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Arthritis & Rheumatology
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DOI 10.1002/art.41108

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Abstract Number: 0001

Interleukin-6 Promotes Osteoclast-like Phenotype in Human Rheumatoid Arthritis Synovial Fibroblasts

Anil Singh,[1] Mahamudul Haque,[1] Bhanupriya Madarampalli,[2] and Salahuddin Ahmed[3], [1]Department of Pharmaceutical Sciences, Washington State University, College of Pharmacy, Spokane, WA, Spokane, WA, [2]University of Washington, Seattle, WA, [3]Department of Pharmaceutical Sciences, Washington State University, College of Pharmacy, Spokane, WA. Division of Rheumatology, University of Washington School of Medicine, Seattle, WA, Spokane, WA

SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disorder characterized by chronic inflammation and joint destruction caused by pro-inflammatory cytokines. Progressive joint damage is also an outcome of the enhanced osteoclast function in synovial microenvironment mediated by IL-6. However, the molecular mechanisms through which IL-6 propels synovial fibroblasts to contribute to bone loss in RA are not fully characterized.

Methods: Human synovial tissue derived RA synovial fibroblasts (RASFs) were treated with IL-6 and IL-6 receptor (IL-6/IL-6R, 100 ng/ml each) alone or in combination with M-CSF (2 ng/ml) and RANKL (5 ng/ml) for 9 days to study differentiation mechanisms to osteoclast-like precursor cells. Osteoclast-like phenotype of RASFs was confirmed by a Tartrate-resistant acid phosphatase (TRAP) staining method. Osteoclast-like characteristics of RASFs were determined using quantitative RT-PCR or Western immunoblotting for markers such as RANKL, OPG, NFATc1, OSCAR and MITF. Signaling mechanisms that contribute to osteoclastogenesis in RASFs were confirmed by transient small-interfering RNA (siRNA). Effect of IL6/IL-6R was further examined on bone marrow-derived macrophages (BMDM) from 7-week old C57BL/6 mice and compared to M-CSF/RANKL treatment groups.

Results: Treatment of human RASFs with IL-6/IL-6R for 9 days resulted in the phenotypic changes to osteoclast-like features confirmed using TRAP staining ($p< 0.05$; n=3). IL6/IL-6R treatment of RASFs also increased the expression of osteoclast-specific expression of OPG, Cathepsin K, and Cathepsin B, which was comparable to the expression in M-CSF/RANKL-stimulated samples ($p< 0.05$; n=4). The increased TRAP staining and osteoclastogenic factors by IL-6/IL-6R were independent of M-CSF receptor expression in human RASFs. In addition to increasing Cathepsin K, Cathepsin B, and traditional osteoclast-specific markers (MITF, RANKL, and OSCAR), IL-6/IL-6R increased the expression transcription factor ETS2 by 3-5-fold when compared to M-CSF/RANKL-differentiated human RASFs. In vitro studies using mouse BMDMs showed a significantly higher expression of Cathepsin B, OPG, MITF and ETS2 in response to IL-6/IL-6R activation when compared to M-CSF/RANKL treatment group ($p< 0.05$; n=3). Silencing ETS2 expression during human RASF differentiation abrogated IL-6/IL-6R-induced Cathepsin K and Cathepsin B production, and osteoclastogenic features of these synovial cells.

Conclusion: IL-6 uniquely contributes to osteoclast-like phenotype of RASFs by directing the molecular reprogramming in these cells mediated through ETS2. Targeting ETS2 to suppress this phenotypic switch of RASFs to osteoclast-like cells may serve as regulatory mechanism of limiting bone resorption in RA.

Disclosure: A. Singh, None; **M. Haque**, None; **B. Madarampalli**, None; **S. Ahmed**, None.

Abstract Number: 0002

Baseline Cytotoxic Gene Expression Associates with Ustekinumab Response in Systemic Lupus Erythematosus

Loqmane Seridi,[1] Matteo Cesaroni,[1] Matthew Loza,[1] Jessica Schreiter,[1] Kristen Sweet,[1] Yevgeniya Orlovsky,[1] Isabelle Baribaud,[1] Ashley Orillion,[1] Peter Lipsky,[2] Ronald van Vollenhoven,[3] Bevra Hahn,[4] George Tsokos,[5] Marc Chevrier,[1] Shawn Rose,[1] Frédéric Baribaud,[1] and Jarrat Jordan[1], [1]Janssen Research & Development, LLC, Spring House, PA, [2]AMPEL BioSolutions, LLC, Charlottesville, VA, [3]Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands, [4]University of California, Los Angeles, CA, [5]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA

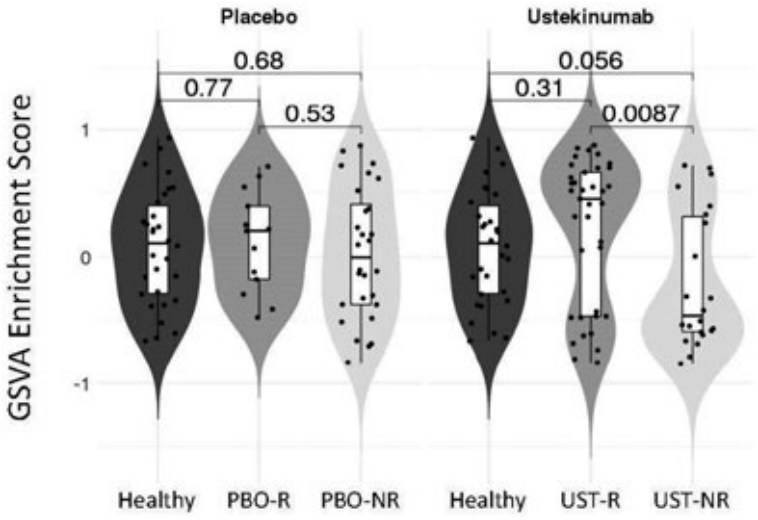
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematous (SLE) is a clinically and biologically diverse disease, for which only one new therapy has been approved in the past 60 years. In a phase 2 trial of mild-to-moderate SLE patients, ustekinumab (UST) improved clinical and laboratory measures of disease activity compared with placebo (PBO).[1]We previously reported an association of IFN-g reduction with response to UST,[2]suggesting an impact on the IL12/Th1 axis. To extend these findings, we performed unbiased transcriptomic analysis from baseline whole blood samples to identify genes that discriminate UST responders (UST-R) from non-responders (UST-NR) using the primary endpoint of Systemic Lupus Erythematosus Responder Index (SRI)-4 at week 24 to define response.

Methods: UST was studied in a Ph2 PBO-controlled study of 102 patients with seropositive SLE and active disease despite standard therapy. Patients were randomized 3:2 to receive IV UST 6 mg/kg or placebo followed by subcutaneous injections of UST 90mg or placebo every 8 weeks. Whole blood gene expression at baseline was measured via microarray using RNA samples from 100 patients, as samples from 2 patients failed quality control. An unbiased approach was used to identify gene signatures present at baseline that associate with UST response. Recombinant IL-12 or IL-23 was incubated in vitro with whole blood from 6 healthy donors for 24h and RNA-Seq was performed to determine the effect of these treatments on representative genes comprising the UST response signature.

Results: A non-biased machine learning algorithm identified a 9-gene whole blood signature composed primarily of cytotoxic cell-associated transcripts (PRF1, KLRD1, GZMH, NKG7, GNLY, FGFBP2, TRGC2, TARP, TRGV2) that was enriched at baseline in UST-R vs UST-NR. By Gene Set Variation Analysis, the cytotoxic signature enrichment in UST-NR was less at baseline than both UST-R and a healthy control cohort (P=0.0087, P=0.056, respectively), whereas UST-R cytotoxic gene enrichment was similar to healthy controls (P=0.31). No significant difference in cytotoxic signature enrichment was observed at baseline between PBO responders and PBO non-responders or healthy controls (Figure). Enrichment levels of the cytotoxic gene signature remained stable over time in PBO and UST-NR groups while a trend of decreased cytotoxic signature was observed in UST-R, although never reaching levels seen in UST-NR. To begin to understand the relationship between IL-12 and IL-23, the targets of UST, and the cytotoxic signature, whole blood was stimulated with these cytokines in vitro. Recombinant IL-12, but not IL-23, resulted in increased expression of representative members of this cytotoxic gene signature.

Conclusion: We identified a novel cytotoxic signature in baseline blood samples that associated with UST response in SLE. The observation that IL-12 can increase this signature in vitro and that IL-12 is a robust inducer of cytotoxic cell activity[3] as well as IFN-γ[3] suggests an important role of IL-12 blockade in the mechanism of action of UST in SLE.



1. van Vollenhoven RF. Lancet. 2018; 392:1330-39
2. Jordan. ACR 2018 Abstract # 29513
3. G. Trinchieri. Nat Rev Immunol. 2003; 3:133-46

Disclosure: L. Seridi, Janssen Research & Development, LLC, 3; **M. Cesaroni**, Janssen Research & Development, LLC, 3; **M. Loza**, Janssen Research & Development, LLC, 3; **J. Schreiter**, Janssen Research & Development, LLC, 3; **K. Sweet**, Janssen Research & Development, LLC, 3; **Y. Orlovsky**, Janssen Research & Development, LLC, 3; **I. Baribaud**, Janssen Research & Development, LLC, 3; **A. Orillion**, Janssen Research & Development, LLC, 3; **P. Lipsky**, Horizon, 5, Janssen Research & Development, LLC, 2; **R. van Vollenhoven**, AbbVie, 2, 5, 8, AbbVie, Arthrogen, Bristol-Myers Squibb, GlaxoSmithKline (GSK), Lilly, Pfizer, and UCB, 2, AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, GSK, Janssen, Lilly, Medac, Merck, Novartis, Pfizer, Roche, and UCB., 5, Amgen, 2, AstraZeneca, 5, 8, Biotest, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, 8, Crescendo Bioscience, 5, 8, GlaxoSmithKline, 2, 5, 8, Janssen, 5, 8, Janssen Research & Development, LLC, 2, Lilly, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, UCB, 2, 5, 8, Vertex, 5, 8; **B. Hahn**, Janssen Research & Development, LLC, 2; **G. Tsokos**, Janssen Research & Development, LLC, 2; **M. Chevrier**, Janssen Research & Development, LLC, 3; **S. Rose**, Janssen Research & Development, LLC, 3; **F. Baribaud**, Janssen Research & Development, LLC, 3; **J. Jordan**, Janssen Research & Development, LLC, 3.

Abstract Number: 0003

Pannexin-1 KO Mice Are Unresponsive to Tenofovir Induced Bone Loss

Ane Larrañaga-Vera,[1] Francisco Conesa-Buendia,[2] Bruce Cronstein,[3] and Aranzazu Mediero[2], [1]NYU Langone Health, New York, NY, [2]IIS-FUNDACION JIMENEZ DIAZ, Madrid, Spain, [3]NYU Langone, New York

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Tenofovir is an anti-retroviral agent commonly used to treat human immunodeficiency virus (HIV)-infected patients as part of the drug regimen known as highly active anti-retroviral therapy (HAART). As many as 15% of patients taking tenofovir develop osteopenia resulting in pathological fractures. Recent studies

in our lab indicate that tenofovir-induced osteopenia is due to reduction of extracellular adenosine resulting from tenofovir-mediated blockade of Pannexin-1, a transporter for ATP which is hydrolysed in the extracellular space to adenosine, and the effect of tenofovir on bone can be reversed by dipyridamole, an agent that blocks adenosine re-uptake. To further confirm this effect we studied the effect tenofovir on bone in Pannexin-1 knockout mice (PANX1KO) mice.

Methods: PANX1KO animals were treated daily with 75mg/Kg of tenofovir, 25 mg/kg tenofovir or both during 4 weeks, after that bone mineral density (BMD) was measured. Additionally, primary osteoclasts were differentiated in the presence of different concentrations of Tenofovir and dipyridamole. The differentiation stage and extracellular ATP levels were studied.

Results: Consistent with previous experiments, tenofovir treatment of extracellular ATP in cultures of wild type (WT) bone marrow-derived primary osteoclasts as well as an increase in osteoclast differentiation. However, the addition of dipyridamole inhibited osteoclast differentiation ($p=0.0068$). The dipyridamole-induced inhibition was reversed with Tenofovir in a dose dependent manner (0.0055). In contrast, osteoclasts from PANX1KO mice did not decrease ATP release when treated with Tenofovir ($p= 0.3292$). Additionally, PANX1KO mice osteoclast differentiation was also inhibited by dipyridamole ($p=0.0005$), which was not reversed by dipyridamole treatment ($p= 0.9756$). In WT mice, Tenofovir treatment reduced bone mineral density by 10% ($p< 0.05$, $n=10$) and this effect was reversed in the animals who received Dipyridamole in addition to Tenofovir. In contrast, tenofovir did not affect bone mineral density in PANX1KO mice ($p >0.99$, $n=4$).

Conclusion: Tenofovir, a commonly used drug, induces osteopenia in many patients. The results presented here support the hypothesis that tenofovir reduces bone density by inhibiting ATP release with subsequent adenosine-mediated inhibition of osteoclast differentiation. These effects can be reversed by treatment with dipyridamole.

Disclosure: A. Larrañaga-Vera, None; **F. Conesa-Buendia**, None; **B. Cronstein**, AstraZeneca, 5, CanFite Biopharmaceuticals, 4, Horizon Pharmaceuticals, 5, Regenosine, Inc., 4; **A. Mediero**, None.

Abstract Number: 0004

AMP Deaminase 2 Surface Expression Counteracting CD73-Driven Generation of Anti-Inflammatory Extracellular Adenosine

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Adenosine and its nucleotides represent crucial immunomodulators in the extracellular environment. ATP and ADP are released from stressed cells in states of inflammation, whereas adenosine serves as a key anti-inflammatory mediator which signalsvia multiple receptors on immune cells. The ectonucleotidases CD39 and CD73 are responsible for the sequential catabolism of ATP to adenosine via AMP, thereby promoting an anti-inflammatory milieu induced by the “adenosine halo”. Great importance has been attributed to these enzymes in the pathogenesis of autoimmune diseases such as RA and as targets in cancer therapy. AMPD2 mediates AMP deamination to IMP, consequently reducing adenosine formation. Here, we postulate that (i) this pathway is also present on

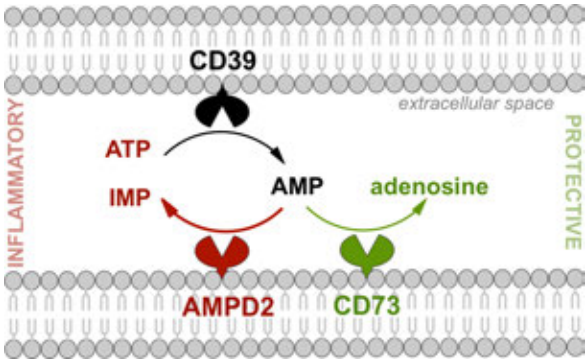

Figure 1. Surface AMPD2 counteracting CD73-driven adenosine generation.

the cell surface of immune cells, and (ii) its predominance may lead to an increased state of inflammation as found in chronic inflammatory diseases (Fig. 1).

Therefore, we analyzed surface AMPD2 expression and its modulation on distinct cell lines and primary immune cells.

Methods: Firstly, AMPD2 surface expression was verified by immunoprecipitation from membrane fractions isolated from cell lines (HEK293 and HMEC1) and CD14+ monocytes analyzed by immunoblot and mass spectrometry. In addition, surface biotinylation of the aforementioned cells was performed. Also, AMPD2 surface expression was evaluated by flow cytometry, analyzing both cell lines (HEK293, HMEC1, THP1, and Jurkat) and primary human immune cells.

Secondly, co-expression of surface AMPD2, CD39 and CD73 on PBMCs was analyzed by flow cytometry directly after isolation as well as after a 24h culture period. Moreover, surface expression was assessed after immunostimulation and Golgi transport inhibition.

Results: AMPD2 surface expression was confirmed by immunoblot and mass spectrometry of (i) precipitated AMPD2 from membrane fractions and (ii) biotinylated surface molecules in HEK293 and HMEC1 as well as CD14+ monocytes. Surface expression was reduced after AMPD2 knockdown in HEK293. AMPD2 was detected on the surface of all examined cell lines, human T cells and monocytes from healthy donors and RA patients by flow cytometric analysis. Flow cytometry revealed a stable surface expression of AMPD2, CD39 and CD73 on lymphocytes after immunostimulation. Golgi transport inhibition slightly reduced AMPD2 surface expression ($p=0.02$), while expression of CD39 and CD73 remained unaffected. However, 24h incubation with substances agonizing TLRs 1, 2, 4, 5, 6, 7, and 8 respectively strongly enhanced the surface expression of AMPD2 ($p< 0.01$) and CD39 ($p< 0.05$) on monocytes, while this effect was attenuated by concomitant incubation with dexamethasone. Agonists of TLRs 3 and 9 did not affect AMPD2 surface expression. CD73 expression was not influenced by immunostimulation. Golgi transport inhibition significantly decreased monocytic AMPD2 surface expression ($p< 0.001$).

Conclusion: We demonstrate AMPD2 surface expression on immune cells for the first time and thereby reveal a novel regulator of the extracellular ATP-adenosine balance. The extracellular conversion of AMP into IMP may constitute a shunt-like mechanism adding to the CD39-CD73 system controlling immunomodulation.

Disclosure: L. Ehlers, None; **A. Kuppe**, None; **C. Strehl**, None; **M. Kirchner**, None; **F. Buttgereit**, Medac, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, Roche/Chugai, 2, 5, 8, Roche-Chugai, 2, 5, 8, Sanofi-Genzyme, 2, 5, 8; **T. Gaber**, None.

Abstract Number: 0005

Interferon Kappa Promotes the Development of Psoriasis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriasis is a one of the most common chronic inflammatory autoimmune skin diseases characterized by hyperproliferation and abnormal differentiation of keratinocytes and infiltration of inflammatory cells. It affects about 3% of the world's population, with unknown etiology. In psoriasis, a complex network of cytokines and chemokines is produced by various types of immune cells, but keratinocytes also play a key role in pathogenesis. Early infiltration of plasmacytoid dendritic cells and detection of an interferon (IFN) signature occurs in many psoriasis lesions. In addition, deletion of the type I IFN receptor is protective in imiquimod-induced psoriasis. Recently, we described keratinocyte production of IFN-κ as an important source of type I IFN production in the epidermis. We thus wanted to explore the role of IFN-κ in psoriasis.

Methods: We used the well-characterized imiquimod (IMQ) psoriasis model for these studies. 10-week old male and female wild type (WT) and mice transgenic for IFN-κ under the K14 promoter (resulting in only epidermal overexpression) were used (n=5-8 per group). Psoriasis was induced by topical application of IMQ on both ears for 8 consecutive days. Control mice received Vaseline. Animals were monitored daily for ear thickness, lesion severity, and body weight. On day nine, mice were euthanized and disease severity was compared between WT and IFN-κ transgenic mice. Skin inflammation was assessed via H&E staining.

Results: Although both IFN-κ transgenic and WT IMQ treated mice exhibited psoriasis lesions in both ears after 8 days of treatment, the lesion size and thickness was significantly increased in IFN-κ transgenic mice vs. WT for both male and female mice. Interestingly, the difference was more exaggerated in IFN-κ transgenic female mice vs. male mice. H&E staining revealed increased inflammatory cell infiltrates in IMQ treated IFN-κ-TG vs. WT mice. Control mice did not show any sign of inflammation or disease. Ongoing studies are characterizing the differences in cell populations that make up the inflammatory infiltrates in WT vs. IFN-κ transgenic mice.

Conclusion: Overexpression of IFN- κ in the epidermis caused accelerated and increased disease severity after topical application of IMQ. This suggests that overproduction of type I IFNs may impact psoriasis development and there may be a role of targeting IFNs in early disease. Further studies will need to elucidate the specific mechanisms that may be at play.

Disclosure: M. Gharaee-Kermani, None; **S. Estadt**, None; **S. Wolf-Fortune**, None; **J. Gudjonsson**, AbbVie, 2, Genentech, 2, genentech, 2, MiRagen, 5, Novartis, 5, Sun Pharma, 2, SunPharma, 2; **J. Kahlenberg**, AstraZeneca, 5, Eli Lilly, 5, Bristol Myers Squibb, 5.

Abstract Number: 0006

A Novel Role for Extracellular Sulfatase-2 in Mediating IL-6-induced Adhesion and Migration Molecules in Human Rheumatoid Arthritis Synovial Fibroblasts

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Cytokines & Cell Trafficking Poster
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Background/Purpose: Interleukin-6 (IL-6) promotes synovial hyperplasia by inducing mediators of adhesion, migration and leukocyte infiltration in rheumatoid arthritis (RA). The extracellular enzymes sulfatase-2 (Sulf-2) and sulfatase-1 (Sulf-1) cleave specific sulfate esters from heparan sulfate proteoglycans (HSPGs) which may affect the receptor/ligand binding and signaling of chemokines, cytokines, and growth factors. However, the potential role of sulfatases in IL-6 signaling remain unexplored. The present study evaluated the effect of the sulfatases on IL-6 signaling and induction of effector molecules in human RA synovial fibroblasts (RASFs).

Methods: Human RASFs were serum-starved overnight followed by treatment with 100 ng/ml each of IL-6 and IL-6 receptor (IL-6/IL-6R) for different time periods. Conditioned media and whole cell lysates were collected to determine the expression of adhesion (cadherin-11, ICAM-1) and migration (podoplanin) molecules using qRT-PCR and Western blotting. IL-6/IL-6R-induced MCP-1 release in conditioned media was measured by ELISA. Effect of sulfatases on IL-6/IL-6R stimulation was evaluated by small inhibitory RNA (siRNA) knockdown of Sulf-1 and Sulf-2. RASFs treated with siRNA were stimulated with IL-6/IL-6R for 24 hr for protein studies, or for 30 min to determine signaling mechanisms.

Results: Compared to IL-1β (10 ng/ml) or TNF-α (20 ng/ml), IL-6/IL-6R selectively induced the expression of Sulf-2 by 1.5-fold, without marked change in Sulf-1 expression in human RASFs (n=3). In a time-dependent study (n=3; 0-48 hr), IL-6/IL-6R caused a significant increase in the expression of cadherin-11 (2-fold; $p< 0.01$), podoplanin (2.5-fold; $p< 0.05$) and ICAM-1 (3.5-fold; $p< 0.0001$), and the production of MCP-1 in the conditioned media (2.6-fold; $p< 0.05$). Additionally, IL-6/IL-6R stimulation caused a ~4-fold increase in expression of syndecan-2, a known HSPG target of Sulf-2, in human RASFs ($p< 0.01$; n=3). Interestingly, densitometric analysis of Western blots showed that knockdown of Sulf-2, but not Sulf-1, preferentially reduced IL-6/IL-6R-induced cadherin-11, podoplanin, and ICAM-1 by 35%, 25%, and 30%, respectively ($p< 0.05$; n=3). However, siRNA targeted for both Sulf-2 and Sulf-1 proved effective in reducing IL-6/IL-6R-induced MCP-1 production by 35% and 56%, respectively ($p< 0.01$; n=3). Evaluation of signaling events showed that inhibition of Sulf-2, but not Sulf-1, suppressed IL-6/IL-6R-induced phosphorylation of JAK-1 (Tyr1022) by ~50% while maintaining the expression of SOCS3, a negative regulator of JAK/STAT3 signaling.

Conclusion: Our study identified a novel role of Sulf-2 in facilitating IL-6-induced signaling in RASFs and suggests potential therapeutic value of targeting Sulf-2-dependent pathways in treatment approaches for RA.

Disclosure: R. Siegel, None; **S. Ahmed**, None.

Abstract Number: 0007

Citrullination of Interleukin 6 Augments Its Pro-inflammatory Capacity and Signaling Potency Through Interleukin-6 Receptor in Rheumatoid Arthritis

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

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory disorder featured by synovial hyperplasia, inflammatory cell infiltration and presence of anti-citrullinated peptide antibodies (ACPAs) in sera. Citrullination, a post-translational modification of arginine to citrulline by peptidylarginine deiminase (PAD), contributes to the development of RA. We have shown that interleukin 6 (IL-6) can be citrullinated and mediates inflammation in RA. Additional experiments were performed to define the receptor for citrullinated IL-6 (citIL-6).

Methods: Recombinant human (rh) IL-6 was incubated with rhPAD4 and the citrullination of IL-6 was verified by liquid chromatography-mass spectrometry (LC-MS). We identified the presence of citIL-6 and ACPAs against citIL-6 in RA synovial fluids (SFs) and sera by performing Western blotting and immunodot blot assay, respectively. In vitro, monocyte (MN) chemotaxis assays were performed with modified Boyden chambers to examine the effect of citIL-6 on MN migration. The role of citIL-6 in RA fibroblast-like synoviocyte (FLS) proliferation and migration was determined using the IncuCyte S3 live-cell analysis system and scratch wound assays. FLS were stimulated with citIL-6 or noncitIL-6 to examine the phosphorylation of signaling molecules by Western blotting without exogenous IL-6 receptor (IL-6R). To define the receptor for citIL-6, RA FLS were transfected with gp130 siRNA or blocked with sarilumab, an IL-6R neutralizing antibody, and signaling molecules were tested by Western blotting after stimulation with citIL-6 or noncitIL-6. In vivo, citIL-6 or noncitIL-6 was injected into mouse knees and joint circumference was measured at 0 hour and 24 hours after injection.

Results: LC-MS confirmed that all of the arginines in rhIL-6 can be citrullinated by rhPAD4. Western blotting showed that citIL-6 was present in the SFs from RA, and immunodot blot assay showed that sera from RA patients but not healthy controls contained ACPAs reactive with citIL-6 but not noncitIL-6. Compared to noncitIL-6, citIL-6 induced more MN migration ($p< 0.001$). We found that citIL-6 induced significantly higher FLS proliferation and migration rates after 24 hours than noncitIL-6. CitIL-6, without exogenous IL-6R, consistently upregulated phosphorylation of Erk1/2, Jnk, and Stat3 in RA FLS while noncitIL-6 did not unless exogenous IL-6R was added. Furthermore, gp130 knock down or monoclonal antibody blockade of the IL-6R abrogated the phosphorylation of Stat3 and Erk1/2 in FLS by both citIL-6 and noncitIL-6, indicating IL-6R and gp130 are necessary for function of both forms of IL-6. The change in mouse knee circumference with citIL-6 injection was approximately 7-fold higher than that with noncitIL-6 injection (0.90 ± 0.13 mm vs 0.13 ± 0.13 mm; $n=14$; $p< 0.05$), indicating that citIL-6 induced much more severe inflammation in mouse knees compared to noncitIL-6.

Conclusion: IL-6 can be citrullinated by PAD, citIL-6 was present in RA SFs, and citIL-6 ACPAs were present in RA sera. CitIL-6 appears to be a more potent ligand of IL-6R and play an important role in the pathogenesis of RA by inducing proliferation as well as migration of FLS and recruitment of monocytes.

Disclosure: C. Lu, None; **R. Ohara**, None; **P. Campbell**, None; **Y. Du**, None; **A. Stinson**, None; **J. Hervoso**, None; **E. Cealey**, None; **D. Fox**, None; **M. Amin**, None.

Abstract Number: 0008

CKD-506, a Selective Histone Deacetylase (HDAC) 6 Inhibitor, Regulates Inflammatory Responses Through NF-kB and AP-1 Signaling

Jieun Shin,[1] Nina Ha,[1] Daekwon Bae,[1] Dong-hyeon Suh,[1] Ji-yeon Baek,[1] Jae Hyun Jun,[1] Yong Jae Lee,[1] Young Il Choi,[1] Keun Ho Ryu,[1] Gi Soo Youn,[2] and Jinseu Park[3], [1]CKD Research Institute, Yongin-si, Republic of Korea, [2]Department of Biomedical Science, Hallym University, Chuncheon, Republic of Korea, [3]Department of Biomedical Science, Hallym University, Chuncheon

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Cytokines & Cell Trafficking Poster

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Session Time: 9:00AM–11:00AM

Background/Purpose: Inhibition of HDAC6 has been proposed beneficial and therapeutic effects in inflammatory diseases. CKD-506, a potent and selective oral HDAC6 inhibitor, has anti-inflammatory and anti-rheumatic effects in arthritis animal models and RA patient samples. Moreover, CKD-506 was generally safe and well tolerated following single and multiple doses in healthy volunteers, and CKD-506 is on clinical investigation to assess the efficacy and safety in patients with rheumatoid arthritis. Herein, we identify the molecular mechanisms of CKD-506 in regulation of inflammation.

Methods: Mouse peritoneal macrophages and Raw264.7 cells were transfected with HDAC6 overexpression vector or pcDNA3.1 vector as control. Cells were cultured in the presence or absence of 0.03~3 μM CKD-506, and the expression and production of inflammatory mediators were determined by RT-PCR and ELISA respectively. For reporter assays, cells were transfected with pNF-kB-luc or pAP-1-luc plasmid and luciferase activity in cell lysates was determined by luminometer. Tubulin acetylation and signaling molecules by CKD-506 in HDAC6 overexpressed cells were checked by immunoblot analysis.

Results: HDAC6 overexpression in both Raw264.7 cells and mouse peritoneal macrophages strongly induced pro-inflammatory mediators such as TNFa, IL-6, IL-1b. However, CKD-506 inhibited the expression and production of TNFa, IL-6, and IL-b at dose dependent manners in HDAC6 overexpressed cells. Moreover, ROS production and NADPH oxidase activity mediated by HDAC6 overexpression were inhibited by CKD-506. In signaling pathway, HDAC6 overexpression strongly induced NF-kB and AP-1 activity and CKD-506 inhibited both signaling pathways. In addition, CKD-506 with methotrexate exhibited better anti-inflammatory effects on macrophages with HDAC6 overexpression.

Conclusion: CKD-506 inhibits inflammatory mediators such as TNFa, IL-6, IL-1b, ROS, and NADPH oxidase activity in HDAC6 overexpressed cells. This anti-inflammatory activities of CKD-506 are mediated through NF-kB and AP-1.

Disclosure: J. Shin, None; **N. Ha**, None; **D. Bae**, None; **D. Suh**, None; **J. Baek**, None; **J. Jun**, None; **Y. Lee**, None; **Y. Choi**, None; **K. Ryu**, None; **G. Youn**, None; **J. Park**, None.

Abstract Number: 0009

Chemokine CXCL 10 Gene Expression as a Potential Activity Biomarker of Systemic Lupus Erythematosus

Julian Torres Vazquez,[1] Alejandro Corzo Cruz,[2] David Alberto Comoto Santacruz,[2] and Omar Eloy Muñoz Monroy[1],
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[2]Universidad del Ejército y Fuerza Aérea/ Esc. Mil. Gdos. Snd., SEDENA, Mexico City, Mexico

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is characterized by a wide range of systemic dysfunctions as well as an elevated erythrocyte sedimentation rate. Chemokine CXCL 10 (IP-10) is a chemotactic chemokine for monocytes and T-Lymphocytes and has been studied as a potential biomarker to detect SLE activity. The clinical manifestations of the activity of this disease are difficult to assess for clinicians as there is no high sensitivity blood test available for diagnostic purposes. The aim of this study was to determine if SLE activity in our patients, evaluated using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), elevates the expression of IP-10 mRNA in leucocytes, measured as Fold Change using qRT-PCR.

Methods: We recruited SLE female patients, diagnosed according to SLICC 2012 classification criteria. The patients were classified in five groups (Control; n=30, Without Activity (WA); n=30, Mild Activity (Mi A); n=30, Moderate Activity (Mo A); n=30, Severe Activity (SA); n=30) according to SLEDAI results, subsequently blood samples were taken, labeled and transported with all preservation precautions to the Molecular Biology Laboratory where total RNA was extracted from leucocytes and quantified. Primers were designed to amplify a specific region in the exon 2 and 3 of the IP-10 gene and gene expression levels were determined using qRT-PCR. ANOVA test was used to compare the expression of IP-10 mRNA between groups and a Spearman test was used to correlate the SLEDAI with the IP-10 mRNA expression levels.

Results: Overexpression of IP-10 mRNA was observed in the SA group with a Fold Change of 3.0171 (p=0.02), SLEDAI correlates with an increased expression of IP-10 (R=0.9029); Group Mo A was omitted from the analysis due to inconsistent results probably caused by methodological errors.

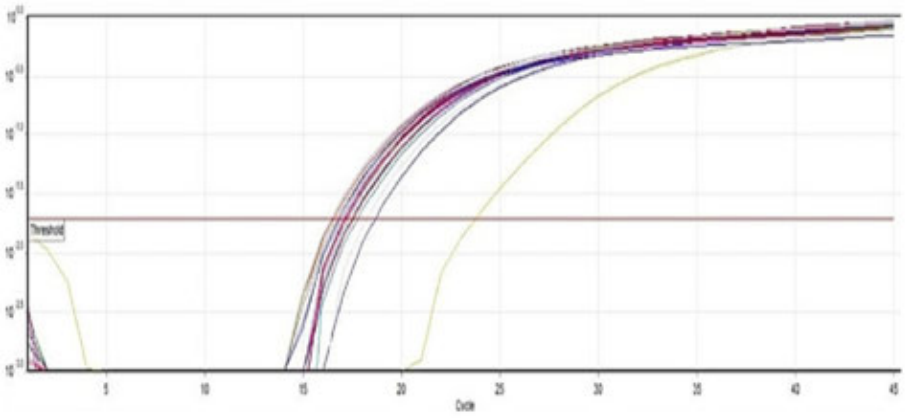

Figure 1. qRT – PCR CTs analysis from IP-10 sequence amplification.

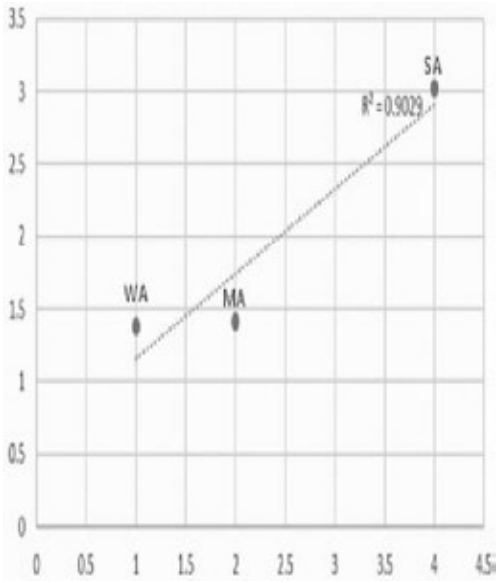

Figure 2. Correlation Activity of SLE with Fold Change $R^2 = 0.9029$ (WA = Without Activity, MA = Mild Activity, SA = Severe Activity)

CTs	Control	Without Activity	Mild Activity	Severe Activity
Fold Change	1	1.381147	1.412124	3.017178

Table 1. Overexpression of IP-10 in different groups

Conclusion: IP-10 mRNA overexpression could be associated with Several Activity of SLE, quantification of IP-10 gene expression has potential as a biomarker to evaluate SLE activity. Complimentary techniques such as IP-10 protein quantification are suggested to confirm our observations.

Disclosure: J. Torres Vazquez, None; **A. Corzo Cruz**, None; **D. Comoto Santacruz**, None; **O. Muñoz Monroy**, None.

Abstract Number: 0010

Roles of Histone Acetyltransferases CBP/p300 and Transcriptional Factor RORα/REV-ERBα Against TNFα-induced CCL2 Expression in RA-FLSs

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SESSION INFORMATION

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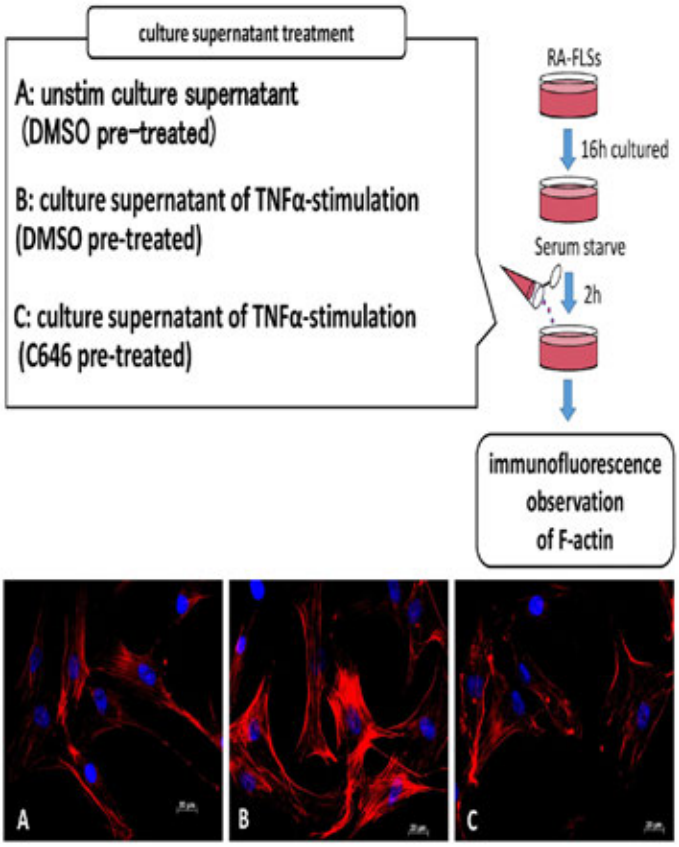

Figure 1. TNFα induced reorganization of the actin cytoskeleton in RA-FLSs (A and B), while C646 significantly inhibited that (C).

Background/Purpose: We have reported that TNFα induced expressions of clock gene*Bmal1*by up-regulating transcriptional activator RORα and down-regulating repressor REV-ERBα in RA fibroblast-like synoviocytes (RA-FLSs), and that histone acetyltransferases CREB binding protein (CBP) and p300 were involved in this process. A chemokine CCL2, associated with cell proliferation and migration of RA-FLSs, is regulated by RORα and REV-ERBα as well as Bmal1. In this study, we investigate the relation between RORα/REV-ERBα, histone acetyltransferases and TNFα-induced CCL2 expression in RA-FLSs.

Methods: To examine the effect of RORα antagonist SR1001 and REV-ERBα agonist GSK4112 on TNFα-induced CCL2 expression, primary cultured RA-FLSs were treated with SR1001 (20μM) and/or GSK4112 (20μM) in the presence of TNFα (10ng/ml) for 24h.

Next, to clarify the role of histone acetyltransferases on TNFα-induced CCL2, cells were incubated with p300/CBP inhibitor C646 or transfected with both p300 and CBP small interfering RNA (siRNA) before stimulation with TNF-α. Thereafter, intracellular CCL2 mRNA and culture supernatant CCL2 were analyzed by qPCR and ELISA, respectively.

To examine the effect of C646 on TNFα-induced cell migration of RA-FLSs, wound healing assay and immunofluorescence observation were performed by using two different culture supernatant of TNFα-stimulation; DMSO pre-treated control and C646 pre-treated one.

Results: TNFα-induced CCL2 expression was strongly inhibited by simultaneous treatment with both SR1001 and GSK4112, as compared with solo treatment of each agents. Further, CCL2 expressions were also suppressed by

pretreatment with C646 and silencing of both*Cbp*and*p300*genes. C646 significantly inhibited both TNFα-induced cell migration and reorganization of the actin cytoskeleton as compared to those with DMSO control (Figure 1).

Conclusion: We newly found that TNFα induced expression of CCL2 through RORα and REV-ERBα, which was associated with CBP/p300 in RA-FLSs, in the same manner as*Bmal1*.

Results propose these molecules as novel therapeutic targets of RA.

Disclosure: I. Okumura, None; **K. Yoshida**, None; **K. Kaneshiro**, None; **K. Uchida**, None; **A. Yaekura**, None; **Y. Oketani**, None; **K. Morii**, None; **K. Tateishi**, None; **Y. Terashima**, None; **Y. Kawasaki**, None; **N. Shibanuma**, None; **Y. Sakai**, None; **A. Hashiramoto**, None.

Abstract Number: 0011

Biomarker Changes for Patients with Rheumatoid Arthritis Receiving Tofacitinib with Methotrexate or Glucocorticoids vs Tofacitinib Monotherapy

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SESSION INFORMATION
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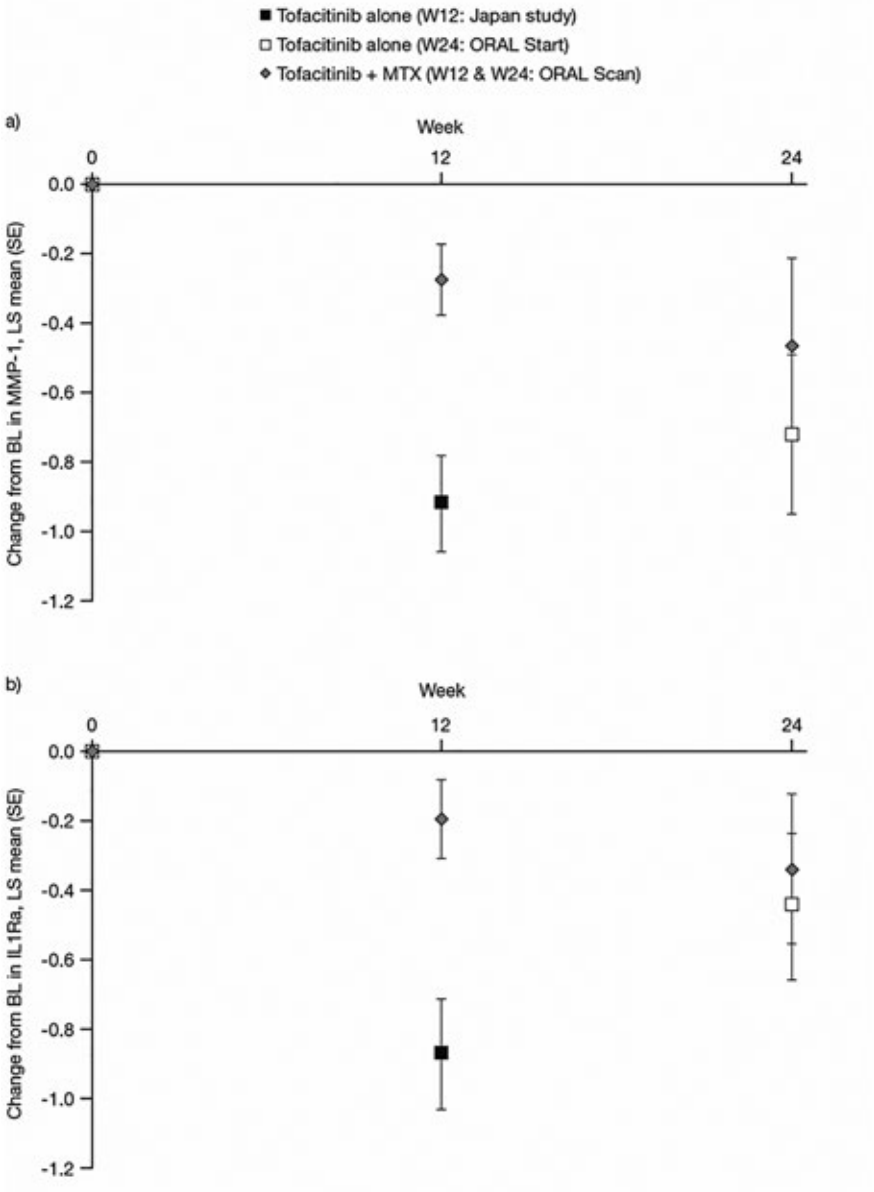
Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Herpes zoster (HZ) is more common in patients (pts) with RA vs the general population.[1]HZ risk is increased with tofacitinib use,[2]and seems to further increase with concomitant use of conventional synthetic DMARDs (eg MTX) or glucocorticoids (GC).[3]This increased risk may be linked to treatment-induced IFN suppression,[3]as varicella-zoster virus replication may be limited by IFN activity.[4]We evaluated whether tofacitinib + MTX and/or GC suppressed IFN pathway proteins to a greater extent than tofacitinib alone.

Methods: This post hoc analysis pooled data from 1 Phase (P) 2 (Japan study [NCT00687193]) and 2 P3 (ORAL Scan [NCT00847613]; ORAL Start [NCT01039688]) tofacitinib studies. Serum samples were collected at baseline (BL), Week (W) 12, and/or W24 from pts with RA treated with tofacitinib 5 or 10 mg twice daily alone (Japan study; ORAL Start) or with stable MTX (15–25 mg/week for ≥ 6 weeks; ORAL Scan), and/or GC (≤ 10 mg/day prednisone or equivalent; all studies). A total of 376 proteins associated with cellular/inflammatory processes, including 6 IFN pathway proteins (CXCL9, CXCL10, CXCL11, IL-12, IFNγ, and IL-20), were measured using a homogeneous, solution-based assay (Olink Proseek®Multiplex Assay, Uppsala, Sweden). Protein-level changes at W12 (Japan study; ORAL Scan) and/or W24 (ORAL Scan; ORAL Start) were compared for both regimens using linear regression models. The dependent variable was change from BL in protein levels at W12 or W24. The independent variable was MTX or GC status. Age, gender, GC status (in MTX model), BL protein levels, and tofacitinib dose were covariates. Separate regressions were performed for each study; GC results were combined via meta-analysis using fixed-/random-effect models. Significance was considered at $p < 0.1$ after controlling for false discovery rate (FDR).

Results: In total, 659 samples were obtained from 321 pts. Of the 6 IFN pathway proteins, IFNγ and IL-20 were below the limit of detection. There were no statistical differences between tofacitinib alone vs tofacitinib + MTX and/or GC

Figure 1. Change from BL to W12 and W24 in a) MMP-1 and b) IL1Ra in patients receiving tofacitinib alone or tofacitinib + MTX



BL protein levels were assessed in all studies (Japan study [NCT00687193]; ORAL Scan [NCT00847613]; ORAL Start [NCT01039688]). Data for protein changes at W12 are from the Japan study (tofacitinib alone) and ORAL Scan (tofacitinib + MTX); data for protein changes at W24 are from ORAL Start (tofacitinib alone) and ORAL Scan (tofacitinib + MTX). All groups included patients who may or may not have received concomitant GC. Significance was considered at $p<0.1$ after controlling for FDR. Data quality control included accounting for plate/batch effects and limits of detection, and removal of samples/analytes with excessive missing data. At W12, FDR-adjusted p=0.08 for MMP-1; FDR-adjusted p=0.09 for IL1Ra. At W24, FDR-adjusted p=1.00 for MMP-1; FDR-adjusted p=1.00 for IL1Ra.

BL, baseline; FDR, false discovery rate; GC, glucocorticoids; IL1Ra, interleukin-1 decoy receptor; LS, least squares; MMP 1, matrix metalloproteinase-1; SE, standard error; W, Week

in changes in levels of the 4 detectable IFN pathway proteins (CXCL9, CXCL10, CXCL11, and IL-12) at W12/W24. Significant differences were observed for 2 of 370 other proteins: MMP-1 (FDR-adjusted p = 0.08) and IL1 decoy receptor (IL1Ra; FDR-adjusted p = 0.09); levels were decreased at W12 for tofacitinib + MTX to a greater extent vs tofacitinib alone (Figure 1).

Conclusion: Tofacitinib + MTX and/or GC may not suppress IFN pathway proteins to a greater extent than tofacitinib alone. There were differences at W12 for tofacitinib + MTX vs tofacitinib alone in MMP-1 and IL1Ra, but it is not clear

whether these were due to ethnicity differences in the study populations receiving these treatments (global vs Japan). Analyses of biomarker changes with tofacitinib are ongoing.

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Abstract Number: 0012

Intraarticular and Circulatory Cytokine Responses to Chlamydia Trachomatis: A Clinical Study in Reactive Arthritis/ Undifferentiated Spondyloarthropathy Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: *Chlamydia trachomatis*-induced reactive arthritis (ReA)/ undifferentiated spondyloarthropathy (uSpA) is an immune-mediated situation where development of disease and maintenance of this pathogen remains elusive. The aim of the study was to estimate the peripheral and localized Th1/ Th2/ Th17 cytokine responses in paired synovial fluid (SF) and serum samples in genitourinary ReA/ uSpA patients infected with *C.trachomatis*.

Methods: With hospital ethical permission, ReA/ uSpA (n = 45)/ Rheumatoid Arthritis (RA) (n = 35)/ Osteoarthritis (OA) (n = 35) patients were enrolled following European spondyloarthropathy study group criteria for ReA/ uSpA and American College of Rheumatology for RA; while OA patients were diagnosed on the basis of clinical and radiological findings. Clinical profile of all arthritic patients was recorded and SF and blood (serum) were collected from each patient. Commercially available kits were used for estimation of SF/ serum cytokines and serum chsp60 by Elisa and HLA B27 by PCR in SF DNA. Statistical analysis of data was done by GraphPad Prism software version 5.0 (GraphPad software, La Jolla, CA, USA).

Results: IFN-gamma was significantly ('p' = 0.0003) elevated in the SF of *C.trachomatis*-positive ReA/ uSpA patients while it was non-significant ('p' = 0.06) in serum. IL-4 was significantly higher in SF ('p' = 0.01) and serum ('p' = 0.006)

of*C. trachomatis*-infected ReA/ uSpA patients in comparison to uninfected ReA/ uSpA, RA and OA patients. IL-17 was comparable ('p' = 0.9) in SF and serum of *C.trachomatis*-infected and uninfected ReA/ uSpA patients and RA. SF and serum IFN-gamma were positively correlated ($r = 0.28$; $p < 0.05$); IL-6 and IFN-gamma in SF were also positively correlated ($r = 0.72$; $p < 0.007$) in ReA/ uSpA patients. IFN-gamma was slightly high ('p' > 0.05, non-significant) in chsp60-positive patients while it was low in HLA B27-positive patients with *C. trachomatis*infection.

Conclusion: Synergistic upregulation of IFN-gamma in SF and serum shows Th-1 dominant immune response which is probably mediated by IL-6 in *C.trachomatis*-induced ReA/ uSpA. HLA B27 and chsp60 do not play any significant role during *C.trachomatis*-induced ReA/ uSpA.

Disclosure: S. Rastogi, None; **P. Kumar**, None; **D. Bhakuni**, None; **G. Khanna**, None.

Abstract Number: 0013

The Effect of Estrogen and Interferon γ on the Immunobiology of Minor Salivary Gland Mesenchymal Stromal Cells

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is a female-predominant autoimmune disease with peak onset in perimenopause. pSS is characterized by severe ocular and oral sicca, leading to reduced quality of life and increased healthcare costs. Minor salivary glands are central to the diagnosis and prognosis of pSS. Although the exact pathogenesis of pSS remains unclear, focal lymphocytic infiltrate, and ultimately, fibrosis of the minor salivary gland, is a key feature of pSS. Mesenchymal stromal cells (MSCs), a cell type with the potential to abrogate inflammation/fibrosis,have been isolated from human minor salivary glands but little is known of their immunobiology. We hypothesize that minor salivary gland-resident MSCs may play a role in pSS pathology. To test this idea, we culture adapted minor salivary gland MSCs and interrogated the hypothesis that treatment with interferon (IFN) γ will have altered immunobiology with and without estrogen treatment.

Methods: All pSS subjects (N=8) fulfilled ACR/EULAR criteria for pSS. Control subjects (N=7) were referred for minor salivary gland biopsy but did not have features or diagnosis of autoimmune disease. MSC cell lines were cultured from minor salivary glands were studied between passages 4 and 6. MSC phenotype was assessed by morphology and flow cytometry using typical MSC surface markers (CD19-,CD45-,HLADR; CD105+,CD90+,CD73+). Estrogen studies were performed on control MSC populations and culture was performed in phenol-free media using charcoal stripped fetal bovine serum. Control MSCs (n=3) were pre-treated for 48 hours with 17 β-estradiol (0.1μM) in the presence or absence of IFN y (25 ng/mL). MSC activity was measured by flow cytometry median fluorescence intensity (MFI) of key mediators of MSC immunobiology including indoleamine 2,3-dioxygenase (IDO), programmed death ligand (PDL)1, and PDL2.

Results: 8 pSS and 7 control MSC cell lines were established with both morphologic and cell marker expression consistent with an MSC phenotype (Figure 1a & Figure 1b). MSCs had minimal expression of CD45, CD19, and HLADR. MSCs had high expression of CD105, CD73, and CD90. Phenotypic cell marker expression did not vary

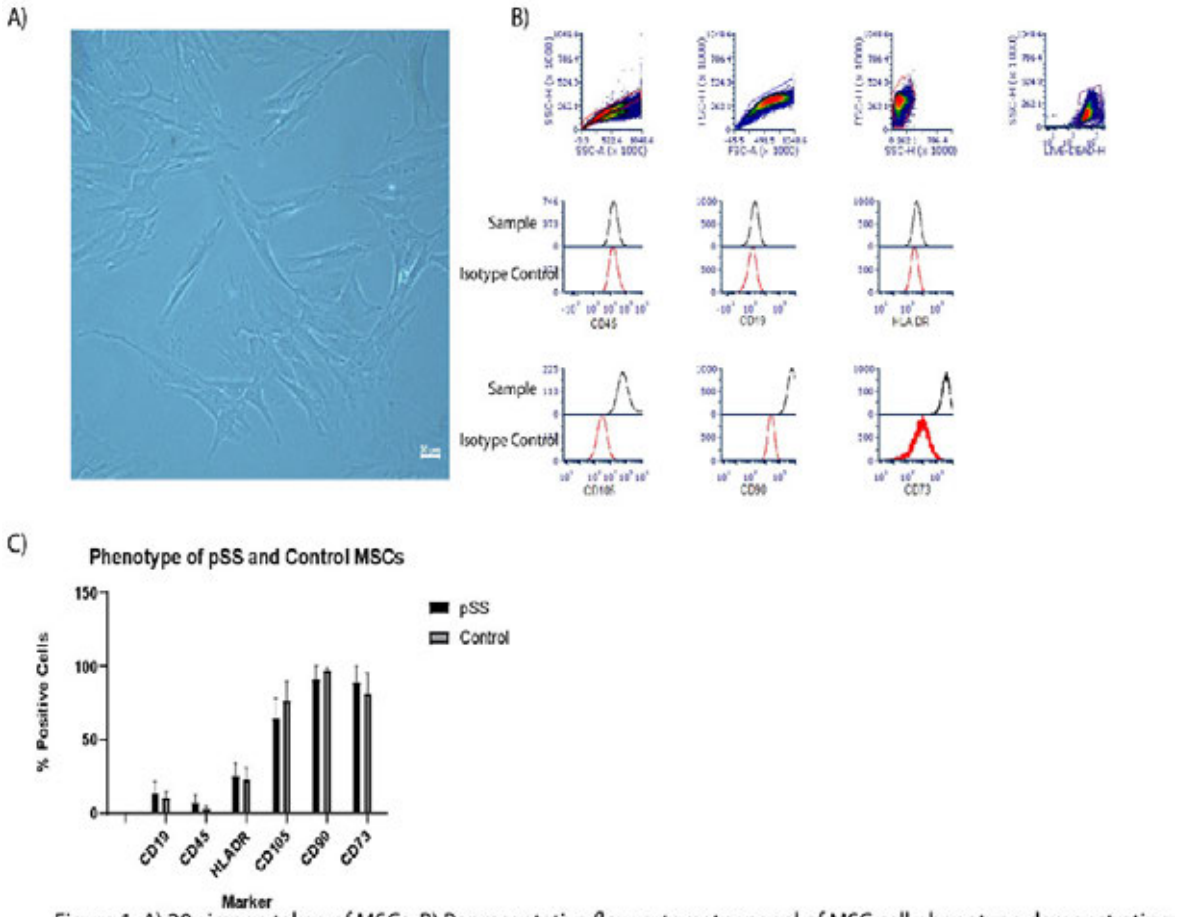

Figure 1. A) 20x image taken of MSCs; B) Representative flow cytometry panel of MSC cell phenotype demonstrating cell populations negative for CD45, CD19, and HLA DR and positive for CD105, CD90, and CD73;
C) Comparison of pSS (n=8) and control (n=7) cell surface markers shows no difference in cell marker expression patterns between these groups.

between pSS and control MSCs (Figure 1c). Control MSCs treated with IFNγ demonstrated increased expression of IDO, PDL1, and PDL2 (Figure 2a & Figure 2b). Estrogen pretreatment did not affect expression of IDO, PDL1, or PDL 2 with or without IFNy licensing.

Conclusion: These results confirm the similarities of MSC phenotype between pSS and controls. Despite increased sicca symptoms around the time of menopause when estrogen is in flux, we did not find that estrogen impacted minor salivary gland MSC immunobiology. Even in the setting IFNγ stimulated MSCs, simulating a high IFN SS-like environment, pulse estrogen exposure did not appear to modify expression of key MSC immunobiology markers. Future investigation will test whether long term pre-conditioning of MSC with estrogens leads to an altered immune plasticity response.

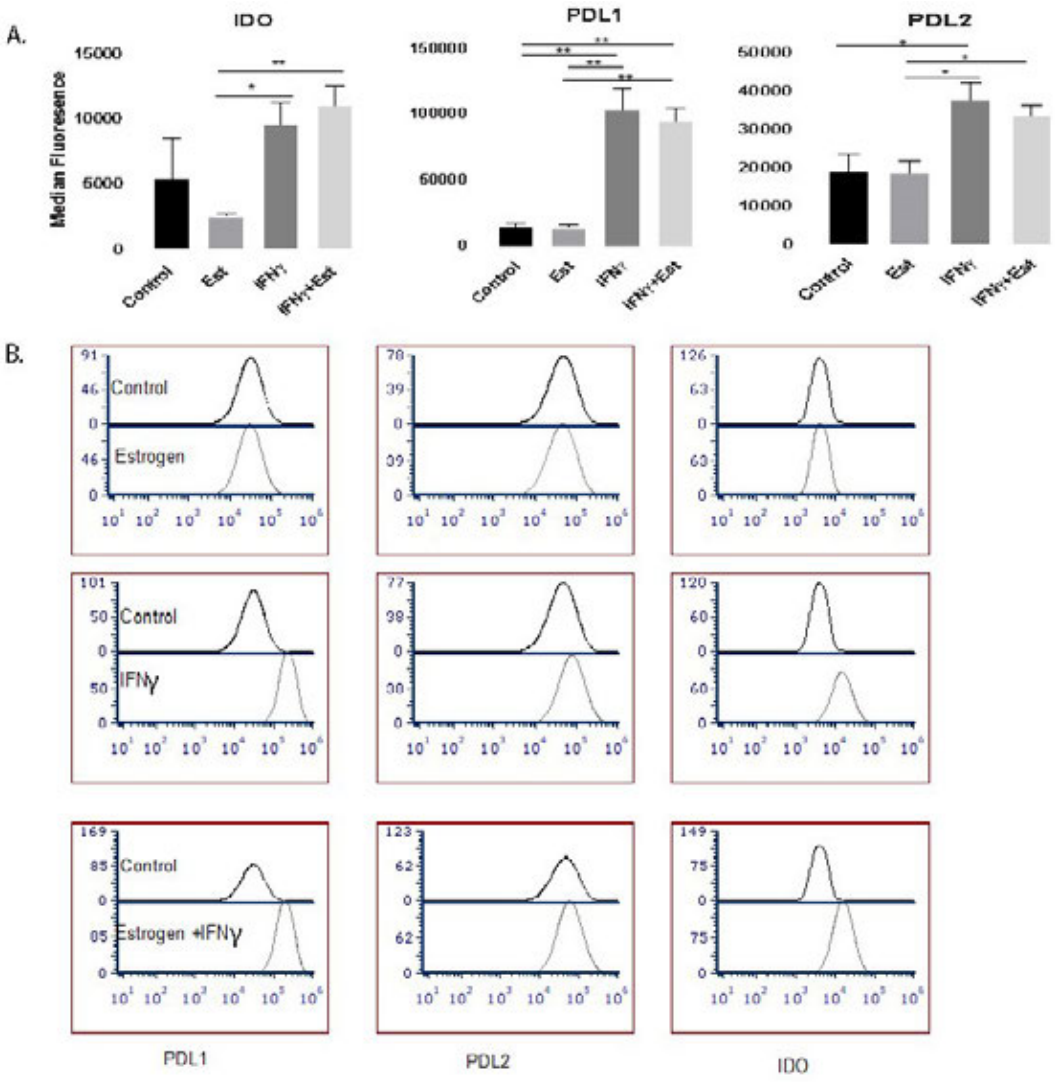

Figure 2. A) IDO, PDL1, and PDL2 have increased median fluoresence after IFNγ licensing. Estrogen treatment does not impace IDO, PDL1, or PDL2 expression (n=3); B) Representative figure demonstrating expression of IDO, PDL1, and PDL2 after treatment with estrogen, IFNγ, or both estrogen and IFNγ. *=p≤0.05; **=p≤0.01.

Disclosure: S. McCoy, None; **J. Giri**, None; **J. Galipeau**, Cambium medical technologies.

Abstract Number: 0014

Sec16A Abnormalities Affect the Intracellular Trafficking of HLA-B27 in the Pathogenesis of Axial Spondyloarthritis

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Background/Purpose: Axial Spondyloarthritis (AxSpA) is a chronic inflammatory arthritis, mainly affecting the axial skeleton. HLA-B27 confers the greatest genetic association in AxSpA. Exome sequencing in a multiplex family had revealed that the incidence of AxSpA in individuals with HLA-B27 and the Sec16A mutation was 100%. Sec16A is a protein that plays a major role in the formation of COPII vesicles and trafficking of proteins from ER to plasma membrane via Golgi Complex. We had previously shown that Sec16A abnormalities not only hinder the assembly of COPII vesicles, leading to abnormal intracellular trafficking and ER stress but also it disrupted the HLA-B27 expression. Here, we aim to investigate whether the Sec16A abnormalities affect the intracellular trafficking of HLA-B27, which is associated with the development of AxSpA, differ from those of HLA-B7, which is not associated. In addition, examining the effect of top 10 interacting proteins of Sec16A, previously identified using BioID, by next generation sequencing help us understanding the pathway associated with intracellular trafficking of HLA-B27.

Methods: Sec16A knockout HeLa cells were generated by transfecting these cells with Sec16A CRISPR/Cas9 KO plasmid (h) and Sec16A HDR plasmid (h) according to manufacturer's instructions. KO efficiency was determined by western blotting. The plasmids encoding YFP (Yellow Fluorescent Protein) tagged HLA-B27

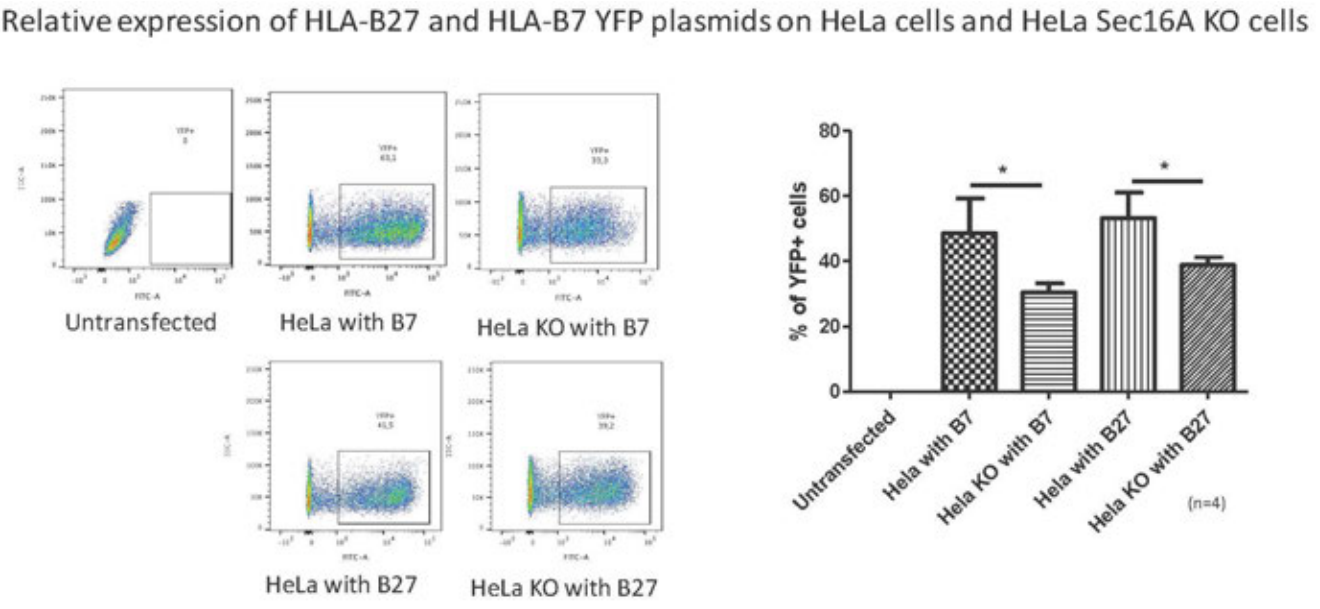

Figure 1.

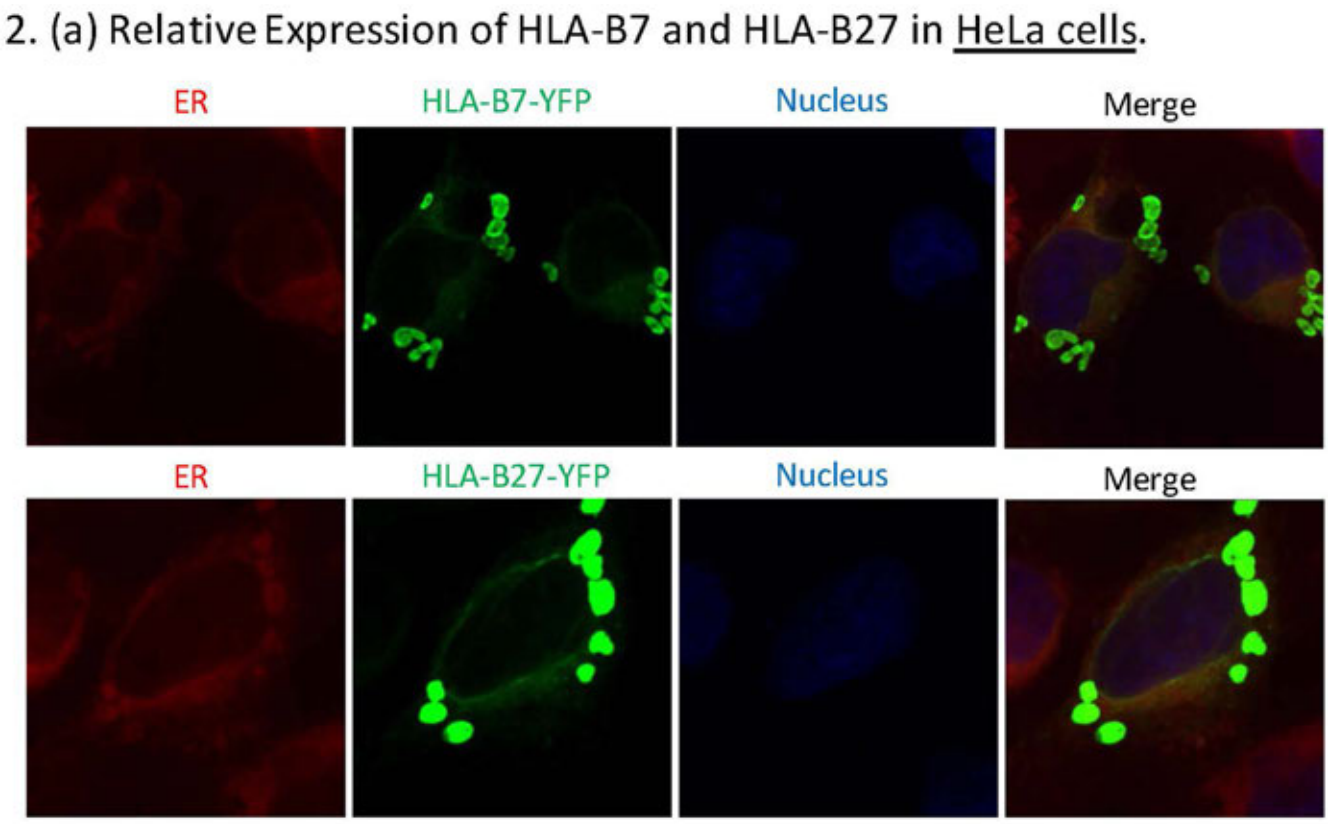

Figure 2.

and HLA-B7 were transfected to HeLa cells and HeLa Sec16A KO cells. The YFP expression of HLA-B7 and HLA-B27 in HeLa cells was assessed by flow cytometry and confocal microscopy at different time points. The real time intracellular trafficking of HLA was monitored using live cell imaging. Also, the expression of properly folded and misfolded HLA-B7 and HLA-B27 were determined using flow cytometry. The top 10 proteins interacting with Sec16A were suppressed using siRNA in C1R-B27 cells and their effect were studied using Next Generation Sequencing.

Results: There was a significant decrease in the expression of both HLA-B7 ($p< 0.05$) and HLA-B27 ($p< 0.05$) in the HeLa Sec16A KO cells compared to wild type cells after transfection. HeLa cells showed an intracellular accumulation of HLA-B27 and HLA-B7 as a result of over expression. On the other hand, we did not observe any such vesicle formation in the HeLa Sec16A KO cells. Sec16 KO cells exhibit an exaggerated unfolded protein response resulting in degradation of the HLA-B proteins. This is also evident from the increased level of intracellular misfolded HLA-B27 and HLA-B7 in the Sec16 KO cells. Using next generation sequencing, we found that Sec16A interacting proteins had an effect in the pathways related to inflammation, ER-to-Golgi vesicle mediated transport and antigen presentation.

Conclusion: Sec16A plays a significant role in the trafficking of HLA-B molecules (HLA-B7 and HLA-B27) irrespective of the subtypes, thereby playing a prospective role in the pathogenesis of AxSpA.

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Abstract Number: 0015

CYR61/TGF-β Axis Promotes Adventitial Fibrosis of Takayasu Arteritis in the IL-17 Mediated Inflammatory Microenvironment

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SESSION INFORMATION
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Background/Purpose: As a novel proinflammatory and potential profibrotic factor, the role of CYR61 on the vascular fibrosis of Takayasu arteritis (TA) has not been investigated.

Methods: CYR61 expression was analysed in aortic vessel samples from TA patients and healthy donors by immunohistochemistry tests. The *in vitro*effect of recombinant human CYR61 (rhCYR61) on the proliferation, migration and activity of adventitial fibroblasts (AFs) in the inflammatory microenvironment was studied.

Results: CYR61 showed obviously higher expression in the TA-affected vessel wall. The proliferation of AFs and the synthesis of ECM components such as collagen I, collagen III and fibronectin were stimulated by rhCYR61. rhCYR61 also partly blocked the migration of AFs. The integrin αvβ1 was identified as the membrane receptor of CYR61, and phosphorylation of the Erk1/2 pathway was also identified. Pretreatment with PD98059, an inhibitor of Erk1/2, resulted in a remarkable decline in the mRNA and protein expression of collagens and fibronectin. Furthermore, rhCYR61 upregulated the expression of TGF-β in AFs, and TGF-β siRNA transfection obviously attenuated the profibrotic effect of rhCYR61. Finnally, recombinant human IL-17 (rhIL-17) could promote the expression of CYR61 in AFs, and the combination of rhIL-17 and rhCYR61 dramatically strengthened the synthesis of ECM. The CYR61 monoclonal antibody diminished these effects of rhIL-17 in AFs.

Conclusion: These findings indicated that CYR61/Erk1/2/TGF-β pathway played a profibrotic role in the pathogenesis of TA, and this was enhanced by IL-17 mediated inflammatory environment. Thus, targeting CYR61 may have potential clinical values in the future.

Disclosure: L. Ma, None; **X. Kong**, None; **X. Cui**, None; **S. Wu**, None; **Y. Wang**, None; **L. Jiang**, None.

Abstract Number: 0016

Monoclonal ACPA Promote Synovial Fibroblasts Migration Through a Peptidylarginine Deiminases (PAD) Dependent Pathway

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
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Background/Purpose: Anti-citrullinated protein antibodies (ACPAs) play an important role in rheumatoid arthritis (RA) pathogenesis. ACPAs have different amino acid motif recognition patterns and show cross-reactivity to other protein modifications. We aimed to investigate the effect of different monoclonal ACPAs on RA synovial tissue derived fibroblast-like synoviocytes (FLS).

Methods: FLS were isolated from synovial tissue of RA patients by enzymatic digestion. ACPA and control monoclonal antibodies (mAbs) were derived from single B cells isolated from RA patients. Whole antibodies and F(ab')2 fragments were tested in synovial fibroblast migration (IncuCyte live-cell analysis) and osteoclast formation assays. Blocking experiments were performed with soluble citrullinated proteins in SF migration. The role of mAbs cross-reactivity was tested in fibroblast migration assays using antibodies with distinct cross-reactivities, inhibitors of peptidylarginine deiminases (Cl-amidine and GSK199), histone acetyltransferase (anacardic acid) and histone deacetylase (trichostatin A). Binding patterns of monoclonal ACPAs were tested in synovial biopsies obtained from both healthy donors and RA patients.

Results: Three monoclonal ACPAs (1325:01B09, 14T+:02D09 and14T+:02H12) enhanced fibroblast migration significantly compared to control mAb 1362:01E02-treated samples (mean±SD fold increase of 1.9±0.5, 1.7±0.4 and 1.8±0.6, respectively, $p< 0.05$), whereas the same antibodies showed no effect on osteoclast formation. Clone 1325:01B09 but neither 14T+:02D09 nor 14T+:02H12 is cross reactive with homo-citrullinated and acetylated targets (acetylated histone). The effect of 1325:01B09 on fibroblast migration was completely abolished by Cl-amidine or by pre-incubating the antibody with citrullinated fibrinogen or histone but not by citrullinated enolase or vimentin. Despite the cross-reactivity with acetylated epitopes, neither anacardic acid nor trichostatin A could modulate the 1325:01B09 effect on fibroblast migration. The fibroblast-promoting ACPA clone 1325:01B09 but not the osteoclastogenic 1325:04C03 co-localized with podoplanin-positive fibroblasts in the inflamed rheumatoid synovium. On the contrary to RA samples, healthy synovia were not stained by ACPAs. F(ab')2 fragments of mAbs show similar effects on synovial fibroblast migration, osteoclast formation and a similar tissue binding pattern as the intact antibodies, indicating an Fc-independent mediated effect.

Conclusion: Some but not all ACPA clones could stimulate synovial fibroblast migration through a mechanism that was dependent on protein citrullination but no other protein modifications or FcR binding. Different clones acted on fibroblasts and osteoclasts suggesting unique pathological roles associated with individual ACPA specificities.

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Abstract Number: 0017

Transcription Factor Fli-1 Impacts Lupus Nephritis by Orchestrating CXCL10/CXCR3 Axis

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SESSION INFORMATION
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Background/Purpose: Lupus nephritis is a major cause of death in both animal models and human patients. Expression of Fli-1, a member of the Ets family of transcription factors, is implicated in the development of nephritis in murine models ofSLE as well as human lupus nephritis. The increased expression of Fli-1 is significantly associated with new or recurrent lupus nephritis in SLE patients with lupus nephritis compared with SLE without lupus nephritis. Reducing the levels of Fli-1 in two lupus mouse strains significantly decreased renal disease with a profound decrease in infiltrating inflammatory cells and prolonged survival. IFN-gamma Inducible Protein (IP-10), also known as C-X-C motif chemokine 10 (CXCL10), is an inflammatory chemokine belonging to the CXC chemokine family. Overexpression of CXCL10 is associated with clinical lupus nephritis. CXCL10 is chemotactic for inflammatory cells including macrophages, monocytes and activated T and NK cells that express the CXCR3, a receptor for CXCL10. Previous reports demonstrated that CXCR3+ cells are recruited into the inflamed kidneys in murine models of lupus and human patients. In this study, we examinedif Fli-1 impacts lupus nephritis by orchestrating CXCL10/CXCR3 Axis.

Methods: The expression of CXCL10 was measured in kidneys from Fli-1 knockout heterozygous MRL/lpr mice, a murine model of lupus (Fli1+/-; Fli-1 homozygous knockout is embryonic lethal), and wild-type (Fli1+/+) MRL/lpr mice. A murine endothelial cell line, human renal glomerular endothelial cells (HRGEC), and human T cells were used in this study. CXCL10 was measured using commercially available ELISA kits. The specific Fli-1 siRNA was used to knock down the expression of Fli-1 in cells.

Results: CXCL10 protein concentration was significantly higher from kidney homogenates from wild-type MRL/lpr mice compared to the kidney homogenates from Fli-1+/- MRL/lpr mice at the age of 25 weeks (WT, 2,264±376 pg/mg vs Fli-1+/-,1322±129 pg/mg, N=11, $p< 0.05$). CXCL-10 concentrations from mouse endothelial cells transfected with Fli-1 siRNA were significant lower compared to the cells transfected with control siRNA following stimulation with LPS (645.7± 167.1 pg/ml versus 336.2± 93.26 pg/ml at 6 hours, $P< 0.001$; and 1493.75± 392.35 pg/ml versus 540.01± 187.37 pg/ml at 24 hours, $p< 0.001$). The CXCL10 concentrations in supernatant from HRGEC transfected with Fli-1 siRNA and stimulated with LPS or TNF-α were significantly lower 6 and 24 hours post LPS or TNF-α stimulation compared to thosetransfected with control siRNA. Fourteen putative Ets binding sites are identified within a 2900 bp region of the CXCL-10 promoter, and four sites in the promoter showed significant enrichment for Fli-1 specific antibodies compared to normal IgG controls by the chromatin immunoprecipitation (ChIP) assay. We have demonstrated that mutation of the Fli-1 DNA binding domain led to a statistically significant reduction in activation from the CXCR3 promoter when compared to wild-type Fli-1 protein, andacetylationand phosphorylationofFli-1play arole in CXCR3activityin Tcell.

Conclusion: Together, the results implicate that one key factor in Fli-1's impact on lupus nephritis is by modulating theCXCL10/CXCR3 Axis.

Disclosure: X. Wang, None; **M. Lennard Richard**, None; **T. Caldwell**, None; **B. Henry**, None; **T. Nowling**, None; **J. Oates**, None; **G. Gilkeson**, None; **X. Zhang**, None.

Abstract Number: 0018

Undifferentiated Connective Tissue Disease at Risk for SSc: Potential Role of Circulating CXCL-10, CXCL-11 and IL-33 in Predicting Disease Evolution

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SESSION INFORMATION

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Session Title: Cytokines & Cell Trafficking Poster

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Session Time: 9:00AM–11:00AM

Background/Purpose: Higher levels of CXCL10 and CXCL11 in patients with a very early diagnosis of systemic sclerosis (SSc) subsequently shifted to SSc were pointed out (1). An intriguing role of IL-33 in early SSc patients was also previously described (2).

Methods: Serum levels of CXCL-10, CXCL-11 and IL-33 were measured in 30 undifferentiated connective tissue disease at risk for SSc (UCTD-risk-SSc) patients (3), otherwise referred to as very early-early SSc, and 34 healthy controls (HC) by multiplex suspension immunoassay. All UCTD-risk-SSc patients were followed-up for 36 (12-101) months.

Results: Serum levels of CXCL-10, CXCL-11 and IL-33 resulted higher in UCTD-risk-SSc patients as compared to HC (respectively: $p< 0.001$; $p< 0.001$ and $p=0.07$). UCTD-risk-SSc subsequently evolved to SSc showed higher baseline cytokines levels versus patients not evolved (CXCL10: $p=0.05$; $p=0.04$ and IL-33: $p=0.03$). At receiver operating characteristic (ROC) analysis the following cut-off values were able to discriminate patients evolving into SSc (CXCL-10 >34.47 pg/mL, area under the curve (AUC)=0.72, $p=0.02$ with 0.63 sensitivity (SE) and 0.82 specificity (SP); CXCL11 >42.38 pg/mL, AUC=0.73, $p=0.02$ with 0.84 SE and 0.54 SP; IL-33 >8.86 pg/mL, AUC=0.73, $p=0.01$ with 0.89 SE and 0.54 SP). In addition a baseline CXCL-11 value >45.21 pg/mL and IL-33 value >8.86 pg/mL were able to discriminate patients developing an interstitial lung disease (AUC=0.80, $p< 0.001$ with 1.0 SE and 0.56 SP and AUC=0.72, $p=0.05$ with 1.0 SE and 0.53 SP).

Conclusion: We confirmed the previous data on CXCL-10 and CXCL-11 and we first highlighted a potential role of IL-33 in predicting disease evolution.

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Abstract Number: 0019

Inhibition of IkB Kinase-IKK Complex of Canonical NF-κB Pathway in Antiphospholipid Antibody-Mediated Endothelial Cell Activation

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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid antibodies (aPL) activate several target cell types leading to inflammatory damage and thrombosis in the antiphospholipid syndrome (APS). NF-κB activation is essential for inducing this inflammatory phenotype but there is limited information on the role of the canonical vs non-canonical NF-κB activation pathways in APS and the inhibition of these pathways as a possible therapeutic strategy in APS. We sought to determine the efficacy of specific inhibitors of the regulatory IκB kinase complex (IKK), which is responsible for initiating nuclear translocation of NF-κB, in ameliorating the effects of aPL.

Methods: Whole IgG fractions were purified from normal (IgG-NHS) and primary APS (IgG-APS) patients by ammonium sulphate precipitation followed by DEAE sepharose chromatography. Increasing doses of purified whole IgG-APS and control IgG-NHS fractions were used to treat human umbilical vein endothelial cells (HUVEC) (100-400μg/ml). Quantitative RT-PCR was used to measure E-selectin (E-sel), tissue factor(TF), interleukin (IL)-6 and IL-8 mRNA expression and western blot was used to evaluate the time course of NF-κB activation in treated HUVEC identifying various subunits over 4-hours post treatment (at time points 0, 15, 30, 60, 120, 240 and 480 minutes). The effectiveness of specific IKK inhibitors Bay-11-7082 and BMS-345541 were evaluated.

Results: IgG-APS increased pro-inflammatory cytokine expression in a dose dependent manner, with a maximum mRNA fold change ranging from 4-18 times over controls. Over the 4-hour time-course cytoplasmic expression of IκBα decreased and nuclear expression of RelA, p50 (strong) and p52, p105 (weak) subunits increased in response to aPL treatment (peaks at 30 to 60 minutes), indicating strong activation via the canonical NF-kB pathway. BMS and Bay-11 significantly inhibited cytokine expression 2.5 to 3.5 fold in aPL-treated HUVEC.

Conclusion: The canonical NF-kB pathway is essential for aPL-medicated EC activation in at least a portion of APS patients. Accordingly, specific IKK inhibitors may prove useful in ameliorating aPL-mediated inflammation in these patients.

Disclosure: R. Willis, None; **E. Papalardo**, None; **M. Jamaluddin**, None; **Z. Romay-Penabad**, None; **A. Schleh**, None; **A. Brasier**, None; **E. Gonzalez**, None.

Abstract Number: 0020

Comparative Efficacy of Beta-2-Glycoprotein I Domain V Structural Analogue Variants in Preventing Antiphospholipid Antibody-Mediated Endothelial Cell Activation

Rohan Willis,[1] Elizabeth Papalardo,[1] Mohammad Jamaluddin,[1] Zurina Romay-Penabad,[1] Alvaro Schleh,[1] Allan Brasier,[1] and Emilio B Gonzalez[2], [1]University of Texas Medical Branch, Galveston, TX, [2]University of Texas Medical Branch, Galveston

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In previous studies, our group has demonstrated that a synthetic 20 amino acid peptide ("TIFI") with structural similarity to Beta-2-Glycoprotein I Domain V (β2GPI DV) prevents endothelial cell (EC) activation and thrombosis in a mouse model of antiphospholipid syndrome (APS). In order to improve its half-life and decrease its immunogenicity, TIFI was PEGylated but this process proved inefficient, with substantial loss of material during the process. Therefore, we have designed two synthetic peptides that would potentially improve efficiency of PEGylation, TIFI Mut1 and TIFI Mut2, and evaluated their ability to inhibit antiphospholipid antibody (aPL)-mediated EC activation.

Methods: Whole IgG fractions were purified from normal (IgG-NHS) and primary APS (IgG-APS) patients by ammonium sulfate precipitation followed by DEAE sepharose chromatography. A dose of 200μg/ml IgG was used to treat human umbilical vein endothelial cells (HUVEC) alone or after 2 hours pre-incubation with 10μM TIFI WT, Mut1 or

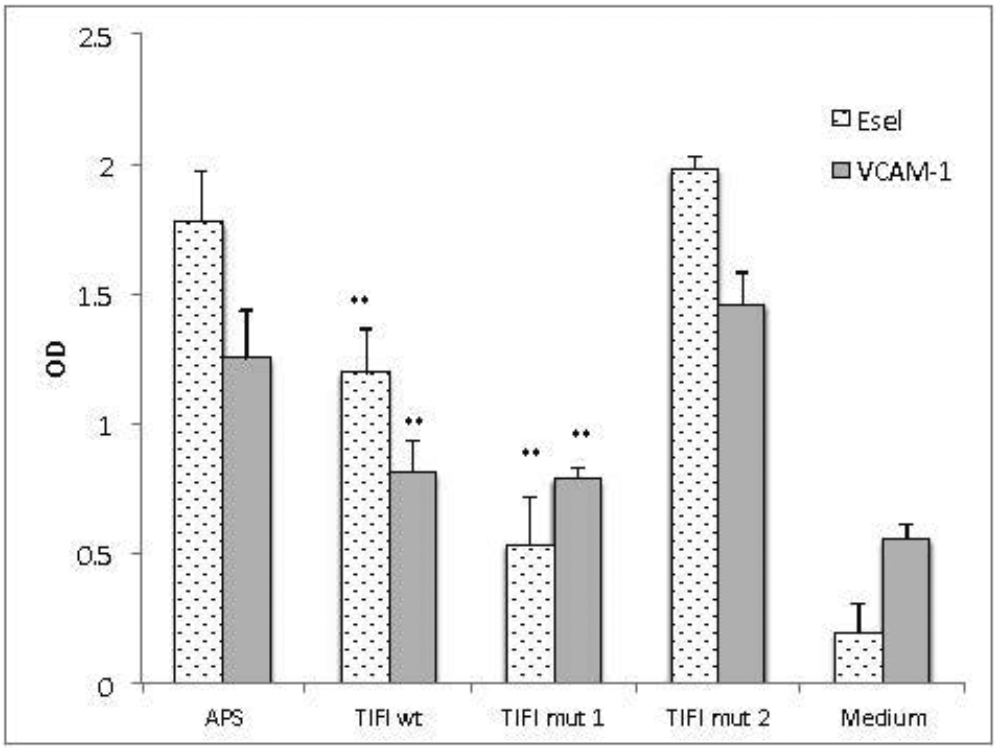

Figure 1. CytoELISA Activity on HUVEC - Effect of non-PEGylated TIFI variants on aPL-mediated cytokine production. **-p<0.001 compared to APS

Mut2. Quantitative RT-PCR was used to measure E-selectin (E-sel), tissue factor (TF), intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) mRNA expression. VCAM-1 and E-sel cell surface expression was also determined by cytoELISA on fixed ECs treated with IgG ± TIFI variants

Results: TIFI-Mut1 was 1.3-2.3 fold more effective than TIFI-WT in inhibiting aPL-mediated inflammatory cytokine mRNA induction. Similarly, TIFI-Mut 1 was 3 times more effective in limiting cell-surface expression of E-sel compared to TIFI-WT and was equally as effective in limiting VCAM-1 surface expression. TIFI-Mut2 was ineffective at inhibiting aPL activation of HUVECs.

Conclusion: TIFI Mut1 peptide reduces aPL-induced inflammatory cytokine gene expression and cell surface expression significantly, indicating that PEGylation of this peptide variant will likely be effective in an in vivo application.

Disclosure: R. Willis, None; **E. Papalardo**, None; **M. Jamaluddin**, None; **Z. Romay-Penabad**, None; **A. Schleh**, None; **A. Brasier**, None; **E. Gonzalez**, None.

Abstract Number: 0021

Immuno-Phenotypic Analysis of Peripheral Blood Mononuclear Cells in Rheumatoid Arthritis Patients Treated with E6011, a Humanized Anti-Fractalkine Monoclonal Antibody

Tomohiro Yamada,[1] Jungo Kakuta,[1] Eri Fusaoka-Nishioka,[1] Jun-ichi Ito,[2] Nobuyuki Yasuda,[3] Tetsu Kawano,[3] and Toshio Imai[3], [1]KAN Research Institute Inc., Kobe, Japan, [2]EISAI Co. Ltd., Tsukuba, Japan, [3]KAN Research Institute, Inc., Kobe, Japan

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Innate Immunity Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fractalkine (FKN) and its solo receptor CX3CR1 are deeply involved in the pathogenesis of rheumatoid arthritis (RA). FKN is expressed on vascular endothelium, while CX3CR1 is expressed on peripheral blood leukocytes such as monocytes/macrophages, NK cells, effector $CD8^+$T cells and a minor fraction of $CD4^+$T cells. E6011, a novel humanized anti-FKN monoclonal antibody (mAb), is under clinical development in RA. In order to continuously assess the E6011 pharmacodynamics by monitoring the alteration of peripheral blood immune cells, including CX3CR1-expressed cell populations, a series of multi-color flow cytometry (FCM) was conducted before and during the course of the E6011 treatment of active RA patients in phase 2 clinical trial.

Methods: Immuno-phenotypic changes were explored by FCM during the E6011 administration in 190 Japanese RA patients with inadequate response to MTX (NCT02960438). Patient's peripheral blood were drawn into fixative tube (Cyto-Chex® BCT, Streck) at each clinics and thereafter transported to the FCM facility at KAN Research Institute. Inc. within 30 hours after the blood collection to operate the FCM analysis by standardized method. Immuno-phenotyping was carried out by multi colors flow cytometry (BD FACSCantoII™, BD LSRFortessa™, BD Biosciences).

Results: Based on these determined conditions, CX3CR1 expression on monocytes, NK cells and a part of $CD8^+$and $CD4^+$T cells were confirmed in this method. Interestingly, during the E6011 treatment, the proportion of CD16+ monocytes, which highly express CX3CR1 within whole monocytes, were significantly decreased at 2 week after initial treatment from the baseline (E6011 : $p< 0.001$, placebo: $p> 0.48$) and sustained up to 24 week, while that of $CD16^-$monocytes were increased. The reduction of the proportion of NK cells, $CD4^+$and $CD8^+$T cells were not ob-

served, but in some certain populations like CX3CR1-expressed $CD56^+CD16^+$NK cells and terminal differentiated effector $CD8^+$T cells, the percentage of these populations tended to increase from the baseline at 2 week and kept increasing up to 24 week by the E6011 treatment.

Conclusion: Our results indicated that the reduction of $CD16^+$monocytes after initial treatment might be a sensitive pharmacodynamic marker of E6011 exposure, possibly reflecting mechanism of action of E6011, since the $CD16^{+-}$ monocytes are the most abundant $CX3CR1^+$cell population in peripheral blood.

Disclosure: T. Yamada, None; **J. Kakuta**, None; **E. Fusaoka-Nishioka**, None; **J. Ito**, None; **N. Yasuda**, None; **T. Kawano**, KAN Research Institute, Inc., 3; **T. Imai**, KAN Research Institute, Inc., 3.

Abstract Number: 0022

Beta-2 Glycoprotein I as a DNA- and NET-binding Protein

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Innate Immunity Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Beta-2 glycoprotein I (β_2GPI) is a prominent autoantigen in antiphospholipid syndrome (APS). As an abundant plasma protein, β_2GPI has variably been suggested to have antioxidant, anticoagulant, and scavenging functions, albeit without a clear consensus regarding its defining role. Many years ago, β_2GPI was shown to be capable of binding cell-free DNA in plasma; however, to our knowledge, this line of investigation was not further pursued. Here, we tested the hypothesis that β_2GPI might bind to not only negatively-charged DNA, but also neutrophil extracellular traps (NETs)—prothrombotic tangles of chromatin and microbicidal proteins extruded from activated neutrophils. We also asked whether β_2GPI-DNA complexes might be detectable*in vivo*, specifically in the blood of patients with APS.

Methods: To induce NET release, control neutrophils were stimulated with either phorbol 12-myristate 13-acetate (PMA) or lipopolysaccharide (LPS) in the presence of human serum as a source of β_2GPI. In parallel, APS neutrophils were cultured in the presence of autologous serum and allowed to undergo spontaneous NET release. To assess a potential direct interaction between β_2GPI and either genomic DNA or purified NETs, we utilized the electrophoretic mobility shift assay (EMSA). Finally, we developed a novel sandwich ELISA to measure plasma concentrations of β_2GPI-DNA complexes in which the capture antibody was specific for β_2GPI and the detection antibody specific for DNA.

Results: By confocal immunofluorescence microscopy, we observed broad decoration of both anuclear neutrophils remnants and NET strands themselves by β2GPI. The pattern of β2GPI decoration of NETs was relatively granular, as compared with linear painting of NETs by neutrophil elastase. β2GPI-decorated NETs were appreciated in the context of PMA-and LPS-stimulated control neutrophils, as well as spontaneous NET release from APS neutrophils. By agarose-gel EMSA, β2GPI triggered dose-dependent electrophoretic retardation of both neutrophil genomic DNA and purified NETs. Using a custom ELISA for β2GPI-DNA complexes, we tested 78 primary-APS plasma samples alongside 41 healthy-control samples. APS plasma demonstrated significantly higher levels of β2GPI-DNA complexes as compared with healthy controls (3.6 μg/ml ± 10 versus 0.57 μg/ml ± 1.6; $p< 0.0001$ by Mann-Whitney test).

Additional analyses are underway to determine whether β2GPI-DNA complexes are associated with particular APS clinical profiles, and the extent to which these complexes are unique to APS versus other inflammatory states.

Conclusion: β_2GPI appears to directly bind both genomic DNA and NETs. In neutrophil cultures, β_2GPI decorates anuclear neutrophil remnants, as well as classic NET strands. Intriguingly, β_2GPI-DNA complexes are on average 6-fold higher in the plasma of patients with primary APS as compared with controls. Future research should endeavor to determine whether β_2GPI is an endogenous DNA scavenger, and the extent to which the β_2GPI-NET association may play a role as an instigator and/or perpetuator of autoimmunity in APS.

Disclosure: K. Gockman, None; **S. Yalavarthi**, None; **G. Sule**, None; **A. Morris**, None; **Y. Zuo**, None; **J. Knight**, None.

Abstract Number: 0023

Covalent High Molecular Weight HMGB1 Complexes in Muscle Regeneration: Implications in Inflammatory Myopathy

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Innate Immunity Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Increased levels of the alarmin high mobility group box one (HMGB1) have been implicated as a possible pathogenic mediator and biomarker for myositis. We have recently published that in response to stress/ inflammation, HMGB1 forms covalent protein complexes (HMGB1c) via transglutaminase-2 (TG2) dependent crosslinking. The purpose of this study is to test the hypothesis that HMGB1c is a driver of skeletal muscle myogenesis and may play a role in the pathogenesis of myositis.

Methods: A combination of in vivo and in vitro studies were used to examine the role of HMGB1c in muscle regeneration. Muscle regeneration and myogenesis were examined in TG2 -/- vs. wild-type mice as well as in mouse C2C12 myoblasts. An in vivo muscle regeneration model using BaCl2 induced injury was used to probe muscle covalent HMGB1 complex expressionand myogenic markers. Samples were analyzed by real time RT-PCR, immunohistochemistry, and western blotting.

Results: HMGB1 formed high molecular weight, heat/denaturing resistant protein complexes (HMGB1c) in differentiating C2C12 cells. Loss of TG2 function via RNAi or genetic ablation reduced HMGB1c formation, impaired C2C12 differentiation, and delayed muscle regeneration in vivo. Impaired muscle regeneration in TG2 -/- mice also correlated with enhanced pro-inflammatory immune cell infiltration and reduced presence of myogenic M2 macrophages.

Conclusion: Our results revealthat TG2 is a novel mediator of myogenesis in vitro and in vivo, which may occur in-part via HMGB1 transamidation and altered pro- to anti-inflammatory transitions during myogenic differentiation. Increased presence of HMGB1c in plasma of myositis patients relative to healthy controls suggests that the crosslinked alarmin could play a role in disease pathogenesis.

Disclosure: W. Willis, None; **J. Petrosino**, None; **G. Valiente**, None; **L. Wu**, None; **W. Jarjour**, None.

Abstract Number: 0024

Role of Trained Immunity in the Pathogenesis of Erdheim-Chester Disease

Giulio Cavalli,[1] Riccardo Biavasco,[1] Marina Ferrarini,[2] Elisabetta Ferrero,[2] Eugenio Montini,[2] Simone Cenci,[2] Cardaci Simone,[2] and Lorenzo Dagna[1], [1]Vita-Salute San Raffaele University, Milan, Italy, [2]IRCCS San Raffaele Hospital, Milan, Italy

SESSION INFORMATION

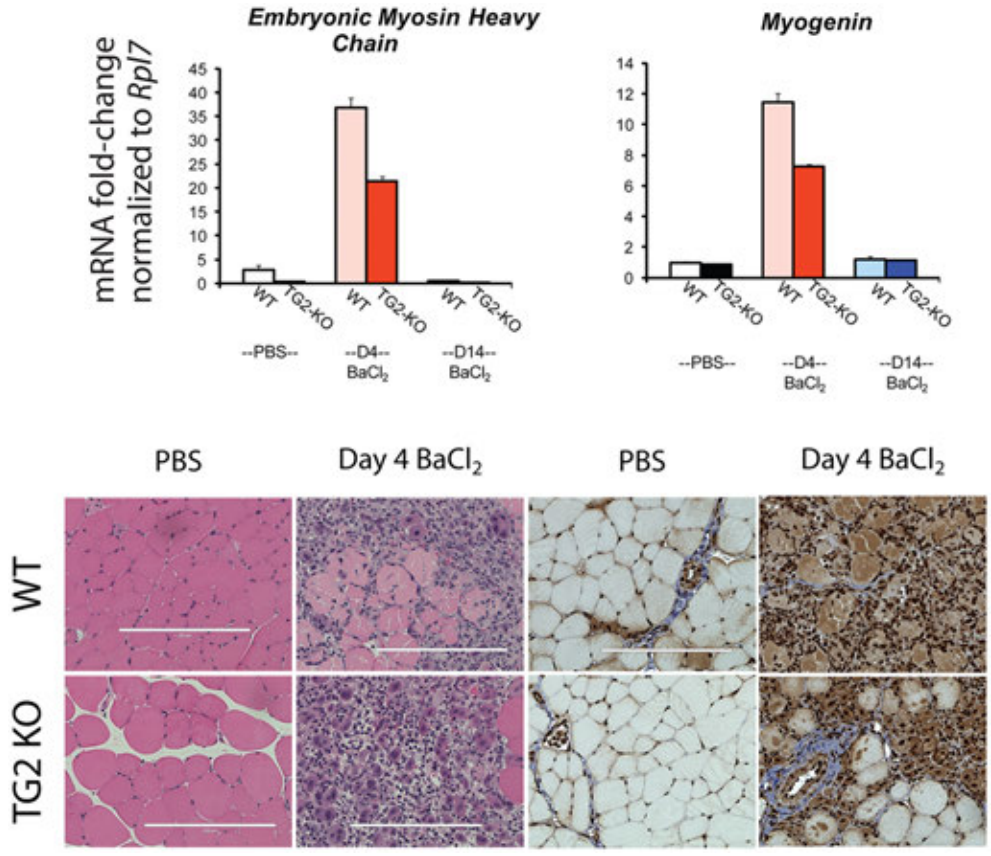
Session Date: Sunday, November 10, 2019

Session Title: Innate Immunity Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Erdheim-Chester disease (ECD) is a chronic inflammatory disease characterized by infiltration of bone and other tissues by foamy macrophages. These cells exhibit activating mutations along the MAPK pathway, most commonly BRAFV600E, and increased production of pro-inflammatory cytokines. Although this dual neoplastic-inflammatory nature of ECD has long fascinated scientists, the mechanistic link between these two features remains elusive. We hypothesized that Trained Immunity (TI), a pro-inflammatory cell program physiologically elicited in monocytes/macrophages upon activation of the MAPK pathway, might represent the missing link between oncogenic transformation and pro-inflammatory activation in ECD. In this study, we aimed at determining the role of



TG2 genetic ablation decreases cytosolic HMGB1 levels, delays regeneration in a BaCl2-induced muscle injury model.

TI in the pathogenesis of ECD, and to evaluate the therapeutic potential of targeting this mechanism for the treatment of ECD.

Methods: We developed innovative models to study ECD pathogenesis*in vitro*and*in vivo*(ectopic expression of BRAFV600E in monocytes and hematopoietic progenitors from healthy donors cultured and/or transplanted into immunocompromised mice), as well as*ex vivo*(3D culture of ECD tissues in bioreactor). Mechanistic features of TI, including typical changes in cell energy metabolism and epigenetics, were investigated by assessing I) cytokine and lactate production; II) mitochondrial respiration with Seahorse flux analyzer; III) glucose and glutamine metabolism with metabolomics analyses; III) chromatin dynamics with ATAC sequencing.

Results: Activation of the MAPK pathway induced by BRAFV600E in ECD macrophages induces changes in the epigenetic landscape, cell energy metabolism, and cytokine production characteristic of TI. In particular, changes in cell energy metabolism of macrophages are characterized by increased glycolysis and glucose and glutamine metabolism. This metabolic rewiring is likely needed to sustain rampant, constitutive production of pro-inflammatory cytokines IL-1β, IL-1α, and IL-6.

Conclusion: A role emerges for TI in the pathogenesis and pro-inflammatory activation of ECD. Since drugs targeting TI programs are already entering the clinical arena, the identification of this mechanism in the pathogenesis of ECD may translate into novel, effective treatment options for ECD patients.

Disclosure: G. Cavalli, None; **R. Biavasco**, None; **M. Ferrarini**, None; **E. Ferrero**, None; **E. Montini**, None; **S. Cenci**, None; **C. Simone**, None; **L. Dagna**, None.

Abstract Number: 0025

Altered Distribution and Enhanced Osteoclastogenesis of Mucosal-associated Invariant T Cells in Gouty Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Innate Immunity Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Mucosal-associated invariant T (MAIT) cells are subsets of innate invariant T cells and rapidly produce Th1/Th17 cytokines including interferon (IFN)-γ, tumor necrosis factor (TNF)-α, and interleukin (IL)-17 in an innate-like manner. Accumulating data indicate that MAIT cells play an important role in immune defense against infection or cancer. Furthermore, recent studies have extended knowledge regarding the clinical relevance of MAIT cells to cardiometabolic diseases, including metabolic syndrome, obesity, diabetes mellitus, and cardiovascular disease. Here, we investigate the role of MAIT cells in gouty arthritis (GA), one of metabolic diseases, and their effects on osteoclastogenesis.

Methods: Patients with GA (n = 61), hyperuricemia subjects (n = 11), and healthy controls (n = 30) were enrolled in this study. MAIT cells, cytokines, CD69, programmed death-1 (PD-1), and lymphocyte-activation gene 3 (LAG-3) levels were measured by flow cytometry.*In vitro*osteoclastogenesis experiments were performed using peripheral blood mononuclear cells in the presence of macrophage colony-stimulating factor and receptor activator of nuclear factor kB ligand.

Results: Circulating MAIT cell levels were significantly reduced in GA patients. However, their capacities for IFN-γ, IL-17, and TNF-α production were preserved. Expression levels of CD69, PD-1, and LAG-3 in MAIT cells were found to be elevated in GA patients. In particular, CD69 expression in circulating MAIT cells was increased by stimulation with monosodium urate monohydrate (MSU) crystals, suggesting that deposition of MSU crystal might contribute to MAIT cell activation. Interestingly, MAIT cells were found to be accumulated in synovial fluid and infiltrated into gouty tophus tissues within joints. Furthermore, activated MAIT cells secreted pro-resorptive cytokines (i.e., IL-6, IL-17, and TNF-α) and facilitated osteoclastogenesis.

Conclusion: This study demonstrates that circulating MAIT cells are activated and numerically deficient in GA patients. In addition, MAIT cells have the potential to migrate to inflamed tissues and induce osteoclastogenesis. These findings provide an important role of MAIT cells in the pathogenesis of inflammation and bone destruction in GA patients.

Disclosure: Y. Park, None; **Y. Cho**, None; **H. Jeong**, None; **H. Jin**, None; **S. Kee**, None.

Abstract Number: 0026

Increased Sodium Accumulation Detected by ^{23}Na-Magnetic Resonance Imaging in Inflamed Knees of Patients with Autoimmune Joint Disease

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Innate Immunity Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Salt, or sodium, has recently emerged as a potent factor involved in modulating inflammatory responses. Sodium is implicated as a dietary risk factor for (ACPA-positive) RA[1]and increased sodium concentrations lead to enhanced Th17 cell differentiation[2]. Furthermore, sodium accumulates locally in certain inflamed and sclerotic tissues such as the skin, both in the context of infection and in autoimmunity, as has been shown in scleroderma patients[3]. To clarify whether sodium, as a possible inflammation-enhancing factor, may also accumulate locally in the joints in autoimmune arthritis, we used a state-of-the-art, non-invasive 7-Tesla^{23}Na MRI technique to measure sodium concentrations in inflamed knees of patients with autoimmune joint disease.

Methods: In 8 patients with autoimmune arthritis of the knee (3 JIA, 2 PsA, 2 RA, 1 peripheral SpA) and 11 healthy controls, we measured synovial Na^+content in the (affected) knee with a birdcage double-tuned proton/^{23}Na sodium transmit/receive coil on a 7-Tesla MR system (Philips Healthcare, Best, the Netherlands). Cartilage, synovium, and synovial fluid (in the intra-articular space and synovial bursae) was manually segmented in the proton image in six sagittal slices, after which the volume of interest was transferred to the^{23}Na image for extraction of^{23}Na MR signal intensity. Average Na^+content in mmol/L was calculated by relating^{23}Na MR signal intensity to three agarose standard gels of known Na^+concentration (20, 50, and 100 mmol/L), scanned in tandem with each knee (see Figure 1).

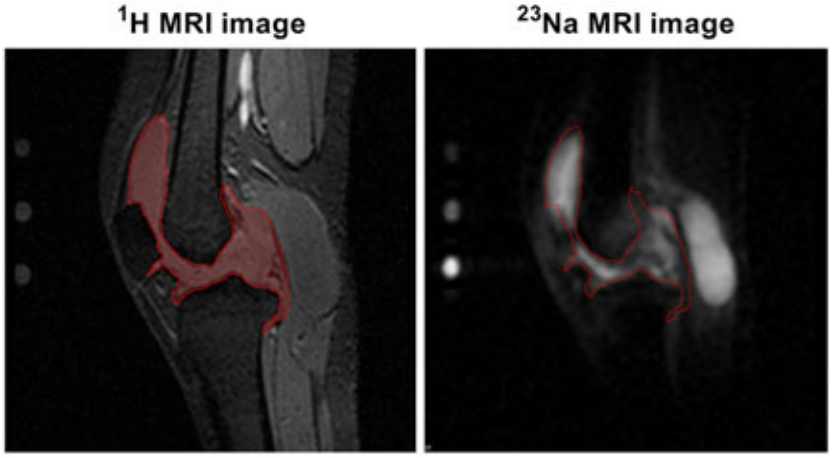

Figure 1. Manual segmentation of a mid-knee sagittal slice of a representative patient. The volume of interest (cartilage, synovium, and synovial fluid in the joint space and synovial bursae) was manually selected in the proton image (left), propagated to adjacent slices, and then transferred to the sodium image (right) for quantification of sodium signal. Cross-sections of three sodium-containing agarose phantom tubes are visible anterior to the knee, from top to bottom: 20, 50, 100 mmol/L sodium. Baker's cysts, as visible in this patient, were not included in the analysis.

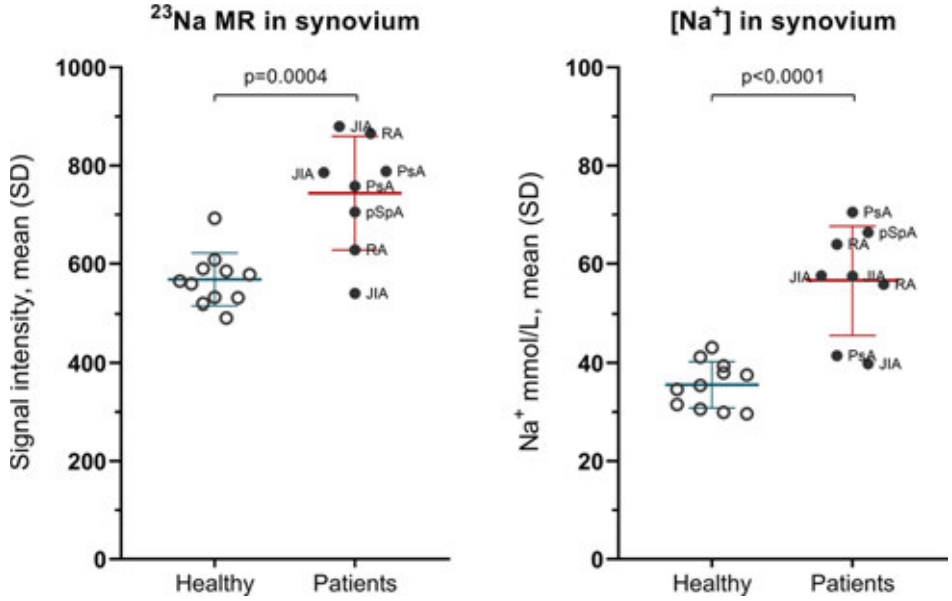

Figure 2 Synovial sodium MR signal intensity (left) and concentration (right) quantified by 23Na-MRI. Each dot, representing one subject, is based on the average of 6 sagittal MRI slices capturing the synovial volume.

Results: ^{23}Na-MRI signal intensity in synovial structures was consistent and reproducible across slices: between slice coefficient of variation in a representative patient was 9.4%.^{23}Na-MRI demonstrated increased^{23}Na MR signal intensity in arthritis knees of patients compared to healthy controls: mean (SD): 744 (116) vs 568 (54), p=0.0004 (Figure 2). When this MR signal intensity was converted to Na^{+}concentration, patients had clearly increased Na^{+}-concentrations compared to controls: mean (SD): 57 (11) vs 36 (5) mmol/L, p< 0.0001. A linear regression with synovial Na^{+}concentration as the outcome indicated that the differences in synovial Na^{+}concentration between patients and healthy controls could not be explained by differences in synovial volume (not shown).

Conclusion: Tissue sodium detection and quantification by 7-Tesla ^{23}Na MRI is feasible and reliable, and indicates significantly higher sodium content in inflamed knees of patients with autoimmune joint disease compared to healthy controls. This suggests that sodium may be involved in modulating inflammation and synovial cell biology. Whether this is specific for chronic autoimmune joint diseases or may be present for more general inflammation remains to be determined.

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Disclosure: E. de Moel, None; **W. Teeuwisse**, None; **T. Huizinga**, Abblynx, 2, 5, 8, Abbott, 2, 5, 8, Biotest AG, 2, 5, 8, Boehringer Ingelheim, 2, 5, 8, Boeringher Ingelheim, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Crescendo Bioscience, 2, 5, 8, Eli Lilly, 2, 5, 8, Epirus, 2, 5, 8, Galapagos, 2, 5, 8, Janssen, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Nycomed, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, Sanofi-Aventis, 2, 5, 8, Takeda, 2, 5, 8, UCB, 2, 5, 8, Zydus, 2, 5, 8; **R. Toes**, None; **A. Webb**, None; **D. van der Woude**, None.

Abstract Number: 0027

Altered Inflammatory Response of Macrophages in the Fosl-2 Transgenic Mouse Model of Systemic Sclerosis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Innate Immunity Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fos-like 2 (Fosl-2) is a transcription factor belonging to the Fos family of proteins which is part of the AP-1 transcription complex. The Fosl-2 transgenic (tg) mouse model has been shown to develop a similar phenotype to patients with SSc, such as vascular changes, dysregulation of innate and adaptive immunity, and fibrosis of the skin and visceral organs. Although the etiology is yet to be found, various studies have indicated immune cells, such as macrophages, to be important contributors to the pathogenesis of SSc. In this study, we aimed to determine the role of Fosl-2 expression in macrophages.

Methods: Bone marrow from Fosl-2 tg and wild type (wt) mice was isolated and differentiated into macrophages by stimulation with recombinant mouse macrophage colony stimulating factor (M-CSF) (20 ng/ml) for 7 days. The bone marrow-derived macrophages (BMDM) were stimulated with LPS (10 ng/ml) or IL-4 (10 ng/ml) for various time points. Expression of Fosl-2 and cJun was checked by Western blot. Levels of inflammatory cytokines IFN-g (wt n=12, tg n=15), TNF-α (wt n=9, tg n=11), IL-1β (wt n=8, tg n=9), IL-6 (n=7), and anti-inflammatory markers MRC1 (wt n=9, tg n=11) and CCL22 (n=8) were determined by qPCR and ELISA. To assess the production of nitric oxide, BMDM were stimulated with LPS (10 ng/ml) (n=17) or LPS + IFN-g (10 ng/ml) (n=9) and a Griess assay was performed. An arginase assay was conducted to evaluate urea concentration post stimulation (wt n=7, tg n=3).

Results: We observed induction of Fosl-2 after LPS and IL-4 stimulation in wt and Fosl-2 tg BMDM, with the peak of expression at 4 to 6 hours in wt mice. Tg mice show a higher induction of Fosl-2 after LPS stimulation than wt mice. After LPS stimulation, Fosl-2 tg BMDM showed a decreased mRNA expression of IFN-g ($p< 0.0001$), TNF-α ($p=0.0036$), as well as a tendency towards decreased expression of IL-1β. Protein levels of IL-6 and TNF-α appeared to peak around 6h post LPS stimulation and were decreased in tg BMDM compared to wt BMDM ($p=0.0044$ and $p=0.02555$). Fosl-2 tg BMDM were characterized by lower concentrations of NO after LPS stimulation ($p=0.0061$) and further decreased after co-stimulation with IFN-g ($p=0.0118$), in comparison to wt mice. After stimulation with IL-4, when comparing wt to tg BMDM, MRC1 ($p=0.0007$) was downregulated and CCL22 ($p=0.0361$) upregulated.

Conclusion: Our data indicates the involvement of Fosl-2 in the regulation of the inflammatory response of macrophages. Decreased levels of inflammatory cytokines suggest a possible alternative activating phenotype-promoting role of Fosl-2. Alternative activation of macrophages induces fibrosis, thus bringing Fosl-2 and macrophages into the spotlight regarding the development of fibrosis in SSc.

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Abstract Number: 0028

Novel *ExVivo* Model of Septic Arthritis Identifies Role of Neutrophils in Joint Destruction

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Innate Immunity Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Septic arthritis (SA) caused by bacterial species, such as *Staphylococcus aureus*, has high morbidity and mortality[1]. Currently diagnosis is often prolonged and unreliable, with no suitable near-patient biomarkers available[2]. To generate more reliable biomarkers and to understand pathogenesis we sought to develop a novel *ex vivo* system to explore the effect of pathogenic and mutant *Staphylococcus* strains in promoting cartilage degradation.

Methods: Human cartilage explants were obtained from femoral heads being surgically removed following trauma. Explants were infected for 48h with 10^6cfu bacteria from two *Staph. aureus* SA-derived patient isolates (28g & 36v) or with a mutated bacterial strain preventing biofilm formation and adhesion, *Staphylococcus epidermidis* RP62A

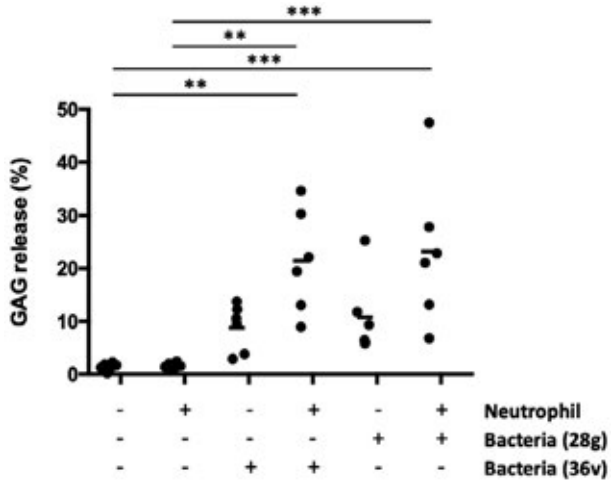

Figure 1 Synovial sodium MR signal intensity (left) and concentration (right) quantified by 23Na-MRI. Each dot, representing one subject, is based on the average of 6 sagittal MRI slices capturing the synovial volume.

wild type strain or RP62A mutated strain. In the final 24h of bacterial infection, neutrophils purified from healthy donor blood were added to explant cultures at 3 x 10^6cells/well. Chondrocyte viability was assessed using CellTracker green CMFDA and propidium iodide. Images were captured using confocal microscopy (LSM880) and cells counted using Imaris software. Structural damage was measured by glycosaminoglycan (GAG) release and statistical analysis performed using GraphPad Prism software.

Results: When cartilage explants were co-cultured with bacteria +/- neutrophils, cell death was significantly increased compared to the negative control or addition of neutrophils alone, (one-way ANOVA, Holm-Sidak's multiple comparisons test, N=3, bacteria - neutrophils $p < 0.05$, bacteria + neutrophils $p < 0.01$). Cartilage breakdown, estimated via GAG release, was induced by*Staph. aureus*alone, whereas it was significantly enhanced upon neutrophil addition in the final 24h of co-culture, Figure 1. Using the model, we investigated the effect of bacterial cell adhesion using a*Staph. epidermidis*adhesion mutant. The mutated strain did not significantly release more GAG compared to the negative control, whereas the wild type strain caused significant damage (2-way ANOVA, Holm-Sidak's multiple comparisons test, N=3, $p < 0.05$). Moreover, the effect of neutrophil stimulation was attenuated when bacteria were unable to adhere to the cartilage.

Conclusion: A co-culture model of septic arthritis has been developed which allows precise examination of the contribution of the host neutrophil response and (mutant) bacterial species to cartilage damage. We used this to define the importance of bacterial adherence to cartilage for subsequent degradation. This novel model will be a valuable tool in understanding pathology and identifying biomarkers of joint infection in the future.

References:

1. Gupta, M. N., Sturrock, R. D. & Field, M. A prospective 2-year study of 75 patients with adult-onset septic arthritis.*Rheumatology***40**, 24–30 (2001).
2. Swan, A., Amer, H. & Dieppe, P. The value of synovial fluid assays in the diagnosis of joint disease: a literature survey.*Ann. Rheum. Dis.***61**, 493–8 (2002).

Disclosure: K. McCall, None; **C. Atherton**, None; **N. Millar**, Novartis, 2, 5, 8; **C. Goodyear**, Celgene, 2, AstraZeneca, 2, 5, MedAnnex, 2, 5, UCB, 2, Jannsen, 2; **T. Evans**, None; **I. McInnes**, Abbott, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, Roche., 2, 8, Abbvie, 5, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Astra Zeneca, 2, 5, AstraZeneca, 5, BI, 2, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 5, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Leo, 5, Lilly, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 0029

Therapeutic Anti-TNF Biologic Agents Exhibit Functional Differences in Blocking TNF-induced Effects on Human Monocytes *In Vitro*

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Innate Immunity Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Therapeutic anti-TNF biologic agents can be distinct in their structure and/or in their binding to TNF. Whether these differences affect the functional properties of these biologics in direct comparison to each other has not been thoroughly investigated. Our objective was to determine the equivalency of all anti-TNF biologic agents approved for RA in preventing a variety of TNF-induced effects on human monocytes *in vitro*.

Methods: Human monocytic U937 NF-kB luciferase reporter cells and human RA PBMC were incubated with 100 ng/mL TNF +/- biologic [adalimumab (ADA), etanercept (ETN), infliximab (IFX), golimumab (GOL) or certolizumab pegol (CZP)] as pre-formed complexes. Surface TNF-RI and –RII levels were monitored by flow cytometry after 1h. Luciferase activity was measured after 4 h. to assess NF-kB activation. After 24 h., U937 cells and CD14+ monocytes from human RA PBMC cultures were analyzed for surface levels of ICAM-1, an adhesion molecule shown to contribute to monocyte migration and arthritis. Apoptosis was assessed using caspase 3/7 fluorescent substrate. Alpha-2,6 sialylation (Sia), a glycosylation modification shown to regulate TNF-RI internalization and apoptosis, was evaluated using FITC-labeled Sambucus nigra lectin (SNA).

Results: Surface levels of TNF-RI and –RII on U937 cells were both reduced by 2.4-fold in presence of TNF. TNF-RI was maintained at baseline levels by 16.7 nM ADA or CZP as pre-formed complexes with TNF; however, those complexes with ETN, IFX or GOL could only preserve a fraction of TNF-RI on the surface (43%, 52% & 62%, respectively). All anti-TNF biologics were equally effective in preventing loss of TNF-RII. TNF stimulation of U937 NF-kB reporter cells led to a 122-fold increase in luciferase activity which was reduced to baseline by only ADA or CZP at a 38 nM conc. Partial inhibition by 65%, 77% or 88% was observed with ETN, IFX or GOL, respectively. TNF-enhanced ICAM-1 surface expression on U937 cells and on CD14+ monocytes from RA PBMC was reduced to baseline by 16.7 nM ADA or CZP, whereas ETN, IFX or GOL were only partially effective (69%, 83% & 86% reduction, respectively). Both ADA:TNF and CZP:TNF complexes also completely inhibited TNF-induced apoptosis in a dose dependent manner unlike ETN, IFX and GOL, which were less effective (42%, 32% & 42% reduction, respectively). According to SNA staining, alpha-2,6 Sia surface levels dropped in presence of TNF specifically on the subset of cells undergoing apoptosis, and this subset was reduced proportionately to the inhibitory properties of anti-TNF biologics on apoptosis.

Conclusion: For each of the conditions tested *in vitro*, many resembling features associated with RA, the pre-formed complexes of ADA:TNF and CZP:TNF were significantly more effective in preventing the TNF-induced effects (decrease of surface TNF-RI and alpha-2,6 Sia; increase in NF-kB activation, ICAM-1 surface levels and apoptosis) on human monocytes than those complexes of TNF with ETN, IFX or GOL. Additional *in vitro* and *in vivo* studies need to be done to further elucidate these mechanistic differences.

Disclosure: B. Harvey, AbbVie, Inc., 3, 4; **Z. Kaymakcalan**, AbbVie, Inc., 3, 4.

Abstract Number: 0030

Aberrant M1 Polarization of Macrophages in Behcet's Disease

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Innate Immunity Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Behcet's disease (BD) is systemic inflammatory vasculitis with unknown *etiology*. As a critical compartment in innate immunity, macrophages may play a role in BD. According to the phenotype and cytokine expression, macrophages can be classified into 2 subtypes, the pro-inflammatory classically activated macrophages (M1) and the anti-inflammatory alternatively activated macrophages (M2). However, the mechanism of how macrophage polarization is involved in BD is yet unidentified. Here we aim to investigate the effect of the BD serum on the phenotype and the functions of macrophages.

Methods: Thirty treatment-naïve active BD patients from our center and 30 gender- and age-matched healthy controls (HC) were included in this study. The monocytes of HC were isolated from PBMCs through $CD14^+$microbeads and further cultured into M0 macrophages. Then the macrophages were polarized to M1 macrophages with LPS and IFNγ, and to M2 macrophages with IL4. Serum from BD patients and HC was applied to the human monocyte-derived macrophages (HMDM). The cell surface markers and the cytokines in the supernatant were detected and compared to the phenotypes of M1 and M2 macrophages. The phagocytosis of different HMDMs was determined by the cellular uptake of Dextran. In order to investigate the effect of different HMDMs on the differentiation of Th1 and Th17 cells, HMDMs were co-cultured with naïve $CD4^+$T cells and the intracellular cytokines as well as the nuclear transcription factor were detected by FACS. Western-blot analysis was performed to detect the expression of JAK1, STAT1 and their phosphorylated forms in the HMDMs when stimulated with BD serum.

Results: Compared to M0 macrophages, BD serum stimulated HMDM had an increased expression of CD86 ($p=0.024$) and a decreased CD163 expression ($p=0.009$). The secretion of IL12 ($p=0.019$) and TNFα ($p=0.0295$) was also increased. The HC serum stimulated HMDM, however, had a similar phenotype with M0 macrophage. All these observations suggested BD serum could promote M1 polarization. BD serum also led to a significant increase in macrophage phagocytosis ($p=0.011$), which was similar with M1 phenotype ($p=0.014$). Moreover, M1 phenotype macrophages and BD serum treated macrophages can both promote naïve $CD4^+$T cells to differentiate into Th1 cells, characterized by increased IFNγ and T-bet (IFNγ: M1 $p=0.037$; M_{BD} $p=0.048$. T-bet: M1 $p=0.0009$; M_{BD} $p=0.0121$). No significant increase of IL17A was noted in both M1 phenotype macrophages as well as BD serum treated macrophages. After stimulating HMDM with BD serum for 5 minutes, the expressions of phosphorylated JAK1 and phosphorylated STAT1 were both elevated ($p_{JAK1}=0.0228$, $p_{STAT1}=0.0101$), indicating a role if JAK1-STAT1 pathway in the BD serum treated macrophage polarization and the pathogenesis of BD.

Conclusion: Serum from patients with BD could promote M1 macrophage polarization via the JAK1-STAT1 pathway, and could also increase the macrophage phagocytosis and drive Th1 differentiation.

Disclosure: J. Shi, None; **X. Wu**, None; **J. Liu**, None; **H. Chen**, None; **W. Zheng**, None.

Abstract Number: 0031

Regulation of Neutrophil Extracellular Traps by Apremilast (phosphodiesterase 4 Inhibition)

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Innate Immunity Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Increased propensity for neutrophil extracellular trap generation has been described in autoimmune diseases such as rheumatoid arthritis. Neutrophil extracellular traps are thought to contribute to disease propensity. Calcium signalling is known to be important for neutrophil extracellular trap generation. Thus, controlling this calcium signalling pathway may allow for regulation of autoimmune disease pathology. Apremilast is a selective phosphodiesterase 4 inhibitor that is currently approved for the treatment of psoriasis and psoriatic arthritis with a positive phase 3 on Behcet`s disease. Inhibition of phosphodiesterase 4 can elevate cAMP levels, decrease adenylate cyclase levels and thus modulate calcium release and store-operated calcium signalling.We hypothesised that by inhibiting phosphodiesterase 4 with apremilast, calcium release can be controlled and in turn decrease the propensity for neutrophil extracellular trap generation.

Methods: Healthy controlswere recruited at the Blood Bank of the Swiss Red Cross, Basel. Patients matching American College of Rheumatology criteria for rheumatoid arthritis were recruited at the University Hospital of Basel (n = 13).

Whole blood was collected into heparin tubes and neutrophils isolated using Dextran-Ficoll density centrifugation. Neutrophils were resuspended in RPMI + 10mM Hepes and were separately treated with apremilast, PDE7 inhibitor (0.1 - 100uM), rolipram (10 uM) and IBMX (300 uM).

For healthy control neutrophils, PMA (20nM) and calcium ionophore (2.5 uM) were used to induce neutrophil extracellular traps. Spontaneous neutrophil extracellular trap formation was measured for rheumatoid arthritis neutrophils. Samples were fixed, then prepared for immunohistochemistryusing mouse anti-human MPO antibody (Abcam)followed by incubation with goat anti-mouse IgG AF555 (Invitrogen Life Technologies). DNA was counterstained with DAPI. Neutrophil extracellular traps were then quantified using NETQUANT and a Nikon EclipseTi-E.

Treated neutrophils were loaded with DHR123 (25uM) for 15 min at 37°C. Once loaded, ROS production was monitored using a Biotek Synergy H1 Hybrid Reader (Biotek) at 0, 15 and 30 minutes (excitation 485 nm, emission 570 nm). In the case healthy control neutrophils, ROS production was induced using PMA (20nM) while for rheumatoid arthritis neutrophils, spontaneous ROS production was monitored.

Results: Reduction in PMA induced ROS production for healthy control neutrophils when treated with apremilast was observed. A decrease in PMA and calcium ionophore-induced neutrophil extracellular trap generation was also observed. Apremilast treatment of rheumatoid neutrophils also displayed a decrease in spontaneous ROS generation and neutrophil extracellular trap generation. We also investigated the effect of phosphodiesterase 7 inhibition. Interestingly, this displayed an opposite effect to phosphodiesterase 4 inhibition.

Conclusion: By reducing neutrophil extracellular traps through modulation of calcium signalling by phosphodiesterase 4 inhibition, the possibility of controlling neutrophil extracellular trap generation in certain autoimmuneconditions might be possible.

Disclosure: S. van Breda, Celgene, 2; **S. Rossi**, None; **P. Hasler**, None.

Abstract Number: 0032

Aberration of Histone Lysine Methylation in Adult-Onset Still's Disease Are Novel Biomarker Candidates Associated with the Disease Activity

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Innate Immunity Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Adult-onset Still's disease (AOSD) is a systemic autoinflammatory disorder characterized by spiking fever, transient rash, arthritis and leukocytosis. Macrophage and neutrophil activation is a hallmark of AOSD. No specific laboratory tests have been known in AOSD. A few serological markers, such as ferritin, CRP, and IL-18, have been used in the clinical settings but their specificity is limited. Although a line of evidence has suggested a genetic contribution to AOSD, the pathogenesis of the disease is still unclear. Non-genetic factors, such as environment, infection and epigenetics, may play pivotal roles in the pathogenesis. Epigenetic mechanisms including posttranslational histone modifications are known to regulate gene expression without altering the genomic sequence. Histone modifications in major rheumatic diseases, such as rheumatoid arthritis, have been investigated, while studies on those in AOSD are limited. From the functional point of view, it is important to analyze the difference of histone modifications in each functional subset of peripheral blood nucleated cells. To examine the pathological condition-specific histone modifications of peripheral white blood cells (WBCs) in AOSD, We have established a novel method for analyzing histone methylation in each subset defined by the surface markers using fluorescence-activated cell sorting (FACS).

Methods: Peripheral WBCs were obtained from patients with active and inactive AOSD and healthy controls (HC). Nine immune cell types were stained with antibodies against surface markers and classified as below: CD4+ T cells, CD8+ T cells, γδT cells, neutrophils, regulatory T cells, B cells, CD14++CD16- monocytes, CD14++CD16+ monocytes and CD14+CD16++ monocytes. All samples were analyzed with a FACSCanto II cytometer. As a quantitative measure of H3K4me3 and H3K27me3, mean fluorescence intensity (MFI) was used. We quantified the serum levels of 10 cytokines (IFN-α, IFN-γ, IL-1β, IL-2, IL-4, IL-6, IL-10, IL-12p70, IL-17A and TNF-α) using multiplex bead array assays and IL-18 using ELISA. The correlation between the level of histone methylation and CRP, ferritin and 11 cytokine levels was examined.

Results: The distinction in H3K27me3 and H3K4me3 MFI levels were observed in several WBC subsets when comparing HC and AOSD. Particularly, histone methylation in neutrophils, B cells, and CD14++CD16- monocytes correlated with the disease activity of AOSD. The levels of serum ferritin, CRP, IFN-γ, IL-2, IL-6 and IL-18 were significantly higher in active AOSD than in inactive AOSD. Histone methylation levels in neutrophils, B cells, or CD14++CD16- monocytes correlated with the levels of either CRP, IFN-γ, IL-2 or IL-18. However, there was no significant correlation between serum ferritin and histone methylation. Focusing on CD14++CD16- monocytes, H3K4me3 MFI levels negatively correlated with the levels of IL-18.

Conclusion: Differences in histone modifications were detected by FACS in different subsets of peripheral WBCs in AOSD patients. Aberrant histone methylations in CD14++CD16- monocytes were associated with the disease activity of AOSD. It is indicated that histone methylation could be a novel biomarker for AOSD.

Disclosure: Y. Aizaki, None; **Y. Araki**, None; **K. Sato**, None; **T. Mimura**, None.

Abstract Number: 0033

GS-4875, a First-in-Class TPL2 Inhibitor Suppresses MEK-ERK Inflammatory Signaling and Proinflammatory Cytokine Production in Primary Human Monocytes

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Innate Immunity Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor progression locus 2 (TPL2, also known as MAP3K8) is a mitogen-activated protein kinase kinase kinase and the primary regulator of ERK-mediated gene transcription downstream of multiple proinflammatory stimuli including bacterial products (eg, LPS and bacterial peptidoglycans), damage-associated molecular patterns (DAMPs), TNFα, and IL-1β.[1]TPL2 regulates the expression of several proinflammatory cytokines, including TNFα, IL-1β, IL-6 and IL-8. As TPL2 acts on both the production of and response to TNFα and IL-1β, it acts to amplify proinflammatory signaling. Dysregulated signaling downstream of these inflammatory signals can drive uncontrolled immune cell activation and inflammation, which is associated with multiple chronic inflammatory and autoimmune diseases. As such, TPL2 inhibition represents a strategy to modulate inflammation in a variety of disease settings. We evaluated the effect of a highly selective TPL2 inhibitor (GS-4875) on inflammatory signaling and cytokine production in primary human cells and in an acute inflammation model.

Methods: GS-4875 selectivity was screened using a KINOMEscan™ selectivity assay (ScanMAX, DiscoveRx, San Diego, CA). Cells were precultured with GS-4875 prior to stimulation with LPS, TNFα, or EGF. Lewis rats were dosed orally with 3, 10, 30 or 100 mg/kg doses of GS-4875 or 1 mg/kg dexamethasone followed by IV dosing of 0.01 mg/kg LPS 2 hours later. Animals were bled for plasma at multiple time points between 0 and 5h after compound dosing and plasma concentrations of TNFα and GS-4875 were measured.

Results: GS-4875 inhibits the TPL2 kinase with an IC50 = 1.3 nM with no significant off-target binding activity. GS-4875 selectively inhibited LPS and TNFα-stimulated phosphorylation of TPL2, MEK, and ERK, with little to no inhibition of phosphorylated p38, JNK or p65 observed. Both the RNA production and secretion of TNFα, IL-1β, IL-6, and IL-8 following LPS stimulation in primary human monocytes was similarly inhibited with GS-4875. In monocyte-derived dendritic cells GS-4875 inhibited the secretion of TNFα and IL-6 following LPS stimulation. To confirm TPL2 requirement for inflammatory, but not Ras-mediated (growth factor stimulated) ERK signaling, A431 cells were stimulated with either TNFα or EGF. Although TPL2 inhibition reduced TNFα-stimulated pERK, no effect on ERK activation downstream of EGF was observed. In vivo activity and PK/PD relationship was established using a rat LPS-TNFα model of acute inflammation. GS-4875 treatment showed dose and exposure dependent inhibition of LPS-stimulated TNFα production at all time points with an estimated EC50 (±SD) of 667 ±124 nM. Inhibition of TNFα production at the highest dose tested inhibited TNFα levels at levels equivalent to that of dexamethasone.

Conclusion: This work demonstrates the selective effects of TPL2 inhibition on ERK-mediated signaling and proinflammatory cytokine production and highlights the potential for TPL2 inhibition to treat diseases associated with dysregulated inflammatory signaling and chronic inflammation.

Reference: 1. Gantke T, Sriskantharajah S, Ley S. Cell Res. 2011; 21:131-145.

Disclosure: M. Warr, Gilead Sciences, Inc., 1, 3, 4; **A. Hammond**, Gilead Sciences, Inc., 1, 3, 4; **G. Park**, Gilead Sciences, Inc., 1, 3, 4; **Z. Cui**, Gilead Sciences, Inc., 1, 3, 4; **N. Wright**, Gilead Sciences, Inc., 1, 3; **J. Taylor**, Gilead Sciences, Inc., 3, 4.

Abstract Number: 0034

The Role of NFAT5-p65 Complex Enhanceosome in the Inflammatory Responses of Rheumatoid Arthritis Synovial Fibroblasts via TLR4 Signaling

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Transcription factors belonging to the family of nuclear factors of activated T cells (NFAT) play an essential role in diverse biological processes, such as inflammation, immune response and cell proliferation. Known NFAT5 target genes are involved in the pathogenesis of rheumatoid arthritis (RA), including inflammation promotion and joint destruction. The TLR4 ligands was shown to trigger the activity of NFAT5 in macrophages through the IKK-NF-κB pathway. Some reports indicated that there is an interaction between NF-κB p65 and NFAT5 for the induction of the expression of the target genes of these transcription factors. These findings suggested that NFAT5 might play an important role in not only innate immune but also autoimmune rheumatic disorders. However, it is still not clear whether the TLR4 pathway induces NFAT5-p65 complex enhanceosome activation in RA synovial fibroblasts (RASFs). The aim of this study to investigate the role of NFAT5-p65 enhanceosome in the inflammatory responses of RASFs via TLR4 signaling.

Methods: Human neutrophil-derived lactoferrin (LTF) was used as TLR4 ligand. RASFs were stimulated with LTF, and the expressions of inflammatory cytokines in RASFs were measured. The expression of IL-6, CCL20 and IL-8 mRNA in RASFs was measured using real-time quantitative PCR. The protein levels of IL-6, CCL20 and IL-8 in culture medium was measured by ELISA. To clarify the TLR4 signalling pathway associated with LTF stimulation, a small molecular inhibitor of TLR4 (TAK242) and NF-κB inhibitor were used. The role of nuclear factor of activated T cells 5 (NFAT5) was identified using small interfering RNA. Cerulenin is an inhibitor of fatty acid synthase, which is isolated from *Cephalosporium caerulens*as an antibiotic agent. Cerulenin was reported as one of agents to disrupt the p65-NFAT5-p300 interaction and inhibited the activity of NF-κB. Therefore, to reveal the interaction between NF-κB and NFAT5, cerulenin, which disrupts their interaction, was used.

Results: Stimulation of RASFs with LTF significantly increased the expressions of inflammatory cytokines and chemokines, such as IL-6, CCL20 and IL-8, in RASFs. LTF enhanced the mRNA expressions of these cytokines in RASFs stimulated by TNF-α. TAK242 almost completely inhibited the expressions of inflammatory cytokines and chemokines in RASFs stimulated by LTF. The NF-κB inhibitor partially repressed the expressions of IL-6 and IL-8 mRNAs induced by LTF, but not CCL20 mRNA expression. On the other hand, NFAT5 silencing decreased the expres-

sions of CCL20 and IL-8 mRNAs induced by LTF, but not IL-6 mRNA expression. Cerulenin repressed the expressions of IL-6, CCL20 and IL-8 mRNAs in RASFs treated with LTF or LPS.

Conclusion: NFAT5-p65 enhanceosome might regulate the expressions of LTF-TLR4-responsive genes in RASFs. NFAT5-p65 enhanceosome has potential as novel therapeutic target in the pathogenesis of RA.

Disclosure: K. Umekita, None; **Y. Kariya**, None; **C. Iwao**, None; **M. Kimura**, None; **R. Kudo**, None; **Y. Rikitake**, None; **S. Miyauchi**, None; **A. Okayama**, None.

Abstract Number: 0035

Mass Cytometry Identifies Enhanced Histone H3 Citrullination and TNFα Production by CD14 Monocytes in Subjects At-Risk for Future Development of Rheumatoid Arthritis

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SESSION INFORMATION
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Our group previously demonstrated that sputum neutrophils from subjects At-Risk for future rheumatoid arthritis (RA) spontaneously form neutrophil extracellular traps with elevated histone H3 (H3) citrullination, which were associated with mucosal inflammation and local anti-citrullinated protein antibody (ACPA) generation (*Okamoto ACR 2018*). Also, enhanced H3 citrullination and functional/metabolomic alterations have been found in peripheral blood CD4 T cells of At-Risk subjects. However, it is unknown in what other cell types elevated H3 citrullination could be observed, and how this phenotype is related to functional alterations in cells. Herein, we explored using mass cytometry and confirmatory flow cytometry H3 citrullination and cytokine/chemokine/metabolomic signatures in peripheral blood immune cells following *ex vivo* toll-like receptor stimulation.

Methods: 13 serum ACPA (+) At-Risk subjects without synovitis, 14 ACPA (+) Early RA patients, and 13 matched healthy controls were included. Freshly drawn whole blood was fixed just after blood draw, or incubated with or without stimulants including LPS and R848 (TLR7/8 agonist) in the presence of protein transport inhibitor for 6 hours and then fixed. Cells were stained with 39 metal conjugated antibodies, and mass cytometry analysis was performed. Batch adjustment was performed before data analysis. Separately, CD14 monocytes were stimulated with R848 after pretreatment with GSK484 (PAD4 inhibitor) or AFM30a (PAD2 inhibitor) to determine effects on H3 citrullination and cytokine production. In addition, CD14 monocytes were cultured on coverslips with stimulant, and immunofluorescence staining was performed to examine H3 citrullination and morphologic changes.

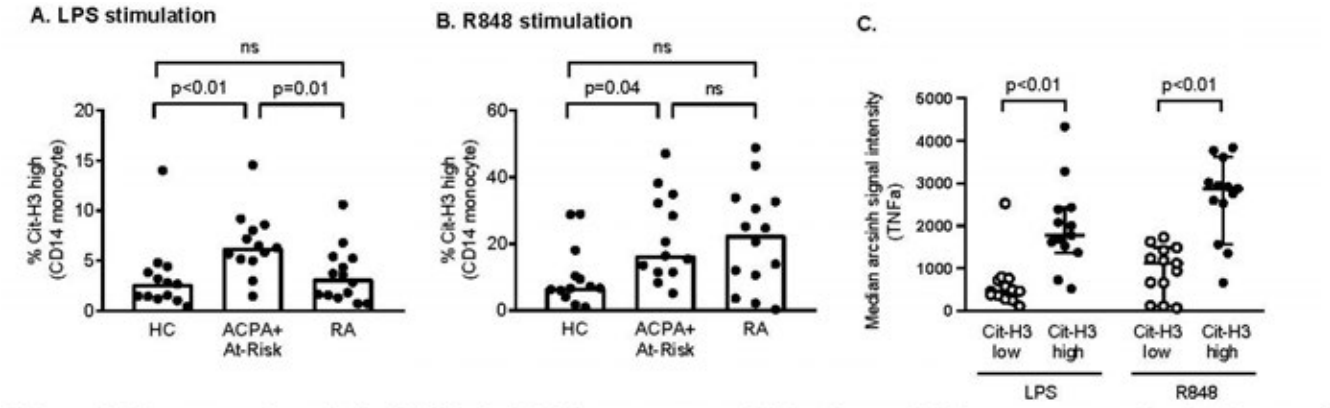

Figure1. Frequencies of cit-H3 high CD14 monocytes following toll-like receptor stimulation and TNFα production in CD14 monocytes. The figure depicts the % of cit-H3 high CD14 monocytes after LPS stimulation (Panel A) and R848 stimulation (Panel B) by mass cytometry. Panel C depicts median arcsinh signal intensity of TNFα in cit-H3 high CD14 monocytes and cit-H3 low CD14 monocytes following LPS and R848 stimulation. P-values were calculated using Kruskal-Wallis test (Panel A and B) and Wilcoxon signed-rank sum test (Panel C), adjusted by Benjamini and Yekutieli method to account for multiple testing. Closed circles=cit-H3 high CD14 monocytes; open circles =cit-H3 low CD14 monocytes.

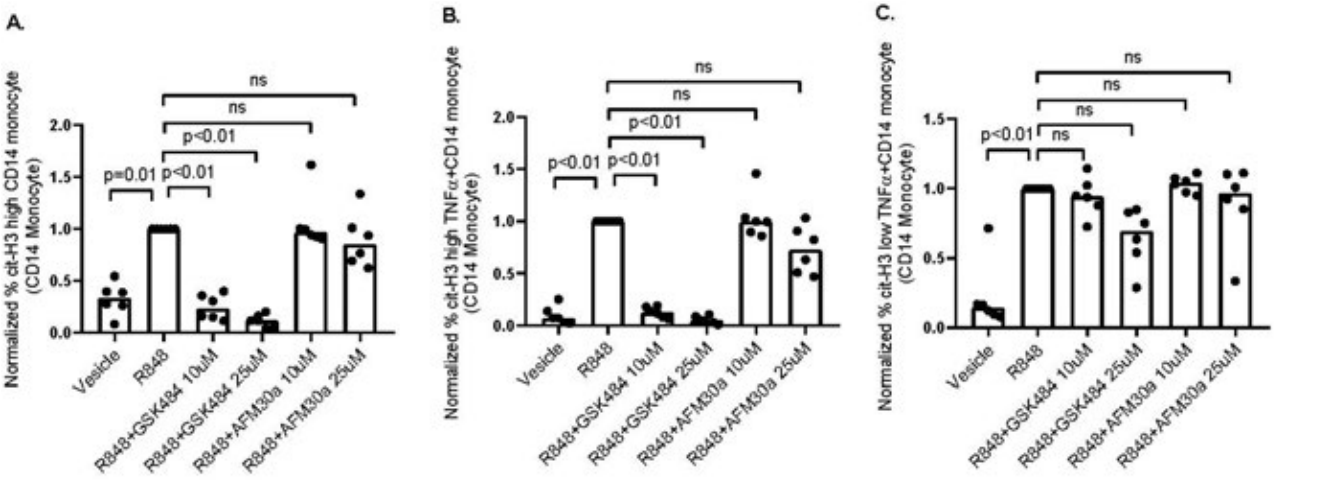

Figure2. H3 citrullination and TNFα production were significantly suppressed by PAD4 inhibitor, but not by PAD2 inhibitor. CD14 monocytes were stimulated with R848 after pretreatment with GSK484 (PAD4 inhibitor) or AFM30a (PAD2 inhibitor) to determine effects on H3 citrullination and TNFα production. The figure depicts the normalized % of cit-H3 high CD14 monocytes (Panel A), cit-H3 high TNFα+ CD14 monocytes (Panel B), and cit-H3 low TNFα+ CD14 monocytes (Panel C) of At-Risk subjects (n=6) by flow cytometry analysis. P-values were calculated using Friedman test and adjusted by Benjamini and Yekutieli method to account for multiple testing.

Results: The % of CD14 monocytes with elevated H3 citrullination following*ex vivo*LPS and R848 stimulation was significantly higher in ACPA (+) At-Risk subjects compared to healthy controls (Figure 1A and 1B). CD14 monocytes in At-Risk subjects with high citrullinated H3 (cit-H3) levels were skewed to produce more TNFα compared to cit-H3 low CD14 monocytes (Figure 1C). H3 citrullination and TNFα production were significantly suppressed by PAD4 inhibitor in cit-H3 high CD14 monocytes, but not by PAD2 inhibitor (Figure 2A and 2B). TNFα production by cit-H3 low CD14 monocytes was not affected by PAD4 or PAD2 inhibitor (Figure 2C). Immunofluorescence staining revealed CD14 monocytes with cit-H3 formed extrusions of DNA with PAD4 co-localization, which was compatible with the development of monocyte extracellular traps (METs).

Conclusion: Peripheral blood CD14 monocytes in subjects At-Risk for RA demonstrate increased cit-H3 expressing MET formation with cytokine skewing to TNFα in a process mediated by PAD4. These finding suggests enhancement of histone H3 citrullination and aberrant TNFα production may play a role in the development of RA. Further studies are needed to determine the role of this phenotype in the generation of ACPA and future development of classified RA.

Disclosure: Y. Okamoto, None; **E. Hsieh**, None; **R. Schuyler**, None; **J. Seifert**, Janssen, 2; **M. Feser**, None; **J. Norris**, Pfizer, 2; **M. Demoruelle**, Pfizer, 2; **K. Deane**, Bristol-Myers Squibb, 5, Inova, 9, Janssen, 2, 5, Janssen R&D, 2, Microdrop, 5, Pfizer, 2; **V. Holers**, AdMIRx, 1, 2, 4, 5, 6, Alexion, 7, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 5, Janssen R&D, 2, 5, Pfizer, 2.

Abstract Number: 0036

Discovery, Verification and Validation of Rheumatoid Arthritis Activity Monitoring Biomarkers

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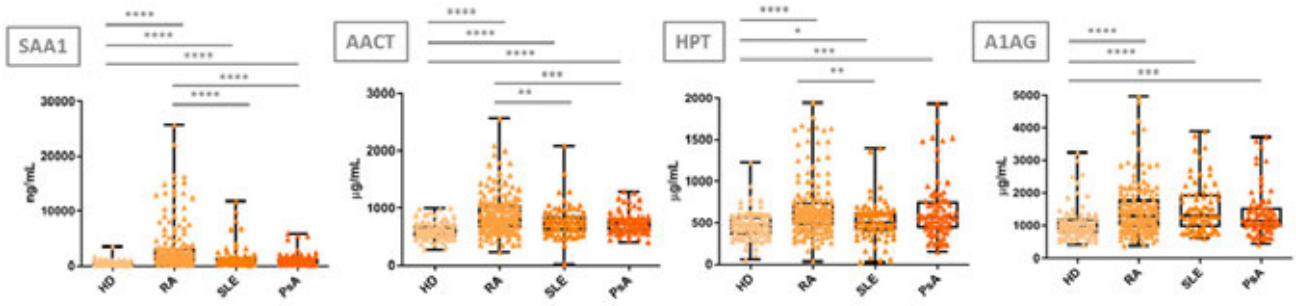
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a long-lasting inflammatory autoimmune disorder that ultimately leads to the destruction of joint architecture. The activity of this disease is measured by the assessment of clinical symptoms (generally using the DAS28). The aim of this study was to find and validate plasma biomarkers able to discriminate patients with different RA activities.

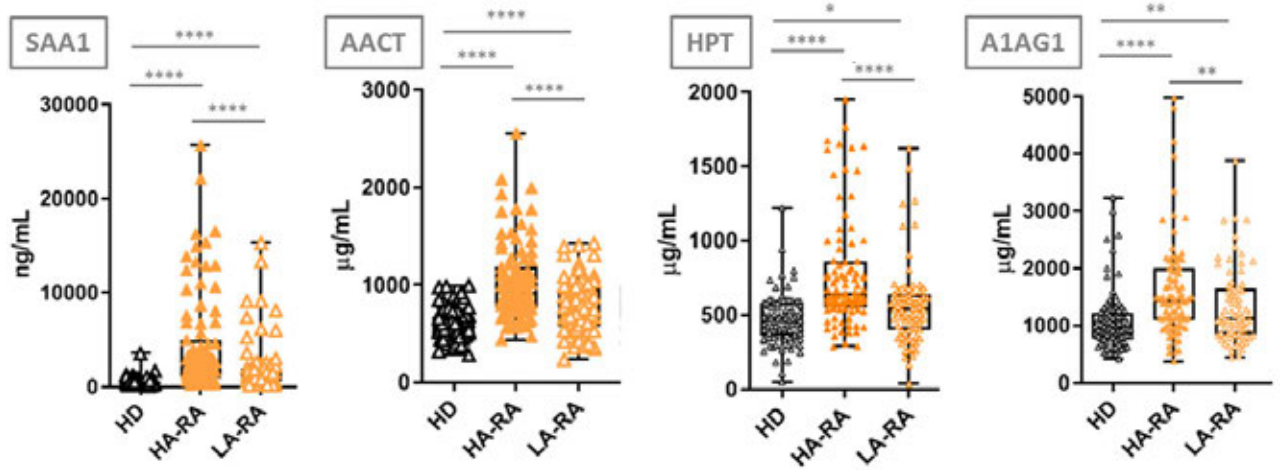
Methods: Plasma samples from patients with different IMIDs (Immune-Mediated Inflammatory Diseases), used in this research belonged to the IMID Consortium. Plasma from RA patients were DAS28-classified as low activity (LA, DAS28: 2,6-3,2) and high activity (HA, DAS28 > 5,1). The study was conducted in three different stages.

Firstly, an initial discovery phase was performed to identify an early panel of proteins with a RA activity differing role. Thus, 80 RA plasma samples (40 LA and 40 HA) were pooled in 8 groups (4 LA and 4 HA). These pools were albumin-depleted, digested, differentially labelled with iTraq 8-plex reagents, combined, desalted using StageTips-C18, HPLC-fractionated and analyzed by shotgun nanoLC-MS/MS. Secondly, the verification of the previously identified possible markers was carried out by a targeted Multiple Reaction Monitoring (MRM) strategy on a QTRAP 5500. Particularly, the same 80 RA plasma samples (40 LA and 40 HA) were individually measured, employing stable isotope-labeled standards (SIS) peptides for absolute protein quantitation. Lastly, the verified proteins were validated by ELISA on additional 420 plasma samples from patients with RA (170), psoriatic arthritis (PsA, 80), systemic lupus erythematosus (SLE, 80) and healthy donors (HD, 90). PsA and SLE patients were used as disease controls.

Results: In the discovery stage, 186 proteins were identified, whereas 11 of these proteins significantly differed between RA patients with LA and HA ($p < 0.05$). A targeted MRM method using SIS peptides was developed for the verification and absolute quantitation of this 11-protein panel on 80 RA plasma samples. A significant increase in the HA condition for Haptoglobin (HPT), Serum Amyloid A1 (SAA1), Alpha-1-antichymotrypsin (AACT) and Alpha-1-acid Glycoprotein 1 (A1AG1) was shown, in accordance with the discovery phase tendency. Equally, the validation results show a significant increase of the 4 verified proteins in HA RA patients from LA RA patients and HD, as well as in LA



SAA1, AACT, HPT and A1AG1 concentrations in plasma from RA, SLE, PsA patients and healthy donors as well as their corresponding significant differences ($p < 0.05$). $p < 0.0001$ (****), $p < 0.001$ (***), $p < 0.01$ (**), $p < 0.05$ (*).



SAA1, AACT, HPT and A1AG1 concentrations in plasma from RA patients with extreme disease activities (LA: low activity; HA: high activity) and healthy donors as well as their corresponding significant differences ($p < 0.05$). $p < 0.0001$ (****), $p < 0.001$ (***), $p < 0.01$ (**), $p < 0.05$ (*).

RA patients from HD, therefore confirming their RA activity monitoring capacity. Furthermore, SAA1 and AACT significantly discriminate among RA, SLE, PsA patients and HD, as well as between RA patients and the related disease controls. Moreover, these proteins are related with the RA process and its effects (inflammation and immune disorder in joints), giving significance to the results obtained.

Conclusion: A three-step proteomic approach (including discovery, verification and validation phases) has been followed for the identification of protein biomarkers for assessing RA disease activity in plasma. A panel of four proteins has been validated as increased in plasma from HA RA patients, and could be useful for the molecular monitoring of the disease, even when they are measured among plasma samples from other IMID patients and/or HD.

Disclosure: L. González-Rodríguez, None; **V. Calamia**, None; **R. Paz-González**, None; **P. Fernández-Puente**, None; **C. Ruiz-Romero**, None; **A. Julià**, None; **A. Fernández-Nebro**, None; **J. Tornero**, None; **S. Marsal**, Vorso Corp, 5; **F. Blanco**, None.

Abstract Number: 0037

Intestinal Microbiota Dynamics in the Progression of Rheumatoid Arthritis

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SESSION INFORMATION
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Intestinal microbial dysbiosis in patients with rheumatoid arthritis (RA) has raised the interest in studying the role of intestinal microbes in the pathogenesis of RA. Animals studies indicate that intestinal microbiota changes prior to the onset of visible inflammatory arthritis. Here, we undertook this study to clarify the intestinal microbiota changes in individuals at high risk for RA with the aim to identify bacteria biomarkers associated with the progression of RA.

Methods: High-risk for RA individuals were defined as having a positive serum antibody for anti-cyclic citrullinated peptide (CCP), without reported arthritis symptoms at the time of enrollment. RA patients were diagnosed according to the American College of Rheumatology (ACR) 2010 classification for RA. Age and gender matched anti-CCP negative healthy individuals were recruited as controls. Individuals having a history of antibiotics treatment in the last six months or other conditions that may affect the study were excluded. The 16S ribosomal RNA of fecal samples from 31 RA patients, 42 high-risk individuals and 38 healthy controls (HC) were sequenced and analyzed.

Results: Alpha diversity analysis showed that the intestinal microbiota communities in high-risk group ("pre" group) had a lower community diversity (Shannon index) than the healthy controls (Fig.1A). Beta diversity using principal coordinate analysis (PCoA) revealed that the intestinal microbiota was significantly different between groups (Fig.1B). Interestingly, we observed that the intestinal microbiota communities dynamically shifted from HCs to high-risk individuals (Pre) to RA patients.

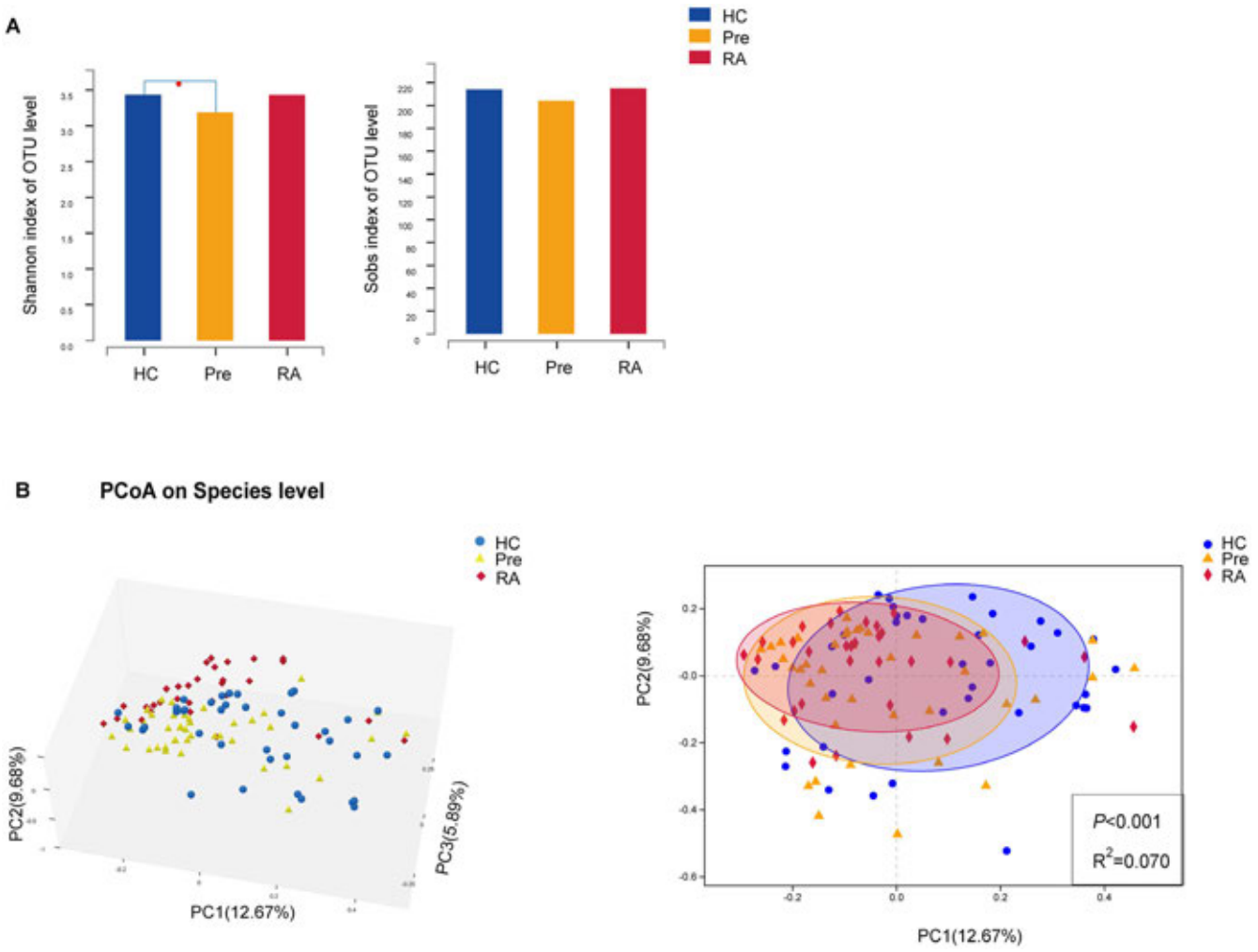

Figure 1. Alpha diversity (A) and beta diversity (B) analysis of the intestinal microbiota communities in rheumatoid arthritis (RA) patients, high-risk individuals for RA (Pre) and healthy controls (HC).

The majority of species (437) were shared by all groups. 35 species were found only in high-risk individuals and RA patients (Fig. 2A). Besides, the abundance of the microflora variant between groups. At the phylum level, the abundance of*Bacteroidetes*gradually decreased from HCs to high-risk individuals to RA patients. The abundance of *Saccharibacteria* were particularly higher in high-risk individuals than in both RA patients and HCs (Fig. 2B). Further to the family level, *Bacteroidaceae*, *Pseudomonadaceae*and*Pasteurellaceae*showed the same trend of gradual reduction from the HCs to high-risk individuals and to RA patients. On the contrary, an enriched abundance of *Streptococcaceae, Lactobacillaceae, Enterococcaceae* and *Leuconostocaceae* were seen in RA patients (Fig. 2C).

To determine taxonomic biomarkers that characterize the differences in the progression of RA, linear discriminant analysis (LDA) analysis was performed (Fig. 3A). We identified potential disease stage specific bacteria. A marker panel of six bacteria species was selected, which had an AUC of 0.78 (95%CI=0.66-0.9) in discriminating RA patients from HCs (Fig. 3B and 3C).

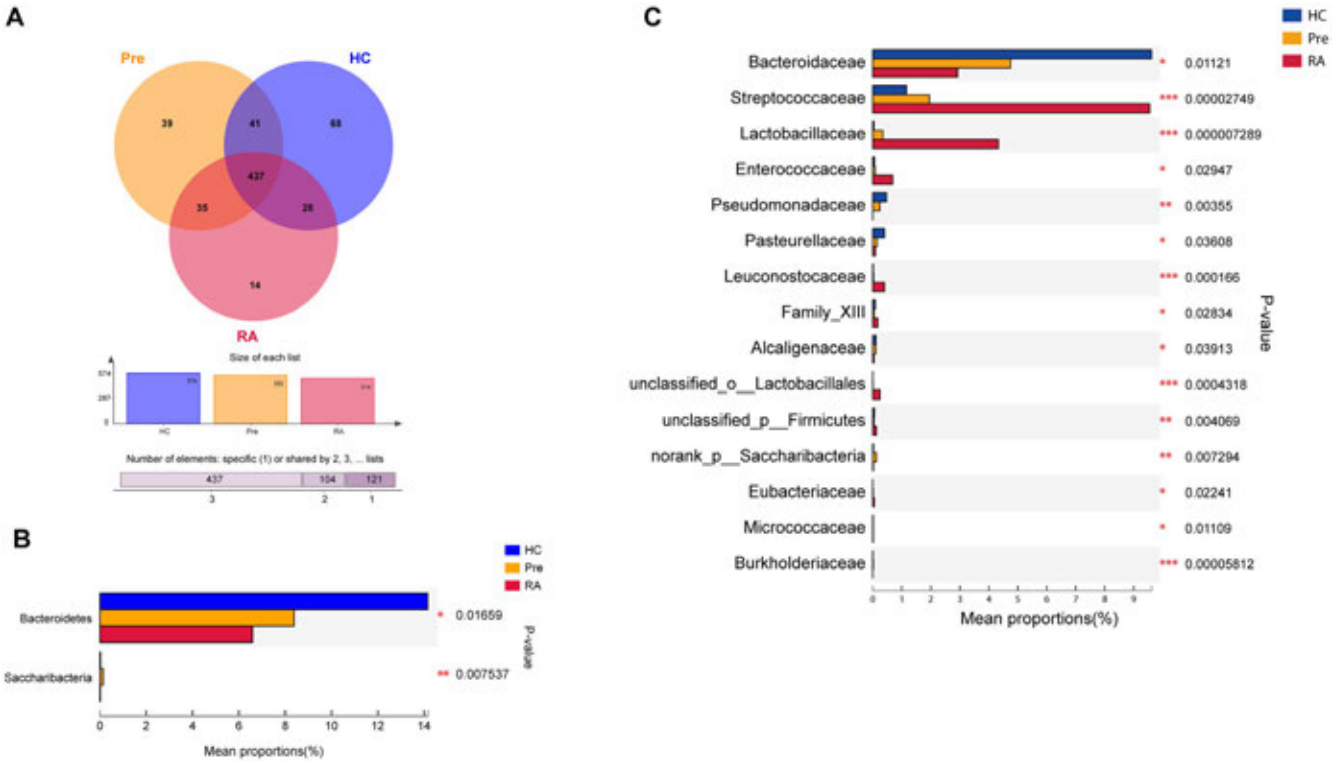

Figure 2 Differential and variant abundance of intestinal bacteria in rheumatoid arthritis (RA) patients, high-risk individuals for RA (Pre) and healthy controls (HC). (A) Venn diagram showing the number of shared and specific species in the three groups of individuals. Bacteria with different abundance in the three groups at the phylum level (B) and the family level (C).

Conclusion: The intestinal microbiota changed gradually during disease progression of human RA. Intestinal dysbiosis occurs prior to the onset of arthritis symptoms in individuals with positive anti-CCP antibody. Identifying the specific microbes characterize individuals at preclinical stage would provide a useful tool for early detection and intervention of RA.

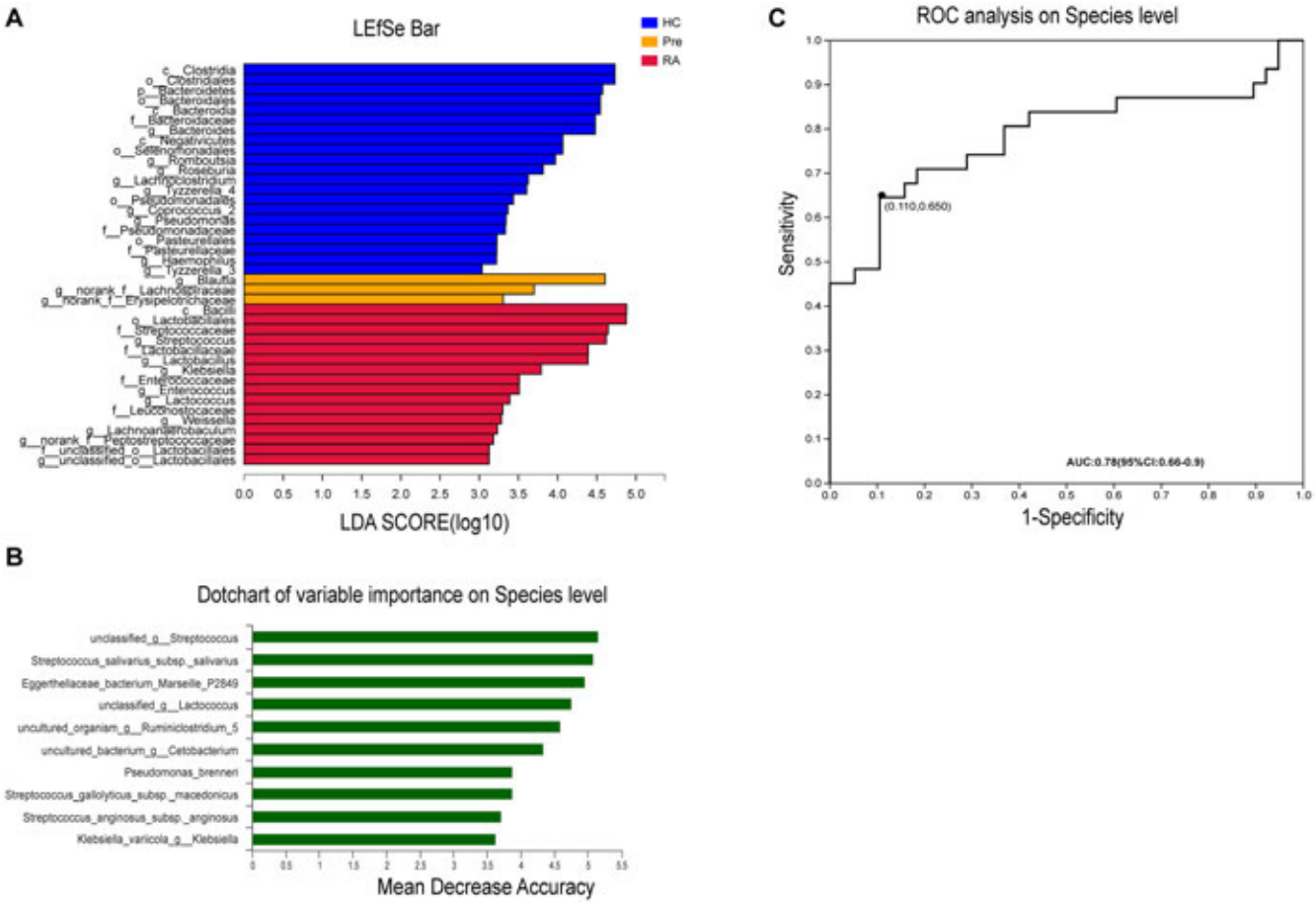

Figure 3 The discriminant taxonomic biomarkers that characterize the stages in the progression of RA. (A) LDA analysis showing the most discriminate bacteria for the specificity of each group. Bacterial marker of six bacteria species (B) yield an AUC of 0.78(95%CI=0.66-0.9) with a specificity of 89% and sensitivity of 65% in discriminating RA patients from healthy controls (C).

Disclosure: Y. Tong, None; **Y. Bai**, None; **Y. Zhao**, None; **Y. Liu**, None; **Y. Luo**, None.

Abstract Number: 0038

Autophagy Receptor Optineurin in Synovial Fibroblasts Plays a Protective Role Against Joint Destruction in Rheumatoid Arthritis

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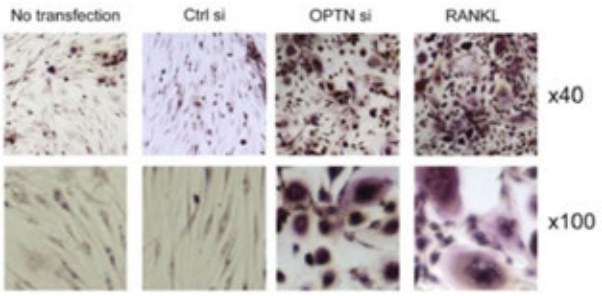
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Joint destructions progress throughout the course of rheumatoid arthritis (RA) without complete remission. Optineurin (OPTN) is an autophagy receptor with multiple functions related to homeostasis of cells and has been reported to negatively regulate osteoclast differentiation *in vivo*. However, the role of OPTN in RA, especially in joint destruction, has been unclear. In this study, we clarify the role of OPTN in the pathogenesis of joint destructions in RA using synovial fibroblasts (RASFs).

Methods: RASFs wereobtained from RA patients who fulfilled theACR 2010 criteria during the knee replacement surgery. RASFs with passages of 4 to 8 were used in this study. RASFs were incubated with pro-inflammatory cytokines and the expression of OPTN was analyzed using quantitative realtime PCR (RT-qPCR) and western blot. RASFs were transfected with siRNA targeting OPTN and the downregulated efficacy was confirmed by RT-qPCR and western blot. The expression of RANKL and osteoprotegerin (OPG) on OPTN-reduced RASFs were analyzed by flow cytometry and RT-qPCR after treatment with TNF-a or IFN-g. CD14+ monocytes isolated from healthy subjects were cocultured with OPTN-reduced RASFs or control RASFs in the presence of M-CSF. RANKL+M-CSF added in cocultured cells were used as positive control. Cocultured cells were stained with Tartrate-Resistant Acid Phosphatase (TRAP). TRAP+ cells with number of nuclei≥3 were considered as osteoclasts. Protein levels of IkBa were analyzed to evaluate the activation of NF-kB signaling. RNA sequencing was performed to analyze further pro-inflammatory/pro-destructive genes regulated by OPTN knockdown. Data within a group were compared using Student's unpaired t-test and data between groups were compared using the analysis of variance (GraphPad Prism). Differences were considered significant if $p < 0.05$.

Results: OPTN levels were upregulated after TNF-a or IFN-g stimulation at both mRNA and protein levels ($n = 5$, $p < 0.05$). The cell surface expression of RANKL was significantly increased following treatment with TNF-a or IFN-g and the effect was further pronounced in OPTN-reduced RASFs compared with that in control RASFs ($n = 5$, $p < 0.05$). The mRNA levels of RANKL were also increased in OPTN-reduced RASFs ($n = 5$, $p < 0.05$) while OPG levels remained unchanged. CD14+ monocytes cocultured with OPTN-reduced RASFs differentiated more into TRAP+ multinucleated cells (osteoclasts) compared to those cocultured with control RASFs ($n = 4$, $p < 0.05$). IkBa degradation following TNF-a treatment was prolonged in OPTN-reduced RASFs. RNA sequencing detected dysregulation of genes related to cartilage degradation, joint inflammation and bone formation, including MMP-3, CHST15, HAS1 and GATA-3, and the results were confirmed by RT-qPCR.



Representative figure of isolated human CD14+ monocytes cocultured with RASFs.

Conclusion: OPTN may play a protective role in RA with its upregulation when immersing with pro-inflammatory cytokines. Absence of OPTN might worsen RA by generating joint destructive state including increased RANKL expression on RASFs and subsequent osteoclast differentiation.

Disclosure: W. Lee, None; **M. Kato**, None; **E. Sugawara**, None; **M. Kono**, None; **Y. Kudo**, None; **M. Kono**, None; **Y. Fujieda**, None; **T. Bohgaki**, None; **O. Amengual**, None; **K. Oku**, None; **S. Yasuda**, None; **T. Atsumi**, AbbVie, 5, 8, Abbvie, 5, 8, Asahi Kasei Pharma Corporation, 8, Astellas Pharma, 8, 9, Astellas Pharma Inc, 8, AstraZeneca, 5, AstraZeneca plc, 5, 8, Bayer Yakuhin, 8, Bayer Yakuhin, Ltd., 8, Bristol-Myers Squibb, 8, 9, Chugai Pharmaceutical Co Ltd, 8, Chugai Pharmaceutical Co., 8, 9, Daiichi Sankyo, 8, 9, Daiichi Sankyo Co Ltd, 8, Eisai Co., Ltd, 8, Eli Lilly and Company, 8, 9, Eli Lilly Japan KK, 8, Elsai Co Ltd, 8, Gilead Sciences, 8, Gilead Sciences, Inc., 8, MEDICAL & BIOLOGICAL LABORATORIES CO., 5, Medical and Biological Laboratories Co Ltd, 5, Mitsubishi Tanabe Pharma, 8, 9, Nippon Shinyaku Co., 8, Novartis, 5, Novartis Pharma KK, 5, Ono Pharmaceutical, 5, ONO Pharmaceutical Co Ltd, 5, Otsuka Pharmaceutical, 8, Pfizer, 5, 9, Pfizer Inc, 5, 8, Sanofi, 9, Takeda Pharmaceutical Company, 8, Takeda Pharmaceuticals, 8.

Abstract Number: 0039

Role of Sialic Acid in the Aggressive Phenotype of RA FLS

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A comprehensive epigenomic characterization of rheumatoid arthritis (RA) fibroblast-like synoviocyte (FLS) has recently been described and can help to identify new critical pathways for RA pathogenesis. Two genes involved in sialylation, β-galactoside α2,3-sialyltransferase I (ST3Gal1) and β-galactoside α2,6-sialyltransferase I (ST6Gal1), were found to be significantly associated with changes in epigenetic marks between RA and osteoarthritis (OA) FLS, suggesting a role of this biological process in the aggressive phenotype of RA FLS. Here, we determined whether the amount of sialic acid (Sia) on FLS regulate its phenotype.

Methods: Sia expression in OA and RA synovial tissue was determined by using lectin immunofluorescence (IF). Sialyltransferases (ST) gene expression and Sia expression after TNF or PDGF stimulation in RA FLS were analyzed

by qPCR and by using lectin western blotting (WB),respectively. Migrative (scratch assay) and invasive (matrigel assay) phenotype after PDGF stimulation were evaluated after treatment with neuraminidase (Neu) from *Clostridium perfringens* (25mU/ml for 60 minutes), which cleaves Sia from glycoconjugates, and with an endogenous neuraminidase inhibitor, N-Acetyl-2,3-dehydro-2-deoxyneuraminic acid (NADNA, 100uM). Metalloproteinases (MMP) and IL6 gene expression after TNF and PDGF stimulation was also analyzed after Neu treatment. For arthritis experiments, mice were injected with K/BxN sera on day 0. Lith-O-Asp (a sialyltransferase inhibitor, 3mg/kg) was injected every other day i.p. beginning on day 0 after serum administrationor starting at the peak of arthritis (from day 4). Clinical arthritis scores were serially assessed.

Results: Maackia amurensislectinI and II IF staining was higher in RA synovial lining.PDGF and TNF stimulation increased the expression of ST3Gal1 and ST6Gal1 and total amount of Sia in FLS. Neu treatment decreased the amount of Sia in FLS determined by WB and inhibited not only migration (Neu:26.94±5.4vs. vehicle:22.5±3.4; $p< 0.001$) and invasion (Neu:12.7±1.6 vs. vehicle:24.0±2.5; $p< 0.001$), but also the expression of MMP and IL-6 after TNF and PDGF stimulation. Conversely, NADNA treatment increased the amount of Sia in RA FLS and enhanced both migration (vehicle:32.0±3.1vs. NADNA:16.5±5.0; $p< 0.001$)and invasion (vehicle:27.0±9.3vs. NADNA:39.5±13.6; $p< 0.001$). Finally, Lith-O-Asptreatment significantly decreased arthritis severity. Day 10 scores were 15.16±1.17 and 12.3±1.4($p=0.003$) for vehicle and Lith-O-Asp-treated mice respectively, when mice were treated from day 0, and 15.2±1.2 and 11.3±2.2($p< 0.001$) for vehicle and Lith-O-Asp -treated mice when mice were treated from day 4.

Conclusion: Sia are abundant on vertebrate glycoproteins and mediate a variety of biological phenomena, including migration and invasion. Our results suggest that in FLS, changes in the amounts of Sia likely mediated by changes in expression of ST3Gal1 and/or ST6Gal1, might be key regulator of FLS phenotype and contribute to joint destruction in RA. Modulation of Sia expression could act as disease modifying factor by directly modulating synoviocyte-mediated cartilage destruction.

Disclosure: P. Oliveira, None; **B. Pedersen**, None; **N. Varki**, None; **M. Fuster**, None; **G. Firestein**, Abbvie, 2, Janssen, 2; **M. Guma**, None.

Abstract Number: 0040

Inflammation and Neuronal Growth Factors in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Depression and cognitive impairment are frequently reported in rheumatoid arthritis (RA). We have recently presented that reduced hippocampus volume may be linked to functional disability and enhanced pain response in patients with RA (Andersson and Wasén et al. 2018). Reduced hippocampus volume and reduced neurogenesis (in hippocampus) was suggested related to insulin-like growth-factor 1 (IGF1) signaling in both RA patients and experimental models.Here, we aim to investigate the relation between growth factors of importance for neuronal growth and inflammation in RA and experimental arthritis.

Methods: Serum of 254 RA patients was analyzed for inflammatory markers IL-1b and IL-6 in addition to growth factors IGF1, brain-derived neurotrophic factor (BNDF) and vascular endothelial growth-factor (VEGF) and compared to the patients' disease activity (DAS28). Mice with collagen-induced arthritis were treated with short hairpin (sh)RNA targeting expression of IGF1 receptor (IGF1R). IBA1$^+$(microglia), DCX$^+$(developing neurons) and serin256-phosphorylated FoxO1$^+$(target of IGF1 signaling) cells in the hippocampal structures dentate gyrus (DG) and cornu ammonis (CA1-3) were identified by immunohistochemistry.

Results: Serum levels of IGF1, BNDF and VEGF all had weak but significant correlations to IL-1b (r= 0.12, 0.20 and 0.19, p= 0.049, 0.0013 and 0.0032, respectively). IGF1 was inversely correlated to IL-6 levels (r= -0.15, p= 0.020) and BNDF was negatively associated with disease activity (r= -0.14, p= 0.038). High serum IGF1 was associated with less expression of IGF1R in human peripheral blood monocytes (r= 0.25 p= 0.023). In IGF1R inhibited mice, the density of IBA1$^+$microglial cells was decreased in DG and CA regions of the hippocampus, indicating reduced local inflammation. The density of pFoxO1$^+$cells was increased in DG (p=0.0046) and CA3 (p=0.0030) when IGF1R was inhibited. The density of pFoxO1$^+$cells in DG and CA3 was positively correlated with serum IGF1 (r= 0.64 and 0.51, p= 0.0006 and 0.0080). However, the density of pFoxO1$^+$cells in DG and CA3 was negatively correlated with the number of DCX$^+$developing neurons (r= -0.46 and -0.65, p= 0.078 and 0.014).

Conclusion: We conclude that systemic inflammation measured as higher disease activity and IL-6 levels were associated with low BNDF, while serum IL-1b may stimulate release of growth factors IGF1, BNDF and VEGF into serum. Inhibition of IGF1R resulted in increased serum levels of IGF1, increased FoxO1 phosphorylation in the hippocampus, but this appeared to be insufficient to rescue neurogenesis.

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Abstract Number: 0041

Liver Dysfunction Associated with Rheumatoid Arthritis: Impact of Obesity and Effects of DMARDs in Hepatic Alterations

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SESSION INFORMATION
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Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: 1) To analyze the impact of rheumatoid arthritis (RA) in the liver function, 2) To evaluate the impact of obesity and the effect of methotrexate (MTX) and leflunomide (LFN) in the liver alterations.

Methods: Human data: cross-sectional study carried out in 300 RA patients (200 non-obese and 100 obese), 100 obese non-RA and 100 healthy donors (HDs). Clinical and laboratory parameters were analyzed.**In vitro model:** Hep

G2 cells were treated with IgG-ACPAs isolated from RA patients. **Mouse model:** Collagen induced arthritis (CIA) was developed in obese and lean mice. 55 C57Bl/6 mice (4-5 weeks) were used. Forty mice were fed with high fat diet (60%) until reaching 30g (obese) (OB). CIA-OB mice were treated with LFN (10 mg/kg daily) or MTX (3mg/kg three times/week) for 15 days. Liver samples were collected. The expression of genes related to fibrogenesis (TGF-b1, CO-L1A1, a-SMA, TIMP1, MMMP-9, MMP-12), lipid metabolism (PLIN, MCAD, CD36, PPARg, DGAT, LPL), insulin signal (AKT, IRS-1, IRS-2 and GLUT-2), endoplasmic reticulum and oxidative stress (AOX and CHOP) and inflammation (TNF-a, IL-6, MCP-1, CD11c, F4/80) was analyzed.

Results: Within the normal range, the percentage of RA patients with altered levels of hepatic enzymes and albumin was significantly increased. Moreover, these levels were associated with autoimmunity and inflammatory markers. The *in vitro* treatment of HepG2 cells with IgG-ACPAs induced the expression of inflammatory and oxidative stress markers and altered the expression of genes involved in lipid and glucose metabolisms.

On the other hand, RA non-OB patients treated with MTX or LFN did not show any differences in the hepatic subclinical alteration associated with RA. As expected OB non-RA subjects had altered levels of hepatic enzymes. Of note, RA OB patients taking MTX had significant increased levels of hepatic enzymes compared to RA non-OB and OB non-RA patients, suggesting the deleterious effect of MTX in those patients with obesity.

The induction of arthritis in both lean and obese mice elevated inflammatory, endoplasmic reticulum, oxidative stress and fibrogenesis related genes compared to non-disease mice. Supporting the data observed in the human study, treatment of CIA-OB mice with MTX significantly increased the hepatic alteration observed in OB mice. In contrast, LFN reduced genes involved in fibrogenesis, inflammation, endoplasmic reticulum and oxidative stress, suggesting an improvement of the liver function.

Conclusion:

1. RA patients display a subclinical alteration of the hepatic enzymes associated with inflammation and autoimmunity, suggesting that RA might be associated with liver abnormalities induced at least partially by the effect of ACPAs.
2. In mice, the generation of arthritis induced inflammation, fibrosis, endoplasmic reticulum and oxidative stress and an alteration in glucose and lipid metabolisms in the liver.
3. Methotrexate could affect the hepatic function as long as there is a subclinical pre-existent alteration of the liver such as obesity.

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Abstract Number: 0042

Subclinical Oral Inflammation Is Common Across the Spectrum of Oral Findings in Rheumatoid Arthritis Patients, Whereas *Porphyromonas Gingivalis* Antibodies Are Primarily a Marker for Clinical Periodontitis

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SESSION INFORMATION
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Background/Purpose: Periodontitis and immune responses to periodontal pathogens such as *Porphyromonas gingivalis* (*Pg*) are associated with rheumatoid arthritis (RA) but the mechanisms underlying these connections are incompletely understood. Our goal here was to gain further insights into inflammatory responses linking periodontal and joint inflammation in RA patients.

Methods: Seventy-three subjects underwent full-mouth dental examinations, including 33 RA patients, the majority with early RA (median symptom duration 5.5 months), all meeting 2010 ACR/EULAR criteria, 20 age and gender matched healthy subjects (HS), and 20 chronic periodontitis subjects who lacked RA (non-RA CP). Thirteen inflammatory mediators and matrix metalloproteinases (MMPs) were measured in serum, saliva, gingival crevicular fluid (GCF) and synovial fluid by bead-based multiplex immunoassay. *Pg* DNA in subgingival plaque *Pg* IgG antibodies in serum and were also measured.

Results: Of the 33 RA patients, 30 (91%) received routine dental care, and only one currently smoked. However, on clinical assessment, only 10 of the 33 patients (30%) had healthy periodontium, 13 (39%) had gingivitis, a periodontitis precursor, and 10 (30%) had periodontitis.

Compared with HS and non-RA CP, RA patients had the most elevated serum levels of inflammatory mediators and MMPs, with exception of MMP-3, which was more enriched in the sera of non-RA CP patients ($P < 0.005$ vs. HS). In RA synovial fluid, the Th1-associated mediator, CXCL10, innate immune mediators, IL-6 and IL-8, and MMPs, particularly MMP-1 and MMP-3, were most concentrated compared with serum ($P \leq 0.0001$).

In saliva, the non-RA CP group had greatest concentration of inflammatory mediators, particularly the neutrophil chemoattractant IL-8, and elevated levels of MMPs, especially MMP-1, MMP-8, and MMP-9 ($P < 0.002$). In GCF, a similar inflammatory profile was observed and additionally levels of the anti-inflammatory cytokine IL-10 were significantly lower than in HS. Although values were somewhat lower, RA patients also had elevation of IL-8 in both saliva and GCF ($P=0.02$), and levels of MMP-8, and MMP-9 were also elevated, particularly in saliva ($P < 0.002$). Similar to the non-RA chronic periodontitis group, levels of IL-10 were decreased in GCF of RA patients compared with HS ($P=0.005$). When RA patients were stratified according to dental status (healthy, gingivitis, or periodontitis), there were no significant differences in the levels of inflammatory mediators. In contrast, *Pg* antibodies in serum or *Pg* DNA in subgingival plaque were found only in RA patients with clinical periodontitis.

Conclusion: While RA patients had systemic and joint inflammation, as expected, they also had elevated levels of periodontitis-associated mediators in oral fluids, even in the absence of clinical periodontitis. Levels of IL-8, a chemoattractant for neutrophils, the major effector cell in periodontitis, and MMPs were particularly elevated. Thus, the

oral mucosa may be a common, but often unrecognized, site of extra-articular inflammation in RA. In contrast, *Pg* antibodies and DNA seem to be a marker only for frank periodontitis.

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Abstract Number: 0043

The Impact of Air Pollution on Extracellular Vesicles as a Potential Pro-inflammatory Stimulus in Rheumatoid Arthritis

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is an heterogeneous chronic autoimmune disorder potentially leading to a progressive joint damage with great impact on quality of life. RA pathogenesis is complex and involves environmental factors that trigger disease in genetically susceptible individuals. Extracellular vesicles (EVs) have been described to play an important role in RA pathogenesis and to modulate autoimmune response following environmental exposures, such as air pollution.

Our aim was to evaluate the effects of particulate matter (PM) with aerodynamic diameter ≤ 10 μm (PM10) and ≤ 2.5 μm (PM2.5) on EVs in RA and osteoarthritis (OA) as control.

Methods: Plasma EVs were analyzed by Nanosight and flow cytometry: CD14 (monocyte/macrophage), CD61 (platelet), CD25 (T-reg), human endogenous retrovirus w (HERV-w), human leukocyte antigen G (HLAG). Demographic and clinical data were collected for each patient. Plasma EV concentrations were measured in RA and OA patients and were analyzed by generalized linear regression models. Daily PM concentrations, estimated by Regional Environmental Protection Agency at municipality resolution, were used to assign short-term exposure (mean of the 7 days preceding the evaluation) to each patient.

Results: 12 consecutive patients with RA (median age 68.1, median disease duration 9.3, 12 female, median DAS28 2.25, 5 positive for rheumatoid factors, 6 positive for anti-citrullinated peptide antibodies) and 12 patients with OA (median age 67.1, median disease duration 9.3, 8 female) were enrolled. Analysis of EVs concentration, according to their dimensions, showed a negative association of exosomes (63-92nm) in RA compared to OA ($p< 0.05$). The increase of PM2.5 led to a decrease of CD14+ microvesicles (MV) (β=-0.13; $p< 0.01$) and CD61+ (β=-0.08; p=0.05) in RA, and of HERV-w in OA (β=-0.09; p=0.01). Similar results were observed analyzing PM10 exposure. PM exposure was not observed to modify CD25+ and HLA-G+ MV release both in RA and OA patients (table below). Moreover, we compared plasmatic EVs mean concentration among patients with RA and OA, and we found a significant difference in the two groups in the HERV-w subpopulations (βAR vs βOA = 0.044 vs - 0.091; p = 0.011). In RA patients we also observed a significant association between EVs (CD14+ and HLA-G+ MV) and DAS28 (βCD14+ = 0.03; p = 0.01 and

EV	RA			OA		
	β	SE	P-value	β	SE	P-value
$PM_{2.5}$ exposure						
EV count						
Total EV	-0.04	0.02	0.08	0.02	0.03	0.49
Exosomes	-0.01	0.02	0.60	0.01	0.03	0.66
MV	-0.02	0.02	0.36	0.01	0.03	0.66
MV subtypes						
CD14+	-0.13	0.03	**<0.01**	-0.04	0.04	0.25
CD61+	-0.08	0.04	**0.05**	0.00	0.05	0.99
CD25+	-0.02	0.02	0.48	-0.02	0.03	0.48
HERV-w+	0.04	0.03	0.08	-0.09	0.04	**0.01**
HLA-G+	-0.03	0.02	0.18	-0.01	0.03	0.67
PM_{10} exposure						
EV count						
Total EV	-0.01	0.01	0.52	0.02	0.02	0.43
Exosomes	-0.02	0.02	0.26	0.04	0.03	0.14
MV	-0.01	0.01	0.63	0.02	0.03	0.52
MV subtypes						
CD14+	-0.09	0.02	**<0.01**	-0.01	0.04	0.72
CD61+	-0.06	0.03	**0.02**	-0.02	0.05	0.76
CD25+	-0.01	0.01	0.53	-0.02	0.03	0.50
HERV-w+	0.03	0.02	0.07	-0.07	0.04	**0.05**
HLA-G+	-0.01	0.02	0.46	0.00	0.03	0.97

βHLA-G+ = 0.04; p = 0.02). Finally, we observed a negative association between exosomes and C-reactive protein (CRP) (β=-1.99; p=0.03), and a positive association between HERV-w and Erythrocyte Sedimentation Rate (ESR) (β=0.53; p=0.06), and HLA-G+ and ESR (β=0.29; p=0.01).

Conclusion: The results of this pilot study show that PM exposure modulates the release of EVs carrying HLA-G and/or HERV-w in RA patients. This might be interpreted as an attempt of immune system to counteract the perturbation provoked by a pro-inflammatory environmental stimulus. More research is still needed to tie the genetic, epigenetic and environmental factors together and to determine their roles in RA pathogenesis.

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Abstract Number: 0044

Validation of New Genes Identified in a Molecular Bayesian Network of Rheumatoid Arthritis Synovitis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: We have previously identified new key regulators of Rheumatoid arthritis (RA) synovial pathology using a systems biology approach that combined RA gene expression datasets, epigenomics data, genetics and rodent studies. The RA fibroblast-like synoviocytes (RA-FLS) have a central role in RA pathogenesis and joint damage, and their in vitro invasive properties correlate with in vivo joint damage. In the present study were examine the effect of different key regulators identified in the systems biology study in phenotypes relevant to disease and joint damage.

Methods: RA-FLS cell lines (n=4-6 cell lines per gene) were treated with siRNA smartpool targeting the top key network and subnetwork regulators, and compared with control siRNA. RA-FLS were then examined in different in vitro phenotypes that strongly correlate with joint damage in RA and rodent models of RA. These phenotypes included FLS invasiveness, FLS proliferation, cell adhesion, the wound healing model, and IL-1b-induced expression and production of IL-1b, IL-6, TNFa and MMPs (MMP1, 2, 3 and 14).

Results: Knock down of LOXL2 and NUSAP with siRNA significantly decreased FLS invasiveness by 30% (p=0.03) and 60% (p=0.002), respectively, compared with siRNA control. RA-FLS mobility in the wound healing assay was inhibited by knock down of AKT3, BACH1 and DLX4 (p=0.008). Knock down of TRIM22, an interferon-induced protein involved in innate immunity, decreased the IL-1b-induced release of IL-6 (p=0.03). RA-FLS proliferation and adhesion were not affected by any of the siRNA tested.

Conclusion: This study validated new key regulators identified in our systems biology discovery approach generating potential new understanding of events regulating FLS behavior in RA and potential new targets for the development of new treatments aimed at reducing joint damage.

Disclosure: T. Laragione, None; **C. Harris**, None; **W. Wang**, None; **J. Zhu**, None; **P. Gulko**, None.

Abstract Number: 0045

bDMARD-experienced Filgotinib-treated Patient Samples Exhibit a Partial Reversion to the Peripheral Molecular Profile of a Demographically Matched Healthy Population

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SESSION INFORMATION
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Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
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Background/Purpose: Filgotinib (FIL), an oral, selective, Janus Kinase 1 (JAK1) inhibitor was effective in Phase 3 studies of active RA in patients (pts) with inadequate response or intolerance to biologic DMARDs (bDMARD-IR; FINCH-2 ClinicalTrials.gov Identifier: NCT02873936). A proteomic and transcriptomic study was conducted to elucidate the effect of FIL on molecular mechanisms and the underlying pathobiology of RA.

Methods: Whole blood was collected from FINCH-2 RA pts on either a stable dose of placebo + MTX (PBO; n = 148), or once daily FIL 100 mg (n = 153), or 200 mg (n = 148) + MTX at baseline, week 4 and week 12. Samples from demographically matched healthy volunteers (HV; n = 50) were also evaluated. Serum concentrations of 28 cytokines known to be associated with RA pathology were quantified by ELISA-based assays. Globin depleted whole-blood mRNA was sequenced using Illumina HiSeq 2500. Differential gene expression analysis was applied comparing baseline RA pts data to HVs and interpreted into pathways using Gene Set Enrichment Analysis (GSEA). Further, we calculated gene signature (GS) scores using single sample GSEA (ssGSEA) to evaluate a reversion to healthy for Hallmark gene sets that had previously shown the strongest magnitude of FIL-associated effects (Taylor *et al*. EULAR 2019). Each GS was tested (Wilcoxon rank sum) comparing treatment arms with time-paired subjects against HVs. All cytokines and GSs were standardized to HV values. Cytokines and GSs not statistically different between RA pts after treatment and HVs were considered to have "reversed" toward a HV phenotype.

Results: Among 28 cytokines evaluated in baseline RA serum, 18 were significantly different from HV. Of these, 6 (chemokine (C-X-C motif) ligand [CXCL13], chemokine (C-C motif) ligand 2 [CCL2], CCL3, CCL4, IL-18, and Osteocalcin) reversed towards a HV phenotype after FIL treatment (Table 1). In contrast, only IL-18 reached HV levels in PBO treated pts (week 4). Of 15,189 genes with expression data, 3,532 (23%) were significantly increased and 4,408 (29%) significantly decreased in pts with RA relative to HV (false discovery rate < 0.05). The baseline transcriptional profile of RA pts was enriched with pathways implicated in RA pathology, including inflammatory responses and IFN, IL-6, TNFα signalling. Reversal of transcriptional profiles was broadly dose- and time-dependent, with fewer genes differ-

Table 1. Impact of FIL on cytokines that were significantly different from HV

		PBO			FIL 100 mg			FIL 200 mg		
Cytokine	**HV group**	**Baseline**	**Week 4**	**Week 12**	**Baseline**	**Week 4**	**Week 12**	**Baseline**	**Week 4**	**Week 12**
CXCL13	-0.08	2.92	2.68	2.65	1.80	1.15	0.54	2.49	0.85	**0.71**
	(-0.66, 0.64)	(0.83, 4.33)	(0.96, 4.07)	(1.16, 4.14)	(0.14, 3.72)	(-0.50, 3.44)	(-0.48, 3.01)	(0.40, 4.66)	(-0.81, 2.57)	**(-1.20, 1.96)**
CCL2	-0.02	0.65	0.55	0.64	**0.48**	**0.10**	0.53	0.61	**0.39**	0.66
	(-0.63, 0.58)	(-0.31, 2.06)	(-0.58, 1.87)	(-0.50, 1.74)	**(-0.63, 1.79)**	**(-1.17, 2.08)**	(-0.78, 1.95)	(-0.72, 1.96)	**(-1.05, 1.78)**	(-0.60, 2.18)
CCL3	0.10	0.87	0.69	0.98	0.54	**0.44**	0.51	1.07	**0.14**	**0.44**
	(-0.63, 0.65)	(-0.46, 2.22)	(-0.37, 2.09)	(-0.28, 2.30)	(-0.54, 2.15)	**(-1.03, 1.81)**	(-0.46, 2.18)	(-0.51, 2.44)	**(-1.22, 1.46)**	**(-1.03, 1.68)**
CCL4	-0.05	0.76	0.55	0.60	0.45	**0.36**	**0.35**	0.58	**-0.32**	**0.11**
	(-0.71, 0.66)	(-0.55, 1.94)	(-0.70, 1.69)	(-0.41, 1.71)	(-0.40, 1.57)	**(-0.69, 1.29)**	**(-0.50, 1.40)**	(-0.52, 1.56)	**(-1.01, 1.10)**	**(-0.96, 1.29)**
IL-18	0.08	0.56	**0.44**	0.63	0.39	**0.11**	**0.09**	0.55	**-0.04**	**0.00**
	(-0.79, 0.78)	(-0.40, 1.40)	**(-0.65, 1.22)**	(-0.46, 1.33)	(-0.35, 1.24)	**(-0.66, 0.90)**	**(-0.81, 0.98)**	(-0.38, 1.44)	**(-1.14, 0.68)**	**(-0.94, 0.76)**
OC	0.00	-0.72	-0.93	-0.74	-0.75	-0.63	-0.63	-0.56	**-0.21**	-0.71
	(-0.81, 0.86)	(-1.91, 0.24)	(-1.96, 0.06)	(-1.90, 0.09)	(-1.60, 0.10)	(-1.41, 0.30)	(-1.49, 0.28)	(-1.49, 0.37)	**(-1.23, 0.61)**	(-1.69, 0.34)

Data presented as median (Q1, Q3). Cytokines levels not statistically different (unadjusted Wilcoxon test) from the HV range are in **bold**.

CCL, chemokine (C-C motif) ligand; CXCL, chemokine (C-X-C motif) ligand; FIL, filgotinib; HV, healthy volunteer; PBO, placebo.

Table 2. Transcriptional impact of FIL treatment on inflammatory pathways implicated in RA pathology

Pathway	HV group	PBO			FIL 100 mg			FIL 200 mg		
		Baseline	Week 4	Week 12	Baseline	Week 4	Week 12	Baseline	Week 4	Week 12
Apoptosis	0.20 (-0.50, 0.67)	0.89 (0.37, 1.42)	0.91 (0.35, 1.41)	0.84 (0.51, 1.38)	0.82 (0.09, 1.46)	0.70 (-0.06, 1.31)	0.60 (0.12, 1.27)	0.91 (0.34, 1.56)	**0.55 (-0.11, 1.10)**	**0.59 (-0.05, 1.04)**
Coagulation	0.12 (-0.32, 0.43)	0.67 (0.15, 1.49)	0.89 (0.05, 1.44)	0.97 (0.12, 1.65)	0.73 (-0.11, 1.39)	0.67 (-0.19, 1.37)	0.70 (-0.12, 1.33)	0.96 (0.17, 1.57)	**0.46 (-0.19, 1.28)**	**0.57 (-0.04, 1.29)**
Complement	0.28 (-0.53, 0.56)	1.03 (0.08, 1.52)	0.77 (0.10, 1.32)	0.90 (0.03, 1.52)	0.75 (0.19, 1.36)	0.56 (-0.13, 1.19)	**0.45 (-0.25, 0.96)**	0.95 (0.20, 1.49)	**0.24 (-0.44, 0.81)**	**0.24 (-0.37, 1.18)**
IL-6 Signalling	0.25 (-0.29, 0.58)	1.06 (0.32, 1.54)	1.00 (0.39, 1.57)	1.06 (0.41, 1.64)	0.84 (0.15, 1.27)	0.62 (-0.02, 1.21)	0.59 (-0.04, 1.19)	0.90 (0.33, 1.40)	**0.19 (-0.41, 0.78)**	**0.38 (-0.14, 1.01)**
Inflammatory Response	0.22 (-0.45, 0.56)	0.96 (0.38, 1.48)	0.92 (0.31, 1.42)	0.81 (0.38, 1.53)	0.78 (0.33, 1.31)	0.64 (-0.02, 1.28)	**0.58 (0.03, 1.15)**	0.96 (0.32, 1.44)	**0.28 (-0.36, 0.97)**	**0.35 (-0.05, 1.06)**
IFN α	-0.12 (-0.77, 0.56)	0.23 (-0.44, 1.67)	0.16 (-0.43, 1.29)	0.39 (-0.56, 1.37)	0.41 (-0.29, 1.35)	**-0.15 (-0.67, 1.16)**	**0.11 (-0.71, 0.74)**	0.66 (-0.20, 1.79)	**-0.18 (-0.95, 1.04)**	**-0.12 (-0.87, 0.78)**
IFN γ	-0.17 (-0.76, 0.72)	0.27 (-0.43, 1.63)	0.14 (-0.51, 1.26)	0.36 (-0.66, 1.33)	0.46 (-0.18, 1.33)	**-0.10 (-0.63, 1.23)**	**0.01 (-0.78, 0.98)**	0.58 (-0.25, 1.62)	**-0.20 (-1.01, 0.92)**	**-0.15 (-0.77, 0.76)**
ROS	0.04 (-0.63, 0.68)	1.02 (0.23, 2.34)	1.42 (0.52, 2.25)	1.14 (0.41, 2.15)	1.41 (0.41, 2.32)	0.97 (0.17, 2.04)	1.31 (0.31, 2.13)	1.46 (0.54, 2.24)	1.11 (-0.11, 1.97)	1.28 (0.43, 2.10)
TNF α	0.22 (-0.42, 0.64)	1.10 (0.56, 1.57)	1.13 (0.52, 1.61)	1.10 (0.57, 1.66)	0.95 (0.42, 1.51)	0.97 (0.38, 1.48)	1.02 (0.31, 1.47)	1.15 (0.47, 1.52)	0.62 (0.03, 1.18)	0.80 (0.32, 1.36)

Data presented as median (Q1, Q3). Pathways significantly (unadjusted Wilcoxon test) reduced from baseline are in **bold**.
FIL, filgotinib; HV, healthy volunteer; PBO, placebo; ROS, reactive oxygen species.

entially expressed from HVs after 12 weeks of FIL compared with those receiving PBO. Expression of IFN response genes in pts who received FIL was statistically indistinguishable from HVs after 12 weeks. Interestingly, reactive oxygen species and TNFα signalling did not show this trend of reversal towards HV.

Conclusion: Differences in the peripheral molecular profile were observed between bDMARD-experienced RA pts and HV. While an overall trend toward the non-diseased molecular profile was observed following FIL, only a subset of cytokines and pathways were statistically indistinguishable from HV after 12 weeks. These results support the clinical efficacy of FIL within the bDMARD-experienced population and provide evidence for the reversal of disease activity to a healthier molecular profile in the periphery.

Disclosure: P. Taylor, AbbVie, 5, Abbvie, 5, Biogen, 5, Celgene, 2, 5, Eli Lilly and Company, 2, 5, Fresenius, 5, Fresenius SE & Co, 5, Fresnius, 5, Galapagos, 2, 5, Gilead, 5, GlaxoSmithKline, 5, Janssen, 2, 5, Lilly, 2, 5, Nordic Pharma, 5, NORDIC Pharma, 5, Pfizer, 5, Pfizer Inc, 5, Roche, 5, Sanofi, 5, UCB, 5; **E. Elboudwarej**, Gilead Sciences, 1, Gilead Sciences, Inc., 1, 3; **B. Downie**, Gilead Sciences, Inc, 3, Gilead Sciences, Inc., 1, 3; **L. Vestergaard**, Gilead, 3; **J. Liu**, Gilead, 1, 3, Gilead Sciences, Inc., 1, 3, Johnson & Johnson, 1, Johnson and Johnson, 1, Roche, 1; **A. Mirza**, Abbott Laboratories, 1, Gilead, 1, 3, Gilead Sciences, Inc., 1, 3; **R. Hawtin**, Gilead, 1, 3, Gilead Sciences, Inc., 1, 3.

Abstract Number: 0046

Key Inflammatory Biomarkers at Baseline Are Associated with Filgotinib Response at Week 12 in Rheumatoid Arthritis Patients with Inadequate Response or Intolerance to Biologic DMARDs

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL), an oral, selective, Janus Kinase 1 (JAK1) inhibitor was effective in Phase 3 studies of active RA in patients (pts) with inadequate response or intolerance to biologic DMARDs (bDMARD-IR; FINCH-2 ClinicalTrials.gov Identifier: NCT02873936). We evaluated blood and urine biomarkers from FINCH-2 pts to better understand the relationship between molecular drivers of RA and identify any association between biomarkers at baseline and therapeutic response.

Methods: Forty-two cytokines known to be associated with RA pathobiology were quantified by single and multiplexed ELISA at baseline and week 12. The multiplicative interaction between each baseline biomarker (low [≤ median] or high [> median]) and q.d. FIL 100mg (n = 153) or FIL 200 mg (n = 148), relative to placebo (PBO; n = 148), was tested for an effect on week 12 response (ACR-N, ACR20, ACR50, ACR70, DAS28-CRP). The relative concentrations of soluble intercellular adhesion molecule 1 (sICAM1) and serum chemokine (C-X-C motif) ligand (CXCL13) was previously associated with clinical outcomes in pts with RA treated with bDMARDs.[1]We similarly evaluated the therapeutic effect of FIL with sICAM1/CXCL13 ratio (low vs. high) on week 12 clinical responses. Odds ratios (OR) from logistic regression and effect estimates from linear regression models (Wald Chi-Square Test) were reported to assess whether the interaction between biomarker and treatment was associated with clinical response (FDR < 0.20).

Results: Comparing FIL 100 mg pts to PBO, high baseline levels of 8 serum cytokines (Chemokine (C-C motif) ligand 3[CCL3], CXCL10, IL-5, IL-6, IL-18, MMP3, serum amyloid A [SAA] and vascular cell adhesion molecule 1 [VCAM1]) were individually associated with improved ACR response or reduction in RA disease activity (DAS28-CRP) by week 12 (Δ ACRN range [27.5, 79.4]; Δ DAS28-CRP range [-0.70, -0.93]). High baseline serum CRP, CXCL13, and vascular endothelial growth factor A [VEGFA] levels were also associated with improved response to FIL 200 mg (Δ ACRN range [15.4, 32.9]; Δ DAS28-CRP range [-0.79, -1.39]; ACR50 OR range [6.13, 7.10]). Additionally, PBO-treated pts with a low sICAM1/CXCL13 ratio had lower ACR50 response rate compared to pts with high sICAM1/CXCL13 ratio (low vs high ratio Δ = -15.2%). In contrast, FIL treated pts exhibited the opposite effect, where a low sICAM1/CXCL13 ratio led to an increased ACR50 response (FIL 100 mg: low vs high ratio Δ = + 10.7%; FIL 200 mg: low vs high ratio Δ = + 19.9%). Relative to PBO with high sICAM1/CXCL13 ratio, a low sICAM1/CXCL13 ratio was significantly associated with an improved likelihood of ACR50 response to FIL 100 mg and 200 mg respectively at week 12 (OR = 7.40, *P* = 0.001; OR = 5.23, *P* = 0.007). Notably, these significant interactions held for ACR20 and ACR70 in FIL 200 mg (Table).

Table. Interactions of ACR response and CXCL13/sICAM1 ratios in FIL treated RA pts with a low CXCL13/sICAM1 ratio compared with PBO treated pts with high CXCL13/sICAM1 ratio

	Week 12 ACR Response Rate (%)	Low CXCL13/sICAM1 ratio FIL treatment vs high CXCL13/sICAM1 ratio PBO		
		Odds Ratio	95% CI	P Value
ACR 20				
PBO	36.2	n/a	n/a	n/a
FIL 100 mg	68.9	ns	ns	ns
FIL 200 mg	80.6	3.43	1.21, 9.93	0.021
ACR 50				
PBO	24.1	n/a	n/a	n/a
FIL 100 mg	39.3	7.44	1.61, 18.5	0.001
FIL 200 mg	53.7	5.31	2.30, 25.6	0.007
ACR 70				
PBO	10.2	n/a	n/a	n/a
FIL 100 mg	21.3	ns	ns	ns
FIL 200 mg	32.8	9.97	1.97, 60.1	0.007

CI, confidence interval; FIL, filgotinib; n/a, not applicable; ns, not significant; PBO, placebo; sICAM1, soluble intercellular adhesion molecule 1.

Biomarkers at Baseline Table Interactions of ACR response and CXCL13/sICAM1 ratios in FIL treated RA pts with a low CXCL13/sICAM1 ratio compared with PBO treated
pts with high CXCL13/sICAM1 ratio

Conclusion: Individually, high baseline levels of key inflammatory serum cytokines, as well as the presence of a low sICAM1/CXCL13 ratio were each indicative of positive outcomes in these bDMARD-IR RA pts treated with FIL. Further evaluation of these biomarkers alone or in combination may suggest a cytokine profile in RA pts that enriches for the probability of high-end responses to therapy.

Reference

1. Dennis G et al. *Arthritis Res Ther*. 2014; 16(2):R90

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Abstract Number: 0047

Autoreactivity to Acetylated Histones Defines a Subset of RA Patients and Is Associated with Acetyl - Citrulline Anti-Modified Protein Autoantibody (AMPA) Cross-Reactivity

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SESSION INFORMATION
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Session Title: RA – Etiology & Pathogenesis Poster I
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Session Time: 9:00AM–11:00AM

Background/Purpose: Serum anti-citrullinated protein autoantibodies (ACPA) in rheumatoid arthritis (RA) display reactivity to a variety of cit-autoantigens. Studies of human ACPA mAbs have revealed that individual clones bind multiple cit-epitopes by recognition of consensus motifs. For certain ACPA, this cross-reactivity may extend also to other post-translational modifications (PTMs). Here we investigated anti-modified protein autoantibody (AMPA) reactivity to acetylated epitopes in RA.

Methods: Serum from 402 RA patients, 317 population controls and 160 SLE patients were screened by ELISA for IgG to an acetylated histone 2B peptide ($His2B_{6-22}$(Ac-K12)). IgG values were normalized towards a reference and reactivities to the native lys-peptide were subtracted. Cutoff for positivity was set based on controls (Mean+3 SD Δac-lys: 4.25). ACPA fine-specificity in the RA cohort was assessed by the ISAC antigen microarray, CCP2 by CCPlus assay and RF IgM/G/A by ELiA. In addition, AMPA reactivity to Ac-His2B and $His4_{1-18}$(Ac-K5,8,12,16) peptides were investigated in 295 RA-derived single-cell cloned human mAbs (23 CCP2+ and 272 non-ACPA clones). A mAb-subset was further evaluated using the JPT Histone Code Array. Fisher's exact test, Kruskal-Wallis analysis, and Spearman correlation were used for statistical analysis.

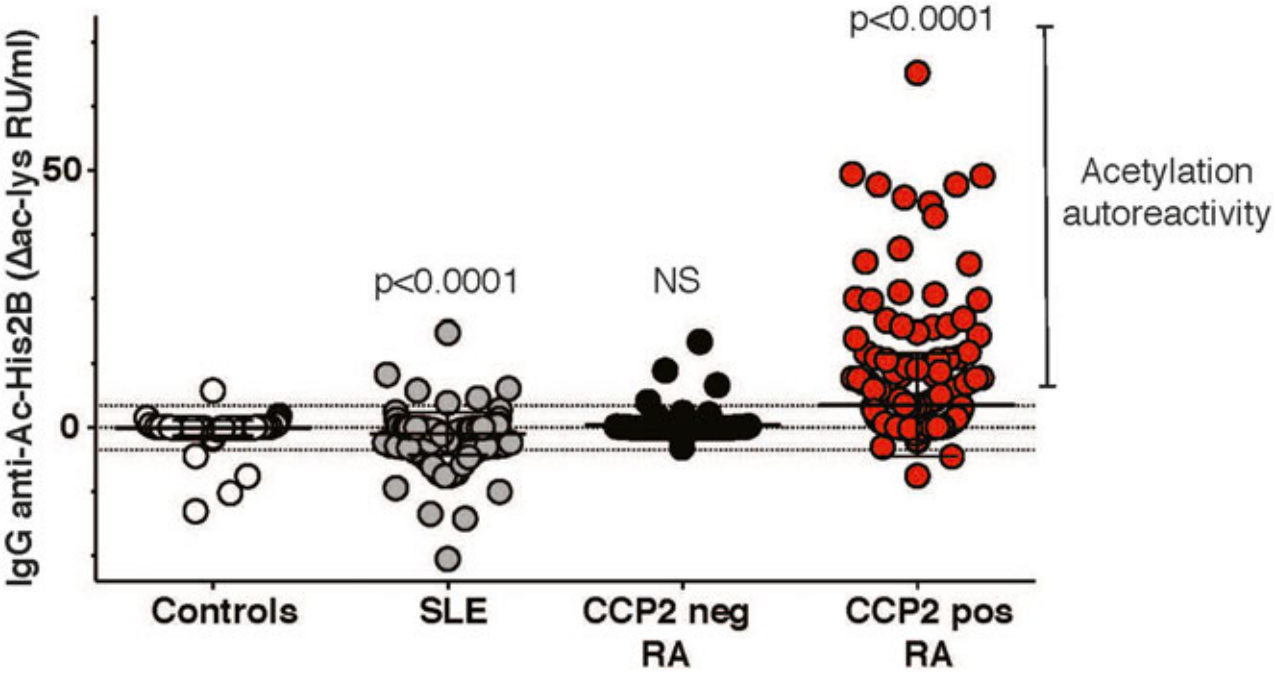
Results: RA patients displayed significant autoreactivity to acetylated histone compared to controls and SLE (Table 1, Fig. 1). Some SLE patients instead had increased reactivity to native His2B. 17% of all RA were positive for IgG anti-Ac-His2B distributing into 23% in the CCP2+ RA subset and 3.2% in CCP2 neg RA, while 0.3% in controls and 3.8% in SLE were positive. The CCP2 neg anti-Ac-His2B pos patients were RF positive and a majority had ACPA fine-specificities. At least one of the positive SLE patients was CCP2 positive. IgG anti-Ac-His2B correlated with IgG anti-CCP2 (R=0.41, p< 0.0001) as well as a range of cit-peptide reactivities (e.g. cit-Vim, cit-Fib, CEP-1). No significant association with DAS28, CRP or shared epitope HLA-DRB1 could be shown. However, levels were increased in smokers (p=0.04; Δac-lys: 3.8±9.6 RU/ml vs 1.9±6.7 RU/ml) and correlated with the number of positive ACPA fine-specificities (R=0.44 p< 0.0001). Among ACPA mAbs, 30% had ac-his reactivity (7/23, derived from 4 different patients and either lung/BAL, synovial plasma cells, or blood memory). None of the non-ACPA mAbs showed any binding. PTM cross-reactivity of these AMPA, and acetyl-lysine consensus motifs, were confirmed by the histone code array. Of note, some ACPA displayed restricted cit-reactivity.

Table 1. Serum IgG autoantibodies to acetylated histone 2B in RA

	Serum IgG anti-Ac-His (Δac-lys) (Mean±SD)		Frequency of IgG anti-Ac-His positivity	
		*p-value**		*p-value**
Controls	-0.1±1.45 RU/ml		0.3% (1/317)	
SLE patients	-1.2±4.18 RU/ml	p<0.0001	3.8% (6/160)	p=0.007
All RA patients	3.2±8.6 RU/ml	p<0.0001	17% (68/402)	p<0.0001
CCP2 neg RA	0.42±2.1 RU/ml	NS	3.2% (4/125)	p=0.03
CCP2 pos RA	4.4±10 RU/ml	p<0.0001	23% (64/277)	p<0.0001

**Compared to healthy population controls; RU=Relative Units*

Figure 1



Conclusion: A subset of ACPA can bind to acetyl-lysine peptides and elevated serum IgG anti-acetylated histone was confirmed in RA patients. We hypothesize that acetyl-autoreactivity in RA is associated with increased levels of cross-reactive AMPA. Notably, while AMPA activity is not restricted to histone motifs, anti-Ac-His may have functional properties by PAD-independent NET-interactions. These novel findings substantially extend our understanding of autoreactivity in RA and provide insight in RA pathogenesis.

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Abstract Number: 0048

Phenotype-based Clustering Along with Analysis of Molecular Profile Might Help to Define Precise CV-risk Profiles in RA Patients

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SESSION INFORMATION
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Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: 1. To identify and characterize specific immunological, inflammatory and epigenetic determinants involved in the enhanced cardiovascular (CV)-risk present in Rheumatoid Arthritis (RA) patients. 2. To evaluate the effects of biological drugs on the reestablishment of this altered profile.

Methods: Serum samples from 52 healthy donors (HD) and 188 selected RA patients -including 100 patients that had suffered previous CV events and 88 without previous CV events- were studied. Inflammatory and oxidative stress biomolecules and Netosis-derived products were quantified, and the CV-Risk Score was calculated following EULAR recommendations. Carotid intima-media thickness (CIMT) was evaluated as early atherosclerosis marker. miRNnomes were identified using next-generation sequencing miRNA assay. The *in vivo* effects of biologic drugs such as Infliximab (IFX), Tocilizumab (TCZ) and Rituximab (RTX) were evaluated before and after 6 months of therapy in parallel cohorts of 45, 25 and 27 patients, respectively.

Results: Circulating biomolecules related to inflammation -interleukins, chemokines, adhesion molecules-, Netosis -cell-free nucleosomes and elastase- and oxidative stress -lipoperoxides and 8-hydroxy-2'-deoxyguanosine (8-OHdG)- were found coordinately altered in the serum of RA patients. 104 circulating miRNAs were found altered in RA patients. Functional classification (Ingenuity Pathway analysis, IPA) recognized their potential involvement in inflammatory response, immunological and hematological diseases, and correlation analyses established the relationship of a number of them with the biomolecules found altered in RA patients. Non-supervised hard clustering analysis differentiated 3 clusters representing different CV-risk profile groups: a) RA patients with elevated CV-risk score (>9), positive for autoantibodies (RF and ACPAs) and with a high incidence (53 %) of CV events; b) RA patients with medium-low CV-risk score (< 4) but positive for autoantibodies and also with a high incidence (47%) of CV events, thus suggesting a relevant role for autoimmunity in this increased CV-risk; and c) RA patients negative for autoantibodies with medium-low CV-risk score and without previous CV events. Those three phenotypes of RA patients further displayed distinctive and specific molecular shapes. In vivo treatments with IFX, TCZ and RTX reduced disease activity and induced the re-establishment of normal levels in these altered biomolecules in an inhibitor-dependent manner.

Conclusion: 1. Phenotype-based clustering combined with the analysis of molecular profiles might help to define precise CV-risk profiles in RA patients. 2. Specific mediators of autoimmunity, inflammation, oxidative damage and Netosis, along with the miRNAs modulating their expression, coordinately contribute to a higher CV-risk score in RA patients. 3. Biological drugs, most likely though distinctive molecular mechanisms, restore the normal levels of these altered biomolecules, reducing the CV risk in RA patients. Funded by PI-0285-2017, ISCIII, PI18/00837 and RIER RD16/0012/0015 co-funded with FEDER

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Abstract Number: 0049

Towards a Single Cell Portrait of Rheumatoid Arthritis – Development of a Single Cell Multiomics Pipeline for Phase 2 of the Accelerating Medicine Partnership (AMP) – RA Network

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Etiology & Pathogenesis Poster I

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Background/Purpose: The goal of the Accelerating Medicines Partnership (AMP) program is to study synovial tissue from individuals with rheumatoid arthritis (RA) using high-dimensional analyses. During phase 1 of the program, we performed cytometric and transcriptomic analyses of synovial tissues and identified subsets of stromal and immune cells that were enriched in inflamed synovium. For phase 2, we have developed a pipeline to generate parallel single cell transcriptomic, proteomic, and epigenetic datasets of RA synovial cells (**Fig.1**).

Methods: Synovial tissues were obtained from individuals meeting the 2010 ACR criteria for RA and undergoing elective surgical procedures or synovial biopsies. We developed a histologic grading system to guide selection of biopsies with sufficient cell number and quality to apply multiple analytic technologies. Synovial tissues were cryopreserved after acquisition and then thawed and disaggregated. Viable synovial cells from each sample were sorted for subsequent analysis by scRNAseq, CITE-seq (combined scRNAseq and surface proteomics), and scATAC-seq using droplet-based technology (10X Genomics).

Results:

1. Histologic grading informs tissue cellularity. High quality synovial tissues (Grade A) predicted high cell yield (>50,000 cells) and whereas low quality (Grade D) predicted low cell yield (< 1,000 cells).
2. CITE-seq on synovial cells. Optimized cell handling enabled CITE-seq analysis on tissues with as low as 50,000 viable cells. After eliminating low-complexity cells (~5% of cells), we consistently recovered >10,000 high quality cells (>2,000 genes/cell) from each tissue. We tested 83 oligo-conjugated antibodies targeting immune and stromal cell surface markers and identified 61 antibodies with high signal specificity (high K-L divergence within gene-defined clusters) and signal intensity (median non-zero expression). Specificity of proteomic signals were markedly improved through serial titration. Importantly, independently clustering based on either transcriptomic or proteomic data revealed concordant signal that identified 19 distinct immune and stromal cell clusters.
3. Single cell ATAC-seq on synovial cells. We optimized nuclei recovery from synovial cells to enable scATAC-seq analysis from 30,000 viable cells. We demonstrated feasibility of performing scATAC-seq on re-cryopreserved synovial cells to facilitate batched processing. After removing low-read-depth barcodes, we obtained robust scAT-

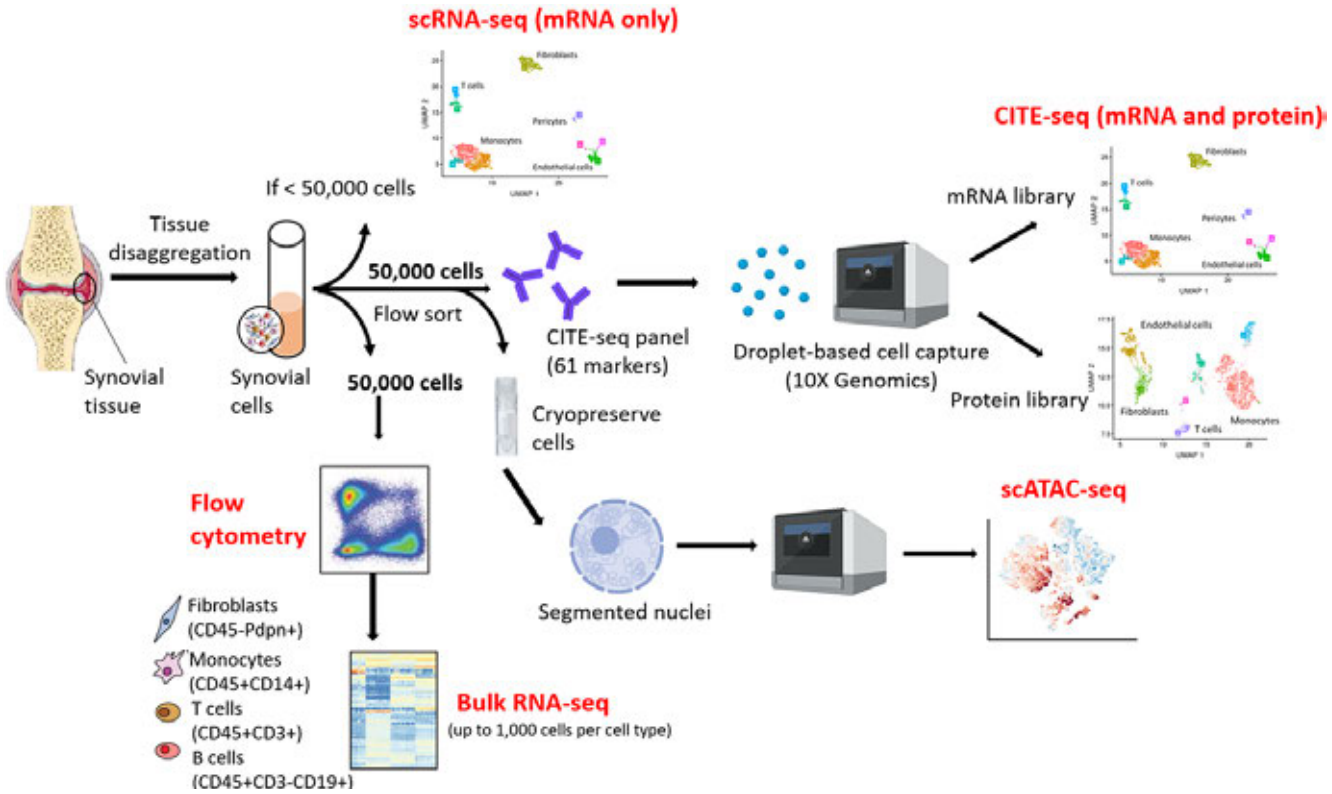

Figure 1. Single cell multiomics analysis of synovial cells.

AC-seq data (>9,000 mapped fragments/nucleus) with high concordance between scATAC-seq with scRNA-seq. We further demonstrated consistent identification of diverse synovial cell types in both once- and twice-cryopreserved synovial cells.

4. Flow Cytometry and bulk RNAseq. A 14-color flow cytometry panel was used to quantify disease-associated cell populations in conjunction with sorting major synovial cell types for low-input RNAseq.

Conclusion: We demonstrate feasibility of implementing multiple single cell profiling techniques in synovial tissue. The collection of multiple modalities of single cell analysis will add new dimensions to our understanding of the cellular pathogenesis of rheumatoid arthritis.

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Abstract Number: 0050

Circulating 25(OH)D, LL-37 and Antimicrobial Protein and Peptide (APP) Levels Are Altered Prior to Onset of Rheumatoid Arthritis

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SESSION INFORMATION
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Epidemiological studies suggest vitamin D deficiency as a potential risk factor for rheumatoid arthritis (RA) development, a chronic autoimmune disorder highly prevalent in indigenous North American (INA) population. Vitamin D improves immune function and protects against infections by inducing the expression of antimicrobial proteins and peptides (APPs) such as LL-37. We therefore profiled the circulating levels of 25-hydroxyvitaminD [25(OH)D], an active metabolite of vitamin D, and APPs in serum samples obtained from a cohort of at-risk first-degree relatives (FDR) of INA RA patients, a subset of whom subsequently developed RA (2010 ACR/EULAR guidelines) and were referred as "progressors".

Methods: 2007 onward, serum samples were collected from at-risk INA FDRs. Anti-citrullinated protein antibodies (ACPA), 25(OH)D, hs-CRP, vitamin-D binding protein (VDBP) and LL-37 (cathelicidin) levels were determined using ELISA and rheumatoid factor (RF) seropositivity was determined by nephelometry. A high-throughput Slow Off-Rate Modified Aptamer (SOMAmer®)-based Protein Array technology (SOMALogic Inc., US) was used for quantification of other APPs.

Results: We demonstrate that seropositive RA patients and FDR had lower 25(OH)D levels compared to ACPA-/FDR ($P< 0.05$, $P< 0.01$ respectively). In contrast, serum LL-37 levels were higher in both study groups compared to ACPA-/FDR ($P = 0.0009$ and $P = 0.0120$ respectively). No difference was observed in LL-37 levels between ACPA+ FDR and RA patients ($P = 0.1090$) Linear regression analysis showed circulating 25(OH)D and LL-37 was inversely associated with anti-CCP antibody levels ($P = 0.005$ and $P = 0.05$ respectively). Longitudinal samples from 14 progressors demonstrated a consistent increase in 25(OH)D, and LL-37 levels at the time they exhibited clinically detectable joint inflammation, without any significant change in VDBP levels. Expression profile of APPs was also significantly altered in progressors at RA onset and at-risk FDRs.

Conclusion: We demonstrate a differential serum abundance in the levels of 25(OH)D and APPs at RA onset in progressors. The interrelationship between vitamin D and these downstream metabolites and their potential role in RA transition requires further investigation.

Disclosure: V. Anaparti, None; **X. Meng**, None; **H. Mahadevappa**, None; **I. Smolik**, None; **N. Mookherjee**, None; **H. El-Gabalawy**, None.

Abstract Number: 0051

Cigarette Smoking Has Different Impacts on ACPA and RF Production Depending on Shared Epitope Allele Status in Japanese RA Patients; A Study with the Two Independent Japanese Cohorts (IORRA and KURAMA)

Yuki Ishikawa,[1] Motomu Hashimoto,[2] Katsunori Ikari,[3] Koichiro Ohmura,[4] Masao Tanaka,[4] Hiromu Ito,[4] Atsuo Taniguchi,[3] Hisashi Yamanaka,[3] Tsuneyo Mimori,[4] and Chikashi Terao[5], [1]Joslin Diabes Center, Boston, MA, [2]Department of Advanced Medicine for Rheumatic Diseases, Kyoto University Graduate School of Medicine, Kyoto, Japan, [3]Tokyo Women's Medical University, Tokyo, Japan, [4]Graduate School of Medicine, Kyoto University, Kyoto, Japan, [5]RIKEN, Tokyo, Japan

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Etiology & Pathogenesis Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In rheumatoid arthritis (RA), cigarette smoking affects both rheumatoid factor (RF) and anti-citrullinated cyclic peptide/protein antibody (ACPA) production, but its association in relation to HLA-DRB1 alleles, especially shared epitope (SE) alleles, have been different among different races[1-5]. Furthermore, the impact of cigarette smoking and its cessation on levels of RF and ACPA have not been well documented. We conducted the present study to investigate the impact of cigarette smoking and cessation on RF and ACPA levels in relation to HLA-DRB1 alleles in the largest RA cohorts in Asians.

Methods: A total of 6,239 subjects from two independent Japanese cohorts were enrolled. Their precise smoking histories both before and after the onset of RA were collected in questionnaires. The latest RF and ACPA levels were used (mean disease duration 15.6 years). We defined top quadrant of levels of RF or ACPA as high levels. Associations between smoking status and positivities or high levels of ACPA or RF as well as effects of HLA-DRB1 alleles on the associations were investigated by multiple logistic regression models.

Results: Smoking at onset (SaO) was an independent risk of not only RF and ACPA positivities (RF, odds ratio (OR) 1.52, 95% confidence interval (CI) 1.26-1.85, $p=1.8x10^{-5}$; ACPA, OR 1.39, 95%CI 1.09-1.76, $p=6.8x10^{-3}$), but also high levels of these autoantibodies, especially RF (Figure1; OR 2.06, 95% CI 1.70-2.48, $p=7.4x10^{-14}$; ACPA OR 1.29, 95%CI 1.06-1.57, $p=1.2x10^{-2}$). The larger ORs of RF than ACPA suggests that RF is more sensitive to cigarette smoking than ACPA. The effects of cigarette smoking were significantly larger in males than in females. The patients who quited smoking before onset had no longer significant risks of high autoantibody levels compared to subjects who had never smoked (RF, OR 1.33, p=0.099; ACPA, OR 1.19, p=0.093), and the risk was gradually attenuated depending on cessation years (RF, 0-10 years OR 1.34, 10-20 years OR 1.31, > 20 years OR 0.97; ACPA, 0-10 years OR 1.38, 10-20 years OR 1.01, > 20 years OR 1.12). The effect of smoking on ACPA positivity and its high level was apparent only in the presence of SE alleles, while the effect on RF positivity and its high level was apparent despite the presence of SE alleles (Figure 2 and 3) .

Conclusion: Cigarette smoking especially at RA onset is a significant risk of future high levels of ACPA and RF preferentially in males, and RF is more sensitive to smoking status than ACPA. The effect on ACPA is apparent only in the presence of SE alleles, indicating that an interaction between cigarette smoking and SE alleles affects ACPA production. On the other hand, the effect of cigarette smoking on RF production may be independent of SE alleles. Our study imply a novel potential mechanism of RA pathogenesis.

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Disclosure: Y. Ishikawa, None; **M. Hashimoto**, Astellas, 8, Ayum, 9, Brystol-Meyers, 8, Chugai, 9, Tanabe-Mitsubishi, 8, 9, UCB Japan, 9; **K. Ikari**, None; **K. Ohmura**, None; **M. Tanaka**, None; **H. Ito**, None; **A. Taniguchi**, None; **H. Yamanaka**, None; **T. Mimori**, None; **C. Terao**, None.

Abstract Number: 0052

Autophagy Protein Microtubule-associated Protein 1 Light chain-3B (LC3B) Regulates Joint Inflammation and Destruction in Rheumatoid Arthritis

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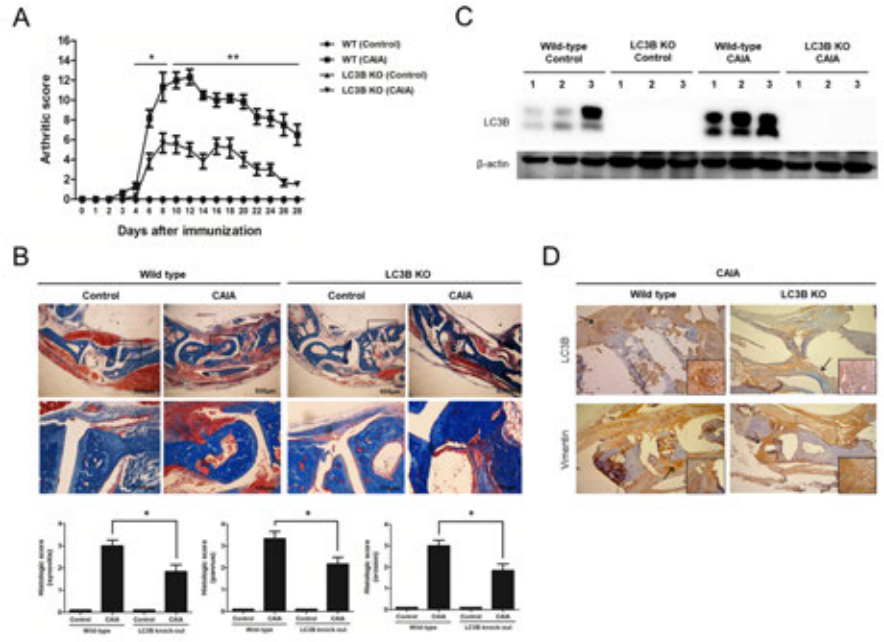
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

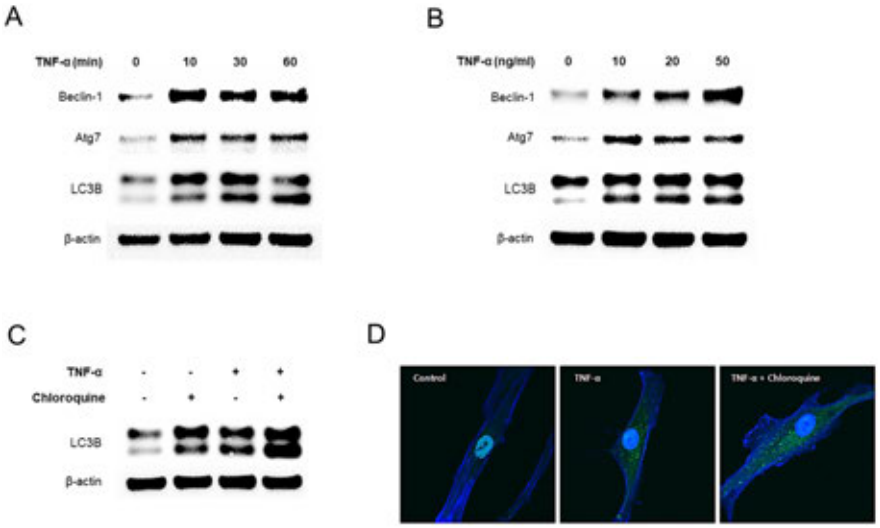
Background/Purpose: Here, we assumed that intracellular autophagy mechanism and its protein microtubule-associated protein 1 light chain-3B (LC3B) play an important role in the synovial fibroblasts of rheumatoid arthritis, and identified it through TNF-α stimulated synovial fibroblasts and animal model of rheumatoid arthritis.

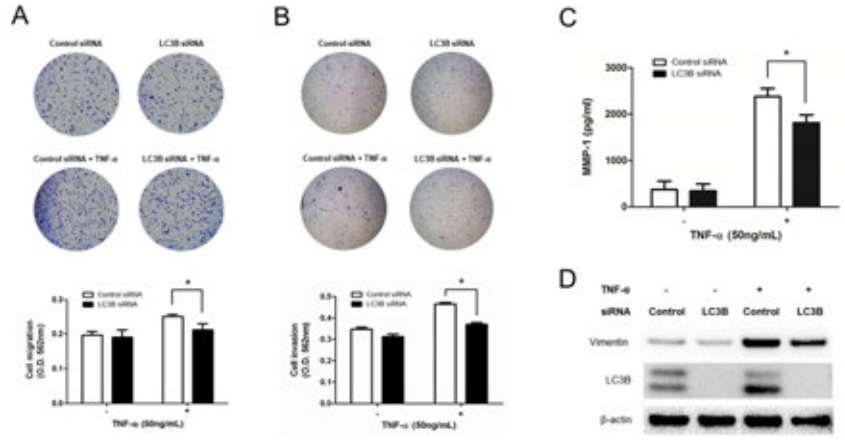
Methods: Mice deficient in microtubule associated protein-1 light chain-3B (LC3B-/-) were induced arthritis by the injection of type II collagen antibody and LPS. The clinical and histologic scores of arthritis and pro-inflammatory cytokines were measured from arthritic mice. Human synovial fibroblasts were obtained from the patients with rheumatoid arthritis. Their autophagic induction and its mechanisms were measured by western blots and ELISA assays after TNF-α treatment.

Results: In the results, we found that the clinical and histologic scores of arthritis and pro-inflammatory cytokines such as TNF-α, IL-1β and IL-6 in joint tissues were significantly decreased in the LC3B-/- arthritic mice compared to wild type littermates. We also identified that autophagy proteins like LC3B were expressed in synovial fibroblasts stimulated with TNF-α, and in this process, the activation of Jun-N terminal kinase (JNK) through reactive oxygen species (ROS) generated by a TNF-α and the expression of early growth response protein-1 (Egr-1) were important to LC3B expression. After knock down of LC3B by siRNA in the TNF-α stimulated synovial fibroblasts, the proliferation, migration and invasion capacities of these cells were significantly reduced and these phenomenons were associated with the decrease of cyclin D1 and vimentin by the increased ROS after autophagy inhibition.

Conclusion: In conclusion, we confirmed that autophagic protein LC3B induced by TNF-α plays an important role in the joint inflammation and destruction of rheumatoid arthritis and suggest this protein as a new therapeutic target in the treatment of rheumatoid arthritis.







Disclosure: **s. jung**, None; **s. lee**, None; **j. choi**, None.

Abstract Number: 0053

Activation of the Desacetylase Sirtuin-1 Counteracts the Activated and Proangiogenic Profile of Endothelial Cells in Rheumatoid Arthritis and Alleviates Experimental Arthritis

Agathe Leblond,[1] Sonia Pezet,[1] Anne Cauvet,[1] Claudine Casas,[1] Julie Pires Da Silva,[2] Roxane Herve,[3] Luca Semerano,[4] Christophe Lemaire,[5] Yannick Allanore,[6] and **Jerome Avouac**[6], [1]INSERM U1016, Paris, France, [2]Paris Sud University, Chateany Malabry, France, [3]Paris 13 University, Bobigny, France, [4]INSERM UMR 1125, Université Paris 13, Bobigny, France, [5]Paris Sud University, Chatenay malabry, France, [6]Paris Descartes University, Cochin Hospital, Rheumatology department, Paris, France

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Session Date: Sunday, November 10, 2019

Session Title: RA – Etiology & Pathogenesis Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To decipher the phenotype of endothelial cells (ECs) derived from circulating progenitors issued from patients with rheumatoid arthritis (RA).

Methods: Proliferation capacities between RA and control ECs was compared using the xCELLigence™ RTCA System. rh-TNFa-induced EC activation was analyzed by adhesion cell expression, VEGF synthesis and stress fiber formation. Angiogenic properties of ECs were assessed *in vitro* by tube formation on Matrigel and migration capacities through VEGF stimulation in modified Boyden chambers, and *in vivo* in a mouse model of tumoral neovascularization. Microarray experiments were then performed on Affymetrix GeneChip® Human Exon 1.0 ST Arrays in ECs issued from 18 RA patients and 11 age and sex-matched healthy controls. Expression of identified candidates was assessed by RT-PCR and western blots in ECs and by immunohistochemistry in the synovium. Their functional importance was then evaluated *in vitro* after gene invalidation by siRNA and adenoviral gene overexpression, and *in vivo* in the mouse model of methyl-BSA-induced arthritis.

Results: RA ECs displayed higher proliferation rate, greater sensitization to TNF-α,with increased VEGF production, ICAM/VCAM expression, and more prominent stress fiber formation, as well as enhanced angiogenic capacities, characterized by accelerated tube formation and increased migration capacities through VEGF stimulation, compared co control ECs. The subcutaneous transplantation of murine colon carcinoma (CT-26) cells with RA ECs in CB17-SCID mice markedly amplified tumor growth and intra-tumoral neovessel density, compared to the transplantation of control ECs.

Supervised microarray analyses identified the NAD-dependent protein deacetylase sirtuin-1 (SIRT1) as a relevant gene candidate. A strikingly decreased SIRT1 gene / protein expression and enzyme activity was detected in RA ECs upon the regulation of miR217 and miR181. A markedly decreased SIRT1 expression was also observed in synovial vessels of RA patients.

Invalidation of SIRT1 with specific siRNA in control ECs was associated with a proliferative and activated profile upon TNFa stimulation, trough the acetylation of p53 and p65, and with the development of proangiogenic capacities through the upregulation of the matricellular protein CYR61. Conditional deletion of SIRT1 in ECs through a Cre-LoxP recombination system increased angiogenesis and worsened signs of arthritis in methyl-BSA-induced arthritis.Conversely, adenoviral overexpression of SIRT1 in RA ECs reversed the activated and proangiogenic phenotype of RA ECs, and activation of SIRT1 with resveratrol alleviated signs of experimental methyl-BSA-induced arthritis.

Conclusion: SIRT1 expression is reduced in synovial vessels of RA patients. SIRT1 invalidation in ECs reproduces the proliferative, activated and proangiogenic profile of RA ECs and exacerbate experimental arthritis. These effects were reversed by SIRT1 activation. These results support the implication of SIRT1 in RA synovial neoangiogenesis and may have direct therapeutic implications, since targeting angiogenesis, and especially SIRT1, might be used as a complementary therapeutic approach in RA.

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Abstract Number: 0054

A Metagenome-wide Association Study of Gut Microbiome Revealed Novel Etiology of Rheumatoid Arthritis in the Japanese Population

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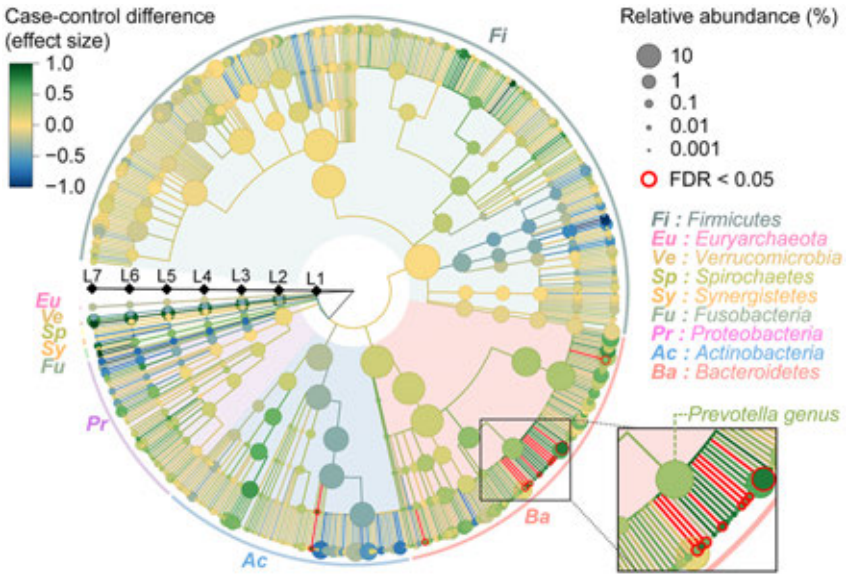
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The causality and pathogenic mechanism of microbiome composition remain elusive in many diseases, including autoimmune diseases such as rheumatoid arthritis (RA). This study aimed to elucidate gut microbiome's role in RA pathology by a comprehensive metagenome-wide association study (MWAS).

Methods: We conducted MWAS of the RA gut microbiome in the Japanese population (n_{case} = 82, $n_{control}$ = 42) by utilizing whole-genome shotgun sequencing of high depth (average 13 Gb per sample). Our MWAS consisted of three major bioinformatic analytic pipelines (phylogenetic analysis, functional gene analysis, and pathway analysis).

Results: Phylogenetic case–control association tests showed high abundance of multiple species belonging to the genus *Prevotella* (but other than previously reported *Prevotella copri*) in the RA case metagenome. The non-linear machine learning method efficiently deconvoluted the case–control phylogenetic discrepancy. Gene functional assessments showed that the abundance of one redox reaction–related gene was significantly decreased in the RA metagenome compared to controls. A variety of biological pathways including those related to metabolism (e.g., fatty acid biosynthesis and glycosaminoglycan degradation) were enriched in the case–control comparison. A population-specific link between the metagenome and host genome was identified by comparing biological pathway enrichment between the RA metagenome and the RA genome-wide association study (GWAS) results. No apparent discrepancy in alpha- or beta-diversities of metagenome was found between RA cases and controls.



Phylogenetic tree. Levels L2–L7 are from the inside layer to the outside layer. The size and color of dots represent relative abundance and effect sizes, respectively. The 12 clades with significant case–control associations ($q < 0.05$) are outlined in red.

Conclusion: Our shotgun sequencing–based MWAS highlights a novel link among the gut microbiome, host genome, and pathology of RA, which contributes to our understanding of the microbiome's role in RA etiology.

Disclosure: T. Kishikawa, None; **Y. Maeda**, Bristol-Myers Squibb Company, 8, Chugai Pharmaceutical Co. Ltd, 8, Eli Lily, 8, Mitsubishi-Tanabe, 8, Pfizer, 8; **T. Nii**, None; **D. Motooka**, None; **Y. Matsumoto**, None; **M. Matsushita**, None; **H. Matsuoka**, None; **M. Yoshimura**, None; **S. Kawada**, None; **S. Teshigawara**, None; **E. Oguro**, None; **Y. Okita**, None; **K. Kawamoto**, None; **S. Higa**, None; **T. Hirano**, None; **M. Narazaki**, None; **A. Ogata**, None; **Y. Saeki**, None; **S. Nakamura**, None; **H. Inohara**, None; **A. Kumanogoh**, None; **K. Takeda**, None; **Y. Okada**, None.

Abstract Number: 0055

A Novel Subclass of Intravascular Non-classical, Tissue Resident Synovial Monocyte Is Critical for Rheumatoid Arthritis Pathogenesis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: There are at least three populations of circulating monocytes; classical, intermediate and non-classical. We demonstrated that circulating non-classical monocytes are required for the effector phase of arthritis and spontaneous models of arthritis in mice. While the vast majority of studies on monocytes have focused those in circulation, very little is known about the monocytes in the synovium. The aim of this study was to examine the heterogeneity of tissue monocytes with those circulation and determine their involvement in inflammation.

Methods: NR4A1$^{-/-}$, CX3CR1$^{ERCre.zsGFP}$, CCR2$^{-/-}$, LFA$^{-/-}$ and C57Bl/6 mice were used in all studies. Intravascular and extravascular monocytes were identified using fluorescent anti-CD45 antibody before perfusion. STIA was induced via I.V. KBxN sera. Monocyte populations were quantified by flow cytometry and FACS sorted for RNA-sequencing (RNA seq). Human synovium was obtained from ultrasound guided synovial biopsies and CD45+ cells were FACSorted for single cell RNA seq.

Results: Single cell profiling of CD45^{+}NK1.1^{-}CD3^{-}CD19^{-}Ly6G^{-}CD64^{-}Tim4^{-}CD11b^{+} cells revealed 4 populations of non-classical monocytes that are distinct from circulating non-classical monocytes. We then identified four populations of Ly6C^{lo} monocytes in the joint; 2 intravascular and 2 extravascular cells using 18 color flow cytometry. Similarly, RA patients also display populations of non-classical monocytes using single cell RNA seq of ultrasound guided synovial tissue biopsies. Lineage tracing studies reveal that the origin of extravascular synovial monocytes are from the embryo while the intravascular monocytes are derived post-natally. The NR4A1-/- mice have fewer intravascular monocytes but still retain the extravascular monocytes, while CCR2-/- mice display similar numbers of intravascular non-classical monocytes yet lack the extravascular MHCII^{+} nonclassical monocytes compared to controls. Nonetheless, NR4A1-/- and CCR2-/- mice develop rheumatoid arthritis (RA)-like disease. Moreover, LFA-/- mice fail to have an expansion of the extravascular non-classical monocytes, which correlates with an ability to develop RA-like disease. Clodronate loaded liposomes depletes the intravascular monocytes as well as the extravascular CD177+MHC- nonclassical monocytes. These data suggest that only the loss of extravascular CD177+MHC- nonclassical monocytes but not the intravascular non-classical monocytes and the MHCII+ extravascular non-classical monocytes are essential for the development of RA.

Conclusion: We have identified and described four novel and uncharacterized populations of non-classical monocytes cells in the joint, an intravascular adherent and an extravascular populations. These cells have distinct origins and phenotype from both tissue resident macrophages and circulating non-classical monocytes. Further, the findings presented here strongly suggest the extravascular CD177+ non-classical monocytes are a key effector cells in inflammatory arthritis.

Disclosure: A. Montgomery, None; **S. Chen**, None; **D. Winter**, None; **H. Perlman**, None.

Abstract Number: 0056

Choline Metabolite Is Associated with Inflammation in Arthritis in the Elderly

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SESSION INFORMATION

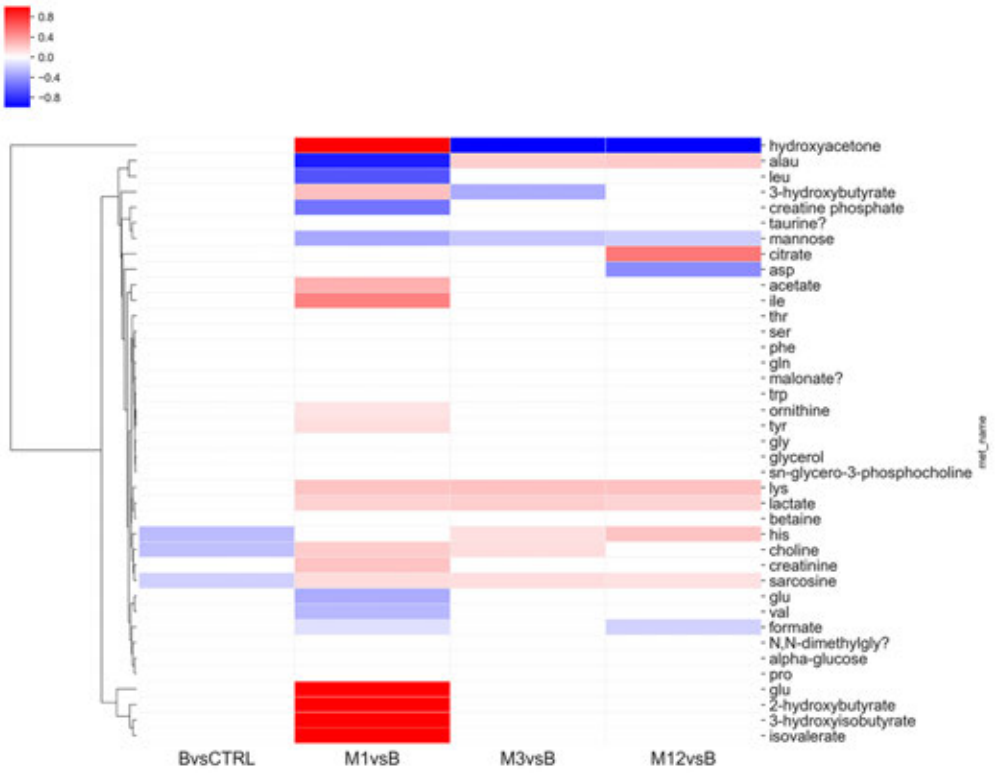
Session Date: Sunday, November 10, 2019

Session Title: RA – Etiology & Pathogenesis Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Elderly-onset RA (EORA) and polymyalgia rheumatica (PMR) are common rheumatic disease in the elderly and their pathogenesis are still not completely understood. Perturbations caused by in-



flammation can lead to correlated changes in concentrations of certain metabolites. Specifically, choline metabolism is strongly related to inflammation. The objective of this study was to explore metabolomic perturbations profiles in blood, utilizing 1H-nuclear magnetic resonance (NMR) and to relate to arthritic symptoms in the elderly.

Methods: ARTIEL (Arthritis in the Elderly) is a cohort with newly diagnosed arthritis in patients older than 60 years, with blood samples collected at baseline (pre-treatment), 1, 3 and 12 months after treatment, along with physician and patient outcome measures through 12 months. They are compared with randomly control individuals of the same age and gender. A Bruker Avance 700 MHz spectrometer was used to acquire NMR spectra of serum samples. Metabolomics data were pqn-normalized prior to the analysis. We conducted a temporal analysis to determine which metabolites were significantly changed between baseline and control, and between months 1,3,12 and baseline. We also examined the correlation between clinical variables of interest with baseline levels of metabolites. We used the Limma tool in R to conduct the analyses, by fitting linear models to the data, and controlling for the possibly confounding factors age, sex and BMI. False discovery rate was accounted for using the Benjamini-Hochberg method.

Results: 65 patients (average: 75, standard deviation (SD) 7) and 18 controls (average: 75.39, SD, 6.04) were analyzed. Of these, 45 were diagnosed with RA (15 patients were rheumatoid factor positive, 23 were ACPA positive and 5 had erosions at diagnosis) and 20 with PMR. At the start of the study, RA patients had a mean DAS28CRP of 5.7 (SD, 1). In addition, 84% of the patients reported scapular pain, and 56% of the patients reported pelvic pain at baseline. After 12 months of treatment, RA patients had a DAS28CRP of 2.46 (SD, 1). As shown in figure 1, levels of choline, histidine and sarcosine, were lower in arthritis patients than in controls. Of interest, after 1 month of treatment (91% were on glucocorticoids (GC) and 51% were on GC and one DMARD), several metabolites significantly changed respect to baseline (Figure 1). Several metabolites, including lactate, glucose, glutamine, formate and acetate also

significantly correlated with clinical scores at baseline. We did not see any difference in metabolites between RA and PMR population.

Conclusion: Inflammation correlates with significant changes in serum metabolites. Interestingly, choline, a metabolite strongly related to inflammation was significantly lower in arthritic patients than in the control population, suggesting a higher choline uptake and metabolism from inflamed tissues. Metabolite profile dramatically changed after therapy. Further analysis is needed to further understand how inflammation and/or treatment have impact on systemic metabolic profiling, and to define elements of inflammation pathobiology in this population.

Disclosure: F. cedola, None; **R. Coras**, None; **E. Sanchez-Lopez**, None; **L. Mateo**, None; **A. Pedersen**, None; **A. Brandy-Garcia**, None; **Á. Prior-Español**, None; **B. rosenthal**, None; **M. Martínez-Morillo**, None; **M. Guma**, None.

Abstract Number: 0057

Endothelial Progenitor Cells in the Pathophysiology of Interstitial Lung Disease Associated with Rheumatoid Arthritis

Veronica Pulito-Cueto,[1] Sara Remuzgo-Martínez,[1] Fernanda Genre,[1] Leticia Lera-Gomez,[1] Veronica Mijares,[1] Pilar Alonso Lecue,[2] Victor Manuel Mora Cuesta,[2] David Iturbe,[3] Sonia M. Fernández Rozas,[2] Ricardo Blanco,[4] Alfonso Corrales,[1] Jose Manuel Cifrian Martínez,[2] Raquel López-Mejías,[1] and Miguel A Gonzalez-Gay[4],
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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is one of the most significant comorbidities that contributes to the increased mortality observed in patients with rheumatoid arthritis (RA) [1,2]. Although the pathogenesis of ILD associated to RA (RA-ILD) remains poorly defined [2], it is known that vascular tissue plays a crucial role in lung physiology [3]. In this context, a population of cells termed endothelial progenitor cells (EPC) are involved in vasculogenesis and endothelial tissue repair [4]. Previous reports suggest the implication of EPC in different conditions such as RA and idiopathic pulmonary fibrosis (IPF), the most common and destructive ILD [5,6]. Nevertheless, little is known about their specific role in RA-ILD. Accordingly, the purpose of this study was to shed light on the potential role of EPC in RA-ILD pathophysiology.

Methods: Peripheral venous blood was collected from a total of 30 patients (13 with RA-ILD, 5 with RA without ILD and 12 with IPF) as well as 13 healthy controls. All subjects were recruited from the Rheumatology and Pneumology departments of Hospital Universitario Marqués de Valdecilla, Santander, Spain. Quantification of EPC by flow cytometry was analyzed for the expression of surface antigens. The combination of antibodies against the stem cell marker CD34, the immature progenitor marker CD133, the endothelial marker VEGF receptor 2 (CD309) and the common

leukocyte antigen CD45 was used. EPC were considered as $CD34^+$, $CD45^{Low}$, $CD309^+$ and $CD133^+$. All statistical analyses were performed using Prism software 5 (GraphPad).

Results: EPC frequency was significantly increased in RA patients, with and without ILD, and IPF patients when compared to controls ($p< 0.0001$, $p= 0.004$ and $p< 0.0001$, respectively). Nevertheless, patients with RA, in particular those with RA-ILD, showed a lower frequency of EPC than those with IPF ($p=0.009$).

Conclusion: Our results provide evidence for a potential role of EPC in the pathophysiology of RA-ILD disease.

References:

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Abstract Number: 0058

In Rheumatoid Arthritis (RA) Decreases in Conventional Dendritic Cell Lineages Are Associated with Adverse Measures of Myocardial Function and Expansions of Anomalous HLA-DR^+ Myeloid Subsets

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Dendritic cells (DC) are specialized antigen-presenting cells (APC) that have a central role in the initiation of immune responses. However, prior studies showed numeric decreases of myeloid (mDC) and plasmacytoid (pDC) DC in RA. This apparent contradiction led us to hypothesize that depletion of these 'canonical' DC is only one manifestation of a more fundamental alteration in this important immunoregulatory compartment in RA and that the overall non-lymphoid APC population ($CD3^-CD19^-$HLA-DR^+) does not decrease due to the appearance

	RA (n=31)	controls (n=4)	p
Live PBMC analyzed (per sample)	188255 [146909,290563]	163257 [147186,194461]	0.593
Dendritic cells analyzed (per sample)	3889 [1465.8,5601.5]	5974 [3916.0,8670.7]	0.165
CD1c⁺ cDC			
% of PBMCs	1.2 [0.7,1.6]	2.6 [2.2,2.9]	0.006
HLA-DR MFI	35067 [24107,40366]	50513 [47347,52586]	0.009
CCR2 MFI	17702 [14611,19381]	13188 [12840,13975]	0.033
CD141⁺ cDC			
% of PBMCs	0.1 [0.1,0.2]	0.2 [0.2,0.3]	0.019
HLA-DR MFI	22279 [14672,25703]	46890 [43845,50418]	0.002
CCR2 MFI	5506 [4190,6937]	3669 [3617,4017]	0.069
CD303⁺ pDC			
% of PBMCs	0.5 [0.3,0.7]	0.8 [0.6,1.1]	0.285
HLA-DR MFI	19115 [14493,23608]	18504 [17768,19496]	0.915
CCR2 MFI	14794 [12798,15978]	11782 [11205,12054]	0.028
Reference APCs			
'Candidate nonlymphoid APC' Frequency in % PBMC	13.7 (5.6)	12.6 (4.3)	0.667
B cell ($CD19^+$) HLA-DR MFI	18943 [16549,23917]	22991 [21605,24727]	0.149
Monocytes ($CD14^+$) HLA-DR MFI	12780 [10321,14755]	16264 [15287,18343]	0.022

MFI: Median fluorescence intensity

Table 1: Numeric and functional characteristics of DC subsets compared between RA and controls. Numbers in average +-(SD) resp. mean [IQR]
'Candidate nonlymphoid APC' defined as $HLA\text{-}DR^+CD3^-CD19^-CD56^-CD14^{lo}$

Table 1. Enumeration and expression of DR and CCR2 Expression in DC subsets in RA. Enumeration and expression of HLA-DR and CCR2 in DC subsets of Rheumatoid Arthritis patients compared with controls

of anomalous APC phenotypes. We further hypothesized that alterations in DC subsets are associated with clinical aspects of RA including those driving RA-associated cardiovascular disease.

Methods: RA patients enrolled in a cohort study and healthy donors underwent immunophenotyping to define known DC subsets, including $CD1c^+$ mDC, $CD141^+$ mDC and $CD303^+$ pDC in peripheral blood mononuclear cells (PMBCs). We correlated DC subset features with disease characteristics and cardiac function. To screen for non-lymphoid cells with putative APC potential not conforming to conventional DC paradigms we defined 'candidate nonlymphoid APC' ($DR^+CD3^-CD19^-CD56^-$) as a DC superset. We used t-Distributed Stochastic Neighbor Embedding (t-SNE) to categorize the entirety of non-lymphoid APC candidate cells and identify possible novel RA APC subsets.

Results: Circulating $CD1c^+$ frequencies were, as expected, remarkably decreased in RA (mean 1.0% of PBMCs vs controls 2.6%; p=0.009). Mean $CD141^+$ frequencies were 0.1% (RA) vs 0.2%; p=0.019. $CD303^+$ pDC frequencies did not differ (p=0.285). HLA-DR intensity in both myeloid subsets was significantly lower in RA whereas CCR2 intensity was higher in $CD1c^+$ DC. In RA, a lower $CD1c^+$ frequency was associated with lower cardiac index (corr.=-0.54, p=0.008) and CCR2 expression of $CD1c^+$ DC was associated with lower Ejection Fraction (EF) (corr.=-0.70, p=0.001). Interestingly, despite the decrease in canonical DC; the overall frequencies of 'candidate non-lymphoid APC' did not differ (Table 1) suggesting that the declines of canonical DC were compensated for by increases in other populations of this DR^+ DC superset. t-SNE analysis of healthy controls allowed clear categorization with distinct clusters of APC subsets as well as a homogenous cluster of $CD14^-CD16^-CD11c^+$(Figure 2; orange circle). RA t-SNE showed a de-

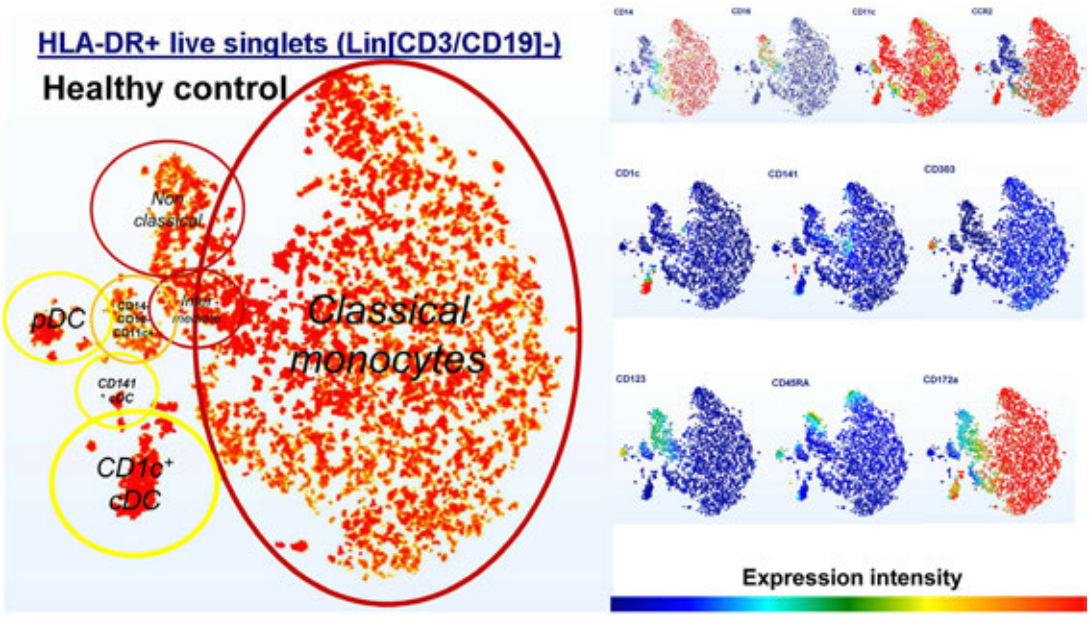

Figure 1. t-SNE representation of non-lymphoid HLA-DR+ cells with APC potential of a healthy donor. Red circles: monocyte populations. Yellow: DC populations. A small homogenous population of CD14-CD16-CD11c+ cells without DC characteristics is shown in orange. Classical monocytes: CD14+CD16+ Intermediate monocytes: CD14+CD16+ Nonclassical monocytes: CD14-CD16+ CD1c+ cDC: CD11c+CD1c+ CD141+ cDC: CD11c+ CD141+ pDC: 11c-CD303+

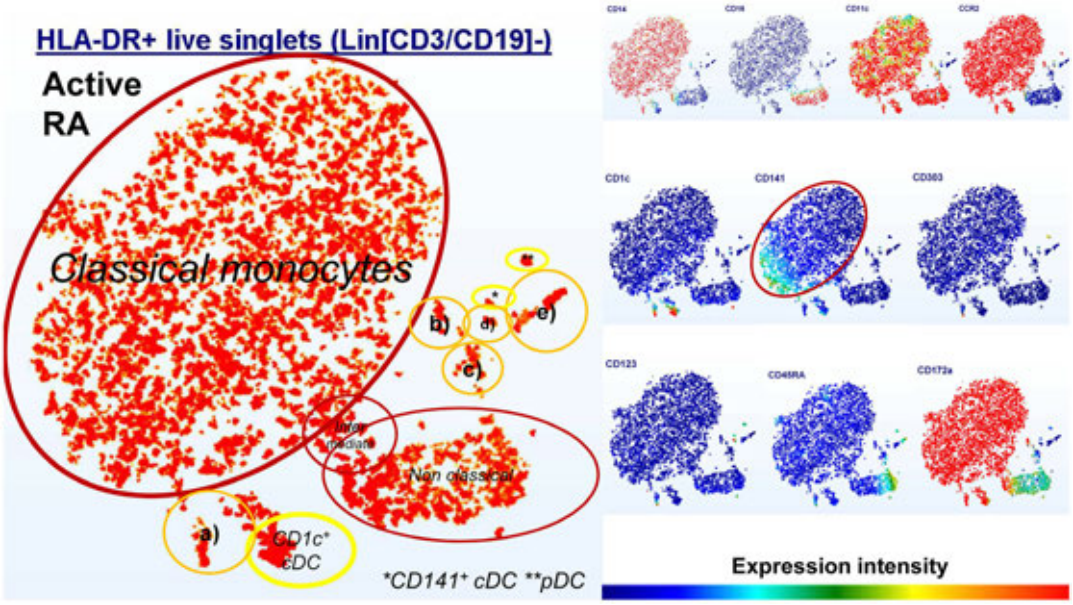

Figure 2. t-SNE representation of non-lymphoid HLA-DR+ cells with APC potential of an RA patient. Red circles: monocyte populations. Yellow: DC populations. Orange: DR+ cells which do not conform to standard DC paradigms but express partial DC markers. a) CD14+ CD1c+ CD141+ CD172a+ CD123+- b) CD14-CD16- 11c+ c) CD14-CD16- CD172a+ d) CD123+ e) CD14- CD16- CD45RA+- Classical monocytes: CD14+CD16+ Intermediate monocytes: CD14+CD16+ Nonclassical monocytes: CD14-CD16+ CD1c+ cDC: CD11c+CD1c+ CD141+ cDC: CD11c+ CD141+ pDC: 11c-CD303+

crease of canonical DC subsets (yellow ellipses) and the appearance of five clusters with some DC features that did not fit accepted definitions (Figure 2a-e)

Conclusion: We found extensive alterations in the DC compartment in RA, including a significant decrease in the major CD1c$^+$ subset and the emergence of anomalous HLA-DR$^+$ non-lymphoid cells with antigen-presenting potential that are candidate DC subsets. The novel subsets included one resembling CD14+ monocyte-derived DC, a subset of which also expressed CD1c in addition to plasmacytoid markers; CD303 and CD123. The remaining populations were distinguished by combinations of CCR2, CD11c, CD123 and CD172a (SIRPα). The association of adverse measures of cardiac function with changes of the DC compartment, including decreases of CD1c$^+$ mDC, emphasize their potential clinical significance.

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Abstract Number: 0059

Evaluation of Potential Mechanisms Underlying the Safety Observations of Filgotinib in Clinical Studies in RA

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Inhibition of the Janus kinase-signal transducers and activators of transcription (JAK-STAT) pathway have demonstrated efficacy in immune-mediated diseases and haves been identified as therapeutic targets for the treatment of rheumatoid arthritis (RA). Differences in JAK inhibitor specificity for JAK1, JAK2, JAK3, and TYK2 may influence their safety profiles, but the mechanism is not known. Selective JAK1 inhibition by filgotinib (FIL) may improve the risk-benefit profile by minimizing non-JAK1–related adverse events. JAK2 inhibition is associated with cytopenias, while JAK3 inhibition has been associated with increased risk for opportunistic infections and chronic low-grade inflammation. In clinical trials, FIL did not negatively impact hemoglobin, LDL/HDL ratios, or natural killer (NK) cell counts.[1-3] Here we compare the in vitro profile of JAK inhibitors with different JAK selectivity profiles at clinically relevant doses to calculate the overall kinetics of suppression of erythroid progenitor cell expansion and maturation, NK cell proliferation, and liver X receptor (LXR) agonist-induced cholesteryl ester transfer protein (CETP) expression.

Methods: JAK inhibitors (FIL, FIL metabolite [GS-829845], baricitinib [BARI], tofacitinib [TOFA], and upadacitinib [UPA]) were evaluated in vitro in human cell-based assays: growth of erythroid progenitors from human cord blood CD34$^+$ cells using a HemaTox™ liquid expansion assay, IL-15–induced NK cell proliferation, and LXR agonist-induced CETP expression in the hepatic cell line (HepG2). Using IC_{50}s generated from these assays and the reported human plasma concentrations of the JAK inhibitors from clinical studies,[4-6] we calculated the target coverage for each compound at clinically relevant doses. The activity of FIL in humans was based on a PK-PD modeling algorithm[7] of FIL + GS-829845.

Calculated Inhibition of Cellular Activity at Clinical Exposures (% inhibition over 24h)								
JAK inhibitor	FIL[a]		BARI		TOFA		UPA	
Dose (mg)	100	200	2	4	5	10	15	30
Early erythroid progenitor	18.9	30.5	17.6	38.2	17.6	28.5	31.1	42.4
Mature erythroid progenitor	42.1	50.4	33.0	45.1	36.7	45.0	46.3	54.7
NK cell proliferation	38.9	52.3	51.7	78.9	75.4	86.0	74.2	84.2
Inhibition of LXR agonist-induced CETP expression	17.3	27.4	inactive					

[a]FIL + GS-829845 composite PD effect

Results: In vitro dose-response assay results were obtained for each inhibitor. Based on these results, human exposure data, and modeled PK-PD relationships, FIL 100 mg and FIL 200 mg result in lower calculated cellular inhibition than the other JAK inhibitors at clinical exposures for NK cell proliferation and CETP expression. There was no obvious difference in the effect of FIL on erythroid progenitor cell differentiation or maturation versus the other JAK inhibitors in these experiments.

Conclusion: JAK1 selectivity of FIL resulted in less inhibition of NK cell proliferation compared with BARI, TOFA, and UPA. FIL also reduced LXR agonist-induced CETP expression, while the other inhibitors did not alter these levels. These results provide a potential mechanistic link to the observed reduction of CETP concentration and activity following FIL treatment, and the observed reduction in LDL:HDL in RA patients.[8]

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Abstract Number: 0060

mTORC1-phosphorylated CXCR3^{+}memory B Cells and Their Potential as a New Mode of Action of TNF Inhibitors in RA

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SESSION INFORMATION
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Background/Purpose: B cells play a crucial role through producing autoantibodies and activating osteoclasts in synovium in rheumatoid arthritis (RA). Recently "Immunometabolism" attract much attention, and mTORC1 is well known as a key player for anabolic change and contributes to B cell activation. However, it remained elusive by which mTORC1 in B cells involved in the pathogenesis of RA.

Methods: PBMCs were obtained from 32 healthy controls (HCs) and 86 patients with RA who were refractory to MTX-treatment and bio-naïve, and analyzed by flow cytometry. In addition, we examined the role of mTORC1 for induction of chemokine receptors on B cells in vitro.

Results: Baseline characteristics of patients with RA in this study were males : females =21:65, age 55.8 years, disease duration 55.8 months, stage I/II/III/ IV:35/33/9/9, MTX dose 13.8mg/week, tender joints 9.1, swollen joints 7.2, DAS28-CRP 4.7, DAS28-ESR 5.4, CDAI 25.9, SDAI 28.2, RF169.6, anti-CCP Abs 336.0, HAQ 1.2. The percentage of $CXCR3^+CD27^+CD19^+$ cells among $CD19^+$ cells decreased in the periphery of patients with RA compared to those of HCs. The level of mTORC1 phosphorylation (p-mTORC1) enhanced in $CXCR3^+CD27^+CD19^+$ cells, but not in $CXCR3^-CD27^+CD19^+$ cells from patients with RA. The level of p-mTORC1 in $CXCR3^+CD27^+CD19^+$ cells were correlated with tender joints, swollen joints, disease activity such as DAS28-CRP, CDAI, SDAI, but not RF and anti-CCP antibodies. We examined the change of percentage of $CXCR3^+CD27^+CD19^+$ cells and the level of p-mTORC1 before and at 1 year after treatment with biologics (37 patients, TNF inhibitors (n=19: adalimumab:11, certolizumab:7, etanercept:1), abatacept (n=16), tocilizumab (n=2)). The percentage of $CXCR3^+CD27^+CD19^+$ cells were recovered and the level of p-mTORC1 decreased selectively in TNF inhibitors treatment group, but not in abatacept treatment group at 1 year. Finally, we examined the role of mTORC1 for induction of chemokine receptor expression on B cells in vitro. Combined stimulation of BCR, CD40L and IFN-γ induced CXCR3 expression on B cells, which were abrogated by mTORC1 inhibitors, Rapamycin. It has been reported that concentration of CXCL10 (IP-10), ligand of CXCR3, increased in RA synovium. We found that TNF-α stimulation induced CXCL10 production from RA patients-derived fibroblast like synoviocytes (FLS), which was abrogated by TNF inhibitors.

Conclusion: Taken together, activation of mTORC1 is involved in the accumulation of CXCR3-positive memory B cells in RA synovium and TNF inhibitors possibly target at this in patients with RA.

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MSD, Astellas, Abbvie, Eisai, 2, Novartis, 8, Ono, 2, Pfizer, 5, 8, Pfizer Inc, 8, Roche, 5, Sanofi, 2, Takeda, 2, 8, Teijin, 8, UCB, 2, YL Biologics, 8.

Abstract Number: 0061

Lyn-Deficient Murine Lupus Is Exacerbated by Glucocorticoid-Induced Leucine Zipper (GILZ) Deficiency

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: *Lyn*-deficient mice develop hyperactive B cells, excess IL-6 production, and nephritis. Mice deficient in glucocorticoid-induced leucine zipper (GILZ), an intracellular protein involved in glucocorticoid effects on immunity, also develop spontaneous lupus-like autoimmunity and excess B cell activation (Jones 2016). However, whether GILZ is operative as a suppressor in lupus-prone *Lyn*-/- mice is unknown.

Methods: We compared WT C57Bl/6 mice to *Lyn* knockout (KO) mice and *Lyn*KO mice crossed to a GILZ-deficient background (GILZ- *Lyn* double knock out (DKO)) mice. The effects of GILZ deficiency on *Lyn*KO phenotype, including spleen weight, autoantibodies, nephritis, and cytokines including Type I interferon-induced genes (ISG) were examined.

Results: Lupus-like autoimmunity was increased in GILZ-*Lyn* DKO mice, compared to *Lyn*KO, including increased spleen weight and more severe glomerulonephritis, especially crescents and segmental necrosis. In contrast, serum autoantibodies (dsDNA, Sm, histone, Jo-1, Scl-70, SSA, SSB, U1RNP, Ro52,) were not increased in GILZ-*Lyn* DKO mice compared to *Lyn*KO mice. Serum IL-6, BAFF, IL-17A, IL-18, and TNF were increased in GILZ-*Lyn* DKO mice. A panel of ISG (*ifi44, usp18, oas3, cxcl10, isg15, mx1, irf7, stat1* and *ifit3)* and an overall ISG score were also significantly increased in GILZ-*Lyn* DKO mice.

Conclusion: The *Lyn*KO lupus-prone model was significantly exacerbated by GILZ deficiency, an effect accompanied by evidence of activation of the Type I IFN program. This suggests that endogenous GILZ exerts an inhibitory effect on IFN pathways in this lupus model, and thus that GILZ regulates inflammation in SLE by inhibiting IFN responses downstream of autoantibodies.

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Abstract Number: 0062

Human Gingiva-derived Mesenchymal Stem Cells Are Therapeutic in Lupus Nephritis Through Targeting of CD39-CD73 Signaling Pathway

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Cell specific and cytokine targeted therapeutics have underperformed in systemic lupus erythematosus (SLE) in spite of numerous targets examined and clinical trials conducted. Mesenchymal stem cells (MSCs), especially bone marrow derived MSCs (BMSCs), have emerged as a novel therapy to address the dysregulation in autoimmune diseases because of their immunomodulatory and tissue regeneration properties. Nonetheless, BMSCs have limitations such as heterogeneous cell populations, dysfunction of autologous BMSCs and tumorigenesis. Compared with BMSCs, human gingiva derived MSCs (GMSCs) are superior in regulating immune responses.

Methods: In this study, we prepared gingiva-derived mesenchymal stem cells and adoptively transferred them to NZM2328 mice, a lupus strain that spontaneously develop lupus nephritis with predilection for female mice.

Results: We demonstrate that the adoptively transferred GMSC home to the kidney quickly and have a robust therapeutic effect. Specifically, the administration of GMSCs limits the development of autoantibodies as well as proteinuria, decreases the frequency of plasma cells and lupus nephritis histopathological scores. We further observed that GMSCs directly targeted B cells through suppression of activation and proliferation, plasmocyte differentiation and autoantibody production in an inflammatory milieu. The blockage of CD39-CD73 pathway dramatically abrogated the suppressive capacities of GMSCs in vitro and in vivo and highlights the significance of this signaling pathway in SLE.

Conclusion: Collectively, manipulation of GMSCs provides a promising strategy for the treatment of patients with SLE and other autoimmune diseases.

Disclosure: S. Zheng, None; **J. Wang**, None; **J. dang**, None; **N. Olsen**, None; **W. Jarjour**, None.

Abstract Number: 0063

The Role of the Intestinal Microbiota in Lupus Nephritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The bacterial gut microbiota (GM) exerts substantial influence over the host immune system and dysbiosis of this microbial community has been associated with end-organ damage in chronic inflammatory conditions. The role that pathobionts and GM dysbiosis play in the pathogenesis of systemic lupus erythematosus (SLE) or lupus nephritis (LN) is not fully appreciated. We hypothesized that the GM potently influences the pathogenesis of LN through the induction of host immune processes and that shifts in the bacterial GM would reflect what has been published in lupus patients. This project was focused on the ability of gut dysbiosis to promote kidney damage in a LN mouse model. The pathobiont commensal, segmented filamentous bacteria (SFB), is applied in this study to test this overall hypothesis.

Methods: Using oral gavage, we colonized NZM2410 mice with SFB- or no SFB-fecal homogenates in a sterile vivarium. Colonization was confirmed via repeated fecal DNA PCR analysis using SFB-specific primers. Serum was collected and mice were euthanized at 26 or 30 weeks. The severity of kidney damage was assessed via immunohistochemistry (IHC) and RNA-ISH. Flow cytometry was also performed on small intestinal lamina propria cells. To analyze the makeup of the fecal bacterial metagenome of these mice through 16S rDNA analysis we used Illumina 16S sequencing technology and compared the resulting reads to the Silva fecal bacterial metagenomics database.

Results: We demonstrated that inoculation with SFB was associated with worse renal dysfunction and glomerulonephritis. We also discovered that serum autoantibodies and proinflammatory cytokines were elevated in SFB positive mice versus controls. Initially, we expected to find infiltrating Th17 cells in the kidneys of SFB positive mice. However, while we did not detect intra-renal Th17 cells by immunohistochemistry, we found that SFB positive mice had significantly increased numbers of M2-like F4/80+CD206+ macrophages when compared to SFB negative mice. Lastly, we show that SFB positive NZM2410 mice may harbor intestinal barrier dysfunction. A very recent human LN study also reported related findings. This particular finding suggests a potential mechanism by which commensal bacteria can activate the host immune system.

We identified unique bacterial compositions at multiple taxonomic levels with respect to time of disease and SFB positivity. We also show that many of the taxonomic shifts observed in our study, even within certain genera, are in congruence with lupus-GM human studies. Finally, we identified a particular *Ruminococcus* species group that is enriched in SFB positive versus SFB negative mice. Importantly, this group is significantly enriched in SFB positive mice during late disease versus SFB positive mice at pre-/early disease which suggests a disease activity.

Conclusion: Collectively, the work presented herein helps to address an unfulfilled knowledge gap in autoimmunity. Our findings suggest that changes to the commensal GM may have an important role in renal dysfunction and promoting an overall proinflammatory state in LN. Importantly, this work provides suggestions for novel therapeutic targets that may be useful in treating patients suffering from LN.

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Abstract Number: 0064

Rab4A Controls mTOR Pathway Activation, Pro-inflammatory Lineage Development, and Disease Pathogenesis in Lupus-prone Mice

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Mouse models of SLE have been indispensable tools for studying disease pathogenesis; however, each model only recapitulates limited aspects of lupus. SLE1.2.3. (TC) mice are mice homozygous for three NZM2410-derive lupus susceptibility loci on the C57Bl/6J background. These mice develop systemic autoimmunity with fatal glomerulonephritis and die typically by 12 months of age. The polymorphic Rab4a locus has been associated with genetic susceptibility and protection from lung disease in SLE patients and has been found to be overexpressed in T cells of patients and mice with SLE. To determine the impact of this gene on disease development, the TC mice has been backcrossed with C57Bl/6 wild-type (WT) mice that carry floxed Rab4A^{Q72L} (TC-FL) alleles or lack Rab4A in T cells (TC-KO).

Methods: Proteinuria was assessed by the Bradford assay. ANA production was measured by ELISA. Mice were sacrificed around 50 weeks of age for analysis via flow cytometry, Seahorse assay and mass spectrometry. Histological scoring for glomerulonephritis (GN) was done blindly by Dr. Mark Haas.

Results: TC mice had increased proteinuria (males 160%, p=0.035, females 230%, p=0.008) over matched controls. Deletion of Rab4A in T cells reduced proteinuria (-50%, p=0.015) in female TC-KO mice relative to TC-FL mice at 21 and 40 weeks of age (TC-FL: 0.85±0.2 mg/ml, n=22; TC-KO: 0.39±0.1 mg/ml; n=12; p=0.041). Similar trends were noted in male mice (TC-FL: 1.01±0.1 mg/ml, TC-KO: 0.79±0.1 mg/ml; p=0.048). ANA production was reduced in male (-70.3%, p=0.009) and female (-24%, p=0.003) TC-KO mice relative to TC mice at 23 weeks of age. GN scores were significantly elevated (425%, p=0.009) in female TC mice compared to WT control at 53 weeks of age. Importantly, TC-KO mice showed a reduction (-40%; p=0.0342) in GN severity over TC-FL mice.

Immunophenotyping unveiled a 45% depletion of CD4$^+$ T cells (p=0.003) and 50% expansion of CD8$^+$ T cells (p=0.016) in TC-KO female mice relative to TC-FL controls. Interestingly, mTORC1 activity in CD4$^+$ was elevated by 100% in TC and by 290% (p=3E-05) in TC-FL mice, an effect that is diminished in TC-KO mice by 47% compared to TL-FL mice (p=0.0395). The same effect was not observed in CD8$^+$ T cells or B cells of TC-KO mice. Additionally, IFNy-producing

Background Model	Genetic modification	Function	Name (in abstract)
C57.Bl6J	WT	Wild type Rab4a	WT
C57.Bl6J	Rab4aQ72L	Constitutively active Rab4a	WT-FL
C57.Bl6J	Rab4aQ72L-CD4Cre	Deletion of Rab4a in CD4$^+$ cells	WT-KO
SLE1.2.3.	WT	Wild type Rab4a	TC
SLE1.2.3.	Rab4aQ72L	Constitutively active Rab4a	TC-FL
SLE1.2.3.	Rab4aQ72L-CD4Cre	Deletion of Rab4a in CD4$^+$ cells	TC-KO

$CD4^+$ T cells were expanded by 370% in TC (p=0.042) and by 310% in TC-FL mice (p=0.025). These proinflammatory cells were depleted by 47% in the TC-KO mice relative to lupus-prone TC mice.

Relative to WT controls, flow cytometry revealed elevated mitochondrial mass (+38%, p=0.0416) and that occurred with a reduction in mitochondrial potential in $CD4^+$ T cells of TC mice (53%, p=0.009). Seahorse metabolic analysis unveiled increased mitochondrial basal respiration (+80%, p=0.024), maximal respiration (+48%, p=0.02), ATP production (+84%, p=0.023) and spare respiratory capacity (+174%, p< 0.001) in $CD8^+$ T cells of TC-WT mice relative to WT controls.

Conclusion: These findings establish how Rab4A promotes mTOR pathway activation, pro-inflammatory T cell lineage development, and disease pathogenesis through its influence on mitochondrial metabolism in SLE. Therefore, inactivation of Rab4A may have therapeutic potential in SLE.

Disclosure: N. Huang, None; **Z. Lai**, None; **B. Wyman**, None; **T. Winans**, None; **M. Duarte**, None; **J. Lewis**, None; **M. Haas**, None; **L. Morel**, None; **A. Perl**, None.

Abstract Number: 0065

CD6 Modulation Ameliorates Skin and Kidney Disease in a Spontaneous Murine Model of SLE

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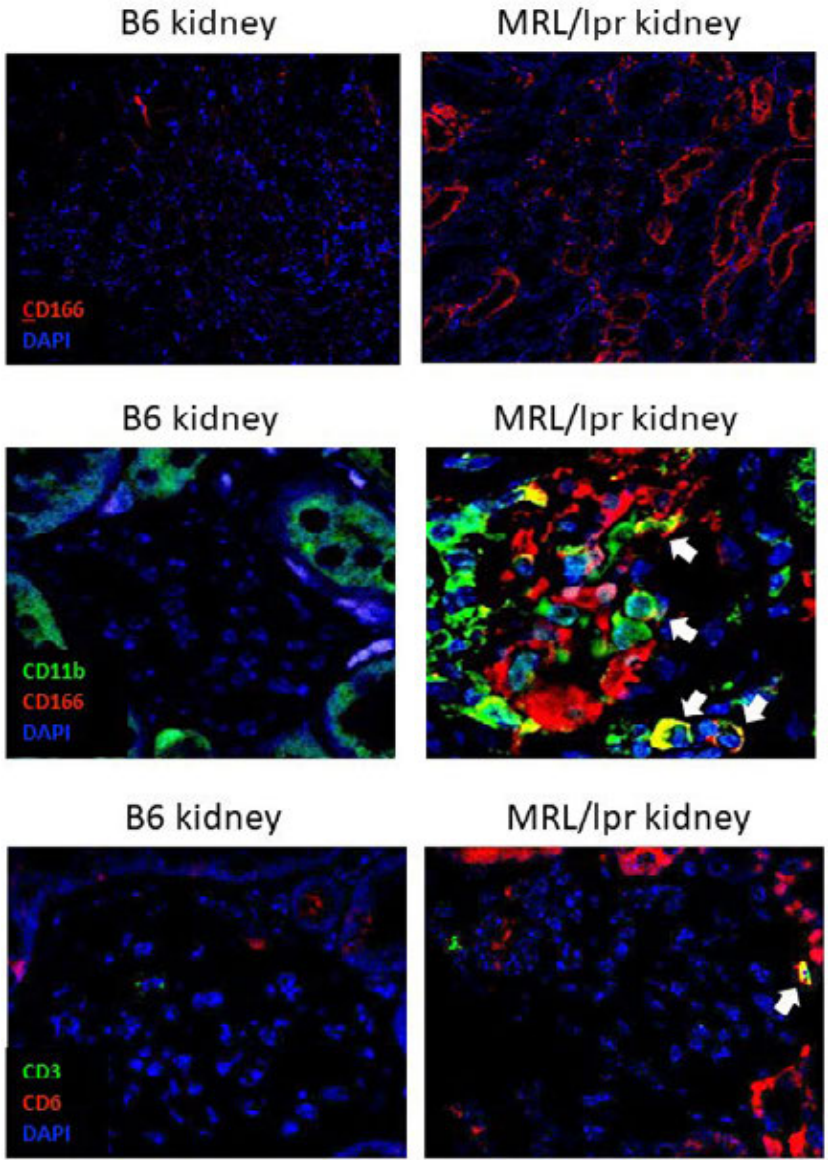
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: T cells are an important contributor the pathogenesis of SLE and its various end organ manifestations. Thus, they present themselves as potential therapeutic targets; however, the optimal approach to targeting T cells in SLE still remains under investigation. CD6 is a co-stimulatory receptor, predominantly expressed on T cells, that binds to activated leukocyte cell adhesion molecule (ALCAM), a ligand expressed on antigen presentation cells and various epithelial and endothelial tissues. The CD6-ALCAM pathway plays an integral role in modulating T cell activation, proliferation, differentiation and trafficking. In this study, we assessed the expression of CD6 and ALCAM within the context of a murine model of SLE, and then subsequently targeted this signaling axis to determine its role in the pathogenesis of disease.

Methods: The MRL/lpr mouse is a spontaneous murine model of SLE, which exhibits systemic autoimmunity, nephritis, and skin disease. In an initial experiment, 6 month old MRL/lpr mice and B6 kidneys were stained for the presence of both ALCAM and CD6. In a separate experiment, female MRL/lpr mice were aged to 9-10 weeks of age, and then treated with either anti-CD6 monoclonal antibody (60 ug/dose, IP twice per week), isotype control (60 ug/dose, twice per week), or cyclophosphamide (25 mg/kg, once per week). We also included a no treatment group, and a group of MRL/MpJ mice, a congenic healthy control strain. Baseline levels of anti-DNA antibodies, weight, and proteinuria in the MRL/lpr groups were similar. Mice were monitored weekly for proteinuria, lymph node swelling, and macroscopic skin lesions.

Results: MRL/lpr mice at 6 months of age show increased levels of ALCAM expression in their kidneys, both within their tubules and glomeruli, compared to B6 healthy control mice (shown are images representative of 3 mice per



group). Additionally, macrophages infiltrating into the glomeruli of MRL/lpr mice were ALCAM+ (white arrows, top panel) and were paired with a concomitant increase in CD6+ T cell infiltration (white arrows, bottom panel). Consequently, in a separate study, we blocked this signaling axis using a monocolonal antibody for CD6. At 19 weeks of age, mice treated with anti-CD6 show improved proteinuria compared to isotype control mice ($p< 0.05$). MRL/lpr mice develop lymphoproliferative disease which results in abnormally large lymph nodes. Assessing lymphadenopathy at 19 weeks of age, we noted a significant improvement in the anti-CD6 treated mice, compared to the isotype control ($p< 0.05$). MRL/lpr mice also develop severe skin lesions that have similar pathology to cutaneous lupus. Macroscopic scoring of these lesions showed a significant improvement in the skin disease of the anti-CD6 treated mice compared to the isotype control group ($p< 0.05$).

Conclusion: Within a spontaneous model of SLE, anti-CD6 treatment ameliorated multiple end organ pathologies, namely in the kidney and skin, while also significantly reducing the lymphoproliferative phenotype of this model. Overall, these results indicate that targeting the CD6-ALCAM pathway may have promising therapeutic potential for multiple end organ pathologies within SLE.

Upregulated expression of ALCAM (CD166, red), is seen in the tubules of 6 month old MRL/lpr mice, compared to age matched B6 mice (top panel). Looking more closely at the glomeruli, we note ALCAM expression is increased in lupus mice, including on macrophages (CD11b+, white arrows) infiltrating into the glomerulus (middle panel). Finally, CD6+CD3+ T cells are also noted infiltrating the glomeruli of MRL/lpr mice (white arrow, bottom panel). Shown are representative images from 3 mice per group.

Disclosure: S. Chalmers, Equillium, Inc, 2; **S. Garcia**, None; **R. Ayilam Ramachandran**, None; **C. Mohan**, Equillium, 5, Equillium, Inc, 5; **J. Ampudia**, Equillium, Inc, 3; **C. Ng**, Equillium, Inc, 3; **S. Connelly**, Equillium, Inc, 3, 6, Equillium, 3; **C. Putterman**, Equillium, 5, Equillium, Inc, 2, 5, Exagen, 2.

Abstract Number: 0066

Amelioration of Immune Complex-Mediated Glomerulonephritis by CD6 Modulation

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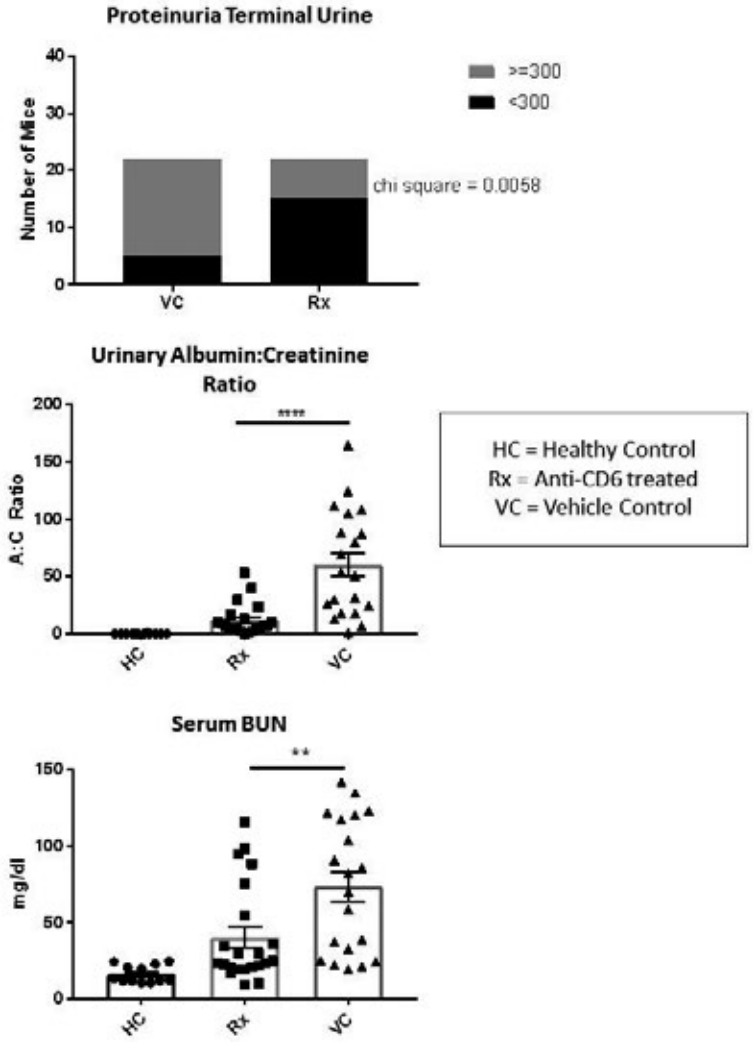
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: CD6 is a co-stimulatory receptor on T cells, that binds to activated leukocyte cell adhesion molecule (ALCAM), a ligand expressed on antigen presentation cells and epithelial and endothelial tissues. The CD6/ALCAM pathway plays an integral role in modulating T cell activation and trafficking, making this an integral pathway in immuno-inflammation. Increased levels of CD6 are associated with pathogenic T cell responses, suggesting that the CD6/ALCAM pathway is a contributor to disease pathogenesis. T cells are a key cellular mediator in both systemic lupus erythematosus (SLE) and lupus nephritis (LN), as they amplify the autoimmune response and inflammation and contribute to end organ damage. Thus, we designed an experiment to target them via CD6 modulation.

Methods: Nephrotoxic serum nephritis (NTN) is a validated, short-term model of LN. Disease was induced in two separate cohorts of female 129/svJ mice, both aged to 10 weeks. Mice were immunized with rabbit IgG and CFA on day 0 to create mouse anti-rabbit antibodies, which then cross-reacted with nephrotoxic rabbit serum given on day 5, causing an antibody-mediated nephritis similar in pathology to LN. To assess the importance of the CD6/ALCAM pathway in LN pathogenesis, mice were treated 3x per week with an anti-CD6 monoclonal antibody (mAb) (60ug/dose, n=23), or with vehicle control (n=23). Healthy mice (immunized with rabbit IgG, but not given nephrotoxic serum) were also included as a control (n=12). We monitored the progress of kidney disease via proteinuria (uristix), urinary albumin:creatinine ratio, and serum blood urea nitrogen (BUN) to assess the effect of the anti-CD6 treatment on both cohorts. To assess the affect of treatment on immune cell infiltration, flow cytometry, RT-PCR, and immunofluorescent staining was completed at termination.

Results: Mice treated with the anti-CD6 mAb displayed decreased levels of proteinuria ($p< 0.001$) compared to vehicle control mice. This result was confirmed by measuring albumin:creatinine ratios in terminal urine ($p< 0.0001$). We also found a significantly improved BUN ($p< 0.01$) when comparing treated mice to vehicle control mice. To ensure that anti-CD6 treatment did not interfere with the induction of the NTN model, we measured mouse anti-rabbit IgG levels and rabbit anti-mouse glomerular basement membrane (GBM) levels and found no difference between the groups. RT-PCR revealed significantly decreased levels of VCAM and RANTES in the kidneys of treated mice, while



anti-inflammatory IL-10 was increased, compared to control sick mice. Flow cytometry results indicated decreased levels of renal-infiltrating activated T cells (CD4+CD25+CD69+, $p < 0.01$). Immunofluorescent staining and histology results are pending.

Conclusion: Inhibiting the CD6-ALCAM pathway with an anti-CD6 treatment is beneficial in ameliorating the nephritis associated with nephrotoxic antibody administration, an inducible model of lupus nephritis. These results indicate a potentially promising therapeutic option which is more selective than the immunosuppressive therapies currently offered.

Mice treated with a monoclonal antibody to CD6 displayed decreased levels of proteinuria as determined by semi-quantitative uristix (top image), improved urinary albumin:creatinine ratios (middle panel) and lower levels of blood urea nitrogen (BUN; bottom panel), compared to vehicle control treated mice.

Disclosure: S. Chalmers, Equillium, Inc, 2; **S. Garcia**, None; **J. Ampudia**, Equillium, Inc, 3; **C. Ng**, Equillium, Inc, 3; **S. Connelly**, Equillium, Inc, 3, 6, Equillium, 3; **C. Putterman**, Equillium, 5, Equillium, Inc, 2, 5, Exagen, 2.

Abstract Number: 0067

Dermal Lymphatic Dysfunction Is Associated with Disease Activity in the MRL/*lpr* Lupus Model

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Lymphatic vessels are important in limiting the extent and duration of peripheral immune response, both by transporting cellular debris, inflammatory cells and excess interstitial fluid away from the site of inflammation, as well as through the direct modulation of the immune response by the lymphatic endothelial cells (LECs). Disruption in lymphatic function has been implicated in several models of chronic inflammatory diseases, including RA, psoriasis, and IBD. Cutaneous inflammation is a major feature of SLE, and is an important impediment to patients' quality of life. The role of the lymphatic system in SLE, and its contribution to the cutaneous inflammatory phenotype of SLE specifically have not been described to date.

Methods: 7-10 weeks old ('pre-diseased') and 12 weeks old ('diseased') MRL/*lpr* (*lpr*) mice and age-/sex-matched MRL controls were evaluated at baseline, and after exposure to 2000-25000 J/m^2 of ultraviolet radiation (UVR). Lymphatic function was assessed in 2 ways: 1) 'Drainage' - 1μL of 2% evans blue (EB) injected intradermally to the ear, followed by measurement of EB concentration in the draining lymph node (dLN) 1 minute later; or 2) 'Effective clearance' - evaluation of the residual dye concentration in the ear 18-24 hours following EB injection. EB concentration was evaluated by extraction of the dye from the tissue by immersion in formamide, followed by spectrophotometric evaluation of the fluid. Flow cytometry of the contralateral ears and dLNs was performed. Groups were compared with the Mann-Whitney *U* test; data is presented as median (interquartile range), with a two-tailed *p*-value of < 0.05 considered significant.

Results: Lymphatic clearance of EB from the ears of 'diseased' *lpr* mice was significantly impaired compared with controls (2.3-times residual EB in *lpr* ears at 24 hours post-EB injection, compared with controls, $p=0.029$). This difference in effective lymphatic clearance was not observed in 'pre-diseased' mice (0.85 (0.53-0.92) vs. 1 (0.79-1.21) in *lpr* vs. controls, $p=0.8$); indicating a possible association of dermal lymphatic dysfunction with disease activity (Figure 1). Similarly, when cutaneous inflammation was induced by UVR in 'pre-diseased' *lpr* and MRL mice, at 1 month-post UVR the *lpr* mice demonstrated significantly higher numbers of ear LECs than controls (1.42 (1.10-16.25) vs. 1 (0.95-1.05) of LECs per ear, normalized to MRL controls, $p=0.009$), but without the expected corresponding improvement in lymphatic drainage (0.92 (0.50-2.74) vs. 1 (0.57-1.43) EB in dLN, normalized to MRL controls, $p=0.937$); likely indicating a relative dysfunction in the *lpr* lymphatic vessel function.

Conclusion: The lymphatic network has long been known to be important in immune response regulation and tolerance mechanisms. SLE is thought to be the prototypical systemic inflammatory disease, but the role of the lymphatic system was never characterized in this setting. Here we provide evidence of impaired lymphatic function in the *lpr* lupus strain associated with increased disease activity, both due to age and UVR-induced inflammation. These findings may potentially point to a novel focus of study and intervention in this often devastating, yet still elusive disease.

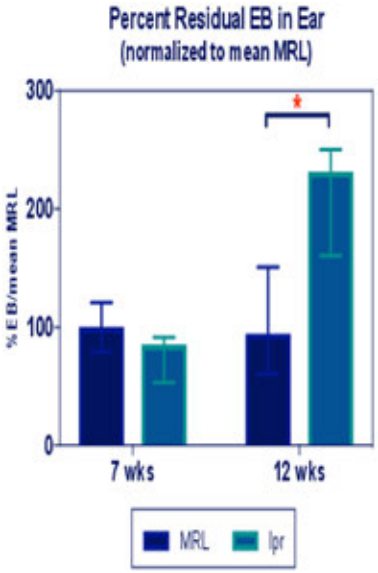

Figure 1. Impaired dermal EB clearance in diseased lpr mice. Quantification of residual EB in ear, 18-24 hours following EB injection. 7 weeks: MRL, n=3; lpr, n=2; 12 weeks: n=4 in both groups. *p<0.05. Bars indicate median with range.

Disclosure: N. Schwartz, None; **T. Li**, None; **S. Chyou**, None; **W. Shipman**, None; **T. Lu**, None.

Abstract Number: 0068

Inactivation of Transaldolase and HRES-1/Rab4 Predisposes to Hepatitis in a Mouse Model of Systemic Lupus Erythematosus

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SESSION INFORMATION
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Background/Purpose: Deficiency of transaldolase (TAL) in systemic lupus erythematosus (SLE) predisposes to oxidative stress mediated autoimmune hepatitis[1, 2]. Along with TAL, HRES-1/Rab4 (Rab4A), a small GTPase responsible for mitochondrial turnover, is overexpressed in T cells of SLE patients[3] and livers of lupus-prone mice[2]. The expression of Rab4A is dependent on TAL activity[2]. Therefore, we investigated the impact of TAL and Rab4A in pristane-induced and spontaneous models of SLE.

Methods: C57Bl/6J wild-type (WT) mice and strains constitutively lacking TAL (TALKO)[1] or Rab4A in T cells were injected intraperitoneally with pristane (500μL/20g body weight). Mice lacking Rab4A were generated on both C57Bl/6J and lupus-prone SLE1.2.3. backgrounds. The number of inflammatory foci was used as a measurement of lymphocytic inflammation within the mouse livers. Vasculitis measurement[4] was adapted for H&E-stained liver sections. Student's T test was used to test significance; p values < 0.05 were considered significant for hypothesis testing.

Results: Among pristane-injected female mice, TALKO mice had more inflammatory cells relative to WT controls (p=0.0309). C57Bl/6J Rab4ACD4-KO mice had fewer inflammatory foci (p=0.0456), inflammatory cells (p=0.0497), and

Female Mice: TAL	Wild Type (n=4)	TALKO (n=2)	P value
Inflammatory Cells	170.750±98.738	878.500±378.5	0.0308*
Inflammatory Foci	1.750±0.750	3.500±1.500	0.147
Cells/Focus	61.250±31.0264	364.250±264.250	0.227

TAL Effects on Female Mice

Female Mice: Rab4A	$Rab4A^{WT}$ (n=5) [A] (Wild Type)	$Rab4A^{CD4\text{-}KO}$ (n=5) [B] (T Cell Knock Out)	$Rab4A^{Q72L}$ (n=5) [C] (Constitutively Active)	P value [A vs B]	P value [A vs. C]	P value [B vs C]
Inflammatory Cells	1138.4±345.284	298.4±113.891	315±116.070	0.0497*	0.0537	0.921
Inflammatory Foci	27±8.081	4±1.304	11.8±5.014	0.0456*	0.149	0.198
Cells/Focus	40.843±8.281	58.695±19.61	32.878±5.977	0.426	0.458	0.266
Number of Vasculitis	22.8±5.860	3±1.049	9.2±5.171	0.0267*	0.120	0.300
Vasculitis Score	3.070±0.113	2±0.324	2.935±0.182	0.00161*	0.524	0.0139*

Rab4A Effects on Female Mice

SLE Genotype Effect: Female and Male	C57Bl/6J WT (n=2) [A; female]	SLE1.2.3. WT (n=2) [B; female]	P value [A vs B]	C57Bl/6J WT (n=3) [C; male]	SLE1.2.3. WT (n=3) [D; male]	P value [C vs D]
Inflammatory Cells	260.5±135.5	1144±222	0.0384*	343.000±195.832	189.333±75.974	0.252
Inflammatory Foci	5.5±2.5	23.5±3.5	0.0263*	10.000±5.196	6.333±2.403	0.278
Cells/Focus	45.583±3.917	51.224±17.0759	0.389	28.442±5.881	28.747±5.967	0.486
Number of Vasculitis	13.5±1.5	28.0±9.0	0.253	11.333±8.838	9.000±1.155	0.408
Vasculitis Score	3.407±0.162	1.875±0.133	<0.0001*	1.735±0.114	1.704±0.176	0.876

SLE Genotype Effects on Female and Male Mice

vasculitis events (p=0.0266) compared to WT controls. The average vasculitis score was also decreased in C57Bl/6J Rab4ACD4-KO animals compared to C57Bl/6J Rab4AWT (p=0.00160) and C57Bl/6J Rab4AQ72L (p=0.0139) animals. The number of inflammatory foci (p=0.0263) and inflammatory cells (p=0.0384) was significantly higher in SLE1.2.3. mice versus C57Bl/6J controls. There was no difference in vasculitis incidents between the two genotypes; the vasculitis score was lower in SLE1.2.3 mice vs. C57Bl/6J (P< 0.0001). Relative to WT C57Bl/6J controls, SLE1.2.3. mice or pristane-injected TALKO male mice failed to show differences in liver inflammation.

Conclusion: Constitutive deletion of TAL or T-cell-specific deletion of Rab4A predisposes to inflammation and vasculitis in the liver, which is also enhanced in lupus-prone mice. These changes were confined to females, which is consistent with a similar gender bias in humans.

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Disclosure: A. Patel, None; **N. Huang**, None; **A. Perl**, None.

Abstract Number: 0069

Treatment of Lupus-prone MRL-*lpr* Mice with the Mitochondrial Antioxidant MitoQ

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Systemic Lupus Erythematosus (SLE) is characterized by a type I Interferon (IFN-I) gene signature in peripheral blood lymphocytes (PBL), which contain enlarged mitochondria and reactive oxygen species (ROS). SLE patients also manifest an unusual population of CD4-CD8- T cells that arise during homeostatic proliferation of CD8+ T cells. We have previously shown that ROS is sufficient to induce oligomerization of MAVS (**m**itochondrial antiviral stimulator) and type I Interferon (IFN-I) production, both of which was reversible with the mitochondrially targeted antioxidant, MitoQ. In addition, SLE patients manifested spontaneous MAVS oligomerization. CD4-CD8- T cells from MRL-*lpr* mice also manifested spontaneous oligomerization of MAVS and an IFN-I gene signature. Based on these collective observations, we elected to test the therapeutic potential of MitoQ in lupus-prone MRL-*lpr* mice.

Methods: MitoQ was administered in drinking water (200 or 400 mM) to MRL-lpr mice from weaning for the next 11 weeks.

Results: MitoQ produced a reduction in MAVS oligomerization in CD4-CD8- T cells and serum IFN-I. There was no effect on adenopathy or autoantibody production, but MitoQ did result in decreased dermatitis, immune complex deposition in kidneys, and NETosis (Fig. 1).

Conclusion: These findings suggest that SLE may be in part a disorder of mitochondrial dysfunction and ROS production, contributing to MAVS oligomerization and IFN-I stimulation. It also suggests mitochondrially targeted antioxidants as a therapeutic intervention for SLE.

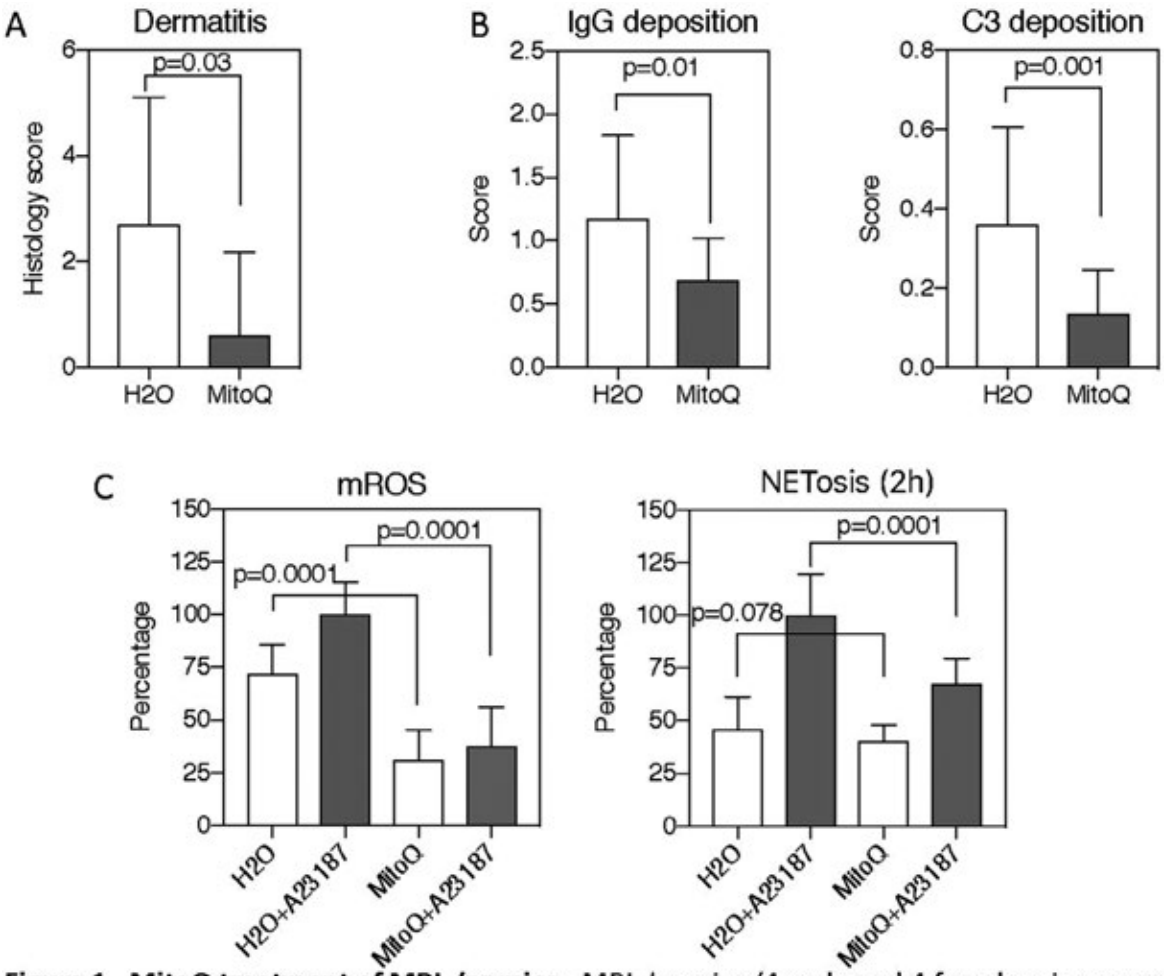

Figure 1. MitoQ treatment of MRL-*lpr* mice. MRL-*lpr* mice (4 male and 4 female mice per group) were administered water alone or MitoQ (200 μM) in drinking water beginning at weaning. After 11 weeks mice were assessed for (A) dermatitis by histologic score, (B) IgG and C3 deposition of kidneys, and (C) neutrophil production of ROS or NET formation without or with A23187 ionophore stimulation.

Disclosure: R. Budd, None; **K. Fortner**, None; **L. Blanco**, None; **M. Kaplan**, None; **A. Perl**, None; **I. Busliewicz**, None; **G. MacPherson**, MitoQ, 3; **M. Murphy**, MitoQ, 4.

Abstract Number: 0070

Angiotensin Receptor Blockers Prevent Loss of Dendritic Complexity in a Lupus Mouse Model of Cognitive Impairment

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: SLE – Animal Models Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Cognitive dysfunction affects the majority of patients with systemic lupus erythematosus (SLE), however it is grossly under-recognized, the pathogenesis is poorly understood, and no treatments are available. The anti-NMDA receptor (NMDA) antibody, a subset of anti-DNA antibodies cross-reactive with the NMDAR, and termed DNRAbs, has been strongly associated with cognitive dysfunction in both mouse models and humans. In a mouse model, DNRAb-mediated brain pathology proceeds through two stages: excitotoxic neuron loss, followed by persistent neuroinflammation resulting in alteration in neuronal integrity and spatial memory impairment. The renin-angiotensin system is emerging as a promising target in neurodegenerative diseases with angiotensin II as the most neuroactive peptide. We have previously shown that ACE inhibition can preserve and treat the dendritic damage and cognitive impairment that occurs in DNRAb-positive mice. We now tested whether direct inhibition of angiotensin signaling with angiotensin receptor blockers (ARBs) has a similar neuroprotective effect.

Methods: Mice immunized with DNRAbs and then treated with lipopolysaccharide (LPS) to breach the blood brain barrier and allow transient access of antibody to the hippocampus, were studied for loss of neuronal dendritic complexity using Golgi and analyzed using Sholl analysis. Mice received the ARB telmisartan in drinking water or control (regular drinking water) for two weeks, starting one week post LPS.

Results: Dendritic complexity was preserved in DNRAb-positive mice treated with telmisartan compared to those not treated ($p< 0.001$, KS). Moreover, dendritic complexity was considered normal in telmisartan-treated mice when compared to DNRAb-negative mice (not significant, KS).

Conclusion: These findings suggest that angiotensin receptor blockers can preserve neuronal dendritic complexity in the DNRAb mouse model. Future studies looking at microglial activation and spatial memory behavioral deficits are warranted. Angiotensin receptor blockers could be a potential therapeutic target for cognitive impairment in SLE and may serve as an alternative to ACE inhibitors in those that cannot tolerate them.

Disclosure: L. El Khoury, None; **N. Kello**, None; **K. Hanna**, None; **B. Volpe**, None; **B. Diamond**, GSK, 5, Jansen, 5, Lilly, 5.

Abstract Number: 0071

Inhibition of Nuclear Pore Export Ameliorates Lupus via Modulation of Plasma Cell Generation and Survival

Javier Rangel-Moreno,[1] Maria de la luz Garcia-Hernandez,[2] Teresa Owen,[3] Jennifer Barnard,[3] Bruce Goldman,[3] Christopher Ritchlin,[2] Douglas Widman,[4] Savanna Gornisiewicz,[4] Sharon Tamir,[4] and Jennifer H Anolik[3], [1]University of Rochester Medical center, Rochester, NY, [2]Division of Allergy, Immunology and Rheumatology, Center for Musculoskeletal Research, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA, Rochester, NY, [3]University of Rochester, Rochester, NY, [4]Karyopharm Therapeutics, Newton, MA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A major challenge in lupus is the elimination of autoreactive plasma cells, which amplify inflammation at peripheral sites via deposition of autoantibody-self antigen complexes. We previously reported that Selective Inhibitors of Nuclear Export (SINEs), developed to treat malignancies including multiple myeloma, prevented lupus nephritis in lupus prone mice (LPM). SINEs potently reduced spontaneous formation of germinal centers (GC) and generation of autoreactive plasma cells in the spleen of LPM. We hypothesized that SINEs mediate their effect by disrupting NF-kB signaling in stromal cells, compromising migration and positioning of T and B cells, and thus affecting production of GC-derived plasma cells. Furthermore, SINEs may directly target plasma cells in the spleen and bone marrow (BM).

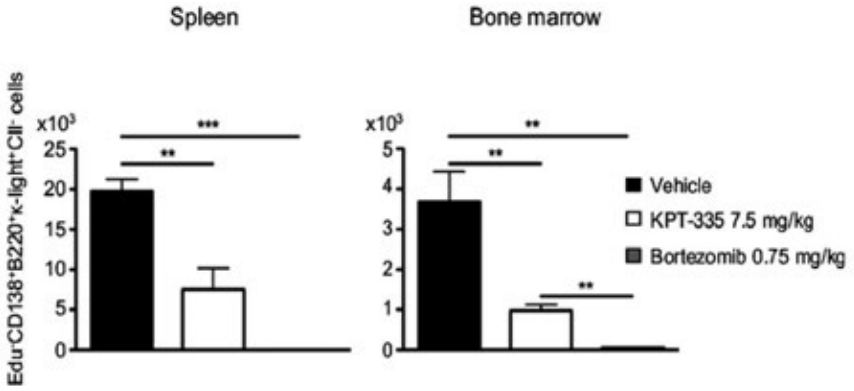

Figure 1. Short-term SINE therapy eliminates long-lived plasma cells in spleen and BM of lupus prone mice. 24 weeks old NZB/NZW female mice with active lupus received 4 i.p. injections of 5-ethynyl-2'-deoxyuridine (Edu, 1 mg/injection) in a period of 2 weeks to label proliferating cells. The following week, two mice cohort received KPT-335 (7.5 mg/kg) or vehicle by gavage, three times a week for one week A third group of mice received 2 ip injections per week of Bortezomib at 7.5 mg/kg. At the end of therapy spleen cells and bone marrow cells were stained with Aqua to eliminate dead cells from analysis, and stained with fluorescent antibodies and Edu. Long lived plasma cells (LLPC) were defined as Aqua⁻ alive cells that did not incorporate Edu, lacked MHC CII and were positive for CD138, B220 and K-light: Aqua⁻Edu⁻CD138⁺B220⁺light⁺CII-. Total number of LLP was calculated based on the number of cells that excluded trypan blue. Stattistically significant differences were calculated by t Test in groups of 8 mice. *: $p = 0.05$, **, $p = 0.005$, ***, $p < 0.0001$.

Methods: We isolated nuclear and cytoplasmic fractions from splenic stromal cells, stimulated with TNFain the presence of SINEs, and evaluated sequestration of NF-kB signaling components in the nuclei by western blot. Fold changes in mRNA expression for stromal cell-derived homeostatic chemokines (HC) were calculated with quantitative PCR. Morphometric analysis of area covered by fluorescent signal revealed the *in vivo* effects of SINEs on splenic HC. Finally, we used flow cytometry to enumerate cycling and non-cycling splenic and BM plasma cells in Edu labelled LPM after short-term therapy with KPT-335 (7.5 mg/kg) or vehicle (n = 8 mice/group).

Results: We demonstrated a significant enrichment for I-kBain the nuclear fraction of stromal cells stimulated with TNFain the presence of SINEs, thus confirming blockade of NF-kB signaling. In addition, fold mRNA expression for CCL19 and CXCL13 - HC that attract CXCR7+T cells and CXCR5+B cells, was significantly reduced in stromal cells incubated with SINEs (Control vs treated, p=0.0028). There was a significant decrease in CXCL13 staining (Control vs treated, p< 0.0001) and the size of follicular dendritic cells networks (Control vs treated, p< 0.0001) in spleens of mice orally treated with KPT-350 at 7.5 mg/kg for 8 weeks (3 administrations/week). As expected, short-term SINE therapy (1 week, 3 administrations/week) caused a two-fold reduction in GC B cells and a significant decrease in T follicular helper cells (Control vs treated, p=0.0043). Of note, short-term SINE therapy caused a global and significant reduction in long-lived plasma cells in spleen (Control vs treated, p=0.004) and BM (Control vs treated, p=0.0071). Unexpectedly, cycling splenic plasmablasts and short-lived plasma cells in the BM were not affected by SINE.

Conclusion: Our data demonstrate that SINEs disrupt NF-kB- dependent production of HC by stromal cells, thus impairing GC formation and compromising autoreactive PC generation. In addition, SINEs have a direct impact on PC survival, including long-lived plasma cells in the BM.

Disclosure: J. Rangel-Moreno, None; **M. Garcia-Hernandez**, None; **T. Owen**, None; **J. Barnard**, None; **B. Goldman**, None; **C. Ritchlin**, AbbVie, 2, 5, 9, Amgen, 2, 5, BMS, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Lilly, 5, Novartis, 5, Pfizer, 2, Pfizer Inc, 5, UCB, 2, 5; **D. Widman**, Karyopharm Therapeutics, 3; **S. Gornisiewicz**, Karyopharm, 3; **S. Tamir**, Karyopharm Therapeutics, 3; **J. Anolik**, None.

Abstract Number: 0072

The Single-cell Transcriptomic Landscape of NZB/W Murine Lupus at Early and Late Stages of Disease

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis is a complex and heterogeneous disease characterized by infiltrating immune cells in damaged kidney tissue. While mouse models have enabled mechanistic studies of lupus nephritis, immune and kidney cell types and states are incompletely characterized. Thus, shared cells and pathways between mouse and human lupus nephritis remain unrecognized and could provide the basis for targeted studies as well as engineering existing mouse models to better reflect human disease. To provide a comprehensive view of active leukocytes in a common model of mouse lupus nephritis, NZB/W, we measured the transcriptomes of single cells from murine kidneys and as well as spleens at early and late stages of kidney disease.

Methods: NZB/W female mice were generated and followed clinically. Kidneys and spleens from NZB/W mice were harvested for analysis from two 22-week-old non-proteinuric and two 37-week-old proteinuric mice. Single immune and parenchymal cells from digested kidney, and immune cells from spleen, were collected by flow cytometric cell sorting. We used the 10X Chromium 5' kit for single-cell encapsulation into droplets for library generation and next-generation sequencing for ~50,000 reads per cell. After normalization, single-cell transcriptomes passing quality metrics (>500 genes and < 25% mitochondrial content) were analyzed with unsupervised clustering (Seurat 3.0).

Results: We profiled 32,969 single cells collected from kidneys and spleens from NZB/W lupus mice at early and late stages of kidney disease (pre- and proteinuric, 2 mice per disease stage). Using unsupervised transcriptome analysis we discovered 27 distinct cellular clusters. Of these, 15 were immune cell clusters reflecting distinct subsets of T, B, and myeloid cells in both damaged kidney tissue and the spleen; the remaining 12 cell clusters were non-hematopoietic cells reflecting kidney cell types and states in early and late stages of kidney disease. Comparing cells from the same organ type (kidney or spleen) harvested from different mice at identical disease stages revealed highly similar immune and non-hematopoietic cell clusters, indicating reproducibility across animals and minimal batch effect.

Conclusion: By measuring the transcriptomes from single cells collected from damaged murine kidney tissue and spleens at early and late stages of kidney disease (pre-proteinuric and proteinuric), this study provides a comprehensive view of active leukocytes of lupus nephritis in a common model, NZB/W. We discovered 27 distinct murine cellular clusters reflecting multiple T, B, and myeloid cell subsets, as well as non-hematopoietic kidney cells types. We will compare NZB/W immune and kidney cellular clusters to those recently discovered in human lupus nephritis patients by single cell transcriptome profiling (Arazi et. al, Nature Immunology, 2019; Der et. al. Nature Immunology, 2019). We expect to identify new and better understand existing cells and pathways shared between human mouse lupus nephritis. We anticipate this approach can incorporate other common mouse models of lupus nephritis to better understand how each is related to human disease.

Disclosure: P. Hoover, None; **T. Eisenhaure**, None; **D. Lieb**, None; **A. Davidson**, None; **N. Hacohen**, None.

Abstract Number: 0073

Potent Anti-neutrophil Properties of the Natural Compound 6-Gingerol in Models of Lupus and Antiphospholipid Syndrome

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: 6-gingerol, the major bioactive compound of ginger root, is known to have anti-inflammatory and anti-oxidative effects. Indeed, ginger has been employed for millennia as an herbal supplement in the treatment of inflammatory diseases. Our group recently revealed that 6-gingerol prevents neutrophil extracellular trap (NET) release triggered by either ribonucleoprotein (RNP)/anti-RNP complexes or antiphospholipid antibodies (aPL). Here, we sought to further elucidate the mechanism by which 6-gingerol suppresses NET release, as well as to test its efficacy in lupus-relevant mouse models.

Methods: For in vitro studies, human neutrophils were prepared from healthy volunteers and stimulated with either immune complexes from lupus patients (RNP/anti-RNP) or total IgG fractions from primary APS patients (aPL). Stimulation was in the presence or absence of 6-gingerol and NET release was quantified via the enzymatic activity of NET-associated myeloperoxidase. Phosphodiesterase 4 (PDE4) activity and cyclic AMP (cAMP) levels were measured by chromogenic assays. In vivo, 6-gingerol (10 mg/kg/day) was tested in two models characterized by accelerated NET release: TLR7 agonist-induced lupus (BALB/c mice) and aPL-accelerated inferior vena cava thrombosis (C57BL/6 mice).

Results: As in our previous study, 6-gingerol completely neutralized RNP/anti-RNP- and aPL-mediated NET release at low micromolar concentrations. We further explored mechanisms of aPL-mediated NET release and found that 6-gingerol suppresses normal PDE4 activity, and thereby raises intracellular levels of cAMP. Indeed, the suppressive effects of 6-gingerol could be mitigated by blocking activity of the cAMP-responsive protein kinase A complex. Administration of 6-gingerol to TLR7 agonist-treated mice (model of lupus) resulted in a marked reduction in plasma NET levels, as well as anti-double-stranded DNA and anti-beta-2 glycoprotein I autoantibodies. In a model of APS, 6-gingerol neutralized the acceleration of large-vein thrombosis by human aPL; importantly levels of plasma NET were reduced in the same model.

Conclusion: We demonstrate for the first time that the natural compound 6-gingerol attenuates lupus-relevant NET release in vitro through a mechanism that at least partially depends on inhibition of PDE4. At the same time, administration of 6-gingerol to mice reduces NET release in models of lupus and APS, while also attenuating other disease-relevant activities such as autoantibody formation and large-vein thrombosis.

Disclosure: R. Ali, None; **J. Weiner**, None; **A. Gandhi**, None; **S. Estes**, None; **J. Knight**, None.

Abstract Number: 0074

LILRA3 Promotes Lupus-like Chronic Graft-versus-Host Disease by Expansion of Follicular Helper T Cells and Anti-dsDNA Autoantibodies

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Leukocyte immunoglobulin-like receptor A3 (LILRA3) is a soluble member of LILR family. We previously reported that *LILRA3* is a novel genetic risk for multiple autoimmune diseases, including systemic lupus erythematosus (SLE). However, it is unclear how LILRA3 contributes to the pathogenesis of SLE. This study was undertaken to examine the *in vivo* role of LILRA3 and its possible mechanism(s) in development of lupus in a chronic graft-versus-host disease (cGVHD) model.

Methods: To functionally study the role of LILRA3 in lupus pathogenesis, we generated a novel *LILRA*3 knock-in (*LILRA3*-KI) mouse and evaluated clinical and immunological phenotypes in the bm12-induced cGVHD model. Human LILRA3 gene (Gene ID: 11026) was inserted into Rosa26 allele in C57BL/6 (B6) mice based on Cas9/sgRNA system. The cGVHD was induced by an intraperitoneal injection of the bm12 donor splenocytes into recipients, either B6 wild-type (B6-WT) or *LILRA3*-KI mice. Mice were assessed for the development of splenomegaly, immune cellular response, autoantibody production, and renal pathology.

Results: Compared with B6-WT recipient mice, the *LILRA3*-KI mice displayed a more pronounced lupus-like phenotype and immune response, which includes an apparent spleen enlargement ($p < 0.001$); expansion of Tfh cells ($p < 0.001$), germinal center (GC) B cells ($p < 0.01$), and plasma B cells ($p < 0.001$); and elevated levels of serum anti-double-stranded DNA IgG autoantibodies ($p < 0.001$).

Conclusion: Our data indicate that LILRA3 promotes lupus-like disease probably through the excessive expansion of Tfh, GC B, and plasma cells, and subsequently leading to an excessive production of anti-dsDNA autoantibodies.

Disclosure: Y. Tang, None; **Y. Wang**, None; **Y. Zou**, None; **M. Liu**, None; **Y. Du**, None; **J. Guo**, None.

Abstract Number: 0075

Microglia-Specific Transcriptional Signatures Correlate with Behavioral Deficits in 'Neuropsychiatric Symptoms of Systemic Lupus Erythematosus'

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune syndrome affecting multiple organs, including the brain. More than 50% of patients experience neuropsychiatric symptoms of SLE (NPSLE) that often occur early in disease and go undiagnosed. Despite the devastating impact of NPSLE on health-related quality of life, underlying disease mechanisms are unknown. Microglia are the resident innate immune cells of the brain; ac-

cumulating evidence points to microglia as drivers of neurological conditions ranging from neurodevelopmental (autism) to neurodegenerative (Alzheimer's disease, chronic pain) disorders. The recently discovered disease-associated microglia (DAM) subset is enriched for lipid metabolism pathways and phagocytosis-related functions. The vast majority of investigations into microglia, particularly DAM, have occurred in neurodegenerative disease models of Alzheimer's disease, amyotrophic lateral sclerosis and multiple sclerosis. However, very few studies have examined microglia, particularly DAM, in the context of NPSLE. Here, we probed microglia from two NPSLE-prone mouse strains at the transcriptional level to potentially correlate gene signatures with behavioral deficits.

Methods: Mice with caspase 8 flanked by *loxP* sites (*Casp8*$^{fl/fl}$, WT) were bred to mice expressing Cre under the CD11c gene promoter to generate CReCOM (Caspase-8 Removed CD11c-specific Overactive MyD88) mice. B6.*Sle1.Sle3* mice were derived from the introgression of 2 NZM2410-derived susceptibility loci onto non-autoimmune C57BL/6 (B6) mice. 3-4 month old WT and CReCOM mice underwent behavioral testing. Microglia were sorted from mice following behavioral tasks and from 10-12 month old WT, CReCOM, B6 and B6.*Sle1.Sle3* mice for RNA-seq analysis (n=4/group).

Results: CReCOM mice develop an inflammatory disease reminiscent of human SLE and exhibit significant impairment in spatial memory, contextual associative learning, startle response and motor coordination, similar to patients with NPSLE. Likewise, the recently validated B6.Sle1Sle3 NPSLE model exhibits depression-like behavior and significant impairment in spatial and recognition memory, symptoms detected in NPSLE patients. Of the significantly upregulated genes (DESeq2, $p< 0.05$, fold change in expression >1.5) observed in CReCOM (256) and B6.Sle1.Sle3 (214) microglia compared to their respective controls, a common 18-gene 'NPSLE signature' is shared ($p< 2.54x10-4$) and enriched for genes associated with lipid metabolism, scavenger receptor activity and downregulating inflammatory responses and cell chemotaxis processes. NPSLE microglia are also enriched for genes associated with the DAM subset. Moreover, microglial expression of 'NPSLE' and 'DAM' signatures significantly correlate with the severity of behavioral deficits in CReCOM mice.

Conclusion: The discovery of our novel 'NPSLE signature', as well as enrichment of the 'DAM signature', represents the first to connect microglia-specific transcriptional signatures with clinical outcomes in NPSLE-like disease. In future studies, we will assess the penetrance of these signatures to further interrogate how defective microglial function may incite NPSLE.

Disclosure: H. Makinde, None; **E. Mike**, None; **C. Putterman**, Equillium, 5, Equillium, Inc, 2, 5, Exagen, 2; **D. Winter**, None; **C. Cuda**, None.

Abstract Number: 0076

Effect of Ifnα and Costimulatory Blockade on Brain Infiltration in a Model of 'Neuropsychiatric Symptoms of Systemic Lupus Erythematosus'

Hadijat Makinde,[1] Chirag Raparia,[2] Anne Davidson,[2] and Carla Cuda[3], [1]Northwestern University, Chicago, IL, [2]Feinstein Institutes for Medical Research, Manhasset, [3]Northwestern University Feinberg School of Medicine, Division of Rheumatology, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease that affects many end organs including the brain. Despite a prevalence of over 50% in SLE patients, neuropsychiatric symptoms of SLE (NPSLE) are among the least understood complications. Similar to SLE patients, the lupus-prone NZB/W strain develops NPSLE-like disease that manifests in mood-related disorders and learning impairment. Despite the paucity of data examining underlying mechanisms, accumulating evidence points to microglia, the resident innate immune cells in the brain, as a driver of disease. The cross-talk between infiltrating monocyte-derived macrophages and microglia plays a critical role in directing microglial responses. Evidence shows that IFNα exacerbates systemic disease and induces early lethality in the NZB/W strain in a T cell-mediated manner. In contrast, blocking the CD28/cytotoxic T lymphocyte antigen (CTLA)-4/B7 interaction (using CTLA4Ig) induces disease remission in NZB/W mice in combination with anti-CD40L antibodies and cyclophosphamide. Here, we elucidate the role of IFNα administration and costimulatory blockade on the infiltration of monocyte-derived macrophages and the corresponding microglial responses in NPSLE-like disease.

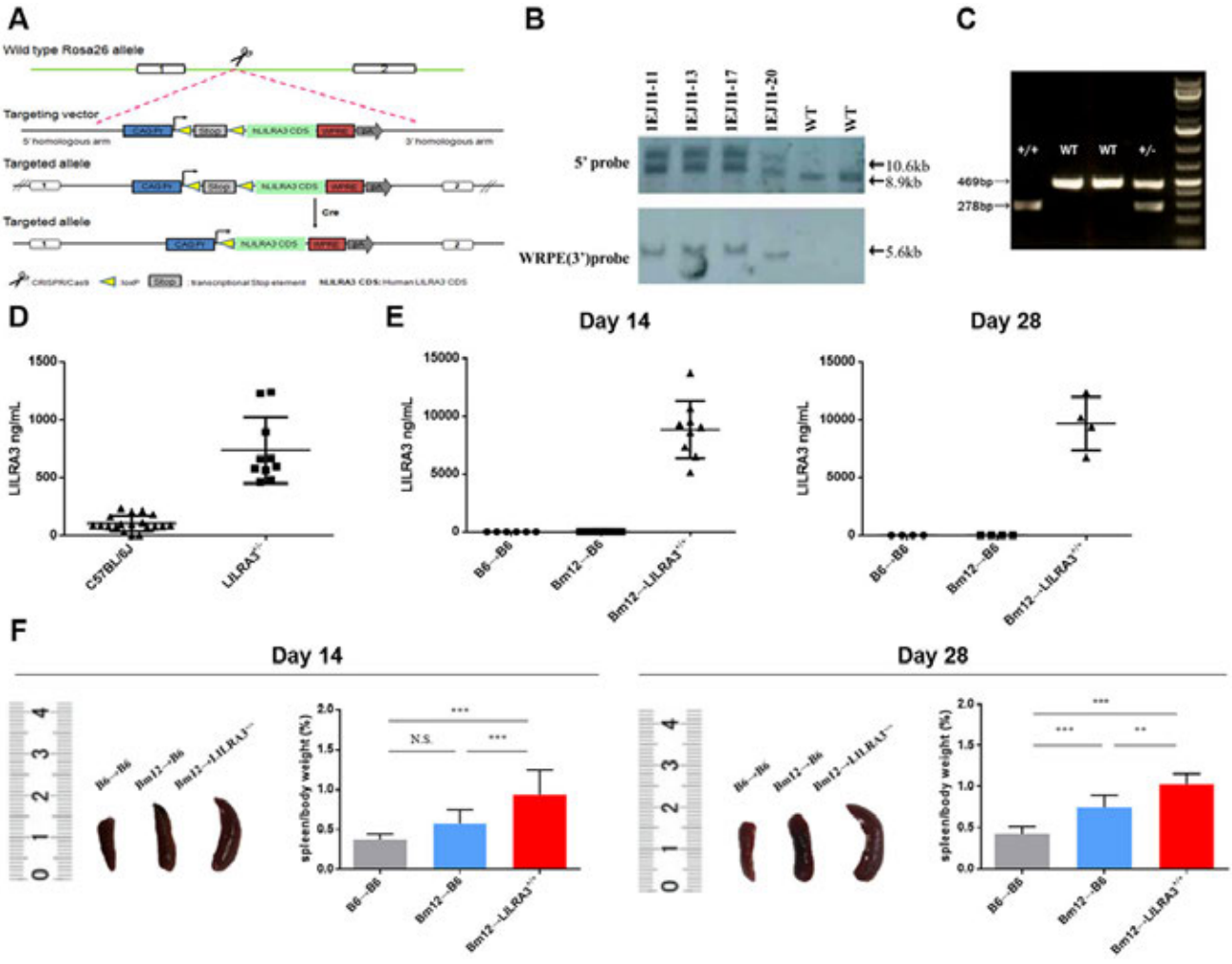

Figure 1. Construction strategy of the LILRA3 knock-in mice. Humanized LILRA3 knock-in (LILRA3-KI) mice were constructed on C57BL/6 background. A full-length sequence of human LILRA3 gene (Gene ID: 11026) was inserted into the C57BL/6 Rosa26 allele based on CRISPR-Cas9 technology (A). LILRA3 expression was confirmed by southern blot (B), PCR (C), and ELISA (D). After cGVHD, serum LILRA3 was highly expressed in bm12→KI mice at both days 14 and 28 (E). The bm12→KI mice showed a significant aggravation of splenomegaly (F). Results from F: data were obtained from 2 independent experiments at day 14 (B6→B6: n=9; bm12→B6: n=12; bm12→KI: n=12). At day 28, data were obtained from a single experiment (B6→B6: n=4; bm12→B6: n=6; bm12→KI: n=4). Data are displayed as mean±SD. ** $p < 0.01$, *** $p < 0.001$.

Methods: One cohort of female NZB/W mice (n= 5) was given a single intravenous injection of adenovirus-IFNα (AD-IFNα) at 12-14 wks of age and tissues were harvested at 18 wks. An additional cohort (n=5) was intraperitoneally injected 3 times/wk for 2 wks with CTLA4Ig/anti-CD40L (costimulatory blockade) at 18-20 wks prior to overt disease and tissues were harvested at 32 wks. Treated animals and age-matched NZB/W control mice were examined for proteinuria and splenic alterations as an indicator of systemic disease. Brain monocytic infiltration was evaluated via flow cytometry as a measure of blood-brain barrier breach. Neurocognitive testing and RNA-seq analysis of sorted microglia are pending.

Results: Mice immunized with AD-IFNα developed proteinuria and splenomegaly, corresponding to an increase in total splenocyte numbers, compared to age-matched control NZB/W mice. In contrast, costimulatory blockade prevented development of proteinuria and splenomegaly compared to their age-matched counterparts. Similar to SLE patients with NPSLE, AD-IFNα-immunized mice showed reduced brain volume compared to age-matched control mice. However, animals placed on the costimulatory blockade treatment showed a trend towards prevention of this brain volume loss compared to age-matched control mice. Furthermore, the increased macrophage infiltration into brains of 18-wk-old AD-IFNα-immunized mice mirrored that found in brains of 32-wk-old NZB/W control mice. Strikingly, costimulatory blockade prevented this infiltration at 32 wks.

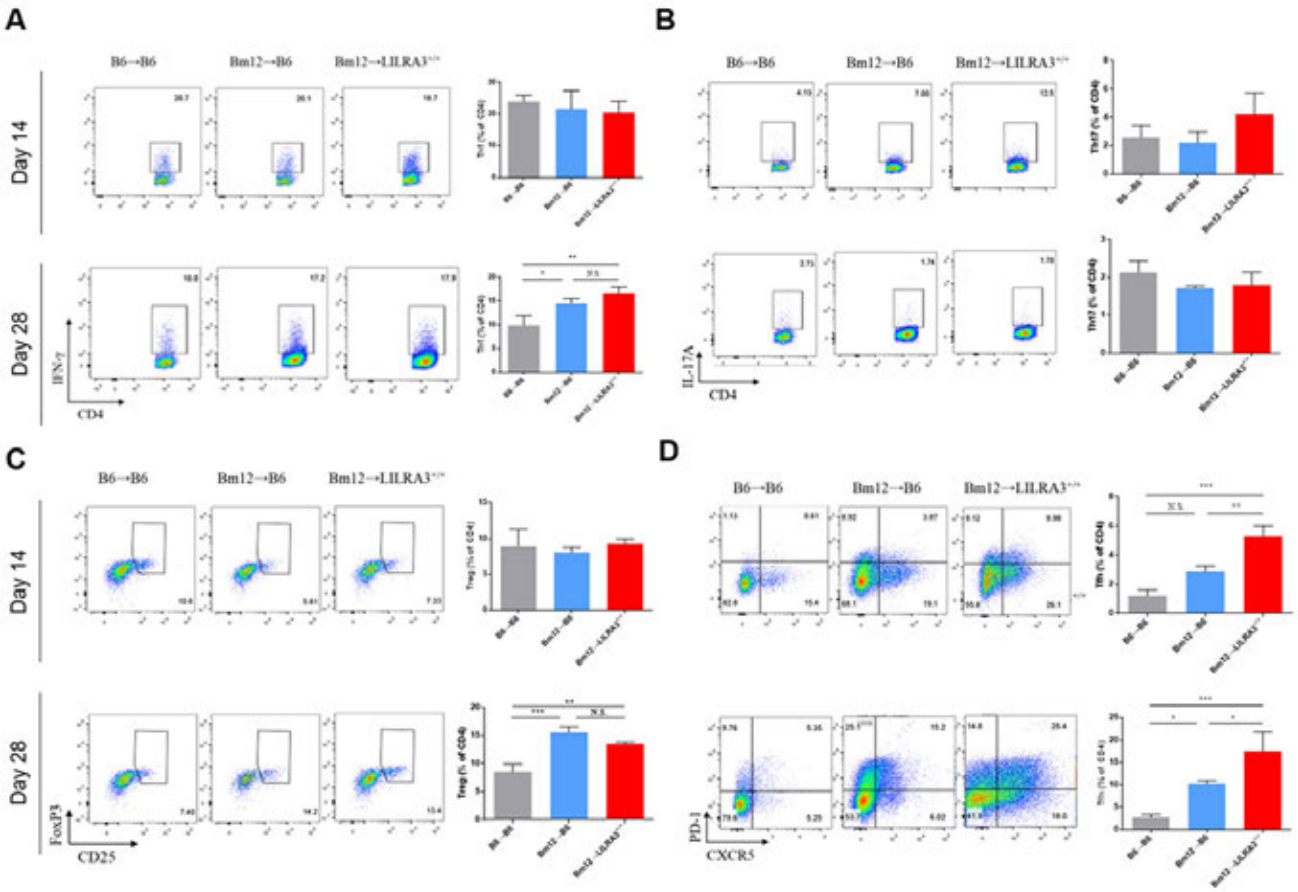

Figure 2. Increased expansion of Tfh cells in LILRA3-KI cGVHD mice. On days 14 and 18, the frequencies of CD4+IFNγ+ Th1 cells (A), CD4+IL-17A+ Th17 cells (B), CD4+CD25+FoxP3+ Tregs (C), and CD4+PD-1+CXCR5+ Tfh cells (D) from splenocytes were determined by flow cytometry. At day 14, data were obtained from 2 independent experiments (B6→B6: n=9; bm12→B6: n=12; bm12→KI: n=12). At day 28, data were obtained from a single experiment (B6→B6: n=4; bm12→B6: n=6; bm12→KI: n=4). Data are displayed as mean±SD. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

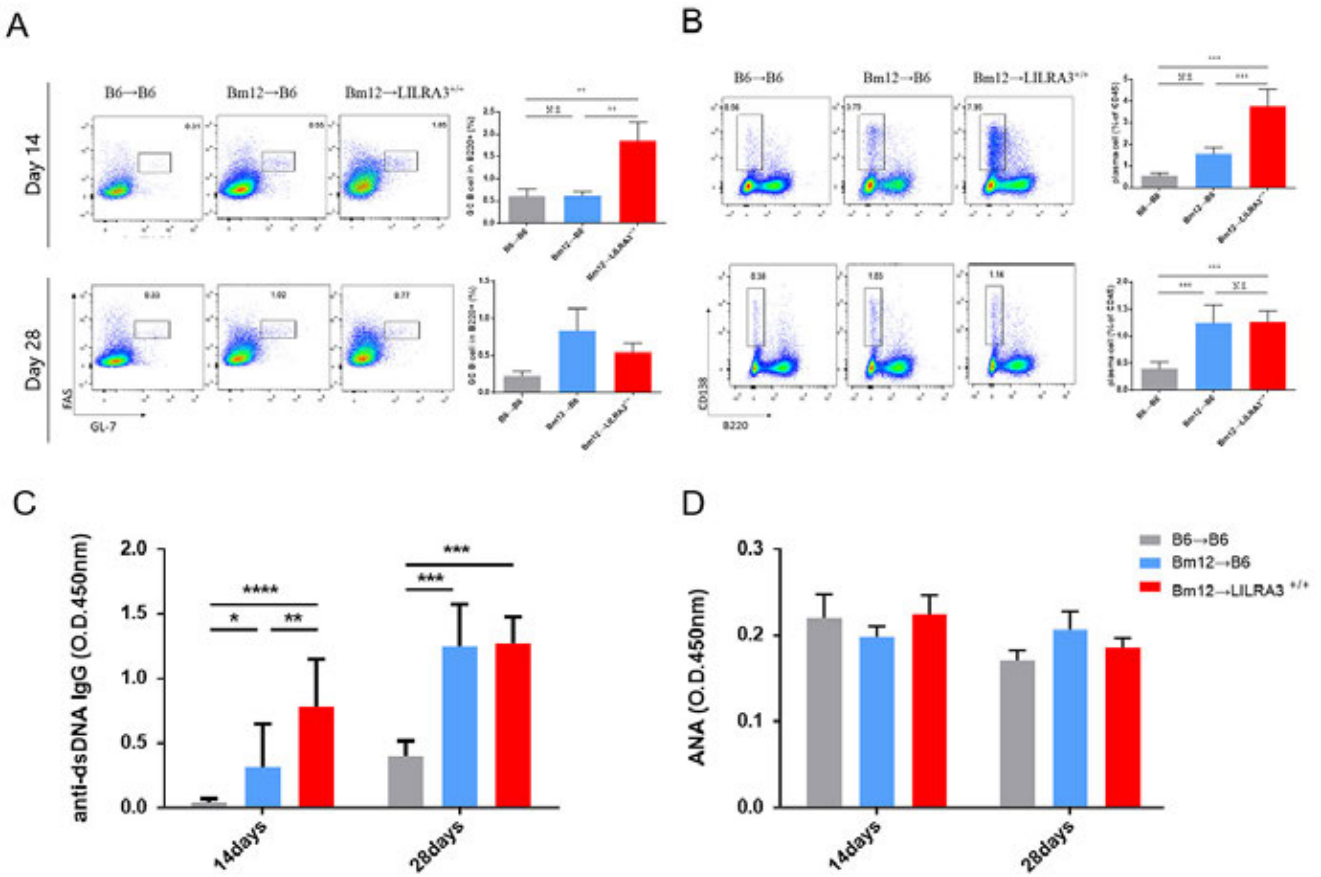

Figure 3. Increased expansion of GC B, plasma cells and anti-dsDNA autoantibody production in LILRA3-KI cGVHD mice. On days 14 and 18, the frequencies of CD19+FAS+GL-7+ GC B cells (A), and CD19+CD138+B220- plasma cells (B) from splenocytes were determined by flow cytometry. Serum levels of anti-dsDNA IgG (C), and ANA (D) were measured by ELISA. At day 14, data were obtained from 2 independent experiments (B6→B6: n=9; bm12→B6: n=12; bm12→KI: n=12). At day 28, data were obtained from a single experiment (B6→B6: n=4; bm12→B6: n=6; bm12→KI: n=4). Data are displayed as mean±SD. ** $p < 0.01$, *** $p < 0.001$.

Conclusion: These data indicate that IFNα accelerates brain macrophage infiltration, potentially impacting repair and regeneration responses of microglia within the injured brain, while costimulatory blockade prevents this insult. Future studies will examine neurocognitive decline and microglial-specific responses to these treatments.

Disclosure: H. Makinde, None; **C. Raparia**, None; **A. Davidson**, None; **C. Cuda**, None.

Abstract Number: 0077

Flux Analysis Reveals Influence of Rab4 Expression on Mitochondrial and Pentose Phosphate Pathway Metabolism of Lupus T Cells

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: SLE – Animal Models Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: HRES-1/Rab4 is a small GTPase enzyme which regulates endosomal trafficking. The protein is overexpressed in T cells of SLE patients (J Immunol. February 15, 2009, 182 (4): 2063-2073) and mice (Ann Rheum Dis. 2014 Oct;73(10):1888-97.), resulting in mitochondrial accumulation through the inhibition of mitophagy (PLoS One. 2014, 9(1): e84392). Since mitochondrial dysfunction in T cells plays an important role in the pathogenesis of SLE, we investigated whether its mouse homologue, Rab4A, regulates metabolism.

Methods: Metabolic flux analysis is an emerging technique capable of offering insight into intracellular metabolism both on an individual metabolite and on a metabolic pathway level (J Ind Microbiol Biotechnol (2015) 42: 317) which makes it a suitable method for the investigation of T cell metabolism.

To study the effects of Rab4A expression in T cells, a site-specific Cre/Lox recombinase system was employed to knock down Rab4A expression in lupus-prone SLE 1.2.3. mice. The metabolic flux of T cells and other lymphocytes was characterized by feeding ^{13}C-stable isotope labeled nutrients, such as glucose or glutamine, to cells in culture and subsequently measuring isotope labeled metabolites using liquid chromatography-mass spectrometry (LC-MS) after the preparation of cell extracts.

Results: The non-oxidative pentose phosphate pathway (PPP) metabolite, sedoheptulose-7-phosphate (S7P) was accumulated in CD4+ T cells (33% elevation, p=0.002) but it was reduced in B cells (24%, p=0.043) of lupus mice. Rab4A deletion in T cells reversed the accumulation of S7P in CD4 T cells in SLE mice (p=0.035).

Mitochondrial tricarboxylic cycle metabolites, glutamate (18% decrease, p=0.029), citrate/isocitrate (37% decrease, p=0.004), alpha-ketoglutarate (32% decrease, p=0.006) and malate (35% decrease, p=0.038) were depleted in CD4+ T cells of SLE mice. Glutamate was also reduced in B cells of SLE mice (7% decrease, p=0.026).

Conclusion: The results suggest that T cell-specific deletion of Rab4A restores the SLE-induced metabolic changes in CD4+ T cells. Therefore, Rab4A may represent a target for correcting T-cell dysfunction in SLE.

Disclosure: T. Faludi, None; **N. Huang**, None; **M. Duarte**, None; **J. Lewis**, None; **A. Perl**, None.

Abstract Number: 0078

Ultraviolet Light Induces Increased T Cell Activation in Lupus-Prone Mice via Type I Interferon-Dependent Inhibition of T Regulatory Cells

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Ultraviolet (UV) light is a known trigger of skin and possibly systemic inflammation in systemic lupus erythematosus (SLE) patients. Although type I interferons (IFN) are upregulated in SLE skin after UV exposure, the mechanisms to explain increased UVB-induced inflammation remain unclear. Here, we identified the role of type I IFNs in regulating immune cell activation between wild-type and lupus-prone mice following UVB exposure.

Methods: 10-week old female lupus-prone (NZM2328), wild-type (BALB/c) and iNZM mice (which lack a functional type I IFN receptor on NZM2328 background) were treated on their dorsal skin with 100mJ/cm^2 of UVB for 5 con-

secutive days. Following UVB treatment, draining lymph node cell populations were characterized via flow cytometry and suppression assays. Treated skin was examined for changes in expression of type I IFN genes by real-time PCR.

Results: Two weeks following UVB exposure, lupus-prone NZM2328 mice showed an increase in draining lymph node size and expansion of T cell numbers and T cell activation in the draining lymph nodes. B cells were not increased. Neither Balb/c nor iNZM mice demonstrated this change. This T cell activation was preceded by a significant increase in UVB-induced type I IFN expression in the skin of NZM2328 mice compared to BALB/c mice. To explain the rise in T cell activation, T regulatory (T_{reg}) cells were examined. Following UVB exposure, both BALB/c and iNZM mice demonstrated an increase in activated T_{Reg} cells in the draining lymph node 24 hours after the fifth UVB treatment; however, this was not seen in NZM2328 mice. In addition, T_{regs} isolated from NZM2328 mice draining lymph nodes were not functional in a T cell suppression assay. and this was dependent on type I IFNs as Tregs from UVB-treated iNZM demonstrated excellent suppressive capacity, similar to Balb/c mice.

Conclusion: These data suggest that an environment rich in type I IFNs, such as seen in lupus skin, promotes a skewed UVB-mediated T cell response in which activation of T cells is enhanced secondary to a type I IFN-dependent suppression of T_{Reg} cells. Thus, we propose that type I IFNs promote are important for UVB-induced inflammation and may be an effective target for prevention of UVB-mediated flares.

Disclosure: S. Wolf-Fortune, None; **S. Estadt**, None; **J. Theros**, None; **T. Moore**, None; **J. Ellis**, None; **J. Liu**, None; **T. Reed**, None; **C. Jacob**, None; **J. Gudjonsson**, AbbVie, 2, Genentech, 2, genentech, 2, MiRagen, 5, Novartis, 5, Sun Pharma, 2, SunPharma, 2; **J. Kahlenberg**, AstraZeneca, 5, Bristol Myers Squibb, 5, Eli Lilly, 5.

Abstract Number: 0079

Unique Primed Status of Microglia Under the Systemic Autoimmune Condition of Lupus-Prone Mice

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the production of various autoantibodies. This disease causes disabling neuropsychiatric symptoms even in the absence of apparent inflammation in the central nervous system (CNS), but the mechanisms involved remain unknown. Innate immune-mediated inflammation has attracted attention as a pathogenic mechanism in neuropsychiatric diseases.

Methods: We investigated the CNS of lupus-prone mice focusing on innate immunity. Three strains of lupus-prone mice, FcγRIIB$^{-/-}$*Yaa*, an F1 hybrid of NZB and NZW (NZB/NZW) mice, and MRL/Fas^{lpr} (MRL/lpr) mice were used to analyze CNS immunopathology.

Results: Flow cytometry analysis demonstrated the numbers of brain CD45^{+} cells were increased compared with controls in lupus-prone mice. Upregulation of MHC class I and PDCA1 were observed in microglia and CD11b^{+} myeloid cells of lupus-prone mice, indicating they were activated in response to interferons (IFN). Microglial gene ex-

pression analysis of FcγRIIB$^{-/-}$*Yaa* mice revealed the upregulation of IFN responsive genes and inflammation-related genes including *Axl*, *Clec7a,* and *Itgax*, which were previously reported in neurodegenerative conditions and primed conditions. Upregulated chemokine gene expressions including *Ccl5* and *Cxcl10* were concurrent with increased numbers of T cells and monocytes, especially Ly6C^{lo} monocytes in the CNS. Upregulation of these genes was also observed in NZB/NZW mice, indicating common lupus pathology. The primed status of microglia in FcγRIIB$^{-/-}$*Yaa* mice was also demonstrated by morphological changes such as enlarged cell bodies with hypertrophic processes, and hyper reactivity to lipopolysaccharide. Immunohistochemistry of FcγRIIB$^{-/-}$*Yaa* mice indicated reactive responses of astrocytes and vascular endothelium.

Conclusion: Our data indicated that microglia in lupus exhibit a unique primed phenotype characterized by the upregulated expressions of neurodegeneration-related genes and IFN responsive genes. Interaction with peripheral cells and brain resident cells was presumed to orchestrate neuroinflammation. Targeting innate immune cells, such as microglia and monocytes, may be a promising therapeutic approach for neuropsychiatric SLE.

Disclosure: A. Nomura, None; **D. Noto**, None; **G. Murayama**, None; **A. Chiba**, None; **S. Miyake**, Bristol myers squibb, 2, Bristol-Myers Squibb, 2, Pfizer, 2, Pfizer Japan Inc., 2, Taiho pharmaceutical, 8, TAIHO PHARMACEUTICAL CO., LTD., 8.

Abstract Number: 0080

The Role of Adopter Protein SH3BP2 in a Murine Systemic Lupus Erythematosus Model

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SESSION INFORMATION
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Session Title: SLE – Animal Models Poster
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Background/Purpose: An adaptor protein SH3BP2 (Src homology 3 domain-binding protein 2) is widely expressed in immune cells and controls intracellular signaling pathways, such as Syk, Src, Vav, and PLCγ. In previous reports, SH3BP2 has been reported to regulate the production of antibodies in B cells. We have previously reported that, in a collagen-induced arthritis model, SH3BP2 loss-of-function mutation suppresses antibody production against type II collagen and markedly prevents the development of arthritis (Mukai T, et al. Arthritis Rheumatol 2015). To further investigate the role of SH3BP2 in autoimmune diseases, we examine the effect of SH3BP2 deficiency in a murine systemic lupus erythematosus (SLE) model.

Methods: For the lupus model, we used Fas^{lpr} mice (C57BL6 background), which possess impaired Fas signaling. SH3BP2-deficient mice and Fas^{lpr} mice were crossed to create SH3BP2-deficient Fas^{lpr} double mutant mice. These mice were observed until 35-week old, and then serum, urine, spleen, inguinal lymph nodes, kidney and bone marrow samples were collected. We evaluated proteinuria, splenomegaly, serum anti-dsDNA antibody titer, and histological renal damage. In addition, we analyzed B- and T-cell subsets by flow cytometry.

Results: Wild-type, SH3BP2-deficient, Fas^{lpr}, and SH3BP2-deficient Fas^{lpr} double mutant mice were analyzed. Fas^{lpr} mice exhibited splenomegaly, proliferative glomerulus lesions, and increased anti-dsDNA antibody levels compared to wild-type and Fas^{lpr} mice. All of them were significantly ameliorated by SH3BP2 deficiency. Furthermore, SH3BP2 deficiency suppressed the accumulation of $CD3^+B220^+CD4^-CD8^-$(double negative) T cells in spleen and lymph nodes, which are characteristic of Fas^{lpr} mice.

Conclusion: In the murine lupus model, SH3BP2 deficiency suppressed the development of the autoantibody (anti-dsDNA antibody), organ damage, and the accumulation of double negative T cells in the spleen. SH3BP2 could be a potential therapeutic target for autoimmune diseases.

Disclosure: K. Kawahara, Chugai Pharmaceutical Co., Ltd., 2, Glaxo Smith Kline K.K., 2; **T. Mukai**, Chugai Pharmaceutical Co., Ltd., 2, Glaxo Smith Kline K.K., 2; **A. Nagasu**, Chugai Pharmaceutical Co., Ltd., 2, Glaxo Smith Kline K.K., 2; **M. Iseki**, None; **H. Nagasu**, None; **S. Tshuji**, Chugai Pharmaceutical Co., Ltd., 2, Glaxo Smith Kline K.K., 2; **T. Akagi**, Chugai Pharmaceutical Co., Ltd., Glaxo Smith Kline K.K., 2; **Y. Ueki**, None; **Y. Morita**, Chugai Pharmaceutical Co., Ltd., 2, Glaxo Smith Kline K.K., 2.

Abstract Number: 0081

UV Light Stimulates a Systemic Neutrophil Response Associated with Transient Kidney Injury

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sensitivity to ultraviolet B (UVB) light affects ~70% of SLE patients and exacerbates both skin disease and systemic flares, including lupus nephritis (LN). Our findings that neutrophils are the dominant infiltrating immune cell in the skin after exposure to UVB light together with the recent discovery that neutrophil gene signature is the strongest predictor of active SLE disease prompted the hypothesis that *neutrophils are the pathogenic link between UVB light-induced inflammation in the skin and kidney injury in SLE*.

Methods: Mice (C57BL/6J, 3-4mo) were exposed to a single dose of UVB light (500mJ/cm2, 280-320 nm). Skin infiltrating neutrophils in photoactivatable mice (UBC-PA-GFP) were photoconverted with violet light (~415nm) 1 day after UVB light exposure. Individual mice were euthanized on 1, 2, or 6 days after UVB and perfused with saline; non-irradiated mice were used as controls. Immune cells isolated from the skin, bone marrow (BM), blood, lung, and kidney were profiled by flow cytometry. Gene expression was evaluated by QPCR, plasma protein concentration by Legendplex Inflammatory Panel, and proteinuria by Bradford assay.

Results: Acute exposure to UVB light caused a 10-fold increase in neutrophil numbers in the skin, associated with their precipitous egress from the BM and a 5-fold increase in circulating neutrophils. Unexpectedly, UVB light injury in the skin caused neutrophil migration to peripheral organs, including the lung and kidney, with up to 10-fold increase in neutrophil numbers in the kidney. Extensive gene profiling of the skin tissue revealed a broad local cutaneous inflammatory response to UVB light injury, while proteomic analysis of plasma samples identified IL17A as the dominant inflammatory mediator found in circulation 6-24hr after skin exposure to UVB light.

Relevant to SLE pathogenesis, neutrophil infiltration into the kidney was accompanied by endothelial activation and inflammation: increased expression of adhesion molecules VCAM-1 and E-Selectin, as well as inflammatory proteins IL1β, s100A8/9, and s100A6. Moreover, we detected increased early (day 1-2) expression in Ngal and Kim1, markers of kidney injury in LN, as well as elevated urine protein levels, findings indicating that skin exposure to UVB light triggers transient kidney damage. Neutrophils in distal sites late (day 6) after UVB light injury demonstrated two phenotypes: aged CXCR4^{hi} and reverse migrating ICAM1^{hi}CXCR1^{lo}. In the kidney, presence of CXCR4^{hi} neutrophil population followed expression of CXCR4 ligand, CXCL12, another marker of kidney injury. In the photoactivatable mouse model, photoconverted GFP+ skin infiltrating neutrophils were detected in the kidneys of mice one day after UVB light exposure.

Conclusion: Our findings provide several novel insights into the neutrophil response to UVB light: i) localized skin injury triggers systemic neutrophil migration, accompanied by inflammatory response and transient kidney injury and ii) presence of CXCR4^{hi} and ICAM1^{hi}CXCR1^{lo} neutrophil populations in peripheral organs suggests that a subset of activated skin-infiltrating neutrophils has migrated to distal organs via reverse transmigration.

Disclosure: S. Skopelja-Gardner, None; **J. Tai**, None; **X. Sun**, None; **L. Tanaka**, None; **P. Hermanson**, None; **K. Elkon**, None.

Abstract Number: 0082

Rab4A Increases Mitochondrial Oxidative Stress and Glutathione Disulfide Accumulation That Underlie Neurobehavioral Changes in Lupus-Prone Mice

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: The human GTPase HRES-1/Rab4 has been identified as a susceptibility locus for systemic lupus erythematosus (SLE) and is overexpressed in T cells of SLE patients [1]. HRES-1/Rab4 depletes DRP-1, a mitochondrial protein that initiates mitophagy, thereby increasing the mass of mitochondria [2]. Rab4A is the mouse orthologue of HRES-1/Rab4, which is overexpressed in lupus-prone mice [2]. Therefore, the role of Rab4A in disease pathogenesis has been modeled in Jurkat cells and investigated in lupus-resistant and lupus-prone strains carrying constitutively active Rab4A^{Q72L} alleles or lacking Rab4A in T cells.

Methods: Methods HRES-1/Rab4 was overexpressed in Jurkat cells using a doxycycline-inducible GFP-encoding bi-cistronic expression vector system. Mitochondrial function was assessed by Seahorse metabolic analyzer. The effect of Rab4A was examined in lupus-prone triple congenic SLE123 (SLE) mice and autoimmune resistant C57Bl/6 mice carrying wildtype (WT), constitutive active Rab4AQ72L, or Rab4-deficient alleles (Rab4KO) created through crossing of floxed Rab4AQ72L and CD4Cre mice. Q-Exactive Hybrid Quadrupole-Orbitrap Mass Spectrometer was used for targeted assessment of >800 metabolites. Mouse behavior was evaluated by the elevated plus maze and open field tests. Statistical analyses were performed by Student's T-test or Tukey's HSD ANOVA using GraphPad software and considered significant at $p< 0.05$ for hypothesis testing.

Results: Overexpression of HRES-1/Rab4 led to a significant increase in ATP production (fold change, FC=1.2, p= 0.03), % spare respiratory capacity (FC=1.2, p= 0.002), increased glutathione disulfide (GSSG, FC=4.3, p=0.04) and malondialdehyde (MDA, FC=1.2, p=0.01) in Jurkat cells. The Rab4A^{Q72L} mice traveled a significantly further distance than the WT mice (FC=1.5, p=0.03). The Rab4A^{Q72L} mice also traveled further than the SLE mice, SLE Rab4A^{Q72L} and SLE Rab4A^{Q72L} CD4Cre. Interestingly the deletion of Rab4A in the T cells in SLE mice increased the distance traveled significantly relative to SLE Rab4A^{Q72L} mice (FC=1.7, p=0.01). The Rab4A^{Q72L} mice entered the open arms of the maze more often than WT (FC=1.6, p=0.008). Rab4A^{Q72L} mice entered the open arm significantly more times than all SLE mice. Similar trends were seen in the open field test.

The brain metabolomes of Rab4A^{Q72L} mice showed a significant increase in GSSG (FC=1.4, p=0.02) and MDA (FC=1.6, p=0.04). SLE and SLE Rab4A^{Q72L} mice also had more GSSG (SLE: FC=1.5, p=0.04; SLE Rab4A^{Q72L}: FC=1.7, p=0.01) and MDA (SLE: FC=1.9, p=0.12; SLE Rab4A^{Q72L}: FC=2.5, p=0.02) than WT controls.

Conclusion: Activation of Rab4A increases mitochondrial oxidative stress and GSSG accumulation, which apparently underlie neurobehavioral changes in lupus-resistant and lupus-prone mice.

Disclosure: T. Winans, None; **T. Faludi**, None; **B. Wyman**, None; **N. Huang**, None; **J. Lewis**, None; **M. Duarte**, None; **L. Morel**, None; **F. Middleton**, None; **A. Perl**, None.

Abstract Number: 0083

Dysfunction of TRIM21 Promotes Aberrant Plasmablast Differentiation in Systemic Lupus Erythematosus Due to the Reduction of TRIM21-mediated Ubiquitylation of IRF5

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Animal Models Poster
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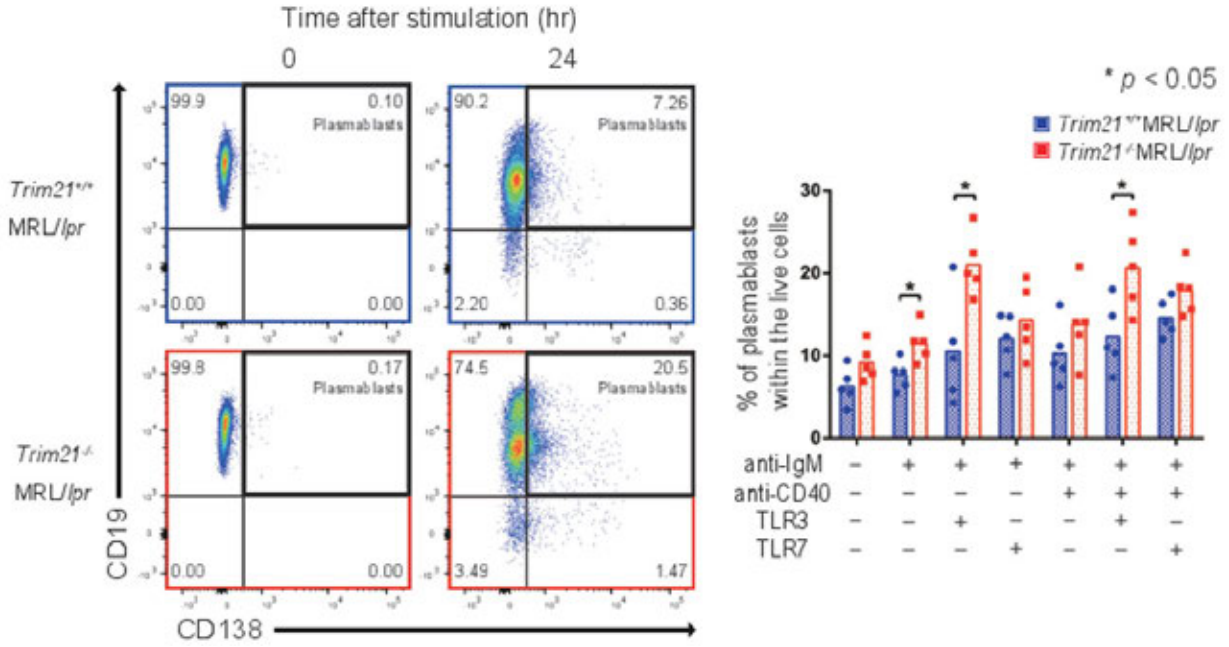
Session Time: 9:00AM–11:00AM

Background/Purpose: TRIM21 is a member of the tripartite motif family proteins and is one of the autoantigens which react with anti-SS-A antibody (Ab) present in sera of patients with systemic lupus erythematosus (SLE) and Sjögren's syndrome. Although TRIM21 has been thought to play a role in B-cell proliferation and apoptosis, the role of TRIM21 in SLE pathogenesis is still unknown. Previous studies have shown the data strongly suggesting that TRIM21 can act as a suppressor for autoimmune and inflammatory response and that its dysfunction can cause the pathological state of SLE. Here we examined the pathological role of TRIM21 in SLE using *Trim21*-deficient lupus model mice and B cells from SLE patients.

Methods: *Trim21*-deficient MRL/*lpr* mice were generated by backcrossing *Trim21*-deficient C57BL/6 mice to MRL/*lpr* mice. Urine albumin/creatinine ratio was measured as the urine protein level. Anti-dsDNA and anti-TRIM21 Abs were measured by enzyme-linked immunosorbent assay. CD43-negative resting B cells were isolated from mouse spleens or peripheral blood of SLE patients by magnetic-activated cell sorting and stimulated with several Toll-like

Figure 1. TRIM21 deficiency promotes aberrant B-cell differentiation in MRL/*lpr* mice.



receptor (TLR) ligands. The abilities to differentiate into plasmablasts and to product Ab were examined by flow cytometry and bead-based immunoassay, respectively.

Results: The levels of urine protein and serum anti-dsDNA Ab at 28 weeks of age were significantly higher in *Trim21*-deficient MRL/*lpr* mice as compared to wild-type MRL/*lpr* mice (p = 0.029 and 0.003, respectively). When we stimulated resting B cells from these mice with TLR ligands for 24 hours, B cells from *Trim21*-deficient MRL/*lpr* mice showed significantly higher abilities to differentiate into plasmablasts (Figure 1) and to produce Ab (Figure 2) as compared to wild-type MRL/*lpr* mice. Due to the reduction of TRIM21-mediated ubiquitylation, IRF5 protein expression was increased in *Trim21*-deficient MRL/*lpr* mice (p = 0.021), which correlated with increased plasmablasts generation. B cells from SLE patients with anti-TRIM21 Ab seropositivity also indicated significantly higher ability to differentiate into plasmablasts and to produce Ab as compared with SLE patients without anti-TRIM21 Ab seropositivity or healthy controls (Figure 3).

Conclusion: TRIM21 dysfunction promotes aberrant B-cell differentiation and Ab production in SLE. Anti- TRIM21 Ab may be related to the TRIM21 dysfunction in human SLE pathogenesis. These findings suggest that TRIM21 and anti-TRIM21 Ab can be promising targets for SLE treatment.Figure 1Figure 2Figure 3

Figure 2. TRIM21 deficiency promotes aberrant Ab production in MRL/*lpr* mice.

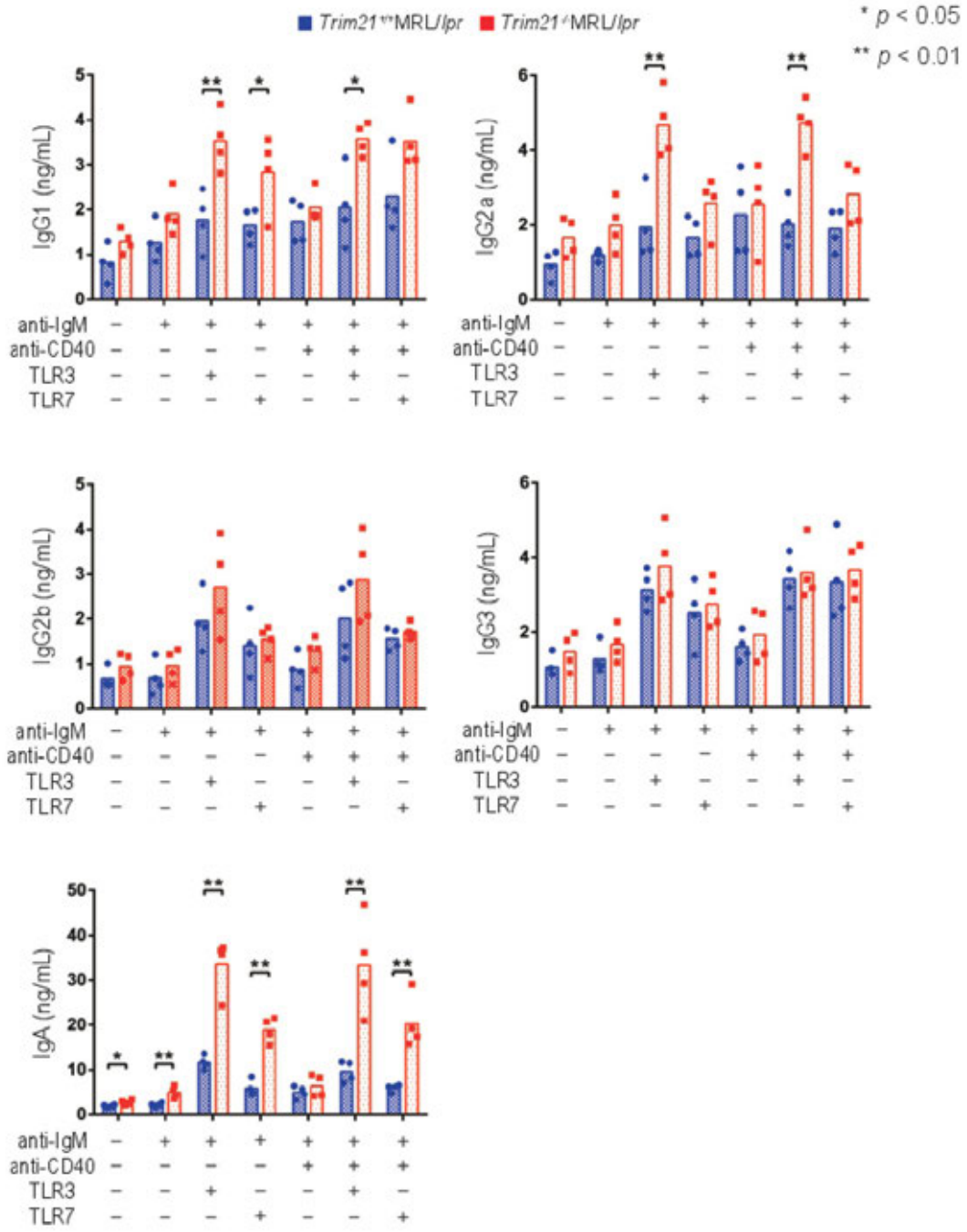
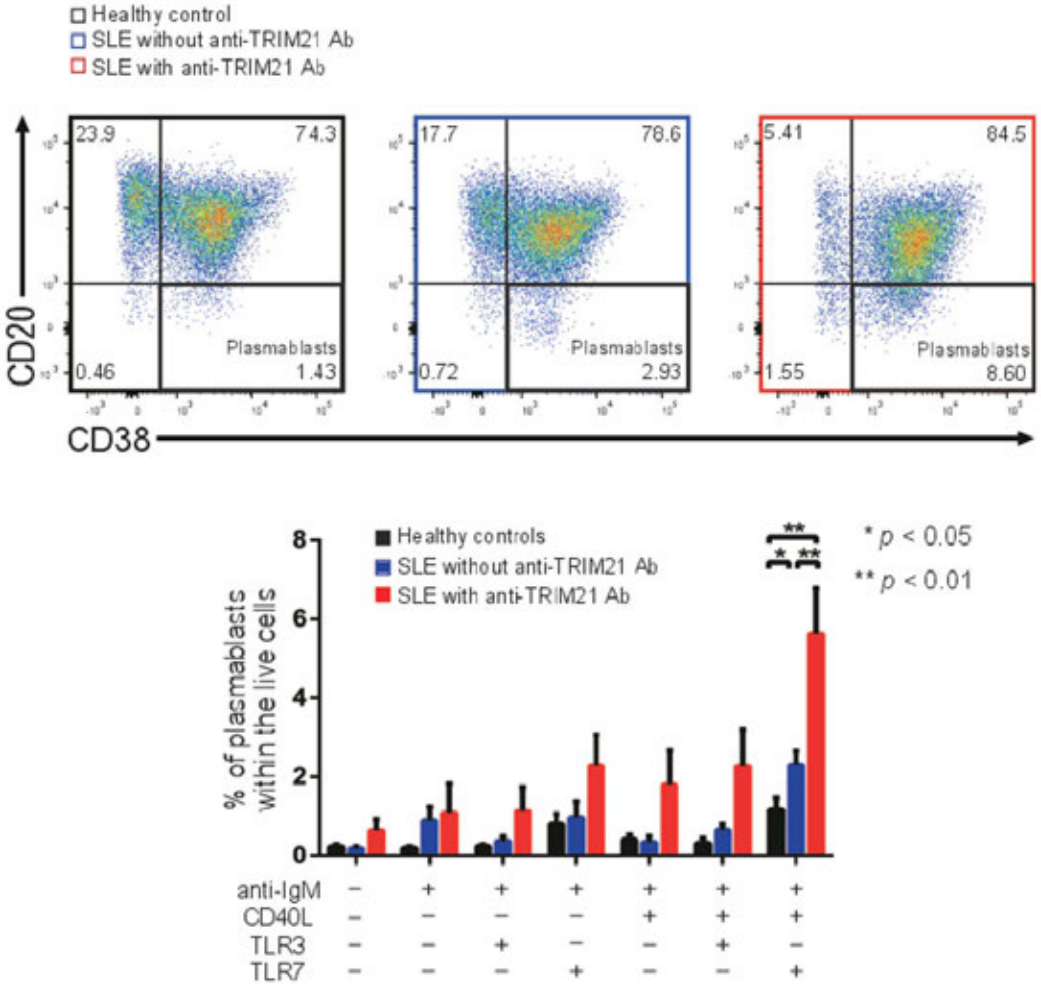


Figure 3. The seropositivity of anti-TRIM21 Ab is related to aberrant B cell differentiation in patients with SLE.



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Abstract Number: 0084

Cenerimod, a Potent and Selective Sphingosine-1-Phosphate Receptor 1 Modulator, Controls Systemic Autoimmunity and Organ Pathology in Mouse Models of Systemic Lupus Erythematosus and Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: SLE – Animal Models Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune diseases including SLE and SS are characterized by aberrant lymphocyte activation and autoantibody production. This results in systemic manifestations and the formation of tertiary lymphoid structures (TLS) leading to organ pathology, loss of organ function, and poor disease prognosis. SLE and SS are challenging to treat and are associated with mortality or severe disabilities.

Reported here are the proof-of-concept and efficacy of cenerimod, a potent, selective, and orally active sphingosine-1-phosphate receptor 1 ($S1P_1$) modulator, in mouse models of systemic (SLE) and organ-specific (SLE and SS) autoimmunity including TLS formation (SS).

Methods: SLE study: MRL/lpr mice were randomly assigned to either a cenerimod or vehicle group; the study was predefined to end when 20% mortality/morbidity was reached in one group. SS study: Salivary gland inflammation was induced in C57BL/6 (B6) mice by cannulation with replication-deficient adenovirus. B6 mice were therapeutically treated with either cenerimod or vehicle and sacrificed 15 days post cannulation. In both studies, target organs were evaluated for immune cell subsets, inflammatory cytokines, disease-relevant biomarkers, histopathology, and organ function.

Results: In the SLE study, all cenerimod-treated mice remained alive after 10 weeks of treatment, whereas >20% died in the vehicle group. Cenerimod-treated mice had significantly fewer circulating immune cells and immune cell infiltrates in kidneys, brain, and salivary glands. This translated to preserved organ function, with significantly reduced urine albumin concentration, kidney and brain histopathologic score, and local inflammatory milieu. Moreover, anti-dsDNA antibody and systemic BAFF and IFN-α levels were significantly reduced. In the SS study, cenerimod-treated mice displayed significantly reduced lymphocyte infiltration into salivary glands and abrogated expression of genes associated with TLS formation. Cenerimod induced TLS disaggregation and resolution of salivary gland inflammation with concomitant decreases in focus score, lymphoid structure size, and T/B-cell follicular organization, resulting in improved organ function with preserved saliva production.

Conclusion: Together, these data demonstrate that cenerimod treatment significantly ameliorated systemic and organ-specific autoimmunity, resulting in decreased inflammation and preserved organ function in animal models of SLE and SS. These results warrant investigation of cenerimod in autoimmune diseases characterized by systemic lymphocyte activation and organ damage. A phase 2b study evaluating the safety and efficacy of cenerimod in patients with SLE is currently recruiting (NCT03742037).

Disclosure: E. Gerossier, Idorsia Pharmaceuticals Ltd., 3, 4, Idorsia Pharmaceuticals Ltd., 3, 4; **S. Nayar**, None; **C. Smith**, None; **S. Froidevaux**, Idorsia Pharmaceuticals Ltd., 3, 4; **F. Barone**, None; **M. Martinic**, Idorsia Pharmaceuticals Ltd., 3, 4.

Abstract Number: 0085

Selective Inhibition of the Immunoproteasome with KZR-616 Blocks Multiple Cell Signaling Pathways, Plasma Cell Signatures and Myeloid Cell Associated Damage in the NZB/W Lupus Nephritis Model

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SESSION INFORMATION
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Background/Purpose: The immunoproteasome is a distinct class of proteasome found predominantly in immune effector cells and has been shown to play a distinct role in the regulation of the immune cell function. We have previously demonstrated that selective inhibition of the LMP7 and LMP2 subunit of the immunoproteasome with KZR-616 effectively blocks the progression of lupus in the NZB/W mouse model of lupus nephritis (LN), including reducing serum levels of anti-dsDNA antibodies**.** Here we describe changes to global gene expression in the spleens and kidneys of diseased mice following KZR-616 treatment.

Methods: The therapeutic effect of KZR-616 was examined in the NZB/W model of SLE. The degree of proteinuria (0 – 4 scale) was used to evaluate the severity of nephritis. Kidneys were harvested and stained with hematoxylin and eosin and anti-immunoglobulin G (IgG). RNA was extracted from spleens and kidneys of NZB/W mice after 11 weeks of subcutaneous KZR-616 treatment and evaluated by RNA sequencing analysis. Canonical pathways were analyzed using Ingenuity Pathway Analysis software.

Results: KZR-616 administration to mice resulted in selective inhibition of LMP7 and LMP2 by 91% and 71%, respectively, similar to levels of inhibition seen *in vitro* and previously reported data in humans at doses ≥ 30 mg (Lickliter et al. ACR 2017). KZR-616 treatment of diseased mice resulted in complete resolution of proteinuria and an absence of renal IgG deposition compared to vehicle treated animals. Consistent with these findings, we noted decreased gene expression associated with inflammation, the T helper (Th) 1 pathway, Th17 activation, interferon signaling, generation of antibody secreting cells, and plasma cell (PC) differentiation in the spleen. In the kidney, immunoproteasome inhibition abrogated transcripts associated with inflammation, cell and myeloid trafficking into the glomerulus as well as expression of renal ortholog genes previously identified to be differentially expressed in the glomerular and tubulointerstitial compartments in LN patients.

Conclusion: KZR-616 effectively blocks disease progression in a mouse model of SLE by regulating expression of genes that are involved in immune response and effector cell function, PC differentiation and antibody secretion, and glomerular and tubulointerstitial renal pathology. These experimental data support the ongoing clinical evaluation of KZR-616 in patients with LN.

Disclosure: T. Muchamuel, Kezar Life Sciences, 1, 3; **J. Anderl**, Kezar Life Sciences, 1, 3; **R. Fan**, Kezar Life Sciences, 3, 4; **H. Johnson**, Kezar Life Sciences, 1, 3, 4; **D. McMinn**, Kezar Life Sciences, 1, 3, 4; **C. Kirk**, Kezar Life Sciences, 3, 4, 6.

Abstract Number: 0086

THOR-809: An IL-2 Engineered from an Expanded Genetic Alphabet for the Potential Treatment of Autoimmune Disorders

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: CD4+ regulatory T cells (Tregs) play a crucial role in maintaining immune homeostasis. Treg dysfunction is associated with multi-organ autoimmune (AI) and inflammatory-related diseases. Treg-mediated

down-modulation of the immune effector function (Teffs and T helpers) that prevents antigen recall may reset immune tolerance in select AI disorders.

A current focus for therapeutic intervention of autoimmune disorders includes cytokine therapies such as IL-2. Administered at low dose, IL-2 induces limited expansion of CD4+ regulatory T cells (Tregs) and showed therapeutic benefit in chronic graft-versus-host disease (cGVHD) and HCV-induced vasculitis and is currently in clinical investigation for treatment of diverse Tcell-mediated autoimmune disorders. However, the sub-optimal pharmacological properties of IL-2 complicate administration and may limit the efficacy of low dose IL-2 therapy. Multiple IL-2 muteins, most of them consisting of fusions to IgG or its Fc domain, are in pre-clinical and clinical development, to address the pharmacokinetic and pharmacodynamic liabilities of low dose IL-2.

Methods: To engineer an improved IL-2 for autoimmune therapy, we applied our recombinant platform technology that expands the genetic code by adding a new DNA base pair. This allows for optimization of proteins through incorporation of novel amino acids encoded by our new DNA base pair, enabling site-specific modifications that enhance the pharmacological properties of these therapeutics. Here we report on the discovery of a site-specific, covalently-pegylated IL-2 that has substantially improved pharmacologic properties over native IL-2 for expansion of Tregs.

Results: Screening of distinct site-specific PEG-IL-2 conjugates in vitro and in mouse identified THOR-809, which showed significantly improved half-life and sustained exposure. In mouse, THOR-809 preferentially stimulated proliferation of peripheral Tregs relative to Teffs (no expansion) and NK cells (minimal expansion). Expanded Treg populations demonstrated significant upregulation of markers that correlate with Treg suppressive function, including FoxP3, CD25, ICOS and Helios. In Cynomolgus monkey, subcutaneous dosing of THOR-809 demonstrated dose-dependent proliferation and activation of peripheral Tregs with no detectable proliferation of Teffs or NK cells up to 200 mcg/kg. We also show that PEG length and shape influences the half-life and pharmacodynamic response for expansion of Tregs in vivo.

Conclusion: Overall, our results indicate that THOR-809 is an IL-2 tuned for biased activation and expansion of Treg cells, with no activation and expansion of Teff or NK cells. These findings support the development of THOR-809 as a treatment for AI disorders.

Disclosure: J. Ptacin, Synthorx, 3; **C. Caffaro**, Synthorx, 3; **L. Ma**, Synthorx, 3; **I. Joseph**, Synthorx, 3; **D. Chen**, Synthorx, 3; **T. Ismaili**, Synthorx, 3; **K. San Jose**, Synthorx, 3; **Y. Pavlova**, Synthorx, 3; **N. Singh**, Synthorx, 3; **L. Koriazova**, Synthorx, 3; **H. Aerni**, Synthorx, 3; **M. Pena**, Synthorx, 3; **J. Mooney**, Synthorx, 3; **M. Milla**, Synthorx, 3, 4.

Abstract Number: 0087

KINE-101, a Novel Synthetic Peptide with Potent Regulatory T Cells Activation to Treat Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Medical and patient unmet needs still existed in rheumatoid arthritis (RA) global market due to the side effects treated for long duration and sometimes non-response to existing medicines. We developed a novel synthetic peptide, KINE-101 with distinct mode of action to activate the regulatory T (Treg) cells.

Methods: The efficacy of KINE-101 was investigated by collagen-induced arthritis (CIA) mouse model. The activity and differentiation of Treg cells by KINE-101 were determined by FACS analysis using various Treg cells markers. Treg cells depletion study was evaluated using CD25 antibody. Autoantibody production was measured by ELISA and germinal center B cells were stained with B cells markers. Osteoclastogenesis was assessed Safranin O staining using joint tissue section. Preliminary toxicology study was accomplished to confirm the safety of KINE-101.

Results: In CIA model, KINE-101 showed similar efficacy in controlling arthritis index compared to MTX. Surprisingly, activation and differentiation of Treg cells were significantly increased by treatment of KINE-101. The effect of KINE-101 mediated by Treg cells was confirmed by Treg cell depletion study in CIA mouse model. Moreover, collagen type II specific autoantibody production were dramatically decreased and germinal center B cells were inactivated by treatment of KINE-101. Safranin-O staining results show KINE-101 suppresses cartilage damage through inhibiting osteoclastogenesis. No significant toxicological findings were observed as a result of preliminary toxicology study.

Conclusion: We developed a novel synthetic peptide, KINE-101, for the treatment of rheumatoid arthritis. KINE-101 shows high remission of RA symptoms in CIA model by activating Treg cells resulting in reduction of autoantibody production. These results suggest that KINE-101 may serve as a first-in-class therapeutic to control autoimmune diseases with Treg cells regulation.

Disclosure: M. Kim, None; **S. Lee**, None; **J. Roh**, None; **J. Kwon**, None; **S. Park**, None; **D. Cho**, None.

Abstract Number: 0088

Type I Interferon Signature Activation in Antiphospholipid Syndrome: Gene Expression Heterogeneity Among Disease Subsets

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
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Background/Purpose: Type I Interferons (IFN) play a key role in the pathogenesis and evolution of various autoimmune diseases. Previous studies have demonstrated that the expression of a number of genes regulated by type I IFN, the so-called "*IFN signature*", has been related with disease activity and clinical features in systemic lupus erythematosus (SLE) patients and other systemic conditions. However, differences in the degree of activation and gene diversification have been reported among diseases and even at the disease level. To date, a limited number of studies have analysed the IFN signature in antiphospholipid syndrome (APS) setting, both primary (PAPS) and when associated with other autoimmune conditions (secondary APS, SAPS). This study aims to describe the activation and structure of the type I IFN signature among different subsets of APS.

Methods: A total of 116 patients were enrolled, including 19 PAPS patients, 13 SAPS, 75 SLE patients, and 9 antiphospholipid antibodies positive individuals ("*aPL carriers*"). Thirty-two subjects were also recruited as healthy controls (HC).

IFI44, IFI44L, IFI6, MX1 and IRF4 gene expression was determined in whole blood in the entire cohort. Expression levels were normalized to Z-scores and averaged into a global IFN signature. Differences were measured by Kruskal-Wallis tests and associations among genes were studied by cluster and correspondence analyses. Correlations were plotted by network analyses.

Results: A global activation of the type I IFN signature was observed (HC: -0.44±0.08, aPL carriers: -0.38±0.12, PAPS: -0.31±0.80, SAPS: -0.17±0.39, SLE: 0.09±0.80; p(Kruskal-Wallis)< 0.001).Certain heterogeneity was observed among interferon regulated genes (IRG): MX1 being increased in all patient groups (all p< 0.001), whereas IFI44 was only increased in SLE (p< 0.001) and PAPS (p< 0.001), and both IFI44L and IFI6 were increased in SLE (both, p< 0.001) and a trend was observed in SAPS (p=0.060 and p=0.080). By means of an unsupervised analysis, 3 clusters (I to III) were identified, which correlated with clinical status of the patients by correspondence analysis (p< 0.0001, Figure 1a). Network analyses revealed different structures of the IRGs networks among groups, from weaker networks in HC and aPL carriers to stronger degree of correlations among IRGs in SAPS and SLE, thus pointing to diverse

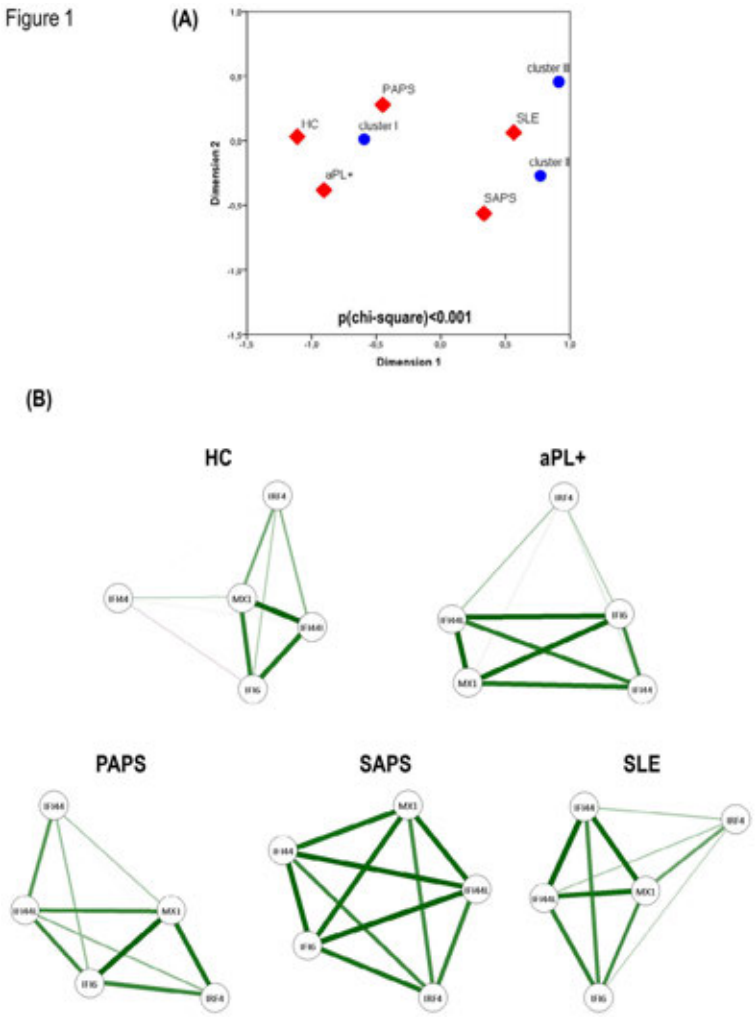

Figure 1. Panel A) Clusters analysis, correlated with clinical status of the patients by correspondence analysis (p<0.0001). Panel B) Network analyses of the interferon regulated genes networks among groups.

expression programs (Figure 1b). Among APS patients (both SAPS and PAPS), the IFN signature was positively associated with anti-phosphatidylserine/prothrombin antibodiesIgG levels (r=0.478, p=0.003), but no associations were observed for the IgM isotype nor with other autoantibodies specificities (all p >0.050). No associations were observed with traditional cardiovascular risk factors or current treatments (all p >0.050).

Conclusion: APS is associated with a broad type I IFN activation, with a notable heterogeneity within the IFN signature structure among clinical subsets.

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Abstract Number: 0089

Difference of Induced CD4+ and Natural Regulatory T Cells in Targeting Inflamed Synovial Tissues in Autoimmune Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
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Background/Purpose: Enhanced evidence supports that autoimmune diseases often result from an imbalance between regulatory T cells (Treg**s**) and interleukin-17-producing T helper (Th17) cells. However, under inflammatory arthritic conditions, natural Treg cells (nTregs) lose Foxp3 expression and undergo transdifferentiation into Th17 cells, which has a key role in the pathogenesis of autoimmune arthritis. Our previous data showed that induced iTregs are able to alleviate collagen-induced arthritis(CIA), which inspired us to study the characteristics and functional difference between nTreg and iTreg especially their interaction with inflamed synovial fibroblast cells (ISFs), since ISFs are the most prominent player in both inflammation and joint destruction in rheumatoid arthritis.

Methods: To determine the stability of iTregs or nTregs in the present of ISFs isolated from CIA mice, iTregs or nTregs were co-cultured with ISFs and the expression of Foxp3 and IL-17a was detected by flow cytometry. We also pretreated nTreg and iTreg with ISFs and then compared their suppressive activities against effector T cells. Additionally, iTregs and nTregs were co-cultured with ISFs, and the production of the pro-inflammatory factors TNF-α, IL-6, IL-12, IL-18, IL-1β, IL-11, IL-15, MCP-1, MMPs, as well as anti-inflammatory cytokines IL-10, IL-1R by ISFs were measured by qPCR, the tumor-like biologic behaviors of ISFs were detected by CCK-8 (proliferation) or crystal violet staining (migration and invasion). To determine the function of nTreg and iTregs on ISFs in CIA mice, ISFs isolated from CIA mice treated with nTregs or iTregs were also subjected to detect the expression of the pro-inflammatory factors and observe their tumor-like biologic behaviors. Finally, we also treated colitis mice with nTregs or iTregs that had been pretreated with or without ISFs to determine their difference in treating an inflammatory disease.

Results: iTregs are more stable functional in the presence of ISFs relative to nTregs. iTreg maintained most Foxp3 and less are converted into Th1 and/or Th17 cells when explored with ISFs. Moreover, ISFs treated with iTregs but not nTregs show reduced expression of pro-inflammatory factors and matrix metalloproteinases and suppressed tumor-like biologic behaviors, with lower proliferation, migration and invasion. In line with results in vitro, infusion of iTregs are more functional to reduce the activation of osteoclasts and bone erosion in CIA mice. ISFs isolated from CIA

treated with iTregs also showed reduced expression of pro-inflammatory factors and matrix metalloproteinases and suppressed tumor-like biologic behaviors when compared to treated with nTregs. Adoptive transfer of iTregs that had been pretreated with ISFs are still able to alleviate colitis, while nTreg lost the therapeutic effects on colitis although they are effective if they are not pretreated with ISFs.

Conclusion: iTregs could be more stable and functional than nTregs in the environment of inflammatory synovial tissues in autimmune arthritis. The manipulation of iTreg therapy may provide an advantage strategy in treating patients with rheumatoid arthritis in the future.

Disclosure: X. Zhang, None; **J. Wang**, None; **N. Olsen**, None; **W. Jarjour**, None; **S. Zheng**, None.

Abstract Number: 0090

SLAMF6 Clustering Is Required to Augment Autoimmune T Cell Activation

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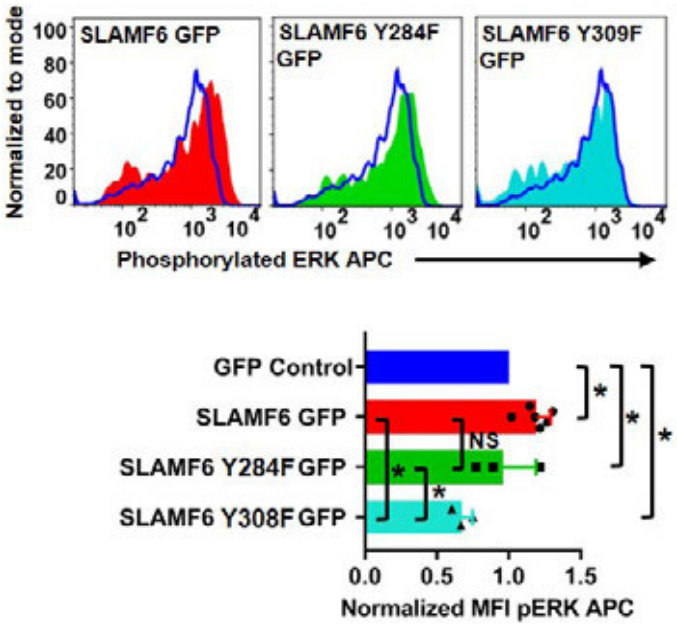
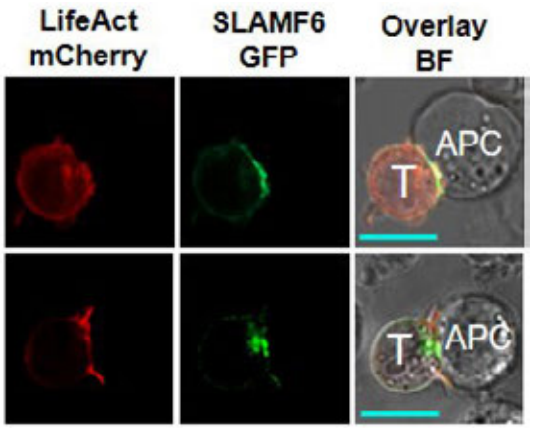
Background/Purpose: The signaling lymphocytic activation molecule (SLAM) family is encompassed by nine distinct receptors that are hematopoietic restricted. Among these, SLAMF6 is highly expressed in autoimmune T cells and genetic variants have been reported in both rheumatoid arthritis and systemic lupus erythematous. Moreover, previous studies as well as our own data, have suggested that anti-SLAMF6 antibodies can have a therapeutic effect in autoimmunity. However, little is known about the role of SLAMF6, specifically in T cell responses. To utilize SLAMF6 interventional approaches, a better understanding of the biology of this receptor in T cell is required. The goal of this





work is to uncover SLAMF6 downstream signaling and function in the context of neutralizing antibodies (Abs). We hypothesis that the SLAMF6 is a co-stimulatory receptor in T cells and that blocking its function should disrupt T cell receptor (TCR) signaling, specifically in activated autoimmune T cells.

Methods: Primary human T cells were collected from healthy volunteers and from patients with rheumatoid arthritis. Cells were treated with anti-CD3 Abs ± anti-SLAMF6 Abs or anti-CD3 abs ± anti-SLAMF6 monobodies. Cytokine release was measured by ELISA and proliferation was recorded by CFSE dilution assay. SLAMF6 gene was deleted in Jurkat T cells using shRNAs and CRISPR-Cas9, prior to a set of rescue experiments with different versions of mutated SLAMF6 gene. These cells were analyzed by western blot and flow cytometry to illustrate signaling downstream of SLAM6. Confocal microscopy imaging was performed to determine the spatial location of SLAMF6 in the immunological synapse during contact with an antigen presenting cell.

Results: Our experimental data shows that SLAMF6 was obligatory for TCR downstream signaling. Remarkably, SLAMF6 ectodomain was required for its function, yet not for its conscription to the immunological (IS) synapse. Flow-cytometry analysis established that tyrosine 308 of the tail of SLAMF6 was crucial for its ability to augment T cell function (Image 1). Imagining studies revealed that SLAMF6 clustering, with the TCR resulted in a dramatic rise in downstream signaling (Image 2). Mechanistically, we showed that SLAMF6 improved T cell function by increasing T cell adhesivity through activation of the small GTPase Rap1.

Conclusion: We have shown that SLAMF6 ligation via antibodies can deliver a vital co-stimulatory signal to increase TCR activation. This behavior includes increasing cytokine secretion, proliferation,ERK, ZAP70 and AKT phosphorylation and cellular adhesion through Rap1 activation. Our findings propose that during TCR engagement SLAMF6 is transported to the IS independent of its ectodomain where it is engaged by another SLAMF6 molecule through the ectodomain to undergo proper function as a stimulatory co-receptor. SLAMF6 is then deliver a co-stimulatory signal dependent on tyrosine 308 into the T cell. By elucidating the mechanism by which SLAMF6 operates in the TCR pathway, we have provided a model for designing interventional approaches for the treatment of autoimmune diseases where SLAMF6 plays a functional role.

Characteristic histograms of phosphorylated ERK. Jurkat T cells were transfected with GFP control, SLAMF6 GFP, SLAMF6 Y284F GFP and SLAMF6 Y308F GFP then stimulated with CD3 antibodies. After fixation and permeabilization the cells were stained and subjected to flow cytometry. Only GFP positive cells were analyzed for phosphorylated ERK APC. Quantification for a minimum of three independent experiments (n=3-6). *$p<0.05$ for an unpaired student t-test. Images and data were adapted from our publication also titled “SLAMF6 Clustering Is Required to Augment T Cell Activation” in press at PLOS ONE (10.1371/journal.pone.0218109).

Jurkat T cells had been transfected with LifeAct mCherry and SLAMF6 GFP then co-cultured with antigen presenting Raji B cells (APC) (top row) or APCs with SEE (bottom row). Scale bar is 10μm. Images were adapted from our publication also titled “SLAMF6 Clustering Is Required to Augment T Cell Activation” in press at PLOS ONE (10.1371/journal.pone.0218109).

Disclosure: M. Dragovich, None; **A. Mor**, None.

Abstract Number: 0091

Histonedeacetylase 1 (HDAC1): A Key Mediator of T Cells for the Pathogenesis of Rheumatoid Arthritis

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SESSION INFORMATION

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

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Background/Purpose: Despite enormous efforts to develop new therapeutic strategies for treatment of rheumatoid arthritis (RA), the large number of non responding patients to currently available drugs underlies the unmet need to identify new therapeutic targets. Certain $CD4^+$T cell subsets, especially Th17 cells, have been shown to be major drivers of inflammation in patients with RA. The expression of their key transcription factors is controlled by histone modifications which includes acetylation of *lysine residues* mediated by histone deacetylases (HDAC). Indeed, pan HDAC inhibitors have been shown to be a potential therapeutic strategy. However, major side effects limited the clinical use and underline the need of more specific HDAC inhibitors. We therefore addressed the individual role of HDAC1 on the development of collagen-induced arthritis model (CIA).

Methods: Methods: Mice with a T cell specific deletion of HDAC1 (HDAC1cKO) were generated by using the CD-4Cre/LoxP system. Collagen induced arthritis (CIA) was induced at week 8. Animals were scored for paw swelling and grip strength. After 10 weeks, mice were sacrificed and paraffin sections of the affected joints were analysed for histomorphologic signs of inflammation, cartilage and bone destruction. Anti-CII antibody levels were determined by ELISA. Serum samples were analysed for various cytokines by multiplex assays. CCR6 expression in CD4 T cells was analysed by flow cytometry.

Results: To address potential effects of HDAC1 in the pathogenesis of RA, CIA was induced in *HDAC1cKO* mice and *WT* mice. Surprisingly *HDAC1cKO* mice were completely protected from the development of arthritis. In line with the clinical data, histological analysis revealed no signs of inflammation, no bone erosion and no osteoclasts in the joints of *HDAC1cKO* mice. Anti-CII antibodies, including total IgG and igG2c were detected in *HDAC1cKO* and *WT* mice. Surprisingly, IL-17 was significantly decreased in the serum of *HDAC1cKO* mice as compared to *WT* mice, suggesting a role of HDAC1 in the development of Th17 cells. To see whether HDAC1 is involved in the regulation of the chemokine receptor 6 (CCR6), the main marker of Th17 cells, we compared the upregulation of CCR6 in $CD4^+$ T

cells from *WT* and *HDAC1cKO* mice. Indeed, CCR6 could not be upregulated in $CD4^+$ T cells from *HDAC1cKO* mice upon IL-6 *in vitro*. These data support the role of HDAC1 in the regulation of CCR6, an important chemokine receptor, which is necessary for the migration of pathogenic Th17 cells and therefore for the development of arthritis.

Conclusion: Our data show the importance of HDAC1 as a key immune regulator in the pathogenesis of T cell driven collagen induced arthritis. Therefore, it might be considered as an interesting novel therapeutic target in RA.

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Abstract Number: 0092

Negative Immune Checkpoint Molecules on T Regulator Cells Distinguish RA, SLE and Healthy Controls

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
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Background/Purpose: T regulatory cells (Treg) play a crucial role in the regulation of the immune response and therefore are of utmost interest when studying autoimmune diseases, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Therefore, targeting specific Treg markers in therapy is now widely discussed. Expression of T cell immunoglobulin 3 (TIM-3) is associated with an enhanced immune suppression and is currently discussed as target in cancer therapy. Fc receptor-like protein 3 (FCLR-3), which regulates Treg proliferation, was shown to be associated with the susceptibility in juvenile RA. Other surface markers, like CD161 enable Treg to produce IL-17A, IFNγ and IL-2, hence promoting inflammation. The aim of this study was to distinguish between RA and SLE using anti-and pro-inflammatory cell markers.

Methods: Peripheral blood samples from 66 patients suffering from RA (mean ± SD; age 60 ± 10 years, female ratio: 0.68, disease duration 18 ± 14 years), 40 SLE patients (age 42 ± 13 years, female ratio 0.85, disease duration 11 ± 13 years) and 72 age-matched healthy participants (age 46 ± 17 years, female ratio 0.68) were drawn over a sampling period of two years. Freshly isolated PBMCs were stained and Treg subsets were identified by the expression of CD25, CD127, FoxP3, CD45RA and CD15 on the surface of $CD3^+CD4^+$ T cells. $CD25^+CD127^+CD45^-$ Treg were further subclassified by the expression of TIM-3 (CD366) and FCLR-3 (CD307c). CD161 was used to identify Th17 type Treg ($CD15S^-CD161^-$) and transitional Treg ($CD15S^-CD161^-$). All cytometric measurements were performed using a standardized BD LSR Fortessa platform.

Results: Transitional Treg ($CD15S^-CD161^-$) were significantly higher ($p < 0.001$) in RA patients compared to the SLE and healthy cohort (40.5 ± 13.4% vs. 28.7 ± 9.6% and 29.7 ± 9.4% respectively). However, differences in the $CD161^+$ Th17 type Treg population could not be detected. Treg expressing TIM-3 were higher in both RA and SLE patients compared to healthy controls (2.8 ± 2.3%, $p = 0.0105$ and 2,.6 ± 1.6%, $p = 0.0031$ vs. 0.8 ± 0.7% respectively), but did not differ between the rheumatic diseases. On the other hand, FCLR-3 positive Treg distinguished RA and SLE

patients (17.8 ± 13.3 vs. 25.3 ± 13.1%, p = 0.0036), as well as SLE patients from healthy controls (16.8 ± 12.9%, p = 0.0112). All findings were not correlated with the disease activity of RA or SLE patients.

Conclusion: Expression of the negative immune checkpoint molecules TIM-3 and FCRL-3 not only distinguish healthy controls from patients suffering from RA or SLE but can be used to differentiate between different autoimmune diseases. These findings indicate that the regulation of the immune response in RA and SLE is triggered by Treg, yet the activation of different Treg subset is disease-specific.

Disclosure: B. Dreo, None; **B. Prietl**, None; **S. Kofler**, None; **H. Sourij**, None; **A. Lackner**, None; **F. Moazedi-Fuerst**, None; **M. D'Orazio**, None; **M. Stradner**, None; **W. Graninger**, None; **H. Brezinschek**, None.

Abstract Number: 0093

Interferon Pathway Activation in T Follicular Helper (Tfh) Cell Subsets in Human Myositis

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Background/Purpose: T and B cells come together in ectopic lymphoid aggregates in myositis, suggesting that local T:B cell interactions could play a role in disease. T follicular helper cells are increased in circulation in patients with active myositis. We studied circulating Tfh cells from myositis patients using single-cell RNA-sequencing and examined the proximity of Tfh cells to B cells in patient biopsies.

Methods: Tfh cells [$CD3^{+}CXCR5^{+}PD\text{-}1^{+}CXCR3^{neg}$ and $CD3^{+}CXCR5^{+}PD\text{-}1^{+}CXCR3^{pos}$] cells were sorted from peripheral blood and subsets were identified by chemokine markers to designate Tfh1 and Tfh2/17 cell subsets. RNA sequencing was performed on individual cells of (3 controls and 3 myositis patients) using Fluidigm C1 HT platform, and data were analyzed using a pseudo-temporal ordering using Monocle. Biopsies were stained using the OPAL standardized sequential immunofluorescence method for PD-1, CXCR5, CD19, and CD4 in human muscle, and machine learning was used to map proximity of B cells to all T-cells compared with Tfh cells.

Results: We found various subsets within the Tfh pool, corresponding to Tfh1 and Tfh2/17 cells and some cells that looked to be transitioning between states. Tfh2/17 were enriched in myositis patients vs. controls. The Tfh2/17 cells demonstrated a type I interferon signature, while the Tfh1 cells had a type II interferon and proteasome signature. In tissue, we demonstrate Tfh cells in close proximity to B cells in lymphoid aggregates.

Conclusion: Tfh cells are present in myositis biopsies juxtaposed to B cells, suggesting productive T:B interactions in the tissue. Tfh subsets in blood from patients demonstrate distinct pathological signatures when compared to controls.

Disclosure: A. Puranik, None; **M. Jensen**, None; **R. Tipon**, None; **Y. Ghodke-Puranik**, None; **V. Mezzano**, None; **S. Selvaraj**, None; **T. Wampler Muskardin**, None; **C. Loomis**, None; **A. Reed**, None; **L. Pachman**, None; **T. Niewold**, None.

Abstract Number: 0094

Tumor Necrosis Factor Receptor 2 Signaling Potentiates Proliferation and Suppressive Activities of Follicular Regulatory T Cells

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Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor Necrosis Factor (TNF) α is a multifunctional cytokine with pro-inflammatory and anti-inflammatory characteristics. Regulatory T cells (Treg) express a remarkably high level of TNF Receptor 2 (TNFR2). TNFα modulates the proliferation and function of Treg via TNFR2. Recently, a subset of CD4+ Treg termed follicular regulatory T (Tfr) cells has been found in the lymphoid organs and blood of animals and humans. Function of human Tfr in vivo is not well understood, however it has been shown that Tfr cells limit the function of Tfh cells and repress immunoglobulin secretion from B cells in vitro. Altered number and ratio of Tfr in several autoimmune diseases have been reported, indicating that Tfr might contribute the immunological abnormality in these patients. TNF-R2 signaling enhances suppressive activities in Treg, on the other hand it is still unclear whether Tfr response to TNF-α via TNF-R2. We examine the role of TNF-R2 signaling in this new regulatory cell subset.

Methods: We sorted Tfr(CD3+ CD4+ CXCR5+ CD25+ CD127low or CD14-CD4+ CXCR5+ CD25+ CD127low) and Treg(CD3+ CD4+ CXCR5- CD25+ CD127low or CD14- CD4+ CXCR5- CD25+ CD127low) from mononuclear cells of healthy donor using FACS Aria.

We examined the proliferation and suppressive ability of these cells stimulated with an anti- TNF-R2 agonistic antibody in vitro and performed the transcriptome analysis by RNA-seq.

Results: Foxp3 expression was upregulated in both cell types after stimulation with TNFR2 agonists. TNFR2 agonists greatly enhanced proliferation of Tfr and Treg. Although unstimulated Tfr did not suppress expansion of Tconv (CD14-CD4+ CXCR5- CD25- CD127high) or Tfh(CD14- CD4+ CXCR5+ CD25- CD127high), Tfr stimulated with TNFR2 agonists suppressed expansion of these cells. In coculture with naïve B cells and Tfh cells, TNF-R2-stimulated Tfr suppressed differentiation of naïve B cells into antibody-producing cells and production of immunogloblin from B cells. RNA-seq revealed altered transcriptome of these TNF-R2-stimulated cells in co-stilmulatory/inhibitory molecules and known Treg associated genes (i.e. Foxp3, CTLA-4, LAG3, etc.). Tfr and Treg showed mostly similar gene expression flux, however part of genes was differently regulated.

Conclusion: TNFR2 agonist enhanced proliferation and suppressive function in Tfr in vitro assays. It suggests that Tfr response to TNF-R2-stimulation similarly with Treg, however in part RNA-seq data showed different response after TNF-R2-stimulation between Treg and Tfr. TNF-R2 agonist might be one of the therapeutic strategies in autoimmune diseases.

Disclosure: S. kawano, None; **H. Mitoma**, None; **S. Inokuchi**, None; **M. Ayano**, None; **Y. Kimoto**, None; **M. Akahoshi**, None; **Y. Arinobu**, None; **K. Akashi**, None; **T. Horiuchi**, None; **H. Niiro**, None.

Abstract Number: 0095

IL-21-mediated Suppression of STAT5 Phosphorylation Underlies Treg Depletion and Dysfunction in SLE

Hiroshi Kato,[1] and Andras Perl[1], [1]SUNY Upstate Medical University, Syracuse, NY

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: IL-21 activates mechanistic target of rapamycin (mTOR) complexes 1 and 2 which in turn block regulatory T (Treg)-cell differentiation and function in patients with SLE. While both IL-21 and IL-6 phosphorylate STAT3 in $CD4^+$ T cells cultured under Treg-polarizing conditions, only IL-21 stimulates mTOR and abrogates Treg-cell differentiation in humans (*Arthritis Rheumatol. 2018 Mar;70(3):427-438*). This suggests that IL-21 blocks Treg-cell differentiation through an mTOR-dependent, but STAT3-independent mechanism. However, it remains unclear how IL-21-driven mTOR activation elicits Treg-cell depletion and dysfunction in SLE.

Methods: Naïve $CD4^+$ T cells from 9 pairs of matched SLE and healthy control (HC) subjects were cultured for 24 hours in the presence of anti-CD3/CD28, TGF-β (5 ng/ml), and IL-2 (50 IU/ml) (hereafter designated Treg-polarizing conditions) with or without IL-21 (10 ng/ml). As a control, $CD4^+$ T cells from 3 matched SLE and HC subjects were cultured for 72 hours in the presence of anti-CD3/CD28 and TGF-β (20 ng/ml) with or without IL-2 (100 IU/ml). Expression and phosphorylation of STAT5 at tyrosine 694 were detected by immunoblotting. The signal intensity of phospho-STAT5 was normalized to that of actin. Statistical significance was determined by a two-tailed t-test using GraphPad Prism version 5 software.

Results: IL-2 induced the phosphorylation of STAT5 in CD4+ T cells from patients with SLE ($p< 0.005$). Conversely, IL-21 suppressed STAT5 phosphorylation in naïve CD4+ T cells cultured under Treg-polarizing conditions both in HC and SLE subjects ($p< 0.05$). Following 24 hours of Treg polarization, CD4+ T cells from SLE patients exhibited diminished STAT5 phosphorylation as compared with those from HC subjects ($p< 0.05$).

Conclusion: In light of the essential roles for STAT5 in Treg-cell differentiation, our data suggests that IL-21-mediated suppression of STAT5 phosphorylation underlies the Treg-cell depletion and dysfunction in patients with SLE.

Disclosure: H. Kato, None; **A. Perl**, None.

Abstract Number: 0096

Characterizing the Brain T Cell Receptor Repertoire in Neuropsychiatric Lupus

Erica Moore,[1] Michelle Huang,[1] and Chaim Putterman[2], [1]Albert Einstein College of Medicine, Bronx, NY, [2]Albert Einstein College of Medicine, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

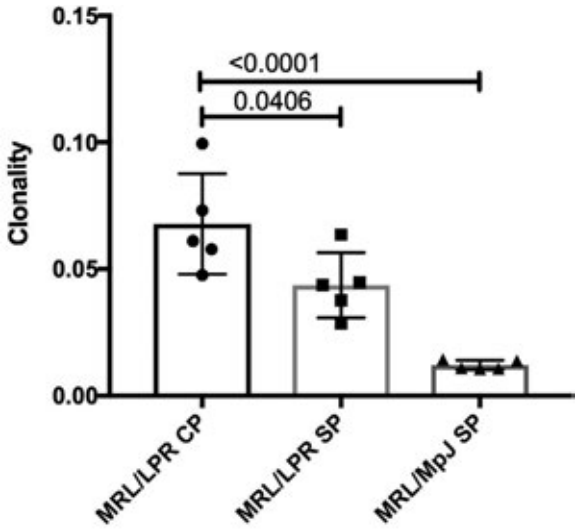

Figure 1A: Sample clonality of MRL/lpr CP T cells, MRL/lpr splenic (SP) T cells, and MRL/MpJ splenic (SP) T cells

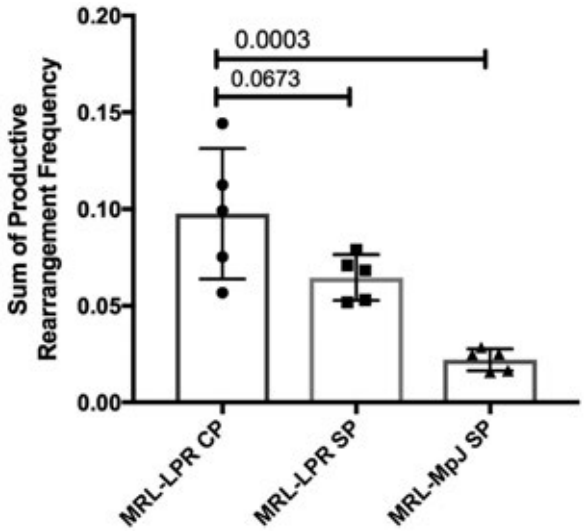

Figure 1B: Abundance of top 10 productive TCR rearrangements for MRL/lpr CP T cells, MRL/lpr splenic (SP) T cells, and MRL/MpJ splenic (SP) T cells

Background/Purpose: Approximately 40% of SLE patients experience neurological and/or psychiatric disorders, including cognitive abnormalities, mood disorders, confusion, psychosis, and seizures. However, the pathogenesis of neuropsychiatric SLE (NPSLE) is complex, and as of yet incompletely understood. We have previously demonstrated that the brain choroid plexus (CP) in the spontaneous MRL/lpr lupus mouse model, a strain which displays affective abnormalities and cognitive dysfunction similar to human NPSLE, is heavily infiltrated with effector T cells. In this study, we investigated T cell receptor (TCR) usage and repertoire diversity in CP infiltrating T cells, to enhance our understanding of this T cell population and its possible contribution to neuropsychiatric disease. In addition, since MRL/lpr mice exhibits T cell proliferation in other parenchymal organs (e.g. lungs and salivary glands), we sought to confirm that the brain T cell infiltration is organ specific.

Methods: Choroid plexuses and spleens were dissected from female MRL/lpr mice (n=5 per group) and MRL/MpJ mice (n=5) (the congenic control) at 16 weeks of age, by which time MRL/lpr mice display profound neurobehavioral deficits. The TCR repertoire was evaluated by isolating genomic DNA from choroid plexus and spleen, and amplifying the CDR3 sequence by multiplex PCR (Adaptive Technologies). The samples were evaluated with the Adaptive Technologies immunoSeq Analyzer and the R package, LymphoSeq.

Results: MRL/lpr CP tissues had significantly increased clonality, derived from the Shannon entropy, as compared to both MRL/lpr and MRL/MpJ splenic tissues ($p = 0.0406$ and $p < 0.0001$ respectively). Similarly, T cells infiltrating the CP demonstrated enhanced oligoclonality, as seen by higher Gini coefficients ($p = 0.0074$ and $p < 0.0001$, respectively, Figure 1A). The abundance of the top 10 productive rearrangements was increased in MRL/lpr CP when compared to the MRL/lpr and MRL/MpJ splenic tissues ($p = 0.0673$ and $p = 0.0003$ respectively), as was the maximum productive frequency (Figure 1B). There was no difference in the gene usage or CDR3 length between the groups. Interestingly, there was an increased sample overlap for tissues originating from the same mouse rather than by organ type.

Conclusion: The results indicate that there is an increased oligoclonal expansion of T cells occurring in the CP of MRL/lpr mice compared to splenic tissues, suggesting antigen-driven brain T cell infiltration and expansion. Further comparative phenotyping of T cells found in different organs (lung, salivary glands, kidney) in the lupus strain is in progress.

Disclosure: E. Moore, None; **M. Huang**, None; **C. Putterman**, Equillium, 5, Equillium, Inc, 2, 5, Exagen, 2.

Abstract Number: 0097

Low Frequency of Circulating T Follicular Helper 1 Cells Is Associated to Adequate Response to Adalimumab Therapy in Rheumatoid Arthritis

Charlotte Lucas,[1] Roussine Codo,[2] Jean-David Albert,[3] Rachel Jean,[2] Stéphane Rodriguez,[4] Patricia Amé-Thomas,[5] and Aleth Perdriger[6], [1]Rheumatology department, Rennes University Hospital, France, Rennes, Bretagne, France, [2]SITI Laboratory, Rennes University Hospital, EFS, INSERM1236, France, Rennes, Bretagne, France, [3]Rheumatology department, Rennes University Hospital and Institut NUMECAN, INSERM U 1241, Rennes, Bretagne, France, [4]PhD, SITI Laboratory, Rennes University Hospital, EFS, INSERM1236, France, Rennes, Bretagne, France, [5]SITI Laboratory, Univ Rennes, Rennes University Hospital, EFS, INSERM1236, France, Rennes, Bretagne, France, [6]Rheumatology department, Rennes University Hospital, France, Rennes, France

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

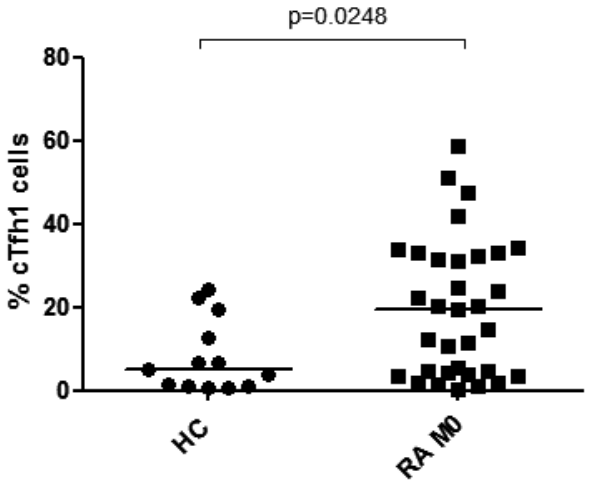

Figure 1 Percentage of cTfh1 cells in RA patients and HC at baseline (M0)

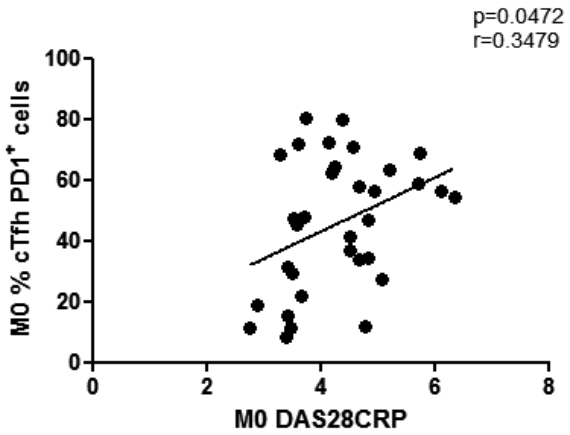

Figure 2 Positive correlation between the percentage of cTfh PD1+ cells and disease activity at baseline (M0)

Background/Purpose: T follicular helper cells (Tfh) constitute a distinct $CD4^+$ helper T-cell subset, promoting B-cell maturation and activation. Circulating Tfh (cTfh) seem to play a critical role in auto-immune diseases. The aim of this study was to analyze cTfh cells involvement in active rheumatoid arthritis (RA), before and after three months of Adalimumab treatment.

Methods: Adalimumab treatment was introduced in biologics-naive RA patients. Disease activity score (DAS) was evaluated at baseline and 3 months later. At baseline, all RA patients have an active disease with a DAS > 3.2 and a corticosteroid treatment > 15 mg per day. All patients vaccinated less than 3 months before Adalimumab initiation were excluded. Three months after Adalimumab initiation, RA patients were classified in responders (R) or non-responders (NR) according to the DAS value (< or > 3.2). cTfh characterization was performed in healthy volunteer controls (HC), and in RA patients before and after 3 months of Adalimumab treatment. Fifteen-color panels of flow cytometry was used to define T helper cells, T regulatory cells, B cells, cTfh cells ($CD3^+CD4^+CD45RA^-CXCR5^+$), effector $PD1^+$ cTfh subset ($CD3^+CD4^+CD45RA^-CXCR5^+$ $PD1^+$), and cTfh1 subset ($CD3^+CD4^+CD45RA^-CXCR5^+CXCR3^+CXCR6^-$). cTfh related cytokine, interleukin 21 (IL21), was also quantified in RA plasma, at baseline and 3 months later.

Results: The results concerned 33 RA patients and 13 HC. Mean age of patients was 58.6 years. Mean RA duration was 8.8 years. Mean DAS value was 4.28. Rheumatoid factors (RF) were positive in 72.7% patients. At baseline, frequency of cTfh1 cells (p=0.0248) (Figure 1), cTfh $PD1^+$ (p=0.004) and IL21 plasma concentration (p=0.003) were higher in RA compared to

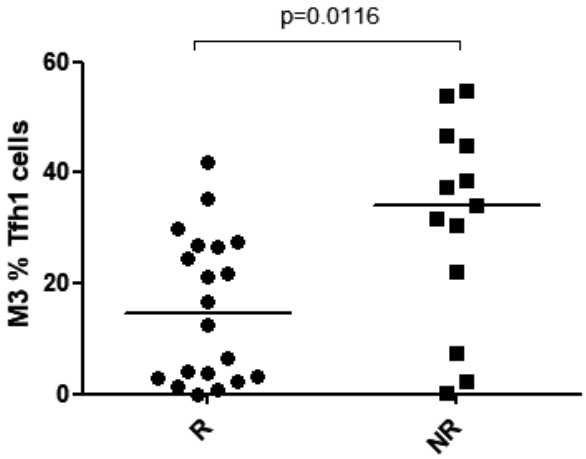

Figure 3 Percentage of cTfh1 cells 3 months after Adalimumab treatment initiation (M3) in responder (R) and non-responder (NR) patients

HC. Moreover, a significant positive correlation was observed between the DAS value, and the percentage of cTfh PD1$^+$ cells (r=0.3479; p=0.0472) (Figure 2) and IL21 plasma concentration (r=0.3755; p=0.0313). After 3 months of treatment, 20 RA patients (60.1%) achieved DAS response. Percentage of cTfh1 was significantly lower in responders than in non-responder patients (p=0.006) (Figure 3). Under treatment, IL21 plasma concentration decreased in all RA patients (p=0.0402).

Conclusion: Our results suggest that cTfh1 cells are involved in RA activation and in a clinical adequate response to adalimumab. Further analysis of these patients is necessary to understand the relationship between cTfh cells, the cTfh1/cTfh2 balance, B cells activation and antibodies production.

Disclosure: C. Lucas, None; **R. Codo**, None; **J. Albert**, None; **R. Jean**, None; **S. Rodriguez**, None; **P. Amé-Thomas**, None; **A. Perdriger**, None.

Abstract Number: 0098

Selective Induction of Functional Regulatory T-Cells in Healthy Volunteers by NKTR-358, a Novel IL-2 Conjugate Treg Stimulator, in Development for the Treatment of Autoimmune Diseases

Christie Fanton,[1] Neha Dixit,[1] Suresh Siddhanti,[1] Lin Lu,[1] Daniel Dickerson,[2] Brian Kotzin,[1] and Jonathan Zalevsky[1], [1]Nektar Therapeutics, San Francisco, [2]PRA Health Sciences, Lenexa

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Regulatory T cell (Treg) dysfunction and impaired IL-2 production have been implicated as key immunological defects in multiple autoimmune diseases. Enhanced sensitivity of Tregs to IL-2 supports use of low-dose IL-2 therapy; however, this treatment is limited by short half-life and relatively poor selectivity for stimulation of Tregs versus other conventional T cell (Tcon) subsets and natural killer (NK) cells. NKTR-358 is a polyethylene glycol (PEG) conjugate of recombinant human IL–2 (aldesleukin sequence with no additional amino acid mutation or substitution), and is being developed with the goal to selectively restore Treg numbers and function in autoimmune disease. NKTR-358 demonstrates prolonged biological activity as well as marked and selective stimulation of Tregs in different animal species as compared to native IL-2.

Methods: In this first-in-human, double-blind, single ascending dose study, healthy volunteers received subcutaneous doses of NKTR-358 ranging from 0.3 to 28.0 μg/kg (9 active: 3 placebo per cohort) and were followed for 50 days. The time course and extent of activation and proliferation of Tregs, Tcons, and NK cells were assessed. In addition, suppressive function of Tregs, as well as changes in gene expression and epigenetic markers in peripheral blood lymphocytes were investigated.

Results: All 8 planned cohorts completed dosing. There were no dose-limiting toxicities, serious adverse events, deaths, or clinically significant abnormalities in vital signs, electrocardiograms, or laboratory test values. The primary effect of NKTR–358 was seen on Tregs. In the 3.0 to 28.0 μg/kg dose cohorts, dose-dependent and sustained increases in the absolute numbers, percentages, and proliferation (Ki67+) of circulating FoxP3+CD25^{bright} Tregs were observed. At 28.0 μg/kg, the mean peak increase in numbers of CD25^{bright} Tregs was 17-fold above baseline, and the mean percentage of Ki67+ CD25^{bright} Tregs was 6-fold above baseline. No increases in numbers of CD4+ or CD8+ Tcons were detected and the number of NK cells was increased < 4-fold at the highest dose tested. In addition to increased Treg numbers, expression of Treg activation markers ICOS and CTLA-4 increased at doses ≥20 μg/kg. NKTR-358-induced Tregs maintained their suppressive capacity as shown by the ability to suppress CD4+ Tcon cell proliferation in an *ex vivo* assay. Induction of Treg numbers was further supported by epigenetic analysis of immune cells demonstrating an increase in demethylated FOXP3. Finally, NKTR-358 administration led to dose-dependent induction of genes associated with Treg regulation, such as IDO1 and CD38.

Conclusion: In continuation of results previously reported, single ascending doses of NKTR-358 led to a dose-dependent increase in proliferation of CD25^{bright} Tregs. The induced Tregs displayed functional activity as evidenced by increased levels of activation markers and the capacity to suppress proliferation of Tcons. These clinical results extend previously reported effects of NKTR-358 on selective Treg stimulation and provide strong support for studying NKTR-358 as a new therapeutic in inflammatory and autoimmune diseases, such as systemic lupus.

Disclosure: C. Fanton, Nektar Therapeutics, 1, 3, 4; **N. Dixit**, Nektar Therapeutics, 1, 3, 4; **S. Siddhanti**, Nektar Therapeutics, 1, 3, 4; **L. Lu**, Nektar Therapeutics, 1, 3, 4; **D. Dickerson**, None; **B. Kotzin**, Nektar Therapeutics, 1, 3, 4; **J. Zalevsky**, Nektar Therapeutics, 1, 3, 4.

Abstract Number: 0099

Mass Cytometry Immunophenotyping of Synovial Fluid from Checkpoint Inhibitor Related Arthritis

Runci Wang,[1] Karmela Kim Chan,[2] Amy Cunningham-Bussel,[3] Laura Donlin,[4] Gregory Vitone,[2] Aidan Tirpack,[2] Caroline Benson,[2] Gregory Keras,[3] Anna Helena Jonsson,[5] Michael Brenner,[6] Anne Bass,[7] and Deepak Rao[1], [1]Brigham and women's hospital, Boston, MA, [2]Hospital For Special Surgery, New York, [3]Brigham and women's hospital, Boston, [4]Hospital For Special Surgery, New York, NY, [5]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [6]Brigham and Women's Hospital:, Boston, [7]Hospital for Special Surgery/Weill Cornell Medicine, New York, NY

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-PD-1/PD-L1 checkpoint inhibitor therapies have produced remarkable results in stimulating immune responses against tumors. Checkpoint inhibitor therapy can also trigger a variety of autoimmune responses; however, the mechanisms underlying these immune-related adverse events (IrAEs) remain unclear. Checkpoint inhibitor-related arthritis (CIrA) occurs in ~5% of treated patients, and synovial fluid from these patients provides

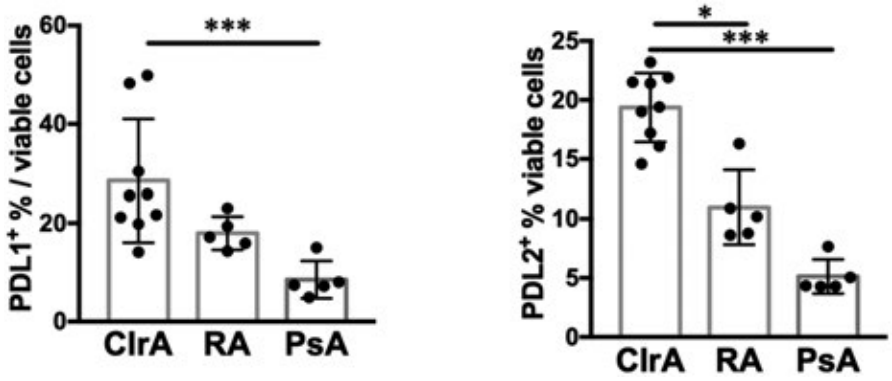

Figure 1. Higher frequencies of PD-L1+ and PD-L2+ cells were found in ClrA.

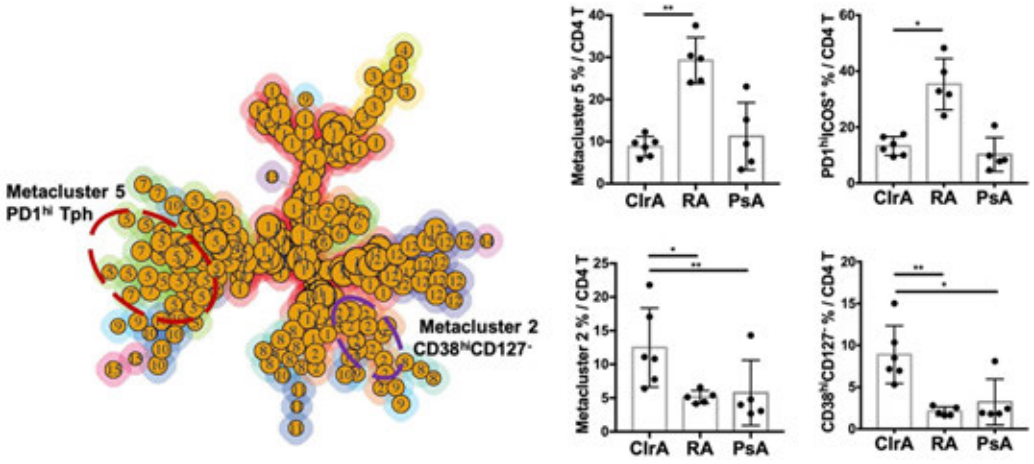

Figure 2. FlowSOM analysis of CD4 T cells revealed expanded PD-1hi Tph cells (CD4 metacluster 5) in RA samples and expanded PD-1+CD38hi CD127- cells (CD4 metacluster 2) in ClrA.

a unique opportunity to study the phenotypes of immune cells from the inflamed site. The extent to which the inflammatory response in ClrA resembles RA or PsA is unknown.

Methods: We conducted detailed immunophenotyping of cryopreserved synovial fluid mononuclear cells (SFMC) from ClrA following anti-PD-1/PD-L1 treatment (n=9), seropositive RA (n=5), and PsA (n=5) patients using a 39-marker mass cytometry (CyTOF) panel. ClrA patients had varied cancers, and 5/9 had mono/oligoarticular arthritis. We identified and custom-conjugated an anti-PD-1 CyTOF antibody using a clone that is not blocked by pembrolizumab or nivolumab, allowing detection of PD-1 in ClrA samples. We used FlowSOM to cluster either CD4 or CD8 T cells into 15 'metaclusters' (cell populations) based on their multi-dimensional phenotypes. We used Kruskal-Wallis or Mann-Whitney tests to identify significantly altered populations ($p< 0.05$), which we confirmed by biaxial gating.

Results: T cells were the most abundant population in ClrA (50% of SFMC. 53% CD4, 40% CD8), followed by monocytes (24%) and NK cells (8%); they were comparable to those in RA and PsA. Cells in ClrA samples showed expression of PD-1 comparable to that in RA and PsA. However, expression of PD-L1 and PD-L2, both frequently expressed on monocytes, was increased in ClrA compared to RA and PsA (Fig. 1, PD-L1: 2.2-fold increased over RA/PsA, $p=0.0021$; PD-L2: 2.4-fold increased over RA/PsA, $p< 0.0001$). FlowSOM analysis of CD4 T cells highlighted distinct cell populations in ClrA and RA. RA samples contained one significantly expanded population (metacluster5, 30% of CD4s in RA, $p=0.006$), which contained PD-1hiICOS+ T peripheral helper (Tph) cells. Tph cells were not expanded in ClrA. In contrast, ClrA samples showed a specific expansion of a distinct population of PD-1+CD38hi

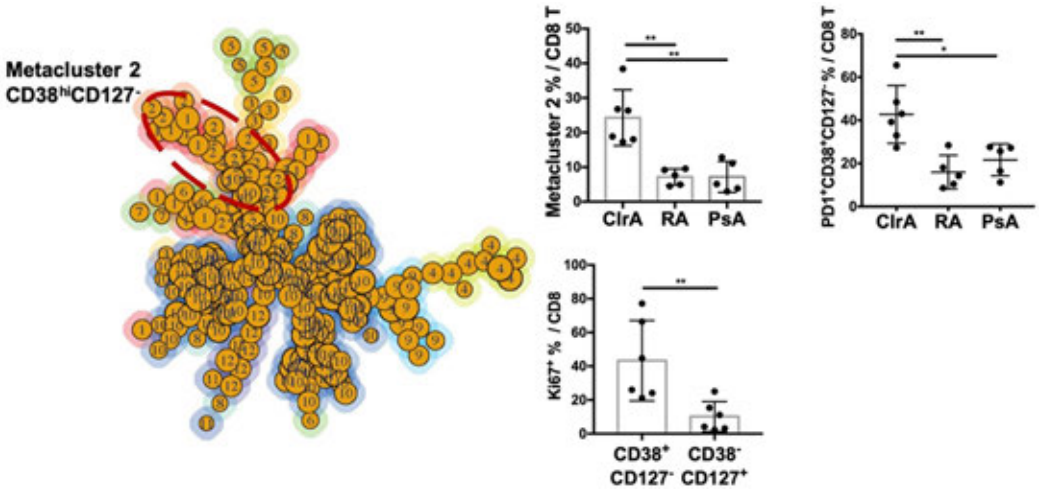

Figure 3. FlowSOM analysis of CD8 T cells revealved the expansion of a PD-1 +CD38hi CD127- population enriched of Ki67+ cells in ClrA.

CD127-cells (metacluster2, 10% of CD4s in ClrA, 2.4-fold increased over RA/PsA, p=0.0047), which we confirmed by biaxial gating (Fig. 2). Interestingly, analysis of CD8 T cells by FlowSOM revealed expansion in ClrA of a CD8 cell population with a similar phenotype to the expanded CD4 population: PD-1+CD38hiCD127-(CD8 metacluster2, 30% in ClrA, 3.4-fold increased over RA/PsA, p=0.0002). Over 40% of PD-1+CD38hi CD127-CD8+T cells in ClrA expressed Ki67, suggesting active proliferation (Fig. 3).

Conclusion: CyTOF analysis of SFMC revealed uniquely expanded CD4 and CD8 T cell populations in ClrA that are not shared with RA or PsA. Both the expanded CD4 and CD8 populations show a PD-1 $^{+}$ CD38 ^{hi} CD127 $^{-}$ phenotype. These cell phenotypes may be directly enhanced by PD-1/PD-L1 blockade and may contribute to the amplified immune response. Functional analysis of these cells may reveal key mechanisms driving CI-associated IrAEs.

Disclosure: R. Wang, None; **K. Chan**, None; **A. Cunningham-Bussel**, None; **L. Donlin**, Karius Inc, 9, Karius, Inc, 2, Stryker, 5; **G. Vitone**, None; **A. Tirpack**, None; **C. Benson**, None; **G. Keras**, None; **A. Jonsson**, Amgen, 2; **M. Brenner**, None; **A. Bass**, None; **D. Rao**, Janssen, 5, Merck, 2, Pfizer, 5.

Abstract Number: 0100

Targeting ITK Signaling Ameliorates Collagen-Induced Arthritis via Shifting the Balance Between Th17 and Regulatory Th17 Cells

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory disease that cannot be cured and current approaches have some severe side effects. Although the pathogenesis is not completely understood, many studies have suggested that the imbalance between Th17 cells/inflammatory cytokines and suppressive Foxp3+ T regulatory (Treg) cells is associated with the pathogenesis and development in RA progression. IL-2 inducible T cell kinase (ITK) is involved in signaling cascades mediating T-lymphocyte proliferation, differentiation, migration, and pro-inflammatory cytokine pro-

duction. The small molecule BMS509744 covalently binds ITK and inhibits the kinase activity of ITK. In this study, we explored whether BMS509744 regulates Th17/Treg balance and could be an effective in RA therapy.

Methods: DBA/1J mice were immunized with Collagen II and CFA to induce a CIA model. BMS509744 was injected i.p. into the mice on day 30 after immunization. To exam the effects of BMS509744 on Th17 and Treg differentiation and function, naïve CD4+ T cells were isolated from Foxp3^{GFP} mice and cultured under Th17 and Treg polarization condition in the absence or presence of BMS509744. Results were analyzed by using Graphpad Prism 7.0 software. Student t test was used to assess statistical significance between two groups and one-way ANOVA were used to assess statistical significance among multi-groups. *p* values less than 0.05 were considered as statistically significant difference.

Results: In the CIA model, infusion of BMS509744 effectively reduced the severity of arthritis, decreased the histopathology scores, improved bone destruction and down-regulated the expression of inflammatory factor IFN-γ/IL-17A. In addition, infusion of BMS509744 increased ratios of Treg cells in CIA mice. BMS509744 effectively skews naïve T cells to Treg cells under Th17 differentiation condition, and promotes Treg induction and enhances Treg function under Treg polarization condition, and also increases Foxp3 expression across TCR doses under Th17 condition, these effects can be reversed by Foxo1 inhibitor. Moreover, we found that BMS509744 decreased mTOR and Akt activity, resulting in inhibiting the phosphorylation of foxo1 and foxo1 translocation to the cytoplasm. Foxo1 expressed in nuclear can stabilize Foxp3 and inhibit the expression of IL-17A. At last, Foxo1 inhibitors significantly reversed the therapeutic effects of ITK inhibitors in CIA model and reversed effects of ITK inhibitors on the balance of Th17 and Treg in CIA model.

Conclusion: ITK inhibitor BMS509744 inhibits the development of CIA by changing the balance between Th17 and Treg cells via mTOR-AKT-Foxo1 signaling. ITK may be an effective RA therapeutic target.

Disclosure: Y. Chen, None; **J. Wang**, None; **N. Olsen**, None; **W. Jarjour**, None; **S. Zheng**, None.

Abstract Number: 0101

CD126 Negative CD4+Foxp3+ Cell Represents a Superior Treg Subset in Treating Autoimmune Diseases

Ye Chen,[1] Julie Wang,[2] Nancy Olsen,[3] Wael Jarjour,[4] and Song Guo Zheng[4], [1]Ohio State University, Columbus, OH, [2]Ohio State University, columbus, [3]Penn State University, Hershey, PA, [4]Ohio State College of Medicine, Columbus, OH

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Regulatory T (Treg) cells play an important role in maintaining immunologic homeostasis. Abnormal Treg cells were found in some autoimmune diseases. Transferred natural Treg (nTreg) cells prevents some autoimmune disease but usually, fails to treat established diseases. Several studies demonstrated that natural CD4+CD25+ Foxp3+ Treg (nTreg) could be transdifferentiated into IL-17A-producing cells and lost its function in the presence of pro-inflammatory cytokines. Given IL-6 is an important inflammatory cytokine and IL-6 binds to its receptor (CD126) to exert functional role, whereas some nTreg cells express CD126, we hypothesize that CD126- Foxp3+ cell subsets could be more stable and functional in the inflammatory condition.

Methods: Flow cytometry were used to analyze CD126 expression on nTreg from collagen induced collagen-induced arthritis (CIA). CD126+ and CD126- nTreg were sorted from CIA mice and analyzed the transcript difference via RNA-sequence. These two subsets were cultured *in* the presence of IL-6 to determine the stability. Moreover, we transferred these two subsets into the established colitis model to analyze the function and stability of CD126+ and CD126- nTreg *in vivo.* Results were analyzed by using Graphpad Prism 7.0 software. Student t- test were used to assess statistical significance between two groups and one-way ANOVA was used to assess statistical significance among multi-groups. *p* values less than 0.05 were considered a statistically significant difference.

Results: Compared to normal mice, the proportion of CD126+ nTreg from CIA mice was significantly higher. CD126- nTreg cells express higher immunosuppressive molecule and present stronger function than CD126+ nTreg not only in the normal condition but also in the presence of IL-6. Moreover, CD126- nTreg was stable while CD126+ nTreg lost Foxp3 expression and trans-differentiated into IL-17A producing cells in the presence of IL-6. Impaired IL-6 signaling in CD126- nTreg was the primary mechanism responsible for the stability, in addition, CD126- nTreg exhibited reduced Hif-1a and glucose transporter 1(Slc2a1) expression, which are two key regulators of glycolytic metabolism and play an important role in the balance of Th17 and Treg. Finally, CD126- Tregs is more effective than CD126+ Tregs when transferred to treat colitis model.

Conclusion: CD126- nTreg cells present stronger function and stability even under inflammatory conditions than CD126+ nTreg cells. Our results suggest that manipulation of CD126- nTreg might be a novel strategy for the treatment of autoimmune diseases.

Disclosure: Y. Chen, None; **J. Wang**, None; **N. Olsen**, None; **W. Jarjour**, None; **S. Zheng**, None.

Abstract Number: 0102

Serine Arginine-Rich Splicing Factor 1 (SRSF1) Restrains IFN-γ and IL-17 Inflammatory Cytokine Production and Its Selective Deficiency in T Cells Exacerbates Experimental Autoimmune Encephalomyelitis (EAE) and Nephrotoxic Nephritis (NTN)

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: CD4 T helper 1 (Th1) and Th17 cells producing IFN-γ and IL-17 are aberrantly increased and contribute to inflammatory responses in autoimmune diseases including systemic lupus erythematosus (SLE) and multiple sclerosis. Better understanding of the molecules and mechanisms that control these aberrant responses are important to design better therapeutic strategies. By discovery approaches we previously identified the multifunctional protein serine arginine-rich splicing factor 1 (SRSF1) in human T cells, and showed that it controls genes involved in signaling and cytokine production. We further showed that SRSF1 is low in T cells from SLE patients and associates with active disease. We recently generated T cell restricted *Srsf1*-conditional knockout (*Srsf1*-ko) mice. *Srsf1*-ko mice develop T cell hyperactivity, systemic autoimmunity, and inflammation in peripheral organs. While SRSF1 is an

important regulator of gene expression, it is unknown how SRSF1 specifically contributes to CD4 T cell activation/differentiation and resulting inflammation in immune-mediated disease. To this end, we evaluated the role of SRSF1 in the Th1/Th17-dependent experimental autoimmune disease (EAE) and nephrotoxic nephritis (NTN) *in vivo*.

Methods: T cell conditional *Srsf1*-heterozygous (het) and homozygous (ko) knockout mice were generated by crossing *Srsf1*-flox mice with d.*Lck.Cre* mice. Peripheral lymphoid organs were analyzed for immune cell phenotype and stimulated ex vivo with PMA/Ionomycin and analyzed by flow cytometry. Naïve CD4 T cells were cultured for 72h with CD3/CD28 and IL-12 for Th1 differentiation. RNA from in vitro generated effector CD4 T cells from WT and Srsf1-ko (n=3 each) mice was subjected to RNA-sequencing. EAE was induced by injecting mice with myelin oligodendrocyte glycoprotein (MOG) peptide with CFA i.p. on day 0, and pertussis toxin i.p. on day 0 and 2. Body weight (BW) and disease scores were recorded daily for 28 days. To induce NTN, mice were preimmunized with sheep IgG (100μg), and 3 days later, nephrotoxic serum (100μl)was administered intravenously. Mice were euthanized on day 24, and tissues collected for analysis. Kidneys were fixed, processed and evaluated blind for histopathology scoring.

Results: CD4 T cells from the Srsf1-ko mice exhibit an increased activated (CD69hi and CD44hi) phenotype and produce increased amounts of IFN-γ and IL-17 upon e*x vivo* stimulation with PMA/Ionomycin. Increased in vitro Th1 differentiation was observed in CD4 T cells from *Srsf1*-ko mice. RNA-seq revealed an overall elevated T cell activation gene signature, increased inflammatory cytokine genes (IL-17A, IL-17F, IFN-γ, IL-4 and IL-21) and increased representation of the Th1/Th17 differentiation pathways in the ko mice. *Srsf1*-ko mice developed more severe glomerular histopathology scores in NTN and the *Srsf1*-het mice developed more severe EAE as evidenced by clinical disease scores and BW loss.

Conclusion: SRSF1 is a novel regulator of CD4 T cell activation/differentiation, and its deficiency in T cells leads to autoimmunity and target organ damage. Therefore, deficiency of SRSF1 in T cells may represent a molecular defect that contributes to the pathogenesis of autoimmune disease.

Disclosure: T. Katsuyama, None; **K. Otomo**, None; **H. Li**, None; **M. Kono**, None; **N. Yoshida**, None; **G. Tsokos**, Janssen Research & Development, LLC, 2; **V. Moulton**, None.

Abstract Number: 0103

Serine Arginine-rich Splicing Factor 1 (SRSF1) Is Indispensable for Homeostasis and Function of Regulatory T Cells

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Regulatory T cells (Tregs) are pivotal in enforcing immune tolerance to prevent and protect from autoimmunity. Defects in Tregs lead to unchecked immune cell activation and promote autoimmune disease. Numbers and/or function of Tregs are frequently impaired in patients with autoimmune diseases. Therefore, understanding mechanisms and molecules that control Treg homeostasis, stability and function is necessary to better target Tregs in autoimmune disease. Serine/arginine-rich splicing factor 1 (SRSF1) is the prototype member of the highly conserved serine arginine (SR) family of RNA-binding proteins. We previously found that SRSF1 expression levels are decreased in T cells from systemic lupus erythematosus (SLE) patients, and associate with active disease.

In addition, using *Srsf1* T cell-conditional knockout (Srsf1-T cell cko) mice, we have shown that deletion of Srsf1 in T cells leads to systemic autoimmunity and lupus-nephritis in vivo through effector T cell hyperactivity. However, the role of Srsf1 in Tregs is unknown.

Methods: Treg specific *Srsf1* conditional knockout (*Srsf1*-Treg cko) mice were generated by crossing B6.*Srsf1*-flox mice with B6.Foxp3.YFP.*Cre* transgenic mice to delete SRSF1 in FoxP3+ Tregs. Peripheral lymphoid organs were analyzed for immune cell phenotype and function by flow cytometry. Serum autoantibodies were measured by ELISA. Tissues were formalin fixed and processed for histopathology. Apoptosis was assessed by Annexin V/7AAD staining and flow cytometry and expression of Bcl-x genes by RT-qPCR. To assess Treg function, Srsf1-deficient Tregs from *Srsf1*-T cell ko mice were utilized. In vitro co-culture assays were performed with CFSE-labeled conventional T (Tconv) cells followed by measurement of Tconv cell proliferation by flow cytometry. In vivo Treg function was assessed by adoptive transfer of Tregs into B6 mice, followed by induction of colitis by oral dextran sodium sulfate.

Results: *Srsf1*-Treg cko mice develop early fatal systemic autoimmune disease and succumb to disease at 3-4 weeks of age. Mice develop systemic autoimmunity, exhibit increased inflammatory cytokine producing T cells, and inflammatory infiltration in vital organs including the lungs and liver. Tregs are reduced in the peripheral lymphoid tissues and display increased levels of apoptosis. Induced (i) Tregs display skewed ratios of the anti-apoptotic Bcl-xL to pro-apoptotic Bcl-xs isoforms of the Bcl-x apoptosis-related gene with a shift towards the pro-apoptotic isoform. *Srsf1*-deficient Tregs from the *Srsf1*-T cell cko mice exhibit defects in suppressive function assessed by both in vitro and in vivo suppressive function assays. In addition, these Tregs produce proinflammatory cytokines including IFN-γ, IL-17 and IL-4. RNA-seq data analysis of *Srsf1*-deficient Tregs reveals that SRSF1 controls the expression of genes involved in homeostasis, inflammatory cytokines and chemokines.

Conclusion: SRSF1 is a novel regulator of Treg homeostasis and function, and its deficiency in Tregs leads to fatal systemic inflammation and autoimmunity. Therefore, deficiency of SRSF1 in Tregs may represent a molecular defect that contributes to the pathogenesis of systemic autoimmune disease.

Disclosure: T. Katsuyama, None; **V. Moulton**, None.

Abstract Number: 0104

Novel, Selective, Orally Active PAD4 Inhibitors for the Treatment of Autoimmune Disorders

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SESSION INFORMATION
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Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Citrullination of proteins is catalyzed by a family of enzymes called the peptidylarginine deiminases (PADs). While the citrullinated proteins may have physiological roles in differentiation, development, cell death, and gene regulation, the pathological protein citrullination has been associated with a range of diseases in-

cluding rheumatoid arthritis (RA), multiple sclerosis, alzheimer's disease, psoriasis and cancer. Notably, the citrulinated proteins are of interest in the pathology in rheumatid arthritis and the citrullinated proteins were detected in the synovium of RA patients. One of the PAD enzymes, PAD4, was reported to be associated with RA and higher levels of PAD4 expression is reported in the synovium. PAD4 co-localizes with citrullinated proteins in the synovium. We hypothesized that inhibition of PAD4 would be beneficial in the treatment of RA and other autoimmune disorders. Our medicinal chemistry efforts have led to the identification and characterization of a series of novel and selective PAD4 inhibitors. The optimization and development of these inhibitors for a variety of autoimmune disorders is underway

Methods: A variety of approaches including the Structure Based Drug Design (SBDD) was employed to identify the hit series and to optimize the leads. The enzymatic activity of hPAD4, PAD1 and PAD2 was assessed using fluorescence based ammonia release assay. The level of citrullinated histones, which is a direct reflection of PAD4 activity, was measured in human neutrophils by ELISA. The mouse model of collagen-induced arthritis, oxazolone induced colitis and Imiquimod induced psoriasis were used to profile the lead compounds

Results: The lead compound PADi showed an IC_{50} of 190 nM against PAD4 in the biochemical assay. It was selective against PAD1 and PAD2 enzymes. In the human neutrophil-based assay, the compound showed significant inhibition of H3-Histone citrullination with an IC_{50} of 320 nM. PADi showed oral bioavailability of greater than 50% across species. Treatment with PADi showed significant improvement in disease index across the various animal models, with efficacies comparable to the standard of care. In Collagen Induced Arthritis and Oxazolone induced colitis models, 50 mpk (BID, P.O.) dose showed >70% reversal of clinical score, with no effect on body weight. The observed pharmacological benefit was accompanied by reduction of histone citrullination in tissue samples, indicating target engagement. In Imiquimod induced psoriasis model, application of 500 ug of compound topically showed a reduction of psoriatic index with a significant decrease in ear thickness and ear weight.

Conclusion: We have identified and optimized a few novel chemical series of PAD4 inhibitors. One of our lead compound, PADi, a selective PAD4 inhibitor, is efficacious in the disease model of arthritis, colitis by oral administration and in psoriasis by topical application. These results suggest that PAD4 inhibition could be a novel therapeutic strategy against unmet medical needs in autoimmune disorders. Further characterization and advanced pre-clinical studies of PADi is in progress.

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Abstract Number: 0105

The DLEU2/miR-15a/16-1 Cluster Inhibit Foxp3+ Treg Cells in Salivary Glands of pSS via Targeting Foxp3

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's Syndrome (pSS) is a systemic autoimmune disease characterized by lymphocytic infiltration of the salivary and lacrimal glands cells form a large part of the lymphocytic infiltrates observed in salivary and lacrimal gland tissues, particularly in the earlier stages of disease, increasing evidence suggests that Treg cells can suppress and control the autoimmune response to protect the body from autoimmune diseases in humans and in animal models. It is also well known that Treg cells play potent roles in the onset and development of SS, but its roles were controversial. This project aimed to claim its role in pSS by investigating ncRNAs related Treg cell.

Methods: Compared to normal controls, we identified the shared and divergent differentially expressed mRNAs (DEmRNAs), miRNAs (DEmiRNAs) and lncRNAs (DElncRNAs) in salivary glands of pSS and non-pSS sicca cases by RNA-sequencing and bioinformatics analysis. Functional annotation of DEmRNAs were performed. Both cis and trans-target DEmRNAs of DElncRNAs were identified. The target DEmRNAs of DEmiRNAs were identified as well. The DEmiRNA-DEmRNA-DElncRNA interaction network was constructed. QRT-PCR was performed to validate the slected miRNAs, mRNA and lncRNAs in salivary tissues. Dual-Luciferase Report Gene System was used to confirm the target of miRNA. The ratio of Th17 and Treg cells (FOXP3+CD25+ CD4+ T cell) in salivary were identified by flow cytometry.

Results: According to RNA-sequencing, 1523 DEmRNAs, 821 DElncRNAs and 19 DEmiRNAs were detected in salivary gland of pSS group, compared to non-pSS sicca group. 20 DElncRNAs related Treg cell were detected in 20 paired of salivary glands, and lncRNA-Dleu2 was upregulated in pSS salivary gland($p< 0.001$) .After the validation by qRT-PCR, the expression of miR15a/miR16-1 cluster was significant up-regulated in salivary glands of pSS patients ($p< 0.001$), which was negative related with the FOXp3 mRNA, and positive related with lncRNA-DLEU2. According the bioinformatics analysis and references confirmation, miR15a/miR16-1 located in gene of lncRNA- DLEU2, known as a gene cluster. And dual-Luciferase Report Gene System confirmed Foxp3 is the target of miR15a/miR16-1.Flow cytometry confirmed FOXP3+Treg cells were decreased in salivary gland of pSS, which was positive related with the expression of miR15a and miR16-1.

Conclusion: LncRNA- DLEU2-miR15a/miR16-1 might be responsible for the reduced FOXp3+Treg cell in salivary gland of pSS via targeting FOXp3.

Disclosure: X. Wang, None; **Z. Wu**, None; **J. Pu**, None; **R. Feng**, None; **J. Tang**, None.

Abstract Number: 0106

Increased T Cell Polyreactivity with Marked Accumulation of TNF-α DP ($CD4^+CD8^+$) in the Synovial Tissue of pre-RA, Arthralgia Subjects

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
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Background/Purpose: Effective treatment of Rheumatoid arthritis (RA) patients is achievable within a short window of opportunity following diagnosis. Identification of pathogenic immune mechanisms at a pre-RA stage would greatly benefit our understating of the early events that govern disease progression and help identify new therapeutic targets and early points for therapeutic intervention. Recent studies illustrate the pathogenic effect of increased T cell poly-

reactivity in autoimmunity, such studies in pre-RA arthralgia subjects have been hindered by the rare availability of synovial biopsy samples and minimal synovial cell recovery. In this study, we describe for the first time, polyreactive T cell responses in the synovial tissue of Arthralgia subjects and RA patients.

Methods: Synovial biopsies of RA patients and arthralgia subjects were obtained by key-hole arthsoscopic surgery. Following enzymatic and mechanical digestion of the tissue, a single cell suspension was obtained. Synovial cells and paired PBMC were stimulated *in vitro* and analysed by 15-colour flow cytometric analysis for the identification of T cell pro-inflammatory cytokine responses. Following multiparametric flow-cytometric analysis, SPICE algorithm and Flowsome unsupervised clustering were utilised to examine peripheral blood and synovial tissue T-cell cytokine polyreactivity of arthralgia subject and RA patients and peripheral blood and synovial fluid Tfh responses.

Results: Higher T cell pro-inflammatory cytokine polyreactivity was identified in arthralgia subjects compared to RA patients. Compared to the periphery, synovial tissue T cell polyreactivity is significantly higher with comparable pro-inflammatory cytokine profiles between arthralgia and RA synovial tissue T cells. Flowsome clustering analysis resulted in the identification of novel T cell clusters that exhibit high polyreactivity and an accumulation of DP ($CD4^+CD8^+$) in the synovial tissue of arthralgia subjects and RA patients. Peripheral blood Tfh cell frequency is significantly higher in arthralgia subjects compared to RA patients, with an accumulation of germinal centre like-Tfh T cells in the synovial fluid of established RA.

Conclusion: Polyreactive pro-inflammatory T cell responses pre-date disease onset as demonstrated by the accumulation of polyreactive T cells in the synovial tissue of pre-RA arthralgia subjects. These data highlight a key early pathogenic role for T cell plasticity and the newly, in autoimmunity, described T cell cluster of DP T cells in RA. We are currently investigating transcription factor profiles that govern polyreactivity of these T cell clusters.

Disclosure: A. Floudas, None; **D. Veale**, Health Beacon, 1; **U. Fearon**, None.

Abstract Number: 0107

Expanded Peripheral T Helper Cells Characterize the Early Rheumatoid Arthritis Synovium

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SESSION INFORMATION
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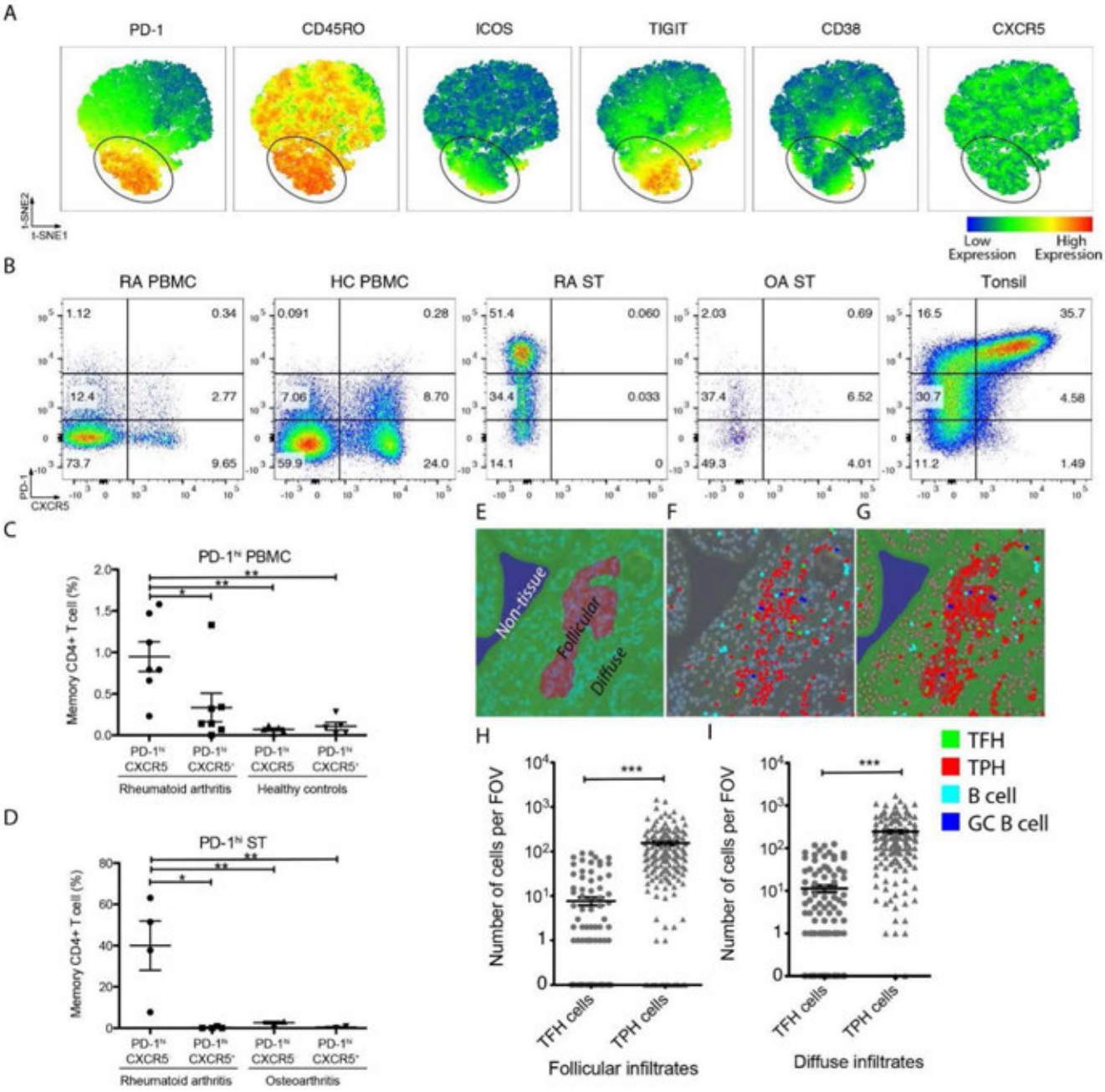
Background/Purpose: Programmed cell death protein 1 (PD-1) expressing T-cells are implicated in the pathogenesis of autoimmune inflammatory diseases such as rheumatoid arthritis (RA). In secondary lymphoid organs, $CXCR5^+$ T follicular helper (TFH) cells secrete IL-21 and provide co-stimulatory signals to germinal centre (GC) B cells, allowing for affinity maturation of antibody responses. Recently a new subset of CXCR5- T-cells, termed T peripheral helper (TPH) cells driving B cell differentiation, have been identified in ectopic lymphoid structures in established RA synovial tissue (ST). Critically, it remains unknown whether TPH cells accumulate in treatment-naïve early RA prior to fully established disease. We aimed to identify TPH cells in treatment naïve early RA patients using flow cytometry (FACS)



and multi-parameter immunofluorescence (IF) microscopy from ST and matched peripheral blood mononuclear cells (PBMCs).

Methods: FACS: Fresh dissociated ST (n=4), and PBMCs (n=7) single cell suspensions were stained with Zombie UV®, CD45RO, PD1, CD3, ICOS, CD8, CD4, CD20, CXCR5, TIGIT and CD38 and analysed using FlowJo 10.5.2.

Histology: 4μm thick RA ST sections were prepared for Opal™ multispectral IF. Primary antibodies for CD45RO, CD20, PD-1 and CXCR5 were sequentially stained, each followed by HRP amplification and specific Opal™ reactive fluorophores. DAPI nuclear staining was performed prior to image acquisition on the Perkin Elmer Vectra 3.0 imaging

system. Images were processed and analyzed using InForm®, a machine learning software package, where the tissue segmentation and TPH and TFH cells quantification was performed.

Results: ST FACS demonstrated T cell infiltration in ST with differential expression of PD-1, CD45RO, ICOS, TIGIT and CD38 (Figure 1A). We observed a higher frequency of PD1hi CXCR5- TPH in RA ST and PBMCs vs. controls (Figure 1B-D). Importantly, no significant difference in TFH frequency was observed in RA and controls. Furthermore, IF identified a 10-fold increase of TPH cells in early RA ST follicular and diffuse regions and identified TPH adjacent to GC B cells (Figure 1E-I).

Conclusion: In this study, we demonstrate, for the first time, the presence and potential role of TPH cells in early RA, with TPH accumulation and close interaction with GC B-cells, potentially contributing to disease pathogenesis and progression. TPH cells may be a novel immune cell target to therapeutic interception of disease progression and warrant further study in early RA.

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Abstract Number: 0108

Mucosal Associated Invariant T Cells in Giant Cell Arteritis

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SESSION INFORMATION

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Background/Purpose: Mucosal Associated Invariant T (MAIT) cells express a semi invariant T-cell receptor (TCR) (TCRVα7.2) restricted to MHC related protein 1 (MR1) and are able to be activated by a TCR-independent pathway involving IL-12 and IL-18. As these cytokines are involved in the pathogenesis of Giant Cell Arteritis (GCA), we investigated the role of MAIT cells in GCA.

Methods: Blood samples from 27 GCA patients, as defined by ≥3/5 ACR criteria, were obtained at diagnosis before starting glucocorticoid (GC) and compared with 16 healthy subjects (age >50 years, CRP≤5 mg/L with no infectious, auto-immune or neoplastic disease). A second blood sample was obtained after 3 months of treatment for 20/27

GCA patients. MAIT cells ($CD3^+CD4^-TCR\gamma d^-TCRV\alpha 7.2^+CD161^+$) were quantified and their phenotype analyzed by flow cytometry. For 4 patients and 5 controls, MAIT cells and MAIT depleted $CD161^+$ T cells were sorted using Fluorescent Assisted Cell sorting (FACS), stained with cell trace violet (invitrogen) and cultured with or without anti CD3/CD28 microbeads or IL-12 and IL-18 (50 ng/ml each). Proliferation index was assessed by flow cytometry after 7 days of culture. MAIT ($CD3^+TCRV\alpha 7.2^+IL\text{-}18R^+$) were stained in positive and negative Temporal Artery Biopsies (TAB) by confocal microscopy on a Leica TCS SP8 confocal microscope. Results are expressed as median [interquartile range] and *P* value is the result of Mann Whitney or Wilcoxon ranked tests, as appropriate.

Results: MAIT frequency among circulating αβ-T cells was similar between patients at diagnosis and controls (0.48% [0.15-1.01] vs. 0.47% [0.28-1.13]; *P*=0.63) and not modified after GC-treatment (0.48% [0.15-0.76] vs. 0.43% [0.14-0.88]; *P*=0.51). By contrast, the phenotype of MAIT cells was modified toward a decreased expression in CXCR3 (6.08% [1.57-13.96] vs. 8.33% [6.13-36.66]; *P*=0.048) and an increased expression in IFN-γ (47.7% [31.8-66.7] vs. 31.0% [16.6-38.7]; *P*=0.03) in patients when compared to controls. This difference was not corrected after GC-treatment: from 8.31% [3.90-16.30] to 4.36% [16.40-17.47] (*P*=0.96) for CXCR3 expression and from 39.8% [23.7-61.3] to 42.4% [23.5-63.3] (*P*=0.85) for IFN-γ expression. Functional analyses revealed that MAIT proliferate in the presence of IL-12 and IL-18 without TCR activation, unlike MAIT-depleted $CD161^+$ T cells. Notably, MAIT from GCA patients displayed a stronger proliferation than the one from controls when stimulated with IL-12 and IL-18: proliferation index 3.39 [2.36-7.15] vs. 1.40 [1.20-2.42] (*P*=0.03). MAIT cells ($CD3^+IL\text{-}18R^+TCRV\alpha 7.2^+$ cells) were identified in the arterial wall of 3 positive TABs and absent in 3 negative TAB.

Conclusion: Although MAIT frequency is not modified in the blood of GCA patients, MAIT infiltrate the arterial wall in GCA patient and their functional characteristics are modified toward a pro-inflammatory phenotype: increased IFN-γ expression and stronger proliferation ability in presence of IL-12 and IL-18. As IL-12 and IL-18 are produced by dendritic cells and macrophages in GCA lesions, MAIT cells might be activated by a TCR-independent pathway and play a role in GCA pathogenesis through the production of IFN-γ.

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Abstract Number: 0109

Targeting CD6 Expression Attenuates T Cell Activity in Murine Collagen Induced Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: CD6, an important regulator of T cell function, interacts with the ligands CD166 and CD318. We previously examined CD318 expression on synovial tissues (STs) and soluble CD318 concentrations in synovial fluids (SFs) of rheumatoid arthritis (RA) patients and demonstrated its potential roles in recruitment and retention of T cells in the RA joints. To further clarify the significance of CD6 in RA, we examined the effects of targeting CD6 in the mouse collagen-induced arthritis (CIA) model, using CD6 knockout mice and CD6 humanized mice that express human CD6 in lieu of mouse CD6 on their T cells.

Methods: We immunized age- and sex-matched WT and CD6 KO mice with a collagen emulsion to induce CIA. Beginning on day 21, CIA clinical scores were recorded by a blinded investigator until day 28. For treatment studies using humanized CD6 mice, we immunized similarly, and injected UMCD6 (a mouse anti-human CD6 IgG) or control IgG on days 7, 14, and 21. We analyzed the joints of the paws for tissue damage, leukocyte infiltration, and local inflammatory cytokine production. We also compared collagen-specific Th1, Th9 and Th17 responses and serum levels of collagen-specific IgG subclasses. Cytokine multiplex assays were used to measure the levels of 32 inflammatory cytokines in homogenates of paw and joint tissues.

Results: CD6 KO mice had markedly lower clinical arthritis scores than WT mice ($p< 0.05$) suggesting that CD6 acts to tune the severity of joint inflammation in CIA. Absence of CD6 reduced 1) collagen-specific Th9 and Th17, but not Th1 responses, 2) many pro-inflammatory joint cytokines, 3) serum levels of collagen-reactive IgG1 and IgG2b, but not IgG2a and IgG3. Significant reductions in joint homogenate hemoglobin (Hb) content in CD6 KO mice were observed compared to WT mice (reduced angiogenesis). Moreover, treating CD6 humanized mice with a mouse anti-human CD6 monoclonal antibody was similarly effective in reducing joint inflammation in CIA as in reducing inflammatory cytokines and chemokines without significantly depleting T cells.

Conclusion: Taken together, these data suggest that CD6 is required for the development of CIA, and that CD6 could be targeted for treating RA.

Disclosure: Y. Li, None; **J. Ruth**, None; **S. Rasmussen**, None; **K. Athukorala**, None; **D. Weber**, None; **M. Amin**, None; **P. Campbell**, None; **N. Singer**, None; **D. Fox**, None; **F. Lin**, None.

Abstract Number: 0110

Bioinformatics Analysis of Transcriptomics Data Reveals That SRSF1 Is a Novel Molecular Brake for the T Cell Activation Program and Controls Key Cytokine Signaling Genes Implicated in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: T cells from systemic lupus erythematosus (SLE) patients exhibit a hyperactive phenotype with defects in homeostasis, signaling and cytokine production. By discovery approaches, we previously identified the serine arginine-rich splicing factor 1 (SRSF1) in human T cells and showed that it controls genes involved in sign-

aling and cytokine production. We further showed that SRSF1 expression is decreased in SLE T cells, and associates with worse disease. We recently found that mice with conditional knockout of *Srsf1* in T cells (Srsf1-T cell ko) exhibit T cell hyperactivity, systemic autoimmunity and lupus nephritis. However, little is known about the molecular targets controlled by SRSF1. Our goal is to identify the genes and pathways controlled by SRSF1 in mice and by comparative analysis evaluate if these are implicated in SLE.

Methods: Effector CD4 T (Teff) cells were generated by stimulating naïve CD4 T cells from spleens of *Srsf1*-T cell-ko or control WT (n=3) mice for 72h with CD3/CD28 antibodies. RNA from CD4 Teffs was subjected to RNA-sequencing (R-seq). Data was analyzed for differentially expressed (DE) genes, gene set enrichment, Kyoto encyclopedia of genes and genomes (KEGG) and gene ontology (GO) pathways. Gene expression omnibus (GEO)2R was used to identify a publicly available dataset (GDS4888) from CD4 T cells in patients with active SLE (n=6, SLEDAI range 6-22, ANA and dsDNA positive) and 4 healthy controls. Comparative analysis of mouse (Srsf1-T cell ko) and human (SLE) gene array data was performed using Metascape to identify overlapping gene signatures in SLE patients controlled by SRSF1.

Results: R-seq analysis from CD4 Teff cells of Srsf1-T cell ko mice revealed 608 significant DE genes compared to WT mice at the 2-fold cutoff with $p < 0.05$. In the human SLE CD4 T cells transcriptomics analysis, SRSF1 was confirmed to be significantly downregulated in active SLE patients compared to healthy controls. 290 genes were significantly ($p < 0.05$) changed between patients with active SLE and healthy controls. The top pathways represented in the DE genes in ko mice were cell cycle, Th1 and Th2 differentiation, Th17 differentiation and cytokine-cytokine receptor interaction. Overall the CD4 Teffs showed an elevated T cell activation gene signature. Pathway analysis of the 290 DE genes in SLE patients identified interferon signaling, cytokine production, cytokine receptor interaction, cell migration and lysosomal clearance pathways. Overlapping genes between human and mouse transcriptomics data were analyzed. Specifically, we found 11 genes (CCR1, RHOG, ELL2, IFI16, IFIT3, OAS2, ZER1, PRKD2, RGS3, SAT1, SOCS1) to be significantly altered in active SLE patients, which were regulated by SRSF1 as confirmed by our mouse R-seq analysis.

Conclusion: SRSF1 controls genes involved in T cell homeostasis, activation, cytokine regulation/signaling and differentiation, which are altered in patients with active SLE. Therefore SRSF1 is an important regulator of T cell function and its deficiency may lead to the hyperactive T cell phenotype in active SLE patients. Targeting SRSF1 to correct the aberrant T cell phenotype may lead to novel therapeutics particularly in SLE patients with decreased SRSF1.

Disclosure: R. Bhargava, None; **M. Lee**, None; **T. Katsuyama**, None; **V. Moulton**, None.

Abstract Number: 0111

The Transcription Factor STAT3 Regulates Pathogenic Th17 Responses in Autoimmune Disease via Noncanonical Roles

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The Th17 lineage of CD4 T cells drives autoimmune diseases such as RA, SLE, IBD, and MS. The JAK2/STAT3 signaling pathway is required for Th17 fate and cytokine production. DMARDs such as JAK inhibitors and anti-IL-6 mAbs exploit this pathway to treat autoimmune diseases. While deletion of STAT3 is known

to abolish Th17 development, little is known about the role of STAT3 in the maintenance of effector Th17 cells. We generated Th17$^{\Delta STAT3}$ mice that delete STAT3 in Th17 cells after upregulation of IL-17. Thus we examined the functional role of sustained STAT3 expression in Th17 cells during a prototypical Th17-driven autoimmune response in experimental autoimmune encephalomyelitis (EAE).

Methods: IL-17^{cre}ROSA26YFP$^{fl/fl}$ mice were crossed with STAT3$^{fl/fl}$ mice (Th17$^{\Delta STAT3}$) and compared to age and gender matched IL-17^{cre}ROSA26YFP$^{fl/fl}$STAT3$^{fl/+}$ littermate controls (Th17^{ctrl}). Mice were immunized with MOG peptide emulsified with CFA and given pertussis toxin on days 0 and 2. Mice were scored daily for disease severity. Cells were isolated from draining lymph nodes (dLN), blood, and/or central nervous system (CNS) and analyzed by flow cytometry and ELISA. For RNA-Seq, YFP^{+} cells were FACS sorted on day 7 post-immunization and RNA-Seq was performed on an Illumina NextSeq500. Results were analyzed using one-way ANOVA or Student's *t*-test, except for EAE clinical data analyzed by Mann-Whitney test on each day of scoring.

Results: Sustained STAT3 expression in Th17 cells is critical for Th17 pro-inflammatory functions, as Th17$^{\Delta STAT3}$ mice had reduced incidence and severity of EAE compared to controls. Similarly, the number of CD4 T cells and macrophages were reduced in the CNS. While Th17 cells develop early after immunization in Th17$^{\Delta STAT3}$ mice, there was a decline in Th17 cell numbers after STAT3 deletion, beginning at the peak of LN priming (day 10). We performed RNASeq of day 10 dLN YFP^{+}Th17$^{\Delta STAT3}$ and YFP^{+}Th17^{ctrl} cells, which revealed that Th17$^{\Delta STAT3}$ cells had reduced expression of genes associated with cell cycle pathways, and confirmed that YFP^{+}Th17$^{\Delta STAT3}$ cells had increased proportions of cells in G0/G1 phase and decreased proportions of cells in S phase and G2/M. Accordingly, we showed that deletion of STAT3 in Th17 cells resulted in an increase in IL-6-mediated phosphorylation of STAT1, which is known to have anti-proliferative effects. Additionally, Th17 cells showed reduced production of the pro-inflammatory cytokines IL-17, GM-CSF, and IFNγ when stimulated with MOG peptide. Surprisingly, cytokine induction by PMA/ionomycin did not require STAT3, suggesting that STAT3 was functioning in a non-transcriptional role. Furthermore, Th17$^{\Delta STAT3}$ cells had reduced mitochondrial membrane potential, which is required for TCR-activated Ca^{2+} flux.

Conclusion: Expression of STAT3 in effector Th17 cells promotes formation and maintenance of pathogenic autoimmune cells by noncanonical functions of STAT3: by reducing STAT1 activation and anti-proliferative effects, and through maintained mitochondrial membrane potential to drive cytokine production in a TCR-dependent manner.

Disclosure: C. Poholek, None; **I. Raphael**, None; **M. McGeachy**, None.

Abstract Number: 0112

Impact of Interleukin-9 on the Immune Suppressive Functions of Regulatory T Cells in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: An important component of the immune tolerance is regulatory T cells (Tregs), which prevents autoimmunity and restrains inflammatory reactions. In Rheumatoid Arthritis (RA), there is a consensus among researchers that Tregs are enriched in the synovial fluid (SF) of individuals with RA. However, despite their synovial

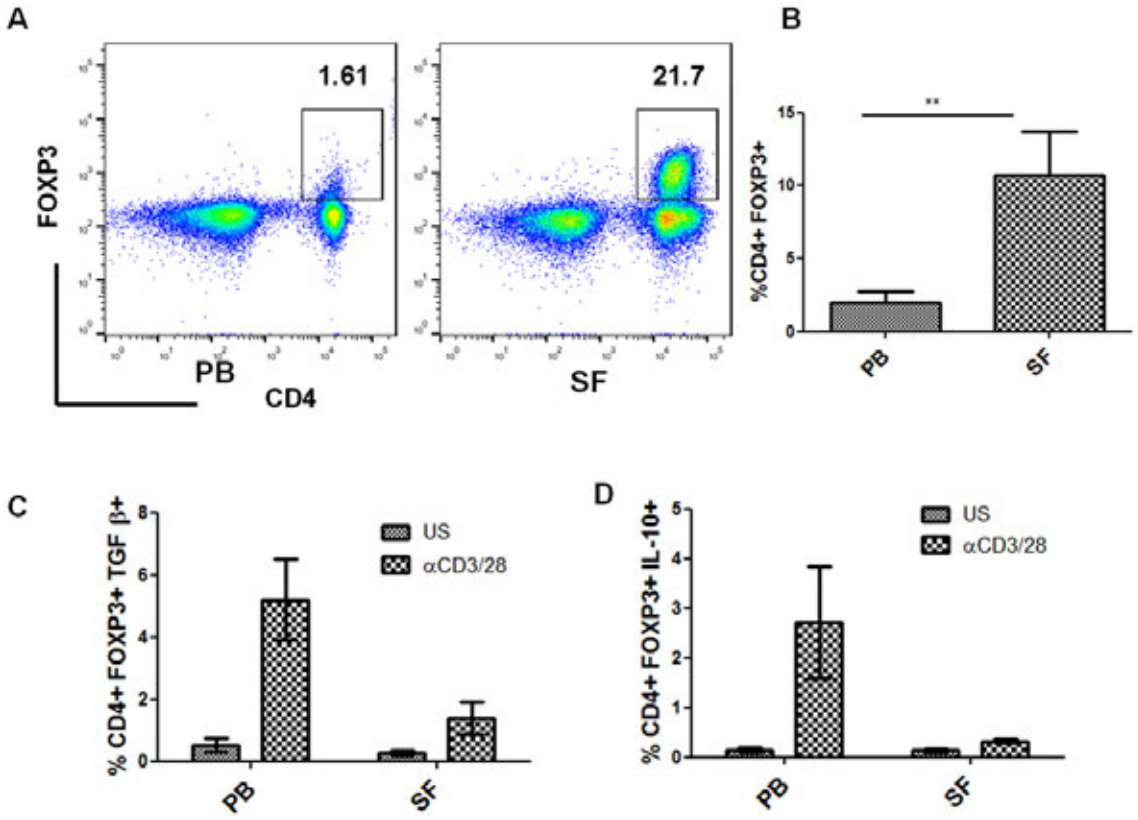

Figure 1: Representative and Cumulative Plots showing Treg frequency in PB and SF of RA patients. Lymphocytes were gated by Forward scatter (FSC) vs. Side Scatter (SSC). Representative dot plots showing CD4+Foxp3+ Tregs in PB (Figure 1A; left panel) and SF (Figure 1A; Right panel) RA patients. Cumulative plots showing frequency of CD4+Foxp3+ cells in PB vs SF in RA patients (Figure 1B; $p<0.05$ is significant). SFMC and PBMC were stimulated . Cumulative plots showing frequency of CD4+Foxp3+IL-10+ cells and CD4+Foxp3+TGFβ+ cells in PB vs SF in RA patients (Figure 1C & D).

accumulation, the synovial inflammation continues in RA suggesting their inability to mediate suppression in the pathogenic site. Recently, our group has shown the enrichment of interleukin-9 (IL-9) producing helper T (Th9) cells in synovial fluid and its positive correlation with disease activity. Therefore, in this study we investigated whether IL-9 plays any role in dysfunctioning of synovial Tregs in RA.

Methods: Mononuclear cells were isolated from peripheral blood (PB) and synovial fluid (SF) of patients with active RA. In vitro stimulation of mononuclear cells was performed by engagement of anti-CD3 and anti-CD28 monoclonal antibodies. We performed IL-9 pathway blocking using a blocking antibody against IL-9 receptor alpha chain. Polychromatic flowcytometry was performed to evaluate the frequencies of IL-10, TGF-β, PD-1 and CTLA-4 positive Tregs (CD4+, CD25+ and FOXP3+).

Results: Treg cells mediate their suppressive function by various ways like contact dependent involving immune inhibitory molecules like programmed cell death protein 1 (PD-1) and contact independent involving suppressive cytokines like IL-10 and TGF-β.We observed that the frequency of $CD4^+$ $FoxP3^+$T cells was significantly higher in the Synovial Fluid (SF) compared to that of Peripheral Blood (PB) from patients. However, Tregs derived from SF are functionally impaired and thus fail to suppress the inflammation at the local site. We observed that *in vitro* stimulation of synovial T cells in presence of IL-9 receptor alpha chain blocking antibody, enhanced the frequency of IL-10 and TGF beta producing Tregs. Also, IL-9 blocking resulted in increase in frequency of PD-1 and CTLA4 expressing Tregs. These observations indicated that IL-9/IL-9 receptor pathway inhibits the suppressive function of synovial fluid derived Tregs. We next checked the effect of recombinant IL-9 on peripheral blood derived Tregs from healthy indi-

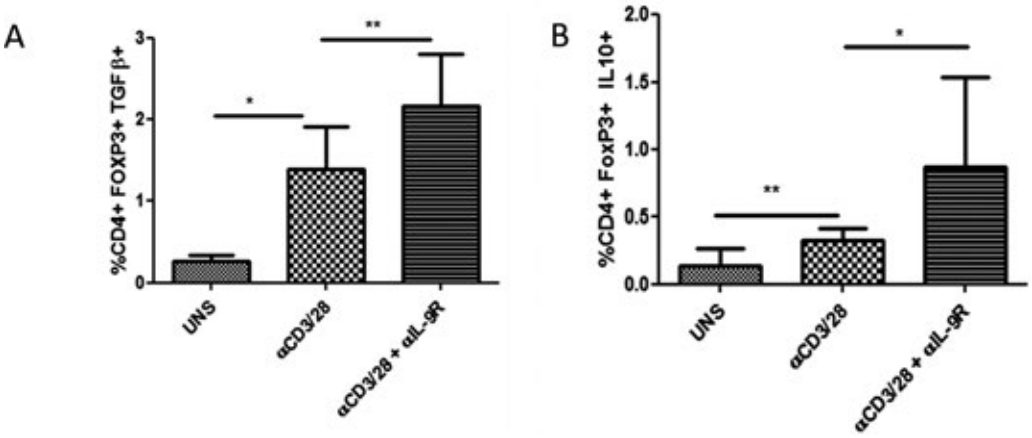

Figure 2: Effect of in vitro blocking IL-9 receptor (IL-9R) on frequency of TGF β and IL10 producing Tregs. Synovial fluid derived mononuclear cells (SMNCs) were stimulated in presence or absence of monoclonal antibody binding to IL-9 receptor alpha . Lymphocytes were gated by Forward scatter (FSC) vs. Side Scatter (SSC).On gated CD4+, the frequency of TGF-β and IL-10 producing Foxp3+ cells were assessed. Cumulative Plots showing frequency of CD4+FOXP3+TGFβ+ (A) and CD4+FOXP3+IL10+(B).

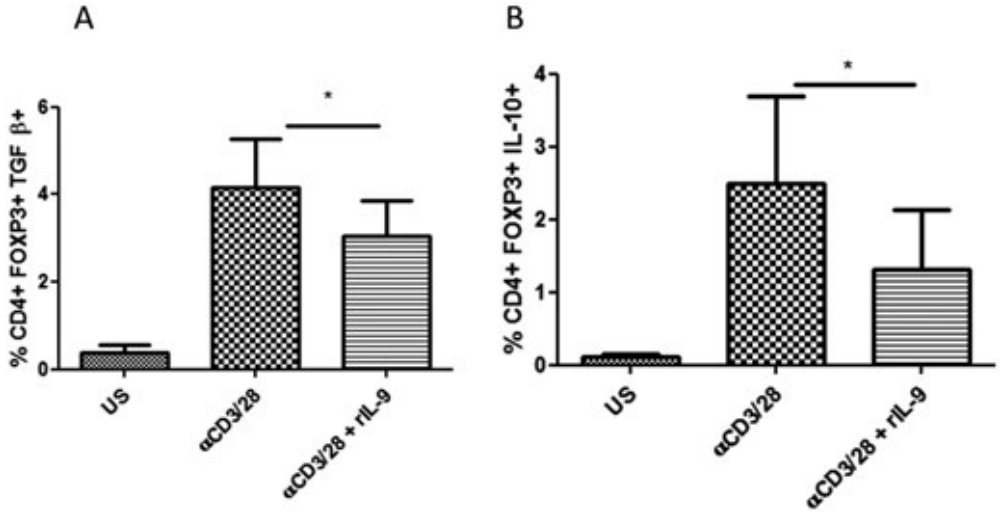

Figure 3. Peripheral blood mononuclear cells (PBMCs) of RA patient were stimulated in presence or absence of recombinant IL-9. On gated CD4+ CD25+ cells, the frequency of TGF-β (A) and IL-10 (B) producing Foxp3+ cells were assessed using Flow cytometry.

viduals. We observed that in vitro stimulation of mononuclear cells in presence of recombinant IL-9 results in reduced frequency of IL-10 and TGF beta producing Tregs, suggesting that IL-9 has negative impact on Tregs.

Conclusion: Our results indicate that IL-9 pathway blocking in RA may contribute in the resolution of inflammation by restoring the Treg function essential for immune tolerance.

Disclosure: S. Chakraborty, None; **R. Gupta**, None; **R. Kumari**, None; **D. Mitra**, None.

Abstract Number: 0113

In Vitro Characterization of the Effect of Cenerimod, a Potent and Selective Sphingosine 1-Phosphate Receptor 1 ($S1P_1$) Modulator, on $S1P_1$ Receptor Expression, Receptor Internalization, and Migration of Primary Human T Cells in the Presence or Absence of Glucocorticoids

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Cenerimod is a potent, selective, and orally active sphingosine 1-phosphate receptor 1 ($S1P_1$) modulator that is currently being evaluated in a Phase 2b study in patients with SLE (NCT03742037). $S1P_1$ receptor modulators sequester circulating lymphocytes within lymph nodes, thereby reducing pathogenic autoimmune cells in the blood stream and in inflamed tissues. Extensive clinical experience has become available for the nonselective S1P receptor modulator fingolimod/Gilenya in relapsing forms of multiple sclerosis, supporting therapeutic concept of sphingosine 1-phosphate for the treatment of autoimmune disorders.

In this study, the mode of action of cenerimod was studied in primary human lymphocytes in a series of in vitro experiments including $S1P_1$ receptor internalization and a newly developed real-time migration assay. As glucocorticoids (GC) are frequently used in the treatment of patients with autoimmune disorders including SLE, the influence of GC on $S1P_1$ receptor expression and function were studied.

Methods: Primary human T lymphocytes from healthy donors were isolated from whole blood cultured with different concentrations of cenerimod to measure $S1P_1$ receptor internalization and sphingosine 1-phosphate (S1P)-directed chemotaxis using flow cytometry and real-time migration assays. In a second series of experiments, the effect of different concentrations of GC (prednisolone and dexamethasone) on $S1P_1$ receptor expression was evaluated. Finally, the effect of physiological concentrations of GCs on cenerimod activity in the receptor internalization and migration assay were tested.

Results: *In vitro,* cenerimod led to a dose-dependent internalization of the $S1P_1$ receptor on primary human CD4 and CD8 T lymphocytes. Cenerimod also blocked migration of activated T lymphocytes towards S1P in a concentration-dependent manner, which is in line with the retention of lymphocytes in the lymph node and the reduction of circulating lymphocytes observed in the clinical setting. Culturing of T cells with GC lead to a slight dose dependent decrease of cell surface expression of $S1P_1$ receptor on CD8 and CD4 T lymphocytes. Importantly, physiological concentrations of GC did not affect the activity of cenerimod in the receptor internalization or the migration assay.

Conclusion: These results show that cenerimod by modulating $S1P_1$ blocks T lymphocyte migration towards its natural chemoattractant S1P and demonstrate compatibility of cenerimod and GC.

Disclosure: P. Kulig, Idorsia Pharmaceuticals Ltd, 1, 3, 4; **M. Murphy**, Idorsia Pharmaceuticals Ltd, 1, 3, 4; **M. Keller**, Idorsia Pharmaceuticals Ltd, 1, 3, 4.

Abstract Number: 0114

Persistent Synovial Resident Memory T Cells Mediate Arthritis Flares

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SESSION INFORMATION

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

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Background/Purpose: Resident memory T cells (TRM) are site-specific memory T cells that take up long-term residence in peripheral tissues and aid in pathogen defense. However, TRM cells can also drive localized, recurrent inflammation. RA and JIA are characterized by recurrent joint inflammation that exhibits a strong tendency to flare at the same sites. We previously created a novel murine model of recurrent, joint-specific inflammation and demonstrated a population of memory T cells with a TRM cell phenotype (CD45+CD3+CD8+CD44+CD62L-CD69hi). Here, we characterize the persistence of these synovial resident memory T cells and their role in arthritis flares.

Methods: Localized arthritis is established by intra-articular (IA) injection of methylated bovine serum albumin (meBSA) or ovalbumin (OVA) with concurrent IL-1beta injections to the footpad to stimulate an immune response. Spontaneous remission occurs after 28 days, but arthritis flares in the original joints when re-stimulated with intraperitoneal meBSA or OVA. To track the site-specific persistence of TRM cells, we labelled synovial T cells using fluorescent reporter mice and IA injection of adeno-associated virus (AAV). To assess the importance of lymphocyte recruitment to an arthritis flare, we treated mice with FTY720, a sphingosine-1 phosphate receptor modulator that sequesters lymphocytes in lymphoid tissues, and evaluated joint inflammation after triggering a flare. Finally, to demonstrate the contribution of synovial TRM cells to the flare response, we locally depleted synovial T cells with a single IA injection of diphtheria toxin into mice with Lck-inducible diphtheria toxin receptors prior to triggering an arthritis flare.

Results: We found that synovial TRM cells persist in previously inflamed joints 8 months after remission and retained their capacity to trigger a flare in a site-specific manner. AAV-labelled TRM cells present in the synovium during remission did not migrate to the contralateral joint. TRM cells enabled joint inflammation by recruiting effector lymphocytes to the joint, and correspondingly localized depletion strongly blunted the capacity to flare arthritis.

Conclusion: Synovial TRM cells persist in arthritic joints and retain their capacity to trigger a site-specific flare after prolonged periods of remission. Our data suggest that synovial resident memory T cells can mediate joint-specific memory in inflammatory arthritis and trigger flares by recruiting circulating lymphocytes, suggesting local depletion of TRM cells as a potential therapeutic strategy.

Disclosure: M. Chang, None; **A. Levescot**, None; **R. Blaustein**, None; **N. Nelson-Maney**, None; **A. Morris**, None; **R. Fuhlbrigge**, CARRA, 6, 9; **P. Nigrovic**, None.

Abstract Number: 0115

CD8+ Cytotoxic T Lymphocytes Are Clonally-expanded in IgG4-related Disease and Home to Affected Tissues

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4-related disease (IgG4-RD) is a chronic immune-mediated fibrotic disease often causing multi-organ involvement. We have previously reported the association of SLAMF7+ CD4+ cytotoxic T lymphocytes (CD4+CTLs) with IgG-4RD including their dominance among the CD4 infiltrate in diseased tissues. In the context of chronic viral infections, such as HIV and CMV, CD4+CTL expansions have been observed to parallel those of CD8+CTLs. CD8+CTLs are additionally reported to be relevant to other autoimmune diseases such as Sjogren's syndrome and Celiac disease. To date, no detailed examination of CD8+ CTLs has been reported in the setting of IgG4-RD.

Methods: We used multi-color flow cytometry to quantitate CD8+CTL subsets in the blood of 48 patients with IgG4-RD and explored correlations with disease severity, serum IgG4 levels and CD4+CTL expansions. We used 20 age-matched healthy individuals and 19 sarcoidosis patients without lung parenchymal fibrosis as controls. We performed TCR repertoire analysis and RNA sequencing using Next Generation Sequencing. Diseased tissues were interrogated for CD8+ T cell infiltrates using multi-color immunofluorescence.

Results: $CD28^{Low}$ $CD57^{Hi}$ CD8+CTLs are expanded in the blood of patients with IgG4-RD and correlate with disease severity, serum IgG4 level and expansion of effector CD4+CTLs. The majority of $CD28^{Low}$ $CD57^{Hi}$ CD8+CTLs in the blood have regained CD45RA expression (CD8+ TEMRA) and dominate over CD8+ TEM. In IgG4-RD, CD8+ TEM and CD8+ TEMRA cells are clonally restricted and highly connected to each other. In contrast to cells from healthy individuals, certain TCR V-beta genes are over-represented among $CD28^{Low}$ $CD57^{Hi}$ CD8+CTLs in IgG4-RD, and dominant V-beta genes are shared across different patients. In the context of IgG4-RD, the transcriptome of these cells suggests conditioning by an inflammatory microenvironment (IL-6, TNF-α, and IFN-γ signaling), heightened metabolic activity, increased cell proliferation, and an enhanced capacity to home to damaged tissues. SLAMF7+ CD8+CTLs infiltrate the involved tissues of IgG4-RD patients in high numbers, comparable to those of SLAMF7+ CD4+CTLs. Tissue infiltrating SLAMF7+ CD8+CTLs are composed of both CD8+ TEM and CD8+ TEMRA cells.

Conclusion: $CD28^{Low}$ $CD57^{Hi}$ CD8+CTLs are expanded in the blood of IgG4-RD and correlate with multiple parameters relevant to the mechanism of disease. In contrast to the same cell type from healthy individuals, these CD8+CTLs from IgG4-RD patients appear to be more active, proliferative and tissue-homing. The highly restricted TCR repertoire shows an over-represented V-beta gene usage that is shared across multiple IgG4-RD patients and differs from the V-beta genes used by the the corresponding T cells in healthy individuals. The TCR V-beta usage suggests the possibility that the CD8+CTL responses are targeting shared class I restricted protein antigens across patients in a

disease-specific manner. The accumulation of CD8+CTLs in disease lesions suggest that they may contribute to the pathogenesis of IgG4-RD. (Supported by NIH U19 AI 110495 and UM1 AI144295)

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Abstract Number: 0116

Defective EZH2 Expression Attenuates Treg Differentiation in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To explore the role of EZH2, a histone methylation regulator, in the pathogenesis of rheumatoid arthritis (RA).

Methods: Forty treatment-naïve patients with active disease and fulfilled the 2010 ACR revised criteria for RA were enrolled in the study.

The expression of EZH2 was further quantified by qPCR, WB, and flow cytometry in T cells. The ability of differentiation, proliferation, and apoptosis of T cells was measured by flow cytometry and qPCR after inhibition of EZH2 through pharmacological inhibitor and siRNA. mTOR signaling pathways were also monitored. The effect of synovial fluid and fibroblast-like synoviocyte (FLS) on EZH2 expression in T cell was determined by flow cytometry and qPCR.

Results: EZH2 expression is lower in PBMC and CD4 + T cells from RA patients. EZH2 inhibition with GSK126 or siRNA ex vivo attenuated the differentiation of naïve T cells into regulatory T cells (Treg). Phenotypically, RA showed decreased Treg frequency in peripheral blood. EZH2 silencing could downregulate SMAD3/4 and increased mTOR expression in vitro. Synovial fluid and FLS from RA patients suppress EZH2 expression in T cells.

Conclusion: Lower expression of EZH2 contributed to decreased Treg differentiation in the CD4+ T cells of RA patients, involved in TGF-β/SMAD signaling and mTOR signaling. The synovial fluid and FLS from RA patients played and role in the reduction of EZH2 expression. Targeting EZH2 might be a potential approach for RA treatment.

Disclosure: X. Xiao, None; **Y. Li**, None; **H. Chen**, None; **X. Zhang**, None.

Abstract Number: 0117

The Indole Derivative NecroX Blocks Th17 Cell Differentiation and Fibroblast-like Synoviocytes-mediated Th1/Th17 Responses in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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

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Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic inflammation of synovium, which causes progressive joint destruction and reduction in quality of life. T-helper-17 (Th17) cells have been implicated to play a crucial role in the development and progression of persistent inflammation. In addition, Th17 cells from patients with early RA induce a pro-inflammatory feedback loop upon RA fibroblast-like synoviocytes (RA-FLS) interaction, including autocrine interleukin (IL)-17A production. NecroX is an inhibitor of necrosis/necroptosis and has been shown to scavenge mitochondrial reactive oxygen and nitrogen species in inflammatory cells, and preventing necrotic cell death against various kinds of oxidative stresses. We aimed to investigate the effects of NecroX on Th17 cell differentiation and T cell – RA-FLS interaction and the production of immune mediators in these interactions.

Methods: RA-FLS were cultured from synovial specimens obtained from RA patients undergoing joint replacement therapy. Inflammatory cytokines/chemokines level was measured by ELISA. Human CD4+ T cells were isolated by magnetic-activated cell sorting from healthy controls and RA patients. Activated naïve CD4+ T cells were pretreated with or without NecroX for Th17 differentiation. The location of phosphorylated signal transducer and activator of transcription 3 (pSTAT3) was detected by immunofluorescence microscope. Human CD4+ T cells were cultured with or without NecroX or co-cultured with RA-FLS by transwell culture system. Th1 or Th17 phenotype was measured by flow cytometry and culture supernatant was collected for analyses of IFN-gamma and IL-17A by ELISA.

Results: NecroX reduced the TNF-alpha induced production of IL-6, CXCL10, MMP-1, 3, 9 and 13 in RA-FLS. When peripheral CD4+ T cells were cultured under Th17 condition, NecroX decreased the population of IL-17+ and CD4+ T cells, and production of IL-17A in dose-dependent manner and also prevented the nuclear translocation of pSTAT3. When RA-FLS were co-cultured with CD4+ T cells, NecroX-7 inhibited RA-FLS-mediated Th1 and Th17 cell expansion both in cell-cell contact-dependent and inflammatory cytokine-dependent manners.

Conclusion: NecroX could be an immune regulator of inflammatory arthritis by suppressing Th17 cell differentiation and RA-FLS activation and inhibiting the pro-inflammatory feedback loop between Th17 cell and RA-FLS. These observations suggest that NecroX might be useful for the development of anti-inflammatory agents.

Disclosure: H. Yoo, None; **S. Kang**, None; **J. Lee**, None; **R. Kim**, None; **Y. Song**, Astellas Pharma, Inc., 9.

Abstract Number: 0118

Polymorphonuclear Neutrophils and Regulatory T Lymphocytes (Treg) Cooperate to Sustain Treg Activity but This Interaction Is Altered in Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Regulatory T cells (Treg) are necessary for immune homeostasis but are functionally deficient in inflammatory/autoimmune diseases such as rheumatoid arthritis (RA). On the other hand, polymorphonuclear neutrophils (PMN) are known for their proinflammatory properties and are highly recruited at inflammation sites such as RA joints. However, recent evidences show that PMN exert also immunoregulatory functions. We hypothesized that Treg/PMN interact and that this interaction is dysregulated in RA. We aimed at deciphering the phenotype and activity of both cells upon *in vitro* Treg/PMN co-cultures and characterized the mechanisms involved. Finally, we analyzed the fate of Treg/PMN interaction in RA patients.

Methods: Splenic mouse Treg and bone marrow PMN (C57BL/6 mice) as well as peripheral blood Treg and PMN of healthy donors and RA patients were freshly purified by magnetic sorting. Co-cultures were unstimulated or exposed to anti-CD3/anti-CD28 antibodies and/or LPS. $CD4^+FoxP3^+$ Treg (mouse and human), $Ly6G^+$ (mouse) and $CD66b^+$ (human) PMN were identified by flow cytometry. Cell activation was further studied by flow cytometry using antibodies against CD25, CTLA-4 (Treg) and CD11b, CD39, PD-L1 (PMN). Treg maintenance was evaluated as the frequency of FoxP3 expression among $CD4^+$ cells, and cell proliferation by CFSE staining followed by flow cytometry analysis. In some case, co-cultures were performed using transwell or Tofacitinib (a JAK inhibitor). Cytokine levels were quantified in culture supernatants by ELISA. Collagen-induced arthritis (CIA) was induced by immunization with type II collagen in complete Freund's adjuvant.

Results: Upon co-culture *in vitro* with PMN, Treg proliferated, showed increased maintenance of FoxP3 expression and up-regulated CTLA-4 as well as CD25 compared to Treg cultured alone, only when both Treg and PMN were stimulated. Reciprocally, upon co-culture with Treg, PMN were activated and expressed regulatory molecules, as evidenced by CD11b, CD39 and PD-L1 up-regulation, as compared to PMN cultured alone, when both cell types were stimulated. The co-culture led to higher secretion of MIP-2/IL-8, IL-6 and IL-17. All these effects were abrogated when co-cultures were done using transwell or when blocking JAK-STAT signalling. Most importantly, PMN sustain Treg suppressive effect on effector ($CD4^+FoxP3^-$) T cells (inhibition of cell proliferation). Similar results were observed in co-cultures of PMN/Treg isolated from mice (both naïve and CIA mice) and healthy donors. However, and importantly, we found out that PMN from RA patients were unable to increase CTLA-4 expression on Treg in co-culture, CTLA-4 being involved in Treg suppressive activity.

Conclusion: Our results reveal the existence of a new link between Treg and PMN, leading to an activation of both cell types and a more suppressive phenotype in healthy conditions. Although cell contacts are clearly required, soluble mediators are also involved and probably as a second signal. This is the first demonstration of an effect of PMN

on Treg phenotype. In RA patients, we evidenced a defect in this Treg/PMN cross-talk. This Treg/PMN interaction might unveil new therapeutic targets against RA.

Disclosure: M. Batignes, None; **F. Santinon**, None; **M. Boissier**, None; **P. Decker**, None; **N. Bessis**, None.

Abstract Number: 0119

Mitochondrial Transplantation Suppressed Muscle Inflammation and Improved the Mitochondrial Dysfunction in C Protein-induced Myositis Model

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SESSION INFORMATION

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Background/Purpose: Polymyositis is a chronic inflammatory myopathy associated with lymphocyte infiltration, especially $CD8^+$T cells to the muscle layer. C protein-induced myositis (CIM) is a murine model of polymyositis (PM). Dexamethasone treatment has an anti-inflammatory effect on polymyositis, but did not improve mitochondrial dysfunction in muscle of CIM mice. In the previous report, mitochondrial function is restored in damaged cells after transfer of mitochondria from human umbilical cord-derived mesenchymal stem cells (UC-MSCs). We investigate whether mitochondrial transplantation may attenuate inflammation and improve mitochondrial dysfunction in CIM model.

Methods: To induce CIM, C57BL/6 mice were immunized with human skeletal muscle C protein fragment. Dexamethasone was administered intraperitoneally at a dose of 0.8 mg/kg/day. Mitochondria from human UC-MSCs were transplanted intravenously on day1 or day7. To evaluate muscle inflammation, ^{18}F-FDG PET/MRI evaluation was performed on day 14. Muscle tissues were stained with hematoxylin and eosin (H&E) for histological evaluation. Pro-inflammatory cytokines were measured by ELISA. The expression of subunits of OXPHOS (oxidative phosphorylation) complexes (I -V) was investigated by immunoblot analysis. To quantitative evaluation of mitochondrial transplantation, the expression of MITO-CO1 and COX4 was evaluated by RT-qPCR.

Results: Mean of histologic summation score of muscles was decreased in day 1 group (0.67 ± 0.60, n = 3), day 7 group (0.75 ± 0.61, n = 10) of mitochondrial transplantation and dexamethasone-treated group (0.5 ± 0.63, n = 10) compared with vehicle (1.5 ± 0.32, n = 7). PET/MRI showed ^{18}F-FDG uptake reduction after mitochondrial transplantation and dexamethasone treatment. IL-6 was reduced in the serum of mitochondrial transplantation and dexamethasone-treated group. However, the protein expression of OXPHOS complex II was increased in day 7 group

of mitochondrial transplantation compared with vehicle or dexamethasone-treated group. As a quantitative evaluation of mitochondrial transplantation, the expression of human mitochondrial encoded gene, MITO-CO1 was increased without altering the expression of COX4, the nuclear-encoded gene in day 7 group of mitochondrial transplantation and these data suggest that isolated mitochondria from human UC-MSC transplanted into CIM mouse muscle.

Conclusion: Mitochondrial transplantation suppressed muscle inflammation and improved the mitochondrial dysfunction through an increase of mitochondrial activity. These findings suggest that mitochondrial transplantation may be used as a new potential therapeutic strategy for inflammatory myopathy.

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Abstract Number: 0120

Administration of a CD45 Antibody Drug Conjugate as a Novel, Targeted Approach to Achieve Immune System Reset: A Single Dose of CD45-targeted ADC Safely Conditions for Autologous Transplant and Ameliorates Disease in Multiple Models of Autoimmune Disease

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SESSION INFORMATION

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

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Background/Purpose: Autologous hematopoietic stem cell transplant (autoHSCT) is a highly effective treatment in selected patients with autoimmune diseases. AutoHSCT can induce long-term remission (up to 15 years) with 70-80% progression free survival in patients with relapsed refractory and secondary progressive multiple sclerosis (Muraro 2017) that is superior to standard of care agents in a randomized study (Burt 2019). Likewise, use of autoHSCT in patients with scleroderma achieved superior outcomes in two randomized studies (Tyndall 2014, Sullivan 2018). These impressive results are achieved by eradication of autoreactive immune cells and re-establishment of a self-tolerant immune system, i.e., immune system reset. However, only a small fraction of eligible patients undergo autoHSCT, in part due to toxicity associated with current conditioning protocols. To address these issues, we are developing antibody drug conjugates (ADCs) that selectively target CD45 to eradicate autoimmune cells and enable autoHSCT as a potentially one-time curative treatment for patients with autoimmune disease.

Methods: We generated a novel ADC targeting murine CD45 that was evaluated as a single conditioning agent for murine congenic transplant. This ADC was further evaluated for its ability to eliminate pathogenic host-reactive cells in the context of multiple murine models of autoimmune disease, including MOG-induced experimental autoimmune encephalitis (EAE), proteoglycan-induced arthritis (PGIA), and sclerodermatous graft-vs-host disease (scGVHD). To translate these encouraging pre-clinical data we generated novel anti-human CD45 ADCs that cross react with nonhuman primates (NHP) and evaluated these for the ability to deplete hematopoietic and immune cells in NHPs.

Fig. 1: Administration of CD45-ADC enables autoHSCT and substantially reduces pathology in murine EAE model

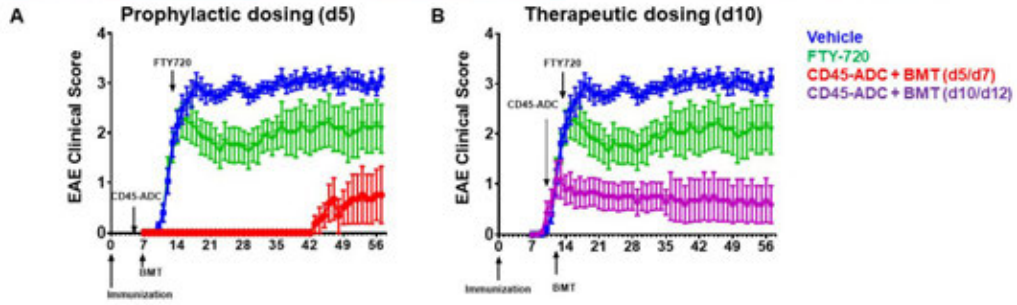

Fig. 1. Administration of CD45-ADC enables autoHSCT and substantially reduces pathology in murine EAE model . Experimental autoimmune encephalitis (EAE) was initiated in C57BL/6 mice via immunization with MOG_{35-55} peptide in complete Freund's adjuvant (CFA) on day 0 with pertussis toxin on days 0 and 1. Groups of immunized mice were conditioned with 3 mg/kg of CD45-ADC on day 5 (**A**) or day 10 (**B**) post-immunization followed by congenic bone marrow transplant ($2x10^7$ BM cells from B6.SJL (CD45.1$^+$)). All animals were scored daily starting at 5 days post immunization. Vehicle (blue) and FTY-720 –treated groups (green) are shown as comparators.

Results: A single-dose of anti-mouse CD45-ADC achieved full myeloablation in recipient mice and enabled full donor chimerism in a congenic mouse transplant model. In EAE, conditioning with anti-mouse CD45-ADC followed by congenic transplant prior to disease onset significantly delayed disease onset and reduced overall disease severity. In active EAE, treatment with anti-mouse CD45-ADC followed by congenic transplant halted progression of disease activity. The disease modifying effect in EAE with anti-mouse CD45-ADC showed comparable efficacy to a traditional conditioning regimen. Evaluation of CD45-ADC in additional autoimmune models of arthritis and scleroderma are ongoing and will be presented. Given these encouraging results we developed an anti-human CD45 ADC that cross-reacts with non-human primates (NHP). Substantial depletion of both lymphocytes and hematopoietic stem cells (HSCs) was observed at well-tolerated doses.

Conclusion: These results suggest that targeted immune depletion with a single treatment of CD45-ADC may be sufficient for auto-HSCT and allow re-establishment of immune tolerance. Targeted CD45-ADCs may represent a safer and better tolerated approach for conditioning patients prior to immune reset through autoHSCT and significantly reduce the side effects associated with current conditioning.

Disclosure: G. Gillard, Magenta Therapeutics, 1, 3, 4; **J. Proctor**, Magenta Therapeutics, 1, 3, 4; **M. Brooks**, Magenta Therapeutics, 1, 3, 4; **T. Lamothe**, Magenta Therapeutics, 1, 3, 4; **S. Hyzy**, Magenta Therapeutics, 1, 3, 4; **S. McDonough**, Magenta Therapeutics, 1, 3, 4; **R. Palchaudhuri**, Magenta Therapeutics, 1, 3, 4; **A. Bhat**, Magenta Therapeutics, 1, 3, 4; **G. Sarma**, Magenta Therapeutics, 1, 3, 4; **P. Bhattarai**, Magenta Therapeutics, 1, 3, 4; **P. Sawant**, Magenta Therapeutics, 1, 3, 4; **B. Pearse**, Magenta Therapeutics, 1, 3, 4; **C. McDonagh**, Magenta Therapeutics, 1, 3, 4; **A. Boitano**, Magenta Therapeutics, 1, 2, 4; **M. Cooke**, Magenta Therapeutics, 1, 3, 4.

Abstract Number: 0121

In Vitro Human Enthesitis Model with Induced IL-17A and TNFα from CD4+ and CD8+ T Cells and Effect of Pharmacological Antagonism with Janus Kinase and Retinoic Acid Receptor-related Orphan Receptor γ Inhibition

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SESSION INFORMATION

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

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Background/Purpose: Animal models of experimental spondyloarthritis (SpA), human genetics and therapies support a central role for adaptive immunity in disease pathogenesis. However, there is very limited data on whether the human enthesis harbours conventional CD4+ and CD8+ T-cells

To investigate whether spinal enthesis including peri-entheseal bone and peripheral blood harboured resident CD4+ and CD8+ conventional T-cells and to evaluate the effects of therapy in blocking the production of pivotal SpA-related cytokines TNF and IL-17A. Additionally, to investigate T cell plasticity via gene expression of Th17 and Treg markers following in vitro induction of entheseal inflammation.

Methods: Healthy interspinous ligament and spinous process with matched blood were harvested from patients undergoing elective surgery for the correction of mechanical spinal defects (n=13). Entheseal soft tissue (EST) and peri-entheseal bone (PEB) were separated and digested. . Following the isolation of CD4+ and CD8+ T-cells lymphocytes from PEB and peripheral blood, the conventional T lymphocytes were investigated using ELISA's and RNA extraction for qRT-PCR to assess T effector cell markers. Cells were stimulated using an anti-CD3/CD2/CD28 beads with and without the presence experimental RORγt inhibitor (RORγti), Tofacitinib, methotrexate (MTX), and phosphodiesterase type 4 inhibitor (PDE4i).

Results: Following stimulation, CD4+ T-cells produced more TNF and IL-17A than CD8+ T-cells ($p< 0.05$), IL-17A was robustly detected in CD4+ but not CD8+ T-cells. TNF and IL-17A production from CD4+ T-cells was effectively inhibited by Tofacitinib ($p< 0.05$), while RORγti only reduced IL-17 secretion highlighting it's specificity in the IL-17A signalling pathway. MTX and PDE4i treated cells had no significant impact on reducing IL-17A production in either cell population. MTX also had no impact on reducing TNF production in either cell population, however PDE4i treated cells did reduce TNF production in both cell populations in blood. CD4+ and CD8+ T-cells showed increased expression of the Treg lineage specific gene FOXP3 compared to DMSO control ($p=0.002$) where PDE4i and methotrexate treatment caused the highest relative expression fold change in CD4+ PEB and CD8+ blood respectively (4.33±0.97, 347.89±347.35). The pleiotropic cytokine TGFβ showed varying results in PEB and blood, with a complete down-regulation in CD4+ PEB and an upregulation in CD8+ Blood, methotrexate treatment caused the highest relative expression fold change (19.66±17.78), which may suggest a Th17 phenotypic shift in PEB and a iTreg shift in CD8

Blood, this is also supported by RORC and IL-6 upregulation in CD4 PEB in PDE4i treated cells (p=0.045 and 0.001 respectively).

Conclusion: This is a novel finding of conventional CD4+ and CD8+ enthesis resident T-cells that exhibit regulatory transcript expression in health. Where TGFβ expression may highlight T cell plasticity, promoting a Th17 phenotype in PEB and iTreg phenotype in blood. Induced IL-17A was robustly inhibited by RORgt inhibition.

Disclosure: H. Rowe, None; **A. Watad**, None; **C. Bridgewood**, None; **T. Russell**, None; **D. Newton**, None; **M. Wittmann**, None; **Q. Zhou**, None; **A. Khan**, None; **R. Dunsmuir**, None; **P. Loughenbury**, None; **R. Cuthbert**, None; **D. McGonagle**, AbbVie, 9, Abbvie, 2, 8, BMS, 9, Celgene, 2, 8, 9, Janssen, 2, 8, Johnson & Johnson, 9, Lilly, 2, 8, MSD, 9, Novartis, 2, 8, 9, Pfizer, 2, 8, 9, UCB, 8, 9.

Abstract Number: 0122

Inhibition of Necroptosis Suppresses Muscle Cell Death and Inflammatory Infiltrate, and Improves Muscle Strength in Experimental Polymyositis

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SESSION INFORMATION
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Background/Purpose: In polymyositis (PM), $CD8^+$ cytotoxic T lymphocytes (CTLs) are assumed to induce muscle cell death. We presumed that the injured muscle cells release pro-inflammatory molecules including damage associated molecular patterns (DAMPs), which would accelerate further CTL-mediated muscle injury. Inhibition of muscle cell death could be a novel therapeutic strategy in PM. We have previously shown that the suppressive effects of perforin deficiency on the severity and incidence of myositis were partial in C protein induced-myositis (CIM), suggesting the involvement of another pathway in addition to the perforin/granzyme pathway. The aims of this study are to clarify the mechanisms of CTL-mediated muscle injury, the pattern of cell death of muscle cells, and the therapeutic effects of inhibition of muscle cell death on *in vitro* and *in vivo* models of PM.

Methods: OT-I CTLs, and their mutants lacking perforin 1 or granzyme B were cocultured with myotubes differentiated from C2C12 cells that were retrovirally transduced with the genes encoding MHC class I ($H2K^b$) and SIINFEKL peptide derived from ovalbumin ($H2K^b$OVA-myotubes) to discern how muscle cell death is mediated *in vitro* by CTL. CIM was used to study the effect of necrostatin-1s (nec1s) on the severity of myositis *in vivo*. The levels of high mobility group box-1 protein (HMGB1), one of the DAMPs, in the supernatant of the coculture and the serum of CIM were measured by ELISA. Muscle biopsy specimens of PM patients were examined with terminal deoxynucleotidyl transferase nick-end labeling (TUNEL) assay, and histologically for the expression of the necroptosis associated proteins including receptor-interacting serine-threonine kinase (RIPK3) and mixed lineage kinase domain-like pseudokinase (MLKL).

Results: OT-I CTLs lacking perforin 1 or granzyme B were as cytotoxic to $H2K^b$OVA-myotubes as wild type OT-I CTLs. Inhibition of Fas ligand by the Fas-Fc chimera protein reduced cytotoxicity of CTLs against the myotubes. The TUNEL assay and time-lapse imaging of cell death visualized by Annexin V and PI revealed that the cell death of

the myotubes was non-apoptotic. The CTL-mediated cell death of myotubes was inhibited by nec1s, a necroptosis inhibitor, or *Ripk3* silencing with siRNA, but not by benzyloxycarbonyl-Val-Ala-Asp-fluoromethylketone, an apoptosis inhibitor. Treatment of myotubes with nec1s inhibited the CTL-induced increase of HMGB1 level in the supernatant of the coculture. Therapeutic administration of nec1s on CIM improved the grip strength of mice and reduced the severity of myositis histologically. The serum level of HMGB1 was lower in nec1s-treated CIM mice compared to that in the untreated mice. Immunohistological staining of muscle tissue of PM patients revealed the expression of Fas, RIPK3, and phosphorylated MLKL on injured muscle cells.

Conclusion: Necroptosis is involved in muscle cell death in PM. Inhibition of necroptosis should be a novel therapeutic strategy in PM.

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Abstract Number: 0123

Blockade of Antigen-specific T Cell Activation by a Non-Depleting Anti-HLA-DR Monoclonal Antibody with a Unique Binding Epitope

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Session Date: Sunday, November 10, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The activation of T helper cells requires cognate recognition of antigen-derived peptides presented by Major Compatibility Complex Class II (MHC II) molecules, which are encoded by the human leukocyte antigen gene complex (HLA)-DR, HLA-DP and HLA-DQ genes. Polymorphisms in the HLA-DR beta chain 1 gene *HLADRB1* are highly associated with many autoimmune diseases. The HLA-DRB1 'Shared Epitope' is the single most significant genetic risk factor for Rheumatoid Arthritis. Blockade of the interaction of HLA-DR with the TCR might inhibit activation of autoreactive T cells while preserve protective antigen presentation by other HLA molecules.

Methods: HLA-DR selective binding Fabs were identified from phage display libraries and cloned as IgG2sigma/kappa antibodies. The affinities of the anti-HLA-DR antibodies for HLA-DR1 or DR4 complexes were measured by Surface Plasmon Resonance (SPR). To evaluate the potency of anti-HLA-DR mabs *in vitro*, peptide-specific T cell hybridoma lines were cocultured with APCs expressing HLA-DR1 or DR4. In addition, a mixed lymphocyte reaction (MLR) assay was established via coculture of human CD4+ T cells with bone marrow-derived dendritic cells (BMDC) from human HLA-DR4 transgenic (Tg) mice. To evaluate the efficacy of anti-HLA-DR mabs *in vivo*, human HLA-DR4 Tg mice were immunized with hemagglutinin (HA) peptide and HA-specific T cell expansion was assessed by *ex vivo* stimulation.

Results: DR4B127 is an anti-HLA-DR monoclonal antibody with a 'silent' Fc (lacking effector function). It selectively binds to HLA-DR1 or DR4 in the presence of various antigen peptides (KD=9~146 nM) but does not binds to HLA-DP or HLA-DQ. Its binding epitope does not overlap with the MHC II/TCR interfaces. However, interaction of MHC II/CD4

could be affected. Unlike other anti-HLA-DR antibodies (e.g. L243), the binding of DR4B127 does not cause apoptosis of primary human B cells *in vitro*. Target-mediated internalization is observed for DR4B127 and other HLA-DR-binding antibodies *in vitro,* and internalization efficiency is correlated with binding affinity. DR4B127 dose-dependently inhibits HLA-DR1- or HLA-DR4-restricted, HA peptide-dependent or HLA-DR4-restricted, type II collagen (CII) peptide-dependent activation of T cell hybridoma cells. DR4B127 also inhibits a human T cell/ HLA-DR4 Tg mouse BMDC MLR. DR4B127 demonstrated a short half-life with $t_{1/2}$ < 24h in both HLA-DR4 Tg mice and cyno monkeys. DR4B127 does not deplete B cells in HLA-DR4 Tg mice *in vivo*. However, quick loss of target engagement is observed as over 90% of total HLA-DR epitopes on B cells are not covered by antibody after 24h. Sustained exposure of DR4B127 by repeated dosing is sufficient to inhibit HA-specific T cell expansion *in vivo*, while single dose treatment is not efficacious.

Conclusion: DR4B127 is differentiated from other anti-HLA-DR mabs, demonstrating a unique binding epitope and non-depleting profile. Although short half-life and transient target engagement preclude further development as a therapeutic for autoimmune indications, DR4B127 may have utility as a research tool for selective uptake into HLA-DR-expressing cells.

Disclosure: F. Shen, Janssen Research, Johnson&Johnson, 1, 3, 4; **K. Duffy**, None; **S. Becart**, Janssen, 3; **R. Kuhn**, None; **M. Swiecki**, None; **B. Jones**, None; **Y. Li**, None; **J. Hall**, None; **R. Malaviya**, Janssen Research, Johnson&Johnson, 1, 3, 4, Janssen Research, Johnson&Johnson, 1, 3, 4; **N. Felix**, Janssen, 3; **M. Zhou**, None; **S. Nagpal**, Janssen Research & Development, 3, Janssen Research, Johnson&Johnson, 1, 3, 4, Johnson & Johnson, 1, 4; **N. Rao**, Janssen Research & Development, 3, Johnson & Johnson, 1, 3, 4.

Abstract Number: 0124

Treatment with Abatacept but Not with TNF Blockers, Is Associated with a Reduction of Constitutively Elevated Circulating Follicular Helper T Cells in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Circulating CD4 T cells that express CXCR5 together with PD-1 and/or ICOS are considered as counterparts of bona fide Tfh cells and function as B cell helpers (Simpson N et al, Arthritis Rheum 2010; Craft J, Nat Rev Rheumatol 2012). In addition, circulating CD4+CXCR5+ T cells can be subdivided into three subpopulations: CXCR5+CXCR3+CCR6- (Tfh-Th1), CXCR5+CXCR3-CCR6+ (Tfh-Th17) and CXCR5+CXCR3-CCR6- (Tfh-Th2). Only Tfh-Th17 and Tfh-Th2 but not Thf-Th1 cells seem to provide B cell help. Altered frequencies of circulating Tfh cells (cTfh) and of cTfh cell subpopulations have been associated with autoinmune conditions. We previously described that patients with RA treated with conventional synthetic DMARDs (csDMARDs), demonstrate constitutively altered frequencies of cTfh and cTfh cell subpopulations that are observed not only in patients with an active disease but also in patients who are in remission. Therefore, our objective was to determine if treatment with biological agents (TNF blockers or abatacept) is able to modify the constitutively altered cTfh and cTfh subpopulation numbers, observed in RA patients receiving csDMARDs.

Methods: Peripheral blood was drawn from RA patients receiving csDMARDS (n=35), TNF blockers (n=27: 10 infliximab, 12 etanercept, 3 certolizumab, 2 adalimumab), or abatacept (n=20). For each patient, an age and gender-matched healthy control was also studied (n=82). cTfh and plasmablast frequencies were determined by flow cytometry of freshly isolated PBMCs.

Results: As described, RA patients receiving csDMARDs demonstrated, whether they had an active or inactive disease, an increased frequency of CD4+CXCR5+PD-1^{hi} and CD4+CXCR5+ PD-1^{hi}ICOS+ T cells, together with an increased frequency of circulating plasmablasts. In addition, the frequency of Tfh-Th1 cells was significantly decreased and the frequency of Tfh-Th17 and Tfh-Th2 cells were significantly increased as compared with HC; subsequently, the ratio (Tfh-Th17+Tfh-Th2)/Tfh-Th1 was increased in RA: that is, RA patients demonstrated a higher proportion of Tfh cell subsets bearing a phenotype associated with B cell helping capacity. Interestingly, these alterations were also observed in RA patients treated with TNF blockers, whether they had an active or inactive disease. In contrast, in patients receiving abatacept, the frequencies of cTfh, cTfh cell subpopulations and plasmablasts, were not different from those observed in HC.

Conclusion: Patients with RA receiving csDMARDs or TNF blockers demonstrated a constitutively increased frequency of cTfh cells and an overrepresentation of cTfh subsets bearing a B cell helper phenotype, suggesting that altered germinal center dynamics play a role in RA pathogenesis. Remarkably, in RA patients treated with abatacept these frequencies and ratio were not altered, indicating that costimulation blockade is able to revert the increased generation of Tfh cells in RA; conversely, TNF neutralization does not seem to affect the generation or recirculation of cTfh.

Disclosure: M. Miranda-Carus, BMS, 2, Roche Pharma, 2; **P. Fortea-Gordo**, BMS, 2; **L. Nuño**, BMS, 2; **A. Villalba**, BMS, 2; **M. Santos-Bornez**, BMS, 2; **D. Peiteado**, BMS, 2; **I. Monjo**, BMS, 2; **A. Balsa**, BMS, 2, Roche Pharma, 2.

Abstract Number: 0125

Elevated Proliferative Capacity of CD8+ T Cells in Giant Cell Arteritis

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SESSION INFORMATION
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Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is the most frequent form of systemic vasculitis affecting the large- and medium-sized vessels. The involvement of innate immune cells and CD4+ T cells in the pathogenesis of GCA has been intensively studied. Interestingly, recent findings suggest a role of CD8+ T cells in disease development. However, CD8+ subsets and their functional capacities have not yet been studied in detail. Therefore, this study aims to investigate the phenotype and function of circulating CD8+ T cells in newly diagnosed GCA patients compared to healthy age- and sex- matched controls.

Methods: Newly diagnosed, untreated GCA patients (n=9), diagnosed according to international GCA consensus criteria, and age- and sex-matched healthy controls (HCs, n= 12) were enrolled. Firstly, peripheral blood mononu-

clear cells (PBMCs) were stained with fluorochrome-conjugated antibodies directed against CD3, CD4, CD8, CCR7, CD45RO, Ki-67, CD69 and CD25 and analyzed by flow cytometry. The following differentiation subsets were defined: CD8+ T naive (CD45RO-CCR7+), central memory (T_{CM}, CD45RO+CCR7+), effector memory (T_{EM}, CD45RO+CCR7-) and effector memory re-expressing CD45RA (T_{EMRA}, CD45RO-CCR7-) cells. Secondly, the proliferative capacity of CD8+ T cells was determined in isolated CD3+ T cells by measuring the intensity of cell proliferation dye (CPD) upon 5 days of stimulation with plate-bound anti-CD3 or anti-CD3 plus soluble anti-CD28. Lastly, the proliferative capacity of whole blood sorted CD8+ T naive, T_{EM} and T_{EMRA} cells from two GCA patients in remission and two HCs was determined.

Results: No differences in the proportions of differentiation subsets were present between GCA patients and HCs. A proportional increase of Ki-67 within CD8+ T_{EM} cells was found in GCA patients compared to HCs ($p < 0.01$) suggesting increased homeostatic proliferation in these cells. After stimulation with anti-CD3, the percentage of divided CD8+ T cells was higher in patients than in HCs ($p< 0.05$). After stimulation with both anti-CD3 and anti-CD28, no differences in proliferative capacity were found. Furthermore, a strong positive correlation between the proportion of CD8+ T_{EMRA} cells and the percentage of divided cells upon CD3 stimulation was found in newly diagnosed GCA patients (R=0.8), and not in HCs. Preliminary data from sorted CD8+ differentiation subsets suggest that CD8+ T_{EMRA} cells from GCA patients indeed have a higher proliferative capacity than those from HCs.

Conclusion: This study demonstrated that CD8+ T_{EM} cells show increased homeostatic proliferation in GCA patients compared to HCs. Functional data on proliferative capacity suggest that CD8+ T_{EMRA} cells from GCA patients are more rapidly activated by crosslinking CD3, suggesting either reduced regulation in these patients or more intrinsic threshold changes. This higher proliferative capacity of CD8+ T_{EMRA} cells is contrary to existing literature, since it is well appreciated that the expansion potential of CD8+ T cells decreases from naive T cells to T_{CM} to T_{EM} and T_{EMRA}. The lower activation thresholds for CD8+ T_{EMRA} cells in GCA imply that these cells are not innocent bystanders but contribute to disease progression in GCA.

Disclosure: R. Reitsema, None; **R. Hid Cadena**, None; **W. Abdulahad**, None; **A. Boots**, Gruenenthal, 5; **P. Heeringa**, None; **E. Brouwer**, Roche, 5, 8.

Abstract Number: 0126

Antibodies Targeting Mitochondrial Antigens Are Associated with Reduced Thrombotic Events in APS

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Mitochondria are intracellular organelles involved in many biological pathways such as energy supply by oxidative phosphorylation and apoptosis. Mitochondria are considered as derived from the endosymbiosis between an α-proteobacterion and a primitive eukaryotic cell. Mitochondria display molecular features derived from their bacterial origin such as N-formylated peptides or a circular double-stranded DNA with hypomethylated

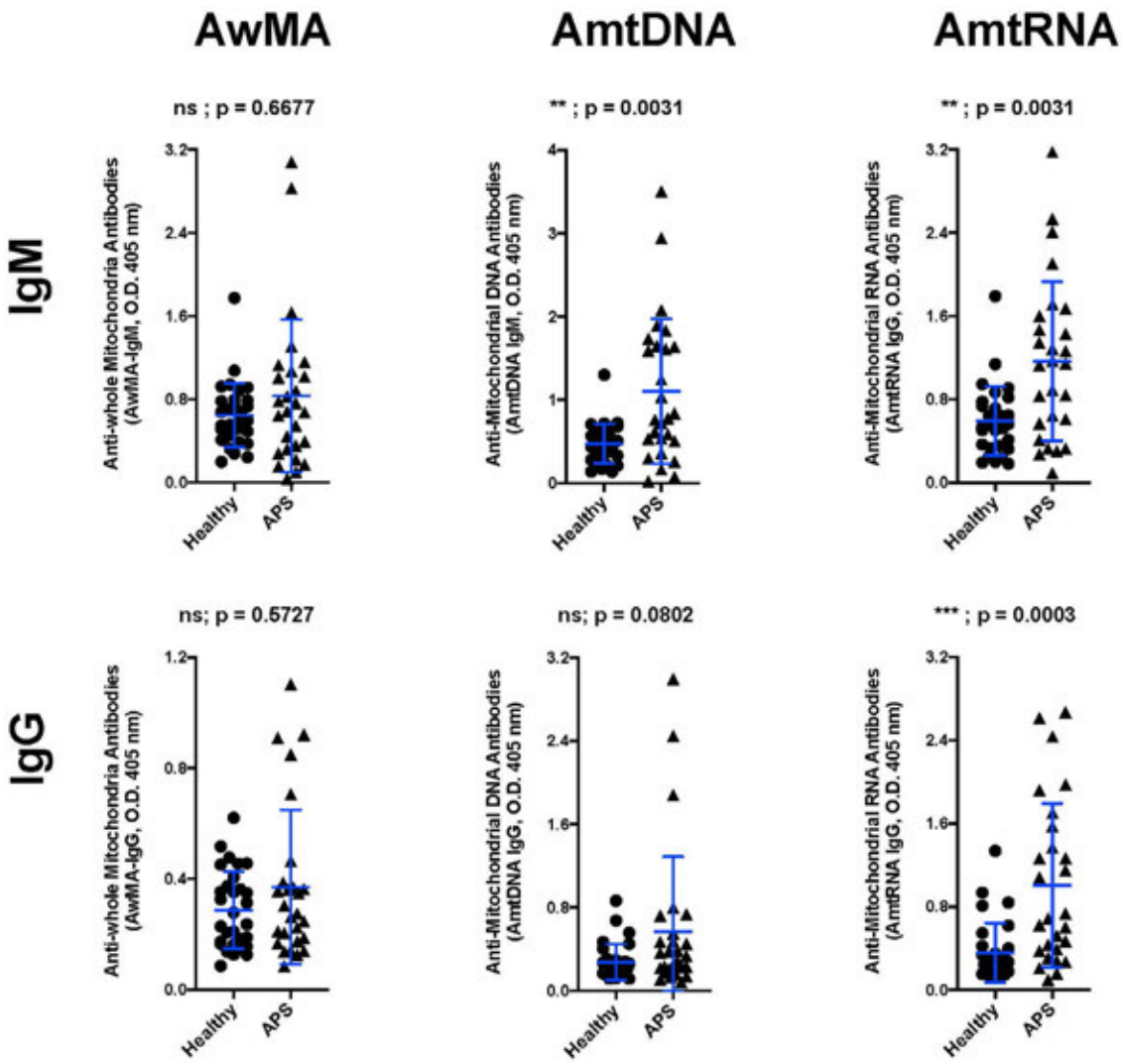

Figure 1. Detection of anti-mitochondrial autoantibodies targeting whole mitochondria (AwMA), mitochondrial DNA (AmtDNA) or RNA (AmtRNA) in healthy donors (n=30) and APS patients (n=27)

CpG motives. When released onto the extracellular milieu upon tissue damage or cell activation, mitochondria may elicit proinflammatory responses through their recognition by the innate immune system. Little is known about interplays between mitochondria and the adaptive immune system, despite descriptions of humoral responses to mitochondria in some diseases. Our laboratory already reported that anti-mitochondrial antibodies (AMA) targeting whole organelles (AwMA), mitochondrial DNA (AmtDNA) or RNA (AmtRNA) are expressed in patients with systemic lupus erythematosus, an autoimmune disease often associated with APS. In this study, we detected AMA in patients with APS and associated their titers with clinical features of APS.

Methods: AwMA, AmtDNA and AmtRNA – IgG and IgM were detected in healthy controls (n=30) and APS patients (n=27) by direct ELISA. All participants agreed to participate to our Systemic Autoimmune Rheumatic Diseases Biobank and Data Base. Demographic and disease characteristic variables were collected according to the standard APS ACTION protocol. Vascular events were defined as arterial, venous or microangiopathic and «any vascular event» was defined as the combination of all types of vascular events Morbidities during pregnancy were defined as spontaneous abortions before the 10^{th} week of pregnancy, miscarriages after the 10^{th} week or premature birth due to eclampsia or preeclampsia before the 34^{th} week and «any pregnancy morbidity» was defined as any combination of one or more items. Kruskall-Wallis and Wilcoxon tests were used to compare groups. Vascular events and morbidities during pregnancy were predicted with logistic regressions.

Table 1. Clinical characteristics of APS patients

Variable	n	Mean ± SD [or n (%)]
Gender		
Male	27	17 (63)
Female		10 (37)
Age (years)	27	50.93 ± 16.20
Tobacco intake		
Non-smokers	27	9 (33.3)
Smokers		6 (22.2)
Ex-smokers		12 (44.4)
Disease duration (years)	27	10.00 ± 9.70
Body mass index (BMI)	27	27.89 ± 6.46
Disease:		
Primary APS (PAPS)	27	7 (25.9)
Secondary APS (SAPS)		20 (74.1)
Lupus anticoagulant (LA):		
Negative	20	5 (18.5)
Positive		15 (55.6)
Anticardiolipin antibodies (aCL):		
IgG	22	32.99 ± 82.30
IgM		32.82 ± 99.49
Anti-β_2 Glycoprotein I (β_2GPI):		
IgG	25	13.77 ± 28.45
IgM		29.18 ± 114.21
History of vascular events:		
Any	27	22 (81.5)
Arterial		10 (37.0)
Venous		15 (55.6)
History of pregnancy:	12	
History of any pregnancy morbidity		4 (33.3)

Results: AmtDNA-IgM and both AmtRNA IgG and IgM were significantly elevated in APS patients compared to controls. AMA failed to discriminate primary APS (n=7) from secondary APS (n=20). AwMA-IgG were associated with positivity to lupus anticoagulant (p=0.01). While the AMA were not associated with morbidities during pregnancy, AwMA-IgM, AmtDNA-IgG and IgM and AmtRNA-IgM were all associated with reduced history of any thrombotic events (respectively p=0.0447, p=0.0414, p=0.0363 and p=0.0481). AmtDNA-IgM was also associated with reduced arterial vascular events (p=0.0463).

Conclusion: Our findings suggest that AMA are represented within the autoantibody repertoire in APS and that various mitochondrial antigens display different clinical associations in the disease.

Disclosure: Y. Becker, None; **A. Julien**, None; **A. Godbout**, None; **É. Boilard**, None; **P. Fortin**, None.

Abstract Number: 0127

Elevated Levels of the Neutrophil Extracellular Trap-binding Protein LILRA3 in Primary Antiphospholipid Syndrome

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The leukocyte immunoglobulin-like receptor A3 (*LILRA3*) gene encodes the only soluble receptor within the LILR family. *LILRA3* polymorphisms have been associated with both rheumatoid arthritis and lupus. Soluble LILRA3 appears to circulate at high levels in patients with rheumatoid arthritis, and has been suggested to have pro-inflammatory functions. Regarding its cellular source, a recent proteomic analysis of neutrophil granules detected LILRA3 as a key component of tertiary granules. To date, the role of LILRA3 in antiphospholipid syndrome (APS) has not been defined. Here, we hypothesized that LILRA3 might be delivered extracellularly via the release of neutrophil extracellular traps (NETs). We also considered whether LILRA3 might function as a NET-binding protein and whether it circulates at high levels in APS patients, where it may promote autoantibody formation or have thromboinflammatory functions.

Methods: LILRA3 expression was assessed in neutrophils of primary APS patients by real-time PCR. Circulating levels of soluble LILRA3 and anti-LILRA3 IgG were measured in primary APS patients and healthy controls by enzyme-linked immunosorbent assay. Electrophoretic mobility shifts assay (EMSA) was performed to determine whether LILRA3 binds neutrophil DNA (the dominant component of NETs). Human neutrophils were activated to release NETs, and co-localization of LILRA3 and NETs was assessed by immunofluorescence microscopy.

Results: Our previous RNA-sequencing of primary APS neutrophils (n=9) revealed ~3-fold upregulation of *LILRA3* in APS patients as compared with matched controls. Here, we verified this overexpression by real-time PCR in an independent cohort of 20 primary APS patients and matched controls (mean 2 fold increase in APS). We also measured LILRA3 protein and anti-LILRA3 IgG in primary APS plasma, and found a positive correlation between LILRA3 protein levels and anti-beta-2 glycoprotein I IgM ($P = 0.009$). Furthermore, as compared with matched controls, primary APS was associated with higher circulating levels of both soluble LILRA3 (1.5 fold) and anti-LILRA3 IgG (1.6 fold), with a positive correlation between the two ($P = 0.041$). To investigate whether LILRA3 might directly interact with NET DNA, LILRA3 was incubated with purified neutrophil genomic DNA and analyzed by EMSA. The addition of 0.25 μM LILRA3 (partial effect) and 1.0 μM (full effect) significantly reduced the migration of genomic DNA (0.1mg/ml) through the agarose gel, suggested a direct interaction between LILRA3 and DNA. Furthermore, by immunofluorescence microscopy, we observed clear co-localization of LILRA3 and NET strands.

Conclusion: We demonstrate for the first time elevated levels of LILRA3 and anti-LILRA3 IgG in patients with primary APS. Furthermore, LILRA3 appears to be a NET-binding protein that can be delivered extracellularly in the context of NETs, where it has potential to play a role in the pathogenesis of APS. Further studies are underway in pursuit of potential thromboinflammatory functions of this NET-binding protein.

Disclosure: H. Shi, None; **S. Yalavarthi**, None; **J. Guo**, None; **J. Knight**, None.

Abstract Number: 0128

Metabolomics Analysis Identifies Biomarkers for APS and Suggests a Potential New Pathway Related to APS Pathogenesis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Antiphospholipid Syndrome Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The metabolic disturbances that underlie antiphospholipid syndrome (**APS**) are currently unknown. The goal of this study was to utilize high-throughput metabolomics screening to identify new biomarkers and dysregulated pathways in primary APS patients.

Methods: Fasting serum samples were collected from 20 primary APS patients and 17 healthy controls. High-throughput metabolomics screening of 247 small molecule metabolites were performed via gas chromatography-coupled mass spectrometry. Multiple variate analysis, principal components analysis, partial least squares discriminant analysis (**PLS-DA**), and pathway analysis were completed. SYTOX Green NETosis assay was performed utilizing freshly-prepared healthy donor neutrophils with various stimulants including normal human IgG, polyclonal antiphospholipid antibodies (**aPL**), sphingosine-1 phosphate (**S1P**), and polyclonal aPL plus various concentrations of S1P.

Results: 50 circulating small molecule metabolites were significantly different between primary APS patients and healthy controls. PLS-DA modeling was performed and demonstrated a clear separation between primary APS patients and healthy controls (**Figure 1**). 15 metabolic molecules that contributed most to the differentiation of primary APS patients and the healthy controls (assessed by variable importance on projection score) had the highest potential to be clinically relevant biomarkers. Pathway analysis revealed that sphingosine metabolism was the most enriched pathway among primary APS patients. Sphingosine metabolism plays paramount roles in membrane biology

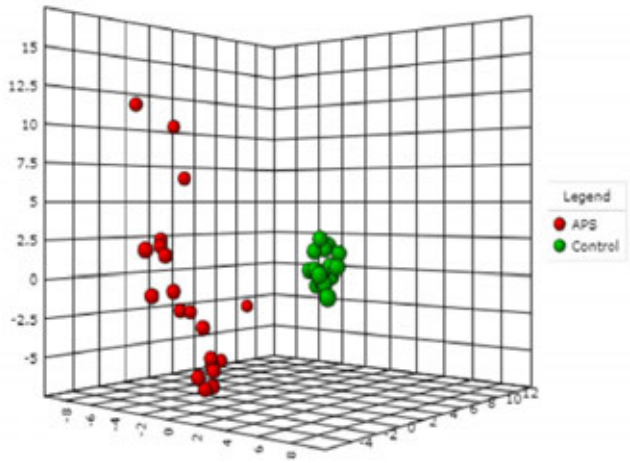

Figure 1. Metabolic analysis of primary APS patients and healthy controls. 3-D PLS-DA modeling to distinguish between APS patients and healthy controls.

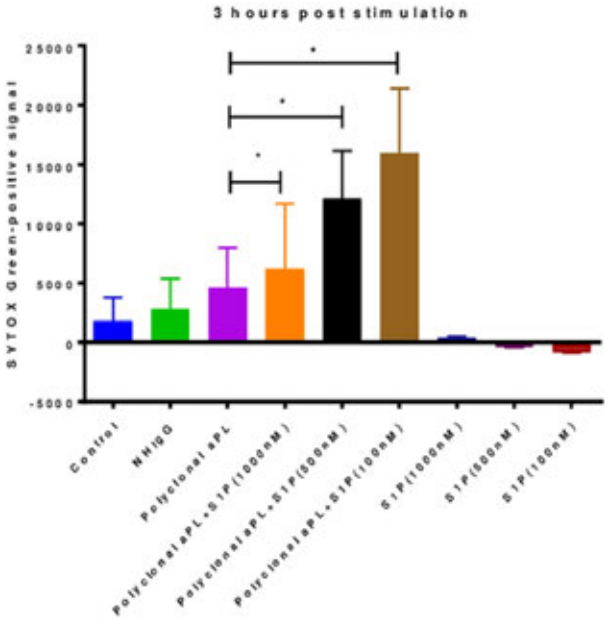

Figure 2. SYTOX Green NETosis Assay on healthy donor neutrophils with various stimulants.

and provides many bioactive metabolites that regulate cellular function. To further elucidate the role of sphingosine metabolism in APS, we examined the effect of S1P (a product of sphingosine metabolism) on aPL-mediated neutrophil extracellular trap release (**NETosis**). aPL-mediated NETosis was significantly potentiated by S1P. Importantly, S1P had no impact on NETosis in the absence of aPL (**Figure 2**).

Conclusion: This study identified metabolomic differences in the serum of primary APS patients and healthy controls. One of the most significant pathways was sphingolipid metabolism. One product of this pathway is S1P, implicated in immunological pathology. The ability of this compound to augment aPL in provoking NETosis suggests a potential role of S1P/S1PR axis in APS pathogenesis.ACR Figure

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Disclosure: C. Li, None; **Y. Zuo**, None; **J. Knight**, None; **J. Feng**, None; **X. Wang**, None; **D. Karp**, None; **Z. Li**, None.

Abstract Number: 0129

Surface Proteins on Exosomes Derived from Plasma of APS Patients Indicate an Altered Immune, Cell Adhesion and Coagulation Profile

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
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Background/Purpose: Antiphospholipid syndrome (APS) is characterized by thromboses and/or obstetric complications in presence of antiphospholipid antibodies (aPL). Extracellular vesicles have been suggested to play a

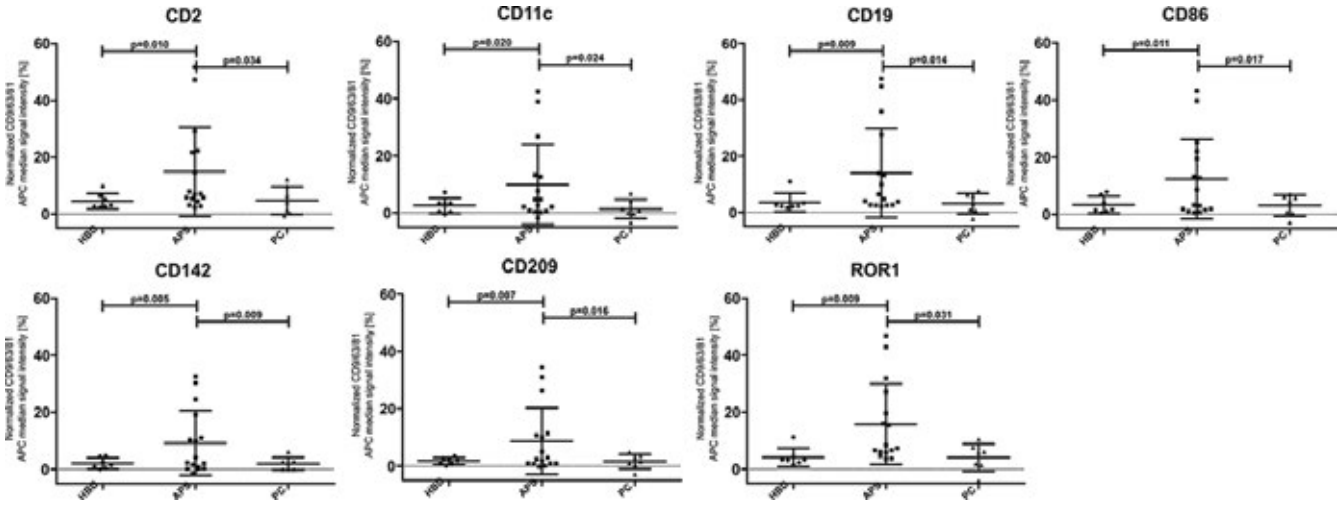
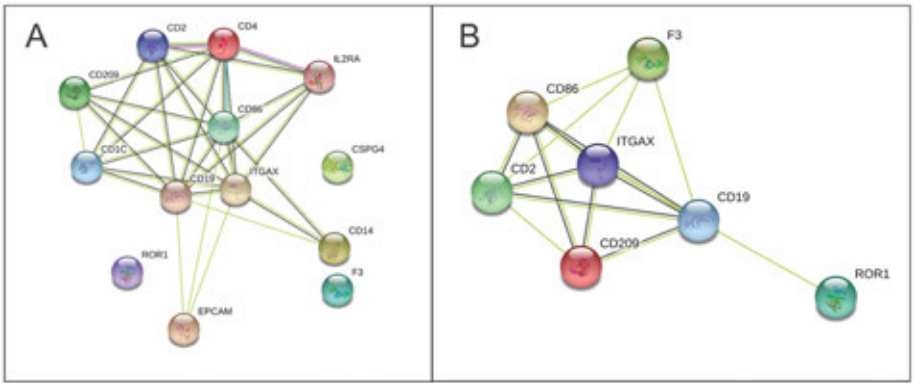


Figure 1. Surface protein profile of circulating exosomes in plasma of APS patients, healthy blood donors (HBD) and aPL negative patient controls (PC).

	HBD (n=7)	APS (n=16)	aPL neg Patient Control (n=7)
mean age (range)	48 (27-65)	46 (27-74)	46 (29-73)
sex (F:M)	6:1	11:5	7:2
Thrombosis (arterial and/or venous)	non	69% (11)	57% (4)
Obstetric complications	non	19% (3)	2 (29%)
Thrombosis and Obstetric complications	non	13% (2)	14% (1)

Table 1. Patients' clinical characteristics



role in the pathogenesis of APS (1,2), however no data till now has been provided for exosomes, representing small (< 100nm), secreted vesicles of endosomal origin. Recent advances show exosomes to be involved in autoimmune cell-cell communication (3). We hypothesize that markers involved in coagulation, hemostasis and the immune system are enriched on exosomes isolated from APS patients and we aimed to determine their surface marker profiles.

Methods: Platelet poor plasma was collected from 16 APS patients and 14 aPL negative controls, (7 healthy blood donors (HBDs) and 7 patient controls (PC)) (Table 1). The groups were sex- and age-matched. LA was determined by clotting tests, aCL, anti-β2GPI, aPS/PT were measured with in-house ELISAs (4). Exosomes were isolated using

CD63-labelled magnetic beads and surface protein profile studied with MACSPlex Exosome kit (both from Miltenyi Biotec), for 37 markers (CD1c, CD2, CD3, CD4, CD8, CD9, CD11c, CD14, CD19, CD20, CD24, CD25, CD29, CD31, CD40, CD41b, CD42a, CD44, CD45, CD49e, CD56, CD62P, CD63, CD69, CD81, CD86, CD105, CD146, CD209, CD326, CD133/1, CD142, MCSP, SSEA-4, ROR1, HLA-ABC and HLA-DRDPDQ). All results were normalized against expression of tetraspanin surface proteins e.g. CD9/81/63. Student t-test and $\chi 2$ test were calculated to compare APC median signal intensities between the groups. The database of known and predicted protein interactions STRING 10.5 was used for analysis of interactions between markers.

Results: 7/37 surface markers (CD2, CD11c, CD19, CD86, CD142, CD209 and ROR1) exhibited significantly higher expression in APS patients vs. both control groups (Fig 1). Specifically, CD86+, CD142+ (TF), ROR+ exosomes were found in 44% (7/16), CD2, CD19+, CD209+ in 38% (6/16) and CD11c+ in 31% (5/16) of APS patients, while there was no positive HBD or PC ($p< 0.05$). Using STRING analysis (Fig 2A), we found strongest GO term assigned to analytes APS vs. HBD, to be cell surface receptor signaling pathway, the immune system process, while weaker association was found for regulation of T cell activation. In the KEGG pathway, the strongest association was shown for hematopoietic cell lineage, and less strong for cell adhesion molecules and complement/coagulation cascades. When comparing APS to both control groups (Fig 2B) in the KEGG pathway the association for complement/coagulation cascades was stronger.

Conclusion: Significant differences in exosomal surface markers of APS patients vs. HBD and PC indicate the involvement of the immune system, surface receptor signaling, cell adhesion molecules and complement/coagulation cascades. Profiles of exosomes thus show activated status of immune cells and coagulation cascade in aPL positive patients. Our study also demonstrates that MACSPlex facilitates sensitive multiparametric phenotyping of exosomes in patient plasma.

1. *Chaturvedi S, Semin Thromb Hemost, 2018*
2. *Lackner KJ, Exp Rev Clin Immunol, 2018*
3. *Tan L, Autoimmunity, 2016*
4. *Zigon P, Clinical and Developmental Immunology, 2013*

Protein association network in STRING analysis showed interactions of positive proteins on exosomes. A: APS vs. HBDs: CD1c, CD2, CD4, CD11c (ITGAX), CD14, CD19, CD25, CD86, CD142(TF-F3), CD209, CD326, ROR1 and MCSP; revealed cell surface receptor signaling pathway (false discovery rate [FDR]: 1.77 × 10–6), the immune system process (FDR 5.34 × 10–5), regulation of T cell activation (FDR 1.1 × 10–4), hematopoietic cell lineage (FDR 1.04 × 10–9), adhesion molecules (FDR 0.0021) and complement/coagulation cascades (FDR 0.0102). B: APS vs. both control groups CD2, CD19, CD11c (ITGAX), CD86, CD142 (TF-F3), CD209 and ROR1 revealed stronger association for complement/coagulation cascades (FDR 0.0079).

Disclosure: U. Štok, None; **E. blokar**, None; **A. Ambrožič**, None; **M. Tomsic**, None; **S. Sodin-Semrl**, None; **S. Čučnik**, None; **P. Žigon**, None.

Abstract Number: 0130

Is There Clinically Relevant Plasma Interference with ELISA Detection of APS Antibodies? Reproducibility of Serum and Plasma Testing in a Real-World Clinical Setting

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Traditionally in ELISA detection of APS antibodies, the use of serum is thought to be preferable over plasma according to international consensus bodies. The dilution effects of citrate in the plasma blood draw tube or matrix effects with fibrinogen are some of the cited concerns. However, there is scarcity of clinical data comparing reproducibility of APS antibody detection in serum versus plasma. The purpose of this study was to determine reproducibility of anti-cardiolipin (aCL), beta2-glycoprotein-1 (β2GP1), and phosphatidylserine-prothrombin (aPS-PT) antibody detection between serum and plasma in a real-world clinical setting.

Methods: Patients with clinical serum draws for IgG/IgM aCL, β2GP1, and aPS-PT antibodies were identified, and same-day, platelet-poor citrated plasma samples were obtained for repeat ELISA testing with commercially available ELISA assays. Quantitative levels were determined for each isotype without citrate volume correction and further stratified into Negative (< 15.0 GPL/MPL or U/mL), Weakly Positive (15.0-39.9), or Positive (≥40.0) reference cutoff categories. Median and mean differences along with inter-sample reliability were compared using Wilcoxon paired signed-rank method and kappa coefficients, respectively.

Results: One hundred fifty patients were identified for study with 134 aCL, 110 β2GP1, and 7 aPS-PT serum samples eligible for repeat plasma testing. Mean age was 49±16 years. About 69% were female, 87% were Caucasian, 21% with APS, and 13% with SLE. As shown in Table 1, median differences were generally 0.0 units and mean differences largely falling within 2 units. The differences were technically statistically significant. There was strong inter-sample agreement in reference cutoff category with kappa coefficients ranging from 0.80 to 1.00.

Conclusion: To our knowledge, we present the largest study examining the reproducibility of APS antibodies on paired serum and plasma samples in a real-world clinical setting. Small differences were detected between serum and plasma for aCL and β2GP1 antibodies with similar trends in aPS-PT antibodies. Although the observed differences were statistically significant, the magnitude of the differences was small and the clinical relevance is likely negligible. Moreover, with kappa coefficients of at least 0.80, there was strong inter-sample agreement in reporting negative, weakly positive and positive categories for aCL and β2GP1 antibodies. These results suggest serum and plasma could be used interchangeably for ELISA detection of antiphospholipid antibodies in a clinical setting.

Table 1 – Reproducibility of aCL, β2GP1, and aPS-PT Antibody Levels in Paired Serum versus Plasma

		Quantitative Levels			Agreement to Reference Category
	N Samples	Median Difference (IQR)[1]	Mean Difference (sd)[1]	*p-value*	Weighted κ Coefficient (95% CI)
IgG aCL	134	0.0 (0.0, 0.0)	1.4 (11.8)	<0.05	0.86 (0.78, 0.94)
IgM aCL	134	0.0 (0.0,2.1)	2.1 (9.4)	<0.05	0.85 (0.76, 0.93)
IgG β2GP1	110	0.0 (0.0, 0.0)	0.8 (5.6)	<0.05	1.00 (1.00, 1.00)
IgM β2GP1	110	0.0 (0.0, 0.05)	1.8 (11.6)	<0.05	0.80 (0.68, 0.92)
IgG aPS-PT	7	0.0 (0.0, 0.0)	1.6 (4.3)	>0.10	†
IgM aPS-PT	7	0.0 (-1.4, 0.0)	-0.9 (1.9)	>0.10	†

1: (Serum)-(Plasma) in units of GPL, MPL, or U/mL. **Abbreviations:** aCL = anti-cardiolipin, β2GP1 = anti-β2 glycoprotein-1, aPS-PT = anti-phosphatidylserine-prothrombin, sd= standard deviation, IQR = Interquartile Range. † Sample number threshold not met for statistical testing

Disclosure: M. Pham, None; **G. Orsolini**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **M. Snyder**, None; **R. Pruthi**, None; **K. Moder**, None.

Abstract Number: 0131

Anti-Phosphatidylserine Prothrombin Antibodies as a Predictor of the LAC in an All-Comer Population

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Antiphospholipid Syndrome Poster

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Background/Purpose: Anti-phosphatidylserine prothrombin antibodies (aPS-PT) are reported to be highly associated with the LAC. Some have suggested a clinically useful role for aPS-PT as a potential surrogate marker for the LAC – especially in the clinical scenario of concurrent anticoagulation where the LAC can have decreased diagnostic performance. However, the studies revealing the aPS-PT and LAC relationship have primarily been carried out on well-established APS and SLE cohorts. Validation studies replicating this relationship in a real-world, all-comer study population are lacking. The purpose of this study was to determine the sensitivity and specificity of aPS-PT to the LAC and other APS serologies in an all-comer population undergoing evaluation for APS and other autoimmune syndromes.

Methods: A cross-section of patients from June 2017 to December 2018 undergoing evaluation for APS across all medical specialties were reviewed for APS testing inclusive of LAC, aPS-PT, anti-cardiolipin (aCL), and anti-β2 glycoprotein-1 (β2GP1). Presence of a LAC was determined by trained hematologists interpreting mixing and neutralization studies. Demographic details were abstracted from the medical record. Cases meeting the SLICC criteria for SLE and the revised Sapporo criteria for APS were enumerated. Sensitivities, specificities, negative-, and positive predictive values with 95% confidence intervals were calculated.

Table 1: Sensitivity and Specificity of IgG and IgM aPS-PT to the LAC and other APS Serologies

	aPS-PT Sensitivity, %		aPS-PT Specificity, %		aPS-PT NPV, %		aPS-PT PPV, %	
	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM
LAC	41 (95%CI: 30-53)	54 (41-65)	100 (96-100)	97 (91-100)	65 (56-73)	69 (59-77)	100 (89-100)	95 (84-99)
IgG aCL	53 (28-77)	72 (47-90)	89 (82-94)	80 (72-87)	93 (87-97)	95 (89-98)	39 (20-61)	34 (20-51)
IgM aCL	20 (4-48)	85 (55-98)	84 (76-90)	85 (77-91)	90 (83-95)	98 (94-100)	13 (3-34)	37 (20-56)
IgG β2GP1	58 (33-79)	74 (49-91)	89 (83-94)	80 (72-87)	93 (88-97)	95 (89-98)	44 (24-65)	36 (21-53)
IgM β2GP1	42 (15-72)	100 (72-100)	84 (76-89)	82 (74-88)	94 (88-98)	100 (97-100)	19 (6-38)	31 (17-49)

Abbreviations: LAC = Lupus Anticoagulant, aCL = anti-Cardiolipin, β2GP1 = anti-β2 Glycoprotein-1, aPS-PT = anti-Phosphatidylserine-Prothrombin, NPV = Negative Predictive Value, PPV = Positive Predictive Value

Results: A sample of 166 eligible patients was identified. Mean age was 49±17 years. Seventy-one percent were female, 89% Caucasian, 15% with SLE, and 21% with APS. At time of testing, 18% were on warfarin, 8% on direct factor Xa inhibitors and 1% on low-molecular weight heparin. The aPS-PT was found to be the most specific to the LAC as seen in table 1. Specificity of IgG aPS-PT was 100% (96-100%) and IgM aPS-PT was 97% (91-100%) to the LAC. This corresponds to a positive predictive value for IgG aPS-PT of 100% (89-100%) and IgM aPS-PT of 95% (84-99%). Specificities of aPS-PT to aCL and β2GP1 antibodies were slightly less in the 80% range. In contrast, the sensitivities of aPS-PT to the LAC were only in the 40-50% range.

Conclusion: In our study with an all-comer population undergoing evaluation for APS and other autoimmune syndromes, aPS-PT had high specificity and high positive predictive value to the presence of the LAC. The sensitivity and negative predictive performance of aPS-PT to LAC however was less robust. This study's findings echo similar findings in past studies on APS and SLE cohorts. And, it corroborates the notion that a positive aPS-PT could be a clinically useful marker for the LAC in the general clinical setting.zACR_PSPT LAC association_PDF TABLE

Disclosure: M. Pham, None; **G. Orsolini**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **M. Snyder**, None; **R. Pruthi**, None; **K. Moder**, None.

Abstract Number: 0132

Anti-phosphatidylserine/prothrombin Antibodies Confer a Distinctive Molecular Profile in Primary Antiphospholipid Syndrome Patients

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: The clinical significance of non-canonical anti-phosphatidylserine/prothrombin (aPS/PT) antibodies in antiphospholipid syndrome (APS) is still controversial. This study assessed the prevalence of aPS/PT antibodies, their association with different APS clinical phenotypes and their involvement in the serum and monocytes molecular profiles.

Methods: Forty APS patients and 40 healthy donors were examined. Anti-cardiolipin (aCL), anti-β2GP-I and aPS/PT antibodies (IgG, IgM and IgA isotypes), as well as lupus anticoagulant (LA) were tested. In parallel, monocytes from peripheral blood were purified by positive immunomagnetic selection. Gene expression microarray (Agilent GF112F) and nCounter microRNA expression array (Nanostring) were performed. Separately, a miRNA array in the plasma of those patients was performed, along with the analysis of their inflammatory profile by multiplex assay. Selected

genes and miRNAs found significantly altered and related to the prothrombotic and obstetric pathology in APS were validated in the whole cohort by qPCR. The involvement of the presence and titers of canonical and non-canonical autoantibodies on the altered inflammatory and gene/miRNA profiles were assessed by multiple comparison tests.

Results: aPS/PT antibodies were detected in 11 out of 26 APS patients (42,3%): 6 carriers of the IgM isotype, 1 carrier of IgA isotype, 1 carrier of both IgM and IgA isotypes and 3 carriers of the three isotypes (IgG/IgA/IgM) simultaneously. The 3 isotypes of aPS/PT antibodies were significantly associated with isolated LA positivity. Among them, there was a prevalence of IgM aPS/PT antibodies in thrombotic patients, and of IgA aPS/PT antibodies in patients with obstetric complications. Levels of IgM aPS/PT were significantly different in APS patients with thrombotic manifestations and those with fetal loss.

Inflammatory profile in plasma of APS patients positive for these non-canonical antibodies showed significantly increased levels of a number of pro-inflammatory mediators (IL2, IL4, IL6, INFg, IL8, IL10, IL12, IL17, GM-CSF, MIP1a, MIP1b) in relation to patients positive for canonical antibodies, along with reduced levels of serum miR26a-5p.

Accordingly, monocytes from APS patients positive for aPS/PT displayed slightly distinctive gene/miRNA profiles related to atherosclerosis and thrombosis than those negative for non-canonical antibodies compared with HDs. Moreover, increased IFNg mRNA classified patients positive or negative for aPS/PT antibodies. This IFNg altered expression might be related to the occurrence of obstetrical complications, as observed by its increased expression in aPS/PT positive obstetric patients in relation to thrombotic patients.

Conclusion: Conclusions: Anti-PS/PT antibodies are frequent in primary APS patients positive for other antiphospholipid antibodies, are associated with different clinical features, and confer distinctive molecular profiles. Thus, anti-PS/PT antibodies might constitute a useful serological tool in the diagnosis, phenotypic and molecular characterization of APS patients.

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Abstract Number: 0133

Anti-β2GPI Domain 1 Antibodies Stratify High Risk of Thrombosis and Pregnancy Morbidity in a Large Cohort of Chinese Patients with Antiphospholipid Syndrome

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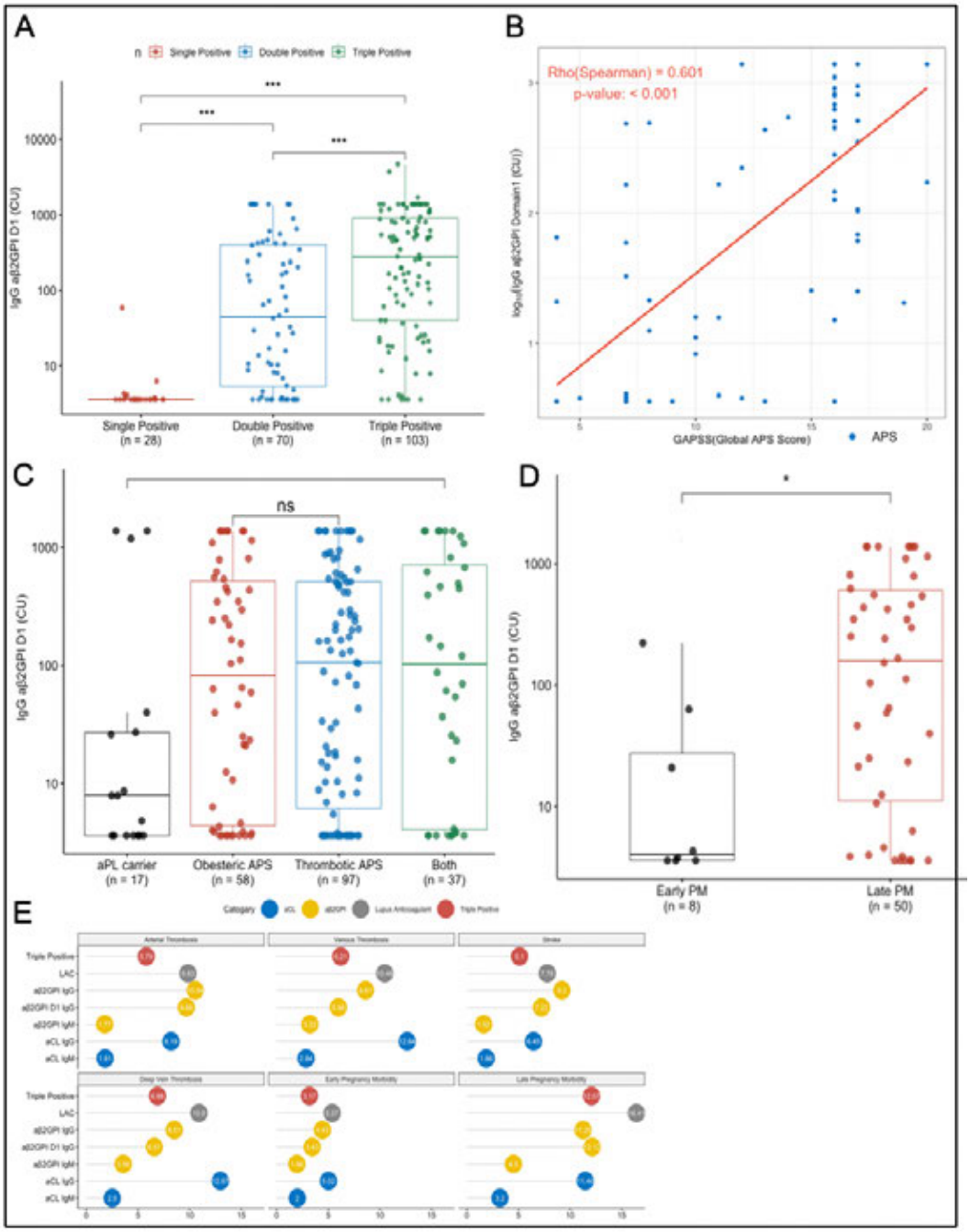
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM



Background/Purpose: Anti-β2GPI-Domain 1 (β2GPI -D1) antibodies are currently considered to be a pathogenic subset of anti-β2GPI antibodies and have been strongly associated with thrombosis and pregnancy morbidity in antiphospholipid syndrome (APS) patients. We evaluated the clinical utility of anti-β2GPI-D1 IgG antibody for stratifying the risk of thrombosis and/or pregnancy morbidity (PM) in a cohort of Chinese patients with APS and also assessed its correlation with the Global Anti-Phospholipid Syndrome Score (GAPSS).

Methods: Sera from 192 APS patients, 17 aPL carriers, 193 patients with other systemic autoimmune diseases, and 120 healthy controls were collected and the presence of aCL IgG/IgM, anti-β2GPI IgG/IgM antibodies and anti-β2GPI-D1 IgG were assessed by chemiluminescence assays (CIA). Anti-phosphatidylserine-prothrombin (aPS/PT) IgG and IgM antibodies were detected by commercial ELISA kits.

Results: Anti-β2GPI-D1 IgG antibodies showed high specificity (97.12%) and moderate sensitivity (64.32%) for the diagnosis of APS. Anti-β2GPI-D1 antibody levels were significantly higher in patients with triple aPL positivity and correlated well with the GAPSS. Anti-β2GPI-D1 antibody presented with a higher prevalence and higher titers in patients with late pregnancy morbidity (≥10 wks) and thrombosis compared to those with early pregnancy (< 10 wks) morbidity. Higher anti-β2GP1-D1 antibody titers effectively distinguished APS from other autoimmune diseases.

Conclusion: This study suggests a predictive role of anti-β2GPI-D1 IgG antibodies as a strong risk factor for both thrombotic and obstetric APS (OAPS), especially for late adverse pregnancy outcomes.

Anti-β2GPI-D1 IgG antibodies act as a strong risk factor for both thrombotic and obstetric APS (OAPS), especially for late adverse pregnancy outcomes.

Disclosure: T. Liu, None; **J. Gu**, None; **L. Wan**, None; **G. Norman**, None; **H. Shi**, None; **C. Yang**, None.

Abstract Number: 0134

'Non-criteria' Antiphospholipid Antibodies Add Value to Antiphospholipid Syndrome Diagnoses in a Large Chinese Cohort

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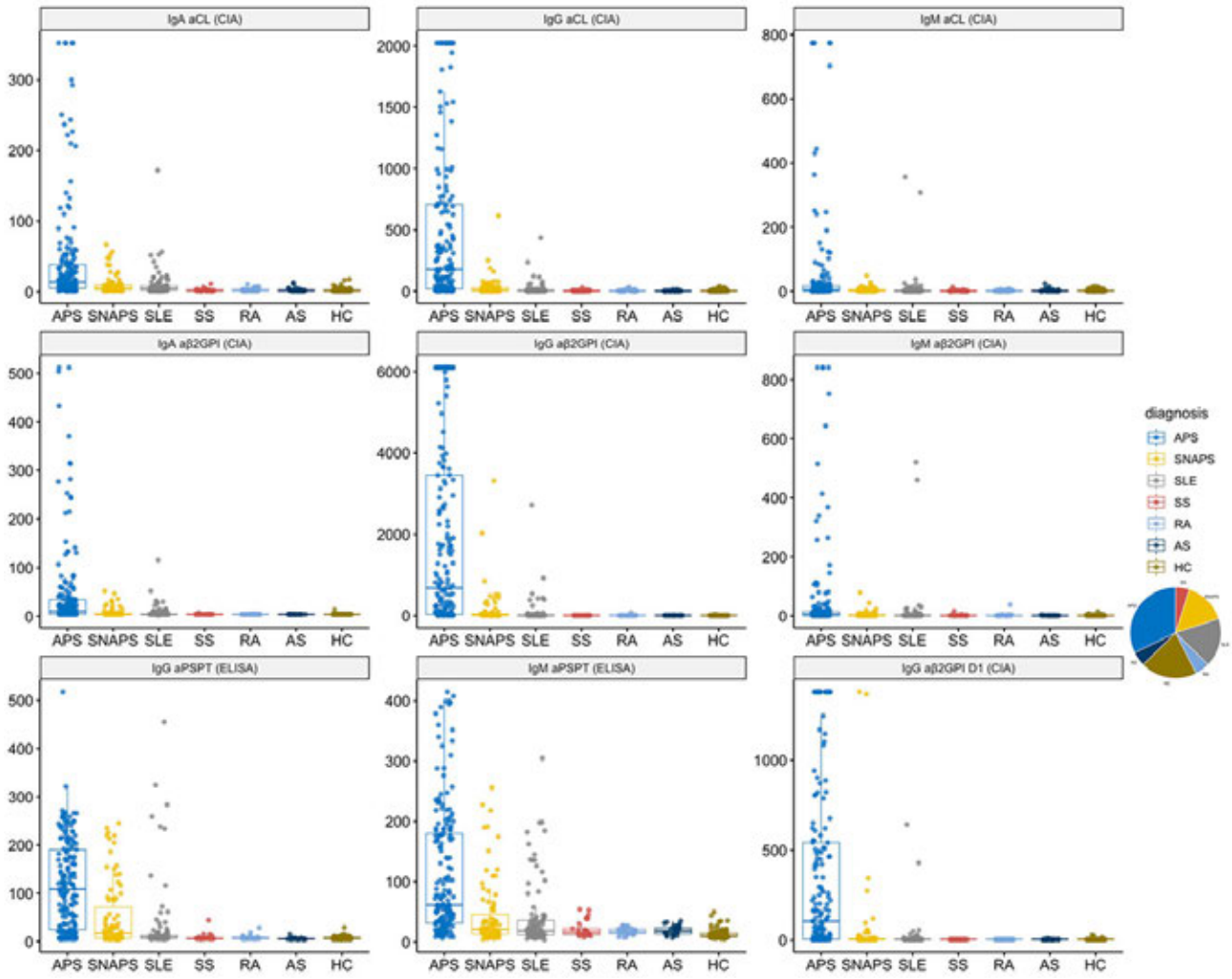
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

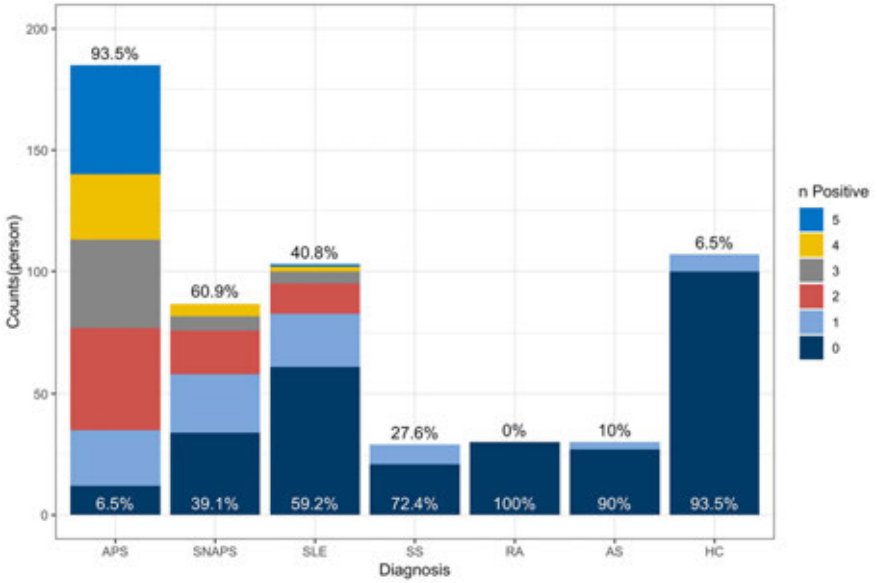
Background/Purpose: The laboratory criteria used in the 2006 Sydney Classification criteria for antiphospholipid syndrome (APS) which is widely used in clinical practice, includes IgG/IgM isotypes of anti-cardiolipin antibodies (aCL), IgG/IgM isotypes of anti β2-glycoprotein I antibodies (aβ2GPI) and lupus anticoagulant (LAC), but there stands a group of patients tagged as seronegative-APS (SNAPS) with clinical manifestation prompting APS but persistent negative criteria antiphospholipid antibodies. Since these patients are at risk of developing recurrent thrombosis and pregnancy morbidities as the APS patients are, it is of great importance to distinguish these patients, meanwhile necessary clinical intervention or preventive measures should be carried out to minimize losses due to the disease. This study aims to assess the value of non-criteria antiphospholipid antibodies in SNAPS patients.

Methods: 192 APS patients fulfilling the 2006 Sydney classification criteria, 90 SNAPS patients, 193 disease control with other autoimmune diseases and 120 healthy controls were included in the survey. A total of 10 different aPLs were tested in the cohort using commercial kits, including 5 non-criteria aPLs: IgG/IgM anti-phosphatidylserine/prothrombin antibodies (aPS/PT), IgA aCL, IgA aβ2GPI, IgG anti-β2GPI Domain 1 (aβ2GPI D1).

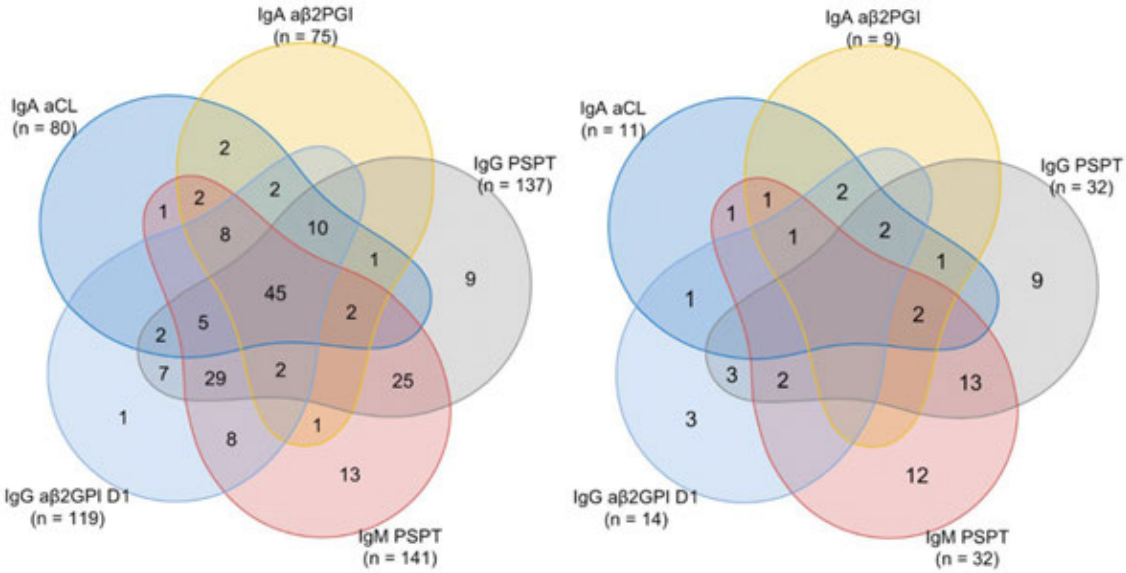
Results: Up to 60.9% SNAPS patients were detected by at least one kind of non-criteria aPLs, and the percentage reaches 93.5% in the APS group. IgG aPS/PT has the biggest Youden Index in classifying APS and SNAPS from the control group, while IgM aPS/PT is a little bit better in sensitivity, just secondary to IgG aβ2GPI. Besides, IgG β2GPI Domain1 is best related with pregnancy morbidities among all the markers. All of the three aforementioned markers can be separately detected in some of the SNAPS patients, while the IgA isotypes of aCL/aβ2GPI tend to appear together with other biomarkers, but they show better diagnostic and prognostic value compared with the IgM



Dot plot of the nine aPL titers among different diagnostic groups, with the box showing the quantile values.



The black percentage above the bars indicates the percentage of patients with any positive non-criteria antibodies while the white percentage on the bottom indicates those without positive non-criteria antibodies.



isotypes of the same aPL. Combined analysis showed better performance of the antibodies profiles with the help of non-criteria aPLs.

Conclusion: SNAPS patients account for a noticeable cohort in the clinical management of thrombotic and obstetric adverse events, and the non-criteria antiphospholipid antibodies help to distinguish a considerable part (40.8%) of these patients in clinical practice.

Numbers in the overlapping region represents the number of patient with specific positive non-criterial aPLs pattern, meanwhile numbers in the non-overlapping region represents the number of patients with single positive non-criterial aPLs. Number in the brackets represents the number of patients in the group with positive outcome of the specific aPL.

Disclosure: J. Gu, None; **T. Liu**, None; **L. Wan**, None; **G. Norman**, None; **C. Yang**, None; **H. Shi**, None.

Abstract Number: 0135

Added Clinical Utility of Testing for Extra-Criteria Antibodies Specificities Beyond Sapporo and Sydney Criteria Recommendations

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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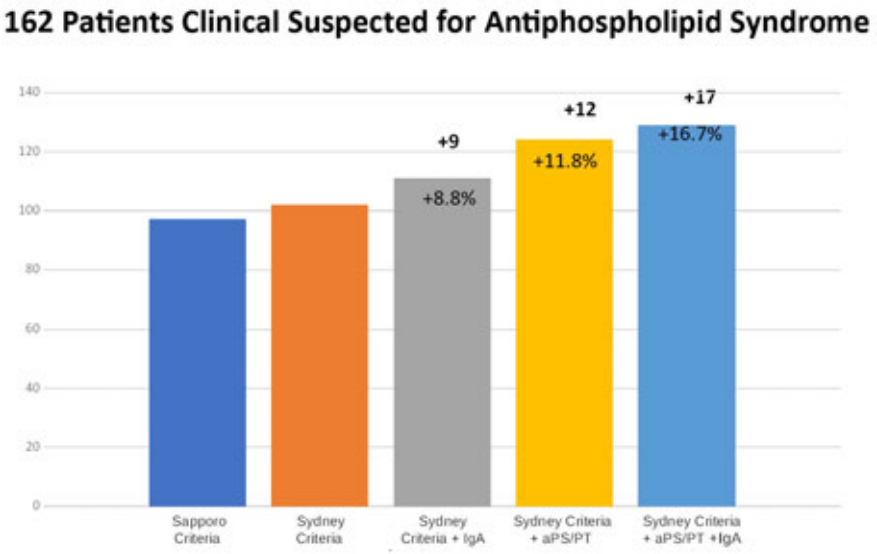
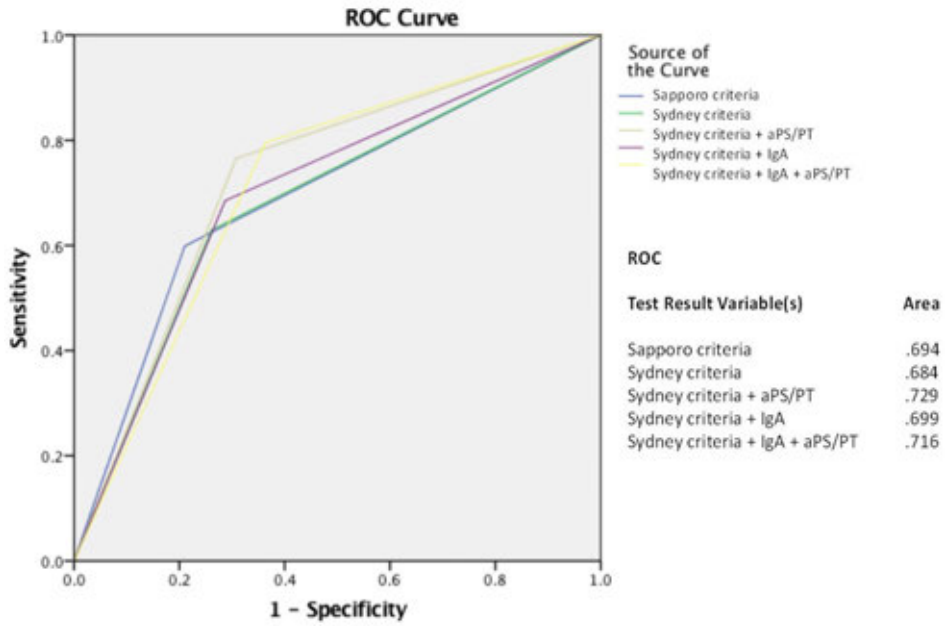
Background/Purpose: The laboratory diagnostics of antiphospholipid syndrome (APS) takes into account the persistent positivity for anticardiolipin (aCL) and/or anti-β2glycoprotein I (anti-β2GPI) antibodies and/or the presence of lupus anticoagulant (LA). However, testing for extra-criteria antiphospholipid antibodies (aPL) is emerging as a poten-





tial tool to improve diagnostic accuracy in patients suspected for APS. In this study we aimed to evaluate the clinical accuracy of aPL specificities both individually and/or in combination, in a wide cohort of patients suspected for APS [on the basis of the presence of thrombosis and/or pregnancy morbidity (PM-)] in an attempt to identify a panel of tests that may provide the best accuracy for diagnosing APS.

Methods: This study included 277 patients affected by an autoimmune systemic disease (234 women, mean age 44.7 ± 13.9 years). One hundred-forty-four patients suffered at least one thrombotic event or PM as described in the current classification criteria for APS. All patients were tested for LA, aCL, anti-β2GPI and anti-phosphatidylserine/prothrombin (aPS/PT). Testing for aCL, anti-β2GPI, and aPS/PT included IgG/M/A isotypes using a novel particle-based multi-analyte technology (PMAT, Aptiva System, Inova Diagnostics, research use only). Sensitivity, specificity, and predictive values were calculated. The diagnostic accuracy for each combination of tests was assessed by receiver operating characteristic (ROC) curve analysis and their area under the curve (AUC) was calculated.

Results: Six possible combinations of results were derived from testing for 4 aPL (Figure 1). Among them, LA+/aCL+/aβ2GPI+/aPS/PT had the best diagnostic accuracy for APS [AUC 0.73, OR 4.0 (95% CI 1.9-6.0)]. Introducing testing for IgA and aPS/PT in the diagnostic workout of patients for suspected APS improved the diagnostic accuracy up to 16.7% (Figure 2).

Conclusion: Combining LA,aCL, aβ2GPI, and aPS/PT improves the diagnostic power and helps in stratifying the risk for each patient, according to their aPL profile

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Abstract Number: 0136

Identifying Phenotypes of Patients with Antiphospholipid Antibodies: Results from a Cluster Analysis in a Large Cohort of Patients

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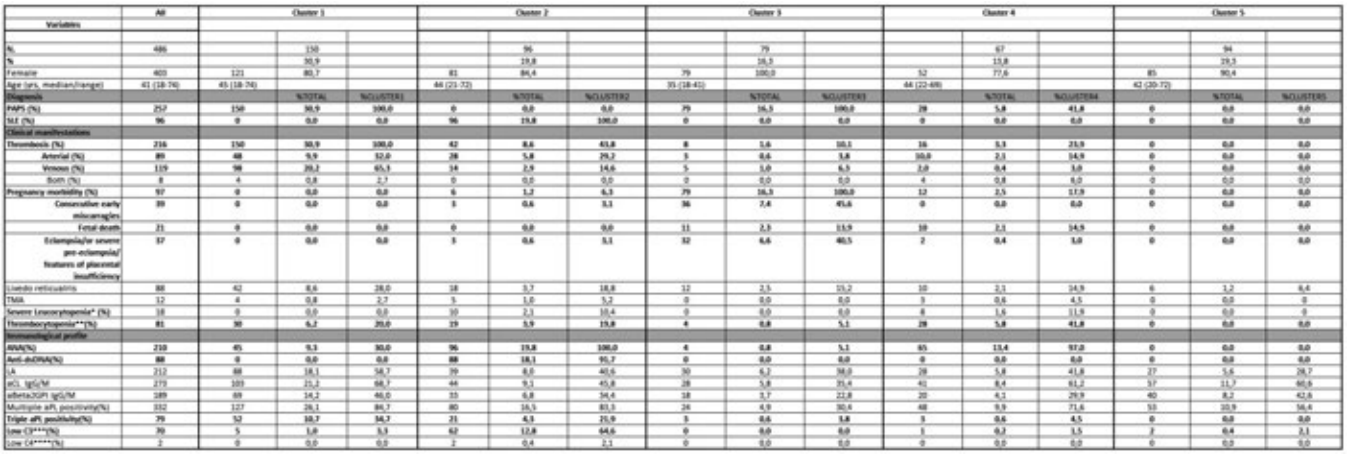
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In this study, we sought to perform an unsupervised hierarchical clustering analysis in a large cohort of antiphospholipid antibodies (aPL) positive patients, to identify the aggregation of patients into different subgroups sharing common characteristics in terms of clinical and laboratory phenotypes.

Methods: We applied a hierarchical cluster analysis from the multiple correspondence analysis to determine subgroups of patients according to clinical and laboratory characteristics in patients with confirmed aPL positivity who presented to our outpatient clinics 2006 to 2018.



Results: We included in this observational, retrospective, and multicentre study 486 patients (403 [83%] women; median age, 41[18-74] years; mean age, 41.7 years±26) with confirmed aPL. Among those 486 subjects, 5 clusters of patients emerged. Cluster 1 (N=150) presented with thrombotic events (65% with a venous thrombosis) in the absence of a confirmed diagnosis of systemic lupus erythematosus(SLE). Up to 85% of patients from Cluster 1 were positive for more than one aPL, triple aPL positivity was found in 35% of the patients, the highest rate observed among the different subgroups($p< 0.01$). All the patients from Cluster 2 (N=91 patients, 84.4% were female) had a confirmed diagnosis of SLE and presented with ANA positivity. These patients had the highest rate of anti-dsDNA positivity(as high as 92%), and up to 64.6% of them presented hypocomplementemia($p< 0.01$). Cluster 3 included 79 women who suffered from pregnancy morbidity, with consecutive early miscarriages in up to 45.6% of the cases. Multiple aPL positivity was found in 30%, with triple positivity in 3.8%, rates significantly lower when compared to Cluster 1(85% and 35%v.s.30 and 4% for multiple and triple positivity, respectively,$p< 0.01$). Cluster 4 included 67 patients (13.8% of the total), 28(42%) of whom with defined diagnosis of APS. Thrombotic events were observed in 16 out of 67(24%) patients. Patients in this group had the highest rate of cytopenia, with thrombocytopenia as high 42%. None of them had anti-dsDNA antibodies positivity. Multiple aPL positivity was found in 72% of the patients, with triple positivity in 4.5%,rate significantly lower when compared to Cluster 1(85% of multiple aPL and 35% of triple aPL positivity) and Cluster 2(83% for multiple aPL and 22% triple aPL positivity, $p< 0.01$). Cluster 5 included 94 subjects. No subjects in this group had a history of thrombosis or pregnancy morbidity. They were all negative for ANA and anti-dsDNA, with normal leukocytes and platelets count.

Conclusion: This study identified 5 clusters emerging from unsupervised analysis. Clusters 1, 2, 3 and 5 corresponded to well-known entities, such thrombotic Primary APS, Secondary APS, obstetric APS and aPL carriers, respectively. Cluster 4 might represent a bridging condition between patients with pure PAPS and defined SLE, with lower thrombotic risk when compared to Primary APS but higher general features such as ANA and cytopenia (mainly thrombocytopenia), representing a group that might benefit of different therapeutic approaches rather than only counterbalancing the pro-thrombotic status.

Demographic, clinical and laboratory characteristics among the Cluster analysed

Disclosure: S. Sciascia, None; **M. Radin**, None; **I. Cecchi**, None; **M. Bertolaccini**, None; **T. Bertero**, None; **E. Rubini**, None; **A. Vaccarino**, None; **M. Bazzan**, None; **O. Giachino**, None; **S. Baldovino**, None; **D. Rossi**, None; **G. Mengozzi**, None; **D. Roccatello**, None.

Abstract Number: 0137

The Clinical and Laboratory Characteristics of Antiphospholipid Antibody Positive Patients Included in the AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository ("Registry")

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SESSION INFORMATION

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Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: APS ACTION "Registry" was created to study the long-term natural history and outcomes of persistently antiphospholipid antibody (aPL)-positive patients with and without other systemic autoimmune diseases (SAID). Our primary objective was to describe baseline demographic, clinical, and laboratory characteristics of patients enrolled since 2010.

Methods: A web-based data capture system is used to store patient demographics and aPL-related medical history. APS ACTION Registry includes adults aged 18 to 60 years with positive aPL, based on the Updated Sapporo APS Classification Criteria, tested on two occasions at least twelve weeks apart within one year prior to enrollment.

Table: Clinical Characteristics of Antiphospholipid Antibody (aPL) Positive Patients in the Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking (APS ACTION) Registry Tested for Three aPL Tests*, Categorized by aPL Profile (n: 668)

Baseline Clinical Characteristics (n: 660)** (Number [%])	LA only Positivity 168 (25%)	Any Single*** aPL Positivity 215 (32%)	Single aPL (excluding LA only) 47 (7%)	Double*** aPL Positivity 167 (25%)	Triple*** aPL Positivity 278 (42%)
Any Vascular thrombosis	123 (73%)	144 (67%)	21 (45%)	113 (68%)	191 (69%)
- Arterial thrombosis	56 (33%)	68 (32%)	12 (26%)	60 (36%)	87 (31%)
- Venous Thrombosis	81 (48%)	92 (43%)	11 (23%)	66 (40%)	130 (47%)
- Small vessel thrombosis	10 (6%)	12 (6%)	2 (4%)	9 (5%)	16 (6%)
- Transient Ischemic Attacks	11 (7%)	13 (6%)	2 (4%)	19 (11%)	20 (7%)
Any Pregnancy Morbidity	61/125 (49%)	75/163 (46%)	14/38 (37%)	55/123 (45%)	77/192 (40%)
- >1 Fetal Death ≥10th week	31 (51%)	39 (52%)	8 (57%)	29 (53%)	43 (56%)
- >1 Preterm Delivery <34th week	12 (20%)	13 (17%)	1 (7%)	14 (25%)	29 (38%)
- 1 or 2 Pre-Emb/Emb Loss <10th week	37 (61%)	45 (60%)	8 (57%)	28 (51%)	34 (44%)
- ≥3 Pre-Emb/Emb Loss <10th week	9 (15%)	14 (19%)	5 (36%)	6 (11%)	6 (8%)
Any Non-Criteria Manifestation	93 (55%)	107 (50%)	14 (30%)	104 (62%)	158 (57%)
- Livedo Reticularis/Racemosa	27 (16%)	28 (13%)	1 (2%)	24 (14%)	32 (12%)
- Persistent Thrombocytopenia	26 (15%)	30 (14%)	4 (9%)	29 (17%)	70 (25%)
- Hemolytic Anemia	9 (5%)	10 (5%)	1 (2%)	7 (4%)	16 (6%)
- Cardiac Valve Disease	11/146 (8%)	12/188 (6%)	1/42 (2%)	12/142 (8%)	32/234 (14%)
- Skin Ulcers	6 (4%)	7 (3%)	1 (2%)	7 (4%)	10 (4%)
- aPL-associated Nephropathy	4/157 (3%)	4/201 (2%)	0	5/160 (3%)	11/256 (4%)
- Cognitive Dysfunction	14 (8%)	17 (8%)	3 (6%)	20 (12%)	33 (12%)
- Multiple Sclerosis-like disease	2 (1%)	3 (1%)	1 (2%)	3 (2%)	0
- Chorea	2 (1%)	2 (1%)	0	4 (2%)	6 (2%)
- Seizure	17 (10%)	21 (10%)	4 (9%)	13 (8%)	23 (8%)
- White Matter Lesions	33/120 (28%)	40/155 (26%)	7/35 (20%)	33/116 (28%)	45/190 (24%)

*Three aPL tested were lupus anticoagulant test [(LA), anticardiolipin antibodies [(aCL), and anti-β_2-Glycoprotein-I antibodies (aβ_2GPI). Only 5/660 (0.8%) of patients had isolated aCL/aβ_2GPI IgA positivity with negative LA and aCL/aβ_2GPI IgG/M

**8 patients had low titer (20-39U) aPL ELISA with negative LA test; thus they were excluded

***: 40U cut-off for aCL and aβ_2GPI IgG/M/A positivity; All groups except LA only and any single aPL were mutually exclusive

Patients are followed every 12±3m with clinical data and blood collection. For this retrospective analysis, we descriptively evaluated the sociodemographic and clinical characteristics of patients overall and in categories by disease manifestation (aPL positive without APS, thrombotic APS, and obstetric APS). We also assessed the clinical characteristics of aPL-positive patients who were tested for all three aPL (lupus anticoagulant [LA] test, anticardiolipin antibody [aCL], and anti-β_2-Glycoprotein-I [aβ_2GPI]) by subgroups based on aPL profiles (LA only, single, double, and triple positivity). Positivity for aCL IgG/M/A and aβ_2GPI IgG/M/A was defined as a titer of ≥40 GPL/MPL/APL units and the highest titer among all test results was taken into consideration during analysis.

Results: As of March 2019, 804 patients were enrolled from 26 centers (mean age: 45 ± 13y; female: 74%; white 68%; and other SAID: 36%). Overall, 172 (21%) were aPL-positive without APS, 453 (56%) thrombotic APS; 73 (9%) purely obstetric APS; and 106 (13%) both thrombotic and obstetric APS. Among thrombotic APS patients, there were slightly higher rates of venous vs arterial thrombosis (62% vs 49%). Slightly higher rates of at least one non-criteria manifestation were observed in APS versus aPL only patients (58% vs 49%). All three aPL were tested in 668 (83%) patients, of whom 278 (42%) were triple positive. While similar frequencies of overall vascular thrombosis, pregnancy morbidity, and non-criteria manifestation were seen across single, double, and triple positivity subgroups, the lowest frequencies were observed in the single aPL positivity (excluding lupus anticoagulant [LA] only) subgroup **(Table).**

Conclusion: One-fifth of APS ACTION patients do not fulfill clinical APS classification criteria; 70% have vascular events; one-fifth have obstetric morbidity; and more than half have at least one non-criteria manifestation. Within single aPL-positivity, LA positivity appears to be an important contributor to aPL-related clinical features. Future prospective analyses, using standardized core laboratory aPL tests, will help better clarify aPL risk profiles.

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Abstract Number: 0138

Relationship Between Recurrent Thrombosis and the Antiphospholipid Antibodies Profile in a Cohort of Patients with Antiphospholipid Syndrome

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SESSION INFORMATION
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Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Recurrent thrombosis is an uncommon complication of patients with antiphospholipid syndrome (APS), usually related with persistent high levels of antiphospholipid antibodies (aPL), specially classic aPL (anticardiolipin antibodies, aCL or lupus anticoagulant, LA). The role of other aPL, including anti-phosphatidylserine/prothrombin (PS/PT) antibodies, anti B2 glycoprotein 1 (B2GP1) and anti domain 1 against B2GP1 as markers of recurrence in APS, it is less well known. Our aim was to determinate the relationship between the presence of different aPL (criteria and non-criteria aPL) with recurrent thrombosis in a cohort of patients with APS, including patients with primary APS and secondary APS (related with SLE)

Methods: We conducted a prospective single center study including patients with diagnosis of APS (Sidney criteria). A wide panel of aPL antibodies were measured at the moment of study inclusion, then, a prospective follow up was made according daily clinical practice. New thrombotic and non-thrombotic manifestations were recorded during follow-up. Anti-D1 B2GPI antibodies were tested using a chemiluminescent immunoassay (QUANTA Flash, Inova Diagnostics). In addition, anti PS/PT (IgG and IgM), aCL (IgG and IgM) and anti B2GP1 (IgG and IgM) were measured at baseline by ELISA. LA was detected according to International guidelines.

Baseline patient characteristics were summarized using counts and percentages or median and for categorical and continuous variables. Comparison across groups was done using Chi-squared, Fisher's Exact, or Mann–Whitney tests as appropriate. Kaplan–Meier for time to event analysis was used to determine risk factors for thrombotic events during follow-up.

Results: One hundred and sixty eight patients were included, 87% of patients were female with a mean age of 34.0 ± 12.8 years. aPL profile was done in 145 patients with secondary APS and 23 patients primary APS. Clinical follow-up was available in 91 patients. Mean follow-up was 20.6 ± 13.8 months (range 1-46 months). New thrombotic episodes occurred in 8 out of 91 (8.8%) of patients (6 DVT and 2 arterial), 5 of them despite anticoagulation therapy (4 vitamin

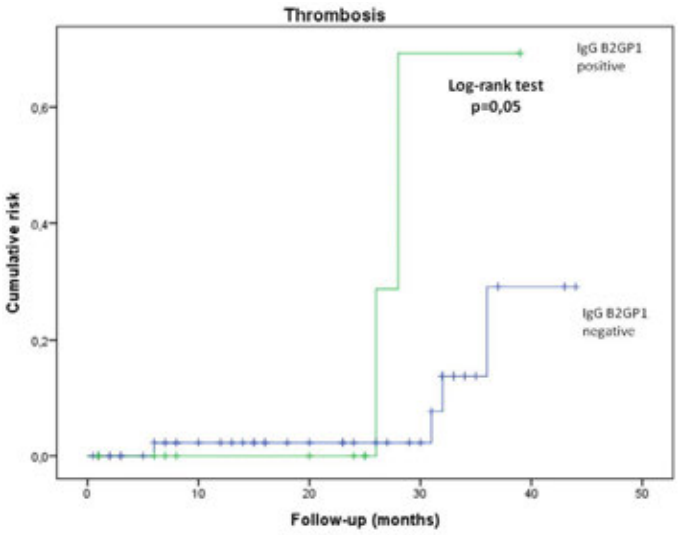

Figure 1. Cumulative risk of thrombosis according IgG B2GP1 antibodies.

K antagonist and 1 Dabigatran).We also documented 6 new episodes of thrombocytopenia and 2 new fetal losses. Overall, anti IgG B2GP1 antibodies were related with recurrent thrombosis (28 vs 7%, p=0,022), arterial thrombosis (6.7 vs 0%, p=0,05) and LA with recurrent thrombocytopenia (12,9 vs 0%, p=0,049). In survival analysis, IgG B2GP1 were related with a significant cumulative risk of thrombosis (Figure). No relationship between non-criteria aPL or triple positivity was found with recurrence. No clinically relevant major or minor bleeding occurred

Conclusion: In our cohort of patients with APS, IgG B2GP1 antibodies were related with recurrent thrombotic events. Given the low rate of new events, a longer follow-up is needed to establish further relationships.

Cumulative risk of thrombosis according IgG B2GP1 antibodies

Disclosure: T. Urrego, None; **B. Frade-Sosa**, None; **A. Hernández**, None; **S. Ruiz**, None; **C. Rua**, None; **J. Duque**, None; **A. Vanegas-García**, None; **C. Muñoz-Vahos**, None; **L. González**, None; **G. Vasquez**, None; **J. Gómez-Puerta**, None.

Abstract Number: 0139

Antiphospholipid Syndrome Damage Index (DIAPS): Distinct Long-term Kinetic in Primary Antiphospholipid Syndrome and APS Related to SLE

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Background/Purpose: Antiphospholipid syndrome (APS) is an acquired thrombophilia that affects young productive individuals with permanent damage and negative impact in quality of life. Recently a damage index specific for APS (DIAPS) was developed. There are, however, no data regarding the comparison of its performance and long-term damage in primary antiphospholipid syndrome (PAPS) and APS related to SLE (APS+SLE). The primary purpose of this study was, therefore, to compare the long-term damage in patients with these conditions.

Table 1. Demographic features and damage scores in PAPS and APS related to SLE patients

	PAPS (N=50)	APS+SLE (N=50)	P
Age (years) mean ± SD	47.10±12.4	44.04±10.80	0.19
Female gender N (%)	41 (83%)	44 (88%)	0.57
Diagnostic delay (years) mean ± SD	4.00±4.20	2.54±3.05	0.04
Time of follow up (years) mean ± SD	9.40±3.60	10.94±4.50	0.06
DIAPS at diagnosis mean ± SD	1.72±1.17	0.82±0.96	<0.001
Final DIAPS mean±SD	2.04±1.50	2.24±1.61	0.52
Patients free of damage	2 (4%)	4(16%)	0.67
Δ DIAPS mean ± SD	0.43±0.30	1.22±1.24	<0.001

Table 2. Comparison of damage domains at the end of follow-up of PAPS and APS+SLE

	PAPS n(%)	*APS+SLE* n(%)	P
Peripheral vascular (total)	31(62)	32 (64)	1.00
Deep vein thrombosis	28(55)	29 (56)	1.00
Intermittent claudication	0 (0)	0 (0)	1.00
Tissue loss: minor	2 (4)	0 (0)	0.49
Tissue loss: major	1 (2)	3 (6)	0.61
Vascular venous insufficiency	4 (8)	13 (25)	**0.03**
Pulmonary (total)	9 (18)	15 (30)	0.24
Pulmonary infarction	7 (14)	12 (23)	0.30
Pulmonary arterial hypertension	0 (0)	1 (2)	1.00
Chronic thromboembolic/Pulmonary hypertension	2 (4)	2 (4)	1.00
Respiratory insufficiency	1 (2)	3 (6)	0.61
Cardiovascular (total)	4 (8)	8 (16)	0.35
Coronary artery bypass	0 (0)	0 (0)	1.00
Myocardial infarction	3 (6)	4 (8)	1.00
Cardiomyopathy	0 (0)	3 (6)	0.24
aPL-associated heart valve disease (with or without replacement)	1 (2)	1 (2)	1.00
Neuropsychiatric (total)	25(50)	29 (58)	0.54
Cognitive impairment	6(12)	2 (4)	0.26
Seizures	2 (4)	5 (10)	0.43
Ischemic stroke with hemiparesia	7 (14)	10 (21)	0.59
Ischemic stroke with hemiplegia	3 (6)	4 (8)	1.00
Multi-infarct dementia	1 (2)	0 (0)	1.00
Cranial neuropathy	1 (2)	0 (0)	1.00
Sudden sensorineural Hearing loss	0 (0)	1 (2)	1.00
Transverse myelitis	1 (2)	1 (2)	1.00
Optic neuropathy	0 (0)	0 (0)	1.00
Peripheral neuropathy	3 (6)	5 (10)	0.71
Abnormal movements	1 (2)	1 (2)	1.00
Ophthalmologic (total)			
Retinal vaso-occlusive disease	0 (0)	2 (4)	0.49
Blindness	1 (2)	1 (2)	1.00
Renal (total)	7 (14)	5 (10)	0.75
Chronic renal failure	5 (10)	3 (6)	0.71
Proteinuria 24 h >3.5g/vol or Renal thrombotic microangiopathy	2 (4)	2 (4)	1.00
Musculoskeletal - Avascular necrosis	1 (2)	4 (8)	0.36
Cutaneous - Chronic cutaneous ulcers	2 (4)	7 (14)	0.15
Gastrointestinal (total)	1 (2)	2 (4)	1.00
Mesenteric thrombosis	1 (2)	1 (2)	1.00
Budd-Chiari syndrome	0 (0)	0 (0)	1.00
Cirrhosis of the liver	0 (0)	1 (2)	1.00
Endocrine (total)	1 (2)	1 (2)	1.00
Suprarenal insufficiency	0 (0)	0 (0)	1.00
Hypopituitarism	1 (2)	0 (0)	1.00
Infertility	0 (0)	1 (2)	1.00

Methods: This is a retrospective analysis of a single tertiary center cohort followed for approximately 10 years, using a standardized prospective electronic chart database. Fifty consecutive PAPS patients age matched with fifty APS+SLE patients were consecutively selected for the study and DIAPS was calculated once-a-year during follow-up. Long term damage and damage kinetics in both groups were compared.

Results: PAPS and APS+SLE had comparable age (47.10±12.4 vs. 44.04±10.80 years, p=0.19) and time of follow-up (9.40±3.60 vs. 10.94±4.50 years, p=0.06). At diagnosis, PAPS group had higher DIAPS than APS+SLE (1.72±1.17 vs. 0.82±0.96, p< 0.001). At the end of 10 years follow-up both groups presented comparable mean damage scores (2.04±1.50 vs. 2.24±1.61, p=0.52). The damage increment throughout the observation period for PAPS was solely 35% whereas for APS+SLE it was gradual, persistent and reached 139% at the end of follow up with a total damage increment for PAPS lower than APS+SLE group (0.43±0.30 vs. 1.22±1.24, p< 0.001). Of note, the frequency of indi-

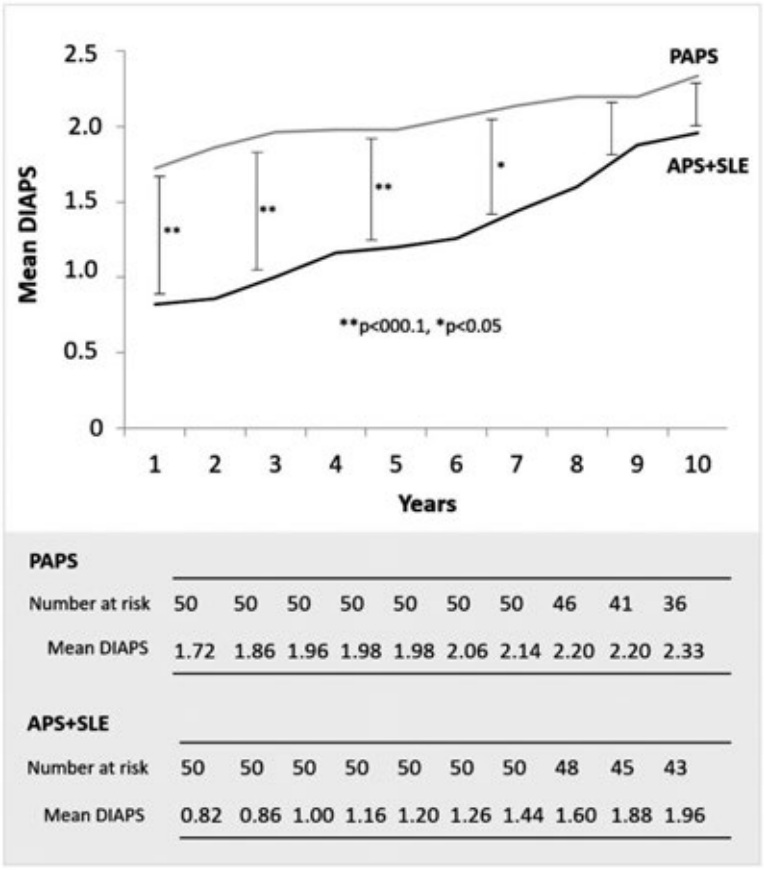

Figure 1. Cumulative incidence of damage along follow-up in PAPS and APS related to SLE

viduals that acquired damage was lower in PAPS than in APS+SLE group (32% vs. 71%, p< 0.001). PAPS had also longer delay in diagnosis than APS+SLE (4.00±4.20 vs. 2.54±3.05 years, p=0.04). This delay was positively correlated to a higher damage score at diagnosis (r=0.36, p< 0.001) in all groups.

Conclusion: We identified a distinct pattern of damage in PAPS and APS related to SLE. Damage in PAPS is an early event while APS+SLE is associated with higher long term damage with a striking increment of damage along the follow-up. Diagnosis delay is correlated with higher damage scores. Damage surveillance requires therefore different approaches for these two conditions.Table 1. Demographic features and damage scores in PAPS and APS related to SLE patients

Disclosure: A. Kühl Torricelli, None; **M. Remião Ugolini-Lopes**, None; **E. Bonfa**, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #305068/2014-8), 2, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4 and #2010/10749-0), 2; **D. Andrade**, None.

Abstract Number: 0140

Early Anticoagulation Improves the Long-term Prognosis in Patients with Antiphospholipid Syndrome Associated Portal Vein Thrombosis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Portal vein thrombosis (PVT) is a rare and severe clinical phenotype of antiphospholipid syndrome (APS) with a poor prognosis. Anticoagulation therapy is efficient, but is associated with potentially severe side-effects, especially bleeding episodes. The aim of this study was to retrospectively analysis our single center experience on long-term anticoagulation in APS patients presenting a PVT.

Methods: Data of 26 APS patients with PVT from 2012 to 2019 were enrolled. The diagnosis of PVT was made according to the 2009 American College of Liver Diseases (AASLD) criteria. Regular imaging was performed to monitor the outcome of PVT. The hemorrhagic complications and the recurrence of the PVT after anticoagulation withdrawal were also analyzed.

Results: A total of 26 patients with APS-PVT were enrolled, 5 males and 21 females, with an average age of 39±12.65 years, 9 cases (35%) with acute thrombosis, 12 cases (46%) with chronic thrombosis, and 5 cases (19%) with portal vein spongiformity. 14 cases (54%) with portal hypertension, 13 cases (50%) with esophageal varices, 4 cases(15%) with spleen infarction, 6 cases (23%) with gastrointestinal bleeding and 2 cases (8%) with abdominal infection. Triple aPLs positive in 5 cases (19%). 14 cases began anticoagulation therapy immediately after diagnosis of thrombus. 7 patients got thrombus recanalization. 3 patients got recurrence. 5 patients died.

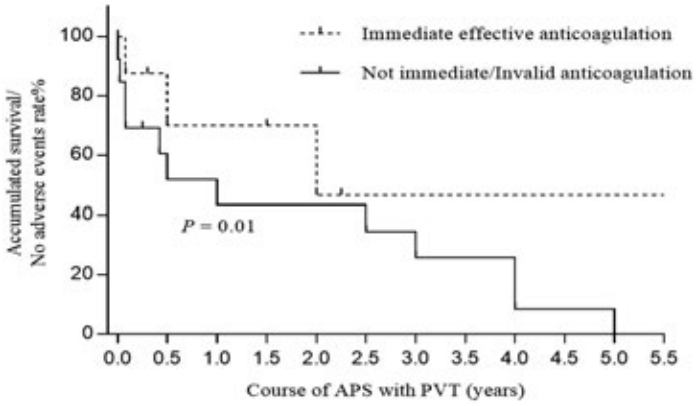

Figure 1 Difference of accumulated survival/no adverse events rate between groups receiving immediate effective anticoagulation and not. Adverse events included recurrent thrombosis, liver cirrhosis and severe portal hypertension complications, such as gastrointestinal bleeding and esophagogastric varices. Effective anticoagulation was defined as sufficient anticoagulant therapy for at least 6 months. Not immediate/invalid anticoagulation was defined as no anticoagulation immediately after the thrombus or course of anticoagulant therapy less than 6 months.

Conclusion: PVT usually had insidious onset with atypical clinical symptoms and easily be misdiagnosed. Early diagnosis and anticoagulation treatment can bring thrombus recanalization thereby significantly improving the prognosis.

Disclosure: H. You, None; **J. Zhao**, None; **X. Tian**, None; **M. Li**, None; **X. Zeng**, None.

Abstract Number: 0141

Pregnancy in Antiphospholipid Syndrome: Outcomes and Risk Factors – Data from a Portuguese Multidisclinary Unit

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Antiphospholipid Syndrome Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Women with antiphospholipid syndrome (APS) are at increased risk of recurrent miscarriage, fetal death, placental insufficiency, preeclampsia and fetal growth restriction (FGR). Although treatment improves outcomes, there are still some unsuccessful pregnancies. A multidisciplinary approach with strict monitoring is essential

Table 1. Comparison of clinical and serological features between adverse pregnancy outcomes and successful pregnancies.

	APO, n=12 (30%)	Successful pregnancies n= 28 (70%)	*p*-value †	OR (CI 95%)
Maternal age, mean	34.1 ± 3.5	33.3 ± 5.7	0.623 ‡	-
Disease duration, mean	7.6 ± 6.3	5.8 ± 4.8	0.334 ‡	-
History of thrombosis	9 (75%)	16 (57.1%)	0.276	-
History of previous APOs	8 (66.7%)	15 (53.6%)	0.443	-
Concomitant SLE	9 (75%)	12 (42.9%)	0.062	-
Lupus anticoagulant	12 (100%)	11 (39.3%)	**<0.001**	38.0 (2.046 – 707.515)
IgG aCL	7 (58.3%)	10 (35.7%)	0.185	-
IgM aCL	0 (0%)	7 (25%)	0.081	-
IgG anti-B2GPI	8 (66.7%)	9 (32.1%)	0.079	
IgM anti-β2GPI	2 (16.7%)	5 (17.9%)	0.999	-
Single Positivity	2 (16.7%)	10 (35.7%)	0.285	-
Double Positivity	3 (25%)	7 (25%)	0.999	-
Triple Positivity	7 (58.3%)	4 (14.3%)	**0.008**	8.4 (1.763 – 40.024)
Negative APL	0 (0%)	7 (25%)	0.081	-
Low complement levels *	4 (44.4%)	5 (25%)	0.396	-
Anti-dsDNA Φ	3 (33.3%)	2 (16.7%)	0.611	

The only patient who had a medical abortion was excluded from this analysis.

† Fisher's exact test or chi-square test, except otherwise indicated.

‡ Independent t-test.

*Data available for 29 pregnancies.

Φ Applied only to patients with SLE (n=21).

in order to attain obstetrical success. Our aim is to assess feto-maternal outcomes in Portuguese pregnant women with antiphospholipid syndrome (APS) who received multidisciplinary care and to determine the risk factors for adverse outcomes.

Methods: Pregnant women fulfilling the Sydney classification criteria for definite APS, who attended our specialized Rheumatology and Obstetrics outpatient clinic between 2010 and 2019, were included in this retrospective observational study. Cases of suspected APS not fulfilling the classification criteria were excluded. All pregnancies were followed up by a multidisciplinary team (rheumatologists, obstetricians and nurses). Data was collected from medical records. Adverse Pregnancy Outcomes (APO) were defined as: spontaneous abortion (< 10w), fetal death (≥10w), neonatal death, FGR and delivery prior to 36 weeks of gestation with or without preeclampsia (PE).

Results: A total of 41 pregnancies were identified in 31 women with APS (58% primary; 42% secondary APS). Forty-five percent had thrombotic APS, 42% obstetric APS and 13% mixed APS. Mean age at conception was 33.4 ± 5.2 years; mean disease duration was 6.3 ± 5.3 years. In regard to antiphospholipid antibody (APL) profile, 32%, 24% and 27% of patients were triple, double and single positive, respectively. Although they had fulfilled laboratorial criteria in the past, 17% of patients were negative for all APL at the time of conception. All patients were instructed to receive prophylactic or therapeutic low-molecular-weight heparin combined with low dose aspirin for the duration of pregnancy. Regarding fetal outcomes, there were 3 (7.3%) cases of first-trimester miscarriage, 1 (2.4%) medical abortion and 4 (9.8%) fetal deaths. There were no cases of neonatal death or other fetal malformations. The rate of live births was 80.5%, with a mean gestational age of 37.7 ± 1.7 weeks and mean birth weight of 2853.9 ± 466 g. Most women (64%) delivered by cesarean section. Preterm birth rate was 18% (6 cases), half corresponding to fetus with FGR. Concerning maternal outcomes, there was one single case (2.4%) of PE. There were no cases of eclampsia or HELLP syndrome. Lupus anticoagulant ($p< 0.001$, OR 38) and triple APL ($p=0.008$, OR 8.4) positivity were associated with adverse pregnancy outcomes. In this cohort, no association was found between poor obstetric outcomes and history of thrombosis, presence of SLE or low complement levels (table 1).

Conclusion: In our study, most pregnancies were uneventful. The presence of lupus anticoagulant and triple APL positivity can represent risk factors for adverse outcomes, despite conventional treatment. We reinforce the importance of a multidisciplinary evaluation and surveillance before, during and after pregnancy in women with APS in order to implement early treatment and to optimize fetal-maternal outcomes.

Disclosure: A. Neto, None; **P. Martins**, None; **M. Centeno**, None; **C. Araújo**, None; **L. Pinto**, None; **S. Capela**, None.

Abstract Number: 0142

Antiphospholipid Antibodies Prevalence in Women with Late Pregnancy Complication and Low-Risk for Chromosomal Abnormalities

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Antiphospholipid Syndrome Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: While current guidelines help defining correct pregnancy standard of care for patients with systemic lupus erythematosus andantiphospholipid syndrome (APS),little is known about the significance of antiphospholipid antibodies (aPL) detection during pregnancy and their association with clinical manifestations of the syndrome in women without history of rheumatic disease.

In this context, we aimed to retrospectively investigate the prevalence of aPL and late-onset pregnancy complications (LO-PC) in a cohort of women with low risk of chromosomal abnormalities.

Methods: For the purpose of this study, we retrospectively collected data from a number of patients ever pregnant attending the S. Anna University Clinic (Turin, Italy) from August 2017 to August 2018, that were found to be negative for triple test and fetal abnormalities and who experienced LO-PC. aPL testing was performed on serum samples derived from pregnancy screening test collected during the fourth month of gestation. aPL detection was performed using both ELISA assay (INOVA Diagnostic) and chemiluminescent immunoassay (INOVA Diagnostic) for the semi-quantitative measurement of antibodies -comprehensive of IgG, IgM, and IgA isotypes for anticardiolipin (aCL) and anti-β2-glycoprotein I (β2GPI), β2GPI domain I, and anti-phosphatidylserine/prothrombin (aPS/PT) IgG and IgM.

	All patients (59)	aPL positive (19)	aPL negative (40)	Chi Square test (p)
Fetal outcomes				
Live births, n (%)	55 (93)	16 (84)	39 (98)	**.007**
Stillbirths, n (%)	4 (7)	3 (16)	1 (3)	.054
IUGR, n (%)	8 (14)	0	8 (20)	N/A
Maternal pregnancy outcomes				
Preeclampsia, n (%)	27 (46)	7 (37)	20 (50)	.9
Eclampsia, n (%)	1 (2)	1 (5)	0	N/A
Gestational diabetes, n (%)	16 (27)	6 (32)	10 (25)	.595
Gestational hypertension, n (%)	32 (54)	12 (63)	20 (50)	.343
HELLP, n (%)	6 (10)	1 (5)	5 (13)	.39
IUGR, n (%)	8 (14)	0	8 (20)	N/A
Obstetric and post-partum complications				
Hypertensive crisis, n (%)	12 (20)	4 (21)	8 (20)	.925
Hemorrhage, n (%)	6 (10)	2 (11)	4 (10)	0.95
Acute renal insufficiency, n (%)	1 (2)	0	1 (3)	N/A
Acute respiratory failure, n (%)	1 (2)	0	1 (3)	N/A
Placental histology				
Malperfusion, n (%)	19 (32)	6 (32)	13 (33)	.943
Fetal thrombotic vasculopathy, n (%)	3 (5)	1 (5)	2 (5)	.965
Subacute villitis, n (%)	1 (2)	0	1 (3)	N/A
Chronic villitis of unknown etiology, n(%)	1 (2)	0	1 (3)	N/A
Subacute deciduitis, n (%)	1 (2)	1 (5)	0	N/A

Results: Fifty-nine patients met the inclusion criteria of the study. Pregnancy complications were as follows: 27 (46%) patients developed preeclampsia, 1 eclampsia, 16 (27%) manifested gestational diabetes, 32 (54%) gestational hypertension, 6 (10%) experienced HELLP syndrome, and 8 (14%) intrauterine growth restriction. Obstetric and post-partum complications were as follows: 12 (20%) patients developed hypertensive crisis, 6(10%) patients developed post-partum hemorrhage, 1 patient developed hypertensive crisis, acute renal failure, and acute respiratory insufficiency concomitantly. Placental histologic examination, when performed, showed that the most frequent histologic finding was placental malperfusion (19 patients, 32%), followed by 3 fetal thrombotic vasculopathy (5%), 1 subacute villitis, 1 subacute deciduitis, and 1 case of chronic villitis of unknown etiology. Nineteen women (32%) were aPL positive, in detail: 15 showed a single positivity (6 aPS/PT IgM, 1 aPS/PT IgG, 8 aCL IgG), 3 double positivity (aCL IgG, aPS/PT IgM), and one triple positivity (aCL IgG, β2GPI IgG, andaPS/PT IgM). Of interest, patients with aPL positivity had significantly lower life births rates (84% vs. 98%, $p< 0.05$). Table 1 shows fetal, maternal outcomes, post-partum complications, and placental histologic findings.

Conclusion: In our experience, the prevalence of aPL in women with LO-PC at low-risk for chromosomal abnormalities was as high as 32%. Our data suggest that testing for both criteria and extra criteria aPL could improve the diagnostic accuracy to identify LO-PC.

Fetal and maternal pregnancy outcomes, obstetric complications and placental findings. aPL means antiphospholipid antibodies; IUGR, intrauterine growth restriction.

Disclosure: S. Foddai, None; **M. Radin**, None; **E. Rubini**, None; **I. Cecchi**, None; **S. Sciascia**, None; **D. Roccatello**, None; **E. Menegatti**, None; **S. Gaito**, None; **L. Marozio**, None; **T. Manetta**, None; **G. Mengozzi**, None.

Abstract Number: 0143

Clinical and Genetic Factors Associated with Thrombosis or Pregnancy Morbidity of Antiphospholipid Antibody-Positive Systemic Lupus Erythematosus Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid syndrome (APS) is characterized by thromboembolic and obstetric morbidity associated with antiphospholipid antibodies (aPL) in systemic lupus erythematosus (SLE). This study aims to evaluate the prevalence of aPL profile, and identify clinical and genetic risk factors associated with thrombotic and obstetric events in Korean patients with SLE.

Methods: Patients with SLE were enrolled and followed from 1998 to 2018 in Hanyang BAE lupus cohort and were investigated clinical and aPL profile [lupus anticoagulant (LAC), anticardiolipin antibodies (aCL), and anti-β_2-glycoprotein1 antibodies (aβ_2-GP1)]. We genotyped SLE patients using genome-wide association study (GWAS) array (Affymetrix Axiom-KOR, 833K SNPs). To determine risk factors for APS, clinical and genetic variables were analyzed by logistic regression.

Table 1. Comparison of antiphospholipid antibody-positive systemic lupus erythematosus patients with and without thrombosis or pregnancy morbidity

	aPL(+) SLE (n = 428)	*Thrombosis or pregnancy morbidity(+) in aPL(+) SLE (n = 79)*	*Thrombosis or pregnancy morbidity(-) in aPL(+) SLE (n = 349)*	*p-value*
Demographics				
Sex: female, n (%)	390 (91.1)	71 (89.9)	319 (91.4)	0.83
Age at clinical diagnosis of SLE, years	26.6 ± 10.6	25.2 ± 9.6	26.9 ± 10.9	0.20
Observation period, years	13.8 ± 6.9	14.0 ± 6.7	13.7 ± 7.0	0.76
Disease activity				
SLEDAI at enrollment	5.2 ± 4.0	5.2 ± 4.1	5.2 ± 4.0	0.98
SLEDAI at last follow-up	4.2 ± 3.7	4.7 ± 3.9	4.1 ± 3.7	0.20
SDI at enrollment	0.4 ± 0.8	0.7 ± 1.1	0.3 ± 0.8	<0.01
SDI at last follow-up	1.1 ± 1.5	1.8 ± 1.7	1.0 ± 1.4	0.04
ACR classification criteria for SLE, cumulative, n (%)				
Malar rash	190 (44.4)	36 (45.6)	154 (44.1)	0.91
Discoid rash	42 (9.8)	6 (7.6)	36 (10.3)	0.60
Photosensitivity	138 (32.2)	25 (31.7)	113 (32.4)	1.00
Oral ulcer	173 (40.4)	31 (39.2)	142 (40.7)	0.91
Arthritis	262 (61.2)	39 (49.4)	223 (63.9)	0.02
Serositis	171 (40.0)	35 (44.3)	136 (39.0)	0.46
Renal disorder	223 (52.1)	45 (57.0)	178 (51.0)	0.41
Neurologic disorder	41 (9.6)	13 (16.5)	28 (8.0)	0.04
Hematologic disorder	398 (93.0)	76 (96.2)	322 (92.3)	0.33
Leukopenia	320 (74.8)	61 (7.2)	259 (74.2)	0.68
Lymphopenia	354 (82.7)	72 (91.1)	282 (80.8)	0.04
Hemolytic anemia	78 (18.2)	13 (16.5)	65 (18.6)	0.77
Thrombocytopenia	169 (39.5)	45 (57.0)	124 (35.5)	<0.01
Immunologic disorder	425 (99.3)	79 (100)	346 (99.1)	1.00
ANA positivity	428 (100)	79 (100)	249 (100)	
Autoantibodies, n (%)				
Anti-dsDNA antibody	373 (87.2)	70 (88.6)	303 (86.8)	0.81
Anti-Smith antibody	86 (20.1)	14 (17.7)	72 (20.6)	0.67
Anti-RNP antibody	400 (93.5)	75 (94.9)	325 (93.1)	0.80
Anti-phospholipid antibody	401 (93.7)	77 (97.5)	324 (92.8)	0.20
LAC	222 (51.9)	60 (76.0)	162 (46.4)	<0.01
aCL IgM	156 (36.5)	30 (38.0)	126 (36.1)	0.86
aCL IgG	244 (57.0)	50 (63.3)	194 (55.6)	0.26
aβ2-GPI IgM	80 (18.7)	11 (13.9)	69 (19.8)	0.30
aβ2-GPI IgG	86 (20.1)	24 (30.4)	62 (17.8)	0.02

Results: Among 1,167 SLE patients, 428 (36.7%) had at least one aPL (aPL(+)). In patients with aPL(+) SLE, the number of patients with LAC, aCL and aβ2-GP1 was 223 (52.1%), 297 (69.4%), and 139 (32.5%), respectively. Triple aPL positivity was observed in 70 (16.4%). Among 428 aPL(+) SLE patients, 79 (18.5%) had thrombosis or pregnancy morbidity as clinical criteria of APS, and 42 (9.8%) were satisfied with classification criteria of APS. When comparing the groups with and without thrombosis or pregnancy morbidity in aPL(+) SLE patients, multivariable regression analysis indicated that thrombocytopenia (p=0.04), positivity of LAC (p< 0.01), and positivity of aβ2-GP1 IgG (p=0.02) were associated with the occurrence of thrombosis or pregnancy morbidity in aPL(+) SLE. We identified eight SNPs were associated with development of aPL in SLE patients (p< 5×10-5). We also identified that two genes have significant effects on thrombosis

Table 2. Factors associated with thrombosis or pregnancy morbidity of antiphospholipid antibody-positive systemic lupus erythematosus patients

	Univariate		*Multivariable*	
	OR (95% CI)	*p-value*	*OR (95% CI)*	*p-value*
Sex: female	0.84 (0.37-1.90)	0.67	1.08 (0.43-2.68)	0.87
Age at clinical diagnosis of SLE	0.99 (0.96-1.01)	0.20	1.01 (0.98-1.04)	0.52
Observation period	1.01 (0.97-1.04)	0.76	1.03 (0.98-1.07)	0.23
Arthritis	0.55 (0.34-0.90)	0.02	0.62 (0.36-1.07)	0.08
Neurologic disorder	2.26 (1.11-4.59)	0.02	2.00 (0.90-4.42)	0.09
Lymphopenia	2.44 (1.08-5.55)	0.03	2.33 (0.97-5.57)	0.06
Thrombocytopenia	2.40 (1.46-3.95)	<0.01	1.74 (1.02-2.97)	0.04
Positivity of LAC	3.65 (2.09-6.36)	<0.01	3.91 (2.08-7.33)	<0.01
Positivity of aß2-GP1 IgG	2.02 (1.16-3.51)	0.01	2.04 (1.11-3.75)	0.02

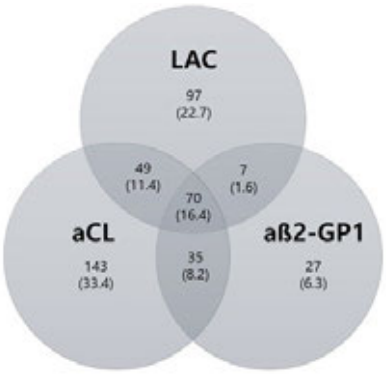

Figure 1. Distribution of antiphospholipid antibody positivity in antiphospholipid antibody-positive in systemic lupus erythematosus patients.
Values are shown number (%).

manifestations in aPL(+) SLE patients (p< 5×10-6). Among them, top gene showed the high risk association with APS(+) SLE (odds ratio=6.2) that influenced on regulation of Wnt pathway and vascular permeability.

Conclusion: In this study, 36.7% of Korean SLE patients showed aPL positivity. Eight SNPs were associated with the development of aPL in SLE, two genes with thrombosis manifestations in aPL(+) SLE, and the top gene with APS(+) SLE. As clinical factors, thrombocytopenia, positivity of LAC, and positivity of aβ_2-GP1 IgG were significantly associated with the occurrence of APS related thrombosis or pregnancy morbidity in aPL(+) SLE. These results may help clinicians to better risk stratify aPL(+) SLE patients.

Disclosure: J. Kim, None; **G. Ahn**, None; **J. Choi**, None; **J. Lee**, None; **Y. Park**, None; **S. Bang**, None; **S. Bae**, None.

Abstract Number: 0144

Antiphospholipid Syndrome-Associated Preeclampsia Is Defined by a Distinct Clinical Phenotype

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Antiphospholipid Syndrome Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid syndrome (APS) significantly increases risk of preeclampsia. It is assumed that APS is associated with a subset of severe preeclampsia, HELLP (Hemolysis; Elevated Liver enzymes; Low Platelet count) syndrome, and that APS-associated preeclampsia presents earlier and with increased severity compared to non-APS associated preeclampsia. However, little data exists that directly compares these groups of patients. Herein we compare clinical characteristics of patients with APS-associated preeclampsia to those of APS-negative preeclampsia patients.

Methods: We used the electronic medical record of a large academic medical system to identify adult APS patients with at least one preeclampsia episode between 2000-2018. APS diagnoses were confirmed using the updated Sapporo APS Classification, and preeclampsia diagnoses (including subsets of severe preeclampsia and HELLP) were classified according to American College of Obstetricians and Gynecologists guidelines. We identified control patients from the same electronic medical record with at least one episode of preeclampsia and negative laboratory testing for antiphospholipid antibodies at the time of the preeclampsia event. Groups were compared with respect to demographic factors, clinical presentation and fetal outcomes (including intrauterine growth restriction, intrauterine fetal demise and infant mortality within the first week of life) using Student's t test and Chi-Square test.

Results: We identified eight APS patients and 29 controls with at least one episode of preeclampsia during the study period (Table 1). APS patients had a mean age of 30 years, 100% were white and BMI was 32 ± 2 (mean ± SD). Controls had similar demographics, with the exception that only 59% of controls were white. Of the eight APS patients, 38% had a pre-existing APS diagnosis (all based on obstetric complications; no thrombotic history), 38% were triple-positive (positive lupus anticoagulant, anti-cardiolipin and anti-β2 glycoprotein antibodies), 38% had at least one prior episode of preeclampsia and 50% had systemic lupus (likely low disease activity based on review of laboratory studies, lack of significant proteinuria, and treatment with few/no lupus medications). Although both groups had similar rates of severe preeclampsia, APS patients were more likely to have preeclampsia associated with at least partial HELLP (75%) compared to non-APS controls (20.7%) (p=0.004). Further, APS patients had more severe liver involvement (p=0.028) and thrombocytopenia (p=0.018). There was a trend for less severe proteinuria in APS-associated preeclampsia (p=0.36). No significant differences were seen in maternal or fetal outcomes, although there was a trend for more frequent intrauterine growth restriction complicating pregnancies of women with APS. Both groups developed preeclampsia at similar gestational ages.

Table 1: Comparison of preeclampsia patients with and without antiphospholipid syndrome

		APS (n=8 patients)	non-APS (n=29 patients)	p
Demographics				
Age*		29.8 ± 4.6	30.6 ± 2.0	0.72
BMI*		31.7 ± 2.4	31.3 ± 2.9	0.89
Race	White	8 (100%)	17 (58.6%)	**0.03**
	Black	0 (0)	7 (24.1%)	0.12
	Other	0 (0)	5 (17.2%)	0.21
Past Medical History				
Hypertension		1 (12.5%)	5 (17.2%)	0.75
APS[1]		3 (37.5%)	0	**0.001**
SLE[2]		4 (50%)	3 (10%)	**0.01**
Preeclampsia		3 (37.5%)	7 (24.1%)	0.45
Current Preeclampsia Episode				
Severity	Severe	8 (100%)	25 (86%)	0.27
	HELLP[3**]	6 (75.0%)	6 (20.7%)	**0.004**
Admission BP*	Systolic (mmHg)	154.1 ± 16.4	154.5 ± 10.1	0.98
	Diastolic (mmHg)	91.4 ± 7.1	95.0 ± 5.9	0.59
Liver*	Peak ALT (U/L)	648.1 ± 667.7	146 ± 105.1	**0.02**
	Peak AST (U/L)	749.9 ± 710.1	193.8 ± 142.4	**0.03**
Platelet nadir (1000 platelets/uL)		81 ± 36	149 ± 25	**0.02**
Peak protein/creatinine ratio*		0.92 ± 0.86	8.3 ± 8.0	0.36
Gestational age (weeks)*		27.3 ± 6.1	29.7 ± 2.1	0.32
Intrauterine growth restriction		5 (62.5%)	10 (34.5%)	0.15
Infant mortality	IUFD[4]	2 (25.0%)	10 (34.5%)	0.61
	Infant death	2 (25.0%)	6 (20.7%)	0.79

[1]Antiphospholipid syndrome

[2]Systemic Lupus Erythematosus

[3]Hemolysis, Elevated Liver Enzymes, and Low Platelets

[4]Intrauterine fetal death

* mean ± SD

** Partial and Complete HELLP

Conclusion: As compared with preeclampsia in the general population, APS-associated preeclampsia has a distinct clinical phenotype, more often presenting in association with HELLP. If verified by other studies, these clinical differences suggest the possibility that distinct disease mechanisms underlie APS-associated preeclampsia.

Disclosure: S. Cheemalavagu, None; **B. Wallace**, None; **W. Marder**, None; **J. Knight**, None; **A. Vreede**, None.

Abstract Number: 0145

Development of New International Classification Criteria for Antiphospholipid Syndrome: Phase II Results

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Antiphospholipid Syndrome Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: An international multi-disciplinary effort is underway to develop rigorous, new, consensus- and evidence-based classification criteria to identify patients with high likelihood of Antiphospholipid Syndrome (APS) for research purposes. The methodological approach includes four phases: item generation (I); item reduction (II); item weighting and threshold identification (III); and criteria refinement and validation (IV). Phase II aimed to reduce items generated in Phase I to approximately 30 items considered most important for distinguishing APS from other conditions. We previously reported the initial item reduction results reducing 261 Phase I items to 64 high specificity items *(Barbhaiya et al., Arthritis Rheumatol. 2018; 70 [suppl 10])*; here we report overall Phase II results.

Methods: We surveyed the APS Classification steering committee by asking members to rank the 64 previously identified items, using a Likert scale (-5 to +5), based on how specifically each item differentiates APS from other similar conditions (survey A). We ranked each item by mean (+SD) survey score and grouped highest scoring items into independent logical domains (Table). During a face-to-face steering committee meeting, we eliminated low specificity items (score < 1); items overlapping or describing similar concepts were combined. We used nominal group technique (NGT) for problem identification, solution generation, and decision-making via teleconferences to further reduce to approximately 30 items. To more precisely define, cluster, and organize items, we formed domain subcommittees to review literature and come to consensus on the definition, reliability, and precision of each potential criterion. Lastly, we surveyed the steering committee to assess proposed entry criteria and the role of provoking risk factors for macrovascular domain outcomes (survey B).

Results: Mean scores of survey A responses (n: 20) ranged between -1.05 to 4.79. Literature reviews, NGT, and subcommittee discussions reduced 64 items to 27 candidate criteria, which we organized into six independent domains (Table). Survey A results also demonstrated different weights for macrovascular domain outcomes with or without "provoking" thrombosis risk factors. Based on survey B results, we eliminated provoking risk factors with low specificity and, depending on the type of macrovascular domain outcome, 72-89% of the committee members agreed with proposed risk factors and definitions. Following a steering committee consensus to use entry criteria to identify the relevant patient population to whom the classification criteria would be applied, 84% voted in survey B in favor of a time restriction between a positive antiphospholipid antibody test and clinical event as an entry criterion for classification.

Conclusion: Twenty-seven candidate criteria for APS classification were retained and organized into six independent domains using Phase II item reduction techniques. In the next phase, these proposed candidate criteria will be used for real-world case collection and further refined, organized, and weighted so that a preliminary threshold for APS classification can be determined.

Table: Candidate Relative Criteria Based on Phase II of New APS Classification Criteria Development
Candidate Relative Criteria (Laboratory)

• **Domain 1A: Antiphospholipid Antibody Testing- Coagulation-based Functional Assays**
  ○ Lupus Anticoagulant Test
• **Domain 1B: Antiphospholipid Antibody Testing- Solid Phase Assays**
  ○ Anticardiolipin Antibody IgG, Anticardiolipin Antibody IgM
  ○ Anti-β_2-glycoprotein-1 IgG, Anti-β_2-glycoprotein-1 IgM

Candidate Relative Criteria (Clinical)

• **Domain 2: Macrovascular**
  ○ Superficial Vein Thrombosis, Venous Thromboembolism, Arterial Thrombosis, Transient Ischemic Attack
• **Domain 3: Microvascular**
  ○ Livedo Racemosa, Livedoid Vasculopathy, Adrenal Hemorrhage or Plexus Thrombosis, Acute Ischemic Encephalopathy, Cardiac Microvascular Disease, Pulmonary Hemorrhage, Acute aPL Nephropathy, Chronic aPL Nephropathy
• **Domain 4: Obstetric**
  ○ Pregnancy Loss <10w of Gestation, Fetal Death Between 10w to <16w of Gestation, Fetal Death Between 16w to 34w of Gestation, Pre-eclampsia with Severe Features <34w of Gestation, Placental Insufficiency with Severe Features <34w of Gestation
• **Domain 5: Cardiac Valve Disease**
  ○ Non-infectious Valve Vegetation, Thickening
• **Domain 6: Hematologic**:
  ○ Platelet count <20 x 10^9 per liter, Platelet count 20-130 x 10^9 per liter, Platelet count 131-150 x 10^9 per liter

Acknowledgement: The project is supported by ACR/EULAR

Acknowledgement: This project is supported by ACR/EULARACR TABLE

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Abstract Number: 0146

Simulated Rheumatology Clinic: Bridging Basic Science and Clinical Application

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Traditional medical school curricula divided the basic sciences from clinical rotations using a compartmentalized approach, though the need for curricular integration in the preclinical years is now well recognized.[1] Simulation offers learners opportunities for active engagement with basic science knowledge in relevant clinical contexts, thereby enhancing knowledge acquisition.[2] We developed a simulated clinic experience for preclinical medical students to reinforce learning content presented in the rheumatology course.

Methods: Students were divided into groups of 3-4 learners to rotate through a series of 3, 20-minute standardized patient (SP) cases during which they were tasked with performing a targeted history and physical exam. Small groups then had 10 minutes to discuss their findings to develop a differential diagnosis and determine next best step in diagnostic testing for each case. The activity concluded with a large-group debrief with a content expert. Learners' evaluation of the activity was assessed through a voluntary, anonymous online survey.

Results: Twenty-five (18%) learners responded to the survey. Eighty-eight percent (22/25) of respondents found the activity extremely or quite relevant to their role as a future physician. All respondents felt the small-group format and the pace and duration of the learning activity were appropriate. Greater than 90% of respondents found the activity to be extremely or quite effective for reviewing and applying learning content from the rheumatology course, practicing how to approach specific chief complaints, practicing history taking skills, practicing physical exam skills, practicing differential diagnosis formation skills, and practicing creating a diagnostic plan for the cases. Eighty-four percent (21/25) of respondents felt the large group debrief was effective. Twenty out of 24 respondents rated the activity's overall effectiveness as ≥ 8 out of 10.

Conclusion: The simulated rheumatology clinic activity was well received by learners, who rated it as effective for reinforcing and applying concepts discussed in the rheumatology basic science curriculum. Simulation-based activities structured like this one can provide opportunities for clinical applications in other domains of the pre-clinical curriculum. Future directions include evaluating higher-order learning outcomes beyond learner perception.

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Disclosure: R. Wolfe, None; **D. Williams**, Certus Critical Care Inc, 4; **J. Jackson**, None.

Abstract Number: 0147

A Qualitative Study of Factors That Influence Interest in a Career in Pediatric Rheumatology

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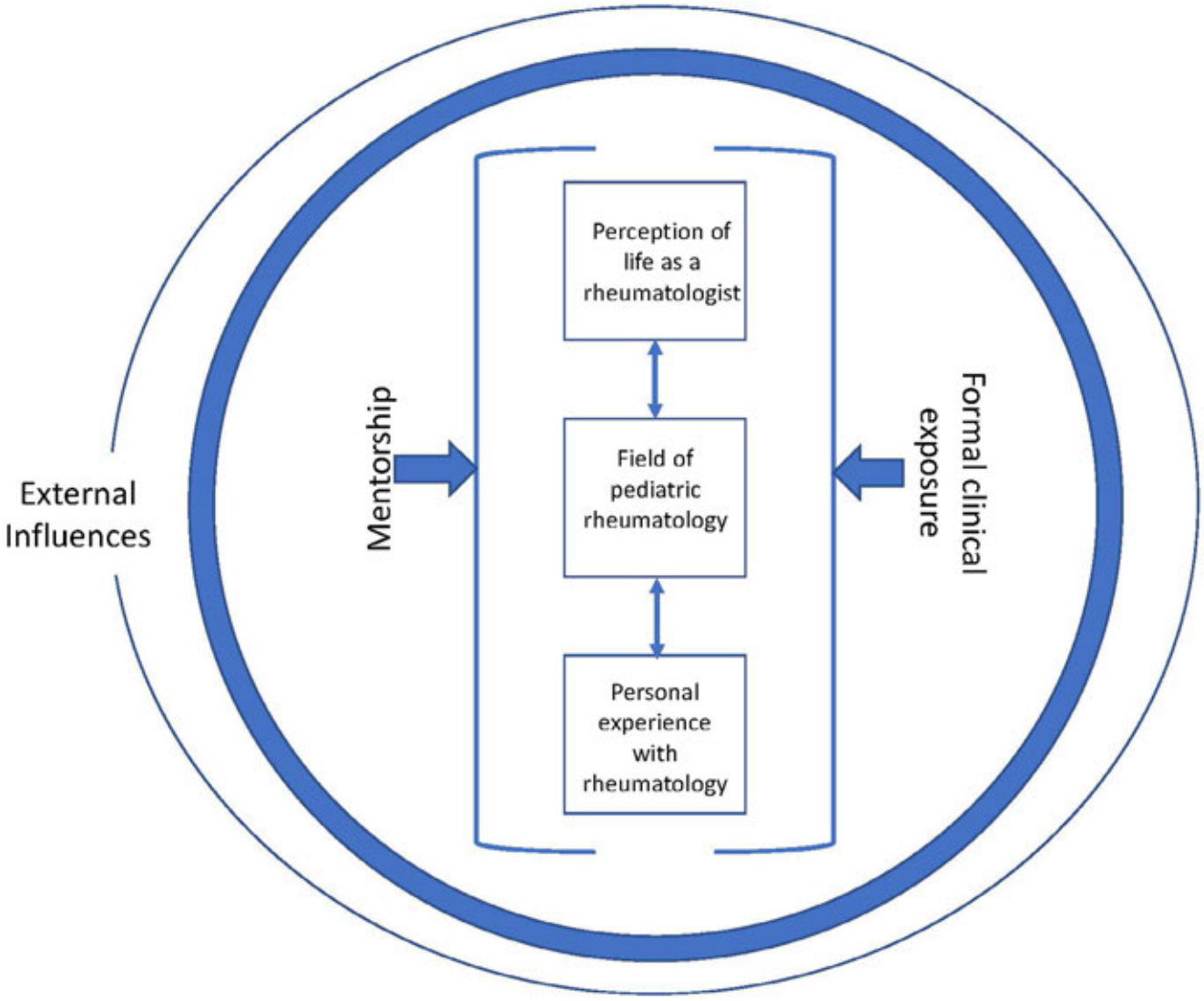
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The American Academy of Pediatrics estimates that one-quarter of children with rheumatic disease live over 80 miles from the nearest pediatric rheumatologist. It has been suggested that half of these children receive care from an adult provider. Contributing to this mismatch between children with rheumatic disease and pediatric rheumatology providers is a relative dearth of pediatric residents who choose to enter pediatric rheumatology fellowship. From 2013-2017, between 28-50% of fellowship spots went unfilled each year. Little is known about the factors that influence pediatrics residents to consider a career in rheumatology.

Methods: Semi-structured interviews were conducted with 15 pediatrics residents who were accepted to the ACR Pediatrics Residents Program, which aims to expose pediatrics residents to the ACR Annual Scientific Meeting. Residents were re-interviewed after making their final specialty decision to understand the factors most influential in their decision. Interviews were transcribed and coded. Codes pertaining to influential factors were organized into an explanatory model.

Results: Most residents expressed their interest in pediatric rheumatology growing with formal clinical exposure during residency. Few residents had exposure to this field as medical students. Some residents reported only considering pediatric rheumatology as a career after completing a rotation during residency. Residents stated the evolving research, immunopathology, complex diseases, and long-term patient disease management were desirable aspects of the field. Some residents stated positively viewing pediatric rheumatology as focused on educating and teaching trainees and reported a collegial and friendly atmosphere. Some residents had mentors in pediatric rheumatology and explored research and career opportunities. Few residents mentioned salary, geography, perception of the field by others, or geographic limitations as barriers to considering pediatric rheumatology as a career.

Conclusion: Residents cite a variety of factors influencing their decision to consider pediatric rheumatology as a career. We organized these factors into a model with major influencing factors of 1) perceptions of life as a rheuma-



Explanatory model for influential factors impacting interest in career in pediatric rheumatology

tologist, 2) qualities inherent to the field such as long-term patient relationships and complex immunopathology and 3) personal experience with rheumatology being modified by formal clinical exposure and mentorship, with external influences having a peripheral, but often important, role. Pediatric rheumatology has aspects that are desirable to residents such as its culture, patient-family relationships, and disease processes. Facilitating exposure to pediatric rheumatology during medical school or earlier in residency may help facilitate interest in the field.Model for ACR abstract Explanatory model for influential factors impacting interest in career in pediatric rheumatology

Disclosure: N. Pandya, None; **C. Sholevar**, None; **R. Frasso**, None; **D. Balmer**, None; **J. Mehta**, None.

Abstract Number: 0148

The Combat Rheumatologist: Long Term Professional Outcomes of Graduates from a Tri-Service Military Rheumatology Fellowship Program

Caleb Anderson,[1] Wayne Bailey,[2] and Jess Edison[1], [1]Walter Reed National Military Medical Center, Bethesda, MD, [2]Fort Belvoir Community Hospital/U.S. Army, Bethesda, MD

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The Walter Reed Army / Walter Reed National Military Medical Center National Capital Consortium (WRNMMC) Rheumatology fellowship program has been in existence since 1973, and in June 2015 graduated its 100th fellow. The military rheumatologist has a unique role and is responsible for leadership as well as rheumatology practice. In an effort to identify the strengths and gaps in the training required of our military rheumatologists, we studied the long-term professional outcome of our graduates. Specifically, we evaluated our graduates' contribution to the advancement of knowledge in the field of rheumatology and medicine, as well as leadership positions held. In an effort to evaluate our graduates' professional military development and contribution to the Defense Health Agency's goal of a medically ready force, we also queried number of deployments, operational tours, and Professional Military Education (PME) participation.

Methods: Email addresses for all graduates of the Walter Reed Army / Walter Reed National Military Medical Center National Capital Consortium Rheumatology fellowship program from 1976 through 2015 were obtained from publicly available registries such as the American College of Rheumatology Annual Directory. An email request was sent to graduates requesting a copy of their curriculum vitae (CV). If no response was received, up to three monthly emails were sent. Data was analyzed for respondents' rank, board certification, hospital committees, professional societies, awards, peer reviewed publications, invited lectures, operational tours, deployments, and PME courses.

Results: Forty-six of 100 contacted graduated fellows provided their CV for review. The highest percentage of respondents were graduates between 2003 and 2015 (26/30). This was the interval chosen for analysis. Twenty one (81%) of respondents were still active duty at the time the survey was taken. The 26 responding graduates had given 415 lectures (16 per graduate), authored 95 peer reviewed publications (3.7 per graduate), and had served on a cumulative total of 95 committees. Seventeen of 26 had been rheumatology service chiefs, four served as assistant department chief, and eighteen (69%) were affiliated with a medical school. Fourteen of the respondents had been deployed with four graduates serving in an operational billet without deployment. Of the 18 Army respondents, three

attended Command and General Staff Intermediate Level Education, six attended Captain's Career Course, two attended Tactical Combat Medical Course, and two attended Brigade Surgeon Course.

Conclusion: Our graduates of the WRNMMC rheumatology fellowship have excelled in medical education and professional development. A gap in completion of PME was noted in the study and led to incorporation of a three week course during fellowship. Overall, scholarly activity, medical education, leadership, and contribution to medical readiness through deployments and operational positions held are among the most consistent findings within the graduates over the previous decade.

Disclosure: C. Anderson, None; **W. Bailey**, None; **J. Edison**, None.

Abstract Number: 0149

Teaching Rare Diseases Through Role Play: Results of an Experimental Workshop About Raynaud Phenomenon

Sébastien Sanges,[1] Sandrine Morell-Dubois,[2] Meryem-Maud Farhat,[3] Morgane Assaraf,[3] Marc LAMBERT,[4] Vincent Sobanski,[3] David Launay,[3] and Eric Hachulla[5], [1]CHRU Lille, Lille, France, [2]Department of Internal Medicine and Clinical Immunology, CHU Lille, University of Lille, Lille, France, [3]CHU Lille, Lille, France, [4]Lille University Hospital, Lille, France, [5]Dept. of Internal Medicine and Clinical Immunology, Hôpital Claude Huriez, University of Lille, Lille, France, Lille, France

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic autoimmune diseases are mostly taught through theoretical lectures, which do not allow for the acquisition of physical examination skills and semiologic confrontation. We report herein the results of a pilot experiment using role-play to teach how to manage patients with Raynaud phenomenon (RP).

Methods: We developed a workshop that consisted of two 30-minute OSCE (Objective and Structured Clinical Examination) stations. Students were divided into groups of 4 to 5 persons. On each station, 2 students were actors and 2 were observers. After a short briefing, students played a 15-minute scenario and then had a 15-minute debriefing.

The first station simulated the case of a 26-year old woman referred for suspected RP. Students were instructed to perform clinical history taking and physical examination of the patient, formulated relevant diagnosis hypotheses and prescribe any additional necessary exams. Students had to suspect the diagnosis of idiopathic RP. The simulated patient was played by a trained facilitator with expertise on RP.

The second station simulated the case of a 56-year-old woman referred for RP complicated by digital ulcers. Students received the same instructions as before. They had to suspect the diagnosis of systemic sclerosis. The patient role was held by a real patient with systemic sclerosis, followed by the physician who was supervising the station, who had received prior training and who agreed to participate in this training.

At the end of the workshop, the students had to complete a satisfaction questionnaire.

Results: A total of 21 students participated in the workshop and 17 completed the survey. The students were "very satisfied" (Likert 4/4) of this training in 94%. They considered this workshop "not very stressful" (Likert 2/4) and "very formative" (Likert 4/4) in 71%, but "a little short" (Likert 2/4) in 88%. After taking this training, all students felt "a little"

(Likert 3/4, 24%) or “much more comfortable” (Likert 4/4, 76%) to manage patients with idiopathic RP; and “a little” (Likert 3/4, 65%) or “much more comfortable” (Likert 4/4, 35%) to manage patients with systemic sclerosis. All would recommend this workshop to other students.

When asked about the strengths of this training, the students mentioned the benefits of being put in an immersive situation, which allowed for a better acquisition of practical skills (especially physical examination) and a more interactive exchange with teachers; as well as the confrontation with a real patient, which allowed for a better retention of semiologic findings and associated a relational component to this experience. The main weak points reported were its short duration and the stress induced by being observed during the simulation.

Conclusion: This workshop suggests the interest and feasibility on a small group of students of a rare diseases awareness workshop using role-play. The evaluation of its pedagogical efficiency and its generalization on large student promotions are being considered.

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Abstract Number: 0150

Comparison of Debate vs. Lecture to Teach Medical Students Pediatric Rheumatology

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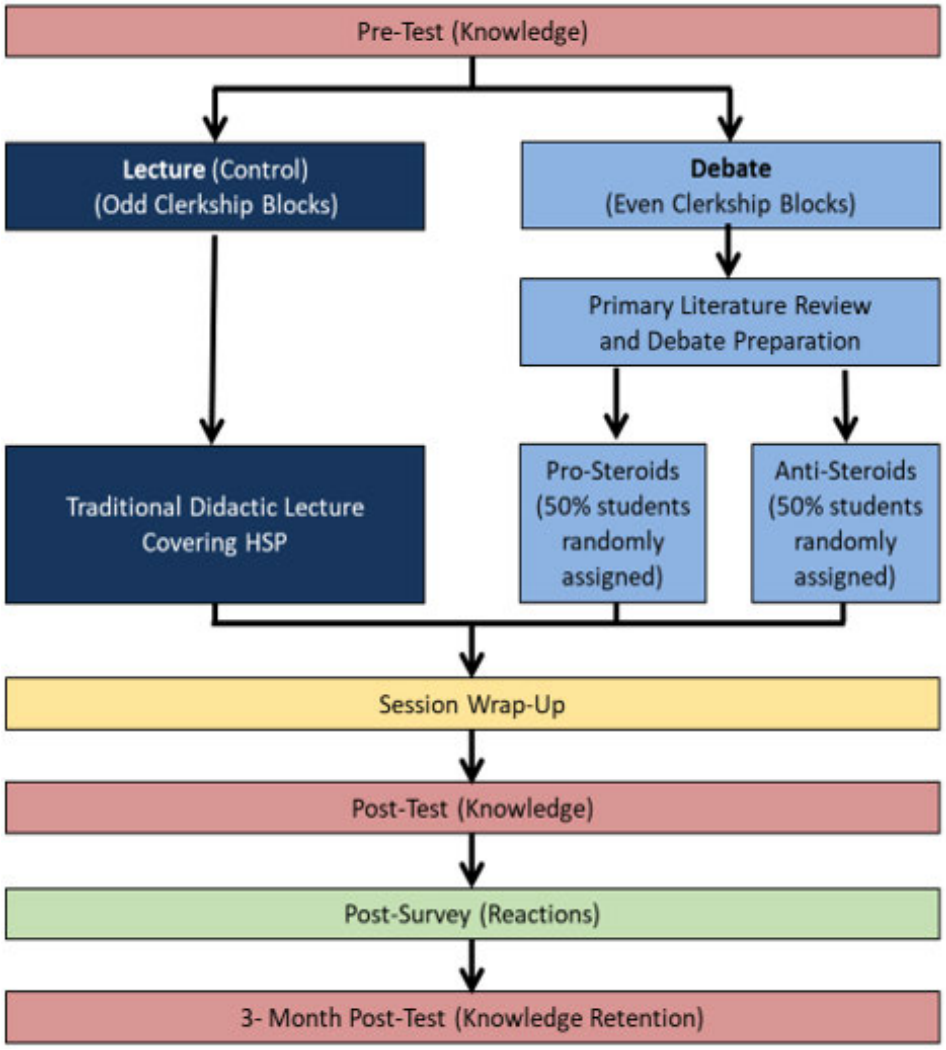
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Medical students at Vanderbilt receive approximately 25 hours of didactic teaching during their pediatric clerkship. Debate format educational sessions employ active learning principles allowing students opportunities to critically evaluate and articulate evidence to support claims. The aim of our study was for students to participate in a debate of two treatment options for Henoch-Schönlein Purpura (HScP), and evaluate learning outcomes, student engagement, and satisfaction with debate compared to traditional lecture.

Methods: We compared medical students on their pediatrics clerkship participating in a debate to a control group receiving a traditional lecture. Debate group students received a case of a patient with HScP and abdominal pain a week prior to the session. Half of the students were randomly assigned to argue in favor of treatment with steroids and half against steroid treatment. Students were asked to prepare by performing a review of primary literature and then met during their pediatrics clerkship to participate in the debate. The control group received a traditional lecture about HScP. Both groups received same wrap-up presentation reinforcing key concepts. Students completed an identical multiple-choice pre-test before and post-test after the session and a follow-up post-test three months later to assess knowledge retention. Surveys immediately following and three months after the session assessed satisfaction with and the efficacy of the session in promoting active learning and clinically relevant skills.

Results: Both groups showed improvement between the pre- and post-tests, and there was no significant difference in the groups’ post-test scores (n=48, p=0.06). Retention of information on the three-month post-test was not significantly



Study Design

different between the two groups (n=18, p=0.61). More students in the debate group agreed or strongly agreed that they practiced researching a clinical question (n=21 and 27, 81.5% vs 44.4% respectively) and articulating their opinion (77.8% vs 37.0% respectively). More students in the debate group agreed or strongly agreed that they used the research skills they used in this session in the direct care of a patient on the three-month follow up survey (n=8 and 10, 87.5% vs 50% respectively). Students in the lecture group who reported higher satisfaction or increased engagement scored significantly better on the initial post-test (n=27, p=0.004 and p=0.016, respectively). Satisfaction and engagement did not correlate with initial post-test scores in the debate group (n=21, p=0.46 and p=0.29 respectively).

Conclusion: Students learned core knowledge about HScP in both groups as evidenced by similarly improved scores on immediate and three-month post-tests. Participation in the debate allowed students to practice critically appraising literature and articulating their opinion. Debate students' immediate post-test scores were less correlated with their perception of engagement or satisfaction with the session. Future sessions will include a debrief session to help students transfer critical appraisal skills to clinical practice. We are interested in utilizing debates to study tolerance of ambiguity in pediatric rheumatology fellows.

Disclosure: J. Dingle, None; **T. Graham**, None; **T. Crook**, None; **M. Neeley**, None; **M. Davidson**, None; **A. Fleming**, None.

Abstract Number: 0151

Implementation of Recommendations for Prevention of Glucocorticosteroid-Induced Osteoporosis in Hospitalized Patients

Tal Gazitt,[1] Muna Elias,[1] Joy Feld,[1] Idit Lavi,[1] Amir Haddad,[1] Rema Bishara-Garzuzi,[1] Muhanad Abu Elhija,[1] Adi Kibari,[1] and Devy Zisman[2], [1]Carmel Hospital, Haifa, Israel, [2]Carmel Hospital and Ruth and Bruce Rappaport Faculty of Medicine, Technion, Israel, Haifa, Israel

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticosteroid-induced osteoporosis (GIO) is the most common cause of secondary osteoporosis but is under-diagnosed and under-treated. Most professional guidelines recommend as a first step calcium and vitamin D (Ca/VitD) supplementation for patients treated with prednisone ≥ 5-7.5 mg daily or equivalent for ≥ 1-3 months.

Rheumatology inpatient consultations are routinely given by our rheumatology unit with emphasis on smooth transition to outpatient care. The study objectives were to examine the real-life implementation of recommendations for Ca/VitD supplementation in patients anticipated to receive long-term corticosteroid treatment and to assess the impact of standardized academic lecture on guideline implementation.

Methods: All rheumatology inpatient consultations given in 4 internal medicine wards in an academic community-based hospital in 2018 were included in the study. The hospital inpatient database was queried by two independent rheumatologists regarding the total number and content of rheumatology consult notes, doses and indications for steroid treatment where applicable, diagnostic codes, and discharge medications including Ca/VitD for patients prescribed ≥ 7.5 mg/day of prednisone with anticipated treatment for ≥ 1 month. Patients who died during hospitalization and patients hospitalized with diagnostic code of sarcoidosis were excluded from this analysis.

During the month of July 2018, standardized academic lectures on GIO prevention were given by rheumatologists in 3 of the 4 internal medicine wards. The fourth internal medicine ward served as control. The percentage of patients for whom Ca/VitD was both recommended and prescribed and the impact of academic lecture on discharge prescriptions was calculated and compared between the 6-month period before and after the instructional intervention and to the corresponding data in the control internal medicine ward. Variables were compared by Chi Square test or Student's t-test, as appropriate. All tests were 2-sided; $p < 0.05$ was considered statistically significant.

Results: Rheumatology consultations were given to 559 inpatients in 2018, 101 of whom had steroid treatment and should have been treated with Ca/VitD. The mean age of the patients was 64.6±16.1 years, 59.4% female. The main rheumatologic indications for corticosteroid treatment were vasculitis (26.7%), connective tissue disease (22.8%), rheumatoid arthritis (18.8%), and crystal-induced arthropathy (14.9%). In 79.2% of cases, rheumatology consultations specifically recommended Ca/VitD, but only 44.3% of patients were discharged on supplementation. No statistically significant differences were found among the four wards. GIO prevention lecture had no impact on discharge prescriptions.

Conclusion: Real-life implementation of GIO prevention guidelines is poor in internal medicine wards. A collaborative learning program not limited only to academic lectures is recommended as measure of intervention to increase GIO awareness and prevention especially among internal medicine staff.

Disclosure: T. Gazitt, None; **M. Elias**, None; **J. Feld**, None; **I. Lavi**, None; **A. Haddad**, None; **R. Bishara-Garzuzi**, None; **M. Abu Elhija**, None; **A. Kibari**, None; **D. Zisman**, Pfizer, 5, 8.

Abstract Number: 0152

A Shoulder to Lean On: Differences in Shoulder Examinations Between Rheumatology Educators and Fellows

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SESSION INFORMATION
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Background/Purpose: The maneuvers to include in a comprehensive shoulder exam are debatable. For rheumatology fellows, rheumatology fellowship program directors (PD) serve as models of competency in performing the musculoskeletal exam. In this pilot study, we investigated exam techniques used by PDs in comparison to rheumatology fellows in their first year of training.

Methods: We recruited 6 rheumatology clinic patients with known causes of shoulder pain to undergo physical exam by 3 rheumatology PDs (32-36 years post medical school), and 3 rheumatology fellows in the first 3 months of training (3-4 years post medical school). Exams were performed in a simulation center with video recording. Exam procedure was not standardized beforehand, but fellows had formal training in shoulder exam both before and during fellowship. Overall diagnosis was noted by participants after each exam. Ultrasound imaging on the day of the exercise and clinical information were used to establish a "gold standard" (GS) diagnosis for each patient.

Videos were reviewed by a 4th PD using a standardized data extraction tool (27 exam techniques) based on a previously published standardized observed clinical exam (OSCE) of the shoulder. Exam findings not included in this tool, as well as total exam duration per room were also recorded.

Table I. Comparison of Program Directors and Trainees in Various Aspects of the Shoulder Exam

	Program Directors	Trainees	P value
% of time arriving at previously established clinical diagnosis	61	33	0.06
Mean % of prespecified exam elements performed*	55	54	0.54
Mean % of neck exam maneuvers performed	58	45	0.03
Mean % of technique measures performed+	75	26	1.7×10^{-11}
Mean time per room	4 min 53 sec.	6 min 24 sec	0.00014

* standardized data extraction tool based on a previously published (OSCE) of the shoulder identifying 27 examination techniques

+ exam technique measures include bilateral palpation, bilateral resisted motion testing, elbows adduction during resisted external rotation, and keeping one of the examiner's hands on the patient's shoulder during passive range of motion determination.

Exam maneuvers employed for each patient, technical methodology of the maneuvers, agreement with GS diagnosis, and duration of each exam were compared between the two groups using the student-t test. Four measures of exam technique assessed for each encounter included bilateral palpation, bilateral resisted motion testing, elbows adducted during resisted external rotation, and keeping one of the examiner's hands on the patient's shoulder during passive range of motion testing.

Results: GS diagnoses were: biceps tendonitis (x2), acromioclavicular joint arthritis, adhesive capsulitis, subacromial bursitis, and fibromyalgia. PDs agreed with the GS diagnosis 61% of the time compared to 33% for fellows. Five exam elements not described in the OSCE tool were noted, all involving the neck.

There was no significant difference in the completed number of prespecified 27 exam elements between PDs and fellows but PDs completed a significantly greater number of cervical spine elements and measures of exam technique then fellows, and spent less time on the exam (Table 1). The Hawkins, Neer, belly press, and horn blower's tests were never performed by any of the PDs.

Conclusion: Exam technique distinguished PDs from fellows most clearly, as did greater attention to exam of the neck for evaluation of shoulder pain. PDs and fellows performed just over half of the exam elements previously described in a shoulder OSCE, and this number did not distinguish the two groups. These results suggest that more emphasis should be placed on exam technique assessment during OSCE examinations in place of performing a greater number of maneuvers.

Disclosure: L. Martirossian, None; **R. Kalish**, None; **K. O'Rourke**, None; **S. Panginikkod**, None; **E. Kissin**, None.

Abstract Number: 0153

Palliative Care Curriculum in Rheumatology: Teaching Serious Illness Conversations

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Background/Purpose: Palliative care is a specialty that focuses on holistic care, promoting quality of life, and providing an extra layer of support for patients and families alongside traditional medical treatment. While these principles are highly relevant to many patients seen by rheumatologists, palliative care education for rheumatologists has been limited. Our aim was to assess the baseline needs of rheumatologists in our division, present an educational program, and identify opportunities for adaptation and expansion of palliative care education.

Methods: We developed an educational program collaboratively with palliative care that was presented to Rheumatology faculty and fellows at the University of Pennsylvania in the fall of 2018. A needs assessment survey was developed based on well-known palliative care concepts to assess baseline skills and attitudes. A two-hour interactive session was held based on the established and validated "Serious Illness Care Program" created by Ariadne Labs, adapting content to rheumatology. This program includes teaching the "Serious Illness Conversation Guide" – a scripted set of questions to guide clinicians through a conversation that includes 1) setting up the conversation, 2) assessing patient understanding, 3) sharing information, 4) exploring patient goals, fears, strengths, wishes, and 5) closing. The session included a

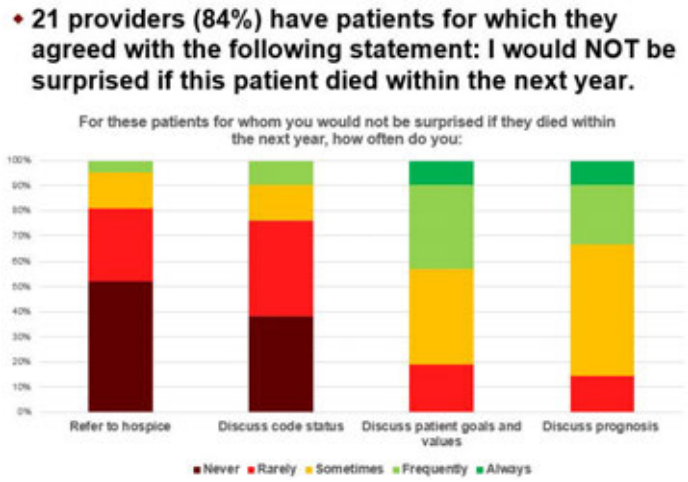

Figure 1.

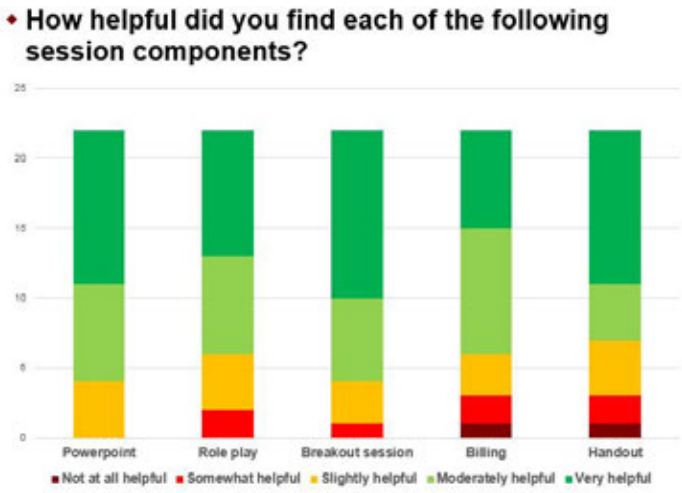

Figure 2.

demonstration of how to utilize the Conversation Guide, break-out sessions to practice conversations led by palliative care specialists using rheumatology-specific cases, and a debrief. Two champions of the program were identified who trialed the guide in clinic over the following four months. All providers received a follow-up survey to evaluate the program.

Results: The needs assessment survey had 25/30 responses. No providers had received previous rheumatology-specific palliative care training and 36% had never received any palliative care training. 21 (84%) reported seeing patients for which they would not be surprised if the patient died within the next year. Few providers referred to hospice or discussed code status, and a minority regularly discussed patient goals/values or prognosis for these patients (Figure 1). Time and uncertainty in prognostication were the most significant barriers to these conversations. The two-hour session was attended by 27 providers. In the follow-up survey, >80% found the program to be interesting, appropriate in length, and appropriate in scope. Each component of the program was favorably rated (Figure 2). Although only two providers were designated as “champions,” 6 providers reported using the Conversation Guide in clinic. Time was the major barrier to using the guide.

Conclusion: This innovation was among the first to adapt a validated palliative care training program to a rheumatology division. The program was highly rated and led to use of the Conversation Guide in clinic. Further adaption of the Conversation Guide to rheumatology specific needs, scheduling changes to allow time for serious illness conversations in clinic, and assessment of benefits to patients are planned.Figure 1.

Disclosure: M. Karpoff, None; **M. George**, AbbVie, 5, Bristol Myers Squibb, 2, Bristol-Myers Squibb, 2; **L. Dingfield**, None.

Abstract Number: 0154

Enhancing Medicine Trainees' Exposure to Gout Diagnosis and Management Through an Interprofessional Approach in the Primary Care Setting

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Background/Purpose: Gout is common in primary care, though patients often have inadequate control or are referred to specialists for evaluation and management. This may be due to limited provider time during routine clinic visits, but may also reflect insufficient preparation of primary care providers (PCPs) in health professions education (HPE). Although excellent clinical training in gout is often provided in rheumatology clinics, learners may not effectively translate the lessons learned in the subspecialty context to primary care.

To increase contact between rheumatologist clinical educators and internal medicine (IM) trainees and to strengthen interprofessional and interdisciplinary collaboration in a new teaching and learning environment, a Primary Care Gout Clinic (PC Gout) was established at a Veterans Affairs (VA) Medical Center affiliated with a large academic institution. The primary purpose was to increase IM trainees' exposure to the appropriate evaluation and management of gout; a secondary goal was to improve patient access to specialty services while aligning with current medical home models.

Methods: The PC Gout clinic was initiated in September 2017, by a rheumatologist with primary care support, and a dedicated pharmacist with advanced training in primary care. The clinic is held one half day per week, with trainees (mainly IM) and HPE students regularly assigned. Patients are referred to the clinic from other providers in primary care, the emergency department, inpatient medicine, and other services. Clinic experiences emphasize the importance of treating to uric acid targets, understanding the interactions of gout and urate-lowering therapies (ULTs) with common comorbidities such as chronic kidney disease and congestive heart failure, and the value of care delivery using a model of interprofessional teamwork.

Results: One hundred seventy-two visits have been completed since September 21st, 2017, representing 80 unique patients (77 male, 3 female). Demographics, referral source, and trainee type involved in the encounter are shown in Table 1.

Mean serum uric acid (sUA) level at initial visit was 7.6 mg/dL (0.9 to 13.1). To date, 53 patients (66%) have at least one additional measurement; mean post-treatment sUA is 5.8 mg/dL (2.9-10.5). Figure 1 shows the individual-matched changes in sUA for these patients.

Conclusion: The PC Gout Clinic represents an innovative method of connecting rheumatologist clinical educators with HPE students and trainees and creates a new context for teaching and learning. It embeds the rheumatologist

Table 1 – Patient Demographic and Clinic Information	
Total Encounters	172
Unique Patients	80
	Average (Range)
Patient Age	67 (40 – 98)
Number of clinic visits per patient	2.2 (1 – 10)
Referral Source	N (% of total)
Primary Care	51 (64)
General Rheumatology	18 (23)
Emergency Room	6 (8)
Inpatient Services	4 (5)
Physical Medicine & Rehab	1 (1)
Trainee Type per Encounter	N (% of 172)
Internal Medicine Resident	158 (92)
Medical Student	4 (2)
Physician Assistant Student	3 (2)
N/A (Attending only)	7 (4)

Table 1. Comparing PGY-1 post-test to pre-test scores

and pharmacist—both of whom bring content expertise—within the primary care environment and enhances clinical teaching by increasing specialists' awareness of learners' perspectives. In addition, the PC Gout Clinic also improves patient access to appropriate care and helps prioritize specialty referrals.

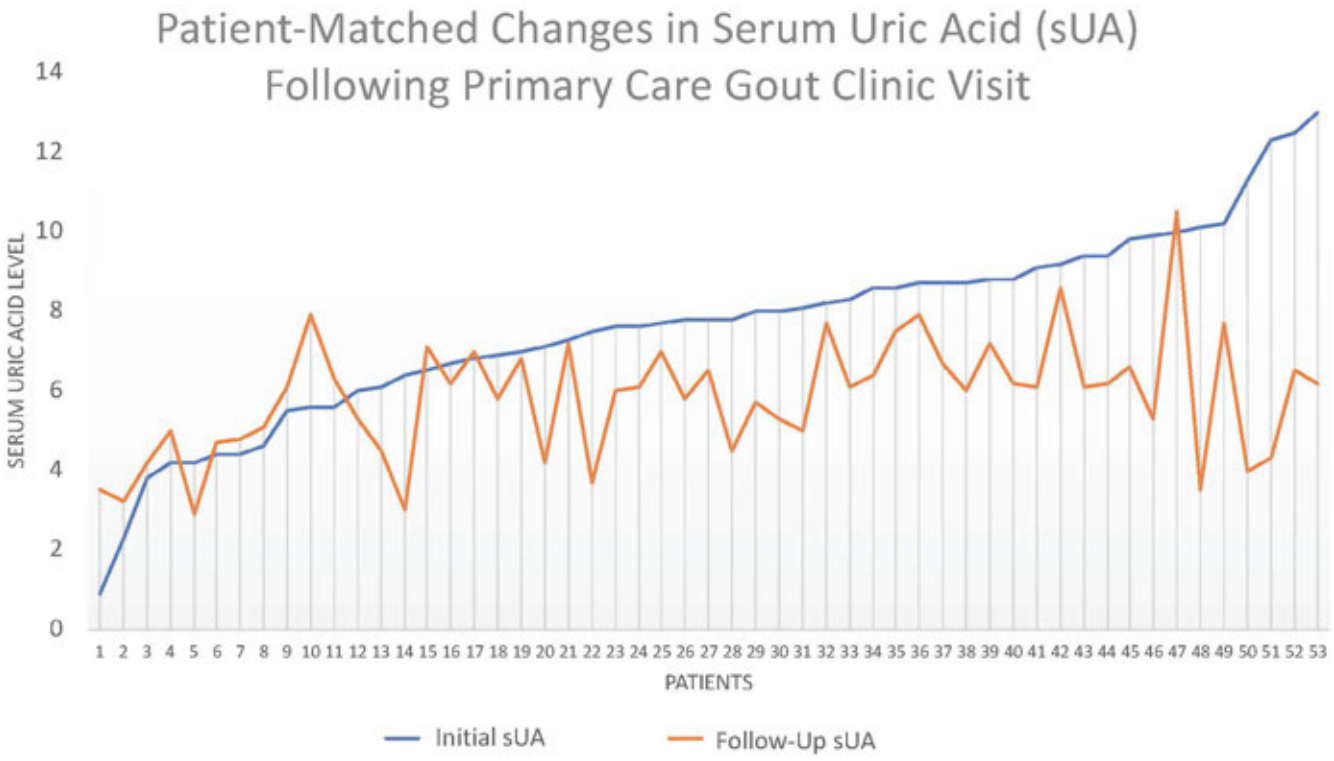

Figure 1

Disclosure: N. Lebedoff, None; **A. Barker**, None; **C. Koening**, None; **C. Gallop**, None; **K. Starman**, None; **M. Battistone**, None.

Abstract Number: 0155

A Prospective, Unblinded, Non-randomized Pilot Study Examining the Effect of a Musculoskeletal Immersion Curriculum for First Year Internal Medicine Residents

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SESSION INFORMATION
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Background/Purpose: Musculoskeletal (MSK) disorders are one of the most common clinic visit complaints. Prior studies evaluating graduate medical training of rheumatology and MSK medicine have shown that a knowledge gap exists in the United States. This gap in knowledge could lead to a delay in medical care and increased healthcare costs. In an attempt to bridge this gap, we designed an introductory curriculum for PGY-1 internal medicine (IM) residents during their first months of residency, aimed at improving knowledge of MSK and rheumatologic conditions, as well as providing early exposure to rheumatology. Our purpose was to assess whether the use of these didactics

Test	Point Range	Mean Change (points)	p-value
Knowledge Exam	0-27	3.68	p<0.001
MSK Exam: Confidence of joint identification	1-5	1.09	p<0.001
MSK Exam: Confidence of assessing joint tenderness	1-5	1.18	p<0.001
MSK Exam: Confidence of assessing joint effusion	1-5	1.45	p<0.001
MSK Exam: Confidence of assessing strength	1-5	1.09	p<0.001
MSK Exam: Confidence of assessing range of motion	1-5	0.86	p<0.001
Rheumatology interest	1-5	0.36	p=0.572

Table 1. Comparing PGY-1 post-test to pre-test scores

Test	Point Range	Mean Difference (points)	p-value
Knowledge Exam	0-27	2.07	p=0.027
MSK Exam: Confidence of joint identification	1-5	0.21	p=0.563
MSK Exam: Confidence of assessing joint tenderness	1-5	0.93	p=0.008
MSK Exam: Confidence of assessing joint effusion	1-5	1.00	p=0.003
MSK Exam: Confidence of assessing strength	1-5	0.86	p=0.002
MSK Exam: Confidence of assessing range of motion	1-5	0.64	p=0.049
Rheumatology interest	1-5	0.29	p=0.390

Table 2. Comparing PGY-1 retention test to PGY-2 control test scores

would: 1) increase rheumatology medical knowledge, 2) result in retention of knowledge, 3) increase confidence of MSK exam skills, and 4) increase rheumatology career interest.

Methods: The study was conducted at Hennepin Healthcare. PGY-1 residents are required to participate in an immersion ambulatory rotation during one of their first three months of residency. We developed a curriculum focused on introductory rheumatology concepts, MSK medicine, and MSK exam that were integrated into their immersion month. We evaluated PGY-1 IM resident knowledge on three separate occasions via a voluntary online test: pre-intervention, post-intervention, and 1-3 months after completing their immersion block (retention test). The test included 27 questions on rheumatology and MSK knowledge, 5 questions on confidence in MSK exam, and one question regarding interest in rheumatology. PGY-2 residents were enrolled as the voluntary comparison control group and completed an identical test to the PGY-1 resident retention test. We provided small gift cards as compensation to increase voluntary

participation. Data was collected and stored on a secure cloud-based program, then analyzed using the student's t-test.

Results: All 22 PGY-1 residents completed the pre- and post-test. Approximately 64% of PGY-1 residents and 64% of PGY-2 residents completed the same retention test. The PGY-1 residents who participated in the rheumatology immersion didactics scored significantly higher on both their post-test and confidence in MSK exam scores (p=< 0.001). There was no significant difference between post-test scores and the retention exam score (p=0.435). The PGY-1 residents also scored significantly higher on their retention test compared to the PGY-2 control group (p=0.027). There was no statistical difference in rheumatology interest either before or after intervention in PGY-1 group or between PGY-1 and PGY-2 groups.

Conclusion: Our pilot study suggests that integrating rheumatology didactics early in residency results in immediate and long-term improvement in rheumatology knowledge and confidence in the MSK exam. The present deficit in rheumatology and MSK medical knowledge, combined with the growing frequency of these conditions in the primary care setting, highlights the importance finding methods to address this gap in knowledge. Our study demonstrates early education in rheumatology and MSK knowledge provides a possible cost-effective solution.

Disclosure: E. Miller, None; **L. Ngo**, None; **Z. Abou Zahr**, None; **C. Mahrer**, None; **R. Nasr**, None.

Abstract Number: 0156

The Impact of Spaced Education and Reciprocal Peer Teaching on Rheumatology Fellows' Long-term Recall from Core Curriculum

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Table 1: Engagement of Four Fellows Included in the "Rheuminder" Spaced Education Intervention

Rheuminder Topic	First Distribution			Second Distribution		
	Days since session*	Response rate (%)	Average correct (%)	Days since session**	Response rate (%)	Average correct (%)
Rheumadermatology	15	75%	67%	66	75%	83%
Innate Immunity & TLRs	8	100%	94%	55	50%	88%
SLE & the lung	11	100%	50%	56	50%	80%
EBV-induced HLH	7	75%	50%	55	50%	50%
PsA Rx & axial disease	7	75%	93%	48	100%	80%
Eosinophilic disorders	7	100%	70%	48	50%	80%
Renal path: SLE mimics	6	25%	100%	43	100%	100%
Inflammatory myositis	N/A***	N/A***	N/A***	41	50%	63%
SLE & the heart	9	75%	67%	****	****	****
Muscle path	8	50%	88%	****	****	****
Infusion medicine	8	75%	75%	****	****	****
Average	8.6	75.0%	75.3%	51.5	65.6%	77.9%

*Time in days between the original core curriculum session and the first distribution of the rheuminder reviewing that session

**Time in days between the original core curriculum session and the second distribution of the rheuminder reviewing that session

***Error in distribution software, the first rheuminder was never sent

****Not enough time between original session and post-SE assessment to send a second rheuminder

Background/Purpose: Spaced education (SE) and reciprocal peer teaching (RPT) are known to promote knowledge retention and learner engagement. We wanted to understand the educational impact of SE and RPT elements in our rheumatology fellowship core curriculum (CC) but were limited by a small number of learners, insufficient time for test question validation, and difficulty isolating the curricular elements of interest from concurrent educational activities. We developed a novel free recall assessment to analyze knowledge retention from CC sessions in our program to evaluate the impact of SE and RPT.

Table 2: Data for Each Core Curriculum Session According to Pre- vs. Post-SE and Non-RPT vs RPT

Core Curriculum Session	Date	# Fellows (n)*	# Concepts (avg)**	Quality Score = 1 (n)	Quality Score = 1 (%)	Quality Score = 2 (n)	Quality Score = 2 (%)	Quality Score = 3 (n)	Quality Score = 3 (%)	Quality Score = 4 (n)	Quality Score = 4 (%)	Avg Quality (avg)***
Pre-SE, non-RPT												
RTX and Cyc	7/24/18	4	5.25	2	9.5%	8	38.1%	9	42.9%	2	9.5%	2.52
Biostatistics	8/2/18	4	3.25	1	7.7%	11	84.6%	1	7.7%	0	0.0%	2.00
PT and OT in rheum	8/9/18	4	4.25	2	11.8%	8	47.1%	6	35.3%	1	5.9%	2.35
MSK Ultrasound	11/8/18	4	4.25	2	11.8%	11	64.7%	3	17.6%	1	5.9%	2.18
Gout management	11/27/18	3	4.00	0	0.0%	8	66.7%	3	25.0%	1	8.3%	2.42
Crystal analysis	11/29/18	4	5.25	0	0.0%	17	81.0%	1	4.8%	3	14.3%	2.33
Renal path: SLE	12/13/18	4	4.25	0	0.0%	8	47.1%	7	41.2%	2	11.8%	2.65
Overall average	-	3.9	4.37	1.0	5.9%	10.1	60.2%	4.3	25.4%	1.4	8.5%	2.36
Pre-SE, RPT												
Baricitinib & sarilumab	7/17/18	4	2.75	0	0.0%	3	27.3%	4	36.4%	4	36.4%	3.09
Extra-articular RA	7/19/18	4	6.25	1	4.0%	19	76.0%	2	8.0%	3	12.0%	2.28
GIOP	8/7/18	3	4.67	0	0.0%	7	50.0%	3	21.4%	4	28.6%	2.79
Vasculitis & mimics	8/14/18	4	2.50	1	10.0%	6	60.0%	3	30.0%	0	0.0%	2.20
RAVE & MAINRITSAN II	8/21/18	4	3.75	1	6.7%	4	26.7%	3	20.0%	7	46.7%	3.07
MRI in AS	9/4/18	4	2.00	1	12.5%	1	12.5%	6	75.0%	0	0.0%	2.63
SpA classification & Rx	9/13/18	4	4.50	0	0.0%	8	44.4%	8	44.4%	2	11.1%	2.67
Autoinflammatory dz	10/3/18	4	4.00	0	0.0%	9	56.3%	3	18.8%	4	25.0%	2.69
SLE & the GI tract	10/25/18	4	5.25	0	0.0%	6	28.6%	15	71.4%	0	0.0%	2.71
BAFF and belimumab	11/6/18	4	3.75	1	6.7%	7	46.7%	6	40.0%	1	6.7%	2.47
CIRT & CANTOS	11/20/18	3	4.33	2	15.4%	4	30.8%	5	38.5%	2	15.4%	2.54
IPAF	12/6/18	4	5.75	1	4.3%	8	34.8%	12	52.2%	2	8.7%	2.65
Overall average	-	3.8	4.11	0.7	4.2%	6.8	43.4%	5.8	37.0%	2.4	15.3%	2.63
Post-SE, non-RPT												
Rheumadermatology	1/8/19	3	1.67	0	0.0%	3	60.0%	2	40.0%	0	0.0%	2.40
Innate Immunity & TLRs	1/22/19	4	2.75	2	18.2%	7	63.6%	1	9.1%	1	9.1%	2.09
Renal path: SLE mimics	2/26/19	3	4.67	0	0.0%	10	71.4%	4	28.6%	0	0.0%	2.29
Muscle path	4/23/19	4	3.75	0	0.0%	8	53.3%	6	40.0%	1	6.7%	2.53
Infusion medicine	4/25/19	4	5.00	1	5.0%	6	30.0%	8	40.0%	5	25.0%	2.85
Overall average	-	3.6	3.61	0.6	4.6%	6.8	52.3%	4.2	32.3%	1.4	10.8%	2.49
Post-SE, RPT												
SLE & the lung	1/24/19	4	4.00	0	0.0%	7	43.8%	6	37.5%	3	18.8%	2.75
EBV-induced HLH	2/5/19	3	3.33	0	0.0%	2	20.0%	5	50.0%	3	30.0%	3.10
PsA Rx & axial disease	2/14/19	4	5.00	0	0.0%	12	60.0%	4	20.0%	4	20.0%	2.60
Esosinophilic disorders	2/19/19	4	4.75	2	10.5%	8	42.1%	7	36.8%	2	10.5%	2.47
Inflammatory myositis	3/5/19	4	3.25	4	30.8%	7	53.8%	1	7.7%	1	7.7%	1.92
SLE & the heart	4/16/19	4	4.50	0	0.0%	5	27.8%	11	61.1%	2	11.1%	2.83
Overall average	-	3.8	4.17	1.0	6.3%	6.8	42.7%	5.7	35.4%	2.5	15.6%	2.60

* Number of fellows present, **Average total number of concepts recalled, ***Average quality score of the concepts recalled

CC = Core Curriculum; SE = Spaced Education; RPT = Reciprocal Peer Teaching

Methods: The SE intervention involved emailing fellows "rheuminder" multiple choice quizzes about key topics covered in CC sessions. There were 19 CC sessions during the pre-SE period. The SE intervention included 11 CC sessions: unique rheuminders were sent about 1 one week after each CC session; 8 rheuminders were re-sent about 1 month later. Pre- and post-SE free recall assessments asked fellows to list every concept they could remember from each CC session over 1 minute. We tallied the total number of concepts listed and scored the quality of each statement according to the following scale: 1 = incorrect or irrelevant; 2 = a general topic that was covered, not an individual learning point; 3 = an individual learning point that is vague or of poor quality; 4 = an individual learning point that is specific and of good quality. Concept quality was independently scored by 2 raters (DL, JG) with discrepancies arbitrated by a third rater (LCS). We defined RPT CC sessions as those in which fellows were required to prepare in advance and teach each other during the session. Non-RPT sessions did not require prep-work and depended on an instructor for content delivery. Both types of sessions occurred throughout the pre and post-SE period. We used student's t-test and Fisher's exact test to analyze the impact of SE (primary analysis) and RPT (secondary analysis) on the average number of concepts recalled and proportions of concept quality.

Results: Metrics on fellow engagement with SE rheuminders are shown in table 1. Data on the number and quality of concepts recalled for each CC topic are shown in table 2. The average number of concepts recalled per session pre- vs. post-SE was 4.21 vs. 3.93 ($p = 0.338$). The quality scores of concepts pre-SE was 1 = 4.9%, 2 = 49.8%, 3 = 32.6%, 4 = 12.7%; post-SE quality was 1 = 5.6%, 2 = 46.5%, 3 = 34.2%, 4 = 13.7% ($p = 0.913$). The average number of concepts recalled per session non-RPT vs. RPT was 4.07 vs. 4.13 ($p = 0.824$). The quality scores of concepts for non-RPT sessions was 1 = 5.4%, 2 = 57.4%, 3 = 27.9%, 4 = 9.3%; quality for RPT sessions was 1 = 4.9%, 2 = 43.2%, 3 = 36.5%, 4 = 15.4% ($p = 0.0148$).

Conclusion: Using a unique free recall assessment, we found that numbers of concepts remembered did not change when analyzed by SE or RPT. However, the quality of concept recall significantly improved for CC sessions employing RPT, and did not change after the SE intervention. These findings suggest that RPT may be more impactful than SE using multiple choice quizzes and offers a unique perspective on the impact of curricular elements within a rheumatology training program.SE Table 2 FINAL Table 2. Data for Each Core Curriculum Session According to Pre- vs. Post-SE and Non-RPT vs RPT

Disclosure: D. Leverenz, None; **J. Golenbiewski**, None; **L. Criscione-Schreiber**, None.

Abstract Number: 0157

We Can Do Better: Evaluating Inpatient Pediatric Rheumatology Inpatient/Consult Service Performance

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Session Time: 9:00AM–11:00AM

Background/Purpose: Analysis of the last five annual program reviews of our fellowship identified repeated concerns raised by both residents and fellows with Rheumatology inpatient rounding and consultation. Thus, one of the specific aims for improvement chosen for our American Council for Graduate Medical Education (ACGME) Self-Study was to obtain feedback regarding our inpatient consult service performance from the Cincinnati Children's Hospital Medical Center (CCHMC) pediatric residents. We know from the adult rheumatology literature that communication,

professionalism, teaching, and pushback have been identified by residents as key measures to evaluate the effectiveness of consultative services. These measures, however, have not been applied to evaluate pediatric rheumatology consultations, and so we modified the existing validated adult survey to 1) determine pediatric resident opinion on the aforementioned areas, and 2) identify areas for improvement.

Methods: Rheumatology consultation patients requiring inpatient admission at CCHMC are primarily admitted to one of the general inpatient teams that is staffed by post graduate year one (PGY-1) through four (PGY-4) residents. Residents on this team from July 2018 through April 2019 were handed and completed a survey during a noon lecture given during the 4-week rotation. Surveys included 6 questions related to the experience and residents' perception of communication, education, etc. All questions were answered on a 5-point Likert scale (not applicable, poor, fair, good, very good, and excellent). The survey was developed by our pediatric rheumatology program director based on a survey described in the adult literature.

Results: 31/38 (82%) of residents completed the survey (75% PGY-1, 23% PGY-2, and 3% PGY-3 or PGY-4). Overall satisfaction with consulting service was good among residents, with 29/31 (94%) of residents reporting "very good" or "excellent satisfaction". Resident opinion on the quality of communication was variable, with 5/31 (16%) reporting "poor" to "good" quality of communication and 26/31 (84%) reporting "very good" or "excellent". The majority of residents reported "very good' or "excellent" professionalism (30/31, 97%). Teaching was also variable, with 6/31 (19%) reporting "poor" to "good" experience. There was little report of pushback, with 31/31 (100%) of residents reporting receiving pushback "rarely" or "never".

Conclusion: Overall, experience with the inpatient consulting service seemed favorable among residents. Areas for improvement included communication and teaching. In regards to communication, more first year residents seemed dissatisfied, which some reporting "poor" or "fair" experiences. Prior investigations through end of year reviews in our program have reported that this dissatisfaction in communication revolves around discussion of rounding times and plans, but further investigation is required to fully illuminate ways to improve this. In regards to teaching, though the majority of responders reported favorably, there were still some who did not have a good experience, and next steps include investigations into ways to improve this.

Disclosure: K. Schultz, None; **B. Gregg**, None; **M. Klein**, None; **F. Real**, None; **J. Huggins**, None.

Abstract Number: 0158

Addressing the Pediatric Rheumatology Physician Shortage: Does Early Exposure Matter?

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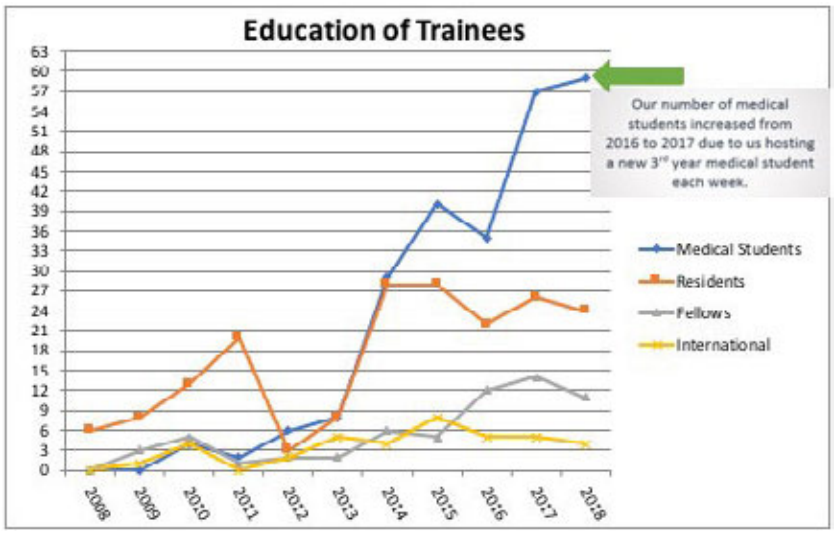
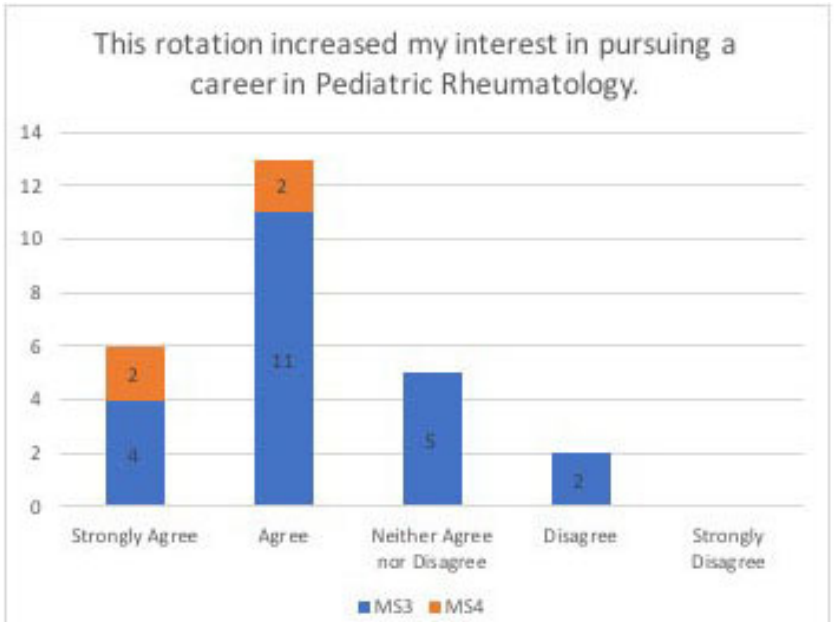
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: There is a shortage of pediatric rheumatologists in the United States, with current demands exceeding provider supply by 33%. This disparity is projected to increase to 61% by 2030 as the anticipated work—that is, residents pursuing pediatric rheumatology fellowships—is expected to decline below current rates. Evidence supports that early exposure to rheumatology increases a learner's interest to pursue rheumatology as a career. For



Increase in medical student exposure over 10 year period



Medical student reported interest in pursuing pediatric rheumatology as a career after rotation exposure

example, an adult study demonstrated 35% of current rheumatology fellows identified a clinical rotation as the most influential factor towards choosing their career. Thus we aimed to 1) increase medical students' exposure to pediatric rheumatology at Cincinnati Children's Hospital and Medical Center (CCHMC); and 2) identify how early educational experiences impact learners' self-assessed career plans.

Methods: A multifaceted approach was used to provide clinical experiences in pediatric rheumatology to medical students starting in 2013, initially by conducting lectures at the medical school. Starting in 2016, third year students were offered a one-week outpatient rotation during their pediatric clerkship. Fourth year students were offered 2- or 4-week electives. From July 2018 to April 2019 third- and fourth-year students participating in these rotations were surveyed at the end of their experiences. Beginning in 2018, a survey was by our pediatric rheumatology program based on previous surveys used in the adult literature. The survey included questions related to the impact of the experiences on interest in pursuing pediatric rheumatology as a career rated on a 5-point Likert scale from strongly agree to strongly disagree.

Results: An increased number of medical students participating in pediatric rheumatology experiences occurred as a result of our curriculum (figure 1). Ninety-three percent (27/29) of third- and fourth-year medical students completed the survey in 2018. All students agreed/strongly agreed that the experience was valuable and increased their awareness of pediatric rheumatologic disease. In addition, 65% (19/29) of students agreed/strongly agreed that the rotation increased their interest in pursuing a career in pediatric rheumatology (figure 2).

Conclusion: There is a growing need for pediatric rheumatologists, and early exposure to the specialty may be one strategy to combat the future shortfall. Most medical students that participated in our curriculum reported increased interest in pursuing a career in pediatric rheumatology. Next steps include long-term follow up of participants to evaluate ultimate career choices.Increase in medical student exposure over 10 year periodMedical student reported interest in pursuing pediatric rheumatology as a career after rotation exposure

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Disclosure: K. Schultz, None; **T. Hennard**, None; **B. Gregg**, None; **M. Klein**, None; **F. Real**, None; **J. Huggins**, None.

Abstract Number: 0159

VA Musculoskeletal "Master Educator" Faculty Development Program for Health Professions Educators: Follow-Up on Changes in Educational Duties and Perceptions of Program Content

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Since 2011, the Veterans Administration (VA) has supported musculoskeletal (MSK) training programs to facilitate provider and trainee MSK education, including a national health professions education (HPE) faculty development course – the MSK Master Educator (ME). The ME program, offered through VA Simulation Learning, Education and Research Network (SimLEARN), was created to teach educators how to systematically train primary care providers and trainees in MSK medicine. The program includes a portable curriculum to be used at ME participants' home institutions. Program development and pilot testing has been previously described. Herein, we describe the long-term effects of the ME training program on the first cohort of learners from 2017-2018.

Methods: The 2.5 day ME program included didactic presentations designed to teach primary care providers how to evaluate and manage shoulder and knee pain, reinforced by a 2-station OSCE. On the final day, participants rotated through an objective structured teaching experience (OSTE) to practice the roles of teacher, student and simulated patient.

Table 1. Demographic and Self-Assessment Information for Master Educator Participants from 2017 to 2018

TABLE 1.
Demographics and Self-Assessment Ratings

Discipline	Primary Care	Rheumatology	Physical Medicine & Rehabilitation	Emergency Medicine	Occupational Medicine, Orthopedics
N (% of total)	17 (49%)	11 (31%)	3 (8%)	2 (6%)	2 (6%)
Years of Experience	> 3	3 to 5	6 to 10	11 to 20	> 20
N (% of total)	7 (20%)	6 (17%)	5 (14%)	11 (31%)	6 (17%)

Anticipated Program Outcomes	Improve personal MSK evaluation & management skills	Improve teaching skills for MSK medicine	Develop an MSK program for practicing providers	Develop an MSK program for trainees
N (% of total)	24 (69%)	31 (89%)	23 (66%)	21 (60%)

Self-Assessment Ratings Variable	Mean pre-course ratings (SD)	Mean post-course ratings (SD)	Mean paired difference (p)
How *important* is it for you to be competent...			
Shoulder			
In the evaluation of shoulder pain?	4.9 (0.4)	5.0 (0.2)	0.1 (ns)
In performing shoulder injections?	4.7 (0.5)	5.0 (0.2)	0.3 (ns)
In teaching others to perform injections?	4.6 (0.6)	4.9 (0.4)	0.3 (ns)
Knee			
In the evaluation of knee pain?	4.9 (0.3)	5.0 (0.2)	0.1 (ns)
In performing knee injections?	4.9 (0.4)	5.0 (0.0)	0.1 (ns)
In teaching others to perform injections?	4.7 (0.6)	4.9 (0.3)	0.2 (ns)
How *confident* are you in your ability to...			
Shoulder			
Evaluate and diagnose shoulder pain (global rating)	3.9 (1.2)	4.9 (0.4)	1.0 (<0.001)
Manage shoulder pain (global rating)	3.8 (1.0)	4.8 (1.0	1.0 (<0.001)
Shoulder Injection			
Understand indications for a subacromial injection?	3.8 (1.2)	4.7 (0.4)	0.9 (<0.001)
Perform a subacromial injection?	3.6 (1.5)	4.5 (1.0)	0.9 (<0.001)
Teach others to perform a subacromial injection?	3.4 (1.6)	4.4 (1.0)	1.0 (<0.001)
Knee			
Evaluate and diagnose knee pain (global rating)	3.9 (1.0)	4.8 (0.6)	0.9 (<0.001)
Manage shoulder pain (global rating)	4.0 (1.0)	4.7 (0.6)	0.7 (<0.001)
Knee Injection			
Understand indications for a knee injection?	3.9 (1.1)	4.8 (0.6)	0.9 (<0.001)
Perform a knee injection?	3.7 (1.4)	4.6 (0.8)	0.9 (<0.001)
Teach others to perform a knee injection?	3.5 (1.6)	4.4 (0.9)	0.9 (<0.001)

Ratings based on a 5-point scale (1, not at all; 2, slightly; 3, moderately; 4, quite; 5, extremely)

Participant evaluation included written surveys assessing learning goals and perceptions of confidence both before and immediately following the training. In 2019, a follow-up survey was developed. The survey collected information about participants' current work environment and any MSK-related duties that may have changed since participation in the ME program. Additionally, the survey collected perceptions about the ME course content and its importance in preparing participants to teach MSK knowledge to other providers. Individual emails with survey links were sent to 31 ME participants (4 excluded with no active email address).

Table 2. Changes in Local MSK Educational Responsibilities for Master Educator Participants

TABLE 2.
Follow-Up Survey Results

Participant involvement in MSK-related activities before and after the ME program

	Pre-Course N (%)	Post-Course N (%)	Change N (% increase)
Involved in teaching MSK-related content in formal didactic sessions	8 (50)	14 (88)	6 (75)
Level of Learners			
Medical Students	6 (38)	7 (44)	1 (17)
Physician Assistant Students	1 (6)	3 (19)	2 (200)
Nurse Practitioner Residents	2 (13)	3 (19)	1 (50)
Medicine Residents	6 (38)	10 (63)	4 (67)
Medicine Fellows	5 (31)	7 (44)	2 (40)
Practicing Providers	6 (38)	12 (75)	6 (50)
Working in an MSK-related clinical role	12 (75)	13 (81)	1 (8)
Precepting learners in MSK-related clinical experiences	11 (69)	14 (88)	3 (27)

Perceived Program Advantage, Compatibility, and Complexity

	N/A	Not	Slightly	Moderately	Quite	Extremely
How *advantageous* was this approach to teaching primary care providers and/or trainees, over the current approach that was being used at your facility?	1	-	-	-	10	5
How *compatible* was this content for integration into your facility's educational programs to train primary care providers and/or trainees?	-	-	-	3	6	7
How *complex* was this approach to teaching MSK skills to primary care providers and/or trainees?	-	4	4	8	-	-

Results: The ME program was held on 6 occasions from 2017 to 2018. Thirty-five learners participated (29 physicians, 5 nurse practitioners, 1 physician assistant). Demographic information and self-assessments collected immediately before and after the program are presented in Table 1. There was a significant increase in all post-course self-assessments of confidence, including the ability to teach shoulder and knee injections.

Sixteen follow-up surveys were completed in 2019 (52% response rate) by 14 physicians, 1 nurse practitioner and 1 physician assistant. Table 2 includes practice changes for MSK-related educational activities and perceptions of pro-

Table 3. Master Educator Schedule and Program Evaluation

Table 3 - Program Schedule and Rating of Course Elements

How important was each module ***in preparing you to teach*** future MSK content?				
1 – Not at all important	2 – A little important	3 – Moderately important	4 – Quite important	5 – Extremely important

Day 1	Ave (SD)	Day 2	Ave (SD)	Day 3	Ave (SD)
Shoulder Physical Examination *Didactic and Small Group Practice*	4.9 (0.3)	Knee Physical Examination *Didactic and Small Group Practice*	4.8 (0.4)	Observed Structured Teaching Experience (OSTE)	4.7 (0.6)
Shoulder Pathology	4.8 (0.4)	Knee Pathology	4.8 (0.6)	Implementation and Local Planning	4.3 (0.5)
Shoulder Simulated Case Practice	4.9 (0.3)	Knee Simulated Case Practice	4.9 (0.3)		
Shoulder Subacromial Injections *Didactic and task-trainers*	3.9 (1.0)	Knee Intra-articular Injections *Didactic and task-trainers*	4.0 (1.1)		
Review Current Literature in MSK Education	4.4 (0.7)	Objective Structured Clinical Examination (OSCE) *Shoulder & Knee*	4.5 (0.7)		

gram advantage, compatibility and complexity. Participant evaluation of the importance of each ME course elements in preparing them to teach future MSK content are represented in Table 3.

Conclusion: The ME program is a national HPE faculty development course that attracts strong multidisciplinary educators and results in improved self-perception of MSK teaching abilities. Participants have reported an improvement in MSK teaching manifested by an increase in their local educational responsibilities in didactic and clinical settings. The curriculum was rated as advantageous and compatible with local programs, and feasible to integrate. To continue the effectiveness of this program, local institutions should support more educators to participate in this VA sponsored program.

Disclosure: A. Barker, None; **T. Anderson**, None; **A. Brahaj**, None; **D. Chandrasekaran**, None; **A. Hansen**, None; **K. Hansen**, None; **M. Hearth-Holmes**, None; **L. Hubbard**, None; **L. Kim**, None; **A. Lazzari**, None; **R. Mckie**, None;

P. Miller, None; **J. Obrien**, None; **V. Osting**, None; **Y. Sayeed**, None; **B. Siaton**, None; **K. Sully**, None; **S. Wiltz**, None; **M. Battistone**, None.

Abstract Number: 0160

Evaluation of ACGME Competencies in a Rheumatology Observed Structured Clinical Examination

Arundathi Jayatilleke,[1] and Al Denio[2], [1]Drexel, Philadelphia, PA, [2]Geisinger, Danville, PA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The Pennsylvania Rheumatology Objective Structured Clinical Examination (ROSCE) is an annual assessment of rheumatology fellows' communication skills. Fellows complete several standardized patient (SP) encounters involving complex communication issues within rheumatology. We revised our assessment tools to align with Accreditation Council of Graduate Medical Education (ACGME) internal medicine subspecialty milestone

ICS1-01	listen carefully to patients and caregivers to create rapport and build a therapeutic relationship.
ICS1-02	explain and counsel patients and caregivers about their problems, proposed examinations and treatments, and findings.
ICS1-03	share decision-making in both diagnostic and therapeutic scenarios.
PC1-01	take a comprehensive, accurate history, including review of all available records, on patients with rheumatic symptoms and signs.
PC1-03	understand and use diagnostic tests including, but not limited to, laboratory, imaging, electrodiagnostic and pathologic studies for the evaluation of the patient with rheumatic symptoms and signs.
PC2-01	form comprehensive treatment plan, based on clinical evidence, clinical context, and patient preferences, counsel patients, and assess response to therapy.
PC3-02	understand disease- and treatment-related complications that may lead to long term morbidity, including the consideration for implications of comorbid diseases and the effects of aging.
PROF1-01	demonstrate respectful professional interactions.
PROF1-02	demonstrate respect for patient dignity and autonomy.
PROF3-02	demonstrate compassion and respect to patients.
MK1-03	explain relevant mechanisms of action and potential adverse effects of agents used in the management of patients with rheumatologic conditions.
MK1-05	explain similarities and differences of the clinical presentation and management between adults and children with rheumatic conditions.
MK1-06	form a differential diagnosis for rheumatologic conditions, including consideration of non-rheumatic diseases.
MK1-08	evaluate complex rheumatic diseases in the setting of multiple coexistent conditions, including the effects of aging.
PBLI1-01	identify knowledge or skills gaps to enhance future clinical interactions.

Figure 1. Description of ACGME milestone categories.

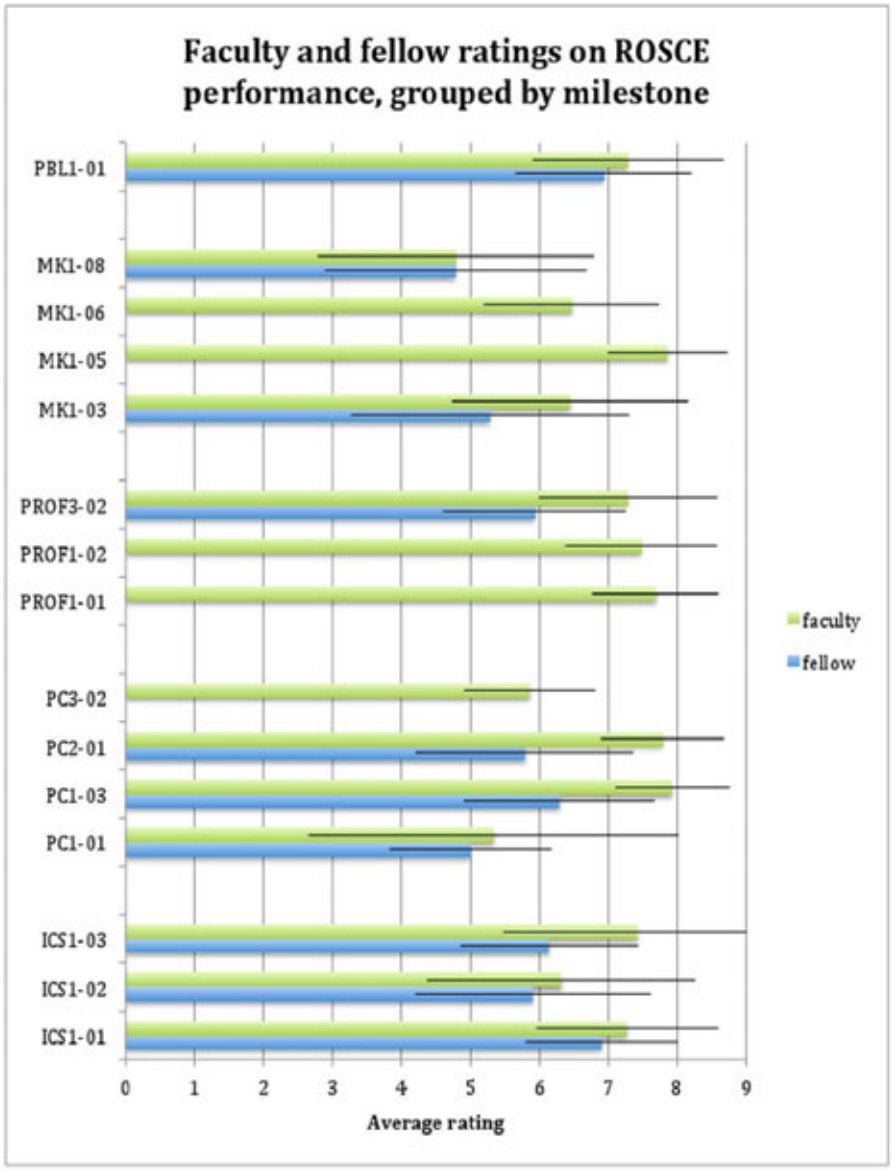

Figure 2. Faculty and fellow ratings on ROSCE performance, grouped by milestone.

areas and compare fellow performance across cases. In this study, we evaluated the comparability of the fellow and faculty ROSCE evaluations within ACGME competency domains.

Methods: 16 trainees from 8 rheumatology programs participated in 7 SP scenarios and were observed by faculty raters. Content validity was determined by consensus of 10 rheumatology fellowship program directors. We recorded faculty and fellow feedback using previously developed 9-point Likert scale instruments. To ensure response process validity, faculty raters were trained on scoring forms prior to the ROSCE; scores were recorded electronically and transferred to Excel for analysis. Fellows completed self-assessment forms afterwards. Items were mapped to milestone categories in the ACGME competencies of medical knowledge (MK), interpersonal and communication skills (ICS), patient care (PC), practice based learning and improvement (PBLI) and professionalism (PROF) (see figure 1). Narrative comments were also recorded.

Results: 16 faculty and 16 fellow feedback forms from 7 ROSCE cases were analyzed. 15 MK, 48 ICS, 9 PC, 1 PBLI, and 26 PROF questions (99 total) were scored across all cases, corresponding to 15 rheumatology milestones.

Overall, average faculty and fellow ratings on milestone categories as well as grouped by competency domains were comparable; however, fellow and faculty ratings were generally poorly correlated except with respect to medical knowledge (r=0.67 for MK1-03, r= 0.70 for MK1-08). Faculty ratings tended to be higher than fellows, most prominently in the MK and PROF domains overall, and in the MK1-03, PROF3-02, PC2-01, and PC1-03 milestones specifically (see figure 2).

Narrative comments from faculty (n=224) largely pertained to use of medical jargon (26%), clarity of explanation (12%), and knowledge base (12%). 24% of fellow comments (n=112) pertained to difficulty of the case, while 33% pertained to areas that they had forgotten during the SP encounter.

Conclusion: Faculty and fellow evaluations of performance were similar in each ACGME competency though fellows tended to self-rate lower than faculty. Correlation between faculty and fellow ratings was generally low, except with regard to more "objective" milestones in medical knowledge; this is likely due to a relatively small spread in ratings of communication skills. We plan to further evaluate validity of our ROSCE and revise our assessments to reflect milestone achievement levels. We hope in future to evaluate correlation of competency evaluation in the ROSCE with program director assessment of fellows.

Disclosure: A. Jayatilleke, None; **A. Denio**, None.

Abstract Number: 0161

Use of a Systematic Consensus Process to Inform Development of the Veterans Health Affairs Simulation Learning, Education and Research Network (SimLEARN) Musculoskeletal Clinician Course

Michael Battistone,[1] Timothy Anderson,[2] Arben Brahaj,[3] Michelene Hearth-Holmes,[4] Lisa Hubbard,[5] Laura Kim,[2] Paul Miller,[2] John O'Brien,[6] Bernadette C. Siaton,[7] Scott A. Wiltz,[2] Nancy Wong,[2] and Steven J. Durning[8,] Andrea Barker[9], [1]Salt Lake City Veterans Affairs Medical Center & University of Utah, Salt Lake City, UT, [2]VHA SimLEARN National Simulation Center, Orlando, FL, [3]VA New England Healthcare System, West Haven, CT, [4]University of Nebraska Medical Center, Omaha, NE, [5]VHA SimLEARN National Simulation Center, Orlando, [6]VA Connecticut Health Care System, West Haven, CT, [7]Baltimore VAMC, Baltimore, MD, [8]Uniformed University of the Health Sciences, Bethesda, MD, [9]Salt Lake City Veterans Affairs Medical Center & University of Utah, North Salt Lake, UT

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Background/Purpose: The Veterans Health Affairs (VHA) Simulation Learning, Education and Research Network (SimLEARN) National Simulation Center has developed a portfolio of continuing professional development (CPD) programs to strengthen the skills of primary care providers (PCPs) in the evaluation and management of common musculoskeletal (MSK) conditions. Instituted in 2015, these 2-day courses are held frequently at the SimLEARN Center in Lake Nona, FL, where they are taught by a rotating consortium of national faculty. The purpose of this study was to engage faculty in a systematic process of course evaluation using a structured consensus procedure inform ongoing curriculum development.

Methods: Eleven educators who had taught in the "MSK Clinician" (MSK-C) course at SimLEARN since 2015 were invited to participate in a 3-step Delphi process. Step 1 involved review of the current curriculum, with invitation to suggest additional content. In step 2, each educator rated every item's importance in a curriculum for PCPs, using

1 Not at all important for Primary Care	2 Slightly important for Primary Care	3 Somewhat important for Primary Care	4 Very important for Primary Care	5 Extremely important for Primary Care

Elements of Current Course	Mean Rating (SD)		Consensus to Retain? Mean ≥ 4 SD ≤ 1 (Final Round)
	First Round	Final Round	
Day 1			
Course Introduction/Precourse Assessments	4.1 (1.1)	4.2 (0.8)	Yes
Introduction to Shoulder Exam (Didactic)	4.8 (0.4)	5.0 (0.1)	Yes
Small Group Shoulder Exam Practice (Hands-on)	4.9 (0.3)	5.0 (0.1)	Yes
Shoulder Pathology (Didactic)	4.7 (0.4)	4.9 (0.2)	Yes
Arthrocentesis Basics (Didactic)	4.2 (0.7)	4.2 (0.6)	Yes
Shoulder Injections (Didactic)	4.0 (0.9)	4.1 (0.7)	Yes
Small Group Shoulder Cases (Hands-on)	4.8 (0.4)	4.9 (0.3)	Yes
Shoulder Injections on Task Trainers (Hands-on)	3.5 (1.2)	3.5 (1.2)	No
Day 2			
Shoulder OSCE (Hands-on)	4.2 (1.2)	4.2 (0.1)	Yes
Introduction to Knee Exam (Didactic)	4.8 (0.4)	4.9 (0.3)	Yes
Small Group Knee Exam Practice (Hands-on)	4.9 (0.3)	4.9 (0.3)	Yes
Knee Pathology (Didactic)	4.7 (0.4)	4.8 (0.3)	Yes
Knee Injections (Didactic)	4.0 (0.9)	4.0 (0.8)	Yes
Small Group Knee Cases (Hands-on)	4.8 (0.4)	4.9 (0.3)	Yes
Knee Injections on Task Trainers (Hands-on)	3.6 (1.2)	3.6 (1.1)	No
Knee OSCE (Hands-on)	3.6 (1.2)	3.6 (1.2)	No
Evaluation Feedback and Closing Remarks	4.4 (0.7)	4.5 (0.4)	Yes
Proposed Elements (Additions Only)			
Pain management, specifically non-opioid choices	4.2 (1.2)	4.2 (1.1)	No
Self-care options: specific exercises or resources to describe home therapy	4.2 (0.8)	4.1 (0.6)	Yes
Exercise prescription	3.8 (1.2)	3.4 (1.1)	No
Documentation of the exam, management plan, and procedures	3.6 (1.3)	3.5 (1.1)	No
Comparative efficacy of treatments (PT, steroids, viscosupplementation)	3.8 (0.6)	3.8 (0.6)	No
Back exam	3.9 (1.3)	3.6 (1.3)	No
Back management	3.8 (1.3)	3.5 (1.3)	No
Hip exam	3.9 (1.2)	3.7 (1.2)	No
Him management	3.8 (1.1)	3.6 (1.2)	No
Addition to shoulder exam—Roos maneuver/costoclavicular maneuver (checking for pectoralis minor shortening)	2.2 (0.9)	2.1 (1.0)	No
Addition to knee exam—tracking of the patella	2.8 (1.3)	2.5 (1.2)	No
Newer treatment options for knee injections (beyond steroids and hyaluronic acid), including efficacy data	3.4 (0.9)	3.4 (0.8)	No
Updates from the literature regarding the use of steroid and hyaluronic acid	3.5 (0.8)	3.7 (0.6)	No
Chronic pain medication options in addition to NSAIDS used for chronic MSK pain, with literature regarding efficacy	3.8 (0.8)	3.6 (1.2)	No
Chondromalacia patella, including role of arthroscopy	3.1 (1.1)	3.0 (0.8)	No
Gout (of the knee)	3.3 (0.7)	3.1 (0.7)	No
Tendonitis (of the knee)	3.5 (0.9)	3.3 (0.6)	No
More detailed approach to history of shoulder pain	2.9 (1.5)	2.9 (1.3)	No
Location	3.1 (1.6)	3.3 (1.4)	No
Trauma	3.0 (1.6)	3.0 (1.5)	No
Pain intensity (0-10)	3.0 (1.6)	2.8 (1.5)	No

MSK-C Curriculum Consensus Table Mean Ratings for Step 2 and Step 3

a 5-point Likert scale (1 = not at all important; 5 = extremely important). In the 3rd step, educators were given the groups' average rating for each item, reminded of their own initial rating, and asked to make a final 5-point rating. Individual responses to each step remained anonymous. After the final step, items meeting the predetermined criteria of mean ³4 and standard deviation ≤1 were retained; these items defined group consensus.

Results: Eleven educators (100%; 8 physicians, 2 physician assistants, 1 nurse practitioner) completed all steps of the project.

In step 1, a total of 59 additional elements of the course were proposed by the group, though only one of these—the inclusion of teaching self-care options and specific elements of a home exercise program—met the criteria for consensus. In addition, three of the existing course elements—two sessions for practicing injections using task trainers, and the objective structured clinical examination of the knee—also were not endorsed by consensus.

Mean ratings of all current and proposed course elements in step 2 and step 3 of the consensus process are shown in the Table.

Conclusion: Using a systematic consensus exercise, the faculty of the SimLEARN MSK-C program have critically evaluated the current CPD course, as well as proposed additions to the existing curriculum. This information, combined with participant feedback, other measures of course effectiveness, and ongoing needs assessments conducted by VHA, will help inform the educational and administrative leadership of SimLEARN and give guidance to efforts for continued development of this important national resource.

Disclosure: M. Battistone, None; **T. Anderson**, None; **A. Brahaj**, None; **M. Hearth-Holmes**, None; **L. Hubbard**, None; **L. Kim**, None; **P. Miller**, None; **J. O'Brien**, None; **B. Siaton**, None; **S. Wiltz**, None; **N. Wong**, None; **S. Durning**, None; **A. Barker**, None.

Abstract Number: 0162

A Shared Mental Model for Teaching and Assessing Examination of the Hand, Wrist, and Elbow in the "Training Rheum" Continuing Professional Development Program

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: An increasing number of nurse practitioners (NPs) and physician assistants (PAs) are pursuing careers in rheumatology. To serve their educational interests, the American College of Rheumatology and the American Association of Physician Assistants will launch "The Training Rheum", a 3-day continuing professional development (CPD) course offered August 2019 and January 2020. This program includes instruction in physical exam skills of the hand, wrist, and elbow, reinforced through low-stakes, formative assessment. An interprofessional group of Training Rheum faculty was engaged in a statistically-guided consensus project to develop a useful learning and assessment tool geared to the needs of advanced clinicians new to the practice of rheumatology.

Methods: A literature review was performed to determine physical exam maneuvers of the hand, wrist and elbow that were relevant to informing a clinical diagnosis. Seven faculty involved in the practice and assessment sessions engaged in a 3-step Delphi process. Step 1 involved reviewing the physical exam maneuvers identified in the literature review, and offering suggestions for additional items for the group to consider. In step 2, each faculty member rated every item's importance relative to a curriculum designed for NPs or PAs working in rheumatology, using a

Rating of Items' Importance for NPs and PAs Working In Rheumatology

1 Not at all important for Training Rheum	2 Slightly important for Training Rheum	3 Somewhat important for Training Rheum	4 Very important for Training Rheum	5 Extremely important for Training Rheum

		Mean Rating (s.d.)		Item Retained? (Mean ≥ 4; s.d. ≤ 1)
	Examination Element	**Round 1**	**Round 2**	
1	**Observation**			
	General			
	Inflammation	5.0 (0.0)	5.0 (0.0)	Yes
	Erythema	5.0 (0.0)	5.0 (0.0)	Yes
	Swelling	5.0 (0.0)	5.0 (0.0)	Yes
	Tenderness	5.0 (0.0)	5.0 (0.0)	Yes
	Warmth	5.0 (0.0)	5.0 (0.0)	Yes
	Rashes	4.7 (0.7)	4.7 (0.5)	Yes
	Ulcers	4.6 (0.7)	4.6 (0.7)	Yes
	Scars	3.7 (0.9)	3.7 (0.7)	No
	Muscle atrophy	4.3 (0.7)	4.3 (0.5)	Yes
	Joint deformity	4.9 (0.3)	4.9 (0.3)	Yes
	Swan-neck	4.9 (0.3)	4.9 (0.3)	Yes
	Boutonniere	4.9 (0.3)	4.9 (0.3)	Yes
	MCP deformity	4.9 (0.3)	4.9 (0.3)	Yes
	Volar subluxation (wrist)	4.7 (0.5)	4.9 (0.3)	Yes
	Fingers			
	Bouchard's Heberden's	4.7 (0.5)	5.0 (0.0)	Yes
	Dactylitis	4.7 (0.5)	4.9 (0.3)	Yes
	Sclerodactyly	4.6 (0.5)	4.9 (0.3)	Yes
	Chieropathy	3.7 (1.2)	3.7 (0.9)	No
	Flexion contractures	4.3 (0.9)	4.4 (0.5)	Yes
	Calcinosis	4.1 (0.8)	4.4 (0.5)	Yes
	Digit resorption	3.6 (1.0)	3.4 (0.7)	No
	Nail Signs			
	Pitting	4.7 (0.7)	4.9 (0.3)	Yes
	Onycholysis	4.6 (0.7)	4.7 (0.7)	Yes
	Nailfold capillary changes	4.1 (1.4)	4.1 (1.0)	Yes
	Splinter hemorrhages	4.1 (0.8)	4.1 (0.8)	Yes
	Clubbing	4.0 (0.9)	3.9 (0.6)	No

5-point Likert scale (1 = not at all important; 5 = extremely important). In the third step, faculty were asked to make a final 5-point rating considering the group's overall average rating for each item and their own initial rating. Individual responses to each step remained anonymous. To determine the final consensus checklists, items meeting the predetermined criteria of mean >/= 4 and standard deviation (s.d.) < /= 1 were retained.

Results: All seven faculty members (4 physicians (rheumatologists), 2 NPs, and 1 PA) completed all three Delphi steps. The initial list, including items added in step 1, consisted of 78 elements. The consensus process eliminated

22 items, leaving 53 in the final version of the checklist. Mean ratings of all elements for step 2 and step 3 are shown in Table 1.

All seven faculty members (4 physicians (rheumatologists), 2 NPs, and 1 PA) completed all three Delphi steps.

The initial list, including items added in step 1, consisted of 78 elements. The consensus process eliminated 22 items, leaving 53 in the final version of the checklist.

Mean ratings of all elements for step 2 and step 3 are shown in Table 1.

Conclusion: Using a systematic consensus exercise, an interprofessional group of faculty participating in the "Training Rheum" CPD program has developed a checklist for use in teaching and assessing learners' physical examination of the hand, wrist, and elbow. The next steps will include an evaluation of the effectiveness of this tool, including its response process, internal structure, relation to other variables, and consequences, when used in actual teaching sessions.

Disclosure: M. Battistone, None; **B. Jonas**, None; **J. Bahr**, None; **S. Chrostowski**, None; **A. Dua**, None; **K. Torralba**, None; **A. Konopasky**, None; **H. Meyer**, None; **A. Barker**, None.

Abstract Number: 0163

Workforce Survey: Career Trends of Combined Adult and Pediatric Rheumatology Fellowship Graduates

Kimberly DeQuattro,[1] and **Cuoghi Edens**[2], [1]University of California, San Francisco, San Francisco, CA, [2]University of Chicago, Chicago, IN

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Future projections deem the rheumatology workforce insufficient to meet patient demand, with certain with catchment areas (micropolitan, rural) already lacking clinicians. Currently there is an inadequate number of pediatric rheumatologists to care for patients, only expected to worsen as the current workforce reaches retirement. Interest in combined adult and pediatric rheumatology training has increased in recent years in concert with medpeds residency applicants and rheumatology fellowship training. One prospect to minimize the workforce gap is to capitalize on physicians trained in both medicine and pediatrics (medpeds) rheumatology who can treat patients of all ages. While combined medpeds rheumatologists exist in clinical practice, the path to this career title has historically not been standardized and there is no governing body to determine this designation. No study has established the number of medpeds rheumatologists in practice, their demographics, practice characteristics, and board certifications of this unique rheumatology workforce.

Methods: Mixed-methods approach of primary and secondary data was used to identify baseline medpeds workforce data. Secondary data derived from query of matriculation, board certification, and practice records of multiple organizations including *Accreditation Council for Graduate Medical Education*, American Board of Pediatrics, American Board of Internal Medicine (ABIM), American Board of Medical Specialties, MedPeds section of American Academy of Pediatrics, and Childhood Arthritis and Rheumatology Research Alliance. Formally medpeds trained rheumatologists were defined as having achieved board certifications in both pediatric and adult medicine and rheumatology. Surveys were used to characterize medpeds physician fellowship training and career experiences. Pediat-

ric rheumatology program directors were queried about past medpeds fellowship trainees. Identified combined medpeds rheumatology fellowship graduates were queried to determine their practice location and type, employment percent (full or part-time), patient population, salary, and board certifications. A similar survey was sent to those who completed a medpeds residency followed by a categorical rheumatology fellowship.

Results: In the United States, there are approximately 5000 rheumatologists, 300 of which are pediatric rheumatologists. Thrirty-four formally trained medpeds rheumatologists were identified in the past 20 years, although the number of dual board-certified rheumatologists is incongruent to this. Additionally, 80 pediatricians were board certified through ABIM in rheumatology in addition to those with combined training. Further survey data collection and analysis is currently ongoing.

Conclusion: Inconsistent data exists on the number of practicing medpeds rheumatologists who care for adult and pediatric patients with rheumatologic conditions. This information is vital to the workforce shortage facing rheumatology, particularly pediatric rheumatology, as medpeds rheumatologists may fill a unique clinical niche and help meet the future provider demand.

Disclosure: K. DeQuattro, None; **C. Edens**, None.

Abstract Number: 0164

Learner Practice Gaps in Osteoporosis: Piloting a Metabolic Bone Disease Curriculum Within a Fracture Liaison Service Framework

Vaneet Sandhu, MBBS,[1] Ajay Kamboj,[1] **Teodor Duro**,[1] Christina Downey, MD,[2] and Karina Torralba[3], [1]Loma Linda University, Loma Linda, CA, [2]Loma Linda University Medical Center, Loma LInda, CA, [3]Loma Linda University School of Medicine, Loma Linda, CA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Targeting community level health outcomes is one of the higher aims of medical education. Osteoporosis care gaps are prevalent. Only 23% of women with a fragility fracture have dual energy x-ray absorptiometry (DXA) or pharmacotherapy within 6 months post-fracture. There is also an overreliance on DXA for diagnosis, overlooking a history of fractures, underrecognition of osteoporosis in men, and underutilization of fracture risk assessment (FRAX) to guide therapy. A Fracture Liaison Service (FLS) was established after a local institutional study showed similar care gaps. In the context of experiential learning, a metabolic bone disease (MBD) curriculum was designed within the framework of the FLS for Internal Medicine (IM) residents. (Figure 1,2) Areas of emphasis include disease recognition and risk assessment. The objectives of this study are to determine osteoporosis practice care gaps among residents who have undergone the MBD rotation with the goal to inform educators about areas needing curricular improvement.

Methods: IM residents who completed an MBD rotation April 2018-2019 who provided consent for practice habit review were included in the study. Patient encounters from electronic medical records of women > 65 and men > 70 years of age seen for routine followup visits in continuity clinics May 2018-April 2019 were reviewed. Osteoporosis practice guidelines and nationally-defined patient outcome measures were reviewed by faculty. Six parameters on disease recognition (DXA, FRAX or prior fracture), and risk assessment (steroid exposure, vitamin D level determination; also FRAX) were selected by consensus. Descriptive statistics were utilized. The IM Core Program approved the curriculum as a one week block within a Rheumatology rotation in lieu of an independent 4 week rotation.

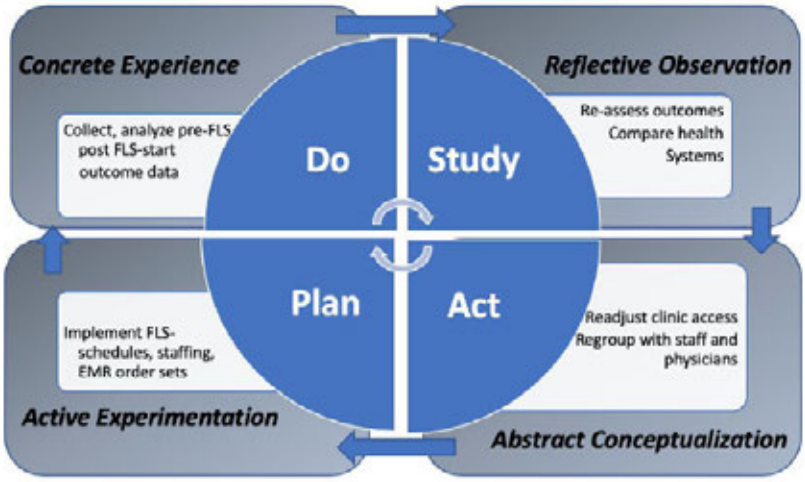

Figure 1. Kolb's Constructivist Theory of Experiential Learning Complements the QI PDSA Cycle

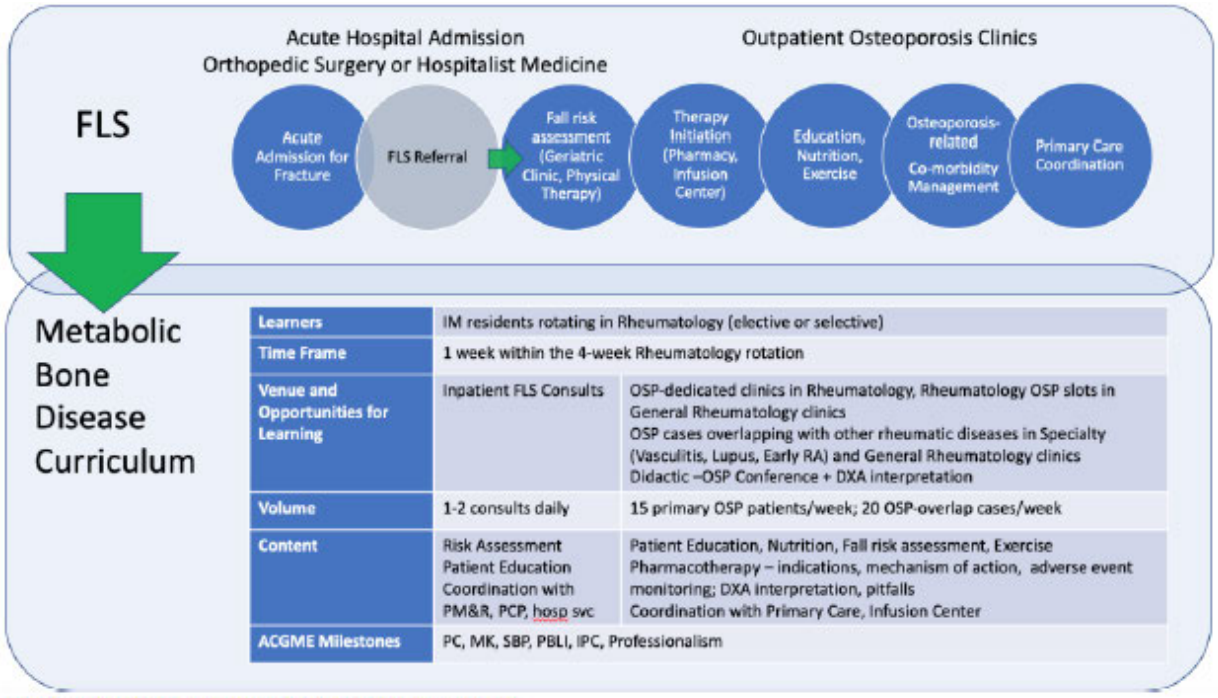

Figure 2. Metabolic Bone Disease Curriculum proposal

Results: 52 residents had gone through the rotation during the designated period of time, and 11 agreed to have a practice review. 2, 6, and 3 were PGY 1, 2, and 3, respectively. 88 charts were reviewed of 54 female and 34 male elderly patient encounters occurring within 3 months of MBD rotation completion. (Figure 3) Fifty (57%) DXAs were ordered by 10 residents. 32 DXAs were completed, and 18 (56%) had osteoporosis. Of these 18 cases, prior fracture was documented in 3 (17%) and long-term steroid use in 4 (22%). No chart had documentation of FRAX. Out of 88 charts, 13 (15%) of patients had a vitamin D level checked within 3 months of provider visit or DXA.

Conclusion: Practice review reveals underutilization of osteoporosis diagnosis and risk assessment strategies. Issues to consider for curricular improvement include reformatting the MBD rotation as a 2-week minimum hands-on rotation providing Orthopedic Surgery, Rheumatology and Endocrinology exposure, and increasing active learning compo-

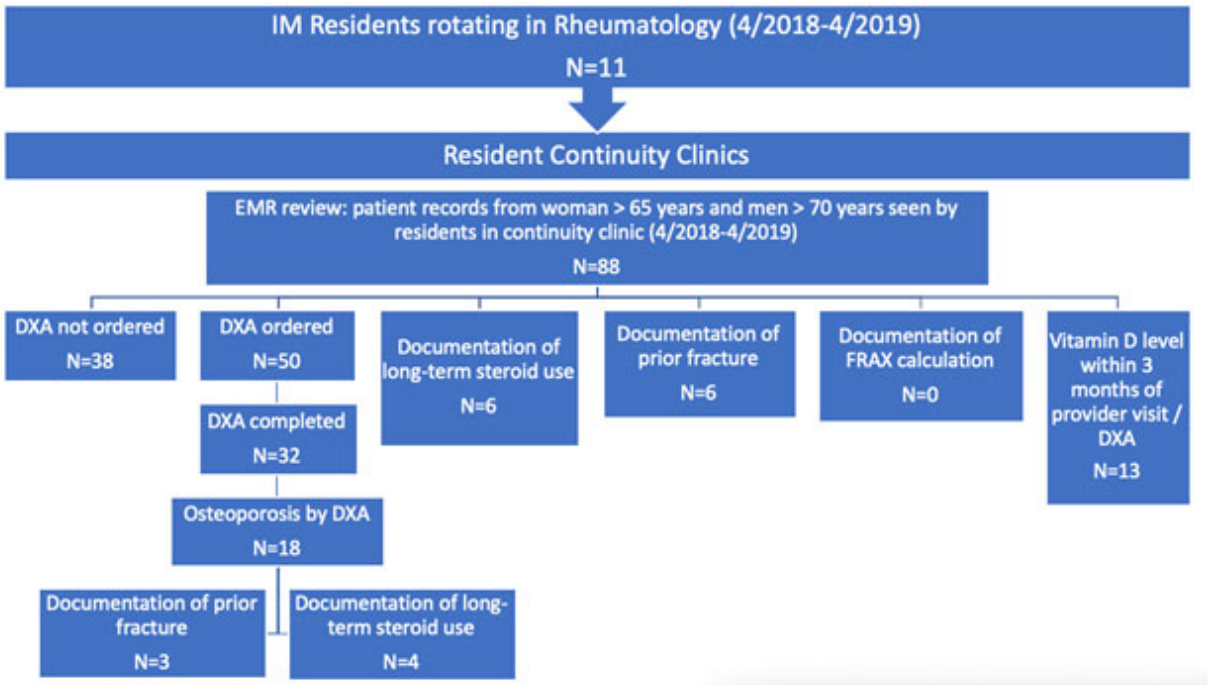

Figure 3. Methodology and Results

nents during the rotation and even throughout the year. The FLS aims to engage primary care physicians, and offering learning opportunities for resident continuity clinic supervising primary care faculty also need to be considered.

Disclosure: V. Sandhu, MBBS, None; **A. Kamboj**, None; **T. Duro**, None; **C. Downey, MD**, None; **K. Torralba**, None.

Abstract Number: 0165

Heterogeneity of Strategies and Methods for Assessment of Competences in Rheumatology Training: Results of a Systematic Literature Review to Inform EULAR Points to Consider

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Education Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The structure and content of Rheumatology training programs vary widely among European countries. Harmonization of assessment methods of competences across EULAR countries could contribute to ensure a minimal standard of care. Our objectives were to To summarize the available information on competence assessment methods and strategies in postgraduate medical training in rheumatology and other specialties.

Author, country, year	Humphrey-Murto S, Canada, 2009	Berman JR, USA, 2009	Kissin EY, USA, 2014	Pascual Ramos V, Mexico, 2015
Competence assessed	CanMEDS roles	Clinical skills, communication skills, professionalism	Practical skills (MSUS)	Clinical skills
Tool	DOPS	OSCE	OSCE	OSCE
Comparator tool	A national 10-station OSCE	Rating by program directors	A 76-question MCQ	Theory Test Board Exam (300 MCQ)
Sample size	73	70 (number of participants to year 4 NA)	35	68
Control population	none	none	3 faculty members	3 certified rheumatologists
MERSQI (0-18)	12.5	11	9.5	14.5
Revised tool by Daly et al (1-5)	5	2	5	1
Internal consistency (Cronbach alpha)	not performed	not performed	0.15-0.57	0.83–0.92
Inter-rater reliability	not performed	Correlation between faculty raters not significant	ICC 0.3 between live assessors and assessors on videotapes ICC 0.7 between assessors on videotapes	not performed
Test-retest reliability/intra-rater reliability	not performed	not performed	not performed	OSCE total and partial scores in Year 1 vs Year 2 r=0.80-0.95
Inter-method (or parallel forms) reliability /concurrent validity	DOPS vs OSCE r=0.48	OSCE vs rating by program directors r=0.48	OSCE vs MCQ r =0.52	OSCE total score vs MCQ Study year 1: r=0.203 Study year 2: r=0.436
Feasibility	14 forms per resident to achieve a g coefficient of 0.80	not performed	not performed	not performed
Construct validity	not performed	not performed	OSCE scores significantly discriminated fellows and fellows vs faculty	Significantly higher scores in higher levels of training

MSUS: musculoskeletal ultrasound; DOPS, direct observation of practical skills; OSCE, objective structured clinical examination; MCQ, multiple choice questionnaire; NA, not available; MERSQI, medical education research study quality instrument; ICC, intraclass correlation coefficient

Table 1. Studies addressing assessment of competences in rheumatology

Methods: As part of a EULAR taskforce on the assessment of competences in rheumatology training, a systematic literature review was performed. Two reviewers independently identified eligible studies according to the PIM framework: P (population): trainees, fellows; I (instrument of interest): assessment strategies and methods; M (measurement of properties of interest): validity, discrimination, feasibility. one search for rheumatology and one for related medical specialties and extracted data on assessment methods. Two searches were conducted: (i) for rheumatology, retrieving original studies; (ii) for related medical specialties, retrieving SLRs through which we identified original studies. Risk of bias was assessed using the medical education research study quality instrument (MERSQI).

Results: Of the 6,276 articles in rheumatology and 2,265 reviews from other specialties, 4 and 31 original studies were included, respectively. Studies in rheumatology were at variable risk of bias and explored only direct observation of practical skills (DOPS) and objective structured clinical examination (OSCE). Rheumatology OSCEs including clinical, laboratory and imaging stations performed best, with a good to very good internal consistency, and inter-rater reliability. OSCEs correlated fairly to moderately with other assessment tools, including DOPS. Studies on OSCEs on clinical skills in other specialties showed a good to very good inter-rater reliability, while OSCEs on communication skills consistently demonstrated a good to very good internal consistency. Other tools such as multisource feedback

(MSF) and mini-clinical evaluation (mini-CEX) exercise showed a good feasibility and internal consistency, with conflicting data on validity and reliability.

Conclusion: Although there is a consistent body of evidence about assessment of competence in postgraduate medical training in several specialities, data in rheumatology is scarce and this partial picture indicates some conflicting evidence. OSCEs represent an appropriate tool to assess clinical competences and correlate fairly well with other assessment strategies; DOPS, MSF and mini-CEX are other feasible alternatives. This SLR informs the ongoing initiative to formulate EULAR 'points to consider' for the assessment of competences in rheumatology training.

Disclosure: A. Alunno, None; **A. Najm**, None; **F. Sivera**, None; **C. Haines**, None; **S. Ramiro**, None.

Abstract Number: 0166

An Analysis of Inpatient Rheumatology Consults at an Academic Military Medical Center over 16 Years: Do Consults Requests Accurately Reflect the Curriculum and Prepare Fellows for Board Certification and Future Practice?

Caitlin Cruz,[1] and Jess Edison[1], [1]Walter Reed National Military Medical Center, Bethesda, MD

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Review inpatient rheumatology consults over the last 16 years at a major military academic medical center to analyze trends in rheumatic disease presentation, consultative requests by other services, and a representation of core educational topics for the fellowship curriculum based on medical content categories for the Rheumatology Board Examination.

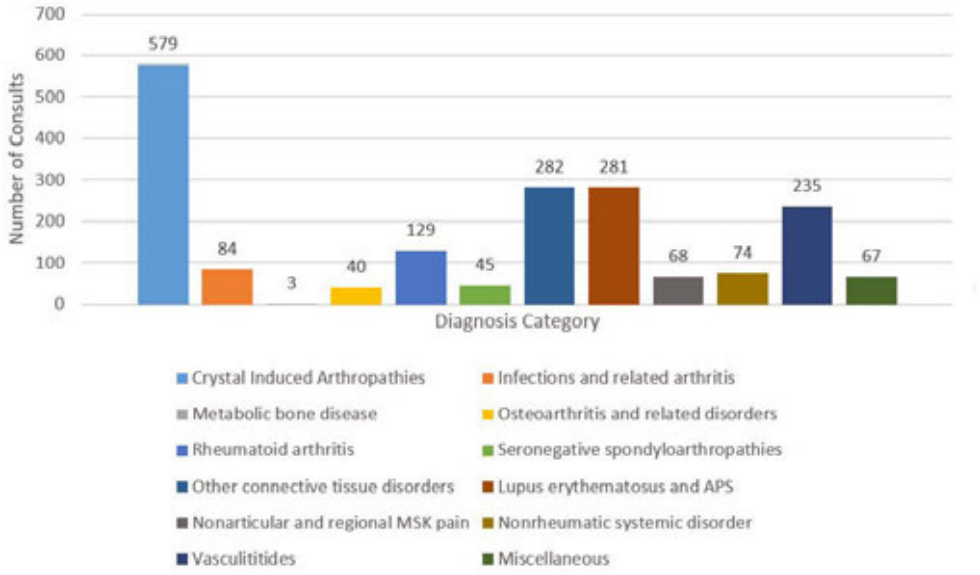

Figure 1. Distribution of rheumatologic disorders evaluated during hospital admission from April 2002 to June 2018.

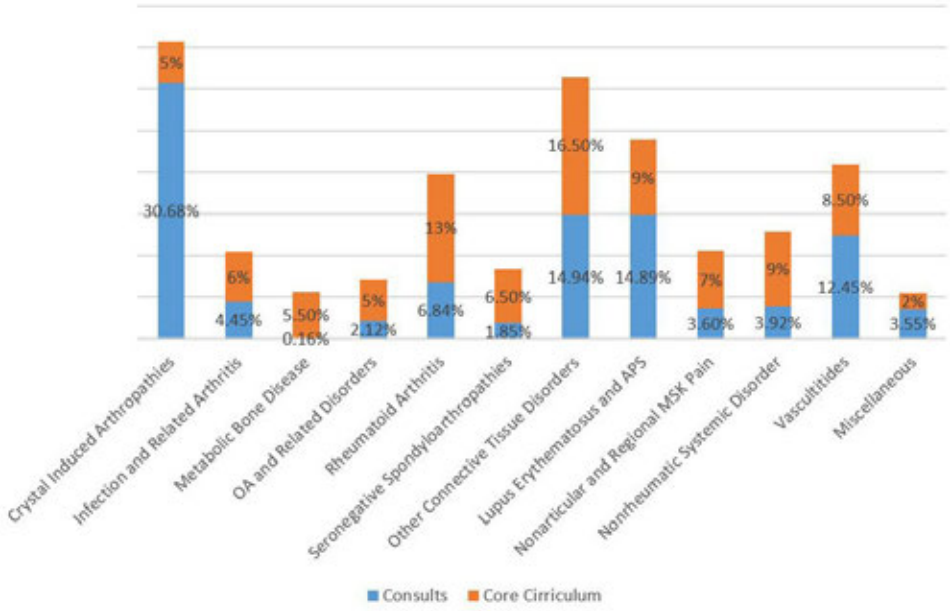

Figure 2. Percentage of consults seen compared to the weighted breakdown of the core curriculum on the board certification examination (based on the 2015 core curriculum outline for rheumatology fellowship program).

Methods: The Rheumatology Fellowship documents every formal inpatient consultation request from any service. The hospital provides services for all active duty, their families, and retirees and inpatients have access to all medical subspecialties. The fellow documents date, reason for consult, and requesting service. Records were categorized by reason for consultation. If the consultation request was unclear, record review was done to determine final rheumatologic diagnosis. Each consultation request was further characterized by diagnoses into pertinent educational core categories as outlined in the 2015 core curriculum outline for rheumatology fellowship program to include: crystal-induced arthropathies, infection and related arthritis, metabolic bone disease, osteoarthritis and related disorders, rheumatoid arthritis, seronegative spondyloarthropathies, other connective tissue disorders, lupus erythematosus and antiphospholipid syndrome, nonarticular and regional musculoskeletal pain, nonrheumatic systemic disorder, vasculititides, and miscellaneous.

Results: From April 2002 until June 2018, a total of 15,0359 adult patients were hospitalized under the care of all inpatient services during this 16-year period. From this population, 1887 consultations were requested for the Rheumatology service. These consultations were completed by 41 fellows over the studied period. Overall 1.25% of admissions required an evaluation by Rheumatology. The most common consult request was evaluation for crystal-induced arthropathies at 30.68% of all consults followed by evaluation for other connective tissue disorders and systemic lupus erythematosus at 14.94% and 14.89% respectively. In comparison to the educational objectives for the board certification examination, crystal-induced arthropathies represents only 5% of tested information while other connective tissue disorders accounts for 16.5% of tested material. For the Rheumatology program, the average fellow evaluated 25 consults per academic year and 46 consults in the 24 months of fellowship.

Conclusion: The adult Rheumatology fellowship at our military academic hospital provides consultation to surgical and medicine services and provides invaluable learning and teaching experiences for the fellowship. As trends in diagnosis and treatment emerge, the fellowship curriculum should continue to change to best prepare future rheumatologists. Continued analysis of the data to identify trends over time can help to optimize graduate medical educational topics at both the residency and fellowship levels as well assist with quality improvement strategies to enhance the curriculum and resources for the future.

Disclosure: C. Cruz, None; **J. Edison**, None.

Abstract Number: 0167

Bioethics for the Rheumatologist: A Needs-Assessment, Curriculum Development, and Knowledge Assessment of Bioethical Topics for Rheumatology Trainees

Alexandra Saltman,[1] Heather McDonald-Blumer,[2] Lynn Spiegel,[3] and Pier Bryden[4], [1]University of Toronto, Mount Sinai Hospital and Princess Margaret Cancer Centre, Toronto, ON, Canada, [2]University of Toronto and Mount Sinai Hospital, Toronto, ON, Canada, [3]The Hospital for Sick Children, Toronto, ON, Canada, [4]University of Toronto; Sick Kids Hospital, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Education Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: An understanding of bioethics and an ability to apply ethical principles in clinical practice should be key components of postgraduate medical training. However, there is no formal bioethics curriculum for Rheumatology residents at the University of Toronto. Instead, the majority of bioethics education is currently delivered via informal role-modelling by staff physicians. The purpose of this study was to determine whether the implementation of a curriculum tailored to the needs of Rheumatology residents, and delivered centrally at the National Rheumatology Residents' Weekend (NRRW), would increase residents' self-perceived knowledge of, and competency in, bioethical issues in clinical practice.

Methods: A literature review was performed to identify bioethical issues that were relevant to Rheumatology trainees. Cases were developed based on three of these issues for interactive, small-group sessions that were piloted at the NRRW in Toronto in December 2017. A clinician with bioethics expertise delivered a lecture on a framework for evaluating ethical dilemmas. Rheumatology faculty physicians facilitated case-based discussions of three key bioethical issues—medical assisted in dying (MAID), resource allocation, and relationships with industry—using group role-play as a tool for examining different perspectives surrounding these ethical controversies. Residents were given access to all study materials following the sessions. Pre- and post-knowledge surveys were distributed to participating residents to assess their comfort and knowledge with bioethical topics before and after participation in these sessions. Survey results were analyzed using descriptive statistics.

Results: 41% of attendees at the NRRW completed the needs assessment. 46% were PGY4s and 54% were PGY5s. Most residents agreed that formal training in bioethics was very important (29%) or somewhat important (51%) to rheumatology training, but the majority rated their knowledge as low in core bioethical topics. Residents identified: end of life care and MAID (41%), assessing capacity and substitute decision-making (34%), doctor-patient relationships and boundaries (32%), caring for the non-adherent patient (59%), medical resource allocation (51%), and cross-cultural issues (51%) as topics they wished to learn more about. 22% of attendees completed the post-rounds survey. The majority (91%) felt that the case-based sessions improved their knowledge of a core bioethical topic, and that they would feel more comfortable addressing this topic in clinical practice (86%). There were statistically significant improvements in self-perceived knowledge of, and comfort with, a number of core topics, including those not explicitly covered by the case-based sessions.

Conclusion: The design and implementation of a bioethics curriculum relevant to Rheumatology trainees is an effective means of increasing residents' self-perceived understanding of, and engagement with, bioethical issues central

to the practice of Rheumatology. Further study is required to assess whether or not residents retain knowledge of an ethical framework as presented in such a setting and can apply its principles to clinical practice.

Disclosure: A. Saltman, None; **H. McDonald-Blumer**, None; **L. Spiegel**, None; **P. Bryden**, None.

Abstract Number: 0168

Development and Usability Testing of Take Charge: An Email Series to Increase Knowledge of Self-Management Skills in People with Lupus

Karin Tse,[1] Lauren Metelski,[1] Reid Dossinger,[1] Mike Donnelly,[1] and **Latifa Boyce**[1], [1]Lupus Foundation of America, Washington, DC

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education/Community Programs Poster – ARP
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Session Time: 9:00AM–11:00AM

Background/Purpose: Email may be a promising approach to expose people with lupus, especially newly diagnosed patients, to educational information, tools, and resources on lupus self-management skills. The Lupus Foundation of America developed an educational email series called Take Charge to increase knowledge of self-management skills among newly diagnosed people with lupus. This study aimed to evaluate satisfaction and usability issues with Take Charge to help improve the email series.

Methods: Six emails containing information on lupus self-management skills were distributed weekly to participants affected by lupus. Skills ranged from coping and communications to medication and symptom management. A post-series survey was distributed to users who opened at least one message of series, and semi-structured phone interviews were conducted among a subset of these users to obtain feedback on functionality, content, and design of the email series. The post-series survey measured users' exposure to information on lupus self-management skills during the series and actions taken (self-management skills attempted) after exposure to email content. The phone interviews provided in-depth insight on users' perceptions of the design and branding of the series, and on the clarity, understandability, relevance, and appeal of its contents.

Results: Usability testing was conducted with 13 Take Charge participants (users) —all participants completed the post-series survey and five completed phone interviews. Sixty-nine percent of users reported trying at least one self-management skill presented in the series. Of the six self-management skills presented in the series, 46% of users said they prepared questions for their next doctor's appointment (this was the most attempted skill reported among users). In general, users liked that the series was short, simple, and easy to understand. Users stated that weekly distribution of the emails was an appropriate frequency to prompt them to take action. The email content was also empowering and motivating, particularly the graphics and tone. Users who completed phone interviews could not tell that the series was sent from lupus health educators, which they all thought was an important feature to highlight in the design, especially for newly diagnosed participants. Users recommended the series provide ways to connect with other people with lupus and more in-depth information, such as information on lupus treatment, research, and financing lupus care.

Conclusion: Usability testing for Take Charge provided valuable insight on the use of emails to expose people with lupus to information on lupus self-management skills and prompt them to take action in the management of their care. While user satisfaction was high, usability testing also revealed important issues to enhance the Take Charge

email series. Overall, email series show promise as a feasible method to deliver patient education. Future iterations of Take Charge will be developed and tested for ability to increase knowledge of self-management skills among people with lupus.

Disclosure: K. Tse, Lupus Foundation of America, 3; **L. Metelski**, Lupus Foundation of America, 3; **R. Dossinger**, Lupus Foundation of America, 3; **M. Donnelly**, Lupus Foundation of America, 3; **L. Boyce**, Lupus Foundation of America, 3.

Abstract Number: 0169

Wikipedia as a Source of Health Information for the Public: Systematic Analysis of Quality and Readability of 8 Common Rheumatic Diseases Articles

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education/Community Programs Poster – ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Wikipedia is the largest open-access online collaborative encyclopedia. Several studies have shown that Wikipedia is one of the most read online source for health information by patients. As of March 2017, the English Wikipedia had over 30,000 medical articles. Data on the quality and readability of rheumatic diseases articles are lacking. At least 36% of the U.S. adults have basic or below basic health literacy; therefore, may face serious challenges in understanding health information. In this study, we aim to systematically analyze the quality of health information and the readability of Wikipedia articles on 8 common rheumatic diseases: osteoarthritis (OA), gout, rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE), scleroderma, and Sjogren's syndrome.

Methods: Quality of health information in the 8 Wikipedia articles was analyzed using DISCERN instrument by 2 independent reviewers trained on this validated scoring system. The readability of articles was evaluated using 7 popular formulas based on the number of sentences, words, syllables, and characters. Medical jargon level was assessed using the De-jargonizer which detects rare medical terms and hence accessibility by the public. Additional data collected include: article views, number of words, and presence of multimedia.

Results: The average DISCERN score for health information quality was found to be 3.5/5. OA article had the highest score of 3.8/5 followed by gout and Sjogren's articles (3.6/5), whereas scleroderma article had the lowest score of 3.2/5. Articles readability ranged from "difficult" to "very difficult" (average grade level: 13th). Scleroderma article was the most difficult to read (college graduate level) whereas gout was the easiest to read (10th-11th grade level). Similarly, the jargon percentage score was highest in scleroderma with 19% rare words used and a general audience suitability score of 73/100. On the other hand, OA article had the lowest jargon percentage (10% rare words) with the highest general audience suitability score of 85/100 followed by gout article with 82/100 score. Page views for the 8 articles between 7/2015-5/2019 was 31,725,957 (average 3,965,744 views per article). Gout article was the most viewed followed by SLE and RA, whereas Sjogren's article was the least viewed. Presence of multimedia averaged 9 images/videos per article with the highest seen in OA article.

Conclusion: Evaluation of 8 common rheumatic diseases articles on Wikipedia revealed a fair quality of health information indicating potentially important shortcomings. The readability level was at college level for most articles making these articles less accessible to the public. There seems to be a positive correlation between disease prevalence and quality of health information as well as the readability scores. Overall, these articles were well viewed and referenced and covered the important aspects of each disease. A more targeted approach and dedicated group effort is needed to improve the quality of information and the readability of these articles.

Disclosure: M. Mohameden, None; **A. Ali**, None; **Z. Li**, None; **S. Mumtaz**, None; **C. Reyes Yuvienco**, None.

Abstract Number: 0170

Evaluating an Illustrated Storybook for Children with Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Education/Community Programs Poster – ARP
Session Type: Poster Session (Sunday)
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Background/Purpose: While juvenile idiopathic arthritis (JIA) is a common pediatric rheumatic disease, there is a lack of available child-friendly patient education materials. An illustrated storybook on JIA was created by medical students to address this gap. The present study evaluated the storybook for its comprehensibility, appropriateness and acceptability from the perspectives of children with JIA and their parents.

Methods: English-speaking children, aged 4–10 years, diagnosed with JIA in the past 36 months were recruited from a pediatric rheumatology clinic at a tertiary academic centre for this qualitative study. All children met the ILAR classification criteria for JIA. Children and parents were observed reading the storybook aloud and then interviewed using a semi-structured interview guide. Data collection tools were developed through an iterative process involving feedback from external experts and were further refined through piloting. The storybook reading and interviews were audio-recorded and transcribed. The transcripts were then analyzed using conventional content analysis within a qualitative data software, NVivo 11.

Results: Twelve child-parent dyads participated. The average age of children was 6 years and 5 months (4 years 2 months–10 years) and the average time from diagnosis was 19 months (3–32 months). Analysis showed that children comprehended the content of the storybook and understood the emotions portrayed by the story's main characters. Children and parents reported that the story appropriately mirrored their own experiences of JIA. The reading level and book length were deemed acceptable to children aged 5–10, with varying degrees of assistance. Minor revisions were suggested regarding background illustrations, word choices and font.

Three key elements regarding patient education materials were identified: (1) Children were most intrigued by anatomical illustrations and interpreted them according to their own experiences. (2) Non-medical details about the story's main characters helped children relate to the storybook on a personal level. (3) Parents desired not only accurate medical information but also a sense of relief and hope.

Conclusion: The storybook on JIA was considered comprehensible, appropriate and acceptable. The findings informed minor modifications to the present storybook and suggest important elements to consider when creating future pediatric patient education materials.

Disclosure: J. Lee, None; **D. Newhook**, None; **K. Eady**, None; **R. Jurencak**, None.

Abstract Number: 0171

Performance of 2010 ACR/EULAR and 1987 ACR Criteria for Classification of Rheumatoid Arthritis in a Population-based Incidence Cohort, 2010-2014

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies evaluated performance of the 2010 American College of Rheumatology (ACR)/European League against Rheumatism (EULAR) criteria for classification of rheumatoid arthritis (RA) in clinical settings. However, information about performance of these criteria in population-based studies is scarce. We aimed to estimate RA incidence during 2010-2014 using 1987 ACR and the 2010 ACR/EULAR criteria and compare the performance of these criteria sets.

Methods: We evaluated RA incidence in a population-based inception cohort of individuals 18 years of age and older based on fulfillment of the 1987 ACR and the 2010 ACR/EULAR criteria between 1/1/2010 and 12/31/2014. Both rheumatoid factor (RF) and cyclic citrullinated peptide antibody (anti-CCP) were considered for criteria fulfillment. Seropositive was defined as RF and/or anti-CCP positive, and seronegative was defined as neither positive. Incidence rates were estimated and were age-and sex-adjusted to the white population in the US in 2010.

Results: There were 221 patients who first fulfilled 1987 or 2010 criteria for RA in 2010-2014 (216 met 1987 criteria and 175 met 2010 criteria). Table shows RA incidence rates per 100,000 population for the 2010-2014 time period overall and by seropositivity. The estimates for the overall age- and sex-adjusted annual RA incidence were higher

Overall	Female	Male	Total
1987 criteria	54 (45, 63)	29 (22, 35)	42 (36, 47)
2010 criteria	44 (36, 52)	22 (16, 28)	34 (29, 39)
Seropositive			
1987 criteria	33 (27, 40)	16 (11, 21)	25 (20, 29)
2010 criteria	32 (25, 39)	17 (11, 22)	24 (20, 29)
Seronegative			
1987 criteria	20 (15, 26)	13 (8, 18)	17 (13, 20)
2010 criteria	12 (8, 16)	6 (3, 9)	9 (7, 12)

Table 1. Incidence rates per 100,000 population (95% CI) for 2010-2014 by criteria

when 1987 ACR criteria were applied as compared to the 2010 ACR/EULAR criteria due to lower estimates for seronegative patients identified with the 2010 ACR/EULAR criteria. There were a total of 36 seronegative patients who met 1987 ACR criteria but not 2010 ACR/EULAR criteria in 2010-2014. When these patients were compared with the other 47 seronegative patients who met both 1987 ACR and 2010 ACR/EULAR criteria in 2010-2014, patients fulfilling both criteria had higher joint counts ($p< 0.001$) and were more likely to be ever smokers ($p=0.02$). The rest of characteristics of these two groups of seronegative patients were similar, including age at RA incidence, sex, race, body mass index, proportion of patients with prolonged morning stiffness, arthritis in 3 or more joints, arthritis in hand joints, rheumatoid nodules, erosions, abnormal erythrocyte sedimentation rate or C-reactive protein, disease duration >6 weeks. There were no differences between these groups in the proportion of patients started on methotrexate, hydroxychloroquine, sulfasalazine, or other disease-modifying antirheumatic drug (DMARD) as their first DMARD.

Conclusion: The incidence of RA and particularly seronegative RA in population-based studies may be underestimated by 2010 ACR/EULAR criteria as compared to the 1987 ACR criteria for classification of RA. Seronegative RA patients who fulfill 1987 ACR criteria but not 2010 ACR/EULAR criteria have lower joint counts but have otherwise similar RA disease characteristics as patients who fulfilled both sets of criteria.

Disclosure: E. Myasoedova, Pfizer, 2; **J. Davis**, Abbvie, 5, Pfizer, 2, 5, Sanofi Genzyme, 5; **E. Matteson**, Boehringer Ingelheim, 5, Pfizer, 2, Sun Pharmaceuticals, 2; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2.

Abstract Number: 0172

Is the Epidemiology of Rheumatoid Arthritis (RA) Changing? Results from a Population-based Incidence Cohort of RA Patients, 2005-2014

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The incidence and prevalence of rheumatoid arthritis (RA) vary substantially between populations in different geographic areas and over time. Recent trends in RA incidence in US populations are unknown. We aimed to examine trends in the incidence of RA from 2005 to 2014 as compared to the previous decades.

Characteristic	Decade of RA incidence			p value
	1985-1994 (N=240)	1995-2004 (N=344)	2005-2014 (N=428)	
Age at RA incidence, years. Mean (SD)	56.6 (16.6)	56.0 (15.5)	55.4 (15.4)	0.736
Female Sex	160 (67%)	240 (70%)	292 (68%)	0.727
Race, white	225 (94%)	321 (93%)	378 (88%)	0.077
Ever smoker at RA incidence	143 (60%)	183 (53%)	186 (43%)	<0.001
BMI≥30 kg/m^2 at RA incidence	57 (24%)	114 (33%)	175 (41%)	<0.001
RF positive	166 (69%)	238 (69%)	217 (51%)	<0.001
Anti-CCP positive in first year after RA incidence	0 (0%)	14/36 (39%)	188/375 (50%)	0.20
Erosion in first year after RA incidence	33 (15%)	65 (19%)	97 (24%)	0.021

Table 1. Patient characteristics by decade of RA incidence

Table 2. Incidence rates by 1987 ACR criteria per 100,000 population (95% CI)

Group	Decade of RA incidence	Female	Male	Total
Overall	1985-1994	48 (40, 56)	31 (24, 38)	40 (34, 45)
	1995-2004	56 (49, 64)	29 (23, 35)	43 (39, 48)
	2005-2014	55 (49, 62)	29 (24, 34)	43 (39, 47)
RF+	1985-1994	33 (27, 40)	23 (17, 29)	28 (23, 32)
	1995-2004	40 (33, 46)	19 (14, 24)	30 (26, 34)
	2005-2014	27 (23, 32)	15 (12, 19)	22 (19, 24)
RF-	1985-1994	15 (11, 19)	8 (5, 12)	12 9, 15)
	1995-2004	17 (13, 21)	10 (7, 14)	14 (11, 16)
	2005-2014	28 (23, 32)	14 (11, 18)	21 (18, 24)

Methods: We evaluated RA incidence trends in a population-based inception cohort of individuals 18 years of age and older who first fulfilled the ACR 1987 classification criteria for RA between 1/1/1985 and 12/31/2014. While both rheumatoid factor (RF) and cyclic citrullinated peptide antibody (anti-CCP) were considered for criteria fulfillment when available, incidence rates were calculated for RF positive vs negative without inclusion of anti-CCP to allow fair comparison of incidence rates over 3 decades during which anti-CCP testing rates were on the rise. Incidence rates were estimated and were age-and sex-adjusted to the white population in the US in 2010. Trends in incidence rates were examined using Poisson regression methods.

Results: The 2005-2014 incidence cohort comprised 428 patients: mean age 55.4 years, 68% female, 51% RF positive, 50% anti-CCP positive (Table 1). There was no statistically significant difference in age at RA incidence, sex distribution or race in 2005-2014 cohort vs 1995-2004 and 1985-1994 cohorts. Smoking rates declined and obesity rates increased from earlier decades to more recent years. Patients in the 2005-2014 cohort were more likely to develop an erosion in the first year of RA incidence as compared to the previous decades.

Table 2 shows RA incidence rates per 100,000 population for 3 most recent decades and by RF status. The overall age- and sex-adjusted annual RA incidence in 2005-2014 was 43/100,000 population with age-adjusted incidence in women 55/100,000 population and 29/100,000 population in men. These estimates were similar to the 1995-2004 decade. There was a decline in the incidence of RF positive RA in 2005-2014 compared to the previous 2 decades ($p=0.006$), with a corresponding increase in RF negative cases ($p< 0.001$, Table 2).

Conclusion: The incidence of RA overall during the 2005-2014 period remained similar to the previous decade. An increase in RF-negative RA disease and decrease in RF positive RA was found using 1987 ACR criteria. Changing prevalence of environmental factors, such as smoking, obesity and others, may have contributed to these trends. Whether these trends represent a changing serological profile of RA requires further investigation.

Disclosure: E. Myasoedova, Pfizer, 2; **J. Davis**, Abbvie, 5, Pfizer, 2, 5, Sanofi Genzyme, 5; **E. Matteson**, Boehringer Ingelheim, 5, Pfizer, 2, Sun Pharmaceuticals, 2; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2.

Abstract Number: 0173

Statin Use Is Associated with Increased Risk of RA in US Population: Results from a Large Nationwide Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Studies evaluating the effect of statin use on the risk of rheumatoid arthritis (RA) onset have shown conflicting results. Most of these studies evaluated European populations while data from the US are scarce. We aimed to assess the association between statin use and RA occurrence using claims data from the US population.

Methods: For this case-control study, we used OptumLabs Data Warehouse database, a large administrative database of commercially insured and Medicare Advantage beneficiaries, to identify cases of RA and matched controls. Cases were defined as patients with 2 or more diagnoses of RA in 2011-2017 who were ≥18 years old, filled ≥1 prescription for a conventional or biologic disease modifying anti-rheumatic drug or glucocorticoid, and had no diagnoses of RA or relevant therapies during ≥12 months of prior medical/pharmacy coverage. Controls were persons without RA matched 1:1 to RA cases on age, sex, census region and calendar year. Statin use was defined as any filled prescription for a statin medication in the 12 months prior to RA incidence/index date. All patients with available data on statins were used in this analysis. Logistic regression models were used to estimate odds ratios (OR) **with 95% confidence intervals (CI).**

Results: The study included 42,865 cases with RA (mean age 57.6, 74.9% female) and 42,848 matched controls (mean age 57.6, 74.9% female). All patients in both groups had at least 12 months of prior medical/pharmacy coverage during which there were 15,391 (36%) statin users among RA patients and 13,892 (32%) statin users among the matched controls. Statin use was associated with increased risk of RA: unadjusted OR 1.17, 95%CI 1.14-1.20; OR adjusting for age, sex, race, calendar year of RA diagnosis and census region: 1.20, 95%CI 1.16-1.23. When we adjusted for additional comorbidities, including myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, diabetes with or without organ damage, hypothyroidism, liver disease, metastatic cancer, obesity, and renal failure, the association remained statistically significant: OR 1.12, 95%CI 1.09, 1.16. With adjustment for age, sex, race, calendar year of RA diagnosis, census region and Charlson's comorbidity index, we had slightly attenuated but overall similar results: OR 1.08, 95%CI 1.04, 1.11.

Conclusion: This large nationwide study showed increased risk of RA in statin-users vs non-users. The underlying mechanisms for this association require further investigation.

Disclosure: E. Myasoedova, Pfizer, 2; **J. Davis**, Abbvie, 5, Pfizer, 2, 5, Sanofi Genzyme, 5; **D. Asante**, None; **L. Sangaralingham**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2.

Abstract Number: 0174

Clinical Presentation and Disease Course Evaluation of Mono- and Bilateral Knee Arthritis: Results from the Leiden Early Arthritis Clinic Cohort

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Patients presenting with arthritis in one or both knees propose a challenge regarding diagnosis, prognosis and treatment decisions. The aim of the current study was to characterize patients with knee arthritis who presented to the Leiden EAC and to evaluate the disease course and treatment decisions in the first year of follow-up.

Methods: Patients with arthritis confined to the knee(s) were selected from all patients included in the EAC between 1993 and 2015. Medical files were revised for information on treatment and clinical outcomes. Baseline characteristics were summarized, treatment and outcome was evaluated at 3 and 12 months. Patients were stratified over 4 groups: 1. Early sustained remission (remission at 3 months and no flare in the first year); 2. Late remission (remission at 12 months); 3. Persistent gonarthritis at 12 months; 4. Progression to oligo- or polyarthritis at 12 months. Baseline characteristics were compared between the patients in early sustained remission and the patients with gonarthritis and/or progression at 12 months. The initial medication choices and cumulative treatment within the first year were evaluated.

Results: In total 206 consecutive patients with mono- (174, 85%), and bilateral- (32, 15%) knee arthritis were evaluated. At 12 months, 120 patients could be evaluated: 27 (23%) were in early sustained remission, 41 (34%) were in late remission, 40 (33%) had persistent gonarthritis, and 12 (10%) had progressed to oligo-/poly arthritis. In total 84 (41%) patients were lost to follow-up before 12 months (most likely not progressive or persistent). No differences in baseline characteristics were identified between the patients in early sustained remission vs. the patients with

Table 1. Baseline characteristics – stratified analysis

	Early sustained remission N=27	Persistent gonarthritis/ progression N=52	P-value
Age, years	46.9 (3.6)	44.7 (2.3)	0.60
Female, %	55.6	53.8	0.89
Mono knee, %	14.8	21.2	0.50
RF positive, %	3.7	13.7	0.25
ACPA positive, %	4.8	17.1	0.25
Symptom duration, days	84 (25-84)	92 (41-175)	0.23
DAS	1.8 (0.35)	2.0 (0.15)	0.69
ESR	45 (16-49)	22 (11-48)	0.53

RF: rheumatoid factor; ACPA: anti citrullinated protein antibodies; DAS: disease activity score; ESR: erythrocyte sedimentation rate. P-value comparing the group in "early sustained remission" and the group with "persistent gonarthritis/progression to oligo-/polyarthritis" using Fishers exact test.

Table 2. Cumulative treatment within the first year of follow-up – stratified analysis

Treatment group	Early sustained remission N=27	Late remission N=41	Persistent gonarthritis N=40	Progression to oligo-/polyarthritis N=12	P-value
NSAID only	**12 (44)**	9 (22)	5 (13)	1 (8)	**0.015**
IA corticosteroid injection(s)	**8 (30)**	21 (51)	28 (70)	9 (75)	**0.005**
Prednisone (oral)	1 (4)	4 (10)	1 (3)	2 (17)	0.23
Antibiotics	4 (15)	5 (12)	2 (5)	2 (17)	0.42
csDMARD(s)	2 (7)	6 (15)	11 (28)	**6 (50)**	**0.013**
bDMARD(s)	-	1 (2)	-	-	-
Yttrium	-	-	1 (3)	-	-
Colchicine/Allopurinol	1 (4)	1 (2)	2 (5)	-	0.89

Values are the number (and % of patients within this stratum) of patients ever using drugs from this class within the first year of follow-up. IA: intra articular. p: Comparing the four stratification groups using Fishers exact test.

gonarthritis or oligo-polyarthritis at 12 months (table 1). The initial therapy was similar in all groups (data not shown). During the first year, in 31% patients treatment remained limited to NSAIDs, most often in group 1 (p =0.015). IACs were (also) administered to 46%, mainly in group 2, 3 and 4 (p=0.005). Prednisone was prescribed in 5% of patients. CsDMARDs (and < 1% subsequently a bDMARD) were (also) prescribed in 15% of patients (most frequently in group 4 (p=0.013)). The frequencies of other treatment did not differ between the groups (table 2).

Conclusion: Of 206 consecutive patients with undifferentiated arthritis limited to the knee(s) the majority were in remission or lost to follow up after 12 months. Progression to arthritis in other joints was relatively rare. Baseline characteristics could not predict the disease course at presentation and initial treatment choices suggest that physicians could not either. To timely start appropriate treatment, more research is needed to identify disease characteristics that predict chronicity or progression and identify patients that could profit from early, more effective therapy.

Disclosure: J. Maassen, None; **X. Matthijssen**, None; **S. Bergstra**, None; **C. Allaart**, None.

Abstract Number: 0175

Associations Between Circulating Cytokines and Incident Inflammatory Arthritis in an Anti-citrullinated Protein Antibody Positive Population

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SESSION INFORMATION

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Background/Purpose: Elevated circulating cytokines are present years before the onset of rheumatoid arthritis (RA). We conducted a prospective cohort study in an at-risk population of anti-cyclic citrullinated peptide (CCP) antibody positive individuals to determine if serum cytokines predict the development of incident inflammatory arthritis (IA).

Table 1. Study population characteristics at baseline by incident IA status, N=137			
Characteristic	**No IA (n=108)**	**Incident IA (n=29)**	**p-value**
Age at baseline, years, mean (SD)	54.5 (13.4)	49.7 (14.9)	0.12
Gender, Female	76 (70.4)	18 (62.1)	0.39
Race/ethnicity, non-Hispanic white	91 (84.3)	21 (72.4)	0.14
Education, > high school	84 (78.5)	25 (86.2)	0.35
Income, > $40,000	76 (76.0)	21 (75.0)	0.91
Shared epitope, positive	49 (45.4)	20 (69.0)	0.02
Smoker, ever	44 (41.1)	11 (37.9)	0.76
All values n% unless otherwise stated.			

Table 2. Hazard ratios for the association of serum cytokines with incident IA (n=29 events)			
	HR	**95% CI**	**p-value**
IL-6	1.27	0.93, 1.74	0.13
IL-8	0.91	0.49, 1.68	0.76
TNF-α	1.97	1.08, 3.58	0.02
Models adjusted for cohort, age at baseline, and shared epitope status.			

Methods: Participants were recruited into the cohort if they were a first degree relative (FDR) of a RA proband or were screened at health fairs. For the present analysis we included n=137 CCP positive participants contributing 508 person-years of follow-up for the appearance of IA (CCP3.1 Inova). During follow-up 29 participants developed IA (defined as having at least 1 joint consistent with RA-like synovitis based on exam), and of those participants 22 were classified as RA by 2010 ACR/EULAR criteria. The concentrations of interleukin (IL)-6, IL-8 and tumor necrosis factor (TNF)-α were quantified from stored serum at baseline and each follow-up visit for a total of n=525 visits. Each of these cytokines and chemokines have previously been implicated in RA pathogenesis. We conducted a survival (i.e. time-to-event) analysis using Cox proportional hazard models with log transformed cytokine concentrations as time-varying predictors and obtained hazard ratios (HRs) and 95% confidence intervals (CIs).

Results: Baseline characteristics by incident IA status are presented in Table 1. Participants who went on to develop IA were significantly more likely to test positive for the shared epitope compared to participants who did not develop IA (p-value = 0.02). We found a significant positive association of serum TNF-α with incident IA risk, adjusting for cohort (FDR or screened), shared epitope status and age at baseline (adjusted HR: 1.97; 95%CI: 1.08, 3.58). The association of IL-6 and IA risk trended in the same direction but did not reach statistical significance (adjusted HR: 1.27; 95%CI: 0.93, 1.74).

Conclusion: In a cohort of DMARD untreated CCP positive individuals, we demonstrated that circulating levels of TNF-α, a potential indicator of systemic inflammation, was positively associated with incident IA. This finding further supports the dysregulation or failure in the ability to resolve inflammation in preclinical RA patients.

Disclosure: K. Polinski, Pfizer, 2; **E. Bemis**, None; **M. Demoruelle**, Pfizer, 2; **M. Feser**, None; **L. Moss**, None; **J. Seifert**, Janssen, 2; **M. Clare-Salzler**, None; **W. Robinson**, None; **V. Holers**, AdMIRx, 1, 2, 4, 5, 6, Alexion, 7, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 5, Janssen R&D, 2, 5, Pfizer, 2; **K. Deane**, Bristol-Myers Squibb, 5, Inova, 9, Janssen, 2, 5, Janssen R&D, 2, Microdrop, 5, Pfizer, 2; **J. Norris**, BMS, 5, Celgene, 5, Janssen R&D, 2, Pfizer, 2.

Abstract Number: 0176

The Epidemiology of Rheumatoid Arthritis in the Czech Republic

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health Poster I: RA

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To describe the epidemiology of Rheumatoid Arthritis (RA) in the Czech Republic (CZ)

Methods: We used the administrative database of the National Registry of Reimbursed Health Services (NRRHS) operated by the Czech Institute of Health Information and Statistics (IHIS) to estimate the incidence and prevalence of RA. NRRHS contains all administrative claims data collected for purposes of health system management as part of all public medical insurance plans for the period 2010-17. Data on all Czech citizens seeking healthcare are captured in this billing database, as medical insurance is mandatory in CZ. Cases of RA were identified using the following algorithm: at least 2 physician service claims (over 1 year) with ICD-10 code for RA (M05, M06) as the main diagnosis, with at least 1 of these claims originating from a rheumatologist AND at least one prescription for an oral glucocorticoid, csDMARD or bDMARD. We calculated crude and age and sex–standardized prevalence and incidence rates (with corresponding 95% confidence intervals [95% CIs]) among patients age ≥18 years over the period 2012–2017. The numerator represents all patients with RA, and the denominator represents all persons age >18 years living in CZ for the relevant year for prevalence or persons age >18 years at risk for incidence. Prevalent cases were carried forward for each year. We used a 2-year "run-in" period (2010-2011) to distinguish between incident and prevalent cases, allowing rates to be reported from 2012 onward. All analyses were performed by IHIS using Vertica database and IBM SPSS statistical software, version 25.0.0.1.

Results: As of 2017, there were 86,906 Czechs with RA, corresponding to a cumulative prevalence of 1.01%. Age and sex–standardized RA prevalence for population in 2017 increased over time from 685 (95% confidence interval [95% CI] 679 – 690) per 100,000 population (0.65 %) in 2012 to 1,015 (95% CI 1,008 – 1,022) per 100,000 population (1.01 %) in 2017. Age and sex–standardized incidence per 100,000 population ranged from 118 (95% CI 116 - 121) in 2012 to 80 (95% CI 78-82) in 2017. See table 1. Mean (SD) age at diagnosis was 59 (14) years, and 73% cases were

	Prevalence					Incidence[2]				
Year	No. of RA cases	Population	[1]Crude estimate	Crude %	[2] Standardized rate (95% CI)	No. of new RA cases	Population at risk	[1]Crude estimate	Crude %	[2] Standardized rate (95% CI)
2012	55,616	8,556,018	650	0.65	685 (679–690)	9,604	8,500,402	113	0.11	118 (116–121)
2013	62,673	8,563,023	732	0.73	765 (759–771)	8,077	8,500,350	95	0.10	99 (97–101)
2014	69,703	8,568,015	814	0.81	841 (835–847)	8,198	8,498,312	96	0.10	99 (97–101)
2015	76,061	8,566,285	888	0.89	908 (901–914)	7,633	8,490,224	90	0.09	92 (89–94)
2016	81,806	8,564,814	955	0.96	966 (959–972)	7,298	8,483,008	86	0.09	87 (85–89)
2017	86,906	8,563,563	1,015	1.01	1 015 (1,008–1,022)	6,754	8,476,657	80	0.08	80 (78–82)

RA = rheumatoid arthritis; 95% CI = 95% confidence interval.
[1] Standardized rates are per 100,000 population (age >18) for prevalence and per 100,000 population at risk (age >18) for incidence.
[2] Standardized by age and sex based on population (age >18) of Czech Republic in 2017 for prevalence and population at risk (age >18) of Czech Republic in 2017.

Table 1. Crude and age and sex–standardized prevalence and incidence of RA by year

female. The direction of the time trends in incidence and prevalence were similar across various age groups and both sexes, and the slopes of the curves appeared to be steeper in older individuals.

Conclusion: Over a 6-year period, we observed an increase in RA prevalence over time. This rise may be attributed to the increasing time to ascertain cases, increasing survival, and/or an increase in the aging background population. Incidence appears to decreasing.

Disclaimer: This study was supported by the project of MHCR for conceptual development of research organization 00023728Table 1. Crude and age and sex–standardized prevalence and incidence of RA by year

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Abstract Number: 0177

Early Retirement Attributed to Rheumatoid Arthritis and Its Predictors in Portugal

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
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Session Time: 9:00AM–11:00AM

Background/Purpose: Work disability is a common consequence of Rheumatoid Arthritis (RA) with economic implications for both the patient and society. Scarce information is available on the possible causes for early retirement of RA patients in Portugal.

Aim: To evaluate the rate of early retirement due to RA in Portugal. Secondary aim consists in the identification of its main predictors.

Methods: Multicentric retrospective cohort study involving eleven portuguese rheumatology centers, including patients with RA according the ACR/EULAR 2010 or the 1987 ACR Classification Criteria for RA, based on Reuma.pt, the Portuguese Register of Rheumatic Diseases. Patients retired prior to RA diagnosis, never-employed or with missing information on current work status were excluded. Retirement due to RA versus non-retirement were compared using T-test or Chi-2 test as adequate. Variables with $p< 0,05$ in univariate analysis, and other potential predictors selected on clinical and epidemiological grounds, were included in multivariable binary logistic regression, while adjusting for potential confounding or contributing factors.

Results: 3231 patients were included (81,5% female, aged 60,8 ± 13,0 years, mean disease duration 18,0 ± 10,3 years). Until the present time, 37,6% (n=1216) of the patients retired, this being due to RA in 59,6% of the cases. Early retirement due to RA translated into 7 years of active work being lost when compared to patients retired to other

Table 1. Clinical and epidemiological characteristics of the study population.

	Early retired due to RA (n=725)	Non-retired (n=2015)	p
Current age (mean ± SD, years)	67,7 ± 9,73	55,64 ± 11,77	<0,001
Gender (female, %)	84,4	82,4	0,249
Smokers (%)	20,2	30,6	<0,001
Hypertension (%)	38,9	22,9	<0,001
Diabetes mellitus (%)	10,7	5,9	<0,001
Cardiovascular disease (%)	10,0	4,1	<0,001
Age of diagnosis (mean ± SD, years)	44,59 ± 12,24	42,74 ± 12,18	0,001
Disease duration (mean ± SD, years)	24,82 ± 10,38	15,03 ± 8,81	<0,001
Time until diagnosis (mean ± SD, years)	2,67 ± 4,58	2,06 ± 4,12	0,003
Rheumatoid factor (%)	75,9	71,9	0,043
Anti-CCP (%)	73,7	72,6	0,679
Erosive disease (%)	83,9	56,7	<0,001
Occupation type (blue collar, %)	58,1	41,9	<0,001
Educational level (mean ± SD, school-years)	5,00 ± 2,78	8,71 ± 4,49	<0,001

causes (49,6 ± 9,5 vs. 56,6 ± 9,8 years). Compared to patients that are still professionally active, patients retired due to RA were diagnosed later in the disease process (2,7 ± 4,6 vs. 2,0 ± 4,1 years from first symptoms to RA diagnosis, p=0,003), had longer disease duration (24,8 ± 10,4 vs. 15,0 ± 8,8 years at the time of retirement, p< 0,001), were more likely positive for rheumatoid factor (75,9% vs. 71,9%, p=0,043), to present erosive disease (83,9% vs. 56,7%, p< 0,001), have a blue collar occupation (58,1% vs. 41,9%, p< 0,001) and have a lower educational level (5,0 ± 2,8 vs. 8,7 ± 4,5 school-years, p< 0,001). After multivariate analysis, independent predictors for early retirement due to RA were: later diagnosis (OR: 2,23; 95% CI 1,18-4,21/year, p=0,013), erosive disease (OR: 2,21 95% CI 1,54-3,16, p < 0,001), need for biologic therapy (OR: 1,32; 95%CI 1,01-1,73, p=0,045) and lower educational level (OR: 0,83; 95%CI 0,79-0,86/year, p< 0,001). Although a blue collar occupation was associated with a higher prevalence of early retirement, this association does not stand after adjusting for educational level (OR: 0,822; 95% CI 0,654-1,033).

Conclusion: RA itself is the leading cause of early retirement in RA patients, being responsible for the loss of an average of 7 years of work. Late diagnosis, presence of poor prognosis factors (such as erosive disease and the need for biologic therapy) and lower educational level are the main predictors of early retirement associated with RA in Portugal.

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Abstract Number: 0178

Depression: A Common Comorbidity in Rheumatic Diseases. a Case-Control Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Depression is a frequent comorbidity in rheumatic diseases (RD) and it is associated with chronic pain and long-term medical treatment in these patients. Furthermore, studies have reported the impact of depression in these population and it is consistently associated with the severity and sensitivity to pain, poor treatment outcomes, disease activity and potentially with early mortality. The Patient Health Questionnaire 9 (PHQ-9) is an extensively validated screening tool. It has several advantages: it is more accurate than other screening tools with 88% of sensitivity and 88% specificity, it is self-applied and able to be used by any clinician. Thus, the aim of this study was to determine the prevalence of depression in a group of RD patients and compare it to non-rheumatic controls.

Methods: An observational, cross-sectional study was designed. Patients were recruited at a community educational healthcare conference. Population was divided into two groups: patients with and without RD. A complete history with information about exercise and the PHQ-9 screening tool were performed to every subject. Subjects without RD

Table 1. Demographic Characteristics

	Case (n= 131)	Control (n =126)	*p*
Female*	117 (89.3)	99 (78.6)	**0.019**
Age**	52 ± 13	53 ± 16	0.837
Active smoking*	9 (7.1)	10 (8.2)	0.755
Sedentary*	72 (56.7)	61 (50.4)	0.322
Arterial hypertension*	28 (21.7)	35 (28.2)	0.231
T2DM*	11 (8.7)	22 (17.9)	**0.033**
Dyslipidemia*	32 (25.6)	47 (29.2)	**0.023**
Rheumatoid Arthritis*	102 (40.1)	-	
Systemic Lupus Erythematosus*	7 (2.7)	-	
Sjögren Syndrome*	7 (2.7)	-	
Spondylitis*	6 (2.3)	-	
Scleroderma*	4 (1.6)	-	
Psoriatic arthritis*	3 (1.2)	-	
Dermatomyositis*	1 (0.4)	-	
*- variable reported as: n (%), **-variable reported as: media ±			

Table 2. Patient Health Questionnaire – 9			
	Case n=131	Control n=126	*p*
PHQ-9*	7 (3-12)	4 (1-9)	**0.009**
Normal 0-4**	48 (18.7)	65 (25.3)	**0.016**
Depression	83 (32.3)	61 (25.3)	
Mild 5-10**	33 (12.8)	32 (12.5)	
Moderate 10-14**	26 (10.1)	13 (5.1)	
Moderate severe 15-19**	14 (5.4)	7 (2.7)	
Severe 20-27**	10 (3.9)	9 (3.5)	
*-variable reported as: n (%), **-variable reported as: median (p25-p75)			

were recruited as controls. Descriptive analysis was done using frequencies (%) and median (q25-q75). Comparisons were done using Chi-square and Mann Whitney-U test, considering $p < 0.05$ as significant.

Results: A total of 257 subjects were included. Demographic characteristics are shown in Table 1. Patients with RD have greater scores of PHQ-9 with a median of 7 points (p25-p75, 3-12) than controls with a median of 4 (q25-q75, 1-9) (p= 0.009). In the case group, 83 patients (32.8%) have diagnosis of depression and 61 (25.3%) of the controls (p= 0.016).

Subjects with an inactive lifestyle have a higher prevalence of depression, being sedentary in both groups has an OR 3.246 (IC 1.92 to 5.47), p< 0.001. Sedentarism is highly significant in controls (p < 0.001), but not in RD (p=0.085).

Conclusion: Patients with RD have a higher prevalence of depression than non-rheumatic subjects. An inactive lifestyle was associated with a higher prevalence of depression in both, those with and without RD. The physicians should be aware of it and use screening tools for early detection and provide a multimodal management.

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Abstract Number: 0179

The Burden of Comorbidity in Patients with RA, PSA or SPA in a General Practice Registry

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SESSION INFORMATION
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Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA), psoriatic arthritis (PSA) and spondyloarthritis (SPA) are the most common inflammatory rheumatic diseases, associated with a high burden of comorbidities and polypharmacy, especially analgesics. Thus, we compared comorbidity burden and usage of pain-related medication in patient with RA, PSA and SPA versus controls in a general practitioner (GP) setting.

Table 1: Comorbidity incidence rates after a 3-year follow up period

	Crude Incidence Rate of comorbidity per 1000-person years					
	RA n=738	Controls n=2952	SPA n=229	Controls n=916	PSA n=167	Controls n=668
Lung Disease	16.73	13.74	8.98	12.39	10.38	13.43
Cardiovascular disease	24.84	17.31	7.04	6.94	20.29	10.98
Hypertension	29.68	21.97	7.21	13.21	10.58	10.74
Fracture	8.58	9.08	10.18	4.74	7.16	5.18
Depression	7.54	11.53	5.39	6.98	11.10	6.24
Diabetes mellitus	17.84	12.33	3.40	7.70	9.73	7.19
Digestive disease	15.04	13.27	22.46	17.39	11.20	10.24
Malignancies	11.86	20.22	5.05	10.64	17.34	8.69

Crude incidence rate per 1000 is calculated as the number of new cases divided by the total persons years of persons at risk (not having comorbidity at baseline) with a maximum of 3 years of follow-up per person.

Table 2: Prevalent medication use in RA, SPA and PSA patients versus controls

Medication	RA n=738	Controls n=2952	SPA n=229	Controls n=916	PSA n=167	Controls n=668
Glucocorticoids	241(33%)	348(12%)	29(13%)	70(8%)	47(28%)	67(10%)
NSAIDs	455(62%)	1156(39%)	161(70%)	340(37%)	114(68%)	267(40%)
Opioids	164(22%)	366(12%)	46(20%)	71(8%)	30(18%)	64(10%)
Paracetamol	233(32%)	598(20%)	63(28%)	165(18%)	51(31%)	141(21%)

Methods: Data over a 13-year time interval (1999-2012) were obtained from a Flemish GP-based morbidity registration network, called Intego that covers 2% of the Flemish general population. Patients classified on the International Classification of Primary Care (ICPC) codes L88 (rheumatoid/seropositive arthritis) and L99 (musculoskeletal disease other) were selected for this study. Experienced rheumatologists verified if the codes corresponded to a diagnosis of RA/SPA/PSA. Diagnosis date in Intego was considered “baseline”. Per case, 4 controls were selected from all other ICPC codes and matched with cases by age, gender, GP practice, and date of diagnosis. The total comorbidity burden was summarised by calculating the Rheumatic Disease Comorbidity Index (RDCI) score at baseline and after 3 years. RDCI ranges from 0-9, with 9 being the highest comorbidity burden. Incidence rates of comorbidities included in this index were calculated. Prevalent analgesic medication use in RA/SPA/PSA patients versus controls was determined. Mann Whitney and $\chi 2$ tests were used when appropriate.

Results: Over the 13-year period, 738, 229 and 167 patients were included with a diagnosis of RA (mean(SD) age 57.7(17.2), 68% female), SPA (mean(SD) age 40.6(15.1), 50% female) and PSA (mean(SD) age of 47(13.2), 48% female), respectively.

The mean(SD) RDCI at baseline was 1.2(1.4), 0.6(1.0) and 1.0(1.3) for RA, SPA or PSA respectively. After 3 years, the mean(SD) RDCI was 1.5(1.6), 0.8(1.2) and 1.3(1.4) for RA, SPA or PSA respectively. The RDCI differed after 3 years between RA and controls (1.5(1.6) versus 1.4(1.5), p=0.008), and PSA and controls (1.3(1.4) versus 1.0(1.4), p=0.009). In RA, at baseline 58% of individuals had an RDCI score ≥1 (versus 53% controls, p=0.01) and after 3 years, 66% of individuals had an RDCI score ≥1 (versus 60% controls, p=0.004). In SPA, at baseline 36% of individuals had an

RDCI score ≥1 (versus 34% controls, p=0.6) and after 3 years, 45% of individuals had an RDCI score ≥1 (versus 41% controls, p=0.4). In PSA, at baseline 52% of individuals had an RDCI score ≥1 (versus 42% controls, p=0.03) and after 3 years, 60% of individuals had an RDCI score ≥1 (versus 48% controls, p=0.003). Table 1 shows the incidences of selected comorbidities over 3 years. All analgesics were statistically significantly prescribed more in patients with a musculoskeletal disease versus controls (table 2).

Conclusion: This study highlights the issue of multimorbidity in patients with musculoskeletal diseases, especially for individuals with RA and PSA. The high cardiovascular burden is substantial in these two populations. The high prevalence of opioids in 1/5 patients with an inflammatory rheumatic disease is to be noted.

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Abstract Number: 0180

Identifying Comorbidities and Seropositivity in Rheumatoid Arthritis Patients Using Single-specialty Electronic Health Record Data

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SESSION INFORMATION
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Comorbidities are associated with worse clinical outcomes among patients with rheumatoid arthritis (RA), as does seropositive disease. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide (CCP) antibody status are often tested at the time of RA diagnosis but may not be repeated and therefore may not appear in a rheumatologists' electronic health record (EHR). Recent ICD10 coding allows discrimination between seropositive (M05) and seronegative (M06) patients, but the validity has not been examined. Moreover, the accuracy of identifying

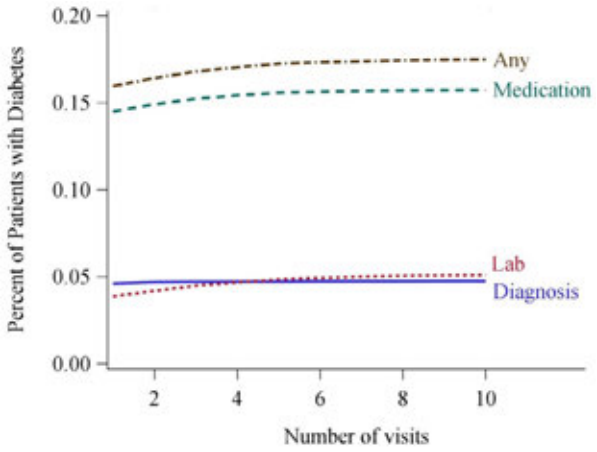

Figure 1. Number of rheumatology visits needed to stabilize diabetes prevalence in the RISE registry.

Table 1. Sensitivity and positive predicted values for identifying seropositive patients using different algorithms

Algorithm	Gold Standard	N	Sensitivity (95% CI)	PPV (95% CI)
Ever M05	RF+			
≥ 1 visit with M05/M06.* code		5941	0.86 (0.85-0.87)	0.82 (0.80-0.83)
≥2 visit with M05/M06.* code		5877	0.86 (0.85-0.87)	0.82 (0.81-0.83)
≥3 visit with M05/M06.* code		5818	0.86 (0.85-0.88)	0.82 (0.81-0.83)
Most Recent RA diagnosis code of M05.*	RF+			
≥1 visit with M05/M06.* code		5941	0.82 (0.81-0.84)	0.84 (0.83-0.85)
≥2 visit with M05/M06.* code		5877	0.82 (0.81-0.84)	0.84 (0.83-0.86)
≥3 visit with M05/M06.* code		5818	0.82 (0.81-0.84)	0.85 (0.83-0.86)
Ever M05	CCP+			
≥1 visit with M05/M06.* code		7090	0.87 (0.86-0.88)	0.68 (0.66-0.69)
≥2 visit with M05/M06.* code		7002	0.87 (0.85-0.88)	0.68 (0.66-0.69)
≥3 visit with M05/M06.* code		6924	0.87 (0.85-0.88)	0.68 (0.67-0.69)
Most Recent RA diagnosis code of M05.*	CCP++			
≥1 visit with M05/M06.* code		7090	0.83 (0.82-0.84)	0.70 (0.68-0.71)
≥2 visit with M05/M06.* code		7002	0.83 (0.82-0.84)	0.70 (0.68-0.71)
≥3 visit with M05/M06.* code		6924	0.83 (0.82-0.84)	0.70 (0.69-0.71)
Ever M05	RF+ or CCP+			
≥1 visit with M05/M06.* code		7953	0.83 (0.82-0.84)	0.83 (0.82-0.84)
≥2 visit with M05/M06.* code		7848	0.83 (0.82-0.84)	0.83 (0.82-0.84)
≥3 visit with M05/M06.* code		7759	0.83 (0.82-0.84)	0.83 (0.82-0.84)
Most Recent RA diagnosis code of M05.*	RF+ or CCP+			
≥1 visit with M05/M06.* code		7953	0.79 (0.78-0.80)	0.85 (0.84-0.86)
≥2 visit with M05/M06.* code		7848	0.79 (0.78-0.81)	0.85 (0.84-0.86)
≥3 visit with M05/M06.* code		7759	0.79 (0.78-0.81)	0.86 (0.85-0.87)

comorbidities that may not be managed, nor coded, in rheumatologists' EHRs has received little attention. We used a national rheumatology-based EHR registry to examine ICD10 coding to assess the accuracy of seropositive RA classification, and used a confluence of data (diagnoses, drugs, and lab results) to identify diabetes as an example of a common comorbidity that might be relevant for RA.

Methods: Using the ACR's Rheumatology Informatics System for Effectiveness (RISE) EHR-based registry, we created a RA cohort requiring patients to have ≥ 2 rheumatologist visits. Seropositive RA patients were defined as ever have any ICD10 diagnosis code of M05 (i.e. 'with RF'), as well as several permutations of the M05 code (requiring >=2 diagnoses, using the last code, etc). Using RF or anti-CCP lab tests as the gold standard, we calculated sensitivity (Se) and positive predicted value (PPV) based on number of diagnosis codes for RA and different combinations of RF and CCP. We identified diabetes based on ≥ 1ICD9/10 diagnosis code (ICD9: 250.*0, 250.*2; ICD10: E11*); prior prescriptions for diabetes, or elevated laboratory test (hemoglobin A1C ≥ 6.5% or random glucose >200 or fasting glucose ≥ 126mg/dl). We also evaluated the number of physician visits needed to stabilize the prevalence estimate for diabetes.

Results: Among 22,340 eligible RA patients, 5,941 (27%) patients had a lab test for RF (ever), 7,090 (32%) had a test for CCP, and 7,953 (36%) had tests for RF or CCP. Using RF result as the gold standard, the Se for seropositivity using any M05 diagnosis code was 0.86, PPV 0.82; similarly, using CCP as the gold standard, the Se was 0.87 and PPV was 0.68. Combining (RF or CCP), the Se was 0.83 and PPV was 0.83. Requiring additional diagnosis codes, or examining the last code, minimally improved Se and PPV.

Among RA patients with diabetes, 90% were identified as having diabetes medications, 32% by diagnosis codes and 28% by laboratory tests. Diabetes medications by themselves accounted for 51% of all diabetes classification. Using all three types of data, the prevalence of diabetes (17% overall) stabilized after 2 physician visits (Figure 1).

Conclusion: Under ICD10, M05 is a reasonable proxy to identify seropositive RA patients with high sensitivity and positive predictive values. Comorbidities not usually managed by rheumatologists can be identified in a single-specialty EHR like RISE, and identification will be greatly facilitated if specific drugs for those conditions are used.

Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.Figure 1: Number of rheumatology visits needed to stabilize diabetes prevalence in the RISE registry

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Abstract Number: 0181

Prevalence of Renal Impairment in a US Rheumatoid Arthritis Population

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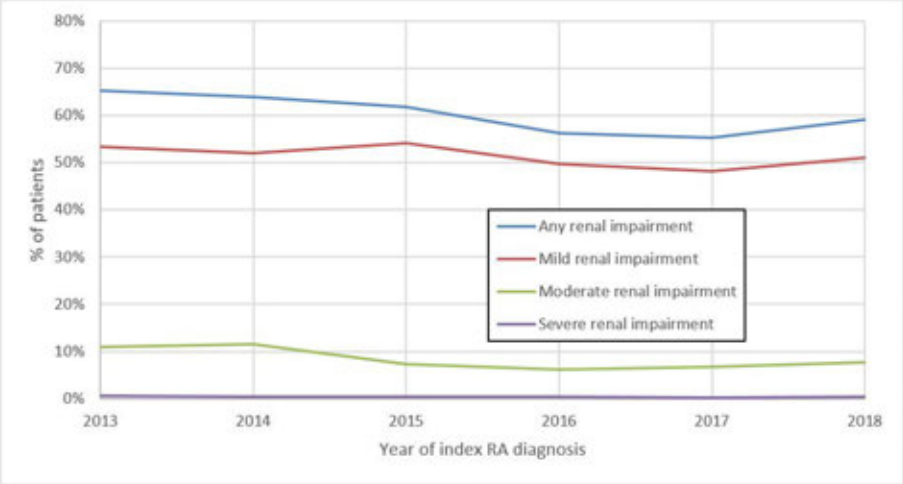
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Table 1. Prevalence of renal impairment overall and by severity category

Severity of renal impairment[a]	All patients[b] (n = 42,173)	Patients treated with advanced therapies[c] (n = 16,197)
Mild (eGFR 60-90 mL/min/1.73m^2), %	52.1	50.9
Moderate (eGFR 30-59 mL/min/1.73m^2), %	9.3	7.0
Severe (eGFR <30 mL/min/1.73m^2), %	0.5	0.3
Overall (any impairment level), %	61.9	58.2

eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; SCr, serum creatinine.
[a] MDRD equation: 175 x standardized SCr$^{(-1.154)}$ x age$^{(-0.203)}$ x 0.742 (if female).
[b] With at least 2 SCr laboratory test results available.
[c] Advanced therapies included abatacept, adalimumab, anakinra, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, sarilumab, tocilizumab, and tofacitinib citrate.

Figure 1. Annual prevalence of renal impairment in patients with RA and ≥2 SCr results



Background/Purpose: Clinical management of rheumatoid arthritis (RA) must consider patient renal function, particularly for medications that rely on renal clearance and require dose adjustment or restriction in the presence of renal impairment. However, estimates of the prevalence of renal impairment/chronic kidney disease (CKD) among patients with RA vary widely (5-50%).[1] This study used the Modification of Diet in Renal Disease (MDRD) equation to calculate the prevalence of estimated glomerular filtration rate (eGFR)-based renal impairment among US patients with RA in a commercially insured population, with the goal of providing current real-world data to inform RA treatment decisions in cases where such decisions may be impacted by CKD.

Methods: Claims data from the HealthCore Integrated Research Database (HIRD®) from January 2013 through December 2018 were used. All adult patients with ≥2 claims with diagnosis codes for RA were included in the study, with index date set as the earliest occurrence of an RA claim. All patients had to have ≥2 serum creatinine (SCr) laboratory measurements ≥90 days apart on or after the index date. Prevalence of eGFR-based renal impairment, including by severity category (i.e., mild, moderate, severe; see Table 1 for definitions), was calculated based on the MDRD equation (as race is a component of the MDRD equation, but is not collected in the database, individuals were designated as non-black for purposes of the calculation). Patients with conflicting severity categories based on their

2 SCr measurements were classified into the less-severe category. Possible variations in prevalence for patients on advanced therapies (biologic DMARDs or tofacitinib) were explored in subgroup analysis.

Results: There were 152,090 adult patients with RA identified in the HIRD®, with 128,062 (84%) meeting the criteria for inclusion in the study. Of these, 42,173 (33%) had ≥2 qualifying SCr laboratory results and 16,197 (13%) also initiated advanced RA therapies. Mean age was 56 years; 76% of patients were female. In this population, the estimated prevalence of renal impairment by severity is approximately 52% for mild, 9% for moderate, and < 1% for severe (Table 1). Prevalence was slightly lower among patients initiating advanced therapy. Prevalence remained relatively consistent from 2013 to 2018 (Figure 1).

Conclusion: Among commercially insured US adults with RA with ≥2 SCr results, approximately 7-10% of patients have moderate or severe CKD (eGFR < 60 mL/min/1.73m^2) that might merit dose adjustment of RA medication. Prevalence in this population was stable from 2013 to 2018. While the reported prevalence of renal impairment may tend to underestimate true prevalence due to all patients being covered by commercial insurance, it highlights that renal monitoring, DMARD dose adjustment and potential for drug toxicity remain important considerations for approximately 10% of RA patients.

Reference: (1) Couderc M, et al. Arthritis Care Res. 2016;68:638-44.

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Abstract Number: 0182

Comparing the Generalizability of Cardiovascular Risk in Different Rheumatoid Arthritis Cohorts

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health Poster I: RA

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular (CV) risk estimation across diverse rheumatoid arthritis (RA) cohorts may be challenging given potential heterogeneity in comorbidities and widely varying prevalence of CV risk factors. The generalizability of CV risk among younger disabled RA patients enrolled in the Medicare program to similarly-aged patients who are commercially insured is unclear. We aimed to compare CV rates in Medicare and Marketscan to assess comparability.

Methods: Three cohorts of rheumatoid arthritis (RA) patients 40≤ age < 65 years were created using 2006-2016 Medicare and Marketscan claims data respectively. In each dataset, Cohort 1 was defined as ≥2 diagnosis codes for RA occurring 7 -365 days apart with ≥1 diagnosis code from a rheumatologist; Cohort 2 was defined as ≥1 diagnosis code for RA from rheumatologist followed by use of disease-modifying antirheumatic drugs (DMARDS, conventional, biologic or small molecule); Cohort 3 was defined as Cohort 2, plus initiation of a new biologic/tofacitinib, used as a proxy for greater RA disease activity. Other autoimmune diseases, malignancy, past myocardial infarction (MI), or stroke were exclusionary.

Table 1. Distribution of characteristics by RA cohort and by data source

	Cohort 1			Cohort 2			Cohort 3		
	Medicare N=135,888	Marketscan N=202,926	SMD	Medicare N=119,517	Marketscan N=186,456	SMD	Medicare N=39982	Marketscan N=49712	SMD
Age in years, mean(sd)	54.8 (6.5)	53.4 (6.7)	0.20	54.7 (6.5)	53.4 (6.7)	0.21	54.3 (6.5)	53.1 (6.6)	0.20
Age			0.20			0.20			0.20
40-44	8.8	12.6		8.8	12.8		9.4	13.0	
45-49	14.0	17.2		14.1	17.5		15.5	17.9	
50-54	21.3	22.6		21.4	22.6		22.2	24.0	
55-59	26.7	25.0		26.7	24.8		26.4	25.3	
60-64	29.2	22.7		29.0	22.3		26.5	19.8	
Male	21.9	23.9	0.05	21.3	23.6	0.06	16.9	20.9	0.10
Diabetes	31.9	15.4	0.40	31.5	15.1	0.40	38.2	19.5	0.42
Hypertension	61.6	38.5	0.48	61.0	37.8	0.48	68.8	46.1	0.47
High Risk CVD	21.1	8.2	0.37	20.4	7.9	0.37	24.8	10.3	0.39
Obesity	7.0	2.7	0.20	6.9	2.7	0.20	9.2	4.6	0.18
Smoking	20.4	4.4	0.50	20.0	4.2	0.50	22.5	5.0	0.53
CKD	5.8	1.6	0.23	5.3	1.5	0.21	5.0	1.7	0.18
Steroid	59.6	53.5	0.12	62.3	56.4	0.12	73.4	72.5	0.03
Statin	31.2	21.8	0.21	31.5	22.3	0.21	31.7	22.1	0.22
Hospitalization	22.9	9.6	0.37	21.8	9.2	0.36	22.4	10.9	0.31
Number of physician visits	16.1 (10.7)	11.3 (7.2)	0.53	15.9 (10.6)	11.1 (7.2)	0.54	17.9 (11.1)	13.6 (7.8)	0.45

CKD: Chronic kidney disease; SMD: standardized mean difference; Other CVD: Other cardiovascular disease.

Cohort: 1=Two diagnosis code for rheumatoid arthritis (RA), at least 1 from rheumatologist;

2=One diagnosis code for RA followed by use of Disease-modifying antirheumatic drugs (DMARDS, biologic or small molecule);

3=Cohort 2 plus initiation of a biologic

Table 2. Crude and adjusted hazard ratios for myocardial infarction and stroke in RA cohorts, comparing Medicare to MarketScan enrollees

Cohort	Outcome	Crude HR (95% CI)	Adjusted HR 1 (95% CI)*	Adjusted HR 2 (95% CI)**	Adjusted HR 3 (95% CI)***
Cohort 1	MI	2.40(2.26-2.54)	2.27 (2.14-2.40)	1.58 (1.48-1.68)	1.50 (1.40-1.59)
	Stroke	1.68 (1.58-1.79)	1.55 (1.45-1.65)	1.10 (1.04-1.19)	1.05 (0.97-1.12)
	MI or stroke	**2.03 (1.95-2.12)**	**1.91 (1.83-1.99)**	**1.34 (1.28-1.41)**	**1.27 (1.21-1.33)**
Cohort 2	MI	2.37 (2.23-2.51)	2.24 (2.11-2.38)	1.57 (1.47-1.67)	1.48 (1.39-1.59)
	Stroke	1.65 (1.54-1.76)	1.51 (1.41-1.62)	1.09 (1.02-1.18)	1.03 (0.96-1.12)
	MI or stroke	**2.01 (1.92-2.10)**	**1.88 (1.79-1.97)**	**1.33 (1.27-1.40)**	**1.27 (1.20-1.33)**
Cohort 3	MI	1.65 (1.37-1.99)	1.65 (1.37-1.99)	1.12 (0.91-1.39)	1.10 (0.89-1.36)
	Stroke	1.64 (1.33-2.02)	1.54 (1.25-1.91)	1.09 (0.86-1.38)	1.04 (0.82-1.32)
	MI or stroke	**1.61 (1.41-1.86)**	**1.57 (1.36-1.81)**	**1.09 (0.93-1.27)**	**1.05 (1.89-1.23)**

Note: hazard ratios shown are for Medicare enrollment compared to Marketscan enrollment

* Adjusted for age and sex

** Adjusted for age, sex, diabetes, hypertension, smoking, and other CVD history

*** Adjusted for age, sex, diabetes, hypertension, other CVD history identified using all available data; Obesity, Steroid use, Statin use, all cause hospitalization and number of physician visits identified using one year baseline data

Follow up started at the earliest date of meeting the cohort definition and the requirement of one year of medical and pharmacy coverage and ended at earliest of: 1) a CV outcome (hospitalized MI or stroke, using validated algorithms); 2) end of enrollment 3) age 65 years; 4) end of biologic exposure plus 90 days (cohort 3 only).

Descriptive statistics including standardized mean differences (SMDs) and CV incidence rates (IR) were calculated, and Poisson regression used to generate confidence intervals (CI). Cox regression was used to generate hazard ratio (HR), comparing enrollment in Medicare vs. Marketscan. Models sequentially adjusted for age and sex (model 1); model 1 + diabetes, smoking, hypertension, high CV risk (model 2): and model 2 + a variety of additional risk factors (model 3).

Results: A total of 380,336 RA patients comprised cohort 1 (mean age 53.3 (SD 8.1) years for Medicare and 51.1 (SD 8.8) years for Market Scan, and 21-23% were male). All co-morbidities and medication use were more prevalent in Medicare than Marketscan. Age- and sex-specific IRs were approximately 1.5-2.5-fold greater in Medicare referent to Marketscan. After intermediate adjustment (model 2), RA patients in Medicare in cohort 2 still had higher CV risk (adjusted HR 1.33, 95% CI 1.27-1.40). However, cohort 3 requirements attenuated MI and stroke risk to be negligibly different between Medicare and Marketscan RA patients (adjusted HR 1.09, 95% CI 0.93-1.27).

Conclusion: The rate of CV events varies substantially between different RA cohorts, but multivariable adjustment and careful attention to RA-related features including medication initiation (used as a proxy to reduce heterogeneity in disease activity) can minimize these differences.

Table 2b. Age and sex-specific incidence rates for myocardial infarction (MI) and stroke by RA cohort and data source

Cohort	Outcome	Age	Sex	Medicare			Market Scan		
				Event	Person year	IR(95%CI)	Event	Person year	IR(95%CI)
1	MI	Overall		4441	596185	0.74 (0.72-0.77)	1724	614483	0.28 (0.27-0.29)
		30-44	F	242	90084	0.27 (0.24-0.30)	72	134245	0.05 (0.04-0.07)
		45-54	F	868	154642	0.56 (0.53-0.60)	326	169276	0.19 (0.17-0.21)
		55-64	F	1956	229585	0.85 (0.82-0.89)	576	171555	0.34 (0.31-0.36)
		30-44	M	109	22023	0.49 (0.41-0.60)	43	31373	0.14 (0.10-0.18)
		45-54	M	424	43257	0.98 (0.89-1.08)	238	48097	0.49 (0.44-0.56)
		55-64	M	842	56594	1.49 (1.39-1.59)	469	59931	0.78 (0.71-0.86)
	Stroke	Overall		2968	599821	0.49 (0.48-0.51)	1656	614812	0.27 (0.26-0.28)
		30-44	F	241	90073	0.27 (0.24-0.30)	125	134128	0.09 (0.08-0.11)
		45-54	F	672	155089	0.43 (0.40-0.47)	360	169173	0.21 (0.19-0.24)
		55-64	F	1395	230962	0.60 (0.57-0.64)	702	171373	0.41 (0.38-0.44)
		30-44	M	51	22214	0.23 (0.17-0.30)	29	31441	0.09 (0.06-0.13)
		45-54	M	196	43979	0.45 (0.39-0.51)	129	48381	0.27 (0.22-0.32)
		55-64	M	413	57504	0.72 (0.65-0.79)	311	60310	0.52 (0.46-0.58)
2	MI	Overall		3886	530685	0.73 (0.71-0.76)	1595	570845	0.28 (0.27-0.29)
		30-44	F	219	81601	0.27 (0.24-0.31)	70	125820	0.06 (0.04-0.07)
		45-54	F	784	138334	0.57 (0.53-0.61)	298	158653	0.19 (0.17-0.21)
		55-64	F	1732	204401	0.85 (0.81-0.89)	528	157952	0.33 (0.31-0.36)
		18-44	M	87	19535	0.45 (0.36-0.55)	42	29021	0.14 (0.11-0.20)
		45-54	M	362	37924	0.95 (0.86-1.06)	221	45053	0.49 (0.43-0.56)
		55-64	M	702	48892	1.44 (1.23-1.55)	436	54340	0.80 (0.73-0.88)
	Stroke	Overall		2556	534038	0.48 (0.46-0.50)	1515	571139	0.27 (0.25-0.28)
		30-44	F	221	81589	0.27 (0.24-0.31)	128	125715	0.10 (0.09-0.12)
		45-54	F	562	138834	0.40 (0.37-0.44)	344	158510	0.22 (0.20-0.24)
		55-64	F	1225	205693	0.60 (0.56-0.63)	642	157739	0.41 (0.38-0.44)
		30-44	M	40	19707	0.20 (0.15-0.28)	27	29097	0.09 (0.06-0.14)
		45-54	M	164	38579	0.43 (0.36-0.50)	120	45320	0.26 (0.22-0.32)
		55-64	M	344	49635	0.62 (0.62-0.77)	254	54753	0.46 (0.41-0.52)
3	MI	Overall		284	55510	0.51 (0.46-0.57)	184	63654	0.29 (0.25-0.33)
		30-44	F	17	8422	0.20 (0.13-0.32)	4	13615	0.03 (0.01-0.08)
		45-54	F	71	15180	0.47 (0.37-0.59)	31	18042	0.17 (0.12-0.24)
		55-64	F	111	22396	0.50 (0.41-0.60)	65	18452	0.35 (0.28-0.45)
		30-44	M	<11	redacted	0.24 (0.09-0.65)	1	2840	0.04 (0.00-0.25)
		45-54	M	26	3630	0.72 (0.49-1.05)	31	4777	0.65 (0.46-0.92)
		55-64	M	55	4242	1.30 (1.00-1.69)	52	5927	0.88 (0.66-1.15)
	Stroke	Overall		229	55565	0.41 (0.36-0.47)	157	63699	0.25 (0.21-0.29)
		30-44	F	17	8407	0.20 (0.13-0.33)	17	13612	0.12 (0.08-0.20)
		45-54	F	50	15213	0.33 (0.25-0.43)	42	18038	0.23 (0.17-0.32)
		55-64	F	121	22392	0.54 (0.45-0.65)	63	18449	0.34 (0.27-0.44)
		30-44	M	<11	redacted	0.18 (0.06-0.57)	2	2841	0.07 (0.02-0.28)
		45-54	M	<11	redacted	0.27 (0.15-0.51)	13	4800	0.27 (0.16-0.47)
		55-64	M	28	4259	0.66 (0.45-0.95)	20	5957	0.34 (0.22-0.52)

Cohort: 1=Two diagnosis code for rheumatoid arthritis (RA), at least is from rheumatologist; 2= One diagnosis code for RA followed by use of Disease-modifying antirheumatic drugs (DMARDS, biologic or small molecule); 3=biologic DMARDS agent naïve user (no prior use for that specific biologic DMARDS), at least one diagnosis code for RA from rheumatologist.

CI: Confidence interval; IR: Incidence rate; MI: myocardial infarction.

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Abstract Number: 0183

Exploring Heterogeneity in Rheumatoid Arthritis: Patient Profiling Through Principal Component and Cluster Analysis of the BRASS Registry

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health Poster I: RA

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Data-driven principal component (PC) and cluster analysis has the potential to identify previously unknown patient subgroups within a rheumatoid arthritis (RA) registry to establish prognosis, predict disease trajectory, and help inform treatment. The Brigham and Women's Rheumatoid Arthritis Sequential Study (BRASS), established in 2003, is a single-center, prospective observational registry cohort providing a comprehensive set of clinical disease activity measures in >1400 patients with RA. Our objective was to use PC and cluster analysis of baseline demographic, socio-economic, health and disease characteristics in BRASS to identify and characterize distinct patient clusters in RA.

Methods: Patient variables recorded at entry into BRASS were refined and combined using PC analysis to reduce dimensionality and collinearity. The number of PCs was established by eigenvalue >1, cumulative variance, and interpretability. Patients were clustered using a k-means approach with non-hierarchical, exclusive, and complete clustering, with minimum cluster size 5% of population, and maximum 19 clusters. The final number of clusters was determined according to the cubic clustering criterion and pseudo F.

Results: Analysis of baseline data from 1443 patients identified 41 PCs that capture the fundamental characteristics involved in RA. Cluster analysis distinguished 5 patient clusters. Each cluster reflected a different profile of PCs, and can be described based on overall health, RA disease activity and duration (Table). Key differentiators between clusters include comorbidity PCs (metabolic comorbidities predominate in cluster 1, neurologic in cluster 4, and orthopedic in cluster 5) and patient characteristics/social PCs (greatest number of doctor visits and family history of MI in cluster 3, greatest BMI in cluster 1, highest income in cluster 2, lowest income in cluster 5, and least emotional support in cluster 1).

Conclusion: Data-driven cluster analysis of RA patient characteristics at entry into the BRASS registry identified five distinct patient phenotypes, providing a convenient method to potentially derive novel insights into the multifactorial drivers, commonly co-occurring health conditions, and manifestations of RA. Investigation of longitudinal outcomes in these different clusters in the BRASS registry and validation in an independent dataset is ongoing.

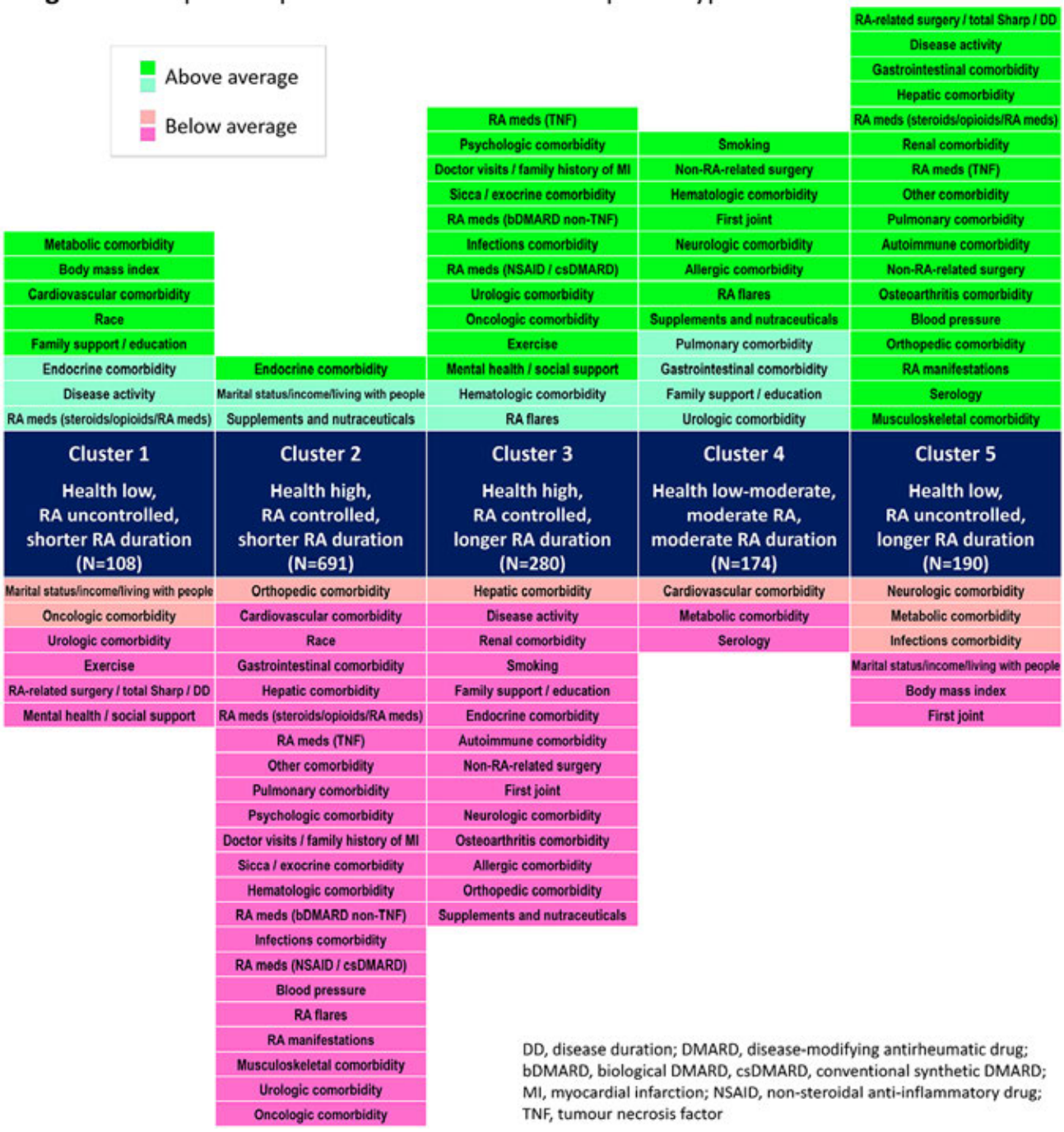
Table. Summary of clusters

	N	Summary descriptor	Patients, %				
					RA duration, years		
			≤1 comorbidity*	CDAI ≤10	<5	5–20	>20
1	108	Health low, RA uncontrolled, shorter RA duration	7%	28%	37%	38%	25%
2	691	Health high, RA controlled, shorter RA duration	59%	43%	46%	37%	17%
3	280	Health high, RA controlled, longer RA duration	48%	46%	24%	45%	31%
4	174	Health low-moderate, moderate RA, moderate RA duration	36%	36%	26%	50%	24%
5	190	Health low, RA uncontrolled, longer RA duration	30%	24%	12%	33%	55%

*Charlson Comorbidity index

Disclosure: J. Curtis, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **M. Weinblatt**, Abbvie, 5, AbbVie, 5, Amgen, 5, BMS, 2, 5, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Canfite, 1, 4, Corrona, 5, Crescendo Bioscience, 2, 5, Eli Lilly and Company, 5, Gilead, 5, Glaxo-Smith Kline, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Lilly, 5, Lily, 5, Lycera, 1, 4, 5, Merck, 5, Novartis, 5, Pfizer, 5, Roche, 5, Samsung, 5, Samsung Bioepis Co., Ltd., 5, Sanofi Regeneron, 2, Sanofi/Regeneron, 2, Sanofi-Regeneron, 2, Scipher, 1, 4, 5, Set Point, 5, SetPoint, 5, Squibb, 5, Vorso, 1; **K. Saag**, Abbvie, 5, AbbVie, 5, Amgen, 2, 5, Ampel, 2, Bayer, 5, Gilead, 5, Horizon, 2, 5, Ironwood/AstraZeneca, 2, 5, Kowa, 5, kowa, 5, Mereo, 2, Radius, 5, Radius Health, 2, 5, Roche/Genentech, 5, SOBI, 2, 5, Sobi, 2, 5, Takeda, 2, 5, Teijin, 5, Tejin, 5; **V. Bykerk**, AbbVie, 5, Amgen, 1, 2, 3, 5, 8, Brainstorm Therapeutics, 1, 2, 3, 5, 8, Bristol-Myers Squibb, 5, Genentech, 5, Gilead, 5, NIH, 2, Pfizer, 1, 2, 3, 5, 8, Regeneron, 5, Regeneron Pharmaceuticals, Inc, 5, Sanofi, 5, Sanofi/Genzyme-Regeneron, 5, Sanofi-Genzyme/Regeneron, 1, 2, 3, 5, 8, Scipher, 1, 2, 3, 5, 8, The Cedar Hill Foundation, 9, UCB, 1, 2, 3, 5, 8, UCB Pharma, 5; **C. Charles-Schoeman**, Abbvie, 2, AbbVie, 2, Amgen, 5, BMS, 2, Bristol Myers Squibb, 2, Gilead, 5, Octapharma, 2, 5, Pfizer, 2, 5, Regeneron, 5, Regeneron/Sanofi, 5, Sanofi, 5; **S. Fiore**, Sanofi, 1, 3; **G. St John**, Regeneron, 1, 3, 4, Regeneron Pharmaceuticals, Inc, 1, 3; **T. Kimura**, Regeneron, 1, 3, Regeneron Pharmaceuticals, Inc, 1, 3; **S. Zheng**, Sanofi, 3, 5; **C. Bingham**, Abbvie, 5, AbbVie, 5, BMS, 2, 5, Bristol Meyer Squibb, 2, 5, Bristol Myers-Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Eli/Lilly, 5, Genentech/Roche, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Pfizer Inc, 5, Regeneron/Sanofi, 5, Sanofi/Regeneron, 5; **G. Wright**, AbbVie, 5, 8, Abbvie, 5, 8, Amgen, 5, 8, Autoimmune, 5, 8, BMS, 5, 8, Exagen, 5, 8, Lilly, 5, 8, Myriad, 5, 8, Myriad Autoimmune, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Regeneron, 5, 8, Sanofi Genzyme, 5, 8, UCB, 5, 8; **M. Bergman**, Abbvie, 5, 8, AbbVie, 5, 8, AbbVie, BMS, Celgene Corporation, Genentech, Janssen, Merck, Novartis, Pfizer, Sanofi, 5, AbbVie, Celgene Corporation, Novartis, Pfizer, Sanofi, 8, Amgen, 5, 8, BMS, 5, 8, Celgene, 5, 8, Genentech, 5, Genentech/Roche, 5, 8, Genentech-Roche, 5,

Figure. Principal components across the five RA phenotype clusters



Gilead, 5, GlaxoSmithKline, 8, GSK, 8, Horizon, 5, Janssen, 5, 8, JNJ (parent of Janssen), 1, JNJ stock, 1, Johnson & Johnson, 1, 4, Johnson and Johnson, 1, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sandoz, 5, Sanofi, 5, 8, Sanofi/Regeneron, 5, 8, Sanofi-Regeneron, 5, 8; **K. Nola**, Coherus, 8, Gilead, 1, 5, Johnson & Johnson, 1, Proctor & Gamble, 1, Regeneron, 5, Sanofi Genzyme, 5; **D. Furst**, Actelion, 2, 5, Actelion Pharmaceuticals, 2, 5, Amgen, 2, 5, BMS, 2, 5, CME, 5, 8, Corbus, 2, 5, Galapagos, 2, 5, Galapogos Novartis, 5, GlaxoSmithKline, 2, GSK, 2, 5, NIH, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche/Genentech, 2, 5, Sanofi, 2, 5; **N. Shadick**, BMS, 2, Crescendo Biosciences, 2, Mallinckrodt, 2, Sanofi Regeneron, 2, Sanofi/Regeneron, 2.

Abstract Number: 0184

No Increased Risk of Incidence Diabetes in Patients with Rheumatoid Arthritis Compared to Patients Without RA

Yinzhu Jin,[1] Sarah Chen,[2] Jun Liu,[1] Rishi Desai,[3] and **Seoyoung C. Kim**[1], [1]Brigham and Women's Hospital and Harvard Medical School, Boston, [2]Brigham and Women's Hospital and Harvard Medical School, Boston, [3]Brigham and Women's hospital, Boston

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Some previously published studies suggest that patients with rheumatoid arthritis (RA) are at an increased risk of developing diabetes mellitus. We examined the risk of incident type 2 diabetes mellitus (T2DM) among RA patients compared to four non-RA comparison cohorts.

Methods: Using a large US commercial insurance database, Optum Clinformatics (2005-2017), we identified RA patients based on ≥2 diagnosis codes for RA and use of ≥1 disease-modifying antirheumatic drugs (index date). We selected four comparison cohorts with ≥2 disease-specific diagnosis codes and ≥1 dispensing of disease-specific drugs: 1) general non-RA patients, 2) hypertension, 3) osteoarthritis (OA), and 4) psoriatic arthritis (PsA) patients as an inflammatory arthritis comparison cohort. All study patients were ≥18 years old with 365 days of continuous enrollment prior to the index date. Patients with diabetes diagnosis or use of any anti-diabetic drugs at baseline were excluded. We also excluded patients with RA or PsA from the non-RA, non-PsA cohorts. RA patients were matched to comparator cohorts (except PsA) with age, sex, and index date. Incidence T2DM was defined as a diagnosis of T2DM plus a new dispensing of anti-diabetic drugs within +/- 30 days. Patients were followed up from the day (for the primary analysis) or one year (for the secondary analysis to minimize surveillance bias) after the index date to the earliest event of: 1) occurrence of T2DM, 2) disenrollment, 3) end of data, 4) death, or 5) occurrence of RA or PsA in other cohorts. We used multivariable Cox-proportional hazards model to estimate hazard ratios (HR) of incident T2DM among RA versus each of comparison cohorts, accounting for >40 baseline covariates including demographics, co-morbidities, co-medications, lab ordered, and healthcare utilizations. To validate our results, we selected hip fracture as a positive control outcome since RA is known to increase the risk of hip fracture.

Results: A total of 108,568 RA patients were 1:1 matched to the hypertension, OA, and general non-RA cohorts on age, sex, and index date. 15,055 of PsA patients were identified. Mean age was 55.6 years among RA/general non-RA/hypertension/OA cohort and 77.3% were female. PsA patients had a mean age of 48.6 years and 48.6% were female (Table 1). During the mean 2.4 years of follow-up, we observed 2,091 incident T2DM events in RA patients, 1,828 in the general non-RA cohort, 3,012 in hypertension, 1,802 in OA, and 366 in PsA cohort. The crude incidence rate of T2DM was the lowest in the RA cohort (7.0 per 1,000 person-years) and highest (12.3 per 1,000 person-years) in the hypertension cohort (Table 2). After adjusting for baseline covariates, RA was associated with a 24-35% lower risk of incident T2DM compared to the comparison groups (Figure 1). The secondary analysis showed consistent results. Our positive control outcome analysis showed over 30% increased risk of hip fracture in RA patients compared to the general non-RA, hypertension, and PsA patients (Figure 1).

Conclusion: In this large cohort study with over 10 years of study period, RA patients had a lower rate of incident T2DM compared to the general non-RA, hypertension, OA, and PsA cohorts.

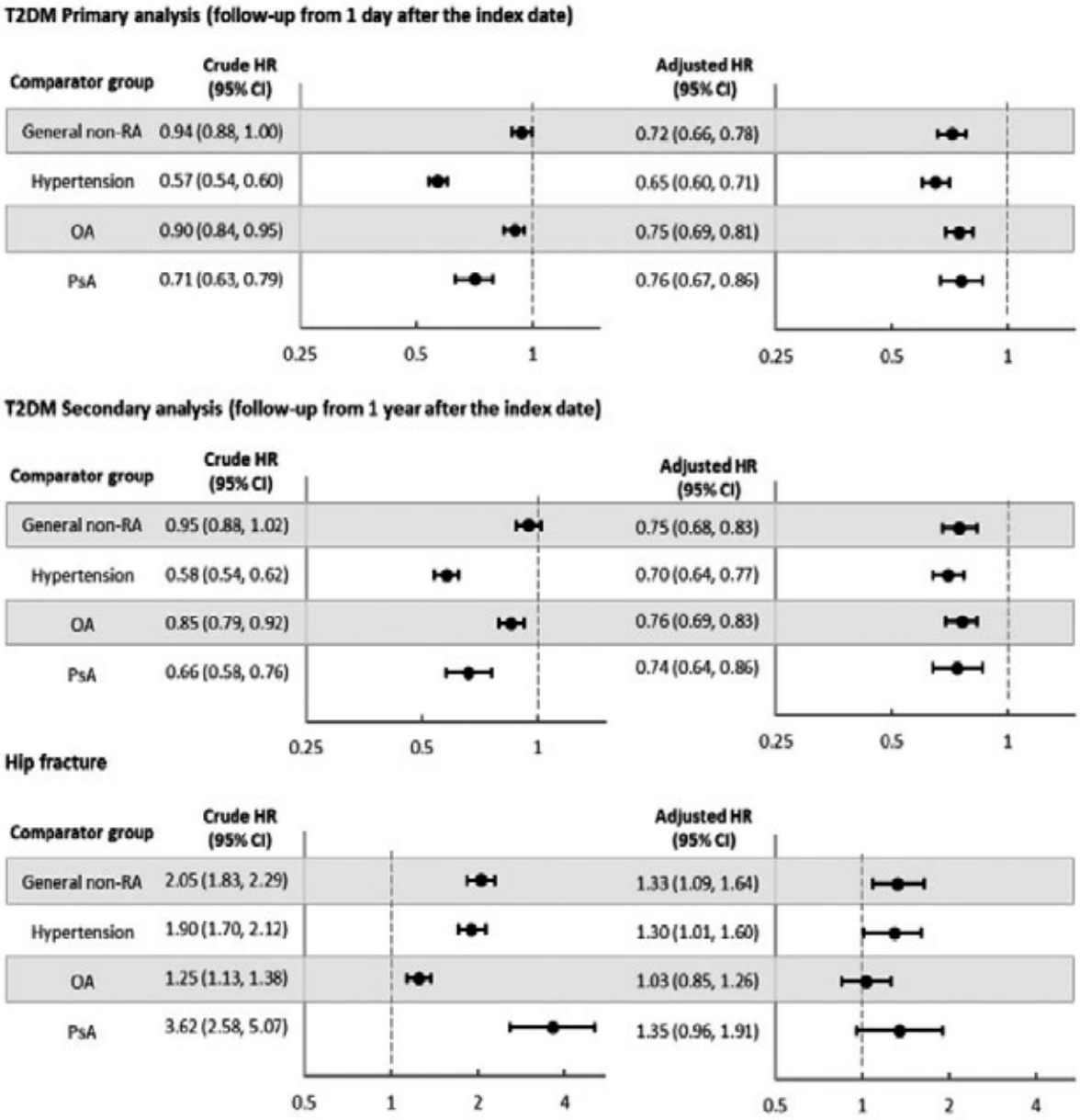
Table 1. Selected baseline characteristics of RA vs. non-RA cohorts

Cohort	RA	Non-RA	Hypertension	OA	PsA
Total N	**108,568**	**108,568**	**108,568**	**108,568**	**15,055**
Demographics					
Age in years, mean (SD)	55.6 (13.5)	55.6 (13.5)	55.6 (13.5)	55.6 (13.5)	48.6 (12.5)
Female, %	77.3	77.3	77.3	77.3	48.3
Comorbidities					
Hypertension, %	38.7	36.0	100	33.4	32.5
Hyperlipidemia, %	34.4	35.6	53.3	38.4	32.5
Hypothyroidism, %	17.3	13.1	14.7	15.0	11.0
Obesity, %	8.9	7.4	14.8	14.4	10.7
Use of DMARDs					
Methotrexate	57.1	-	-	-	51.4
Hydroxychloroquine	35.8	-	-	-	2.5
TNF inhibitors	27.5	-	-	-	60.3
Other biologic DMARDs	18.7	-	-	-	6.2
Use of other medications					
Oral steroids	56.5	12.6	14.7	21.6	34.4
Cumulative steroid dose (365 days, prednisone equivalent) (Q1, median, Q3)	300, 705, 1575	0, 0, 0	105, 200, 390	105, 200, 360	0, 0, 205
NSAIDs	45.1	18.6	21.2	58.0	43.8
Coxibs	10.9	2.4	2.6	12.5	8.9
ACE inhibitors/ARB	22.3	21.4	63.1	15.3	20.7
Beta blockers	15.7	13.6	33.6	10.9	12.2
Calcium channel blockers	12.3	10.0	26.7	7.3	8.1
Diuretics	22.8	19.2	52.1	17.7	17.2
Statin	19.2	21.5	31.4	21.1	18.3
Proton pump inhibitors	24.2	11.8	15.9	18.5	16.8
Lab test ordered					
HbA1c, %	9.6	8.6	13.0	9.3	9.6
Healthcare utilization					
Emergency room visits	22.3	15.8	24.4	23.6	17.2
Any hospitalization	11.2	6.9	12.3	18.2	6.6
Number of physician visits (Q1, median, Q3)	6, 9, 13	2, 3, 6	3, 5, 8	5, 7, 11	5, 8, 12
Number of unique prescription drugs (Q1, median, Q3)	6, 9, 13	2, 4, 7	4, 6, 9	4, 7, 11	5, 8, 12

Table 2. Incidence rates (95% CI) of primary T2DM RA and non-RA comparison cohorts

Cohort	Number of patients	Number of events	Total person-years	Incidence rate per 1,000 person-years (95% CI)
RA	108,568	2,091	297,987	7.0 (6.7, 7.3)
General	108,568	1,828	246,020	7.4 (7.1, 7.8)
Hypertension	108,568	3,012	244,214	12.3 (11.9, 12.8)
OA	108,568	1,802	232,361	7.8 (7.4, 8.1)
PsA	15,055	366	36,903	9.9 (9.0, 11.0)

Figure 1. Forest plots for crude and adjusted HR (95% CI) of T2DM and hip fracture in RA versus comparison cohorts



Disclosure: Y. Jin, None; **S. Chen**, None; **J. Liu**, None; **R. Desai**, Merck, 2, Vertex, 2; **S. Kim**, AbbVie, 2, AstraZeneca, 2, Bristol-Myers Squibb, 2, Merck, 2, Pfizer, 2, research grants to Brigham and Women's Hospital from Pfizer, AbbVie, Bristol-Myers Squibb, and Roche for unrelated topics, 2, Roche, 2, Roche/Genentech, 2.

Abstract Number: 0185

Accrual of Multimorbidity After Incident Rheumatoid Arthritis and Matched Comparators Using a Large Prospective Cohort with 30 Years of Follow-up

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

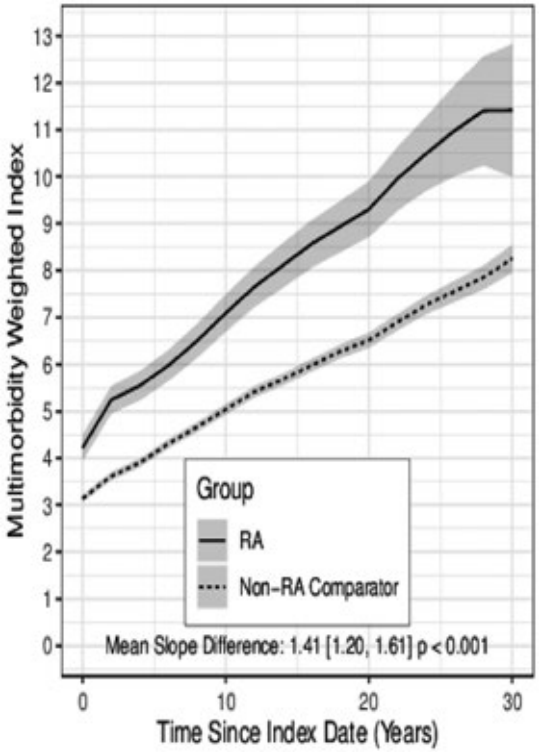
Session Title: Epidemiology & Public Health Poster I: RA

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

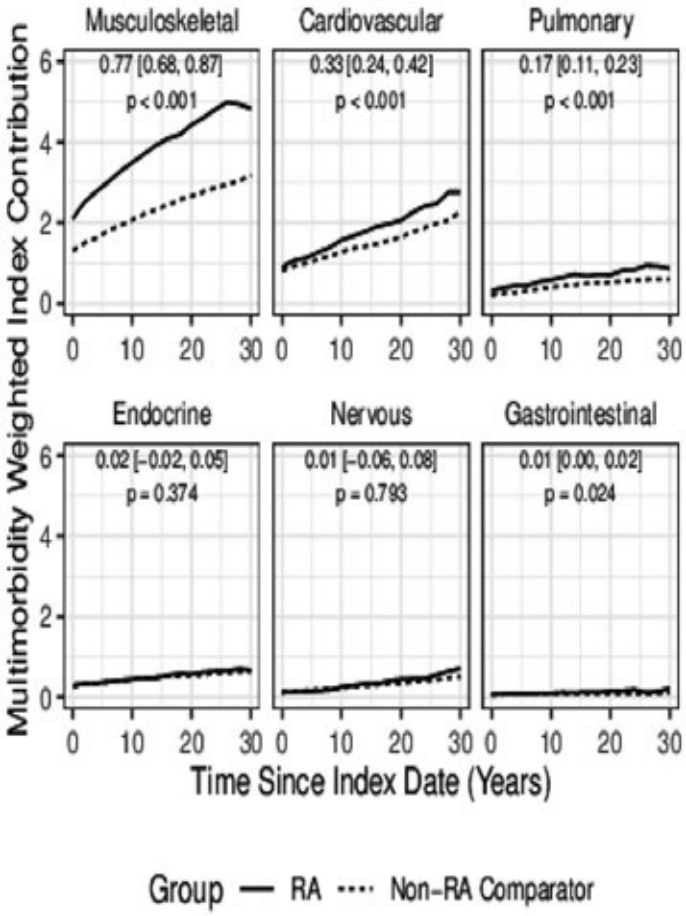
Background/Purpose: Rheumatoid arthritis (RA) patients often suffer from multimorbidity, the coexistence of multiple chronic morbidities. However, little is known about how multimorbidity accrues over time among RA patients compared to similar individuals without RA. Thus, we aimed to describe the longitudinal trajectories of multimorbidity after incident RA and compared to age- and calendar year- matched non-RA comparators, both from a large prospective cohort of female nurses.

Methods: We conducted a prospective cohort study utilizing the Nurses' Health Study, an ongoing (n = 121,700) prospective cohort of female registered nurses that began in 1976. Biennial questionnaires collected information on items such as sociodemographics, anthropometrics, dietary intake, and health conditions. Incident RA and date of



diagnosis were determined by medical record review (all meeting 1987 ACR or 2010 ACR/EULAR classification criteria). For each woman with incident RA, we matched 10 non-RA comparators who had never reported RA at or prior to the index date (time of RA diagnosis) by age and calendar year. To quantify the potentially differential accumulation of multimorbidity over time, we used the validated Multimorbidity-Weighted Index (MWI), previously associated with physical function, mortality, and cognitive decline. We modified the MWI to exclude RA (exposure of interest), analyzing a total of 61 morbidities, each weighted according to their impact on the Short Form-36 physical functioning scale. The conditions included common and rare but debilitating conditions and spanned all organ systems; e.g., musculoskeletal (gout, osteoarthritis, osteoporosis, fractures, joint replacements), cardiovascular, and pulmonary systems. We demonstrated the trajectories of the overall MWI and components of the MWI over time in RA patients and their matched comparators. The between-group difference in trajectories was tested using linear mixed effect models.

Results: We identified 1,007 incident RA patients and matched 10,003 non-RA participants. Both had mean ages of 60 years (SD 10). Need to include mean follow-up time (big strength of the study). Past and current smoking was more common among RA individuals (65%) than comparators (56%). At baseline (**Figure 1**), the MWI was higher for the RA patients (mean 4.2) than matched comparators (mean 3.1). During the follow-up, MWI accrued more rapidly for RA patients than their matched comparators. For each decade, MWI score increased by 1.41 [95% confidence interval (CI) 1.20, 1.61] in RA patients. The largest contributor to the baseline difference and difference in trajectories over time was the musculoskeletal component of the MWI (**Figure 2**). Although similar at baseline, cardiovascular and pulmonary components of the MWI accrued more rapidly over time for the RA patients than the matched comparators.



Conclusion: Women with RA and their non-RA comparators exhibited differential accumulation of multimorbidity after incident RA. Since the MWI concomitantly captures current physical functioning and predicts future physical functioning, cognitive decline, and increased mortality, potential strategies to mitigate the accumulation of multimorbidity in RA patients are urgently needed.

Accumulation of multimorbidity after the index date of RA diagnosis (n=1,007) or matched date for comparators (n=10,003) as quantified by the Multimorbidity Weighted Index.

Accumulation of the major components (musculoskeletal, cardiovascular, pulmonary, endocrine, gastrointestinal, and nervous) of the Multimorbidity Weighted Index after the index date of RA diagnosis (n=1,007) or matched date for comparators (n=10,003)

Disclosure: K. Yoshida, None; **T. Lin**, None; **M. Wei**, None; **S. Malspeis**, None; **S. Chu**, None; **C. Camargo**, None; **B. Raby**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5; **S. Tedeschi**, None; **M. Barbhaiya**, None; **B. Lu**, None; **K. Costenbader**, Astra-Zeneca, 2, Glaxo Smith Kline, 2, Janssen Scientific Affairs, LLC, 2, Lupus Foundation of America, 2, Lupus Research Alliance, 2, Merck, 2; **E. Karlson**, None; **J. Sparks**, None.

Abstract Number: 0186

Asthma, Chronic Obstructive Pulmonary Disease, and Subsequent Risk for Incident Rheumatoid Arthritis Among Women: A Prospective Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: While RA patients are known to have excess respiratory morbidity and mortality, less is known about the role of chronic respiratory diseases in the development of RA. Prior studies using retrospective cohort or case-control studies suggest an association between asthma and increased RA risk, but were limited by potential for recall bias and lack of data on smoking and RA serostatus. Chronic obstructive pulmonary disease (COPD) as a risk factor for incident RA has not previously been studied. We investigated whether asthma or COPD are associated with subsequent risk of developing RA, independent of smoking.

Methods: We performed a prospective cohort study investigating asthma, COPD, and incident RA risk in two prospective cohorts, the Nurses' Health Study (NHS, 1988-2014) and NHSII (1991-2015). Self-reported asthma and COPD were confirmed using validated supplemental respiratory questionnaires. Medical record review determined incident RA (meeting 1987 ACR or 2010 ACR/EULAR criteria), serostatus, and date of diagnosis. Covariates including smoking pack-years were self-reported every 2 years. Two separate pooled analyses were performed: 1) asthma as primary exposure, and 2) COPD as primary exposure, each compared to women who never reported asthma or COPD. Cox regression models estimated hazard ratios (HR) and 95% confidence intervals (CI) for RA (overall and by serostatus), adjusting for smoking and other potential confounders. We performed subgroup analyses among never and ever smokers and by age to evaluate possible effect modification for asthma and RA risk by smoking and age.

Table 1. Hazard ratios for incident rheumatoid arthritis according to time-updated asthma, compared to women without asthma or COPD in the Nurses' Health Studies (n=196,409).

	No asthma or COPD	Asthma
	HR (95%CI)	HR (95%CI)
Outcome: All RA		
Cases/person-years	874/3,841,747	100/265,359
Age-adjusted model	1.00 (Ref)	**1.67 (1.35, 2.05)**
Multivariable model*	1.00 (Ref)	**1.53 (1.24, 1.88)**
Outcome: Seropositive RA		
Cases/person-years	562/3,834,291	60/264,341
Age-adjusted model	1.00 (Ref)	**1.51 (1.15, 1.97)**
Multivariable model*	1.00 (Ref)	**1.42 (1.08, 1.86)**
Outcome: Seronegative RA		
Cases/person-years	312/3,833,574	40/264,329
Age-adjusted model	1.00 (Ref)	**1.98 (1.42, 2.76)**
Multivariable model*	1.00 (Ref)	**1.75 (1.25, 2.45)**

*Multivariable model was adjusted for age, questionnaire period, cohort, US geographic region (West, Midwest, Mid-Atlantic, New England, Southeast), median household income (quartile), smoking pack-years (continuous), smoking status (never/past/current), cumulative average physical activity (<3, ≥3 MET-hours/week), parity/breastfeeding in months (nulliparous, parous/<1 month, parous/1-11 months, parous/≥12 months), menopausal status/postmenopausal hormone use (premenopausal, postmenopausal/never, postmenopausal/ever), cumulative average Alternate Healthy Eating Index (quartile), body mass index category (<25.0, 25.0 to <30.0, ≥30.0 kg/m^2), parents smoked in house when growing up (yes/no), lived with smoker (ever/never), and physical exam in the last two years (yes/no).

Table 2. Hazard ratios for incident rheumatoid arthritis according to time-updated COPD, compared to women without asthma or COPD in the Nurses' Health Studies (n=205,153).

	No asthma or COPD	COPD
	HR (95%CI)	HR (95%CI)
Outcome: All RA		
Cases/person-years	1,029/4,337,186	31/47,285
Age-adjusted model	1.00 (Ref)	**2.39 (1.66, 3.43)**
Multivariable model*	1.00 (Ref)	**1.89 (1.31, 2.75)**
Outcome: Seropositive RA		
Cases/person-years	642/4,328,257	21/47,134
Age-adjusted model	1.00 (Ref)	**2.69 (1.73, 4.18)**
Multivariable model*	1.00 (Ref)	**2.07 (1.31, 3.25)**
Outcome: Seronegative RA		
Cases/person-years	387/4,327,740	10/47,121
Age-adjusted model	1.00 (Ref)	**1.93 (1.02, 3.64)**
Multivariable model*	1.00 (Ref)	1.59 (0.83, 3.05)

*Multivariable model was adjusted for age, questionnaire period, cohort, US geographic region (West, Midwest, Mid-Atlantic, New England, Southeast), median household income (quartile), smoking pack-years (continuous), smoking pack-years squared (continuous), smoking status (never/past/current), cumulative average physical activity (<3, ≥3 MET-hours/week), parity/breastfeeding in months (nulliparous, parous/<1 month, parous/1-11 months, parous/≥12 months), menopausal status/postmenopausal hormone use (premenopausal, postmenopausal/never, postmenopausal/ever), cumulative average Alternate Healthy Eating Index (quartile), body mass index category (<25.0, 25.0 to <30.0, ≥30.0 kg/m^2), parents smoked in house when growing up (yes/no), lived with smoker (ever/never), and physical exam in the last two years (yes/no).

Results: We identified 1,060 incident RA cases (63% seropositive) during 4,384,471 person-years of follow-up. In the asthma analysis, the RA incident rate (IR) for 15,148 women with validated asthma was 0.38 per 1000 person-years compared to an IR of 0.23 per 1000 person-years for women without asthma or COPD. Asthma was associated with increased risk for all RA (HR 1.53, 95%CI 1.24, 1.88) compared to no asthma/COPD after adjusting for covariates including continuous pack-years and smoking status (Table 1). Among never-smokers, asthma was associated with increased risk for all RA (HR 1.53, 95%CI 1.14, 2.06) and seronegative RA (HR 1.91, 95%CI 1.22, 2.97), but not seropositive RA. In the COPD analysis, the RA IR for 3,573 women with validated COPD was 0.66 per 1000 person-years. COPD was associated with increased risk of all RA (HR 1.89, 95%CI 1.31, 2.75) and seropositive RA (HR 2.07,

95%CI 1.31, 3.25) after adjusting for covariates including continuous pack-years and smoking status (Table 2). The association of COPD with seropositive RA was most pronounced in the subgroup of ever-smokers who were >55 years old (HR 2.71, 95%CI 1.55,4.76).

Conclusion: In this large prospective cohort study, asthma and COPD were both associated with increased risk for incident RA, independent of smoking status/intensity. Identifying asthma and COPD patients as at-risk populations for RA can help develop prevention and screening strategies as well as provide insight into the role of chronic airway inflammation in RA pathogenesis.

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Abstract Number: 0187

Epidemiology of JIA-Associated Uveitis: Environmental Factors and Disease Characteristics of a JIA-Associated Uveitis Cohort

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health Poster I: RA

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: JIA-associated uveitis (JIA-U) is the most prevalent extra-articular manifestation of JIA and the most common type of uveitis in children. To date, environmental factors such as smoke exposure, early life infection, pets, breast feeding, residential areas, stressful life events and prematurity have been investigated for potential associations with the development of JIA. Prematurity was found to have a possible correlation with JIA; while in adults, cigarette smoke has been reported to have an association with the onset of uveitis. Our objective is to identify

Figure 1. Baseline Socio-Cultural Questions

BIRTH AND SOCIAL HISTORY	Yes	No	Prefer Not to Answer
7. Child's birth weight: _____lbs. _____oz.			
8. Did the pregnancy require hormone treatment or IVF?	▫	▫	▫
9. During the pregnancy did the mother smoke? If yes, how frequently? _____Cigarettes per ▫ day ▫ week ▫ month	▫	▫	▫
10. During the pregnancy did the mother drink alcohol?	▫	▫	▫
11. During the pregnancy did the mother use drugs or medications?	▫	▫	▫
12. Was initial feeding: ▫Breast ▫Formula ▫Both ▫Prefer not to answer			
13. Does anyone in your home or who cares for your child smoke?	▫	▫	▫
14. Did the child live at home with a smoker anytime during the 6 months prior to onset?	▫	▫	▫
15. Did the child live at home with a smoker anytime more than 6 months prior to onset?	▫	▫	▫

Table 1. Socio-cultural and Disease Characteristics of a JIA Cohort at Cincinnati Children's Hospital
N (%) unless otherwise indicated

	JIA (n = 120)	JIA-U (n = 51)	T / χ^2 Value (Probability)
Age at Enrollment, mean years (SD)	11.0 (4.8)	11.4 (5.3)	t = -0.43 (p = 0.666)
Female	87 (74.4)	42 (92.4)	χ^2 = 1.27 (p = 0.259)
Caucasian	113 (95.8)	46 (90.2)	χ^2 = 1.98 (p = 0.159)
Non-Hispanic	111 (98.2)	47 (94.0)	χ^2 = 2.09 (p = 0.149)
Labs			
ANA Positive	59 (50.9)	35 (77.8)	χ^2 = 9.67 (p = 0.002)*
ESR at JIA Diagnosis, mean (SD)	22.5 (21.1)	23.1 (20.5)	t = -0.19 (p = 0.846)
JIA Characteristics			
Age at JIA Diagnosis, mean years (SD)	6.7 (4.4)	4.8 (4.3)	t = 2.47 (p = 0.015)*
Duration of JIA, mean years (SD)	4.4 (3.6)	6.4 (4.9)	t = -3.04 (p = 0.003)
Oligoarticular Persistent	57 (49.1)	12 (26.7)	χ^2 = 6.68 (p = 0.010)*
Oligoarticular Extended	12 (10.3)	11 (24.4)	χ^2 = 5.26 (p = 0.022)*
Polyarticular RF-	47 (40.5)	16 (35.6)	χ^2 = 0.34 (p = 0.563)
Uveitis Characteristics			
Age at Uveitis Diagnosis, mean years (SD)	-	5.0 (4.6)	
Duration of Uveitis, mean years (SD)	-	5.6 (4.1)	
Bilateral Disease	-	27 (52.9)	
Anterior Location	-	41 (84.3)	
History of Ocular Complications	-	20 (39.2)	
Pregnancy Related History			
IVF	8 (7.0)	0 (0.0)	χ^2 = 3.66 (p = 0.050) [a]
Smoking	11 (9.7)	4 (8.0)	χ^2 = 0.12 (p = 0.223) [a]
Alcohol	2 (1.7)	1 (2.0)	χ^2 = 0.01 (p = 0.446) [a]
Drugs/meds	16 (14.2)	6 (12.0)	χ^2 = 0.15 (p = 0.695)
Premature (birth weight < 5lb 8oz)	12 (10.2)	3 (5.9)	χ^2 = 0.81 (p = 0.168)
Initial Feeding			
Breast Milk	57 (50.0)	27 (55.1)	
Formula	42 (36.8)	15 (30.6)	
Both, Breast Milk & Formula	15 (13.2)	7 (14.3)	
Smoke Exposure			
Currently in Home	21 (18.3)	5 (10.0)	χ^2 = 1.79 (p = 0.181)
Lived with Smoker Previously	15 (13.2)	4 (8.2)	χ^2 = 0.83 (p = 0.362)
6 Months Prior to Onset JIA	14 (12.3)	4 (8.2)	χ^2 = 0.59 (p = 0.442)
>6 Months Prior to Onset JIA	14 (12.3)	4 (8.2)	χ^2 = 0.65 (p = 0.420)

NOTE: n =number; SD = Standard Deviation; % = Percentage; χ^2 = Chi square value; [a] = Fisher's exact test; * = significant p values

environmental factors (pregnancy history, smoking exposure and initial feeding regimen) and disease characteristics (clinical lab values, disease duration and disease subtype) associated with uveitis development in children with JIA.

Methods: We reviewed records for a JIA cohort comprised of 171 children (120 oligoarticular or polyarticular RF- JIA without uveitis [JIA-no-U], and 51 JIA-U) enrolled in a prospective study on uveitis outcomes who are seen at an outpatient clinic at Cincinnati Children's Hospital. Data collected included JIA and uveitis clinical characteristics, and a baseline ESR at JIA diagnosis. Parents or guardians completed a questionnaire on socio-cultural factors including pregnancy history (fertility treatments, substance use and birth weight), initial feeding regimen and smoke exposure (Figure 1). Means were used to compare JIA-no-U and JIA-U patients using Chi Square (χ2) and T-test.

Results: Of 171 children, mean age was 11 (SD, 5 years), 75% female, 93% Caucasian and 93% non-Hispanic (Table 1). Compared to JIA-no-U, those with JIA-U were more likely to be ANA positive (50.9% vs. 77.8%, p = 0.002), diagnosed with JIA at a younger age (6.7 vs. 4.8 years, p = 0.015), and be of the oligoarticular extended JIA category (24.4%, p = 0.022). ESR (nearest JIA diagnosis) of JIA-no-U and JIA-U children at JIA diagnosis was not significantly

different (22.5 vs. 23.1, p = 0.846). Environmental factors such as initial feeding regimens, pregnancy history and smoke exposure were also not significantly different. A portion of our JIA population report a history of in-vitro fertilization (JIA-no-U: 8 vs. JIA-U: 0, p = 0.050).

Conclusion: Our results are consistent with previous findings suggesting children with JIA-U more commonly have a positive ANA and are diagnosed with JIA at a younger age. In our Midwest regional cohort, we were not able to identify environmental factors significantly-associated with uveitis development in children with JIA. Further, we were not able to confirm associations with smoking or baseline ESR levels. Future studies are needed in a larger cohort to examine environmental factors in relation to healthy controls and JIA-U children, and other reported environmental factors such as birth order, delivery type or family medical history.

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Abstract Number: 0188

The Importance of Diagnosis: Clinical Distinctions Between Adult JIA and RA, and a Characterization of Patients with JIA Reclassified as RA in Adulthood

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SESSION INFORMATION
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Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Upon transitioning from pediatric to adult care, many patients with JIA are labeled as having RA, despite the two diagnoses being distinct in care and treatment. We investigated differences between adult patients with JIA and those with RA, and between adult patients with JIA who retain their diagnosis and those who are reclassified to RA, in a 20-year observational study.

Methods: Patients enrolled in a large, US-wide longitudinal study of rheumatic disease outcomes from 1998 to 2018 were eligible. Random observations from adults with JIA were analyzed descriptively and matched 1:3 with patients with RA. Matching was performed based on sex, calendar year of observation, and calendar year of diagnosis to produce matching disease duration and treatment era comparisons. Demographics, disease activity and status assessments, medications, co-morbidities and biomarkers were compared using t-tests and Chi-square tests. Logistic regression models for JIA versus RA diagnosis and for JIA diagnosis type were generated using backward elimination at $p < 0.05$.

Results: In the JIA cohort (n=933), 25.8% of patients had physician-confirmed or self-reported JIA and 74.2% had physician-confirmed RA with symptom onset prior to age 16 (Table 1). Nearly all (92.3%) patients with JIA who were given an RA diagnosis had symptoms prior to the terminology change from juvenile RA to a JIA diagnosis, versus 57.7% of other patients with JIA. Biomarkers were identified in a subset of patients: 38.6% of all patients with JIA (n=44) and 68.9% of matched patients with RA (n=135) were RF+ and/or anti-CCP+ (data not shown). After ad-

Table 1. Demographics, disease activity and status assessments, medications, comorbidities and biomarkers for JIA, RA, and JIA subcategories

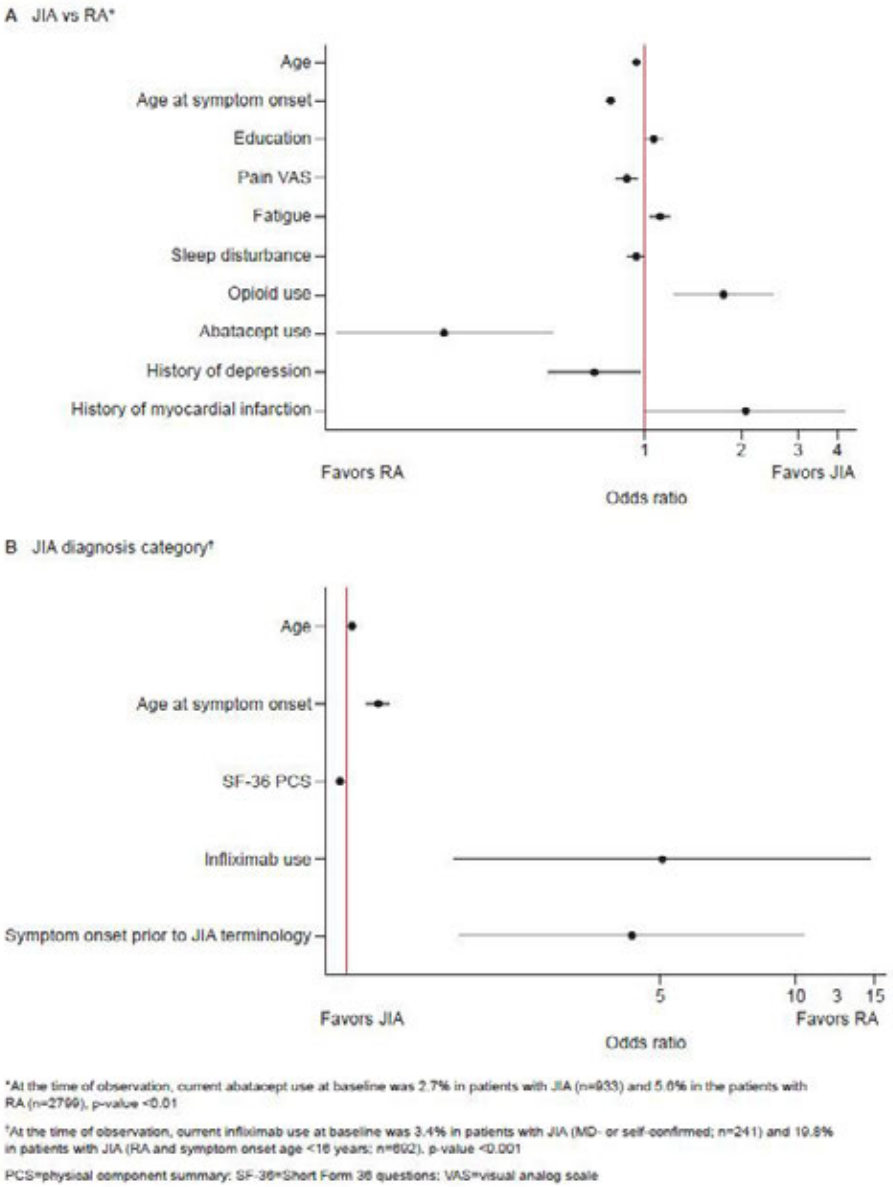
	Patients with JIA (n=933)	Patients with RA (n=2799)	p value	Patients with JIA (MD- or self-confirmed) (n=241)	Patients with JIA (RA and symptom onset age <16 years) (n=692)	p value
Demographics						
Age, years	40.0 ± 13.8	63.0 ± 12.1	**<0.001**	33.3 ± 12.2	42.3 ± 13.7	**<0.001**
Age at onset, years	9.9 ± 4.9	34.4 ± 14.8	**<0.001**	7.5 ± 4.8	10.5 ± 4.7	**<0.001**
Female, %	86.9	86.9	1.00	83.4	88.2	0.06
Caucasian, %	85.2	90.0	**<0.001**	87.8	84.5	0.31
Education, years	14.3 ± 2.5	13.6 ± 2.8	**<0.001**	14.7 ± 2.7	14.2 ± 2.4	**0.03**
Married, %	54.8	63.5	**<0.001**	46.0	57.0	**0.02**
History of smoking, %	27.8	32.1	**0.03**	24.5	28.6	0.32
BMI, kg/m^2	26.9 ± 7.7	27.5 ± 6.7	0.05	25.7 ± 6.9	27.1 ± 7.9	0.09
Household income, US$1000	51.4 ± 33.7	49.3 ± 33.1	0.17	53.7 ± 36.8	50.9 ± 33.0	0.44
Disabled (self-reported work status), %	24.6	17.6	**<0.001**	20.2	25.5	0.24
Disease activity and status assessments						
Pain, 0–10	4.5 ± 2.9	4.2 ± 2.8	**<0.01**	4.2 ± 2.8	4.6 ± 2.9	0.07
Global severity, 0–10	4.0 ± 2.6	3.8 ± 2.5	0.27	3.7 ± 2.7	4.1 ± 2.6	**0.02**
Fatigue, 0–10	5.1 ± 3.0	4.6 ± 3.0	**<0.001**	4.3 ± 3.1	5.3 ± 3.0	**<0.001**
Sleep disturbance, 0–10	4.3 ± 3.2	4.0 ± 3.1	**0.013**	4.0 ± 3.2	4.4 ± 3.2	0.20
SF-36 PCS, 0–100	35.9 ± 11.1	35.0 ± 11.0	0.07	38.0 ± 12.4	35.5 ± 10.8	**0.04**
SF-36 MCS, 0–100	47.1 ± 11.9	49.0 ± 11.5	**<0.001**	47.4 ± 10.9	47.0 ± 12.1	0.77
Medications						
Non-opioid analgesic, %	43.4	58.5	**<0.001**	27.4	49.0	**<0.001**
Any opioid, %	23.7	29.8	**<0.001**	12.0	27.7	**<0.001**
Prednisone, %	33.6	37.6	0.05	19.5	37.9	**<0.001**
Any DMARD, %	65.9	73.7	**<0.001**	55.7	69.3	**<0.01**
Any biologic, %	45.1	45.1	0.98	28.2	50.8	**<0.001**
Any TNFi, %	40.5	38.1	0.24	21.3	46.9	**<0.001**
Comorbidities						
Depression (ever), %	46.5	40.5	**<0.01**	44.7	46.9	0.67
Current depression, 0–10	2.8 ± 1.9	2.5 ± 1.8	**<0.01**	1.9 ± 1.3	2.9 ± 1.9	**<0.01**
Current anxiety, 0–10	4.2 ± 2.2	3.4 ± 2.0	**<0.001**	3.6 ± 1.9	4.2 ± 2.2	0.11
Hypertension (ever), %	37.3	55.8	**<0.001**	32.5	38.4	0.23
Myocardial infarction (ever), %	3.6	7.8	**<0.001**	5.3	3.3	0.31
Stroke (ever), %	4.3	7.5	**<0.01**	5.3	4.1	0.56
Cancer (ever), %	7.6	16.2	**<0.001**	7.0	7.7	0.80
Diabetes, %	7.9	13.7	**<0.001**	8.8	7.7	0.71
Fibromyalgia (criteria), %	35.3	29.5	**<0.01**	38.2	34.7	0.50
Biomarkers						
RF+, %	34.1	60.0	**<0.01**	33.3	34.4	0.95
CRP+, %	13.6	22.2	0.22	0.0	18.8	0.11
Anti-CCP+, %	31.8	60.0	**<0.01**	16.7	37.5	0.19

Values are mean ± SD unless indicated otherwise. Bolded p values indicate statistical significance

MCS=Mental Component Summary; PCS=Physical Component Summary; SF-36=Short Form-36 questions; TNFi=TNF inhibitor

dressing confounding in logistic regression models, several parameters were associated with JIA (vs RA) diagnosis, including younger age, lower pain and abatacept use, and higher fatigue among others (Figure 1A). In comparing the diagnosis type within the JIA cohort, older age, older age at symptom onset, lower Short Form-36 physical component summary score, symptom onset prior to the JIA terminology change and higher infliximab use were associated with labeling patients with RA in adulthood (Figure 1B).

Figure 1. Odds Ratios of Significant Covariates in Logistic Regression Models for (A) Any JIA vs Matched RA Diagnosis and (B) Retained JIA Label vs Relabeled With RA in Adulthood



*At the time of observation, current abatacept use at baseline was 2.7% in patients with JIA (n=933) and 5.6% in the patients with RA (n=2799), p-value <0.01

†At the time of observation, current infliximab use at baseline was 3.4% in patients with JIA (MD- or self-confirmed; n=241) and 19.8% in patients with JIA (RA and symptom onset age <16 years; n=602), p-value <0.001

PCS=physical component summary; SF-36=Short Form 36 questions; VAS=visual analog scale

Conclusion: Matched adults with JIA or RA had important differences in patient-reported outcomes, medication use and co-morbidities. Diagnoses given to adults with JIA have an important impact on their treatments, as reclassification to RA leads to differences in those treatments, particularly with use of infliximab.

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*at the time of the analysis

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Abstract Number: 0189

Validation of Claims-based Algorithms to Identify Interstitial Lung Disease in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health Poster I: RA

Session Type: Poster Session (Sunday)

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Background/Purpose: The prevalence of interstitial lung disease (ILD) among rheumatoid arthritis (RA) patient ranges between 5-10%. ILD leads to high morbidity and mortality in patients with RA and has economic implications. Validation of ILD among patients with RA in administrative datasets will enable future studies to describe clinical courses and treatment patterns on a large scale using real-world data. Therefore, we aimed to validate claims-based algorithms to identify ILD in RA patients.

Methods: We selected RA patients aged ≥65 years who had ≥2 diagnostic codes for RA and ≥1 disease-modifying antirheumatic drugs in Medicare Parts A/B/D linked to the Partners Healthcare electronic medical records from 2012-to 2014. To identify ILD in RA patients, we evaluated 8 claims-based algorithms using a combination of ICD-9 diagnosis codes and procedure codes related to the diagnosis or management of ILD. The algorithms were: (1) ≥1 diagnosis code for ILD by any physician; (2) ≥2 diagnosis codes for ILD by any physician; (3) ≥1 diagnosis code for ILD by any physician and ≥1 procedure code within 6 months from the ILD code; (4) ≥1 diagnosis code for ILD by any physician and ≥1 diagnostic procedure after the ILD diagnosis code; (5) ≥1 diagnosis code for ILD by pulmonologist or rheumatologist; (6) ≥2 diagnostic codes for ILD by pulmonologist or rheumatologist; (7) ≥1 diagnostic code for ILD by pulmonologist or rheumatologist and ≥1 procedure code within 6 months from the ILD code; (8) ≥1 diagnosis of ILD by pulmonologists or rheumatologist and ≥1 relevant diagnostic procedure after the ILD code. We performed manual medical record review and used presence of ILD on the clinical radiology report of chest computerized tomography (CT) scans or lung biopsy as the gold standard. In ambiguous cases of ILD, three rheumatologists and one pulmonologist discussed the case to determine if ILD was present. We calculated the positive predictive value (PPV) of each algorithm as the percentage of ILD confirmed by the gold standard ILD diagnosis over the denominator of patients who had chest CT or lung biopsy data available.

Results: A total of 5,214 RA patients were included in this study. In each algorithm, 181-993 patients were identified. Of those, 40.9-58.0% had adequate records of chest CT or lung biopsy reports. The PPV of algorithm 1 was 43.4% and requiring more than 2 ILD diagnosis codes improved the PPV to 52.0% in algorithm 2. When procedure codes related with the diagnosis or management for ILD was added to diagnostic code (algorithms 3 and 4), PPV did not increase, although the algorithms considering the time sequence between procedure and diagnosis codes improved the PPV slightly. However, the PPV of algorithm 5 (≥1 diagnosis code by pulmonologist or rheumatologist) increased to 61.5%. Requiring more than 2 ILD diagnostic codes by specialists improved the PPV to 72.4% in algorithm 6 (**Table**).

Table. Predictive Values of Proposed Algorithms for Identifying ILD in RA patients

	Algorithm Definition	No. of patients with CT chest or lung biopsy	No. of ILD cases identified	PPV* % (95% CI)
ILD Diagnosis by any physician				
1	≥1 ICD-9 diagnosis of ILD in any position	406	176	43.4 (38.5-48.3)
2	≥2 ICD-9 diagnosis of ILD in any position	248	129	52.0 (45.6-58.4)
3	≥1 ICD-9 diagnosis of ILD in any position and at least one relevant diagnostic procedure within 6 months from the diagnostic code for ILD	373	157	42.1 (37.0-47.3)
4	≥1 ICD-9 diagnosis of ILD in any position and at least one relevant diagnostic procedure† after diagnostic code	303	136	44.9 (39.2-50.7)
ILD Diagnosis by specialist				
5	≥1 ICD-9 diagnosis of ILD in any position by pulmonologist or rheumatologist	166	102	61.5 (53.6-68.9)
6	≥2 ICD-9 diagnosis of ILD in any position by pulmonologist or rheumatologist	105	76	72.4 (62.8-80.7)
7	≥1 ICD-9 diagnosis of ILD in any position by pulmonologist or rheumatologist and at least one relevant diagnostic procedure within 6 months from the diagnostic code for ILD	166	101	60.8 (53.0-68.3)
8	≥1 ICD-9 diagnosis of ILD in any position by pulmonologists or rheumatologist and at least one relevant diagnostic procedure† after diagnostic code	154	94	61.0 (52.9-68.8)

*Gold standard was defined by ILD cases confirmed by chest computerized tomography (CT) or lung biopsy report, and cases with ambiguous ILD on chest CT who were determined to have ILD after adjudication.
†bronchoscopy, biopsy(surgical/transbronchial), chest CT/high resolution CT/positron emission tomography (PET)-CT, pulmonary function testing, oxygen therapy
No.: Number, ILD: interstitial lung disease, PPV: positive predictive value, CI: confidence interval

Conclusion: Among RA patients, the algorithm that required ≥2 ICD-9 diagnosis codes for ILD by pulmonologist or rheumatologist demonstrated adequate PPV of 72.4% to identify ILD. These results demonstrating support the use of the claims-based algorithm for RA-associated ILD for generating more generalizable real-world evidence

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Accuracy of Administrative Algorithms for Identifying Interstitial Lung Disease in Rheumatoid Arthritis

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) affects 10-15% of RA patients leading to significant disability and premature mortality. While large administrative datasets have been widely leveraged in outcomes research, the accuracy of algorithms used to identify RA-ILD cases has not been adequately studied. Our objective was to evaluate the accuracy of administrative algorithms for identifying ILD in RA.

Methods: We selected participants in the Veterans Affairs Rheumatoid Arthritis (VARA) registry for detailed medical record review using a stratified sampling technique. Those with ≥2 outpatient or ≥1 inpatient ILD International Classification of Diseases (ICD) codes were reviewed as well as a 10% random sample of those without ILD codes. After standardizing the review process, three rheumatologists abstracted data from clinical notes, imaging/pathology reports, and pulmonary function testing (PFT). 'Stringent' and 'relaxed' ILD definitions based on medical record review were constructed a priori. Administrative data was obtained from the VA Corporate Data Warehouse and included outpatient and inpatient ICD codes, ICD codes from non-VA providers, provider specialty, diagnostic testing (imaging, biopsy, PFTs), and corresponding dates. We tested the algorithms in phases: 1) number and type of encounters, 2) specific ICD codes, 3) provider specialty and diagnostic testing, and 4) exclusion of 'other' ILD. Sensitivity, specificity, positive and negative predictive value (PPV), and agreement (Kappa statistic) with medical record classification were assessed. Analyses accounted for the stratified sampling design using inverse probability weighting. Several sensitivity analyses were completed.

Results: Characteristics of selected participants (n=536) were reflective of the VARA registry (n=2640) and VA population. ILD was confirmed in 182 (stringent) and 203 (relaxed), with pulmonologist diagnosis and chest computed tomography (CT) evidence in the majority. Initially, we identified ≥2 ILD ICD codes from inpatient or outpatient encounters as the best discriminating factors (PPV 65.5%, Kappa 0.70). Optimal ICD codes were ICD-9 515, 516.3, 516.8, and 516.9 and ICD-10 J84.1, J84.89, and J84.9 (PPV 69.5%, Kappa 0.72). Algorithms including a pulmonologist diagnosis, chest CT, PFTs, lung biopsy, or combinations improved performance (PPV 77.4-81.9%, Kappa 0.75). Exclusion of 'other' ILD modestly improved PPV further (78.5-82.9%). In sensitivity analyses, comparisons against even more sensitive ILD reference-standards resulted in PPVs of 82.4-86.3% while other minor algorithm modifications did not significantly affect algorithm performance.

Conclusion: The administrative algorithms identified in this study demonstrate substantial agreement with medical record review in classifying ILD in RA patients, though PPV is limited by the relatively low prevalence of RA-ILD. Optimal algorithms with PPV ≥80-85% contained multiple ILD encounters, specific ICD codes, pulmonologist diagnosis or diagnostic testing, and exclusion of 'other' ILD. These algorithms can be leveraged for RA-ILD outcomes research.

Disclosure: B. England, None; **P. Roul**, None; **T. Mahajan**, None; **N. Singh**, None; **F. Yu**, None; **H. Sayles**, None; **G. Cannon**, Amgen, 2; **B. Sauer**, Amgen, 2; **J. Baker**, Bristol-Myers Squibb, 2, 5, Burns-White LLC, 5; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **T. Mikuls**, BMS, 2, Horizon, 2.

Abstract Number: 0191

Associations of Self-Reported Inhalant Exposures with Autoantibodies and Disease Severity in U.S. Veterans with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health Poster I: RA

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Cigarette smoke is a known inhalant exposure that contributes substantially to the risk and severity of rheumatoid arthritis (RA). Less is known about the link between other inhalant exposures and RA related factors. The aim of this study was to determine the association between inhalant exposures (occupational, agricultural, and military) with RA-related autoantibodies and severity in U.S. Veterans with RA.

Methods: Participants at 9 sites in the Veterans Affairs Rheumatoid Arthritis (VARA) Registry, a multicenter, longitudinal observational cohort of U.S. Veterans with RA, were mailed surveys assessing occupational, agricultural, and mili-

Table 1. Association of self-reported burn pit exposure with anti-CCP antibody status and concentration by shared epitope status.

Anti-CCP positivity	**OR (95% CI)**	**P value**
Among SE positive	3.06 (1.26, 7.41)	0.01
Among SE negative	1.25 (0.50, 3.10)	0.63
Anti-CCP concentration (log)	**β (95% CI)**	**P value**
Among SE positive	0.67 (0.21, 1.14)	0.005
Among SE negative	-0.20 (-1.13, 0.74)	0.68

Adjusted for age, sex, race, and tobacco use.
Abbreviations: SE, shared epitope; anti-CCP, anti-cyclic citrullinated peptide

Table 2. Association of combined self-reported burn pit exposure and shared epitope status on anti-CCP antibody positivity in RA.		
	Odds Ratio (95% CI)	**P value**
Neither SE nor burn pit	1 (Ref)	-
SE alone	2.78 (1.80, 4.30)	<0.001
Burn pit alone	1.33 (0.56, 3.17)	0.52
SE and burn pit	8.56 (3.46-21.20)	<0.001
Adjusted for age, sex, race, and tobacco use. Abbreviations: SE, shared epitope; anti-CCP, anti-cyclic citrullinated peptide		

tary inhalant exposures. Demographics, disease activity, functional status, and extra-articular features were obtained from the VARA registry database while HLA-DRB1 shared epitope (SE) status, anti-CCP antibodies, and rheumatoid factor (RF) were measured using banked serum from VARA enrollment. Cross sectional associations between self-reported inhalant exposures and RA-related factors (autoantibodies, severity, extra-articular features) were assessed using multivariable linear and logistic regression models adjusting for age, sex, race, and tobacco use. Associations between inhalant exposures and autoantibody status were further examined in models stratified by SE status.

Results: Of 1566 registry participants mailed surveys, 797 returned completed surveys (50.9% response rate). Responders were older, more frequently white, less frequently current smokers, and had better disease activity and functional status. Self-reported occupational dust exposures were present in 67.6%, living or working on a farm in 44.8%, Agent Orange exposure in 29.2%, and military burn pit exposure in 18.6%. Military service periods between 1965-1973 were most common among those self-reporting burn pit exposure, with 19% serving during periods characterized by open-air burn pits on military bases. There were no significant associations between occupational dust, farm, or Agent Orange exposures with RA autoantibodies or disease severity. Self-reported burn pit exposure was significantly associated with anti-CCP positivity (odds ratio [OR] 2.22, 95% CI 1.23-3.99) and higher anti-CCP concentrations (log-transformed; b0.50, 95% CI 0.07-0.93) independent of tobacco use. In analyses stratified by SE status, these associations were limited to individuals with SE alleles (**Table 1**). In models examining combined self-reported burn pit exposure and SE status, those with both risk factors demonstrated a substantially higher risk of anti-CCP positivity (OR 8.56, 95% CI 3.46-21.20) compared to either risk factor in isolation (**Table 2**). Self-reported burn pit exposure was not associated with RF positivity, disease activity, or extra-articular disease.

Conclusion: Self-reported burn pit exposure was associated with anti-CCP antibodies in those with HLA-DRB1 SE alleles independent of, and to a similar degree as tobacco use. While limited by the cross-sectional design and self-report exposure history, these findings suggest that other inhalant exposures may similarly influence RA autoantibody expression and confer risk for RA

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Abstract Number: 0192

A Healthy Plant-Rich Diet and the Risk of Rheumatoid Arthritis in Women

Nathalie Marchand,[1] Shilpa Bhupathiraju,[2] Megu Baden,[2] Jeffrey Sparks,[3] Susan Malspeis,[3] Karen Costenbader,[3] Elizabeth Karlson,[3] and Bing Lu[3], [1]Brigham and Women's Hospital, Boston, [2]Harvard T.H. Chan School of Public Health, Boston, [3]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Consuming an overall healthy diet has been associated with a reduced risk of developing rheumatoid arthritis (RA), but the impact of consuming a diet rich in healthy plant-based foods and low in unhealthy plant-based foods and animal foods has not been investigated previously. The aim of this study was to examine the association between a healthy plant-rich diet and RA in women.

Methods: We prospectively studied 79,465 women from the Nurses' Health Study (NHS) (1984-2012) and 95,741 women from NHS II (1991-2011), who did not have RA at baseline. Information on health, diet, and lifestyle was collected biennially. A diet score was previously created to define a healthy plant-rich diet with higher intake in fruit, vegetable, whole grain, nut, legume, vegetable, coffee and tea consumption, lower intake in fruit juice, refined grain, potato, sugar-sweetened beverage, sweets and dessert consumption, and lower intake in animal foods (animal fats, dairy, eggs, fish, seafood, meat). Cox proportional hazards models, adjusted for age, smoking, physical activity, hormone use, multivitamin use, parity, and duration of breastfeeding, alcohol and total energy intake, were used to estimate hazard ratios (HR) and 95% confidence intervals (CI). Additional adjustment of BMI in separate models assessed the potential mediation effect. Because type of RA and diagnosis at earlier ages can be indicative of differences in disease prognosis, we further stratified our analyses by age at diagnosis and serostatus (seropositive and seronegative).

Results: Over 3,421,592 person years, 1,091 women developed RA in pooled analyses. In age-adjusted models, women with the highest adherence to a healthy plant-based diet had a decreased risk of RA (quartile 4 vs quartile 1 of dietary intake, HR = 0.82; 95% CI = 0.69-0.97, p trend = 0.01). In multivariable adjusted model, the association was attenuated (HR=0.84; 95% CI = 0.70-1.01, p trend=0.05). Additional adjustment for BMI attenuated the association to null. We did not observe significant associations of a healthy plant-based diet with seropositive and seronegative RA separately in multivariable adjusted models, and did not observe a significant difference among women with age ≤55 years and age >55 years.

Conclusion: Consuming a healthy plant-based diet, rich in whole grains, fruits, vegetables, and nuts, may be associated with a modest reduction in RA risk. BMI may mediate the association. Replication of these findings in other prospective studies are needed to confirm if increased consumption of a healthy plant-based diet leads to reduced risk of RA.

Table. Associations between healthy plant-based diets and risk of rheumatoid arthritis in NHS (1984-2012) and NHS II (1991-2011)

	Categories of plant-based diet intake				
	Q1	Q2	Q3	Q4	*P* trend
All RA					
Number of cases	290	287	267	250	
Number of person-years	1,093,230	1,124,540	1,105,186	1,098,635	
HR (95% CI) Age-adjusted	1.00 (Ref)	0.95 (0.81-1.12)	0.88 (0.75-1.04)	0.82 (0.69-0.97)	0.01
HR (95% CI) Multivariable-adjusted	1.00 (Ref)	0.95 (0.80-1.12)	0.88 (0.74-1.05)	0.84 (0.70-1.01)	0.05
HR (95% CI) Multivariable-adjusted + BMI	1.00 (Ref)	0.95 (0.80-1.12)	0.88 (0.74-1.05)	0.86 (0.71-1.03)	0.08
Seropositive RA					
Number of cases	177	191	165	159	
Number of person-years	1,090,991	1,122,243	1,102,891	1,096,607	
HR (95% CI) Age-adjusted	1.00 (Ref)	1.05 (0.86-1.29)	0.91 (0.74-1.13)	0.88 (0.71-1.09)	0.14
HR (95% CI) Multivariable-adjusted	1.00 (Ref)	1.04 (0.85-1.29)	0.90 (0.72-1.13)	0.89 (0.70-1.13)	0.21
HR (95% CI) Multivariable-adjusted + BMI	1.00 (Ref)	1.05 (0.85-1.29)	0.91 (0.73-1.13)	0.91 (0.72-1.15)	0.28
Seronegative RA					
Number of cases	113	96	102	91	
Number of person-years	1,090,623	1,121,908	1,102,679	1,096,306	
HR (95% CI) Age-adjusted	1.00 (Ref)	0.79 (0.60-1.04)	0.83 (0.64-1.09)	0.72 (0.55-0.95)	0.03
HR (95% CI) Multivariable-adjusted	1.00 (Ref)	0.79 (0.60-1.05)	0.84 (0.63-1.12)	0.76 (0.56-1.02)	0.10
HR (95% CI) Multivariable-adjusted + BMI	1.00 (Ref)	0.79 (0.60-1.05)	0.84 (0.64-1.12)	0.77 (0.57-1.04)	0.13

Adjusted for age, cigarette smoking status (never, past, current), alcohol consumption (<5.0, 5.0–<15.0, or 15+ g/d), parity and breastfeeding (nulliparous, parous with no breastfeeding, parous with 1–12 months breastfeeding, or parous with 12+ months breastfeeding), hormone use (premenopausal, postmenopausal with never use, current use, or past use), physical activity (0-<3, 3–<9, 9–<18, 18–<27, or 27+ metabolic equivalent hours/wk), BMI (<18.5, 18.5-<25, 25-<30, 30+ kg/m^2), total energy (kcal), multivitamin use (yes, no).

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Abstract Number: 0193

Diet as a Risk Factor for Rheumatoid Arthritis

Chelsea Guan,[1] and **Shazia Beg**[2], [1]University of Central Florida, Orlando, [2]University of Central Florida College of Medicine, Orlando

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disease affecting the joints that typically affects women more than men. An exact cause has yet to be identified, but the disease is thought to manifest due to both genetic and environmental factors. The predominant theory is that RA is an autoimmune disease with en-

vironmental triggers. Recently, diet as a risk factor for RA has become of interest. The objective of this literature review is to determine which dietary factors have an influence on developing RA by examining existing literature on this topic.

Methods: PubMed was searched for relevant articles. Articles that contained a sample size of ≥10, were published in the last 30 years, and were in English were included. A search was built using the following MeSH terms: "rheumatoid arthritis," "risk factors," "diet," "nutritional status," "nutrition therapy," "nutrition assessment," "nutrition disorders," "diet, food, and nutrition," and "nutritional requirements." Each MeSH search included "rheumatoid arthritis" AND "risk factors" AND one of the aforementioned terms. The abstracts were first screened for suitability, and suitable articles were reviewed. Additional relevant articles were found from the references of reviewed articles. A total of 121 articles were reviewed and 53 were included.

Results: Because categorization of each dietary item varied across studies, ensuring consistency among categorization was necessary for data analysis. For example, alcohol intake may refer to only wine, only beer, both wine and beer, depending on the study. Variations in phrasing (e.g. "fruits" sometimes included citrus, other times it was not defined at all), methods of data collection, and cohort chosen were found. Some studies also reported results on RA risk based on RA serostatus. Thus, variation in results across studies is likely multifactorial, including number of cases and region of cohort chosen.

When the variations were considered, moderate alcohol consumption and increased β-cryptoxanthin (a carotenoid) consumption most notably reduced risk of developing RA. Increased coffee consumption may also be a risk factor for developing RA, but more studies are needed to draw conclusions. Fish, protein, red meat, vegetables, fruits, fats, dairy, other vitamins, tea, carbohydrates, legumes, flavonoids, sugary drinks, and sodium intake had variable significance or no significant association with RA risk.

Conclusion: Moderate alcohol consumption and increased β-cryptoxanthin are protective against developing RA. Overall, specific dietary elements and their influence on RA risk is a promising topic, and significant findings may be helpful in preventing the development of RA.

Disclosure: C. Guan, None; **S. Beg**, None.

Abstract Number: 0194

Predicting Remission in Rheumatoid Arthritis: External Validation for Tocilizumab Monotherapy Using Corrona Real World Data

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Predicting remission in rheumatoid arthritis (RA) is an important goal for tailoring therapy. Tocilizumab (TCZ) has been found in randomized controlled trials (RCT) to have similar efficacy when used as mon-

Table 1: Cohort characteristics of RWD and RCT data.
N (%) presented for categorical variables. Median (25th, 75th percentile) for continuous variables.

Variables	RWD (n=452)	RCTs (n=853)
Age (Years)	59.0 (49.0, 67.0)	53.0 (44.0, 61.0)
Sex: Female	370 (82.0%)	680 (79.7%)
Race: White	420 (94.4%)	680 (79.7%)
Region:		
Other*	0 (0.0%)	88 (10.3%)
Europe	0 (0.0%)	412 (48.3%)
North America	452 (100.0%)	205 (24.0%)
South America	0 (0.0%)	148 (17.4%)
BMI	28.7 (24.7, 33.7)	26.5 (23.5, 30.5)
HAQ-DI	1.2 (0.6, 1.6)	1.6 (1.1, 2.0)
Disease duration (Years)	10.0 (5.0, 17.0)	1.8 (0.5, 7.3)
Past DMARD / MTX:		
Both No	14 (3.1%)	291 (34.1%)
Both Yes	400 (88.5%)	441 (51.7%)
DMARD Yes / MTX No	38 (8.4%)	121 (14.2%)
Baseline CDAI	21.8 (12.0, 32.6)	40.1 (30.7, 49.4)
Follow-up duration (Weeks)	25.8 (22.7, 28.4)	24.0 (24.0, 24.0)

otherapy or in combination with csDMARDS. We recently derived a remission prediction score for TCZ monotherapy (TCZm) using data from four RCTs to predict remission (CDAI < 2.8) at 24 weeks follow-up (Collins, ARD, 2019). Herein, we describe external validation for the prediction score using "real world data" (RWD) from Corrona.

Methods: We identified patients in the RWD who used TCZm for a minimum of 3 months with at least 1 follow-up visit no later than 9 months after TCZm initiation. Patients starting TCZ in combination with other DMARDs were included if TCZm initiation was within 3 months of first TCZ. We followed patients to determine whether they were in remission (CDAI < 2.8) at the next visit closest to 24 weeks (follow-up) after TCZm initiation. The cohort and remission criteria were chosen to mimic the characteristics of the population in the TCZm RCTs. We compared the performance of prediction models derived in our prior work to an additional baseline model, both in the RCTs and RWD. Each of the 3 models is a logistic regression based on a different selection of variables measured before TCZ initiation (baseline): Model A (variables selected based on odds ratio), Model B (selection based on AIC/BIC) and Model C (baseline CDAI only). We studied both a) application of model parameters learned in the RCTs to RWD, and b) cross-validation of models fit to the RWD. We examined the area under the receiver operating characteristic curve (AUROC) as a measure of discrimination and the calibration slope, comparing predicted remission probability with observed remission.

Results: We identified 453 patients from the RWD (out of 54646) who met the inclusion criteria. The 4 RCTs comprise a total of 853 patients with demographics generally similar to the RWD cohort (see Table 1). The number of patients reaching remission on TCZm by their follow-up visit was 12% (n=53) in RWD vs 15% (n=127) in RCTs. The baseline disease activity and history differed considerably: median CDAI 22 in RWD vs 40 in RCTs, and median RA duration 10 years in RWD vs. 2 years in RCTs. We found that discrimination was as good in RWD given baseline covariates as in the RCTs (see Table 2). The AUROC for Model A trained in RCTs and evaluated in RWD was 0.70 vs. 0.71 in the RCTs, and for Model B 0.69 and 0.65, respectively. The CDAI-only (Model C) achieved AUROC of 0.75 in RWD and 0.59 in RCTs.

Table 2: Internal and external validation of 3 remission prediction models.				
Variables		Model A	Model B	Model C (CDAI only)
Baseline CDAI		✓	✓	✓
Age		✓	✓	
Sex (Female)		✓	✓	
RA disease duration		✓		
Region of the world		✓	✓	
Past DMARD / MTX use		✓	✓	
ESR		✓		
Baseline HAQ-DI		✓	✓	
Baseline Hematocrit		✓		
History of CV disease		✓		
History of diabetes		✓		
Model fit in RCTs (derived in RCT)	AUROC	0.71 (0.67-0.76)	0.65 (0.60-0.69)	0.59 (0.54-0.64)
	AUROC 10-fold CV	0.67 (0.62-0.72)	0.62 (0.57-0.67)	0.59 (0.54-0.64)
	AIC	681.03	702.60	711.82
	BIC	757.01	731.10	721.32
	Calibration slope	1.03	0.95	1.04
Model fit in RWD (derived in RWD)	AUROC	0.79 (0.73-0.84)	0.76 (0.70, 0.82)	0.75 (0.69-0.81)
	AUROC 10-fold CV	0.72 (0.66-0.79)	0.74 (0.68-0.80)	0.75 (0.69-0.81)
	AIC	303.77	296.94	295.00
	BIC	357.25	321.63	303.22
	Calibration slope	1.12	1.13	1.19
Transfer to RWD (derived in RCTs)	AUC	0.70 (0.64-0.77)	0.69 (0.62-0.76)	0.75 (0.69-0.81)
	Calibration slope	1.30	0.95	1.70

Notes: ✓ signifies that a variable was included in the specific model. Transfer refers to a model fit to subjects in the RCTs and evaluated for subjects in the RWD. **Abbreviations:** CDAI, clinical disease activity index, RA, rheumatoid arthritis, DMARD, disease modifying antirheumatic drug, MTX, Methotrexate, ESR, erythrocyte sedimentation rate, HAQ-DI, health assessment Questionnaire without disability index, CV, cardiovascular, RCT, randomized controlled trial, AUROC, area under the receiver operating characteristic curve, 10-fold CV, 10-fold cross-validation, AIC, Akaike information criterion, BIC, Bayesian information criterion, RWD, real-world data.

Conclusion: We found that the remission prediction scores derived in RCTs, based on demographics, baseline disease activity and treatment history, discriminated patients in RWD about as well as in RCTs, despite notable cohort differences in treatment history and disease duration. We found that baseline CDAI alone was highly discriminative in the RWD cohort, but not in the RCTs. We believe that this is because the rapid changes in disease activity in early, untreated RA, characteristic of the RCT cohort, is more unpredictable from previous CDAI only than the slow progression of established RA, as in the RWD cohort. Therefore, we consider models A and B more robust to future changes in treatment practice.

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Abstract Number: 0195

The Clinical Characteristics of Patients with Inflammatory Arthritis and a Persistently Low Alkaline Phosphatase Level in a Veteran Affairs Rheumatology Clinic

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SESSION INFORMATION
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Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
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Background/Purpose: The biochemical hallmark of hypophosphatasia (HPP) is a low alkaline phosphatase (ALP) level. It is recognized that some forms of HPP present in adulthood and have been associated with common signs and symptoms seen in patients with rheumatic disease, including fatigue, muscle pain, weakness, bone pain, recurrent fracture, joint dislocation, and chondrocalcinosis[1]. The clinical implications of low ALP levels in patients with inflammatory arthritis is not well established.

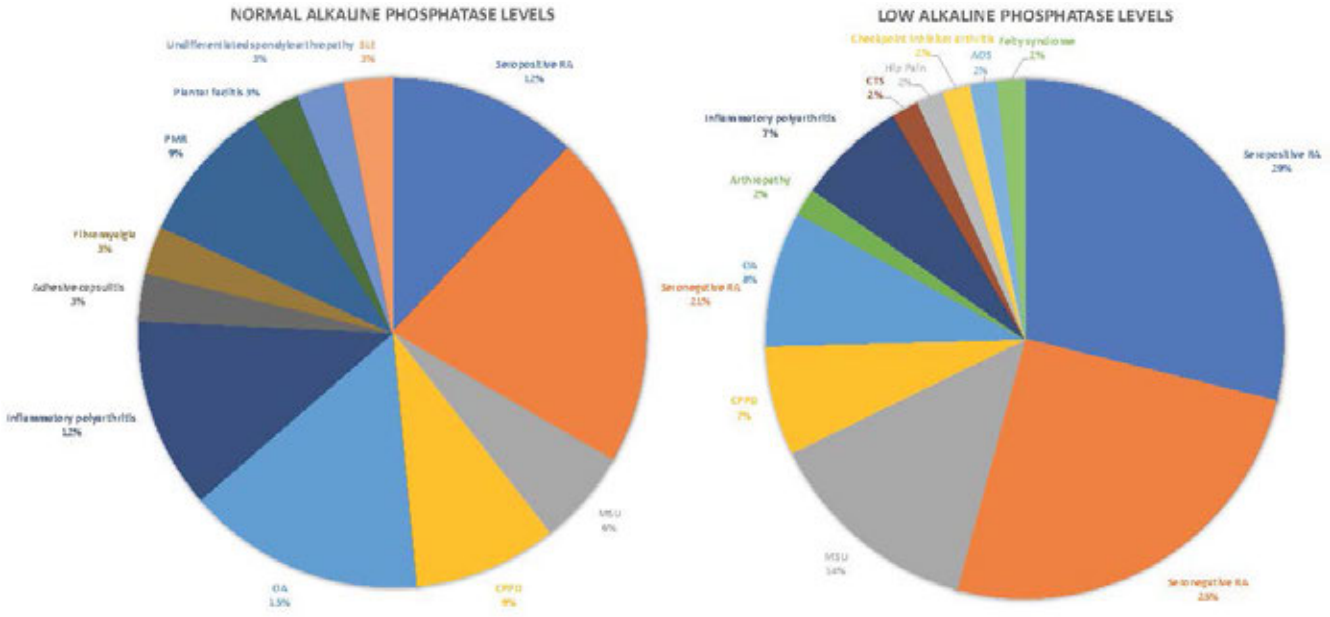

Figure 1. Comparing Diagnoses Between Patients with Normal and Low Alkaline Phosphatase Levels.

Patient Characteristics

Variable	Low Alkaline Phosphatase Level Group	Normal Alkaline Phosphatase Level Group	P Value	
Age				
Mean	68	61	0.048	
Rheumatoid Factor Positive				
no	35 (70%)	15 (75%)	0.6757	
yes	15 (30%)	5 (25%)		
anti-CCP Positive				
no	27 (68%)	15 (83%)	0.2120	
yes	13 (32%)	3 (17%)		
Chondrocalcinosis				
no	46 (90%)	25 (96%)	0.356	
yes	5 (10%)	1 (4%)		
Seropositive Rheumatoid Arthritis Diagnosis				
no	33 (65%)	22 (85%)	0.067	
yes	18 (35%)	4 (15%)		
CPPD Diagnosis				
no	47 (92%)	23 (88%)	0.593	
yes	4 (8%)	3 (12%)		
On DMARD Therapy				
no	18 (35%)	13 (50%)	0.213	
yes	33 (65%)	13 (50%)		
Number of Agents Tried				
Mean	1.55	0.92	0.040	
Prescribed Biologic				
no	44 (86%)	18 (69%)	0.074	
yes	7 (14%)	8 (31%)		
Prescribed Narcotics				
no	44 (86%)	24 (92%)	0.435	
yes	7 (14%)	2 (8%)		
Prescribed Oral NSAIDs				
no	28 (55%)	18 (69%)	0.225	
yes	23 (45%)	8 (31%)		
Prescribed Steroids				
no	35 (69%)	23 (88%)	0.056	
yes	16 (31%)	3 (12%)		

Figure 2. Characteristics of Patients with Low and Normal Alkaline Phosphatase Levels.

Purpose: To analyze the clinical features associated with low ALP in patients with inflammatory arthritis in a rheumatology clinic.

Methods: This single center cross-sectional retrospective chart review of patients with low ALP levels and inflammatory arthritis, defined as rheumatoid arthritis (RA) or inflammatory arthritis encounter diagnoses, was performed using the VA electronic medical record. Patients with two or more ALP levels below 40 U/L were compared to patients with consistently normal ALP levels. We excluded patients with co-morbid disease and medications known to cause low ALP levels. The

age, race, rheumatoid factor, anti-citrullinated peptide (anti-CCP) of these two groups were extracted. We looked at the bivariate relationships of these variables, comparing each separately in relation to the group. Clinical diagnoses and pharmacologic history of disease modifying agents and analgesics were extracted and compared between the two groups. Two Sample T test and Pearson's Chi-Square test were used to compare population means and binary variables, respectively.

Results: There was no significant difference in the prevalence of seropositivity or in clinical diagnoses between the two groups, however there was a trend towards patients with low ALP levels having seropositive RA (35% vs 15%, p=0.064). The mean number of disease modifying anti-rheumatic drugs tried was greater in the low ALP group than the control group (1.55 vs 0.92, p= 0.040). Patients in the low ALP group were also older (68 vs 61, p= 0.048). There was no difference in analgesic use between the two groups.

Conclusion: Patients with low ALP and inflammatory arthritis were older and had been tried on a greater number of DMARDs. These findings may suggest that these patients represent a cohort who have disease that is more severe or longstanding. There was no difference in prevalence of seropositive RA or seronegative RA in patients with low ALP levels. However, we did see a trend towards patients with low ALP having seropositive RA. Future work could evaluate for a stronger association between low ALP, RA, gout, pseudogout, and atypical forms of osteoarthritis using a larger sample size to detect this difference.

Reference

1. Lefever, E. et al. Hypophosphatasia in Adults: Clinical Spectrum and Its Association With Genetics and Metabolic Substrates. *Journal of Clinical Densitometry*. https://doi.org/10.1016/j.jocd.2018.12.006

Disclosure: L. Monteagudo, None; **A. Gravely**, None; **P. Valen**, None; **D. Ewart**, None.

Abstract Number: 0196

Risk of Subsequent Atherosclerotic Cardiovascular Disease After the First Unprovoked Venous Thromboembolism in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: With the advent of JAK inhibitors has come increased concerns for the risk of venous thromboembolism (VTE), which was already known to be increased in RA due to inflammation. Although it can be potentially a fatal condition, the other adverse outcomes of VTE, particularly the risk of atherosclerotic cardiovascular disease (CVD), are not well-known in RA. As this potential association has clinical implications regarding screening and risk factor modification, we performed a cohort study to determine the risk of subsequent ASCVD in RA patients with unprovoked first VTE.

Methods: RA patients with ≥1 year participation in FORWARD, The National Databank for Rheumatic Diseases, from 1998 through 2018 were assessed for incident nonfatal or fatal ASCVD (myocardial infarction and stroke) validated

Table 1. Baseline characteristics of RA patients with VTE and without any CVD

Variables	Without any CVD, N=25,070	With VTE, N=506	P value
Age, years	57.9 (13.1)	67.0 (11.8)	<0.001
Female, %	81.7	79.1	0.125
Caucasian, %	93.6	93.1	0.672
RA duration, years	13.5 (12.0)	20.0 (13.1)	<0.001
BMI, kg/m^2	28.3 (6.4)	30.4 (7.8)	<0.001
Obesity, %	29.3	41.9	<0.001
Exercise, %	13.7	5.7	<0.001
RDCI (0-9)	1.6 (1.5)	2.7 (1.80)	<0.001
Ever-smoked, %	42.3	43.5	0.599
Diabetes, %	8.7	17.8	<0.001
Hypertension, %	43.5	59.9	<0.001
Pulmonary disease, %	6.2	19.4	<0.001
Prior fracture, %	2.3	6.9	<0.001
Prior cancer, %	20.3	27.5	<0.001
HAQ disability (0-3)	1.1 (0.7)	1.4 (0.7)	<0.001
PAS (0-10)	3.9 (2.2)	4.6 (2.2)	<0.001
Medications			
Glucocorticoid current, %	40.1	50.4	<0.001
Glucocorticoid ever, %	70.7	85.4	<0.001
MTX, %	56.3	48.2	0.001
Hydroxychloroquine, %	25.4	18.2	0.001
TNFi, %	33.2	36.0	<0.001
Other b/tsDMARDs, %	10.0	20.8	<0.001

from hospital/death records. We excluded patients with prior VTE/ASCVD and active cancer. Among these patients, we identified patients with first unprovoked VTE (deep venous thrombosis [DVT] and pulmonary emboli [PE] not associated with cancer, recent surgery, hospitalization, fracture, or pregnancy). We calculated event rates and estimated the risk of subsequent ASCVD in patients with incident VTE compared to patients with no history of VTE and ASCVD by using Cox proportional hazards with adjustment for sociodemographics, comorbidities, and RA severity measures.

Table 2. Crude incidence rates and risk of ASCVD in patients with RA by unprovoked VTE

	Events/ patients	Patient-years	Incidence rate (95% CI)*	Unadjusted HR (95% CI)	Adjusted HR† (95% CI)
Patients without VTE or ASCVD	1,283/25,070	147,735	8.68 (8.22-9.17)	-	-
Patients with first unprovoked VTE (no prior ASCVD or VTE)	38/506	16,152	23.53 (17.12-32.33)	2.50 (1.81-3.44)	2.05 (1.43-2.95)
DVT only	21/325	11,150	18.83 (12.28-28.87)	2.03 (1.32-3.12)	1.93 (1.22-3.05)
Pulmonary emboli	17/181	5,002	33.99 (21.13-54.67)	3.78 (2.50-5.70)	2.52 (1.57-4.04)

**Per 1,000 patient-years*
†Adjusted for age, sex, disease duration, socioeconomic status (annual income, insurance, location of residency), ethnicity, smoking, hypertension ,diabetes, comorbidity index, BMI, HAQ, patient global and pain scores, glucocorticoid use DMARDs including MTX, HCQ, TNFi and nonTNFi bDMARDs, NSAIDs, statins, fracture, pulmonary disease, prior count of csDMARDs and bDMARDs, calendar year

Results: In 25,070 RA patients with no VTE or ASCVD and 506 patients with first unprovoked VTE (without prior ASCVD), we identified 1,283 and 38 first ASCVD events during median (IQR) 4.7 (2.4-8.9) years of follow-up. Baseline characteristics of patients with VTE and without any CVD are presented in *Table 1*. Patients with unprovoked VTE had worse RA characteristics (disease duration, HAQ, disease activity, glucocorticoid use) and more frequent traditional CV risk factors (diabetes, hypertension, and obesity). The incidence rate (95% CI) of ASCVD was higher in patients with VTE vs. patients without any CVD (8.68 [8.22-9.17] vs. 23.53 [17.12-32.33] per 1,000 patient-years) (*Table 2*). After multivariable adjustment for baseline differences, we found that patients with an unprovoked VTE had a significantly increased risk of ASCVD (HR [95% CI], 2.05 [1.43-2.95]). The risk increase persisted when we assessed patients with only DVT (HR [95% CI], 1.93 [1.22-3.06]) and the risk in patients with PE was even higher (HR [95% CI], 2.52 [1.57-4.04]) (*Table 2*).

Conclusion: RA patients with unprovoked VTE as the first CVD, even with only DVT, had twofold risk of ASCVD. Future studies are needed to clarify to what extent chronic inflammation and traditional CV risk factors contribute to this association. Nevertheless, RA patients with unprovoked VTE should be evaluated carefully for ASCVD in the presence of concerning symptoms. Also, more vigilant CV risk screening and treatment should be considered in these patients.

Disclosure: G. Ozen, None; **S. Pedro**, None; **R. Schumacher**, None; **T. Simon**, Bristol-Myers Squibb, 3; **K. Michaud**, FORWARD, The National Databank for Rheumatic Diseases, 3, Pfizer, 2, Pfizer & Rheumatology Research Foundation, 2, Rheumatology Research Foundation, 2, University of Nebraska Medical Center, 3.

Abstract Number: 0197

The Relationship Between Pain and Patient Demographics, Clinical Features, and Health Outcomes in a Cohort of Rheumatoid Arthritis Patients Recruited and Studied Using a Mobile Application

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SESSION INFORMATION
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Background/Purpose: Pain is one of the most pressing problems for Rheumatoid Arthritis (RA) patients and contributes substantially towards fatigue and disability. Experiences of pain in real world settings may be captured through the use of innovative mobile apps. This study investigates the relationship between pain and patient demographics, clinical features, and health outcomes in a cohort of RA patients recruited via a mobile app.

Methods: A novel mobile app, funded by GSK, known as the PARADE app (PAtient Rheumatoid Arthritis Data from the rEal world) was developed using Apple ResearchKit™ software in 2016. This app obtained informed consent and captured patient demographics, comorbidities, medication use, and PRO instruments - i.e. the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) and Health Assessment Questionnaire – Disability Index (HAQ-DI). Participants self-reported as being diagnosed with RA and being 18 years or older. A cross-sectional design with week 1 data was used, and Pearson correlations calculated. Pain was measured on a 0 to 10 scale and grouped into: low (0-2), mild (3-5), moderate (6-8) and severe (9-10) pain.

Results: Pain scores were recorded for 421 RA patients; 28.5% of with low pain, 39.0% with mild, 23.3% with moderate, and 9.3% with severe pain, regardless of medication use. Most patients were female (79.1%) and Caucasian (80.5%), however 28.2% of the severe pain group were Hispanic (vs only 9.3% of the low-to-moderate pain group).

Pain score was correlated with tender joint count (correlation r 0.30, $p < .0001$) and degree of morning stiffness (r 0.41, $p < .0001$). The most bothersome RA symptom was joint pain (ranging from 74.2% to 94.9% across pain groups), followed by fatigue (60.8% to 79.3%). Pain was highly correlated with FACIT-F and HAQ-DI scores (r 0.38 and 0.54 respectively, both $p < .0001$). Pain was also correlated with each HAQ-DI subcategory (all $p < .0001$).

Osteoarthritis (OA) was more common in those with moderate pain (34.7%), than low or severe pain (14.2% and 23.1%, respectively). Fibromyalgia was most common in moderate pain patients (36.7%), but less frequent in low and severe pain patients (3.3% and 20.5% respectively). Mood was not associated with pain, and while depression was present in 34.7% of moderate pain patients, it was less common in severe (23.1%) or low (16.7%) pain patients.

Pain medication was frequently used by those with moderate pain (85.7%), but lower levels of use were reported in low (55.0%) or severe (66.7%) pain patients. Conventional Disease-Modifying Anti-Rheumatic Drug (cDMARD) use was common in both low-to-moderate pain groups (61.0% to 68.3%), but only 35.9% in the severe pain subgroup. Biologic DMARDS (bDMARDs) were used by 49.0% of moderate pain patients, but only by 35.9% of severe pain patients.

Conclusion: Pain remains an area of high unmet need in this RA patient cohort. Pain was highly associated with measures of fatigue and disability. However, comorbidities such as OA, fibromyalgia, and depression may be more common in patients with moderate pain than severe or low pain. Patients with severe pain reported lower levels of cDMARD and bDMARD treatment, indicating possible undertreatment of pain in this group.

Disclosure: H. Dickinson, GSK, 1, 2, 3, 4, AZ, 1, 2, 3, 4; **Y. Liu**, GSK, 1, 2, 3, 4; **R. Williams**, GSK, 1, 2, 3, 4.

Abstract Number: 0198

Assessing Care Quality in Rheumatology Services

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SESSION INFORMATION
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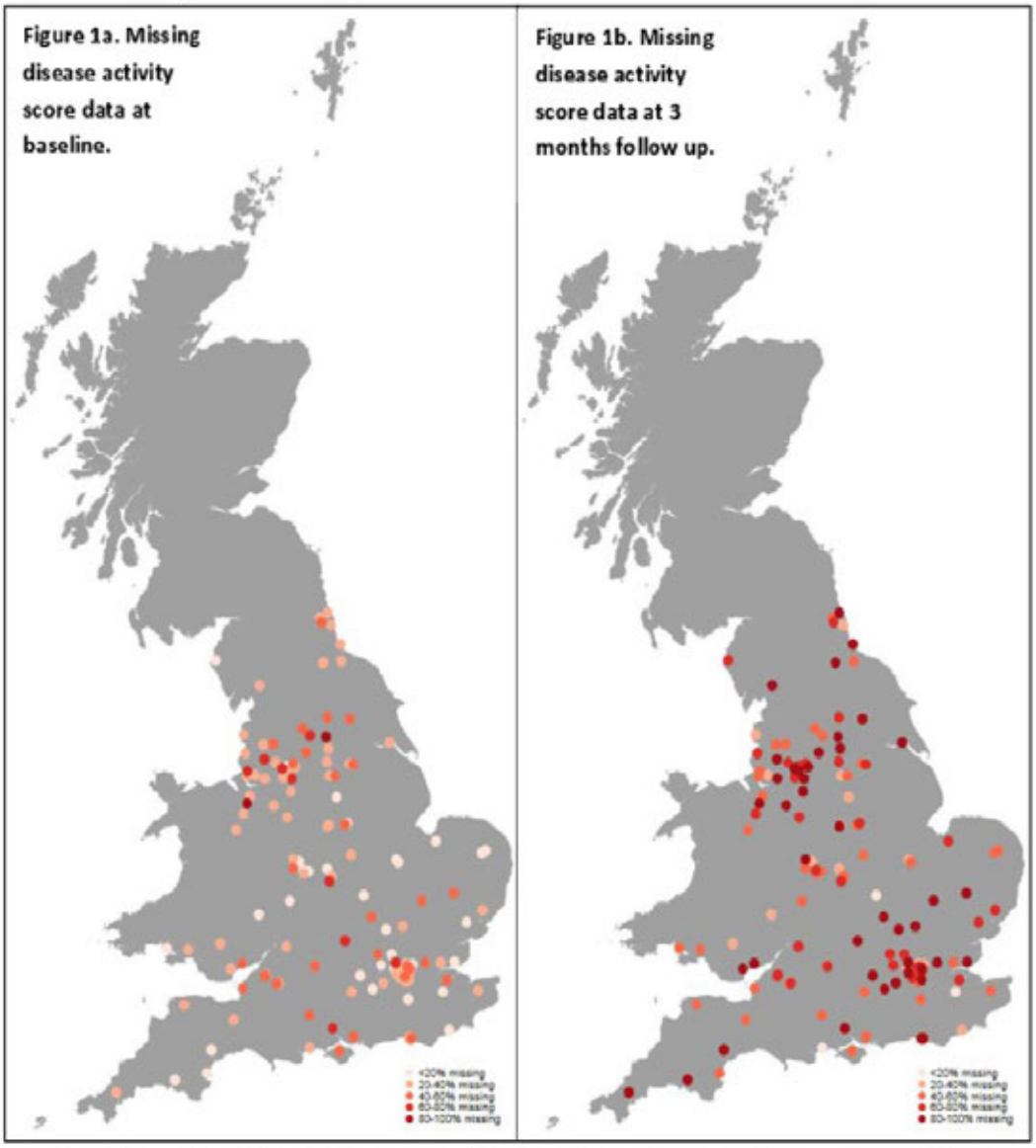
Background/Purpose: There is high-quality evidence that prompt diagnosis and treatment have beneficial impact on outcomes in RA. Current guidelines from both North America and Europe reflect this evidence base. Despite this, there is marked variation in how clinicians follow guidance. We conducted a national survey of practice in England and Wales to assess adherence to guidelines focussing on time to first disease modifying treatment. We have already published from this, demonstrating that over a third of patients experience significant delays. Accepting that data collected outside of a clinical trial or research environment tend to be less complete, we hypothesized that the completeness of data returned would be directly correlated with the quality of care provided.

Table 1. Baseline characteristics, disease activity, and quality of care received stratified by complete and incomplete Das-28 baseline and follow up data.

	Complete DAS-28 data at baseline and follow up	Incomplete DAS-28 data at baseline or follow up	p values
	(N = 1983)	(N = 4222)	
Age, mean (SD)	59.6 (14.2)	57.5 (15.6)	<0.0001
Female	63.8%	63.6%	NS
IMD rank, median (Q1, Q3)	626 (297, 1016)	640 (300, 1022)	NS
White European	91.7%	90.4%	NS
Current Smoker	24.4%	21.2%	0.009
Full time paid employment	36.8%	40.7%	0.008
Seropositive	84.1%	74.3%	<0.0001
DAS-28 at baseline, mean (SD)	5.2 (1.3)	4.9 (1.4)	<0.0001
Symptom duration in days, median (Q1, Q3)	96 (51, 204)	107 (54, 234)	0.003
Referral letter states EIA	90.8%	90.2%	NS
Referral within 3 days	16.0%	17.5%	NS
Review within 21 days	38.8%	36.4%	NS
Treatment within 90 days	70.1%	55.5%	<0.0001

Patients who were positive for RF and/or anti-CCP were considered seropositive. NS = non-significant.

Figure 1. Mapping of departmental proportions of missing disease activity score data at baseline and 3 months follow up.



Departmental proportions of missing disease activity data mapped using the grmap software package in stata 15. Darker colors indicate higher degrees of missing data.

Methods: Data were collected between January 2014 and December 2015 on patients referred to specialist rheumatology services across England and Wales with a suspected diagnosis of inflammatory arthritis. Baseline demographic and clinical details, including a disease activity score (DAS-28), were collected. Patients with a confirmed diagnosis of RA had follow up data collected at three months. Demographic differences in patients with missing DAS-28 data at baseline or three months follow up were tabulated. Departmental proportions of missing DAS-28 data across England and Wales were mapped. A mixed effects logistic regression model adjusted for patient and department level variables was conducted to assess if completeness of baseline DAS-28 data associated with prompt disease modifying treatment commencement.

Results: 6,205 patients diagnosed with RA from 136 rheumatology departments had data, of whom 3,733 (60%) commenced a DMARD within 3 months of referral to specialist rheum care. Disease activity data (measured using

Table 2. Mixed effects logistic modelling of missing DAS-28 data at baseline as a predictor of prompt treatment commencement.

Prompt treatment commencement	Odds Ratio	p values	95% Confidence Interval
Patient level			
Missing baseline DAS-28	0.50	<0.0001	0.41 to 0.60
Age	1.00	0.518	0.99 to 1.00
Gender	1.07	0.447	0.90 to 1.28
In paid work	1.09	0.379	0.90 to 1.32
Socioeconomic position	0.98	0.573	0.92 to 1.05
Smoking status	0.97	0.760	0.79 to 1.18
White European ethnicity	1.03	0.861	0.75 to 1.41
Symptom duration	1.00	0.181	0.99 to 1.00
Seropositive	1.11	0.320	0.90 to 1.37
Department level			
EIA clinic	1.16	0.465	0.78 to 1.71
Departmental proportion missing baseline DAS-28	1.79	0.339	0.54 to 5.87
Departmental proportion missing follow up DAS-28	0.44	0.105	0.16 to 1.19
Specialist nurse density	1.53	0.041	1.02 to 2.31
Consultant density	0.71	0.031	0.52 to 0.97
Random effect			
Department			
var(_cons)	0.86		0.58 to 1.27

DAS-28) was available for 4,075 (66%) at baseline and 2,341 (38%). Patients with missing DAS-28 data had distinct characteristics to those with complete data, see table 1.

Patients without a baseline DAS-28 score recorded were 50% less likely (odds ratio 0.50, 95%CI 0.41 to 0.60) to commence a DMARD within three months. This effect was independent of all patient level factors included in the analysis. Unit level factors including staff ratios did correspond to data quality, and in particular greater specialist nurse support correlated with higher quality care. See table 2 for further details.

There were broad geographic variations in departmental proportions of missing data, illustrated in figure 1. The departmental proportion of missing DAS-28 data ranged from 0 to 91% at baseline, and 0.1 to 100% at 3 months follow up.

Conclusion: These data from a large national survey demonstrate a clear relationship between the completeness of data collected and the quality of care provided. This supports the view that clinician engagement in quality assessment is likely to be a good surrogate for the quality of care that they are delivering. Measuring quality in healthcare has climbed up the rheumatology community's agenda in the last decade, reflected in the ACR white paper on performance outcome measure in 2016. Data completeness is a simple but useful additional metric as a surrogate for quality.

Disclosure: M. Yates, None; **S. Norton**, None; **A. MacGregor**, None; **K. Bechman**, None; **S. Rampes**, None; **J. Galloway**, AbbVie, 8, Bristol-Myers Squibb, 8, Celgene, 8, Janssen, 8, Pfizer, 8, Union Chimique Belge., 8.

Abstract Number: 0199

Obesity and Incident Opioid Use in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
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Background/Purpose: Prevalent chronic use of opioids approximately 17% among patients with rheumatoid arthritis (RA) and has increased over the last decade.(1) Obesity may be a risk factor for chronic opioid use through an association with greater comorbidity, non-inflammatory musculoskeletal disorders, disability, and pain sensitization. We therefore hypothesized a higher rate of use of chronic opioid use in obese patients with RA. We further hypothesized that this relationship would be at least partially explained by worse pain and quality of life scores reported over time in this group.

Methods: RA participants in *Forward*, the National Databank for Rheumatic Diseases, were asked about use of opioid medications on semi-annual surveys between 1999 and 2018. Incident chronic opioid use was defined as new use extending over two contiguous surveys as previously defined. Cox proportional hazards models evaluated associations between body mass index (BMI) category at enrollment and incident chronic opioid use. Initial models considered demographics, smoking, disease duration, and baseline treatments. Subsequent models incorporated time-varying measures depression, pain scores, fibromyalgia severity scores, and physical and mental health status from the SF-36 in order to determine the contribution of these factors to the association between obesity and opioid use.

Results: A total of 25,775 participants were included in this analysis and there were 4,861 incident cases of incident opioid use in 108,864 person-years of follow-up. Higher BMI category was associated a higher risk of incident chron-

Table 1: Risk of chronic opioid use in partially adjusted and fully adjusted models among participants with no data missing for key variables.

	Model 1 *N=19,101 PY= 69,068 Incident Cases 3,345*	**Model 2** *N=19,101 PY= 69,068 Incident Cases 3,345*
	aHR (95% CI)	aHR (95% CI)
BMI Category		
Underweight	1.16 (0.89, 1.50)	1.05 (0.81, 1.36)
Normal	1 (reference)	1 (reference)
Overweight	1.32 (1.21, 1.44)	1.17 (1.07, 1.28)
Obese	1.58 (1.43, 1.74)	1.21 (1.09, 1.34)
Severely Obese	2.11 (1.90, 2.35)	1.26 (1.14, 1.41)

Model 1: Age, sex, race, RA disease duration, smoking, methotrexate use, biologic use, total number of biologics used at baseline.
Model 2: Model 1 plus adjustment for time-varying depression, pain scale, fibromyalgia severity scale, and physical and mental health status.

Table 2: Estimated number of attributable cases of chronic opioid use to obesity based on Model 1.

	N	Predicted 5-year Incidence	Expected Cases at Normal BMI	Cases Attributable to Obesity	% of Cases Explained by Obesity
Underweight	499	120	100	20	0
Normal	8757	1751	1751	0	0
Overweight	8016	1924	1603	321	17%
Obese	4370	1179	874	305	26%
Severely Obese	3152	1040	630	410	39%
All	24794	6004	4958	1046	17%

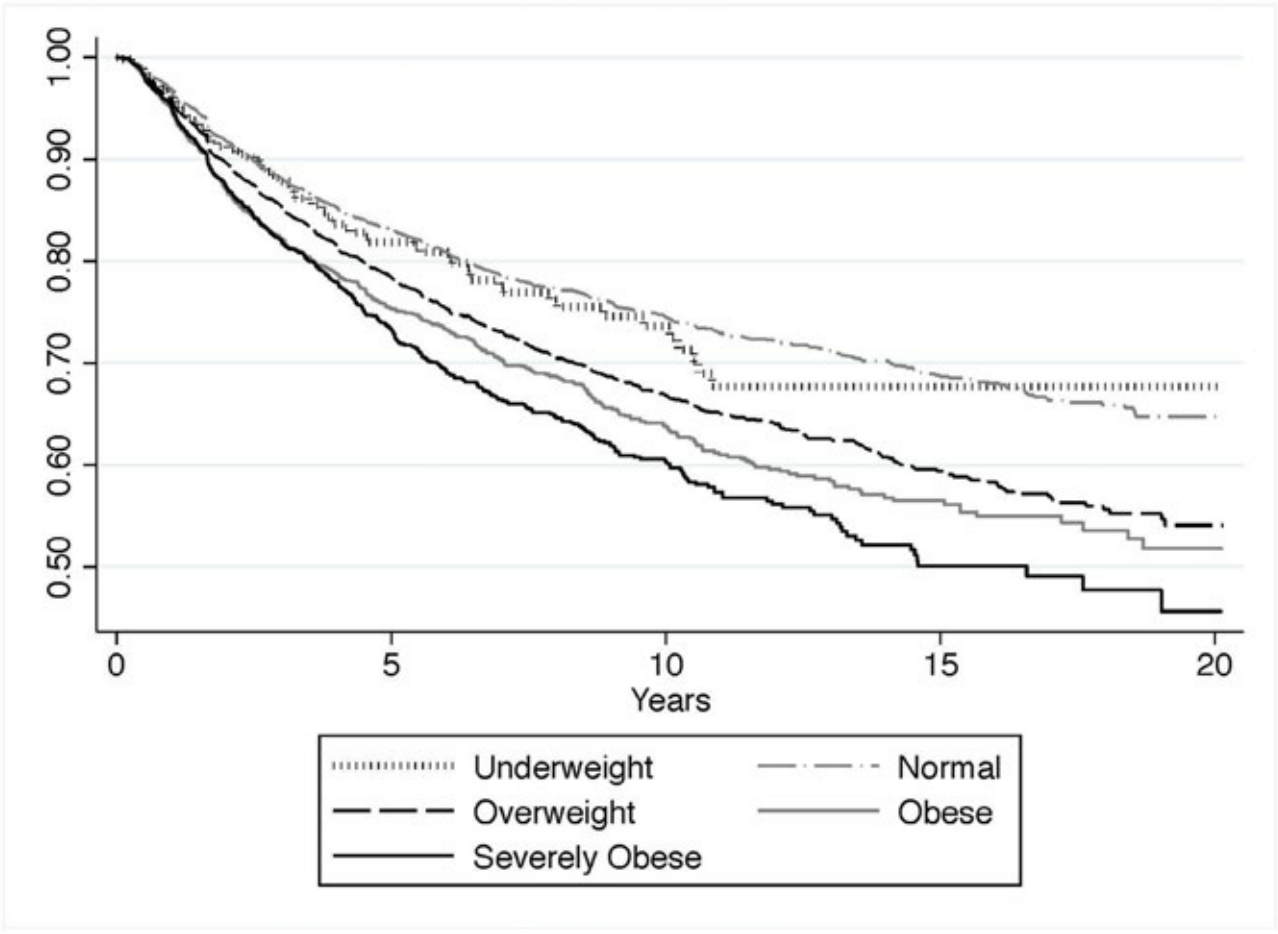

Figure: Survival without use of chronic opioids by BMI category after adjusting for age, sex, race, and smoking status.

ic opioid in a dose-dependent manner. In initial models, severe obesity was associated with a much higher risk of incident use [HR 1.87 (1.72, 2.04) p< 0.0001] compared to normal BMI. Among participants with data for all variables, adjusting for time-varying pain, fibromyalgia, and quality of life scores partially attenuated the relationship (Table 1), suggesting that 69% of the risk was explained by these factors. Based on the absolute incidence at 5 years predicted by Model 1 (Table 2), obesity is expected to account for 39% of use among severely obese individuals. Based on the risk difference of 13%, the prevention or reversal of severe obesity in 8 patients would be expected to prevent one case of chronic opioid use at 5 years.

Conclusion: Obesity is associated with a substantially higher incident chronic use of opioids. This relationship is largely explained by greater reported pain, depression, and poor quality of life over time. Approximately 39% of incident use among severely obese individuals might be attributed to the obesity itself, suggesting a major public health impact on this problem. Interventions to prevent or reduce obesity and related complications could have a substantial impact on chronic use of opioids in this population.

Disclosure: J. Baker, Bristol-Myers Squib, 5, Burns-White LLC, 5, Myriad RBM, 2; **S. Pedro**, None; **K. Michaud**, FORWARD, The National Databank for Rheumatic Diseases, 3, Pfizer, 2, Pfizer & Rheumatology Research Foundation, 2, Rheumatology Research Foundation, 2, University of Nebraska Medical Center, 3.

Abstract Number: 0200

A Validated Text-mining Algorithm to Extract Rheumatoid Arthritis Medication Contained in Format-free Fields of Electronic Medical Records

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SESSION INFORMATION
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Background/Purpose: Rapidly expanding collections of Electronic Medical Records (EMR) form a valuable resource for clinical research. Besides entries with a standardized format, EMRs often also contain free text fields intended for noting specifications of the treatment policy. While these free text fields contain essential information, their free nature makes them hard to parse, as they contain typos or acronyms. As a result, data extraction from EMR is often performed manually, or is performed while excluding the format-free fields. The purpose of this study is to develop and validate a text-mining approach to extract medication prescribed for Rheumatoid Arthritis as contained in format-free fields of an EMR.

Methods: The EMR dataset consisted of 45,012 entries from 2,771 patients that visited the rheumatology outpatient clinic from the Leiden University Medical Centre between 2007 and 2018. We randomly selected 15% and 7,5% of the entries to create a training and test set, with 5,992- and 2,993 entries respectively. The training set was used to design the algorithm, whereas the test set was used as an independent validation of the algorithm's performance of identifying each of the DMARDs and biologicals routinely prescribed for treating RA.

Using methods derived from Natural Language Processing, we developed an algorithm that consecutively performs three tasks: 1. Text pre-formatting 2. Acronym recognition and 3. Typo correction. Text pre-formatting consisted of several simple operations to deal with the most prevalent textual artifacts, including separation of special characters and punctuation sticking to words. Ten independent clinicians compiled acronym lists for each of the routinely prescribed RA medication. Lastly, for typo correction, we employed the Damerau-Levenshtein[1] (DL) distance that determines the similarity between two words by counting the number of single character operations (remove, add, move or replace) required to transform one word into another. Using the training set, we computed for each drug DL distances between all words in the free fields of the EMRs and a particular drug name or its acronym. Using the annotations created in the training set we then determined the DL distance optimally distinguishing between a typo and two similar words with a different meaning.

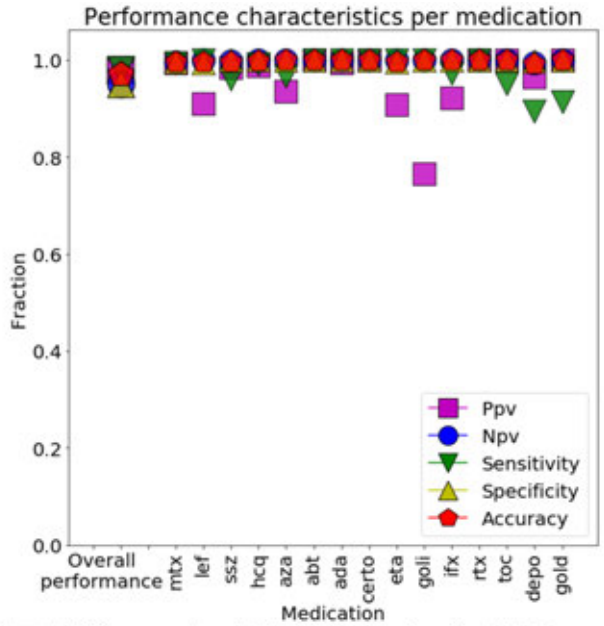

Figure 1: Performance characteristics for the extraction of medication in general and for each medication individually. With the fraction on the Y-scale and the different medications on the X-scale. Where mtx=methotrexate, lef=leflunomide, ssz=sulfasalazine, hcq=hydroxychloroquine, aza=azathioprine, abt=abatacept, ada=adalimumab, certo=certolizumab, eta=etanercept, goli=golimumab, ifx=infliximab, rtx=rituximab, toc=tocilizumab and depo=depomedrol.

Results: Fifteen medications for the treatment of RA were present in our sample (see figure 1). In total, medication was present in 1,789 out of the 2,993 entries. The median DL cutoff for typos was 2 with a standard deviation of 0.96. The overall accuracy of our drug-identification-algorithm was very good per medication in general (0.97) and the individual test characteristics were high: sensitivity=0.98 and specificity=0.95, PPV=0.98, NPV=0.95. Also on an individual drug-level the performance was high: accuracy >=0.99, sensitivity >=0.89 and specificity >=0.99, NPV >=0.99 and PPV >=0.90 for all medication except golimumab.

Conclusion: We developed and validated an algorithm enabling a highly accurate automated extraction of RA medication from format-free fields of Electronic Medical Records.

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Abstract Number: 0201

Identification of Patients with Rheumatoid Arthritis Treated with Biologics Using Standardized Vocabularies

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health Poster I: RA

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To improve efficiency and transportability of observational research, common data models have been developed and maintained to translate data from source vocabularies into standardized vocabularies using vocabulary mapping. The accuracy of mapping International Classification Codes to Systematized Nomenclature of Medicine – Clinical Terms (SNOMED-CT) of rheumatoid arthritis (RA) has been examined at the cohort level, however, its accuracy, in combination with standardized medication coding system RxNorm, has never been examined at the patient level. The objective of this study is to examine the positive predictive value (PPV) of identifying patients with rheumatoid arthritis treated with biologics using Observational Medical Outcomes Partnership (OMOP) common data model.

Methods: NewYork-Presbyterian/Columbia University Irving Medical Center (NYP/CUIMC) EHR has been translated and maintained in OMOP common data model. We searched NYP/CUIMC clinical data warehouse for prevalent cases of patients with rheumatoid arthritis treated with biologics using standardized codes for RA and biologics from 01/01/2013 to 12/31/2018, and excluded patients with other potential indications for biologics. We randomly selected 100 patients from the search result for chart review. We used documentation of a diagnosis of rheumatoid arthritis and a biologics at the index date (+/-4 days) as the gold standard. For patients who had rheumatology visit notes, we examined whether they fulfilled 2010 Rheumatoid Arthritis Classification Criteria.

Results: One hundred and two medical records were identified, and 11 were not accessible. Among the 91 records that were retrieved and examined, 77 patients (84.6%) had a documented RA diagnosis and prescription of biologics, by either rheumatology providers or non-rheumatology providers. Four patients did not have a documented diagnosis of RA, and ten did not have a documented use of biologics. Of the 47 patients who had rheumatology visits, 41 (87.2%) fulfilled the 2010 RA classification criteria.

Conclusion: Using OMOP common data model and standardized vocabularies, we can identify RA patients treated with biologics with a PPV of 84.6% in a single center EHR system.

Disclosure: R. Wang, None; **T. Falconer**, None; **G. Hripcsak**, None.

Abstract Number: 0202

Risk Factors Associated with Serious Infections Among Users of Biosimilar and Originator Infliximab Therapies

Cristiano S. Moura,[1] Jeffrey Curtis,[2] Denis Choquette,[3] Gilles Boire,[4] Vivian P. Bykerk,[5] Carter Thorne,[6] Walter P. Maksymowych,[7] Peter L. Lakatos,[8] Larry Svenson,[9] Laura Targownik,[10] Waqqas Afif,[8] and **Sasha Bernatsky**[11], [1]McGill University Health Centre, Montreal, QC, Canada, [2]University of Alabama at Birmingham, Birmingham, AL, [3]Institut de Recherche en Rhumatologie de Montréal, University of Montreal, Québec, Canada., Montreal, QC, Canada, [4]Sherbrooke University, Sherbrooke, QC, Canada, [5]Hospital for Special Surgery, New York, NY, [6]Southlake Regional Health Centre, Newmarket, ON, Canada, [7]University of Alberta/CARE ARTHRITIS, Edmonton, AB, Canada, [8]McGill University, Montreal, QC, Canada, [9]University of Alberta, Edmonton, AB, Canada, [10]University of Manitoba, Winnipeg, MB, Canada, [11]Research Institute of the McGill University Health Centre, Montreal, QC, Canada

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health Poster I: RA

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Biosimilar use in North America is relatively low, and real-world comparisons of biosimilars and their originator biologics are lacking. We assessed risk factors associated with serious infections in new users of originator infliximab or infliximab biosimilar.

Table 1. Baseline characteristics according to the initial treatment

Characteristic	Originator infliximab (n=2584)	Infliximab biosimilar (n=92)
Female sex (%)	56 (60.9)	1556 (60.2)
Mean age in years, (SD)	48.3 (15.8)	43.9 (15.0)
Age-adjusted CCI score, mean (SD)	1.9 (2.3)	1.4 (2.0)
Past hospitalized infection (%)	5 (5.4)	265 (10.3)
Underline disease indication[1]		
RA	34 (38.2)	546 (22.5)
AS	4 (4.5)	107 (4.4)
Psoriasis/PsA	13 (14.6)	260 (10.7)
IBD	38 (42.7)	1517 (62.4)
Any DMARD use (%)	46 (50.0)	876 (33.9)
Any systemic glucocorticoid use (%)	80 (87.0)	2082 (80.8)
Prior biologic use (%)		
Adalimumab	24 (26.0)	662 (25.6)
Etanercept	8 (8.7)	185 (7.1)
Abatacept	2 (2.2)	27 (1.0)
Certolizumab	3 (3.3)	76 (2.9)
Rituximab	1 (1.1)	25 (1.0)
Tocilizumab	0 (0)	22 (0.9)

[1]Based on the date of diagnosis closest to the start of treatment.
CCI: Charlson comorbidity index; RA: rheumatoid arthritis, AS: ankylosing spondylitis, PsA: psoriatic arthritis, IBD: inflammatory bowel disease, including Crohn's disease and ulcerative colitis.

Methods: We used MarketScan administrative health data to create a cohort of adult new users of infliximab (originator infliximab or infliximab biosimilar), between Jan.-Dec. 2017. The first infusion was the cohort entry date. A 90-day current exposure period was assigned for every infusion and individuals could contribute person-time through the observation period. We assessed frequency and time to first serious infection, defined as those associated with hospitalization. Crude incidence rates were generated to compare infection risk between originator infliximab and infliximab biosimilar. Cox proportional hazards regression models were adjusted to identify risk factors associated with serious infections: current infliximab therapy (originator or biosimilar), age, sex, prior biologic use, prior and current use of DMARDs and systemic glucocorticoids, past hospitalized infection, age-adjusted Charlson comorbidity index (CCI), and underlying conditions (rheumatoid arthritis, ankylosing spondylitis, psoriasis/psoriatic arthritis, Crohn's disease, ulcerative colitis).

Results: We studied 2676 individuals, including 2584 originator infliximab and 92 infliximab biosimilar. Most (60%) were women and the mean age was 44±15 years. Baseline characteristics (stratified by the initial treatment) are presented in Table 1. We identified 115 hospitalized infections during follow-up. Infection rates were 5.5 (95% confidence interval, CI 1.4-22.1) for current infliximab biosimilar and 8.5 (95% CI 7.0-10.3) for originator infliximab. We were unable to identify an association between infliximab therapy and hospitalized infection (adjusted hazard ratio, HR: 0.75, 95%CI 0.18-3.1). Age-adjusted CCI, past hospitalized infection, and prior and current use of glucocorticoids were associated with risk of hospitalized infection (Table 2).

Conclusion: We were unable to detect differences in serious infectious between originator infliximab and infliximab biosimilar. High comorbidity score, occurrence of past infections and use of glucocorticoids were associated with

Table 2. Risk factors associated with hospitalized infections

Variable	HR	95% CI
Infliximab biosimilar	0.75	0.18-3.07
Female sex	0.91	0.61-1.35
Age	0.99	0.98-1.01
Age-adjusted CCI score	1.17	1.07-1.27
Past hospitalized infection	3.69	2.44-5.58
Underline disease indication[1]		
RA	0.23	0.03-1.66
AS	0.48	0.20-1.17
Psoriasis/PsA	0.72	0.39-1.33
Past use of DMARD	0.97	0.56-1.68
Current use of DMARD	0.78	0.38-1.61
Past use of systemic glucocorticoid	1.77	0.93-3.37
Current use of systemic glucocorticoid	1.59	1.04-2.41
Any prior biologic use	1.06	0.70-1.60

[1]IBD was the reference category.

increased risk of hospitalized infections. Additional long-term studies would be of additional help in establishing safety profiles.

Disclosure: C. Moura, None; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **D. Choquette**, AbbVie, 5, 8, AbbVie Canada, 5, 8, 9, Amgen, 5, 8, Amgen Canada, 5, 8, 9, BMS, 5, 8, BMS Canada, 5, 8, 9, Celgene, 5, 8, Celgene Canada, 5, 8, 9, Eli Lilly Canada, 5, 8, 9, Eli-Lilly, 5, 8, Merck, 5, 8, Merck Canada, 5, 8, 9, Novartis, 5, 8, Novartis Canada, 5, 8, 9, Pfizer, 5, 8, Pfizer Canada, 5, 8, 9, Sandoz Canada, 5, 8, 9, Sanofi-Genzime, 5, 8, Sanofi-Genzyme, 5, 8, 9; **G. Boire**, Abbvie, 2, Amgen, 2, 5, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, Eli Lilly, 2, 5, Lilly, 2, 5, Merck, 2, 8, Novartis, 2, Pfizer, 2, 5, 8; **V. Bykerk**, Amgen, 5, Pfizer Pharmaceuticals, 5, Sanofi-Genzyme/Regeneron, 5, Schiper, 5, UCB, 5; **C. Thorne**, Abbvie, 2, 5, Amgen, 2, 5, CaREBiodam, 2, Celgene, 2, 5, Centocor, 5, Janssen, 5, Lilly, 5, Medexus/Medac, 5, 8, Merck, 5, Novartis, 2, 5, Pfizer, 2, 5, Sandoz, 5, Sanofi, 5; **W. Maksymowych**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, AbbVie Inc., 2, 5, 8, Abbvie, Amgen, Eli Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, and UCB Pharma], 2, 5, 8, Amgen, 2, 5, 8, Boehringer, 5, 8, Boehringer-Ingelheim, 5, 8, Canadian Research and Education Arthritis, 6, CARE ARTHRITIS, 3, 6, 9, Celgene, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi, 2, 5, 8, Synarc, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5, 8; **P. Lakatos**, Abbvie, 2, 5, 8, Arena Pharmaceuticals, 5, 8, Celltrion, 5, 8, Falk Pharma GmbH, 5, 8, Ferring, 5, 8, Genetech, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 2, Pfizer, 2, 5, 8, Pharmacosmos, 5, 8, Roche, 5, 8, Shire, 5, 8, Takeda, 5, 8; **L. Svenson**, None; **L. Targownik**, None; **W. Afif**, Abbvie, 2, 5, 8, Ferring, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Prometheus, 2, 5, 8, Takeda, 2, 5, 8, Theradiag, 2, 5, 8; **S. Bernatsky**, None.

Abstract Number: 0203

Recent Use, Missed Doses and Discontinuation of Infliximab in a Population-Based Cohort: Comparisons of Biosimilar and Originator Exposures

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health Poster I: RA

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In North America, biosimilars were approved only relatively recently, and real-world data are few. We described users of infliximab in the US, comparing patient tolerability of biosimilar and originator, in terms of missed doses and discontinuation.

Methods: We used Marketscan® data (Jan-Dec. 2017) to identify adult (age >18) new users of infliximab biosimilar and originator, and switchers from originator to biosimilar. Characteristics (age, sex, comorbidities, medication use) were described. In new users, we assessed missed doses in both the induction (among subjects with >2 months follow-up) and maintenance phases. 'Missed dose' was defined as any gap between infusions beyond recommended intervals

Table 1. Baseline characteristics of new users of infliximab biosimilar and originator, and switchers from originator to biosimilar

Characteristic	Infliximab biosimilar new users (n=112)	Infliximab originator new users (n=3076)	Infliximab biosimilar switchers (n=206)
Female sex, N (%)	69 (61.6)	1848 (60.1)	128 (62.4)
Mean age in years, (SD)	47.3 (15.8)	43.8 (14.9)	52.4 (16.5)
Age-adjusted CCI, mean (SD)	1.9 (2.3)	1.4 (2.1)	1.8 (1.9)
Underline disease[1]			
RA	39 (36.5)	638 (22.2)	69 (35.8)
AS	4 (3.7)	127 (4.4)	9 (4.7)
Psoriasis/PsA	15 (14.0)	300 (10.4)	28 (14.5)
IBD	49 (45.8)	1813 (63.0)	87 (45.1)
Ever DMARDs (%)	53 (47.3)	1024 (33.3)	82 (39.8)
Ever glucocorticoids (%)	95 (84.8)	2424 (78.8)	131 (63.6)
Biologic use (%)			
Adalimumab	32 (28.6)	796 (25.9)	13 (6.3)
Etanercept	11 (9.8)	218 (7.1)	3 (1.5)
Others[2]	8 (7.1)	216 (7.0)	5 (2.4)

[1]Based on the date of diagnosis closest to the start of treatment; 216 missing diagnosis.

[2]Including abatacept, golimumab, certolizumab, tocilizumab, and rituximab.

CCI: Charlson comorbidity index; RA: rheumatoid arthritis, AS: ankylosing spondylitis, PsA: psoriatic arthritis, IBD: inflammatory bowel disease, including Crohn's disease and ulcerative colitis.

Table 2. Factors associated with missed dose and discontinuation during the maintenance phase

	Missed dose		Discontinuation	
Variable	HR	95% CI	HR	95% CI
Infliximab biosimilar	0.32	0.18-3.07	0.82	0.11-6.02
Female sex	1.13	0.61-1.35	0.77	0.41-1.46
Age	1.00	0.98-1.01	0.98	0.96-1.01
Age-adjusted CCI score	1.00	1.07-1.27	1.03	0.85-1.26
Underline disease indication[1]				
RA	1.39	0.88-2.20	1.42	0.32-6.21
AS	1.10	0.53-2.29	0.89	0.25-3.23
Psoriasis/PsA	1.34	0.83-2.17	2.05	0.78-5.33
Past use of DMARD	0.93	0.63-1.35	0.31	0.31-1.64
Past use of systemic glucocorticoid	0.98	0.68-1.42	0.59	0.59-3.41
Any prior biologic use	0.78	0.58-1.06	0.36	0.36-1.37

[1]IBD was the reference category.

(0, 2, and 6 weeks for induction and Q8 weekly for maintenance). Discontinuation (≥ 90-day gap between infusions without restarting therapy) in the maintenance phase was also assessed. We used Cox regression to compare both times to first missed dose and complete discontinuation. All models were adjusted for age, sex, prior use of DMARDs, biologics, and systemic glucocorticoids, comorbidities (Charlson comorbidity index) and underlying disease indication (rheumatoid arthritis, ankylosing spondylitis, psoriasis/psoriatic arthritis, Crohn's disease, and ulcerative colitis).).

Results: We identified 318 users of infliximab biosimilar, including 206 switchers from the originator infliximab (Table 1). Among the 92 new users of infliximab biosimilar with ≥2 months follow-up, the frequency of ≥1 missed dose during induction was 22%, similar to 25% in new users of the originator. For patients completing the induction phase, the adjusted hazard ratio (HR) showed a nonsignificant trend for a longer time to first missing dose in maintenance (adjusted HR 0.33, 95% CI 0.08-1.30, Table 2). We were unable to determine if complete discontinuation differed between the two groups (HR: 0.82; 95% CI: 0.11-6.02).

Conclusion: We documented low use of infliximab use in these US data during 2017; most infliximab biosimilar initiators are switchers from the originator. For previously infliximab-naïve patients, the frequency of ≥1 missed dose during infliximab induction phase was similar in the originator and the biosimilar new users. As the frequency of biosimilar use grows, additional analyses with more follow-up time may help determine if there are differences in persistence between biosimilars and their reference therapy.

Disclosure: C. Moura, None; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **D. Choquette**, AbbVie, 5, 8, AbbVie Canada, 5, 8, 9, Amgen, 5, 8, Amgen Canada, 5, 8, 9, BMS, 5, 8, BMS Canada, 5, 8, 9, Celgene, 5, 8, Celgene Canada, 5, 8, 9, Eli Lilly Canada, 5, 8, 9, Eli-Lilly, 5, 8, Merck, 5, 8, Merck Canada, 5, 8, 9, Novartis, 5, 8, Novartis Canada, 5, 8, 9, Pfizer, 5, 8, Pfizer Canada, 5, 8, 9, Sandoz Canada, 5, 8, 9, Sanofi-Genzime, 5, 8, Sanofi-Genzyme, 5, 8, 9; **G. Boire**, Abbvie, 2, Amgen, 2, 5, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, Eli Lilly, 2, 5, Lilly, 2, 5, Merck, 2, 8, Novartis, 2, Pfizer, 2, 5, 8; **V. Bykerk**, AbbVie, 5, Amgen, 1, 2, 3, 5, 8, Brainstorm Therapeutics, 1, 2, 3, 5, 8, Bristol-Myers Squibb, 5, Genentech, 5, Gilead, 5, NIH, 2, Pfizer, 1, 2, 3, 5, 8, Regeneron, 5, Regeneron Pharmaceuticals, Inc, 5, Sanofi, 5, Sanofi/Genzyme-Regeneron, 5, Sanofi-Genzyme/Regeneron, 1, 2, 3, 5, 8, Scipher, 1, 2, 3, 5, 8, The Cedar Hill Foundation, 9, UCB, 1, 2, 3, 5, 8, UCB Pharma, 5; **C. Thorne**, Abbvie, 2, 5, Amgen, 2, 5, CaREBiodam, 2, Celgene, 2, 5, Centocor, 5, Janssen, 5, Lilly, 5, Medexus/Medac, 5, 8, Merck, 5, Novartis, 2, 5, Pfizer, 2, 5, Sandoz, 5, Sanofi, 5; **W. Maksymowych**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, Ab-

bVie Inc., 2, 5, 8, Abbvie, Amgen, Eli Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, and UCB Pharma], 2, 5, 8, Amgen, 2, 5, 8, Boehringer, 5, 8, Boehringer-Ingelheim, 5, 8, Canadian Research and Education Arthritis, 6, CARE ARTHRITIS, 3, 6, 9, Celgene, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi, 2, 5, 8, Synarc, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5, 8; **P. Lakatos**, Abbvie, 2, 5, 8, Arena Pharmaceuticals, 5, 8, Celltrion, 5, 8, Falk Pharma GmbH, 5, 8, Ferring, 5, 8, Genetech, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 2, Pfizer, 2, 5, 8, Pharmacosmos, 5, 8, Roche, 5, 8, Shire, 5, 8, Takeda, 5, 8; **L. Svenson**, None; **L. Targownik**, None; **W. Afif**, Abbvie, 2, 5, 8, Ferring, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Prometheus, 2, 5, 8, Takeda, 2, 5, 8, Theradiag, 2, 5, 8; **S. Bernatsky**, None.

Abstract Number: 0204

Real-World Evidence: Clinical and Economic Burden of Anemia, Venous Thromboembolism, and Malignancy Among Rheumatoid Arthritis Patients Switching from First Biologic DMARD to Another Treatment in the US

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
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Session Time: 9:00AM–11:00AM

Background/Purpose: RA patients have an increased risk of malignancy[1] and deep-vein thrombosis and pulmonary embolism (DVT/PE)[2] and high prevalence of anemia.[3] The risks of anemia and malignancy vary by prior DMARD exposure.[1] Comorbidities and treatment side effects may lead to treatment discontinuation and increase healthcare costs. Existing estimates of anemia, DVT, PE, and malignancy are outdated or not specific to patients initiating next treatment after first biologic (b)DMARD. This study aimed to estimate prevalence, incidence, and associated costs of these conditions in RA patients switching from a first bDMARD to another treatment.

Methods: In a US health-plan claims database, we selected adult RA patients (≥2 RA diagnoses ≥30 days apart) who initiated their first bDMARD (1/1/2012–3/31/2017) and switched to another bDMARD or Janus kinase inhibitor (JAKi; index date, ID). Patients had continuous health plan enrollment for 12 months pre-ID and ≥12 months post-ID. The prevalence and incidence of anemia, DVT, PE, DVT or PE, and malignancy (excluding nonmelanoma skin cancer) were assessed by index therapy. Incidence counted patients with new events per 100 patient-years (P100PY) while on treatment. We compared mean per-patient-per-year (PPPY) costs (total, medical, and pharmacy) in patients with and without these conditions.

Results: In 4656 patients who switched from first bDMARD (median age 54 years, 78% female), median RA duration was 1.5 years. Upon discontinuation of the first bDMARD, 46% of patients received a monotherapy (61% TNF-α inhibitor (TNFi), 24% non-TNFi, 15% JAKi), and 54% received a conventional synthetic (cs)DMARD-combination therapy (69% TNFi + csDMARD, 23% non-TNFi + csDMARD, 8% JAKi + csDMARD). The 12-month pre-ID prevalence ranged 14.6–19.8% for anemia, 1.0–2.5% for DVT, 0.7–2.2% for PE, 1.8–3.7% for DVT or PE, and 3.5–8.8% for malignancy (Table 1). Overall, P100PY incidence rates were 6.9 for anemia, 0.7 for DVT, 0.3 for PE, 0.9 for DVT or PE, and 2.0 for malignancy. Incidence rates varied among different treatment classes (Table 2). Total PPPY unadjusted healthcare costs were higher in RA patients with vs without condition: anemia $66,896 vs $53,853; DVT $78,461 vs

Table 1. Prevalence of Anemia, DVT, PE, or Malignancy During Pre-index Period, by Index Treatment

	Pre-index Prevalence				
	Anemia	DVT	PE	DVT or PE	Malignancy
All patients (n=4656)	16.2%	1.7%	0.9%	2.1%	5.2%
Index monotherapy (n=2149)	16.8%	2.0%	1.0%	2.4%	5.4%
TNFi (n=1305)	15.4%	1.8%	0.7%	2.2%	4.4%
Non-TNFi (n=521)	19.8%	1.9%	1.0%	2.3%	8.8%
JAKi (n=323)	17.6%	2.5%	2.2%	3.7%	4.0%
Index combination therapy (n=2507)	15.7%	1.6%	0.8%	1.8%	5.0%
csDMARD + TNFi (n=1740)	16.0%	1.5%	0.7%	1.8%	4.7%
csDMARD + Non-TNFi (n=569)	14.6%	1.9%	1.1%	1.9%	6.5%
csDMARD + JAKi (n=198)	15.7%	1.0%	1.5%	2.0%	3.5%

csDMARD, conventional synthetic DMARD; DVT, deep venous thromboembolism; JAKi, Janus kinase inhibitor; PE, pulmonary embolism; TNFi, TNF-α inhibitor.

Table 2. Incidence Rate (IR) per 100 Patient-years (PYs) of New Anemia, DVT, PE, or Malignancy Patients During Index therapy, by Index Treatment

	Mean treatment duration (months)	Anemia		DVT		PE		DVT or PE		Malignancy	
		IR	PY	IR	PY	IR	PY	IR	PY	IR	PY
All patients	13.2	6.9	4032	0.7	4937	0.3	5001	0.9	4911	2.0	4699
Index monotherapy	9.9	6.6	1410	0.7	1691	0.4	1724	1.1	1679	1.9	1619
TNFi	9.3	6.9	822	0.7	976	0.6	993	1.3	971	1.9	939
Non-TNFi	10.7	5.9	358	1.1	436	0.2	449	1.4	432	1.7	408
JAKi	10.8	6.5	229	0.0	278	0.0	282	0.0	277	2.2	272
Index combination therapy	16.1	7.1	2622	0.7	3246	0.3	3278	0.8	3231	2.1	3080
csDMARD + TNFi	15.5	6.6	1740	0.6	2172	0.3	2187	0.7	2160	2.2	2060
csDMARD + Non-TNFi	17.7	8.5	660	0.7	807	0.1	822	0.9	806	1.6	766
csDMARD + JAKi	16.7	7.2	222	1.1	267	0.4	269	1.1	266	2.8	254

csDMARD, conventional synthetic DMARD; DVT, deep-vein thrombosis; JAKi, Janus kinase inhibitor; PE, pulmonary embolism; TNFi, TNF-α inhibitor

$54,462; PE $99,321 vs $54,483; DVT/PE $88,610 vs $54,305; malignancy $76,741 vs $54,172, all p< 0.001. Cost differences were primarily associated with medical costs (Table 3).

Conclusion: Anemia, DVT, PE, and malignancies affected patients who switched from first bDMARD to another treatment; new cases occurred and varied by treatment received. These conditions were associated with increased unadjusted healthcare costs, primarily driven by medical costs. Future studies are needed to adjust costs by accounting for differences in patient cohorts. The prevalence of these conditions (and the risk of their development as treatment side effects) should be factored into the selection of most optimal treatment.

Table 3. Per-patient-per-year (PPPY) Healthcare costs (USD) During Index Treatment in Patients with and without Anemia, DVT, PE, or Malignancy

	Mean PPPY cost with condition	Mean PPPY cost without condition
Anemia		
Total costs*	$66,896	$53,853
Medical costs*	$32,542	$19,305
Pharmacy costs	$34,353	$34,548
DVT		
Total costs*	$78,461	$54,462
Medical costs*	$48,745	$19,890
Pharmacy costs	$29,716	$34,572
PE		
Total costs*	$99,321	$54,483
Medical costs*	$60,337	$19,962
Pharmacy costs	$38,984	$34,521
DVT/PE		
Total costs*	$88,610	$54,305
Medical costs*	$55,466	$19,756
Pharmacy costs	$33,145	$34,550
Malignancy		
Total costs*	$76,741	$54,172
Medical costs*	$40,172	$19,678
Pharmacy costs	$36,569	$34,493

*p<0.0001.
DVT, deep-vein thrombosis; PE, pulmonary embolism.

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Disclosure: R. Dore, AbbVie, 2, 5, 8, AbbVie, Inc., 5, 8, 9, Abbvie, Inc., 2, 5, 8, Amgen, 2, 5, 8, 9, Biogen, 2, 9, Gilead Science, 2, 5, Gilead Sciences, Inc., 2, 5, 9, Lilly, 2, 5, 8, 9, Novartis, 2, 5, 9, Pfizer, 2, 8, 9, Radius, 8, Regeneron, 8, Sanofi, 8, UCB, 2, 8, 9, VCB, 8; **J. Antonova**, Gilead Science, 1, 3, Gilead Sciences, Inc., 1, 3; **M. Gorritz**, IQVIA, 9; **L. Chang**, Gilead Science, 9, Gilead Sciences, Inc., 1, 3, Lilly, 9; **J. He**, IQVIA, 9; **M. Genovese**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 9, Astellas, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck Serono, 2, 5, Galapagos, 2, 5, Galapagos NV, 2, 5, 9, Genentech/Roche, 2, 5, Gilead, 2, 5, Gilead Science, 9, Gilead Sciences, Inc., 2, 5, 9, GSK, 5, Lilly, 2, 5, 9, Novartis, 2, 5, Pfizer, 2, 5, 9, Pfizer Inc, 2, 5, Pfizer, Inc., 9, Pzier, 9, RPharm, 5, Sanofi Genzyme, 2, 5, Vertex, 2, 5.

Abstract Number: 0205

Does a Mandatory Non-medical Switch from Originator to Biosimilar Etanercept Lead to Increase in Healthcare Use and Costs? A Danish Register-based Study of 1620 Patients with Inflammatory Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Marketing of cheaper biosimilar biological agents has created financial incentives for switching from the corresponding originator drugs (=non-medical switch). The economic benefit might potentially be outweighed by extra costs due to patient education or closer monitoring. However, only few studies have previously explored the use of health care resources associated with non-medical switching.[1] In year 2016, Danish national guidelines recommended switch of patients with inflammatory rheumatic diseases treated with originator etanercept (ETA) to biosimilar SB4 in routine care.[2] We aimed to explore if switching lead to increased health care utilization and costs.

Methods: Observational cohort study. Adult patients who switched from ETA to SB4 were identified in the Danish nationwide DANBIO registry. In the National Patient Registry we identified health utilization (hospital admissions/hospital days/outpatient visits/prescription medication use) and comorbidities. Estimation of health utilization included average use and costs one year before/after the switch, changes after the switch, and whether patient characteristics

Figure

Monthly average in-patient and out-patient costs 12 months before and after switch from originator to biosimilar etanercept (n=1620 patients). Black dotted vertical line illustrates time of switch.

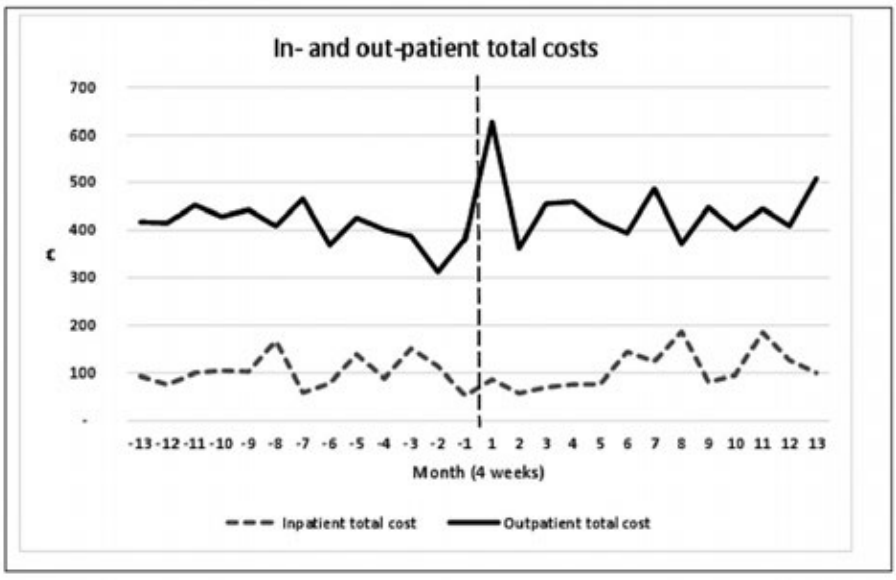

Table 1
A: Health utilization, and B: health costs per patient 12 months before and after switch, unadjusted and adjusted (=predicted)*
N=1620 patients

A. Total health utilization per patient		Unadjusted number, mean (SD)		Adjusted number, mean (95% CI)*	
		Pre-switch	Post-switch	Pre-switch	Post-switch
In-patient services	Number of in-patient admissions	0.25 (0.64)	0.11 (0.40)	0.15 (0.03-0.67)	0.06 (0.01-0.69)
	Number of days in hospital	1.19 (5.26)	0.49 (2.73)	0.66 (0.06-7.25)	0.20 (0.004-10.47)
Outpatient	Number of outpatient visits	12.30 (9.40)	13.31 (9.75)	9.42 (7.91-11.22)	11.09 (9.34-13.16)
Medication**	Pain medication	171 (254)	170 (250)	168 (88-320)	165 (86-315)
	Other medication	937 (1119)	955 (1135)	659 (355-1223)	678 (364-1262)
	Total	1108 (1225)	1124 (1241)	832 (447-1549)	848 (455-1584)

B. Total health costs per patient		Unadjusted average cost, mean (SD)		Adjusted average cost, mean (95% CI)*	
		Pre-switch, €	Post-switch, €	Pre-switch, €	Post-switch, €
In-patient services	Diseases of musculoskeletal syst	315 (1645)	306 (2330)	122 (58-258)	385 (144-1030)
	Other diseases	1014 (4326)	1121 (4607)	491 (268-902)	297 (150-587)
	Total	**1330 (4720)**	**1428 (5501)**	**660 (355-1227)**	**500 (255-977)**
Out-patient services	Diseases of musculoskeletal syst	4445 (6898)	4700 (7381)	4051 (2171-7559)	4040 (2150-7589)
	Other diseases	860 (2623)	1069 (3498)	368 (197-688)	484 (253-928)
	Total	**5305 (7369)**	**5769 (8107)**	**4436 (2529-7779)**	**4593 (2618-8059)**
Primary sector	General practitioner	201 (208)	208 (218)	171 (93-314)	174 (95-318)
	Other practicing specialist	105 (229)	103 (211)	98 (53-180)	89 (48-164)
	Physiotherapist, chiropractor, foot specialist	397 (807)	384 (801)	423 (222-807)	388 (200-751)
	Other	75 (112)	70 (97)	66 (35-124)	63 (33-118)
	Total	**778 (936)**	**765 (921)**	**756 (408-1404)**	**709 (381-1321)**
Medication**	Pain medication	75 (239)	74 (231)	63 (33-119)	62 (32-118)
	Other medication	391 (638)	372 (595)	255 (136-478)	250 (134-466)
	Total	**466 (721)**	**446 (682)**	**321 (172-601)**	**312 (167-584)**
Total costs		**7880 (9427)**	**8408 (10489)**	**6176 (3685-10353)**	**6264 (3741-10491)**

*Predicted costs are for female, 55 years old, not dead in the post-switch period, not withdrawn SB4 within 0-180 days, previous duration of ETA treatment >5 years and with no previous comorbidities
** Defined daily dose of medication total costs (DDD)

affected changes. Analyses were by adjusted 2-step gamma distributed regression models, and for changes over time a GEE model was applied. Impact of comorbidities was explored as interaction terms in the model. Medication costs of ETA and SB4 were not included in model, because these drugs are provided by the hospital department responsible for the therapy and not by private pharmacies.

Results: 1620 patients were included (mean age 55 years(SD 14.7), 40% male). Costs before and after switching were mainly driven by outpatient visits (67% and 72% of all costs, respectively) (Table 1). In general, the adjusted health costs were lower than the unadjusted costs e.g. number of in-patient admissions, hospital days and in-patient costs due to the adjustment for previous comorbidities in the regression (Table 1). Monthly fluctuations of costs were similar before/after switch (Figure). After switching, an increase was observed in the use (8%) and costs (7%) of out-patient services. Number of in-patient days and number of days in hospital decreased (Table 2), but the total number of patients with in-patient services was low (Table 1). Medication costs decreased (5%) (Table 2). Patients with longer ETA treatment duration had increased number of outpatient visits after the switch, higher out-patient total costs and costs related to general practitioners. Higher age (3% per year increase) was associated with higher in-patient total costs related to diseases of the musculoskeletal system and connective tissue diseases. Gender and comorbidities had no impact on costs before and after the switch.

Table 2
A: Changes in health utilization, and B: changes in costs per patient 12 months before and after switch including adjusting variables*

A. Changes in health utilization per patient		After* Exp (estimate), 95% CI	P-value
In-patient services	Number of in-patient admissions	**0.45 (0.37-0.54)**	**<0.0001**
	Number of days in hospital	**0.36 (0.25-0.51)**	**<0.0001**
Outpatient	Number of outpatient visits	**1.08 (1.05-1.11)**	**<0.0001**
Medication**	Pain medication, DDD	0.99 (0.96-1.03)	0.702
	Other medication	1.03 (1.00-1.05)	0.051
	Total	1.02 (1.00-1.04)	0.100
B. Changes in health costs per patient		**After* Exp (estimate), 95% CI**	**P-value**
In-patient services	Diseases of musculoskeletal system	0.70 (0.44-1.10)	0.119
	Other diseases	0.81 (0.62-1.05)	0.114
	TOTAL	0.82 (0.65-1.04)	0.100
Out-patient services	Diseases of musculoskeletal system	1.05 (1.00-1.10)	0.057
	Other diseases	**1.24 (1.09-1.41)**	**0.001**
	TOTAL	**1.07 (1.03-1.12)**	**0.001**
Primary sector	General practitioner	1.03 (0.99-1.08)	0.130
	Other practicing specialist	0.97 (0.85-1.10)	0.603
	Physiotherapist, chiropractor, foot specialist	0.97 (0.92-1.02)	0.258
	Other	0.94 (0.88-1.02)	0.140
	TOTAL	0.99 (0.95-1.02)	0.426
Medication	Pain medication	0.98 (0.93-1.03)	0.331
	Other medication	0.95 (0.91-1.00)	0.061
	TOTAL	**0.95 (0.92-0.99)**	**0.019**
TOTAL COSTS		1.04 (0.99-1.09)	0.138

Statistically significant results are marked with bold types
*Adjusted for gender, age, dead in post period, duration of ETA before index date, stopped SB4 treatment within 180 days and comorbidities (WHO chapters) 12-24 months before index date
** Defined daily dose of medication total costs (DDD)

Conclusion: We demonstrated no obvious changes in overall use and costs of health care services following a mandatory non-medical switch from originator to biosimilar etanercept. Longer ETA treatment duration and higher age were associated with increased use and costs of some services.

Reference List:

1. Glintborg B, et al. RMD Open 2018; 4(2):e000710.
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Abstract Number: 0206

Efficacy of Etanercept on Radiographic Progression in Adult Patients with Rheumatoid Arthritis or Psoriatic Arthritis: Final Results from a German Non-Interventional, Prospective, Multi-Center Study

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health Poster I: RA

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical trials showed that Etanercept (ETN) is highly effective in reducing clinical disease activity and often leading to remission and radiographic non-progression in patients with Rheumatoid Arthritis (RA) or Psoriatic Arthritis (PsA). However, the course of radiographic progression in everyday clinical practice is not known. This German non-interventional study (NIS) assessed radiographic progression in patients with RA or PsA managed in routine outpatient care in private practices with a time interval up to 36 months.

Methods: Throughout the study up to 10 visits (V) were performed (V1 at baseline, V2-7 every 3 months until month 18 – phase 1, V8-10 every 6 months until month 36 – phase 2). Radiographs of hands and feet were taken at baseline (±3 months start of ETN treatment), at month 12 to 18 and/or at months 30-36. All radiographs were scored by 2 blinded readers by the 'van der Heijde modified Total Sharp Score' ($mTSS^{RA}$) for RA patients and the 'van der Heijde modified Total Sharp Score adapted' ($mTSS^{PsA}$) for PsA patients. Additional parameters such as Disease Activity Score (DAS28) and (serious) adverse events were documented.

Results: 1,821 patients were available for the final analysis, 75.7% (N=1,378) were diagnosed as RA and 24.2% (N=440) as PsA patients. The median disease duration at baseline was 4.9 years (range: 0;54 RA) and 8.9 years (0;38 PsA). In RA patients the mean $mTSS^{RA}$ increased from 25.1±42.4 (n=504) at baseline to 26.2±43.6 (n=284) at the end of phase 1 (12-18 months) and to 29.8±48.6 (n=74) at the end of phase 2 (30-36 months). In PsA patients the mean $mTSS^{PsA}$ was 14.7±25.7 (n=166) at baseline, 14.6±23.5 (n=80) at the end of phase 1 and 12.6±23.2 (n=35) at the end of phase 2. Median changes compared to baseline at the end of phase 1 and phase 2 were 0.0, suggesting no radiographic progression on the group level. Calculating normalized progression with yearly intervals about two thirds of the patients showed no radiographic progression after 24 months, i.e. radiographic non-progression defined as a change of $mTSS^{RA/PsA} \leq 0.5$ was observed in 64.2% of RA- and 68.9% of PsA patients after 24 months. The DAS28 decreased from a mean baseline value of 4.6±1.2 (n=1,014) in RA and 4.2±1.1 (n=327) in PsA patients, respectively, to 2.6±1.2 (RA, n=190) and 2.5±1.1 (PsA, n=88) at month 36 indicating an important decrease of disease activity under ETN treatment. Moreover, at month 36, 61.6% of RA and 64.8% of PsA patients were considered to be in remission (DAS< 2.6). A total of 1,993 Treatment Emergent Adverse Events (TEAE) occurred in 849 (46.6%) patients. Most of the AEs were of 'mild' (768 events in 377 patients, 20.7%) or 'moderate' (825 events in 481 patients, 26.4%) severity. 446 patients (24.5%) experienced a total of 753 AEs which were assessed as 'treatment related' to Etanercept (i.e. as adverse drug reactions). 62 out of them in 47 patients (2.6%) were considered to be serious adverse drug reactions.

Conclusion: The final results of this NIS demonstrated that treatment with ETN slows or even stops radiographic progression and reduces disease activity in RA and PsA patients in routine clinical care. The treatment with ETN was well tolerated and no new safety signals were observed.

Disclosure: S. Wassenberg, AbbVie, 5, 8, Chugai, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8; **T. Klopsch**, AbbVie, 1, Amgen, 1, AstraZeneca, 1, Clinuvel, 1, Fresenius, 1, Morphosys, 1, Evotec, 1, Johnson & Johnson, 1; **A. Plenske**, Pfizer, 3, 4; **S. Behnck-Knoblau**, Pfizer, 1, 3; **J. Jobst**, Pfizer, 1, 3, 4; **P. Klaus**, Pfizer, 3; **T. Meng**, Pfizer, 3; **P. Löschmann**, Pfizer, 3; **R. Rau**, Pfizer, 2.

Abstract Number: 0207

Effects of Successive Switches to Different Biosimilars Infliximab on Immunogenicity in Chronic Inflammatory Diseases in Daily Clinical Practice

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SESSION INFORMATION
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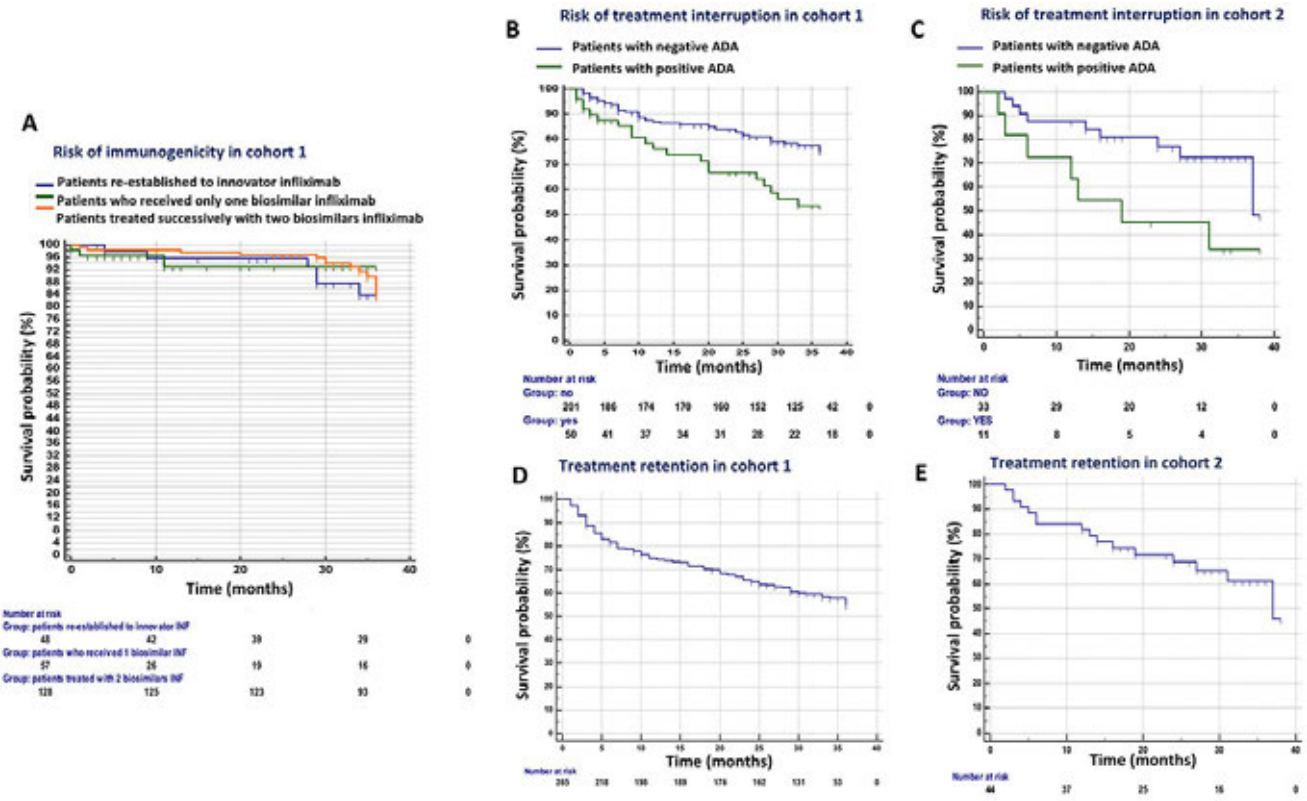
Session Title: Epidemiology & Public Health Poster I: RA
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To determine whether the successive switches from innovator infliximab to a first then a second biosimilar infliximab, or from a first to a second infliximab biosimilar, increase the risk of immunogenicity during a 3-year observation period.

Methods: This is a usual care study performed in the Rheumatology, Gastroenterology and Internal Medicine departments of Cochin Hospital, Paris, France. Two independent cohorts were constituted; Cohort 1 included patients on maintenance therapy with the original treatment who successively switched to CT-P13 in October-December 2015 then to SB2 in December 2017. Cohort 2 included biologic-naïve patients who received CT-P13 starting from November 2015 before being switched to SB2 in December 2017.The end of the observation period was December 2018. Immunogenicity was defined by the detection of positive anti-drug antibodies (ADA >10 ng/mL), at least at two consecutive time points.

Results: Cohort 1 consisted on 265 patients on maintenance therapy with innovator infliximab who switched to CT-P13. Then, 140 patients switched to SB2, 26 remained treated with CT-P13, and innovator infliximab was re-established in 55 patients. 30 patients (16 females) had positive ADA at baseline visit (11.3%), before the switch to CT-P13. These patients were more likely to have a BMI >30 (45% vs. 17%, p< 0.001) and received less innovator infliximab infusions (28±20 vs. 40±25 infusions, p=0.012) than patients without ADA. Among the 235 ADA-free patients at baseline, 20 patients developed ADA during the observation period, corresponding to a rate of 3 for 100 patient years. The mean time to positive ADA detection was 21±14 months (range: 1-37 months). Kaplan Meyer curve illustrating immunogenicity-free survival showed no influence of the number of biosimilars infliximab received on immunogenicity (Figure 1A). Cohort 2 consisted of 44 biologic-naïve patients who initiated CT-P13. Among these patients,



29 switched to SB2, 4 remained treated with CT-P13 and 11 discontinued the treatment before the second switch. 11/44 (25%) patients developed ADA during the observation period, corresponding to a rate of 14 for 100 patients years. Only a single patient developed ADA after the switch to SB2. The mean time to positive ADA detection was 13±11 months (range: 1-31 months). The risk of treatment discontinuation was significantly higher in patients with positive ADA in both cohorts (cohort 1: Hazard Ratio, HR: 2.37, 95% CI 1.38-4.05, p=0.002 and cohort 2: HR: 2.79, 95% CI 1.04-7.52, p=0.042) (Figure 1B-C).Predictors of immunogenicity were only identified in cohort 2: a BMI >30 at baseline visit and mean infliximab through levels < 2 mg/mL from baseline visit to ADA detection were predictive of the development of ADA with HR (95% CI) of 5.54 (1.30-23.65) and 5.53 (1.30-23.43), respectively. The retention rate of infliximab was 58% (154/265) in cohort 1 and 66% (29/44) in cohort 2 at the end of observation period (Figure 1D-E).

Conclusion: Immunogenicity was not favored by switches to biosimilars infliximab in our study. Thus, immunogenicity does not constitute a barrier to interchangeability between biosimilars infliximab in chronic inflammatory diseases.

Kaplan Meyer Survival Analyses. Risk of immunogenicity according to the number of biosimilars infliximab received (A); risk of treatment interruption according to the presence of anti-drug antibodies (ADA) in cohort 1 (B) and 2 (C); and treatment retention within the observation period in cohort 1 (D) and 2 (E)

Disclosure: A. Lauret, None; **A. Moltó**, None; **V. Abitbol**, Pfizer, 8, Biogen, 8; **L. Guterlann**, None; **O. Conort**, None; **F. Chast**, None; **C. Goulvestre**, None; **C. Le Jeunne**, None; **S. Chaussade**, None; **C. Roux**, None; **F. Batteux**, None; **M. Dougados**, AbbVie, 2, 5, 8, Amgen, 5, Biogen, 5, BMS, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, Merck, 2, 5, Merck Inc, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8; **Y. Allanore**, None; **J. Avouac**, Pfizer, 2, 8.

Abstract Number: 0208

Self-Reported Sleep Disturbances in Rheumatoid Arthritis (RA)

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health Poster I: RA – ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sleep disturbances (SD) are reported to be common in RA but relatively few studies have addressed the issue. We examined the frequency and severity of self-reported poor sleep quality, symptoms of restless leg syndrome (RLS), and risk of obstructive sleep apnea (OSA) among individuals with RA, and identified predictors of SD.

Methods: Data were from FORWARD, the National Data Bank for Rheumatic Diseases, for which participants complete questionnaires every 6 months. In one questionnaire, items querying symptoms of RLS, the STOP-BANG questionnaire, a validated measure of OSA risk, physician diagnoses of OSA and RLS, and the Medical Outcomes Study Sleep Scale (MOS-S) were included. The MOS-S yields 5 subscales; results are shown here only for one (Sleep Problems Index I, SPI-I, sleep quality). was also included. Frequencies of reports of OSA risk, RLS symptoms were tabulated. Bivariate regression analyses identified predictors of OSA and RLS (logistic regression) and SPI-I scores (linear regression). Potential predictors included age, sex, race, education, smoking, Rheumatic Disease Comorbidity Index (RDCI)1, low income, obesity (BMI ≥ 30 kg/m2 and < 35), morbid obesity (BMI ≥ 35), RA duration, prednisone

Table 1. Subject characteristics (n = 2623)

	Mean ± SD or % (n)		Mean ± SD or % (n)
Demographic, general health		RA-specific	
Age, years	67.2 ± 11.3	RA duration, years	23.0 ± 11.3
Female	82.7 (2168)	Pain rating (0 – 10)	3.2 ± 2.5
White	93.4 (2449)	Fatigue rating (0 – 10)	3.8 ± 2.9
Current smoker	3.6 (94)	RA Disease Activity Index (RADAI)	2.2 ± 1.5
BMI	28.2 ± 6.7	Prednisone use	25.2 (657)
Obese (BMI≥30)	32.8 (861)	Mean prednisone dose (mgs)	7.6 ± 11.5
COPD	7.9 (208)	Biologic use	51.5 (1349)
Rheumatic Disease Comorbidity Index (RDCI; 0 – 9)	2.1 ± 1.7		
Sleep			
Mean hours	6.8 ± 1.5		
Sleep Problem Index I	33.4 ± 18.9		

Table 2. Self-reported sleep conditions

	Sleep apnea				Restless legs syndrome		
	Diagnosed				Diagnosed		
At risk based on self-report	No	Yes	Total	At risk based on self-report	No	Yes	Total
No	77.3 (2027)	8.7 (227)	85.9 (2254)	No	71.4 (1821)	2.6 (66)	74.0 (1887)
Yes	6.9 (181)	7.2 (188)	14.1 (369)	Yes	17.1 (436)	8.9 (227)	26.0 (663)
Total	84.2 (2208)	15.8 (415)		Total	88.5 (2257)	11.5 (293)	

Table 3. Significant independent predictors of sleep disturbances

	High risk for OSA*	RLS symptoms*	Sleep Problems Index I † (model 1)	Sleep Problems Index I † (model 2)
Age	(ns)	(ns)	-0.2 (.01)	-0.2 (<.0001)
Female	0.5 (0.4, 0.7)	(ns)	2.8 (.0009)	3.2 (.0001)
Low income	(ns)	(ns)	2.0 (.0083)	2.0 (.008)
Obese (BMI 30 – 35)	2.1 (1.6, 2.8)	(ns)	(ns)	(ns)
Morbid obesity (BMI ≥35)	3.4 (2.5, 4.6)	1.3 (1.03, 1.7)	(ns)	(ns)
Current smoking	1.8 (1.1, 3.1)	(ns)	4.4 (.01)	3.7 (.03)
RDCI	1.2 (1.1, 1.3)	(ns)	1.1 (<.0001)	0.9 (<.0001)
RA duration	(ns)	(ns)	-0.1 (.005)	-0.1 (.006)
RADAI	1.3 (1.2, 1.4)	1.3 (1.2, 1.3)	5.8 (<.0001)	5.3 (<.0001)
High risk OSA	---	---	---	7.1 (<.0001)
RLS symptoms	---	---	---	4.2 (<.0001)

* Tabled values are odds ratio (95% CI) from multiple logistic regression analyses
† Tabled values are beta (p-value) from multiple linear regression analysis. Higher scores reflect greater sleep problems

and other medication use, and RA disease activity (Rheumatoid Arthritis Disease Activity Index, RADAI). Variables significant in the bivariate analyses were included in multivariate regression analyses.

Results: Subject characteristics are shown in Table 1 (n = 2623). 16% reported physician-diagnosed OSA, and 14% were at high risk of OSA based on self-reported symptoms (Table 2), compared to 2-4% in the general population. Only half at high risk had an OSA diagnosis. 12% reported physician-diagnosed RLS, and 26% reported RLS symptoms, compared to ~10% in the general population. Only one third with RLS symptoms reported a physician diagnosis. Mean SPI-I was 33.4 (±18.9), ~0.5 standard deviation worse than a population sample mean. Independent predictors of high risk of OSA were male sex, obesity, current smoking, RDCI, and disease activity (Table 3). Predic-

tors of RLS symptoms were morbid obesity and disease activity. Worse scores on SPI-I were associated with younger age, female sex, smoking, higher RDCI, shorter RA duration, and greater disease activity. OSA and RLS symptoms were also independently associated with SPI-I scores.

Conclusion: Symptoms of both OSA and RLS were more common in RA than in the population; self-reported sleep quality was also worse. Some predictors of SDs were similar to predictors in the population (e.g., age, obesity), but disease activity was also consistently associated with SD. Research in RA has linked SDs to worse outcomes. Previous research in other conditions suggests that SDs might also be a cause of increased disease activity through heighted inflammation. Further research is needed to tease out disease-specific causes and effects of SD in RA.

References

1 England BR et al. *Arthritis Care Res* 2015; 6: 865

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Disclosure: P. Katz, None; **S. Pedro**, FORWARD, the National Data Bank for Rheumatic Disease, 3, FORWARD, The National Data Bank for Rheumatic Diseases, 3; **K. Michaud**, Pfizer, 2, Rheumatology Research Foundation, 2.

Abstract Number: 0209

Joint Overuse in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: The development of drug therapies for rheumatoid arthritis (RA), and control of synovitis has now become easier. However, once patients are relieved of pain, they become physically more active and sometimes overuse their joints. Such overuse can result in progression of joint deformity, joint destruction, and in some cases, tendon rupture. However, the actual situation of joint overuse in RA patients remains insufficiently recognized. Here we analyzed the clinical characteristics of such patients who had overused their joints.

Methods: In-depth history taking about joint overuse and physical examinations were performed prospectively for 3148 consecutive patients with RA who visited our outpatient department between August 2016 and October 2016. The patients who satisfied the following inclusion criteria were diagnosed as having joint overuse: (i) met the 2010 American College of Rheumatology/European League against Rheumatism criteria for RA, (ii) had experienced preceding events that exerted a strain on the joints, and (iii) had joint pain and/or swelling of the strained joints. Patients who were suspected of having other conditions such as infection, trauma, pseudogout, and gout were excluded. Among the patients, 41 (10 men and 31 women) were diagnosed as

having joint overuse. The patients' clinical features and laboratory data before they developed joint overuse were collected from their medical records. As comparative controls, we selected 123 age- and sex-matched contemporary patients with RA who had no joint overuse from among 3148 patients. Comparisons between the parameters at different time points were performed using the Friedman test, and a post hoc analysis was performed using the Wilcoxon signed-rank test with Holm correction. The data were expressed as median (interquartile range).

Results: Forty-one patients with a mean age of 62.0 years (range, 54.0–69.0 years) were diagnosed as having joint overuse. The different joints affected by overuse were the wrist (16), hand (thumb and fingers, n = 12), shoulder (4), knee (3), ankle (3), and forefoot (3). The reasons for overuse were occupational in 25 patients, housework in 10, hobbies in 5, and ceremonial occasions in 1. The clinical disease activity index at baseline was 5.00 (2.60–9.00), which increased to 9.00 (6.00–11.3) owing to overuse, and improved to 4.80 (2.20–9.00) at the next visit ($p < 0.001$ and $p < 0.001$, respectively). The 28-joint Disease Activity Score based on erythrocyte sedimentation rate, C-reactive protein, visual analog scale score for pain, and swollen joint count was also elevated transiently. Logistic regression analysis revealed that treatment with biological disease-modifying antirheumatic drugs (bDMARDs; odds ratio [OR], 3.28; 95% confidence interval [CI], 11.32–8.17), low health assessment questionnaire disability index (HAQ-DI; OR, 0.301; 95% CI, 0.11–0.85), and Steinbrocker stage III or IV (OR, 6.89; 95% CI, 2.57–18.5) were significantly associated with the development of joint overuse.

Conclusion: When patients with advanced RA have low HAQ-DI using bDMARDs, they are at risk of joint overuse. Appropriate education would be important for such patients to prevent the overuse.

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Abstract Number: 0210

Associations of Clinical Biomarkers with Radiographic Progression of Rheumatoid Arthritis (RA) in African Americans with Early Disease

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SESSION INFORMATION
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Session Title: Epidemiology & Public Health Poster I: RA – ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To analyze longitudinal data from the Consortium for the Longitudinal Evaluation of African Americans with Early Rheumatoid Arthritis Registry (CLEAR) for the association between biomarkers including the HLA-DRB1 shared epitope (SE), anti-cyclic citrullinated peptide (CCP), and rheumatoid factors IgA and IgM (RFIgA and RFIgM) with changes in radiographic progression from study enrollment (< 2yrs disease duration) to 60-month disease duration. Cross-sectional studies have shown an association between SE, CCP, and RF and disease severity in various cohorts of patients with RA. This study seeks to determine the independent effects of these biomarkers as predictors of radiographic progression among African American patients while controlling for the effects of other comorbidities, socioeconomic factors, age, sex, and RA medication.

Table 1. Baseline Characteristics of the CLEAR Consortium who participated in the 60-month fol

Characteristic	Baseline
Demographics	
Age, Mean (Std Dev)	51.07 (12.3)
Female, N (%)	166 (85.6%)
Months of Disease Duration, Mean (Std Dev)	14.05 (7.2)
Years of Follow up, Mean (Std Dev)	4.09 (0.7)
On Methotrexate and/or Leflunomide, N (%)	125 (64.4%)
Number of Comorbidities (Std Dev)	3.09 (2.2)
BMI, Mean (Std Dev)	31.83 (7.5)
Ever Smoker, N (%)	107 (55.2%)
Biomarkers	
CRP, Mean (Std Dev)	17.21 (42.6)
ACCP Positive, N (%)	227 (64.2%)
RGFIgA Positive, N (%)	248 (70.1%)
RGFIgm Positive, N (%)	257 (72.7%)
Has Shared Epitope, N (%)	150 (42.5%)

Table 2. Radiographic measures over time in the Consortium for the Longitudinal Evaluation of African Americans with Early Rheumatoid Arthritis Registry (CLEAR) (n=194)

	Baseline	60 Months
Radiographic Disease Scores		
Erosion Score, Mean (Std Dev)	1.27 (3.8)	2.12 (7.6)
JSN Score, Mean (Std Dev)	1.79 (5.0)	5.29 (12.6)

Methods: We analyzed data on 194 African American patients with information on biomarkers including SE, CRP, CCP, RFIgA and RFIgM as well as radiographic outcomes including erosion scores and joint space narrowing (JSN) at baseline and after 60 months of disease duration. Radiographic disease progression was determined by increase in disease scores from baseline to 60-month disease duration follow-up, and individuals with severe progression were identified as those in the top worst quintile of disease score increase (Erosion≥1; JSN≥7). Demographics, comorbidities, medications, and measures of SES were also collected at the baseline assessment. Multiple imputation was used to impute missing values. Multivariable multi-level linear and logistic regression models with study site adjusted for as a random effect were used to estimate linear coefficients (β), odds ratios (aOR) and 95% confidence intervals (CI) for disease prevalence and progression in relation to biomarkers at baseline. All models were adjusted for gender, age, BMI, number of comorbidities, cigarette smoking, disease duration at study entry, methotrexate/leflunomide (MTX/LEF) use, education level (< high school [HS] vs ≥ HS), home ownership, professional occupation, as well as simultaneous adjustment for all biomarker predictors.

Table 3. Adjusted[§] associations of predictors of RA joint damage at baseline

	EROSION SCORES				JSN SCORES			
	Baseline Cross-Sectional	Baseline to 5 years Progression			Baseline Cross-Sectional	Baseline to 5 years Progression		
Biomarkers[‡]	Estimate (β)				Estimate (β)			
CRP (continuous)	0.00 (-0.01,0.01)				0.00 (-0.02,0.02)			
ACCP Positive		ACCP Positive	Cases/Controls		ACCP Positive		ACCP Positive	Cases/Controls
No, Mean (Std Dev)	0.52 (0.61)	Erosion Score increased <1	93/52		No, Mean (Std Dev)	1.83 (8.5)	Erosion Score increased <1	99/55
Yes, Mean (Std Dev)	2.01 (0.59)	Erosion Score increased ≥1	33/16		Yes, Mean (Std Dev)	2.46 (8.2)	Erosion Score increased ≥1	27/14
Estimate (95% CI)	1.49 (-0.08,3.06)	Odds Ratio (95% CI)	0.73 (0.18-2.94)		Estimate (95% CI)	0.62 (-1.53,2.78)	Odds Ratio (95% CI)	0.85 (0.23-3.16)
RGFIgA Positive		RGFIgA Positive	Cases/Controls		RGFIgA Positive		RGFIgA Positive	Cases/Controls
No, Mean (Std Dev)	1.54 (0.65)	Erosion Score increased <1	98/47		No, Mean (Std Dev)	2.31 (9.0)	Erosion Score increased <1	106/48
Yes, Mean (Std Dev)	0.99 (0.56)	Erosion Score increased ≥1	37/12		Yes, Mean (Std Dev)	1.98 (7.8)	Erosion Score increased ≥1	30/11
Estimate (95% CI)	-0.55 (-2.15,1.05)	Odds Ratio (95% CI)	1.60 (0.51-4.98)		Estimate (95% CI)	-0.33 (-2.55,1.88)	Odds Ratio (95% CI)	1.26 (0.36-4.45)
RGFIgM Positive		RGFIgM Positive	Cases/Controls		RGFIgM Positive		RGFIgM Positive	Cases/Controls
No, Mean (Std Dev)	1.44 (0.67)	Erosion Score increased <1	104/41		No, Mean (Std Dev)	1.78 (9.3)	Erosion Score increased <1	113/41
Yes, Mean (Std Dev)	1.09 (0.63)	Erosion Score increased ≥1	39/10		Yes, Mean (Std Dev)	2.51 (8.8)	Erosion Score increased ≥1	30/10
Estimate (95% CI)	-0.35 (-2.20,1.50)	Odds Ratio (95% CI)	1.36 (0.31-5.90)		Estimate (95% CI)	0.73 (-1.85,3.31)	Odds Ratio (95% CI)	0.87 (0.15-4.90)
Has Shared Epitope		Has Shared Epitope	Cases/Controls		Has Shared Epitope		Has Shared Epitope	Cases/Controls
No, Mean (Std Dev)	0.91 (0.50)	Erosion Score increased <1	57/88		No, Mean (Std Dev)	2.20 (7.0)	Erosion Score increased <1	58/95
Yes, Mean (Std Dev)	1.63 (0.56)	Erosion Score increased ≥1	22/27		Yes, Mean (Std Dev)	2.09 (7.8)	Erosion Score increased ≥1	21/20
Estimate (95% CI)	0.72 (-0.39,1.83)	Odds Ratio (95% CI)	1.15 (0.56-2.36)		Estimate (95% CI)	-0.12 (-1.60,1.37)	Odds Ratio (95% CI)	1.71 (0.80-3.66)

[§]Adjusted for age, sex, BMI, use of Methotrexate/Leflunomide, ever smoking, number of comorbidities, education, home ownership, occupation; study site adjusted for as a random effect

[‡]All biomarkers simultaneously adjusted in models

Results: At baseline the mean age was 51 years, 86% were female, average RA disease duration was 14.05 months, and 64.4% patients were on MTX/LEF (Table 1). Radiographic measures at baseline and 60 months are shown in Table 2. Beta estimates for the cross-sectional association between baseline biomarkers and baseline radiographic measures are shown in Table 3. Also in Table 3 are odds ratios for the association between baseline biomarkers of interest and severe radiographic progression. Results did not indicate an association of CCP, RF, or SE with severe radiographic progression in this cohort.

Conclusion: Our findings show modest associations between biomarkers and radiographic severity in cross-sectional analyses. However, when analyzing biomarker predictors of radiographic progression, CCP, RFIgM, RFIgA, and SE are not significantly associated with disease progression in African Americans over a 60-month disease duration with early RA. Future larger longitudinal studies are needed to confirm our results.

Disclosure: E. Astrike-Davis, None; **R. Cleveland**, None; **B. Jonas**, None; **L. Callahan**, None.

Abstract Number: 0211

Effects of Deep Haptic Massage in Fibromyalgia (pilot Study)

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The management of fibromyalgia is difficult, combining pharmacological and non-drug treatments, including massage. Its pathophysiology, still poorly understood, is complex, including muscle anomalies with reduced ATP and microcirculation. To date, only superficial massages have been tested in fibromyalgia. Deep haptic massage, used in athletes, have an action on muscle structures by reaching the free nerve endings present in

the muscle and to ensure a “gate control” of the pain. The purpose of this pilot study was to evaluate the effects of deep haptic massage in fibromyalgia.

Methods: Preliminary monocentric open ended prospective study from october 2015 to november 2017.

Inclusion criteria : women, 18 to 65 years, fibromyalgia by ACR criteria, with a White Spread Index (WPI) ≥ 7 and severity score (SS) ≥ 5 or WPI between 3 and 6 and SS ≥ 9, with stable treatment for 1 month without modification expected within the next 6 months.

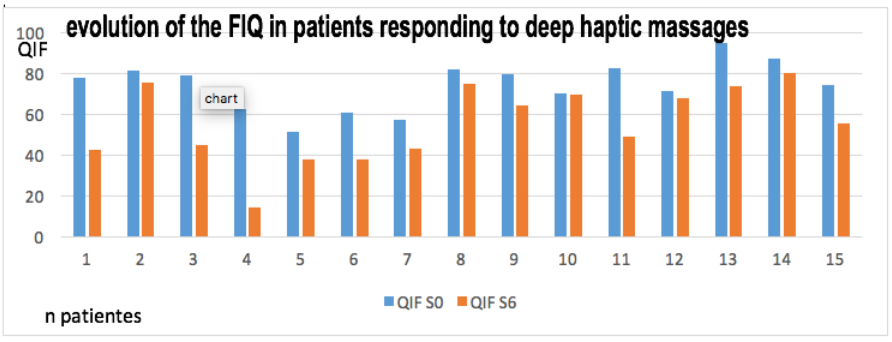
Non inclusion criteria : pregnant women, chronic inflammatory rheumatism, infection disease, individualized psychiatric pathology, severe visceral impairment, non-drug combination therapy, skin lesions contraindicating massages.

Intervention : 2 sessions of deep haptic massage of 30 minutes per week for 6 weeks.

Evaluation at week 0 (S0), S6, S12 and S24. Main evaluation criteria at S6 : fibromyalgia Impact Questionnaire (FIQ). Secondary criteria FIQ to S12 and S24 and sub-items from FIQ to S6, S12 and S24. EVA patient and physician satisfaction at S6, S12 and S24. The analysis of the evolution of the FIQ score carried out using a T Test for a sample.

Results: 21 patients were included (1 study discharge at 3 months), including an age median of 53 (47-57), medians WPI 15 (13-18) and SS 9 (8-11). The average FIQ was from 68.8±16.1 to S0, 60.1±16à S6, 65.7±18.8 à S12 and 68.4±14.5 to 6 months. An average variation between S0 and S6 of -8 percent (ns). No change in sub-items of the FIQ is not significant. The medians of EVA satisfaction at S6 for the patient and physician were similar, respectively 7,5/10 and 6/10. At 3 and 6 months from the massage, EVA satisfaction decreases in a similar way in patients and doctors (5/10 and 4.5/10 respectively). In a subgroup of 14 patients “deep haptic massage reponders”, there is an average variation between S0 and S6 of -26 percents (FIQ means : S0 : 74.03±12.8; S6 : 55.37±19.7).

	J0/J45 (n=21)	J0/J90 (n=21)	J0/J180 (n=20)
Score QIF moyenne	-7,7 (-25,8 - 11,9) *p 0,1293*	2,4 (-19,5 – 12,4) *p 0,5389*	-1,5 (-10,7 – 8,1) *p 0,7538*



Evolution of QIF in patients responding to deep haptic massages

Conclusion: In our study, deep haptic massage does not appear to be effective in the management of fibromyalgia. Nevertheless, positive effects in a subgroup representing more than 50 percents of patients encourage further investigation on a larger scale.

Disclosure: a. FELCE, None; **a. aubrun**, None; **y. allam**, None; **A. Choplin**, None; **L. Euller Ziegler**, None; **V. Breuil**, None.

Abstract Number: 0212

Utility of Mood Disorders Questionnaire in Fibromyalgia: Data from the Cleveland Clinic Fibromyalgia Registry

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Background/Purpose: Patients with comorbid fibromyalgia syndrome (FMS) and bipolar disorder (BD) were found to have more severe FMS. The Mood disorders questionnaire (MDQ), a self-reported inventory of lifetime history of manic and hypomanic symptoms has been proposed as a screening tool for BD, but its specificity for BD has been controversial. We evaluated the relationship between MDQ and a history of self-reported prior clinical diagnosis of BD.

Methods: Consecutive patients diagnosed clinically with FMS were enrolled and demographic, socioeconomic and clinical data were collected. Patients completed the following standardized questionnaires; for depression PHQ-9 (patient health questionnaire), anxiety GAD-7 (generalized anxiety disorder questionnaire), disability HAQ-DI (health assessment questionnaire disability index), PDI (pain disability index), PSD (polysymptomatic distress scale/fibromyalgianess scale), WPI (widespread pain index), SS (symptom severity scale), FIQ (fibromyalgia impact questionnaire).

Results: We enrolled 430 patients with FMS who completed the MDQ and also reported a history of psychiatric evaluation, of which 118 (27.5%) had bipolar disorder by either MDQ or prior psychiatric diagnosis. The mean age was 43.3 (12.0), 89.3% female and 87.7% met the ACR 2010 criteria for FMS. The mean MDQ was 3.9 (3.3) and 20.9% had an MDQ >=7. A psychiatric diagnosis of BD was made in 59 (13.7%) of patients; 6.7% (29%) had a BD diagnosis by psychiatry and an MDQ of < 7. Thirty patients (7%) had a diagnosis of BD both by MDQ and psychiatry. Correlation between MDQ and a past psychiatric diagnosis of BD was low, r= 0.293 (p< 0.005). The sensitivity of an MDQ ³7 for a prior diagnosis of BD was 42.4% and the specificity was 13.5%. Patients with MDQ³ 7 had significantly higher scores on depression and anxiety as well as higher fibromyalgianess, fibromyalgia severity and disability scores (Table 1). We performed three separate linear regression analyses to predict FMS severity measured by FIQ from depression (PHQ-9), anxiety (GAD-7) and bipolar disorder determined by MDQ, psychiatric diagnosis or both. Depression and anxiety but not a positive screen for BD either by MDQ, prior clinical diagnosis of BD or either, remained independent predictors of FIQ variance.

Conclusion: The utility of MDQ as a screening tool for BD in patients with FMS, as well as the impact of a psychiatric diagnosis of BD on FMS measures and severity, needs to be further evaluated. Nevertheless, patients with high MDQ scores seem to have more severe depressive and anxiety symptoms and score higher on FMS measures of severity and impact.

Table 1. Comparison between FMS patients with BD and those without BD diagnosed by MDQ, psychiatric diagnosis, or both

Variable	MDQ*		Prior psychiatric diagnosis of BD**		Either MDQ≥7 or psychiatric diagnosis***		*P*
	MDQ<7 N 340 79.1%	MDQ≥7 N 90 20.9%	No N 371 86.3%	Yes N 59 13.7%	No N 312 72.6%	Yes N 118 27.4%	
PHQ-9	12.7 (6.4) N 339	16.6 (5.5) N 90	13.2 (6.4) N 370	15.7 (5.7) N 59	12.6 (6.3) N 310	16.4 (5.6) N 118	*0.000 **0.006 ***0.000
GAD-7	8.5 (6.0) N 334	13.9 (5.7) N 89	9.3 (6.3) N 365	11.5 (6.4) N 58	8.3 (6.0) N 305	12.8 (6.1) N 118	*0.000 **0.016 ***0.000
FIQ	62.3 (20.1) N 241	70.7 (16.5) N 69	63.5 (20.1) N 271	68.7 (15.3) N 39	61.9 (20.3) N 224	70.1 (16.2) N 86	*0.002 **0.127 ***0.001
WPI	11.8 (4.1) N 330	13.4 (4.1) N 88	12.1 (4.2) N 360	12.9 (4.0) N 58	11.7 (4.1) N 301	13.3 (4.0) N 117	*0.003 **0.161 ***0.001
SS	8.8 (2.3) N 328	9.7 (2.2) N 88	8.9 (2.3) N 358	9.7 (2.2) N 58	8.7 (2.3) N 299	9.7 (2.1) N 117	*0.001 **0.011 ***0.000
PSD	20.7 (5.4) N 325	23.1 (5.3) N 88	21.0 (5.5) N 355	22.6 (5.0) N 58	20.5 (5.4) N 296	23.0 (5.0) N 117	*0.000 **0.033 ***0.000
PDI	5.5 (2.2) N 292	6.3 (1.9) N 81	5.6 (2.2) N 321	6.3 (1.8) N 52	5.4 (2.3) N 296	6.4 (1.8) N 117	*0.004 **0.055 ***0.000
HAQ-DI	1.0 (0.6) N 317	1.2 (0.5) N 83	1.0 (0.6) N 342	1.3 (0.5) N 58	1.0 (0.6) N 288	1.2 (0.5) N 112	*0.011 **0.006 ***0.000

FMS Fibromyalgia, BD Bipolar disorder, PHQ-9 Patient health questionnaire 9, GAD-7 Generalized anxiety disorder questionnaire, FIQ Fibromyalgia impact questionnaire, WPI Widespread pain index, SS Symptom severity scale, PSD Polysymptomatic distress scale /Fibromyalgianess scale, PDI Pain disability index, HAQ-DI Health assessment questionnaire disability index.

Table 2: Linear regression to predict FIQ variability from depression, (PHQ-9) anxiety (GAD-7) and bipolar disorder determined by either MDQ, psychiatric diagnosis or both						
Dependent variable	Predictors	B	Beta	*p*	95% CI for Lower limit of B	95% CI for Upper limit of B
BD by MDQ	constant	38.972		0.000	34.879	43.066
	PHQ-9	1.52	0.499	0.000	1.152	1.893
	GAD-7	0.527	0.178	0.006	0.153	0.901
	BD by MDQ	-1.626	-0.035	0.474	-6.091	2.84
This model predicted 38.3% of FIQ variability, F (63.696)=233.645, p<0.000						
BD by psychiatric diagnosis	constant	39.017		0.000	34.916	43.111
	PHQ-9	1.519	0.189	0.000	1.147	1.891
	GAD-7	0.489	0.165	0.008	0.129	0.849
	BD psychiatric diagnosis	-0.028	0.000	0.999	-5.237	5.182
This model predicted 38.2% of FIQ variability, F (63.416)=234.045, P<0.000						
BD by MDQ and/or psychiatric diagnosis	Constant	39.018		0.000	34.924	43.112
	PHQ-9	1.526	0.500	0.000	1.153	1.898
	GAD-7	0.505	0.171	0.007	0.137	0.872
	BD by MDQ and/or psychiatric diagnosis	-0.859	-0.020	0.687	-4.943	3.225
This model predicted 38.8% of FIQ variability, F (63.510)=233.912, p<0.000						
BD Bipolar disorder, FIQ Fibromyalgia impact questionnaire, PHQ-9 Patient health questionnaire 9, GAD-7 General anxiety disorder questionnaire, MDQ Mood disorder questionnaire						

Disclosure: C. Gota, None; **S. Kaouk**, None; **K. Yaseen**, None; **N. Jhala**, None; **W. Wilke**, None.

Abstract Number: 0213

Relationship Between a History of Abuse and Fibromyalgia Symptoms and Severity: Data from the Cleveland Clinic Fibromyalgia Registry

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: It has been proposed that the fibromyalgia syndrome (FMS) phenotype is determined by genetic factors, lack of physical exercise, mood disorders, maladaptive pain responses, and both current and past stressors, including a history of abuse. In this study we examined the predictive role of a history of abuse on FMS severity measures, and the association between self-reported abuse and socioeconomic status, symptoms, psychiatric comorbidities, and disability.

Methods: All consecutive patients clinically diagnosed with FMS who answered the question 'Do you have a history of abuse?" were enrolled. Patients' characteristics were compared between those who reported a history of abuse and those how did not. Linear regression analysis was performed to determine the predictive effect of a history of abuse on fibromyalgia impact questionnaire and fibromyalgianess scale, used as FMS severity measures.

Results: We enrolled 593 consecutive patients with FMS, mean age 43.8 (12.3), 87% female, of which 85.2% met the ACR 2010 criteria. A history of abuse was reported by 223 patients, sexual abuse by 125 (56.5%), physical abuse by 155 (69.5%) and both by 78 (34.9%). Fibromyalgia patients with a history of abuse had worse socioeconomical status as measured by higher percentages of single and divorced patients, lower education level, lack of private insurance and greater reliance on Medicare and Medicaid, lower employment rates, and higher disability compared with those without abuse. A higher prevalence of personal and family history of psychiatric comorbidity was found in patients with a history of abuse. Fibromyalgia severity scores, including fibromyalgianess scale, pain disability index, fibromyalgia impact questionnaire and the health assessment disability index were all higher in patients with FMS and a history abuse compare to those without abuse (Table 1). A linear regression model predictied 46% of FMS severity measured by fibromyalgia impact questionnaire variability, $p< 0.0005$, from abuse, exercise, non-refreshing sleep, current stressors, depression and anxiety (Table 2). A similar model, $p< 0.0005$, predicted 32% of fibromyalgianess scale variability (Table 3).

Conclusion: Our results suggest that stressors such as abuse have a wide range of detrimental effects on FMS. We recommend that abuse should be inquired about in all patients evaluated for FMS as this may give more clarity to the nature and severity of the FMS presentation and prompt the need for psychological interventions.

Table 1. Characteristics of FMS patients with and without a history of abuse			
Variables	History of abuse		*P*
	No N 370	Yes N 223	
Gender	Female N 313 84.6% Male N 50 13.5%	Female N 203 91.0% Male N 16 7.2%	0.058
Ethnicity	White N 313 84.6% African American N 20 5.4% Other N 8 2.1%	White N 179 80.3% African American N 24 10.8% Other N 4 1.7%	0.057
Marital status	Single N 89 24.1% Living with partner N 5 11.4% Married N 223 60.3% Divorced N 42 11.4% Widowed N 5 1.4%	Single N 36 16.1% Living with partner N 2 0.9% Married N 119 53.4% Divorced N 58 26% Widowed N 5 2.2%	0.000
Insurance type	Medicaid N 38 10.3% Medicare N 30 8.1% No insurance N 42 11.3% Private N 273 73.8%	Medicaid N 41 18.4% Medicare N 26 11.7% No insurance N 5 2.2% Private N 139 62.3%	0.020
Education	<12th grade N 11 9.5% High school graduate N 69 18.6% Some college N 89 24.1% College graduate	<12th grade N 15 13.5% High school graduate N 30 13.5% Some college N 64 28.7% College graduate	0.040

Table 2: Linear regression analysis predicting fibromyalgia severity variance measured by FIQ from waking up unrefreshed, aerobic exercise, ongoing stressors, history of abuse, PHQ-9 and GAD-7					
				95% CI for B	
	B	Beta	*p*	Lower bound	Upper bound
Constant	31.404		0.000	25.699	37.110
Aerobic exercise	-5.115	-0.104	0.007	-8.818	-1.413
Unrefreshing sleep	8.677	0.126	0.001	3.395	13.960
History of abuse	6.114	0.151	0.000	3.011	9.216
Ongoing stressors	-2.568	-0.60	0.134	-5.929	0.794
PHQ-9	1.514	0.489	0.000	1.204	1.824
GAD-7	0.486	0.160	0.002	0.185	0.787
FIQ- Fibromyalgia impact questionnaire, PHQ-9 Patient health questionnaire -9 , GAD-7 General anxiety disorder questionnaire					

Table 3: Linear regression analysis predicting Fibromyalgianess scale (Polysymptomatic distress scale) from waking up unrefreshed, aerobic exercise, ongoing stressors, history of abuse, PHQ-9 and GAD-7					
				95% CI for B	
	B	Beta	*p*	Lower bound	Upper bound
Constant	13.524		0.000	11.954	15.094
Aerobic exercise	-0.841	-0.059	0.118	-1.895	0.214
Unrefreshing sleep	1.578	0.082	0.036	0.104	3.052
History of abuse	1.636	0.140	0.000	0.753	2.520
Ongoing stressors	-0.475	-0.40	0.311	-1.395	0.445
PHQ-9	0.463	0.521	0.000	0.374	0.551
GAD-7	-0.005	-0.006	0.912	-0.094	0.084
PHQ-9 Patient health questionnaire -9, GAD-7 General anxiety disorder questionnaire					

Disclosure: C. Gota, None; **S. Kaouk**, None; **K. Yaseen**, None; **N. Jhala**, None; **W. Wilke**, None.

Abstract Number: 0214

How Well Do Visual Analogue Scales Used in the Fibromyalgia Impact Questionnaire (FIQ) Correlate with Other Measures of Pain, Fatigue, Sleep, Sleep Disturbance, Anxiety and Depression in Patients with Fibromyalgia

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia syndrome (FMS), is a biopsychosocial condition characterized by widespread pain, fatigue, non-refreshing sleep, and various degrees of anxiety and/or depressive symptoms. Visual analogue scales (VAS) for pain, fatigue, sleep, anxiety, depression, are patient reported, uni-dimensional continuous scales, widely used in FMS as measures of symptom intensity and as outcome measures in drug trials. There is limited data on how well these VAS scales correlate with other "alternative measures" of pain, fatigue, sleep, anxiety and depression and with global measures of FMS severity and impact.

Table 1: Pearson correlations between VAS pain, VAS fatigue, VAS waking up unrefreshed, VAS anxiety and "alternate measures" of sleep, pain, anxiety and depression (WPI, ESS, hours of sleep, GAD-7 , PHQ-9) and FMS measures of severity and impact: PSD, FIQ, HAQ-DI and PDI.

Variable	VAS fatigue	VAS waking up unrefreshed	VAS depression	VAS anxiety	WPI	Hours of sleep	ESS	PHQ-9	GAD-7	SS	FIQ	PSD	HAQDI	PDI
VAS pain	0.298*	0.256*	0.298*	0.290*	0.218*	-0.241*	0.125**	0.315*	0.271*	0.301*	0.642*	0.428*	0.451*	0.515*
VAS fatigue		0.553*	0.338*	0.351*	0.261*	-0.101**	0.236*	0.483*	0.357*	0.541*	0.631*	0.420*	0.287*	0.408*
VAS waking up unrefreshed			0.255*	0.312*	0.218*	-0.133**	0.197*	0.470*	0.313*	0.501*	0.545*	0.377*	0.243*	0.338*
VAS depression				0.707*	0.218*	-0.184*	0.193*	0.648*	0.668*	0.375*	0.587*	0.321*	0.342*	0.412*
VAS anxiety						-0.183*	0.194*	0.586*	0.739*	0.388*	0.608*	0.335*	0.344*	0.420*
WPI						-0.128**	0.214*	0.377*	0.263*	0.356*	0.227*	0.919*	0.398*	0.404*
Hours of sleep							-0.003 NS	-0.211*	-0.252*	-0.144*	-0.211*	-0.147*	-0.258*	-0.223*
ESS								0.327*	0.249*	0.311*	0.276*	0.294*	0.245*	0.218*
PHQ-9									0.657*	0.585*	0.636*	0.533*	0.437*	0.510*
GAD-7										0.400* 0.000	0.518* 0.000	0.368* 0.000	0.355* 0.000	0.405* 0.000

VAS Visual analogue scale, ESS Epworth sleepiness scale, GAD-7 Generalized anxiety disorder scale, PHQ-9 Patient health questionnaire 9, WPI Widespread pain index, SS Symptom severity scale, PSD Polysymptomatic distress scale /Fibromyalgiaeness scale, FIQ Fibromyalgia impact questionnaire, HAQ-DI Health assessment questionnaire disability index , PDI Pain disability index

*P<0.000, **p<0.05 NS-not statistically significant

Methods: Consecutive patients diagnosed clinically with FMS were enrolled. Patients completed the following VAS scales: VAS pain, VAS fatigue, VAS waking up unrefreshed, VAS anxiety and VAS depression. As " alternative measures" we used: for pain the Widespread pain index (WPI), for sleep the mean hours of sleep per night and the Epworth sleepiness scale (ESS), for anxiety the Generalized anxiety disorder questionnaire (GAD-7) and for depression the Patient health questionnaire (PHQ-9). The following severity/impact measures were used: Fibromyalgia impact questionnaire (FIQ), the Polysymptomatic distress scale/Fibromyalgianess scale (PSD), calculated as the sum of the Widespread pain index (WPI) and Symptom severity scale (SS), the Health assessment questionnaire (HAQ-DI), and the Pain disability index (PDI). Pearson correlation, r was used to measure two-way linear association between two continuous variables; strong correlations are defined as r ³ 0.7, moderate r ³ 0.5, < 07, weak ³ 03,< 05, and very weak r < 0.3.

Results: We enrolled 763 consecutive patients, 82.4% who met the ACR 2010 criteria for FMS. Patients had the following characteristics: 86.6% were female, 80.3% white, age 44.3 (12.4), PHQ-9 12.7 (8.0), GAD-7 8.8 (6.3), VAS pain 7.1 (2.1), VAS fatigue 7.8 (2.1), VAS waking up rested 7.7 (2.4), VAS anxiety 5.1 (3.3), VAS depression 4.5 (3.3), WPI 11.9 (4.3), hours slept per night 5.9 (2.1), ESS 9.5 (5.6), GAD-7 8.8 (6.3), PHQ-9 12.7 (6.3), FIQ 61.7 (20.3), PSD 20.8 (17.0), PDI 5.5 (2.3), HAQ-DI 1.0 (0.6). Correlations between variables are presented in Table 1.

Conclusion: We found that VAS pain and WPI are poorly correlated with each other which suggests that they cannot be used interchangeably and probably both should be used when characterizing the pain of FMS patients.

The very poor correlation of VAS waking up unrefreshed with daytime sleepiness measured by ESS and the mean hours of sleep per night, suggests that a more complex and multidimensional measure of sleep is needed to characterize sleep in FMS patients.

The VAS measures of depression and anxiety had moderate and strong correlations with the alternative measures, PHQ-9 and respectively GAD-7, which indicates VAS depression and anxiety can be used as quick measures of current depressive and anxiety symptoms.

Many studiers of FMS severity report only the FIQ total score and use only the VAS components for more specific measures. This analysis suggests that if alternative measures of specific symptoms rather than VAS FIQ components are used, results and/or conclusions may be different.

Disclosure: C. Gota, None; **S. Kaouk**, None; **K. Yaseen**, None; **N. Jhala**, None; **W. Wilke**, None.

Abstract Number: 0215

Opioid Treatment Pattern in a Community Based Rheumatology Clinic

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatologic pain, especially fibromyalgia, is difficult to treat. While Nonsteroidal anti-inflammatory drugs (NSAIDs) are traditionally prescribed as the first line treatment for fibromyalgia, when patients are unable to tolerate, or the pain persists, or when other treatment modalities have failed, opioids have been prescribed.

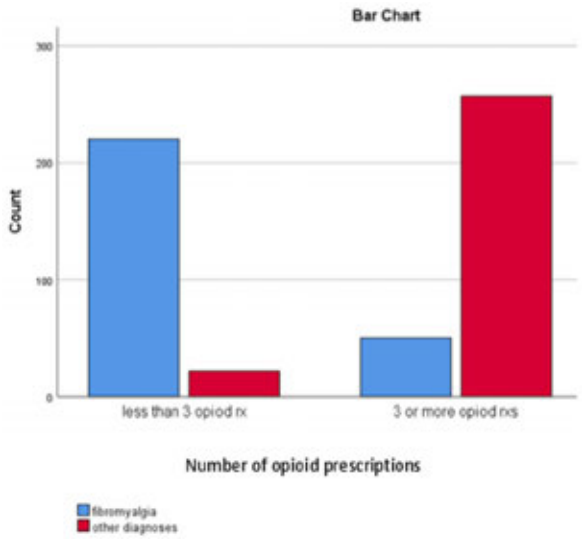


Table 1. Primary diagnosis and Number of opioid prescription ≥ 3

Primary Diagnosis		
Fibromaylgia	Other	No diagnosis
51 (16.4%)	258 (83.0%)	2 (0.6%)
χ^2 =26.65 , p<0.001		

Table 2. Type of opioid and number of opoid prescription ≥ 3

	Weak	Strong	Statistical Significance
Fibromyalgia	7 (14%)	43 (86%)	X^2 =187.25 , p< 0.001
Other	48 (18.7%)	209 (81.3%)	χ^2 = 0.623 , p= 0.43
Total	55	263	

BASDAI

Even though the guidelines do not recommend opioids for the routine treatment of pain in rheumatologic conditions, they are frequently used.

Purpose: To identify the rheumatologic diagnosis for which opioids are most frequently prescribed at one community-based outpatient clinic.

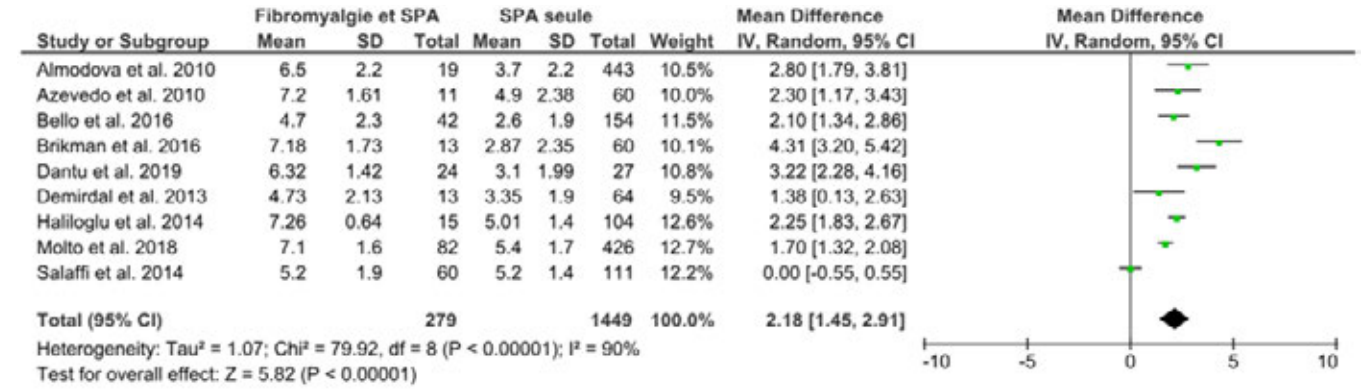
Methods: The medical records of 553 patients treated at the rheumatology clinic from January 1, 2016 until December 31, 2017 were reviewed. To be included in the study, the patients had to have received at least one opioid prescription, but only those who received three or more opioid prescriptions were considered to be reliant on opioids for pain control. The variables used for data collection were age, gender, the primary and secondary rheumatology diagnoses, NSAID prescription as well as the number, name and dose of opioid prescribed. Tramadol and codeine were considered weak opioids, while Fentanyl, Morphine, Oxycodone, Hydrocodone were classified as strong opioids.

Results: Fibromyalgia (FM) was the most common patient diagnosis at 49%, the other 51% had a variety of rheumatologic diagnoses with the next most frequent being rheumatoid arthritis 7%, followed by lupus, 3%, then primary osteoarthritis 2%,, and Sjogren's 1.4%(Image1). Data was missing on 4 patients. Fifty-six per cent (n=311) of the sample had received three or more opioid prescriptions. Of those who received three or more opioid prescriptions, 84% had a diagnoses other than FM, a difference that was statistically significant (χ_2 = 302, p < .001)(Table1). When receiving three or more opioids, 86% (n = 43) of the 51 FM patients who were opioid-dependent for pain control had

been prescribed a strong opioid compared to the other diagnoses, 253 (81.4%) of whom were receiving a strong opioid(Table 2).

Conclusion: Although most research on opioid prescription for rheumatologic pain control has found that FM is the most common diagnosis, this was not the case for one community-based clinic. These results may be attributable to differences in prescribing practices in a community clinic versus a tertiary setting where most of the research has been conducted. Or perhaps patient preferences for treatment accounted for the differences. Additionally the disease duration and degree of suffering for our sample could not be ascertained and it may be that this sample was intrinsically different from others who have been studied.

Disclosure: R. Andrade, None; **P. Roe - Prior**, None; **O. Doan**, None; **J. Ramos**, None.



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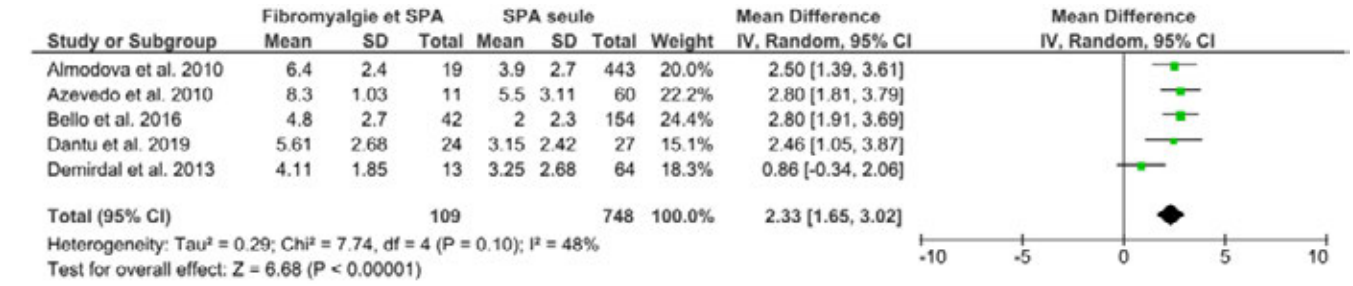

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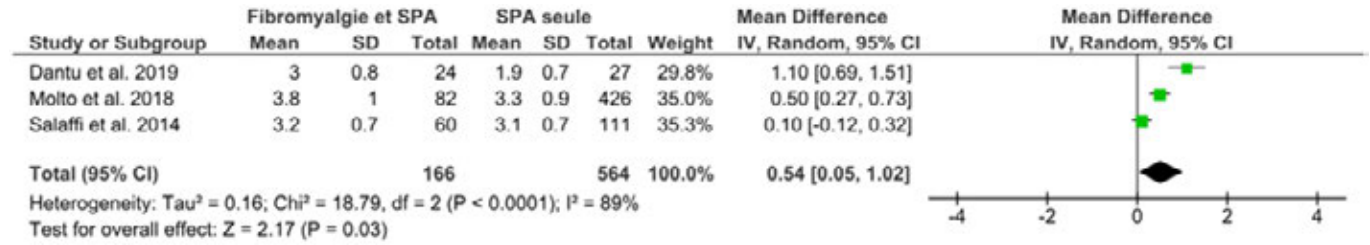

ASDAS-CRP

Abstract Number: 0216

Does Fibromyalgia Change the Evaluation of Spondyloarthritis Activity? A Meta-analysis of Observational Studies

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent studies evaluated the prevalence of Fibromyalgia (FM) in Spondyloarthritis (SpA) and its impact on disease activity scores, but none meta-analysis exists yet. Therefore, we performed a meta-analysis to evaluate the impact of fibromyalgia on activity scores in SpA.

Methods: We performed a systematic review of the literature until May 2019 using database including: MEDLINE (via PUBMED), EMBASE and abstracts from the ACR and EULAR congresses 2016-2019. We selected observational studies comparing characteristics of SpA patients (defined by ASAS, NY modified or CASPAR criteria) with or without fibromyalgia (defined by ACR 1990, 2011 fibromyalgia criteria or FiRST survey).

Two readers extracted the prevalence of FM in SpA, female ratio, HLAB27 status, disease duration, radiographic sacroiliitis, C-reactive protein (CRP), BASDAI, BASFI, ASDAS-CRP and Quality of Life (QoL).

Statistical analysis determined in each study theeffect size. Data was analyzed using the inverse variance approach.

Results: The literature search identified 433 articles. Finally, 15 studies met the inclusion criteria.

The prevalence of FM in SpA was 17% IC95% [0.12, 0.23] with a significant female ratio of 5.13 IC95%[3.02, 8.70] in SpA with FM.

FM impacted significantly all the activity scores of SpA: BASDAI: OR= 2.18 IC95%[1.45, 2.91]; BASFI: OR= 2.33 IC95%[1.65, 3.02]; ASDAS-CRP: OR= 0.54 IC95%[0.05, 1.02]; AsQoL: OR=5.50 IC95%[4.28, 6.71]

No statistical difference was found concerning HLAB27 status, disease duration and CRP level.

Conclusion: In this meta-analysis, the prevalence of FM in SpA was 17%, whereas 2-8% in general population. The coexistence of FM with SpA led to higher activity scores, including ASDAS-CRP, although CRP trends to be lower in the FM group.

Rheumatologist have to be aware of the association of FM and SpA, activity scores may be biased.

Disclosure: A. Beck, None; **L. SOLE**, None; **T. Barnetche**, None; **P. Vergne-Salle**, None.

Abstract Number: 0217

Fibromyalgia and Multiple Switching of Biologics in Spondylarthritis

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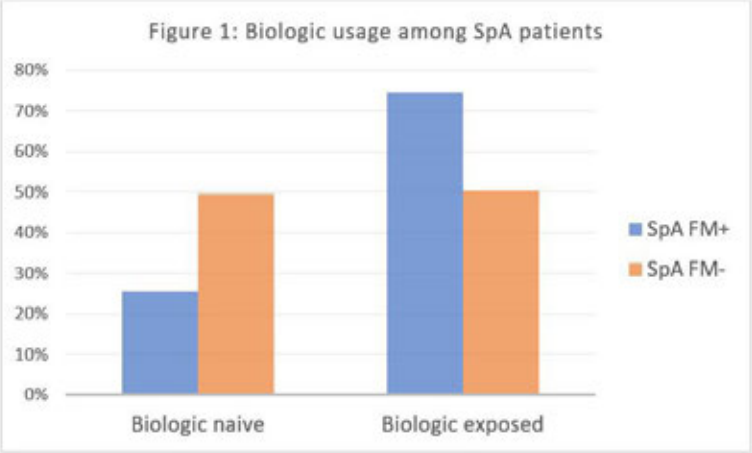
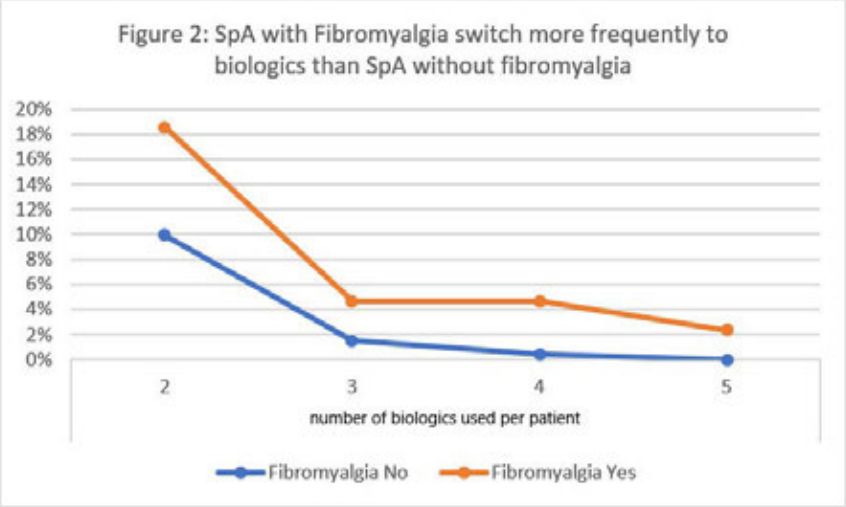
SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster

Gender, Female, n (%)	175 (57.4)
Age, mean ±SD (min- max), years	44.07 ± 11.85 (18- 78)
Type of SpA, n (%)	
Axial	117 (38.4)
Peripheral	188 (61.6)
Fibromyalgia, n (%)	43 (14.1)
FM in axial SpA	18 (41.9)
FM in Peripheral SpA	25 (58.1)
SpA Disease duration (months)	
FM+, mean ±SD	107.7± 50.4
FM-, mean ±SD	86± 57.9
SpA initial clinical features, n (%)	
IBP	157 (51.5)
Arthritis	117 (38.4)
Sacroiliitis	107 (35.1)
Uveitis	6 (2)
Enthesitis	67 (22)
Dactylitis	29 (9.5)
Psoriasis	95 (31.1)
IBD	11 (3.6)
Family history of SPA	30 (9.8)
SpA established diagnosis according to ESSG, n (%)	
Ankylosing Spondylitis	51 (16.7)
Psoriatic arthritis	128 (41.9)
Undifferentiated SpA	110 (36.1)
IBD associated SpA	9 (3)
Reactive SpA	6 (2)
Acute anterior Uveitis	1 (0.3)
Elevated CRP, n (%)	62 (20.3)
HLA B27 in 180 patients, n (%)	
Positive	32 (17.8)
Negative	148 (82.2)
ASDAS score in 210 patients	
ASDAS- ESR, mean ±SD (min- max)	1.63 ±0.69
ASDAS- CRP, mean ±SD (min- max)	1.45 ± 0.75
Abnormal MRISIJ, n (%)	92 (30.2)
Bone marrow edema	33 (10.8)
Subchondral sclerosis	21 (6.9)
Fatty transformation of bone marrow	5 (1.6)
Erosion	2 (0.7)
Number of conventional DMARDs ever tired, n (%)	
None	81 (26.6)
One	166 (54.4)
Two	46 (15.1)
Three	12 (3.9)
Number of biologic DMARDs ever tried, n (%)	
None	141 (46.25)
One	120 (39.35)
Two	34 (11.1)
Three	6 (2)
Four	3 (1)
Five	1 (0.3)
Frequency of DMARDs usage, n, (%)	
Conventional DMARDs	224 (73.4)
Prednisolone	56 (18.4)
Biologic DNARDs	164 (53.8)





Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia (FM) is a condition characterized by chronic widespread pain, tender points, fatigue and disturbed sleep rhythm. Some of these symptoms such as fatigue, tender points and diffuse pain seen in patients with spondylarthritis (SpA). Moreover, FM and SpA can coexist creating a diagnostic challenge, particularly in early disease course and influence clinical disease activity assessment. With this cross-sectional study, we aim to estimate the prevalence of FM in SpA and to elaborate its effect on biological treatments.

Methods: FM was identified according to the ACR 2010 diagnostic criteria. SpA patients identified according to rheumatologist using various SpA subsets criteria. A review of the electronic medical files for SpA patients attending the rheumatology outpatient clinic and infusion unit at a major tertiary hospital during the period from June to December 2018 were included. Patients' demographics, disease characteristics were explored. Regarding SpA medications, number, frequency and dose of DMARDs and biological agents were obtained. Continuous variables were reported by their mean and standard deviation (SD) and qualitative variables by frequency and percentage. Statistical significance was set at $p < 0.05$. Statistical analysis was performed using SPSS version 23.

Results: Of the 305 enrolled SpA patients, 43 (14.1%) had FM. Females represents 57.4% of the patients, mean age was 44.07 ± 11.85 years. Arab ethnicity represents most of our cohort 84.9%, the majority were Emirati 64.6%. Smokers were 8.2% and ex-smokers were 3.3%. HLA B27 tested in a sample of 180 patients; it was positive in only 17.8%. Abnormal MRI SIJ bone marrow edema changes were found in 10.8%, while other SIJ changes was seen in additional 20.6%. The prevalence of FM showed no statistically significant difference between axial and peripheral SpA. Patients with SpA and FM have longer disease duration than SpA alone, P= 0.034. Table.1 show demographics and clinical data. Regarding medication, the use of biologics in SpA patients with FM is more frequent than SpA patients without FM (74.4% vs 51.5 % respectively), P= 0.005 (Figure: 1). Interestingly, the likelihood ratio testing showed that SpA patient with Fibromyalgia switch more frequently to another biologics, P= 0.015 (Figure: 2). Cramer's V test showed that there is a high statistically significant (P= 0.002) and very strong association (> 0.25) between presence of Fibromyalgia and multiple switching of biologics in SpA. There was no difference in the exposure to prednisolone nor conventional DMARDs between SpA patients with or without FM, P= 0.64 & 1 respectively.

Conclusion: FM coexistence with SpA might impact clinical evaluation of disease activity and negatively affect measures of treatment response. In our study, SPA patients exposed to more biologics if they have coexisting FM; Moreover, they are more frequent switchers among biologics including TNFi and IL17i.

Disclosure: A. Negm, None; **N. Elsidig**, None; **A. Al Marzooqi**, None; **N. Zamani**, None; **A. Hossaini**, None; **J. Al Saleh**, None.

Abstract Number: 0218

Effects of Tai Chi versus Aerobic Exercise on Mindfulness in Fibromyalgia

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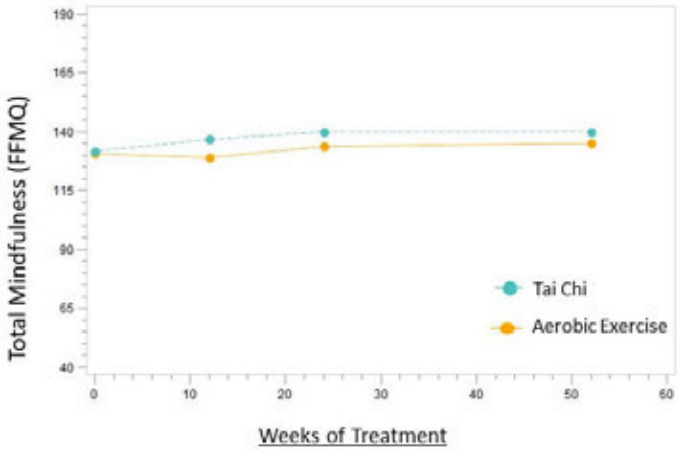
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Emerging evidence shows that Tai Chi mind–body practice may result in greater benefits in pain and psychological symptoms of Fibromyalgia (FM). Mindfulness is the ability to maintain a heightened awareness of moment-to-moment experiences without judging or reacting, and its improvement through mind-body

Table. Change in Total Mindfulness Levels After Intervention

Variable	Mean change from baseline (95% CI)		Mean Between group difference (95% CI)	Interaction p- value
	TC (n=151)	AE (n=75)		
Total FFMQ				0.11
Week 12	3.58 (1.08, 6.08)	-1.24 (-4.84, 2.35)	4.8 (0.45, 9.20)	
Week 24	7.27 (4.55, 9.98)	2.50 (-1.46, 6.46)	4.8 (-0.03, 9.57)	
Week 52	5.97(2.63, 9.32)	3.89 (-1.01, 8.79)	2.08 (-3.85, 8.02)	

Table FAST3 indices vs 2011 FM CriteriaTable. Percent agreement and kappa of 3 FAST3 (fibromyalgia assessment screening tool3) indices vs 2011 FM Criteria



practice is widely believed to contribute to the therapeutic benefits of Tai Chi. Observational studies have shown that mindfulness is associated with improved health outcomes among patients with FM. However, little is known about the contribution of mindfulness to the treatment effect of Tai Chi interventions among patients with chronic musculoskeletal pain. Therefore, our purpose was to investigate the effects of Tai Chi mind–body practice compared to aerobic exercise (AE) on mindfulness among adults with FM.

Methods: Secondary analysis of a single-blind trial randomizing adults with FM (ACR 1990 and 2010 Criteria) to either AE (twice per week for 24 weeks) or 1 of 4 Tai Chi intervention groups (once or twice weekly for 12 or 24 weeks). Participants completed the Five Facet Mindfulness Questionnaire (FFMQ) and other health outcome measures before and after intervention. Repeated measures regression models with interaction of evaluation (0, 12, 24, 52 weeks) and treatment group were used to compare change over time in total and facet FFMQ scores between the AE group versus the average of the 4 Tai Chi groups based on the intention to treat principle.

Results: Among 226 randomized participants (mean age 52 years, BMI 30kg/m^2, 92% female, 61% white), baseline mean total FFMQ score was 131.3 ± 20.7. FFMQ significantly improved from Tai Chi at all timepoints (**Table**). However, change in FFMQ from AE did not reach significance. Between group difference for total FFMQ favored Tai Chi at all timepoints and trended toward significance (**Figure**, p=0.11). Similar results were found for the Observing (p=0.11) and Acting-With-Awareness (p=0.18) facets of mindfulness, while the Non-Judging, Describing, and Non-Reacting facets did not significantly improve than from AE (p=0.41 to 0.62).

Conclusion: This is the first study to evaluate the effects of Tai Chi mind–body practice with active exercise in FM. Although Tai Chi significantly improved mindfulness from baseline, these differences did not reach significance when compared to changes from AE group. This suggests that mindfulness may not primarily account for the distinct health benefits from Tai Chi compared with AE shown in prior studies among these patients. Further study is needed to identify underlying mechanisms of effective mind–body interventions to advance treatment-making decisions for clinicians and patients.

AE = Aerobic Exercise; CI= Confidence Interval; FFMQ = Five Facet Mindfulness Questionnaire; total score = 39 to 195, higher scores reflect higher mindfulness; TC= Tai Chi. P≤0.05 was considered statistically significant.

Figure. Change in Mindfulness Between Treatment Groups: FFMQ = Five Facet Mindfulness Questionnaire; total score = 39 to 195, higher scores reflect higher mindfulness. Evaluations were completed at 0, 12, 24, and 52 weeks.

Disclosure: A. Lee, None; **L. Price**, None; **R. Bannuru**, None; **C. Wang**, None.

Table. Percent agreement and kappa of 3 FAST3 (fibromyalgia assessment screening tool3) indices vs 2011 FM Criteria

FAST3 indices vs 2011 FM Criteria	FAST3-P (pain)= Symptom checklist +RADAI+pain	FAST3-F (fatigue)= Symptom checklist +RADAI+fatigue	FAST3-nJC (no RADAI JC)= Symptom checklist +pain+fatigue
% Agreement	84.3%	86.6%	81.5%
Kappa	0.63 (0.56–0.70)	0.68 (0.60–0.75)	0.58 (0.50–0.66)

Abstract Number: 0219

A Fibromyalgia Assessment Screening Tool on a Multidimensional Health Assessment Questionnaire (MDHAQ) Which Does Not Include a Self-Report RADAI Painful Joint Count (RADAI), FAST3nJC, Recognizes Fibromyalgia Similarly to Other FAST3 Indices Which Include a RADAI

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
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Background/Purpose: Fibromyalgia (FM) generally is easily recognized, but a diagnosis may be difficult, particularly in patients with secondary FM who have other primary diagnoses. Criteria for FM initially were reported in 1990, and revised in 2010, 2011 and 2016. The 2 most recent criteria are based entirely on patient self-report, which is not collected in most routine clinical care, as multiple patient questionnaires are not feasible in busy clinical settings. MDHAQ/RAPID3 (multi-dimensional health assessment questionnaire/routine assessment of patient index data) is informative in all diseases studied. Cumulative indices based on MDHAQ scales known as FAST3 (fibromyalgia assessment screening tool3) recognize FM at levels of agreement with revised FM criteria of >80% and correlations of >0.80, p< 0.001), and might provide clues to recognize FM in patients with non-rheumatic diseases, as most components of the MDHAQ (as well as the HAQ) appear generic rather than disease-specific, other than a RADAI self-report painful joint count. Therefore, we analyzed a FAST3-nJC (no RADAI JC) index versus 2011 FM criteria as a reference standard, and compared to other FAST3 indices which include a painful RADAI JC.

Methods: All patients with all diagnoses complete an MDHAQ at all visits in routine care at one setting. The self-report questionnaire to recognize the 2011 FM Criteria was added over a 6-month period to be completed by consecutive patients. The MDHAQ includes 0-10 scores for physical function, and pain and patient global visual analog scales (VAS), compiled into 0-30 RAPID3, as well as a 0–10 fatigue VAS, 0–54 self-report painful joint count, and 0–60 symptom checklist. Each MDHAQ scale was analyzed for agreement with FM Criteria according to receiver-operator-characteristic (ROC) curves for area under the curve (AUC). Optimal cut points for each measure were identified, based on specificity and sensitivity, to develop optimal cumulative indices for clues to FM versus the 2011 Criteria as "gold standards."

Results: Among 502 patients with complete data, primary ICD-10 diagnoses were FM in 49, OA in 74, RA in 78, SLE 88 and other rheumatic diseases in 213. Primary or secondary FM was identified in 131 (26%) who met 2011 FM criteria. The 4 MDHAQ scales with the highest AUC vs FM Criteria (0.829-0.889) and optimal cut-points, were symptom

checklist 16/60, RADAI JC 16/54, fatigue VAS 6/10, and pain VAS 6/10. FAST3 0-3 measures were calculated as 0 or 1 based on cut-points for each measure, FM=2 or 3: FAST3-P= symptom checklist+RADAI JC+pain VAS; FAST3-F=symptom checklist+RADAI JC+fatigue VAS; FAST3nJC=symptom checklist+painVAS+fatigue VAS(no RADAI). All FAST3 indices agreed with FM Criteria >80% and kappas were >0.58, indicating good agreement (Table). Lowest agreement was seen for FAST3nJC, expected as FM criteria include a self-report painful joint count, but differences are small.

Table: Baseline Factors Associated with Response to 24-week Treatment

Characteristics	OR* (95% CI)	p-value
Gender, female	1.33 (0.46,3.83)	0.60
Age, yrs	0.98 (0.96,1.01)	0.17
Race		
White	0.77 (0.42,1.43)	0.41
Education		
High School	0.90 (0.21,3.87)	0.88
Living Alone	**0.56 (0.31,1.02)**	**0.06**
BMI, kg/m^2	1.00 (0.96,1.05)	0.97
Duration of Body Pain, yrs	0.98 (0.95,1.02)	0.31
Widespread Pain Index	1.01 (0.93,1.09)	0.83
Symptom Severity	**1.14 (0.99,1.32)**	**0.08**
FIQR	**1.02 (1.01,1.04)**	**0.01**
Patient's Global Assessment	1.00 (0.86,1.16)	0.98
Beck Depression Inventory-II	**1.03 (1.00,1.05)**	**0.05**
HADS Anxiety	1.05 (0.97,1.13)	0.24
HADS Depression	1.04 (0.97,1.12)	0.29
Arthritis Self Efficacy Scale	1.06 (0.92,1.22)	0.45
Coping Skills Questionnaire	**1.19 (0.97,1.46)**	**0.09**
Pittsburgh Sleep Quality Index	0.95 (0.88,1.02)	0.17
6-minute Walk Test, m	1.00 (1.00,1.00)	0.76
Physical Component Score of Short Form-36	1.01 (0.97,1.05)	0.55
Mental Component Score of Short Form-36	**0.97 (0.95,1.00)**	**0.08**
Analgesics	0.84 (0.45,1.60)	0.60
NSAIDs	1.12 (0.48,2.60)	0.80
Narcotics	0.69 (0.38,1.26)	0.22
Hypertension	0.98 (0.52,1.86)	0.95
Diabetes	0.74 (0.26,2.15)	0.54
Heart Disease	1.67 (0.56,4.98)	0.35
Outcome Expectations for Exercise	0.96 (0.64,1.44)	0.85
Tai Chi vs. Aerobic Exercise	1.24 (0.65,2.34)	0.51

*OR = Odds ratio, CI = confidence interval

Conclusion: FAST3nJC had slightly lesser agreement with 2011 and 2016 FM criteria than FAST3-P and FAST3-F but would appear satisfactory to provide clues to recognize FM in patients with non-rheumatic diseases, although a diagnosis of FM ultimately is made by a physician.

Disclosure: T. Pincus, Helath Services, 7, Medical History Services LLC, 6, 7, 9, Medical history services LLC, 6, 7; **I. Castrejon**, None; **J. Block**, None.

Abstract Number: 0220

A Positive Response to Nonpharmacological Therapies in Patients with Fibromyalgia

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Identifying the factors associated with response to nonpharmacological therapies in patients with fibromyalgia will help personalize treatments and provide information to improve the design and interpretation of future research. We used results from a large comparative effectiveness trial of Tai Chi versus aerobic exercise to investigate baseline characteristics associated with clinical response at 24 weeks in patients with fibromyalgia.

Methods: We analyzed data from a randomized trial which enrolled 226 adults with fibromyalgia as defined by the ACR 1990 and 2010 criteria. Participants were assigned to aerobic exercise (2x/week for 24 weeks) or one of four Tai Chi interventions (1x or 2x/week for 12 or 24 weeks) and followed for 52 weeks. Results from the trial showed that all treatment groups demonstrated improvement in revised fibromyalgia impact questionnaire (FIQR) scores, but the combined Tai Chi groups improved significantly more in FIQR score at 24 weeks than the aerobic exercise group. Although a minimal clinically important difference (MCID) in response has not yet been determined for the FIQR, FIQR scores correlate closely with scores of the original fibromyalgia impact questionnaire (FIQ) ($r=0.88$, $P< 0.001$). Based on the established MCID of the FIQ, we estimated the MCID of the FIQR to be 14% or 8.1 units on a 0-100 scale. We performed a stepwise multivariable analysis to investigate baseline variables associated with positive response (our criteria for entry was univariate $p< 0.10$). Baseline variables included demographics (sex, age, race, education, and whether they live alone) and clinical measurements (BMI, duration of body pain, pain index, symptom severity, FIQR, global assessment, depression, anxiety, self-efficacy, coping skills, sleep quality, 6-minute walk test, physical and mental quality-of-life components of the Short-Form 36, analgesic use, comorbidities, and outcome expectations).

Results: Mean age of the 181 participants with complete data at 24 weeks was 52.3 years, 91.7% were female, average BMI was 30.1 kg/m2, and average duration of body pain was 12.4 years. Mean FIQR at baseline was 55.5. There were 108 participants (60%) who responded to either treatment. When the six variables which were significant ($p< 0.10$) in the univariate analyses were included in the multivariate analysis, only FIQR remained significant (**Table**). Having a higher FIQR score or greater impact of symptoms was significantly associated with clinically meaningful improvement at 24 weeks (**$p = 0.01$**). Response did not significantly differ by treatment.

TABLE 1. FIBROMYALGIA EMERGENCY DEPARTMENT UTILZATION

Age	Total number of visits: N	Percent of visits	Rate of Visits per 100,000 persons	Age (mean)	Total number of admissions to same hospital: N
<17	135	0.82	0.2	13.33	9
18-44	7,475	45.46	6.4	35.1	253
45-64	7,058	42.93	8.4	52.96	365
65-84	1,676	10.19	3.9	71.81	152
85+	98	0.6	1.5	86.93	19
all ages	16,442	100	5.1	46.64	800

TABLE 2: FIBROMYALGIA EMEGENCY UTILIZATION BY GENDER

GENDER	Total number of visits: N	Percent of visits	Rate of Visits per 100,000 persons	Age (mean)	Total number of admissions to same hospital: N	Percentage admissions to same hospital: %
Male	1,020	6.2	0.6	45.21	59	5.80
Female	15,417	93.8	9.4	46.73	742	4.80

Conclusion: Individuals with fibromyalgia who had more severe symptoms seem to experience greater clinical improvement from nonpharmacological interventions such as Tai Chi or aerobic exercise than those who are less impacted by their condition. More studies are warranted to confirm whether other clinical variables may be associated with positive response. These findings will aid in improving the design of future trials for patients with fibromyalgia.

Disclosure: R. Bannuru, None; **M. Park**, None; **L. Price**, None; **C. Wang**, None.

Abstract Number: 0221

Emergency Department Utilization for Fibromyalgia Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia (FMS) is a common pain syndrome affecting millions of people in the USA. It is normally managed in the outpatient setting by rheumatologists, pain physicians, and primary care physicians but

some FMS patients seek care in emergency departments (ED). In this abstract, we describe ED visit utilization for patients with FMS based on billing codes.

Methods: Data were abstracted from the National Inpatient Sample Databases. This database is the largest longitudinal collection of inpatient admission and emergency department data in the USA. It is a nationally representative sample from approximately 1000 hospitals. The numbers in the databases are weighted to optimize both national estimates and longitudinal analysis. The databases were searched for ED visits in 2016 with a listed ICD-10 code for fibromyalgia M79.7 as the principal diagnosis. Total number of FMS ED visits, gender, age, number of hospital admissions, and inpatient charges were recorded.

Results: 16,442 ED visits had an ICD-10 FMS code listed as the principal diagnosis in 2016. This is estimated to be 5.1 ED FMS visits per 100,000 persons. The age breakdown was as follows: < 17 =135 (0.82%), 18-44 =7,474 (45.46%), 45-64 = 7,058 (42.93%), and 65-84 =1,676 (10.19%), and ≥85= 98 (0.6%); see table 1. Gender breakdown of ED FMS visits were as follows 15,417 (93.8%) females and 1,020 (6.2%) males; see table 2. Only a small number of ED visits 800/16,442 (4.9%) resulted in an inpatient admission to the same hospital. A similar percentage of females 4.8% and males were admitted 5.8%. The charges for hospital admission were on average $29,431 and had a median of $25,806. This type of analysis is severely limited by the ED's ability to diagnose FMS and the quality of subsequent coding. These numbers may underestimate ED utilization by FMS patients.

Conclusion: This data gives us valuable information on FMS care in the USA. 16,442 visits to EDs were coded with a principal diagnosis of FMS during the year 2016. Females between the ages 18-64 were the most common to seek ED care for FMS. Patients < 18 years, > 84 years and males were the least likely to visit an ED for FMS. Fortunately only a small fraction of these ED visits led to an inpatient admission to the same hospital. Even though the overall number of ED FMS visits was small, there seems to be an opportunity to improve coordination of outpatient care to avoid unnecessary ED visits.

Disclosure: S. Kambhatla, None; **E. Gauto-Mariotti**, None; **A. MANADAN**, None.

Abstract Number: 0222

Acupuncture for Chronic Musculoskeletal Pain: A Review of Randomized Controlled Trials

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Acupuncture has been widely used for pain relief in adults. Evidence on effects of acupuncture for pediatric chronic musculoskeletal pain is scarce. We have reviewed existing randomized controlled trials, expecting to summarize the high-quality evidence of acupuncture on chronic musculoskeletal pain before advocating it in the pediatric population.

Methods: We performed a comprehensive search in MEDLINE as well as reference lists until June 2019. Selection criteria included: chronic musculoskeletal pain, randomized controlled trials, sample size ≥20.

Table 1: Randomized Controlled Trials Evaluating Effects of Acupuncture in Chronic Musculoskeletal Pain*

Author/Year Country	Mean Age (range)	N	Duration (Week)	Intervention(s) [Blinding]	Control(s)	Indication	Author favors acupuncture
Kim E, 2019, Korea	42	106	4	TEA weekly for 4 sessions	Usual Care	chronic neck pain	Yes
Moura CC, 2018, Brazil	47	110	5	eA weekly for 5 sessions (D)	1. Sham 2. Usual care	chronic pain in spinal column	Yes
Seo BK, 2017, Korea	49	54	3	6 sessions of BVA over 3 wks [D]	Sham	chronic low back pain	Yes
Yeh CH, 2015, US	60 (20-82)	61	4	AP weekly for 4 sessions [D]	Sham	chronic low back pain	Yes
Hinman R, 2014 Australia	64	282	12	1. CA 1-2/ week for 12 wks, <=12 sessions [Tr] 2. Laser once weekly for 12 weeks [Tr]	1. Sham 2. Usual care	chronic knee pain	No, pain reduced at 12 weeks, not at 1 year
Vas J, 2014, Spain	51	265	8	AP once weekly for 8 weeks [D]	Sham	chronic pain in spine	Yes
Glazov G, 2014, Australia	57 (18-75)	144	8	1. LD Laser once weekly for 8 weeks [Tr] 2. HD Laser once weekly for 8 weeks [Tr]	Sham Laser	chronic low back pain	Yes
Ferreira LA, 2013, Brazil	32	40	12	Laser 12 sessions over 3 months [D]	Sham laser	temporomandibular dysfunction	Yes
Cho YJ, 2013, Korea	42	130	6	CA twice weekly for >=6 weeks [D]	Sham	low back pain	Yes
Mavrommatis CI, 2012, Greece	62	120	8	Pharm+ CA biweekly for 8 weeks	1. Pharm+ Sham 2. Pharm	Osteoarthritis of knee	Yes
Ahsin S, 2009, Paskistan	51	78	10 days	EA once daily for 10 days	Sham	osteoarthritis of knee	Yes
Haake M, 2007, Germany	26	1162	5	VA Twice a week for 10 sessions [D]	1. Sham 2. Usual care	chronic low back pain	No Similar to sham
Scharf HP, 2006, Germany	62	1039	6	CA 10 sessions over 6 weeks	1. Sham 2. Usual care	osteoarthritis of knee	No Similar to sham
Witt C, 2005, Germany	64	300	8	CA 12 sessions over 8 weeks	1. Sham 2. Usual care	osteoarthritis of knee	Yes, more effective than sham
Assefi NP, 2005, Afghanistan	46	96	12	CA twice weekly for 12 weeks [D]	1. Unrelated point CA* 2. Sham 3. Simulated+	fibromyalgia	No Similar to sham
Kleinhenz J, 1999, Germany	33-37	52	4	CA 8 sessions over 4 weeks	Sham	rotator cuff tendinitis	Yes Needling important

TEA: thread-embedding acupuncture; eA: ear acupuncture; BVA: bee venom acupuncture; AP: auricular acupressure; CA: traditional acupuncture; pharm: usual pharmacological therapies (etoricoxib in this trial); LD: low dose; HD: high dose; [D]: double blinding; [Tr]: triple blinding *Unrelated: acupuncture at the points unrelated to fibromyalgia; +Simulated: noninsertive simulated

Results: We identified 16 randomized controlled trials with a total of 4039 subjects met the eligibility criteria. All the subjects were age 18 or older, with most of them middle aged. Number of trials included chronic pain in temporomandibular joint (1), neck (1), back or spine (7), knee (5), fibromyalgia (1) and rotator cuff tendinitis (1). Seven trials used traditional Chinese acupuncture, two used auricular acupressure, two used verum or bee venom acupuncture, one used electro-acupuncture, two used laser with acupuncture, and one used thread-embedding acupuncture. Ten of the 16 trials (62.5%) were either double or triple blinded. Mean treatment duration was 6.6 weeks (range from 10 days to 12 weeks). **Table 1** summarizes the trials evaluating the effect of acupuncture on pain and the authors' conclusions whether the acupuncture therapies were favorable. Of the 16 trials, 12 (75%) reported that the acupuncture therapy was effective compared to a variety of control groups; nine of those trials reported better pain reduction of acpunture s than sham/placebo groups. Among those 10 trials with double or triple blinded design, 7 out of 10 trials (70%) suggested acupuncture favorable. However, 4(25%) suggested that acupuncture was not more effective than the controlled/sham groups. One trial did show a pain reduction in acupuncture groups at 12 weeks but effects did not sustain at 1-year follow up.

Conclusion: Our review showed a mixed result in the effect of acupuncture in pain relief for chronic musculoskeletal pain. The majority of the trials suggested that acupuncture maybe effective beyond the placebo effect. To date, there are no high-quality trials in pediatric population. Rigorous and well-controlled randomized trials in pediatric population are warranted.

Disclosure: Y. Zhang, None; **C. Wang**, None.

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Abstract Number: 0223

Correlation Between Heart Rate Variability Parameters and Circulating Neuropeptides in Fibromyalgia

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Heart rate variability analyses in fibromyalgia patients have shown changes consistent with sympathetic hyperactivity that theoretically could lead to chronic pain. There is little investigation on dysautonomia associated circulating neuropeptides in fibromyalgia. There are no studies correlating serum neuropeptide levels with heart rate variability parameters. The purpose of this study was to measure dysautonomia-associated serum neuropeptides levels in women with fibromyalgia and in age, sex, body mass index comparable healthy controls. Additionally to correlate neuropeptide levels with heart rate variability parameters and disease severity.

Methods: We studied 23 women with fibromyalgia without comorbid conditions and 15 matched healthy controls. At the time of the study, patients were free from medications that could affect autonomic-related neuropeptide levels. Time domain parameters were extracted from 24 hours heart rate variability recording. All participants filled out the Revised Fibromyalgia Impact Questionnaire (FIQR), Widespread Pain Index (WPI), Symptom Severity Scale (SSS), Polysymptomatic Distress Scale (PDS) and the Small Fiber Neuropathy Symptoms Survey (SFNSS). The following 7 neuropeptides levels were measured using the 7-Plex Human Neuropeptide Magnetic KitMilliplex MAP: aMSH, beta-endorphin, cortisol, neurotensin, orexin, oxytocin and substance P. The protocol was approved by the institution review board and required a written informed consent from participants. Kolmorogov-Smirnov test was used for normality analysis, Student's T test or Mann Whitney U test for comparisons and Pearson or Spearmen test for correlations. SPSS version 23.0 was used for the analyses.

Results: Beta-endorphin (669.24 ± 186.28 vs 541.71 ± 146.26pg/ml, p=0.028) and neurotensin (156.23 ± 58.15 vs 116.64 ± 47.93pg/ml, p=0.016) levels were higher in fibromyalgia patients. Both neuropeptides levels had a negative correlation with heart rate RR interval standard deviation (Rho -0.5 and Rho -0.6, p< 0.05) and with FIQR "tenderness to touch" (Rho -0.4 and Rho -0.4, p< 0.05).

Conclusion: Heart rate variability parameters suggesting sympathetic hyperactivity correlate with circulating beta-endorphin and neurotensin levels in fibromyalgia patients. Future research will define the possible clinical implications of this novel finding.

Disclosure: L. Martínez-Martínez, None; **C. Lerma Gonzalez**, None; **M. Navarro Gonzalez**, None; **O. Infante Vázquez**, None; **F. López Trejo**, None; **E. Aranda Cano**, None; **A. Salgado Aguayo**, None; **D. Paz Gómez**, None; **M. Barrera Villalpando**, None; **L. Silveira**, None; **V. Higuera Ortiz**, None; **A. Vargas Guerrero**, None; **M. Martínez-Lavín**, None.

Abstract Number: 0224

A Functional Exercise Program Improves Pain and Health Related Quality of Life in Patients with Fibromyalgia: A Randomized Controllel Trial

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia (FM) is a syndrome characterized mainly by chronic generalized pain that affects the physical fitness and functional capacity of patients. There is increasing evidence of the benefits of physical exercise in improving FM symptoms, making these interventions part of therapeutic arsenal.

Methods: It is a controlled and randomized study, with blind evaluator. A total of 82 female patients with FM were included, with age between 18 and 65 years, randomized into two groups, intervention and control. The intervention group (FEG) performed functional exercise training for 45 minutes twice a week for 14 weeks. The control group (SEG) performed stretching exercises with the same duration and frequency. Evaluation instruments were: VAS - Visual Analogue Scale for pain assessment; FIQ- Fibromyalgia Impact Questionnaire, for assessing health-related quality of life; Time-up and go test for functional performance evaluation; 1RM, for evaluation of muscle strength; Bank of Welss, for the assessment of flexibility; Berg Balance Scale, to evaluate balance; and SF-36 to evaluate general quality of life. Also, the amount of analgesics used during the intervention period was assessed.

Results: 41 patients were randomized to the FEG and 41 patients to the SEG. After intervention, the FEG presented a reduction in pain and an improvement in the quality of life related to the disease, which was statistically significant compared to SEG. Regarding general quality of life, functional capacity, muscle strength, flexibility and balance, there was no difference between the groups.

Conclusion: Functional exercise training proved to be effective in reducing pain and improving the health-related quality of life of patients with FM when compared to stretching exercises.

Disclosure: G. Fernandes, None; **F. Jennings**, None; **M. Nery**, None; **R. Santos**, None; **J. Natour**, None.

Abstract Number: 0225

Evaluating Fibromyalgia Symptoms in Transgender Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia Syndrome (FMS), characterized by widespread pain and fatigue, is known to be more prevalent in women, and has frequently been associated with stress is various models. In the current study we have evaluated the prevalence of fibromyalgia symptoms among Transgender men and women, in attempt to correlate such symptoms with gender dysphoria and gender transformation due to hormonal therapy.

Methods: Participants were recruited among patients followed at a specialized transgender clinic at the endocrinology institute of a large tertiary medical center. Participants were at various stages of the process of gender reassignment, including hormonal treatment.

After providing informed consent, participants were asked to answer the Widespread Pain Index (WPI) and the Symptom Severity Scale (SSS), in order to document the presence of symptoms related to the fibromyalgia spectrum and in order to determine the prevalence of fibromyalgia, according to the 2010-2011 diagnostic criteria.

Results: Thirty-six transgender men [Female-to-male (FTM)] and 29 transgender women [Male-to-female (MTF)] answered the questionnaires. Eight individuals form the FTM group met fibromyalgia criteria (22.2%). Only 1 individual from the MTF group met the criteria for fibromyalgia (3.4%). Among FTM individuals, 13 were evaluated both before and after initiating androgen-based hormonal treatment, in order to evaluate the effect of such treatment on symptoms.

Out of 4 individuals fulfilling fibromyalgia criteria before receiving hormonal therapy, 3 remained unchanged when re-evaluated on treatment, while 1 reported alleviation of symptoms. One individual developed fibromyalgia symptoms after 1 year of hormone treatment.

Conclusion: In this preliminary study, Fibromyalgia symptoms were found to be highly prevalent among Transgender men (FTM), at a rate significantly higher than reported in the general population. Fibromyalgia symptoms appeared to be less frequent among Transgender women (MTF).

These results are relevant for professionals treating transgender individuals in the medical or psychological field. Further research into the effects of gender and of hormone treatment on fibromyalgia and chronic pain are indicated.

Disclosure: D. Levit, None; **J. Ablin**, None; **V. Aloush**, None; **I. Yaish**, None.

Abstract Number: 0226

Hypersensitivity Beyond Pain: Hyperacusis and Hyperalgesia of Patients with Fibromyalgia

Roland Staud,[1] **Gabriella Tom**,[1] Melyssa Godfrey,[1] and Michael Robinson[1], [1]University of Florida, Gainesville, FL

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
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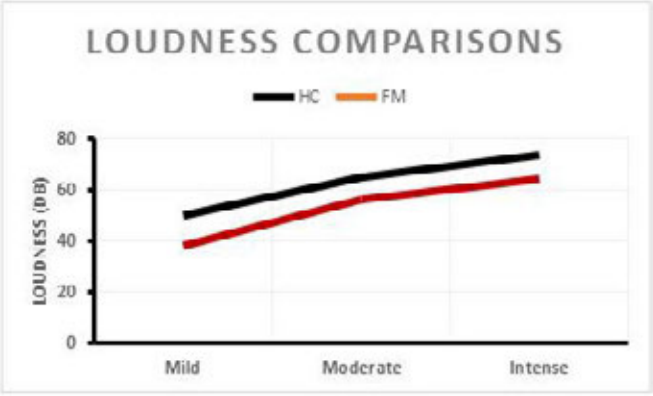
Background/Purpose: Fibromyalgia (FM) is a condition in which patients are afflicted with unexplained chronic musculoskeletal pain, insomnia and fatigue. The underlying mechanisms of this disorder is only partially understood. FM patients frequently report not only hypersensitivities to noxious but also to non-noxious sensations like light touch, sounds, and smells encountered in everyday life. Despite anecdotal reports of unusual sensory sensitivities of FM patients, there has been little or no empirical validation of these complaints in current research. The presence of such sensitivities may contribute to difficulties in function by creating an additional source of stress, anxiety, and fatigue

Hypothesis: Compared to age-sex matched healthy controls (HC), FM patients are not only hypersensitive to A) noxious heat and pressure but also to B) auditory stimuli across 3 different sound intensity levels

Methods: FM subjects fulfilled the 1990 FM Criteria and were not taking pain or psychotropic medications. HC had to be without pain and without any medications. All subjects underwent heat and pressure sensory testing at the hand using sensitivity adjusted stimuli that elicited pain rating of 5 ± 1 VAS (0-10). The subjects underwent auditory threshold testing to ensure normal hearing at frequencies between 1,000 and 4,000 Hz using a GSI 61 Clinical Audiometer. Subsequently, they received auditory stimuli of mixed frequencies at intensities that resulted in mild (12.5 dB, moderate 32.5 dB, and intense (67.5 dB) loudness. All tests were performed in triplicates.

Results: We enrolled 26 HC and 20 FM subjects (all females). Their ages were 52.3 years and 47.5 years, respectively. Avg pain of FM subjects was 4.6 VAS (0-10). Independent t-test demonstrated significantly lower temperature and pressure to achieve 5 VAS for FM subjects than HC (all $p < .001$). A mixed model ANOVA showed that FM subject required significantly less sound intensity (dB) to rate similar loudness compared to HC ($p < .001$). Pearson's product moment correlations demonstrated significant associations between auditory and heat/pressure sensitivity ($p < .05$)

Conclusion: Patients with FM are more sensitive to sensory stimuli in daily life than patients who do not experience chronic pain. Their hypersensitivity, however, seems to extend beyond heat and pressure to auditory and possibly to taste/smell and visual sensations. Our findings suggest that FM patients not only demonstrate hypersensitivity to painful but also auditory stimuli. Furthermore, auditory hypersensitivity predicted heat/pressure pain hypersensitivity. Besides genetic predisposition other factor could explain our findings, specifically the "Cognitive Activation Theory of Stress (CATS)", a theoretical model tying together chronic pain and hyperacusis. CATS postulates that sustained



arousal and lack of appropriate arousal resolution (i.e., restful sleep) can result in dysfunction of the central nervous system. In particular, chronic arousal and lack of restorative sleep, can lead to increased sensitivity to peripheral neural input, resulting in chronic pain and hyperacusis

Sound intensity ratings of FM and HC participants who received auditory stimuli of mixed frequencies that resulted in mild, moderate, and intense loudness. All tests were done in triplicates

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Disclosure: R. Staud, None; **G. Tom**, None; **M. Godfrey**, None; **M. Robinson**, None.

Abstract Number: 0227

Metabolomic and Symptom Comparison in Women With/without Fibromyalgia: A Pilot Study

Victoria Menzies,[1] Angela Starkweather,[2] Yingwei Yao,[3] Timothy Garrett,[4] Debra Lynch-Kelly,[3] Param Patel,[2] and Debra E. Lyon[3], [1]Virginia Commonwealth University School of Nursing, Richmond, VA, [2]University of Connecticut School of Nursing, Storrs, CT, [3]College of Nursing, University of Florida, Gainesville, FL, [4]Southeast Center for Integrated Metabolomics, University of Florida, Gainesville, FL

SESSION INFORMATION
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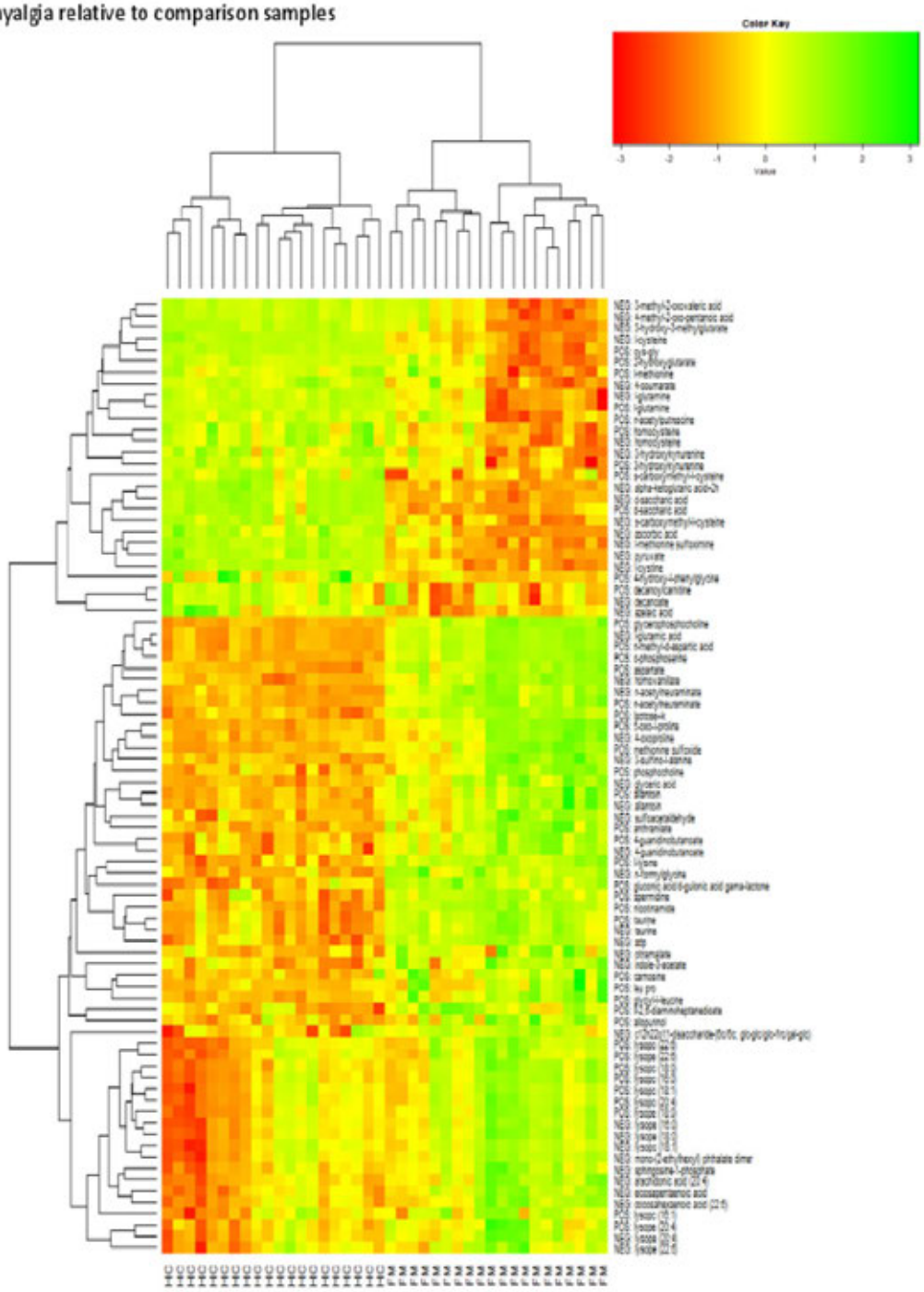
Background/Purpose: The biological perturbations associated with fibromyalgia (FM) remain unclear. The recognition of objective measures to confirm FM diagnosis have not been identified. The obscurity regarding the pathogenesis of FM underscores the pressing need to enhance understanding of the biological mechanisms that may distinguish patients with FM from individuals without FM. The purpose of this pilot study was to examine levels of global metabolites and relationships among metabolites, symptoms of pain, fatigue and depression in women with FM (*n*=20) and without FM (*n*=20).

Methods: Using a cross-sectional design, we analyzed banked plasma specimens and symptom data from two FM studies and a newly recruited age-matched comparison group. Global metabolomics analysis was performed using state-of-the-art high resolution mass spectrometry coupled with ultra-high performance liquid chromatography. SIMCA-Q software, unsupervised principal component analysis (PCA) and supervised orthogonal partial least-squares discriminant analysis (OPLS-DA) were used to investigate differential metabolite concentrations between groups (fold change; FC >2 or < 0.5). Variable Importance in Projection (VIP) was calculated for each metabolite to provide a quantitative estimation of the discriminatory power of each individual metabolite to classify FM. Means and standard deviations were computed for pain, fatigue and depression scores and metabolite concentrations. Logistic regression analysis was used to compare differences among metabolites and symptoms of pain, fatigue and depression between groups. Pearson correlation coefficients were assessed between significantly differentiated metabolites and symptom severity scores.

Results: Of 1462 significantly differentiated metabolites or unknown compounds between women with and without FM, there were 48 with an FC >2 and VIP >1 and 23 with an FC< 0.5 and VIP >1 (Figure 1). These differential metabolites correctly classified women with FM from women without FM with 100% accuracy (Figure 2). Of the significantly differentiated metabolites between groups, 15 metabolites with FC >2 and 7 metabolites with FC< 0.5 had moderately strong association (r=0.51-0.63) with depressive symptoms in women with FM (Table 1). The metabolite, anthranilate, is associated with the tryptophan/kynurenine pathway, which, when dysregulated is related to depression, a

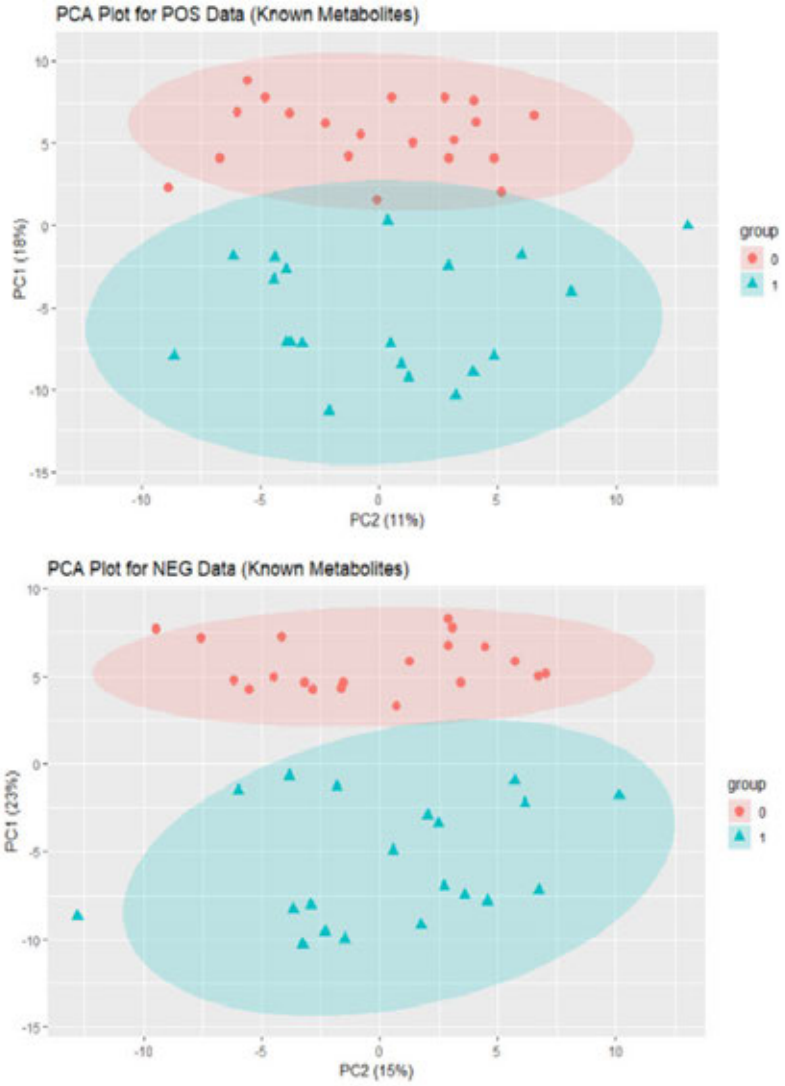
Figure 1: Statistically significant differential metabolites with FC>2.0 or FC<0.5 in women with fibromyalgia relative to comparison samples



symptom with a prevalence up to 80% in persons with FM. Additional metabolites significantly differentiated between women with FM compared to women without FM were correlated with symptom severity of fatigue (r=0.64-0.86) and pain (r=0.63-0.83), and pain interference (r=0.63-0.86).

Conclusion: The preliminary data presented suggests that metabolomic profiles can be used to classify women with and without FM, with specific metabolite concentrations contributing to symptom severity in women with FM. Future

Figure 2. Principal Component Analysis (PCA) Plot for Positive and Negative Ion Mode Data (Known Metabolites)



Note: Group 0 = Women without Fibromyalgia

Group 1 = Women with Fibromyalgia

Table 1: Significant correlations among metabolites and symptoms of depression, pain severity, pain interference and fatigue in Fibromyalgia**

METABOLITE FC>2	Depression (CES-D)	Pain severity (BPI-S)	Pain Interference (BPI-I)	Fatigue (BFI)
Energy Metabolism				
lactose+k	0.58*	0.71*	0.79*	0.80*
nicotinamide	0.59*	0.72*	0.77*	0.79*
Amino Acid Metabolism				
3 sulfino-l-alanine	0.51*	0.69*	0.68*	0.64*
5-oxoproline	0.55*	0.83*	0.79*	0.74*
anthranilate	0.52*	0.70*	0.66*	0.65*
aspartate	0.59*	0.79*	0.83*	0.81*
gluconic acid	0.58*	0.72*	0.78*	0.79*
glycerophosphocholine	0.53*	0.80*	0.82*	0.79*
homovanillate	0.52*	0.78*	0.77*	0.73*
l-glutamic acid	0.60*	0.79*	0.82*	0.82*
l-lysine	0.62*	0.75*	0.80*	0.81*
n-acetylneuraminate	0.63*	0.81*	0.86*	0.86*
n-formylglycine	0.59*	0.65*	0.74*	0.76*
n-methyl-d-aspartic acid	0.59*	0.78*	0.82*	0.82*
o-phosphoserine	0.58*	0.80*	0.82*	0.81*
METABOLITE (FC<0.5)	**Depression (CES-D)**	**Pain severity (BPI-S)**	**Pain Interference (BPI-I)**	**Fatigue (BFI)**
Energy Metabolism				
alpha-ketoglutaric acid	-0.60*	-0.69*	-0.76*	-0.82*
pyruvate	-0.62*	-0.76*	-0.81*	-0.83*
Amino Acid Metabolism				
4-coumarate	-0.56*	-0.79*	-0.69*	-0.64*
l-cystine	-0.56*	-0.72*	-0.71*	-0.73*
Unclassified Metabolism				
ascorbic acid	-0.54*	-0.73*	-0.63*	-0.72*
d-saccharic acid	-0.56*	-0.64*	-0.72*	-0.78*
l-methionine sulfoximine	-0.63*	-0.75*	-0.75*	-0.75*

Note: CES-D=Center for Epidemiological Studies-Depression; BPI-S=Brief Pain Inventory-Severity; BPI-I=Brief Pain Inventory-Interference; BFI=Brief Fatigue Inventory

*adjusted $p<0.01$; **Correlations between 2 or less symptoms not shown

work will confirm these findings in a large, comparative cohort, targeting metabolites and symptomology and examine if a nonpharmacologic intervention can affect change in symptom severity, interference, and identified metabolite/symptom relationships.

Disclosure: V. Menzies, None; **A. Starkweather**, None; **Y. Yao**, None; **T. Garrett**, None; **D. Lynch-Kelly**, None; **P. Patel**, None; **D. Lyon**, None.

Abstract Number: 0228

Good Pain, Bad Pain: Illness Perception and Physicians Attitude Towards Rheumatoid Arthritis and Fibromyalgia Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
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Background/Purpose: Rheumatoid arthritis and fibromyalgia are common diagnoses encountered in rheumatology practice. While rheumatoid arthritis is perceived as a valid medical condition and patients receive appropriate consideration and treatment, patients with fibromyalgia do not always get the same recognition for their painful condition. The aim of this study was to examine the physician's illness perceptions of these two rheumatologic disorders, and evaluate how they correlate with their frustration or resistance to admit such patients. We also aimed to check if factors such as physician's empathy and burnout influence illness perceptions and doctor- patient relationship.

Methods: Fifty-two rheumatologists attending one of the two rheumatologic national conferences during the study period were enrolled in the study. Demographic data was registered. Measures collected included the Brief Illness Perception Questionnaire (BIPQ) and the Difficult Doctor- Patient Relation Questionnaire (DDPRQ-10). Both of them were recorded twice, addressing fibromyalgia (FM) and rheumatoid arthritis (RA). Empathy and burnout were assessed by the Jefferson scale of physician empathy (JSPE) and the Shirom–Melamed Vigor Measure (SMVM)/ Shirom-Melamed Burnout Measure (SMBM).

Results: Of 52 physicians included in the study (58% men, mean age 50, mean years of practice 15), 56% were willing to accept fibromyalgia patients whereas 98% will accept rheumatoid arthritis patients. Fibromyalgia was considered a more severe disease than rheumatoid arthritis (FM- BIPQ mean score 58.6, SD 5.5 versus RA-BIPQ mean 49.7 SD 6.5, $p< 0.00$) especially in terms of consequences (beliefs about illness impact on physical, psychological and social functioning), treatment control (belief in cure through treatment), understanding and emotional response generated by the disease. Doctor-patient relationship was perceived more difficult with fibromyalgia patients compared to RA patients (FM-DDPRQ mean score 36.9, SD9.2 versus RA-DDPRQ mean 16.6, SD 7.1, $p< 0.00$). Difficult doctor-patient relationship with FM patients was significantly correlated to the lack of personal patient control over the disease ($p=0.03$), the impact of patient's emotional response ($p=0.01$), and the burden of symptoms perceived as related to fibromyalgia ($p=0.021$). Resistance to accept FM patients was not correlated with illness perception but significantly correlated with higher scores of DDPRQ ($p=0.024$), especially with feeling discomfort towards and during a meeting with a patient with fibromyalgia. No correlation was found between empathy, burnout, years of practice and illness perceptions or willingness to accept fibromyalgia patients.

Conclusion: Fibromyalgia patients were perceived as more difficult than RA patients, with a large burden of symptoms and emotional response and a lack of control on their disease. A high proportion of physicians were reluctant to accept them because they feel emotional/psychological difficulties meeting and coping with these patients. Improving illness understanding and providing coping skills to rheumatologists may improve doctors-patients relationships and outcomes.

Disclosure: V. Aloush, None; **D. Niv**, None; **J. Ablin**, None; **I. Yaish**, None; **O. Elkayam**, None; **O. Elkana**, None.

Abstract Number: 0229

Is Fibromyalgia Associated with Structural or Functional Abnormalities in Skeletal Muscle?

Carlos Pineda,[1] Héctor García,[2] Gabriela Pineda,[2] Angélica Peña,[3] Laura Aline Martínez-Martínez,[4] Melisa Valdivieso-Ruiz,[2] Jaime Mendoza,[2] Luis Rodríguez,[2] Mariana Moreno,[5] Jessica Gutiérrez,[2] Araceli Bernal-González,[2] Marwin Gutierrez,[1] and Manuel Martínez-Lavín[6], [1]Division of Musculoskeletal and Rheumatic Diseases, Instituto Nacional de Rehabilitación "Luis Guillermo Ibarra Ibarra", Mexico, Mexico, Mexico, [2]Instituto Nacional de Rehabilitación Luis Guillermo Ibarra Ibarra, Mexico City, Mexico, [3]Hospital General Regional no. 1 IMSS, Querétaro, Mexico, [4]Departamento de Reumatologia del Instituto Nacional de Cardiologia Ignacio Chavez, Mexico City, Mexico, [5]Hospital General Fernando Quiroz ISSSTE, Mexico City, Mexico, [6]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia (FM) is a chronic nonarticular pain syndrome of unknown etiology characterized by diffuse muscular pain, fatigue and mood disturbances. Previous studies indicated the absence of skeletal muscle degeneration, regeneration or inflammation. Altered muscle fiber size distribution and decreased capillary density were the only abnormalities reported.

From the clinical point of view some FM symptoms (fatigue, pain, myalgias, trigger points, and stiffness) suggest involvement of the skeletal muscle.

The objective of this study is to determine if there are structural and functional abnormalities in the skeletal muscle in patients with primary FM assessed through a non-invasive multi-modality approach.

Methods: Female patients older than 18 years with primary FM diagnosis (fulfilling 2016 revision to the 2010/2011 ACR criteria), and a group of healthy controls matched by age and gender. Skeletal muscle morpho-structure and function were assessed by the following tests/evaluations: body mass index (BMI), total fat mass and total muscle mass calculated by direct segmental multi-frequency bioelectrical impedance analysis. Cross-sectional measurements of rectus femoris muscle area and tissue echogenicity evaluated by ultrasound and post-processing pixel analysis. Maximum handgrip strength by digital dynamometry, gait speed by 6-meter time walk test, and Fibromyalgia Health Assessment Questionnaire (FHAQ).

Results: Ninety-four FM patients and 140 healthy controls were included, mean age was 51.8 years +/- 10.8 vs 50.2 +/- 11.3, respectively (p = 0.27). FM patients compared with controls had similar BMI (27.9 kg/m^2 +/- 4.9 vs 26.8 +/- 4.5, p = 0.14), higher total body fat mass (27.8 kg +/- 9.2 vs 25.1 +/- 7.6, p = 0.04); the rectus femoris muscle area was also higher for FM patients (44.6 cm^2 +/- 11.4 vs 41.7 +/- 13.9, p = 0.05); regarding ultrasound tissue echogenicity, FM patients demonstrated higher mean brightness in rectus femoris (157.2 pixels +/- 19.4 vs 149.9 +/- 22.4, p = 0.01); lesser handgrip strength (22.0 kg +/- 6.6 vs 26.2 +/- 5.4 p = 0.0001); slower gait speed (1.14 m/s +/- 0.2 vs 1.3 +/- 0.2 p = 0.0001); and major impairment in daily activities by FHAQ (47% vs 2.90% p = 0.0001).

Conclusion: This non-invasive multimodal evaluation discloses the presence of structural and functional skeletal muscle abnormalities in women with FM. These changes can be attributed to sedentary and hypoactive lifestyle with consequent higher total body fat mass, muscular fat infiltration, and functional impairment of activities of daily living.

Alternatively, these abnormalities may also be an expression of a small-fiber polyneuropathy (myoneurovascular dysregulation). Further studies are required to elucidate its underlying pathological process.

Disclosure: C. Pineda, None; **H. García**, None; **G. Pineda**, None; **A. Peña**, None; **L. Martínez-Martínez**, None; **M. Valdivieso-Ruiz**, None; **J. Mendoza**, None; **L. Rodríguez**, None; **M. Moreno**, None; **J. Gutiérrez**, None; **A. Bernal-González**, None; **M. Gutierrez**, None; **M. Martínez-Lavín**, None.

Abstract Number: 0230

Patients with Fibromyalgia Associated with Rheumatoid Arthritis and Patients with Primary Fibromyalgia Differ in Depression, Anxiety, Stress-related Disorders and Events: A Cross-sectional Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: The aim was to evaluate the differences in depression-, anxiety- and stress-related events and trauma between patients with rheumatoid arthritis + Fibromyalgia [AR+FM] (SFM) and those with primary FM (PFM).

Methods: Study design: observational cross- sectional. Patients were consecutively recruited. The inclusion criteria were an age of 18-70 years; a diagnosis of RA according to the 2010 ACR criteria and FM according to the 1990 and 2016 ACR criteria. Lifetime diagnoses of major depression disorder (MDD), panic disorder (PD) and post-traumatic stress disorder (PTSD), three of the most frequently described psychiatric disorders among FM patients were made by a senior psychiatrist using the Structured Clinical Interview for DSM-5 Axis I Disorders-Clinician Version and a single, cross-sectional assessment. Depressive symptoms were measured using the Zung Self-rating Depression Scale (ZSDS). Childhood trauma was measured using the short form of the Childhood Trauma Questionnaire (CTQ). Stressful events were assessed using the validated Italian version of Paykel's Interview for Recent Life Events, a semi-structured interview investigating 64 life events. Pain was assessed using a VAS. The Italian version of the FIQ was used. Two-sided Fisher or T-test and multivariable logistic regression were performed.

Results: Seventy-seven patients were originally screened, but six were excluded. The final analysis therefore involved 70 patients, all Caucasians: 30 with PFM and 40 with AR+FM. All patients with PFM and 38 (95%) of the 40 with AR+FM were treated for FM symptoms (antidepressants, pregabalin). The rates of lifetime MDD and PD were significantly higher in the PFM patients vs RA+FM (76.7% vs 40%, p =0.003), whereas there was no between-group difference in the rates of PTSD (50% in PFM vs 15% in SFM, p.003). The PFM patients reported significantly higher levels of physical (p=0.020) and sexual abuse (p=0.011) and physical neglect (p< 0.001), whereas there was no between-group difference in the levels of emotional abuse (p=0.912) and neglect (p=0.542); consistently, the proportion of sexually abused (p=0.005) or phsically neglected patients was also higher in the PFM group (p=0.023). The rates of emotional neglect were high in both groups, without any significant difference between them. The vast ma-

jority of AR+FM patients (90%) said that only event occurring in the year preceding the onset of FM was RA, whereas the PFM patients mainly reported non-physical events (36%, particularly the ending of a relationship, or working or financial problems) or no event at all (40%), ($p< 0.001$). Multivariable logistic regression used to identify the factors predicting association of PFM/AR+FM status, showed and association with lifetime major depression, life events preceding the development of FM, and BMI ($p < 0.05$ for all).

Conclusion: The study indicate that psychiatric co-morbidities and predisposing and precipitating environmental factors are different in patients with PFM from those in AR+FM patients, thus suggesting that the putative common pathogenetic condition of sensitisation may develop through different pathways.

Disclosure: F. Atzeni, None; **M. Cirillo**, None; **I. Masala**, None; **P. Sarzi-Puttini**, None; **A. Alciati**, None.

Abstract Number: 0231

Duloxetine for Chronic Pain Management in a Tertiary Care Rheumatology Practice: How Patients Are Doing in the Real World

Rupal Shastri,[1] Sonali Khandelwal,[2] and Najia Shakoor[2], [1]Rush University, Chicago, IL, [2]Rush University Medical Center, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic pain is a complicated issue that has received a significant amount of attention. In particular, studies suggesting the role of central sensitization in chronic pain conditions, have supported the utility of centrally acting agents in the management of these conditions. Duloxetine, a selective serotonin and norepinephrine reuptake inhibitor, has central nervous system activity and has been has been approved for these syndromes. It was initially approved in 2004 for treatment of depression and neuropathic pain. In 2008, it use extended to the management of FMS and in 2010 to the treatment of chronic musculoskeletal pain, including OA. The utility of this agent in the "real world" is not clear. Here, we evaluated the trends of duloxetine use in a tertiary care rheumatology practice for chronic pain conditions, with emphasis on length of therapy and improvement in patient-reported outcomes.

Methods: IRB approval was obtained. A single center retrospective study was performed of patients with ICD-10 diagnoses of OA, chronic pain syndromes and FMS who were prescribed duloxetine between 2010 and 2019. Age, sex, ethnicity, dose of medication, length of use and multidimensional health assessment questionnaire (MDHAQ) scores pre and post treatment were recorded. Individuals with any diagnosis of mood disorder were excluded. Chi squared and paired t tests were used to analyze differences in prescribing patterns and improvement in patient reported outcomes.

Results: Of 1700 charts reviewed, 250 met inclusion criteria. Of the patients being prescribed duloxetine, 149 had a primary diagnosis of FMS, 71 had OA and 28 had chronic pain. Results are summarized in the Tables. MDHAQ scores significantly improved with duloxetine use in FMS and OA groups, however there was no significant improvement in scores in the chronic pain group . In addition, there was significant improvement of MDHAQ scores in Caucasian and African American patients prescribed duloxetine, while this improvement was not observed in Hispanics patients. Duloxetine 30 mg daily was the most frequently prescribed dose in each condition. In total, over 54% of the patients continued therapy for over 6 months, with a mean duration of therapy in those that continued as high as 26 months in

Table 1.

Disease	Percent of total patients	Sex M/F	Mean Age (Years)	Continued therapy for 6 months or longer	Mean duration of therapy (Months)	Pretreatment MDHAQ	Posttreatment MDHAQ	P-value for change in MDHAQ
FMS	60%	7/142	50± 14	54%	18.0±18.7	17.9±6.4	16.0±6.6	0.008*
OA	29%	6/66	63±10	56%	26.0±27.8	17.8±5.7	15.4±6.4	0.003*
Chronic pain	11%	6/22	57±11	44%	19.0±23.2	18.0±4.6	16.8±6	0.326

Table 2.

Ethnicity	FMS	OA	Chronic Pain	Pretreatment MDHAQ	Posttreatment MDHAQ	P-value for change in MDHAQ
Caucasian	44%	32%	50%	15.0±5.6	13.1±6.2	0.004*
African American/Black	28%	40%	29%	21.0±4.9	18.0±5.7	0.005*
Hispanic	24%	25%	18%	19.0±5.9	18.4±6.1	0.391

the OA group. In addition, our data suggest that physicians in practice for over 15 years prescribed more duloxetine compared to those in practice less than 15 years ($p< 0.03$).

Conclusion: The results of the current study are supportive of previous clinical trial studies in that patient reported outcomes improve significantly during the period of use of duloxetine. Although this improvement cannot directly be attributed to medication use alone, its potential efficacy is also supported by the continued use of the medication for an extended period of time. Chronic pain syndrome patients did not demonstrate significant improvements, however this may be limited by the small number of patients. Interestingly, improvements varied by ethnicity, and these differences could be evaluated in future studies. Finally, considering differences in prescribing based on years in practice, education for younger professionals on the potential utility of this drug may be warranted.

Disclosure: R. Shastri, None; **S. Khandelwal**, None; **N. Shakoor**, None.

Abstract Number: 0232

Hand Digital Thermography Findings in Patients with Primary Fibromyalgia

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster

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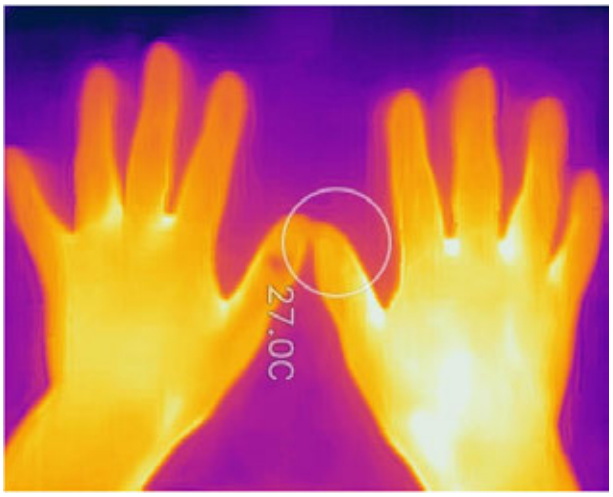

Hands thermography in primary fibromyalgia

Background/Purpose: Fibromyalgia is a diffuse chronic painful disease, with prevalence of 0.5% -12%, with a female:male ratio 3:10. Because of unexplained symptoms, particularly as disability pain, the primary differential diagnosis is inflammatory arthritis. Few studies have evaluated whether digital thermography can differentiate primary from secondary fibromyalgia with arthritis.

Our primary objective was identification of joint inflammation in patients with primary fibromyalgia; secondary objective, to correlate ultrasound findings hand with digital thermography, besides joint exploration of hands.

Methods: We selected patients with primary FM (Criteria ACR 2016) from January-April 2019. We did a clinical, termographic and ultrasound evaluation of the carpal, metacarpophalangeal and proximal interphalangeal joints. The clinical evaluation was made by 2 blinded rheumatologists. For the thermographic evaluation we used a digital photograph of hands at 50 cm perpendicular distance with a thermal camera Flir-One -Pro; for the analysis, the software included in the thermography equipment was used; through the thermal delta of the average temperature of the hand with respect to the joints (we considered an inflamed joint with an increase of > 0.5 ° C). Finally, we did an articular ultrasound of 22 hand joints.

Results: we included 22 patients with primary FM, of whom 3 showed inflammatory changes by thermography, the median age of these patients was 54 years (IQR 7.5) and median of BMI 23.1 (IQR 1.9). All patients had negative rheumatoid factor and anti-CCP, median erythrosedimentation rate 34 (IQR 15). With ultrasound 2 patients had joint effusion, 3 synovitis and 11 synovial hypertrophy, only 1 patient had the three features. We did not find any correlation between thermography and ultrasound ($p = 0.9$). Articular examination showed poor concordance between inflammed and painful joints (Kappa < 0.4); although with certain correlation in left (kappa 0.42) and right carpal inflammation (kappa 0.49), as well as left (kappa 0.43) and right carpal pain (kappa 0.7).

Conclusion: In patients with primary fibromyalgia without joint pain, the use of tools such as digital thermography does not provide information for ruling out inflammatory arthropathy.

Disclosure: D. Garcia, None; **D. Herrera-Van Oostdam**, None; **R. moreno Valdés**, None; **E. Santillan Guerrero**, None; **C. Abud-Mendoza**, Pfizer, 5, 8, Eli Lilly, 5, 8, Takeda, 5, 8.

Abstract Number: 0233

Intensive CBT Is Effective in the Treatment of Significant Functional Impairment and Psychological Distress Found in Fibromyalgia: But Can We Improve Depressive Symptoms?

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
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Background/Purpose: The study was designed to evaluate the effectiveness and durability of an intensive cognitive behavioral intervention on functioning and depression in patients with Fibromyalgia (FM). Despite significant statistical improvements observed in functional status and level of depression, high rates of depression remained at follow-up. Analyses were designed to determine why depression rates remained high in order to identify more effective interventions

Methods: The patients included in the study were 141 adults with a diagnosis of FM who participated in an intensive two day treatment program for FM provided at a tertiary medical center. The Center for Epidemiologic Studies of Depression Scale (CES-D) and the FM Impact Questionnaire-Revised (FIQR) were completed at the time of admission to the 2-day structured FM Treatment Program and at 3 and 6 month follow-up. The FM Treatment Program is a cognitive behavioral treatment program that focuses upon strategies to decrease central sensitization including management tools to decrease pain, fatigue, assist with sleep disturbance and improve cognitive issues associated with FM. Strategies of behavioral activation, exercise, sleep hygiene and cognitive strategies are integral aspects of the treatment program.

Results: Table 1 contains demographic information for the sample. As seen, patients were majority (85.1%) female and the average age was 52.26 years. Table 2 shows statistically significant improvements ($p < 0.001$) in depression levels (CES-D) and functional status (FIQR) at both 3 and 6 month follow up. 79.4% of patients met the clinical threshold for depression at intake. Following intervention, 52.5% and 53.9% of patients met the clinical threshold for depression at 3 and 6 month follow-up, respectively. As in Table 2, there was a significant effect of treatment on each of the CES-D subscales (Negative Affect: $p=.002$, Positive Affect: $p=.002$, Somatic Symptoms: $p < .0001$, Interpersonal Distress: $p=.019$). Of 20 CES-D items, 14 were significantly improved by treatment ($p < .05$). 6 items did not change significantly after treatment: 'I felt depressed,' 'I felt hopeful about the future,' 'I felt lonely,' 'People were unfriendly,' 'I

Table 1: Demographics

Variable	Categorical: n (%) Continuous: average (standard deviation)
Age	52.26 (14.00)
Gender (Female)	120 (85.1%)
Duration of symptoms (months)	133.86 (138.91)
Time since FM was diagnosed (months)	70.41 (101.00)
FDA Approved Meds at time of admission	35 (24.8%)
Opioids at time of admission	42 (29.8%)

Table 2: Repeated Measures ANOVA

Item	P-value*
CES-D	**<.0001**
FIQR	**<.0001**
Met clinical threshold for depression	**<.0001**
Met severe threshold for functional impairment	**<.0001**
CES-D Subscales	
Negative Affect	**.002**
Positive Affect	**.002**
Somatic Symptoms	**<.0001**
Interpersonal Distress	**.019**
CESD Items (1-20)	
I was bothered by things that don't usually bother me.	**<.0001**
I did not feel like eating; my appetite was poor.	**<.0001**
I felt that I could not shake off the blues even with the help of my family or friends.	**.001**
I felt that I was just as good as other people.	**.008**
I had trouble keeping my mind on what I was doing.	**<.0001**
I felt depressed.	.260
I felt everything I did was an effort.	**<.0001**
I felt hopeful about the future.	.135
I thought my life had been a failure.	**.026**
I felt fearful.	**.001**
My sleep was restless.	**<.0001**
I was happy.	**<.0001**
I talked less than usual.	**.005**
I felt lonely.	.062
People were unfriendly.	.611
I enjoyed life.	.133
I had crying spells.	**.007**
I felt sad.	.052
I felt that people disliked me.	**.001**
I could not get 'going'.	**<.0001**

***Bold** signifies statistical significance p<.05

enjoyed life,' 'I felt sad' (p >.05) (Table 2). Three paired samples t-tests with Bonferroni corrections to make post hoc comparisons between time points for each significant effect (Table 3).

Conclusion: The intensive CBT treatment program was successful in improving functional impairment and psychological distress in a sample of Fibromyalgia patients. The improvements were maintained at 6 month follow-up. Despite statistically significant improvements in levels of depression, more than half of subjects continued to meet the clinical threshold for depression following CBT intervention. While CBT is regarded as the gold-standard treatment

Table 3: Post-hoc test

Item*	Admission	3 month	6 month	Admission vs. 3 month**	Admission vs. 6 month**	3 month vs. 6 month**
CES-D	23.22 (9.89)	17.13 (10.31)	17.30 (10.09)	**<.0001**	**<.0001**	1.000
FIQR	56.86 (17.54)	42.84 (21.12)	42.13 (21.03)	**<.0001**	**<.0001**	1.000
Clinical threshold depression	79.4% (112)	52.5% (74)	53.9% (76)	**<.0001**	**<.0001**	1.000
Severe functional impairment	46.1% (65)	25.5% (36)	23.4% (33)	**<.0001**	**<.0001**	1.000
CES-D Subscales						
Negative Affect	5.932 (4.70)	4.549 (4.28)	4.579 (4.38)	**.003**	**.005**	1.000
Positive Affect	5.029 (2.76)	3.964 (3.23)	4.109 (3.03)	**.002**	**.007**	1.000
Somatic Symptoms	11.689 (3.78)	8.459 (4.01)	8.570 (4.31)	**<.0001**	**<.0001**	1.000
Interpersonal Distress	.7554 (1.20)	.4676 (.879)	.6187 (1.05)	**.024**	.695	.231
CESD Items						
I was bothered by things that don't usually bother me.	1.295 (.896)	.9065 (.833)	.8705 (.833)	**<.0001**	**<.0001**	1.000
I did not feel like eating; my appetite was poor.	1.022 (.974)	.7194 (.917)	.6547 (.823)	**.002**	**<.0001**	1.000
I felt that I could not shake off the blues even with the help of my family or friends.	1.000 (.978)	.6763 (.895)	.729 (.877)	**.002**	**.005**	1.000
I felt that I was just as good as other people.	1.324 (1.118)	1.065 (1.137)	.9712 (.985)	.108	**.005**	1.000
I had trouble keeping my mind on what I was doing.	1.856 (.947)	1.532 (.943)	1.460 (.950)	**.001**	**<.0001**	1.000
I felt depressed.	.9424 (.969)	.871 (.992)	.7986 (.942)	1.000	.301	1.000
I felt everything I did was an effort.	2.225 (.863)	1.551 (.944)	1.594 (1.04)	**<.0001**	**<.0001**	1.000
I felt hopeful about the future.	1.201 (.949)	1.022 (1.01)	1.050 (1.031)	.158	.399	1.000
I thought my life had been a failure.	.4891 (.815)	.2993 (.611)	.3723 (.675)	**.021**	.286	.638
I felt fearful.	.7754 (.936)	.5217 (.812)	.4855 (.707)	**.019**	**.001**	1.000
My sleep was restless.	2.261 (.890)	1.645 (1.024)	1.717 (.996)	**<.0001**	**<.0001**	1.000
I was happy.	1.331 (.904)	.9209 (.941)	1.094 (.955)	**<.0001**	.056	.117
I talked less than usual.	1.094 (.966)	.7536 (.903)	.8551 (.925)	**.004**	**.049**	.792
I felt lonely.	.899 (1.045)	.676 (.919)	.748 (.918)	.056	.344	.912
People were unfriendly.	.324 (.616)	.273 (.612)	.331 (.630)	1.000	1.000	1.000
I enjoyed life.	1.196 (.895)	1.000 (.928)	1.014 (.989)	.170	.256	1.000
I had crying spells.	.715 (.899)	.511 (.749)	.438 (.766)	**.025**	**.007**	.912
I felt sad.	1.101 (.898)	.906 (.800)	.906 (.879)	.067	.090	1.000
I felt that people disliked me.	.432 (.771)	.194 (.470)	.288 (.651)	**.001**	.169	.157
I could not get 'going'.	1.87 (.895)	1.348 (.851)	1.442 (.952)	**<.0001**	**<.0001**	.704

* Categorical: n (%), Continuous: average (standard deviation)

** **Bold** signifies statistical significance p<.05

for depression in Fibromyalgia, some patients may require additional strategies for improvement. Factors important to address in this population to improve treatment effectiveness are contained in Table 2.

Disclosure: B. Bruce, None; **M. Allman**, None; **J. Gehin**, None; **L. Oliphant**, None; **F. Rivera**, None; **A. Abril**, None.

Abstract Number: 0234

Oxytocin Attenuates Tactile Allodynia in Experimental Fibromyalgia Rats

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia is a chronic disease characterized by widespread musculoskeletal pain throughout the body accompanied by fatigue, sleep, and memory issues, but there are no effective drugs in clinical. Oxytocin is synthesized within the paraventricular nucleus and supraoptic nucleus of the hypothalamus, and well known to facilitate the parturition and suckling. In addition to these pharmacological effects, oxytocin has been reported to have antinociceptive effect on neuropathic pain. However, the effect of oxytocin on fibromyalgia has not been reported. In this study, we examined the effect of oxytocin using experimental fibromyalgia model rats.

Methods: SD rats were exposed to repeated cold stress (23°C for 2 h and -3°C for 2 h for 5 cycles, -3°C for 4 h for 1 cycle; for 5 days) in the automatically controlled chamber. Two days after repeated cold stress, rats were intranasally treated with vehicle or oxytocin (25 μL/body), or orally treated with Pregabalin. Mechanical sensitivity was assessed by von Frey filament at 1 and 3 h after treatment. Corticosterone and ACTH in plasma were measured.

Results: Repeated cold stress induced significant tactile allodynia in rats. Pregabalin a drug used for fibromyalgia, significantly improved allodynia at 1 and 3 h after treatment. Intranasal oxytocin significantly attenuated allodynia in a dose-dependent manner. Plasma ACTH and corticosterone were decreased in repeated cold stress rats. Intranasal oxytocin inhibited the decreases in plasma ACTH and corticosterone levels, but pregabalin failed.

Conclusion: This is the first report showing that oxytocin attenuates tactile allodynia in fibromyalgia model. Intranasal oxytocin is expected to be therapeutic option for fibromyalgia.

Disclosure: H. Takahashi, None; **K. Kuki**, None; **J. Nomura**, None; **T. Kobayashi**, None.

Abstract Number: 0235

Muscle Pressure Correlates with Pain Levels in Fibromyalgia Patients and Muscle Tension May Be the Cause of Their Pain

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
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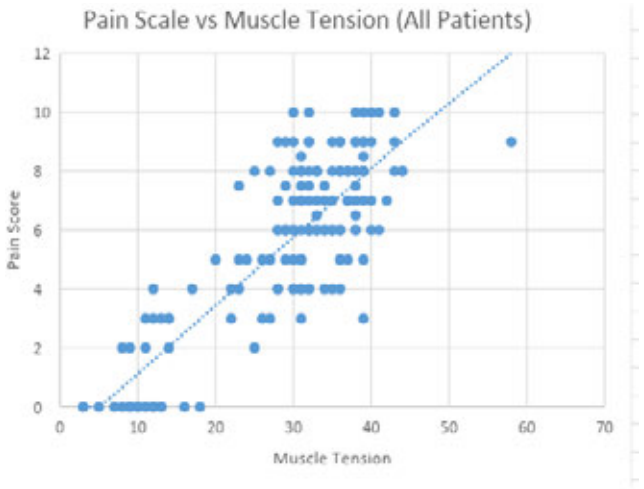
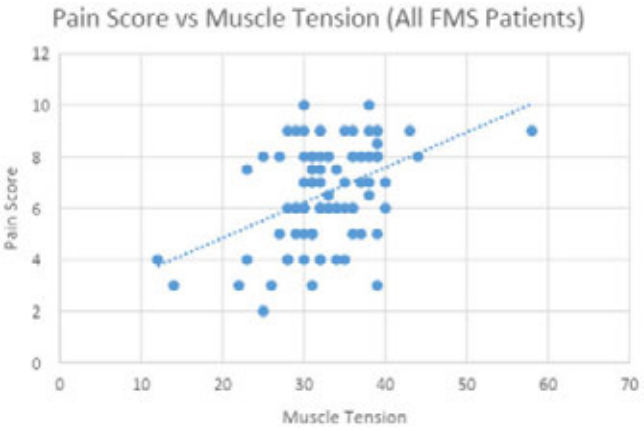
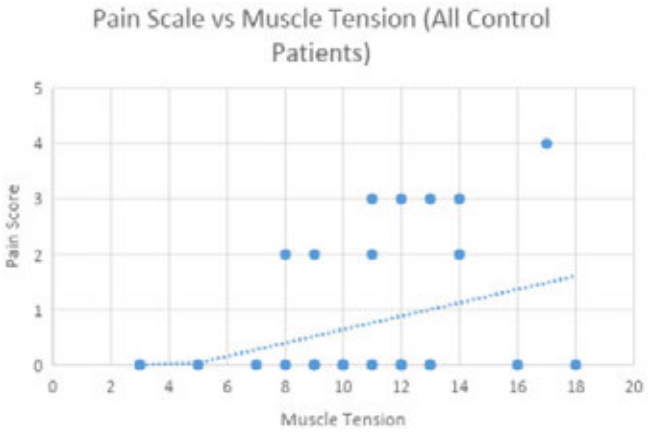
Background/Purpose: Previous research has found that muscle pressure as measured by a pressure gauge is three times higher in the trapezius muscle in fibromyalgia patients compared with non-fibromyalgia controls. We evaluated patients with fibromyalgia to determine whether there is a correlation between pain scores based on visual analog scale (VAS) 0 to 10 and the muscle pressure.

Methods: Patients signed a consent form if they were willing to have a muscle pressure measured by inserting a 22-gauge needle into the left trapezius muscle. After consent from patient, a trained nurse or physician experienced in determining muscle pressure performed the procedure and found the muscle pressure in mmHg. The muscle pressure was then correlated with the pain score of 0 to 10.

Results: For this analysis, all subjects (N=180) - regardless of diagnoses - were combined together in order to assess the correlation between the muscle tension and pain scale scores. Subjects had a median age of 47 years (range 20- 75 years), 81% were female. 79% had a diagnosis of fibromyalgia syndrome (FMS), followed by 7% having a diagnosis of rheumatoid arthritis. FMS patients had a median age of 49 years (range 20 to 75 years); 84.5% were female and 15.5 % male. In the non-FMS group (non-FMS rheumatic disease patients and controls) the median age was 45 years (range 24 to 68 years); and 68.4% were females and 31.6 % males. 142 patients had fibromyalgia and their mean (SD) pain score was 6.6 (1.84) on a 0-10 VAS. The mean (SD) pain score in the non-FMS subjects was 0.7 (1.26). The mean (SD) total population pain score was 5.5 (2.91). The calculated Pearson correlation coefficient for muscle tension vs pain scale for 175 subjects was 0.8312 (R-squared 0.6909; p-value < 0.0001). This indicates a highly significant association between subject's muscle tension and pain scores.







Conclusion: These findings demonstrate that muscle pressure directly correlates with pain scores, and this provides further evidence that muscle pressure may be the cause of much of the pain in fibromyalgia. Attempts to reduce muscle pressure with medication or other treatments could be successful in reducing pain in patients with fibromyalgia.

Disclosure: A. Katz Small, None; **B. Small**, None; **J. Anilao**, None; **J. Polyak Wokurka**, None; **R. Katz**, None.

Abstract Number: 0236

Repeat Muscle Pressures Measured in Fibromyalgia Patients and Compared with Pain Scores

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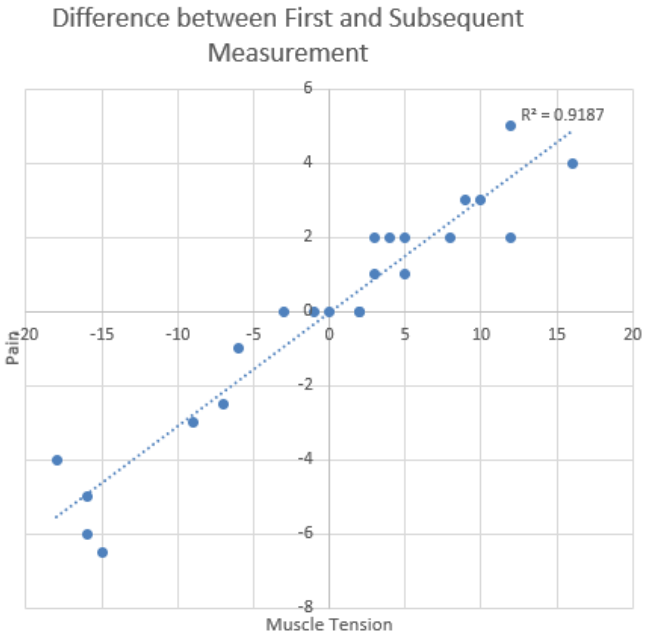
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients meeting the ACR criteria for the diagnosis of fibromyalgia were evaluated for intramuscular pressure using a pressure gauge from a trained physician or nurse. Some of these patients had a repeat muscle pressure determined using the same technique of measuring intramuscular pressure. The visual analog scale pain scores were compared and correlated with the muscle pressures.

Methods: Patients filled out a consent form after agreeing to have a repeat muscle pressure performed. A nurse or physician trained in measuring muscle pressures inserted a 22-gauge needle into the trapezius muscle, injected 0.3 cc of saline, and determined the muscle pressure using a pressure gauge. The pain score was correlated with the muscle pressure.

Results: Twenty three patients had a repeat muscle pressure done on a subsequent office visit after having an initial muscle pressure determined using the pressure gauge. The mean (SD) change in patients' muscle pressure and pain was 0 (9.81) mmHg and -0.04 (3.14). Although some patients showed improvement in muscle tension and/or pain score between visits, and some worsened, 19/23 (83%) of patients' change in both scales was in a consistent direction (both scales showed improvement or both scales showed worsening or both scales showed no change). In addition, when the change in muscle tension was correlated with the change in pain score, the resulting Pearson correlation coefficient was 0.9585 (R-squared 0.9187; p-value < 0.0001), indicating a very strong association between



the two values. The closer a correlation coefficient or R-squared is to 1, the stronger the relationship (with 1 being a perfect correlation between two variables).

Conclusion: The data show that those patients who had less pain at a subsequent office visit also had lower muscle pressure, whereas those patients who had a similar pain score based on the visual analog scale had a muscle pressure in the same range as the initial muscle pressure determination.

These findings further demonstrate that muscle pressure correlates strongly with pain scores, and this provides additional evidence that muscle pressure may be the cause of much of the pain in fibromyalgia. Attempts to reduce muscle pressure with medication or other treatments could be successful in reducing pain in patients with fibromyalgia.

Disclosure: A. Katz Small, None; **B. Small**, None; **R. Katz**, None.

Abstract Number: 0237

Determination of Muscle Pressure in Patients with Fibromyalgia by Two Examiners; The Examiners Get Similar Results

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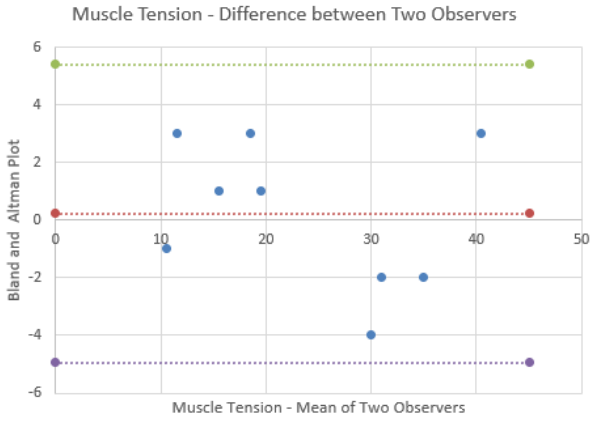
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Muscle pressure is increased in fibromyalgia as measured by a pressure gauge with a needle inserted into the trapezius muscle. We attempted to evaluate whether different examiners found the same muscle pressure using the recommended technique.



Green line = upper Bland and Altman limit of agreement
Red line = indicates the mean difference between Observer 1 and Observer 2
Purple line = lower Bland and Altman limit of agreement

Methods: Two nurses and two physicians separately determined the muscle pressure on fibromyalgia patients who met the ACR criteria for the diagnosis. A needle was inserted at a 45 degree angle up to ½ inch into the left trapezius muscle, 0.3 cc of saline was injected, and the pressure was determined using a manometer. A paired t-test and a Bland-Altman analysis were used to assess the agreement between the two professionals' muscle pressure measurements.

Results: Nine fibromyalgia patients had two muscle pressure evaluations performed by different professionals. Two rheumatology nurses, one rheumatologist and one rheumatology fellow performed the examinations. Visual analog scales were determined based on patient evaluation, and the muscle pressure was measured in mmHg. The mean (SD) of the differences between the pairs of professionals' scores was 0.2 (2.59), and this difference was determined to be insignificant (p = 0.803). Per the Bland-Altman analysis, the 95% limits of agreement are -4.9525 to 5.3970, and all the pair differences fell within these limits, indicating a high level of agreement between the data obtained by the nurses and physicians in determining the muscle pressure in fibromyalgia patients.

Conclusion: This study demonstrates that there is strong agreement - or reproducibility - between the muscle pressures measured by trained rheumatology professionals. Therefore, the measurement of muscle pressure is a reliable indicator of muscle tension in fibromyalgia patients and is a technique that is relatively easy to teach.

Disclosure: A. Katz Small, None; **B. Small**, None; **J. Polyak Wokurka**, None; **R. Katz**, None.

Abstract Number: 0238

Muscle Pressure as Measured by a Manometer Correlates with Dolorimetry in Patients with Fibromyalgia

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SESSION INFORMATION
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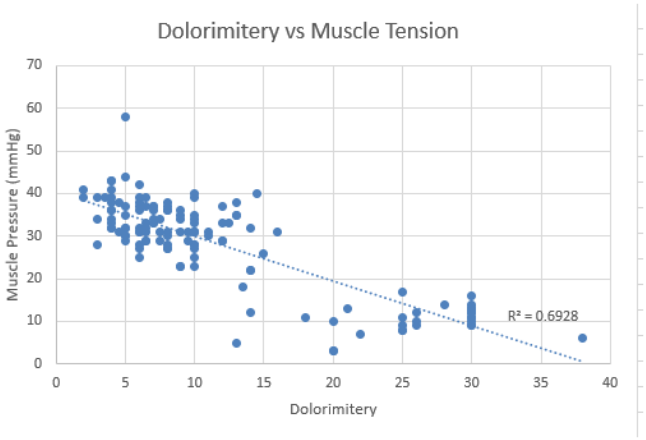

Background/Purpose: Muscle pressure is elevated in fibromyalgia patients compared to controls. We have demonstrated this finding in previous studies. We wanted to determine whether a noninvasive measure such as dolorimetry correlates with muscle pressure and would be a surrogate measure for muscle tension and tightness.

Methods: Patients meeting the 2010 ACR criteria for the diagnosis of fibromyalgia syndrome (FMS) signed a consent form if they were willing to have muscle pressure obtained. The pressure was determined using a manometer inserted into the left trapezius muscle by trained rheumatologists and rheumatology nurse clinicians. Dolorimetry was used to assess the amount of muscle tenderness resulting in moderate pain. A 60-pound dolorimetry gauge was used to apply pressure to the trapezius muscle, and the patient indicated when pain intensity became moderately intense.

Results: For this analysis, all subjects (N=133) - regardless of diagnoses - were combined together in order to assess the correlation between the muscle pressure and pain scale scores. Subjects had a median age of 51 years (range 20 - 75 years), 81% were female. 77% had a diagnosis of fibromyalgia. FMS patients had a median age of 52 years (range 20 to 75 years); 85.3% were female and 14.7 % male. In the non-FMS group the median age was 47 years (range 24 to 68 years); and 64.5% were females and 35.5 % males. 102 patients had fibromyalgia and their mean (SD) dolorimetry score was 8.0 (4.36). The mean (SD) dolorimetry score in the non-FMS subjects was 25.2 (5.42). The mean (SD) total population dolorimetry score and muscle tension were 12.0 (12.0) and 27.8 (27.85), respectively. The calculated Pearson correlation coefficient for muscle tension vs pain scale for 133 subjects was -0.8323 (R-squared 0.6928; p-value < 0.0001). This indicates a highly significant association between muscle tension and subject's dolorimetry scores.

Conclusion: Dolorimetry correlates with muscle pressure in patients with fibromyalgia. Dolorimetry indicates the amount of muscle tenderness present. It could be used as a surrogate measure for muscle pressure in patients with fibromyalgia

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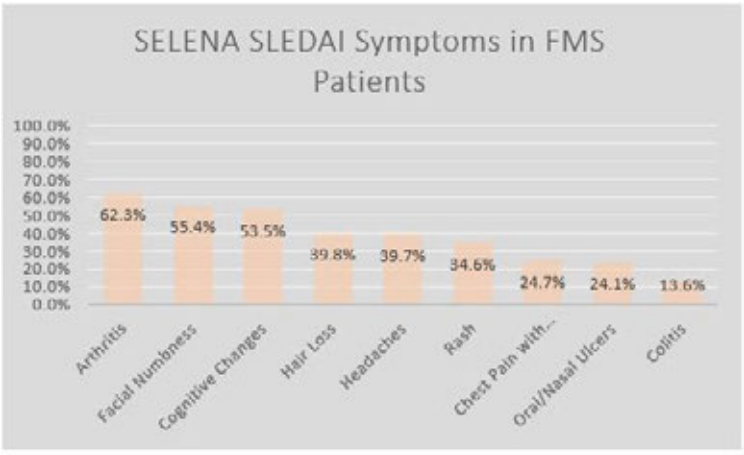
Disclosure: A. Katz Small, None; **B. Small**, None; **J. Polyak Wokurka**, None; **R. Katz**, None.

Abstract Number: 0239

The SELENA SLEDAI Is an Imperfect Measure of Lupus Disease Activity in Patients with Concomitant Fibromyalgia

Robert Katz,[1] Jessica Polyak Wokurka,[2] and Ben Small[2], [1]Rush University Medical Center, Chicago, IL, [2]Rheumatology Associates, Chicago, IL



SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The SELENA-SLEDAI is a tool for measuring the activity of systemic lupus. It is frequently used in clinical drug trials, but what is the value of this index in patients with lupus and concomitant fibromyalgia?

Methods: Patients were given an office questionnaire in which many of the SELENA-SLEDAI symptoms were listed.

Results: The fibromyalgia syndrome and non-fibromyalgia syndrome rheumatic disease groups did not significantly differ in age or education. In the fibromyalgia syndrome group, there were 191 patients (160 females and 31 males). In the control non-fibromyalgia syndrome rheumatic disease group, there were 130 patients (82 females and 48 males). The mean age for the fibromyalgia patients was 5

Analyzing the fibromyalgia syndrome sample, the SELENA-SLEDAI results were “arthritis” 119 patients (62.3%): cognitive changes 102 patients (53.5%); severe persistent headaches 74 patients (39.7%); hair loss 76 patients (39.8%); oral or nasal ulcers 46 patients (24.1%); facial numbness 106 patients (55.4%); chest pain with deep breathing 47 patients (24.7%); colitis 26 patients (13.6%); rash 66 patients (34.6%).

Conclusion: Patients with fibromyalgia frequently report symptoms that are part of the SELENA-SLEDAI disease activity scale. Therefore, patients with concomitant fibromyalgia and lupus may report these symptoms more commonly, and they may appear to be more resistant to treatment.

This has an important impact on clinical drug trials because the inclusion of patients with lupus and fibromyalgia together can lead to an apparent lack of efficacy for a new drug. In an evaluation of lupus patients by Wolfe, et al in 2014, of those given a diagnosis of lupus by a rheumatologist, 31% also met the criteria for fibromyalgia, based on the 2010 ACR criteria for the diagnosis.

New lupus treatments may appear to be ineffective, when actually they could be quite valuable if concomitant fibromyalgia is excluded. Using the SELENA-SLEDAI as an instrument for assessing lupus disease activity may be confounded by patients also having concomitant fibromyalgia.

Disclosure: R. Katz, None; **J. Polyak Wokurka**, None; **B. Small**, None.

Abstract Number: 0240

Whom Do Patients with Fibromyalgia Turn to for Emotional Support?

Robert Katz,[1] Jessica Polyak Wokurka,[2] and Ben Small[2], [1]Rush University Medical Center, Chicago, IL, [2]Rheumatology Associates, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia patients often have intense symptoms, especially pain and fatigue. We asked them in an in-office questionnaire whom they turn to for emotional support.

Methods: One hundred and fifteen fibromyalgia patients completed the questionnaire concerning emotional support.

Results: See Chart

Conclusion: Fibromyalgia patients most often find emotional support from their spouse (63%), but also frequently from friends (57%). They less commonly turn to professional support (21%) for their stressful symptoms. Fibromyalgia likely puts a significant strain on relationships and quite possibly fibromyalgia patients should be encouraged to receive professional support. Rheumatologists should help fibromyalgia patients find professional help for the emotional stress of their somatic symptoms.

FMS		%	Rheumatic Disease Controls		
Spouse	72	63%	Spouse	57	67%
Friends	66	57%	Friends	50	59%
Children	50	43%	Children	44	52%
Parents	38	33%	Parents	32	38%
Siblings	37	32%	Siblings	20	24%
Professional	24	21%	Professional	14	16%

Disclosure: R. Katz, None; **J. Polyak Wokurka**, None; **B. Small**, None.

Abstract Number: 0241

Comparing Patients with Fibromyalgia Syndrome with Non-Fibromyalgia Rheumatic Disease Patients Regarding Exercise

Robert Katz,[1] and Jessica Polyak Wokurka[2], [1]Rush University Medical Center, Chicago, IL, [2]Rheumatology Associates, Chicago

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Exercise is reported to help patients with the fibromyalgia syndrome (FMS). We wanted to know whether FMS patients, compared to non-FMS rheumatic disease patients, did try to exercise regularly and whether they felt they benefited from it.

Methods: We administered an in-office questionnaire to 191 FMS patients meeting the 2010 ACR criteria and 130 non-FMS rheumatic disease patients. Patients were asked about whether they exercise, what type of exercise they did, the duration and frequency, and whether they felt that exercise helped their symptoms.

Results: 77.4% of the FMS patients exercise compared to 89.2% of the non-FMS rheumatic disease patients ($p< 0.007$). With respect to whether the exercise helped their symptoms, non-FMS rheumatic disease patient benefited more. The mean VAS for pain improvement (0-10) was 6.19 in the non-FMS group, compared with 4.64 for FMS patients ($p< 0001$). The mean improvement in energy (VAS 0-10) for non-FMS patient was 7.08, vs 4.92 in the FMS group ($p< 0001$). The mean improvement in sleep (VAS 0-10) was 6.78 in non-FMS patients and 4.77 in FMS patients ($p< 0001$). Patients exercised using different methods including using a stationary bike, an outdoor bike, running outside or on the treadmill, walking, swimming, muscle strengthening, yoga, stretching. Although walking was the most common activity chosen by the FMS and non-FMS groups, there was no significant difference between the types of exercise in the two groups. Also exercise frequency and duration did not differ statistically between the two groups.

Conclusion: In this study there was no impact, good or bad, on pain, in fibromyalgia patients who exercised. There was also no improvement in energy or sleep related to exercise in fibromyalgia patients. On the other hand, non-fibromyalgia rheumatic disease patients did benefit from exercise in terms of pain, energy and sleep.

It is unclear why fibromyalgia patients don't respond to exercise favorably. Possibly they do not feel they can exercise vigorously and don't become physically fit. But for whatever reason, we did not find that exercise benefits fibromyalgia patients.

Disclosure: R. Katz, None; **J. Polyak Wokurka**, None.

Abstract Number: 0242

The Effectiveness of Medications for Fibromyalgia Based on Patient Experiences

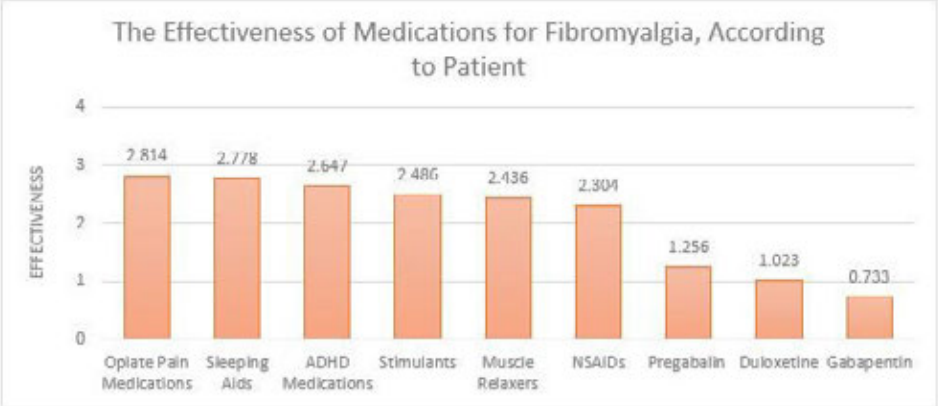
Robert Katz,[1] Jessica Polyak Wokurka,[2] and Ben Small[2], [1]Rush University Medical Center, Chicago, IL, [2]Rheumatology Associates, Chicago, IL

SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To assess patients' global assessment of frequently used treatments for the fibromyalgia syndrome (FMS), we asked patients with fibromyalgia to rank medications they have tried for their effectiveness.

Methods: 95 patients (mean age of 50.5) diagnosed with fibromyalgia based on the 2011 ACR criteria, 88 females and 7 males, completed an in-office questionnaire regarding the effectiveness of various medications often used to treat fibromyalgia. The study ranked 9 medications, which include Pregablin, Gabapentin, Duloxetine, Muscle Relax-



Medications	Patient	Mean
Opiate Pain Medications	70	2.814
Sleeping Aids	72	2.778
ADHD Medications	34	2.647
Stimulants	35	2.486
Muscle Relaxers	78	2.436
NSAIDs	81	2.304
Pregabalin	43	1.256
Duloxetine	44	1.023
Gabapentin	30	0.733

ants, Sleep Aids, Stimulants, ADHD Medications, Opiate Pain Medications, and NSAIDS. Patients rated the medications using this scale: 1=minimally helpful, 2=somewhat helpful, 3=moderately helpful, 4=very helpful.

Results: The three medications that were most positively rated by patients were opiate pain meds (mean=2.8), medications to improve sleep (mean= 2.8), and ADHD stimulants for fibro fog symptoms (mean=2.6).

The medications with the lowest effectiveness ratings by fibromyalgia patients included: gabapentin (mean=0.73); duloxetine (mean=1.02); pregabalin (mean=1.26). 59.1% of FMS patients reported little or no help from pregabalin, and 83.3 % found gabapentin to be little help.

Conclusion: Fibromyalgia patients rated the effectiveness of various medications that they tried. Pain medication, sleep aids and stimulants given for the attention deficit component of fibro fog were judged by patients to be the most helpful.

Disclosure: R. Katz, None; **J. Polyak Wokurka**, None; **B. Small**, None.

Abstract Number: 0243

Concomitant Fibromyalgia in Patients with Other Rheumatic Diseases and Response to Treatment

Robert Katz,[1] Jessica Polyak Wokurka,[2] and Ben Small[2], [1]Rush University Medical Center, Chicago, IL, [2]Rheumatology Associates, Chicago, IL

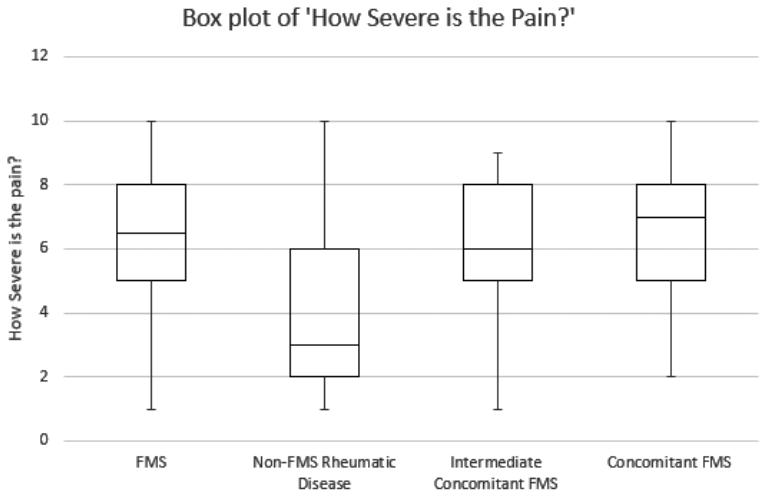
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

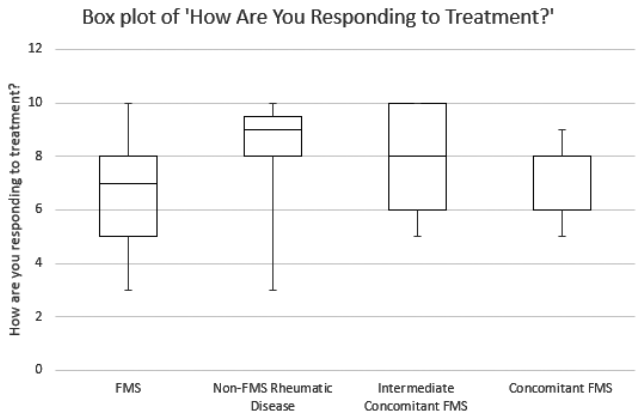
Background/Purpose: Some rheumatic disease patients have concomitant fibromyalgia. We wanted to determine treatment response in patients with and without concomitant fibromyalgia.

Methods: Patients were diagnosed by a rheumatologist. All patients also filled out a form to determine the presence of fibromyalgia based on the 2012 modifications of the ACR approved criteria for the diagnosis. The cut-off point was for the diagnosis of fibromyalgia was 12 or more points on a 1 to 31-point scale. Summarized counts and percentages of sex by derived DX group and for the total

- Descriptive statistics (N, mean, SD, median, min, max, etc) for the FMS score by derived DX group and for the total
- Descriptive statistics (N, mean, SD, median, min, max, etc) for the responses to “How are you responding to tx” by DX group and for the total but also summary of the counts and percentages of the number of patients having each tx score (1, 2, 3, etc).
- A Kruskall-Wallis test to compare all 4 dx groups’ pain score and also the tx response score.
- Upon confirming that there’s indeed a difference between all 4 groups for both scores, comparisons were done, using the Mann-Whitney test and the Bonferroni correction

Results: There were 503 patients analyzed in this study; 75% were female and 25% were male. Of these, 108/503 (22%) had FMS diagnosis, 273/503 (54%) were determined to have other rheumatic diseases but no concomitant





FMS (FMS score < 10), 39/503 (8%) were determined to have other rheumatic diseases and potential FMS (FMS score 10 or 11), and 83/503 (17%) were determined to have other rheumatic diseases and concomitant FMS (FMS score > 11). See table below for a summary of these patients' pain scores and response to treatment scores.

The Kruskall-Wallis test for both scores and showed a significant difference between the 4 diagnosis groups for the pain score ($p < 0.0001$) and the response to treatment score ($p < 0.0001$), indicating that indeed there are differences in pain sensation and response to treatment between the 4 diagnosis groups. When multiple comparisons were performed, the ones that were statistically significantly different for the pain score were

Concomitant FMS vs No Concomitant FMS ($p < 0.0001$)

No Concomitant FMS vs FMS ($p < 0.0001$)

No Concomitant FMS vs Intermediate/potential Concomitant FMS ($p < 0.0001$)

This means that there are significant differences between each of those pairs of dx groups in terms of the pain score. One can conclude from this that having FMS or Concomitant FMS seems to be associated with higher pain scores.

Conclusion: Those patients who scored 12 or more points on the ACR diagnostic criteria scale were diagnosed with having fibromyalgia. Some patients scored 10 to 12 on that scale and were considered to be intermediate in the

How are you responding to tx?				
N	21	39	5	7
Mean	6.4	8.3	7.8	7.1
SD	2.06	1.72	2.28	1.57
Median	7	9	8	8
Min	3	3	5	5
Max	10	10	10	9

determination of a fibromyalgia diagnosis. Patients with inflammatory rheumatic diseases in addition to fibromyalgia (concomitant fibromyalgia) were evaluated for treatment response based on a visual analog scale.

There was a clear difference in patients' response to therapy in those rheumatic disease patients who had concomitant fibromyalgia and those that do not.

Disclosure: R. Katz, None; **J. Polyak Wokurka**, None; **B. Small**, None.

Abstract Number: 0244

Real-World Evidence Associated with the Treatment of Systemic Lupus Erythematosus in the USA, UK, France, and Germany: A Structured Review

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research Poster I – ACR/ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is an autoimmune multi-system disease characterized by flares and more rarely remissions. Emerging biologic therapies for SLE are expected to change the treatment landscape. A study was conducted to: (1) review the safety and efficacy outcomes associated with treatment of SLE in the real world; (2) compare results of real-world studies with those of randomized controlled trials (RCTs) and their extension studies; (3) understand real-world patterns of medication use. Searches focused on belimumab, as it is the only biologic agent approved for the treatment of SLE.[1]

Methods: A targeted literature search was conducted in MEDLINE on Jan 2, 2019, with no limitations for publication year. A total of 546 articles underwent title and abstract screening to identify English-language real-world studies of belimumab conducted in USA, UK, France, and Germany. Long-term extension studies for belimumab were identified in a separate systematic literature review of RCTs.

Results: Real-world studies showed reduced disease activity after belimumab treatment in 51% and 77% of patients with SLE at 6 months and 1 year, respectively. In comparison, RCTs of belimumab treatment showed similar

efficacy for this endpoint at 6 months (44%–57%) and lower efficacy at one year (43%–58%). Reductions in disease activity were maintained over 7 years of follow-up in long-term extension studies.

The real-world studies additionally showed that belimumab treatment led to reductions in corticosteroid dosages (24%–58% at 6 months) and discontinuation of corticosteroids in up to 11% of patients with SLE. Similar reductions in corticosteroid dosages and discontinuations were seen in long-term extension studies for up to 7 years. In contrast, claims data showed no effect of belimumab treatment on the number of patients taking corticosteroids.

Numerous reasons for discontinuation of belimumab were reported in the real-world studies, such as patient request, ineffective medication, disease progression, infection, no clinical response, adverse events (AEs), or disease persistence. In contrast, discontinuation was primarily due to AEs in RCTs and withdrawal in the long-term extension studies. Claims data showed that discontinuation of belimumab typically occurred within 6 months of treatment initiation. Rates of AEs remained stable over the course of therapy in the long-term extension studies, with infections being most common.

Conclusion: The current study found that real-world studies of belimumab show similar or better reductions in disease activity vs those observed in RCTs and that these reductions are maintained during long-term treatment. Real-world studies also showed that belimumab is associated with reductions in corticosteroid dosages and even discontinuation of corticosteroid use, two important outcomes for patients with SLE. Longer follow-up of more detailed real-world studies would further improve the understanding of outcomes of belimumab and other biologic therapies in the treatment of SLE.

[1]Navarra SV, Guzman RM, Gallacher AE, et al. (2011) Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial. *Lancet* 377 (9767): 721-731.

Disclosure: J. Lofland, Janssen Scientific Affairs, LLC, 3; **P. Berry**, Janssen Scientific Affairs, LLC, 3; **F. Pan**, Janssen Scientific Affairs, LLC, 3; **C. Karyekar**, Abbott, 3, BMS, 3, Janssen, 1, 3, Janssen Scientific Affairs, LLC, 3, Novartis, 3; **H. Guiang**, Janssen Scientific Affairs, LLC, 5; **R. McTavish**, Janssen Scientific Affairs, LLC, 5; **M. Thompson**, Janssen Scientific Affairs, LLC, 5.

Abstract Number: 0245

Comorbidities, Health Care Utilization, and Cost of Care in Systematic Lupus Erythematous Increase with Disease Severity During 1 Year Before and After Diagnosis: A Real-World Cohort Study in the United States, 2004–2015

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research Poster I – ACR/ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is associated with high economic burden. This real-world study assessed health care resource utilization (HRU) and costs in a US cohort of patients with newly diagnosed SLE.

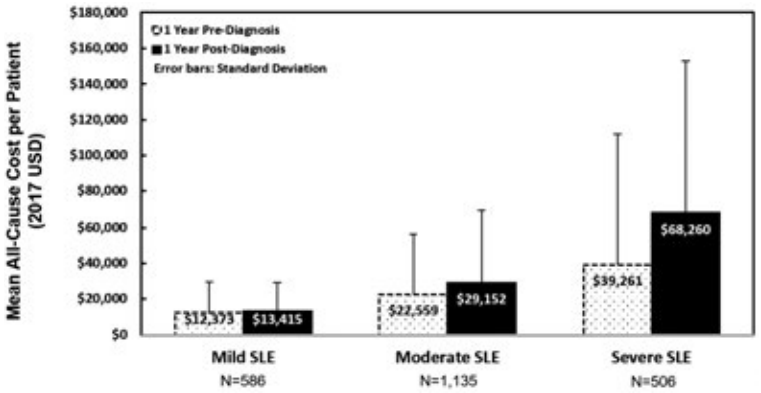

Figure. Mean All-Cause Health Care Costs per Patient by Disease Severity Among Patients With Newly Diagnosed SLE 1 Year Before and After Diagnosis; United States 2005–2014.

Methods: Using linked Truven Health MarketScan® commercial claims data and IQVIA's GE Centricity electronic medical record (EMR) database, we identified patients ≥18 years old with SLE diagnosis (index) between January 1, 2005 and December 31, 2014, with no prior SLE or lupus nephritis diagnosis 1 year pre-index, who had ≥1 year of continuous enrollment pre- and post-index date. Disease severity was classified as mild, moderate, or severe over 1 year post diagnosis using claims-based algorithms, which combined SLE diagnosis, disease activities/SLE-related conditions, medications, and health services use,[1] supplemented with EMR. HRU and costs (2017 US$) were reported over 1 year pre and post diagnosis. All-cause costs were evaluated with a generalized linear model, adjusting for demographics, clinical characteristics, Charlson comorbidity index, and pre-index cost.

Results: In total, 2,227 patients with SLE were included in this analysis; 586 (26.3%) with mild, 1,135 (51.0%) with moderate, and 506 (22.7%) with severe SLE. Mean (SD) age was 50.2 (13.0) years, 90.6% female, and 54.4% White. Patients were prescribed corticosteroids (76.1%), hydroxychloroquine (59.7%), methotrexate (14.7%), and biologics (2.7%).

Patients with moderate/severe SLE had more comorbid disease during the year before SLE diagnosis; 26.5% of severe patients had ≥3 Charlson comorbidities compared with 13.8% moderate and 6.1% mild SLE. Moderate/severe patients also had significantly higher mean per-patient costs 1 year before SLE diagnosis, representing a 1.8- and 3.2-fold increase, respectively, vs mild SLE (mild $12,373 [SD $17,171], moderate $22,559 [SD $33,674], severe $39,261 [SD $72,768]; $P< 0.0001$).

During the first year after SLE diagnosis, the proportion of patients with ≥1 inpatient stay increased with SLE severity (mild 12.8%, moderate 22.4%, severe 51.2%; $P< 0.0001$), as did the average hospital stay days (0.47 [SD 1.69], 1.31 [SD 3.69], 5.52 [SD 12.33], respectively; $P< 0.0001$). Similarly, the proportion of patients with ≥1 ED visit increased with disease severity (mild 26.8%, moderate 41.3%, severe 57.9%; $P< 0.0001$).

Moderate/severe patients had 2.2- and 5.1-fold higher health care costs, respectively, vs mild SLE (average yearly cost: mild $13,415 [SD $15,707], moderate $29,512 [SD $40,466], severe $68,260 [SD $84,712]; $P< 0.0001$; **Figure**). Adjusted cost ratio (95% CI) was 1.81 (1.65, 1.98) for moderate vs mild SLE and 4.24 (3.80, 4.73) for severe vs mild SLE.

Conclusion: Prior to SLE diagnosis, health care costs increase with disease severity. For patients with newly diagnosed moderate/severe SLE, total all-cause health care costs during the first year after diagnosis are significantly higher (4.2- and 1.8-fold increase, respectively) compared with mild SLE. This pattern of increased health care costs

is also observed during the year before SLE diagnosis. Earlier diagnosis may ensure better health care outcomes and lower associated costs.

[1] Garris C, et al. *J Med Econ*. 2013;16:667–677.

Disclosure: M. Jiang, AstraZeneca, 3; **A. Near**, IQVIA, 3; **B. Desta**, AstraZeneca, 3; **X. Wang**, AstraZeneca, 3; **E. Hammond**, AstraZeneca, 3.

Abstract Number: 0246

Smoking Exposure in Pack-Years Predicts Cutaneous Manifestations of Lupus

Nnenna Ezeh,[1] Trevor McKown,[1] Shivani Garg,[1] and Christie Bartels[1], [1]University of Wisconsin School of Medicine and Public Health, Madison, WI

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research Poster I – ACR/ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients of color are more likely to have systemic lupus erythematosus (SLE) and a smoking history. Prior literature notes that both smoking and race impact odds of cutaneous manifestations. Thus, we examined the impact of cumulative smoking and race on cutaneous manifestations of SLE.

Methods: For this cohort study, electronic health records at an academic center were manually abstracted to include adult patients meeting ACR 1997 or SLICC 2012 classification criteria and with at least one ambulatory rheumatology encounter with an SLE ICD- 9 or 10 code from 2003 - 2016. Our cohort included 632 consecutive SLE patients; 552 met ACR and 80 met SLICC SLE criteria only. The primary outcomes were ACR or SLICC cutaneous criteria and SLICC Damage Index (DI) cutaneous criteria. The primary explanatory variable was smoking exposure defined as low (< 5 pack-years), medium (5-10 pack-years), and high (>10 pack-years), compared to nonsmokers. Covariates included age category at diagnosis (early onset < 18 years old, 18-50 years, or late onset >50 years), sex, and race. Analysis was performed using multivariate logistic regression to calculate odds ratios and 95% confidence intervals (OR, (95% CI)).

Results: Among 632 SLE patients, mean age was 42 ±14 years, 91% female, 82% white, and 40% were ever smokers**.** Figure 1 compares age at SLE diagnosis of ever smokers and never smokers. Never smokers were on average younger with a wider age distribution observed among ever smokers. Patients with low smoking exposure were nine times more likely to develop any mucocutaneous manifestations (OR 9.0, (1.2, 67.7)), four times more likely to meet any SLICC cutaneous criteria (OR 3.7, (1.3, 10.6)), and twice as likely to meet ACR cutaneous criteria (OR 2.0 (1.0, 3.8)) compared to non-smokers (Table 1). Patients with medium smoking exposure were twice as likely to meet acute cutaneous SLICC criteria (OR 2.3, (1.1, 5.1)), whereas those with high smoking exposure had two-fold higher odds of discoid lupus (OR 2.1, (1.1, 4.1)). Chronic cutaneous SLICC criteria and SLICC DI cutaneous criteria showed linear pack-year trends that met significance with high smoking exposure (OR 2.2, (1.2, 4.2) and OR 4.2, (0.9, 9.2) respectively). Patients of color had increased risk for alopecia, discoid lupus, chronic cutaneous lupus, and DI skin damage. Limitations included sample size and just 18% patients of color.

Table 1. Multivariate odds ratios & 95% CI of cutaneous lupus by smoking exposure in pack-years

	Acute SLICC Cutaneous	Chronic SLICC Cutaneous	Any SLICC Cutaneous	Any ACR Cutaneous	Any Muco-cutaneous *	Any SLICC-DI Skin Damage
Nonsmoker (0 pk-yrs)	Referent	Referent	Referent	Referent	Referent	Referent
Low (<5 pk-yrs)	1.6 (0.8, 2.9)	1.7 (0.8, 3.9)	**3.7 (1.3, 10.6)**	**2.0 (1.0, 3.8)**	**9.0 (1.2, 67.7)**	1.8 (0.6, 5.7)
Medium (5-10 pk-yrs)	**2.3 (1.1, 5.1)**	2.0 (0.8, 4.9)	2.1 (0.8, 5.8)	2.0 (0.9, 4.3)	7.3 (0.95, 56.2)	2.6 (0.8, 8.3)
High (>10 pk-yrs)	1.1 (0.7, 1.7)	**2.2 (1.2, 4.2)**	1.3 (0.7, 2.2)	1.2 (0.7, 1.9)	0.9 (0.5, 1.7)	**4.2 (1.9, 9.2)**
Unknown	0.6 (0.4, 1.2)	**2.6 (1.3, 5.2)**	0.9 (0.5, 1.6)	0.9 (0.5, 1.5)	0.7 (0.4, 1.4)	0.7 (0.2, 3.1)
Early onset	0.6 (0.3, 1.3)	0.9 (0.3, 2.7)	0.6 (0.2, 1.7)	0.7 (0.3, 1.6)	0.6 (0.2, 2.2)	0.8 (0.2, 3.7)
Usual onset	Referent	Referent	Referent	Referent	Referent	Referent
Late onset	**0.3 (0.1, 0.8)**	1.0 (0.3, 3.0)	**0.3 (0.1, 0.97)**	0.5 (0.2, 1.1)	0.4 (0.1, 1.6)	1.3 (0.3, 6.4)
Male	Referent	Referent	Referent	Referent	Referent	Referent
Female	**2.6 (1.5, 4.7)**	1.1 (0.5, 2.6)	**4.6 (2.6, 8.1)**	**2.5 (1.4, 4.4)**	**5.2 (2.9, 9.4)**	1.1 (0.4, 3.4)
White	Referent	Referent	Referent	Referent	Referent	Referent
Black	**0.4 (0.2, 0.6)**	1.8 (0.97, 3.4)	0.9 (0.5, 1.8)	**0.5 (0.3, 0.8)**	0.7 (0.4, 1.6)	**2.6 (1.1, 5.9)**
Other	0.6 (0.3, 1.1)	**3.6 (1.6, 8.1)**	0.6 (0.3, 1.5)	0.5 (0.3, 1.4)	0.5 (0.2, 1.2)	2.2 (0.6, 8.2)

*Any Mucocutaneous included any SLICC or ACR cutaneous or mucosal criteria.

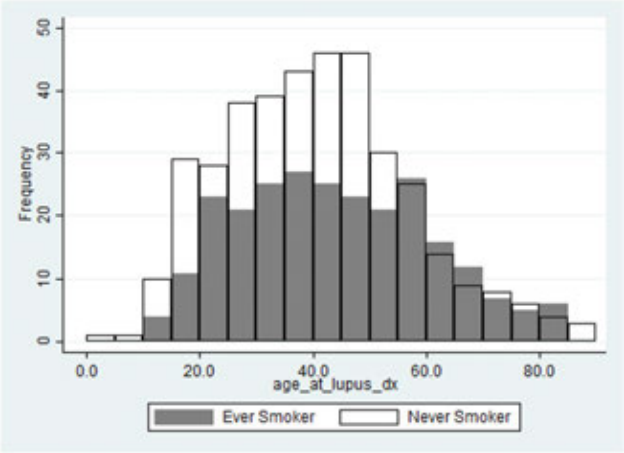

Figure 1. Frequency of ages at SLE diagnosis for SLE ever smokers compared to never smokers.

Conclusion: Any smoking exposure was an independent risk factor for nearly all cutaneous manifestations of SLE, whereas high smoking exposure and patients of color had significantly increased risk of chronic cutaneous manifestations and persistent skin damage. Findings suggest a dose relationship between smoking exposure and cutaneous manifestations/damage, making cessation an important strategy to potentially reduce disparities and improve cutaneous outcomes in SLE.

Disclosure: N. Ezeh, None; **T. McKown**, None; **S. Garg**, None; **C. Bartels**, Pfizer, 2, Pfizer Independent Grants for Learning and Change, 2.

Abstract Number: 0247

Health Literacy, Adherence, and Quality of Life of Uveitis Patients

Claire Mueller,[1] and **Ghazala O'Keefe**[1], [1]Emory University School of Medicine, Atlanta, GA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research Poster I – ACR/ARP
Session Type: Poster Session (Sunday)
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Table 1: Uveitis Etiologies

	Etiology	Number of Patients	Infectious (%)	All Cases (%)
Infectious Etiology	Tuberculosis	7	41	12
	Toxoplasmosis	3	18	5
	HIV	3	18	5
	Syphilis	2	12	3
	CMV Retinitis and Immune Reconstitution Uveitis	1	6	2
	Lyme Disease	1	6	2
Non-Infectious Etiology	**Etiology**	**Number of Patients**	**Non-Infectious (%)**	**All Cases (%)**
	Idiopathic	18	38	30
	Sarcoidosis	8	17	13
	HLA B27	8	17	13
	Systemic Lupus Erythematosus	5	11	8
	Vogt-Koyanagi-Harada Disease	2	4	3
	Multiple Sclerosis	2	4	3
	Inflammatory Bowel Disease	2	4	3
	Rheumatoid Arthritis	1	2	2
	Retinal vasculitis c-ANCA+ and HLA B51+	1	2	2

Table 2. Comparison of Necessity and Concerns Scores of the Beliefs about Medicines Questionnaire

		BMQ Necessity		BMQ Concerns	
Covariate of interest	**Covariate Level**	**Mean (Std), (n=)**	**p-value**	**Mean (Std), (n=)**	**p-value**
Health Literacy*	SAHL ≤14 SAHL > 14	3.7 (1.1) (n=26) 3.6 (0.9), (n=30)	0.7867	3.0 (1.3), (n=26) 3.0 (0.9), (n=30)	0.9813
Co-Management by Rheumatology	Yes No	3.9 (0.8), (n=27) 3.3 (1.1), (n=24)	0.0275	3.4 (1.1), (n=27) 2.6 (1.0), (n=24)	0.0076
Number of Providers**	1 Provider 2 Provider 3 Provider	3.2 (1.1), (n=24) 4.0 (0.9), (n=25) 4.0 (0.4), (n=5)	0.0220	2.7 (1.0), (n=24) 3.3 (1.2), (n=25) 3.4 (1.5), (n=5)	0.2184
Annual Household Income	< $5,000 $5,000 - $29,999 > $30,000	3.7 (0.9), (n=16) 3.8 (0.9), (n=27) 2.8 (1.4), (n=8)	0.0489	3.0 (1.1), (n=16) 3.0 (1.1), (n=27) 3.2 (1.5), (n=8)	0.8720
Immune Modulating Therapy or Biologics	Yes No	3.8 (0.8), (n=20) 3.5 (1.1), (n=34)	0.3944	3.4 (0.9), (n=20) 2.8 (1.2), (n=34)	0.0561

*Health literacy score out of 18, with 14 or less indicating poor health literacy
**Ophthalmology is included as one of the providers. 2 providers represent a provider in addition to Ophthalmology

Table 3. Comparison of Physical and Mental Component Scores of the SF-12

		Physical Component Score (PCS)		Mental Component Score (MCS)	
Covariate of interest	**Covariate Level**	**Mean (Std), (n=)**	**p-value**	**Mean (Std), (n=)**	**p-value**
Co-Management by Rheumatology	Yes Referral* No	35.8 (10.2), (n=28) 40.5 (5.9), (n=5) 43.7 (10.1), (n=26)	0.0174	44.1 (11.0), (n=28) 43.2 (12.2), (n=5) 46.8 (11.8), (n=26)	0.6382
Number of Providers**	1 Provider 2 Provider 3 Provider	43.1 (9.6), (n=27) 36.9 (10.5), (n=26) 33.3 (7.7), (n=5)	0.0318	45.1 (11.8), (n=27) 39.9 (10.1), (n=5) 45.8 (11.1), (n=26)	0.5747
Annual Household Income	< $5,000 $5,000 - $29,999 > $30,000	35.7 (11.9), (n=17) 39.6 (9.5), (n=30) 46.3 (6.3), (n=8)	0.0510	45.7 (9.9), (n=17) 50.3 (10.7), (n=8) 44.9 (11.7), (n=30)	0.4865
Correlation of BMQ and SF-12					
		Physical Component Score (PCS)		**Mental Component Score (MCS)**	
		Correlation Coefficient	**p-value**	**Correlation Coefficient**	**p-value**
BMQ Necessity		-0.2352	0.0900	-0.1837	0.1879
BMQ Concerns		-0.3271	0.0168	-0.5255	<0.0001

*Patients who have been referred to rheumatology, but have not had an appointment or missed their first appointment with rheumatology
**Ophthalmology is included as one of the providers. 2 providers represent a provider in addition to Ophthalmology

Background/Purpose: To determine health literacy, medication adherence, and quality of life (QOL) of uveitis patients in order to understand how to deliver better and improved quality of care given uveitis patients' multidisciplinary needs.

Methods: We performed a cross-sectional quality improvement study of uveitis patients treated at an outpatient ophthalmology clinic at a 953-bed county hospital in Atlanta, Georgia. A prospective assessment of health literacy using the Short Assessment of Health Literacy survey (SAHL), adherence using the Beliefs about Medicine Questionnaire (BMQ), and QOL using the 12-item Short Form Health Survey (SF-12) were obtained from 60 consecutive patients, as well as baseline data on uveitis diagnosis and etiology.

Results: Demographics: 57% of patients were women and 80% identified as Black. 42% of patients had schooling beyond high school. 32% of patients earned < $5,000 in annual household income, and 79% earned < $30,000. 27% of patients were uninsured.

Uveitis description and etiology: 70% of cases were bilateral and 43% were anterior in location. 25% were infectious etiologies and 51% were related to inflammatory disease or markers.

Health Literacy: 43% of patients had poor health literacy. Mean SAHL was significantly lower for those with less schooling ($p< 0.0001$).

Beliefs about Medicines: Mean necessity scores (3.7/5) were higher than concerns scores (3.2/5). Necessity scores were higher for multiple providers ($p=0.0220$) as well as those co-managed by rheumatology ($p=0.0275$). Concerns scores were higher ($p=0.0076$) for patients co-managed by rheumatology.

Quality of Life (QOL): Uveitis patients scored lower than the general US population for physical ($p< 0.0001$) and mental QOL ($p=0.002$). Physical QOL was lower for patients co-managed by rheumatology ($p=0.0174$), those managed by multiple providers ($p=0.0318$), or those on immune modifying therapy ($p=0.0345$).

Conclusion: Uveitis patients reported many barriers to care, have significantly poorer QOL compared to normal subjects, and have poor health literacy. Despite strong perceptions of treatment necessity there were also treatment concerns. Rheumatology patients have worse physical QOL but indicated increased adherence. Co-management with other specialties and patient education may be beneficial in improving medication adherence and QOL.

Disclosure: C. Mueller, None; **G. O'Keefe**, None.

Abstract Number: 0248

Adherence to Biologic Disease-modifying Anti-rheumatic Drugs (DMARDs) —a Comparison of Long-term Adherence Among Patients with Various Inflammatory Conditions by Primary Dispensing Channel

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research Poster I – ACR/ARP
Session Type: Poster Session (Sunday)
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Background/Purpose: Medication adherence to biologic DMARDs has been associated with optimal clinical outcomes. Adherence varies with primary dispensing channel among rheumatoid arthritis patients. Prior studies have primarily focused on individual inflammatory conditions. This research compared adherence among patients diagnosed with rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis or a combination of these conditions over a two-year follow-up period by primary dispensing channel.

Methods: A retrospective cohort analysis of patients continuously eligible for pharmacy/medical benefits, with biologic DMARD claims and corresponding diagnoses for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis or a combination of these diagnoses. Dispensing channel was determined by a threshold of 75% of biologic DMARD therapy through a 2-year follow-up period. Adherence was calculated using medication possession ratio during each 1-year period of analysis. Adherent patients were defined as those whose biologic DMARD adherence was at least 80%. Patients were classified as new or continuous users based on 6 months prior to index biologic DMARD claim. Patients were matched between channels based on age, gender, new or continuous use, and diagnosed condition using propensity score matching. Logistic regression was used to assess impact of dispensing channel and to control for age, gender, new or continuous use, diagnosed condition, and comorbidity burden in year one. Year two adherence results also controlled for year one adherence behavior.

Results: Final sample included 2,436 patients on biologic DMARD therapy meeting selection criteria, with an index prescription between July 1 and December 31, 2015. Likelihood of adherence was found to be significantly lower during the first year of follow-up among patients primarily filling their biologic DMARD through retail compared to specialty pharmacy (37.6% [95% CI: 23.7%-48.9%] lower compared to our specialty pharmacy, and 29.0% [95% CI: 10.6%-43.7%] lower compared to other specialty pharmacy). Average adherence, based on MPR, was lower in the second year for all channels, and no significant difference in the change in average adherence was found ($p > 0.05$). Likelihood of adherence in the second year of analysis was influenced by adherence behavior in the first year, with adherent patients in the first year being 11 times more likely to be adherent in the second year (aOR=11.18, 95% CI: 9.09-13.73).

Conclusion: Among patients with diverse inflammatory condition diagnoses, those using specialty pharmacy as primary dispensing channel for biologic DMARDs have higher adherence in the first year of measurement after controlling for other factors influencing adherence. Adherence in the second year was lower for all channels; however, dispensing channel does not appear to impact the magnitude of change in adherence between years. Given that the largest single predictor of adherence in the second year is prior adherence, choice of primary dispensing channel during the first year of therapy should be considered upon starting or continuing biologic DMARD therapy for patients with inflammatory conditions.

Disclosure: C. Swift, Express Scripts, 3; **Y. Viteri**, Accredo, 3; **G. Bridges**, Accredo, 3; **M. Dorholt**, Accredo, 3; **M. Kohli**, Express Scripts, 3.

Abstract Number: 0249

Evaluation of Real-World Early-Line Abatacept versus Tumor Necrosis Factor Inhibitors Persistence in Rheumatoid Arthritis Patients with Anti-Citrullinated Protein Antibody or Rheumatoid Factor Positivity

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SESSION INFORMATION
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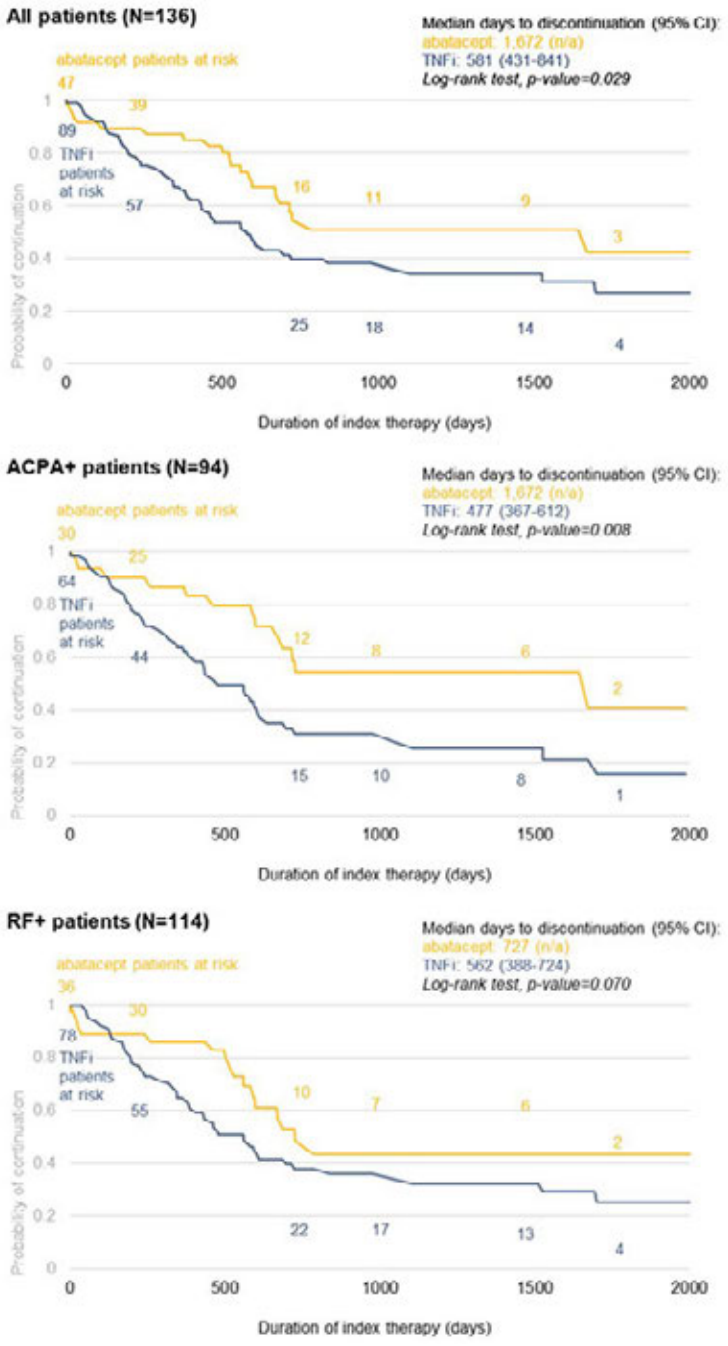
Table 1 Baseline characteristics and persistence	Abatacept N=47	TNFi N=89	P-Value
Anti-CCP and RF status			0.075
ACPA+ only	11	11	
RF+ only	17	25	
ACPA+ and RF+	19	53	
Age in years, mean (SD)	64.87 (12.99)	60.48 (11.82)	0.049
Female, n (%)	38 (80.85)	62 (69.66)	0.160
Charlson comorbidity index (CCI), mean (SD)	0.87 (1.17)	0.61 (0.98)	0.182
Duration of treatment at site (years), mean (SD)	5.09 (3.95)	4.74 (3.11)	0.581
Index drug with 12 months of persistence, n (%)	39 (82.98)	57 (64.04)	0.021
Reason for discontinuation (among patients who discontinued index treatment), n (%)			0.015
Disease progression – uncontrolled symptoms	4 (20.00)	28 (51.85)	
Adverse effects of medication	0 (0)	6 (11.11)	
Insurance coverage	5 (25.00)	7 (12.96)	
Adherence issues	1 (5.00)	0 (0.0)	
Physician preference	1 (5.00)	1 (1.85)	
Patient preference	3 (15.00)	2 (3.70)	
Unknown/not specified	1 (5.00)	0 (0.0)	
Other	5 (25.00)	10 (18.52)	

Background/Purpose: Abatacept is recommended as first-line biologic therapy in adult patients with moderate to severe RA. We aimed to assess real-world 1-year treatment persistence in early-line abatacept versus TNFi treated RA patients who were ACPA+ and RF+, which predict poorer functional and radiographic outcomes.

Methods: As part of a multicenter retrospective medical record review of adult RA patients with poor prognostic factors, patients were treated with abatacept or TNFi as the first biologic treatment at participating clinics (defined as early line) and had ACPA positivity, RF positivity, increased CRP, elevated ESR, or joint erosions. This analysis only included ACPA+ and/or RF+ patients. Patients in the TNFi group were treated with adalimumab, etanercept, infliximab (and biosimilars), certolizumab pegol, or golimumab. Data were collected ≥1 year from treatment initiation (8/9/11-11/14/16). Patients with Crohn's disease, ankylosing spondylitis, ulcerative colitis, psoriatic arthritis, or anal fistula were excluded. Demographic, disease, and treatment data (start, stop, reason for discontinuation) were abstracted. Treatment persistence (continuation of index treatment with gap ≤60 days) at 1 year and time to discontinuation were reported. Multivariate logistic and Cox modeling with forward selection compared abatacept and TNFi 1-year persistence, risk of overall discontinuation, and discontinuation for disease progression, controlling for demographic and clinical characteristics (age, sex, Charlson comorbidity index (CCI), RA duration), baseline utilization, and clinic. Analyses will be repeated when >300 patients are recruited.

Results: Data on 136 patients (47 abatacept, 89 TNFi) were available at the time of analysis (Table 1). Abatacept patients were older than TNFi patients. There were no significant differences in gender, CCI, or duration of treatment at the clinic. Risk of discontinuation was lower in abatacept vs. TNFi overall (p=0.029) and for both ACPA+ (p=0.008) and RF+ (p=0.070) patients. Median time to discontinuation for ACPA+ and RF+ patients was 1,672 and 727 days for abatacept vs. 477 and 562 days for TNFi, respectively (Figure 1). At 1 year, 83% of abatacept vs. 64% of TNFi patients were persistent (p=0.021) (Table 1). Adjusted risk of discontinuation was higher in TNFi patients, although not statistically significant (Table 2). Odds of 1-year persistence was lower in TNFi than abatacept patients, but not statistically significant (Table 2). TNFi patients were at significantly higher risk of discontinuing index treatment due to disease progression.

Figure 1 Time to discontinuation of index treatment



Conclusion: In this analysis of ACPA+ and RF+ RA patients, unadjusted analyses demonstrate these patients are significantly more likely to be persistent to abatacept than TNFi at 1 year in a real-world setting. Abatacept patients also experienced a longer time to discontinuation than the TNFi cohort, which may be explained by the significantly lower proportion of patients discontinuing abatacept due to disease progression. Perhaps due to limited sample size, the adjusted comparison of abatacept and TNFi persistence is not significant, however, numeric trends are consistent.

Table 2 Adjusted persistence and discontinuation of index treatment

	Persistence at 12 months: OR (95% CI)	*p*-value	Risk of all-cause discontinuation: HR (95% CI)	*p*-value	Risk of discontinuation for disease progression: HR (95% CI)	*p*-value
Age, years	1.033 (0.998 - 1.069)	0.064	0.998 (0.979 - 1.017)	0.822	0.988 (0.960 - 1.017)	0.425
Male vs. female	0.254 (0.102 - 0.637)	0.003	1.400 (0.831 - 2.357)	0.206	1.442 (0.663 - 3.136)	0.356
CCI	1.246 (0.802 - 1.934)	0.328	0.995 (0.796 - 1.243)	0.963	1.054 (0.753 - 1.476)	0.758
Anti-CCP and RF status						
Positive anti-CCP only vs dual positive	2.812 (0.712 - 11.107)	0.140	0.493 (0.228 - 1.069)	0.073	0.337 (0.077 - 1.479)	0.149
Positive RF only vs dual positive	2.607 (0.996 - 6.826)	0.051	0.495 (0.281 - 0.871)	0.015	0.507 (0.221 - 1.164)	0.109
TNFi vs. Abatacept	0.559 (0.217 - 1.439)	0.228	1.525 (0.897 - 2.594)	0.119	3.759 (1.289 -10.966)	0.015

The initial models included age, gender, CCI, ACPA and RF status, and cohort as independent variables. We then used a forward selection method to include additional significant covariates ($p<0.05$) in the final models. The following covariates were considered: time from RA diagnosis to index, number of physician office visits (1-year pre-index), number of hospitalizations (1-year pre-index), and clinic site. None of those covariates were significant and therefore were not included.

Disclosure: D. Paul, Bristol-Myers Squibb, 3; **X. Han**, Bristol-Myers Squibb, 3, Bristol-Myers Squibb Company, 3; **I. Yermilov**, Partnership for Health Analytic Research (PHAR LLC), 9, CareminDr, 4, 6; **S. Gibbs**, Partnership for Health Analytic Research (PHAR LLC), 9; **M. Broder**, Partnership for Health Analytic Research (PHAR LLC), 9.

Abstract Number: 0250

Treatment Patterns, Dose Change, and Treatment Discontinuation in RA Patients Switching from First Biologic DMARD to Another Treatment in the US

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Background/Purpose: For RA patients not meeting their treat-to-target goals despite treatment with their first biologic (b)DMARD, ACR guidelines recommend switching to a different bDMARD or Janus kinase inhibitor (JAKi).[1] Shorter treatment duration was reported for TNF-α inhibitors (TNFi) than non-TNFi bDMARDs;[2,3] little data exist for JAKi. Understanding treatment and dosing patterns and persistency among treatment classes can optimize next-treatment selection in RA patients switching from initial bDMARD to another treatment.

Methods: In a US health-plan claims database, we identified adult RA patients who initiated a bDMARD (1/1/2012–3/31/2017) and switched (index date) to another bDMARD or JAKi (as monotherapy or in combination with a conventional synthetic [cs]DMARD). Patients had ≥2 RA diagnoses ≥30 days apart and 12-month pre- and ≥12-month post-ID continuous enrollment. Treatment patterns before and after the switch were assessed. Index-treatment dose modifications (≥10% daily-dose increase or decrease) were evaluated. Persistency was evaluated as the risk of treatment discontinuation (via Cox proportional hazards models) – among all, within index monotherapy, within index combination therapy.

Results: A total of 4656 patients switched from a first (pre-index) bDMARD to another (index) treatment (78% female, median age 54 years, RA duration 1.5 years). As pre-index bDMARD, 90.0% of patients used TNFi. Upon changing

Table 1. Prior (Pre-Index) Treatments by Subsequent (Index) bDMARD (n=4656)

	Index TNFi (n=3045, 65%)	Index non-TNFi bDMARD (n=1090, 23%)	Index JAKi (n=521, 11%)	Total (n=4656, 100%)
Prior bDMARD – TNFi	2843 (68%)	940 (22%)	407 (10%)	4190 (100%)
Prior bDMARD – non-TNFi	202 (43%)	150 (32%)	114 (25%)	466 (100%)

Table 2. Dose Change (Increase or Decrease) and Time to Dose Change, by Index Treatment

	% of patients with dose increase within:			Time to dose increase, days	% of patients with dose decrease within:			Time to dose decrease, days
	3 months	6 months	12 months		3 months	6 months	12 months	
All patients (n=4656)	4.6%	8.8%	12.0%	196	3.3%	4.5%	5.6%	207
Index monotherapy (n=2149)	5.6%	8.7%	11.0%	164	3.4%	4.4%	5.3%	160
TNFi (n=1305)	3.7%	6.5%	8.9%	173	3.9%	4.4%	5.4%	134
Non-TNFi (n=521)	13.7%	18.6%	20.2%	111	4.3%	7.0%	8.2%	195
JAKi (n=323)	0.6%*	2.5%*	5.3%*	351*	0.0%*	0.3%*	0.6%*	239
Index combination therapy (n=2507)	3.8%	8.9%	12.8%	218	3.2%	4.5%	5.9%	238
TNFi + csDMARD (n=1740)	2.3%	7.6%	11.6%	215	3.0%	4.1%	5.1%	223
Non-TNFi + csDMARD (n=569)	9.4%	15.1%	18.9%	178	4.9%	7.6%	10.5%	247
JAKi + csDMARD (n=198)	1.0%†	2.0%†	6.6%†	444†	0.0%†	0.0%†	0.5%†	541†

*p<0.001 for JAKi vs. bDMARD within monotherapy.
†p<0.05 for JAKi vs. bDMARD within combination therapy.

treatment, 65.4% started another TNFi, 23.4% non-TNFi, and 11.2% JAKi. Most (68%) patients on pre-index TNFi cycled to another TNFi, 22% switched to a non-TNFi, and 10% switched to JAKi. Patients with non-TNFi as first bDMARD switched to TNFi (43%), another non-TNFi (32%), or JAKi (25%; Table 1).

Within 3, 6, and 12 months, the percentages of patients with dose increase ranged: 0.6–6.6% JAKi, 2.3–11.6% TNFi, 9.4–20.2% non-TNFi; dose decrease: 0–0.6% JAKi, 3.0–5.4% TNFi, 4.3–10.5% non-TNFi. Time to dose change was longer in JAKi than in bDMARD treatments (Table 2).

Patients were significantly more likely to discontinue monotherapy than combination therapy (hazard ratio [HR]=2.0). Within monotherapy, patients were more likely to discontinue TNFi than JAKi (HR=1.25). Within combination therapy, TNFi + csDMARD where more likely to be discontinued than JAKi + csDMARD (HR=1.31). In all models, discontinuation risk increased in patients with unknown vs commercial types of insurance (overall HR=1.62, monotherapy HR=1.72, combination therapy HR=1.54); treatment discontinuation risk increased with shortened duration of RA (HR=0.92 for all) and increased number of concomitant medications (HR=1.02 for all; Table 3).

Conclusion: For RA patients switching from first bDMARD to another treatment, TNFi was the most common drug class before and after switch. After switch, JAKi demonstrated higher treatment persistency than TNFi. Dose increases were most common in non-TNFi, followed by TNFi, and least common in JAKi.

References:

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2. Chastek B, et al. Adv Ther. 2017; 2422-35.
3. Wilke T, et al. BMC Musculoskelet Disord. 2017; 332-42.

Table 3. Cox Proportional Hazards Models for Time to Discontinuation of Index Regimen after First bDMARD: Among All Patients (Model 1), Among Patients Treated with Monotherapy (Model 2), and Among Patients Treated with Combination Therapy (Model 3)

	Model 1: All patients N=4,656		Model 2: Monotherapy patients n=2,149		Model 3: Combination therapy patients n=2,507	
Predictor	Hazard Ratio	p-value	Hazard Ratio	p-value	Hazard Ratio	p-value
Index regimen (monotherapy vs combination)	2.00	<0.001	N/A	N/A	N/A	N/A
Index regimen among monotherapy (vs. JAKi mono)	N/A	N/A	N/A	N/A	N/A	N/A
TNFi mono	N/A	N/A	1.25	0.002	N/A	N/A
Non-TNFi bDMARD mono	N/A	N/A	1.06	0.49	N/A	N/A
Index regimen among combination therapy (vs. JAKi + csDMARD)	N/A	N/A	N/A	N/A	N/A	N/A
TNFi + csDMARD	N/A	N/A	N/A	N/A	1.31	0.01
Non-TNFi bDMARD + csDMARD	N/A	N/A	N/A	N/A	1.00	0.97
Age (vs 18–34)						
35–44 years	1.03	0.72	0.98	0.85	1.14	0.30
45–54 years	1.08	0.34	1.10	0.37	1.09	0.48
55–64 years	0.95	0.54	0.96	0.69	0.98	0.85
65+ years	0.87	0.19	0.89	0.41	0.91	0.52
Female (vs Male)	1.10	0.03	1.15	0.02	1.04	0.51
Region (vs Northeast)						
South	1.09	0.10	1.16	0.03	0.99	0.89
Midwest	1.01	0.88	1.06	0.47	0.93	0.34
West	1.12	0.09	1.11	0.26	1.11	0.27
Payer type (vs. Commercial)						
Self-insured†	0.98	0.56	1.01	0.80	0.91	0.09
Medicaid/Medicare	1.19	0.07	1.36	0.02	0.94	0.66
Unknown	1.62	<0.001	1.72	<0.001	1.54	0.003
Physician specialty (non-rheumatology vs. rheumatology)	0.98	0.56	1.01	0.90	0.96	0.46
Index year (vs ≤2013)						
2014	1.07	0.18	0.99	0.86	1.17	0.03
2015	1.08	0.13	0.98	0.80	1.18	0.02
2016	1.07	0.19	1.01	0.92	1.15	0.06
2017	0.83	0.06	0.78	0.09	0.89	0.42
Duration of RA in years (as continuous variable)	0.92	<0.001	0.92	<0.001	0.92	<0.001
Total number of comorbidities (as continuous variable)	0.99	0.10	0.99	0.61	0.98	0.11
Total number of drugs (as continuous variable)	1.02	<0.001	1.02	<0.001	1.02	<.0.001

N/A: Results were not applicable because the corresponding covariate was not included in the model.
†Self-insured plan was the plan in which the employer took full financial risk for providing health care benefit to its employees.

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Abstract Number: 0251

Long-term Financial Impact of Switching from Reference to Biosimilar Etanercept When Considering Short-term Formulary Management Costs in the US

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SESSION INFORMATION
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Session Title: Health Services Research Poster I – ACR/ARP
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Background/Purpose: Biosimilars have enabled some US institutions and payers to achieve significant financial savings after implementing a formulary change from the reference biologic. However, within integrated delivery networks (IDN), health-systems, and outpatient practices, there are short-term administrative costs to clinically implement such a change and additional labor associated with formulary management. The objective of this study is to assess the long-term financial implications of implementing a formulary change from a reference biologic to a biosimilar when considering the short-term costs incurred in select, chronic rheumatologic conditions.

Methods: We evaluated the short- and long-term costs of implementing a formulary change from reference to biosimilar etanercept for the treatment of RA, JIA, and AS from a US IDN perspective over a 5-year time horizon. The number of existing and new patients to be treated with etanercept was calculated based on a hypothetical population of 1 million (M) within an IDN, taking into consideration population growth, etanercept treatment patterns, and incidence/prevalence rates of RA, JIA, and AS derived from the literature (see data table for population inputs). For the price of biosimilar etanercept, a base case discount from reference etanercept was estimated from US market experience with biosimilars in general using Average Sales Price data from the Centers for Medicare and Medicaid Services. For patients switching from reference etanercept, the biosimilar market share was assumed to be 95% in year 1 and 100% by year 5. Initial short-term administrative costs to implement a formulary change vary by institution, so three different scenarios (low: $50,000; medium: $100,000; and high: $200,000) were explored. Labor costs to implement a switch included nurse time for additional patient education and pharmacist time to manage non-formulary requests.

Results: For this hypothetical population of 1 M patients within an IDN, a total of 1,331 (0.1%) patients were treated with etanercept for all three indications by year 5. When considering short-term administrative costs, the total non-pharmacy costs of implementing a formulary conversion program over 5 years was $55,518, $105,518, and $205,518 for the low, medium, and high administrative cost scenarios, respectively. When considering pharmacy cost savings within this particular model, the total 5-year savings were $62.4 M, $62.4 M, and $62.3 M for the low, medium, and high administrative cost scenarios, respectively ($10,076, $10,067, and $10,049 savings per switched patient per year on average).

Conclusion: Substantial cost savings may be realized in the long term for an institution when changing the formulary from the reference etanercept to a biosimilar etanercept, even when factoring the short-term administrative costs and labor associated with managing a formulary change within a relatively small population.

Parameter	Value	Source
Total IDN population	1,000,000	Assumption
Annual population growth (%)	3	Assumption
Prevalence rates (per 100,000)		
RA	890	Kawatkar AA, et al. *Rheumatol Int.* 2019; 39(3):541-549
JIA	44.7	Harrold LR, et al. *J Rheumatol.* 2013; 40(7):1218-25
AS	107	Curtis JR, et al. *Perm J.* 2016; 20(4):15-151
Incidence rates (per 100,000)		
RA	53	Kawatkar AA, et al. *Rheumatol Int.* 2019; 39(3):541-549
JIA	11.9	Harrold LR, et al. *J Rheumatol.* 2013; 40(7):1218-25
AS	3.1	Wright KA, et al. *Arthritis Care Res (Hoboken).* 2015; 67(6):836-41
Proportion treated with a biologic (%)		
RA	32.5	Curtis JR, et al. *Clin Ther.* 2014; 36(7):996-1004
JIA	13	Zamora-Legoff JA, et al. *Clin Rheumatol.* 2016; 35(6):1493-9
AS	52.5	Reveille JD, et al. *Am J Med Sci.* 2012; 343(5):371-4
Proportion treated with etanercept (%)		
RA, JIA, AS	41.5	Curtis JR, et al. *Clin Ther.* 2014; 36(7):996-1004

Table 1. Model Assumptions for Population Calculations

Disclosure: D. Mezzio, Xcenda, 3, Xcenda, 3; **E. Li**, Sandoz, 3; **S. Balu**, Sandoz, 1, 3.

Abstract Number: 0252

Treatment Sequences, Effectiveness, and Costs of Tumor Necrosis Factor Inhibitor Cycling Compared with Swapping to a Novel Disease-modifying Anti-rheumatic Drug in Rheumatoid Arthritis Patients

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Background/Purpose: To evaluate the sequences of therapeutic drugs used by rheumatoid arthritis (RA) patients whose initial tumor necrosis factor inhibitor (TNFi) therapy failed, as well as mean time to therapy discontinuation and costs of TNFi and non-TNFi drugs.

Methods: Using the IBM MarketScan Research Databases, we analyzed claims of adult RA patients who switched to their second biological or targeted disease-modifying antirheumatic drug between January 2008 and December 2015. We determined the most common treatment sequences and estimated the time to therapy discontinuation. We compared drug and other health care costs between adherent and non-adherent patients.

Results: Among 10,442 RA patients identified, 36.5% swapped to a non-TNFi drug, most commonly (54.2%) abatacept. The remaining 63.5% switched to a cycling regimen (second TNFi), most commonly adalimumab (41.2%). For subsequent lines of therapy, non-TNFi drugs were more common. Patients who swapped were significantly older and sicker than those who cycled ($p < 0.001$). Survival analysis showed a longer time to discontinuation for second-line non-TNFi drugs than for TNFi (median 471 days compared with 370 days, $p < 0.001$), but no difference in subsequent lines of therapy. Although non-TNFi drugs were less expensive for adherent patients, cycling was associated with lower costs overall.

Conclusion: Although patients are more likely to cycle to a second TNFi than swap, those who swap to a non-TNFi drug are more likely to persist with the second-line therapy. However, cycling appears to be the less costly strategy.

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Abstract Number: 0253

A Systematic Review and Meta-analysis of Observational Studies Reporting on the Use of Checkpoint Inhibitors in Patients with Cancer and Pre-existing Autoimmune Disease

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SESSION INFORMATION
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Background/Purpose: Immune checkpoint inhibitors (ICI) are increasingly used in the treatment of cancer. To date, no clinical trials exist evaluating the use of ICI in patients with autoimmune disease. Therefore, we have systematically reviewed observational studies reporting the outcomes of cancer patients with pre-existing autoimmune disease to determine the frequency of flares, *de novo* immune-related adverse events (irAEs), and deaths.

Methods: We searched in 5 electronic databases through August 2018. Study selection, data collection and quality assessment were performed by one investigator and cross-checked by another. A meta-analysis was performed to pool occurrence of flares, *de novo* irAEs, and deaths.

Results: Eleven observational studies were included (868 patients with cancer and preexisting autoimmune disease). Four studies were comparative. All studies included patients with advanced cancer stages. Seven studies reported therapy with PD-1/PD-L1, three CTLA-4, and one both. The mean age of the participants ranged from 54 to 72 years of age. The risk of bias score for cohort studies ranged from four to seven points (out of a maximum of 9). Pooled occurrence of any irAEs (flares or *de novo*) was 55% (95% confidence interval (CI) 44%, 66%); for flares it was 29% (95% CI 11%, 49%), and for *de novo* irAEs 30% (95% CI 24%, 35%). Flares were more commonly reported in patients with rheumatoid arthritis (33%) and psoriasis (20%). Pooled occurrence of deaths was 31% (95% CI 11%, 56%), one due to *de novo* colitis, however none were considered to be related to the pre-existing autoimmune disease. The pooled proportion of permanent discontinuation of the ICI was 12% (95% CI 4%, 24%), and for patients with partial cancer response 25% (95% CI 15%, 36%).

Conclusion: Over 40% of the patients with pre-existing autoimmune disease received ICI blockade with no subsequent flares or *de novo* irAE. These results suggest that ICI can be used in these patients, but careful monitoring is required as close to one third of the patients will experience a flare of their autoimmune disease.

Disclosure: M. Lopez-Olivo, None; **N. Abdel-Wahab**, None; **M. Suárez-Almazor**, Bristol-Myers Squibb, 5, Pfizer Inc, 5, Eli Lilly, 5.

Abstract Number: 0254

Interstitial Lung Disease Associated Health Care Resource Utilization and Cost in Rheumatoid Arthritis Patients in an Insured Population

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SESSION INFORMATION
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Background/Purpose: Interstitial lung disease (ILD) is a frequent extraarticular manifestation of rheumatoid arthritis (RA) that imposes substantial economic burden on patients and healthcare systems. However, the impact of the incidence of ILD on healthcare resource utilization (HCRU) and medical cost in RA patients (pts) has not been well documented. The objective of this study was to assess the HCRU and cost attributed to incident ILD in RA pts.

Table 1: Baseline characteristics by cohort

	RA-ILD pts (n=8,214)	RA only pts (n=104,101)	p-value
Age (years), mean (SD)	69.38 (12.05)	59.76 (15.32)	<.0001
Female, n (%)	5,901 (71.84%)	76,254 (73.25%)	0.0208
Charlson Comorbidity Index, mean (SD)	2.76 (2.00)	0.83 (1.32)	<.0001
ACPA, n (%)			
Non-Missing	543 (6.61%)	11,349 (10.90%)	0.4397
Positive	*94 (17.31%)*	*1,823 (16.06%)*	
Negative	*449 (82.69%)*	*9,526 (83.94%)*	
Missing	7,671 (93.39%)	92,752 (89.10%)	
RF, n (%)			
Non-Missing	951 (11.58%)	20,741 (19.92%)	<.0001
Positive	*420 (44.16%)*	*7,749 (37.36%)*	
Negative	*531 (55.84%)*	*12,992 (62.64%)*	
Missing	7,263 (88.42%)	83,360 (80.08%)	
Comorbidities, n (%)			
COPD	3,004 (36.57%)	8,716 (8.37%)	<.0001
Asthma	1,505 (18.32%)	7,674 (7.37%)	<.0001
Bronchitis	59 (0.72%)	191 (0.18%)	<.0001
Pneumonia	1,588 (19.33%)	2,645 (2.54%)	<.0001
Pulmonary fibrosis	45 (0.55%)	4 (0.00%)	<.0001
Pulmonary Nodules	1,039 (12.65%)	1,583 (1.52%)	<.0001
Tuberculosis	30 (0.37%)	104 (0.10%)	<.0001
Diabetes	2,194 (26.71%)	18,152 (17.44%)	<.0001
Dyslipidemia	3,611 (43.96%)	32,219 (30.95%)	<.0001
Hypertension	5,783 (70.40%)	46,846 (45.00%)	<.0001
Felty's syndrome	1 (0.01%)	0 (0.00%)	0.0731
Sjögren's syndrome	362 (4.41%)	2,254 (2.17%)	<.0001
Prior Medications, n (%)			
Biologic DMARDs	724 (8.81%)	3,650 (3.51%)	<.0001
Conventional DMARDs	3,115 (37.92%)	20,935 (20.11%)	<.0001
Corticosteroids	5,162 (62.84%)	48,474 (46.56%)	<.0001
NSAIDs	2,858 (34.79%)	41,070 (39.45%)	<.0001

Table 2: HealthCare Resource Utilization and Costs 12 months pre- and post-ILD diagnosis in the RA-ILD cohort

	12-month pre-ILD diagnosis (n=8,214)	12-month post-ILD diagnosis (n=8,214)	p-value
Number of healthcare services utilized, mean (SD)			
Inpatient admissions	2.43 (3.89)	3.13 (4.74)	<.0001
Length of stay, days	14.51 (24.31)	24.31 (37.81)	<.0001
Outpatient visits	27.24 (24.34)	35.77 (30.28)	<.0001
Emergency visits	3.33 (5.41)	4.17 (6.60)	<.0001
Urgent care visits	1.47 (0.98)	1.57 (1.04)	0.0474
Pharmacy prescriptions	32.93 (20.99)	36.51 (21.57)	<.0001
All- cause visits	**56.21 (39.10)**	**68.68 (44.95)**	**<.0001**
Costs incurred by patients, mean (SD)			
Inpatient costs	$38,062.28 ($76,384.27)	$59,216.59 ($124,432.68)	<.0001
Outpatient costs	$17,308.30 ($38,633.09)	$26,089.92 ($54,560.66)	<.0001
Emergency costs	$3,799.42 ($9,911.56)	$5,260.95 ($12,212.22)	<.0001
Urgent care costs	$227.51 ($247.75)	$267.71 ($330.67)	0.2098
Pharmacy costs	$6,364.00 ($12,063.77)	$7,659.26 ($18,245.37)	<.0001
All- cause costs	**$38,898.04 ($71,440.06)**	**$67,843.37 ($120,567.15)**	**<.0001**

Table 3: Comparison of the Change in HealthCare Resource Utilization and Costs Over Time in RA-ILD and RA Only Patients

	RA-ILD pts (n=8,214)	Only RA pts (n=104,101)	p-value
***Difference in number of healthcare services utilized per pt, mean (SD)**			
Inpatient admissions	0.82 (3.30)	0.25 (2.20)	<.0001
Length of stay, days	8.33 (29.13)	1.64 (13.12)	<.0001
Outpatient services	7.68 (23.29)	4.68 (15.89)	<.0001
Emergency visits	0.49 (3.56)	0.18 (3.12)	<.0001
Urgent care visits	-0.01 (0.38)	0.00 (0.30)	0.0048
Pharmacy prescriptions	3.58 (14.52)	5.01 (11.63)	<.0001
All-cause visits	**12.58 (31.61)**	**10.13 (22.42)**	**0.0017**
Difference in costs per patient, mean (SD)			
Inpatient costs	$19,122.83 ($101,609.71)	$3,240.38 ($33,088.83)	<.0001
Outpatient costs	$7,808.52 ($42,668.47)	$3,372.53 ($21,237.32)	<.0001
Emergency costs	$754.83 ($6,009.36)	$244.30 ($3,864.66)	<.0001
Urgent care costs	-$0.31 ($88.27)	$1.21 ($221.04)	0.0034
Pharmacy costs	$1,248.57 ($12,660.92)	$1,632.07 ($9,564.75)	<.0001
All-cause costs	**$28,934.43 ($112,904.91)**	**$8,490.49 ($42,804.70)**	**<.0001**

**Difference = (HCRU or Costs post diagnosis – HCRU or Costs prior diagnosis), positive difference means an increase over time.*

Methods: Adult pts from administrative claims database Optum Clinformatics Data Mart with incident RA (≥2 claims with ICD-9: 714.0 or ICD-10: M05.xxx/ M06.0xx/ M06.8xx /M06.9) between July 2002 to Jun 2018 were included in the analysis. Pts were split into 2 mutually exclusive cohorts of incident RA-ILD pts (Pts having ≥1 ILD diagnosis before and after the chest X-ray/CT scan/Lung Biopsy/Pulmonary Function Test conducted post first RA diagnosis) and RA only patients (no ILD diagnosis in the study period). All-cause healthcare resource use and costs were calculated for the 12 months prior to and 12 months after diagnosis in both cohorts. Statistical differences between the RA-ILD

and RA only cohort were assessed using chi-square and Kruskal-Wallis tests with significance level of 0.05. For the incident RA-ILD cohort, an additional McNemar and Wilcoxon sign rank tests was conducted for the comparion between per and post ILD diagnosis period with significance level of 0.05.

Results: A total of 8,214 incident RA-ILD pts and 104,101 RA only pts were included in the analysis. RA-ILD pts were significantly older, had more comobididities and a lower percentage of female as compared to RA only patients (Table 1). In RA-ILD pts, all healthcare service use including inpatient visits, length of hospital stay, outpatient visits, pharmacy prescriptions increased significantly after the diagnosis of ILD for the RA-ILD cohort, resulting in a 74% increase in all-cause cost. (Table 2) Compared with RA only pts, RA-ILD pts showed a statistically greater increase in overall and all components of healthcare use over the study period (Table 3). The increase of all-cause medical cost was $20,444 higher in RA-ILD pts, primarily driven by the increase in the inpatient and outpatient cost.

Conclusion: RA-ILD pts had a substantial increase in healthcare resource utilization and a nearly doubled medical cost after the diagnosis of ILD. The greater cost was primarily driven by the higher use of inpatient and outpatient service. This indicates the need of more targeted treatment strategy to prevent ILD and improve clinical and economic outcomes of RA-ILD pts.

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Abstract Number: 0255

Designing and Testing Treat to Target as a New Care Model in JIA Across a Network of Pediatric Rheumatology Centers

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Background/Purpose: In 2018 an international task force published a recommended Treat to Target (T2T) approach to juvenile idiopathic arthritis (JIA) treatment. In February 2019, 17 centers participating in the Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) began a collaborative improvement project using quality

Figure 1. Network aggregate and one example centers' progress on Step 1

Step 1 Standardized assessment and review of components of the clinical juvenile arthritis disease activity score (cJADAS10)

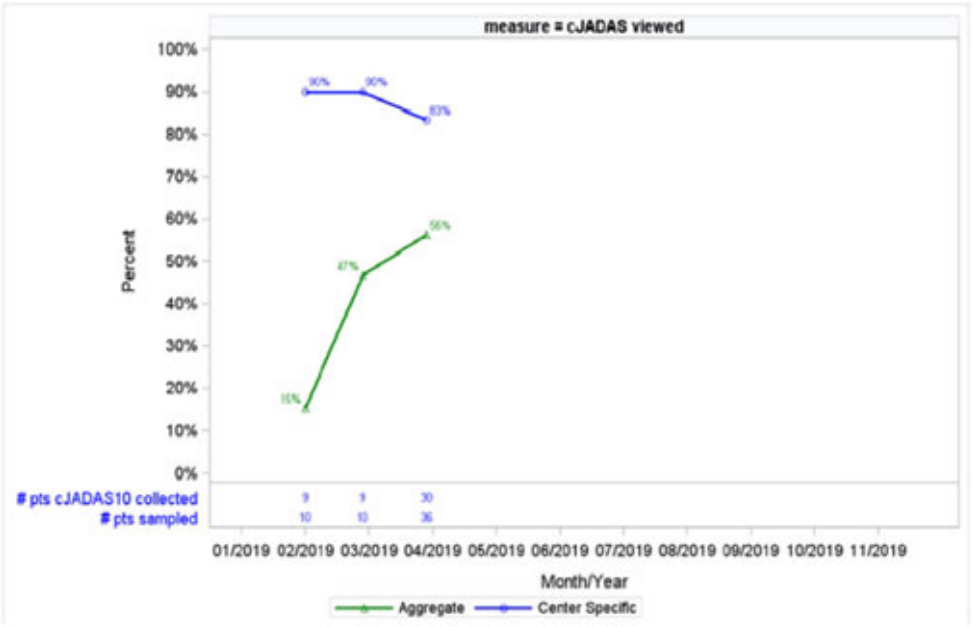
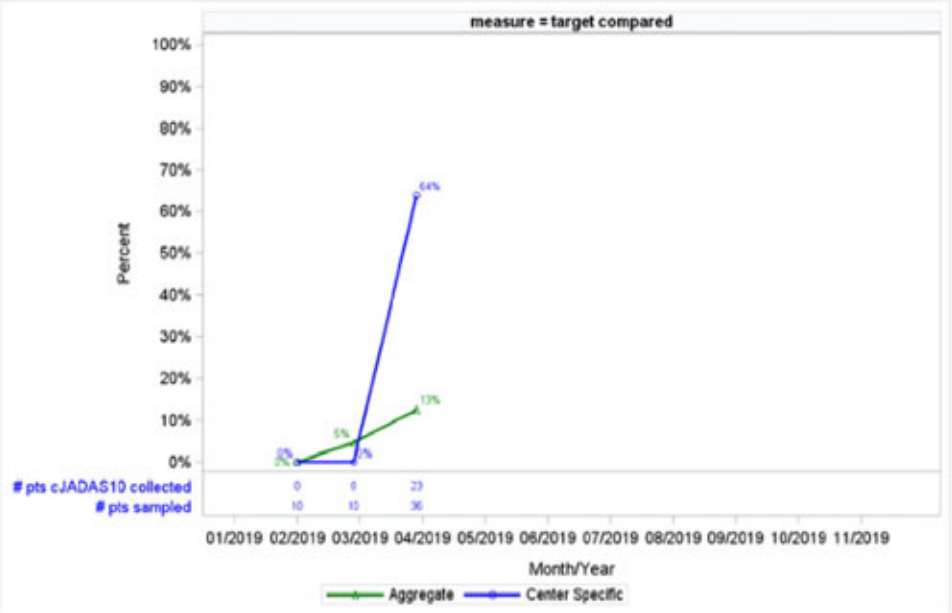


Figure 2. Network aggregate and one example centers' progress on Step 2

Step 2 Use shared decision making (SDM) concepts to select treatment target with the family and compare it to current disease activity



improvement (QI) methods to test and implement T2T interventions. Based upon published literature and one center pilot experience, PR-COIN designed an approach to introduce interventions to support successful and reliable deployment of three T2T component processes: standardized disease activity assessment, setting a treatment target with patient/family, and use of polyarticular JIA (Poly-JIA) clinical decision support (CDS). Our objective is to implement T2T with high reliability in 80% of PR-COIN centers by October 2019.

Methods: With patient/family partners, PR-COIN co-produced educational materials to train providers on implementation of T2T and to introduce families to the concept. The network adapted an evidence and consensus-based treatment algorithm, and designed a step-by-step implementation plan to support local implementation with a data submission platform to evaluate the interventions. Interactive monthly webinars feature best practices and performance reports, and QI/T2T process coaching. The interventions are being implemented in three steps: 1) standardized assessment and review of components of the clinical juvenile arthritis disease activity score (cJADAS10), including the physician global assessment, active joint count, patient assessment, 2) use shared decision making (SDM) concepts to select treatment target with the family and compare it to current disease activity and 3) use of CDS. Sites progress to the next step once reliable process implementation (>80%) is demonstrated in a representative sample of patients with Poly-JIA.

Results: As of April 2019, 16 centers are participating. All centers completed on-site training, 9/16 (56%) submitted at least one QI tool, and 11/16 (69%) eligible centers submitted performance data. A sample of patient-level data indicate 157/279 (56%) of patients are receiving Step 1 activities (Figure 1). Four of the sixteen centers (25%) are performing Step 1 activities with high reliability and have progressed to Step 2, with 4 / 35 (13%) of sampled patients engaged in SDM to set treatment targets (Figure 2). Figures show aggregate data alongside an example single center performance. Centers are demonstrating progressive improvement over time towards the reliability criteria to full implementation of T2T and performance goals.

Conclusion: Introduction of novel interventions required for fidelity of T2T implementation in pediatric rheumatology clinical practice requires a tiered approach with demonstrated commitment from trained providers, buy-in from leadership, and an identified QI lead. Co-producing support materials with families, infrastructure to support QI, and reliable data submission are key to success. We predict that center-level cJADAS10 improvement will correlate with reliability of the implementation of interventions.

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Abstract Number: 0256

Chronic Musculoskeletal Pain and Its Initial Management in Children, Adolescents and Young Adults in the United States

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Background/Purpose: Chronic musculoskeletal pain can affect up to 20% of persons under the age of 25 and is a risk factor for persistent chronic musculoskeletal pain in adulthood. Among those who consult a physician, prescribed treatment approaches vary and can be pharmacologic and nonpharmacologic. The goal of this study was to investigate chronic musculoskeletal pain in young people. Specifically we sought to 1) present a portrait of persons with chronic musculoskeletal pain in terms of sex, race/ethnicity, smoking status, and the various diagnoses related to chronic musculoskeletal pain in a representative sample of young Americans; 2) describe the initial clinical management of chronic musculoskeletal pain in this group; and 3) explore factors associated with prescribed treatments.

Methods: We analyzed data from the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey-Out Patient Department (NAMCS) between 2007 and 2015. Visits among persons under the age of 25, with a new chronic musculoskeletal pain condition were identified using pre-determined diagnostic criteria. We documented the following treatment prescriptions: opioids, non-opioid pain medication, physical therapy, counseling and other non-pharmacological treatments. We describe the sample according to sex, age group (< 15 and 15-24), race/ethnicity, payment type for services (serving as a proxy for socioeconomic status), and type of physician (pediatrician, family doctor, specialist). Logistic regression models to determine factors associated with treatment prescription will be calculated.

Results: There were 1,316 initial visits over the 9-year period with a diagnosis of chronic musculoskeletal pain in the NAMCS database for persons under the age of 25, translating into 32,423,549 weighted initial visits, for a frequency of 3.4% of Americans < 25 years of age. Opioid prescription was low for those under the age of 15 years at 1.2% but increased to 13.9% in the 15-24 year old group. Non-opioid pain medications were prescribed in 33.2% of the cases for the younger group and 40.6% in the older group. The proportions prescribed physical therapy, counseling and other nonpharmacological treatments were respectively, 6.3%, 8.3% and 15.4% in those under 15 years and 13.6%, 10.4% and 9.4% in those 15-24 years.

Conclusion: Nearly 3.5% of young Americans consult a physician for a **c**hronic musculoskeletal pain condition. Pharmacologic treatment is used much more than nonpharmacologic treatment, and opioid prescription in the adolescent and young adult group nears estimates of opioid prescription in adults with these problems. Reasons for the low use of nonpharmacologic treatments need to be elucidated.

Disclosure: D. Ehrmann Feldman, None; **R. Nahin**, None.

Abstract Number: 0257

Alcohol Use Hospitalizations in People with Gout, Osteoarthritis, Rheumatoid Arthritis, Fibromyalgia, and Low Back Pain Are Increasing: A Time-trends Study Using the U.S. National Data

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Background/Purpose: Alcohol abuse and associated mortality is an important public health problem in the U.S. To our knowledge, limited data are available on alcohol use disorder-related hospitalizations in people with common musculoskeletal diseases.

Methods: We used the U.S. National Inpatient Sample (NIS) data from 1998-2014 to examine the rates of alcohol use disorder-related hospitalizations without overdose, detoxification or rehabilitation services, based on the presence of International Classification of Diseases, Ninth or Tenth Revision, Clinical Modification (ICD-9-CM or ICD-10-CM) diagnostic codes for alcohol dependence or abuse in the primary diagnosis position. We assessed five common rheumatic diseases using the respective diagnostic codes in a secondary position: Gout, rheumatoid arthritis (RA), fibromyalgia, osteoarthritis (OA), and low back pain (LBP). Incidence of alcohol use disorder claims was assessed per 100K NIS claims overall.

Results: The incidence of alcohol use disorder-related primary hospitalizations was low in 1998-2000 for the five musculoskeletal conditions and increased over the 19-year study period (**Table1**). The increase was 2-fold higher in people with gout, osteoarthritis or LBP, 2.5-fold for RA versus 3-fold higher in people with fibromyalgia. Rates of alcohol use disorder per 100K total NIS claims showed similar trends, with an increase ranging 3-fold in people with

Table 1. Number of alcohol use disorder as the primary reason for hospitalizations from 1998 to 2016 by five common musculoskeletal diseases

	Gout	OA	Fibromyalgia	RA	Low Back Pain
1998 - 2000	5.69	8.09	1.36	1.82	4.93
2001 - 2002	6.27	10.06	1.64	2.27	6.36
2003 - 2004	6.12	11.08	1.69	1.74	6.93
2005 - 2006	7.30	12.03	2.25	2.23	8.59
2007 - 2008	9.95	15.33	3.15	2.84	10.62
2009 - 2010	12.63	17.97	3.82	3.14	12.93
2011 - 2012	15.24	20.80	5.31	4.22	15.34
2013 - 2014	16.82	21.70	6.58	4.65	16.45
2015-2016	17.02	28.32	6.15	5.06	14.05
% change	199.4%	250.2%	351.0%	177.8%	185.0%

Table 2. Rate of alcohol use disorder primary hospitalizations from 1998 to 2016 per 100k total NIS claims by five common musculoskeletal diseases

	Gout	OA	Fibromyalgia	RA	Low Back Pain
1998 - 2000	5,894	8,382	1,414	1,888	5,112
2001 - 2002	4,550	7,308	1,194	1,646	4,621
2003 - 2004	4,566	8,265	1,259	1,298	5,168
2005 - 2006	5,545	9,136	1,710	1,692	6,522
2007 - 2008	7,595	11,709	2,406	2,165	8,109
2009 - 2010	9,482	13,490	2,865	2,355	9,709
2011 - 2012	11,191	15,280	3,899	3,101	11,268
2013 - 2014	11,935	15,395	4,670	3,300	11,675
2015-2016	12,160	20,230	4,395	3,615	10,040
% change	106.3%	141.4%	210.8%	91.5%	96.4%

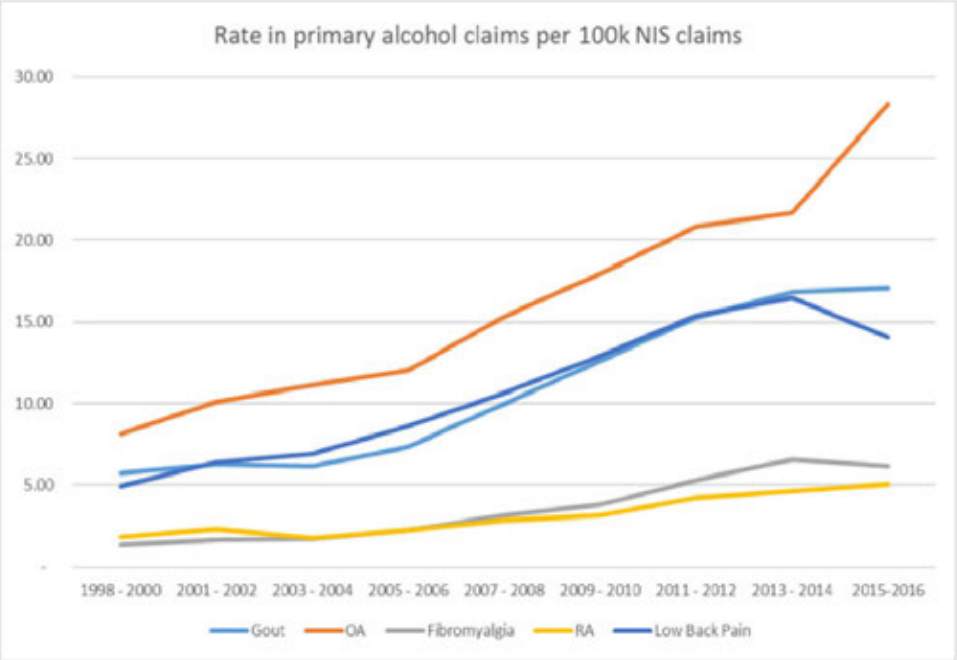

Figure 1. Trends in rates of primary alcohol abuse claims per 100K NIS claims, by five musculoskeletal conditions

gout, osteoarthritis, LBP or RA to 4.5-fold in people with fibromyalgia (**Table 2**). There was a plateauing of alcohol use disorder claims for all conditions except osteoarthritis (**Figure 1**).

Conclusion: The rate of increase in alcohol use disorder hospitalizations occurred in all 5 musculoskeletal conditions, but the rate differed by the condition. Providers need to counsel their patients with these musculoskeletal conditions regarding the risk and impact of alcohol use, in order to prevent associated morbidity and mortality. Findings are also important for policy makers with regards to resource allocation.

Disclosure: J. Singh, Amarin pharmaceuticals, 1, 4, Clearview healthcae partners, 5, Clearview healthcare partners, 5, Clinical Care options, 5, Horizon, 5, Medisys, 5, OMERACT, 6, Putnam associates, 5, Spherix, 5, the American College of Rheumatology, 5, The American College of Rheumatology, 5, The National Institues of Health, 5, the National Institutes of Health, 5, Viking therapeutics, 1, 4, WebMD, 5; **j. Cleveland**, None.

Abstract Number: 0258

Health Services Utilization as Recommended by the American Diabetes Association Among Middle-Aged Patients Disabled with Rheumatoid Arthritis and Diabetes Mellitus

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Background/Purpose: Medicare beneficiaries who are disabled (coverage by the Social Security Disability Insurance (SSDI)) with rheumatoid arthritis (RA) and diabetes mellitus (DM) and under 65 years of age are complex patients with heavy healthcare use. These young disabled patients cost 31% more than older Medicare patients, but we do not know whether they are receiving the basic standards of diabetes care given their disability and complexities related to also having RA. Our purpose was to assess the standard of care for diabetes measured by health services utilization in patients under 65 years of age who are disabled with RA and DM by race and ethnicity.

Methods: We conducted a longitudinal analysis from 2010– 2014 of patients who were beneficiaries of the SSDI with both RA and DM. RA was defined in 2010 as either 1) two RA diagnoses (ICD9-714.xx) by a rheumatologist between 7 and 365 days apart; OR 2) one RA diagnosis by a rheumatologist and at least 1 prescription for a disease modifying anti-rheumatic drug. DM was defined as one diagnosis from any physician (ICD-9 250.xx) in 2010. Patients were followed for 4 years (2011 – 2014) and outcomes were the testing and visit standards defined by the 2010 American Diabetes Association. We used Poisson models to adjust for age, gender, and Charlson-Deyo Comorbidity Index and examined the differences between racial/ethnic groups.

Results: In 2010, there were 5,380 patients under the age of 65 disabled with RA and DM receiving SSDI benefits. The cohort was 78% female and 61% had 5 or more comorbidities. These patients had high health services utilization with a mean number of visits to the doctor of about 18 visits a year (Table 1). More than half (53.5%) of all patients did not receive a foot exam and almost a quarter (23.3%) did not receive an eye exam in 2011-2014. After multivariable

Table 1. Unadjusted Annual Mean of Services Utilization According Standards of Diabetes Care for Medicare SSDI recipients (Disabled) under 65 years with Rheumatoid Arthritis and Diabetes in 2011 - 2014

Standards of Diabetes Care	White N = 3,281	Black N = 1,119	Hispanic N = 742	Other N = 238	Total N = 5,380
Total HbA1c tests					
Annual Mean+	2.11	2.07	2.28	1.80	2.11
None (%)*	6.2	5.1	4.7	16.8	6.2
Total Lipid Tests					
Annual Mean+	1.61	1.63	1.89	1.43	1.65
None (%)*	5.2	2.9	2.8	16.0	4.9
Total Urine Albuminuria tests					
Annual Mean+	1.54	1.68	2.00	1.40	1.62
None (%)*	13.8	10.7	7.5	20.6	12.6
Total Eye Exams					
Annual Mean+	0.77	0.95	1.01	0.82	0.85
None (%)*	25.3	20.2	20.1	19.7	23.3
Total Foot Exams					
Annual Mean+	1.19	1.05	0.99	0.82	1.12
None (%)*	55.5	47.1	53.1	57.1	53.5
Total visits (Evaluation and Management)					
Annual Mean+	17.62	17.95	18.06	17.03	17.72
Total visits to Rheumatologist					
Annual Mean+	2.82	3.06	3.23	2.87	2.93
None (%)	6.9	6.1	5.9	7.6	6.6
Total visits to Primary Care†					
Annual Mean+	4.85	4.91	5.40	4.94	4.94
None (%)*	5.6	4.9	8.4	5.0	5.8

* Significant Chi square test ($p < 0.05$)

+ Total tests over 4 years averaged (divided by 4)

†Primary care was defined as family medicine and internal medicine

Table 2. Adjusted Annual Means of Testing and Visits for Standards of Diabetes Care among Medicare SSDI (Disabled) recipients under 65 years with Rheumatoid Arthritis and Diabetes in 2011 - 2014

	Cohort in 2010 followed from 2011 to 2014		
Race/Ethnicity++	White N = 3,281	Black N = 1,119	Hispanic N = 742
Annual mean of HbA1c Tests	2.19 (2.03 - 2.37)	2.14 (1.96 - 2.33)	2.39 (2.18 - 2.61)*
Annual mean of Urine Albuminuria Tests	2.28 (2.10 - 2.48)	2.40 (2.15 - 2.61)	2.80 (2.53 - 3.09)*
Annual mean of Lipid Tests	1.67 (1.54 - 1.81)	1.70 (1.55 - 1.85)	1.96 (1.79 - 2.15)*
Annual mean of eye exams	0.88 (0.79 - 0.98)	1.03 (0.91 - 1.17)*	1.16 (1.12 - 1.32)*
Annual mean of foot exams	1.18 (0.95 - 1.46)	1.04 (0.83 - 1.32)*	1.01 (0.80 - 1.29)*
Annual mean of visits (Evaluation and Management)	19.19 (18.21 - 20.23)	19.15 (18.04 - 20.32)	19.97 (18.76 - 21.25)
Annual mean of visits to rheumatologist	2.69 (2.48 - 2.92)	2.88 (2.63 - 3.14)*	3.08 (2.81 - 3.38)*
Annual mean of visits to primary care†	5.36 (4.81 - 6.21)	5.35 (4.88 - 5.87)	6.03 (5.47 - 6.64)*

+ Poisson model to estimate the counts, adjusted for age, gender, and Charlson-Deyo Comorbidity Index
++ Race/Ethnic category of Other were dropped from the tables to improve readability
*Indicates significant difference with White group, $p<0.05$

adjustment, Hispanic patients had a statistically significant higher annual mean of testing (HbA1c 2.39 vs 2.19, urine albuminuria 2.8 vs 2.28, and lipid 1.96 vs 1.67) than White patients in 2011-2014 (Table 2). Both Hispanic and Black patients had a higher annual mean of eye exams (1.16 and 1.03, respectively, vs 0.88) but lower annual mean of foot exams (1.01 and 1.04, respectively, vs 1.18) than the White patients.

Conclusion: Disabled patients with RA and DM had high utilization of health services and received most of the recommended standard of care for diabetes, which was similar across all racial/ethnic groups. The exception was for eye exams, which was lower among Whites. However, there was low utilization of specialty services related to DM care such as ophthalmology evaluations or foot exams by any physician.

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Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **I. Navarro-Millan**, None.

Abstract Number: 0259

Describing Treatment Patterns and Healthcare Costs in Newly Diagnosed Psoriatic Arthritis Patients by Physician Specialty

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Table 1. Patient Characteristics of Early Vs. Untreated/Delayed Treated (N = 3,520)

	Delayed/Non-Treatment*		Early Treatment	
	N = 1,588		N = 1,932	
Provider Type	**N/Mean**	**%/SD**	**N/Mean**	**%/SD**
Rheumatologist + Dermatologist	1	0.0%	21	1.1%
Rheumatologist	683	19.4%	1257	65.1%
Dermatologist	144	4.1%	124	6.4%
Primary Care Physician	68	1.9%	379	19.6%
Non-traditional	692	19.7%	151	7.8%
Gender				
Male	679	19.3%	874	24.8%
Female	909	25.8%	1058	30.1%
Age	50.4	12.9	49	11.7
18-34	200	5.7%	238	6.8%
35-44	297	8.4%	409	11.6%
45-54	445	12.6%	639	18.2%
55-64	471	13.4%	519	14.7%
65-74	125	3.6%	97	2.8%
75+	50	1.4%	30	0.9%
Baseline Comorbidities				
Anxiety	238	6.8%	296	8.4%
Depression	178	5.1%	212	6.0%
Cardiovascular Disease	814	23.1%	997	28.3%
Type 1 Diabetes	39	1.1%	32	0.9%
Type 2 Diabetes	251	7.1%	286	8.1%

**Patients in the early treatment group-initiated therapy with either an OSM, biologic, or newer OSM within 90 days of the index PsA diagnosis claim. Patients in the delayed/non-treatment group either initiated treatment sometime following the initial 90-day period post-index or did not initiate treatment during the 12-month follow-up period.*

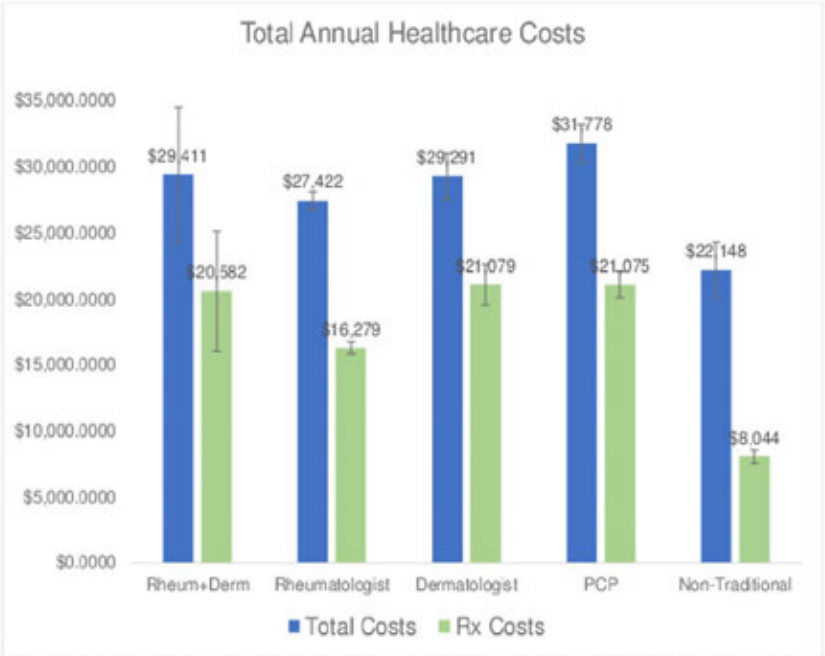
Background/Purpose: The clinical heterogeneity of psoriatic arthritis (PsA) presents a variety of diagnostic and treatment challenges, which may be reflected in the way different health care providers approach the treatment of their patients. Differences in clinical practice between physician specialties may have lasting consequences on patient health outcomes, though there is a dearth of real-world evidence available on the topic.

Objective: To describe treatment patterns and healthcare costs between PsA patients stratified by their treating provider's specialty.

Methods: This study used administrative claims from the IBM® MarketScan® commercial and supplemental Medicare databases from 2014-2017. The sample included patients ≥18 newly diagnosed with PsA (first diagnosis=in-

Table 2. Pharmacologic Treatment Utilization (N = 1,932)

	Rheum+Derm N = 21		Rheumatologist N = 1,257		Dermatologist N = 124		PCP N = 379		Other N = 151		All N = 1,932	
Oral Small Molecules (OSMs)	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Methotrexate	11	52.4%	690	54.9%	34	27.4%	193	50.9%	81	53.6%	1009	52.2%
Other	0	0.0%	176	14.0%	1	0.8%	59	15.6%	28	18.5%	264	13.7%
TNFi and other Biologics												
Adalimumab	7	33.3%	199	15.8%	46	37.1%	63	16.6%	21	13.9%	336	17.4%
Etanercept	0	0.0%	120	9.5%	17	13.7%	36	9.5%	12	7.9%	185	9.6%
Infliximab	1	4.8%	24	1.9%	2	1.6%	4	1.1%	4	2.6%	35	1.8%
Other	0	0.0%	22	1.8%	11	8.9%	10	2.6%	1	0.7%	44	2.3%
Newer Oral Small Molecules												
Apremilast	2	9.5%	76	6.0%	15	12.1%	26	6.9%	12	7.9%	131	6.8%



Note: Annual healthcare costs include medical services (hospitalization, ER visits. Physician office visits, and other outpatient services). Total costs equal all medical services plus all outpatient prescription costs.

Figure 1. Mean Total Annual Healthcare Costs by Provider Group

dex date) with continuous plan enrollment for 12 months both preceding and following index date, an absence of infectious diseases, cancer, and any additional autoimmune disease excluding psoriasis, and an absence of any pharmacologic treatments indicated for PsA during the pre-index period. Patients treated with a medication for PsA were assigned to a physician specialty as observed during the 30-day period preceding the earliest medication claim. Patient not treated with PsA medications within the first 90 days after diagnosis were assigned to the provider listed on their diagnostic index claim. One-year outcomes included medication utilization including switching rates, and healthcare expenditures. Descriptive analyses were conducted by provider specialty and medication and included measures of central tendency and dispersion.

Results: 3,520 patients qualified for the study; the majority were female (56%) with an average age of 49.7. Of all rheumatologist's PsA patients, about two thirds (65%) had early pharmacologic treatment, in contrast to approximately 46% of dermatologist's patients (*p*s < 0.001). Of those with a medication, about 55% of these were prescribed by a rheumatologist; 8% by a dermatologist; < 1% by combination of both; 13% by a primary care provider (PCP); and 24% by others (e.g., pain management, physical medicine & rehab, etc.) (Table 1). Dermatologists were more likely to prescribe a TNFi (73%) compared to remaining provider groups (ranges 33%-48%; *p*s < 0.001) (Table 2). Mean total annual prescription and healthcare expenditures exhibited great variation for all provides, with rheumatologists and dermatologists having similar total costs despite lower prescription costs for rheumatologists (Figure 1).

Conclusion: There is significant variation in the pharmacologic treatment for PsA by different physician specialties. Our findings begin to uncover the impact of rheumatology practice patterns compared to other specialties. While more research is needed to confirm the findings, they highlight potential differences between rheumatologists and other physicians in managing costs and adherence to the recommended clinical guidelines for the management of PSA.

Disclosure: J. Tkacz, Amgen, 5; **E. Maksabedian**, Amgen, 1, 3, 4; **P. Chan**, Amgen, 5; **B. Limone**, Amgen, 5; **A. Ogdie**, Abbvie, 5, 8, Amgen, 5, 8, BMS, 5, Celgene, 5, 8, Corrona, 5, Lilly, 5, Novartis, 2, 5, 7, Pfizer, 2, 5; **E. Karis**, Amgen, 1, 3, Amgen Inc., 3, 4; **B. Stolshek**, Amgen, 1, 3, 4, Amgen, Inc, 3, 4.

Abstract Number: 0260

Rheumatoid Arthritis Associated with Longer Hospital Stays in Patients Admitted with Venous Thromboembolism: A Nationwide Analysis 2010-2014

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research Poster I – ACR/ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM.

Background/Purpose: Venous thromboembolism (VTE) is a major health problem and can be potentially fatal when complicated by lethal pulmonary embolism (PE). Previous hospital-based studies have reported an increased risk of VTE among hospitalized patients with rheumatoid arthritis (RA), particularly in the first year after admission for RA (1). The relative risk of VTE in patients with RA hospitalized for other causes besides joint surgery was 1.99. (2) Data describing differences in mortality and morbidity of patients with a history of rheumatoid arthritis is limited in current

Table 1: Baseline Characteristics of patients with Venous thromboembolism National Inpatient Sample 2010-2014

Characteristics	VTE patients without RA	VTE patients with RA	P value
Age in years (Mean ± SE)	63.19±0.06	68.42±0.17	<0.001
Female [%]	52.16	73.86	<0.001
Males [%]	47.84	26.14	<0.001
Race [%]			<0.001
White	73.11	75.52	
African american	17.23	15.39	
Hispanic	6.14	6	
Asian/pacific islander	0.92	0.49	
Native american	0.44	0.85	
Other	2.16	1.75	
Charlson category (%)			<0.001
0	39.96	0	
1	22.44	35.61	
2	14.94	26.46	
3	8.21	17.47	
>=4	14.44	20.46	
Insurance (%)			<0.001
Medicare	54.88	69.91	
Medicaid	9.69	6.44	
Private	29.94	21.96	
Self-pay	5.29	1.69	
Mean income (%)			0.01
1-38,999	28.81	28.98	
39000-47999	25.86	27.04	
48000-62999	24.22	24.37	
>63000	21.1	19.61	
Hospital bed size (%)			0.60
Small	14.84	14.4	
Medium	26.59	26.85	
Large	58.57	58.76	
Teaching status of hospital (%)			<0.001
Non-teaching	53.78	56.47	
Teaching	46.22	43.53	
Hospital region (%)			<0.001
Northeast	18.75	15.92	
Midwest	24.97	26.17	
South	39.43	41.23	
West	16.85	16.68	

literature. In our study, we discuss the potential impact on mortality, length of stay, and cost of hospitalization in patients admitted with VTE with a history of RA.

Methods: We analyzed hospitalizations for VTE (both Deep Venous Thrombosis and PE) among adults in the Nationwide Inpatient Sample (NIS). Patients were stratified into two groups based on the status of RA; using ICD-9 CM diagnostic codes. Descriptive statistics were represented as means/medians for continuous and as frequencies and percentages for categorical variables. A survey weighted multivariate regression analysis was used to adjust for confounders when comparing mortality, length of stay, and total charges.

Results: A total of 1,481,777 admissions with a primary diagnosis of VTE were identified from 2012-2014, and amongst these patients, 33,152 patients had an underlying diagnosis of RA. Patients with underlying RA were older (average age 68.42years vs. 63.19 years), more often females (73.86% vs. 52.16%), and had multiple comorbidities, as described in Table 1. Patients with RA had a significantly longer length of stay (LOS) compared to those without RA (Avg LOS 5.1 days vs. 4.9 days, p value=0.00), but mortality rates were lower in this population (1.67% vs. 2.01%,p value=0.05).

Conclusion: VTE is a major healthcare burden in the US population, and RA has been associated with an increased risk of VTE. Endothelial dysfunction in inflammatory diseases accelerates microvascular thrombosis cascade. Even though RA may not affect the mortality in patients with VTE, this study shows increased morbidity with increased length of stay and cost per hospitalization. Hospitalized RA patients should be evaluated for known risk factors for VTE and should be initiated on VTE prophylaxis at admission unless contraindicated. We also recommend additional analytic studies in other databases to confirm these findings, further quantify the risks, and also develop appropriate monitoring and prophylactic strategy in the hospitalized RA population.

Disclosure: S. Jatwani, None; **K. Jatwani**, None; **K. Chugh**, None.

Abstract Number: 0261

Impact of Rheumatoid Arthritis on Outcomes of Atrial Fibrillation: Results for National Inpatient Sample

Shraddha Jatwani,[1] Karan Chugh,[1] Bikramjit Bindra,[2] and Karan Jatwani[3], [1]St. Vincent Evansville, Evansville, [2]Government Medical College & Hospital, Chandigarh, India, [3]Mount Sinai West - St Luke's Hospital, New York

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research Poster I – ACR/ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Atrial Fibrillation (AF) is a common cardiac arrhythmia related to increased cardiovascular morbidity and mortality. There is a significant association of systemic inflammation with the pathogenesis of AF. Several studies have assessed the relationship of AF with Rheumatoid Arthritis (RA) with variable results. Some studies suggest 29-40% higher incidence of AF with RA, while others did not find any increased risk of AF in RA. In this study, we used the National Inpatient Sample (NIS) to assess the impact of RA on demographics, mortality, length of stay, and cost per hospitalization for AF in comparison to non-RA hospitalizations.

Methods: Healthcare Cost and Utilization Project's NIS is the largest all-payer inpatient database in the United States with discharge data from >1200 hospitals, located across the nation. We queried the National Inpatient Sample from 2010-2014 to identify adult hospitalizations for AF with and without RA, using validated ICD-9 CM codes. Logistic regression analysis was used to identify independent associations with in-hospital mortality. Multivariate regression was applied to adjust for confounders.

Results: There were an estimated 43910 adult hospitalizations for AF with a secondary diagnosis of RA, from 2010 to 2014. On univariate analysis, the average age for hospitalizations with AF in the non-RA group was 70.03years, whereas, in the RA group, the average age for was 73.26 years ($p< 0.001$). 72.15% of all hospitalizations with AF & RA were females (significantly higher, p-value < 0.001). Unadjusted logistic regression suggested an increased risk of mortality in patients with AF & RA with an odds ratio of 1.297 (p value=0.01), but after adjusting for confounders, a relative decrease in mortality was identified patients with AF & RA (Adjusted Odds Ratio=0.781; p value=0.025). Unadjusted Linear regression for length of stay (LOS) per hospitalization suggested longer length of stay for patients with AMI & RA (3.837 days vs. 3.41 days, p-value < 0.001), but when adjusted for confounders with multivariate regression, LOS was found to be lower (Coefficient = -0.243; p value< 0.001)

Conclusion: This study reports contemporary data of AF & RA hospitalizations over five years in the United States. It suggests that patients with AF and RA have similar and possibly better outcomes for mortality compared to the

Table 1: Baseline Demographics of hospitalizations for Atrial Fibrillation (AF) without and with underlying Rheumatoid Arthritis (RA)

Demographic Characteristics	Adult Hospitalizations for AF without RA	Adult Hospitalizations for AF with RA	p value
Mean Age (in years)	70.03	73.26	<0.001
Sex (%)			<0.001
Male	50.21	27.85	
Females	49.79	72.15	
Race (%)			<0.001
White	82.67	85.19	
African American	8.22	7.34	
Hispanic	5.28	4.69	
Asian/pacific islander	1.34	0.81	
Native American	0.46	0.43	
Other	2.04	1.55	
Charlson Category (%)			<0.001
0	33.53	0	
1	27.4	29.24	
2	17.21	28.39	
3	10.34	19.16	
4	5.79	11.8	
5	2.8	5.88	
>=6	2.93	5.53	
Insurance status (%)			<0.001
Medicare	67.78	80.86	
Medicaid	4.8	2.7	
Private insurance	24.21	15.2	
Self-pay	3.2	1.24	
Median household income for patient's zip code (%)			0.037
0-25th percentile	26.25	25.99	
26th to 50th percentile (median)	26.264	26.76	
51st to 75th percentile	24.82	26.04	
76th to 100th percentile	22.29	21.21	
Hospital location (%)			0.1419
Rural	13.21	13.79	
Urban	86.79	86.21	
Hospital size (%)			0.0432
Small	14.56	14.86	

non-RA population when adjusted for confounding factors like age, gender, and other demographic factors. Further prospective studies are needed to understand the relationship between AF and RA.

Disclosure: S. Jatwani, None; **K. Chugh**, None; **B. Bindra**, None; **K. Jatwani**, None.

Abstract Number: 0262

Outpatient Healthcare Utilization Among Incident Cases of Systemic Sclerosis: Results from a Population-based Cohort (1988-2016)

Caitrin Coffey ,[1] Avneek Singh Sandhu,[2] Cynthia Crowson,[3] Dennis Asante,[1] Eric Matteson,[4] Thomas Osborn,[5] Kenneth Warrington,[6] and Ashima Makol[5], [1]Mayo Clinic, Rochester, MN, [2]kettering health, dayton, OH, [3]Mayo Clinic Rochester, Rochester, [4]Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA, Rochester, [5]Mayo Clinic Minnesota, rochester, MN, [6]Mayo Clinic Rochester, Rochester, MN

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Health Services Research Poster I – ACR/ARP

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a chronic autoimmune disorder which results in multi-organ dysfunction and high morbidity and mortality. There is limited data on healthcare resource usage in patients with SSc. The purpose of this study was to compare healthcare utilization among incident cases of SSc vs age- and sex-matched comparators without SSc.

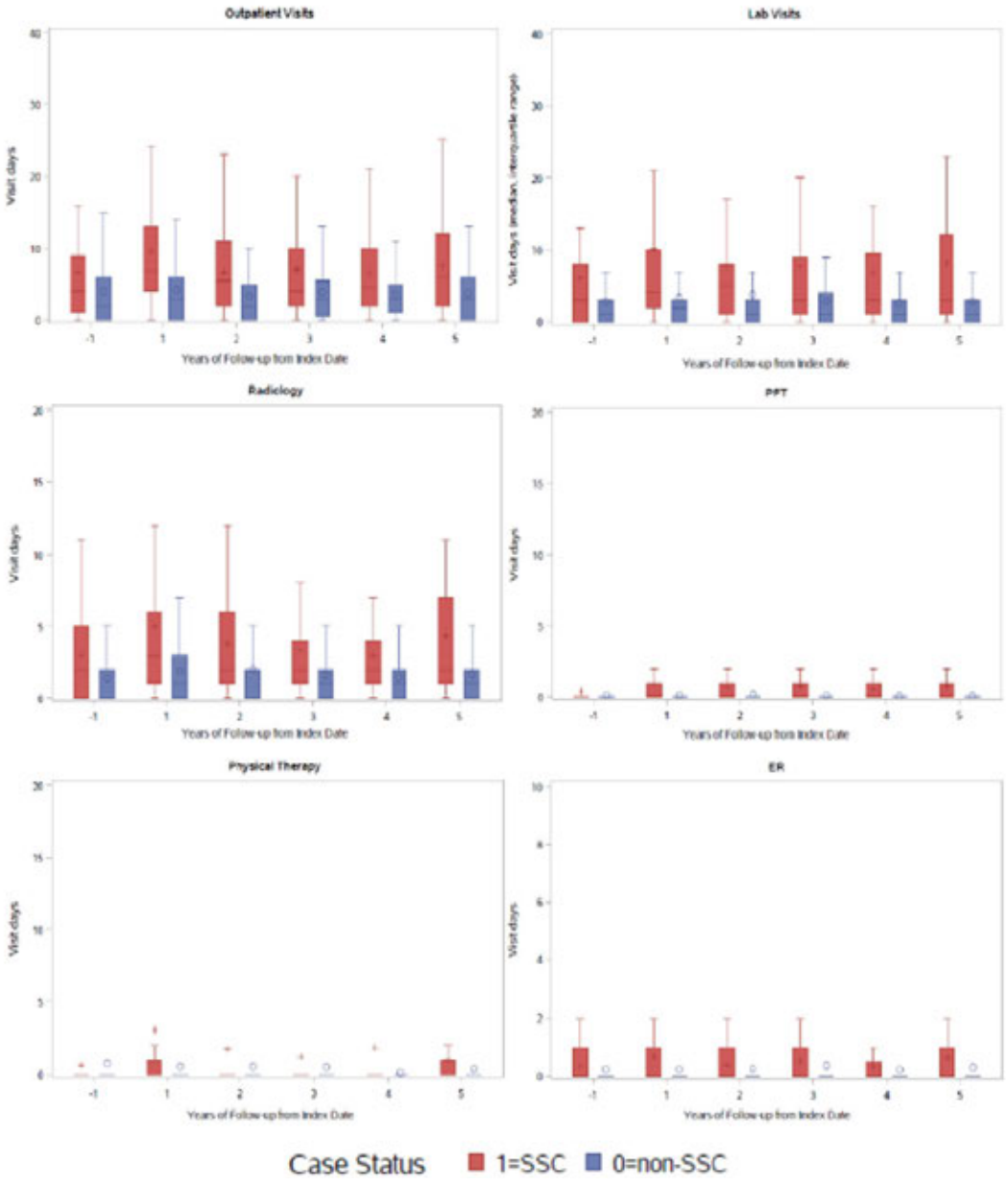
Table. Comparison of outpatient visits, laboratory testing visit-days and imaging visit-days in patients with and without incident systemic sclerosis.

Services	Time Interval (years)	Number of patients, SSc / Non-SSc	SSc Median visit-days (IQR)	Non-SSc Median visit-days (IQR)	Rate Ratio (95% CI)
Outpatient visits	-1-0	69/138	4 (1–9)	2 (0–6)	1.7 (1.1-2.6)
	0-1	69/138	7 (4–13)	3 (0–6)	2.3 (1.7-3.1)
	1-2	66/132	5.5 (2–11)	2 (0–5)	2.1 (1.5-2.9)
	2-3	54/108	4 (2–10)	3 (0.5-5.5-)	1.8 (1.3-2.6)
	3-4	48/96	4.5 (2–10)	3 (1–5)	1.8 (1.3-2.6)
	4-5	43/86	6 (2–12)	3 (0–6)	2.0 (1.4-3.0)
Laboratory testing	-1-0	69/138	3 (0-8)	1 (0-3)	2.1 (1.4–3.3)
	0-1	69/138	4 (2-10)	2 (0–3)	3.0 (2.0–4.6)
	1-2	66/132	5 (1-8)	1 (0–3)	2.0 (1.3–3.2)
	2-3	54/108	3 (1-9)	1 (0–4)	2.6 (1.7–4.3)
	3-4	48/96	3 (1-10)	1 (0–3)	2.7 (1.7–4.1)
	4-5	43/86	3 (1-12)	1 (0–3)	2.9 (1.7–4.7)
Radiology Services	-1-0	69/138	2 (0–5)	0 (0–2)	2.1 (1.6–4.2)
	0-1	69/138	3 (1–6)	1 (0–3)	2.6 (1.8–3.9)
	1-2	66/132	2 (1–6)	0 (0–2)	1.9 (1.8–3.1)
	2-3	54/108	2 (1–4)	1 (0–2)	2.1 (1.3–3.1)
	3-4	48/96	2 (1–4)	1 (0–2)	2.0 (1.3–3.1)
	4-5	43/86	2 (1–7)	1 (0–2)	2.6 (1.6–4.2)

IQR: interquartile range; CI: confidence interval

Methods: A retrospective, population-based cohort of physician-diagnosed patients with SSc in a geographically well-defined area from Jan 1, 1988 to Dec 31, 2016 was assembled. Fulfillment of 2013 ACR/EULAR classification criteria for SSc was ascertained. A 2:1 cohort of age- and sex-matched non-SSc subjects from the same population base was randomly selected for comparison. Outpatient utilization data were obtained beginning 12 months prior to the SSc incidence/index date. Patients were followed until death, migration from the area, or December 31, 2017. A maximum of 5 years following the incidence/index date was used for analysis and the

Figure. Comparison of outpatient visits-days by type of visit between SSc subjects and non-SSc comparators.



ER: Emergency room visit, PFT = Pulmonary function test

follow-up of each matched triple was further truncated at the shortest length of follow-up for any member, to ensure similar periods of observation for SSc cases and non-SSc comparators. Services were summarized as visit-days (number of days at least one service in the category was billed) to avoid overestimation of services provided. Utilization was compared between SSc and non-SSc cohorts using negative binomial and multinomial models.

Results: The cohort included 69 incident SSc cases and 138 non-SSc comparators (mean age of 57 ± 16 years at diagnosis/index, 90% female for both cohorts; 87% [SSc] and 95% [non-SSc] Caucasian). Patients with SSc had the highest utilization of outpatient physician visit-days, laboratory visit-days and combined radiology visit-days during the year of the SSc diagnosis compared with the year prior to diagnosis or years 1 to 4 after diagnosis of SSc (Table, Figure). They also had higher utilization of outpatient physician, laboratory and combined radiology visit-days annually for the year prior to SSc diagnosis and for each of the first 5 years after SSc diagnosis compared to patients without SSc (Table). Rate ratios comparing utilization in patients with and without SSc ranged from 1.8 to 3.0 for all comparisons.

In the year of SSc diagnosis, visit-days specifically for X-rays, computed tomography scan, ultrasound, cardiovascular and gastroenterological testing and procedures, pulmonary function testing, emergency department visit, and physical therapy were higher for SSc subjects than non-SSc comparators, with rate ratios ranging from 2.5 to 13.0. Utilization of magnetic resonance imaging, nuclear medicine imaging, and musculoskeletal procedures were similar between groups in the year of diagnosis.

Conclusion: A higher utilization of outpatient physician visit-days, laboratory visit-days and radiology visit-days was observed among patients with SSc compared to non-SSc subjects throughout 5 years of disease duration, indicating high and continued care needs in this patient population. Highest utilization of services among SSc subjects occurred during the year of SSc diagnosis.

Disclosure: C. Coffey, None; **A. Sandhu**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **D. Asante**, None; **E. Matteson**, Boehringer Ingelheim, 5, Pfizer, 2, Sun Pharmaceuticals, 2; **T. Osborn**, None; **K. Warrington**, Eli Lilly, 2, GlaxoSmith-Kline, 2, roche, 2, 8, Roche, 2, 5, 8, Sanofi, 5, sanofi, 5; **A. Makol**, None.

Abstract Number: 0263

Health Professionals Agreed with Recommendations to Evaluate and Optimize Adherence to Disease-modifying Treatments, but Perceived Feasibility Was Lower: A Study of 357 Physicians and Health Professionals in France

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research Poster I – ACR/ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In chronic inflammatory rheumatic diseases (CIRDs), including rheumatoid arthritis, spondyloarthritis, connective tissue diseases and crystal-induced arthritis, long-term adherence to disease-modifying drugs (DMARDs) is only moderate. In 2017, a group of 105 experts developed recommendations to facilitate the evaluation and management of non-adherence to DMARDs in daily practice [1]. Five overarching principles and 10 recommendations were developed [1].

The objective of this study was to evaluate the agreement of French rheumatologists and health professionals (HPs) with these recommendations, their perceived feasibility/ ease of application and participants' characteristics linked to perceived feasibility.

Methods: Face-to-face meetings were organized across France in 2018 by the program sponsor (Abbvie) with the support of the program committee. During these meetings, the key data and the recommendations were presented and discussed [1]. Participants then informed on paper, their personal data, agreement (from 1 to 5, where 5 is highest) and perceived feasibility (1-5) for each recommendation. Mean agreement and perceived feasibility were calculated for each recommendation. A univariate and multivariate logistic regression identified the characteristics of the participants who rated feasibility the highest (pooled mean above the median).

Results: A total of 38 meetings were held involving 377 physicians/other HPs: 357 (95%) provided analyzable data. The respondents had an average age of 46 years [standard deviation, SD 13]; 223 (63%) were female. Among the 247 (69%) rheumatologists, one third were hospital based (N=90, 37%). Other HPs were nurses (N=81, 23%) or pharmacists (N=14, 4%). Pooled agreement with the overarching principles was very high (mean 4.4 [0.5]). Agreement with the 10 recommendations was also high: pooled mean 4.3 [0.4]; the recommendation with the lowest agreement (mean 3.9 [0.9]) was recommendation 3 on assessing adherence by complex methods. Perceived feasibility was lower (pooled mean 3.4 [0.5]) with a range of means from 2.8 [0.9] (recommendation 3) to 3.9 [0.9] (recommendation 2: assess adherence by an open-ended question). More than 30% of participants rated the feasibility as low (score 1 or 2) for recommendations 3 and 8 (specific intervention in case of non-adherence). The only factor correlated with

greater perceived feasibility was being a HP other than a rheumatologist: odds ratio 2.52 [95% confidence interval 1.23-5.15], while age, gender and type of exercise were not significant. Thus, perceived feasibility seemed higher among non-physician HPs, which may be due to the selection of HPs with a strong interest on patient education.

Conclusion: French HPs are in agreement with recently-published recommendations for the evaluation and optimization of adherence to DMARDs [1]. However, feasibility was lower, especially with regard to complex evaluation of non-adherence, and targeted interventions. This initiative has contributed to the dissemination of the recommendations; the next step will be their implementation. [1] L. Gossec et al. Joint Bone Spine. 2019;86(1):13-19.

Disclosure: L. Gossec, Abbvie, 5, AbbVie, 5, Abbvie, Biogen, BMS, Celgene, Lilly, Novartis, Pfizer, SAnofi-Aventis, UCB, 5, Amgen, 5, Biogen, 5, BMS, 2, 5, Celgene, 5, Celgene Corporation, 2, Janssen, 5, Lilly, 2, 5, MSD, 5, Nordic Pharma, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 5, Sanofi-Aventis, 5, UCB, 5; **A. Moltó**, None; **C. Beauvais**, None; **E. Senbel**, None; **R. Flipo**, Janssen, 8, Novartis, 8; **S. Pouplin**, None; **C. Richez**, astrazeneca, 5, 8, BMS, 5, 8, Glenmark, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8; **A. Saraux**, None; **P. Gaudin**, None; **D. WENDLING**, None; **M. Dougados**, AbbVie, 2, 5, 8, Amgen, 5, Biogen, 5, BMS, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, Merck, 2, 5, Merck Inc, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 0264

Gaps in Patient Safety Performance in Patients with Immunosuppressive Therapy: Results of Screening for Infections and Vaccination Status in a Large Real-life Cohort

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SESSION INFORMATION
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Background/Purpose: Patients with chronic inflammatory rheumatic diseases (CIRD) are known to have an increased risk of infections compared to the general population. Therefore, prevention of infections by vaccination strategies is mandatory. The aim of this study was to evaluate the vaccination status in patients with CIRD.

Methods: Consecutive patients with CIRD were prospectively recruited. Disease characteristics, vaccination status and screening for latent tuberculosis infection (LTBI) and hepatitis B (hepB) were analyzed. Antibodies against measles and hepB were measured. The vaccination status was assessed by a predefined vaccination score (range 0-26): 3 points for a complete vaccination, 2 points for a basic immunization and 1 point for an incomplete vaccination status for tetanus, diphtheria, poliomyelitis or pertussis. For hepB, pneumococcal, influenza, meningococcal, measles, rubella and varicella 2 points were given for a complete vaccination status and 1 point for an incomplete vaccination status. Finally, patients were categorized into 3 immunization states: low (0-6), moderate (7-13), good (14-20) and high (21-26).

Results: A total of 975 patients with CIRD were included (table 1). All patients on bDMARDs (n=499) were screened for LTBI, and 469 also for hepB (94%). Only 16 patients with LTBI received prophylaxis with isoniazid (3.2%) and only

Table 1. Patients characteristics of our cohort

	RA (n=424)	axSpA (n=145)	PsA (n=132)	SLE (n=41)	Other diseases (n=233)
Age, years	60,7 (13,4)	43,7 (12,4)	51,3 (12,7)	48,4 (17,6)	56,1 (16,9)
Gender, male, n (%)	137 (32,3)	95 (65,5)	55 (41,7)	4 (9,8)	64 (27,5)
Current use of bDMARDs, n (%)	163 (38,4)	103 (71,0)	76 (57,6)	9 (22,0)	59 (25,3)
Physical function*	1,30 (0,76)	4,0 (2,55)	1,28 (0,68)	1,12 (0,67)	1,03 (0,69)
CRP (mg/dl), median (IQR)	0,3 (0,1-0,7)	0,2 (0,1-0,6)	0,2 (0,1-0,7)	0,2 (0,0-0,4)	0,3 (0,1-0,6)
Vaccination card available	230 (54,2)	76 (52,4)	66 (50,0)	28 (68,3)	140 (60,1)
Received information about vaccination	273 (64,4)	101 (69,7)	81 (61,4)	28 (68,3)	146 (62,7)
Complete pneumococcal vaccination status	129 (30,4)	33 (22,8)	26 (19,7)	12 (29,3)	66 (28,3)
Complete influenza vaccination status	85 (20,0)	17 (11,7)	20 (15,2)	8 (19,5)	50 (21,5)
Complete hepatitis B vaccination status	36 (8,5)	26 (17,9)	13 (9,8)	10 (24,4)	37 (15,9)

Table 1: Patients characteristics of our cohort

All values are given in mean (SD) otherwise indicated

*Physical function was assessed with HAQ except in axSpA patients in whom the BASFI was used.

16 patients with hepatitis B received prophylaxis with lamivudine (3.4%). The mean anti-HBs titer was 251.1±258.1 IU/l. Protective measles specific IgG-antibodies were found in 901 patients (92.4%). No more than 30% of patients had undergone pneumococcal vaccination and less than 20% were protected against hepB and influenza. Although 629 patients had been educated about vaccination strategies (64.5%), only 540 patients could show a vaccination certificate (55.4%). The mean vaccination score was 12.8±4.9 with 5.3% of patients categorized having a low, 24.3% a moderate, 26.1% a good and 1.8% a high score.

Conclusion: Screening for tuberculosis and hepatitis is successfully implemented in clinical routine in Germany but many patients are not sufficiently vaccinated against pneumococci, hepatitis B, influenza and measles. Our vaccination strategy is based on cooperation with GPs. However, this strategy did not seem to work. The overall rate of successful vaccination was low to moderate although patients received professional information about vaccine strategies.

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Abstract Number: 0265

Frequency of Performing Anti dsDNA Antibody in an ANA Negative Patient with Clinical Suspicion of SLE in a Single Centre Trial Before and After the Publication of National Guideline

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Health Services Research Poster I – ACR/ARP

Session Type: Poster Session (Sunday)

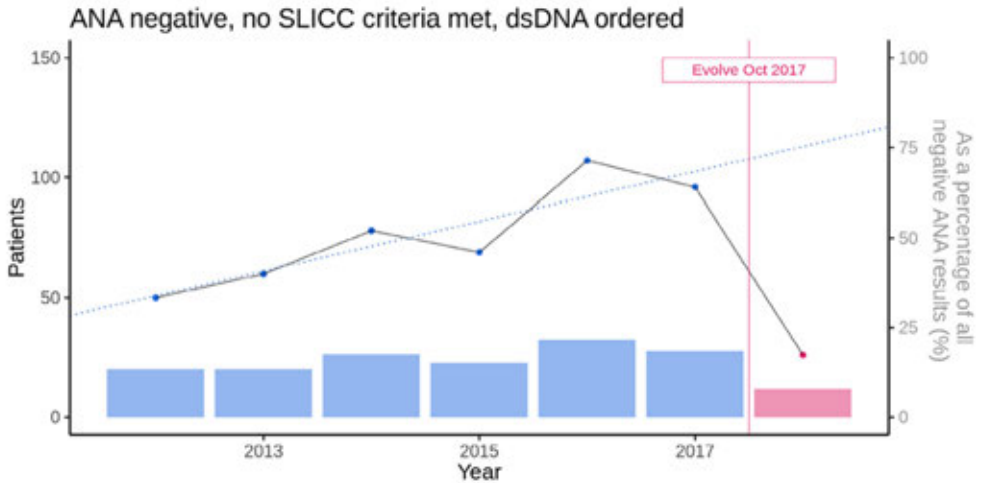
Session Time: 9:00AM–11:00AM

Background/Purpose: In October 2017, the Australian Rheumatology Association widely promoted a list of five recommendations on low-value practices to general clinicians and patients as part of the peer-reviewed Evolve initia-

Table 1. Results

	Jan-Mar 2012	Jan-Mar 2013	Jan-Mar 2014	Jan-Mar 2015	Jan-Mar 2016	Jan-Mar 2017	Jan-Mar 2018	Total
ANA ordered	714	721	784	770	777	782	668	5216
ANA neg	377	451	444	453	495	520	331	3071
ANA neg, anti dsDNA antibody ordered	95	141	120	124	168	180	40	868
ANA neg, anti dsDNA antibody ordered & pos	7	7	2	7	4	6	1	34
ANA neg, anti dsDNA antibody ordered, clinical history available	87	137	108	115	152	168	36	803
ANA neg, at least one SLICC criteria met, anti dsDNA antibody ordered	37	77	30	46	45	72	10	317
ANA neg, no SLICC criteria met, anti dsDNA antibody ordered	**50**	**60**	**78**	**69**	**107**	**96**	**26**	**486**
ANA neg, no SLICC criteria met, anti dsDNA antibody ordered and positive	1	1	2	3	2	1	1	11
ANA neg, no SLICC criteria met, anti dsDNA antibody ordered & >15IU/ml	0	0	0	0	0	0	0	0
ANA neg, anti dsDNA antibody ordered, no SLICC criteria met, anti dsDNA antibody pos relevant to eventual diagnosis	0	0	0	0	0	0	0	0

Figure 1. Reduction of anti dsDNA antibody ordering after publication of national recommendation



tive. One recommendation in keeping with international guidelines suggested avoiding ordering anti-double-stranded DNA antibodies (dsDNA) in anti-nuclear antibody (ANA) negative patients unless there was a high clinical suspicion of Systemic Lupus Erythematosus (SLE). Inappropriate anti dsDNA antibody ordering confers a substantial and unnecessary cost on health resources.

We sought to compare ANA and anti dsDNA antibody ordering practices in a large tertiary teaching hospital before and after the Evolve recommendations were promoted.

Methods: Results of ANA and dsDNA testing ordered through the institutional laboratory of a large tertiary teaching hospital between 2012-2018 inclusive were captured, as were data paired to these tests including age, gender and the ordering medical specialty. Analysis was performed on results ordered between January 1 and March 31 of each year. Retrospective chart review of ANA negative patients with dsDNA testing ordered was performed to review the indication for testing and the presence of component clinical criteria from the Systemic Lupus International Collaborating Clinics Classification (SLICC) Criteria for Systemic Lupus Erythematosus.

Results: A total of 24,501 ANA tests were performed between January 1, 2012 and August 16, 2018. Of these, 5216 patients had ANA tests ordered between January 1 and March 31 in any year, with 3071 having returned a negative ANA result and 803 of these having also had a dsDNA ordered (Table 1). The majority of these patients had no history of any SLICC clinical criteria (486, 60.5%). Very few ANA negative patients who did not meet SLICC criteria had positive dsDNA (14, 2.8%) and all were low titre. None of these dsDNA results were relevant to the patient's eventual diagnosis. There was a marked reduction in dsDNA ordering following the promotion of the Evolve recommendations starting October 2017, from 96 patients during January - March 2017 to 28 patients during Januaryy – March 2018 (Figure 1).

Conclusion: A majority of patients who had dsDNA testing ordered despite a negative ANA result had no clinical features of SLE. There has been a marked reduction in the ordering of dsDNA testing in ANA negative

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Abstract Number: 0266

Measuring Advanced/Extended Practice Roles in Arthritis and Musculoskeletal Care in Canada: Stand up and Be Counted Too (2)!

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SESSION INFORMATION
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Background/Purpose: Arthritis and musculoskeletal disorders are the most common chronic health conditions in Canada but there is a critical and growing shortage of rheumatologists relative to the needs of an aging population. Models of care involving advanced or extended role health disciplines practitioners to augment provision of arthritis care are emerging. Research supports these roles, however there are no studies to date documenting the workforce capacity or learning needs of advanced and extended role health disciplines.

Study Objectives

1. To capture descriptive information on the current workforce practices/attributes of advanced or extended role practitioners (ERPs) working in arthritis care in Canada.
2. To determine perceived opportunities and barriers in the pursuit of formal academic/clinical training to support these roles.

Methods: This Pan-Canadian exploratory cross-sectional self-report study was developed and based on the original Stand Up and Be Counted Rheumatologist Workforce Survey.

Data were collected using anonymous, online questionnaires deployed in early 2018 to groups of non-physician health disciplines professionals across Canada with potential to have undertaken formal and informal post-licensure training in arthritis care. Descriptive statistics were generated to describe the demographics and practice information of the sample. Qualitative responses were analyzed using Grounded Theory techniques.

Results: There were 141 respondents; 91 were identified as practising in an extended role capacity. Respondents were further characterized by profession (PT >OT >RN >Chiropractor/Pharmacist) and by their post-licensure training in arthritis care (ACPAC >CPSIA >ACR >Institutional-apprenticeship >ISAEC). Mean age of ERP respondents was 49±9 years, 87% (n=79) were female, and 41% (n=38) of ERPs planned to retire within 5-10 years. Geographic practice sites were Ontario > Alberta > British Columbia > Newfoundland and practice settings were urban academic (46.2%), community (38.5%) and rural (13.2%). Almost 50% (n=45) of ERPs treated patients with inflammatory arthritis. 54% (n=20) of non-ERP respondents had received some form of advanced training but were not deployed as ERPs; almost all 98% (n=89) of ERP respondents had undertaken advanced training. 95% (n=103) of all respondents agreed that formal training is necessary to work as an ERP but only half (n=52) felt that they had sufficient opportunities to pursue training. Barriers to pursuing training are various: from personal, geographic, and patient-care/patient-needs related, to administrative, post-program recognition and financial/remuneration concerns.

Conclusion: No previous studies have assessed the workforce attributes of non-physician, advanced practice arthritis care providers or the perceived need for the training of ERPs working in arthritis/MSK care. It is important to measure the workforce capacity of these health disciplines practitioners as they evolve and integrate into the Canadian healthcare system.

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Abstract Number: 0267

Develop Risk Prediction Model and Drug Withdrawl Road Map Through Pattern Extraction and Data Mining: Create a Master Algorithm from the Smart System of Disease Management (SSDM)

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SESSION INFORMATION

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Session Title: Health Services Research Poster I – ACR/ARP

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Session Time: 9:00AM–11:00AM

Background/Purpose: Combination therapy with DMARDs for treating RA is considered as a standard of care. However, certain rates of adverse events (AEs) are unavoidable. The stigma are how to predict the risk and how to define drug withdrawl sequence for optimal risk reductions if AEs persist. The decisions made are always empirical. To develop a risk prediction model and an algorithm for drug withdrawl sequence based on data mining from the SSDM

Methods: SSDM is an interactive mobile disease management tool, including two application systems (APPs) for both the doctors and the patients. The patients can input medical records (including medication and laboratory test results) and perform self-evaluation (DAS28, HAQ) via App. The patients' data synchronizes to mobiles of authorized rheumatologists through cloud and doctors' advices could be delivered. In previous studies, we demonstrated that patients could master SSDM after training.

In order to develop a prediction model and the master algorithm, abnormal white blood cell counts (WBC) and alanine aminotransferase (ALT) elevation were targeted. Data was collected, extracted, validated, and Bayesian networking, data mining, modeling were performed. WBC under 4k/ml is defined as leukocytopenia (LP), over 10k/ml as infection predisposing (IP), and ALT > 40 U/L as ALT elevation.

Results: From Jun 2014 to May 2019, 54,149 RA patients from 587 centers registered in SSDM. 135 different drugs and 1,220 combination therapies are identified. LP happens at 341 and IP at 344, ALT elevation at 325 cases in 752 treatment regiments. Among them, MTX based regiments are 291 types, and the risk ratio (RR) are profiled as prediction model by comparing each AE rate of combination regiment with that of MTX monotherapy (Fig 1). The RR ranges from 0.28 to 6.28. The highest risk combination of prednisone (Pred), leflunomide (LEF), methotrexate (MTX), hydroxychloroquine (HCQ) and Celecoxib (Cel) is selected (RR=6.28) to develop a master algorithm. Figure 2 shows Bayesian network, in which, quartet correlates with 31 different regiments. Based on Bayesian method, the probabilities of LP, IP and ALT elevation are plotted through 64 modeling, and the algorithm for drug withdrawl strategies is generated. Drug withdrawl sequence for LP is HCQ, then Cel, then LEF, then Pred, the risks of LP are reduced by 41%, 22% 36% and 15%, respectively. For IP, withdrawl sequence is Pred, then LEF, then Cel, then HCQ, the risks of IP are reduced by 45%, 28%, 23% and 4%, respectively, For ALT elevation, withdrawl sequence is MTX, then Pred, LEF, then Cel, the risks of ALT elevation are reduced by 48%, 8%, 7% and 6%.

Fig.1 AE rate of combination regiment with that of MTX monotherapy.

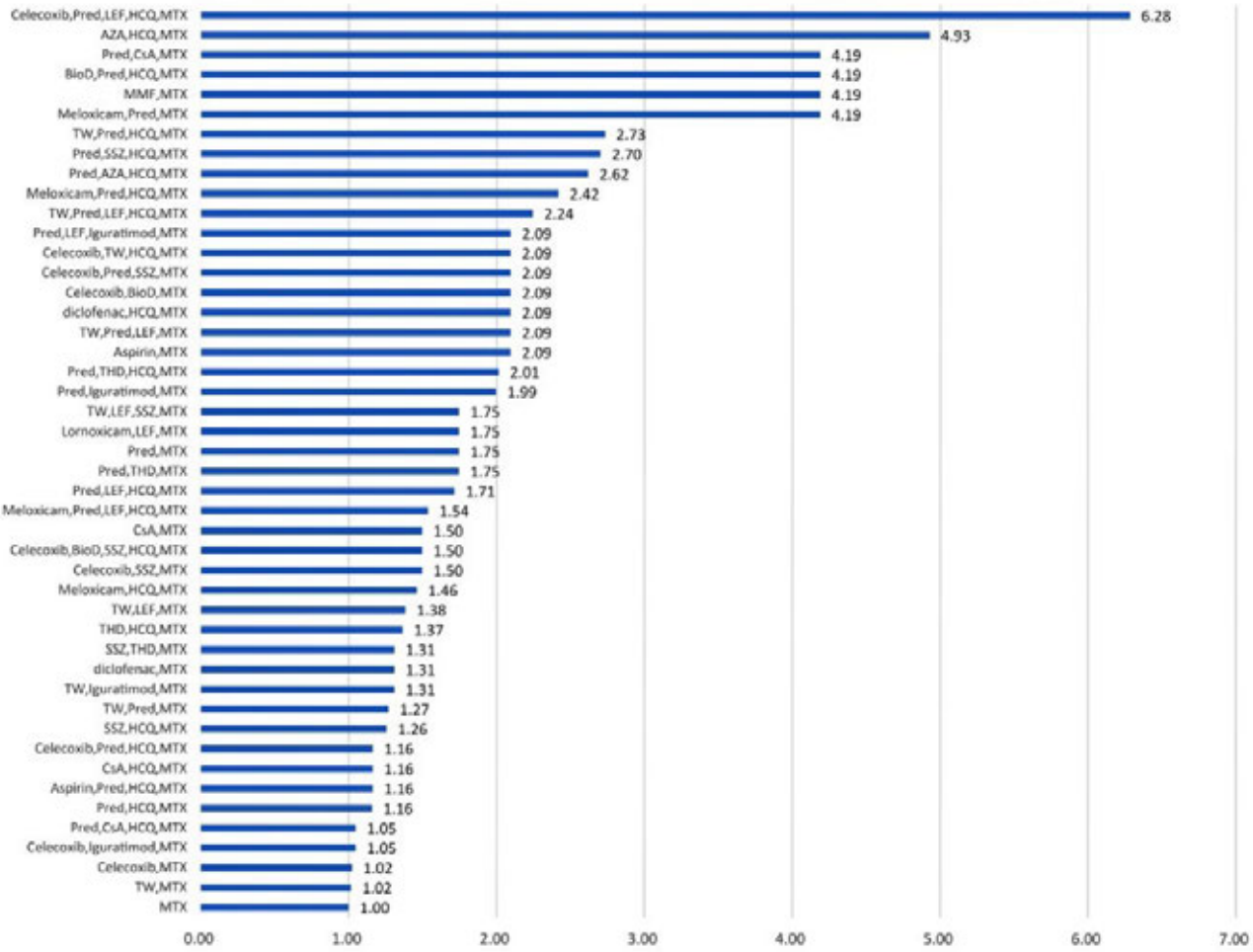
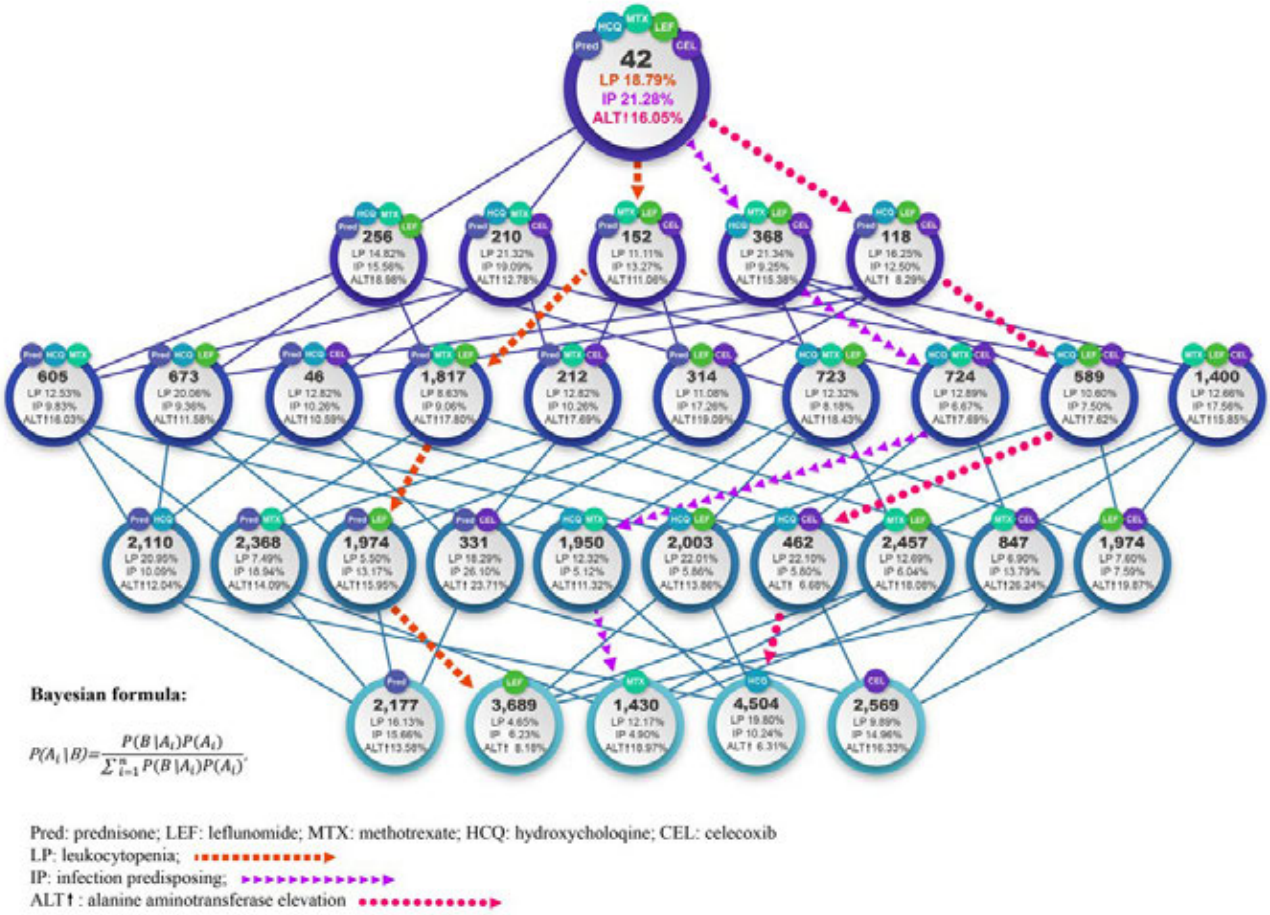


Figure 2. Bayesian network and date processing: Patients number (black as blow) and the rate of LP, IP and ALT elevation in 31 regiments.



Conclusion: Through patterns extraction, data mining, modeling, and Bayesian networking, a risk prediction model and a master algorithm for drug withdrawl strategy in reduction of AEs are developed, which are expendable and replicatable. Via continuing data inputs and machine leaning, an artificial intelligent system in assisting clinical forecast and decision-making may be achieved with SSDM.

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Abstract Number: 0268

LARS Study: Latin American Rheumatologist Survey

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SESSION INFORMATION
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Background/Purpose: Currently, Latin America does not have detailed information of rheumatologists in the region based on: education, working conditions, productivity, distribution of time between work activities and job satisfaction.

The purpose of this survey was to provide more information on the rheumatology community in Latin America.

Methods: A digital survey was created using the Google Forms platform, it was approved and endorsed by the scientific committee of PANLAR and later sent to the different rheumatology associations of the region. The data was analyzed in the statistical program SPSS v.23.

Results: 600 surveys of rheumatologists from 23 countries were received. The majority were females (53%). The mean age was 46.8 ± 11.7 [25-78] years, with a majority of mixed race 58%. 63.2% are married, 22.5% are single, 7.8% are divorced, 5.2% in free union and 1.3% are widowed. The mean number of children was 1 [0-7]. Birthplaces included Argentina (25.8%), Brazil (15.8%). The setting of the professional practice after obtaining the title of specialists was: public hospital (36.7%), private (23.8%), private / teaching in a university hospital (12.5%), public / teaching in a university hospital (12.6%), and industry (0.2%). The main place of work was in public / government hospitals by 33.5% followed by private practice 28.8%, private hospital 20.8%, university hospital 15.5%, nonprofit organizations 1% and retired 0.3%. The average of weekly working hours was 37.8 ± 17.7. 87.5% of the sample practices adult rheumatology, 12.7% pediatric rheumatology, 1.5% immunology and 3.5% another specialty. 30.2% had an early arthritis care center at their workplace, 70% had an infusion unit, 56.2% had ultrasound, 48% had a densitometer, 48.7% had a resonator and 78.5% had X-rays. 28.7% have training in ultrasound and 9.5% are in training period, 74.8% have training in reading densitometry and 3% in training period, 52.7% have training in resonance reading and 12.2% in training period. The average satisfaction with practice as a rheumatologist was 5.3/7, career options 4.3/7, geographic location 4.7/7, income 3.5/7, job security 3.7/7, colleagues and co-workers 4.5/7. 33.5% had an annual compensation of < 19,000 US dollars. Only 57.2% have malpractice insurance and 87.5% have medical insurance. 38.2% present at least one clinical comorbidity.

Conclusion: The majority of rheumatologists in the region feel satisfied with their clinical practice. This survey shows a low level of income for the region, however, more data should be obtained. This is the first study of its kind in Latin America, being an initiative for similar projects.

Disclosure: G. Maldonado, None; **M. Intriago**, None; **E. Soriano**, Abbvie, 2, 5, 8, ABBVIE, 2, 5, 8, AbbVie, 2, 5, 8, Amber, 8, Amgen, 5, 8, AMGEN, 5, 8, BMS, 8, BRISTOL, 8, Bristol MS, 8, BRISTOL MYERS SQUIBB, 8, Bristol-Myers Squibb, 8, eli lilly, 5, 8, Genzyme, 8, GENZYME, 8, GLAXO, 2, Glaxo, 2, glaxosmithkline, 2, GlaxoSmithKline, 2, GSK, 2, Janssen, 8, Lilly, 5, 8, LILLY, 5, 8, Novartis, 2, 5, 8, NOVARTIS, 2, 5, 8, PFIZER, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, 8, Roche, 2, 8, ROCHE, 2, 8, Sandoz, 5, SANDOZ, 5, Sanofi, 5, SANOFI, 5, SANOPHY, 5, UCB, 8; **L. Moreno**, None; **C. Rios**, None.

Abstract Number: 0269

Attitudes and Beliefs About Opioid Medications: Determining Treatment Use in Osteoarthritis

Ernest Vina ,[1] Jazmin Dagnino,[1] and C. Kent Kwoh[1], [1]University of Arizona, Tucson, AZ

SESSION INFORMATION
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Table 1. Patient knowledge and attitudes towards opioid medications that may determine opioid medication use (vs. no opioid medication use) in the last 6 months [a]

	Odds Ratio	95% CI
Perception of benefit [b]	2.05*	1.24, 3.41
Perception of risk [b]	0.77	0.52, 1.16
Have family/friends that received opioid medication for OA	7.56*	2.51, 22.77
Have a good understanding of opioid medication treatment	1.71	0.43, 6.86

[a] Logistic regression model adjusted for age, sex, race (White vs. not), education, income, Patient Health Questionnaire-8 (Depression) score, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total score, comorbidity score.
[b] OR for a one-point increase in a scale ranging from 1 to 5.
*p<0.05

Background/Purpose: Considering the growing opioid epidemic in the US, it is imperative to have a good understanding of what patient characteristics predict the use of these types of medication. Patients' attitudes and beliefs about treatments may influence perceptions of need and use of health treatments. Their significance as determinants of utilization of opioid medications for osteoarthritis (OA) treatment is unknown, however. The objective of this study is to determine if patient familiarity with and perceptions of efficacy and risk of opioid medications are associated with opioid medication use for OA.

Methods: Participants with chronic, frequent pain due to knee or hip OA were recruited from a university medical center. A self-administered questionnaire was used to determine use of an opioid medication to treat OA in the last 6 months. The questionnaire also assessed patient familiarity with (3 items, yes/no), and perceptions of efficacy (4 items) and risk (3 items) of opioid medications. Responses to perceptions of efficacy and risk question items were based on a five-category ordinal response scale (score 1-5). Items were averaged, with higher values indicating higher perception of efficacy/risk. Chi-squared or t-tests were conducted to determine if the familiarity and perception of efficacy/risk items were associated with opioid treatment use. Logistic regression was used to determine if observed associations persisted after adjustment for sociodemographic and clinical variables.

Results: Our sample consists of 100 participants who had used and 249 who had not used an opioid medication for OA treatment in the last 6 months. Users, compared to non-users, were younger (mean age 62.5 vs. 64.8), less likely to have an Associate's Degree or higher (34.0% vs. 51.0%), and less likely to have ≥$40,000 annual household income (25.5% vs. 45.8%). They also had higher mean WOMAC pain (54.75 vs. 46.76), WOMAC disability (56.64 vs. 44.89), and comorbidity (4.12 vs. 3.23) scores. Opioid medication users were also more likely to have heard about opioids as treatment for OA (95.9% vs. 71.4%), to have family/friends that received a opioid for OA (77.4% vs. 40.4%), and to have a good understanding of what happens after opioid medication treatment (92.2% vs. 64.7%) [all p-values < 0.005]. Mean [SD] perceived efficacy score was higher (3.90 [0.94] vs. 3.27 [0.94], p< 0.005) while perceived risk score was lower (3.20 [1.18] vs. 3.84 [1.07], p< 0.005) among opioid medicine users than non-users. When adjusted for sociodemographic and clinical factors, perception of medication benefit (OR 2.05 [95% CI 1.24, 3.41]) and having family/friends that received the medication for OA (OR 7.56 [95% CI 2.51, 22.77]) remained significantly associated with opioid treatment use (Table 1).

Conclusion: Among patients with knee or hip OA, those who used opioid medications, compared to those who did not, were more familiar with opioids, more likely to believe in their efficacy, and less likely to believe in their risks. Perceived medication efficacy and having family/friends who use the medication were associated with opioid medication use even after controlling for patient sociodemographic and clinical characteristics.

Disclosure: E. Vina, None; **J. Dagnino**, None; **C. Kwoh**, Abbvie, 2, Astellas, 5, Astellas and Thusane, 5, EMD Serono, 2, 5, Express Scripts, 5, Novartis, 5, Taiwan Liposome Co., 5, Thusane, 5, TissueGene, 5.

Abstract Number: 0270

Outcomes of a Fracture Liaison Service at an Academic Health Center

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Background/Purpose: Osteoporosis is associated with increased morbidity and mortality. There is a 60% risk of a subsequent fracture for patients who have had one fracture, with vertebral compression fractures having the highest rate of recurrent fragility fracture, and hip fractures being the most common recurrent fracture type at 3 years. Fracture Liaison Services (FLS) are secondary fracture prevention systems that channel hospital-admitted patients to an osteoporosis clinic that have been shown to lower recurrent fracture rates. An FLS at our institution addresses care gaps; a local study showed that up to 90% of fracture patients are never offered screening or treatment for osteoporosis by their primary care physician (PCP). The purpose of this study is to determine the effectiveness of the FLS by analyzing outcome measures related to initiation of treatment, DXA utilization and risk factor assessment.

Methods: Hospital admission data extraction from our Epic® electronic health record (EHR) was done using ICD 10 codes on fragility fracture for pre-FLS data (September 2015-March 2017) and post-FLS (September 2017-February 2019). Chart review was done to retrieve the following data: patient demographics (age, sex, ethnicity), body mass index, weight, height, circumstances of fracture (fragility vs traumatic), anatomic location, prior fractures, primary care provider location, treatment initiation, calcium and vitamin D supplementation, and laboratory data (TSH, PTH, 25-OH-Vitamin D). A 10% improvement in outcome measures related to treatment initiation and DXA utilization were previously set. Percent improvement in these measures, including p-values were calculated, and barriers to care were identified.

Results: Patient demographics, medication initiation, calcium and vitamin D supplementation and risk factor assessment between pre- and post-FLS groups were noted. (Table 1 and 2) Patient populations pre and post-FLS were similar. Overall, a 10% improvement in outcome measures were met except for pharmacotherapy initiation and DXA scan post-fracture. The barrier to medication initiation was most commonly due to reluctance of patients to take medications for prevention of further fractures which typically stems from inability to understand the risk of side effects as compared to the risk of a subsequent fracture.

Out of 92 FLS referrals inpatient, only 27 (29.3%) were adherent with osteoporosis clinic visits. Many patients admitted to the academic medical center are referred from other centers and have outside PCPs, and at an institutional level, primary care services are limited. (Figure 1) A Primary Care Institute was established 2018. It is hoped this would increase patient adherence to visits.

Conclusion: The Fracture Liaison Service met targeted improvements in outcomes in calcium and vitamin D supplementation but not in DXA post-fracture or pharmacotherapy initiation. Improving risk communication physician skills, while necessary, also need to consider patient perspectives on treatment recommendations. Improving access to

Table 1. FLS Patient population demographics and risk factors

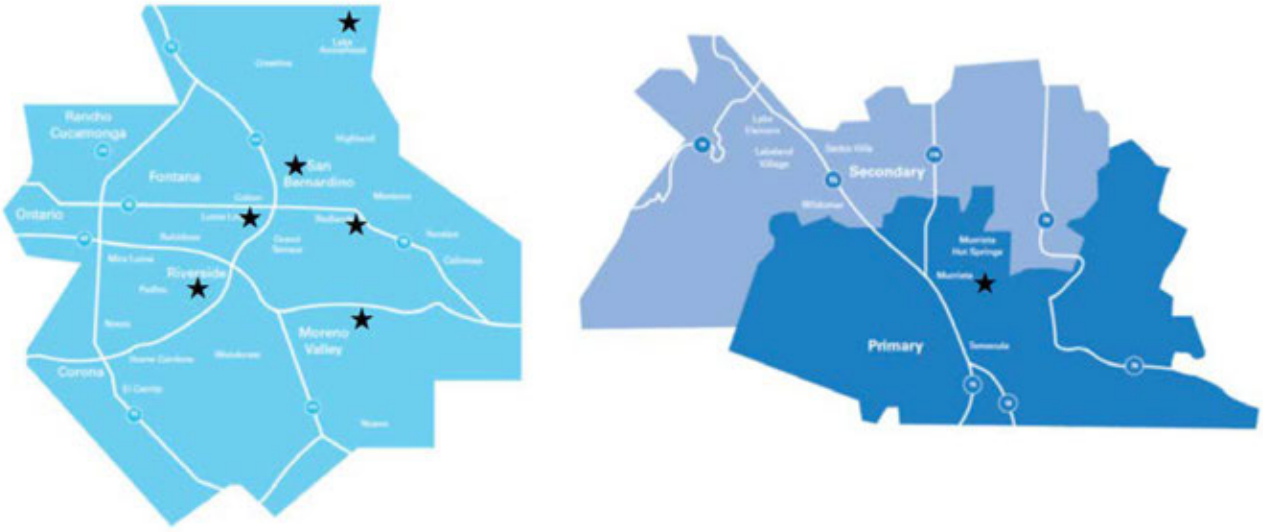
	Pre-FLS (N-216)	Post-FLS (N=102)
Demographics		
Mean Age	77.1 years	78.2 years
% Female	72.8%	67.6%
% Caucasian	75.5%	66.9%
Risk factors for Osteoporosis		
Prior fracture	27.6%	41%
Current tobacco use	10.6%	9.7%
Ever tobacco smoker	37%	31.1%
Alcohol use	4.60%	18.4%

Table 2. Determination of FLS impact based on comparison of performance on outcome measures post-FLS vs Pre-FLS

FLS Outcomes	Pre-FLS (%) N = 216	Post-FLS (%) N = 105	% difference* (Post-Pre)	p value
DXA post-fracture	5.6	11.6	+6	<0.001
Pharmacotherapy initiation	10.3	17	+7.2	0.075
Vitamin D supplementation	25.4	44	+18.6	<0.001
Calcium supplementation	20.4	39.4	+19	<0.001

*A minimum +10% difference was set as a target goal for each outcome measure

Figure 1. Geographic regions serviced by the academic health system. Despite a large catchment area of at least 27,313 square miles, primary care services (*) are only offered in a few places.



local Primary Care can improve adherence to osteoporosis specialty clinic visits. Tracking re-fracture events in these patients is also needed.

Disclosure: M. Yu, None; **D. Jose**, None; **P. Hudson**, None; **C. Downey, MD**, None; **W. Phipatanakul**, None; **S. Giannelli**, None; **K. Codorniz**, None; **K. Torralba**, None.

Abstract Number: 0271

Who Prescribed Which Osteoporosis Medication to Whom

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Several osteoporosis (OP) medicines came on the market in the past two decades, each with its own indications. However, there is no clear information on how the medicines were prescribed in the real world. Using Medicare data, we assessed who prescribed which OP medication for what type of patients.

Methods: Using the 2011-2015 Medicare 20% random sample database, we identified patients who initiated an OP medication during a two years period - October 1, 2013, to September 30, 2015, and the specialty of the initial prescribers. OP medications included alendronate, ibandronate (oral and IV formats, separately), risedronate, zoledronic acid, teriparatide, denosumab, raloxifene, and calcitonin; prescriber's specialties included orthopedic, OB/GYN, geriatric, rheumatologic, endocrinologic, internal medicine or family, and "other." Patients were aged ≥65 years at initiation and covered by Medicare Parts A and B for at least 2 years and by Medicare Part D for at least 1 year before initiation. Initiation was defined as first use in the period and no use of the same medicine for at least 1 year before. Patients could be on other OP medications before this initiation. For each medication group, we assessed patient demographics (age, race, sex, and geographic regions), history of fractures (hip, vertebral, other), comorbid conditions, which may be associated with increased fracture risk, and previous OP medication use.

Results: In all, 203,305 patients were included; 4.6% initiated more than one medicine (one by one, not simultaneously) in this period. The largest medication group was denosumab users (123,128), followed by alendronate (50,559) users; the smallest groups were IV ibandronate (548) and teriparatide (3,779) users. Calcitonin users were the oldest (mean age 78.9 years) and denosumab users the youngest (72.8). About 10% of users were men for all medicines except for raloxifene (< 1%) and denosumab (34.5%). More calcitonin and teriparatide users were at high risk of fracture (with previous fracture or more comorbidity) and a large percentage had recent fractures, especially vertebral; more ibandronate and teriparatide users switched from (other) bisphosphonates. OP medication was mostly prescribed by internal/family (47.2%) and "other" (32.1%) doctors. However, this varied by medication; except for high percentages of internal/family and "other" doctors, about 40% of IV bisphosphonates were prescribed by rheumatologists; 10.4%, 18.5%, and 14.8% of teriparatide by orthopedists, rheumatologist, and endocrinologists; 11.8% of raloxifene by OB/GYN; and 11.9% of risedronate by rheumatologists. For details, see Table 1.

Conclusion: This study found that, in the Medicare population, denosumab was prescribed for the most patients and was used by more men; calcitonin was mainly prescribed for older women; calcitonin and teriparatide were prescribed for more patients at high risk of fracture; and OP medications were mainly prescribed by internal/family

Table 1. Patient Characteristics and Prescriber Specialty by Osteoporosis Medication

	Oral Bisphosphonates			IV Bisphosphonates					
	Alendronate	Ibandronate	Risedronate	Ibandronate	Zeledronic Acid	Prolia	Teriparatide	Raloxifene	Calcitonin
Total N	50559	9449	4784	548	9837	123128	3779	3875	7118
Demographic									
Age(Mean years, SD)	77.09(7.11)	75.22(9.06)	75.41(9.08)	75.04(9.81)	74.70(9.34)	72.82(12.29)	74.91(10.95)	74.20(8.18)	78.94(10.43)
Age									
<= 74 years	44.42	49.28	49.81	46.72	50.10	54.17	47.61	56.59	32.94
75-79 years	22.54	21.64	19.52	22.08	21.61	18.15	18.55	21.11	16.75
80-84 years	17.18	15.32	16.16	16.97	15.56	13.85	16.62	12.15	19.23
85+ years	15.86	13.76	14.51	14.23	12.73	13.83	17.23	10.14	31.08
Sex									
Male	11.90	7.60	10.90	10.80	10.40	34.50	12.40	0.90	16.70
Female	88.10	92.40	89.10	89.20	89.60	65.50	87.60	99.10	83.30
Race									
White	83.29	84.09	83.63	81.93	91.82	85.45	87.54	81.94	91.12
Black	5.67	4.72	4.87	4.01	3.50	7.75	2.28	4.62	2.98
Asian	4.37	5.05	4.74	6.39	1.50	2.13	4.00	6.94	2.22
Other	6.67	6.14	6.75	7.66	3.18	4.67	6.19	6.50	3.68
Fracture within 2 Years									
HIP fracture									
No	96.61	97.71	97.74	98.36	97.15	98.46	90.71	97.99	95.6
Month 1-3	1.15	0.56	0.54	* (≤11 Pts)	0.41	0.23	2.36	0.49	1.12
Month 4-6	0.74	0.48	0.61	*	0.70	0.30	2.75	0.46	0.89
Month 7-12	0.70	0.58	0.63	*	0.93	0.42	2.20	0.44	0.93
Month 13-24	0.81	0.67	0.48	*	0.81	0.60	1.98	0.62	1.46
Vertebral fracture									
No	93.45	94.08	93.42	92.15	89.33	95.69	67.77	95.77	72.60
Month 1-3	3.20	2.40	2.78	*	3.69	1.51	16.22	1.65	18.81
Month 4-6	1.13	0.92	1.19	*	2.08	0.80	8.26	0.90	3.84
Month 7-12	1.03	1.15	1.19	2.19	2.23	0.92	4.79	0.75	1.85
Month 13-24	1.19	1.44	1.42	2.37	2.67	1.08	2.96	0.93	2.89
Other fracture									
No	95.21	95.34	95.21	95.8	94.32	96.75	85.02	96.98	91.81
Month 1-3	1.29	1.08	0.63	*	0.60	0.62	4.39	0.72	2.66
Month 4-6	0.93	0.78	1.17	*	1.09	0.52	3.68	0.41	1.55
Month 7-12	1.06	0.97	1.40	*	1.50	0.79	3.41	0.65	1.42
Month 13-24	1.52	1.82	1.59	*	2.49	1.31	3.49	1.24	2.57
Osteoporosis Medication									
Oral Bisphosphonate									
No use within 1 year	89.94	73.82	79.31	76.46	81.15	90.85	76.40	80.52	84.41
Month 1-3	8.14	20.06	15.09	16.42	11.61	6.52	16.59	13.96	11.2
Month 4-6	0.88	2.84	2.36	2.92	3.03	1.05	3.20	2.32	1.95
Month 7-12	1.04	3.29	3.24	4.20	4.21	1.58	3.81	3.20	2.44
IV Bisphosphonate									
No use within 1 year	99.50	98.84	99.39	95.99	99.41	97.7	95.53	98.14	98.15
Month 1-3	0.15	0.42	*	*	0.34	0.59	1.61	0.52	0.97
Month 4-6	0.08	0.22	*	*	0.12	0.30	0.87	0.34	0.32
Month 7-12	0.28	0.52	0.42	3.47	0.13	1.40	1.98	1.01	0.56
Teripatatide									
No use within 1 year	99.37	99.30	98.98	98.18	98.3	99.12	100.00	98.74	99.21
Month 1-3	0.43	0.42	0.59	*	0.81	0.52	*	0.72	0.42
Month 4-6	0.10	0.13	0.25	*	0.49	0.16	*	*	*
Month 7-12	0.11	0.15	*	*	0.40	0.20	*	0.36	0.24
Denosumab(Prolia)									
No use within 1 year	95.77	95.18	95.17	87.59	93.32	100	88.86	93.78	92.98
Month 1-3	2.66	3.08	2.93	7.85	3.81	*	7.78	4.03	4.76
Month 4-6	0.54	0.7	0.71	2.01	1.21	*	1.24	0.77	0.91
Month 7-12	1.03	1.04	1.19	2.55	1.66	*	2.12	1.42	1.35
Baseline Comorbid conditions									
Myocardial infarction	4.77	3.5	4.08	4.56	4.41	7.45	6.51	2.68	8.47
Congestive Heart Failure	11.46	9.3	8.97	15.88	9.91	15.19	16.46	6.17	21.48
Chronic pulmonary disease	20.01	19.61	19.17	24.45	20.93	22.24	27.47	15.92	29.18
Chronic Kidney Disease	16.60	13.99	13.75	15.33	13.12	22.89	21.06	11.92	27.00
Rheumatoid arthritis	6.43	7.01	8.72	21.17	11.91	5.13	12.41	4.54	6.60
Osteoarthritis	37.42	38.13	40.45	54.20	41.81	37.14	53.03	35.79	45.35
Parkinson disease	1.79	1.59	1.69	2.55	1.79	1.73	3.02	1.19	3.33
Multiple sclerosis	0.40	0.77	0.69	*	0.93	0.64	1.30	0.46	0.70
Stroke	4.96	4.09	4.37	6.20	4.91	5.62	6.67	3.20	8.13
Hypertension	76.94	74.11	74.12	76.64	70.79	77.74	75.97	69.34	81.58
Depression	19.54	20.51	19.63	24.82	23.45	22.34	32.73	17.57	30.04
Anxiety	15.47	16.43	17.33	18.07	19.07	18.27	25.46	14.84	24.12
Dementia	7.51	5.81	5.96	6.02	4.95	5.85	10.08	4.21	15.82
Fall	22.53	20.85	19.86	20.44	25.19	20.74	43.74	15.82	43.35
Diabetes	26.89	25.27	25.59	27.19	21.16	33.54	25.35	23.05	27.56
Specialty									
Missing	3.28	2.90	3.03	27.55	57.59	59.31	3.41	2.53	4.50
Non-missing									
Orthopaedic	0.62	0.63	0.61	*	0.05	5.97	10.39	0.45	6.57
OB/GYN	2.80	5.36	7.33	1.26	1.13	1.87	1.35	11.76	0.72
Geriatric	2.00	1.46	1.36	0.25	0.19	0.29	1.70	1.35	3.50
Rheumatolog,	6.67	6.37	11.92	39.56	40.29	9.56	18.54	3.52	3.10
Endocrinology	4.00	3.79	7.26	5.54	6.98	3.81	14.80	3.87	1.50
Internal/Family	68.17	66.10	57.21	42.07	22.58	22.25	31.34	63.91	62.05
Other	15.75	16.29	14.31	11.34	28.78	56.25	21.89	15.14	22.57

and “other” doctors. Internal medicine and family doctors should remain updated regarding osteoporosis treatment-related research results. A study limitation is that prescriber information was not complete for IV medications.

Disclosure: J. Liu, None; **H. Guo**, None; **T. Gong**, None; **Y. Peng**, None.

Abstract Number: 0272

Osteoporosis Management Outcomes in a Southern California County Health System

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research Poster I – ACR/ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fragility fractures (FF) are a sentinel event in osteoporosis and world-wide only 20% of patients with a FF receive treatment, a large care gap. A 2016-2017 study done at a university-based academic medical center (AMC) found up to 90% of patients admitted for FF did not receive treatment after discharge. A Fracture Liaison Service (FLS) has subsequently been implemented at AMC. The same rheumatologists serve AMC and 20 miles away, Academic Medical Center 2 (AMC2). The objective of this study is to determine the quality of care received by AMC2 FF patients and determine the health disparities among patients seen in these two health systems.

Methods: Medical records of patients with FF who were at least 50 years of age who presented to AMC2 between July 2017 and June 2018 were reviewed. Those with ICD10 codes for FF were reviewed for dual x-ray absorptiometry (DXA) utilization, pharmacotherapy initiation, adequate calcium and vitamin D supplementation. Patient ethnicity and access to AMC2 vs. out of system primary care were also noted.

The objective of this study is to determine factors contributing to gaps in patient care in the AMC2 system with the goal of informing health improvement efforts as part of a Plan-Do-Study-Act (PDSA) cycle. An outcomes comparison between the two medical centers was subsequently done, directed toward socioeconomic status and access to care.

Results: 144 AMC2 patient charts were analyzed. 120 (83%) were female. 36.8% of encounter cases at AMC2 involved Hispanic or Latino patients who were Hispanic or Latino, similar to the ethnicity profile at AMC. 83 (58%) had femoral neck fractures, 13 (9%) had vertebral fractures. 3.47% were subsequently seen at outpatient AMC2 primary care clinics within 6 months post-hospital discharge, 2.96% of which had a post-fracture DXA scan. Similarly, 5% of patients at AMC had a post-fracture DXA completed.

2.78% of AMC2 patients with previous FF were on pharmacologic therapy prior to their ED encounter, vs. 14.4% of AMC patients with prior FF. Though very few patients seen at AMC2 were on treatment for osteoporosis, previous fracture rates were similar: 23% of patients at AMC and 20% at AMC2. At AMC2, 4.1% had osteoporosis treatment after discharge, which was lower than the 10.3% of patients at AMC who were given pharmacotherapy post-fracture.

Table 1. Comparison of Osteoporosis Health Outcomes at AMC (University) and AMC2 (County)

Outcomes	AMC-university	AMC2-county
% Patients on OSP medications prior to FF	8.90%	2.78%
% Treated after discharge	10.30%	4.10%
% Received calcium after discharge	20.8%	12%
% Received vitamin D after discharge	31.2%	21%
Post-fracture DXA	5%	3.47%

At AMC, 20.8% received calcium and 31.25% received vitamin D supplement after discharge. Comparatively, 12% of patients at AMC2 were given calcium and 21% were given vitamin D. (Table 1)

Conclusion: A minority of patients with FF presenting to AMC2 for FF are receiving optimal care post-hospital discharge. Between AMC and AMC 2, the post-fracture treatment rates were disproportionate among FF patients. Similarities in ethnicity remove this as an explanation of disparities in treatment rates. A limitation of this study is the inability to analyze data for patients who leave the AMC2 system post discharge. An FLS would be a good way to improve care and awareness among physicians and patients alike, but the inadequacies of healthcare access will most likely continue to hamper improvement efforts.

Disclosure: L. Ahn, None; **J. Thompson**, None; **N. Collado**, None; **M. Yu**, None; **A. Lafian**, None; **C. Downey, MD**, None; **K. Torralba**, None.

Abstract Number: 0273

Bone Health in Lupus: Findings from the Southern California Lupus Registry

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: The association of vitamin D deficiency with SLE is well established. While disease activity can itself cause pathologic bone remodeling and reduced vitamin D, SLE flares often necessitate steroid treatment, which can lead to decreased vitamin D absorption and decreased bone mineral density. Some rheumatologists recommend a goal serum 25(OH)D of 40ng/mL to reduce the probability ratio for a high disease activity score and to also improve urine protein-to-creatinine ratio. In addition, the ACR recommends vitamin D replacement for all patients receiving steroids, irrespective of steroid dose or duration of treatment. The objective of this study is to identify practice care gaps among rheumatologists in their adherence to vitamin D replacement in SLE patients currently on steroid therapy. An additional practice review of evaluating for vitamin D deficiency is noted.

Methods: Data collected from the Southern California Lupus Registry (SCOLR), an academic cohort of 182 patients with SLE, was analyzed. Cross-sectional review of medical records of patients seen from June 2016 to April 2019 included the following data: 1) Current or prior use of systemic steroids, 2) Vitamin D replacement in patients receiving steroid therapy, 3) Evaluation of vitamin D level within 6 months of patient encounter. Independent review was completed on medications prescribed. Abnormal vitamin D level was deemed < 30ng/mL. Descriptive statistics were utilized. This study is approved by the Loma Linda University IRB.

Results: Of 182 patients enrolled in SCOLR, data was available to be analyzed in 176 (Figure 1). Current, prior and never use of steroids was noted in 56 (32%), 73 (41%), 47 (27%), respectively. In patients currently on steroids, vitamin D replacement was provided to 30 (54%).Vitamin D levels were tested in 49/176 (28%) and noted to be abnormal in 27/49 (55%) (Table 1). Contrary to our expectations, patients with current or prior use of systemic steroids did not

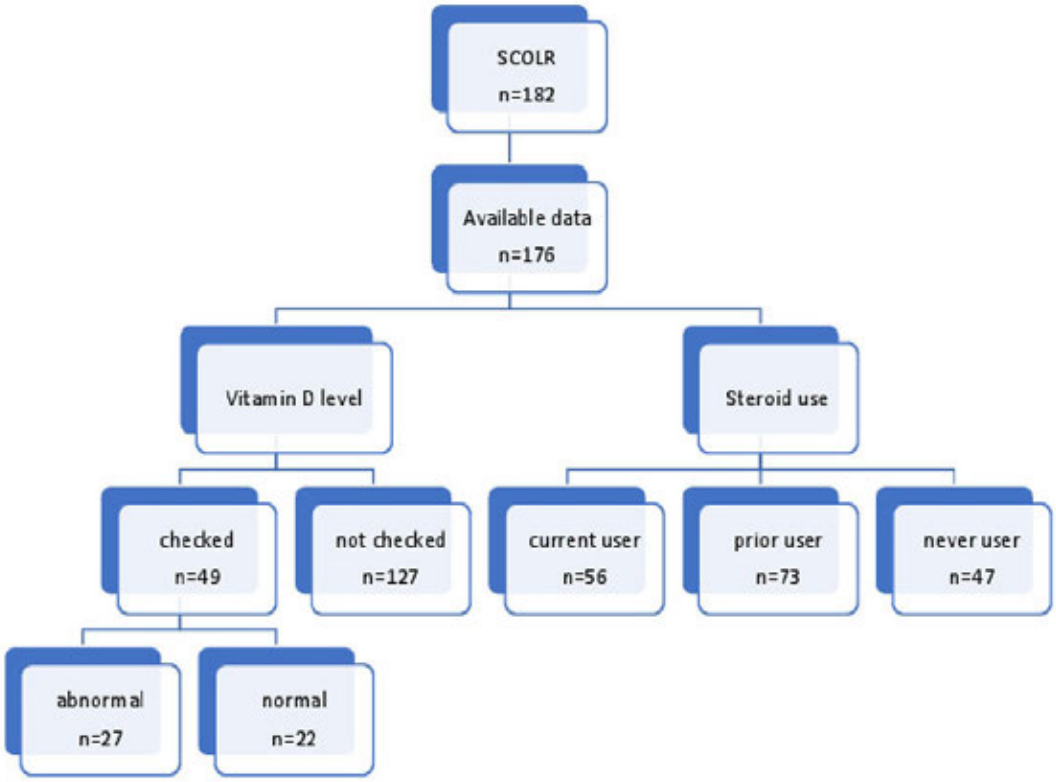
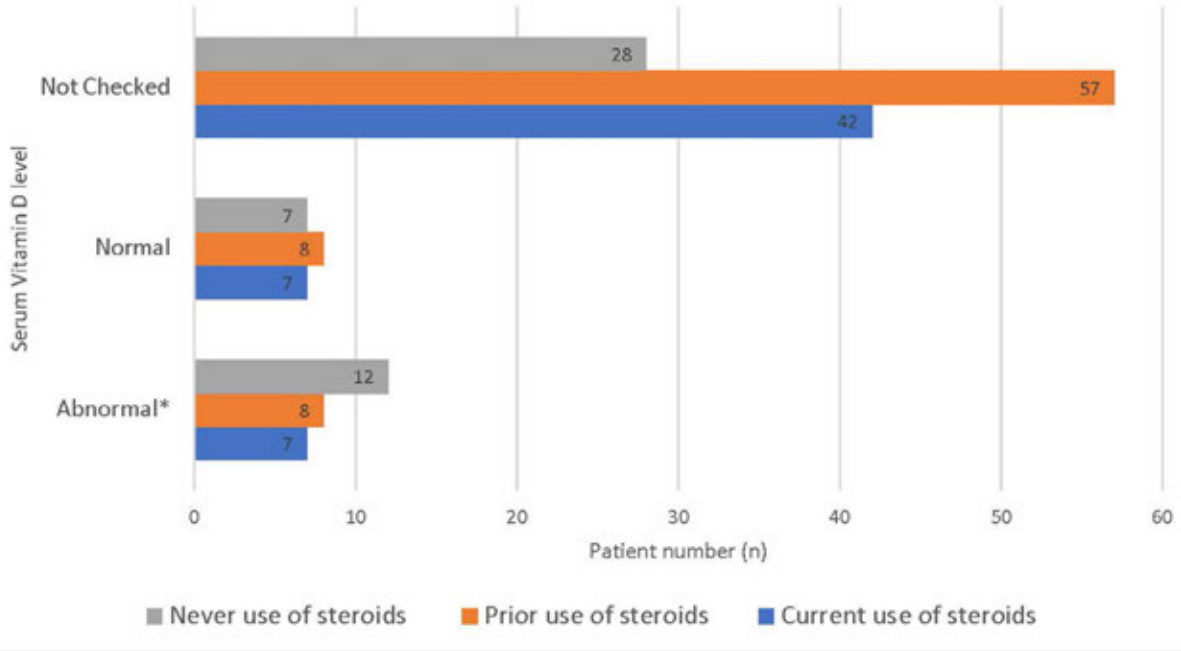


Figure 1. Methodology and Results

Figure 2. Monitoring serum vitamin D in SLE patients on systemic steroids



** serum 25(OH)D <30ng/mL*

Table 1. Vitamin D level crosstabulation with steroid use

		Vitamin D level		Total
		Normal (n)	Abnormal (n)	
Steroid use	Never user	7	12	19
	Current or prior use of steroids	15	15	30
Total		22	27	49

Pearson Chi^2 test of independence, (χ^2 (df), *p*-value) = 1.07 (1), $p = 0.899$

experience a significantly increased risk of abnormal vitamin D levels (OR 0.583, 95% CI (0.18, 1.89). However, vitamin D level was not checked in 42/56 (24%) patients currently on steroids and 57/73 (78%) patients with prior use of steroids, which limits the ability to formulate more meaningful conclusions.

Conclusion: Rheumatologists are infrequently screening for vitamin D deficiency in SLE. Further, vitamin D supplementation is inadequate in those individuals receiving systemic steroids. We acknowledge our gaps in the power of this study but bring to light the need for increased awareness of bone health in SLE in addition to the appropriate management of such individuals exposed to systemic steroids. With this information, we will plan to implement a best practice advisory warning in the electronic medical record of all individuals receiving steroid therapy to trigger both screening for and treating vitamin D abnormalities. Additional attention is warranted in monitoring and replacing vitamin D a complementary treatment of SLE, which will be the studied further as a continuation of this analysis.

Disclosure: V. Sandhu, MBBS, None; **S. Johnson**, None.

Abstract Number: 0274

Participation in the Stanford University Chronic Pain Self-Management Program in a Population with a High Prevalence of Arthritis

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SESSION INFORMATION
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Background/Purpose: In 2016, 1 in 5 US adults reported chronic pain (CP). Osteoarthritis and rheumatoid arthritis are top causes of CP. The Stanford University Chronic Pain Self-Management Program (CPSMP) is a 6-week, low-cost

community-delivered workshop that increases participants' confidence in self-managing their CP. We describe baseline participation in a randomized, wait-list (6 months) controlled trial on CPSMP's short- and longer-term outcomes in West Virginia, a population with a high prevalence of arthritis, CP, opioid deaths, and socio-economic deprivation.

Methods: Community-dwelling adults, aged ≥ 18, with CP of ≥ 3 months, were eligible. Ineligibility criteria were cancer, an open wound, planned surgery in next year, or participation in a similar self-management program in the past year. Participants were recruited from clinics and the community via direct mailings, newspaper articles/advertisements, word-of-mouth, social media, and an electronic patient portal. Baseline data collected included age, sex, arthritis status (yes/no), and pain severity (Stanford Pain Visual Numeric Scale [0=no pain, 10=severe pain]), categorized as no (0), low (1-4), moderate (5-6), or severe (7-10) pain. Participation was the number enrolled divided by the number of eligible participants, multiplied by 100. Barriers to enrollment were identified. Descriptive statistics determined the characteristics of those who enrolled in the study. Statistical tests were conducted to determine if pain severity (categories) varied by: 1) age (Spearman's correlation) or 2) sex and arthritis (Cochran-Mantel-Haenszel tests).

Results: From June 2018 to March 2019, 336 people inquired about the study, 323 (96%) were screened for eligibility, 281 of the 323 (87%) were eligible, and 176 of the 281 enrolled, for a total of 63% participation. Enrollment barriers to participation were: not understanding what CP meant, the stigma associated with having CP, low socioeconomic status, and competing life priorities. At baseline, participants were primarily women (76%); mean age ± SD was 65 ± 13 years (range, 28 to 88). Most participants had arthritis (88%). The mean ± SD, range, and median (interquartile range) pain severity scores were 6.6 ± 1.9, 0-10, and 7.0 (3.0), respectively, with 1% with no pain, 10% mild pain, 39% moderate pain, and 50% with severe pain. Among those with severe pain (n=86), 71% were women and 89% had arthritis. The prevalence of severe pain was lower among older participants (43%, aged ≥ 65) compared to younger ones (61%, aged 18-64) (p=0.006). The distribution of pain severity was similar by sex (p=0.23) or arthritis status (p=0.66).

Conclusion: In a population with multiple challenges, including high arthritis prevalence, participation seemed moderate, possibly due to barriers identified during recruitment. One in 2 trial participants reported severe pain indicating that the recruitment strategy captured individuals in West Virginia with a substantial need for pain management interventions. Because some barriers to trial participation may also be barriers to implementing CPSMP in the community, strategies to increase understanding of CP and reduce its stigma may be important ways to eventually increase CPSMP's reach.

Disclosure: D. Jones, None; **L. Murphy**, None; **R. Misra**, None; **A. Vargovich**, None; **D. Guglielmo**, None; **M. Robinson**, None; **S. Shawley-Brzoska**, None; **S. Wen**, None; **M. Burkart**, None; **R. Vaglienti**, None.

Abstract Number: 0275

Exercise Is Medicine® in Primary Care Practice: Provider Characteristics and Physical Activity Counseling for Patients with Arthritis, DocStyles, 2018

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SESSION INFORMATION

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Background/Purpose: Physical activity (PA) can reduce pain, prevent or delay disability, and improve physical functioning and mood in people with arthritis. However, only 36% of US adults with arthritis met the *2008 Physical Activity Guidelines for Americans* aerobic guideline. The American College of Sports Medicine's global initiative, Exercise is Medicine® (EIM), encourages health care providers to perform PA evaluations and refer patients to evidence-based PA programs or fitness professionals to manage chronic conditions, including arthritis. Primary care providers (PCPs) frequently treat rheumatologic conditions and are well positioned to influence patient PA through counseling consistent with EIM guidance. This study examined PA counseling behaviors for patients with arthritis among PCPs, and how adoption of EIM guidance for PA counseling differed across PCP characteristics.

Methods: We analyzed 2018 DocStyles cross-sectional data from 1,389 PCPs (family practitioners, internists, obstetrician/gynecologists [OB/GYNs], and nurse practitioners). PCPs were asked about frequency of assessing and recommending PA to their patients with arthritis, which align with the evaluation and prescription components of EIM guidance, respectively. Responses were classified into three counseling levels: *Does Not Follow, Partially Follows, and Follows* EIM guidance (Table). Prevalence and 95% confidence intervals (CIs) were calculated for each level overall and across selected PCP characteristics. Differences between PCP subgroups were determined using pairwise *t*-tests and linear trends in ordinal variables using orthogonal linear contrasts.

Results: PCPs most commonly reported that they *Follow* EIM guidance for their patients with arthritis (39.7% [95% CI: 37.2-42.3]), while 27.4% (95% CI: 25.0-29.7) *Partially Follow* and nearly a third (32.9% [95% CI: 30.4-35.4]) *Do Not Follow* EIM guidance. Prevalence of PCPs who *Follow* EIM guidance rose with increasing provider age (range: 32.8% among aged 21-39 years to 47.3% among aged > 50 years), years practicing medicine (range: 32.4% among practicing < 10 years to 51.0% among > 30 years), and number of total patients (range: 35.3% among < 75 patients to 46.4% among > 125 patients) and patients with arthritis seen per week (range: 30.2% among 1-9 patients to 56.4% among > 20 patients). Prevalence of PCPs who *Do Not Follow* EIM guidance was highest among OB/GYNs (49.5% [95% CI: 42.2-56.7]), those working in inpatient settings (41.7% [95% CI: 33.8-49.6]), those seeing fewer patients (1-9/week) with arthritis (41.3% [95% CI: 37.4-45.2]), younger providers (21-39 years) (39.9% [95% CI: 34.3-45.5]), those practicing medicine < 10 years (37.8% [95% CI: 32.3-43.4]), or living in the South (37.7% [95% CI: 33.4-42.0]).

Table. Definition of Following Exercise is Medicine® Guidance

		DocStyles: Assess Physical Activity[1] (EIM: Evaluate)	
		Always	Sometimes/Never
DocStyles: Recommend Physical Activity[2] (EIM: Prescribe)	Always	Follows EIM guidance	Partially Follows EIM guidance
	Sometimes/Never	Partially Follows EIM guidance	Does Not Follow EIM guidance

EIM: Exercise is Medicine®

[1]Measured by the question, "When you see patients with arthritis/rheumatic conditions, how often do you ask them about their level of physical activity to assess whether they are sedentary, meeting guidelines (150 minutes per week), or somewhere in between?"

[2]Measured by the question, "When you see patients with arthritis/rheumatic conditions how often do you recommend physical activity/exercise for management of their condition?"

Conclusion: Only about 2-in-5 PCPs *Follow* EIM guidance for PA counseling for patients with arthritis. PCPs who *Do Not Follow* EIM guidance are younger, less experienced, and see fewer patients with arthritis per week compared to PCPs who *Follow* EIM guidance. These PCPs may benefit from additional training and education to help increase their confidence and skills in PA counseling for patients with arthritis.

Disclosure: D. Guglielmo, None; **L. Murphy**, None; **K. Theis**, None; **C. Helmick**, None; **J. Omura**, None; **J. Croft**, None.

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Effectiveness of Screening by Nurse with Predetermined Questionnaire on Infections Before Administration of Intravenous Biologics in Patients with Rheumatoid Arthritis

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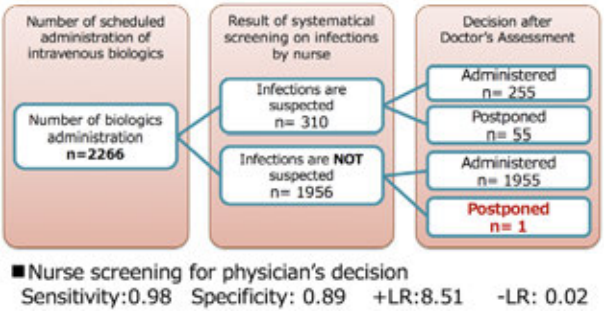
Background/Purpose: Biologics are widely used as treatment for rheumatoid arthritis (RA), and pre-administration screening of active infection is imperative for the safety use. There is no standardized way in the assessment of infection by nurse and it is often difficult and time-consuming. We implemented new method in which nurses systemati-

Table 1. Baseline characteristics and infections

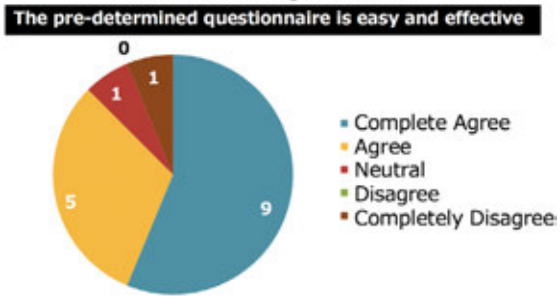
	Overall (n=271)	Conventional Method (n=143)	New method (n=128)	p value
Age	64.1 (15.3)	63.8 (15.0)	64.6(15.7)	0.638
Female (%)	229 (84.5)	124 (86.7)	105 (82.0)	0.316
RF positive (%)	238 (87.8)	125 (87.4)	113 (88.3)	0.855
Anti-CCP antibody positive (%)	201 (74.2)	104 (72.7)	97 (75.8)	0.581
Biologics				
Infliximab (%)	56 (20.7)	34 (23.8)	22 (17.2)	0.229
Tocilizumab (%)	106 (39.1)	54 (37.8)	52 (40.6)	0.709
Abatacept (%)	121 (44.6)	61 (42.7)	60 (46.9)	0.541
Glucocorticoid (%)	133 (49.1)	71 (49.7)	62 (48.4)	0.903
csDMARDs				
Methotrexate (%)	146 (53.9)	81 (56.6)	65 (50.8)	0.393
Salazosulfapyridine (%)	104 (38.4)	50 (35.0)	54 (42.2)	0.26
Bucillamine (%)	59 (21.8)	32 (22.4)	27 (21.1)	0.883
Iguratimod (%)	60 (22.1)	33 (23.1)	27 (21.1)	0.77
Mizoribine (%)	20 (7.4)	7 (4.9)	13 (10.2)	0.109
Tacrolimus (%)	33 (12.2)	15 (10.5)	18 (14.1)	0.457
Serious Infection (%)	**22 (8.1)**	**11 (7.7)**	**11 (8.6)**	**0.827**
Hospitalization (%)	22 (8.1)	11 (7.7)	11 (8.6)	0.827
IV antibiotics	22 (8.1)	11 (7.7)	11 (8.6)	0.827
Death due to infection(%)	1 (0.4)	0 (0.0)	1 (0.8)	0.472
Opportunistic Infection				
Tuberculosis (all latent) (%)	26 (9.6)	14 (9.8)	12 (9.4)	1
Zoster (%)	11 (4.1)	4 (2.8)	7 (5.5)	0.359
Candida (%)	14 (5.2)	7 (4.9)	7 (5.5)	1
Pneumocystis Pneumonia (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA

Figure 1. Results of nurse screening and decisions after physician's assessments



■Nurse screening for physician's decision
Sensitivity:0.98 Specificity: 0.89 +LR:8.51 -LR: 0.02

Figure 2. Results of questionnaire about new screening method



cally use pre-determined questionnaires on infections before doctors examine the patients for confirmation. Our aim of this study is to reveal effectiveness of this new method of assessments.

Methods: We retrospectively reviewed charts of patients with RA who received intravenous biologics at St. Luke's International Hospital, Tokyo, Japan from January 2016 to April 2019. We investigated basic demographics, kinds of biologics and other treatments, underlying diseases, incidence of serious infection(SI), and opportunistic infections. SI was defined as bacterial infections requiring intravenous antibiotics, hospitalization, or resulting in death. We calculated the number of scheduled administrations and evaluated results of screening by nurse and doctor's assessment. We compared the number of infections in the new method with those in conventional one. Univariate analysis and Chi-square test were performed. We also asked nurses for their feeling about this new screening method with questionnaire.

Results: We identified 271 cases in total. There are 143 and 128 patients who received intravenous biologics from January 2016 to August 2017 with conventional assessment and from September 2017 to April 2019 with new-style assessment. There are no significant differences in the baseline characteristics and the number of SI between new and conventional methods (7.7% vs 8.6%; p= 0.827)(Table1). New screening method showed high sensitivity (0.98) and specificity (0.89) and there was just 1 case in which doctors postponed biologics even the patient was assessed not to have active infections by nurse (Fig 1). Eighty eight % of nurses answered new method is easy and efficient, and 30% answered time-efficient. (Figure2)

Conclusion: Systematical screening by nurse with pre-determined questionnaires is effective as a screening with high sensitivity and nurses are satisfied with its convenience and time-efficiency. Doctors can carefully see cases in which infections are suspected by nurse. Our new-method of pre-administration assessments can contribute to time-efficient practice without any increasing risk of SI.

Disclosure: S. Furukawa, None; **S. Fukui**, None; **S. Tamaki**, None; **T. Nakasone**, None; **M. Okada**, None.

Abstract Number: 0277

Efficacy of a Counselling Program to Promote Physical Activity in People with Inflammatory Arthritis

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SESSION INFORMATION
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Background/Purpose: Being physically active is key to successful management in people with inflammatory arthritis (IA). This study aimed to assess efficacy of a physical activity counselling program, with the use of a Fitbit® and FitViz (a personalized Fitbit-compatible web-based app), for promoting physical activity and improving health outcomes in people with IA.

Methods: Eligible participants had physician-confirmed diagnosis of rheumatoid arthritis (RA) or systematic lupus erythematosus (SLE). After baseline assessment (T0) and stratified randomization by diagnosis, the *Intervention Group (IG)* received standardized education, a Fitbit, access to FitViz, and phone calls from a physical therapist (PT) every 2 weeks to counsel activity goals over an 8-week period. The *Control Group (CG)* received a monthly e-newsletter from the research team. Participants were assessed again at the end of 8 weeks (T1). The primary outcome was time in daily moderate/vigorous physical activity at ≥3 METS and in bouts of ≥10 mins (**3+ MVPA**) measured with a SenseWear® monitor. Secondary outcomes were: 1) daily step count, 2) MVPA at ≥4 METS and in bouts of ≥10 mins (4+ MVPA, reflects purposeful activities), 3) time in sedentary activity in bouts of >20 mins, 4) pain (McGill Pain Questionnaire Short Form), 5) fatigue (Fatigue Severity Scale), and 6) self-management capacity (Partners in Health Scale). We used Analysis of Covariance (ANCOVA) to assess the effect of the intervention on outcome measures at T1 after adjusting for T0. Post-hoc subgroup analysis was done to explore the effect of diagnosis on outcomes.

Results: We recruited 118 participants (*IG*: n=59, 86.4% women; *CG*: n=59, 91.5% women); of those, 83 had RA (*IG*: n=42, 71.2%; *CG*: n=41, 69.5%). Both groups were similar in age [*IG:* 53.5 (SD 14.7) years; *CG*: 53.1 (SD 12.6) years] and body mass index [*IG*: 27.1 (SD 6.5); *CG*: 28.7 (SD 8.9)].The adjusted mean difference in 3+ MVPA was 9.4 mins (95% CI: -0.5, 19.3, p=0.06). A significant effect was found in pain [-0.16 (95% CI: -0.32, -0.01, p=0.04)]. The remaining secondary outcomes improved, but not statistically significant -- step count: 644.1 (95% CI: -103.8, 1,392.0, p=0.09); 4+ MVPA: 0.5 mins (95%CI: -4.6, 5.6, p=0.85); sedentary time: -10.4 mins (95% CI: -53.4, 32.6, p=0.63); fatigue: -0.31 (95% CI: -0.63, 0.00, p=0.05); self-management capacity: 0.13 (95% CI: -0.09, 0.35, p=0.23). Post-hoc analysis revealed a significant effect in 3+ MVPA (13.1; 95% CI: 1.9, 24.3) and pain (-0.25; 95% CI: -0.4, -0.08) in participants with RA, but not those with SLE.

Conclusion: Counselling by a PT has potential to improve physical activity behaviour in people with IA, but further study is needed to understand the intervention effect on different diagnosis. We found a significant improvement in pain, suggesting the intervention might have a positive effect on symptom management.

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Abstract Number: 0278

Improving a SLE-Quality Indicator Tool in an Outpatient Tertiary Care Setting

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Background/Purpose: The care for patients with lupus is complex as they may exhibit multiple concomitant medical and socioeconomic issues. To address all their needs according to the current guidelines is a daunting task in busy outpatient practices. However, incorporating quality indicators in patient care has been found to decrease mortality and morbidity, improve patient satisfaction, and reduce costs. To improve the quality of care following recommendations from published guidelines, ACR, and EULAR, we embarked on a comprehensive quality improvement project by developing a checklist tool that incorporates the major SLE-Quality indicators (SLE-QI).

Methods: The project was launched in October 2017. A SLE-QI checklist detailing quality indicators was created based on published recommendations for standard of care. The checklist included a set of 20 SLE-QIs that address several important aspects of SLE care including diagnosis and disease monitoring, general prevention strategies, screening for comorbidities, drug toxicity monitoring, assessment of renal disease, reproductive health, and quality of life in daily practice. A standardized document template for clinic visits was developed that incorporated these quality indicators. Clinic progress notes were reviewed weekly to determine if these indicators were used and addressed. If SLE-QIs were missing, efforts were made to reach out to providers to address the missing QIs.

Results: At the beginning of the assessment, documentation of SLE-QIs was generally poor and inconsistent. For example, vaccinations was only at 60% compliance while screening for cardiovascular risk was only at 3% compliance. Since documentation was not standardized, it was difficult to assess if SLE-QIs were being done. Implementing SLE-QI in standardized notes resolved these concerns, bringing compliance close to 100% compliance for the 20 identified SLE quality indicators.

Conclusion: Standardized progress notes incorporating QI indicators is a feasible strategy that helps streamline data extraction for future clinical research. Additionally, incorporating patient outcome tools improves the ability to perform treat-to-target strategies for SLE. This ongoing QI project may potentially improve overall patient outcomes and lead to reduce health care costs.

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Abstract Number: 0279

Comparison of Carotid Ultrasound and Coronary Artery Calcium Score in Cardiovascular Risk Stratification of Patients with Inflammatory Rheumatic Diseases

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SESSION INFORMATION
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Background/Purpose: The value of non-invasive vascular imaging for cardiovascular (CV) risk stratification of patients with inflammatory rheumatic diseases is unclear. Measures of atherosclerosis including coronary artery calcification score (CACS) on computerized tomography (CT) scan and both total plaque area (TPA) and carotid intima-media thickness (cIMT) by carotid ultrasound (US) have been reported to improve risk stratification beyond the Framingham Risk Score (FRS). We determined the ability of CACS and US to correctly identify high CV risk patients with inflammatory rheumatic diseases.

Methods: In this cross-sectional study, patients with ankylosing spondylitis (AS), psoriatic arthritis (PsA) and rheumatoid arthritis (RA), who had no history of CV disease, underwent assessment of CV risk factors from July 2017 to March 2019 in a Cardio-Rheumatology clinic. CACS, cIMT and TPA were measured. The correlation between CACS and cIMT, between CACS and TPA, and between cIMT and TPA was assessed by Pearson correlation coefficient.

Table 1. Baseline characteristics of the study population (N = 139)

Variable	Mean ± SD / Frequency (%)
Age (years)	61.2 ± 10.9
Sex: Female (%)	93 (66.9)
Disease duration (years)	13.7 ± 12.0
Tender joint count	1.8 ± 3.5
Swollen joint count	1.0 ± 1.9
DMARDs – current use (%)	117 (84.2)
Use of anti-hypertensive medication (%)	38 (27.3)
BMI (kg/m^2)	28.5 ± 6.0
Current smoker (%)	7 (5.0)
Systolic blood pressure (mmHg)	127.2 ± 17.5
Diastolic blood pressure (mmHg)	78.4 ± 8.8
ESR (mm/hr)	19.6 ± 12.8
CRP (mg/L)	5.2 ± 10.5
Total Cholesterol (mmol/L)	4.9 ± 1.1
LDL cholesterol (mmol/L)	2.7 ± 0.9
HDL cholesterol (mmol/L)	1.6 ± 0.5
Triglycerides (mmol/L)	1.6 ± 1.1
CACS	140.0 ± 400.1
cIMT (mm)	0.665 ± 0.119
TPA (cm^2)	0.079 ± 0.176
Unilateral plaques (%)	30 (21.6)
Bilateral plaques (%)	18 (12.9)

Table 2. Framingham Risk Score categories versus Imaging-based risk groups

Table 2. Framingham Risk Score groups versus imaging-based risk categories

	FRS 10-year CV risk		
	Low risk (<10%) (n=77)	**Intermediate risk (10-19%) (n=34)**	**High risk (≥20%) (n=28)**
US-based risk categories			
Low risk (No plaque and cIMT ≤ 0.9mm) (%)	61 (79.2)	17 (50)	10 (35.7)
Intermediate risk (unilateral plaques) (%)	12 (15.6)	9 (26.5)	8 (28.6)
High risk (bilateral plaques and/or cIMT > 0.9mm) (%)	4 (5.2)	8 (23.5)	10 (35.7)
CACS-based risk categories			
Low risk (CACS=0) (%)	57 (74.0)	11 (32.4)	3 (10.7)
Intermediate risk (0-100) (%)	14 (18.2)	11 (32.4)	12 (42.9)
High risk (>100) (%)	6 (7.8)	12 (35.3)	13 (46.4)
FRS vs. US: Weighted κ = 0.33 FRS vs. CACS: Weighted κ = 0.42			

Table 3. Carotid US versus CACS-based risk categories

	CACS-based risk categories		
US-based risk categories	Low risk (CACS=0) (n=71)	Intermediate risk (0-100) (n=37)	High risk (>100) (n=31)
Low risk (No plaque and cIMT ≤ 0.9mm) (%)	59 (83.1)	20 (54.1)	9 (29.0)
Intermediate risk (unilateral plaques) (%)	10 (14.1)	10 (27.0)	9 (29.0)
High risk (bilateral plaques and/or cIMT > 0.9mm) (%)	2 (2.8)	7 (18.9)	13 (41.9)
Weighted κ = 0.39			

Based on the FRS, patients were classified into low (< 10%), intermediate (10-20%) and high risk categories (>20%). Risk categories for US were defined as low (zero plaque and cIMT< 0.9mm), intermediate (unilateral plaque) and high risk (cIMT >0.9mm and/or bilateral plaques). CACS risk categories were defined as low (CACS=0), intermediate (0-100) and high risk (>100). The weighted Kappa statistic was used to assess agreement between score categories.

Results: 139 patients with RA (49.6%), PsA (37.4%) and AS (12.9%) were assessed (mean age 61.2 ± 10.9 years, 66.9% female) (Table 1). CACS correlated moderately with TPA (r=0.42, p< 0.0001), while there was very weak correlation between CACS and cIMT (r=0.08), and between TPA and cIMT (r=0.14). 29.7% and 16.2% of patients classified into the low and intermediate risk categories based on the FRS had significant atherosclerosis in the carotid (TPA >0) and coronary arteries (CACS >100), respectively (Table 2). 50% of patients in the FRS intermediate risk category were reclassified into an US low risk group, while 35.7% of patients in the FRS high risk category were reclassified into an US low risk group. Importantly, when comparing US and CACS risk categories, 54% of patients in the intermediate CACS risk category were reclassified into a low risk US group (Table 3). There was generally good agreement between the FRS and CACS risk categories in stratifying low and high risk patients, while stratification among intermediate risk patients was poor. Overall, agreement between FRS and US (weighted k = 0.33), CACS and US (weighted k = 0.39), and FRS and CACS (weighted k = 0.42) risk categories was fair to moderate.

Conclusion: There is a moderate agreement between non-invasive carotid vascular and coronary calcium imaging in assessment of atherosclerosis burden in patients with IRDs. The results of the study highlight potential added value of using CACS and TPA in combination with traditional risk scores to improve CV risk stratification.

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Abstract Number: 0280

Ultrasound versus Conventional Treat-To-Target Strategies in Early Rheumatoid Arthritis: Magnetic Resonance Imaging Outcome Data from a 2-year Randomized Controlled Strategy Trial

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SESSION INFORMATION
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Background/Purpose: It has been debated whether treatment outcomes in early RA would be improved by targeting imaging remission, assessed by ultrasound or MRI, in addition to clinical remission. The primary analyses of the ARCTIC and TaSER trials (Haavardsholm et al. *BMJ* 2016; Dale et al. *ARD* 2016) did not show a beneficial effect of adding structured ultrasound assessment to a treat-to-target strategy. However, both studies reported a trend toward less radiographic progression in the ultrasound arm. We aimed to investigate whether an ultrasound-guided strategy would lead to reduced MRI inflammation or structural damage compared to a conventional treat-to-target strategy.

Methods: The ARCTIC trial included 230 DMARD-naïve early RA patients aged 18-75, randomized 1:1 to an ultrasound strategy targeting DAS < 1.6, no swollen joints and no power-Doppler signal in any joint, or a conventional strategy targeting DAS < 1.6 and no swollen joints. All patients were treated by the same DMARD escalation algorithm starting with MTX, then combination therapy MTX/SSZ/HCQ, then biologic DMARD. In the ultrasound arm, treatment was stepped up if indicated by the ultrasound score, overruling the DAS and swollen joint count. MRI of dominant hand was performed at 6 times and scored in chronological order by a blinded reader. MRI acquisitions and scoring were done according to the OMERACT RA MRI Scoring System (Østergaard et al. *J Rheum* 2017). 218 patients (ultrasound n=116, conventional n=102) had MRI at baseline and ≥ 1 follow-up visit, and were analyzed. A combined inflammation score was computed by normalized summation of the synovitis, tenosynovitis and bone marrow edema scores, and a combined damage score by normalized summation of the erosion and joint space narrowing scores (Sundin et al. *J Rheum* 2019). Mean change from baseline to each follow-up was estimated by a linear mixed model adjusted for baseline score, age, gender, center and anti-CCP status. The proportion of patients in each treatment arm with MRI erosive progression after 2 years was calculated, using the smallest detectable change (0.61) as cut-off.

Results: Demographic composition was comparable to the ARCTIC primary sample. There were no statistically significant baseline differences between the arms in either of the combined MRI scores. The mean combined MRI inflammation score decreased during the first year (1-year change in ultrasound arm –64.2 (–71.3; –57.1), conventional arm –59.4 (–66.9; –51.9) p=0.34), and maintained at the same level throughout the 2nd year. There was no significant difference in change from baseline between the study arms at any time (**figure 1a**). The mean combined MRI damage score showed a small increase over time, without any significant difference between study arms (**figure 1b**). In the ultrasound arm 39% of patients had MRI erosive progression vs. 33% in the conventional arm, RR: 1.16 (95% CI 0.81; 1.66), *p*=0.40.

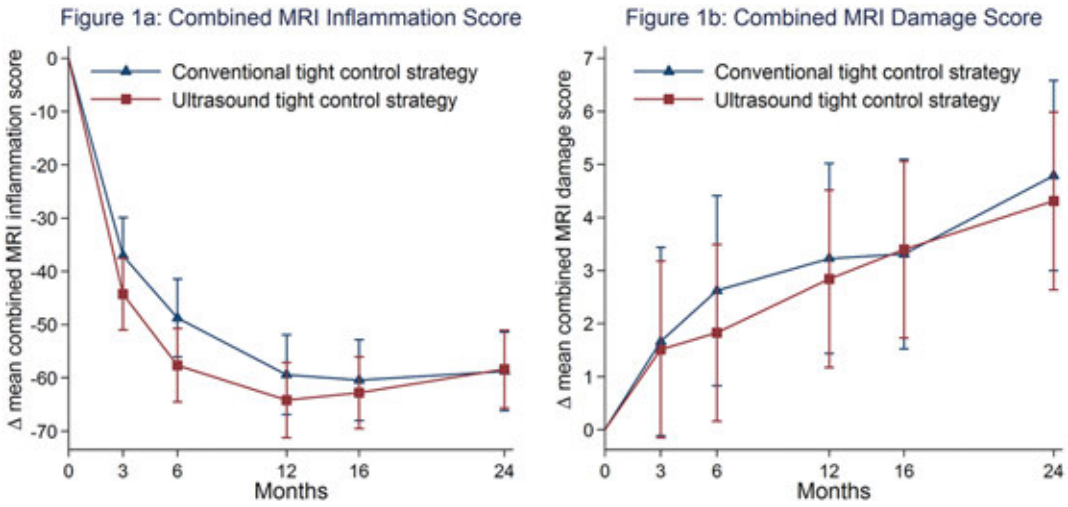

Figure 1 a-b. Change from baseline level to 3, 6, 12, 16 and 24 months of the mean combined MRI inflammation score (range 0-750) and the mean combined MRI damage score (range 0-500). Estimates based on a linear mixed model adjusted for baseline score, age, gender, center and anti-CCP status. Error bars represent 95% CI.

Conclusion: Incorporating ultrasound information in treatment decisions did not lead to reduced MRI inflammation or less structural damage, compared to a conventional treatment strategy. The findings support that systematic use of ultrasound does not provide benefit in treat-to-target follow-up of patients with early RA.

Disclosure: U. Sundin, None; **A. Aga**, AbbVie, 2, 8, Eli Lilly, 8, MSD, 2, Norwegian Research Council, 2, Norwegian Rheumatism Association, 2, Norwegian South-Eastern Health Region, 2, Norwegian Women's Public Health Association, 2, Novartis, 8, Pfizer, 2, 8, Roche, 2, UCB, 2, 8; **Ø. Skare**, None; **L. Nordberg**, None; **T. Uhlig**, None; **H. Hammer**, None; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **T. Kvien**, AbbVie, 2, 8, Biogen, 5, 8, Biogen, Egis, Eli Lilly, Hikma, Mylan, Novartis/Sandoz, Oktal, Hospira/Pfizer, Sanofi and UCB, 5, BMS, 8, Celltrion, 8, Egis, 5, 8, Eli Lilly, 5, 8, Hikma, 5, 8, Hospira/Pfizer, 2, 5, 8, MSD, 2, 8, Mylan, 5, 8, Novartis, 8, Novartis/Sandoz, 5, 8, Oktal, 5, 8, Orion Pharma, 8, Roche, 2, 8, Sandoz, 8, Sanofi, 5, 8, UCB, 5, 8; **S. Lillegraven**, AbbVie, 2, MSD, 2, Norwegian Research Council, 2, Norwegian South-Eastern Health Region, 2, Pfizer, 2, Roche, 2, UCB, 2; **E. Haavardsholm**, AbbVie, 2, 8, Cellgene, 8, Eli Lilly, 8, Janssen, 8, MSD, 2, Norwegian Research Council, 2, Norwegian South-Eastern Health Region, 2, Pfizer, 2, 8, Roche, 2, UCB, 2, 8.

Abstract Number: 0281

Frequency of Ultrasound Features of Knee Osteoarthritis and Their Association with Radiographic Features and Symptoms in a Community-Based Cohort

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SESSION INFORMATION

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Background/Purpose: To evaluate the frequency and associations of osteoarthritis (KOA) features on knee ultrasound (KUS) in a community-based cohort study with radiographic and symptomatic data in the same knees.

Table 1. Spearman correlations* between ultrasound (US) features and radiographic (XR) features for RIGHT knees.

KUS Feature (range)	Kellgren-Lawrence Grade (0-4)	Comparable XR feature†
	Spearman correlation p value	*Spearman correlation p value*
Gray scale effusion/synovitis (0-3)	**0.30 (0.16, 0.43) <0.0001**	na
Gray scale synovitis (0-3)	**0.29 (0.15, 0.43) <0.0001**	na
Gray scale effusion (0-1)	**0.16 (0.02, 0.30) 0.0257**	na
Suprapatellar color power Doppler signal (0-3)	**0.14 (0.00, 0.28) 0.0347**	na
Osteophytes, medial (0-3)	**0.62 (0.52, 0.71) <0.0001**	**0.58 (0.50, 0.66) <0.0001**
Osteophytes, lateral (0-3)	**0.54 (0.43, 0.64) <0.0001**	**0.57 (0.46, 0.67) <0.0001**
Meniscal extrusion, medial (0-1, compared with XR medial JSN, 0-3)	**0.42 (0.31, 0.54) <0.0001**	**0.36 (0.23, 0.49) <0.0001**
Meniscal extrusion, lateral (0-1, compared with XR lateral JSN, 0-3)	**0.15 (0.01, 0.29)** 0.0798	0.11 (-0.04, 0.25) 0.1818
Calcium deposition, medial (0-1)	0.08 (-0.06, 0.22) 0.1814	**0.24 (0.07, 0.42) <0.0001**
Calcium deposition, lateral (0-1)	**0.21 (0.08, 0.34) 0.0073**	**0.34 (0.18, 0.50) <0.0001**
Cartilage damage, medial (compared with XR medial JSN, both 0-3)	**0.15 (0.01, 0.28)** 0.0792	0.10 (-0.04, 0.23) 0.1369
Cartilage damage, lateral (to XR lateral JSN, both 0-3)	0.13 (-0.00, 0.27) 0.0526	0.13 (-0.01, 0.27) 0.0570
Popliteal cyst (0-2)	**0.25 (0.11, 0.39) 0.0001**	na

Correlation estimates with 95% confidence intervals (95% CI) excluding the null, and 0.05 p-value level significant statistics for nonzero correlation, are shown in **bold.*

†The feature most comparable to the US feature that was assessed on radiograph (e.g., medial osteophytes on US are compared to medial osteophytes on XR, while US cartilage damage and meniscal extrusion are both compared to XR JSN)

na=not applicable (no comparable XR feature)

Table 2. Spearman correlations* between US features or XR features with KOOS pain subscale scores or sxKOA for RIGHT knees.

KUS Feature (range)	KOOS pain subscale (continuous)	Symptomatic KOA (present/absent)
	Spearman correlation p value†	*Spearman correlation p value*
Gray scale effusion/synovitis (0-3)	0.07 (-0.07, 0.21) 0.3406	0.15 (-0.00, 0.30) 0.0059
Suprapatellar color power Doppler signal (0-3)	0.03 (-0.11, 0.17) 0.6696	0.12 (-0.02, 0.27) 0.4238
Osteophytes, medial (0-3)	**0.34 (0.23, 0.46) <0.0001**	**0.43 (0.32, 0.54) <0.0001**
Osteophytes, lateral (0-3)	**0.22 (0.08, 0.36) 0.0020**	**0.30 (0.16, 0.44) <0.0001**
Meniscal extrusion, medial (0-1)	**0.15 (0.01, 0.29) 0.0371**	**0.26 (0.12, 0.39) 0.0011**
Meniscal extrusion, lateral (0-1)	0.06 (-0.08, 0.20) 0.3963	0.07 (-0.07, 0.20) 0.4181
Calcium deposition, medial (0-1)	-0.05 (-0.18, 0.09) 0.5002	0.03 (-0.11, 0.18) 0.5214
Calcium deposition, lateral (0-1)	-0.10 (-0.24, 0.03) 0.1384	0.06 (-0.09, 0.20) 0.5069
Cartilage damage, medial (0-3)	**0.16 (0.03, 0.29) 0.0263**	**0.15 (0.03, 0.27) 0.0397**
Cartilage damage, lateral (0-3)	0.10 (-0.03, 0.24) 0.1518	0.13 (-0.00, 0.26) 0.0970
Popliteal cyst (0-2)	0.07 (-0.07, 0.21) 0.3310	**0.19 (0.05, 0.33) 0.0096**
Radiographic Features		
Kellgren-Lawrence grade (KLG, 0-4)	**0.25 (0.11, 0.38) 0.0005**	**0.52 (0.43, 0.61) <0.0001**
Osteophytes, medial (0-3)	**0.16 (0.03, 0.30) 0.0217**	**0.33 (0.22, 0.45) <0.0001**
Osteophytes, lateral (0-3)	0.13 (-0.01, 0.27) 0.0671	**0.22 (0.08, 0.36) 0.0008**
Chondrocalcinosis, medial (0-1)	-0.06 (-0.19, 0.07) 0.3968	0.13 (-0.03, 0.28) 0.0782
Chondrocalcinosis, lateral (0-1)	-0.10 (-0.24, 0.04) 0.1623	0.11 (-0.04, 0.26) 0.1214
Joint space narrowing (JSN), medial (0-3)	0.10 (-0.04, 0.24) 0.1554	**0.43 (0.30, 0.55) <0.0001**
Joint space narrowing (JSN), lateral (0-3)	**0.17 (0.02, 0.31) 0.0197**	**0.17 (0.01, 0.33) 0.0054**

Correlation estimates with 95% confidence intervals (95% CI) excluding the null, and 0.05 p-value level significant statistics for nonzero correlation, are shown in **bold.*
†Using modified ridit scores

Methods: A radiology technologist trained in standardized KUS imaging (SSG) scanned both knees in consecutive individuals enrolled in the Johnston County OA Project, using a written protocol. The KUS protocol included 7 views per knee: longitudinal and transverse suprapatellar in 30 degrees flexion (grading for effusion, gray scale synovitis and color power Doppler [CPD]), medial and lateral longitudinal (for osteophytes, meniscal damage, calcium deposition), maximally flexed suprapatellar transverse (for cartilage damage, calcium deposition) and posterior transverse (for popliteal cysts). Each set of images was scored using an atlas by 2 readers (previously shown to be reliable) whose scores were averaged. Radiographs (XR) were scored separately by an expert radiologist (JBR); all readers were blinded to other imaging and clinical data. Radiographic KOA (rKOA) was defined as a Kellgren-Lawrence grade (KLG) of 2 or more; osteophytes and joint space narrowing (JSN) were scored 0-3 using the OARSI atlas. Symptomatic KOA (sxKOA) was defined as rKOA with symptoms experienced in the same knee. Pain was assessed via the Knee Injury and OA Outcome Score (KOOS) pain subscale for each knee. We produced unadjusted Spearman correlations and additionally tested for nonzero correlation using the Cochran-Mantel-Haenszel statistic to describe

associations with each KUS and XR feature and pain. All results shown are for right knees; left knees demonstrated similar patterns.

Results: Participants (n=203) had a mean (±SD) age of 73 ± 8 years and a mean BMI of 29.4 ± 7 kg/m2; about 1/3 were male and 1/3 were African-American. About a third of knees had symptoms and 5% had a history of knee injury. About half of knees met the above definition for rKOA, while almost a quarter met the sxKOA definition. The majority of knees had US evidence (score >0) of at least one of the following: effusion/synovitis, osteophytes, and/or cartilage damage (data not shown). Correlations between US and XR features are shown in Table 1. The strongest correlations were seen for osteophytes (r=0.6); similar correlations were seen between US osteophytes and XR KLG. Correlations for calcium deposition detected by each modality (r=0.2-0.3) were significant. Non-identical constructs such as medial US meniscal extrusion and XR JSN (r=0.4) were also significantly correlated. Medial XR JSN was more closely related to US meniscal extrusion (r=0.4) than to US cartilage damage (r=0.1). Osteophytes by US, compared with XR, had slightly stronger correlations with KOOS pain (Table 2). Medial meniscal extrusion and cartilage damage by US were significantly correlated with KOOS pain while medial JSN by XR was not; all three were correlated with presence of sxKOA.

Conclusion: US assessment of KOA is accessible and reliable and provides information complementary to XR; KUS may provide increased sensitivity for early KOA changes. Future work will further examine the associations between US and radiographic features, including effect modification by key covariates.

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Abstract Number: 0282

Ultrasound Is More Sensitive Compared to Conventional Radiography to Detect Joint Erosions in ACPA-positive Patients with Musculoskeletal Pain

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

Background/Purpose: Circulating anti-citrullinated protein antibodies (ACPA) are associated with an increased risk of developing rheumatoid arthritis (RA), particularly in patients with erosive disease. We previously showed that erosions detected by ultrasound predict arthritis development in ACPA-positive patients with musculoskeletal (MSK) pain. We now aimed to compare ultrasound with conventional radiography to detect joint erosions during 2 years follow-up of ACPA positive patients with MSK pain.

Methods: We prospectively followed 82 ACPA-positive patients with MSK pain without arthritis at baseline clinical examination. Ultrasound at baseline and after 2 years assessed joint erosions, defined as intraarticular discontinuity

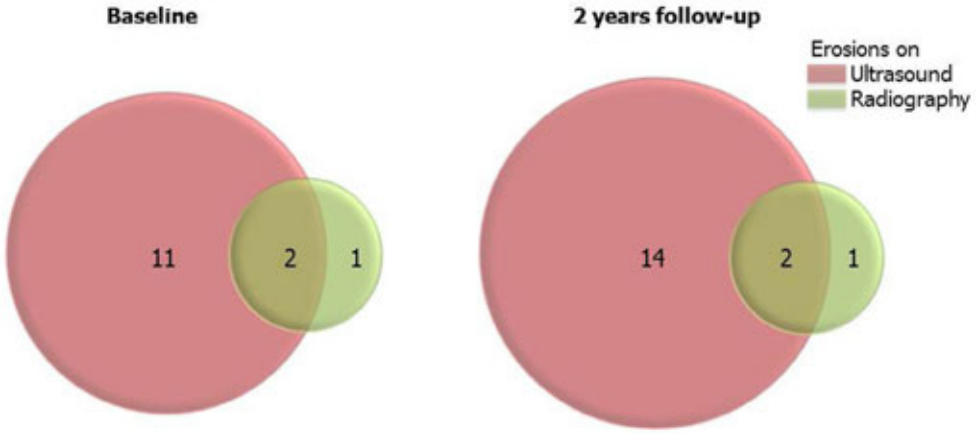

Figure 1. Number of patients with joint erosions according to ultrasound and/or conventional radiography in a cohort of 82 ACPA-positive patients with musculoskeletal pain.

of the bone surface visible in 2 planes, in 36 joints in hands and feet. Radiographs of hands and feet were taken at baseline and after 2 years, and evaluated by experienced radiologists according to clinical routine. In cases where erosions had been identified by the radiologist, and in all cases with indistinct findings as well as the radiographs of all patients with erosions by ultrasound, the radiographs were reevaluated by an experienced rheumatologist to confirm presence of erosions. We used Fisher's exact test to compare the prevalence of erosions as evaluated by ultrasound and radiography.

Results: Baseline joint erosion(s) were detected in 13 (16%) patients by ultrasound and in 3 (4%) patients by conventional radiography (p=0.016, Fig. 1). After 2 years follow-up, 30 of the patients (37%) had developed clinical arthritis. By ultrasound, erosion(s) were detected in 16 patients (19%) and in 3 (4%) by conventional radiography (p=0.018, Fig. 1). During follow-up, the total number of ultrasound erosions had increased from 16 to 20, while radiographic erosions had increased from 3 to 5 (p >0.05). Development of new erosions at 2 years occurred in 8 patients (12%) as evaluated by ultrasound, and in one patient (1%) by radiography (p=0.013) among patients without baseline erosions (by corresponding imaging techniques). In 5 out of the 13 patients (38%) with baseline ultrasound erosions, no further abnormality was detected at 2 years. The corresponding finding concerning radiographic erosion was made in 1 patient.

Conclusion: Ultrasound is more sensitive compared to conventional radiography to detect erosive abnormalities during follow-up of an ACPA-positive at-risk population. To some extent, erosive joint abnormalities show dynamic, and possibly reversible, features in very early phases of RA.

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Abstract Number: 0283

Can Synovial Hypertrophy in the Feet Without Doppler Change During Treatment - Results from a Longitudinal Study of Rheumatoid Arthritis Patients Initiating Biological DMARD

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SESSION INFORMATION
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Background/Purpose: Ultrasound is used to assess disease activity in rheumatoid arthritis (RA). Gray scale (GS) ultrasound shows the synovial hypertrophy (SH) and Doppler the amount of hyperemia. SH Both with and without Doppler change during treatment in the hands– even grade 1. However, SH grade 1 without Doppler is a common finding in the feet of both RA patients and healthy controls. If low grade SH in metatarsophalangeal joints (MTPs) does not have the ability to change during treatment this should be taken in to consideration in the ultrasound evaluation of disease activity and treatment effect in the feet.The aim was to investigate if joints with SH without Doppler activity (Doppler negative SH) in MTPs differ in ability to change during treatment with biological DMARD (bDMARD) as compared to metacarpophalangeal joints (MCPs) in RA patients.

Methods: RA patients initiating biological DMARD treatment were included. US examination was performed at baseline, 3 and 6 months using Siemens Antares US equipment with optimized Doppler settings for slow flow. Bilateral MCP 1-5 and MTP 1-5 were evaluated at each visit. SH and Doppler activity were graded from 0-3 according to the US atlas by Hammer et al. The GS score for SH in Doppler negative joints was registered for the individual joints using

Table 1. The frequency of synovial hypertrophy grades at different time points and the relative frequency of improvement for joints with Doppler negative SH and Doppler positive SH

	SH grade 1				SH grade 2				SH grade 3			
n = total number of joints per grade	MCP (n = 219)		MTP (n=382)		MCP (n=216)		MTP (n=261)		MCP (n=223)		MTP (n=104)	
	With Doppler	Without Doppler	With Doppler	Without Doppler	With Doppler	Without Doppler	With Doppler	Without Doppler	With Doppler	Without Doppler	With Doppler	Without Doppler
Baseline Percentage (number of joints)	12% (26)	88% (193)	9% (34)	91% (348)	77% (166)	23% (50)	49% (128)	61% (133)	96% (215)	4% (8)	80% (83)	20% (21)
3 months Percentage (number of joints)	7 % (15)	33% (72)	5% (18)	53% (204)	35% (76)	9% (20)	20% (51)	22% (57)	42% (94)	1% (2)	38% (39)	4% (4)
6 months Percentage (number of joints)	7% (16)	30% (66)	6% (22)	53% (202)	26% (55)	7% (15)	18% (48)	23% (61)	35% (79)	1% (1)	22% (23)	5% (5)
	MCP		MTP		MCP		MTP		MCP		MTP	
Percentage of joints with improvement in SH (n= number of joints at baseline)	With Doppler (n=26)	Without Doppler (n=193)	With Doppler (n=34)	Without Doppler (n=348)	With Doppler (n=166)	Without Doppler (n=50)	With Doppler (n=128)	Without Doppler (n=133)	With Doppler (n=215)	Without Doppler (n=8)	With Doppler (n=83)	Without Doppler (n=21)
From baseline to 3 months	42%	63%	47%	41%	54%	60%	60%	57%	56%	75%	53%	81%
From baseline to 6 months	38%	66%	36%	43%	67%	70%	62%	55%	63%	88%	74%	76%

SH=synovial hypertrophy, MCP= metacarpophalangeal joints, MTP=metatarsophalangeal joints

GS SH >1 as threshold and were compared to changes in SH score in joints with Doppler activity (Doppler positive SH) in both MCPs and MTPs. Doppler positive was defined as Doppler score ≥1.

Results: 157 patients (83.2% women, 81.3% seropositive for anti-CCP and 75.8% for rheumatoid factor) were included, with a mean (SD) age of 51.5 (13.3) years and disease duration of 9.9 (8.1) years. At baseline, 52.2% used prednisolone (mean (SD) 7.7 (4.6) mg, range 2.5-25mg). The patients had a mean (SD) baseline DAS28 of 4.5 (1.5).1570 MTPs and 1570 MCPs were examined and of these 502 MTPs (32%) had Doppler negative SH and 245 (16%) Doppler positive SH. For MCPs, 251 (16%) had Doppler negative SH and 407(26%) Doppler positive SH. Doppler negative Grade 1 SH were more frequent in MTP than MCP joints and Doppler negative grade 3 SH was rare in MCPs (table 1). The percentage of joints exhibiting a decrease in SH was similar for both MTPs and MCPs, both for joints with Doppler negative SH and Doppler positive SH at baseline. However, adjusting for the grade of SH at baseline, joints with Doppler negative SH appeared to have a somewhat greater tendency towards change. For joints with Doppler negative SH grade 1 at baseline the tendency to change was somewhat lower for MTPs than MCPs (41% vs 63% respectively at 3 months and 43% vs 66% respectively at 6 months follow-up).

Conclusion: Most joints with Doppler negative SH had low grades of SH with the majority having a grade 1 – especially in MTPs. Doppler negative SH in MTPs and MCPs can improve during treatment and exhibit the same tendency to change. For joints with Doppler positive SH, MTPs have the same tendency to change as MCPs except that MTPs with Doppler negative grade 1 SH showed a somewhat lower tendency to change than the corresponding MCPs.

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Abstract Number: 0284

Impact of Body Mass Index on the Agreement Between Ultrasound- and Clinical Assessments of Disease Activity in Rheumatoid Arthritis : Multicenter and Cross-sectional Study

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Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical evaluation of synovitis in rheumatoid arthritis (RA) is difficult in obese (O) and overweight patients, due to the fat pad located around the joint, that can over- or under estimate the number of joints regarded as swollen by clinical examination.

Objectives: To compare the level of agreement between the number of joints considered abnormal by Power Doppler ultrasound (PDUS) and clinical examination (swollen joint count (SJC) as component of SDAI) in O (i.e. Body Mass Index (BMI) >30) versus non-obese (NO) (BMI≤30) RA patients.

Methods: RA patients ≥18 years fulfilling 2010 ACR-EULAR criteria, treated with conventional synthetic (cs) or biologic (b) DMARDs were included in the cross-sectional multicenter (13 centers) French observational RABODI study (ClinicalTrials.gov Identifier: NCT03004651). Clinical synovitis was evaluated on 44 joints. ESR and CRP were collected and several composite scores were calculated: SDAI, DAS28, DAS. A standard US examination on 44 joints for the presence of synovial hypertrophy (SH) and PD signal according to the EULAR-OMERACT scoring system was performed in each center by an independent investigator blinded to clinical data. Presence of US synovitis was defined by a SH≥1 and PD signal≥1 on a semi-quantitative scale. Levels of agreement between number of synovitis defined by PDUS and clinical examination were compared in O versus NO patients using Chi2 test, and Kappas (k) and ORs were calculated. A patient was considered "discordant" if ≥1 joint was discordantly classified by PDUS and clinical examination. SDAI was calculated and compared, with SJC defined either by clinical examination or PDUS.

Results: 121 patients were included: mean (SD) age of 58.5 (12.7) years, mean disease duration of 11.1 (9.7) years. 81% were female, 84.3% anti-CCP positive, 63.6% had erosive disease. Mean SDAI was 12,6 (±10,2). 53 (43.8%) had a BMI >30 and 68 (56.2%) ≤30. 59 (48.7%) and 62 (51.2%) had a SDAI≤11 and >11, respectively. 78.5% received csDMARD, 58.7% bDMARD and 40.5% glucocorticoids. The 2 groups were comparable, except for weight (mean (SD) 65.4 (13.5) vs 96.7 (14.7) kg, p< 0.001), some comorbidities (diabetes, asthma and fibromyalgia more frequent in O patients, anemia less frequent), tender joint count (mean 4.04 (±5.23) in NO vs 7.38 (±8.64) in O, p=0.021). Mean

Table: Level of agreement between PDUS synovitis and SJC in obese versus normally weighted RA patients

		BMI <= 30 N=68	BMI > 30 N=53	OR (95%CI)	P*
SDAI (with PDUS) vs. SDAI (with SJC)	Non-Discordant	63	46	1.92 (0.57-6.42)	0.28
	Discordant	5	7		
	Kappa	0.85	0.73		
DAS28 (with PDUS) vs. DAS28 (with SJC)	Non-Discordant	62	47	1.32 (0.4-4.35)	0.64
	Discordant	6	6		
	Kappa	0.81	0.77		
DAS44 (with PDUS) vs. DAS44 (with SJC)	Non-Discordant	63	52	0.24 (0.03-2.14)	0.23
	Discordant	5	1		
	Kappa	0.83	0.96		
PDUS vs. SJC	Non-Discordant	51	35	1.54 (0.7-3.4)	0.28
	Discordant	17	18		
	Kappa	0.50	0.32		

*Chi^2 test

number of clinical synovitis was 2.4 (3.3), and 6.7 (±6.3) by PDUS. Levels of agreement between clinical and PDUS findings were comparable in O vs. NO patients regarding SDAI and other scores (Table). Patients with ≥3 discordant joints was numerically higher in O patients compared to NO (26/53 (49.1%) vs 22/68 (32.4%), p=0.062). Results were similar when overweighted patients (BMI >25) were compared with normally weighted patients (BMI≤25) or when SH≥1 was considered in place of PDUS synovitis. At the joint level, discordance was higher in O patients in some specific joints: MCP4 (p=0.057), wrist (p=0.089).

Conclusion: In RA patients, despite a perceived higher difficulty to clinically detect synovitis (SJ) in O patients, the discrepancy between clinically- and PDUS defined synovitis was not significantly higher than in NO patients, and did not impact the extend of the definition of disease activity level.

Disclosure: G. Mouterde, None; **F. Manna**, None; **B. Le Goff**, None; **J. Albert**, None; **S. Jousse-Joulin**, None; **F. Gandjbakhch**, None; **D. Loeuille**, None; **P. Gaudin**, None; **M. Piperno**, None; **F. Banal**, None; **B. Jamard**, None; **C. Salliot**, None; **N. Molinari**, None; **B. Combe**, AbbVie, 5, BMS, 5, 8, Chugai, 5, 8, Eli Lilly, 5, Eli Lilly and Company, 5, 8, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, UCB, 5, USD, 5; **M. D'Agostino**, None; **C. Lukas**, None.

Abstract Number: 0285

Thermal Imaging in Rheumatoid Arthritis: A Comparative Analysis with Ultrasonography and Clinical Joint Assessment

York Kiat Tan ,[1] Cassandra Hong,[1] HuiHua Li,[2] John Carson AllenJr,[3] and Julian Thumboo[1], [1]Department of Rheumatology and Immunology, Singapore General Hospital, Singapore, Singapore, [2]Health Services Research, Singapore General Hospital, Singapore, Singapore, [3]Centre for Quantitative Medicine, Duke-NUS Medical School, Singapore, Singapore

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Imaging Of Rheumatic Diseases Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The potential of thermal imaging in detecting joint inflammation in rheumatoid arthritis (RA) has not been well studied or compared with other approaches in assessing joint inflammation. Therefore, we aimed

Table 1. Comparing thermographic parameters between joints based on ultrasound findings.

Thermographic Parameter	Mean values within ultrasound category		Difference (95% CI)	P-value
	PD negative	PD positive		
Tmax (°C)	31.2	32.5	1.37 (0.86, 1.87)	**<0.001**
Tmin (°C)	29.3	30.2	0.91 (0.46, 1.36)	**<0.001**
Tavg (°C)	30.1	31.3	1.16 (0.67, 1.64)	**<0.001**
Tmax-min (°C)	1.82	2.29	0.46 (0.28, 0.64)	**<0.001**
	GS negative	GS positive		
Tmax (°C)	31.1	32.2	1.09 (0.67, 1.52)	**<0.001**
Tmin (°C)	29.3	30.0	0.66 (0.32, 1.00)	**<0.001**
Tavg (°C)	30.1	31.0	0.86 (0.47, 1.26)	**<0.001**
Tmax-min (°C)	1.79	2.23	0.45 (0.28, 0.62)	**<0.001**

PD, power Doppler; GS, grey-scale; Tmax, maximum temperature; Tmin, minimum temperature; Tavg, average temperature; Tmax-min, maximum minus minimum temperature.

Table 2. Comparing thermographic parameters and ultrasound scores between joints based on their clinical status.

Thermographic/ ultrasound Parameter	Mean values within Clinical joint category				F-test P-value	Differences (95% CI) S0T0 vs			P-values S0T0 vs		
	S0T0	S0T1	S1T0	S1T1		S0T1	S1T0	S1T1	S0T1	S1T0	S1T1
Tmax (°C)	31.3	31.1	31.6	31.7	0.324	0.25 (-0.66, 0.16)	0.30 (-0.88, 1.47)	0.44 (-0.44, 1.33)	0.238	0.620	0.325
Tmin (°C)	29.4	29.2	29.7	29.9	0.249	-0.21 (-0.68, 0.26)	0.27 (-0.67, 1.21)	0.52 (-0.12, 1.15)	0.385	0.572	0.110
Tavg (°C)	30.3	30.1	30.4	30.7	0.485	-0.17 (-0.60, 0.25)	0.14 (-0.98, 1.25)	0.44 (-0.32, 1.19)	0.423	0.808	0.259
Tmax-min (°C)	1.89	1.82	1.95	1.84	0.886	-0.07 (-0.29, 0.15)	0.06 (-0.33, 0.45)	-0.05 (-0.40, 0.31)	0.527	0.769	0.793
PD score	0.08	0.16	0.53	0.75	**<0.001**	0.08 (-0.03, 0.19)	0.46 (0.07, 0.84)	0.67 (0.39, 0.96)	0.171	**0.021**	**<0.001**
GS score	0.18	0.31	1.01	1.04	**<0.001**	0.13 (-0.04, 0.29)	0.83 (0.37, 1.29)	0.86 (0.54, 1.18)	0.140	**<0.001**	**<0.001**

S0T0, non-swollen and non-tender; S0T1, non-swollen but tender; S1T0, swollen but non-tender; S1T1, swollen and tender; Tmax, maximum temperature; Tmin, minimum temperature; Tavg, average temperature; Tmax-min, maximum minus minimum temperature; PD, power Doppler; GS, grey-scale.

to gain further insight into the role of thermal imaging in RA by performing a comparative analysis with ultrasound (US) and clinical joint assessment.

Methods: 22 joint (including bilateral wrists, metacarpophalangeal joints, thumbs interphalangeal joints and proximal interphalangeal joints) were studied per patient. At the joint sites, thermographic parameters included maximum (Tmax), minimum (Tmin), average (Tavg) and Tmax minus Tmin (Tmax-min) temperatures, US parameters collected at the same study visit included power Doppler (PD) and grey-scale (GS) joint inflammation (graded semi-quantitatively 0-3), while clinical assessment included joint swelling and tenderness (graded yes=1 or no=0). As imaging findings for different joints in the same patient may not be independent, Generalized Estimating Equations (GEE) analysis was used to (a) compare the differences in mean values of thermographic parameters between joints based on their PD or GS positivity/negativity status (b) compare the differences in mean values of thermographic parameters, US PD and GS scores between joints based on their clinical swelling and tenderness status. Differences in means and 95% CIs were estimated using GEE with robust Huber-White variance estimates.

Results: 814 joints were studied in 37 RA patients with the following baseline characteristics: mean age, 56.5 years; 75.7% female; 75.7% Chinese; mean (SD) disease duration, 30.9 (45.3) months; mean (SD) DAS28, 4.43 (1.12). Comparing joints with PD positivity versus those with PD negativity (table 1), the differences in mean values (95% CI) for thermographic parameters Tmax, Tmin, Tavg and Tmax-min had all attained statistical significance (P-values were all < 0.001). The corresponding differences in mean values (95%CI) for the thermographic parameters comparing joints with GS positivity versus those with GS negativity (table 1) were similarly statistically significant (P-values were all < 0.001). The differences in mean values (95% CI) for PD and GS scores—but not for thermographic parameters—were statistically significant for (a) swollen and tender joints (PD: 0.67 (0.39, 0.96), $P< 0.001$; GS: 0.86 (0.54, 1.18), $P< 0.001$) and (b) swollen and non-tender joints (PD: 0.46 (0.07, 0.84), $P=0.021$; GS: 0.83 (0.37, 1.29), $P< 0.001$) when compared to non-swollen and non-tender joints (table 2)

Conclusion: Thermographic parameters were useful in discriminating between US PD and GS positivity versus negativity status at the RA joints, although they were not useful—unlike ultrasonography—for discriminating between joints based on clinical swelling and tenderness status.

Disclosure: Y. Tan, None; **C. Hong**, None; **H. Li**, None; **J. Allen Jr**, None; **J. Thumboo**, None.

Abstract Number: 0286

Imaging Neoangiogenesis in Rheumatoid Arthritis (INIRA): Whole-Body Synovial Uptake of a 99mTc-Labelled RGD Peptide Is Highly Correlated with Power Doppler Ultrasound

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Imaging Of Rheumatic Diseases Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Power doppler ultrasound (PDUS) is superior to clinical examination in the detection of synovitis in patients with rheumatoid arthritis (RA). Although dynamic and cheap it is impractical to scan large numbers of joints in routine clinical settings. MRI, whilst sensitive for synovitis, is expensive, and routine use is limited to targeted joints. Bone scintigraphy produces whole body images but due to lower specificity is not routinely used to detect synovitis

^{99m}Tc-maraciclatide (Serac Healthcare) is a radio-labelled tracer which binds with high affinity to integrin $\alpha_v\beta_3$, a cell-adhesion molecule up-regulated on neoangiogenic blood vessels. It therefore has the potential to image synovial inflammation at the whole-body level. We previously showed in a pilot study that uptake was seen in the inflamed joints of 5 RA patients and that this correlated with PDUS[1]. This study explores correlation with PDUS in a larger groups of patients with a range of disease activities

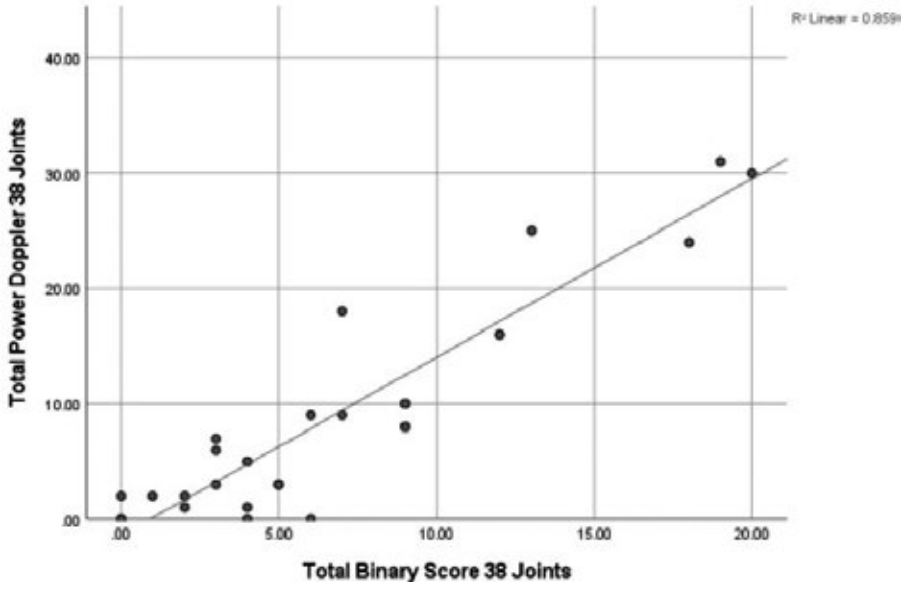

Figure 1. Correlation between total power doppler and 99mTc-maraciclatide binary scores

Methods: 25 patients with RA, fulfilling ACR 2010 classification criteria, were recruited. Patients underwent 66/68 swollen/tender joint counts followed by an ultrasound scan of 38 joints with grey scale (GS) and PD quantification. As per OMERACT guidelines, each joint was scored on a scale of 0-3 for GS and PD with a total score calculated for each patient. Within 3 hours of the ultrasound, patients were injected with 740 MBq of ^{99m}Tc-maraciclatide. Using a

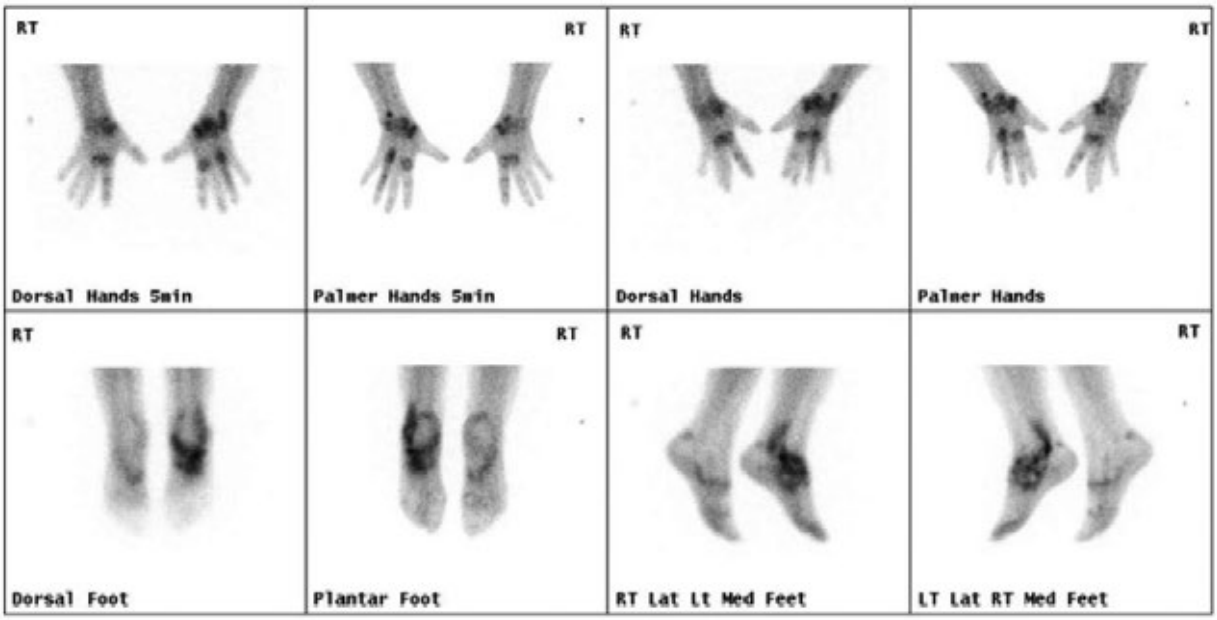

Figure 2. 99mTc-maraciclatide imaging with dedicated hand and foot views

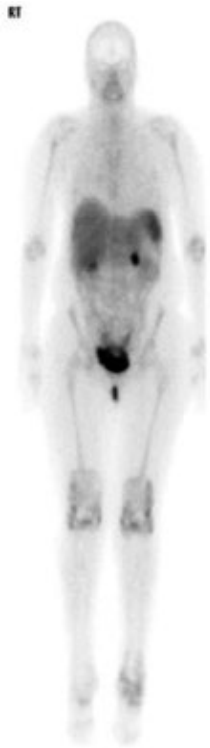

Figure 3. 99mTc-maraciclatide whole body image

gamma camera, whole body planar views and dedicated hand and foot views were taken 2 hours after injection. Acquisition time was 20 minutes for whole body, and 20 minutes for hand and foot views. Nuclear medicine images were scored as positive or negative uptake for each joint (binary score). Binary scores were summed individually to derive a total score for each patient. Ultrasound and ^{99m}Tc-maraciclatide scores were tested for correlation with Pearson's correlation coefficient. Significance was set at $p< 0.05$

Results: Strong correlation was seen between total PDUS and binary scores ($r=0.93$, $r^2=0.86$, $p< 0.001$). In the wrists and ankles ^{99m}Tc-maraciclatide uptake was seen not only in synovitic joints but in inflamed tendons/ tendon sheaths. The imaging procedure was well-tolerated

Conclusion: ^{99m}Tc-maraciclatide uptake was highly correlated with PDUS highlighting its potential as a viable alternative imaging modality. ^{99m}Tc-based planar imaging has the unique capacity to image the whole body and hence the total synovial inflammatory load in a quick acquisition. Furthermore the imaging equipment to perform these scans is already widely available in nuclear imaging departments. Interpretation of scans is also much simpler compared to US and MRI. It could therefore have a role in key decision-making points in pathways for diagnosis, treatment failure, and remission prior to dose tapering. Recruitment is underway to expand the data to a larger group of patients

Reference:

1. Garrood T, Morrison M, Shivapatham D, Chaabo K, Ul-Hassan F, Ballinger J, Cook G, Cope AP. Whole-Body Synovial Uptake of a 99mtc-Labelled RGD Peptide Is Highly Correlated with Power Doppler Ultrasound [abstract]. *Arthritis Rheumatol.* 2015; 67 (suppl 10)

Disclosure: L. Attipoe, None; **T. Garrood**, None; **S. Subesinghe**, None; **M. Opena**, None; **C. Blanco-Gil**, None; **M. Rosser**, Serac Life Sciences, 4, Serac Life Sciences, 4; **G. Cook**, Guy's and st Thomas' Hospitals NHS Trust, 2; **A. Cope**, None.

Abstract Number: 0287

Ultrasound Evaluation of the Achilles Enthesis in Inflammatory and Non-inflammatory Processes: A Systematic Review

Nancy Desai ,[1] Justin Bucci,[1] and Eugene Kissin[2], [1]Boston Medical Center, Boston, [2]Boston University, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Imaging Of Rheumatic Diseases Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Ultrasound (US) evaluation of the Achilles tendon has been utilized to assess involvement at the entheses in the setting various inflammatory, metabolic and mechanical processes. The purpose of this systematic review is to determine if US evaluation has been reported to show different findings at the Achilles enthesis with inflammatory (IT) versus non-inflammatory tendinopathy (NIT).

Methods: We conducted a systematic review of all studies involving US evaluation of IT or NIT (mechanical or metabolic) affecting the Achilles enthesis using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We systematically searched the Embase, PubMed, Medline databases from start until August 2018. One author applied predefined exclusion criteria, excluding poster or conference abstracts, as well as studies without original data, without description of US findings, studies not focused on the Achilles tendon or studies in children. An additional author was utilized to perform secondary review of these articles and any differences were then mitigated by a 3rd reviewing author. Data was extracted from selected articles assessing tendon thickness, Doppler signal and erosions.

Results: Our initial search yielded 574 articles, limited to 174 by initial abstract review and to 46 through full text review. Of these, 30 studies investigated an underlying IT, 14 studies focused on NIT, and 2 articles evaluated both. At the enthesis, the Achilles was abnormally thickened in 12.0% of all patients reported in IT and 29.4% in symptomatic IT groups in comparison to 27.9% of those with NIT and 7.4% of those in the healthy control group. The average Achilles enthesis thickness was 5.24mm in 147 tendons in 4 studies of all patients with underlying IT, 5.65mm in patients from 3 studies focused only on symptomatic tendons in those with IT, compared to 5.72mm in 340 tendons from 6 studies including NIT, and 4.16mm in 243 healthy tendons (5 studies) (Figure 1). NIT increased incidence of Doppler signal at the Achilles enthesis to 28.2% (n=306 tendons, studies = 7, range from 0 to 96.4%) in comparison to 7.6% in IT (n=2746 tendons, studies =24, range 0 to 100%), 12.2% in those with specifically symptomatic IT (n=131 tendons, studies=4, range 1.1 to 100%) and 0.5% for healthy controls (n=953 tendons, studies = 12, range 0 to 6.25%) (Figure 2). Incidence of erosions was similar between IT, 10.9% (n=3108 tendons, studies = 31, range 0.9 to 95.6%) and NIT, 11.1% (n=227 tendons, studies = 5, range 1.2 to 31.1%) and 1.93% in healthy controls (n=973 tendons, studies =12, range 0 to 23.3%) (Figure 3).

Conclusion: Achilles enthesis thickening and even erosions are reported at a similar incidence and degree in both patients with IT and NIT. Surprisingly Doppler signal is more commonly reported in NIT even compared to studies

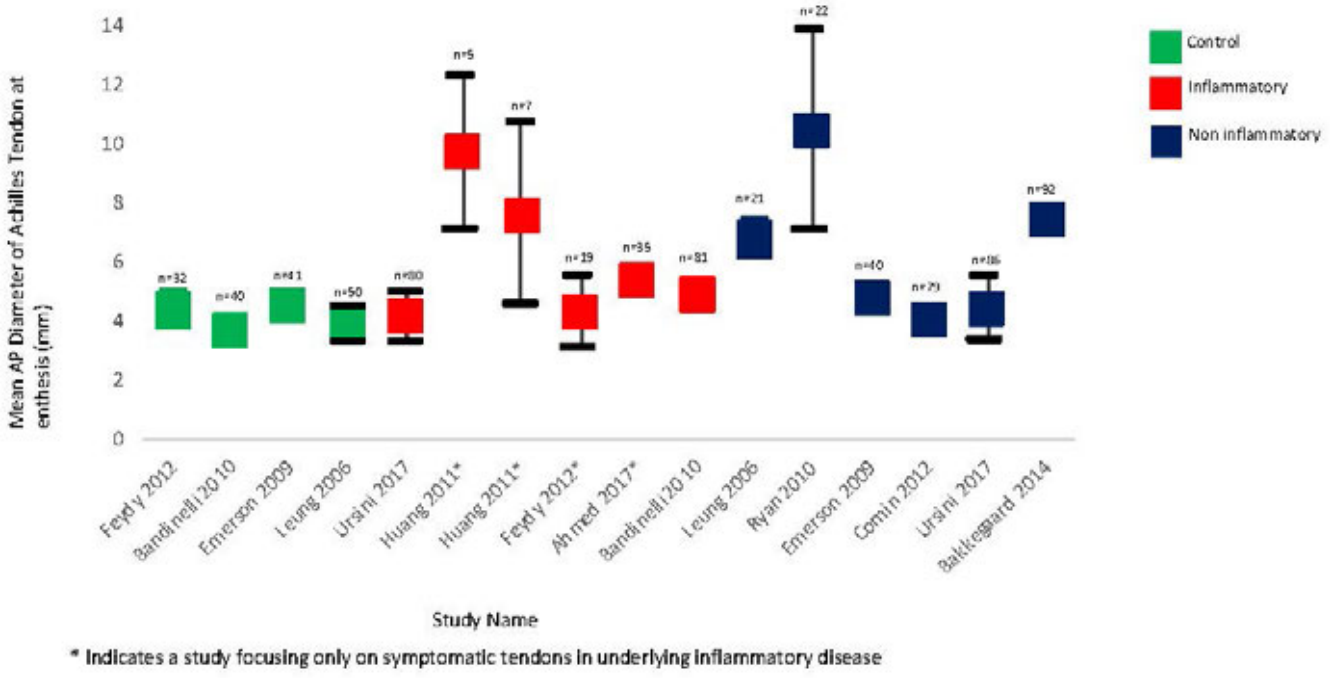

Figure 1. Studies with Increased Thickness Noted at Achilles Enthesis (mm)

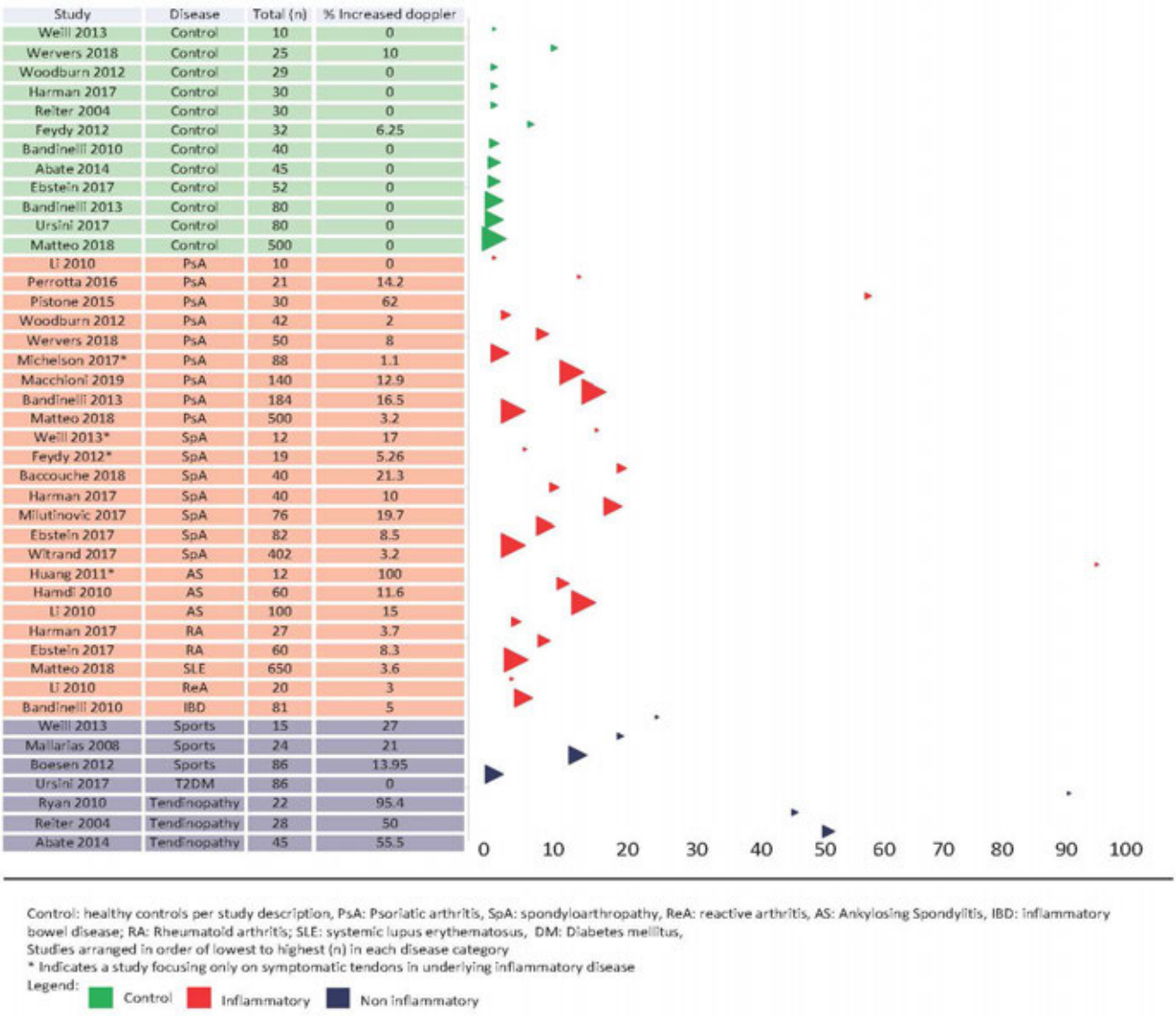

Figure 2. Studies with Doppler Signal Noted at the Achilles Enthesis

looking only at symptomatic tendons with underlying inflammatory conditions. These typical US abnormalities at the Achilles enthesis may not be helpful in distinguishing inflammatory from non-inflammatory causes.

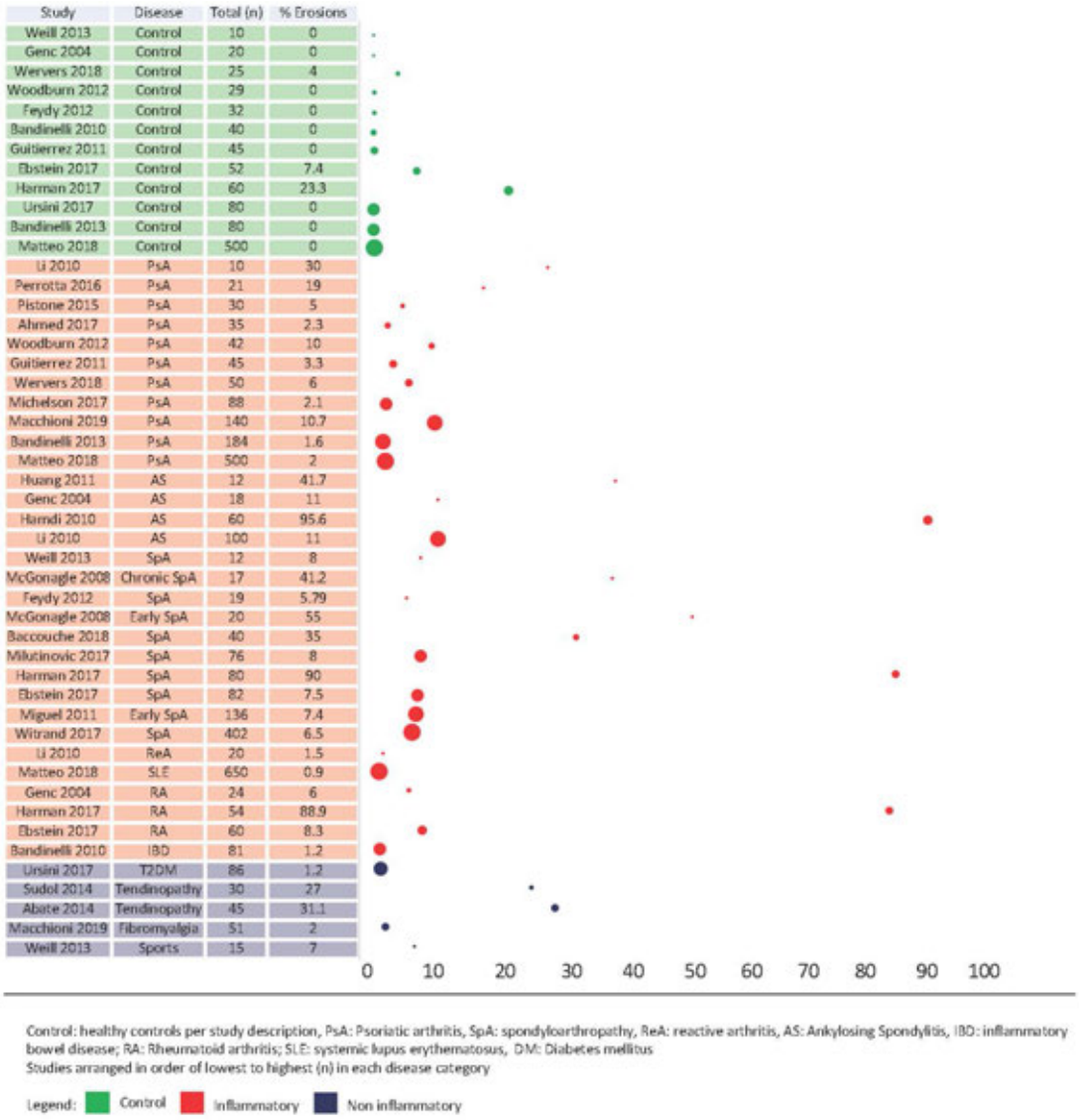

Figure 3. Studies with Erosions Noted at the Achilles Enthesis

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Disclosure: N. Desai, None; **J. Bucci**, None; **E. Kissin**, None.

Abstract Number: 0288

Evaluating the Performance of a Single-site Musculoskeletal Ultrasound Clinic Associated with an Academic Rheumatology Practice: Diagnostic and Therapeutic Impact on Patient Care and Survey of Patient and Physician Satisfaction

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: Imaging Of Rheumatic Diseases Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Growing utilization of musculoskeletal ultrasound (MSUS) for the management of rheumatologic disorders has led to integration of dedicated MSUS clinics in many rheumatology practices. However, there is limited published data on patient/physician satisfaction with such clinics and their clinical impact. This study aimed to analyze the performance of our MSUS clinic by assessing (1) reasons for referral, (2) patient/physician satisfaction and (3) subsequent diagnostic and therapeutic impact.

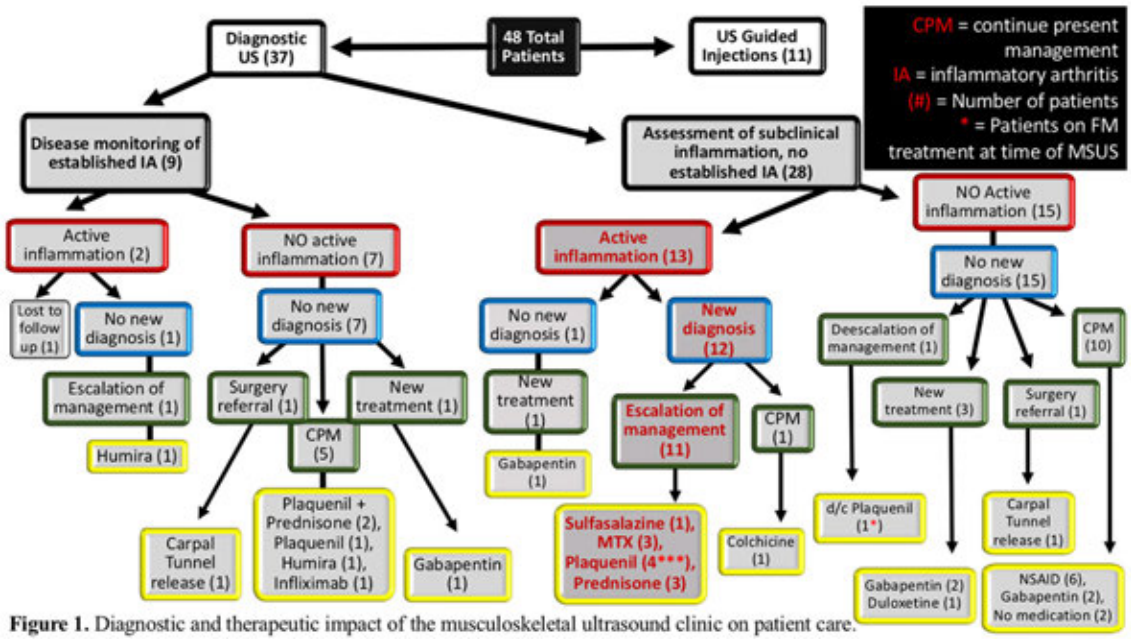

Figure 1. Diagnostic and therapeutic impact of the musculoskeletal ultrasound clinic on patient care.

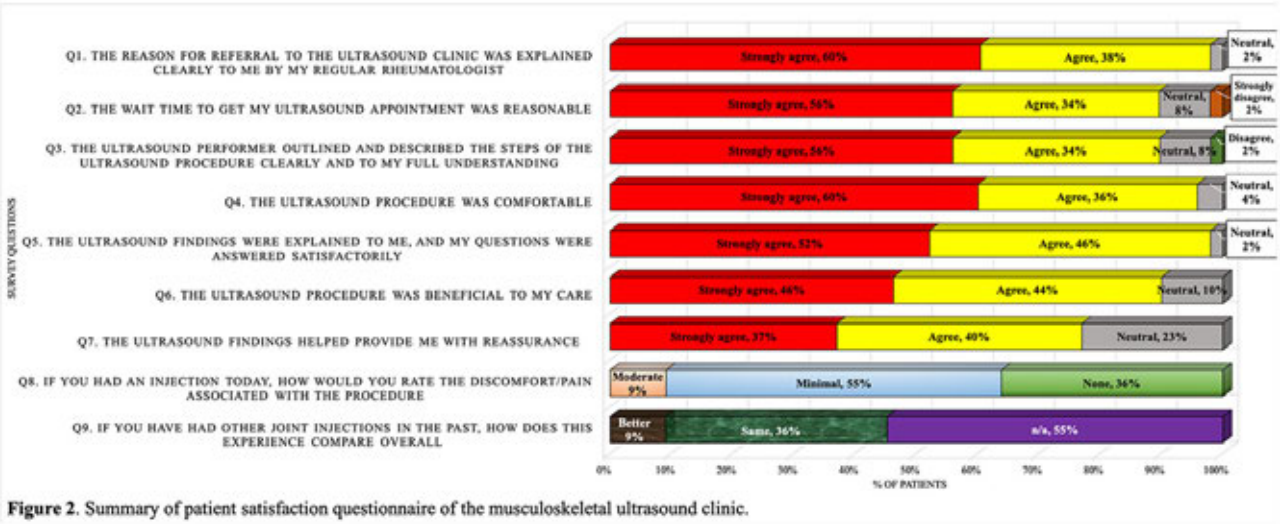

Figure 2. Summary of patient satisfaction questionnaire of the musculoskeletal ultrasound clinic.

Figure 3. Summary of physician questionnaire on satisfaction and perceived utility of the musculoskeletal ultrasound clinic.
(#%): Percentage of physicians with labeled response.

Methods: Patients (pts) and referring rheumatologists anonymously completed and returned a single written in-office questionnaire-based survey, at the end of the visit or study, respectively. For all pts seen for diagnostic MSUS, a retrospective chart review was conducted, and post-MSUS diagnosis and management were documented. Positive MSUS findings, indicative of inflammatory arthritis (IA), were defined as synovitis, tenosynovitis, dactylitis, erosions, synovial thickening or crystal deposition.

Results: Of 48 total pts, seen over 5 months, 23% (n=11) received US guided joint injections and 77% (n=37) had diagnostic US for disease monitoring/management of established IA (n=9) or assessment of subclinical/suspected IA (n=28). Of the 28 pts with suspected IA, 46% (n=13) had MSUS findings of IA, prompting initiation of DMARD (n=8) or prednisone (n=3). Remaining 54% of pts (n=15) had no inflammation on MSUS, leading to de-escalation (n=1) or no escalation of management (n=14). Of 9 pts with established IA, 78% (n=7) showed no active synovitis, with no consequent escalation of management (figure).

The patient survey had 100% response rate, 9.6 mean satisfaction score (1-10 scale) and > 75% positive feedback (strongly agree or agree) for every question (Q); 89-98% explanation of procedure/results (Q1, 3, 5), 89% appointment wait time (Q2), 95% comfort (Q4), 90% benefit to care (Q6), 77% reassurance (Q7). Of pts who received injections, 82% had minimal to no pain, and 100% had similar to improved overall experience, compared to prior injections (figure 2).

Of the 83% (n=10) physician survey response, 100% indicated plan for future referral (figure 3). The most frequent reason given for referral was assessment of subclinical/suspected IA (n=10), followed by US injections (n=9) and disease monitoring (n=4). The majority of physicians (75%, n=3) with experience performing MSUS referred most often (>10 pts/12 months). However, in regards to perceived impact on clinical decision making or benefit to patient care, there was no statistical difference between physicians with more MSUS or rheumatology experience, compared to their less experienced colleagues.

Conclusion: The MSUS clinic was most impactful in the evaluation of patients with subclinical/suspected IA. This group of patients comprised the most referrals to the clinic and 46% of patients had positive US findings, which helped to confirm a new diagnosis of IA. Overall, the MSUS clinic received high patient and physician satisfaction scores and was perceived as beneficial to patient care by both patients and referring rheumatologists.

Disclosure: N. Nensey, None; **S. Hassan**, None.

Abstract Number: 0289

Doppler in Entheses: A Potential Useful Outcome in Active Spondyloarthritis and Psoriatic Arthritis

Juan Molina Collada ,[1] Cristina Macía-Villa,[2] Chamaida Plasencia,[3] Diana Peiteado,[4] Laura Nuño,[5] Irene Monjo,[6] Alejandro Villalba,[7] Carolina Tornero,[8] Patricia Bogas,[1] Luis Coronel,[9] Gabriela González,[1] Diego Benavent,[10] Elisa Fernández,[11] Pablo Rodríguez,[1] Gerardo Napky,[1] Alejandro Balsa,[5] and Eugenio de Miguel[12], [1]La Paz University Hospital, Madrid, Spain, [2]Severo Ochoa University Hospital, Madrid, Spain, [3]Immuno-Rheumatology Research Group, IdiPaz & Rheumatology Department. La Paz University Hospital, Madrid, Spain, [4]Hospital Universitario La Paz, Madrid, [5]Rheumatology Department, Hospital Universitario La Paz, Madrid, Spain, Madrid, Spain, [6]FIBHULP-IdiPAZ-Hospital La Paz-Rheumatology, Madrid, Spain, [7]FIBHULP-IdiPAZ-Hospital La Paz-Rheumatology, Madrid, [8]Rheumatology Department. La Paz University Hospital., Madrid, [9]Nuestra Señora de la Candelaria University Hospital, Tenerife, Spain, [10]Hospital Universitario La Paz, Madrid, Spain, [11]Rheumatology Department, La Paz University Hospital, Madrid, Madrid, Spain, [12]Rheumatology Department, Hospital Universitario La Paz, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Imaging Of Rheumatic Diseases Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The assessment of activity in spondyloarthritis (SpA) and psoriatic arthritis (PsA) involves several domains, including enthesitis. Clinical enthesitis has shown low sensitivity, specificity and reliability. The inclusion of ultrasound (US) can be an objective outcome in the assessment of the disease. Our objective is to assess the prevalence of peripheral US enthesitis using an US score, at patient level, among active SpA and PsA patients

		Total n= 36	AS n=19 (52.8%)	PsA n=10 (27.8%)	nr-axSpA n=7 (19.4%)	p
Age		49.8±13	50.3±14.5	51.1±12.9	46.3±9.9	0.7
Sex	Female	18 (50%)	9 (47.4%)	5 (50%)	4 (57.1%)	0.9
CRP (mg/L)		11.5±12.6	13.7±11.4	11±17	6.8±9.1	0.4
DAS28 n= 22		3.5±1.3	3.1±1.1	4±1.4	3.2±1.4	0.4
ASDAS n= 17		3.7±0.9	3.7±1	4.1±0.6	3.5±0.6	0.5
BASDAI n=24		5.7±2.2	5.3±2.5	5.4±0.8	7.1±1	0.2
MASEI score ≥18		30 (83.3%)	18 (94.7%)	7(70%)	5(71.4%)	0.2
Mean number of enthesis with PD OMERACT		1.7±1.3	1.7±1.3	1.7±1.3	1.6±1.7	0.9
Mean number of enthesis with PD MASEI		1.8±1.4	1.9±1.4	1.8±1.2	1.7±1.7	0.9
PD OMERACT	≥1	29 (80.6%)	15 (78.9%)	9 (90%)	5(71.4%)	0.8
	≥2	18 (50%)	11 (57.9%)	4 (40%)	3 (42.9%)	0.6
PD MASEI	≥1	29 (80.6%)	15 (78.9%)	9 (90%)	5(71.4%)	0.8
	≥2	21 (58.3%)	12 (63.2%)	5 (50%)	4 (57.1%)	0.8

Table 1. Baseline characteristics of active SpA patients

	Reader 1	Reader 2	Reader 3
ICC reader 1		0.784 (95% CI 0.58 to 0.89)	0.909 (95% CI 0.82 to 0.95)
ICC reader 2	0.784 (95% CI 0.58 to 0.89)		0.855 (95% CI 0.72 to 0.93)
ICC reader 3	0.909 (95% CI 0.82 to 0.95)	0.855 (95% CI 0.72 to 0.93)	

Table 2. Inter-reader reliability

Methods: A cross-sectional study in patients with SpA and PsA active disease (defined as patients who were going to start or switch biological therapy according to physician criteria and in agreement with clinical guidelines) was undertaken. Basal assessment included clinical features, physical examination and laboratory tests. Patients underwent bilateral US examination of peripheral entheses according to the MAdrid Sonographic Enthesitis Index (MASEI). MASEI and OMERACT enthesitis Power Doppler (PD) definitions were checked. Each enthesis was scanned in both the longitudinal and transverse planes, and 5 second videos were recorded for reliability. An inter-reader analysis by three readers was performed. For statistical analysis Mann-Whitney U test, Kruskal-Wallis test and intraclass correlation coefficients (ICCs) were used

Results: 36 patients were included, of whom 19(52.8%) were ankylosing spondylitis (AS) patients, 10(27.8%) PsA, and 7(19.4%) non radiographic axial spondyloarthritis (nr-axSpA). Mean age was 49.8±13.1 years and 18(50%) were females. Mean DAS28 (3.5±1.3), ASDAS (3.7±0.9), BASDAI (5.7±2.2) and CRP values (11.5±12.6) reflect moderate-high disease activity. Demographic and clinical baseline characteristics are shown in Table 1. Mean global MASEI score was 28.1(±9.1) and 30 patients (83.3%) scored ≥18 (proposed cut-off point to diagnose SpA). Abnormal US findings consistent with at least one enthesis showing PD signal (whether using MASEI or OMERACT PD definition) were observed in 29(80.6%) of patients while two or more PD in entheses were observed in 21(58.3%) patients (PD MASEI definition) or 18(50%) patients (PD OMERACT definition), without significant variation among the different SpA subtypes. The sites most commonly affected were the distal patellar, quadriceps and distal Achiles tendon (52.8%, 41.7% and 16.7%, respectively). The inter-reader reliability among the three readers was high (mean ICC of 0.85). Table 2 shows the ICC of every reader pair

Conclusion: Presence of PD enthesitis is found in 80% of patients with active SpA and PsA. This finding is independent of SpA subtype and support the usefulness of PD US in the assessment of enthesitis

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Abstract Number: 0290

In Psoriatic Arthritis Patients Considered in Remission by Their Rheumatologist, Can Discordance in Disease Activity Assessment Between Patient and Rheumatologist Be Explained by Residual Inflammation as Measured by Ultrasonographic Examination?

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SESSION INFORMATION
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Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous disease and its assessment is sometimes difficult. Perception of disease activity by patient and physician is frequently discordant in patients in clinical remission

	N (%)
Ultrasound remission	26 (41.9)
Ultrasound minimal disease activity	44 (71)
Patients with ≥1 grey scale synovitis	55 (88.7)
Patients with ≥1 Power Doppler synovitis	12 (19.4)
Patients with ≥1 grey scale tenosynovitis	15 (24.2)
Patients with ≥1 Power Doppler tenosynovitis	1 (1.6)
Patients with ≥1 grey scale enthesitis lesion (thickness, hypo echogenicity, calcification, enthesophyte, erosion, bursitis)	59 (95.2)
Patients with ≥1 Power Doppler enthesitis	32 (51.6)

Table 1. Ultrasound characteristics of the 62 PsA patients

(1). Ultrasound (US) is an imaging technique, which can detect inflammation in PsA. The aim of our study was to assess whether persistence of disease activity evaluated by the patient, considered in remission by his rheumatologist, was associated with inflammation measured by US.

Methods: We performed a transversal monocentric study. PsA patients were included if they met the CASPAR criteria and were considered in remission by their rheumatologist. Demographic data, characteristics of the disease and treatments were collected. Discordance was defined by a difference between patient's and rheumatologist's global assessment ≥30/100 on a Visual Analogic Scale. An US examination was performed on 50 joints, 28 tendons and 14 entheses by an independent investigator. Synovial or tendon sheath hypertrophy and PD signal were evaluated on a semi-quantitative scale, B Mode and PD signal abnormalities on entheses were searched, according to the EULAR-OMERACT scoring system. US remission was defined by no power Doppler (PD) signal on joints, tendons and entheses and minimal US activity by maximum one PD signal on the same sites. Univariate and multivariate analyses were performed to evaluate factors associated with US abnormalities

Results: Sixty-two PsA patients were included. 40.3% were women, the mean (SD) age was 55 (14) years, 42% were in US remission and 71% in minimal US activity *(Table 1*), 19.4% had ≥1 PD synovitis and 88.7% had a B mode synovitis, 95.2% had a B mode abnormality on entheses and 51.6% had ≥1 PD signal on entheses. Thirty nine percent had a discordant disease activity assessment with their rheumatologist. In univariate analysis, discordance was not associated with US remission (OR=1.71 (95%CI 0.61-4.83), p=0.224) or US minimal disease activity (OR=0.99 (95%CI 0.32-3.05), p=0.602). In multivariate analysis, US remission was independently associated with female gender (OR=3.94 (95%CI 1.20-12.9), p=0.024) and younger age (OR=0.95 (95%CI 0.91-0.99), p=0.027). Minimal US activity was associated with history of enthesis lesion (OR=11.26 (95%CI 1.34-94.93), p=0.026) and age (OR=0.95 (95%CI 0.90-1), p=0.044).

Conclusion: Our study showed persistent inflammation evaluated by US in PsA patients considered in remission by their rheumatologist. However, prevalence of residual inflammation evaluated by US was not higher in patients with self-assessment of their disease discordant from their rheumatologist.

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Abstract Number: 0291

Factors Explaining Patient Perspective in Psoriasis and Psoriatic Arthritis: The Role of Inflammation and Structural Damage Detected by Ultrasound

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SESSION INFORMATION
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Background/Purpose: Patient reported outcomes (PROs) reflect patients' opinion on disease activity, impact of disease, quality of life (QoL), disability and are essential in the assessment of PsA patients. PROs may be influenced by several factors other than disease activity and severity. US is an objective tool to evaluate inflammation and structural damage in PsA. This cross-sectional study aimed at evaluating the role of US-detected inflammation (synovitis, tenosynovitis, enthesitis, dactylitis) and structural damage (erosions, enthesophytes, osteophytes and cortical irregularities), according to the OMERACT definitions and scoring [1], to explain PROs in PsA and to compare that to psoriasis (PsO) patients with and without musculoskeletal (MSK) symptoms.

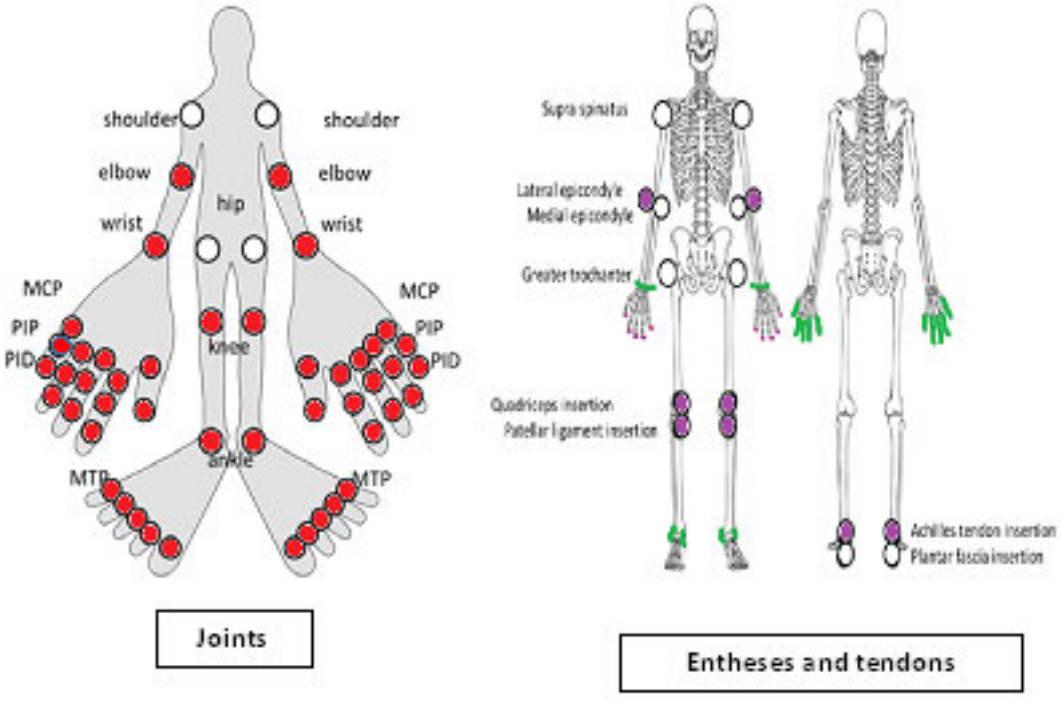

Figure 1. Anatomical sites of US evaluation: joints, entheses and tendons

	PsA N=54	symptoPsO N=52	asymptoPsO N=52	p
Males, N (%)	28 (51.9)	25 (48.1)	34 (65.4)	NS
Age, mean±SD	54.2 ± 11.7	52.1 ± 16.3	50.6 ± 15.8	NS
Years of education, mean±SD	13.6 ± 4.4	13.3 ± 3.6	13 ± 3.3	NS
Psoriasis duration, mean±SD	17.8 ± 12.9	18.4 ± 15.6	14.3 ± 12.5	NS
PsA duration	7 (0.3- 43)	NA	NA	
PASI, median (min, max)	0 (0, 36)	3 (0, 15.8)	11 (0, 60)	<0.001
68 TJC, median (min, max)	4.5 (0, 21)	2 (0, 20)	0	<0.001
66 SJC, median (min, max)	0 (0, 23)	0 (0, 3)	0	0.005
Number of enthesitis*, median (min, max)	3 (0, 13)	1 (0, 10)	0	<0.001
Number of dactylitis, median (min, max)	0 (0, 5)	0	0	NS
Patient global assessment of disease activity (NRS), mean±SD	4.2 ± 2.6	NA	NA	NA
Minimal disease activity, N (%)	17 (31.5)	NA	NA	NA
C-reactive protein, median (min, max)	3 (0, 182)	3 (0, 28)	2 (0, 21)	NS
Fibromyalgia, N (%)	5 (9.3)	3 (5.8)	0	NS
Depression, N (%)	8 (14.8)	8 (15.4)	2 (3.8)	NS
Biologic treatment, N (%)	28 (51.9)	14 (26.9)	8 (15.4)	<0.001
Number of joints with US synovitis, median (min, max)	1 (0, 32)	0 (0, 5)	0 (0, 6)	0.006
Number of US enthesitis, median (min, max)	0 (0, 11)	0 (0, 2)	0 (0, 2)	0.001
Number of US tenosynovitis, median (min, max)	0 (0, 7)	0 (0, 1)	0 (0, 1)	0.011
Number of joints with US osthephytes and/or cortical irregularities, median (min, max)	2 (0, 22)	1 (0, 25)	1 (0, 21)	0.041
Number of joints with US erosions, median (min, max)	0 (0, 4)	0 (0, 2)	0 (0, 2)	0.020
Number of US enthesis with	2 (0, 8)	1 (0, 10)	1 (0, 8)	NS

Table 1. Characteristics of the patients included in the 3 groups: PsA patients, patients with psoriasis with MSK symptoms (symptoPsO) and patients with psoriasis and no MSK symptoms (asymptoPsO) PsA: psoriatic arthritis; PsO: psoriasis; PASI: Psoriasis Area and Severity Index; TJC: total tender joint count; SJC: total swollen joint count; N: number; SD: standard deviation; NRS: numeric rating scale; SF36: Medical Outcome Study Short Form-36; PF: Physical Functioning; RP: Physical Role functioning; BP: Bodily Pain; GH: General Health; VT: Vitality; SF: Social role Functioning; MH: Mental Health; RE: Emotional Role functioning * Number of enthesitis was calculated according to the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index

Methods: PsA (CASPAR criteria) [2], PsO with MSK symptoms without fulfilling CASPAR criteria (symptoPsO) and PsO with no MSK symptoms (asymptoPsO) were included. Socio-demographic characteristics, comorbidities, disease duration and treatment were collected. All patients underwent dermatological and rheumatologic assessment: PsO severity, swollen joint count (SJC), tender JC (TJC), number of dactylitis and enthesitis, fibromyalgia criteria; and US evaluation on joints, tendons and entheses as shown in figure 1. PROs were evaluated in all patients: assessment of skin psoriasis and of fatigue on a numeric rating scale (NRS), HAQ and QoL assessed by SF36. Variables were compared across groups (chi square or one-way ANOVA test). Correlations were evaluated using Spearman's test.

Results: One hundred fifty eight patients (54 PsA, 52 symptoPsO and 52 asymptoPsO) with similar socio-demographic characteristics and PsO duration were included (table 1). Most of PsA patients had low/moderate disease activity. With the exception of US enthesophytes, all US changes were significantly higher in PsA, followed by symptoPsO patients.

Across all 3 groups, all PROs correlated mainly with demographic variables, comorbidities, TJC, number of enthesitis, skin severity, depression and fibromyalgia (r=0.29-0.66). SymptoPsO and PsA reported similar scores of fatigue and impact on some QoL domains (vitality, pain, general health, social and mental), significantly higher than asymptoPsO. Only in PsA, HAQ correlated with the total number of US enthesitis (r=0.35, p=0.01) and of joints with ostheophytes/cortical irregularities (r=0.28, p=0.04) as well as the physical function domain of SF36 with the number of joints with ostheophytes/cortical irregularities (r=-0.33, p=0.02).

Conclusion: Quality of life, disability and fatigue were more impaired in PsA and symptoPsO patients than asymptoPsO. In all groups, PROs were mostly associated with socio-demographic characteristics, comorbidities and some clinical variables rather than objective measures such as US changes.

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References:

1. Bruyn GA et al. J Rheumatol 2019
2. Taylor W et al. Arthritis Rheum 2006

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Abstract Number: 0292

Is Shoulder Involvement an Early Feature of Rheumatoid Arthritis in Clinically Suspect Arthralgia? *A Longitudinal Ultrasound Study*

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SESSION INFORMATION
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Background/Purpose: Multiple studies have demonstrated that shoulder involvement is frequent in Rheumatoid Arthritis (RA). Previous research also showed that a swollen shoulder joint has a similar predictive value as small joint involvement for developing RA in patients with undifferentiated arthritis (UA). The phase of clinically suspect arthralgia (CSA) precedes the phase of clinically apparent arthritis; in this phase subclinical tenosynovitis of the hands, visualized with MRI or US, is predictive for developing RA. Given the similarities in predictive values between the shoulder and small joints in UA, and the predictive value of tenosynovitis in CSA, we hypothesized that subclinical tenosynovitis of the shoulder is a predictor for RA development in CSA. Within the shoulder the biceps tendon is the most obvious to investigate, because it passes though the shoulder joint and is covered with a synovial sheet.

Objective: Therefore, the aim of this study is to examine the predictive value of tenosynovitis of the bicep tendon by ultrasound (US) on developing inflammatory arthritis (IA) in CSA patients.

Methods: The SONAR (Sonographic evaluation of hands, shoulders and feet in patients presenting with inflammatory arthralgia to identify subclinical arthritis)-study is a multi-center observational cohort study in which patients were followed on the development of clinically apparent inflammatory arthritis (IA). Visits were done at baseline and every 6 months thereafter. At baseline a US of both shoulders was made. 1-year follow-up data were used. IA was defined as having an arthritis verified by the treating physician. We investigated whether there was a relation between the development of IA and the presence of (1) biceps tenosynovitis (TS); (2) a thickened biceps tendon without power

	Patients that developed IA (n =37)	Patients that did not develop IA (n = 133)	P value
Gender, female, n (%)	30 (81)	110 (83)	0.82
Age, years, mean (SD)	47(12)	44 (12)	0.28
BMI, mean (SD)	27 (5)	28 (5)	0.38
Morning stiffness, minutes median (IQR)	45 (30-90)	30 (15-60)	0.16
TJC44, median (IQR)	5 (3-8)	5 (3-8)	0.81
Shoulder pain, n	0 (0)	9 (6.8)	0.10
SJC44, median (IQR)	0 (0-0)	0 (0-0)	-
ESR, median (IQR)	9 (5-22)	11 (5-21)	0.66
RF-positive, n (%)	12 (34)	34 (26)	0.33
ACPA-positive n (%)	10 (29)	16 (12)	0.019

Abbreviations: BMI: IA: Inflammatory Arthritis, Body Mass Index, TJC44: Tender Joint Count in 44 joints, SCJ44: Swollen Joint Count in 44 joints, , ESR: Erythrocyte sedimentation rate, RF: Rheumatoid Factor, ACPA: Anti-citrullinated Protein Antibody

Table 1. Baseline characteristics (n=170)

	Patients that developed IA, n (%)	Patients that did not develop IA, n (%)	P-value
Bicep tendon TS (n= 164)	5 (15)	14 (11)	0.48
Bicep tendon thickness (n=164)	0 (0)	6 (5)	0.19
Effusion joint (n=157)	0 (0)	0 (0)	-
Subdeltoid bursa effusion (n=159)	3 (9)	26 (21)	0.094

Table 2. Abnormalities identified with US of the shoulders at baseline

Doppler; (3) joint effusion and (4) subdeltoid bursa effusion on US. Reference values for tendon thickness and effusion of the bursa were determined according to Schmidt et al.(1)

Results: A total of 170 patients were included and underwent bilateral US of the shoulder joint. Shoulder symptoms were infrequent (Table 1). After one year 37 patients developed IA (22%). ACPA positivity was associated with the development of IA (Table 1). As presented in Table 2, US abnormalities of the shoulder were infrequent and not associated with IA-development. In particular biceps tenosynovitis was not increased in the patients that developed IA.

Conclusion: Subclinical tenosynovitis of the shoulder is not an early feature of RA in patients with CSA.

Reference:

1. Schmidt WA, Schmidt H, et al. *Standard reference values for musculoskeletal ultrasonography.* Ann Rheum Dis. 2004 Aug;63(8):988-94.

Disclosure: C. Rogier, None; **P. de Jong**, None; **A. van der Helm-van Mil**, None.

Abstract Number: 0293

False Positives in the Ultrasound Diagnosis of Giant Cell Arteritis: Some Diseases Can Also Have Halo Sign

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Background/Purpose: Giant cell arteritis (GCA) is the most common systemic vasculitis in the elderly. The halo sign is an accepted valid test for the diagnosis of GCA in trained units. However, other conditions can also produce a hypoechoic increase of the arterial wall thickness and mimic the halo sign. Our aim was to describe the frequency and causes of false positives in the diagnosis of GCA by color Doppler ultrasound (CDUS).

Methods: We performed an observational retrospective study of 305 patients with temporal artery CDUS findings compatible with GCA. Their medical records were reviewed to collect demographic, physical examination, clinical and analytical data. The medical diagnosis based on the clinical evolution of the patient during at least 1 year of follow-up was established as the gold standard for definitive diagnosis.

Results: 14 of the 305 included cases (4.6%) were false positives. The characteristics of these 14 patients and their final diagnoses are shown in table 1. 64% were female. The median age was 72 (interquartile range 68-79) years. The median erythrocyte sedimentation rate was 55 (32-110) mm/h, C-reactive protein 15.1 (7.3-100.9) mg/L and hemoglobin 13.3 (11.2-14.1) g/dL. Five patients (36%) fulfilled the 1990 American College of Rheumatology classification criteria. A temporal artery biopsy was performed in 9 patients (64%), with negative results in all of them. Twelve

Table 1. Final diagnoses for false positive halo signs and associated ultrasound findings

Patient	Definitive diagnosis	Biopsy result	Artery involved	Number of arterial branches
1	Non-Hodgkin's T lymphoma	Negative	Temporal	3
2	Narrow-angle glaucoma	No done	Temporal	1
3	Osteomyelitis of the skull base	No done	Temporal	4
4	Polymyalgia rheumatica	Negative	Temporal	2
5	Urinary sepsis	Negative	Temporal	1
6	Polymyalgia rheumatica	Negative	Temporal	1
7	Polymyalgia rheumatica	Negative	Temporal	1
8	Amyloidosis due to multiple mieloma	Negative (deposit of amyloid material)	Temporal	4
9	Atherosclerosis	No done	Axilar	
10	Atherosclerosis	No done	Axilar	
11	Polymyalgia rheumatica	Negative	Temporal	1
12	Atherosclerosis	Negative	Temporal	2
13	ANCA-associated vasculitis	No done	Temporal	2
14	Neurosyphilis	Negative	Temporal	3

patients (86%) had CDUS involvement of the superficial temporal arteries. Five had 1 branch involved (42%), three 2 branches (25%), two 3 branches (17%) and two 4 branches (17%). In addition, two patients (14%) had an isolated halo sign in the axillary arteries, one unilateral and the other bilateral. Regarding the definitive diagnosis, in four patients it was polymyalgia rheumatica (29%), in three atherosclerosis (21%), and there was one case each of non-Hodgkin's Lymphoma type T, osteomyelitis of the skull base, primary amyloidosis associated with multiple myeloma, granulomatosis with polyangiitis, neurosyphilis, urinary sepsis and narrow-angle glaucoma.

Conclusion: CDUS diagnosis of GCA yields a low percentage of false positives. These are attributable either to operator-dependent technical mistakes or to the presence of other medical conditions that alter the US signal of the arterial wall, resulting in a halo sign. The clinician must be aware of the existence of these conditions when interpreting this test, in order to improve the diagnostic accuracy of the CDUS.

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Abstract Number: 0294

Tendons Involvement at Early Onset of Gouty Arthritis, Ultrasonographic Study

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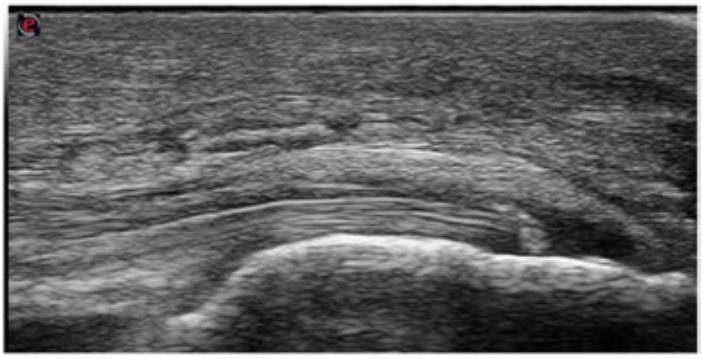
Background/Purpose: Gout is the commonest form of inflammatory arthritis and is caused by the longstanding elevation of serum uric acid levels causing crystal deposits. monosodium urate deposits are the hallmark sign of gouty arthritis, and tendons in many sites represtents a potential target for urate deposits.

Methods: The current study was based on a cross sectional hospital-based survey, conducted among patients presenting at outpatient rheumatology clinics between August 2018- March 2019

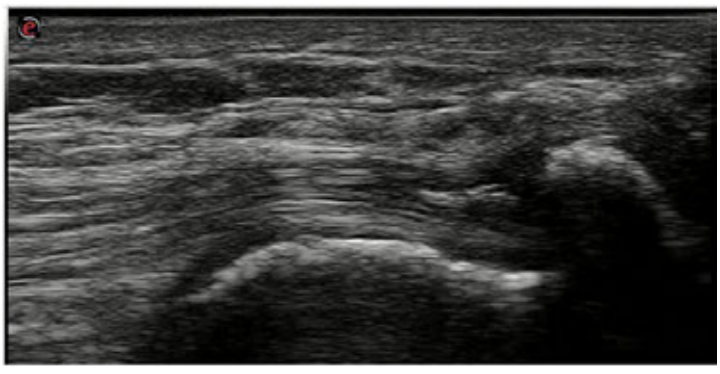
Inclusion criteria: First attack of acute gouty arthritis, diagnosed according to 2015 ACR/EULAR Gout Classification Criteria. Age 45 years or less. Exclusion criteria: Patients with other causes of arthritis, either degenerative or inflammatory. Previous related joint surgery, malalignment, congenital or acquired joint abnormality. Metabolic or endocrinopathies: Diabetes mellitus, dyslipidemia, thyroid dysfunctions. Chronic renal or hepatic diseases.

Grouping: Group I: 65 patients with acute gouty arthritis, Group II: 20 normal subjects as a control group. All patients were subjected to the following: Full clinical assessment, of 5 tendon sites, Achilles, Infrapatellar, Quadriceps, Triceps, and Supraspinatus tendons. Blood assay for serum uric acid level.

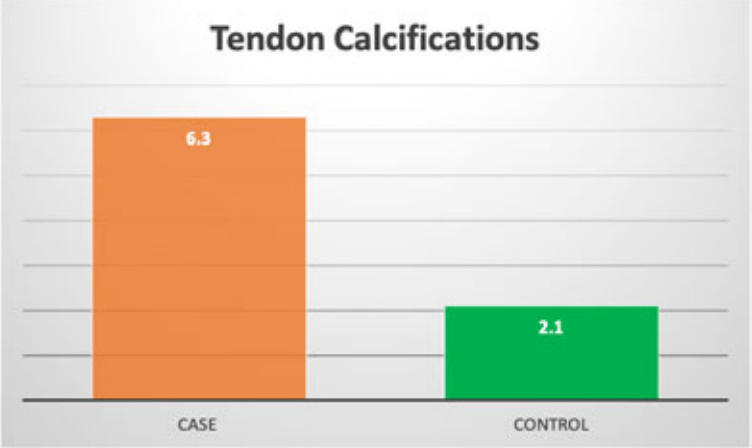
Ultrasonography: was performed for 5 tendon sites; Achilles, infrapatellar ligament, quadriceps, Triceps, supraspinatus tendons. All tendons were evaluated bilaterally according to the EULAR guidelines for performing US in rheumatology. using a scanner with a multi-frequency 12 megahertz linear array transducer (Esaote MYLAB7&General electric Systems; LOGIQU-E). Ultrasonography (US) has been used to detect features of crystal deposits in the tendons, US elementary lesion defined sas intra-tendinous deposits, inhomogeneous, circumscribed, and hyperechoic shadows with or without posterior acoustic shadowing and may be surrounded by a small anechoic halo.



triceps calcification



Achilles Calcification



calcifications in both groups

Results: both groups were matched as regards the age and BMI with no significant difference in means. In the study group; among 650 tendon sites examined by US calcifications were detected in 41 tendon sites 6.3%. 19 at the Achilles tendon unilateral in 13 cases and bilateral in 3 cases, 7 at infrapatellar ligament, 2 at the quadriceps, 7 at the Triceps, and 6 at the supraspinatus tendon. In the other hand clinically, symptomatic tendons presented only in 6 tendon sites with 0.9 %. While in the control group; 190 sites examined by US, and calcifications were detected in 4 sites with 2.1%.

Conclusion: Tendons appears to be involved with the gouty urate deposits, and tendon calcifications could happen and detected early in the course of the disease.

Disclosure: A. Abogamal, None; **s. abdallatif**, None; **M. Hegazy**, None; **k. Fathy**, None.

Abstract Number: 0295

Assessing the Vascularization of Salivary Glands in Patients with Sjögren's Syndrome - An OMERACT Ultrasound Group Reliability Exercise

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Imaging Of Rheumatic Diseases Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The vascularization of salivary glands (SG) in Sjögren's syndrome (SS) has not been extensively studied by imaging methods, and currently no agreement exists on how this should best be evaluated. Color Doppler (CD) ultrasonography (US) might represent a good tool for the assessment of vascularization in SS.

The aim of the exercise of the OMERACT Sjögren US subtask group was to test the reliability of SG vascularization assessment in SS patients using a consensual developed semiquantitative CD US scoring system.

Methods: Nine sonographers participated in the reliability exercise, evaluating the vascularization of bilateral parotid and submandibular glands in 9 SS patients using CD US with previously standardized and optimized Doppler settings. The participants were not allowed to modify the settings while scanning. The superficial lobe of parotid glands was scanned in both longitudinal and transverse plane, while submandibular glands were scanned in longitudinal plane only. A previously agreed four grade semiquantitative score was applied: Grade 0, no visible vascular signals; Grade 1, focal, dispersed vascular signals; Grade 2, diffuse vascular signals detected in less than 50% of the gland; Grade 3, diffuse vascular signals in more than 50% of the gland. Intrareader and interreader reliability of grading SG was determined by Light's weighted kappa analysis.

Results: Light's weighted kappa of intrareader and interreader reliability showed good to excellent agreement. Data are presented in Table 1.

Conclusion: The consensual CD US scoring for the evaluation of SG vascularization in SS showed a good interreader reliability and excellent intrareader reliability. Next step should be further testing for clinical application in a larger group of SS patients and controls. In addition, a potential correlation between SG structural changes seen on B-mode US and vascularization should be studied.

Prevalence of Doppler grades (%) in 9 patients with Sjögren's syndrome	
Grade 0	15.2%
Grade 1	33.8%
Grade 2	44.5%
Grade 3	6.4%
Intrareader reliability (Light's weighted kappa (mean and 95%CI):	
Parotid glands (longitudinal)	0.89 (0.85-0.94)
Parotid glands (transverse)	0.91 (0.83-0.96)
Submandibular glands (longitudinal)	0.72 (0.48-0.87)
All four salivary glands	0.84 (0.73-0.92)
Interreader reliability (Light's weighted kappa (mean and 95%CI):	
Parotid glands (longitudinal)	0.70 (0.61-0.77)
Parotid glands (transverse)	0.76 (0.71-0.81)
Submandibular glands	0.65 (0.57-0.73)
All four salivary glands	0.70 (0.64-0.76)

Legend: CI confidence interval

Table 1. The prevalence of grades, intrareader, and interreader reliability of the proposed CD US scoring for the assessment of SG vascularization

Disclosure: A. Hocevar, None; **S. Jousse-Joulin**, None; **N. Perko**, None; **S. FINZEL**, None; **P. HANOVA**, None; **A. IAGNOCCO**, None; **N. Inanc**, None; **E. NAREDO**, None; **W. SCHMIDT**, None; **L. Terslev**, None; **A. ZABOTTI**, None; **M. Tomšič**, None; **G. Bruyn**, None.

Abstract Number: 0296

Prevalence of Elbow Arthritis in Patients with Rheumatoid Arthritis: A Prospective Ultrasound Study

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Imaging Of Rheumatic Diseases Poster I

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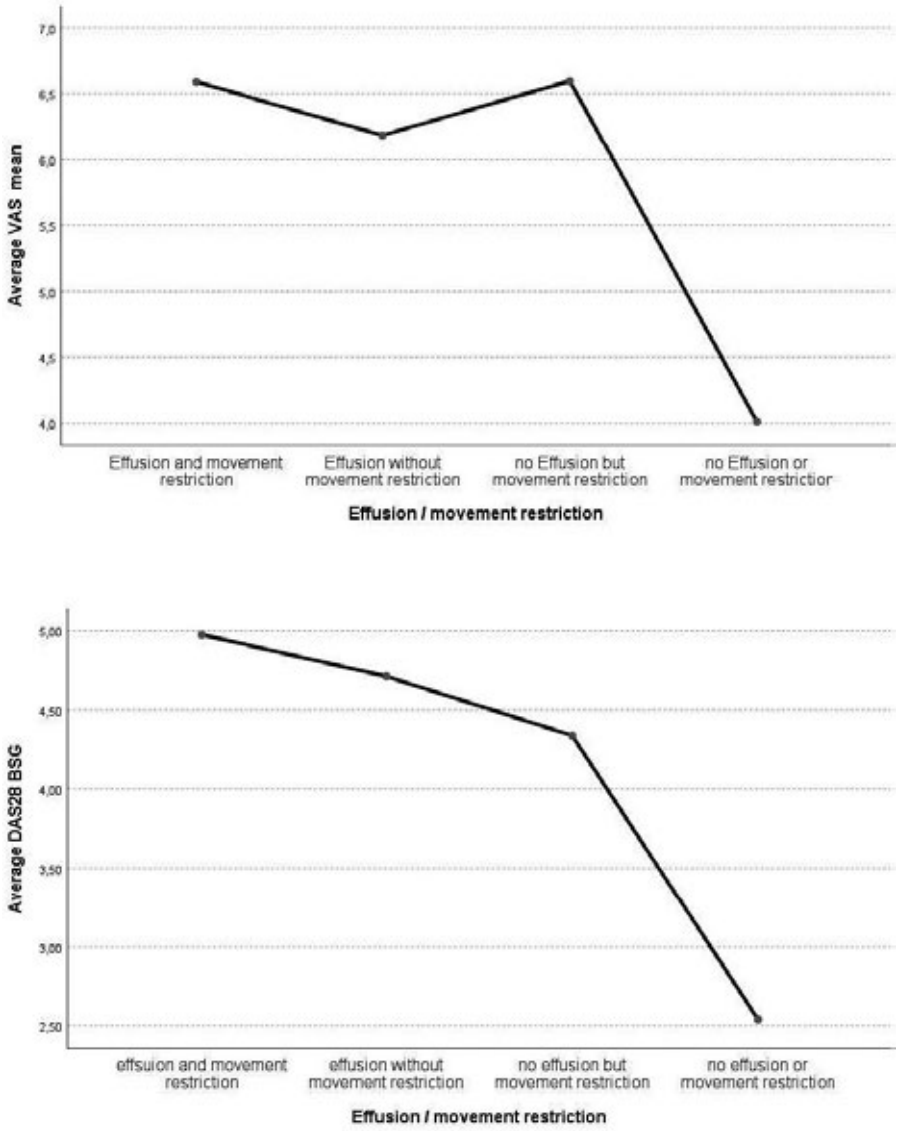
Session Time: 9:00AM–11:00AM

Background/Purpose: Musculoskeletal ultrasound is an important imaging method in the diagnosis of arthritis, especially rheumatoid arthritis (RA). The prevalence of elbow joint arthritis in RA has not yet been specifically investigated sonographically and correlated with the clinical examination and other parameters.

Methods: In 100 patients with RA and 50 patients without rheumatological disease both cubital joints were examined according to the 3 most relevant standard planes (anterior longitudinal humeroradial and humeroulnar as well as posterior longitudinal scans) of the German Society for Ultrasound in Medicine (DEGUM). A complete clinical examination was performed and baseline characteristics (age, sex, etc.), DAS28 and visual analogue scale (VAS) were recorded. Elbow arthritis was defined as joint effusion grade II and/or hyperperfusion of the synovial proliferation. The patients were recruited in the department of Rheumatology of the University Hospital Bonn as well as in the Rheinischen Rheumazentrum Meerbusch. The ultrasound examination was performed by two very experienced physicans (DEGUM level I and DEGUM level II, equals EFSUMB levels). The statistical evaluation was performed with IBM SPSS (Version 25). A p-value < 0.05 was considered significant. The interrater analysis was assesed by Cohen's kappa, as well as by an independent blinded assessor (DEGUM III, equal EFSUMB III).

Results: Mean age was 59.8 years (±SD 15.9) in the RA cohort and 59.8 years (±SD 16.2) in the control group. The RA cohort displayed relevant joint effusion in 54.9%, in 6.9% hypervascularization was visible, whereas in the control group 16% displayed joint effusion and none showed hypervascularization. The mean DAS28 in the RA cohort was 5.3 (±SD 1.1; high activity 56.9% (DAS28 > 5.1), moderate activity 41.1% (DAS28 > 3.2), low activity (DAS28 > 2.6) 2%). The mean VAS in RA patients was 6.41 (±SD 2.3), and 2.42 (± 2.9) in the control group.

In the RA cohort there was a significant correlation between movement restriction (MR) and joint effusion (p-value = 0.001), between DAS28 and MR (p-value = 0.02) and between DAS28 and sonographic joint effusion (p-value = 0.022). The overall collective showed a significant correlation of DAS28 with MR and joint effusion [figure 1].



Graphs elbow study
figure 1 and figure 2

In overall analysis, a highly significant correlation of VAS with MR (p-value 0.001), the presence of joint effusion (p-value 0.001) and the diagnosis of RA (p-value 0.001) was observed.

Interrater analysis showed good agreement with Cohen´s kappa of 0,896 and a highly significant p-value of 0.001.

Conclusion: This is the first study to investigate the prevalence of elbow joint effusion and synovitis in RA patients. It shows, that the prevalence of elbow joint arthritis is high, with over 54% in the RA cohort. Movement restriction is a good indicator of elbow joint arthritis in RA, but not in all RA patients. In the overall analysis of both cohorts, there is a strong correlation between VAS with joint effusion and MR (p-value 0.001) [Figure 2].

Disclosure: D. Vossen, None; **V. Schaefer**, None; **F. Recker**, None; **I. Geffken**, None; **E. Matuschek**, None; **W. Hartung**, None.

Abstract Number: 0297

Ultrasound and Magnetic Resonance Imaging Evaluation of the Fingers' Joints of Psoriatic Arthritis Patients – Interim Analysis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Imaging Of Rheumatic Diseases Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is an inflammatory disease affecting up to 30% of psoriasis patients. PsA can involve both the peripheral and axial skeleton and manifest with inflammatory and structural changes such as synovitis, tenosynovitis and erosions. Ultrasound (US) and magnetic resonance imaging (MRI) are the leading imaging modalities for peripheral arthritis assessment. However, little is known about the discrepancies between these two modalities in PsA patients. The aim of the study was to evaluate the agreement between US and MRI in the detection of fingers lesions in PsA patients and to evaluate the sensitivity and specificity of US with MRI as gold standard.

Methods: Consecutive PsA patients (all fulfilled the CASPAR criteria) were recruited prospectively. All patients underwent US and MRI assessment of MCP, PIP and DIP joints of one matched hand. The time interval between US and MRI scans was at most 3 days and the US and MRI assessors were blinded to the clinical data. NSAIDs treatment was hold for 3 days before assessment. Agreement between MRI and US was calculated based on absolute agreement and Cohen's Kappa values. Sensitivity and specificity of US was evaluated with MRI as gold standard.

Characteristics	
Age, mean (± s.d)	52.2 (12.9)
Gender, Female, n (%)	36 (60)
BMI, mean (± s.d)	27.7 (4.4)
PSO duration, mean (± s.d)	21.7 (16.5)
PsA duration, mean (± s.d)	10.97 (12.87)
TJC, mean (± s.d)	9.60 (10.72)
SJC, mean (± s.d)	0.95 (1.93)
CRP mg/l, mean (± s.d)	8.50 (9.24)
ESR, mm/h, mean (± s.d)	22.79 (13.38)
MDA, n (%)	19 (27.7)
CPDAI, mean (± s.d)	8.62 (3.54)
DAPSA, mean (± s.d)	21.26 (15.82)
Treatment	
sDMARDs, n (%)	31 (51.7)
Otezla, n (%)	3 (5.0)
Biologics, n (%)	33 (55.0)

Table 1. Baseline characteristics (60 patients with matched scanned hand)

	US	MRI
Synovitis		
MCP (total 300), n (%)	58 (19.3)	41 (13.7)
MCP US Doppler, n (%)	13 (4.3)	
PIP (total 300), n (%)	23 (9.6)	18 (7.5)
PIP US Doppler, n (%)	1 (0.4)	
DIP (total 240) , n (%)	13 (5.4)	12 (5)
DIP US Doppler, n (%)	2 (0.8)	
Flexor tenosynovitis		
MCP (total 300)	17 (5.7)	19 (6.3)
MCP US Doppler, n (%)	3 (1)	
PIP (total 300)	11 (4.6)	10 (4.2)
PIP US Doppler, n (%)	2 (0.8)	
DIP (total 240), n (%)	5 (2.1)	4 (1.7)
DIP US Doppler, n (%)	0	
Erosions		
MCP (total 300), n (%)	4 (1.3)	6 (2)
PIP (total 300), n (%)	4 (1.7)	7 (2.5)
DIP (total 240) , n (%)	1 (0.4)	7 (2.5)

Table 2. Prevalence of lesions for each group of joints

	US vs MRI
Synovitis	
MCP (total 300)	84%; K= 0.411
PIP (total 300)	95%; K=0.654
DIP (total 240)	95%; K=0.451
Flexor tenosynovitis	
MCP (total 300)	94%; K=0.468
PIP (total 300)	95%; K=0.353
DIP (total 240)	97%;K=0.208
Erosions	
MCP (total 300)	98%; K=0.211
PIP (total 300)	98%; K=0.492
DIP (total 240)	98%; K=0.329

Table 3. Agreement and Kappa values between US and MRI

Results: Sixty PsA patients with mean age of 52 years (± 12.9) and female:male ratio of 60%:40% were included (Table 1). Three hundred MCP, 300 PIP and 240 DIP were assessed by US and MRI. The prevalence of synovitis, flexor tenosynivitis and erosions were comparable between the US and MRI assessments (Table 2). Synovitis (19.3% for US and 13.7% for MRI) and flexor tenosynovitis (5.7% for US and 6.3% for MRI) were more prevalent in the MCP joints compared to the PIP and DIP joints in both modalities. Absolute agreement and kappa values between US and MRI were 84%-95% with moderate to substantial kappa values (0.411-0.654), 94%-97% with fair to moderate kappa values for tenosynovitis (0.208-0.468) and 98% with fair to moderate kappa values for erosions (0.211 to 0.492) (Table 3). The sensitivity and specificity of US with MRI for synovitis ranged between 0.5-0.78 and 0.87-0.97 according to the specific type of joint (DIP, PIP and MCP), and for flexor tenosynovitis 0.25-0.47 and 0.97, respectively.

Conclusion: US and MRI have moderate to good agreement for the detection of inflammatory and destructive changes, while the sensitivity is better for synovitis compared to flexor tenoseynovitis.

Disclosure: A. Polachek, None; **V. Furer**, None; **M. Zureik**, None; **S. Nevo**, None; **L. Mendel**, None; **D. Levartovsky**, None; **J. Wollman**, None; **V. Aloush**, None; **M. Berman**, None; **I. Kaufman**, None; **Y. Lahat**, None; **H. Sarbagil-Maman**, None; **S. Borok**, None; **A. Broyde**, None; **L. Eder**, Abbvie, 2, 5, 8, Celgene, 5, Janssen, 5, Lily, 2, 5, Novartis, 2, 5, Pfizer, 2, 8, UCB, 2; **D. Paran**, None; **I. Eshed**, None; **O. Elkayam**, Pfizer, 2, 5, 8.

Abstract Number: 0298

In CCP Positive "At Risk of Rheumatoid Arthritis" Individuals, the Presence of Sub-clinical Synovitis in 4-10joints Universally Results in Clinical Synovitis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Imaging Of Rheumatic Diseases Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In a cohort of Anti-Cyclic Citrullinated Peptide Positive (Anti-CCP+) At-Risk of developing inflammatory arthritis (IA) individuals without clinical synovitis, previous univariable analysis showed that the presence of a Power Doppler signal (PD) in at least one joint was predictive of progression (Nam, 2016).

Further analysis is required to examine the influence of the number of joints PD positive on the progression rates and incorporate this data in the already established 2010 ACR/EULAR criteria for Rheumatoid Arthritis (RA), replacing the swollen joint count by the PD positive joint count.

Table 1: Demographic data

	Overall	Progressors	Non-progressors	P-value
N (%)	361	102 (28%)	259 (72%)	/
Mean follow-up (Months (SD))	24.71 (25.96)	19.55 (24.05)	26.75 (24.44)	0.017
High CCP titre	69.2%	92.2%	59.9%	<0.001
Smokers (Ever/Never) Ever smoker	186/142 56.7%	74/24 75.5%	112/118 48.7%	<0.001
Sex ratio (F/M) Women	262/95 72.6%	(190/65) 72.5%	(72/30) 70.6%	0.338
Age (years (SD))	50.95 (13.23)	53.51 (13.28)	49.91 (13.10)	0.021
Alcohol consumption (Unit/week (SD))	7.91 (13.71)	6.21 (9.46)	8.66 (15.20)	0.144
Meet ACR criteria for RA at progression (n/N)	/	80.5% (70/87)	/	/

Objectives:

1. To investigate the association between the number of joints with a Power Doppler signal and progression to IA.
2. To include the PD positive joint count in the 2010 ACR/EULAR criteria for RA to improve prediction in individuals without synovitis.

Methods: Participants were selected by an anti-CCP positive test and a new musculo-skeletal symptom. Individuals with intermittent symptoms or clinical synovitis were excluded.

Using univariable cox regression, we described for the first time the predictive value of the number of joints with a Power Doppler signal.

By replacing the number of swollen joints, with the number of joints PD positive in the 2010 ACR/EULAR criteria for RA, we then analysed IA-free survival curves for participants without clinically swollen joints.

Figure 1: Number of joints with Power Doppler and risks of progression

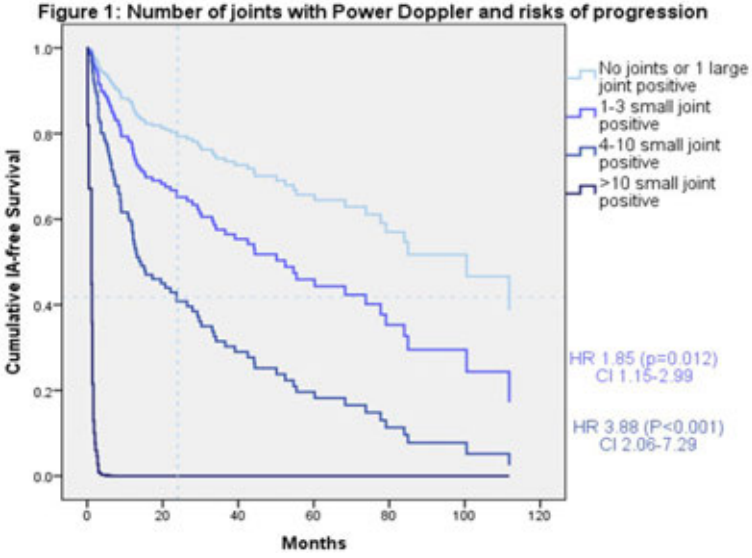
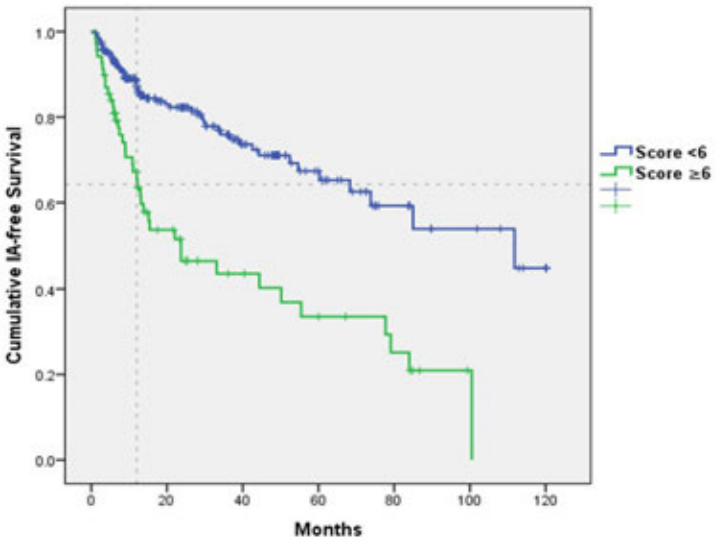


Figure 2: 2010 ACR/EULAR criteria for RA using PD positive joint count in At-Risk of RA individuals



Results: 361 patients were followed for a mean of 24 months (Table 1). Of the 28% of participants who developed IA, 81% met the ACR/EULAR criteria for RA at progression. There were significantly more participants with high anti-CCP titres in the progressor group.

Using Cox univariable analysis, the results show that the probability of developing IA is significantly increased by a Hazard ratio of 1.89 if 1 to 3 small joints present a PD signal (p=0.012), and of 3.81 if 4 to 10 joints are PD positive (p< 0.001) (Figure 1). Furthermore, all participants presenting with 4 to 10 joints progressed, 60% of them in the first 2 years (Figure 1).

Using multivariable analysis and adding CCP titre and inflammatory markers to the PD positive joint count, Hazard Ratio for the probability of progression shows a risk 2.97 times higher (p >0.001, CI 1.96-4.49) for the participants who met the 2010 ACR/EULAR criteria for RA replacing the swollen joint score with the PD positive joint count (Figure 2).

Conclusion:

1. All of the participants with 4 to 10 joints with a Power Doppler Signal progressed to IA (mainly RA), 60% of them in the first 2 years.
2. The predictive value for progression to IA of ultrasound scans is not improved by the addition of CCP titres and inflammatory markers (*when included in the 2010 ACR/EULAR criteria for RA using Power Doppler positive joint count in patient without clinical synovitis*).

Disclosure: L. Duquenne, None; **K. Mankia**, None; **J. Nam**, None; **A. Di Matteo**, None; **L. Garcia-Montoya**, None; **P. Emery**, AbbVie, 2, 5, 9, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, 9, Gilead, 5, Lilly, 2, 5, 9, MSD, 2, 5, 9, Novartis, 2, 5, 9, Pfizer, 2, 5, 9, Roche, 2, 5, 9, Samsung, 2, 5, 9, Samsung Bioepis Co., Ltd., 2, Sandoz, 2, 5, 9, UCB, 2, 5, 9.

Abstract Number: 0299

Definition of New Ultrasound Enthesophytes Score: Application in a Consecutive Series of IBD Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Imaging Of Rheumatic Diseases Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent studies have developed criteria for US definition of entheseal abnormalities (1), however no actual scores are available to determine the extension and severity of enthesophyte growth at patient level.

To evaluate the feasibility of two new scores to measure enthesophytes occurrence and their dimensional changes with time.

Methods: We evaluated 816 enthesis in a consecutive series of 68 IBD patients for the presence and size of enthesophytes. Images were collected at baseline and after 24 months using an Esaote MyLabClass, 18-6 MHz linear multi-frequency transducer both in B-mode and power Doppler-mode. The following sites were evaluated bilaterally: lateral epicondyle of the humerus, distal quadriceps femoris insertion into the patella, inferior pole of the patella, tibial distal insertion of the patellar tendon, calcaneal insertion of the Achilles tendon, and plantar aponeurosis insertion. The presence of enthesophyte was scored dichotomously as present (=1) or absent (=0) for each site and summed up to generate the ARES (Anatomical ReggioEmilia Enthesophytes Score). Enthesophytes were also scored semiquantitatively in a 0-3 scale (0 = absent, 1 = minimal, 2 = discrete, 3 = massive) according to previous studies (2) for each site and summed up to generate RESS (ReggioEmilia Enthesophytes Severity Score). All the stored images were reviewed and scored by 4 rheumatologists (FM, GC, PM, NG) well trained in US examination of enthesis. Four patients were evaluated independently by the 4 ultrasonographers and new ARES and RESS were calculated for each patient. Intraclass correlation coefficients (ICC) were calculated for inter- and intra-observer reliability.

Results: Both intra- and interobserver reliability analyses for presence or absence of enthesophytes showed an excellent ICC for each site. ICC for ARES was excellent for intra and inter observer (Cronbach alfa = 0.930, 95%CI 0.72-0.98 and 0.969, 95% CI 0.942-0.998 respectively). ICC was excellent also for the semiquantitative RESS for almost all the examined sites, but moderate for the plantar fascia (Cronbach alfa = 0.571, 95%CI -0.72-0.89). The total RESS had an excellent ICC both for intra and inter-examiner (Cronbach alfa = 0.963, 95%CI 0.85-0.99 and 0.983, 95%CI 0.913-0.999).

Conclusion: The present study demonstrates that the ARES and RESS scores are easily feasible, highly reproducible and have excellent intra and interobserver reliability.

Disclosure: P. Macchioni, None; **f. Martinis**, None; **G. Citriniti**, None; **N. Girolimetto**, None; **C. Salvarani**, None.

Abstract Number: 0300

Proliferative Globular Synovitis, an Ultrasound Pattern Associated with Seropositive Rheumatoid Arthritis

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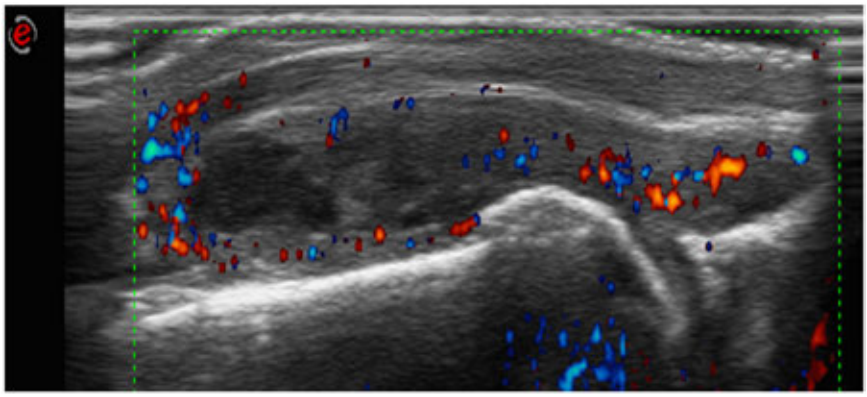
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Imaging Of Rheumatic Diseases Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

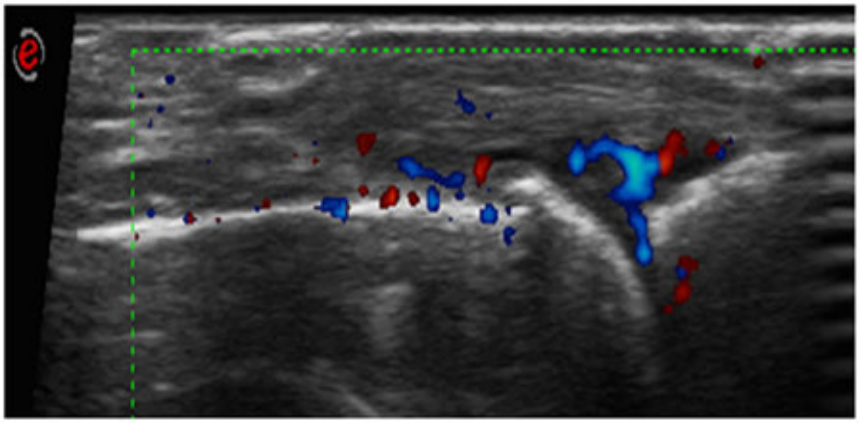
Background/Purpose: Rheumatoid Arthritis (RA) has a synovial ultrasound (US) pattern, while soft tissue involvement is more frequently found in Psoriatic Arthritis (PsA). No previous studies have analyzed if US findings differ between seropositive and seronegative RA patients. The objective is to analyze differences in the ultrasound pattern among patients with seropositive and seronegative RA. To assess if proliferative globular synovitis is associated to seropositive RA.

Methods: Retrospective Analysis. We collected clinical, epidemiological and ultrasound images of patients with RA who met ACR/EULAR 2010 criteria with bilateral carpal and hand ultrasonography carried out during the last five years. Synovial hypertrophy (SH) and Power Doppler signal (PD) in wrist and 1-5 metacarpophalangeal (MCP) were evaluated. We calculated the SH score (sum of the SH degrees of each joint), PD (sum of the PD degrees of each joint) and the total score (sum of the score of SH and PD) for each patient. We also evaluated the presence of proliferative globular synovitis, defined as big synovial hypertrophy with exophytic growth and a convex upper limit

Results: 145 RA patients were collected. 80% were women. Mean age was 59.06 (14.8) years and the mean time of disease evolution was 114.6 (112.8) months. 68.3% were RF positive and 74.5% ACPA positive. Overall, 115 of the 145 (79.3%) patients were seropositive for RF/ACPA. 53.1% had radiographic erosions, 73.1% used conventional synthetic Disease-modifying drugs (DMARDs), 29.7% biological therapy, and 57.2% low doses of corticosteroids (< 5 mg prednisone). The mean DAS28 was 2.81 (1.14), the number of swollen joints was 3 (3.4), and CRP was 0.99 mg/dl (1.6). No significant differences between seropositive and seronegative patients in terms of disease activity (swollen joints count [SJC], tender joint count [TJC], CRP, DAS28), treatment (use of corticosteroids, DMARDs, biological), time of evolution or US scores (SH, PD and total scores) were found. Globular synovitis was present in 71 patients 61.7% and 10.3% (62% and 13.7%) of seropositive and seronegative RA patients, respectively (p< 0.0001). Globally, 75 (51.7%) out of 145 patients had “globular” synovitis by US (Figure 1). 71 out of 75 patients were FR /ACPA positive (95.9%). Only three patients with seronegative RA had this US pattern (p < 0.001). Furthermore, patients with “globular” synovitis had more erosions (72% vs 32.9%, p 0.000), higher SJC (3.3and higher SH and PD scores (p< 0.001).



Globular synovitis in MCP joint of a FR and ACPA positive RA patient. The synovial has an exophytic growth with globular shape and convexity in the upper limit of joint capsule.



Synovitis in MCP joint of a patient with FR and ACPA negative RA. Synovial proliferation is low and the upper limit of the joint capsule has a flat shape.

Conclusion: The presence of proliferative globular synovitis was significantly associated with the presence of RF/ACPA in patients with RA. This US pattern identified a subgroup of RA patients with poor prognosis: more erosions and greater inflammatory activity both at clinical and ultrasound level.

Disclosure: A. Azuaga-Piñango, None; **B. Frade-Sosa**, None; **R. Gumucio**, None; **K. Cajiao-Sanchez**, None; **S. Mandelikova**, None; **V. Ruiz-Esquide**, None; **R. Castellanos-Moreira**, None; **R. Sanmarti**, None; **J. Cañete**, Eli Lilly and Company, 5, Janssen, 5, 8, Novartis, 5, 8, Mylan, 5, Pfizer, 5, UCB, 5; **J. Ramirez**, None.

Abstract Number: 0301

PANLAR Ultrasound Study Group Recommendations for the Use of Imaging in the Management of Patients with Gout

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SESSION INFORMATION
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is a metabolic disease caused by deposition of monosodium urate (MSU) monohydrate crystals in different tissues. Imaging may be useful to evaluate the extent of MSU deposition, the presence of acute and chronic inflammation, and tissue structural damage. The aim of the current study was to develop evidence-based and expert opinion recommendations for the use of imaging techniques in the diagnosis, monitoring, prognosis and treatment of patients with gout.

Methods: A selected group of experts (rheumatologists, radiologists, rheumatologist sonographers, methodologists and statisticians) from different PANLAR countries were included in the gout imaging task force. Imaging modalities evaluated were: conventional radiography (CR), ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI) and dual-energy computed tomography (DECT). Seven clinical questions were selected using the Delphi technique with RAND/UCLA modified methodology. Each question was scored in a visual analogue scale from 1 to 9 (1: complete disagreement; 9: complete agreement). With the information obtained, questions were reformulated

Table 1.

Recommendations	Level of evidence	Grade	Level of agreement [&] Task force	Level of agreement [&] Independent committee
1. When clinical diagnosis is doubtful, detection of elementary US lesions defined by OMERACT and/or deposits of MSU by DECT, are sensitive and specific complementary tools for diagnosis of gout.	II	B	9 (100%)	9 (100%)
2. US and DECT have a lower sensitivity for gout diagnosis in patients with less than 2 years of disease duration. However, due to their high specificity, their use is recommended as complementary diagnostic method, regardless time of disease duration.	II	B	8 (100%)	8 (77%)
3. CR and CT show poor sensitivity for gout diagnosis. However, due to its high specificity and low cost, initial evaluation by CR is recommended for all patients with suspected gout, for both differential diagnosis and evaluation of structural damage.	II	B	9 (100%)	8 (92%)
4. MRI and US are valid tools for measurement of synovitis in patients with gout, regardless of disease duration.	III	B	8 (100%)	9 (92%)
5. CR is the choice technique for quantification of structural damage in patients with gout, using the Sharp van der Heijde method modified for this pathology. CT represents an alternative, more sensitive, but more expensive, for evaluation of structural joint damage.	II	B	8 (100%)	8 (85%)
6. US and MRI are alternative tools to detect structural damage in patients with gout. However, currently both techniques do not have a validated scale that allows its quantification. DECT should not be used for detection and quantification of structural damage.	III	B	8 (100%)	8 (77%)
7. US and DECT are the methods of choice to detect and quantify MSU deposits in the different tissues.	III	B	8 (100%)	8 (100%)
8. Current evidence is insufficient to recommend the use of images as a method of follow-up and treatment guidance in patients with gout. However, according to expert opinion, detection of synovitis by US or MRI and/or quantification of deposits of MSU by US or DECT, can be used as complementary tools for monitoring these patients.	IV	D	8 (100%)	8 (92%)

[&]Each question was graduated from 1 to 9 (1: totally disagree; 9: totally agree); median (percentage of response between 7-9)

and re-evaluated using the same scoring system. One question did not reach agreement. Finally, six questions were selected. A systematic literature review was performed using Medline, LILACs, Embase and Cochrane databases from January 1966 to February 2018. The search resulted in a total of 8657 articles, of which 1957 were duplicated. Of the 6700 remaining, 6020 were excluded based on the title and/or summary, leaving 680 for full text review. After that, 639 were excluded, leaving a total of 41 articles as supporting evidence, by two independent reviewers (agreement 97%, kappa 0.91). Recommendations were developed by consensus following similar methodology utilized for clinical question selection. Such recommendations were graded according to levels of evidence from the Oxford Center of Medicine in 2011. Final recommendations were eventually presented to an independent committee including representatives from several PANLAR rheumatologist societies.

Results: Eight recommendations were developed for the use of imaging techniques in the diagnosis, monitoring, prognosis and treatment of patients with gout. The strength of each recommendation was established based on the evidence level as well as rate of agreement. Both gout imaging task force and independent committee agreed with the final recommendations (Table 1).

Conclusion: To the best of our knowledge, these are the first evidence-based and expert opinion recommendations for the use of imaging in patients with gout, providing some guidelines for their use in daily clinical practice.

Disclosure: M. Gutierrez, None; **C. Pineda**, None; **J. Vazquez-Mellado**, None; **M. Moreno Alvarez**, None; **J. Rosa**, ABBVIE, 8, BRISTOL, 8, JANSSEN, 8, LILLY, 8, NOVARTIS, 8, PFIZER, 8; **A. Reginato**, Eli Lilly and Company, 5, Novartis, 5, Horizon, 5; **M. Chavez**, None; **M. Alva Linares**, None; **M. Audisio**, None; **J. Mendonca**, None; **T. Cazenave**, None; **O. Sedano**, None; **L. Ventura Ríos**, None; **E. de Miguel**, AbbVie, 2, 5, 8, BMS, 8, BMS, MSD, UCB, Roche, 8, MSD, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 8, UCB, 8; **G. Kaeley**, None; **E. Scheines**, None; **F. Hofmann**, None; **G. Aguilar**, None; **C. Waimann**, None; **F. Marengo**, None; **S. Ruta**, None.

Abstract Number: 0302

Clinical Impact of a Rheumatology Musculoskeletal Ultrasound Clinic at a U.S. Academic Center

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Routine use of musculoskeletal ultrasound (MSK-US) to aid in clinical decision-making for rheumatology patients is less common in the United States than in Europe, and while MSK-US is widely perceived as additive to the clinical impression, the measured clinical impact is unknown. Our aim was to evaluate diagnostic and therapeutic outcomes of patients with rheumatic disease referred to a rheumatology MSK-US clinic.

Methods: All patients seen at an MSK-US clinic over a 12-week period were reviewed for the study. Subjects referred for non-rheumatologic queries as well as subjects lacking referral documentation were excluded. Data were extracted from the referral documentation, MSK-US clinic notes, and clinic notes from the referring provider pre- and post-US visit (± 6 months). Subjects were categorized into groups pertaining to diagnostic and clinical impact of the MSK-US visit: 1) No diagnostic or clinical impact 2) US findings leading to subsequent clinical action by the referring provider 3) Unknown impact (follow-up data unavailable). All MSK-US examinations were performed using a GE Logiq e ultrasound (GE Healthcare, WI) with 12-L and 18-L transducers. Diagnostic regional MSK exams were performed according to published EULAR protocols, enthesitis exams utilized the Madrid Sonographic Enthesis Index (MASEI), and synovitis exams utilized the ARCTIC protocol (Aiming for Remission in rheumatoid arthritis: a randomized trial examining the benefit of ultrasound in a Clinical Tight Control regimen).

Results: 86 referrals met inclusion criteria. Mean age was 53 ± 14 years, 81% were female, and mean time from referral to US visit was 24 ± 25 days (Table 1). Most referrals were generated from rheumatologists (93%, n=80), and disease activity assessment was the most frequent referral reason (60%, n=51). Overall, MSK-US led to a change in the underlying diagnosis in 28% (n=24) of cases (Table 1). In 58% (n=50) of cases, MSK-US examination led to a subsequent clinical action by the referring provider (Figure 1); the majority of these cases were subjects referred for diagnostic exam or disease activity assessment (Table 1). Discordance between the US visit recommendations and the subsequent referring provider's treatment plan occurred in 11% (n=3) of patients with non-inflammatory US findings.

Conclusion: The most common referral reason in an academic rheumatology MSK-US clinic was for disease activity assessment. MSK-US findings led to a change in the underlying existing rheumatologic diagnosis or clinical impression of the chief complaint in 28% of cases and led to a change in clinical management in 58% of cases. These findings suggest that rheumatologists utilize MSK-US findings to make significant clinical decisions and support the utility of a dedicated MSK-US clinic to aid in the diagnosis and management of patients with rheumatic disease.

Table 1. Cohort characteristics of subjects evaluated in a rheumatology MSK-US clinic over a 12-week period			
		Referral Reason	
	Total Cohort n=86	**Diagnostic/ Disease Activity Assessment*** n=65 (76%)	**Procedure (Injection/Aspiration)** n=21 (24%)
Mean age (years)	53 ± 14	51 ± 13	59 ± 16
Female	70 (81%)	54 (84%)	16 (76%)
Mean time to MSK-US (days)	24 ± 25	21 ± 18	31 ± 38
Referring provider specialty			
Rheumatology	80 (93%)	62 (95%)	18 (86%)
Other	6 (7%)	3 (5%)	3 (14%)
Diagnosis at referral			
Rheumatoid arthritis/JIA	14 (16%)	12 (18%)	2 (10%)
Osteoarthritis/Fibromyalgia	20 (23%)	10 (15%)	10 (48%)
Seronegative inflammatory arthritis	18 (21%)	17 (26%)	1 (5%)
Spondyloarthropathy	15 (17%)	12 (18%)	3 (14%)
Other**	19 (22%)	14 (22%)	5 (24%)
Change in diagnosis***	24 (28%)	22 (34%)	2 (9%)
Change in clinical action****	50 (58%)	49 (75%)	1 (5%)

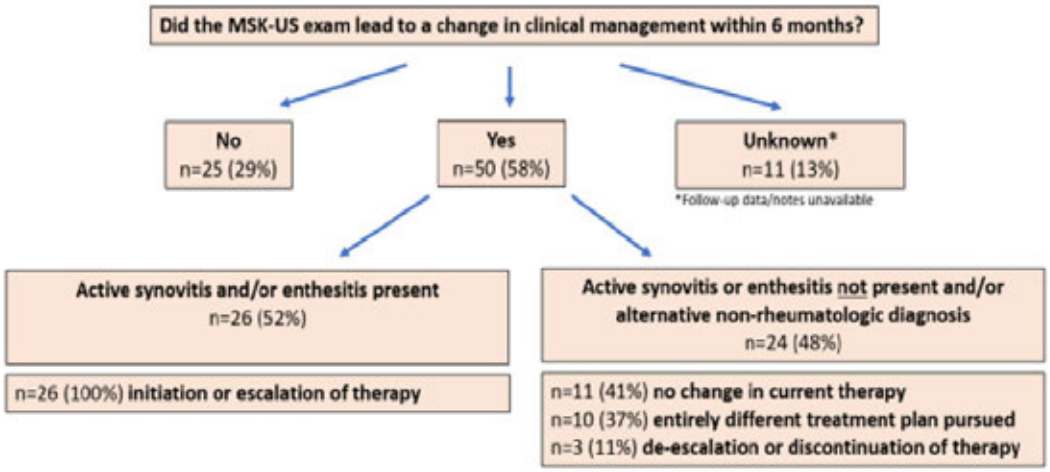
*Refers to diagnostic regional MSK, synovitis, and enthesitis exams

**_Other diagnoses_ refer to the following: systemic lupus erythematosus (SLE), systemic sclerosis (SSc), Sjogren's syndrome (SS), sarcoidosis, anti-neutrophil cytoplasmic antibody (ANCA) vasculitis, polymyalgia rheumatica (PMR), Cogan syndrome, anti-synthetase syndrome, gout, stiff person syndrome, large granular lymphocytic (LGL) leukemia, remitting seronegative symmetric synovitis with pitting edema (RS3PE)

***_Change in diagnosis_ refers to the underlying rheumatologic diagnosis at time of referral and/or the clinical impression of the chief complaint that generated the referral

****_Change in clinical action_ refers to decisions made regarding dosages of current rheumatologic medications, additions/subtractions of medications, referrals to other specialists (i.e. physical therapy, sports medicine), referrals for advanced imaging (i.e. MRI) or specialized tests (i.e. EMG)

Figure 1. Clinical impact of MSK-US exam results on treatment decisions by referring provider, total cohort n=86. No change in clinical management (n=25) includes subjects in whom MSK-US was unable to answer the provider's query as well as subjects in whom there was discordance between the MSK-US visit recommendations and the referring provider's subsequent treatment plan. A change in clinical management (n=50) refers to subjects in whom MSK-US findings led to a subsequent clinical action.



Abstract Number: 0303

Utility of Power Doppler Ultrasound–Detected Synovitis for the Prediction of Flare in Psoriatic Arthritis Patients in Clinical Remission

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Imaging Of Rheumatic Diseases Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Power Doppler ultrasound (PDUS) has been shown to detect subclinical synovitis in psoriatic arthritis (PsA). The aim of this study was to evaluate PDUS features at joint level in patients with PsA in clinical remission and to investigate its value for predicting flares after one year of follow up.

Methods: Consecutive patients with PsA in clinical remission according to the attending rheumatologist and who fulfill minimal disease activity criteria and/or 28-joint Disease Activity Score in remission criteria underwent PDUS examination of 18 joints. All patients were followed up for 12 months. Disease flare was defined as any increase of disease activity generating the need of any of the following: changes in therapy with disease-modifying antirheumatic drugs (DMARD) by the attending rheumatologist: dose increase, switch or addition of a different DMARD, and/or switch or addition of biological therapies.

Results: Sixty patients with PsA in clinical remission (15 [25%] by DAS28, 12 [20%] by MDA, and 33 [55%], by both), were included. Fourteen patients (23%) were receiving biologics (5 as monotherapy and 9 combined with methotrexate (MTX), 27 (45%) were receiving MTX, 2 (3%) sulfasalazine, 1 (2%) leflunamide, and 16 patients were not receiving treatment. 18 (32%) experienced a flare within the next 12 months. Seventeen patients had at least 1 joint with PDUS synovitis at baseline, and 8 (44%) of these had a disease flare during the follow up period compared with only 10 of the 43 patients (21%) without baseline PDUS synovitis (relative risk = 2.1 (95% CI: 0.95 – 4.5; p=0.0698). On logistic regression analysis, PDUS synovitis was associated with short term flares: OR: 4.8, 95% CI: 1.12 - 20.9; p= 0.034), after adjusting for use of biologics, sex, age, disease duration, and baseline disease activity.

In 28 patients without flares a second US was performed within 12 months, in 6 (21%) the PDUS was positive (2 already positive in the first evaluation)

Conclusion: Among patients with PsA in clinical remission, PDUS-detected synovitis was present in around 20% of the patients and was predictor of short-term flares independently of treatment.

Disclosure: J. Zacariaz Hereter, None; **J. Marin**, None; **M. Acosta Felquer**, Eli Lilly, 8, Pfizer, 8, Montpellier, 8, Jannsen, 8, Novartis, 8; **M. Brom**, None; **J. Rosa**, ABBVIE, 8, BRISTOL, 8, JANSSEN, 8, LILLY, 8, NOVARTIS, 8, PFIZER, 8; **R. Garcia Monaco**, None; **E. Soriano**, Abbvie, 2, 5, 8, ABBVIE, 2, 5, 8, AbbVie, 2, 5, 8, Amber, 8, Amgen, 5, 8, AMGEN, 5, 8, BMS, 8, BRISTOL, 8, Bristol MS, 8, BRISTOL MYERS SQUIBB, 8, Bristol-Myers Squibb, 8, eli lilly, 5, 8, Genzyme, 8, GENZYME, 8, GLAXO, 2, Glaxo, 2, glaxosmithkline, 2, GlaxoSmithKline, 2, GSK, 2, Janssen, 8, Lilly,

5, 8, LILLY, 5, 8, Novartis, 2, 5, 8, NOVARTIS, 2, 5, 8, PFIZER, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, 8, Roche, 2, 8, ROCHE, 2, 8, Sandoz, 5, SANDOZ, 5, Sanofi, 5, SANOFI, 5, SANOPHY, 5, UCB, 8.

Abstract Number: 0304

The ACR's Rheumatology Informatics System for Effectiveness (RISE) Demonstrates Improvements in Many Measures of Quality of Care Between 2015 and 2017

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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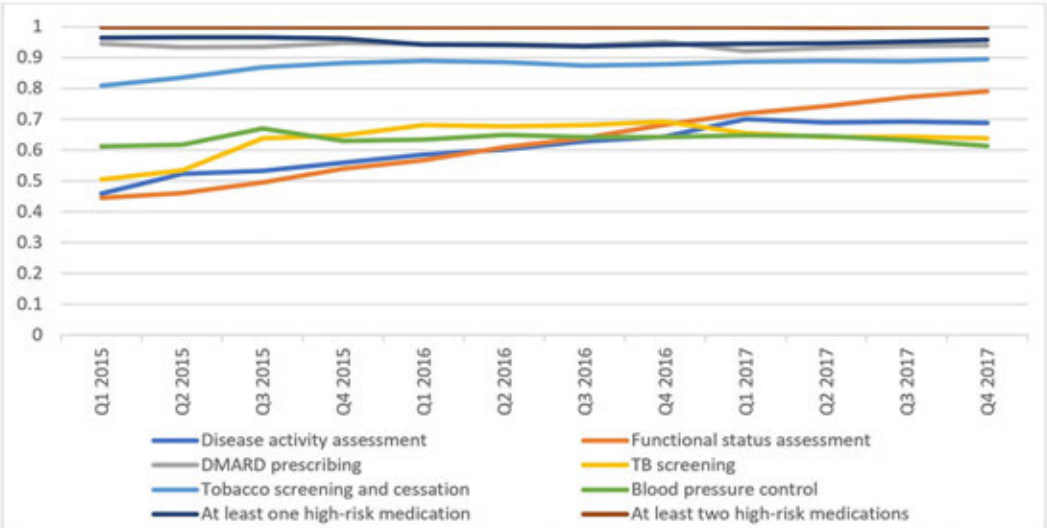
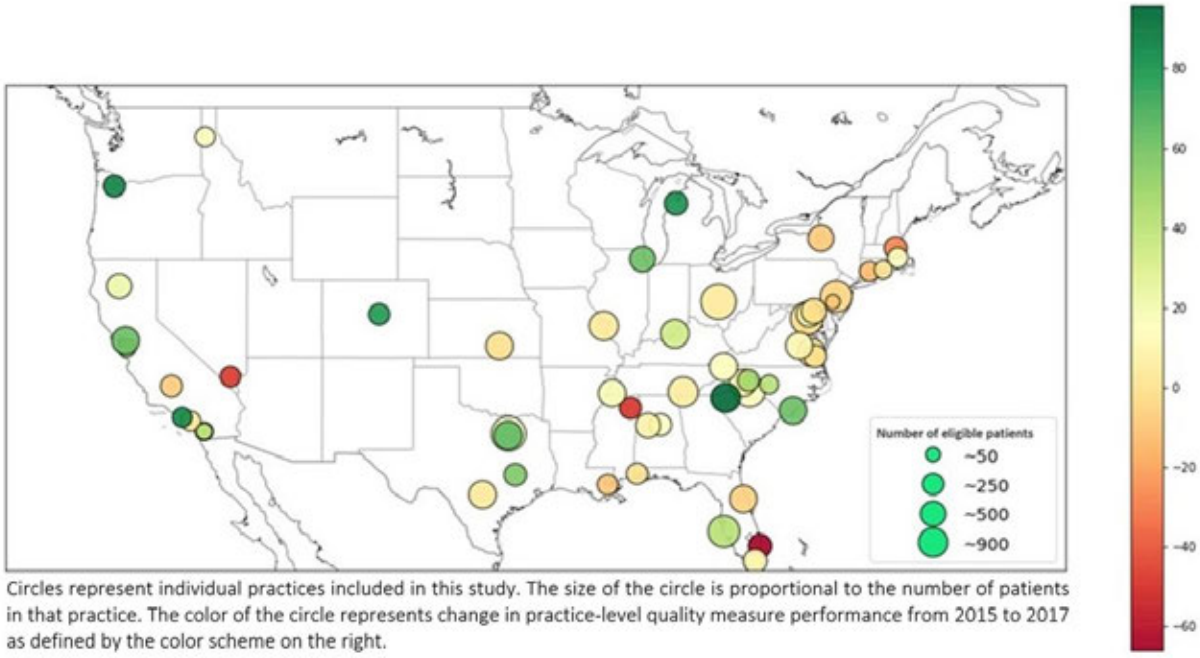
Background/Purpose: The ACR's Rheumatology Informatics System for Effectiveness (RISE) is an EHR-enabled registry that represents over 36% of the U.S. clinical rheumatology workforce and calculates patient-level performance on over 24 quality measures. RISE allows rheumatologists to track their performance on quality measures, but aggregate trends in performance have not been studied. The objectives of our study were to examine changes in performance over time on selected quality measures in patients with RA and assess variations in performance across practices.

Figure 1. Proportion of patients with rheumatoid arthritis meeting the quality measures from 2015 to 2017



Disease activity assessment: Percentage of patients ≥18 years with rheumatoid arthritis (RA) whose disease activity is assessed using a standardized measurement tool at 50% or more encounters for RA with the same clinician during the measurement period; *Functional status assessment:* Percentage of patients ≥18 years with RA whose functional status is assessed using a standardized measurement tool at least once during the measurement period; *DMARD prescribing:* Percentage of patients ≥18 years with active RA who are treated with a DMARD during the measurement period; *TB screening:* Percentage of patients ≥18 years with RA that are newly prescribed a biologic therapy during the measurement period and whose medical record indicates TB testing in the 12 months preceding the biologic prescription; *Tobacco screening and cessation:* Percentage of patients ≥18 years who were screened for tobacco use ≥ 1 time within 24 months AND who received cessation counseling intervention if identified as a tobacco user; *Blood pressure (BP) control:* Percentage of patients 18-85 years of age who had a diagnosis of hypertension and whose BP was adequately controlled (<140/90mmHg) during the measurement period; *Use of high-risk medications in the elderly*: Two rates were reported: a) Percentage of patients ≥66 years who were ordered ≥1 high-risk medication; b) Percentage of patients ≥66 years who were ordered ≥2 different high-risk medications. These are inverse measures but, in this study, they were inverted again such that higher percentages indicated better performance – e.g., a performance of 1% on the inverted measure became 99% in the modified measure.

Figure 2. Variability in within-practice change in measure performance (%) from 2015 to 2017 across states. Measures included: disease activity assessment, functional status assessment and tuberculosis screening.



Circles represent individual practices included in this study. The size of the circle is proportional to the number of patients in that practice. The color of the circle represents change in practice-level quality measure performance from 2015 to 2017 as defined by the color scheme on the right.

Methods: We analyzed data from practices enrolled in RISE between January 1, 2015 and December 31, 2017. Eight quality measures in the areas of RA management (disease activity assessment, functional status assessment, DMARD prescribing, and tuberculosis (TB) screening), and risk reduction (tobacco use screening and cessation, blood pressure (BP) control, and two measures on high risk medication use in elderly) were examined. Practice-level performance was defined as the percentage of eligible patients receiving recommended care for each measure separately. We used hierarchical multivariate linear models to predict change in performance as a function of practice type (single-specialty group practice, multi-specialty group practice, solo practitioner vs. health system), after adjusting for patient demographics, number of providers, EHR vendor and geographic region.

Results: Data from 59,986 patients from 54 practices was examined. Mean age was 62±14 years, 77% were female, 69% were Caucasian, and 81% had private insurance. The most common practice structure was a single-specialty group practice (46%), most practices had 1-4 providers (59.3%), and NextGen was the most commonly used EHR vendor (63%). From 2015 to 2017 there were clinically meaningful and statistically significant changes for disease activity assessment (8.4% per year, $p< 0.001$), functional status assessment (13.9% per year, $p< 0.001$), and TB screening (4.3% per year, $p< 0.001$), but only very modest changes for DMARD prescribing (1.0% per year, $p=0.004$), tobacco screening and cessation (2.9% per year, $p< 0.001$), and BP control (1.6% per year, $p=0.022$) (Figure 1). The degree of change in performance varied considerably across practices and regions (Figure 2). In adjusted analyses, single specialty group practices had the highest rates of improvement on disease activity assessment (12.8% per year), functional status assessment (17.3%) and TB screening (5.7%), while health systems were worsening over time on these measures (-18.5%, -4.2%, -19.3%, respectively; p-value for interaction ≤0.008).

Conclusion: Among practices participating in RISE from 2015 to 2017, aggregated performance, especially on RA-specific measures improved, although we found significant variation in performance over time between practices. These findings suggest that future work to identify workflow patterns leading to high performance or to dramatic improvements in quality are warranted.

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

Disclosure: Z. Izadi, None; **G. Schmajuk**, None; **J. Kay**, None; **M. Evans**, None; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2.

Abstract Number: 0305

Naming Is Everything! the Cost of Inappropriate "Lupus Panel" Testing

Caleb Anderson ,[1] Roger Stitt,[2] and Robert O'Brian[1], [1]Walter Reed National Military Medical Center, Bethesda, MD, [2]US Army, Ft Eustis

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Greater emphasis has been placed on cost saving measures due to ballooning healthcare cost in the U.S. ACGME now evaluates trainee ability to practice cost conscious care through the systems based practice competency. In the rheumatology clinic at Walter Reed National Military Medical Center (WRNMMC), we observed inappropriate ordering of the so called "lupus panel." The "lupus panel" lab is better known as the lupus anticoagulant test (LAC), which may be associated with the antiphospholipid syndrome (APS) and its clinical features of thromboembolic events and recurrent pregnancy loss. We suspected the misleading name led physicians to order the "lupus panel" to screen for systemic lupus erythematosus (SLE) rather than to evaluate for APS. We retroactively evaluated the rate and cost of inappropriate ordering of the "lupus panel" and found thousands of dollars spent annually on inappropriate ordering. The lab name was changed from "lupus panel" to "lupus anticoagulation panel" based on our recommendation. We then set out to evaluate a change in ordering pattern and resulting cost over a three month period.

Methods: Results of the "Lupus Panel" from 1 January 2015 – 31 December 2015 were collected. The rationale for ordering each test was analyzed in the EMR by two rheumatologists. The test was considered inappropriate if it was

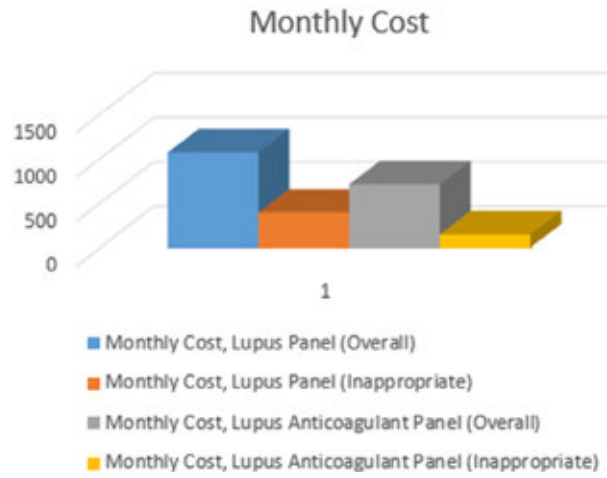


Table One. Monthly cost of total and inappropriate lupus anticoagulant lab tests. Total monthly cost of "lupus panel" was $1072.18, with inappropriate lab tests costing $393.56. Total monthly cost of "lupus anticoagulant panel" was $711.60, with inappropriate lab tests costing $147.79.

ordered for anything other than thrombophilia, initial SLE evaluation by a rheumatologist, or pregnancy loss. The name of the lab was changed to “Lupus Anticoagulant Panel” on 1 April 2018. The ordering pattern from 1 April 2018 – 30 June 2018 was similarly evaluated. The lab processing cost, excluding labor, was estimated by our lab manager. Fisher’s exact test was utilized to evaluate the association between lab name and ordering pattern.

Results: 403 “lupus panel” lab tests were processed in the National Capital Region in 2015, at a rate of 33.6 per month. 148 (37%) samples were considered inappropriate, costing $4,722.68 ($393.56 per month) to process. The three most common reasons for inappropriate testing were musculoskeletal complaints 63 (43%), fatigue 13 (8%), and paresthesias 6 (4%). 65 LAC tests were ordered in the first three months after the name change, at a rate of 22.3 per month. Of the 62 tests that had sufficient documentation to analyze, 14 were considered inappropriate (22.6%). The most common reasons for inappropriate testing were musculoskeletal complaints 6 (43%) and rash 5 (36%). The monthly cost of inappropriate lab tests was $147.79.

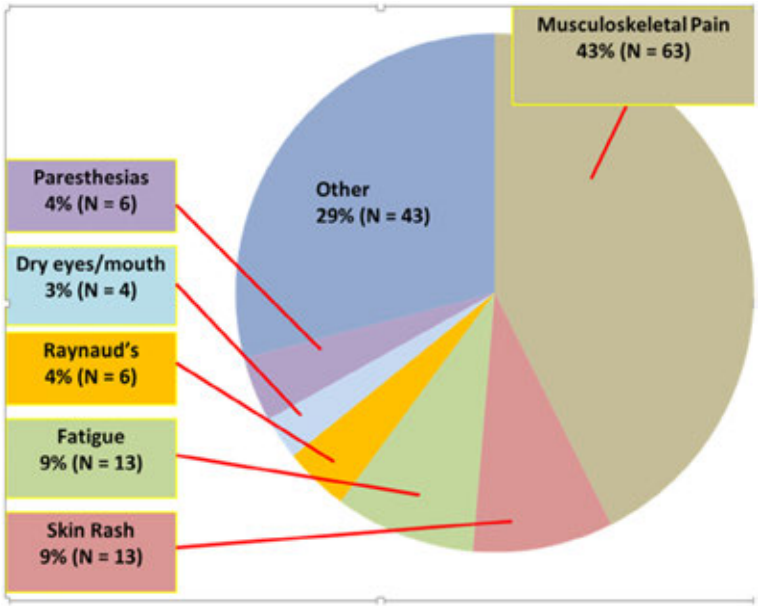


Figure Two: Reasons for inappropriate “lupus anticoagulant panel” testing

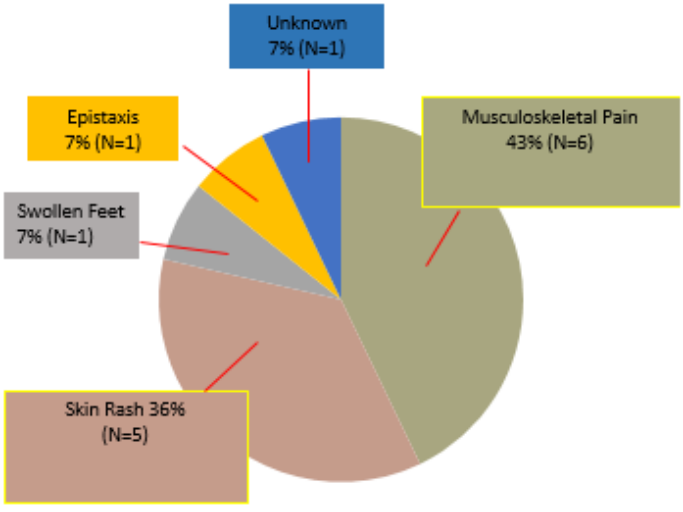


Figure One: Reasons for inappropriate “lupus panel” testing

Conclusion: Inappropriate ordering of the "lupus panel" cost WRNMMC approximately $4,722.68 in lab processing for the calendar year 2015. Changing the name of the lab to better describe the test yielded a significant reduction in the percentage of inappropriate lab tests (37% vs 22.6%, p=0.0318) and reduced annual and monthly cost by approximately $2,949.20 and $245.77, respectively.

Disclosure: C. Anderson, None; **R. Stitt**, None; **R. O'Brian**, None.

Abstract Number: 0306

Infrequent Screening but High Prevalence of Antinuclear Antibodies in Patients with Neuropsychiatric Disorders

Jihad Ben Gabr ,[1] and Andras Perl[1], [1]SUNY Upstate Medical University, Syracuse, NY

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The American College of Rheumatology (ACR) established case definitions of 19 specific neuropsychiatric syndromes seen in patients with systemic lupus erythematosus (SLE) (*1*). Therefore, we evaluated the frequency of antinuclear antibody (ANA) screening by immune that has the greatest sensitivity to detect SLE (*2*).

Methods: This quality improvement project examined the electronic medical records (EMR) of patients diagnosed with 17 neuropsychiatric conditions documented at our institution between 2013 until 2019 (Table 1). Patients with existing SLE have been excluded. ANA testing was done by indirect immunofluorescence using HEp-2 cells as antigen (*2*). Significant ANA titer was defined as titer >1:50. Our findings were compared to published studies in similar patient populations which were available in PubMed for 8/17 conditions. Statistical analysis was performed with chi-square test using GraphPad version 5.0 software.

Results: Table 1 outlines the findings in a total number of 178,585 patients with 17 neuropsychiatric diagnosis in our cohort. ANA was assessed in 19,369 subjects (10.7%). Rates of testing ranged between 6.7% (seizure) and 23.8% (Guillain-Barre syndrome, GBS). Surprisingly, ANA testing was done in 8.9% of patients with psychosis. Each population was evaluated for the numbers of patients who were screened and found to have elevated ANA. Compared to peer-reviewed literature our cohort was larger in number with greater prevalence of positive ANA with the exception of myasthenia gravis, which unveiled similar levels of prevalence.

Conclusion: Up to 80% of SLE manifest a neuropsychiatric disorder, which may benefit from treatment targeting the immune system and inflammation. The prevalence ANA testing was surprisingly low in patients with neuropsychiatric disorders. However, among the tested patients, the prevalence of ANA exceeded those in the literature in 7/8 conditions, which likely reflects a preference for testing in cases where disease manifestations occurred outside the nervous system. Further studies are clearly warranted to substantiate the role of systemic inflammatory diseases, such as SLE, in neuropsychiatric disorders.

Disclosure: J. Ben Gabr, None; **A. Perl**, None.

	Upstate Data					Literature Data				
	Total Dx	ANA Testing Done	% tested	ANA+	%ANA+	Total Dx	ANA+	%ANA+	χ2 p	Ref.
Anxiety	37320	3851	10.0	1882	48.87					
Aseptic Meningitis	75	14	19.0	6	42.86					
Autonomic Neuropathy	1398	277	20.0	143	51.62					
CVA	18959	1821	9.6	1374	75.45	481	35	7.28	<0.0001	3
Cognitive Disorder	3346	337	10.0	184	54.6	30	9	30	0.0097	4
Confusional State	5247	573	11.0	319	55.67					
Demyelinating Disease	3185	495	15.5	235	47.47	174	47	27.01	<0.0001	5
Headache	29353	3128	10.7	1576	50.38					
Movement Disorder	6583	518	7.9	261	50.39	108	20	18.52	<0.0001	6
Myelopathy	6433	504	7.8	258	51.19					
Seizure	19865	1325	6.7	609	45.97	232	40	17.24	<0.0001	7,8
GBS	110	26	23.8	9	34.62					
Mononeuropathy	13646	2031	14.9	1083	53.23					
Polyneuropathy	6978	1616	23.2	851	52.66					
Myasthenia Gravis	498	79	15.9	33	41.77	78	30	38.46	0.6722	9
Mood Disorder	19034	2188	11.5	1391	63.57	63	12	19.05	<0.0001	10
Psychosis	6555	586	8.9	424	72.35	188	15	7.98	<0.0001	11, 12

Table 1. Prevalence of ANA testing in patients with 17 neuropsychiatric conditions. Total Dx, total population at SUNY Upstate. ANA testing done = Total number of each population at Upstate screened for ANA. ANA+, patients with positive ANA not including SLE patients. %ANA+, percent of positive ANA screened from total population not including SLE patients. Total dx (lit)= Total diagnosis found in the literature screened for ANA. ANA+, number of positive ANA found within the population from the outside literature; %ANA+, percent positive ANA found within the literature; X2 p, chi square values comparing prevalence of ANA between our cohorts and ones in the published literature. Ref.= references that can be seen under reference section

Abstract Number: 0307

ANA-lysis: Utility of Repeated Antinuclear Antibody Testing in a Single Center

Ai Li Yeo ,[1] Jason Ong,[1] Kathryn Connelly,[2] Suong Le,[2] Ronnie Ptsaznik,[2] Jane Ross,[2] Eric Morand,[3] and Michelle Leech[1], [1]Monash University, Melbourne, Australia, [2]Monash Health, Melbourne, Australia, [3]Monash University, Melbourne, Victoria, Australia

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating
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Session Time: 9:00AM–11:00AM

Background/Purpose: Reducing unnecessary laboratory investigations is a health economic priority. Anti-nuclear antibody (ANA) testing is performed as part of the diagnostic work up for autoimmune disease, or in patients with inflammatory or musculoskeletal symptoms. The value of serial ANA testing is unclear, but anecdotal evidence suggests it is frequent. We sought to evaluate the utility of repeated ANA testing in a large tertiary healthcare network, to determine the evidence base for decision support actions.

Methods: The primary endpoint was whether a longitudinal change in ANA resulted in new ANA associated diagnoses. Secondary endpoints included calculation of the total cost associated with repeated testing and the examination of baseline ANA testing behaviours. We retrospectively analysed data from a multi-centre tertiary health network across a 7-year period (March 2011 to July 2018). ANA and other autoimmune test results were obtained from the hospital systems. The laboratory positive ANA cut off of 1:160 was used. Clinical information was sourced from medical records on all patients who had a change in ANA result from negative to positive on repeat testing. The cost of repeated ANA testing was calculated based on the baseline cost to the payer. Descriptive statistics were performed using Stata version 15.

Results: A total of 36,715 ANA tests (excluding 980 cancelled same-day requests) were performed in 28,840 patients. Of these, 14,058 (38.3%) were positive, with females accounting for 9,265 (65.9%, $p< 0.001$). The most frequent ANA patterns were homogenous (47.4%) and nucleolar (23.3%). The distribution of ANA titres was: 1:160 (41.4%), 1:320 (15.3%), 1:640 (13.1%) and 1:1280 (29.2%). 7,875 (21.4%) tests were repeat tests in 4,887 patients, with test frequency in an individual patient ranging from 2-45. Of repeated tests, 79% of results remained the same, while 541 (11.1%) results changed from negative to positive. In the 501 of these in whom medical records were available, a change to positive ANA was associated with a new ANA-associated diagnosis in only 7 cases (2 SLE, 1 scleroderma, 2 undifferentiated connective tissue disease and 2 autoimmune hepatitis), resulting in a positive predictive value of 0.014. When comparing patients with a new diagnosis to those with no new diagnosis, there was no difference between ANA titre, pattern, age, time interval between negative and positive ANA, location or ordering clinician. The direct total cost to the payer of all ANA testing was USD$624,691, of which repeat testing contributed USD$133,990.

Conclusion: Repeat ANA testing was frequent. After a negative result, repeat ANA testing has limited utility in the diagnosis of ANA-associated conditions with a very low positive predictive value, and was associated with excess cost. Clinical alert systems to reduce unnecessary repeat ANA testing may result in significant direct cost savings.

Disclosure: A. Yeo, None; **J. Ong**, None; **K. Connelly**, None; **S. Le**, None; **R. Ptsaznik**, None; **J. Ross**, None; **E. Morand**, AstraZeneca, 2, 5, 8, Bristol Myers Squibb, 2, Eli Lilly, 5, Janssen, 2, 5, Merck Serono, 2, 5, UCB, 2; **M. Leech**, None.

Abstract Number: 0308

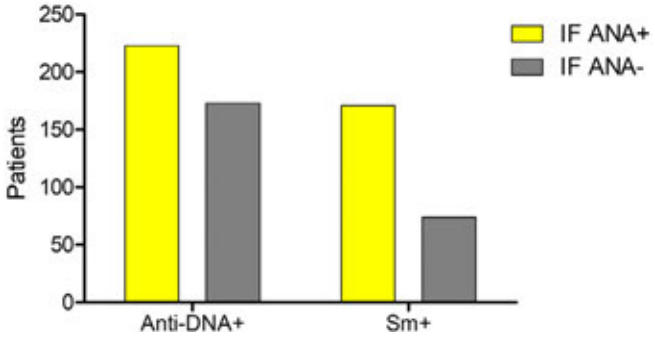
Quality Control of Antinuclear Antibody Detection by Indirect Immunofluorescence and Flow Cytometry-based Recombinant Antigen Assays

Konrad Dziamski ,[1] and Andras Perl[1], [1]SUNY Upstate Medical University, Syracuse, NY

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Indirect immunofluorescence (IF) is the recommended initial test for detection of antinuclear antibodies (ANA) by the American College of Rheumatology (*Ann Rheum. Dis* **69**:1420-2), (*Clin. Immunol.* **124**:18-21). Because the staining pattern does not identify the responsible autoantibody, additional testing using Flow Cytometry-

TEST	dsDNA	TEST	Smith
Homogeneous (+)	223	Speckled (+)	171
Homogeneous (-)	173	Speckled (-)	74
Sensitivity (%)	56	Sensitivity (%)	70
Specificity (%)	30	Specificity (%)	44
p value vs Smith	0.0007	p value vs dsDNA	0.0007



Detection of ANA by IF in patients with SLE that have positive anti-DNA or anti-Sm antibodies.

based Recombinant Antigen Assays (FCA) is required. We were interested in assessing the correlation of this method for ANA detection with the results of specific autoantibodies identified by FCA at our institution between 2012-2019.

Methods: 5,474 instances of simultaneous testing with ANA by IF and FCA were identified. All tests were performed in house (SUNY Upstate, Syracuse, NY). Positive autoantibody detection by FCA for dsDNA, anti-Smith, centromere, histone, RNP, Scl-70, SSA, and SSB were individually compared to results of ANA by IF. Sensitivities, specificities, positive and negative predictive values were assessed by 2-tailed Chi-square tests using GraphPad software.

Results: Of 396 positive dsDNA results, 223/396 were associated with a homogeneous pattern and 173/396 were not (sensitivity: 56%; $p< 0.0007$ relative to anti-Smith, $p< 0.0021$ relative to RNP and $p< 0.0001$ to all others). Anti-Smith antibodies had association with speckled pattern in 171/245 instances (70%) while 74/245 (30%) did not (statistical significance only achieved in comparison to dsDNA ($p< 0.0007$ and centromere (0.0009)). There were 562 instances of multiple positive autoantibodies detected by FCA associated with positive IF, and an additional 17 instances of multiple positive autoantibodies associated with negative IF.

Conclusion: This analysis of lupus patients suggests that quality control issues likely exist when IF is used for ANA screening given the high number of negative homogeneous and speckled patterns when compared to positive dsDNA and Sm autoantibody detection by FCA.

Disclosure: K. Dziamski, None; **A. Perl**, None.

Abstract Number: 0309

Increasing Capacity and Reducing Costs of Rituximab Administration

Zachary Wallace ,[1] Tyler Harkness,[1] Kimberly Blumenthal,[1] Hyon K. Choi,[2] John Stone,[3] and Rochelle Walensky[1],
[1]Massachusetts General Hospital, Boston, [2]Massachusetts General Hospital, Boston, MA, [3]Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab (RTX) is associated with a large cost burden on the healthcare system and treatment delays that often exceed one month because the long infusion duration (>4 hours) limits daily capacity. Time-drive activity-based costing (TDABC) is a novel method to estimate costs that can identify opportunities for economic and process efficiencies. The TDABC approach examines actual time spent with each resource and its per-unit cost. We performed TDABC of RTX administration in rheumatology to identify key cost drivers, project potential cost- and time-saving opportunities, and enable future cost-effectiveness research.

Methods: We implemented TDABC throughout the care pathway (e.g., orders, pharmacy preparation, scheduling, administration) for 26 patients receiving a total of 30 RTX infusions in an academic hospital-based infusion center (IC). The base-case was one treatment cycle which included two 1,000mg RTX infusions administered using standard rates over two visits. We assumed a 23% rebate on drug costs. After collecting base-case data on provider timing, pre-treatment regimens, and infusion rates, we then varied these in sensitivity analyses paying particular attention to varying (1) the drug (biosimilar vs originator), and (2) administration, including the use of subcutaneous (SQ) or rapid (e.g., 90-minute) infusion protocols. We estimated the mean number of RTX infusions per day using 3 months of IC scheduling data and associated visit length (hours) using estimates from TDABC. We then assessed the potential effect of two alternative strategies on annual capacity: a) SQ RTX and b) rapid 2nd infusion protocols. We assumed that SQ RTX would require a 30-minute appointment based on oncology practice.

Results: In the base-case, RTX administration costs $18,840 (**Table 1**), 92% ($17,380) from drug costs; the remaining costs were due to personnel ($780, 4%), non-drug consumables ($60, 0.3%), and space ($630, 3%). In one-way

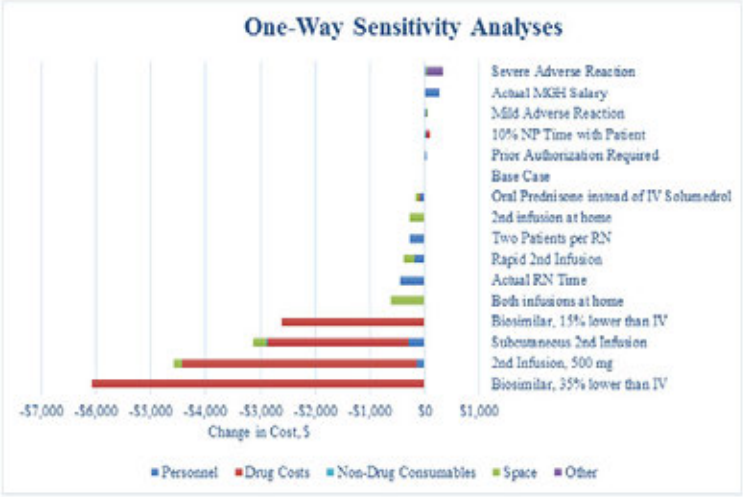
Infusions	Cost	% of Total
Long (First) Infusion Total		
Drug Costs	$8,690	91%
Personnel Costs	$440	5%
Space Costs	$350	4%
Non-Drug Costs	$30	0.3%
Total Cost	$9,510	100%
Short (Second) Infusion Total		
Drug Costs	$8,690	93%
Personnel Costs	$340	4%
Space Costs	$280	3%
Non-Drug Costs	$30	0.3%
Total Cost	$9,330	100%
Total Base Case Cost	$18,840	

Base Case Costs

	Number of Infusions			Hours of Infusions		
	Overall	First Tx	Second Tx	Overall	First Tx	Second Tx
Baseline Infusion Capacity						
per Day*	3	1	2	11	3	9
per Year†	680	130	550	2980	680	2,290
Subcutaneous Substitution^						
Maintain Current Volume (/day)	3	1	2	4	3	1
Newly Available Capacity (/day)				8	--	--
All Available Time for SQ	15	0	15	8	0	8
One Add'l First Infusion, Rest SQ	6	1	5	8	5	3
Newly Available Capacity (/year)†						
All Available Time for SQ	4,030	0	4,030	2,020	0	2,020
One Add'l First Infusion, Rest SQ	1,550	260	1,290	2,020	1,370	650
Rapid 2nd Infusion Substitution						
Maintain Current Volume (/day)	3	1	2	6	3	3
Newly Available Capacity (/day)				6	--	--
All Available Time for 2nd Infusion	3	0	3	5	0	5
One Add'l First Infusion	1	1	0	5	5	0
Newly Available Capacity (/year) †						
All Available Time for 2nd Infusion	980	0	980	1,460	0	1,460
One Add'l First Infusion	260	260	0	1,370	1,370	0

*Number of infusions/day based on Infusion Center scheduling over a 3 month period and hours of infusions based on TDABC estimates; †Based on infusion center open for 261 days/year; ^30 minutes reserved for SQ injection based on oncology practice

Projected Increases in Capacity



One-Way Sensitivity Analyses Using TDABC

sensitivity analyses (**Figure**), the greatest cost savings were associated with biosimilar RTX at a 35% cost reduction (-$6,080) and substitution of the 2nd dose with SQ RTX (-$3,170). SQ RTX use led to savings on personnel (-$290, -37%), consumable (-$2,640, -15%), and space (-$250, -39%) costs. In a "best case" scenario, when we used IV biosimilar RTX for the 1st dose, SQ RTX for the 2nd dose, assigned two patients per RN, and used oral prednisone (rather than IV solumedrol) as pre-treatment for the 1st dose, total savings reached -$6,350 (-34%). Using SQ RTX would increase the number of RTX treatments available by up to 15 patients per day, a 6-fold increase in capacity (**Table 2**). Using a rapid 2nd infusion would increase the number of RTX treatments available in one day by up to 3, an increase in capacity of 2-fold (**Table 2**).

Conclusion: Using a novel costing method, we found that drug price is the primary driver of the cost of RTX treatment and that varying non-drug factors has minimal impact on overall costs. The ultimate list price of biosimilar RTX may substantially impact the cost of RTX administration on the healthcare system. However, use of biosimilar and SQ RTX may reduce costs by 34% and appreciably increase administration capacity, thereby reducing delays in treatment.

Disclosure: Z. Wallace, National Institute of Arthritis, Musculoskeletal, and Skin Diseases, 2, Rheumatology Research Foundation, 2; **T. Harkness**, None; **K. Blumenthal**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5; **J. Stone**, Genentech, 2, 5, Roche, 2, 5, Xencor, 2, 5; **R. Walensky**, None.

Abstract Number: 0310

Efficacy, Immunogenicity and Cost Analysis of a Systematic Switch from Originator Infliximab to Biossimilar CT-P13 of All Patients with Inflamatory Arthritis from a Single Center

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating

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Background/Purpose: Biotechnological drugs are a fundamental resource for the treatment (Tx) of rheumatic patients (Pts). Biosimilar drugs are intended to be as effective as the originator product but with a lower cost to healthcare systems.

In our center we promoted a switch from originator infliximab (IFXor) to biosimilar infliximab (CT-P13). We analyzed efficacy, safety, immunogenicity and cost savings of switching.

Methods: Eligible Pts were those older than 18 years old with the diagnosis of rheumatoid arthritis (RA), spondylarthritis (SpA) and psoriatic arthritis (PsA) on Tx with IFXor for at least 6 months and with stable disease activity (DA). In December 2016 all eligible Pts were proposed to switch to CT-P13. At the day of the last Tx with IFXor, informed consent, data and blood samples were collected. On the next Tx day, CT-P13 was administered after standard evaluation of efficacy and safety. Efficacy was measured considering change from baseline in DAS in 28 joints for RA and PsA and in Ankylosing Spondylitis Disease Activity Score (ASDAS) for SpA. Disease worsening was considered when an increase of 1.2 from baseline in DAS28 or an increase of 1.1 in ASDAS occurred. Serum Infliximab levels (sIFX) were dichotomized as low (< 3 µg/mL) and high (>6 µg/mL). Anti-drug antibody (ADA) levels were dichotomized into detectable (>10 ng/ml) or non-detectable (< 10 ng/ml). CT-P13 Tx withdrawal and drug persistence were used as effectiveness outcomes. A cost analysis was done based on the purchasing prices of the 2 drugs at our center.

Table 1. Variation in disease activity of patients switched to biosimilar infliximab (CT-P13). *Median values (IQ)

	Baseline (n=60)	3 months after switch (n=59)	6 months after switch (n=58)	9 months after switch (n=56)	12 months after switch (n=55)	Variation from baseline to 12 months after switch (p-value)
ESR (mm/h)*	15.5 (11-22)	17 (10-30)	15 (10-24)	19 (11-26)	20 (12-35)	4.5
CRP (mg/dL)*	0.18 (0.08-0.59)	0.17 (0.06-0.50)	0.19 (0.11-0.49)	0.20 (0.10-0.63)	0.15 (0.08-0.5)	-0.03
PtGA (0-100)*	30 (20-50)	30 (20-50)	27 (10-50)	30 (10-50)	30 (20-50)	0
PhGA (0-100)*	20 (10-30)	20 (10-30)	15 (0-30)	20 (10-30)	30 (10-40)	10

ESR – Erythrocytes sediment rate; CRP – C-Reactive protein; PtGA – Patient Global assessment; PhGA – Physician global assessment.

Results: During a period of 1 year switch to CT-P13 was performed in 60 Pts for non-medical reasons.

We had a total of 36 Pts with SpA, 16 with RA and 8 with PsA. 65% were females with a median age of 53 years, median disease duration previous to switch of 17 years and median time on IFXor Tx of 8 years.

DA was stable over the observation period and similar to the values observed with IFXor. Median follow-up time was 15 months during which 5 Pts stopped CT-P13. Three Pts had disease worsening, 1 Pt had a minor adverse event (lip edema) and 1 Pt moved to another country. One patient returned to IFXor and the other 3 switched to another drug.

42 switchers had blood samples collected before and after switch. A total of 27 Pts had unaltered sIFX levels and ADA status during follow up.

At baseline, 5 Pts had low sIFX, with no detectable ADAs, that reverted after switch. These Pts had no variation in DA before and after switch.

3 Pts had detectable ADA at baseline with low sIFX levels. After switch, ADAs became negative in 2 of those Pts, with normalization of sIFX. The other Pt kept detectable ADA levels after switch and had a minor elevation of DAS28, based on patient global assessment.

ADAs became positive in 5 Pts after switch. Of these, sIFX changed from high to low accompanied by an elevation of ASDAS in 3 Pts. The other 2 Pts maintained ADA levels detectable with sIFX >3 µg/mL during all the evaluation period.

Apart from the Pts that developed ADAs, no other Pt changed from high to low sIFX.

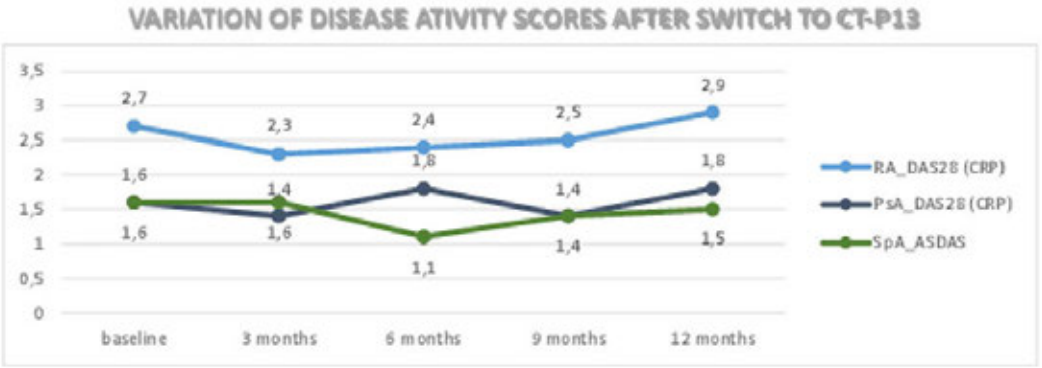

Figure 1. Variation in disease activity of patients switched to biosimilar infliximab (CT-P13). *Median values (IQ)

	RA (n=13)			PsA (n=2)			SpA (n=27)			Total (n=42)		
	Baseline	After switch (3-9 m)	After switch (≥ 12 m)	Baseline	After switch (3-9 m)	After switch (≥ 12 m)	Baseline	After switch (3-9 m)	After switch (≥ 12 m)	Baseline	After switch (3-9 m)	After switch (≥ 12 m)
IFX serum concentration* (µg/mL)	11.5 (9.7)	9.6 (8.9)	7.4 (4.2)	6.9 (2.3)	6.7 (2.3)	6.7 (1.8)	6.1 (3.9)	6.2 (8.1)	5.4 (3.7)	7.6 (6.8)	7.9 (8.9)	6.1 (3.9)
Positive ADA, n/total	2/13	1/13	1/13	0/2	0/2	0/2	1/27	5/27	5/27	3/42	6/42	6/42

Table 2. ADA and sIFX concentration at baseline and after switch. *mean values (SD)

The switch to CT-P13 represented a 26.4 % reduction of costs in the use of IFX Tx in these Pts.

Conclusion: The switch in routine care of a group of RA, SpA and PsA patients from IFXor to CT-P13 did not affect efficacy, safety or immunogenicity and reduced costs in 26.4%.

Disclosure: A. Valido, None; **J. Silva-Dinis**, None; **M. Saavedra**, None; **I. Iria**, None; **J. Gonçalves**, None; **J. Cruz**, None; **N. Bernardo**, None; **J. Eurico Fonseca**, None.

Abstract Number: 0311

Documenting Bone Health for Veterans with Rheumatoid Arthritis in an Outpatient Academic Clinic: A Multiphase Quality Improvement Project

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) is associated with an increased risk of osteopenia and osteoporosis, which may result in fragility fractures and significant cost and morbidity. Bone density assessments are often overlooked in routine clinical practice, resulting in missed opportunities for early interventions and prevention of disease progression. In the first phase of this multi-phase quality improvement project, a “Bone Health” prompt was added to the RA note template to remind physicians to document bone health status, Fracture Risk Assessment Tool scores, and management. Initial documentation rate of bone health (ie, osteoporosis, osteopenia, normal bone density) was 65%. We found that post-intervention documentation rates improved among residents (70%) and rheumatology fellows (82%). It was unclear whether these changes could be sustained and, importantly, if the intervention would improve the quality of bone health management for RA patients. The aim of this second phase of the project is to evaluate the sustainability of bone health documentation and the impact on clinical management in Veterans with RA in an academic clinic.

Methods: Pre-intervention documentation rates of bone health and appropriate management (defined as evaluation with DEXA or use of pharmacotherapy) were measured by reviewing 50 residents’ (internal medicine, PM&R) and 50

rheumatology fellows' notes from August-October of 2017. The "Bone Health" prompt (intervention) in the note template was implemented in December of 2017. We reviewed 50 resident and 50 fellow notes from January-March of 2019 to evaluate the sustainability of bone health documentation and the rate of appropriate management 12 months after intervention implementation.

Results: One year after the original template intervention was introduced, the post-intervention documentation rate of bone health was sustained in both residents' (88%) and fellows' (82%) notes. For bone health management, in the pre-intervention group, documentation was higher among residents (70%) than fellows (62%). Twelve months after the intervention, rates of documentation of appropriate management dropped among residents (68%) but improved among fellows (74%). Among the Veterans, three had significant medical comorbidities requiring emergency care or discontinuation of therapy, therefore, documenting bone health was less of a priority during these encounters. A subgroup analysis including only Veterans with reduced bone density demonstrated documentation of appropriate management of 84% and 73% in the resident and fellow notes, respectively.

Conclusion: Adding a "Bone Health" prompt demonstrated sustained improvement of assessment over 12 months. As compared to the pre-intervention data, documentation of management of bone disease improved in the fellow group but dropped in the resident group (possibly because they rotate more frequently); however, if Veterans with normal bone density were excluded, documentation of appropriate management improved in both groups. Future projects can evaluate if prompting trainees to document bone health results in fewer fragility fractures.

Disclosure: M. DeFoe, None; **R. Nayfe**, None; **U. Makris**, None; **R. Arora**, None; **S. Reddy**, None.

Abstract Number: 0312

Timely Glucocorticoid Tapering in Vasculitis: A Need for Improved Knowledge Translation to Limit Toxicity

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating
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Background/Purpose: High dose glucocorticoids (GC) are part of the initial treatment of ANCA-associated (AAV) and large vessel vasculitides (LVV). Prompt subsequent tapering limits toxicity. Adherence to tapering recommendations has not been studied. Among patients referred to a tertiary vasculitis clinic for either AAV or LVV, we aimed to determine the frequency of adherence to GC tapering recommendations, barriers to appropriate GC tapering, and possible improvement strategies.

Methods: Consenting new patients assessed July 2017-March 2019 for AAV (including GPA, EGPA, MPA) and LVV (GCA, Takayasu arteritis) were included. Referral specialty, diagnosis, wait time, GC dose and duration were recorded. Patients taking >10 mg prednisone above their target dose based on tapering recommendations were classified as taking 'excessive' GC. Physicians who referred 2 patients in the last year (n=31) were invited to complete a survey to identify barriers to GC tapering and potential solutions.

Results: Of 231 patients referred for AAV/LVV during the study period, 128 (55%) were taking GC at their first visit. Mean prednisone start dose was 53.5 mg (SD 14) and 33/111 (30%) received pulse GC. At the first visit (mean wait time 63 days, SD 31), mean GC dose was 30 mg (SD 18). 35 (27%) patients were taking excessive GC (17 AAV, 18 LVV), 11 of whom had not started tapering entirely. There were no significant differences in referral specialty, diagnosis, or wait times among patients taking 'excessive' vs 'appropriate' doses. Initial GC 'pulses' had been given to 14/31 (45%) of the 'excessive' group patients vs 19/80 (24%) in the 'appropriate' group (NS). 73% of survey respondents (n=14, 93% rheumatologists) felt "very comfortable" tapering GC in GCA, but only 43% and 21% in AAV or Takayasu arteritis, respectively. Challenges with tapering were managing the risk of disease flare (79%) and differentiating active disease from damage (64%). Most (93%) felt that providing GC tapering suggestions at the time of referral would improve timely tapering, and 64% felt reducing wait times would help.

Conclusion: Nearly one third of patients referred for LVV or AAV were taking excessive GC doses at their first visit. There may be a referral bias to our clinic, and excessive GC use may reflect more challenging cases. Providing a GC tapering "action plan" at the time of referral may help to promote timely GC tapering.

Disclosure: A. Mendel, None; **D. Ennis**, None; **S. Lake**, None; **S. Carette**, None; **C. Pagnoux**, ChemoCentryx, 5, Chemocentryx, 5, Genetech/Roche, 5, Genzyme/Sanofi, 5, GlaxoSmithKline, 5, Hoffman-La Roche, 2, 5, 8, Hoffman-LaRoche, 2, 5, 8, Sanofi, 5.

Abstract Number: 0313

Screening and Treating Hyperlipidemia in Patient's on Tofacitinib, Tocilizumab, Sarilumab, and Baricitinib

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Background/Purpose: Tofacitinib and baricitinib (JAK inhibitors) are agents used for rheumatoid arthritis (RA), seronegative spondyloarthropathy (SpA), and juvenile idiopathic arthritis (JIA). Tocilizumab and sarilumab are biologics (IL6 inhibitors) for the management of inflammatory arthritis, and giant cell arteritis. Aforementioned drugs elevate total cholesterol and LDL levels. Primary aim is to assess compliance for screening and treatment per guidelines of the American College of Rheumatology (ACR) (ARP Practice Committee, 2017) for hyperlipidemia in patients receiving tofacitinib, tocilizumab, sarilumab, and baricitinib at Lehigh Valley Health Network (LVHN).

Methods: Data reviewed on 146 patients within LVHN, from December 2018 to April 2018. Subjects were retrieved from Epic by searching for orders for the drugs of interest. Manual Chart Review was utilized to determine: age, gender, ethnicity, pathology, medication, steroid dose, additional DMARDs, medication duration, date of drug initiation, previous statin, baseline lipid panel, frequency of lipid screenings, and statin initiated.

Results: Table 1 shows demographic and clinical variables of the charts reviewed. Medications used were the following: tofacitinib (64%), tocilizumab (27%), sarilumab (8%), and baricitinib (0.68%). Patients examined were afflicted with the following disease processes: RA (90%), GCA (4%), SpA (4%), and JIA (2%). Prior to the intervention 29% of patients were on a statin, and 28% had indications for a statin yet were not prescribed one. Additionally, only 17%

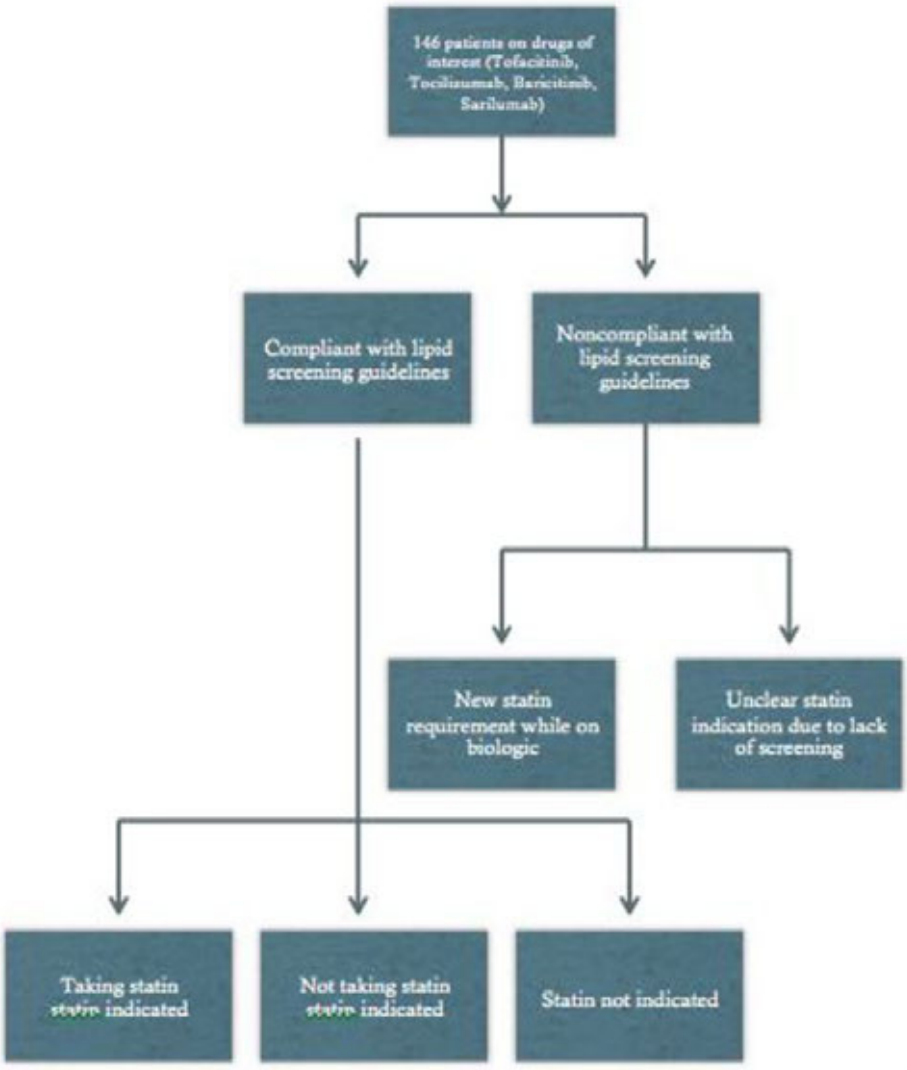

Figure 1.

of patients had a proper baseline lipid screening 4-8 weeks after starting the drug. Only 13% of patient had lipid screenings every 6 months after institution of the drug. Mean age was 56 years old, with 77% female, and average duration on drug of interest was 760.5 days.

Conclusion: According to ACR guidelines, laboratory monitoring for patients on JAK and IL6 inhibition is recommended due to treatment related changes in neutrophils, platelets, lipids, and liver specific enzymes (ARP Practice Committee, 2017). Additionally, British Society for Rheumatology (BSR) advocates for baseline lipid screenings, and rescreening every 3 months (Malaviya, 2014). After analyzing patients in LVHN there is room for improvement. Twenty eight percent of patients in the project have an indication for statin therapy, and are not being treated. Eighty two percent of patients lacked baseline lipid screening 4-8 weeks after starting JAK and IL6 inhibition. An intervention educating rheumatology providers on guidelines for these medications, and options for managing subjects with lipid lowering agents will follow initial data assessment. Data will be re-collected and assessed for improvement in guideline compliance and treatment following the intervention. After the intervention we expect to see increased compliance with lipid screening and management with patients on the drugs of interest within LVHN.

Table 1.

Table 1.		
Demographics	**Drugs**	**Disease Process**
Average Age: 55.8 years	Tocilizumab 27.39% (40)	RA 89.72% (131)
Gender: Female 77.40% (113)	Sarilumab 8.21% (12)	GCA 4.10% (6)
Average days on drug: 760.5 days	Baricitinib 0.684% (1)	SpA 4.10%(6)
Race	Tofacitinib 63.69% (93)	JIA 2.05%(3)
Causasion: 78.76% (115)	Chronic Steroids 26.71%	**Statin Statistics**
African American 6.84% (10)	Other DMARD 36.31%	On Statin (start of study) 28.96%
Multi-racial 6.84% (10)	MTX 24.65% (36)	Statin indicated: 28.08%
Hispanic 1.36% (2)	HCQ 5.47% (8)	Statin not indicated: 35.61%
Asian 0.685% (1)	LEF 4.10% (6)	Baseline lipid panel checked 17.21%
Other 5.47% (8)	SZS 0.684 (1)	Lipid Screening per guidelines 13.10%

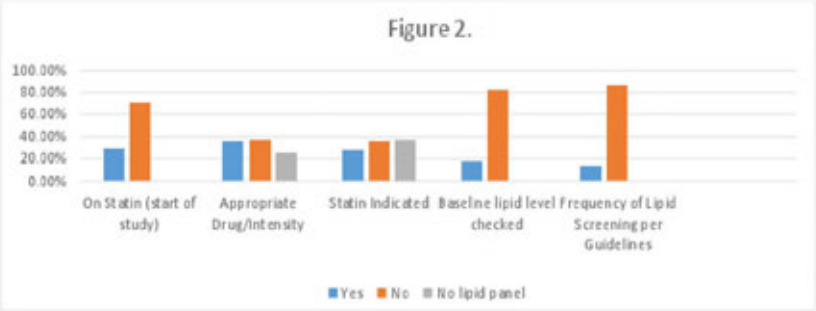

Figure 2.

Disclosure: W. Torelli, None; **J. Ross**, None; **T. Quinn**, None; **K. Erickson**, None; **A. Soliman**, None; **A. Harit**, None.

Abstract Number: 0314

Pre-treatment Screening for Hepatitis B and C Among Users of Biologics or New Synthetic Disease Modifying Drugs: An Analysis Using RISE Data

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating
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Session Time: 9:00AM–11:00AM

Background/Purpose: Testing for hepatitis B virus (HBV) and hepatitis C virus (HCV) is recommended for patients initiating biologics or new synthetic DMARDs, which can increase the risk of viral hepatitis reactivation. We examined pre-treatment screening for HBV and HCV among practices participating in ACR's RISE registry for patients who were new users of biologics or new synthetic DMARDs.

Methods: Data derived from Rheumatology Informatics System for Effectiveness (RISE), a national EHR-enabled rheumatology registry that passively collects data on all patients seen by participating practices. As of 2017, RISE held validated data from 1,257 providers in 236 practices, representing an estimated 36% of the U.S. clinical rheumatology workforce. Patients included in this study were ≥ 18 years old and had ≥ 1 prescription for a biologic or

Table. Proportion of documented pretreatment screening for HBV and HCV, N (%)

Total N=23,597	HBV*	HCV†	Composite measure (HBV and HCV testing)
No test	18,226 (77.2%)	20,203 (85.6%)	17,732 (75.1%)
Complete testing	1,428 (6.1%)	3,394 (14.4%)	1,373 (3.7%)
Partial testing	3,943 (16.7%)	-	4,992 (21.2%)

* HBV (Hepatitis B virus): Complete testing was defined as documentation of a HBV surface antigen AND HBV core antibody. If an HBV viral load was documented, this counted as an HBV surface antigen. Partial testing included at least one of these tests.
†HCV (Hepatitis C virus): Complete testing was defined as documentation of an HCV antibody or HCV viral load.

new synthetic DMARD between Jan 1 and Dec 31, 2017; the "index date" was defined as the first prescription date. New medication users were identified if they had ≥ 2 visits in the 12 months prior to their index date without any biologic or new small synthetic DMARD use. HBV screening was defined as "complete" if HBV surface antigen AND HBV core antibody were documented or "partial" if only one test was documented; HBV viral load satisfied the HBV surface antigen requirement. HCV screening was defined as having a documented HCV antibody or viral load test. We assessed screening across several windows (before the index date; allowing for a 60-day grace period after the index date; or allowing up to a 1-year grace period after the index date). We assessed practice-level performance for practices reporting on ≥ 20 patients.

Results: 23,597 patients were included from 196 practices. 71.9% were female, mean age of 57.3±14.4 years. 37% were non-white, including 6.9% Hispanic. The most common class of medication was TNFi (62.9%). Overall, only 22.8% patients had any documented HBV screening and 14.4% had any documented HCV screening (Table). Among those with complete testing, most screening was completed prior to the index date (82.6%); 96.9% completed screening by 60 days after the index date. Patterns were similar for HCV screening. Among 168 practices in the practice-level analysis, median performance was 0% (range 0-62.7%) for HBV, 0% (range 0-80.4%) for HCV screening, and 0% (range 0-62.7%) for the composite (HBV and HCV) screening measure.

Conclusion: Only a small proportion of RISE patients who were new users of biologics or new synthetic DMARDs had documented screening for HBV or HCV. It is likely that some patients were tested outside the rheumatology practice and also possible that results are documented in clinical notes or scanned documents, which are not currently accessible for use in electronic clinical quality measures. In order to meet criteria for measures that assess performance of pre-treatment HBV and HCV screening, practices will need to adjust workflows to ensure these patient safety measures are captured consistently in structured fields within the electronic health record.

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

Disclosure: J. Li, None; **J. Kay**, None; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2; **G. Schmajuk**, None.

Abstract Number: 0315

Improving the Rate of Tuberculosis Screening Among High Risk Rheumatoid Arthritis Patients on Biologic Agents Using a Proposed Questionnaire

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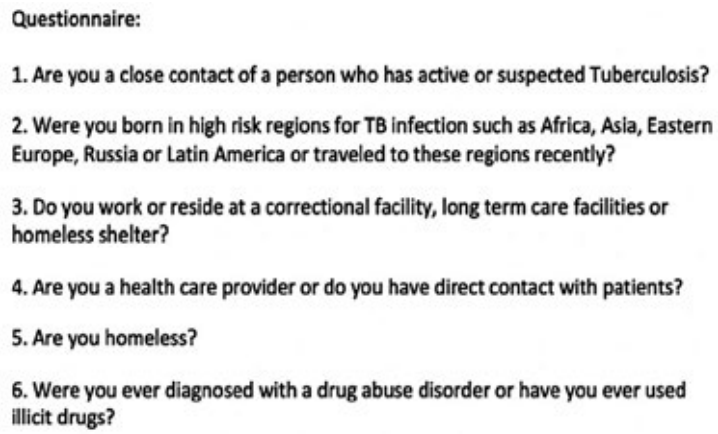
Background/Purpose: The use of biologics has transformed the treatment paradigm for RA; however, reactivation of Mycobacterium Tuberculosis is still a concern. Frequent TB screenings without consideration of risk factors can lead to potential clinical dilemmas including indeterminate Interferon-Gamma Release Assays in immunosuppressed patients. Current American College of Rheumatology guidelines recommend annual tuberculosis screening test for high risk patients while on biologics for management of RA. Our goal was to identify the high risk RA patients on biologics (tumor necrosis factor inhibitors, abatacept, IL-6 inhibitors, and tofacitinib)using a guideline based questionnaire and improving the rate of annual Tuberculosis screening among those patients.

Methods: This study was conducted in two large academic centers in Florida and Pennsylvania, which serve a diverse population across multiple clinics. A Plan-Do-Study-Act cycle model was implemented for this project. RA patients chosen for this study were on biologics for more than a year and had a negative baseline interferon-gamma release assay. Chart review was performed to obtain baseline data of how many of these patients were asked high risk questions for Tuberculosis exposure and were screened for Tuberculosis within one year of their visit. Our baseline data was based on one month worth of clinic visits. We put into effect our intervention to improve this rate by educating our Rheumatology providers and creating a questionnaire using American College of Rheumatology guidelines to identify high risk patients (please see attached), which could be easily accessed in our Electronic Medical Record. Post intervention, we gathered data over the course of two months to assess whether there was any improvement in the rate of Tuberculosis screening using the questionnaire.

Results: Our baseline data included 65 patients and postintervention included 175 patients. Analysis of our baseline data revealed that only 4.6% of the time any of the high risk questions were documented in EMR. Post Intervention, our compliance rate using the questionnaire improved to 26.3%. Using the questionnaire we noted an increase in interferon gamma release assay testing from 21 %to 23 % . Moreover, interestingly the rate Tuberculosis conversion to positivity was 0% for all patients in the project.

Conclusion: Our baseline data revealed that we were inadequately identifying high risk patients for Tuberculosis screening. Our post intervention data analysis showed an overall improvement in the rate of appropriate Tuberculosis screening. Despite the slight increase in the percentage of interferon gamma release assays checked in the intervention group, patients were appropriately rescreened based on risk factors. Further intervention such as Electronic Medical Record alerts will be implemented in the future aspects of this study to improve compliance among provid-



Tuberculosis Screening Questionairre

ers.Given the importance of Tuberculosis screening among high risk patients, we want to raise awareness about this quality measure and work towards providing the highest quality of care to our patients.

Disclosure: H. Babary, None; **S. Afroz**, None; **J. Carter**, None; **Y. Lin**, None; **M. O'Brien**, Janssen Pharmaceuticals, Janssen Pharmaceuticals, 5; **M. Maldonado**, None; **H. Bateman**, None; **G. Montes-Rivera**, None; **G. Berlin**, None; **D. Tseytlin**, None; **M. MacDonald**, None; **Y. Ayoubi**, None; **M. Nguyen**, None; **S. Setty**, None; **R. Mhaskar**, None; **J. Valeriano-Marcet**, None.

Abstract Number: 0316

Implementation of Cardiovascular Screening in Hispanic Patient Population with RA, SLE and PsA

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Evidence suggests that the tools used for cardiovascular disease (CVD) risk assessment in the general population underestimate the true risk when they are applied to patients with proatherogenic diseases such as RA, SLE and PsA. High inflammatory state increases atherogenesis and myocardial microvascular abnormalities leading to increased morbidity and mortality risks from cardiovascular (CV) causes. EULAR recommends that it is the rheumatologist who should ensure that CV disease risk assessment and management are performed regularly.[1]

Hispanic population has been underrepresented in the CV risk assessment research. We aimed to identify the RA, SLE and PSA patients' CV risk in clinic with predominantly underserved Hispanic patient population using the Atherosclerotic Cardiovascular Disease (ASCVD) calculator as recommended by the American Heart Association and American College of Cardiology. ASCVD 10-year-risk score of ≥5% is the recommended threshold for statin consideration/initiation. LDL >70 in a diabetic or LDL >190 in a nondiabetic are additional recommendations for statin treatment regardless of the ASCVD 10-year-risk score.[2]

ASCVD Score Data

#	Ethnicity	Age	Sex	Disease	Lipid Total	HDL	LDL	A1C	Diabetes	Smoker	HTN	systolic BP	ASCVD score
1	Hispanic	43	F	RA	164	47	95	5.1	no	no	no	104	0.40%
2	Hispanic	53	F	RA	136	60	65	5.7	no	no	no	109	1.10%
3	Hispanic	52	F	RA	241	67	133	5.7	no	no	yes	118	1.90%
4	Hispanic	45	F	RA	145	47	78	7.9	no	no	yes	163	1.90%
5	Hispanic	45	F	PsA	252	57	174	6.9	yes	no	no	137	4.40%
6	Hispanic	40	M	RA	274	44	120	5.9	no	no	no	137	2.80%
7	Hispanic	44	F	SLE	142	40	84	5.7	no	no	no	116	0.60%
8	Hispanic	41	F	RA	144	62	69	5	no	yes	no	102	0.40%
9	Hispanic	55	F	RA	198	63	111	5.5	no	no	no	106	1.20%
10	Hispanic	49	F	SLE	146	39	82	5.8	no	no	yes	105	1.30%
11	Hispanic	59	F	RA	253	55	131	5.8	no	no	no	128	3.60%
12	Hispanic	43	M	SLE	210	66	115	5.8	no	no	no	140	1.40%
13	Caucasian	48	M	PsA	176	49	69	5.4	no	no	no	157	1.70%
14	Hispanic	45	M	RA	138	46	76	5.6	no	yes	no	104	0.80%
15	Hispanic	53	F	RA	145	59	63	6.7	yes	no	yes	149	3%
16	Hispanic	48	M	RA	178	57	98	5.2	no	yes	no	128	2%
17	Asian	41	F	SLE	213	102	95	5.3	no	no	no	133	0.40%
18	Hispanic	40	F	RA	163	39	103	5.8	no	no	no	95	0.40%
19	Hispanic	48	M	SLE	232	91	116	5.5	no	yes	no	115	1.60%
20	Hispanic	49	F	RA	178	59	75	5.6	no	no	no	139	1%
21	Hispanic	47	F	RA	154	49	86	5.5	no	no	no	101	0.50%
22	Hispanic	58	F	RA	278	62	214	5.7	no	no	no	115	2.70%
23	Hispanic	71	F	RA	179	57	91	5.8	no	no	no	133	10.90%
24	Hispanic	40	F	SLE	117	67	39	5.1	no	no	no	122	0.20%
25	Hispanic	41	F	RA	197	78	92	4.8	no	no	no	138	0.40%
26	Hispanic	42	F	SLE	162	41	100	5.1	no	no	no	116	0.60%
27	Hispanic	50	F	RA	200	45	126	5.8	no	no	no	112	1.20%
28	Caucasian	68	M	RA	168	44	101	5.4	no	yes	No	101	8.30%
29	Hispanic	42	F	SLE	242	58	140	4.8	no	no	Yes	150	1.60%
30	Hispanic	40	F	SLE	142	62	69	5.6	no	no	No	101	0.10%
31	African American	66	F	RA	114	39	57	7.3	yes	no	Yes	116	19.30%
32	African American	67	F	RA	163	48	86	5.6	no	yes	Yes	179	6.80%
33	Hispanic	69	F	RA	153	46	82	5.8	no	yes	No	130	8.40%
34	Hispanic	44	M	PsA	147	42	82	4.9	no	yes	No	136	4.10%
35	Hispanic	55	F	SLE	189	45	148	4.8	no	yes	No	138	2.60%
36	Hispanic	42	F	SLE	157	41	63	5.2	no	no	No	104	0.50%
37	Hispanic	44	F	RA	224	45	127	6	no	no	no	117	1.10%
38	Hispanic	40	F	RA	172	40	98	5.4	no	no	no	105	0.50%
39	Hispanic	43	F	SLE	217	86	89	4.7	no	yes	no	103	0.20%
40	African American	55	F	SLE	165	64	90	5.8	no	yes	no	124	1.10%
41	Hispanic	55	F	PsA	237	73	133	5.6	no	yes	no	129	4.50%
42	Hispanic	46	F	RA	164	45	79	5.9	no	no	no	134	1%
43	African American	50	F	RA	188	80	100	5.4	no	yes	yes	162	1.50%
44	Hispanic	41	F	PsA	209	48	117	5.3	no	no	no	111	0.70%
45	Hispanic	43	F	RA	264	66	149	5.5	no	no	no	101	0.50%
46	Hispanic	52	F	RA	145	47	61	5.1	no	no	no	103	1%
47	Hispanic	45	F	SLE	205	60	84	5.3	no	no	no	117	0.60%
48	Hispanic	42	F	SLE	174	35	102	5.5	no	no	Yes	126	1.50%
49	Caucasian	61	F	RA	132	48	68	5.5	no	no	yes	166	3.40%
50	Hispanic	45	M	RA	216	42	111	5.8	no	no	no	124	4.20%
51	Hispanic	45	M	RA	204	55	130	5.4	no	yes	no	142	3.50%
52	Hispanic	47	F	SLE	138	32	88	5.6	no	no	no	101	0.70%
53	Hispanic	61	F	RA	132	48	68	5.5	no	no	yes	130	4.10%

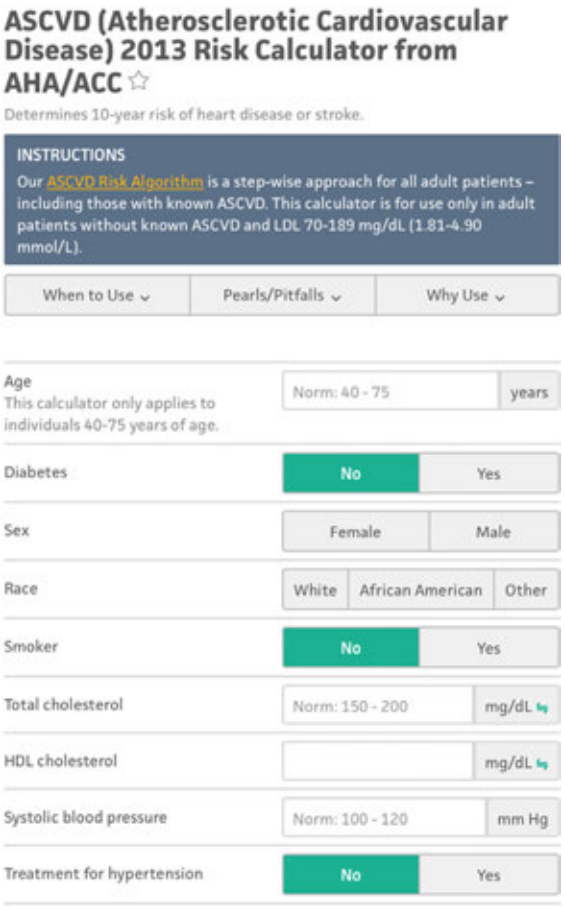
Diabetes with LDL >70
LDL >190
ASCVD score >5%

Table 1

Methods: RA, SLE and PsA patients were assessed during routine follow up visits from 1/2019 to 6/2019. Rheumatology fellows identified patients over the age of 40 who did not have an established diagnosis of CV disease and not treated with lipid lowering therapy. We calculated the ASCVD score based on patients' age, gender, ethnicity, smoking status, systolic blood pressure and antihypertensive treatment, lipid panel (total cholesterol, HDL) by using the *MDCalc Medical Calculator App*. The ASCVD score may also be obtained by going on www.mdcalc.com or tools.acc.org websites.

Results: The ASCVD score was calculated for 53 patients (32 RA, 16 SLE, 5 PsA). Out of these patients, 85% were Hispanic, 6% Caucasian, 7% African American, 2% Asian; 82% were females.We identified 7 (13%) out of 53 rheumatology patients who met the ASCVD criteria for statin initiation. Five (9%) patients had ASCVD score above >5%, 1 patient with diabetes had LDL >70 and 1 patient had LDL level >190. The patients with elevated ASCVD score were all over the age of 60 and carried the diagnosis of RA.

Conclusion: This abstract highlights the importance of CV disease screening in rheumatology clinic to identify patients with the highest risk for life-threatening CV events by calculating the ASCVD score. Thirteen percent of our 53 screened patients satisfied the criteria for statin initiation. Of interest, our study identified 7% of the Hispanic population with autoimmune diseases at risk for CV disease – a population frequently not included in cardiovascular



ASCVD 2013 Risk Calculator from AHA/ACC. Available at: https://www.mdcalc.com/ascvd-atherosclerotic-cardiovascular-disease-2013-risk-calculator-aha-acc Accessed June 4, 2019.

risk assessment studies. Although we have a small sample size, this study demonstrates the ease and feasibility of performing CV risk assessment in clinical practice.

Disclosure: L. Gandrabur, None; **W. Kim**, None; **A. Sen**, None; **D. Nes**, None; **J. Ash**, None; **A. Wasserman**, None; **K. Sperber**, None.

Abstract Number: 0317

Improving Adherence to Pregnancy Screening in Patients on Teratogenic Medications Using an Electronic Medical Record Alert System: A Quality Improvement Initiative

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating

Session Type: Poster Session (Sunday)

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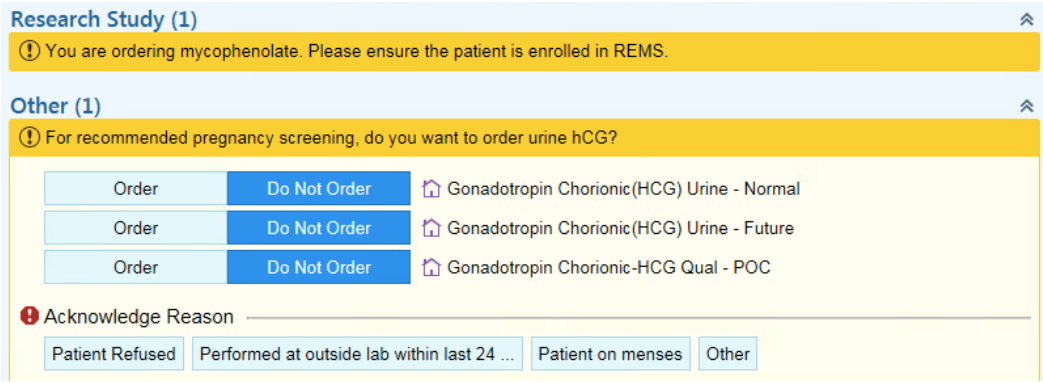

Figure 1. A BPA alert system was implemented in the pediatric rheumatology clinic setting.

Background/Purpose: Mycophenolate is widely prescribed in the rheumatology setting. However, usage of mycophenolate during the first trimester of pregnancy is associated with an increased risk of congenital malformations and miscarriages. The Risk Evaluation and Mitigation Strategy (REMS) from the Food and Drug Administration recommends pregnancy screening at routine follow-up visits. However, there is currently no standardized method of ensuring routine pregnancy screening. After a patient required pregnancy termination due to major fetal abnormalities, this quality improvement project sought to improve physician adherence in pregnancy screening for female patients on mycophenolate.

Methods: This project was conducted in the pediatric rheumatology clinic setting at a single tertiary care center. Female patients age 10 and older prescribed mycophenolate mofetil or mycophenolic acid were included in the study. Process mapping was utilized to identify potential areas of improvement. Two Plan-Do-Study-Act (PDSA) cycles were completed. The identified intervention included leveraging the electronic medical record through the development of a Best Practice Advisory (BPA) tool (Figure 1). The BPA alert was designed to prompt ordering of a urine human chorionic gonadotropin (hCG) test for female patients age 10 and older prescribed mycophenolate. The current PDSA cycle included analysis from March 2018 to March 2019, and missed opportunities for pregnancy screening were identified. A missed opportunity was defined as an encounter where mycophenolate was prescribed but a urine hCG was not ordered within 7 days.

Results: At baseline, pregnancy screening was performed at 11% (8/71) of the encounters where mycophenolate was prescribed. Implementation of the BPA alert resulted in marked improvement in routine pregnancy screening to

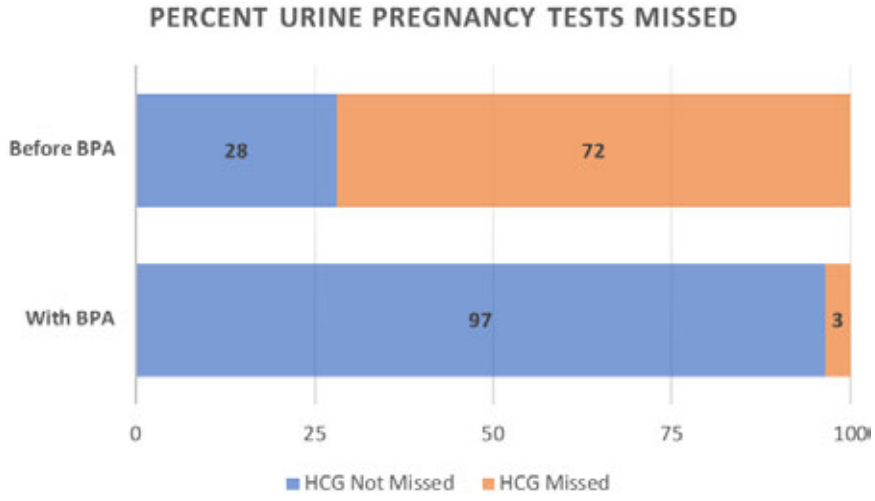

Figure 2. Significant reduction of missed opportunities for routine pregnancy screening after implementation of BPA alert.

79% (114/144, p< 0.00001). An opportunity for routine urine pregnancy screening was missed 72% (51/71) of the time at baseline. Implementation of the BPA alert resulted in reduction of the missed opportunities to 3% (5/144, p< 0.00001), shown in Figure 2. Authorization of a medication refill prior to the next visit was the most common reason for a missed opportunity. Analysis revealed that the BPA alert was not triggered if mycophenolate was prescribed outside a clinic visit.

Conclusion: Pregnancy screening in our female patients of childbearing age on a teratogenic medication is paramount. Effective utilization of an alert system embedded in the electronic medical record resulted in a striking improvement in routine urine pregnancy screening. This systems-based approach provides a sustainable infrastructure for improvement in patient care.

Disclosure: V. Do, None; **M. Nguyen**, None; **K. Akamine**, None; **J. Fuller**, None; **L. Nassi**, None; **T. Wright**, None; **K. Stewart**, None.

Abstract Number: 0318

Improving Safe Prescribing of Hydroxychloroquine in a Safety Net Hospital Rheumatology Clinic

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Hydroxychloroquine (HCQ) prescribing is standard of care for patients with SLE. The main potential side effect is retinal toxicity, especially at higher doses and with prolonged use. In 2016, the American Acad-

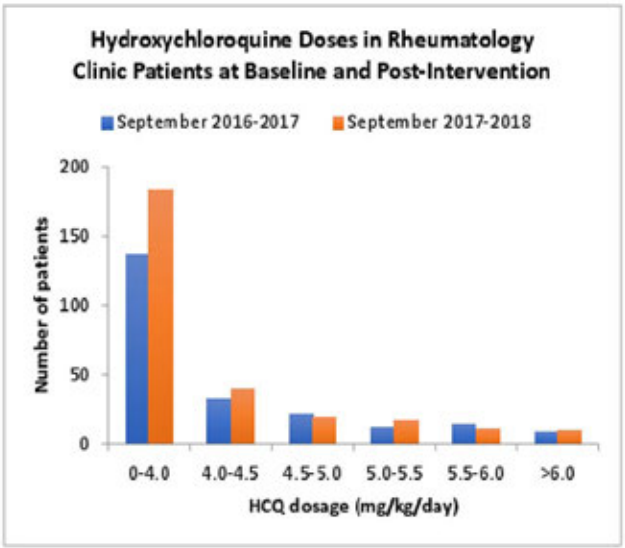

Figure 1. Distribution of hydroxychloroquine doses prescribed to rheumatology clinic patients in the periods prior to and after intervention.

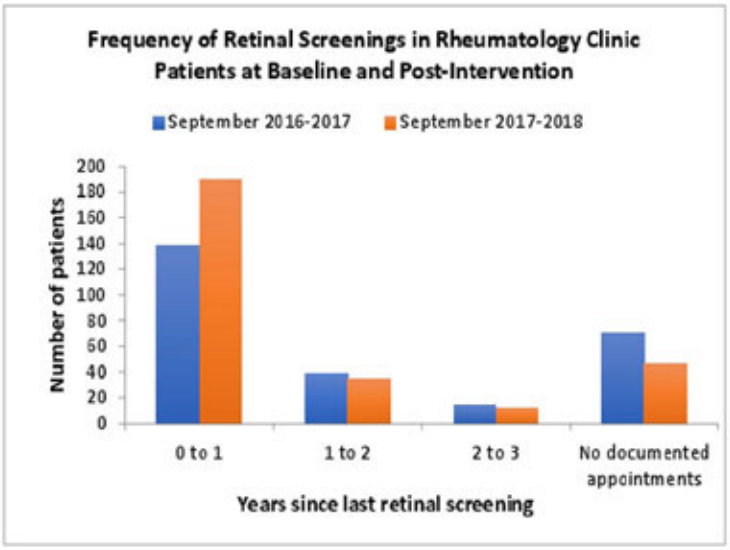

Figure 2. Frequency of retinal screenings among rheumatology clinic patients treated with hydroxychloroquine in the periods prior to and after intervention.

emy of Ophthalmology (AAO) modified its HCQ dosing and screening guidelines to recommend a maximum daily dose of 5 mg/kg of actual body weight and retinal examinations at baseline, then annually after 5 years of taking HCQ. We undertook a quality improvement project in a safety net rheumatology clinic that had two aims: 1) to increase the proportion of patients prescribed hydroxychloroquine at recommended doses from 85% at baseline to 95% and 2) to improve the proportion of patients receiving appropriate retinal screening from 52% at baseline to 80% at one year.

Methods: Using the Institute for Healthcare Improvement's Model for Improvement, we first mapped the existing clinical workflow for HCQ prescribing and monitoring. We developed and applied two process measures to track our progress: the proportion of patients prescribed hydroxychloroquine receiving a dose less than or equal to 5 mg/kg at their last encounter and the proportion of patients prescribed hydroxychloroquine at their last encounter with a retinal screening test over the last 18 months. After identifying baseline values for our two process measures, we worked with clinicians and clinic support staff over four Plan-Do-Study-Act (PDSA) cycles to develop our intervention. The final optimized workflow involved the clinic's nurse using a weekly report to identify patients who were overdue for retinal screening for an ophthalmology referral and to alert physicians whose patients were on a higher than recommended dose of HCQ. In September 2018, we queried the electronic health record again for data on our clinic's adherence rates to AAO guidelines between September 2017 to August 2018 to analyze the impact of our intervention.

Results: The percentage of clinic patients prescribed HCQ at doses less than 5.0 mg/kg daily increased from 84% to 86% during the study period, and the percentage receiving retinal screening increased from 64% to 76%. Of note, only 8 out of the 243 SLE patients on HCQ with a rheumatology office visit in 2018 did not have an ophthalmology appointment scheduled. The remainder of those that did not have retinal screening had an ophthalmology appointment scheduled, but either cancelled or did not appear to their appointments.

Conclusion: Using the Model for Improvement, we were able to develop and integrate an intervention to increase adherence to the AAO recommendations for HCQ dosing and retinal screening measures, although we fell short of our pre-specified improvement goals. Although the intervention has been moderately effective at improving patient safety practices for this drug, efforts are ongoing to further understand barriers to further improvement, including root cause analysis of individual-level and systems-level factors.

Disclosure: F. Castillo, None; **M. Dodge**, None; **J. Noh**, None; **L. Trupin**, None; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2; **S. Goglin**, None.

Abstract Number: 0319

A Pragmatic Randomized Trial to Improve Safe Dosing of Hydroxychloroquine

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Although generally well tolerated, the long-term use of hydroxychloroquine (HCQ) may lead to irreversible and potentially vision-threatening retinal toxicity. The American Academy of Ophthalmology (AAO) issued guidelines in 2011, and again in 2016 that recommended dosing HCQ based on an individual's body weight, and also outlined how and when to screen for retinal toxicity. While providers have been aware of the potential side effects of HCQ for decades, studies have shown that many patients continue to receive higher than recommended doses. We conducted a pragmatic randomized trial to assess the utility of a new e-prescribing (eRX) interface to support appropriate dosing of HCQ.

Methods: Rheumatology providers at a large university health center were randomized into either an intervention (n=12) or control (n=12) group. In the intervention group, providers were presented with an eRX interface which automatically pulled in a patient's weight from the electronic health record each time a new order for HCQ was entered. A suggested HCQ dosage was provided in accordance with the 2016 AAO recommendation, defined as ≤ 5.0 mg/kg (Figure 1). The interface rounded dosage to the nearest half tablet. The control group received no change to the standard ordering interface. Chi-squared tests were used to compare the proportion of all HCQ prescription dosages > 5.0 mg/kg prior to (May 1, 2016-April 30, 2017) and all new orders after eRX implementation (May 1, 2017-April 31, 2019). Mixed effects models were used to examine the association between group assignment and HCQ dosage > 5.0mg/kg, controlling for patient factors and clustering by provider.

Results: A total of 551 patients contributed 1,664 HCQ prescription orders. Most patients were white (62%) and female (87%), with a mean age of 43.2 (+/- 18.5). Prior to the eRX intervention, 69% of HCQ orders were within guidelines across groups. We found no significant difference between groups with respect to the proportion of prescribed dosages > 5.0mg/kg both before and after the eRX implementation (p=0.71 and p=0.45, respectively) (Table 1). After introduction of the eRX interface, the intervention group prescribed 32% of HCQ prescriptions at higher than recommended doses, similar to the control group (29%). The null association remained after controlling for patient level

Table 1. Characteristics of individuals prescribed HCQ before and after implementation of a new eRX interface

	Intervention Group	Control Group	p-value
Patient Characteristics			
Female	191 (89%)	288 (86%)	0.29
Non-white	75 (35%)	136 (40%)	0.19
Age	45.7 (± 15.2)	41.6 (± 20.3)	0.01
*Pre-Intervention (before May 1, 2017)**			
HCQ Dosage (mg/kg)	4.4 (± 1.7)	4.3 (± 1.7)	0.90
Proportion HCQ Doses > 5.0 mg/kg	32%	31%	0.71
*Post Intervention (after May 1, 2017)***			
HCQ Dosage (mg/kg)	4.5 (1.5)	4.5 (1.5)	0.78
Proportion HCQ Doses > 5.0 mg/kg	32%	29%	0.45

*New orders and reorders
**New orders only

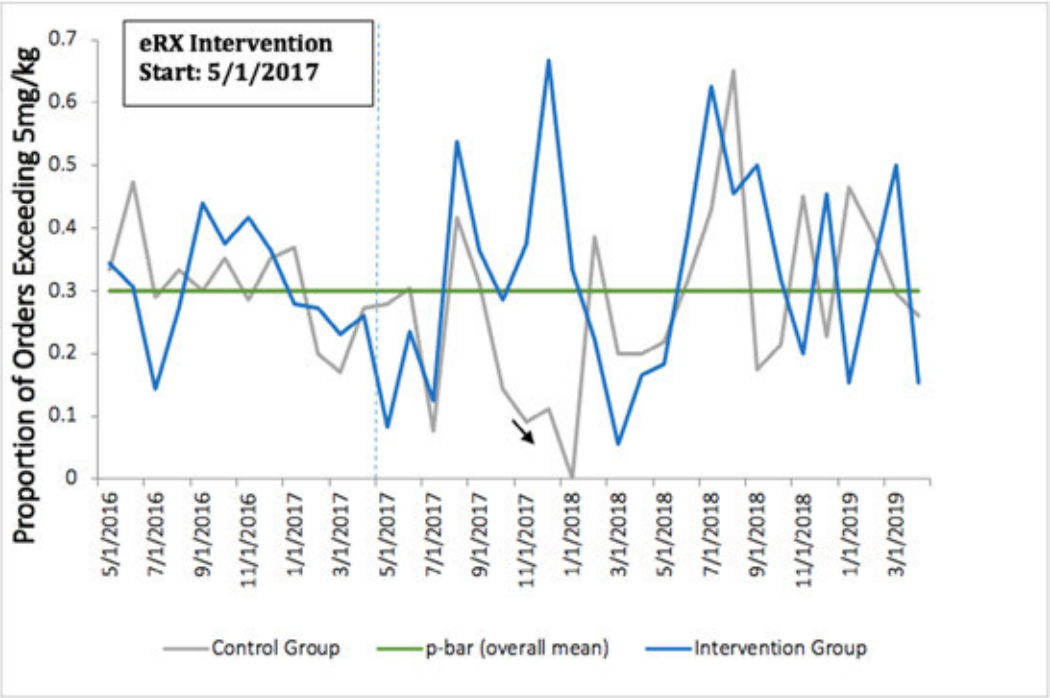

Figure 1. P-Chart demonstrating the proportion of HCQ orders exceeding 5mg/kg over the study period.

factors and clustering by provider. Our control chart also did not show any significant change in prescribing patterns over time (Figure 1).

Conclusion: This study demonstrates that the eRX interface in its current state was insufficient to significantly reduce HCQ dosing to levels recommended in current guidelines. However, the small sample size, rounding of dosage to nearest half tablet, and restriction to new HCQ orders may have limited our ability to detect differences between groups. Additional iterations of the eRX interface should address these issues. Qualitative studies could also help elucidate reasons for lack of improvement, including clinical reasons such as uncertainty about guideline cutpoints or concerns about efficacy, or implementation issues such as the design of the eRX interface and associated workflows.

Disclosure: M. Gianfrancesco, None; **S. Murray**, None; **M. Evans**, None; **G. Schmajuk**, None; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2.

Abstract Number: 0320

Hydroxychloroquine (HCQ) Prescribing Habits and Provider Opinion on Dosing Guidelines in the Rheumatology and Dermatology Practices of an Academic Institution

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

TABLE 1. HYDROXYCHLOROQUINE DOSING AND DEMOGRAPHICS

	Rheumatology				Dermatology				
	Female n (%)	*Male n (%)*	*Avg Wt (kg)*	*Sub-Total n (%)*	*Female n (%)*	*Male n (%)*	*Avg Wt (kg)*	*Sub-Total n (%)*	*Total n (%)*
≤ 5 MG/KG	626 (80)	152 (20)	86.5	778 (69)	122 (71)	50 (29)	89.3	172 (61)	950 (67)
5.1 - 6.5 MG/KG	256 (92)	21 (8)	69.2	277 (25)	65 (84)	12 (16)	67.8	77 (27)	354 (25)
≥ 6.6 MG/KG	70 (96)	3 (4)	56.3	73 (6)	33 (94)	2 (6)	54.2	35 (12)	108 (8)

Background/Purpose: Research has shown potential retinal toxicity rates from HCQ as high as 7.5%. Research suggests toxicity is dose-related. In 2016, the American Academy of Ophthalmology (AAO) issued weight-based guidelines for HCQ dosing recommending that daily dose not exceed 5 mg/kg. Two years into the guideline's release, we analyzed our institution's HCQ prescribing habits and opinions on these guidelines.

Methods: We collected cross-sectional data from all prescribers in rheumatology and dermatology, from all patients with an active hydroxychloroquine prescription in a 20-month period (June 2017 – January 2019). We collected sex and the most current weight. We grouped and compared patients according to weight-based HCQ dose. Concurrently, we constructed and administered a multiple-choice survey to gauge understanding and perceived utility of these guidelines. Survey responses were compared using Fisher's exact test with an assigned p-value < 0.05.

Results: We reviewed 1,128 rheumatology charts. 778 (69%) were prescribed ≤ 5 mg/kg. 80% were female. 277 (25%) were prescribed 5.1 - 6.5 mg/kg. 92% were female. 73 (6%) were prescribed ≥ 6.6 mg/kg. 96% were female. We reviewed 284 dermatology charts. 172 (61%) were prescribed ≤ 5 mg/kg. 71% were female. 77 (27%) were pre-

Figure 1. Hydroxychloroquine dose ≥ 6.6 mg/kg

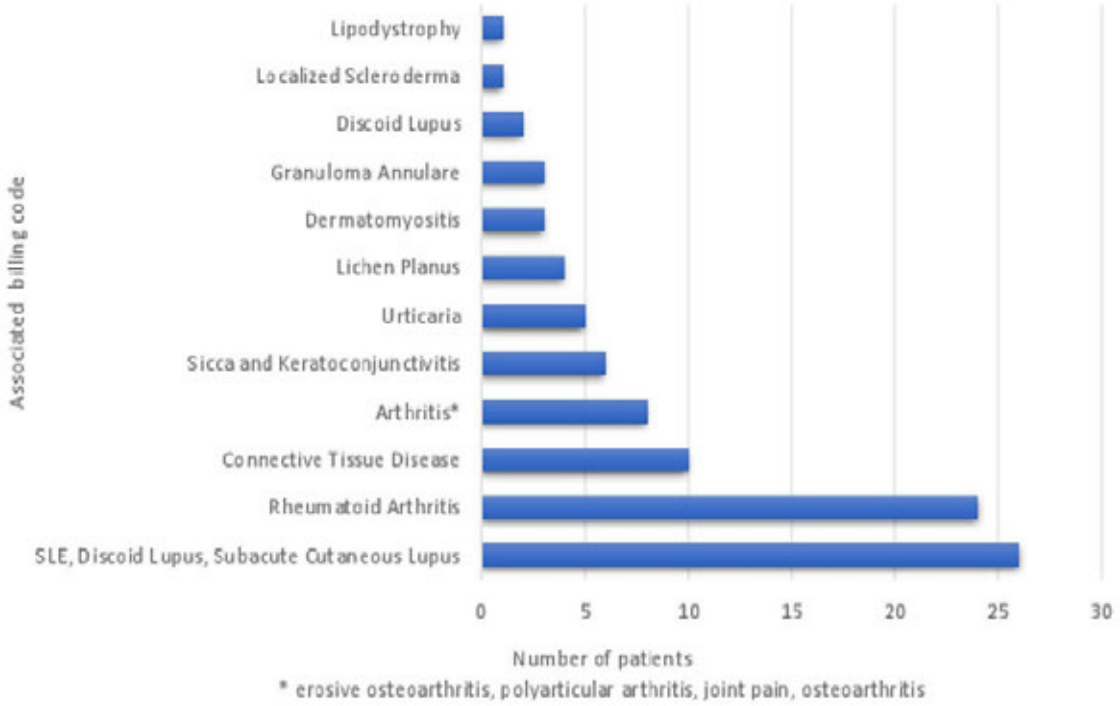
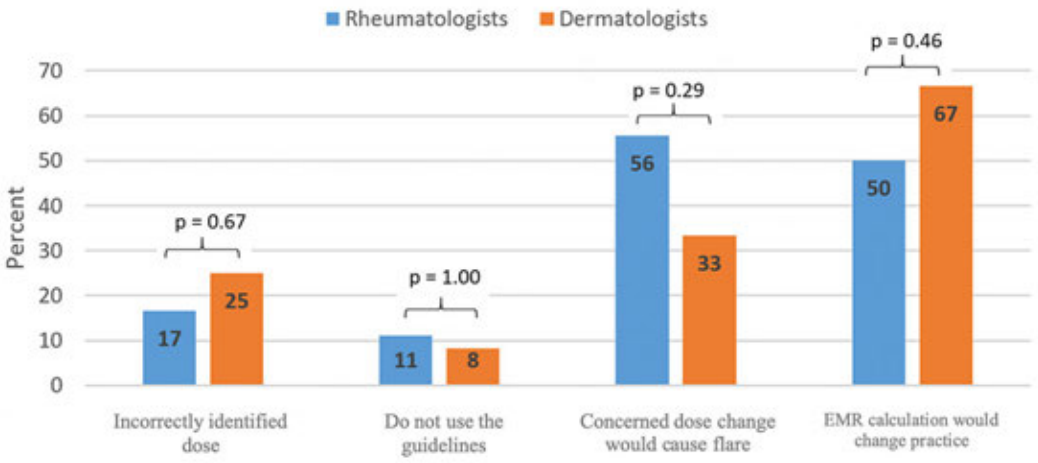


Figure 2. Survey responses



scribed 5.1 - 6.5 mg/kg. 81% were female. 35 (12%) were prescribed ≥ 6.6 mg/kg. 94% were female (Table 1). In rheumatology patients with HCQ dose ≥ 6.6 mg/kg, use was most often for rheumatoid arthritis and systemic lupus erythematosus (SLE). In dermatology patients, indications for this higher dose included SLE, lichen planus, discoid lupus, dermatomyositis, and urticaria (Figure 1). We compiled 18 surveys from rheumatology and 12 surveys from dermatology. 3 (17%)/3 (25%) incorrectly identified the recommended weight-based dose. 2 (11%)/1 (8%) said they did not use these guidelines in their practice. 10 (56%)/4 (33%) were concerned that changing HCQ dose based on these guidelines would lead to disease flares. 9 (50%)/8 (67%) reported that if their electronic medical record (EMR) automatically calculated a weight-based dose that this would change their practice (Figure 2). There were no statistically significant differences in the survey responses between the subspecialties.

Conclusion: Despite prescribers' declared familiarity with the 2016 recommendations regarding weight-based dosing of HCQ, and the belief that they are using these guidelines, HCQ doses often exceeded the recommended daily dose (33%). Survey data suggests that this discordance may be due to concern for causing disease flares. This could also suggest a gap between intended practice and actual practice that could be attributed to guideline misunderstanding or lack of knowledge of these guidelines. Findings are similar in rheumatology and dermatology settings. Smaller patients, and presumably therefore women, are more often prescribed a higher and potentially toxic weight-based dose. Further research should be a combined effort of rheumatology, dermatology and ophthalmology to explore tools, including EMR interventions, for bridging this gap between perceived guideline use and "real-world" implementation.

Disclosure: R. Overbury, None; **J. Pupaibool**, None; **C. Hansen**, None; **D. Clegg**, None; **D. Lebiedz-Odrobina**, None.

Abstract Number: 0321

Adherence to Weight-Based Dosing Guidelines in Patients Receiving Hydroxychloroquine for Rheumatoid Arthritis and Systemic Lupus Erythematosus

Tara Skorupa ,[1] and Robert Shmerling[1], [1]Beth Israel Deaconess Medical Center / Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
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Background/Purpose: Hydroxychloroquine (HCQ) is a commonly prescribed medication for systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and other rheumatic diseases. However, HCQ may cause retinal toxicity leading to permanent vision loss. The risk of HCQ-related retinopathy correlates with both daily dose and duration of use[1]. In addition to screening ophthalmologic examinations, the most recent guidelines by the American Academy of Ophthalmology recommend limiting the dose of HCQ to 5mg/kg/day of actual body weight[1]. The goal of this study was to determine the proportion of patients in our practice receiving HCQ in compliance with these recommendations.

Methods: We performed a single-center retrospective analysis of 1066 adult patients receiving HCQ for SLE or RA in our rheumatology practice at Beth Israel Deaconess Medical Center between January 1, 2018 and December 1, 2018. To account for "loading dose" adjustments just after beginning the medication, we included only patients who had two rheumatology provider interactions separated by at least 6 months. For patients who stopped taking the drug, the reason for discontinuation was noted but these patients, patients who were lost to follow up, and those who died during the period of study were excluded from the dosing analysis. For each provider interaction, we collected the patient's HCQ dose and weight. We used this data to calculate the daily weight-based dose at each time point.

Results: 830 patients met inclusion criteria: of these, 181 (22%) had weight-based doses above the current recommended dose of 5mg/kg/day. 35 (4%) patients had doses above 6.5mg/kg/day (a cut-off suggested by older guidelines). Of the 81 patients who discontinued HCQ during the period of study, the most commonly cited reasons for discontinuation were medication ineffectiveness (27%), de-escalation of therapy (19%), gastrointestinal side effects (14%), and retinal changes (6%).

Conclusion: At least 2 years after the publication of updated HCQ dosing guidelines, 22% of our patients were taking a dose that was higher than recommended by current guidelines. Further analysis is underway to understand the reason(s) for these finding and to provide feedback that may lead to higher compliance. In addition, we hope to study the impact of these new guidelines on retinal toxicity and the effectiveness of HCQ within our practice.

Disclosure: T. Skorupa, None; **R. Shmerling**, None.

Abstract Number: 0322

Hydroxychloroquine Retinal Screening and Dosing in an Unique Rheumatologic Patient Population

Leanna Wise ,[1] Stavros Savvas,[2] and Elizabeth Ortiz[2], [1]LAC+USC/Keck Medicine of USC, Los Angeles, CA, [2]LAC+USC/Keck Medicine of USC, Los Angeles

SESSION INFORMATION
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Background/Purpose: Hydroxychloroquine (HCQ) is used in many rheumatologic diseases. The American Academy of Ophthalmology (AAO) put forth guidelines in 2012 regarding retinal screening and dosing in regards to HCQ. These include a retinal exam in the first year after initiation of HCQ and a maximum dose of 5mg/kg/day of actual body weight. The Los Angeles County + University of Southern California Medical Center (LAC+USC MC) serves a largely underinsured urban population and is associated with an academic institution. LAC+USC MC utilizes an online third-party system for ophthalmology referrals. Our aim is to evaluate the LAC+USC MC rheumatology clinic's effectiveness at pursuing ophthalmologic care for HCQ patients and adhering to the appropriate dosing recommendations put forward by the AAO.

Methods: This is a retrospective chart review of rheumatology clinic patients prescribed HCQ in the LAC+USC MC rheumatology clinic. Charts of patients with clinic visits between March 2018 and May 2018 were reviewed. Patients were included if they had a clear first-time HCQ initiation date. Gender, age, ethnicity, diagnosis, prescribed dose and recommended weight-based dose of HCQ, and date of ophthalmology referral and exam were noted. Fisher's exact test was used for statistical analysis to see if there was any difference in screening or dosing between different groups of patients.

Results: One hundred and thirty-eight patients qualified for analysis. They were predominantly female (121; 87.7%). Average age was 45.7 (range 18 – 88). Forty-two (30.4%) had lupus, 55 (39.9%) had rheumatoid arthritis, and 41 (29.7) had . Of the 138 patients, 30 (21.7%) received ophthalmologic assessment within the first year of HCQ use. Of the remaining patients who were not screened, 97 patients (89.8%) lacked a timely referral to ophthalmology. Thirty-nine (28.3%) patients were prescribed a HCQ dose higher than the AAO guidelines; the average amount in excess of the recommended dose was 24.3% (range 1-122%). The rheumatoid arthritis patients tended towards lower rates of screening; however, this was not statistically significant.

Conclusion: To our knowledge, this is the first review that has evaluated compliance to AAO recommendations for HCQ retinal screening and dosing in an underserved population at an academic institution. Our findings are congruent with the literature, which demonstrate that providers are not meeting the guidelines for ophthalmologic screening when prescribing HCQ. Additionally, a large proportion of our patients are prescribed more than the recommended HCQ dose. It is important to note that a lowest effective dose of HCQ has not been established for the various rheumatologic conditions for which it is used, and at times, there may be a need for a higher than recommended dose for any particular patient. We hope to use this data to better pinpoint barriers rheumatologists face when following the AAO guidelines. Given our results, possible difficulties include a cumbersome referral system, a lack of knowledge about the guidelines, or difficulty with individualized dosing. Educating providers on AAO guidelines and working with third party referral systems to ensure ease of referrals could help providers meet recommendations.

Disclosure: L. Wise, None; **S. Savvas**, None; **E. Ortiz**, None.

Abstract Number: 0323

Compliance with Hydroxychloroquine Dosage According to 2016 American Academy of Ophthalmology (AAO) Guidelines: A Study with 6591 Patients

Thein Swe ,[1] and Andras Perl[1], [1]SUNY Upstate Medical University, Syracuse, NY

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating

Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) induced retinal toxicity remains a major concern because it can lead to irreversible damage to retinal pigment epithelium and blindness. American Academy of Ophthalmology (AAO) 2016 guidelines recommend to use HCQ at dosages ≤5 mg/kg real body weight to minimize toxicity [1]. Important risk factors for retinal toxicity are daily and cumulative dosage of HCQ, duration of treatment, patient age and concomitant renal or liver diseases [1].

Methods: This is a quality improvement project, a retrospective electronic medical records (EMR) review of patients who have been treated with HCQ since April 2016 through February 2019 at the State University of New York Upstate Medical University. Primary outcome was to identify patients whose dose exceeded the recommended dosage (≤5 mg/kg real body weight) according to 2016 AAO guidelines. Data on cumulative dosages, real body weight, height, age, adherence to the screening ophthalmologic exams within the last 5 years and concomitant renal or liver disease were extracted from EMR. Importantly, we also identified the details of number of patients who were discontinued HCQ use due to retinal toxicity.

Results: A total of 6591 patients on HCQ were identified. The average age was 50 years. Most common indications for HCQ usage were 33% for systemic lupus erythematous, 32% for undifferentiated connective tissue disease, 15.5% for rheumatoid arthritis. 2036/6591 (30.8%) patients were receiving more than 5 mg/kg/day of HCQ. 827/6591 (12.5%) patients had eye exams. Eight patients (0.96%) were diagnosed with HCQ induced retinal toxicity by ophthalmologists (Table 1) and discontinued HCQ. Among eight patients with retinal toxicity, 6 patients were taking > 5 mg/kg/day real body weight of HCQ. Their cumulative dosage ranged from 511 grams to 1,168 grams. Two patients have comorbid chronic kidney disease and two other patients have deranged liver function tests. Their duration of HCQ therapy ranged from 3 years to 8 years. The more than 5 mg/kg/day dosages were associated with increased retinal toxicity {chi-square = 5.378; p=0.02} (Table 2).

Patient	Age (in years)	Daily Dosage	Duration of use	Total Cumulative dose (grams)	Height (feet. inches.)	Weight	Daily mg/kg dosage	Overdose (>5 mg/kg/d real body weight of HCQ) Yes or No	Liver or Renal comorbidities (Present or Absent)
Patient 1	62	400 mg	5 years	730	5 ft	61 kg	6.55	Yes	Absent
Patient 2	32	400 mg	7 years	1,022	5ft 5in	62 kg	6.45	Yes	Absent
Patient 3	73	400 mg	5.5 years	803	5ft 2in	56 kg	7.14	Yes	Present (Deranged liver function tests)
Patient 4	36	400 mg	3.5 years	511	5ft 2 in	60 kg	6.66	Yes	Absent
Patient 5	41	700 mg	3 years	766	5ft 5in	103 kg	6.79	Yes	Absent
Patient 6	68	400 mg	7 years	1,022	5ft	46 kg	8.69	Yes	Present (Chronic kidney disease)
Patient 7	47	400 mg	6.1 years	890	5ft 3in	91 kg	4.39	No	Present (Chronic kidney disease)
Patient 8	62	400 mg	8 years	1,168	4ft 10in	89 kg	4.49	No	Present (Deranged liver function tests)

Table 1. Details of 8 patients who had HCQ induced retinal toxicity.

Table Analyzed	Data 1		
Chi-square			
Chi-square, df	5.378, 1		
P value	0.0204		
One- or two-sided	Two-sided		
Statistically significant? (alpha<0.05)	Yes		
Data analyzed	Number of patients who are taking ≤5 mg/kg of HCQ	Number of patients who are taking >5mg/kg of HCQ	Total
Retinal toxicity +	2	6	8
Retinal toxicity -	4553	2030	6583
Total	4555	2036	6591

Table 2. Chi- Square analysis of HCQ dosage and retinal toxicity

Conclusion: 69.2 % of patients were correctly administered HCQ with dosages based on the 2016 AAO guidelines. Retinal toxicity from HCQ is a rare phenomenon (0.96%) and apparently related to more than 5mg/kg/day of real body weight dosing. It is imperative to adjust the HCQ dosage according to body weight.

References: 1. Marmor MF, Kellner U, Lai TY, et al.; American Academy of Ophthalmology. Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision). Ophthalmology. 2016 Jun; 123(6):1386-94. https://doi.org/10.1016/j.ophtha.2016.01.058. PMID: 26992838

Disclosure: T. Swe, None; **A. Perl**, None.

Abstract Number: 0324

Adherence to Guideline Directed Management of Gout Among VA Providers

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is the most common inflammatory arthritis, affecting about 4% of the adult population in the United States. Management is often costly, with estimates around one billion dollars in yearly spending. The American College of Rheumatology recommends serum uric acid level (sUA) less than 6 mg/dL for the appropriate management of gout and prevention of recurrences. Despite the gout-related burden on the general patient population and its impact on the health-care system, guideline-directed management of patients with gout remains inconsistent among general practitioners. The degree to which general practitioners at the Miami VA adhere to guideline-directed management of veterans with gout is unknown – understanding discrepancies in care of veterans with gout

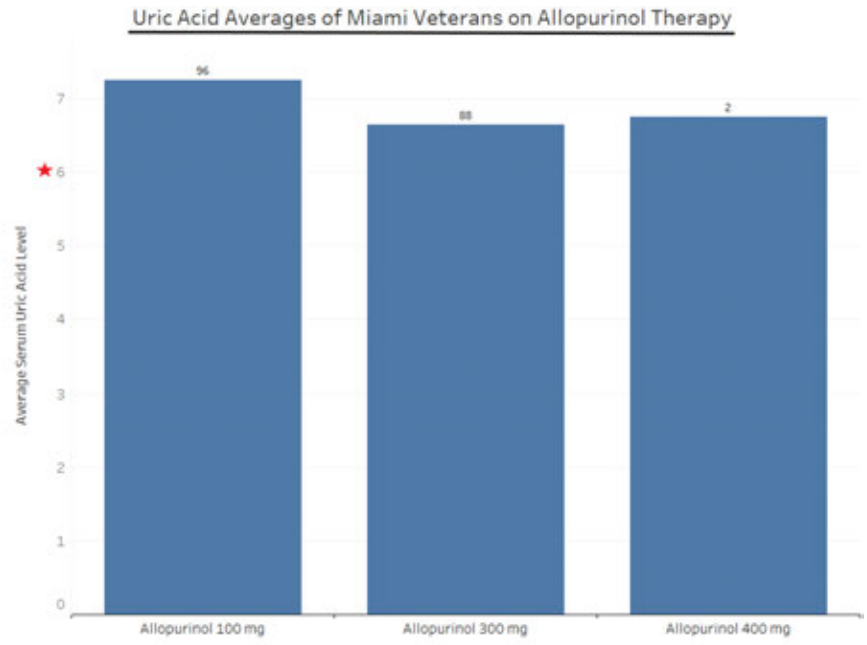

Figure 1. Average Uric Acid levels for varying Allopurinol tablet dosages

can allow us to formulate and implement quality improvement projects to address these deficiencies and standardize care.

Methods: Retrospective chart review of veterans seen at the Miami VA primary care outpatient clinics was performed by searching ICD-9 and ICD-10 codes (274 and M10, respectively) between the years of 2017 to 2018. Patients not seen by a general practitioner within the last year were excluded. The dose of uric acid lowering drugs, as well the value and date of the last serum uric acid level were recorded. Descriptive analysis of these data points was conducted.

Results: We identified 398 veterans with an ICD-9 or 10 diagnosis of gout managed by primary care providers, out of which 186 veterans were prescribed allopurinol. Of the 186 veterans prescribed allopurinol, 96 veterans were on 100 mg daily dosing, 88 veterans on 300 mg daily dosing, and 2 veterans on 400 mg daily dosing. The average sUA of veterans on the 100 mg dosing was 7.24 mg/dL, the average sUA level on the 300 mg dosing was 6.64 mg/dL, and the average sUA on the 400 mg dosing was 6.75 mg/dL.

Among the 398 veterans with a diagnosis of gout, 171 of them had sUA checked in the past year, with an average sUA value of 6.94 mg/dL, irrespective if they were on allopurinol therapy. Of the 186 patients on allopurinol, 36% (67 patients) had no sUA level obtained over a one-year span to assess uric acid lowering response.

Conclusion: Our results reveal that adherence to guideline-directed management of veterans with gout is lacking. We found that a large number of veterans with gout did not have a follow-up sUA level over a one-year span, while

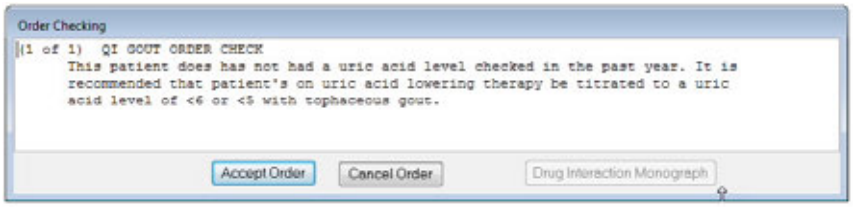

Image 1. Order check prompting primary care provider to order uric acid level

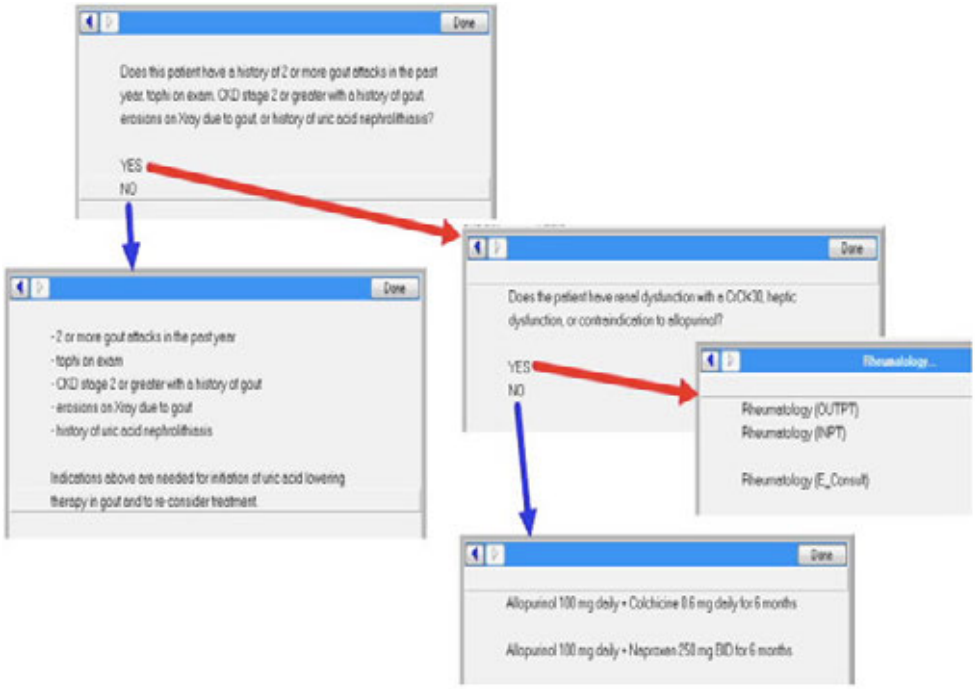

Figure 2. Order set for initiating uric acid lowering therapy for primary care providers

among veterans whose sUA levels were recorded, the average sUA level failed to meet the guideline-accepted sUA level of less than 6 mg/dL, irrespective of allopurinol dosage. In an effort to improve standardization of care for the management of gout among our patients, several quality improvement measures were developed. First, an electronic alert in the VA electronic medical record was created to prompt primary care providers to order a repeat sUA when attempting to place a refill for urate lowering medications if this was not ordered within the year. The goal for sUA level is also displayed via the alert system. An order set has also been developed to assist providers in initiating uric acid lowering agents that includes sUA checks at appropriate intervals. We hope that implementation of these quality improvement measures will lead to improved management of veterans with gout.

Disclosure: K. Corbitt, None; **I. Lopez**, None; **D. Dillon**, None.

Abstract Number: 0325

Frailty and Sarcopenia in Inflammatory Rheumatic Disease

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcopenia, the loss of skeletal muscle mass, is associated with adverse individual physical and metabolic changes contributing to morbidity and mortality. Sarcopenia is a core component of physical frailty that together impact negatively on an individual's capability to live independently.

Sarcopenia and frailty are important problems among elderly individuals.

Although relationships between sarcopenia and various chronic inflammatory diseases have been shown, the role in rheumatologic disease is currently unknown. The aim of this study was to assess the prevalence of sarcopenia and frailty syndrome in patients with Rheumatoid arthritis (RA) and spondyloarthritis SpA).

Methods: Cross-sectional, observational and descriptive study in patients with RA and SpA (ACR and ASAS criteria) older than 50 years.

-Sarcopenia was defined as per the European Working Group on Sarcopenia in Older People definition as Skeletal muscle mass index (SMI) $\leq$ 8.87 kg/m^2 in men and $\leq$ 6.42 kg/m^2 in women. Body composition analysis was performed using bioelectrical impedance analysis (BIA): fat mass, fat-free mass and predicted skeletal muscle mass were collected. Skeletal muscle mass index (SMI) was calculated by appendicular skeletal muscle mass (sum of predicted muscle mass in all 4 limbs) divided by height squared.

- Fragility was measured according to the 5 criteria proposed by Fried, using the Frail scale, and it was considered fragile to the patient who met at least 3 and prefragiles to those who met at least 2.We applied the Frail Scale and registered data (demographic and diseased related data) using a cross-sectional, observational, and descriptive study design.

Frail scale: Based on five items, reflecting performance, selfreports and common co-morbidities (*Morley JE et al., J Nutr Health Aging. 2012;16(7):601-8*).

Did you feel worn out? or Did you feel tired?

Ability to climb one flight of stairs

Ability to walk 100 m

Self-report of >5% weight los

≤5 of: dementia; heart Disease; depression; arthritis; asthma;bronchitis/ emphysema; diabetes; hypertension; osteoporosis; stroke.

Results: 523 consecutive RA and SpA patients were included, 79.3 %) were female. Mean age was 55.4 years. Patients with spondyloarthritis were 39.3% ankylosing spondylitis, 31.6% psoriasis arthritis, 20.1% undifferentiated spondyloarthritis, 9% spondyloarthritis associated with inflammatory bowel disease.

Mean number of comorbidities was 1.47, with systemic hypertension and obesity as the most frequent ones (32.6 % and 27.1 %, respectively). Polypharmacy was found in 94.2 % and 63.9 % received more than five drugs simultaneously.

RA patients: 21.5 % met frailty criteria (42% in $\geq$ 65 years old patients). SpA patients:18.9% met frailty criterio (37% in $\geq$ 65 years old patients).

Conclusion: Prevalence of frailty in this study was high. Rheumatologists should make an early detection of signs of frailty.

The screenig and early detection of frailty can spur reforms to make routine care less hazardous, can focus on outcomes most relevant to patients and can aid in understanding effectiveness of health care interventions, including at the population level.

Disclosure: E. Trujillo, None; **A. Aznar**, None; **H. Sanchez**, None; **M. Hernandez**, None; **A. García**, None; **M. Trujillo Martin**, None.

Abstract Number: 0326

Cardiac Sarcoidosis Awareness: Are We Underdiagnosing?

Yvonne Lee ,[1] Patil Injean,[1] and Mehrnaz Hojjati[1], [1]Loma Linda University Health, Loma Linda

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis, a multiorgan granulomatous disorder, may involve the heart at any time and often presents with cardiac conduction disturbances, heart failure, and sudden death. 5% of patients with sarcoidosis have clinically significant cardiac involvement and up to 25% of patients have sub-clinical asymptomatic cardiac involvement. The prevalence of cardiac sarcoidosis (CS) may be higher than published statistics. We query the Loma Linda University Medical Center (LLUMC) patient database to investigate.

Methods: A single center retrospective analysis of patients with sarcoidosis from January 2014 to June 2019 at LLUMC was undertaken. Data collected included demographics, specialties involved, diagnostic tests such as cardiac magnetic resonance imaging (CMRI), positron emission tomography (PET) scan, and serologies.

Table 1: Baseline clinical features and initial organ manifestation

Patient Number	Initial organ manifestation of sarcoidosis	Method of sarcoidosis diagnosis	# Organ involvement prior to CS diagnosis?	# Year between diagnosis of sarcoidosis and CS	# Year between cardiac symptoms and diagnosis of CS	Initial Cardiac Manifestation
1	skin	skin biopsy	4	2	14	Heart Failure
2	pulmonary	lung biopsy	2	1	0	Heart Failure
3	skin	node biopsy	6	9	8	AV conduction abnormality
4	unknown	CT scan	1	18	unknown	Heart Failure
5	cardiac	lung biopsy	1	missed diagnosis	missed diagnosis	Heart Failure
6	pulmonary	node biopsy	1	3	3	Heart Failure
7	unknown	skin biopsy	1	9	11	Heart Failure
8	pulmonary	lung biopsy	3	4	1	Heart Failure
9	unknown	unknown	1	unknown	unknown	"stiff heart"
10	hypercalcemia	node biopsy	1	missed diagnosis	missed diagnosis	Heart Failure & AV conduction abnormality
11	pulmonary	node biopsy	4	3	1	Heart Failure
12	cardiac	unknown	3	0	1	AV conduction abnormality
13	gastrointestinal	liver biopsy	2	4	1	Chest Pain
14	cardiac	cardiac MRI	0	1	1	AV conduction abnormality

Table 2 : Methods and specialties involved in cardiac sarcoidosis diagnosis

Method of CS diagnosis	Specialty that suspected diagnosis of CS	After CS diagnosis, was rheumatology involved?	After CS diagnosis, was cardiology involved?	Cardiac MRI	Cardiac PET scan	Left Ventricular Ejection Fraction	EKG
PET scan	rheumatology	yes	yes	N/A	FDG +	15%	normal
Cardiac MRI	internal medicine	yes	yes	scarring	normal	60-65%	Abnormal*
Cardiac biopsy	unknown	yes	yes	N/A	N/A	55-60%	Abnormal*
unknown	rheumatology	yes	no	N/A	N/A	45%	N/A
missed diagnosis	missed diagnosis	missed diagnosis	missed diagnosis	N/A	N/A	35-40%	Abnormal+
unknown	unknown	no	yes	scarring	N/A	25%	normal
Echocardiogram	cardiology	no	yes	N/A	N/A	40%	Abnormal+
Cardiac MRI	unknown	yes	yes	scarring	FDG +	30%	Abnormal*
unknown	unknown	yes	yes	N/A	N/A	65%	Abnormal*+
missed diagnosis	missed diagnosis	missed diagnosis	missed diagnosis	N/A	N/A	50%	Abnormal*+
Cardiac biopsy	cardiology	yes	yes	N/A	N/A	45%	Abnormal*
complete heart block	unknown	unknown	yes	N/A	N/A	55-60%	Abnormal+
Cardiac MRI	pulmonology	yes	yes	scarring	FDG +	55-60%	normal
Cardiac MRI	cardiology	no	yes	scarring	normal	70-75%	Abnormal*+

FDG - Fluorine-18-deoxyglucose; N/A – not applicable
* AV conduction abnormality
+ arrhythmia

Results: Out of 496 patients diagnosed with sarcoidosis, 14 patients had CS in accordance with the Heart Rhythm Society diagnostic criteria. The median age was 58, 2:5 male-to-female ratio, and an average body mass index of 30.3 of all 14 patients. 50% patients had Medicare insurance. 42.8% of patients were African American. 71.4% of patients had biopsy proven diagnosis of sarcoidosis. 93% had other sarcoidosis organ involvement at the time of CS diagnosis (Table 1).CS was the only manifestation of sarcoidosis in 1 patient. 0% had another autoimmune disease. The average time between diagnosis of sarcoidosis and CS was 5 years and the average time between cardiac symptoms and diagnosis of CS was 4 years (Table 1). 64% had heart failure, 29% had AV conduction abnormality, and 4 patients had arrhythmias on presentation (Table 1).

14.3% of patients met the diagnostic criteria of CS but the diagnosis was missed. Out of 7 patients diagnosed with CS at LLUMC, cardiologists, rheumatologists, pulmonologist, and internists were the first to suspect diagnosis of CS in 3, 2, 1, and 1 patients, respectively (Table 2). There was an increase in specialty consultations after diagnosis of

Table 3: Serologies

Troponin	CKMB	pro-BNP	Hemoglobin	ESR	CRP
normal	normal	elevated	decreased	normal	normal
elevated	normal	elevated	decreased	elevated	elevated
N/A	normal	Elevated	decreased	elevated	elevated
N/A	N/A	Normal	normal	elevated	elevated
normal	normal	Elevated	decreased	normal	normal
normal	N/A	Elevated	decreased	N/A	N/A
N/A	N/A	N/A	normal	normal	N/A
N/A	N/A	Elevated	decreased	normal	normal
elevated	normal	Elevated	normal	elevated	elevated
elevated	normal	Elevated	decreased	elevated	N/A
normal	N/A	elevated	normal	normal	normal
N/A	N/A	N/A	N/A	N/A	N/A
normal	N/A	N/A	normal	N/A	N/A
normal	N/A	elevated	decreased	normal	normal

CS. Out 14 patients, 93% were followed by cardiology and 57% were followed by rheumatology after the diagnosis of CS; this was an increase from 90% and 14%, respectively. 42.8% had abnormal CMRI and 42.8% had abnormal PET scans. Only 2 patient's diagnosis was confirmed by cardiac biopsy. Additionally, 57% had ejection fraction (EF) reduction only explainable by their CS diagnosis (Table 2).

Most patients with CS had an elevated Pro-BNP (71%), low hemoglobin (61.5%), and/or elevated ESR (45%) at the time of diagnosis (Table 3).

Conclusion: A high clinical suspicion is warranted for prompt diagnosis of CS, since missed diagnosis is possible. Patients with multisystem sarcoidosis involvement should be evaluated for CS. Abnormal EKG followed by low EF or new onset heart failure was the most frequent finding in our cohort of CS at the time of diagnosis. CMRI and PET Scan are useful diagnostic modalities and diagnosis of CS was confirmed in 42.8% of patients using one of these 2 modalities. Serologies are less helpful in diagnosing CS. Cardiologists are at the forefront of diagnosing CS and there needs to be improved rheumatology awareness for screening CS. Multidisciplinary collaboration between subspecialties is important in the diagnosis of CS.

Disclosure: Y. Lee, None; **P. Injean**, None; **M. Hojjati**, None.

Abstract Number: 0327

Presentation Order Bias in Rheumatology Journals: A Content Analysis

Sarah Stewart ,[1] Greg Gamble,[2] Andrew Grey,[2] and Nicola Dalbeth[2], [1]University of Auckland, Auckland, Auckland, New Zealand, [2]University of Auckland, Auckland, New Zealand

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Measures Of Healthcare Quality Poster I: Testing, Screening, & Treating
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Presentation order can influence the prominence of an academic article. Earlier-listed items or those at the top of tables of contents are more likely to be seen and read, and the serial ordering of articles within a journal issue can influence article citations over many years. The aim of this study was to analyse what rheumatology journals prioritize through the presentation order of research articles within journal issues.

Methods: A content analysis of original articles published in general rheumatology journals from 2013-2018 was undertaken. All included journals produced regular issues, reported original research, and had 2016 Thomas Reuters Impact Factor > 3.0. The following data were extracted: gender of first and last author, country of origin, industry funding, and disease category. Analysis of the overall distribution of article placement within issues was computed using cumulative density function plots and area under the curve (AUC) analysis. The odds ratio (OR) for articles published in one of the first three places of an issue compared with one of the last three places was also calculated. Downloads and altmetrics were analysed.

Results: A total of 6,787 articles were included. There were no differences in presentation order based on gender, country of origin, or industry funding (Figure). However, there were significant differences in presentation order based on disease category (Figure). Articles about rheumatoid arthritis were more likely to be ordered towards the front of an issue ($P < 0.001$), and were more likely to be ordered in the first three places compared to the final three places (OR [95% CI] 5·77 [4·80, 6·92]). In contrast, articles about crystal arthritis, pain syndromes, pediatric rheumatic diseases,

systemic lupus erythematosus, systemic sclerosis, and vasculitis were more likely to be ordered at the end of the issue (P for all < 0.001). Journals presenting content grouped by disease category exhibited greater disease category prioritization compared to journals without disease category content groupings. Articles ordered in the first three places of an issue had higher download rate/article year (rate [95% CI] difference 441.9 [292.9, 591.0]) and mean altmetric scores (mean [95% CI] difference 4.88 [1.62, 8.15]), compared to articles in the last three places.

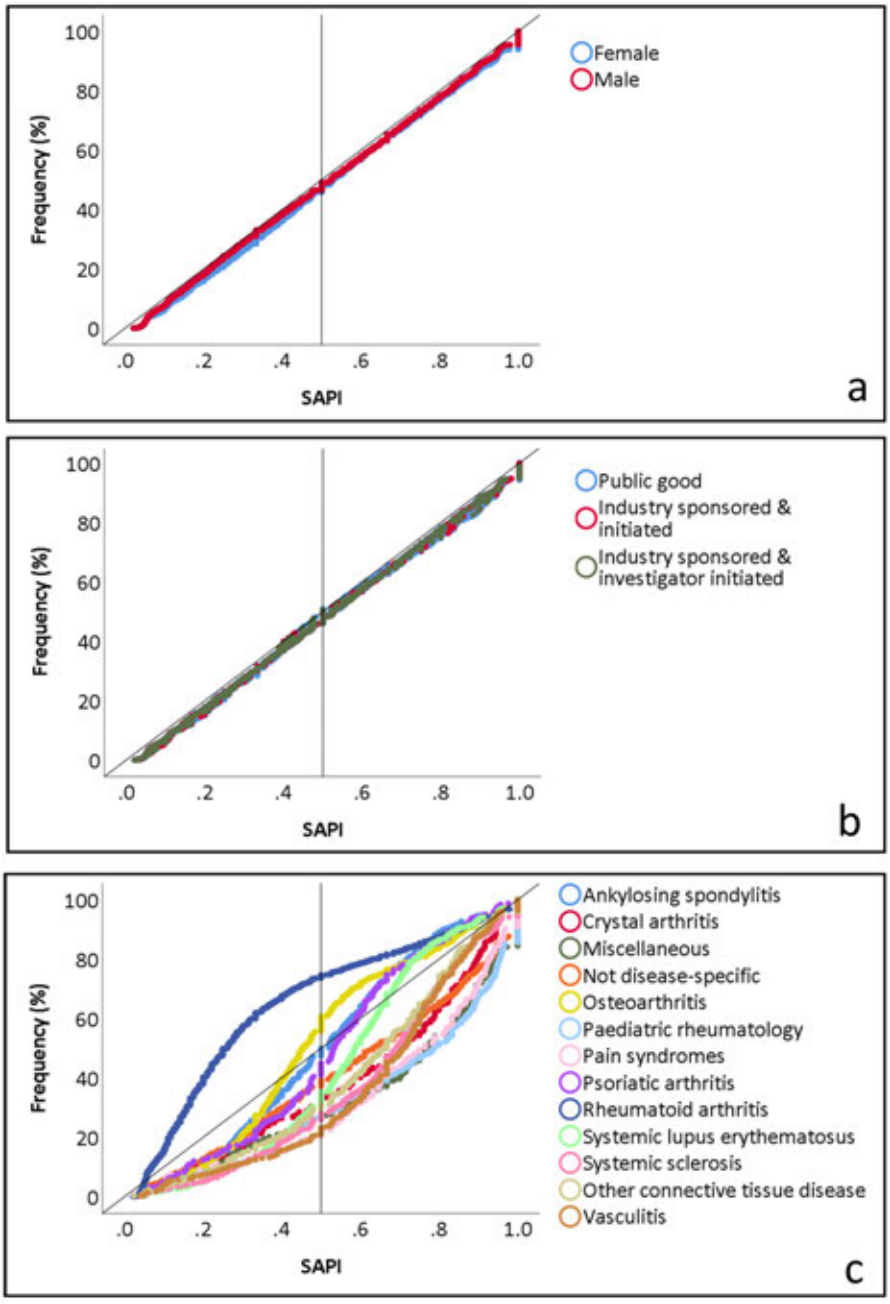

Figure. Cumulative distribution function plots of Standardised Article Placement Indices (SAPI) for (a) first author gender; (b) industry funding; and (c) disease categories. Left skewed distributions suggest publication prioritisation.

Conclusion: Contemporary rheumatology journals do not demonstrate presentation order bias for author gender, country of origin, or industry funding. However, differences in the presentation order of disease categories are evident. Editorial choices about the serial position of articles within journals can influence prioritization of certain rheumatic diseases.

Disclosure: S. Stewart, None; **G. Gamble**, None; **A. Grey**, None; **N. Dalbeth**, Abbvie, 5, 8, 9, Amgen, 2, AMGEN, 2, AstraZeneca, 2, 5, 8, 9, Dyve, 5, 8, 9, Dyve BioSciences, 5, Hengrui, 5, 8, 9, Horiaon, 5, 8, Horizon, 5, 8, 9, Janssen, 5, 8, 9, Kowa, 5, 8, 9, Pfizer, 5, 8, 9.

Abstract Number: 0328

Adverse Events During Colchicine Use: A Systematic Review and Meta-Analysis of Randomized Controlled Trial Events

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Colchicine is a widely used drug used to treat rheumatic and inflammatory conditions. Due to its long historical use in medicine, controlled clinical trials of colchicine have been small, precluding clear understanding about safety profile. The aim of the study was to systematically examine the adverse event (AE) profile of colchicine in randomized controlled trials (RCTs) across all published indications.

Methods: A systematic search was undertaken using electronic databases and manual searching of reference lists. The analysis included double-blind RCTs that compared the effects of oral colchicine to placebo or active comparator. Trials were included if they reported the incidence of AEs per group. AE data were extracted under pre-defined categories: diarrhoea, gastrointestinal events (including diarrhoea), liver events, hematology events, muscle events, sensory events, infection events and death, and any reported AE. Meta-analyses were undertaken to determine the pooled risk ratios (RR) of AEs in the colchicine group compared to the placebo and/or active comparator groups. Subgroup analyses were used to explore the effects of disease indication, dose, and exposure duration.

Results: Thirty-two studies were included involving participants with liver diseases (n = 6), gout (n = 5), Bechet's and related conditions (n = 4), pericarditis and related conditions (n = 6), and other (n = 11). The pooled sample size was 3,774 participants. Any adverse event was reported in 26.6% of colchicine users compared to 20.9% of comparator groups, with an estimated risk ratio (RR) (95% confidence interval (CI)) of 1.72 (1.33-2.23) (**Table**). Sub-group meta-analyses showed no significant difference in RR of AEs in colchicine users between placebo and active comparator groups, or between different disease indications, duration of drug exposure, daily dose or cumulative dose. The RR (95% CI) in colchicine users compared to comparator groups for diarrhoea was 2.63 (1.67-4.16), and for any gastrointestinal AE was 1.97 (1.50-2.58), both $P < 0.001$. The RRs of liver, muscle (including myalgia, cramps, myotoxicity, and weakness), sensory, and infection AEs in colchicine users compared to comparators were not significant (**Table**). No study reported rhabdomyolysis, hematology AEs or deaths.

Table. Meta-analysis results showing pooled risk ratio of adverse events between colchicine and pooled comparator groups

	N. studies	n/N, % (95% CI) participants		Pooled risk ratio (95% CI)	I^2 (p-value)	Overall effect, Z (p-value)[a]
		Colchicine	Comparator			
Any event	26	437/1641, 26.6% (24.5, 28.8)	370/1773, 20.9% (19.0, 22.8)	1.72 (1.33, 2.23)	86% (<0.001)	4.16 (**<0.001**)
Diarrhoea	17	189/797, 23.7% (20.0, 26.8)	54/712, 7.6% (5.8, 9.7)	2.32 (1.51, 3.57)	39% (0.05)	3.83 (**<0.001**)
Gastrointestinal[b]	27	299/1744, 17.1% (15.4, 19.0)	121/1874, 6.5% (5.4, 7.6)	1.97 (1.50, 2.58)	29% (0.08)	4.88 (**<0.001**)
Liver	12	15/1129, 1.3% (0.8, 2.1)	11/1343, 0.8% (0.4, 1.4)	1.63 (0.76, 3.50)	0% (0.82)	1.24 (0.21)
Muscle[c]	8	33/851, 3.9% (2.7, 5.3)	23/850, 2.7% (1.8, 4.0)	1.41 (0.87, 2.30)	0% (0.90)	1.40 (0.16)
Sensory	2	3/201, 1.5% (0.4, 4.0)	2/190, 1.1% (0.2, 3.4)	1.35 (0.27, 6.74)	0% (0.58)	0.37 (0.71)
Infection	4	42/327, 12.8% (9.5, 16.8)	74/548, 13.5% (10.8, 16.6)	1.19 (0.65, 2.16)	47% (0.13)	0.55 (0.58)

[a]Bolded p-values indicate a significant overall effect in the risk ratio for an adverse event between colchicine and comparator groups. [b]The gastrointestinal category includes diarrhoea. [c]The muscle category includes myalgia, muscle cramps, myotoxicity, muscle weakness and elevated CPK. No study assessed or reported rhabdomyolysis.

Conclusion: Although AEs are more common with colchicine compared with placebo or active comparator, these relate mostly to well-recognized gastrointestinal AEs. Increased incidence of liver, sensory, muscle, infection, or haematology AEs or death was not observed.

Disclosure: S. Stewart, None; **K. Yang**, None; **K. Atkins**, None; **N. Dalbeth**, Abbvie, 5, 8, 9, Amgen, 2, AMGEN, 2, AstraZeneca, 2, 5, 8, 9, Dyve, 5, 8, 9, Dyve BioSciences, 5, Hengrui, 5, 8, 9, Horiaon, 5, 8, Horizon, 5, 8, 9, Janssen, 5, 8, 9, Kowa, 5, 8, 9, Pfizer, 5, 8, 9; **P. Robinson**, None.

Abstract Number: 0329

Excessive Alcohol Intake Is Associated with Tophi Formation in Gout Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Dietary factors have been recognized as risk factors of hyperuricemia and gout. However, their association with tophi formation remain elusive. The aim of this study was to identify the dietary factors associated with the presence of tophi in gout patients.

Methods: Consecutive gout patients who fulfilled the 2016 ACR/EULAR classification criteria were recruited from July 2017 to April 2019. A 10-items food frequency questionnaire was developed which included alcohol, red meat, animal offal, seafood, hotpot, slow-cooking soup, fructose-containing beverages (FCB), tea, coffee and milk/milk products. Patients were asked to report the average consumption frequency over the one year prior to the first gout

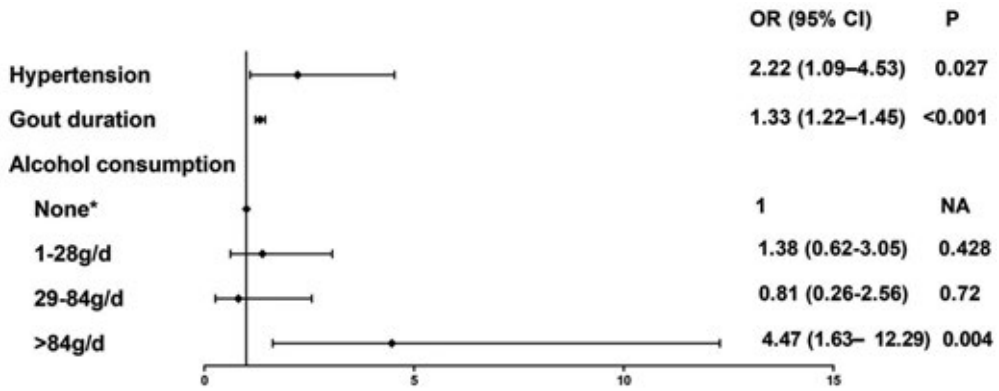

Figure 1. Risk factors of tophi formation by multivariate logistic regression analysis. Independent variables included age, gender, gout duration, sUA, eGFR, obesity, hypertension, diabetes, dyslipidemia, coronary heart disease and ten dietary factors. *: reference group.

attack. The alcohol intake was divided into four categories: none, 1-28 grams per day (g/d), 29-84 g/d, > 84 g/d. Intake of red meat was recorded as < 100 g/d, 101-200 g/d, 201-300 g/d and > 300 g/d. The consumption of other dietary factors were categorized as < 1 time/w, 1-2 times/w, 3-4 times/w, and > 4 times/w. Tophi was identified by physical examination, ultrasonography or dual energy CT.

Results: Among 430 recruited gout patients, 96.0% were male with median age of 39 (IQR 30-53) years and gout duration 3 (IQR 2-7) years. The median serum uric acid (sUA) was 9.3 (IQR 7.8-10.4) mg/dl. There were 14.0% gout patients consuming alcohol >84 g/d and 4.4% patients eating red meat >300 g/d. There were 41.4% patients drinking tea, 18.8% drinking FCB and 11.6% drinking slow-cooking soup >4 times/w, respectively. Tophi were identified in 77 patients (17.9%). Compared with non-tophi group , the tophi group presented higher age (median 47 vs. 38 years), longer gout duration (median 8 vs. 3 years), more affected joints (median 7 vs. 3), higher prevalence of hypertension (59.7% vs. 34.8%) and diabetes (18.2% vs. 8.5%), but lower estimated glomerular filtration rate (eGFR, 79.5±18.3 vs. 84.7±16.4 ml/min/1.73 m2, all P< 0.05). For dietary factors, there were more patients in tophi group consumed alcohol >84g/day (31.2% vs. 10.2%, P< 0.01). To evaluate the risk factors of tophi, multivariate logistic regression analysis was performed with independent variables including age, gender, duration of gout, sUA, eGFR, obesity, hypertension, diabetes, dyslipidemia, coronary heart disease and ten dietary factors, The result showed gout duration (OR=1.33, 95%CI: 1.22-1.45), hypertension (OR=2.22, 95%CI: 1.09-4.53) and alcohol intake >84g/day compared with those without alcohol intake (OR=4.47, 95%CI: 1.63-12.29) were associated with the presence of tophi (Figure 1).

Conclusion: Excessive alcohol intake may promote tophi formation.

Disclosure: Q. Li, None; **C. Deng**, None; **L. Yang**, None; **J. Liang**, None; **J. Lin**, None; **Y. Mo**, None; **L. Dai**, None.

Abstract Number: 0330

Acute Gout Attacks Among Patients Admitted Due to Heart Failure: Analysis of NIS Database

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Acute gout arthropathy is a well-described side effect of aggressive diuresis in patients hospitalized with heart failure. This study aims to determine the prevalence and predictors of acute gout attacks of patients admitted primarily for heart failure exacerbation as well as analyze its impact on health care resource utilization.

Methods: Data were obtained from the National Inpatient Sample (NIS) between 2009 and 2015. ICD-9-CM codes were captured to identify patients with a principal diagnosis of heart failure (ICD-9 428.x; 402.01, 402.11, 402.91; 404.01, 404.03, 404.11, 404.13, 404.91, 404.93) and a secondary diagnosis of acute gouty arthropathy (ICD-9 274.01). Outcomes measured were length of stay (LOS), inpatient total cost, and prevalence of acute kidney injury (ICD-9 584.x). Multivariable logistic regression was used to identify predictors of acute gout arthropathy.

Results: We identified a total of 1,130,374 patients (>18years) who were admitted for heart failure exacerbation over the study period with 4116 (0.4%) having an acute gout attack during that admission. Patients who developed gout were younger (67.9 vs. 61.7 years, P-value < 0.001) and had a higher prevalence of alcohol abuse, iron deficiency anemia, coagulopathy, diabetes, and obesity (all P< 0.05). With regards to the observed outcomes, acute kidney injury (AKI) rates were higher in patients who developed acute gout attacks compared to those who did not (43.8% vs. 22.0%, P< 0.001). Total hospital cost ($ 9,999 vs.$ 6,941; P< 0.001) and LOS (6 days vs. 4 days; P< 0.001) were higher in patients that had acute gout attacks.Of the patients with acute gout and heart failure, only 8.9% of them received either an intra-articular joint injection or arthrocentesis. Multivariable logistic regression revealed that some significant predictors of gout were chronic kidney disease (OR 2.43; 95% CI 2.27-2.60; P-value < 0.001), chronic alcohol use (OR 1.27; 95% CI 1.08 -1.49; P-value < 0.004), Obesity (OR: 1.84; 95% CI 1.71-1.98; P-value < 0.0001), dyslipidemia (OR 1.16; 95% CI 1.09-1.24; P-value < 0.001).

Conclusion: Inpatient gout attacks result in an increment of days of hospital stay, AKI rates, and total charges in patients hospitalized with heart failure exacerbation. CKD, chronic alcohol use, obesity, and dyslipidemia showed a statistically significant increase in the risk of development of gouty arthritis flare in heart failure patients. Intra-articular injections or arthrocentesis were not commonly done in these patients per coding records. Our analysis indicates acute gout during a hospitalization for heart failure negatively impacts health care resource utilization.

Disclosure: E. Gauto-Mariotti, None; **S. Kambhatla**, None; **S. Fugar**, None; **A. MANADAN**, None.

Abstract Number: 0331

Gout Management in the Medical Community: A Claims-Based Analysis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Table 1. Patient sample sizes, gout codes, and claims history in database

Gout Category	Patient Counts	>1 Idiopathic Gout Code*	>1 Secondary Gout Code**	>1 Unspecified Gout Code***	>1 Year of Pre and Post Gout Claims History
Acute Gout	987,127	196,364 (19.9%)	20,679 (2.1%)	834,968 (84.6%)	751,722 (76.1%)
Non-Tophaceous Chronic Gout	122,162	75,295 (61.6%)	11,265 (9.2%)	71,197 (58.3%)	96,137 (78.7%)
Tophaceous Chronic Gout	27,769	17,762 (64.0%)	4,075 (14.7%)	20,171 (72.6%)	21,522 (77.5%)
Uncontrolled Gout	25,689	14,885 (57.9%)	2,716 (10.6%)	22,248 (86.6%)	18,829 (82.8%)

* Idiopathic gout diagnosis codes include ICD-10: M10.0* and M1A.0*

** Secondary gout diagnosis codes include ICD-10: M10.1*, M10.2*, M10.3*, M10.4*, M1A.1*, M1A.2*, M1A.3*, and M1A.4*

*** Unspecified gout diagnosis codes include M10.9* and M1A.9*

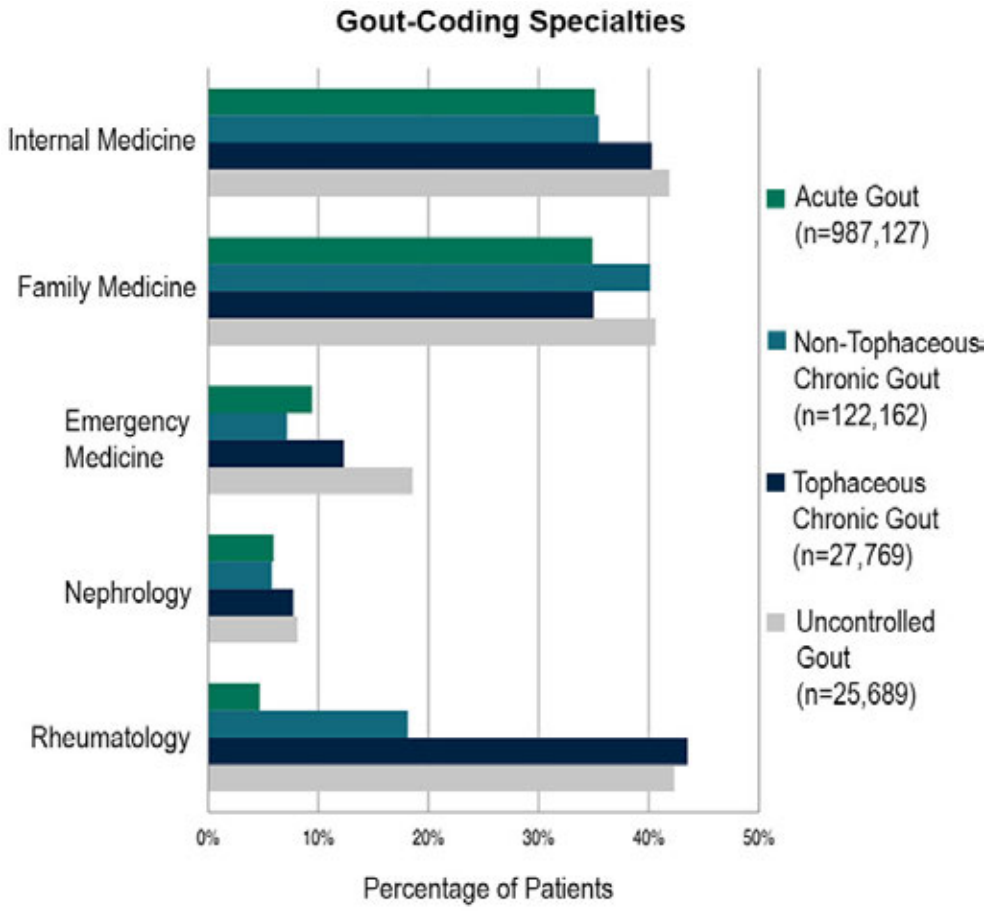

Figure 1. Frequency with which gout subsets are seen by various physicians.

Background/Purpose: Gout is one of the most common inflammatory arthropathies. Despite available urate lowering therapies (ULT), many patients progress to chronic or advanced gout, characterized by the development of tophi, chronic inflammatory arthritis, and other manifestations resulting from persistent urate deposition. Although numerous guidelines exist for the management of gout, there is little information on the frequency of their implementation in the medical community.

Population	Urate Tests / Year			ULT Prescriptions / Patient		
	With Rheumatology Visit	No Rheumatology Visit	p-value	With Rheumatology Visit	No Rheumatology Visit	p-value
Acute Gout	0.68	0.55	<0.001	5.66	4.27	<0.001
Non-Tophaceous Chronic Gout	0.93	0.59	<0.001	6.70	5.10	<0.001
Tophaceous Chronic Gout	1.35	0.75	<0.001	7.20	4.97	<0.001
Uncontrolled Gout	3.17*	3.12*	0.06	8.25	5.77	<0.001

* Definitional

ULT = urate lowering therapies

Table 2. Comparison of annual frequency of urate testing and urate lowering therapies in patients with or without a history of a rheumatology visit

The objective of this research was to evaluate the real-world practice patterns in patients diagnosed with gout using a large administrative claims database from the United States.

Methods: We carried out a retrospective analysis to identify patients with gout over an approximately 6-year period from October 2012 to August 2018. This study used data from the Symphony Integrated Dataverse, an administrative database covering over 250 million patients across the United States. Patients were identified as having gout if they were >18 years of age and had at least two medical claims for the diagnosis of gout on different days, separated by at least 3 months. Patients with acute gout were identified by ICD-10 code M10.*, chronic non-tophaceous gout (M1A.***0), tophaceous gout (M1A.***1) and uncontrolled gout (M10.*, M1A.*), the latter manifested by three gout codes (any) in the primary diagnosis position and three urate tests within the same calendar year. Percent and frequency of urate testing, rheumatology specialist visits, and prescriptions for ULT (allopurinol, febuxostat, probenecid, and lesinurad) were evaluated for each diagnostic group.

Results: We identified 1,162,747 gout patients (Table 1). The median age was 63 (range: 19-80), 74.1% were male, and the average duration of claims history in the database was 5.6 years. As shown in Figure 1, gout patients were seen most frequently by internists and family medicine practitioners. Patients with acute gout were infrequently see by rheumatologists, but the likelihood of encountering a rheumatologist progressively increased in subjects with advanced gout (chronic nontophaceous< tophaceous=uncontrolled). In all groups, the frequency of serum urate testing and receipt of a prescription for ULT significantly increased in gout patients seen by a rheumatologist (Table 2).

Conclusion: Most subjects with acute gout are not seen by a rheumatologist and less than half of those with advanced gout encounter a rheumatologist. However, measurement of serum urate and prescriptions for ULT are more frequent in those seen by a rheumatologist, but measurement of serum urate and prescriptions of ULT are not uniform. More frequent referral to rheumatologists and closer adherence to guidelines may improve outcomes for gout patients.

Disclosure: N. Edwards, Astra Zeneca, 5, Horizon, 5, Ironwood Pharmaceuticals, 5, Selecta, 5; **N. Schlesinger**, amgen, 2, Astra Zeneca, 2, Horizon, 5, horizon, 5, IFM Therapeutics, 5, Mallinckrodt Pharmaceuticals, 5, Novartis, 5, olatec, 5, pfizer, 2, selecta, 5; **S. Clark**, None; **J. Paige**, None; **T. Arndt**, None; **P. Lipsky**, Horizon, 5, Janssen Research & Development, LLC, 2.

Abstract Number: 0332

Incident Gout After Renal Transplantation in Gout-naïve Patients: Large Database Analysis

Brian LaMoreaux ,[1] Megan Francis-Sedlak,[1] and Robert Holt[1], [1]Horizon Therapeutics plc, Lake Forest, IL

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients undergoing kidney transplantation are at increased risk for developing hyperuricemia and gout compared to the general population (generally attributed to the frequent use of calcineurin inhibitors, cyclosporine and tacrolimus). However, the proportion of renal transplant patients that develop gout and the timing in which this occurs post-transplant is less established. This study sought to describe and quantify the incidence of gout in gout-naïve patients undergoing renal transplantation.

Methods: This retrospective analysis of Humana Research Database 2007-2017 claims data (private insurance and Medicare) was performed by identifying kidney transplant patients who were in plan for at least 6 months before and 5 years after transplant. Only patients without an ICD-9/10 gout diagnostic code within 6-months prior to transplant were included. Included patients were then examined for cumulative incidence of gout post-transplant.

Results: The database contained 16,454 patients that underwent kidney transplant. Of these, 920 patients underwent renal transplant, were in plan for at least 6 months before and 5 years after transplant, and did not have a gout diagnostic code before transplant. Of these, 212 patients (23%) had a post-transplant gout code while in plan, and 175 (19%) developed gout within 5 years post-transplant. The proportion of patients with gout progressively increased over time post-transplant and did not plateau. (**Figure 1**)

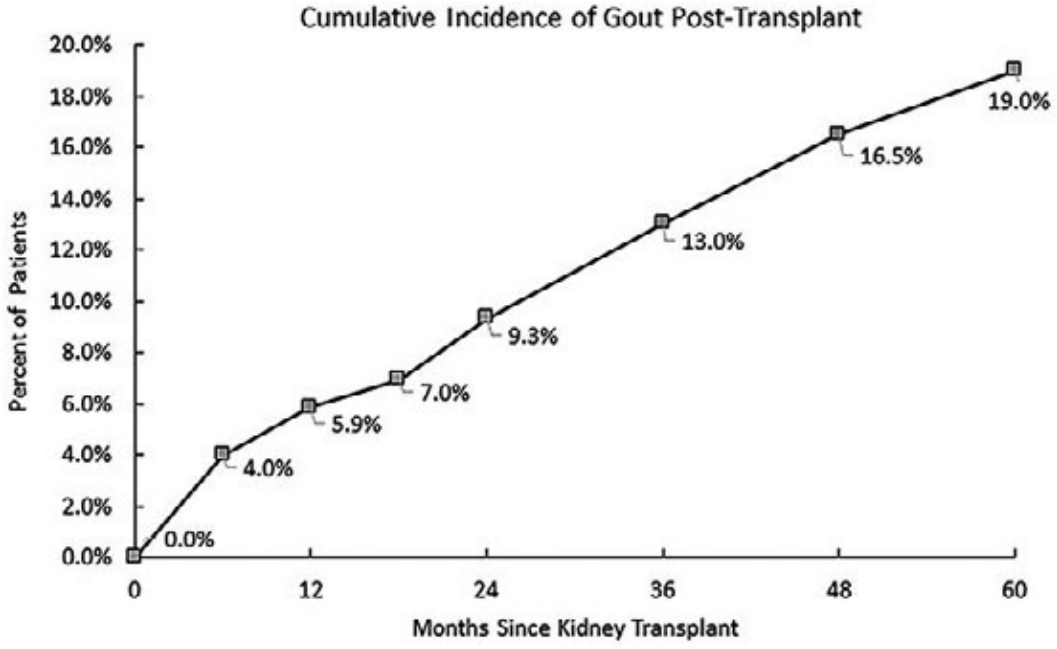

Figure 1. Proportion of gout-naïve kidney transplant patients who developed gout over 5 years post-transplant

Conclusion: Gout is a known frequent comorbidity in solid organ transplant patients, but the timing and proportion of transplant patients who develop gout is not well described. Using a large database analysis, this analysis showed that the proportion of gout-naïve patients undergoing kidney transplantation who develop gout is high and that this proportion only increases as patients are followed over a longer period of time.

Disclosure: B. LaMoreaux, Horizon, 3, 4; **M. Francis-Sedlak**, Horizon, 3, 4, Horizon Therapeutics, 3, 4; **R. Holt**, Horizon, 3, 4, Horizon Therapeutics, 3, 4.

Abstract Number: 0333

Assessing the Relationship Between Gout and Return to Hemodialysis Among U.S. Renal Transplant Patients

Justin Li ,[1] David Yin,[1] Zheng Wang,[1] Mark Brigham,[1] Brian LaMoreaux,[2] Jeffrey Kent,[2] Megan Francis-Sedlak,[2] Richard Johnson,[3] Nandini Hadker,[1] and Gavin Miyasato[1], [1]Trinity Partners, Waltham, MA, [2]Horizon Therapeutics plc, Lake Forest, IL, [3]University of Colorado Denver, Aurora, CO

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Although gout has been shown to be associated with poor renal outcomes among chronic kidney disease populations, this relationship is not well understood among renal transplant recipients. This analysis compared rates of return to maintenance hemodialysis, a negative transplant outcome, across three primary renal transplant patient cohorts based on gout status: non-gout, pre-existing gout, and new-onset gout following transplantation.

Methods: This retrospective study of the United States Renal Data System examined Medicare beneficiaries who received a primary renal transplant between 2008-2013. Patients' Medicare claims data were used to identify pre-existing gout in the 2 years prior to transplant and new-onset gout in the 3 years post-transplant. To mitigate the effect of complications associated with acute allograft rejection/ failure, recipients who died, returned to dialysis, or received re-transplantation within 3 years after primary renal transplantation were excluded. Patients' return to hemodialysis was observed in the period between 3-5 years post-transplantation. The association between gout status (non-gout, pre-existing, and new-onset) and 5-year return to dialysis was evaluated via chi-squared tests.

Results: 39,780 patients received a primary renal transplant between 2008-2013 with Medicare as their primary payer after exclusions. Of these patients, 33,105 (83.2%) were non-gout, 4,747 (11.9%) had pre-existing gout, and 1,928 (4.8%) developed new onset gout post-transplant. 2,211 (5.6%) primary renal transplant recipients returned to hemodialysis between 3 and 5 years post-transplantation. The rate of return to hemodialysis 3 to 5 years after transplantation for non-gout, pre-existing gout, and new onset gout was 5.6, 4.6, and 7.5%, respectively (all pairwise comparisons yielded $p < 0.05$).

Conclusion: Compared to non-gout and pre-existing gout patients who received a primary renal transplant, patients who developed new-onset gout after transplantation were more likely to require maintenance hemodialysis, a negative renal transplant outcome. Further investigation is needed to determine if the presence and timing of gout relative to renal transplantation is an independent predictor for return to dialysis.

Disclosure: **J. Li**, Horizon Pharma, 2; **D. Yin**, Horizon Therapeutics plc, 2; **Z. Wang**, Horizon Therapeutics plc, 2; **M. Brigham**, Horizon Therapeutics plc, 2; **B. LaMoreaux**, Horizon, 3, 4; **J. Kent**, Horizon, 3, 4; **M. Francis-Sedlak**, Horizon, 3, 4, Horizon Therapeutics, 3, 4; **R. Johnson**, XORT Therapeutics, 1, 4, 5, Colorado Research Partners LLC, 1, 4, Danone Research Foundation, 2, 5, Horizon Therapeutics plc, 5; **N. Hadker**, Horizon Therapeutics plc, 2; **G. Miyasato**, Horizon Therapeutics plc, 2.

Abstract Number: 0334

The Role of a 'Treat-to-Target' Approach on Long-term Renal Outcomes in Patients with Gout

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
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Background/Purpose: Although gout is accompanied by the substantial burden of kidney disease, there is limited data to assess renal function as a therapeutic target. There remains some discordance between the indication and goal of urate-lowering therapy (ULT) and unanswered questions about its effects on renal function. Thus, we evaluated the clinical importance of implementing the "treat-to-target" approach in the long-term management of gout in relation to renal function and the factors influencing this outcome.

Methods: In this 10-year retrospective study, the research subjects consisted of patients with gout who were newly treated with allopurinol (n = 42), febuxostat (n = 145), or benzbromarone (n = 57) and had continued ULT for at least 1 year. The upward titration of ULT doses was recommended according to the "treat-to-target" approach proposed by major international rheumatology groups such as the American College of Rheumatology and the European League Against Rheumatism. The efficacy of ULT in improving renal function was investigated through a sequential comparison of the estimated glomerular filtration rate (eGFR) after the duration of ULT. Multivariate logistic regression was used to assess the factors associated with the improvement in renal function.

Results: Out of 719 patients, a total of 244 subjects with a diagnosis of gout who received ULT for more than 12 months were enrolled in this study. The study population was predominantly male (96.7%). The mean age was 50.9 ± 14.2 years, and 17.6% were ≥65 years old. A serum uric acid (SUA) target concentration of < 6 mg/dL was attained for 191 patients (78.3%). Improvement in renal function was only demonstrated in the subjects in whom the SUA target was achieved (76.40 ± 18.81 mL/min/1.73 m2 vs. 80.30 ± 20.41 mL/min/1.73 m2, $p < 0.001$). A statistically significant difference in the mean change in eGFR with respect to SUA target achievement was apparently shown in individuals with chronic kidney disease (CKD) stage 3 (-0.35 ± 3.87 mL/min/1.73 m2 vs. 5.33 ± 11.64 mL/min/1.73 m2, $p = 0.019$). The patients who developed acute kidney injury during ULT had a considerable decline in the mean eGFR as opposed to the rest of the patients (-13.21 ± 16.26 mL/min/1.73 m2 vs. 4.23 ± 12.73 mL/min/1.73 m2, $p < 0.001$). There was no significant difference in the proportion of subjects with improved renal function ($p = 0.543$) and the mean change in eGFR ($p = 0.101$) among the three groups of urate-lowering agents selected for ULT. Multivariate analysis predicted that patients ≥65 years old had a decreased likelihood of improvement in renal function (OR 0.35, 95% CI 0.15-0.85, $p = 0.020$).

Conclusion: This study clarifies that long-term SUA lowering to below 6 mg/dL after initiation of ULT is associated with the significant improvement of renal function in patients with gout, which has proven to be highly beneficial for conditions associated with renal impairment. The proper utilization of the "treat-to-target" approach in clinical practice would provide implications for better management and outcomes not only in gouty arthritis but also in comorbid kidney disease.

Disclosure: W. Kim, None; **J. Song**, None; **S. Choi**, None.

Abstract Number: 0335

Renal Transplant Complications in Patients with and Without Gout

Megan Francis-Sedlak ,[1] Brian LaMoreaux,[1] and Robert Holt[1], [1]Horizon Therapeutics plc, Lake Forest, IL

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Graft-related complications are among the most serious issues solid-organ transplant recipients and their healthcare teams face post-operatively. Gout is a known frequent co-morbidity in transplant patients. Whether renal transplant patients with gout suffer from higher rates of transplant-related complications, as compared to transplant patients without gout, has not been investigated. We analyzed a large US population database to determine the overall transplant complication rate in patients having a renal transplant with and without gout.

Methods: A retrospective review of Humana Research Database claims data (2007-2017) was undertaken to identify kidney transplant patients with ≥6 months in plan before and after transplant. Diagnostic gout codes (ICD 9/10) were used to categorize patients into gout and non-gout groups. Additionally patients were classified as having gout pre- or post-transplant based on when the first gout code occurred. Transplant complications were determined using the ICD 9 code for complications of transplanted kidney and ICD 10 codes for unspecified and other complications of kidney transplant, kidney transplant rejection, failure, and infection.

Results: The database contained 6085 patients with a kidney transplant and ≥6 months in plan both pre and post-transplant. Of these, 1504 patients had ≥1 gout codes (the first code occurred in 909 patients pre-transplant and 595 post-transplant), and 4581 patients never had a gout code. The renal transplant complication rate in the overall cohort was 36.0%. Patients with gout had a higher complication rate (40.4%) than those without gout (34.6%, OR: 1.28, 95% CI: 1.136–1.443, p< 0.001). The higher complication rate in gout patients was driven by those who developed gout post-transplant.(Table 1)

Group	Number of Patients	Number with Complications	% with Complications
Enrolled Patients:	6085	2191	36.0%
-Gout and Transplant:	1504	607	40.4%
Gout Pre-Transplant	909	304	33.4%
Gout Post-Transplant	595	303	50.9%
-No Gout	4581	1584	34.6%

Table 1. Renal transplant-related complications in patients with and without gout

Conclusion: Our analysis indicates that patients with gout, especially those with gout arising post-transplant, suffered from higher rates of overall transplant-related complications. In addition to more research on this topic, an increased focus on awareness and screening of renal transplant patients for gout is warranted.

Disclosure: M. Francis-Sedlak, Horizon, 3, 4, Horizon Therapeutics, 3, 4; **B. LaMoreaux**, Horizon, 3, 4; **R. Holt**, Horizon, 3, 4, Horizon Therapeutics, 3, 4.

Abstract Number: 0336

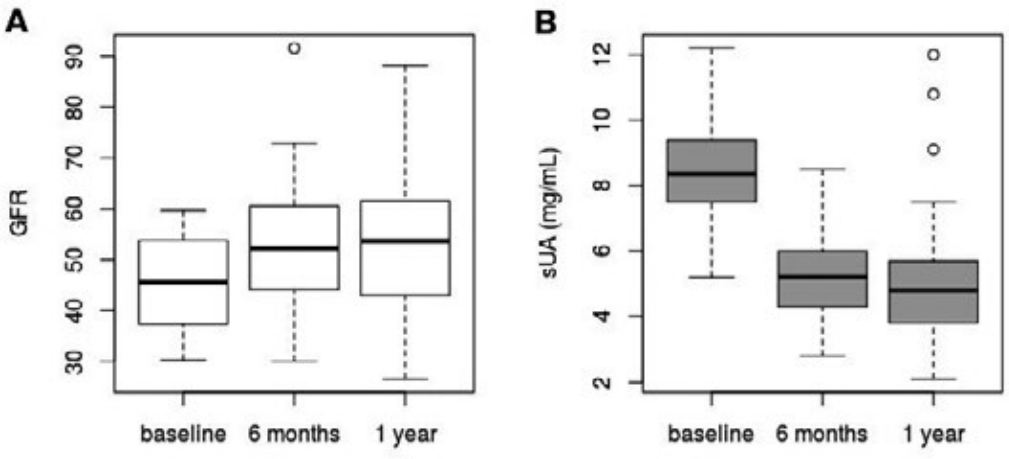
Treating Gout to Target Entails Renoprotective Effect in Patients with Moderate Chronic Kidney Disease

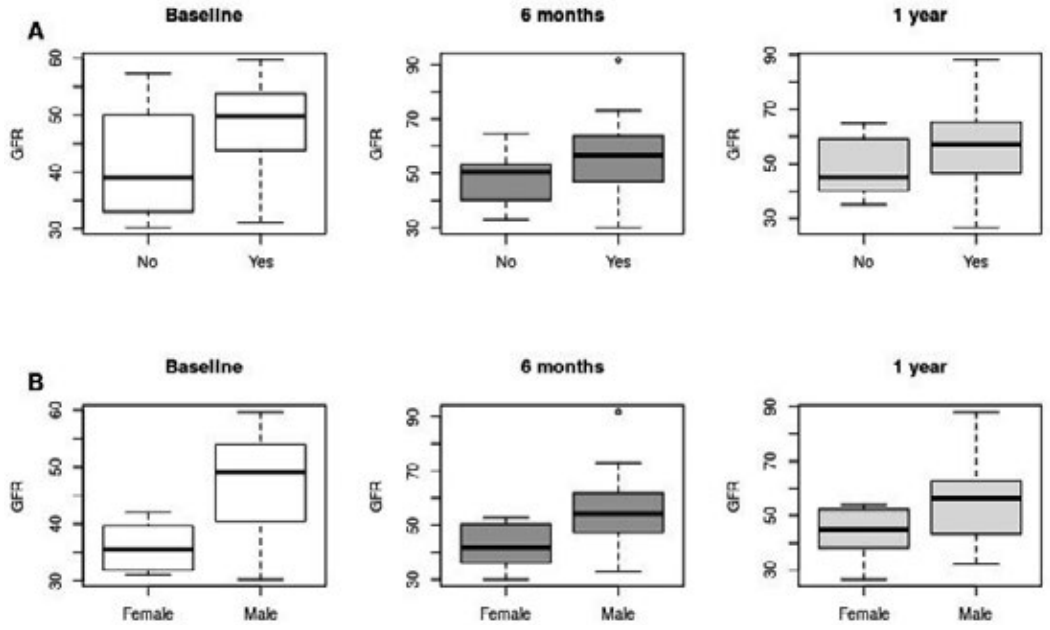
enrique Calvo-Aranda ,[1] Marta Novella-Navarro,[2] jOSE LUIS CABRERA-ALARCON,[3] Francisco Aramburu,[2] Iustina Janta,[4] Alejandro Prada-Ojeda,[5] Luis Sala-Icardo,[5] Maria del Carmen Ortega de la O,[6] Cesar Diaz-Torne,[7] and A. Urruticoechea-Arana[8], [1]Hospital Universitario Infanta Leonor, Madrid, Spain, [2]Hospital Universitario HM Sanchinarro, madrid, Spain, [3]Bioinformatica CNIC, madrid, Spain, [4]Hospital General Universitario Gregorio Marañón, madrid, Spain, [5]Hospital Universitario de Torrejon, madrid, Spain, [6]Hospital Universitario Santa Elena, madrid, Spain, [7]Hospital de la Santa Creu i Sant Pau, barcelona, Catalonia, Spain, [8]HU Can Misses, Ibiza, Spain

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Approximately 25% of patients with gouty arthritis suffer from chronic kidney disease (CKD). High serum uric acid (sUA) levels have been related to glomerular filtration-rate (eGFR) imbalance. Beneficial effect of treatment with xanthine oxidase inhibitors (XOI), mostly allopurinol, has already been proved in patients with CKD and asymptomatic hyperuricemia. Although several studies have described the efficacy and renal safety of treatment with XOI in gout, few authors have analyzed the effect of treating gout to target (T2T) on eGFR in patients with gouty arthritis and moderate CKD. Our objective is to assess the effect of treating gout to target in patients with gouty arthritis and moderate CKD, in terms of eGFR changes.

Methods: In this multicenter, longitudinal, observational study, we included patients from 7 different hospitals, between January 2014 and December 2018. All diagnosed with gout (ACR/EULAR 2015 criteria) and stage-3 CKD according to Cockroft-Gault formula (eGFR 30-59 ml/min/m2) who received XOI (febuxostat or allopurinol) with a





follow-up for 6 and 12 months. Exclusion criteria were: primary kidney disease, kidney transplantation or single-kidney. Data were provided from clinical records at baseline visit, 6 and 12 months. Those patients whom data were not collected at that schedule were also excluded. Demographic and clinical features included were: age, sex, age at gout onset, pattern of joint involvement, presence of tophi, sUA levels, nephrolithiasis, comorbidities, concomitant treatments, smoking and alcohol intake. Statistical analysis: linear mixed-effects model was used. To fit this model a stepwise approach was adopted considering p-value < 0.05 statistically significant for feature coefficients. Nmlev-3.1-137 R package.

Results: Complete data were obtained from 50 patients (44 males and 6 females). Mean age 72.90±8.94 years. Mean baseline sUA was 8.55±1.57 mg/dl and mean eGFR 45.52±9.21 ml/min/m^2. Time, sUA levels, smoking and sex were variables with significant effects according to the linear mixed effects model for eGFR. A significant improvement in eGFR was observed in first 6 months (16.7±5.1 ml/min/m^2) (p=0.004), associated to an inverse relation in sUA levels (p=0.04). Non-smokers presented better eGFR than smokers (p=0.01) and males had higher eGFR in all considered points than females (p=0.008). No significant differences were obtained between allopurinol or febuxostat administration regarding eGFR variations.

Conclusion: Reduction of sUA levels in patients with gout and CKD stage-3 treated with XOI following the T2T approach entitles an improvement of eGFR. These findings suggest that the response to urate-lowering treatment takes place in the first 6 months, leading to a significant improvement in eGFR in this period, and both (sUA and eGFR) remain stable between 6 and 12 months. So that, an optimal management of gout can preserve and improve kidney function in patients with arthritis and moderate CKD.

Disclosure: e. Calvo-Aranda, None; **M. Novella-Navarro**, None; **j. CABRERA-ALARCON**, None; **F. Aramburu**, None; **I. Janta**, None; **A. Prada-Ojeda**, None; **L. Sala-Icardo**, None; **M. Ortega de la O**, None; **C. Diaz-Torne**, None; **A. Urruticoechea-Arana**, None.

Abstract Number: 0337

Gout in the US: Significant Association with Cardiovascular and Renal Disease Hospitalizations - A Nationwide Study

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Session Date: Sunday, November 10, 2019
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Background/Purpose: Gout is a disorder of uric acid metabolism and often presents as acute severe joint pain. Previous work from our group suggests that all-cause hospitalizations in patients with gout in the United States (US) have significantly increased in the last 22 years. The current study focused on identifying potential reasons for the excess hospitalizations.

Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in the NIS in 2016 among patients 40 years or older with a primary or secondary diagnosis of gout and compared them to total all-cause hospitalizations in patients without a gout diagnosis in the same age group during the same period. Over 69,800 ICD 10 diagnoses codes were collapsed into a smaller number of clinically meaningful categories, consistent with the Centers for Disease Control (CDC) Clinical Classification Software. The top 15 primary causes for hospitalization were evaluated and compared between the two cohorts.

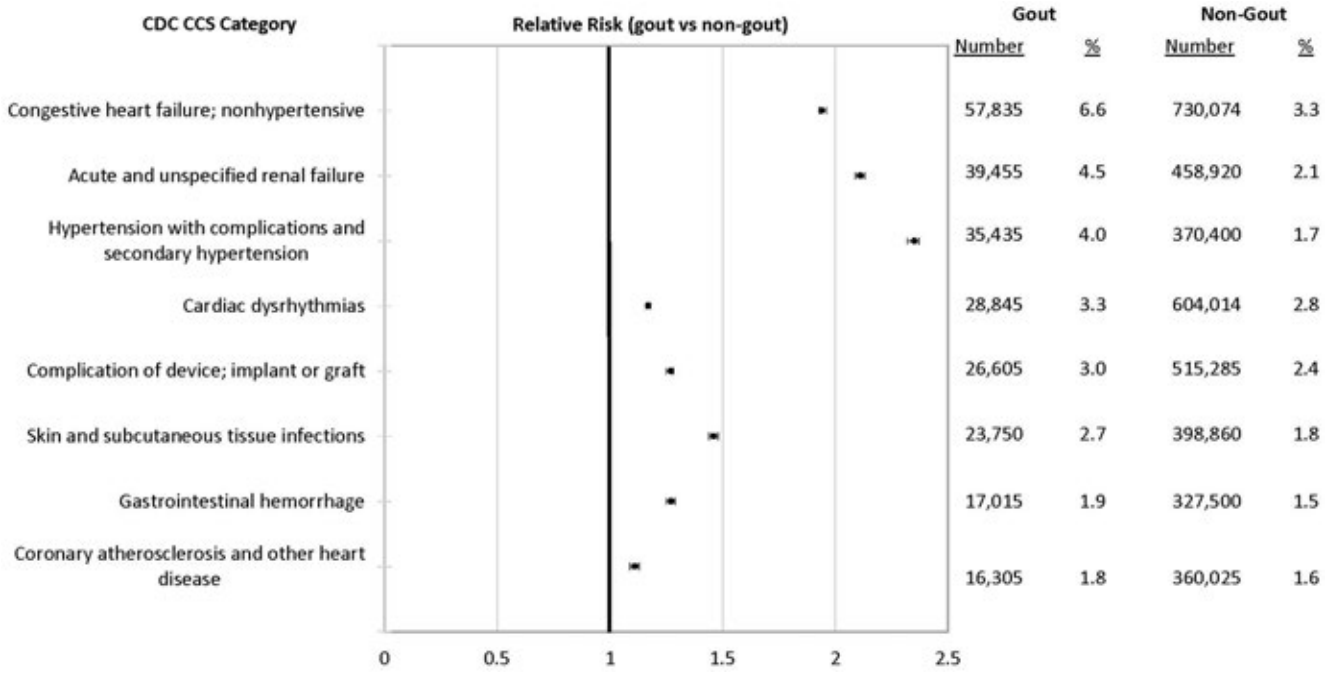

Figure Relative risk of comorbidities in Gout vs No Gout

Results: In 2016, there were 892,379 all-cause hospitalizations in the US in patients with gout with 14,135 (1.6%) of these for primary diagnosis of gout. The primary diagnoses for remaining 878,244 hospitalizations in patients with gout were compared with those in 21.9 million hospitalizations in the general US population without gout. The most common primary cause of hospitalizations in both cohorts was septicemia (7.8% in gout vs. 7.4% in general population). Significant differences were seen in several other categories. For example, acute renal failure was twice as frequent among gout patients (39,455 hospitalizations, 4.5%) compared to the general population (458,920 hospitalizations, 2.1%) (Relative Risk (RR) 2.11, 95% CI 2.08 – 2.13, p< 0.0001). Hospitalizations for "hypertensive complications and secondary hypertension" were also higher (35,435, 4.0% in gout vs 370,400, 1.7% in general population, RR 2.35, 95% CI 2.32 – 2.37, p< 0.0001). Hospitalizations from gastrointestinal bleeding were 30% more common in gout patients, perhaps associated with concomitant NSAID treatments (Figure).

Conclusion: Among patients with gout, a far greater proportion of serious hospitalizations are related to renal and cardiovascular complications as compared to age-matched general population.

This calls for an increased awareness and management of serious co-morbid conditions in patients with gout.

Disclosure: A. Mithal, None; **M. Sehgal**, None; **G. Singh**, Horizon Pharma, 2, 5.

Abstract Number: 0338

Effect of Serum Urate Lowering with Allopurinol on Blood Pressure in Young Adults

Angelo Gaffo ,[1] David Calhoun,[2] Elizabeth Rahn,[1] Suzanne Oparil,[2] Peng Li,[2] Tanja Dudenbostel,[2] David Redden,[2] Amy Mudano,[2] Jeffrey Foster,[1] Daniel Feig,[2] Stephanie Biggers,[2] and Kenneth Saag[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham, Birmingham

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Background/Purpose: The association between serum urate and hypertension continues to be a matter of controversy. Studies in adolescents provided evidence for the efficacy of urate lowering therapy to improve early hypertension, while at least one study in adults failed to find benefit. The Serum Uric acid Reduction to Prevent HypERtension (SURPHER) study tested whether serum urate reduction with allopurinol would lead to blood pressure reductions in pre-hypertensive young adults.

Methods: Single center, double-blinded, crossover trial in which participants were randomly assigned to allopurinol (300 daily mg) or placebo for a period of one month each separated by a 2-4 week washout. Adults ages 18-40 with baseline systolic blood pressure (SBP) ≥ 120 and < 160 mm Hg or diastolic blood pressure ≥ 80 and < 100 mm Hg, and serum urate ≥ 5.0 mg/dL for men or ≥ 4.0 mg/dL for women were enrolled. Main exclusion criteria included chronic kidney disease, gout, or use of urate-lowering therapies. The primary outcome was change from study treatment period baseline (allopurinol or placebo) in SBP assessed by 24 hour ambulatory blood pressure monitoring at four time points. Missing data was handled with a multiple imputation approach. Safety assessments were conducted as part of the study.

Results: 99 participants were randomized and 73 completed study participation. The characteristics of study participants are shown in Table 1. Serum urate decreased by 1.33 ± 1.21 mg/dL during the allopurinol period (p< 0.001) and by a non-significant 0.04 ± 0.75 mg/dL while taking placebo. SBP changed by -0.71 ± 8.21 mmHg during the period assigned to allopurinol versus -0.16 ± 7.33 mmHg during the period assigned to placebo. The difference between these changes in SBP was not significant (p=0.52) (Table 2). Changes in diastolic blood pressure and mean ambulatory blood pressure also were not significantly different during allopurinol and placebo exposure periods. There was a trend to significant blood pressure decreases in the small participant subset with average serum urate of >6.5 mg/dL at the initiation of study periods (Figure). No allopurinol hypersensitivity events or other serious adverse events were observed.

Conclusion: In the intention-to-treat analysis urate-lowering therapy with allopurinol in young adults did not lead to reductions in blood pressure when compared with placebo. Blood pressure reductions were observed in participants with high baseline serum urate levels.

Table 1. Baseline characteristics of participants (n=99)

	Mean or frequency
Age (years)	28.0 ± 7.0
Gender	
Male	62 (63%)
Female	37 (37%)
Race/Ethnicity	
African American	40 (40%)
Not African American	59 (60%)
Serum urate at baseline	
Male	6.4 ± 1.0 mg/dL
Female	4.9 ± 0.7 mg/dL
Blood pressure at enrollment	
Mean Systolic (mmHg)	133.8 ± 10.0
Mean Diastolic (mmHg)	84.3 ± 8.8

Table 2. Change in blood pressure parameters during allopurinol and placebo treatment phases (n=99). Mean (SD)

Outcomes (mmHg)	Placebo	Allopurinol	p
Systolic Blood Pressure	- 0.16 (7.33)	-0.71 (8.21)	0.52
Diastolic Blood Pressure	-0.22 (5.81)	-0.28 (6.58)	0.68
Mean Arterial Pressure	-0.43 (5.63)	-0.54 (6.86)	0.54

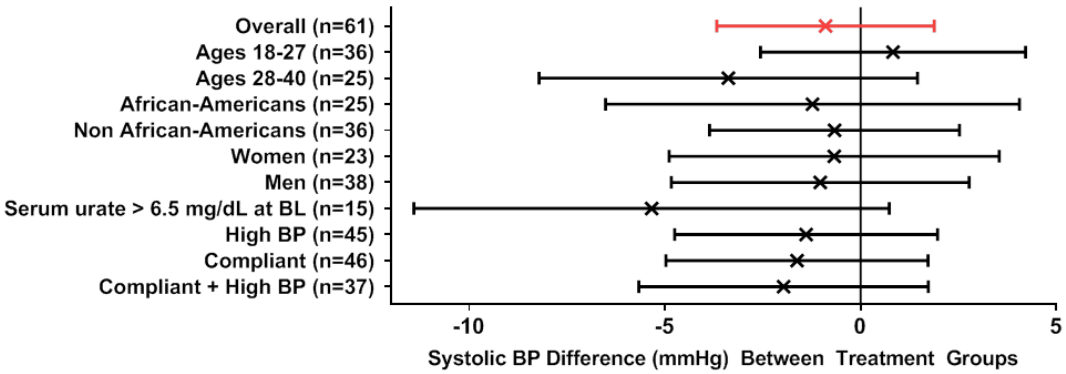

Figure. Change in systolic blood pressure between allopurinol and placebo treatment phases in selected participant subgroups. BL = average baseline at the initiation of treatment phases (allopurinol and placebo), BP= blood pressure, Compliant = any detectable oxypurinol at end of allopurinol phase

Disclosure: A. Gaffo, Amgen, 2; **D. Calhoun**, None; **E. Rahn**, None; **S. Oparil**, None; **P. Li**, None; **T. Dudenbostel**, None; **D. Redden**, None; **A. Mudano**, None; **J. Foster**, None; **D. Feig**, None; **S. Biggers**, None; **K. Saag**, Abbvie, 5, AbbVie, 5, Amgen, 2, 5, Ampel, 2, Bayer, 5, Gilead, 5, Horizon, 2, 5, Ironwood/AstraZeneca, 2, 5, Kowa, 5, kowa, 5, Mereo, 2, Radius, 5, Radius Health, 2, 5, Roche/Genentech, 5, SOBI, 2, 5, Sobi, 2, 5, Takeda, 2, 5, Teijin, 5, Tejin, 5.

Abstract Number: 0339

Depressive Symptoms Influence Success of Allopurinol in Reducing Serum Urate

Sylvie Mrug,[1] Catheryn Orihuela,[1] Elizabeth Rahn,[2] Amy Mudano,[1] Kenneth Saag,[2] Jeffrey Foster,[2] and **Angelo Gaffo** [2], [1]University of Alabama at Birmingham, Birmingham, [2]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
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Background/Purpose: Elevated levels of serum urate (sUA) are central to the pathogenesis of gout and have been associated with cardiovascular disease. Urate-lowering therapies are effective at treating gout and are being explored as novel approaches for cardiovascular disease. However, less is known about factors that influence the effectiveness of urate-lowering therapies. Depression has shown strong relationships with treatment noncompliance, which may translate into reduced effectiveness of urate-lowering therapies. This study tested the role of depressive symptoms in the effectiveness of allopurinol for lowering sUA and treatment compliance in the context of a clinical trial.

Methods: Within a larger within-subject cross-over clinical trial of allopurinol vs. placebo, 67 patients had complete data for depressive symptoms at the beginning of each treatment period, as well as sUA before and after a 4-week treatment period with allopurinol and a 4-week placebo period (order of allocation was randomized). The 67 patients had average age 27.01 years (SD=6.5, range 18-40), 39% were African-Americans and 64% were males. Depressive symptoms were assessed with the Center for Epidemiologic Studies Depression Scale (CESD) 10 tool. Treatment compliance was assessed by oxypurinol levels being present at the end of the allopurinol allocation study period. Paired samples t-test evaluated change in sUA from pre- to post-treatment during active treatment and placebo. Then, linear regressions predicted change in sUA over each treatment period from pre-treatment depressive symptoms, adjusting for sex and race which were associated with baseline sUA levels. Logistic regression predicted treatment compliance during the medication period based on the same predictors.

Results: Over the 4-week active treatment period with allopurinol, sUA levels decreased from average 5.8 mg/dL (SD=1.2) to 4.4 mg/dL (SD=1.2), p< 0.001. However, sUA did not change during the 4-week placebo period (both 5.8 mg/dL, SD=1.1 and 1.3, p=0.707). Pre-treatment depressive symptoms ranged from “no symptoms” (0) to “severe symptoms” (16 or 20), with mean in the “no to mild” range (M=4.6, SD=4.1 before active treatment; M=6.1, SD=4.8 before placebo). After adjusting for pre-treatment sUA, sex and race, pre-treatment depressive scores predicted higher levels of sUA at the end of the active treatment period (b=.07, beta=.25, p=0.028) but not at the end of the placebo period (b=.03, beta=.11, p=0.102). After 4 weeks of allopurinol, the estimated difference in sUA between individuals with pre-treatment depressive scores of 0 vs. 16 was 1.12 mg/dL, which was similar to the average treatment effect of 1.4 mg/dL. Depressive symptoms did not predict treatment compliance (OR=0.93, p=0.39), perhaps because of reduced sample size (N=55).

Conclusion: Even in the absence of clinical diagnosis of depression, depressive symptoms are associated with reduced effectiveness of allopurinol treatment for hyperuricemia in the context of a clinical trial. We could not associate this with reduced compliance, assessed by presence of measurable oxypurinol. Our findings could have implications in gout and hyperuricemia research and clinical practice.

Disclosure: S. Mrug, None; **C. Orihuela**, None; **E. Rahn**, None; **A. Mudano**, None; **K. Saag**, Abbvie, 5, AbbVie, 5, Amgen, 2, 5, Ampel, 2, Bayer, 5, Gilead, 5, Horizon, 2, 5, Ironwood/AstraZeneca, 2, 5, Kowa, 5, kowa, 5, Mereo, 2, Radius, 5, Radius Health, 2, 5, Roche/Genentech, 5, SOBI, 2, 5, Sobi, 2, 5, Takeda, 2, 5, Teijin, 5, Tejin, 5; **J. Foster**, None; **A. Gaffo**, Amgen, 2.

Abstract Number: 0340

Increased Physical Activity in Gout Patients Correlates with Better Prognosis, Decreased Pain, and Suppressed C-Reactive Protein Levels

Naomi Schlesinger ,[1] Kyle Jablonski,[2] Peter Harb,[3] Caitlin Henry,[3] Emily Schwarz,[3] Ifeoma Okafor,[3] Wael Jarjour,[4] and Nicholas Young[5], [1]Rutgers Health- RWJ Medical School, New Brunswick, NJ, [2]The Ohio State University Wexner Medical Center, Division of Immunology and Rheumatology, Columbus, [3]Ohio State College of Medicine, Columbus, [4]Ohio State College of Medicine, Columbus, OH, [5]The Ohio State University Wexner Medical Center, Division of Immunology and Rheumatology, Columbus, OH

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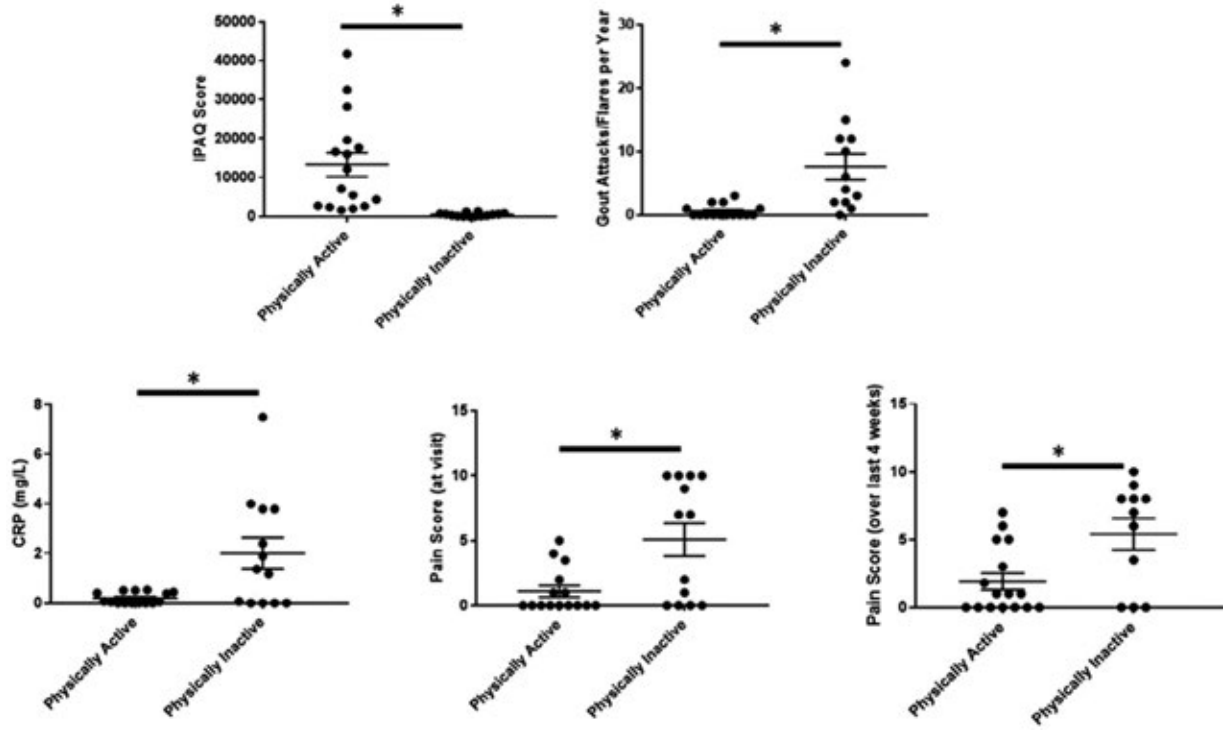

Physically active gout patients have lower C-reactive protein levels, less flares per year, and decreased pain perception compared to those that are not physically active.

Background/Purpose: Regular exercise programs were previously thought to be inappropriate in patients with rheumatic diseases because of the potential to exacerbate inflammation. However, while recent paradigm-shifting studies have demonstrated that moderate physical activity can suppress inflammatory burden in chronic disease states, the impact in patients with gout has not been studied extensively hitherto. Consequently, clinical practice guidelines for gout released by the ACR (2012) and the ACP (2017) do not even address exercise as an interventional strategy. In a mouse model of gout, we have recently demonstrated that regular low/moderate intensity exercise regimens can reduce localized MSU crystal-induced inflammation. Therefore, the objective of this study was to examine the correlation of physical activity levels with clinical data in gout patients.

Methods: During scheduled appointments, gout patients not experiencing a flare at the time of visit were recruited from our clinics and consented to participate in the study (N = 30). International physical activity questionnaires (IPAQ) were completed to access current levels of daily/weekly physical activity. Clinical data was collected during the patient visit, including BMI, age, years since diagnosis, flares per year, perceived pain at the time of visit and in the past 4 weeks, and C-reactive protein (CRP) levels. Results were analyzed with individual unpaired t-tests with Welch's correction and one-way ANOVA without Gaussian distribution and multiple comparisons to analyze the mean rank of each data set with that of every other to obtain p-values. Statistical significance was determined to be $p < 0.05$.

Results: The IPAQ survey, which has been previously used in studies of rheumatologic diseases, separated the gout patients in this study into physically active (IPAQ > 1400; N = 16) and physically inactive cohorts (IPAQ < 1400; N = 14) ($p < 0.001$). Average age, BMI, or years since diagnosis did not significantly differ between cohorts. However, physically active gout patients had 7 fewer flares per year, which corresponded to a 12-fold reduction ($p < 0.01$). Furthermore, physical activity correlated with a 10-fold decrease in CRP levels by an average of 2 mg/L ($p < 0.01$). In addition, perceived pain at the time of visit and over the past 4-week period was down 4.6-fold ($p < 0.01$) and 2.8-fold ($p < 0.05$), respectively.

Conclusion: These epidemiological and clinical data suggest that increased physical activity is beneficial in patients with gout and should be explored further as a therapeutic intervention. Regular exercise may be efficacious during intervals between flares and could function as a flare prophylaxis. While rest and decreased movement will still be recommended to a patient experiencing a gout flare, further characterization of exercise therapy may lead to a standardized exercise regimen to be performed during times of clinical inactivity and serve as part of the treatment for flare prophylaxis.

Disclosure: N. Schlesinger, amgen, 2, horizon pharma, 5, IFM Therapeutics, 5, Mallinckrodt Pharmaceuticals, 5, Novartis, 5, olatec, 5, pfizer, 2, Selecta Biosciences, 5; **K. Jablonski**, None; **P. Harb**, None; **C. Henry**, None; **E. Schwarz**, None; **I. Okafor**, None; **W. Jarjour**, None; **N. Young**, None.

Abstract Number: 0341

Development of a Multivariable Improvement Measure for Gout

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Background/Purpose: Gout is a multifactorial inflammatory disease in which patients experience a wide range of signs and symptoms, including flares, inflammatory arthritis, tophi and disability. Most assessments of gout and response to urate-lowering therapy (ULT) have focused primarily on the ability to lower serum urate and decrease the frequency of flares. Recognition that assessment of ULT and other treatments for gout could be facilitated by endpoints that more closely reflect the multidimensional impact of the disease has prompted an interest in developing composite measures, although there is no consensus on the most appropriate composite measure to employ.

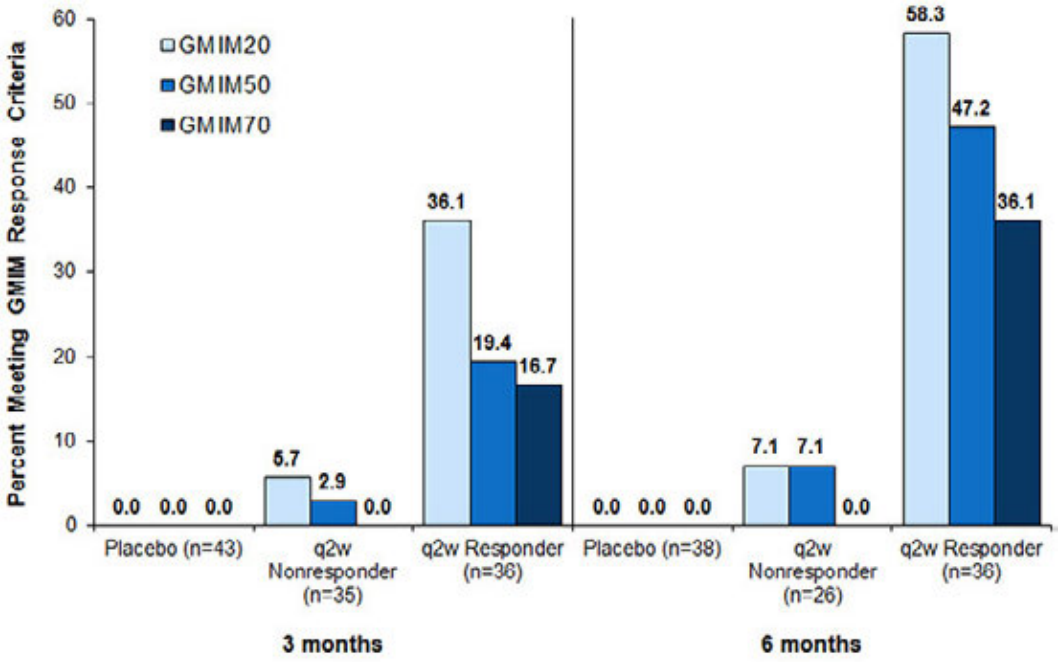

Figure 1. Percentage of subjects attaining GMIM 20/50/70 criteria

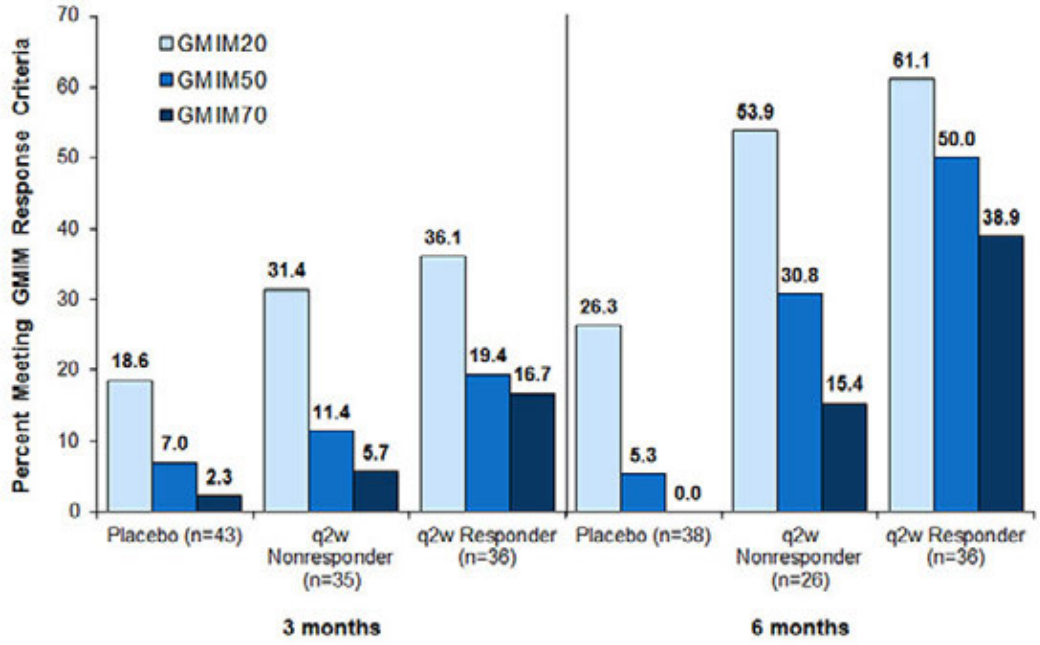

Figure 2. Percentage of subjects attaining GMIM 20/50/70 criteria omitting the requirement for urate <6mg/dL

The goal of this research was to develop an evidence-based gout multivariable improvement measure (GMIM) that captures the spectrum of gout manifestations and is sensitive to change.

Methods: Databases from patients with chronic refractory gout who participated in two randomized 6-month clinical trials (RCTs) of pegloticase were reviewed. Sub-sets who had persistent urate lowering (responders) to biweekly pegloticase (n=36) and those who had only transient urate lowering (non-responders, n=49) were identified and compared to those who received placebo (n=43). Initially individual patients were assessed for achievement of previously reported criteria for remission: serum urate < 6 mg/dL, absence of tophi and flares, patient global assessment, and pain (each < 2 on a 10-point visual analog scale). A repeated measures mixed effects model controlling for repeated observations with backward elimination using data from these patients was employed to determine the model components that best correlated with time to maximum benefit. This analysis resulted in the addition of swollen and tender joints to the outcome measure. In order to assess the degree of improvement, each subject was scored based upon a serum urate < 6 mg/dL and 20, 50 or 70% improvement in ≥4 of the 6 clinical evaluations and termed GMIM20, 50, 70.

Results: GMIM was able to capture gradation of change in the treated populations and also distinguish responses in those with persistent versus those with transient urate lowering and subjects treated with placebo (Figure 1). At 3 and 6 months, achievement of GMIM20, 50 and 70 in persistent responders occurred significantly more often vs placebo and versus non-responders without persistent urate lowering. By eliminating the requirement for urate < 6mg/dL, the improvement in clinical features could be assessed (Figure 2). Improvement greater than that noted in subjects receiving placebo could be discerned in both responders and non-responder to pegloticase. Sensitivity analysis indicated that flares and pain contributed minimally to the model.

Conclusion: GMIM effectively captures changes in disease severity in response to treatment in patients with advanced gout treated with pegloticase. GMIM20,50,70 may serve as an evidence-based tool for assessment of the quality of response to therapies in subjects with gout in medical practice or in clinical trials.

Disclosure: N. Schlesinger, amgen, 2, Astra Zeneca, 2, Horizon, 5, horizon, 5, IFM Therapeutics, 5, Mallinckrodt Pharmaceuticals, 5, Novartis, 5, olatec, 5, pfizer, 2, selecta, 5; **N. Edwards**, Astra Zeneca, 5, Horizon, 5, Ironwood Pharmaceuticals, 5, Selecta, 5; **A. Yeo**, Horizon, 3; **P. Lipsky**, Horizon, 5, Janssen Research & Development, LLC, 2.

Abstract Number: 0342

Rheumatologist Care Is Associated with Fewer Emergency Room Visits by Persons with Gout

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Background/Purpose: Gout is one of the most common inflammatory arthropathies, although care of gout patients is not always optimal. By searching a large administrative data base (Symphony Integrated Dataverse), we found

that persons with acute gout see a rheumatologist infrequently, whereas those with advanced gout are seen by a rheumatologist more often, but still less than 50% of advanced gout patients are seen by a rheumatologist. Notably, however, gout patients seen by rheumatologists have more frequent urate measurements and are prescribed urate lowering therapy more frequently. The objectives of this study were to validate these results using an additional administrative data base and also to determine whether involvement of a rheumatologist in gout care had a positive impact on health outcomes.

Methods: We carried out a retrospective analysis to identify persons with gout over an approximately 3-year period from October 2015 to December 2018. This study used data from the Truven Marketscan® database, an administrative database covering over 190 million patients across the United States and based on fully adjudicated and paid insurance claims. Patients were identified as having gout if they were >18 years of age and had at least two medical claims for the diagnosis of gout on different days, separated by at least 3 months. Patients with acute gout were identified by ICD-10 code M10.*, chronic nontophaceous gout (M1A.***0), tophaceous gout (M1A.***1) and uncontrolled gout (M10.*, M1A.*), the latter manifested by three gout codes (any) in the primary diagnosis position and three urate measurements within the same calendar year. Particular attention was placed on Emergency Room (ER) visits by individuals in each category and by individuals who had been evaluated by a rheumatologist.

Results: We identified 284,877 gout patients. The median age was 59.2 years and 79.0% were male. Of the 230,998 persons coded as acute gout, 10.7% were seen by a rheumatologist, whereas 26.9% of the 32,942 coded as chronic nontophaceous gout, 47.2% of the 7,723 coded as tophaceous gout and 43.6% of the13,514 coded as uncontrolled gout were seen by a rheumatologist. In each gout category, the frequency of ER visits was significantly reduced in persons who had been seen by a rheumatologist. In acute gout, the frequencies of ER visits in those with and without rheumatologist care were 5.6% vs 6.6% ($p< 0.001$), respectively. In chronic nontophaceous gout it was 5.5% vs 6.7% ($p=0.001$); in tophaceous gout it was 10.3% vs 14.7% ($p< 0.001$); and in uncontrolled gout it was 12.8% vs 19.0%, respectively. If the frequencies of rheumatologist-associated gout patient ER visits were applied to all gout subjects, there would have been 3,088 less ER visits in this cohort of gout patients.

Conclusion: Most subjects with acute gout are not seen by a rheumatologist and only about half of those with advanced gout encounter a rheumatologist. However, there appears to be a positive impact of rheumatologist care, manifested by a significant decrease in the frequency of ER visits. Considering the inconvenience and cost of ER visits, rheumatologist care may have a significant impact on the well-being of gout patients and on the overall cost of their care.

Disclosure: N. Schlesinger, amgen, 2, Astra Zeneca, 2, Horizon, 5, horizon, 5, IFM Therapeutics, 5, Mallinckrodt Pharmaceuticals, 5, Novartis, 5, olatec, 5, pfizer, 2, selecta, 5; **N. Edwards**, Astra Zeneca, 5, Horizon, 5, Ironwood Pharmaceuticals, 5, Selecta, 5; **S. Clark**, None; **P. Lipsky**, Horizon, 5, Janssen Research & Development, LLC, 2.

Abstract Number: 0343

Emergency Department Length of Stay in Patients with Acute Gout

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical

Session Type: Poster Session (Sunday)

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Background/Purpose: Emergency department (ED) visits for acute gout increased by approximately 20% between 2006 and 2014 in the United States. (1) Reducing ED length of stay (LOS) can help reduce ED crowding and cost of care for gout patients. The aim of our study was to assess ED LOS and to identify factors associated with prolonged ED LOS in patients with acute gout.

Methods: In this retrospective analysis, we included the first ED visit of adult patients (>18 years) with acute gout who presented to the 3 EDs affiliated with Lifespan Health Systems, the largest healthcare provider in Rhode Island. The study period was between 3/30/2015 and 9/30/2017. We calculated ED LOS as the time spent by patients in the ED until they were discharged. Patients presenting to the ED and subsequently admitted to the hospital were excluded given the differential effect of systems factors in these patients. We assessed the following factors' association with being in the upper quartile of ED LOS: (a) patient factors – demographics, comorbidities and clinical presentation of gout (number of joints involved, severity as gauged by an ED triage nurse on a scale of 1 to 5; 1 being the worst) and (b) systems factors – time of day, day of the week, and time of year at presentation to the ED, and teaching versus non-teaching hospital setting. We performed univariate and multivariable analyses.

Table 1. factors associated with longer ED length of stay for patients with acute gout

	< 4.3 hours in ED (n = 265)	> 4.3 hours in ED (n = 90)
Patient factors		
Age < 65	185/265 (69.8%)	51/90 (56.7%)
Male gender	213/264 (80.7%)	75/90 (83.3%)
Comorbidities		
Diabetes	68/228 (29.8%)	29/76 (38.2%)
Hyperlipidemia	132/228 (57.9%)	53/76 (69.7%)
History of gout	160/228 (70.2%)	54/76 (71.1%)
Hypertension*	162/228 (71.1%)	65/76 (85.5%)
Coronary artery disease	49/228 (21.5%)	21/76 (27.6%)
Heart failure*	32/228 (14.0%)	26/76 (34.2%)
Chronic kidney disease	44/228 (19.3%)	21/76 (27.6%)
Cerebrovascular disease	19/228 (8.3%)	4/76 (5.3%)
Other inflammatory arthritis	10/228 (4.4%)	3/76 (4.0%)
Clinical presentation of gout		
Oligo/polyarticular gout	33/265 (12.4%)	13/90 (14.4%)
Arthrocentesis*	21/265 (7.9%)	51/90 (56.7%)
ED Severity Score*		
Score 2 and 3	117/265 (44.1%)	67/90 (74.4%)
Score 4 and 5	148/265 (55.8%)	23/90 (25.6%)
Systems factors		
Type of Hospital*		
Academic center	204/265 (77%)	82/90 (91.1%)
Community center	61/265 (23%)	8/90 (8.9%)
Time of Day		
Time of day (12 AM – 8 AM)	52/265 (19.6%)	20/90 (22.2%)
Time of day (8 AM – 12 PM)	124/265 (46.8%)	51/90 (56.7%)
Time of day (12 PM – 12 AM)	89/265 (33.6%)	19/90 (21.1%)
Time of Year		
January to March	43/265 (16.2%)	21/90 (23.3%)
April to June	94/265 (35.5%)	28/90 (31.1%)
July to September	78/265 (29.4%)	19/90 (21.1%)
October to December	50/265 (18.9%)	22/90 (24.2%)
Weekend presentation	94/265 (35.5%)	24/90 (26.7%)

*Represents statistically significant results (p <0.05)

Results: A total of 355 patients (mean age 56.6 ± 16.03 years, 81.3% males) were included. The median ED LOS was 2.65 hours (1.75, 4.3 hours). In the univariate analysis, older age (> 65 years), comorbidities (hypertension, congestive heart failure) and worse ED severity score among patient factors and being treated at a teaching hospital ED among systems factors were associated with being in the upper quartile of ED LOS. Performing arthrocentesis was also associated with being in the upper quartile of ED LOS (Table 1). In a multivariable analysis, age > 65 years, performing arthrocentesis, and worse acuity score continued to be associated with longer ED LOS.

Conclusion: In our study settings, patients with acute gout spent a longer time in the ED than the national median of 120-150 minutes. (2) We noted that older age and higher acuity score in addition to procedural delays led to longer length of stay in the ED.

References:

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2. Centers for Disease Control and Prevention. (2014). QuickStats: median emergency department (ED) wait and treatment times, by triage level–National Hospital Ambulatory Medical Care Survey, United States, 2010-2011. *Morb Mortal Wkly Rep*, *63*, 439. (https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6319a8.htm)

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Abstract Number: 0344

Factors Associated with the Disappearance of Calcifications Following Ultrasound Guided Percutaneous Lavage of Rotator Cuff Calcific Tendinopathy: A Post Hoc Analysis of a Randomized Controlled Trial

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SESSION INFORMATION

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Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical

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Background/Purpose: Rotator cuff calcific tendinopathy is a common condition causing up to 20% of the painful shoulder. Ultrasound guided percutaneous lavage (UGPL) is indicated after failure of conservative treatments. We have shown that this treatment led to clinical improvement and complete resorption of the calcification in 43 % of the patients at 3 months (1). However, it is currently unclear if the baseline characteristics of the calcification or the success of the procedure (withdrawal of calcium) are associated with the disappearance of the calcific deposit. The goal of this post-hoc analysis was to find characteristics associated with the resorption of the calcific deposit 3 months after UGPL.

Table 1.

	Disappearance (n=53)	Persistance (n=70)	p
Age, years, mean	49,5	50,6	NS
Sexe (F/M), n	39/14	43/27	NS
Symptoms duration (years), mean	2,6	2,7	NS
Nocturnal pain, n (%)	44 (83%)	56 (80%)	NS
Baseline VAS at rest, mm, mean	30,1	30	NS
Baseline VAS during activities, mm, mean	72,7	66,4	0,007
Maximum size (mm), mean	16,1	15,3	NS
Calcification > 2cm, n (%)	17 (32%)	20 (28,6%)	NS
X-Ray Calcification type (A/B)	25/27	23/47	NS
Doppler signal on ultrasound, n (%)	14(26%)	11 (15,7%)	NS
Calcium extraction, n (%)	48 (90.6%)	53 (75%)	0,033
Large amount extracted, n (%)	33 (62%)	36 (51%)	NS
Communication SAB and calcifc deposit, n (%)	37 (69%)	31 (45%)	0,008
Hard calcification, n (%)	12 (23%)	36 (51%)	0,002
Blurred aspect on X-Ray at day 7, n (%)	30 (63%)	19 (27,5%)	<0.001
Day 7 VAS at rest, mean	14,5	15,8	NS
Day 7 VAS during activities, mean	35,7	31	NS

Methods: This was a post-hoc analysis of a multicentric prospective double blinded randomized controlled study (1). Patients with shoulder pain for more than 3 months and a type A (dense) or B (split/separated with clear contours) calcification > 5 mm on X-Ray were included. Patients were treated with UGPL using a single needle technic. X-Ray was performed at 3 months and resorption of the calcific deposit defined as more than 90% of decrease of size or complete disappearance of the calcific deposit. Clinical, radiological and procedure characteristics was compared between patient with or without resorption. Multivariate logistic regression was performed to identify baseline and procedure characteristics associated with the disappearance of the calcific deposit.

Results: 134 patients were included in the study, mean age 49.8 (+/-9.7) years, 89 were females (67.4%). X-Ray at 3 months were available for 123 patients. At this time point 53 (43%) of the patients had more than 90% decrease or complete disappearance of their calcification. Baseline and procedure characteristics of the 2 groups are summarized in table 1. None of the baseline radiological characteristics were significantly different between the 2 groups (size of the calcific deposit (even calcification more than 2 cm wide) or radiologic type). Baseline pain at activity was the only clinical variable higher in patients that had resorption of their calcification. Consistence of the calcification during the procedure, the possibility of calcium extraction and the presence of a communication between the calcification and the sub-acromial bursa (SAB) at the end of the procedure were all associated with the calcific disappearance. However, no difference was found according to the amount of calcium extracted. Finally, blurred aspect of the calcification at 7 days but not pain at this time point was associated with resorption. In multivariate logistic regression, we found that only the pain during activity (p=0.046) at baseline and the communication between the subacromial bursa (p=0.046) remains significant.

Conclusion: Disappearance of the calcification after UGPL occurs more frequently in patients in which a communication can be created between the calcification and the SAB, leading to the migration of the calcium deposit and its resorption. Importantly nor the size of the calcification neither the radiological aspect seemed important showing that UGPL can be offered to any patients with symptomatic calcific tendonitis.

Reference

1. Darrieutort-Laffite at al., Ann Rheum Dis, 2019

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Abstract Number: 0345

Associations of Serum Uric Acid with Cardiovascular Disease Risk: Data from the Korea National Health and Nutrition Examination Survey

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
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Background/Purpose: The cardiovascular risk of gout is already well known, and the debate over the cardiovascular risk of uric acid lower agents is currently hot. Although hyperuricemia has been reported to be associated with a higher cardiovascular risk, it is not yet conclusive and guidelines for the management in patients with hyperuricemia are still lacking. We investigated associations of serum uric acid level with cardiovascular disease (CVD) risk in general population.

Methods: We examined data from a survey conducted during the first and second years of the seventh Korea National Health and Nutrition Examination Survey (KNHANES,2016-2017). We included subjects who were aged from 30 to 74 years without prevalent CVD. We estimated CVD risk by 10-year CVD risk score prediction formula. Fractional polynomial model was chosen to estimate relationship of serum uric acid, physical activity, and BMI with 10-year CVD risk score.

Results: There was no significant difference of 10-year CVD risk score in men by serum uric acid level, but there was significant difference in women. In the fitted fractional polynomial model, an approximate U-shaped association between serum uric acid level and 10-year CVD risk score with an inflection point at 6.9 mg/dL of serum uric acid level in men was found. An approximate J-shaped association between serum uric acid level and 10-year CVD risk score in women was found.

Table 1. Associations of serum uric acid, physical activity and body mass index with 10-year cardiovascular disease risk by gender

Parameter	Men			Women		
	β-coefficient	SE	*p* value	β-coefficient	SE	*p* value
Serum uric acid #1	-0.241	0.033	< 0.001	0.075	0.013	< 0.001
Serum uric acid #2	0.023	0.031	< 0.001			
Aerobic physical activity	-1.071	0.214	< 0.001	-0.834	0.172	< 0.001
Muscular strength exercise	0.432	0.234	0.066	0.039	0.214	0.854
Body mass index	0.146	0.032	< 0.001	0.505	0.030	< 0.001

There was no significant difference of 10-year CVD risk score in men by serum uric acid level, but there was significant difference in women. In the fitted fractional polynomial model, an approximate U-shaped association between serum uric acid level and 10-year CVD risk score with an inflection point at 6.9 mg/dL of serum uric acid level in men was found. An approximate J-shaped association between serum uric acid level and 10-year CVD risk score in women was found.

Conclusion: Our study showed that hyperuricemia is associated with increased CVD risk, hypouricemia is also associated with increased CVD risk in men and practicing aerobic physical activity and lower BMI is associated with reduced CVD risk.

Disclosure: K. Jung, None; **S. Lee**, None; **W. Park**, None; **Y. Suh**, None; **M. Lim**, None; **S. Kwon**, None; **J. Lee**, None; **Y. Joo**, None.

Abstract Number: 0346

Subtypes of Gout Based on Comorbidity Patterns Among Black Patients in the US General Population - Cluster Analysis of the National Health and Nutrition Examination Survey 2007-2016

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Gout is a very prevalent condition associated with many metabolic and cardiorenal comorbidities. A few studies have investigated the comorbidity subtypes of gout patients by cluster analyses; however, such analyses have not yet been performed among Blacks nor confirmed in a general population cohort. As such the generalizability of these findings remains unknown. Thus, our objective was to identify gout subtypes based on comorbidities using cluster analysis among Black adults with gout in the US general population. Furthermore, we sought to compare these findings to that of White adults with gout.

Methods: We used data from 371 Black and 656 White participants in the 2007-2016 cycle of the National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of adults in the US with detailed clinical and physical examination data. Diagnosis of gout was based on survey of physician- or health professional-diagnosed gout. We employed Ward's minimum variance method of clustering to group patients with gout into clusters (i.e., subtypes) based on distinct comorbidity patterns according to 8 variables: obesity, hypertension, diabetes, dyslipidemia (i.e., hypercholesterolemia and/or hypertriglyceridemia), coronary heart disease (CHD), heart failure (HF), chronic kidney disease (CKD), and non-alcoholic fatty liver disease (NAFLD).

Results: Metabolic and cardiorenal comorbidities were prevalent among both Black and White participants with gout (**Table 1**). Cluster analysis identified 5 comorbidity subgroups among Black patients with gout (**Table 2**). All patients in Group 1 had dyslipidemia and hypertension. Group 2 had the highest proportion of patients with diabetes (95%), and nearly all patients with NAFLD belonged to this group. Group 3 consisted of patients with gout but few

other comorbidities. All patients in Group 4 had CKD. Group 5 had the highest proportion of patients with CHD and HF. Cluster analysis among Whites also identified subgroups with isolated gout (Group 2) and dyslipidemia and hypertension (Group 1) (**Table 3**). It also identified a subgroup that combined cardiac and renal disease (Group 5). Key differences among Whites was the presence of obese (Group 3) and hypertension only (Group 4) clusters, and the lack of a diabetes group. The higher prevalence of obesity in Blacks and the smaller number of Black participants likely contributed to these differences.

Conclusion: These findings from a nationally representative sample of Black US adults identified 5 subgroups of gout based on comorbidities: dyslipidemia/HTN, diabetes, isolated gout, CKD, and heart disease. Notable differences from the European population and American White cohorts included the separation of CKD and cardiac disease

Table 1: Characteristics of Patients with Gout

Characteristics	Blacks (n=371)	Whites (n=656)
Demographics		
Age, years (SD)	66.1 (13.7)	63.2 (12.0)
Number Missing	0	0
Body Mass Index, kg/m^2 (SD)	33.1 (8.2)	31.4 (6.8)
Number Missing	24	36
Comorbidities		
Obesity (%)	213 (57.4)	321 (48.9)
Number Missing	24	36
Hypertension (%)	200 (53.9)	243 (37.0)
Number Missing	45	193
Diabetes (%)	195 (52.6)	236 (36.0)
Number Missing	0	0
Dyslipidemia (%)	251 (67.7)	508 (77.4)
Number Missing	31	19
Hypercholesterolemia (%)	242 (65.2)	483 (73.6)
Number Missing	47	35
Hypertriglyceridemia (%)	31 (8.4)	140 (21.3)
Number Missing	64	44
Metabolic Syndrome (%)	212 (57.1)	401 (61.1)
Number Missing	141	222
Coronary Heart Disease (%)	38 (10.2)	108 (16.5)
Number Missing	2	7
Heart Failure (%)	71 (19.1)	98 (14.9)
Number Missing	5	1
Cerebrovascular Disease (%)	46 (12.4)	81 (12.4)
Number Missing	0	1
Chronic Kidney Disease (%)	49 (13.2)	182 (27.7)
Number Missing	161	44
Nephrolithiasis (%)	33 (8.9)	143 (21.8)
Number Missing	0	1
Non-Alcoholic Fatty Liver Disease (%)	14 (3.8)	44 (6.7)
Number Missing	236	354
Malignancy (%)	61 (16.4)	182 (27.7)
Number Missing	0	1

Table 2: Subgroups of Black Patients with Gout Based on Comorbidities

Characteristics	Group 1 (n = 66)	Group 2 (n = 96)	Group 3 (n = 103)	Group 4 (n = 41)	Group 5 (n = 65)
Demographics					
Age, years (SD)	62 (12)	64 (11)	60 (14)	68 (9)	66 (11)
Male gender, n (%)	44 (67)	55 (57)	64 (62)	41 (100)	38 (59)
Body Mass Index, kg/m^2 (SD)	32 (7)	35 (10)	32 (7)	30 (6)	37 (10)
Increased Abdominal Circumference, n (%)	53 (80)	79 (82)	74 (72)	31 (76)	43 (66)
Comorbidities, n (%)					
Obesity	32 (49)	65 (68)	53 (52)	18 (44)	45 (69)
Hypertension	**66 (100)**	94 (98)	65 (63)	41 (100)	64 (99)
Diabetes	0 (0)	**91 (95)**	35 (34)	26 (63)	43 (66)
Dyslipidemia	**66 (100)**	90 (94)	19 (19)	29 (71)	47 (72)
Hypercholesterolemia	**62 (94)**	88 (92)	19 (19)	28 (68)	45 (69)
Hypertriglyceridemia	**10 (15)**	11 (12)	2 (2)	3 (7)	5 (8)
Non-Alcoholic Fatty Liver Disease	0 (0)	**12 (13)**	1 (1)	0 (0)	1 (2)
Coronary Heart Disease	0 (0)	0 (0)	1 (1)	1 (2)	**36 (55)**
Heart Failure	0 (0)	12 (13)	1 (1)	8 (20)	**50 (77)**
Stroke	8 (12)	10 (10)	11 (11)	7 (17)	10 (15)
Chronic Kidney Disease	0 (0)	0 (0)	0 (0)	**41 (100)**	8 (12)
Malignancy	11 (17)	19 (20)	11 (11)	9 (22)	11 (17)

and the absence of a group defined by obesity among US Blacks. Overall, these subgroups could be broadly classified as i) isolated gout, ii) dyslipidemia/hypertension, iii) obese or diabetes, and iv) cardiorenal disease (separately or together). These subgroups may shed light on pathophysiologic mechanisms that contribute to gout and have implications for personalized interventions to reduce the burden of gout and its comorbidities.

Table 3: Subgroups of White Patients with Gout Based on Comorbidities

Characteristics	Group 1 (n = 139)	Group 2 (n = 116)	Group 3 (n = 178)	Group 4 (n = 87)	Group 5 (n = 136)
Demographics					
Age, years (SD)	72 (10)	59 (14)	62 (14)	65 (15)	72 (9)
Male gender, n (%)	92 (66)	76 (72)	126 (71)	60 (69)	97 (71)
Body Mass Index, kg/m^2 (SD)	27 (2)	30 (6)	36 (7)	31 (7)	32 (7)
Increased Abdominal Circumference, n (%)	104 (75)	96 (83)	164 (92)	65 (75)	105 (77)
Comorbidities, n (%)					
Obesity	0 (0)	47 (41)	**159 (89)**	37 (43)	78 (57)
Hypertension	**127 (91)**	0 (0)	160 (90)	**81 (93)**	117 (86)
Diabetes	53 (38)	19 (16)	75 (42)	25 (29)	64 (47)
Dyslipidemia	**137 (99)**	90 (78)	167 (94)	0 (0)	114 (84)
Hypercholesterolemia	**136 (98)**	85 (73)	149 (84)	0 (0)	113 (83)
Hypertriglyceridemia	**19 (14)**	29 (25)	66 (37)	0 (0)	26 (19)
Non-Alcoholic Fatty Liver Disease	0	0	41 (23)	0 (0)	3 (2)
Coronary Heart Disease	1 (0.7)	5 (4)	4 (2)	0 (0)	**98 (72)**
Heart Failure	15 (11)	1 (0.9)	2 (1)	2 (2)	**78 (57)**
Stroke	20 (14)	3 (3)	20 (11)	8 (9)	30 (22)
Chronic Kidney Disease	56 (40)	0 (0)	46 (26)	25 (29)	55 (40)
Malignancy	47 (34)	27 (23)	51 (29)	18 (21)	39 (29)

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Abstract Number: 0347

Patterns and Clinico-Radiological Correlates of Symptomatic Atlantoaxial Joint Involvement in Patients with Calcium Pyrophosphate Deposition Disease

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SESSION INFORMATION

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Background/Purpose: Atlantoaxial joint involvement in calcium pyrophosphate deposition disease (CPPD) may present as crowned dens syndrome (CDS), a clinico-radiological tetrad defined as the presence of periodontoid calcifications, acute cervical pain with neck stiffness, fever, and raised inflammatory markers. Though 40-60% of CPPD patients exhibit periodontoid calcifications, only a small percentage develop CDS. Risk factors associated with CDS development in these patients remain unknown. The purpose of this study was to identify differences between symptomatic and asymptomatic CPPD patients with periodontoid calcifications.

Methods: Single-center cross-sectional analysis of CPPD patients with periodontoid calcifications identified by cervical or head CT done for various unrelated reasons. All the analyses were performed using STATA 14.2.

Results: Forty-one patients with CPPD and periodontoid calcifications were identified. Median age at diagnosis was 78 years (73-83) and 26 (63.4%) were female. Peripheral arthritis was present in 27 patients (65.9%) as monoarthritis

Patients with symptomatic atlantoaxial joint involvement	n=25
Symptoms at presentation	
CDS - acute cervical pain with neck stiffness, fever, and raised inflammatory markers, n (%)	2 (8.0%)
Incomplete CDS - acute cervical pain with raised inflammatory markers, without fever or neck stiffness, n (%)	9 (36.0%)
Fever of unknown origin, n (%)	1 (4.0%)
Polymyalgia rheumatica-like, n (%)	6 (24.0%)
Chronic neck pain, n (%)	6 (24.0%)
Retrodontoid pseudotumor with tetraparesis, n (%)	1 (4.0%)
Fever, n (%)	6 (24.0%)
Raised inflammatory markers, n (%)	14 (56.0%)
Median ESR - mm/h (IQ)	72 (48 – 110)
Median CRP - mg/dL (IQ)	6.9 (2.4 – 16.3)

Table 1. Clinico-laboratorial presentation of symptomatic atlantoaxial joint involvement

Variable	Asymptomatic (n=16)	Symptomatic (n=25)	p-value
Median age (IQ)	79 (73-82)	78 (67-83)	0.544
Male gender, n (%)	7 (43.8%)	8 (32.0%)	0.517
Presence of peripheral arthritis, n (%)	12 (75.0%)	15 (60.0%)	0.501
Monoarthritis, n (%)	7/12 (58.3%)	1/15 (6.7%)	0.008
Oligo/polyarthritis, n (%)	5/12 (41.7%)	14/15 (93.3%)	0.008
CT findings			
Transverse (cruciform) ligament calcifications, n (%)	16 (100%)	23 (92.0%)	0.512
Apical and/or alar ligament calcifications, n (%)	4 (25.0%)	16 (64.0%)	0.025
C1 erosions, n (%)	1 (6.3%)	4 (16.0%)	0.632
C1-C2 subluxation, n (%)	0	1 (4.0%)	N.A.
Transverse ligament involvement stage			
Stage 1, n (%)	2 (12.5%)	6 (24.0%)	0.468
Stage 2, n (%)	10 (62.5%)	13 (52.0%)	
Stage 3, n (%)	4 (25.0%)	4 (16.0%)	
Stage 4, n (%)	0	2 (8.0%)	

Table 2. Comparative analysis between patients with asymptomatic versus symptomatic periodontoid calcifications

(8), oligoarthritis (11), or polyarthritis (8). All patients had radiographic chondrocalcinosis at other sites. Metabolic changes were present in 20 patients (48.8%): low 25(OH)D (17), hyperparathyroidism (9), hypomagnesemia (2), and hypophosphatemia (1). Eleven patients had chronic kidney disease (26.8%). Periodontoid calcifications were documented at the transverse (cruciform) ligament in 39 patients (95.1%), alar ligaments in 19 (46.3%), and apical ligament in 6 (14.6%). CT staging of the transverse ligament changes identified curvilinear deposits (>1mm) in a single band (stage 2) in 23 patients (56.1%).

Twenty-five patients (61.0%) had symptomatic atlantoaxial joint involvement (Table 1). All symptomatic patients were treated with a combination of colchicine (16; 64.0%), NSAIDs (13; 52.0%), and/or systemic corticosteroids (13; 52.0%). Four patients (16.0%) with peripheral polyarthritis were treated with methotrexate.

Comparative analysis (Table 2) showed that, in patients with peripheral arthritis, monoarthritis was more frequent in patients with asymptomatic periodontoid calcifications and oligo/polyarthritis was more common in patients with symptomatic disease. Apical and/or alar ligament calcifications were more frequent in patient with symptomatic atlantoaxial joint involvement.

Conclusion: Atlantoaxial joint involvement in CPPD is heterogeneous, classical CDS being uncommon. The pattern of peripheral arthritis and ligament calcification is associated with the presence of symptoms in CPPD patients with periodontoid calcifications.

Disclosure: J. Silva-Dinis, None; **C. Tenazinha**, None; **N. Khmelinskii**, None; **V. Teixeira**, None; **P. Ávila-Ribeiro**, None; **J. Eurico Fonseca**, None; **J. Romeu**, None.

Abstract Number: 0348

Patterns of Newer Gout Medication Use in a U.S. Electronic Health Record-Based Registry

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A variety of newer gout therapies have been introduced in recent years, some with potential safety concerns. However, uptake of these therapies and associated dose/duration of use is not clear. We used the American College of Rheumatology's electronic health record-based registry (RISE) to examine patterns of gout drug use over time.

Methods: We used RISE data to identify gout patients by ICD9/10 diagnosis (ICD9: 274.*; ICD10: M10.*, M1A.*) with at least one physician visit in 2016, excluding patients with diagnoses for other types of inflammatory arthritis. Gout medications were identified based on written prescriptions and infusion orders and classified in the following hierarchy so as to assign uniquely: pegloticase, lesinurad, febuxostat, allopurinol, and probenecid. Baseline characteristics including demographics, comorbidities, serum uric acid, and estimated glomerular filtration rate (eGFR) were classified on the date of initiation or using the most recent preceding value. Descriptive characteristics compared initiators of various gout drugs over calendar time 2015-2018.

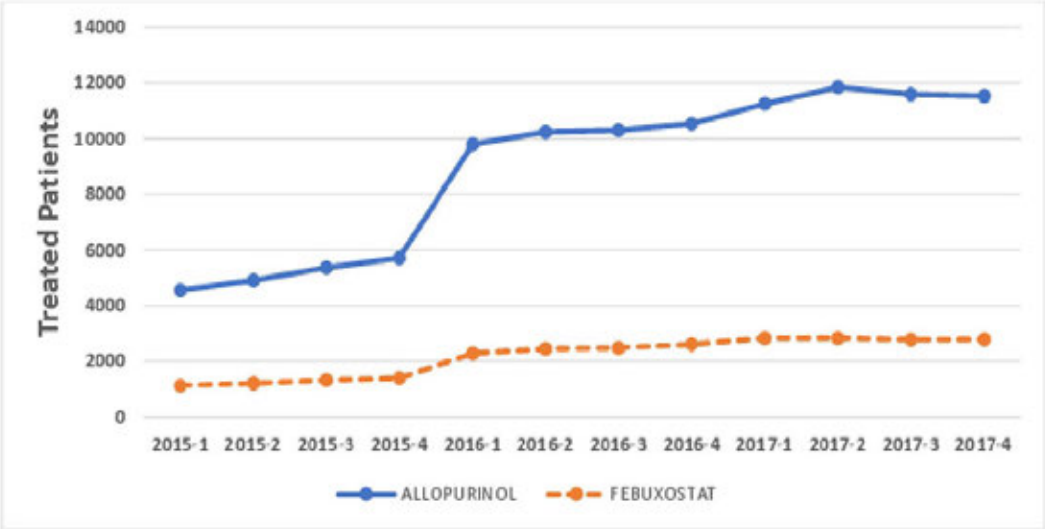

Figure 1. Use of Allopurinol and Febuxostat Over Time in RISE

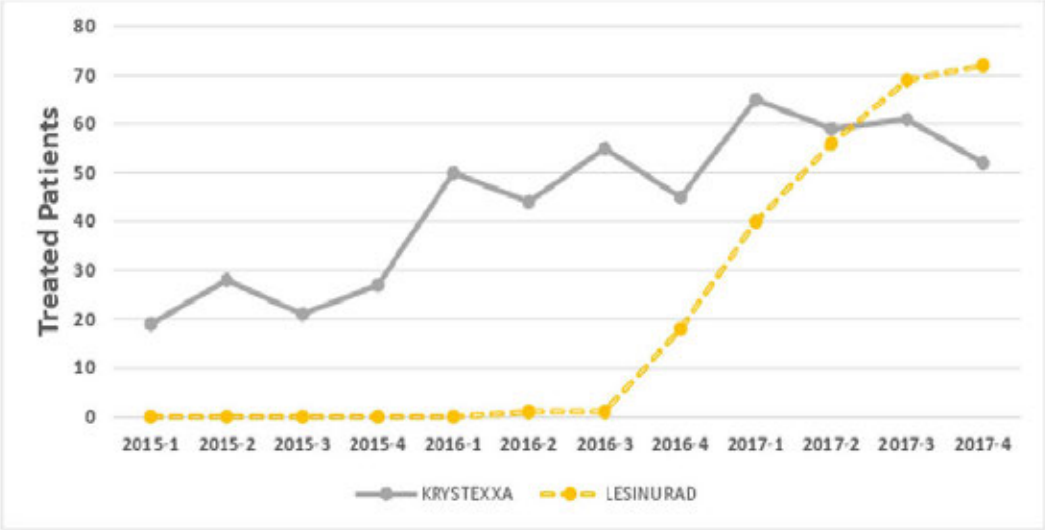

Figure 2. Use of Pegloticase and Lesinurad Over Time in RISE

Results: Patterns of gout drug use are shown in Figures 1 and 2. Allopurinol was the most common drug used, followed by febuxostat. Krystexa and lesinurad were used much less frequently, approximately 1/200 of allopurinol use. In total, 338 patients received pegloticase, prescribed by approximately 150 unique clinicians. Of these, 53% of patients receive only 1 pegloticase dose. For those who received more than 1 dose, the median (IQR) duration of treatment was 105 (24, 294) days.

Overall a total of 19,763 met eligibility criteria for the gout cohort. Mean [SD] age was highest in the febuxostat group: 64 [14] years compared to allopurinol (63 [14]) and pegloticase (61 [16]). Black race was most common in the febuxostat group (12.3%) and lowest in allopurinol (7.8%). Febuxostat-treated patients had a higher prevalence of coronary atherosclerosis (4.8%) vs. allopurinol users (2.8%), and chronic kidney disease was more common in febuxostat patients (median eGFR 57 ml/min) vs. allopurinol patients (68 ml/min). NSAIDs were used by approximately one-third of allopurinol (36%) and febuxostat (31%) users and more than half (56%) of pegloticase patients. Colchicine was used even more frequently (allopurinol: 50%; febuxostat: 59%; pegloticase: 83%). Opioids were commonly used as concomitant treatment: 24%, allopurinol; 32%, febuxostat; and 40%, pegloticase.

Conclusion: The EHR-based ACR RISE registry appears useful to examine prescribing trends for gout medication use, even for relatively uncommonly used therapies. Febuxostat users had a higher prevalence of cardiovascular-related comorbidities compared to allopurinol users, inviting caution in the selection of patients to receive this therapy given recent FDA warnings.

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

Disclosure: K. Saag, Abbvie, 5, AbbVie, 5, Amgen, 2, 5, Ampel, 2, Bayer, 5, Gilead, 5, Horizon, 2, 5, Ironwood/AstraZeneca, 2, 5, Kowa, 5, kowa, 5, Mereo, 2, Radius, 5, Radius Health, 2, 5, Roche/Genentech, 5, SOBI, 2, 5, Sobi, 2, 5, Takeda, 2, 5, Teijin, 5, Tejin, 5; **A. Reimold**, None; **L. Chen**, None; **H. Yun**, BMS, 2, Bristol-Myers Squibb, 2, Pfizer, 2; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5.

Abstract Number: 0349

Carotid Atherosclerosis and Sonographic Signs of Urate Crystal Deposits in Patients with Gout: An Association Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Carotid subclinical atherosclerosis is prevalent in patients with gout, although poorly predicted by cardiovascular risk assessment tools. Gout itself is deemed to contribute to its development. However, a previous report did not show association between clinical characteristics of gout and the presence of subclinical atherosclerosis [Ann Rheum Dis. 76:1263]. The aim of this study was to explore the association between sonographic signs of urate crystal deposits and carotid atherosclerosis.

Methods: Consecutive new patients with crystal-proven gout attended in a tertiary Rheumatology unit were eligible for the study. This included musculoskeletal and carotid ultrasound assessment, performed by a trained sonographer blinded to clinical data. Patients were examined during intercritical periods; flare prophylaxis with low-dose colchicine or other agents was permitted, but patients under urate-lowering treatment were excluded. The musculoskeletal scans evaluated wrists, 2nd MCPs and 1st MTPs joints, and triceps and patellar tendons, for the presence of signs suggestive of urate crystal deposits (double contour, hyperechoic aggregates, and tophi), following OMERACT definitions. Also, local power-Doppler (PD) signal was registered and graded as 0 to 3. The sum of locations showing crystal deposits or positive PD signal (≥1) was chosen to assess the crystal and inflammatory burden, respectively. Carotid arteries were scanned for increased intima-media thickness (IMT) and presence of atheroma plaques, according to Mannheim consensus. The association analysis was done by logistic regression, considering increased IMT or atheroma plaques as the independent variable.

Table 1. Results of the association analysis by simple logistic regression.

	Increased IMT		Atheroma plaques	
	OR (95%CI)	p	OR (95%CI)	p
Sum of locations with deposits	1.03 (0.90-1.19)	0.653	1.05 (0.93-1.19)	0.436
Sum of locations with DC	0.92 (0.51-1.65)	0.778	0.87 (0.55-1.39)	0.556
Sum of locations with HA	0.95 (0.77-1.17)	0.620	0.98 (0.83-1.16)	0.785
Sum of locations with tophi	1.26 (0.95-1.67)	0.108	1.27 (1.00-1.60)	0.047
Sum of locations with positive PD	0.85 (0.48-1.52)	0.591	1.93 (1.12-3.34)	0.019

95%CI: 95% confidence interval; DC: double-contour; HA: hyperechoic aggregates; IMT: intima-media thickness; OR: odds ratio; PD: power Doppler.

Results: Seventy-four new patients with gout were enrolled, mean aged 62.2 years (SD 14.7), 89.2% males. Mean gout duration was 5.6 years (SD 9.2), clinical tophi were observed in 15.9% of patients and mean serum urate level at diagnosis was 8.2 mg/dl (SD 1.6). All participants showed at least one sonographic sign of crystal deposits at the examined locations, with a mean sum of locations of 9 (SD 3.9). Regarding individual signs, their mean (SD) sum was as follows: 4.4 (2.2) for tophi, 3.7 (2.8) for aggregates and 0.8 (1.0) for double contour. The mean sum of locations with positive PD signal was 1.1 (SD 1.0). Regarding carotid scans, increased IMT was seen in 17 patients (24.3%), and atheroma plaques in 41 (55.4%). Table 1 shows the results of the association analysis. Tophi and positive PD signal were significantly associated with the presence of atheroma plaques, while no sonographic sign showed association with an increased IMT.

Conclusion: Sonographic deposits were consistently observed in new patients with gout. Tophi and positive PD signal, indicators of crystal and inflammatory burden, were significantly associated with carotid atheroma plaques. This new finding may contribute to understand the complex relationship between gout and atherosclerosis.

Disclosure: I. Calabuig, Fundación Valenciana de Reumatología (FVR), 2, Instituto de Investigación Sanitaria y Biomédica de Alicante (ISABIAL), 2; **A. Martínez-Sanchis**, None; **M. Andrés**, Astra-Zeneca, 5, Grunenthal, 2, 5, 8, Horizon, 5, Menarini, 8.

Abstract Number: 0350

Rapid Reduction in Uric Acid Is Associated with Recurrent Cardiovascular Events

Su Jin Choi ,[1] Jung Sun Lee,[1] So Hye Nam,[1] Doo-Ho Lim,[2] Ji Seon Oh,[3] Seokchan Hong,[4] Yong-Gil Kim,[1] Chang-Keun Lee,[1] and Bin Yoo[1], [1]Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea, [2]Division of Rheumatology, Department of Internal Medicine, Ulsan University Hospital, Ulsan, Republic of Korea, [3]Department of Biomedical Informatics, Asan Medical Center, Seoul, Korea, Seoul, Republic of Korea, [4]Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea, Seoul, Republic of Korea

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: A recent study showed that febuxostat had a higher risk of cardiovascular and all-cause mortality than allopurinol. Because febuxostat is more potent than allopurinol, we hypothesized that an abrupt change in serum uric acid levels caused by urate-lowering agent might influence the risk of cardiovascular events.

Methods: We included patients with cardiovascular disease (CVD) treated with allopurinol or febuxostat. Cardiovascular events were defined as follows: nonfatal myocardial infarction, nonfatal stroke, unstable angina requiring coronary revascularization procedure, and cardiovascular death. The change in serum uric acid level was determined by the difference or reduction rate in uric acid within 6 months after exposure to allopurinol or febuxostat. The factors associated with cardiovascular events were evaluated by Cox regression analysis.

Results: In total, 207 patients with CVD exposed to allopurinol or febuxostat were included. Cardiovascular events occurred in 25 patients (12.1%). In univariate analysis, hypertension, difference in uric acid levels between baseline and post-exposure to urate-lowering agent, and reduction rate in uric acid levels were associated with cardiovascular events. In multivariate analysis, hypertension [hazard ratio (HR) 3.450, 95% confidence interval (CI), 1.167–10.202, $p = 0.025$] and reduction rate in uric acid to the lowest levels (HR 26.133, CI, 6.876–99.319, $p < 0.001$) were associated with cardiovascular events.

Conclusion: Rapid reduction in serum uric acid levels was associated with the recurrence of cardiovascular events in patients with CVD. Thus, careful attention should be paid to abruptly changed serum uric acid levels after treating urate lowering agent in high-risk CVD patients.

Disclosure: S. Choi, None; **J. Lee**, None; **S. Nam**, None; **D. Lim**, None; **J. Oh**, None; **S. Hong**, None; **Y. Kim**, None; **C. Lee**, None; **B. Yoo**, None.

Abstract Number: 0351

Risk Factors for Cutaneous Reactions to Allopurinol in Kinh Vietnameses: Results of a Prospective Study in Ho Chi Minh City

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Allopurinol (ALLO), the leading hypouricemic drug worldwide, exposes to mild (M) and severe (S) cutaneous adverse reactions (CARs). SCARS have been associated with HLA*B-58 01. However, the reported strength of the association has varied across ethnicities and has been little studied in Vietnam. Little is known about risk factors for MCARs.

The aim of this prospective study was to investigate risk factors, including HLA*B-58 01, for MCARs and SCARs in the predominant Kinh ethnicity of Vietnam.

Methods: All patients were Kinh Vietnamese and were prospectively recruited in Ho Chi Minh City, after Ethics committee approval. SCARs were recruited in dermatology and allergy hospital departments, MCARs in the same departments and at the Vien Gut clinic (specialized in gout care), and tolerant gouty patients (no skin reaction after at least 3 months from the last increment in ALLO dose) at the Vien Gut clinic. Clinical data were prospectively collected and HLA*B-58 01 genotype was obtained using the PG5801 DNA detection kit (Pharmigene-Taiwan). Fisher exact test for categorical variables and Kruskal/Wilkonson test for quantitative variables were used for statistics.

Results: Between March 2017 and May 2019, 31 patients with a non-fatal SCAR. (29 toxic necrotic epidermolysis/ Stevens-Johnson syndrome and 2 DRESS), 74 patients who stopped ALLO because of MCAR and 395 ALLO-tolerant patients were recruited. Table 1 shows the main features of interest in the 3 groups. The Odds ratios of lack of dose escalation, HLA*B-58 01 presence and GFR< 60 ml/min to develop SCARs were calculated at 883 (, 95%CI:128; 4504), 185(95 % CI: 43; 1595) and 104 (95%CI:28;454), respectively.

Conclusion: In the studied Vietnamese Kinh population, lack of ALLO titration was the strongest risk factor for SCARs. HLA*B-58 01 and other known factors, including renal failure but not high ALLO dose, were also significantly associated with SCARs. MCARs associated with lack of ALLO titration and renal failure but not with HLA*B-58 01

	SCARs N=31	MCARs N=74	Controls N=395	Global p	P SCARs vs controls	P MCARs vs controls
NO Gout N (%)	15/27 (55,6 %)	2 (2,7 %)	0 (0 %)	<0.0001	<0.0001	0.025
Women N (%)	9 (29.3)	0	0	<0.0001	<0.0001	1
Age Mean (95%CI)	60.03 (15.94 %)	45.68 (11.67 %)	45.37 (10.28 %)	<0.0001	<0.0001	0.99
History of CAR to ALLO N (%)	2/27 (7.4 %)	2 (2.7 %)	0	0.0005	0.004	0.025
Diuretic intake N (%)	7/26 (26.9 %)	! (1.35 %)	0	<0.0001	<0.0001	<0.0001
Mean ALLO dose mg/d Mean (95%CI)	303.4 (97.22)	243.2 (110.2)	369.1 (103.8)	<0.0001	0.0003	<0.0001
Lack of ALLO titration N (%)	28/29 (96.55 %)	35 (47.30 %)	11 (2.80 %)	<0.0001	<0.0001	<0.0001
eGFR < 60 ml/min N (%)	12/18 (66.67 %)	6 (8.11 %)	7 (1.77 %)	<0.0001	<0.0001	0.009
Type 2 diabetes N (%)	6/15 (40%)	3 (4.05 %)	24 (6.08%)	0.002	0.0008	0.80
Hypertension N (%)	8/15 (53.33 %)	4 (5.41%)	99 (25.06 %)	<0.0001	0.030	<0.0001
Coronary heart disease N (%)	1/15 (6.67 %)	0	9 (2.28%)	0.16		
Dyslipemia N (%)	6/13 (46.15 %)	6 (8.11 %)	69 (17.47 %)	0.03	0.018	0.056
HLA-B*5801 N (%)	29 (93.55 %)	6 (8.11)	28 (7.09%0	<0.0001	<0.0001	0.81

Table 1. Factors associated with SCARs and MCARS to ALLO in the Kinh population of Ho Chi Minh City (Vietnam)

Disclosure: T. Bardin, None; **L. Le**, None; **Q. Nguyen**, None; **A. Do**, None; **H. Le**, None; **M. Do**, None; **A. Vu**, None; **A. Le**, None; **K. Bui**, None; **P. Richette**, Janssen, 8; **M. Resche-Rigon**, None; **T. Mai**, None.

Abstract Number: 0352

Primary Hyperparathyroidism Is Associated with a Higher Level of Serum Uric Acid: A Systematic Review and Meta-analysis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Studies have suggested that primary hyperparathyroidism could be a risk factor for hyperuricemia although the results were inconsistent across the studies. This systematic review and meta-analysis was performed in order to identify all available studies and summarize their results together.

Methods: A systematic review was performed using EMBASE and MEDLINE from inception to August 2018 to identify all cohort studies that consisted of two cohorts, cohort of patients with primary hyperparathyroidism and cohort of individuals without hyperparathyroidism. Eligible studies must provide data on mean serum uric acid level and standard deviation of both cohorts, which would be extracted to calculate mean difference (MD). Pooled MD was then calculated by combining MDs of each study using random-effects model. Funnel plot was used for evaluation for publication bias.

Results: A total of nine cohort studies met the inclusion criteria and were included into the meta-analysis. The pooled analysis found that patients with primary hyperparathyroidism had a significantly higher level of serum uric acid than individuals without hyperparathyroidism with the pooled MD of 65.00 µmol/L (95% CI, 37.74 - 92.25). The statistical heterogeneity was high with I^2 of 90 %. The forest plot of this meta-analysis is shown as figure 1. The funnel plot was relatively symmetric and did not provide evidence for publication bias (figure 2). Reduced renal tubular secretion of urate due to the direct effect of PTH on renal tubules is one of the possible explanations for this observation.

Conclusion: Patients with primary hyperparathyroidism had a significantly higher level of serum uric acid compared to individuals without hyperparathyroidism.

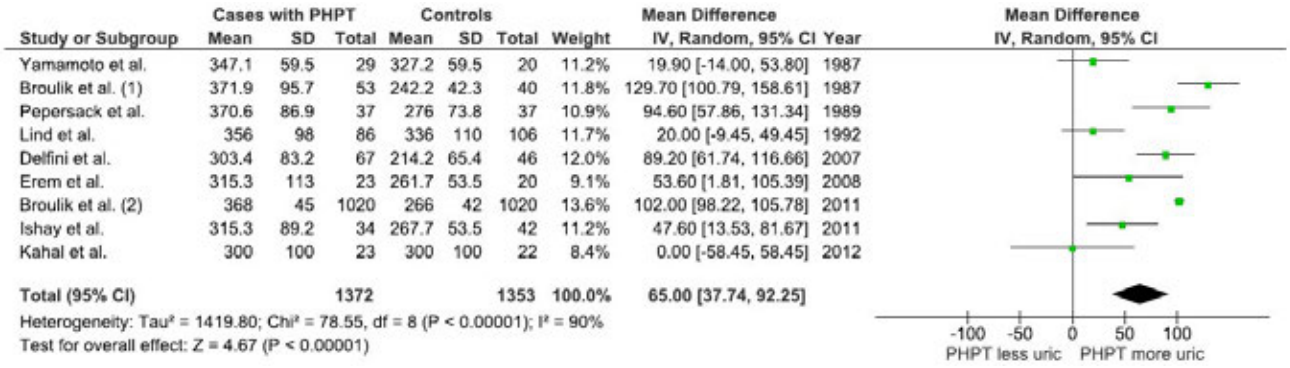

Figure 1. Forest plot of the meta-analysis

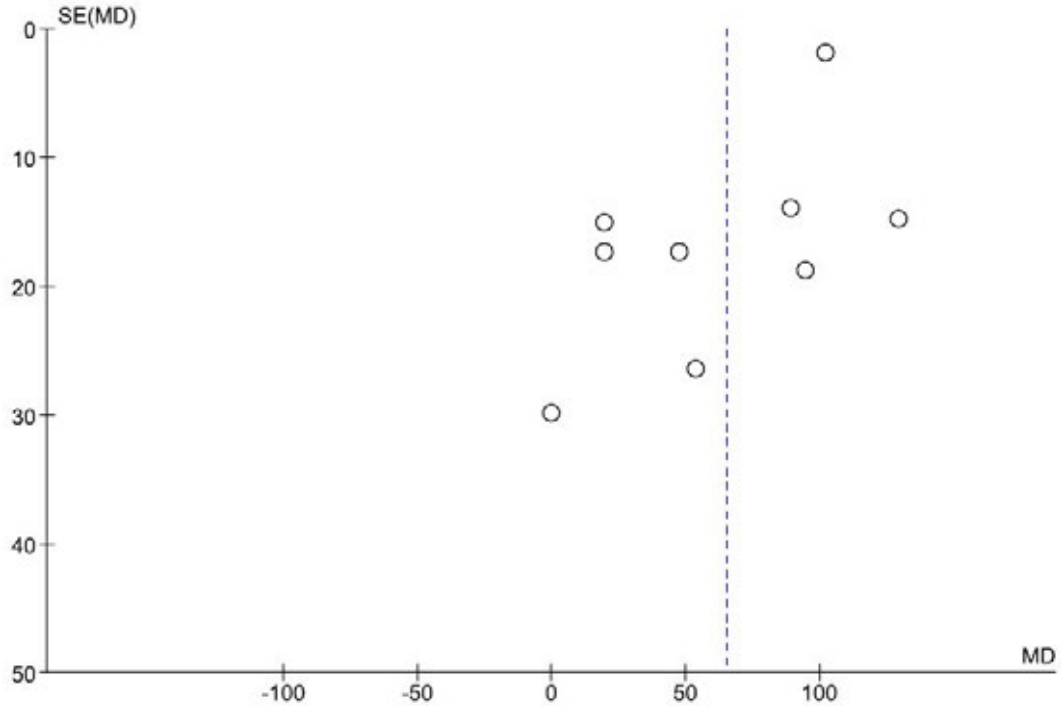

Figure 2. Funnel plot of the meta-analysis

Disclosure: B. Ponvilawan, None; **N. Charoenngam**, None; **P. Ungprasert**, None.

Abstract Number: 0353

Allopurinol Use and Type 2 Diabetes Incidence Among Patients with Gout: A VA Cohort Study

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SESSION INFORMATION

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Background/Purpose: Several studies implicate gout and/or xanthine oxidase activity as risk factors for type 2 diabetes. However, no studies have directly evaluated the effect of the xanthine oxidase inhibition on type 2 diabetes development. We therefore assessed the impact of allopurinol use on diabetes incidence in a retrospective cohort study of Veterans' Affairs patients with gout.

Methods: The New York Harbor VA Computerized Patient Record System was searched to identify patients with an ICD-9 code for gout also meeting at least 4 1977 American Rheumatology Association gout diagnostic criteria. Pharmacy records were reviewed, and subjects divided into subgroups based on >30 continuous days of allopurinol prescription, versus no allopurinol. Incident diagnoses of diabetes, defined as first hemoglobin A1c ≥ 6.5% or physician documentation, were identified during an observation period from January 1, 2000 through December 31,

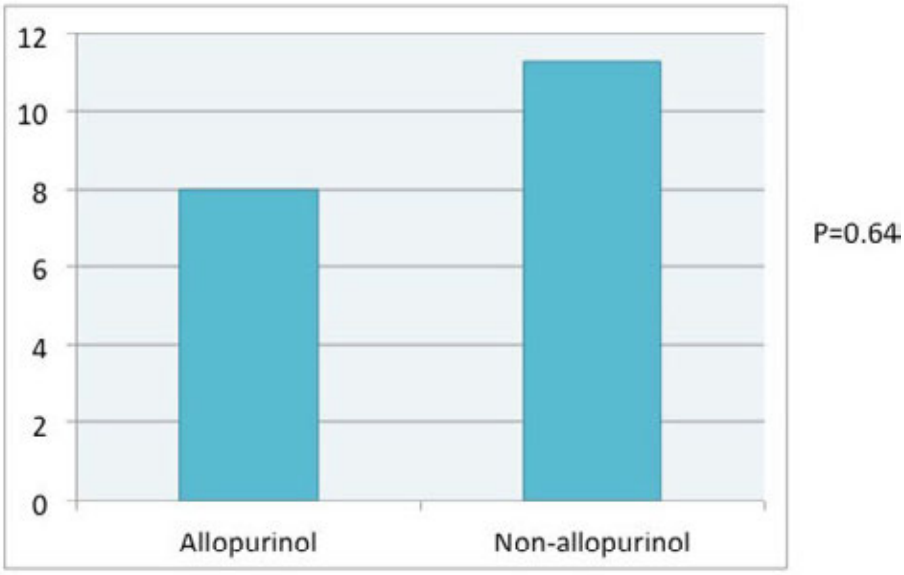

Figure 1. Diabetes incidence per 1000 person-years

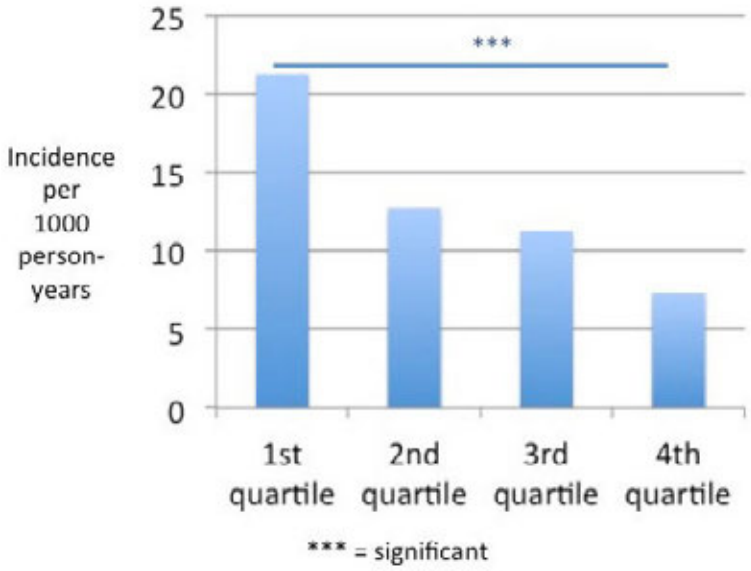

Figure 2. Diabetes incidence by duration of allopurinol use/observation

2015. Categorical variables, including the primary endpoint, were analyzed utilizing Fisher's exact test. Continuous variables were analyzed using binomial regression and the Student's T test.

Results: 1032 subjects were allopurinol users, and 485 subjects were allopurinol never-users. The average duration of allopurinol use was 48.4 months. There were significantly more Black subjects in the allopurinol group, whereas there were significantly more Asian subjects and subjects with chronic kidney disease in the non-allopurinol group. Over a mean 94.3 months of follow-up, there was no significant difference in diabetes incidence between the allopurinol and non-allopurinol groups (8.0/1000 person-years versus 11.3/1000 person-years, p=0.64). There was also no significant difference in diabetes incidence when subjects were analyzed by baseline serum urate level, colchicine use, allopurinol dose, extent of urate lowering with allopurinol or achieving target urate level. When stratified into quartiles by duration of allopurinol use, a significant difference was observed between diabetes incidence in the

longest and shortest quartiles among subjects in the allopurinol cohort (7.3 per 1000 person-years versus 21.3 per 1000 person-years, p=0.007).

Conclusion: In this study, allopurinol use was overall not associated with reduced diabetes incidence, but longer durations of allopurinol use may have been associated with decreased diabetes. Prospective studies may further elucidate the relationship between hyperuricemia, gout, xanthine oxidase activity and diabetes, and the potential impact of gout treatments on diabetes incidence.

Disclosure: A. Slobodnick, None; **M. Toprover**, None; **C. Pike**, None; **D. Crittenden**, Amgen Inc., 1, 9; **J. Greenberg**, Corrona, LLC, 1, 3; **M. Pillinger**, Sobi, 5, Horizon, 5.

Abstract Number: 0354

Evaluation of Opioid Analgesia in Hospitalized Patients with Acute Crystal Induced Arthritis

Sukhraj Singh ,[1] Anthony Ocon,[1] Mark Riley,[2] Jennifer Tchervenkov,[1] and Ruben Peredo-Wende[1], [1]Albany Medical Center, Albany, NY, [2]Albany Medical Center, Albany

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Session Time: 9:00AM–11:00AM

Background/Purpose: The Opioid Epidemic has been declared a public health emergency since 2017. The use of opioids in the acute crystal induced arthritis (ACIA) population has not been well evaluated. Despite availability of effective gout treatments, opioid use remains prevalent in hospitalized patients [1]. Traditionally, treatment for acute flares includes non-steroidal anti-inflammatories, colchicine, and glucocorticoids. Anakinra is a relatively new immunomodulator that has been shown to be non-inferior to traditional treatments for acute gout flares, suggesting that anakinra is an effective alternative treatment for acute gout flares [2]. We proposed to look at the total amount of opioid use in the inpatient population suffering from acute crystal induced arthritis and also evaluate whether anakinra use may reduce opioid prescribing.

Methods: Retrospective chart review of all adult in-patients who were admitted between 2015 through 2018 with gout or pseudogout flare were evaluated. A total of 204 patients met ACR/EULAR criteria for ACIA. Of those, seventeen had received anakinra for ACIA and thirty-four patients receiving traditional treatment were matched with the anakinra group in a 1:2 ratio. The two groups were matched for age, gender and number of joints affected. Data collection included demographics, home medications, comorbidities, and Visual Analog Pain Scale (VAS-pain). Response to treatment was defined as decrease in VAS-pain by more than 2 points on a 0-10 scale at 24, 48, and 72 hours. The total opioid dose in morphine milliequivalents was reviewed for both groups. Repeated measures ANOVA was used to compare each group at each time-point of pain assessment. Tukey-Kramer multiple comparisons test was used for post-hoc comparisons. Significance was set at $p< 0.05$.

Results: All the patients in traditional treatment group had significantly more use of opioids for their joint pains compared to the anakinra group ($p< 0.05$). All patients receiving anakinra had statistically significant improvement in VAS-pain compared to the conventional group ($p< 0.001$). Within the anakinra group, pain was significantly improved at 24 hours ($p< 0.05$) and at 48 hours ($p< 0.001$) compared to baseline. The conventional group had significant improvement at 48 hours compared to baseline ($p< 0.05$) but was not significantly improved at 24 hours ($p >0.05$). Between

Table 1: Patient Characteristics and Outcomes by Group

Variable	Treatment as usual (n=34)	Anakinra Group (n=17)
Age, mean [95% CI]	64.0 [60.6 – 67.4]	67.6 [61.7 – 73.5]
Sex		
Male [%]	22 [64.7%]	11 [64.7%]
Female [%]	12 [35.3%]	6 [35.3%]
Race		
Caucasian	14 [41%]	14 [82%]
African American	14 [41%]	2 [12%]
Hispanic	3 [9%]	0 [0%]
Other	3 [9%]	1 [6%]
Crystal Type		
Uric Acid	31 [91%]	14 [82%]
CPPD	3 [9%]	3 [18%]
Flare Duration, Days [95% CI]	3.6 [2.7-4.5]	2.8 [2.1 – 3.6]
Diabetes Mellitus [%]	14 [41%]	7 [41%]
CKD Stage 3 or Greater [%]	10 [29%]	9 [53%]
Uric Acid, Mean [95% CI]	7.2 [6.0 – 8.4]	6.2 [5.0 – 7.4]
Mean Number of Joints [95% CI]	2.1 [1.7 – 2.6]	2.3 [1.6 – 2.9]
Mean ESR [95% CI]	67.2 [55.8 – 78.4]	54.1 [36.2 – 71.9]
Mean Renal Function		
Blood Urea Nitrogen [95% CI]	28.9 [23.8 – 34.0]	25.6 [19.7 – 31.5]
Serum Creatinine [95% CI]	1.59 [1.26 – 1.93]	1.79 [1.01 – 2.58]
Glomerular Filtration Rate [95% CI]	44.4 [38.6 – 50.1]	46.6 [38.1 – 55.1]
•Mean VAS-pain Scores [95% CI]		
Before Treatment	7.8 [7.1 – 8.4]	7.9 [6.9 - 8.9]
24 hours after Treatment	7.3 [6.6 – 8.1]	6.3 [5.3 – 7.4]
48 hours after Treatment	6.7 [5.7 – 7.8]	4.0 [2.5 – 5.5]
72 hours after Treatment	6.7 [5.7 – 7.6]	3.1 [1.3 – 4.9]
•Mean Morphine Milliequivalents [95% CI]	120.8 [64.2 – 177.3]	46.7 [0 – 95.4]
Odds Ratio for Opioid prescription at Discharge [95%CI]	3.35 [0.37-30.9]	0.30 [0.03-2.7]
Mean Number of Days in Hospital after Flare diagnosis, [95% CI]	7.2 [5.2 – 9.2]	5.2 [CI 3.9 – 6.5]
Mean doses of Anakinra [95% CI]	0	3.1 [2.3 – 3.9]

•Indicates statistically significant with $p<0.05$

groups pain was not different at baseline or at 24 hours ($p > 0.05$). On average the number of days of hospitalization since treatment initiation was nearly 2 days shorter in the anakinra group compared to conventional. In addition, prescription for opioids at discharge was more likely in the traditional treatment group [OR = 3.34, (CI 0.37-30.70)], but this did not reach statistical significance. No significant adverse events were noted in the anakinra group.

Conclusion: A significant amount of opioid analgesia is employed in treating inpatients with ACIA. Significant pain reduction with anakinra highlights the availability of safe alternative for inpatients with ACIA. Additional investigations are warranted to evaluate the appropriate role of opioids in ACIA population and how to control its utilization.

Disclosure: S. Singh, None; **A. Ocon**, None; **M. Riley**, None; **J. Tchervenkov**, None; **R. Peredo-Wende**, None.

Abstract Number: 0355

Comparative Risk of Cardiovascular Events in US Veterans with Gout Treated with Febuxostat versus Allopurinol

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
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Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is the most common inflammatory arthritis and is particularly common among veterans. Recent studies, a randomized controlled trial (CARES, White et al. NEJM 2018) and an observational study using administrative claims data (Zhang et al. Circulation 2018) point to a higher all-cause and cardiovascular mortality with febuxostat relative to allopurinol. However, the CARES trial was limited to patients with a history of major cardiovascular disease and 45% subjects were lost to follow up. Therefore, the objective of our study was to evaluate the comparative risk of cardiovascular events in veterans with gout on allopurinol versus febuxostat.

Methods: We identified patients age >=18 with gout who initiated allopurinol during 2009-2017 using encounter and claims data from the Corporate Data Warehouse housed within the Veteran Affairs Informatics and Computing Infrastructure (VINCI). The Index date was the date of first allopurinol fill. Patients were followed in monthly increments for up to 8 years and, for patients who subsequently initiated febuxostat, the date of first febuxostat fill was noted. Exclusion criteria included patients with end stage renal disease or on dialysis; use of pegloticase or rasburicase in the 365 days before the index date. The primary outcome was development of major adverse cardiovascular events (MACE) defined as hospitalization for myocardial infarction (MI), stroke (including TIA), or heart failure (new-onset heart failure or heart failure exacerbation). The secondary outcomes were myocardial infarction, stroke, new and recurrent heart failure, and all-cause mortality. Marginal structural models (MSM) were used to determine the hazard of MACE events with febuxostat relative to allopurinol while accounting for changes in patient characteristics over time that influence the use of febuxostat (serum uric acid and glomerular filtration rate). Censoring events included death, date of last available allopurinol or febuxostat, or end of follow up (whichever comes first).

Results: We identified 151,184 new allopurinol users, of which 3,693 (2.4%) subsequently initiated febuxostat over the study period. Allopurinol-only users were predominantly male (98.4%) and white (63.7%), respectively, with similar attributes in those switching to febuxostat. 56% of allopurinol users had uric acid >8-< 12 mg/dl compared to 70.3% of febuxostat group at drug initiation. There were 186 MACE events over 8,768 patient years of febuxostat use (crude incidence rate (IR)=2.12/100 patient-yrs) compared to allopurinol 6,623 events over 554,916 patient years (crude IR=1.19/100 patient-yrs); adjusted hazard ratio (HR) being 1.11 (95% CI 0.95-1.29, p=0.19) after multivariable adjustment. We also observed no statistically significant differences between months of allopurinol use or febuxostat use for MI, stroke or composite of MACE and all-cause mortality (Table 1).

Table 1 Risk of major adverse cardiovascular events in allopurinol compared to febuxostat use

	Febuxostat (n=3693)			Allopurinol (n=147491)			
	Event (n)	Patient-Years	Crude IR	Event (n)	Patient-Years	Crude IR	Adjusted HR (95%CI)
Primary Outcome							
MI, stroke, or heart failure	186	8768	2.12	6623	554916	1.19	1.11 (0.95-1.29)
Secondary Outcomes							
MI	51	9146	0.56	1632	565442	0.29	1.22 (0.92-1.63)
Stroke	31	9194	0.34	1343	564948	0.24	1.09 (0.76-1.56)
Heart failure	139	8924	1.56	4483	560443	0.80	1.09 (0.91-1.31)
All-cause mortality	718	8768	8.19	32248	554916	5.81	1.02 (0.95-1.11)

CI = confidence intervals; IR = incidence rate is per 100 person-years; MI = myocardial infarction

Conclusion: By using marginal structural model to reduce bias caused by non-random censoring and treatment assignment, we found no differences in the risk of MACE events between febuxostat and allopurinol users in a large cohort of veterans with gout.

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Abstract Number: 0356

Gout Flares Become Infrequent During a Treat-to-target Strategy over One Year: Data from the NOR-Gout Study

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SESSION INFORMATION

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Background/Purpose: Urate lowering therapy (ULT) is expected to prevent new gout flares. Treat-to-target ULT is however often not performed, and more evidence on how often patient experience flares during ULT is needed.

We studied how many patients had a gout flare during months 6-12 in the first year during a treat-to-target strategy, and which factors predicted a flare during that time.

Methods: In a prospective observational study, 208 patients with crystal-proven gout with a recent gout attack and insufficiently treated serum urate (sUA) level (>360 μmol/L/ >6 mg/dl) were included. They received ULT with drug escalation during monthly follow-up until the target sUA level was met (sUA < 360 μmol/L, or < 300 μmol/L if clinical tophi). Assessments in this ongoing data collection included demographic and clinical variables, serum urate levels, previous medication with allopurinol, colchicine and NSAIDs, co-morbidities, and health related quality of life (SF-36). Flares during the last six months in the first year of follow-up with "treat-to-target" were recorded. Bivariate analyses and logistic regression analyses examined factors associated with and prediction (odds ratio with 95% confidence interval) of a flare during months 6-12.

Results: 208 patients were included, and 164 completed a 12-month follow-up: 94.3% males, 90.5% Caucasian, mean (SD) age 56.3 (13.7) years, disease duration 7.9 (7.7) years), body mass index 28.8 (4.6), sUA level 496 (81) μmol/L, and 17.9% had tophi. Allopurinol had previously been used by 27.2% (57/186), colchicine by 50.7% (106/200), NSAIDs by 75.6 % (158/203), and prednisolone by 43.5% (91/198). 67.7% of patients had no flare between 6 and 12 months. After 12 months 87.0% (141/162) had reached the treatment target sUA < 360 μmol/l, but this was not related to whether patients had a flare between months 6-12 (p=0.83). A number of variables at baseline were bivariately related to a flare: higher BMI (p< 0.002), presence of tophi (p=0.02), co-morbidities (p=0.03), previous use of colchicine (p< 0.001) or NSAIDs (p=0.04), worse physical function summary score (SF-36) (p< 0.03), and high level joint pain during strongest attack ever (p=0.001).

In multivariate logistic regression analyses, also adjusting for age and gender in the final model, a high BMI (OR 1.11 per unit (95% CI 1.02-1.21), low baseline serum urate (OR 1.006 per unit, 95% CI 1.001-1.012) and previous use of colchicine (OR 4.8, 95% CI 2.1-11.1) predicted a flare during months 6 and 12. Also, NSAID use (OR 5.1, 95% CI 1.6-16.0), when substituting colchicine, was a predictor of a flare-free period during this period.

Conclusion: One of three patients experienced a flare during the second half of one year with treat-to-target ULT strategy. A low baseline level of sUA and high BMI increased the risk of a flare, as did previous experience with colchicine or NSAID.

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Abstract Number: 0357

Longitudinal Variation in Repeat Serum Urate Levels: Relationship with Hyperuricemia Classification

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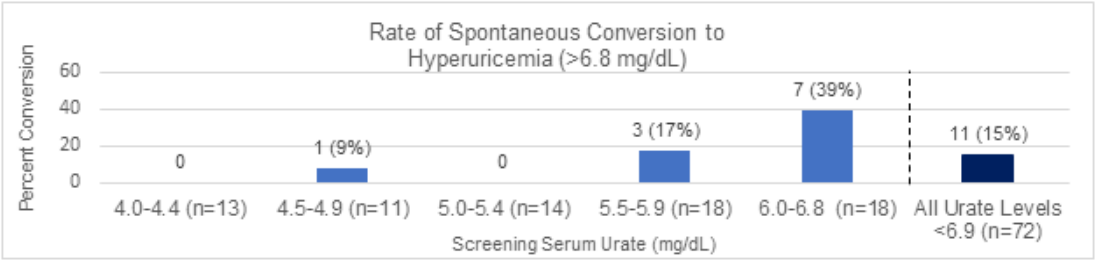
Background/Purpose: Previous studies have noted significant variation in serum urate (sUA) levels, and it is unknown how this influences the accuracy of hyperuricemia classification based on single data points. Despite this known variability, hyperuricemic patients are often used as a control group in gout studies. Our objective was to determine the accuracy of hyperuricemia classifications based on single data points versus multiple data points given the degree of variability observed with serial measurements of sUA.

Methods: Data was analyzed from 85 young adults without a gout diagnosis participating in a single center, double-blinded, crossover trial in which participants were randomly assigned to receive allopurinol (300 mg daily) or placebo for a period of 4 weeks. Serum urate levels were measured at five clinic encounters (2 -4 week intervals between measurements). For this analysis, sUA levels collected at screening, post-placebo and post-washout (i.e., no intervention) were considered (up to 4 sUA levels per participant). Mean coefficient of variation for sUA was determined. The rates of conversion from normouricemia (sUA ≤6.8 mg/dL) to hyperuricemia (sUA >6.8 mg/dL), and from hyperuricemia to normouricemia at were calculated. The rates of conversion to hyperuricemia were then compared across subgroups defined by the sUA level at initial screening (4-4.4, 4.5-4.9, 5-5.4, 5.5-5.9, 6-6.8).

Results: Mean study participant (n = 85) age was 27.8±7.0 years and mean body mass index was 31.1±7.9. 39% of participants were women. 41% of participants were African-American. Mean sUA coefficient of variation was 8.5% ± 4.9% (1% to 23%). There was no significant difference in the coefficient of variation between men and women, or between participants whose screening values were normouricemic (sUA ≤6.8 mg/dL) and those whose values were hyperuricemic (sUA >6.8 mg/dL). Among those with an initial sUA value in the range of normouricemia (n=72), 15% converted to hyperuricemic levels during at least one subsequent measurement (figure 1). The subgroup with initial sUA < 6.0 (n=54) was much less likely to have future values in the range of hyperuricemia compared to the group with screening sUA values between 6.0-6.8 (n=18) (20% vs 39%, p = 0.0037). Of the study participants with a screening



Rate of spontaneous conversion from normouricemia to hyperuricemia at any later measurement by groups stratified by initial (screening) serum urate level

sUA value in the range of hyperuricemia (n=13), 46% had values in normouricemia ranges during at least one later measurement.

Conclusion: Single sUA measurements were unreliable in hyperuricemia categorization (defined as sUA >6.8 mg/dL) due to spontaneous variation in urate levels. This is likely a result of multiple factors such as time of sample collection, diet, and change in weight. Those with an sUA measurement of < 6.0 mg/dL were less likely to demonstrate sUA values classified as hyperuricemic at future evaluations, and this could be considered a safer threshold to rule out intermittent hyperuricemia based on a single measurement point.

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Abstract Number: 0358

Emergency Department Encounters in a Large US Payer Database: Tophaceous versus Non-tophaceous Gout Patients

Meron Mezgebe ,[1] Megan Francis-Sedlak,[1] Brian LaMoreaux,[1] and Robert Holt[1], [1]Horizon Therapeutics plc, Lake Forest, IL

SESSION INFORMATION
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Background/Purpose: From 2006 to 2012, gout was the primary indication for ~0.2% of all emergency department visits for adults, as reported in the Nationwide Emergency Department Sample (NEDS).[1] The rate of emergency department visits for gout in the NEDS increased by 14% between 2006 and 2012 rising from 75.0 to 85.4 per 100,000 US adults.[1] A cross-sectional study of 296 gout patients reported that a composite gout severity score, composed of mean serum uric acid, patient-rated and physician-rated gout severity, was a significant predictor of emergency/urgent care service utilization for gout treatment.[2] The relationship between the presence or absence of tophi, visible monosodium urate crystal masses representing an uncontrolled stage of gout,[3] and emergency department utilization has not been previously reported. The objectives of this study were to analyze the utilization of emergency department services and compare the diagnostic codes present among tophaceous and non-tophaceous gout patients.

Methods: A retrospective review of Humana Research Database data from 2007 to 2017 in private pay and Medicare patients was performed to identify patients with at least 1 gout ICD-9 diagnosis code and enrolled in the plan for at least 6 months (N=370,484). Patients were divided by gout codes into patients with at least one tophi code (tophaceous group) and patients without any tophi codes (non-tophaceous group). To decrease bias non-tophaceous patients were matched to tophaceous patients based on age, gender and race. Relevant comorbidity codes were grouped and examined. Occurrence of ICD codes during emergency department encounters were analyzed in the two groups.

Results: The tophaceous and non-tophaceous group included 6,889 patients each. The patients were mean age 70.7 years, 69.4% male, and 71.7% white. Patients in the tophaceous group had a shorter time in plan since gout diagnosis (average of 3.3 years) compared to non-tophaceous patients (average 3.7 years in plan). During the time in plan analyzed, more patients with tophaceous gout had at least one emergency department encounter than patients

	Tophaceous N=6889 n (%)	Non-tophaceous N=6889 n (%)	OR	95% CI	P-value
Joint/Limb Pain	1042 (15.1)	847 (12.3)	1.27	1.153-1.402	<0.001
Renal Disease	734 (10.7)	598 (8.7)	1.25	1.120-1.405	<0.001
Chronic Kidney Disease (Stage 1-4)	131 (1.9)	81 (1.2)	1.63	1.233-2.154	<0.001
End Stage Renal Disease (Stage 5)	59 (0.9)	30 (0.4)	1.98	1.271-3.069	0.003
Acute Kidney Injury	369 (5.4)	231 (3.4)	1.63	1.379-1.930	<0.001
Calculus of kidney	102 (1.5)	118 (1.7)	0.86	0.660-1.126	0.277
Heart Failure	649 (9.4)	518 (7.5)	1.28	1.134-1.443	<0.001
Gout	543 (7.9)	319 (4.6)	1.7623	1.528-2.032	<0.001
Hypertension	491 (7.1)	453 (6.6)	1.09	0.955-1.245	0.200
Atrial Fibrillation	341 (5.0)	290 (4.2)	1.19	1.010-1.391	0.038
Diabetes	232 (3.4)	195 (2.8)	1.20	0.986-1.452	0.069

Table 1. ICD- Codes during an Emergency Department Encounter

without tophi (71.2% tophaceous vs. 67.4% non-tophaceous; OR 1.19, 95%CI of 1.109 to 1.282, p< 0.001). On average, during this period, patients with tophi had 4.01 visits to the emergency department and the patients without tophi had 3.51.The percentage of patients with renal and cardiovascular comorbid emergency department codes were increased in the tophaceous group. Table 1 compares the percentage of patients with and without tophi with emergency department codes.

Conclusion: In this large matched database study more patients with visibly tophaceous gout had at least one emergency department encounter during the time in plan analyzed as compared with their non-tophaceous gout counterparts. Additionally, patients with tophi had a greater number of emergency department encounters in this time period. In these encounters renal and cardiovascular complications were increased in the tophaceous group.

Disclosure: M. Mezgebe, Horizon Therapeutics, 3, 9; **M. Francis-Sedlak**, Horizon, 3, 4, Horizon Therapeutics, 3, 4; **B. LaMoreaux**, Horizon, 3, 4; **R. Holt**, Horizon, 3, 4, Horizon Therapeutics, 3, 4.

Abstract Number: 0359

Impact of Hospital Admissions on Adherence to Allopurinol Therapy After Discharge

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SESSION INFORMATION
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Background/Purpose: Gout is a common disease with effective medical therapies, yet many cases are complicated by providers' hesitancy to prescribe an adequate dose of urate-lowering therapy (ULT), or patients' reluctance to take it. In addition, patients with gout often have comorbidities resulting in frequent and complex interactions with the

healthcare system. In this study, we sought to investigate the effect of inpatient admission on adherence to allopurinol therapy in patients with gout.

Methods: All hospital admissions to the Salt Lake City (SLC) Veterans Affairs (VA) Health Care System (HCS) between March 2018 and March 2019 involving patients who had an active prescription for allopurinol, and who had been requesting regular refills at the time of hospitalization, were identified. Prevalence of allopurinol prescription rates and adherence to refill requests following discharge were determined, and medical records of patients who had discontinued therapy were reviewed.

Results: From March 7, 2018 through March 25, 2019, 193 patients with an active prescription of allopurinol were admitted for inpatient care at the SLC VA HCS. These data are summarized in Figure 1. Thirty-one (16%) had not refilled their prescription in the 90 days preceding admission, and were excluded from further analysis. Of the 162 remaining patients, 91 (56%) continued to take allopurinol without change after discharge. The remaining 71 patients did not fill their allopurinol prescription for 90 days after discharge, and were assumed to have stopped taking it. Of these 71 patients, 22 were excluded from the final analysis because they were either taking allopurinol for Tumor Lysis Syndrome (TLS) prophylaxis and no longer needed it (11), were deceased within 90 days of leaving the hospital (7), or filled their prescriptions outside of the VA system (4). Medical records of the remaining 49 patients were reviewed to determine why they stopped taking allopurinol; the findings are summarized in Table 1. In 42 cases (86%), patients did not continue allopurinol despite the inpatient physician recommending they continue it after discharge. The

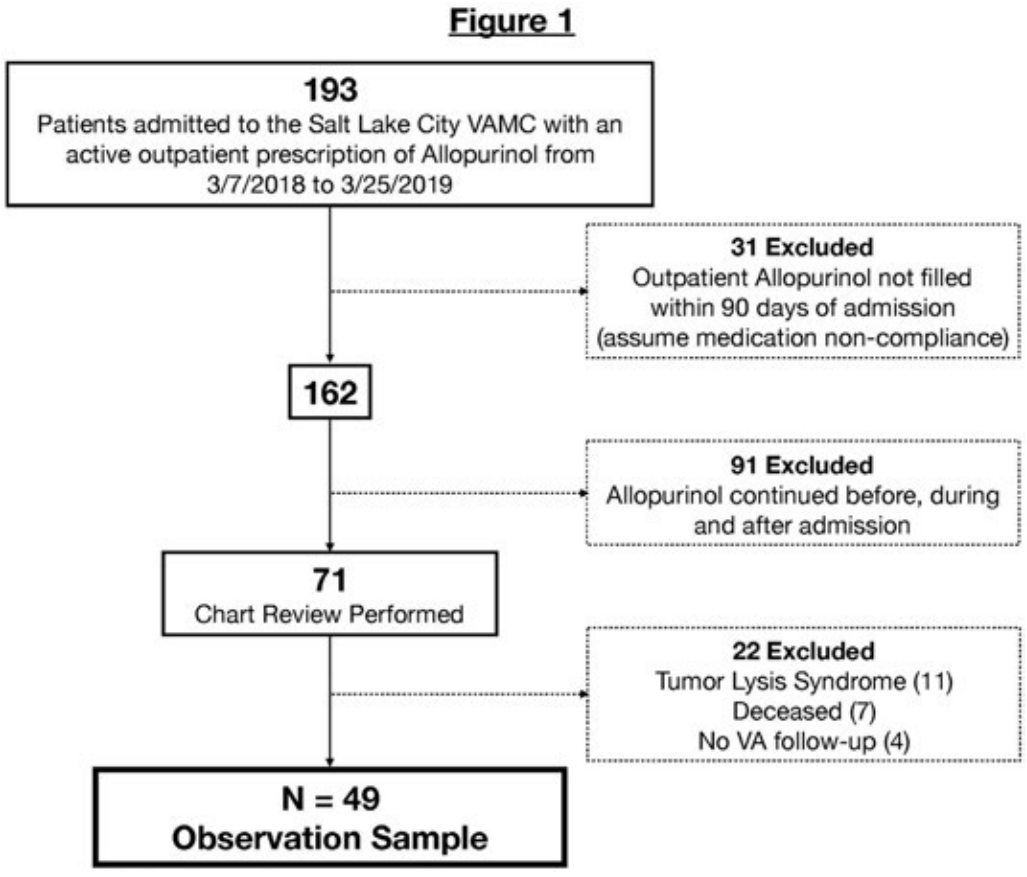

Figure 1. Patient Admissions with Active Outpatient Allopurinol Prescriptions

Table 1 – Summary of Findings for Patients with Active Outpatient Allopurinol Prescriptions Prior to Hospital Admission in Whom Allopurinol was Not Continued Following Hospital Discharge

	N	(% of 49)
Patient Compliance Issue – Did not refill the outpatient Allopurinol following discharge	42	(86%)
Patient expressed the preference to discontinue Allopurinol during admission	3	(6%)
Inpatient provider discontinued Allopurinol for undetermined reasons	2	(4%)
Unknown	2	(4%)
Total	49	

remaining 7 patients had it stopped while inpatient and did not resume it after discharge. The reasons for this were provider recommendation (2), patient preference (3), and unknown (2).

Conclusion: Admission to the hospital is strongly associated with the development of poor adherence to allopurinol therapy in gout patients, even for those who appear to be taking this medication as prescribed before hospitalization. Since patients with gout often have other health problems that require inpatient treatment, this phenomenon may contribute substantially to the major problem of nonadherence to ULT. Additional work is needed to better understand patients' motivations for stopping treatment, as well as to identify timely and effective interventions in the post-discharge period.

Disclosure: N. Lebedoff, None; **A. Barker**, None; **C. Koening**, None; **T. Jones**, None; **R. Rose**, None; **P. Yarbrough**, None; **M. Battistone**, None.

Abstract Number: 0360

Colchicine Prophylaxis of Gout Flares When Commencing Allopurinol Is Very Cost Effective: A Health Economic Analysis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Metabolic & Crystal Arthropathies Poster I: Clinical
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Prophylaxis of acute gout flares when commencing urate lowering therapy is recommended by international guidelines. Whether this is a cost-effective intervention is currently unknown. Colchicine was awarded orphan drug status by the US Food and Drug Administration in 2009 and the price increased from 9 cents per tablet to $5 per tablet (Kesselheim, 2015). Therefore, the economics of using colchicine for all of its indications altered substantially.

To perform a cost effectiveness analysis of co-prescribing colchicine when initiating urate lowering therapy for gout using both a United States healthcare system input model and an Australian healthcare system cost input model.

Methods: This cost-effectiveness analysis was completed from the point of view of the third-party payer (This therefore excluded costs such as the cost of the patient driving to their doctor or the hospital). We used a two decision-tree with one arm commencing allopurinol with no colchicine prophylaxis and the other with colchicine prophylaxis. Model inputs were drawn from published literature, where available. We completed univariate and probabilistic sensitivity analysis to confirm the robust nature of the modelling. The time frame for the model was 6 months.

Results: In the US model, the colchicine prophylaxis arm resulted in a cost of US$1109 and 0.49 quality adjusted life-years (QALYs). This was cost-effective compared to placebo (cost of US$536 and 0.47 QALYs, Incremental cost-effectiveness ratio of $25,666 per QALY gained). In the Australian model the colchicine arm dominated placebo (AUD228 in colchicine arm vs. AUD523 in placebo) due to lower colchicine cost. Univariate and probability sensitivity analysis demonstrated that results were robust to changes in input parameters, but were most sensitive to cost of colchicine and the rate of reduction of flares from colchicine treatment. In probabilistic sensitivity analysis, the probability of colchicine prophylaxis being the most cost-effective option was 78% in the US and 99% in Australian setting, at a willingness-to-pay threshold of $50,000 per QALY gained.

Conclusion: Colchicine prophylaxis of gout flares whilst commencing allopurinol in gout appears to be cost effective both in the US healthcare system with elevated unit cost for colchicine and in the Australian healthcare system where the unit cost of colchicine is substantially lower.

Disclosure: P. Robinson, None; **N. Dalbeth**, Abbvie, 5, 8, 9, Amgen, 2, AMGEN, 2, AstraZeneca, 2, 5, 8, 9, Dyve, 5, 8, 9, Dyve BioSciences, 5, Hengrui, 5, 8, 9, Horiaon, 5, 8, Horizon, 5, 8, 9, Janssen, 5, 8, 9, Kowa, 5, 8, 9, Pfizer, 5, 8, 9; **P. Donovan**, None.

Abstract Number: 0361

Frequency of Allopurinol Dose Reduction in Hospitalized Patients with Gout Flares

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Background/Purpose: It is a common misconception that allopurinol should either be held or reduced during gout flares and renal insufficiency. However, current guidelines recommend the continuation of allopurinol during flares as long as an effective anti-inflammatory therapy is in place [Khanna, et al 2012]. Additionally, allopurinol has been shown in recent studies to have no association with worsening renal function or increased risk of allopurinol hypersensitivity syndrome in acute renal insufficiency [Vargas-Santos, et al 2018]. In this retrospective observational study, we assessed the frequency of allopurinol dose reduction or discontinuation in patients with gout who had acute flares during inpatient admissions.

Variables	All admissions N = 73	Allopurinol decreased or discontinued N = 15	Allopurinol unchanged or increased N = 58
Median age (IQR), years	58 (16)	57 (15)	58.5 (16)
Male gender	67 (92%)	14 (93%)	53 (91%)
Caucasian ethnicity	43 (59%)	9 (60%)	34 (59%)
Acute kidney injury	30 (41%)	9 (60%)	21 (36%)
Chronic kidney disease	53 (73%)	10 (67%)	43 (74%)
Tophaceous disease	19 (26%)	3 (20%)	16 (28%)
Flare prophylaxis	39 (53%)	4 (27%)	35 (60%)
Rheumatology consult	29 (39%)	2 (13%)	26 (45%)
Flare within 3 months of discharge	21 (29%)	8 (53%)	13 (22%)*

*p=0.03 for this comparison

Table Baseline demographics, comorbidities, and post-hospitalization gout flares between exposed and comparator groups.

Methods: A clinical database was utilized to query patients with ICD-10 diagnosis of gout with prescriptions for allopurinol, who were admitted to two medical centers from 2014-2019. Patients with acute gout flares during the hospitalization were included in the study. Charts were reviewed for patient demographics, comorbidities, allopurinol dose on admission and discharge, reasons for dose changes, use of flare prophylaxis, rheumatology consultation, and gout flares within three months after discharge. Descriptive statistics were performed for patient baseline characteristics and outcomes. We used Fisher's exact test to assess for the difference between post-hospitalization gout flares between allopurinol dosage change groups.

Results: We identified 59 patients with a total of 73 admissions who met inclusion criteria (Table). Of all the admissions, 92% were males with a median age of 58 years. Allopurinol was either reduced or discontinued in 15 admissions (allopurinol reduced group), which comprised 21% of total admissions. Allopurinol was increased or unchanged in the other 58 admissions (comparator group). The proportion of chronic kidney disease was similar between the groups, while there was a greater proportion of admissions with acute kidney injury in the allopurinol reduced versus the comparator group (60% vs. 36%, respectively). The allopurinol reduced group also had a significantly higher rate of gout flares within three months of discharge at 53% compared to the comparator at 22% (P =0.03).

Conclusion: In hospitalized patients with gout who experienced acute flares, allopurinol was decreased or discontinued in nearly a quarter of admissions despite current recommendations. There were significantly more gout flares following these admissions, compared to those in which allopurinol dose was unchanged or increased. Improved clinician awareness of the current gout recommendations, as well as the risks and benefits of allopurinol in the setting of concomitant renal disease, is necessary to improve patient outcomes.

Disclosure: I. Huang, None; **A. Bays**, None; **J. Liew**, None.

Abstract Number: 0362

Methods to Efficiently Recruit Minority Patients with Gout for Clinic-Based Registries

Giovanni Adami ,[1] Giovanna Rosas,[2] Joshua Melnick,[3] Jeffrey Foster,[2] Elizabeth Rahn,[2] Amy Mudano,[4] Jeffrey Curtis,[2] Tony Merriman,[5] S Louis Bridges,[4] and Kenneth Saag[2], [1]University of Verona, Verona, Italy, [2]University of Alabama at Birmingham, Birmingham, AL, [3]University of Alabama at Birmingham, Birmimgham, AL, [4]University of Alabama at Birmingham, Birmingham, [5]University of Otago, Birmingham, AL

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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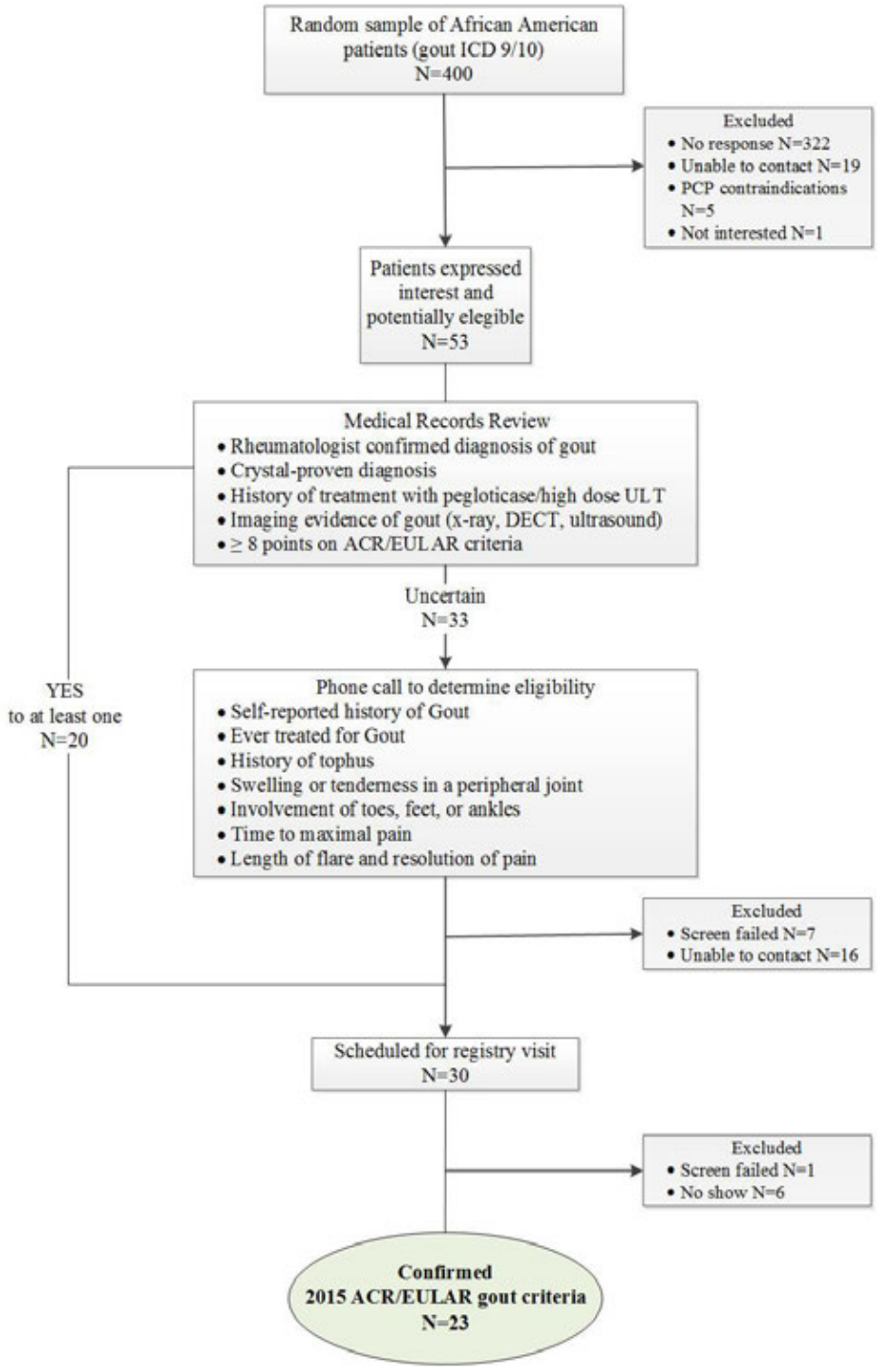
Background/Purpose: Gout is frequently misdiagnosed and/or miscoded, making approaches to identifying eligible patients for observational and interventional studies more challenging. Ethnic and racial minorities are underrepresented in many gout studies. Methods to better identify minorities and patients with confirmed gout will ensure studies have better validity and more generalizability. We defined efficient methods for identifying African Americans (AA) interested in participating in a gout registry who satisfied the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) gout classification criteria.

Methods: We identified all AA patients seen at University of Alabama at Birmingham from 01/09/2017 to 31/08/2018 with an ICD 9/10 code for gout. Patients not "opted out" by their primary care provider (PCP) were invited to participate via electronic letters and/or mailed invitations. Those interested underwent detailed medical record review followed by phone contact to determine gout eligibility. Those with a high likelihood of meeting gout diagnostic criteria were invited for an in-person visit to confirm diagnosis (Figure 1). We compared descriptive characteristic of participants enrolled in the registry with the larger populations of potentially eligible subjects.

Results: From 3,032 AA patients with an ICD 9 /10 gout diagnosis we generated a random sample of 400 patients. 5 patients were excluded by their PCPs, thus 395 patients were preliminarily eligible who we attempted to contact. 1 patient (< 1%) communicated lack of interest, 19 (4.8%) were unreachable, 322 (81.5%) did not respond to our invitation, and 53 (13.4%) expressed preliminary interest and underwent medical record review. We successfully scheduled 30 subjects for a registry visit, 24 completed the visit, and 23 (6% of initial sample) satisfied 2015 ACR/EULAR gout classification criteria (see **Table 1**). We found no significant difference in age, sex, and the number of medical encounters in the last year between enrolled patients and the remaining population.

Conclusion: We present an efficient strategy for identifying and recruiting AA patients with ACR/EULAR classified gout into a population-based registry. Among a randomly selected cohort of AAs with an initial ICD 9/10 diagnosis code of presumed gout, slightly under 15% expressed interest and eventually 6% satisfied the 2015 ACR/EULAR criteria and successfully enrolled in the registry. Our experience emphasizes a potential approach as well as some challenges in creating a generalizable gout registry of under-represented minority patients.


Random sample of African American patients (gout ICD 9/10) N=400
Excluded
• No response N=322
• Unable to contact N=19
• PCP contraindications N=5
• Not interested N=1
Patients expressed interest and potentially elegible N=53
Medical Records Review
• Rheumatologist confirmed diagnosis of gout
• Crystal-proven diagnosis
• History of treatment with pegloticase/high dose ULT
• Imaging evidence of gout (x-ray, DECT, ultrasound)
• ≥ 8 points on ACR/EULAR criteria
Uncertain N=33
YES to at least one N=20
Phone call to determine eligibility
• Self-reported history of Gout
• Ever treated for Gout
• History of tophus
• Swelling or tenderness in a peripheral joint
• Involvement of toes, feet, or ankles
• Time to maximal pain
• Length of flare and resolution of pain
Excluded
• Screen failed N=7
• Unable to contact N=16
Scheduled for registry visit N=30
Excluded
• Screen failed N=1
• No show N=6
Confirmed 2015 ACR/EULAR gout criteria N=23

Characteristic	Participants (*n*=24)
Gender	
Men (%)	12 (50%)
Women (%)	12 (50%)
Age years, mean (SD)	62.7 (8.3)
2015 ACR/EULAR criteria ≥8 (%)	23 (96%)
2015 ACR/EULAR criteria, mean (SD)	9.5 (0.9)
Sufficient criteria (%): MSU crystals present	0 (0%)
Joint/bursa involvement (%)	
Ankle or midfoot	1 (4%)
First metatarsophalangeal joint	23 (96%)
Characteristics of gout flare(s) ever (%)	
One	0 (0%)
Two	2 (8%)
Three	22 (92%)
Time course of gout flare(s) ever (%)	
One	0 (0%)
Recurrent	24 (100%)
Clinical evidence of tophus (i) (%)	0 (0%)
Serum urate (uricase method) (%)	
<4 mg/dl	0 (0%)
4-6	2 (8%)
6-8	9 (37.5%)
8-<10	10 (42%)
≥10	3 (12.5%)
Synovial fluid analysis (%)	
Negative	1 (4%)
Not done	23 (96%)
Imaging evidence of urate	0 (0%)
Imaging evidence of damage	1 (4%)
Gout medication	
Allopurinol	
Current (%)	15 (62.5 %)
Past (%)	2 (8%)
Colchicine	
Current (%)	10 (42%)
Past (%)	2 (8%)
Gout flare history	
Last year (%)	18 (75%)
Number of flares last year, mean (SD)	3 (6.0%)
Age at diagnosis, mean (SD)	52.7 (11.9%)
Positive family history (%)	10 (42%)
Gout attack at screening visit (%)	3 (12.5%)

Table 1. Characteristics of African Americans (n = 24) who completed an scheduled in-person visit for a gout registry

Disclosure: G. Adami, None; **G. Rosas**, None; **J. Melnick**, None; **J. Foster**, None; **E. Rahn**, None; **A. Mudano**, None; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **T. Merriman**, Ardea Biosciences, 2, 5, AstraZeneca, 2, 5, Ironwood Pharmaceuticals, 2; **S. Bridges**, None; **K. Saag**, Abbvie, 5, AbbVie, 5, Amgen, 2, 5, Ampel, 2, Bayer, 5, Gilead, 5, Horizon, 2, 5, Ironwood/AstraZeneca, 2, 5, Kowa, 5, kowa, 5, Mereo, 2, Radius, 5, Radius Health, 2, 5, Roche/Genentech, 5, SOBI, 2, 5, Sobi, 2, 5, Takeda, 2, 5, Teijin, 5, Tejin, 5.

Abstract Number: 0363

Efficacy and Outcomes of Telephone-Based Management Program in Patients with Gout

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SESSION INFORMATION
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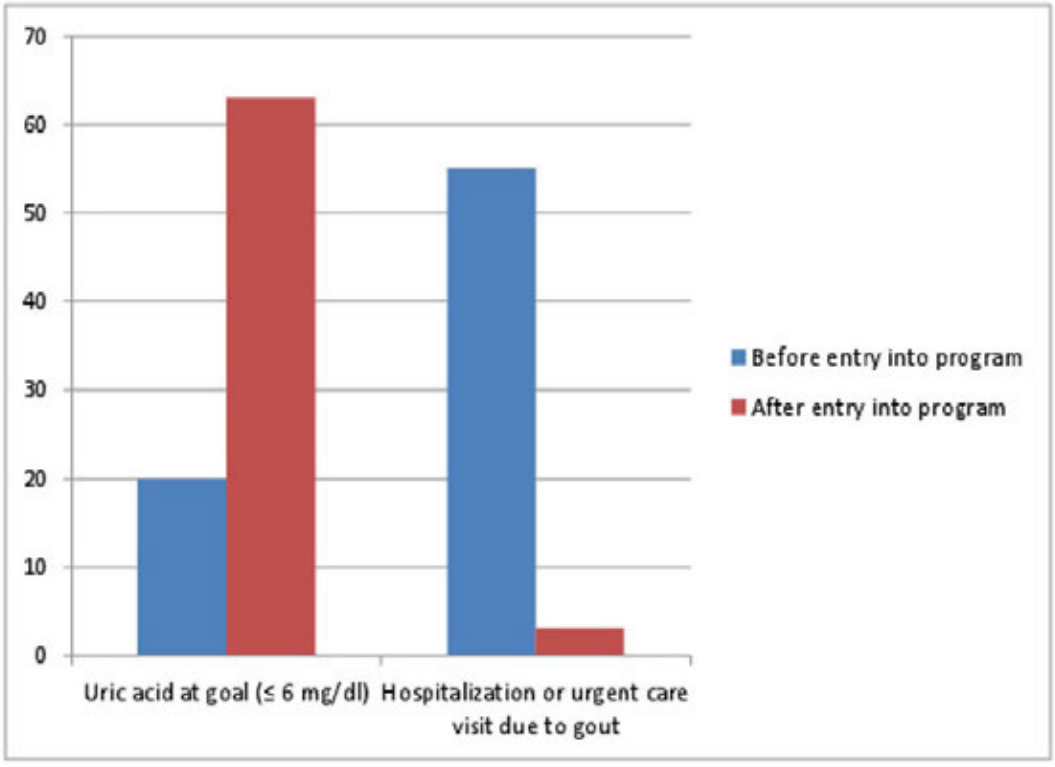
Background/Purpose: Gout is the most common inflammatory arthritis in the US, and causes significant morbidity. Despite published guidelines and available effective treatment, management remains suboptimal, leading to unnecessary morbidity and increased cost of care. We have designed the gout disease management program (GDMP) to improve outcomes and to decrease healthcare cost in gout patients. To date, no such study was conducted to evaluate healthcare utilization, patients' satisfaction and clinical outcomes.

Methods: Gout patients were seen at their usual rheumatology clinical visit and offered participation in the GDMP. Enrollees were contacted by phone every 2-4 weeks until serum uric acid (SUA) level is at goal. Data were analyzed on patients enrolled between April 2017 and May 2019. During telephone encounters, made by a rheumatology provider, recent hospitalizations since last encounter, and emergency visits due to gout were ascertained. Self-reported gout medication usage and adherence were determined. SUA levels were measured at initial outpatient encounter, when entered into the GDMP and checked every 2-4 weeks until SUA is at goal, and the most recent SUA while in



Chart

the telephone phase. Patient satisfaction with GDMP (compared with usual care of office visits) was surveyed using a 5-point Likert scale.

Results: 125 patients have enrolled into the GDMP; 66 have ≥1 telephone encounter for follow-up and are reported here. At enrollment, 15 (23%) had a crystal proven diagnosis, 15 (23%) had tophaceous gout, and 13 (20%) had SUA levels at goal (≤6.0 mg/dl). Prior to enrollment, 7 (10%) had been hospitalized due to gout, and 23 (45%) had required emergency or urgent care service due to gout. After entry into GDMP, 65 patients were treated with a urate lowering agent coupled with appropriate prophylaxis (one patient lost to follow up). Allopurinol was prescribed in most patients (56/66, 85%) as a urate lowering therapy. Forty-one (63%) have achieved the serum uric acid level goal of ≤6.0 mg/dl. Two patients (3%) required hospitalization or visits to an emergency department or urgent care center due to gout flare (chart). Patients were extremely satisfied with the telephone encounters, 62 (95%) have rated their encounter as a 5 on a 5-point Likert scale.

Conclusion: A gout disease management program consisting of typical visit with rheumatology provider followed by a novel telephone-based follow-up management program leads to improved clinical outcomes as defined by the ACR guidelines, may prevent hospitalization and urgent care visits, and has high patient satisfaction.

Disclosure: A. Al Harash, None; **T. Sharma**, None; **B. Dunmire**, None; **M. Wasko**, None; **W. Ayoub**, None.

Abstract Number: 0364

Calcium Pyrophosphate Crystal Arthritis During Hospitalizations: A Prospective, Crystal-Proven Case Series

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Background/Purpose: Despite more than fifty years after its initial description, key questions for calcium pyrophosphate (CPP) crystal disease, such as clinical spectrum, diagnosis or management schemes, remain unsolved. Acute flares often occurred during hospitalizations, but scant reports have addressed this common setting for CPP crystal disease. Whether these patients behave similarly to ambulatory cases is unknown. Our aim was to describe a prospective, crystal-proven case series of patients developing acute CPP crystal arthritis during hospitalizations for other conditions.

Methods: Observational, cross sectional descriptive study, conducted in two Spanish centers from November 2013 to December 2018. A prospective convenience sampling was used to select patients with crystal-proven CPP acute arthritis occurred during hospital admissions. Demographic, clinical and CPP-related variables were collected. X-rays of pelvis, knees, hands, and affected joint when different - to assess chondrocalcinosis (CC) - and laboratory tests - to rule out associated metabolic conditions - were systematically requested. A descriptive analysis is presented.

Results: We included 90 episodes of acute CPP arthritis in 87 patients, with an average age of 81.8 years (SD 7.7), 50.6% of them men. 26.4% of patients referred prior flares, most of them (68.4%) as outpatients. Three patients were

on flare prophylaxis (colchicine in two, low-dose glucocorticoids in one). The reasons for admission were diverse, with a mean of 7.7 days (SD 9.1) from admission to flare. Flares were mostly monoarticular (81.0%) and involving knees (46.0%). In X-rays, 23.8% of patients showed absence of CC [61/80]; in 57.1%, CC was noted in the affected joint [44/77], while in 74.3% in knees [55/74], 51.5% in triangular carpal ligaments [34/66], 25.4% in metacarpophalangeal joints [17/67], 20% in pubic symphysis [14/70], and 17.6% in coxofemoral joints [12/68]. Secondary osteoarthritis was seen in 10 patients (12.5%). Hyperuricemia was noted in 12 patients (13.3%), hypomagnesemia at the time of the flare in five (5.7%), and one case of primary hyperparathyroidism was diagnosed. In all six patients with a polyarticular presentation, rheumatoid factor and ACPA were negative.

Conclusion: From this prospective, crystal-proven series of CPP crystal arthritis during hospitalizations, we can remark: i) the low numbers of prior flares as outpatients may suggest a different clinical entity; ii) CC was absent in around a quarter of patients despite an extensive assessment, so synovial fluid analysis remains essential for accurate diagnosis; and, iii) the rarity of associated metabolic diseases runs against systematic screening for secondary causes of CPP disease in this setting.

Disclosure: L. Ranieri, None; **F. Sivera**, None; **M. Andrés**, Astra-Zeneca, 5, Grunenthal, 2, 5, 8, Horizon, 5, Menarini, 8.

Abstract Number: 0365

Classifying Pseudogout Using Machine Learning Approaches with Electronic Health Record Data

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Background/Purpose: Identifying pseudogout in large administrative datasets has been difficult due to lack of specific billing codes for this acute subtype of calcium pyrophosphate (CPP) crystal deposition disease. While several machine learning approaches exist to phenotype patients using electronic health record (EHR) data, they are largely validated in chronic conditions with relatively accurate billing codes. Pseudogout poses unique challenges due to its lack of specific billing codes and episodic nature. We evaluated a novel machine learning approach for classifying definite/probable pseudogout using EHR data.

Methods: We created an EHR dataset of 30,089 patients with ≥1 relevant billing code (Table 1 footnote) or ≥2 natural language processing (NLP) mentions of pseudogout or chondrocalcinosis in narrative notes, 1990-2017. We randomly selected 900 patients for gold standard chart review to label as: (1) definite pseudogout, synovitis+synovial fluid CPP crystals; (2) probable pseudogout, synovitis+chondrocalcinosis; (3) not pseudogout. Presence of synovial fluid CPP crystals was determined by manual review of lab results recorded as free text in the EHR. To develop an algorithm for identifying definite/probable pseudogout vs. not, we applied a semi-supervised topic modeling approach; presence of CPP crystals was not included since it required manual review. The approach included the score from an unsuper-

Table 1. Performance of algorithms to identify definite/probable pseudogout in an electronic health record datamart

	Performance among gold-standard labels (N=900)				Cases identified in datamart (N=30,089)
Algorithm	**Sensitivity**	**Specificity**	**PPV**	**AUC**	
Billing codes [a]	0.65	0.63	0.22	0.64	12,035
Semi-supervised topic modeling [b]	0.29	0.98	0.79	0.86	1,870
Presence of CPP crystals [c]	0.29	1.00	0.92	0.64	1,630
Combined algorithm: semi-supervised topic modeling + presence of CPP crystals	0.42	0.98	0.81	0.70	2,490

[a] ≥1 ICD-9 or 10 code for chondrocalcinosis or calcium metabolism disorder (ICD-9 712.1*, 712.2*, 712.3*, 275.49; ICD-10 M11.1*, M11.2*, M11.8*, E83.59). Adapted from Bartels CM, et al. J Clin Rheumatol 2015;21(4):189-92, which only included ICD-9 codes, by also including ICD-10 codes

[b] Semi-supervised topic modeling model includes: topic modeling score for propensity of pseudogout from an unsupervised topic modeling method including all relevant features, NLP mentions of pseudogout, whether synovial fluid crystal analysis was performed regardless of result

[c] Presence of synovial fluid CPP crystals was ascertained via manual review of lab results recorded as free text in the EHR

Table 2. Comparison of cohorts identified by three algorithms for definite/probable pseudogout applied to a datamart of 30,089 patients

	Billing codes	Presence of CPP crystals	Combined algorithm: semi-supervised topic modeling + presence of CPP crystals
Number of patients (n)	12,035	1,630	2,490
Age at last medical visit, years	72.8 (15.6)	76.4 (13.0)	76.3 (12.8)
Female	55.6	50.6	50.8
Race			
White	84.7	79.5	81.0
African American	4.8	8.8	7.8
Other	10.5	11.7	11.2
≥1 pertinent billing code	100.0	72.6	74.1
≥1 NLP mention of pseudogout	34.3	86.1	90.8
Synovial fluid crystal analysis performed regardless of result	18.9	100.0	86.0
Synovial fluid CPP crystals present	9.8	100.0	65.5
Prescription medications in EHR			
Colchicine	17.3	35.1	43.4
NSAID	59.1	69.1	72.7
Oral glucocorticoids	44.4	62.9	67.4

Presented as mean (SD) or percentage unless otherwise indicated

vised topic modeling method including all relevant features; NLP mentions of pseudogout; and whether synovial fluid crystal analysis was performed regardless of result. We created a combined algorithm including information from the semi-supervised topic modeling approach and the manually reviewed CPP crystal results. We compared algorithm accuracy and cohorts identified by: (1) billing codes, (2) presence of CPP crystals, (3) the combined algorithm.

Results: Among the 900 subjects, 123 (13.7%) had pseudogout by chart review (68 definite, 55 probable). Billing codes alone had a sensitivity 65% and PPV 22% for definite/probable pseudogout (**Table 1**). Presence of CPP crystals had a sensitivity 29% and PPV 92%. Without using the CPP crystal result, the semi-supervised topic modeling algorithm had a sensitivity 29% and PPV 79%. The combined algorithm yielded a sensitivity 42% and PPV 81%. The cohort identified by the combined algorithm (n=2490) was 50% larger than that identified by presence of CPP crystals (n=1630); the latter only captured patients with definite pseudogout and did not identify patients with probable pseudogout. **Table 2** demonstrates important differences between cohorts identified via billing codes vs. the combined algorithm, and similarities between cohorts identified by the presence of CPP crystals vs. the combined algorithm.

Conclusion: For pseudogout, a condition without a specific billing code, combining NLP and machine learning methods with synovial fluid CPP crystal lab results yielded an algorithm that significantly boosted PPV compared to billing codes alone, with modest sensitivity. This balance allows classification of a large pseudogout cohort for future research.

Disclosure: S. Tedeschi, None; **T. Cai**, None; **Z. He**, None; **Y. Ahuja**, None; **C. Hong**, None; **K. Yates**, None; **K. Dahal**, None; **C. Xu**, None; **H. Lyu**, None; **K. Yoshida**, None; **D. Solomon**, AbbVie, 2, Abbvie, 2, Amgen, 2, AstraZeneca, 2, Corrona, 2, Genentech, 2, Janssen, 2, Lilly, 2, Pfizer, 2; **T. Cai**, None; **K. Liao**, None.

Abstract Number: 0366

Serum Uric Acid Level and Subclinical Coronary Atherosclerosis in Asymptomatic Individuals: An Observational Cohort Study

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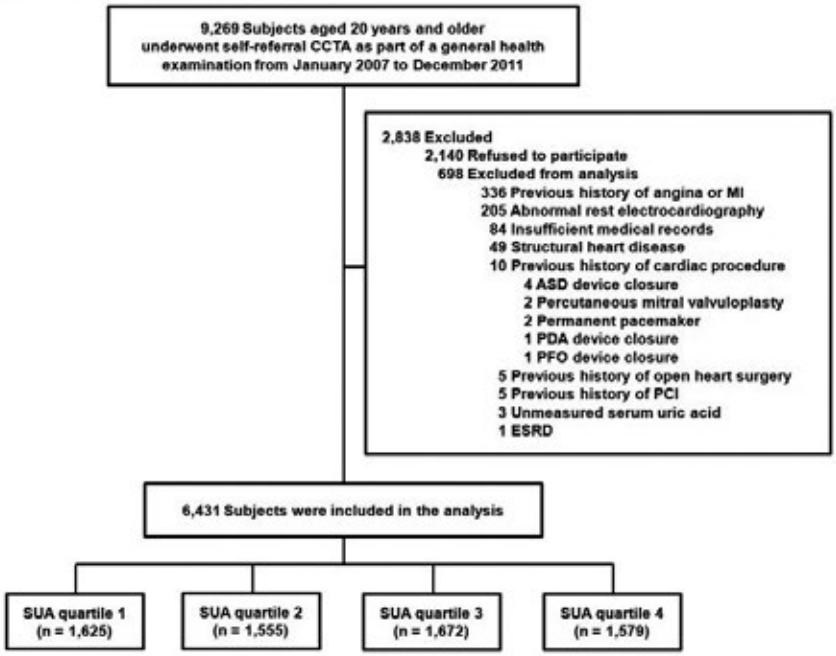
Background/Purpose: High serum uric acid (SUA) level is the main prerequisite for gout, and it might be associated with obesity, hypertension, glucose intolerance, insulin resistance, and dyslipidemia which are the known risk factors for coronary artery disease. Although the association of SUA level with coronary artery disease has been investigated in previous studies, the results are conflicting**.** Further, there are limited data regarding the association between SUA and subclinical coronary atherosclerosis in asymptomatic individuals. This study investigated the influence of SUA level on subclinical coronary atherosclerosis, as detected by coronary computed tomography angiography (CCTA), in an asymptomatic population.

Methods: We evaluated 6,431 asymptomatic individuals with no prior history of coronary artery disease who voluntarily underwent laboratory tests and CCTA as part of a general health examination. The participants were stratified

Figure. Overview of the study population



CCTA = coronary computed tomographic angiography; MI = myocardial infarction; ASD = atrial septal defect; PDA = patent ductus arteriosus; PFO = patent foramen ovale; PCI = percutaneous coronary intervention; ESRD = end-stage renal disease; SUA = serum uric acid

Table 1. Comparison of coronary computed tomography angiographic findings according to the quartiles of serum uric acid

Overall	Overall	Serum uric acid				
		Quartile 1	Quartile 2	Quartile 3	Quartile 4	p value
Mean coronary artery calcium score	40.8 ± 140.0	25.1 ± 107.3	39.2 ± 131.8	46.3 ± 151.1	52.5 ± 160.5	<0.001
Coronary artery calcium score, no. (%)						<0.001
0	4,144 (64.7)	1,216 (75.1)	992 (64.1)	1,032 (61.9)	904 (57.4)	
1–10	598 (9.3)	113 (7.0)	143 (9.2)	164 (9.8)	178 (11.3)	
11–100	1,026 (16.0)	181 (11.2)	260 (16.8)	284 (17.0)	301 (19.1)	
101–400	490 (7.6)	94 (5.8)	119 (7.7)	139 (8.3)	138 (8.8)	
>400	151 (2.4)	16 (1.0)	34 (2.2)	48 (2.9)	53 (3.4)	
Any atherosclerotic plaque, no. (%)	2,698 (41.8)	490 (30.2)	654 (42.1)	734 (43.9)	811 (51.4)	<0.001
Plaque characteristics, no. (%)						
Calcified plaque	1,808 (28.1)	326 (20.1)	454 (29.2)	503 (30.1)	525 (33.2)	<0.001
Non-calcified plaque	1,179 (18.3)	212 (13.0)	264 (17.0)	330 (19.7)	373 (23.6)	<0.001
Mixed plaque	570 (8.9)	99 (6.1)	128 (8.2)	149 (8.9)	194 (12.3)	<0.001
Significant stenosis, no. (%)	494 (7.7)	92 (5.7)	105 (6.8)	140 (8.4)	157 (9.9)	<0.001

Values are shown as the mean ± standard deviation or number (%).

into quartiles according to their SUA levels (Figure). Coronary atherosclerotic plaques (calcified, mixed, and non-calcified plaques) were assessed using CCTA. Logistic regression analysis was used to determine the association between SUA levels and subclinical coronary atherosclerosis.

Results: Among the 6,431 individuals (mean age, 53.6 ± 7.6 years) in the study, 72.9% were male. The prevalence of any atherosclerotic, calcified, mixed, and non-calcified plaques increased with SUA quartiles (all $p < 0.001$) (Table 1). After adjustment for cardiovascular risk factors including age, sex, obesity, diabetes mellitus, hypertension, hyperlipidemia, current smoking status, family history of coronary artery disease, and high-sensitivity C-reactive protein ≥2 mg/L., there were no statistically significant differences in the adjusted odds ratios for calcified plaques (1.19; 95% confidence interval [CI] 0.98–1.45; $p = 0.087$) and mixed plaques (1.25; 95% CI 0.93–1.67; $p = 0.139$) in the fourth SUA quartile compared to the

Table2. Association between serum uric acid level and coronary computed tomography angiographic findings

Variables	Univariable		Multivariable	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Coronary artery calcification*				
Quartile 1 (reference)	1		1	
Quartile 2	1.65 (1.39–1.95)	<0.001	1.10 (0.91–1.34)	0.320
Quartile 3	1.77 (1.50–2.01)	<0.001	1.04 (0.85–1.27)	0.688
Quartile 4	2.05 (1.74–2.41)	<0.001	1.19 (0.97–1.46)	0.100
Any atherosclerotic plaque				
Quartile 1 (reference)	1		1	
Quartile 2	1.68 (1.45–1.95)	<0.001	1.11 (0.94–1.32)	0.228
Quartile 3	1.81 (1.57–2.10)	<0.001	1.02 (0.86–1.22)	0.809
Quartile 4	2.45 (2.12–2.83)	<0.001	1.39 (1.15–1.67)	0.001
Calcified plaque				
Quartile 1 (reference)	1		1	
Quartile 2	1.64 (1.40–1.94)	<0.001	1.13 (0.94–1.37)	0.201
Quartile 3	1.72 (1.46–2.01)	<0.001	1.04 (0.86–1.26)	0.679
Quartile 4	1.99 (1.69–2.33)	<0.001	1.19 (0.98–1.45)	0.087
Non-calcified plaque				
Quartile 1 (reference)	1		1	
Quartile 2	1.36 (1.12–1.66)	0.002	1.02 (0.83–1.26)	0.856
Quartile 3	1.64 (1.36–1.98)	<0.001	1.11 (0.90–1.37)	0.341
Quartile 4	2.06 (1.71–2.48)	<0.001	1.38 (1.11–1.71)	0.004
Mixed plaque				
Quartile 1 (reference)	1		1	
Quartile 2	1.38 (1.05–1.82)	0.020	0.91 (0.67–1.22)	0.510
Quartile 3	1.51 (1.16–1.96)	0.002	0.88 (0.66–1.18)	0.379
Quartile 4	2.16 (1.68–2.78)	<0.001	1.25 (0.93–1.67)	0.139
Significant stenosis				
Quartile 1 (reference)	1		1	
Quartile 2	1.21 (0.90–1.61)	0.203	0.88 (0.64–1.20)	0.416
Quartile 3	1.52 (1.16–2.00)	0.002	1.02 (0.75–1.39)	0.897
Quartile 4	1.84 (1.41–2.40)	<0.001	1.26 (0.92–1.71)	0.147

CI = confidence interval
*Coronary artery calcification is defined as coronary artery calcium score >10.
Covariates in the multivariable model include age, sex, obesity, diabetes mellitus, hypertension, hyperlipidemia, current smoking status, family history of coronary artery disease, and high-sensitivity C-reactive protein ≥2 mg/l.

first quartile. However, the adjusted odds ratios for any atherosclerotic plaque (1.39; 95% CI 1.15–1.67; p = 0.001) and non-calcified plaque (1.38; 95% CI 1.11–1.71; p = 0.004) were significantly higher in the fourth SUA quartile (Table 2).

Conclusion: In asymptomatic individuals, high SUA level was an independent predictor of non-calcified plaques, suggesting an increased cardiovascular risk.

Disclosure: D. Lim, None; **G. Park**, None; **S. Choi**, None; **S. Choi**, None; **S. Nam**, None; **S. Hong**, None; **Y. Kim**, None; **C. Lee**, None; **B. Yoo**, None.

Abstract Number: 0367

Understanding the Mystery of Sarcoidosis: An Academic Rheumatology Center Experience

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies

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Session Time: 9:00AM–11:00AM

		Pulmonary	Cutaneous	Lymph Node	Uveitis	GI	Hematologic	Neurosarcoidosis	Renal	Arthritis	URT
Gender	Female	78.7	22.7	72.7	77.8	16 (p value- 0.024	5	6.2	77.8	7	5
	Male	21.3	17.6	27.3	22.2	0	1	5.7	22.2	0	0
Race	African American	67.7 (p value 0.005)	23.4	12	23	16	4	4.9	6.3	6	4
	Caucasian	33.3	9.5	23.8	19	0	2	14.3	0	1	1

Figure 1: Organ manifestation distributed by Gender and Race demographics (in percentage) with statistically significant values highlighted and p value indicated.

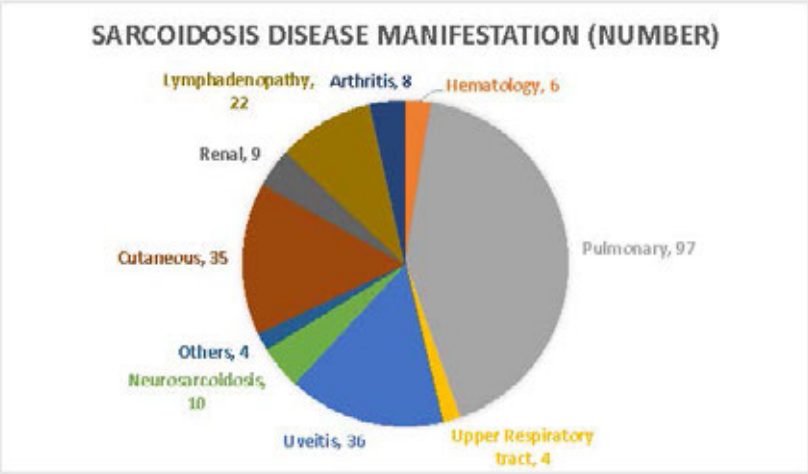

Figure 2. Number of patients with the various organ manifestations of Sarcoidosis

Treatment Drug	Pulmonary	Cutaneous	Lymph Node	Uveitis	GI	Hematologic	Neurosarcoidosis	Renal	Arthritis	URT
Prednisone	58	22	7 (p value – 0.015)	17	8	3	6	5	4	3
Hydroxychloroquine	8	6 (p value 0.025)	1	3	0	1	2	0	0	0
Methotrexate	20	10	5	6	6 (p value- 0.033)	1	2	1	1	1
Azathioprine	4	1	2	1	3 (P value - 0.019)	0	1	1	1	1
Leflunomide	6	5 (p value- 0.024)	1	1	1	0	1	0	0	0
Mycophenolate Mofetil	3	1	0	1	1	1	2	0	1	0
Adalimumab	5	3	1	2	1	0	2	0	1	0
Infliximab	6	3	1	4	4 (p value- 0.016)	0	3 (p value- 0.027)	1	1	0
Rituximab	3	0	0	1	1	0	1	0	0	0
Cyclophosphamide	1	0	0	2	1	0	2 (p value- 0.019)	3 (p value- <0.01)	0	0

Figure 3. The Treatment used for each organ manifestation (Number) with statistically significant values highlighted and p value indicated.

Background/Purpose: Sarcoidosis is an inflammatory disorder of unknown etiology characterized by tissue infiltration with non-caseating granulomas which can affect any organ. The most common organ involved is the lungs but involvement of eyes (Uveitis), skin (Cutaneous), lymph nodes, gastrointestinal (GI), upper respiratory tract (URT), musculoskeletal system (Arthritis), heart and central nervous system can be seen as well. Systemic glucocorticoid therapy has been proven to improve and stabilize pulmonary and extrapulmonary Sarcoidosis but are associated with a plethora of undesirable side effects. There is a paucity of guidelines and clinical trial data are limited for the steroid sparing agents to treat chronic Sarcoidosis, so majority of the treatment decisions are based solely on extrapolation from studies done for other autoimmune diseases and expert opinion. This study aims to review the various organ manifestations and treatment options used to successfully treat patients of Sarcoidosis at our academic center.

Methods: This is a retrospective chart review of 172 patients seen in our rheumatology clinic with the diagnosis of Sarcoidosis. Categorical analysis was performed by Chi-squared analysis unless the underlying assumptions were violated when Fisher's exact test was used instead. Continuous measures, such as age, were compared between groups by a Student's t test. P value of < 0.05 was considered significant.

Results: Sarcoidosis was seen to affect patients between the age of 17 – 83 years (Mean 49.3). Females diagnosed with Sarcoidosis were older than males (p value 0.006). There was no association found between the age, gender and race except that Pulmonary Sarcoidosis was significantly associated with African American population (p value 0.005) and GI involvement was seen in females (p value 0.024) (Fig. 1). The most common organ manifestations were Pulmonary Sarcoidosis seen in 97 patients (56.4%), Uveitis in 36 patients (20.9%) and cutaneous Sarcoidosis in 35 patients (20.3%) (Fig 2). 81 patients (46.8%) had more than one organ involvement. Amongst the treatment agent for each organ manifestations, statistically significant associations were found with Prednisone for Lymph node involvement (p value 0.015); Hydroxychloroquine for Cutaneous Sarcoidosis (p value 0.025); Methotrexate (p value 0.033), Azathioprine (p value 0.019) and Infliximab (p value 0.016) for GI involvement; Infliximab (p value 0.027) and Cyclophosphamide (p value 0.019) for Neurosarcoidosis; and Cyclophosphamide for renal involvement (p value < 0.01). The Prednisone dose was variable between 5 mg to 60 mg with a mean of 15 mg.

Conclusion: The most common manifestation was noted to be Pulmonary involvement followed by Uveitis and cutaneous Sarcoidosis and Pulmonary Sarcoidosis was more common in African Americans. The prescribing practice at our center for chronic Sarcoidosis with statistical significance included Hydroxychloroquine for Cutaneous; Methotrexate and Azathioprine for GI involvement, Infliximab for GI and Neurosarcoidosis. Long term prospective studies need to be done to outline a treatment protocol for patients with chronic Sarcoidosis to limit the use of long term steroids.

Disclosure: M. Tariq, None; **M. Katikaneni**, None; **K. Malhotra**, None; **J. McLarty**, None; **S. Umer**, None; **S. Hayat**, None.

Abstract Number: 0368

Practice Patterns in Bone Health and Vitamin D Management in Sarcoidosis: A Survey of Physicians Who Manage Sarcoidosis

Huzaefah Syed ,[1] Thieroff George,[2] Thomas Iden,[1] Aamer Syed,[1] Alicia Gerke,[3] and Trang Le[1], [1]VCU Medical Center, Richmond, VA, [2]VCU Medical Center, Richmond, VA, [3]University of Iowa, Iowa City, IA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis is a multisystem disease caused by granulomatous inflammation of unclear etiology. Hypercalcemia, seen in 2-30% of patients with sarcoidosis, is caused by calcitriol overproduction by macrophages within granulomas. Low Vitamin D 25OH (VitD) is common and contributes to low bone mass. VitD repletion can lead to hypercalcemia, but there are limited data regarding safe VitD repletion in these patients. We surveyed physicians from varying specialties who manage patients with sarcoidosis to assess current practice patterns.

Methods: Two clinical vignettes regarding bone health and VitD in sarcoidosis were presented. Clinical Vignette #1 presented a patient with hypercalcemia, elevated calcitriol, and VitD insufficiency. Clinical Vignette #2 presented a patient with normal calcium and calcitriol, VitD insufficiency, and low bone mass. These were followed by questions regarding evaluation and therapy. The survey was distributed to physicians (1) in the divisions of Pulmonary/Critical

Care, Rheumatology, Neurology, Endocrinology, and Cardiology at the Virginia Commonwealth University, (2) who attended the 2019 annual Americas Association of Sarcoidosis and other Granulomatous Disorders meeting, and (3) in a national listserv for sarcoidosis which includes approximately 100 physicians with an interest in sarcoidosis. Participants were asked to complete the vignettes they felt were pertinent to their practice and were informed that there were no incorrect answers.

Results: 45 physicians responded to the survey; the majority were pulmonologists (55.5%), followed by rheumatologists (26.7%) and endocrinologists (8.9%). They were predominantly from an academic hospital setting (93.4%). Over 75% of all physicians assessed patients for 6 of the 9 listed risk factors related to bone health. Only 31.1% assessed for symptoms of male hypogonadism. More than half of all respondents chose PTH, DXA scan, VitD, and calcitriol as part of their evaluation, while response rates to obtain serum ACE level varied between 0 to 33% among specialists. In patients with hypercalcemia, 46.7% opted not to give VitD supplementation for the VitD level that was presented. In patients without hypercalcemia, 33.3% chose not to supplement VitD at the presented level, while at least 28.9% would supplement with low dose VitD. In patients with osteopenia, 80% of respondents would recommend weight-bearing exercise and 35.6% would recommend a bisphosphonate. For patients with osteoporosis, 71.1% recommend a bisphosphonate and only 35.6% would opt to maintain VitD above 30ng/mL.

Conclusion: Maintaining strong bone health in a patient with sarcoidosis can be complicated given the risk of hypercalcemia. Though not all patients are hypercalcemic at baseline, it is unclear if Vitamin D supplementation can lead to

Table 1. Baseline Characteristics of Survey Responders for Bone Health/Vitamin D Vignettes

Practice Details		N = 45, n (%)
What is your area of specialty?	Pulmonary	25 (55.5%)
	Rheumatology	12 (26.7%)
	Endocrinology	4 (8.9%)
	Cardiology	3 (6.7%)
	Critical Care	1 (2.2%)
What is your degree?	MD/DO	44 (100%)
How many years since you have completed training?	<5	9 (20%)
	6-10	14 (31.1%)
	11-20	10 (22.2%)
	>20	12 (26.7%)
How would you describe your practice setting?	Academic Hospital	42 (93.4%)
	Private Practice	1 (2.2%)
	Other	2 (4.4%)
How many patients with sarcoidosis do you see per month?	<5	13 (28.9%)
	5-15	11 (24.4%)
	15-25	10 (22.3%)
	>25	11 (24.4%)

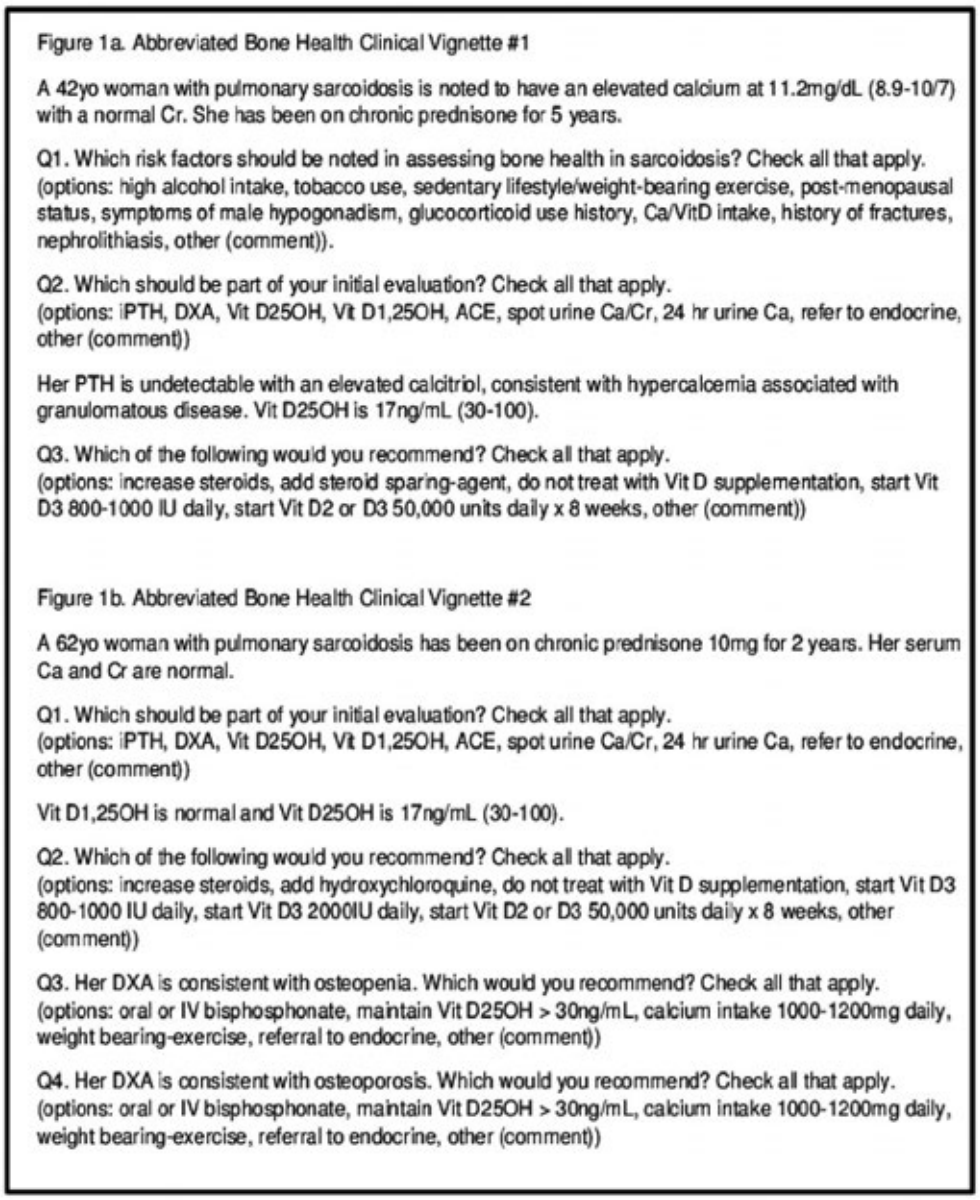

Figure 1 a&b. Abbreviated Bone Health Clinical Vignette s

hypercalcemia. This survey highlights the differences in practices in promoting healthy bones in sarcoidosis patients, stressing the importance of developing guidelines for safe Vitamin D repletion.

Table 2. Survey Answers for Bone Health/Vitamin D Vignettes

Question	Answers	N=45, n (%)	Comments
Case 1. Hypercalcemic patient, normal GFR, chronic prednisone daily x 2.5 years			
1. Which risk factors are parts of your routine history-taking for assessing bone health in sarcoidosis?	a. high alcohol intake	30 (66.7%)	
	b. tobacco use	30 (66.7%)	
	c. sedentary lifestyle / weight-bearing exercise	38 (84.4%)	
	d. post-menopausal status	35 (77.8%)	
	e. symptoms of male hypogonadism	14 (31.1%)	
	f. glucocorticoid use history	43 (95.6%)	
	g. calcium / vitamin D intake (supplements or dietary)	39 (86.7%)	
	h. history of prior fractures	39 (86.7%)	
	i. nephrolithiasis	34 (75.6%)	
2. Which of the following would be part of your initial evaluation?	a. iPTH	33 (73.3%)	
	b. DXA scan	27 (60%)	
	c. 25-OH Vitamin D	39 (86.7%)	
	d. 1,25OH Vitamin D (calcitriol level)	37 (82.2%)	
	e. ACE level	8 (17.8%)	
	f. Spot urine calcium / creatinine ratio	9 (20%)	
	g. 24 hour urine calcium	22 (48.9%)	
	h. refer to endocrinology	10 (22.2%)	
3. PTH undetectable, calcitriol elevated, Vit D 17.0ng/mL (30.0-100.0). Which would you recommend?	a. increase glucocorticoid dosage	23 (51.1%)	"Other":
	b. add steroid sparing agents	27 (60%)	• Refer to endocrinology
	c. do not treat with any vitamin D supplementation	21 (46.7%)	• Add HCQ
	d. Start vitamin D3, 800-1000 IU daily.	3 (6.7%)	• Stop Vit D and calcium
	e. Other	12 (26.7%)	• Replete Vit D only when Ca level normalized
			• Encourage hydration
			• Replete with Vitamin D 400 IU daily
			• Decision is contingent on other studies
Case 2. Post-menopausal woman with normal Ca and GFR, on chronic prednisone 10mg daily x 2 years.			

Disclosure: H. Syed, None; **T. George**, None; **T. Iden**, None; **A. Syed**, None; **A. Gerke**, None; **T. Le**, None.

Abstract Number: 0369

Methotrexate and Interstitial Lung Disease in Patients with Inflammatory Articular Disease: A Systematic Review

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies
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Background/Purpose: Methotrexate (MTX) is a commonly used drug for inflammatory joint diseases. Occasionally, its use has been associated with diffuse interstitial lung disease (DILD) development[1]. A systematic review (SR) has been carried out using the PRISMA methodology[2] in order to determine the extent of involvement of MTX in DILD development in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), psoriasis (Pso), juvenile idiopathic arthritis (JIA) or Crohn's disease-associated arthritis (CD-A).

Methods: Regarding the study selection, eligible studies were SR of randomized controlled trials (RCTs) with/without meta-analysis, RCTs, cohort studies, case-control studies and abstracts with relevant content, published from the year 2008 onwards, with adult population (≥18 years, except in JIA studies) diagnosed with any of the aforementioned pathologies and treated with MTX. The outcome was the onset/exacerbation of DILD.

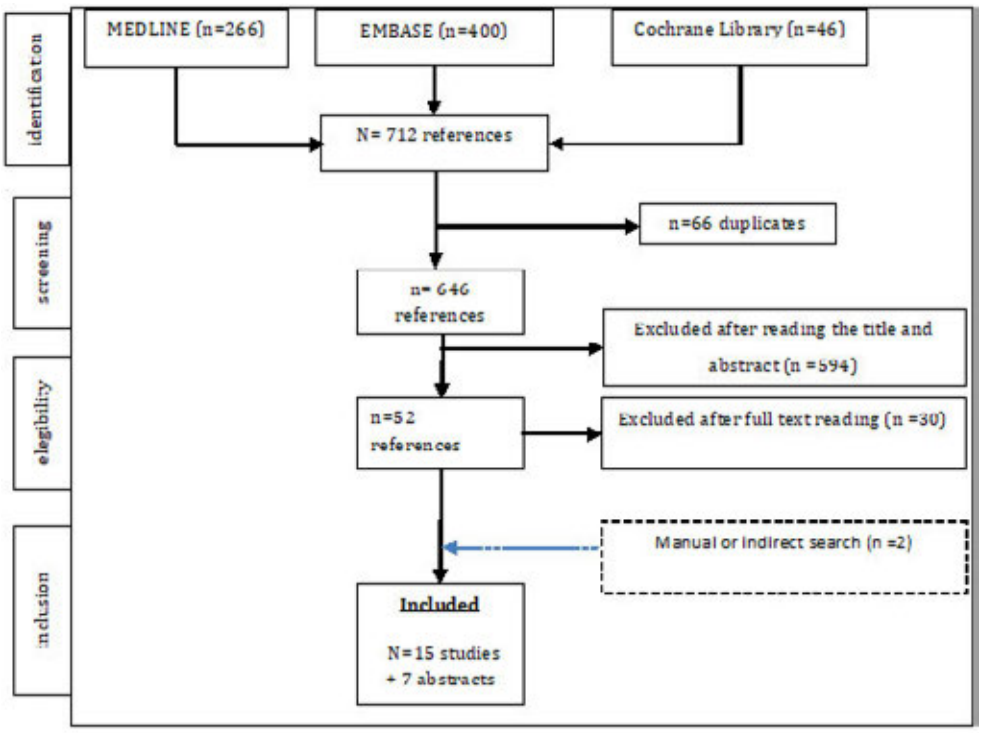

Figure 1. Flow-chart of the systematic review according to the PRISMA

1. Koduri G, Norton S, Young A, Cox N, Davies P, Devlin J, et al. Interstitial lung disease has a poor prognosis in rheumatoid arthritis: results from an inception cohort. Rheumatology (Oxford, England). 2010;49:1483-9.
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The search and selection of studies for the SR was performed in Medline, Embase and Cochrane, as well as among conference abstracts. Quality assessment and grading of the level of evidence was performed using SIGN[3].

According to the attached flow chart (Figure 1), 712 documents were initially retrieved. After full-text selection 15 studies of interest were identified. A meta-analysis was ruled out due to the heterogeneity of the papers.

Results: RA: Conway 2015[4] evaluated the relative risk (RR) of DILD/RA in patients treated with MTX, and detected a small increase in pneumonitis cases among these patients . Rojas-Serrano 2017[5] prospectively evaluated the role of MTX in a RA/DILD cohort, and observed better survival in the MTX cohort. England 2018[6] assessed the association of MTX with mortality risk in patients with/without lung diseases in a large RA cohort, and found no statistical significance. Kiely 2019[7] performed a multivariate analysis on two early RA cohorts, and found no association between MTX and RA/DILD development; on the contrary, MTX may delay DILD development.

PsA, Pso and CD-A: Conway 2015[4] found no association between MTX and RR of respiratory adverse events, respiratory infections, or non-infectious respiratory events. Cabello-Zurita 2017[8] retrospectively evaluated the overall

safety related to MTX in a cohort of patients with Pso without finding strong associations with any type of respiratory event.

JIA: Leiskau 2012[9] performed a retrospective analysis on the influence of cumulative MTX dose and its impact on respiratory function tests or the onset of new long-term respiratory events without finding any association. Alkady 2012[10] conducted a case-control study evaluating cardiopulmonary evolution in children with asymptomatic JIA. Impairment of lung function parameters was inversely correlated to longer MTX use.

Conclusion: The analysed studies offer no data to establish an association between the use of low-dose MTX and DILD onset in patients with inflammatory diseases. The association of MTX with recurrent acute episodes of previously established lung disease has also not been confirmed.

Disclosure: E. Rubio, Gebro, 2; **A. Muñoz**, Gebro, 2; **N. Casamira**, Gebro, 3.

Abstract Number: 0370

Use of Serum Lung Injury Biomarkers for Predicting the Severity of Interstitial Lung Disease in Patients with Connective Tissue Disease Associated Interstitial Lung Disease and Interstitial Pneumonia with Autoimmune Features

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SESSION INFORMATION

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Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Fibrotic lung diseases encompass a wide spectrum of clinical entities including connective tissue disease related interstitial lung disease (CTD-ILD) and interstitial pneumonia with autoimmune features (IPAF). Prior research on serum Krebs von den Lungen-6 (KL-6), surfactant proteins A (SP-A) and D (SP-D) levels have shown independent correlation to disease severity in patients with CTD-ILD. To our knowledge, no studies have evaluated the utility of all three biomarkers in predicting disease severity among US patients with CTD-ILD/IPAF. The goal of this study is to assess 1) the correlation between these biomarkers and lung disease severity; 2) their combined use with forced volume capacity (FVC, % predicted) in predicting lung disease severity using high resolution computed tomography (HRCT) as reference for disease severity.

Methods: This retrospective cross-sectional study involves 20 patients who had testing performed for ILD autoantibodies and KL-6, SP-A, and SP-D biomarkers at ARUP laboratories. In addition, they were diagnosed with CTD-ILD/IPAF per ACR criteria and had HRCT and pulmonary function testing available within 3 months from the date of the laboratory assessments. Positive KL-6, SP-A and SP-D levels were defined as >500 U/mL, >200 ng/mL and >300 ng/mL respectively. Extent of pulmonary fibrosis on HRCT was estimated as 0 to 100 percent using the Athol-Wells

Table 1. *Summary statistics for serum biomarker levels (KL-6, SP-A and SP-D) are given as median and range and as mean ± standard deviation and range for age, FVC and HRCT. They are otherwise reported as total number and percentage. ** ILD autoantibodies includes: ANA, RF, CCP, Jo-1, EJ, OJ, PL-7, PL-12, SRP, SCL-70, centromere, RNAP III, U1RNP, PM/SCL-100, Ku, SSA-52, and SSA-60. Testing performed at ARUP Inc.

Table 1. Cohort demographics and clinical characteristics (n = 20)

Variable	Summary Statistics*
Gender, female (%)	13 (65)
Age, years (SD)	61.4 ± 11.6, (41-84)
Ethnicity, white (%)	15 (75)
Positive ILD autoantibodies panel** (%)	20 (100)
Positive KL-6 (%)	15 (75)
Serum KL-6 level (U/ ml)	771 (328-6175)
Positive SP-A (%)	5 (25)
Serum SP-A level (U/ ml)	137 (63-491)
Positive SP-D (%)	15 (75)
Serum SP-D level (U/ ml)	383 (91- 861)
FVC, % predicted (0 – 100)	66.8 ± 15.7, (42 – 94)
HRCT score (0 -100%)	33.5 ± 20.9, (5 – 88)

method. We evaluated correlations between each biomarker and disease severity and assessed the individual and combination weights of KL-6, SP-A and SP-D levels and FVC in predicting disease severity (dependent variable) using HRCT as reference for disease severity.

Results: 75% of patients were white and 65% were females. 75, 25 and 75% had positive KL-6, SP-A and SP-D levels respectively (Table 1). All three biomarkers had positive correlations with disease severity, but only SP-D level had significant correlation with disease severity (r = 0.51, p: 0.02) (Table 2). KL-6 levels had significant negative correlation with FVC (r = 0.50, p: 0.03), but not with HRCT. In addition, SP-A levels were elevated in patients with severe disease as compared to those without (p: 0.03) (Table 3). In univariate regression analyses of KL-6, SP-A, SP-D and FVC only SP-D level had significant correlation in predicting disease severity (r = 0.05, p: 0.02) whereas in a multiple regression model using KL6, SPA, SPD, and FVC as independent variables, SPD (r = 0.08, p: 0.006) and FVC (r =

Table 2. Associations are shown in terms of magnitude (correlation coefficients, r), direction and statistical significance defined as p-value of < 0.05 *Quantitative high resolution CT score used to determine disease severity **Forced vital capacity used to determine disease severity

Table 2. Association of KL-6, SP-A and SP-D biomarkers with disease severity using HRCT and FVC as references for disease severity

		HRCT*		FVC, % predicted**	
	N	r	p	r	p
KL-6	20	0.22	0.36	-0.50	0.03
SP-A	20	0.18	0.45	-0.09	.72
SP-D	20	0.51	0.02	-0.07	.78

Table 3 Serum biomarker (KL-6, SP-A and SP-D) levels are reported as mean ± standard deviation. Severe and mild disease were defined as HRCT total score of > 20 and < 20 % respectively. P-value < 0.05 is considered statistically significant.

Table 3. Difference in serum biomarker levels between patients with severe and mild disease using HRCT as reference

Serum Biomarkers	Severe disease* (n=14)	Mild Disease* (n=6)	p
KL-6	1611.8 ± 1564. 3	710.5 ± 499.3	0.19
SP-A	242.9 ± 150.6	99.1 ± 33.2	0.03
SP-D	487 ± 219.6	319.8 ± 156.1	0.11

- 0.74, p: 0.03) were found to have statistically significant coefficients. Thus, all other predictor variables being equal, a one unit increase in SP-D is associated on average with a 0.064 increase in disease activity (R^2: .47, F-Value: 0.03).

Conclusion: The findings in this single-center retrospective study of patients with CTD-ILD/IPAF suggest that use of lung injury specific biomarkers and FVC together may be valuable in predicting disease severity and offer a cost-effective approach in monitoring disease progress. To our knowledge, this is the first US cohort study evaluating the utility of all three biomarkers in predicting disease severity among patients with CTD-ILD/IPAF.

Disclosure: S. Amjadi, None; **T. Frech**, None; **J. Chan**, None; **M. Scholand**, advisory board for Genetech and Boerhinger-Ingelheim., 5; **T. Jaskowski**, None; **S. La'ulu**, None; **J. Genzen**, None; **D. Lebiedz-Odrobina**, None; **A. Tebo**, None.

Abstract Number: 0371

Role of Alternative Immunosuppressant Therapy in Management of Cardiac Sarcoidosis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiac sarcoidosis (CS) is a rare, life-threatening disease and the second leading cause of death in patients with sarcoidosis. Currently, the recommended treatment for CS includes corticosteroids, optimal heart failure therapy, arrhythmia management, and prevention of heart block complications. The role of steroid sparing agents in the treatment of CS is not well described. Our aim was to review the clinical characteristics and treatment modalities of CS in our center and analyze patient outcomes who received oral immunosuppressive agents or a Tumor Necrosis Factor-alpha inhibitor (TNFi) as a part of their CS management.

Methods: We performed a retrospective chart review of all patients diagnosed with sarcoidosis from 2014 to 2019 at Loma Linda Medical Center. Patients that were diagnosed with CS (as defined by the Heart Rhythm Society diagnostic criteria) were included in the analysis.

	Immunosuppresive therapy					Conventional heart therapy					Cardiac Intervention	
Patient	Steroids	Methotrexate	Azathioprine	Infliximab	Mycophenolate	Aspirin	Statin	ACEi/ARB	Beta Blocker	Spironolactone	Pacemaker	AICD
1	+	-	-	+	-	+	+	+	+	+	-	+
2	-	-	+	-	-	+	+	+	+	-	-	-
3	+	+	+	+	-	+	-	+	-	+	-	-
4	+	-	+	-	-	+	+	+	-	-	-	+
5	-	-	-	-	-	-	+	+	+	-	-	+
6	-	-	-	-	-	-	-	+	+	-	-	-
7	+	-	-	-	-	+	+	+	+	+	-	+
8	+	+	-	-	-	+	+	-	+	+	+	-
9	+	-	-	-	-	+	+	+	-	-	-	-
10	+	-	+	-	-	+	+	+	+	-	-	+
11	+	+	+	-	+	+	-	-	+	-	-	-
12	+	-	-	-	-	+	-	+	-	-	-	+
13	+	-	-	+	-	+	-	-	-	-	-	-
14	-	-	-	-	-	-	-	+	+	-	-	-

Table 1: Immunosuppresive therapy and Conventional Heart Therapy of Patients Diagnosed with CS

Results: Out of 496 patients who have been diagnosed with sarcoidosis, 14 patients were diagnosed with CS in accordance with the Heart Rhythm Society guidelines. The average age was 58, 2:5 male to female ratio, and an average body mass index of 30.3. Seventy one percent of patients had biopsy proven sarcoidosis and the remaining 29% were diagnosed by clinical and imaging criteria. The most common presenting cardiac manifestation was new onset heart failure (64%), followed by cardiac arrhythmias (46%) of which more than half of patients presented with AV blocks (29%). All patients except one were initially diagnosed with sarcoidosis involving other organs (lungs (71%), skin (28%), lymph node (28%) joints (14%), GI tract manifestation (21%), neurological manifestations (21%). Cardiac manifestation was the initial presenting symptomatology of sarcoidosis in one patient. The average duration between initial diagnosis of sarcoidosis until diagnosis of CS was 5 years. The average duration between initial cardiac symptom onset and CS diagnosis was 4 years. Abnormal findings were noted on echocardiography (46%), cardiac magnetic resonance imaging (46%) noted as patchy myocardial scar, myocardial late gadolinium enhancement and positron emission tomography scan (40%). Patients were treated with corticosteroids (78%), azathioprine (36%), methotrexate (14%), infliximab (21%), mycophenolate (7%), hydroxychloroquine (7%), adalimumab (14%), cyclophosphamide (14%), and tacrolimus (7%) in addition to their conventional heart therapy. (Table 1). Three patients did not undergo any treatment for CS given their subclinical/asymptomatic status. Six of the analyzed patients had echocardiogram after initiation of immunosuppressive therapy. All patients except for one demonstrated either improvement, or no worsening of their left ventricular ejection fraction (LVEF) (table 1). One patient showed worsening of the LVEF due to noncompliance.

Conclusion: There are no formal guidelines for management of CS. We describe clinical manifestations and treatment outcomes of 14 patients with CS managed with an oral immunosuppressive agent or TNFi with favorable outcomes. Further larger scale prospective studies are required to identify the most appropriate immunosuppressant regimen and conclude its efficacy in management of CS.

Disclosure: P. Injean, None; **Y. Lee**, None; **M. Hojjati**, Exagen, 2.

Abstract Number: 0372

Periaortitis and Coronary Arteritis in IgG4-Related Disease: Eastern Mediterranean Experience

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated fibroinflammatory condition that may involve multiple organ systems. IgG4-RD can also lead to large vessel vasculitis and chronic periaortitis have been reported in patients with IgG4-RD. Furthermore, a Classification of IgG4-related periaortitis/periarteritis distribution was also reported.

This study is aimed to compare demographic and clinical features of IgG4RD patients with periaortitis/periarteritis with patients without periaortitis/periarteritis patients. Also distribution of patients according to classification reported is analyzed.

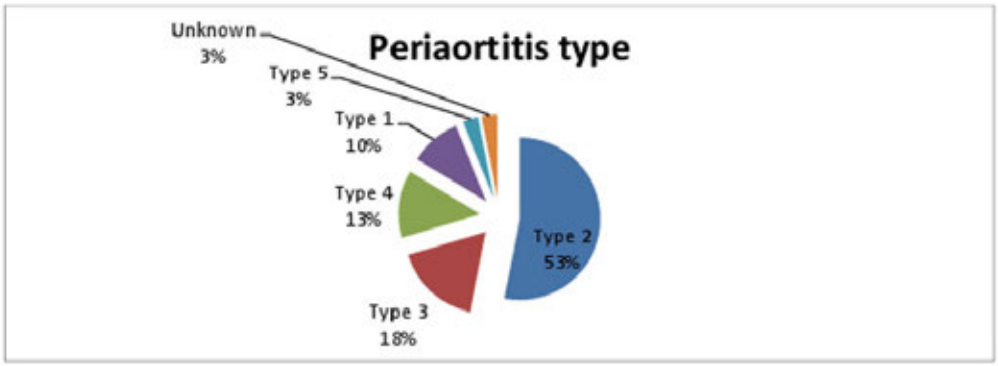
Methods: A total of 66 patients fulfilling the Comprehensive Diagnostic Criteria for IgG4-RD and admitted our vasculitis center between 2014 and 2018 were included in the study. Periaortitis and coronary arteritis was defined as

Table. Demographic characteristics and clinical findings of IgG4-RD patients with and without periaortitis

	Patients with periaortitis (n=29)	Patients without periaortitis (n=37)	p
Male	**19 (65.0)**	**15 (40.0)**	**0.038***
Age (years)	52 (±11)	51 (±19)	0.739
Age at disease onset (years)	49 (±13.6)	49 (±14.2)	0.832
Allergy	3/23 (13.0)	5/27 (18.5)	0.448
Ever smoked	13/23 (56.5)	8/27 (30.0)	0.051
Hypertension	**8/23 (34.8)**	**3/27 (11.0)**	**0.047***
Elevated acute phase reactants at diagnosis	22 (75.8)	18 (48.6)	0.025*
Elevated serum IgG4 level	15.0 (60.2)	14 (53.8)	0.303
Involved organ systems			
Multiple organ involvement	**23 (79.3)**	**17 (45.9)**	**0.006***
Lacrimal glands	4 (13.8)	11 (29.7)	0.107
Salivary glands	**2 (6.8)**	**10 (27.0)**	**0.034***
Respiratory organs	9 (31.0)	7 (18.9)	0.197
Pancreas	7 (24.1)	8 (21.6)	0.519
Biliary tract/liver	5 (17.2)	3 (8.1)	0.227
Kidney/urinary tract	9 (31.0)	3 (8.1)	0.019*
Lymph nodes	13 (44.8)	12 (32.4)	0.245
Coronary periarteritis	**6 (21.4)**	**0**	**0.005***
Periorbital involvement	4 (13.8)	11 (29.7)	0.107

* Data was shown as n(%) and mean (standart deviation) *Elevated serum IgG4 level is defined >135mg/dl and was available in 50 patients.

Figure. Classification of IgG4-related periaortitis type



vessel wall thickness, wall enhancement and perivascular soft tissue thickening on CT or MR angiography. Type 1 aortitis was localized at the infra-renal artery portion of the abdominal aorta, Type 2 added continuation to medium sized arteries, Type 3 added seperate location at the ascending aorta, Type 4 affected medium-sized arteries only and Type 5 was other involvement. Demographic, clinical, laboratory and imaging features of IgG-RD patients with and without periaortitis were compared.

Results: Among 66 (F/M=32/34) patients, 29 had periaortitis (43.9%). Mean age and disease duration was 51.4 ± 13.5 and 2.6 ± 2.7 years, respectively. Demographic and clinical characteristics of patients were summarized in Table. Male sex, hypertension, elevated acute phase reactants at diagnosis, urinary/kidney involvement and coronary arteritis was more frequent in periaortitis (+) patients whereas salivary gland involvement was more frequently observed in patients without periaortitis (Table).Median number of involved organ systems was 2 (1-5) and 1 (1-4) in patients with and without periaortitis, respectively (p=0.02).There was no difference in terms of serum IgG4 levels between groups.

In our cohort the most common periaortitis type was Type 2 that localized at the infra-renal artery portion of the abdominal aorta and was seen in 15 patients (53%). Second most common type was Type 3 (18%) followed by Type 4 (13%), Type 1 (10%) and Type 5 (3%) respectively. Classification of IgG4-related periaortitis type was given in Figure. Of the 66 IgG4-RD patients 6 (9%) had coronary arteritis. All patients with coronary involvement also had periaortitis and IgG4-RD patients without periaortitis had no coronary involvement (21.4% vs. 0%, p=0.005). In Type 3 periaortitis patients coronary artery involvement was significantly higher than other types of periaortitis (80% vs 8%, p=0.003).

Conclusion: Periaortitis is frequent in our IgG4-RD cohort and seen more in patients with male sex, hypertension, increased acute phase reactants at diagnosis and urinary/kidney involvement. The most common periaortitis type was Type 2 as reported. Since coronary arteritis is a serious involvement, screening of patients with periaortitis, especially Type 3 for coronary involvement might be rational.

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Abstract Number: 0373

Prognostic Factors and Long-term Outcomes in Cardiac Sarcoidosis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To identify prognostic factors and to assess the effects of immunosuppressive drugs on relapse risk in patients presenting with cardiac sarcoidosis (CS).

Methods: From a cohort of 157 patients with CS with a median follow-up of 7 years, we analysed all cardiac and extra-cardiac data and treatments, and assessed relapse-free and overall survival.

Results: The 10-year survival rate was 90% (95% CI, 84-96). Baseline factors associated with mortality were the presence of high degree atrioventricular block (HR, 5.56, 95% CI 1.7-18.2, p=0.005), left ventricular ejection fraction below 40% (HR, 4.88, 95% CI 1.26-18.9, p=0.022), hypertension (HR, 4.79, 95% CI 1.06-21.7, p=0.042), abnormal pulmonary function test (HR, 3.27, 95% CI 1.07-10.0, p=0.038), delayed myocardial hypersignal enhancement on cardiac magnetic resonance (HR, 2.26, 95% CI 0.25-20.4, p=0.003), and older age (HR per 10 years 1.69, 95% CI 1.13-2.52, p=0.01). The 10-year relapse-free survival rate for cardiac relapses was 53% (95% CI, 44-63). Baseline factors that were independently associated with cardiac relapse were kidney involvement (HR, 3.35, 95% CI 1.39-8.07, p=0.007), wall motion abnormalities (HR, 2.30, 95% CI 1.22-4.32, p=0.010), and left heart failure (HR 2.23, 95% CI 1.12-4.45, p=0.023). After adjustment for cardiac involvement severity, treatment with intravenous cyclophosphamide was associated with a lower risk of cardiac relapse (HR 0.16, 95% CI 0.033-0.78, p=0.024).

Conclusion: Our study identifies putative factors affecting morbidity and mortality in cardiac sarcoidosis patients. Intravenous cyclophosphamide is associated with lower relapse rates.

Disclosure: P. Cacoub, Abbvie, 5, AstraZeneca, 5, Bristol meyer squibb, 5, Gilead, 5, Glaxo Smith Kline, 5, Janssen, 5, Merck Sharp Dohme, 5, Roche, 5, Servier, 5, Vifor, 5; **C. Chapelon Abric**, None; **M. Resche-Rigon**, None; **D. Saadoun**, None; **A. Desbois**, None; **L. Biard**, None.

Abstract Number: 0374

The INBUILD Trial of Nintedanib in Patients with Progressive Fibrosing Interstitial Lung Diseases: Subgroup with Autoimmune Diseases

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SESSION INFORMATION

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Background/Purpose: Some patients with autoimmune disease develop progressive fibrosing interstitial lung disease (ILD) characterized by increasing fibrosis on HRCT, decline in lung function, worsening symptoms and high mortality. Nintedanib, a tyrosine kinase inhibitor, has established efficacy and safety in patients with idiopathic pulmonary fibrosis (IPF) and is an approved treatment for IPF. Recently nintedanib was shown to reduce the rate of decline in lung function in patients with systemic sclerosis-associated ILD. The efficacy and safety of nintedanib in patients with chronic fibrosing ILDs with a progressive phenotype are being investigated in the INBUILD trial. Here we describe the subgroup of patients with autoimmune disease-related ILDs enrolled in this trial.

Table. Baseline characteristics of patients with autoimmune disease-related ILDs in the INBUILD trial

Characteristic	All autoimmune ILDs (n=171)	Rheumatoid arthritis-associated ILD (n=88)	Systemic sclerosis-associated ILD (n=40)	Mixed connective tissue disease ILD (n=20)	Other fibrosing autoimmune ILDs (n=23)
Female	91 (53.2)	34 (38.6)	31 (77.5)	16 (80.0)	10 (43.5)
Age, years	64.3±10.6	66.9±9.7	58.6±10.0	64.4±9.3	63.9±12.5
Weight, kg	72.9±16.9	76.8±16.8	64.5±14.6	73.0±18.1	72.5±15.8
Race					
White	114 (66.7)	63 (71.6)	24 (60.0)	16 (80.0)	11 (47.8)
Asian	51 (29.8)	23 (26.1)	14 (35.0)	2 (10.0)	12 (52.2)
Other/missing	6 (3.5)	2 (2.3)	2 (5.0)	2 (10.0)	0
Criteria for ILD progression met in 24 months before screening*					
Relative decline in FVC ≥10% predicted	88 (51.5)	48 (54.5)	20 (50.0)	9 (45.0)	11 (47.8)
Relative decline in FVC ≥5–<10% predicted and increased extent of fibrotic changes on HRCT	49 (28.7)	22 (25.0)	13 (32.5)	8 (40.0)	6 (26.1)
Relative decline in FVC ≥5–<10% predicted and worsened respiratory symptoms	27 (15.8)	11 (12.5)	5 (12.5)	7 (35.0)	4 (17.4)
Worsened respiratory symptoms and increased extent of fibrotic changes on HRCT	57 (33.3)	34 (38.6)	13 (32.5)	5 (25.0)	5 (21.7)
FVC % predicted	70.8±14.8	71.4±16.2	69.5±12.6	71.3±12.2	70.4±15.5
DLco, % predicted	49.1±19.0	47.5±15.6	53.2±26.4	50.7±19.8	46.7±14.1
Usual interstitial pneumonia (UIP)-like fibrotic pattern only† on HRCT	127 (74.3)	77 (87.5)	24 (60.0)	12 (60.0)	14 (60.9)

Mean±SD or n (%) of patients treated with ≥1 dose of trial drug. *≥1 category could be ticked.
†Based on criteria used to identify UIP in the INPULSIS trials (Richeldi et al. N Engl J Med 2014;370:2071–82).

Methods: Patients with a physician-diagnosed ILD other than IPF were eligible to participate in the INBUILD trial if they had features of diffuse fibrosing lung disease of >10% extent on HRCT, forced vital capacity (FVC) ≥45% predicted, diffusing capacity of the lungs for carbon monoxide (DLco) ≥30–< 80% predicted, and met ≥1 of 4 criteria for ILD progression (Table) in the 24 months before screening, despite treatment of ILDs in clinical practice as applicable.

Patients were randomized to receive nintedanib 150 mg bid or placebo double-blind. Randomization was stratified by HRCT pattern (usual interstitial pneumonia [UIP]-like fibrotic pattern only or other fibrotic patterns). The primary endpoint is the annual rate of decline in FVC (mL/year) assessed over 52 weeks.

Results: Of 663 patients in the trial, 171 (25.8%) had autoimmune disease-related ILDs, of which the most common were rheumatoid arthritis-associated ILD (RA-ILD) (n=88), systemic sclerosis-associated ILD (n=40), and mixed connective tissue disease ILD (n=20) (Table). At baseline, the mean±SD age of patients with autoimmune ILDs was 64.3±10.6 years, FVC was 70.8±14.8% predicted and DLco was 49.1±19.0% predicted; about half had a relative decline in FVC ≥10% predicted in the 24 months before screening. Almost three-quarters of patients with autoimmune ILDs (74.3%) had a UIP-like fibrotic pattern only on HRCT. This pattern was most common in patients with RA-ILD (87.5%). The trial is ongoing.

Conclusion: The INBUILD trial will provide insights into the efficacy and safety of nintedanib in patients with progressive fibrosing ILDs, including those with autoimmune diseases. The results will be presented at the conference.

Disclosure: E. Matteson, Boehringer Ingelheim, 5, Pfizer, 2, Sun Pharmaceuticals, 2; **C. Kelly**, Boehringer Ingelheim, 5, 8; **J. Distler**, 4D Science, 4, Actelion, 5, Actelion Pharmaceuticals, 5, Active Biotech, 2, 5, AnaMar, 2, 5, Array Biopharma, 2, aTyr, 2, Bayer, 2, 5, BMS, 2, Boehringer Ingelheim, 2, 5, Bristol-Myers Squibb, 2, Celgene, 2, 5, Galapagos, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, JB Therapeutics, 5, medac, 5, Medac, 5, Novartis, 2, Pfizer, 5, RedX, 2, RuiYi, 5, Sanofi, 2, Sanofi-Aventis, 2, UCB, 2, 5; **A. Hoffmann-Vold**, Actelion, 5, 8, Boehringer Ingelheim, 2, 5, 8, GSK, 5, 8; **J. Seibold**, Boehringer Ingelheim, 5, Camurus AB, 5, Octapharma, 5, Corbus, 5, Bayer, 5, Indalo, 5, Blade, 5, Mitsubishi Tanabe Pharma, 5, Eicos Sciences, 5, Athersys, 4, Pacific Therapeutics, 4, BriaCell, 4; **S. Mittoo**, The Clinic Network, 1, 3; **O. Distler**, A. Menarini, 5, Abbvie, Acceleron, 5, Acceleron Pharma, 5, Actelion, 2, 5, 8, Actelion Pharmaceuticals, 2, 5, 8, 9, Amgen, 5, AnaMar, 2, 5, Bayer, 2, 5, 8, 9, Biogen Idec, 2, 5, Blade Therapeutics, 5, Boehringer Ingelheim, 2, 5, 8, 9, Catenion, 5, 9, ChemomAb, 2, 5, ChemomAB, 5, CSL Behring, 5, Ergonex, 5, espeRare Foundation, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 5, GSK, 2, 5, Holds Patent mir-29 for the treatment of systemic sclerosis, 9, Inventiva, 2, 5, iQvia, 5, Italfarmaco, 2, 5, Italfarmco, 5, Lilly, 2, 5, med, 5, 8, medac, 5, Medac, 2, 5, MedImmune, 2, 5, Medscape, 5, 8, 9, Menarini, 8, Mepha, 8, Mitsubishi Tanabe, 2, 5, Mitsubishi Tanabe Pharma, 2, 5, MSD, 5, 8, Novartis, 2, 5, 8, 9, Patent, 9, Patent issued, 9, Pfizer, 2, 5, 8, Pharmacyclics, 2, 5, Roche, 5, 8, 9, Sanofi, 2, 5, Sinoxa, 2, 5, Target Bio Science, 5, Target BioScience, 5, UCB, 2, 5, 9, UCB in the area of potential treatments of scleroderma and its complications, 2, 5; **R. Goeldner**, Boehringer Ingelheim, 3; **R. Schlenker-Herceg**, Boehringer Ingelheim, 3; **S. Stowasser**, Boehringer Ingelheim, 3; **M. Quaresma**, Boehringer Ingelheim, 3; **K. Flaherty**, Bellepheron, 5, Blade, 5, Boehringer Ingelheim, 5, Roche/Genentech, 5, Veracyte, 5.

Abstract Number: 0375

Experience with Biologic Agents for the Treatment of Cardiac Sarcoidosis in a U.S. Academic Medical Center

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis is a multisystem granulomatous disease of unclear etiology characterized histologically by non-caseating granulomas. While clinically manifest cardiac involvement occurs in only about 5% of patients with sarcoidosis, a significant proportion have clinically silent disease. Symptomatic cardiac involvement portends a poorer prognosis with manifestations varying from heart failure and conduction abnormalities to ventricular arrhythmias including sudden death. Immunosuppression with corticosteroids and DMARDs has been the mainstay of treatment despite a paucity of data. There is a subset of patients that are either non-responders to these agents or in whom the side effect profile is prohibitive for their long-term use. Biologic agents, mainly TNF alpha antagonists, have been used as salvage therapies in these patients. However, the evidence regarding their efficacy and safety is limited to a few case reports. In fact, there remains much apprehension regarding the use of TNF alpha antagonists in patients with systolic heart failure due to concerns that they can exacerbate heart failure. Our objective was to study the efficacy and safety of using biologics for the treatment of cardiac sarcoidosis.

Methods: We conducted a retrospective and prospective observational study of all adult patients with cardiac sarcoidosis treated with biologics at an academic medical center in Washington D.C, USA between 2013 and 2018.

Results: We identified 9 patients (3 men and 6 women) diagnosed with cardiac sarcoidosis at our institution. The mean age at diagnosis was 49.9 ± 8.6. 1 patient was Caucasian and the rest (n=8) were African American. Lungs were the most common extra cardiac organ involved (n=7) followed by CNS (n=4), liver (n=4) and skin (n=3). 5 of the patients presented with systolic heart failure (EF< 50%), 3 with arrhythmias and 1 was found to have incidental abnormal myocardial uptake on PET imaging. 8 of the 9 patients had abnormal myocardial uptake on PET imaging. All patients were initially treated with oral steroids and 7 of the 9 patients also received oral DMARDs; MTX (n=6), AZA (n=2), HCQ (n=2) and MMF (n=1). Biologics used were adalimumab (n=5), infliximab (n=3) and rituximab (n=1). The most common indication for biologics was progression of disease despite optimal doses of standard therapy, followed by intolerance or contraindication to standard therapy. 75% of the patients were noted to have marked clinical improvement with the addition of a biologic. 5 out of 9 patients had decreased myocardial uptake on PET following treatment with a biologic. 1 patient had no change on PET and 3 have not had repeat imaging done yet. None of the patients had worsening of left ventricular systolic function with the addition of a TNF alpha antagonist. There were no reported major infections or significant adverse events that were attributable to the use of biologics.

Conclusion: Based on our small cohort, biologics (mainly TNF alpha antagonists) appear to be safe and efficacious as salvage therapy for cardiac sarcoidosis. However, there is a need for prospective studies to further validate these findings as well as to identify the subset of patients that would benefit from early initiation of these therapies.

Disclosure: A. Pillarisetty, None; **M. Devraj**, None; **F. Sheikh**, None; **F. Constantinescu**, None.

Abstract Number: 0376

Long-term Outcome and Prognostic Factors of Patients with Interstitial Pneumonia with Autoimmune Features: A Single Center Large-scale Observational Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with idiopathic interstitial pneumonia (IIP) may have features of connective tissue diseases (CTDs). The term interstitial pneumonia with autoimmune features (IPAF) has been recently proposed for such patients. Factors reported to indicate a poor prognosis in IPAF include age, smoking history, non-specific interstitial pattern in HRCT, anti-RNP antibody positivity, decline in %DLCO and presence of a multi-compartment feature within the morphological domain [1-3]. To date, however, no study has comprehensively described outcomes over a long-term period and factors of exacerbation. The aim of study was to identify prognostic factors for exacerbation in patients with IPAF, and compare long-term outcomes among patients with IPAF, IIP, and CTD-ILD.

Methods: Six hundreds- and seventy-two patients who visited our department between April 2009 and March 2019 and were evaluated by chest HRCT scan. Then, they were clinically and radiologically diagnosed as having interstitial lung disease (ILD), IIP or connective tissue diseases associated ILD were enrolled. We applied IPAF criteria to these patients and then purified 68 patients. The prognostic factors for exacerbation were prospectively calculated and statistically analyzed using clinical, laboratory and imaging data collected from medical records.

Results: Of 68 patients with IPAF, 60% were women and mean age at diagnosis was 64.2 ± 13.8 years old. Mean observation period was 27.1 ± 29.6 months. Exacerbation rate was 25% (n=17). Overall death rate was 5.9% (n=4). Comparison of characteristics at diagnosis between the exacerbation group and non-exacerbation group showed that the exacerbation group had a significantly elevated rate of smoking, KL-6, and SP-D (P=0.034, 0.016, and 0.007). When we compared characteristics at diagnosis between the treatment group and non-treatment group in patients with IPAF, and those between the exacerbation group and non-exacerbation group in IPAF patients with treatment, the treatment group was significantly associated with signs of mechanic's hands, arthritis, anti-SS-A antibody positivity, and anti-ARS antibody positivity (P=0.009, 0.05, 0.05, and 0.007), and the exacerbation group in IPAF patients with treatment had a significantly elevated rate of smoking and KL-6 (P=0.008 and 0.019). When we compared

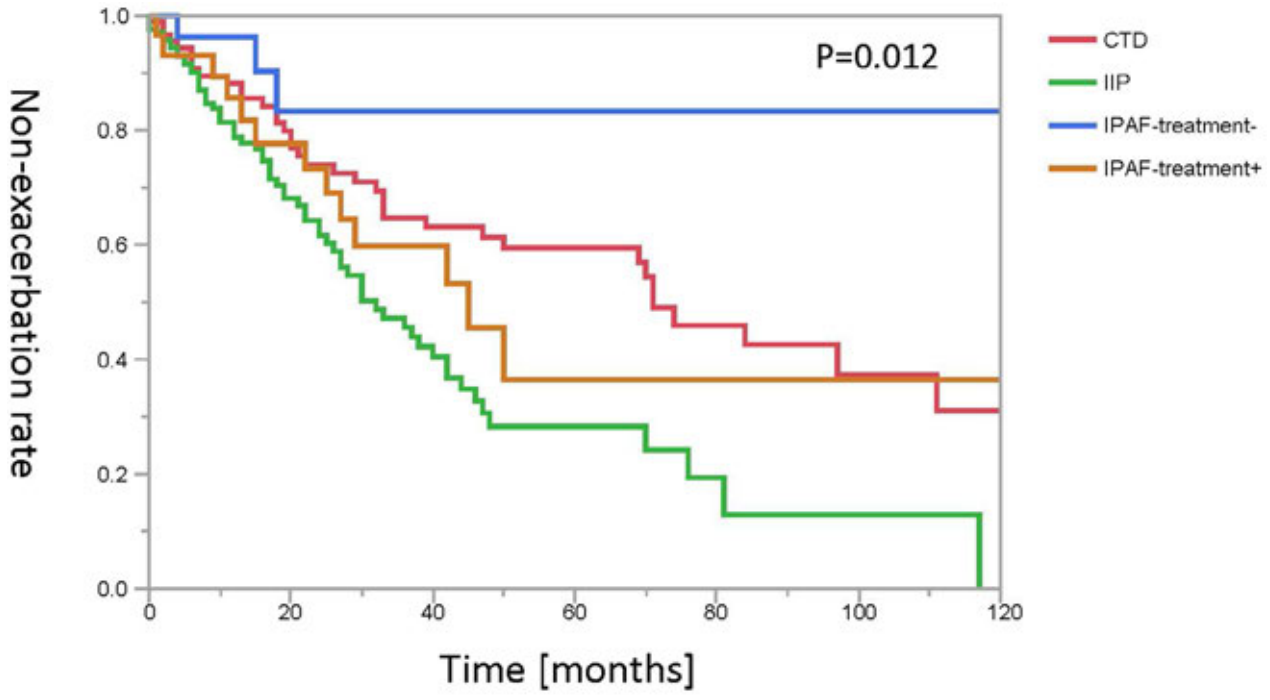

Figure 1. Kaplan-Meier survival curves of interstitial pneumonia with autoimmune features (IPAF) with or without treatment (n=38 and 30), idiopathic pulmonary fibrosis (IIP) (n=170) and connective tissue disease (CTD)-interstitial lung disease (ILD) (n=92).

long-term outcomes among patients with IPAF, IIP, and CTD-ILD, 5-year non-exacerbation rate in IPAF patients with treatment, those without treatment, CTD-ILD patients, and IIP patients was 36.5%, 83.3%, 59.5%, and 28.3%, respectively. (Figure 1)

Conclusion: Our large-scale cross-sectional cohort study identified unique prognostic factors of exacerbation and long-term outcome in patients with IPAF.

References: [1] *BMC Pulmonary Medicine*. (2017), [2] *Eur Respir J.* (2016), [3] *Clin Rheumatol.* (2018)

Disclosure: O. Murata, None; **K. Suzuki**, AbbVie, 2, Bristol-Myers Squibb, 2, Chugai, 2, Daiichi-Sankyo, 2, Eisai, 2, Fuji Film, 2, Kissei, 2, Mitsubishi Tanabe, 2, Ono, 2, Pfizer, 2, Takeda Pharmaceutical, 2; **N. Sasaki**, None; **T. Takeuchi**, Mitsubishi Tanabe Pharma Co., 2, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8; **M. Maemondo**, None.

Abstract Number: 0377

Novel Approach to the Treatment of Cardiac Sarcoidosis with TNF-alpha Inhibition

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis is a systemic inflammatory disease characterized by the presence of noncaseating granulomas. When it affects the myocardium, it can result in electrical conduction abnormalities, heart failure, and sudden death. There are no FDA-approved treatments for cardiac sarcoidosis, but the standard of care includes glucocorticoids and disease modifying anti-rheumatic drugs (DMARDs). When these therapies fail, tumor necrosis factor alpha (TNF-a) inhibitors are considered as a possible option. No formal studies have examined TNF-a inhibitors in cardiac sarcoidosis, and there is a theoretical concern that they may worsen heart failure. The aim of this retrospective review is to characterize cardiac sarcoidosis patients treated at Stanford University and to evaluate the response to TNF-a inhibitor treatment.

Methods: This is a retrospective study conducted at Stanford University. Sarcoidosis patients were identified by searching all patients seen between 2009 and 2017, ages 18 years and older, with an ICD-9/10 code for sarcoidosis, and at least one clinical note mentioning “sarcoidosis.” Each chart was manually reviewed to verify the sarcoidosis diagnosis, to determine which patients had cardiac involvement, and to extract relevant data for analysis. Continuous variables were summarized as mean and standard deviation. Categorical variables were summarized as frequencies and percentage of the total.

Results: A total of 1,186 potential sarcoidosis patients were identified (*Figure 1*), and 250 patients were excluded for not meeting diagnostic criteria. Of the 936 sarcoidosis patients remaining, 77 were identified as having cardiac sarcoidosis (8.2%). Baseline demographics (*Table 1*) demonstrate that the mean age at diagnosis was 55 years, 39% of patients were female, and the most common clinical presentations were heart block and tachyarrhythmia. Twenty patients (26%) received a TNF-a inhibitor (*Table 2*). The mean dose of prednisone before starting a TNF-a inhibitor was 23 milligrams (mg) daily, which decreased to 4 mg daily within 6 months after treatment initiation. Likewise, the mean left ventricular ejection fraction (LVEF) within one year before TNF-a inhibitor treatment was 44%, which

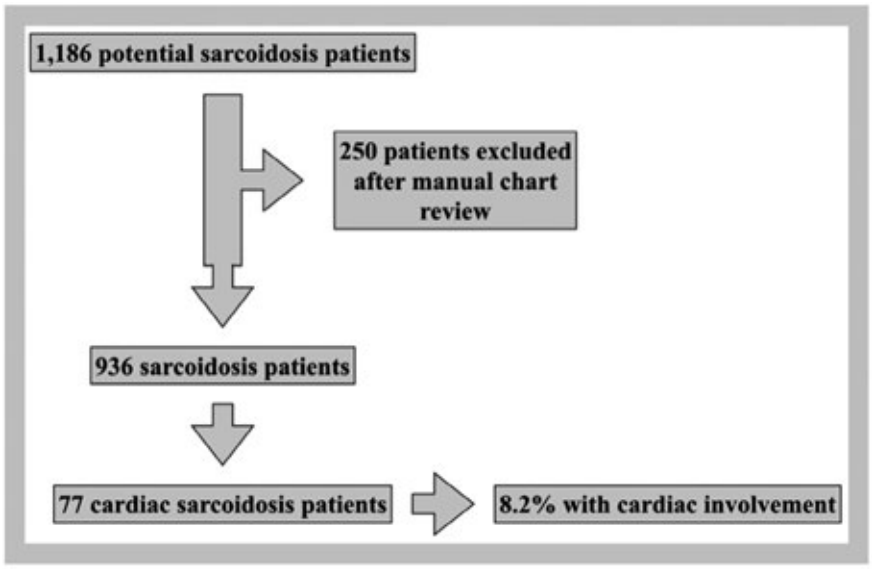

Figure 1: Sarcoidosis cohort patient selection

Table 1: Baseline characteristics of 77 cardiac sarcoidosis patients seen at Stanford University between 2009 and 2017

Clinical Characteristic	n (%)
Age at diagnosis in years, mean (SD)	55 (11.8)
Women	30 (39)
Race	
White	51 (66)
Black	12 (16)
Asian	7 (9)
Hispanic	7 (9)
Smoking (ever)	16 (21)
Body mass index at diagnosis, mean (SD)	28 (4.9)
Normal weight (< 25)	18 (23)
Overweight (≥ 25 and < 30)	30 (39)
Obese (≥ 30)	29 (38)
Initial clinical presentation	
Heart block	36 (47)
1st degree	10 (13)
2nd degree	3 (4)
3rd degree	23 (30)
Tachyarrhythmia	37 (48)
Palpitations	22 (29)
Heart failure	28 (36)
Syncope	16 (21)
Extracardiac sarcoidosis present	52 (68)
Isolated cardiac sarcoidosis	25 (32)
Follow-up in years, mean (SD)	4.8 (5.6)
Time to diagnosis from first symptom in years, mean (SD)	3.3 (4.7)
When extracardiac sarcoidosis present, mean (SD)	2.7 (3.8)
When isolated cardiac sarcoidosis, mean (SD)	4.6 (6.1)

*Data are number (%) except for age, BMI, follow-up, and time to diagnosis, which are mean (SD).

Table 2: Treatment outcomes for 20 cardiac sarcoidosis patients treated with TNF-α inhibitors

TNF-α Inhibitor Indication/Outcome	n (%)
Reason for initiating TNF-α inhibitor	
Worsening heart failure	3 (15)
Worsening arrhythmia	8 (40)
Worsening findings on imaging	17 (85)
Improvement in imaging after TNF-α inhibitor initiation	16 (94)
Time from diagnosis to TNF-α inhibitor initiation in months, mean (SD)	16 (14.0)
Prednisone dose 6 months before TNF-α inhibitor initiation in mg, mean (SD)	23 (11.9)
Prednisone dose 6 months after TNF-α inhibitor initiation in mg, mean (SD)	4 (8.6)
Time to stop prednisone after TNF-α inhibitor initiation in months, mean (SD)	9 (8.9)
LVEF within 12 months before TNF-α inhibitor initiation, mean (SD)	44 (14.1)
LVEF within 12 months after TNF-α inhibitor initiation, mean (SD)	47 (14.8)
Serious infections	
Patients on TNF-α inhibitors	0 (0)
Patients on non-TNF-α inhibitor immunosuppression	7 (9)

remained stable at 47% within one year after starting treatment. This included 5 patients with an LVEF £ 30% at the time of TNF-a inhibitor initiation.

Conclusion: Twenty cardiac sarcoidosis patients in our cohort (26%) received a TNF-a inhibitor, with the overall experience being positive. Despite concerns that TNF-a inhibitors can worsen heart failure, no patients had a notable decline in LVEF within one year after treatment initiation, and most saw an improvement. This included 5 patients who had a LVEF £ 30% at the time of starting a TNF-a inhibitor. In addition, those patients who were on glucocorticoids at the time of TNF-a inhibitor initiation were all able to reduce their dose. This study supports the notion that patients with cardiac sarcoidosis who continue to have active disease despite conventional therapies can be treated with TNF-a inhibitors, and it provides a strong rationale for larger, prospective studies to be conducted in the future.

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Abstract Number: 0378

Systemic and Ocular Sarcoidosis Study of 381 Patients from a Single Universitary Centre in the Last 20 Years

Lara Sanchez-Bilbao ,[1] Belén Atienza-Mateo,[1] Iñigo Gonzalez-Mazon,[2] Jose Luis Martín-Varillas,[1] Rosalia Demetrio,[3] Vanesa Calvo-Río,[4] Eva Peña Sainz-Pardo,[5] Raul Fernandez-Ramon,[3] Jorge Javier Gaitan-Valdizan,[3] Miguel A Gonzalez-Gay,[1] and Ricardo Blanco[1], [1]Rheumatology, Hospital Universitario Marques de Valdecilla, Santander, Spain, [2]Rheumatology, Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain, [3]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [4]Hospital Universitario Marques de Valdecilla, Santander, Spain, [5]Pediatrics, Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain

SESSION INFORMATION

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Background/Purpose: Sarcoidosis is a multisystemic inflammatory disease characterized by non-caseating epitheliod granulomas. Ocular involvement is the presenting symptom in approximately 20-30% in form of uveitis, conjunctivitis, episcleritis/scleritis, optical nerve disease or orbital inflammation. Our objective was to define an epidemiological context in the last 2 decades, focusing on the ocular affectation and its correlation with the IWOS (International Workshop on Ocular Sarcoidosis) criteria, which classify ocular sarcoidosis as definitive, presumed, probable and possible, according to certain ophthalmological and analytical findings. They are very useful if a biopsy is not obtained or it is negative

Methods: Retrospective study of patients admitted to a single reference University Hospital between 01/01/1999 and 01/01/2019 with diagnosis of sarcoidosis trough biopsy and/or compatible symptoms and imaging tests. Demographics features, clinical findings, complementary tests and treatment were recorded.

	Patients (n=50)
Age, mean (SD) years	45.5 (16.7)
Sex, men/women, n/n	23/27
Affected organs, n (%)	
Lung	30 (60)
Skin	14 (28)
Liver	4 (8)
Kidney	3 (6)
Musculoskeletal system	3 (6)
Central nervous system	3 (6)
Hearth	2 (4)
Ocular signs, n (%)	
Bilaterality	22 (44)
Snowballs/strings of pearls	19 (38)
Mutton-fat KPs	12 (24)
Multiple chorioretinal peripheral lesions	7 (14)
Periphlebitis	5 (10)
Anterior synechiae	1 (2)
Optic disc granulomas	1 (2)
IWOS criteria, n (%)	
Definite	22 (44)
Presumed	13 (26)
Possible	4 (8)
Treatment, %	
Prednisone (oral)	44 (88)
Methylprednisolone (bolus)	5 (10)
Conventional immunosuppressor	
.....Methotrexate	21 (42)
.....Azathioprine	9 (18)
.....Cyclosporine	2 (4)
.....Mycophenolate mofetil	2 (4)
Biologic therapy	
.....Infliximab	5 (10)
.....Adalimumab	4 (8)
.....Golimumab	2 (4)

Results: We studied 381 patients (190 women/191 men), mean age at diagnosis 45.5±15.4 years, 94.8% of Spanish nationality. 33% were smokers and 6.3% had had tuberculosis. The incidence rate of sarcoidosis was 3.3 cases/ 100,000 people/year, like other national series. The most affected organ was lung (72.3%), followed by skin (31%) (TABLE 1). In addition, at diagnosis 11.5% and 0.5% of patients had a Löfgren and a Heerdfort syndrome, respectively. A simple x-ray chest was performed in all patients, with alterations in 83.7%, the majority at stages I and II. Moreover, 29.9% and 10.5% presented pathological scintigraphy and PET scan, respectively. A biopsy was performed in 81.9% of the cases, with a mediastinal approach in 43.3%. After a median follow-up of 11.0 [6.0-17.0] years, 32% had never received treatment and in the remaining 68% the most used therapy was oral glucocorticoids. Other therapies were conventional and/or biological immunosuppressants (TABLE 2).

	Patients diagnosed with sarcoidosis (n=381)
DEMOGRAPHIC PARAMETERS	
Sex, n (%)	191♂/190♀ (50.1/49.9)
Age at disease onset (years), mean ± SD	45.5 ± 15.4
Current age (years), mean ± SD	59.0 ± 16.3
Follow-up, median [ICR]	11.0 [6.0-17.0]
Nationality (Spanish), n (%)	361 (94.8)
Smokers, n (%)	126 (33.1)
Asthma, n (%)	24 (6.3)
Tuberculosis, n (%)	24 (6.3)
Tumors, n (%)	23 (6.0)
CLINICAL MANIFESTATIONS	
Pulmonary symptoms, n (%)	**277 (72.3)**
- Dyspnea, n (%)	103 (26.9)
- Cough, n (%)	35 (9.1)
- Pleuritic pain, n (%)	10 (2.6)
- Adenopathy, n (%)	129 (33.7)
Ocular involvement, n (%)	**50 (13.0)**
Skin involvement, n (%)	**119 (31.1)**
- Erythema nodosum, n (%)	72 (18.8)
- Lupus pernio, n (%)	7 (1.8)
- Parotid gland hypertrophy, n (%)	7 (1.8)
- Granulomatous dermatitis, n (%)	33 (8.6)
Joint involvement, n (%)	**107 (27.9)**
- Arthralgia, n (%)	66 (17.2)
- Arthritis, n (%)	40(10.4)
- Sarcoid myopathy, n (%)	1 (0.3)
Digestive disorders, n (%)	**36 (9.3)**
- Hypertransaminasemia, n/N (%)	20 (5.2)
- Hepatic granulomas, n/N (%)	13 (3.3)
- Other granulomas, n/N (%)	3 (0.8)
Neurological symptoms, n (%)	**25 (6.5)**
- Headache, n (%)	13 (3.5)
- Meningitis, n (%)	2 (0.5)
- Neuropathy, n (%)	6 (1.5)
- Others, n (%)	4 (1.0)
Cardiological manifestations, n (%)	**6 (1.6)**
- Dilated cardiomyopathy, n (%)	4 (1.0)
- Pericarditis, n (%)	1 (0.3)
- SMVT, n (%)	1 (0.3)
Nephrological manifestations, n (%)	**18 (4.7)**
- Acute renal failure, n (%)	12 (3.1)
- Chronic kidney disease, n (%)	5 (1.3)
- Lithiasis, n (%)	1 (0.3)
Systemic symptoms, n (%)	**143 (37.3)**
- Fever, n (%)	36 (9.4)
- General syndrome, n (%)	107 (27.9)
Lymphadenopathy as incidental finding, n (%)	44 (11.5)
Löfgren syndrome, n (%)	44 (11.5)
Heerdfort syndrome, n (%)	2 (0.5)

	Patients diagnosed with sarcoidosis (n=381)
LABORATORY TESTS	
CRP (mg/dl), median [ICR]	0.2 [0.0-1.2]
ESR (mm/1ªh), median [ICR]	22.0 [10.0-38.0]
ACE, mean ± SD	78.7 ± 46.2
Calcium, mean ± SD	9.4 ± 0.9
Thrombocytosis, n (%)	9 (2.4)
Lymphopenia, n (%)	43 (11.3)
Hypercalciuria, n (%)	29 (7.6)
CD4/CD8 > 3.5, n (%)	122 (32.0)
IMAGING TESTS	
Patients with abnormal radiological patterns:	**319 (83.7)**
- Stage I, n (%)	156 (41.4)
- Stage II, n (%)	122 (32)
- Stage III, n (%)	29 (7.6)
- Stage IV, n (%)	14 (3.8)
Confirmed lymphadenopathy in CT, n (%)	**300 (78.7)**
Pathological scintigraphy, n (%)	**114 (29.9)**
Pathological PET, n (%)	**40 (10.5)**
Non-caseating granulomas in biopsy, n (%)	**290 (75.7)**
- Mediastinum, n (%)	166 (43.3)
- Lung, n (%)	67 (17.5)
- Liver, n (%)	9 (2.4)
- Skin, n (%)	45 (11.7)
- Lymphadenopathy, n (%)	3 (0.8)
TREATMENT	
Not treated, n (%)	**122 (32.0)**
Glucocorticoid treatment	
- Topical treatment, n (%)	39 (10.2)
- Prednisone, n (%) / mean dose (mg/day), mean±SD	206 (54.1) / 43.4±19.1
- Bolus MTP, n (%)	15 (3.9)
Conventional immunosupressants	
- Methotrexate, n (%) / mean dosage (mg/week), mean±SD	53 (13.9) / 15.4±5.5
- Azathioprine, n (%) / mean dosage (mg/day), mean±SD	17 (4.5) / 91.6±32.2
- Cyclophosphamide, n (%)	2 (0.5)
- Mycophenolate mofetil, n (%)	2 (0.5)
Biological agents	
- Infliximab, n (%)	14 (3.7)
- Adalimumab, n (%)	19 (5.0)
- Etanercept, n (%)	1 (0.3)
- Golimumab, n (%)	2 (0.5)
- Tocilizumab, n (%)	3 (0.8)
- Rituximab, n (%)	3 (0.8)
- Secukinumab, n (%)	1 (0.3)

Besides, patients with ocular involvement were selected (n=50, 13%), 40 of them with uveitis. Thirty-nine patients (78%) met one of the 4 IWOS diagnostic categories: 22 definite (44%), 13 presumed (26%) and 4 possible (8%) sarcoidosis. The most common ocular signs were bilaterality (44%), snowballs or strings of pearls (38%), mutton-fat KPs (24%), multiple chorioretinal peripheral lesions (14%) and periphlebitis (10%). Regarding the treatment of this group, 44 patients (88%) received oral corticosteroids, 21 (42%) methotrexate, 11 (21%) another conventional immunosuppressor and 11 (21%) a biological treatment. TABLE 3 shows the main demographic and clinical features of this group.

Conclusion: The results obtained are reproducible to those published in national and international series, except for the non-predominance of females and the highest percentage of ocular involvement in our study. Currently, biological treatment (especially anti-TNF) is used more frequently. In our population the IWOS criteria had a sensitivity of 78%.

Even though there is no gold standard for diagnosing ocular sarcoidosis yet, IWOS signs can help clinicians suspect it.

Disclosure: L. Sanchez-Bilbao, None; **B. Atienza-Mateo**, None; **I. Gonzalez-Mazon**, None; **J. Martín-Varillas**, None; **R. Demetrio**, None; **V. Calvo-Río**, None; **E. Peña Sainz-Pardo**, None; **R. Fernandez-Ramon**, None; **J. Gaitan-Valdizan**, None; **M. Gonzalez-Gay**, Abbvie, 2, 5, 8, Celgene, 5, 8, Janssen, 2, MSD, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, Sanofi, 5, 8, Sobi, 5, 8; **R. Blanco**, None.

Abstract Number: 0379

Neurosarcoidosis: An Evaluation Based on the Neurosarcoidosis Consortium Consensus Group

Thieroff George ,[1] Huzaefah Syed,[2] Thomas Iden,[2] Aamer Syed,[2] Trang Le,[2] and Alicia Zukas[3], [1]VCU Medical Center, Richmond, VA, [2]VCU Medical Center, Richmond, VA, [3]Virginia Commonwealth University, Richmond, VA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The 2018 Neurosarcoidosis Consortium Consensus Group (NCCG) attempted to increase specificity in diagnosing neurocsarcoidosis from the 2013 World Association of Sarcoidosis and Other Granulomatous Diseases (WASOG) Organ Assessment Criteria. We assessed whether treatment response varied within these new classifications.

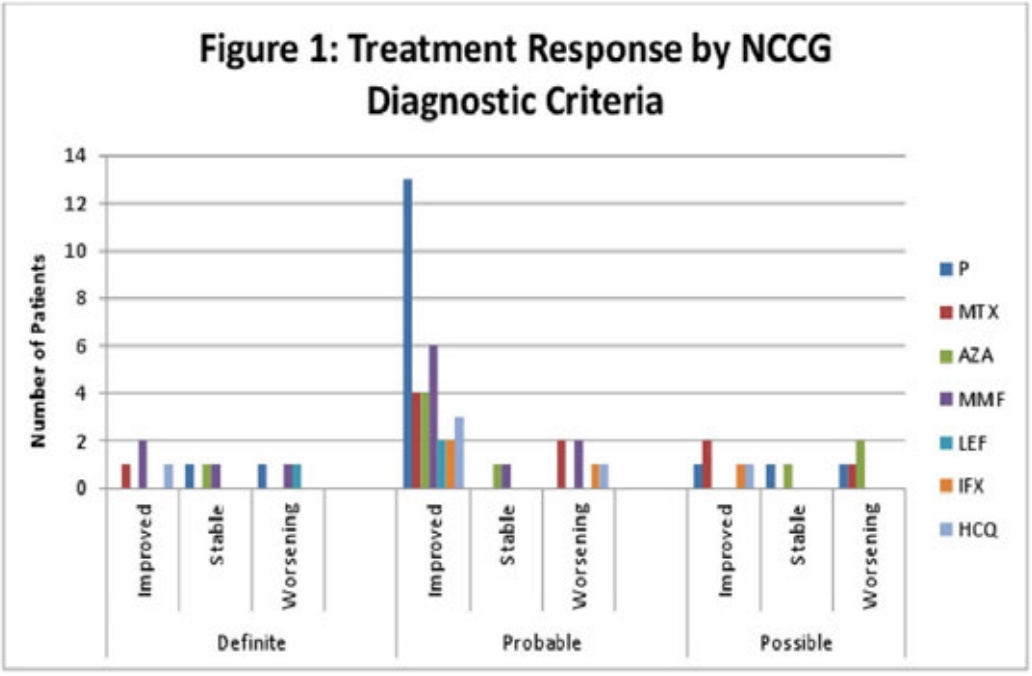

Table 1: Demographics (n=48)	
Age (years)	Median (49), IQR (42.5 – 54.5)
Race (%)	Black (83), White (15), Other (2)
Sex (%)	Male (50)
MRI n = 40, % abnormal	97.5
CSF n = 24, % abnormal	60
Brain bx n = 7, % abnormal	100

Methods: We performed a single center, retrospective study of patients with diagnosis of neurosarcoidosis from the VCU Sarcoidosis database containing data on 1298 patients from 2009 to 2019. Patients were classified by WASOG and NCCG criteria. Response to therapy was defined as improvement in symptoms on most recent therapeutic agent.

Results: 48 subjects (50% male, 83.3% black) were enrolled with a median of age 49. Of the 46 previously diagnosed as Highly Probable or Probable by WASOG criteria, 32 (66.7%) dropped from Highly Probable to Probable or from Probable to Possible by NCCG criteria. 7 (14.6%) dropped from Highly Probable to Possible due to lack of tissue biopsy from any source. 7 patients were defined as Definite by NCCG criteria due to positive brain biopsy and were previously Highly Probable by WASOG criteria. 28 (58.3%) patients improved on any therapy and 16 (33.3%) improved with exposure to glucocorticoids. There was no appreciable response to any specific therapy, both between NCCG classifications or the group as a whole (Figure 1).

Table 3: Change in Diagnosis Group

	NCCG		
WASOG	Definite	Probable	Possible
Highly Probable	7	31	8
At Least Probable	0	2	0

Conclusion: NCCG criteria likely increase specificity for neurosarcoidosis by placing a greater emphasis on tissue biopsy. There was no observable difference in response to therapy, regardless of classification, emphasizing the need for future randomized controlled trials.

Disclosure: T. George, None; **H. Syed**, None; **T. Iden**, None; **A. Syed**, None; **T. Le**, None; **A. Zukas**, None.

Abstract Number: 0380

Seasonal Clustering of Acute Sarcoidosis in South-West Germany and Associations with Particulate Matter Air Pollution

Philipp Rustler ,[1] Dirk Schindler,[2] Reinhard Voll,[1] and Florian Kollert[3], [1]Division of Rheumatology and Clinical Immunology, Medical Centre - University of Freiburg, Freiburg, Germany, [2]Environmental Meteorology, University of Freiburg, Freiburg, Germany, [3]Department of Rheumatology, Immunology and Allergology, Inselspital, University Hospital Bern, Bern, Switzerland

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis is a multisystemic granulomatous disorder of unknown origin. The central role of macrophages and granuloma formation, the predominant involvement of lung and skin, and risk populations (e.g. fire fighters) points towards causative airborne antigen(s). This study has been set to analyze seasonal clustering of acute sarcoidosis in south-west Germany and correlations to particulate matter air pollution.

Methods: Patients with acute sarcoidosis (as defined by bihilar lymphadenopathy, ankle swelling and/ or erythema nodosum) who presented between January 1994 and December 2018 were included in this retrospective study. Disease onset (seasonal clustering) and associations to air pollution (particulate matter (PM_{10})) were analyzed.

Results: We were able to include 186 patients (47.3% female, mean age 37, complete Löfgren triad in 72%) with acute sarcoidosis. Over the whole study period disease onsets peaked in the first third of the year (January 17.7 % of cases, February 11.8 %, March 12.4 %, April 12.4 %, May 9.7 %, June 9.7 %, July 7.5 %, August 3.2 %, September 2.7 %, October 1.1 %, November 2.1 %, December 9.7 %). Increase of local PM_{10} (values ranging between 15 and 40 µg/m^3) was followed by a higher number of disease cases in the study period from 2004 to 2015.

Conclusion: In south-west Germany the onset of acute sarcoidosis clusters in the first third of the year. Particulate matter air pollution might be one factor involved.

Disclosure: P. Rustler, None; **D. Schindler**, None; **R. Voll**, None; **F. Kollert**, None.

Abstract Number: 0381

Effect of Vitamin D Supplementation on Calcium Levels in Patients with Sarcoidosis: A Retrospective Analysis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Hypercalcemia is seen in 2-30% of patients with sarcoidosis and is caused by the overproduction of Vitamin D (VitD) 1,25OH (calcitriol) by macrophages within granulomas. Low VitD 25OH is also commonly seen, but VitD repletion can potentially cause hypercalcemia. There are currently limited data regarding safe VitD

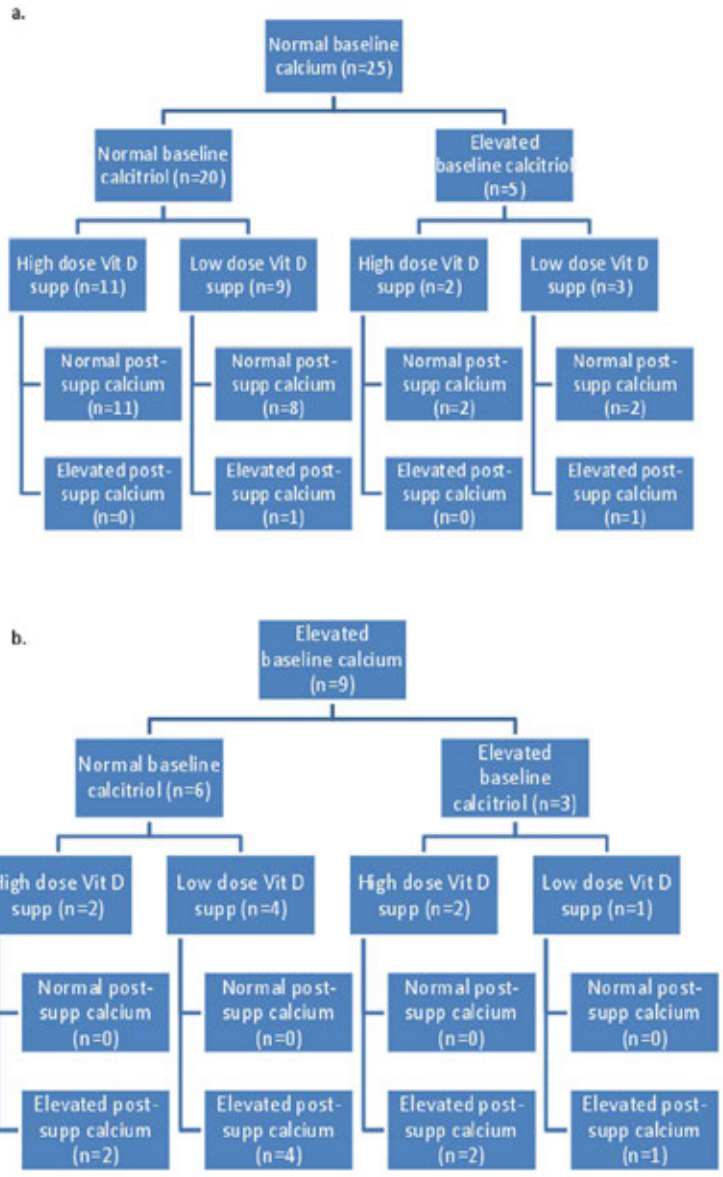


Figure 1. Levels of post-supplementation calcium in patients with normal baseline calcium (a) and elevated baseline calcium (b). Stratified by baseline calcitriol and dosage of Vitamin D supplementation. Only patients with a documented baseline calcitriol included. All patients with baseline hypercalcemia remained hypercalcemic post-supplementation, but only two with normal baseline calcium developed hypercalcemia.

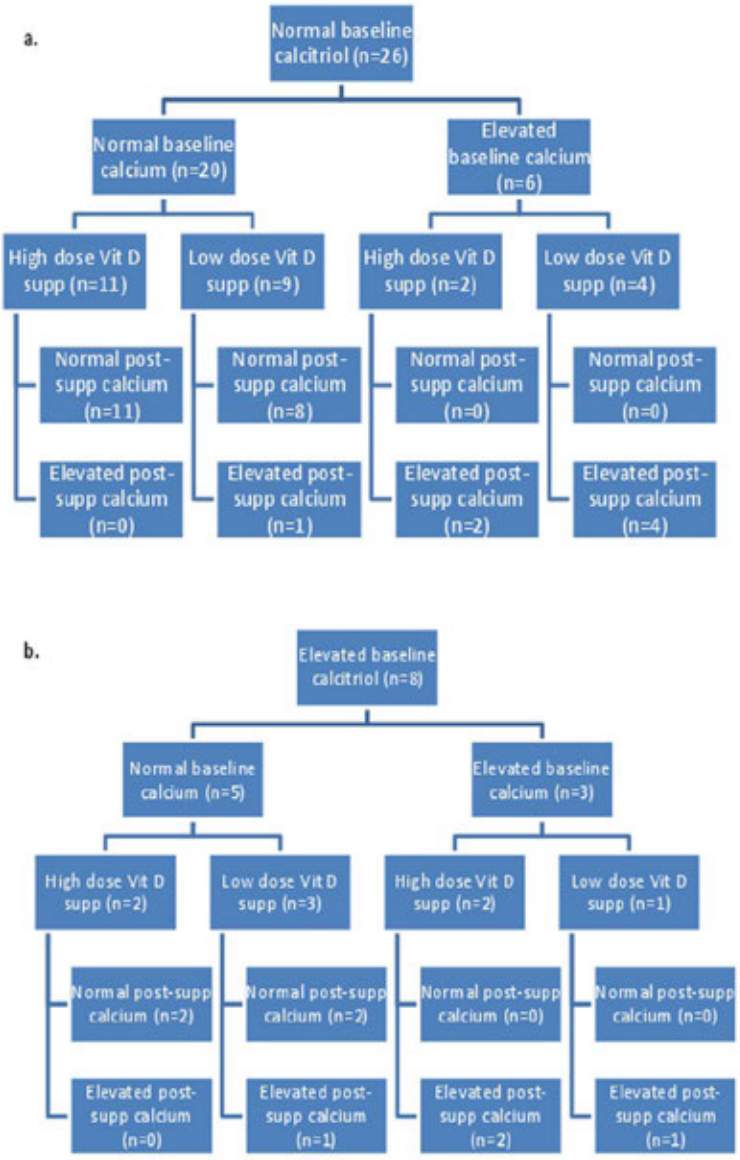
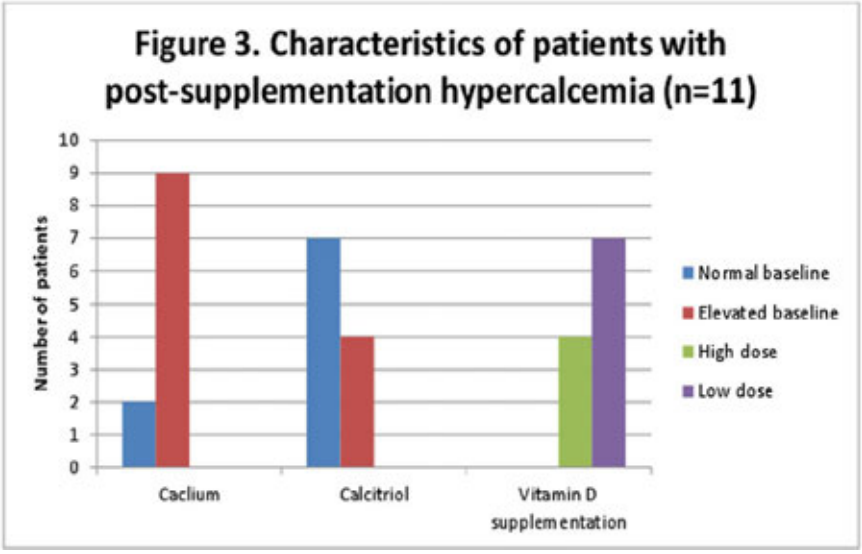


Figure 2. Levels of post-supplementation calcium in patients with normal baseline calcitriol (a) and elevated baseline calcitriol (b). Stratified by baseline calcium and dosage of Vitamin D supplementation. All patients with elevated baseline calcium remained hypercalcemic after receiving supplementation, whereas only 2 patients with normal baseline calcium developed hypercalcemia after supplementation.

repletion in sarcoidosis patients. We sought to identify patients with sarcoidosis receiving VitD supplementation and determine the incidence of hypercalcemia among them.

Methods: Records of patients with at least one visit for sarcoidosis between January 2010 and December 2015, one recorded baseline calcium, and at least two recorded VitD 25OH levels were reviewed. Serum calcium, VitD 25OH, and calcitriol levels and VitD supplementation data were collected. Hypercalcemia was defined as > 10.7mg/mL. Elevated calcitriol level was defined as >79.3pg/mL. High dose VitD supplementation was defined as vitamin D2 or D3 ^{3}50,000 units weekly, or its equivalent.



Results: One hundred twenty patients were identified (70.8% female, 84.3% African-American, median age of 50 years). Sixteen (13%) patients demonstrated baseline hypercalcemia. Of the 36 patients with available baseline calcitriol, 8 (22%) were elevated. The mean baseline VitD 25OH level was 15.64ng/mL (SD 6.88). For patients in whom repletion duration was available (n=71), median duration for repletion was 12 weeks. Two of the 25 (8%) patients with normal baseline calcium developed post-supplementation hypercalcemia, whereas 9 of the 9 (100%) patients with elevated baseline hypercalcemia had hypercalcemia after supplementation. Seven of the 26 (26.9%) patients with normal baseline calcitriol were hypercalcemic post-supplementation, whereas 4 of the 8 (50%) patients with elevated baseline calcitriol were hypercalcemic after supplementation. Of the total cohort, 11 (9.2%) patients were noted to be hypercalcemic after supplementation. Of these, 9 (81.8%) had baseline hypercalcemia, 4 (36.4%) had elevated baseline calcitriol, and 4 (36.4%) received high dose supplementation. Only one patient who received VitD supplementation developed VitD levels above the normal limit, but did not develop hypercalcemia.

Conclusion: Our data suggests that VitD supplementation can be considered in those with normal baseline calcium, but should be given with caution in those with elevated baseline calcium. Baseline calcitriol did not appear to be a risk factor for hypercalcemia induced by VitD supplementation, but additional data are needed to inform more standardized supplementation algorithms.

Disclosure: C. Overton, None; **T. Le**, None; **T. Iden**, None; **A. Syed**, None; **M. Kashiouris**, None; **H. Syed**, None.

Abstract Number: 0382

Neurofilament Light Chain Levels in Cerebrospinal Fluid and Plasma in Neurosarcoidosis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Neurofilament Light Chain (NFL) is an emerging biomarker that is specific for neuronal and axonal damage/degeneration but unspecific regarding the origin of destruction. NFL has been suggested as biomarker in neurological diseases. No study has so far examined relation between neurosarcoidosis (NS) and NFL.

The purpose is to compare NFL levels in plasma and cerebrospinal fluid (CSF) in sarcoidosis patients with NS compared to healthy controls (HC).

Methods: Plasma and CSF from consecutive biopsy positive sarcoidosis patients with suspected NS and/or relapsing NS (n=19). Based on WASOG-criteria, patients were characterized into two groups: highly probable NS (n=14) and a non-NS group (n=5). Results were compared to the HC (n=11). NFL concentrations were analyzed using Single Molecular Array (SIMoA) from Quanterix. NFL Levels above 807.5pg/ml in CSF and 13.0 pg/ml in plasma were considered elevated. Group medians were compared using Kruskal-Wallis and Mann-Whitney tests. Range is given in brackets.

Results: The average mean age of NS patients was 45 years (23-59) and disease duration median 5.5 (2-259) months. Of the patients with NS 79 % (n=11) initially presented with CNS symptoms. The remaining patients: one developed NS after 4 months under glucocorticoid treatment, one had chronic NS with symptom aggravation under immunosuppression and one had skin sarcoidosis with relapse of NS. Elevated serum angiotensin converting enzyme (ACE) was found in 14 % (n=2) and elevated plasma Interleukin-2 in 57 % (n=8). Abnormal MRI of brain was found in 50% (n=7) and medulla 21 % (n=3). Pleocytosis (LKC >5/ml) of the CSF was found in 79 % (n=11) and protein elevation in 79% (n=11). Oligoclonal bands were found in 21% (n=3). NFL was elevated in 64% (n=9) in plasma and 57% (n=8) in CSV. The average mean age in the non-NS group was 45 years (26-60), and disease duration median 45 (11-272) months. 20% (n=1) had elevated ACE, 40% (n=2) had elevated IL-2. Median CSF NFL was significantly higher ($p< 0.005$) in NS (1537 pg/ml; 184-43961) compared to non-NS (426 pg/ml; 249-689) and HC (336 pg/ml; 81-499). Also, median plasma NFL level was significantly higher ($p< 0.05$) in NS (16.8 pg/ml; 4.8-191.8) compared to non-NS (9.2 pg/ml; 5.1-11.4) and HC (7.1 pg/ml; 3.0-10.9). Plasma and CSF NFL in NS patients was not found to be significantly different between NS patients with or without MRI pathology. No patient in non-NS group and HC group had abnormal NFL in plasma or CSV.

Conclusion: Both plasma and CSF NFL were significantly higher in NS patients compared to non-NS patients and HC´s. Plasma and CSF NFL were elevated in 64% and 57% of NS patients, respectively, compared to none of the patients in non-NS or HC group. NFL could be related to extend of CNS affection, but our study was underpowered to demonstrate a significant different difference in NS patient with and without MRI and CSF abnormalities. This is the first study demonstrating elevation of NFL in both blood and CSF in patients with NS. Further studies are needed to evaluate the potential use of NFL as a biomarker supporting the diagnosis of NS, prognosis of the disease and if NFL could be used clinically to monitor response of immunological treatment.

Disclosure: K. Byg, Eli Lilly, 9; **T. Sejbaek**, Biogen, 9, Roche, 9; **H. Nielsen**, None; **Z. Illes**, None; **J. Madsen**, None; **D. Olsen**, None; **T. Ellingsen**, None.

Abstract Number: 0383

Retroperitoneal Fibrosis- a Single Center Experience

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

Background/Purpose: Idiopathic retroperitoneal fibrosis (iRPF) is a rare, chronic, progressive disorder of unknown etiology and characterized by the presence of inflammatory and fibrous retroperitoneal tissue that often encompasses the ureters or abdominal organs. We evaluated iRPF cases of a single institution cohort to describe the features of patients (pts) with iRPF.

Methods: Twenty-eight iRPF patients who were being followed in our outpatient clinic between 2009 and 2018 were reviewed retrospectively. The demographic characteristics, clinical and radiologic findings,medical and interventional therapies were retrospectively collected and reported.

Results: We evaluated the data of 28 patients (17M/11F). The mean age at the time of diagnosis was 53±10,57, median follow up was 46 (IQR:23-67) months. Fifteen (%50) patients were presented with abdominal-pain which was the most common initial complaint. Twenty-one patients had hydronephrosis (11 bilateral hydronephrosis, 5 right) at

Table 1: Types of medical and surgical therapy

Types of medical therapy	**n, (%)**
Glucocorticoid	27(96,5)
Glucocorticoid only	3 (10,5)
Tamoxifen	8 (28)
Azathioprine	8 (28)
Cyclophosphamide	1 (3,5)
Methotrexate	10(35)
Rituximab	13(46)
Mycofenolate Mofetil	1 (3,5)
Types of interventional therapy	n, (%)
Left ureteral stents	15(53,5)
Right ureteral stents	16(57)
Right nephrostomy	4 (14)
Left nephrostomy	2 (7)
Ureterolysis	2 (7)
Temporary Hemodialysis	1 (3,5)

Table 2: Baseline clinical,laboratory and radiologic findings

Characteristic	Value
General characteristics	
Age,mean (S.D), years	53±10,57
Male, n (%)	17 (60)
Follow-up duration, median (IQR),months	46 (23-67)
Clinical symptoms, n (%)	
Abdominal pain	15 (50)
Flank pain	9 (32)
Nausea	2 (8)
Anuria	1 (5)
Nocturia	1 (5)
Laboratory	
ESR, median (IQR), mm/h	39 (17-88)
CRP, median (IQR), mg/L	11 (5,5-46,5)
Serum creatinine mean (IQR), mg/dL	1,14 (0,83-1,9)
Radiologic findings	
Hydro-ureteronephrosis, n(%)	21 (75)
Bilateral	10 (48)
Unilateral	11 (52)
^{18}F-FDG-PET scan, n(%)	19 (69)
Positivity	16 (84)

initial visit and one patient diagnosed while on temporary hemodialysis therapy. Laboratory tests showed that ESR was elevated in 15 of 23 cases with a median value of 39 mm/h (IQR:17-88); CRP was elevated in 19 of 28 patients (68%), with median value 11 (IQR:5,5-46,5). Mean serum creatinine level was 1,14 mg/dl IQR (0,83-1,9). Tissue involvement was detected with computed tomography in 25 (89%) patients. In addition, 18 F-FDG-PET was ordered for 19 patients and 16 of them (84%) was positive for tissue involvement of iRPF. Among these 16 pts, control 18 F-FDG-PET scan was obtained in 13 after at least 6 months of follow-up. Remission was observed in 7 pts in control 18 F-FDG-PET scan.Histopathological samples were available for further analysis in 8 cases and 5pts' findings were consistent with iRPF (storiform fibrosis and dense lymphoplasmacytic infiltration were observed). Medical and interventional therapies are presented in Table 2. Twenty-seven pts were initially treated with glucocorticoids and the mean initial oral prednisone dose was 45,5±13,8 mg/day. Prednisone was discontinued in 4 patients after remission and for the remaining 23 pts; 12 pts' prednisone was tapered < 5 mg/day at mean 9 (IQR:6,7-22,5) months. The remaining patient was treated with tamoxifen. One patient diagnosed AML-M2 during the follow-up and had allogenic stem cell transplantation. Final median values of ESR and CRP were 10 mm/h (IQR:4,7-17,7) and 4,4 mg/l (1,9-7,7), respectively (p= 0.001 and p=0.002). Final median serum creatinine level was 1,03 (IQR:0,78-1,28) (p=0,2). Thirteen pts (%46) were treated successfully with Rituximab who were not responded initial prednisone therapy. Twenty-one pts had ureteral stents and 11 of them are stent free at the final visit. 2 pts had ureteroysis but the procedure was failed in one patient. None of the pts was deceased on the follow-up.

Conclusion: Steroids are the mainstay treatment for iRPF and steroid resistant cases could be treated with rituximab rescue therapy. Prompt interventional approaches are valuable bridging therapies for pts who presented with hydronephrosis. Obtaining a biopsy sample could be hazardous or not possible; so imaging modalities add great value on the diagnose of İRPF.

Disclosure: M. Oztas, None; **E. Cerme**, None; **I. Altun**, None; **S. Ugurlu**, None.

Abstract Number: 0384

Prevalence and Predictors of Fibrosis in Rheumatological Patients on Therapy and Risk Factors for Chronic Liver Disease

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The assessment of liver stiffness using liver elastography (Fibroscan) has facilitated early diagnosis of hepatic fibrosis in patients with chronic liver disease, but its use has not been evaluated extensively in rheumatological patients. The use of methotrexate in these patients is considered first-line disease modifying therapy for many inflammatory arthritides, and one of its potential adverse effects is hepatotoxicity which can present either as asymptomatic transaminitis, progressive liver fibrosis, or liver cirrhosis.

This is the first Australian study to examine the predictors for abnormal liver elastography in rheumatological patients, and its clinical utility in the management of methotrexate users.

Methods: A retrospective chart review of patients attending a Melbourne metropolitan rheumatology practice between 2011-2018, who has had liver elastography done as part of their liver assessment, was studied. Liver stiffness measure (LSM) of >8 kPa was used as a surrogate for liver fibrosis. Baseline diagnosis, comorbidities, laboratory results, and medication use were correlated to abnormal liver elastography using univariate and multivariate analysis.

Results: One hundred twenty nine patients were identified with rheumatological conditions that underwent LSM assessment during the 7-year period. Commonest indications for assessment were methotrexate use (47.3%), non-alcoholic steatohepatitis (27.9%), and chronic viral hepatitis (9.3%) and at-risk alcohol consumption (3.9%). Elevated LSM was associated significantly with the diagnosis of spondyloarthritis (OR 1.22 p=0.008) and with high BMI (OR 4.64 p=0.058). Biochemically, GGT was the only significant predictor of abnormal LSM. The presence or absence of methotrexate use, nor its duration, were associated with abnormal LSM. There was no difference in baseline demographic features between users and non-users of methotrexate. Median LSM were similar in methotrexate exposed patients compared to non-exposed patients (4.8kPa respectively p=0.707). The proportions of patients with LSM >8 were similar in methotrexate exposed and non-exposed group (6.6% vs 13.2% respectively, p=0.202). The discontinuation of methotrexate was associated with increased LSM (13.8% discontinued versus 2.1% that did not p=0.046) and those with increased LSM were less likely to be commenced on MTX following LSM assessment (0.0% vs 31.8% p=0.002).

Conclusion: Abnormal liver elastography in rheumatological patients was associated with high BMI and the diagnosis of seronegative spondyloarthritis. Methotrexate use was not associated with increased fibrosis but LSM did affect its use. Positive correlation with the diagnosis of spondyloarthritis with increased LSM is consistent with current theories suggesting an increase in insulin resistance and therefore an increased risk of fatty liver that may be observed in this group.

Disclosure: C. Lam, None; **S. Bloom**, None; **A. Hoi**, Merck, 2.

Abstract Number: 0385

Distinctive Clinical Features and Biomarkers of Connective Tissue Disease Associated Interstitial Lung Disease

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SESSION INFORMATION
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Session Type: Poster Session (Sunday)
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Background/Purpose: The connective tissue diseases (CTD) are a group of rheumatologic diseases characterized by inflammation and immune-mediated organ damage including interstitial lung disease (ILD). The reported frequency of ILD associated with CTD (CTD-ILD) is variable, depend on definitions of disease and demographic factors. However, studies of clinical risk factor and serologic biomarkers on CTD-ILD in Korean patients are sparse.The aim of this study is to investigate clinicoserologic biomarkers associated with development, progression, and prognosis of CTD-ILD in Korean patients

Methods: We conducted a single center, a retrospective study including 70 incident patients diagnosed with CTD-ILD and 70 age-, sex-, type of CTD-matched patients without ILD at Kyung Hee University medical center. Clinical information including the time of developing ILD, pulmonary function test, and imaging findings of chest CT were reviewed using medical record. To find serologic biomarkers, serum concentrations of interferon-r-induced protein 10 (IP-10), interleukin (IL)-6, IL-8, IL-10, and matrix metalloproteinase 7 (MMP-7) in patients with CTD-ILD and CTD without ILD were measured using Luminex multiplex bead assay.

Results: Total 140 patient (70 CTD-ILD, 70 CTD without ILD) were enrolled, the mean age of the study group was 63.4 ± 11.2 years, 103 (73.6%) patients were female. To analyze clinical risk factors for developing ILD in CTD, we compared clinical features and laboratory findings between CTD-ILD group and CTD without ILD group. Raynaud`s phenomenon (OR 8.1, 95% CI 2.1-31.2) was the risk factor for developing ILD in CTD in multivariable logistic regression analysis. Rheumatoid arthritis (RA) was the most common type of CTD associated with ILD and idiopathic inflammatory myopathy (IIM)-ILD group had more deteriorated pulmonary functions. Non-specific interstitial pneumonia (NSIP) pattern was the most frequent radiographic pattern (41/70, 58.6%). For analysis of distinctive clinical features according to the onset of ILD, we stratified CTD-ILD patients into three groups: ILD-preceding (12/70, 17.1%), simultaneous (25/70, 35.7%), and CTD-preceding (33/70, 47.1%). In the ILD-preceding group, ILD preceded CTD by 27 months on average, UIP and NSIP had similar proportion. Majority of ILD-preceding group (75%) had worse baseline pulmonary function which required treatment (DLCO < 65%), while 51.5% of in CTD-preceding group did. In CTD-preceding group, NSIP was more common than UIP. Initial DLCO was the risk factor for ILD progression. Serum MMP-7 levels were associated with the developing ILD in CTD patients and had a significant correlation with CT extent score in the present study.

Conclusion: In this study, Raynaud`s phenomenon was a clinical risk factor for ILD in CTD. Patients with preceding ILD prior to CTD had more deteriorated lung function at baseline, and it was associated with poor prognosis. Serum MMP-7 levels had a correlation with ILD development and CT score. Therefore, it is necessary to pay attention to the clinicoserologic biomarkers assoiated with ILD in patients with CTD, this will be beneficial to provide more proper management

Disclosure: S. Chung, None; **S. Lee**, None; **S. Lee**, None; **S. Hong**, None; **Y. Lee**, None.

Abstract Number: 0386

Idiopathic Granulomatous Mastitis: The Role of Rheumatologists in Treating This Rare Cause of Breast Pain

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Table 1: Baseline Characteristics of 28 patients with Idiopathic Granulomatous Mastitis

Baseline Characteristic	N (%)
Mean age at diagnosis (years)	32 years
Mean follow-up period (months)[1]	27 months
Female	28 (100)
Race/Ethnicity	
White, Hispanic	17 (61)
White, non-Hispanic	6 (21)
Asian	2 (7.1)
Black	1 (3.6)
Pacific Islander	1 (3.6)
Other	1 (3.6)
Specialties of treating MDs[2]	
Breast Health	22 (47)
Surgical Oncology	12 (26)
Rheumatology	8 (17)
Primary Care	3 (6.4)
General Surgery	1 (2.1)
Obstetrics-gynecology	1 (2.1)
Smoking (ever)	
No	24 (86)
Yes	4 (14)
Gestational history	
Ever	26 (93)
In past 5 years prior to symptom onset[1]	19 (83)
Breastfeeding history	
Ever[1]	23 (92)
In past 5 years prior to symptom onset[1]	15 (83)
Hormonal-based birth control	
Ever[1]	14 (56)
At time of symptom onset[1]	6 (29)

1. Data not available in the following numbers of patients, as listed by baseline characteristic: mean follow-up period- 2; Gestational history/in past 5 years prior to symptom onset- 5; breastfeeding history/ever- 3; breastfeeding history/in past 5 years prior to symptom onset- 10; hormonal-based birth control/ever- 3; hormonal-based birth control/at time of symptom onset-4
2. Patients sometimes treated by more than one specialist

Table 2: Clinical Features of Idiopathic Granulomatosis Mastitis at Time of Diagnosis in 28 Patients

Clinical Feature	N (%)
Max size at diagnosis (mean)[1]	4.69 centimeters
Bilaterally	
At time of diagnosis (n, %)	1 (3.6)
Ever (n,%)	7 (25)
Positive bacterial culture or gram stain	
Any positive[1]	7 (26)
Corynebacterium[2]	2 (7.4)
Positive tuberculosis[1,3]	4 (15)
Symptoms at diagnosis	
Pain (n,%)	27 (96)
Nipple discharge (n,%)	5 (18)
Erythema (n,%)	16 (57)
Inflammatory arthritis/arthralgias (n,%)	4 (14)
Erythema nodosum (n,%)	5 (18)

1. Data not available in the following numbers of patients, as listed by clinical feature: max-size at diagnosis- 6; positive bacterial culture or gram stain/any positive-1; positive tuberculosis-2
2. Two additional patients with gram stain showing gram positive bacilli
3. Defined as positive acid fast bacilli (AFB) culture, interferon gamma release assay (IGRA), tuberculin skin test (TST), chest x-ray (CXR) with suggestive findings. Of the 4 positive results, 1 patient with history of previously treated latent tuberculosis (TB), 1 patient with positive TST but negative CXR and IGM biopsy specimen with negative AFB staining, 1 patient had history of treated pulmonary TB 20 years prior and IGM biopsy specimen with negative AFB staining, 1 patient with positive IGRA and PPD and chest x-ray with transient hilar lymphadenopathy, however AFB staining, broad range polymerase chain reaction from biopsy was negative

Background/Purpose:: Idiopathic granulomatous mastitis (IGM) is an inflammatory breast disease occurring primarily in young to middle-aged women (1, 2). IGM typically presents with a tender, firm breast mass that may be accompanied by redness, irritation, and drainage. The diagnosis of IGM is made by breast biopsy showing non-caseating granuloma after other causes of granulomatous mastitis have been excluded (1, 4). IGM is a poorly understood disease; there is no consensus regarding underlying cause, risk factors, and optimal treatment of this condition (3). However, IGM is being increasingly recognized as an inflammatory condition and referred to rheumatologists to aid in immunomodulatory management. IGM is primarily managed by breast surgeons and most of our understanding about this disease comes from surgical literature. However, a growing body of evidence, including this case series, suggests that IGM is a systemic inflammatory disease, and that rheumatologists are important and well situated to help care for these patients.

Methods:: IGM patients were identified via the OHSU Cohort Discovery tool who carried a diagnosis of “granulomatous mastitis”. 30 patients seen between 2007-2018 where identified. Retrospective chart review was used to verify that IGM diagnosis was accurate, collect data on baseline characteristics, clinical features and treatment course/outcomes. 2 patients were excluded (1 diagnosed with alternative condition and 1 without adequate follow-up).

Results:: Of the 28 IGM patients, all were female, the mean age was 32, the majority (60.7%) were Hispanic. The mean follow-up was 27 months and 17% of patients were treated by rheumatologists. Consistent with previous reports, the majority of patients had a history of pregnancy (93%) and breastfeeding (92%). Interestingly, 4 patients had inflammatory arthritis/arthralgias and 5 had erythema nodosum. 23 patients had adequate follow-up to assess treatment response. Treatment groups were divided into surgery plus high dose steroids (n=3), high dose steroids alone (n=12), methotrexate (MTX) and high dose steroids (+/- surgery) (n=3) and other (n=5). A rheumatologist saw all patients who received MTX. 7 patients (30%) had disease relapse after initial treatment and 4 patients (17%) had

Table 3: Idiopathic Granulomatous Mastitis Treatment Outcomes in 23 patients

	All treatment groups	High dose steroids + surgery[1] N=3	High dose steroids alone[1] N=12	Methotrexate and high dose steroids (+/- surgery)[1] N=3	Other (none, surgery alone, antibiotics/surgery alone, antibiotics alone) N=5
Remission without relapse	12 (52%)	2 (66%)	5 (42%)	3 (100%)	2 (40%)
Relapse	7 (30%)	0	5 (42%)	0	2 (40%)
1 relapse	5 (22%)	0	4	0	1
> 1 relapse	2 (8.7%)	0	1	0	1
Mean length of time until 1st remission (mo)	7.9	15	7.3	8	5.3
Mean length of time until 1st relapse (mo)	11.4	n/a	9.6	n/a	16
Persistent disease	4 (17%)	1 (33%)	2 (17%)	0	1 (20%)
Disease free off of treatment	19 (83%)	2 (66%)	10 (83%)	3 (100%)	4 (80%)

1. All patients received varying courses of antibiotics, without significant clinical improvement except in 1 case (listed in "other")

Note: Total number of patients included in outcomes table is 23. Of the 5 excluded patients, 3 had insufficient follow-up to determine outcomes and 2 excluded because treatment still ongoing

persistent disease. The highest rates of relapse were in the steroids alone group (42%) and lowest rate of relapse was in the methotrexate group (0%). Overall, 83% of patients eventually achieved a disease free remission with post-remission follow-up of over 1 year in 74%.

Conclusion:: This case series of 28 IGM patients suggests that MTX in combination with high dose steroids may successfully treat IGM, although larger prospective studies are needed. We also report a higher incidence of arthritis/arthralgia and erythema nodosum than previously described—it is possible that these systemic findings are more likely to be recognized by a rheumatologist. IGM is an inflammatory disease and a rheumatologist is a valuable addition to the treatment team for IGM patients.

Disclosure: S. Ringsted, None; **M. Friedman**, None.

Abstract Number: 0387

Early Mortality in IgG4-Related Disease

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster I: Fibroinflammatory & Granulomatous Disorders & Therapies

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4-related disease (IgG4-RD) is a fibroinflammatory disorder characterized by tumefactive lesions that can occur in nearly any organ or anatomic site. Manifestations can include pancreatitis, sclerosing cholangitis, tubulointerstitial nephritis, retroperitoneal fibrosis, aortitis, and pulmonary disease. Prior to treatment and as a complication of treatment (e.g., Whipple procedure, glucocorticoids), IgG4-RD patients are at risk of organ dysfunction and failure which can lead to death. However, the risk of death in IgG4-RD is poorly understood, especially in reference to the general population. We evaluated all-cause mortality and investigated cause of death in a large cohort of IgG4-RD patients.

Methods: We identified patients seen in the Center for IgG4-RD at Massachusetts General Hospital who were diagnosed with IgG4-RD between 2010 and 2018 and had complete baseline records available for review. We determined patients' vital statuses through the electronic medical record (EMR) and by contacting patients or next of kin. Patients were followed from the date of their first visit until date of death, last visit, or December 31st, 2018, whichever came first. Person-years (PY) of follow-up were measured and the all-cause mortality rate was calculated. We used CDC WONDER to extract expected deaths for the US general population and calculated age- and sex-standardized mortality ratios (SMR). Cause of death was determined by review of the EMR.

	IgG4-RD Cases
N	205
Male	129 (63%)
Baseline Age (Years, Mean, SD)	57.8 (13.1)
White	152 (74%)
Selected Features of IgG4-RD	
Number of Organs	2.9 (2.1)
HEENT	106 (52%)
Orbital	20 (10%)
Lacrimal	44 (21%)
Salivary Gland	84 (42%)
Thyroid	5 (2%)
Pulmonary	40 (19%)
Renal	41 (20%)
Pancreato-Hepatobiliary	72 (35%)
Retroperitoneal Fibrosis	39 (19%)

N (%), unless otherwise specified.

Demographics of Cases and Controls

Case	Age at Death	Sex	Cause of Death	Related to IgG4-RD?
1	74	Male	Hemorrhagic shock secondary to gastrointestinal bleed	Yes
2	70	Male	Hemorrhagic shock secondary to retroperitoneal bleed	Yes
3	55	Male	Septic shock secondary to cholangitis	Yes
4	80	Male	Complications of cholangitis	Yes
5	81	Male	Intraparenchymal hemorrhage secondary to trauma	No
6	69	Male	Infection vs. adrenal insufficiency	No
7	69	Male	Liposarcoma	No
8	78	Male	Pneumonia in the setting of dementia	No
9	74	Male	Myocardial infarction due to paroxysmal nocturnal hemoglobinuria	No
10	74	Male	End-stage renal disease due to diabetes	No

Cause of Death in IgG4-Related Disease

Results: We included 205 IgG4-RD patients with a mean age of 57.8 (±13.1) years; 63% were male (**Table 1**). During 647.7 PY of follow-up, ten patients died, yielding an all-cause mortality rate of 15.4 (95% CI 7.8-27.5) /1,000 PY. Death was associated with IgG4-RD in four (40%) cases. The first patient had pancreatic involvement and died of hemorrhagic shock secondary to a GI bleed in the setting of treatment-refractory disease. The second patient had aortic involvement and died from a retroperitoneal bleed. The third patient died of hemorrhagic shock bacteremia with gram negative bacilli in the setting of progressive cholangitis. The fourth patient died from complications related to progressive cholangitis (**Table 2**). Compared to the general US population, the overall SMR was 1.30 (95% CI 0.70-2.41). During follow-up, all deaths occurred in male patients. Among male patients, the all-cause mortality rate was 26.6 (95% CI: 13.5-47.4) / 1,000 PY and the corresponding SMR was 1.75 (95% CI 0.94-3.26).

Conclusion: In the early period following diagnosis, IgG4-RD mortality appears similar to that of the general population. Of the deaths related to IgG4-RD, severe pancreato-hepatobiliary disease contributed in three cases. We observed few deaths and had a relatively short follow up which may limit our power to detect significant differences in mortality. However, we observed a trend suggesting that male IgG4-RD patients may have a higher rate of death compared to the general population. Future studies with larger cohorts are necessary to further evaluate the risk of death in IgG4-RD, especially differences in late mortality. Our findings may be useful for discussing overall prognosis with IgG4-RD patients.

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Abstract Number: 0388

Treating Statin-induced Anti-HMGCR Myopathy with Normal Muscle Strength: A New Window of Opportunity

Alain Meyer ,[1] Yves Troyanov,[2] Julie Drouin,[3] Josiane Bourre-Tessier,[4] Genevieve Oligny-Longpre,[5] Océane Landon-Cardinal,[6] Baptiste Hervier,[7] Sabrina Hoa,[8] Anne-Marie Mansour,[9] Eric Rich,[4] Jean-Richard Goulet,[4] Sandra Chartrand,[10] Marie Hudson,[11] Jessica Nehme,[9] Jean-Paul Makhzoum,[12] Farah Zarka,[9] Sara Hussein,[13] Vincent Morin,[14] Edith Villeneuve,[15] Jean-Pierre Raynauld,[16] Marianne Landry,[17] Erin O'Ferrall,[18] Jose Ferreira,[19] Benjamin Ellezam,[20] Jason Karamchandani,[18] Sandrine Larue,[21] Rami Massie,[18] Catherine Isabelle,[21] isabelle Deschênes,[5] Valérie Leclair,[22] Helene Couture,[23] Ira Targoff,[24] Marvin Fritzler,[25] and Jean-Luc Senecal[4], [1]Centre de Reference des Maladies Autoimmunes Rares, Hôpitaux Universitaires de Strasbourg, Strasbourg, France, [2]Division of Rheumatology, Department of Medicine, Hôpital du Sacre-Coeur de Montreal, Montreal, QC, Canada, [3]Centre hospitalier regional de Trois-Rivieres, Trois-Rivieres, QC, Canada, [4]Centre hospitalier de l'Universite de Montreal, Montreal, QC, Canada, [5]Hôpital du Haut-Richelieu, Saint-Jean-sur-Richelieu, QC, Canada, [6]Division of Rheumatology, Centre hospitalier de l'Université de Montréal; Department of Medicine, Université de Montréal, Montreal, QC, Canada, [7]Hopital Pitie-Salpetriere, Paris, France, [8]University of Montreal, Montreal, QC, Canada, [9]Hôpital du Sacre-Coeur de Montreal, Montreal, QC, Canada, [10]Hôpital Maisonneuve-Rosemont, Montreal, QC, Canada, [11]Jewish General Hospital, Lady Davis Institute for Medical Research, and Department of Medicine, McGill University, Montreal, QC, Canada, [12]Vasculitis Clinic, Hopital du Sacre-Coeur de Montreal, Montreal, QC, Canada, [13]Centre hospitalier regional de Lanaudiere, Saint-Charles-Borromée, QC, Canada, [14]Universite Laval, Quebec, QC, Canada, [15]Institut de Recherche en Rhumatologie de Montréal, Montreal, QC, Canada, [16]Institut de Rhumatologie de Montréal, Montreal, QC, Canada, [17]Hôpital LaSalle, Montreal, QC, Canada, [18]Montreal Neurological Institute, Montreal, QC, Canada, [19]Hopital Maisonneuve-Rosemont, Montreal, QC, Canada, [20]Centre hospitalier universitaire Sainte-Justine, Montreal, QC, Canada, [21]Hôpital Charles-Le Moyne, Greenfield Park, QC, Canada, [22]Division of Rheumatology, Department of Medicine, Jewish General Hospital; Clinical Epidemiology Unit, Department of Medicine, Karolinska Institutet, Montreal, QC, Canada, [23]Hôpital Enfant-Jesus, Quebec, QC, Canada, [24]University of Oklahoma Health Sciences Center, Oklahoma City, OK, [25]Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Muscle Biology, Myositis & Myopathies Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-HMGCR myopathy has recently been defined as a subset of immune-mediated necrotizing myopathies characterized by proximal muscle weakness, elevated CK levels and the presence of anti-HMGCR autoantibodies (aAbs). Statin-induced anti-HMGCR myopathy with elevated serum CK but normal muscle strength has scarcely been reported. Our objective was to describe the natural history of this subset.

Methods: All our patients with elevated serum CK, anti-HMGCR aAbs and statin exposure were studied retrospectively for demographics, myologic features, chronology of events leading to induction as well as maintenance therapy. Early treatment was defined as treatment when muscle strength was still normal, whereas delayed treatment was defined as treatment when proximal weakness was apparent. Remission was defined by serum CK ≤ 500 UI/L, and successful steroid sparing immunosuppressant (SSI) maintenance as remission for 1 year with ≤ 5 mg/day of prednisone. Anti-HMGCR aAbs were detected by ALBIA or ELISA.

Results: Fifty-five patients with statin-induced anti-HMGCR myopathy were identified. Twenty-two patients (40%) presented with normal muscle strength, with median CK of 1501 IU/L (range 500-5613) and median age of 64.7 years. Of these 22 patients, 9 (41%) had early treatment and 13 (59%) had delayed treatment. All patients were treated with at least one SSI, with or without steroids and/or intravenous immunoglobulins (IVIg). All patients achieved remission.

- ***Early treatment group (n=9):*** median time from presentation (defined as first CK elevation) to treatment was 13.4 months (range 2.6-78.4). Median CK at presentation and at treatment initiation were 1501 IU/L (range 617-2132) and 2684 IU/L (554-13339), respectively. Successful steroid-free induction was used in 5 patients (56%), and IVIg induction in 2 patients (22%). Successful SSI monotherapy maintenance was possible in 5 patients (56%), with only one patient still on IVIg and steroids. At last follow-up, all patients had normal strength.
- *Delayed treatment group (n=13):* median time from presentation to treatment was 21.6 months (range 7-95). Median CK at presentation and at treatment initiation were 1700 IU/L (range 500-5613) and 6400 IU/L (1556-14098), respectively. Successful steroid-free induction was used in 1 patient (8%), and IVIg induction in 8 patients (62%). Successful SSI monotherapy maintenance was possible in 4 patients (31%) while 6 patients were on maintenance IVIg and 3 (23%) on steroids. At last follow-up, normal strength was present in 9 patients (69%).
- Thus, steroid-free induction was proposed by the treating physicians and used successfully in 56% of patients in the early treatment group versus only 8% of patients in the delayed treatment group (p=0.023).

Conclusion: In this cohort of statin-induced anti-HMGCR myopathy, 22 patients (40%) presented with normal strength. While successful in all patients, steroid-free induction was proposed in 5 patients (56%) with normal strength, but only once (8%) in patients in whom proximal weakness had ensued (p=0.023). Anti-HMGCR myopathy presenting with normal strength may be an ideal subset for initiating steroid-free induction.

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Abstract Number: 0389

ACR/EULAR Criteria for Myositis and Systemic Sclerosis Lack Sensitivity for Scleromyositis

Alain Meyer ,[1] Valérie Leclair,[2] Océane Landon-Cardinal,[3] Benjamin Ellezam,[4] Julie D'Aoust,[5] Margherita Giannini,[6] Bernard Geny,[6] Laurent Arnaud,[7] Jacques-Eric Gottenberg,[8] Jean Sibilia,[9] Minoru Satoh,[10] Marvin Fritzler,[11] Yves Troyanov,[12] and Marie Hudson[13], [1]Centre de Reference des Maladies Autoimmunes Rares, Hôpitaux Universitaires de Strasbourg, Strasbourg, France, [2]Division of Rheumatology, Department of Medicine, Jewish General Hospital; Clinical Epidemiology Unit, Department of Medicine, Karolinska Institutet, Montreal, QC, Canada, [3]Centre Hospitalier de l'Université de Montréal, Montréal, Canada, [4]Department of Pathology, Centre Hospitalier Universitaire Sainte-Justine, Montréal, Canada, [5]McGill University, Montreal, QC, Canada, [6]CHU de Strasbourg, Strasbourg, France, [7]Service de Rhumatologie, Centre National de Référence des Maladies Autoimmunes Systemiques Rares (RESO), Hôpitaux Universitaires de Strasbourg, Strasbourg, France, Strasbourg, France, [8]Department of Rheumatology, Strasbourg University Hospital, Strasbourg, France, [9]CHU Strasbourg, Strasbourg, France, [10]Department of Clinical Nursing, School of Health Sciences, University of Occupational and Environmental Health, Kitakyushu, Japan, [11]Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, [12]Division of Rheumatology, Department of Medicine, Hôpital du Sacre-Coeur de Montreal, Montreal, QC, Canada, [13]Jewish General Hospital, Lady Davis Institute for Medical Research, and Department of Medicine, McGill University, Montreal, QC, Canada

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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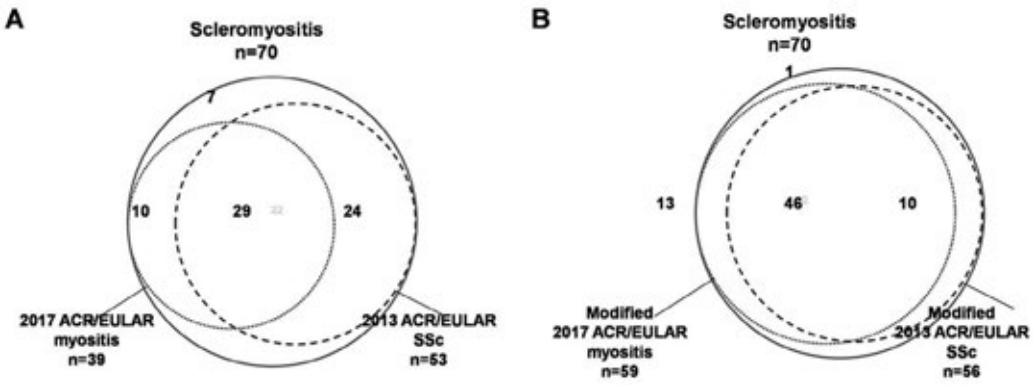
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune myositis consists of a group of diseases with heterogeneous muscular and systemic manifestations. Prognosis also varies widely across the spectrum. Thus, myositis subgroups are being identified to facilitate personalized care. Systemic sclerosis (SSc) is a disease characterized by vasculopathy, autoimmunity, inflammation and fibrosis affecting multiple organs including muscle. The association of myositis and SSc is referred to as "scleromyositis". Classification criteria for both myositis and SSc have been endorsed by ACR/EULAR but their performance for scleromyositis is unknown.

Methods: Patients with scleromyositis were identified in two centers. Diagnosis of scleromyositis was based on the co-existence of myositis and features of SSc according to expert opinion. Patients were systematically assessed for the presence or absence of items in the 2017 ACR/EULAR criteria for myositis and 2013 ACR/EULAR criteria for SSc at last follow-up. Additional organ involvement and auto-antibodies associated with myositis and SSc were also systematically recorded.

Results: Seventy (70) patients with scleromyositis (sex ratio F/M 3.7) were included. Age at myositis onset was 51.5 ± 15.8 years. Only 39 (56%) patients fulfilled the 2017 ACR/EULAR criteria for myositis (21 definite, 14 probable, 4 possible) and 53 patients (76%) fulfilled the 2013 ACR/EULAR criteria for SSc (Figure 1). Of these, only 29 (41%) fulfilled both sets of criteria. Seven (10%) patients fulfilled neither set of criteria (Figure 1a). The ACR/EULAR criteria that were most frequently lacking for myositis were anti-Jo1 antibodies (n=70, 100%) and dermatomyositis rash (Gottron sign, Gottron papule and/or heliotrope rash n=61, 87%). The criteria that were most frequently lacking for SSc were pulmonary arterial hypertension (n=68, 97%) and "classical" SSc auto-antibodies (anti-Scl70, -centromere, -RNA polymerase III, n= 63, 90%). The 7 patients fulfilling neither ACR/EULAR criteria for myositis nor SSc all had increased creatinine kinase and Raynaud's phenomenon, but the frequency of the other items in the criteria were all < 50%. Four of the 7 patients (56%) had well-known complications of SSc some of which are not included in the criteria: interstitial lung disease (n=3), calcinosis (n=1) and/or renal crisis (n=1). All 7 patients had auto-antibodies associated with scleromyositis that are also not included in ACR/EULAR criteria: anti-Ku (n=3), anti-SMN1 (n=2), anti-PM/Scl (n=1), anti-U1RNP (n=1) and/or anti-RuvBL1/2 (n=1), When ACR/EULAR criteria for myositis and SSc were modified to take into account these additional clinical features and auto-antibodies, the rate of patients who fulfilled myositis and SSc criteria increased from 41% to 66% (Figure 1b).

Conclusion: In our cohort, ACR/EULAR criteria for myositis and SSc alone and together had low sensitivity for scleromyositis. Additional clinical features and serologies could lead to improved sensitivity. Studies of scleromy-



ositis will require careful consideration of inclusion criteria to ensure that the full spectrum of this important subset is included.

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Abstract Number: 0390

Preliminary Response to Janus Kinase (JAK) Inhibition with Baricitinib in Refractory Juvenile Dermatomyositis

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

Background/Purpose: Juvenile dermatomyositis (JDM) is a systemic autoimmune disease with a prominent interferon (IFN) signature. Treatment often requires prolonged high-dose steroids and other immunosuppressive medications. In a compassionate use program, we assessed efficacy and safety of baricitinib (JAK 1/2 inhibitor) in active refractory JDM.

Methods: Active (based on ≥3 core set measures (CSM)) and refractory (use of high dose steroids and ≥2 other medications, including ≥1 biologic therapy) patients with JDM were enrolled after washing out biologic agents other than IVIG. Baricitinib was dosed based on weight and renal function. Primary outcome was reduction in symptom daily diary score (DDS) of weakness, fatigue, musculoskeletal pain, and rash. Other assessments included International Myositis Assesment and Clinical Studies (IMACS) disease activity CSMs and Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI). Peripheral 28 gene inteferon-regulated gene (IRG) score and serum CXCL10 (IP-10) were assessed. Paired t-test was used to compare baseline to 24 weeks. Safety and tolerability were also assessed.

Results: Four JDM patients (5.8-20.7 years old) were enrolled (NCT01724580).Patients received baricitinib 4-8 mg/day PO divided BID. After 24 weeks, DDS reduced from a mean of 2.0 (range 1.1-2.3) to 1.0 (0.7-1.1; mean decrease 49%, p=0.02) (Figure or Fig 1A). Physician global activity visual analog scale (VAS) decreased from a mean of 5.1 (3.5-7.4) to 3.9 (3.0-6.1; 24% decrease, p=0.04) (Fig 1B). Extramuscular global activity VAS decreased from mean 5.1 (3.0-7.3) to 3.6 (1.0-5.0; mean 34% decrease, p=0.03). CDASI activity score reduced from mean 43 (27-53) to 26 (14-48; mean improvement 41%, p=0.04) (Fig 1C). In 2/4 with baseline weakness, manual muscle testing (MMT8) increased from 108 to 135 and 116 to 142 (mean improvement 24%) (Fig 1D). By the ACR-EULAR JDM response criteria, the Total Improvement Score (TIS) was mean 39, range 17.5-62.5. In 2 pts with baseline weakness, the TIS

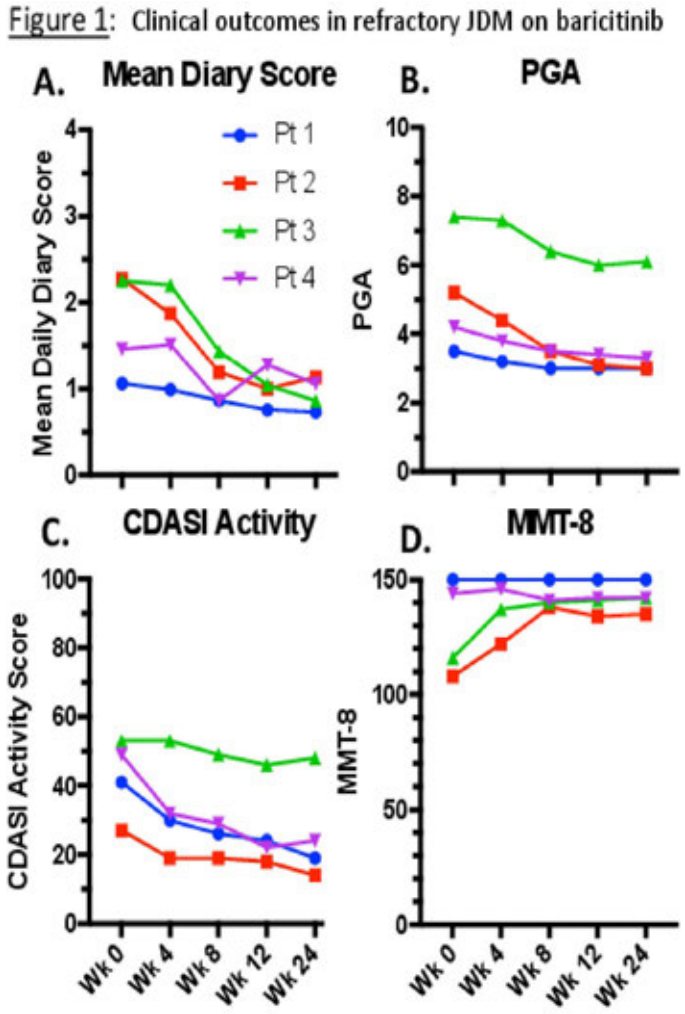

Figure 1. Clinical outcomes are shown at baseline (week or wk 0), and then at week 4, 8, 12, and 24 for (A) mean daily diary score (DDS) out of 4 (B) Physician Global Activity (PGA) out of 10, (C) Cutaneous Dermatomyositis Disease Area and Severity (CDASI) Activity Score out of 100, and (D) Manual Muscle Testing-8 out of 150

improved moderately, with a change of 55 and 62.5. Two patients reduced prednisone (21 to 15 and 10 to 7.5 mg/day); 2 patients' doses remained unchanged (5 and 10 mg/day). Baricitinib was generally well tolerated. One patient had an increase in plasma BK viral titer; the other 3 patients were negative for BK virus in blood and urine. No adverse events required holding/discontinuing baricitinib. IRG score was significantly lower at 24 weeks (p value < 0.01) and serum IP-10 at 12 weeks was trending lower ($p = 0.056$).

Conclusion: Preliminary data on the use of baricitinib (JAK 1/2 inhibitor) in 4 refractory JDM patients are encouraging, showing improvement in symptom DDS as well as in validated measures of rash (4/4) and strength (2/2 with baseline weakness), and other CSMs. Patients with baseline weakness met clinically significant moderate improvement by the ACR-EULAR response criteria. A corresponding decrease in IRG and trend down in IP-10 was observed. Baricitinib was generally well tolerated and further evaluation in JDM should be considered.

Disclosures: Baricitinib provided by Eli Lilly and Company, expanded access program sponsor. Other support: IRP of NIH, NIAMS, NIEHS, CC.Figure 1. Clinical outcomes are shown at baseline (week or wk 0), and then at week 4, 8, 12, and 24 for (A) mean daily diary score (DDS) out of 4 (B) Physician Global Activity (PGA) out of 10, (C) Cutaneous Dermatomyositis Disease Area and Severity (CDASI) Activity Score out of 100, and (D) Manual Muscle Testing-8 out of 150.>

Disclosure: H. Kim, Cure JM Foundation, 2; **S. Dill**, None; **M. O'Brien**, None; **M. Jain**, None; **S. Lu**, None; **W. Tsai**, None; **Y. Shi**, None; **L. Vian**, None; **M. Gadina**, None; **M. Millwood**, None; **A. Brundidge**, None; **L. Rider**, ., 2, 9, aTyr, 9, Bristol Myers Squibb, 2, Cure JM Foundation, 2, 9, Eli Lilly and Company, 9, Hope Pharmaceuticals, 2, Lilly-drug, 9, MedImmune / AstraZeneca, 9, MedImmune/AstraZeneca, 9, NIEHS, 2, NIEHS, NIH, 2, NIH, 2; **R. Colbert**, Eli Lilly and Company, 2, 9.

Abstract Number: 0391

The Beneficial Effects of Rituximab Treatment in Myositis May Be Due to the Binding of a Non B-Cell Protein, SMPDL3B, in Skeletal Muscle

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Muscle Biology, Myositis & Myopathies Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab was developed to treat B cell lymphomas but has now been shown to have clinical efficacy in multiple disease conditions (endocrine, neurological, dermatological etc) where B cells are not the primary mediators of pathogenic processes. Likewise, beneficial effects of Rituximab appear to outweigh the relative contribution of B cells to disease pathogenesis in inflammatory myopathies. Therefore, we hypothesized that Rituximab is recognizing proteins other than CD20 that are expressed outside of the B cell lineage (e.g., skeletal muscle cells) in myositis. We have tested this hypothesis by evaluating effects of Rituximab in CD20+ B cells (Raji cells), macrophages (THP-1 cells) and human skeletal muscle cells.

Methods: CD20 expression was assessed in Raji B-cells (ATCC CCL-86), THP-1 macrophages (ATCC TIB-202) and immortalized human myoblasts by Fluorescent Activated Cell Scanning. These cells were treated with 5, 10, 20, or 40 μg/mL Rituximab to assess cell viability (CCK-8 reagent and Trypan Blue), cytokine production by ELISA and activation of down stream transcriptional targets by RTqPCR. Protein sequence homology search has identified previously known protein, Sphingomyelin Phosphodiesterase Acid Like 3B (SMPDL3B) as the alternate target for Rituximab.

Results: CD20 was only expressed in Raji cells but not human myoblasts or macrophages. As expected, Rituximab treatment at higher concentrations (>20ug/ml) induced cell death in Raji cells but not in macrophages and muscle cells. However, Rituximab treatment increased IL-13 production by Raji cells and decreased TNF-alpha production by macrophages suggesting that Rituximab recognized non-CD20 proteins expressed on macrophages. More interestingly, Rituximab showed an effect neither on cell survival nor on cytokine production in human muscle cells. However, analysis of transcripts from treated muscle cells showed dose dependent increase in Estrogen receptor 1 (ESR1), a protein known to be associated with reduction of pro-inflammatory NF-κB activation as well as increased mitochondrial function. These observations also demonstrated that Rituximab binds to non-CD20 protein target in proliferating muscle cells. We have identified SMPDL3B as the alternative target of Rituximab in skeletal muscle cells.

Conclusion: Our data suggests that binding of Rituximab to a non-CD20 target such as SMPDL3B in muscle cells activates ESR1 which is known to down regulate inflammation and enhance muscle mitochondrial function. Likewise, Rituximab by binding to macrophages also reduces TNF-alpha leading to overall reduction in pro-inflammatory signaling in muscle microenvironment of myositis patients. Our results explain reasons for the clinical efficacy of Rituximab in a variety of non-B lymphocyte mediated disease conditions.

Disclosure: J. Parkes, None; **J. Boehler**, None; **N. Li**, None; **K. Nagaraju**, None.

Abstract Number: 0392

Management of Idiopathic Inflammatory Myopathies Using Intravenous Immunoglobulin Therapy: A Retrospective Cohort Study

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SESSION INFORMATION
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Session Title: Muscle Biology, Myositis & Myopathies Poster I
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Background/Purpose:: Dermatomyositis (DM) and polymyositis (PM) are idiopathic inflammatory myopathies characterized by weakness and inflammation of the muscles. First line therapy typically involves high dose systemic steroids to establish disease control along with steroid sparing agents to minimize steroid induced morbidities. Other immunosuppressive agents are typically initiated as an adjunct to systemic steroids, with scarce evidence supporting use of various agents in the clinical context. Intravenous immunoglobulin therapy (IVIG) in particular has demonstrated evidence in severe refractory disease. Our study aims to investigate the efficacy of IVIG in the treatment of various clinical manifestations of inflammatory myopathies.

Methods: A retrospective chart review was performed on patients identified through the Sunquest Laboratory Information System who had received IVIG for the treatment of DM or PM between January 1st, 2012 to January 1st, 2018 at the University of Alberta Hospital. Data extracted included patient's age at initiation of treatment, sex, duration of treatment, presenting symptoms (weakness, myalgias, skin rashes, calcinosis, dysphagia and interstitial lung disease [ILD]) and outcome of treatment.

Results: A total of 46 DM and 19 PM patients were identified. Median age of treatment onset was 54 (interquartile range [QR], 40 – 64) years, with 49 (75%) female patients. The median duration of treatment was 13 (QR, 3 – 37) months. Fifty-six of sixty-five (86%) patients had weakness, 7/65 (11%) patients had myalgias, 40/65 (62%) patients had rashes, 5/65 (8%) had calcinosis, 16/65 (25%) had dysphagia and 6/65 (9%) had ILD. Initiation of IVIG improved symptoms of weakness for 41/56 (73%) patients, myalgias for 6/7 (86%) patients, rashes for 33/40 (83%) patients, calcinosis for 0/5 (0%) patients and dysphagia for 12/16 (75%) patients. IVIG improved the ILD for 1/6 (17%) patients and the remaining 5/6 (83%) patients did not demonstrate progression of their ILD.

Conclusion: This large retrospective cohort study indicates the utility of IVIG in the management of idiopathic inflammatory myopathies. The results of our study suggest that a course of IVIG at 2 g/kg per month administered over 2-5 days is effective in treating refractory inflammatory myopathies and particularly effective in treating symptoms of weakness, myalgias, rashes and dysphagia. IVIG however appears generally ineffective in treating calcinosis as well as ILD.

Disclosure: R. Chu, None; **S. Nahirniak**, None; **J. Cohen Tervaert**, None; **E. Yacyshyn**, None.

Abstract Number: 0393

Surfactant Protein D as a Useful Predictor for Mortality in Myositis-associated Interstitial Lung Disease: A Dimorphic Model Based on anti-MDA5 Antibody

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Muscle Biology, Myositis & Myopathies Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Surfactant protein D (SP-D) is considered a serum biomarker of various forms of interstitial lung disease (ILD). However, the usefulness of SP-D for prediction of mortality remained unknown in detail in patients with ILD associated with polymyositis/dermatomyositis (myositis-associated ILD). Thus, we aimed to examine the utility of SP-D as a predictive biomarker for mortality in patients with myositis-associated ILD using our large-scale multicentre cohort data.

Methods: We recently established a multicentre retrospective cohort of Japanese patients with myositis-associated ILD (JAMI), which involved 44 institutions across Japan. We enrolled 381 patients with incident myositis-associated ILD in the JAMI cohort based on the availability of serum SP-D at the baseline. Demographic and clinical characteristics as well as the presence of autoantibodies to melanoma differentiation-associated gene 5 (MDA5) and aminoacyl tRNA synthetase were measured at the time of diagnosis, and follow-up survival data were collected prospectively.

Results: Seventy-eight patients died during the median observation period of 18 months, and the majority of patients died of ILD. The mortality rate was significantly higher (P = 0.0057) in a subset of patients with SP-D < 95.4 ng/mL, the cut-off value estimated by the receiver operating characteristic curve (ROC), than a subset with SP-D ≥95.4 ng/mL. (P = 0.0065; Figure 1A). However, interestingly, the survival curves intersected at 78 months, suggesting a dimorphic role of the SP-D level in the survival of patients with PM/DM-associated ILD:, i.e., short-term mortality was associated with a lower SP-D level, while long-term mortality was associated with a higher SP-D level. Therefore, we divided the enrolled patients into two subsets, anti-MDA5-antibody-positive group and negative group. In anti-MDA5 antibody-positive patients, survival rates were similar between those with SP-D levels at diagnosis < 95.4 ng/mL and ≥95.4 ng/mg (P = 0.90; Figure 1B). In contrast, in anti-MDA5 antibody-negative patients, survival rates were significantly worse in patients with SP-D levels ≥95.4 ng/mL than in those with SP-D levels < 95.4 ng/mL (P = 0.02; Figure 1C). Surprisingly, in anti-MDA5 antibody-negative patients, none of the patients with SP-D levels < 95.4 ng/mL died . In other words, all deceased patients with SP-D level < 95.4 ng/mL were positive for the anti-MDA5 antibody. We re-estimated the optimal cut-off value of SP-D for mortality in anti-MDA5 antibody-positive and anti-MDA5 antibody-negative patients individually with ROC curve analyses, resulting in optimal cut-off levels of 59.8 ng/mL in

Figure 1.

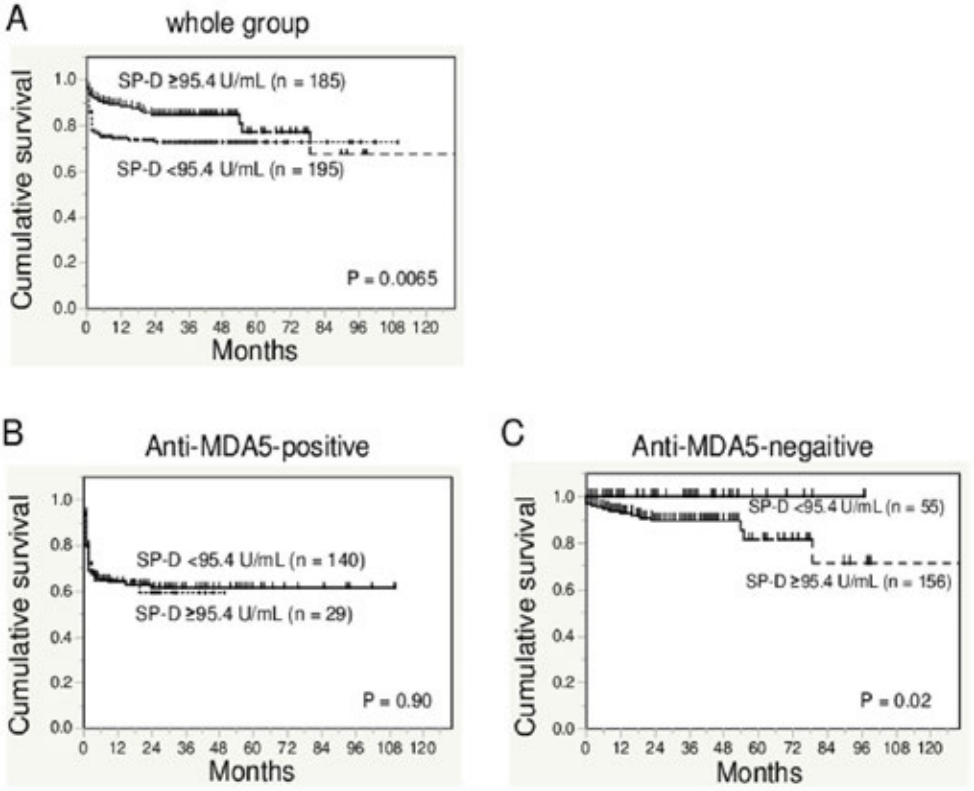
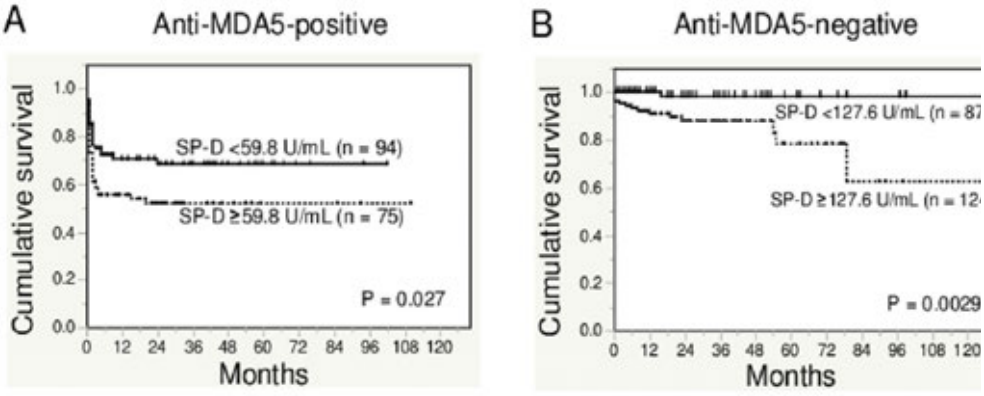


Figure 2



anti-MDA5 antibody-positive patients (P = 0.027;Figure2A) and 127.6 ng/mL in anti-MDA5 antibody-negative patients (P = 0.0029;Figure2B).

Conclusion: Serum SP-D is a useful predictor for the prognosis of patients with myositis-associated ILD. We successfully demonstrated the dimorphic role of the SP-D level in the prediction of outcomes on the basis of the presence or absence of anti-MDA5 antibody.

Disclosure: S. Kaieda, None; **T. Gono**, Astellas, 8, Astellas Pharma, 8, Boehringer-ingelheim Pharma, 8, Chugai, 8, Janssen, 8, MBL, 8, MEDICAL & BIOLOGICAL LABORATORIES CO., LTD, 8, Ono, 8, Ono Pharma, 8, Tanabe-Mitsubishi, 8, UCB Japan, 8; **K. Masui**, None; **N. Nishina**, None; **S. Sato**, MBL, 7, MEDICAL & BIOLOGICAL LABO-

RATORIES CO., LTD, 7; **M. Kuwana**, Abbvie, 2, 8, Actelion, 2, 8, Actelion Pharmaceuticals, 2, 8, Astellas, 2, 8, Bayer, 5, Boehringer Ingelheim, 5, Boehringer-Ingelheim, 5, Chugai, 2, 5, 8, Corbus, 5, CSL Behring, 5, CSL Berling, 5, Eisai, 2, 8, Eli Lilly, 2, Janssen, 8, Japan Blood Products Organization, 8, MBL, 7, 8, Ono, 2, 8, Pfizer, 2, Reata, 5, Tanabe-Mitsubishi, 2, 8.

Abstract Number: 0394

Sexual Health in 39 Female Patients with Idiopathic Inflammatory Myopathies

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Muscle Biology, Myositis & Myopathies Poster I
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Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are characterized by inflammation and weakness of skeletal muscles, pulmonary and articular involvement, which can have a negative impact on all aspects of quality of life including sexual life. The aim of this study was to assess sexual functioning in female IIM patients compared to age-/sex-matched healthy controls (HC) and to determine the association between sexual health impairment and disease activity, treatment, physical and psychological aspects of the disease.

Methods: In total, 39 women (29 currently have a partner) with IIM [mean age: 54.7, disease duration: 11.8 years, dermatomyositis (DM, 19)/ polymyositis (PM, 16)/ necrotizing myopathy (IMNM, 3)/ inclusion body myositis (IBM, 1)], who fulfilled the Bohan/Peter 1975 criteria for DM/PM, and 39 healthy controls (30 currently have a partner, mean age: 54.7 years) without rheumatic diseases filled in 11 well-established and validated questionnaires assessing sexual function (FSFI, SFQ28, BISFW, PISQ-12), quality of sexual life (SQoL-F), pelvic floor function (PFIQ-7), fatigue (FIS, MAF), physical activity (HAP), and depression (BDI-II). A standard laboratory testing was performed. Data are presented as mean ± SEM.

Results: Patients with IIM had significantly higher prevalence and greater severity of sexual dysfunction (FSFI, BISF-W, SFQ28, PISQ-12) and worse sexual quality of life (SQoL-F) compared to HC (table). Worse scores in IIM patients were associated with increased inflammation [CRP: FSFI (r=-0.378, p=0.0190), SFQ-28 Satisfaction domain (r=-0.346, p=0.0356), SQoL-F (r=-0.331, p=0,0479], greater muscle weakness of m. gluteus maximus/ m. gluteus medius/ m. iliopsoas [FSFI: (r=0.426, p=0.0368), (r=0.370, p=0.0368), (r=0.394, p=0.0252), SQoL-F (r=0.504, p=0.0044), (r=0.421, p=0.0204), (r=0.462, p=0.0100)], greater fatigue [FIS: FSFI (r=-0.358 , p=0.0154), BISF-W (r=-0.415, p=0.0084), SQoL-F (r=-0.327, p=0.0481)], more severe depression [BDI-II: FSFI Arousal domain (r=-0.357, p=0.0299)], deteriorated quality of life [HAQ: BISF-W (r=-0.464, p=0.0033)], and worse ability to perform physical activities [HAP: FSFI (r=0.405, p=0.0105), BISF-W (r=0.480, p=0.0019)]. No associations were found with disease duration, prednisone dose or serum levels of muscle enzymes.

Questionnaire: score range (meaning)	Idiopathic inflammatory myopathies (n=39)	Healthy controls (n=39)	p-value
FSFI: Female Sexual Function Index: 2(worst)-36(best)	15.7±2.1	20.7±2.0	p=0.0421
BISF-W: Brief Index of Sexual Function for Women: -16(worst)-75(best)	14.6±2.8	24.5±3.0	p=0.0134
SFQ28 Desire domain: Sexual Function Questionnaire: 5(worst)-31(best)	11.7±1.0	14.7±1.0	p=0.0457
PISQ-12: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form: 0(best)-48(worst)	14.9±0.8	10.1±1.0	p=0.0005
SQoL-F: Sexual Quality of Life Questionnaire – Female: 0(worst)-100(best)	31.8±5.1	80.7±2.5	p<0.0001
PFIQ7: Pelvic Floor Distress Inventory Questionnaire – short form 7: 0(best)-300(worst)	24.7±6.3	10.1±2.7	*p=0.0820*
FIS: Fatigue Impact Scale: 0(best)-160(worst)	55.3±5.5	33.2±4.3	p=0.0025
MAF: Multidimensional Assessment of Fatigue Scale: 1(best)-50(worst)	22.0±2.0	15.7±1.4	p=0.0021
BDI-II: Beck's Depression Inventory II: 0(best)-63(worst)	12.8±1.5	6.6±0.9	p=0.0013
HAP: Human Activity Profile – adjusted activity score: 0(worst)-94(best)	51.0±3.5	80.2±1.6	p<0.0001
HAQ: Health Assessment Questionnaire: 0(best)-3(worst)	1.1±0.1	0.1±0.1	p<0.0001

Conclusion: Women with IIM reported significantly impaired sexual function and sexual quality of life compared to age-matched healthy controls. Worse scores in IIM were associated with disease activity, physical activity, fatigue, depression and quality of life.

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Abstract Number: 0395

Younger Age at Presentation Is a Risk Factor for Failure to Achieve Remission in Adult Dermatomyositis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: A subset of patients with dermatomyositis may fail to achieve remission despite treatment. Nevertheless, the risk factors for failure to achieve remission in dermatomyositis are largely unknown.

Methods: We conducted a retrospective chart review of patients seen between 2006 and 2011 at John H. Stroger Medical Center of Cook County (Illinois, USA) with a diagnosis of dermatomyositis. All patients met 1975 Bohan and Peter criteria for "probable" or "definite" dermatomyositis. Remission could occur at any time point during follow-up and was defined as normal strength, creatine kinase < 200 mg/dL, and the absence of active dermatomyositis rash. Clinical features were defined at baseline within 1 month of presentation. We compared demographics, dermatomyositis-related clinical and serologic parameters, and treatments between those who achieved remission

Table 1. Characteristics of patients with dermatomyositis who failed to achieve remission versus those who achieved remission			
Values listed as mean (95% CI) or % (N/Total)	No remission (N=22)	Remission (N=43)	P value
Age at first visit in years	40.6 (35.1-46.2)	49.1 (44.6-53.6)	0.025
Female sex	81.8 (18/22)	79.1 (9/43)	0.793
Race			0.810
African-American	54.6 (12/22)	53.5 (23/43)	
Hispanic	36.4 (8/22)	39.5 (17/43)	
Other	9.2 (2/22)	7.0 (3/43)	
Myositis features			
Follow-up time, months	45.9 (20.6-71.3)	60.7 (47.1-74.3)	0.253
Biopsy-proven myositis	50.0 (11/22)	48.8 (21/43)	0.929
Full strength at first visit	38.9 (7/18)	18.0 (7/39)	0.314
Initial creatine kinase, mg/dL	3955.4 (793.2-7117.7)	4031.5 (1920.7-6142.2)	0.967
Neck weakness	50.0 (4/8)	33.3 (6/18)	0.664
Dysphagia	42.9 (6/14)	46.2 (12/26)	0.842
Fever	9.5 (2/21)	2.4 (1/42)	0.256
Raynaud's	27.3 (6/22)	20.9 (9/43)	0.566
Myalgias	52.9 (9/17)	44.1 (15/34)	0.552
Arthritis	44.4 (8/18)	57.1 (20/35)	0.380
ILD	27.3 (6/22)	32.6 (14/43)	0.662
Anti-Jo1 antibodies	25.0 (3/12)	36.0 (9/25)	0.711
ANA	66.7 (14/21)	55.0 (22/40)	0.379

and those who did not. We used Chi square tests to compare categorical variables and Student's t-tests to compare continuous variables. We then conducted a multivariable logistic regression to examine the outcome of failure to achieve remission. We forced age, sex, race, and follow-up time into the model and included clinical variables based on a p-value of < 0.2 in univariate screen. Treatments were not included in the multivariable model due to inability to adjust for confounding by treatment severity in this small sample.

Results: 65 patients, of whom 92.3 % (60/65) were African-American or Hispanic, were included in this study. Mean follow-up time for patients who did not achieve remission was 45.9 months vs. 60.7 months for those who did

Table 2. Multivariable logistic regression model of factors associated with failure to achieve remission in dermatomyositis				
	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age, per year increase	0.96 (0.92-1.00)	0.030	0.95 (0.90-0.99)	0.030
Female sex	1.19 (0.32-4.41)	0.793	1.61 (0.26-9.91)	0.610
African-American race	1.04 (0.37-2.93)	0.936	1.66 (0.43-6.44)	0.463
Months of follow-up	0.99 (0.98-1.01)	0.256	0.98 (0.97-1.00)	0.077
Full muscle strength at baseline	2.91 (0.83-10.17)	0.095	3.17 (0.73-13.8)	0.125
OR=odds ratio				

achieve remission (p-=0.253). 33.8% (22/65) of patients failed to achieve remission at any point during follow-up. Patients who failed to achieve remission were younger (mean age 40.6 years vs. 49.1 years; p=0.025) at first visit than patients who achieved remission. Patients who failed to achieve remission were more likely to have been treated with intravenous immunoglobulin (27.3% vs. 4.7%; p=0.009) at any point during follow-up. A multivariable logistic regression with age at presentation, female sex, African-American race, follow-up time, and full strength on presentation as predictors demonstrated that younger age at presentation was an independent risk factor for failure to achieve remission (OR 0.95 [95% CI 0.91-0.99] per 1-year increase in age; p=0.030).

Conclusion: In this small cohort of largely African-American and Hispanic patients with dermatomyositis seen at a US medical facility largely serving poor and uninsured patients, younger age at presentation was an independent risk factor for failure to achieve remission. Patients who failed to achieve remission were more likely to have been treated with second-line agents than those who achieved remission. Given that patients who failed to achieve remission were more likely to have normal baseline muscle strength than those who achieved remission, we hypothesize that younger age at presentation may be associated with more treatment-refractory cutaneous disease.

Disclosure: S. Kambhatla, None; **C. Richardson**, RUSH University Medical Center, 3; **P. Lingamaneni**, None; **A. Manadan**, RUSH University Medical Center, 3.

Abstract Number: 0396

Clinical Manifestations and Comparison of Subtypes of Juvenile Idiopathic Inflamatory Myopathies: Data from the REMICAM Registry

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
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Background/Purpose: Juvenile idiopathic inflammatory myopathies (JIIM) are a heterogeneous group of autoimmune diseases affecting children, characterized by symmetric muscular weakness, cutaneous rash and systemic organ involvement. The clinical manifestations of the IIMs differ between children and adults, for example, JIIM have a higher prevalence of calcinosis, lipodystrophy and vasculopathy, as well as a minor incidence of neoplastic disease or interstitial pneumonia. Given the low incidence of the JIIM, there are few studies describing the characteristics of this disease and its different subtypes.

The objective of this study is to describe the demographic, clinical and analytical characteristics of patients with JIIM from the multicentric REMICAM registry, and to compare those measures between polymyositis (PM) and juvenile dermatomyositis (JDM) subgroups.

Methods: A multicenter retrospective study from the REMICAM registry was performed. Patients were selected if they were 18 years or younger at onset of JIIM and met definite or probable criteria for IIM as defined by the modified Bohan and Peter criteria. We included patients with JDM or PM subgroups, overlap myositis patients were excluded.

Results: A total of 86 patients were included, 12 (14%) classified as PM and 74 (86%) as JDM. 70% were women, most of the subjects were Caucasian (96%). Disease characteristics are shown in Table 1. 13% of the patients had fever and 15% weight loss. Regarding musculoskeletal manifestations, 44% and 28% had arthralgias and arthritis, respectively, and 93% presented muscular weakness. Gottron sign was present in 76% of the patients, and calcinosis was present in 31.4%. CPK and aldolase levels at diagnosis are 431 U/L and 8 U/L respectively. Antinuclear antibody (ANA) was positive in 40% of the sample, but only 2 cases were anti-Jo1 positive. The rest of the complementary analysis are shown in table 2.

Clinical features	Total (n=86)	PM (n=12)	JDM (n=74)	p-value
Fever	23 (29,1%)	6 (50,0%)	17 (25,4%)	0,084
Weight loss	12 (15,2%)	1 (8,3%)	11 (16,4%)	0,680
Arthralgia	38 (44,2%)	7 (58,3%)	31 (41,9%)	0,287
Arthritis	24 (28,4%)	6 (50%)	18 (24,7%)	0,071
Gottron'sign	66 (76,7%)	-	65 (87,8%)	
Heliotrope erythema	46 (53,5%)	-	46 (62,2%)	
Mechanic hands	10 (12,3%)	-	10 (14,5%)	
Skin ulcers	3 (3,7%)	-	3 (4,3%)	
Raynaud	12 (13,9%)	3 (25,0%)	9 (12,2%)	0,362
Calcinosis	27 (31,4%)	2 (16,7%	25 (33,8%)	0,325
Muscular weakness	80 (93,0%)	11 (91,7%)	69 (93,2%)	1,000
Myalgias	68 (83,9%)	8 (66,7%)	60 (87,0%)	0,095
Miocarditis	2 (2,3%)	-	2 (2,7%)	
Arrhytmia	3 (3,5%)	1 (8,3%)	2 (2,7%)	0,370
Heart failure	1 (1,2%)	-	1 (1,4%)	1,000
Interstitial lung disease	1 (1,2%)	1 (8,3%)	-	0,140
Dysphagia	19 (22,1%)	2 (16,7%)	17 (23,0%)	1,000
GE reflux	7 (8,1%)	1 (8,3%)	6 (8,1%)	1,000
GI hemorrhage	1 (1,2%)	-	1 (1,3%)	1,000

Table 1. Clinical features.

Laboratory features	Total (n=86)	PM (n=12)	JDM (n=74)	p-value
Anemia	13 (15,1%)	4 (33,3%)	9 (12,2%)	0,079
Leucopenia	4 (4,6%)	1 (8,3%)	3 (4,0%)	0,458
Trombopenia	3 (3,5%)	2 (16,7%)	1 (1,3%)	0,050
ANA+	34 (40,5%)	7 (58,3%)	27 (37,5%)	0,173
CPK at diagnosis	431 (97-3131)	206 (36-7428)	659 (104-3110)	0,730
Aldolasa at diagnosis	12 (9-18)	9 (5-12)	12 (9-19)	0,230
CRP	0,35 (0-1,3)	0,12 (0-2,8)	0,42 (0-1,3)	0,817
ERS	19 (11-29)	25 (13-42)	19 (11-29)	0,450
Anti-Jo1	2 (2,6%)	-	2 (3,0%)	1,000
Myopathic pattern (EMG)	72 (92,3%)	12 (100%)	60 (90,1%)	0,508

Table 2. Laboratory features and complementary diagnosis

Conclusion: JDM was the most frequent clinical form of JIIM in our study, which corresponded to more than 80% of the cases, like other cohorts. The most frequent manifestations in patients with JIIM of our registry were the muscular and dermatological ones, but an important group also presented arthralgia/arthritis and fever. There was no statistical difference between both groups, regardless, cutaneous manifestations, myalgias and dysphagia were more common in JDM group, as well as higher CPK values and aldolase. PM group patients were older at diagnosis, had more fever and arthritis, also, cytopenia and ANA positivity were more frequent in this subtype.

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Abstract Number: 0397

Clinical Features of Polymyositis and Dermatomyositis Patients with Severe Dysphagia

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SESSION INFORMATION
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Background/Purpose: Polymyositis (PM) and dermatomyositis (DM) are autoimmune inflammatory diseases characterized by proximal myositis. Dysphagia has been reported to develop in 35 to 62% of PM/DM patients and known as poor prognosis factor. This study aimed to determine the clinical feature of PM/DM patients presenting severe deglutition disorder.

Methods: Consecutive patients with PM/DM who visited National Hospital Organization Tokyo Medical Center between April 2010 and March 2019 are included in this study. We compared the following clinical features between the patients with and without severe dysphagia: age of onset, maximum levels of serum creatine kinase (CK), sense

of dysphagia, manual muscle test (MMT) score, and complication of malignancy. Severe dysphagia was defined as having difficulty swallowing which needed gastrostomy.

Results: A total of 73 patients with PM/DM were identified. Among them, 5 patients developed severe dysphagia. Patients with severe dysphagia presented older age of onset (mean age 69.4 ± 12.0 vs 51.8 ± 15.7, p = 0.016), more frequent muscle weakness (MMT grade ≦ 4)(100% vs 56.6%, p = 0.048), more frequent complication of malignancy (80.0% vs 11.8%, p= 0.0005) and sense of dysphagia (100% vs 10.7%, p< 0.0001). On the other hand, there were no significant differences in maximum serum CK levels between the patients with and without severe dysphagia (21884.0 ± 10275 U/L vs 5544.5 ± 3043 U/L, p = 0.1788).

Conclusion: These results indicate that severe dysphagia develops frequently in PM/DM patients with older onset, muscle weakness, complication of malignancy and sense of dysphagia. When any of these clinical features are noticed, it is necessary to consider the risk of severe dysphagia.

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Seasonal Variation in Idiopathic Inflammatory Myopathies Incidence and Presentation: A Retrospective Study in Beijing and Hong Kong

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SESSION INFORMATION
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Background/Purpose: Seasonal patterns of disease onset and severity in idiopathic inflammatory myopathies (IIMs) as a whole are conflicting. In recent years, over 10 myositis-specific antibodies (MSAs) have been identified. They are able to divide patients into homogenous subgroups and inform on prognosis. We conducted a large multicentred study of a homogeneous disease group, based on serology and ethnicity, aiming to investigate the seasonal variation of IIMs.

Methods: This was a retrospective observational study. Consecutive Chinese patients with IIMs admitted to the rheumatology wards of the participating major regional hospitals in Beijing and Hong Kong from July 2013 to June 2018 were recruited. The diagnosis of IIMs was based on the Bohan and Peter's criteria with definite or probable cases being included. Patients with clinically amyopathic disease must have the typical Gottron's papules or heliotrope rash as determined by rheumatologists or dermatologists, and with no symptoms or signs of muscle involvement according to Sontheimer. Patients with juvenile myositis, inclusion body myositis, cancer-associated myositis and myositis associated with a previously diagnosed connective tissue disease were excluded. A commercial line blot immunoassay kit (EUROIMMUN) was used to detect the MSAs. The primary objective of the study was to investigate the seasonal variation of onset of IIMs characterised serologically. The secondary objective was to examine the seasonal patterns of the various clinical manifestations.

Results: All together 416 patients were studied. The mean age of the patients at disease onset was 48.1 years (S.D. 13.3). There was a female predominance (68.5%). The subgroups of IIMs were: dermatomyositis (63.9%), polymyositis (22.4%), clinically amyopathic dermatomyositis (10.1%), immune mediated necrotising myopathy (3.1%) and nonspecific myositis (0.5%). No particular seasonal pattern in disease onset was observed in IIM patients as a whole or in any classical subgroups. However, significantly more patients with any one MSA had their disease started in the first half of the year (p=0.013). The same pattern was also seen in the hospitalisation rate in patients with either anti-synthetase or anti-MDA5 antibodies (p=0.029). It was also found that rapidly progressive interstitial lung disease (RPILD) which was a well known severe complication associated with the anti-MDA5 antibody occurred more in the first half of the year (p=0.044). At the same time, most of the mortalities in our patients happened in the first quarter of the year (January to March) (p=0.013). Further analyses showed that infection was significantly associated with anti-MDA5 antibody, RPILD and mortality (p< 0.001).

Conclusion: Apparent seasonal patterns were noticed in our ethno-serologically defined IIM patients. Certain environmental factors, particularly infection, could be potential triggers. Our findings could shed light on the identification of etiologic factors and enhance our understanding of disease pathogenesis. They could also increase our awareness of the disease and its complications during the peak seasons.

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Seasonal and Temporal Analyses of Disease Onset and Diagnosis in Myositis Autoantibody Phenotypes in Juvenile Dermatomyositis (JDM)

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Background/Purpose: Published studies suggest seasonal occurrence of disease onset and disease activity in patients with adult idiopathic inflammatory myopathies (IIM).Our objective was to evaluate seasonal variation of disease onset and diagnosis and the distribution over time of myositis autoantibodies in JDM.

Methods: This study includes disease onset and diagnosis data of 383 myositis patients enrolled in NIH studies from 1994 to 2015. We tested myositis-specific autoantibodies (MSA) by standard immunoprecipitation (IP) and IP-immunoblotting methods and identified five autoantibody subtypes: 35 patients with JDM diagnosed before age 18 years with anti-melanoma-differentiation gene 5 (MDA5) autoantibodies, 157 with anti- transcriptional intermediary factor 1 (TIF1), 116 with anti-nuclear matrix protein 2 (NXP2), 15 with anti-synthetase (ARS) autoantibodies and 60 MSA-negative JDM patients, all meeting probable or definite Bohan and Peter criteria. We studied overall seasonable patterns of disease onset and diagnosis dates (by month) and performed comparisons between autoantibody subtypes. Circular statistics were used with seasonality and differences between the groups assessed by the Rayleigh

test and Watson two sample test for homogeneity, respectively. Proportion trend test was used to assess the trend of anti-MDA5 Ab over time compared to anti-TIF1 and anti-NXP2 autoantibodies.

Results: There was no seasonal clustering of the month of disease onset in JDM patients as a whole nor in the anti-ARS, anti-MDA5, anti-TIF1, anti-NXP2 autoantibody-positive and MSA-negative JDM subgroups. Anti-ARS autoantibody positive JDM patients had a seasonal pattern of disease diagnosis, with a peak time of diagnosis from May to July, and no patients with anti-ARS autoantibodies were diagnosed from January to April (p=0.03, Figure 1a). There were no differences in the seasonal patterns of disease onset and disease diagnosis of anti-MDA5 autoantibody-positive JDM patients compared to anti-TIF1 and anti-NXP2 autoantibody-positive, and MSA-negative patients (p >0.1, Figure 1b). In examining temporal trend of anti-MDA5 autoantibodies compared to anti-TIF1 and anti-NXP2 autoantibodies over time, from 1988 to 2015, we found no significant differences in the trend of occurrence of these subgroups based on year of symptom onset or of diagnosis (p >0.2).

Conclusion: Similar to adult IIM patients, JDM patients with anti-ARS autoantibodies demonstrate a spring to early summer seasonal peak in diagnosis, suggestive of certain environmental factors contributing to illness onset in these patients. In contrast, other MSA groups, including anti-MDA5, anti-TIF1, anti-NXP2 autoantibodies and MSA-negative JDM groups, did not exhibit seasonality in onset or diagnosis. In contrast to non-US cohorts, the frequency of anti-MDA5 autoantibodies has not increased over the past three decades and did not differ compared to anti-TIF1 and anti-NXP2 autoantibody-positive groups.

Figure 1a. Seasonal distribution was significantly skewed (p=0.03) based on month of diagnosis for anti-ARS autoantibody-positive JDM.

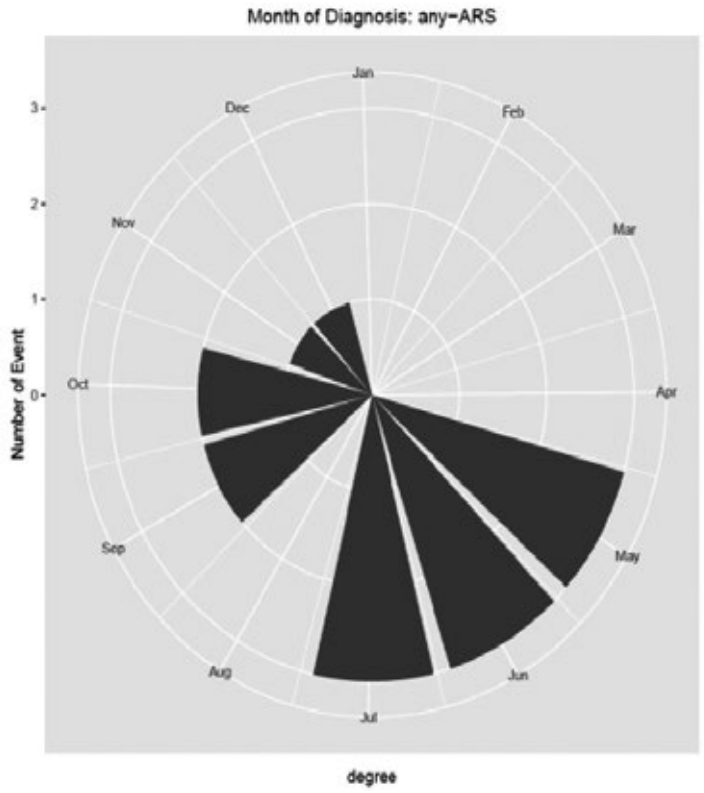
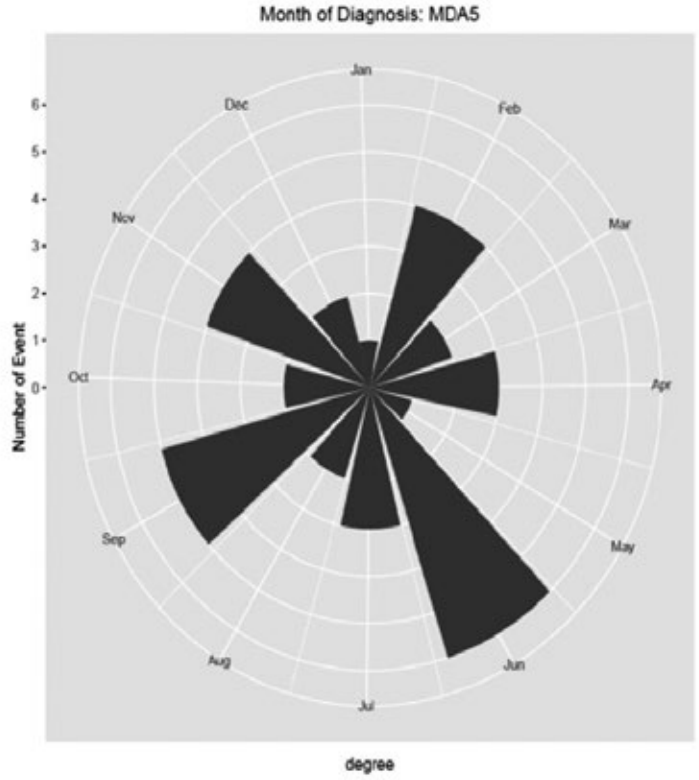


Figure 1b. Seasonal distribution was not significantly skewed based on month of diagnosis for anti-MDA5 autoantibody-positive JDM.



Disclosure: G. Mamyrova, Cure JM Foundation, 2; **M. Shi**, None; **I. Targoff**, Oklahoma Medical Research Foundation, 5; **R. Curiel**, Cure JM Foundation, 2, Bristol Myers Squibb, 2; **F. Miller**, aTyr Pharma, 9, Biogen, 9, Hope Pharmaceuticals, 9, Idera Pharmaceuticals, 9, MedImmune, 9, Momenta Pharmaceuticals, 9; **L. Rider**, ., 2, 9, aTyr, 9, Bristol Myers Squibb, 2, Cure JM Foundation, 2, 9, Eli Lilly and Company, 9, Hope Pharmaceuticals, 2, Lilly-drug, 9, MedImmune / AstraZeneca, 9, MedImmune/AstraZeneca, 9, NIEHS, 2, NIEHS, NIH, 2, NIH, 2.

Abstract Number: 0400

Performance of the European League Against Rheumatism/American College of Rheumatology Idiopathic Inflammatory Myopathies Classification Criteria in a Myositis Cohort from Argentina

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SESSION INFORMATION

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Table 1. Performance of all criteria in our cohort. EULAR-ACR criteria were considered positive if patient fulfilled probable or definitive criteria

	EULAR/ACR Criteria with muscle biopsy		EULAR /ACR criteria without muscle biopsy		Boham and Peter Criteria	
	Positive	Negative	Positive	Negative	Positive	Negative
Patients with biopsy N=37	29 (78%)	8 (21%)	29 (78%)	8 (22%)	37 (100%)	0
Patients without biopsy N= 95			76 (80%)	19 (20%)	72 (76%)	23 (24%)
All patients N= 132			105 (79%)	27 (20%)	109 (83%)	23 (17%)

Table 2. Sensitivity of EULAR/ACR criteria according to the physician diagnosis as gold standard

EULAR/ACR criteria	True positive	False negative	Sensitivity % (95% CI)
Probable IIM	39	24	61.9 (4-84.6)
Definitive IIM	66	24	73 (56.7-93.3)

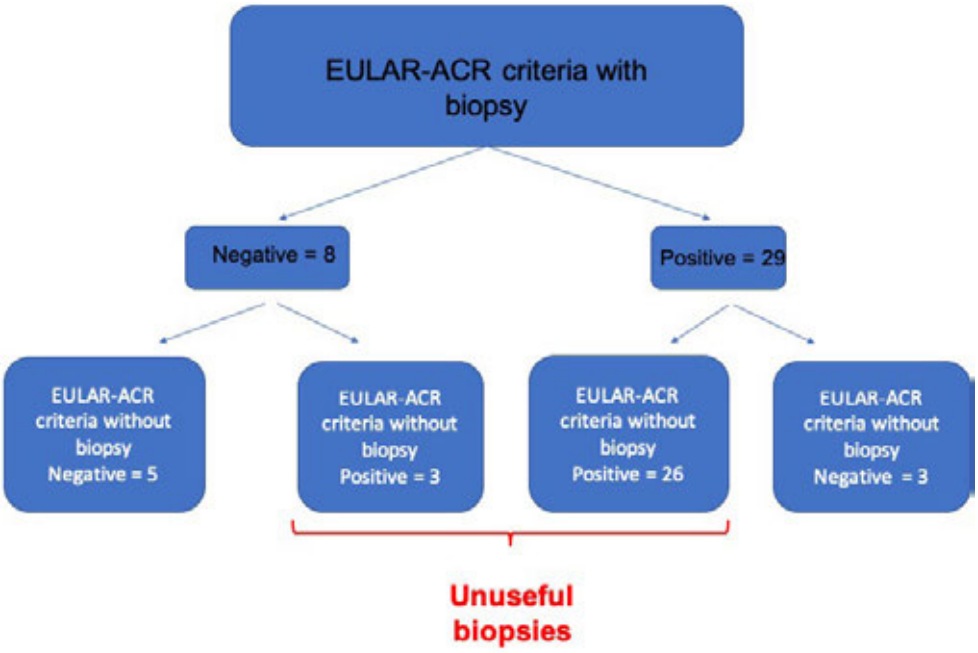

Figure 1. Performance of EULAR/ACR criteria in patients who underwent muscle biopsy

Background/Purpose: Patients with Idiopathic Inflammatory Myopathies (IIM) have been classified mainly according to Bohan and Peter (B&P) criteria, proposed in 1975. In 2017 the new EULAR/ACR criteria were proposed. They are able to classify patients with IIM and they are applicable even without results of a muscle biopsy.

The objective of this study was to evaluate the performance of the new EULAR-ACR myositis classification criteria in a large retrospective cohort of IIM patients from Argentina.

We applied the EULAR-ACR criteria in an external real-world cohort of consecutive IM cases from the Argentinean Rheumatology Society Myositis study group. Consecutive patients with IM based on physician diagnosis were included in the database. Data were collected form a preexisting database.

Methods: B&P criteria and EULAR-ACR were applied to each patient. For the purpose of this study we applied the non-biopsy EULAR/ACR criteria to non-dermatomyositis (DM) patients without biopsy (in the original paper those criteria only applied to DM patients). And we also applied the non-biopsy criteria to patients with a biopsy to be able to evaluate whether IM diagnosis might have been done without a biopsy.

We compared the performance of EULAR-ACR criteria with physician diagnosis and with B&P criteria.

Results: A cohort of 132 patients with physician diagnosis of IM were included in the study.

Seventy-seven percent were females, mean age at IM diagnosis was 45 (SD 17) years. Ninety- four (71%) without muscle biopsy and 37 (29%) with biopsy.
Table 1 shows the performance of all criteria in our cohort. EULAR-ACR criteria were considered positive if patient fulfilled probable or definitive criteria.

Figure 1 shows the performance of EULAR/ACR criteria (with and without biopsy) in patients who underwent muscle biopsy (37 patients)

Table 2 shows sensitivity of EULAR/ACR criteria according to the physician diagnosis as gold standard.

When we analyzed the sensitivity of EULAR-ACR (criteria without biopsy) according to B&P criteria as gold standard, the sensitivity was 86% (73.2-94.9). We were not able to evaluate the sensitivity of EULAR/ACR criteria with biopsy according to B&P criteria because all patients with biopsy fulfilled this criteria.

Conclusion: The sensitivity of EULAR-ACR criteria according to physician diagnosis in our cohort was lower than previous reports for both probable and definitive cut-off points. Sensitivity of EULAR-ACR criteria performed better using B&P criteria as gold standard. If criteria without biopsy are applied to patients with biopsy most of them fulfill criteria. Only in 6 patients of 37 the biopsy would change diagnosis.

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Abstract Number: 0401

Performance of EULAR/ACR Classification Criteria for Idiopathic Inflammatory Myopathies in a Real-life Cohort of Adult Patients

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SESSION INFORMATION
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Background/Purpose: Idiopathic Inflammatory Myopathies (IIM) are rare and heterogenous diseases, remaining a clinical challenge and persisting with high morbidity and mortality. The lack of consensus in their classification has added difficulties to the development of novel and effective therapeutic strategies, precluding clinical trials with significant and reproductible results. The recently published EULAR/ACR criteria were developed to overcome the fragilities of the previous most used criteria.

The objective of this study is to evaluate the performance of the new classification criteria in a real-life cohort of adult patients with IIM.

Methods: Retrospective review of the cohort of adult patients followed in a dedicated unit of a tertiary hospital, between January 2008 and December 2018. Clinical, serological and histological data were collected. EULAR/ACR classification criteria were applied to each individual patient using the web calculator. Clinical diagnosis was obtained from 2 experts, for each case, and all the patients with a definitive IIM were included in the analysis. Sensibility, sensitivity, positive and negative predictive values were calculated for each of the classification subtypes.

Results: Ninety-two patients were included, 79 women (85.9%) and 15 men, with a medium age at diagnosis of 47 years-old and a medium follow-up period of 12 years. Muscle biopsy results were available in 43.5% of cases, but only 62.5% presented parameters compatible with the criteria specifications. EULAR/ACR classification criteria re-

Table 1. EULAR/ACR classification criteria performance

Classification criteria-assigned IIM subtype	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
PM	30	90	27	91
DM	100	66	51	100
IBM	100	100	100	100
ADM*	63	99	83	96

*ADM: amyopathic dermatomyositis

sulted in a definitive diagnosis of IIM in 52/92 cases (56.5%) and a probable diagnosis in 25/92 cases (27.2%), with the remaining 15 cases (16.3%) having a probability of IIM of less than 50%. Regarding IIM assigned subtypes, we found overall high negative predictive values and good specificity (table 1). Sensitivity was heterogenous among the subtypes: very high for Dermatomyositis (DM) and Inclusion-Body Myositis (IBM) and low for Polymyositis (PM). The most strinking differences between expert clinical diagnosis and classification criteria-assigned subtypes were in PM, reducing drastically the sensitivity. Overlap myositis, anti-synthetase syndrome and paraneoplastic myositis were the cases that contributed the most for the group that did not score enough for a diagnosis of IIM using the criteria, as well as for the differences between clinical diagnosis and classification results in PM and DM.

Conclusion: EULAR/ACR criteria applied to this cohort presented high specificity but only moderate sensitivity, particularly in some subtypes, as PM. A number of factors may be contributive, namely the absence of pulmonar involvement in the clinical variables and the stringicity of cutaneous involvement parameters and histological features. The most recent developments in the pathogenesis of IIM, particularly regarding myositis-specific antibodies, could be of interest to be added to the classification in order to include those patients with an atypical clinical presentation.

Disclosure: A. Campar, None; **C. Vasconcelos**, None.

Abstract Number: 0402

Chronic Disease Course and IVIg-dependance in Long-term Follow-up of Anti-HMGCR Immune-mediated Necrotizing Myopathy

Océane Landon-Cardinal ,[1] Kuberaka Mariampillai,[2] Céline Anquetil,[3] Aude Rigolet,[2] Baptiste Hervier,[4] Nicolas Champtiaux,[2] Olivier Benveniste,[3] and Yves Allenbach[3], [1]Centre Hospitalier de l'Université de Montréal, Montréal, Canada, [2]Pitié-Salpêtrière University Hospital, Paris, France, [3]Sorbonne Université, Paris, France, [4]Hopital Pitie-Salpetriere, Paris, France

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

Background/Purpose: Anti-HMGCR antibodies have been associated with a severe form of immune-mediated necrotizing myopathy (IMNM) with a poor muscle strength recovery and early muscle damage. These patients tend to require aggressive immunosuppressive therapy and present relapsing disease course. Our objective was to evaluate real-life treatment strategies in anti-HMGCR IMNM patients.

Methods: This monocentric study included all patients with anti-HMGCR IMNM with at least 12 months of follow-up. Medical records were retrospectively reviewed to assess clinical features at diagnosis, HLA typing, treatment

strategies over the follow-up period (including corticosteroid (CS) use, number of immunosuppressive (IS) agent and intravenous immunoglobulin (IVIg) duration), disease course, and clinical status and therapeutic profile at last follow-up. Remission was defined as the presence of CK level ≤ 2 times the upper limit of normal associated with a stable manual muscle testing for ≥3 months. Quantitative variables are reported as median [IQR1-IQR3].

Results: Thirty-five patients were included. Age at diagnosis was 47.1 [26.1-60.2] years, 74% of patients were female, 29% were statin-exposed, all patients presented with muscle weakness (deltoid and psoas MRC-5 was 4.0 [2-4] and 4.0 [3-4], respectively) and highest CK level was 8146 [5000-12090] IU/L. Time from symptoms onset to treatment initiation was 0.8 [0.3-4.7] years. During the follow-up period, 91% of patients were treated with CS in combination with an IS agent, the majority of patients received IVIg (91%) and the number of treatment intensification was 2 [1-4]. Fourty percent of patients also received plasma exchanges as part of induction therapy.

All patients demonstrated a chronic disease course and no patients were in treatment-free remission at last follow-up after 4.9 [3.1-8.9] years. At last follow-up, 60% of patients were in remission - most of which with IVIg (71%) -, 57% of patients were still receiving CS (CS dose was 8 [5-10] mg/day) and 54% of patients had an IS agent. At last follow-up, only 40% of patients had a normal muscle strength, deltoid and psoas MRC-5 was 5 [4-5] and 4 [3-5], respectively, and CK level was 299 [200-559] IU/L. No predictors of remission or IVIg use at last follow-up were identified, including demographic features, HLA-DRB1*11:01 and HLA-DRB1*07:01 status, muscle disease severity at onset and statin use. Therapy-related side effects were reported in 26% of patients.

Conclusion: In our population, anti-HMGCR IMNM was associated with a chronic disease course associated with IVIg-dependance.

Disclosure: O. Landon-Cardinal, None; **K. Mariampillai**, None; **C. Anquetil**, None; **A. Rigolet**, None; **B. Hervier**, None; **N. Champtiaux**, None; **O. Benveniste**, None; **Y. Allenbach**, None.

Abstract Number: 0403

Single-specificity Anti-SMN Autoantibodies Are Associated with a Novel Scleromyositis Overlap Syndrome

Alexandra Baril-Dionne,[1] **Océane Landon-Cardinal** ,[2] Alain Meyer,[3] Josiane Bourre-Tessier,[1] Yves Troyanov,[4] Anne-Marie Mansour,[5] Farah Zarka,[5] Jean-Paul Makhzoum,[6] Jessica Nehme,[5] Eric Rich,[1] Jean-Richard Goulet,[1] Tamara Grodzicky,[1] Isabelle Richard,[7] Marie Hudson,[8] Valérie Leclair,[9] Ira Targoff,[10] Minoru Satoh,[11] Marvin Fritzler,[12] and Jean-Luc Senecal[1], [1]Centre hospitalier de l'Universite de Montreal, Montreal, QC, Canada, [2]Division of Rheumatology, Centre hospitalier de l'Université de Montréal; Department of Medicine, Université de Montréal, Montreal, QC, Canada, [3]Centre de Reference des Maladies Autoimmunes Rares, Hôpitaux Universitaires de Strasbourg, Strasbourg, France, [4]Division of Rheumatology, Department of Medicine, Hôpital du Sacre-Coeur de Montreal, Montreal, QC, Canada, [5]Hôpital du Sacre-Coeur de Montreal, Montreal, QC, Canada, [6]Vasculitis Clinic, Hopital du Sacre-Coeur de Montreal, Montreal, QC, Canada, [7]CISSS AT Rouyn-Noranda, Rouyn-Noranda, QC, Canada, [8]Jewish General Hospital, Lady Davis Institute for Medical Research, and Department of Medicine, McGill University, Montreal, QC, Canada, [9]Division of Rheumatology, Department of Medicine, Jewish General Hospital; Clinical Epidemiology Unit, Department of Medicine, Karolinska Institutet, Montreal, QC, Canada, [10]University of Oklahoma Health Sciences Center, Oklahoma City, OK, [11]Department of Clinical Nursing, School of Health Sciences, University of Occupational and Environmental Health, Kitakyushu, Japan, [12]Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

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Background/Purpose: Autoantibodies (aAbs) to proteins comprising the survival of motor neuron (SMN) macromolecular complex have not been thoroughly studied. Only two publications described clinical associations related to anti-SMN: the seminal publication reported three patients for which anti-SMN was associated with myositis and myositis/SSc overlap, while the second reported a patient with necrotizing myopathy and aAbs to SMN1 and gemin3. aAbs to the SMN complex may be suggested by indirect immunofluorescence (IIF) on HEp-2 cells showing a pattern referred to as few nuclear dots (known as AC-7 in the International Consensus on ANA patterns). The AC-7 pattern has been reported to have a low predictive value for any disease. Interestingly, deletion or mutation of SMN gene causes spinal muscular atrophy. The aim of this study was to describe the ANA pattern of patients with a SSc/myositis (scleromyositis) overlap syndrome (SMOS) with no known other SSc or myositis-specific aAbs; and to evaluate the clinical features of patients with a SMOS and anti-SMN aAbs.

Methods: Patients with a SMOS with no known SSc or myositis-specific aAbs were identified from 2 retrospective cohorts of patients with myositis and/or SSc. Both the diagnosis of myositis and SSc were made by expert opinion, since fulfilling the new classification criteria for both SSc and myositis may be insensitive in early disease. Sera from patients with the AC-7 pattern were tested for anti-SMN by an addressable laser bead immunoassay (ALBIA) and validated by immunoprecipitation (IP) of homogenates of metabolically labelled cells. ALBIA results were expressed as median fluorescence units (MFU) and the cut-off was set at 3 standard deviations above normal and unrelated disease controls.

Results: Twenty-one patients with SMOS and no known SSc or myositis-specific aAbs were identified, 6 of whom had an AC-7 IIF pattern. Anti-SMN aAbs were present on ALBIA in 5/6 (83.3%) of these patients (median 13 661 MFU; range 7433–21146). In these 5 patients positive on ALBIA, IP confirmed the reactivity to SMN and gemins 2, 3 or 4. Key myopathic features at presentation of these 5 patients were proximal weakness in all, with a mean CK elevation of 2564 IU/L (range 1738-3675). SSc features at the time of myositis diagnosis included Raynaud phenomenon (100%), limited (60%) or sine (40%) skin involvement, and bilateral trigeminal neuropathy (20%). At last follow-up, all patients met the ACR/EULAR classification criteria for SSc and notable SSc features included calcinosis (60%), pneumatosis intestinalis (20%), retro-pneumoperitoneum (20%) and interstitial lung disease (20%). Although all patients had been treated with corticosteroids, SSc renal crisis did not occur. Other overlap features included arthritis (60%), Sjögren syndrome (40%) and SLE (20%). One patient had 3 siblings with spinal muscular atrophy.

Conclusion: Single-specificity anti-SMN complex aAbs may define a novel SMOS, with absent or limited skin involvement at myositis diagnosis. The few nuclear dots (AC-7) pattern may be associated with clinically relevant information and be a sensitive screening test for anti-SMN aAbs in SMOS.

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Abstract Number: 0404

Autoantibody Profiles Delineate Three Distinct Subsets of Scleromyositis

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Background/Purpose: Myopathy is an important cause of morbidity in systemic sclerosis (SSc). Nevertheless, scleromyositis remains incompletely characterized owing at least in part to its clinical heterogeneity. Sub-classifying patients with either SSc or autoimmune inflammatory myositis (AIM) by autoantibody profiles is a useful way of identifying more homogeneous subsets. We hypothesized that grouping patients with scleromyositis based on their autoantibody profile would also allow us to identify distinct clinical phenotypes.

Methods: Thirty-six subjects from a referral centre were identified as having a concomitant diagnosis of SSc and AIM by two rheumatologists. A retrospective chart review was performed and data on demographics, clinical features, laboratory tests and other relevant investigations were extracted. Autoantibodies were assessed by indirect immunofluorescence (IIF) on Hep-2 substrates and line immunoassay (LIA, myositis and systemic sclerosis profiles: Euroimmun, Lübeck, Germany). Subjects were divided into 3 groups based on their autoantibody profiles: group 1 included subjects with SSc-specific autoantibodies (anti-centromere, -topoisomerase 1, -RNA polymerase III, -Th/To, -fibrillarin), group 2 with SSc-overlap autoantibodies (anti-PM/Scl, -U1RNP, -Ku), and group 3 without any fine specificities (hereinafter referred to as 'seronegative').

Results: Of the 36 subjects with scleromyositis, 8 (22%) had SSc-specific autoantibodies, 11 (31%) had SSc-overlap autoantibodies and 17 (47%) were seronegative on LIA (Table 1). However, 14 (82%) of the seronegative subjects had positive IIF staining: 6 nuclear speckled and cytoplasmic; 5 nuclear speckled; 2 cytoplasmic; and 1 nucleolar. Most of the subjects were women (83%), had Raynaud's phenomenon (92%), and abnormal nailfold capillaroscopies (79%). One third of the scleromyositis subjects had no skin involvement and the absence of skin disease was seen more frequently in SSc-overlap and seronegative subjects. Subjects with SSc-specific autoantibodies had lower median creatine kinase (CK) levels (290 IU/L (48-1344)). Subjects with SSc-overlap autoantibodies presented a more classical pattern of weakness associated with significant CK elevation (median (range) 2860 IU/L (159-5075)). Distal weakness was a major feature of seronegative subjects (65%) and head drop was found more frequently in both SSc-associated (38%) and seronegative individuals (29%).

Table 1. Comparison of scleromyositis subjects based on autoantibody profiles

	SSc-specific ab (ACA, ATA, RNApol, Th/To, fibrillarin) (n = 8)	Overlap SSc-myositis ab (PM/Scl, Ku, U1RNP) (n = 11)	No SSc-associated ab (n = 17)
Female n,%	7 (88)	11 (100)	12 (71)
Age at diagnosis mean, SD	47 (21)	52 (10)	57 (12.8)
Skin thickening			
Diffuse	4 (50)	3 (27)	6 (35)
Limited	4 (50)	2 (18)	5 (29)
Sine	0	6 (55)	6 (35)
Raynaud	6 (75)	11 (100)	16 (94)
Pitting scars	2 (25)	0	3/16 (19)
Digital ulcers	2 (25)	0	4 (24)
Telangiectasias	6 (75)	3 (27)	4 (24)
Abnormal nailfold capillaroscopy*	2/2	7/8	10/14
Calcinosis	1 (13)	2 (18)	1 (6)
Muscle weakness			
Distal weakness	2 (25)	5 (45)	11 (65)
Proximal weakness	6 (75)	10 (91)	14 (82)
Head drop	3 (38)	1 (9)	5 (29)
Diaphragmatic weakness	0	1 (9)	1 (6)
Dysphagia	3 (38)	4 (36)	8 (47)
Classic dermatomyositis rash	1 (13)	3 (27)	3 (18)
Mechanics' hands	0	0	1 (6)
Elevated creatinine kinase	5 (63)	10 (91)	15 (88)
Peak creatinine kinase median, range	290 (48-1344)	2860 (159-5075)	946 (63-3489)
Myopathic electromyography	4 (50)	9/10 (90)	14/16 (88)
Arthritis	1 (13)	5 (45)	4 (24)
Interstitial lung disease on HRCT	2 (25)	6 (55)	9 (53)
Pulmonary hypertension**	0/7	0	1 (6)
Trigeminal neuropathy	0	2 (13)	0

Abbreviations: ACA, anti-centromere antibodies; ATA, anti-topoisomerase I (Scl-70) antibodies; HRCT, high resolution computed tomography; PM/Scl, antibodies to polymyositis/scleroderma exosome antigen; RNAP, RNA polymerase III antibodies; Th/To, mitochondrial RNA processing (MRP) complex (note LIA detects only anti-hPOP1); U1-RNP, U1-ribonucleoprotein.

*Including scleroderma and scleroderma-like patterns.

**Right heart catheterization available for only 7 patients of which one had pulmonary arterial hypertension. The rest of the cohort was screened by cardiac echocardiography and showed no signs of pulmonary hypertension.

Conclusion: In this carefully phenotyped cohort, autoantibody profiles identified three subsets of scleromyositis associated with distinct patterns of muscle involvement. Just under 50% of subjects had no SSc- or myositis-specific autoantibody identified by LIA, although most of these had positive IIF. Studies are underway to correlate these results with muscle histopathology and to identify novel autoantibodies associated with scleromyositis.

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Abstract Number: 0405

Anti-MDA5 Dermatomyositis: A Case Series, Systematic Review and Meta-analysis of the Literature

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Background/Purpose: Anti-MDA5 dermatomyositis is characterized by little or no muscle involvement, distinct cutaneous features and an increased risk of severe interstitial lung disease (ILD) with high mortality. We aim to describe clinical presentation, radiological features and disease course in 6 patients and to perform a systematic review and meta-analysis of the literature on proportions of clinically-amyopathic form and ILD/rapidly progressive ILD (RPILD) in anti-MDA5 dermatomyositis according to the ethnicity of the published cohorts.

Methods: A total of six patients fulfilling diagnostic criteria of dermatomyositis with MDA5 antibodies, followed between 2014 and 2018 at the Department of Internal Medicine of Lille University Hospital and Roubaix Hospital, were retrospectively reviewed.

For the systematic review, we searched MEDLINE up to May 2019 for cohorts describing clinical and radiological features in dermatomyositis with MDA5 antibodies, using the following search terms (dermatomyositis OR interstitial lung disease) AND (MDA-5 OR (melanoma differentiation-associated protein 5) OR anti-CADM-140) AND English [language]. We calculated weighted pooled summary estimates of proportions of clinically amyopathic dermatomyositis, ILD and RPILD. For each meta-analysis, we used the DerSimonian and Laird method. A random-effects model was used to combine data. The overall effect was estimated using a weighted average of individual effects, with weights inversely proportional to variance in observed effects.

Results: In our case series, median age at diagnosis was 54.4 years (39.3-55.4). There were four women. Five patients had clinically amyopathic dermatomyositis. Three patients had a characteristic cutaneous phenotype consisting of skin ulcerations and palmar papules (Figure 1 A, B). Among five patients with ILD, one patient had a rapidly progressive course leading to respiratory failure (Figure 1 C) one week after admission, three patients had a severe

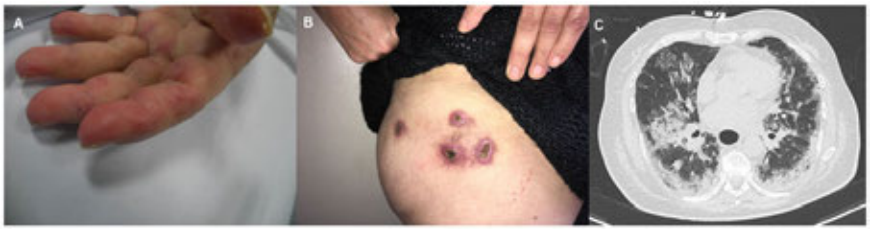

Figure 1. Distinct features Anti-MDA5 dermatomyositis A) palmar papules B) skin ulcerations and C)Chest CT scan of rapidly progressive interstitial lung disease

Table 2. N: number of anti-MDA5 dermatomyositis patients, ♀: females, Age is expressed as mean ± standard deviation or median (interquartile), CADM: clinically amyopathic dermatomyositis, ILD: interstitial lung disease; RPILD: rapidly progressive interstitial lung disease.

Table 2. Systematic review of the literature

Author	Country /Period	MDA5 antibody assay	N	♀ (%)	Age	CADM (%)	PID /PIA (%)
Allenbach	France /NA	IB	9	78	44±17.7	NA	67/NA
Borges	Brazil/2000-2016	ELISA	21	71	NA	24	38/NA
Cao	China /2009-2011	ELISA	15	60	46.2±9.6	20	100/60
Chen	China /2007-2011	ELISA	19	58	NA	26	NA/79
Chen	China /2010-2011	ELISA	26	38	46.7±13.1	35	100/38
Fiorentino	USA /2004-2010	IP	10	88	51.5±8.8	50	67/22
Fujikawa	Japan /1999-2007	IP	8	88	60.5±10.9	75	100/100
Gono	Japan /1992-2009	IP ELISA	14	79	43.6±14.6	57	100/71
Gono	Japan /1993-2009	ELISA	27	74	48±13	81	NA/74
Hall	USA /2006-2012	IP	11	NA	NA	45	73/NA
Hoshino	Japan /NA	IP	21	81	47±15	95	95/NA
Hozumi	Japan /1996-2015	IP	15	73	52 (33-68)	53	100 /87
Ikeda	Japan /2000-2009	IP	6	50	46.6±12	17	83 /50
Ikeda	Japan /2005-2014	IP ELISA	10	40	63 (58.0-64.8)	100	100 /NA
Kang	Korea /1993-2007	IP	9	56	45.8±16	0	67 /67
Koga	Japan /1999-2010	IP	17	88	55.5±13	82	94 /71
Labrador-Horrillo	Spain /1983-2012	ELISA IB	14	64	52.5 (42.3-54)	57	64 /57
Matsushita	Japan /2009-2015	IP ELISA	12	67	56±12	83	100 /92
Moghadam-kia	USA /1985-2013	ELISA	16	NA	NA	NA	50/44
Nakashima	Japan /NA	IP	13	69	57(52-64)	15	92/54
Sato	Japan /NA	IP	8	75	44.5±12.7	100	88/50
Sato	Japan /2011-2014	ELISA IP	55	73	50.8±14.3	82	91/84

ILD and received pulsed methylprednisolone and intravenous cyclophosphamide. Among these three patients, add-on immunosuppressant therapy with rituximab was given in one case, mycophenolate mofetil in another, and plasma exchange with intravenous immunoglobulin in the last case.

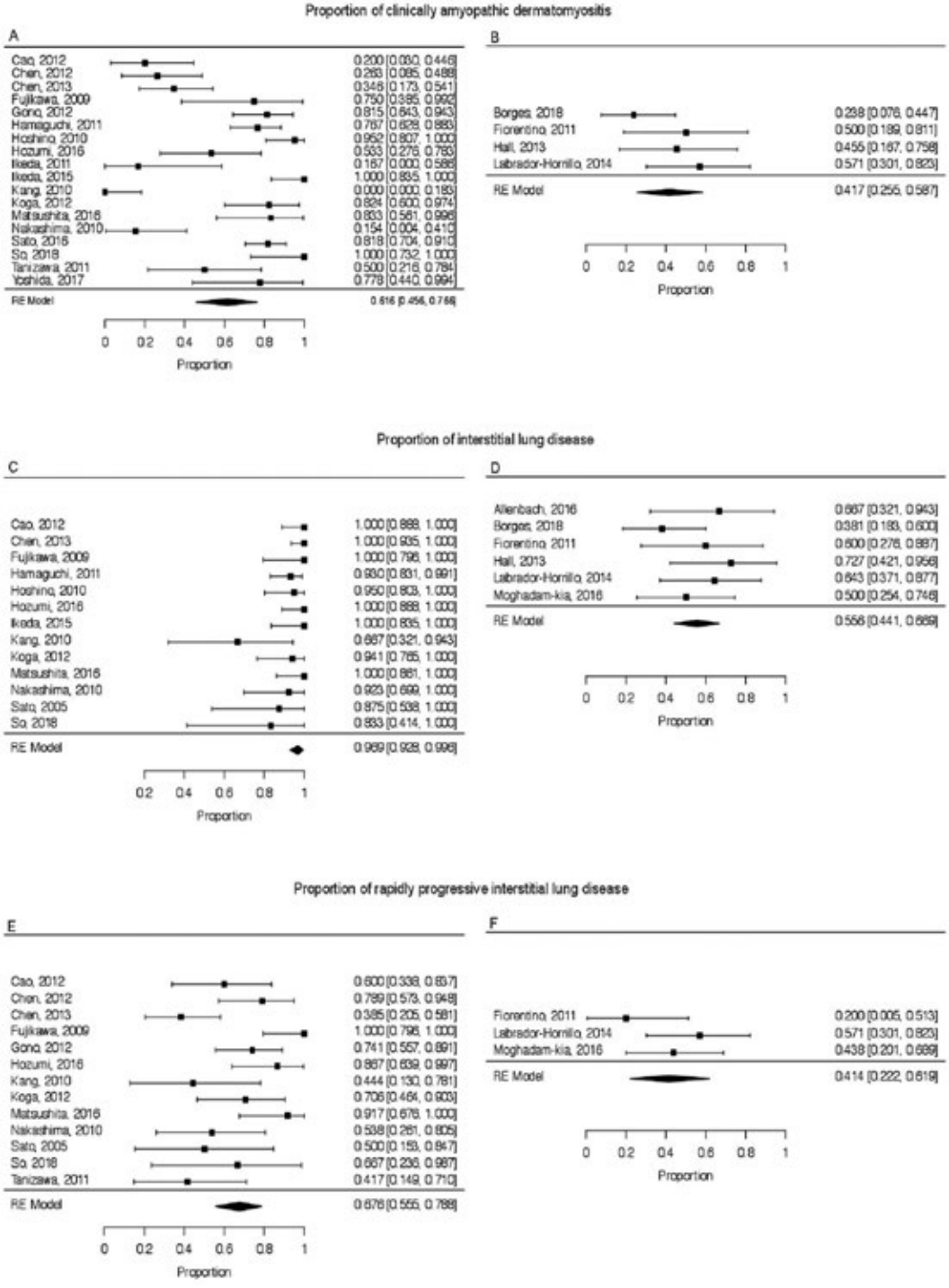

Figure 2. Forest plots of meta-analysis of proportion of clinically amyopathic dermatomyositis in A) Asian cohorts and B) American/European cohorts; proportion of interstitial lung disease in C) Asian cohorts and D) American/European cohorts; proportion of rapidly progressive interstitial lung disease in E) Asian cohorts and F) American/European cohorts.

A total of 25 studies (Table 2), consisting of 19 Asian cohorts and 6 American/European cohorts were included in the meta-analysis. Pooled proportion of clinically amyopathic dermatomyositis was 61.6% [95% CI 45.6%-76.6%] in Asian cohorts and 41.7% [25.5%-58.7%] in American/European cohorts (Figure 2). Pooled proportion of ILD was 96.9% [92.8%-99.6%] in Asian cohorts and 55.6% [44.1%-66.9%] in American/European cohorts. Pooled proportion of RPILD was 67.6% [55.5%-78.8%] in Asian cohorts and 41.4% [22.2%-61.9%] in American/European cohorts.

Conclusion: Our results show higher proportions of clinically amyopathic dermatomyositis and ILD/RPILD in Asian cohorts than in American/European cohorts.

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Abstract Number: 0406

Myositis Related Antibodies and Interstitial Lung Disease: Variables Associated with Baseline Lung Function and Functional Improvement: Results from a Multicentric Latin-american Cohort

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SESSION INFORMATION
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Background/Purpose: Idiopathic inflammatory myopathies (IIM) comprise a group of autoimmune diseases associated to different myositis related antibodies (MRA), that determine distinct phenotypes but share some symptoms, including myositis, skin rash and high prevalence of interstitial lung disease (ILD), the latter being particularly associated with some MRA. Some patients with MRA and ILD will fulfill IIM classification criteria, but others will not and may be classified as ILD with autoimmune features (IPAF). The aim of our study is to describe the clinical and radiological features of a group of patients with ILD and MRA, and their association with baseline and longitudinal pulmonary function (PF).

Methods: Descriptive study of a multicentric cohort of 211 patients evaluated between 2016-2018 in 3 multidisciplinary ILD clinics in Argentina, Chile and México. Every patient was confirmed to have ILD by thoracic high-resolution computed tomography (HRCT). Descriptive statistics, univariate and multivariate analysis were performed.

Results: 211 patients were included, (Chile = 119, México = 50 and Argentina = 42). Most patients were women (77,4%), mean age of 57 +-12 years. In 146 patients (70%) ILD was diagnosed first, in 43 patients (18%) ILD and connective tissue disease (CTD) were diagnosed simultaneously, and CTD was diagnosed first in 25 patients (12%). Mean interval between ILD and CTD diagnosis was 7.6 months (Table 1). Anti-Synthetase (AS) antibodies were the most frequent (Jo-1, PL12, PL-7), followed by Ro-52, PM-Scl 75-100 and Ku. Most frequent CTD diagnoses were AS syndrome and IPAF. Most prevalent HRCT patterns were non-specific interstitial pneumonia /organizing pneumonia

Table 1

Variable	N: 211	Variable	N: 211
Demographics		**Laboratory**	
Female: n (%)	164 (77,4%)	Creatin kinase serum levels U/L (n= 178)	81 (12 - 10.053)
Age (years old)	57 ± 12	Antinuclear antibodies (ANAs (n= 207)	135 (65,2%)
Primary Dignosis		Ro (n= 211)	59 (28,5%)
Initial ILD diagnosis n (%)	146 (69,9%)	Ro52 (n= 211)	104 (54,2%)
Simultaneous diagnosis n (%)	38 (18,2%)	Jo1 (n= 211)	54 (25%)
Interval between the diagnosis of ILD and CTD. (month).	7,6 (0,03- 279,7)	PL12 (n =208)	39 (18,4%)
Rheumatological diagnosis		PM- Scl (n= 194)	30 (15,5%)
Anti-synthetase syndrome (AS)	135 (64,3%)	Other IIM antibodies (208)*	32 (15,4%)
Interstital pneumonia with autoimmune features (IPAF)	43 (20,5%)	PL7 (n= 208)	29 (13,7%)
Amyopathic dermatomyositis (CADM)	13 (6,2%)	Ku (n= 208)	25 (12%)
Dermatomyositis (DM)	11 (5,2%)	MDA5 (n= 165) **	13 (7,9%)
Polymyositis (PM)	8 (3,8%)	OJ (n= 167)**	10 (4,7%)
HRCT Pattern (n=198)		Ej (n= 167)**	8 (3,8%)
NSIP/OP	90 (45,5%)	**Baseline pulmonary function**	
NSIP (Non specific interstitial pneumonia)	69 (34,5%)	FVC (L) (n= 164)	1970 (850 - 4350)
UIP (Usual interstitial pneumonia)	19 (9,6%)	% FVC (n=164)	66% (30 - 119%)
OP (Organizing pneumonia)	19 (9,6%)	% DLCO (n = 124)	49,5% (11- 127%)
LIP (Lymphocytic interstitial pneumonia)	1 (0,5%)	**First line treatment**	
Main symptoms		Corticosteroids (CS)	13 (6,1%)
Dyspnea, mMRC ≥2	137 (64,6%)	CS + Cyclophosphamide	33 (15,6%)
Sicca (xerostomia and / or xerophthalmia)	122 (59,2%)	CS + Mycophenolate mofetil	72 (34%)
Arthritis	113 (53,6%)	CS + Azathioprine	54 (25,5%)
Mechanic's hands	102 (48,3%)	CS + Methotrexate (MTX)	8 (3,8%)
Raynaud's Phenomenon	95 (45%)	Rituximab	1 (0,5%)
Proximal muscle weakness	82 (38,9%)	Calcineurin inhibitors	1 (0,5%)
Gottron's papules/heliotrope rash	62 (29,4%)	CS + MTX + Leflunomide***	17 (8%)
Dysphagia	29 (14,8%)		

* Other antibodies of IIM: Mi2, TIF1gamma, NXP2, SAE1, SRP
** This Antibodies are not avalilabe in Argentina
*** This combination is used in México to treat IIM-ILD

Table 2: Variables associated with *worse baseline* PF

Univariate analysis	OR	p value	CI 95%
ILD alone as first manifestation of disease	**2.12**	**0.045***	**[1.00 - 4.48]**
Raynaud's Phenomenon	0.5	0.057	[0.24 - 1.02]
Xerophthalmia	0,53	0,095	[0,25 - 1,12]
Arthritis	0,54	0,092	[0,26 - 1,19]
Abcense of Dermatomyositis rash	**2,87**	**0.049***	**[0.16 - 0.72]**
Abcense of positive Antinuclear antibodies (ANA)	**2,26**	**0.049***	**[0.19 - 1.01]**
Absence of positive Ro	**2.10**	**0,044***	**[0,22 - 0,98]**
Ro52	0.47	0.053	[0.21 - 1.01]
Creatin kinase serum levels < 250 U/L	3.09	0.069	[0.86 - 11.04]
Jo1	2.37	0.069	[0.91 - 6.14]
NSIP/OP	**2.67**	**0.011***	**[1.23 - 5.78]**
Multivariate analysis	**OR**	**p value**	**CI 95%**
ILD alone as first manifestation of disease	**4,97**	**0.015***	**[0,56 - 0,73]**
NSIP/OP	**2,56**	**0,05***	**[0,15 - 1,0]**

* p value ≤ 0,05

overlap (NSIP/OP) and NSIP (Table 1). Worse baseline PF was defined as forced vital capacity (FVC) < 70% and/or diffusion capacity of carbon monoxide (DLCO) < 60% at debut. Worse baseline PF was associated to ILD alone as initial diagnosis, NSIP/OP HRCT pattern, absence of dermatomyositis rash and absence of positive ANA and Ro (uni/ multivariate analysis, Table 2). Functional improvement was defined as an increase of FVC greater than 10% in follow up. 121 patients with > 3 months of follow-up were included. Functional improvement was associated with absence of ILD as the first manifestation of disease and absence of sclerodactily, presence of OP HRCT pattern and mechan-

Table 3: Variables associated with *functional improvement* (n = 121)			
Univariate analysis	**OR**	**p value**	**CI 95%**
Abcense of ILD alone as first manifestation of disease	**3.24**	**0.013***	**0.12-0.78**
Mechanic´s hands	**2.3**	**0.035***	**1.05-5.01**
Dermatomiositis Rash	2.02	0.078	0.92 - 4.66
Abcense of sclerodactily	4.33	0.06	0.04 - 1.06
Positive Jo-1	**2,57**	**< 0.001***	**0.24 - 0.61**
OP pattern in HRCT	**5.22**	**0.002***	**1.81 - 14.99**
Multivariate analysis	**OR**	**p value**	**CI 95%**
Abcense of ILD alone as first manifestation of disease	**2.75**	**0.051**	**0.99 - 7.63**
Mechanic´s hands	1,78	0.22	0.69 - 4.58
Dermatomiositis Rash	1.57	0.61	0.26 - 9.26
Abcense of sclerodactily	**8.15**	**0.053**	**0.97 - 68.05**
Positive Jo-1	1.43	0.49	0.51 . 4.02
OP pattern in HRCT	**4.30**	**0.009***	**1.43 - 12.92**

* p value ≤ 0,05

ic´s hands (uni/mulitvariate analysis, Table 3). First line immunosuppressive treatments consisted in corticosteroids (CS) associated with a CS sparing agent like mycophenolate mofetil, azathioprine, cyclophosphamide, leflunomide, tacrolimus or rituximab (Table 1).

Conclusion: In our MRA-ILD cohort, AS antibodies and AS Syndrome were the most common findings, followed by IPAF. NSIP and NSIP/OP were the most prevalent HRCT patterns. Worse baseline PF could be related to the absence of extra-thoracic symptoms and “classic” antibodies of CTD (e.g ANA, Ro), causing delay in diagnosis and treatment. On the contrary, better functional improvement could be related to the presence of extra-thoracic signs that allow an opportune diagnosis and therapy, and more acute-subacute forms of ILD, as OP HRCT pattern.

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Abstract Number: 0407

Utility of Anti-SSA/SSB Assay and Anti-Ro 52 Antibody Assay in Routine Clinical Practice for Risk Assessment of Patients with Idiopathic Inflammatory Myositis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Muscle Biology, Myositis & Myopathies Poster I
Session Type: Poster Session (Sunday)
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Background/Purpose: Idiopathic inflammatory myopathies (IIM) are chronic autoimmune diseases affecting multiple organ systems and associated with a diverse autoantibody profile. Anti-SSA/SSB are the most frequent myositis associated antibodies. Historically, anti-Ro/SSA reporting has been combined for autoantigens Ro 52 and Ro 60

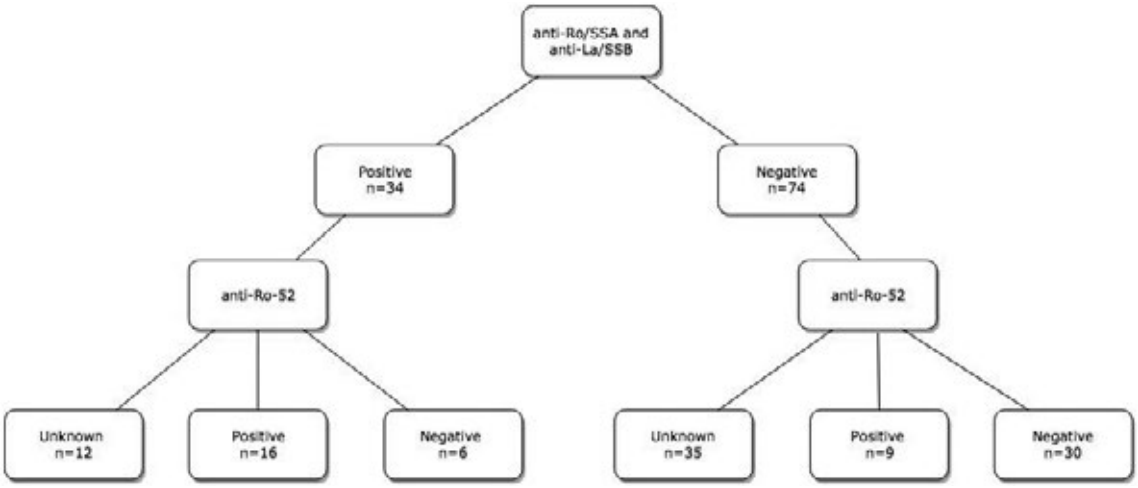

Table 1. Patient stratification based on autoantibody profile.

kDa. Recent data suggest that anti-Ro 52 and anti Ro 60 differ significantly in their clinical associations. Correlation of anti-Ro 52 with higher frequency of ILD has been demonstrated, but not been verified for commercially available anti-SSA/SSB assay.

Table 2. Comparison of demographics, clinical characteristics and autoantibody subtypes in anti-Ro 52 positive and anti-Ro 52 negative groups

	anti-Ro 52 positive (n=25)	anti-Ro 52 negative (n=36)
Age (yrs)	54	55
Sex	72% female 28% male	71% female 29% male
Race	36% African-American 28% Caucasian 20% Asian or Pacific Islander 4% American Indian or Alaskan Native 12% Unknown	45% Caucasian 33% African-American 11% Asian or Pacific Islander 0% American Indian or Alaskan Native 11% Unknown
Myositis subset	48% DM 36% PM 12% DM and IMNM 4% PM and IMNM	59% DM 32% PM 3% DM and IMNM 15% PM and IMNM
Antibody Subtypes	16% Anti-Jo-1 Ab 0% Anti-PL-7 Ab 4% Anti-PL-12 Ab 0% Anti-EJ Ab 0% Anti-OJ Ab 16% Anti-MDA5 Ab 8% Anti-PM/Scl-100 Ab 8% Anti-RNP Ab	6% Anti-Jo-1 Ab 0% Anti-PL-7 Ab 0% Anti-PL-12 Ab 6% Anti-EJ Ab 0% Anti-OJ Ab 3% Anti-MDA5 Ab 3% Anti-PM/Scl-100 Ab 8% Anti-RNP Ab

DM = dermatomyositis, PM = polymyositis, IMNM= immune-mediated necrotizing myopathy, UCTD= undifferentiated connective tissue disease.

Aim: To compare commercially available anti-SSA/SSB assay positivity and anti-Ro52 assay positivity as determinants of Interstitial Lung Disease (ILD) in IIM.

Methods: We queried the Northwell Myositis Center database for patients with IIM and available data for anti SSA/SSB and anti Ro52 between 1/1/2007 to 4/6/2018. All patients met 2017 EULAR/ ACR classification criteria for IIM. Anti-SSA and anti-SSB was measured by commercially available multiplexed bead-based immunoassay. Anti-SSA and anti-SSB were combined and analyzed as a single group because SSB was only found in association with positive SSA in our cohort. Anti-Ro52 was measured by commercially available immunoenzymatic assay (EIA). Patients were divided in 6 groups based on positivity/availability of each test (Table1)**.** The frequency of ILD was calculated for each group. Statistical analyses included Chi-square, Fisher's Exact test, and Wilcoxon Rank Sum test to determine statistical differences in group distributions and McNemar's test was performed to compare groups.

Results: There were 108 patients that met criteria for inclusion of which 31% (34/108) were anti-SSA/SSB positive. Anti-Ro 52 data were available for 61 patients and was positive in 41% (25/61). Some Ro 52 positive patients were nested in SSA/SSB negative group 36% (9/25) but majority of these had low titers of Ro 52. Both Ro 52 positive and negative patient groups had similar distribution for age, gender and race, as well as subtypes of IIM. Demographics, clinical characteristics and distribution of myositis associated antibodies in both groups are listed in Table 2**.**

As anticipated, the frequency of ILD was significantly higher in anti-Ro 52 positive compared with anti-Ro52 negative patients (64% vs 25%, p value= 0.0041). Similarly, anti-SSA/SSB positive status was associated with higher rate of ILD, independent of anti-Ro 52 status (56% vs 28%, p = 0.0084). Likewise, when patients with unknown anti-Ro 52 status were excluded from analysis, the difference remained statistically significant although weaker (55% vs 33%, p = 0.0038). There was no statistically significant difference in frequency of ILD between anti-Ro52 positive and anti SSA/SSB positive individuals (64% vs 56% p=0.5).

Conclusion: Both commercially available assays for anti-SSA/SSB and anti-Ro 52 positivity conferred the increased rate of ILD in our IIM cohort. Our data suggests that commercially available anti SSA/SSB assay can be used as a surrogate to the Ro52 assay to determine risk of ILD in IIM in clinical practice.

Disclosure: G. Marder, GSK, 2; **S. Narain**, Exagen, 2; **M. Barilla-Labarca**, None; **A. Valle**, None.

Abstract Number: 0408

Frequency of Concomitant Non-aminoacyl-transfer-RNA Synthetase Autoantibodies in Patients with Antisynthetase Syndrome

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SESSION INFORMATION
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Background/Purpose: Antisynthetase syndrome (ASSD) is an autoimmune disease with features including interstitial lung disease (ILD), myositis, inflammatory arthritis, Raynaud phenomenon, and mechanic's hands.[1] Eight aminoacyl-transfer-RNA (tRNA) synthetase autoantibodies (Ab) have been described so far: Jo-1, PL-7, PL-12, EJ, OJ, YRS, KS, and Zo.[1] Sometimes, additional autoantibodies associated with other autoimmune rheumatologic dis-

orders can be detected in patients with ASSD including ANA, anti-U1-RNP, anti-Sm, anti-ds-DNA, rheumatoid factor (RF), and anti-CCP.[2,3,4] In ASSD, the coexistence of these autoantibodies may increase the prevalence of Raynaud phenomenon, dermatomyositis, and deforming arthropathy.[2,3,4] Also, copresence of anti-SSA/Ro antibody in ASSD has been variably correlated with more severe interstitial lung disease.[2,4,5] We completed a subset analysis evaluating the presence of other (non-tRNA synthetase) antibodies in patients with ASSD.

Table 1. Overall summary of antibody

Factor	Total (N=88)	Jo-1 (N=62)	PL-7 (N=8)	PL-12 (N=13)	EJ (N=2)	OJ (N=3)
ANA	63(71.6)	54(87.1)	4(50.0)	3(23.1)	2(100.0)	0(0.0)
SSA	41(46.6)	27(43.5)	4(50.0)	8(61.5)	1(50.0)	1(33.3)
SSB	3(3.4)	1(1.6)	1(12.5)	0(0.0)	1(50.0)	0(0.0)
Sm	4(4.5)	3(4.8)	0(0.0)	1(7.7)	0(0.0)	0(0.0)
RNP	10(11.4)	8(12.9)	0(0.0)	2(15.4)	0(0.0)	0(0.0)
Scl	2(2.3)	2(3.2)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cardiolipin	10(11.4)	8(12.9)	0(0.0)	1(7.7)	1(50.0)	0(0.0)
Centromere	1(1.1)	1(1.6)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
RF	13(14.8)	7(11.3)	0(0.0)	5(38.5)	1(50.0)	0(0.0)
Smooth Muscle	4(4.5)	3(4.8)	1(12.5)	0(0.0)	0(0.0)	0(0.0)
dsDNA	5(5.7)	4(6.5)	1(12.5)	0(0.0)	0(0.0)	0(0.0)
CCP	4(4.5)	2(3.2)	0(0.0)	2(15.4)	0(0.0)	0(0.0)
Chromatin	4(4.5)	3(4.8)	0(0.0)	1(7.7)	0(0.0)	0(0.0)

Statistics presented as N (column %).

Table 2. Comparison of PL-12 vs Non-PL-12 ASSD antibodies

Factor	Total (N=88)	PL-12 (N=13)	Non-PL-12 ASSD (N=75)	p-value
ANA	63(71.6)	3(23.1)	60(80.0)	*<0.001*[c]
SSA	41(46.6)	8(61.5)	33(44.0)	0.24[c]
SSB	3(3.4)	0(0.0)	3(4.0)	0.99[d]
Sm	4(4.5)	1(7.7)	3(4.0)	0.48[d]
RNP	10(11.4)	2(15.4)	8(10.7)	0.62[c]
Scl	2(2.3)	0(0.0)	2(2.7)	0.99[d]
Cardiolipin	10(11.4)	1(7.7)	9(12.0)	0.65[c]
Centromere	1(1.1)	0(0.0)	1(1.3)	0.99[d]
RF	13(14.8)	5(38.5)	8(10.7)	*0.009*[c]
Smooth muscle	4(4.5)	0(0.0)	4(5.3)	0.99[d]
dsDNA	5(5.7)	0(0.0)	5(6.7)	0.99[d]
CCP	4(4.5)	2(15.4)	2(2.7)	0.10[d]
Chromatin	4(4.5)	1(7.7)	3(4.0)	0.48[d]

Statistics presented as N (column %).
p-values: c=Pearson's chi-square test, d=Fisher's Exact test.

Table 3. Comparison of Jo-1 vs Non-Jo-1 ASSD antibodies

Factor	Total (N=88)	Jo-1 (N=62)	Non-Jo-1 ASSD (N=26)	p-value
ANA	63(71.6)	54(87.1)	9(34.6)	<0.001[c]
SSA	41(46.6)	27(43.5)	14(53.8)	0.38[c]
SSB	3(3.4)	1(1.6)	2(7.7)	0.21[d]
Sm	4(4.5)	3(4.8)	1(3.8)	0.99[d]
RNP	10(11.4)	8(12.9)	2(7.7)	0.48[c]
Scl	2(2.3)	2(3.2)	0(0.0)	0.99[d]
Cardiolipin	10(11.4)	8(12.9)	2(7.7)	0.48[c]
Centromere	1(1.1)	1(1.6)	0(0.0)	0.99[d]
RF	13(14.8)	7(11.3)	6(23.1)	0.16[c]
Smooth muscle	4(4.5)	3(4.8)	1(3.8)	0.99[d]
dsDNA	5(5.7)	4(6.5)	1(3.8)	0.99[d]
CCP	4(4.5)	2(3.2)	2(7.7)	0.58[d]
Chromatin	4(4.5)	3(4.8)	1(3.8)	0.99[d]

Statistics presented as N (column %).
p-values: c=Pearson's chi-square test, d=Fisher's Exact test.

Methods: We obtained clinical data by retrospective review of electronic medical records from 2004 – 2017. The diagnosis of ASSD was confirmed by a rheumatologist, based on clinical phenotype and presence of one of the following autoantibodies: Jo-1, PL-7, PL-12, EJ, or OJ. Additional autoantibody positivity was determined by positive or negative values. Categorical variables were summarized using frequencies and percentages, and were compared using Pearson's chi-square tests or Fisher's exact tests. For all measures, a p-value of < 0.05 was considered significant.

Results: A total of 88 ASSD patients met criteria for inclusion in this study. The mean age was 57 years; 64% were female. The largest subset of patients was positive for Jo-1 Ab (N = 62). A positive ANA was noted in 63/88 patients (71.6%). ANA was more frequently positive in Jo-1 (87.1%) than those with 'non-Jo-1 ASSD antibody' (34.6%, p< .001) and PL-12 groups (23.1%, p< 0.001). RF was positive more frequently in PL-12 positive patients 5/13 (38.5%) than both in Jo-1 (11.3%, p=0.015) or 'Non-PL-12 ASSD antibody' groups (10.7%, p=0.009). Only 2/15 RF positive patients had radiographic evidence of deforming arthropathy, one of whom was also anti-CCP antibody positive and had erosions. No statistical comparisons were made for PL-7, EJ, and OJ antibodies due to small sample sizes.

Conclusion: Concomitant non-tRNA synthetase antibodies are common in patients with ASSD. Eighty five percent of our ASSD patients had at least one additional non-tRNA synthetase autoantibody, and almost 30% had at least three such additional autoantibodies, the most common ones being ANA, SSA, and RF. The impact of these autoantibodies on the phenotype and prognosis of ASSD patients remains unclear, and additional research is needed in this field.

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Abstract Number: 0409

Antisynthetase Syndromes: Correlation of Indirect Immunofluorescence Patterns with Diagnosis Criteria Fulfillment

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SESSION INFORMATION
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Background/Purpose: The antisynthetase syndromes (ASSD) are characterized by the presence of anti-aminoacyl transfer RNA synthetase (ARS) autoantibodies and a clinical classic triad of myositis, arthritis, and interstitial lung disease (ILD). Two ASSD diagnosis criteria have been proposed; those from Connors, and the stricter from proposed by Solomon.
Regarding ARS detection, previous studies have shown differences in the specificity between different myositis immunoblots. Nevertheless, an adequate clinical correlation and the ARS positivity in another monospecific-assays or HEp-2 indirect immunofluorescence assay (IIFA), can safeguard a high specificity of myositis-specific autoantibodies in the immunoblots.
Objective:
To evaluate the performance of IIFA patterns in the ASSD diagnosis in patients with ARS positivity and adequate ASSD or IIM clinical suspicion.

Methods: We analyzed data from one center (period 06/2008-06/2018). We searched all the myositis immunoblots (Euroimmun assay) requested by Rheumatologists under suspicion of ASSD or myositis and assessed: 1) the rate of cases with positive ARS; 2) the rate of cases with Connor´s or Solomon´s diagnosis criteria fulfillment; and 3) their relation with the IIFA patterns (Hep-2 cells; ≥1/80).

Results: A total of 140 myositis immunoblots were searched. Twenty-seven cases (19.3%) presented positive ARS: anti-Jo1 (n=13), anti-PL-12 (n=7), anti-PL-7 (n=1), anti-EJ (n=2), and anti-OJ (n=4). Twenty-five of these (92.6%) fulfilled Connors´ criteria, and 15 (55.5%) also met Solomon´s criteria. Additionally, all cases with positive ARS presented positive IIFA: 19 (70.4%) showed a cytoplasmic speckled pattern (10 of them with an associated nuclear pattern) and 8 cases (29.6%) presented only a nuclear pattern. Correlating, 13 of 27 cases with clinical suspicion of IIM or ASSD and positive ARS (48.1%) presented a cytoplasmic speckled IIFA pattern and also fulfilled Solomon´s criteria; representing the 68.4% of the cases with these IIFA patterns and the 86.6% of those that met Solomon´s criteria. On the other hand, 71 of the 113 cases (62.8%) with negative ARS presented positive IIF: 29 of them (40.8%) showed a cytoplasmic pattern (21 with an associated nuclear pattern) and 42 cases (59.2%) presented only a nuclear pattern.

Conclusion: Our results suggest that in patients evaluated by a Rheumatologist, with an adequate clinical suspicion of ASSD or IIM and with ARS positivity, the probability of fulfilling Solomon´s criteria is higher when the IIFA presents a cytoplasmic speckled pattern than when only a nuclear pattern is observed.

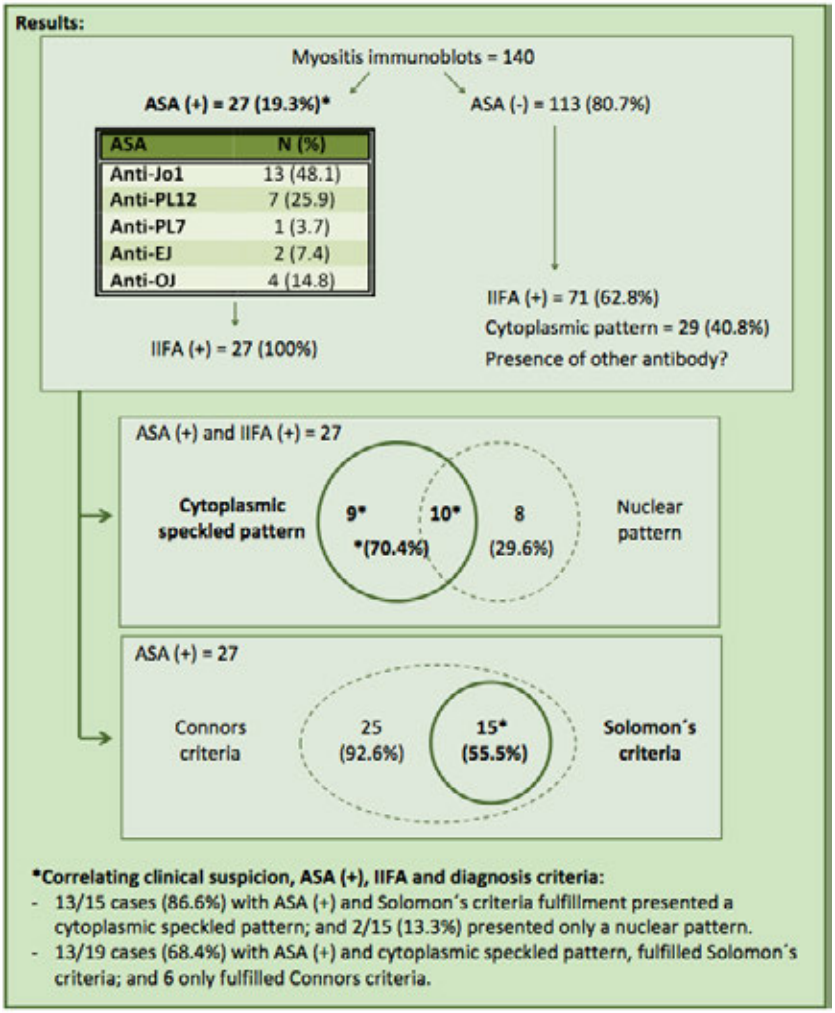

Image 1. Correlation of clinical suspicion, antisynthetase antibodies (ASA) and indirect immunofluorescence assays (IIFA).

Additionally, the high rate of positive IIFA in patients without positive ARS, suggests the presence of other positive antibodies and is in favor of good clinical judgment of the Rheumatologists when requesting the tests and of the auto-immunity expert when accepted them. This highlights the importance of the International Autoantibody Standardization (IAS) and the International Consensus on Antinuclear antibodies Patterns (ICAP) initiatives; whose implementation clinical laboratories could facilitate the harmonization of these tests and consequently the development of multicenter studies.

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Abstract Number: 0410

Prevalence of Malignancy in Myositis Patients with Anti-aminoacyl-tRNA Synthetase Antibodies: A Single Center Retrospective Study and Literature Review

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SESSION INFORMATION
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Background/Purpose: Anti-aminoacyl-tRNA synthetase antibodies (anti-ARS antibodies) are related to Idiopathic Inflammatory Myopathy (IIM) and Anti-Synthetase Syndrome (ASS). While anti-TIF1-γ antibody and anti-NXP-2 antibody are highly related to malignancy, anti-Jo-1 antibody is reported as protective factor against complicating malignancy. We recently experienced a case of anti-PL-7 antibody positive clinically amyopathic dermatomyositis (CADM) with rapidly progressive interstitial lung disease (RP-ILD) and colon cancer (stage IIIa). Regarding clinically difficult situation of this case with severe ILD activity and massive tumor indication for surgery, we thought it is important to clarify the risk factors and incidence of malignancy in myositis patients with anti-ARS antibodies.

Methods: Anti-ARS antibodies were detected by EUROLINE Myositis Profile 3. IIM diagnosis was made by the 2017 EULAR/ACR classification criteria and 'probable' cases meeting Bohan And Peter classification were included in this study between 2009 and 2018. Clinical features, laboratory and instrumental data were reviewed in this single center retrospective study. Cancer associated myositis(CAM) was defined by incidence of malignancy within 3 years from the diagnosis of IIM.

Results: We identified 38 patients positive for Anti-ARS antibodies (Anti-Jo-1 13 cases, Anti-PL-7 12 cases, Anti-PL-12 5 cases, Anti-EJ 8 cases, Anti-OJ 0 case). Malignancies were complicated in 6/38 patients (15.8%, Anti-Jo-1 1/13 case, Anti-PL-7 5/12 cases), while patients negative for anti-ARS antibodies showed lower incidence (8/83 patients, 12.0%). All 6 patients with malignancy complicated with ILD and 3/6 patients (50%) developed RP-ILD. Prevalence of malignancy in Anti-PL-7 antibody positive patients was significantly high compared to other myositis associated antibodies. We then analyzed clinical features, laboratory data of Anti-PL-7 antibody positive patients with or without malignancy. No significant differences in clinical characteristics were seen but interestingly all 3 CADM patients complicated with malignancy.

We identified 429 cases of anti-ARS antibody positive IIM and ASS in the literature. Incidence of malignancy in anti-ARS antibody positive patients was reported around 6% up to 16% and controversial. No patients positive for Anti-PL-7 antibody complicated with malignancy. Anti-Jo-1 antibody showed the highest incidence of malignancy contrary to the previous reports.

Conclusion: We should pay attention to malignancy screening in anti-ARS antibody positive patients same as other IIMs. Since all CADM patients positive for anti-PL-7 antibody complicated with malignancy, we may need to be cautious of malignancy in anti-PL-7 antibody positive CADM patients. Regarding the high frequency and severity of ILD in anti-ARS antibody positive patients even with malignancy, early detection and intervention of malignancy may lead to beneficial prognosis.

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Abstract Number: 0411

Frequency and Staining Patterns of Antinuclear Antibodies in Myositis Patients Without Known Myositis-specific Autoantibodies

Maria casal-Dominguez ,[1] Iago Pinal-Fernandez,[1] Ana Marin,[2] Maria Teresa Sanz-Martinez,[2] Andres Baucells-de la Pena,[3] Katherine Pak,[4] Yuji Hosono,[1] Lisa Christopher-Stine,[5] and Andrew L Mammen[4], [1]NIH, Bethesda, [2]Vall d'Hebron Hospital, Barcelona, Spain, [3]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [4]National Institutes of Health, Bethesda, [5]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Muscle Biology, Myositis & Myopathies Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To determine the frequency and staining patterns of antinuclear antibodies (ANA) in myositis patients who do not have known myositis-specific autoantibodies.

Methods: Sera from dermatomyositis (DM), inclusion body myositis (IBM), and polymyositis (PM)patients without known myositis-specific autoantibodies, as well as serum from healthy control patients, were tested for ANA by indirect immunofluorescence (IIF) assay on HEp-2 cells. In sera from ANA-positive patients and controls, the pattern of positivity was classified according to the International Consensus on ANA Patterns (ICAP). The prevalence and pattern of ANA in different myositis subgroups was compared to those of healthy sera.

Results: Sera from189 myositis-specific autoantibody-negative myositis patients (76 DM, 50 IBM and 63 PM) and 91 healthy comparators were included in the study. Most DM sera were moderately or strongly ANA positive (53%, $p< 0.001$). Only 33%, 22%, and 15% were moderately or strongly ANA positive in the PM, IBM, and healthy control groups, respectively (all $p >0.05$). ANA positivity was mostly nuclear (as opposed to cytoplasmic or mitotic) and the most common pattern was fine speckled. The only difference in ANA pattern among myositis subgroups was a higher prevalence of a nuclear fine speckled pattern in DM patients (61%, $p=0.02$).

Conclusion: Most myositis-specific autoantibody-negative DM patients have moderate/strong ANA positivity, predominantly in a fine speckled pattern. In contrast, myositis-specific autoantibody-negative PM and IBM patients show similar rates of ANA positivity as healthy controls. These findings suggest that currently ANA-positive unidentified autoantibodies are more likely to exist in DM patients than in IBM or PM.

Disclosure: M. casal-Dominguez, None; **I. Pinal-Fernandez**, None; **A. Marin**, None; **M. Sanz-Martinez**, None; **A. Baucells-de la Pena**, None; **K. Pak**, None; **Y. Hosono**, None; **L. Christopher-Stine**, AstraZeneca (Medimmune) Kezar, 5, Corbus Pharmaceuticals, 2, CSL Behring, 2, Inova Diagnostics, 7, Kezar, 2, Mallinckrodt Pharmaceuticals, 5, Novartis, 2, OptionCare, 5, Pfizer, 2; **A. Mammen**, None.

Abstract Number: 0412

Elevated Serum BAFF Levels in Patients with Dermatomyositis: Association with Interstitial Lung Disease

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: Muscle Biology, Myositis & Myopathies Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with dermatomyositis (DM) frequently have myositis-specific autoantibodies (MSAs), which are closely associated with different clinical features. Patients with anti-aminoacyl-tRNA synthetase (ARS) antibody (Ab) and anti-melanoma differentiation-associated gene-5 (MDA5) Ab often have interstitial lung disease (ILD); however, anti-MDA5 positive ILD is rapidly progressive and a life-threatening disease. Recently, anti-MDA5 Ab levels have been shown to correlate with disease activity in DM patients.Thus, B cells that are stimulated by excess B-cell activating factor (BAFF) play an important role in the pathogenesis of DM through autoAb production. In this study, we investigatedthe role of BAFF in DM patients.

Methods: We measured the serum BAFF levels in 56 adult DM patients (14 patients with anti-ARS Ab, 18 with anti-MDA5 Ab, 7 with anti-Mi-2 Ab, and 17 with anti-TIF1-γ Ab)using ELISA. For a longitudinal study, 130 serum specimens from 10 DM patients with anti-MDA5 Ab were analyzed.

Results: Serum BAFF levels were significantly higher in DM patients [median (range); 1.51 (0.39 – 6.11) ng/mL] than in healthy controls [0.65 (0.46 – 0.99)]. DM patients with elevated serum BAFF levels more frequently had ILD. In subgroup analysis, DM patients with anti-ARS Ab [1.74 (0.47 – 4.08)] and DM patients with anti-MDA5 Ab [2.42 (0.55 – 6.11)] exhibited increased BAFF levels compared to those in healthy controls, while DM patients with other MSAs showed BAFF levels comparable to those of healthy controls (Figure 1). In the longitudinal study, serum BAFF levels in DM patients with anti-MDA5 Abwere decreased after immunosuppressive therapy along with anti-MDA5 Ab level, which is a biomarker of the disease activity (Figure 2).

Conclusion: These results suggest that BAFF plays an important role in the pathogenesis of ILD in DM patients with anti-ARS and anti-MDA5 Abs.Furthermore, serum BAFF level is associated with disease activity in DM patients with anti-MDA5 Ab.

Disclosure: T. Matsushita, None; **T. Kobayashi**, None; **M. Kano**, None; **Y. Hamaguchi**, None; **K. Takehara**, None.

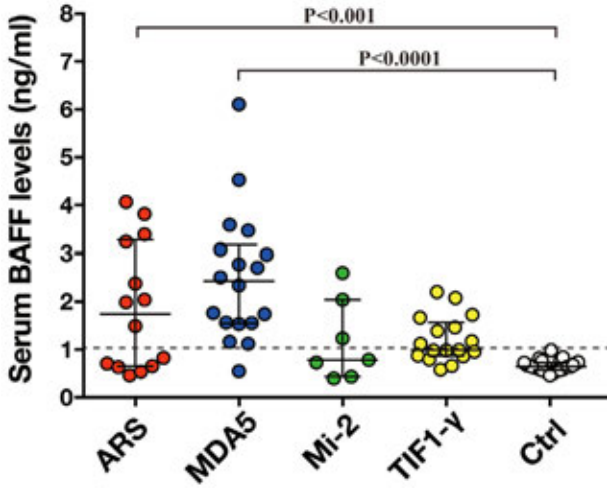

Figure 1

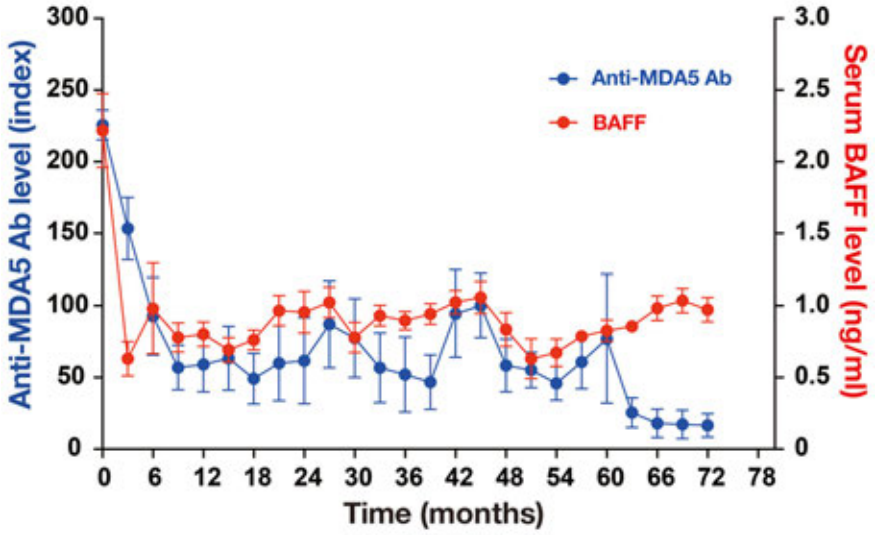

Figure 2

Abstract Number: 0413

Performance of the Patient Reported Outcomes Measurement Information System 29-item Profile in Comparison to the Clinical Disease Activity Index (CDAI) and Routine Assessment of Patient Index Data 3 (RAPID3) in an Australian Rheumatoid Arthritis Cohort

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The Patient-Reported Outcomes Measurement Information System (PROMIS) was developed to improve measurement of patient-reported outcomes. A large study from the US reported guarded support for the use of PROMIS-29 in RA, OA, FM and SLE patients[1]. Validity of PROMIS-29 for assessing quality of life in an Australian limited scleroderma cohort was demonstrated by comparison to SF36 and the HAQ-DI[2]. Our objective was to examine performance of the static 29 item PROMIS profile (PROMIS-29) compared to two legacy disease activity measures in RA, the CDAI and the RAPID3. We report a cross-sectional analysis of PROMIS-29 domain T scores according to CDAI and RAPID3 high, moderate, low and remission disease activity scores in a cohort of Australian patients with RA.

Methods: All patients attending one academic Rheumatology center complete the Multidimensional Health Assessment Questionnaire (MDHAQ) and PROMIS29 questionnaires at each visit. PROMIS29 questionnaires are scored on a 0 to 100 scale normed to the US population and reported as a T score (mean=50; 1 standard deviation (SD) =10). RAPID3 scores (range=0-30) are the sum of the patient physical function score (0-10), patient global assessment (0-10 VNS) and physician global assessment (0-10 VNS) derived from the MDHAQ. CDAI (range=0-76) is the sum of the patient global assessment (0-10 VAS), physician global assessment (0-10 VAS), tender joint count (0-28) and swollen joint count (0-28). T scores were compared across CDAI and RAPID3 disease activity (DA) categories by ANOVA. Minimum clinically important differences (MCIDs) from the population mean of 50 were estimated at 0.5 of the population SD, equivalent to 5 points[3].

CDAI	Remission (n=15)	Low (n=35)	Medium (n=33)	High (n=13)	*P value
Physical function	48.6 (6.4)	42.2 (8.7)	35.8 (6.2)	35.4 (9.9)	0.0001
Satisfaction with social role	56.5 (6.1)	48.6 (11.1)	42.2 (9.2)	40.6 (10.9)	0.0004
Fatigue	44.3 (9.3)	49.3 (10.2)	57.8 (9.5)	60.2 (14.6)	0.0008
Pain interference	48.5 (7.6)	58.5 (7.5)	62.8 (6.6)	67.6 (8.7)	0.0008
Sleep	46.9 (6.6)	51.9 (7.3)	58.0 (7.9)	58.6 (9.8)	0.02
Anxiety	46.4 (8.0)	53.3 (10.8)	54.1 (11.1)	58.6 (11.6)	0.04
Depression	44.8 (6.5)	51.4 (10.4)	55.5 (10.9)	55.5 (11.8)	0.04
RAPID3	Remission (n=22)	Low (n=8)	Medium (n=28)	High (n=55)	*P value
Physical function	51.0 (6.4)	46.6 (6.9)	41.9 (4.4)	33.6 (6.0)	<0.0001
Satisfaction with social role	57.8 (6.4)	54.0 (6.9)	47.6 (7.6)	40.0 (9.4)	<0.0001
Fatigue	44.8 (7.8)	42.8 (8.2)	51.2 (10.0)	57.5 (11.3)	<0.0001
Pain interference	47.9 (6.6)	54.9 (6.1)	58.1 (4.3)	66.0 (5.9)	<0.0001
Sleep	46.9 (5.4)	48.9 (7.2)	55.3 (7.8)	57.1 (8.2)	<0.0001
Anxiety	46.1 (7.5)	43.9 (6.8)	51.5 (10.4)	56.9 (11.1)	0.0003
Depression	44.1 (5.5)	44.5 (6.5)	51.0 (10.5)	56.2 (10.)	<0.0001

*** P values refer to the difference between high disease activity and remission**

Results: The mean (SD) CDAI was 12.4+/-10.4 with 15.6% in remission, 36.5% in low DA, 34.4% in moderate DA and 13.5% in high DA. All PROMIS domains were significantly worse in patients with high CDAI DA (>22) compared to remission (≤2.8) (Table). The mean (SD) RAPID3 score was 12.0+/-7.9 with 19.5 % in remission, 7.1% in low DA, 24.8% in moderate DA and 48.7% in high DA. All PROMIS domains were significantly worse in patients with high RAPID3 DA (>12) compared to remission (≤3.0) (Table). The majority of PROMIS scores in the high and moderate disease activity groups (23 out of 28) by CDAI and RAPID3 met MCID for worse scores than the population mean. Patients in CDAI or RAPID3 remission had PROMIS T scores equivalent to or better than the population mean.

Conclusion: All PROMIS domains in people with high RAPID3 or CDAI disease activity were significantly worse than in people in RAPID3 or CDAI remission. As expected, most PROMIS scores in those with high and moderate disease activity met MCID for being worse than the population mean. Further examination with larger patient numbers in each CDAI and RAPID3 DA category is required to confirm these findings.

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Abstract Number: 0414

Treat-to-Target Approach in the Management of Elderly Rheumatoid Arthritis Patients

Vivek Joseph,[1] Swetha Vontela,[2] **Surjeet Dheer** ,[3] Molly Weinberg,[4] Zuhayr Haq,[2] and Arundathi Jayatilleke[5], [1]Drexel University, PHILADELPHIA, PA, [2]Drexel University, Philadelphia, [3]Mercy Catholic Medical Center, Philadelphia, [4]Drexel University, Philadlephia, [5]Drexel, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: With the advent of biologic therapy for RA, the American College of Rheumatology advocates a treat to target (TTT) approach in the treatment of RA with the goal of achieving remission or low disease activity. In this study we analyse the frequency of use of clinical disease activity measures such as DAS28 and the clinical disease activity index (CDAI) in elderly RA as a measure of how aggressively rheumatologists treat elderly RA patients to minimal disease activity. We hypothesized that rheumatologists are less likely to measure disease activity in elderly patients and less likely to treat them to minimal disease activity with biologic and targeted synthetic DMARDs.

Methods: In this retrospective cohort study, patient data was collected by review of electronic medical records of patients in our academic rheumatology clinic for 34 months (March 2015-December 2017). Patients over the age of 75 with a diagnosis of RA based on two ICD9 or ICD10 codes on at least 2 office visits were included in the study. A control group consisted of RA patients of ages 41-70. Patients with history of positive TB testing, HIV infection, active viral hepatitis, liver disease with AST/ALT 2x normal limits, history of organ transplantation, and/or active malignancy were excluded from the study.

Results: A total of 72 elderly RA patients were included in the study group; the control group had a total of 459 patients. 23% (n=17) of study group patients had disease activity measures as compared to 53% (n=246) in the control group. Out of the patients who had disease measurements, 64% (n=11) of the study group had low/minimal disease activity as compared to 59% (n=140) of controls.

Conclusion: Our results suggest a provider bias in treating elderly patients with RA with a less aggressive approach. Rather than using objective disease activity scores with a TTT approach to achieve minimal levels of disease activity and better patient outcomes, our clinic experience shows that providers less frequently use disease activity measures

	Elderly RA	Non-Elderly RA
Females	86% (63)	81% (405)
Clinical Disease Activity Measures (CDAI or DAS-28)	23% (17)	53% (264)
Steroids >5mg/day	25% (18)	27% (113)
Oral DMARD use	63% (45)	73% (363)
Biologic/Synthetic DMARD use	14% (10)	40% (201)
Osteoporosis Screening	60% (43)	59% (294)

Elderly and Non-Elderly RA demographics

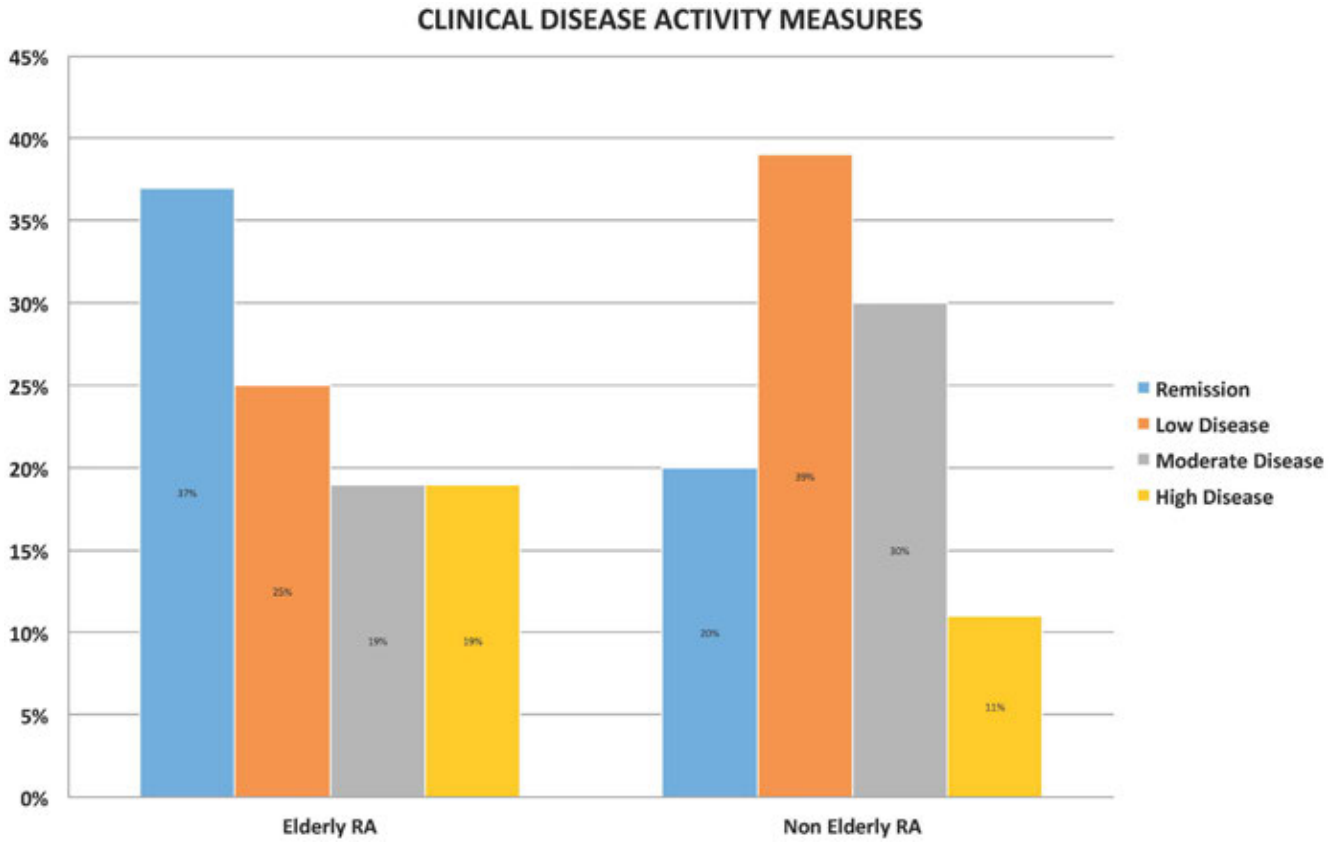

Figure 2. Clinical Disease Activity Measures in Elderly and Non-Elderly RA Patients

in elderly patients, and less frequently use biologic and targeted synthetic DMARDs. As rheumatologists increasingly adopt the TTT approach in management of RA, including objective documentation of disease activity, it is important to extend this to all segments of the population, including older patients.

Disclosure: V. Joseph, None; **S. Vontela**, None; **S. Dheer**, None; **M. Weinberg**, None; **Z. Haq**, None; **A. Jayatilleke**, None.

Abstract Number: 0415

Validation of a Satisfaction Measure for Use in Total Joint Replacement Clinical Trials

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient satisfaction after total hip (THR) and total knee replacement (TKR) is a core outcome selected by the Outcomes Measurement in Rheumatology (OMERACT), yet up to 30% of THR/TKR patients are dissatisfied. Improving patient satisfaction is hindered by the lack of a validated measurement tool that can accurately measure change.

Methods: This was a retrospective analysis using prospectively collected data of 10011 patients undergoing unilateral THR and TKR between 5/ 2007 and 2/2011 in The Hospital for Special Surgery arthroplasty registry. We tested psychometric properties of a proposed satisfaction instrument composed of 4 primary questions rated on a Likert scale, scored 1-100 **(Figure 1)**. Validity was assessed through correlation with similar constructs. We tested reliability with Cronbach's α, and sensitivity to change was assessed through the change corresponding to minimal change or a large change in two global questions, satisfaction with TJR outcome and Quality of Life (QOL).

Results: We included 4,796 TKR and 5215 THR **(Table 1)**; 90% were somewhat/very satisfied with pain relief, and almost 90% of TKR and 95% of THR were somewhat/very satisfied overall. Satisfaction correlated moderately with pain relief (TKR ρ=0.61, THR ρ=0.47) and function (TKR ρ=0.65, THR ρ=0.51) at 2 years; there was no correlation with baseline values. Reliability was demonstrated with overall Cronbach's alpha > 9. HOOS/KOOS improvement of >30 points corresponds to a mean Satisfaction score of 93.25 (11.53) after THR and 90.37 (SD 13.76) after TKR. When HOOS/KOOS pain and function were divided in to quartiles, increasing relief of pain and functional improvement increased the strength of the association of 2 core domains with satisfaction.

Figure 1. Patient questionnaire

1) How satisfied are you with the results of your knee/hip surgery in the following areas? (Please circle one answer for each question).					
	Very Satisfied	**Somewhat Satisfied**	**Neither Satisfied nor Dissatisfied**	**Somewhat Dissatisfied**	**Very Dissatisfied**
a. For relieving pain?	☐	☐	☐	☐	☐
b. For improving your ability to do housework or yard work?	☐	☐	☐	☐	☐
c. For improving your ability to do recreational activities?	☐	☐	☐	☐	☐
d. Overall, how satisfied are you with the results of your knee surgery?	☐	☐	☐	☐	☐

2) How much did your knee/hip surgery improve the quality of your life?					
More improvement than I ever dreamed possible	Great improvement	Moderate improvement	A little improvement	No improvement	The quality of my life is worse
☐	☐	☐	☐	☐	☐

Table 1. Demographic factors by TKR/THR including satisfaction score and quartiles.

	Overall (N=10011)	TKR (N=4796)	THR (N=5215)	p-value
Age	67.0 [59.0, 74.0]	68.0 [61.0, 75.0]	65.0 [58.0, 73.0]	<.0001
Sex				
Female	6397 (59.4%)	3248 (62.5%)	3149 (56.5%)	<.0001
Male	4378 (40.6%)	1952 (37.5%)	2426 (43.5%)	
Race				
Asian	53 (0.5%)	28 (0.5%)	25 (0.5%)	
Black	440 (4.1%)	256 (4.9%)	184 (3.3%)	
Hispanic	224 (2.1%)	134 (2.6%)	90 (1.6%)	<.0001
Native/Pacific Islander	17 (0.7%)	10 (0.2%)	7 (0.1%)	
Other	242 (2.3%)	143 (2.8%)	99 (1.8%)	
White	9788 (90.9%)	4620 (89.0%)	5168 (92.7%)	
SF-12 PCS	33.28 [28.0, 38.8]	33.5 [28.4, 39.0]	33.01 [27.58, 38.6]	0.001
SF-12MCS	53.18 [42.5, 60.7]	53.7 [43.6, 60.9]	52.72 [41.58, 60.43]	<.0001
Charlson Comorbidity Index	0.0 [0.0, 1.0]	0.0 [0.0, 1.0]	0.0 [0.0, 0.0]	<.0001
KOOS Pain Score	47.2 [37.5, 58.3]	47.2 [37.5, 58.3]	----------	---
KOOS Function Score	52.9 [42.7, 66.2]	52.9 [42.7, 66.2]	----------	---
HOOS Pain Score	45.0 [35.0, 57.5]	----------	45.0 [35.0, 57.5]	---
HOOS Function Score	48.5 [37.5, 61.8]	----------	48.5 [38.2, 61.8]	---
ASA Status				

Conclusion: Satisfaction with THR/TKR can be measured with 4 primary item questions. Moderate correlations with pain and function confirm that satisfaction is a separate construct. This satisfaction measure can be included in a TJR core measurement set for TJR trials.

Disclosure: S. Goodman, BMC Rheumatology, 5, 6, Calgene, 5, Celgene, 5, Current Rheumatology reports, 5, Current Rheumatology Reports, 6, Horizon, 2, 5, horizon, 2, Novartis, 2, 5, NYU College of Medicine, 3, NYU Langone College of Medicine, 3, Pfizer, 2, 5, Regenosine, 4, 9, Roche, 2, UCB, 5; **B. Mehta**, None; **C. Kahlenberg**, None; **J. Finik**, None; **M. Figgie**, Insight, 4, Lima, 7, Mekanika, 4, Wishbone, 4, 5, 7; **M. Parks**, Zimmer Biomet, 5, Orthopaedic Research and Education Foundation, 6, Orthopedic Learning Center (OLC), 6; **D. Padgett**, DJ Orthopaedics, 5, 7, 8, Journal of Arthroplasty, 6, The Hip Society, 6; **V. Antao**, None; **A. Yates**, None; **B. Springer**, AJRR, 4, 6, ICJR, 4, 6, Stryker, 5, 7, Convatec, 5, Osteoremedies, 5, JPS, 5; **S. Lyman**, JBJS, 9, JOSKAS, 5, OMNI, Inc, 5, Universal

Research Solutions, 5; **J. Singh**, Amarin pharmaceuticals, 1, 4, Clearview healthcae partners, 5, Clearview healthcare partners, 5, Clinical Care options, 5, Horizon, 5, Medisys, 5, OMERACT, 6, Putnam associates, 5, Spherix, 5, the American College of Rheumatology, 5, The American College of Rheumatology, 5, The National Institues of Health, 5, the National Institutes of Health, 5, Viking therapeutics, 1, 4, WebMD, 5.

Abstract Number: 0416

Global Management of Patients with Knee Osteoarthritis Begins with Quality of Life Assessment: A Systematic Review

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Knee OA (KOA) associates with remarkable functional restrictions due to pain that seriously affect social and emotional well-being, reducing the quality of life (QoL). The identification of therapies and factors that influence QoL in KOA patients may mitigate the clinical, economic, and social burden of this disease. Thus, the assessment of QoL in KOA, and individual factors associated has a great interest in research and clinical practice. Still, a general recompilation of these data is missing. Our aim was to recapitulate the existing information on QoL in KOA patients as an international tool to raise awareness on their condition and guide future actions for patient's management.

Methods: We conducted a systematic review examining the breadth of the literature regarding the QoL in patients with KOA (up to 2017). We identify articles in MEDLINE, EMBASE, Cochrane, and PsycINFO using relevant. All articles were reviewed for inclusion by 3 independent reviewers. QoL domains and items relevant to patients with knee OA were extracted. Inclusion criteria were QoL compared to one or more demographic factors (age, gender), lifestyle factor (functional independence), or comorbidity factor diabetes, obesity) or a control group. The quality of included studies was assessed using a quality appraisal tool.

Results: We retrieved 610 articles, 62 fulfilled the inclusion criteria. The instrument used to assess QoL were SF-36 and EQ-5D. The participants' mean in the studies was 561, the majority were female, the mean age was 63 years. KOA patients report a worse QoL compared to a control group, having women a worse QoL than men. Obesity, little or too much physical activity correlate with worse QoL. Higher educational level and mindfulness can improve QoL while poverty, physiological distress, depression and having dysfunctional families can reduce it. The delivery of a knee self-management program by health professionals can improve QoL. Surgical interventions result in good outcomes but the results were influenced by individual factors.

Conclusion: This is the first review pertaining to QoL in KOA patients. KOA has a strong impact on QoL. Individual factors (sex, weight, exercise, mental health, education) can influence QoL. These factors affect treatment outcomes and should be considered for a better patient's management. These data are a valuable tool for health professionals,

to better understand the disease and to implement a more adequate standard of care. This study was coordinated by representatives of patient organizations aiming to shed light on OA patient's condition and the need for a broader evaluation of the individual and human factors affecting their QoL.

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Abstract Number: 0417

Contribution of Pain Relief to Function, Fatigue, and Quality of Life When Inflammation Is Controlled in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Baricitinib, an oral selective Janus kinase 1 and 2 inhibitor, has shown clinical efficacy and patient-reported pain relief in patients (pts) with RA and an inadequate response to conventional, synthetic DMARDs (RA-BEAM[1]) or biologic DMARDs (RA-BEACON[2]); and in DMARD-naïve pts (RA-BEGIN[3]). The objective of this post-hoc analysis is to quantify the contribution of pain relief to other patient-reported outcomes (PROs) using pooled data from pts who achieved control of inflammation in three phase 3 trials, regardless of treatment.

Methods: Well-controlled inflammation in RA was defined[4] as swollen joint count (SJC) of 28 joints examined ≤1 and CRP ≤1 mg/dL at week 24. Among pts with well-controlled inflammation, PROs were compared between pts who also achieved thresholds of pain relief (defined as ≤20 mm or ≤40mm on a 0-100 mm visual analogue scale) at week 24 versus those who did not. PROs included: HAQ-Disability Index (HAQ-DI) normative value (< 0.5 for RA-BEAM and RA-BEACON, < 0.25 for RA-BEGIN) and minimum clinically important difference (MCID, ≥0.22), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) normative value (≥40.1) and MCID (≥3.56), and the 36-item Short Form Health Survey (SF-36) physical and mental component scores (PCS and MCS) MCID (≥5). Logistic regression models were adjusted for age, gender, body mass index, geographic region, duration of disease, and baseline SJC, CRP, pain, and value of the outcome. Missing data were imputed using modified last observation carried forward.

Results: Of the pts included in these phase 3 trials, 263 pts from RA-BEGIN, 371 pts from RA-BEAM, and 81 pts from RA-BEACON achieved inflammation control at week 24 (Table 1). Among pts who achieved inflammation control in RA-BEGIN and RA-BEAM, those who also achieved pain threshold ≤20 mm were more likely ($p< 0.05$) to report benefit in physical function (HAQ-DI), fatigue (FACIT-F), and general quality of life (SF-36) than pts who did not reach the pain relief threshold (Table 2). Generally, pts in RA-BEACON (inadequate responders to biologic DMARDs) were

Table 1. Inflammation control at Week 24

	RA-BEGIN			RA-BEAM			RA-BEACON		
	BARI 4-mg	BARI 4-mg + MTX	MTX	BARI 4-mg	ADA	PBO	BARI 2-mg	BARI 4-mg	PBO
Total patients, N	159	215	210	487	330	488	174	177	176
Patients achieving inflammation control[₸], n (%)	90 (56.6)	110 (51.2)	63 (30.0)	187 (38.4)	121 (36.7)	63 (12.9)	28 (16.1)	38 (21.5)	15 (8.5)

₸ Swollen joint count ≤1 and C-reactive protein ≤1 mg/dL at Week 24
ADA: Adalimumab; BARI: baricitinib; MTX: methotrexate; PBO: placebo

Table 2. Percentage of patients achieving improvement in PROs by pain relief (20 mm threshold) at Week 24

Outcome	RA-BEGIN			RA-BEAM			RA-BEACON		
	≤20 mm (N=162)	>20 mm (N=101)	p-value	≤20 mm (N=212)	>20 mm (N=159)	p-value	≤20 mm (N=47)	>20 mm (N=34)	p-value
HAQ-DI<0.5*†	60.5	15.8	<0.0001	66.5	19.0	<0.0001	55.3	5.9	0.0008
HAQ-DI MCID ≥0.22	96.3	85.1	<0.0001	89.2	72.2	<0.0001	87.2	76.5	0.2061††
FACIT-F≥40.1*	72.8	38.6	<0.0001	76.3	36.1	<0.0001	67.4	29.4	0.0141
FACIT-MCID, ≥3.56	87.0	77.2	<0.0001	76.3	63.9	<0.0001	91.3	70.6	0.0085
SF-36 PCS MCID, ≥5	90.1	72.3	<0.0001	80.6	57.0	<0.0001	87.0	44.1	0.0003
SF-36 MCS MCID, ≥5	45.7	48.5	0.0095	47.9	43.7	0.0154	34.8	41.2	0.2909

* Normative score to facilitate comparison with general population
† For RA-BEGIN, HAQ-DI normative value was <0.25
†† P-value from Chi-square test due to the small sample size
FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI: Health Assessment Questionnaire-Disability Index; MCID: minimum clinically important difference; MCS: mental component score; PCS: physical component score; SF-36: 36-item Short Form Health Survey.

less likely to achieve all PRO thresholds than pts in other trials. In RA-BEACON, achieving pain ≤20 mm resulted in statistically greater percentages of pts achieving FACIT-F MCID, as well as HAQ-DI and FACIT-F normative values and numerically, but not statistically higher, percentages of pts for HAQ-DI MCID. The statistical insignificance may be due to the small number of RA-BEACON pts included in the analysis. Similar patterns were observed with the pain relief thresholds of ≤40 mm compared to >40 mm.

Conclusion: Despite apparently well-controlled inflammation (SJC ≤1 and CRP ≤1 mg/dL), residual pain may persist. Higher levels of pain >20mm are associated with worse physical function, fatigue, and quality of life. This may have implications for management decisions beyond treating to disease activity targets alone.

References: [1]*N Engl J Med*. 2017, 376:652; [2]*N Engl J Med*. 2016, 374:1243; [3]*Arthritis Rheumatol*. 2017, 69:506; [4]*Arthritis Rheum*. 2011, 63:573

Disclosure: M. van de Laar, Abbvie, 2, 5, Eli Lilly and Company, 2, 5, 8, Merck, 2, 5, Pfizer, 2, 5, 8, Sanofi Genzym, 5, Grünenthal B.V., 2, Swedish Oprhan Biovitrum AB, 2; **J. Pope**, AbbVie, 5, Abbvie, 5, Actelion, 5, Actellion, 5, Amgen, 2, 5, AstraZeneca, 2, Astra-Zeneca, 2, Bayer, 2, 5, BMS, 2, 5, Eicos Sciences, 5, Eli Lilly & Company, 5, Eli Lilly and Company, 5, EMERALD, 5, Emerald, 5, Genzyme, 5, Janssen, 5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8; **Y. Lee**, Cigna Corp, 1, Eli Lilly, 2, 5, Eli Lilly and Company, 2, Express Scripts, 4, Pfizer, 2; **B. Fautrel**, AbbVie, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Boehringer Ingelheim, 8, Celgene, 5, 8, Eli Lilly and Company, 2, 5, Janssen, 5, 8, Lilly, 8, Medac, 5, 8, MSD, 2, 5, 8, NORDIC Pharma, 5, 8, Novartis, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, Sanofi-Aventis, 5, SOBI, 5, 8, UCB, 5, 8; **K. Ikeda**, Abbvie Japan, 8, AbbVie Japan, 8, Bristol-Myers Squibb Japan, 8, Mitsubishi Tanabe Pharma, 2, Novartis Japan, 8; **A. Quebe**, Eli Lilly & Company, 3, 4, Eli Lilly and Company, 1, 3; **X. Zhang**, Eli Lilly and Company, 1, 3; **C. Gaich**, Eli Lilly & Company, 3, 4, Eli Lilly and

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Abstract Number: 0418

Work Productivity Is Associated with Disease Activity and Functional Ability in Chinese Patients with Axial Spondyloarthritis Using a Smart-Phone Management System: A Prospective Cohort Study

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SESSION INFORMATION
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Background/Purpose: Axial spondyloarthritis (axSpA) usually affects young people and may lead to work disability(WD). We used the "Smart-phone SpondyloArthritis Management System", an interactive mobile health tool to evaluate clinical characteristics and the status of work ability disorders, to determine the prevalence of axSpA unemployment due to illness and the loss of work efficiency, and to analyze the association between the clinical characteristics and WD in patients with axSpA.

Methods: 1187 patients with axSpA were included. WD was assessed with the Work Productivity and Impairment questionnaire (WPAI) reporting WD as the absenteeism, presenteeism, overall work impairment and activity impairment. Demographic properties, pharmacotherapy, co morbidities, disease activity (BASDAI and ASDAS), functionality (BASFI),spinal mobility (BASMI), C-reactive protein, erythrocyte sedimentation rate (ESR),nocturnal pain, total back pain, patient's global assessment of disease activity and Assessment of Spondyloarthritis International Society health index (ASAS-HI) were investigated and compared in employed and un-employed patients. Logistic regressions were used to investigate the associations between work status and clinical characteristics. The relationships between WPAI scores and disease activity were assessed using Spearman correlation coefficients.

Results: Among them, 60(5.05%) participants were unemployed. 793 patients(66.81%)were employed. Absenteeism, presenteeism, overall work impairment and activity impairment in all employed patients were 7%, 24%, 29%

and 27%, respectively. The predictive factors for not being employed were suffering from inflammatory bowel disease and higher ASAS HI scores (OR value was 0.431, 0.696, respectively). Factors significantly associated with a higher absenteeism, overall work impairment and activity impairment loss were BASDAI,BASFI,ASAS HI,ASDAS, nocturnal pain, total back pain and patient's global assessment of disease activity (r >0.5), while NSAIDs treatment were significantly associated with a lower Absenteeism loss. A decrease in work productivity was related to an increase ASDAS score.

Conclusion: We determined that axSpA had a significant influence on the working conditions and the factors related to the disease had a significant correlation with work productivity using a Smart-Phone Management System.

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Abstract Number: 0419

Real-World Evidence on the Early Effects of Golimumab on Work Productivity and Activity Impairment in Patients with Spondyloarthritis: Interim Results from a Prospective, Observational Study

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SESSION INFORMATION
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Background/Purpose: There are limited real life data regarding the effect of golimumab on work productivity and activity impairment in rheumatic diseases. The aim of our study was to evaluate these work-related patient reported outcomes (PROs) in spondyloarthritis (SpA) patients treated with golimumab in daily clinical practice.

Methods: This is a 12-month multicenter, non-interventional, prospective study of working adults with active axial SpA (axSpA) or psoriatic arthritis (PsA) treated with golimumab. Prospectively collected data regarding work productivity and activity impairment (using the specific health problem WPAI:SHP instrument) from the first 60 patients who completed the 3-month visit (or were prematurely withdrawn prior to 3 months) are reported here.

Results: Sixty patients, 34 (56.7%) with axSpA and 26 (43.3%) with PsA were enrolled over a 7.7-month recruitment period (from 06-Apr-2017 to 27-Nov-2017) by 10 public/private sector hospitals and 3 private offices in Greece. Fifty-nine patients attended the 3-month visit, while one patient was withdrawn 12.1 weeks after enrollment due to golimumab discontinuation for lack of therapeutic response. The overall SpA population included 47% males with a mean age of 44.8 years at enrollment. Overall, 23% of patients had previously received biologics, while 31.7% were receiving concomitant conventional disease-modifying antirheumatic drugs (csDMARDs) during the study period. At baseline, the mean DAS28-ESR of the overall SpA population was 4±1.2, while the mean BASDAI score among axSpA patients was 5.8±1.8 In the overall SpA population, 72.9% (43/59), 91.4% (53/58), 94.9% (56/59), and 96.7%

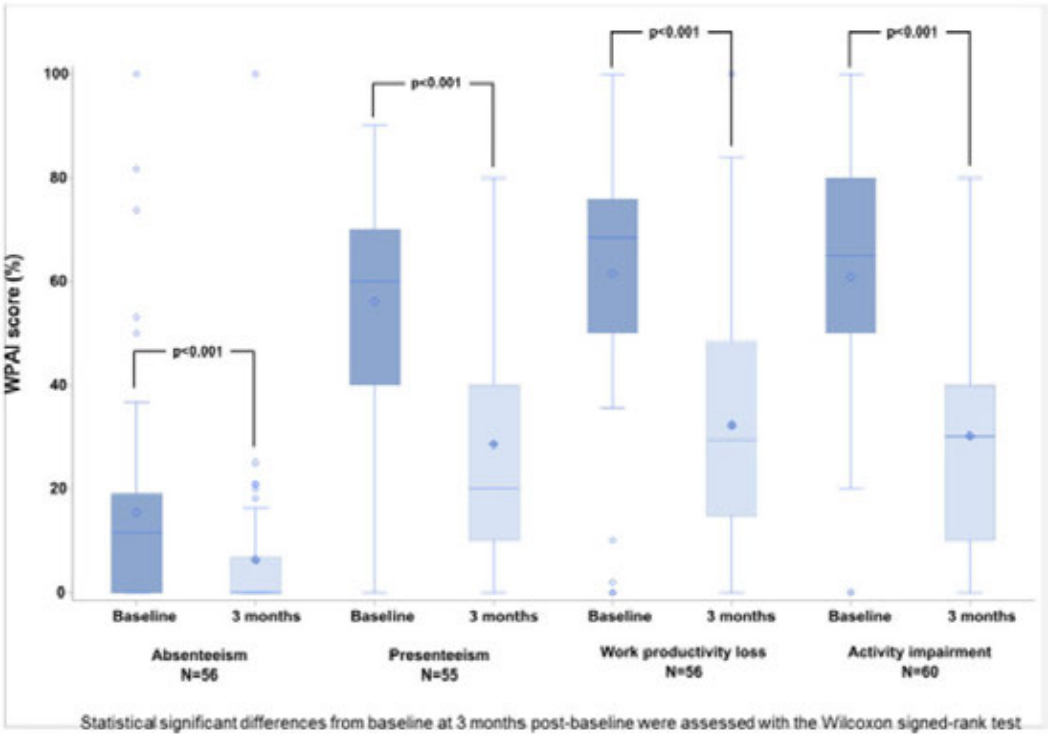

Figure 1. WPAI outcomes at baseline and at 3 months post-baseline in the SpA population

(58/60) of patients, reported absenteeism, presenteeism, work productivity loss, and activity impairment due to SpA, respectively, at baseline. At 3 months the respective rates were 46.4% (26/56), 89.3% (50/56), 91.1% (51/56), and 88.3% (53/60). In the overall SpA population, the median scores for absenteeism, presenteeism, work productivity loss, and activity impairment significantly decreased ($p < 0.001$ for all) by 5.7%, 40.0%, 38.1%, and 40.0%, respectively (Figure 1).

Conclusion: Actively working patients with SpA treated with golimumab in real life settings demonstrated significant improvements in all domains of the work-related PROs as early as 3 months after treatment initiation. These preliminary data, if confirmed at 6 and 12 months, provide valuable work-related information on the effect of a golimumab treatment of SpA patients in real life practice.

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Abstract Number: 0420

Assessment of Fatigue in Adults with Moderate to Severe Systemic Lupus Erythematosus (SLE): A Qualitative Study to Explore What Patients Feel Should Be Measured in Clinical Trials

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Background/Purpose: Fatigue is one of the most common symptoms reported by patients with systemic lupus erythematosus(SLE) and is responsible for considerable loss of time at work and greatly impaired quality of life. There is a lack of patient reported outcome (PRO) instruments developed with input from patients with SLE. To collect evidence of content validity required by regulatory agencies for a PRO tool to support label claims, this qualitative study aimed to understand SLE patients' experience of fatigue and to assess the FACIT-F (Functional Assessment of Chronic Illness Therapy-Fatigue) questionnaire used extensively in health research to evaluate fatigue. Evaluation of the FACIT-F content was informed by a literature review and guided by a project steering committee (PSC; consisting of a patient advocate, a clinical expert, and an outcomes measure expert).

Methods: The study, approved by an institutional review board, involved focus groups (Round 1) and cognitive interviews (Round 2) with adults with moderate to severely active SLE. All participants provided written informed consent. In Round 1, three focus groups were conducted to understand the disease and fatigue-related concepts that were most important to patients; participants also provided high-level feedback on the FACIT-F. Round 2 included 13 one-on-one cognitive interviews to collect more nuanced feedback on the relevance of content, clarity, and comprehensiveness of the FACIT-F. The qualitative interviews were audio-recorded and transcribed; content analysis methods were used to analyze the transcripts to achieve the study objectives. The PSC reviewed the results and contributed to decision making. Specific attention was given to determine the comprehensiveness and participant understanding of the FACIT-F and any gaps in concept coverage to evaluate fatigue in the context of a clinical trial.

Results: A total of 28 adult patients with moderate to severe SLE, mostly female (n=27) with a mean age of 45.5 ± 12.1 years (range: 18–75 years) participated in the study; 23 (82%) had moderate disease activity and five (18%) severe SLE. All participants were receiving treatment to manage their SLE at the time of the study and most (n=23, 82%) reported fatigue among the top three most important SLE-related symptoms. Fatigue was described as profoundly impacting their daily life, including the ability to perform chores, work-related activities, maintain personal hygiene, exercise, and participate in hobbies. Study participants reported that the FACIT-F covered concepts most relevant to their experience of fatigue. Participants were able to understand the instructions, items, and response options of the instrument and felt that the recall period of 7 days was appropriate.

Conclusion: Fatigue was one of the most important symptoms that had a significant impact on adults with moderate to severely active SLE, limiting their ability to perform activities they needed or wanted to do. The FACIT-F was found to be an appropriate measure for the assessment of fatigue in this sample. Evidence of content validity of the FACIT-F in adults with SLE was confirmed for its use to support endpoints in Idorsia's Cenerimod Assessing $S1P_1$ Receptor Modulation in SLE (CARE) clinical trial.

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Abstract Number: 0421

An Examination of Patient-Reported Outcomes Data from a Randomized Trial Examining Etanercept and Methotrexate as Monotherapy or in Combination in Patients with Psoriatic Arthritis

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Background/Purpose: Health-related quality of life is impacted in patients (pts) with psoriatic arthritis (PsA). Patient-reported outcomes (PROs) are an important means of measuring treatment improvements in PsA pts receiving systemic therapies such as methotrexate (MTX) and tumor necrosis factor inhibitors. PROs reported in the SEAM PsA randomized, controlled trial (RCT)* included SF-36 physical and mental component (PCS, MCS) scores and Health Assessment Questionnaire -Disability Index (HAQ-DI). Results showed significant differences in the SF-36 PCS mean change from baseline (BL) at week 24 in the etanercept (ETN)-containing arms compared to MTX-monotherapy (mono); similar improvements were seen across treatment groups in MCS and HAQ-DI.* Here we report results from analyses of all PROs measured in this RCT.

Methods: Pts with active PsA (N = 851) were randomized to receive 48 weeks of: MTX 20 mg weekly (N = 284), ETN 50 mg weekly (N = 284), or ETN 50 mg plus MTX 20 mg weekly (Combo; N = 283). PROs included: Patient global assessment of disease activity (PtGA); Patient global assessment of joint pain (PtGAJP); HAQ-DI; and SF-36 PCS, MCS, and 8 domains. Analyses included: least squares mean (LSM) changes from BL to week 24 comparing the ETN-containing arms to MTX mono; the proportion of pts reporting improvements ≥ minimal clinically important differences (MCID) at week 24, and the proportion of pts reporting scores ≥ age and gender matched normative values (A/G norms) at 24 weeks in HAQ-DI and SF-36 PCS, MCS, and 8 domains. Tests were not adjusted for multiplicity; P-values are nominal.

Results: PRO BL values were generally balanced across treatment arms. The largest LSM changes from baseline at week 24 were evident in PtGA, PtGAJP, and SF-36 PCS, with significant differences in both ETN-arms compared to MTX mono (Table 1). Compared to MTX mono, significantly larger differences were reported with ETN mono in the SF-36 Bodily Pain (BP) and General Health (GH) domains and with Combo in the SF-36 BP and Vitality (VT) domains (Figure 1).

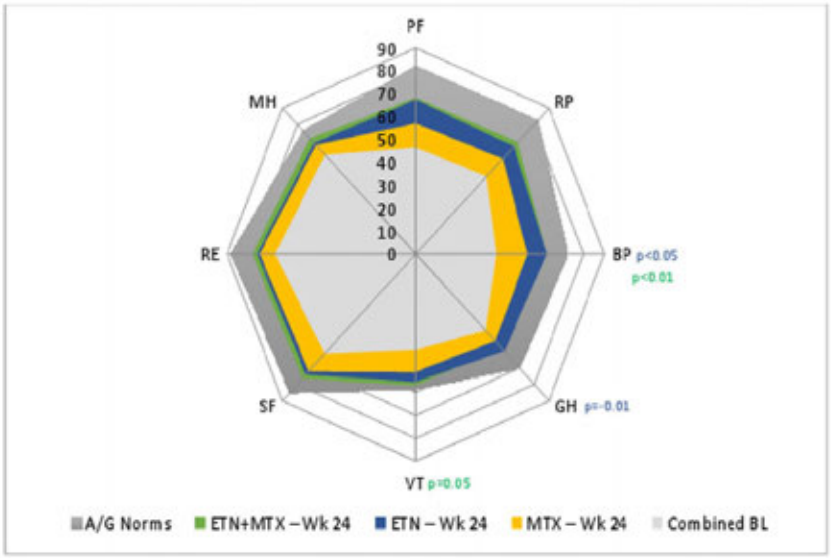
Compared to MTX mono at week 24, significantly more pts reported improvements ≥ MCID with ETN mono in PtGA and with Combo in PtGAJP (Figure 2A).

Significantly higher proportions of pts in both the ETN mono and Combo arms reported scores ≥ A/G norms at week 24 compared to MTX mono in HAQ-DI; SF-36 PCS; and SF-36 physical function (PF), role physical (RP), BP, and GH domains. In addition to these, significantly higher proportion of patients receiving Combo reported scores ≥ A/G norms in SF-36 VT and mental health (MH) domains compared to MTX mono (Figure 2B). Continued improvements across PROs were reported through week 48.

Table 1. Patient-reported outcomes: least square mean changes from baseline at week 24

Patient Reported Outcome	Methotrexate Monotherapy N = 284	Etanercept Monotherapy N = 284	Methotrexate + Etanercept N = 283
HAQ DI	-0.39	-0.41	-0.44
PtGA	-22.70	-31.64; **P<0.001**[a]	-29.04; **P=0.012**[a]
PtGAJP	-18.95	-24.12; **P=0.032**[a]	-24.90; **P=0.014**[a]
SF-36 PCS	5.68	7.38; **P=0.033**[a]	7.62; **P=0.015**[a]
SF-36 MCS	3.48	2.99	3.46
SF-36 Domain Scores			
Physical Functioning	14.47	17.42	17.54
Role Physical	13.81	16.28	17.66
Bodily Pain	16.03	20.47; **P=0.034**[a]	21.66; **P=0.007**[a]
General Health	7.77	11.93; **P=0.01**[a]	10.9
Vitality	10.46	10.99	13.94; **P=0.05**[a]
Social Functioning	14.58	11.37	13.22
Role Emotional	8.58	9.76	8.08
Mental Health	6.92	7.5	8.91

HAQ-DI, Health Assessment Questionnaire- Disability Index; LSM, least squares mean; MCS, mental component summary; PCS, physical component summary; PtGA, patient global assessment; PtGAJP, patient global assessment of joint pain; SF-36, Short Form (36) health survey version 2.
[a]P-values are for comparison with methotrexate monotherapy. Only P-values ≤ 0.05 are shown.



Missing values were not imputed; spydergrams were generated using domain raw scores (range: 0.100); US age-gender norms were matched to the protocol population. Spydergrams are for illustrative purposes only.
A, age; BL, baseline; BP, bodily pain; ETN, etanercept; G, gender; GH, general health; MH, mental health; MTX, methotrexate; PF, physical functioning; RE, role emotional; RP, role physical; SF, social functioning; VT, vitality; Wk, week.

Figure 1. Spydergram of domain scores from baseline to week 24 versus age- and gender-matched normative scores

Figure 2A. Percentages of patients reporting improvements ≥ MCID at week 24.

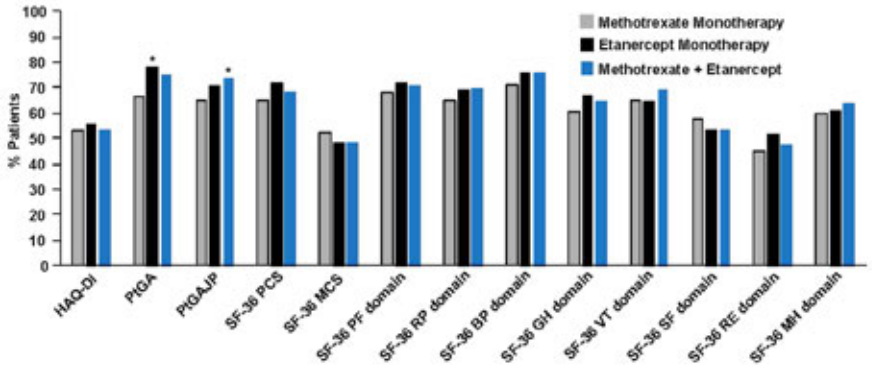
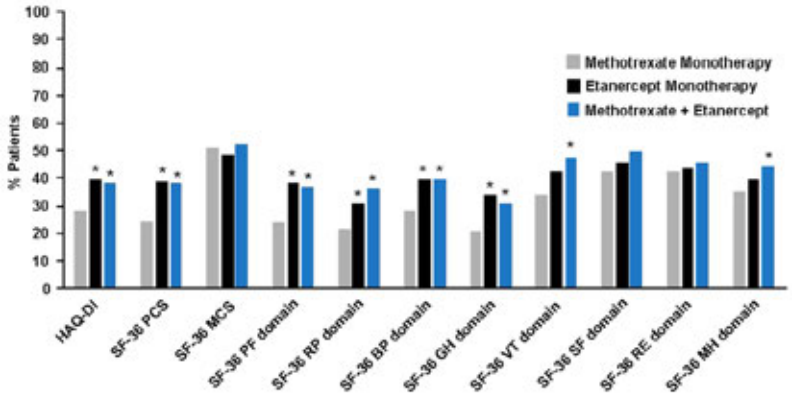


Figure 2B. Percentages of patients reporting HAQ-DI and SF-36 PCS, MCS, and domain scores ≥ A/G normative values at week 24.



A, age; BP, bodily pain; G, gender, GH, general health; HAQ-DI, Health Assessment Questionnaire- Disability Index; MCID, minimal clinically important difference; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical function; PtGA, patient global assessment; PtGAJP, patient global assessment of joint pain; RE, role emotional; RP, role physical; SF, social function; SF-36, Short Form (36) health survey; VT, vitality.
*P-values compared with methotrexate monotherapy that were ≤ 0.05.
MCID values were change from baseline ≤ -0.35 for HAQ-DI, ≤ -10.0 for PtGA, ≤ -10.0 for PtGAJP, ≥ 2.5 for SF-36 PCS, ≥ 2.5 for SF-36 MCS, and ≥ 5.0 for each SF-36 domain. Normative values were ≤ 0.25 for HAQ-DI; ≥ 50 for SF-36 PCS, and ≥ 50 for SF-36 MCS. Age/gender normalized values for the SF-36 domains were 82.01 for PF, 82.55 for RP, 72.86 for BP, 70.31 for GH, 58.89 for VT, 85.11 for SF, 88.12 for RE, and 75.94 for MH.

Figure 2. Percentage of patients with scores ≥ MCID or ≥ A/G normative values at week 24

Conclusion: In this RCT, significant and clinically meaningful improvements in PROs were reported with ETN mono and Combo compared to MTX mono. In general, pts in ETN-containing arms had greater improvements from BL in several PROs at week 24 compared to MTX mono, with higher percentages reporting improvements ≥ MCID and/or scores ≥ A/G norms.

*Mease et al. Arthritis Rheumatol. 2019 Feb 12. https://doi.org/10.1002/art.40851 [Epub ahead of print].

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Janssen, Pfizer, UCB, 8, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Abbvie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer and UCB., 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB, 2, Abbvie, Amgen, Brsitol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Brsitol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Brsitol Myers Squibb,Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, Amgen, 2, 5, 6, 8, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, and UCB, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 2, 5, Boerhinger Ingelheim, 5, Bristol Myers Squibb, 2, 5, 8, Bristol Myers Squibb Co., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8, Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8; **E. Maksabedian**, Amgen, 1, 3, 4; **B. Stolshek**, Amgen, 1, 3, 4, Amgen, Inc, 3, 4; **L. Liu**, Amgen Inc., 1, 3, 4; **D. Collier**, Amgen Inc., 1, 3, 4, Amgen, Inc, 1, 3; **G. Kricorian**, Amgen Inc., 1, 3, 4; **J. Merola**, AbbVie, 2, 5, 8, Aclaris, 2, 5, Almirall, 2, 5, Amgen, 5, Biogen, 2, 5, Biogen Idec, 2, 5, Biogen IDEC, 5, Brigham and Women's Hospital, Harvard, 3, Burrage Capital Management Boston Advisory Board, 6, Celgene, 2, 5, Dermavant, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 5, GlaxoSmithKline, 5, GSK, 2, 5, Incyte, 2, 5, Janssen, 2, 5, Leo Pharma, 2, 5, Lilly, 5, Merck, 5, Merck Research Laboratories, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Regeneron, 5, Samumed, 2, 5, Sanofi, 5, Sanofi Regeneron, 2, 5, Science 37, 5, Sun Pharma, 2, 5, UCB, 2, 5.

Abstract Number: 0422

The Impact of Adalimumab vs Placebo on Patient-Reported Outcomes and Utility Measures Among Patients with Moderately to Severely Active Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Physical function and health-related quality of life (HRQoL) are negatively impacted in patients (pts) with PsA, and treatment with conventional and biological (b) DMARDs improved patient-reported outcomes (PROs), including HRQoL measures. The objective of this analysis was to assess the impact of adalimumab (ADA) vs placebo (PBO) on PROs following 12-week (wk) treatment in the randomized-controlled ADEPT trial.

Methods: Pts (n=315) with moderately to severely active PsA who were bDMARD naive (50% were receiving MTX) were randomized to ADA 40 mg or PBO every other wk. This analysis assessed PROs at baseline (BL) and wk 12 using the 36-item Short-Form (SF-36) Health Survey physical (PCS) and mental component summary (MCS) scores,

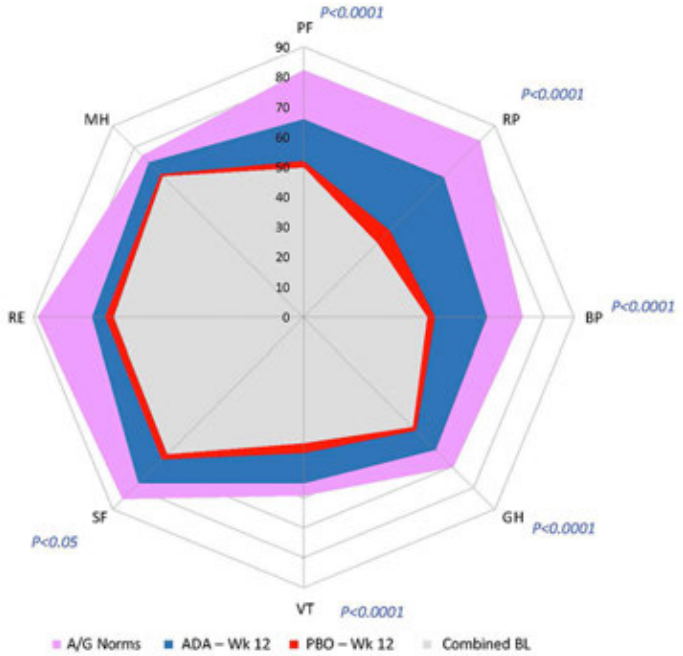
Table 1. Mean Disease Characteristics and SF-36 Domain Scores by Treatment Group at Baseline and Week 12 Compared With Age- and Gender-Matched Normative Values

	ADA 40 mg eow		PBO		A/G norms
	Baseline	Week 12 (change from baseline to week 12)	Baseline	Week 12 (change from baseline to week 12)	
SF-36 PCS	33.2	42.5 (9.3**)	33.3	34.7 (1.4)	≥50
SF-36 MCS	48.1	49.8 (1.6)	46.6	48.4 (1.2)	≥50
SF-6D	0.653	0.724 (0.071)	0.641	0.659 (0.018)	—
PtGA	47.1	25.9 (−21.7**)	48.1	47.5 (0.2)	—
Pt pain	51.1	26.8 (−24.1**)	48.8	49.1 (1.3)	—
HAQ-DI	1.0	0.6 (−0.4**)	1.0	0.9 (−0.1)	≤0.25
	Baseline (vs A/G norms)	Week 12 (vs A/G norms)	Baseline (vs A/G norms)	Week 12 (vs A/G norms)	
Physical Functioning	50.8 (−31.5)	65.9*** (−16.4)	48.2 (−34.1)	52.0 (−30.3)	82.3
Role Physical	37.1 (−45.9)	65.9*** (−17.1)	32.6 (−50.4)	40.6 (−42.4)	83.0
Bodily Pain	41.3 (−31.6)	61.0*** (−11.9)	40.2 (−32.7)	43.7 (−29.2)	72.9
General Health	49.5 (−20.8)	62.1*** (−8.2)	52.1 (−18.2)	53.0 (−17.3)	70.3
Vitality	41.4 (−17.8)	55.1*** (−4.1)	41.6 (−17.6)	45.0 (−14.2)	59.2
Social Functioning	66.3 (−19.0)	77.8† (−7.5)	61.7 (−23.6)	66.7 (−18.6)	85.3
Role Emotional	65.1 (−23.4)	70.4 (−18.1)	59.1 (−29.4)	66.0 (−22.5)	88.5
Mental Health	67.6 (−8.5)	72.9 (−3.2)	64.9 (−11.2)	67.3 (−8.8)	76.1

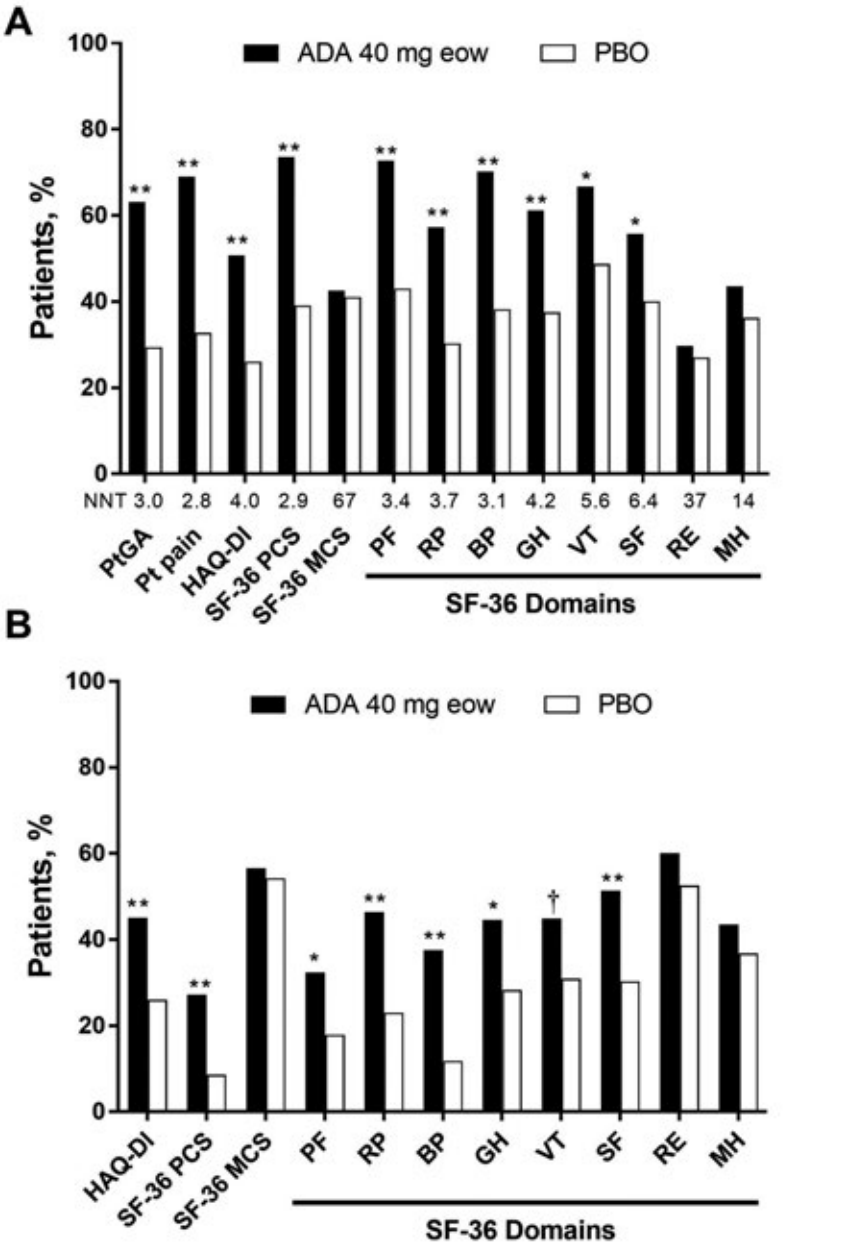
ADA, adalimumab; A/G norm, age- and gender-matched normative value; eow, every other week; DI, disability index; MCS, mental component summary; MID, minimally important difference; PBO, placebo; PCS, physical component summary; PtGA, Patient Global Assessment of disease activity; SF-36, 36-item Short-Form Health Survey; SF-6D, Short-Form 6D.
SF-6D MID=0.041.
Statistical analysis ADA vs PBO: †$P<0.05$; *$P<0.01$; **$P<0.001$; ***$P<0.0001$.

8 domain scores ranging from 0 (worst) to 100 (best), and the SF-6D utility measure derived from all 8 SF-36 domains with scores ranging from 0.296 (worst) to 1.00 (full health) and a minimally important difference (MID) of 0.041. Patient Global Assessment of disease activity (PtGA) and pain (both utilizing 100 mm visual analog scale [VAS]) and HAQ disability index (DI) also were assessed. Mean changes from BL, percentages of pts with improvements ≥minimum clinically important differences (MCID), and scores ≥US age- and gender-matched normative values (A/G norms) were

Figure 1. Spydergram of Mean Changes in SF-36 Domain Scores at Week 12: ADA vs PBO vs Age- and Gender-Matched Normative Scores



ADA, adalimumab; A/G norm, age- and gender-matched normative value; BL, baseline; BP, bodily pain; GH, general health; MH, mental health; PBO, placebo; PF, physical functioning; RE, role emotional; RP, role physical; SF, social functioning; SF-36, 36-item Short-Form Health Survey VT, vitality.



ADA, adalimumab; eow, every other week; BP, bodily pain; DI, disability index; GH, general health; MCID, minimal clinically important difference; MCS, mental component summary; MH, mental health; NNT, number needed to treat; PBO, placebo; PCS, physical component summary; PF, physical functioning; RE, role emotional; RP, role physical; PtGA, Patient Global Assessment of disease activity; SF, social functioning; SF-36, 36-item Short-Form Health Survey VT, vitality.
MCIDs: SF-36 PCS=2.5; HAQ-DI= –0.35; PtGA=10; Pt pain=10.
A/G normative values: SF-36 ≥50; HAQ-DI ≤0.25.
Statistical analysis ADA vs PBO: †P<0.05; *P<0.01; **P<0.001

Figure 2. Proportion of Patients Reporting Improvements ≥MCID and (B) Scores ≥Age- And Gender-Matched Normative Values at Week 12

analyzed, based on as observed data. *P* values were assessed by analysis of variance model for continuous variables and Cochran–Mantel–Haenszel test for binary outcomes, adjusting by baseline MTX use and extent of psoriasis; no *P* value adjustments for multiplicity were performed. Numbers needed to treat (NNTs) are reported using proportions of pts reporting improvements ≥MCID in SF-36, PtGA, pain, and HAQ-DI.

Results: In general, BL PRO scores were similar between ADA (n=151) and PBO (n=162; **Table 1**). Improvements from BL at wk 12 with ADA vs PBO were significant in PtGA, pain, HAQ-DI, and SF-36 PCS (change: 9.3 vs 1.4; $P<$ 0.001) but not in SF-36 MCS (1.6 vs 1.2; **Table 1**). Six of 8 SF-36 domains (physical functioning, role physical, bodily pain, general health, social functioning, and vitality) significantly improved from BL to wk 12 with ADA vs PBO (all $P\leq0.05$; **Table 1** and **Figure 1**). SF-6D improvements exceeded MID with ADA (change: 0.071) vs PBO (0.018); the ADA SF-6D score (0.724) also approached the A/G norm of 0.778 at wk 12 (**Table 1**). Proportions of pts reporting improvements ≥MCID at wk 12 were significantly greater with ADA vs PBO in all PROs, except SF-36 role emotional and mental health domains, with corresponding NNTs ≤6.4 (**Figure 2**). Proportions of pts who reported scores ≥A/G norms in HAQ-DI, SF-36 PCS, and 6 of 8 SF-36 domains were significantly greater with ADA vs PBO (**Figure 2)**.

Conclusion: Statistically significant and clinically meaningful improvements and scores ≥A/G norms (higher definition of response) at week 12 were reported with ADA treatment vs PBO in pts with moderately to severely active PsA. These data are consistent with improvements in PROs reported with other bDMARDs in patients with PsA.

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Abstract Number: 0423

Patient Reported Outcomes over 2 Years in Psoriatic Arthritis Patients Initiating Treatment with 1st, 2nd or 3rd TNF Inhibitor in Routine Care – Was PRO Remission Achieved? Results from the EuroSpA Collaboration

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patient Reported Outcomes (PROs) provide important information on assessment of pain, disease activity, fatigue and physical function in patients with psoriatic arthritis (PsA). Knowledge of the evolution in PROs over time in patients, who initiate treatment with their 1st, 2nd or 3rd Tumour Necrosis Factor inhibitor (TNFi) in routine practice is limited. Hence, the aim of this was study was to investigate PROs at 6, 12 and 24 months after TNFi start and the changes from baseline to 6, 12 and 24 months in PsA patients, who initiated their 1st, 2nd or 3rd TNFi in clinical practice.

Methods: Pooled data on PsA patients from 13 European registries participating in the EuroSpA Research Collaboration were analysed (1). Patients were included in the study cohort if they had been followed in the registry from initiation of the 1st TNFi. PROs included Visual Analogue Scale (VAS) scores on a 0-100 mm scale for pain, global disease activity and fatigue, while physical function was captured with Health Assessment Questionnaire (HAQ). The distribution of PROs at 6, 12 and 24 months after TNFi start and the changes from baseline to 6, 12 and 24 months were investigated with descriptive statistics. PRO remission rates were defined as the proportion of patients achieving a state of pain score ≤20 mm, global score 20 mm, fatigue score ≤20 mm and HAQ score ≤0.5. Crude and LUNDEX-adjusted (2) PRO remission rates were assessed for the overall cohort and the individual registries.

Results: Of the 25,988 axSpA patients, who initiated 1st TNFi, 8,294 patients switched to a 2nd TNFi, while 2,842 patients subsequently switched to a 3rd TNFi. Baseline characteristics of the study cohort are shown in Table 1. The 6, 12 and 24 month PRO status and changes in PROs for 1st, 2nd and 3rd TNFi in the pooled cohort are summarized in Table 2. For the 1st, 2nd and 3rd TNFi, median PROs after 6 months ranged from 20mm to 30mm, 27mm to 40mm and 35mm to 50mm, respectively. Similarly, median decreases in PROs from baseline to 6 months ranged from 18 to 30mm, 8 to 18mm and 8 to 18mm for the 1st, 2nd and 3rd TNFi. In the overall cohort 6 month LUNDEX-adjusted PRO

Table 1: Baseline characteristics of pooled PsA cohort at 1st, 2nd and 3rd TNFi start

	1st TNFI (n =16,230)		2nd TNFi (n =5,367)		3rd TNFi (n = 1,863)	
	Available data, n	Median (IQR) or percentage	Available data, n	Median (IQR) or percentage	Available data, n	Median (IQR) or percentage
Age, years	16,230	49 (40-57)	5,367	50 (41-58)	1,863	50 (41-59)
Male	16,230	49%	5,367	44%	1,863	38%
Time since diagnosis	9,162	4 (1-9)	2,914	5 (2-11)	1,015	7 (4-13)
TNFi drug	16,230		5,367		1,863	
Adalimumab		31		33		30
Certolizumab		4		4		5
Etanercept		35		38		27
Golimumab		10		13		20
Infliximab		20		12		18
DAS28, units	9,549	4.3 (3.4-5.1)	3,197	4.0 (3.1-4.9)	1,085	4.1 (3.2-5.0)
DAPSA28, units	9,809	26 (17-39)	2,997	25 (15-37)	1,037	25 (16-39)
28TJC	12,030	4 (2-9)	3,642	4 (1-9)	1,276	4 (1-10)
28SJC	12,042	2 (0-6)	3,638	2 (0-4)	1,273	2 (0-4)
CRP, mg/L	12,787	6 (2-15)	2,008	5 (2-13)	1,310	5 (2-14)
Pain score, mm	11,616	60 (40-75)	3,534	63 (40-78)	1,233	65 (41-80)
Global score, mm	11,616	60 (40-75)	3,662	63 (44-80)	1,263	67 (47-81)
Fatigue score, mm	5,228	64 (40-80)	2,395	67 (43-81)	812	70 (48-84)
HAQ score, mm	11,000	0.850 (0.5-1.375)	3,477	1.00 (0.625-1.50)	1,206	1.125 (0.625-1.625)

Data are as observed. TNFi; Tumour Necrosis Factor Inhibitor; DAS28: Disease Activity Score in 28 joints; DAPSA28: Disease Activity in Psoriatic Arthritis in 28 joints; 28SJC: 28 Swollen joint count; 28TJC: 28 Tender Joint Count; CRP; C-reactive protein; HAQ: Health Assessment Questionnaire.

Table 2: PROs after 6, 12 and 24 months of TNFi treatment in the pooled PsA cohort									
	1st TNFi			2nd TNFi			3rd TNFi		
	6 months	12 months	24 months	6 months	12 months	24 months	6 months	12 months	24 months
Pain, mm	25 (10-50)	23 (9-49)	21 (8-46)	37 (17-60)	35 (15-60)	30 (13-57)	40 (20-64)	40 (20-63)	40 (16-63)
Global, mm	27 (10-50)	25 (10-50)	22 (9-50)	40 (18-63)	36 (17-60)	32 (13-58)	42 (20-65)	43 (20-65)	44 (20-61)
Fatigue, mm	33 (11-61)	31 (10-60)	30 (10-57)	44 (19-70)	45 (20-70)	41 (17-67)	52 (25-73)	49 (22-73)	47 (19-70)
HAQ	0.5 (0.0-1.0)	0.5 (0.0-1.0)	0.375 (0.0-0.875)	0.75 (0.25-1.25)	0.75 (0.25-1.25)	0.625 (0.125-1.125)	0.875 (0.375-1.375)	0.875 (0.375-1.375)	0.875 (0.375-1.375)
Changes in PROs from baseline to 6, 12 and 24 months									
	0-6 months	0-12 months	0-24 months	0-6 months	0-12 months	0-24 months	0-6 months	0-12 months	0-24 months
Pain, mm	-25 (-47;-5)	-16 (-39;0)	-28 (-50;-7)	-15 (-38;0)	-27 (-49;-6)	-17 (-40:0)	-16 (-39;0)	-15 (-40;0)	-14 (-37;1)
Global, mm	-26 (-49;-6)	-30 (-50;-7)	-30 (-50;-8)	-16 (-40;0)	-16 (-30;0)	-18 (-39;0)	-17 (-38;0)	-16 (-41;0)	-15 (-37;0)
Fatigue score, mm	-18 (-40;0)	-19 (-41;0)	-20 (-41;-1)	-10 (-31;1)	-10 (-31;3)	-11 (-31;3)	-14 (-33;2)	-9 (-32;4)	-11 (-36;2)
HAQ	-0.250 (-0.625;0.0)	-0.325 (-0.750;0.0)	-0.375 (-0.750;0.0)	-0.125 (-0.5;0.0)	-0.125 (-0.5;0.0)	-0.175 (-0.625;0.0)	-0.125 (-0.50;0.0)	-0.125 (-0.5;0.0)	-0.125 (-0.50;0.125)
PRO remission rates (%) at 6, 12 and 24 months									
	1st TNFi			2nd TNFi			3rd TNFi		
	Crude* 6/12/24		LUNDEX adjusted**	Crude*		LUNDEX adjusted**	Crude*		LUNDEX adjusted**
Pain ≤ 20	44%/48%/49%		36%/33%/25%	31%/34%/38%		23%/20%/17%	26%/28%/31%		18%/15%/11%
Global ≤20	42%/46%/48%		35%//31%/24%	31%/32%/35%		23%/19%/15%	27%/26%/28%		18%/14%/10%
Fatigue ≤20	36%/39%/40%		29%/27%/20%	28%/27%/29%		20%/16%/12%	21%/24%/28%		15%/13%/10%
HAQ ≤0.5	54%/56%/58%		44%/38%/29%	41%/42%/46%		31%/25%/19%	33%/33%/36%		24%/18%/13%

Data are as observed. Percentage of available data varied from 40-86%. Values are median (Inter Quartile Range (IQR)) unless otherwise stated. PRO: Patient reported outcome; TNFi: Tumour Necrosis Factor inhibitor; HAQ: HIealth Assessment Questionnare.
*Crude value: the fraction of patients in PRO remission of those still on drug with available data at 6, 12 and 24 months.
** LUNDEX-adjusted: Crude value adjusted for drug retention.

remission rates varied from 33% to 41%, 23% to 33% and 17% to 24% for the 1st, 2nd and 3rd TNFi, respectively (Table 2). In the individual registries, LUNDEX-adjusted 6 months PRO remission rates for the 1st TNFi ranged from 32% to 51%, 24% to 50%, 28% to 48%, 32% to 51% and 21% to 47% for pain, global, BASDAI, BASFI and fatigue scores, respectively.

Conclusion: In this large observational study cohort, one-third of patients achieved a state of PRO remission after 6 months of treatment with their first TNFi with significant variation between registries. As expected, improvements in PROs and PRO remission rates were lower in those who had switched to the 2nd or 3rd TNFi, reflecting selection of non-responders and more severe cases (confounding by indication).

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Abstract Number: 0424

A Novel Patient-Reported Outcome Measure in IgG4-Related Disease: The Symptom Severity Index

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4-related disease (IgG4-RD) causes symptoms, the severity of which vary by organ involvement. The Responder Index (RI) captures physicians' judgement of disease activity, but no disease-specific patient-reported outcome measure (PROM) exists. We sought to develop and validate the Symptom Severity Index (SSI), a PROM that measures the frequency of IgG4-RD-specific symptoms and associated distress.

Methods: 40 common IgG4-RD symptoms were identified by three expert clinicians to create a pilot SSI. This was tested in a convenience sample to test usability in a clinic setting and to obtain feedback on the symptom list. Several gaps were identified. Semi-structured qualitative transcribed interviews were then performed with new patients to expand the item set and explore issues that were absent. Newly identified patients described symptoms they attributed to IgG4-RD, associated distress, and other concerns. We reached saturation regarding symptoms and language at 20 patients. The SSI was revised based on these interviews and administered to 5 subjects for feedback on face validity. Minor changes yielded the final SSI which 45 patients completed at routine visits along with SF-36, EQ-5D, and feeling thermometer surveys. For each SSI symptom, a score is calculated by multiplying frequency (range "Never" [0] to "Every Day" [3]) by associated distress (range "None" [0] to "Very Much" [4]). Each symptom score is then summed (e.g., SSI score). We assessed construct validity by measuring known-group and convergent/divergent validity.

Results: The final SSI assesses the frequency and distress of 24 symptoms in 8 categories: General Health, Orbit, Sino-nasal Area, Salivary Glands, Chest, Abdomen, Skin and Extremities, and Genitourinary (Figure). A question on fear of more serious or severe disease was included based on qualitative interview findings. 45 patients completed the SSI 64 times (Table 1). The mean (SD) SSI score was 27.4 (27.1) and the range was 0-138. Fear of more severe disease was reported by 21 (46.7%) patients. The SSI inversely correlated well with the SF-36 (r= - 0.47, p< 0.001) and the feeling thermometer (r= - 0.50, p< 0.001). The symptom frequency score correlated with the RI (r=0.3, P=0.03) but the total SSI score did not (r=0.2, P=0.1). The SSI inversely correlated weakly with the EQ-5D (r= - 0.26, p=0.09). The fear score inversely correlated with the SF-36 item regarding role limitation due to emotional problems (r= - 0.36, p=0.003). Trends suggested that the median (IQR) SSI score was higher in active vs inactive disease (26 [12, 41] vs. 12 [6, 31]) and multi-organ vs one or two-organ disease (25 [12, 33] vs. 13 [6, 33]).

Conclusion: The SSI is an IgG4-RD-specific PROM developed with patient and clinician input to achieve face and content validity. In addition to symptoms and distress related to organ-specific disease, fear of worsening or more serious disease is common. The SSI has good construct validity in comparison with generic quality of life measures.

Example:

	In the past 30 days, how often, if at all, have you experienced this symptom? (Check one)					How much distress does the symptom cause you? (Check one)				
Symptom	**Never**	**A few days a month**	**A few days a week**	**Every Day**		**None**	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**
Orbit (Eye Area)										
Swelling or pressure around the eyes	X					X				
Change in vision	X					X				
Dry or itchy eyes			X				X			

Example of the IgG4-Related Disease Symptom Severity Index

	Overall (N = 43)
Mean (SD) Age (yrs) at SSI Completion	64.8 (11.5)
Male (N, %)	30 (69.8%)
Race	
White	39 (90.7%)
Black	1 (2.3%)
Asian	2 (4.6%)
Other	1 (2.3%)
Organ Involvement	
Single or Two-Organ (N, %)	27 (62.8%)
Multi-Organ (N, %)	16 (37.2%)
Symptom Severity Index (SSI)	
Mean (SD) Score	27.4 (27.1)
Range	0 – 138
Any Fear of Worsening Disease	21 (46.7%)
Mean (SD) Fear Symptom Score*	1.8 (3.0)
Range	0 – 12

*Frequency of fear (Range 0-3) multiplied by distress associated with fear (Range 0-4)

Cohort Characteristics

The symptom frequency score correlated with the RI but the overall SSI score did not, suggesting that the SSI better reflects patient-reported severity. The validity of the SSI should be further investigated in multi-center studies.

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Abstract Number: 0425

Differences in Correlation Between Objective Disease Measurements and Patient's/physician's Global Assessment in the Large Non-interventional Study SUSTAIN

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SESSION INFORMATION
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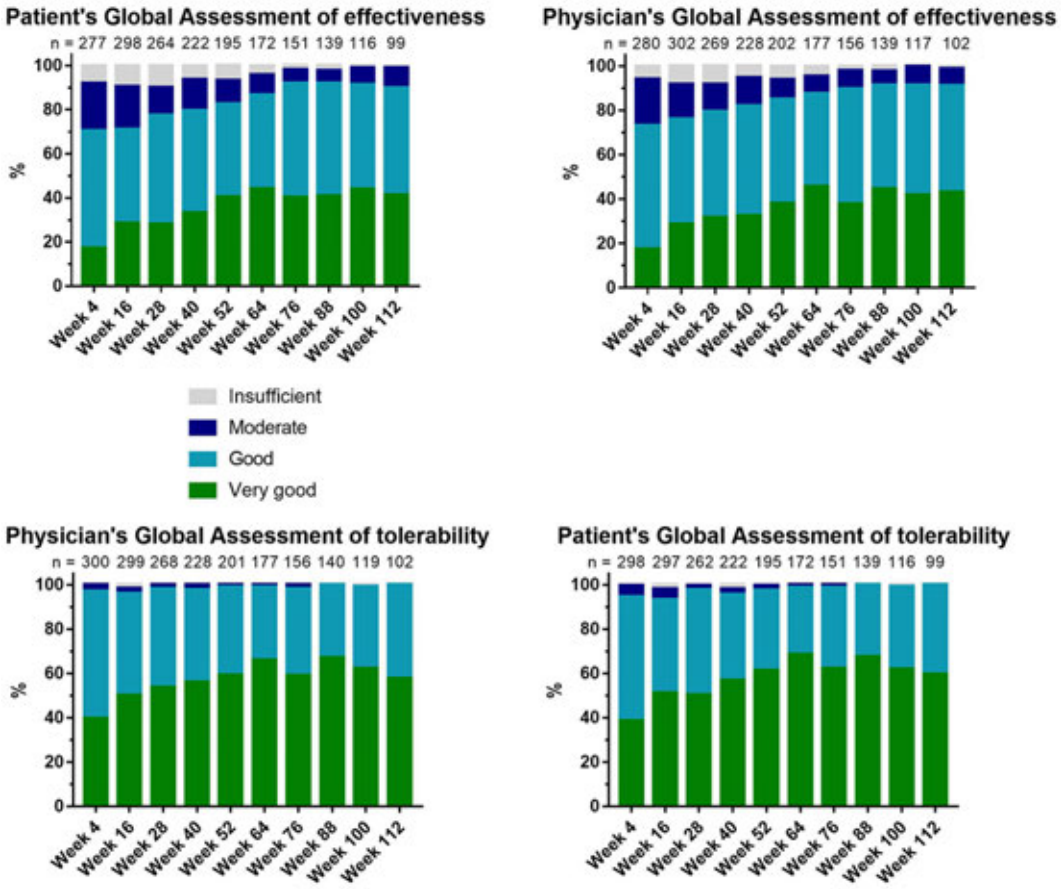
Background/Purpose: The wish of a treating physician is to make sure, that the patient gets an effective and safe therapy and is satisfied with the treatment. The question is how to measure the patient's satisfaction with the therapy.

SUSTAIN is a prospective, multi-center non-interventional study in Germany to observe long term efficacy and safety, quality of life and other patient reported outcomes (PROs) in patients with active psoriatic arthritis (PsA) under treatment with ustekinumab in routine clinical care. In this ongoing study, up to 400 patients were planned to be included at 75 centers for 160 weeks with visit intervals at week 0 and 4 and then every 12 weeks of treatment with ustekinumab according to the label. In this non-interventional study, all patients were diagnosed with psoriatic arthritis according to the CASPAR Criteria.

Here we examine the correlation between treatment satisfaction of the patients with satisfaction of the physicians. Furthermore, we correlate satisfaction with the effectiveness of the therapy for both patients and physicians, regarding the joints and the skin.

Methods: In this interim analysis, results of baseline data of 336 patients and of the documented visits up to week 112 were evaluated. Reported outcomes on satisfaction of patients and physicians with effectiveness and tolerability of therapy were assessed and correlated with disease severity measures such as number of swollen and tender joints and psoriasis affected body surface area (BSA).

The correlation between measured variables was assessed using Spearman's Rank Correlation Coefficient (CC). With a possible range from -1 to +1, a correlation coefficient between -0.3 and 0.3 was defined as no /weak correlation, between -0.3 and -0.7/ 0.3 and 0.7 as moderate correlation, and values below -0.7 or above 0.7 as strong correlation.



Patient's and physician's global assessments of effectiveness and tolerability.

Patient's global assessment of effectiveness	Physician's global assessment of effectiveness N	Physician's global assessment of effectiveness Correlation coefficient	Physician's global assessment of tolerability N	Physician's global assessment of tolerability Correlation coefficient
Week 4	269	0.854	293	0.809
Week 16	294	0.825	292	0.776
Week 28	262	0.802	260	0.722
Week 40	221	0.798	221	0.747
Week 52	194	0.834	194	0.826
Week 64	171	0.822	172	0.830
Week 76	150	0.830	150	0.819
Week 88	138	0.826	139	0.770
Week 100	116	0.846	116	0.802
Week 112	99	0.895	99	0.832
The global assessments range from 1 (=very good) to 4 (=insufficient).				

Correlation Coefficients between patient's and physician's assessments.

Results: The patients' and physicians' global assessments of effectiveness and tolerability were evaluated at every 12 weeks of treatment (Figure 1). The CCs between patient's and physician's assessments over 112 weeks of treat-

ment were in the range of 0.798 and 0.895 for effectiveness and 0.722 and 0.832 for tolerability (Table 1). Therefore, the CCs for global assessments can be classified as strong.

The CCs between physicians' and patients' assessments of effectiveness for tender joint count, based on 78 joints at week 112, were 0.321 (n=96) and 0.247 (n=94) respectively. The CCs between physicians' and patients' assessments of effectiveness for swollen joint count based on 76 joints also at week 112 of treatment, were 0.232 (n=96) and 0.193 (n=94) respectively. The CCs between physicians' and patients' assessments of effectiveness for BSA were 0.227 (n=86) and 0.216 (n=85) respectively. Thus, the correlation between patients' and physicians' satisfaction with the effectiveness of the therapy can mostly be classified as weak.

Conclusion: The results showed strong correlation between patients' and physicians' global assessments of both effectiveness and tolerability with high treatment satisfaction. However, the PROs correlate weakly to moderately with disease measures of tender and swollen joint counts and BSA.

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Abstract Number: 0426

Time to Response for Clinical and Patient-Reported Outcomes in Patients with Psoriatic Arthritis Treated with Tofacitinib, Adalimumab, or Placebo

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SESSION INFORMATION
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Background/Purpose: With many disease domains affected in PsA, clinical and patient-reported outcome (PRO) measures are important to assess disease improvement following treatment. Rapid, meaningful improvements in disease activity are a priority for physicians and patients (pts). Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. Higher proportions of pts achieved responses in PROs and clinical measures when treated with tofacitinib for 3 months vs placebo (PBO).[1-5] Proportions of responders were also similar between tofacitinib and adalimumab (ADA) after 3, 6, and 12 months.[2,3,5] We aimed to determine the time to initial response using responder definitions for selected PROs and clinical endpoints in pts with active PsA treated with tofacitinib, ADA, or PBO switching to tofacitinib.

Methods: In this post hoc analysis, data were collected from two Phase 3 studies (OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439]).[3,4] Pts receiving tofacitinib 5 or 10 mg twice daily (BID), subcutaneous ADA 40 mg once every two weeks (Q2W; OPAL Broaden only), or PBO, switching to tofacitinib 5 or 10

Table 1. Time to initial response

	OPAL Broaden			OPAL Beyond		
	Responders		Median time to initial response	Responders		Median time to initial response
	N at baseline	Number of subjects achieving initial response	Days (95% CI)	N at baseline	Number of subjects achieving initial response	Days (95% CI)
HAQ-DI						
Tofacitinib 5 mg BID	96	84	30.0 (27.0, 57.0)**	115	88	37.0 (29.0, 61.0)
Tofacitinib 10 mg BID	92	71	53.5 (29.0, 90.0)**	123	80	64.0 (57.0, 113.0)
ADA 40 mg SC Q2W	96	73	29.0 (29.0, 57.0)**	---	---	---
PBO → tofacitinib 5 mg BID	48	30	162.0 (85.0, NE)**	57	40	85.0 (57.0, 169.0)
PBO → tofacitinib 10 mg BID	45	36	112.0 (57.0, 169.0)**	59	38	113.0 (84.0, 169.0)
FACIT-F						
Tofacitinib 5 mg BID	107	87	31.0 (29.0, 43.0)	127	95	32.0 (30.0, 85.0)
Tofacitinib 10 mg BID	104	84	85.0 (34.0, 92.0)	132	91	84.0 (32.0, 91.0)
ADA 40 mg SC Q2W	106	83	85.0 (61.0, 92.0)	---	---	---
PBO → tofacitinib 5 mg BID	52	42	86.0 (85.0, 169.0)	65	48	84.0 (35.0, 164.0)
PBO → tofacitinib 10 mg BID	53	41	85.0 (31.0, 170.0)	65	41	92.0 (81.0, 175.0)
MDA						
Tofacitinib 5 mg BID	107	55	337.0 (256.0, NE)	131	46	NE (173.0, NE)
Tofacitinib 10 mg BID	104	54	337.0 (171.0, NE)	132	39	NE (NE, NE)
ADA 40 mg SC Q2W	106	53	339.0 (171.0, NE)	---	---	---
PBO → tofacitinib 5 mg BID	52	21	342.0 (337.0, NE)	66	17	189.0 (NE, NE)
PBO → tofacitinib 10 mg BID	53	25	338.0 (176.0, NE)	65	21	176.0 (174.0, NE)
PASDAS						
Tofacitinib 5 mg BID	107	67	253.0 (174.0, 335.0)	123	49	NE (170.0, NE)
Tofacitinib 10 mg BID	103	67	176.0 (166.0, 258.0)	129	51	182.0 (169.0, NE)
ADA 40 mg SC Q2W	104	59	253.0 (169.0, NE)	---	---	---
PBO → tofacitinib 5 mg BID	52	24	344.0 (251.0, NE)	63	22	189.0 (169.0, 189.0)
PBO → tofacitinib 10 mg BID	52	31	241.0 (170.0, 323.0)	65	28	173.0 (169.0, 190.0)

Response definitions: HAQ-DI ≥0.35-point improvement from baseline, FACIT-F total score ≥4-point improvement from baseline, MDA yes/no composite response (meeting at least five of seven criteria), and PASDAS post-baseline score of ≤3.2 and >1.6-point improvement from baseline
Log rank (Mantel-Haenszel) tests comparing Kaplan-Meier curves across treatments; p-value based on Chi square test with degrees of freedom = number of treatments -1; **p<0.01
PBO → tofacitinib 5 or 10 mg BID groups began treatment with tofacitinib at Month 3.
ADA, adalimumab; BID, twice daily; CI, confidence interval; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, Minimal Disease Activity; NE, not estimable; PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; Q2W, once every two weeks; SC, subcutaneous

mg BID at Month (M)3, were included. Responder definitions included: HAQ-DI ≥ 0.35-point improvement from baseline (BL), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) total score ≥ 4-point improvement from BL, Minimal Disease Activity (MDA) yes/no composite response (meeting at least 5/7 criteria), and PsA Disease Activity Score (PASDAS) post-BL score of ≤ 3.2 and > 1.6-point improvement from BL. First post-BL data were collected at Week 2 (eg for HAQ-DI) or M1. Time-to-event analyses were performed using the Kaplan-Meier (KM) method, with pts censored at last observed visit. Log-rank tests compared time to initial response across treatment groups.

Results: KM analyses show days to initial response (Table 1, Figure 1). Time to initial HAQ-DI responses was significantly different between treatment groups in OPAL Broaden ($p < 0.01$): faster in pts receiving tofacitinib 5 mg BID, tofacitinib 10 mg BID, and ADA, vs pts who switched from PBO to tofacitinib at M3. A similar, but not significant (ns) trend was observed for HAQ-DI responses in OPAL Beyond. Generally, initial FACIT-F responses were achieved faster in pts receiving tofacitinib 5 mg BID vs other treatment groups in both studies (ns). Times to initial MDA and PASDAS responses were similar between tofacitinib and ADA treatment groups.

Conclusion: Times to initial response in functional ability and disease activity were similar in pts treated with either tofacitinib or ADA. Time to initial response prior to first post-BL observation (Week 2 or M1) was not estimable in this analysis. These results may help physicians better understand the time frame for a meaningful response in pts receiving tofacitinib.

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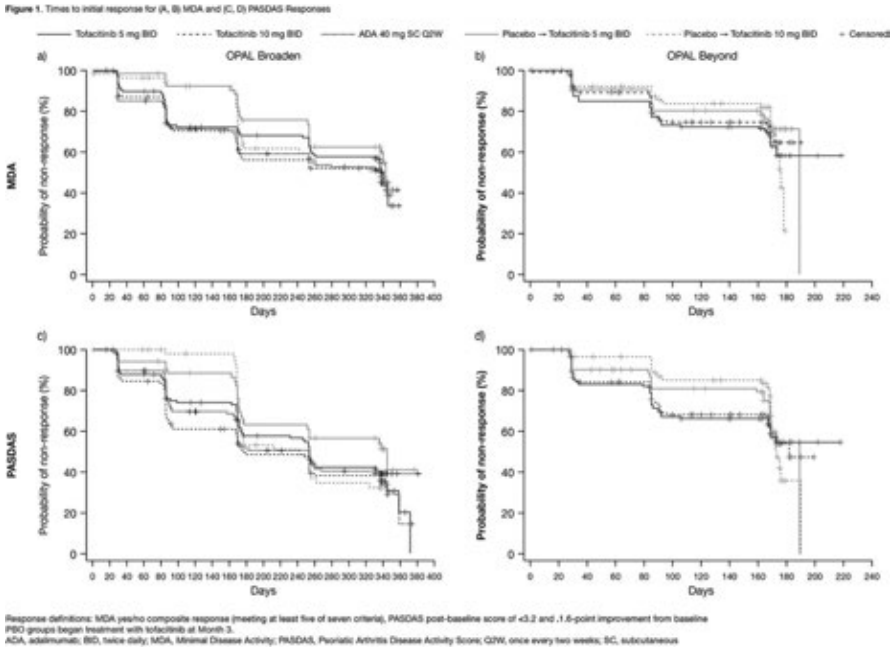

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Abstract Number: 0427

Correlation Between Patient Reported Outcomes Measurement Information System (PROMIS) and RAPID3 in Rheumatoid Arthritis Patients Starting a New Biologic DMARD

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SESSION INFORMATION
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Background/Purpose: RAPID3 is a disease activity measure which relies on patient-reported outcomes (PROs) to assess physical function, pain, and global health but does not require joint count or lab values. Patient Reported Outcomes Measurement Information System (PROMIS) is a validated instrument used to collect PROs across multiple diseases. Compared to RAPID3, PROMIS offers the ability to assess more targeted domains such as fatigue, global mental health, and pain interference. It also allows comparison of patient responses to a normalized US population. The purpose of this study was to assess whether changes in PROMIS domains correlate with changes in RAPID3 in RA patients starting a new biologic DMARD and whether PROMIS could complement a composite measure such as RAPID3 to optimize patient outcomes.

Methods: A retrospective chart review was conducted of RA patients in a tertiary outpatient rheumatology practice starting a new biologic DMARD. Computer Adaptive Testing (CAT) PROMIS domains (global physical health, global mental health, physical function, pain interference, and fatigue) were collected along with RAPID3 at baseline and follow-up visits. CAT uses item response theory and branching logic to quickly assess patient scores. Correlations between PROMIS domains and RAPID3 were calculated using Spearman's correlations.

Results: 126 patients were included in the final analysis. Mean age was 56.2 ± 13.8 years and 75% were female. Disease duration was greater than 2 years in 80% of patients. 81% of patients had been on at least 1 or 2 prior DMARDs. All PROMIS domains, with the exception of global mental health, were significantly associated with changes in RAPID3 ($p \leq 0.05$) and the coefficients suggest moderate correlation ($|r| = 0.48 - 0.60$). Number of days between

Table 1: Demographic characteristics

	Total (N = 126)
Age (mean ± SD)	56.2 ± 13.8
Female (%)	95 (75.4%)
Disease duration	
≤ 2 years	25 (19.8%)
> 2 years	101 (80.2%)
Treatment history	
None	6 (4.8%)
1 or 2 prior DMARDs	102 (81.0%)
3 or more prior DMARDs	18 (14.3%)
Current DMARD	
Yes	108 (85.7%)
No	18 (14.3%)

Table 2: Change in RAPID3 and PROMIS domains from baseline

Measure	Respondents (total = 126)	Median (min, max)	Mean + SD	P-value [a]
RAPID3	126	-0.75 (-7.6, 2.1)	-0.89 ± 1.7	**< 0.001**
PROMIS global physical health	94	2.6 (-7.5, 19.8)	3.3 ± 5.3	**< 0.001**
PROMIS global mental health	93	0.0 (-8.6, 14.5)	0.99 ± 5.1	0.064
PROMIS physical function	125	1.7 (-37.7, 20.3)	2.3 ± 6.5	**< 0.001**
PROMIS pain interference	126	-3.3 (-70.3, 8.9)	-4.2 ± 8.6	**< 0.001**
PROMIS fatigue	125	-1.1 (-39.5, 12.9)	-2.6 ± 7.5	**< 0.001**
Pain intensity (VAS [b])	94	-1.0 (-8.0, 5.0)	-1.3 ± 2.1	**< 0.001**

[a] *Paired T-test*
[b] *VAS = visual analog scale*

initial and follow-up visit was 111.7 ± 48.6. There was no significant difference found between a follow-up period < 90 days compared to a follow-up period > 90 days. At follow up, patients in near remission by RAPID3 (≤ 1.3, n=12) had a PROMIS physical global health median score of 52.5 (min, max = 37.4, 61.9), while patients with high severity RAPID3 (≥ 4.3, n=55) had a PROMIS global health median of 34.9 (min, max = 26.7, 47.79; p< 0.001). A change of > 1.2 for RAPID3 and > 5 for PROMIS domains has been considered the minimal clinically important difference. 52% of patients had a RAPID3 change of >1.2. Of these, 80% had a change of > 5 in PROMIS pain interference, while 76%, 65%, and 59% had changes of > 5 in PROMIS fatigue, physical function, and global physical health respectively.

Table 3: Disease activity by RAPID3 and PROMIS global health percentile at baseline and follow-up

Disease Activity	Baseline n (%)	PROMIS global health median (min,max)	Follow-up n (%)	PROMIS global health median (min,max)	P-value [a]
RAPID3 Near remission [b]	3 (2.4)	54.1 (54.1,54.1)	12 (9.5)	52.5 (37.4,61.9)	**<0.001**
RAPID3 Low severity [c]	8 (6.3)	44.9 (39.8,47.7)	20 (15.9)	47.7 (37.4,57.7)	**<0.001**
RAPID3 Moderate severity [d]	40 (31.7)	42.3 (32.4,54.1)	39 (31.0)	42.3 (32.4,47.7)	**<0.001**
RAPID3 High severity [e]	75 (59.5)	34.9 (19.9,47.7)	55 (43.7)	34.9 (26.7,47.7)	**<0.001**

[a] *p-value by Kruskal-Wallis test refers to comparison of both baseline and follow-up PROMIS global health across RAPID3 groups*
[b] *near remission ≤ 1.3*
[c] *low severity ≤ 2.3*
[d] *moderate severity ≤ 4.2*
[e] *high severity ≥ 4.3*

Conclusion: In RA patients starting a new biologic DMARD, changes in all studied PROMIS domains, with the exception of global mental health, were significantly associated with changes in RAPID3. Compared to RAPID3, use of PROMIS can allow for the assessment of additional domains in a format which is normalized to a broad population. Insight gained from these additional domains can help focus follow-up visits and facilitate joint decision making between patients and providers. A composite index of PROMIS domains predictive of changes in RAPID3 is being developed. Additional studies are needed to validate the use of PROMIS as a tool for disease activity measure in RA patients.

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Abstract Number: 0428

Assessing Meaningful Changes in Disease Activity as Clinical Trial Efficacy Measures for Cutaneous Lupus Erythematosus

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SESSION INFORMATION

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Background/Purpose: To date, there are no approved treatments for cutaneous lupus erythematosus (CLE), a disease known to significantly burden a patient's quality of life (QoL). Clinical trials are important for the advancement of new treatments for CLE and outcome measures should reflect clinically meaningful improvement in disease activity and its effect on QoL. Currently, trials use an efficacy measure of ≥50% improvement in disease activity, defined by the Cutaneous Lupus Disease Area and Severity Index score for activity (CLASI-A), in patients with an initial CLASI-A of ≥10. However, the degree of improvement in disease activity needed to predict a meaningful impact on QoL, an important variable in the design and interpretation of future clinical trials, has not been defined.

Methods: This study included 126 patients seen at the Hospital of the University of Pennsylvania who participate in a longitudinal research database. Patients with mild, moderate or severe initial CLASI-A were analyzed separately and using a linear regression model, we calculated the percent change and difference needed in CLASI-A to have an important impact on QoL, defined as a 9.38-point and a 7.37-point improvement in the Emotions and Symptoms subscales of Skindex-29, respectively.

Results: In patients with an initial CLASI-A ≥8, a decrease by 42.1% or 7-points and a decrease by 31.0% or 5-points in disease activity is associated with a meaningful impact in the Emotions and the Symptoms subscales, respectively. For both subscales, patients with increasingly severe initial disease required a smaller percent change in CLASI-A to predict a meaningful change in QoL.

Conclusion: We find that using a CLASI-A ≥8 for trial entry allows for the inclusion of patients with milder disease for whom improvement of CLASI-A by ≥50% results in a meaningful impact on QoL, as determined by the Emotions and Symptoms subscales of Skindex-29. In patients with CLASI-A ≥8, a decrease in activity by seven and five-points is not only a clinically significant improvement but also indicates a meaningful impact on the Emotions and Symptoms subscales, respectively. For trials enrolling a larger proportion of patients with severe disease activity, or CLASI-A ≥20, we recommend stratifying patients by disease severity, as a smaller magnitude of percent change in disease activity predicts meaningful improvement in QoL. Our findings establish appropriate trial endpoints by determining clinically significant change in disease activity associated with meaningful changes in patients' QoL.

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Concordance Between Physician and Patient Assessment of Disease Activity in Rheumatoid Arthritis Using Disease Activity Score: Phase II Results

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SESSION INFORMATION
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Background/Purpose: Involving patients with rheumatoid arthritis (RA) in the assessment of their disease may increase adherence to treatment, improve disease outcomes and reduce consultation time. Concordance between Disease Activity Score (DAS-28) performed by physicians and patients was substantial in the phase 1 (baseline visit) of this prospective study.

The purpose of the study is to evaluate the persistence of the concordance between physician and patient assessment of disease activity in RA using DAS-28 after 3 months of the baseline visit.

Methods: At baseline visit, patients with RA from 7 Middle Eastern Arab Countries (MEAC) were briefed about DAS-28 by their rheumatologist and were given a smartphone access to a video in easy Arabic language explaining the performance of DAS-28. At visit 2, scheduled 3 months later, patients were asked to self-report DAS-28, blinded to the physician's assessment. Concordance between DAS-28 at each visit was calculated using paired T-Test. Agreement between physician- and patient-DAS categories (remission, low-, moderate- and high disease activity) was calculated at baseline and at 3 months using weighted kappa for category comparison. Predictive factors of positive concordance between physician and patient-DAS were identified using logistic regression.

Table 1. Patients characteristics

Characteristic	
N	229
Age, years, mean (SD)	47.8 (13.4)
Female N (%)	188 (82.1)
Educational level N (%)	
- Illiterate	14 (6%)
- Primary	34 (15%)
- High school	76 (33%)
- University	100 (44%)
Disease duration, years (SD)	11.3 (8.8)
Gap between symptom onset and RA diagnosis, years (SD)	2.8 (8.6)
Positive rheumatoid factor, N (%)	161 (70%)
Positive ACPA, N (%)	138 (60%)
Radiographic erosions, N	84 (37%)
Current treatment, N (%)	
- Corticosteroids	101 (44%)
- cs DMARDs	214 (93%)
- bDMARDs	79 (34.5%)
- tsDMARDs	21 (9%)
Compliance Questionnaire for Rheumatology (CQR) score % (SD)	78.9 (11.8)
Physician DAS-28, mean (SD)	3.76 (1.39)

Results: Two hundred and twenty-nine patients were included in AUTODAS phase II (Characteristics in Table 1). At baseline, mean DAS-28 was 3.76 [SD 1.39] in physicians and 3.94 [SD 1.42] in patients, with a difference delta1 of -0.19 [95% CI -0.26; -0.11] ($p < 0.0001$). At 3 months, mean DAS-28 was 3.57 [SD 1.44] in physicians and 3.75 [SD 1.47] in patients, with a difference delta2 of -0.18 [95% CI -0.25; -0.11] ($p< 0.0001$). The difference between deltas was not statistically significant ($p = 0.81$). Agreement between physician- and patient-DAS categories was 76% at baseline (Weighted Kappa = 0.71), and 73% at 3 months (Weighted Kappa = 0.73). Concordance at 3 months was statistically associated with DAS-patient category ($p = 0.045$) and concordance at baseline ($p = 0.036$) and did not correlate with education, treatment or country.

Conclusion: DAS-28 is numerically slightly overestimated by patients compared to physicians but the concordance between DAS-28 categories was substantial and remained stable at the 3-months follow-up visit.

Self-assessment of disease activity should be decided according to the physician's clinical judgment.

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Abstract Number: 0430

Axial Spondyloarthritis Patients Report Important Impairments in Daily Life and Work Ability – a Web Survey in 472 Patients

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SESSION INFORMATION
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Background/Purpose: Axial spondyloarthritis (axSpA) can be associated with significant burden and impaired work activity. In Chile, several barriers impede adequate treatment, such as insufficient access to specialists and biologic treatment. Furthermore, there is an important lack of insight into the local situation. This hampers the development of adequate national treatment standards and financial support.

Table 1 **Patient characteristics of the 472 axial SpA patients.**

	Overall (n = 472)	Men (n = 173)	Women (n = 299)	p=	Biologics (n= 92)	No Biologics (n=372)	p=
Men, n (%)	173 (37)				45 (49)	124 (33)	<0.01
Age, yrs, mean (SD)	42 (10)	43 (11)	41 (9)	0.02	41 (9)	41 (10)	ns
Age at diagnosis, yrs, mean (SD)	35 (10)	34 (11)	35 (9)	ns	32 (9)	35 (10)	ns
Age onset symptoms, yrs, mean (SD)	28 (10)	28 (11)	28 (10)	ns	27 (9)	28 (11)	ns
Diagnostic delay, yrs, median (IQR)	4 (1-10)	3 (1-10)	5 (1-11)	ns	4 (1-9)	4 (1-10)	ns
HLA-B27 positive, n (%)	232 (49)	110 (77)	121(52)	<0.01	47 (57)	180 (61)	ns
HLA-B27 unknown	94(20)	30(17)	65(22)		15 (16)	138 (37)	
Current treatment, n (%)							
DMARD	261 (55)	88 (51)	173 (59)	ns	41 (46)	217 (59)	0.02
NSAIDs	370 (78)	126 (73)	244 (82)	0.02	59 (65)	305 (82)	<0.01
Biological	92 (20)	45 (26)	47 (16)	<0.01			
Opiates	158 (34)	43 (25)	115 (39)	<0.01	25 (28)	130 (35)	ns
Patient global disease, mean (SD)	6 (3)	6 (3)	6 (2)	ns	5 (3)	6 (2)	<0.01
BASDAI, mean (SD)	6.1 (2.1)	5.8 (2.3)	6.3 (2.0)	0.03	5.2 (2.2)	6.3 (2.1)	<0.01
BASDAS ≥4, n (%)	390 (83)	131 (76)	258(86)	<0.01	64 (70)	318 (85)	<0.01
BASFI, mean (SD)	5 (3)	5.1 (2.8)	5.4 (2.4)	ns	4.7 (2.4)	5.5 (2.6)	<0.01
ASAS Health Index, mean (SD)	10 (4)	9 (4)	10 (3)	<0.01	9 (3)	10 (4)	ns
Normal[a], n (%)	44 (9)	24(19)	10(4)		10 (11)	34 (9)	
Moderate impaired[a], n (%)	267 (57)	60(48)	138(56)	<0.01	62 (67)	199(53)	0.02
Severely impaired[a], n (%)	161 (34)	40(32)	99(40)		20 (22)	139(37)	

a. normal functioning (ASAS HI sum score ≤5.0), moderate impairment of functioning (>5.0 to ≤11.9) and severe impairment of functioning (≥12.0). ASAS HI, ASAS Health Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; DMARD, disease modifying anti-rheumatic drug; HLA-B27, Human Leukocyte Antigen B27; NSAIDs, nonsteroidal anti-inflammatory drugs; SpA, spondyloarthritis.

Table 2 Work participation in the last 7 days, in axial spondyloarthritis patients of working-age (n = 457)

	Overall	Gender			Biological Treatment		
		Men	Women	P	Yes	No	P
Number	457	166	291		90	358	
Currently paid job, n (%)	296 (65)	127 (77)	169 (58)	<0.01	68 (76)	221 (62)	.01
Absenteeism –patients[b1], n (%)	121 (41)	41 (32)	81 (48)	<0.01	21 (31)	100 (45)	0.04
Absenteeism - % time [c], median (IQR)	30 (9-100)	40 (12-100)	23 (8-100)	ns	17 (7-100)	33 (10-100)	ns
Presenteeism–patients[b2]*, n (%)	197 (82)	78 (75)	119 (88)	<0.01	45 (79)	147 (84)	ns
Presenteeism - %[d], mean (SD)	45 (25)	42 (27)	48 (24)	ns	43 (23)	46 (26)	ns
Overall work impairment[b3], n (%)	237 (80)	95 (79)	142 (90)	0.01	51 (81)	181 (87)	ns
Work impairment -%[e], median (IQR)	55 (30-86)	50 (20-83)	60 (37-90)	ns	50 (30-78)	60 (30-92)	ns
Overall activity impairment[b4], n (%)	425 (93)	144 (87)	281 (97)	<0.01	83 (92)	334 (93)	ns
Activity impairment - %[f], mean (SD)	53 (27)	57 (29)	60 (26)	ns	51 (26)	61 (27)	<0.01

a. Number of patients who answered 'yes'. b. Number of the patients with a job (N=304) that reported [1]absenteeism,[2] presenteeism, [3] Work impairment (absenteeism ór presenteeism), [4] Activity impairment. c. % of work time lost, in employed patients with >0% absenteeism (n=123). d. % of work time with less productivity, in employed patients with >0% presenteeism (n=202). e. % of work time with less productivity (due to absenteeism or presenteeism), in all employed patients with >0% work impairment. f. % of time with activity impairment in all patients of working age. *Presenteeism was only mentioned for patients that were not 100% absent.

Table 3 Gender differences in disease burden and work participation – female versus male patients

	BASDAI			BASFI			Severe daily impairment (ASAS HI)[e]			Work absenteeism			Work presenteeism		
	β	95% CI	p	β	95% CI	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Crude	0.5	0.1 – 0.9	0.02	0.4	-0.1 – 1.0	ns	1.6	1.1 – 2.5	0.03	2.1	1.3-3.4	<0.01	2.3	1.1-4.6	0.02
Adjusted 1[a]	0.5	0.1 – 0.9	0.02	0.6	0.1 – 1.1	0.02	1.8	1.1 – 2.8	0.02	2.1	1.3-3.6	<0.01	2.5	1.2-5.0	0.01
Adjusted 2[b]	0.4	-0.1 – 0.8	ns	0.5	0.02 – 1.0	0.04	1.6	1.0 – 2.6	0.03	2.0	1.2-3.4	<0.01	2.5	1.2-5.0	0.01
Adjusted 3[c]	0.3	-0.1 – 0.8	ns	0.4	-0.1 – 0.9	ns	1.6	1.0 – 2.5	0.05	2.0	1.1-3.2	0.02	2.2	1.1-4.7	0.03
Adjusted 4[d]	0.2	-0.3 – 0.6	ns	0.2	-0.3 – 0.7	ns	1.3	0.8 – 2.2	ns	1.3	0.9-2.7	ns	*		

Female versus male patients. a. Correction for age and disease duration. b. Correction for age, disease duration and biological treatment. c. Correction for age, disease duration, biological treatment and NSAIDs. d. Correction for age, disease duration, biological treatment, NSAIDs and opiates. e. Severe daily impairment (ASAS HI sum score ≥12) versus no or moderate impairment (ASAS HI sum score <12). * Additional correction for opiates was not performed because 100% of the patients with opiate treatment reported presenteeism. B, linear regression coefficient; CI, confidence interval; ns, non-significant; OR, odds ratio; p, p-value.

The objectives were to (1) evaluate the disease burden, quality of life, work participation and treatment status in Chilean axSpA patients and (2) to assess the influence of gender.

Methods: A cross sectional online survey among Chilean axSpA patients, recruited via the Chilean SpA Patient Foundation ("Espondilitis Chile") between July and October 2018. The survey requested information on gender, age, disease characteristics (diagnosis, disease duration, treatment), disease burden (BASDAI and BASFI), quality of life (ASAS Health Index) and work participation (WPAI). The association between BASDAI, quality of life or work participation (presenteeism, absenteeism) and subgroups (gender, biologics) was assessed through univariable and multivariable regression analyses, correcting for age, disease duration and concomitant treatment (NSAIDs, opiates).

Results: AxSpA was reported by 472 participants (91% radiographic, 63% women, mean age 42+10 years), and the levels of disease activity (BASDAI ≥4: 83%; ASAS HI ≥moderately impaired: 91%; table 1) and work disability (absenteeism: 41%; presenteeism 82%; table 2) were high. Thirty-four percent used opiates. Biologics use was very low (20%) but significantly associated with lower BASDAI, BASFI, ASAS HI, and risk of absenteeism. Females had significantly higher BASDAI, BASFI and ASAS HI, although were less likely to receive biologics (26% versus 16%, p< 0.01). After correction for treatment, these gender differences were not significant anymore (table 3).

Conclusion: This web survey strongly suggest a high disease burden and work impairment in Chilean axSpA patients. The use of biologics is low, while the use of opiates was alarmingly high. Women used significantly less biologics despite reporting a worse disease state and work disability, which could be due to treatment inequity. This is the first large web survey on axSpA patients in Latin America and the first to describe labor participation and gender differences in disease activity and treatment in Chilean axSpA patients.

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Abstract Number: 0431

Psychometric Properties of the Pediatric Patient-Reported Outcomes Measurement Information System (PROMIS®) Item Banks in a Dutch Clinical Sample of Children with Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

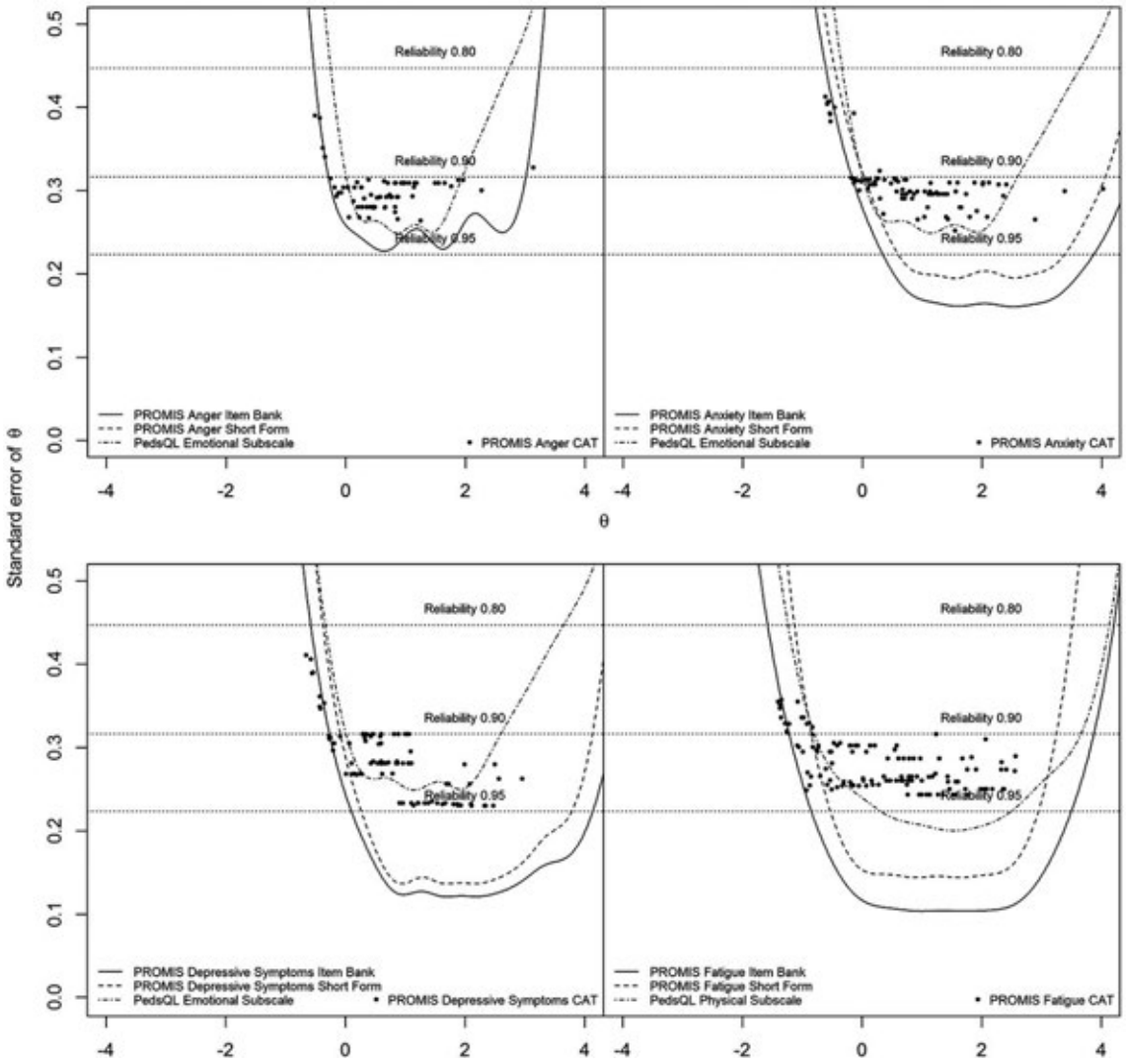
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes

Session Type: Poster Session (Sunday)

Item Bank/Scale	Mean FL SE(θ)	FL SE(θ) <0.32* N(%)	Mean SF SE(θ)	SF SE(θ) <0.32* N(%)	Mean CAT SE(θ)	CAT SE(θ)<0.32* N(%)	Mean CAT items administered	FL Amount of items	SF Amount of items	ICC (95% CI) FL**	ICC SF**	SDC**
PROMIS Anger Scale	0.37	89 (57.4%)	0.51	89 (57.4%)	0.40	89 (57.4%)	3.6	5	5	0.70 (0.59 – 0.70)	0.70	15.3
PROMIS Anxiety Item Bank	0.36	86 (55.5%)	0.52	73 (47.1%)	0.41	84 (54.2%)	5.6	13	8	0.77 (0.68 – 0.84)	0.76	13.5
PROMIS Depressive Symptoms Item Bank	0.34	89 (57.4%)	0.75	78 (50.3%)	0.40	88 (56.8%)	5.2	13	8	0.79 (0.70 – 0.85)	0.77	14.2
PROMIS Fatigue Item Bank	0.20	123 (79.4%)	0.40	108 (69.7%)	0.31	114 (73.5%)	4.7	23	10	0.87 (0.82 – 0.91)	0.85	17.2
PROMIS Mobility Item Bank	0.30	106 (67.5%)	0.54	79 (50.3%)	0.37	99 (63.1%)	5.3	23	8	0.84 (0.76 – 0.89)	0.81	13.3
PROMIS Pain Interference Item Bank	0.27	108 (69.7%)	0.40	103 (66.5%)	0.36	106 (68.4%)	4.5	13	8	0.83 (0.77 – 0.89)	0.82	13.6
PROMIS Peer Relationships Item Bank	0.29	112 (72.3%)	0.41	82 (52.9%)	0.36	97 (62.6%)	5.8	15	8	0.69 (0.58 – 0.78)	0.72	18.7
PROMIS Upper Extremity Item Bank	0.38	76 (48.7%)	0.84	65 (41.7%)	0.45	70 (44.9%)	6.0	29	8	0.86 (0.80 - 0.90)	0.84	12.1

Note: SE(θ), Standard Error of theta; FL, full-length item bank; SF, short-form; CAT, computerized adaptive testing; ICC, intraclass correlation coefficient; CI, confidence interval; SDC, smallest detectable change; * amount of patients with a SE(θ)lower than 0.32. A SE(θ)of 0.32 equals a reliability of 0.90; ** n = 101

Reliability and test-retest reliability of measurements for the full-length (FL) item banks, short-forms (SF) and computerized adaptive test (CAT)s of the pediatric PROMIS item banks in a sample of children with juvenile idiopathic arthritis (n = 155).

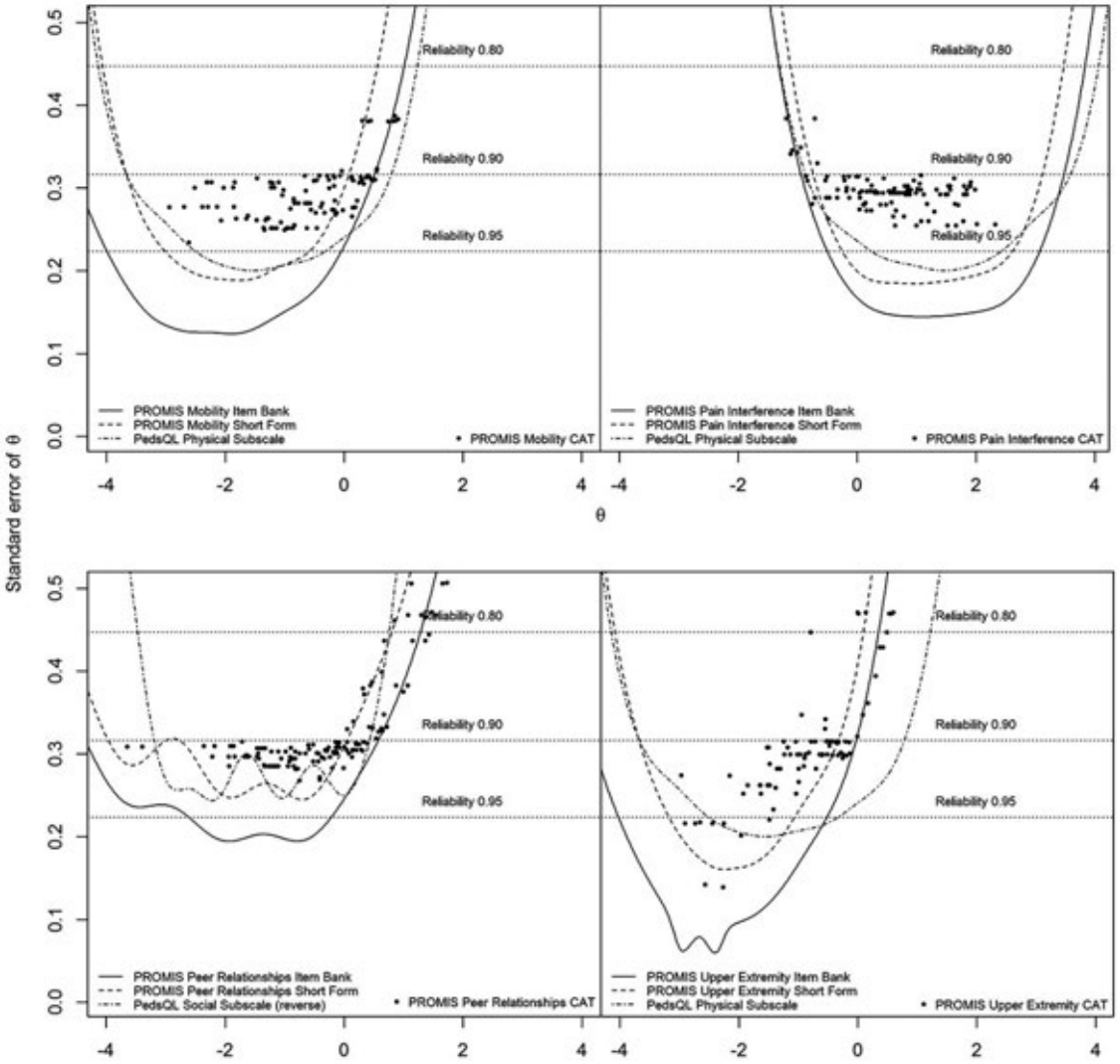


Reliability of measurement (expressed as SE of the theta) plots for the PROMIS item banks: Anger, Anxiety Depressive Symptoms and Fatigue and their associated PedsQL subscale across the range of theta.

Session Time: 9:00AM–11:00AM

Background/Purpose: Patient-reported outcome measures (PROMs) are often used to include the patients perspective on treatment (outcome). However, the choice of PROMs is difficult, as there are multiple PROMs available to measure a single construct. These PROMs differ in psychometric properties, length and scoring methods and often suffer from ceiling effects. To improve measurements the National Institute of Health (NIH) initiated the development of the Patient Reported Outcomes Measurement Information System (PROMIS®), which contains multiple item banks to assess different construct of Health-Related Quality of Life (HRQoL), symptoms and psychosocial functioning.The purpose of this study was to assess the psychometric properties of eight pediatric PROMIS item banks in a clinical sample of children with Juvenile Idiopathic Arthritis (JIA).

Methods: 154 Dutch children (8-18 years, mean=14.4, SD=3.0) with JIA completed eight pediatric v1.0 PROMIS item banks (Anger, Anxiety, Depressive Symptoms, Fatigue, Pain Interference, Peer Relationships, Physical Function Mobility, Physical Function Upper Extremity) twice and the Pediatric Quality of Life Inventory (PedsQL) and the Childhood Health Assessment Questionnaire (CHAQ) once. Structural validity of the item banks was assessed by fitting a Graded Response Model (GRM) and inspecting GRM fit (CLI, TLI, RMSEA) and item fit (S-X^2). Convergent validity



Reliability of measurement (expressed as SE of the theta) plots for the PROMIS item banks: Mobility Pai Interference, Peer Relationships and Upper Extremity and their associated PedsQL subscale across the range of theta.

(with PedsQL/CHAQ subdomains) and discriminative validity (active/inactive disease) were assessed. Reliability of the item banks, short-forms and CATs was expressed as standard error of theta (SE(θ)). Test-retest reliability was assessed using intraclass correlation coefficients (ICC) and Smallest Detectable Change (SDC).

Results: All item banks had sufficient overall GRM fit (CFI >.95, TLI >.95, RMSEA< .08) and no item misfit (all S-X2 p >.001). High correlations (>.70) were found between most PROMIS T-scores and hypothesized PedsQL/CHAQ (sub) domains. Mobility, Pain Interference and Upper Extremity item banks were able to discriminate between patients with active and inactive disease. Regarding reliability PROMIS item banks outperformed legacy instruments. Post-hoc CAT simulations outperformed short-forms. Test-retest reliability was strong (ICC >.70) for all full-length item banks and short-forms, except for Peer Relationships.

Conclusion: The pediatric PROMIS item banks displayed sufficient psychometric properties in children with JIA. CATs outperformed short-forms in terms of test length and amount of patients reliably estimated. PROMIS item banks are ready for use in clinical research and practice in children with JIA.

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Abstract Number: 0432

Does Improvement in Patient Pain and Fatigue Lag Behind Clinical Remission in Rheumatoid Arthritis Patients? Data from a Rheumatoid Arthritis Registry

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes
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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) patients are often not in remission due to patient global assessment of disease activity (PtGA) which is included in the formula of all disease activity indices. Given that PtGA may reflect pain or fatigue, the aim of this analysis was to assess the relative timing and perhaps lag of patient-reported outcomes (PRO) after remission is obtained as measured by clinical disease activity index (CDAI) or swollen joint count (SJC28) in a large observational database of RA patients followed in routine clinical care.

Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) registry that were not in low disease state at baseline based on the CDAI, SJC28, PtGA, pain and fatigue criteria below, and had at least six months of follow-up, were included in the analysis. Low disease state was defined as CDAI≤10, SJC28≤2, PtGA≤2cm, pain score≤2cm, or fatigue score≤2cm. Remission was defined as CDAI≤2.8, SJC28≤1, PtGA≤1cm, pain score≤1cm, or fatigue score≤1cm. Kaplan-Meier survival analysis was used to assess the time to first low disease state / remission based on each definition.

Results: A total of 986 patients were included with a mean (SD) age and disease duration of 57.4 (12.9) years and 8.3 (9.9) years, respectively, and mostly women (80.0%). Mean (SD) of CDAI, SJC28, PtGA, pain, and fatigue at enrolment was 29.8 (11.7), 8.3 (4.6), 6.4 (1.9), 6.6 (1.9), and 6.7 (2.0), respectively.

Figure 1 shows the time to first low disease state and time to first remission based on different definitions. The median (95%CI) time in months to CDAI≤10 was 12.4 (11.4-13.6), SJC28≤2 was 9 (8.2-10), PtGA≤2cm was 18.9 (16.1-22), pain≤2cm was 24.5 (19.4-30.5), and fatigue≤2cm was 30.4 (24.8-31.7). For remission, the median (95%CI) time to CDAI≤2.8 was 46.5 (42-54.1), SJC28≤1 was 12.5 (11.4-13.4), PtGA≤1cm was 39.6 (34.6-44.8), pain≤1cm was 54.7 (43.6-57.5), and fatigue≤1cm was 42.6 (36.8-48).

Conclusion: Time to achieving low disease state or remission based on PROs is considerably longer compared to swollen joint count which may have significant impact on the time to CDAI low disease activity and remission. Remission and low disease activity composite scores, and PROs lag behind SJCs. Careful interpretation of PROs and composite scores could impact management including prevention of overtreatment and unnecessary switching of DMARDs.

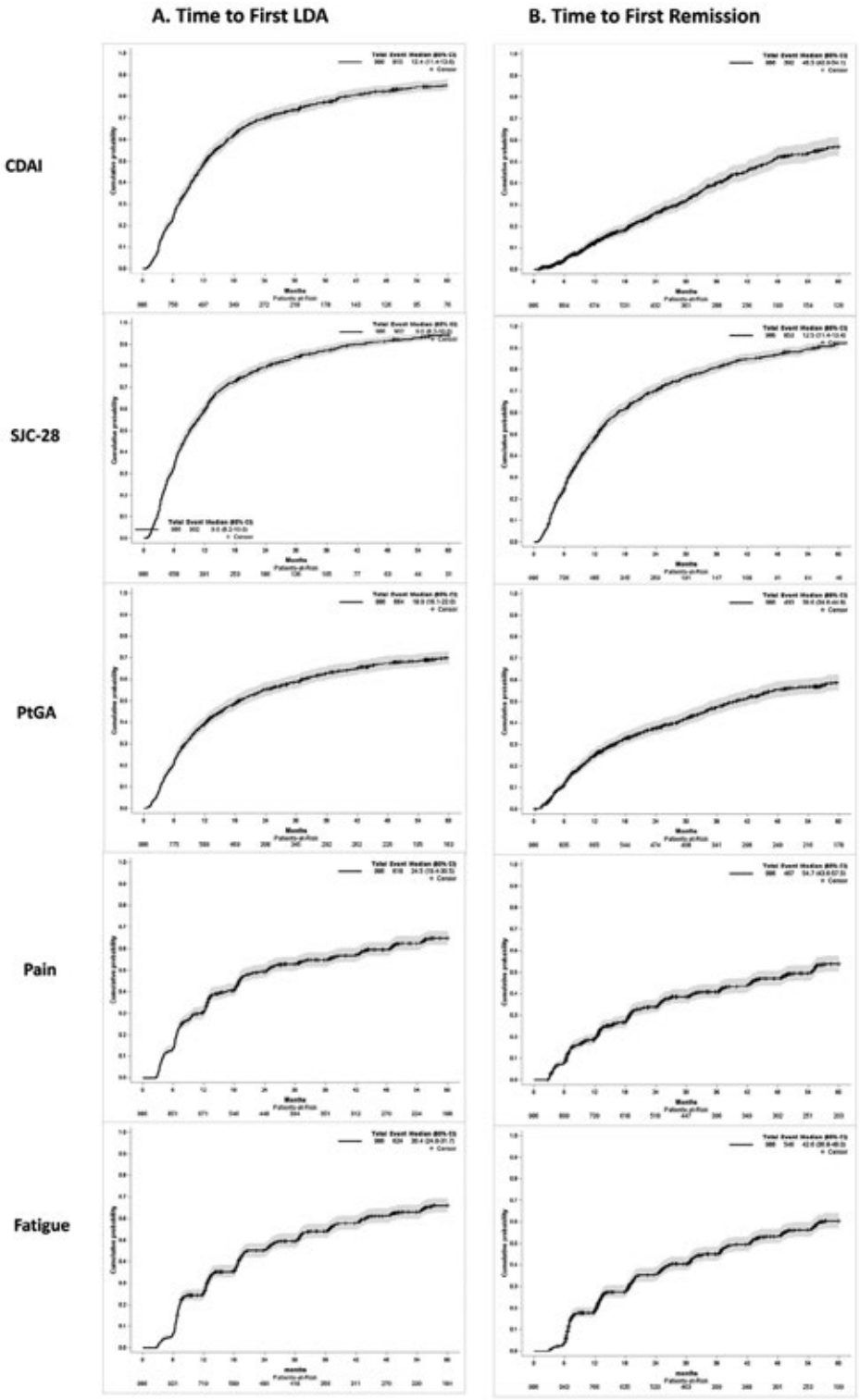

Figure 1. Time to First Low Disease State and Time to First Remission Based on Different Definitions

Disclosure: J. Pope, AbbVie, 5, Abbvie, 5, Actelion, 5, Actellion, 5, Amgen, 2, 5, AstraZeneca, 2, Astra-Zeneca, 2, Bayer, 2, 5, BMS, 2, 5, Eicos Sciences, 5, Eli Lilly & Company, 5, Eli Lilly and Company, 5, EMERALD, 5, Emerald, 5, Genzyme, 5, Janssen, 5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8; **E. Rampakakis**, None; **M. Movahedi**, None; **A. Cesta**, None; **J. Sampalis**, None; **C. Bombardier**, AbbVie, 2, 5, AbbVie Medical, 2, Amgen, 2, ECHO Project Co-PI for Rheumatology, 9, Genzyme, 2, GSK, 5, 9, Hospira, 2, Janssen, 2, 5, Medexus, 2, Merck, 2, 5, Novartis, 2, 5, 9, Pfizer, 2, 5, 9, Schering, 2.

Abstract Number: 0433

Comparison of PROMIS Computerized Adaptive Testing-Administered Item Banks versus Fixed Short Forms in Juvenile Myositis

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

Background/Purpose: Compared to healthy children, youth with juvenile myositis (JM) often report poorer health-related quality of life (HRQoL). Legacy HRQoL measures may underestimate the impact of JM due to floor/ceiling effects. Patient-Reported Outcomes Measurement Information System® (PROMIS) HRQoL measures have undergone initial validation in pediatric rheumatic diseases, including JM. PROMIS can be administered by using computerized adaptive testing (CAT) item banks or fixed short forms (FSF), but the relative benefits of CAT vs FSF are not known. The purpose of this study was to compare CAT and FSF.

Table 1. Comparison of PROMIS Computerized Adaptive Testing (CAT)-Administered Item Banks and Fixed Short Forms (FSF)

		CAT			FSF			CAT vs FSF		
	Domain	n	Median # Questions Administered [IQR]	Median T-Score* [IQR]	n	# Questions Administered	Median T-Score* [IQR]	Pearson's Correlations	t-Test (p-value)	Cohen's D (effect size)
CHILD	Anxiety	49	12 (6,12)	38.7 [31.9, 47.1]	48	8	33.5 [33.5, 44.6]	0.91	0.7864873	0.0393214
	Depression	49	6 (5,12)	44.6 [31.8, 55.0]	48	8	43.1 [35.2, 52.4]	0.89	0.9493802	0.0092124
	Fatigue	49	11 (6,12)	36.3 [25.6, 51.1]	49	10	37.3 [30.3, 46.4]	0.92	0.6970946	0.0559414
	Mobility	49	12 (5,12)	56.4 [46.4, 61.7]	49	8	58.5 [48.2, 58.5]	0.92	0.5942272	-0.0766145
	Pain Interference	49	12 (5,12)	32.0 [32.0, 44.8]	49	8	34.0 [34.0, 43.4]	0.87	0.4046734	0.1201029
	Upper Extremity	49	12 (12,12)	57.3 [46.0, 57.3]	49	8	56.7 [56.7, 56.7]	0.92	0.0781128	-0.2571733
PARENT-PROXY	Anxiety	67	5 (5,12)	44.4 [33.7, 52.2]	66	8	34.6 [34.6, 47.6]	0.90	0.0001066	0.5080356
	Depression	67	5 (5,12)	44.7 [33.2, 53.6]	66	6	36.2 [36.2, 48.9]	0.79	0.0556075	0.2399114
	Fatigue	67	5 (5,12)	43.9 [33.2, 52.4]	66	10	38.8 [34.1, 49.0]	0.83	0.0123592	0.3167688
	Mobility	67	12 (5,12)	54.0 [43.6, 60.2]	66	8	56.5 [44.2, 56.5]	0.84	0.5333983	0.0770758
	Pain Interference	67	12 (5,12)	40.6 [36.8, 50.5]	66	8	37.8 [37.8, 47.6]	0.82	0.1239677	0.1918397
	Upper Extremity	67	12 (5,12)	47.1 [38.6, 55.7]	66	8	54.7 [39.8, 54.7]	0.86	0.2806785	-0.1339051

*higher score for anxiety, depression, fatigue and pain interference indicates worse symptoms while higher score for mobility and upper extremity indicates better function

	Group (by t-Score)	Anxiety				Depression				Fatigue				Mobility				Pain Interference				Upper Extremity			
		n	Corr[a]	P[b]	ES[c]	n	Corr[a]	P[b]	ES[c]	n	Corr[a]	P[b]	ES[c]	n	Corr[a]	P[b]	ES[c]	n	Corr[a]	P[b]	ES[c]	n	Corr[a]	P[b]	ES[c]
CHILD	<45	33	0.66	0.26	-0.20	25	0.66	0.05	-0.42	34	0.61	0.13	-0.27	9	0.82	0.01	-1.21	38	0.71	0.55	-0.10	11	0.71	0.221	-0.39
	45-55	7	0.41	0.19	0.56	12	0.59	0.18	0.41	6	0.86	0.05	1.03	12	0.71	0.03	-0.70	7	-0.02	0.26	0.47	7	0.63	0.005	-1.65
	>55	8	0.64	0.68	0.15	11	0.58	0.33	0.31	9	0.43	0.03	0.92	28	NA*	0.00	0.67	4	0.46	0.03	2.05	31	NA*	NA*	Inf**
PARENT-PROXY	<45	34	0.61	0.24	0.21	35	0.30	0.73	-0.06	35	0.65	0.04	-0.36	19	0.85	0.02	-0.56	41	0.64	0.05	-0.32	28	0.72	0.08	-0.34
	45-55	25	0.72	0.00	1.02	20	0.33	0.00	0.90	21	0.52	0.00	1.07	20	0.61	0.07	-0.43	17	0.19	0.01	0.74	7	0.39	0.44	-0.31
	>55	7	0.80	0.99	0.00	11	0.63	0.94	-0.02	10	0.86	0.02	0.89	27	NA*	0.00	2.06	8	0.64	0.36	0.34	31	NA*	NA*	Inf**

[a] Pearson Correlations between FSF and CAT
[b] Paired t-test p-value
[c] Effect size = mean difference/standard deviation of differences.
*NA = not applicable as CAT and FSF values were the same
**Inf = infinite value

Table 2. Comparison of CAT and FSF by specific T-score ranges

Methods: JM patients (5-17 yo) and their parents were recruited at clinic visits. Demographic and clinical assessments were collected, including: Physician Global Assessment of Disease Activity (PGA); Disease Activity Score (DAS-Muscle/-Skin); muscle enzymes; and Childhood Myositis Assessment Scale (CMAS). Patients (8-17 yo) completed self-report versions and parents (of patients 5-17 yo) completed parent proxy versions of the following PROMIS domains in both CAT and FSF: Fatigue, Pain Interference, Upper Extremity Function, Mobility, Anxiety and Depressive Symptoms. To study the extreme scorers and middle scorers, participants were split into three groups by PROMIS CAT T-scores (< 45, 45-55, >55). Pearson correlations, paired t-tests, and Cohen's d were used to compare PROMIS CAT and FSF for the entire cohort and for each of the three T-score groupings.

Results: Data from 67 patient-parent dyads were analyzed. Most patients were 8-17 yo (n=49; 73%), diagnosed with juvenile dermatomyositis (n=61; 91%), female (n=56; 84%), and white (n=51; 76%). Median [IQR] age of onset was 5.2 [3.9, 7.1] and age at initial study visit was 11.8 [7.4, 15.2]. Median [IQR] clinical data were: PGA 0.5 [0.0, 1.5]; DAS-Muscle 0.0 [0.0, 1.0]; DAS-Skin 1.0 [0.0, 5.0]; and CMAS 52.0 [50.0, 52.0]. Median [IQR] muscle enzyme values were: CPK 92.0 [69.0, 130.0]; AST 28.5 [23.0, 32.8]; ALT 14.0 [11.2, 17.8]; LDH 257.0 [223.0, 307.0]; and Aldolase 5.5 [4.8, 6.0]. PROMIS CAT and FSF were highly correlated (Pearson's correlation coefficients ranging 0.79-0.92) (Table 1). Mean scores between CAT and FSF were not significantly different except in parent proxy anxiety and fatigue, though effect sizes were modest (0.508 and 0.317, respectively). Correlations between CAT and FSF varied based on domains, patient vs parent report, and T-score groupings (Table 2). Review of scatterplots showed floor/ceiling effect at the less symptomatic extreme in all FSF domains (Figure 1).

Conclusion: PROMIS CAT is feasible in clinical settings and is comparable to FSF. Additionally, CAT had less pronounced floor/ceiling effects than FSF, allowing detection of individual differences in low symptom/disability scorers. CAT is recommended for long-term follow-up of JM patients given that deconditioning often persists even in remission. Future studies should focus on multicenter replication of these findings, benefits of CAT vs FSF in patients with more severe symptoms, and clinical interpretability (e.g. minimal important differences, severity strata).

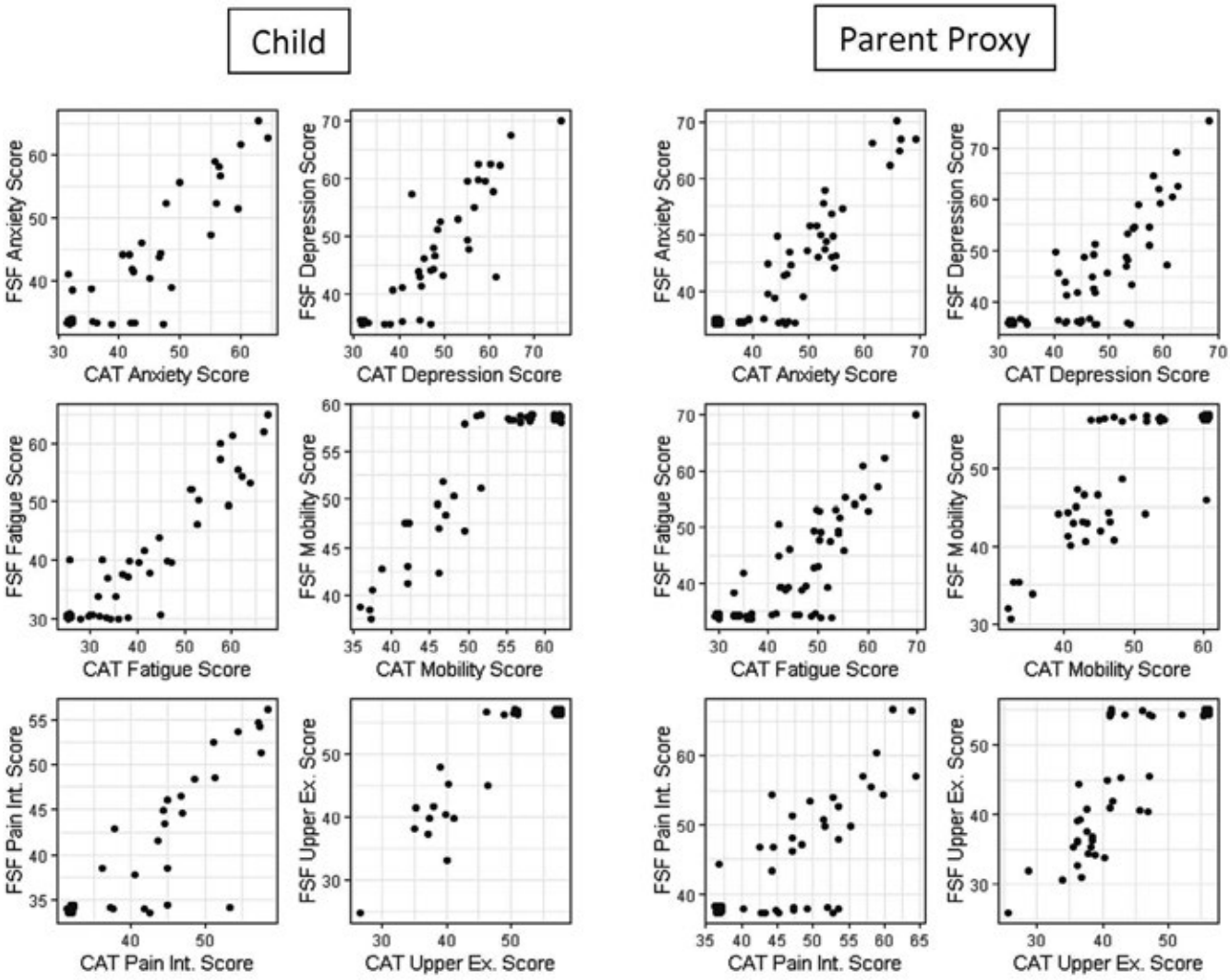


Figure 1. Child self-report and parent-proxy report PROMIS CAT vs FSF score scatterplots by domain

Disclosure: R. Patel, None; **V. Esparza**, None; **J. Lai**, None; **E. Gray**, None; **R. Chang**, None; **D. Cella**, AbbVie, 5, Alexion Pharmaceuticals, 5, Astellas Pharma, 5, Bayer AG, 5, Board of Directors for PROMIS Health Organization, 6, Bristol-Myers Squibb, 5, Clovis Oncology Inc, 5, Clovis Oncology Inc., 5, Evidera, 5, Exelixis Inc., 5, FACITtrans LLC (FACIT.org), 4, Functional Assessment of Chronic Illness Therapy (FACIT.org), 4, Horizon Pharma Inc., 5, Janssen Pharmaceuticals Inc, 5, Janssen Pharmaceuticals Inc., 5, Merck/Schering-Plough Pharmaceuticals, 5, National Academy of Sciences, 5, Novartis Pharma K.K. (Japan), 5, Pfizer Inc, 5, Pfizer Inc., 5, Pled Pharma, 5, PROMIS Health Organization, 6, Regeneron Pharmaceuticals Inc., 5; **K. Ardalan**, None.

Abstract Number: 0434

Ixekizumab Significantly Improves Patient-reported Overall Health as Measured by SF-36 in Patients with Active Ankylosing Spondylitis/ Radiographic Axial Spondyloarthritis: 52-Week Results of Two Phase 3 Trials

Cheng-Chung Wei ,[1] Theresa Hunter,[2] Filip Van den Bosch,[3] Jessica Walsh,[4] Uta Kiltz,[5] Yan Dong,[6] David Sandoval,[6] Luis Leon,[6] Vibeke Strand,[7] and Xiaoqi Li[2], [1]Chung Shan Medical University, Taichung City, Taiwan (Republic of China), [2]Eli Lilly and Company, Indianapolis, [3]Ghent University Hospital, Ghent, Belgium, [4]Division of Rheumatology, University of Utah, Salt Lake City, UT, [5]Rheumazentrum Ruhrgebiet/Ruhr University Bochum, Herne, Germany, Herne, Germany, [6]Eli Lilly and Company, Indianapolis, IN, [7]Division of Immunology/Rheumatology, Stanford University, Stanford, CA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

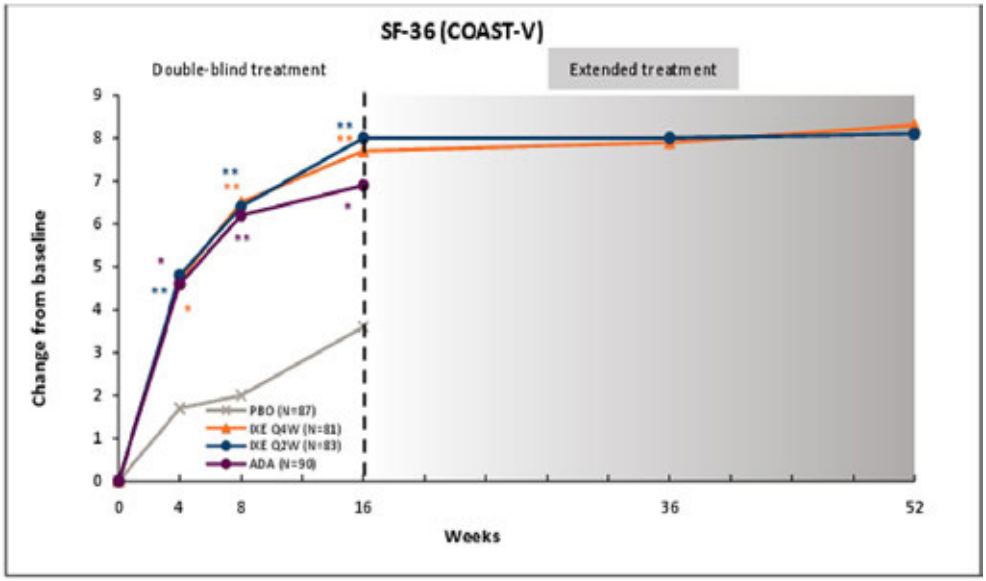
Background/Purpose: Previous trials have used the Short Form (SF)-36 questionnaire to evaluate the impact of ankylosing spondylitis/radiographic axial spondyloarthritis (AS/r-axSpA) on health-related quality of life (HRQoL).[1] Ixekizumab (IXE), is a high-affinity monoclonal antibody that selectively targets interleukin-17A and helps improve HRQoL in patients with AS/r-axSpA.[2] The purpose of this analysis was to evaluate the effect of 52 weeks of treatment with IXE on self-reported HRQoL by SF-36 in patients with active AS/r-axSpA who fulfilled ASAS and modified New York criteria and were naïve to biologic therapy or had failed on/were intolerant to ≥1 but not more than 2, TNF inhibitors (TNF-IRs).

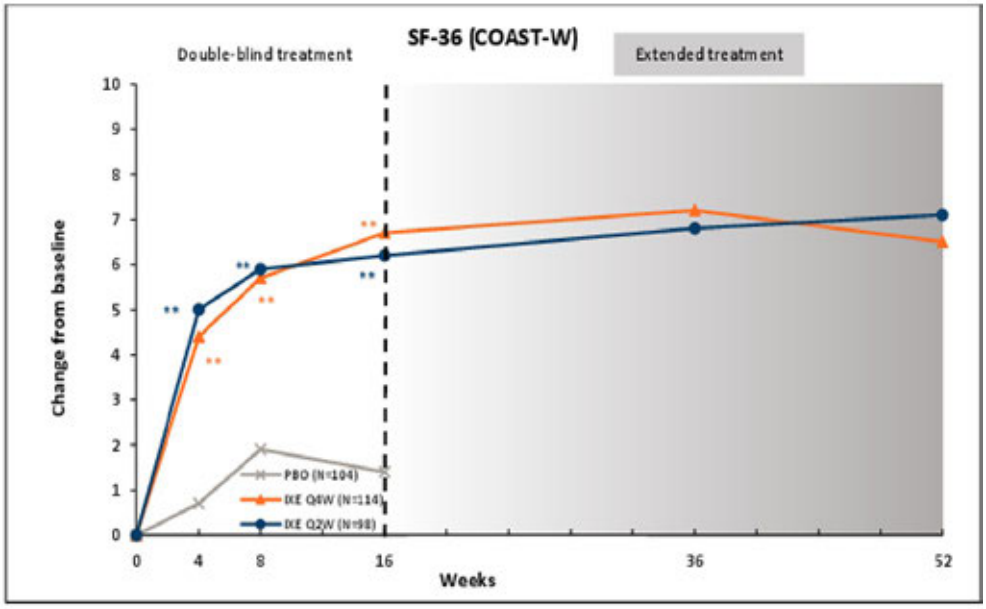
Methods: COAST-V and COAST-W are Phase 3 randomized controlled trials (RCTs) including active and placebo (PBO) comparators in the first 16 weeks in patients with active AS/r-axSpA; BASDAI and back pain scores ≥4; no prior treatment with biologic agents (COAST-V) or TNF-IR (COAST-W). During the double-blind treatment period, patients were randomized 1:1:1:1 to 80 mg IXE every 4 weeks (Q4W) or every 2 weeks (Q2W), active reference arm (adalimumab [ADA] 40mg), or PBO (COAST V) and 1:1:1 to IXE 80 mg Q4W, IXE 80 mg Q2W or PBO (COAST W). At Week 16, patients entered the extended treatment period (Weeks 16-52). Patients initially assigned to PBO/ADA were reassigned to IXEQ4W or IXEQ2W at Week 16. Patients already receiving IXE remained on their assigned treatment regimens through Week 52. Changes from baseline in SF-36 up to Week 16 were analyzed by mixed model for repeated measures. Changes from baseline in SF-36 over Weeks 36-52 were summarized using raw mean with modified baseline observation carried forward (mBOCF) for missing data imputation.

Results: Statistically significant differences in SF-36 Physical Component Summary (PCS) scores were reported in Weeks 4-16 between PBO and IXE Q4W and Q2W groups in COAST-V and COAST-W ($P \leq 0.002$ and $P \leq 0.001$, respectively). Improvements in PCS scores continued at Week 36 and sustained to Week 52 in both COAST RCTs (Figure; Table). Changes in Mental Component Summary scores were modest (Table). Improvements in all domains were reported at 52 weeks with both Q4W and Q2W doses of IXE in both trials (Table).

Conclusion: Improvements in patient-reported HRQoL in A/r-axSpA patients measured with SF-36 were observed at Weeks 4 and 16 and sustained up to 52 weeks of continuous IXE treatment.

Figure 1: SF-36 Physical Component Summary Mean Change from Baseline (COAST-V and COAST-W)





*p≤0.002, **p≤0.001 vs. PBO. Mixed model for repeated measures used to compare least-squares means up to Week 16. No model applied for Weeks 36-52. Missing data imputation was used for Weeks 36-52 only.

Disclosure: C. Wei, AbbVie, 2, 5, BMS, 2, 5, Celgene, 2, 5, Chugai, 5, Eisai, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi-Aventis, 5, TSH Biopharm, 2, 5, UCB Pharma, 2, 5; **T. Hunter**, Eli Lilly, 1, 3, Eli Lilly and Company, 1, 3; **F. Van den Bosch**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, Bristol-Myers Squibb, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sanofi and UCB, 5, 8, ABBVIE, CELGENE, ELI LILLY, GALAPAGOS, MERCK, NOVARTIS, PFIZER, VCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **J. Walsh**, AbbVie, 2, 5, ABBVIE, NOVARTIS, LILLY, AMGEN, UCB, 5, Amgen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, PFIZER, ABBVIE, 2,

Table: SF-36 Baseline Scores and Mean Change at Week 52

	COAST-V				COAST-W			
Parameter	IXE Q4W (N=81)		IXE Q2W (N=83)		IXE Q4W (N=114)		IXE Q2W (N=98)	
	BL	ΔWk 52	BL	ΔWk 52	BL	ΔWk 52	BL	ΔWk 52
Physical Component Summary	36.4	8.3	36.6	8.1	30.3	6.5	30.7	7.1
Mental Component Summary	50.7	2.2	46.9	4.5	46.5	4.1	45.2	4.0
Physical Function	39.2	7.0	38.1	8.0	31.5	6.1	31.7	7.6
Role-Physical	39.3	6.9	38.6	6.7	34.5	4.7	34.3	5.3
Bodily Pain	36.7	9.7	36.4	9.3	31.4	8.7	31.2	8.4
General Health	41.8	4.2	40.2	5.8	36.0	4.9	36.3	4.7
Vitality	45.9	6.1	44.9	6.9	41.6	6.3	41.4	6.4
Social-Functioning	46.2	4.1	42.9	6.0	40.4	5.0	38.6	5.3
Role-Emotional	46.2	4.3	43.3	5.0	40.9	3.6	40.2	4.1
Mental Health	48.2	2.5	44.4	5.7	43.5	5.3	42.6	5.3

BL=baseline; Wk=Week

UCB, 5; **U. Kiltz**, AbbVie, 2, 5, 8, ABBVIE, NOVARTIS, CHUGAI, JANSEN, MSD, UCB, 8, ABBVIE, NOVARTIS, LILLY-,BIOCAD, GRUNENTHAL,UCB, 5, ABBVIE, NOVARTIS, PFIZER,BIOGEN, 2, Biocad, 2, 5, Biogen, 2, 5, Chugai, 2, 5, 8, Eli Lilly, 2, 5, Eli Lilly and Company, 5, Grünenthal, 2, 5, 8, Janssen, 8, Jasnssen, 2, 5, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8; **Y. Dong**, Eli Lilly, 1, 3; **D. Sandoval**, Eli Lilly, 1, 3, Eli Lilly and Company, 1, 3; **L. Leon**, Eli Lilly, 1, 3; **V. Strand**, Abbvie, 5, AbbVie, 5, Amgen, 5, Amgen, Abbvie, Bayer, BMS, Boehringer Ingelheim, Celltrion, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, UCB, 5, AstraZeneca, 5, AURA, 8, Bayer, 5, BMS, 5, Boehringer Ingelheim, 5, Celgene, 5, Celltrion, 5, Cleveland Clinic, 8, CORRONA, 5, Crescendo, 5, Crescendo Bioscience, 5, Eli Lilly, 5, EMD Serono, 5, Genentech, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Inmedix, 5, Janssen, 5, Kezar, 5, Lilly, 5, Merck, 5, NACCME, 8, Novartis, 5, Pfizer, 5, Purdue, 8, RA Forum, 8, RAN, 8, Regeneron, 5, Roche, 5, Samsung, 5, Sandoz, 5, Sanofi, 5, Servier, 5, Setpoint, 5, SLRA, 8, UCB, 5, Up to Date, 7, Washington University, 8, WIR, 8, WRA, 8; **X. Li**, Eli Lilly and Company, 1, 3.

Abstract Number: 0435

Understanding Which Patient-Reported Outcomes Are Important to Rheumatology Patients: Findings from ArthritisPower

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient-reported outcomes (PROs) are important indicators of treatment effectiveness and their role is increasing in comparative effectiveness studies. Little is known about PRO measures patients find most

important for their disease, treatment effectiveness and health outcomes. In this study, we examined PROs voluntarily selected by patients with rheumatologic conditions to further elucidate which disease symptoms they found most important to track within the ArthritisPower registry. These findings will be useful to inform future data collection efforts for trial and clinical study planning. As the study is ongoing, this abstract will discuss initial PRO selections of study participants.

Methods: Adult US patients with self-reported rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), osteoporosis (OP), osteoarthritis (OA), or fibromyalgia syndrome (FMS) in the ArthritisPower registry were invited to participate via an email invitation. Participants were prompted to select up to ten PRO (symptom) measures they felt were important to track for their condition at baseline via the ArthritisPower smartphone and web-based app. Patient-Reported Outcomes Measurement Information System (PROMIS) instruments focusing on symptoms of pain, physical and cognitive function, mental health, fatigue, social function, work impact, sexual function, and sleep were offered. The Outcomes Measures in Rheumatology (OMERACT) RA flare instrument (only for those with RA) and the Lilly-developed morning joint stiffness duration question were also offered. At three subsequent time points (Month [m] 1, m2, m3), participants were given the option to continue tracking their previously selected PRO measures or change to different measures. At m3, participants complete an exit survey to prioritize all measures selected during study participation and to specify other symptoms not available that they would have wanted to track. Descriptive statistics were conducted on baseline data.

Table. **Patient Reported Outcome Measures Selected by Rheumatology Patients**

Domain	N = 251 n (%)
Fatigue	**211 (84.1)**
Mental Health	**206 (82.1)**
Depression	136 (54.2)
Anxiety	108 (43.0)
Applied Cognition Ability	104 (41.4)
Anger	40 (15.9)
Pain (effect on function, behavior)	**205 (81.7)**
Pain Interference	126 (50.2)
Pain Intensity	123 (49.0)
Pain Behavior	107 (42.6)
Physical Function	**181 (72.1)**
Social Function	**167 (66.5)**
Social Isolation	83 (33.1)
Ability to Participate Social	77 (30.7)
Emotional Support	38 (15.1)
Social Satisfaction Discretionary Social Activities	37 (14.7)
Satisfaction Roles Activities	22 (8.8)
Sleep	**162 (64.5)**
Morning Joint Stiffness	**142 (56.6)**
Sexual Function	**27 (10.8)**
Impact on Work	**22 (8.8)**
RA Flare*	**86 (69.9)**

*Measure offered only to participants with RA; N=123

Results: As of May 2019, 292 participants enrolled in this study and 251 completed baseline assessments. Mean age was 55.6 (9.2) years, 89.6% female, 91.2% White, mean disease duration of 12 (10.7) years. These characteristics were similar to the overall ArthritisPower population. The majority (64.1%) self-reported OA, followed by RA (49.0%), FMS (40.6%), PsA (26.3%), OP (20.3%), AS (15.5%) and SLE (5.6%), not mutually exclusive. The top 3 PRO domains that participants chose at baseline, were fatigue, mental health, and pain (Table). The average number of instruments selected for baseline completion was 6.9 (2.4).

Conclusion: Participants prioritized tracking fatigue, aspects of mental health, pain, physical function, social function, sleep, and morning stiffness. These findings provide insights into symptoms rheumatology patients find most important and will be useful to inform the design of future patient-centric clinical trials and real-world evidence generation.

Disclosure: W. Nowell, AbbVie, 1, Allergan, 1, Biogen, 1, BMS, 1, CVS, 1, Eli Lilly, 1, Global Healthy Living Foundation, 3, GSK, 1, Merck, 1, Pfizer, 1, Stryker, 1; **C. Gaich**, Eli Lilly & Company, 3, 4, Eli Lilly and Company, 1, 3, 4; **K. Gavigan**, Global Healthy Living Foundation, 3; **Z. Cai**, Eli Lilly and Company, 4, Eli Lilly and Company, 3; **A. Cardoso**, Eli Lilly and Company, 1, 3; **T. Hunter**, Eli Lilly, 1, 3, Eli Lilly and Company, 1, 3; **J. Birt**, Eli Lilly and Company, 3, Eli Lilly and Company, 4; **J. Workman**, Eli Lilly and Company, 1, 3, 4; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5.

Abstract Number: 0436

Poor Concordance Between Remission Judged by Physicians and a Patient-Acceptable Symptom State in Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Both the evaluation of disease activity in psoriatic arthritis (PsA) and the determination of the impact of the disease on patients' lives are subjects of intense research at present. Our objective was to evaluate the concordance between the state of clinical remission and an acceptable symptomatic state for patients.

Methods: Post hoc analysis of a multicentre study that included 223 patients with PsA treated with biologic and non-biologic drugs. Remission was defined according to the evaluating physicians and DAPSA definitions. DAPSA score was calculated by adding the number of tender and swollen joints, VAS pain, patient-reported global assessement (PtGA), and CRP (mg/dl). The cDAPSA was calculated without the contribution of CRP. DAPSA and cDAPSA score ≤ 4 identified clinical remissions.

Table 1. Demographic and clinical characteristics of PsA patients with a PsAID score < 4

	Total N (122)
Male, n (%)	70 (57.4)
Age, mean (SD), yrs.	54.5 (12.7)
BMI, mean (SD) (kg/m²)	27.1 (3.9)
CRP (mg/L), mean (SD)	2.8 (3.3)
Comorbidities, n (%)	
Dyslipidemia	40 (32.8)
HBP	33 (27.0)
Obesity	30 (24.6)
DM	12 (9.8)
PsA clinical patterns, n (%)	
Axial	3 (2.5)
Peripheral	107 (87.7)
Mixed	12 (9.8)
DIP disease	45 (36.9)
Familial history, n (%)	
Psoriasis	60 (49.2)
PsA	11 (9.0)
Ankylosing spondylitis	2 (1.6)
PsA duration, mean (SD), yrs.	9.6 (7.9)
Skin symptoms duration, mean (SD), yrs.	21.6 (14.5)
Articular symptoms duration, mean (SD), yrs.	11.9 (8.7)
Radiologic findings	
Erosions in hands, n (%)	40 (32.8)
Erosions in feet, n (%)	33 (27.0)
PASI, mean (SD)	1.2 (3.8)
HAQ, mean (SD)	0.2 (0.3)
HAQ ≤ 0.5, n (%)	104 (85.2)
MDA, n (%)	76 (62.3)
Kappa [$CI_{95\%}$] HAQ ≤ 0.5 vs. PsAID < 4	0.53 [0.42–0.64]
Kappa [$CI_{95\%}$] MDA vs. PsAID < 4	0.36 [0.24–0.48]

MDA: Minimal disease activity; SD: Standard deviation; BMI: Body mass Index; CRP: C-Reactive Protein; HBP: High blood pressure; DIP: distal interphalangeal joint disease; DM: Diabetes mellitus; PASI: Psoriasis Area and Severity Index; HAQ: Health Assessment Questionnaire; PsAID: Psoriatic Arthritis Impact of Disease; CI : Confidence intervals.

A descriptive statistical analysis of all the variables was performed, including central tendency and dispersion measures for continuous variables, and absolute and relative frequencies for categorical variables. Student's t-test, Mann-Whitney-U test or Kruskall Wallis H test were used to compare quantitative variables and Pearson's chi-square or Fisher's exact tests for qualitative variables. Concordance was assessed using Cohen's κappa (k) and was considered as follows: < 0.20 = poor, 0.21–0.40 = fair, 0.41–0.60 = moderate, 0.61–0.80 = good, and 0.81–1.00

Table 2. Kappa agreement between remission and patient-acceptable symptoms state

			Skin and joint remission*	
			No	Yes
PASS = PsAID <4	No	N	86	15
		%	50,9%	27,8%
	Yes	N	83	39
		%	49,1%	72,2%
Total		N	**169**	**54**
		%	**75,8%**	**24,2%**
Kappa [$CI_{95\%}$]			0,16 [0,05-0,26]	

PASS: Patient-Acceptable Symptoms State. PsAID: Psoriatic Arthritis Impact of Disease.
CI: Confidence Interval. *according to the evaluating rheumatologist.

= very good. Tests were two-tailed with a significance level of 5%. Data were analysed using SPSS V19.0 statistical software.

The PsAID questionnaire reflects the impact of PsA from the patients' perspective. It is comprised of 12 physical and psychological domains. Each domain is rated from 0 to 10 with a different weighting. Total score is divided by 20. The final score has a range from 0 (best status) to 10 (worst status) with a cutoff of 4. A PsAID value below 4 defines a PASS state.

Results: Of the 223 patients analysed, 122 (54.7%) met the PsAID criterion below 4. The characteristics of this sub-population are shown in Table 1. There was fair (k: 0.23) and poor (k: 0.17) agreement between joint and cutaneous remission respectively (according to the evaluating physician) and PASS status. the degree of agreement between a complete clinical remission (both cutaneous and articular according to the evaluating physician) and the PASS status was low (k: 0.16, Table 2). There was a moderate agreement (k: 0.46) between DAPSA remission and PASS, while there was almost a good concordance (k: 0.58) between cDAPSA remission and PASS.

Conclusion: The agreement between the state of remission judged by doctors and PASS is quite low. The degree of agreement between DAPSA remission and PASS is better, but it is still moderate. Both DAPSA and PsAID should be included in the routine clinical assessment of patients with PsA, since both offer a superior overall view to that given by each instrument separately. It is also better to define remission in accordance to a composite index rather than according to physicians´ opinion.

Disclosure: R. Queiro, None; **E. Pardo**, None; **L. Charca**, None; **S. Alonso**, None; **L. Arboleya**, None; **M. Alperi-López**, None.

Abstract Number: 0437

Is There Any Relationship Between Cardiovascular Comorbidity and a Patient-Acceptable Symptom State in Psoriatic Arthritis?

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Background/Purpose: Psoriatic arthritis (PsA) is accompanied by a high prevalence cardiovascular (CV) comorbidity. This comorbidity has been associated with worse therapeutic results as well as worse quality of life. We aimed to evaluate if the presence of this CV comorbidity could be associated with a greater impact of PsA on patients´ lives according to the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire.

Methods: Post hoc analysis of a multicentre cross-sectional study that included 223 patients with PsA according to CASPAR criteria and under systemic treatment. The impact of the disease was assessed by the PsAID questionnaire. The impact of disease was evaluated by the PsAID, a questionnaire recently developed by the EULAR that reflects the impact of PsA from the patient's perspective. It is comprised of 12 physical and psychological domains. Each domain is rated from 0 to 10 with a different weighting. The total score is divided by 20. The final score has a range from 0 (best status) to 10 (worst status) with a cut-off of 4. A PsAID value less than four has been defined as a patient-acceptable symptom state (PASS). A descriptive statistical analysis of all the variables was performed, including central tendency and dispersion measures for continuous variables, as well as absolute and relative frequencies for

Table 1. Demographic and clinical characteristics of PsA patients with a PsAID score < 4

	Total N (122)
Male, n (%)	70 (57.4)
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PsA clinical patterns, n (%)	
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Familial history, n (%)	
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HAQ ≤ 0.5, n (%)	104 (85.2)
MDA, n (%)	76 (62.3)
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Kappa [$CI_{95\%}$] MDA vs. PsAID < 4	0.36 [0.24–0.48]

MDA: Minimal disease activity; SD: Standard deviation; BMI: Body mass index; CRP: C-Reactive Protein; HBP: High blood pressure; DIP: distal interphalangeal joint disease; DM: Diabetes mellitus; PASI: Psoriasis Area and Severity Index; HAQ: Health Assessment Questionnaire; PsAID: Psoriatic Arthritis Impact of Disease; CI: Confidence intervals.

categorical variables. Student's t-test, the Mann-Whitney U test, and the Kruskall-Wallis H-test were used to compare quantitative variables, and Pearson's chi-square test or Fisher's exact tests were used for qualitative variables. Concordance between different PsA outcomes was assessed using Cohen's κappa (k) and was considered as follows: < 0.20 = poor, 0.21–0.40 = fair, 0.41–0.60 = moderate, 0.61–0.80 = good, and 0.81–1.00 = very good. The tests were two-tailed with a significance level of 5%. The data was analysed using SPSS V19.0 statistical software.

Results: Out of the 223 patients included in this analysis, 122 (54.7%) were in PASS status. The main characteristics of this subpopulation are shown in Table 1. There were more smokers among patients who did not achieve the PASS (25% vs. 13%, p= 0.08). However, there were more obese among those who did reach a PASS (24.6% vs. 15.8%, p= 0.108). No differences were found in the distribution of other CVRF between patients with and without PASS. Among PASS patients there was a significantly higher frequency of coronary heart disease (6.6%) than in non-PASS patients (1%), p = 0.035. The number of CV risk factors did not differ between the two groups.

Conclusion: In this multicentre study, we found no association between CV risk factors and the achievement of a PASS status in patients with PsA under systemic therapy. All in all, patients with PsA should be encouraged to maintain healthy lifestyle habits.

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Abstract Number: 0438

Longitudinal Construct Validity and Responsiveness of MDHAQ and HAQDI in PsA: Can MDHAQ Replace HAQDI?

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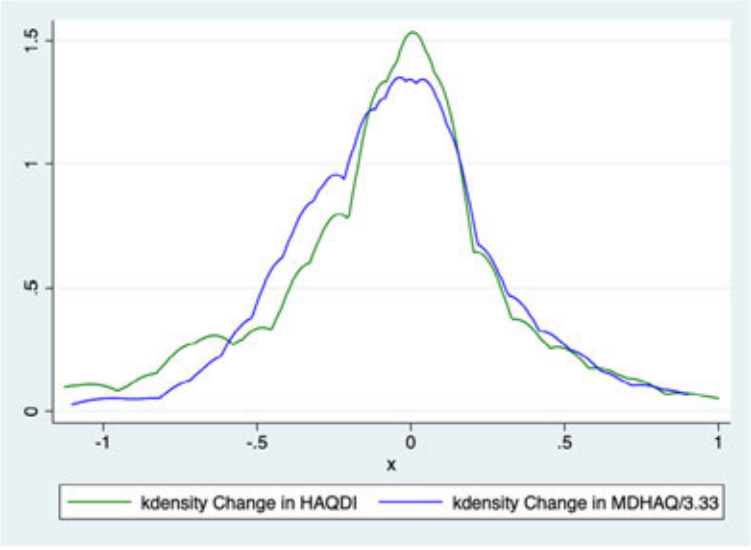

Figure 1. Distribution of change in HAQDI vs change in MDHAQ/3.33

Variable	N	Mean	SD	p50	p25	p75	min	max
Age	278	51.53	14.59	52.00	41.00	62.77	19.00	94.41
Body Mass Index (kg/m^2)	273	29.88	6.89	28.19	25.03	33.47	16.96	55.74
Total Tender Joint Count	251	4.32	6.37	2.00	0.00	6.00	0.00	40.00
Total Swollen Joint Count	252	2.27	4.45	1.00	0.00	3.00	0.00	34.00
Body Surface Area (%)	245	1.95	7.44	0.20	0.00	1.00	0.00	70.00
HAQDI	278	0.64	0.62	0.50	0.00	1.13	0.00	2.38
MDHAQ	278	1.89	1.65	1.67	0.33	3.00	0.00	7.33
	N	Yes	No					
Minimal Disease Activity >5	243	64	179					
Dactylitis	251	20	231					
Enthesitis	252	66	186					

Table 1. Baseline characteristics of patient cohort (n=278)

	Any Visit		At Baseline Visit		Change between two visits							
	N	rho (p-value)	N	rho (p-value)	N	HAQDI			MDHAQ			rho over time, longitudinal (p-value)
						Mean Change	SD	SRM	Mean Change	SD	SRM	
All patients	438	0.84 (<.001)	278	0.83 (<.001)	160	-0.07	0.38	0.19	-0.16	1.11	0.14	0.55 (<0.001)
Patients with:												
Tender joint counts ≥4	191	0.80 (<.001)	115	0.77 (<.001)	76	0.001	0.45	0.003	0.009	1.28	0.007	0.47 (<0.001)
Swollen joint count ≥4	117	0.83 (<.001)	98	0.83 (<.001)	43	-0.02	0.43	0.04	-0.11	1.19	0.09	0.35 (0.02)
C-DAPSA≥14	197	0.80 (<.001)	127	0.80 (<.001)	70	-0.001	0.45	0.004	-0.03	1.24	0.03	0.48 (<0.001)

Table 2. Correlation among HAQDI and MDHAQ and Responsiveness to change

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes

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Background/Purpose: The multi-dimensional health assessment questionnaire (MDHAQ) is a patient-reported outcome that is commonly used in clinical practice in the US and comprises of 10 items. Although the validated Health Assessment Questionnaire Disability Index (HAQDI) measures similar constructs as the MDHAQ, is less commonly used and has 16 items. Therefore, the objective of this study is to assess if the MDHAQ (divided by 3.33 to transform to the same scale as HAQDI) can substitute for the HAQDI in ACR20 assessment and cohort studies.

Methods: Between 2016-2019, patients with PsA were enrolled in the Psoriatic Arthritis Research Consortium (PARC), a longitudinal observational cohort at four United States institutions: University of Pennsylvania, Cleveland

Clinic, New York University, and University of Utah. Baseline patient characteristics were descriptively reported. A priori we hypothesized that the MDHAQ and HAQDI would have high correlation at baseline (>0.8) and among the change scores (>0.8) and that responsiveness would be similar. Correlations were calculated among the total scores using Spearman's correlation coefficients at baseline and follow-up visit. Change scores (e.g., score at visit 1 minus score at visit 2) and standardized mean responses were calculated. Sensitivity analyses excluding patients with low disease activity were calculated. We additionally examined agreement with the 20% improvement cut-off to determine the potential effect of using MDHAQ in the ACR20 criteria in place of HAQDI.

Results: HAQDI and MDHAQ data were available in 438 visits in which both questionnaires were completed and 161 patients with HAQDI and MDHAQ at two time points. The mean age was 51.5 ± 14.6 years old, 53% were male, and most had low disease activity with mean swollen (66) and tender (68) joint counts 2.3 ± 4.4 and 4.3 ± 6.4, respectively. At baseline, the mean HAQDI was 0.64 ± 0.62 (range 0-3) and the mean MDHAQ was 1.9 ± 1.7 (range 0-10; Table 1). Dividing the MDHAQ by 3.33 to transform it to the same scale as the HAQDI resulted in a transformed MDHAQ mean of 0.56 ± 0.48 with a mean excursion from the HAQDI score of 0.07 ± 0.35 (Figure 1). Among all time points, the Spearman's correlation coefficient between the two instruments was 0.84 and among the first visit only, the coefficient was 0.83. The mean change over two visits in the HAQDI was -0.07 ± 0.4, with a standardized response mean (SRM) of 0.19 and mean change in the MDHAQ was -0.16 ± 1.1 with an SRM of 0.14. The Spearman's correlation coefficient among the two change variables was 0.55 (Table 2). Using the 20% criteria for the ACR20, the agreement among use of HAQ-DI and MDHAQ is 74%. When excluding patients with a clinical Disease Activity index for Psoriatic Arthritis (c-DAPSA) score < 14 (i.e., low disease activity), the correlation coefficients were similar.

Conclusion: Although the HAQDI consists of more questions than the MDHAQ, the total scores correlated well when analyzed cross-sectionally. However, the correlation was moderate between the change over time. Using the 20% improvement cut-off, most were correctly classified with MDHAQ but MDHAQ cannot directly replace HAQDI for the ACR20 criteria.

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Abstract Number: 0439

Improved Patient-Reported Outcomes in Patients with Persistently Active Rheumatoid Arthritis Following Treatment with Repository Corticotropin Injection

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes
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Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disorder characterized by progressive inflammation and irreversible joint damage. Treatment of active disease includes disease-modifying anti-rheumatic drugs (DMARDs) and short-term corticosteroid (CS) use. A comprehensive assessment of clinical treatment outcomes should include validated patient-reported outcome (PRO) instruments. Repository corticotropin injection (RCI) is approved by the FDA for short-term adjunctive use in the treatment of RA.[1] A naturally sourced complex mixture of purified adrenocorticotropic hormone ($ACTH_{1-39}$) analogues and other pituitary peptides, RCI stimulates endogenous CS production and is an agonist for all 5 melanocortin receptors (MCRs).[1,2] MCR activation by ACTH has been shown to have direct and indirect anti-inflammatory and immunomodulatory effects.[2] A 2-part, multicenter, placebo-controlled Phase 4 trial explored the effect of RCI treatment on PROs with the greatest impact on quality of life (ie, for pain, fatigue, physical functioning, and ability to work) in patients with persistently active RA. Data presented are from the open-label period (ClinicalTrials.gov ID: NCT02919761).

Methods: Adults with persistently active RA (defined as DAS28-ESR >3.2) despite DMARD and CS use received 80 U of RCI subcutaneously, twice weekly during a 12-week open-label period. PRO measurements included the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scale, the Work Productivity and Activity Impairment (WPAI) questionnaire, and the Health Assessment Questionnaire – Disability Index (HAQ-DI). Mean changes from baseline were assessed at Weeks 4, 8, and 12. Patients' global assessments of disease activity and pain were also evaluated.

Results: Of the 259 patients in the modified intent-to-treat population, 89.2% were female and 65.6% were Caucasian (mean age, 51 years). During the 12-week open-label treatment period (wherein 62.9% of patients [163/259] achieved low disease activity by Week 12), mean improvements from baseline were clinically and statistically significant at all time points for HAQ-DI and FACIT-F scores. Clinically and statistically significant improvements in 3

PRO Assessment	Baseline, Mean (SD)	Week 4	Week 8	Week 12
		Mean Change From Baseline (SD)		
FACIT-F	22.8 (8.4)	−5.0 (8.2)*	−6.5 (8.4)*	−8.7 (8.4)*
HAQ-DI	1.7 (0.6)	−0.5 (0.5)*	−0.6 (0.6)*	−0.84 (0.6)*
Patient global assessment of disease activity[b]	63.4 (20.0)	−17.8 (23.6)*	−25.7 (25.2)*	−35.0 (27.3)*
WPAI-RA				
Percent work time missed due to RA[c]	24.9 (27.6)	−7.0 (26.6)	−5.2 (28.0)	−10.8 (26.5)**
Percent impairment while working due to RA[c]	50.3 (27.1)	−18.7 (24.4)*	−18.0 (23.9)*	−25.2 (25.3)*
Percent overall work impairment due to RA[c]	58.1 (28.6)	−17.6 (27.0)*	−17.6 (27.5)*	−25.5 (29.2)*
Percent activity impairment due to RA[c]	63.2 (24.2)	−18.1 (24.3)*	−22.5 (25.3)*	−32.8 (27.4)*
Patient global assessment of pain[d]	64.9 (20.4)	−20.8 (23.3)*	−27.6 (25.3)*	−37.4 (27.4)*

of 4 WPAI subscores – percent impairment while working, percent activity impairment, and percent overall work impairment – were observed at all time points; for percent work time missed, significant improvement was achieved by Week 12. Clinically and statistically significant improvements from baseline at Weeks 4, 8, and 12 were found for patient-reported global assessments of disease activity and pain (see **Table** for results).

Conclusion: During the 12-week open-label treatment period, RCI significantly improved patient-reported pain, fatigue, physical functioning, and work-related impairment as early as Week 4. RCI treatment resulted in rapid and clinically meaningful improvements in PROs deemed most relevant to quality of life by patients with persistently active RA.

1. Acthar® Gel (repository corticotropin injection) [prescribing information]. Mallinckrodt ARD, LLC, 2019.

2. Catania A, et al. *ScientificWorldJournal*. 2010;10:1840-53.

*P<0.001 vs baseline. **P<0.01 vs baseline. a mITT population (all patients who received study drug and had any post-treatment efficacy assessment). b MCID = 15% absolute/20% relative improvement.2 c MCID = 7% absolute change.3 d MCID = 11.4 Abbreviations and MCID references: FACIT-F; Functional Assessment of Chronic Illness Therapy – Fatigue (MCID = 3-41); HAQ-DI, Health Assessment Questionnaire – Disability Index (MCID = 0.21); MCID, minimum clinically important difference; mITT, modified intent-to-treat; PRO, patient-reported outcome; RCI, repository corticotropin injection; SD, standard deviation; WPAI-RA, Work Productivity and Activity Impairment Questionnaire – Rheumatoid Arthritis. 1 Wells GA, et al. J Rheumatol. 1993;20(2):557-60. 2 Tubach F, et al. Arthritis Care Res (Hoboken). 2012;64(11):1699-1707. 3 Reilly MC, et al. Gut. 2007;56(Suppl 3):159. 4 Hawker GA, et al. Arthritis Care Res. 2011;63(Suppl 11):S240-52.

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Abstract Number: 0440

Disease Activity and Quality of Life in Behçet's Syndrome: The Role of Patient Reported Outcome

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SESSION INFORMATION

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Background/Purpose: Behçet's syndrome (BS) is a systemic vasculitis, characterised by recurrent oro-genital ulcers, ocular inflammation and skin manifestations; articular, vascular, gastro-enteric and neurological involvement may also occur.The complex pattern of BS profile can effect negatively on patients' quality of life. The primary aim of this study was to explore the role of quality of life in BS patients by means of patient reported outcome (PRO); the secondary aim was to study any correlation between disease activity, psychiatric symptoms and quality of life.

Methods: The study enrolled 147 patients (86 M, 61 F), all fulfilling the International Study Group (ISG) criteria for BS. Their mean age was 41 ± 7 years (18-77), while the disease duration was 11 ± 4 years (5-18) and the mean follow-up of 7 ± 3 years. Disease activity was evaluated by means of the Behçet's Disease Current Activity Form (BDCAF), while Short-form-36 (SF-36) was used to evaluate quality of life. Disease activity was compared with the global SF-36 score and with each dimension, that includes physical functioning, physical disability, body pain, general health, vitality, social functioning, emotional disability, mental health according the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV). The statistical analysis was performed using Student t-test, Mann-Whitney-U test, ANOVA, and Pearson correlation.

Results: At time of evaluation, according BDCAF, 48 BS patients (33%) had clinically active disease characterized by concomitant types of involvement (40 muco-cutaneous involvement, 18 ocular involvement 8 joint involvement, 5 neurological involvement, 4 gastro-enteric). As expected, the overall SF- 36 scores were significantly lower in patients with clinically active disease. Notably, female BS patients had statistically significant lower scores in all SF-36 domains compared with male patients. When each domain of SF-36 was evaluated, we found that physical disability ($p=0.004$), body pain ($p=0.006$), general health ($p=0.001$), and vitality ($p=0.001$) were significantly lower in patients with disease activity. Notably, vitality ($p=0.001$), physical disability($p=0.004$), social functioning ($p=0.001$), emotional disability ($p=0.003$) and mental health ($p=0.001$) were significantly lower in patients with muco-cutaneous active disease, compared with the other patients with active disease. Moreover, we found a significant correlation between disease activity, high frequency of bipolar disorder and worsening of quality of life.

Conclusion: The combination of PRO measures and disease activity have been demonstrated to add more information compared to the evaluation of disease activity alone. These considerations suggest that the correct assessment of BS needs a multi-dimensional approach, that includes disease activity, disease damage and quality of life.

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Multidimensional Health Assessment Questionnaire (MDHAQ) Scores in Spain vs USA: Similar Scores for Clinical Status and Self-report of Depression in Rheumatoid Arthritis (RA) but Poorer Scores for Both in Spondyloarthropathies (SpA) in Spain

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Background/Purpose: Associations of depression with clinical status in RA[1] and differences in clinical status in different countries[2] have been reported. We compared MDHAQ (multidimensional health assessment questionnaire) scores for clinical and psychological status, including RAPID3 (routine assessment of patient index data) and psychological index, in patients with rheumatoid arthritis (RA) or spondyloarthropathies (SpA) at one setting in the USA vs another in Spain.

Methods: The MDHAQ is a 2-page self-report questionnaire, which is completed by all RA and SpA patients before seeing the rheumatologist at certain rheumatology settings, including one in the USA and another in Spain. MDHAQ data in the 2 settings were compared in a cross-sectional study of patients with RA or SpA. The MDHAQ includes 0-10 scores for physical function (FN), visual analogue scales (VAS) for pain (PN), and patient global estimate (PATGL), compiled into 0-30 RAPID3, for which minimum clinically important improvement (MCII) is 3.8[3]. The MDHAQ also includes a 0-10 fatigue VAS, 0-48 RADAI self-reported painful joints count, 0-60 symptom checklist, as well as 3 psychological queries in the traditional patient-friendly HAQ format concerning depression, anxiety, and sleep quality

Table. MDHAQ demographic, clinical, and psychological scores of RA and SpA patients at two sites, one in USA and the other in Spain. Data are presented as mean (SD) and %.

	RA patients (n=566)			SpA patients (n=209)		
Site	USA N=464	Spain N=102	p	USA N=141	Spain N=68	p
Demographic data						
Age	55.6 (14.8)	58.8 (12.1)	0.043	46.3 (15.0)	55.6 (12.1)	<0.001
Female	86.2%	82.3%	0.317	36.2%	47.0%	0.132
White	141 (40.9%)	93 (91.2%)	<0.001	80 (57.7%)	66 (97.0%)	<0.001
BMI	29.4 (8.1)	26.1 (4.4)	<0.001	29.8 (7.2)	27.7 (5.0)	0.050
MDHAQ scores						
Physical Function	2.6 (2.0)	2.4 (1.8)	0.214	1.9 (1.7)	3.0 (2.1)	<0.001
Pain	5.7 (2.9)	4.5 (2.8)	0.001	4.3 (3.2)	4.9 (3.0)	0.209
PATGL	5.4 (3.0)	4.6 (2.8)	0.022	4.0 (3.0)	5.3 (2.9)	0.001
RAPID3	13.7 (7.2)	11.6 (6.8)	0.009	9.1 (7.5)	13.3 (7.3)	<0.001
Depression (0-3.3)	0.7 (0.9)	0.8 (1.0)	0.476	0.5 (0.8)	1.1 (1.0)	<0.001
Anxiety (0-3.3)	0.8 (0.9)	0.9 (0.9)	0.907	0.7 (0.9)	1.3 (1.0)	<0.001
Sleep problems (0-3.3)	1.3 (1.0)	1.1(1.0)	0.156	1.0 (0.9)	1.5 (1.0)	<0.001

(scores 0 to 3.3). MDHAQ demographic, clinical, and psychological data were compared by diagnostic groups at the 2 settings using Student t-test and Chi^2 test.

Results: Among 775 patients with RA or SpA, 605 were from USA, 464 with RA and 141 with SpA, and 170 from Spain, 102 with RA and 68 with SpA (Table). Patients in the USA were younger than in Spain. Patients with RA were 82-86% female, while SpA patients were 36–47% female - no significant sex differences by site. Patients in the USA were 41-58% white versus 91-97% in Spain (Table). Mean BMI was higher in the USA in both diagnoses. MDHAQ clinical variables in RA patients were higher in the USA vs Spain, statistically significant for pain and RAPID3, although the RAPID3 difference in RA of 2.2 (13.7 in the USA versus 11.6 in Spain) did not meet MCII of 3.8. No significant differences in self-report psychological scores were seen in RA patients in the 2 settings. By contrast, in SpA patients, MDHAQ clinical and psychological variables were higher in Spain vs USA (Table). The difference in RAPID3 of 4.2 (13.3 in Spain versus 9.1 in the US) was greater than the MCII, indicating statistical and clinical significance. Statistically significantly poorer status for depression, anxiety and poor sleep quality also was seen in SpA patients in Spain versus USA, similar to differences in clinical scores.

Conclusion: In comparisons of a setting in the USA vs one in Spain, somewhat higher scores were seen for RA patients in the USA for clinical measures, which did not meet criteria for MCII, and no differences were seen in psychological status. In patients with SpA, poorer status was seen in Spain vs the USA in both clinical and psychological MDHAQ measures. The findings are consistent with associations between self-report of depression and RAPID3, and component physical function, pain, patient global assessment scores.

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Abstract Number: 0442

Multidimensional Health Assessment Questionnaire (MDHAQ) as an Effective Screening Tool to Identify Concomitant Depression in Patients with Rheumatoid Arthritis and Spondyloarthritis in Routine Care

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes

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Background/Purpose: Patients with rheumatoid arthritis (RA) or spondyloarthritis (SpA) are more likely to report depression than the general population, and depression has been associated with poorer outcomes[1,2]. A multidi-

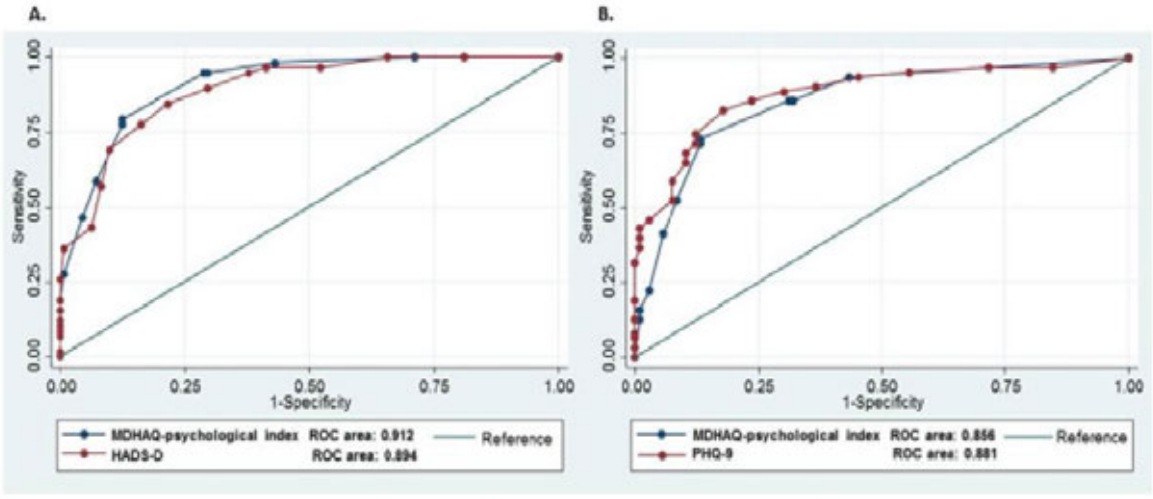
Table: Spearman rank correlations between 3 MDHAQ psychological items and psychological index versus PHQ9 and HADS scores. *p<0.001

MDHAQ/RAPID3: Patient self-report scores	PHQ9	HADS		
		Depression	Anxiety	Total
MDHAQ-psychological items (0-3.3)				
- Sleep problems	0.75*	0.63*	0.62*	0.67*
- Anxiety/being nervous	0.69*	0.64*	0.75*	0.74*
- Depression/feeling blue	0.72*	0.70*	0.70*	0.75*
Total MDHAQ psychological index sleep+ anxiety+ depression (0-9.9)	0.80*	0.73*	0.76*	0.79*
PHQ-9 (0-27)	–	0.78*	0.77*	0.82*

mensional health-assessment questionnaire (MDHAQ) has been found informative in many rheumatic diseases[3], and includes two queries to screen for depression. We compared these 2 MDHAQ depression items to 2 widely-used depression indices: the Patient Health Questionnaire (PHQ-9), and the Hospital Anxiety Depression Scale (HADS).

Methods: Consecutive patients attending two rheumatology clinical settings with a primary diagnosis of either RA or SpA completed a MDHAQ, which includes a 60 Yes/No symptom checklist (one symptom is depression), and a psychological index as the sum of 3 queries in the patient-friendly HAQ format (ranging from "without any difficulty" to "unable to do") concerning dealing with depression, anxiety and sleep quality (each scored 0-3.3 for a total score=0-9.9). Patients also completed the PHQ-9, a depression screening tool (total=0-27, ≥10=depression), and HADS, a 14-item screening tool, 7 for depression (HADS-D) and 7 for anxiety (HADS-A) (total=0-21, ≥8=depression). Spearman correlations between the MDHAQ-psychological index and its 3 individual index items versus PHQ-9 and HADS were computed. Agreement and confidence intervals (CI) between MDHAQ-depression in the symptom checklist versus PHQ-9 ≥10 and HADS-D ≥8 as positive screens for depression was calculated. Receiver-operator characteristic (ROC) curves were analysed for the MDHAQ psychological index, using PHQ-9≥10 or HADS-D≥8 as reference standards.

Figure: ROC curves for MDHAQ psychological index versus 2 external standards: A. PHQ-9≥10 B. HADS-D≥8 (B)



Results: Among 170 patients studied, 102 had RA and 68 had SpA, 82% and 47% females, mean age 58.8 and 55.6 years, respectively. In RA, depression screening was positive in 26% of patients by MDHAQ-depression, 28% by PHQ-9 ≥10, and 33% by HADS-D ≥8, versus 35%, 43%, and 45%, respectively in SpA. Agreement between MDHAQ-depression and PHQ-9≥10 was 83% (kappa= 0.60, 95% CI 0.47, 0.73), and with HADS-D≥8 was 79% (kappa= 0.52, 95% CI 0.39, 0.66). Agreement between PHQ-9≥10 and HADS-D≥8 was 82% (kappa= 0.60 95% CI 0.48, 0.72). Correlations between the MDHAQ psychological index and individual items with PHQ-9 and HADS ranged from 0.62 to 0.82 (p< 0.001) (Table). The area under the ROC curve for the total MDHAQ psychological index was 0.91 (95% CI 0.87, 0.95) with PHQ-9≥10 and 0.86 (95% CI 0.79, 0.91) with HADS-D≥8 (Figure).

Conclusion: The prevalence of positive screening for depression was higher in SpA patients versus RA patients according to each screening tools. MDHAQ self-report of depression showed good agreement with PHQ-9 ≥10 and HADS ≥8 to screen for depression. The three psychological queries on the MDHAQ can be combined into a psychological index to provide a useful clue to screen for depression in busy clinical settings.

References: 1.Matcham F. Rheumatology 2013,52:2136-48. 2.Zhao S. Arthritis Res Ther 2018,20:140. 3. Castrejon I. Bull Hosp Jt Dis 2017;75:93-100.

Disclosure: R. Morlà, None; **M. Riad**, None; **V. Ruiz-Esquide**, None; **F. Espi**, None; **J. Ramirez**, None; **N. Del Castillo**, None; **J. Gomez-Puerta**, None; **R. Sanmarti**, None; **T. Pincus**, Helath Services, 7, Medical History Services LLC, 6, 7, 9, Medical history services LLC, 6, 7; **I. Castrejon**, None.

Abstract Number: 0443

Validation of a Risk Perception Questionnaire Developed for Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment recommendations directed to rheumatoid arthritis patients (RA) may be more easily adopted if they are patient-centered. The adoption of health behaviors is associated with the recognition of risks. Risk perception (RP) is a multidimensional phenomenon that describes the individual's judgment of the likelihood of experiencing something unpleasant (1). Assessing perceived risk helps to explain how RA patients integrate their ideas concerning the disease and its treatments, and how this understanding impacts their self-care management. There is no validated instrument to assess RP in RA patients. The objective of the study was to develop and validate the RP Questionnaire (RPQ) for Spanish speaking patients with RA.

Methods: RPQ development and validation was performed in 3 steps, using convenience samples (**Table 1**). Step-1 included the conceptual model construction (literature review), 20 patient's interviews to identify components from the conceptual model-dimensions and 11 healthcare provider´s consultations who identified RA-related manifestations/complications (network and frequencies analysis). Step-2 consisted of item generation and reduction and ques-

tionnaire feasibility (n=100); for scaling response we selected a direct estimation method of responses, on a visual analogue scale and for item scoring we proposed the method of standard scores to be able to compare our results with those eventually described in other populations. Step-3 consisted of RPQ psychometric validation (n=270), which included content, face, construct (exploratory factor analysis) and criterion validity (logistic regression analysis) and consistency and stability (Cronbach's α and test-retest). The study received IRB approval and patients included signed informed consent form.

Results: Patients included in the 3 samples were representative of typical RA outpatients attending a tertiary care level center (**Table 1**).

Step 1. The initial conceptual model included 7 dimensions, 3 for probability and 1 each, for responsibility, prevention, control and for severity.

Step 2. The final version of the RPQ included 27 items distributed in 5 dimensions (**Table 2**)**,** and was feasible: mean of time required to fill it was of 13 minutes and all patients agreed the time was convenient; 89% of the patients agreed about instructions and item´s semantic clarity and 97% of them agreed about adequacy of the RPQ format. (Mean±SD) RPQ score for the sample was 50±6.69.

Table 1. Description of the sample´s characteristics, and steps of RPQ development and validation.

	N=20 (Step 1) (Conceptual model construction)	N=100 (Step 2) (Item generation and reduction)	N=270 (Step 3) (Psychometric Validation)
Females[1]	19 (95)	95 (95)	262 (97)
Years of age	52 (45-50)	53.5 (42-63)	57 (50-63)
Years of formal education	9 (9-12)	9 (9-11)	7 (7-9)
Patients with medium-low SE level[1]	19 (95)	90 (90)	251 (93)
Years of disease duration	20 (16-24)	13 (7.9-21.5)	12 (7-18)
Patients in remission status[1]	12 (60)	NA	146 (54)
CRP, mg/dL	0.42 (0.15-1.1)	NA	0.59 (0.21-1.9)
ESR, mm/H	8 (3-16)	NA	14 (7-28)
Patients with RF[1]	20 (100)	NA	240 (89)
Patients with ACCP[1]	20 (100)	NA	170 (74)*
Patients with major comorbidities[1]	2 (10)	23 (23)	57 (21)
Patients with joint replacement[1]	4 (20)	12 (12)	43 (16)

Data as presented as median (25th-75th interquartile range) unless otherwise indicated. [1]Number (%); SE=socioeconomic; CRP=C reactive protein; ESR=erythrocyte sedimentation rate; RF=rheumatoid factor; ACCP=antibodies to cyclic citrullinated peptides; NA=not available. *Data limited to 230 patients with sample available.

Table 2. Psychometric characteristics of the RPQ by dimension

RPQ Dimension	Cronbach´s α	ICC 95% CI	Mean of inter-item correlations	Floor effect/ceiling effect (%)
Likelihood to develop articular and extra-articular manifestations (9 items)	0.93	0.93 0.91-0.94	0.59	0 / 0.7
Likelihood to develop complications and/or comorbidities and disease severity (7 items)	0.86	0.86 0.81-0.89	0.52	0 / 0.7
Likelihood to develop socioeconomic unfavorable consequences (8 items)	0.89	0.87 0.84-0.90	0.51	0 / 0
Perception of personal responsibility to prevent and develop RA-related complications (2 items)	0.81	0.80 0.74-0.85	0.69	15.9 / 0
Perception of personal control over the disease (1 item)	NA	NA	NA	3.3 / 3.7

NA=not applicable; ICC=intraclass correlation coefficient; CI=confidence interval

Table 3. Logistic regression analysis of RP (presence) based on number of external criteria

	2 vs ≥ 3 external criteria	1 vs ≥ 3 external criteria	None vs ≥ 3 external criteria
OR to RP	2.307	2.934	8.730
95% CI	1.622-3.281	2-4.293	3.715-20.514
R^2	0.296	0.269	0.278
p value	0.000	0.000	0.000

OR= odds ratio; RP=risk perception; CI=confidence interval

Step 3. A five-factor model was most appropriated and resulted in 68.8% of the variance explained; Cronbach's α=0.90, intraclass-correlation-coefficient=0.93 (95% CI=0.90-0.95). Psychometric properties by dimension are summarized in **table 2**. A positive relation between number of external criteria recorded from the charts and RP was found as summarized in **table 3**.

Conclusion: The RPQ was valid and reliable to evaluate RP in RA outpatients; it can be incorporated to routine care and clinical research, and guide interventions to improve patient's health behaviors.

Disclosure: I. Contreras-Yáñez, None; **P. Lavielle**, None; **P. Clark**, None; **V. Pascual-Ramos**, None.

Abstract Number: 0444

Criterion Validity of the Flare Assessment in Rheumatoid Arthritis (FLARE-RA) Questionnaire and FLARE-RA Cut-offs for Clinical Decision Making: International Collaboration

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Patient Reported Outcomes

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Background/Purpose: Flares are inherent to the rheumatoid arthritis (RA) disease course and associated with poor clinical outcomes including low quality of life, joint damage and disability, suggesting the need for their early detection and timely management. The self-administered Flare Assessment in Rheumatoid Arthritis (FLARE-RA) questionnaire was devised and validated for detection of current and recent flares in RA, taking into account both patient and provider perspectives [1]. The FLARE-RA questionnaire includes arthritis-related subscale and general subscale. The overall score for the questionnaire is defined as the global scale, with scoring from 0 (no flare) to 10 (maximum flare). We aimed to define the cross-cultural criterion validity of the FLARE-RA questionnaire and cut-off(s) for definition and decision in four different countries, using different anchor items in patients with RA.

Methods: This cross-sectional study included adult patients with prevalent RA (per 2010 ACR/EULAR criteria) attending outpatient rheumatology clinics in four countries. Flare occurrence over the past 3 months was assessed using the FLARE-RA questionnaire. The cut-offs for the FLARE-RA score were defined using the following anchor items obtained at the same encounter: 1) Patient report of flare; 2) DAS28-CRP >3.2; 3) Change of anti-rheumatic treatment, based on the area under the receiver operating characteristic curve (AUC) and distance to (0,1).

Results: The study included 571 patients with RA (mean age 56.9 years, 75.3% female). The discrimination for the FLARE-RA was acceptable-to-excellent: AUC for the global FLARE-RA score ranged from 0.71 to 0.92. The summary of optimal cut-offs for the FLARE-RA questionnaire is presented in the Table. The cut-offs for the FLARE-RA score

Table: Summary of FLARE-RA optimal cut-offs by RA disease duration using different anchor selection methods

	Disease duration 2-5 years			Disease duration > 5 years		
	Arthritis subscale	General subscale	Global scale	Arthritis subscale	General subscale	Global scale
Patient report of flare	2.80	1.00	1.82	2.20	1.40	2.18
DAS28 CRP >3.2	4.40	3.67	4.09	1.80	1.67	2.18
Change of anti-rheumatic treatment	4.00	4.50	4.55	4.80	2.33	3.18

were overall lowest using “patient’s report of flare” and highest using “change of anti-rheumatic treatment” as an anchor item: cut-offs for the global score for patients with RA duration 2-5 years: 1.82 and 4.55, respectively; for patients with RA duration >5 years – 2.18 and 3.18, respectively. The cut-offs corresponding to DAS28-CRP >3.2 were lower in patients with RA disease duration >5 years than in those with RA duration 2-5 years.

Conclusion: The FLARE-RA questionnaire has acceptable-to-excellent discriminative capacity across the tested anchor items. Patient report of flare corresponds to a lower FLARE-RA cut-off score than DAS28-CRP and change of anti-rheumatic treatment, suggesting the hierarchy of flare recognition from flare self-perception to its detection by DAS28 to treatment change by the rheumatology provider. More studies are needed to ensure the early recognition of flares and the appropriate alignment between flare and the adjustment of anti-rheumatic and other medications.

Reference:

1. Fautrel B, et al. Validation of FLARE-RA, a Self-Administered Tool to Detect Recent or Current Rheumatoid Arthritis Flare. *Arthritis Rheumatol* 2017, 69(2):309-319.

Disclosure: E. Myasoedova, Pfizer, 2; **A. De Thurah**, Central Region Denmark Health Research Foundation, 2, The Danish Rheumatism Foundation, 2, The Novo Nordisk Research Foundation, 2, The Hede Nielsen Family Foundation, 2; **M. Erpelding**, AbbVie, 2; **E. Schneeberger**, None; **T. Maribo**, Central Region Denmark Health Research Foundation, 2, the Danish Rheumatism Foundation, 2, the Novo Nordisk Research Foundation, 2, the Hede Nielsen Family Foundation, 2; **G. Citera**, AbbVie, 5, 8, Abbvie, 2, 5, 8, BMS, 5, BRISTOL MYERS SQUIBB ARGENTINA, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, Gema Biotech, 2, 5, 8, Genzyme, 5, Janssen, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi Genzyme, 5, 8; **J. Davis**, Abbvie, 5, Pfizer, 2, 5, Sanofi Genzyme, 5; **E. Matteson**, Boehringer Ingelheim, 5, Pfizer, 2, Sun Pharmaceuticals, 2; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **B. Fautrel**, AbbVie, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Boehringer Ingelheim, 8, Celgene, 5, 8, Eli Lilly and Company, 2, 5, Janssen, 5, 8, Lilly, 8, Medac, 5, 8, MSD, 2, 5, 8, NORDIC Pharma, 5, 8, Novartis, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, Sanofi-Aventis, 5, SOBI, 5, 8, UCB, 5, 8; **F. Guillemin**, AbbVie, 2.

Abstract Number: 0445

What Is the Effect of Statins on the Risk of Rheumatoid Arthritis? Results of a Systematic Review and Meta-Analysis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The anti-inflammatory and immune-modulating effects of statins suggest that these drugs may influence the risk of developing autoimmune diseases, such as rheumatoid arthritis (RA). We aimed to perform a systematic review and meta-analysis of studies assessing the risk of RA in statin-users versus non-users.

Methods: We searched Medline from inception to 01/22/2019 and Embase from 1988 to week 03 2019 for all comparative studies that examined the association between statin use and the risk of RA without restrictions on language. Two reviewers independently selected studies with very good inter-rater agreement (Cohen’s Kappa coefficient 0.90).

Data on study characteristics and adjusted effect estimates were extracted. A random-effects model was used to pool estimates and generate risk ratio (RR) and 95% confidence intervals (CI).

Results: The literature search identified 1,161 references; of which 8 studies (5 cohort and 3 case-control studies) were included in the systematic review. Six studies comparing statin users vs non-users were included in the meta-analysis and showed no significant difference in the risk of developing RA (RR 1.01; 95%CI 0.88-1.15; I^2=65%). Similar results were shown when cohort studies (RR 1.01; 95%CI 0.93-1.10, I^2=17%) or case-control studies (RR 1.01; 95%CI 0.36-2.87, I^2=92%) were analyzed separately. Two studies assessing persistence with or intensity of treatment with statins showed lower risk of RA in persons with higher as opposed to lower treatment persistence or intensity of statin use (pooled RR 0.66; 95%CI 0.5-0.87; I^2=83%).

Conclusion: In this systematic review and meta-analysis, observational evidence suggested that statin users had similar risk of RA as non-users. Considering some imprecision of the effects based on the 95% CIs, potentially with either meaningful benefit or harm of statin exposure on the risk of RA, it appears premature to conclude the lack of effect at this point. The risk of RA may be lower in patients who have higher as opposed to lower treatment persistence or intensity of statin use, suggesting potential heterogeneity of treatment effect. More studies at lower risk of bias are needed to further elucidate the impact of statin use on the risk of RA, considering potential differences by dosage, duration of use, study population and other factors.

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Abstract Number: 0446

High MDHAQ/RAPID3 (Multidimensional Health Assessment Questionnaire/Routine Assessment of Patient Index Data) Scores in RA Patients Who Have Depression According to a Screening Questionnaire

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Depression in rheumatoid arthritis (RA) patients may be pre-existent, amplified, or may develop after the onset of RA[1]. The Patient Health Questionnaire (PHQ9) is a widely-used tool to screen for depression in primary care[2]. A multidimensional health assessment questionnaire (MDHAQ)[3] includes two screening queries for depression. MDHAQ also includes routine assessment patient index data (RAPID3), an index which is correlated significantly with disease activity score (DAS28) and clinical disease activity index (CDAI), and also is informative in all rheumatic diseases in which it has been studied[4]. We investigated possible associations of PHQ9 scores for depression with MDHAQ demographic, clinical, psychological and laboratory measures.

Table. Demographic and clinical characteristics of rheumatoid arthritis (RA) patients who have or do not have depression according to Patient Health Questionnaire (PHQ9). Data are presented as mean (SD) or %. *p<0.05.

All patients (n=102)	PHQ9	
	Cut-off below 10 N=74 (71.1%)	Cut-off = 10 or above10 N=28 (27.4%)
Demographic variables		
Age, years	60.1 (12.0)	54.4 (12.2)
% Female	77%	96%*
Education level, years	12.2 (4.7)	10.4 (3.5)
MDHAQ/RAPID3: Patient self-report scores		
Physical function (0-10)	1.8 (1.4)	3.7 (1.8)*
Pain (0-10)	3.6 (2.6)	6.8 (1.6)*
Patient global estimate (0-10)	3.7 (2.6)	7.0 (1.7)*
RAPID3 (0-30)	9.2 (6.1)	17.8 (4.3)*
% RAPID3 high severity	34%	82%*
Fatigue (0-10)	3.1 (2.4)	7.0 (2.0)*
RADAI Self-reported joint pain (0-48)	9.2 (9.1)	20.7 (2.1)*
Symptoms checklist (0-60)	9.0 (7.2)	22.1 (10.1)*
% Depression on symptom checklist (0/1)	9%	70%*
Poor sleep quality (0-3.3)	0.7 (0.8)	2.2 (0.8)*
Dealing with depression/feeling blue (0-3.3)	0.4 (0.6)	1.7 (1.0)*
Dealing with anxiety/being nervous (0-3.3)	0.6 (0.7)	1.6 (1.0)*
Laboratory data		
% Abnormal CRP	35%	32%
% Abnormal ESR	49%	46%
Treatment		
% Taking DMARD – Biologic	68%	63%
% Taking DMARD – Non Biologic	31%	33%
% Taking antidepressant	14%	43%*

FINAL TABLE FINAL VERSION

Methods: Consecutive patients with RA, who met EULAR/ACR 2010 criteria, completed both an MDHAQ and a PHQ9 as part of a routine rheumatology visit between November 2018 and February 2019. The 2-page MDHAQ includes 0-10 scores for physical function (FN), and visual analogue scales (VAS) for pain (PN) and patient global estimate (PATGL), compiled into 0-30 RAPID3 (≤3 =remission, 3.1-6=low, 6.1-12=moderate, and >12=high severity), 0-10 fatigue (FT) VAS, 0-48 RADAI self-report painful joint count, and 0-60 symptom checklist, which includes depression. The MDHAQ also includes 3 psychological queries in the patient-friendly HAQ format for depression, anxiety, and poor sleep quality, as well as demographic data. PHQ9 is a 9-item self-report screening tool for depression in primary care (range 0-27); PHQ9 scores ≥ 10 indicate positive screening for depression. MDHAQ demographic, self-report clinical, psychological and laboratory variables were compared according to PHQ9 depression group, ≥10 vs < 10.

Results: 102 RA patients were included in the analysis: 82.3% were females, mean age was 58.8 years and mean formal educational level of 11.7 years. 28 patients (27.4%) had PHQ9 ≥ 10, positive for depression (Table). PHQ9 ≥ 10 patients did not differ significantly from PHQ9 < 10 patients in age and educational level, while 96% of PHQ9 ≥ 10 patients were female (p=0.02). Patients who reported PHQ9 ≥ 10 had significantly higher scores vs those with PHQ9 < 10 for physical function, pain, PATGL, and RAPID3 (Table). High RAPID3 severity (>12) was seen in 82% of PHQ9 ≥ 10 patients versus 34% of PHQ9 < 10 patients. Patients with PHQ9 ≥ 10 also had significantly higher scores on the two MDHAQ depression queries vs those with PHQ9 < 10 (Table). No differences in the two groups were seen in acute

phase reactants ESR and CRP or in treatment with DMARDs. 43% of patients with a PHQ9 ≥ 10 were being treated for depression vs 14% of PHQ9 < 10 patients (Table).

Conclusion: RA patients screening positively for depression according to PHQ9 have high scores for all MDHAQ, including depression scale as well as physical function, pain, RAPID3, fatigue, and others, indicating a high self-report disease burden.

Reference:

1. J Clin Rheumatol. 2017;23:425-434. 2. J Gen Intern Med. 2001;16:606-13. 3. Rheum Dis Clin North Am. 2009;35:787-98. 4. Bull Hosp Jt Dis. 2017;75:93-100.

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Abstract Number: 0447

Nail Abnormalities in a Cohort of Rheumatoid Arthritis Patients: Repetitive Trauma-Related Findings in Toenails Are Associated with Radiographic Damage

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SESSION INFORMATION
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Classification of nail findings and number (%) of affected RA patients		
RA-associated nail findings	**Non-specific nail findings**	**Nail diseases**
Hands		
Bywaters 1 (0.8%)	Longitudinal ridging 14 (11.5%) Short linear vessels 16 (13.1%) Beau lines 5 (4.1%)	Onychomycosis 0
Feet		
Bywaters 1 (0.8%)	Xantonychia 25 (20.5%)* Traumatic melanonychia 19 (15.6%)* Subungual hyperkeratosis 15 (12.3%)* Longitudinal ridging 11(9%) Beau lines 8 (6.6%)* Subungual hematoma 8 (6.6%)* Mycotic leukonychia 7 (5.7%) Onicoatrophy 6 (4.9%) Onychocryptosis 5 (4.1)* Splinter hemorrhages 4 (4.1%)* Onycholysis 3 (2.5%)*	Onychomycosis 11 (0.9%)

* Findings associated with repetitive trauma

	Trauma-associated toenail findings		
Variable	Present (n=58)	Absent (n=64)	p value
Age	53(39.8-60.3)	43(32.3-52)	**<0.001**
Disease duration	10(5.8-13)	6.5(4-11.75)	**0,034**
Positive rheumatoid factor	50(80.6)	49(81.7)	1
Positive ACPAs	54(87.1)	55(91.7)	0,56
Erosions in hands and/or feet	36(62.1)	21(32.8)	**0,002**
Erosions in hands	25(43.1)	9(14.1)	**0,001**
Erosions in feet	28(48.3)	20(31.3)	0,065
Cumulative DAS28 first two years	2.39(2-3)	2.2(1.7-2.6)	**0,026**
Cumulative DAS28 previous year	2.04(1.57-2.6)	1.86(1.27-2.49)	0,19
Disease remission	44(75.9)	54(84.4)	0,262
HAQ	0(0-0.25)	0(0-0)	0,05

Background/Purpose: Different dermatological changes and nail abnormalities have been reported in rheumatoid arthritis (RA) patients, some of which are specifically associated with the disease, while others are non-specific. Whether nail changes are associated with disease activity and/or damage has not been properly assessed.

Methods: We performed a cross-sectional study in patients from an early RA cohort, which was initiated in 2004. Up to April 2019, the cohort had 145 patients with active follow-up. All patients were invited to participate and 122 agreed to have a standardized dermatological and nail screening exam. Toenail findings were classified as RA-related findings, RA-unrelated findings and nail-specific diagnoses, using standardized definitions. We described the main findings of the toenail evaluation, as well as their association with different disease parameters.

Results: At study entry, patients had a median age of 45.5 years (IQR 36-58), and most of them were female (91%), with substantial disease duration (median of 9 years [5-13]). The majority of patients (80.3%) had DAS28 remission and 46.7% had erosive disease.

There were 79 patients (64.8%) with nail findings: 62 (78.5%) in toenails, 44 (55.7%) in fingernails and 27 (34.2%) in both (Table 1). Patients with toenail abnormalities (n=60) showed higher disability, as per the HAQ-DI (p=0.019).

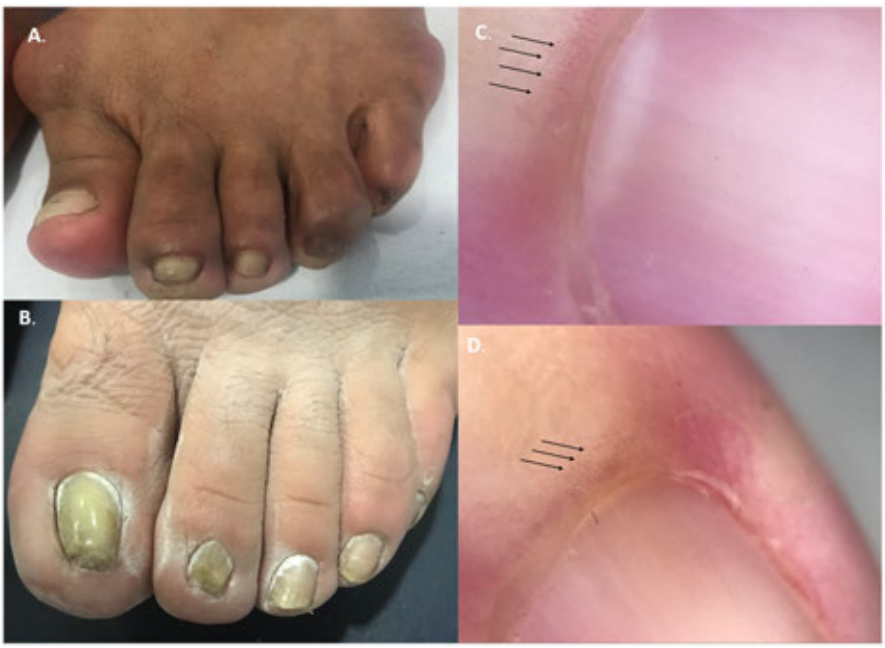

Figure 1. 1A and 1B. Nails changes due to trauma showing xantonychia and melanonychia. 1C and 1D

Onychomycosis was found in 11 patients (9%), and the only associated variable was a higher cumulative DAS28 within the previous year: median (IQR) DAS28 of 2.57 (1.97-3.03) vs. 1.89 (1.47-2.48), p=0.047.

We grouped patients with toenail findings which could be attributed to trauma (Table 1); there were 58 patients (47.5%) with one or more lesions and their data were compared to those without these abnormalities (Table 2). Patients from the former group were older (p≤0.001), had a longer disease duration (p=0.034), a higher prevalence erosive disease (p=0.002) and a higher cumulative DAS28 during the first 2 years of follow-up in the cohort (p=0.026). After multivariate analysis, age (Exp β 1.04, 95% CI 1.008-1.073, p=0.014) and erosive disease (Exp β 2.564, 95% CI 1.175-5.598, p=0.018) remained significantly associated with traumatic toenail lesions.

Conclusion: Nail lesions, particularly in toenails, are highly prevalent in RA patients. Although most of them are non-specific, toenail findings suggestive of repetitive trauma may be considered a surrogate marker of disease damage. Routinely performing dermatological exams to RA patients may detect clinically relevant information and foster a multidisciplinary care.

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2. Sayah A, et al. J Am Acad Dermatol 2005; 53(2):191-209

3. Parra-Salcedo F, et al. Arthritis Res Ther 2015; 17:34

Disclosure: V. Pascual-Ramos, None; **S. Méndez-Flores**, None; **J. Domínguez-Cherit**, None; **A. Sánchez-Cárdenas**, None; **A. Barrera-Vargas**, None; **J. Merayo-Chalico**, None; **I. Contreras-Yáñez**, None.

Abstract Number: 0448

Central Sensitization in Patients with Rheumatoid Arthritis Using the Central Sensitization Inventory

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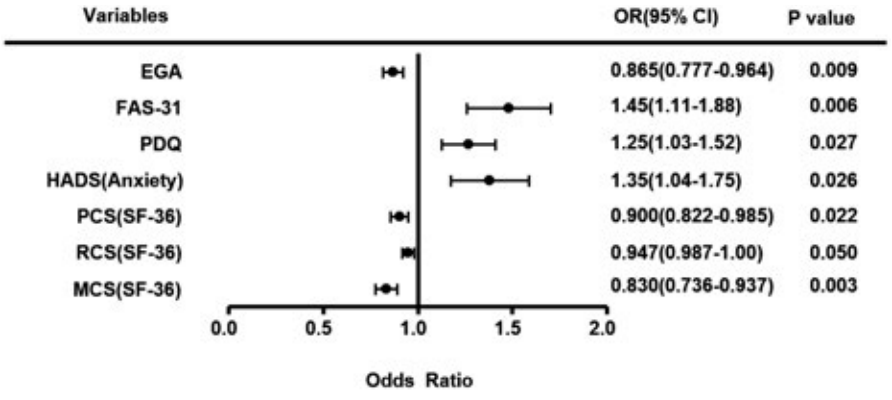
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM



Background/Purpose: Pain of rheumatoid arthritis (RA) is thought to be nociceptive. However, recent studies indicate that RA pain also includes the mechanism of central sensitization (CS). Therefore, we examined the prevalence of CS among RA patients and these patients' clinical characteristics.

Methods: The central sensitization inventory (CSI) was used to evaluate in 240 outpatients (63 Male, 177 Female) with RA from May 2017 to September 2018. The disease activity was evaluated using the disease activity score of 28 joint (DAS28), clinical disease activity index (CDAI), and simplified disease activity index (SDAI). The following parameters were evaluated: swollen joint count on 28 joints (SJC), tender joint count on 28 joints (TJC), patient global assessment (PGA), estimator global assessment (EGA), pain visual analogue scale (PainVAS), serum C-reactive protein (CRP), and ESR. Physical function was evaluated using mHAQ-DI. Health-related quality of life (HRQOL) was evaluated using short-formed 36-Item health survey (SF-36). Fibromyalgia was evaluated using the fibromyalgia activity score 31 (FAS-31). Neuropathic-like pain was evaluated using the painDETECT questionnaire. Depression and anxiety were evaluated using the hospital anxiety and depression scale (HADS). We compared the clinical parameters between the patients with CS (CSI ≧ 40) and without CS (CSI < 39).

Results: Eighteen (7.5 %) of 240 patients had CS according to the CSI. In patients with CS, EGA, PainVAS, mHAQ-DI, FAS-31, HADS scores, physical component summary scores (PCS), and mental component summary scores (MCS) on the SF-36 were significantly higher than in patients without CS. Multivariate analysis of clinical parameters contributing CS showed significant differences in EGA ($p = 0.009$, OR 0.865), PDQ ($p = 0.027$, OR 1.25), FAS-31 ($p = 0.006$, OR 1.45), HADS(Anxiety) ($p = 0.026$, OR 1.35), PCS ($p = 0.022$, OR 0.900) and MCS ($p = 0.003$, OR 0.830) on the SF36.

Conclusion: CS in RA patients was associated with neuropathic-like symptoms, fibromyalgia, anxiety, and decrease of HRQOL. Neuropathic-like symptoms in RA may be helpful to detect CS. Proper treatment of CS in RA patients may improve HRQOL.

Disclosure: K. Noda, None; **M. Saitou**, None; **T. Ukichi**, None; **Y. Oto**, None; **K. Yoshida**, None; **D. Kurosaka**, None.

Abstract Number: 0449

The Course of Disability Related to Function of the Upper Extremities in Early Rheumatoid Arthritis over 10 Years of Follow-up

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) have increased disability, in particular due to involvement of the joints of the upper extremities. The Stanford Health Assessment Questionnaire (HAQ) includes questions related to both upper and lower extremity function. The objective of this study was to investigate the course of

Table 1. Change in HAQ-DI UE between every follow-up visit in the early RA cohort

HAQ-DI UE, median (IQR)		Δ HAQ-DI UE
From	To	Mean (95 % CL)
Inclusion (n=207) 0.80 (0.40-1.20)	**6 months** (n=207) 0.60 (0.00-1.00)	-0.26 (-0.18; -0.34)
6 months (n=203) 0.60 (0.00-1.00)	**1 year** (n= 203) 0.40 (0.00-1.00)	0.02 (-0.08 to 0.04)
1 year (n= 199) 0.40 (0.00-1.00)	**2 years** (n= 199) 0.40 (0.00-1.00)	0.03 (-0.02 to 0.08)
2 years (n=166) 0.40 (0.00-1.00)	**5 years** (n=´166) 0.60 (0.20-1.00)	0.10 (0.03 to 0.17)
5 years (n=109) 0.40 (0.20-1.00)	**10 years** (n=109) 0.60 (0.20-0.90)	0.08 (0.04 to 0.16)

Patients with data at both time points; paired samples t-test

disability related to the upper extremities in early RA, using a subset of the HAQ disability index (HAQ-DI upper extremities; HAQ-DI UE), and to assess associations between HAQ-DI UE and disease parameters, including grip force.

Methods: An inception cohort of patients with early RA (symptom duration ≤12 months), recruited in 1995-2005, was investigated and followed in a structured program (5 examinations over 10 years), including clinical evaluation and grip force measurement. Disability was assessed using the validated Swedish version of the HAQ. In order to more specifically address disability of the upper extremities, we calculated the HAQ-DI UE, based on the 10 questions that cover activities that are mainly dependent on function of the upper extremities. Grip force was measured using the electronic instrument Grippit (AB Detektor, Gothenburg, Sweden). Average grip force values of the dominant hand were evaluated at each visit, and compared to the expected, based on age- and sex-specific reference values from the literature. Grip force was expressed as % of predicted values. Changes in HAQ-DI UE between two consecutive follow-up visits over time, baseline to 10 years follow-up, in the early RA cohort with data on both time points, were estimated using the paired samples t-test. Spearman's test was used to further explore correlations between HAQ-DI UE and grip force, swollen and tender joint counts (SJC and TJC), visual analogue scales for patient global assessment (VAS global) and pain (VAS pain), ESR and CRP at each visit.

Results: A total of 222 patients with early RA (71 % women, mean age 61 years, median symptom duration 7 months) were investigated. At inclusion, the mean DAS28 was 4.6 (SD 1.4), and the median HAQ-DI was 0.75 (IQR 0.38-1.25). Data on both HAQ-DI UE and average grip force of the dominant hand were available for 222 patients at inclusion, 207 patients at 6 month, 209 at 1 year, 200 at 2 years, 167 at 5 years and 110 at 10 years. In the paired analysis of patients with available data at both time points there was a significant decrease in HAQ-DI UE from inclusion to 6 months follow-up (Table 1). HAQ-DI UE levels were stable between 6 month and 2 years, whereas between 2 years and 5 years, there was a significant increase. (Table 1) The mean average grip force of the dominant hand increased from 40 % of expected at inclusion to 66 % of expected at 10 years. There were strong correlations for HAQ-DI UE with grip force, VAS global and VAS pain at all time points, and moderate to weak correlations with SJC, TJC, ESR and CRP (Table 2).

Conclusion: In this study of patients with early RA, disability related to the upper extremities decreased from inclusion to the 6 month follow-up, and increased again after 2 years. HAQ-DI UE scores correlated strongly with grip force and patient reported outcomes, and to a lesser extent with joint counts and laboratory markers of inflammation.

Table 2. Correlations for disease parameters with HAQ-DI UE

	Inclusion	6 months	1 year	2 years	5 years	10 years
Grippit average score, dominant hand (% of predicted)	r: -0.62 p<0.001	r: -0.50 p<0.001	r: -0.58 p<0.001	r: -0.55 p<0.001	r: -0.54 p<0.001	r: -0.45 p<0.001
CRP (mg/l)	r: 0.35 p<0.001	r: 0.35 p<0.001	r: 0.22 p=0.001	r: 0.12 p=0.09	r: 0.21 p=0.007	r: 0.12 p=0.25
DAS28 (0-10)	r: 0.66 p<0.001	r: 0.62 p<0.001	r: 0.55 p<0.001	r: 0.52 p<0.001	r: 0.52 p<0.001	r: 0.29 p=0.003
ESR (mm 1st h)	r: 0.33 p<0.001	r: 0.30 p<0.001	r: 0.26 p<0.001	r: 0.25 p<0.001	r: 0.24 p=0.003	r: 0.09 p=0.35
Patient's global assessment (VAS 0-100)	r: 0.53 p<0.001	r: 0.53 p<0.001	r: 0.64 p<0.001	r: 0.60 p<0.001	r: 0.58 p<0.001	r: 0.44 p<0.001
Pain (VAS 0-100)	0.58 p<0.001	0.57 p<0.001	0.60 p<0.001	0.55 p<0.001	0.54 p<0.001	r: 0.36 p<0.001
Swollen joint count (0-28)	r: 0.39 p<0.001	r: 0.27 p<0.001	r: 0.22 p=0.002	r: 0.22 p=0.002	r: 0.32 p<0.001	r: 0.00 p=0.99
Tender joint count (0-28)	r: 0.50 p<0.001	r: 0.49 p<0.001	r: 0.49 p<0.001	r: 0.42 p<0.001	r: 0.43 p<0.001	r: 0.26 p=0.006

Spearman's test

Disclosure: M. Rydholm, None; **I. Wikström**, None; **M. Mellblom Bengtsson**, None; **S. Hagel**, None; **L. Jacobsson**, None; **C. Turesson**, None.

Abstract Number: 0450

ACPA-positive versus ACPA-negative Rheumatoid Arthritis: Two Distinct Erosive Disease Entities on Radiography and Ultrasonography

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Several studies have shown that ACPA-positive (ACPA+) patients were more likely to develop erosive disease on radiography (RX) than ACPA-negative (ACPA-) patients, but it has never been demonstrated

on ultrasonography (US). The characteristics of bone erosions on both RX and US according to ACPA status has never been studied before. The objective of this study was to assess the prevalence, localization and severity of bone erosions on RX and US according to ACPA status in patients with rheumatoid arthritis (RA).

Methods: 78 patients with ACPA+ RA and 30 patients with ACPA- RA fulfilling the ACR 1987 and/or ACR/EULAR 2010 criteria were consecutively included. On RX, a modified Sharp erosion score (SHSe) was evaluated by two blinded readers and one adjudicator for discordant cases (number of eroded joints ≤ three). On US, erosions were scored on six bilateral joints (MCP2,3,5; MTP2,3,5) with a four-point scale to calculate the total US score for erosions (USSe).

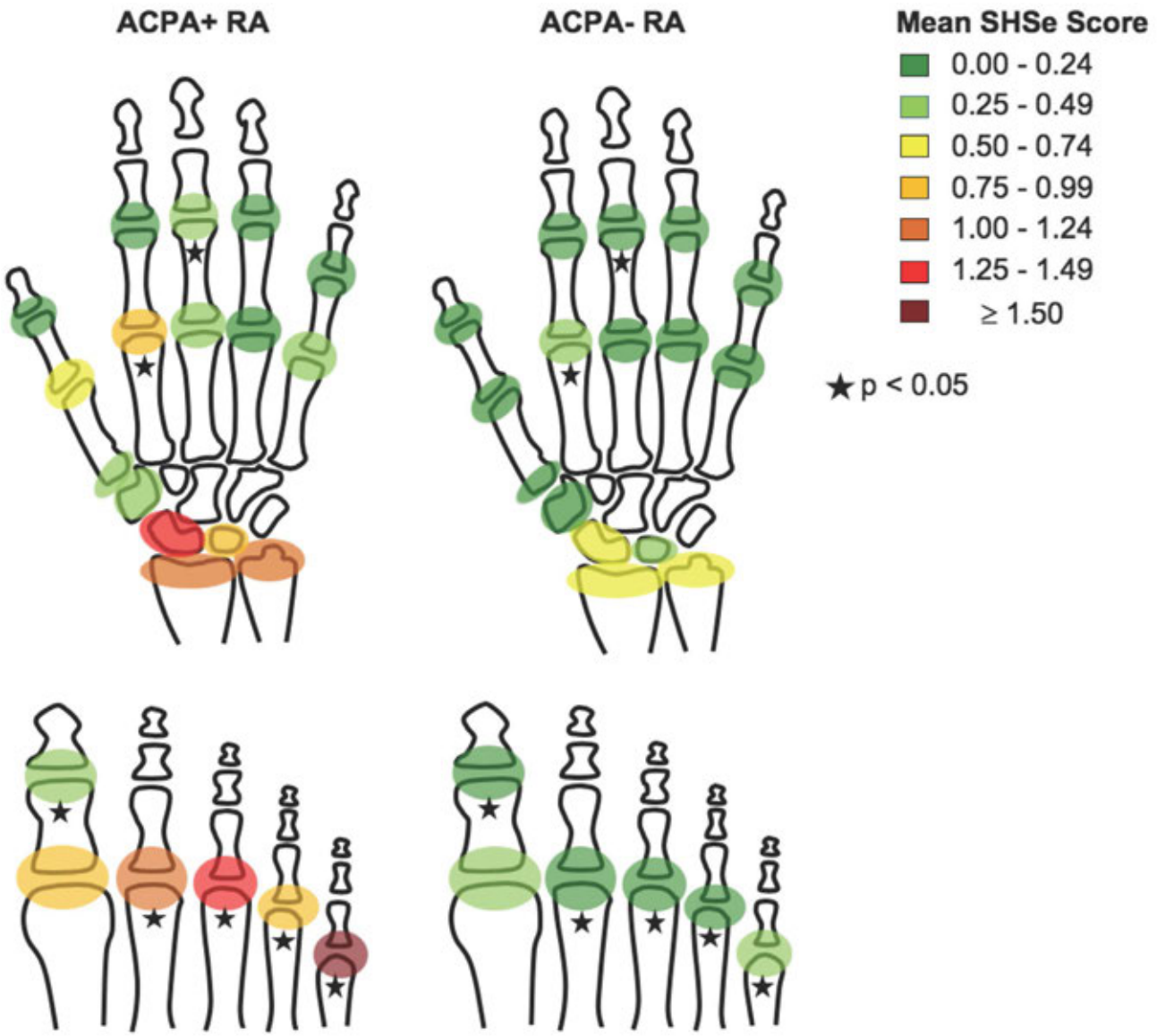

Figure 1. Topography of erosions according to the mean SHSe score for ACPA-positive (ACPA+) and ACPA-negative (ACPA-) Rheumatoid Arthritis

Results: On RX, 33 ACPA+ RA patients (42.3%) and 4 ACPA- RA patients (13.3%) had an erosive disease according to the EULAR 2013 definition criteria. On US, 61 and 63 ACPA+ RA patients (78.2% and 80.8%) versus 14 and 10 ACPA- RA patients (46.7% and 33.3%) had an erosive disease according to the following two definitions: the presence of at least two eroded joint facets (def1) or at least one grade 2 eroded joint facet (def2), respectively.

Erosion patterns were different between ACPA+ RA patients and ACPA- RA patients. On RX, erosions were preferentially observed in MTP joints in the ACPA+ group and in wrists in the ACPA- group (Figure 1). On US, erosions were preferentially found in the lateral facets of MTP5 joints, followed by MCP2 and MCP5 joints in both groups (Figure 2).

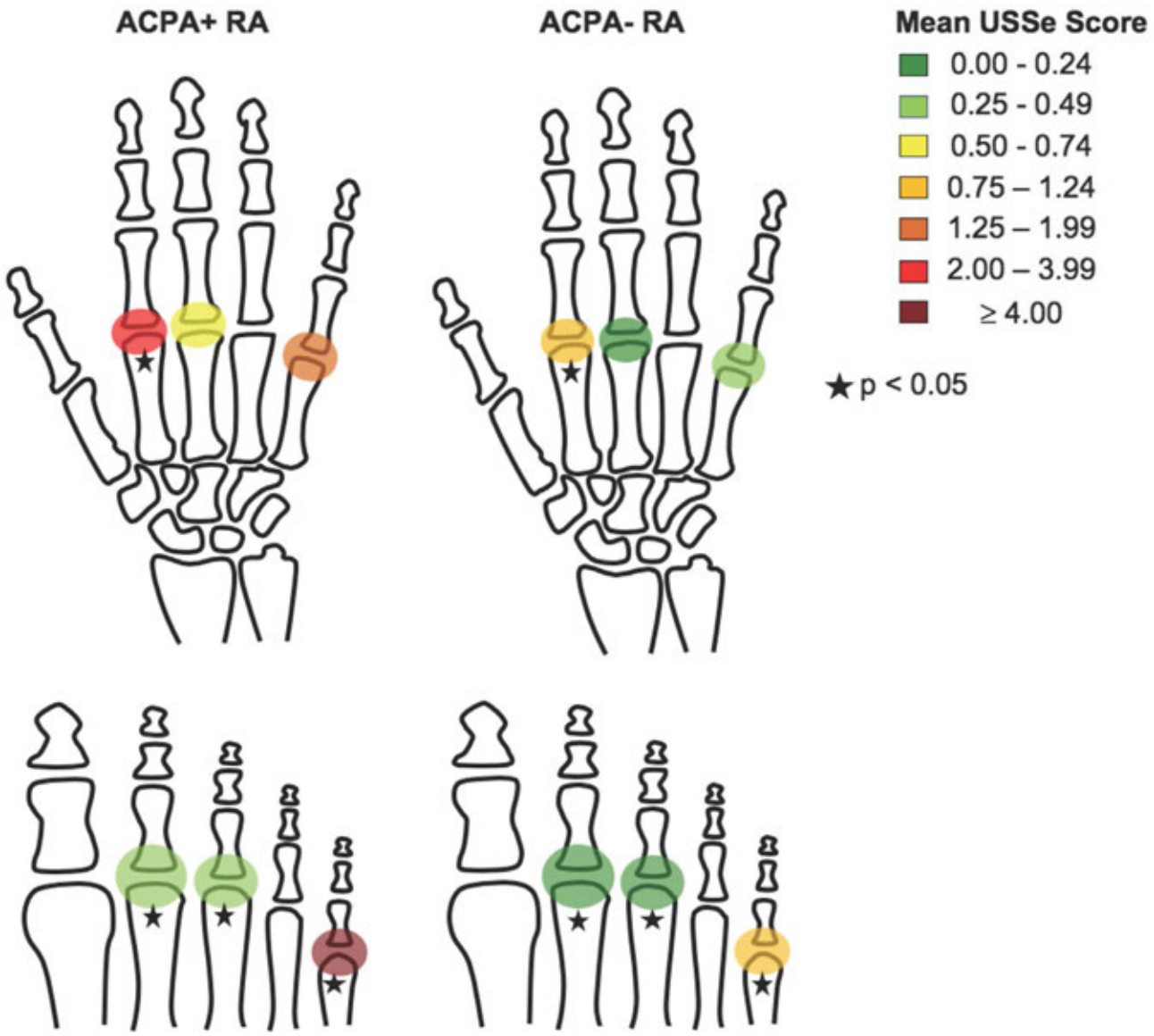

Figure 2. Topography of erosions according to the mean USSe score for ACPA-positive (ACPA+) and ACPA-negative (ACPA-) Rheumatoid Arthritis

On both RX and US, the most discriminating joint between the two groups was MTP5, especially in cases with bilateral erosion (17 ACPA+ RA patients versus 0 ACPA- RA patients on RX, 45 ACPA+ RA patients versus 1 ACPA- RA patient on US; p<0.001). The mean total SHSe were 15.3±22.1 and 4.1±8.3 in the ACPA+ and ACPA- groups, respectively (p< 0.001). The mean total USSe were 12.2±11.7 in the ACPA+ group and 2.8±4.4 in the ACPA- group (p< 0.001).

Based on multivariate analyses, ACPA+ status was associated with erosive RA on RX according to the EULAR 2013 definition criteria (OR 4.4 (95% CI 1.2-16.4)), and on US according to def1 (OR 3.7 (95% CI 1.4-9.9)) and def2 (OR 9.0 (95% CI 2.8-28.4)).

Conclusion: Compared to ACPA- RA, ACPA+ RA is associated independently with more severe erosive disease on RX and US. Both US and RX bilateral erosions in MTP5 joints are highly discriminant for ACPA+ RA patients (97.8% in US, 100% in RX).

Disclosure: J. Grosse, None; **E. Allado**, None; **C. Roux**, None; **A. Pierreisnard**, None; **M. Couderc**, None; **I. Clerc-Urmès**, None; **T. Remen**, None; **E. Albuisson**, None; **M. De Carvalho**, None; **I. Chary-Valckenaere**, None; **D. Loeuille**, None.

Abstract Number: 0451

Persistent and Non-Articular Regional and Widespread Pain Are Common in Early Rheumatoid Arthritis, Impacting Remission Rates and Reflected in Patient Global Scores

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Persisting pain (NRS ≥4,) (PP) and non-articular pain (NAP), reduces quality of life for patients with RA. NAP is often attributed to fibromyalgia (FM), though FM prevalence could be overestimated in patients with unrecognized regional pain (RP) syndromes. Our goal was to understand pain patterns (regional vs. widespread) and its impact on achieving remission in real-world early inflammatory arthritis (EIA) patients.

Methods: Data were from EIA patients (symptoms < 1 year) enrolled in a national prospective cohort study between Mar 2017 – Mar 2019 who completed body pain diagrams (BPD) at baseline (n=317) and repeat assessments every 3-months over 1 year follow up (n=122). Patients were grouped by pattern of NAP reported in left, right, upper, lower and central regions (max 5 regions) as follows: 1. none, 2. regional pain (RP) if 1 or 2 painful regions and 3. widespread pain (WSP) if 3-5 painful regions. We compared sociodemographic, RA clinical and patient reported outcome measures across patient pain groups at baseline as well as associations between pain patterns and achievement of

Pain Measures:	Non-Articular Pain (NAP) identified on Body Pain Diagram (n=317)		
Groups:	Group 1 No NAP N=149 (47%)	Group 2 Regional Pain (RP) 1-2 of 5 regions n=106 (33%)	Group 3 Widespread Pain (WSP) ≥3 BPD regions n=62 (20%)
Age, years, mean (SD)	57 (14)	56 (14)	53 (15)
Female, n (%)	94 (63%)	62 (58%)	43 (69%)
Caucasian, n (%)	115 (77%)	87 (82%)	46 (74%)
RDCI^ (0-9), mean (SD)	1.1 (1.3)	1.3 (1.4)	1.4 (1.9)
Current Smoking status, n (%)	22 (15%)	16 (15%)	14 (23%)
Finished High school+ n (%)	84 (56%)	63 (59%)	38 (61%)
Obese BMI > 30, n (%)	77 (66%)	64 (76%)	36 (75%)
Symptom duration, mos, mean (SD)	5.5 (3.1)	5.5 (3.0)	5.2 (2.6)
Meet ≥1 of 1987/2010 RA criteria, n (%)	101 (68%)	84 (79%)	40 (65%)
Seropositive (RF/ ACPA), n (%)	33 (75%)	35 (76%)	17 (61%)
DAS28 (ESR or CRP if ESR missing)	4.7 (1.4)	5.1 (1.2)	5.0 (1.2)
ESR, mean (sd)	27.4 (20.2)	26.8 (19.6)	23.8 (19.3)
CRP mean (sd)	14.5 (18.3)	13.7 (19.1)	11.9 (15.6)
Swollen Joint Count (0-28)	7 (5)	7 (5)	7 (5)
Tender Joint Count (0-28)	8 (7)	9 (6)	9 (7)
Persistent pain ≥4, n (%)*	84 (56%)	89 (84%)	56 (90%)
Pt GA (0-10), mean (SD)	4.3 (2.9)	5.4 (2.3)	6.1 (2.4)
MDGA (0-10), mean (SD)	5.0 (2.7)	5.5 (2.4)	5.4 (2.2)
RA-FQ Score*	22.8 (13.5)	30.9 (11.5)	34.1 (10.2)
RA-FQ Fatigue*	4.3 (3.0)	5.8 (2.7)	6.6 (2.4)
MDHAQ (0-10)*	2.0 (1.7)	3.1 (1.8)	3.7 (1.8)
Depressive Symptoms (PHQ-8)			
Moderate (10-19)	16 (11%)	24 (23%)	24 (41%)
Severe (≥ 20)	4 (3%)	6 (6%)	5 (9%)
DAS28-ESR	4.8 (1.4)	5.1 (1.2)	5.1 (1.2)
DAS28-ESR MDA/HDA$^{\Phi}$	81 (85%)	69 (92%)	39 (98%)
^RDCI Rheumatic Disease Comorbidity Index, *p<0.05			

Table 1. Baseline Characteristics Across EIA Patients Reporting Absence of Non-Articular Pain, Non-Articular Regional Pain and Widespread Pain

ACR Boolean Remission and DAS Remission, with and without inclusion of patient global assessment at 6 and 12 months. Logistic regression was used to estimate age and sex, and multiple adjusted associations between RP and WSP with remission.

Results: Of 317 eligible patients, the mean (sd) age was 56 (14), baseline DAS28 was 4.9 (1.3); 199 (63%) were female, 225 (71%) met one or both 1987/2010 RA criteria and 287 (91%) were treated with csDMARDS +/- MTX. There were more patients with RP compared to WSP throughout the study period (Figure 1). Patients with no NAP (Gp 1) and RP (Gp 2) had lower scores on the RA-FQ, MDHAQ, and Fatigue. Similarly, patient pain ratings, PtGA, PHQ scores were lower in groups 1 and 2 vs group 3 (Table 1). PtGA was most discordant from MDGA in the WSP group. Depressive Symptoms were lowest in the no pain group as was the mean(sd) DAS28 at baseline (4.8 (1.4)). Patients with RP or no pain smoked less than those with WSP. Age/sex adjusted and fully adjusted logistic regression models predicting associations with remission are shown in table 2. Regional pain was significantly associated with reduced odds of Boolean remission at 6 months, and widespread pain tended to be associated with lower odds of Boolean remission at 6- and 12 months and lower odds of DAS28 remission at 12-months though the sample with widespread pain was small and confidence intervals were inconclusive.

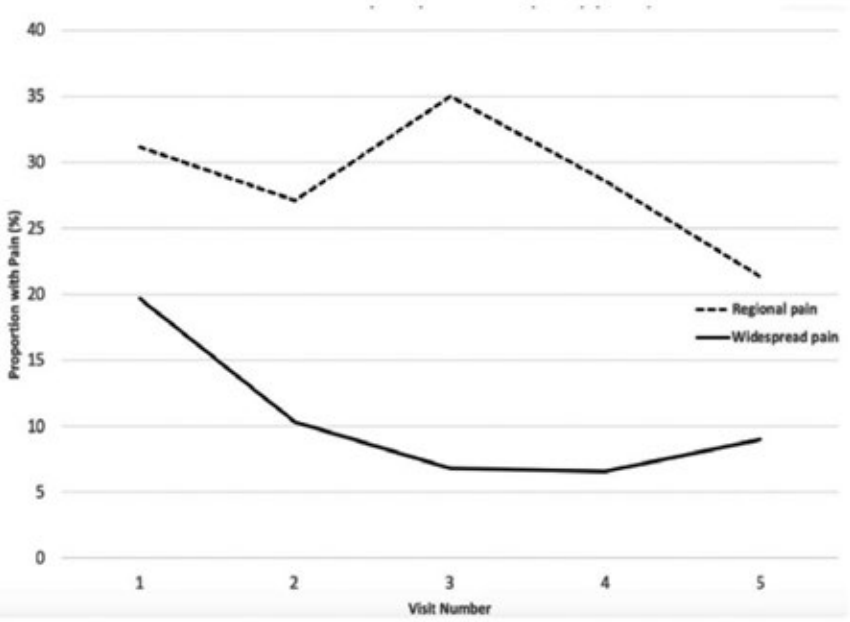

Figure 1. Proportion of EIA patients reporting regional and widespread pain over the first year of follow up

	REMISSION					
	ACR/ EULAR Boolean		DAS28		DAS28 3-Variable	
Pain Pattern by BPD	Age & Sex Adjusted OR (95% CI)	Fully Adjusted OR (95% CI)	Age & Sex adjusted OR (95% CI)	Fully Adjusted OR (95% CI)	Age & Sex Adjusted OR (95% CI)	Fully Adjusted OR (95% CI)
6- Months						
No NAP	Ref	Ref	Ref	Ref	Ref	Ref
Regional pain	**0.27 (0.08, 0.88)**	**0.34 (0.07, 0.86)**	0.91 (0.39, 2.11)	1.02 (0.41, 2.57)	1.22 (0.53, 2.81)	1.43 (0.57, 3.60)
Widespread pain	0.39 (0.08, 1.96)	0.37 (0.07, 2.02)	0.99 (0.28, 3.56)	0.92 (0.24, 3.49)	0.72 (0.19, 2.68)	0.65 (0.16, 2.64)
12- Months						
No NAP	Ref	Ref	Ref	Ref	Ref	Ref
Regional pain	0.71 (0.21, 2.41)	0.64 (0.15, 2.66)	1.31 (0.44, 3.89)	1.13 (0.33, 3.85)	1.09 (0.38, 3.19)	0.90 (0.27, 2.98)
Widespread pain	0.33 (0.04, 3.00)	0.59 (0.06, 6.37)	0.37 (0.08, 1.76)	0.38 (0.07, 2.15)	0.61 (0.14, 2.72)	0.58 (0.11, 3.10)
Model adjusted for baseline age, sex, education, baseline swollen joint count (SJC28), RA Disease Comorbidities Index (RDCI) and smoking						

Table 2. Logistic Regression Examining Associations Between Pain Pattern and Remission at 6- and 12-months Follow Up in Patients with EIA

Conclusion: Early RA patients frequently experienced regional and widespread non-articular pain, though regional pain is more common, perhaps reflecting strain injuries following a period of active RA with consequent sarcopenia. Results suggest non-articular pain tended towards fewer patients achieving remission. Clinicians should consider whether their patients have non-articular pain and address these separately to provide more holistic care. Non-articular pain may falsely lower remission status. Awareness of this is needed when implementing targeted care strategies.

Disclosure: V. Bykerk, Amgen, 5, Pfizer Pharmaceuticals, 5, Sanofi-Genzyme/Regeneron, 5, Schiper, 5, UCB, 5; **O. Schieir**, None; **M. Valois**, None; **G. Boire**, Abbvie, 2, Amgen, 2, 5, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, Eli Lilly, 2, 5, Lilly, 2, 5, Merck, 2, 8, Novartis, 2, Pfizer, 2, 5, 8; **G. Hazlewood**, None; **L. Bessette**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, Amgen, BMS, Janssen, Roche, UCB Pharma, AbbVie Inc, Pfizer, Merck, Celgene, Sanofi, Eli Lilly, and Novartis., 2, 5, 8, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Bristol-Myers-Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5; **C. Hitchon**, Pfizer, 2, UCB, 2, UCB Canada, 2; **D. Tin**, None; **C. Thorne**, Abbvie, 2, 5, Amgen, 2, 5, CaREBiodam, 2, Celgene, 2, 5, Centocor, 5, Janssen, 5, Lilly, 5, Medexus/Medac, 5, 8, Merck, 5, Novartis, 2, 5, Pfizer, 2, 5, Sandoz, 5, Sanofi, 5; **E. Keystone**, Abbvie, 2,

5, 8, Amgen, 2, 5, 8, AstraZeneca, 5, Astra-Zeneca, 5, Biotest, 5, BMS, 2, 5, 8, Celltrion, 5, Crescendo, 5, Crescendo Bioscience, 5, F. Hoffmann-La Roche Inc, 2, 5, 8, Genentech, 5, Genentech Inc., 5, Genzyme, 5, Gilead, 2, 5, Gilead Sciences, Inc., 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 5, 8, Pfizer, 2, 5, 8, Pfizer Pharmaceuticals, 2, 5, 8, Roche, 2, 5, 8, Sandoz, 5, Sanofi, 2, 5, 8, Sanofi-Aventis, 2, 8, UCB, 5, 8; **J. Pope**, AbbVie, 5, Abbvie, 5, Actelion, 5, Actellion, 5, Amgen, 2, 5, AstraZeneca, 2, Astra-Zeneca, 2, Bayer, 2, 5, BMS, 2, 5, Eicos Sciences, 5, Eli Lilly & Company, 5, Eli Lilly and Company, 5, EMERALD, 5, Emerald, 5, Genzyme, 5, Janssen, 5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8; **S. Bartlett**, Abbie, 2, Abbvie, 2, 5, Bayer, 5, International Society of QOL Research, 6, Janssen, 5, 8, Lilly, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, Pfizer Inc, 8, PROMIS International, 6, UCB, 5, 8; **C. (CATCH) Investigators**, Amgen, 2, Pfizer Canada, 2, AbbVie Corporation, 2, Medexus Inc., 2, Eli Lilly Canada, 2, Merck Canada, 2, Sandoz Canada Biopharmaceuticals, 2.

Abstract Number: 0452

Anti-citrullinated Vimentin Antibodies Are Associated to Early Deterioration of Cortical Bone and Volumetric Bone Mineral Density in Finger Joints in RA-at-risk Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmunity, characterized by the presence of anti-modified protein antibodies (AMPA), recognizing citrullinated, carbamylated or acetylated proteins, as well as rheumatoid factor (RF) precedes the onset of manifest rheumatoid arthritis (1,2).High resolution peripheral quantitative (HR-pQCT) technique is able to visualize marginal cortical changes in peripheral joints (3).To evaluate presence of deterioration of cortical bone as well as volumetric bone mineral density in finger joints using HR-pQCT technique and correlate these findings to arthritis specific autoimmunity, particularly osteoclast-inducing citrullinated vimentin (cVIM) antibodies and their impact on the later development of RA.

Methods: Patients were part of our individuals at risk cohort Erlangen (ethics approval 333_16B) comprising patients with AMPAs but without clinical manifest arthritis. These patients are regularly followed for arthritis development. Patients receive HR-pQCT scans as part of the protocol analyzing cortical micro-channels (CoMiCs) as well as volumetric cortical and trabecular bone densities of MCP joints as described before (3). Anti-modified protein antibody (AMPA) response was profiled including reactivities against citrullinated proteins (vimentin, enolase, fibrinogen) as well as carbamylated and acetylated vimentin from serum samples at time points

Results: 75 RA at risk patients were included. Patients with high-level (>1000U) cVIM antibodies showed a broader AMPA response. Those patients also displayed more severe deterioration of cortical bone (higher CoMiCs, lower cortical and trabecular bone volume) compared to subjects with low/no cVIM reactivity. High cVIM antibodies and microstructural changes (>15 radial CoMiCs/joint) were associated with the presence of arthralgia. Furthermore, progression to RA was high in subjects with high cVIM (53%) vs. those with low (22%) or no (5%) antibodies and those with microstructural changes (46%) vs. those without such changes (16%).

Conclusion: HR-pQCT technique detects earliest deterioration of cortical bone and volumetric bone mineral density in finger Joints with association to cVIM antibodies. These data support the concept of a non-silent form of autoimmunity regarding bone changes before the onset of RA.

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Abstract Number: 0453

Including Pain, Fatigue and Functionality Regularly in the Assessment of Patients with Early Rheumatoid Arthritis Separately Adds to the Evaluation of Disease Status

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) level of disease activity, cannot be evaluated by a single clinical or laboratory measurement. Hence, composite indices have been created via factor analysis (FA). FA uncovers the fact that multiple observed variables have similar patterns of responses because they are all associated with a latent, not directly observable, variable. Yet, only one directly patient-reported outcome (PRO), the patient's global (PaGH), has been included in the composite indices. The PaGH answers a very general question of "Considering all the ways your RA has affected you how would you say your health is?", making it easy to apply but hard to interpret. Lately, more specific PROs have been proven to add valuable and unique information on the patient's disease state. We wanted to see if this is the case in early RA.

Methods: In the Care in early rheumatoid arthritis (CareRA) trial, patients with early RA (≤1 year) (n=379) naïve to DMARDs were randomized to one of four remission induction treatment schemes and followed up over 2 years (Verschueren et al, 2015). Key clinical variables such as swollen (SJC) and tender joint count (TJC), patient (PaGH) and physician (PrGH) global health assessment, CRP or ESR; along with pain, fatigue and physical function (Health As-

Table 1: Factor analysis extracted 2 factors when using classical variables from composite scores

Variables	Factor 1: Clinical assessment	Factor 2: Laboratory
CRP		0.88
ESR		0.77
SJC28	0.82	
TJC28	0.87	
PaGH	0.72	
PrGH	0.90	

Cross-loadings were negligible (<0.3), not presented
CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, SJC28: 28 swollen joint count, TJC28: 28 tender joint count, PaGH: patient's global health assessment, PrGH: health provider's global health assessment

Table 2: Pearson correlations of all measured variables after combining 15 000 datasets

	CRP	ESR	SJC28	TJC28	PrGH	PaGH	Fatigue	Pain	HAQ
CRP	1	0.464	0.292	0.247	0.228	0.204	0.144	0.193	0.209
ESR		1	0.319	0.271	0.293	0.231	0.145	0.219	0.263
SJC28			1	0.756	0.680	0.403	0.236	0.394	0.407
TJC28				1	0.679	0.470	0.312	0.465	0.464
PrGH					1	0.564	0.385	0.570	0.492
PaGH						1	**0.650**	**0.834**	**0.588**
Fatigue							1	0.632	0.430
Pain								1	0.572
HAQ									1

CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, SJC28: 28 swollen joint count, TJC28: 28 tender joint count, PaGH: patient's global health assessment, PrGH: health provider's global health assessment, Pain and Fatigue: measured on a visual analogue scale 0-100, HAQ: Health Assessment Questionnaire

sessment Questionnaire-HAQ) were recorded at every consultation. Exploratory factor analysis (EFA) was performed for all observations and per time point as well on (1) key set variables only and (2) when also including other PROs. Pearson correlations of all variables were calculated. Firstly, missing data was handled using multiple imputation resulting in 15 complete datasets. Next, clustering was removed by performing multiple outputation 1000 times on the 15 datasets. Each of the 15 000 datasets was analyzed by EFA with oblimin rotation. The analyses were combined after re-ordering the factors by maximizing factor congruence.

Table 3: Factor analysis extracted 3 factors when using all variables			
Variables	Factor 1: Patient's assessment	Factor 2: Clinical assessment	Factor 3: Laboratory
CRP			0.87
ESR			0.78
SJC28		0.92	
TJC28		0.89	
PrGH		0.76	
PaGH	0.87		
Fatigue	0.90		
Pain	0.86		
HAQ	0.57		
Cross-loadings were negligible (<0.3), not presented CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, SJC28: 28 swollen joint count, TJC28: 28 tender joint count, PaGH: patient's global health assessment, PrGH: health provider's global health assessment, Pain and Fatigue: measured on a visual analogue scale 0-100, HAQ: Health Assessment Questionnaire			

Results: The different factor analyses (FAs) based on the classical components of disease activity scores, supported the traditional approach of composite indices extracting 2 factors that are stable over time, meaning no substantial cross-loadings between factors (Table 1). Still, pain (0.83), fatigue (0.65) and HAQ (0.59) were strongly correlated with PaGH in our cohort (Table 2). When rerunning the FA including also these variables, the 2-factor model was no longer stable with variables changing the factors in which they loaded over time. However, when a 3-factor model was extracted, there were large positive loadings on Factor 1 describing the patient's personal assessment, Factor 2 clinical assessment and Factor 3 laboratory (Table 3).

Conclusion: The classical FA with the key variables gives a 2-factor model that bundles everything in one, except for acute phase reactants (CRP and ESR). However, PaGH seems to be associated with pain, fatigue, and functionality. By including these variables, a third factor dedicated to the patient's perceptions is extracted and a very clear factor structure showing three latent factors is present. This could indicate that these patient's assessments should be added to the standard measurements of disease state.

Disclosure: S. Pazmino, None; **A. Lovik**, None; **A. Boonen**, AbbVie, 2, Amgen, 2, Celgene, 2, Eli Lilly and Company, 5, Janssen, 8, Lilly, 5, 8, Novartis, 5, Sandoz, 5, 8, UCB, 5, 8; **D. De Cock**, None; **V. Stouten**, None; **J. Joly**, None; **K. Van der Elst**, None; **D. Bertrand**, None; **R. Westhovens**, Celltrion, 5, 8, 9, Celltrion, Inc., 2, 5, Galapagos, 5, 8, Galapagos NV, 5, 9, Galapagos/Gilead, 2, 5, Gilead Sciences, Inc., 5, 8, 9; **P. Verschueren**, None.

Abstract Number: 0454

Principal Component Analysis Identifies Unique Sub-Populations in Rheumatoid Arthritis Using a Combination of Serological Biomarkers: A Cross Sectional Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Determining the prognosis of rheumatoid arthritis (RA) could guide more precise treatment selection, optimizing outcomes while minimizing unnecessary therapeutic exposures. It is important that potential biomarkers have widespread availability and provide meaningful input in clinical decision making. While CRP and ESR have been shown to be moderately associated with disease activity and severity, there continues to be uncertainty regarding the utility of these as they may be elevated in other conditions, or be normal even during severe clinical inflammation. While RF and anti-CCP positivity are considered to be associated with more treatment refractory RA, those who are autoantibody negative may experience a negative disease trajectory as well due to lack of recognition of disease and introduced delays in treatment initiation. Our objective was to employ principal component analysis to investigate if biomarkers could determine sub-groups of disease severity.

Figure 1.

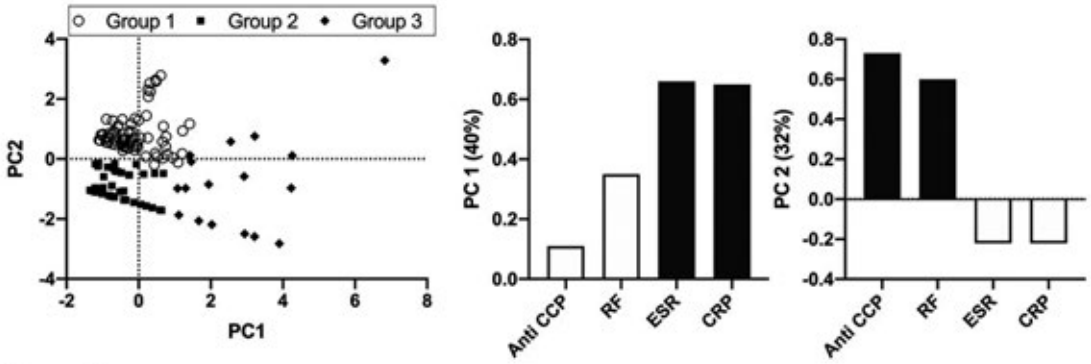
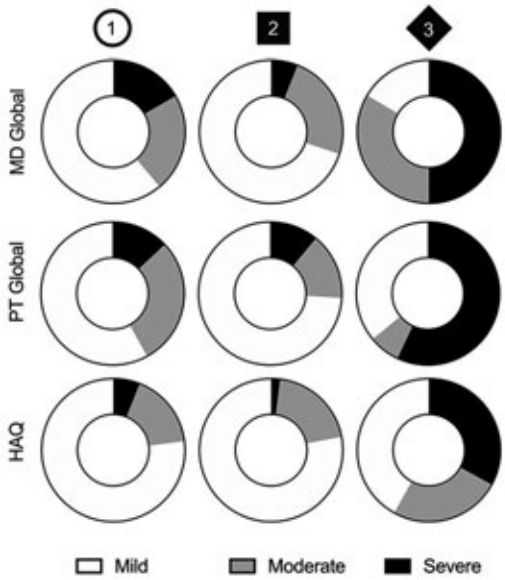


Figure 2.



Methods: RA patients were recruited from a single centre to a cross sectional study initiated to investigate influences on disease trajectory (n=145). ESR, CRP, RF, and anti-CCP collected at enrolment to the study were used in the principle component analysis (PCA) to create 2 components, which were subsequently used in k-means clustering (K=3) to demarcate the patient groups. Function (Health Assessment Questionnaire), Physician Global Assessments (MD Global), and Patient Global Assessments (Pt Global) were divided into 3 tertiles of disease activity (mild, moderate, and severe) and used as metrics of disease severity to describe the patient groups identified by PCA and K-means.

Results: Based on correlation analysis, ESR and CRP had a moderate positive relationship with each other (r=0.67), but no correlation with HAQ, Pt Global, or MD Global. Furthermore, there was no relationship between individual serological markers and disease activity as reported by HAQ, Pt Global, or MD Global (r< 0.25 for all). PCA revealed the presence of three visual groupings of data points (PC1, PC2 and PC3), that were then confirmed with K-means clustering (Figure 1). ESR and CRP weighed most heavily in PC1, while PC2 was predominantly influenced by anti-CCP and RF. Disease severity assessments illustrate that PC3 had a higher percentage of severe disease and PC2 showed a higher percentage of mild disease (Figure 2).

Conclusion: Sub-populations with unique serological biomarker combinations that predict disease severity are identifiable. The sub-group that was not influenced as strongly by serology was the group identified to have the largest proportion of patients with mild disease. Furthermore, the group with the highest proportion of patients with severe disease was most heavily influenced by ESR and CRP, and the group with the next highest percentage of severe disease was influenced predominantly by anti-CCP and RF. This suggests 2 unique populations with higher serological values and various weighted combinations of ESR and CRP, or anti-CCP and RF, seem to display RA with a more severe phenotype. Further studies will need to be undertaken to identify factors that make these RA groups unique.

Disclosure: J. Van Dyk, None; **B. Heard**, None; **C. Barnabe**, None.

Abstract Number: 0455

Anti-Protein-Arginine Deiminase (PAD) 4 IgA Are Present in the Sera of Rheumatoid Arthritis Patients and Are Associated with Joint Erosion and Biological Treatment Use

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SESSION INFORMATION
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Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Over the past years, novel biomarkers have been described in rheumatoid arthritis (RA) patients, including autoantibodies to the protein-arginine deiminase (PAD) enzymes. Anti-PAD4 IgG are associated with anti-citrullinated protein antibodies (ACPA), worse baseline radiographic joint damage and a better response to treatment escalation. These data suggest that anti-PAD antibodies might play a role in RA pathogenesis. The objective of this study was to evaluate the presence of anti-PAD4 IgG and IgA in the sera of RA patients and to investigate their association with joint erosion and biological treatment use.

Methods: All the samples included in this study were tested for anti-PAD4 IgG and IgA using the novel particle-based multi-analyte technology (PMAT, research use only, research use only). In a first phase, sera from RA patients (n=70) and controls (n=155) were included (Figure 1). Next, anti-PAD4 IgG and IgA were measured in a second cohort of RA patients (n=40) for whom information on erosion status and biological treatment was available. ACPA IgG was also measured in these patients by QUANTA Flash CCP3 (Inova Diagnostics, CA, US).

Results: Anti-PAD4 IgA but not IgG levels were significantly higher in RA patients vs. controls (p=0.0080 and p=0.2740, respectively) (Figure 1). Receiver operating characteristics (ROC) analysis showed significant discrimination in the clinically relevant area (high specificity) for both IgG and IgA (Figure 2). Using the 95th percentile of the controls as cut-offs, anti-PAD4 IgG reported a sensitivity and specificity of 17.1%/94.8% for IgG and 20.0%/94.8% for IgA. Significantly higher levels of anti-PAD4 IgA but not anti-PAD4 IgG or ACPA were found in the RA patients with erosive disease vs. individuals without erosions (p=0.0419, p=0.2126, and p=0.7417, respectively) (Figure 3A), and in patients under biological treatment vs. those that were not on biologics (p=0.0240, p=0.1261, and p=0.8202, respectively) (Figure 3B).

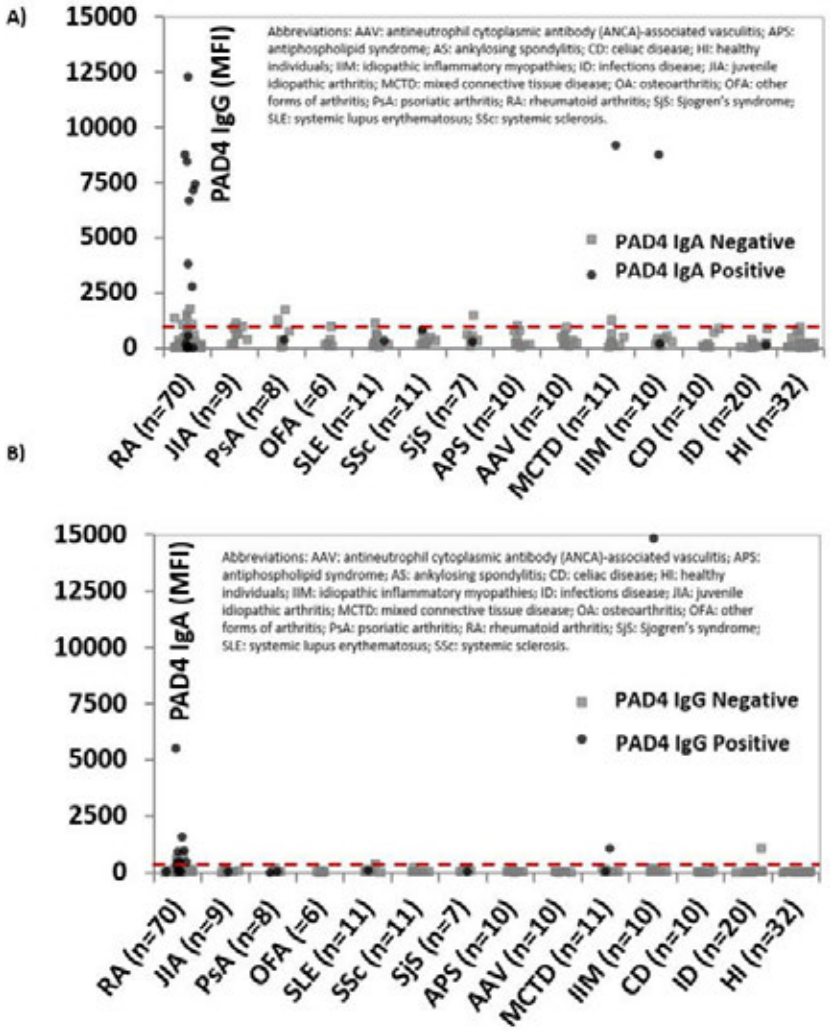

Figure 1. Levels of anti-PAD4 IgG (A) and IgA (B) in the different disease groups. The positivity for the other anti-PAD4 isotype is also represented in each graph. Red dashed lines represent the preliminary cut-offs.

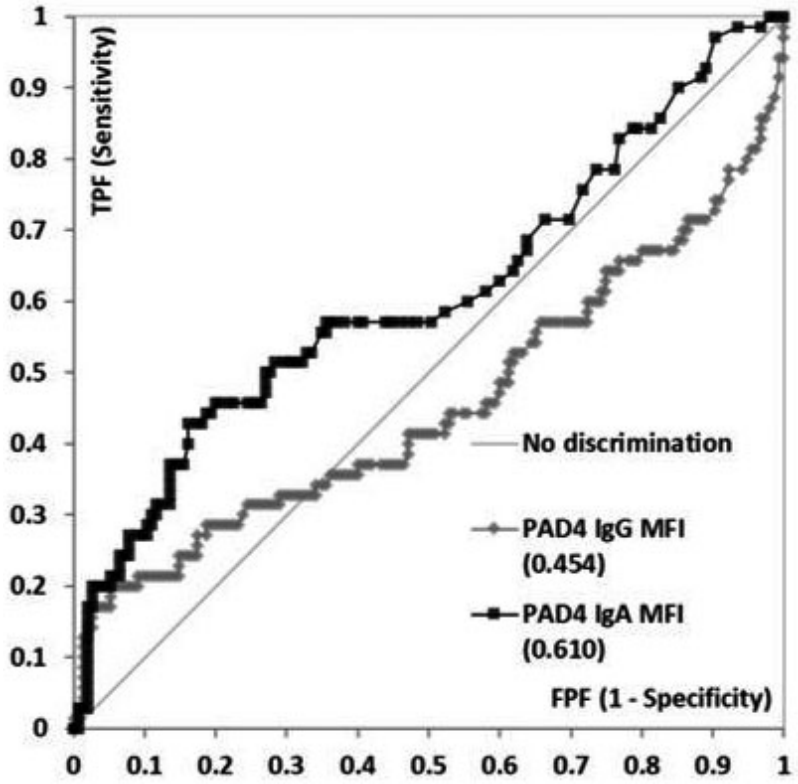

Figure 2. Receiver Operating Curve (ROC) analysis of anti-protein arginine deiminase (PAD) 4 IgG (grey) and IgA (black) for the discrimination of rheumatoid arthritis (RA) versus controls. Area under the curve (AUC) is shown for each isotype.

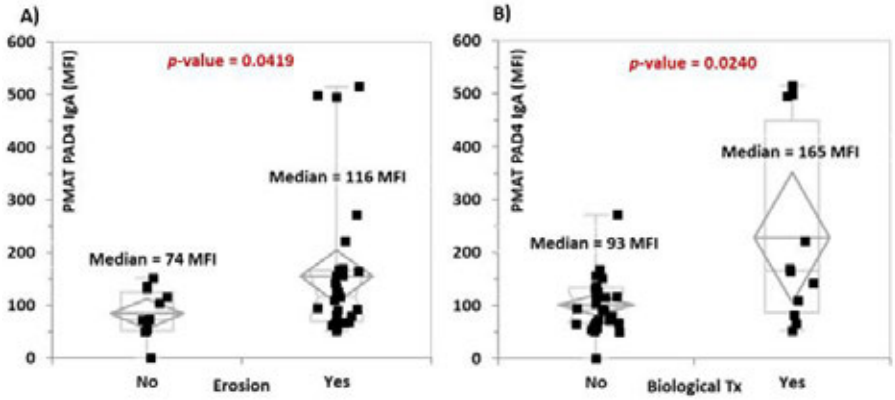

Figure 3. Pairwise comparison (Wilcoxon Mann-Whitney analysis) of anti-protein arginine deiminase (PAD) 4 IgA in RA patients based on erosive status (A) and on the biological treatment use (B). Median of each subgroup and p-values are shown in the figures.

Conclusion: Our study is the first to report anti-PAD4 IgA as a highly specific marker for RA showing strong association with erosive disease as well as biological treatment, suggesting a more severe phenotype. Anti-PAD4 antibodies of the IgA isotype represent a novel biomarker for RA patient stratification and prediction of prognosis.

Disclosure: L. Martinez-Prat, Inova Diagnostics, 3; **V. Martínez Taboada**, None; **M. Lopez-Hoyos**, None; **M. Mahler**, Inova Diagnostics, 3.

Abstract Number: 0456

Vitamin D Is Not Associated with Treatment Responses in Patients with Newly Diagnosed Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
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Background/Purpose: Vitamin D is known to have immunomodulatory properties and had shown a relationship with susceptibility and disease activity in rheumatoid arthritis (RA). We investigated the relationship between response to treatment and vitamin D levels in patients newly diagnosed with RA.

Methods: This was a retrospective study of 249 patients who were newly diagnosed with RA. They were assessed for 25-hydroxyvitamin D (25OHD) level at diagnosis of RA and after 6 months of treatment. All patients with vitamin D insufficiency (25OHD < 30 ng/ml) received vitamin D supplementation. Correlation between vitamin D levels and disease activity measured by Disease Activity Score 28 calculated with erythrocyte sedimentation rate (DAS28-ESR) at diagnosis and after 6 months were assessed.

Results: The proportion of patient with low, moderate, and high disease activity at diagnosis were 9.2%, 59.4%, and 31.3%, respectively. Mean level of 25OHD was 18.8 ± 11.3 ng/ml. Vitamin D level showed no significant correlation with disease activity at diagnosis with a mean 25OHD value of 17.4 ± 8.6 ng/ml, 19.1 ± 11.3 ng/ml, and 18.8 ± 12.1 ng/ml, respectively. After 6 months of treatment, the proportion of patients in remission, low, moderate, high disease activity were 41.7%, 22.4%, 29.4%, and 6.1%, respectively. Vitamin D significantly increase to mean 25OHD value of 24.7 ± 11.1 ng/ml after 6 months of treatment of RA and vitamin D supplementation in patients with insufficiency. However, it showed no significant correlation with treatment response at 6 months with a mean value of 23.2 ± 11.4 ng/ml, 25.1 ± 10.5 ng/ml, 26.2 ± 10.5 ng/ml, and 26.3 ± 11.9 ng/ml.

Conclusion: Patients showed vitamin D insufficiency at diagnosis of RA, but vitamin D was not correlated with treatment response of RA.

Disclosure: J. Kang, None; **C. Choi**, Eisai Korea, 2.

Abstract Number: 0457

Serum Myostatin in Patients with Rheumatoid Arthritis and Its Correlations with Body Compositions and the Disease Activity

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Altered body composition is a common feature of patients with rheumatoid arthritis (RA), up to two-thirds of affected patients showing loss of muscle mass and strength and a concomitant increase in fat mass, so-called “rheumatoid cachexia”. Despite great advances in the treatment of RA, such as biological agents and small-molecule compounds, rheumatoid cachexia persists even after joint inflammation has improved. Myostatin, a member of the transforming growth factor-beta superfamily, is a potent negative regulator of skeletal muscle growth and its inactivation can induce skeletal muscle hypertrophy, whereas its overexpression or systemic administration causes muscle atrophy. As it enhances proteolysis and inhibits protein synthesis in skeletal muscle, it has generated considerable interest as a potential regulator of cachexic status in patients with conditions such as cancers, cardiac failure, and HIV infection. In this study, we investigated the possible role of myostatin in body composition alteration in patients with RA.

Methods: This was a cross-sectional study. Ninety-six RA patients who visited Niigata University Hospital between April and June 2017 were recruited. Body composition in each subject was measured by bioelectrical impedance analysis with a tetrapolar impedance meter (InBody S-10, InBody Japan Inc., Tokyo, Japan). The serum myostatin level was measured by enzyme-linked immunosorbent assay with a commercially available kit (Quantikine ELISA GDF-8/Myostatin Immunoassay, R&D Systems, MN, USA). Patients’ laboratory findings and disease activities were also measured, and the correlations between the titer of serum myostatin and these factors were analyzed by Spearman’s correlation coefficient and stepwise multiple regression. In addition, 70 female patients from the cohort were divided into two groups according to their fat-free mass index (FFMI) (low FFMI group (FFMI< 13.82, n=20) and normal FFMI group (n=50)), and their clinical findings and serum myostatin levels were compared by Mann-Whitney U test. Differences at $p < 0.05$ were considered to be statistically significant.

Results: Spearman’s correlation coefficient analysis showed that the serum myostatin level was positively correlated with skeletal muscle mass index and FFMI, and negatively correlated with percentage body fat (%BF), fat mass index (FMI), the swollen joint count, ESR, and DAS28(4)-ESR. Stepwise multiple regression analysis selected FFMI as a positive independent variable (rho=0.3620, p=0.00019) and DAS28(4)-ESR as a negative independent variable (rho=-0.2298, p=0.0154) against the serum myostatin level, respectively. In these 70 female patients, %BF and FMI/FFMI ratio were significantly higher in the low FFMI group than in the normal FFMI group.

Conclusion: The serum myostatin level was significantly correlated with body composition and disease activity in patients with RA. Patients with a lower level of myostatin showed a tendency to have decreased skeletal muscle and increased body fat, suggesting that serum myostatin could be a possible biomarker of rheumatoid cachexia.

Disclosure: Y. Wada, None; **M. Sudo**, None; **D. Kobayashi**, None; **T. Kuroda**, None; **M. Nakano**, None.

Abstract Number: 0458

The Influence of Mediterranean Diet in Rheumatoid Arthritis: A Monocenter Cross-sectional Study

Francesca Ingegnoli ,[1] Tommaso Schioppo,[1] Isabella Scotti,[2] Giuseppe Marano,[2] Patrizia Boracchi,[2] Orazio De Lucia,[3] Antonella Murgo,[3] and Roberto Caporali[1], [1]Division of Clinical Rheumatology, ASST Pini-CTO, Università degli Studi di Milano, Department of Clinical Sciences and Community Health, Milan, Italy, Milano, Italy, [2]Università degli Studi di Milano, Milano, Italy, MILANO, Italy, [3]Division of Clinical Rheumatology, ASST Pini-CTO, Milan, Italy, Milano, Italy

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Mediterranean diet (MD) is considered a well-balanced and potentially anti-inflammatory diet characterized by high consumption of olive oil, unrefined cereals, fresh or dried fruit and vegetables, fish, dairy products, meat and with a moderate amount of red wine. Currently, there is conflicting data for the benefits of MD in rheumatoid arthritis (RA), and not enough evidence to support a role of MD in the prevention and treatment of RA.

The aim of our study was to evaluate the association between MD adherence and disease activity, general health (GH) and comorbidities in patients with RA.

Methods: Consecutive patients with RA (ACR/EULAR Criteria 2010) were enrolled in this cross-sectional study. For each patient, Disease Activity Score on 28 joints (DAS28), Simple Disease Activity Index (SDAI), patient GH and a self-reported questionnaire called MD score were recorded. The association between MD score and the above mentioned variables was assessed through univariate regression models (MD score as response variable and the variables of interest as independent variables). Results from each model were reported in terms of: 1) test of association (Likelihood Ratio test, with a Chi-square distribution); 2) categorical independent variables, estimated differences of mean MD score between groups, with respective 95% CI; 3) numerical independent variables, estimate of correlation coefficient and regression slope coefficient, with respective 95% CI. The analysis was performed using the R software.

Results: 205 RA patients (197 Italian) were enrolled: median age at visit 53 (q1-q3: 44-59) years, age at onset 38 (q1-q3: 28-47), disease duration 12 (q1-q3: 7-19), female 80.49%, rheumatoid factor and/or anti–citrullinated protein antibody positivity 58.54%, radiographic damage 41.79%. Comorbidities were also assessed: gastrointestinal 19% (gastro-esophageal reflux disease; inflammatory bowel disease; gastritis; esophagitis), chronic renal failure 1%, arterial hypertension 21.95%, diabetes mellitus 3.9% and coronary artery disease 1.95%. A significant positive correlation was found between MD score and GH, as shown in the table. This suggests a low/moderate tendency of having better GH with higher MD score. Although not statistically significant, a negative correlation was found with DAS28 and SDAI, suggesting an association between higher MD score with lower disease activity. Among comorbidities, a significant difference of mean MD score values between subjects with and without arterial hypertension was also found (mean difference -2.0 CI: -3.7, -0.2; p=0.029).

Conclusion: In this Italian RA cohort, the adherence to MD was significantly associated with a better GH, but higher MD score was not significantly associated with lower disease activity. Arterial hypertension was the only comorbidity

	Mediterranean diet score		
	Correlation coefficient (r): est (95% C.I.)	Regression coefficient (slope): est (95% C.I.)	LR test: p-value
DAS28	-0,10 (-0.23, 0.04)	-0.45 (-1.05, 0.16)	0.149
SDAI	-0.12 (-0.25, 0.02)	-0,12 (-0.38, 0.15)	0.088
GH	0.19 (0.05, 0.31)	0.05 (0.01, 0.09)	0.007*
Body mass index	-0.05 (-0.18, 0.09)	-0,06 (-0.22, 0.08)	0.483

associated with lower MD score, probably due to the fact that the prevalence of the other comorbidities was low. Our study suggests an overall beneficial effect of MD in RA patients. Further studies are needed to better understand the impact of lifestyle modification (*e.g.* diet) in achieving RA disease control.

Disclosure: F. Ingegnoli, None; **T. Schioppo**, None; **I. Scotti**, None; **G. Marano**, None; **P. Boracchi**, None; **O. De Lucia**, None; **A. Murgo**, None; **R. Caporali**, None.

Abstract Number: 0459

The Effects of Erythrocytes and Platelets on Disease Activity in Patients with RA - ANSWER Longitudinal Cohort Study -

Akira Onishi ,[1] Kengo Akashi,[1] Sadao Jinno,[2] Yonsu Son,[3] Hideki Amuro,[3] Toru Hirano,[4] Yuichi Maeda,[5] Motomu Hashimoto,[6] Wataru Yamamoto,[6] Kosaku Murakami,[6] Ryota Hara,[7] Masanori Katayama,[8] Tohru Takeuchi,[9] Takuya Kotani,[9] Jun Saegusa,[1] and Akio Morinobu[1], [1]Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, [2]Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Osaka, Japan, [3]First Department of Internal Medicine, Kansai Medical University, Osaka, Japan, [4]Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University, Osaka, Japan, [5]Department of Respiratory Medicine and Clinical Immunology, Osaka University Graduate School of Medicine, Osaka, Japan, [6]Department of Advanced Medicine for Rheumatic Diseases, Kyoto University Graduate School of Medicine, Kyoto, Japan, [7]The Center for Rheumatic Disease, Department of Orthopedic Surgery, Nara Medical University, Nara, Japan, [8]Department of Rheumatology, Osaka Red Cross Hospital, Osaka, Japan, [9]Department of Internal Medicine IV, Osaka Medical College, Osaka, Japan

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

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Session Time: 9:00AM–11:00AM

Background/Purpose: Experimental models suggested both erythrocytes and platelets activated immune cells and enhanced inflammation in inflammatory arthritis. Although previous cross-sectional studies showed the form and number of erythrocytes and platelets were associated with disease activity, the cross-sectional design cannot assess the causal relationship between erythrocytes/platelets and disease activity. Other limitations include no adjustment with confounding factors and small sample size. The objective of this multi-center longitudinal large cohort study is, therefore, to identify the effects of erythrocytes and platelets on disease activity in patients with RA.

Methods: Hemoglobin concentrations, mean corpuscular volume (MCV), red blood cell distribution width (RDW), platelet counts, and mean platelet volume (MPV) were measured as exposures. Disease activity was assessed using clinical disease activity index (CDAI) for primary outcome. Considering the estimation of effects of time-varying exposures and clustering effects by individual, linear mixed-effect models were used to examine the association between the indices of erythrocytes and platelets on the previous visit and disease activity on the next visit. The indices of erythrocytes and platelets, and disease activity were used as time-dependent variables while participant identification number and time from baseline were included as random factors. Age, sex, disease duration, RF, ACPA, prednisolone, and DMARDs were included as covariates. Sensitivity analyses were also conducted based on secondary outcomes of DAS28-CRP and simplified disease activity index (SDAI).

Results: A total of 63913 samples (median sampling interval: 66.2 days) from 3973 patients was included. The median age at baseline was 63.0 years with 78.3 % of women and mean disease activity were moderate (CDAI:10.9). Regarding erythrocytes, the next disease activity was significantly higher in patients with lower hemoglobin concentrations (-0.53/mg/dL, $P < 0.001$), MCV (-1.18/fL, $P < 0.001$), and RDW (-0.09/fL, $P < 0.001$) on the previous visit after

adjusting by potential confounding factors. For platelets, higher platelet counts and lower MPV were associated with the next higher disease activity (0.20/μL, $P < 0.001$ and -0.55/fL, $P < 0.001$, respectively). These results were similar using DAS28-CRP and SDAI.

Conclusion: These results suggest the number and form of erythrocytes and platelets capture disease activity that remain unmeasured by established disease activity measures in RA. These may also support erythrocytes and platelets influence immune and inflammatory processes in patients with RA as well as the established opposite causal relationship.

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Abstract Number: 0460

Fertility of Women with Rheumatoid Arthritis: Disease Activity Negatively Correlates with Serum AMH Levels

Camille Valdeyron ,[1] Martin SOUBRIER,[2] Bruno Pereira,[1] Arnaud Constantin,[3] Jacques Morel,[4] Philippe Gaudin,[5] Bernard Combe,[6] and Florence Brugnon[1], [1]CHU CLERMONT-FERRAND, Clermont-Ferrand, France, [2]CHU Gabriel Montpied, Clermont Ferrand, Auvergne, France, [3]CHU TOUOUSE, TOULOUSE, France, [4]CHU MONTPELLIER, MONTPELLIER, France, [5]Rheumatology Department, CHU Grenoble Alpes Hôpital Sud and GREPI - Université Grenoble Alpes, EA7408, Grenoble - Echirolles, France, [6]CHU Montpellier, Montpellier University, Montpellier, France

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) display a higher infertility prevalence compared with the general population. Disease-related inflammation and RA treatments are likely to be the main factors explaining the RA patients' infertility. Nevertheless, the tangible link between these different factors and the decline in women's fertility has never been clearly demonstrated. This study sought to examine the impact of RA disease activity and treatments on ovarian reserve measured by serum AMH levels in a large patient cohort over 36 months. Using this analysis, we sought to better define the indications for fertility preservation in RA patients.

Methods: Patient and serum analysis data were derived from the French national prospective cohort ESPOIR (Etude et Suivi des POlyarthrites Indifférenciées Récentes). Enrolled patients (n= 117; 18-37-year-olds) fulfilling ACR/EULAR2010 criteria for RA were not receiving any medication at enrolment time (T0). Patients were examined and serum AMHs level measured at T0, 6(T6), 12(T12), 24(T24), and 36(T36) months post-diagnosis.

Serum AMH measurements were performed using the electrochemiluminescence method (analyser Cobas® e411). The impact of both RA activity (evaluated by DAS28 scores and CRP levels) and treatments (methotrexate and corticosteroids) was evaluated at each study visit.

Results: Overall, 117 women from the ESPOIR cohort, aged 18-37 years, were included. The mean age was 29.2+/-5.3 years, mean body mass index 22.96 (+/-3.57)Kg/m^2, mean DAS 28 4.95 (+/-1.24) (range: 1.57-8.30), thus reflecting moderate RA activity, and mean CRP 22.5+/-34mg/L.

A gradual decrease in patients' serum AMH levels was observed over time, in line with the descending curve described in the literature for healthy women (Kelsey *et al*.,2011). Serum AMH levels of RA patients in comparison with the values considered normal for age did not reveal any significant differences at T6, T12, T24, and T36 ($p > 0.05$). We did not observe any impact of RA treatments on serum AMH levels, irrespective of the medication administered, and even after adjusting for age and DAS 28 score ($p=0.81$). We demonstrated an inverse correlation between serum AMH level variations and inflammation parameters (DAS28: r=-0.27, $p=0.003$; CRP: r=-0.16, $p=0.06$).

Conclusion: This is the first study to determine serum AMH levels of a large cohort of young RA patients over 36 months. A quick disease activity limitation appears required to limit ovarian reserve alterations. Oocytes or ovarian tissues are not likely to be necessary if inflammation is promptly controlled. No impact of RA treatments was observed. More studies are required to further explain the pathophysiological mechanisms underlying these associations.

Disclosure: C. Valdeyron, None; **M. SOUBRIER**, None; **B. Pereira**, None; **A. Constantin**, Novartis, 8, Pfizer, 5, Sanofi, 5, SANOFI, 8, UCB, 5, 8; **J. Morel**, None; **P. Gaudin**, None; **B. Combe**, AbbVie, 5, BMS, 5, 8, Chugai, 5, 8, Eli Lilly, 5, Eli Lilly and Company, 5, 8, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, UCB, 5, USD, 5; **F. Brugnon**, None.

Abstract Number: 0461

Maximal Improvement in Fatigue Lags Behind Achievement of Sustained Remission in Early Rheumatoid Arthritis

Melissa Holdren ,[1] Orit Schieir,[2] Susan J. Bartlett,[3] Louis Bessette,[4] Gilles Boire,[5] Glen Hazlewood,[6] Carol Hitchon,[7] Edward Keystone,[8] Diane Tin,[9] Carter Thorne,[10] Vivian Bykerk,[11] Janet Pope,[12] and Canadian Early Arthritis Cohort (CATCH) Investigators[13], [1]The University of Western Ontario, London, ON, Canada, [2]University of Toronto Dalla Lana School of Public Health, Toronto, ON, Canada, [3]McGill University, Montreal, QC, Canada, [4]Laval University, Quebec City, QC, Canada, [5]Sherbrooke University, Sherbrooke, QC, Canada, [6]University of Calgary, Calgary, AB, Canada, [7]University of Manitoba, Winnipeg, Canada, [8]Mount Sinai Hospital and University of Toronto, Toronto, ON, Canada, [9]Southlake Regional Health Centre, Newmarket, Canada, [10]Southlake Regional Health Centre, Newmarket, ON, Canada, [11]Hospital for Special Surgery, New York City, NY, [12]Western University, London, ON, Canada, [13]Canadian Early Arthritis Cohort (CATCH) Study, Toronto, Canada

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Up to 80% of rheumatoid arthritis patients report clinically relevant fatigue. Fatigue is a complex multi-factorial process that can result in adverse affects on patients' physical and emotional well-being.

The purpose of this study was to examine the relationship between disease activity and fatigue over time in early rheumatoid arthritis (ERA).

Methods: Data were from patients with ERA (symptoms ≤ 12 months) enrolled in the Canadian Early Arthritis Cohort (CATCH). CATCH participants completed repeat clinical assessments, laboratory investigations and self-reported questionnaires including rating their fatigue over the past week using a 0-10 point numerical rating scale (NRS). Fatigue severity was classified as low (≤2); moderate (>2 but < 5) and high (≥5) based on other published RA studies. T-tests and repeated measures ANOVA were used to compare differences in fatigue in patient who did vs. did not achieve a low disease state using ESR (DAS28 ≤ 3.2) or REM (DAS28 < 2.6) within 3-months of cohort entry. Paired t-tests were used to compare fatigue at different time points in patients achieving remission (DAS < 2.6) at three or more consecutive visits within the first year of follow-up.

Results: Of the 1864 patients included, 1640 (88%) met ACR criteria for RA, 1342 (72%) were women and most had moderate-high baseline disease activity with a mean (SD) DAS28 of 4.9 (1.5). Fatigue was common with 19% reporting moderate and 59% high fatigue at baseline. Patients who reported low fatigue severity by three months continued to have significantly lower fatigue throughout follow-up compared to those with moderate or high fatigue (p< 0.001). Patients who achieved DAS28 REM or LDA within 3-months of cohort entry (N=539) had significantly lower mean fatigue throughout 5 years of follow-up compared to those who did not achieve REM or LDA within 3 months (p< 0.001) (Figure 1). Patients who achieved sustained remission in the first 3-months of cohort entry (N=236) had significantly decreased fatigue at time of first achieving DAS REM and 6 months after initially achieving DAS REM (Figure 2). Patients who first achieved sustained remission after 6-months of cohort entry (N= 141) had significantly decreased fatigue at both 3 and 6-months after cohort entry as well as 6-months after the first time in DAS REM (Figure 3).

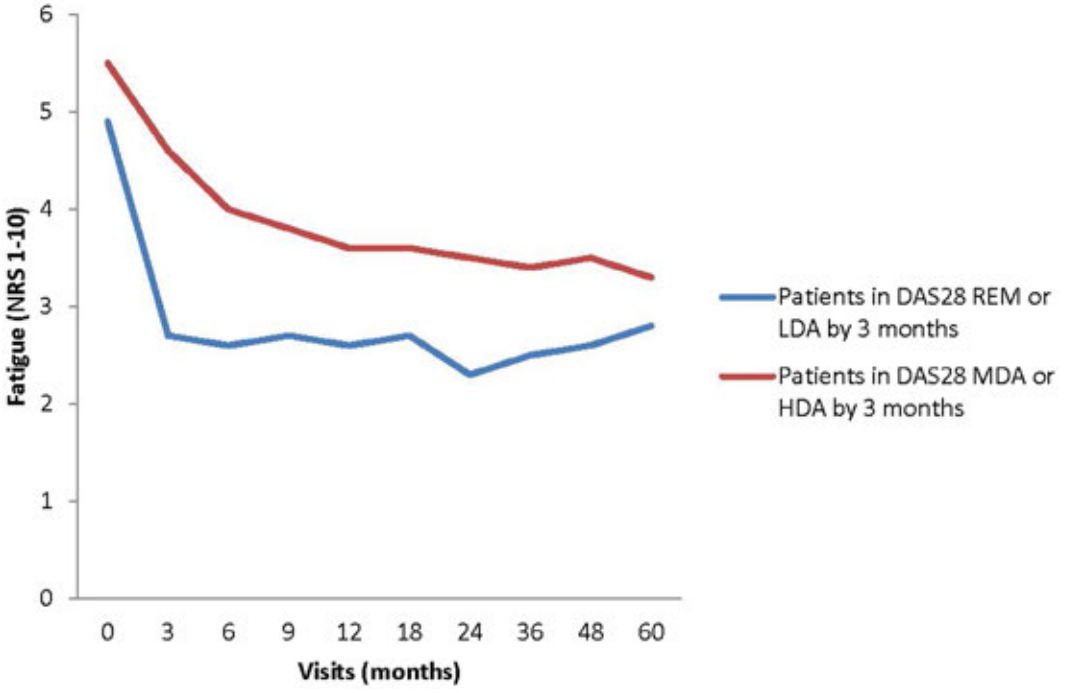

Figure 1. Differences in fatigue scores over time in ERA patients comparing patients in DAS28(ESR) REM or LAD to patients in DAS28(ESR) MDA or HDA at 3 months. DAS28(ESR): disease activity score in 28 joints using Erythrocyte Sedimentation Rate; REM: remission; LDA: low disease activity; MDA: moderate disease activity; HDA: high disease activity.

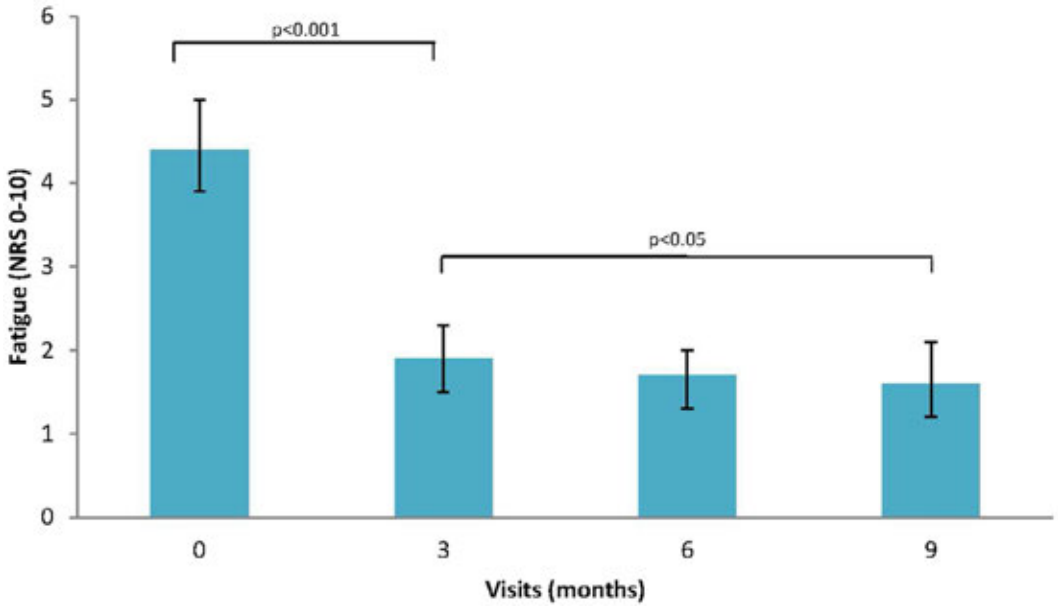

Figure 2. Change in fatigue over time in patients achieving sustained remission (DAS <2.6) from months 3 to 9 (N=236)

Conclusion: Fatigue is common in ERA and is significantly decreased at time of first remission in those with sustained remission within the first year of diagnosis. Maximal improvement in fatigue lags behind with further improvement in fatigue seen 6 months after first remission. Early treatment response within 3-months was associated with short and long-term improvements in fatigue over time. This may have implications for counselling patients.

Disclosure: M. Holdren, None; **O. Schieir**, None; **S. Bartlett**, Abbie, 2, Abbvie, 2, 5, Bayer, 5, International Society of QOL Research, 6, Janssen, 5, 8, Lilly, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, Pfizer Inc, 8, PROMIS International, 6, UCB, 5, 8; **L. Bessette**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, Amgen, BMS, Janssen, Roche, UCB Pharma, AbbVie Inc, Pfizer, Merck, Celgene, Sanofi, Eli Lilly, and Novartis., 2, 5, 8, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Bristol-Myers-Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5; **G. Boire**, Abbvie, 2, Amgen, 2, 5, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, Eli Lilly, 2, 5, Lilly, 2, 5, Merck, 2, 8, Novartis, 2, Pfizer, 2, 5, 8; **G. Hazlewood**, None; **C. Hitchon**, Pfizer, 2, UCB, 2, UCB Canada, 2; **E. Keystone**, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 5, Astra-Zeneca, 5, Biotest, 5, BMS, 2, 5, 8, Celltrion, 5, Crescendo, 5, Crescendo Bioscience, 5, F. Hoffmann-La Roche Inc, 2, 5, 8, Genentech, 5, Genentech Inc., 5, Genzyme, 5, Gilead, 2, 5, Gilead Sciences, Inc., 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 5, 8, Pfizer, 2, 5, 8, Pfizer Pharmaceuticals, 2, 5, 8, Roche, 2, 5, 8, Sandoz, 5, Sanofi, 2, 5, 8, Sanofi-Aventis, 2, 8, UCB, 5, 8; **D. Tin**, None; **C. Thorne**, Abbvie, 2, 5, Amgen, 2, 5, CaREBiodam, 2, Celgene, 2, 5, Centocor, 5, Janssen, 5, Lilly, 5, Medexus/Medac, 5, 8, Merck, 5, Novartis, 2, 5, Pfizer, 2, 5, Sandoz, 5, Sanofi, 5; **V. Bykerk**, AbbVie, 5, Amgen, 1, 2, 3, 5, 8, Brainstorm Therapeutics, 1, 2, 3, 5, 8, Bristol-Myers Squibb, 5, Genentech, 5, Gilead, 5, NIH, 2, Pfizer, 1, 2, 3, 5, 8, Regeneron, 5, Regeneron Pharmaceuticals, Inc, 5, Sanofi, 5, Sanofi/Genzyme-Regeneron, 5, Sanofi-Genzyme/Regeneron, 1, 2, 3, 5, 8, Scipher, 1, 2, 3, 5, 8, The Cedar Hill Foundation, 9, UCB, 1, 2, 3, 5, 8, UCB Pharma, 5; **J. Pope**, AbbVie, 5, Abbvie, 5, Actelion, 5, Actellion, 5, Amgen, 2, 5, AstraZeneca, 2, Astra-Zeneca, 2, Bayer, 2, 5, BMS, 2, 5, Eicos Sciences, 5, Eli Lilly & Company, 5, Eli Lilly and Company, 5, EMERALD, 5, Emerald, 5, Genzyme, 5, Janssen, 5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8; **C. (CATCH) Investigators**, Amgen, 2, Pfizer Canada, 2, AbbVie Corporation, 2, Medexus Inc., 2, Eli Lilly Canada, 2, Merck Canada, 2, Sandoz Canada Biopharmaceuticals, 2.

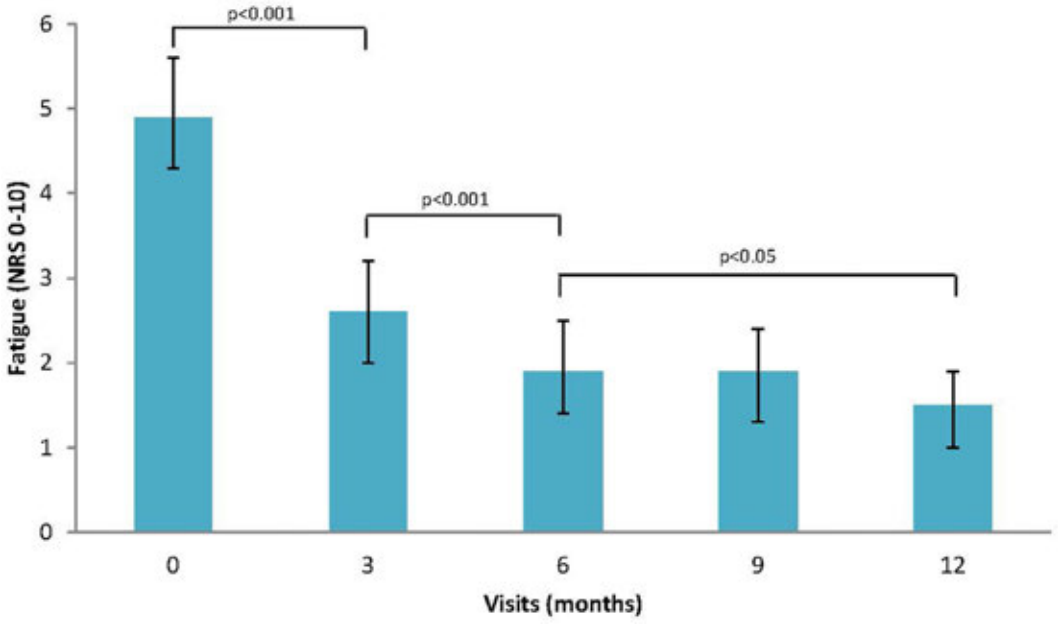

Figure 3. Change in fatigue over time in patients achieving sustained remission (DAS <2.6) from months 6 to 12 (N=141).

Abstract Number: 0462

The Endogenous Plasma Small RNAome of Rheumatoid Arthritis

Michelle Ormseth ,[1] Joseph Solus,[2] Quanhu Sheng,[2] Fei Ye,[2] Haocan Song,[2] Qiong Wu,[2] Yan Guo,[3] Annette Oeser,[2] Ryan Allen,[2] Kasey Vickers,[2] and C. Michael Stein[2], [1]Vanderbilt University Medical Center and Veterans Administration: TN Valley Healthcare System, Nashville, [2]Vanderbilt University Medical Center, Nashville, [3]University of New Mexico, Albuquerque

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Small RNA (sRNA) sequencing has revealed new classes of sRNAs beyond microRNAs. These sRNAs can regulate genes and are also useful biomarkers of disease. The aim of this study was to determine if the endogenous plasma sRNA landscape of patients with RA is altered compared to control subjects and determine their association with disease-related parameters in RA.

Methods: sRNA sequencing was performed on plasma from 165 RA and 90 control subjects who were frequency-matched for age, race and sex. TIGER pipeline was used to quantify endogenous sRNAs including microRNAs and sRNAs derived from small nuclear RNAs (snDRs), small nucleolar RNAs (snoDRs), YRNAs (yDRs), transfer RNAs (tDRs), long non-coding RNAs (lncDRs), miscellaneous sRNAs (miscRNAs), and sRNAs aligning to the human genome but not annotated sRNAs categories (such as sRNAs aligning to messenger RNAs or precursors such as pre-rRNAs). Sequencing reads were normalized to million total reads. The reads in each sRNA category were compared between RA and control subjects and correlated with disease activity measures and general laboratory measures with Spearman correlation. The correlations were presented using heatmap with hierarchical clustering.

Results: The largest proportion of endogenous plasma sRNAs was yDRs, followed by microRNAs. Patients with RA had more microRNAs (1.42-fold, P=0.01), more tDRs (1.14-fold, P=0.04), and fewer yDRs (-1.41-fold, P=0.009) compared to control subjects (Figure 1), but other sRNAs as classes were not significantly different in RA. Disease duration was inversely associated with yDRs (Figure 2). Disease-related parameters such as DAS28 score, swollen

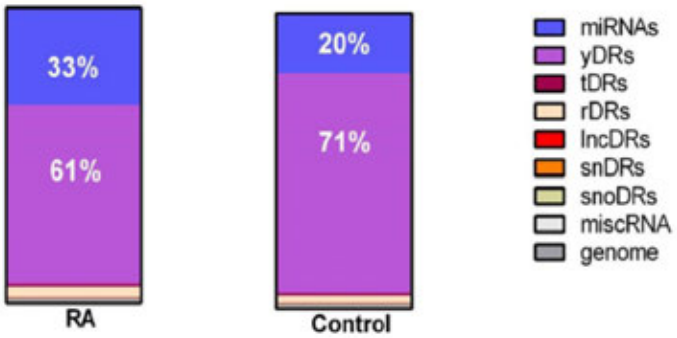

Figure 1. Proportions of endogenous plasma sRNAs in RA and control subjects. Proportions were calculated using the geometric mean of the sRNAs due to skewness.

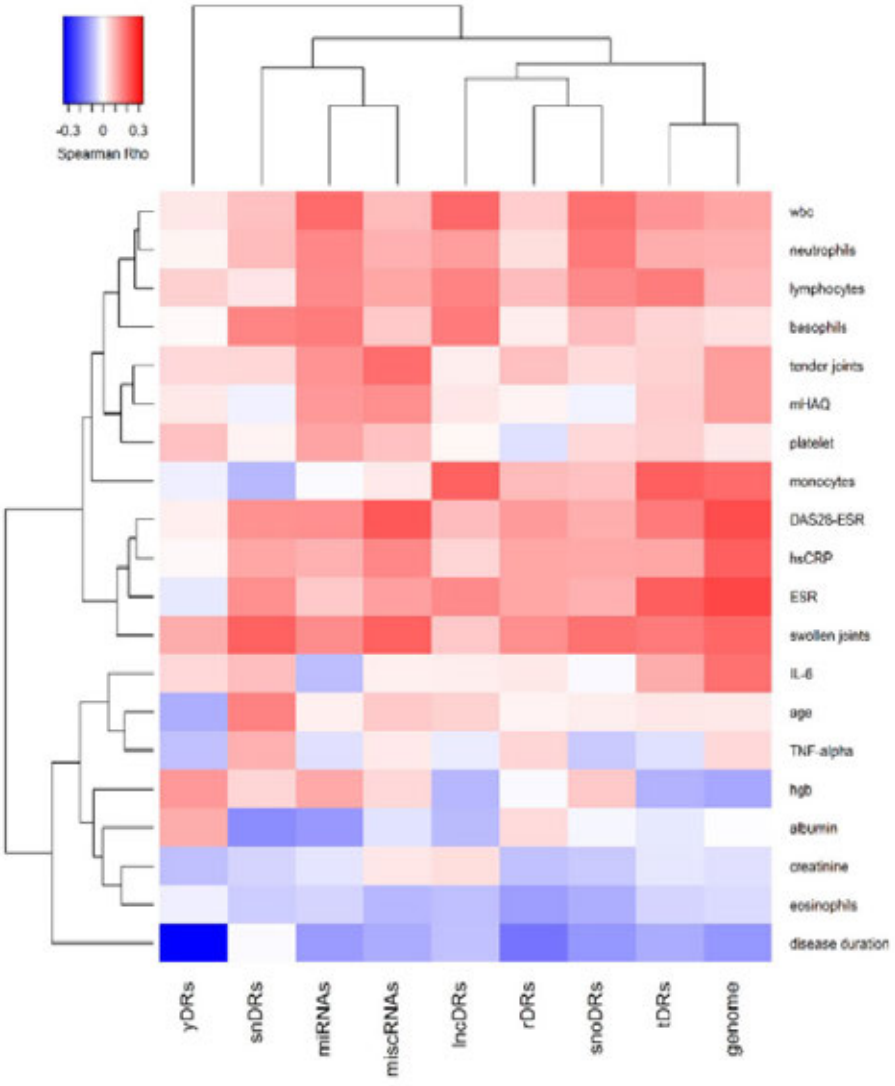

Figure 2. Heatmap with hierarchical clustering demonstrating the relationship between sequencing reads of plasma sRNAs based on category.

joint count, and inflammatory markers were significantly positively associated with genome reads not classified as a sRNA category, tDRs and miscRNAs (Figure 2).

Conclusion: Endogenous plasma sRNAs are altered in patients with RA compared to control subjects. While individual miRNAs have been well studied and many are excellent biomarkers in RA, non-miRNA sRNA and unclassified sRNAs were significantly associated with disease related parameters as classes and may represent novel biomarkers for RA.

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Abstract Number: 0463

High-titer Rheumatoid Factor Impacts Real-life Management Outcomes of Rheumatoid Arthtitis

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SESSION INFORMATION
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Background/Purpose: The rheumatoid factors (RF) have established roles in rheumatoid arthritis (RA) diagnosis, prediction of disease onset and drug response, and in classifying patients as to prognosis. We assessed the influences of RF presence and titration on real-life management outcomes in a large multicenter RA cohort.

Methods: From August, 2015 to April, 2016, the REAL Study enrolled adult patients diagnosed with RA, according to ARA (1987) or ACR/EULAR (2010) criteria, from eleven Brazilian tertiary healthcare centers. Structured clinical interview and assessment of medical records were performed. DAS28-ESR score, treat to target (T2T) goal attainment (DAS28-ESR < 3.2), disability (HAQ), RF titers, and the presence of erosive disease (EULAR definition) were assessed, as well as several other clinical and demographic variables. A high-titer RF was defined as ≥ 3x the upper limit of normality. Student's t test, Mann-Whitney U, Kruskal-Wallis test, chi-square, and Fisher's exact test were used as appropriate.

Results: 1116 patients were included; 89.4% female and 56.8% white. The mean (SD) age was 57.1 (11.5) years; disease duration: 174.7 (115.1) months; schooling years: 8.3 (4.7). Mean DAS28-ESR was 3.6 (1.5); HAQ score 0.943 (0.769). Only 41.3% of patients were within the T2T goal for DAS28. RF was positive in 78.6% of all patients, and in high titers in 56.1%. Erosive disease was found in 54.9%. The median delay from first symptoms to first DMARD was 12 months (IQR=36). RF titers categories (negative, low and high positive) were comparable as to background characteristics: gender, race, age, disease duration, schooling years, and delay from first symptoms to first DMARD ($p > 0.05$ for all comparisons). The high-titer RF category as compared to the non-high (combined negative or low-titer) RF category showed higher DAS28-ESR scores [3.8(1.5) vs. 3.4(1.5); $p < 0.001$]; higher HAQ scores [0.999(0.796)

vs. 0.870(0.728); p=0.012]; lower attainment of T2T goals [37.2% vs. 46.9%; OR 0.67 (95%CI: 0.51—0.87)]; higher usage of corticosteroids [52.4% vs. 40.2%; OR 1.64 (95%CI: 1.29—2.08)]; higher biological DMARD usage [39.3% vs. 30.9%; OR 1.45 (95%CI: 1.12—1.86)], and higher frequency of extra-articular manifestations [26% vs. 19.6%; OR 1.45 (95%CI: 1.08—1.92)]. Negative and positive low-titer RF categories showed no significant differences between themselves, as to any of the aforementioned outcome variables. Erosive disease was not associated with the RF titer categories (p=0.097).

Conclusion: High-titer RF was associated with worse outcomes in real-life management of RA, with higher disease activity and disability, lower attainment of T2T goals, higher usage of both corticosteroids and biological DMARDs, and higher frequency of extra-articular manifestations. Erosive disease was not associated with RF titer categories in this study, possibly because of the long delay in initiating DMARDs in all RF titer categories, and the overall high frequency of erosions in this population. Negative and low-titer RF categories seemed to perform similarly, regarding clinical outcomes in real-life management of rheumatoid arthritis.

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Abstract Number: 0464

Continuous Decrease in Serum RF Titer During Anti-TNF Therapy Was Associated with Suppression in Progression of RA Joint Damage

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SESSION INFORMATION
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Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
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Session Time: 9:00AM–11:00AM

Background/Purpose: A number of studies have investigated the association between serum RF and joint damage in early and established RA patients, and positive and high-titer RF has been a risk or predictive factor of joint damage in RA patients. However, it still remains unclear whether the changes in serum RF titers were correlated with progressions of joint damage in RA. The purpose of this study is to clarify whether continuous decrease in RF titer during anti-TNF therapy was associated with suppression in progression of RA joint damage.

Methods: The subjects were 55 RA patients who filled RA criteria 2010, were treated with adalimumab, certolizumab pegol or golimumab, had serum RF titer ≥45 IU/ml at entry (at starting anti-TNF therapy, month 0), and were followed up until month 12. Their medical records were reviewed retrospectively. Serum RF titers were measured at the entry, month 4 and 12 months after starting TNF inihibitor. More than 10% reduction in RF titer was considered as significant decrease, and continuous decrease in RF titer was defined as significant reductions during both month 0-4 and 4-12. RA disease activity and radiographic progression were assessed by DAS28-CRP and modified total Sharp score (mTSS) at month 0 and 12. In case of withdrawal from anti-TNF therapy during month 4-12 due to some causes, data upon the discontinuation of TNF inhibitor was used as that at month 12 using the last observation carried forward method.

Results: Subjects were 9 male and 46 female, were median age 54.8 years with 3.5 years of disease duration, and were treated with 8 mg/week of median MTX dosage. Median DAS28-CRP and mTSS were 3.23 (interquartile range [IQR] 2.15–4.46) and 6 (IQR 1-20), respectively. After starting TNF inhibitor, the serum RF titer decreased from 104 IU/ml (median) at month 0 to 72 at month 4 ($p< 0.0001$) and 52 at month 12 ($p=0.0122$). Although median DAS28-CRP decreased from 3.23 at month 0 to 1.81 at month 12 ($p< 0.0001$), mTSS increased from 6 (IQR 1-20) to 6 (IQR 2-22) ($p< 0.0001$) and the radiographic progression (yearly change in mTSS >0.5) was found in 43.6%. During anti-TNF therapy, 26 of 55 subjects showed continuous decrease (CD) in serum RF titer, and 29 cases did not (non-CD). Between these groups, there were no differences in baseline characteristics at the entry, and DAS28-CRP at month 0, 4 and 12. The median changes in mTSS during month 0-12 were 0 in CD patients and 1.09 in non-CD, and the yearly radiographic change in mTSS was greater in non-CD group ($p=0.0015$). The radiographic remission (yearly change in mTSS ≤0.5) was found in 71.4% of CD patients and 13.3% of non-CD, and ratio of radiographic remission was higher in CD group ($p=0.0036$). The yearly progression in bone erosion score during month 0-12 was greater in RA patient with non-CD than with CD ($p=0.0037$), but no significant difference between CD and non-CD was observed in the joint space narrowing score. Multiple regression analysis revealed that the continuous RF decrease as well as RA disease activity was significantly correlated with yearly change in bone erosion score during month 0-12.

Conclusion: Continuous decrease in serum RF titer was associated with less progression in mTTS, especially in bone erosion score, of RA patients treated with TNF inhibitors.

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Abstract Number: 0465

Prognostic Factors and Clinical Outcome Modifiers in Patients with Rheumatoid Arthritis: A Review

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SESSION INFORMATION
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Background/Purpose: The current goal in treatment of RA is to deliver therapies tailored to individual patients' characteristics. Establishing disease prognosis is a crucial first step in this process. This review maps the current understanding of prognostic factors in the natural history of RA.

Methods: A comprehensive search for the period of Jan. 2000 to Oct. 2018 was conducted using Doctor Evidence LLC's proprietary search platform (DOC Search) containing all relevant databases and RSS feeds. This was supplemented by a search of EULAR and ACR conferences (2017-2019). The search included systematic and narrative reviews, meta-analyses, clinical trials, and observational studies in which prognostic factors in RA were investigated or described.

Results: The results of the search and screening identified 56 publications that were included in the qualitative evidence synthesis (Figure 1).

Qualitative synthesis of the included studies showed that the term “prognostic factor” can be subdivided into 7 broad categories: socio-demographic data, clinical presentation, comorbidities and toxic habits, questionnaire data, biomarkers, genetic markers, and imaging data (Table 1). Once diagnosed, the clinical course of RA is highly variable, which underscores the utility of prognostic factors for predicting the natural history of disease. In clinical settings, the most commonly used factors to strongly predict worsened prognosis are very young age at onset, swollen and tender joint counts at diagnosis, presence of RF, ACPA antibodies, and radiographic erosions. Comorbidities, such as obesity, low bone-mineral density, cardiovascular disease, and extra-articular manifestations, are perceived as moderately associated with prognosis; nevertheless, they are used widely by practicing rheumatologists. Genetic biomarkers and osteitis by magnetic resonance are less accessible for use in daily practice. Prognostic factors that are also outcome modifiers are specific to each therapy . For instance, predictors of remission for treatment with methotrexate include male sex, young age, late-onset RA, low disease activity, RF negative status, and ACPA negative status. For biologics like TNF alpha inhibitors (TNFi), positive treatment response is most strongly correlated with male sex, young age, non-smokers, RF and ACPA negative status, exposure to fewer previous biologic DMARD therapies, low drug immunogenicity, and non-obesity. For patients treated with abatacept, several studies correlate ACPA positive status with greater response when compared with response of patients with the same prognostic factors to TNFi.

CATEGORY	EXAMPLE FACTORS
Socio-demographic data	Gender, Age, Educational level, Family background, Socio-economic status
Clinical Presentation	Swollen joint count, Tender joint count, Morning stiffness, Early onset, RA duration, VAS score
Comorbidities and Toxic Habits	Smoking, Obesity, Diabetes, Depression, Cardiovascular disease
Questionnaire data	Disease activity score, Simplified disease activity index, Clinical disease activity index, Health assessment questionnaire
Biomarkers	Rheumatoid factor, Anti-citrullinated protein antibodies, C-reactive protein, Erythrocyte sedimentation rate, Interleukin-6, Tumor necrosis factor receptor type 1, Calcium binding protein (S100A8/A9), Soluble intercellular adhesion molecule 1, Matrix metalloproteinase 3, C-telopeptide of type II collagen, Tumor necrosis factor α, Fibrinogen, Interleukin 1 α, Anti-perinuclear factor, B lymphocyte chemokine, Myeloid progenitor inhibitory factor 1, Transforming growth factor α, Tumor necrosis factor receptor superfamily member 9, Macrophage colony stimulating factor, Cartilage oligomeric matrix protein, Pyridinoline, Tissue inhibitor of metalloproteinases 1, Deoxypyridinoline glycosylated Pyr, Oncostatin M, Matrix metalloproteinase 10, Matrix metalloproteinase 8, CCL8/monocyte chemotactic protein 2, Chemokine (C-X-C motif) ligand 11, Lymphotactin, Fibroblast growth factor 4, Ciliary neurotrophic factor receptor α, Follistatin, Interleukin 9, Lymphotoxin β receptor, Interleukin 2 (IL-2), Apolipoprotein A-I, Platelet factor 4, CCL8/Myeloid progenitor inhibitory factor 1
Genetic markers	HLA-DR1 and shared epitope, PTPN22, PADI4, CTLA-4
Imaging data	Radiological erosion, MRI and ultrasound signs of inflammation

Table 1. Typology of Prognostic Factors in RA

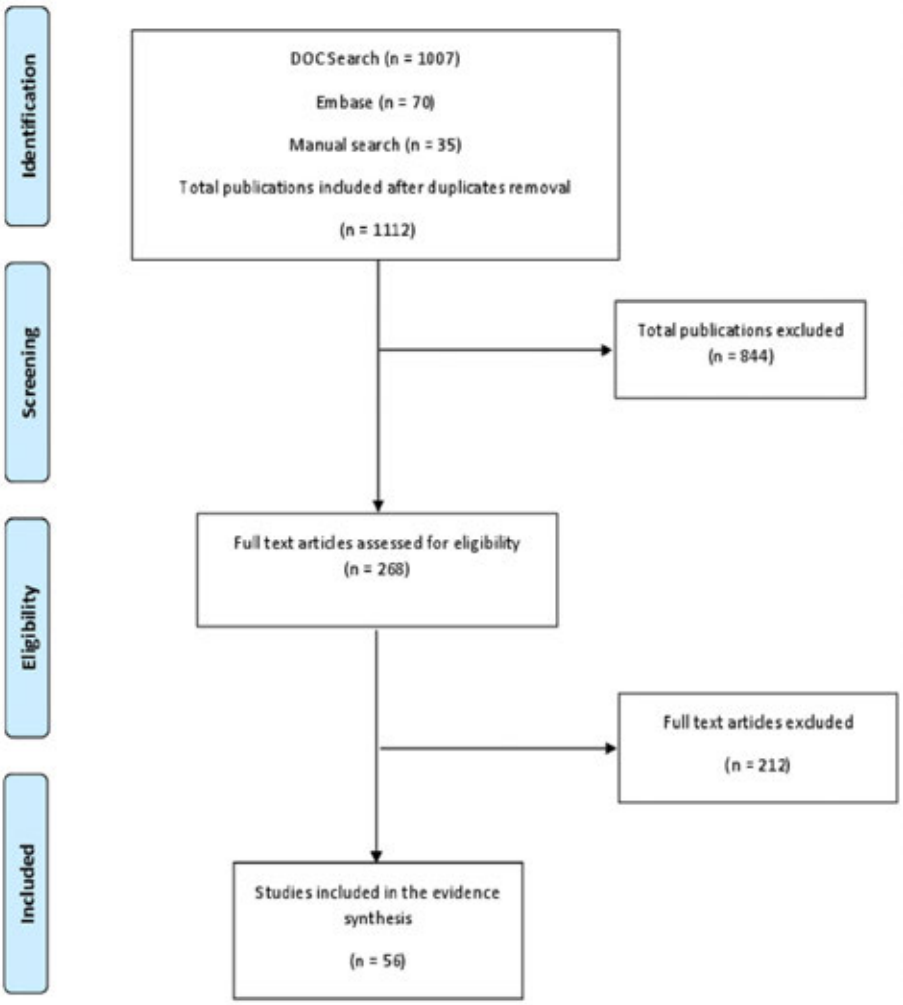

Figure 1. PRISMA Diagram

Conclusion: Although the published literature reports several prognostic factors for RA, only a small subset is routinely assessed in practice and mentioned in clinical guidelines. Interestingly there are already some factors being reported as predictors of response to TNFi and abatacept; specifically the seropositivity (particularly ACPA+) seems to favor abatacept efficacy over TNFi. The barriers to wider and more accurate use of available prognostic factors are both technological, as well as informational, via lack of expert consensus.

Disclosure: L. Ferri, Bristol-Myers Squibb, 1, 3, 4, Bristol-Myers Squibb Company, 1, 3; **G. Crocket**, Bristol-Myers Squibb, 9, Rutgers University, 3; **X. Han**, Bristol-Myers Squibb, 3, Bristol-Myers Squibb Company, 3; **B. Breznen**, Doctor Evidence, 3; **M. Fazeli**, Doctor Evidence, 3.

Abstract Number: 0466

Predicting Risk of Radiographic Progression for Patients with Rheumatoid Arthritis

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SESSION INFORMATION

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Background/Purpose: The multi-biomarker disease activity (MBDA) blood test has been shown to be a predictor of risk for radiographic progression in patients with rheumatoid arthritis (RA). Subsequently, the MBDA score was adjusted to account for the effects of age, sex and adiposity and was shown in two cohorts to be better than conventional disease activity measures for predicting risk for radiographic progression [Curtis, J.R., et al. *Rheumatology (Oxford).* 2018. PMID: 30590790]. Here, we combined data from four separate cohorts to validate the adjusted MBDA score as a predictor of radiographic progression. We also evaluated the ability of the adjusted MBDA score, as a continuous variable, to predict risk for radiographic progression.

Methods: Four cohorts with requisite data were identified and combined: the BRASS registry (N=401) and OPERA study (N=154), which have been previously evaluated; and the SWEFOT study (N=235) and Leiden registry (N=163), which are new to these analyses. The associations of radiographic progression (change per year in total Sharp score [ΔTSS]) with the adjusted MBDA score, seropositivity (RF and/or ACPA positive), DAS28-CRP, SDAI, CDAI, CRP, baseline total TSS, age, and sex, were evaluated using linear regression. Logistic regression was used to estimate risk for four levels of radiographic progression (ΔTSS >2, >3, >4 or >5), each as a function of the adjusted MBDA score.

	Pooled Cohort		
Variable	N	Coefficient (95% CI)	p-value
Adjusted MBDA score	953	0.061 (0.044, 0.076)	2.5×10^{-13}
Seropositivity	952	1.47 (0.89, 2.06)	9.9×10^{-7}
log(CRP + 1)	946	0.58 (0.33, 0.83)	4.7×10^{-6}
Baseline TSS	953	0.0074 (0.0028, 0.012)	0.0018
DAS28-CRP	927	0.31 (0.11, 0.50)	0.0024
Male sex	243/953	-0.45 (-1.04, 0.14)	0.14
Age	953	-0.0043 (-0.024, 0.015)	0.66

Table 1. Univariate analyses of risk for radiographic progression (ΔTSS) in four cohorts combined.

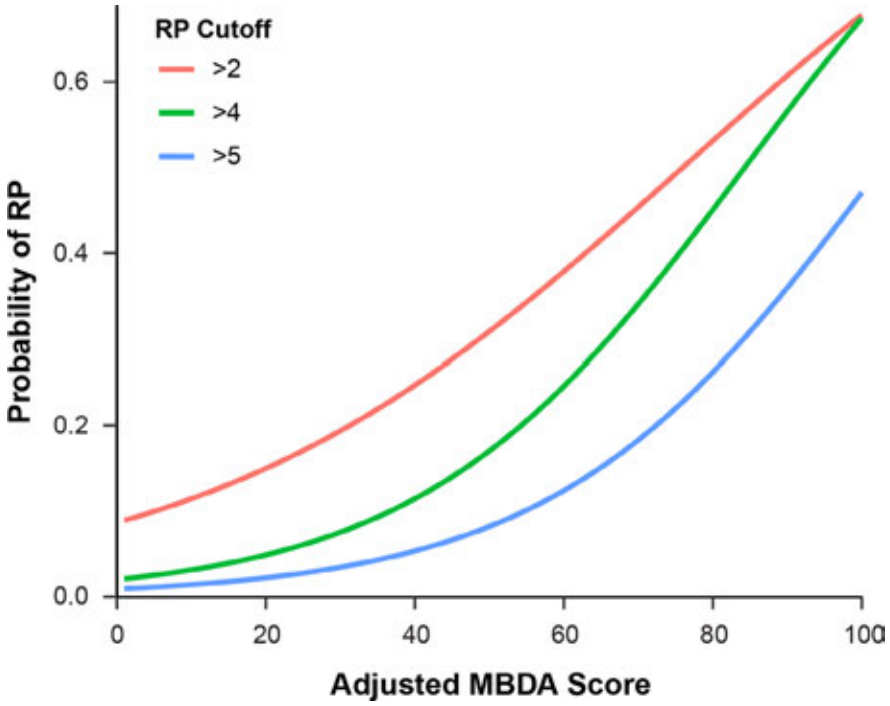

Figure 1. Probability of RP Based on Adjusted MBDA Score.

Results: The four cohorts were similar in age, adjusted MBDA score, and DAS28-CRP, with mean ages ranging from 55.2 to 56.4 years, mean adjusted MBDA scores from 39.9 to 42.5 and mean DAS28-CRP from 3.4 to 5.6. Patients in the OPERA and SWEFOT cohorts had early onset RA (mean durations 87 days and 6.1 months, respectively). Patients in the BRASS and Leiden cohorts tended to have established RA (mean durations 13.8 and 4.6 years, respectively). In a pooled analysis combining all four cohorts (N=953), the adjusted MBDA score was the most statistically significant univariate predicator of radiographic progression ($p=2.5 \times 10^{-13}$) among the tested measures of disease activity, followed by CRP ($p=4.7 \times 10^{-6}$) (Table 1). Curves were generated to display risk for four levels of radiographic progression, relative to the adjusted MBDA score as a continuous variable (Figure 1). The risk for the most severe level of progression that was evaluated, ΔTSS >5, ranged from 1% to 3% in the low (1-30) adjusted MBDA category to 7% to 47% in the high (45-100) adjusted MBDA category (Figure 1).

Conclusion: In a combined analysis of four cohorts of patients with RA, risk of radiographic progression (ΔTSS >5) was nearly absent when the adjusted MBDA score, as a continuous variable, was low, and exceeded 40% for patients with the highest MBDA scores.

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8, Abbvie, Celgene, Centocor, Merck, and Novartis, 2, Abbvie, Celgene, Centocor, Merck, Novartis, 2, BMS, 2, 5, 8, 9, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8; **M. Lund Hetland**, Abbvie, 2, AbbVie, 2, Biogen, 2, BMS, 2, CellTrion, 2, 9, MSD, 2, Novartis, 2, Orion, 2, Pfizer, 2, Samsung, 2, UCB, 2; **K. Hambardzumyan**, None; **S. Saevarsdottir**, None; **M. Horton**, Myriad Genetics, Inc., 3, 4; **B. Mabey**, Myriad Genetics, 3; **D. Flake**, Myriad Genetics, Inc., 1, 3, 4; **A. Gutin**, Myriad Autoimmune, 1, 3, 4; **R. Ben-Shachar**, Myriad Genetics, Inc., 3, 4; **E. Sasso**, Crescendo Bioscience, 3, 4; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5.

Abstract Number: 0467

Serum Long-chain n-3 and -6 Fatty Acids Are Associated with Disease Feature at Onset and with 6-month Disease Activity in Early RA: Results from the ESPOIR Cohort

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Long-chain polyunsaturated fatty acids (PUFAs) of the n3 and n6 families can contribute to modulate inflammatory processes. Dietary intake of n3PUFA is inversely associated with the incidence of RA in different populations. In subject at risk of developing RA, a high erythrocyte content in long-chain n3-PUFA is associated with lower ACPA prevalence and less progression to RA. While long-chain n6PUFA are considered mainly proinflammatory, the erythrocyte content in n6 linoleic acid was inversely associated with the development of RA in a nested-case control study. This study aims to characterize serum profiles of PUFA and to determine their association with baseline variables, with 6-month disease activity and 2-year radiographic progression in a cohort of patients with early RA.

Table 1 Baseline association between PUFA patterns and patient variables

	Pattern 1	Pattern 2	Pattern 3
Active Smoking	p<0.05	ns	p<0.05
BMI	p<0.001	ns	p<0.001
Caucasian ethnicity	p<0.001	ns	ns
Education level	ns	p=0.05	p<0.001*
ACPA positivity	ns	ns	p=0.01
Baseline CRPc	24,2 (+/-34,3) p : ns	17,6 (+/-28,1) p<0.05*	26,5 (+/-49,5) p<0.01
Baseline DAS28 >5.1	p=0.09	p<0.05*	p<0.01

*: inverse association. n.s. : not significant

Methods: Serum PUFAs were quantified by gas chromatography-mass spectrometry in 594 patients with early RA at recruitment in the French ESPOIR cohort. Cluster analysis on 19 serum fatty acids with 14 to 22 carbon atoms allowed to determine 3 patterns of baseline serum PUFA. Pattern 1 included high proportions of n7 and n9 PUFA, pattern 2 was high in n3 long-chain PUFA (EPA et DHA), pattern 3 was rich in n6 long-chain PUFA. Those patterns were not mutually exclusive (i.e. each patient could fit at different level into different profiles). Patients were stratified in tertiles according to how much the fitted into the pattern (tertile 1 meaning lowest and tertile 3 highest fitting into the pattern). The association of PUFA patterns with baseline variables was tested at univariate analysis. The association with 6-month high disease activity (DAS28 >5.1) was tested at multivariate analysis after adjustment on baseline CRP, corticosteroid and/or NSAIDs, socioeconomic status, ACPA, RF, traditional and biologic DMARDs treatment between 0 and 6 months after inclusion. The same model was used to test the association with 2-year radiographic progression.

Results: At baseline, pattern 1 was associated with high BMI, active smoking and with non-Caucasian origin (table 1). Profile 2 was associated with higher socioeconomic status and inversely associated with DAS28 and CRP. Profile 3 was associated with ACPA positivity and higher baseline CRP. At multivariate analysis, fitting into pattern 2 or 3 was associated with lower odds of having active disease after 6 months (OR for tertile 3 vs. tertile 1: 0.49 (95% CI 0.25 to 0.97, p< 0.05) for pattern 2 and 0.51 (0.28 to 0.95) for pattern 3, respectively). None of the patterns associated with 6-month disease activity was associated with 2-year radiographic progression.

Conclusion: In a cohort of early RA patients, we identified a favorable high serum long-chain n3PUFA profile, associated with low baseline inflammation and persistently low disease activity between 0 and 6 months of follow-up in the cohort. This is consistent with a presumed immunomodulatory action of n3PUFA. Despite a clear baseline association with disease severity features, like ACPA positivity and high CRP, a high serum long-chain n6PUFA profile was also associated with 6-month lower disease activity. Despite the longitudinal association with disease activity, none of the baseline PUFA patterns predicted radiographic progression.

Disclosure: J. Sigaux, None; **C. Buscail**, None; **C. Julia**, None; **R. Flipo**, MSD, 5, Sanofi, 5; **A. Cantagrel**, None; **B. Bannwarth**, None; **F. Laporte**, None; **S. Challal**, None; **M. Boissier**, None; **L. Semerano**, None.

Abstract Number: 0468

Effect of Body Mass Index on the Disease Activity of Patients with Rheumatoid Arthritis in a Gender Specific Manner and Association of Respective Serum C - Reactive Protein Levels with the Body's Inflammatory Status

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Current literature evaluating the effect of high Body Mass Index (BMI) on the disease activity of patients with rheumatoid arthritis (RA) is mixed as some studies have shown a positive, linear relationship between BMI and disease activity while others have demonstrated an inverse correlation. Through this study we have expanded upon the relationship between BMI and disease activity in RA. We have further expanded on whether BMI has an effect on the disease activity depending on the gender being studied. Finally, we have studied whether there is a correlation between high BMI values and rising C- reactive protein (CRP) levels.

Methods: This observational study was conducted at the outpatient clinical department of Buffalo Rheumatology and Medicine. The study was ethically approved by Catholic Health Institutional Review Board. The minimum sample size (n=358) was calculated via the World Health Organization sample size calculator. A total number of 451 patients' clinical data was selected on the basis of inclusion/exclusion criteria. The patients were divided into different BMI categories based on the guidelines of National Obesity Education Initiative of the National Heart, Lung, and Blood Institute. The following clinical parameters were studied: BMI, serum CRP level, and severity of disease activity assessed through Routine Assessment of Patient Index Data questionnaire (RAPID3). All data was entered and analyzed through SPSS 16.0.

Results: Our study sample included 98 males and 353 females (22% and 78% respectively). The baseline data of the recruited patients is shown in table 1. Collective data for both the genders showed significantly increased disease activity in RA patients with high BMI values (p=0.04); the highest disease activity was observed in a subgroup of severely obese patients (mean RAPID3 score 13.0 + 7.3 SD) (Figure 1). When the data sets were categorized according to the two genders, it was noted that the aforementioned results remain significant for the females only (p=0.02 for

Table 1. Baseline data for recruited patients. Through independent sample t-test, p values for mean within a group were calculated. Foot notes: BMI= Body Mass Index; RAPID3= Routine Assessment of Patient Index Data; CRP= C Reactive Protein; p value= Pearson's chi-square probability.

Characteristics	Males (n=98) (Mean ± S.D.)	Females (n=353) (Mean ± S.D.)	P values
Age	63.4 ± 13.1	61.3 ± 14.4	0.192
BMI	30.7 ± 7.8	30.9 ± 9.5	0.869
RAPID3 Score	8.3 ± 6.6	10.5 ± 7.3	0.006
CRP	3.2 ± 5.5	4.1 ± 7.5	0.291

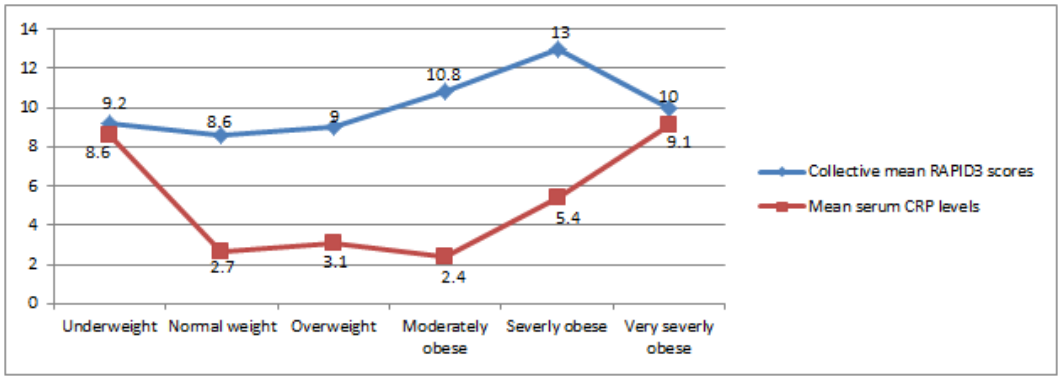

Figure 1. Plots are mean RAPID 3 scores and mean serum CRP levels with BMI categories mentioned on the x-axis. Foot notes: BMI= Body Mass Index; RAPID3= Routine Assessment of Patient Index Data; CRP= C Reactive Protein.

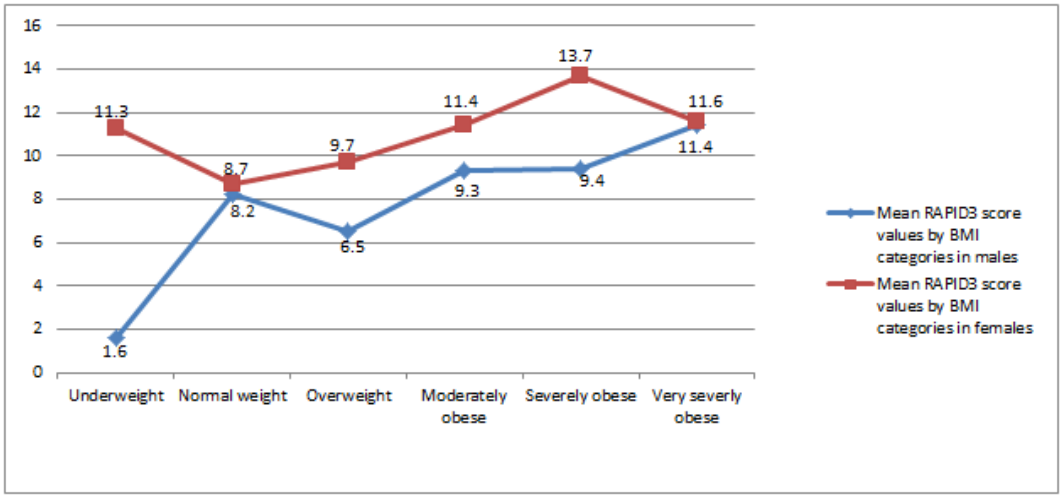

Figure 2. Plots are mean values for RAPID3 scores in individual gender with BMI mentioned on the x-axis. Foot notes: BMI= Body Mass Index; RAPID3= Routine Assessment of Patient Index Data.

females and p=0.57 for males). At all BMI values, mean RAPID3 scoring remained significantly higher for females as opposed to their male counterparts (p=0.006) (Figure 2). Among all three components of the RAPID3 questionnaire, the pain was recorded at the higher side of the scale as stated by the patients. Mean serum CRP levels increased linearly with increasing BMI (p< 0.001); however for the underweight patient population, mean CRP levels were the highest as compared to normal weight, overweight, moderately obese, and severely obese patients (Figure 1)

Conclusion: We conclude that the association between the BMI and the severity of disease remains elusive. High BMI values increases the risk for a pro-inflammatory state of the body due to higher serum CRP levels. Estimating the clinically significant benefit of this theory would require a large scale clinical trial that would highlight the role of losing weight in improving the patients' quality of life, pain control, and mortality.

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Abstract Number: 0469

Location and Size of Affected Joints Are Useful to Predict Prognosis of Patients with Rheumatoid Arthritis

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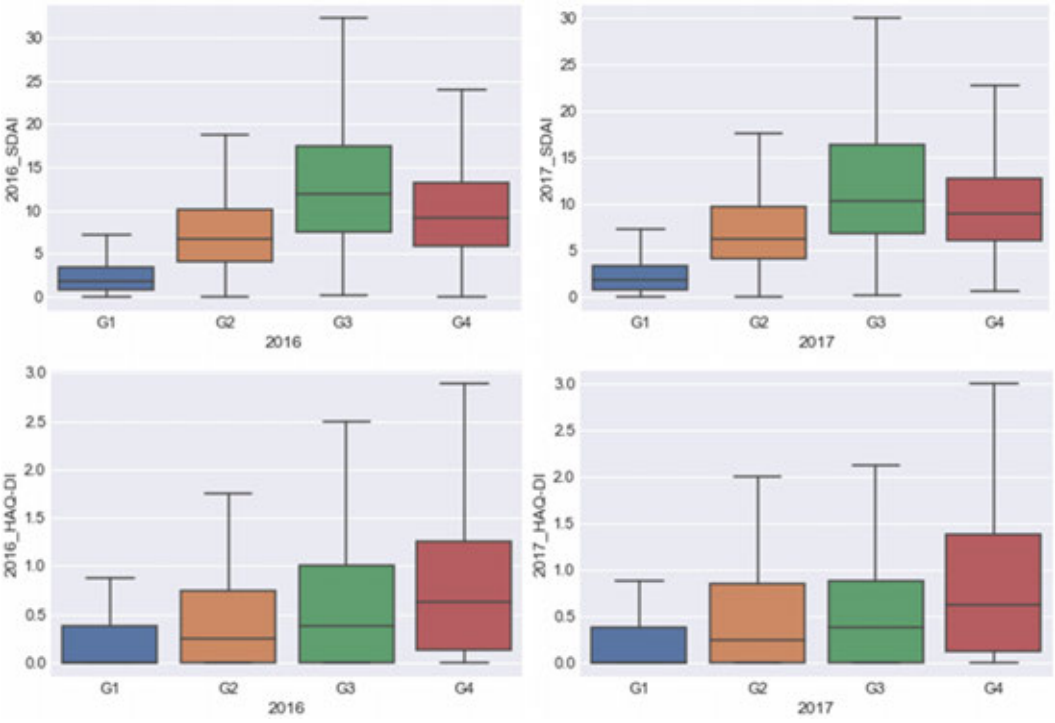
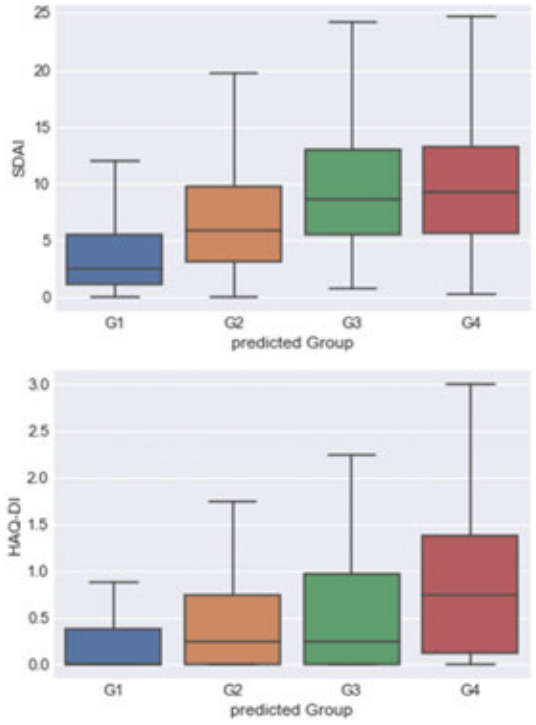
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To predict prognosis of patients with rheumatoid arthritis (RA) from the location and the size of affected joints.

Methods: Data of 7,776 patients with RA, who were serially registered from 2016 to 2017 without data missing, were extracted from the National Database of Rheumatic Diseases in Japan (NinJa). The joint index (JI) was calculated as the sum of the number of tender and swollen joints divided by the number of evaluable joints in four categories, i.e., upper/large, upper/small, lower/large, and lower/small (Nishiyama S, et al. Proposing a method of regional assessment and a novel outcome measure in rheumatoid arthritis. Rheumatol Int 32:2569-2571. https://doi.org/10.1007/s00296-011-2058-9). Next, the joint index vector V (x, y, z) was calculated as $x = JI_{UL} + JI_{US}$, $y = JI_{LL} + JI_{LS}$, and $z = JI_{UL} + JI_{LL} - JI_{US} - JI_{LS}$, where JI_{UL}, JI_{US}, JI_{LL}, and JI_{LS} indicate the joint indices of the upper/large, upper/small, lower/large, and lower/small joint categories, respectively. Patients were classified into four groups by $|Vxy|$ ($= \sqrt{(x2+y2)}$) and z values (G1: $|Vxy| \leqq 0.1$, G2: $|Vxy| > 0.1$ & $|z| \leqq 0.2$, G3: $|Vxy| > 0.1$ & $z < -0.2$, G4: $|Vxy| > 0.1$ & $z > 0.2$). Transformation matrix was computed using serial registration data of patients with RA who were treated with MTX from the NinJa database





from 2013 to 2014 (Nishiyama S, et al. Joint index vector: a novel assessment measure for stratified medicine in patients with rheumatoid arthritis. Journal of Big Data 2018;5:37. https://doi.org/10.1186/s40537-018-0148-1).

Results: SDAI was the highest in patients of the G3 (small-dominant joint involvement group) and HAQ-DI was the worst in patients of the G4 (large-dominant joint involvement group) independent of registration year (Fig.1). Groups in 2017 were predicted from the vectors estimated using the transformation matrix applied on 4,811 MTX users in 2016, and then 456 patients were classified as the predicted G4. The rest of 4,355 patients had lower SDAI and better HAQ-DI than patients of the predicted G4 (Fig. 2). The concordance rate of the G4 or the others between the predicted group and the real group in 2017 was 82.8%. In 1,001 patients of the G4 in 2016, 452 were predicted to be in the G4 next year, whose SDAI (mean±standard error: 9.90±0.30) and HAQ-DI (0.95±0.04) were significantly higher than those of the rest of 549 patients (7.12±0.22 and 0.67±0.03, respectively).

Conclusion: Classification of RA patients according to the joint index vector which has the affected joints information of the location and the size discriminated patients with a relatively poor prognosis from those with lower SDAI and better HAQ-DI.

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Abstract Number: 0470

Obesity Is a Robust Predictor of Persistent High Fatigue at 1 Year in Women and Men with Early Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: While treat-to-target strategies can dramatically reduce inflammation in RA, persistently high levels of fatigue are present in many patients and represent an important unmet need. Proposed underlying causes include RA disease activity, cognitive/emotional/behavioral factors (CEB), and personal (health) factors. We identified risk factors for persistent high fatigue at 12 months in women and men with ERA receiving guideline-based treatment.

Table 1. Baseline characteristics of participants by sex.

Mean (SD) or N (%)	Women N=714	Men N=288	P value
Age	52 (15)	59 (13)	<0.0001
College Education	405 (57%)	134 (47%)	0.0034
RA Disease			
Symptom duration (month)	5.7 (3.0)	5.6 (2.9)	0.6485
RF+ or ACPA +	526 (84%)	177 (75%)	0.0038
DAS28 > 3.2	688 (96%)	272 (94%)	0.1712
Pain (0-10)	5.8 (2.8)	5.7 (2.8)	0.5509
HAQ-DI	1.1 (0.7)	1.0 (0.7)	0.0220
Cognitive/Emotional/Behavioral (CEB)			
Baseline fatigue (0-10)	5.6 (3.0)	4.9 (2.9)	0.0007
Obese (BMI≥30)	223 (31%)	93 (32%)	0.7440
Current Smoking	110 (15%)	54 (19%)	0.1954
Depressive Symptoms (SF12 MCS <45.6)	356 (53%)	92 (35%)	<0.0001
Major stress in past year	401 (56%)	123 (43%)	0.0001
Personal/Health			
Work full- or part-time	401 (56%)	149 (52%)	0.2026
Rheumatoid Disease Comorbidity Index	1.1 (1.3)	1.3 (1.3)	0.0605
OA or backpain	164 (23%)	57 (20%)	0.2723
Fibromylagia	20 (3%)	3 (1%)	0.0919
Poor Sleep	5.2 (3.2)	5.0 (3.3)	0.4108

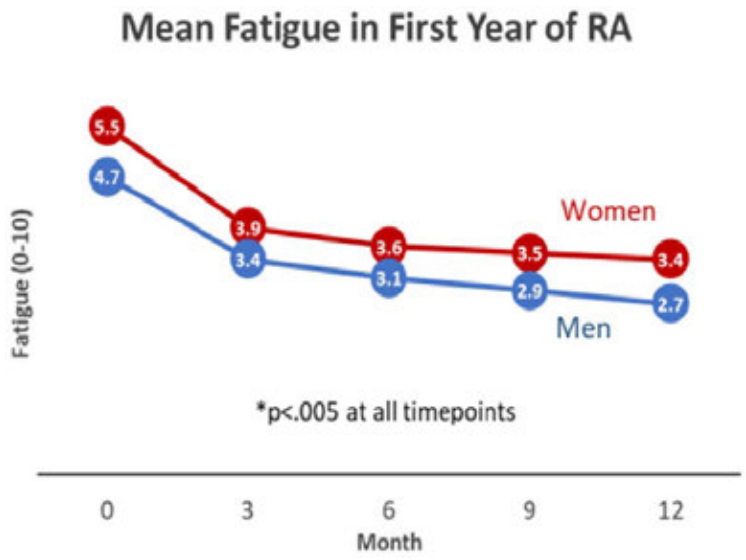

Table 2. Predictors of persistent fatigue at 1 year in early rheumatoid arthritis by sex.

	Women (N=714)		Men (N=288)	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Age (10 years)	0.95	0.80, 1.14	0.79	0.56, 1.13
College Education	0.89	0.57, 1.40	0.79	0.34, 1.81
RA Characteristics at Baseline				
Symptom duration (month)	1.05	0.98, 1.12	1.08	0.95, 1.24
RF+ or ACPA+	0.60	0.35, 1.02	0.78	0.32, 1.89
DAS28 > 3.2	0.75	0.23, 2.43	0.49	0.10, 2.33
Pain (0-10)	0.96	0.85, 1.08	1.10	0.90, 1.22
Poor Sleep (0-10)	**1.12**	**1.02, 1.23**	1.05	0.90, 1.22
HAQ-DI	1.33	0.88, 2.02	0.88	0.41, 1.89
Cognitive/Emotional/Behavioral				
Obese (BMI≥30)	**1.68**	**1.07, 2.62**	**2.36**	**1.09, 5.11**
Current Smoking	0.96	0.55, 1.68	0.66	0.24, 1.86
Depression (SF12 MCS <45.6)	1.05	0.66, 1.66	1.59	0.65, 3.86
Major stress in past year	1.28	0.82, 2.01	0.80	0.36, 1.77
Personal/Health				
Work (full- or part-time)	1.17	0.72, 1.90	0.64	0.25, 1.64
Rheumatoid Disease Comorbidity Index	1.06	0.89, 1.25	1.23	0.89, 1.68
OA or backpain	1.17	0.69, 1.97	1.25	0.47, 3.37
Fibromylagia	1.83	0.64, 5.27	--	--
Initial Treatment				
No MTX	Reference		Reference	
MTX < 20 mg	1.08	0.59, 1.97	1.45	0.42, 4.97
MTX ≥ 20 mg	0.71	0.43, 1.19	0.73	0.24, 2.17
Oral steroids	**1.69**	**1.06, 2.69**	0.93	0.40, 2.19

Methods: Data were from patients enrolled in the Canadian Early Arthritis Cohort (CATCH) between 01-2007 and 03-2017 who met 1987 or 2010 ACR/EULAR RA criteria, had active disease treated with DMARDS, and had complete data on DAS28, BMI, and fatigue severity (0-10) over 12-months. Persistent high fatigue was defined as fatigue ≥ 4

at baseline with < 20% improvement by 12 months. Multivariable logistic regression was used to identify RA disease, CEB, and personal / health factors associated with persistent high fatigue in women and men.

Results: Patients (N=1002) were mostly white (81%), female (71%), with a mean (SD) age of 54 (15), symptom duration of 6 (3) months, and BMI of 28.0 (6.1); 32% were obese (BMI≥30). Women were generally younger, better educated, seropositive, and had greater disability, fatigue, depressive symptoms, and major stress in the year prior to diagnosis (p< .05). 21% of women and 19% of men reported persistent high fatigue throughout the first year (p=.13). Mean fatigue was significantly higher (p< .005) in women at all time points (Figure).

In multivariable regression that included all variables, predictors of persistent high fatigue in women were obesity (OR 1.7; 95% CI 1.1, 2.6), initial steroid use (OR 1.7; 95% CI 1.1, 2.7), seronegativity (OR 0.6; 95% CI 0.4, 1.0) and poor sleep (OR 1.1; 95% CI 1.0, 1.2). In men, obesity was the only significant predictor and was associated with a 2.4 times higher odds (95% CI 1.1, 5.1) of persistent fatigue at 1 yr. Other sociodemographic and RA characteristics, CEB and personal/health factors were not associated with persistent high fatigue in either sex in multivariable models.

Conclusion: Obesity is common in ERA and an important contributor to persistent high fatigue in both women and men. In obese RA patients on guideline-based treatment, lifestyle interventions targeting weight loss may play an important role and strategies to improve mood and manage stress may help reduce persistent high fatigue that does not improve with RA treatment.

Disclosure: S. Bartlett, Abbie, 2, Abbvie, 2, 5, Bayer, 5, International Society of QOL Research, 6, Janssen, 5, 8, Lilly, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, Pfizer Inc, 8, PROMIS International, 6, UCB, 5, 8; **O. Schieir**, None; **M. Valois**, None; **J. Pope**, AbbVie, 5, Abbvie, 5, Actelion, 5, Actellion, 5, Amgen, 2, 5, AstraZeneca, 2, Astra-Zeneca, 2, Bayer, 2, 5, BMS, 2, 5, Eicos Sciences, 5, Eli Lilly & Company, 5, Eli Lilly and Company, 5, EMERALD, 5, Emerald, 5, Genzyme, 5, Janssen, 5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8; **L. Bessette**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, Amgen, BMS, Janssen, Roche, UCB Pharma, AbbVie Inc, Pfizer, Merck, Celgene, Sanofi, Eli Lilly, and Novartis., 2, 5, 8, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Bristol-Myers-Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5; **C. Hitchon**, Pfizer, 2, UCB, 2, UCB Canada, 2; **C. Thorne**, Abbvie, 2, 5, Amgen, 2, 5, CaREBiodam, 2, Celgene, 2, 5, Centocor, 5, Janssen, 5, Lilly, 5, Medexus/Medac, 5, 8, Merck, 5, Novartis, 2, 5, Pfizer, 2, 5, Sandoz, 5, Sanofi, 5; **D. Tin**, None; **G. Hazlewood**, None; **G. Boire**, Abbvie, 2, Amgen, 2, 5, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, Eli Lilly, 2, 5, Lilly, 2, 5, Merck, 2, 8, Novartis, 2, Pfizer, 2, 5, 8; **E. Keystone**, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 5, Astra-Zeneca, 5, Biotest, 5, BMS, 2, 5, 8, Celltrion, 5, Crescendo, 5, Crescendo Bioscience, 5, F. Hoffmann-La Roche Inc, 2, 5, 8, Genentech, 5, Genentech Inc., 5, Genzyme, 5, Gilead, 2, 5, Gilead Sciences, Inc., 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 5, 8, Pfizer, 2, 5, 8, Pfizer Pharmaceuticals, 2, 5, 8, Roche, 2, 5, 8, Sandoz, 5, Sanofi, 2, 5, 8, Sanofi-Aventis, 2, 8, UCB, 5, 8; **V. Bykerk**, AbbVie, 5, Amgen, 1, 2, 3, 5, 8, Brainstorm Therapeutics, 1, 2, 3, 5, 8, Bristol-Myers Squibb, 5, Genentech, 5, Gilead, 5, NIH, 2, Pfizer, 1, 2, 3, 5, 8, Regeneron, 5, Regeneron Pharmaceuticals, Inc, 5, Sanofi, 5, Sanofi/Genzyme-Regeneron, 5, Sanofi-Genzyme/Regeneron, 1, 2, 3, 5, 8, Scipher, 1, 2, 3, 5, 8, The Cedar Hill Foundation, 9, UCB, 1, 2, 3, 5, 8, UCB Pharma, 5; **C. (CATCH) Investigators**, Amgen, 2, Pfizer Canada, 2, AbbVie Corporation, 2, Medexus Inc., 2, Eli Lilly Canada, 2, Merck Canada, 2, Sandoz Canada Biopharmaceuticals, 2.

Abstract Number: 0471

When Will I Get past This Exhaustion? Predictors of Improved Fatigue in the First Year of RA

Susan J. Bartlett,[1] Orit Schieir,[2] Marie-France Valois,[3] Carol Hitchon,[4] Louis Bessette,[5] Glen Hazlewood,[6] Carter Thorne,[7] Janet Pope,[8] Gilles Boire,[9] Diane Tin,[10] Edward Keystone,[11] Vivian Bykerk,[12] and Canadian Early Arthritis Cohort (CATCH) Investigators[13], [1]McGill University, Montreal, QC, Canada, [2]University of Toronto, Montreal, Canada, [3]McGill University, Montreal, Canada, [4]University of Manitoba, Winnipeg, Canada, [5]Laval University, Quebec City, QC, Canada, [6]University of Calgary, Calgary, Canada, [7]Southlake Regional Health Centre, Newmarket, ON, Canada, [8]Western University, London, ON, Canada, [9]Sherbrooke University, Sherbrooke, QC, Canada, [10]Southlake Regional Health Centre, Newmarket, Canada, [11]Mount Sinai Hospital and University of Toronto, Toronto, ON, Canada, [12]Hospital for Special Surgery, New York City, NY, [13]Canadian Early Arthritis Cohort (CATCH) Study, Toronto, Canada

SESSION INFORMATION

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Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Although overwhelming fatigue is common at the onset of RA, some patients continue to experience debilitating high levels of fatigue that impact mood, interfere with work and home life, social participation,

Table 1. Baseline characteristics of early RA patients with low, improved and persistently high fatigue levels.

MEAN (SD) OR N (%)	LOW FATIGUE	HIGH FATIGUE		SIG	
	Low (n=301)	Improved (n=493)	Persistent (n=208)	Low v. High	Imp v. Persist
Age	55 (15)	54 (15)	54 (15)	0.13	0.97
Female sex	202 (67%)	360 (73%)	152 (73%)	0.06	0.99
>High School	169 (56%)	267 (54%)	103 (50%)	0.33	0.26
PERSONAL/HEALTH					
Work (full/part time)	161 (53%)	274 (56%)	115 (55%)	0.56	0.94
RD Comorbidity Index	1.1 (1.3)	1.1 (1.3)	1.4 (1.4)	0.42	0.001
OA or backpain	52 (17%)	114 (23%)	55 (26%)	0.02	0.35
Fibromyalgia	3 (1%)	10 (2%)	10 (5%)	0.07	0.04
Poor sleep	2.6 (2.7)	6.3 (2.9)	6.1 (2.7)	<0.001	0.38
COGNITIVE/BEHAVIORAL					
Obese (BMI≥30)	78 (26%)	152 (31%)	86 (41%)	0.01	0.01
Smoking	48 (16%)	83 (17%)	33 (16%)	0.81	0.75
Depression (SF12 MCS<45.6)	62 (22%)	273 (59%)	113 (57%)	<0.001	0.59
Major stress past year	138 (46%)	268 (54%)	118 (57%)	0.01	0.58
RA					
Symptom duration (mth)	5.7 (2.9)	5.5 (3.0)	6.1 (3.2)	0.79	0.02
RF+/ACPA+	221 (85%)	349 (81%)	133 (76%)	0.07	0.21
DAS28 (MDA/HDA v. LDA/REM)	280 (93%)	481 (98%)	199 (96%)	<0.01	0.18
Pain (0-10)	3.8 (2.6)	6.7 (2.4)	6.4 (2.2)	<0.001	0.08
HAQ-DI	0.7 (0.6)	1.3 (0.7)	1.2 (0.7)	<0.001	0.15
Baseline fatigue (0-10)	1.6 (1.2)	7.2 (1.9)	6.6 (1.7)	<0.001	<0.001

and result in poor QoL. Among people with high fatigue at diagnosis, we examined characteristics and identified predictors associated with improved vs. persistent fatigue in the first year of RA.

Methods: Data were from early RA patients (symptoms < 1 year) enrolled in the Canadian Early Arthritis Cohort (CATCH) from 01-2007 to 03-2017. All met ACR1987 or 2010 ACR/EULAR criteria, had active disease, were on DMARDS, and complete fatigue (0-10 NRS) data over ≥ 12 months. Patients were classified at baseline with low (< 4) or high (≥ 4) fatigue; patients who reported high fatigue at baseline were categorized at 12 months as having improved (↓ ≥ 2) or persistently (↓ < 2) high fatigue and multivariable logistic regression was used to identify baseline predictors of improvement.

Results: Participants (N=1002) were mostly white (81%) and female (71%) with a mean (SD) age of 54 (15); 32% were obese. At diagnosis, 70% reported high levels of fatigue; as compared to those with low fatigue, high fatigue patients were significantly (p >.05) more likely to have high disease activity and OA/back pain, be obese, and report greater pain, disability, sleep disturbance, depression, and major stressors in the previous year (Table 1). There was a trend for high fatigue patients to be female and seropositive.

At 12 months, 70% of patients with high fatigue reported significant improvements in fatigue. Patients with improved fatigue were significantly less likely to be obese or have fibromyalgia, and had fewer comorbidities, a shorter symptom duration, and lower initial fatigue (Table 2). In adjusted multivariable models, baseline predictors of improved fatigue at 1 year was BMI < 30 (OR 0.6; 95% CI 0.4, 0.9) after controlling for other Table 1 characteristics.

Conclusion: Debilitating fatigue is common around the time of RA diagnosis and is associated with more active disease, worse pain and disability, and OA/back pain, obesity, depression, poor sleep, and major stressors in the previous year. In patients who presented with high fatigue, 70% improved by the end of the first year. Obesity decreased the odds of improved fatigue at 12 months by 40%. In contrast, other RA presenting characteristics were not associated with improvement. Early MTX use and optimizing weight, sleep, and mood may help address persistent fatigue when RA inflammation is well controlled. These results underscore the potential benefits of multidisciplinary interventions in ERA.

Disclosure: S. Bartlett, Abbie, 2, Abbvie, 2, 5, Bayer, 5, International Society of QOL Research, 6, Janssen, 5, 8, Lilly, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, Pfizer Inc, 8, PROMIS International, 6, UCB, 5, 8; **O. Schieir**, None; **M. Valois**, None; **C. Hitchon**, Pfizer, 2, UCB, 2, UCB Canada, 2; **L. Bessette**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, Amgen, BMS, Janssen, Roche, UCB Pharma, AbbVie Inc, Pfizer, Merck, Celgene, Sanofi, Eli Lilly, and Novartis., 2, 5, 8, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Bristol-Myers-Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5; **G. Hazlewood**, None; **C. Thorne**, Abbvie, 2, 5, Amgen, 2, 5, CaREBiodam, 2, Celgene, 2, 5, Centocor, 5, Janssen, 5, Lilly, 5, Medexus/Medac, 5, 8, Merck, 5, Novartis, 2, 5, Pfizer, 2, 5, Sandoz, 5, Sanofi, 5; **J. Pope**, AbbVie, 5, Abbvie, 5, Actelion, 5, Actellion, 5, Amgen, 2, 5, AstraZeneca, 2, Astra-Zeneca, 2, Bayer, 2, 5, BMS, 2, 5, Eicos Sciences, 5, Eli Lilly & Company, 5, Eli Lilly and Company, 5, EMERALD, 5, Emerald, 5, Genzyme, 5, Janssen, 5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8; **G. Boire**, Abbvie, 2, Amgen, 2, 5, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, Eli Lilly, 2, 5, Lilly, 2, 5, Merck, 2, 8, Novartis, 2, Pfizer, 2, 5, 8; **D. Tin**, None; **E. Keystone**, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 5, Astra-Zeneca, 5, Biotest, 5, BMS, 2, 5, 8, Celltrion, 5, Crescendo, 5, Crescendo Bioscience, 5, F. Hoffmann-La Roche Inc, 2, 5, 8, Genentech, 5, Genentech Inc., 5, Genzyme, 5, Gilead, 2, 5, Gilead Sciences, Inc., 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 5, 8, Pfizer, 2, 5, 8, Pfizer Pharmaceuticals, 2, 5, 8, Roche, 2, 5, 8, Sandoz, 5, Sanofi, 2, 5, 8, Sanofi-Aventis, 2, 8, UCB, 5, 8; **V. Bykerk**, AbbVie, 5, Amgen, 1, 2, 3, 5, 8, Brainstorm Therapeutics, 1, 2, 3, 5, 8, Bristol-Myers Squibb, 5, Genentech, 5, Gilead, 5, NIH, 2, Pfizer, 1, 2, 3, 5, 8, Regeneron, 5, Regeneron Pharmaceuticals, Inc, 5, Sanofi, 5, Sanofi/Genzyme-Regeneron, 5, Sanofi-Genzyme/Regeneron, 1, 2, 3,

5, 8, Scipher, 1, 2, 3, 5, 8, The Cedar Hill Foundation, 9, UCB, 1, 2, 3, 5, 8, UCB Pharma, 5; **C. (CATCH) Investigators**, Amgen, 2, Pfizer Canada, 2, AbbVie Corporation, 2, Medexus Inc., 2, Eli Lilly Canada, 2, Merck Canada, 2, Sandoz Canada Biopharmaceuticals, 2.

Abstract Number: 0472

Sleep Quality in Women with Rheumatoid Arthritis Is Associated with Disease Activity and Depressive Symptoms

Deborah Da Costa ,[1] Teresa Szlachetka,[2] and Diane Lacaille[3], [1]McGill University, Montreal, QC, Canada, [2]University of British Columbia, Vancouver, BC, Canada, [3]Arthritis Research Canada and University of British Columbia, Vancouver, BC, Canada

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sleep disturbances, including difficulty initiating sleep, maintaining sleep, and/or early morningawakenings are prevalent in persons with rheumatoid arthritis (RA) and can significantly impact quality of life and worsening of other RA symptoms including fatigue and pain. Despite their high prevalence and negative consequences, sleep disturbances remain poorly understood and inadequately managed in persons with RA. This study aimed to characterize sleep disturbances in RA and identify the role of disease-related, lifestyle behaviors and depressive symptoms in relation to sleep quality in women with RA.

Methods: We conducted a cross-sectional study using 2018 data from an annual survey administered to an RA cohort derived from a population-based cohort from British Columbia. The sample was comprised of 146 women with RA (mean age = 73.7 years ± 10.9). Participants completed self-report questionnaires assessing sociodemographics, anthropometrics, disease activity, functional impairment, leisure time physical activity, alcohol consumption, smoking and depressive symptoms. Sleep quality was measured with the Pittsburgh Sleep Quality Index (PSQI). Descriptive statistics were performed to characterize the sleep parameters. Bivariate associations with the potential determinants of poorer sleep (PSQI global score) were first calculated, followed by multivariate linear regression with variables found to be significantly associated with sleep in the bivariate analyses.

Table 1. Results of bivariate and multivariate regression analyses to identify determinants of poorer sleep quality. * Standardized beta coefficients; Sleep quality assessed with the global PSQI score, with higher scores associated with poorer sleep quality. Abbreviations: RADAI: Rheumatoid Arthritis Disease Activity Index; HAQ: Health Assessment Questionnaire

Variables	Bivariate B* (p-value)	Multivariate B* (p-value)
RADAI	0.51 (<0.001)	0.25 (0.005)
HAQ	0.36 (<0.001)	0.02 (0.228)
> 150 min/wk physical activity	-0.17 (0.035)	-0.08 (0.267)
Alcohol intake		
None	Ref	Ref
Monthly	0.02 (0.813)	0.09 (0.279)
Weekly	-0.02 (0.820)	0.08 (0.282)
Daily	-0.22 (0.027)	-0.05 (0.526)
Depressive symptoms	0.61 (<0.001)	0.46 (<0.001)

Results: The mean global PSQI score was 8.1 (SD=4.1), with 70.5% of the sample classified as poor sleepers (PSQI global score >5). Sleep latency was greater than 30 minutes in 24% of the sample and 35% reported sleep duration < 7 hours. A sleep efficiency of less than 75% was reported by 26% of the sample. Awakening at night three or more times a week was reported by 62.8% of the patients, and this was most commonly attributed in part due to requiring use of the washroom (80.7%) and pain (60.7%). Of the total participants, 44.5% reported using medication to aid sleep in the past month, with 31.5% using sleep medication 3 or more times per week. Significant bivariate relationships with sleep quality are shown in the Table. Age, education, obesity, disease duration, menopausal status, and smoking were not associated with sleep quality. In the multivariate analysis, disease activity and depressive symptoms remained independently associated with poorer sleep quality.

Conclusion: Sleep problems are prevalent among patients with RA. Our findings suggest that in addition to disease activity, depressed mood contributes to poor sleep in RA. Multimodal interventions which include nonpharmacological methods to target sleep require evaluation to optimize the management of sleep disruptions in RA.

Disclosure: D. Da Costa, None; **T. Szlachetka**, None; **D. Lacaille**, None.

Abstract Number: 0473

RA Presents in Disease Patterns Impacting Treatment Response

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite significant research on rheumatoid arthritis (RA), disease courses have not been clearly described. Like systemic lupus erythematosus and multiple sclerosis, RA displays a diversity of disease patterns across patients. The purpose of this study was to describe the range of RA disease courses and how they relate to rheumatology treatment including time to diagnosis and degree of improvement with DMARDs.

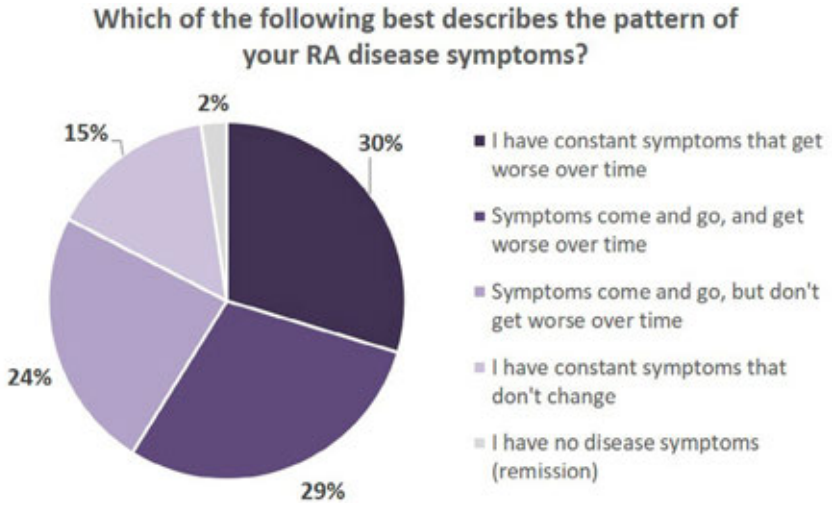

Figure 1. RA disease symptoms can be divided into five categories.

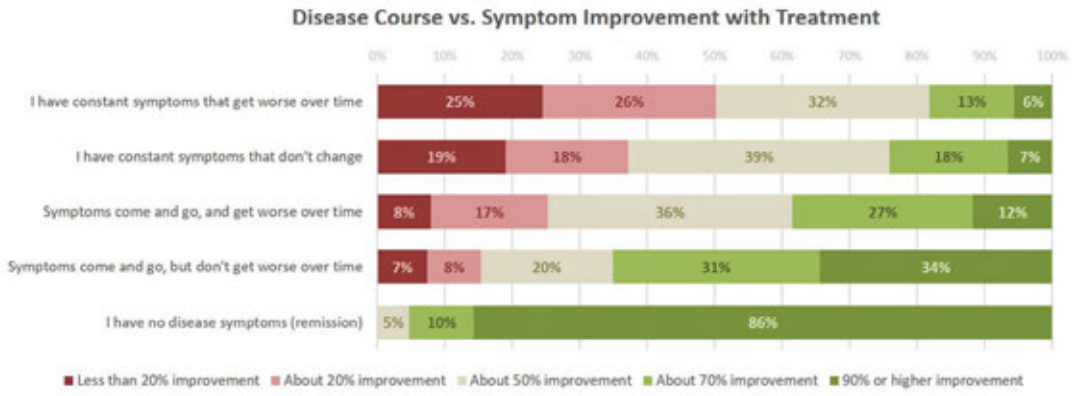

Figure 2. Symptom improvement with DMARDs is associated with particular disease courses.

Which of the following best describes the pattern of your RA disease symptoms?	How long did you experience RA symptoms prior to diagnosis?			
	≤ 1 Year	Between 1-5 Years	5+ Years	Total
I have constant symptoms that get worse over time	24.3%	32.7%	**36.6%**	30%
Symptoms come and go, and get worse over time	27.2%	29.3%	**33.0%**	29%
I have constant symptoms that don't change	14.6%	15.7%	**15.5%**	15%
Symptoms come and go, but don't get worse over time	30.8%	20.3%	**13.9%**	24%
I have no disease symptoms (remission)	3.2%	2.0%	**1.0%**	2%
Grand Total	**100.0%**	**100.0%**	**100.0%**	**100%**

Figure 3. Disease courses are related to length of time between symptom onset and RA diagnosis.

Methods: An anonymous, web-based questionnaire was developed, pilot-tested and presented over 7 days in 2019 on a secure survey system preventing multiple entries. Eligible participants were U.S. residents age ≥18 years with a self-reported diagnosis of RA by a medical professional. Participants recruited by email and social media answered closed and open-ended questions about socio-demographics, their RA disease activity, diagnosis and DMARD history, and improvement from RA treatment. Patients were also asked which of a list of disease patterns best described their RA: "I have constant symptoms that don't change"; "I have constant symptoms that get worse over time"; "I have no disease symptoms"; "Symptoms come and go, and get worse over time"; and "Symptoms come and go, but don't get worse over time". These patterns were categorized in 2 dimensions: (1) constant vs flaring and remitting and (2) progressive vs non-progressive.

Results: 907 people responded (90% women, 10% men), with a mean age of 58 years and 11.1 years since diagnosis (SD 10.1). Patients were asked which of a list of disease patterns best described their RA. The responses as listed above were 15%, 30%, 2%, 29%, and 24%, respectively (Fig 1).

Of respondents who reported a flaring and remitting pattern, 50% reached ≥ 70% improvement from treatment while only 20% of respondents reporting constant disease reached ≥ 70% improvement (Fig 2). Furthermore, 49% of respondents with a non-progressive disease course reached ≥ 70% improvement, while conversely 28% of those with a progressive disease course reached ≥ 70% improvement.

Only 5% of respondents reporting constant progressive symptoms were diagnosed within 3 months of symptom onset. Respondents with this disease pattern were more likely to have had symptoms >10 years before diagnosis compared to other patterns. Those having >10 years between first symptoms and diagnosis were more likely to have progressive disease than non-progressive disease. Thirty-six percent of those who experienced symptoms ≥5 years before diagnosis considered their disease constant and progressive (Table 1). Respondents were 95% more likely to achieve ≥70% improvement if diagnosed within a year of symptom onset versus ≥5 years after symptom onset.

Conclusion: RA patients experience a variety of disease patterns not readily reflected in literature describing RA disease activity. Disease courses may be related to time to diagnosis and treatment and also may impact levels of improvement from RA treatment. While RA is a heterogeneous disease, recognizing patterns of the disease may assist both research and treatment decisions. Further research should explore more thoroughly how RA disease patterns affect rheumatology treatment.

Disclosure: K. Marks, None; **D. Symons**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **P. Sinicrope**, None; **K. O'Neill**, None.

Abstract Number: 0474

Associations of Plasma Extravesicular (EV) MicroRNA Levels in Seropositive and Seronegative Rheumatoid Arthritis (RA)

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA) are biomarkers that allow early diagnosis of RA in seropositive (ACPA+ or RF+) patients. However, some subjects are seronegative (ACPA-/RF-). In addition to a lack of markers to identify ACPA- patients, researchers hypothesize that different serotypes reflect distinct pathogenic and disease entities. RA is mediated by a complex interplay between genetic and environmental factors that mirrors epigenetic deregulation. Recent research has focused on understanding the role of microRNAs (miRNAs), a type of epigenetic modification, in RA. Studies have identified altered expression patterns for miRNAs in synovial fluid and plasma of RA patients, suggesting that changes in miRNA underly the molecular mechanisms of the disease. However, research has not investigated whether miRNA expressions differ by serotype status. In this study, we investigate plasma extravesicular miRNAs associations with serotype and other clinical features of RA. We also attempt to identify whether miRNAs can discriminate seronegative from seropositive RA.

Methods: We recruited 20 patients who satisfied the ACR criteria for RA. The population included 14 seropositive (ACPA+ and/or RF+), and 6 seronegative (ACPA- and RF-) patients. 800 EV miRNAs were extracted from plasma circulating extra-vesicles, and measured using a Nanostring nCounter Human v3 miRNA expression panel. Data was normalized using nSolver software. Statistical analysis was carried out to determine miRNA differences by serotype and to identify miRNA correlations with rheumatoid factor (RF), anti-citrullinated peptide antibodies (ACPA), disease activity index (CDAI), Simple Erosive Narrowing Score (SENS), neuropathic pain (ID pain), Toronto Clinical Neuropathy Score (TCNS), Neuropathy Symptom Score (NSS), and disease duration. Discriminant function analysis was used to investigate whether miRNAs could discriminate between serotypes.

Results: Five miRNAs (*miR-1261, miR-4532, miR-802, miR-595, miR-373-3p*) were differentially expressed between seropositive and seronegative RA ($p \leq 0.05$). *miR-802* and *miR-1261* positively correlated with ACPA levels (Pearson Coeff.ACPA= 0.608, p=0.001) and ID Pain (Pearson Coeff.ID Pain= 0.472, p=0.041), respectively. No other RA clinical

	Seronegative (ACPA-/RF-)	Seropositive (ACPA+ and/or RF+)	p-value
Demographic Characteristics			
Age			
Men, (years)	57.7 ±4.9	56.0 ± 18.4	-
Women, (years)	57.0 ±6.2	53.2 ± 12.6	-
Race/ Ethnicity (n)			
Hispanic	6	12	-
African-American	1	2	-
Clinical Characteristics (% or mean ±SE)			
% ACPA+	0	100%	-
% RF+	0	75%	-
Disease duration (years)	10.4 ± 14.0	8.1 ± 8.2	0.73
CRP	0.60 ± 0.39	0.87 ± 0.34	0.55
WBC	7.20 ± 0.94	6.38 ± 0.59	0.49
CDAI	19.58 ± 2.73	11.18 ± 2.13	0.06

variables were correlated with miRNA levels. Discriminant function analysis identify *miR-1261* (p=0.004) and ACPA (p=0.002) as the strongest biomarkers differentiating seronegative from seropositive RA.

Conclusion: Our findings suggest that EV miRNAs might underlie serotype pathogenesis in RA. One of these, *miR-595*, has been previously identified as upregulated in RA. We identified four new miRNAs related to RA serotype. Of all these, *miR-1261* was as powerful as ACPA differentiating seronegative from seropositive patients. Interestingly, *miR-1261* did not correlate with ACPA, which suggests independent roles for each biomarker in serotype biology. Further studies are needed to explore the potential of these miRNAs as biomarkers of development and progression of the disease in this population.

Disclosure: L. Delgado-Cruzata, None; **M. Rodriguez Alvarez**, None; **N. Almodovar**, None; **T. Bravo**, None; **S. Hinson**, None.

Abstract Number: 0475

Myopenia in Elderly Female Patients with Rheumatoid Arthritis Is Associated with Severe Joint Damage: A Cross-sectional Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Our previous study reported myopenia is associated with joint damage in rheumatoid arthritis (RA). However, little is known about body composition (BC) disorder in elderly patients with RA. Here we aimed to explore the characteristics of BC in elderly RA patients and their clinical significance.

Methods: Consecutive female patients with RA who fulfilled the 1987 revised criteria of ACR or 2010 ACR/EULAR classification criteria for RA were recruited from August 2015 to March 2018. Clinical data including disease activity, function and radiographic assessment were collected. BC was assessed by bioelectric impedance analysis. Overfat was defined by body fat percentage (BF%) as ≥35% in women. Myopenia was defined by appendicular skeletal muscle mass index (ASMI) ≤5.7kg/m^2 in women.

Results: ①There were 425 female RA patients recruited with median age 50 (IQR 40, 58) years, median disease duration 60 (IQR 24, 120) months. There were 65.6% patients with active RA (DAS28-CRP≥2.6), 15.5% patients with functional limitation (HAQ-DI >1) and 56.5% with radiographic joint damage (RJD, mTSS >10). ②There were 23.1% elderly RA patients (age ≥60 years). Compared with young patients (age < 60 years), elderly RA patients had longer disease duration (median 92 months vs. 50 months), higher ESR (43 mm/h vs. 26mm/h), higher rate of functional limitation (24.5% vs. 12.8%) and RJD (67.2% vs. 51.0%), and higher rate of overfat (49.0% vs. 28.7%) and myopenia (54.1% vs. 41.9%, all P< 0.05). ③Compared with RA patients without myopenia, RA patients with myopenia (44.7%) had longer disease duration (median 72 months vs. 48 months), higher DAS28-CRP (median 3.48 vs. 3.02), higher rate of functional limitation (25.8% vs. 7.2%) and RJD (68.4% vs. 46.8%, all P< 0.05). ④There were 44.7% young patients without myopenia, 32.2% young patients with myopenia, 10.6% elderly patients without myopenia, and 12.5% elderly patients with myopenia. Elderly patients with myopenia had the highest rate of RJD (84.9%) in comparison with other three subgroups respectively. They also had higher rate of functional limitation (37.7%) when compared with young patients without myopenia as well as elderly patients without myopenia subgroups respectively (Table 1, all P< 0.0083, Bonferroni correction). ⑤After adjustment for confounding factors including age, smoking habits, disease duration, RF and ACPA status, multivariate logistic regression analysis showed that both young and elderly patients with myopenia had higher probabilities accompanied by functional limitation (young patients with myopenia: OR=3.479, 95%CI: 1.713~7.063; elderly patients with myopenia: OR=5.727, 95%CI: 2.467~13.292) and RJD (young patients with myopenia: OR=1.896, 95%CI: 1.171~3.068; elderly patients with myopenia: OR=4.627, 95%CI: 1.946~10.999) when compared with young patients without myopenia. Moreover, significant additive interaction was observed between the elderly and myopenia in RJD (AP=0.554, 95%CI: 0.125~0.983).

Table 1 Comparisons of disease characteristics among RA patients in age and myopenia subgroups

Characteristics	Young without myopenia (n=190)	Young with myopenia (n=137)	Elderly without myopenia (n=45)	Elderly with myopenia (n=53)	P#
Age, yrs, median (IQR)	47 (39,52)	45 (34,52)	64 (61,69)*è	63 (62,69)*è	<0.001
Disease duration, month, median (IQR)	48 (23,95)	64 (25,109)	83 (24,144)	108 (39,192)*	<0.001
Smoking habits					0.212
Active smoking, n (%)	3 (1.6)	1 (0.7)	0 (0.0)	3 (5.7)	
Exposure to second hand smoke, n (%)	77 (40.5)	46 (33.6)	17 (37.8)	15 (28.3)	
Without exposure to smoke, n (%)	110 (57.9)	90 (65.7)	28 (62.2)	35 (66.0)	
Positive RF, n (%)	116 (61.1)	88 (64.2)	25 (55.6)	37 (69.8)	0.484
Positive ACPA, n (%)	136 (71.6)	94 (68.6)	29 (64.4)	32 (60.4)	0.429
Core disease activity indicators					
Morning stiffness, min, median (IQR)	0 (0,10)	0 (0,13)	0 (0,21)	0 (0,13)	0.909
28TJC, median (IQR)	2 (0,4)	2 (1,7)	2 (0,6)	4 (0,10)	0.091
28SJC, median (IQR)	1 (0,3)	2 (0,4)	1 (0,4)	2 (0,7)	0.070
PtGA, median (IQR)	2 (0,5)	3 (1,6)	2 (2,5)	4 (2,7)*	0.001
PrGA, median (IQR)	2 (0,4)	3 (1,6)	2 (2,5)	4 (2,6)*	<0.001
Pain VAS, median (IQR)	2 (1,4)	3 (2,4)	2 (2,4)	4 (2,5)	0.007
ESR, (mm/h), median (IQR)	24.00 (14.50,36.00)	27.00 (13.50,52.50)	40.00 (20.50,60.50)	45.00 (23.00,75.50)*	<0.001
CRP, (mg/L), median (IQR)	3.30 (3.28,8.07)	5.54 (3.28,22.85)	3.98 (3.28,10.55)	6.46 (3.28,22.50)	0.008
DAS28-CRP, median (IQR)	3.00 (1.85,3.93)	3.42 (2.43,4.66)	3.11 (2.08,4.27)	3.68 (2.55,5.50)	0.004
DAS28-ESR, median (IQR)	3.48 (2.46,4.75)	3.88 (2.82,5.28)	3.87 (2.85,5.08)	4.38 (3.06,6.49)*	0.002
SDAI, median (IQR)	8.34 (2.89,16.86)	12.12 (5.37,24.84)	11.00 (4.36,21.44)	16.33 (7.31,33.85)*	0.001
CDAI, median (IQR)	8.00 (2.00,16.00)	12.00 (4.00,20.50)	10.00 (4.00,18.50)	14.00 (6.50,30.00)*	0.003
Functional indicators					
HAQ-DI, median (IQR)	0.12 (0.00,0.50)	0.25 (0.00,0.94)*	0.25 (0.00,0.75)	0.63 (0.12,1.25)*	<0.001
Functional limitation, n (%)	13 (6.8)	29 (21.2)*	4 (8.9)	20 (37.7)*ƒ	<0.001
Radiographic assessment					
mTSS, median (IQR)	8.50 (2.50,23.50)	21.50 (4.50,64.00)*	11.50 (5.00,34.25)	28.00 (12.50,81.75)*	<0.001
JSN subscore, median (IQR)	1.00 (0.00,9.00)	7.00 (0.50,31.75)*	2.00 (0.00,7.50)	10.00 (2.00,35.75)*	<0.001
JE subscore, median (IQR)	6.50 (2.00,15.00)	12.50 (3.75,31.50)*	10.00 (4.25,27.50)	18.50 (9.50,47.00)*	0.001
Bony erosion (%)	172 (90.5)	123 (89.8)	44 (97.8)	51 (96.2)	0.199
RJD, n (%)	85 (44.7)	85 (62.0)*	25 (55.6)	45 (84.9)*èƒ	<0.001

Myopenia, ASMI<5.7kg/m² in women; Functional limitation, HAQ-DI>1; Bony erosion, JE subscore>0; RJD, radiographic joint damage (mTSS>10); IQR, interquartile range.

#Comparison in four groups by Kruskal-Wallis test.

* Compared with young patients without myopenia in Bonferroni correction, P<0.0083.

è Compared with young patients with myopenia in Bonferroni correction, P<0.0083.

ƒ Compared with elderly patients without myopenia in Bonferroni correction, P<0.0083.

Conclusion: Elderly female patients with myopenia is associated with severe joint damage in rheumatoid arthritis and the underlying mechanism is worth further study.

Disclosure: C. Chen, None; **J. Lin**, None; **J. Ma**, None; **L. Yang**, None; **Q. Li**, None; **L. Chen**, None; **Y. Mo**, None; **L. Dai**, None.

Abstract Number: 0476

Decreased Muscle Mass, a Novel Predicting Indicator for One-year Radiographic Progression in Rheumatoid Arthritis: A Real-world Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Obesity paradox based on body mass index (BMI) in rheumatoid arthritis (RA) remain elusive. Our previous cross-sectional study has reported myopenia is associated with joint damage in RA. Here we aimed to explore the association of body composition (BC) with RA clinical outcomes in a real-world cohort.

Methods: Consecutive Chinese patients with RA who fulfilled the 1987 revised criteria of ACR or 2010 ACR/EULAR classification criteria for RA were recruited from August 2015 to January 2018. RA patients were treated according to the T2T strategy and completed at least one-year follow-up. BC was assessed by bioelectric impedance analysis and clinical data were collected at baseline, 3rd, 6th, 9th and 12th months. Myopenia was defined by appendicular skeletal muscle mass index (ASMI) ≤7.0kg/m^2 in men and ≤5.7kg/m^2 in women. One-year radiographic progression was defined as a change of Sharp/van der Heijde modified total sharp score (mTSS) ≥0.5 units.

Results: There were 305 RA patients [median age 49 (IQR 39-58) years old with 84.6% women] completed one year follow-up and 31.8% showed radiographic progression. RA patients with radiographic progression showed worse disease characteristics, lower BMI and lower muscle mass with higher prevalence of myopenia (62.9%-67.0% vs. 30.8%-38.0%) compared with those without radiographic progression during one-year follow-up. After treatment, all muscle indicators increased at almost all visits in all RA patients group especially in those without radiographic progression. Compared with those without baseline myopenia, RA patients with baseline myopenia (45.9%) had worse disease activity indicators at the 12th month, worse functional indicators at each visit, and higher percentage of radiographic progression (43.6% vs.21.8%, all P< 0.05, Figure 1). Multivariate logistic regression analysis showed baseline myopenia was associated with a significantly higher likelihood of radiographic progression (OR=2.139, 95%CI: 1.221-3.747). ROC curve analysis and multivariate logistic regression analysis showed that in patients without baseline myopenia, decreased ASMI from baseline to the 3rd (OR=2.849, 95%CI: 1.156-7.018), 9th (OR=2.837, 95%CI: 1.116-7.209) and 12th (OR=3.791, 95%CI: 1.467-9.794) months revealed significantly higher likelihoods of radiographic progression, with cutoff values of -0.021, -0.156 and -0.083 kg/m2 respectively.

Conclusion: Our data indicated decreased muscle mass, a novel predictive indicator for one-year radiographic progression in RA which imply the importance of dynamic monitoring of BC especially muscle mass during RA treatment.

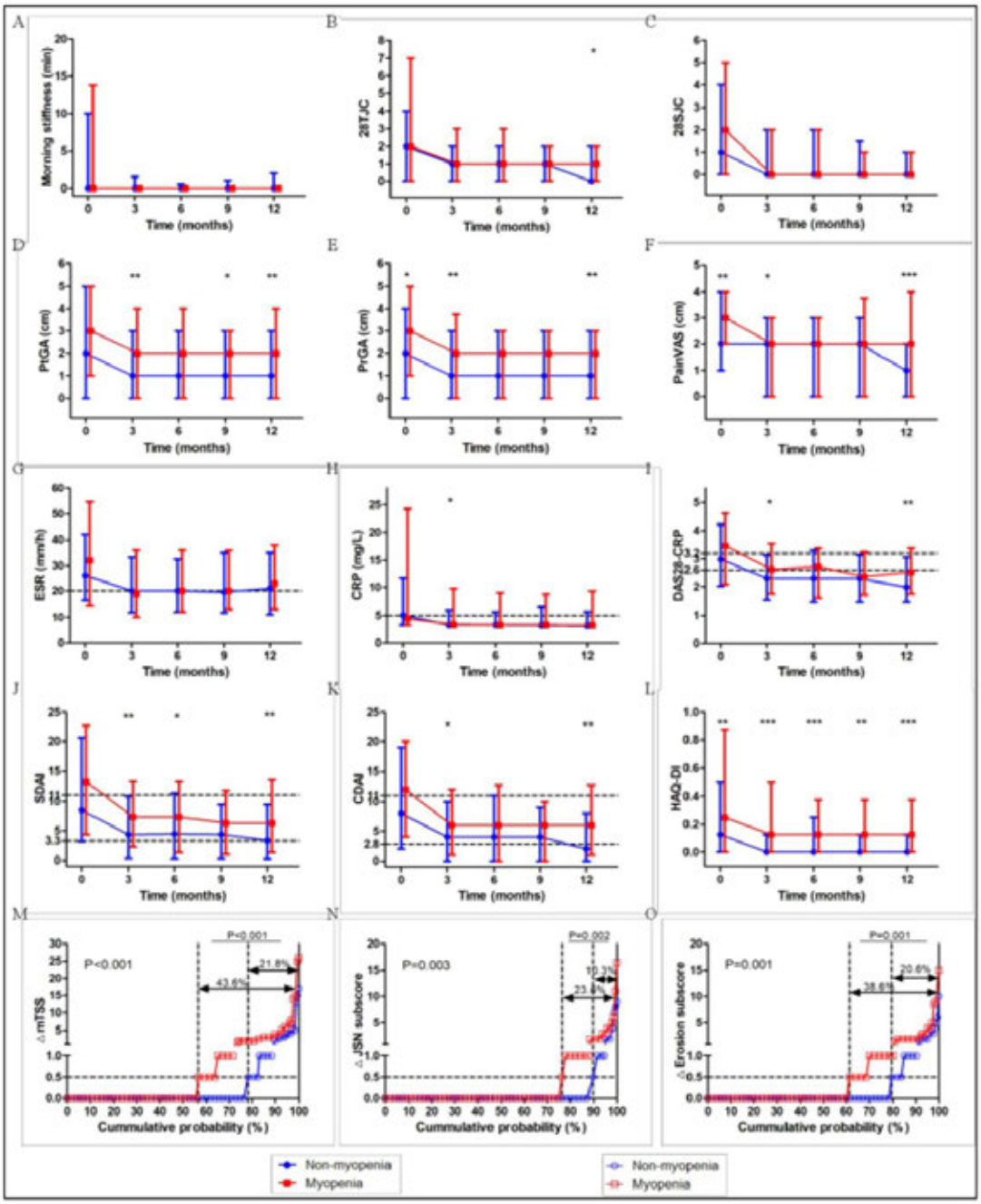

Figure 1 Comparisons of dynamic disease activity indicators (A-K), functional indicator (L) and one-year radiographic change (M-O) between RA patients with and without baseline myopenia.

Myopenia, ASMI≤7.0kg/m^2 in men and ≤5.7kg/m^2 in women; ΔmTSS, a change in mTSS from baseline to the 12th month; ΔJSN subscore, a change in joint space narrowing subscore from baseline to the 12th month; ΔErosion subscore, a change in erosion subscore from baseline to the 12th month.

* P<0.05, ** P<0.01, *** P<0.001.

Disclosure: **J. Lin**, None; **J. Ma**, None; **Q. Li**, None; **Y. Mo**, None; **L. Yang**, None; **L. Chen**, None; **C. Chen**, None; **J. Wang**, None; **D. Zheng**, None; **L. Dai**, None.

Abstract Number: 0477

Inflammation but Also Pain and Function, and Psychological Impact Is Related to Non-Acceptable Status in Patients with Rheumatoid Arthritis: A Factorial Analysis in 643 Patients

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patient Acceptable Symptom State (PASS) represents the maximum level of symptom intensity that a patient considers acceptable. Control of disease activity is associated with the attainment of PASS, but many patients do not reach this status despite being in disease remission. Recognizing the factors associated with PASS status can be helpful in identifying the need for adjunctive treatments besides immunosuppressive therapy, aiming at improving the satisfaction and well-being of patients with rheumatoid arthritis (RA). This study aimed to explore domains of health associated with being in non-PASS in RA patients.

Methods: Data of patients with a diagnosis of RA from 3 databases (NOR-DMARD, RAID study and RAID.Pt) were included. PASS was assessed using the anchored method based on patients' perspective, through the question: "*Think about all the ways your RA has affected you during the last week. If you were to remain for the next few months as you were during the last week, would this be a) Acceptable b) Unacceptable*". Age, gender, disease duration, disease activity based on DAS28-3 variable (joint counts and ESR) and its individual components, the RA Impact of

Table 1: Factor Analysis explaining non-PASS status in RA

	Factor		
	1 "Psychological Impact"	2 "Pain and Function"	3 "Inflammation"
RAID Pain	0.236	0.855	0.172
RAID Function	0.278	0.860	0.139
RAID Fatigue	0.709	0.390	-0.004
RAID Sleep	0.879	0.102	0.052
RAID Emotional well being	0.653	0.549	0.098
RAID Physical well-being	0.719	0.437	0.014
RAID Coping	0.482	0.619	0.060
DAS28-ESR- 3v	0.032	0.174	0.982

Values correspond to rotated loading factors obtained by the Varimax Rotation Method

Disease (RAID) score and its individual components, Patient Global Assessment (PGA) and Physician Global Assessment (PHGA) were collected. Patients who considered themselves in a non-acceptable status and without missing data were selected for statistical analysis. An exploratory factor analysis using the principal components method and Varimax rotation with Kaiser Normalization was performed. A correlation analysis (Pearson's correlation) between the identified factors with PGA and PhGA was performed.

Results: In total, 643 RA patients in non-acceptable status from the three datasets (NOR-DMARD: 388; RAID Study: 179 and RAID.Pt: 76) were included (female: 79.6%, mean age (±SD): 54.0±15.2 years; mean disease duration: 13.4±1.5 years). On average, patients in non-PASS status scored ≥ to 5 in all RAID domains, except Coping (mean:4.79±2.33) and had moderate disease activity (mean DAS28-ESR-3v: 3.77±1.46). Three principal components were identified: "Psychological Impact", "Pain and Function", and "Inflammation" explaining respectively 32.3%, 31.7%, and 12.9% of the total variance (table 1). PGA was moderately correlated with "Psychological Component" (r= 0.43) and with "Pain and Function Component" (r=0.68), but not with the "Inflammation Component". Conversely, PhGA correlated moderately with the "Inflammation component" (r=0.55), but not with the other two factors.

Conclusion: This exploratory analysis suggested that non-PASS status can be due to three main factors: "Psychological impact", "Pain and Function and Inflammation. This suggests the need for a holistic evaluation and consideration of tailored interventions to optimize outcomes, from the patients' perspective.

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Abstract Number: 0478

The Influence of Gender on Composite Disease Activity Indices for Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Disease activity of patients with rheumatoid arthritis should be assessed equally independent of gender, age, or disease duration. However, at present, they are not taken into account consideration in the calculation of any composite measure indices. The aim of this study is to clarify how "gender" affect DAS28-ESR, DAS28-CRP, SDAI and CDAI.

Table. Coefficients of gender in each disease activity category for all of composite disease activity indices in generalized liner model

	Remission		LDA		MDA		HAD	
	Estimate	p-value	Estimate	p-value	Estimate	p-value	Estimate	p-value
DAS28-ESR(Complete Case)	-0.21	<0.001	-0.0041	0.83	-0.052	0.26	-0.006	0.97
DAS28-ESR(Imputed dataset)	-0.19	<0.001	-0.0027	<0.05	-0.0065	<0.05	-0.015	<0.05
DAS28-CRP(Complete Case)	0.022	0.36	0.012	0.6	0.012	0.85	-0.27	0.19
DAS28-CRP(Imputed dataset)	0.026	<0.001	0.011	<0.001	0.037	<0.001	0.043	<0.001
SDAI(Complete Case)	0.0061	0.92	0.15	0.36	0.56	0.26	-2.43	0.3
SDAI(Imputed dataset)	0.048	<0.001	0.049	<0.001	0.21	<0.001	-0.036	0.75
CDAI(Complete Case)	0.00075	0.99	0.12	0.42	0.18	0.64	1.25	0.54
CDAI(Imputed dataset)	0.016	<0.001	0.025	<0.001	0.065	<0.001	-0.34	<0.001

LDA: low disease activity MDA: moderate disease activity HAD: high disease activity
Dummy variable(male=1, female=0) is used in each models
Coefficients of other independent variables are not shown
Standard Errors are not shown

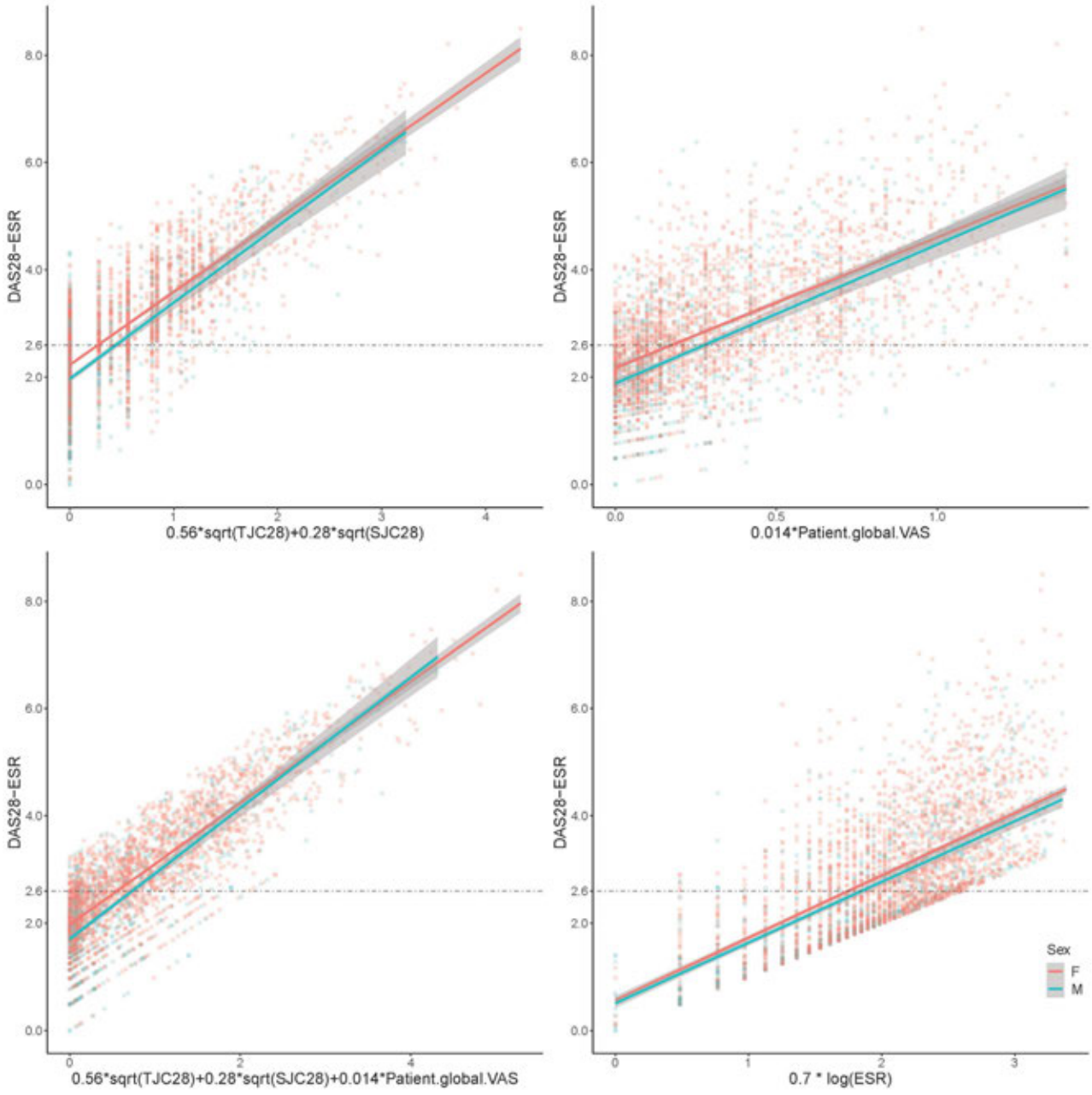

Figure. scatter plots in complete case with regression line(gamma distribution and identity link)

Methods: We analyzed 15056 of patients with rheumatoid arthritis registered in the nationwide observational cohort database(National Database of Rheumatic Diseases in Japan; NinJa) in 2017. We performed regression analysis in each disease activity category (remission, low disease activity, moderate disease activity, high disease activity) for all of DAS28-ESR, DAS28-CRP, SDAI and CDAI using generalized liner model with gamma distribution and identity link: each disease activity indices as a dependent variable and duration of disease, gender, number of artificial joints, BMI, Stage, HAQ-DI, HADS-A and smoking as independent variables. The results of regression analysis are dually confirmed in complete case analysis(listwise deletion) and dataset imputed by chained equation(iteration number:100 × sample size:15056 = 1505600).

Results: In complete case analysis, coefficients of gender in each disease activity category are not significant, except for remission based on DAS28-ESR: -0.21 (Table). In analysis using dataset imputed by chained equation, all coefficients of gender in each disease activity category are significant, except for high disease activity based on SDAI. From the view of clinical knowledge, only the coefficient value of remission based on DAS28-ESR:-0.19 is large enough to affect interpretation of disease activities. To investigate the reason of discrepancy by gender in remission based on DAS28-ESR, we drew scatter plots in complete case with regression line(gamma distribution and identity link):DAS28-ESR as a dependent variable and components of DAS28-ESR as independent variables respectively(Figure). Discrepancy by gender in remission is negligible only in scatter plot of ESR as an independent variable, suggesting gender difference of ESR mainly contribute to the discrepancy. Additionally, we calculated the number of male patients who achieve remission criteria defined as 2.4 for male in DAS28-ESR on the assumption that gender difference is at least -0.2 from the coefficient values. As a result, remission criteria as 2.6 may be overestimated by about 10% in male.

Conclusion: This study indicates we may have to pay attention to gender only when assessing remission based on DAS28-ESR. Considering the current treatment strategy targeting “remission” by composite measures in rheumatoid arthritis, the influence of gender on remission assessed by DAS28-ESR cannot be ignored.

Disclosure: T. NIshino, None; **A. Hasimoto**, None; **S. Tohma**, None; **T. Matsui**, Chugai Pharmaceutical Co., LTD,, 2, Janssen Pharmaceutical K.K., 2.

Abstract Number: 0479

Impact of Achieving Early-sustained Remission on Preventing Long-term Functional Loss in Patients with Early Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Preventing functional loss is crucial to early RA (ERA) patients in order to maintain usual activities of daily living. However, whether achieving early and sustained remission could predict long-term functional status remain uncertain. The aim of this study is to ascertain whether early-sustained remission can prevent loss of functional ability in ERA patients.

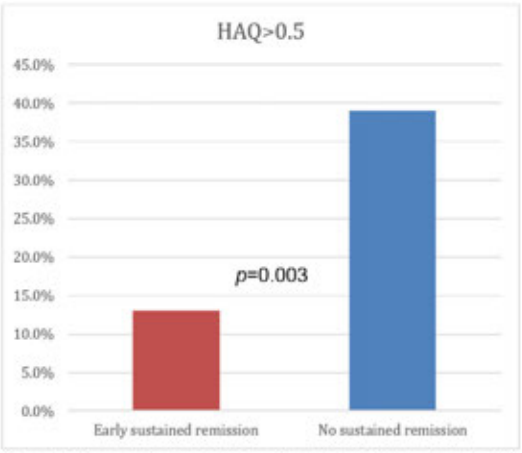

Figure 1. Proportion of patients with substantial functional ability loss at year 4

Methods: ERA patients with symptom onset < 2 years were enrolled into the Clinical Rheumatology Systematic Treat-to-target in Asia Leadership (CRYSTAL) Project. All subjects satisfied the 2010 ACR classification criteria for RA. Clinical assessments were performed for every three months in the first year, then yearly until the sixth year. Disease Activity Score 28 (DAS-28) and Health Assessment Questionnaire Disability Index (HAQ-DI) were recorded each visit. Early-sustained remission is defined as achieving DAS28-CRP < 2.6 consecutively from month 6 to year 4. Substantial functional ability loss is defined as HAQ-DI >0.5 at year 4. Potential independent predictors including baseline characteristics and early-sustained remission at year 4 were determined using multivariate logistic regression analysis.

Results: One-hundred-and-thirteen patients (age: 52.8±12.0 years, female: 90/113 (80%)) who completed year 4 assessment were included. Significant improvement in disease activity is observed (DAS28-CRP: 4.42±1.29 at baseline vs 2.34±0.99 at year 4, p< 0.001). Majority of patients (103/113, 91.2%) were on conventional synthetic DMARDs and 8/113 (7.1%) on biologic DMARDs. 47/113 (42%) patients achieved early-sustained remission, with 5/47 (11%) achieving drug-free remission. Patients with early sustained remission had a milder disease at baseline (Table 1). At year 4, there were less patients with substantial functional loss in the early-sustained remission group (6/46 (13%) vs 25/66 (40%), p=0.003) (Figure 1).

Using multivariate logistic regression, early-sustained remission is a protective factor for substantial functional loss at year 4 (OR: 0.26, 95% CI: 0.09-0.77, *p*=0.015) after adjusting baseline variables. Whereas independent risk factors for functional loss include female gender and HAQ-DI at baseline (Table 2).

Table 1. Baseline characteristics

	In sustained remission = 47	No sustained remission = 66	*p* value
Age	52.83±11.92	55.15±11.04	0.289
Symptom onset, month	9.57±6.75	9.89±6.49	0.800
Gender (Female), n	37 (78.7%)	53 (80.3%)	0.837
VAS[1] Pain Score, 0-100	43.09±26.82	47.8±22.05	0.308
VAS[1] Patient Global, 0-100	48.96±27.67	55.89±22.19	0.143
VAS[1] Physician Global, 0-100	46.51±28.72	58.33±24.31	**0.020**
DAS28-CRP[2]	3.97±1.36	4.74±1.14	**0.001**
HAQ-DI[3], 0-3	0.65±0.67	0.87±0.64	0.080

[1]Visual Analogue Scale, range 0-100; [2]Disease Activity Score-28; [3]Health Assessment Questionnaire Disability Index, range 0-3

Table 2. Multivariate logistic regression

	Odds ratio (OR)	95% C.I.	*p* value
Early sustained remission	0.26	[0.09,0.77]	0.015
Female gender	5.17	[1.01,26.46]	0.049
Baseline HAQ-DI	3.31	[1.58,6.96]	0.002

Conclusion: Long-term functional ability loss can be prevented in ERA patients who achieved early-sustained remission. Baseline HAQ-DI indicates a risk factor for substantial functional loss, therefore early disease control aiming for consistent remission is crucial.

Disclosure: E. Chow, None; **I. Cheng**, None; **L. Tam**, None; **C. Hong Kong**, None.

Abstract Number: 0480

Not Achieving Clinical Remission Predicts a Poor Health-Related Quality of Life in Rheumatoid Arthritis Patients: Results of a Latin American *Real World* Database

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Uncontrolled Rheumatoid Arthritis (RA) leads to disability, damage, and poor health-related quality of life (HRQoL). Current treatment recommendations emphasize the importance of achieving remission or Low Disease Activity (LDA) [(1)] to avoid the aforementioned results. In Latin American, RA patients have been shown to achieve low remission but high disability rates. [(2-4)] and the alternative LDA, could be a reasonable treatment goal. Objective: To explore the impact of not achieving remission over time on the HRQoL in RA patients.

Methods: RA patients from a longitudinal established RA cohort (ACR1987/ACR-EULAR2010 criteria) from a single center were studied. This cohort was established to describe the clinical outcomes of RA Peruvian patients; for this analysis, subjects with at least two evaluations (half-yearly) were included. In each visit clinical remission state was defined if they achieved a 3.3 value in the Simple Disease Activity Index (SDAI). Also, non-remission categories were defining in according to SDAI definition (>3.3 to ≤11.0; >11.0 to ≤26 and > 26 to low, moderate and high activity disease, respectively). HRQoL was explored with the Short Form 36 Health Survey Questionnaire (SF-36). A generalized estimating equation model was used to explore each SDAI category as a predictor of the summary measures, mental (MCS), and physical (PCS) of the SF-36 obtained on the subsequent visit. The multivariable models were adjusted for other predictors: gender, age at diagnosis, education, socio-economic level (measured by the Graffar scale), disease

duration, tobacco use, anti-citrullinated protein antibodies level, disability (MDHAQ), use of conventional (c), and biologic (b) DMARDs, use of corticosteroids (current use, past use or non-use) and the baseline score of the corresponding SF-36 summary measure.

Results: Four hundred thirteen patients were included, 375 (90.8%) were women; age at diagnosis was 43.9 (13.5) years, disease duration was 16.7 (11.4) years. At the baseline visit, the SDAI was 25.6 (22.8); only 4.1% patients were in remission; 14.3%, 41.9% and 39.7 were in low, moderate and high disease activity, respectively; MDHAQ was 0.7 (0.5); current corticosteroid use was 31.6%, cDMARD 59.2% and only 7.8% were in bDMARD treatment. The PCS was 40.5(18.4) and the MCS 45.7 (16.6). One thousand and nineteen visits were analyzed in the follow-up (2.71 per patient). In the multivariable analysis, not achieving remission state was associated with a worse HRQoL; these data are depicted in table 1.

Conclusion: Not achieving remission states predicted a worse HRQoL in the follow-up of RA patients, in our *real world* cohort. These results reinforced the importance of remission as a goal of RA management in clinical practice in our region.

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Table 1: Not achieving remission as a predictor of HRQoL in RA patients.

	SF36-PCS		SF36-MCS	
	B (SE)	p value	B (SE)	p value
SDAI category				
Remission	Ref.		Ref.	
Active				
Low	-5.18 (2.39)	0.030	-4.03 (2.03)	0.015
Moderate	-5.81 (-2.30)	0.011	-6.30 (1.98)	0.001
High	-5.27 (2.40)	0.028	-5.62 (2.09)	0.007
Age at diagnosis	-0.10 (0.03)	0.003	NA	
Disease duration	-0.13 (0.04)	<0.001	NA	
MDHAQ	-3.40 (0.96)	<0.001	-2.96 (0.82)	<0.001
SF36-PCS at baseline	0.57 (0.03)	<0.001		
SF36-MCS at baseline			0.60 (0.03)	<0.001

NA: Not associated. SDAI=Simple Disease Activity Index, MDHAQ= Multidirectional Disease Health Assessment Questionnaire, SF36-PCS=Physical Short Form 36 Health Survey Questionnaire, SF36-MCS=Physical Short Form 36 Health Survey Questionnaire

Disclosure: R. Gamboa-Cárdenas, None; **M. Ugarte-Gil**, None; **C. Reátegui-S**, None; **V. Pimentel-Quiroz**, None; **M. Medina**, None; **Z. Rodríguez-Bellido**, None; **S. Garcia-H**, None; **P. Zeña-Huancas**, None; **L. Gil**, None; **E.**

Noriega, None; **F. Zevallos-M**, None; **J. Alfaro-Lozano**, None; **R. Perich-Campos**, None; **C. Pastor-A**, None; **G. Alarcón**, None.

Abstract Number: 0481

Production of IL17A in Synovial Tissue Correlates with MRI RAMRIS Scores in ACPA Positive Early Rheumatoid Arthritis

Thomas Kirchgesner ,[1] Christine Galant,[2] Bernard Lauwerys,[3] Bruno Van de Berg,[1] Tatiana Sokolova,[4] Laurent Meric de Bellefon,[5] Adrien Nzeusseu,[5] and Patrick Durez[6], [1]Musculoskeletal Imaging Unit, Cliniques universitaires Saint-Luc - Université Catholique de Louvain - Institut de Recherche Expérimentale et Clinique (IREC), Brussels, Belgium, Bruxelles, Belgium, [2]Histopathology, Cliniques universitaires Saint-Luc - Université Catholique de Louvain - Institut de Recherche Expérimentale et Clinique (IREC), Brussels, Belgium, Bruxelles, Belgium, [3]Rheumatology, Cliniques universitaires Saint-Luc - Université Catholique de Louvain - Institut de Recherche Expérimentale et Clinique (IREC), Brussels, Belgium, Brussels, Belgium, [4]Rheumatology, Cliniques universitaires Saint-Luc - Université Catholique de Louvain - Institut de Recherche Expérimentale et Clinique (IREC), Brussels, Belgium, Bruxelles, Belgium, [5]Cliniques universitaires Saint-Luc - Université Catholique de Louvain - Institut de Recherche Expérimentale et Clinique, Bruxelles, Belgium, [6]Pôle de Recherche en Rhumatologie, Institut de Recherche Expérimentale et Clinique, UCL Saint-Luc, Brussels, Belgium

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: We previously studied evolution of MRI RAMRIS scores in a group of 28 early rheumatoid (RA) patients treated with first-line infliximab (IFX) versus placebo. After 4 months, we observed a significant improvement of the scores in IFX-treated patients, while the changes in placebo-treated individuals were minimal. Here, we used synovial tissue samples obtained at baseline and 4 months after initiation of therapy, in order to study correlations between synovial IL17A and clinical/MRI scores of disease activity.

Methods: Twenty eight patients with treatment naive early ACPA positive RA were enrolled. Disease activity measures (DAS28-CRP) were evaluated at baseline, weeks 2 and 4, and every 4 weeks until week 52. OMERACT RAMRIS scores (and each of their components: erosion, osteitis, synovitis, tenosynovitis), synovial biopsy inflammation and quantitative evaluation of IL17A immunostained sections were evaluated at baseline and month 4.

Results: 28 pts were randomized (mean age: 48 +/- 12 yrs; mean duration of arthritis: 0.34 +/- 0.53 yr; mean CRP level: 1.67 +/- 2.23 mg/dL). A synovial biopsy was performed in 18 patients. A strong correlation was observed between IL17A expression and total RAMRIS score or any of its components (see table and graph). No association of IL17A expression was observed across the different pathotypes (pauci-immune vs myeloid-lymphoid).

Higher synovial IL17A was also associated with a better improvement of the RAMRIS score at month 4 in IFX-treated patients (0.2799 ± 0.2102 vs 0.0216 ± 0.0223, p=0.029).

No correlation was observed between synovial IL17A and disease activity measures.

Conclusion: In this small randomized cohort of ACPA positive early RA patients, we observed a good correlation between IL17A expression in the synovium and MRI RAMRIS score, underlining the potential role of the cytokine in disease severity and progression.

Figure: IL17A expression and baseline total RAMRIS score correlation

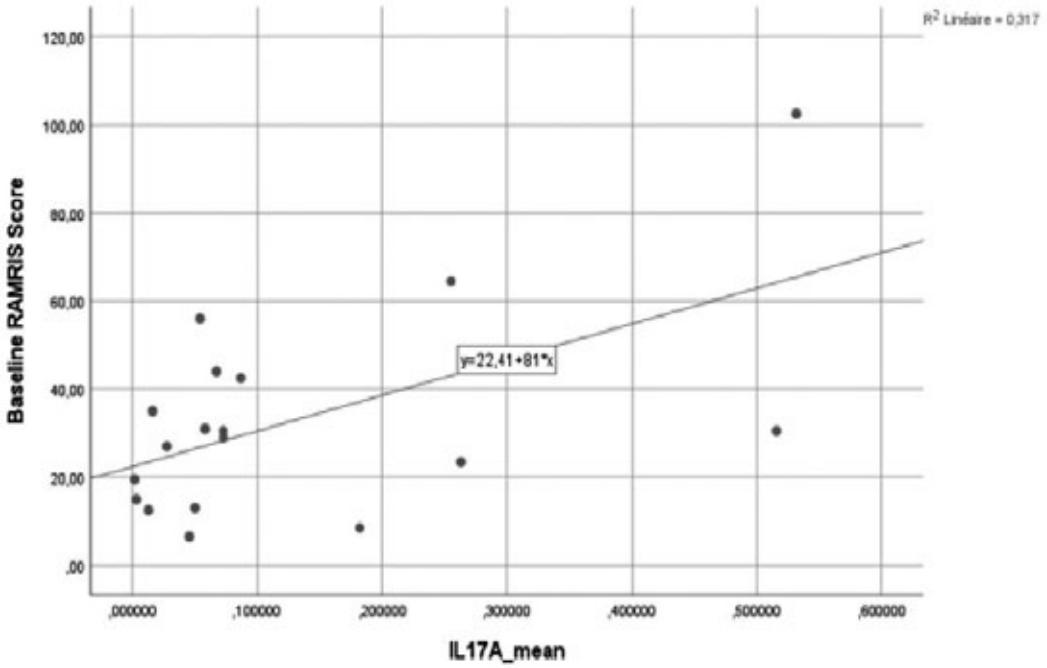

Table: IL17A expression and RAMRIS scores correlations

Correlations Table

		baseline						
		Synovitis	Tenosynovitis	Peritendinitis	Edema	Erosions	RAMRIS Score	RAMRIS-Peritendinitis Score
IL17A	Pearson's Test	0.472*	0.077	0.338	0.598**	0.577**	0.563*	0.580*
	p value	0.048	0.761	0.171	0.009	0.012	0.015	0.012
	Covariance	0.635	0.071	0.106	0.818	0.630	2.155	2.261
	N	18	18	18	18	18	18	18

Disclosure: T. Kirchgesner, None; **C. Galant**, None; **B. Lauwerys**, None; **B. Vande Berg**, None; **T. Sokolova**, None; **L. Meric de Bellefon**, None; **A. Nzeusseu**, None; **P. Durez**, BMS, 8, Bristol-Myers Squibb, 8, Celltrion, 8, Eli Lilly, 8, Hospira, 8, Mundipharma, 8, Pfizer, 8, Samsung, 8, Sanofi, 8, UCB, 8.

Abstract Number: 0482

Antibody Repertoire Sequencing, Antigen Array Analysis, and Cytokine Profiling of Blood from Individuals at High-risk for RA Reveals Candidate Immunoglobulin V Genes, ACPA, and Cytokines That May Promote the Transition to Arthritis

Radhika Iyer ,[1] Amin Zia,[1] Michelle Bloom,[1] Sunil Nagpal,[2] Navin Rao,[2] Frédéric Baribaud,[3] George Vratsanos,[4] Wei Wang,[5] Gary Firestein,[6] David Boyle,[5] Jane Buckner,[7] V. Michael Holers,[8] Kevin Deane,[9] and William Robinson[10], [1]Stanford University, Stanford, [2]Janssen R&D, Spring House, PA, [3]Janssen Research & Development, LLC, Spring House, PA, [4]JNJ, Raritan, NJ, [5]University of California, San Diego, San Diego, CA, [6]University of California, San Diego, San Diego, [7]Benaroya Research Institute, Seattle, WA, [8]University of Colorado Denver, Division of Rheumatology, Aurora, CO, USA, Denver, [9]University of Colorado Denver, Division of Rheumatology, Aurora, CO, USA, Aurora, CO, [10]Stanford University, Stanford, CA

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The "Targeting Immune Responses for Prevention of RA" (TIP-RA) collaboration studies individuals at high risk for developing rheumatoid arthritis (RA) because of serum anti-citrullinated protein antibody (ACPA) positivity in absence of arthritis at baseline, and is focused on defining how they transition from at-risk to classifiable disease. One potential mechanism is through the development, expansion and class-switching of B cells expressing pathogenic ACPA. Previous studies identified blood plasmablasts expressing ACPA in pre-clinical and established RA. Individuals enrolled in the TIP-RA cohort were analyzed by antibody repertoire sequencing, serum ACPA profiling, and serum cytokine analysis to identify features associated with progression to RA.

Methods: Cytokine array and ACPA array profiling were performed on serum samples from CCP- controls (n=156), (n-78), RA converters (n=3), and seropositive early-RA (n = 32). RNA was extracted from PAXgene whole blood tubes from CCP- (n=170), CCP3+ at risk (n=85), RA converters (n=3) and early RA individuals (n=41). Purified RNA was used for paired-end sequencing of immunoglobulin heavy-chain and run on a HiSeq 2500. Bulk IgH data was de-multiplexed with adapter sequences trimmed using MIGEC. Overlapping paired end reads were merged using MiTools. MIXCR was used to align sequencing reads to germline VDJ genes of B cell receptors obtained from IMGT, and subsequently group clones. VDJ gene family usage was analyzed using Alakazam (Immcantation).

Results: ACPA array analysis demonstrated development of ACPA targeting citrullinated fibrinogen and histone 2B as well as native vimentin as associated with transition to clinical arthritis. Cytokine profiling revealed increased levels of multiple pro-inflammatory cytokines and chemokines in the blood. Immunoglobulin heavy chain sequencing identified persistent clones (based on shared V and J gene usage, identical CDR3 lengths, and >60% amino acid homology) that underwent both expansion and class switching to IgA and IgG. Specifically, we identified clones encoding IgH-V3-23/IgHJ4 and IgHV1-2/IgHJ4 that switched and expanded from IgM pre-conversion to IgA and IgG isotypes post-conversion to RA (Figure 1).

Conclusion: Asymptomatic anti-CCP+ individuals that converted to RA exhibited increased levels of blood cytokines and ACPA. These individuals also exhibited expression, expansion and class-switching of B cell clones encoding IgH-V3-23/IgHJ4 and IgHV1-2/IgHJ4, antibody V genes previously identified as being expressed by RA plasmablasts and encoding anti-citrullinated protein antibodies (ACPA). IgH-V3-23/IgHJ4 and IgHV1-2/IgHJ4 may encode ACPA

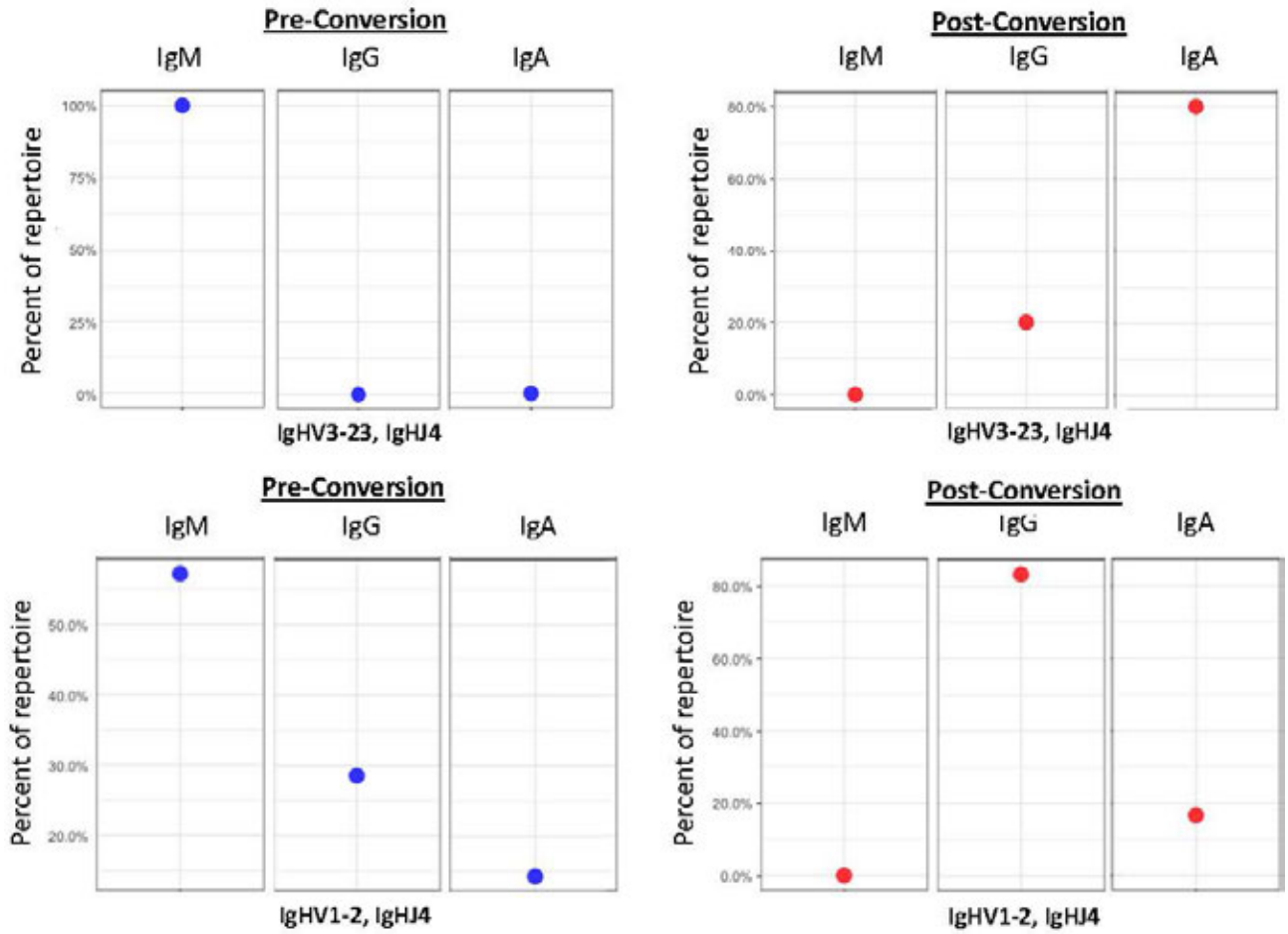

Figure 1. B cell clones encoding IgH-V3-23/IgHJ4 and IgHV1-2/IgHJ4 class switch from IgM pre-conversion to IgA and IgG isotypes post-conversion in TIP-RA converters.

that promote the transition to clinical RA, and further investigation is needed to fully define their citrullinated antigen targets and potential role in promoting the transition to clinical RA.

Disclosure: R. Iyer, None; **A. Zia**, None; **M. Bloom**, None; **S. Nagpal**, Janssen Research & Development, 3, Janssen Research, Johnson&Johnson, 1, 3, 4, Johnson & Johnson, 1, 4; **N. Rao**, Janssen Research & Development, 3, Johnson & Johnson, 1, 3, 4; **F. Baribaud**, Janssen Research & Development, LLC, 3; **G. Vratsanos**, Janssen Research & Development, 1, 3; **W. Wang**, None; **G. Firestein**, Abbvie, 2, Janssen, 2; **D. Boyle**, Janssen, 2; **J. Buckner**, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Janssen, 2, Novo Nordisk, 2, Pfizer, 2; **V. Holers**, AdMIRx, 1, 2, 4, 5, 6, Alexion, 7, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 5, Janssen R&D, 2, 5, Pfizer, 2; **K. Deane**, Bristol-Myers Squibb, 5, Inova, 9, Janssen, 2, 5, Janssen R&D, 2, Microdrop, 5, Pfizer, 2; **W. Robinson**, None.

Abstract Number: 0483

Can a Single Question on Functional Impairments Facilitate the Diagnosis of Early Inflammatory Arthritis? A Cross-Sectional Derivation and Validation Study in Two Early Arthritis *Recognition* Clinics

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Early treatment initiation in RA is associated with improved outcomes but requires early identification of synovitis. Joint swelling in early inflammatory arthritis (IA) may be subtle, making it difficult to detect at joint palpation, especially for general practitioners (GPs) who have limited experience with this. To promote early recognition of IA, two Early Arthritis *Recognition* Clinics (EA*R*C) were initiated in our country. EA*R*Cs are easy-access outpatient rheumatology clinics, intermediary between primary and secondary care, to which GPs can refer patients if in doubt about the presence of IA (instead of 'watchful waiting'). Although this approach markedly reduced referral delay, it may not be easily implemented in other places. New tools are needed. Since it is unknown if inquiring about functional impairments is helpful in the early detection of IA, we used the unique EA*R*C data of patients with suspected IA to investigate this. Aiming for simple and time-efficient use in daily practice, we evaluated whether a single question on functional impairments could aid the diagnosis of early IA.

Methods: From September 2010 to April 2014, 997 patients with suspected but uncertain IA visited one of the two EA*R*Cs and were included in a derivation cohort. In addition, 557 other patients visiting the same EA*R*C (November 2015-December 2018) and 506 patients visiting another EA*R*C (September 2010-January 2014) served as validation cohorts. IA was assessed by joint examination by rheumatologists, physical functioning with the Health Assessment Questionnaire Disability Index (HAQ-DI). Discriminative abilities of its 20 questions for IA were compared based on the area under the receiver operating characteristics curve (AUC) and test characteristics. Associations between the best discriminating question and IA were assessed with logistic regression. Odds ratios (ORs) were adjusted for age, sex and for six other, previously reported variables predictive of the presence of IA. Overall discriminative ability of multivariable logistic regression models was assessed with the AUC.

Results: IA was diagnosed in 43%, 35% and 53% of patients in the derivation and validation cohorts, respectively. In the derivation cohort, patients with IA had higher mean HAQ-DI-scores (0.84 compared to 0.73, p=0.003). Discriminative characteristics of one question on difficulties with dressing (AUC (95%CI) 0.57 (0.54–0.61); OR 1.83 (1.41-2.38)) paralleled the total HAQ-DI score (AUC 0.55 (0.52–0.59)). In the validation cohorts, ORs were 2.14 (1.48-3.10) and 2.00 (1.39-2.87) in univariable analyses, which remained similar in multivariable analyses. However, the difference in AUC for multivariable models with and without 'difficulties with dressing' was small: 0.73 (0.70–0.77) and 0.72 (0.69–0.76), respectively. Test characteristics are shown in the table.

Conclusion: A yes/no answer on a simple question ("Are you able to dress yourself, including shoelaces and buttons?") was helpful in discriminating patients with and without IA. Findings were validated in independent 1.5-line

	Sens. % (95%CI)	Spec. % (95%CI)	PPV % (95%CI)	NPV % (95%CI)
Derivation cohort n = 997, IA in 43%	60 (55–65)	54 (50–58)	50 (45–54)	65 (60–69)
1st validation cohort n = 557, IA in 35%	67 (60–73)	52 (47-57)	42 (37–48)	74 (70–80)
2nd validation cohort n = 506, IA in 53%	66 (60–72)	51 (44–57)	60 (54–66)	57 (50–64)

Table. Test characteristics of the presence of difficulties with dressing (scores ≥1 on the corresponding HAQ-DI question), with IA at physical examination as outcome.

settings and need to be validated further in primary care. This is a step forward to arrive at practical tools that are helpful for GPs in diagnosing IA.

Disclosure: B. van Dijk, None; **H. van Steenbergen**, None; **E. Niemantsverdriet**, None; **A. van der Helm-van Mil**, None.

Abstract Number: 0484

Effectiveness of Platelet-derived Microparticles for the Diagnosis and Clinical Evaluation of Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Platelet-derived microparticles (PDMP) are membrane vesicles released from activated platelets and contain various inflammatory or angiogenetic factors; therefore, PDMP may be a new biomarker for the diagnosis of rheumatic disease. Previous studies regarding PDMP levels in rheumatoid arthritis (RA) have compared patients with osteoarthritis or less active RA but not those with undifferentiated arthritis (UA), which requires more differentiation from RA. Moreover, reports on the clinical characteristics of RA patients with high PDMP levels are limited. We conducted the analysis of plasma PDMP levels obtained from 65 patients, including those with RA and UA. Furthermore, we examined the clinical features of RA cases with high PDMP levels.

Methods: In total, plasma PDMP levels in 65 cases (RA, n = 28; polymyalgia rheumatica [PMR], n = 11; UA, n = 6; others, n = 20; and healthy controls, n = 7) were analyzed using PDMP ELISA kit employing anti-GPIX and anti-GPIb monoclonal antibodies (Protein Purify Ltd., Gunma, Japan). In addition, we compared PDMP levels with clinical char-

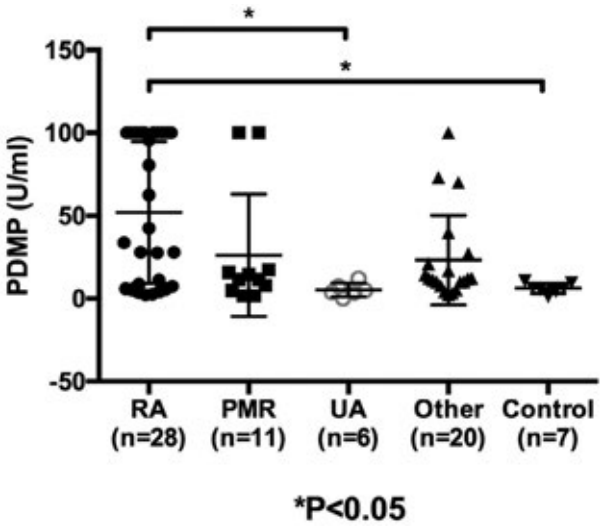

Figure 1. PDMP levels in each disease group. RA, rheumatoid arthritis; PMR, polymyalgia rheumatica; UA, undifferentiated arthritis; Other includes rheumatic diseases, such as systemic lupus erythematosus and dermatomyositis.

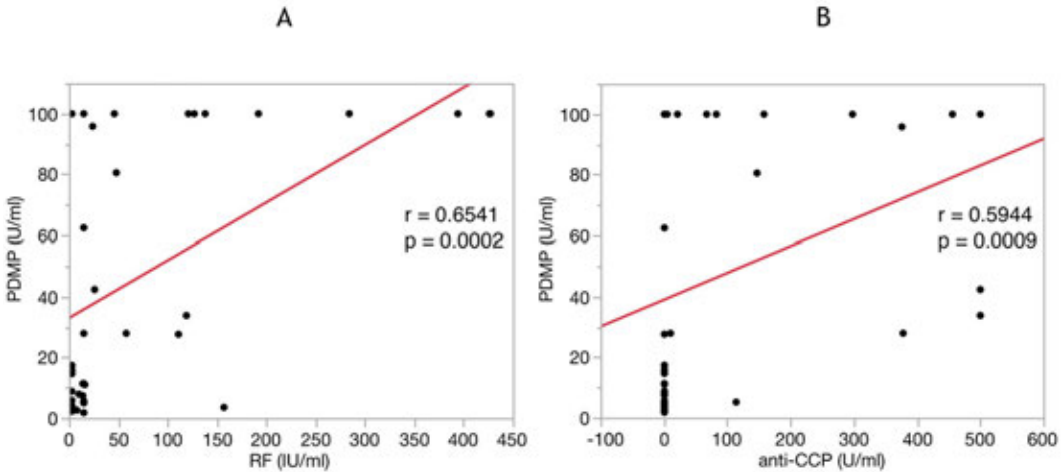

Figure 2. Correlation of PDMP levels with RF (A) and anti-CCP titers (B) PDMP levels positively correlated with RF and anti-CCP. RF, rheumatoid factor; anti-CCP, anticyclic citrullinated peptide antibody.

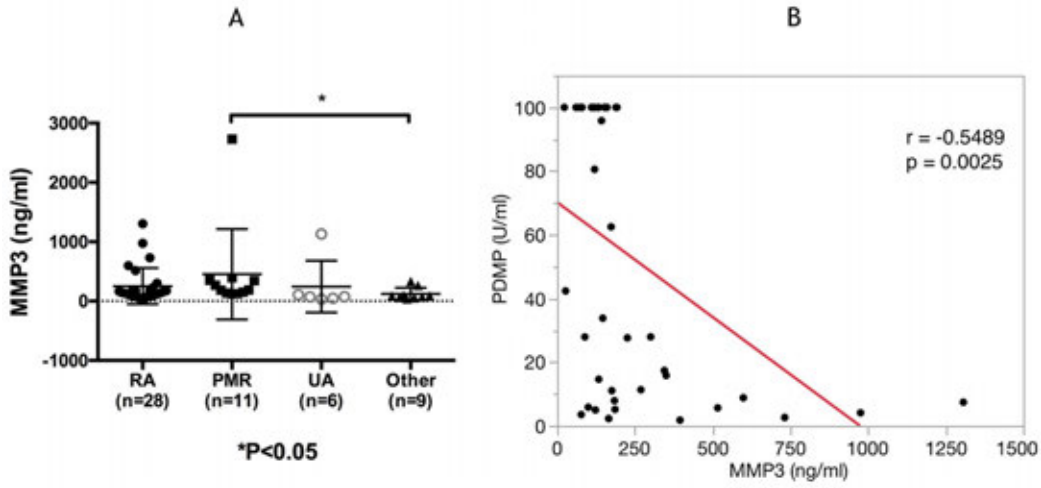

Figure 3. (A) MMP3 level for each disease group. MMP3 level between RA and UA was not significant. (B) PDMP levels negatively correlated with MMP3. RA, rheumatoid arthritis; PMR, polymyalgia rheumatica; UA, undifferentiated arthritis; Other includes rheumatic diseases such as systemic lupus erythematosus and dermatomyositis; MMP3, matrix metalloproteinase-3

acteristics and other biomarkers, including C-reactive protein, erythrocyte sedimentation rate, matrix metalloproteinase-3 (MMP3), rheumatoid factor (RF), and anticyclic citrullinated peptide antibody (anti-CCP).

Results: Mean PDMP levels (± SD) for each disease group and controls were as follows: RA, 51.96 ± 42.87 U/ml; PMR, 26.10 ± 36.92 U/ml; UA, 5.27 ± 4.13 U/ml; others, 23.28 ± 26.93 U/ml; healthy controls, 6.20 ± 3.13 U/ml. Plasma PDMP levels were significantly higher in RA patients than in UA patients and control. Furthermore, in RA patients, PDMP levels positively correlated with RF ($r = 0.6541$; $p = 0.0002$) and anti-CCP ($r = 0.5944$; $p = 0.0009$). Notably, PDMP levels negatively correlated with MMP3 ($r = –0.5489$; $p = 0.0025$); MMP3 levels between RA and UA patients were not significant. In addition, compared with 22 RA patients without interstitial pneumonia, 6 RA patients complicated with interstitial pneumonia showed elevated PDMP levels (85.72 ± 26.60 U/ml vs. 42.76 ± 42.19 U/ml; $p = 0.0281$).

Conclusion: Plasma PDMP levels are useful in the differential diagnosis of RA and UA. Plasma PDMP levels were correlated with RA-associated autoantibody and the complication of interstitial pneumonia, moreover, negatively

correlated with MMP3; therefore, plasma PDMP can be a candidate for an independent biomarker for the diagnosis and clinical evaluation of RA.

Disclosure: H. Horikoshi, None; **K. Takamatsu**, None; **R. Suzuki**, None; **Y. Kusanagi**, None; **F. Kimura**, None; **K. Itoh**, None.

Abstract Number: 0485

Comparison of Clinical Features, Synovial Histology and Immunohistochemistry in Seropositive Arthralgia, Rheumatoid Arthritis, and Osteoarthritis

Candice Low ,[1] Richard Conway,[2] Francis Young,[1] Eamonn Molloy,[3] Anne Barbara Mongey,[3] Gerry Wilson,[3] Ursula Fearon,[4] and Douglas Veale[5], [1]Saint Vincent's University Hospital, Dublin, Ireland, [2]Blackrock Clinic, Dublin, Ireland, [3]St Vincent's University Hospital, Dublin, Ireland, [4]Molecular Rheumatology, Trinity Biomedical Sciences Institute, TCD, Dublin, Ireland, [5]EULAR Centre For Arthritis And Rheumatic Diseases and The Conway Institute, Dublin, Ireland

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Table 1. Characteristics of patients with seropositive arthralgia, RA, and OA

Characteristic	Seropositive Arthralgia	Rheumatoid Arthritis	p value	Osteoarthritis	p value
N	33	14		7	
Age, years, mean (range)	54 (33-81)	55 (36-67)	0.724	62 (49-80)	0.137
Female, n (%)	22 (67)	6 (43)	0.195	6 (86)	0.318
Tender Joint Count	0 (0, 4)	6 (2, 11)	0.008	1 (1, 2)	0.261
Swollen Joint Count	0 (0, 0)	7 (3, 10)	<0.0005	1 (1, 2)	0.169
C Reactive Protein (mg/dL)	3.00 (2.00, 7.00)	14.00 (4.30, 35.00)	0.018	3.00 (1.73, 15.83)	0.805
Erythrocyte Sedimentation Rate (mm/hr)	17 (9, 25)	29 (21, 44)	0.028	15 (5, 18)	0.493
Patient Global Assessment (mm)	50 (28, 70)	52 (70, 90)	0.045	84 (70, 90)	0.013
DAS28-CRP	3.43 (2.38, 4.82)	4.88 (3.45, 5.90)	0.015	3.85 (2.53, 4.58)	0.781
Arthroscopic synovitis (mm)	60 (35, 80)	80 (80, 90)	0.011	80 (30, 80)	0.442
Arthroscopic vascularity (mm)	50 (30, 75)	80 (65, 90)	0.027	50 (30, 60)	0.889

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Seropositive arthralgia is defined as joint pain in patients positive for rheumatoid factor (RF) or anti-citrullinated protein antibodies (ACPA). It is a precursor to rheumatoid arthritis (RA) in some individuals. Clinical and synovial findings in seropositive arthralgia when compared to RA and osteoarthritis (OA) have not been fully

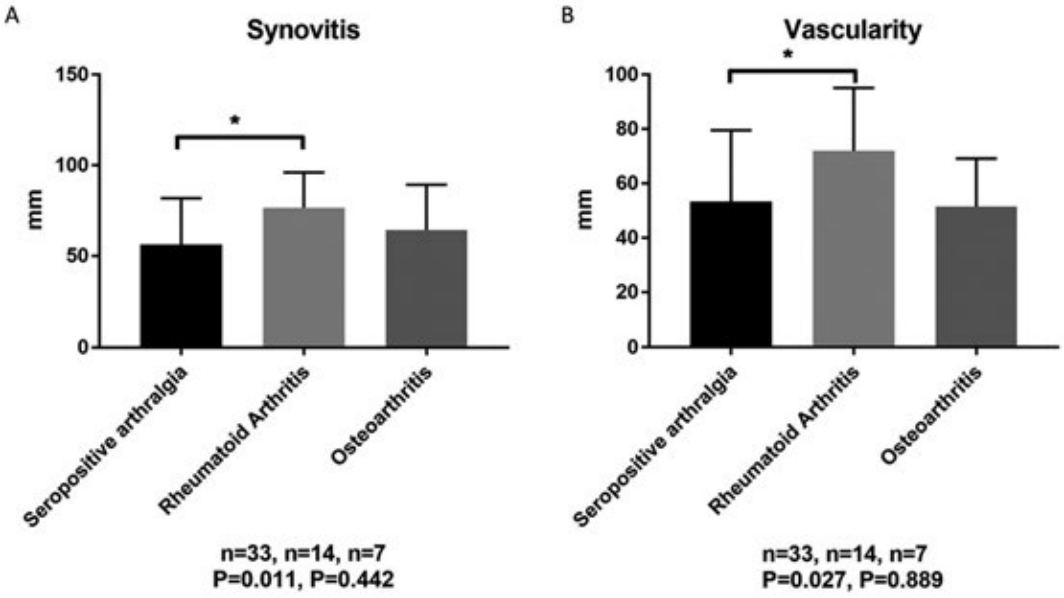

Figure 1. Macroscopic synovitis and vascularity in seropositive arthralgia, RA, and OA.

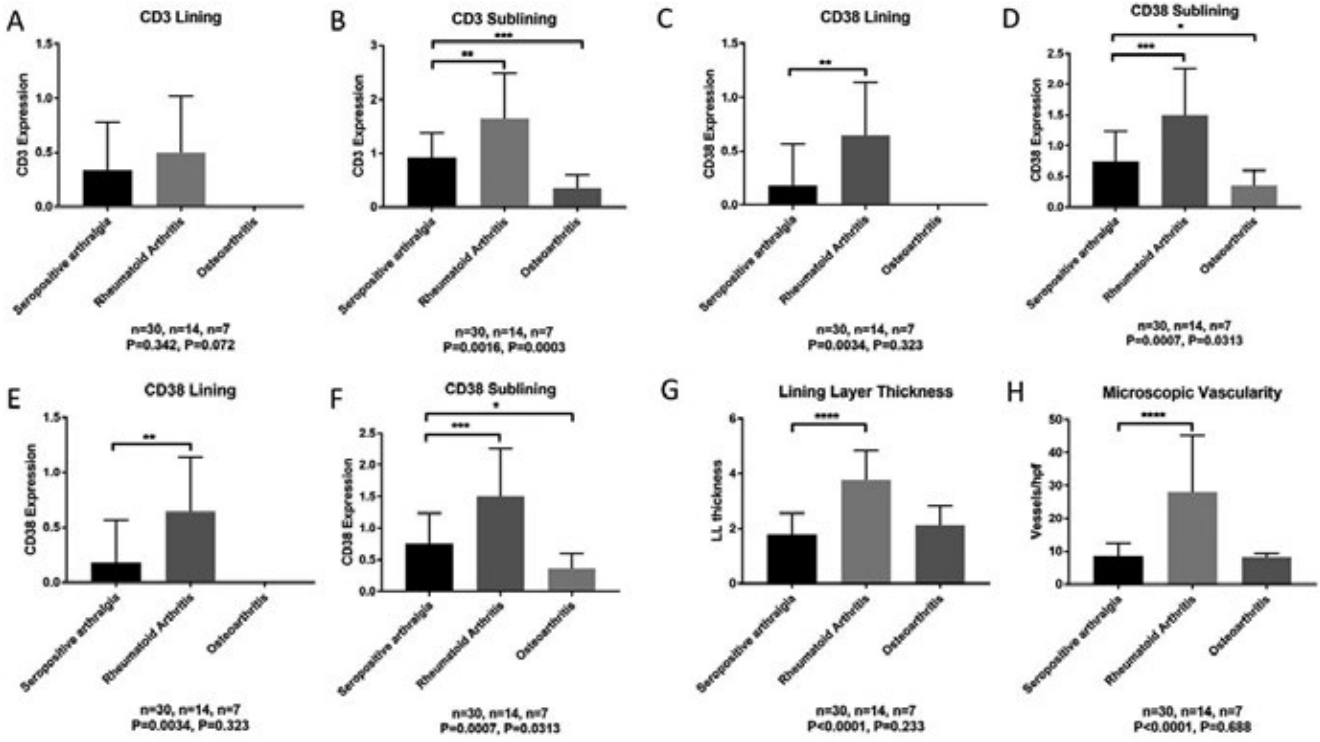

Figure 2. Comparison of synovial biopsy and immunohistochemical findings in seropositive arthralgia, RA, and OA.

defined. Our aim was to compare clinical characteristics, macroscopic arthroscopy findings, and synovial immunohistochemical findings in those with seropositive arthralgia, RA, and OA.

Methods: We performed a prospective study of consecutive patients with seropositive arthralgia. All patients were seropositive for RF and/or ACPA. Demographic and clinical characteristics were collected on all patients. Synovial biopsy was performed by needle arthroscopy in all patients, and macroscopic and histologic features recorded. The degree of synovitis and vascularity were recorded on a 0–100-mm visual analog scale. We compared the findings in this group to 2 other cohorts; patients with established diagnoses of either RA or OA as per ACR classification criteria. Whitney U test was used to compare groups. GraphPad Prism Version 8 and IBM SPSS Statistics Version 24 were used for data analysis.

Results: 54 patients were recruited, 33 with seropositive arthralgia, 14 with RA, and 7 with OA. Compared to seropositive arthralgia, established RA patients had higher tender and swollen joint counts, CRP and ESR, patient global assessment (PGA) of disease activity, and DAS28-CRP, Table 1. In contrast, the only difference between seropositive arthralgia and OA patients was higher PGA in the OA group, Table 1. RA patients had significantly greater macroscopic synovitis and synovial vascularity than seropositive arthralgia patients who were not significantly different to OA patients, Table 1, Figure 1. On synovial biopsy, synovial lining layer thickness and microscopic vascularity were increased in RA compared to seropositive arthralgia; there was no difference between seropositive arthralgia and OA. On immunohistochemical analysis of synovial tissue, CD3 and CD38 but not CD138 expression were higher in RA compared to seropositive arthralgia, Figure 2. CD3 and CD38 but not CD138 expression, were higher in seropositive arthralgia compared to OA, Figure 2.

Conclusion: Baseline clinical characteristics, macroscopic arthroscopic findings, and microscopic histologic findings in seropositive arthralgia are more similar to OA than established RA patients. However, key differences in synovial inflammatory cell populations are identifiable in seropositive arthralgia on immunohistochemical analysis.

Disclosure: C. Low, None; **R. Conway**, None; **F. Young**, None; **E. Molloy**, None; **A. Mongey**, None; **G. Wilson**, None; **U. Fearon**, None; **D. Veale**, Health Beacon, 1.

Abstract Number: 0486

Evolution of Seropositive Arthralgia over Time: Predictors of Evolution to Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Seropositive arthralgia is defined as joint pain in patients positive for rheumatoid factor (RF) or anti-citrullinated protein antibodies (ACPA). In some individuals it is a precursor to rheumatoid arthritis (RA). The factors which determine progression and outcomes in seropositive arthralgia patients remain to be fully defined. Our

Table 1. Baseline characteristics of 37 patients with seropositive arthralgia

Age, years	50 (13)
Sex, female, n (%)	26 (70%)
Tender Joint Count	3 (5)
Swollen Joint Count	0 (0)
Patient Global Assessment (mm)	47 (29)
DAS28-CRP	3.24 (1.31)
Arthroscopic synovitis (mm)	54 (25)
Arthroscopic vascularity (mm)	52 (25)

aim was to evaluate outcomes and prognostic factors, including arthroscopic findings, in a cohort of patients with seropositive arthralgia.

Methods: We performed a prospective study of consecutive patients with seropositive arthralgia. All patients were seropositive for RF and/or ACPA. Demographic and clinical characteristics were collected on all patients. Synovial biopsy was performed by needle arthroscopy in all patients, and macroscopic and histologic features recorded. The degree of synovitis and vascularity were recorded on a 0–100-mm visual analog scale. Diagnosis at last follow-up was recorded in all patients. Mann-Whitney U test was used to compare groups. GraphPad Prism Version 8 and IBM SPSS Statistics Version 24 were used for data analysis.

Results: 37 patients were recruited. Mean (SD) age was 50 (13) years. 26 (70%) were female. 31 (84%) were positive for RF and 32 (86%) for ACPA with 26 (70%) dual positive. Mean (SD) follow-up was 38 (13) months. Baseline characteristics are shown in Table 1. Final diagnosis was RA in 26 (70%), psoriatic arthritis in 2 (5%), connective tissue disease in 1 (3%), calcium pyrophosphate arthritis in 1 (3%), and remained seropositive arthralgia in 7 (19%). Baseline CRP was significantly higher in patients who developed RA than those who remained seropositive arthralgia, median (SD) 3.50 (2.00, 8.25) vs 1.00 (1.00, 2.00) mg/dL (p=0.0096), Figure 1. Baseline macroscopic synovitis and vascularity at arthroscopy were both significantly higher in those who developed RA than in those who remained as seropositive arthralgia, median (IQR) 60 (30, 80) vs 40 (20, 40) mm (p=0.021), and median (IQR) 50 (30, 73) vs 40 (20, 40) mm (p=0.021), Figure 1. Baseline DAS28-CRP, tender joint count, swollen joint count, and patient global assessment were not different between the groups. Baseline synovial cell immunophenotyping did not predict final diagnosis.

Conclusion: Elevated baseline CRP and arthroscopically determined macroscopic synovial inflammation and vascularity predict the development of RA in patients with seropositive arthralgia.

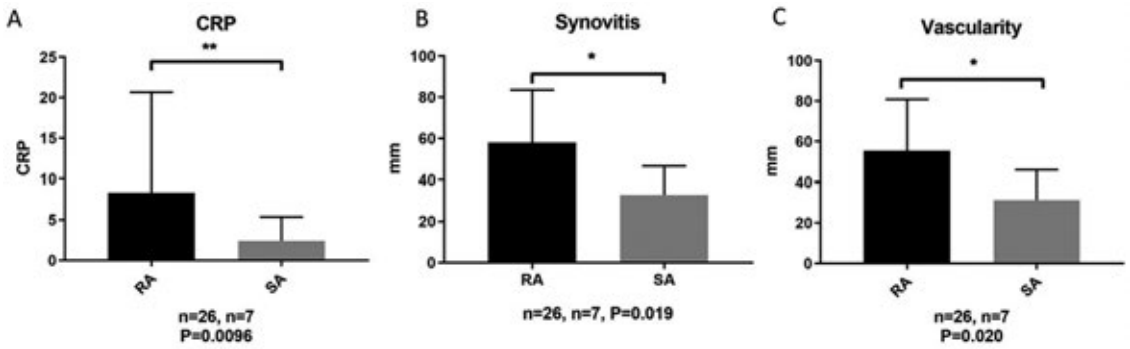

Figure 1. Comparison of CRP, macroscopic synovitis, and synovial vascularity in patients with seropositive arthralgia who did or did not progress to RA (RA: progressed to rheumatoid arthritis; SA: remained seropositive arthralgia)

Disclosure: C. Low, None; **R. Conway**, None; **F. Young**, None; **E. Molloy**, None; **A. Mongey**, None; **G. Wilson**, None; **U. Fearon**, None; **D. Veale**, Health Beacon, 1.

Abstract Number: 0487

Third Generation Anti-cyclic Citrullinated Peptide Antibodies Improve Prediction of Clinical Arthritis in Second Generation Anti-cyclic Citrullinated Peptide Positive Subjects at Risk of Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: ACPA positive individuals with musculoskeletal symptoms are at increased risk of developing RA. In such individuals, ACPA are conventionally identified on the basis of a positive serum IgG anti-CCP2 antibody (Ab) test.

Third-generation anti-CCP (CCP3) tests (Inova Diagnostic) have been recently introduced and their diagnostic value has been evaluated in patients with early and established RA.

The value of anti-CCP3 for predicting progression to RA in at-risk individuals is less understood. Consequently, the main aims of the study were:

- to determine the prevalence of anti-CCP3 Ab in anti-CCP2 positive at-risk individuals and the agreement between the 2 tests;
- to investigate the association between anti-CCP3 Ab and progression to RA;
- to explore the stability of anti-CCP3 Ab status over time.

Methods: Anti-CCP3 Ab were tested on stored serum samples obtained from 337 anti-CCP2 positive (BioRad, USA) at-risk individuals without synovitis from the Leeds CCP study.

Table 1. Agreement between anti-CCP2 and anti-CCP3 tests

	CCP2	
CCP3	***Low +ve***	***High +ve***
-ve	79	59
Low +ve	10	9
High +ve	12	168

Anti-CCP2 and anti-CCP3 tests positivity threshold was >2.99 IU/ml and >20 units, respectively. Anti-CCP2 and anti-CCP3 Ab were considered low titre (LT) or high titre (HT) if < or > than 3 times the positivity threshold, respectively.

Only subjects with at least one follow-up visit were included in the progression analysis (n=308). Sequential samples were tested for CCP3 in 132 individuals.

Results: Anti-CCP3 Ab tended to be either negative (138/337; 40.9%) or HT positive (180/337; 53.4%), with a few subjects showing a LT (19/337; 5.6%). In contrast, for anti-CCP2, more LT were observed (101/337; 30%). The Cohen's k agreement between anti-CCP2 and anti-CPP3 test was 0.22 (0.17-0.26) (p< 0.001) (Table 1). Eighty-three/308 subjects (27%) developed arthritis (median follow up 273 days, min 3 – max 3402), 73 of whom fulfilled 2010 ACR/EULAR classification criteria for RA. The proportions of patients progressing to arthritis (ever) according to anti-CPP2 and anti-CPP3 Ab status are illustrated in Table 2. The rate of progression of LT and HT anti-CCP2, when anti-CCP3 was negative, fell from 6.5% to 2.7%, and from 45.6% to 9.4%, respectively. Progression in anti-CCP2 HT increased

Table 2. Proportions of patients progressing to arthritis (ever) according to CCP2 and CCP3 status

				Progressed (ever) n (%)
CCP2: Low positive	n=92			6 (6.5%)
High positive	n=216			77 (35.6%)
CCP3: Negative	n=126			7 (5.5%)
Low positive	n=16			4 (25%)
High positive	n=166			72 (43.4%)
CCP3: Negative		**CCP2:** Low positive	n=73	2 (2.7%)
		High positive	n=53	5 (9.4%)
Low positive		**CCP2:** Low positive	n=7	1 (14.2%)
		High positive	n=9	3 (33.3%)
High positive		**CCP2:** Low positive	n=12	3 (25%)
		High positive	n=154	69 (44.8%)

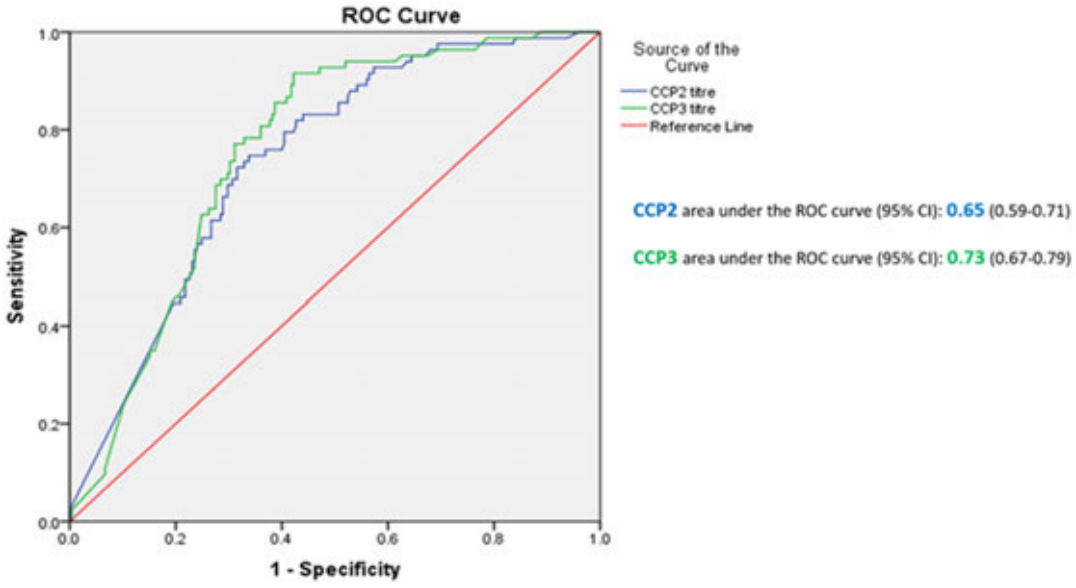

Figure 1. ROC curves for anti-CCP2 and anti-CCP3 tests predicting progression (ever)

from 35.6% to 44.8%, when anti-CCP3 was positive. The hazard ratio for HT anti-CCP2 and HT anti-CPP3 Ab was 4.9 (CI 2.1-11.2) and 6.9 (CI 3.1-15.0) ($p< 0.001$), respectively. The ROC curves for anti-CCP2 and anti-CCP3 tests are shown in Figure 1.

At baseline, 33/132 (25%) individuals who had CCP3 tested at ≥1 timepoint for sequential samples were anti-CCP3 negative and 99/132 (75%) were anti-CCP3 positive (5 LT, 94 HT). The anti-CCP3 Ab titer remained stable in 125/132 (94.7%) individuals, in 559/575 (97.6%) sequential samples (mean follow-up 551 days ±623.53).

Conclusion: The distributions of anti-CCP2 and anti-CCP3 assays differed and their agreement was poor.

Our results suggest a potential value of anti-CCP3 antibodies in improving prediction of clinical arthritis in both LT and HT CCP2 positive at-risk subjects.

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Abstract Number: 0488

Citrullinated Antigens with Multiple Citruline Similar Motif Could Be Used for RA Diagnosis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic joint inflammation that ultimately leads to joint destruction. Diagnosis of RA is important as new therapies can halt the disease progression in its early stages. In the past decade, ACPA measured by antiCCP assay was widely accepted as RA diagnostic biomarker. ACPAs are auto-antibodies produced against proteins of the body modified by citrullination. Although anti-ACPA test specificity reaches around 95%, about 20 to 40 percent of RA patients are ACPA negative.

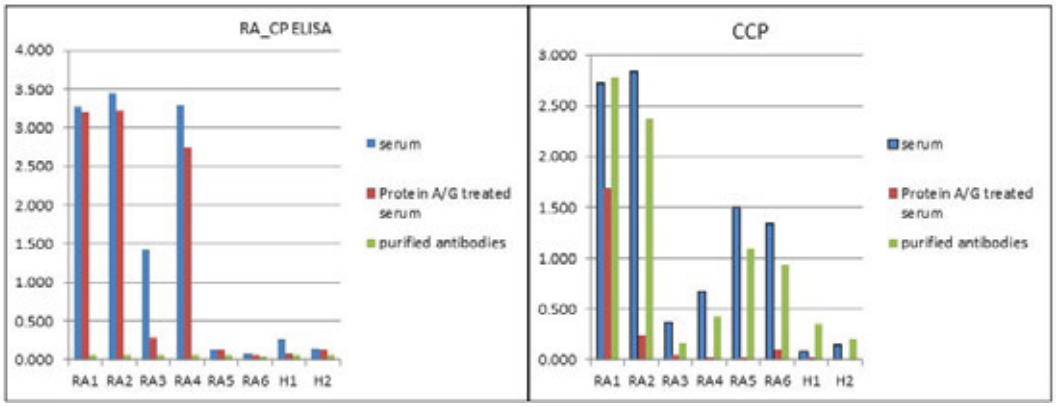
Methods: Peptides with Multiple Citruline Similar Motif (MCSM) were synthesized and used to produce anti-MCSM antibodies. Anti-MCSM antibody recognized MCSM in the citrullinated proteins such as fibrogen, vimentin and enolase which were found in the RA patients. RA_CP ELISA was developed using anti-MCSM antibodies. Clinical samples were collected under the Investigational Review Board approval protocol and RA patients met 2010 ACR classification criteria for RA. Receiver operating characteristic (ROC) curve was used for the analysis of optimal cut-off point for the evaluation of diagnostic capacity. CCP2 assay kits were purchased from European Diagnostic. Protein A/G resin was used to extract IgG/IgM from serum samples.

Fig1 : Total 136 RA patients and 214 health person's samples were used to evaluate RA-CP

RA_CP	Clinical Diagnosis		Total
	Positive (+)	Negative (-)	
Positive (+)	117	8	125
Negative (-)	19	206	225
Total	136	214	350

Positive Coincidence Rate	86.0%
Negative Coincidence Rate	96.3%
Total Coincidence Rate	92.3%

Fig 2: Protein A/G resin separate antibodies from serum of 6 RA patients and two health person's. RA_CP and CCP ELISA were used to test the serum with and without Protein A/G resin treatment. After antibodies removed, RA_CP still can detect target in the serum. RA_CP cannot react with purified Protein A/G fraction. After Protein A/G resin treatment, CCP kit cannot detect target in the serum. But CCP can recognize all purified Protein A/G fractions(antibodies)



Results: Among 25 Anti-ACPA negative RA samples, citrullinated antigens recognized by anti-MSCM antibodies were detected in 11 samples (44%). In the anti-ACPA+ samples, 95.5% samples were RA_CP positive. After antibodies in anti-ACPA+/RA_CP+ samples were depleted by Protein A/G resins, significant RA_CP signals were remained in the serum fraction and no signal was detected in the Protein A/G fraction. However, Anti-CCP signals were greatly reduced in Protein A/G treated serum and its signals were recovered in Protein A/G fraction. A total of 350 clinical samples were further analyzed by anti-ACPA and RA_CP Elisa. The sesentivity for RA_CP is 86.0% which is higher than anti-ACPA assay while maintaining the specificity at 96.3%.

Conclusion: It was well known that up to 40% RA patient samples were ACPA negative and the diagnostic sensitivity in this population needs to be improved to meet patient's clinical management. In this study, anti-MCSM antibodies were developed and detected citrullinated antigens with MCSM in the serum samples. Protein A/G experiments clearly demonstrated that MCSM antigen can be present in the free form or with antigen/antibody immune complex. It was very interesting that MCSM antigens were found in 44% of anti-ACPA- RA samples and over 95% anti-ACPA+

RA samples. Since antigen normally emerges earlier than the antibody, theoretically, RA_CP could be used in early RA diagnosis which needs further study to confirm.

Disclosure: z. ru, None; **X. Chen**, None; **X. huang**, None; **J. Lou**, None; **Y. peng**, None; **X. Yang**, None.

Abstract Number: 0489

S100A11 (calgizzarin) Is Released During Neutrophil Extracellular Traps (NETs) Formation in Rheumatoid Arthritis (RA)

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: S100A11 protein, a member of S100 family, has been associated with several autoimmune inflammatory conditions such as rheumatoid arthritis (RA). Moreover, its pro-inflammatory effect on mononuclear cells has been reported (1). Although the pathogenesis of autoimmune diseases is not fully understood, the formation of NETs seem to play a certain role. Recent data indicate that some DAMPs including S100A8/A9 are released via NETosis and can further augment inflammatory responses.

Methods: To assess the expression of S100A11 by neutrophils of RA synovial tissue (n=5), immunofluorescence staining of S100A11 and myeloperoxidase (MPO) was performed. The levels of S100A11 and MPO in RA synovial fluid (n=24) and serum (n=36) were measured by ELISAs (RayBiotech and Abcam). For in vitro experiments, NETosis was induced by adding phorbol 12-myristate 13-acetate (PMA) to the neutrophils purified from peripheral blood of RA patients (n=7). Release of NETs was visualised by immunocytochemistry (n=4-7) and the presence of S100A11 in supernatants was analysed by ELISA (RayBiotech). Neutrophils purified from healthy donors were stimulated by S100A11 and the release of cytokines TNFα, IL-6 was measured by ELISA (RayBiotech).

Results: S100A11 was expressed by synovial tissue neutrophils of the RA patients (n=5). The levels of S100A11 in the serum and in the synovial fluid of patients with RA were significantly associated with the levels of neutrophil MPO (r=0.463, p=0.005 and r=0.500, p=0.013). We demonstrated that the neutrophils treated by LPS (n=7) did not up-regulate the secretion of S100A11 compared to unstimulated controls (0.28±0.07 vs. 0.25±0.06; p=ns). However, the release of S100A11 was significantly up-regulated in PMA stimulated neutrophils undergoing NETosis compared to untreated controls (0.30±0.08 vs. 1.14±0.22; p=0.006). Moreover, our results showed that DPI treatment abolished PMA-induced S100A11 secretion. By immunofluorescence staining we demonstrated that the neutrophils activated by PMA release NETs containing S100A11 protein whereas cells stimulated by DPI+PMA were not able to form NETs. In addition, extracellular S100A11 did not modulate the secretion of pro-inflammatory cytokines TNFα and IL-6 by human neutrophils (n=5).

Conclusion: Here we show for the first time that the release of S100A11 by neutrophils could be dependent on NETosis. Moreover, extracellular S100A11 does not further augment the inflammatory response of neutrophils in RA.

Acknowledgement: Supported by MHCR 023728 and SVV – 260373

Reference

1. Andrés Cerezo et al., Arthritis Research & Therapy (2017) 19:79, https://doi.org/10.1186/s13075-017-1288-y

Disclosure: A. Navrátilová, None; **J. Baloun**, None; **H. Hulejová**, None; **K. Pavelka**, AbbVie, 8, Abbvie, 5, 8, Amgen, 5, 8, BMS, 8, Egis, 5, 8, Lilly, 5, 8, MSD, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 8; **J. Vencovský**, projeMinistry of Health, Czech Republic, project 00023728, 2; **L. Senolt**, None; **L. Andrés Cerezo**, None.

Abstract Number: 0490

Validation of Risk Scores for Predicting Progression in Individuals "At Risk of Rheumatoid Arthritis"

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Risk scores for progression have been described in 2015 in a cohort of 100 anti-cyclic citrullinated peptide (anti-CCP) positive individuals at risk of developing Inflammatory Arthritis (IA) (Rakieh, 2015). The first score, designed for primary care, was based on anti-CCP and rheumatoid factor (RF) titres, small joints tenderness and early morning stiffness (EMS). A second score developed for secondary care added power Doppler presence (PD+) and/or at least one allele positive for the shared epitope (SE+).

The objective is to validate previous data by scoring risk factors in a new cohort of 318 individuals.

Methods: Individuals at risk of developing IA selected by a positive anti-CCP test and a new musculoskeletal symptom have been followed in a single-centre prospective observational cohort since 2008. Previous risks analysis were founded on the data collected among 100 patients, a sequential 318 patients' data are analysed here with the same recruitment and follow-up pathways (Full data were available for 263 patients for secondary care).

Table 1. Patients characteristics

Score	2015	2019	p-value
N	100	318	
Percentage of progression n/N (%)	50/100 (50)	63/318 (19.8)	<0.001
Mean of follow-up before progression to IA (Months (SD))	15.35 (15.27)	13.62 (13.11)	0.511
Mean follow-up of non progressors (Months (SD))	39.74 (15.82)	21.72 (18.10)	<0.001
Overall Follow-up duration (Months (SD)	27.68 (19.36)	20.11 (17.51)	<0.001
High CCP titre (%)	83	66.2	>0.001
Women (%)	72	70.2	0.360
Smoker ever (%)	71.9	54	0.007
Age (Mean (SD))	51.2 (11.9)	50.44 (13.7)	0.299

Table 2.

A. Multivariable Cox regression analysis of time to progression to inflammatory arthritis.

Primary care model	2015 (n=98)			2019 (n=318)		
	HR	p-value	CI	HR	p-value	CI
High anti-CCP or RF titre	4.86	0.031	1.16-20.43	8.73	<0.001	2.73-27.9
EMS≥30min	1.86	0.039	1.03-3.37	2.52	0.004	1.51-4.2
Small Joints Tenderness	1.42	0.252	0.78-2.57	1.62	0.067	0.97-2.73
Secondary care model	**2015 (n=98)**			**2019 (n=263)**		
	HR	p-value	CI	HR	p-value	CI
High anti-CCP or RF titre	3.04	0.147	0.68-13.6	5.55	0.001	1.95-15.78
EMS≥30min	1.56	0.167	0.83-2.92	2.82	0.001	1.53-5.19
Small Joints Tenderness	1.54	0.178	0.82-2.88	2.01	0.033	1.06-3.8
PD signal	1.92	0.033	1.06-3.50	1.74	0.081	0.94-3.23
Shared epitope	1.57	0.272	0.70-3.49	1.12	0.739	0.57-2.20

B. Progression rates

Primary care model score	2015 (n=98) % (n/N)	2019 (n=318) % (n/N)	Risk grade
3	60 (21/35)	29.2 (26/89)	High
4	65 (13/20)	60.0 (27/45)	
Secondary care model score	**2015 (n=98) % (n/N)**	**2019 (n=263) % (n/N)**	**Risk grade**
4	74 (14/19)	39.5(14/43)	High
5	67 (4/6)	77.8 (7/9)	

Participants who had a negative anti-CCP test at first visit control and those followed for less than 6 weeks without progression were excluded.

Results: Participants from both cohorts were similar in terms of age and sex. Although the mean time to progression was comparable, there were significantly more participants with a high titre anti-CCP test in the 2015 cohort (Table 1). Cox multivariable analysis showed similar Hazard Ratios (HR) of progression for the two groups with a better predictive value of the CCP high titre in the 2019 group (Table 2.A). There was consequently a good correlation with progression rates in the highest scores (Table 2.B). The Kaplan-Meier curves in Figure 1 confirms survival rates according to level of risk in 2019. The secondary care score identified 10% more progressors at one year (HR 5.4 for High risk scores, $p< 0.001$).

Conclusion: These data from a new large cohort confirm the validity of previous Leeds Risk Scores for primary and secondary care and the fidelity of the risk factors over time to predict progression.

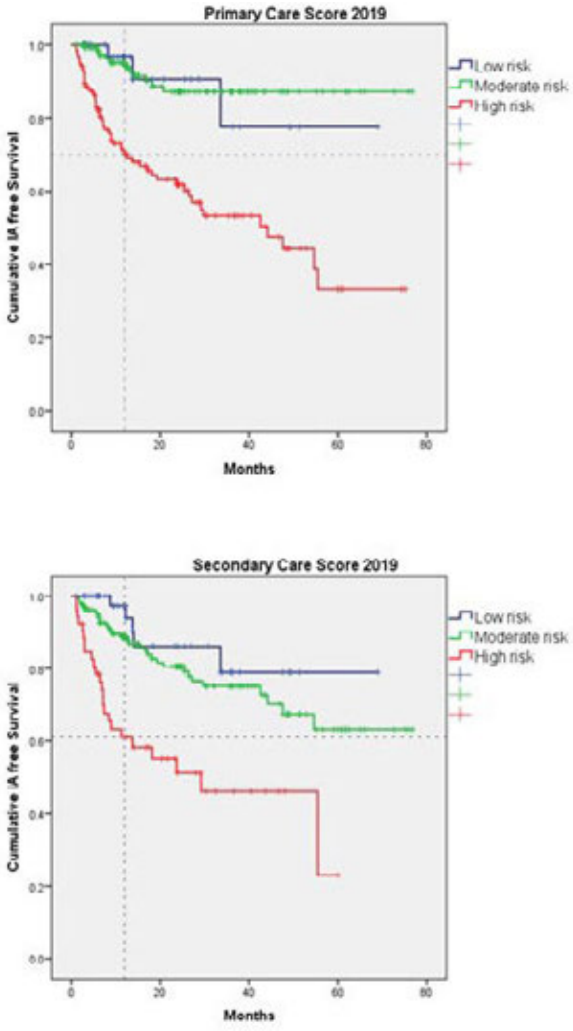

Figure 1. Probability of IA free survival over up to 75 Months of follow-up, according to categories of risk.

Disclosure: L. Duquenne, None; **J. Nam**, None; **K. Mankia**, None; **A. Di Matteo**, None; **L. Garcia-Montoya**, None; **P. Emery**, AbbVie, 2, 5, 9, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, 9, Gilead, 5, Lilly, 2, 5, 9, MSD, 2, 5, 9, Novartis, 2, 5, 9, Pfizer, 2, 5, 9, Roche, 2, 5, 9, Samsung, 2, 5, 9, Samsung Bioepis Co., Ltd., 2, Sandoz, 2, 5, 9, UCB, 2, 5, 9.

Abstract Number: 0491

Diagnostic Performance of Anti-cyclic Citrullinated Peptide (CCP) 2 and CCP3.1 Assays in Early Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

	CCP3.1	CCP2 IgG	CCP2 IgA
Cut-off (U/ml)	20	10	10
Patients positive (n)	102	96	56
Specificity % (healthy subjects)	95.9	99.0	98.0
Specificity % (disease controls)	90.8	98.9	99.4
Sensitivity %	55.4	52.2	30.4
LR+ (healthy)	13.5	52.0	15.2
LR+ (disease controls)	6.0	47.5	50.7

Table 1. Specificity, sensitivity and positive likelihood ratio (LR+) of CCP2 (IgG, IgA) and CCP3.1 assays

Background/Purpose: Anti-cyclic citrullinated peptide (CCP) antibodies are the most specific markers for rheumatoid arthritis (RA). Different generations of assays (CCP1-CCP3) have been developed which show variability regarding their performance. This may have considerable impact on diagnostic decision making because serological testing is an important diagnostic tool especially in the early stages of disease. Therefore the comparability of different assays is an important issue to address.

Methods: This study aimed to investigate the diagnostic performance of IgG and IgA anti-CCP2 detected by EliA™ (Thermo Fisher Scientific) compared to the combined IgG/IgA Quanta Lite® anti-CCP3.1 assay (Inova Diagnostics) in sera of 184 early RA patients, 98 healthy subjects and 360 disease controls.

Results: Anti-CCP2 IgG and IgA assays were found having very high specificities versus healthy subjects (98.9%; 98%) as well as disease controls (98.8%; 99.4%). Sensitivities were 52.2% for anti-CCP2-IgG and 30.4% for anti-CCP2 IgA, respectively. This resulted in high positive likelihood ratios (LR+) of 47.5 for the IgG and 50.7 for the IgA assay. However, anti-CCP2 IgA antibodies did not show an added diagnostic value since all positive patients were also anti-CCP IgG positive. The anti-CCP3.1 assay was found to be slightly more sensitive than the anti-CCP2 IgG assay with 55.4% of early RA patients being positive. However, specificity was markedly lower and amounted to 95.9% versus healthy subjects and 90.8% versus disease controls which resulted in a relatively low LR+ of only 6.0. The data are summarized in Table 1. When adjusting the cut-off value of the CCP3.1 assay to >98% specificity against disease controls, sensitivity (52.7%) became comparable to the anti-CCP2 assay and LR+ increased to 26.4 which was still somewhat lower than the LR+ of the CCP2 assays.

Conclusion: Thus, when interpreting the results of diagnostic assays the issue of test to test variability must be taken into account as reduced specificity might lead to an increase in false positive diagnosis.

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Abstract Number: 0492

'It Felt Like I Was Walking on Rocks" Patients Share First Symptoms of RA

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SESSION INFORMATION
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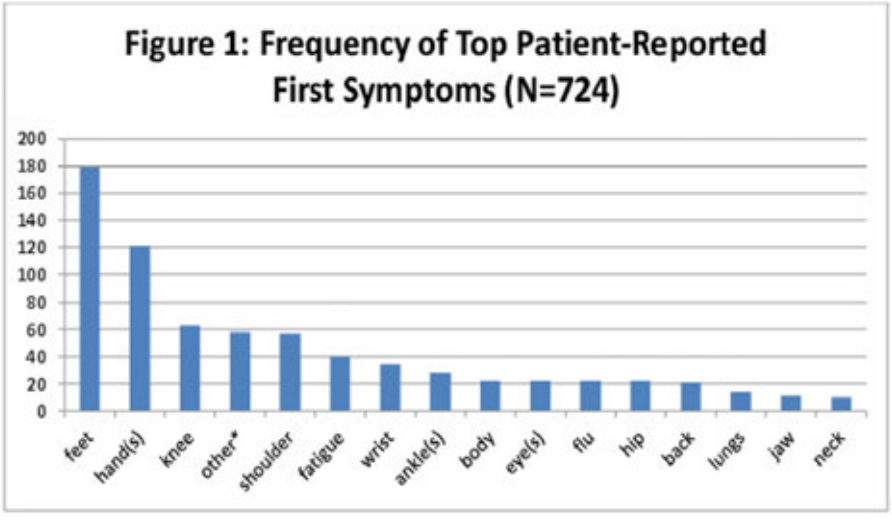
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Although early diagnosis and treatment are pivotal for successful outcomes in rheumatoid arthritis (RA), a gap remains in our understanding of its earliest symptoms. Current diagnosis requires physician evaluation for joint involvement, serology, inflammatory markers and symptom duration to allow accumulation of at least 6 points by the 2010 ACR/EULAR criteria. Patients may experience symptoms not accounted for in the criteria, a discrepancy which could impede early identification of RA. Data on patient perceptions of early RA symptoms and first body parts affected could provide important information to help facilitate the earliest recognition of disease and enable earlier treatment. To examine first symptoms, a non-profit organization collaborated with an academic rheumatology center to describe early RA symptoms as reported by patients in their own words.

Methods: From 2009-2017, people with RA who visited an RA-specific blog site or Facebook page were asked to describe their first RA symptom. Responses were extracted and de-identified. Data collected included: date of response, text of response, and source. Responses from moderators and those who said they did not have RA, or who shared unrelated information were not included in the analysis; responses from the same person were combined. Content analysis was performed to identify themes of response and to tabulate: 1) very first symptom reported; 2) number of symptoms reported per respondent (1-4+), 3) data source (RA patient or other), and 4) length or ease of diagnosis experience.

Results: 724 unique responses (99% RA patients self-reporting), 564 (77%) from the blog and 160 (23%) from Facebook were reviewed. People with RA reported 37 different first symptoms, with 83.3% reporting a symptom outside of the hand(s), with feet (24.7%), hands (16.7%), knees (8.7%), fatigue (7.9%) and wrists (4.7%) being most common. When categorizing first reported symptom, we found the top four were: 1) small joints (51.4%), 2) large joints (16.7%), 3) general (e.g. fatigue, pain) (8.7%), and 4) extra articular (e.g. pleurisy, iritis) (7.9%) Overall, we found that among those describing the number and pattern of first symptoms (from 1-4+), the majority reported more than four (50.6%). For example, one respondent wrote: “My eyes were my first symptom, followed by my feet, spine then ankles…my GP [general practitioner] continually said ‘no not RA’, that affects the hands first.” Themes included in responses



*the other category represents a variety of first symptoms reported at a frequency ≤8.

Table 1: Quotes Illustrating Themes Related to Patient-Reported First RA Symptoms

Category	Representative Quote
Traditional Onset	My early symptoms were my feet and hands together. My feet hurt so bad I would dread getting up and having to walk on them while my hands were so stiff and swollen, I could not close my hand to make a fist. Hands. Knuckles and 4 fingers on dominant right hand. Fatigue. Swelling, lack of mobility and function. Fatigue. Yes, I put it twice because I was exhausted. 7 years later still right hand, plus neck, knees, right ankle and general malaise.
Non-Traditional Onset	My first symptoms were iritis (imflammation) in eyes, then ankle problems (torn achilles tendons resulting in surgery on both sides). Not until extreme fatigue hit me last year coupled with finger swelling and pain did I get diagnosed with RA and start on treatment. While my symptoms did eventually spread to all fingers, wrists, elbows, and knees (my latest big battle), it all started with "non typical" RA symptoms that didn't meet the traditional RA patterns. My RA started in my feet 7 years ago. I spent the first 4 thinking I had "hurt" my foot while walking in a Christmas parade. Now, it's in my hands. Even after diagnosis, I still doubted the doctor because I had never heard of anyone getting RA in their feet first. I thought it had to be in your hands or it wasn't RA.
Difficult Diagnosis over long period of time	Left ankle first. Swollen all to heck – looked exactly like I'd sprained my ankle. Except I hadn't. Then left wrist and right knee. Took about a year to settle into a nice, easily diagnosed, bilateral wrists and MCP joints pattern. I wasn't diagnosed until my hands and fingers started acting up. However I can go back 15 years and it was my feet that hurt for years first. My neck and back too. I always blamed it on something else. When I was diagnosed they said I already had holes in my bones in my toes, ankles, fingers and writs.
Straightforward diagnosis over short period of time	All of this summer i had aches and pains in my feet knees back and hips then my elbow and one of my fingers and i was also very tired and would sleep all afternoon at least 2 hours. I went to my dr and he gave me some blood work to do and he sent me to a reumy. I was diagnosed with RA. Mine was very typical. My pinky finger hurt one day. By the end of the week, all my fingers felt tight and strange. Very tight in the morning, and comfortable by 10am. One google search and I knew what it was. My primary care listened to me and confirmed the dx the next month with labs. I was lucky.

were: 1) first symptom(s) and co-morbidities; 2) timing of symptoms to diagnosis/treatment, including pattern of onset and barriers; 3) life events surrounding symptoms (e.g. illness, accident); 4) patient/physician experience, among others.

Conclusion: Results show people with RA report a wide variety of first symptoms that do not always include hands or joints with varying patterns of onset over time. Such findings could provide valuable information to help patients and physicians decrease the time between diagnosis and treatment by considering the possibility of more non-traditional RA presentations.

Disclosure: P. Sinicrope, None; **D. Symons**, None; **A. P. Tafti**, None; **C. Patten**, None; **M. Bock**, None; **J. Tilburt**, None; **C. Crowson**, None; **E. Myasoedova**, Pfizer, 2; **J. Davis**, None; **K. O'Neill**, None.

Abstract Number: 0493

Diversity Analysis of Intestinal Flora in Patients with Rheumatoid Arthritis

Xu-fang Yin,[1] **Sheng-xiao Zhang** ,[1] Ming-xing Zhang,[2] Min-jing Chang,[1] Xiao-juan Mao,[2] Jia Wang,[2] Jia-qian Zhang,[2] Meng-ting Qiu,[2] Chong Gao,[3] and Xiao-feng Li[2], [1]The Second Hospital of Shanxi Medical University, Taiyuan, Shanxi, China (People's Republic), [2]The Second Hospital of Shanxi Medical University, Taiyuan, China (People's Republic), [3]Brigham and Women's Hospital, Harvard Medical School, Boston

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

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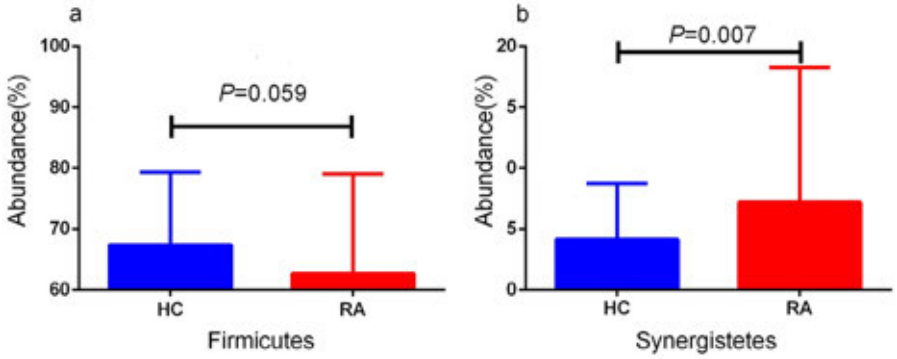

Figure 1. The phylum-level profile for RA patients and healthy control.

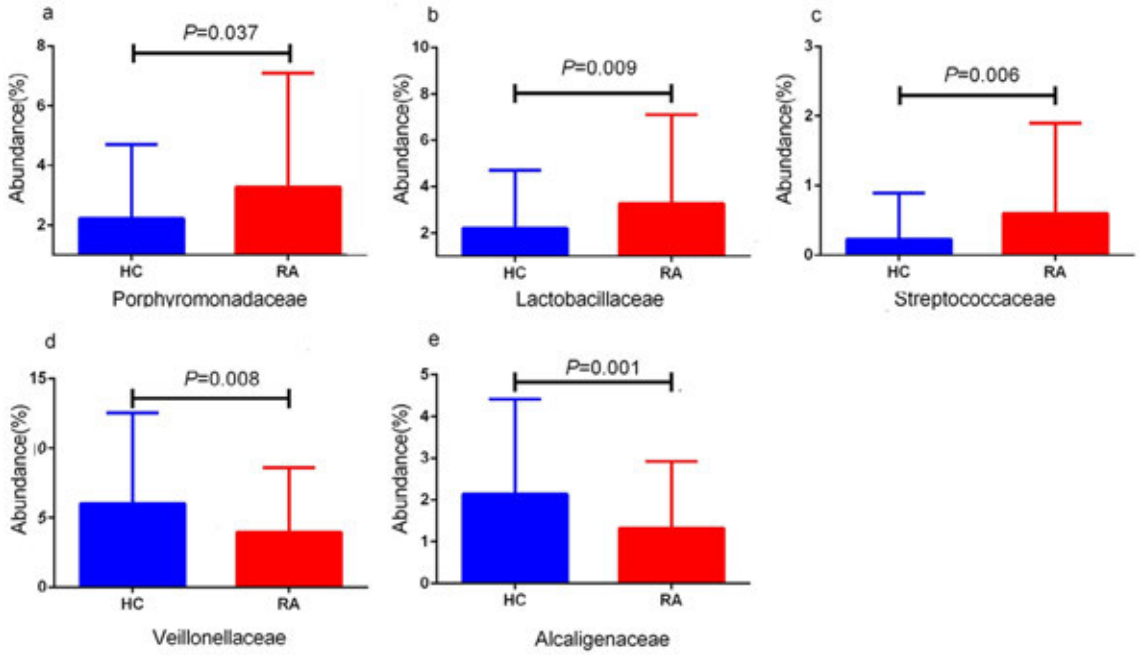

Figure 2. The family-level profile for RA patients and healthy control.

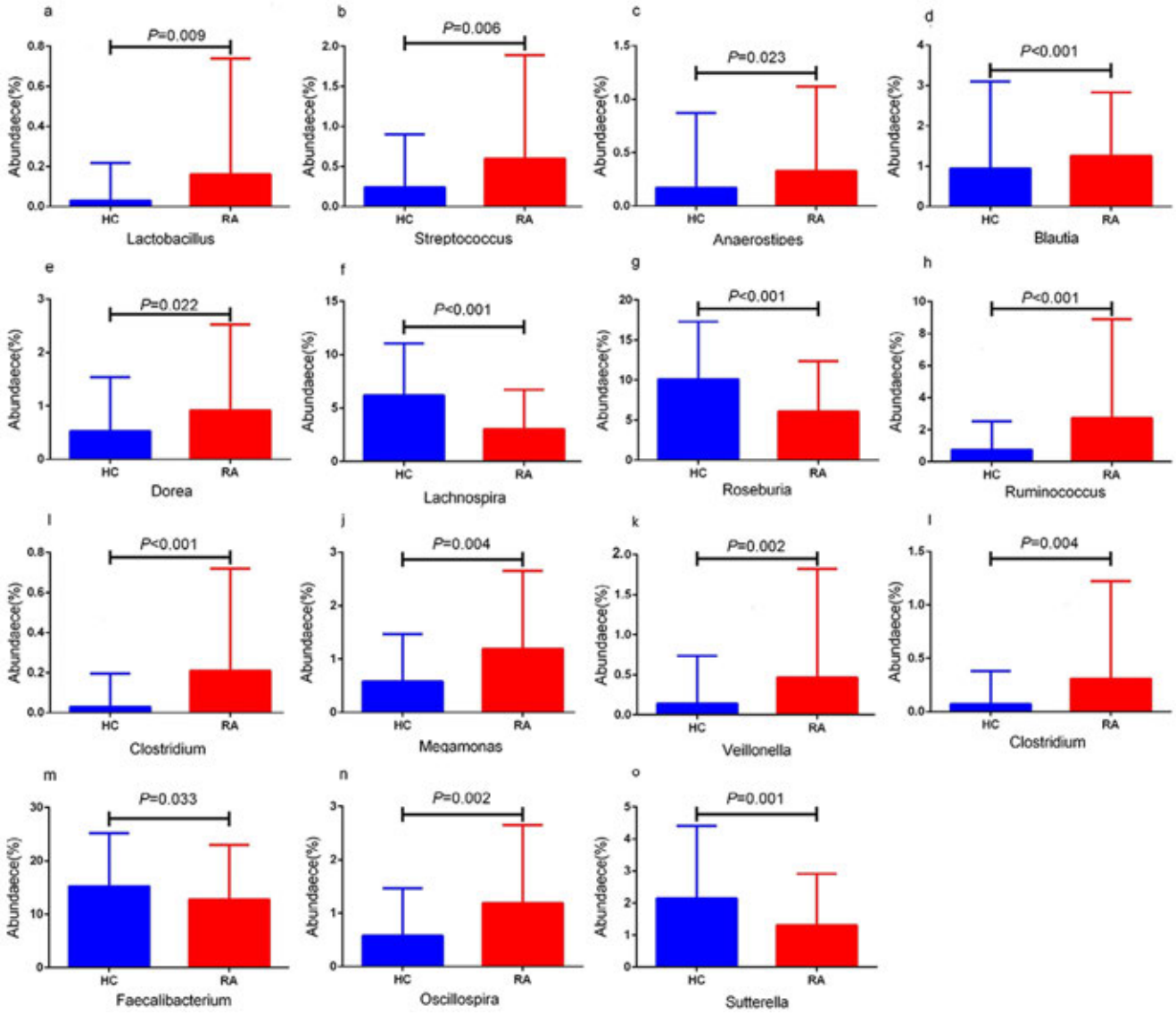

Figure 3. The genus-level profile for RA patients and healthy control.

Background/Purpose: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammation of the synovial joints. The gut microbe with RA has been reported recently, though the specific components of the microbiota that affect the host response leading to disease remain unknown. This study aimed to study the diversity and the abundance of intestinal microbes in patients with RA and further provide new strategy and target for the treatment of RA.

Methods: The stool specimens of 100 RA patients were analyzed at the level of the phylum, family and genus, and compared with that of 125 healthy controls(HC).

Results: Compared with controls,the abundance of intestinal microbiota in patients with RA was significantly different (P< 0.05).At the level of Phylum,the abundance of Proteobacteria was significantly increased (P< 0.05),and the abundance of Firmicutes was significantly reduced (P=0.05),the abundance of Actinomycetes and Bacteroidetes increased in RA patients compared with that of HC(P >0.05).Compared with healthy individules,Patients had more abundance of Micrococcaceae, Porphyromonadaceae, Enterococcaceae, Lactobacillus, Streptococcus, Turicibacteraceae, Hyphomicrobiaceae and Enterobacteriaceae(P< 0.05), but less abundance of Veillonellaceae and Alcaligenes was significantly lower (P< 0.05)

at the level of family. At the genus level, in the RA group, the abundance of Rothia, Enterococcus, Lactobacillus, Streptococcus, Turicibacter, Anaerostipes, Blautia, Lauterium, Dorea, Ruminococcus, Clostridium, Veillonella, Oscillospira, Devosia and Halomonas were significantly increased (P< 0.05), but the abundance of Lachnospira, Roseburia, Faecalibacteriu, Megamonas and Sutterella was significantly lower than that of healthy controls. (P< 0.05).

Conclusion: The diversity and balance of bacterial community in intestinal microecological environment of patients with RA are significantly different from the healthy control. Intestinal microbiota disorder may be related to the pathogenesis of RA, which might provide theoretical foundation for the regulation of intestinal flora for disease intervention.

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Abstract Number: 0494

Clinical and Biomarker Factor Associations with Symptoms and Future Development of RA: TIP-RA Collective

Kevin Deane ,[1] Sunil Nagpal,[2] V. Michael Holers,[3] Gary Firestein,[4] David Boyle,[5] Jennifer Seifert,[3] Jane Buckner,[6] Eddie James,[6] Laurakay Moss,[7] Saman Barzideh,[7] Sylvia Posso,[6] William Robinson,[8] Kristen Polinski,[7] Roger Gilmore,[7] Frédéric Baribaud,[9] Navin Rao,[2] and George Vratsanos[10], [1]University of Colorado Denver, Division of Rheumatology, Aurora, CO, USA, Aurora, CO, [2]Janssen R&D, Spring House, PA, [3]University of Colorado Denver, Division of Rheumatology, Aurora, CO, USA, Denver, [4]University of California, San Diego, San Diego, [5]University of California, San Diego, San Diego, CA, [6]Benaroya Research Institute, Seattle, WA, [7]University of Colorado Denver, Aurora, CO, [8]Stanford University, Palo Alto, CA, [9]Janssen Research & Development, LLC, Spring House, PA, [10]JNJ, Raritan, NJ

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
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Background/Purpose: The Targeting Immune Responses for Prevention of RA (TIP-RA) Collaborative prospectively studies individuals at high risk for developing RA because of serum ACPA positivity in absence of inflammatory arthritis (IA) at baseline. The objectives of the analyses presented herein are to evaluate ACPA+ ACPA- individuals to identify factors associated with each of these states, and to identify factors associated with incident inflammatory arthritis and classifiable RA.

Methods: 87 ACPA+ subjects were identified who at their baseline study visit did not have historical or examination (66/68 count) evidence of IA, and 160 ACPA- matched controls. ACPA+ was defined as a serum elevation of anti-CCP3 (IgG, Inova) on ≥2 occasions above the manufacturer's suggested cut-off (≥20 units). Subjects were recruited through screening of health-fair particiants, first-degree relatives of patients with RA and individuals referred to rheumatology clinics. Subjects were followed annually or sooner if they had changes in joint symptoms. Clinical and biomarker factors, including RF IgA and M (Inova) and C-reactive protein (CRP), were assessed. Comparisons between ACPA+/- subjects were performed, and factors associated with incident IA/RA within the ACPA+ subjects were evaluated.

Results: The baseline characteristics of ACPA+/- subjects are presented in Table 1. Self-reported fatigue was higher in ACPA+ vs ACPA- subjects. In addition, within ACPA+ subjects, current smoking was associated with increased morning stiffness, and higher CRP was associated with increased fatigue. Within ACPA+ subjects, 15 (17%) developed IA/RA a median of 330 days after baseline. At baseline, higher BMI, greater number of self-reported swollen

Table 1. Baseline characteristics of ACPA+/- subjects			
Characteristics	**ACPA-**	**ACPA+**	**p-value**
N	160	87	-
Age, median (IQR 25-75)	61 (52-66)	60 (51-68)	0.96
% Female	66	67	0.60
% Non-Hispanic White	82	85	0.36
% Ever smoker	35	32	0.88
BMI kg/m^2, median (IQR 25-75)	26 (23-30)	27 (25-31)	0.07
% Shared epitope positive	49	52	0.30
% Self-reported first-degree relative with RA	27	21	0.35
% with swollen joints on exam consistent with synovitis	0	0	1.00
Number of tender joints on examination, median (IQR 25-75)	1 (0-0)	0 (0-0)	0.74
Number of self-reported painful joints, median (IQR 25-75)	0 (0-0)	1 (1-2)	0.27
Minutes of morning stiffness, median (IQR 25-75)	0 (0-5)	1 (1-10)	0.17
Self-reported level of pain, median (IQR 25-75) VAS 0-10	0 (0-2)	1 (1-2)	0.19
Self-reported level of fatigue, median (IQR 25-75) VAS 0-10	**0 (0-2)**	**1 (1-3)**	**<0.05**
Self-reported overall well-being, median (IQR 25-75) VAS 0-10	0 (0-2)	1 (1-2)	0.15
Abbreviations: BMI=body mass index; VAS=visual acuity scale; SD=standard deviation; IQR=inter-quartile range			

joints, the presence of the shared epitope (SE) and positivity for RFIgA and M were each associated with increased risk for developing incident IA/RA (Table 2).

Conclusion: Within this cohort, a greater level of fatigue is associated with ACPA positivity. Furthermore, within ACPA+ subjects, smoking and elevated hsCRP are associated with clinical symptoms of stiffness and fatigue, respectively. These symptoms may be part of a prodrome for future RA, but also may indicate a unique 'autoimmunopathy' that warrants further investigation into pathogenesis and treatment. These findings also suggest a role for smoking and increased joint-related symptoms. The association of high BMI with incident IA/RA has been identified prior (de Hair 2013) and the replication of that herein may identify this as a potentially modifiable risk factor for future RA. Furthermore, the risk of incident IA/RA with a higher number of self-reported swollen joints at baseline suggests that individuals may sense joint abnormalities prior to detection of swelling on physical examination. The risk of incident RA with RFIgA and M positivity also highlights the importance of a combination of ACPA and RF in the pathogenesis of joint disease, and the potential role of the SE in transition from ACPA positivity to arthritis is also intriguing. This study will continue with further evaluation of factors that may be predictive of or causally linked to the future onset of RA.

Disclosure: K. Deane, Bristol-Myers Squibb, 5, Inova, 9, Janssen, 2, 5, Janssen R&D, 2, Microdrop, 5, Pfizer, 2; **S. Nagpal**, Janssen Research & Development, 3, Janssen Research, Johnson&Johnson, 1, 3, 4, Johnson & Johnson, 1, 4; **V. Holers**, AdMIRx, 1, 2, 4, 5, 6, Alexion, 7, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 5, Janssen R&D, 2, 5, Pfizer, 2; **G. Firestein**, Abbvie, 2, Janssen, 2; **D. Boyle**, Janssen, 2; **J. Seifert**, Janssen, 2; **J. Buckner**, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Janssen, 2, Novo Nordisk, 2, Pfizer, 2; **E. James**, Janssen, 2; **L. Moss**, Janssen, 2; **S. Barzideh**, Janssen, 2; **S. Posso**, Janssen, 2; **W. Robinson**, Janssen, 2; **K. Polinski**, Pfizer, 2; **R. Gilmore**, Janssen, 2;

Table 2. Baseline characteristics of 15 ACPA+ individuals who developed incident IA/RA compared to 72 ACPA+ who did not			
Characteristics	**Did not develop IA/RA**	**Developed IA/RA**	**p-value**
N	72	15	
Median time to RA, or median time of total follow-up (in days)	360	330	-
% Meeting 2010 criteria at time of onset of synovitis	-	80	-
Age, median (IQR 25-75)	62 (47-68)	56 (52-66)	0.67
% Female	67	67	1.00
% Non-Hispanic White	67	83	0.57
% Ever smoker	33	36	1.00
% Current smoker	7	7	1.00
BMI kg/m^2 median (IQR 25-27)	**27 (24-30)**	**31 (26-35)**	**0.03**
% Shared epitope positive	**49**	**67**	**0.05**
% Self-reported first-degree relative with RA	20	21	1.00
Self-reported number of swollen joints, median (IQR 25-75)	**0 (0-0)**	**0 (0-1)**	**<0.01**
Self-reported number of painful joints, median (IQR 25-75)	1 (1-2)	2 (2-8)	0.13
Self-reported level of pain median (IQR 25-75) VAS 0-10	1 (1-2)	3 (3-3)	0.11
Self-reported level of fatigue median (IQR 25-75) VAS 0-10	1 (1-3)	1 (1-4)	0.46
Self-reported overall well-being median (IQR 25-75) VAS 0-10	1 (1-2)	2 (2-2)	0.11
Minutes of morning stiffness, median (IQR 25-75)	**0 (0-5)**	**2 (2-60)**	**0.04**
Number of tender joints on examination, median (IQR 25-75)	0 (0-0)	0 (0-1)	0.34
CCP3 level, median (IQR 25-75)	41 (29-79)	61 (34-262)	0.23
%RFIgA positivity	**40**	**11**	**0.01**
%RFIgM positivity	**60**	**29**	**0.01**
CRP level, median (IQR 25-75)	1.54 (0.83-3.93)	2.05 (0.80-4.13)	0.54
Abbreviations: BMI=body mass index; VAS=visual acuity scale; SD=standard deviation; RF=rheumatoid factor; Ig=immunolglobulin; CRP=C reactive protein			

F. Baribaud, Janssen Research & Development, LLC, 3; **N. Rao**, Janssen Research & Development, 3, Johnson & Johnson, 1, 3, 4; **G. Vratsanos**, Janssen Research & Development, 1, 3.

Abstract Number: 0495

Pre-Rheumatoid Arthritis Diagnosis Prevalence of Commercial CCP Antibody Positivity Increases over Time with Strong Agreement Between Commercial Assays and Positivity Is Predicative of Developing Rheumatoid Arthritis Within 3 Years

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) related autoantibodies, in particular antibodies to citrullinated proteins (ACPA), predict likelihood of developing future RA. Indeed, clinical trials for RA prevention are underway using ACPA positivity as an inclusion factor. However, there are multiple commercial ACPA assays including several versions of cyclic citrullinated protein (CCP) assays that may differ in diagnostic accuracy for future RA. For this project, we propose to use a novel sample set to evaluate the diagnostic accuracy in preclinical RA of 3 commercial CCP assays that are widely used in the USA.

Methods: Cases who developed classifiable RA (n=196) during military service were identified and up to 3 pre-RA diagnosis and 1 post-RA diagnosis stored serum samples were selected from the Department of Defense Serum Repository along with serum from 208 matched controls. For the analyses herein, the pre-RA diagnosis Case samples were assigned as >3 or < =3 years from diagnosis, with each subject contributing only 1 sample per interval. Case and Control samples were tested using 3 commercially available CCP assays: CCP2 (ELISA IgG, Axis-Shield), CCP3

Table 1. Prevalence of positivity of each CCP assay pre- and post-RA diagnosis and using manufacturer recommended cut-offs for positivity

	Prevalence of positivity >3 years pre-RA diagnosis	Prevalence of positivity <=3 years pre-RA diagnosis	Prevalence of positivity Post-RA diagnosis
N samples/subjects per interval*	196	196	196
Mean (SD) of time of sample from diagnosis within each interval, in years	-12.1 (4.9)	-1.5 (0.6)	+1.2 (0.9)
CCP2	16.3%	64.8%	72.8%
CCP3	20.9%	71.4%	76.5%
CCP3.1	16.8%	67.3%	77.4%
p-value**	0.43	0.36	0.53
Kappa***	0.82-0.87	0.81-0.86	0.85-0.90

*For these analyses, in each interval, only one sample per subject was included. The sample selected was the one closest in time of collection to the middle of the interval.
**p-value comparing positive rates across all 3 CCP assays for each interval
***Kappa values are the range of findings from pairwise comparisons of each CCP assay

Table 2. Likelihood of positivity of each CCP assay at different cut-offs for interval <=3 years prior to RA diagnosis	
	Odds ratio for positivity <=3 years compared to >3 years
Standard cut-off	
CCP2	OR 9.4 (5.8,15.2), p=<0.01
CCP3	OR 9.45 (5.9,15.0), p=<0.01
CCP3.1	OR 10.2 (6.3,16.4), p=<0.01
>=2x standard cut-off	
CCP2	OR 9.1 (5.6,14.8), p=<0.01
CCP3	OR 11.2 (6.9,18.3), p=<0.01
CCP3.1	OR 10.3 (6.3,17.0), p=<0.01
>=3x standard cut-off	
CCP2	OR 8.7 (5.3,14.2), p=<0.01
CCP3	OR 10.6 (6.4,17.3), p=<0.01
CCP3.1	OR 9.7 (5.9,16.0), p=<0.01

(ELISA IgG, Inova) and CCP3.1 (ELISA IgG/A, Inova) with positivity based on the manufacturer recommendations, and specificity determined in a single sample from Controls. The prevalence of CCP positivity in each interval was evaluated using three-way chi-square and kappa analyses. The relationship of positivity for a given test >3 and < =3 years of RA diagnosis was evaluated using a 2x2 table and Mantel-Haenszel odds ratio estimate.

Results: CCP2, CCP3 and CCP3.1 were positive in 72.8 to 77.4% of RA cases post-diagnosis (Table 1). The specificity, using Controls, of CCP2, CCP3 and CCP3.1 was 99.0, 98.6 and 96.6%, respectively; in addition, the specificity for all tests at >=2x the manufacturer recommended cut-off was 99%. In samples >3 years prior to diagnosis, the CCP assays were positive in 16.3 to 20.9% of Cases (Table 1). While CCP3 was positive in this interval in ~5% more subjects than CCP2 and ~4% than CCP3.1, these differences were not statistically significant. In samples < =3 years prior to diagnosis, the CCP assays were positive in 64.8 to 71.4% of Cases. While CCP3 was positive in this interval in ~7% more subjects than CCP2 and ~4% more subjects than CCP3.1, these differences were not statistically significant. For each CCP assay, cases were more likely to be positive < =3 years pre-RA diagnosis compared to >3 years (Table 2).

Conclusion: These results can help inform interpretation of CCP tests in individuals who may be positive in the absence of RA, as well as the choice of assay in clinical trials of RA prevention where the assay or cut-off level (e.g. >=2x) may impact diagnostic accuracy. Furthermore, the finding that positivity for these CCP assays was more likely to occur < =3 years prior to RA diagnosis is useful for informing CCP positive individuals about the potential timeline of development of RA, and in the development of clinical trials where this timeframe can inform trial design. Replication of these findings in additional cohorts is warranted, as well as comparison with additional ACPA assays that are in common use.

The identification of specific products or scientific instrumentation is considered an integral part of the scientific endeavor and does not constitute endorsement or implied endorsement on the part of the author, DoD, or any com-

ponent agency. The views expressed in this abstract are those of the author and do not reflect the official policy of the Department of Army/Navy/Air Force, Department of Defense, or U.S. Government.

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Abstract Number: 0496

Assessment of Anti-Cyclic Citrullinated Protein and Connective Tissue Disease Screening Questionnaire in Healthy Adults from the Oklahoma Immune Cohort

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SESSION INFORMATION
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Background/Purpose: Anti-CCP antibodies are present in the serum of healthy individuals who are at risk of developing RA and serve as an important tool for diagnosing an individual with RA and providing prognostic information. The Connective Tissue Disease Screening Questionnaire (CSQ) is an assessment designed to help identify individuals who may be at risk for CTDs including RA, SLE, and SS. We hypothesize that healthy individuals with elevated levels of anti-CCP antibodies will have higher CSQ scores.

Methods: Demographic information (race, gender, and age) and CSQ scores were obtained from the datasets of 954 individuals who consented to be part of the Oklahoma Immune Cohort (OIC). These individuals were not diagnosed with RA or another autoimmune rheumatic disease. Anti-CCP3 levels were determined by ELISA. Individuals were identified as: < 20 EU/mL = negative, 20-39 EU/mL = weakly positive, 40-59 EU/mL= moderately positive, and ≥60EU/mL as strongly positive for anti-CCP3 antibodies. Associations between CSQ scores and age were determined by Kruskal-Wallis analysis and associations between CSQ scores, race, and gender were determined by Chi-square analysis. Logistical regression was used to determine the relationship between CSQ scores and anti-CCP3 levels while controlling for age, gender, and race.

Results: CSQ scores and anti-CCP3 levels were both found to be significantly different based upon age or race (Table 1). Healthy Native Americans were more likely to have elevated CSQ scores (OR=1.68) than healthy African Americans (OR=0.86) or heathy European Americans. African-American healthy individuals had the lower rate of anti-CCP3 responses. Logistic regression analysis, controlling for race, age and gender, showed that there were no significant associations between CSQ and anti-CCP3 levels (Table 2).

Conclusion: In this cohort of healthy adults, anti-CCP3 levels did not associate with variations in the CSQ score. However, anti-CCP3 levels and CSQ scores both varied with age and race, suggesting that these demographic factors may be relevant when screening for risk of developing rheumatic disease.

Table 1: Demographics and Screening Results, Stratified by CSQ Score and CCP3 Interpretation

Factors	Total (N=954)	CSQ Score			CCP3		
	N (%)	0 (N=715) N (%)	1,2,3, and 4 (N=236) N (%)	p-value	Negative (N=907) N %	Positive (N=47) N %	p-value
Age, years	18-86			**<0.0001**[a]			**0.018**[a]
Mean ± SD	38.4±13.8	36.2±13.1	45.0±13.9		38.0±13.5	45.8±16.5	
Gender				0.068[b]			0.527[b]
Female	649 (68.03)	475 (73.19)	174 (26.81)		619 (95.38)	30 (4.62)	
Male	305 (31.97)	240 (78.69)	65 (21.31)		288 (94.43)	17 (5.57)	
Race				**0.025**[b]			**0.032**[b]
European American	534 (55.97)	409 (76.59)	125 (23.41)		500 (93.63)	34 (6.37)	
African American	131 (13.73)	104 (79.39)	27 (20.61)		130 (99.24)	1 (0.76)	
Native American	171 (17.93)	113 (66.08)	58 (33.92)		162 (94.74)	9 (5.56)	
Others	118 (12.37)	89 (75.42)	29 (24.58)		115 (97.46)	3 (2.54)	
CSQ scores							0.655[c]
0	715 (74.95)				682 (95.38)	33 (4.62)	
1	135 (14.15)				127 (94.07)	8 (5.93)	
2	62 (6.50)				57 (91.94)	5 (8.06)	
3	32 (3.35)				31 (96.88)	1 (3.12)	
4	10 (1.05)				10 (100.00)	0 (0.00)	
CCP3				0.543[c]			
Negative	907 (95.07)	682 (75.19)	225 (24.81)				
Weak positive	33 (3.46)	23 (69.70)	10 (30.30)				
Moderate positive	7 (0.74)	4 (57.14)	3 (42.86)				
Strong positive	7 (0.73)	6 (85.71)	1 (14.29)				

[a] From Kruskal-Wallis test results
[b] From Chi-Square test results
[c] From Fisher exact test results

Table 2: Logistic Regression of Demographics, Stratified by CSQ Score and CCP3 Interpretation

Factors	CCP3						CSQ Score					
	Univariate logistic regression			Multivariate logistic regression			Univariate logistic regression			Multivariate logistic regression		
	OR	95%CI	p-value	OR	95%CI	p-value	OR	95%CI	p-value	OR	95%CI	p-value
Age	1.04	(1.02-1.06)	**<0.0001**	1.03	(1.01-1.06)	**0.002**	1.05	(1.04-1.06)	**<0.0001**	1.05	(1.03-1.06)	**<0.0001**
Race												
European American	1			1			1			1		
African American	0.11	(0.01-0.78)	**0.028**	0.13	(0.02-0.98)	**0.047**	0.86	(0.54-1.35)	0.499	1.14	(0.71-1.64)	0.597
Native American	0.82	(0.39-1.74)	0.600	0.77	(0.36-1.64)	0.493	1.68	(1.07-2.34)	**0.007**	1.58	(1.07-2.34)	**0.022**
Others	0.42	(0.15-1.64)	0.152	0.49	(0.15-1.64)	0.247	1.08	(0.67-1.74)	0.760	1.38	(0.83-2.27)	0.214
CSQ												
0	1			1								
1-4	1.29	(0.68-2.45)	0.443	0.95	(0.48-1.86)	0.877						
CCP3												
Negative							1			1		
Positive							0.92	(0.46-1.83)	0.810	0.92	(0.46-1.83)	0.810

Disclosure: M. Muse, None; **L. Tran**, None; **C. Guthridge**, None; **N. Redinger**, None; **J. James**, Abbvie, 5, Janssen, 5, Progentec, 2, Progentec Diagnostics, Inc., 2, Xencor, 2, Xencor, Inc., 2.

Abstract Number: 0497

Women with Rheumatoid Arthritis Have Higher Lifetime Occupational and Non-occupational Exposure to Silica Dust Compared to French General Population

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Occupational exposure to silica dust is a well-known risk factor for ACPA positive rheumatoid arthritis (RA). The role of non-occupational exposure has not been explored so far, as there are no available tools to measure it in clinical practice.

The Dust Exposure Life-Course Questionnaire (DELCQ), developed within a European Research Council Advanced Grant, provides clinical research with a tool derived from social sciences. The DELCQ, longitudinally quantifies both occupational and non-occupational (e.g. body care; hobbies such as DIY, stone cutting etc.) exposure to silica during lifetime.

In the DELCQ, the sources of silica exposure are grounded on an extensive list of products and activities summed up by the International Agency on Research on Cancer (IARC) and on a wide overview of the literature that in medicine, epidemiology and industrial hygiene has been addressing silica exposure and silica-related diseases.

The aim of this study was to use this novel tool to explore occupational and non-occupational silica exposure in a series of consecutive RA patients and to explore the association of quantified silica dust exposure with major disease features (ACPA positivity) or outcomes (erosive disease).

Methods: We administered the DELCQ to 97 consecutive RA patients (77F, 20M, mean age 59.1+/- 13.3 yrs.,75 ACPA positives, 66 with erosive disease) attending the department of rheumatology of the Avicenne teaching Hospital (Bobigny, FRANCE). Patient scores were compared to those of 261 controls, matched for sex, age and smoking status, from a 2739 -subject national cohort (ELIPSSilice), representative of the French general population. Within RA subjects, the association of the scores with ACPA positivity and with erosive disease was assessed after adjustment for tobacco use.

Results: RA patients had higher scores of occupational (10 [0, 17] vs. 0 [0, 4]) silica exposure vs. controls ($p< 0.0001$) (fig 1). In both men and women with RA, occupational exposure was higher compared to sex-matched controls (23.5

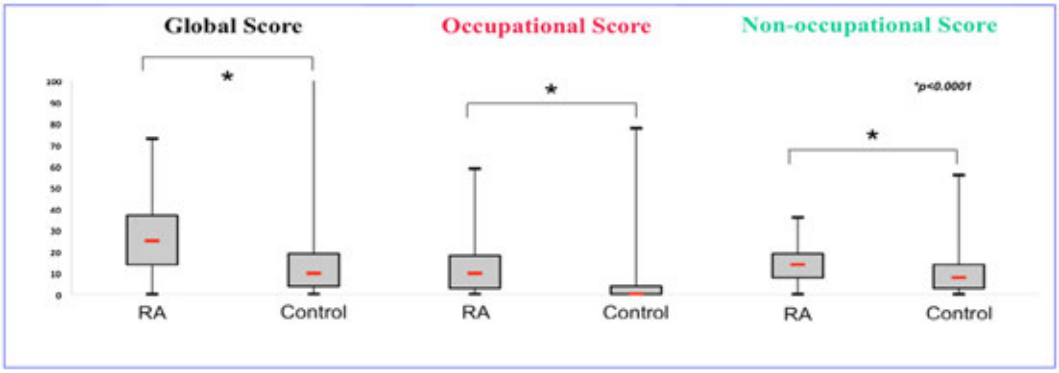

Figure 1. Comparison RA patients vs. Controls of global, occupational and non-occupational silica exposure scores.

[18, 34.5] vs. 2.5 [0, 12] for men and 7 [3, 14] vs. 0 [0, 5] for women p< 0.0001 for both). Non-occupational exposure was higher only in women with RA (15 [9, 21] vs. 12 [5, 21], p< 0.05) (fig 2). Male vs. female RA patients had higher occupational scores of exposure (12 [2, 18] vs. 0 [0, 3] p< 0.005), while non-occupational exposure was not significantly different (fig 3). After adjusting for smoking, neither occupational of non- occupational scores were associated with erosive disease.

Conclusion: RA patients have higher lifetime exposure to silica dust compared to age and sex-matched subjects from the French general population. Women with RA have higher exposure from both occupational and non-occupational sources. In this series, constituted mainly of non-smoking women, exposure to silica may be a relevant environmental factor for the development of RA. In men, only occupational exposure is higher RA patients vs. controls. Neither occupational nor non-occupational exposure was associated with disease severity, likely due to the high prevalence of ACPA positivity and erosive disease in the patient series.

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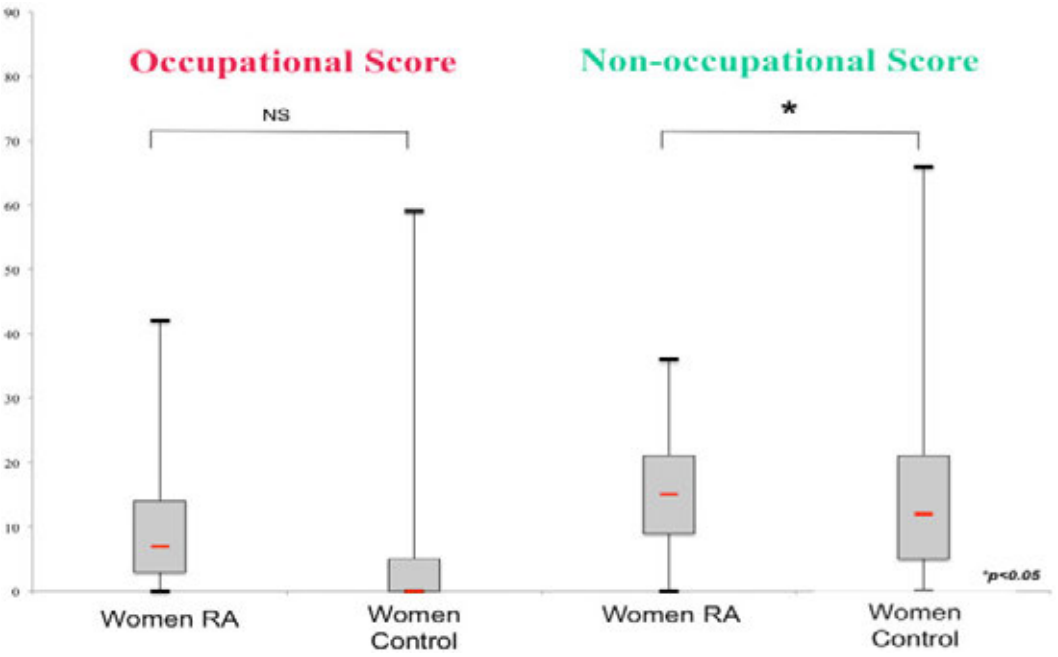

Figure 2. Comparison among women RA patients vs. Controls of occupational and non-occupational silica exposure scores.

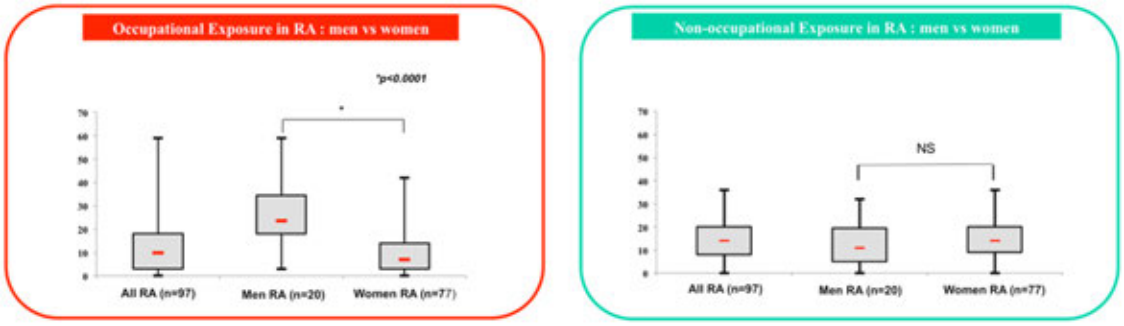

Figure 3. Comparison among RA patients men vs. women of occupational and non-occupational silica exposure scores.

Abstract Number: 0498

Should There Be Hierarchical Scoring Applied to Serologic Testing in the 2010 ACR/EULAR Classification Criteria?

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The 2010 ACR/EULAR classification criteria for Rheumatoid Arthritis (RA) are based on a combination of clinical, laboratory, and imaging investigations. Positive serology contributes to the final score when subjects are either positive to CCP or RFIgM; scoring increases based on the strength of an individual test. No more points are awarded to a patient having one versus two serologies positive.

TABLE 1	Reference	Pooled Sensitivity	Pooled Specificity
ACR Criteria – Full algorithm	Radnar et al., 2014 (Systematic Literature Review and Meta-Analysis)	78%+13%	59%+16%
CCP "and" RF IgM	Sun et al., 2014 (Systematic Literature Review and Meta-Analysis)	57% [55%-59%]	96% [96%-97%]
CCP "or" RF IgM	Sun et al., 2014 (Systematic Literature Review and Meta-Analysis)	78% [76%-80%]	82% [81%-84%]

TABLE 2	True Positives	False Negatives	False Positives	True Positives	Corr Classif	Incorr Classif
ACR Criteria – Full algorithm	139	39	337	485	62%	38%
CCP "and" RF IgM	102	76	33	789	89%	11%
CCP "or" RF IgM	139	39	148	674	81%	19%

The aim of this study was to model the clinical diagnostic outcomes between the ACR/EULAR full algorithm versus serology alone analyzing different combinations of serological positivity (single versus double positive).

Methods: We simulated a cohort of 1000 RA-suspected individuals and calculated the number of correctly/incorrectly classified subjects using the diagnostic accuracies listed in Table 1; results were compared to the ones generated by the full 2010 ACR/EULAR algorithm.

Results: Compared with the 2010 ACR/EULAR diagnostic criteria (Table 2), serology used in isolation in the current ACR/EULAR definition "CCP or RFIgM" reduces False Positives from 337 to 148 respectively, thereby diminishing the misclassification rate by 50%. Combined positivity to both tests ("CCP and RFIgM") decreases False Positives by 90%, but False Negatives increase from 39 to 76 (49% increase); overall, misclassification by this methodology drops to 11% from 38% compared to the full ACR/EULAR criteria.

Conclusion: Results show that serology used in isolation and interpreted as "CCP and RFIgM" can reduce misclassifications and may be useful in adding to the 2010 ACR/EULAR classification criteria. Individuals either positive to one test or seronegative should be re-assessed with the other examinations listed within the criteria to reach a final diagnosis.

Diagnostic accuracies (pooled sensitivities, pooled specificities, and 95% Confidence Intervals) from the two Systematic Literature Review and Meta-Analysis used in input to the simulation model.

By simulating a cohort of 1,000 individuals, all tested with CCP and RF and classified with teh 2010 ACR /EULAR Classification Criteria, this table summarises the number of True Positives, False Negatives, False Positives, True Positives, as well as the total number of correctly / incorrectly classified subjects obtained in each case using the diagnostic accuracies listed in Table 1.

Disclosure: B. Mascialino, Thermo Fisher Scientific, 3; **T. Tarrant**, Thermo Fisher Scientific, 5, 8.

Abstract Number: 0499

The Generation of Anti-CCP Tests Affects Diagnostic Accuracy in Rheumatoid Arthiritis: A Systematic Literature Review and Meta-Analysis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The detection of antibodies to cyclic citrullinated peptides (anti-CCP) may occur long before the onset of rheumatoid arthritis (RA) symptoms.

Several versions of CCP antigen peptide mixtures exist in commercial laboratory testing and are labelled CCP 2, CCP 3.0, CCP 3.1. However, despite the sequential numbering of these antigens, newer generations are not necessarily associated with improved clinical performance [Mathsson-Alm et al., 2018].

The objective of this study was to perform a systematic literature review and meta-analysis aimed at comparing the diagnostic accuracy of the most accurate anti-CCP 2 test as identified in the most recent systematic literature review and meta-analysis published on CCP tests [Mathsson-Alm et al., 2018], with anti-CCP 3.0 and CCP 3.1 tests for the diagnosis of RA, with a focus on early RA.

Methods: Our systematic literature review identified studies from 2004-2018. Estimates for pooled sensitivity, pooled specificity, Area Under the Curve (AUC), Diagnostic Odds Ratios (DOR), positive/negative likelihood ratio (LR+/LR-) were calculated; sub-analyses stratified by study design (single-gated, which are cross-sectional studies, or double-gated studies, which are case-control studies), by test generation, and by early RA (defined as symptoms durarion less than two years).

Results: Out of 5,074 papers, 113 met the inclusion criteria reporting the diagnostic accuracy of anti-CCP tests, and included 84 studies from early RA patients.

The results displayed in the Table show that the CCP 2 test has a stable performance across study designs for un-differentiated RA. As expected, when used in single-gated study designs, the test is characterized by a slightly lower sensitivity (non significant difference). It is worth noting here that single-gated studies are more representative of the scenario in which the tests would be used in practice to diagnose RA. The two CCP 3 tests are characterized by overall good and comparable performance, CCP 3.1 being characterized by a slightly lower sensitivity.

In early RA it was not possible to stratify the analysis by study design due to lack of articles passing the inclusion criteria. Moreover, not enough data was found in the literature for the test CCP 3.1 for this RA sub-type, so the comparison is limited to two tests only. The meta-analysis results show that the CCP 2 test is characterized by significantly higher sensitivity ($p< 0.05$) and by similar specificity compared to the test CCP 3.1.

Conclusion: The meta-analysis highlights that the CCP 2 test considered is in general characterized by higher diagnostic accuracy, demonstrating the greatest combination of sensitivity and specificity for RA, in undifferentiated RA

Test Generation	RA-type	Number of Included studies	Study design	AUC	Pooled Sensitivity (%) [95% CI]	Pooled Specificity (%) [95% CI]	DOR [95% CI]
CCP2	Mixed	10	Double-gated	0.92	73 [64-75]	97 [93-98]	75 [41-135]
CCP3.0	Mixed	11	Double-gated	0.86	76 [72-80]	92 [87-96]	40 [22-73]
CCP3.1	Mixed	6	Double-gated	0.93	70 [54-82]	93 [89-95]	33 [15-72]
CCP2	Mixed	3	Single-gated	0.70	71 [66-76]	96 [91-99]	74 [19-294]
CCP2	Early	3	Double-gated	0.85	78 [69-85]	86 [69-94]	20 [8-50]
CCP 3.0	Early	3	Double-gated	0.64	58 [51-63]	89 [77-96]	15 [3-65]

as well as in early RA. These results suggest that using CCP 3.0 or CCP 3.1 assays may result in the misclassification of some RA patients.

Meta-Analysis results (pooled sensitivity, pooled specificity, Area Under the Curve, Diagnostic Odds Ratio and their 95% Confidence Intervals), stratified by RA type (mixed RA or early RA), and by study design (double-gated, which means case-control, or single-gated, which means cross-sectional).

Disclosure: B. Mascialino, Thermo Fisher Scientific, 3; **L. Mathsson-Alm**, Thermo Fisher Scientific, 3; **M. Pooraf-shar**, Thermo Fisher Scientific, 3; **T. Tarrant**, Thermo Fisher Scientific, 5, 8.

Abstract Number: 0500

The Dysregulation of NK Cells and Non-Conventional NK-T and γδ-T Cells in Individuals at Risk of Developing Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The positivity of antibodies against citrullinated proteins (ACPA) precedes the clinical manifestation and significantly increases the risk of rheumatoid arthritis (RA). EULAR characterised individuals with arthralgia suspicious for progression to RA based on their clinical features (clinically suspect arthralgia, CSA). Natural killer (NK) cells and non-conventional T cells (NK-T and γδ-T cells) are involved in the regulation of immune system and their alteration was previously described in patients with established RA. We aimed to study lymphocyte subpopulations in individuals at risk of developing RA.

Methods: Our study included 71 individuals with arthralgia at risk of developing RA based on ACPA positivity and/or meeting CSA definition and 70 age and gender matched healthy controls (HC). Whole blood samples were analysed by flow cytometry. The % and absolute count of CD3+ T cells and subsequently CD3-CD16/56+ NK cells, CD3+CD16/56+ NK-T cells and CD3bright γδ-T cells were evaluated in CD45+CD14- lymphocyte population. Data were analysed using Mann Whitney test.

Results: Out of 71 individuals with arthralgia (mean age 46.33±12.17 years; 93% females), 46 were ACPA+ and 46 met CSA definition (22 of them were ACPA+). Median symptom duration was 12.5 months [IQR=53], CRP 2.94 mg/L [IQR=3.55 and DAS28-FW score 2.38 [IQR=1.53] that was used as a surrogate parameter of disease activity. As per definition, there was no evidence of clinical arthritis on examination of 66 joints at baseline. Thirteen individuals developed RA within a median of 4 months of follow up.

Analysis of lymphocyte subpopulations showed higher %CD3+ T cells (p=0.004) and lower %NK (p=0.005), %NK-T (p=0.043) as well as absolute count of NK (p≤0.001), NK-T (p=0.012) and γδ-T cells (p=0.027) in all individuals with arthralgia compared to HC. Similarly, higher %CD3+ T cells (p=0.015) and lower %NK (p=0.009), %NK-T (p=0.040) and absolute count of NK (p=0.001), NK-T (p=0.008) and γδ-T cells (p=0.017) were confirmed in a subgroup of ACPA+ individuals (especially those who also met CSA criteria) compared to HC. Also individuals who met CSA criteria irrespective of ACPA status had higher %CD3 T cells (p=0.010) and lower %NK cells (p=0.002) and absolute count of NK (p=0.004), NK-T (p=0.031) and γδ-T cells (p=0.046) compared to HC. Moreover, absolute count of γδ-T cells in individuals with arthralgia negatively correlated with disease activity score DAS28-FW (r=-0.245, p=0.040). There were no differences in lymphocyte subsets in individuals who have developed RA as yet and patients with arthralgia or at the time of RA manifestation.

Conclusion: We show lower numbers of NK cells as well as NK-T and γδ-T cells in individuals at risk of developing of RA irrespective of autoantibody or clinical definition. The decrease of non-conventional T cells was observed despite the increased percentage of the classical T cells. The altered distribution of these lymphocyte subtypes was previously described in established RA. We hypothesize that the dysregulation observed in at-risk individuals may reflect a predisposition leading to further development of RA.

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Disclosure: K. Gibson, Janssen, 8, Novartis, 2, UCB, 8, 9; **D. Gerogevsky**, None; **F. Huang**, None; **R. Fang**, None; **J. Descallar**, None.

Abstract Number: 0501

EULAR Definition of "Arthralgia Suspicious for Progression to Rheumatoid Arthritis" in a Cohort of Patients Included in a Program for Rapid Diagnosis: Role of Ultrasound and Antibodies

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the performance of the EULAR definition of arthralgias suspicious for progression to rheumatoid arthritis (RA) in a group of patients admitted to "Reuma-check" ® program with hand arthralgias and to estimate the added value of ultrasound (US) and the determination of antibodies.

Methods: Consecutive patients older than 18 years admitted for predominantly hand arthralgias to "Reuma-check" ® program were included. At baseline, laboratory tests (including ESR, CRP, RF and anti-CCP), US of hands and wrists with power Doppler (PD) technique including 22 joints (bilateral wrist, MCP and PIP) and X-ray of hands and feet were performed. Sociodemographic, clinical and clinimetry data were also collected. EULAR defined characteristics describing arthralgia at risk for RA were recorded: history taking: Joint symptoms of recent onset (duration < 1 year), symptoms located in MCP joints, duration of morning stiffness ≥60 min, most severe symptoms present in the early morning, presence of a first-degree relative with RA; physical examination: difficulty with making a fist, positive squeeze test of MCP joints. Each evaluator (laboratory, images and clinician) was blinded to the data of the other studies. In successive visits, definitive diagnosis of RA according to the ACR/EULAR 2010 criteria was established or not. Only patients with at least 2 visits were included for the final analysis.

Results: A total of 192 patients were included. 74% were women and mean age was 53 years (SD 14.2). Of the 192 patients, 23 (12%, 95% CI: 7-16) were diagnosed with RA at follow-up. Mean of baseline characteristics describing arthralgia at risk for RA was 3.7 (SD 2.2) in patients with final diagnosis of RA vs 2.7 (SD 1.7) in non-RA patients (p= 0.02). The area under the ROC curve for the EULAR defined characteristics describing arthralgia at risk for RA for the final diagnosis of RA was 0.6302, adding US with PD and anti-CCP data, the area under the ROC curve were 0.6845 (p= 0.0009) and 0.6554 (p= 0.02), respectively. Table shows features associated with final diagnosis of RA. In the multivariate regression logistic analysis, the only features associated with a final diagnosis of RA were anti-CCP (OR: 11, CI 95%: 1.6-74.3) and US with PD in at least one joint assessed (OR: 22.1, CI 95%: 3.7-129.5).

Conclusion: The EULAR definition of arthralgia suspicious for progression to rheumatoid arthritis had an acceptable performance to predict the development of RA in patients with arthralgias in our cohort of patients and improves adding information of both US with PD and anti-CCP. 12% of patients (23/192) were diagnosed as RA at follow-up. Anti-CCP and US with PD were the main features associated with final diagnosis of RA.

	RA	Non RA	p
Age, mean(SD)	49.4 (13.7)	54.1 (14.3)	0.92
Female sex, % (CI 95%)	73 (55-91)	74 (68-81)	0.53
Joint symptoms of recent onset (duration <1 year), % (CI 95%)	70 (50-88)	55 (47-62)	0.17
Symptoms located in MCP joints, % (CI 95%)	56 (36-76)	49 (41-59)	0.52
Duration of morning stiffness ≥60 min, % (CI 95%)	43 (23-63)	20 (14-26)	0.16
Most severe symptoms present in the early morning, % (CI 95%)	78 (61-95)	65 (58-72)	0.22
Presence of a first-degree relative with RA, % (CI 95%)	13(0-26)	20 (14-26)	0.38
Difficulty with making a fist, % (CI 95%)	43 (23-63)	19 (13-24)	0.008
Positive squeeze test of MCP joints, % (CI 95%)	65 (45-84)	45 (38-53)	0.08
ESR, mean (SD)	31.86 (26.3)	20 (14.2)	0.0007
CRP, mean (SD)	14.1 (27.5)	4.5 (8.11)	0.0003
RF, % (CI 95%)	34 (15-54)	10 (6-14)	0.0008
anti-CCP, % (CI 95%)	30 (11-49)	2 (0-4)	< 0.0001
HAQ, mean (SD)	0.63 (0.43)	0.51 (0.41)	0.1
Swollen joints, mean (SD)	4.69 (3.39)	3.29 (2.99)	0.0198
Tender joints, mean (SD)	1.86 (2.63)	0.75 (1.49)	0.0015
DAS28, mean (SD)	4.27 (1.29)	3.57 (1.18)	0.0054
US with PD in at least one joint, % (CI 95%)	43 (23-63)	1 (0-3)	< 0.0001
Bone erosions by X-ray, % (CI 95%)	13 (0-26)	4.7 (1-8)	0.0560

Disclosure: J. Torres Chichande, None; **S. Ruta**, None; **E. Sanchez Prado**, None; **A. Ruta**, None; **S. Magri**, None; **F. Salvatori**, None; **R. Garcia Salinas**, None.

Abstract Number: 0502

Disease Activity Measures at Baseline and 3 Months as Predictors of Rapid Radiographic Progression in Methotrexate Naïve Patients with Early Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Risk Factors, Predictors, & Prognosis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Progressive rheumatoid arthritis (RA) is responsible for disabilities in this patient population, characterized by radiographic joint damage. Achieving low disease activity (LDA) in RA is associated with reduction in radiographic progression. We aimed to compare different measures of disease activity and patient reported outcomes including disease activity score (DAS), C-reactive protein (CRP), modified (M) DAS28 (CRP), clinical disease

activity index (CDAI), DAS28(CRP) change ≥1.2, and health assessment questionnaire disability index (HAQ-DI) to predict rapid radiographic progression (RPP) in early RA patients.

Methods: Data from the PREMIER study, a 2-year, multicenter, double-blind active comparator–controlled study with methotrexate (MTX) naïve RA patients with active disease of < 3 years, were used. For this analysis, only patients in the MTX arm were analyzed. RRP was defined as change in modified total Sharp (mTSS) > 3.5 at month 12. Logistic regression analysis was used to assess impact of disease activity measures at baseline and 3 months to predict RRP at 12 months. The area under the receiver operating characteristic curve (ROC AUC) was also calculated.

Results: A total of 149 MTX treated patients were included in this analysis with the majority being female (n=113; 75.8%), positive RF (n=127; 85.2%), mean (SD) baseline age 52.9 (13.3) years, disease duration 0.8 (0.9) year, DAS28(CRP) 6.3 (0.9). After adjusting for potential confounders, only M-DAS28(CRP) at baseline ($_{adj}$OR=3.29; 95% CI: 1.70-6.36) and 3 months ($_{adj}$OR=2.56; 95% CI: 1.43-4.56) strongly predicted RRP at 12 months. Analysis of ROC curves also showed that compared with other measures, M-DAS28(CRP) at baseline and 3 months had highest predictive values (AUC: 0.66 and 0.74 respectively). We found the value of MDAS28(CRP) 4.5 and 2.6 at baseline and 3 months, respectively as optimal cut-off points to maximize sensitivity and specificity for prediction of RRP at 12 months.

Conclusion: M-DAS28(CRP) is a stronger predictor at baseline and 3 months for rapid radiographic progression compared with other disease activity measures and patient reported outcomes in early RA patients initiating MTX.

Disclosure: M. Movahedi, None; **D. Weber**, None; **P. Akhavan**, None; **E. Keystone**, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 5, Astra-Zeneca, 5, Biotest, 5, BMS, 2, 5, 8, Celltrion, 5, Crescendo, 5, Crescendo Bioscience, 5, F. Hoffmann-La Roche Inc, 2, 5, 8, Genentech, 5, Genentech Inc., 5, Genzyme, 5, Gilead, 2, 5, Gilead Sciences, Inc., 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 5, 8, Pfizer, 2, 5, 8, Pfizer Pharmaceuticals, 2, 5, 8, Roche, 2, 5, 8, Sandoz, 5, Sanofi, 2, 5, 8, Sanofi-Aventis, 2, 8, UCB, 5, 8.

Abstract Number: 0503

A Pilot Phase 1, Randomized, Double-blind, Two-arm, Parallel Group, Single-dose Study to Evaluate the Safety and Pharmacokinetics of CT-P17 and Humira in Healthy Male Subjects

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: CT-P17 is a recombinant humanized monoclonal antibody that was developed as a biosimilar to the reference product, adalimumab. This was a first in human study of CT-P17 (100 mg/mL) designed to evaluate the safety including immunogenicity and pharmacokinetics (PK) compared to European Union (EU)-reference adalimumab (100 mg/mL) in healthy male subjects

Table 1 Overall Summary of Adverse Events (Safety Population)

Category, n (%) Relationship	CT-P17 (N=15)	EU-reference adalimumab (N=15)	Overall (N=30)
Total number of TEAEs	19	14	33
Total number of SAEs	0	0	0
Number of subjects with at least 1 TEAE	10 (66.7)	8 (53.3)	18 (60.0)
Related Unrelated	5 (33.3) 8 (53.3)	4 (26.7) 5 (33.3)	9 (30.0) 13 (43.3)
Number of subjects with at least 1 SAE	0	0	0
Number of subjects with at least 1 TESAE	0	0	0
Number of subjects with at least 1 TEAE leading to study discontinuation	0	0	0
Number of subjects with at least 1 TEAE leading to death	0	0	0
Number of subjects with at least 1 TEAE due to hypersensitivity/allergic reactions	0	0	0
Number of subjects with at least 1 TEAE due to injection site reactions	0	1 (6.7)	1 (3.3)
Number of subjects with at least 1 TEAE due to infection	5 (33.3)	2 (13.3)	7 (23.3)
Related Unrelated	1 (6.7) 5 (33.3)	1 (6.7) 1 (6.7)	2 (6.7) 6 (20.0)
Number of subjects with at least 1 TEAE due to malignancy	0	0	0

Table 2 Treatment-Emergent Adverse Events (Safety Population)

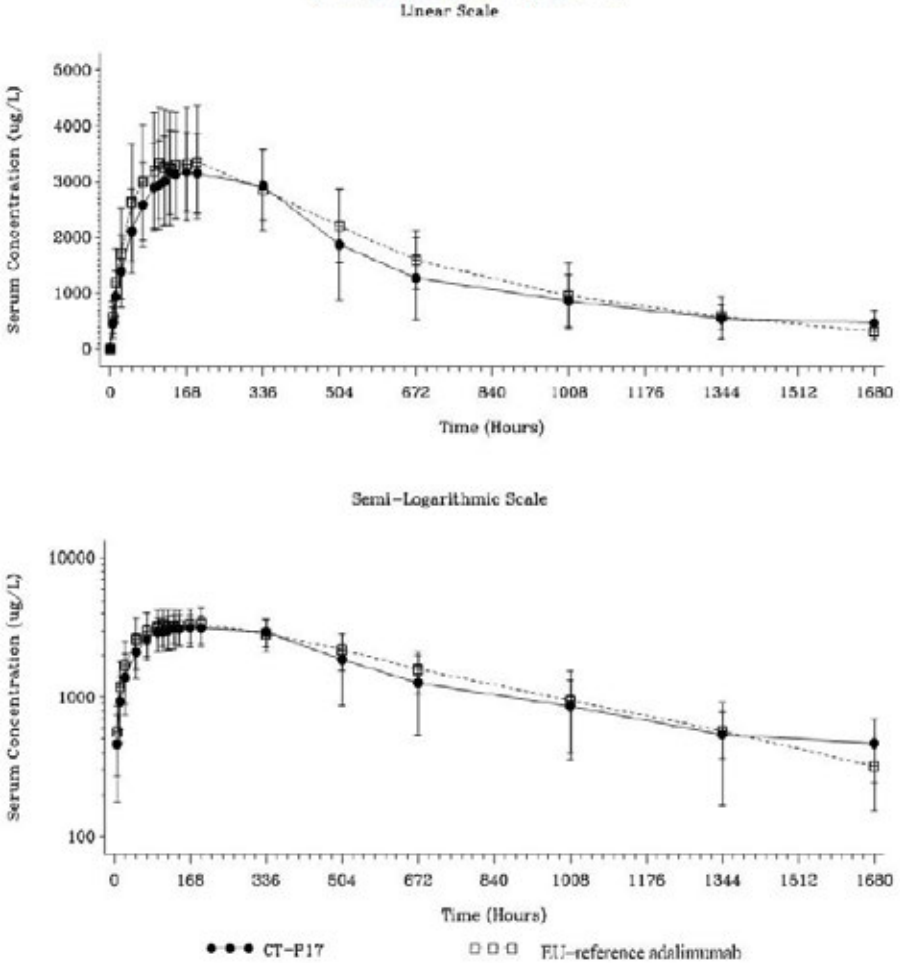
System Organ Class, n (%)	CT-P17 (N=15)	EU-reference adalimumab (N=15)	Overall (N=30)
Ear and labyrinth disorders	1 (6.7)	0	1 (3.3)
Gastrointestinal disorders	3 (20.0)	0	3 (10.0)
General disorders and administration site conditions	1 (6.7)	1 (6.7)	2 (6.7)
Infections and infestations	5 (33.3)	2 (13.3)	7 (23.3)
Musculoskeletal and connective tissue disorders	1 (6.7)	2 (13.3)	3 (10.0)
Nervous system disorders	1 (6.7)	4 (26.7)	5 (16.7)
Respiratory, thoracic and mediastinal disorders	1 (6.7)	2 (13.3)	3 (10.0)
Skin and subcutaneous tissue disorders	1 (6.7)	0	1 (3.3)

Methods: This was a phase 1, randomized, double-blind, two-arm, parallel group, single dose, active comparator study, designed to evaluate the safety and PK of CT-P17 compared to that of EU-reference adalimumab in healthy male subjects. Healthy male subjects aged 18 to 55 years (N=30) were randomized in a 1:1 Ratio to receive 40 mg of either CT-P17 or EU-reference adalimumab by subcutaneous (SC) injection. The primary objective was to evaluate safety in terms of treatment-emergent adverse events (TEAEs). The secondary objective was to evaluate PK parameters and additional safety including immunogenicity.

Results: Demographics and baseline characteristics were similar between the 2 treatment groups. Overall, 33 TEAEs were reported and 10 (66.7%) subjects in the CT-P17 and 8 (53.3%) subjects in the EU-reference adalimumab treatment groups reported at least 1 TEAE (Table 1, 2).

The most commonly reported TEAE was nasopharyngitis (4 [26.7%] in CT-P17 and 1 [6.7%] in EU-reference adalimumab). All TEAEs were grade 1 or grade 2 in intensity. There were no deaths, serious AEs, TEAEs leading to study discontinuation, hypersensitivity/allergic reaction or malignancy case for both treatment groups. One (6.7%) subject in the EU-reference adalimumab treatment group reported grade 1 TEAE of injection site reaction. There were no clinically notable abnormalities reported from other safety assessments, including clinical laboratory testing, vital signs, hypersensitivity/allergic reaction monitoring, ECG, physical examination, chest x-ray and tuberculosis assessment.

Figure 1 **Mean (± SD) Serum Concentrations of Adalimumab by Treatment (Pharmacokinetic Population)**



None of the subjects had a positive anti-drug antibody (ADA) test result at baseline. In the CT-P17 treatment group, 14 (93.3%) and 13 (86.7%) subjects developed at least 1 positive ADA and neutralizing antibodies (NAb) post-dose, respectively. In the EU-reference adalimumab treatment group, 15 (100%) and 14 (93.3%) subjects developed at least 1 positive ADA and NAb post-dose, respectively. Overall, the proportion of subjects with positive ADA and NAb results after study drug administration was similar in the 2 treatment groups.

The mean serum concentrations of adalimumab following a single SC dose of 40 mg of CT-P17 or EU-reference adalimumab were comparable up to Day 71 (Figure 1).

The mean values of $AUC_{0\text{-inf}}$ were 2383.0 h*ug/mL and 2661.1 h*ug/mL and the mean values of C_{max} were 3.415 ug/mL and 3.667 ug/mL for CT-P17 and EU-reference adalimumab, respectively, and were comparable between the 2 treatment groups. All other PK parameters were also comparable between the 2 treatment groups.

Conclusion: Single SC doses of 40 mg of CT-P17 or EU-reference adalimumab were well-tolerated and the safety profile of CT-P17, including immunogenicity, was comparable to that of EU-reference adalimumab in these healthy male subjects.

Pharmacokinetic results were also comparable between the 2 treatment groups.

Abbreviations: AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event. Note: A subject with 2 or more TEAEs within the same system organ class, preferred term, and relationship is counted only once using the most severe intensity.

Disclosure: E. Keystone, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, Gilead Sciences, 2, 5, Lilly Pharmaceuticals, 2, 5, Merck, 2, 5, 8, Pfizer Pharmaceuticals, 2, 5, 8, PuraPharm, 2, Sanofi, 2, 5, 8, AstraZeneca Pharma, 2, Bristol-Myers Squibb Company, 5, 8, Celltrion, 5, Crescendo Bioscience, 5, F. Hoffmann-La Roche Inc, 5, 8, Genetech Inc, 5, Janssen Inc, 5, 8, Sandoz, 5, Samsung Bioepis, 5, UCB, 8; **D. Furst**, Actelion, 2, 5, Actelion Pharmaceuticals, 2, 5, Amgen, 2, 5, BMS, 2, 5, CME, 5, 8, Corbus, 2, 5, Galapagos, 2, 5, Galapogos Novartis, 5, GlaxoSmithKline, 2, GSK, 2, 5, NIH, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche/Genentech, 2, 5, Sanofi, 2, 5; **M. Boyce**, None; **F. van den Berg**, None; **S. Lee**, Celltrion, Inc., 3; **S. Kim**, Celltrion, Inc., 3; **Y. Bae**, None; **G. Yang**, None; **J. Koo**, None; **E. Choi**, None; **J. Kay**, AbbVie, 5, Abbvie, 5, Abbvie, Boehringer Ingelheim, Celltrion, Horizon Therapeutics, Merck, MorphoSys AG, Norvartis AG, Pfizer, Samsung Bioepis, Sandoz Inc., UCB Pharma, 5, AbbVie, Inc., 5, Boehringer Ingelheim GmbH, 5, Boehringer-Ingelheim, 5, Boehringer-Ingelheim GmbH, 5, Celltrion Healthcare, 5, Celltrion Healthcare Co. Ltd, 5, Celltrion Healthcare CO. Ltd, 5, Celltrion Healthcare Co. Ltd., 5, Gilead, 2, Gilead Sciences, 5, Gilead Sciences, Inc, 2, Gilead Sciences, Inc., 2, Gilead Sciences, Inc., Novartis AG, Pfizer, UCB Pharma, 2, Horizon Therapeutics, 5, Horizon Therapeutics PLC, 5, Merck Sharp & Dohme, 5, Merck Sharp & Dohme Corp, 5, Merck Sharp & Dohme Corp., 5, MorphoSys AG, 5, Novartis AG, 2, 5, Novartis Pharmaceuticals, 5, Pfizer, 2, 5, Pfizer Inc, 2, 5, Pfizer Inc., 2, 5, Samsung Bioepis, 5, Samsung Bioepis Co., Ltd., 5, Sandoz, 5, Sandoz Inc, 5, UCB, 2, 5, UCB Pharma, 2, 5, UCB, Inc., 2, 5.

Abstract Number: 0504

A Subgroup Analysis of the Efficacy of Filgotinib in Demographic and Clinical Subgroups of Patients with Refractory Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: RA patients who have failed biologic DMARDs represent an unmet medical need. We explored the impact of baseline demographics and clinical characteristics on filgotinib efficacy in patients with active RA who have inadequate response to ≥1 prior bDMARD (bDMARD-IR).

Methods: In the global, phase 3 FINCH-2 study (NCT02873936), 449 patients with moderately-to-severely active RA and inadequate response to ≥1 prior bDMARDs were randomized 1:1:1 to once-daily filgotinib 200 mg, filgotinib 100 mg, or placebo.[1] We evaluated prespecified subgroups including baseline demographic and clinical characteristics such as sex at birth, seropositivity for RF and/or ACPA, disease duration, disease activity, hsCRP levels, concurrent use of corticosteroids, and different classes of DMARDs on filgotinib efficacy as measured by ACR20 and DAS28(CRP) for low disease activity and remission in patients with active RA who were bDMARD-IR.

Table 1. Proportion of Patients Achieving ACR20 Response at Week 24 Unless otherwise noted, data presented as n/N (%) CI, confidence interval; csDMARD, conventional synthetic DMARD; hsCRP, high-sensitivity CRP; QD, once daily.

	Treatment			Δ in Response vs Placebo, 95% CI, p-value	
	Filgotinib 200 mg QD n = 147	Filgotinib 100 mg QD n = 153	Placebo n = 148	Filgotinib 200 mg QD	Filgotinib 100 mg QD
Sex at birth					
Male	15/27 (55.6)	19/34 (55.9)	7/27 (25.9)	29.6 (0.9, 58.3), 0.051	30.0 (3.1, 56.8), 0.022
Female	87/120 (72.5)	65/119 (54.6)	44/121 (36.4)	36.1 (23.6, 48.7), <0.001	18.3 (5.0, 31.5), 0.006
Seropositivity					
RF or ACPA positive					
Yes	83/112 (74.1)	65/118 (55.1)	39/113 (34.5)	39.6 (26.8, 52.4), <0.001	20.6 (7.2, 34.0), 0.002
No	19/35 (54.3)	19/35 (54.3)	12/35 (34.3)	20.0 (−5.7, 45,7), 0.15	20.0 (−5.7, 45.7), 0.15
Disease duration, years					
<5	22/35 (62.9)	12/28 (42.9)	12/34 (35.3)	27.6 (2.0, 53.1), 0.031	7.6 (−20.1, 35.2), 0.61
5–<10	34/41 (82.9)	24/44 (54.5)	15/41 (36.6)	46.3 (25.2, 67.5), <0.001	18.0 (−5.2, 41.1), 0.13
≥10	46/71 (64.8)	48/81 (59.3)	24/73 (32.9)	31.9 (15.0, 48.8), <0.001	26.4 (9.9, 42.9), 0.001
Disease activity					
DAS28(CRP) ≤5.1	22/33 (66.7)	17/34 (50.0)	10/28 (35.7)	31.0 (3.7, 58.2), 0.021	14.3 (−13.4, 42.0), 0.31
DAS28(CRP) >5.1	80/114 (70.2)	67/119 (56.3)	41/120 (34.2)	36.0 (23.2, 48.8), <0.001	22.1 (9.0, 35.3), <0.001
hs CRP level, mg/L					
≥4	90/128 (70.3)	67/124 (54.0)	41/120 (34.2)	36.1 (23.7. 48.6), <0.001	19.9 (6.8, 32.9), 0.002
<4	12/19 (63.2)	17/29 (58.6)	10/28 (35.7)	27.4 (−5.0, 59.9), 0.081	22.9 (−5.8, 51.6), 0.11
Oral corticosteroid use					
Yes	48/68 (70.6)	36/68 (52.9)	18/71 (25.4)	45.2 (29.0, 61.5), <0.001	27.6 (10.6, 44.6), <0.001
No	54/79 (68.4)	48/85 (56.5)	33/77 (42.9)	25.5 (9.1, 41.9), 0.002	13.6 (−2.9, 30.1), 0.12
csDMARD					
0–1	92/133 (69.2)	76/135 (56.3)	47/136 (34.6)	34.6 (22.7, 46.6), <0.001	21.7 (9.4, 34.0), <0.001
≥2	10/14 (71.4)	8/18 (44.4)	4/12 (33.3)	38.1 (−5.3, 81.5), 0.11	11.1 (−31.0, 53.2), 0.71
Methotrexate use					
Yes	86/124 (69.4)	71/127 (55.9)	41/116 (35.3)	34.0 (21.3, 46.7), <0.001	20.6 (7.5, 33.6), 0.002
No	16/23 (69.6)	13/26 (50.0)	10/32 (31.3)	38.3 (9.8, 66.8), 0.007	18.8 (−9.8, 47.3), 0.18

Table 2. Proportion of Patients Achieving Low Disease Activity at Week 24 Unless otherwise noted, data presented as n/N (%). CI, confidence interval; csDMARD, conventional synthetic DMARD; hsCRP, high-sensitivity CRP; QD, once daily.

	Treatment			Δ in response vs placebo, 95% CI, p-value	
	Filgotinib 200 mg QD n = 147	Filgotinib 100 mg QD n = 153	Placebo n = 148	Filgotinib 200 mg QD	Filgotinib 100 mg QD
DAS28(CRP) ≤3.2					
Sex at birth					
Male	11/27 (40.7)	13/34 (38.2)	6/27 (22.2)	18.5 (−9.5, 46.5), 0.24	16.0 (−10.0, 42.0), 0.27
Female	60/120 (50.0)	45/119 (37.8)	25/121 (20.7)	29.3 (17.0, 41.7), <0.001	17.2 (5.0, 29.3), 0.004
Seropositivity					
RF or ACPA positive					
Yes	54/112 (48.2)	42/118 (35.6)	21/113 (18.6)	29.6 (17.0, 42.4), <0.001	17.0 (4.9, 29.1), 0.005
No	17/35 (48.6)	16/35 (45.7)	10/35 (28.6)	20.0 (−5.2, 45.2), 0.14	17.1 (−8.0, 42.3), 0.22
Disease duration, years					
<5	13/35 (37.1)	10/28 (35.7)	9/34 (26.5)	10.7 (−14.0, 35.4), 0.44	9.2 (−17.1, 35.6), 0.58
5–<10	26/41 (63.4)	16/44 (36.4)	9/41 (22.0)	41.5 (19.6, 63.3), <0.001	14.4 (−7.0, 35.8), 0.16
≥10	32/71 (45.1)	32/81 (39.5)	13/73 (17.8)	27.3 (11.3, 43.2), <0.001	21.7 (6.6, 36.8), 0.004
Disease activity					
DAS28(CRP) ≤5.1	24/33 (72.7)	20/34 (58.8)	11/28 (39.3)	33.4 (6.5, 60.4), 0.011	19.5 (−8.2, 47.3), 0.20
DAS28(CRP) >5.1	47/114 (41.2)	38/119 (31.9)	20/120 (16.7)	24.6 (12.5, 36.6), <0.001	15.3 (3.7, 26.8), 0.007
hsCRP level, mg/L					
<4	11/19 (57.9)	17/29 (58.6)	8/28 (28.6)	29.3 (−2.9, 61.5), 0.069	30.0 (2.0, 58.1), 0.033
≥4	60/128 (46.9)	41/124 (33.1)	23/120 (19.2)	27.7 (15.8, 39.7), <0.001	13.9 (2.2, 25.6), 0.019
Corticosteroid use					
Yes	33/68 (48.5)	22/68 (32.4)	15/71 (21.1)	27.4 (10.8, 44.0), <0.001	11.2 (−4.8, 27.3), 0.18
No	38/79 (48.1)	36/85 (42.4)	16/77 (20.8)	27.3 (11.8, 42.9), <0.001	21.6 (6.5, 36.7), 0.004
csDMARD					
0–1	64/133 (48.1)	54/135 (40.0)	29/136 (21.3)	26.8 (15.1, 38.5), <0.001	18.7 (7.2, 30.2), <0.001
≥2	7/14 (50.0)	4/18 (22.2)	2/12 (16.7)	33.3 (−8.0, 74.7), 0.11	5.6 (−29.9, 41.0), 1.00
Methotrexate use					
Yes	61/124 (49.2)	50/127 (39.4)	25/116 (21.6)	27.6 (15.3, 40.0), <0.001	17.8 (5.7, 30.0), 0.003
No	10/23 (43.5)	8/26 (30.8)	6/32 (18.8)	24.7 (−3.4, 52.8), 0.071	12.0 (−13.8, 37.8), 0.36

Table 3. Proportion of Patients Achieving Remission at Week 24 Unless otherwise noted, data presented as n/N (%). CI, confidence interval; csDMARD, conventional synthetic DMARD; hsCRP, high-sensitivity CRP; QD, once daily.

	Treatment			Δ in response vs placebo, 95% CI, p-value	
	Filgotinib 200 mg QD n = 147	Filgotinib 100 mg QD n = 153	Placebo n = 148	Filgotinib 200 mg QD	Filgotinib 100 mg QD
DAS28(CRP) <2.6					
Sex at birth					
Male	7/27 (25.9)	11/34 (32.4)	3/27 (11.1)	14.8 (−9.2, 38.9), 0.29	21.2 (−1.8, 44.3), 0.068
Female	38/12 (31.7)	29/119 (24.4)	15/121 (12.4)	19.3 (8.3, 30.3), <0.001	12.0 (1.4, 22.5), 0.02
Seropositivity- RF or ACPA positive					
Yes	32/112 (28.6)	31/118 (26.3)	13/113 (11.5)	17.1 (6.0, 28.2), 0.002	14.8 (4.0, 25.5), 0.005
No	13/35 (37.1)	9/35 (25.7)	5/35 (14.3)	22.9 (0.2, 45.5), 0.054	11.4 (−10.0, 32.8), 0.37
Disease duration, years					
<5	9/35 (25.7)	4/28 (14.3)	7/34 (20.6)	5.1 (−17.6, 27.9), 0.78	−6.3 (−28.3, 15.7), 0.74
5–<10	17/41(41.5)	12/44 (27.3)	4/41 (9.8)	31.7 (11.7, 51.8), 0.002	17.5 (−0.8, 35.9), 0.053
≥10	19/71 (26.8)	24/81 (29.6)	7/73 (9.6)	17.2 (3.5, 30.9), 0.009	20.0 (6.7, 33.4), 0.002
Disease activity					
DAS28(CRP) ≤5.1	18/33 (54.5)	15/34 (44.1)	8/28 (28.6)	26.0 (−1.2, 53.1), 0.068	15.5 (−11.3, 42.4), 0.29
DAS28(CRP) >5.1	27/114 (23.7)	25/119 (21.0)	10/120 (8.3)	15.4 (5.3, 25.4), 0.002	12.7 (3.0, 22.3), 0.006
hsCRP level, mg/L					
<4	9/19 (47.4)	16/29 (55.2)	7/28 (25.0)	22.4 (−9.6, 54.4), 0.13	30.2 (2.5, 57.9), 0.031
≥4	36/128 (28.1)	24/124 (19.4)	11/120 (9.2)	19.0 (8.8, 29.1), <0.001	10.2 (0.7, 19.7), 0.028
Corticosteroid use					
Yes	16/68 (23.5)	17/68 (25.0)	7/71 (9.9)	13.7 (0, 27.3), 0.040	15.1 (1.3, 29.0), 0.024
No	29/79 (36.7)	23/85 (27.1)	11/77 (14.3)	22.4 (7.9, 36.9) 0.002	12.8 (−0.7, 26.3) 0.054
csDMARD use					
0–1	40/133 (30.1)	38/135 (28.1)	17/136 (12.5)	17.6 (7.3, 27.9), <0.001	15.6 (5.5, 25.8), 0.001
>2	5/14 (35.7)	2/18 (11.1)	1/12 (8.3)	27.4 (−9.9, 64.7), 0.17	2.8 (−25.5, 31.1), 1.00
Methotrexate use					
Yes	37/124 (29.8)	34/127 (26.8)	14/116 (12.1)	17.8 (6.9, 28.6), <0.001	14.7 (4.2, 25.2), 0.006
No	8/23 (34.8)	6/26 (23.1)	4/32 (12.5)	22.3 (−4.0, 48.6) 0.095	10.6 (−12.7, 33.9) 0.32

Results: Of the 448 patients randomized and treated at baseline, 80.4% were female with a mean age of 56 years and a mean RA duration of 12.4 years. Clinical efficacy outcomes at week 24 as measured by ACR20, DAS28(CRP) ≤3.2 and DAS28(CRP) < 2.6 by patient demographics and clinical baseline characteristics are described in **Tables 1**, **2**, and **3**, respectively.

Conclusion: Compared with placebo, filgotinib consistently improved clinical outcomes in bDMARD-refractory patients. Benefits were observed for filgotinib across subgroups defined by various demographic and clinical baseline characteristics. There was an absence of impact of disease duration, seropositivity, disease activity and concurrent medication use, notably on the effectiveness of filgotinib.

Reference:

1. Genovese MC, et al. Safety and Efficacy of Filgotinib in a Phase 3 Trial of Patients with Active Rheumatoid Arthritis and Inadequate Response or Intolerance to Biologic Dmards [abstract]. Arthritis Rheumatol. 2018; 70 (suppl 10).

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Abstract Number: 0505

Low-grade Total Rheumatoid Arthritis MRI Scoring System Can Predict Successful Half-dose Reduction of MTX in Patients with RA in Clinical Remission

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

Background/Purpose: It has been recommended that tapering csDMARDs should be considered if a patient is in persistent remission. However, methods for tapering csDMARDs, including MTX, without RA flare have not been established. Previously, we reported that baseline RAMRIS synovitis score predicted half-dose reduction of MTX without disease flare until week 24, in an RA patient who achieved clinical remission. In this study, we extended the study duration to week 52 to determine whether baseline MRI findings can predict successful half-dose reduction of MTX for a full year.

Methods: Outpatients of our hospital's department of rheumatology were included in this study. Inclusion criteria were as follows: diagnosis of RA based on 2010 ACR/EULAR classification criteria; achievement of clinical remission, defined by DAS28-CRP, over 4 weeks; treatment with methotrexate reduced by half according to the patient's wishes; and availability of MRI images of the hand at the time of MTX reduction. Exclusion criteria were as follows: treatment with leflunomide or tacrolimus, tsDMARDs, or bDMARDs; or oral prednisolone > 5 mg/day. In this study, we examined DAS28-CRP until week 52 every 4–8 weeks. Disease flare was defined as DAS28-CRP of ≥ 2.3 at two sequential visits, an increase in dose of MTX, and addition of other DMARDs. MRI of the patient's dominant wrist and second through fifth metacarpophalangeal (MCP) joints was performed using a 1.5 T whole-body MRI unit with contrast enhancement. MR images were assessed for bone erosions, synovitis, and bone marrow edema according to the original OMERACT Rheumatoid Arthritis MRI Scoring System (RAMRIS).

Results: Fifteen patients were enrolled in this study (10 women, 5 men). We evaluated all 15 patients' data until week 52. Mean (±SD) age, disease duration, MTX dose before reduction, and DAS28-CRP at baseline were 66.6 ± 9.8 y, 6.0 ± 3.6 y, 8.8 ± 3.4 mg/w, and 1.32 ± 0.26. Thirteen patients were positive for anti-CCP antibody and RF. Subclinical MRI inflammation was detected in all patients. Median (range) synovitis, bone edema, and bone erosion score were 2 (0–7), 0 (0–4) and 7 (1–22). Two patients experienced disease flare until week 24 and one patients after week 24. Two patients without clinical remission before week 24 had significantly higher RAMRIS synovitis scores (4.5 vs. 1.9, $p < 0.05$). RAMRIS bone erosion score of 3 patients experiencing disease flare until week 52 tended to be higher, and total RAMRIS score (synovitis + bone edema + bone erosion score, but not synovitis score alone) was significantly higher in these patients (18.3 vs. 8.0, $p < 0.05$). Analysis of the ROC curve determined that the most sensitive and specific cut-off value for total RAMRIS score was 11 (AUC = 0.917, 95% CI 0.737–1.000, $p < 0.001$).

Conclusion: MRI evaluation was useful for prediction of successful dose reduction of MTX during clinical remission. In the early phase of reduction, synovitis was an important factor in disease flare, and as reduction became long-term, bone erosion was also important. We conclude that half-dose reduction of MTX in RA patients who achieve clinical remission and have low total RAMRIS scores might be a beneficial option for tapering MTX.

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Abstract Number: 0506

Efficacy and Safety of Filgotinib for Patients with Rheumatoid Arthritis with Inadequate Response to Methotrexate: FINCH1 Primary Outcome Results

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Background/Purpose: Filgotinib (FIL) is an orally administered, potent and selective inhibitor of Janus kinase 1 (JAK1) that has shown good efficacy and was well tolerated for treatment of rheumatoid arthritis (RA). The objective of this study is to evaluate efficacy and safety of FIL treatment in patients with RA who have had an inadequate response to methotrexate (MTX).

Methods: This phase 3, double-blind, active- and placebo (PBO)-controlled study randomized patients with active RA (3:3:2:3) to FIL 200 mg, FIL 100 mg, active comparator (adalimumab [ADA] 40mg every 2 weeks), or PBO daily for up to 52 weeks; results through week 24 are presented. Patients were also receiving MTX for ≥12 weeks with a stable dose of MTX for ≥4 weeks before initiation of study drug. Primary efficacy endpoint was proportion of patients achieving ACR20 response at week 12; additional clinical assessments were ACR50 and ACR70 responses, DAS28-CRP score ≤3.2 and < 2.6, van der Heijde modified total Sharp score (mTSS), and patient-reported outcomes were HAQ-DI, SF-36 PCS, and FACIT-Fatigue. Safety endpoints included types and rates of adverse events. Logistic regression adjusting for stratification factors with nonresponder imputation was used for superiority test of FIL vs PBO for ACR response and other binary endpoints. Mixed-effect model adjusting for baseline value, stratification factors, treatment, visit, and treatment by visit interaction as fixed effects with observed cases was used for continuous endpoints. Non-inferiority test of FIL to ADA (preserving >50% of ADA response) was performed for DAS28-CRP ≤3.2 and < 2.6.

Results: Of 1,759 patients randomized, 1,755 received study drug and were analyzed, with 475 FIL 200mg; 480 FIL 100mg; 325 ADA; and 475 PBO, of which 89.5%, 90.4%, 88.9%, and 81.3%, respectively, completed week 24 study drug. Most patients (81.8%) were female, mean (standard deviation [SD]) duration of RA was 7.8 (7.6) years, and mean (SD) DAS28-CRP was 5.7 (0.9). At week 12, significantly more patients in the FIL 200mg and 100mg arms

Table 1. Efficacy at Week 12 (Primary Analysis) and Week 24[a]

	FIL 200 mg (N = 475)		FIL 100 mg (N = 480)		ADA 40 mg Q2W (N = 325)		PBO (N = 475)	
	Week 12	Week 24	Week 12	Week 24	Week 12	Week 24	Week 12	Week 24
ACR20, %	76.6***	78.1	69.8***	77.7	70.8	74.5	49.9	59.2
ACR50, %	47.2***#	57.9	36.3***#	52.7	35.1	52.6	19.8	33.3
ACR70, %	26.3***#	36.2	18.5***#	29.4	14.2	29.5	6.7	14.9
DAS28-CRP ≤ 3.2, %	49.7***§	60.6	38.8***	53.1	43.4	50.5	23.4	33.7
DAS28-CRP < 2.6, %	33.9***#	48.4	23.8***#	35.2	23.7	35.7	9.3	16.2
mTSS, mean change from BL	0.08	0.13***	0.11	0.17***	0.13	0.16	0.25	0.38
HAQ-DI, mean change from BL	–0.69***	–0.82	–0.56***	–0.75	–0.61	–0.78	–0.42	–0.62
SF-36 PCS, mean change from BL	9.2***#	10.4	8.5***#	10.3	8.4	10.4	5.8	7.7
FACIT-Fatigue, mean change from BL	9.2***#	10.5	9.1***#	10.8	8.8	10.3	6.8	8.4

[a]All patients who were randomized and received at least 1 dose of study drug were included in efficacy analyses. *P*-values are shown only for primary time points (all at week 12 except mTSS, which was at week 24).
***$P<0.001$ vs PBO; §$P<0.01$ vs ADA non-inferiority test; ‡$P<0.001$ vs ADA non-inferiority test; *$P<0.01$ vs ADA superiority test; #Comparison not adjusted for multiplicity.
ACR20/50/70, 20%/50%/70% improvement in American College of Rheumatology criteria; ADA, adalimumab; BL, baseline; DAS28-CRP, Disease Activity Score based in 28 joints with C-reactive protein; FIL, filgotinib; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire Disability Index; mTSS, modified total Sharp score; SD, standard deviation; SF-36 PCS, Short-Form 36 Physical Component Summary; Q2W every 2 weeks.

Table 2. Safety Events of Interest through Week 24

Patient with event, n (%)	FIL 200 mg (N = 475)	FIL 100 mg (N = 480)	ADA 40 mg Q2W (N = 325)	PBO (N = 475)
Serious AEs	21 (4.4)	24 (5.0)	14 (4.3)	20 (4.2)
Serious infections	8 (1.7)	8 (1.7)	8 (2.5)	4 (0.8)
Herpes zoster	2 (0.4)	2 (0.4)	2 (0.6)	2 (0.4)
Adjudicated MACEs	0	1 (0.2)	1 (0.3)	2 (0.4)
Venous thrombotic events	1 (0.2)	0	0	2 (0.4)
Malignancies	0	1 (0.2)	1 (0.3)	3 (0.6)
Deaths	2 (0.4)	1 (0.2)	0	2 (0.4)

AE, adverse event; MACE, major adverse cardiovascular event

achieved an ACR20 response compared to PBO (Table 1). Similarly, compared to PBO, more patients receiving FIL achieved ACR50 and ACR70 responses, DAS28-CRP scores ≤3.2 and < 2.6, had lower radiographic progression, and reported improvements in HAQ-DI, SF-36 PCS, and FACIT-Fatigue scores (Table 1). Non-inferiority of FIL 200mg to ADA was met based on DAS28-CRP ≤3.2. The FIL safety profile was consistent with prior studies through week 24 (Table 2).

Conclusion: The selective JAK1 inhibitor FIL, at doses of 200mg and 100mg led to significant improvement in signs and symptoms of RA, prevented radiographic progression, and improved physical function compared to PBO, and was well tolerated among patients with RA with prior inadequate response to MTX. Efficacy of FIL 200mg was non-inferior to ADA based on DAS28-CRP ≤3.2.

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Abstract Number: 0507

Inhibition of Joint Destruction in Patients with Rheumatoid Arthritis Treated with Peficitinib in Combination with Methotrexate: A Randomized, Double-Blind, Placebo-Controlled Trial in Japan

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

Table 1. Sensitivity analyses for change from baseline in mTSS at W28 with rank analysis of covariance

	Summary statistics							Treatment difference vs PBO[1]
Treatment group	N	Mean (SD)	Min	Q1	Median	Q3	Max	P value
1. Rank ANCOVA with LOCF imputation (FAS)								
PBO	153	2.19 (3.84)	-5.5	0.00	0.50	3.00	26.0	
PEF100	164	1.60 (4.22)	-2.0	0.00	0.00	1.50	30.3	0.013
PEF150	164	1.01 (2.85)	-4.0	0.00	0.00	1.00	15.0	<0.001
2. Rank ANCOVA as observed data (FAS)								
PBO	73	2.72 (4.78)	-1.5	0.00	0.50	3.50	26.0	
PEF100	159	1.59 (4.25)	-2.0	0.00	0.00	1.50	30.3	0.082
PEF150	160	1.01 (2.88)	-4.0	0.00	0.00	1.00	15.0	0.002
3. Rank ANCOVA using PPS-mTSS as the analysis set								
PBO	148	3.30 (5.44)	-11.8	0.00	1.08	5.50	31.9	
PEF100	159	1.63 (4.26)	-2.0	0.00	0.00	1.50	30.3	0.002
PEF150	161	1.01 (2.85)	-4.0	0.00	0.00	1.00	15.0	<0.001

Treatment group	N	Mean (SD)	Treatment difference versus PBO[2]		
			LS Mean (SE)	95% CI	P value
4. ANCOVA (FAS)					
PBO	153	3.37 (5.46)			
PEF100	164	1.62 (4.23)	-1.69 (0.48)	(-2.63, -0.75)	<0.001
PEF150	164	1.03 (2.86)	-2.27 (0.48)	(-3.22, -1.33)	<0.001
5. ANCOVA with multiple imputation method (FAS)					
PBO	153	3.37 (5.46)			
PEF100	164	1.62 (4.23)	-1.18 (0.44)	(-2.04, -0.31)	0.008
PEF150	164	1.03 (2.86)	-1.76 (0.44)	(-2.63, -0.90)	<0.001

[1]Based on rank analysis of covariance model: Rank of mTSS Change = Treatment + Baseline Rank of mTSS.
[2]Based on analysis of covariance model: mTSS Change = Treatment + Baseline mTSS. ANCOVA, analysis of covariance; ET, early termination; FAS, full analysis set; PPS, per protocol set; PBO, placebo; PEF100, peficitinib 100 mg/day; PEF150, peficitinib 150 mg/day; SD, standard deviation; SE, standard error; Q1, first quartile; Q3, third quartile.

Background/Purpose: Peficitinib (PEF), a novel oral Janus kinase (JAK) inhibitor, has demonstrated efficacy in Phase 3 studies of patients with RA (NCT02305849).[1] We report the evaluation for suppression of joint destruction of PEF compared with placebo (PBO) in this study.

Methods: This randomized, double-blind, PBO-controlled study was conducted in Japan. Patients with RA (< 10 years' duration) and inadequate response (IR) to MTX were randomly assigned 1:1:1 to receive PEF 100 or 150 mg/day (PEF100 or PEF150) or PBO once daily, plus MTX. Patients receiving PBO were switched to PEF100 or PEF150 at Week (W) 28, or W12 for IR. Hand and foot X-rays were taken at baseline (BL), W12, 28 and 52. Mean change from BL (linear extrapolation) in van der Heijde modified Total Sharp Score (mTSS) at W28 in the full analysis set (FAS) was a primary endpoint, and was analyzed with rank analysis of covariance (rank ANCOVA) with treatment group as factor and BL rank mTSS as covariate in the primary analysis. Sensitivity analyses of the primary efficacy analysis were:

Table 2. Proportions of patients with changes in mTSS of ≤0.5 or >5

	N/n	%	Difference	95% CI	P value[1]
Change in mTSS of ≤0.5: Week 28/ET					
PBO	153/70	45.8			
PEF100	164/110	67.1	21.3	10.0, 32.6	<0.001
PEF150	164/119	72.6	26.8	15.7, 37.9	<0.001
Change in mTSS of ≤0.5: Week 52/ET					
PBO	153/65	42.5			
PEF100	164/105	64.0	21.5	10.2, 32.9	<0.001
PEF150	164/113	68.9	26.4	15.2, 37.6	<0.001
Change in mTSS of >5: Yearly progression					
PBO	153/54	35.3			
PEF100	164/17	10.4	-24.9	-34.5, -15.4	<0.001
PEF150	164/16	9.8	-25.5	-35.0, -16.1	<0.001

[1]Fisher's exact test.
CI, confidence interval; ET, end of treatment; mTSS, modified Total Sharp Score; PBO, placebo; PEF100, peficitinib 100 mg/day; PEF150, peficitinib 150 mg/day

1. rank ANCOVA with LOCF imputation; 2. rank ANCOVA as observed data; 3. rank ANCOVA using the per protocol set-mTSS as the analysis set; 4. ANCOVA; 5. ANCOVA with multiple imputation method. The proportions of patients with no joint damage (mTSS < 0.5) and yearly progression of mTSS >5 were calculated. Subgroup analyses of mTSS for different demographic and BL characteristics were presented, in which interaction term with treatment group was significant at a two-sided significance level of 0.15 by ad hoc analysis.

Results: In total, 518 patients were included in the FAS: PBO n=170; PEF100 n=174; PEF150 n=174. BL demographics were similar between groups. The primary and secondary endpoint results from RAJ4 were met and have been described previously.[1] Sensitivity analyses showed that the change in mTSS at W28 was similar to the primary analysis result, showing the robustness of the primary analysis (**Table 1**). At W28, a significantly greater proportion of patients achieved a change in mTSS of ≤0.5 for both PEF100 and PEF150 compared with PBO (67.1% and 72.6% vs 45.8%, respectively; p< 0.001 for both). This was maintained at W52 (64.0% and 68.9% vs 42.5%, respectively; p< 0.001 for both) (**Table 2**). The proportion of patients showing rapid radiographic progression (yearly progression of mTSS ≥5) was also significantly lower for both PEF100 and PEF150 compared with PBO (10.4% and 9.8% vs 35.3%, respectively; p< 0.001 for both: **Table 2**).

Selected parameters from the subgroup analysis showing significant results for their interaction with treatment group were age group, BL mTSS, BL DAS28-CRP, duration of RA, BL CRP, concomitant steroid at BL, prednisone dose at BL, and body weight at screening at a two-sided significance level of 0.15 by ad hoc analysis (**Table 3**).

Conclusion: Peficitinib 100 mg and 150 mg both demonstrated significant inhibition of joint destruction compared with PBO**.**

Reference:

1. T. Takeuchi et al. Arthritis Rheumatol 2018; 70 (Suppl 10): Abstract 888

Table 3. Subgroup analysis of change from baseline in mTSS at W28 (FAS)

	PBO		PEF100		PEF150		P value for interaction term with treatment group
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	
Age group (years)							
<65	117	3.73 (5.74)	109	1.88 (4.86)	125	1.24 (3.11)	0.072
≥65	36	2.17 (4.32)	55	1.08 (2.49)	39	0.35 (1.74)	
Baseline mTSS							
≤Median	67	2.18 (3.74)	86	1.25 (3.74)	87	1.04 (2.55)	0.109
>Median	86	4.29 (6.37)	78	2.01 (4.69)	77	1.02 (3.19)	
Baseline DAS28-CRP							
≤3.2			3	1.67 (2.89)	3	-0.83 (1.04)	0.116
>3.2–≤5.1	58	2.78 (5.32)	69	0.82 (2.26)	57	0.34 (1.81)	
>5.1	95	3.72 (5.55)	92	2.21 (5.21)	104	1.46 (3.26)	
Duration of RA (years)							
<5	89	4.21 (5.56)	100	2.05 (5.01)	101	1.43 (3.16)	<0.001
≥5	64	2.20 (5.14)	64	0.94 (2.44)	63	0.39 (2.18)	
Baseline CRP							
<1.0	27	1.63 (6.85)	42	0.38 (1.41)	39	0.08 (0.80)	0.006
≥1.0	126	3.74 (5.08)	122	2.04 (4.76)	125	1.32 (3.19)	
Concomitant steroid at baseline							
No	78	4.40 (6.31)	77	1.21 (3.92)	77	1.14 (3.30)	0.018
Yes	75	2.29 (4.19)	87	1.98 (4.47)	87	0.93 (2.42)	
Prednisone dose at baseline (mg/day)							
None	78	4.40 (6.31)	77	1.21 (3.92)	77	1.14 (3.30)	0.045
0–≤5	60	2.51 (4.52	71	1.68 (3.34)	66	0.86 (2.43)	
>5	15	1.40 (2.39)	16	3.30 (7.76)	21	1.12 (2.45)	
Body weight (kg) at screening							
≤40	3	11.47 (8.65)	4	3.00 (3.83)	6	4.06 (6.55)	0.003
>40–≤60	87	4.03 (6.13)	101	2.22 (5.14)	95	0.96 (2.82)	
>60–≤80	54	1.95 (3.52)	49	0.44 (1.04)	52	0.70 (2.05)	
>80	9	2.80 (4.41)	10	0.78 (2.33)	10	1.63 (3.21)	

CRP, C-reactive protein; DAS, Disease Activity Score; FAS, full analysis set; mTSS, modified Total Sharp Score; PBO, placebo; PEF100, peficitinib 100 mg/day; PEF150, peficitinib 150 mg/day; SD, standard deviation; ULN, upper limit of normal

Disclosure: T. Takeuchi, AbbVie, 2, 5, 8, AbbVie GK, 2, 9, Asahi Kasei, 2, Asahikasei, 2, Asahikasei Pharma Corp., 2, Astellas, 2, 8, 9, Astellas Pharma Inc, 2, Astellas Pharma, Inc., 2, 5, 8, 9, Astra Zeneca, 2, AstraZeneca, 8, AYUMI, 2, 9, AYUMI Pharmaceutical Corporation, 2, BMS, 2, 8, Boehringer-ingelheim, 9, Bristol–Myers K.K., 9, Bristol-Myers, 2, Bristol-Myers Squibb, 8, Chugai, 2, 8, 9, Chugai Pharmaceutical Co, Ltd., 2, Daiichi Sankyo, 2, 8, 9, Daiichi Sankyo Co., Ltd., 2, Eisai, 2, 5, 8, 9, Eisai Co., Ltd., 2, Eli Lilly, 2, 8, Eli Lilly Japan, 9, Gilead Sciences, Inc., 9, GlaxoSmithKline K.K, 9, GSK, 8, Janssen, 2, 8, Janssen Pharmaceutical K.K, 9, Mitsubishi Tanabe, 2, 9, Mitsubishi Tanabe Pharma Co., 2, Mitsubishi-Tanabe Pharma Corp, 2, 8, 9, Nippon Kayaku, 2, Nipponkayaku, 2, 9, Nipponkayaku Co.Ltd., 2, Novartis, 2, 8, Novartis Pharma K.K, 2, 9, Novartis Pharma K.K., 2, Pfizer, 2, 8, Pfizer Japan, 2, 9, Pfizer Japan Inc., 2, Sanofi, 8, Sanofi K.K, 9, Shionogi & Co., 2, Shionogi & Co., LTD., 2, Taiho, 2, 8, 9, Taisho, 9, Taisho Toyama, 2, 8, Takahashi Industrial and Economic Research Foundation, 2, Takeda, 2, 8, Takeda Pharmaceutical Co., Ltd., 2, Teijin, 2, 8, UCB, 8, 9, UCB Japan, 9; **Y. Tanaka**, Abbvie, 8, AbbVie, 5, 8, Asahi-kasei, 2, Asahi-Kasei, 2, Asahi-kasei, BMS, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Ono, Pfizer, Sanofi, Takeda, UCB, 2, Astellas, 8, Astellas Pharma, 9, Astellas Pharma, Inc., 2, 3, 5, 8, 9, Astellas, BMS, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi-Tanabe, Pfizer, Sanofic, UCB, YL Biologics, 8, BMS, 2, 5, 8, Bristol-Myers, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Daiichi-Sankyo, 2, 8, Daiichi-Sankyo, Astellas, Eli Lilly, Chugai, Sanofi, Abbvie, Pfizer, YL Biologics, Bristol-Myers, 8, Eisai, 2, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 8, Genzyme, 5, Glaxo-Smithkline, UCB, Mitsubishi-Tanabe, Novartis, Eisai, Takeda, Janssen, Asahi-kasei, 8, Janssen,

8, Mitsubishi-Tanabe, 2, 8, Mitsubishi-Tanabe, Bristol-Myers, Eisai, Chugai, Takeda, Abbvie, Astellas, Daiichi-Sankyo, Ono, MSD, Taisho-Toyama., 2, Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, 2, Novartis, 8, Ono, 2, Pfizer, 5, 8, Pfizer Inc, 8, Roche, 5, Sanofi, 2, Takeda, 2, 8, Teijin, 8, UCB, 2, YL Biologics, 8; **M. Rokuda**, Astellas Pharma, Inc., 3, 9; **H. Izutsu**, Astellas Pharma, Inc., 3, 9; **Y. Kaneko**, Astellas Pharma, Inc., 3, 9; **M. Fukuda**, Astellas Pharma, Inc., 3, 9; **D. Kato**, Astellas Pharma, Inc., 3, 9; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5.

Abstract Number: 0508

Longer Term Safety and Efficacy of Peficitinib in Patients with Rheumatoid Arthritis After 22.7 Months Mean Treatment Exposure: Interim Data from a Long-Term, Open-Label Extension Study in Japan, Korea and Taiwan

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

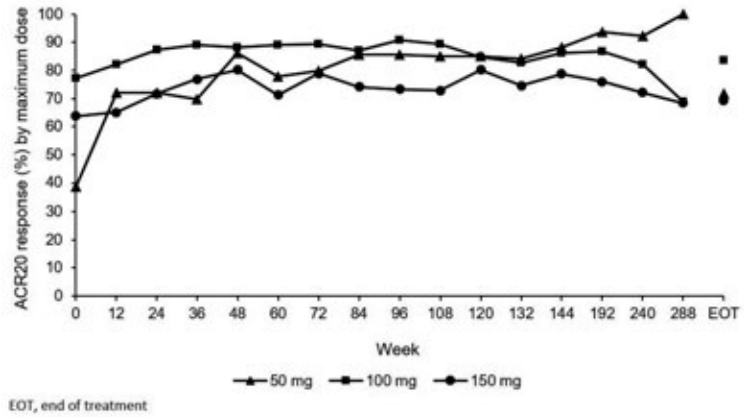
Session Title: RA – Treatments Poster I: Novel Treatments

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Peficitinib, a novel oral Janus kinase (JAK) inhibitor, demonstrated efficacy and an acceptable safety profile in a Phase 2b study (RAJ1 study, NCT01649999) and in Phase 3 studies (RAJ3 study [inadequate

Figure: ACR20 response at each visit by maximum dose level (full analysis set)



EOT, end of treatment

Table: Overview of treatment-emergent adverse events in the overall period (safety analysis set)

	RAJ1 (N=201)	RAJ3 (N=225)	RAJ4 (N=417)	Total (N=843)
All TEAEs, n (%)	193 (96.0)	201 (89.3)	363 (87.1)	757 (89.8)
All SAEs, n (%)	49 (24.4)	40 (17.8)	49 (11.8)	138 (16.4)
Drug-related[1] TEAEs, n (%)	172 (85.6)	148 (65.8)	266 (63.8)	586 (69.5)
Drug-related[1] SAEs, n (%)	19 (9.5)	27 (12.0)	30 (7.2)	76 (9.0)
≥ Grade 3 TEAE[2], n (%)	63 (33.8)	51 (22.7)	70 (16.8)	189 (22.4)
Most common TEAEs occurring in ≥10% of patients in the overall period, n (%)				
Nasopharyngitis	109 (54.2)	79 (35.1)	147 (35.3)	335 (39.7)
Rheumatoid arthritis	47 (23.4)	21 (9.3)	37 (8.9)	105 (12.5)
Herpes zoster	31 (15.4)	25 (11.1)	43 (10.3)	99 (11.7)
TEAEs leading to permanent discontinuation, n (%)				
All	39 (19.4)	19 (8.4)	29 (7.0)	87 (10.3)
Drug-related[1]	22 (10.9)	12 (5.3)	21 (5.0)	55 (6.5)
SAEs	20 (10.0)	12 (5.3)	18 (4.3)	50 (5.9)
Drug-related SAEs	9 (4.5)	8 (3.6)	13 (3.1)	30 (3.6)
Deaths[3]	0	0	1 (0.2)	1 (0.1)
Mean duration of study drug exposure (months)[4]	41.6	17.9	16.2	22.7
Incidence rates (95% confidence interval) of TEAEs of special interest per 100 patient years*				
Serious infections	1.1 (0.6, 2.3)	4.3 (2.6, 7.3)	2.5 (1.5, 4.2)	2.3 (1.6, 3.1)
Herpes zoster-related disease	4.9 (3.4, 6.9)	7.8 (5.3, 11.5)	8.5 (6.4, 11.4)	6.8 (5.6, 8.3)
Malignancy	0.7 (0.3, 1.7)	1.5 (0.6, 3.5)	1.4 (0.7, 2.8)	1.1 (0.7, 1.8)

Treatment-emergent adverse events were defined as any AE that started or worsened in severity after initial dose of study drug in the extension study until the end of the final observation.

*Patient-years definition: PYs = from initial dose date up to first incidence of infections that require intravenous anti-infectious therapy for patients who had at least 1 event. Otherwise, the duration of the patients are summed as from initial dose through follow-up; count = number of patients who had at least 1 infection that require intravenous anti-infectious therapy; incidence rate = calculated as (100 × number of patients who had at least 1 incidence / total patient-year).

[1]Possible or probable, as assessed by the investigator or records where relationship is missing.

[2]National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE): grade 3, severe or medically significant; grade 4, life-threatening; grade 5, death related to AE.

AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

[3]One death during the study due to diffuse large B-cell lymphoma, considered probably related to the study drug, and one death after the end of the study due to uterine sarcoma, considered possibly related to the study drug.

[4]Duration of exposure for overall period (days) was calculated as: date of the last dose of study drug - date of initial dose of study drug + 1

response to DMARDs], NCT02308163, and RAJ4 study [inadequate response to MTX], NCT02305849). In this long-term interim extension study (NCT01638013), we report the safety and efficacy data for peficitinib (mean treatment exposure, 22.7 months) in patients who previously completed these Phase 2b and 3 studies.

Methods: This multicenter, open-label extension study was conducted in Japan, Korea and Taiwan. All patients had RA previously diagnosed according to 1987 ACR criteria or 2010 ACR/EULAR criteria (RAJ1 study followed 1987

ACR criteria exclusively). Patients received oral peficitinib (50 mg, 100 mg or 150 mg) once daily. The starting dose was 100 mg (RAJ3/4) or 50 mg (RAJ1). Doses could be increased to 150 mg/day or reduced (from 100 mg/day or 150 mg/day) to 50 mg/day according to clinical response and safety assessment, as judged by the investigator. Prior and concomitant administration of study-specific non-biological DMARDs was dependent upon the preceding study. For patients in the RAJ1 study and RAJ3 monotherapy study with peficitinib, administration of DMARDs was prohibited from the end of the assessments to the initiation of administration of peficitinib in this extension study. For the RAJ3/RAJ4 peficitinib combination studies, with DMARDs (including MTX) and MTX, respectively, subjects received the concomitant drug concerned from the termination of study to the initiation of administration of peficitinib and throughout the treatment period in this extension study. Discontinuation of the concomitant drug or alteration of the dose was permitted within the range not exceeding or falling below the baseline dose in the previous study. Efficacy outcomes were assessed in the total patient population and grouped according to their preceding study.

Results: In total, 843 patients received peficitinib: RAJ1, n=201; RAJ3, n=225; RAJ4, n=417. During long-term treatment, ACR20 responses were maintained from baseline for patients receiving maximum doses of 100/150 mg/day, and were improved then maintained in patients receiving maximum doses of 50 mg/day **(Figure)**. ACR components and DAS28-CRP also demonstrated continuous improvements from the baselines of preceding studies. Treatment-emergent adverse events (AEs) were reported in 757 (89.8%) patients **(Table)**, primarily grade 1/2 in severity; the most common were nasopharyngitis, RA and herpes zoster. Rates of AEs of special interest (serious infections, herpes zoster-related disease and malignancies) were greater for patients from RAJ3/4 than RAJ1. There was no evidence to support a trend towards increasing incidence rate/100 patient years with treatment duration. One death during and one death after the study were considered probably and possibly related to study drug, respectively **(Table)**.

Conclusion: This interim analysis after 22.7 months mean treatment exposure demonstrated no additional safety concerns were observed with longer term administration of peficitinib in RA patients, and efficacy was maintained for the study duration.

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Abstract Number: 0509

Safety Profile of Upadacitinib in Rheumatoid Arthritis: Integrated Analysis from the SELECT Phase 3 Clinical Program

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Treatments Poster I: Novel Treatments

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA), an oral JAK1-selective inhibitor, was evaluated in a comprehensive clinical program of 5 pivotal Phase 3 randomized-controlled trials (RCTs) across the full spectrum of RA patient (pt) populations[1-5].

Assess the overall safety of UPA as monotherapy (mono) and as combination therapy with background csDMARDs in pts with moderately to severely active RA from the safety database of the Phase 3 clinical program.

Methods: Treatment-emergent adverse events (TEAEs) from 5 pivotal, randomized, double-blind, placebo- or active-controlled Phase 3 trials of UPA 15 mg (included in all 5 trials) or 30 mg QD (included in 4 trials) in RA pts were analyzed and summarized for the integrated placebo (PBO) (3 trials; 12/14 weeks), the integrated methotrexate (MTX) (2 trials; mean exposure: 36 weeks), the originator adalimumab (ADA) (mean exposure: 42 weeks), the UPA 15 mg (mean exposure: 53 weeks) and the UPA 30 mg (mean exposure: 59 weeks) groups as exposure adjusted event rates (EAERs; events/100 patient-years [E/100PY]).

ACR/ARP 2019 *Submission deadline: Tuesday, June 4, 2019, noon Eastern Time*

ISS Overall Safety_Modified Encore

Table. Overall TEAEs and AESIs in patients treated with UPA compared to PBO and active controls

				UPA All Phase 3 Long-term	
	PBO Pooled N=1042, PYS=256.8, E/100 PY (95% CI)	MTX, Pooled[a] N=530, PYS=368.7, E/100PY (95% CI)	ADA 40 mg EOW N=579, PYS=467.8, E/100PY (95% CI)	Any UPA 15 mg QD N=2630, PYS=2655.1 E/100PY (95% CI)	Any UPA 30 mg QD N=1204, PYS=1365.0 E/100PY (95% CI)
Any AE	447.4 (421.9, 474.1)	321.7 (303.6, 340.5)	294.8 (279.4, 310.8)	295.7 (289.2, 302.3)	368.7 (358.6, 379.0)
Any SAE	9.3 (6.0, 13.9)	11.9 (8.7, 16.0)	15.6 (12.2, 19.6)	15.0 (13.6, 16.6)	21.3 (18.9, 23.9)
Any AE leading to discontinuation	10.9 (7.2, 15.8)	9.5 (6.6, 13.2)	11.1 (8.3, 14.6)	8.4 (7.4, 9.6)	13.3 (11.5, 15.4)
Deaths[b]	0.8 (0.1, 2.8)	0.3 (0.0, 1.5)	0.9 (0.2, 2.2)	0.5 (0.3, 0.8)	1.0 (0.5, 1.7)
AESIs					
Serious Infections	3.1 (1.3, 6.1)	2.7 (1.3, 5.0)	4.3 (2.6, 6.6)	3.8 (3.1, 4.7)	6.2 (5.0, 7.7)
Herpes Zoster	1.2 (0.2, 3.4)	1.4 (0.4, 3.2)	1.3 (0.5, 2.8)	3.7 (3.0, 4.5)	7.0 (5.7, 8.6)
MACE (adjudicated)	1.2 (0.2, 3.4)	0.5 (0.1, 2.0)	0.4 (0.1, 1.5)	0.6 (0.4, 1.0)	1.0 (0.5, 1.6)
VTE (adjudicated)	0.4 (0.0, 2.2)	0.5 (0.1, 2.0)	1.1 (0.3, 2.5)	0.6 (0.3, 1.0)	0.3 (0.1, 0.8)
Any non-melanoma skin cancer (NMSC)	0.4 (0.0, 2.2)	0.3 (0.0, 1.5)	0.2 (0.0, 1.2)	0.3 (0.1, 0.6)	1.1 (0.6, 1.8)
Any malignancy other than NMSC	0.4 (0.0, 2.2)	0.8 (0.2, 2.4)	0.6 (0.1, 1.9)	0.9 (0.5, 1.3)	1.4 (0.8, 2.2)

[a]Includes patients on MTX monotherapy censored at time of rescue to combination therapy (either to UPA + MTX or addition of csDMARD); [b]Deaths included non-treatment emergent deaths (3 on UPA 15 mg, 3 on UPA 30 mg and 1 on ADA). MACE was defined as CV death, non-fatal MI, and non-fatal stroke. VTE was defined as deep vein thrombosis and pulmonary embolism.

ADA, adalimumab, AE, adverse events; E, events; EOW, every other week; MACE, major adverse cardiovascular events; MTX, methotrexate; PBO, placebo; PYS, patient years; QD, once-daily; SAE, serious adverse events; TEAEs, treatment-emergent AEs; UPA, upadacitinib; VTE, venous thromboembolic events.

Results: Across the Phase 3 trials, 3834 pts received ≥1 dose of UPA 15 mg (n=2630) or 30 mg QD (n=1204), with no option to switch doses, for a total of 4020.1 PY of UPA exposure. The EAERs of overall SAEs and AEs leading to discontinuation on UPA 15 mg were comparable to ADA; while the rates of both were higher on UPA 30 vs UPA 15 mg and MTX. Across the studies, upper respiratory tract infection, nasopharyngitis and urinary tract infections were the most commonly reported AEs and occurred more frequently in the UPA compared with PBO. Rates of deaths were comparable across the treatment groups. Serious infection (SIEs) rates were comparable between UPA 15 mg and ADA while higher on UPA compared with MTX. Rates of herpes zoster (HZ) were higher in both UPA groups vs MTX and ADA. The rates of SIE and HZ were higher on UPA 30 vs 15 mg. Rates of malignancies (excluding non-melanoma skin cancer [NMSC]) and adjudicated MACE and VTE were comparable across the treatment groups. The rate of NMSC in UPA 15 mg, MTX and ADA groups were similar with higher rates in the UPA 30 mg group, however the rates for both UPA groups were in the range reported for RA patients treated with DMARDs[3]. The age-gender adjusted standardized incidence ratio (SIR, 95% CI) for malignancies other than NMSC (15 mg: 0.98 [0.61, 1.49], 30 mg: 1.49 [0.85, 2.42]) was within the range expected for the general population (SEER 18 Registry 2000-2015).

Conclusion: The rate of SIE on UPA 15 mg was similar to ADA. The rate of HZ was higher on both UPA doses compared to MTX and ADA. The rates of VTE, MACE, and malignancy were comparable with that observed in the MTX and ADA groups while also being consistent with reported rates in the RA population.

References:

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4. Fleischmann R et al. Arth & Rheum. 2018;70.
5. van Vollenhoven R, et al. Arthritis Rheumatol. 2018;70 (S 10) [Abs].

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Bristol-Myers-Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5; **Y. Zhang**, AbbVie, 3, 4, Abbvie Inc, 1, 4; **N. Khan**, Abbvie Inc, 1, 4; **B. Hendrickson**, AbbVie, 3, 4, Abbvie Inc, 1, 4; **J. Enejosa**, AbbVie, 3, 4, Abbvie Inc, 1, 4; **G. Burmester**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma., 5, 8, AbbVie Inc., 5, 8, BMS, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Merck Shar & Dohme, 5, 8, MSD, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche, Sanofi-Genzyme, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Union Chimique Belge, 2, 5, 8.

Abstract Number: 0510

Treatment with Upadacitinib Is Associated with Improvements in Reverse Cholesterol Transport in Patients with Rheumatoid Arthritis: Correlation with Changes in Inflammation and HDL Levels

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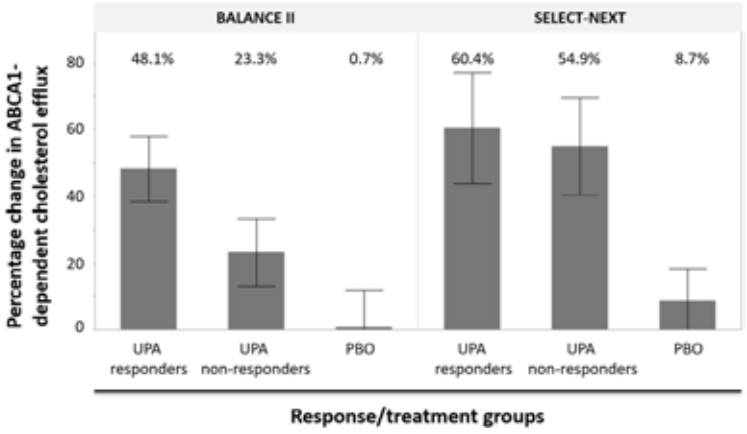
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic inflammatory condition associated with increased rates of atherosclerotic progression via pathogenic remodeling of high-density lipoprotein (HDL)-associated proteins, resulting in reduction of HDL function.[1] Upadacitinib (UPA), a selective JAK1 inhibitor, has demonstrated efficacy in patients (pts) with moderate-to-severe RA.
We assess UPA treatment on cholesterol efflux capacity (CEC) and evaluate CEC with changes in inflammation and serum lipids.

Methods: A subset of pts from the Phase 2 BALANCE II study[2] and the Phase 3 SELECT-NEXT study[3] were selected from the pool of pts with serum samples available at baseline and Week (Wk) 12. Pts were matched for age and sex, and selected based on level of response to UPA therapy (BALANCE II, UPA 6mg BID: 39 responders [mean change in DAS28-CRP at Wk 12 -3.22] and 30 non-responders [mean change in DAS28-CRP -0.33]; SELECT-NEXT, UPA 15mg

Figure: Changes in ABCA1-dependent cholesterol efflux are significantly elevated in UPA-treated patients at Week 12



QD: 20 responders [mean change in DAS28-CRP -3.78] and 20 non-responders [mean change in DAS28-CRP -0.67]). A demographically similar placebo (PBO) group without selection based on degree of response was also included (20 pts from each study). J774 macrophages labeled with [^{3}H]-cholesterol (treated with cAMP to express ABCA1 or left untreated) were exposed to patient sera. The difference between cholesterol efflux from serum-exposed and unexposed cells provided a measurement of CEC. Results were compared between the responder, non-responder, and PBO groups using Tukey's mean comparison method; correlations were calculated using the Pearson method; all statistical analyses were performed in JMP 13.10 (SAS Institute).

Results: In both studies, changes in global and ABCA1-dependent CEC, and to a lesser extent non-ABCA1-dependent CEC, were significantly higher in the UPA-treated group compared with the PBO group (Figure). In the BALANCE II study, there was a significant increase in CEC among UPA responders relative to PBO and a numerically apparent difference observed between UPA non-responders and PBO. Notably, in the SELECT-NEXT study, a similar and highly significant improvement in CEC was observed for both UPA-treated groups relative to PBO (without a significant difference between the responder and non-responder groups). Despite the lack of a consistent association between change in CEC and change in clinical disease activity, observed increases in CEC correlated significantly with reductions in CRP levels in all groups across all active treatment groups. Additionally, increases in CEC at Wk 12 correlated well with changes in total blood cholesterol and HDL levels, but weakly with changes in blood low-density lipoprotein (LDL) levels.

Conclusion: UPA treatment is associated with significant improvement in CEC. This effect was observed even among those demonstrating minimal clinical response (but not in those treated with PBO). The effect seems to be primarily driven by ABCA1-dependent cholesterol efflux and is strongly correlated with a rise in HDL cholesterol as well as reduction in systemic inflammation as measured by change in CRP.

Reference:

1. Charles-Schoeman C, et al. Arthritis Rheumatol 2017;69:46–57; 2. Genovese MC, et al. Arthritis Rheumatol 2016;68:2857–66; 3. Burmester GR, et al. Lancet 2018;391:2503–12

Disclosure: C. Charles-Schoeman, Abbvie, 2, AbbVie, 2, Amgen, 5, BMS, 2, Bristol Myers Squibb, 2, Gilead, 5, Octapharma, 2, 5, Pfizer, 2, 5, Regeneron, 5, Regeneron/Sanofi, 5, Sanofi, 5; **T. Sornasse**, AbbVie, 3, 4; **J. Sokolove**, AbbVie, 3, 4.

Abstract Number: 0511

A Comparative Analysis of Upadacitinib Monotherapy and Upadacitinib Combination Therapy for the Treatment of Rheumatoid Arthritis from Two Phase 3 Trials

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA), a selective JAK1 inhibitor, has demonstrated efficacy and safety in patients with rheumatoid arthritis (RA) as monotherapy and in combination with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) such as methotrexate (MTX).[1,2] However, UPA monotherapy has not been compared directly with UPA combination therapy in the Phase 3 program.
We compare the efficacy of UPA monotherapy and UPA in combination with MTX using data from two Phase 3 trials of RA patients with an inadequate response (IR) to prior MTX therapy.

Methods: In SELECT-MONOTHERAPY, 648 MTX-IR patients were randomized to receive UPA 15 mg or 30 mg monotherapy once daily (QD), or continue with MTX monotherapy (cMTX; given as a blinded study drug), for 14 weeks. In SELECT-NEXT, 661 csDMARD-IR patients were randomized to receive UPA 15 mg or 30 mg QD or placebo (PBO) for 12 weeks on a background of csDMARDs. Only patients receiving concomitant MTX (with or without additional csDMARDs) at baseline in SELECT-NEXT were included in this analysis. The primary endpoints of both studies were the proportion of patients achieving ACR20 and DAS28(CRP) ≤3.2. Additional endpoints included ACR50/70, DAS28(CRP) < 2.6, CDAI remission (≤2.8), CDAI low disease activity (LDA; ≤10), and change from baseline in HAQ-DI. Logistic regression or ordinary least squares analyses were used to compare outcomes with monotherapy versus combination therapy, adjusting for demographics and baseline disease characteristics.

Results: A total of 1114 patients were included in the analysis, of whom 648 received monotherapy in SELECT-MONOTHERAPY and 466 received combination therapy in SELECT-NEXT. Of the patients receiving combination therapy, 338 (72.5%) were receiving MTX background therapy only and 128 (27.5%) were receiving MTX plus other csDMARDs. Baseline characteristics were generally similar between the study cohorts; the majority of patients in both studies were female and of white ethnicity, with a mean age of approximately 55 years and a mean MTX dose of approximately 17 mg/week. Consistent with previously reported results from SELECT-MONOTHERAPY[1] and SELECT-NEXT,[2] both UPA monotherapy and UPA combination therapy led to significant improvements in efficacy outcomes versus cMTX/PBO+MTX (Table). No significant differences were observed between UPA monotherapy and UPA combination therapy across a range of clinical endpoints, including ACR20/50/70 responses and measures of LDA and remission. In addition, improvements in quality of life as measured by HAQ-DI were similar with UPA monotherapy and combination therapy. Efficacy was comparable between the two UPA doses in the combination therapy group, whereas in the monotherapy group numerically higher responses were observed with UPA 30 mg versus UPA 15 mg.

Table. Week 12/14 efficacy outcomes in patients receiving monotherapy and combination therapy.

Endpoint	Monotherapy (Week 14) (SELECT-MONOTHERAPY)			Combination therapy with MTX (Week 12) (SELECT-NEXT)			p-value (mono vs combo)[a]	
	cMTX (n=216)	UPA 15 mg QD (n=217)	UPA 30 mg QD (n=215)	PBO+MTX (n=165)	UPA 15 mg QD+MTX (n=148)	UPA 30 mg QD+MTX (n=153)	UPA 15 mg QD	UPA 30 mg QD
ACR20, %	41.2	67.7	71.2	38.2	66.2	65.4	0.962	0.561
DAS28(CRP) ≤3.2, %	19.4	44.7	53.5	18.2	48.6	49.7	0.564	0.878
ACR50, %	15.3	41.9	52.1	16.4	41.2	43.1	0.578	0.217
ACR70, %	2.8	22.6	33.0	4.8	20.9	26.1	0.172	0.134
DAS28(CRP) <2.6, %	8.3	28.1	40.9	9.7	28.4	30.7	0.594	0.142
CDAI ≤2.8, %	0.9	12.9	19.5	3.0	9.5	13.7	0.063	0.069
CDAI ≤10, %	24.5	34.6	46.5	20.6	41.2	43.8	0.164	0.661
HAQ-DI change from baseline	-0.22	-0.56	-0.63	-0.32	-0.61	-0.60	0.593	0.108

[a]Based on logistic regression (binary outcomes) or ordinary least squares (continuous outcome) analyses for the comparison of monotherapy versus combination therapy, with treatment group as the fixed factor and various demographic (age, sex, race, region, weight, and smoking status) and baseline characteristics (hsCRP, DAS28[CRP], HAQ-DI, RA duration, and RF and anti-CCP positivity) as covariates.

Conclusion: In MTX-IR patients with RA, the efficacy of UPA appears comparable when administered as monotherapy or when given in combination with MTX.

Reference:

1. Smolen J, et al. Ann Rheum Dis 2018;77:67—8 2. Burmester GR, et al. Lancet 2018;391:2503–12

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Abstract Number: 0512

Efficacy and Safety of Upadacitinib Monotherapy in MTX-naïve Patients with Early Active RA Receiving Treatment Within 3 Months of Diagnosis: A Post-hoc Analysis of the SELECT-EARLY

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SESSION INFORMATION
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Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Early treatment of RA within the therapeutic window (0-3 months from symptom onset), has been associated with improved clinical outcomes and physical function. However, ≤42% of RA patients (pts) visit a rheumatologist within 90 days of symptom onset[1,2]. Upadacitinib (UPA), an oral, reversible, potent JAK-1 selective inhibitor[3] demonstrated efficacy in pts with moderate to severely active RA who were MTX-naïve or had an inadequate response to csDMARDs/bDMARDs[4-6].

Methods: In SELECT–EARLY, MTX-naïve pts with active RA and poor prognosis were randomized 1:1:1 to once-daily UPA monotherapy at 15 or 30 mg or weekly MTX (titrated up to 20 mg/week through Week 8). Efficacy (including ACR, DAS28(CRP), CDAI responses and change in mTSS) and safety outcomes from a post-hoc analysis of patients who received treatment within 90 days from diagnosis are reported here. The statistical significance defined as $p< 0.05$ was exploratory in nature.

Results: A total of 270 pts commenced treatment within 90 days from RA diagnosis (median: 44 days [11, 89]). Pts in each arm were mostly female (70%), had moderately to severely active RA with mean DAS28(CRP) =5.9±1.02, had structural joint damage (mean mTSS =7.7±21.5) and were seropositive for both ACPA and RF at baseline (72%)4.

Table 1: Efficacy at Week 24 in Early RA patients who received treatment within 90 days of diagnosis

	MTX N=99	UPA 15 mg QD N=98	UPA 30 mg QD N=73
ACR20, % (95% CI)	61 (51, 70)	85 (78, 92)***	84 (75, 92)**
ACR50, % (95% CI)	38 (29, 48)	66 (57, 76)***	75 (66, 85)***
ACR70, % (95% CI)	22 (14, 30)	49 (39, 59)***	62 (51, 73)***
DAS28CRP≤3.2, % (95% CI)	34 (25, 44)	64 (55, 74)***	69 (58, 79)***
DAS28CRP<2.6, % (95% CI)	20 (12, 28)	55 (45, 65)***	60 (49, 72)***
ΔDAS28CRP, LSM (95% CI)	-2.5 (-2.8, -2.2)	-3.3 (-3.6, -3.1)***	-3.8 (-4.1, -3.5)***
CDAI≤10 (LDA), % (95% CI)	42 (33, 52)	59 (50, 69)*	69 (58, 79)***
CDAI≤2.8 (REM), % (95% CI)	11 (5, 17)	38 (28, 47)***	40 (29, 51)***
Boolean REM, % (95% CI)	7 (2, 12)	34 (24, 43)***	37 (26, 48)***
ΔHAQ-DI, LSM (95% CI)	-0.7 (-0.9, -0.6)	-1.0 (-1.1, -0.9)**	-0.9 (-1.1, -0.8)
ΔPain, mm, LSM (95% CI)	-34.1 (-39.4, -29.1)	-44.5 (-49.4, -39.7)**	-48.9 (-54.9, -43.0)***
ΔmTSS, LSM (95% CI)	1.2 (0.64, 1.68)	0.2 (-0.3, 0.7)**	-0.1 (-0.7, 0.5)**
Pts with no radiographic progression, % (95% CI)	66 (56, 76)	83 (76, 91)*	95 (90, 100)***

Values are either response rates (%) or least square mean differences from baseline with 95% CI values. Results are based on following analyses: binary endpoints: NRI; DAS28CRP, Pain, HAQ-DI, data after first rescue overwritten by LOCF; mTSS: Imputation by Linear extrapolation; Pts with no radiographic progression = ΔmTSS≤0; Boolean remission definition: TJC ≤1, SJC ≤1, CRP ≤1 mg/dL and PtGA ≤1 [0–10 scale]; ***, **, * p-value ≤ 0.001, 0.01, and 0.05 level for UPA vs MTX comparison, respectively.

Δ, Change from baseline; QD, once daily; ACR20/50/70, 20, 50 or 70% improvement in ACR criteria; CDAI, clinical disease activity index; DAS28CRP, 28-joint disease activity score using C-reactive protein; HAQ-DI, health assessment questionnaire disability index; LDA, low disease activity; LOCF, Last observation carried forward; LSM, least-square means; mTSS, modified total Sharp score; Pts, patients; REM, remission; SJC, swollen joint count; TJC, tender joint count.

ACR/ARP 2019 *Submission deadline: Tuesday, June 4, 2019, noon Eastern Time*
EARLY_RA Duration

Table 2: Summary of TEAEs through Week 24 in Early RA patients who received treatment within 90 days of diagnosis, n (%)

	MTX N=99, n (%)	UPA 15 mg QD N= 98, n (%)	UPA 30 mg QD N=73, n (%)
Any Adverse Event (AE)	70 (70.7)	63 (64.3)	53 (72.6)
Any Serious AE	5 (5.1)	3 (3.1)	8 (11.0)
AE Leading to Discontinuation of Study Drug	8 (8.1)	2 (2.0)	3 (4.1)
Deaths*	0	0	2 (2.7)
Infection	36 (36.4)	25 (25.5)	24 (32.9)
-Serious Infection	0	2 (2.0)	4 (5.5)
-Opportunistic Infection	0	0	1 (1.4)
-Herpes Zoster ¥	0	2 (2.0)	2 (2.7)
Hepatic disorder	4 (4.0)	6 (6.1)	5 (6.8)
Gastrointestinal perforation ϕ	0	0	1 (1.4)
Malignancy (including NMSC)	0	0	0
MACE (adjudicated) δ	0	0	2 (2.7)
VTE (adjudicated)	0	0	0
	*Deaths: UPA 30, 1 CV death, 1 death due to pneumonia and sepsis ¥Herpes zoster: All events were mild to moderate ϕ Gastrointestinal perforation: UPA 30, 1 pt with large intestinal perforation δ MACE, major adverse cardiovascular events (adjudicated): UPA30, 1 non-fatal MI and 1 CV death (sudden).		

AE, adverse event; NMSC, non-melanoma skin cancer; VTE, venous thromboembolic events; PE, pulmonary embolism. DVT, deep vein thrombosis.

At Week 24, compared to MTX, significantly greater proportions of pts receiving UPA 15 or 30 mg monotherapy achieved efficacy outcomes including ACR20, 50 and 70 responses, DAS28CRP< 2.6, CDAI≤2.8 or Boolean remission. Improvements in physical function (HAQ-DI) and decrease in pain were also significantly greater in pts receiving UPA 15 and 30 mg vs MTX at Week 24. Treatment with UPA was also associated with a greater inhibition of structural joint damage compared with MTX (Table 1). Safety outcomes were consistent with the full study and the integrated

safety analysis (all phase 3 studies of UPA). Compared to MTX, higher frequencies of serious infections and herpes zoster were reported in both UPA groups. There were 2 deaths in total (UPA 30 mg: 1 due to cardiovascular death and 1 due to pneumonia and sepsis) (Table 2).

Conclusion: In RA pts, early initiation of treatment with UPA 15 mg and 30 mg monotherapy within 3 months from diagnosis was associated with clinically meaningful improvements in efficacy, including remission and inhibition of progression of structural joint damage compared to MTX. The safety profile was consistent with the overall study and the integrated phase 3 safety analysis[7]. UPA was more effective than MTX in enabling more patients to reach their treatment targets of remission or low disease activity when treated within 3 months of diagnosis.

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Abstract Number: 0513

Upadacitinib as Monotherapy in Patients with Rheumatoid Arthritis: Results at 48 Weeks

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Treatments Poster I: Novel Treatments

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In the SELECT-MONOTHERAPY trial, upadacitinib (UPA), an oral JAK1-selective inhibitor, showed efficacy when used as monotherapy over 14 weeks (wks) in rheumatoid arthritis (RA) patients (pts) with an inadequate response to methotrexate (MTX).[1]

Safety and efficacy of UPA monotherapy were assessed through 48 wks in an ongoing long-term extension period of SELECT-MONOTHERAPY.

Methods: At baseline (BL), pts on stable MTX were randomized to either continue MTX (cMTX, given as a blinded study drug) or switch to once-daily (QD) UPA at 15 (UPA15) or 30 mg (UPA30) monotherapy for 14 wks. From Wk14, the start of a long-term blinded extension, pts randomized to cMTX were switched to UPA15 or 30mg per pre-specified assignment at BL, pts randomized to UPA15 or 30 continued their initial treatment. No dose adjustments

Table 1. Efficacy Endpoints at Week 48 (as observed); Percentage of patients with a response; n/N (%)

	cMTX→ UPA 15 MG	cMTX→ UPA 30 MG	UPA 15 MG	UPA 30 MG
ACR20	77/96 (80)	75/91 (82)	150/172 (87)	162/186 (87)
ACR50	63/94 (67)	55/92 (60)	121/174 (70)	133/185 (72)
ACR70	44/94 (47)	39/93 (42)	80/176 (46)	99/183 (54)
DAS28-CRP≤3.2	67/96 (70)	66/92 (72)	126/174 (72)	148/185 (80)
DAS28-CRP<2.6	56/96 (58)	50/92 (54)	96/174 (55)	126/185 (68)
CDAI≤10	69/95 (73)	65/90 (72)	123/172 (72)	142/185 (77)
CDAI≤2.8	26/95 (27)	19/90 (21)	48/172 (28)	77/185 (42)
Change from BL in HAQ-DI	-0.69	-0.73	-0.73	-0.83

Table 2. Adverse event (AE) summary; E/100PY

	UPA 15 MG N=318 PYs=336.0 E/100PYs	UPA 30 MG N=311 PYs=337.1 E/100PYs
Any Adverse Event (AE)	254.2	319.2
Serious AE	19.6	17.8
AE Leading To Discontinuation Of Study Drug	8.9	10.1
Serious Infection[§]	5.1	4.4
Herpes Zoster[‡]	3.3	7.7
Hepatic disorder[*]	7.7	12.5
Any Malignancy (excluding NMSC)[Y]	1.5	1.2
MACE (adjudicated)[δ]	0.9	1.5
Venous Thromboembolism (adjudicated)	1.2	0
Death[†]	0.9	0.3

E/100PY, events per 100 patient-years; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular (CV) event (CV death, non-fatal myocardial infarction [MI], non-fatal stroke)

[§]Serious Infection: Most frequently reported SI were pneumonia, bronchitis, cellulitis, HZ and UTI

[‡]Herpes zoster: mostly 1 or 2 dermatomes,1 opthalmic

[*]Hepatic disorder: mostly transaminase elevations that were mild to moderate in severity.

[Y]Malignancies: 5 breast cancers (UPA15: 3 pts, UPA30: 2 pts), 2 colorectal cancers (UPA15:1 pt, UPA30:1 pt), 1 non-Hodgkin's lymphoma (UPA15), 1 malignant melanoma (UPA30)

[δ]MACE : UPA15: 3 CV deaths; UPA 30: 2 non-fatal MI, 2 non-fatal stroke; 1 CV death

[†]Deaths: UPA15: 1 hemorrhagic stroke (ruptured aneurysm), 1 congestive cardiomyopathy and 1 sudden cardiac death; UPA30: 1 fatal MI.

for UPA were allowed. Starting at Wk26, for pts who did not achieve CDAI ≤10, background csDMARDS could be initiated. Efficacy data up to the Wk48 visit are reported "As Observed". Adverse events (AE) per 100 pt yrs (PYs) are summarized up to May 25 2018.

Results: Of 648 pts randomized at BL, 598 (92%) completed 14 wks and continued on to the extension period. By May 25 2018, 16% discontinued study drug; 5% due to AE, 0.5% due to lack of efficacy, 4% withdrew consent, 1% were lost to follow-up, and 6% discontinued due to other reasons. Cumulative exposures to UPA15 and UPA30 were 336.0 PYs and 337.1 PYs, respectively. Starting from Wk26, background csDMARDs were initiated for approximately18% of pts. Based on As Observed data, for pts on UPA from BL through Wk48 on UPA15 [250/300 (83%)] and UPA30 [251/298 (84%)], clinical and functional outcomes continued to improve, or were maintained (Table 1). For pts continuing UPA15 and 30, DAS28-CRP< 2.6 was 55% and 68%, and CDAI≤2.8 was 28% and 42%, respectively. Pts who were switched from cMTX to UPA15 or 30 at Wk14 had similar responses at Wk 48. The most frequently reported treatment-emergent AEs were urinary tract infection, blood creatine phosphokinase increase, upper respiratory tract infection, nasopharyngitis, worsening of RA, herpes zoster (HZ), alanine aminotransferase increase, and bronchitis. The most frequently reported serious AE was pneumonia (8 events). Events/100PYs were numerically higher in the UPA30 vs UPA15 arm for HZ, and hepatic disorders, and were comparable for serious infections and malignancies excluding non-melanoma skin cancer (Table 2). Adjudicated venous thromboembolic events (VTE) were observed only on UPA15 (2 pts with deep vein thrombosis and 2 pts with pulmonary embolism; all patients had at least one risk factor for VTE).

Conclusion: UPA 15 or 30 monotherapy resulted in similar improvements in signs and symptoms and physical function through 48 wks. The overall benefit-risk profile of both doses of UPA was favorable based on the safety and efficacy data through Wk48 but will be confirmed through an integrated safety analysis across all the phase 3 trials.

Reference:

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Abstract Number: 0514

A Pooled Analysis of 1-year Clinical Outcomes Among 6-month Responders and Non-responders from Three Randomized Controlled Studies of TNF Inhibitor Biosimilars in Patients with Rheumatoid Arthritis

Josef Smolen,[1] Michael Weinblatt,[2] Paul Emery,[3] Jung Yoon Choe,[4] Jonathan Kay,[5] Jieun Lee,[6] Gihyun Myung,[6] Hyoryeong Seo,[6] and Jeehoon Ghil[6], [1]Medical University of Vienna, Vienna, Austria, [2]Brigham and Women's Hospital, Boston, MA, [3]Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom, [4]Division of Rheumatology, Daegu Catholic University Medical Center, Daegu, Republic of Korea, [5]UMass Memorial Medical Center and University of Massachusetts Medical School, Worcester, MA, [6]Samsung Bioepis Co., Ltd., Incheon, Republic of Korea

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Treatments Poster I: Novel Treatments

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: SB4, SB2, and SB5 are biosimilars of etanercept, infliximab, and adalimumab. Phase III randomized, double-blind studies were conducted to compare efficacy and safety between biosimilars and reference products.

The objective of this study is to assess and compare 1-year outcomes among 6-month responders and non-responders.

Methods: Patients who had 6-month data from each phase III study were pooled and categorized, based on their disease status at 6 months (week 24 for etanercept and adalimumab and week 30 for infliximab) and 1 year (week 52 for etanercept and adalimumab and week 54 for infliximab).

Responders included patients who achieved an ACR20 response or low disease activity (including remission) by DAS28, SDAI, or CDAI at 6 months. Those who did not or dropped out were considered non-responders.

Table 1. Proportion of responders at 1 year based on 6-month clinical outcomes

Group	ACR20 responders at 1 year (n,%)		DAS28 (Remission + LDA) at 1 year (n,%)		SDAI (Remission + LDA) at 1 year (n,%)		CDAI (Remission + LDA) at 1 year (n,%)	
	Responder at 6 month	Non-responder at 6 month	Responder at 6 month	Non-responder at 6 month	Responder at 6 month	Non-responder at 6 month	Responder at 6 month	Non-responder at 6 month
All Tx Combined	850 (81.9%)	140 (35.1%)	302 (70.4%)	193 (19.1%)	509 (78.8%)	215 (27.3%)	489 (78.0%)	206 (25.4%)
BS Combined	465 (83.2%)	85 (38.3%)	177 (74.1%)	118 (21.8%)	287 (80.8%)	112 (26.5%)	275 (79.5%)	114 (26.2%)
RP Combined	385 (80.4%)	55 (31.1%)	125 (65.8%)	75 (16.1%)	222 (76.3%)	103 (28.2%)	214 (76.2%)	92 (24.5%)
SB4+ETN	359 (83.9%)	46 (37.7%)	121 (69.9%)	73 (19.4%)	219 (82.0%)	77 (27.2%)	207 (82.1%)	73 (24.5%)
SB2+INF	252 (76.6%)	49 (27.8%)	83 (63.8%)	51 (13.6%)	157 (74.1%)	59 (20.2%)	156 (73.2%)	54 (18.5%)
SB5+ADA	239 (85.1%)	45 (44.6%)	98 (77.8%)	69 (27.0%)	133 (79.6%)	79 (37.1%)	126 (77.8%)	79 (35.9%)
SB4	183 (84.3%)	27 (41.5%)	67 (72.8%)	41 (21.6%)	118 (82.5%)	36 (25.9%)	111 (82.2%)	39 (26.5%)
ETN	176 (83.4%)	19 (33.3%)	54 (66.7%)	32 (17.1%)	101 (81.5%)	41 (28.5%)	96 (82.1%)	34 (22.5%)
SB2	123 (77.4%)	24 (27.6%)	44 (68.8%)	28 (15.4%)	80 (75.5%)	25 (18.0%)	79 (74.5%)	25 (17.9%)
INF	129 (75.9%)	25 (28.1%)	39 (59.1%)	23 (11.9%)	77 (72.6%)	34 (22.2%)	77 (72.0%)	29 (19.1%)
SB5	159 (86.9%)	34 (48.6%)	66 (79.5%)	49 (28.8%)	89 (84.0%)	51 (35.2%)	85 (81.0%)	50 (33.8%)
ADA	80 (81.6%)	11 (35.5%)	32 (74.4%)	20 (23.3%)	44 (72.1%)	28 (41.2%)	41 (71.9%)	29 (40.3%)

ACR, American college of rheumatology; ADA, reference product adalimumab; BS, biosimilars; CDAI, Clinical Disease Activity Index scores; DAS28, disease activity score based on 28-joint count; ETN, reference product etanercept ; INF, reference product infliximab; RP, reference products; SDAI, Simplified Disease Activity Index scores, Tx, treatments

The primary outcome was the proportion of responders who maintained responses from 6 months to 1 year or non-responders at 6 months who achieved responses at 1 year.

Results: Data from 1,437 patients were included in the analysis. For all treatments combined, 81.9% of ACR20 responders, 70.4%, 78.8%, and 78.0% of responders with DAS28, SDAI, and CDAI low disease activity (LDA) at 6 months maintained their responses at 1 year, and 35.1%, 19.1%, 27.3%, and 25.4% of 6-month non-responders achieved responses at 1 year, respectively. The proportions of patients maintaining or achieving an ACR20 response or DAS28, SDAI, and CDAI LDA at 1 year were similar across different treatment groups (Table 1).

Conclusion: A pooled analysis of TNF inhibitor biosimilars and reference products showed that about 20-30% of responders lost their response, while about 20-30% gained it. Thus, the overall stability of disease fluctuation in our 1-year phase III studies is a consequence of a similar success and failure rate. The validity of these data can be seen by the similarities in these outcomes between different types of TNF-inhibitors and similarity between biosimilars and respective reference products.

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Abstract Number: 0515

Clinical Responses in Patients with Inadequate Response to bDMARDs upon Treatment with Upadacitinib

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Treatments Poster I: Novel Treatments

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA), a JAK1-selective inhibitor, demonstrated efficacy in the SELECT-BEYOND study in patients (pts) with moderate to severe rheumatoid arthritis (RA) on a stable dose of csDMARDs who had inadequate response (IR) or intolerance to bDMARDs,. In this analysis we evaluated clinical responses among pts receiving UPA and placebo (PBO) based on the number and mechanism of action (MOA) of prior bDMARDs.

Methods: 498 pts were randomized to UPA 15mg or UPA 30mg once daily (QD) or PBO for 12 weeks (wks), after which pts on PBO received UPA 15 or 30mg QD from Wk 12 onwards.[1] Pts were subgrouped by the number and/or MOA of bDMARD(s) received prior to enrollment: 1) lack of efficacy (LoE) to ≥1 anti-TNF, 2) LoE to an anti-IL-6, and 3) the number of prior bDMARDs (1 vs 2 vs ≥3). ACR20/50/70 responses, DAS28-CRP low disease activity (LDA, ≤3.2), CDAI LDA (≤10), and CDAI remission (≤2.8) were evaluated at Wk 12. The frequency and percentage of treatment-emergent adverse events (TEAE) in each subgroup was assessed over the first 12 wks. Missing values of the efficacy endpoints were imputed using non-responder imputation (NRI). Nominal *P*-values are reported without multiplicity adjustment.

Table 1

	LoE to Anti-TNF			LoE to Anti-IL-6			Overall		
	PBO (%) N=152	UPA 15 (%) N=146	UPA 30 (%) N=151	PBO (%) N=40	UPA 15 (%) N=38	UPA 30 (%) N=47	PBO (%) N=169	UPA 15 (%) N=164	UPA 30 (%) N=165
ACR20	29.6	65.1***	55.0***	20.0	55.6**	58.1**	28.4	64.6***	56.4***
ACR50	11.8	36.3***	35.1***	10.0	18.5	29.0	11.8	34.1***	35.8***
ACR70	6.6	13.0	23.8***	0	3.7	16.1*	6.5	11.6	23.0***
DAS28-CRP≤3.2 (LDA)	14.5	46.6***	42.4***	10.0	22.2	38.7*	14	43.0***	42.0***
CDAI≤10 (LDA)	14.5	33.6***	33.1***	3.3	22.2*	35.5**	14	32.0***	34.0***
CDAI≤2.8 (REM)	5.3	8.9	11.9*	0	0	9.7	4.7	7.9	11.5*

***, **, * statistically significant at 0.001, 0.01, and 0.05 level comparing either UPA dose vs PBO using Cochran-Mantel-Haenszel test adjusting for stratification factor, respectively.
ACR20/50/70, 20%, 50% or 70% improvement in ACR core criteria; DAS28-CRP, 28-joint disease activity score using C-reactive protein; CDAI, clinical disease activity index; LDA, low disease activity; REM, remission

Table 2

	IR/intolerance to 1 Prior bDMARDs			IR/intolerance to 2 Prior bDMARDs			IR/intolerance to ≥3 Prior bDMARDs			Overall		
	PBO (%) N=83	UPA 15 (%) N=86	UPA 30 (%) N=66	PBO (%) N=46	UPA 15 (%) N=40	UPA 30 (%) N=51	PBO (%) N=40	UPA 15 (%) N=38	UPA 30 (%) N=47	PBO (%) N= 169	UPA 15 (%) N= 164	UPA 30 (%) N= 165
ACR20	28.9	61.6***	57.6***	32.6	70.0***	58.8**	22.5	65.8***	51.1**	28.4	64.6***	56.4***
ACR50	12	32.6**	39.4***	15.2	32.5	35.3*	7.5	39.5**	29.8**	11.8	34.1***	35.8***
ACR70	7.2	14.0	27.3***	8.7	5.0	21.6	2.5	13.2	17.0*	6.5	11.6	23.0***
DAS28-CRP≤3.2 (LDA)	16.9	43***	47***	13.0	45.0**	37.3**	10.0	42.1**	40.4**	14	43.0***	42.0***
CDAI≤10 (LDA)	15.7	32.6**	39.4***	17.4	27.5	31.4	7.5	34.2**	27.7*	14	32.0***	34.0***
CDAI≤2.8 (REM)	6.0	9.3	18.2	4.3	5.0	5.9	2.5	7.9	8.5	4.7	7.9	11.5*

***, **, * statistically significant at 0.001, 0.01, and 0.05 level comparing either UPA dose vs PBO using Cochran-Mantel-Haenszel test adjusting for stratification factor, respectively.
ACR20/50/70, 20%, 50% or 70% improvement in ACR core criteria; DAS28-CRP, 28-joint disease activity score using C-reactive protein; CDAI, clinical disease activity index; LDA, low disease activity; REM, remission

Results: Overall baseline disease duration was ~13 years. The majority of pts had LoE to ≥1 anti-TNF (449, 90%); 88 (18%) had LoE to an anti-IL-6; 235 (47%), 137(28%), and 125 (25%) had been treated with 1, 2, or ≥3 prior bDMARDs, respectively.[1] At Wk 12, clinical responses were numerically, and often statistically, better for pts receiving either dose of UPA vs PBO, irrespective of their prior bDMARD exposure and the number of prior bDMARDs received. As most pts had LoE to ≥1 anti-TNF, responses in this group were comparable to the overall study population **(Table 1)**. Pts with LoE to an anti-IL-6 receiving UPA 15 or 30 mg QD experienced improvements vs PBO, particularly in achieving LDA and remission, although responses in these pts were generally lower compared to the overall study population. As expected, there was a trend towards lower responses as the number of prior bDMARDs increased **(Table 2).** Responses at Wk 24 were generally consistent with those at Wk 12 (data not shown). TEAEs across the subgroups were consistent with the overall study population (data not shown).

Conclusion: At Wk 12, treatment with UPA at either 15 or 30 mg QD led to significantly better clinical responses vs PBO in this treatment-refractory population, including in pts with LoE to an anti-TNF or an anti-IL-6, and those who had IR/intolerance to 1, 2 or ≥3 prior bDMARDs, with consistent safety profiles as to the overall study population.

Disclosure: M. Weinblatt, AbbVie, 5, Amgen, 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Can Fite, 4, CanFite, 4, Canfite, 1, Corrona, 5, CORRONA, 5, Crescendo Bioscience, 2, 5, Gilead, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Inmedix, 4, Lilly, 5, Lycera, 4, 5, Lycero, 1, Merck, 5, Novartis, 5, Pfizer, 5, Regeneron, 2, Roche, 5, Samsung, 5, Sanofi, 2, Sanofi-Regeneron, 2, Scipher, 1, 4, 5, Set Point, 5, SetPoint, 5, UCB, 5, Vorso, 4; **G. Thomson**, AbbVie, 2, Amgen, 5; **K. Chen**, AbbVie, 3, 4; **S. Meerwein**, AbbVie, 3, 4, Abbvie Inc, 1, 4; **C. Schlacher**, AbbVie, 3, 4; **J. Cush**, AbbVie, 5, Amgen, GSK, Lilly, Merck, Novartis, Pfizer, Sanofi-Aventis, Servier and Roche., 2, Celgene, 5, Janssen, 5, Merck, Pfizer, Sanofi-Aventis, 5, 8, Novartis, 5, Pfizer, 5.

Abstract Number: 0516

Impact of Baseline Demographics and Disease Activity on Outcomes in Patients with Rheumatoid Arthritis Receiving Upadacitinib

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA), an oral selective JAK1 inhibitor, has demonstrated favorable efficacy and acceptable safety in five Phase 3 global studies in patients with moderately to severely active rheumatoid arthritis (RA).[1–5] This analysis reports the efficacy and safety of UPA in predefined RA patient subgroups based on differences in baseline demographics and disease activity.

Methods: Data were pooled from three pivotal, double-blind, PBO-controlled, multicenter, Phase 3 studies in patients with RA who had an inadequate response (IR) to conventional synthetic DMARDs (csDMARD-IR: SELECT-NEXT [N=661]), MTX (MTX-IR; SELECT-COMPARE [N=1629]), or biologic DMARDs (bDMARD-IR: SELECT-BEYOND

Table. Proportions of patients in each subgroup achieving ACR20 or DAS28(CRP) ≤3.2 at Week 12.

	ACR20				DAS28(CRP) ≤3.2			
n/N (%)	PBO (UPA 15 mg analysis set)	UPA 15 mg	PBO (UPA 30 mg analysis set)	UPA 30 mg	PBO (UPA 15 mg analysis set)	UPA 15 mg	PBO (UPA 30 mg analysis set)	UPA 30 mg
Sex								
Male	82/220 (37)	133/196 (68)	34/81 (42)	41/74 (55)	37/220 (17)	95/196 (49)	17/81 (21)	32/74 (43)
Female	282/821 (34)	573/840 (68)	93/309 (30)	197/310 (64)	115/821 (14)	376/840 (45)	45/309 (15)	143/310 (46)
Age								
<65 years	284/814 (35)	558/822 (68)	93/286 (33)	180/284 (63)	122/814 (15)	378/822 (46)	47/286 (16)	133/284 (47)
≥65 years	80/227 (35)	148/214 (69)	34/104 (33)	58/100 (58)	30/227 (13)	93/214 (44)	15/104 (14)	42/100 (42)
Weight								
<60 kg	61/168 (36)	130/164 (79)	19/68 (28)	41/62 (66)	26/168 (16)	93/164 (57)	9/68 (13)	31/62 (50)
60 – <100 kg	260/738 (35)	489/715 (68)	86/257 (34)	150/246 (61)	113/738 (15)	326/715 (46)	46/257 (18)	113/246 (46)
≥100 kg	43/135 (32)	87/157 (55)	22/65 (34)	47/76 (62)	13/135 (10)	52/157 (33)	7/65 (11)	31/76 (41)
BMI								
<18.5 kg/m²	4/16 (25)	15/22 (68)	0/7 (0)	4/10 (40)	2/16 (13)	11/22 (50)	0/7 (0)	5/10 (50)
18.5 – <25 kg/m²	98/275 (36)	212/272 (78)	32/102 (31)	62/93 (67)	43/275 (16)	146/272 (54)	15/102 (15)	46/93 (50)
25 – <30 kg/m²	141/373 (38)	219/318 (69)	51/127 (40)	67/105 (64)	67/373 (18)	156/318 (49)	28/127 (22)	54/105 (51)
≥30 kg/m²	119/371 (32)	260/424 (61)	44/152 (29)	105/175 (60)	39/371 (11)	158/424 (37)	19/152 (13)	70/175 (40)
Race								
White	324/891 (36)	631/906 (70)	110/330 (33)	207/334 (62)	136/891 (15)	427/906 (47)	55/330 (17)	154/334 (46)
Non-white	40/150 (27)	75/130 (58)	17/60 (28)	31/50 (62)	16/150 (11)	44/130 (34)	7/60 (12)	21/50 (42)
Geographic region								
North America	90/321 (28)	186/319 (58)	53/200 (27)	117/198 (59)	41/321 (13)	131/319 (41)	25/200 (13)	85/198 (43)
South/Central America	92/181 (51)	146/183 (80)	N/A	N/A	34/181 (19)	103/183 (56)	N/A	N/A
Western Europe	29/92 (32)	59/89 (66)	17/57 (30)	37/55 (67)	18/92 (20)	41/89 (46)	9/57 (16)	30/55 (55)
Eastern Europe	126/359 (35)	256/360 (71)	41/97 (42)	60/95 (63)	49/359 (14)	155/360 (43)	19/97 (20)	41/95 (43)
Asia	12/37 (32)	32/38 (84)	N/A	N/A	6/37 (16)	19/38 (50)	N/A	N/A
Other	15/51 (29)	27/47 (57)	16/36 (44)	24/36 (67)	4/51 (8)	22/47 (47)	9/36 (25)	19/36 (53)
RA duration								
<5 years	156/456 (34)	310/461 (67)	54/155 (35)	104/154 (68)	66/456 (15)	195/461 (42)	25/155 (16)	77/154 (50)
5 – <10 years	82/221 (37)	154/228 (68)	21/70 (30)	45/89 (51)	29/221 (13)	106/228 (47)	8/70 (11)	37/89 (42)
≥10 years	126/364 (35)	242/347 (70)	52/165 (32)	89/141 (63)	57/364 (16)	170/347 (49)	29/165 (18)	61/141 (43)
RF								
Positive	282/794 (36)	573/803 (71)	89/277 (32)	174/259 (67)	114/794 (14)	392/803 (49)	43/277 (16)	126/259 (49)
Negative	82/247 (33)	132/232 (57)	38/113 (34)	64/125 (51)	38/247 (15)	79/232 (34)	19/113 (17)	49/125 (39)
ACPA status								
Positive	292/813 (36)	587/818 (72)	92/284 (32)	186/275 (68)	115/813 (14)	408/818 (50)	44/284 (16)	137/275 (50)
Negative	72/225 (32)	118/217 (54)	35/105 (33)	52/109 (48)	37/225 (16)	62/217 (29)	18/105 (17)	38/109 (35)
RF and ACPA status								
Both positive	259/727 (36)	534/740 (72)	81/252 (32)	163/238 (69)	100/727 (14)	370/740 (50)	37/252 (15)	117/238 (49)
≥1 negative	105/311 (34)	170/294 (58)	46/137 (34)	75/146 (51)	52/311 (17)	100/294 (34)	25/137 (18)	58/146 (40)
Both negative	49/160 (31)	80/155 (52)	27/80 (34)	41/88 (47)	23/160 (14)	41/155 (27)	12/80 (15)	29/88 (33)
≥1 positive	315/880 (36)	626/881 (71)	100/309 (32)	197/296 (67)	129/880 (15)	430/881 (49)	50/309 (16)	146/296 (49)
1 positive, 1 negative	56/151 (37)	90/139 (65)	19/57 (33)	34/58 (59)	29/151 (19)	59/139 (42)	13/57 (23)	29/58 (50)
hs-CRP[a,b]								
Tertile 1	134/341 (39)	218/345 (63)	53/134 (40)	74/123 (60)	80/341 (24)	165/345 (48)	34/134 (25)	58/123 (47)
Tertile 2	108/340 (32)	237/345 (69)	37/128 (29)	77/132 (58)	36/340 (11)	160/345 (46)	14/128 (11)	57/132 (43)
Tertile 3	122/360 (34)	251/346 (73)	37/128 (29)	87/129 (67)	36/360 (10)	146/346 (42)	14/128 (11)	60/129 (47)

[a]UPA 15 mg set: Tertile 1: 0.2 – <6.5 mg/L; tertile 2: 6.5 – <15.6 mg/L; tertile 3: 15.6 – ≤198.0 mg/L
UPA 30 mg set: Tertile 1: 0.2 – <5.7 mg/L; tertile 2: 5.7 – <14.1 mg/L; tertile 3: 14.1 – ≤150.0 mg/L
[b]Patients were required to have CRP >3 mg/L (SELECT-NEXT and SELECT-BEYOND) or >5 mg/L (SELECT-COMPARE)

[N=498]). Two integrated analysis sets were evaluated: one comparing UPA 15 mg QD vs PBO (SELECT-NEXT, SELECT-COMPARE, SELECT-BEYOND) and the other comparing UPA 15 mg QD and UPA 30 mg QD vs PBO (SELECT-NEXT, SELECT-BEYOND). All patients received background treatment with csDMARDs. The proportion of patients achieving ACR20 and DAS28(CRP) ≤3.2 at Week 12 was evaluated by predefined baseline demographics and disease activity measure groups, including age, sex, weight, BMI, race, geographic region, duration of RA, RF, and ACPA status, and level of high sensitivity CRP. Non-responder imputation was used for missing data. Subgroup analyses for safety were performed for age, race, sex, weight, BMI, and Asian region.

Results: Across the three Phase 3 studies, 1036, 384, and 1041 patients received UPA 15 mg QD, UPA 30 mg QD or PBO, respectively. The demographic and baseline disease characteristics in the two integrated analysis sets were balanced across treatment groups. ACR20 and DAS28 ≤3.2 response rates at Week 12 were consistently higher with UPA 15 mg and UPA 30 mg vs PBO across the evaluated demographic and baseline disease characteristics (Table).

The efficacy of UPA 15 mg QD was generally similar to that observed with UPA 30 mg QD. At 12 weeks, the proportion of patients with treatment-emergent AEs, serious AEs, severe AEs, and AEs leading to discontinuation were generally comparable across different age, sex, race, weight, and BMI groups. Compared with the global population, patients receiving UPA in the Asian region had a higher rate of CPK elevations (UPA 30 mg only) and herpes zoster; herpes zoster also has been observed to be higher in the Asian region with other JAK inhibitors.[6,7]

Conclusion: In this analysis of pooled integrated efficacy data in csDMARD-IR or bDMARD-IR patients with RA, UPA 15 mg or 30 mg QD in combination with csDMARDs improved efficacy outcomes at Week 12 when compared with PBO across all predefined subgroups evaluated.

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Disclosure: M. Weinblatt, AbbVie, 5, Amgen, 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Can Fite, 4, CanFite, 4, Canfite, 1, Corrona, 5, CORRONA, 5, Crescendo Bioscience, 2, 5, Gilead, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Inmedix, 4, Lilly, 5, Lycera, 4, 5, Lycero, 1, Merck, 5, Novartis, 5, Pfizer, 5, Regeneron, 2, Roche, 5, Samsung, 5, Sanofi, 2, Sanofi-Regeneron, 2, Scipher, 1, 4, 5, Set Point, 5, SetPoint, 5, UCB, 5, Vorso, 4; **E. Mysler**, AbbVie, 2, 5, 8, BMS, 2, 5, Bristol-Myers Squibb, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Lilly, 2, 5, Novartis, 2, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sandoz, 2, 5; **A. Östör**, AbbVie, 2, 5, 8, 9, BMS, 2, 5, 8, 9, Celgene, 2, 5, 8, 9, Eli Lilly, 2, 5, 8, 9, Gilead, 2, 5, 9, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, Roche, 2, 5, 8, 9, Sanofi, 2, 5, 8, 9, UCB, 2, 5, 8, 9; **A. Broadwell**, AbbVie, 5, 8, Amgen, 5, 8, AstraZeneca, 5, Celgene, 5, 8, Eli Lilly, 2, 5, GSK, 8, Horizon, 8, Janssen, 2, 5, 8, Janssen Research & Development, LLC., 2, Mallinckrodt, 8, Novartis, 5, 8, Pfizer, 5, 8, Radius, 8, Sandoz, 5, Sanofi-Regeneron, 8, UCB, 8; **S. Jeka**, None; **K. Dunlap**, AbbVie, 3, 4; **J. Suboticki**, AbbVie, 1, 3, 4; **J. Enejosa**, AbbVie, 3, 4, Abbvie Inc, 1, 4; **B. Hendrickson**, AbbVie, 3, 4, Abbvie Inc, 1, 4; **S. Zhong**, AbbVie, 3, 4; **K. Cherny**, AbbVie, 3, 4; **G. Wright**, AbbVie, 5, 8, Amgen, 5, 8, BMS, 5, 8, Exagen, 5, 8, Janssen, 5, Lilly, 5, 8, medac, 5, Myriad Autoimmune, 5, 8, Novartis, 5, 8, Pfizer, 5, Sanofi-Regeneron, 5, 8, UCB, 5, 8, Medical Education Resource, 8, Vindico, 8, Association of Women in Rheumatology, 3.

Abstract Number: 0517

A Subgroup Analysis of Clinical Efficacy Response and Quality of Life Outcomes from Phase 3 Study of Filgotinib in Patients with Inadequate Response to Biologic DMARDs

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	FIL 200 mg QD (n =147)	FIL 100 mg QD (n = 153)	PBO (n = 148)	Δ in response vs PBO (95% CI), p-value FIL 200 mg	FIL 100 mg
ACR20					
No. of prior bDMARDs					
1	45/73 (61.6)	49/86 (57.0)	28/77 (36.4)	25.3 (8.5, 42.1), 0.003	20.6 (4.4, 36.8), 0.012
2	26/37 (70.3)	19/33 (57.6)	12/36 (33.3)	36.9 (12.9, 61.0), 0.002	24.2 (−1.5, 50.0), 0.055
≥3	26/37 (70.3)	20/34 (58.8)	6/34 (17.6)	52.6 (30.3, 75.0), <0.001	41.2 (17.3, 65.0), <0.001
Prior bDMARD MOAs					
1 MOA	63/97 (64.9)	66/110 (60.0)	31/92 (33.7)	31.3 (16.6, 45.9), <0.001	26.3 (12.0, 40.6), <0.001
>1 MOA	34/50 (68.0)	22/43 (51.2)	15/55 (27.3)	40.7 (21.3, 60.1), <0.001	23.9 (2.8, 45.0), 0.021
Prior TNF inhibitor					
Yes	79/121 (65.3)	73/134 (54.5)	39/124 (31.5)	33.8 (21.2, 46.4), <0.001	23.0 (10.5, 35.5), <0.001
No	18/26 (69.2)	15/19 (78.9)	7/24 (29.2)	40.1 (10.7, 69.5), 0.010	49.8 (19.2, 80.3), 0.002
Prior IL-6 inhibitor					
Yes	26/34 (76.5)	19/35 (54.3)	10/32 (31.3)	45.2 (20.7, 69.7), <0.001	23.0 (−3.0, 49.1), 0.084
No	71/113 (62.8)	69/118 (58.5)	36/116 (31.0)	31.8 (18.7, 44.9), <0.001	27.4 (14.3, 40.5), <0.001
DAS28(CRP) ≤2.6					
No. of prior bDMARDs					
1	22/73 (30.1)	25/86 (29.1)	8/77 (10.4)	19.7 (5.9, 33.6), 0.004	18.7 (5.7, 31.7), 0.003
2	7/37 (18.9)	8/33 (24.2)	4/36 (11.1)	7.8 (−11.2, 26.8), 0.52	13.1 (−7.6, 33.9), 0.21
≥3	4/37 (10.8)	6/34 (17.6)	0	10.8 (−2.0, 23.6), 0.12	17.6 (1.9, 33.4), 0.025
Prior bDMARD MOAs					
1 MOA	28/97 (28.9)	32/110 (29.1)	9/92 (9.8)	19.1 (7.2, 31.0), <0.001	19.3 (7.9, 30.7), <0.001
>1 MOA	5/50 (10.0)	7/43 (16.3)	3/55 (5.5)	4.5 (−7.6, 16.7), 0.47	10.8 (−3.8, 25.5), 0.100
Prior TNF					
Yes	24/121 (19.8)	32/134 (23.9)	11/124 (8.9)	11.0 (1.5, 20.5), 0.017	15.0 (5.4, 24.6), 0.001
No	9/26 (34.6)	7/19 (36.8)	1/24 (4.2)	30.4 (6.5, 54.4), 0.011	32.7 (4.8, 60.5), 0.014
Prior IL-6 inhibitor					
Yes	7/34 (20.6)	7/35 (20.0)	2/32 (6.3)	14.3 (−4.7, 33.3), 0.15	13.8 (−4.9, 32.4), 0.15
No	26/113 (23.0)	32/118 (27.1)	10/116 (8.6)	14.4 (4.2, 24.6), 0.003	18.5 (8.1, 28.9), <0.001
DAS28(CRP) <3.2					
No. of prior bDMARDs					
1	36/73 (49.3)	37/86 (43.0)	14/77 (18.2)	31.1 (15.5, 46.8), <0.001	24.8 (10.1, 39.6), <0.001
2	13/37 (35.1)	11/33 (33.3)	8/36 (22.2)	12.9 (−10.3, 36.2), 0.30	11.1 (−12.8, 35.1), 0.42
≥3	11/37 (29.7)	9/34 (26.5)	1/34(2.9)	26.8 (8.2, 45.4), 0.003	23.5 (4.7, 42.4), 0.013
Prior bDMARD MOAs					
1 MOA	43/97(44.3)	47/110(42.7)	16/92(17.4)	26.9 (13.3, 40.6), <0.001	25.3 (12.3, 38.4), <0.001
>1 MOA	17/50(34.0)	10/43(23.3)	7/55(12.7)	21.3 (3.6, 39.0), 0.011	10.5 (−6.9, 28.0), 0.19
Prior TNF inhibitor					
Yes	47/121 (38.8)	49/134 (36.6)	21/124 (16.9)	21.9 (10.2, 33.6), <0.001	19.6 (8.4, 30.9), <0.001
No	13/26 (50.0)	8/19 (42.1)	2/24 (8.3)	41.7 (15.5, 67.8), 0.002	33.8 (4.3, 63.3), 0.013
Prior IL-6 inhibitor					
Yes	16/34 (47.1)	11/35 (31.4)	4/32 (12.5)	34.6 (11.2, 57.9), 0.003	18.9 (−3.2, 41.1), 0.082
No	44/113 (38.9)	46/118 (39.0)	19/116 (16.4)	22.6 (10.5, 34.7), <0.001	22.6 (10.7, 34.5), <0.001

Table 1. Efficacy outcomes ACR20, DAS28(CRP) for low disease activity and remission at week 12 relative to prior bDMARD use Data presented as n (%) unless otherwise specified. bDMARD, biologic DMARD; CI, confidence interval; FIL, filgotinib; MOA, mechanism of action; PBO, placebo; QD, once daily.

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Treatments Poster I: Novel Treatments

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: There is an unmet medical need to treat RA in patients who have failed prior biologic DMARD treatments (biologic DMARD inadequate response; bDMARD-IR), some of which target the IL-6 pathway. Patients who are bDMARD-IR are considered more treatment resistant and have more variable responses to treatment than treatment- or bDMARD-naïve patients. Questions remain as to whether the clinical efficacy of the oral, selective Janus kinase (JAK)-1 inhibitor filgotinib differs among patients with prior exposure to IL-6 inhibitors. We explored the efficacy of filgotinib in bDMARD-IR patients with active RA based on number and mechanism of action (MOA) of prior biologics.

Methods: The global, phase 3 FINCH-2 (NCT02873936) study enrolled 449 bDMARD-IR patients with active RA, who were randomized in a 1:1:1 manner to receive once-daily filgotinib 200 mg, filgotinib 100 mg, or placebo for 24 weeks.[1] This subgroup analysis evaluated filgotinib efficacy respective to the number and MOA of prior bDMARD use. Clinical efficacy was assessed using ACR20, DAS28(CRP) for low disease activity and remission, and patient-reported outcomes at weeks 12 and 24. Quality-of-life outcomes were assessed by change in HAQ disability index (HAQ-DI), change in SF-36-Physical Component score, and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) at weeks 12 and 24.

	Δ from baseline			LSM of treatment difference, 95% CI, p-value	
	FIL 200 mg QD (n = 147)	FIL 100 mg QD (n = 153)	PBO (n = 148)	FIL 200 mg	FIL 100 mg
A HAQ-DI					
No. of prior bDMARDs					
1	−0.51 (0.609)	−0.50 (0.604)	−0.29 (0.617)	−0.24 (−0.43, −0.06), 0.011	−0.25 (−0.43, −0.07), 0.006
2	−0.69 (0.602)	−0.45 (0.706)	−0.20 (0.475)	−0.47 (−0.75, −0.19), 0.001	−0.24 (−0.53, 0.05), 0.099
≥3	−0.49 (0.533)	−0.48 (0.486)	−0.12 (0.408)	−0.34 (−0.58, −0.09) 0.007	−0.36 (−0.61, −0.11), 0.005
Prior bDMARD MOAs					
1 MOA	−0.57 (0.614)	−0.56 (0.610)	−0.26 (0.591)	−0.31 (−0.48, −0.14), <0.001	−0.33 (−0.49, −0.16), <0.001
>1 MOA	−0.51 (0.547)	−0.28 (0.589)	−0.19 (0.463)	−0.32 (−0.58, −0.12) 0.002	−0.10 (−0.32, 0.11), 0.34
Prior TNF inhibitor					
Yes	−0.51 (0.571)	−0.46 (0.577)	−0.23 (0.572)	−0.27 (−0.41, −0.13), <0.001	−0.24 (−0.37, −0.10), <0.001
No	−0.76 (0.649)	−0.65 (0.760)	−0.21 (0.427)	−0.56 (−0.91, −0.21), 0.002	−0.56 (−0.94, −0.18), 0.005
Prior IL-6 inhibitor					
Yes	−0.83 (0.684)	−0.49 (0.769)	−0.25 (0.310)	−0.57 (−0.88, −0.26), <0.001	−0.28 (−0.59, 0.03), 0.079
No	−0.47 (0.538)	−0.48 (0.555)	−0.23 (0.594)	−0.24 (−0.39, −0.10), <0.001	−0.27 (−0.42, −0.13), <0.001
SF-36 PCS score					
No. of prior bDMARDs					
1	7.7 (8.4)	7.2 (8.2)	5.4 (8.6)	2.6 (−0.1, 5.2), 0.057	2.0 (−0.5, 4.6), 0.11
2	8.2 (7.4)	6.3 (9.5)	1.9 (7.7)	5.6 (1.7, 9.4), 0.005	3.5 (−0.4, 7.5), 0.081
≥3	7.0 (6.6)	6.3 (7.1)	1.0 (6.4)	6.9 (3.6, 10.2), <0.001	6.6 (3.1, 10.1), <0.001
Prior bDMARD MOAs					
1 MOA	7.7 (8.3)	7.6 (8.3)	4.8 (8.8)	3.0 (0.6, 5.3), 0.014	2.9 (0.6, 5.2), 0.013
>1 MOA	7.6 (6.5)	4.5 (7.6)	1.5 (6.4)	6.4 (3.6, 9.2), <0.001	3.6 (0.6, 6.5), 0.018
Prior TNF inhibitor					
Yes	7.1 (7.2)	6.4 (8.6)	3.8 (8.7)	3.7 (1.6, 5.7), <0.001	3.1 (1.0, 5.1), 0.003
No	10.3 (9.6)	9.4 (4.6)	2.9 (4.6)	6.9 (3.0, 10.7), <0.001	6.3 (2.2, 10.3), 0.003
Prior IL-6 inhibitor					
Yes	10.6 (8.1)	6.6 (8.5)	3.7 (6.3)	7.6 (3.8, 11.5), <0.001	3.6 (−0.3, 7.5), 0.067
No	6.8 (7.4)	6.9 (8.2)	3.6 (8.6)	3.2 (1.2, 5.3), 0.002	3.5 (1.4, 5.5), 0.001
FACIT-F					
No. of prior bDMARDs					
1	9.4 (12.1)	8.9 (10.5)	5.4 (11.1)	3.3 (−0.1, 6.7), 0.055	2.6 (−0.6, 5.8), 0.11
2	9.3 (10.8)	6.0 (11.4)	5.4 (9.4)	5.0 (0.1, 9.8), 0.044	0.1 (−4.9, 5.1), 0.97
≥3	10.0 (10.4)	9.2 (11.1)	1.6 (9.0)	8.8 (3.9, 13.7), <0.001	8.1 (3.0, 13.1), 0.002
Prior bDMARD MOAs					
1 MOA	9.9 (11.5)	9.5 (10.3)	5.0 (10.7)	4.4 (1.4, 7.3), 0.004	3.6 (0.7, 6.4), 0.014
>1 MOA	9.0 (10.9)	5.3 (11.6)	3.8 (9.7)	6.0 (1.8, 10.1), 0.005	2.0 (−2.4, 6.4), 0.37
Prior TNF inhibitor					
Yes	9.0 (11.0)	7.8 (10.4)	4.7 (10.7)	4.5 (1.9, 7.2), <0.001	2.9 (0.3, 5.5), 0.027
No	12.6 (12.4)	11.9 (12.7)	3.9 (8.8)	6.3 (0.6, 12.0), 0.032	6.2 (0.2, 12.3), 0.044
Prior IL-6 inhibitor					
Yes	14. 3 (11.7)	8.9 (13.6)	4.8 (8.4)	9.3 (3.6, 15.1), 0.002	4.3 (−1.4, 10.0), 0.14
No	8.2 (10.8)	8.2 (10.0)	4.5 (10.8)	3.8 (1.2, 6.4), 0.005	3.2 (0.6, 5.8), 0.017

Table 2. Quality of life outcomes HAQ-DI, SF-36 physical component, and FACIT-F change from baseline at week 12 with respect to prior bDMARD use Data presented as mean (SD) unless otherwise specified. bDMARD, biologic DMARD; CI, confidence interval; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; FIL, filgotinib; LSM, least squares mean; MOA, mechanism of action; PBO, placebo; PCS, physical component summary; QD, once daily; SD, standard deviation.

Results: Of the 448 patients randomized and treated at baseline, 80.4% were female with a mean age of 56 years and a mean RA duration of 12.4 years. Prior bDMARD exposure, including the total number and MOA, was well balanced amongst the 3 treatment arms. Clinical efficacy outcomes—as measured by ACR20, DAS28(CRP) ≤3.2, and DAS28(CRP) < 2.6—are provided in **Table 1**. Quality-of-life outcomes—as measured by change in HAQ-DI, change in SF-36-Physical Component score, and FACIT-F at week 12—are provided in **Table 2**.

Conclusion: Compared with placebo, filgotinib demonstrated improved clinical outcomes in bDMARD refractory patients. The efficacy observed with filgotinib was maintained with no significant effects based on the number and MOA of prior bDMARD use, including in patients with prior exposure to IL-6 inhibitors.

Reference:

1. Genovese MC, et al. Safety and Efficacy of Filgotinib in a Phase 3 Trial of Patients with Active Rheumatoid Arthritis and Inadequate Response or Intolerance to Biologic Dmards [abstract]. Arthritis Rheumatol. 2018; 70 (suppl 10).

Disclosure: M. Genovese, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 9, Astellas, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck Serono, 2, 5, Galapagos, 2, 5, Galapagos NV, 2, 5, 9, Genentech/Roche, 2, 5, Gilead, 2, 5, Gilead Science, 9, Gilead Sciences, Inc., 2, 5, 9, GSK, 5, Lilly, 2, 5, 9, Novartis, 2, 5, Pfizer, 2, 5, 9, Pfizer Inc, 2, 5, Pfizer, Inc., 9, Pzier, 9, RPharm, 5, Sanofi Genzyme, 2, 5, Vertex, 2, 5; **K. de Vlam**, Celgene, 5, 8, Eli Lilly, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **J. Gottenberg**, Abbvie, 8, BMS, 2, 5, Lilly, 5, 8, Pfizer, 2, 5, Roche, 8, Sanofi-Genzyme, 5, 8, UCB, 5, 8; **B. Bartok**, Gilead Sciences, Inc., 3, 4; **I. Tiamiyu**, Gilead Sciences, Inc., 3, 4; **Y. Guo**, Gilead Sciences,

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Abstract Number: 0518

Upadacitinib in Patients with Rheumatoid Arthritis and Inadequate Response or Intolerance to Biological DMARDs: Results at 60 Weeks

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SESSION INFORMATION
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Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
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Background/Purpose: In patients (pts) with active rheumatoid arthritis (RA) and inadequate response or intolerance to bDMARDs, treatment with upadacitinib (UPA), a JAK1-selective inhibitor resulted in significant improvements over 24 weeks (wks).[1]

We assessed UPA safety and efficacy through Wk60 in an ongoing extension of the phase 3 SELECT-BEYOND study.

Methods: SELECT-BEYOND enrolled a population of patients with active RA who had failed at least one prior biologic therapy.[1] Pts received UPA 15mg or 30mg once daily (QD) or placebo (PBO) on top of background csDMARD treatment for 12 wks. From Wk12, pts randomized to UPA at baseline (BL) continued their assigned doses, while pts initially randomized to PBO received UPA 15mg or 30mg QD per pre-specified assignment at BL. Patients who completed Wk 24 entered the blinded long-term extension. Dose adjustments to UPA were not allowed. Adverse events (AE) per 100 pt years (PY) are summarized based on a cut-off date of 16 April 2018. Efficacy data up to the Wk60 visit are reported "As Observed".

Results: 418/498 (84%) pts were randomized, completed 24 wks and entered the extension on study drug. By the safety data cut-off date, 19% pts discontinued study drug: 5% due to AE, 4% due to lack of efficacy, 3% withdrew consent, 2% were lost to follow-up, and 5% discontinued due to other reasons. Cumulative exposures to UPA15 and UPA30 were 301.7 and 290.7 PYs, respectively. Rates (Events/100PYs) of treatment-emergent AEs are reported (Table 1), and were numerically higher in the UPA30 vs UPA15 arm for serious AEs, AEs leading to discontinuation, serious infections, herpes zoster and hepatic disorders. Based on As Observed analysis, for pts completing Wk60 on UPA15 [172/216 (80%)] and UPA30 [168/202 (83%)], clinical and functional outcomes continued to improve compared to Baseline, or were maintained from Wk24 onwards1 in pts initially randomized to UPA15 or 30; Remission by CDAI≤2.8 at Wk60 was achieved by 20% and 32%, respectively, and DAS28-CRP< 2.6 was achieved by 53% and 52%. Pts who were switched to UPA from PBO at Wk12 had comparable efficacy to pts initially randomized to UPA (Table 2).

Table 1. Treatment-Emergent Adverse Events; Event Rate in E/100PYs		
	UPA 15 MG N=236 PYs=301.7 E/100PYs	UPA 30 MG N=240 PYs=290.7 E/100PYs
Any Adverse Event (AE)	353.3	435.8
Serious AE	17.9	29.2
AE Leading To Study Drug D/C	9.6	15.1
Serious Infection[§]	3.0	8.3
Herpes Zoster[ǂ]	4.6	8.9
Hepatic disorder[¥]	4.6	8.3
Any Malignancy (exc NMSC)[γ]	1.7	1.0
MACE (adjudicated)[δ]	1.0	0.3
VTE (adjudicated)[β]	2.3	0.7
Deaths[†]	0.7	1.0

E, events; PYs, patient-years; E/100PYs, events per 100 patient-years; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular event (cardiovascular death, non-fatal myocardial infarction (MI), non-fatal stroke); VTE, venous thromboembolism (DVT, deep vein thrombosis; PE, pulmonary embolism).
[§]Most frequently reported serious infections were pneumonia, HZ, influenza, and respiratory tract infections.
[ǂ]HZ: most involved 1 or 2 dermatomes. No meningoencephalopathic/ noncutaneous involvement. Two HZ events were reported as ophthalmic.
[γ]Malignancy (excluding NMSC): UPA15: 1 malignant melanoma in situ, 1 bladder cancer, 1 pancreatic carcinoma Stage IV, 1 colon cancer, 1 non-small cell lung cancer metastatic; UPA30: 2 prostate cancers, 1 rectal cancer metastatic.
[δ]MACE (adjudicated): UPA15: 1 CV death, 1 non-fatal MI, 1 non-fatal stroke; UPA30: 1 pt with 2 concurrent events (non-fatal MI and acute congestive heart failure) adjudicated to non-fatal MI
[β]VTE:UPA15: 3 pts with PE, 1 pt with DVT, 2 pts with PE and DVT, 1 pt with non-assessable thrombotic event; UPA30: 1 pt with PE, 1 pt with PE and DVT; no dose relationship in the rates of VTE or patterns in the time to onset of the events, were observed.
[†]Deaths: UPA15: 1 due to other CV causes, 1 due to cardiac arrest; UPA30: 1 pt with cardiac decompensation, 1 pt with presumed MI, 1 pt with rectal cancer metastasized to liver

Table 2. Efficacy Endpoints at Week 60 (as observed); Responses compared to Baseline, n/N (%)				
	PBO→ UPA 15 MG	PBO→ UPA 30 MG	UPA 15 MG	UPA 30 MG
ACR20	48/59 (81)	52/62 (84)	102/133 (77)	97/116 (84)
ACR50	36/60 (60)	40/61 (66)	70/134 (52)	71/117 (61)
ACR70	20/60 (33)	24/61 (39)	45/135 (33)	49/118 (42)
DAS28-CRP≤3.2	37/59 (63)	46/64 (72)	92/133 (69)	86/118 (73)
DAS28-CRP<2.6	31/59 (53)	36/64 (56)	70/133 (53)	61/118 (52)
CDAI≤10	40/60 (67)	45/63 (71)	91/132 (69)	74/117 (63)
CDAI≤2.8	18/60 (30)	17/63 (27)	26/132 (20)	37/117 (32)
SDAI≤3.3	19/59 (32)	20/63 (32)	26/161 (20)	36/114 (32)
HAQ-DI≤-0.22	40/60 (67)	49/61 (80)	91/130 (70)	87/118 (74)
Change from BL in HAQ-DI	-0.52	-0.61	-0.52	-0.65

References:
1. Genovese et al 2018; Lancet.18;31116-4

Conclusion: The benefit:risk of upadacitinib treatment in this refractory population remains favorable. No new safety signals were identified. Some AEs were numerically higher for UPA30 vs 15; however the clinical significance of this, the assessment of rare safety events in this study, and the overall benefit:risk of upadacitinib 15mg and 30mg in the treatment of RA are best evaluated in an integrated analysis across the phase 3 program. UPA15mg and 30mg continued to be effective in treating RA signs and symptoms, and in improving physical function.

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Science, 9, Gilead Sciences, Inc., 2, 5, 9, GSK, 5, Lilly, 2, 5, 9, Novartis, 2, 5, Pfizer, 2, 5, 9, Pfizer Inc, 2, 5, Pfizer, Inc., 9, Pzier, 9, RPharm, 5, Sanofi Genzyme, 2, 5, Vertex, 2, 5; **B. Combe**, AbbVie, 5, BMS, 5, 8, Chugai, 5, 8, Eli Lilly, 5, Eli Lilly and Company, 5, 8, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, UCB, 5, USD, 5; **S. Hall**, AbbVie, 2, 5, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, UCB Pharma, 2, 5; **A. Rubbert-Roth**, AbbVie, 5, 8, Amgen, 5, 8, Chugai, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8; **S. Zhong**, AbbVie, 3, 4; **S. Meerwein**, AbbVie, 3, 4, Abbvie Inc, 1, 4; **A. Pangan**, AbbVie, 3, 4, AbbVie Inc., 3, 4; **R. Fleischmann**, AbbVie, 2, 5, Acea, 2, 5, Akros, 5, Amgen, 2, 5, AstraZeneca, 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, 5, Celltrion, 5, Celtrion, 2, 5, Centrexion, 2, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck-Serono, 2, 5, EMD Serono, 2, EMD-Serano, 2, EMD-Serono, 2, Genentech, 2, 5, Genetech, 2, GlaxoSmithKline, 2, 5, GSK, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Merck, 2, Nektar, 2, Novartis, 2, 5, Pfizer, 2, 5, Pfizer Inc, 2, 5, Regeneron, 2, Resolve, 2, Roche, 2, Samsung, 5, Sandoz, 5, Sanofi Genzyme, 2, Sanofi-Aventis, 2, 5, Sanofi-Aventis, 2, 5, Sanofi-Genzyme, 2, Selecta, 2, Tahio, 5, Taiho, 5, UCB, 2, 5.

Abstract Number: 0519

Efficacy of Biosimilar Candidate ABP 710 in a Phase 3 Study in Subjects with Moderate to Severe RA: Additional Analysis Focusing on the ACR Individual Components

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SESSION INFORMATION
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Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
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Background/Purpose: ABP 710 is being developed as a biosimilar to infliximab. Both ABP 710 and infliximab reference product (RP) inhibit tumor necrosis factor-alpha. Following demonstration of analytical (structural and functional) similarity and clinical pharmacokinetic equivalence in a phase 1 study, a comparative phase 3 clinical trial in patients with moderate to severe RA was conducted. The objective of this analysis was to show the results of the ACR individual components for ABP 710 in comparison with infliximab RP.

Methods: In this multicenter, randomized, double-blind study, the efficacy and safety of ABP 710 was compared with the RP in subjects with moderate to severe RA. Subjects were maintained on a stable 7.5 to 25 mg/week dose

Table 1. Response (≥ 20% Improvement) Difference at Week 22 in ACR Components

ACR Component	ABP 710 n/N (%)	Infliximab n/N (%)	RD (%) and 90% CI
Swollen joint count	238/260 (91.5)	233/256 (91.0)	0.24 (-3.91, 4.43)
Tender joint count	237/260 (91.2)	225/256 (87.9)	3.23 (-1.27, 7.77)
Subject's global health assessment	183/260 (70.4)	174/256 (68.0)	2.67 (-4.01, 9.33)
Investigator's global health assessment	229/260 (88.1)	223/256 (87.1)	1.32 (-3.48, 6.15)
Subject's assessment of disease-related pain	196/260 (75.4)	169/256 (66.0)	9.71 (3.12, 16.21)
HAQ-DI	172/260 (66.2)	154/255 (60.4)	5.83 (-1.16, 12.75)
C-reactive protein	146/253 (57.7)	148/252 (58.7)	-0.70 (-7.89, 6.51)

Table 2. Change From Baseline in ACR Components at Week 22

ACR Component	ABP 710 Mean (SD)	Infliximab Mean (SD)	Difference Between Means	90% CI for Difference Between means	95% CI for Difference Between Means	MCII
Subject's assessment of disease-related pain	-30.8 (28.75)	-25.1 (29.33)	-3.77	(-7.38, -0.16)	(-8.08, 0.53)	-20
HAQ-DI	-0.53 (0.59)	-0.44 (0.56)	-0.07	(-0.15, 0.01)	(-0.17, 0.02)	-0.375

of methotrexate and received 3 mg/kg infusions of the investigational products at predetermined intervals. The primary endpoint of the study was response difference (RD) of at least 20% improvement compared with baseline in ACR core set of measurements (ACR20) at week 22. Individual components of ACR were summarized descriptively at each visit, which included swollen joint count and tender joint count, Subject's Global Health Assessment, Investigator's Global Health Assessment, Subject's Assessment of Disease-related Pain, Health Assessment Questionnaire - Disability Index (HAQ-DI) total score, and C-reactive protein (CRP).

Results: Of the 558 randomized subjects, 556 were treated (ABP 710 n=278; RP n=278); 484 subjects continued in the study through week 22 to be re-randomized (ABP 710/ABP 710: n=244; infliximab RP/infliximab RP: n=121; infliximab RP/ABP 710: n=119), and 435 subjects completed the study. Results of the ACR components (based on a response of ≥20% improvement) at week 22 are shown in Table 1. ACR components with the largest RD between treatment groups were Subject's Assessment of Disease-related Pain and HAQ-DI; yet the difference in mean change from baseline and associated 90% and 95% confidence intervals (CIs) were well below the thresholds of minimal clinically important improvement and thus, not clinically meaningful (Table 2).

Conclusion: This analysis of ACR individual components further supports the similarity of ABP 710 and infliximab RP.

Abbreviations: CI = confidence interval; HAQ-DI = Health Assessment Questionnaire - Disability Index; RD = response difference. Note: The point estimate of RD was estimated by the Mantel-Haenszel estimate and the 90% CI was estimated using stratified Newcombe confidence limits adjusting for actual stratification factors.

Abbreviations: ANOVA = analysis of variance; CI = confidence interval; HAQ-DI = Health Assessment Questionnaire - Disability Index; MCII = minimal clinically important improvement; RD = response difference. Note: Difference between means, 90% and 95% CIs for difference between means was based on ANOVA model with change from baseline in HAQ-DI or pain as the response and adjusted for baseline HAQ-DI or pain and the actual stratification factors: geographic region and prior biologic use for RA.

Disclosure: M. Genovese, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 9, Astellas, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck Serono, 2, 5, Galapagos, 2, 5, Galapagos NV, 2, 5, 9, Genentech/Roche, 2, 5, Gilead, 2, 5, Gilead Science, 9, Gilead Sciences, Inc., 2, 5, 9, GSK, 5, Lilly, 2, 5, 9, Novartis, 2, 5, Pfizer, 2, 5, 9, Pfizer Inc, 2, 5, Pfizer, Inc., 9, Pzier, 9, RPharm, 5, Sanofi Genzyme, 2, 5, Vertex, 2, 5; **J. Sanchez-Burson**, Amgen, 5; **É. Balázs**, Celltrion, Inc., 2, Amgen, 5; **A. Everding**, Amgen, 5, Eli Lilly, 5, Novartis, 5; **M. Oh**, Amgen, 1, 3, 4; **G. Fanjiang**, Amgen, 1, 3, 4; **S. Cohen**, AbbVie, 2, 5, Abbvie, 5, Amgen, 5, Amgen Inc., 2, 5, AstraZeneca, 2, 5, Biogen-IDEC, 2, 5, Bristol Meyer Squibb, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5.

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Efficacy and Safety Results from a Phase 3 Study of Biosimilar Candidate ABP 710 in Subjects with Moderate to Severe RA

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SESSION INFORMATION

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Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: ABP 710 is being developed as a biosimilar to infliximab. Both ABP 710 and infliximab reference product (RP) inhibit tumor necrosis factor-alpha and have been shown to be structurally and functionally similar in analytical assessments. In a phase 1 clinical pharmacokinetic (PK) study, both were shown to be bioequivalent for PK parameters. The final step in the demonstration of biosimilarity is a comparative phase 3 clinical trial in a representative indication. The objective of this study was to evaluate the similarity of ABP 710 compared to RP with respect to efficacy across time in patients with active RA.

Methods: In this multicenter, randomized, double-blind, active-controlled, multiple-dose study, the efficacy and safety of ABP 710 was compared with the RP in subjects with moderate to severe RA while being maintained on a stable 7.5 to 25 mg/week dose of methotrexate. Subjects were randomized to receive a 3 mg/kg intravenous infusion of either ABP 710 or RP on day 1 (week 0), at weeks 2 and 6, and every 8 weeks thereafter until week 22. At week 22, subjects initially randomized to RP were re-randomized to either continue RP or transition to receive ABP 710 through week 46. Subjects initially randomized to ABP 710 continued receiving the same treatment through week 46. The primary endpoint of the study was response difference (RD) of ≥20% improvement in ACR (ACR20) at week 22; secondary endpoints included RD of ACR20, ≥50% improvement (ACR50), and ≥70% improvement (ACR70) across time (weeks 2, 6, 14, 30, 34, 38, 36, and 50). Efficacy data were analyzed by initial treatment (ABP 710 or RP) prior to re-randomization and by initial/re-randomized treatment (ABP 710/ABP 710, RP/RP, RP/ABP 710) after re-randomization.

	ACR20 (%); RD (90% CI)		ACR50 (%); RD (90% CI)		ACR70 (%); RD (90% CI)	
	RP – ABP 710	RP/ABP710 - RP	RP – ABP 710	RP/ABP710 – RP	RP – ABP 710	RP/ABP710 - RP
Week 2	8.03 (1.15, 14.81)	NA	4.41 (-0.56, 9.38)	NA	-2.50 (-5.84, 0.83)	NA
Week 6	4.96 (-1.80, 11.64)	NA	1.62 (-4.71, 7.94)	NA	-2.43 (-7.47, 2.64)	NA
Week 14	6.22 (-0.51, 12.87)	NA	2.30 (-4.45, 9.03)	NA	5.46 (-0.01, 10.91)	NA
Week 22	9.37 (2.67, 15.96)	NA	7.09 (0.27, 13.83)	NA	4.58 (-1.21, 10.34)	NA
Week 30	3.05 (-5.26, 11.73)	8.50 (-1.18, 17.97)	-1.33 (-10.40, 7.62)	3.24 (-7.28, 13.67)	0.20 (-8.12, 8.02)	-0.08 (-9.39, 9.28)
Week 34	3.31 (-4.61, 11.70)	4.06 (-5.40, 13.40)	6.52 (-2.62, 15.48)	10.74 (0.12, 21.03)	1.50 (-7.00, 9.51)	7.49 (-2.39, 17.22)
Week 38	0.82 (-7.34, 9.40)	2.79 (-6.86, 12.34)	0.56 (-8.54, 9.59)	2.93 (-7.62, 13.39)	-0.50 (-9.03, 7.59)	3.39 (-6.41, 13.14)
Week 46	-3.74 (-12.27, 5.17)	1.12 (-8.89, 11.08)	-1.04 (-10.11, 7.93)	6.14 (-4.44, 16.54)	-0.43 (-8.98, 7.66)	7.87 (-2.13, 17.68)
Week 50	-5.25 (-13.24, 3.29)	-1.49 (-11.01, 8.04)	-5.43 (-14.39, 3.71)	2.98 (-7.51, 13.37)	1.95 (-6.81, 10.29)	12.06 (1.74, 22.04)

Results: Of the 558 randomized subjects, 556 were treated (ABP 710 n=278; RP n=278); 484 subjects completed the study through week 22 and were re-randomized (ABP 710/ABP 710 n=244; RP/RP n=121; RP/ABP 710 n=119), with 435 subjects completing the study. Results of the ACR20, ACR50, and ACR70 response rates across time for the initial or initial/re-randomized treatment groups were similar, with overlapping 95% confidence intervals (CIs) of ACR response rates between the treatment groups at all time points and narrow RD at all time points (see Table for RDs with 90% CI). Efficacy was consistently maintained throughout the study, with no impact of the single transition from RP to ABP 710. Through week 22, the percentage of subjects reporting any serious adverse events was 4.1% (ABP 710=3.2%; RP=5.0%) and the binding/neutralizing antibody positive post-baseline in subjects was 58.9%/19.4% (ABP 710=57.1%/18.0%; RP=60.6%/20.8%).

Conclusion: As demonstrated by the narrow RD of ACRs across the entire study, the efficacy of ABP 710 is similar to the RP. Safety was also found to be similar between treatment groups. In addition to previously reported primary efficacy endpoints, these secondary efficacy results support clinical similarity between ABP 710 and infliximab RP with respect to safety and efficacy.

Disclosure: M. Genovese, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 9, Astellas, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck Serono, 2, 5, Galapagos, 2, 5, Galapagos NV, 2, 5, 9, Genentech/Roche, 2, 5, Gilead, 2, 5, Gilead Science, 9, Gilead Sciences, Inc., 2, 5, 9, GSK, 5, Lilly, 2, 5, 9, Novartis, 2, 5, Pfizer, 2, 5, 9, Pfizer Inc, 2, 5, Pfizer, Inc., 9, Pzier, 9, RPharm, 5, Sanofi Genzyme, 2, 5, Vertex, 2, 5; **J. Sanchez-Burson**, Amgen, 5; **É. Balázs**, Celltrion, Inc., 2, Amgen, 5; **A. Everding**, Amgen, 5, Eli Lilly, 5, Novartis, 5; **M. Oh**, Amgen, 1, 3, 4; **G. Fanjiang**, Amgen, 1, 3, 4; **S. Cohen**, AbbVie, 2, 5, Abbvie, 5, Amgen, 5, Amgen Inc., 2, 5, AstraZeneca, 2, 5, Biogen-IDEC, 2, 5, Bristol Meyer Squibb, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5.

Abstract Number: 0521

Discontinuation of Disease Modifying Drugs Due to Inefficacy in Patients with Incident Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
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Background/Purpose: The treatment of Rheumatoid Arthritis (RA) has undergone a big change in the last two decades with the Disease Modifying Drugs (DMARDs). These drugs are widely used in clinical practice, but we have little information about their discontinuation in this conditions especially due to inefficacy. Purpose: to describe the discontinuations of DMARDs due to inefficacy, their causes in patients with incident RA, and to evaluate possible associated factors to inefficacy.

Methods: We conducted an observational longitudinal study. Patients: all recent onset RA diagnosed between January 1st 2007 and December 31st 2015 followed in outpatient clinic at Hospital Clinico San Carlos until January 1st 2017, which used any DMARD (synthetic and biologic) during at least 3 months. Primary outcome: discontinuation of the DMARD due to inefficacy. Covariables: sociodemographic, clinical and treatments. Incidence rates of discontinuation

Table 1	DISCONTINUATIONS			
	Patients/year	N	IR	95%CI
Total	3706.14	149	4.02	3.42-4.7
By gender				
Female	2976.78	130	4.36	3.65-5.15
Male	729.36	19	2.61	1.66-4.08
Age at diagnosis				
Under 45	908.4	56	6.16	4.7-8.0
Between 45 and 70	1963.64	72	3.66	2.9-4.6
Over 70	834.1	21	2.51	1.6-3.8
By treatment course				
First course	1666.32	34	2.04	1.45-2.85
Following courses	2039.82	115	5.63	4.65-6.72
By biological DMARD use				
No	3319.50	99	2.98	2.40-3.6
Yes	386.64	50	12.9	9.8-17.06
By type of biological DMARD				
Non biological	3319.50	99	2.98	2.40-3.63
Anti-TNF	295.10	39	13.2	9.65-18.1
Others	91.54	11	12.02	6.66-21.70
By combined therapy				
Monotherapy	2556.41	57	2.23	1.72-2.89
Combined therapy	1149.73	92	8.0	6.5-9.8
Synthetical DMARDs				
CQ	684.53	36	5.25	3.7-7.3
HCQ	626.88	25	3.99	2.70-5.90
LEF	482.83	23	4.76	3.17-7.17
MTX	2234.58	82	3.66	2.92-4.51
MTX sc	242.69	10	4.12	2.22-7.66
ORO	136.77	18	13.16	8.29-20.89
SSZ	224.45	20	8.9	5.7-13.8
AZA	37.61	2	5.32	1..3-21.26
Biological DMARDs				
ABA	12.68	3	23.66	7.63-73.36
ADA	123.95	11	8.88	4.92-16.03
CERTO	31.36	11	35.07	19.4-63.3
ETN	101.30	14	13.82	8.19-23.34
GOLI	14.77	1	6.77	0.95-48.05
INF	23.72	2	8.43	2.11-33.71
RTX	62.30	7	11.24	5.36-23.57
TOCI	16.56	1	6.04	0.85-42.86

(IR) per 100 patient-years were estimated using survival techniques with their respective 95% confidence interval [CI]. Factors associated with DMARDs discontinuation due to inefficacy was performed using Cox regression models, and results were expressed in Hazard ratio (HR) and [CI].

	Multivariate		
	Hazard ratio	**CI 95%**	**p**
Age at diagnosis	0.98	0.97-1.00	0.07
Depression	1.68	1.06-2.67	0.025
RF positive	1.32	0.9-1.9	0.1
Other treatment courses vs first one	1.81	1.1-2.38	0.018
Combined therapy vs monotherapy	1.87	1.14-3.05	0.012
Classical DMARDs Anti-TNF Other biologicals	1 3.2 2.8	 1.92-5.3 1.3-6.28	 0.000 0.009
Glucocorticoids (Dose)	1.99	1.6-2.4	0.000
ESR>55	0.7	0.7-2.0	0.1

Results: We included 2388 courses of DMARD treatment in 814 patients (3706.14 patient-years). 77.52% were women with a mean age at diagnosis of 57.53±15.50 years. There were 1094 DMARDs discontinuations of the 2388 courses (45.81%) in 438 patients, of these 149 in 110 patients (13.5%) were due to inefficacy (IR: 4.0[3.4-4.7]). Most patients discontinuing due to inefficacy were women (87.50%) with a mean age at diagnosis of 52.40±13.50 years. 33.5% of the discontinuations due to inefficacy were biological DMARDs. 61.7% were in combined therapy and most of them (77.18%) discontinued during successive courses of therapy. IRs are shown in table 1. The multivariate analysis (table 2) was adjusted by age, gender and disease activity (ESR). Interestingly, younger age and depression also increased the risk of inefficacy. Combined therapy, second courses, dose of glucocorticoids and biologic vs synthetic DMARDs (HR: 3.12 [1.8-5.2]) increased the risk. We repeated the multiple regression model with all the sociodemographic and clinical variables shown in table 2 but changing the reference category of DMARD and found that Certolizumab (HR: 5.0[2.5-9.8]) had the highest risk of discontinuation due to inefficacy compared to the other drugs followed by Abatacept (HR: 4.9[1.9-12.7]), Etanercept (HR: 2.3[1.3-4.2]) and Gold (HR: 1.9 [1.1-3.4]). MTX use (HR: 0.6 [0.42-0.87]) was a protective factor against discontinuation due to inefficacy.

Conclusion: Discontinuations of DMARDs in clinical practice due to inefficacy are frequent (13.5%) with an IR of 4%. We have found differences in discontinuation rates among DMARD with Certolizumab, Abatacept, Etanercept, and Gold being the drugs with the highest risk. MTX is a protective factor for discontinuation due to inefficacy. Caution should be taken in regard to discontinuation due to inefficacy in patients receiving glucocorticoids, biological DMARDs, combined therapy, in subsequent treatment courses, and those with depression.

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Abstract Number: 0522

Treatment with Upadacitinib Results in the Normalization of Key Pathobiologic Pathways in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients with moderate-to-severe rheumatoid arthritis (RA) with an inadequate response (IR) to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) or biologic DMARDs (bDMARDs) in the SELECT-NEXT[1] andSELECT-BEYOND[2] trials, respectively. The pivotal immune regulatory pathway targets served by JAK1 in patients have not been comprehensively explored.

We investigate the mode of action (MoA) of UPA in patients with RA via a proteomic approach that evaluates a set of plasma proteins associated with inflammation.

Methods: Patients from the SELECT-NEXT and SELECT-BEYOND (PBO, n=167; UPA 15 mg QD, n=200) studies were randomly selected from the pool of patients with plasma samples available at baseline, Week 2, and Week 12. Samples from 24 age- and sex-matched healthy controls were included. The levels of 92 proteins were analyzed using the Olink® Inflammation Panel. Results from both studies were combined. Data were clustered using the Ward (unsupervised) method; correlations were calculated using the Pearson method; and multiple comparisons were corrected using the Benjamini–Hochberg method; all statistical analyses were performed in JMP 13.10 (SAS Institute). Pathway analysis was performed with Ingenuity® Pathway Analysis (Qiagen Inc.) version 45868156.

Results: At baseline, levels of IL-6, CXCL9, CXCL10, and CCL7 correlated significantly with baseline DAS28-ESR, consistent with effector roles for IL-6 and interferon (IFN) in intercurrent disease activity. Clustering of the differential protein fold change at Weeks 2 and 12 for UPA and PBO groups revealed four clusters enriched for proteins related to: 1) IL-6, IFN, leukocyte trafficking, and macrophage activation (↓↓↓); 2) T helper cell differentiation (↓); 3) T and B cell signaling (↓↓); and 4) hematopoiesis and myeloid cell differentiation (↑). Pathway analysis based on the differential expression of 37 significantly modulated proteins suggests that treatment with UPA results in the normalization of key pathways associated with the pathobiology of RA including: 1) pathways associated with IL-1, IL-6, IL-12, IL-15, IL-18, IFNα, IFNβ, IFNγ, CSF2, and TNF; and 2) pathways associated with behaviors of leukocytes (lymphocytes, myeloid cells, and granulocytes), including leukocyte migration, T cell response, and inflammatory response. In keeping with the latter, the changes in IL-6, CCL23, CCL7, MMP1, and S100A12 levels at Week 12 correlated significantly with the relative change in DAS28-ESR, suggesting a link between UPA MoA and macrophage activation.

Conclusion: In keeping with its selectivity for JAK1, UPA operates via inhibition of multiple JAK1-dependent upstream pathways that result in the normalization of key functional downstream effects associated with the pathobiology of RA, including T cell and myeloid cell-related pathways. Notably, non-JAK signaling pathways also normalize, suggesting functional integration of JAK1 with parallel pathogenic signaling in RA effector cells.

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Abstract Number: 0523

The Impact of Upadacitinib versus Methotrexate or Adalimumab on Individual and Composite Disease Measures in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: In Phase 3 trials, upadacitinib (UPA), an oral JAK1-selective inhibitor, has been assessed as monotherapy vs MTX (SELECT-EARLY[1]) and in combination with MTX vs adalimumab + MTX (ADA; SELECT-COMPARE[2]) in RA pts who were MTX naïve or with inadequate responses to MTX (MTX-IR), respectively. In this analysis we assessed individual and composite measures of disease activity in SELECT-EARLY and SELECT-COMPARE.

Methods: In SELECT-EARLY, MTX-naïve pts received UPA 15 mg or 30 mg monotherapy once daily (QD), or MTX monotherapy, for 12 wks. In SELECT-COMPARE, MTX-IR pts on stable background MTX received UPA 15 mg QD, PBO, or ADA 40 mg every 2 wks for 12 wks. For this analysis, responses at Wk 12 were defined as ≥50% improvement in the 7 components of the ACR response criteria. Among ACR50 responders, the proportions of pts with ≥50% improvement in all 7 components of the ACR criteria was assessed. The proportion of pts achieving TJC68=0 and SJC66=0 was also determined. All analyses were based on observed data without imputation.

Results: 947 pts were randomized in SELECT-EARLY, and 1629 pts in SELECT-COMPARE. Mean time since RA diagnosis was 2.7 years in SELECT-EARLY (median 6 months) and 8.2 years in SELECT-COMPARE; mean DAS28(CRP) was 5.9 and 5.8, respectively. In SELECT-EARLY, significantly more MTX-naïve pts receiving UPA 15 mg or 30 mg monotherapy achieved ≥50% improvements in all ACR components at Wk 12 compared with MTX (Table). In SELECT-COMPARE, significantly more MTX-IR pts on UPA 15 mg + MTX achieved ≥50% improvement in the ACR components vs PBO (all components) and ADA + MTX (all components except SJC and PhGA). Among pts with ACR50 responses at Wk 12, approximately half of the MTX-naïve pts on UPA 15 mg and 30 mg in SELECT-EARLY had ≥50%

Table. Proportions of pts achieving 50% improvements in core components of the ACR score at Wk 12

Parameter	Group	SELECT-EARLY (MTX-naive)		Group	SELECT-COMPARE (MTX-IR)[a]	
		N	n (%)		N	n (%)
TJC68 ≥50% improvement	MTX	279	179 (64.2)	PBO	619	300 (48.5)
	UPA 15	302	234 (77.5)***	UPA 15	619	456 (73.7)***,##
	UPA 30	298	235 (78.9)***	ADA 40	309	201 (65.0)***
SJC66 ≥50% improvement	MTX	279	198 (71.0)	PBO	619	324 (52.3)
	UPA 15	302	251 (83.1)***	UPA 15	619	494 (79.8)***
	UPA 30	298	252 (84.6)***	ADA 40	309	231 (74.8)***
Pain ≥50% improvement	MTX	278	107 (38.5)	PBO	617	155 (25.1)
	UPA 15	302	181 (59.9)***	UPA 15	617	339 (54.9)***,###
	UPA 30	298	196 (65.8)***	ADA 40	309	126 (40.8)***
PtGA ≥50% improvement	MTX	278	115 (41.4)	PBO	617	161 (26.1)
	UPA 15	302	170 (56.3)***	UPA 15	617	323 (52.4)***,###
	UPA 30	298	182 (61.1)***	ADA 40	309	123 (39.8)***
PhGA ≥50% improvement	MTX	277	156 (56.3)	PBO	607	238 (39.2)
	UPA 15	301	216 (71.8)***	UPA 15	608	376 (61.8)***
	UPA 30	291	222 (76.3)***	ADA 40	299	180 (60.2)***
HAQ-DI ≥50% improvement	MTX	278	93 (33.5)	PBO	617	131 (21.2)
	UPA 15	302	166 (55.0)***	UPA 15	617	241 (39.1)***,##
	UPA 30	298	166 (55.7)***	ADA 40	309	88 (28.5)*
hsCRP ≥50% improvement	MTX	279	132 (47.3)	PBO	589	135 (22.9)
	UPA 15	301	244 (81.1)***	UPA 15	585	422 (72.1)***,###
	UPA 30	295	236 (80.0)***	ADA 40	292	173 (59.2)***
≥50% Improvement in five ACR components in pts achieving ACR50[b]	MTX	89	25 (28.1)	PBO	96	16 (16.7)
	UPA 15	165	81 (49.1)***	UPA 15	288	99 (34.4)***
	UPA 30	177	97 (54.8)***	ADA 40	93	26 (28.0)
Proportion of pts achieving 0 joint counts at Wk 12						
TJC68=0	MTX	279	27 (9.7)	PBO	619	29 (4.7)
	UPA 15	302	64 (21.2)***	UPA 15	619	101 (16.3)***
	UPA 30	298	62 (20.8)***	ADA 40	309	37 (12.0)***
SJC66=0	MTX	279	57 (20.4)	PBO	619	64 (10.3)
	UPA 15	302	90 (29.8)**	UPA 15	619	163 (26.3)***,##
	UPA 30	298	95 (31.9)**	ADA 40	309	52 (16.8)**

*,**,*** p<0.05, p<0.01, and 0.001, respectively, vs PBO/MTX;
##,###, p<0.01 and 0.001, respectively, vs ADA
[a]All pts were receiving background MTX
[b]Pain, PtGA, PhGA, HAQ-DI, hsCRP (SJC and TJC not included as ACR50 responders must achieve 50% improvement in these parameters)

improvements in all 5 remaining ACR components (pain, PtGA, PhGA, HAQ-DI, hsCRP) compared with 28% with MTX. Corresponding proportions in MTX-IR pts in SELECT-COMPARE were 34% for UPA 15 mg + MTX, 28% for ADA + MTX, and 17% for PBO. UPA treatment also significantly increased the proportions of pts achieving both TJC68=0 and SJC66=0 vs PBO or MTX, and SJC66=0 vs ADA + MTX (Table).

Conclusion: In MTX-naïve and MTX-IR pts, treatment responses at 12 wks occurred in significantly higher proportions of pts receiving UPA monotherapy vs MTX and UPA + MTX vs PBO for all 7 components of the ACR response criteria, and for 5 of 7 ACR components for UPA + MTX vs ADA + MTX. Favorable outcomes with UPA treatment were evident both in composite and individual parameters.

Reference:

1. van Vollenhoven R, et al. Arthritis Rheumatol 2018;70(Suppl. 10): Abstract 891
2. Fleischmann R, et al. Arthritis Rheumatol 2018;70(Suppl. 10): Abstract 890

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Abstract Number: 0524

A Comparison of Upadacitinib Plus Methotrexate and Upadacitinib Plus Other CsDMARDs in Patients with Rheumatoid Arthritis: An Analysis of Two Phase 3 Studies

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
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Background/Purpose: Upadacitinib (UPA), a selective JAK1 inhibitor, has shown efficacy in patients with rheumatoid arthritis (RA) when combined with methotrexate (MTX) or other conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).[1,2] However, the efficacy of UPA plus MTX has not been directly compared with UPA plus other csDMARDs.

We compare the efficacy of UPA in combination with MTX versus UPA in combination with other csDMARDs in patients with an inadequate response (IR) to csDMARDs (SELECT-NEXT[1]) or biologic DMARDs (bDMARDs; SELECT-BEYOND[2]).

Methods: 661 patients in SELECT-NEXT and 498 patients in SELECT-BEYOND received UPA 15 mg or 30 mg once daily (QD) or placebo (PBO) for 12 weeks; all patients received concomitant csDMARD(s). The primary endpoints

Table. Week 12 efficacy outcomes by concomitant treatment.

csDMARD-IR (SELECT-NEXT)							
Patients (%)	MTX			Non-MTX csDMARDs[a]			p-value[b] (MTX vs non-MTX)
	PBO (n=191)	UPA 15 mg QD (n=169)	UPA 30 mg QD (n=175)	PBO (n=29)	UPA 15 mg QD (n=51)	UPA 30 mg QD (n=44)	
ACR20	37.2	65.1	67.4	27.6	58.8	61.4	0.990
DAS28(CRP) ≤3.2	16.8	49.1	49.1	20.7	45.1	43.2	0.878
DAS28(CRP) <2.6	8.9	29.6	29.1	17.2	33.3	25.0	0.468
CDAI ≤10	18.3	41.4	42.3	24.1	35.3	40.9	0.635
CDAI ≤2.8	2.6	8.9	13.1	6.9	7.8	6.8	0.319
bDMARD-IR (SELECT-BEYOND)							
Patients (%)	MTX			Non-MTX csDMARDs[a]			p-value[b] (MTX vs non-MTX)
	PBO (n=139)	UPA 15 mg QD (n=136)	UPA 30 mg QD (n=135)	PBO (n=29)	UPA 15 mg QD (n=24)	UPA 30 mg QD (n=29)	
ACR20	27.3	65.4	57.0	31.0	66.7	55.2	0.979
DAS28(CRP) ≤3.2	13.7	43.4	42.2	13.8	45.8	41.4	0.834
DAS28(CRP) <2.6	8.6	29.4	25.9	10.3	25.0	13.8	0.661
CDAI ≤10	14.4	33.8	34.1	10.3	25.0	34.5	0.351
CDAI ≤2.8	5.8	8.8	11.9	0	4.2	10.3	0.588

[a]Sulfasalazine, leflunomide, hydroxychloroquine, or chloroquine.
[b]Based on logistic regression analyses for the comparison of UPA in combination with MTX versus UPA in combination with non-MTX csDMARDs, with treatment group and background csDMARD type as fixed factors (as well as the interaction between treatment group and background csDMARD type), adjusting for demographic and baseline factors.

References:
1. Burmester GR, et al. Lancet 2018;391:2503–12
2. Genovese MC, et al. Lancet 2018;391:2513–24

for both studies were rates of ACR20 response and DAS28(CRP) ≤3.2. Additional endpoints included DAS28(CRP) < 2.6, CDAI low disease activity (≤10), and CDAI remission (≤2.8). Patients were grouped according to concomitant csDMARD use (MTX vs non-MTX csDMARDs); patients receiving both MTX and a non-MTX csDMARD were included in the MTX group. p-values were calculated based on a logistic regression model with treatment group and type of background csDMARD as fixed factors, adjusting for demographic and baseline factors. p-values from the interaction between treatment group and background csDMARD were also calculated, to assess the consistency of the effects of study treatments for different background csDMARD type. Non-responder imputation was used for missing data.

Results: In SELECT-NEXT and SELECT-BEYOND, 535 and 410 patients, respectively (~80%), were receiving concomitant MTX (mean dose 17 mg/week), and 124 and 82 patients were receiving non-MTX csDMARDs. Demographics and disease characteristics were broadly similar between treatment groups; the majority of patients were female and of white ethnicity, and around half were using oral corticosteroids at baseline. Across all subgroups, the proportion of patients achieving efficacy outcomes was higher with both UPA doses compared with PBO (Table). There were no significant differences between efficacy outcomes with UPA in combination with MTX versus UPA in combination with non-MTX csDMARDs in either patient population. This included ACR20 response as well as low disease activity and remission defined by DAS28(CRP) and CDAI.

Conclusion: In this post hoc analysis, the efficacy of UPA in patients with RA appeared comparable whether administered in combination with MTX or non-MTX csDMARDs.

Disclosure: J. Kremer, AbbVie, 2, 5, Amgen, 5, Bristol-Myers Squibb, 2, 5, Corrona, 1, Genentech, 2, 5, Gilead, 5, Lilly, 2, 5, Novartis, 2, Pfizer, 2, 5, Regeneron, 5, Sanofi, 5; **F. Van den Bosch**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, Bristol-Myers Squibb, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sanofi and UCB, 5, 8, ABBVIE, CELGENE, ELI LILLY, GALAPAGOS, MERCK, NOVARTIS, PFIZER, VCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **A. Rubbert-Roth**, AbbVie, 5, 8, Amgen, 5, 8, Chugai, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8; **S. Radominski**, AbbVie, 5, 8, Celgene, 5, 8, Genentech, 5, 8, Roche, 5, 8, Janssen, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **G. Burmester**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma., 5, 8, AbbVie Inc., 5, 8, BMS, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Merck Shar & Dohme, 5, 8, MSD, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche, Sanofi-Genzyme, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Union Chimique Belge, 2, 5, 8; **H. Camp**, AbbVie, 1, 3, 4, Abbvie Inc, 1, 4; **S. Meerwein**, AbbVie, 3, 4, Abbvie Inc, 1, 4; **M. Howard**, AbbVie, 3, 4; **Y. Song**, AbbVie, 3, 4, Abbvie, 1, 4; **S. Zhong**, AbbVie, 3, 4; **B. Combe**, AbbVie, 5, BMS, 5, 8, Chugai, 5, 8, Eli Lilly, 5, Eli Lilly and Company, 5, 8, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, UCB, 5, USD, 5.

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Factors Associated with Persistent Drug-free Remission in Patients with Rheumatoid Arthritis

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Background/Purpose: Persistent drug-free remission of RA is a condition close to “cure” of the disease. Long-term drug-free remission is considered rare and challenging to reach, little data are available that report how often persistent drug-free remission can be achieved and what kind of clinical characteristics are associated with such state.

Methods: We analyzed the long-term observational follow-up phase of the randomized controlled RETRO study on tapering and stopping of DMARDS in RA patients in stable remission (DAS28-ESR < 2.6) (1,2). We included patients having completed the 1-year randomized controlled phase of RETRO, in which DMARD treatments were either continued, tapered or stopped. In the long-term extension, (i) patients who successfully stopped, continued DMARD stop, (ii) patients who relapsed in any of the 3 groups continued DMARD treatment, (iii) patients in the continuation arm remaining in remission underwent 50% DMARD tapering follwoed by stopping after 6 months if still being in

remission and (iv) patients in the tapering arm remaining in remission underwent DMARD stop. We assessed the percentage of patients in persistent drug-free remission in the overall population and the three randomization groups, the probability of persistent drug-free remission in the intervention groups compared to controls adjusted by baseline aCCP, erosive changes and use of biologic DMARDs in a logistic regression model and the baseline characteristics associated with reaching persistent drug-free remission.

Results: All 141 patients being in the long-term observational follow-up phase of the RETRO study for at least 1 year were analyzed. Among them DMARDs were initially continued (Control, n=38), tapered (Taper, n=50) or stopped (Taper/Stop n=53). 19/141 patients were lost to follow-up and the worst case scenario was assumed that all of them did not reach persistent drug-free remission. Median time after study entry (Q1-Q3) was 69 (37-96) months as by December 2018. Overall number of patients in drug-free remission was 34/141 (24.1%), 10/38 (26%) in the control group, 6/50 (12%) in the taper group and 18/53 (34%) in the taper/stop group. After adjustment for baseline risk factors in the likelihood to reach persistent drug-free remission between the groups (OR:0.76, 95%CI: 0.29-1.99) was highly uncertain. Positive ACPA (OR: 3.38, 1.01 – 11.31) and erosive-state (3.05, 1.32 – 7.06) at baseline were associated with a lower likelihood to reach persistent drug-free remission.

Conclusion: These data show that persistent drug-free remission can be reached in a subset of RA patients following a structured DMARD tapering approach after being in stable long-term DMARD control.

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Factors Influencing Discontinuation in Long-term RA Treatment

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Background/Purpose: While medication persistence can act as a substitute metric for effectiveness, few studies have examined real-world patterns of bDMARD persistence by line of treatment and by patient-reported reasons for discontinuation in patients with RA.

Methods: From 2006 to 2018, participants with RA in FORWARD, The National Databank for Rheumatic Diseases, a US-wide observational longitudinal study, reported medication use and reasons for discontinuation. Discontinuation was defined as stopping the use of biologic medications for RA or adding another DMARD. We determined discontinuation rates of individual bDMARD initiators and grouped by action mechanism, delivery method, previous bDMARD history, concomitant use of csDMARDs such as methotrexate and prednisone and self-reported reasons for discontinuation. The latter were randomly assigned when more than 1 reason was given. Propensity score (PS) analyses were conducted overall and by line of treatment, defined as the conditional probability of being treated with

Table 1. Median Survival (IQR) of discontinuation and annual rate of discontinuation of individual biologics, by mechanism of action, line of treatment, and reasons of discontinuation

Biologic	N	N of failure (%)	Median Survival (IQR)	Annual rate of discontinuation
Biologic	4230	1693 (40)	3.50 (1.49 -10.00)	0.17 (0.17 - 0.18)
TNF	3129	1453 (46)	2.51 (1.00 - 7.00)	0.21 (0.20 - 0.22)
Etanercept	974	476 (49)	2.50 (1.00 - 7.00)	0.23 (0.21- 0.25)
Adalimumab	1213	633 (52)	2.00 (1.00 - 6.50)	0.25 (0.24 - 0.28)
Infliximab	605	341 (56)	2.00 (1.00 - 5.00)	0.28 (0.25 - 0.31)
Golimumab	305	158 (52)	2.00 (0.50 - 3.00)	0.38 (0.32 - 0.44)
Certolizumab	640	354 (55)	1.50 (0.50 - 3.50)	0.35 (0.31 - 0.38)
Non-TNF	1833	747 (41)	3.00 (1.42 - 7.50)	0.20 (0.18 - 0.21)
Abatacept	884	507 (57)	2.00 (1.00 - 4.00)	0.31 (0.29 - 0.34)
Rituximab	567	274 (48)	2.50 (1.42 - 5.41)	0.23 (0.20 - 0.26)
Tocilizumab	480	265 (55)	1.50 (0.50 - 3.00)	0.39 (0.34 - 0.43)
Anakinra	29	18 (62)	1.00 (0.50 - 2.00)	0.54 (0.34 - 0.86)
Tofacitinib	380	130 (34)	2.00 (1.00 - .)	0.27 (0.23 - 0.32)
Line of treatment	**N**	**Failure (%)**	**Median Survival (IQR)**	**Annual rate of discontinuation**
TNF-First	1785	473 (26)	5.5 (1.5- .)	0.13 (0.12 –0.14)
TNF-Second	1086	462 (43)	2.5 (1.0-6.0)	0.25 (0.23 –0.27)
TNF-Third+	878	518 (63)	1.5 (0.5-3.0)	0.42 (0.39 –0.46)
NTNF-First	315	89 (28)	3.0 (1.5- .)	0.18 (0.14 –0.22)
NTNF-Second	544	180 (33)	3.5 (1.4-8.5)	0.19 (0.16 –0.21)
NTNF-Third+	1144	478 (42)	2.9 (1.4-7.0)	0.21 (0.19 –0.23)
Reason of discontinuation*	**N**	**Failure (%)**	**Median Survival (IQR)**	**Annual rate of discontinuation**
TNF - No reason	3129 (1229 failures)	510 (16)	1.50 (1.00 – 3.00)	0.44 (0.40 – 0.48)
TNF Inefficacy		300 (10)	1.49 (1.00 – 2.50)	0.50 (0.45 – 0.56)
TNF - Cost		55 (3)	1.49 (1.00 – 3.00)	0.47 (0.36 – 0.61)
TNF -Side effects		204 (11)	1.00 (0.50 – 2.00)	0.63 (0.55 -0.72)
TNF -Other		160 (9)	2.00 (1.00 – 3.50)	0.36 (0.31 – 0.42)
NTNF - No reason	1833 (621 failures)	404	1.91 (1.00 – 2.92)	0.45 (0.41 – 0.49)
NTNF Inefficacy		80	1.00 (1.00 – 2.00)	0.59 (0.47 – 0.73)
NTNF - Cost		12	1.49 (1.00 – 2.00)	0.57 (0.32 – 1.00)
NTNF -Side effects		73	1.00 (0.50 – 2.00)	0.62 (0.50 – 0.79)
NTNF -Other		52	2.00 (1.00 – 3.00)	0.45 (0.34 – 0.59)

*For reason of discontinuation: the definition of discontinuation used was to consider stopping a biologic only (failures =TNF 1229, NTNF =240)

TNF or Non-TNF (NTNF). The goal was to remove the baseline characteristics of patients being assigned to one of the two treatments and reduce the channeling bias. Propensity scores were calculated using a logistic regression with treatment (TNF vs NTNF) as dependent variables and several independent variables used as adjustments in the Cox models to evaluate drug survival.

Table 2 Propensity score adjustment overall and by line of treatment

TNF vs Non-TNF	HR (95% CI) Ending drug or adding other DMARD
Overall	1.09 (0.96 – 1.23), P=0.175
First line	0.85 (0.65 – 1.11), P=0.247
Second line	1.13 (0.86 – 1.48), P=0.387
Third line or more	1.30 (1.07 – 1.57), P=0.008

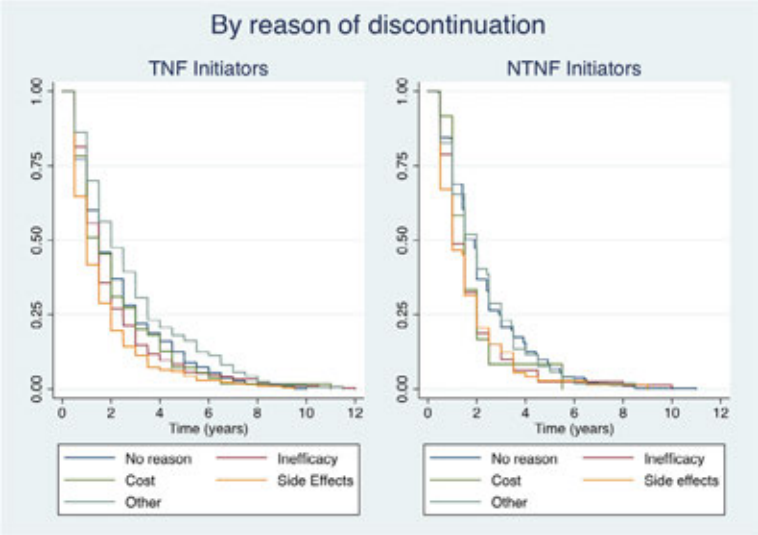

Figure 1 Kaplan Meier curves for reason of discontinuation by TNF and NTNF initiators.

Results: Strict inclusion criteria requiring an observation before and after bDMARD initiation resulted in 4,230 RA patients studied, 3129 initiating a TNF and 1833 initiating NTNF bDMARD or tsDMARD. Mean age of patients was 58 years with a median RA duration of 16 years. TNF had annual discontinuation rates of 0.13 (0.12-0.14) as first line, 0.25 (0.23-0.27) as second line, and 0.42 (0.39-0.46) as third line treatment. NTNF bDMARDs and tsDMARDs showed discontinuation rates of 0.18 (0.14-0.22) per year as first line bDMARD, 0.19 (0.16-0.21) as second line, and 0.21 (0.19-0.23) as third line (see Table 1 for more details). By line of treatment, TNF had lower discontinuation rates used as a 1st line medication compared to NTNF bDMARDs and tsDMARDS, which showed similar persistence regardless of treatment line. However, after adjustment for baseline characteristics through the PS analyses (see Table 2) in the comparison of TNF vs NTNF, only 3rd line treatment showed a difference with TNFs having an 30% increased likelihood of discontinuing compared with NTNF patients. Importantly, long-term persistence was similar for TNF and non-TNF overall. Side effects followed by inefficacy were the most frequent reasons for discontinuation for both action mechanisms (see Figure 1). Cost was also a significant reason among NTNF patients.

Conclusion: While our findings showed relatively low discontinuation rates, the more recently-available non-TNF bDMARDs had similar rates as TNF after propensity score adjustment, which aligns with the latest ACR RA treatment guidelines. With additional follow-up, similar analyses should be done with jakinibs.

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Safety and Effectiveness of Upadacitinib or Adalimumab in Patients with Rheumatoid Arthritis: Results at 48 Weeks

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Background/Purpose: In the SELECT-COMPARE study in rheumatoid arthritis (RA) patients (pts) with inadequate response to methotrexate (MTX), upadacitinib (UPA), a JAK1- selective inhibitor, was superior to placebo (PBO) or adalimumab (ADA), for treatment of signs & symptoms and for inhibition of radiographic progression vs PBO up to 26 weeks (wks). All pts were on stable background MTX. [1]

We report safety and efficacy of UPA plus stable background MTX up to 48 wks in this phase 3 study.

Methods: Pts were randomized to once-daily (QD) UPA 15mg, PBO, or ADA 40mg every other wk, with all patients continuing background MTX. The study was double-blind for 48 wks. Between Wks14-26, pts were rescued (from PBO to UPA, UPA to ADA, or ADA to UPA) if there was < 20% improvement in tender/swollen joint count (Wks 14/18/22) or if Clinical Disease Activity Index (CDAI) was >10 (Wk26); all PBO pts who were not rescued were switched to UPA at Wk 26. Efficacy was analyzed by randomized group. Non-responder imputation (NRI) was used

Table 1

Endpoint	Week 12			Week 26			Week 48	
	PBO N=651	UPA N=651	ADA N=327	PBO N=651	UPA N=651	ADA N=327	UPA N=651	ADA N=327
ACR20 (%)	36	71*** #	63	36	67*** ##	57	65##	54
ACR50 (%)	15	45*** ###	29	21	54*** ###	42	49##	40
ACR70 (%)	5	25*** ###	13	10	35*** ###	23	36###	23
DAS28CRP ≤3.2 (%)	14	45*** ###	29	18	55*** ###	39	50###	35
DAS28CRP <2.6 (%)	6	29*** ###	18	9	41*** ###	27	38##	28
CDAI ≤10 (%)	16	40*** ##	30	22	53*** ###	38	47###	34
CDAI ≤2.8 (%)	3	13*** ##	8	6	23*** ###	14	25##	17
SDAI ≤11.0 (%)	15	40*** ##	30	22	54*** ###	39	49###	35
SDAI ≤3.3 (%)	3	12*** #	7	5	24*** ###	14	25##	17
Boolean REM	2	10*** ##	4	4	18*** ###	10	21#	15
ΔPain	-15.7	-32.1***###	-25.6	-18.6	-36.8*** ##	-31.9	-36.7#	-32.1
ΔHAQ-DI	-0.28	-0.60***##	-0.49	-0.33	-0.69*** ##	-0.57	-0.73##	-0.6
ΔmTSS†	NA	NA	NA	0.94	0.16***	0.19	0.28***	0.39
No Rad Progression (%)†	NA	NA	NA	74	87***	88	86	88

Results are based on following analyses: binary endpoints, NRI, with Wk26 rescue handled by LOCF; mTSS, ANCOVA with linear extrapolation (LE); other continuous endpoints, ANCOVA with rescue handling via LOCF. **, *** p≤ .01 and .001 for UPA vs PBO; #, ##, ### p≤.05, .01 and .001 for UPA vs ADA. For ADA vs PBO, 95%CI are mostly non-overlapping

Table 2. Treatment-emergent adverse event summary; E/100PY in Patients (EAER)		
	Any UPA, N=1417,PY=1243.3	Any ADA, N=579,PY=467.8
Any Adverse Event (AE)	266.4	294.8
Serious AE	12.9	15.6
AE Leading To Discontinuation Of Study Drug	7.4	11.1
Serious Infection	4.1	4.3
Herpes Zoster‡	3.1	1.3
Hepatic disorder¥	17.7	13.9
Any Malignancy (excluding NMSC)ɣ	0.4	0.6
MACE (adjudicated)δ	0.4	0.4
Venous Thromboembolic Events (adjudicated)§	0.3	1.1
Deathsφ	0.4	0.9

†For pts randomized to PBO at BL, ΔmTSS at Wk48 was 1.73; 74% pts had no progression (based on LE). Results are based on 2nd Reading Session.
‡Herpes zoster: majority of cases on UPA were nonserious and involved 1 dermatome
¥Hepatic disorders: majority based on ALT/AST elevations
ɣMalignancies excl.non-melanoma skin cancer: UPA:1 laryngeal cancer, 1 endometrial adenocarcinoma, 1 malignant melanoma, 1 adenocarcinoma gastric; 1adenocarcinoma of colon; ADA: 1 malignant melanoma; 1 colon cancer metastatic), 1 lung neoplasm malignant
δMACE (includes CV death, non-fatal myocardial infarction [MI], non-fatal stroke): UPA : 1 non-fatal stroke; 3 non-fatal MI, 1 CV death; ADA:1 non-fatal stroke, 1 CV death
§VTE: UPA, 1 deep vein thrombosis (DVT), 2 pts with PE, 1 pt with DVT and PE; ADA: 4 pts with PE, 1 pt with DVT.
φDeaths (includes non-treatment emergent deaths): UPA : 2 deaths (undetermined/unknown), 1 cardiac failure, 1 sudden death, 1 arteriosclerosis coronary artery; ADA :1 left ventricular failure, 1 craniocerebral injury, 1 colon cancer, 1 mixed connective tissue disease

for binary endpoints for rescue prior to Wk26. Last observation carried forward (LOCF) was used for continuous endpoints and binary endpoints after Wk26. Treatment-emergent adverse events (AE) per 100 pt yrs (PY) were summarized up to July 6 2018 for pts with any exposure to ADA or UPA.

Results: In SELECT-COMPARE, 1629 pts were randomized at BL. Among 651 pts randomized to UPA, 38.7% were rescued between Wks 14-26; of those who remained on UPA, 86% completed Wk 48, while 5.8% and 0.3% discontinued study drug between BL and Wk 48 due to AE and lack of efficacy (LoE), respectively. Among 327 pts randomized to ADA, 48.6% were rescued between Wks 14-26; of those who remained on ADA, 76% completed Wk48, while 13.1% and 0 discontinued study drug between BL and Wk48 due to AE and LoE, respectively. The cumulative exposures were 1243.3 and 467.8 PYs for UPA and ADA, respectively. At Wk26, and Wk48, significantly more pts in the UPA vs ADA group achieved ACR20/50/70, low disease activity and remission (Table); this was also true for visits between Wks 26 and 48. Similarly, improvements in pain and function were significantly greater in the UPA vs ADA group through Wk48. At Wk26, there was significantly less radiographic progression for UPA vs PBO, which was maintained through Wk48 (based on linear extrapolation).

Adverse events are reported in the table (in events per 100 PY). The rate of AE leading to discontinuation was higher with “any ADA” vs “any UPA”, while the rate of Herpes zoster was higher with “any UPA” exposure.

Conclusion: UPA continued to demonstrate superior clinical and functional responses vs ADA through Wk48. Inhibition of structural joint damage with UPA was also maintained through 48 wks vs PBO. Safety was consistent with observations in the first 26 wks.[1]

Reference:

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Disclosure: R. Fleischmann, AbbVie, 2, 5, Acea, 2, 5, Akros, 5, Amgen, 2, 5, AstraZeneca, 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, 5, Celltrion, 5, Celtrion, 2, 5, Centrexion, 2, Eli

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Abstract Number: 0528

Assessment of Bone and Cartilage Turnover Markers Following Treatment with Repository Corticotropin Injection in Patients with Persistently Active Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Persistently active rheumatoid arthritis (RA) is an autoimmune disorder characterized by chronic inflammation and bone loss.[1] Although short-term administration of corticosteroids (CSs) is recommended alongside use of disease-modifying anti-rheumatic drugs (DMARDs) for active disease, CS use is often associated with exacerbation of bone loss.[2] Repository corticotropin injection (RCI) is FDA approved for short-term adjunctive use in the treatment of RA. A naturally sourced complex mixture of purified adrenocorticotropic hormone ($ACTH_{1-39}$) analogues and other pituitary peptides, RCI acts as an agonist for all 5 melanocortin receptors (MCRs). RCI activation of MCRs exhibits anti-inflammatory and immunomodulatory effects. *In vivo* data have shown RCI suppression of bone resorption via osteoclast reduction.[3] As an exploratory aim of a broader 2-part, multicenter, placebo-controlled

Marker	Mean (SD)		*P* Value[b]
	Baseline	Week 12	
Bone degradation			
CTX, ug/L	4.8 (2.1)	4.8 (1.9)	0.866
CTX-I, ug/L	0.4 (0.2)	0.4 (0.2)	0.956
sRANKL, pmol/L	2057.7 (3592.9)	2107.6 (3794.6)	0.284
Bone formation			
OPG, pmol/L	4.7 (1.8)	4.7 (2.0)	0.997
PINP, ug/L	52.2 (28.2)	47.4 (26.2)	**0.004**
Cartilage degradation			
CTX-II, ug/L	3.5 (2.3)	3.0 (2.2)	**0.006**
CTX-II CRT, ng/mmol	452.4 (325.4)	362.5 (273.1)	**<0.001**

a All patients who received study drug and had any post-treatment efficacy assessment. b From one-sample t test. Bold values are statistically significant. Abbreviations: CRT, creatinine; CTX, C-terminal cross-linking telopeptide; CTX-I, C-terminal cross-linking telopeptide of type I collagen; CTX-II, C-terminal cross-linking telopeptide of type II collagen; mITT, modified intent-to-treat; OPG, osteoprotegrin; PINP, N-terminal propeptide of type I collagen; SD, standard deviation; sRANKL, soluble receptor activator of nuclear factor kappa-β ligand.

Marker	Mean (SD)						*P* Value[b] (RCI vs Placebo)	
	Baseline		Week 12		Week 24		Week 12	Week 24
	Placebo (n=76)	RCI (n=77)	Placebo (n=76)	RCI (n=77)	Placebo (n=76)	RCI (n=77)		
Bone degradation								
CTX, ug/L	4.6 (2.0)	4.8 (1.9)	4.6 (1.6)	4.6 (1.4)	4.5 (1.7)	4.8 (2.8)	0.751	0.968
CTX-I, ug/L	0.4 (0.2)	0.4 (0.2)	0.4 (0.2)	0.5 (0.2)	0.4 (0.2)	0.4 (0.2)	0.586	0.127
sRANKL, pmol/L	2416.3 (3825.9)	1519.4 (2378.3)	2358.6 (4401.7)	2451.8 (4417.6)	2105.6 (4116.9)	2939 (5006.2)	**0.036**	**0.010**
Bone formation								
OPG, pmol/L	4.7 (1.8)	4.9 (1.8)	4.7 (1.9)	4.8 (2.2)	5.1 (2.1)	4.9 (2.0)	0.500	0.701
PINP, ug/L	52.5 (26.4)	54.8 (28.8)	48.7 (25.1)	51.2 (29.1)	53.1 (26.2)	54.3 (40.1)	0.674	0.934
Cartilage degradation								
CTX-II, ug/L	3.6 (2.4)	3.7 (2.5)	3.2 (2.4)	2.9 (2.2)	3.3 (2.1)	3.1 (1.9)	0.940	0.732
CTX-II CRT, ng/mmol	460.5 (368.3)	463.7 (316.9)	382.5 (257.5)	368.0 (228.6)	391.6 (236.0)	339.4 (189.7)	0.426	0.250

a mITT population, n=153. b From two-sample t test. Bold values are statistically significant. Abbreviations: CRT, creatinine; CTX, C-terminal cross-linking telopeptide; CTX-I, C-terminal cross-linking telopeptide of type I collagen; CTX-II, C-terminal cross-linking telopeptide of type II collagen; mITT, modified intent-to-treat; OPG, osteoprotegrin; PINP, N-terminal propeptide of type I collagen; RCI, repository corticotropin injection; SD, standard deviation; sRANKL, soluble receptor activator of nuclear factor kappa-β ligand.

Phase 4 efficacy and safety study, biomarkers associated with bone loss were assessed to evaluate the impact of RCI treatment on bone turnover in patients with persistently active RA.

Methods: Adults with persistently active RA despite DMARD and CS use were enrolled and remained on their current stable DMARD and CS doses throughout the study. During the initial 12-week open-label (OL) period (Part 1), all patients received 80 U RCI (subcutaneously [SC], 2x/wk). Those who achieved low disease activity (defined as DAS28-ESR < 3.2) at Week 12 were subsequently entered into the double-blind (DB) period (Part 2) and randomized to RCI (80 U) or matching placebo SC 2x/wk for an additional 12 weeks. Mean levels of bone turnover biomarkers (C-terminal cross-linking telopeptide [CTX], C-terminal cross-linking telopeptide of type I collagen [CTX-I], osteoprotegrin [OPG], N-terminal propeptide of type I collagen [PINP], and soluble receptor activator of nuclear factor kappa-β ligand [sRANKL]) and cartilage degradation biomarkers (C-terminal cross-linking telopeptide of type II collagen [CTX-II] and CTX-II creatinine [CRT]) were assessed at baseline (BL) and at Weeks 12 and 24.

Results: Of the 153 patients who entered the DB period (RCI, n=77; placebo, n=76), 127 (83%) completed the study. At completion of the OL period (Week 12), mean levels of bone biomarkers (with the exception of bone formation marker PINP) remained unchanged compared with BL, and significant decreases in mean levels of cartilage degradation markers

CTX-II (P=0.006) and CTX-II CRT (P< 0.001) were observed **(Table 1)**. For those who underwent an additional 12 weeks of RCI treatment during the DB period (n=77), there was a significant increase from BL in mean sRANKL levels at both Week 12 (P=0.036) and Week 24 (P=0.010) compared with placebo, suggesting a potential increase in osteoclast differentiation; however, mean levels of all other bone and cartilage biomarkers remained stable at these time points **(Table 2)**.

Conclusion: Bone and cartilage biomarker levels were mostly stable throughout the study, suggesting a potential bone-sparing effect of RCI.

References:

1. Fardellone P, et al. *Mediators Inflamm*. 2014:484280.
2. Tada M, et al. *Osteoporos Int*. 2016;27(2):729-35.
3. Wright D, et al. *Arthritis Rheumatol*. 2018;70(Suppl 9):1-3553.

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Abstract Number: 0529

Characterization of Remission in Patients with Rheumatoid Arthritis Treated with Upadacitinib or Comparators

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SESSION INFORMATION

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Background/Purpose: Across all phase 3 studies, treatment with upadacitinib (UPA), a JAK1-selective inhibitor, was associated with significantly higher remission (REM) rates, compared to placebo (PBO) or active comparators in RA patients (pts) who were methotrexate (MTX)-naive, had inadequate response to conventional synthetic (csDMARD-IR) or had inadequate response or intolerance to biologic DMARDs (bDMARD-IR).

	SELECT EARLY (MTX-naïve)			SELECT COMPARE (MTX-IR)			SELECT BEYOND (bDMARD-IR)		
Parameter at 12 weeks	MTX N=314	UPA 15 mg QD N=317	UPA 30 mg QD N=314	PBO +MTX N=651	ADA 40 mg EOW +MTX N=327	UPA 15 mg QD +MTX N=651	PBO +csDMARD N=169	UPA 15 mg QD +csDMARD N=164	UPA 30 mg QD +csDMARD N=165
Proportion of patients achieving REM by various criteria (NRI), (%)									
DAS28-CRP <2.6	14	36***	41***	6	18	29*** ###	10	29***	24***
CDAI ≤2.8	6	16***	21***	3	8	13*** ##	5	8	12*
SDAI ≤3.3	6	16***	22***	3	7	12*** #	5	9	11*
Boolean REM	6	13**	15***	2	4	10*** ##	2	7*	8**
Mean Change from BL (mean)†									
SJC28	-7.3	-8.4***	-8.8***	-5.0	-7.3	-8.0*** #	-4.6	-7.8***	-6.9***
TJC28	-8.2	-10.11***	-10.7***	-5.6	-8.5	-9.7*** ##	-5.3	-10.0***	-9.5***
PtGA	-24.6	-34.9***	-38.0***	-15.2	-23.6	-30.4*** ###	-10.0	-26.0***	-29.3***
PhGA	-35.2	-45.6***	-47.0***	-24.6	-35.6	-38.5***	-25.5	-38.8***	-40.5***
hsCRP	-10.6	-17.5***	-16.4***	-1.7	-9.4	-12.5*** ##	-1.1	-11.0***	-11.5***
Proportion of patients achieving individual components of the Boolean REM criteria (NRI), (%)									
PtGA ≤10 (mm)	13	25***	30***	7	12	20*** ###	8	15*	19**
TJC28 ≤1	22	38***	37***	13	25	33*** #	13	30***	26**
SJC28 ≤1	32	44**	48***	19	32	42*** ##	23	32$^{\delta}$	33*
hsCRP ≤1 mg/L	62	84***	87***	50	69	78*** ##	49	87***	79***

† For continuous endpoints, results are based on MMRM
For EARLY: *P<.05; **P<.01; ***P<.001 for UPA 15 mg or 30 mg vs MTX.
For COMPARE: *P<.05; **P<.01; ***P<.001 for UPA 15 mg vs PBO. #P<.05; ##P<.01; ###P<.001 for UPA 15 mg vs ADA. Comparison not indicated for ADA vs PBO.
For BEYOND: $^{\delta}$P<.1 *P<.05; **P<.01; ***P<.001 for UPA 15 mg or 30 mg vs PBO
DAS28-CRP, 28-joint disease activity score using C-reactive protein; CDAI, clinical disease activity index; SDAI, simplified disease activity index; SJC28, swollen joint count of 28 joints; TJC28, tender joint count of 28 joints; PtGA, patients' global assessment of disease activity, PhGA, physician's global assessment of disease activity; hsCRP, high-sensitivity C-reactive protein

REM definitions are based on composite scores of various individual assessments of disease activity. To determine the response to UPA on REM and component assessments, we assessed the proportions of pts achieving REM using multiple REM definitions, and the improvement in their respective individual components, compared to PBO or active comparators, in 3 different RA pt populations spanning a range of RA pt populations.

Methods: Three phase 3 studies included pts who were MTX naïve (SELECT EARLY, n=945), MTX-IR (SELECT COMPARE, n=1629) and bDMARD-IR (SELECT BEYOND, n=498). The proportion of pts achieving REM at Week (Wk) 12 by 4 definitions (DAS28-CRP< 2.6; CDAI ≤2.8; SDAI ≤3.3 and Boolean, defined as ≤1 for TJC, SJC, patient's global assessment of disease activity [PtGA], and CRP ≤1 mg/L) were determined. For each definition of REM, the mean change in each of the respective component scores was also assessed. Binary endpoints are based on Non-responder imputation (NRI), and continuous endpoints on mixed-effect model repeat measurement (MMRM). Comparisons were made between UPA-treated groups vs respective control arms (MTX, adalimumab [ADA] or PBO).

Results: Pt demographics and disease characteristics have been previously reported. 1-3 At 12 wks, in EARLY and COMPARE, a significantly greater proportion of pts receiving UPA 15 mg or 30 mg QD achieved REM by all 4 definitions vs MTX, PBO or ADA (Table). In BEYOND, (a refractory population many of whom had inadequate response to multiple bDMARDs), a significantly greater proportion of pts receiving UPA 30mg achieved all REM definitions vs PBO within the first 12 wks, with significantly greater proportions receiving UPA 15mg achieving DAS28-CRP< 2.6 and Boolean REM (Table). Rates of REM in BEYOND further increased through Wk 24 for both dose groups.1 Compared to respective control groups, pts receiving UPA 15 or 30 mg QD had significantly greater improvements in each REM disease component (except for PhGA vs ADA in COMPARE). Significantly more pts

receiving UPA also achieved the required cutoffs on the individual components of Boolean REM compared to respective controls.

Conclusion: Significantly greater proportions of pts receiving UPA 15 or 30mg achieved REM by multiple definitions at 12 wks compared to PBO, MTX or ADA. All disease activity components of each REM definition were significantly improved in pts receiving UPA compared to MTX or PBO, and all Boolean components were significantly improved in pts receiving UPA 15mg compared to ADA.

Reference:

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Abstract Number: 0530

Phase I Evaluation of the PDE4 Inhibitor LY2775240: Head to Head Comparison with Apremilast Using an Ex Vivo Pharmacodynamic Assay

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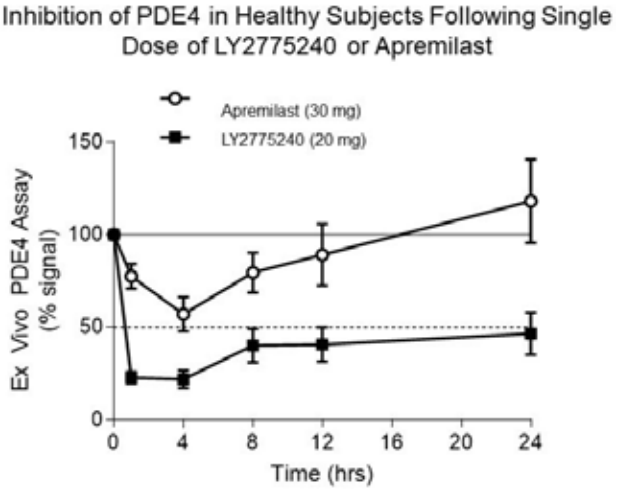
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM



Inhibition of PDE4 using an ex vivo PD assay with LPS as the stimulus. Data for n=11 subjects shown. Mean +/- SEM

Background/Purpose: LY2775240 is a potent and selective phosphodiesterase (PDE4) inhibitor being investigated as a potential treatment for inflammatory disorders, such as psoriasis. PDE4 is expressed primarily in immune cells, and enzymatically degrades cyclic adenosine monophosphate (cAMP). Inhibition of PDE4 leads to increased cytoplasmic cAMP and reduced pro-inflammatory immune responses. Pharmacodynamic (PD) effect measured as inhibition of PDE4 activity can be assessed with an ex vivo whole blood assay where the stimulant is the bacterial endotoxin lipopolysaccharide (LPS) and the readout is secretion of the cytokine TNF alpha.

Methods: In the first part of a Phase 1 (First-in-Human), single-center, randomized, 2-part study evaluating safety, tolerability and pharmacokinetics of LY2775240 in healthy subjects; subjects received LY2775240 or placebo (8:2) in a blinded manner. LY2775240 at 0.1, 0.5, 1.5, 5, 10, 20, 30, or 40 mg was given orally as a single dose. Ex vivo PDE4 inhibition assays were conducted at pre-dose, 4, 12, and 24 hours. The second part was an open-label, 2-period, crossover design in healthy subjects (n=11) that included a single dose of either LY2775240 (20 mg) or apremilast (30 mg) in each period. Ex vivo PDE4 inhibition assays were conducted at pre-dose, 1, 4, 8, 12, and 24 hours. TruCulture (Myriad RBM) assay tubes containing LPS with a 24-hour incubation at 37°C were used for the ex vivo PD assay, with TNF alpha levels measured by MSD assay at Covance (Durham NC).

Results: LY2775240 was safe and well tolerated in this Phase 1 study. The most common AEs were nausea, diarrhea and headache, consistent with those reported with other drugs in the PDE4 inhibitor class. No SAEs were reported. LY2775240 PK was well characterized over the dose range studied, and the half-life supports a once-a-day dosing regimen. In the first part, the ex vivo PD assay showed dose dependent decreases of TNF alpha across the dose range studied. The 20 mg dose of LY2775240 led to near maximal inhibition in this assay and was selected for comparison with the clinical dose (30 mg) of apremilast. LY2775240 maintained >50% inhibition of TNF alpha induction over the 24-hour duration, while apremilast achieved peak inhibition of 50% at 4 hours, while returning to ~10% inhibition within 12 hours post dose.

Conclusion: The 20 mg dose of LY2775240 demonstrated an increased and sustained inhibition of PDE4 activity over 24 hours when compared to the clinical dose of apremilast.

Disclosure: D. Dairaghi, Eli Lilly and Company, 1, 3; **K. Cox**, Eli Lilly and Compahy, 1, 3; **S. Ho**, Eli Lilly and Company, 1, 3; **P. Klekotka**, Eli Lilly and Company, 1, 3; **D. Phillips**, Eli Lilly and Company, 1, 3; **J. Lim**, Eli Lilly and Company, 1, 3; **S. Urva**, Eli Lilly and Company, 1, 3; **D. Patel**, Eli Lilly and Company, 1, 3.

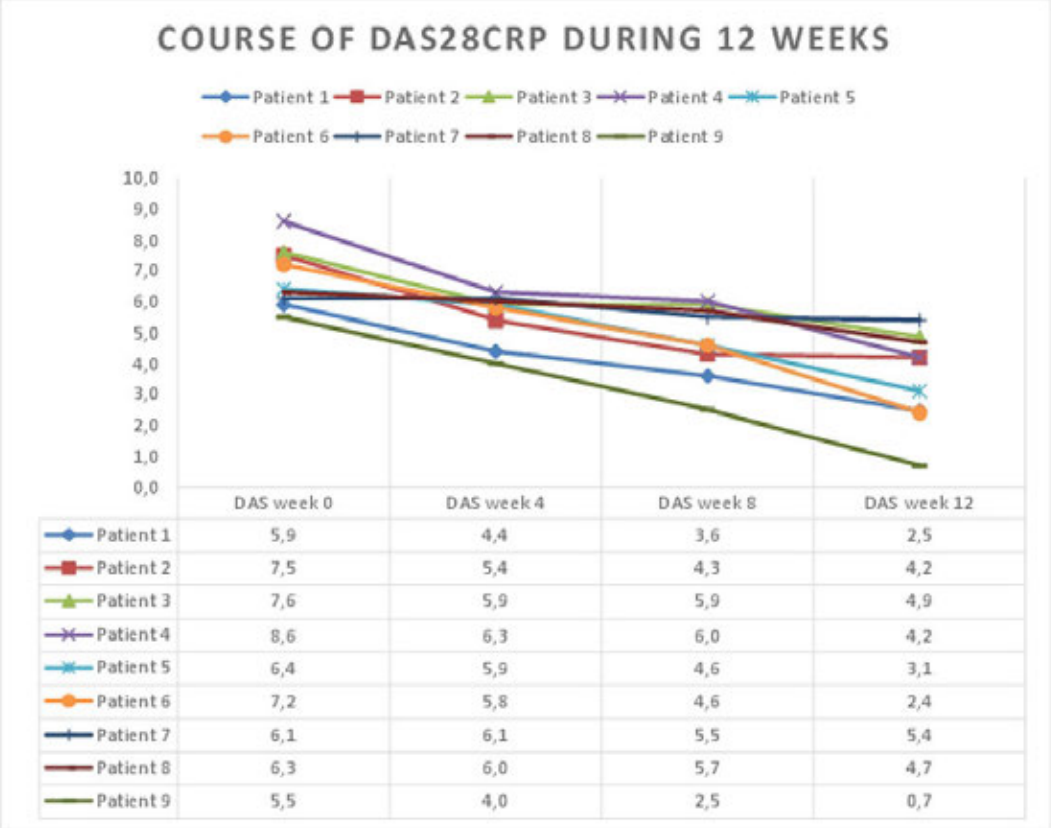
Abstract Number: 0531

Efficacy and Safety of Gonadotropin-Releasing Hormone Antagonism in Severe Biologic Refractory Rheumatoid Arthritis

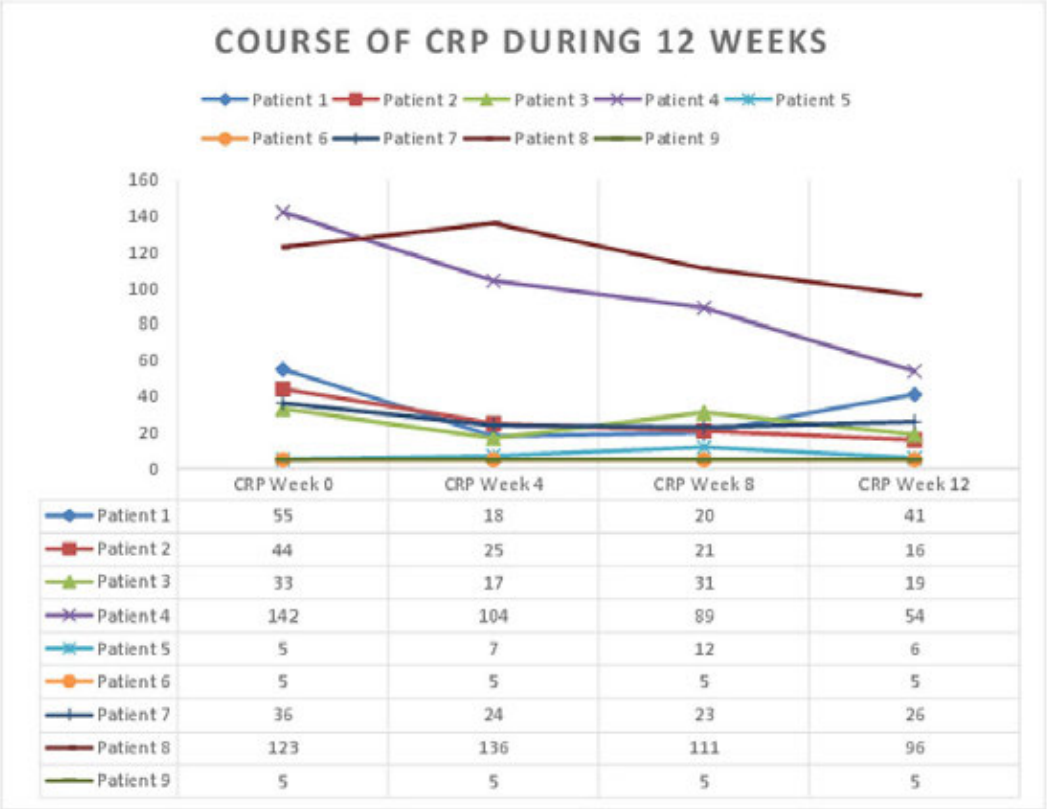
Anita Kass,[1] Hans Christian Gulseth,[1] and Camilla Zettel[1], [1]Betanien Hospital, Skien, Norway

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The pathogenesis of rheumatoid arthritis (RA) is unclear, and additional therapeutic approaches are needed. The improvement of RA disease activity during pregnancy, and flares during the postpartum has been described. Control of the reproductive axis originates in the hypothalamus with the periodic pulsatile release of gonadotropin-releasing hormone (GnRH). Non-reproductive functions of GnRH include stimulation of immune responses (1), and this hormone has shown proinflammatory effects. A proof-of-concept, double blind, randomized controlled trial of GnRH antagonism in RA showed promising results, including a significant reduction in TNF (2). Here, the efficacy and safety of long-term GnRH antagonism therapy to patients with severe, biologic refractory RA is reported.



	DAS week 0	DAS week 4	DAS week 8	DAS week 12
Patient 1	5,9	4,4	3,6	2,5
Patient 2	7,5	5,4	4,3	4,2
Patient 3	7,6	5,9	5,9	4,9
Patient 4	8,6	6,3	6,0	4,2
Patient 5	6,4	5,9	4,6	3,1
Patient 6	7,2	5,8	4,6	2,4
Patient 7	6,1	6,1	5,5	5,4
Patient 8	6,3	6,0	5,7	4,7
Patient 9	5,5	4,0	2,5	0,7



	CRP Week 0	CRP Week 4	CRP Week 8	CRP Week 12
Patient 1	55	18	20	41
Patient 2	44	25	21	16
Patient 3	33	17	31	19
Patient 4	142	104	89	54
Patient 5	5	7	12	6
Patient 6	5	5	5	5
Patient 7	36	24	23	26
Patient 8	123	136	111	96
Patient 9	5	5	5	5

Methods: Nine patients (8 females and 1 male, mean age 59 years, mean disease duration 22 years, baseline mean DAS28CRP 6.79) with biologic refractory RA, fulfilling the ACR 2010 criteria, received off-label subcutaneous GnRH antagonist treatment in the form of either cetrorelix 0.75mg daily or degarelix 240mg loading dose, tapered down to 80mg approximately every 2 weeks. 12 week efficacy and safety data are reported. All patients were primary non-responders to the last biologic therapy administered. Stable concomitant csDMARDs and oral steroids were allowed. No intra-articular injections were received.

Results: DAS28CRP was significantly reduced ($p < 0.001$, Figure 1) at week 12 compared to baseline. The clinical and laboratory courses during 12 weeks are shown. All outcome measures were reduced, including joint counts, morning stiffness, MHAQ, and VAS patient reported outcomes. GnRH antagonism was well tolerated during this period, although hot flushes and mild to moderate injection site reactions were observed. Patient 3 developed a skin abscess on her foot where she had previously had several infections prior to GnRH antagonist therapy.

Conclusion: This data indicates that long-term GnRH antagonism may be beneficial in therapy-resistant RA patients. A plausible explanation involves the interruption of GnRH signaling on peripheral T cells. Further randomized controlled trials are required to verify these results and further assess safety.CRPcourses

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Disclosure: A. Kass, Kaass Discovery, 1; **H. Gulseth**, None; **C. Zettel**, None.

Abstract Number: 0532

A Phase 2 Study of E6011, an Anti-Fractalkine Monoclonal Antibody, in Patients with Rheumatoid Arthritis Inadequately Responding to Biologics

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to dual actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1, during their migration. We have conducted clinical trials of E6011, a novel humanized anti-FKN monoclonal antibody, for patients with rheumatoid arthritis (RA) in Japan[1]. This is the report of a Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group comparison study of E6011 in RA patients inadequately responding to biologics (NCT02960490).

Methods: During the 24-week double-blind period, patients with moderately to severely active RA of inadequate response to biologics were randomly assigned to E6011 400 mg or placebo groups at a 1:1 ratio. Patients who continued the study beyond Week 12 were further allocated to E6011 200 mg or 400 mg at a 1:1 ratio within the initially assigned group. Patients received either E6011 400 mg or placebo at Weeks 0, 1, 2, and every 2 weeks subsequently until Week 10 and then E6011 200 mg or 400 mg every 2 weeks between Weeks 12 and 22 in a double-blind manner.

Results: A total of 64 subjects (33 in the placebo group and 31 in the E6011 400 mg group) received study drug. Of the 64 subjects, 55 completed and 9 discontinued study treatment prematurely during the 12-week placebo controlled double-blind period. The ACR20 response rate at Week 12 (non-responder imputation), the primary endpoint, was 27.3% (9/33 subjects) in the placebo group and 22.6% (7/31 subjects) in the E6011 group. ACR50 and ACR70 response rate at Week 12 were 3.0%, 0% in the placebo group and 9.7%, 3.2% in the E6011 group, respectively. No statistically significant differences were found in any of the ACR components between the placebo and E6011 groups.

After completion of Week 12, 55 subjects were re-randomized and treated with E6011 200 mg or 400 mg (15 subjects for placebo/200 mg, 14 subjects for placebo/400 mg, 14 subjects for 400/200 mg, 12 subjects for 400/400 mg). Of the 55 subjects, 48 completed the planned treatment regimen and 7 discontinued study treatment prematurely between Week 12 and Week 24. During the Weeks 12-24, no apparent differences were found in any of the efficacy endpoints between the each groups during the Weeks 12–24 (after re-randomization). ACR20 response rate at Week 24 was 46.7% (7/15 subjects) in the placebo/200 mg group, 28.6% (4/14 subjects) in the placebo/400 mg group, 21.4% (3/14 subjects) in the 400/200 mg group and 33.3% (4/12 subjects) in the 400/400 mg group.ACR50 and ACR70 response rate at Week 24 were 20.0%, 0% in the placebo/200 mg group, 0%,

0% in the placebo/400 mg group, 7.1%, 0% in the 400/200 mg group and 16.7%, 0% in the 400/400 mg group respectively.

During the Weeks 0-24, Adverse events that occurred in at least 2 subjects in the 400/200 mg group or 400/400 mg group were injection site erythema and nasopharyngitis.

Conclusion: E6011 was well tolerated with no notable safety concerns, but did not show clear efficacy when administered subcutaneously for up to 24 weeks in RA patients with inadequately responding to biologics. Further investigation to seek an optimal clinical dose and evaluation period of E6011 are warranted.

Disclosure: Y. Tanaka, Abbvie, 8, AbbVie, 5, 8, Asahi-kasei, 2, Asahi-Kasei, 2, Asahi-kasei, BMS, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Ono, Pfizer, Sanofi, Takeda, UCB, 2, Astellas, 8, Astellas Pharma, 9, Astellas Pharma, Inc., 2, 3, 5, 8, 9, Astellas, BMS, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi-Tanabe, Pfizer, Sanofic, UCB, YL Biologics, 8, BMS, 2, 5, 8, Bristol-Myers, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Daiichi-Sankyo, 2, 8, Daiichi-Sankyo, Astellas, Eli Lilly, Chugai, Sanofi, Abbvie, Pfizer, YL Biologics, Bristol-Myers, 8, Eisai, 2, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 8, Genzyme, 5, Glaxo-Smithkline, UCB, Mitsubishi-Tanabe, Novartis, Eisai, Takeda, Janssen, Asahi-kasei, 8, Janssen, 8, Mitsubishi-Tanabe, 2, 8, Mitsubishi-Tanabe, Bristol-Myers, Eisai, Chugai, Takeda, Abbvie, Astellas, Daiichi-Sankyo, Ono, MSD, Taisho-Toyama., 2, Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, 2, Novartis, 8, Ono, 2, Pfizer, 5, 8, Pfizer Inc, 8, Roche, 5, Sanofi, 2, Takeda, 2, 8, Teijin, 8, UCB, 2, YL Biologics, 8; **T. Takeuchi**, AbbVie, 2, 5, 8, AbbVie GK, 2, 9, Asahi Kasei, 2, Asahikasei, 2, Asahikasei Pharma Corp., 2, Astellas, 2, 8, 9, Astellas Pharma Inc, 2, Astellas Pharma, Inc., 2, 5, 8, 9, Astra Zeneca, 2, AstraZeneca, 8, AYUMI, 2, 9, AYUMI Pharmaceutical Corporation, 2, BMS, 2, 8, Boehringer-ingelheim, 9, Bristol–Myers K.K., 9, Bristol-Myers, 2, Bristol-Myers Squibb, 8, Chugai, 2, 8, 9, Chugai Pharmaceutical Co, Ltd., 2, Daiichi Sankyo, 2, 8, 9, Daiichi Sankyo Co., Ltd., 2, Eisai, 2, 5, 8, 9, Eisai Co., Ltd., 2, Eli Lilly, 2, 8, Eli Lilly Japan, 9, Gilead Sciences, Inc., 9, GlaxoSmithKline K.K, 9, GSK, 8, Janssen, 2, 8, Janssen Pharmaceutical K.K, 9, Mitsubishi Tanabe, 2, 9, Mitsubishi Tanabe Pharma Co., 2, Mitsubishi-Tanabe Pharma Corp, 2, 8, 9, Nippon Kayaku, 2, Nipponkayaku, 2, 9, Nipponkayaku Co.Ltd., 2, Novartis, 2, 8, Novartis Pharma K.K, 2, 9, Novartis Pharma K.K., 2, Pfizer, 2, 8, Pfizer Japan, 2, 9, Pfizer Japan Inc., 2, Sanofi, 8, Sanofi K.K, 9, Shionogi & Co., 2, Shionogi & Co., LTD., 2, Taiho, 2, 8, 9, Taisho, 9, Taisho Toyama, 2, 8, Takahashi Industrial and Economic Research Foundation, 2, Takeda, 2, 8, Takeda Pharmaceutical Co., Ltd., 2, Teijin, 2, 8, UCB, 8, 9, UCB Japan, 9; **H. Yamanaka**, Teijin Pharma Limited, 5; **T. Nanki**, Eisai Co., Ltd., 2, 5, 8, Takeda Pharmaceutical Co., 8, Teijin Pharma Ltd., 2, 8, Eli Lilly Japan K.K., 2, 8, Bristol-Myers K.K., AbbVie GK., 2, Ono Pharmaceutical Co., Ltd., 2, 8, Novartis Pharma K.K., 2, 8, Asahikasei Pharma Corp., 2, 5, 8, Mitsubishi-Tanabe Pharma Co., 2, 8, Chugai Pharmaceutical Co., 2, 5, 8, Astellas Pharma Inc., 2, 8, Ayumi Pharmaceutical Corporation, 2, 8, Pfizer Japan Inc., 2, 8, Daiichi Sankyo Co., Ltd., 2, Shionogi & Co., Ltd., 2, Sanofi K.K., 2, Nippon Kayaku Co., Ltd., 2, 8, Yutoku Pharmaceutical Ind. Co., Ltd., 2, UCB Japan Co., Ltd., 2, 5, Nihon Pharmaceutical Co., Ltd., 2, Bayer Yakuhin, Ltd., 2, Janssen Pharmaceutical K.K., 8, AbbVie GK, 8, Boehringer Ingelheim, 8; **H. Umehara**, None; **N. Yasuda**, KAN Research Institute, Inc., 3; **F. Tago**, Eisai Co., Ltd., 3; **Y. Kitahara**, Eisai Co., Ltd., 1, 3; **M. Kawakubo**, Eisai Co., Ltd., 1, 3; **H. Hisaki**, Eisai Co., Ltd., 3; **S. Hojo**, Eisai Co., Ltd., 3; **T. Kawano**, KAN Research Institute, Inc., 3; **T. Imai**, KAN Research Institute, Inc., 3.

Abstract Number: 0533

Impact of Formulary Change on TNFi Treatment Patterns and Healthcare Utilization Costs in RA Patients

Jennifer Schenfeld,[1] Scott Stryker,[2] Hafiz Oko-osi,[1] and Bradley Stolshek[2], [1]Amgen, Inc, Thousand Oaks, CA, [2]Amgen Inc., Thousand Oaks, CA

SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Changes in formulary tiers can potentially have unintended impact on outcomes. Moderate-to-severe rheumatoid arthritis (RA) is often treated with Tumor Necrosis Factor inhibitors (TNFi). A large payer implemented a formulary change on January 1, 2015 that switched the tiering and modified the copayment for two TNFi's: etanercept (ETN) and adalimumab (ADA). The purpose of this study was to assess the effect of formulary changes on treatment patterns and healthcare utilization (HCU) costs among RA patients (pts) on TNFi, specifically ETN compared to other TNFi medications.

Methods: This claims-based, retrospective cohort study utilized Optum Clinformatics Data Mart from UnitedHealth Group. The calendar year 2015 was evaluated. Jan 1, 2015 served as the index-date; the 6 months preceding Jan 1, 2015 served as the pre-index period (baseline); and Jan 1 to Dec 31, 2015 served as the follow-up period. The cohort included pts ages ≥18, with a confirmed RA diagnosis prior to Jan 1, 2015; continuous enrollment from beginning of baseline through end of follow-up; and ≥1 TNFi claim(s) during baseline. The most proximal TNFi to the end of baseline served as the index TNFi. Pts were categorized as ETN or Other TNFi and assessed during follow-up for the first occurrence of a treatment outcome: continuer (no changes or gap ≤59 days); early-gap-restart (EGR) (≥60 but ≤180 day gap then restart index TNFi); early-switch (ES) (prescribed a different TNFi than index ≤180 days); discontinuers (no refills; restart; or switch during entire length of follow-up). HCU and mean costs were measured during follow-up.

Results: In 2015, n=9,058 pts met the inclusion criteria. At baseline, ETN accounted for 44.5% (n = 4,033) of pts, of which, 62.1% continued; 14.2% EGR;10.9% ES; 9.4% discontinued, and 3.4% had a gap-restart or switch occurring ≥ 180 days. Among Other-TNFi pts (55.5%) at baseline, 77.2% continued; 7.8% EGR; 4.4% ES; 8.8% discontinued; and 1.8% had a gap-restart or switch occurring ≥ 180 days (T.1). The total mean HCU costs were lower for ETN continuers compared to Other-TNFi continuers ($36,005, $40,102; p < .0001), and for ETN EGR pts compared to Other-TNFi EGR pts ($29,482, $37,121; p = .0002) (T.2). ES ETN pts were costlier than ETN continuers (T.2). Medical costs (inpatient/outpatient) of continuers and EGR were significantly lower

Table 1: Baseline Demographics and Characteristics

Baseline Demographics and Characteristics	Baseline Characteristics of Patients Enrolled in 2015 Cohort (n = 9,058)															
	Baseline Enbrel Patients (n = 4,033)								Baseline Other TNFi Patients (n = 5,025)							
	Treatment Outcomes								Treatment Outcomes							
	TNFi Continuer		Early Gap-Restart		Early-Switch		Discontinuer		TNFi Continuer		Early Gap-Restart		Early-Switch		Discontinuer	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Total Patients	**2,505**	**62.1**	**571**	**14.2**	**441**	**10.9**	**378**	**9.4**	**3,880**	**77.2**	**391**	**7.8**	**222**	**4.4**	**440**	**8.8**
Gender: Female**	1,890	75.4	439	76.9	328	74.4	273	72.2	3,015	77.7	320	81.8	178	80.2	324	73.6
Age Categories at Baseline																
18-44	421	16.8	95	16.6	103	23.4	61	16.1	525	13.5	52	13.3	49	22.1	68	15.5
45-54	591	23.6	158	27.7	122	27.7	82	21.7	849	21.9	93	23.8	59	26.6	74	16.8
55-64	810	32.3	164	28.7	160	36.3	115	30.4	1,165	30.0	96	24.6	67	30.2	114	25.9
65+	683	27.3	154	27.0	56	12.7	120	31.7	1,341	34.6	150	38.4	47	21.2	184	41.8
Use of Oral Glucocorticoids during Baseline (Yes)	916	36.6	194	34.0	213	48.3	169	44.7	1,509	38.9	148	37.9	132	59.5	207	47.0
Use of csDMARDs during Baseline (Yes)	1,498	59.8	295	51.7	291	66.0	215	56.9	2,318	59.7	229	58.6	145	65.3	257	58.4

*Footnote: **For Baseline Enbrel patients, early switch, there was 1 patient with unknown gender*

Table 2: Healthcare Utilization Covariates Measured during Patient Follow-up

Health Care Utilization Covariates	TNFi Continuer			Early Gap-Restart			Early Switch			Discontinuer		
	Enbrel	Other TNFi	p-value	Enbrel	Other TNFi	p-value	Enbrel	Other TNFi	p-value	Enbrel	Other TNFi	p-value
Health Care Utilization (HCU) Total Costs: Mean	$36,005	$40,102	<0.0001	$29,482	$37,121	0.0002	$45,640	$35,366	0.9709	$17,286	$18,747	0.9996
Inpatient and Outpatient Claims HCU Costs: Mean	$8,420	$21,415	<0.0001	$8,999	$18,573	<0.0001	$23,203	$9,737	0.7543	$12,526	$14,888	0.9633
RA-related HCU Total Costs: Mean	$26,921	$29,962	<0.0001	$19,630	$24,037	<0.0001	$18,789	$27,093	0.7180	$3,104	$4,098	0.9984
RA-related Inpatient & Outpatient Claims HCU Costs: Mean	$2,493	$12,770	<0.0001	$2,661	$8,275	<0.0001	$1,259	$3,900	1.0000	$2,719	$3,553	0.9997
Total Drug Costs (Any Rx Claim): Mean	$27,696	$20,703	<0.0001	$20,546	$19,654	0.9991	$22,437	$25,752	0.9999	$5,125	$4,843	1.0000
Total Drug Costs: TNFi and Biologic Medications: Mean	$24,352	$27,079	<0.0001	$16,894	$20,230	<0.0001	$17,022	$25,039	0.2877	.	.	.
Physician Visits (Any Reason): Mean number of Visits	19.0	22.6	<0.0001	18.7	23.2	0.0091	22.4	18.6	0.9999	21.2	23.5	0.8729
Physician Visits (RA-related): Mean number of Visits	6.0	8.2	<0.0001	5.5	7.3	0.0175	7.7	6.4	1.0000	5.7	6.3	0.9984
Inpatient Hospitalizations with at least 1 Overnight Stay (Any Reason): Mean	1.5	1.4	0.9422	1.3	1.6	0.9763	5.0	1.4	0.1237	1.8	2.0	0.9999
Duration (Days) of Inpatient Hospitalizations (Any Reason): Mean	10.5	10.6	1.0000	7.2	12.4	0.9024	55.0	8.3	0.3851	18.9	16.2	0.9993
Average Inpatient Hospitalization Days (Any Reason): Mean	6.8	7.2	1.0000	5.6	7.0	0.9998	11.0	5.3	1.0000	9.7	8.7	1.0000
Inpatient Hospitalizations with at least 1 Overnight Stay (RA-related): Mean	1.3	1.3	1.0000	1.3	1.4	0.9977	4.0	1.2	0.0170	1.5	1.4	1.0000
Duration (Days) of Inpatient Hospitalizations (RA-related): Mean	10.1	10.9	1.0000	6.9	12.5	0.8886	51.0	8.7	0.5117	16.6	14.5	1.0000
Average Inpatient Hospitalization Days (RA-related): Mean	7.4	7.7	1.0000	5.6	8.0	0.9922	12.8	6.3	1.0000	10.7	9.0	0.9995
Emergency Room Visits (Any Reason): Mean Number	1.9	1.8	0.9364	1.8	2.5	0.3728	1.3	1.7	1.0000	2.4	2.2	0.9990
Emergency Room Visits (RA-related): Mean Number	1.8	1.5	0.9352	1.5	2.0	0.8971	.	1.5	.	1.8	1.8	N/A
RA Procedures (Surgery for Hand, Wrist, Shoulder, Hip, Spine and Knee): Mean Number	2.0	2.0	0.9999	1.9	2.8	0.2801	.	1.7	.	2.3	2.6	N/A
Lab Tests: Mean Number	101.5	113.9	0.0051	91.9	93.6	1.0000	55.6	90.3	0.9978	105.7	107.2	1.0000
RA-related Lab Tests: Mean number	1.3	1.3	1.0000	1.3	1.0	0.8535	.	1.2	.	1.1	1.2	N/A
Radiology Orders (X-ray, CT Scan, MRI, Ultrasonography): Mean	3.8	3.8	1.0000	3.7	4.5	0.2031	6.1	3.6	0.7936	4.2	4.9	0.6052

for ETN compared to similar pts on Other-TNFi. While total mean drug costs based on pharmacy claims for any medication were higher for ETN continuers compared to Other-TNFi continuers, and for ETN ES compared to Other-TNFi ES pts, when evaluating specifically mean costs of TNFi and biologic (pharmacy or physician-administered) they were lower for ETN continuers, EGR, and ES compared to Other-TNFi pts with the same treatment outcomes (T.2).

Conclusion: In this plan, a formulary policy change did not result in healthcare cost savings during the first year of implementation. Continuing and EGR pts using Other-TNFi incurred higher costs than similar ETN pts. Pts switching away from ETN cost more than pts switching away from Other TNFi medications. Overall, ETN patients who experienced a formulary change resulted in higher costs.

Disclosure: J. Schenfeld, Amgen, Inc, 3, 4; **S. Stryker**, Amgen Inc., 3, 4, Amgen, Inc, 3, 4; **H. Oko-osi**, Amgen, Inc, 3, 4; **B. Stolshek**, Amgen, 1, 3, 4, Amgen, Inc, 3, 4.

Abstract Number: 0534

CXCL13 Serum Levels and Circulating Follicular Helper T-Cells Decrease After Co-stimulation Blockade with Abatacept in Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: CXCL13 chemokine, by interacting with CXCR5 receptor, attracts B-lymphocytes and CD4+CXCR5+ICOS+ follicular helper T-lymphocytes (THFs) in lymphoid follicles. In rheumatoid arthritis (RA) CXCL13 is expressed by synovial follicular dendritic cells and activated mature antigen-experienced T-helper cells. CXCL13 serum levels are increased in RA and associated with synovial infiltration by lymphoid aggregates, as well as with a preferential response to anti-IL-6R as compared to anti-TNFα monotherapy (1).

Abatacept (ABA), a T-cell co-stimulation blocker, reduces circulating THFs number in RA. This reduction is correlated with CXCL13 serum levels decrease in primary Sjögren's Syndrome, but not much information is available on this issue in RA (2).

The purposes of this study were to analyze the effect of ABA on CXCL13 serum levels in RA and to verify whether they predict the response to the drug.

Methods: 32 RA patients (F/M=25/7; median (25th-75th percentile) age=62 (52-66) years; CRP- DAS28=4.6 (4.0-5.3); ACPA positive: 81%), before and after 6 months of treatment with ABA were evaluated. Serum CXCL13 levels were dosed by commercial ELISA. Circulating TFHs were identifiedby flow-cytometry in 25 subjects. Response to treatment was evaluated with the EULAR criteria.

Results: At baseline, a positive correlation between CXCL13 levels and CRP-DAS28 values was found (r=0.34; p=0.05). After therapy with ABA + methotrexate, a reduction of CXCL13 was observed (158 (109-274) vs 96 (59-154) pg/ml; p< 0.01). It was significant only in responders (n: 22: 158 (104-293) vs 96 (89-182)) pg/ml; p< 0.01; in non-responders (n:10) =164 (95-240) vs 101 (57-142) pg/ml; p=0.06). At baseline, no significant difference was found between the two subgroups (p=0.47) and among patients seropositive for ACPA if compared with the negative ones (ACPA+ vs ACPA-=174 (117-287) vs 96 (73-194) pg/ml; p=0.07). A reduction of THFs was found (0.6 (0-3) vs 0.1 (0-0.7) % of CD4+ T cells; p=0.05), without correlation with the decrease of CXCL13 levels (r=0.20; p=0.33).

Conclusion: Our results confirmed that CXCL13 serum levels are directly correlated with disease activity and demonstrated that ABA therapy induces their reduction, as well as that of circulating THFs. These findings suggest that the co-stimulation blockade at central level and/or in the synovium lead to a reduced generation of THFs and production of CXCL13. We could not demonstrate that CXCL13 levels predict, or are correlated with, clinical response to ABA in this small cohort of patients.

References:

1.Dennis G, Arthritis Res Ther 2014; 2. Verstappen GM, Arthritis Rheumatol 2017.

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Abstract Number: 0535

Exploratory Analysis of a Phase 2b Study Confirms Substantial Pain Improvement with Anti-GM-CSF Monoclonal Antibody Otilimab (GSK3196165) in Patients (Pts) with Active RA

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SESSION INFORMATION

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Session Title: RA – Treatments Poster I: Novel Treatments

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Background/Purpose: Treatment of pain remains a priority for patients (pts) with RA. Otilimab (GSK3196165) is a human mAb that inhibits GM-CSF, a key driver in a broad range of immune-mediated conditions that is involved in the regulation of musculoskeletal pain. In the Phase 2b dose-ranging BAROQUE study (201755)[1] in pts with moderate to severe RA who failed MTX, otilimab plus MTX provided rapid and substantial improvement from baseline (BL) in pain vs placebo (PBO) as assessed by a 100 mm Visual Analogue Scale (VAS). The objective of this post hoc analysis was to further define the clinical relevance of the effect of otilimab on pain through assessment of responder rates.

Table 1. Repeated measures analysis of change from baseline in pain score up to Week 12 by otilimab dose (ITT population)

	Placebo (N=37)	Otilimab 22.5 mg (N=37)	Otilimab 45 mg (N=37)	Otilimab 90 mg (N=37)	Otilimab 135 mg (N=37)	Otilimab 180 mg (N=37)
Baseline Pain VAS						
Mean (SD)	66.1 (16.68)	71.2 (15.84)	70.1 (17.27)	65.8 (20.38)	67.1 (19.27)	61.6 (20.62)
Week 4						
n	34	34	36	37	36	36
Mean (SD)	60.5 (20.16)	61.4 (21.86)	53.3 (18.64)	48.5 (25.51)	53.4 (20.52)	45.1 (22.65)
LS mean change from BL (SE)	−5.44 (3.08)	−8.47 (3.11)	−14.83 (3.03)	−17.65 (2.99)	−13.39 (3.04)	−19.40 (3.04)
Difference to placebo		−3.03	−9.38	−12.21	−7.94	−13.96
(95% CI)		(−11.67, 5.61)	(−17.91, −0.86)	(−20.67, −3.74)	(−16.47, 0.58)	(−22.47, −5.44)
P-value		0.490	0.031	0.005	0.068	0.001
Week 8						
n (%)	34	34	35	37	35	34
Mean (SD)	61.5 (21.74)	60.4 (22.75)	49.6 (23.94)	48.3 (25.64)	46.5 (26.44)	41.4 (22.74)
LS mean change from BL (SE)	−3.98 (3.56)	−9.60 (3.58)	−18.55 (3.52)	−17.92 (3.46)	−20.49 (3.52)	−24.38 (3.54)
Difference to placebo		−5.61	−14.57	−13.94	−16.51	−20.39
(95% CI)		(−15.57, 4.34)	(−24.43, −4.70)	(−23.72, −4.16)	(−26.38, −6.65)	(−30.27, −10.52)
P-value		0.268	0.004	0.005	0.001	<0.001
Week 12						
n (%)	34	35	35	37	35	36
Mean (SD)	58.5 (22.49)	55.0 (23.01)	46.7 (22.99)	41.0 (28.30)	46.7 (25.74)	40.0 (19.88)
LS mean change from BL (SE)	−7.07 (3.71)	−14.09 (3.70)	−21.22 (3.66)	−25.25 (3.59)	−19.07 (3.66)	−25.01 (3.65)
Difference to placebo		−7.02	−14.15	−18.18	−12.00	−17.94
(95% CI)		(−17.36, 3.32)	(−24.42, −3.87)	(−28.35, −8.01)	(−22.27, −1.73)	(−28.18, −7.70)
P-value		0.182	0.007	<0.001	0.022	<0.001

BL, baseline; CI, confidence interval; ITT, intent to treat; LS, least squares; SE, standard error; VAS, visual analog score

Table 2. Summary of MCID, 30%, 50%, and 70% pain response and percentage difference vs placebo at Weeks 4, 8, and 12 by otilimab dose (ITT population)

	Placebo (N=37)	Otilimab 22.5 mg (N=37)	Otilimab 45 mg (N=37)	Otilimab 90 mg (N=37)	Otilimab 135 mg (N=37)	Otilimab 180 mg (N=37)
MCID pain response						
Week 4						
N	34	34	36	37	36	36
n (%)	9 (26)	15 (44)	24 (67)	21 (57)	17 (47)	25 (69)
Difference to placebo (%)		18	40	30	21	43
(95% CI)		(−0.05, 0.40)	(0.17, 0.64)	(0.07, 0.53)	(−0.02, 0.43)	(0.20, 0.66)
Week 8						
N	34	34	35	37	35	34
n (%)	12 (35)	18 (53)	21 (60)	23 (62)	23 (66)	23 (68)
Difference to placebo (%)		18	25	27	30	32
(95% CI)		(−0.06, 0.41)	(0.01, 0.48)	(0.04, 0.50)	(0.07, 0.54)	(0.09, 0.56)
Week 12						
N	34	35	35	37	35	36
n (%)	10 (29)	23 (66)	24 (69)	24 (65)	24 (69)	27 (75)
Difference to placebo (%)		36	39	35	39	46
(95% CI)		(0.13, 0.60)	(0.16, 0.63)	(0.12, 0.59)	(0.16, 0.63)	(0.22, 0.69)
30% pain response						
Week 4						
N	34	34	36	37	36	36
n (%)	7 (21)	10 (29)	12 (33)	14 (38)	15 (42)	16 (44)
Difference to placebo (%)		9	13	17	21	24
(95% CI)		(−0.12, 0.29)	(−0.08, 0.34)	(−0.04, 0.39)	(−0.01, 0.43)	(0.02, 0.46)
Week 8						
N	34	34	35	37	35	34
n (%)	5 (15)	10 (29)	17 (49)	16 (43)	19 (54)	18 (53)
Difference to placebo (%)		15	34	29	40	38
(95% CI)		(−0.05, 0.34)	(0.12, 0.56)	(0.07, 0.50)	(0.17, 0.62)	(0.16, 0.61)

Methods: BAROQUE was a Phase 2b multicenter, PBO-controlled study in 222 pts with RA (ACR 2010 criteria). Pts were randomized (1:1:1:1:1:1) to subcutaneous PBO or otilimab (22.5, 45, 90, 135, or 180 mg) plus MTX once weekly for 5 weeks, then every other week until Week 50. Pts without a good/moderate EULAR response at Week 12 or with DAS28(CRP) >3.2 at Week 24 escaped to otilimab 180 mg until study end. Change from BL in pain was assessed using a 100 mm VAS. Percentage of pts with pain improvement ≥minimal clinically important difference (MCID; 10% VAS response) and improvement in pain from BL of ≥30%, ≥50%, and ≥70% were compared by treatment groups at each visit up to Week 12. The analysis was restricted to pts with complete information; missing data or dropouts prior to Week 12 were not imputed.

Results: The BAROQUE study population had high baseline pain VAS (mean 67.0; standard deviation 18.49). Change from BL in pain VAS is shown in **Table 1.** Overall, otilimab dose groups showed a higher proportion of pts with pain improvement ≥MCID vs PBO, with the largest difference vs PBO in the 180 mg dose group at Week 12: 46% (95% CI 22%, 69% [75% vs 29% of pts with MCID]) (**Table 2**). At most timepoints, more pts achieved 30%, 50%, and 70% pain responses in the otilimab groups vs PBO and the difference generally increased with increasing treatment duration (**Table 2**). At Week 12 in the 90–180 mg dose groups, the difference vs PBO in 30% pain response ranged from 25% to 43% (greatest difference with otilimab 180 mg), 50% pain response ranged from 19% to 26% (greatest difference with otilimab 90 mg), and 70% pain response ranged from 5% to 21% (greatest difference with otilimab 90 mg).

Conclusion: Further to the observed clinically relevant change from baseline in VAS pain with otilimab plus MTX in the overall BAROQUE study population, this post hoc analysis shows that a greater number of pts had substantial (≥50%) improvement from BL in pain levels when treated with otilimab plus MTX vs PBO over 12 weeks. Phase 3

studies are ongoing in pts with moderate to severe active RA and will further assess the overall clinical benefit and sustained improvement in pain symptoms with weekly dosing of otilimab plus MTX.

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1. Buckley C et al. ACR 2018; abstract 1938 (oral)

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PERFUSE: A French Prospective/Retrospective Non-interventional Cohort Study of Infliximab-naïve and Transitioned Patients Receiving Infliximab Biosimilar SB2; An Interim Analysis

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Background/Purpose: SB2 is approved in the EU as an infliximab (IFX) biosimilar, having demonstrated bioequivalence and similar efficacy, safety and immunogenicity as the reference. There is limited real-world evidence published on persistence or safety of SB2, either in IFX-naiive patients or in those transitioning from originator or another IFX biosimilar. PERFUSE is an ongoing non-interventional study intending to enroll over 1,000 patients receiving SB2 as routine therapy, with the objective of describing clinical characteristics, effectiveness, treatment persistence and safety in patients initiating SB2 in routine clinical practice and followed for 12 months at 6 specialist rheumatology sites across France.

Methods: Eligible adult patients have a diagnosis of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Ankylosing Spondylitis (AS) and initiated SB2 in routine clinical practice after September 2017, either as their first IFX or transitioning from treatment with IFX originator or another IFX biosimilar. Data are captured prospectively and/or retrospectively from patient records obtained during routine clinic visits for up to 12 months (M12) following initiation. Outcome measures include persistence on SB2, clinical characteristics at baseline (time of initiation of SB2), disease scores (DAS28, BASDAI and Serious Adverse Events (SAEs).

Results: This interim analysis (IA) includes 177 patients (41 with RA, 23 with PsA and 113 with AS); of these, 24 patients with RA, 8 patients with PsA and 62 patients with AS reached M12 by the data extraction date. Persistence on

Table 1 (to go in Results section)

Table 1: Baseline characteristics, SB2 persistence, and disease scores	RA (N=41)		PsA (N=23)		AS (N=113)	
Age (mean, SD)	42 (12.3)		40.7 (9.9)		34.9 (12.6)	
Disease duration (mean, SD)	15.7 (7.9)		11.1 (8.2)		12.9 (10.9)	
Female (n) (%)	36 (87.8)		7 (30.4)		38 (33.6)	
Prior IFX (n) (%)						
Naiive	5 (12.2)		0 (0.0)		26 (23.0)	
Originator	19 (46.3)		16 (69.6)		57 (50.4)	
CTP13	17 (41.5)		7 (30.4)		30 (26.5)	
SB2 persistence						
Available M12 visit (n)						
Naïve	1		0		12	
Originator	10		7		30	
CTP13	13		1		20	
Overall**	24		8		62	
Patients remaining on SB2 at M12						
Naïve (n)	1		0		8	
Originator (n)	10		7		28	
CTP13 (n)	13		1		18	
Overall** (n) (%; 95% CI*)	24 (100; 85.8, 100)		8 (100; 63.1, 100)		54 (87; 76, 94.2)	
Disease score	**n**	**mean DAS-28 (95% CI)**	**n**	**mean DAS-28 (95% CI)**	**n**	**mean BASDAI (95% CI)**
Disease score in switched patients						
Baseline	34	2.4 (2.1, 2.8)	13	3.8 (0.7, 6.9)	76	7.6 (4.4, 10.7)
M6	32	2.5 (2.0, 2.9)	8	2.2 (1.4, 2.9)	67	5.2 (2.5, 7.9)
M12	22	2.7 (2.1, 3.2)	6	1.5 (0.9, 2.0)	43	2.6 (2.1, 3.2)
Mean change from baseline in switched patients						
M6	30	0.1 (-0.4, 0.7)	7	-2.3 (-8.8, 4.2)	59	-1.9 (-3.6, -0,1)
M12	21	0.3 (-0.2, 0.8)	5	-0.3 (-1.5, 1.0)	41	-1.6 (-3.8, 0.7)
Data extract: 6 May 2019 * Clopper Pearson 95% Confidence Interval ** Originator + CTP13 (+ Naïve where applicable)						

SB2 at M12 was 100% (95% CI 85.8, 100), 100% (95% CI 63.1, 100) and 87% (95% CI 76, 94.2) in RA, PsA and AS respectively. In the patients with prior IFX, no clinically meaningful difference in disease activity score from baseline to M6 was observed; BASDAI mean individual change was -1.9 (95% CI -3.6, -0.1) in AS (n= 59) and DAS28 mean individual change was 0.1 (95% CI -0.4, 0.7) in RA (n=30). Low sample size precluded effectiveness analysis of IFX-naiive patient data. Four SAEs were reported: One related to SB2 (infected cyst) and three unrelated (two RA disease flares and one overdose of vitamin K antagonists).

Conclusion: This IA indicates that patients with chronic inflammatory rheumatism can be successfully transitioned from originator or biosimilar IFX to SB2, with no loss of disease control and without safety concerns. Over 85% of patients initiated de novo or transitioned from originator or another IFX biosimilar continued SB2 treatment at M12 post-initiation. Subsequent to these preliminary data, the study will provide ongoing, pertinent information about long-term outcomes in these populations, helping to inform evidence-based treatment decisions.

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Abstract Number: 0537

Efficacy and Safety Results from a Randomized Double-Blind Study That Compared the Proposed Biosimilar ABP 798 with Rituximab in Subjects with Moderate to Severe RA

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SESSION INFORMATION
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Background/Purpose: ABP 798 is being developed as a biosimilar to rituximab, a CD20-directed cytolytic antibody that is approved in the US and EU for treatment of moderate-to-severe RA (US), severe RA (EU), non-Hodgkin's lymphoma, chronic lymphocytic leukemia, granulomatosis with polyangiitis and microscopic polyangiitis, and moderate-to-severe pemphigus vulgaris (US). A phase 1-phase 3 study was conducted to evaluate the pharmacokinetics (PK), safety and efficacy of ABP 798 in comparison with rituximab reference product (RP) in patients with moderate-to-severe RA. The key efficacy and safety results of this trial comparing ABP 798 with rituximab RP are presented here.

Methods: This was a randomized, double-blind, active-controlled study conducted in adult subjects with moderate-to-severe RA who had an inadequate response or intolerance to other DMARDs. Subjects were randomized (1:1:1) to receive 2 IV infusions of 1000 mg, 2 weeks apart as first dose of either ABP 798, rituximab sourced from the US (rituximab US), or rituximab sourced from the EU (rituximab EU). At Week 24, subjects in ABP 798 and rituximab EU arms received the second dose of the same treatment, while those in the rituximab US arm transitioned to receive ABP 798 for their second dose.

The key efficacy endpoint was defined as the evaluation of change from baseline at Week 24 in DAS28-CRP. Other efficacy endpoints included ACR20, ACR50, and ACR70 at Week 24. Since PK similarity was established between rituximab US and rituximab EU (results presented separately), the 2 rituximab RP arms were pooled for efficacy equivalence assessment.

Results: A total of 311 subjects were randomized (ABP 798, n=104; rituximab EU, n=104; rituximab US, n=103); all subjects were treated with at least one infusion of investigational product. Clinical equivalence between ABP 798 and rituximab RP was established with the 90% confidence interval (CI; -0.225, 0.264) and 95% CI (-0.273, 0.312) for DAS28-CRP change from baseline at Week 24 being within the prespecified equivalence margin of (-0.6, 0.6). The 90% and 95% CIs for the mean differences between ABP 798 and the individual rituximab RP arms were also within the pre-defined margin. Over the first 24 weeks, results from other efficacy endpoints (ACR20, ACR50, ACR70) also supported clinical similarity. Overall safety and immunogenicity profiles of ABP 798 were consistent with that reported for rituximab RP with no unexpected events over this period. Treatment-emergent adverse events (TEAEs) were reported in 50%, 42.3%, and 42.7% of patients that received ABP 798, rituximab EU, and rituximab US, respectively. Infusion reactions including hypersensitivity was the most common event of interest reported. Binding antibodies developed in 13.4%, 10.6%, and 19.6% of patients that received ABP 798, rituximab EU, and rituximab US, respectively; and neutralizing antibodies in 8.2%, 2.1%, and 8.2%, respectively.

Conclusion: Based on the results of this study. clinical equivalence of ABP 798 to rituximab RP was established for efficacy and safety in subjects with moderate-to-severe RA.

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Abstract Number: 0538

Long-Term Safety and Efficacy of Upadacitinib in Patients with Rheumatoid Arthritis and an Inadequate Response to CsDMARDs: Results at 60 Weeks

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Background/Purpose: Upadacitinib (UPA), an oral, JAK1-selective inhibitor showed efficacy over 12 weeks (wks) in patients (pts) with moderately to severely active rheumatoid arthritis (RA) and inadequate response to csDMARDs (SELECT-NEXT).[1]

We assessed safety and efficacy of UPA through Wk60 in an ongoing extension of the phase 3 SELECT-NEXT study.

Methods: Pts received once-daily (QD) UPA at 15 mg (UPA15), 30 mg (UPA30) or placebo (PBO) for 12 wks on stable background csDMARDs. From Wk12, the start of a long-term blinded extension, pts initially randomized to PBO at

BL were switched to UPA15mg or 30mg per pre-specified assignment at BL. Pts randomized to UPA continued their assigned dose. No dose adjustments of UPA were allowed; however, starting at Wk24, adjustments to background RA medications were permitted. Sites/subjects remain blinded to UPA dose throughout the extension period. Efficacy data up to Wk60 are reported "As Observed". Adverse events (AE) per 100 pt yrs (PY) are summarized based on a cut-off date of Mar 22 2018.

Results: 611/661 (92%) pts completed Wk12 and continued on to the extension. By the safety data cut-off date, 125/611 (20%) had discontinued study drug, 50 (8.2%) due to an AE, and 10 (1.6%) discontinued due to lack of efficacy. Cumulative exposure was 393.3 PYs and 372.4 PYs for UPA15 and UPA30 respectively. Based on As Observed analysis, for pts who continued on UPA15 (262/310 [85%]) and UPA30 (243/301 [81%]), clinical and functional outcomes continued to improve or were maintained through Wk60, with 59% and 56% of pts achieving DAS28-CRP < 2.6 and 35% and 32% achieving CDAI remission (≤2.8) with UPA 15 and 30 mg, respectively (Table 1). Pts who switched from PBO to UPA15 or UPA30 showed comparable efficacy to those initially randomized to UPA. The most frequently reported AEs were nasopharyngitis, urinary tract infection, upper respiratory

Table 1. Efficacy Endpoints at Week 60 (as observed); n/N (%)

	PBO→UPA 15 MG	PBO→UPA 30 MG	UPA 15 MG	UPA 30 MG
ACR20	84/93 (90)	71/82 (87)	147/173 (85)	148/170 (87)
ACR50	64/92 (70)	55/84 (65)	122/168 (73)	120/169 (71)
ACR70	46/95 (48)	43/84 (51)	88/171 (51)	77/168 (46)
DAS28-CRP LDA (≤3.2)	74/95 (78)	56/82 (68)	129/173 (75)	125/167 (75)
DAS28-CRP<2.6	60/95 (63)	46/82 (56)	102/173 (59)	93/167 (56)
CDAI LDA (≤10)	72/93 (77)	56/83 (67)	129/171 (75)	123/169 (73)
CDAI REM (≤2.8)	28/93 (30)	29/83 (35)	59/171 (35)	54/169 (32)
Change from BL in HAQ-DI	-0.79	-0.68	-0.83	-0.73

Table 2. Treatment- emergent Adverse events; E/100PYs

	UPA 15 mg, N=324 PYs=393.3 E/100PYs	UPA 30 mg, N=321 PYs=372.4 E/100PYs
Any Adverse Event (AE)	334.6	371.9
Serious AE	16.3	24.2
AE Leading To D/C of Study Drug	8.4	17.2
Serious Infection†	2.3	7.5
Herpes Zoster‡	3.1	7.5
Hepatic disorder¥	14.2	13.7
Malignancy (excl. NMSC)	1.0	2.7
MACE (adjudicated)δ	0.8	0.8
VTE§ (adjudicated)	0.3	0.3
Deathsφ	0	0.8

E, events; PYs, patient-years; E/100PY, events per 100 patient-years; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular event (cardiovascular death, non-fatal myocardial infarction (MI), non-fatal stroke); VTE, venous thromboembolism(DVT, deep vein thrombosis; PE, pulmonary embolism)

†Most frequently reported serious infection were pneumonia, sepsis, staphylococcal wound infection and bronchitis.

‡Herpes zoster: most involved 1 or 2 dermatomes. No meningoencephalopathic/ noncutaneous involvement, except one primary varicella zoster pneumonia (chicken pox). Two HZ events were reported as ophthalmic.

¥Hepatic disorders: Most were asymptomatic lab abnormalities.

δMACE: UPA15: 1 pt with non-fatal MI, 2 pts with non-fatal stroke; UPA30: 1 cardiovascular death, 1 non-fatal MI, 1 non-fatal stroke

§VTE: UPA15: 1 pt with DVT and PE; UPA30:1 pt with DVT

φDeaths: UPA30: 1 CV death in pt prior history of diabetes, hypertension, hyperlipidemia, non-fatal MI with coronary bypasses; 1 due to colon adenocarcinoma; 1 due to lymphangiosis carcinomatosa

References:

Burmester et al. Lancet. 2018 Jun 23;391(10139):2503-2512

tract infection, bronchitis, blood creatine phosphokinase increased, alanine aminotransferase increased, herpes zoster (HZ) and nausea. Most frequent AEs (≥0.8/100PYs) leading to premature study drug discontinuation were pneumonia, transaminase elevations, HZ and pyrexia. Event rates (E/100PYs) were numerically higher in UPA30 vs UPA15 for serious AE, AE leading to discontinuation, serious infections, HZ and malignancies, and were similar in UPA15 and UPA30 for adjudicated major adverse cardiovascular events and venous thromboembolic events (Table 2).

Conclusion: UPA15mg and 30mg on background csDMARD therapy demonstrated consistent efficacy and safety over 60 weeks in RA patients with inadequate response to csDMARDs. Both doses of UPA showed a similar efficacy profile at week 60, with numerically higher rates for certain safety events noted in the UPA30 group. An integrated safety analysis of upadacitinib across the phase 3 program is required to fully characterize the benefit:risk of UPA in RA.

Disclosure: G. Burmester, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma., 5, 8, AbbVie Inc., 5, 8, BMS, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Merck Shar & Dohme, 5, 8, MSD, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche, Sanofi-Genzyme, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Union Chimique Belge, 2, 5, 8; **F. Van den Bosch**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, Bristol-Myers Squibb, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sanofi and UCB, 5, 8, ABBVIE, CELGENE, ELI LILLY, GALAPAGOS, MERCK, NOVARTIS, PFIZER, VCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **L. Bessette**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, Amgen, BMS, Janssen, Roche, UCB Pharma, AbbVie Inc, Pfizer, Merck, Celgene, Sanofi, Eli Lilly, and Novartis., 2, 5, 8, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Bristol-Myers-Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5; **A. Kivitz**, AbbVie, 5, Amgen, 1, 4, 5, Boehringer Ingeleheim, 5, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 5, 8, Flexion Therapeutics, 8, Genzyme, 5, 8, Gilead, 1, 4, 5, Gilead Sciences, Inc., 4, Horizon, 8, Janssen, 5, Janssen Research & Development, LLC, 2, Merck, 8, Novartis, 1, 4, 8, Pfizer, 1, 4, 5, 8, Regeneron, 1, 5, 8, Sanofi, 1, 4, 5, 8, Sun Pharma, 5, SUN Pharma Advanced Research, 5, UCB, 5; **Y. Li**, AbbVie, 3, 4; **A. Friedman**, AbbVie, 1, 3, Abbvie, 1, 4; **A. Pangan**, AbbVie, 3, 4, AbbVie Inc., 3, 4; **H. Camp**, AbbVie, 1, 3, 4, Abbvie Inc, 1, 4; **J. Kremer**, AbbVie, 2, 5, Amgen, 5, Bristol-Myers Squibb, 2, 5, Corrona, 1, Genentech, 2, 5, Gilead, 5, Lilly, 2, 5, Novartis, 2, Pfizer, 2, 5, Regeneron, 5, Sanofi, 5.

Abstract Number: 0539

A Randomized Double-Blind Study Comparing Pharmacokinetics (PK) and Pharmacodynamics (PD) of ABP 798 with Rituximab in Subjects with Moderate to Severe RA

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: ABP 798 is being developed as a biosimilar to rituximab, a CD20-directed cytolytic antibody that is approved in the US and EU for treatment of moderate-to-severe RA (US), severe RA (EU), non-Hodgkin's lympho-

ma, chronic lymphocytic leukemia, granulomatosis with polyangiitis and microscopic polyangiitis, and moderate-to-severe pemphigus vulgaris (only US). A phase 1-phase 3 study was conducted to evaluate the pharmacokinetics (PK), pharmacodynamics (PD), safety, and efficacy of ABP 798 in comparison with rituximab reference product (RP) in patients with moderate-to-severe RA. Here, we report the results of PK and PD similarity of ABP 798 versus rituximab RP.

Methods: This was a randomized, double-blind, active-controlled study conducted in adult subjects with moderate-to-severe RA who have had an inadequate response or intolerance to other DMARDs. Subjects were randomized (1:1:1) to receive 2 IV infusions of 1000 mg, 2 weeks apart of first dose of either ABP 798, rituximab RP sourced from the US (rituximab US), or rituximab RP sourced from the EU (rituximab EU). After Week 24, subjects continued treatment with ABP 798 or rituximab EU. The primary endpoint was area under the serum concentration-time curve [AUC] from time 0 extrapolated to infinity [AUC_{inf}] and the maximum observed serum concentration [C_{max2}] following the 2nd infusion of 1st dose; secondary PK endpoints were AUC from time 0 on Day 1 prior to the 1st infusion of the 1st dose to 14 days post-dose ($AUC_{0\text{-}14\ day}$), AUC from time 0 to week 12 ($AUC_{0\text{-}12\ wk}$), and C_{max1} following the 1st infusion of the 1st dose. The PD was evaluated based on the percent of subjects with complete depletion in CD19+ cell count from Day 1 to Day 3.

Results: A total of 311 subjects were randomized (ABP 798, n=104; rituximab EU, n=104; rituximab US, n=103); all subjects were treated with at least one infusion of investigational product. For the primary PK endpoints, the study established PK similarity between ABP 798, rituximab (US) and rituximab (EU) based on 90% confidence intervals (CIs) of the adjusted geometric mean ratio (GMR) for AUC_{inf} and C_{max2} following the 2nd infusion of 1st dose being within prespecified equivalence margin of 0.8 and 1.25. PK similarity was also established between rituximab US and rituximab EU for AUC_{inf} and C_{max2} following the 2nd infusion of 1st dose. In addition, 90% CIs for the GMR for the secondary PK parameters ($AUC_{0\text{-}14\ day}$, $AUC_{0\text{-}12\ wk}$, and C_{max1} following the 1st infusion of the 1st dose) were also within the (0.8, 1.25) margin, supporting PK similarity. PD effects of complete CD19+ B-cell depletion were similar between ABP 798 and rituximab RP arms, with 92/97 (94.8%), 93/96 (96.9%), and 90/97 (92.8%) subjects showing complete B-cell depletion in ABP 798, rituximab EU, and rituximab US arms, respectively.

Conclusion: Results of this study demonstrated PK similarity of ABP 798 to rituximab RP in subjects with moderate-to-severe RA. The PD of ABP 798 and rituximab RP were also found to be similar.

Disclosure: G. Burmester, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma., 5, 8, AbbVie Inc., 5, 8, BMS, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Merck Shar & Dohme, 5, 8, MSD, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche, Sanofi-Genzyme, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Union Chimique Belge, 2, 5, 8; **S. Cohen**, AbbVie, 2, 5, Abbvie, 5, Amgen, 5, Amgen Inc., 2, 5, AstraZeneca, 2, 5, Biogen-IDEC, 2, 5, Bristol Meyer Squibb, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5; **D. Chien**, Amgen, 1, 3; **V. Chow**, Amgen, 1, 3; **Z. Pan**, Amgen, 1, 3.

Abstract Number: 0540

Comparing Real-world Retention Rates in a Matched Cohort of Rheumatoid Arthritis Patients Who Either Remained on the Etanercept Originator or Switched to a Biosimilar

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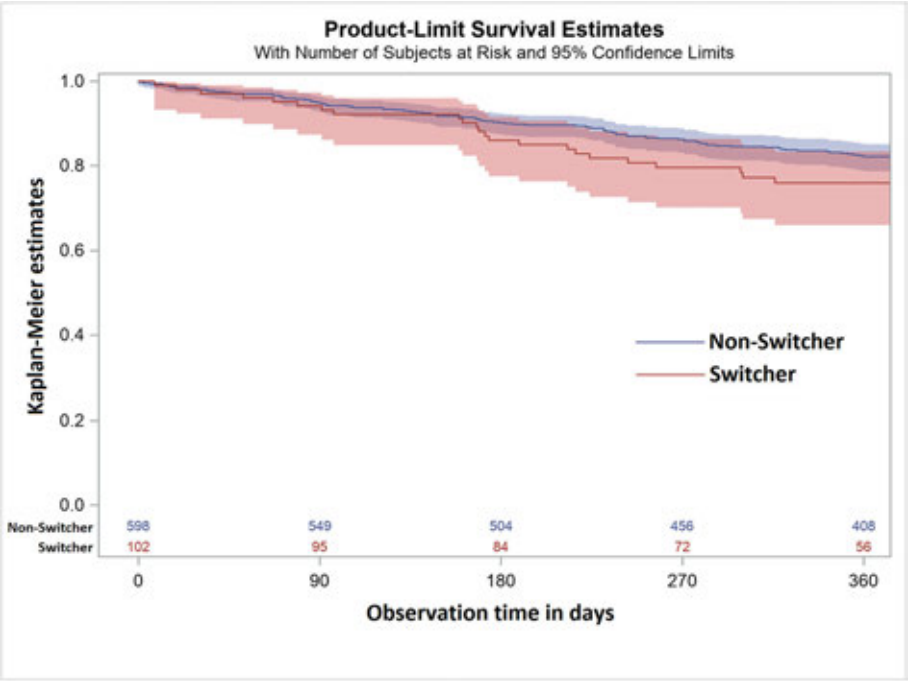
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In Germany, the first etanercept biosimilar was licensed in 2016. In contrast to other European countries there is no uniform recommendation for the prescription of biosimilars. The aim of this study was to compare treatment survival between patients who were switched from the etanercept originator to the etanercept biosimilar SB4 and patients who stayed on the originator treatment.

Methods: We used data of rheumatoid arthritis patients observed in the prospective, longitudinal RABBIT (*R*heumatoid *A*rthritis: *O*bservation of *bi*ologic *t*herapy) cohort until November 2018 who were treated with the etanercept originator (oETA) for at least six months. Patients who thereafter were switched to the biosimilar SB4 (bsETA) were matched (1:n) to patients who stayed on the original treatment using prescription time distribution matching [1] to control for survival bias. Matching criteria were sex, time of switch or corresponding duration of originator treatment in non-switchers and age as well as DAS28 at the time of switching or corresponding time point in non-switchers. The retention rates over one year were analyzed using Kaplan-Meier curves.

[1] Zhou Z et al., Am J Epidemiol. 2005.

Results: Overall, 1,751 patients fulfilled the inclusion criteria of whom 113 were switched to bsETA. Of these, 102 switchers could be matched to 598 patients who remained on oETA. In both groups, 78% of the patients were female, mean age was about 59 years, DAS28 was 3.2 and physical function as well as numbers of prior biologics were similar. Patients who remained on oETA were more often rheumatoid factor positive (71% vs. 63%), had more erosions (56% vs. 47%) and had more frequently three or more comorbidities (34% vs. 28%) than those who were switched to bsETA. The most common reason for switching was costs (79%). After one year, 23% (n=23) of bsETA patients and



Treatment continuation with 95% confidence intervals in etanercept patients who were either switched to the biosimilar SB4 or stayed on the originator.

17% (n=99) oETA patients had stopped the respective treatment. The main reason for discontinuation was “adverse events” in bsETA patients (56%, n=13, thereof 2 serious and 1 planned surgery) and “loss of response” in oETA patients (66%, n=65). Kaplan-Meier curves showed similar retention rates over 12 months for bsETA and oETA (figure). Nine bsETA patients were switched back to oETA.

Conclusion: Retention rates of etanercept treated RA patients who were either switched to the biosimilar SB4 or who stayed on the originator are comparable. Only few patients switched back to the originator.

Disclosure: L. Baganz, None; **A. Strangfeld**, AbbVie, BMS, MSD, Pfizer, Roche, Takeda and UCB, 8; **P. Herzer**, Pfizer, 8; **A. Krause**, Pfizer, 5, 8; **H. Tony**, Abbvie, 5, 8, Astra-Zeneca, 5, BMS, 5, 8, Chugai, 5, 8, Janssen, 5, 8, Lilly, 2, 8, MSD, 5, Novartis, 5, 8, Pfizer, 5, Roche Pharma, 5, 8, Sanofi, 5, 8; **A. Zink**, Astra Zeneca, BMS, Lilly, Pfizer, Roche und UCB, 5, 8.

Abstract Number: 0541

Multicenter, Evaluator-blinded, Randomized, Non-inferiority Study, to Assess the Efficacy, Safety and Immunogenicity of Etanercept Biosimilar (EtaBS) vs. Reference Etanercept (EtaRef) in Combination with Methotrexate for the Treatment of Patients with Rheumatoid Arthritis

Ingrid Strusberg,[1] Daniel Siri,[2] Maria Correa,[3] Santiago Scarafia,[4] Rodolfo Pardo Hidalgo,[5] Alberto Spindler,[6] Patricio Tate,[7] Horacio Venarotti,[8] Jorge Velasco Zamora,[9] Gustavo Citera,[10] Eduardo Mysler,[11] Ezequiel Klimovsky,[12] Andrea Federico,[12] Gabriela Eizikovits,[12] Lucas Cordeiro,[13] and Nestor Lago[13], [1]Instituto Strusberg, Córdoba, Argentina, [2]Paediatric Rheumatology International Trials Organisation (PRINTO), Genoa, Italy, [3]Consultorios Reumatológicos Pampa, Ciudad Autónoma de Buenos Aires, Buenos Aires, Argentina, [4]Hospital Municipal “San Cayetano”, Buenos Aires, Buenos Aires, Argentina, [5]CER San Juan, San Juan, Argentina, [6]Centro Médico Privado de Reumatología, Tucumán, Argentina, [7]OMI Centro Médico, Buenos Aires, Argentina, [8]Atención Integral en Reumatología – AIR, Buenos Aires, Argentina, [9]Instituto Médico CER, Quilmes, Argentina, [10]Instituto de Rehabilitación Psicofísica, Ciudad Autónoma de Buenos Aires, Buenos Aires, Argentina, [11]Organización Médica de Investigación, Buenos Aires, Argentina, [12]QUID Quality In Drugs SRL, BUENOS AIRES, Argentina, [13]Gema Biotech SAU, Buenos Aires, Argentina

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Enerceptan® (EtaBS) has been developed as a proposed biosimilar of etanercept. Phase I study demonstrated pharmacokinetic equivalence with EtaRef.

Methods: A multicenter, non-inferiority, randomized, assessor -blinded, parallel-group, controlled study was conducted in Argentina (NCT03332719). Adults with active moderate or severe RA (2010 ACR/EULAR criteria) with inadequate response to MTX (stable for ≥90 days and throughout the study) were included. Active RA was defined as ≥6 painful joints and ≥8 swollen joints (using 68 and 66-joint assessment respectively) and DAS28 (ESR) ≥ 3.2 and at least one erosion in hands or feet on X-ray at entry. Subjects were randomized in a 2:1 ratio to 32 weeks treatment with EtaBS or EtaREF in a weekly 50 mg dose subcutaneously. Stratification was based on prior use of biological DMARDS and concomitant use of steroids. The primary efficacy endpoint was ACR20 response rate at week 32. Safety, immunogenicity and steady state concentration of both drugs was evaluated. The non-inferiority margin for ACR20 was estimated in 12% with a power of 80%.

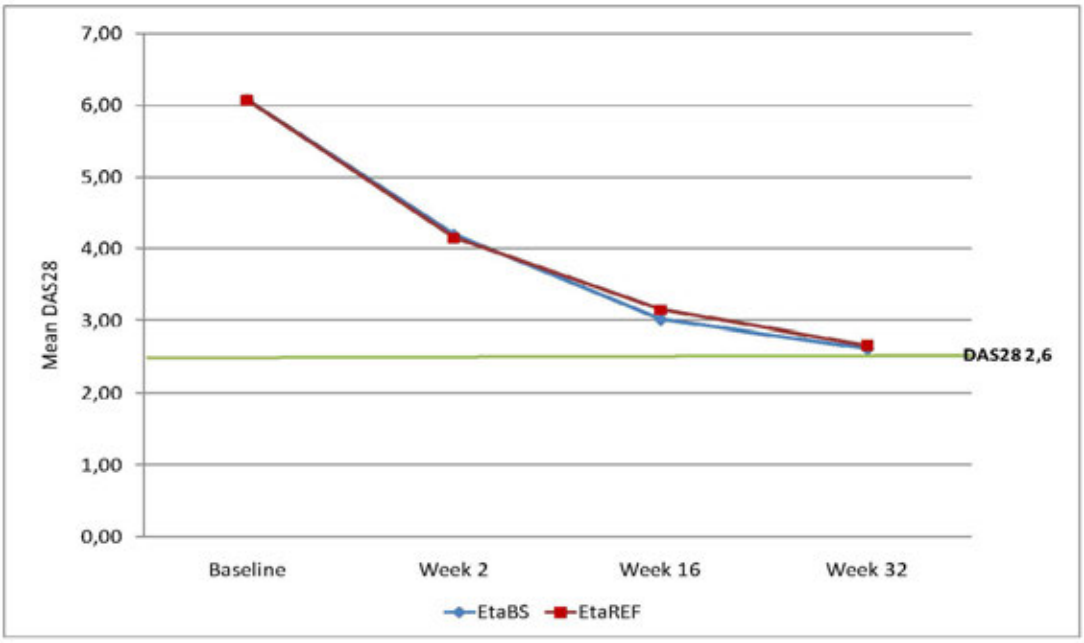


Figure 1. DAS28 average result from baseline to week 32. Per protocol analysis

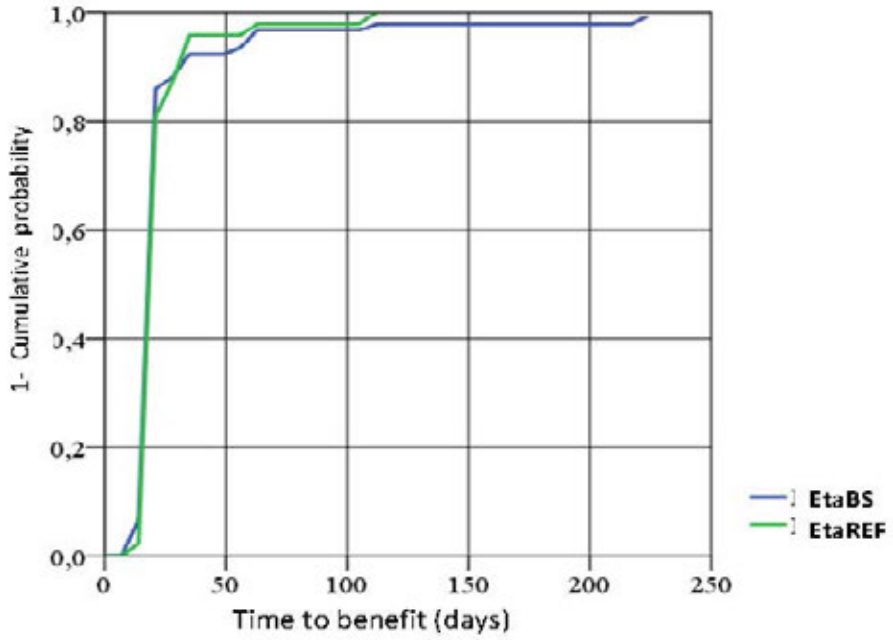


Figure 2. Cumulative probability of benefit. Per protocol analysis

Results: A total of 150 subjects were randomized, 99 were treated with EtaBS and 51 with EtaREF. Five (5) subjects discontinued treatment, 3 subjects treated with EtaBS and 2 treated with EtaREF. *Efficacy:* Per protocol analysis: 85 (92.4%) subjects treated with EtaBS and 44 (93.6%) subjects treated with EtaREF achieved ACR20 (Difference -1.2% CI 95% -10.1; 7.6%). ITT Analysis: 88 (88.9%) subjects treated with EtaBS and 46 (90.2%) treated with EtaREF achieved ACR20 (Difference -1.3%, CI 95% -11.6; 8.9%). ACR50 was achieved by 68.5% and 59.6% subjects and ACR 70 by 48.9% and 42.6%. Sharp/van der Heijde score without radiological progression was maintained by 98.9% and 97.9% respectively. DAS28 results are observed in **Figure 1**. **Figure 2** shows Time to benefit. *Safety*: Frequent

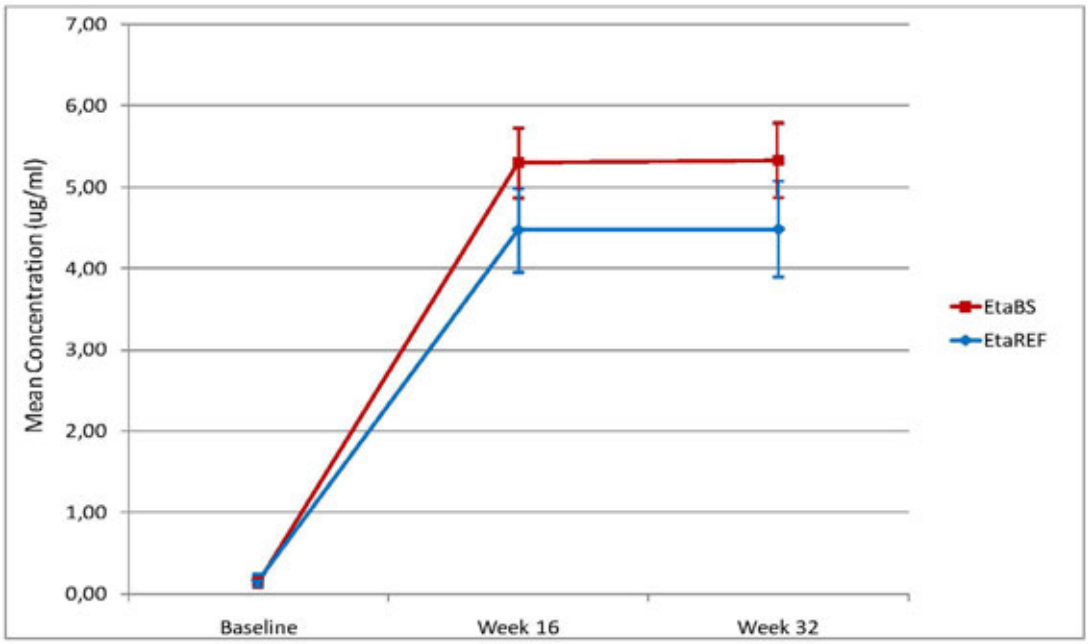


Figure 3. Steady State Concentration

ADRs were developed by 34 subjects (34.3%) treated with EtaBS and by 19 (38.0%) subjects with EtaREF. The most common reaction was upper respiratory tract infection. Six SAEs were developed by 4 subjects treated with EtaBS (lung cancer, epigastralgia, trombophlebitis of left forearm, spondylodiscitis -probably infective- renal colic and colelithiasis). Three subjects treated with EtaREF developed SAEs (unstable angina, acute pelvic inflammatory disease and carpus surgery). No hepatic alterations were developed. Injection site reactions were developed by 67 subjects (67.7%) treated with EtaBS and 33 subjects (66.0%) with EtaREF. Most frequent local reactions were pain and ecchymosis. No subject discontinued due to these reactions. *Immunogenicity*: Three subjects, 2 treated with EtaBS and 1 treated with EtaREF developed antibodies by week 32. All of them had good treatment response. Steady State Concentration results are shown in **Figure 3.**

Conclusion: In this non-inferiority 32 weeks trial, clinical and functional outcomes for EtaBS were not inferior to EtaREF. Both products showed similar safety, immunogenicity and radiographic profiles in patients with moderate to severe active RA on background MTX. EtaBS was granted biosimilarity.

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Abstract Number: 0542

'BENEFIT' Pan-European Observational Study to Evaluate the Real-world Effectiveness of SB4 Transition from Originator Etanercept (ETN) in Patients with Rheumatoid Arthritis or Axial Spondyloarthritis: A Switch Success Story

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SESSION INFORMATION
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Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: SB4, a biosimilar to the reference ETN, received EU marketing authorisation in January 2016, based on the totality of evidence from pre-clinical and clinical Phase I and III studies that demonstrated similar efficacy, bioequivalence, and comparable safety and immunogenicity to ETN. The BENEFIT study describes real world evidence on outcomes of transition from originator to biosimilar in both rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA) in 4 EU countries, outside the controlled setting of a randomised clinical trial, with the purpose of providing real world evidence on transition and outcomes of treatment switch in routine clinical practice.

Methods: Eligible patients had RA or axSpA and had initiated SB4 following treatment with a stable dose of originator ETN in a 6-month window. Data were captured from clinic records, retrospectively for 6 months prior and prospectively and/or retrospectively for 6 months after switch. Outcomes include disease score (DAS-28 for RA, BASDAI for axSpA) over time, clinical characteristics and management, and serious adverse events (SAEs).

Results: Of the 557 patients included, 358 had RA and 199 axSpA; data at baseline and after transition are illustrated in Table 1.

One adverse event of pneumonia was reported as Serious (SAE) and related to SB4. Six SAEs unrelated to SB4 were reported: Uveitis, umbilical hernia, relapsing pancreatitis, coronary artery disease, chronic obstructive pulmonary disease and lithium overdose.

Conclusion: These data from clinical practice indicate maintenance of disease status post-switch from ETN to SB4, without the need for dose adjustment, and with high persistence at 6 months after switch, in both RA and axSpA patients**.** No safety concerns were observed. The study data provide pertinent information about 6-month outcomes in these populations, helping to inform evidence-based treatment decisions.

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Table 1: Baseline characteristics of patients at transition, and 6-month outcomes				
	RA (N=358)		AxSpA (N=199)	
	Mean (SD)	Q1, Q3	Mean (SD)	Q1, Q3
Age in years	60.9 (11.09)	53.0, 69.0	49.9 (13.3)	40.0, 60.0
Women n (%)	264 (73.3)	–	54 (27.1)	–
Duration of disease, years	14.6 (9.43)	7.3, 21.0	12.9 (10.27)	5.9, 16.6
	Mean (SD)	95% CI	Mean (SD)	95% CI
Disease score (DAS-28, BASDAI) in 6 months prior to transition to SB4 (n =342 RA, 187 axSpA)	2.0 (0.84)	1.9, 2.1	2.5 (1.93)	2.2, 2.8
Disease score (DAS-28, BASDAI) at 6 months post-transition to SB4 (n =256 RA, 139 axSpA)	2.1 (0.85)	2.0, 2.2	2.3 (1.81)	2.0, 2.6
Individual change in disease score (DAS-28, BASDAI) from baseline to 6 months post-transition to SB4 (n= 252 RA, 136 axSpA)	0.0 (0.81)	-0.1, 0.1	-0.1 (1.22)	-0.3, 0.1
Outcomes at 6 Months Post-initiation (M6):				
Disease Activity:				
Patients in remission (DAS28 ≤2.6):				
At transition, n (%)	277 (81.0)		–	
At M6	194 (76.0)		–	
Patients with low disease activity (DAS28 ≤3.2, BASDAI <4):				
At transition, n (%)	313 (91.5)		146 (78.1)	
At M6, n (%)	226 (88.0)		110 (79.1)	
Persistence on SB4 at M6:				
Patients continuing SB4 at M6 (% and 95% CI)*	90.8 (87.2, 93.4)		92.4 (87.5, 95.4)	
SB4 Dose Regimen:				
ETN: SB4 regimen at transition, n (%):				
50mg QW: 50mg QW	267 (74.6)		132 (66.3)	
50mg Other: 50mg Other	59 (16.5)		46 (23.1)	
Other**	32 (8.9)		21 (10.5)	
SB4 regimen at transition and 6 months, n (%):				
50mg QW: 50mg QW	268 (79.5)		132 (69.8)	
50mg Other: 50mg Other	53 (15.7)		43 (22.8)	
25 mg Other: 25 mg Other	16 (4.7)		14 (7.4)	
DAS-28, Disease Activity Score 28; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; SD, standard deviation, CI, Confidence interval * Based on Kaplan-Meier (KM) approach ** Includes 25mg Other: 50mg Other; 25mg Other: 25mg Other; 50mg Other: 25mg Other				

Table 1 (to be placed following first paragraph of Results section)

5, 8, Roche, 5, 8, Sanofi, 5, 8, Sanofi-Aventis, 5, UCB, 5, 8; **A. Cantagrel**, Lilly France, 5, 8, Médac, 5, MSD France, 5, 8, Novartis, 5, 8, Roche, 5, 8, Sandoz, 5, Sanofi Aventis, 5, Biogen, 8, Celgene, 8, Nordic-Pharma, 8, Sanofi, 8, AbbVie, 2, 8, Chugai, 2, 5, 8, MSD, 2, Pfizer, 2, 5, 8, UCB, 2, 5, 8, BMS, 5, 8, Janssen, 5, 8; **A. Hernández**, None; **U. Freudensprung**, Biogen, 3, 4; **M. Rezk**, Biogen, 3, 4; **J. Addison**, Biogen, 3, 4.

Abstract Number: 0543

Cytokine Signaling Pathways Inhibited by Different Biologics in Rheumatoid Arthritis Patients

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Treatments Poster I: Novel Treatments

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Different types of cells play pathogenic roles in Rheumatoid Arthritis (RA). The immunogenetics of RA suggests a key role of aberrant pathways of T cell activation in the onset and/or perpetuation of the disease. The differentiation of the naïve CD4 T cell is aimed at differentiating into Th_1, Th_2 and Th_{17}. These molecules probably play a key role in the local generation of specific autoantibodies participating in the autoimmune cascade. Biological treatments for RA interfere different signaling pathways (CD28/CTLA4 system, TNF-α inhibitor, CD20 B cell depleting, IL-6 inhibition, JAKs inhibitors). There are no reports dealing about the impact of serological expression of cytokine profile in RA patients.

Methods: RA patients treated with DMARDs (>3 months) (Methotrexate) and/or biological drugs (Abatecept, Certolizumab pegol, Rituximab, Tocilizumab, Tofacitinib and Baricitinib) attending to two rheumatology outpatient clinics

Table 1. Cytokine profile according to treatment by ANOVA

Variable mean (SD)	Abatacept	Certolizumab	Rituximab	Tocilizumab	Tofacitinib	Baricitinib	Methotrexate	*P* value
IL-1	18.4 (7.7)	10.9 (9.7)	5.6 (6.1)	13.6 (6.8)	2.8 (0)	13.8 (16)	6.4 (7.8)	**0.004**
IFNa	130 (146.7)	76.5 (83.2)	4.7 (4.9)	89.6 (142.5)	30.7 (57.9)	107.2 (92.3)	33.1 (36.3)	0.071
IFNg	12.8 (40.2)	0.8 (0.1)	0.9 (0.1)	80.8 (240.1)	1 (0)	414.7 (339.1)	117.6 (260)	**0.003**
TNFa	8 (1.5)	6 (3.1)	4.3 (2)	7.4 (3.4)	3.4 (0)	3.4 (0)	4 (1.4)	**0.001**
CCL2	3043.1 (4023.7)	829.5 (522.4)	737.5 (509.2)	1603.1 (1039.9)	821.4 (828.4)	1146.8 (655.5)	926.2 (432.3)	0.081
IL-6	67.8 (19)	50.2 (57.4)	15 (27.1)	203.5 (318.9)	2.8 (0)	56.5 (71.9)	23.5 (35)	**0.045**
IL-8	150.8 (332.3)	15.4 (14.4)	17.5 (35.1)	87.3 (116.5)	3.1 (0.6)	28.1 (39.3)	12.2 (7.2)	0.313
IL-10	11.5 (3.6)	7.1 (6.2)	3.8 (3.9)	12.3 (7.5)	2.1 (0.6)	25.4 (31.7)	13.3 (20.5)	0.085
IL-12	34.6 (11.8)	16.7 (19.6)	6.8 (14.8)	28.2 (23.6)	0.2 (0)	0.2 (0)	0.2 (0)	**0.001**
IL-17	213.8 (295.2)	255.9 (269.2)	329.8 (299.5)	344.1 (317.9)	150.9 (135.6)	513.4 (475.1)	532.2 (516.6)	0.32
IL-18	270.3 (310.5)	304.2 (193.3)	251.8 (90.6)	331.4 (438.4)	292.5 (0)	585 (349.4)	353.3 (135.5)	0.466
IL-23	102.3 (130.1)	51.1 (60)	15.1 (27.3)	49.8 (30.8)	2.6 (0)	45.1 (32.5)	17.2 (24.4)	**0.039**
IL-33	69.9 (69.7)	51.8 (24.9)	33.9 (16.2)	85 (49.7)	21 (13.4)	252.3 (182.3)	112.5 (89.1)	**0.001**

were recruited. Blood sample were analyzed by the LEGENDplex Human Inflammation Panel method to perform the profile of cytokines. Disease activity was measured by DAS28-ESR scale, physical functionality with HAQ questionnaire and quality of life of the patient through the EuroQol 5-D questionnaire.

Statistical analysis: Data were presented as numbers, percentage, mean±SD. ANOVA test was performed to compare treatment between groups. P value ≤ 0.05 were considered statistical significant.

Results: Seventy-two RA patients were included, 64 (89%) were female and 19 (26%) smokers. Patients had different comorbidities: 6 (8%) diabetes mellitus, 14 (19%) high blood pressure, 4 (5%) ischemic cardiopathy and 10 (14%) osteoporosis. Ninty-eigth percent were positive for rheumatoid factor and 96% for anti-CCP. Treatment for RA were as follow: Abatacept 11 (15%), Certolizumab nine (13%), Rituximab 11 (15%) Tocilizumab nine (13%), Tofacitinib 10 (14%), Baricitinib 11 (15%), and Methotrexate monotherapy 11 (15%). Cytokine profile according to treatment is presented in Table 1.

Conclusion: Tofacitinib seems to have a better performance inhibiting the cytokine profile in RA patients. More studies and bigger sample are needed to replicate these finding.

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Abstract Number: 0544

Tolerance, Survival, and Adherence to Methotrexate Treatment in Patients with Rheumatoid Arthritis

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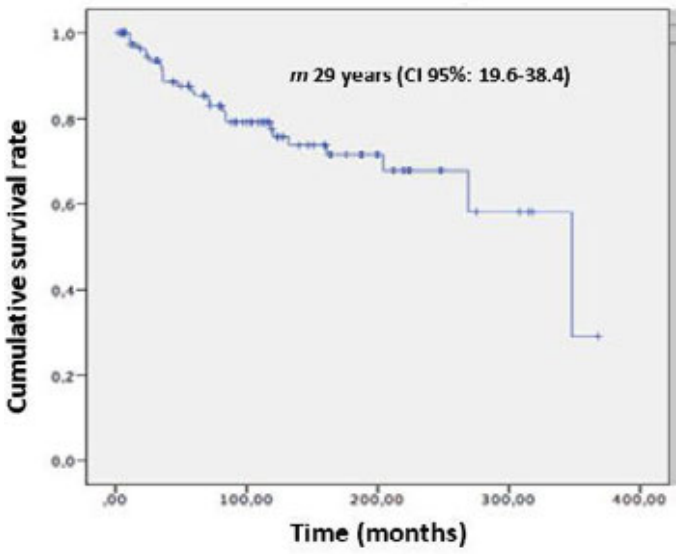
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate (MTX) is the most frequently used medication in patients with Rheumatoid Arthritis (RA). However, several authors have questioned its success due to the presence of adverse events and the lack of adherence.

Objectives: To determine cumulative survival of MTX, frequency and type of adverse events and causes of discontinuation in patients with RA

Methods: Consecutive patients 18 years and older with a diagnosis of RA (ACR / EULAR 2010 criteria), who had begun treatment with MTX during their disease were included. Sociodemographic, clinical and therapeutic data were collected. Date of initiation and suspension of MTX, route of administration, concomitant treatments, consumption of



m: median; CI: confidence interval

coffee and tobacco, presence of adverse events (AE) were all consigned. Adherence was evaluated using the Compliance Questionnaire Rheumatology questionnaire 5-item summary version (CQR5). Statistical Analysis: Descriptive statistics. Chi² test or Fisher's exact test; Survival of treatment by Kaplan-Meier and log Rank. Multiple logistic regression. A p value < 0.05 was considered significant.

Results: We included 118 patients, 101 were women (85.6%), with a median age (*m*) of 56 years (IQR 49-64) and disease duration *m* 10 years (IQR 6-18). Thirty-five patients (29.7%) were smokers and 56 patients (47.5%) consumed coffee. Eighty-five patients (72%) received MTX orally. 43.2% presented AE associated with MTX, but only 20 patients (16.9%) had to discontinue MTX. Gastrointestinal intolerance was the most frequent AE (27.1%), followed by laboratory test abnormalities (12.7%). 86.6% of the patients presented an adherence ≥80%. The median cumulative survival of MTX treatment was 348 months (95% CI: 235-460.9). In the univariate and multivariate analysis, there was no association of survival of MTX with sociodemographic variables, disease characteristics, concomitant treatment, route of administration, coffee consumption nor level of adherence.

Conclusion: In our cohort, adherence and survival of MTX treatment were good. The cumulative survival was almost 30 years. The presence of AE did not determine the suspension of treatment in most cases.

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Abstract Number: 0545

Molecular Analysis of the Mode of Action of Upadacitinib in Rheumatoid Arthritis Patients: Whole Blood RNA Expression Data from the SELECT-NEXT Study

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients with moderate-to-severe rheumatoid arthritis (RA) with an inadequate response to conventional synthetic disease-modifying anti-rheumatic drugs in the SELECT-NEXT[1] trial. This study provides the translational opportunity to evaluate the pivotal immune regulatory pathway targets affected by UPA in RA patients.

The purpose of the study is to investigate the mode of action (MoA) of UPA in patients with RA by assessing genome-wide RNA expression in whole blood.

Methods: A subset of patients with whole blood samples at baseline, week 2, week 4, and week 12 from the SELECT-NEXT (PBO N = 100; UPA 15 mg QD N = 99) study were analyzed. Gene expression was measured using the Affymetrix Clariom S HT microarray. Out of 800 whole blood samples, 775 passed quality control. Expression intensities were normalized with SCAN,[2] using the BrainArray V23 annotation to map probes to Ensembl gene IDs. For each treatment arm, change in expression from baseline to weeks 2, 4, and 12 was estimated in R using limma,[3] accounting for correlation between samples from the same patient. Association of transcripts with specific immuno-

Upstream Pathways	Activation Z Score UPA W2	Activation Z Score UPA W4	Activation Z Score UPA W12	B-H P Val UPA W2	B-H P Val UPA W4	B-H P Val UPA W12
CSF2	-0.577	-0.563	-1.162	0.0509	0.0029	< 0.0001
CSF3	-1.703	-1.597	-1.209	< 0.0001	0.0007	< 0.0001
IFN Beta	-3.341	-2.325	-0.358	< 0.0001	0.0026	0.0015
IFNG	-2.256	-1.012	0.292	< 0.0001	< 0.0001	< 0.0001
Interferon alpha	-3.308	-1.583	-1.082	< 0.0001	< 0.0001	< 0.0001
IL15	-2.424	-2.959	-2.125	0.0409	0.0188	0.0006
IL2	-0.067	-1.165	-2.25	< 0.0001	0.0026	< 0.0001
IL21	-3.344	-2.374	-2.089	0.0004	0.0095	0.0016
IL7	-1.573	-1.291	-0.922	0.0089	0.0126	0.0021
IL6	-2.919	-2.254	-0.798	0.0029	0.0047	< 0.0001
OSM	-2.636	-1.795	-0.043	0.0016	0.0093	0.0122
TGFB3	-0.943	-1.044	-1.673	0.0453	0.0449	0.0274
TNF	-2.946	-2.462	-1.224	< 0.0001	0.0001	< 0.0001
JAK	-1.463	-0.555	-0.555	0.0016	0.0398	0.0243
PI3K (complex)	-2.76	-1.314	-1.457	0.0003	0.0201	0.0001
PRKCA	-1.723	-1.605	-0.596	0.0021	0.0180	0.0115
STAT1	-1.722	-0.731	0.639	0.0005	0.0114	< 0.0001
STAT2	-2.386	-2.213	-1.076	0.0003	0.0038	0.0004
SYK	-1.592	-1.89	0.000	0.0029	0.0033	1.0000
TLR2	-1.492	-1.39	-1.054	0.0223	0.0258	0.0417
TLR3	-2.36	-1.937	-1.254	0.0006	0.0030	0.0379
TLR4	-1.315	-0.894	0.595	0.0022	0.0008	0.0001
TLR9	-2.48	-1.105	0.711	0.0116	0.0147	0.0098
Downstream Pathways	**Activation Z Score UPA W2**	**Activation Z Score UPA W4**	**Activation Z Score UPA W12**	**B-H P Val UPA W2**	**B-H P Val UPA W4**	**B-H P Val UPA W12**
Development of B lymphocytes	2.007	2.007	2.415	0.0011	0.0001	0.0005
Development of hematopoietic system	0.570	1.615	0.610	< 0.0001	< 0.0001	< 0.0001
Lymphopoiesis	0.575	0.529	1.598	< 0.0001	< 0.0001	< 0.0001
Quantity of T lymphocytes	1.381	1.189	-0.576	< 0.0001	< 0.0001	< 0.0001
Activation of leukocytes	-1.908	-1.029	-0.705	< 0.0001	< 0.0001	< 0.0001
Activation of lymphocytes	-1.213	-0.520	-0.228	< 0.0001	< 0.0001	< 0.0001
Degranulation of phagocytes	-1.856	-1.709	-1.132	< 0.0001	< 0.0001	< 0.0001
Response of mononuclear leukocytes	-1.209	-1.496	-0.831	0.0009	0.0002	0.0021
Phagocytosis	-1.780	-0.816	-1.594	< 0.0001	0.0002	< 0.0001
Inflammatory response	-3.046	-2.004	-1.519	< 0.0001	< 0.0001	< 0.0001
Adhesion of immune cells	-2.021	-1.525	-2.727	< 0.0001	0.0002	< 0.0001
Chemotaxis of myeloid cells	-3.283	-2.646	-2.365	< 0.0001	< 0.0001	< 0.0001

Activation Z Score = IPA predicted activation status (< 0 = inhibited; > 0 = activated)
B-H P value = IPA generated prediction p value corrected for multiple testing (Benjamini – Hochberg)

logical cell type was based on the public domain BLUEPRINT expression database. Pathway analysis was performed with Ingenuity® Pathway Analysis (Qiagen Inc.) version 47547484.

Results: Analysis of the top 100 most affected transcripts by UPA at week 2, week 4, and week 12 identified modest but highly significant modulation of a set of genes known to be differentially expressed in RA peripheral blood. mRNA associated with B and T lymphocytes were increased, while mRNA associated with neutrophils and monocytes were decreased, likely reflecting at least in part changes in leukocyte recirculation. Pathway analysis demonstrated a broad inhibitory effect by UPA on cytokine cytokines associated with the pathobiology of RA (IFNA, IFBNB, IFNG, IL2, IL5, IL6, IL7, IL15, IL21, CSF 2 – 3, OSM, TGFB, TNFA), on intracellular signaling-(STAT, JAK, SYK, PI3K, PRKCA), and on Toll-Like Receptor-pathways (TLR2, TLR3, TLR4, TLR9). Similarly, pathways related to both innate and adaptive immune activation, leukocyte movement, phagocytic cell activity, and leukocyte adhesion were predicted based on mRNA modulation, to be inhibited by UPA. Reciprocally, pathways associated with the numbers of B, T, and hematopoietic cells were predicted to be activated by UPA.

Conclusion: UPA directly inhibits several JAK-dependent pathways, indicative of a key role for JAK1 in multiple pathologic processes. Our data suggest also indirect modulation of a range of JAK-independent pathways. We conclude that UPA normalizes key pathobiological pathways in RA consistent with its clinical effect.

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2. Piccolo SR, et al. Genomics 2012;100(6):337-344.
3. Phipson B, et al. Ann Appl Stat 2016;10(2):946-963.

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Abstract Number: 0546

Change in Rheumatoid Arthritis (RA)-Related Autoantibody Profile and Risk of Disease Flare After Withdrawal of Therapy in Patients with Early RA Treated with Abatacept and MTX

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: An emerging concept of "immunologic remission" in RA raises questions about the relevance of the RA autoantibody profile in patients (pts) who are otherwise in clinical remission.[1] The presence of RA autoantibodies indicates adaptive immune activation; several autoantibodies (anti-citrullinated protein antibody [ACPA],

Figure 1. Autoantibody Reactivity Profile and Median Number of Reactivities at Baseline and Month 12 for All Randomized and Treated Patients in the AVERT Trial

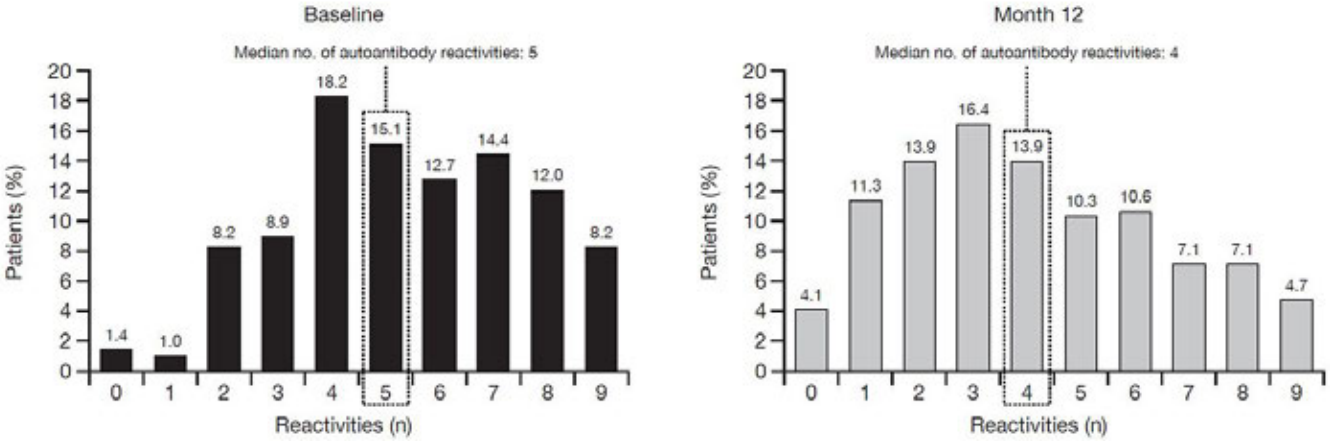
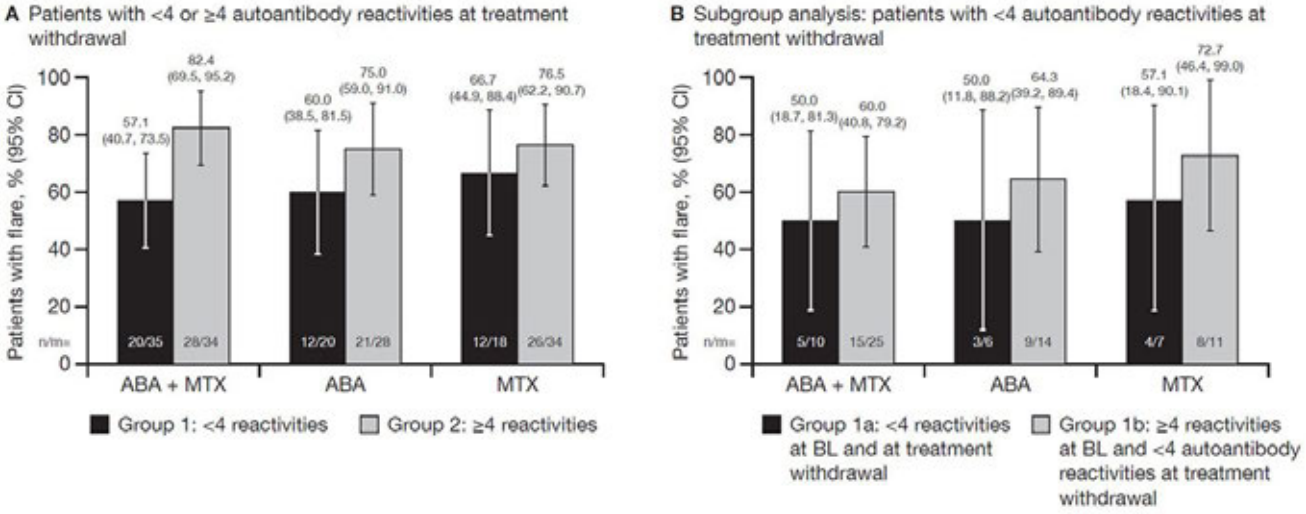


Figure 2. Percentage of Flares by Median Number of Autoantibody Reactivities in Patients Who Entered the Treatment Withdrawal Period of the AVERT Trial With DAS28 (CRP)-Defined Remission (<2.6) at Month 12 of the Treatment Period

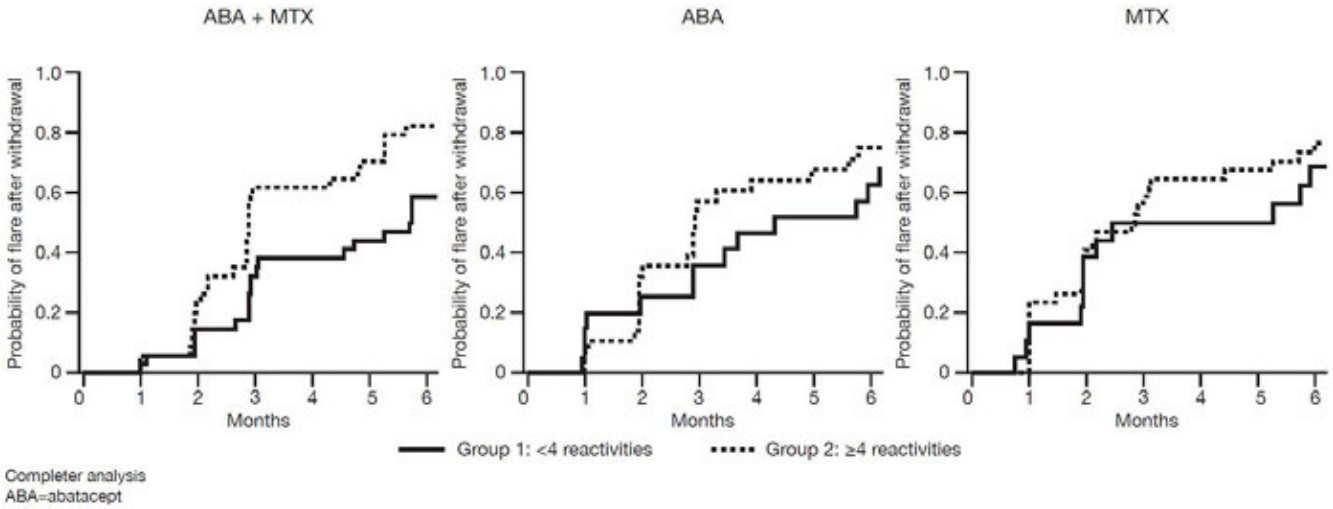


ABA=abatacept; m=number of patients with clinical and autoantibody data available who entered the withdrawal period with DAS28 (CRP) <2.6; n=number of patients with flare after 6 months of treatment withdrawal

anti-carbamylated protein [CarP], RF) and their isotypes (IgG, IgM, IgA) have been identified, but few studies have evaluated the clinical relevance of changes in the complexity of the combined RA autoantibody profile. This *post hoc* analysis of AVERT[2] explored the impact of treatment on the RA autoantibody profile and the relationship between such changes and flare rates following treatment withdrawal for pts in DAS28 (CRP)-defined remission.

Methods: Serostatus of 9 autoantibody reactivities (ACPA, anti-CarP, RF; IgG, IgM, IgA) was assessed by treatment (abatacept [ABA]+MTX, ABA, MTX) at baseline (BL) and Month 12 of the treatment period for pts with clinical and autoantibody data available at both time points. For pts entering the withdrawal period with DAS28 (CRP) < 2.6, the relationship between number of autoantibody reactivities and flare was assessed. Pts were divided into two groups using median number of autoantibody reactivities (4) at treatment withdrawal as a threshold (Group 1: < 4, Group 2: ≥4). Group 1 was further divided: 1a, < 4 reactivities at BL and treatment withdrawal; 1b, ≥4 reactivities at BL and < 4 autoantibody reactivities at treatment withdrawal.

Figure 3. Time to Flare, by Median Number of Autoantibody Reactivities, After 6 Months of Complete Treatment Withdrawal in Patients From the AVERT Trial With DAS28 (CRP)-Defined Remission (<2.6) at Month 12 of the Treatment Period



Completer analysis
ABA=abatacept

Results: In an early RA population (disease duration < 2 years), median number of autoantibody reactivities for 292 pts was 5 at BL and 4 at Month 12 (Fig. 1). Seroconversion rates from + to – for each autoantibody were numerically greater with ABA+MTX than MTX, except for IgA anti-CarP. After 12 months, 169 pts with DAS28 (CRP) < 2.6 with clinical and autoantibody data available entered the withdrawal period. At time of withdrawal, disease characteristics were similar between groups. Following treatment withdrawal, fewer pts in Group 1 vs Group 2 (< 4 vs ≥4 autoantibody reactivities at withdrawal) experienced disease flare (Fig. 2A). In Group 1 subanalysis, fewer pts in 1a vs 1b (< 4 vs ≥4 autoantibody reactivities at BL) experienced disease flare (Fig. 2B). Time to flare was more rapid in patients with ≥4 vs < 4 autoantibody reactivities at withdrawal (Fig. 3).

Conclusion: Differential autoantibody reactivity profile changes were observed following 12 months of abatacept + MTX, abatacept, or MTX. Following complete treatment withdrawal, a less complex autoantibody reactivity profile at both BL and after treatment was associated with a lower rate of disease flare. This suggests that autoantibodies are a modifiable risk factor for disease flare in pts in clinical remission. Additional studies are needed to confirm these findings.

[1]Figueiredo CP, et al. *Ann Rheum Dis* 2017;**76**:399–407.

[2]Emery P, et al. *Ann Rheum Dis* 2015;**74**:19–26.

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Abstract Number: 0547

Inhibition of Structural Joint Damage with Upadacitinib as Monotherapy or in Combination with Methotrexate in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Long-term prevention of structural joint damage is a key treatment goal in the management of RA[1]. Upadacitinib (UPA), a JAK1-selective inhibitor, inhibited the progression of structural joint damage at 6 months as monotherapy in methotrexate (MTX)-naïve RA patients (pts)[2] and in combination with MTX in pts with inadequate response (IR) to MTX[3].

We evaluate the progression of structural joint damage (radiographic) through Week 48 in pts with moderately to severely active RA treated with UPA monotherapy or in combination with MTX.

Methods: Radiographic progression was assessed in 2 phase 3 randomized controlled trials (RCTs), as previously described[2,3]. MTX-naïve pts were randomized to UPA 15 or 30mg QD or MTX monotherapy [SELECT-EARLY, N=945], while MTX-IR pts were randomized to UPA 15mg QD or adalimumab (ADA) 40 mg eow or placebo (PBO), with continuous background MTX [SELECT-COMPARE, N=1629]. Both RCTs specifically enrolled pts at high risk for progression of joint damage (high disease activity including elevated hsCRP, presence of baseline erosions and ACPA and/or RF positivity[2,3]). The mean changes (Δ) from baseline (BL) in modified Total Sharp Score (mTSS), joint space narrowing (JSN), and erosion scores (ES) as well as the proportion of pts with no radiographic progression (ΔmTSS ≤0) at Weeks 24/26 and 48 were determined in both RCTs. Data were analyzed by linear extrapolation (LE) for missing data imputation and treatment switching, and as observed (AO).

Results: BL demographics have been reported previously[2,3]. At Weeks 24/26, UPA as monotherapy and in combination with background MTX significantly inhibited radiographic progression measured by mean ΔmTSS and the proportion of pts with no radiographic progression vs MTX and PBO, respectively (LE and AO, **Table**). The significant inhibition of radiographic progression with UPA was maintained through Week 48 vs MTX (LE and AO) in EARLY and vs PBO (LE) in COMPARE. Following the switch of all PBO pts to UPA in COMPARE by Week 26, no further change in mean mTSS was observed through Week 48 (AO, **Table**). The inhibition of radiographic progression vs comparators was not only observed for the overall mTSS scores but also its components – the JSN and ES in both RCTs (LE and AO).

Conclusion: UPA both as monotherapy, and in combination with background MTX, was effective in inhibiting the progression of structural joint damage through Week 48 in MTX-naïve, and MTX-IR patients, respectively.

Table: Radiographic Progression at Weeks 24/26 and 48 in SELECT-EARLY and SELECT-COMPARE trials.

METHOD of IMPUTATION: Linear Extrapolation

	MTX-naïve (SELECT-EARLY)						MTX-IR (SELECT-COMPARE)					
	Week 24			Week 48			Week 26			Week 48		
	MTX (N=264)	UPA 15 mg QD (N=280)	UPA 30 mg QD (N=273)	MTX (N=268)	UPA 15 mg QD (N=287)	UPA 30 mg QD (N=283)	PBO (N=601)	ADA 40 mg EOW (N=297)	UPA 15 mg QD (N=596)	PBO→UPA 15 mg QD (N=599)	ADA 40 mg EOW (N=298)	UPA 15 mg QD (N=604)
LSM differences in ΔmTSS (within group)	0.66	0.03	0.10	1.00	0.03	0.14	0.94	0.19	0.16	1.73	0.39	0.28
LSM differences in ΔmTSS (UPA or UPA-MTX vs Control)	---	-0.63***	-0.56***	---	-0.97***	-0.87***	---	---	-0.79*** (vs PBO)/ -0.03 (vs ADA)	---	---	-1.44*** (vs PBO)/ -0.11 (vs ADA)
Non-progressors, %	78.0	90.4***	90.8***	74.3	89.9***	90.8***	73.9	88.2	87.4***	74.1	87.9	86.4***

METHOD of IMPUTATION: None (As Observed)

	MTX-naïve (SELECT-EARLY)						MTX-IR (SELECT-COMPARE)					
	Week 24			Week 48			Week 26			Week 48		
	MTX (N=268)	UPA 15 mg QD (N=281)	UPA 30 mg QD (N=275)	MTX (N=247)	UPA 15 mg QD (N=264)	UPA 30 mg QD (N=262)	PBO (N=588)	ADA 40 mg EOW (N=291)	UPA 15 mg QD (N=584)	PBO→UPA 15 mg QD (N=574)	ADA 40 mg EOW (N=276)	UPA 15 mg QD (N=569)
LSM differences in ΔmTSS (within group)	0.65	0.03	0.10	0.85	0.07	0.09	0.67	0.14	0.16	0.51	0.14	0.26
LSM differences in ΔmTSS (UPA or UPA-MTX vs Control)	---	-0.62***	-0.55***	---	-0.78***	-0.76***	---	---	-0.52*** (vs PBO)/ 0.01 (vs ADA)	---	---	-0.26 (vs PBO)/ 0.11 (vs ADA)
Non-progressors, %	78.4	90.4***	90.9***	74.9	89.0***	91.6***	74.1	88.3	86.6***	75.8	85.9	84.7***

Results are summarized by randomized group. In SELECT-EARLY, non-responders (<20% improvement in SJC 66/TJC68 counts) were rescued from MTX monotherapy and UPA monotherapy to UPA+MTX at Week 26. In SELECT-COMPARE, non-responders were rescued from PBO to UPA, UPA to ADA and ADA to UPA at Weeks 14 to 26 (and all remaining non-rescued PBO pts were switched to UPA at Week 26). In AO analysis, observed data at Week 48 are summarized under the randomized group regardless of rescue. In LE analysis, data after rescue are imputed by linear extrapolation. The above mTSS values are from a second reading session of radiographs from Weeks' 24/26 and 48 in both RCTs; previously presented data were from the first reading session and consisted of data for Weeks' 24 and 26 for EARLY and COMPARE RCTs, respectively.

Non-progressors are defined as patients in whom ΔmTSS ≤0. Comparison to control (EARLY: MTX or COMPARE: PBO/ADA) was calculated by ANCOVA; *$p<0.05$, **$p<0.01$, ****$p<0.001$.

ΔmTSS, change from baseline in modified total Sharp score; ADA, adalimumab; EOW, every other week; LSM, least-square means; MTX, methotrexate; PBO, placebo; QD, once-daily.

Reference:

1. Smolen JS et al. Ann Rheum Dis 2017;0: 1–18 2. van Vollenhoven R et al. Arthritis Rheumatol. 2018; 70 (suppl 10) [ACR 2018 abstract] 3. Fleischmann R et al. Arthritis Rheumatol. 2018; 70 (suppl 10) [ACR 2018 abstract]

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5, Cleveland Clinic, 8, CORRONA, 5, Crescendo, 5, Crescendo Bioscience, 5, Eli Lilly, 5, EMD Serono, 5, Genentech, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Inmedix, 5, Janssen, 5, Kezar, 5, Lilly, 5, Merck, 5, NACCME, 8, Novartis, 5, Pfizer, 5, Purdue, 8, RA Forum, 8, RAN, 8, Regeneron, 5, Roche, 5, Samsung, 5, Sandoz, 5, Sanofi, 5, Servier, 5, Setpoint, 5, SLRA, 8, UCB, 5, Up to Date, 7, Washington University, 8, WIR, 8, WRA, 8.

Abstract Number: 0548

Efficacy and Safety of a Novel Subcutaneous Formulation of CT-P13 over the 1-year Treatment Period and After Switching from Intravenous CT-P13 in Patients with Active Rheumatoid Arthritis: Results from Part 2 of Phase I/III Randomized Controlled Trial

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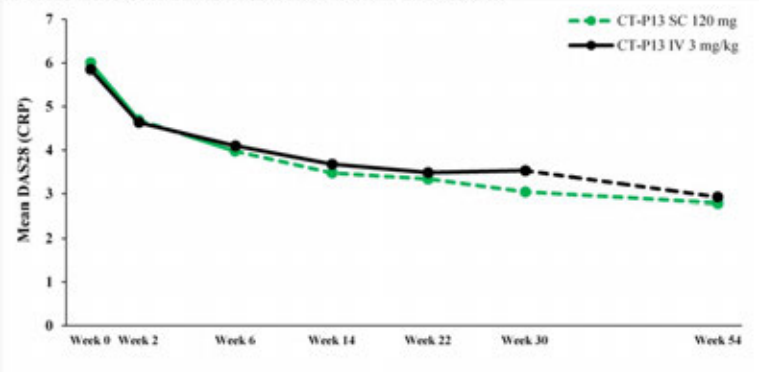
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Efficacy and safety of a new subcutaneous (SC) formulation (CT-P13 SC) were evaluated up to Week 30. The phase I/III randomized controlled trial in patients with active rheumatoid arthritis (RA) study demonstrated non-inferiority of efficacy (mean change [decrease] from baseline in DAS28 [CRP] at Week 22) for CT-P13 SC 120 mg versus CT-P13 IV 3 mg/kg and showed similar safety profile between 2 arms [1]. This is to investigate the efficacy and safety of CT-P13 SC when used over 1-year and after switching from CT-P13 IV in patients with active RA.

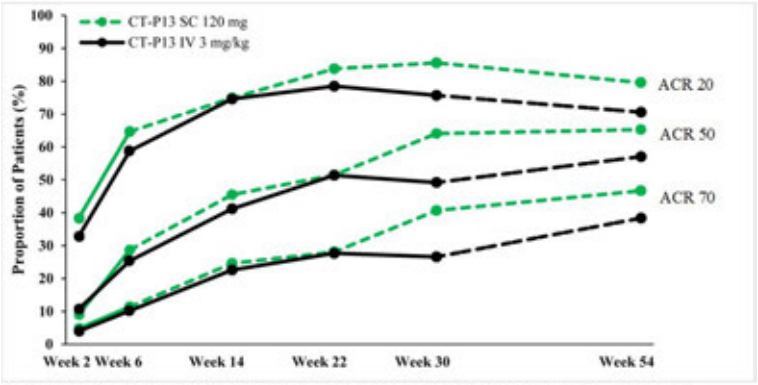
Methods: In this randomized, controlled, double-blinded, phase I/III study, patients who received full doses of CT-P13 IV 3 mg/kg at Weeks 0 and 2 were randomly assigned to receive either CT-P13 SC 120 mg via pre-filled syringe

Figure 1. The Mean Scores of DAS28 (CRP) up to Week 54



Note. All patients in IV 3 mg/kg arm received CT-P13 SC 120 mg from Week 30 to Week 54.
Solid line = IV treatment, Dotted line = SC treatment

Figure 2. The Proportion of Patients Achieving ACR response criteria



Note. All patients in IV 3 mg/kg arm received CT-P13 SC 120 mg from Week 30 to Week 54.
Solid line = IV treatment, Dotted line = SC treatment

Table 1. Summary of Safety Results up to Week 54

Number of patients (%)		Maintenance phase (W6-54)		On or after Week 30 (W30-54)	
		SC 120 mg (N=170)	IV 3 mg/kg (N=178)	SC 120 mg (N=170)	IV 3 mg/kg (N=178)
TEAEs	Total	92 (54.1)	113 (63.5)	72 (42.4)	80 (44.9)
Administration-related Reactions	Total	3 (1.8)	10 (5.6)	2 (1.2)	2 (1.1)
	IRR[1]	0	7 (3.9)	0	0
	SIR[2]	2 (1.2)	3 (1.7)	2 (1.2)	2 (1.1)
	DEL[3]	2 (1.2)	0	1 (0.6)	0
Localized Injection Site Reaction	Total	28 (16.5)	22 (12.4)	22 (12.9)	20 (11.2)
Infection	Total	48 (28.2)	54 (30.3)	31 (18.2)	34 (19.1)

1. Infusion related reaction: occurred between start of administration and 24 hours from the end of IV infusion
2. Systemic injection reaction: occurred between start of administration and 24 hours from the SC injection
3. Delayed hypersensitivity: occurred after 24 hours from the study drug administration

biweekly or CT-P13 IV 3 mg/kg every 8 weeks from Week 6 to Week 28. From Week 30, all patients received CT-P13 SC 120 mg via pre-filled syringe biweekly up to Week 54. Efficacy and safety were evaluated for 54 Weeks.

Results: A total of 362 patients were enrolled, of whom 348 patients were randomly assigned at Week 6 into 2 arms in a 1:1 ratio (169 and 179 patients in SC 120 mg and IV 3 mg/kg arms, respectively). The mean DAS28 (CRP) and ACR response rates were similar between 2 arms up to Week 22 with a slightly greater response in SC 120 mg arm at Week 30. After switching from CT-P13 IV 3 mg/kg to CT-P13 SC 120 mg at Week 30 in IV 3 mg/kg arm, the mean DAS28 (CRP) was similar between 2 arms (Figure 1) whereas ACR response rates were slightly higher in SC 120 mg arm compared to IV 3 mg/kg arm at Week 54 (Figure 2). The safety profiles which occurred on or after Weeks 6 and 30 in SC 120 mg arm were generally comparable to IV 3 mg/kg arm. The majority of the localized injection site reactions were grade 1 or 2 in intensity (Table 1).

Conclusion: The effectiveness and tolerability were confirmed over the 1-year treatment of CT-P13 SC 120 mg. The results after switching from CT-P13 IV 3 mg/kg to CT-P13 SC 120 mg at Week 30 were comparable to that of maintaining CT-P13 SC 120 mg up to Week 54. These results show that the novel SC formulation of CT-P13 via pre-filled syringe could provide a favorable benefit to patients with an alternative convenient way of administration.

Reference:

1. R. Westhovens, et al., Ann Rheum Dis, volume 78, supplement 2, year 2019, page A1158

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Abstract Number: 0549

US Rheumatologists' Beliefs and Knowledge About Biosimilars – an Ongoing Survey

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
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Background/Purpose: A systematic review of survey literature from 2014-2018 found that clinicians in the US and Europe are cautious about biosimilar use (*JMCP;* 2019;25:102). We sought to evaluate current perceptions of biosimilar products among US rheumatologists who prescribe tumor necrosis factor (TNF) α inhibitors now that 8 TNFα inhibitor biosimilars and 1 rituximab biosimilar are FDA approved (thus far, only 1 is marketed in the US).

Methods: A 19-question self-administered online survey was administered by WebMD, LLC from May 7-28, 2019. Rheumatologists (n=9050) who were members of medscape.com and its partner panels were invited to participate via email. The target sample size is 320 board-certified US rheumatologists (self-report); the survey is ongoing and here we present interim results.

Results: Data have been collected from 291 US rheumatologists, 84% are ACR fellows. Nearly all respondents were familiar with the US FDA's definition of a biosimilar product (very/extremely familiar, 82%; moderately familiar, 16%). While 97% of rheumatologists were aware that an infliximab biosimilar was FDA approved, fewer realized that adalimumab, etanercept, and rituximab biosimilars were FDA approved (57%, 62%, and 40%, respectively). When asked to rank what factors are considered when selecting a biosimilar product vs its corresponding reference product (1, most important to 7, least important), responses were varied: 78% selected effectiveness as most important (ranked either 1 or 2), whereas 51% selected physicochemical/functional characteristics as least important (ranked 6 or 7). Most respondents (84%) were aware that an approved biosimilar was not automatically deemed interchangeable by the FDA; 85% felt it important/very important for interchangeable approval to be on the label. Overall, 80% were familiar with the term "totality of evidence." When provided with different patient scenarios, rheumatologists were more likely to initiate biosimilar treatment for a biologic treatment-naïve patient with RA (72%) than they were to switch to

Table. Likelihood of using a biosimilar in different patient scenarios (n=291)

Question	Very Likely/ Likely	Neither Likely or Unlikely	Very Unlikely/ Unlikely
INITIATE treatment with a biosimilar for a biologic treatment-naïve patient who has the **SAME** rheumatologic condition on which the biosimilar approval was based (eg, RA)	72%	18%	10%
INITIATE treatment with a biosimilar for a biologic treatment-naïve patient who has a **DIFFERENT** rheumatologic condition than the one on which the approval was based (eg, extrapolation of RA to psoriatic arthritis)	41%	31%	29%
SWITCH to the biosimilar for a patient **DOING WELL** on the reference product; patient has the **SAME** rheumatologic condition on which the biosimilar approval was based (eg, RA)	33%	22%	45%
SWITCH to the biosimilar for a patient **DOING WELL** on the reference product; patient has a **DIFFERENT** rheumatologic condition than the one on which the approval was based (eg, extrapolation of RA to psoriatic arthritis)	21%	18%	61%
SWITCH to the biosimilar for a patient **NOT DOING WELL** on the reference product; patient has the **SAME** rheumatologic condition on which the biosimilar approval was based (eg, RA)	18%	21%	61%
SWITCH to the biosimilar for a patient **NOT DOING WELL** on the reference product; patient has a **DIFFERENT** rheumatologic condition than the one on which the approval was based (eg, extrapolation of RA to psoriatic arthritis)	16%	19%	65%

Numbers in each row may not total 100% due to rounding.

the biosimilar for a patient with RA doing well on the reference product (33%); see table. About half (54%) of respondents were familiar with the term “non-medical switching” (a misnomer for a biosimilar); among those responding yes, about half (51%; 80/158) had patients for whom this switch had been suggested. The main reasons for non-medical switching included pharmacy benefit insurance/formulary coverage (80%), hospital system formulary (68%) and requirement for a stepped therapy (63%).

Conclusion: This survey suggests that US rheumatologists have an increased understanding and acceptance of biosimilar products, particularly for the initiation of treatment in biologic-naïve individuals. Physicians are hesitant to switch from a reference product to a biosimilar for a patient doing well on the reference product. Additional education on biosimilars is required to help inform treatment decisions by rheumatologists.

Biosimilar Knowledge Among US Rheumatologists_3June_Table Only

Likelihood of using a biosimilar in different patient scenarios (n=291)

Disclosure: A. Gibofsky, Abbvie, 4, 5, 8, Amgen, 4, Pfizer, 4, 5, 8, Regeneron, 4, Johnson & Johnson, 4, Boehringer Ingelheim, 5, Merck, 1, 5, Celgene, 5, 8, Novartis, 5, 8; **D. McCabe**, Boehringer Ingelheim, 3, 4; **S. Badawi**, Boehringer Ingelheim, 3, 4.

Abstract Number: 0550

Rheumatoid Arthritis Treatment with Filgotinib: Week 156 Safety and Efficacy Data from a Phase 2b Open-Label Extension Study

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Treatments Poster I: Novel Treatments

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL) is an oral selective Janus kinase (JAK1) inhibitor. In studies to date, FIL has been shown to be effective and safe in patients with RA and other inflammatory diseases (IBD/AS/PsA). DARWIN 3 (NCT02065700) is an ongoing, open-label, long-term extension study of earlier phase 2b studies evaluating the longer-term safety and efficacy of FIL in RA.[1,2]

Methods: All patients who were inadequate responders to MTX completing the 24-week DARWIN 1 (FIL + MTX) and DARWIN 2 (FIL monotherapy) studies were eligible to enter DARWIN 3. All patients in DARWIN 3 received FIL 200 mg/day, with the exception of 15 males, who received FIL 100 mg/day (7 in FIL + MTX, 8 in FIL). Here we present week

Table 1. Event Rates of Adverse Events of Special Interest at Weeks 132 and 156 Interim Analysis a) For week 132, subjects who received MTX for at least 50% of the time while they were receiving FIL in parent study and DARWIN 3, subjects were counted in FIL+ MTX group. b) For week 156, all patients from DARWIN 1 were counted as FIL + MTX and from DARWIN 2 were counted as FIL monotherapy. c) 19 patients in DARWIN 2 started MTX during DARWIN 3 but are categorized as FIL monotherapy. d) Week 132 interim analysis includes adverse events occurring during placebo/screening period, pre-FIL dose. Week 156 interim analysis only includes adverse events that began on or after FIL start date. FIL, filgotinib; NMSC, nonmelanoma skin cancer; PYE, patient-years of exposure.

	Week 132[a]		Week 156[b]	
	FIL + MTX n = 500 (PYE = 1443)	FIL Monotherapy n = 224 (PYE = 599)	FIL + MTX n = 497 (PYE = 1511)	FIL Monotherapy[c] n = 242 (PYE = 692)
Events/100 PYE (# events)[d]				
Herpes zoster	1.5 (21)	1.5 (9)	1.5 (23)	1.6 (11)
Serious infections	0.8 (11)	1.7 (10)	0.9 (13)	2.0 (14)
Malignancy excluding NMSC	0.6 (8)	0.7 (4)	0.4 (6)	0.7 (5)
Deep vein thrombosis and pulmonary embolism	0.1 (2)	0	0.1 (2)	0
Active tuberculosis	0	0	0	0

Table 2. Changes in Mean Lab Values from Baseline to Week 156 and Grade 1, 2, and ≥3 Treatment-Emergent Lab Toxicity All treatment-emergent lab toxicity events were in the same direction as the change from baseline to week 156 except where shown. a) 19 patients in DARWIN 2 started MTX during DARWIN 3 but are categorized as FIL monotherapy. b) Decreased lymphocytes; no increases reported. c) Patients with decreased lymphocytes; 34 (6.8%) patients had Grade 2 increased lymphocytes. d) Patients with decreased lymphocytes; 25 (10.3%) patients had Grade 2 increased lymphocytes. e) All lipids reported using fasting data. FIL, filgotinib; HDL, high-density lipoproteins; LDL, low-density lipoproteins.

	FIL + MTX (n = 497)					FIL Monotherapy[a] (n = 242)				
	Baseline Mean (SD)	Week 156 Mean (SD)	Grade 1 Lab Toxicity n (%)	Grade 2 Lab Toxicity n (%)	≥Grade 3 Lab Toxicity n (%)	Baseline Mean (SD)	Week 156 Mean (SD)	Grade 1 Lab Toxicity n (%)	Grade 2 Lab Toxicity n (%)	≥Grade 3 Lab Toxicity n (%)
Leukocytes, $10^3/\mu L$	8.6 (2.9)	6.6 (1.9)	63 (12.7)	13 (2.6)	2 (0.4)	9.0 (2.9)	6.5 (1.8)	32 (13.2)	5 (2.1)	1 (0.4)
Lymphocytes, $10^3/\mu L$	1.9 (0.74)	1.6 (0.65)	23 (4.6)[b]	89 (17.9)[c]	21 (4.2)[b]	2.1 (0.80)	1.7 (0.69)	9 (3.7)[b]	36 (14.9)[d]	5 (2.1)[b]
Neutrophils, $10^3/\mu L$	6.1 (2.5)	4.5 (1.6)	35 (7.1)	25 (5.0)	5 (1.0)	6.4 (2.5)	4.4 (1.6)	17 (7.0)	12 (5.0)	3 (1.2)
Platelet count, $10^3/\mu L$	321 (94.9)	270 (71.4)	22 (4.4)	1 (0.2)	2 (0.4)	314 (88.3)	272 (74.7)	4 (1.7)	1 (0.4)	0
Creatinine, mg/dL	0.68 (0.15)	0.78 (0.16)	11 (2.2)	10 (2.0)	1 (0.2)	0.69 (0.17)	0.79 (0.17)	6 (2.5)	13 (5.4)	0
Alanine aminotransferase, U/L	18 (11.5)	24 (16.1)	127 (25.6)	14 (2.8)	4 (0.8)	17 (11.2)	20 (11.4)	46 (19.0)	1 (0.4)	1 (0.4)
Total cholesterol, mg/dL[e]	191 (39.9)	212 (45.2)	193 (42.8)	48 (10.6)	3 (0.7)	196 (40.5)	225 (45.7)	92 (43.4)	35 (16.5)	1 (0.5)
HDL cholesterol, mg/dL[e]	55 (16.2)	65 (18.8)	Not defined	Not defined	Not defined	56 (15.3)	66 (21.1)	Not defined	Not defined	Not defined
LDL cholesterol, mg/dL[e]	111 (32.9)	120 (39.8)	Not defined	Not defined	Not defined	113 (35.2)	132 (41.5)	Not defined	Not defined	Not defined
HDL/LDL ratio	2.15 (0.86)	1.98 (0.86)	Not defined	Not defined	Not defined	2.14 (0.85)	2.19 (0.90)	Not defined	Not defined	Not defined
Triglycerides, mg/dL	125 (57.5)	132 (67.5)	114 (25.3)	50 (11.1)	10 (2.2)	137 (69.2)	134 (69.3)	55 (25.9)	28 (13.2)	7 (3.3)

156 interim analysis data from the first dose of FIL in the parent studies through 30 May 2018. Patients were analyzed by FIL + MTX (from DARWIN 1) or FIL monotherapy (from DARWIN 2). The event rate was calculated as the total events/total years of exposure of FIL. If the subjects were continuing the study at the time of analysis, the exposure was calculated up to the data cut date.

Results: Of 877 patients completing the parent studies, 739 patients enrolled in DARWIN 3 (497 from DARWIN 1, 242 from DARWIN 2); the majority of patients in DARWIN 1 and 2 were female (81.5%, 81.8%) and white (75.3%, 74.8%) with a mean age of 53 and 52 years, respectively. The mean baseline MTX dose in the FIL + MTX group was 16.8 mg/week. At week 156, 59.9% of patients remained on study treatment. The most common reasons for discontinuation were adverse events (26.5%) and subject request (9.1%). Total exposure to FIL was 2203 patient years; mean ± standard deviation (SD) exposure was 2.86 ± 1.21 years for FIL + MTX and 3.04 ± 1.22 years for FIL monotherapy. Treatment-emergent adverse events (TEAEs) occurred in 419 (84.3%) and 203 (83.9%) patients receiving FIL + MTX and FIL monotherapy; serious TEAEs occurred in 45 (9.1%) and 33 (13.6%), respectively. Event rates of adverse events of special interest remained low at week 156 (**Table 1**). There were 5 deaths (meningococcal meningitis, pneumonia, non-Hodgkin's lymphoma [2], and deep vein thrombosis with pulmonary embolism); none of which occurred after the week 132 analysis (2 in FIL + MTX; 3 in FIL monotherapy). Laboratory values are presented in **Table 2**. Clinical efficacy up to week 156, as measured by ACR20/50/70 responses, and DAS28(CRP) ≤3.2 and DAS28(CRP) < 2.6 using observed cases are shown in **Figure 1**.

Conclusion: FIL was generally well tolerated. No new safety signals emerged. There was no safety difference in patients receiving combination therapy with MTX vs filgotinib monotherapy. Efficacy could be sustained up through week 156 in both the monotherapy and MTX combination groups. Clinical correlations with laboratory value changes are being explored and will be presented at the meeting.

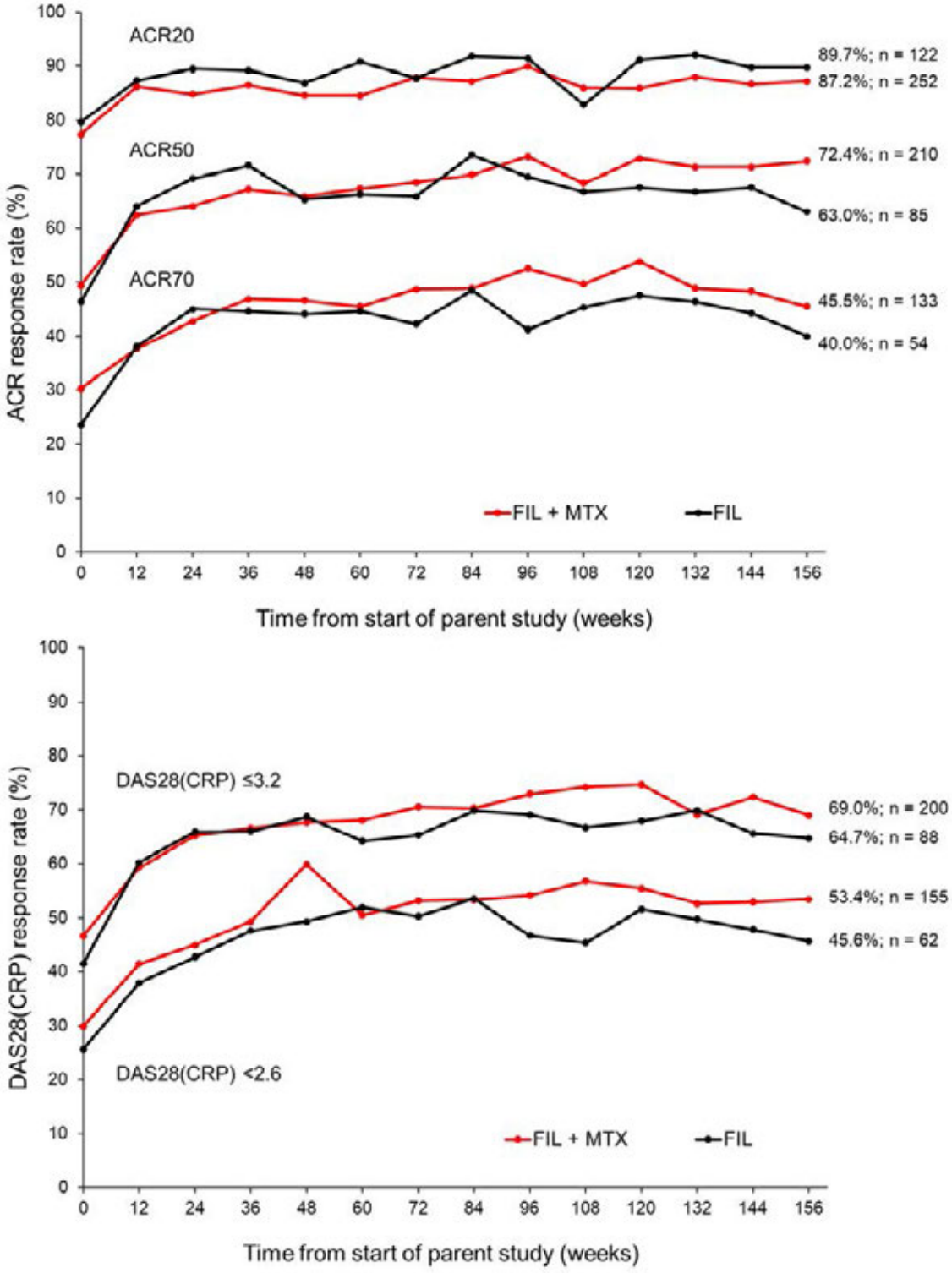

Figure 1. Clinical Efficacy Using Observed Cases by (top) ACR20/50/70 Response by Visit and (bottom) DAS28(CRP) ≤3.2 and DAS28(CRP) <2.6 Response by Visit FIL, filgotinib.

References:

1. Westhovens R, et al. Ann Rheum Dis 2017;76:998-1008.
2. Kavanaugh A, et al. Ann Rheum Dis 2017;76:1009-1019.

Disclosure: A. Kavanaugh, Abbott, 2, Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, 2, Amgen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 2, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, Pfizer Inc, 2, Roche, 2, UCB Pharma, 2; **R. Westhovens**, Celltrion, 5, 8, 9, Celltrion, Inc., 2, 5, Galapagos, 5, 8, Galapagos NV, 5, 9, Galapagos/Gilead, 2, 5, Gilead Sciences, Inc., 5, 8, 9; **K. Winthrop**, AbbVie, 5, Abbvie, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, Gilead Sciences, Inc., 5, GSK, 5, Lilly, 5, Pfizer, 2, 5, Roche, 5, UCB, 5, UCB Pharma, 5, UCB Pharma, Pfizer, Bristol-Myers Squibb, Eli Lilly, AbbVie, and Roche., 2, 5; **S. Lee**, Gilead Sciences, Inc., 3, 4; **J. Greer**, Gilead Sciences, Inc., 3, 4; **A. DeZure**, Gilead Sciences, Inc., 3, 4; **D. An**, Gilead Sciences, Inc., 3, 4; **L. Ye**, Gilead Sciences, Inc., 3, 4; **J. Sundy**, Gilead Sciences, Inc., 3, 4; **R. Besuyen**, Galapagos NV, 3, 4; **L. Meuleners**, Galapagos NV, 3, 4; **R. Alten**, Galapagos, 2, Galapagos NV, 2, Gilead, 2, Gilead Sciences, Inc., 2, Novartis, 2, Pfizer, 2, 8; **M. Genovese**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 9, Astellas, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck Serono, 2, 5, Galapagos, 2, 5, Galapagos NV, 2, 5, 9, Genentech/Roche, 2, 5, Gilead, 2, 5, Gilead Science, 9, Gilead Sciences, Inc., 2, 5, 9, GSK, 5, Lilly, 2, 5, 9, Novartis, 2, 5, Pfizer, 2, 5, 9, Pfizer Inc, 2, 5, Pfizer, Inc., 9, Pzier, 9, RPharm, 5, Sanofi Genzyme, 2, 5, Vertex, 2, 5.

Abstract Number: 0551

Upadacitinib Treatment and the Routine Assessment of Patient Index Data 3 (RAPID3) Among Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
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Background/Purpose: Upadacitinib (UPA) is an oral reversible JAK inhibitor engineered for greater selectivity for JAK1 vs JAK2, JAK3, and TYK2, and is currently being assessed for the treatment of RA. RAPID3 is a pooled index of the three key patient-reported measures: patient global assessment, pain, and physical function. In this analysis we assessed the effect of UPA treatment on RAPID3 in the SELECT-BEYOND, SELECT-COMPARE, and SELECT-MONOTHERAPY trials.

Methods: In SELECT-BEYOND[1], bDMARD-IR pts received UPA 15 mg or 30 mg once daily (QD), or PBO for 12 wks while continuing stable csDMARD therapy. In SELECT-COMPARE[2], MTX-IR pts received UPA 15 mg QD, PBO, or ADA 40 mg every 2 wks for 12 wks while continuing MTX. In SELECT-MONOTHERAPY[3], pts received UPA monotherapy 15 mg or 30 mg QD, or continued MTX monotherapy (cMTX) for 14 wks. We assessed the least squares mean changes from baseline (BL) in RAPID3 and the proportion of pts reporting RAPID3 remission (≤3), low (LDA, >3 to ≤6), moderate (MDA, >6 to ≤12), and high disease activity (HDA, >12). Correlations between RAPID3 remission and remissions defined by CDAI, SDAI, and DAS28(CRP) were also assessed using Pearson correlation coefficients. Non-responder imputation was used for categorical endpoints, and last observation carried forward for continuous endpoints in pts who received rescue therapy in SELECT-COMPARE. Other continuous data are as observed. Data were analyzed descriptively.

Table. Change from baseline in RAPID3 at Wk 12 in SELECT-BEYOND and -COMPARE, and Wk 14 in SELECT-MONOTHERAPY

Phase III study	Group	N	Mean (SD) change from BL
SELECT-BEYOND (bDMARD-IR)	PBO	148	-3.5 (7.1)
	UPA 15 mg QD	159	-6.9 (6.7)
	UPA 30 mg QD	150	-7.4 (6.9)
SELECT-COMPARE (MTX-IR)	PBO	616	-4.2 (6.4)
	UPA 15 mg QD	613	-8.6 (6.6)
	ADA 40 mg EOW	307	-7.0 (6.1)
SELECT-MONOTHERAPY (MTX-IR)	cMTX	203	-3.5 (6.5)
	UPA 15 mg QD	201	-7.2 (7.1)
	UPA 30 mg QD	205	-8.5 (6.3)

ADA, adalimumab; bDMARD, biologic disease-modifying antirheumatic drug; BL, baseline; MTX, methotrexate; IR, inadequate response; PBO, placebo; QD, once daily; SD, standard deviation; UPA, upadacitinib

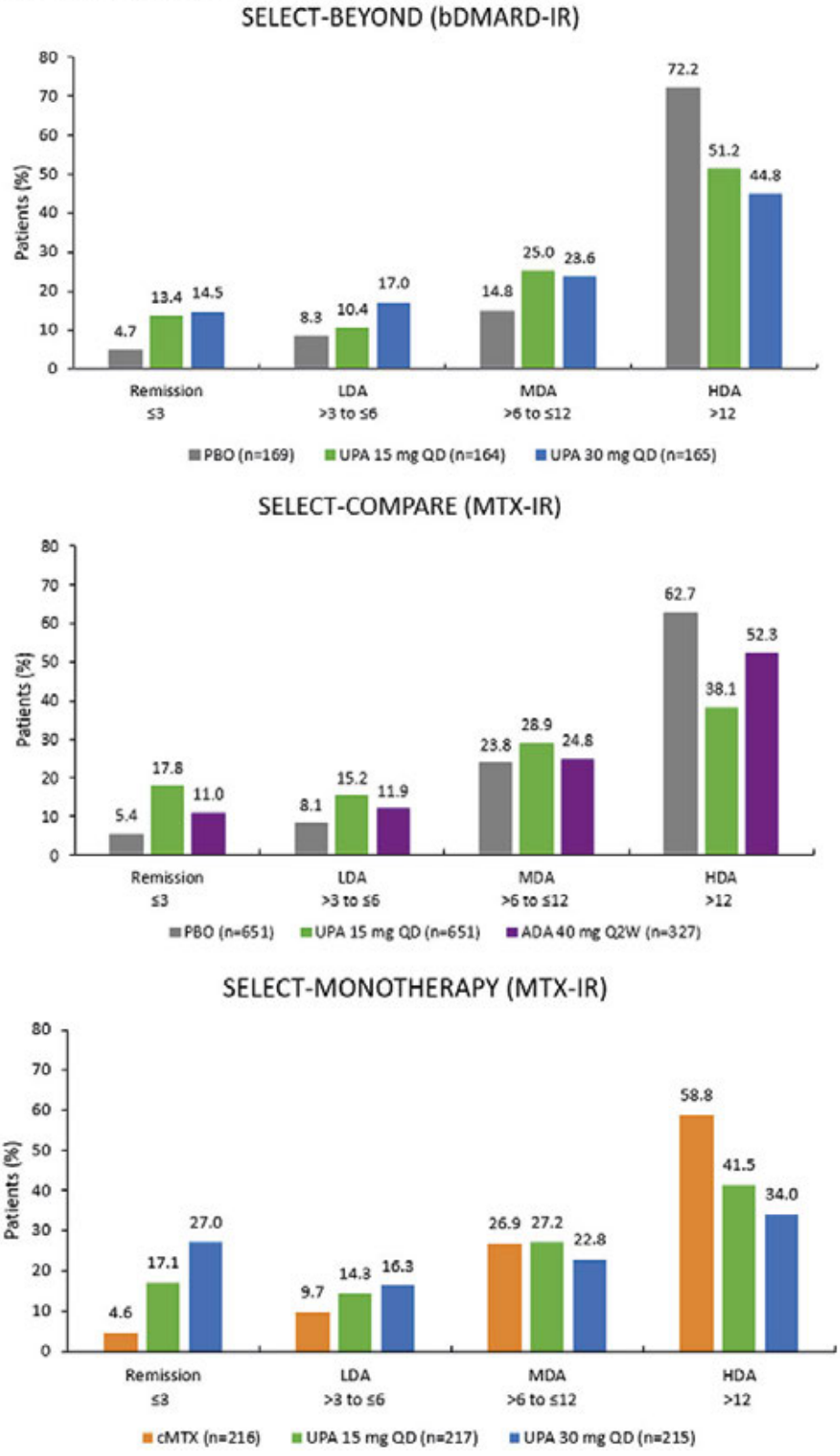
Results: 498, 648, and 1629 pts were randomized in SELECT-BEYOND, -MONOTHERAPY, and -COMPARE, respectively. Numerically higher improvements from BL in RAPID3 were reported with UPA 15 mg and 30 mg treatment vs PBO in SELECT-BEYOND, and vs cMTX in SELECT-MONOTHERAPY (Table). UPA 15 mg QD was also associated with greater reductions from baseline in RAPID3 vs PBO and ADA in SELECT-COMPARE (Table). Of note, the improvements in RAPID3 with UPA and ADA exceeded the minimal clinically important difference (MCID = 3.8[4]). The proportions of pts achieving RAPID3 remission were numerically higher in the UPA 15 mg and 30 mg groups vs PBO and cMTX in SELECT-BEYOND and SELECT-MONOTHERAPY, respectively (Figure). In addition, the proportions of pts in RAPID3 HDA were lower with UPA vs PBO and cMTX in these trials. In SELECT-COMPARE, higher rates of RAPID3 remission, with fewer pts in HDA, were evident with UPA 15 mg treatment vs PBO and ADA (Figure). Correlations between RAPID3 and other remission endpoints were significant ($p< 0.001$; $r=0.35–0.75$) in all three trials at both baseline and Wk 12/14.

Conclusion: UPA was associated with improvements in RAPID3, both as monotherapy and in combination, in MTX-IR (SELECT-COMPARE and SELECT-MONOTHERAPY) or bDMARD-IR (SELECT-BEYOND) pts. UPA treatment can result in improved patient-reported disease activity, pain, and physical function in RA.

References:

1. Genovese MC, et al. Lancet 2018; 391:2513–24
2. Fleischmann R, et al. Arthritis Rheumatol 2018;70(Suppl. 10): Abstract 890
3. Smolen JS, et al. Arthritis Rheumatol 2018;70(Suppl. 10): Abstract 889
4. Ward MM, et al. J Rheumatol 2019;46:27–30

Figure. Proportion of pts achieving RAPID3 remission, LDA, MDA, and HDA at Wk 12 in SELECT-BEYOND and -COMPARE, and Wk 14 in SELECT-MONOTHERAPY



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Abstract Number: 0552

In the Real World Clinical Setting Etanercept Biosimilar SB4(BENEPAIL®) Demonstrates Equivalent Safety and Effectiveness in Biological Naïve as Well as with ENBREL® Pretreated RA,SPA, and PSA Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Background: Biosimilar TNFα inhibitors have only become available in the last few years. Etanercept bisosimilar SB-4 Benepali® has been launched in March 2016 in Germany. Although controlles studies have shown equivalent efficacy and safety compared to the originator, so far only limited data about using biosimilar agents in the daily clinical settiing are availalbe.

Purpose: Assessment of safety and effectiveness of etanercept biosimilar (BioETA) SB4 in the daily clinical setting.

Primary study endpoints:

1) To assess the effectiveness of biosimilar SB4 in biologic naive RA, SpA and PsA patients at baseline and 3, 6 and 12 months after SB4 initiation.

2) To assess safety and effectiveness at Baseline and 3, 6 and 12 months post switch to etanercept biosimilar SB4 from etanercept reference product (Enbrel®) in RA, SpA and PsA patients. Mean disease activity will be assessed during the 12 months treatment periods.

Methods: Prospective and retrospective non-interventional study

Number of included patients: n=40 (RA:14, SpA: 8, PsA:4)

Switch patients: n=14 (RA: 8, SpA: 4, PsA: 2)

All patients re3ceived commervially available BioETA SB4 50 mg sc. per weel. Controlled treatment Phase: Data have been collected prior to BioETA therapy and during aq treatment period of 12 months. At Baseline and after 3, 6, and 12 months clinical disease activity scores (DAS28, Haq, BASDAI, BASFI and BASMI, PASI) and lab tests (CRP, ESR) were performed. Also safety data were acquired.

Results: 40 patients (m= 19, f= 21) were included in this IIT. Average diease duration prior to study entry was 5.9 years (RA); 10.1 (AS), 8.1 (PsA) in therapy naive patients and 8.2 years (RA), 15.2 (AS) and 6.1. (PsA) respectively in switchers.

Clinical disease activity indices (DAS28) improved in ETA-naive RA from 5.5 to 3.4, Haq from 1.9 to 1.4 and FFbH from 50 to 90 %. In ETA-naive SpA patients the BASDAI decreased from 5.9 to 3.2, BASMI from 4.8 to 4.2. ETA naive PsA patients showed improvement of skin (PASI 23.1 to 10.1) and musculoskeletal (Haq 2.1 versus 1.2). CRP and ESR rates improved accordingly.

In switched patients, no significant changes in clinical disease activity scorea as well as lab test results were observed.

Regarsding safety aspects, one patient had to stop ETA- Biosimilar therapy due to side effects (developed psoriatic skin lesions).

Conclusion: The result of the observational study confirm the effectiveness and safety of BioETA SB4 (Benepali) in all real-life Setting, which has previously been investigated in controlled studies in ETA naive patients as well as in patients being switched from Enbrel (R) to SB4. These data may support decision making by prescribers as well as on patients' acceptance towards their choice for BioETA.

Disclosure: H. Kellner, Roche, 5.

Abstract Number: 0553

Etanercept Biosimilar GP 2015 (Erelzi®) in Rheumatic Diseases: Interim Analysis of Real-World Data from COMPACT: A Multicentric, Prospective, Observational Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Treatments Poster I: Novel Treatments

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: GP2015 is an etanercept biosimilar approved for moderate to severely active rheumatoid arthritis (RA), severe active ankylosing spondylitis (AS), and active and progressive psoriatic arthritis (PsA), besides other indications. The COMPACT study is a multicentric, prospective, observational cohort study to evaluate drug persistence, effectiveness, safety and quality of life with GP2015 treatment in patients with rheumatic diseases under

Table 1: Patient enrollment per disease and patient groups*

	Group A n (%)	Group B n (%)	Group C n (%)	Group D n (%)	Total n (%)
Enrolled	162	32	199	37	430
Primary indication RA	96 (59.3)	16 (50.0)	141 (70.9)	3 (8.1)	256 (59.5)
Primary indication AS	39 (24.1)	12 (37.5)	14 (7.0)	28 (75.7)	93 (21.6)
Primary indication PsA	27 (16.7)	4 (12.5)	44 (22.1)	6 (16.2)	81 (18.8)

Group A: switched from reference etanercept (ref ETN; ie., stable, in remission or low disease activity);

Group B: switched from other anti-TNFs (uncontrolled, progressive, high disease activity);

Group C: biologic-naïve (failed treatment with conventional synthetic disease-modifying anti-rheumatic drugs including methotrexate);

Group D: DMARD-naïve (recently diagnosed with severe, active disease).

Table 2: DAS28-ESR scores over 12 Weeks – (RA Patients only)

DAS28-ESR n; Mean (SD)	A (N=96)	B (N=16)	C (N=141)	D (N=3)	Total (N=256)
Baseline	76; 2.1 (0.9)	12; 3.64 (1.2)	119; 3.3 (1.5)	3; 2.2 (1.0)	210; 2.9 (1.4)
Week 12	32; 1.9 (0.8)	3; 3.6 (1.2)	45; 3.0 (1.4)	1; 4.0 (0)	81; 2.6 (1.3)

real world conditions. Here, we report data form an interim analysis in different patient subgroups with first effectiveness data focusing on the largest indication RA as well as safety data for all enrolled patients.

Methods: Patients aged ≥18 years with RA, AS or PsA were initiated treatment with GP2015 prior to enrollment. Patients are categorized based on prior treatment status: (Group A) switched from reference etanercept (ref ETN; ie., stable, in remission or low disease activity); (Group B) switched from other anti-TNFs (previous failure); (Group C) biologic-naïve (failed treatment with conventional synthetic disease-modifying anti-rheumatic drugs including methotrexate (csDMARD–MTX); (Group D) DMARD-naïve (recently diagnosed with severe, active disease). Effectiveness assessments included Disease Activity Score 28-joint count erythrocyte sedimentation rate (DAS28-ESR) until week 12 after enrollment into the study. Functional disability was measured by the Health Assessment Questionnaire Disability Index (HAQ-DI). Incidences of adverse events (AEs), serious AEs (SAE) and adverse drug reactions (ADRs) were reported.

Results: In total, 430 patients were recruited in Germany, UK, Spain, Poland, and Canada until the interim analysis cut-off date in April 2019. Of these, 37.7% of patients were switched from ref ETN, 7.4% were switched from other anti-TNFs, 46.3% were biologic-naïve, and 8.6% were DMARD-naïve. Most patients had RA (59.5%), followed by AS (21.6%) and PsA (18.8%) (Table 1). Comorbidities were more frequent in RA patients (77.7%) than PsA (66.7%) or AS (57%) patients and systemic corticosteroids use was highest in RA patients (47.7%). For RA patients as the largest population, total mean DAS28-ESR scores were 2.9 (1.4) for all 4 groups at baseline, and decreased to 2.6 (1.3) by week 12 (Table 2). HAQ-DI scores in RA patients changed from 0.88 to 0.76 until week 12. Overall, 33% of the patients had at least one AE, while 2.8% of the patients discontinued due to AEs and 8.4% required interruption of the study drug due to AEs (Table 3). No deaths occurred in the study.

Conclusion: COMPACT study is an ongoing observational study of treatment of RA/PsA/AS patients with GP2015 etanercept biosimilar. This interim analysis on real-world treatment with GP2015 showed initial results of effectiveness and safety. Patient distribution in the different patient groups reflect real-life situation. Comorbidities in RA patients were more frequently reported than in AS and PsA. No new safety signals were observed compared to previously published data on etanercept[1-3].

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Abstract Number: 0554

Evidence to Guide Glucocorticoid Tapering Is Lacking in RA

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments Poster I: Novel Treatments
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Over a third of RA patients are managed with long-term oral glucocorticoids (GC), defined as daily GC use for ≥3 months[1]. Due to dose-dependent toxicity concerns, current ACR guidelines for RA management recommend tapering GC when possible[2]. Despite this, GC tapering is under-studied in RA. This is particularly true among patients with established RA (>2 years' duration) who use long-term GC. These patients often have high cumulative GC exposure levels and GC-associated comorbidities, and are prone to withdrawal symptoms when GC are tapered. Our aim was to review existing clinical trials that evaluate GC tapering in RA.

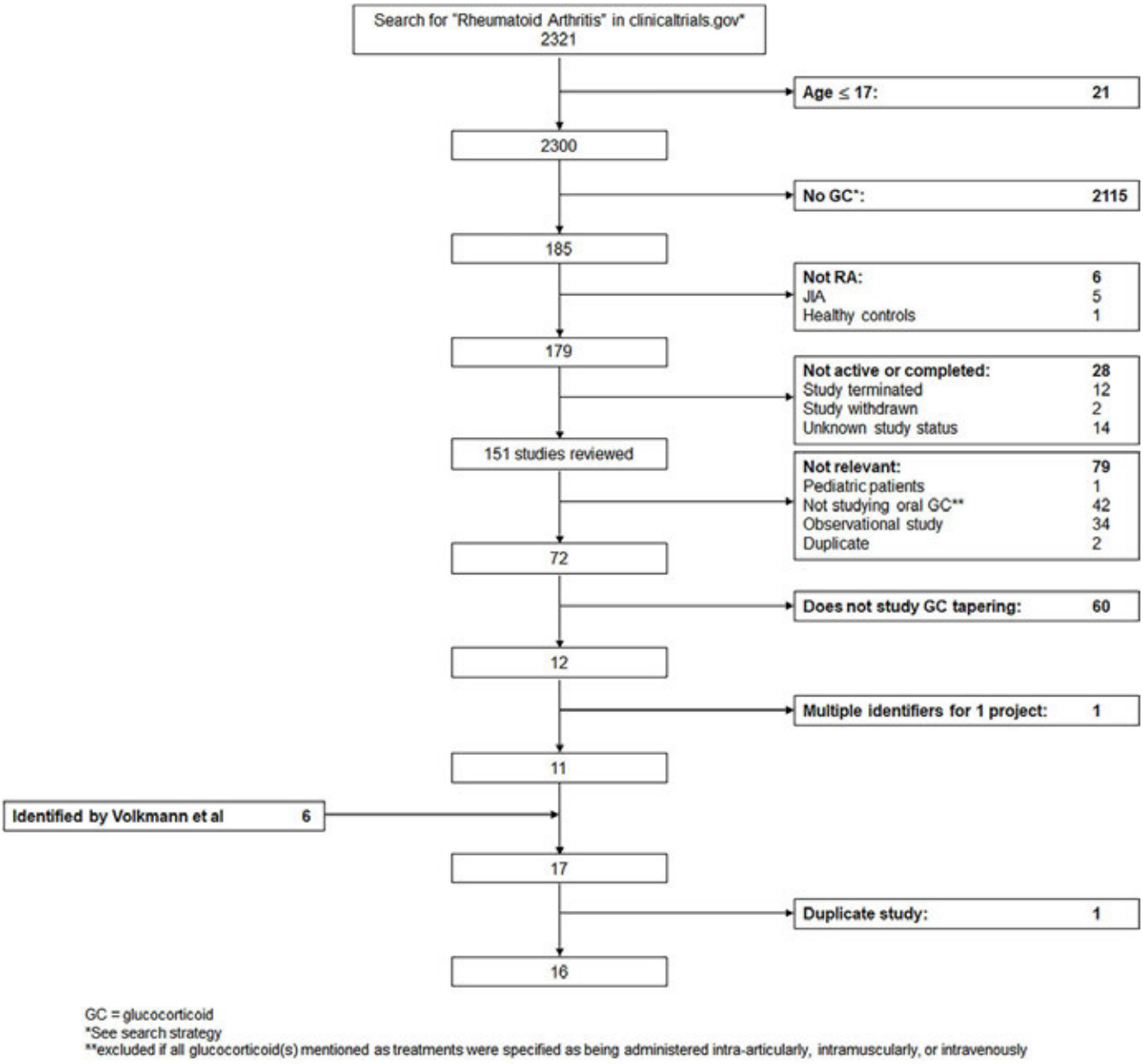

Figure 1. Study selection

Search for "Rheumatoid Arthritis"	N = 2321
Search for "Rheumatoid Arthritis", limiting to patients age 18-64 or ≥65 ("adult")	N = 2300
Search for "Rheumatoid Arthritis" and "corticosteroid", limiting to adult	N = 73
Search for "Rheumatoid arthritis" and "glucocorticoid", limiting to adult	N = 88
Search for "Rheumatoid arthritis" and "prednisolone", limiting to adult	N = 59*
Search for "Rheumatoid arthritis" and "prednisone", limiting to adult	N = 48
Search for "Rheumatoid arthritis" and "dexamethasone", limiting to adult	N = 5
Search for "Rheumatoid arthritis" and "cortisone", limiting to adult	N = 4
Search for "Rheumatoid arthritis" and "hydrocortisone", limiting to adult	N = 16
Search for "Rheumatoid arthritis" and "betamethasone", limiting to adult	N = 3
Search for "Rheumatoid arthritis" and "triamcinolone", limiting to adult	N = 0
Total:	296
Duplicates:	111
Unique Total:	**185**

*also captures all studies using methylprednisolone

Figure 2. Search strategy from clinicaltrials.gov (4/18/19)

Table 1 Included studies

Identifier or citation(s)	Acronyms	Subjects	Population	Design	Study groups	Primary Outcome	Initial daily GC dose	GC tapering strategies
Clinicaltrials.gov								
NCT02466581 NCT01491815	NORD-STAR	812	Early RA	Multicenter randomized, open-label, assessor-blinded	MTX + (1a) SSZ + HCQ + IA GC (1b) Oral GC taper (2) Certolizumab (3) Abatacept (4) TCZ	Remission (CDAI), week 24	Prednisone 20mg	Taper over 9 weeks to 5mg/day, stop after 9 months
NCT02930343		150	Early RA	Single-center randomized, open-label	1) MTX + LEF + HCQ + oral GC bridge 2) MTX + SSZ + HCQ + oral GC bridge	EULAR good response, 3 months	Prednisolone 7.5mg	7.5 mg/day for 2 weeks, 5mg/day for 2 weeks, 5mg every other day for 2 weeks
NCT02997605	STAR	122	Long-term oral GC users	Multicenter randomized, double-blinded, placebo-controlled	Pre-enrollment DMARDs + 1) Prednisone taper + hydrocortisone placebo taper 2) hydrocortisone taper + prednisone placebo taper	GC discontinuation, 1 year	Per treating physician	Prednisone: reduce 1mg/mo from pre-enrollment dose until off or 1 year Hydrocortisone: 20 mg/day for 3 months, 10mg/day for 3 months
NCT03649061 Verschuren et al Ann Rheum Dis 2015	CareRA	442	Early RA	Multicenter randomized, double-blinded	MTX + oral GC taper + 1) leflunomide 2) etanercept	Area under DAS-28 curve, 104 weeks	Prednisone 30mg	30-20-12.5-10-7.5mg for 7 days each, 5mg until week 28, 2.5mg for 2 weeks, stop
NCT01219933 Ribbens et al Ann Rheum Dis 2014	ACT-ALONE	68	Current oral GC users	Multicenter open-label, single-arm	Phase 1: tocilizumab + oral GC per treating physician until LDA (DAS-28-CRP) or 6 months Phase 2: Oral GC taper per physician if persistent LDA	Phase 1: Median cumulative GC dose Phase 2: GC discontinuation with continued LDA (DAS-28), 20 weeks	Methylprednisolone 1-20mg	Per treating physician
NCT02644499		186	Early RA	Single-center randomized, open-label	1) MTX + LEF + HCQ + oral GC bridge 2) MTX + oral GC bridge	EULAR good response, 3 months	Prednisolone 15mg	15 mg/day for 2 weeks, 10 mg/day for 2 weeks, 5mg/day for 2 weeks, 2.5mg (duration not given), stop

Methods: We searched clinicaltrials.gov for registered studies of oral GC use in RA patients since 2008 (Fig. 1). In addition, we reviewed studies captured by a previous systematic review of clinical trials of GC tapering in RA, which included years 1972 to 2011 [3].

Results: Results: 2300 entries from clinicaltrials.gov were screened (Fig. 1-2). 179 entries evaluated GC, and 11 evaluated oral GC tapering. Five additional studies were identified from the previous systematic review, for a total of 16 studies. Of the 11 clinicaltrials.gov entries, seven incorporated GC tapers as induction treatment or bridge therapy for early RA patients (Table 1). Two entries did not specify starting GC dose or taper duration. One entry (NCT02573012) compared RA disease activity among patients on tocilizumab randomized to continue vs. stop vs taper off long-term oral GC. The last (NCT02997605) compared efficacy of prednisone vs. hydrocortisone tapers in allowing RA patients to discontinue long-term oral GC. Of the five studies identified from the previous systematic review, three incorporated GC tapers as induction treatment for early RA patients. The remaining two studies compared RA disease activity (Tengstrand et al) or radiographic progression (Pincus et al) among patients randomized to continue vs taper off long-term GC. Of the 16 studies reviewed, only one (NCT02997605) evaluated GC withdrawal symptoms as a secondary outcome. Another (Tengstrand et al) allowed for slower GC taper if "withdrawal symptoms" occurred, but did not specify how these were defined.

Conclusion: There is little published trial data to guide clinicians attempting to taper long-term GC among patients with established RA. We identified only one trial directly comparing two GC tapering regimens, which is currently unpublished. Further work is needed to develop data-driven protocols for GC tapering that account for GC withdrawal symptoms.

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Disclosure: B. Wallace, None; **D. Wallace**, None; **A. Waljee**, None; **D. Clauw**, Aptinyx, 2, 5, Daiichi Sankyo, 5, Daiichi Snakyo, 5, Eli Lilly, 5, Intec Pharma, 5, Nix Paterson LLP, 8, Nix Patterson LLP, 8, Pfizer, 2, 5, Pfizer Inc, 2, 5, 8, Samumed, 5, Theravance, 5, Tonix, 5, Williams & Connolly LLP, 8, Williams and Connolly LLP, 8, Zynerba, 5.

Abstract Number: 0555

Oncostatin M Receptor (OSMR) Underexpression in Patients with Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Oncostatin M receptor (OSMR), that binding to oncostatin M (OSM) cytokine are associated with inflammation and cell's growth and differentiation. OSM uses the OSMR to powerfully induce RANKL production and osteoclast formation and downregulate the expression of Wnt signalling antagonists such as sclerostin in osteocytes, suggesting these cytokines mediate the enhanced bone formation. Our hypothesis is that OSMR are

implicated on physiopathology of syndesmophytes formation in ankylosing spondylitis (AS) patients. The objective of this study was to evaluate the OSMR levels in AS patients compared to health controls and correlate with disease activity and treatment.

Methods: Seventy two adults patients with AS and 32 healthy age and sex-matched healthy controls were enrolled. The disease activity was calculated by both Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and An-

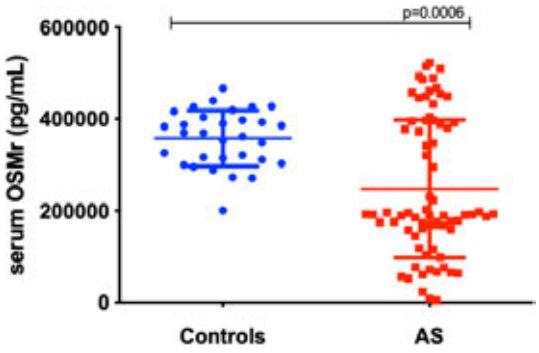

Figure 1. Serum OSMR levels in ankylosing spondylitis patients (AS; n=72) compared with controls (n=31) (CI=95%; Mann Whitney test)

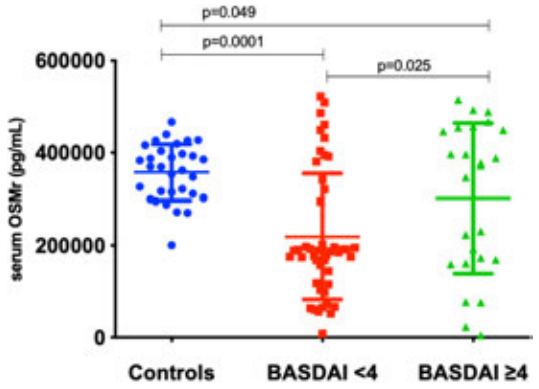

Figure 2. Serum OSMR levels in ankylosing spondylitis patients with low disease activity (BASDAI <4; n=47), high disease activity (BASDAI≥4; n=25) and controls (n=31) (CI=95%; Mann Whitney test)

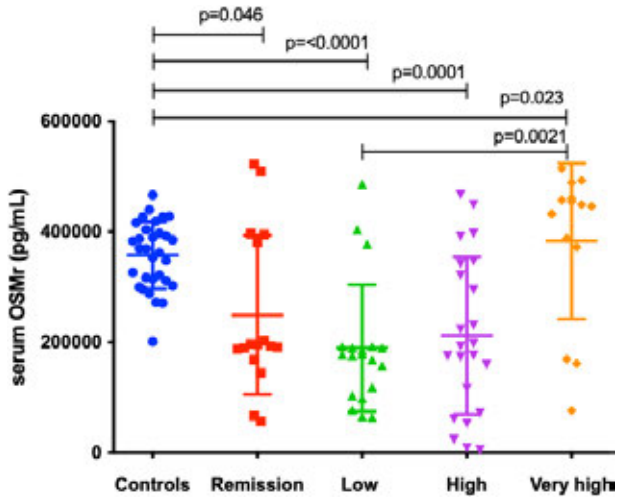

Figure 3. Serum OSMR levels in ankylosing spondylitis patients comparing controls (n=31) and ankylosing spondylitis disease activity using ASDAS cutoff points: remission (2.1 to 3.5; n=23) and very high (>3.5; n=14) (CI=95%; Mann Whitney test).

kylosing Spondylitis Disease Activity Score (ASDAS/CRP). Cytokines in serum samples were quantified by human sandwich ELISA (R&D Systems, Minneapolis, USA and eBioscience, San Diego, CA). The lower limits of detection according to our standard curves were 156.25 – 20000 pg/mL for OSMR.

Results: Among the 72 patients with AS, the majority were male (71.2%; n=52), with a mean age 46.6 (10.5), of the diagnostic time of 8.7 (9.8) years. The mean of BASDAI was 3.18 (2.19) and ASDAS/PCR was 2.32 (1.33). Serum OSMR levels were significantly lower in AS patients than in controls (Figure 1). When the AS group was stratified by disease activity, a statistically significant difference was observed between OSMR levels in patients with low (BASDAI < 4) and high disease activity (BASDAI³ 4) when compared to controls (p=0.001 and 0.049, respectively). Statistical difference was also observed among and patients with low and high disease activity (p=0.025) (Figure 2). These results were similar when we used ASDAS cutoff points to assess disease activity (Figure 3). When patients were stratified by treatment, OSMR levels were similar in those that had not yet been treated and in those using anti-TNF alone (p=0.999). Patients who used only SSZ or NSAID had higher OSMR levels at levels similar to controls.

Conclusion: OMSR expression is reduced in patients with AS compared to healthy controls, and these levels are lower in patients who are either on low disease activity or treated with anti-TNF. These results suggest that despite the control of clinical activity, the OSMR mediates the enhanced bone formation in the form of syndesmophytes in an independent way and may eventually become a potential therapeutic target in ankylosing spondylitis.

Disclosure: M. Correia, None; **C. Marques**, None; **A. Almeida**, None; **V. Silva**, None; **N. Cavalcanti**, None; **M. Rego**, None; **A. Duarte**, None; **M. Pitta**, None.

Abstract Number: 0556

The Correlation of Bone Bridge and Low Bone Mineral Density Measured by Quantitative Computed Tomography in Patients with Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic inflammation of the spine leads not only to new bone formation in axial joints and vertebral spaces, but also to bone resorption leading to osteoporosis, which is increased in ankylosing spondylitis . We planned this study to know whether the formation of bone bridge correlate with low bone mineral density measured by quantitative computed tomography in patients with ankylosing spondylitis.

Methods: The patient's BMD and medical records were analyzed retroactively through chart review. BMD of the lower thoracic and lumbar spine was assessed using QCT. Vertebrae from T11 to L4 were scanned in the supine position. For the BMD of spinal trabecular bone, thresholds of 120 mg/cm^3 for osteopenia (equivalent to a DXA T-score of –1.0 SD) and 80 mg/cm^3 for osteoporosis (equivalent to a DXA T-score of –2.5 SD) were suggested by the International Society for Clinical Densitometry in 2007 and by the American College of Radiology in 2008. We analyzed the near total or total bone bridge on X-rays at the thoracic and lumbar spine (T11-L5 level). R software packages was used for statistical analysis.

Results: Total 52 AS patients were enrolled : 78% male, mean age 47.3 years, mean disease duration 8.2 years, mean ESR 20.6 mm/h, mean CRP 0.7 mg/dL, all patients fulfil modified New York criteria. The trabecular BMD of the lower thoracic and lumbar spine (T11-L5) ranged from 29.1 to 178.8 mg/cm3 (mean 104.8 ± 34.1 mg/cm3), and lumbar spine (L1-L5) ranged from 22.5 to 177.7 mg/cm3 (mean 102.7 ± 35.5 mg/cm3) as measured by QCT. The lumbar BMD measurements showed that 15 (28.8%) had osteoporosis and 19 (36.5%) had osteopenia. Bone bridge formation showed negative correlation with BMD. Low BMD was significantly correlated with bone bridge of lateral side in vertebral body ($p< 0.05$), but not with bone bridge of anterior side in vertebral body. In particular, the correlation was found to be higher in the lumbar spine than the lower thoracic spine ($p< 0.05$).

Conclusion: The reducing mobility of vertebrae due to bone bridge formation affects low BMD in ankylosing spondylitis patients.

Disclosure: S. Lee, None; **S. Chung**, None; **R. Song**, None; **H. Yang**, None; **S. Lee**, None.

Abstract Number: 0557

Comparing Symptoms, Treatments Patterns, and Quality of Life of Non-radiographic Axial Spondyloarthritis and Ankylosing Spondylitis Patients: Findings from a US Survey

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To better understand the symptoms, clinical characteristics, treatment patterns, and quality of life (QoL), of non-radiographic axial spondyloarthritis (nr-axSpA) patients and how they compare to ankylosing spondylitis (AS) patients.

Methods: Data from a cross-sectional survey conducted with rheumatologists and their consulting patients in the United States were analyzed. Data were collected from Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Patients who had physician confirmed diagnoses of AS and nr-axSpA were eligible to participate. Demographics, disease status (improving, stable, deteriorating slowly, deteriorating rapidly), symptoms, and medication use were reported by the physician, while work disability and QoL measures were reported by the patient using validated questionnaires. QoL and treatment patterns of nr-axSpA and AS patients were compared using parametric tests and non-parametric tests where appropriate.

Results: Data from 88 rheumatologists, 515 AS patients, and 495 nr-axSpA patients were included in this analysis. A higher proportion of nr-axSpA patients were female (46.7% vs. 28.7%; $p< 0.0001$) and had a younger mean age (44.2 vs. 46.3; $p=0.014$) compared to AS patients. Nr-axSpA patients were less likely to be prescribed biologic therapy (59.6% vs. 73.6%; $p< 0.0001$) than AS patients. On average, AS patients experienced slightly more symptoms at diagnosis (2.31 vs. 2.61; $p=0.023$), however, more nr-axSpA patients were reported to experience enthesitis (24.9% vs. 19.3%; $p=0.048$) and synovitis (20.6% vs. 13.1%; $p=0.003$). Patient reported outcomes such as the Assessment of SpondyloArthritis international Society Health Index (ASAS HI;5.24 vs. 5.74; $p=0.171$), Ankylosing Spondylitis

Quality of Life (ASQoL; 5.81 vs. 6.29; p=0.296), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; 2.92 vs. 3.19; p=0.124), and Work Productivity and Activity Impairment (WPAI; 27.6 vs. 30.2; p=0.183) were similar between nr-axSpA and AS patients.

Conclusion: Nr-axSpA and AS being part of the same disease spectrum (i.e. axial spondyloarthritis) share the same clinical features. The burden of the disease, as assessed by QoL measurements, is also similar in AS and nr-axSpA patients, but despite these similarities, patients with nr-axSpA are less likely to be treated with a biologic. The treatment approach for nr-axSpA needs to be similar to AS.

Disclosure: T. Hunter, Eli Lilly, 1, 3, Eli Lilly and Company, 1, 3; **D. Sandoval**, Eli Lilly, 1, 3, Eli Lilly and Company, 1, 3; **N. Booth**, Adelphi Real World, 3; **E. Holdsworth**, None; **A. Deodhar**, AbbVie, 2, 5, 9, Abbvie, 5, 8, Abbvie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, and UCB Pharma, 5, 8, AbbVie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GSK, Galapagos, Janssen, Novartis, Pfizer and UCB, 5, AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Glaxo Smith and Klein, Janssen, Novartis, Pfizer, UCB, 5, Amgen, 5, 8, 9, BMS, 2, 5, 8, BMS, Eli Lilly, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, 2, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, UCB Pharma, 2, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, 8, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, 9, Eli Lilly and Company, 2, 5, Eli Lilly,, 5, Eli Lilly, GSK, Novartis, Pfizer and UCB, 2, Galagagos, 5, Galapagos, 5, 8, 9, Glaxo Smith & Klein, 2, Glaxo Smith & Kline, 2, 5, 8, Glaxo Smith Klein, 5, Glaxo SmithKlein, 2, 5, GlaxoSmithKlein, 2, 5, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, Janssen, 2, 5, 8, 9, Janssen Pharmaceutica, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9.

Abstract Number: 0558

Frequency and Characteristics of Inflammatory Bowel Disease in Spondyloarthritis with Biological Therapy: Study of 270 Patients from the Same Center

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory bowel disease (IBD) is an extra-articular manifestation that can appear in spondyloarthritis (SpA), as well as uveitis and psoriasis. Its prevalence is 5-10%, although subclinical intestinal inflammation has been found in up to 60%. Biological therapy(BT) can be the treatment for IBD or produce it paradoxically. Fecal calprotectin (FC) is an intestinal inflammation marker, useful for early diagnosis and monitoring disease activity.

Methods: Descriptive and retrospective study (January 2003-January 2019) of patients with SpA that develop IBD in a single center. Epidemiological variables, type of SpA, presence of IBD and its characteristics, levels of FC, presence of BT at IBD onset and treatment received were registered.

TABLE 1. CHARACTERISTICS OF IBD IN SpA SUBTYPES

	AS (n=16, 64%)	PsA (n=6, 24%)	uSpa (n=3, 12%)	TOTAL= 25
MEN/WOMEN	14/2	4/2	2/1	20/5 (80%/20%)
AGE AT IBD DX (average in years)	37.56	45.8	34	39.12
HLA B27+ (n, patients)	13	1	1	15 (60%)
CD/UC/IC (n, patients)	9/6/1	2/2/2	2/1/0	13/9/3 (52%/36%/12%)
ESR (average in mm1ª h)	30.07	39.75	21.5	31.15
CPR (average in mg/dL)	2.44	3.08	3.42	2.7
FC (average in µg/g) *(24 patients with levels> 50 included)*	369.2	409.67	1009	459.29
BEFORE / SIMUL / AFTER (IBD in relation to SpA DX)	6/2/8	0/0/6	1/1/1	7/3/15 (28%/12%/60%)
BT AT IBD DX (n, patients)	3	2	1	6 (24%)
BT	ETN (n=1), IFX (n=1), SCK (n=1)	ADA (n=1), UST (n=1)	ETN (n=1)	ETN (n=2), IFX (n=1), ADA (n=1), SCK (n=1), UST (n=1)

IBD: inflammatory bowel disease, AS: ankylosing spondylitis, PsA: psoriatic arthritis, uSpA: undifferentiated spondyloarthritis, CD: Crohn´s disease, UC: ulcerative colitis, IC: indeterminate colitis, ESR: erythrocyte sedimentation rate, CPR: C-reactive protein, FC: fecal calprotectin, BEFORE/SIMUL/AFTER: before the diagnosis of SpA/ simultaneously/after, DX: diagnosis, BT: biological therapy, ETN: etanercept, ADA: adalimumab, IFX: infliximab, SCK: secukinumab, UST: ustekinumab

TABLE 2. BT IN 270 PATIENTS WITH SpA.

	Patients (n)	IBD development after BT (n)	IBD development after BT (%)
ETN	57	2	3.50%
ADA	98	1	1.02%
IFX	36	1	2.78%
SCK	22	1	4.54%
UST	15	1	6.67%
CZP	25	0	0 %
GLM	15	0	0 %
VDZ	2	0	0 %
TOTAL	270	6	2.22%

BT: biological therapy, IBD: inflammatory bowel disease, ETN: etanercept, ADA: adalimumab, IFX: infliximab, SCK: secukinumab, UST: ustekinumab, CZP: certolizumab, GLM: golimumab, VDZ: vedolizumab

For the analysis, frequencies and percentages were used in qualitative variables and mean±standard deviation(SD) in quantitative variables. Statistical analysis was performed with IBM SPSS v.23.

Results: We studied 270 patients with SpA, 70.4% male with a mean age of 39.9±12 years. The subtypes of SpA were: ankylosing spondylitis (AS) (n=133; 49.3%), psoriatic arthritis (PsA) (n=116; 43%), undifferentiated SpA (n=16; 5.9%), SpA non-Rx axial (n=3; 1.1%) and reactive arthritis (n=2; 0.7%).

IBD was observed in 25 patients (9.26%), 80% male. At the time of IBD onset, they had a mean age of 39.12±9.8 years, the mean ESR was 31.15±24mm1ªh, CRP 2.7±2mg/dL and BASDAI 4.6. 16 patients had AS, 6 PsA and 3 undifferentiated SpA. TABLE 1.

Regarding SpA diagnosis, IBD appeared after in 15 patients with an average time of development of 8.39±8 years, before in 7 and was simultaneous in 3. The subtypes of IBD were: Crohn's disease (CD) in 13 patients, ulcerative colitis (UC) in 9 and indeterminate colitis (IC) in 3. The FC was > 200µg/g in 17 patients (68%), normal (< 50µg/g)

in 1 and between 50-200μg/g in 7. The incidence rate adjusted for follow-up of the 25 cases was 7.7 cases/1000 patients-year.

At the time of the IBD onset, 6 patients were with BT: Etanercept (ETN) (n=2), Infliximab (IFX) (n=1), Adalimumab (ADA) (n=1), Secukinumab (SCK) (n=1) and Ustekinumab (UST) (n=1). The BT had been initiated the previous 12 months in 5 of them. The incidence rate adjusted for follow-up of the 6 cases of IBD after BT was 1.83 cases/1000 patient-years. TABLE 2.

The treatment of the 25 patients with IBD was mesalazine (n=15), oral corticoid (n=5), methotrexate (n=7) and BT in all cases. The BT was: ADA (n=11; 44%), IFX (n=6; 24%), UST (n=3; 12%), golimumab (n=3; 12%), SCK (n=1; 4%) and vedolizumab (n=1; 4%). The indication was intestinal in 4 patients, joint in 8 and both in 13.

The clinical and analytical evolution in all patients was satisfactory, with a mean ESR of 11.6±9mm1ªh, CRP 0.6±0.3mg/dL and BASDAI 2 in the last control, after an average time of evolution of 12.5±9 years.

Conclusion: In our series, IBD was observed in 9.26% of patients with SpA of which 64% were AS. The most frequent form was CD and it was diagnosed after SpA in 60% of the cases. 6 patients were with BT at the time of IBD onset. High FC (> 200μg/g) was observed in the majority of patients.

Therefore, we recommend assessing of digestive manifestations presence (abdominal pain, weight loss or diarrhea) in patients with SpA due to their possible association with IBD.

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Abstract Number: 0559

Diagnostic Utility of Individual Inflammatory Back Pain Parameters in Patients with Axial Spondyloarthritis

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Background/Purpose: A recent study in German chronic back pain (CBP) patients (pts) with a suspicion of axial spondyloarthritis (axSpA) report on the performance of, among others, the ASAS inflammatory back pain (IBP) criteria and the individual IBP parameters. Pts were diagnosed by a rheumatologist blinded for all clinical features but IBP and by a rheumatologist with all diagnostic tests available as in daily practice (reference standard). Data show high

Table 1. Frequencies (1a) and performance (1b) of IBP criteria and the individual parameters in early SpA patients and patients with chronic back pain

1a	Be-Giant cohort	SPACE cohort	
	axSpA N=205	axSpA* N=307	No axSpA^ N=252
IBP (ASAS criteria), n (%)	172 (83.9)	228 (74.3)	122 (48.4)
Age at onset <40 years	197 (96.1)	277 (90.2)	224 (88.9)
Insidious onset	185 (90.2)	261 (85.0)	212 (84.1)
Improvement with exercise	181 (88.3)	252 (82.1)	151 (59.9)
No improvement with rest	172 (83.9)	264 (86.0)	193 (76.6)
Pain at night	162 (79.0)	172 (56.0)	165 (65.5)
No. of IBP parameters present, n (%)			
0	0	1 (0.3)	0
1	1 (0.5)	5 (1.6)	5 (2.0)
2	7 (3.4)	22 (7.2)	22 (8.7)
3	25 (12.2)	51 (16.6)	51 (20.2)
4	53 (25.9)	116 (37.8)	116 (46.0)
5	119 (58.1)	112 (36.5)	112 (44.4)

1b	Sensitivity (95%CI)		Specificity (95%CI)	LR+	
	Be-Giant cohort N=205	SPACE cohort N=307	SPACE cohort∞ N=252	Be-Giant cohort	SPACE cohort
IBP (ASAS criteria)	83.9% (78.0-88.5)	74.3% (68.9-79.0)	51.6% (45.2-57.9)	1.7	1.5
Age at onset <40 years	96.1% (92.2-98.2)	90.2% (86.2-93.2)	11.1% (7.6-12.9)	1.1	1.0
Insidious onset	90.2% (85.1-93.8)	85.0% (80.4-88.7)	15.9% (11.7-21.1)	1.1	1.0
Improvement with exercise	88.3% (82.9-92.2)	82.1% (77.2-86.1)	40.1% (34.0-46.4)	1.4	1.3
No improvement with rest	83.9% (78.0-88.5)	86.0% (81.5-89.6)	23.4% (18.4-29.2)	1.1	1.1
Pain at night	79.0% (72.7-84.3)	56.0% (50.3-61.6)	34.5% (28.7-40.8)	2.1	1.5

axSpA, axial spondyloarthritis; IBP, inflammatory back pain; ASAS, Assessment of Spondyloarthritis international Society; CI, confidence interval.
* axSpA diagnosis according to rheumatologist with a level of confidence of ≥7 on a 0–10 scale
^ No axSpA patients according to rheumatologist with a level of confidence of ≥7 on a 0–10 scale
∞ Only patients without axSpA diagnosis according to rheumatologist (level of confidence of <7 on a 0–10 scale) are used as control group to calculate specificity

sensitivity but low specificity of the ASAS IBP criteria and individual IBP parameters(1). Performance of IBP in other countries is less studied. Therefore our objective was to investigate what the diagnostic utility of IBP and the individual IBPpar according to the ASAS IBP criteria is in several rheumatology settings in West- and Northern-Europe?

Methods: Data of the multicentre, observational BelGian inflammatory arthritis and spondylitis (Be-Giant) and international SPondyloArthritis Cause Early (SPACE) cohorts were used. The Be-Giant cohort included ≥18 years old, newly diagnosed axSpA patients who were diagnosed by a team of expert rheumatologists and fulfilled the ASAS axSpA criteria. The SPACE cohort included patients, ≥16 years, with (almost) daily chronic back pain for ≥3 months and ≤2 years, with a symptom onset < 45 years. All patients underwent a diagnostic workup according to a predefined protocol of the corresponding cohort, including data on the individual parameters of the ASAS IBP criteria. AxSpA

patients from the SPACE cohort diagnosed by a rheumatologist with a level of confidence on the diagnosis (LOC) of ≥7 on a 0–10 scale were included as 'axSpA'. All patients in SPACE without axSpA diagnosis (LOC ≥7 for no axSpA) were categorised as 'no axSpA'. For patients with a LOC < 7, diagnosis was considered not sufficiently certain and these patients were excluded from primary analyses. Sensitivity, specificity and positive likelihood ratios (LR+) were calculated using axSpA patients from each cohort separately and no axSpA patients as control group.

Results: Information on IBP parameters was available in 228 patients (Be-Giant) and 559 patients (SPACE) of whom 49.6% and 39.5% were male and mean age was 34.7 (SD9.7) and 30.7 (SD8.0) years, respectively. Few axSpA patients had < 2 IBP parameters (table 1a; Be-Giant 3.9%, SPACE 9.1%). The individual IBP parameters show high sensitivity (>80%) but low specificity (< 36%) with 'pain at night' as exception with slightly better specificity. LR+ of IBP were in both cohorts much lower (table 1b) than the LR+ for IBP of 3.1 previously reported as diagnostic estimate in routine practice.

Conclusion: This study shows that the diagnostic utility of IBP criteria in a rheumatology setting in several European countries is lower than previously assumed with a (very) low specificity and LR+. This suggests that the distinctive impact of IBP is almost fully expressed when physicians refer their patient to the rheumatologist.

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Abstract Number: 0560

Dactylitis Occurrence in Early Spondyloarthritis: Five Years Data from a French National Prospective Cohort

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SESSION INFORMATION

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Background/Purpose: Dactylitis is a particular feature shared across the several phenotypical forms of spondyloarthritis (SpA), part of the classification criteria. There are only few data available about incidence of dactylitis in early stage of SpA, and factors associated with dactylitis.

Aim: To study, over 5 years in the DESIR cohort, the prevalence and incidence of dactylitis and to look at the factors associated with presence/incidence of dactylitis.

Methods: DESIR is a prospective observational cohort of patients with recent onset (less than 3 years) inflammatory back pain, beginning before 50 years, suggestive of axial SpA, All available factors in the database (clinical, biological, imaging and medico economic) were compared between patients with and without past or present dactylitis at 5 years (for categorical variables : odds-ratio +/- 95% CI and chi-square/Fisher tests, for continuous variables : unpaired t-tests / Mann-Whitney) , by uni and then multivariate analysis (logistic regression). Baseline factors associated with new cases of dactylitis occurrence were also analyzed. Significance: p less than 0.05.

Results: After 5 years, 138 cases of dactylitis were recorded in 480 patients with complete follow-up : prevalence 28.75 % [CI 95% 24.75-32.75]. At 5 years, dactylitis was significantly associated (multivariate analysis) with : Achilles enthesitis (OR : 3.3), history of psoriasis (OR: 3.9), cumulative number of ASAS criteria (OR: 7.2), modified New York criteria fulfillment (OR: 0.35), DMARD use (OR: 2.7) and elevated CRP (OR:0.9).

Incident new cases were recorded in 41 patients, with an estimated incidence of 1.7/100 patient-years. These incident cases were significantly associated with some baseline factors (multivariate analysis) : female gender (OR: 3.6), psoriasis (OR:3.4), HAQ over median (OR: 5.7), IL-31 levels over median (OR: 1.04), ASQol over median (OR: 0.84), IL-6 over median (0.83).

Conclusion: In the DESIR cohort of patients suspected for early SpA, dactylitis presence or history is recorded in 28.7 % of the cases at 5 years, with an estimated incidence of 1.7/100 p-y over 5 years. It is an early feature associated with peripheral involvement, psoriasis, more frequent use of DMARDs, but with less structural damage. Female gender and psoriasis are associated with incidence of new cases of dactylitis over 5 years in this population.

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Analysing Impairments in Physical Performance as Assessed by the as Performance Index (ASPI) in Patients with Axial Spondyloarthritis (axSpA)

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Background/Purpose: In patients with axial spondyloarthritis (axSpA) physical functioning is frequently impaired. The current gold standard to assess physical functioning is self-reported questionnaires (i.e. BASFI), which, however, are of subjective nature. Therefore, a performance-based test-battery was designed to measure physical functioning more objectively: the ankylosing spondylitis (AS) performance index (ASPI)) [1]. To imitate activities of daily living (ADL), tasks based on BASFI domains, were designed. Although the ASPI had previously been evaluated, a thorough analysis of the deficits of physical functioning and factors which influence the performance of patients with axSpA has not been performed to date.

Methods: Consecutive patients diagnosed with axSpA fulfilling the ASAS classification criteria underwent standardized assessments concentrating on the following variables: patient and disease characteristics, patient-reported outcomes (ASDAS, BASFI, BASMI, ASAS Health Index (ASAS HI), PHQ-9, IPAQ), mSASSSand ASPI (ASPI 1: Bending, 2. Putting on socks, 3. Getting up from the floor) [1]. Performance was measured in seconds as time to complete a task based on published instructions given to the patients. Impairment in physical performance was defined as the inability of patients to perform ≥ 1 ASPI test. Spearman Rho correlation was used to compare self-reported functioning and performed physical functioning. Logistic regression analysis was used to identify factors associated with impaired physical performance.

Results: A total of 200 patients (AS 66%, nr-axSpA 34%) was included: 69% males, 44.3±12.5 years old, mean symptom duration 17.9±12.6 years, BMI 27.2±5.5, mean ASDAS 2.5±1.1, BASFI 4.0±2.7, BASMI 3.5±1.8, ASAS HI 7.0±4.1, PHQ-9 8.8±6.2, and mSASSS(n=157) 10.2±18.8. 133 patients were treated with bDMARDs (66.5%). In total 44 patients (22%) were not able to perform one or more ASPI tests. The mean time for bending was 18.6±9.5 sec (n=179/90%), for putting on socks 12.8±6.4 sec (n=156/78%), and for getting up from floor 6.5±5.0 sec (n=187/94%). A significant correlation was found for all three ASPI-tests with BASFI (0.5-0.7), ASAS HI (0.4-0.6). Self-reported physical activity (IPAQ) correlated weakly with ASPI (all 0.2) and structural damage correlated only with the task putting on socks (r=0.3), whereas the other tests did not correlate. Logistic regression showed an influence of obesity, spinal mobility and global functioning on actual performance but not of disease activity and self-reported physical function (Table 1)

Conclusion: This study confirms a good correlation of the ASPI with standard questionnaires of physical functioning and disease activity. However, the ASPI showed a substantial floor effect, since 22% of patients were unable to perform the tests. This striking finding strongly suggests that more information on the actual performance of patients with axSpA is needed. Our data confirm that self-reported physical activity cannot be used as a substitute for the actual performance of axSpA patients. Moreover, obesity as a potential modifying factor that definitely contributes to limitations in actual performance should also be more carefully addressed in patients with axSpA.

	Univariate		Multivariate	
	OR (CI)	p	OR (CI)	p
Age	1.08 (1.04-1.11)	**<0.001**	1.03 (0.97 - 1.09)	0.45
Male sex	1.46 (0.68-3.11)	0.332		
BMI	1.17 (1.01-1.25)	**<0.001**	1.20 (1.09-1.32)	**<0.001**
ASDAS	2.35 (1.67-3.41)	**<0.001**	0.79 (0.36 - 1.75)	0.56
BASFI, 0-10	1.95 (1.58-2.40)	**<0.001**	1.12 (0.75 - 1.69)	0.57
ASAS HI 0-17	1.41 (1.26-1.60)	**<0.001**	1.41 (1.07-1.87)	0.019
BASMI, 0-10	2.44 (1.87-3.19)	**<0.001**	2.80 (1.78-4.41)	**<0.001**
PHQ-9 0-27	1.15 (1.08-1.21)	**<0.001**	1.04 (0.91 - 1.19)	0.58

Association between clinical characteristics of patients with SpA and physical performance

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Abstract Number: 0562

Development of a Set of ASAS Quality Standards for Adults with Axial Spondyloarthritis

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Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: There is wide variation in the management of patients with axial spondyloarthritis (axSpA) worldwide with significant unmet needs such as delayed diagnosis. One way to achieve improvement in quality of care is to define quality standards (QS) in order to identify resources and processes which may need to be optimized. To develop ASAS QS to ultimately improve the quality of care for adults with axSpA.

Methods: The Assessment of SpondyloArthritis international Society (ASAS) QS group developed a step-wise approach starting with (I) open discussions resulting in a proposal for possible key areas for quality improvement. Thereafter, (II) ASAS members and invited patients discussed a provisional list with the possibility to propose additional

Table. ASAS quality standards for patients with axial spondyloarthritis

No	Quality statement
1	People with suspicion of axial SpA are referred to a rheumatologist for diagnostic assessment within 3 working days.
2	People with suspicion of axial SpA are assessed by a rheumatologist within 3 weeks after referral.
3	People with suspected axial SpA have their diagnostic work-up completed within 2 months.
4	Disease activity of people with axial SpA is monitored under the supervision of a rheumatologist with validated composite scores at least twice a year.
5	In people with axial SpA and active disease despite conventional therapy, treatment escalation with biologics is discussed.
6	People with axial SpA are informed about the benefits of regular exercise.
7	People with axial SpA are offered education on the disease including self-management within two months of diagnosis.
8	People with axial SpA and disease flare or possibly drug-related side effects receive advice within 2 working days of contacting the rheumatologist.
9	People with axial SpA have a comprehensive annual review by the rheumatologist.

key areas. (III) The complete list was then evaluated by ASAS members and invited patients. (IV) ASAS QS group prioritized key areas, and (V) phrased QS for the most important key areas. Finally (VI), a draft version was commented on, discussed and finally agreed by ASAS members.

Results: The ASAS QS group, consisting of 20 rheumatologists, 2 physiotherapists and 2 patients, provided 34 potentially key areas for quality improvement which were commented by 140 participants (86 physicians, 42 patients). Within that process 3 new key areas were proposed and all 37 key areas were again evaluated by 120 participants (86 physicians, 29 patients). 5 key areas were identified to be most important to phrase QS: referral, rheumatologic assessment, treatment, education/self-management and comorbidities. Altogether, 9 QS (table) were endorsed by ASAS.

Conclusion: ASAS successfully developed the first QS set for improvement of health care provided for adults with axSpA.

Disclosure: U. Kiltz, AbbVie, 2, 5, 8, ABBVIE, NOVARTIS, CHUGAI, JANSEN, MSD, UCB, 8, ABBVIE, NOVARTIS, LILLY,BIOCAD, GRUNENTHAL,UCB, 5, ABBVIE, NOVARTIS, PFIZER,BIOGEN, 2, Biocad, 2, 5, Biogen, 2, 5, Chugai, 2, 5, 8, Eli Lilly, 2, 5, Eli Lilly and Company, 5, Grünenthal, 2, 5, 8, Janssen, 8, Jasnssen, 2, 5, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8; **R. Landewé**, Abbott, 2, 5, 8, Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers

Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **M. Rudwaleit**, Abbott, 5, AbbVie, 5, 8, BMS, 5, 8, Bristol Myers-Squibb, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Eli Lilly, 5, 8, Eli Lily, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB Pharma, 5, 8; **M. Weisman**, AbbVie, 9, Boehringer Ingelheim, 9, Eli Lilly, 5, Lilly, 5, 9, Novartis, 5, Paul Hastings, 9, SetPoint Medical, 9, Takeda, 9, Tharpe & Howell LLP, 9, UCB, 5; **N. Akkoç**, None; **A. Boonen**, AbbVie, 2, Amgen, 2, Celgene, 2, Eli Lilly and Company, 5, Janssen, 8, Lilly, 5, 8, Novartis, 5, Sandoz, 5, 8, UCB, 5, 8; **J. Brandt-Jürgens**, AbbVie, 5, 8, Abbvie, 5, 8, BMS, 5, 8, Eli Lilly, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Medac, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi-Aventis, 5, 8, UCB, 5, 8; **P. Carron**, None; **M. Dougados**, None; **L. Gossec**, Abbvie, 5, AbbVie, 5, Abbvie, Biogen, BMS, Celgene, Lilly, Novartis, Pfizer, SAnofi-Aventis, UCB, 5, Amgen, 5, Biogen, 5, BMS, 2, 5, Celgene, 5, Celgene Corporation, 2, Janssen, 5, Lilly, 2, 5, MSD, 5, Nordic Pharma, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 5, Sanofi-Aventis, 5, UCB, 5; **M. Jongkees**, None; **P. Machado**, None; **H. Marzo-Ortega**, AbbVie, 5, 8, AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, 5, Abbvie, Celgene, Janssen, Lilly, Novartis, Pfizer, Ucb, 5, 8, AbbVie, Celgene, Janssen, Lilly, Novartis,Pfizer and UCB, 8, Celgene, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 2, 5, 8, Janssen and Novartis, 2, Janssen, Novartis, 2, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **A. Molto**, None; **V. Navarro-Compán**, AbbVie, 5, 8, Bristol, 8, Bristol, Roche, 8, Eli Lilly and Company, 5, 8, Eli Lilly, Novartis, Abbvie, UCB, MSD, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, Roche, 8, UCB, 5, 8; **K. Niedermann-Schneider**, None; **P. Sampaio-Barros**, None; **G. Slobodin**, None; **F. Van den Bosch**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, Bristol-Myers Squibb, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sanofi and UCB, 5, 8, ABBVIE, CELGENE, ELI LILLY, GALAPAGOS, MERCK, NOVARTIS, PFIZER, VCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **A. van Tubergen**, Abbvie, 2, Biogen, 2, Novartis, 2, 8, Pfizer, 2, UCB, 2; **S. van weely**, None; **D. Wiek**, None; **J. Braun**, Abbott, 2, 5, AbbVie, 2, 5, 6, 8, Amgen, 2, 5, 8, Baxter, 2, 5, 8, Biogen, 2, 8, 9, BMS, 2, 5, 8, Boehringer, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Celgene, 2, 3, 5, 8, Celltrion, 2, 5, 8, Centocor, 2, 5, 8, Chugai, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Hexal, 2, 5, 8, Janssen, 2, 5, 8, Johnson & Johnson, 2, 5, Medac, 2, 5, 8, MSD, 2, 5, MSD (Schering-Plough), 2, 5, 8, Mundipharma, 2, 5, 8, Mylan, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, Pfizer (Wyeth, Hospira), 2, 5, 8, Roche, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, UCB Pharma, 2, 5, 8.

Abstract Number: 0563

The Impact of Sex and Disease Classification on Patient-reported Outcome Measures in Axial Spondyloarthritis: *A Descriptive Prospective Cross-sectional Study*

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To explore the impact of sex and disease classification on outcomes in axial spondyloarthritis (axSpA) patients, including both ankylosing spondylitis (AS) and non-radiographic (nr-) axSpA, in males and females respectively.

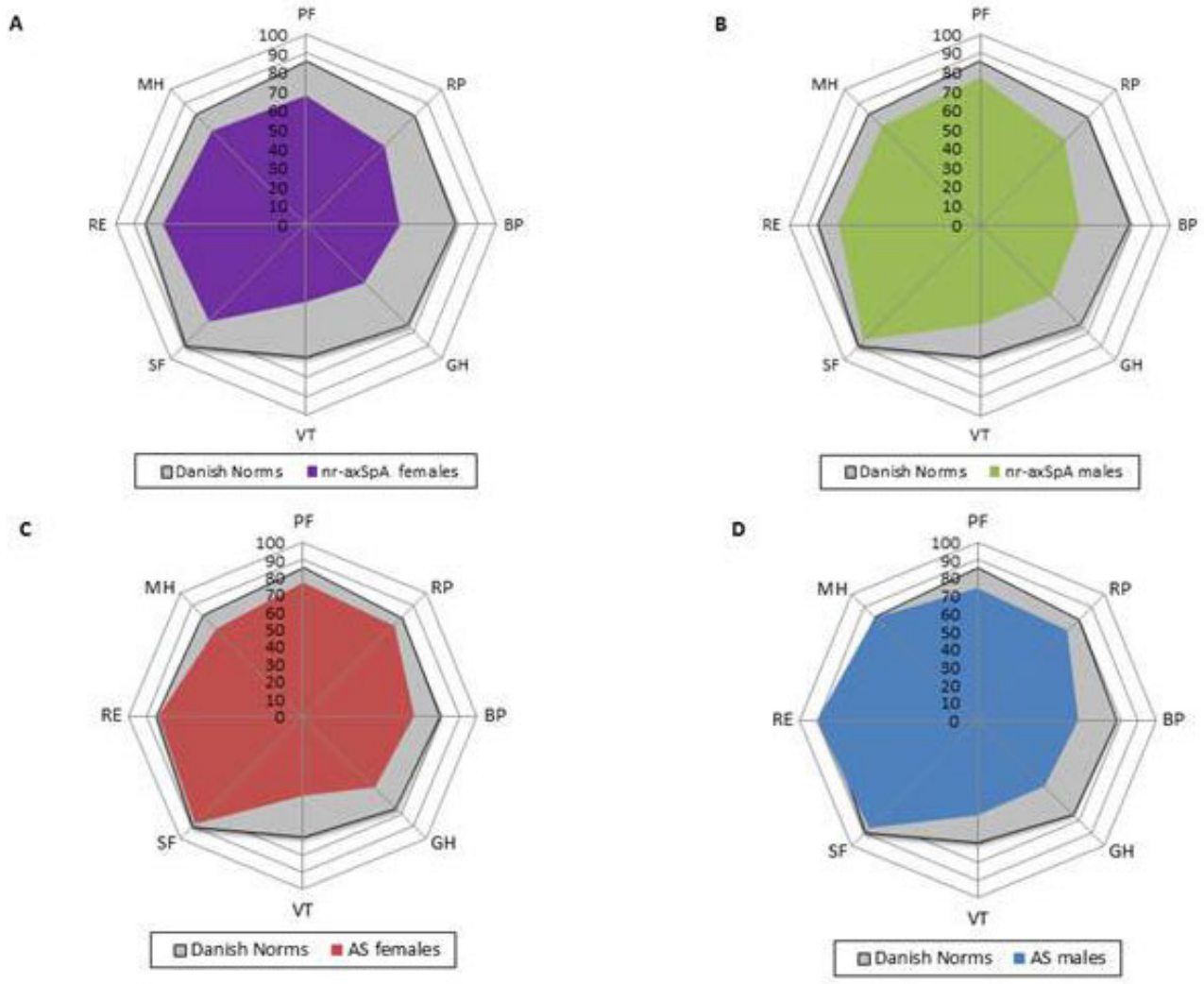

Figure 1. Mean SF-36 scores for Danish axSpA patients stratified on sex and axSpA classification. (A) nr-axSpA females (B) nr-axSpA males (C) AS females (D) AS males. Mean SF-36 scores for Danish norms are also shown. PF, physical function; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health.

Methods: AxSpA patients were consecutively recruited from 2 rheumatology outpatient university clinics. We explored how sex and axSpA disease classification affected patient-reported outcome measures (PROMs). Statistical tests were applied for group comparisons and interactions. We analyzed the relationship between tender point count (TPC) and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). The prevalence of extra-articular manifestations (EAMs) and the Charlson comorbidity index (CCI) were determined.

Table 1. Clinical characteristics and patient-reported outcome measures

Table 1. Clinical characteristics and patient-reported outcome measures

	AS n = 40		Nr-axSpA n = 60		P	P(Sex)	P(AxSpA)	P(AxSpA*Sex)
Demographics	**Male (n = 30)**	**Female (n = 10)**	**Male (n = 25)**	**Female (n = 35)**	0.001	0.002	<0.001	0.18
Age, years, median [Q_1; Q_3]	48 [41 ; 55]	46 [38 ; 62]	40 [29 ; 51]	48 [36 ; 52]	0.18[a]	0.39	0.04	0.67
BMI, kg/m^2, median [Q_1; Q_3]	25.7 [23.2 ; 30.9]	22.7 [20.6 ; 24.8]	28.1 [23.3 ; 30.2]	24.5 [23.3 ; 28.8]	0.02[a]	0.002	0.12	0.21
Smoking (current), n (%)	8 (27)	0 (0)	11 (44)	12 (34)	0.06[b]	0.73	0.29	0.85
Symptom duration, month, median [Q_1; Q_3]	233 [132 ; 384]	192 [132 ; 336]	78 [60 ; 120]	90 [48 ; 152]	<0.001[a]	0.84	<0.001	0.79
Peripheral joint involvement, n (%)	17 (57)	7 (70)	12 (48)	17 (49)	0.62[b]	0.73	0.29	0.85
Medication								
NSAIDs daily use, n (%)	12 (40)	5 (50)	13 (52)	17 (49)	0.82[b]	0.79	0.94	0.55
MTX use, n (%)	2 (7)	4 (40)	3 (12)	11 (31)	0.02[b]	0.09	0.61	0.40
MTX dose (mg/week), median [Q_1; Q_3]	0.0 [0.0 ; 10.0]	0.0 [0.0 ; 20.0]	0.0 [0.0 ; 0.0]	0.0 [0.0 ; 10.0]	0.005[a]	<0.001	0.32	0.31
Sulfasalazine use, n (%)	1 (3)	1 (10)	1 (4)	4 (11)	0.48[b]	0.33	0.90	0.98
No. of previous bDMARD used, median [Q_1; Q_3]	0.0 [0.0 ; 1.0]	0.0 [0.0 ; 1.0]	0.0 [0.0 ; 1.0]	0.0 [0.0 ; 1.0]	0.94[a]	0.89	0.93	0.38
Current bDMARD, n (%)	15 (50)	3 (30)	12 (48)	10 (29)	0.25[b]	0.13	0.93	0.99
Glucocorticoid use, n (%)	0 (0)	1 (10)	0 (0)	0 (0)	0.10[b]	0.02	0.02	0.21
Glucocorticoid use (mg/day), median [Q_1; Q_3]	0.0 [0.0 ; 0.0]	0.0 [0.0 ; 0.0]	0.0 [0.0 ; 0.0]	0.0 [0.0 ; 0.0]	0.03[a]	0.02	0.02	0.02
Patient reported outcome measures (PROMs)								
BASDAI (0-10), median [Q_1; Q_3]	25 [13 ; 45]	25 [16 ; 35]	25 [10; 52]	47 [21 ; 60]	0.07[a]	0.30	0.11	0.29
BASFI (0-100), median [Q_1; Q_3]	18 [7 ; 46]	19.0 [3 ; 49]	16 [7 ; 48]	36 [16 ; 51]	0.37[a]	0.47	0.34	0.57
SF-36: PCS (0-100), median [Q_1; Q_3][†]	43.3 [37.0 ; 52.0]	51.3 [45.4 ; 54.5]	43.8 [37.1 ; 50.4]	43.4 [34.4 ; 46.7]	0.22[a]	0.83	0.29	0.10
SF-36: MCS (0-100), median [Q_1; Q_3][†]	56.9 [50.1 ; 59.3]	50.4 [38.7 ; 60.4]	52.3 [39.1 ; 55.4]	46.7 [42.4 ; 52.2]	0.005[a]	0.09	0.03	0.21
VAS pain (0-100 mm), median [Q_1; Q_3]	24 [12 ; 43]	17 [12 ; 36]	25 [13 ; 47]	49 [20 ; 61]	0.10[a]	0.79	0.06	0.57
VAS fatigue (0-100 mm), median [Q_1; Q_3]	22 [12 ; 45]	39 [16 ; 54]	33 [12 ; 67]	54 [20 ; 61]	0.02[a]	0.08	0.16	0.38
VAS global (0-100 mm), median [Q_1; Q_3]	26 [14 ; 45]	19 [12 ; 57]	20 [12 ; 57]	53 [22 ; 69]	0.25[a]	0.39	0.30	0.41
Clinical examination								
Tender point count (0-18), median [Q_1; Q_3]	0 [0 ; 2]	4 [0 ; 6]	0 [0 ; 4]	5 [2; 8]	<0.001[a]	<0.001	0.28	0.24
Swollen joint count (0-44), median [Q_1; Q_3]	0 [0 ; 0]	0 [0 ; 0]	0 [0 ; 0]	0 [0; 0]	0.67[a]	0.89	0.32	0.23
Tender joint count (0-44), median [Q_1; Q_3]	0 [0 ; 2]	2 [0 ; 4]	0 [0 ; 2]	2 [1; 4]	0.02[a]	0.07	0.67	0.74
BASMI (0-100), median [Q_1; Q_3]	20 [10 ; 40]	10 [0 ; 30]	10 [10 ; 20]	10 [0; 20]	0.006[a]	0.12	0.02	0.30
SPARCC, SI (0-16), median [Q_1; Q_3]	0 [0 ; 2]	0 [0 ; 2]	1 [0 ; 3]	1 [0; 1]	0.05[a]	0.33	0.09	0.33
ASDAS-CRP, median [Q_1; Q_3]	2.0 [1.3 ; 3.1]	1.95 [1.3 ; 3.2]	2.1 [1.5 ; 3.1]	2.6 [1.4 ; 3.1]	0.95[a]	0.76	0.88	0.98
VAS physician (0-100), median [Q_1; Q_3]	11 [5 ; 21]	11 [9 ; 16]	10 [2.0 ; 17.0]	5 [2; 13]	0.63[a]	0.24	0.42	0.57
Extra-articular manifestations*								
Uveitis, n (%)	12 (40)	3 (30)	3 (12)	7 (20)	0.09[b]	0.42	0.51	0.33
Inflammatory bowel disease, n (%)	3 (10)	0 (0)	3 (12)	6 (17)	0.63[b]	0.58	0.81	0.58
Psoriasis, n (%)	12 (40)	2 (20)	11 (44)	14 (40)	0.64[b]	0.76	0.26	0.42
Dactylitis, n (%)	6 (20)	3 (30)	6 (24)	11 (31)	0.75[b]	0.53	0.93	0.87
Achilles entheseitis, n (%)	13 (43)	5 (50)	3 (12)	10 (29)	0.03[b]	0.14	0.21	0.43
Nephrolithiasis, n (%)	6 (20)	0 (0)	3 (12)	4 (11)	0.50[b]	0.95	0.43	0.49
Comorbidities								
Charlson Comorbidity Index, median [Q_1; Q_3]	1 [0 ; 1]	0 [0 ; 0]	1 [0 ; 1]	1 [0; 1]	0.14[a]	0.03	0.83	0.52
Paraclinic assessment								
HLA-B27 positive, n (%)	27 (90)	9 (90)	15 (60)	19 (54)	0.004[b]	0.66	0.06	0.86

Results: According to the protocol a total of 100 outpatients with axSpA were enrolled (AS males 30; AS females 10; nr-axSpA males 25; nr-axSpA females 35). The BASDAI scores appeared higher among nr-axSpA females (median [Q1; Q3] 47 [21; 60]) compared with the combined median for the three other subgroups 25 [12; 25]. Being classified as nr-axSpA was associated with a lower SF-36 MCS (median SF-36 MCS for the four subgroups: nr-axSpa females: 46.7, nr-axSpA males: 52.3 vs. AS males: 56.9 and AS females: 50.4). Females had a higher tender point count (TPC) compared with females (P< 0.001). TPC and BASDAI were correlated for female nr-axSpA patients (r= 0.44, P=0.008) and male nr-axSpA patients (r= 0.56, P=0.003). EAMs were frequent (up to 50 %) and no difference in the CCI between the subgroups was observed (P=0.14).

Conclusion: This is to our knowledge the first study to evaluate the impact of sex and axSpA classification on PROMs in axSpA patients. AS patients appeared less affected on most PROMs compared with nr-axSpA patients.

Disclosure: R. Andreasen, None; **L. Kristensen**, Pfizer, 8, AbbVie, 8, Amgen, 8, UCB, 8, Biogen, 8, MSD, 8, Sanofi, 8, Novartis, 8, Eli Lilly and company, 8, Janssen pharmaceutical, 8; **K. Egstrup**, None; **X. Baraliakos**, AbbVie, 2, 8, Pfizer, 2, 8, Novartis, 2, 8, MCD, 2, 8, UCB, 2, 8, Roche, 2, 8, Celgene, 2, 8, Janssen, 2, 8; **V. Strand**, Abbvie, 5, AbbVie, 5, Amgen, 5, Amgen, Abbvie, Bayer, BMS, Boehringer Ingelheim, Celltrion, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, UCB, 5, AstraZeneca, 5, AURA, 8, Bayer, 5, BMS, 5, Boehringer Ingelheim, 5, Celgene, 5, Celltrion, 5, Cleveland Clinic, 8, CORRONA, 5, Crescendo, 5, Crescendo Bioscience, 5, Eli Lilly, 5, EMD Serono, 5, Genentech, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Inmedix, 5, Janssen, 5, Kezar, 5, Lilly, 5, Merck, 5, NACCME, 8, Novartis, 5, Pfizer, 5, Purdue, 8, RA Forum, 8, RAN, 8, Regeneron, 5, Roche, 5, Samsung, 5, Sandoz, 5, Sanofi, 5, Servier, 5, Setpoint, 5, SLRA, 8, UCB, 5, Up to Date, 7, Washington University, 8, WIR, 8, WRA, 8; **H. Horn**, None; **I. Hansen**, None; **R. Christensen**, AbbVie, 2, Amgen, 2, Axellus A/S, 2, Biogen, 2, BMS, 2, cambridge weight plan, 2, Celgene, 2, Eli Lilly, 2, Hospira, 2, MSD, 2, Norpharma, 2, Novartis, 2, Oak Foundation (OCAY-13-309), 2, Orkla Health, 2, Pfizer, 2, Research Unit for Musculoskeletal Function and Physiotherapy, Institute of Sports science and Clinical biomechanics, University of Southern Denmark, 9, Roche, 2, Sobi, 2, Takeda, 2; **T. Ellingsen**, None.

Abstract Number: 0564

ASDAS Is More Important Than BASDAI in Advanced Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with ankylosing spondylitis, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is used to measure disease activity to initiate or maintain TNF inhibitor therapy. However, despite a low disease activity measured by BASDAI, some patients complain of pain or are found in high inflammatory status. In such cases, other disease activity measurement tools such as the Ankylosing Spondylitis Disease Activity Score

Table 1. Difference in disease activity status according to treatment with TNF inhibitors

	Non-TNF inhibitor			TNF inhibitor		
	BASDAI < 4 (N=2,925)	BASDAI ≥ 4 (N=2,184)	p-value	BASDAI < 4 (N=6,569)	BASDAI ≥ 4 (N=1,637)	P-value
Duration of follow up (year, mean±SD)	7.8±4.3	6.3±4.5	<0.001	7.1±4.1	8.0±4.4	<0.001
mSASSS (mean±SD)	18.7±18.1	19.8±19.5	0.064	20.5±20.7	23.0±22.2	<0.001
Available ASDAS-CRP	1,058 (36.2%)	690 (31.6%)		2,186 (33.3%)	644 (39.3%)	
ASDAS-CRP < 2.1	566 (53.5%*)	0 (0.0%*)	<0.001	1,243 (56.9%*)	0 (0.0%*)	<0.001
ASDAS-CRP ≥ 2.1	**492 (46.5%*)**	690 (100.0%*)		**943 (43.1%*)**	644 (100.0%*)	
Available ASDAS-ESR	1,468 (50.2%)	920 (42.1%)		2,846 (43.3%)	832 (50.8%)	
ASDAS-ESR < 2.1	1,113 (75.8%*)	96 (10.4%*)	<0.001	2,347 (82.5%*)	121 (14.5%*)	<0.001
ASDAS-ESR ≥ 2.1	**355 (24.2%*)**	824 (89.6%*)		**499 (17.5%*)**	711 (85.5%*)	

*Percentage of available ASDAS in the BASDAI

Table 2. Difference in disease activity status according to treatment with mSASSS

	mSASSS < 36			mSASSS ≥ 36		
	BASDAI < 4 (N=5,920)	BASDAI ≥ 4 (N=2,184)	p-value	BASDAI < 4 (N=1471)	BASDAI ≥ 4 (N=652)	P-value
Duration of follow up (year)	7.0 (4.0-10.0)	6.3 (3.0-9.0)	<0.001	8.0 (5.0-11.0)	7.0 (5.0-11.0)	0.950
TNF inhibitor user	4,197 (70.9%)	874 (40.0%)	<0.001	1,100 (74.8%)	319 (48.9%)	<0.001
mSASSS (mean±SD)	7.7 (5.5-14.2)	7.6 (5.5-14.0)	0.424	54.4 (43.1-68.0)	53.0 (44.0-68.0)	0.609
Available ASDAS-CRP	2,124 (35.9%)	782 (35.8%)		540 (36.7%)	267 (41.0%)	
ASDAS-CRP < 2.1	1,252 (58.9%*)	0 (0.0%*)	<0.001	217 (40.2%*)	0 (0.0%*)	<0.001
ASDAS-CRP ≥ 2.1	**872 (41.1%*)**	782 (100.0%*)		**323 (59.8%*)**	267 (100.0%*)	
Available ASDAS-ESR	2,852 (48.2%)	1,039 (47.6%)		686 (46.6%)	345 (52.9%)	
ASDAS-ESR < 2.1	2,331 (81.7%*)	130 (112.5%*)	<0.001	506 (73.8%*)	40 (11.6%*)	<0.001
ASDAS-ESR ≥ 2.1	**521 (18.3%*)**	909 (87.5%*)		**180 (26.2%*)**	305 (88.4%*)	

*Percentage of available ASDAS in the BASDAI

(ASDAS) may be recommended. The aim of this study was to identify patients with advanced AS who show high disease activity with ASDAS and require active treatment despite low BASDAI.

Methods: In a single center cohort, 1,240 patients with AS were followed up to 18 years. The BASDAI, ASDAS, and modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) were obtained from electronic medical records. The mSASSS was measured almost every 2 years. We used the interpolation method to estimate the mSASSS at the time point when the BASDAI or ASDAS was measured. High disease activity was defined as BASDAI ≥ 4 or ASDAS ≥ 2.1 and low disease activity as BASDAI < 4 or ASDAS < 2.1 at each disease activity measurement. Changes in the distribution of high and low disease activities were investigated by assessing TNF inhibitor use and mSASSS.

Results: A total of 13,315 BASDAI, 4,578 ASDAS-CRP, and 6,066 ASDAS-ESR measurements were obtained from 1,240 patients. The mean duration from diagnosis of AS to the date of measuring the disease activity was 10.2 ± 3.9 years. Of these measurements, 1,435 (44.2%) had ASDAS-CRP ≥ 2.1 and 3,244 measurements had BASDAI < 4. In the TNF inhibitor group, the percentage of measurements with ASDAS-CRP ≥ 2.1 and BASDAI < 4 was similar to that in the non-TNF inhibitor group (492/1,058, 46.5% vs. 943/2,186, 43.1%) (Table 1). The percentage of measurements with ASDAS-CRP ≥ 2.1 and BASDAI < 4 was elevated in patients with mSASSS ≥ 36 compared to that in patients with mSASSS < 36 (323/540, 59.8% vs. 872/2,124, 41.1%) (Table 2).

Conclusion: Despite treatment with TNF inhibitors, some patients remain with high disease activity measurable by tools other than BASDAI. Moreover, the proportion of patients with high disease activity was high in the advanced radiographic progression group. These patients may need active treatment with therapies other than TNF inhibitors.

Disclosure: J. Jun, None; **B. Koo**, None; **S. Lee**, None; **J. Kim**, Novartis Korea Ltd., 3; **J. Kang**, None; **T. Kim**, None.

Abstract Number: 0565

Evidence-Based Recommendations for the Management of Enteropathic Arthritis: A Rheumatology – Gastroenterology Collaborative Initiative

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Management of enteropathic arthritis may be challenging due to differences in treatment response of inflammatory bowel diseases and arthritis to different therapeutic modalities, which may even cause worsening of some manifestations while improving others. Enteropathic arthritis was not addressed in the management recommendations for spondyloarthritis. The aim of this project was to develop a set of evidence based recommendations for the management of patients with enteropathic arthritis

Methods: A task force was formed that included ten rheumatologists and 8 gastroenterologists. Research questions were determined using a Delphi approach. A systematic literature search, data extraction, and statistical analyses were performed according to a pre-specified protocol. Studies that assessed the efficacy of an intervention on inflammatory bowel disease-related outcomes and/or spondyloarthritis related outcomes in patients with enteropathic arthritis were included. Risk ratios were calculated for binary outcomes and mean difference for continuous outcomes, whenever possible. Results of the systematic literature review were presented to the experts and recommendations were formulated after thorough discussions and voting.

Results: A total of 4 overarching principles and 10 recommendations were formulated. The recommendations addressed the use of NSAIDs, corticosteroids, sulfasalazine and 5-ASA derivatives, TNF inhibitors, tofacitinib, secukinumab, ustekinumab, and vedolizumab among patients with active inflammatory bowel disease, active arthritis, active disease regarding both inflammatory bowel disease and arthritis, and among patients in remission. Final voting showed a good agreement among the group on all recommendations.

Conclusion: These recommendations are intended to help rheumatologists, gastroenterologists and other clinicians dealing with enteropathic arthritis and to point out to the shortcomings of the available data on the management of this challenging condition.

Disclosure: G. Hatemi, Abbvie, Mustafa Nevzet, UCB, 8, Bayer, Eli Lilly, 5, BMS, Celgene Corporation, Silk Road Therapeutics, 2, Silk Road Therapeutics, 2; **S. Akar**, Abbvie, 2, 5, Amgen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5; **H. Akpinar**, None; **P. Atagunduz**, None; **G. Bengi**, None; **G. Can**, None; **A. Celik**, None; **S. Esatoglu**, None; **O. Gercik**, None; **H. Hamzaoglu**, None; **M. Inanc**, None; **G. Kabacam**, None; **I. Kalkan**, None; **L. Kilic**, None; **F. Onen**, Tofacitinib (Pfizer), 8; **A. Tezel**, None; **M. Toruner**, None; **S. Kiraz**, None.

Abstract Number: 0566

Temporal Relationship Between Enteropathic Spondylitis Symptoms/ diagnosis and Inflammatory Bowel Diseases Diagnosis: HUR-BIO Real Life Results

Bayram Farisoğulları,[1] Gozde Kubra Yardımcı,[1] Alper Sarı,[1] Berkan Armagan,[2] Emre Bilgin,[1] Ertugrul Cagri Bolek,[1] Levent Kilic,[3] Omer Karadag,[4] Ali Akdoğan,[1] Şule Apras Bilgen,[3] Ali İhsan Ertenli,[1] Sedat Kiraz,[3] and Umut Kalyoncu[5], [1]Hacettepe University Vasculitis Centre, Ankara, Turkey, Ankara, Turkey, [2]Department of Internal Medicine, Hacettepe University, Faculty of Medicine, Ankara, Turkey., Ankara, Turkey, [3]Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey, [4]Hacettepe University Vasculitis Centre, Ankara, Turkey / Vasculitis and Lupus Clinic, Addenbrooke's Hospital, University of Cambridge, UK, Ankara, Turkey, [5]Hacettepe University Department of Rheumatology, Ankara, Turkey

Table 1. Temporal relationship spondylitis between IBD

Temporal relationship Spondylitis and IBD		All patients n=59	Crohn Disease n=28	Ulcerative Colitis n=31	P
Spondylitis symptoms	Spondylitis symptoms before IBH diagnosis n (%)	49 (83)	27 (96.4)	22 (71)	0.009*
	Spondylitis symptoms after IBH diagnosis	10 (17)	1 (3.6)	9 (29)	0.009*
Spondylitis diagnosis	Spondylitis diagnosis before IBH diagnosis n (%)	21 (35.6)	12 (42.8)	9 (29)	0.27
	Spondylitis diagnosis after IBH diagnosis	23 (39)	7 (25)	16 (51.6)	0.036*
	Concomitant spondylitis and IBH diagnosis	15 (25.4)	9 (60)	6 (40)	0.26

IBD: inflammatory bowel disease, *p <0.05

enteropatik artrit süre tablosu-dönüştürüldü

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The correlation between the time frame of the symptoms/diagnosis of spondylitis and the diagnosis of inflammatory bowel disease (IBD) on patients of enteropathic spondylitis (eSpA) is not precisely known. Aim of this study was to determine the timing of symptoms/diagnosis of SpA and the diagnosis of IBD on the patients with eSpA.

Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a prospective, single center database of biological treatments since 2005. HUR-BIO SpA registry included 2576 SpA patients, and 90 (3.5%) patients had enteropathic arthritis (EA). Sacroiliitis was defined at 59 (65.5%) patients as modified New York criteria or based on ASAS magnetic resonance imaging. Enteropathic spondylitis defined as inflammatory bowel disease and radiological sacroilitis with inflammatory back pain/spine symptoms. Demographic, clinical, laboratory, therapeutic data and imaging features were collected from this database. Patients with available data about the timing of IBD diagnosis, SpA symptoms and SpA diagnosis were included in the analysis. The temporal relationship between the diagnosis of IBD and the symptom and / or diagnosis of SpA was assessed.

Results: Fifty nine (44.1% female) eSpA patients enrolled in this study. Mean age was 45.0 ± 13.0 years, mean disease duration was 9.9 ± 7.8 years.IBD type was UC in 31 (52.5%) patients, CD in 28 (47.5%) patients. The symptoms of spondylitis were present in 49 (83%) patients before the diagnosis of IBD [CD 96.4% vs UC 71.0%, p=0.009] (Table 1). In 23 patients, SpA diagnosis was made after IBD diagnosis [CD 25% vs UC 51%, p=0.036]. The median time lag between the diagnosis of IBD and SpA was 2 (1-9) years for CD, 7.5 (2-23) years for UC, p=0.027. The mean delay time for the diagnosis of SpA in patients with eSpA was 4 (0-31) years [4 (0-31) years in CD vs 3 (0-22) years UC patients, p:0.57].

Conclusion: In most of eSpA patients, spondylitis symptoms were present before diagnosis of IBD and this finding was more prominent in CD. On the other hand, the diagnosis of spondylitis was made after the diagnosis of IBD in almost 40% of patients. In UC, this condition was more distinct**.**

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Abstract Number: 0567

Worse Outcomes for Female Patients with Axial Spondyloarthropathy

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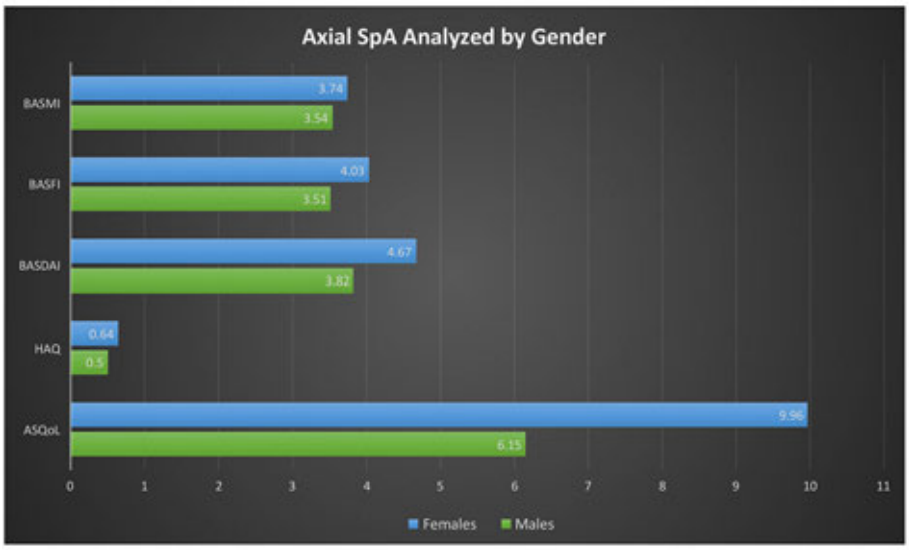
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial Spondyloarthritis(axSpA) is known to have a male predominance. There is little available literature examining affected female patients. Previous studies have included small numbers of females, leading to a lack of detailed analysis of variations between genders. The Ankylosing Spondylitis Registry of Ireland (ASRI) is a source of epidemiological data on patients with axSpA in Ireland. The purpose of this study was to determine if there is a significant difference in disease activity and patterns of disease between genders.

Methods: Analysis of the patient population registered in the ASRI using IBM SPSS version 25. Patients were analyzed on the basis of gender. Mean ASQoL, HAQ, BASDAI, BASFI and BASMI scores were compared. Difference between the two groups was tested for statistical analysis using an independent two tailed t test and a Mann Whitney

	Females (n=171)	Males (n=563)	Total (n=734)	p-value
Age	42.73	45.72	45.02	0.01
Disease duration	17.01	19.13	18.64	0.05
Caucasian	22.8% (168)	73.6% (540)	94.5% (708)	0.4
Delay to diagnosis	7.79	8.56	8.39	0.27
HLA B27 +	67% (115)	69% (387)	68% (502)	0.45
Measures of Disease:				
BASDAI	4.66	3.82	4.02	< 0.01
ASQoL	7.96	6.15	6.57	< 0.01
BASFI	4.03	3.51	3.63	0.03
BASMI	3.74	3.54	3.58	0.38
HAQ	0.64	0.5	0.54	< 0.01
Extra-articular Manifestations:				
Uveitis	43.9% (75)	32.1% (181)	34.9% (256)	0.01
Psoriasis	17% (29)	18.1% (102)	17.8% (131)	0.28
IBD	15.8% (27)	7.8% (44)	9.7% (71)	< 0.01
Co-morbidities:				
IHD	4.1% (7)	3% (17)	3.3% (24)	0.47
CVD	0% (0)	2.1% (12)	1.6% (12)	0.08
HTN	18.1% (31)	22% (124)	21.1% (155)	0.29
Hyperlipidaemia	15.2% (26)	16.5% (93)	16.2% (119)	0.72
DM	3.5% (6)	5% (28)	4.6% (34)	0.54
PUD	7% (12)	7.1% (40)	7.1% (52)	0.97
TB	2.9% (5)	3.7% (21)	3.5% (26)	0.62
Osteoporosis	7.6% (13)	4.6% (26)	5.3% (39)	0.13
Depression	13.5% (23)	9.4% (53)	10.4% (76)	0.13
Cancer	4.1% (7)	3% (17)	3.3% (24)	0.49



U test. Further analysis was performed to determine difference in patterns of disease, extra-articular manifestations, medication usage and co-morbidities using a chi-squared test for independence.

Results: Data for 734 patients were reviewed via the registry. The patient population was 14.6% (171) females, 85.4%(563) males, with mean age of 45 years and a mean disease duration of 18 years (means: ASQoL 6.57, HAQ 0.54, BASDAI 4.02, BASFI 3.63, BASMI 3.58). Female patients had higher ASQoL (7.96 vs. 6.15, $p < 0.01$), HAQ (0.64 vs. 0.50, $p < 0.01$), BASDAI (4.66 vs. 3.82, $p < 0.01$), and BASFI scores (4.03 vs. 3.51, $p=0.03$). No significant difference between BASMI was found between genders (3.74 vs. 3.54, $p=0.83$) (Figure 1). No significant difference was found in delay to diagnosis (7.79 years in females vs. 8.56 years in males, $p=0.05$) or HLA B27 positivity (67% vs. 69%, $p=0.45$). Both genders had comparable incidence of arthritis(39.8% vs. 30.4%, $p=0.07$) and enthesitis (18.8% vs. 16.7, $p=0.74$), however females had higher rates of MRI sacroiliitis(48.5% vs. 42.6%, $p=0.02$) and dactylitis(12.3% vs. 5.2%, $p < 0.01$). Analysis of medication usage showed no significant difference in use of sDMARD (18.7% vs 19.7%, $p=0.7$) or biologic exposure (70% vs. 76.8%, $p=0.96$). A higher proportion of females used NSAIDs (58.5% vs. 48.5%, $p=0.02$) while a lower proportion of women are currently on biologic therapy (77.7% vs. 87.2%, $p=0.01$). Regarding extra-articular manifestations, females had higher rates of both inflammatory bowel disease (15.8% vs. 7.8%, $p < 0.01$) and uveitis (43.9% vs. 32.1%, $p=0.01$). A range of co-morbidities were also analyzed, however no statistically significant difference in incidence was found (table 1).

Conclusion: There are significant differences between genders in patients with axSpA. This analysis demonstrates that females tend to have higher disease activity, worse levels of function leading to greater impact on their quality of life. Perhaps as a reflection of this, female patients have higher rates of NSAID usage. Females also have higher rates of extra-articular manifestations including inflammatory bowel disease and uveitis. Dedicated research into female patient with axSpA is needed to appropriately address and treat their disease.

Disclosure: S. Maguire, AbbVie, 9; **G. Fitzgerald**, AbbVie, 9, Pfizer, 9, Novartis, 9, UCB, 9; **C. Sheehy**, None; **F. O'Shea**, None.

Abstract Number: 0568

Understanding mNY Radiograph Score Discordance in Axial Spondyloarthritis Clinical Trials Using Imaging Criteria for Subject Eligibility

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

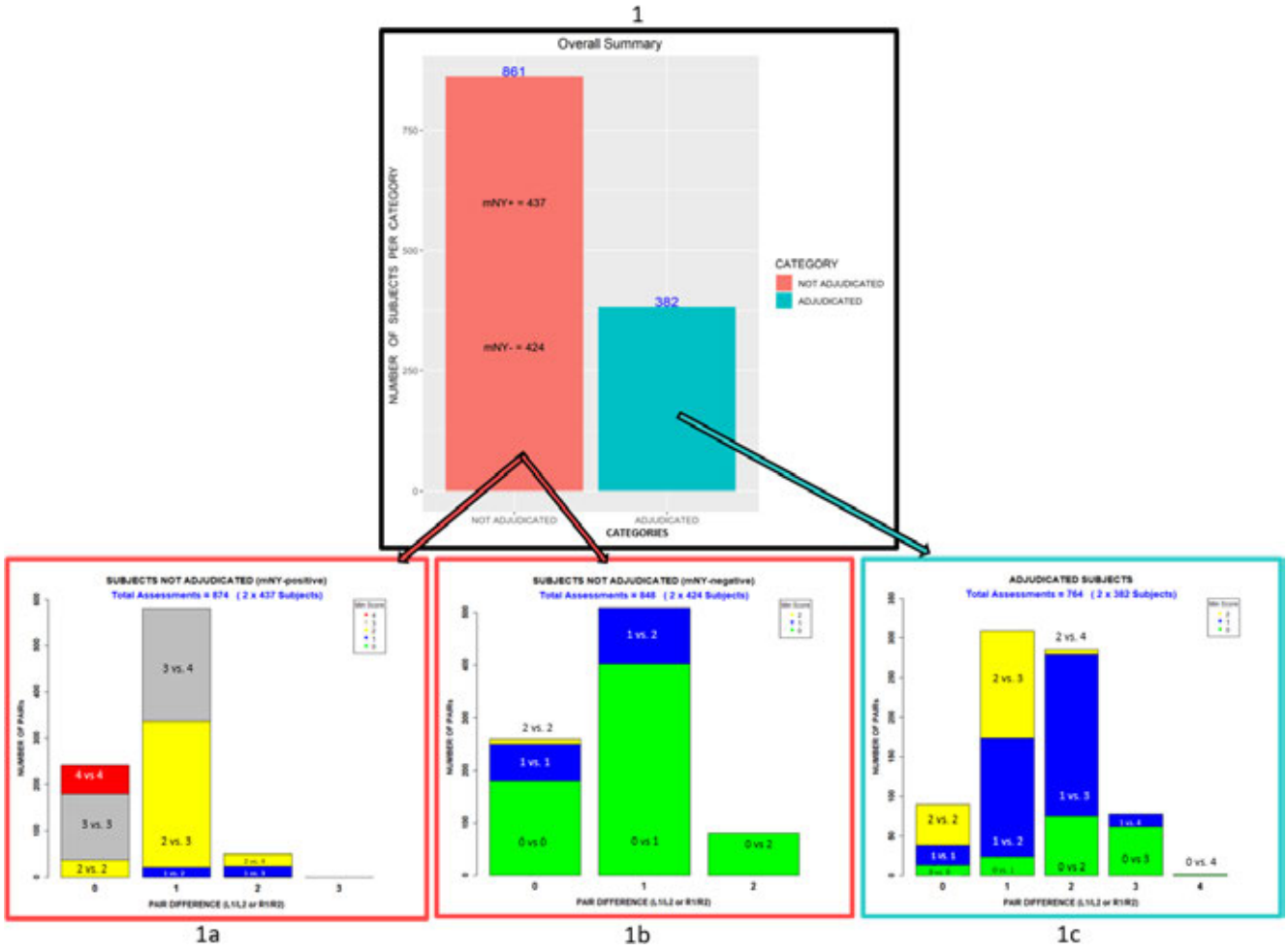
Background/Purpose: Axial spondyloarthritis (axSpA) is typically radiographically confirmed on the sacroiliac joint (SIJ) as assessed by the modified New York (mNY) criteria. In clinical trials, the mNY criteria is used to support determination of subject eligibility for study enrollment. Thus, it is important to analyze the mNY scores most likely to result in disagreement between reviewers and to better understand the impact on enrollment of the target axSpA population.

Methods: Data from central independent review of anterior-posterior (AP) pelvis radiographs in a double read model with adjudication for a total of 1,648 subjects from 3 clinical trials (phases 2 and 3) was analyzed for mNY +/- and individual left (L) and right (R) SIJ score discordance. The mNY scores were categorized per joint (R and L) as follows: 1) independent reviewers agreed on SIJ scores, 2) independent reviewers did not agree on individual joint scores, but mNY +/- was not impacted, and 3) independent reviewers did not agree and mNY +/- was impacted (i.e., adjudication triggered). To identify the score combinations which most often resulted in mNY +/- adjudication discrepancy, the frequency of each combination of scores that led to a discrepancy in categories 2 and 3 was determined.

Results: In 69% of the cases with individual score discrepancies per joint (R or L), the mNY assessment was not impacted; whereas, in 31% of these cases, adjudication was triggered (i.e., the mNY assessment was impacted by the R/L score discrepancy; Fig 1a). The score combinations most often associated with at least one joint for a timepoint where adjudication was triggered were: 1 vs. 2, 2 vs. 3, and 1 vs. 3. The score combination most often discrepant, but did not impact the mNY assessment (i.e., did not trigger adjudication) was 0 vs. 1. Overall, the score of 2 was associated with the most ambiguity.

Conclusion: Discrepancies in SIJ scores per joint (R and L) were not significant in approximately 2 out of 3 (69%) of the cases, considering impact on subject population enrollment. However, in approximately 1 out of 3 (31%) of the cases, the SIJ score discrepancies were associated with a disagreement in subject eligibility for study enrollment resulting in an adjudication.

Based on the data presented (Fig 1), a score of 2 was the most frequently involved score in inter-reader 1-step discordance. This may be related to the definition of a score of 2, which is open to a wider scope of interpretation. These results support the use of a double read and adjudication model for eligibility in clinical trials and potential use



Breakdown of Data from 1,648 subjects (1,243: Evaluable with at least one discrepant joint; 18: Not Evaluable; 8: Incomplete; and 379: no discrepancy)

of other non-radiographic assessments (e.g. MRI) to improve accuracy of classification and appropriate inclusion of subjects into axSpA clinical trials.

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Abstract Number: 0569

Sarcopenia, Segmental Muscle Strength and Body Composition in Young Axial Spondylarthritis Patients: Results from MyoSpA Study

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SESSION INFORMATION

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Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcopenia is a generalized skeletal muscle disorder characterized by the loss of muscle strength and muscle mass, leading to functional limitation, worse quality of life and increased mortality. Although frequently attributable to ageing, sarcopenia due to inflammatory processes has been recognized. However, data on sarcopenia in axial Spondylarthritis (axSpA) are scarce. Our purpose is to determine the prevalence of sarcopenia in young patients with axSpA; in addition, to assess the muscle strength and body composition of different body segments.

Methods: A cross-sectional study was conducted on 54 participants aged 18 to 50 years, 27 patients with axSpA (according to ASAS classification criteria, with symptoms duration ≤ 10 years), and 27 healthy controls (HC), matched by gender and age (1:1).

Sarcopenia was defined as per the European Working Group on Sarcopenia in Older People 2 (EWGSOP2).

Muscle strength of three different body segments (trunk, upper and lower limbs, on both sides) was measured by resisted hand-held dynamometer performed by a single reader and through five times sit-to-stand test. The criteria for low muscle strength was chair stand test >15 seconds for five rises.

Body composition was measured by octapolar multifrequency bioelectrical impedance analysis (InBody770). Low skeletal muscle mass was defined according to the equipment's inbuilt and personalized reference values.

Physical activity was assessed by the International Physical Activity Questionnaire (IPAQ). Appropriate statistical tests were used to compare differences between groups.

Results: A total of 27 axSpA patients and 27 HC were included. Mean age was 36.5 ± 7.5 years, 67% were males. There was no significant difference between both groups in terms of age, gender, body mass index and physical activity. AxSpA patients had a mean symptoms duration of 6.5 ± 3.2 years, BASDAI 2.7±2.3 and BASFI 0.9±3.1.

Variable	Patients *n*=27	Controls *n*=27	*p*-value
Age*	36.8 ± 7.4	36.3 ± 7.8	0.79
Gender (male), *n* (%)	18 (66.7%)	18 (66.7%)	0.99
Body height (cm)	170.2 (164.1 – 176.9)	173.0 (165.4 – 178.0)	0.52
Body weight (Kg)	73.1 (66.9 – 85.6)	69.7 (64.8 – 79.6)	0.35
BMI (Kg/m^2)	25.0 (22.9 – 29.9)	23.6 (23.1 – 25.8)	0.30
IPAQ (%)			0.80
Low	29.2%	20.8%	
Moderate	37.5%	41.7%	
High	33.3%	37.5%	
BASDAI*	2.7 ± 2.3	-	
BASFI*	0.9 ± 3.1	-	
Disease duration*	6.5 ± 3.2	-	
Sarcopenia, *n* (%) ɵ	0	0	-
Low muscle strength (5-times sit-to-stand >15s), *n* (%)	2 (8.3%)	0	0.15
Low skeletal muscle mass, *n* (%)	2 (8.3%)	1 (4.2%)	0.55
Strength (Nm/s)			
Trunk	56.3 (37.6 – 67.2)	57.3 (51.2 – 63.0)	0.67
Upper Limb	47.6 (40.2 – 73.2)	71.8 (51.9 – 80.5)	**0.02**
Lower Limb	51.0 (38.5 – 57.1)	59.8 (54.6 – 64.5)	**0.001**
Lean Mass (Kg)			
Trunk	24.9 (21.9 – 27.0)	25.3 (20.4 – 27.6)	0.92
Upper Limb	3.1 (2.56 – 3.5)	3.1 (2.3 -3.5)	0.81
Lower Limb	8.0 (7.2 – 9.5)	9.2 (7.5 – 10.0)	0.15
Fat Mass (Kg)			
Trunk	10.3 (6.3 – 15.9)	8.1 (5.1 – 11.1)	**0.045**
Upper Limb	1.3 (0.6 – 2.2)	0.9 (0.5 – 1.5)	**0.050**
Lower Limb	2.9 (1.9 – 4.0)	2.5 (1.6 – 3.4)	0.21
Body water (L)			
Trunk	19.6 (17.1 – 21.3)	18.8 (14.4 – 21.1)	0.84
Upper Limb	2.4 (2.0 – 2.7)	2.3 (1.6 – 2.7)	0.38
Lower Limb	6.5 (5.8 – 7.4)	6.5 (5.1 – 7.5)	0.82

Table 1. Comparison of subjects characteristics between axSpA patients and healthy controls. Values are median (25^{th} - 75^{th} percentiles), except otherwise indicated.
***** Mean ± SD.
ɵ Available for 48 subjects (24 patients and 24 HC).

BMI: Body Mass Index. IPAQ: International Physical Activity Questionnaire. BASDAI: Bath AS Activity Index. BASFI: Bath AS Functional Index.

Comparison of subjects characteristics between axSpA patients and healthy controls.

There were no participants (patients or controls) fulfilling the definition of sarcopenia. Low muscle strength, measured by the chair rise test, was found in 8.3% of patients vs 0% of HC (p=0.15). Skeletal muscle mass was reduced in 8.3% of patients vs 4.2% of HC (p=0.55).

Regarding the different body segments, axSpA patients had median lower muscle strength in the upper limbs (47.60 vs 71.75, p=0.023) and lower limbs (51.0 vs 59.83, p=0.001), compared to HC. Trunk muscle strength did not show any difference between groups (56.3 vs 57.30, p=0.67).

There were no significant differences in lean mass and body water, between both groups, for each segment (upper limbs, lower limbs and trunk). Fat mass was marginally higher in the trunk (10.3 vs 8.1, p=0.045) and upper limbs (1.3 vs 0.89, p=0.05) of axSpA patients, but not in the lower limbs (2.9 vs 2.5, p=0.21) – Table 1.

Conclusion: In our cohort, young patients with axSpA with short disease duration did not show higher prevalence of sarcopenia according to EWGSOP2 definition. However, a reduced appendicular muscle strength was found com-

pared with HC, with no differences in lean mass, suggesting a possible muscle dysfunction. New criteria for sarcopenia in young populations are needed and further studies should be conducted to confirm these findings.

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Abstract Number: 0570

Pattern and Influential Factors in Promoting Treat-to-Target (T2T) for Follow-up of Ankylosing Spondylitis (AS) Patients with a Rheumatologist-patient Interactive Smart System of Disease Management (SSDM): A Cohort Study from China

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing Spondylitis Disease Activity Score (ASDAS) is adopted to evaluate the degree of disease activity and the inflammatory response in AS patients. ASDAS score ≤ 1.3 represents inactive disease status and achievement of T2T.

The objective of this study is to evaluate the patterns of T2T and related influential factors among AS patients after applying SSDM in the real world.

Table 1 The T2T results at baseline and in final follow up.

Baseline\Last follow-up	Number	%	ASDAS≤1.3	%	ASDAS≥1.3	%
ASDAS≤1.3	227	28.34%	147	64.76%	80	35.24%
ASDAS≥1.3	574	71.66%	178	31.01%	396	68.99%
Total	801	100%	325	40.57%	476	59.42%

Table 2 The patients were stratified according to their frequency of self-assessment: more than 3 times, less than or equal to 3 times self-assessments within 6 months follow-up.

Self-Assessments	Number	Baseline (T2T rate)	Last follow-up (T2T rate)	Improvement
≤3 times	467	26.77%	35.12%	8.35%
> 3 times	334	30.54%	48.20%	17.66%

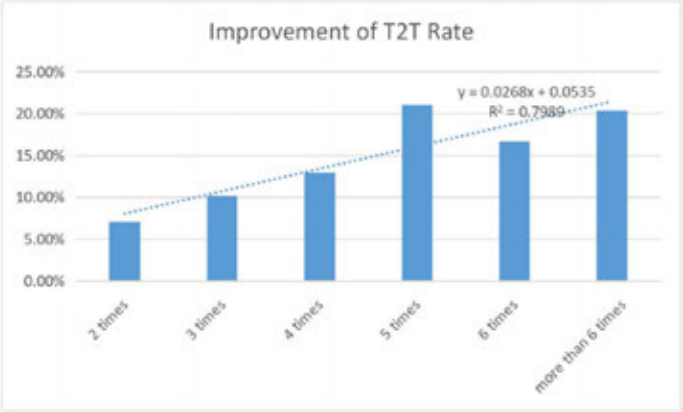

Figure 1. The improvement of T2T rate(y) was positively correlated with times of self-assessment for ASDAS(x) independently. The regression equation as "y = 0.0268x + 0.0535 R2 = 0.7989", p<0.01.

Methods: SSDM is a mobile application for disease management. Patients were trained to master SSDM by healthcare professionals and to conduct ASDAS self-assessments. Patients were also required for repeating self-assessments after leaving the hospital. After entry by patients, data can synchronized to the SSDM terminal of authorized rheumatologists.

Results: From Jan 2015 to May 2019, 13,820 AS patients enrolled in SSDM with the mean age of 33.92±12.61 years old. And median disease duration is 2.91 years. 801 AS patients from 120 hospitals across China were followed up for more than 6 months through SSDM. The results at baseline and in final follow up were summarized in Table 1.

The rate of T2T achievers were 28.34% (227/801) at baseline, and improved significantly to 40.57% (325/801) after 6 months follow up, p< 0.01. Among T2T achievers at baseline, 64.76% (147/227) maintained T2T, 35.24% (80/227) relapsed. Of patients who didn't achieve T2T at baseline, only 31.01% (178/574) of the other AS patients achieved T2T after 6 months follow up. We further analyzed the impact of the times of self-assessment for ASDAS on T2T. The patients were stratified according to their frequency of self-assessment: more than 3 times, less than or equal to 3 times self-assessments within 6 months follow-up. Results show that the more frequent of the self-assessment, the higher improvement of T2T rate (17.66% vs. 8.35%, Table 2). A linear regression analysis of variables in statistics and

parameter estimation was conducted by least square method. The improvement of T2T rate(y) was positively correlated with times of self-assessment for ASDAS(x) independently. The regression equation as "y = 0.0268x + 0.0535 R2 = 0.7989", p< 0.01. (Figure 1)

Conclusion: Significant improvement was observed under applying SSDM through empowering AS patients. After proactive disease management via SSDM for more than 6 months, Patients with ASDAS≤1.3 score at baseline had a significantly higher retention rate of disease activity. The patients who performed more self-assessments through SSDM had lower probability of relapse and higher rate of T2T. SSDM is a valuable tool for long term follow-up through empowering patients.

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Abstract Number: 0571

Effect of Long-term Treatment with TNF-α Inhibitor on Lipid Profile in Spondyloarthritis: Data from Nationwide Korean College of Rheumatology Biologics (KOBIO) Registry

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In spondyloarthritis (SpA), the lipid profile changes due to the systemic inflammatory response. Theoretically, the proinflammatory state is associated with a decrease in total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG) than expected, and an increase in these lipid levels after anti-inflammatory therapies, such as tumour necrosis factor alpha (TNF-α) inhibitor. This study aimed to assess the influence of long-term treatment with TNF-α inhibitor on lipid profile and atherogenic index (AI) in patients with SpA.

Methods: Lipid data and AI of SpA patients treated with TNF-α inhibitor were analysed from the Korean College of Rheumatology Biologics (KOBIO) registry between 2012 and 2017. Patients exposed at least for one year to SpA approved dosage regimens of etanercept, infliximab, adalimumab or golimumab as first line treatment were included. The baseline lipid profile and AI were compared with between 0 - 12 months, 12 - 18 months, 18 - 24 months, > 24 months. AI was derived according to the logarithmic (TG/HDL-C).

Results: The records of 361 patients (male 279, female 82) were reviewed. Mean follow-up duration was 2.25 ± 0.03 year (0.24 - 5.66 years) and baseline Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was 6.0 ± 0.1. Treatment with TNF-α inhibitor was associated with increased levels of TC (173.66 ± 1.82 mg/dL at baseline, 191.93 ± 3.51 mg/dL; p = 0.001 at 0 - 12 months, and 188.88 ± 1.61 mg/dL; p < 0.001 at > 24 months), HDL-C (48.50 ± 0.80 mg/dL at baseline, 55.92 ± 2.83 mg/dL; p = 0.023 at 0 - 12 months, and 53.38 ± 0.88 mg/dL; p= 0.002 at > 24

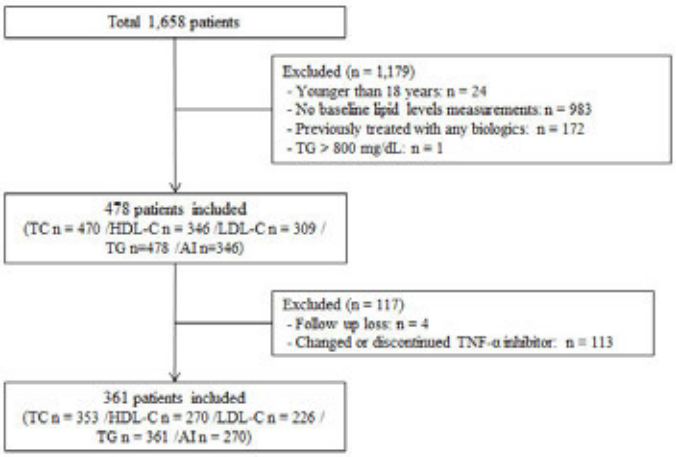

Figure 1. Overview of study design and patient disposition

TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglycerides; AI: atherogenic index

Table 1. Effects of TNF-α inhibitor on lipid profile

		Time				
		baseline value before treatment	0 - 12 months	12 - 18 months	18 - 24 months	> 24 months
TC	Mean±SE	173.66±1.82	191.93±3.51	186.14±2.37	188.12±4.20	188.88±1.61
	p value		<0.001	<0.001	0.001	<0.001
	Multivariate model[a] *p*-value		0.001	0.003	0.022	<0.001
HDL-C	Mean±SE	48.50±0.80	55.92±2.83	56.09±1.94	50.22±1.93	53.38±0.88
	p-value		0.001	<0.001	0.419	<0.001
	Multivariate model[a] p-value		0.023	<0.001	0.936	0.002
LDL-C	Mean±SE	107.23±2.22	116.66±3.63	108.41±2.74	109.10±4.79	113.53±1.84
	p-value		0.034	0.741	0.724	0.035
	Multivariate model[a] *p*-value		0.589	0.719	0.605	0.321
TG	Mean±SE	118.14±4.04	130.79±9.99	140.55±7.06	157.05±12.31	159.90±5.62
	p-value		0.189	0.004	0.001	<0.001
	Multivariate model[a] *p*-value		0.195	0.350	0.029	<0.001
AI	Mean±SE	0.77±0.04	0.78±0.09	0.79±0.06	1.10±0.11	1.00±0.04
	p-value		0.902	0.720	0.004	0.001
	Multivariate model[a] *p*-value		0.601	0.480	0.007	<0.001

[a]Adjusted for age, gender, disease duration, body weight, height, body mass index, systolic blood pressure, diastolic blood pressure, smoking, hypertension, ischemic heart disease, dyslipidemia, congestive heart failure, peripheral artery disease, stroke, diabetes mellitus, and obesity.
TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglycerides; AI: atherogenic index; SE: standard error

months) and TG (118.14 ± 4.04 mg/dL at baseline, 157.05 ± 12.31 mg/dL; p = 0.029 at 18 - 24 months, and 159.90 ± 5.62 mg/dL; p < 0.001 at > 24 months), but no significant change in LDL-C. After treatment, AI increased from 0.77 ± 0.04 at baseline to 1.00 ± 0.04 (p < 0.001) at > 24months.

Conclusion: In patients with SpA, long-term treatment of TNF-α inhibitor was associated with increased TC, HDL-C, and TG levels and AI, whereas it presented no effect on LDL-C levels. Increased HDL-C may have beneficial effects, but evaluation of cardiovascular event rates during long-term treatment is needed to further characterize these findings and their possible clinical implications.

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Abstract Number: 0572

Early Recognition of Patients with Axial Spondyloarthritis by Using a Practical Referral System – Evaluation of the Recently Proposed 2-step Strategy

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Early recognition of axial spondyloarthritis (axSpA) in primary care (PC) is difficult due to the high prevalence of low back pain resulting in a major delay for a diagnosis of axSpA. Recently we proposed a 2-step referral strategy (1) which concentrates on patients ≤45 years with chronic back pain who are to be referred to a rheumatologist if fulfilling 2 of 3 features: buttock pain, improvement by movement, psoriasis (Step 1), or, in case of ≤1 feature, positive testing for HLA-B27 (Step 2). We prospectively evaluated this 2-step referral strategy in PC.

Methods: Consecutive patients ≤45 years who presented in PC to general practitioners or orthopedic surgeons working in PC with back pain lasting ≥2 months who had not been diagnosed before received questionnaires (Q1) relevant for the referral process. Thereafter, the PC physician asked the same questions in a separate questionnaire (Q2), including the decision on HLA-B27 testing. All patients were then referred to two experienced rheumatologists in a tertiary center who performed a complete workup including clinical, laboratory and imaging with radiographs and magnetic resonance imaging (MRI) examinations before their final diagnosis of axSpA or non-SpA (Q3).

Results: A total of 320 patients (mean age 35.9±10.3 years) was recruited. The proposed referral strategy (prS) was fulfilled by 127 patients in Q1 (39.7%), 160 in Q2 (50%), 102 by both, Q1 and Q2 (31.9%), and 83 with either Q1 or Q2 (25.9%). Overall, 47 patients were diagnosed with axSpA by the rheumatologist at Q3 (14.7%), 66% of which were male, mean age 34.7±10.1 years, 70.2% HLA-B27 positive, mean CRP 0.8±1.4mg/dl, mean ASDAS 3.2±0.8, mean BASDAI 5.1±2.0. Of these, 37 patients had fulfilled the prS in Q1 or Q2 (78.7%), and 31 in both Q1 and Q2 (66%), respectively. In the latter, the HLA-B27 prevalence was significantly higher (27/31, 87.1%) as compared to patients diagnosed with axSpA at Q3 but who did not fulfill the prS in Q1 and Q2 (5/16, 31.3%) ($p< 0.001$). The sensitivity and specificity of the prS was 78.7% and 69.2% in Q1, 78.7% and 62.2% in Q2, and in both, Q1 and Q2, 66% and 74%, respectively. AxSpA patients correctly identified by the prS in Q1 and Q2, were significantly more frequently positive for HLA-B27 and CRP and fulfilled more frequently the ASAS definition of inflammatory back pain in Q3.

Conclusion: A simple two-step referral strategy using a combination of clinical features for identifying axSpA patients in PC without laboratory and imaging examinations was confirmed in a large population from daily practice. This strategy performed well as selection for referral at the patient and PC physician level.

1. Braun A et al, ARD 2011

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Abstract Number: 0573

Identification of Factors Associated with Magnetic Resonance Images Changes Suggestive of Axial Spondyloarthritis in the Axial Skeleton of Individuals < 45 Years - Evaluation of Data from a Large Community Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Active (bone marrow edema, BME) and structural (fatty lesions, FL) lesions in the spinal and the sacroiliac joints (SIJ), as assessed by magnetic resonance imaging (MRI), have been described in patients with axSpA but may also occur in healthy individuals (1,2).

We assess factors associated with occurrence of BME and FL in spinal- and SIJ-MRIs in a population-based study.

Methods: Spinal- (sagittal T1/T2-) and SIJ- (semi-coronal STIR sequences) MRIs were evaluated by two trained blinded readers. MRIs were analyzed for BME (SIJ and spine) and FL (spine) 'positive' for axSpA. Degenerative lesions were excluded. BME was quantified using Berlin MRI scores. Clinical information included, sex, smoking (yes/

no), spinal pain (NRS≥4/10 in last 3 months), CRP, HLA-B27 and body mass index (BMI) categories (WHO definition of under- (cat.1), normal (cat.2), overweight (cat.3)). Associations between clinical factors and MRI lesions were analyzed for the presence/absence of lesions using univariate logistic regression and for number and size of lesions using negative binomial count regression.

Results: MRIs of 793 participants (49.4% male, 5.7% CRP-positive, 8.4% HLA-B27+, 62.7% ever smokers) were evaluated. BME lesions were found in 136 SIJ-MRIs (17.2%) and 218 (27.5%) spinal MRIs, and FL in 645 spinal MRIs (81.3%). The median hsCRP was 0.09 [0.05-0.20] mg/dl, 45 (6.4%) had an elevated hsCRP level (cut off < 5 mg/dl); 8.9% were HLA-B27+; 62.7% reported smoking, 45.0% were in the under- or normal weight BMI category. 36.2% in the overweight and 18.8% in the obese BMI category. More and larger SIJ-BME lesions were independently associated with HLA-B27+ (exp(β)=2.8, 1.5-4.9), spinal pain (exp(β)=1.7, 1.2-2.6), and higher BMI (cat. 1 vs 3, exp(β)=1.7, 1.0-3.0). Also, more and larger spinal BME were associated with older age (exp(β)=1.5, 1.2-2.0), while more and larger spinal FL were associated with higher BMI, (cat. 1 to cat. 3 (exp(β)=1.9, 1.5-2.2), older age (exp(β)=1.6, 1.5-1.8) and male sex (exp(β)=1.4, 1.2-1.6). Presence of spinal BME (OR 1.3, 1.0±1.7) and/or spinal FL (OR 1.7, 1.3-2.3) was associated with older age, while alone were associated with a higher BMI (cat. 1 to cat.3, OR 3.3, 1.8-6.1). In total, 22 subjects (16.2%) had large (>33% of surface involvement) and 114 had small (≤33% of surface involvement) SIJ-BME. Large SIJ-BME were found in 4.5% HLA-B27-positive vs. 2.6% HLA-B27-negative subjects (p=0.40). Overall, 35.3% quadrants with SIJ-BME was located in the upper sacral quadrant. Most SIJ lesions (83.4%) were small. For spinal BME, 42% was located in the lower (T7/8-T11/12) thoracic spine. Most spinal lesions (90.9%) were small.

Conclusion: In this large population-based study, higher numbers of large SIJ-BME lesions were significantly associated with HLA-B27, back pain and BMI. Spinal BME and FL were associated with older age, male sex and BMI but not HLA-B27. The association for HLA-B27 was only shown on the quadrant but not on the patient level.

1. Weber U et al, Arthritis Rheumatol 2018
2. De Winter J et al, Arthritis Rheumatol 2018

Disclosure: X. Baraliakos, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, BMS, 2, 5, 8, 9, Bristol-Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, 9, Chugai, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Lilly, 2, 8, 9, Merck, 2, 5, 8, MSD, 2, 5, 8, 9, Novartis, 2, 5, 8, 9, Novatis, 2, 5, 8, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9, UCB Pharma, 2, 5, 8, Werfen, 2, 5, 8; **A. Richter**, None; **D. Feldmann**, None; **A. Ott**, None; **R. Buelow**, None; **C. Schmidt**, None; **J. Braun**, Abbott, 2, 5, AbbVie, 2, 5, 6, 8, Amgen, 2, 5, 8, Baxter, 2, 5, 8, Biogen, 2, 8, 9, BMS, 2, 5, 8, Boehringer, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Celgene, 2, 3, 5, 8, Celltrion, 2, 5, 8, Centocor, 2, 5, 8, Chugai, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Hexal, 2, 5, 8, Janssen, 2, 5, 8, Johnson & Johnson, 2, 5, Medac, 2, 5, 8, MSD, 2, 5, MSD (Schering-Plough), 2, 5, 8, Mundipharma, 2, 5, 8, Mylan, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, Pfizer (Wyeth, Hospira), 2, 5, 8, Roche, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, UCB Pharma, 2, 5, 8.

Abstract Number: 0574

Localization and Morphology of Magnetic Resonance Imaging Features of Pathologic Changes in the Sacroiliac Joints Suggestive of Axial Spondyloarthritis – a Systematic Comparison of Patients and Controls with Chronic Back Pain

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Bone marrow edema (BME), fat metaplasia (FL) and erosions are relevant for magnetic resonance imaging (MRI) changes in the sacroiliac joints (SIJ) in axial spondyloarthritis (axSpA). However, MRI changes have recently also been reported in subjects with no axSpA (1,2). We mapped MRI lesions suspicious of axSpA in patients diagnosed with axSpA and compared them to patients with chronic back pain (cBP, non-SpA).

Methods: Consecutive patients with cBP< 45 years were included with at least one pathologic lesion (any type) in SIJ-MRIs performed during cBP symptoms. AxSpA patients diagnosed by 2 experienced rheumatologists in consensus also had to fulfil ASAS classification criteria. Two experienced readers, blinded for patient´s information) evaluated all MRIs independently. Lesions were only counted positive if readers were in agreement. Both coronal (assessing upper and lower sacral and iliac SIJ) and axial (assessing ventral, middle and retroauricular) MRI orientations were analyzed for localization of BME, FL, sclerosis and erosions. In addition, length and width were digitally measured for BME, FL and sclerosis, and signal intensity was measured in each individual patient (no units). Mann-Whitney-U-test was applied for patients classified as positive by both readers for respective lesions.

Results: 200 consecutive patients (100 axSpA, 100 non-SpA), mean age 36.1±11.3 and 40.3±11.0 years, respectively, were analyzed. BME was found in 85% vs. 80% patients, while 80% vs. 69% had FL, 54% vs. 40% had sclerosis and 64% vs. 12% had erosions, respectively. The largest surface area covered by BME in axSpA vs. non-SpA was found in lower and dorsal SIJ: 60±10.1mm3 in the iliac and 47.3±9.4mm3 in sacral part vs. upper and ventral SIJ: 18.7±3.4mm3 in sacral and 5.2±0.1 mm3 in the iliac part. AxSpA-patients showed larger surface area covered by FL in upper and anterior sacral SIJ (305.5±56.3 mm3), whereas non-SpA-patients showed larger FL areas in lower and posterior sacral SIJ (197.9±1.2 mm3). Upper and anterior iliac part larger sclerosis involvement in both SpA (139.3±11.6 mm3) and non-SpA (81.8±2.8 mm3). Mean signal intensity of all lesions and MRI planes differed between axSpA (102.385) and non-SpA (48.995) patients for BME (p< 0.001) but not for FL. AxSpA patients had significantly more SIJ quadrants with pathologic changes, except for BME and sclerosis in ventral and fat in retroauricular SIJ-part. Erosions in the mid (61 vs. 7) and the ventral (51 vs. 8) part of the SIJ could discriminate best between axSpA and non-SpA (both p< 0.001).

Conclusion: Although all lesion types may be found in both groups, the anatomic pattern of SIJ involvement can still distinguish axSpA from non-SpA. The most frequently involved sites were not necessarily also the best differentiating sites. The localization and morphological appearance of SIJ-MRI features suggestive of axSpA may serve as an additional feature in the definition of a 'positive' MRI both for diagnosis and classification.

References:

1. Weber U et al. Arthritis Rheumatol 2018

2. De Winter et al. Arthritis Rheumatol 2018

Disclosure: X. Baraliakos, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, BMS, 2, 5, 8, 9, Bristol-Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, 9, Chugai, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Lilly, 2, 8, 9, Merck, 2, 5, 8, MSD, 2, 5, 8, 9, Novartis, 2, 5, 8, 9, Novatis, 2, 5, 8, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9, UCB Pharma, 2, 5, 8, Werfen, 2, 5, 8; **j. tomaschoff**, None; **M. Fruth**, None; **J. Braun**, Abbott, 2, 5, AbbVie, 2, 5, 6, 8, Amgen, 2, 5, 8, Baxter, 2, 5, 8, Biogen, 2, 8, 9, BMS, 2, 5, 8, Boehringer, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Celgene, 2, 3, 5, 8, Celltrion, 2, 5, 8, Centocor, 2, 5, 8, Chugai, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Hexal, 2, 5, 8, Janssen, 2, 5, 8, Johnson & Johnson, 2, 5, Medac, 2, 5, 8, MSD, 2, 5, MSD (Schering-

Plough), 2, 5, 8, Mundipharma, 2, 5, 8, Mylan, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, Pfizer (Wyeth, Hospira), 2, 5, 8, Roche, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, UCB Pharma, 2, 5, 8.

Abstract Number: 0575

Facet Joint Ankylosis on Whole Spine Low-Dose CT in Radiographic Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In radiographic axial spondyloarthritis (r-axSpA), whole spine low-dose CT (ldCT) is superior to conventional radiography (CR) in detecting syndesmophytes, mainly due to inclusion of the thoracic spine. Facet joint ankylosis has been studied in r-axSpA in parts of the spine with CR and CT, but not in the whole spine. We aimed to assess readability and interreader reliability of facet joint ankylosis as detected by whole spine ldCT and to describe the prevalence of facet joint ankylosis in each spinal segment in patients with r-axSpA.

Methods: In an observational cohort, r-axSpA patients with syndesmophytes on at least one but no more than 75% of spinal levels of the cervical and lumbar segments on CR and at least one inflammatory lesion on spinal MRI, underwent ldCT (about 4 mSv) of the whole spine. Images were assessed independently by two trained readers and left

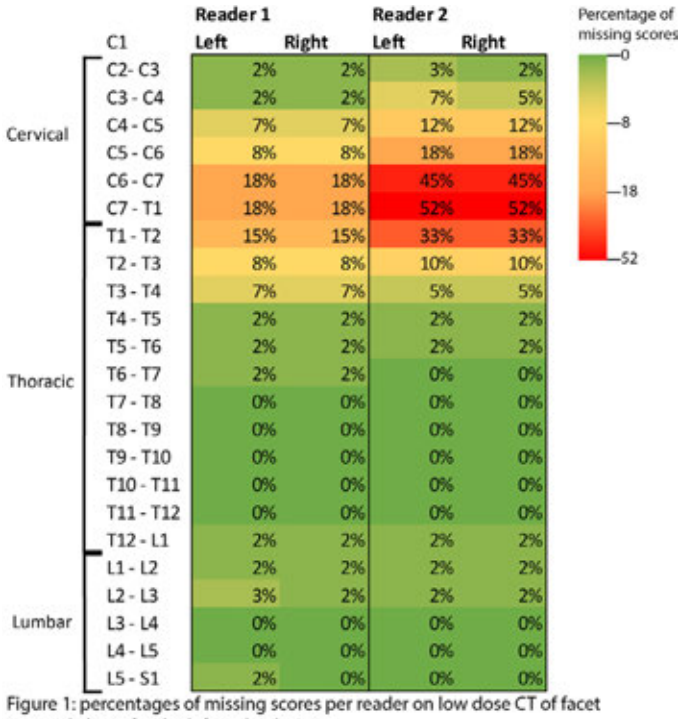

Figure 1: percentages of missing scores per reader on low dose CT of facet joint ankylosis, for the left and right joint.

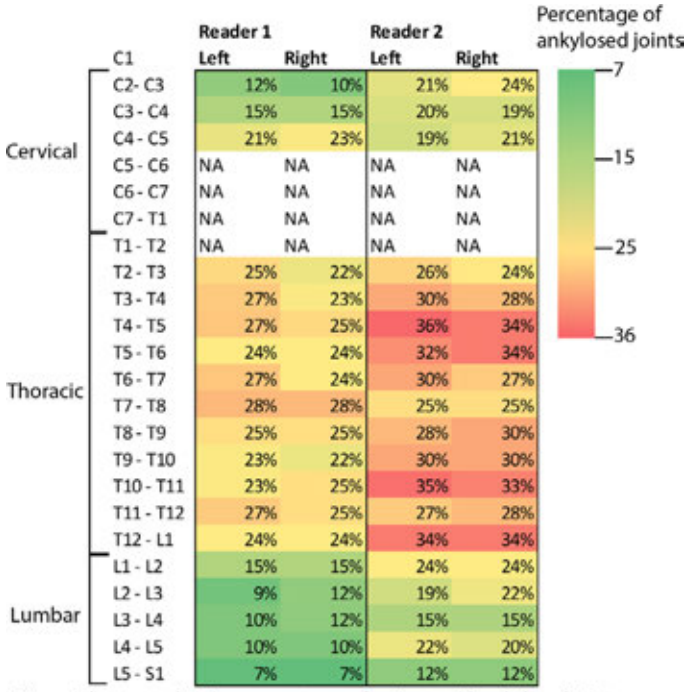

Figure 2: heatmap showing percentages of patients with ankylosed joint per joint level. Levels with >15% missing joint scores for one or both readers are not applicable (NA).

Table: facet joint ankylosis scores per reader and interreader reliability

	Reader 1 mean (SD) *range*	Reader 2 mean (SD) *range*	ICC (95% CI)
Whole spine excluding C5-T2 *max score 38*	7.3 (10) *0 - 34*	9.4 (10.9) *0 - 37*	0.93 (0.87-0.96)
Cervical segment excluding C5-T1 *max score 6*	0.9 (1.8) *0 - 6*	1.1 (2) *0 - 6*	0.84 (0.73-0.90)
Thoracic segment excluding T1-T2 *max score 22*	5.4 (7.4) *0 - 22*	6.5 (7.6) *0 - 22*	0.91 (0.85-0.95)
Lumbar segment *max score 10*	1.0 (2.5) *0 - 10*	1.8 (3.1) *0 - 10*	0.81 (0.67-0.89)

and right C2-C3 to L5-S1 facet joints were scored as ankylosis present (1) or absent (0). The percentage of missing joint scores due to inability to assess, were calculated per reader and joint level. Joint levels with >15% missing joint scores for ≥1 reader were deemed unreliable to score and were excluded from the study. Interreader reliability was assessed by calculating intraclass correlation coefficients (ICCs), two-way average, absolute agreement. Ankylosis scores were summed per patient per segment and for the whole spine and presented as mean scores per reader. The percentage of patients with an ankylosed joint were presented per joint level in a heatmap.

Results: A total of 60 r-axSpA patients were analyzed (mean age 47.7 years, 85% male, 80% HLA-B27+). Reader 1 had between 0% and 18% missing scores per joint, reader 2 had between 0% and 52% missing scores per joint (figure 1). There were >15% missing joint scores for ≥1 reader on levels C5-T2, which were excluded from analyses. Interreader reliability was good to excellent with ICCs ranging from 0.81 to 0.93 (table). Ankylosis occurred at every joint level, but was most prevalent in the thoracic spine (figure 2). Means (SD) of sum-scores for the whole spine and cervical, thoracic and lumbar segments for both readers are presented in the Table.

Conclusion: Facet joints around the cervicothoracic junction were difficult to score in a relatively high percentage of patients and are therefore excluded from scoring. The interreader reliability of the remaining levels was good to excellent. In patients with r-axSpA and at least one syndesmophyte, facet joint ankylosis was detected in all spinal levels, but most ankylosis occurred in the thoracic spine. These results show that ldCT can be used to study facet joint ankylosis in r-axSpA in all spinal segments except the cervicothoracic junction.

Disclosure: R. Stal, None; **F. van Gaalen**, None; **A. Sepriano**, None; **J. Braun**, Abbott, 2, 5, AbbVie, 2, 5, 6, 8, Amgen, 2, 5, 8, Baxter, 2, 5, 8, Biogen, 2, 8, 9, BMS, 2, 5, 8, Boehringer, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Celgene, 2, 3, 5, 8, Celltrion, 2, 5, 8, Centocor, 2, 5, 8, Chugai, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Hexal, 2, 5, 8, Janssen, 2, 5, 8, Johnson & Johnson, 2, 5, Medac, 2, 5, 8, MSD, 2, 5, MSD (Schering-Plough), 2, 5, 8, Mundipharma, 2, 5, 8, Mylan, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, Pfizer (Wyeth, Hospira), 2, 5, 8, Roche, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, UCB Pharma, 2, 5, 8; **M. Reijnierse**, None; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **X. Baraliakos**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, BMS, 2, 5, 8, 9, Bristol-Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, 9, Chugai, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Lilly, 2, 8, 9, Merck, 2, 5, 8, MSD, 2, 5, 8, 9, Novartis, 2, 5, 8, 9, Novatis, 2, 5, 8, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9, UCB Pharma, 2, 5, 8, Werfen, 2, 5, 8.

Abstract Number: 0576

Spinal Bone Formation as Assessed by Low-Dose CT Scan in Patients with Radiographic Axial Spondyloarthritis – Comparison of the Progression Observed in Vertebrae and Facet Joints

Rosalinde Stal,[1] Floris van Gaalen,[1] Alexandre Sepriano,[1] Jürgen Braun,[2] Monique Reijnierse,[1] Désirée van der Heijde,[1] and Xenofon Baraliakos[3], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Rheumazentrum Ruhrgebiet/Ruhr University, Herne, Germany, [3]Rheumazentrum Ruhrgebiet-Ruhr-University Bochum, Herne, Germany, Herne, Germany

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: By using low dose computed tomography (ldCT) in patients with radiographic axial spondyloarthritis (r-axSpA) we have recently shown that there is substantial progression of new bone formation in the facet joints within two years. We now aimed to assess the added value of scoring progression of whole spine facet joint ankylosis in addition to whole spine syndesmophytes in the quantification of spinal bone formation by ldCT.

Methods: In an observational cohort, patients with r-axSpA (≥1 inflammatory lesion on spinal MRI and 1-18 syndesmophytes in cervical and lumbar spine on conventional radiography) underwent whole spine ldCT (circa 4 mSv) at baseline and after 2 years. Two trained readers independently assessed paired ldCTs, blinded to chronology. Left and

Table: progression of whole spine facet joint ankylosis and syndesmophytes

Progression	FJA	CTSS	FJA and CTSS	FJA not CTSS	CTSS not FJA	Not FJA not CTSS
Change >0.5	21(48%)	39(89%)	17(39%)	4(9%)	22(50%)	1(2%)
Change >SDC	12(27%)	13(29%)	4(9%)	8(18%)	9(20%)	23(52%)

For facet joint ankylosis (FJA), SDC=2; for Computed Tomography Syndesmophyte Score (CTSS), SDC=14.4

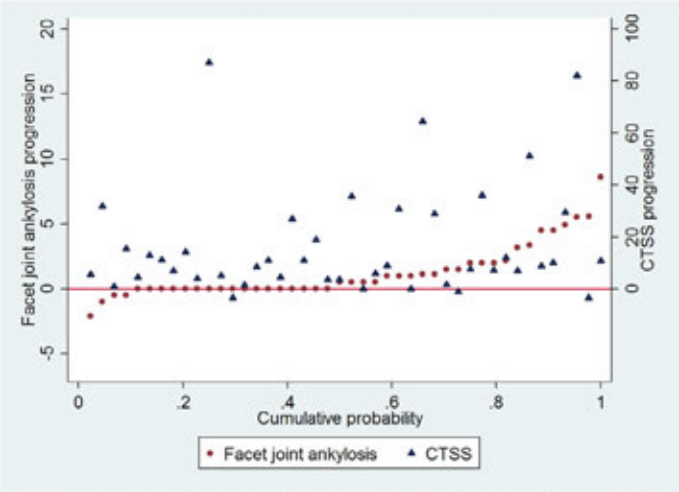

Figure: cumulative probability plot showing 2-year facet joint ankylosis progression and syndesmophyte progression scored with the Computed Tomography Syndesmophyte Score (CTSS). The plot is ordered by the facet joint ankylosis progression scores.

right facet joints from C2-S1, with the exception of C5-T2 due to low visibility, were scored as ankylosis present (1) or absent (0). Syndesmophytes were scored on a scale 0-552 according the Computed Tomography Syndesmophyte Score (CTSS)[1]. Average scores of the readers were used. Patients were included if at baseline they had < 80% ankylosed facet joints and < 80% bridged syndesmophytes on ldCT and had scores from both readers for both time-points. Change scores are calculated as the total change in the whole spine per patient. The proportion of patients with a change score >0.5 and >SDC are presented and in addition net progression, defined as number of patients with change >0.5 minus number of patients with change < -0.5 divided by the total number of patients. Percentage agreement between progression in facet ankylosis and syndesmophyte formation is presented and a cumulative probability plot is shown.

Results: A total of 44 patients was included in the analysis (mean age 49.4, 84% male, 79% HLA-B27+). At the group level, net progression of facet joint ankylosis was 43% (19/44) and net progression of syndesmophytes was 82% (36/44). The proportion of patients with progression is given in the Table. The percentage of patients with progression of facet joint ankylosis >0.5 was 48% and with syndesmophyte progression >0.5 was 89%. Using a more conservative cut-off for progression (>SDC), the percentage of patients with progression of facet joint ankylosis was 27% and syndesmophyte progression was seen in 29%. Bone formation in the facet joints only occurred in 9% and 18% of the patients, and syndesmophytes progression only in 50% and 20% of the patients for the cut-offs of 0.5 and SDC, respectively. The figure shows that there is a tendency that patients with more facet joint ankylosis progression also had more syndesmophyte progression. However, in a number of patients these processes occurred independently.

Conclusion: These data show that scoring facet joint ankylosis in addition to syndesmophyte formation is useful to get full insight in the progression of spinal bone formation in patients with r-axSpA.

Reference:

[1] de Bruin, F., et al. (2018). “Development of the CT Syndesmophyte Score (CTSS) in patients with ankylosing spondylitis: data from the SIAS cohort.” Annals of the rheumatic diseases **77**(3): 371-377

Disclosure: R. Stal, None; **F. van Gaalen**, None; **A. Sepriano**, None; **J. Braun**, Abbott, 2, 5, AbbVie, 2, 5, 6, 8, Amgen, 2, 5, 8, Baxter, 2, 5, 8, Biogen, 2, 8, 9, BMS, 2, 5, 8, Boehringer, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Celgene, 2, 3, 5, 8, Celltrion, 2, 5, 8, Centocor, 2, 5, 8, Chugai, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Hexal, 2, 5, 8, Janssen, 2, 5, 8, Johnson & Johnson, 2, 5, Medac, 2, 5, 8, MSD, 2, 5, MSD (Schering-Plough), 2, 5, 8, Mundipharma, 2, 5, 8, Mylan, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, Pfizer (Wyeth, Hospira), 2, 5, 8, Roche, 2, 5, 8, Sanofi-Aventis, 2, 5, 8,

UCB Pharma, 2, 5, 8; **M. Reijnierse**, None; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **X. Baraliakos**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, BMS, 2, 5, 8, 9, Bristol-Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, 9, Chugai, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Lilly, 2, 8, 9, Merck, 2, 5, 8, MSD, 2, 5, 8, 9, Novartis, 2, 5, 8, 9, Novatis, 2, 5, 8, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9, UCB Pharma, 2, 5, 8, Werfen, 2, 5, 8.

Abstract Number: 0577

Gender Contrasts in Patient Reported Outcomes Don't Alter the Disease Activity Score in Axial Spondyloarthritis Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Disease activity in axial spondyloarthritis (axSpA) is often quantified by the Ankylosing Spondylitis Disease Activity Score (ASDAS), a composite index which combines 4 patient reported outcome (PRO) measures and C-reactive protein (CRP) as an acute phase reactant. ASDAS commonly acts as a target in treat-to-target approaches in axSpA patients. This study aims to identify the impact of gender on ASDAS in newly diagnosed axSpA patients and to determine whether possible differences are PRO- or CRP-driven.

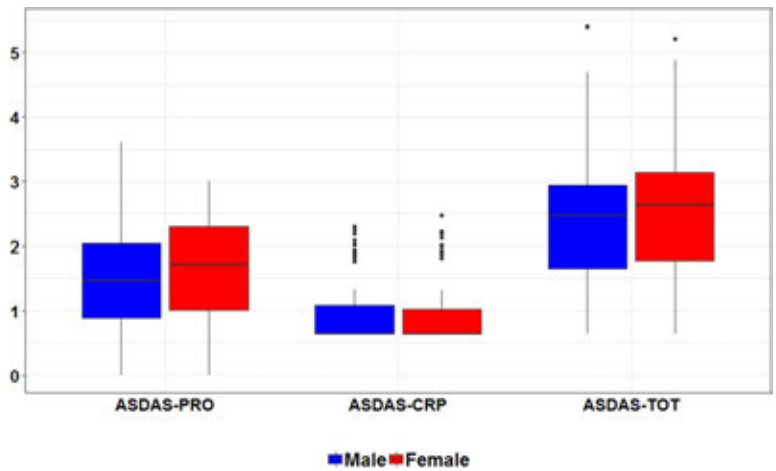

Figure 1. Total ASDAS score (ASDAS-TOT), subdivided in a PRO-component (ASDAS-PRO) and a CRP-component (ASDAS-CRP) in male and female axSpA patients.

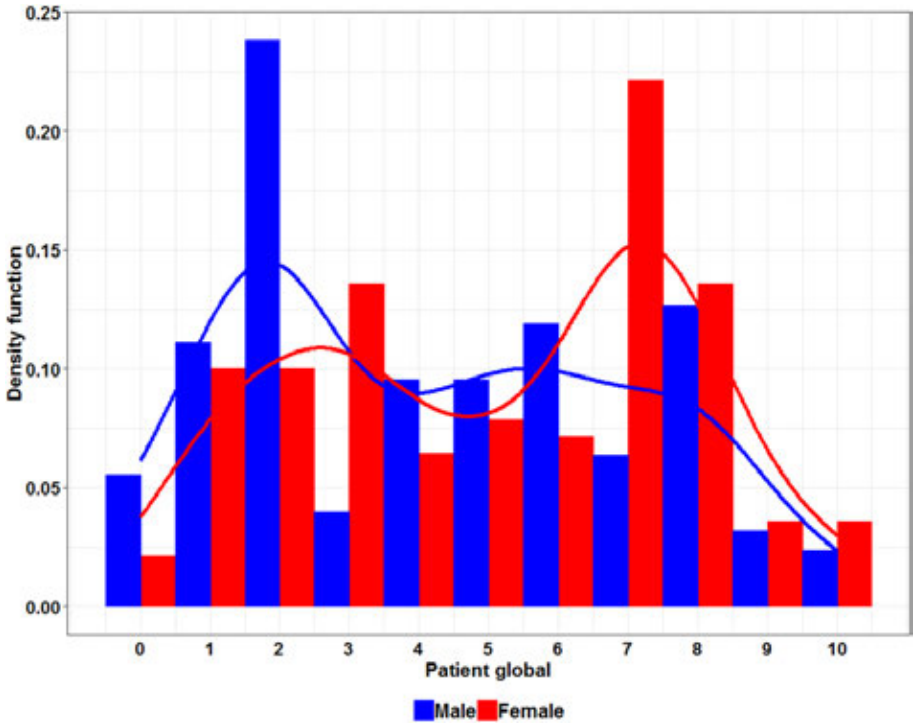

Figure 2. Patient global score in male and female axSpA patients.

Methods: Patients originate from an observational registry of newly diagnosed axSpA patients (expert opinion). Included patients fulfill the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA and are anti-TNF naïve prior to inclusion. An extensive patient description was performed at baseline, including PRO and laboratory investigations with CRP (mg/L). ASDAS was calculated for each patient and subdivided in a PRO-component (ASDAS-PRO) and a CRP-component (ASDAS-CRP).

Results: By January 2019, 291 axSpA patients were included (138 male, 153 female). At baseline, ASDAS could be calculated in 262 patients. ASDAS-PRO was significantly higher in women compared to men (1,66 vs. 1,48, p = 0,04), while ASDAS-CRP did not differ significantly (0,90 for both genders, p = 0,96). No significant difference was found between the total ASDAS of women and men (2,54 vs. 2,38, p = 0,09) (Figure 1). When categorizing the score into 4 disease activity states, 60,8% (76/125) of men show high or very high disease activity (ASDAS > 2.1) at baseline compared to 67,2% (92/137) of women (p = 0,35).

Concerning the 5 ASDAS components, the discrimination between male and female axSpA patients was most pronounced for *patient global* scores (Figure 2). Men reported a baseline patient global score of 4,3 (95% CI 3,8 – 4,8), compared to a score of 5,1 (95% CI 4,7 – 5,6) in women (p = 0,01).

Conclusion: Female axSpA patients report a significantly higher *patient global* score compared to men. This contributes to a significantly higher ASDAS-PRO in women. However, neither the ASDAS itself nor the ASDAS disease activity categories are significantly affected by gender contrasts in PRO.

Disclosure: A. De Craemer, None; **T. Renson**, None; **L. Deroo**, None; **M. de Hooge**, None; **P. Carron**, None; **F. Van den Bosch**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, Bristol-Myers Squibb, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sanofi and UCB, 5, 8, ABBVIE, CELGENE, ELI LILLY, GALAPAGOS, MERCK, NOVARTIS, PFIZER, VCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **D. Elewaut**, None.

Abstract Number: 0578

Restricted Work Participation Relates to High Disease Activity in Spondyloarthritis Patients

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Spondyloarthritis (SpA) generally affects patients at a working age. Despite therapeutic improvements, SpA remains responsible for a significant burden for patients and society in terms of sick leave and work disability. This study aims to assess the determinants of work participation in a Belgian SpA cohort.

Methods: Between May 1st 2018 and April 1st 2019, a cross-sectional survey was conducted amongst patients included in a Belgian SpA cohort ((Be-)Giant), all fulfilling ASAS classification criteria for axial or peripheral SpA. Information on work participation was collected using the Work Productivity and Activity Impairment (WPAI) ques-

Table 1. Demographic and clinical characteristics

	All patients (n = 262)	Axial SpA (n = 192)	Peripheral SpA (n =70)
Male, n (%)	148 (56,4)	107 (55,7)	41 (58,8)
Age, years (mean, SD)	41 (11,0)	40 (11,4)	43 (11,8)
Current smoker, n (%)	40 (15,3)	26 (13,5)	14 (20,0)
HLA B27 positive, n (%)	168 (64,1)	139 (72,4)	29 (41,4)
Modified New York +, n (%)	-	67 (3,9)	-
Symptom duration, years (median, IQR)	5,7 (4,2 – 11,5)	10,1 (6,4 – 19,8)	4,8 (3,6 – 5,7)
TJC, /72 (median, IQR)	0 (0 – 0)	0 (0 – 0)	0 (0 – 1)
SJC, /72 (median, IQR)	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)
BASDAI, /10 (median, IQR)	2,9 (1,4 – 4,5)	3,0 (1,6 – 4,5)	2,8 (1,0 – 4,2)
BASFI, /10 (median, IQR)	2,3 (0,4 – 3,6)	2,4 (0,5 – 3,9)	1,8 (0,3 – 3,0)
ASDAS-CRP (median, IQR)	1,9 (1,1 – 2,6)	2,0 (1,2 – 2,6)	1,6 (0,9 – 2,3)
NSAID index (median, IQR)	26 (0 – 50)	28 (0 – 50)	0 (0 – 4)
csDMARD use, n (%)	48 (18,3)	18 (9,4)	30 (42,9)
bDMARD use, n (%)	121 (46,2)	88 (45,8)	33 (47,1)
Higher education, n (%)	162 (61,8)	124 (64,6)	38 (54,3)
Manual labour, n (%)	51 (19,5)	33 (17,2)	18 (25,7)

Table 2. Association between patient characteristics and work-related outcomes. (*p<0.05)

Predictor	Model 1: Being employed (yes/no) OR (95% CI)	Model 2: Absenteeism (yes/no) OR (95% CI)	Model 3: Presenteeism (yes/no) OR (95% CI)	Model 4: Work impairment (yes/no) OR (95% CI)
Male gender	0.9 (0.48 – 1.72)	0.9 (0.33 – 2.41)	1.1 (0.64 – 2.04)	1.1 (0.63 – 2.00)
Age (y)	1.0 (0.96 – 1.02)	1.0 (0.96 – 1.06)	1.0 (0.97 – 1.02)	1.0 (0.97 – 1.02)
Symptom duration (y)	1.0 (0.95 – 1.00)	**1.1 (1.02 – 1.11)***	1.0 (0.98 – 1.05)	1.0 (0.98 – 1.04)
Higher education vs. lower education	**5.5 (2.74 – 10.82)***	**0.3 (0.12 – 0.90)***	0.7 (0.39 – 1.42)	0.7 (0.38 – 1.33)
Manual labour	**0.2 (0.08 – 0.39)***	**3.1 (1.04 – 9.04)***	**2.3 (1.10 – 4.90)***	**2.4 (1.14 – 4.94)***
ASDAS-CRP	**0.4 (0.29 – 0.62)***	**2.5 (1.44 – 4.53)***	**3.1 (1.89 – 5.22)***	**3.3 (1.99 – 5.48)***
BASFI (/10)	**0.6 (0.52 – 0.72)***	**1.7 (1.35 – 2.24)***	**2.1 (1.60 – 2.79)***	**2.1 (1.61 – 2.79)***
Axial vs. peripheral disease	0.8 (0.37 – 1.63)	3.0 (0.67 – 13.69)	1.6 (0.82 – 2.97)	1.6 (0.83 – 2.94)

tionnaire. Physicians' assessment included standardized clinical and laboratory evaluations. Outcomes of interest were employment status (being employed yes/no), absenteeism (percentage of time absence from the workplace), presenteeism (percentage of productivity loss while at work) and percentage of overall work impairment. Continuous outcomes were categorized because of skewed (zero inflated) distributions. The associations between the four outcomes of interest and patient characteristics were modelled using univariate and multivariate logistic regression. The sample was restricted to SpA patients of working age (≤65 years old).

Results: Data were collected on 262 patients: 214 (81.7%) were employed, 26 (9.9%) work disabled, 8 (3.1%) unemployed, 8 (3.1%) student, 5 (1.9%) early retired and 1 (0.4%) housekeeper. Table 1 summarizes demographic and clinical characteristics. Table 2 shows univariate associations between patient characteristics and the outcomes of interest. Gender, age, symptom duration and SpA subtype are not significantly associated with any of the four outcomes. Higher education increases the odds of being employed and reduces the odds of absenteeism. Manual labour, high ASDAS-CRP and high BASFI show a negative association with employment and significantly increase the odds of absenteeism, presenteeism and overall work impairment. After multivariate adjustment, only ASDAS-CRP and BASFI showed a significant association with employment status (OR 0.39 and 0.69), absenteeism (OR 2.54 and 1.71), presenteeism (OR 2.58 and 1.81) and work impairment (OR 2.67 and 1.82) (all $p < 0,05$).

Conclusion: High disease activity and functional impairment are significantly associated with work participation and overall work impairment in a Belgian SpA cohort. Of interest, neither gender, age, symptom duration, type of work nor SpA subtype significantly affect any of the work-related outcomes. Given the important health economic impact of employment rate in our society, this underscores the need for tight disease control in patients with SpA.

Disclosure: A. De Craemer, None; **T. Renson**, None; **L. Deroo**, None; **P. Carron**, None; **A. Boonen**, AbbVie, 2, Amgen, 2, Celgene, 2, Eli Lilly and Company, 5, Janssen, 8, Lilly, 5, 8, Novartis, 5, Sandoz, 5, 8, UCB, 5, 8; **X. Janssens**, None; **D. Elewaut**, None; **F. Van den Bosch**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, Bristol-Myers Squibb, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sanofi and UCB, 5, 8, ABBVIE, CELGENE, ELI LILLY, GALAPAGOS, MERCK, NOVARTIS, PFIZER, VCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8, UCB, 5, 8.

Abstract Number: 0579

Is There an Impact of Uveitis, Psoriasis and Inflammatory Bowel Disease on Musculoskeletal Disease Activity and Function in Axial Spondyloarthritis?

Imke Redeker,[1] Johanna Callhoff,[2] Falk Hoffmann,[3] Hildrun Haibel,[4] Joachim Sieper,[4] Angela Zink,[5] and Denis Poddubnyy[6], [1]Charité – Universitätsmedizin Berlin and German Rheumatism Research Centre, Berlin, Germany, [2]German Rheumatism Research Centre, Berlin, Germany, [3]Carl von Ossietzky University, Oldenburg, Germany, [4]Charité Universitätsmedizin Berlin, Germany, Berlin, Germany, [5]German Rheumatism Research Centre and Charité University medicine, Berlin, Germany, [6]Charité - Universitätsmedizin Berlin and German Rheumatism Research Centre, Berlin, Germany, Berlin, Germany

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Uveitis, psoriasis and inflammatory bowel disease (IBD) are common in axial spondyloarthritis (axSpA) but data on their impact on activity of musculoskeletal manifestations and functional status, in general, are

contradictory. The aim of this study was to assess the impact of uveitis, psoriasis, and IBD on disease activity and functional status in a population-based cohort of patients with axSpA.

Methods: A stratified random sample of patients with axSpA (ICD-10 M45) was drawn from health insurance data in Germany. Patients in the sample received a survey on demographic, socioeconomic, and disease-related parameters including history of uveitis, psoriasis, and IBD.

Survey data were linked to health insurance data gathering additional information on recent/current occurrence (within one year) of uveitis, psoriasis, and IBD as well as drug prescriptions and non-pharmacological treatment.

Differences between patients with and without uveitis, psoriasis, and IBD were assessed. Separate multivariable linear regression models were calculated to determine the effect of uveitis, psoriasis, and IBD on disease activity and functional impairment after adjustment for other relevant parameters including treatment.

Results: A total of 1,729 patients with axSpA were included in the analyses. The patients' main characteristics are shown in **Table 1**: The mean age was 55.9 years and 46.1% were female. The prevalence for recent (ever) uveitis, psoriasis, and IBD is illustrated in **Figure**: 9% (27%) of the patients had recently (ever) uveitis, 10% (15%) had recently (ever) psoriasis, and 6% (9%) had recently (ever) IBD. In 1.6% (6.9%) of the patients two of these conditions were recently (ever) present, and in 0% (0.5%) of the patients, all three conditions were recently (ever) present.

Results from the multivariable linear regression analyses are presented in **Table 2** and revealed that history of psoriasis was significantly associated with both higher level of disease activity and higher level of functional impairment. History of IBD was also associated with higher disease activity, whereas recent psoriasis or IBD showed no strong association with disease activity and functional status.

In contrast, history of uveitis showed no strong association with disease activity and functional status while recent uveitis was significantly associated with lower disease activity according to the BASDAI even after adjustment for treatment.

Table 1 Main demographic, disease-related, and socioeconomic characteristics of patients with axial spondyloarthritis (N=1,729)

Parameter	
Sex, female (%)	46.1
Age, years (mean±SEM)	55.9±0.1
Symptom duration, years (mean±SEM)	25.2±0.3
BASDAI, 0-10 (mean±SEM)	4.5±0.0
BASFI, 0-10 (mean±SEM)	4.1±0.1
Body Mass Index, kg/m^2 (mean±SEM)	27.0±0.1
Smoking (%)	18.9
Rheumatologic care (%)	45.7
Lack of exercise (%)	24.1
Suffering from stress (%)	39.4
NSAIDs (%)	59.1
Non-opioid analgesics (%)	22.3
Opioids (%)	15.8
bDMARDs (%)	17.2
Systemic steroids (%)	19.6
Physical therapy (%)	52.3

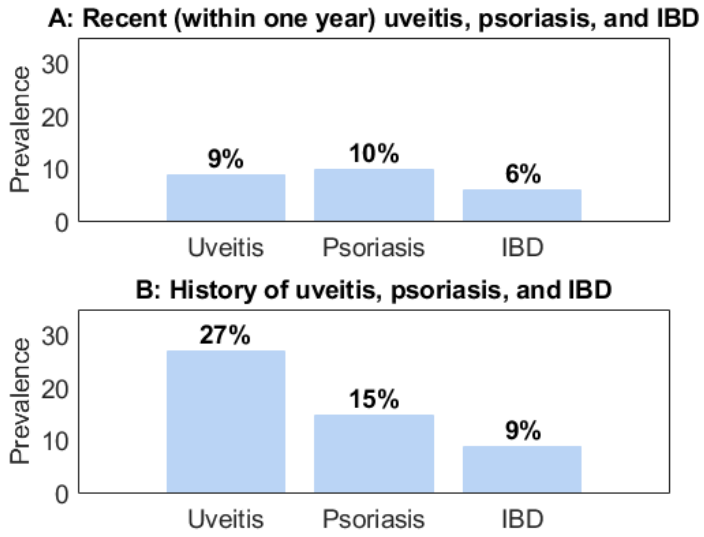
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; bDMARDs, biological disease-modifying anti-rheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs; SEM, standard error of the mean.

Table 2 Results from multivariable linear regression models showing the association of psoriasis, inflammatory bowel disease and uveitis with disease activity (BASDAI) and functional impairment (BASFI) in patients with axial spondyloarthritis (N=1,729)

Recent (within one year) psoriasis, inflammatory bowel disease, and uveitis (based on health insurance data)				
		Reference	**BASDAI* β (95% CI)**	**BASFI** β (95% CI)**
Model 1a	Psoriasis, recently present	not present	0.07 (-0.27, 0.40)	0.30 (-0.09, 0.70)
Model 1b	Inflammatory bowel disease, recently present	not present	0.30 (-0.10, 0.71)	0.33 (-0.14, 0.80)
Model 1c	Uveitis, recently present	not present	**-0.44 (-0.77, -0.10)**	-0.38 (-0.77, 0.02)
History of psoriasis, inflammatory bowel disease, and uveitis (based on survey data)				
		Reference	**BASDAI* β (95% CI)**	**BASFI** β (95% CI)**
Model 2a	Psoriasis, ever present	not present	**0.31 (0.05, 0.58)**	**0.37 (0.05, 0.68)**
Model 2b	Inflammatory bowel disease, ever present	not present	**0.37 (0.01, 0.73)**	0.35 (-0.07, 0.77)
Model 2c	Uveitis, ever present	not present	-0.10 (-0.31, 0.11)	-0.01 (-0.26, 0.24)

*Model adjusted for age, sex, body mass index, rheumatologic care, smoking, suffering from stress, NSAIDs, bDMARDs, non-opioid analgesics, opioids, systemic steroids, physical therapy; **Model adjusted for age, sex, body mass index, rheumatologic care, lack of exercise, smoking, suffering from stress, non-opioid analgesics, opioids, systemic steroids, physical therapy.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; bDMARDs, biological disease-modifying anti-rheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs.

Figure Prevalence of uveitis, psoriasis, and inflammatory bowel disease in patients with axial spondyloarthritis (N=1,729)



Conclusion: Disease activity and functional impairment are higher in axSpA patients with a history of psoriasis or IBD, whereas history of uveitis does not have a major impact on activity of musculoskeletal manifestations and functional status in axSpA. However, recent uveitis showed a somewhat unexpected association with lower disease activity. The latter might be related to a higher likelihood of being treated with TNF inhibitors in the presence of uveitis.

Disclosure: I. Redeker, None; **J. Callhoff**, None; **F. Hoffmann**, None; **H. Haibel**, AbbVie, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8; **J. Sieper**, AbbVie, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Novartis, 5, 8; **A. Zink**, Astra Zeneca, BMS, Lilly, Pfizer, Roche und UCB, 5, 8; **D. Poddubnyy**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 2, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8.

Abstract Number: 0580

Association of Comorbidities with Disease Activity and Functional Impairment in Axial Spondyloarthritis: Results from a Nationwide Population-Based Study

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Table 1 Main demographic, disease-related, and socioeconomic characteristics of patients with axial spondyloarthritis (N=1,776)

Parameter	
Sex, female (%)	46.4
Age, years (mean±SEM)	56.1±0.1
Symptom duration, years (mean±SEM)	25.3±0.3
Uveitis, present (%)	8.6
Number of comorbidities, 0-31 (mean±SEM)	2.6±0.0
In rheumatologic care (%)	45.6
BASDAI, 0-10 (mean±SEM)	4.5±0.0
BASFI, 0-10 (mean±SEM)	4.1±0.1
Body Mass Index, kg/m^2 (mean±SEM)	26.9±0.1
Lack of exercise (%)	24.3
Smoking (%)	18.6
Suffering from stress (%)	39.3
NSAIDs (%)	59.0
Non-opioid analgesics (%)	22.5
Opioids (%)	16.0
bDMARDs (%)	16.9
Systemic steroids (%)	19.7
Number of pharmaceuticals* (mean±SEM)	7.7±0.1
Physical therapy (%)	52.1

* except axSpA-related medication.

AxSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; bDMARDs, biological disease-modifying anti-rheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs; SEM, standard error of the mean.

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Data on the prevalence of comorbidities and their association with disease activity and functional impairment in axial spondyloarthritis (axSpA) are scarce. The aim of this study was to investigate the prevalence of comorbidities and to analyse their association with disease activity and functional impairment in a large population-based cohort of patients with axSpA.

Methods: A stratified random sample of patients with axSpA (ICD-10 M45) was drawn from health insurance data in Germany. Patients in the sample received a survey on demographic, socioeconomic, and disease-related parameters including disease activity (assessed using BASDAI) and functional impairment (assessed using BASFI).

Survey data were linked to health insurance data gathering additional information on comorbidities and drug prescriptions. Comorbidities were based on Elixhauser coding algorithms (excluding rheumatic diseases and augmented upon osteoporosis).

The prevalence of comorbidities in axSpA patients was compared to a sex- and age-matched control group of patients without axSpA drawn from health insurance data.

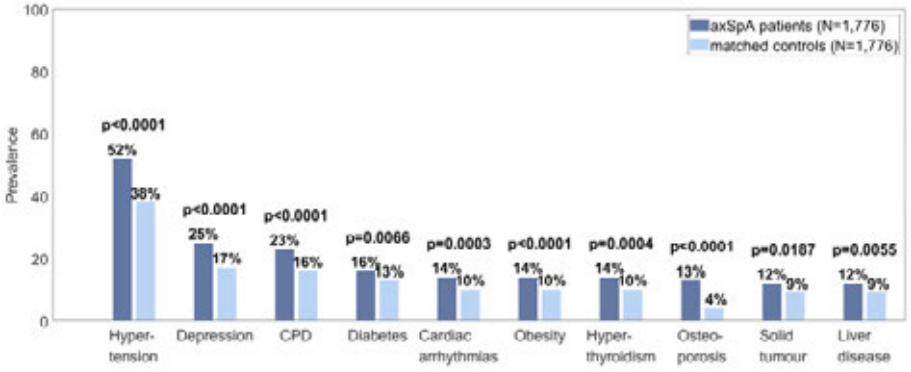
Table 2 Impact of comorbidity on disease activity (BASDAI) and functional impairment (BASFI) in patients with axial spondyloarthritis (N=1,776): Results from multivariable linear regression models

	Reference	BASDAI β (95% CI)	BASFI β (95% CI)
Number of comorbidities	per unit	0.12 (0.07, 0.17)	0.10 (0.04, 0.17)
Number of pharmaceuticals*	per unit		0.03 (0.01, 0.06)
Age	per 10 years	0.11 (0.04, 0.19)	0.51 (0.42, 0.60)
Sex, female	male	0.55 (0.37, 0.73)	-0.02 (-0.24, 0.21)
Uveitis, present	not present	-0.42 (-0.74, -0.09)	
In rheumatologic care	no	0.29 (0.09, 0.50)	0.60 (0.37, 0.82)
Body mass index	per unit	0.02 (0.00, 0.04)	0.07 (0.05, 0.10)
Lack of exercise	no		0.62 (0.37, 0.88)
Smoking (current)	no	0.28 (0.05, 0.52)	0.54 (0.28, 0.80)
Suffering from stress	no	0.76 (0.57, 0.95)	0.23 (0.01, 0.46)
NSAIDs	no	0.43 (0.24, 0.62)	
bDMARDs	no	-0.37 (-0.63, -0.11)	
Non-opioid analgesics	no	0.34 (0.12, 0.56)	0.43 (0.15, 0.71)
Opioids	no	1.02 (0.76, 1.27)	1.64 (1.32, 1.97)
Steroids	no	0.26 (0.02, 0.49)	
Physical therapy	no	0.31 (0.13, 0.50)	0.37 (0.15, 0.59)

* except axSpA-related medication.

AxSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; bDMARDs, biological disease-modifying anti-rheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs.

Figure Comorbidities defined by Elixhauser coding algorithms* in patients with axial spondyloarthritis (N=1,776) and matched controls (N=1,776)



* excluding rheumatic diseases and augmented upon osteoporosis. AxSpA, axial spondyloarthritis; CPD, chronic pulmonary disease.

Separate multivariable linear regression models were calculated to determine the association of comorbidities with disease activity and functional impairment.

Results: A total of 1,776 patients with axSpA were included in the analyses. The patients' main characteristics are shown in **Table 1**: The mean age was 56.1 years and 46.4% were female. The most prevalent comorbidities are illustrated in **Figure**: 52% of the patients presented with hypertension, 25% with depression, and 23% with chronic pulmonary disease. The prevalence of the majority of comorbidities was higher in axSpA as compared to controls. Results from the multivariable linear regression models are presented in **Table 2** showing that the number of comorbidities was significantly associated with both disease activity and functional impairment: each comorbidity was associated with BASDAI increase by 0.11 and BASFI increase by 0.10 points independently of other factors including treatment.

Conclusion: Comorbidities are common in axSpA patients and are independently associated with higher disease activity and higher level of functional impairment. Higher disease activity and a higher level of functional disability might be indicators of a severe disease resulting in the development of comorbid conditions.

Disclosure: I. Redeker, None; **J. Callhoff**, None; **F. Hoffmann**, None; **H. Haibel**, AbbVie, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8; **J. Sieper**, AbbVie, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Novartis, 5, 8; **A. Zink**, Astra Zeneca, BMS, Lilly, Pfizer, Roche und UCB, 5, 8; **D. Poddubnyy**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 2, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8.

Abstract Number: 0581

Allograft Inflammatory factor-1 Drives Th17 Like Pathologic Signature and Predict Poor Response to TNF Inhibitor in Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is an inflammatory disease that commonly treated with TNF inhibitors for controlling active inflammation. To predict treatment response to TNF inhibitors upon clinical disease activity, differentially expressed genes were screened and AIF-1 was identified and validated in serum protein level in our previous study.

To elucidate the mechanism of how systemically elevated allograft inflammatory factor-1(AIF-1) could affect refractoriness of TNF inhibitors in AS, we focused on the change of $CD4^+$ helper T cells and monocytes induced by AIF-1. The effect of AIF-1 on the response to TNF inhibitors was also investigated.

Methods: Flow cytometry including intracellular staining, ELISA, and whole transcriptome analysis using RNA sequencing were performed in whole PBMCs, $CD4^+$ T cells, and $CD14^+$ monocytes after stimulating by AIF-1 in vitro. Healthy volunteers and AS patients provided peripheral blood. The effect of TNF inhibitors (adalimumab, etanercept) and tofacitinib were also examined in AIF-1 induced inflammatory response.

Results: AIF-1 aggravated inflammatory response via both directly increased TNF secretion from $CD4^+$ T cells and monocytes (TNF dependent) and IL-17 associated pathways (TNF independent). This effect resulted in shifting of $CD4^+$ T cell repertoire toward T helper 17 (Th17) rather than T helper 1 (Th1)(Figure 1). For the monocyte aspect, AIF-1 activated monocytes and increased surface expression of IL-17 receptor. In addition, TNF inhibition lost its positive effect of decreasing Th17 in the AIF-1 high environment. Whole transcriptome analysis showed that increased differentiation of Th17 cells by AIF-1 stimulation was prominent in both isolated $CD4^+$ T cell and monocytes.

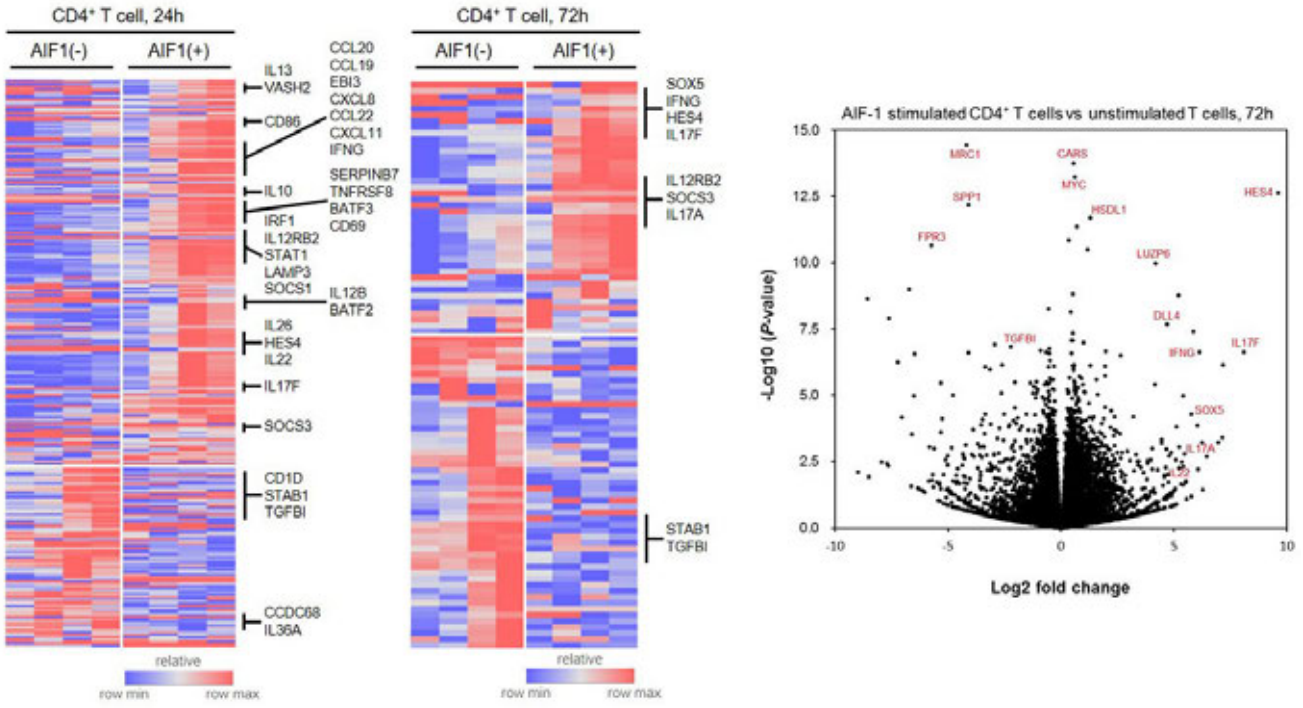

Figure 1. CD4+ T cell transcriptome changed toward Th17 by AIF-1 (n=4)

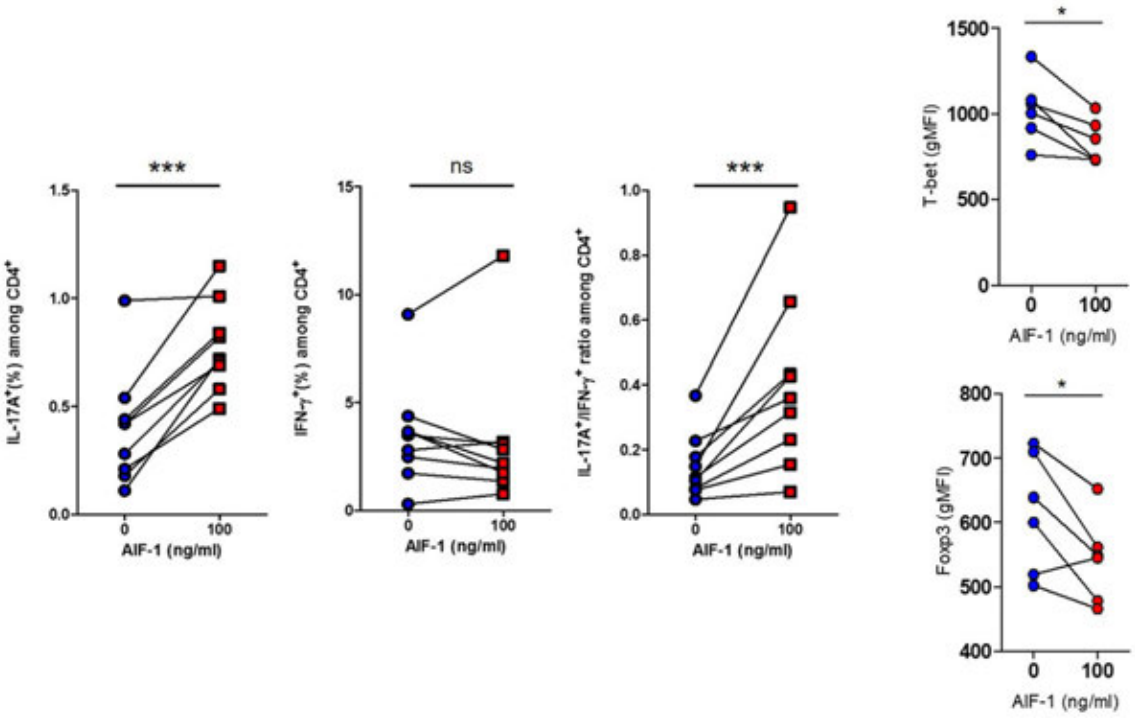

Figure 2. AIF-1 increased Th17/Th1 ratio

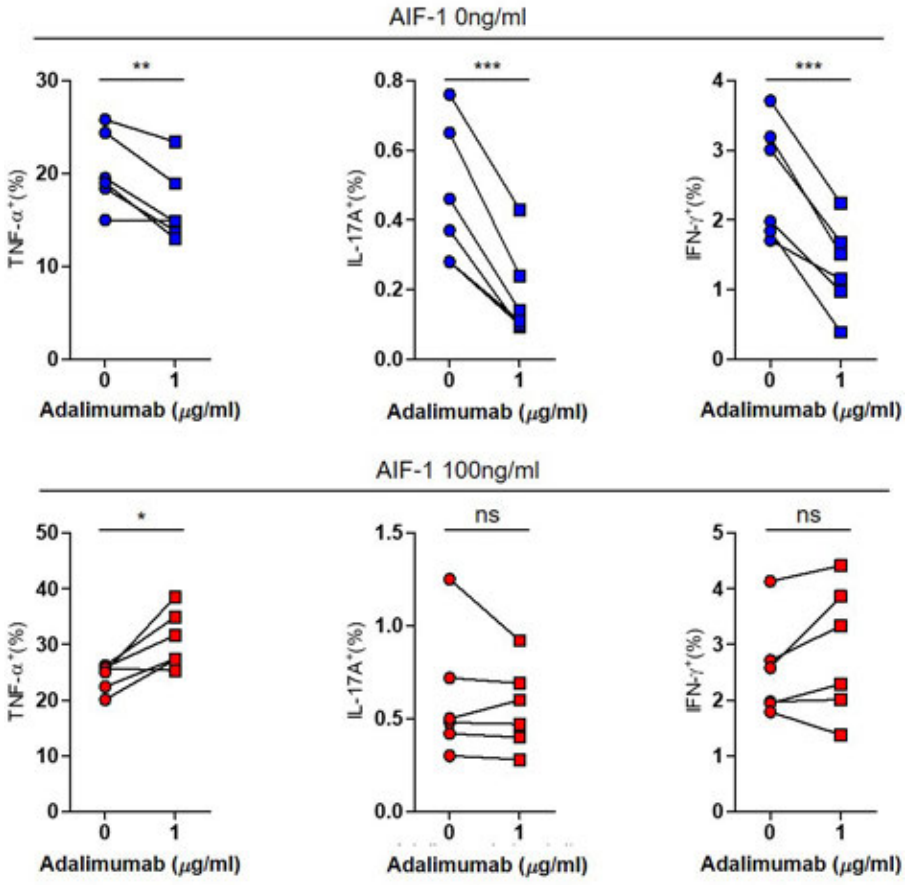

Figure 3. Anti-inflammatory effect or anti-Th17 effect of TNF inhibition may be diminished in the AIF-1 high environment.

Conclusion: AIF-1 aggravated Th17 response of AS and contribute to poor response to TNF inhibitors. Use of IL-17 blockade could be an effective alternative therapy in AS patients who has high AIF-1 level.

Disclosure: J. Lee, None; **E. Lee**, None; **J. Choi**, None; **Y. Song**, Astellas Pharma, Inc., 9; **E. Shin**, None; **E. Lee**, None.

Abstract Number: 0582

Rheumacheck - Spondyloarthritis: Comprehensive Fast-track Diagnosis Program. What Benefits Does It Offer in a Developing Country?

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In our region, the lack of knowledge, timely referral and access to laboratory tests and images are the main causes in the diagnostic delay of spondyloarthritis (SpA), which is estimated between 6 and 10 years.

	PsA (36)	SpA (47)	chronic back pain (52)	*p*
Male (%)	44,4	51	42	0,38
Age (SD)	48,8 (12,5)	45,8 (11,7)	42,3 (10,3)	0,2
Age at onset symptoms (SD)	45,5 (11,2)	39,6 (11,7)	38,8 (10,1)	0,9
IBP (%)	22	93,6	63,5	**0,003**
SpA features (%)	83	36,2	17,3	0,57
Family history SpA (%)	36	32	19,2	0,22
Good response to NSAIDs		66	31	0,14
Sacroiliac test (%)	20	62	29	**0,003**
Morning stiffness mint (IQR)		30 (15-45)	15 (5-15)	**0,002**
AVS pain (IQR)	6 (3-7)	7 (6-8)	7 (5-7)	0,03
AVS Night pain (IQR)		7 (5-8)	5 (3,5-7)	**0,008**
Anterior chest pain (%)		25,5	17,3	0,45
CDAI (IQR)	12 (5-19)	10 (7-17)	10 (5-10)	0,09
MASES (IQR)	0 (0-2)	0 (0-2)	0 (0-1)	**0,016**
BASFI (IQR)		4,3 (3,9-6,2)	3,4 (1-4,6)	**0,01**
BASDAI (IQR)		4,7 (3,8-6)	3,3 (2,2-4,5)	**0,000..**
HAQ (IQR)	0,5 (0,3-0,85)	0,6 (0,5-0,8)	0,5 (0,3-0,8)	0,1
HLA-B27 + (%)	2,8	47	2	**0,0001**
CRP (IQR)	2 (1-5)	2 (1-6)	1 (1-2,25)	0,2
VGS (IQR)	15 (9-34)	15,5 (10-22,5)	10 (5,5-17)	**0,02**
Sacroiliac X-rays + (%)	14	53	4	**0,0001**
Peripheal X-rays + (%)	25	12,8	4	0,14
Sacroiliac MRI + (%)	8,3	68.1	4	**0,000...**
Enthesis US + (%)	50	32	4	**0,000...**
Joints US + (%)	25	10,6	4	0,15
Referred by orthopedics - derm (%)		25,5	56	**0,002**
Smoking (%)	39	42,6	27	0,22
Time since referral and check (mths)	0,23 (0,2-0,5)	0,8 (0,7-1,2)	0,8 (0,6-1,5)	0,7
Time since the beginning of the symtoms (mth	51 (17-87)	38 (13-121)	24 (12-63)	0,12

Objectives: To evaluate the delay between the onset of symptoms, referral and access to the fast-track diagnosis program. To compare the differential characteristics in patients with axial symptoms**.**

Methods: Patients older than 18 years who entered a Rheumacheck-SpA were included according to the following criteria: peripheral arthritis plus at least one SpA feature (ASAS 2006) or low back pain of 3 months of evolution that began before 45. Patients were perfomored at the same day: blood analysis with acute phase reactants, HLA B27 (low back pain), sacroiliac X-r, sacroiliac MRI, joint and entheses ultrasonography (regardless of symptoms), sociodemographic data , characteristics of the disease (eg: age of onset), clinimetry and treatments. The symptom evaluator was unaware of the results of the complementary studies that were collected by another observer. Previously, a plan of awareness was made to the local community, physicians and health personnel involved (media campaigns, social networks and referral talks). Statistical analysis: descriptive statistics were carried out and, Chi2 and Fisher's exact test (categorical variables) and Student's Test or Mann Whitney (continuous variables) were applied.

Results: 135 patients entered the fast-track diagnosis program for 18 months, 99 with axial symptoms and 36 with peripheral symptoms. 53% female, average age 45.5 yrs (11.3), 74% were employed. SpA feature 40% (77% psoriasis, 10% uveitis, 3% IBD), SpA family history 26% (70% psoriasis, 15% SpA, 10% IBD). Of the patients with peripheral symptoms, 100% met criteria for psoriatic arthritis; and patients with axial symptoms 47.5% (95% CI 33-58) met ASAS criteria for axial SpA. Median delay since symptoms began at diagnosis were 37.7 months (RIC 12-85). Those patients referred by specialists (orthopedics-Dherm) had a delay of 0.75 months (RIC: 0.55-1.3). 25% of patients with a diagnosis were referred after the awareness campaign and 55% attended because saw the social media ads. Table 1 shows the differences between patients.

Conclusion: The delay from the onset of symptoms and access to the program (final diagnosis) was 3 years, and the delay of referral by another specialist was less than one month, 70% attended after the awareness campaign. Patients with axial SpA diagnoses had distinctive clinical, laboratory and imaging characteristics.

Disclosure: E. Sanchez Prado, None; **A. Ruta**, None; **J. Torres Chichande**, None; **S. Ruta**, None; **S. Magri**, None; **F. Salvatori**, None; **R. Garcia Salinas**, None.

Abstract Number: 0583

A Biomarker of Type VI Collagen Degradation (C6M) Is Associated with Changes in ASDAS MRI Measures of Inflammation in Patients with Axial Spondyloarthritis During TNF Inhibitor Therapy

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (AxSpa) is characterized by inflammation in the sacroiliac joints and spine and associated with extracellular matrix (ECM) remodelling of affected tissues. Type VI collagen (COL6) is an ECM protein located in the interface between the basement membrane and interstitial matrix, where is binds to other ECM proteins and support cell-cell interactions. C6M is a metabolite of COL6 that is released from the inflamed tissue and can be measured in serum as a biomarker of tissue remodelling. The aim of this study was to investigate the association of C6M in patients with AxSpA, and its relationship with treatment of TNF-α inhibitors for 46 weeks in the prospective Biomarkers in Spondyloarthritis (BIOSPA) study.

Methods: C6M was measured in serum from the BIOSPA study (n=55) at baseline, week 2, 22, 46 after treatment with TNF-inhibitors (infliximab, etanercept or adalimumab). Differences between the biomarker levels at the four different timepoints were calculated using repeated measures ANOVA. A t-test was used to calculate the improvement is ASDAS, while Spearman correlations were performed to explore the association of C6M and MRI measures.

Results: Patients included were 82% males, with median age of 40 years (IQR: 32-48), and 84% were human leucocyte antigen-B27 positive. They had a median disease duration of 5.5 years (IQR: 2-10), and a median baseline level of ASDAS 3.9 (IQR: 3.0-4.5). The levels of C6M can be found in Table 1. Levels of C6M were significantly decreased after 2 and 22 weeks of treatment compared to baseline (p=0.0014 and p=0.0015, respectively). C6M was significantly decreased in patients with clinical important improvement after 22 weeks (ASDAS $\geq\Delta$1.1) (p=0.010) and major improvement after 22 and 46 weeks (ASDAS $\geq\Delta$2.0) (p=0.0002 and p=0.018, respectively) as shown in Table 2 and 3. Baseline and week 22 levels of C6M correlated to the total SPARCC Spine and Sacroiliac Joint Inflammation score measured by MRI (Spearmans Rho=0.496, p< 0.001 and Spearmans Rho=0.297, p=0.031 respectively).

Conclusion: The biomarker C6M was associated with changes in ASDAS and MRI measures of inflammation during TNF-inhibitor treatment. This indicates that C6M may be a tissue-based marker of disease activity.

Table 1. Levels of C6M

	Baseline	2 weeks	22 weeks	46 weeks
C6M levels, ng/mL (IQR)	24.9 (14.7-35.0)	15.9 (12.4-21.0)	15.8 (11.4-26.3)	19.5 (15.1-29.9)

Table 2. C6M in relation to changes in ASDAS from baseline to week 22.

Biomarker	Baseline to week 22 Clinically important improvement		P-value	Baseline to week 22 Major improvement		P-value
	ASDAS <Δ1.1; n=17	ASDAS ≥Δ1.1; n=31		ASDAS <Δ2.0; n= 26	ASDAS ≥Δ2.0; n= 22	
	% Week 0-22			% Week 0-22		
C6M	16.70 (-15.97-49.37)	-31.16 (-46.58;-15.75)	0.010	10.11 (-12.28-32.50)	-44.24 (-60.42; -28.06)	0.0002

Table 3. C6M in relation to changes in ASDAS from baseline to week 46.

Biomarker	Baseline to week 46 Clinically important improvement		P-value	Baseline to week 46 Major improvement		P-value
	ASDAS <Δ1.1; n=11	ASDAS ≥Δ1.1; n=30		ASDAS <Δ2.0; n=24	ASDAS ≥Δ2.0; n=17	
	% Week 0-46			% Week 0-46		
C6M	47.36 (-23.36-118.07)	9.28 (-37.27-55.83)	0.341	53.23 (-4.06-110.51)	-28.13 (-65.39-9.14)	0.018

Disclosure: S. Holm Nielsen, Nordic Bioscience, 3; **A. Bay-Jensen**, Nordic Bioscience, 1, 2, 3; **M. Østergaard**, AbbVie, 2, 8, 9, Abbvie, 2, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, UCB, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, 5, 8, Abbvie, Celgene, Centocor, Merck, and Novartis, 2, Abbvie, Celgene, Centocor, Merck, Novartis, 2, BMS, 2, 5, 8, 9, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8; **A. Siebuhr**, Nordic Bioscience, 3; **M. Karsdal**, Nordic Biosceince, 1, 3, Nordic Bioscience, 1, 2, 3, 4, 5; **i. Sørensen**, None; **U. Weber**, None; **A. Loft**, None; **G. Kollerup**, None; **G. Thamsborg**, None; **O. Rintek Madsen**, None; **J. Møller**, None; **S. Juhl Pedersen**, None.

Abstract Number: 0584

Radiographic Association of Hip and SI Joints in Ankylosing Spondylitis Patients

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) is a representative tool for assessing radiographic progression in spine of ankylosing spondylitis (AS) patients. However, also other joint involvement than spine is common in AS patients. In particular, involvement of hip joints is common in AS patients, but there is not enough assessment of the involvement of the hip joint. The purpose of this study was to investigate the association between radiographic progression of the hip and SI joints and mSASSS in patients with AS.

Table 1. Multivariable linear regression analysis of associated factor of mSASSS

Variables	mSASSS (range 0-72)			
	Univariable analysis		Multivariable analysis	
	B (95% CI)	p-value	B (95% CI)	p-value
Age, years	0.83 (0.59 – 1.06)	<0.001*	0.49 (0.28 – 0.85)	<0.001*
BASDAI (range 0-10)	0.79 (-0.49 – 1.93)	0.242		-[a]
BASFI (range 0-10)	3.02 (1.86 – 4.18)	<0.001*	1.35 (0.37 – 2.33)	0.007*
ESR (mm/hr)	0.02 (-0.10 – 0.14)	0.760		-[a]
CRP (mg/dL)	0.06 (-2.10 – 2.23)	0.953		-[a]
†Use NSAIDs	-6.61 (-20.37 – 7.15)	0.345		-[a]
†Use Sulfasalazine	-6.30 (-10.82 – -1.78)	0.007*		-[a]
†Use Methotrexate	-1.71 (-6.54 – 3.13)	0.487		-[a]
†Use Glucocorticoids	-7.70 (-12.24 – -3.15)	0.001*	-5.63 (-9.09 – -2.16)	0.002*
†Use Biologic DMARDs	4.48 (-0.45 – 9.42)	0.074		-[a]
Hip joint grade	2.61 (1.76 – 3.47)	<0.001*	1.21 (0.46 – 1.96)	<0.001*
SI joint grade	6.84 (5.51 – 8.16)	<0.001*	4.72 (3.38 – 6.04)	<0.001*

B refers to the influence on mSASSS

*Statistically significant variables

[a]These variables were not tested in multivariable regression analysis because the value of the regression coefficient explained by the items already analyzed is the largest

†All drugs were analyzed for the presence or absence of the drug

BASDI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; HLA, Human leukocyte antigen; NSAID, Nonsteroidal anti-inflammatory drug; DMARD, Disease-modifying anti-rheumatic drug

Methods: In a total of 210 patients, simple x-ray images of spine, hip, and sacroiliac (SI) joints were obtained. The changes in SI joints were graded based on New York criteria, and the hip joint changes were assessed as joint space narrowing and osteophyte. The correlation between mSASSS and each joint was analyzed using Spearman's correlation. In addition, the factors were associated with radiographic progression were analyzed using multivariable regression.

Results: The mean age of the patients was 36.02 ± 8.89 years, and males were 91.9%. the grade of joint space narrowing and osteophyte were significantly correlated with mSASSS (r=0.31, r=0.22, r=0.34, p< 0.01), and the grade of SI joint was also significantly correlated with mSASSS (r=0.66, p< 0.01). In the correlation between mSASSS and other variables, Bath Ankylosing Spondylitis Functional Index (BASFI) showed significant correaltion with mSASSS (r=0.39, p< 0.01). In regression analysis, the radiographic progression of hip and SI joints was associated with mSASSS. In addition, age and BASFI were associated with mSASSS (Table 1).

Conclusion: Radiographic change of hip and SI joint was associated with mSASSS. Therefore, when evaluating the radiographic progression of the spine, we should consider hip joint change to evaluate the joint movement in patients with AS.

Disclosure: J. Kang, None; **S. Nam**, None; **H. Sung**, None; **K. Joo**, None; **B. Koo**, None; **S. Lee**, None; **T. Kim**, None.

Abstract Number: 0585

Effect of Testosterone on Spinal Ankylosis in Ankylosing Spondylitis : *in Vivo* and *in Vitro*

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is a predominantly male disease and spinal ankylosis more severely affect male AS[1] suggesting role of testosterone on spinal ankylosis. In previous studies, dihydrotestosterone (DHT) exhibited promoting osteoblast differentiation in *in vitro* experiment[2]. However, testosterone suppressed IL-17 expression[3] and exogenous IL-17A to primary bone-driven cells from AS promoted osteoblast activity and differentiation[4]. But the effect of testosterone on bony ankylosis in AS is still debated. This study aims to investigate the effect of testosterone on spinal ankylosis and osteoblast differentiation with curdlan-induced SKG mice and human primary osteoprogenitors.

Methods: Eight-week-old male SKG mice were intraperitoneally injected 3mg of curdlan (curdlan group, n=10) or PBS alone as control (n=6) at 0 and 2 weeks. Experimental diet with dutasteride (41.2mg/kg/day), 5α reductase inhibitor that block the conversion of testosterone into DHT, was begun at 9 weeks after the first curdlan injection (dutasteride group, n=10). Clinical scores of peripheral arthritis were monitored weekly, and at 15 weeks after first curdlan injection, whole-body imaging of mice using fluorescent *in vivo* bisphosphonate agent was performed using OsteoSense® 680 EX. At 17 weeks after first curdlan injection, mice were sacrificed and sera and splenocytes were collected. Bone metabolism-related molecules (RANKL, osteoprotegerin, DKK1, and sclerostin) were analyzed using luminex multiplex assay and IL-17A by single molecule arrays. T cell population in the spleen was measured using flow cytometry. Additionally, human bone tissues were obtained at surgery from facet joints of 10 patients with noninflammatory spinal disease from traffic trauma or spinal compression disease. Primary osteoprogenitor cells were cultured to assess osteoblastic activity. the effect of DHT on primary preosteoblasts was assessed by alkaline phosphatase (ALP) activity and staining, alizarin red staining (ARS) for calcium deposit, and qPCR

Results: The accumulation of hydroxyapatite that suggested spinal mineralization and osteoblast activity was increased in dutasteride group compared with curdlan group, and the osteoblast activities were correlated with levels of serum IL-17A. Among bone metabolism-related molecules, level of sclerostin was decreased in dutasteride group compared with curdlan group. Interestingly, increased frequency of Th17 frequency and increased IL-17A secretory Treg population was evident from splenocytes in dutasteride group. In *in vitro* human experiments, continuous exposure of DHT to osteoprogenitors resulted in low calcium deposit with ARS during osteoblasts differentiation, but

not intercellular ALP activity and ALP staining. In terms of gene expressions, DHT treated cells showed decreased *osteocalcin* and increased *DKK1* and *SOST1*.

Conclusion: Conclusively, treatment with dutasteride results in more aggressive mineralization of spine in curdlan-induced SKG mice and DHT treatment attenuates osteoblasts differentiation in *in vitro* model. Therefore, anti-androgen treatment in AS patients may be undertaken with caution when considering the progression of spinal ankylosis.

Disclosure: S. Jo, None; **E. Lee**, None; **J. Kang**, None; **S. Lee**, None; **J. Youn**, None; **Y. Kim**, None; **T. Kim**, None.

Abstract Number: 0586

Drug Concentrations and Anti-drug Antibodies Influence in Response to Adalimumab: Results from the BioEfficacySpA Clinical Trial

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Almost all protein-based biotherapeutics can induce immunogenicity, which may result in loss of efficacy and/or increased risk of adverse reactions. Despite all the efforts of protein engineering to reduce drug immunogenicity, recent assays still show unexpectedly high immunogenicity rates, even in fully human products. Pre-existing endogenous antibodies (Pre-Abs) (before first biotherapeutic administration) may be a contributing factor to these findings, leading to new challenges in assessing immunogenicity and its clinical relevance. We aim to assess if the levels of anti-drug antibodies (ADA) and drug concentrations influence response to first Tumor Necrosis Factor inhibitor (TNFi), Adalimumab (ADL).

Methods: Patients from the BioEfficacySpa study (Biomarkers identification of anti-TNF alfa agents efficacy in axial spondyloarthritis (axSpA) patients using a transcriptome analysis and mass spectrometry) were included. Data and blood samples (including ADA levels and serum ADL concentrations) were collected at bl (before first ADL infusion) and at w14 post-treatment with ADL. To be considered responders, patients had to achieve both ASAS 20 and AS-DAS clinically important improvement responses. Association between ADA titer/drug concentrations, at both bl and/or w14, and response to TNFi was assessed through logistic regression models, adjusted for relevant confounders.

Results: In total, 30 patients were included (70% males with median age of 43 (IQR: 17.6) years at bl) (Table 1). The majority (n=18; 60%) fulfilled the predefinition of responder at w14. Anti-TNFi antibodies titer at bl was much higher

Table 1. Baseline patient- and disease-characteristics of the overall population¥ and across subgroups according to responder/non responder category

Variables	Overall (N= 30) ¥	Responders (N=18) ‡	Non responders (N=12) £	p-value *
Age (years), median (IQR)	43.0 (17.6)	39.7 (18.0)	46.1 (16.9)	0.55
Gender (male), n (%)	21 (70.0)	13 (72.2)	8 (66.7)	0.75
BASDAI (0-10), median (IQR)	6.5 (2.8)	6.9 (2.3)	5.3 (4.5)	0.20
BASDAI≥4, n (%)	26 (86.7)	17 (94.4)	9 (75)	0.13
ASDAS-CRP, median (IQR)	3.6 (1.2)	4.1 (1.3)	3.3 (1.1)	**<0.01**
ASDAS inactive disease, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	
ASDAS low disease activity, n (%)	2 (6.7)	0 (0.0)	2 (16.7)	**0.05**
ASDAS high disease activity, n (%)	11 (36.7)	5 (27.8)	6 (50.0)	
ASDAS very high disease activity, n (%)	17 (56.7)	13 (72.2)	4 (33.3)	
CRP, mg/L, median (IQR)	14.0 (14.7)	14.9 (15.4)	3.5 (17.4)	**0.02**
Elevated CRP, n (%) **	23 (76.7)	18 (100.0)	5 (41.7)	**<0.01**
BASFI (0-10), median (IQR)	6.7 (2.7)	7.1 (2.5)	6.2 (3.0)	0.53
Co-medication				
NSAIDs, n (%)	21 (70.0)	13 (72.2)	8 (66.7)	0.75
csDMARDs, n (%)	8 (26.7)	5 (27.8)	3 (25.0)	0.87
ADA titer (baseline), ng/mL, median (IQR)	30.4 (131.1)	25.9 (79.7)	34.5 (156.6)	0.72

¥ axSpA patients who fulfilled the inclusion criteria, submitted to drug concentration and ADA detection assays. ‡ patients who achieved ASAS 20 and ASDAS CII responses after 14 weeks of ADL treatment. £ patients who achieved neither the ASAS 20, nor the ASDAS CII responses after 14 weeks of ADL treatment. * comparison between subgroups according to responder/non-responder to ADL (Wilcoxon-Mann Whitney test for continuous variables and Chi2 for categorical variables). BASDAI, Bath Ankylosing Spondylitis Disease Activity Index. ASDAS, Ankylosing Spondylitis Disease Activity Score. CRP, C Reactive Protein. BASFI, Bath Ankylosing Spondylitis Functional Index. NSAIDs, Non-Steroid Anti-inflammatory Drugs. csDMARDs, conventional synthetic Disease Modifying Anti-Rheumatic Drugs. ADA, Anti-drug Antibodies.

Table 2. Association between ADA levels and response to ADL according to different definitions of responder/non responder

Predictors	Response to Adalimumab ‡
ADA titer at baseline (ng/mL), OR (95% C)	0.9 (0.9;1.0)
ADA titer at week 14 (ng/mL), OR (95% C)	0.9 (0.9;1.0)
ADL concentration at week 14 (µg/mL), OR (95% C)	1.1 (0.8;1.5)
Age (years), OR (95% C)	0.9 (0.8;1.0)
Gender, OR (95% C)	3.0 (0.7; 12.8)

* logistic regression models with ADA title and drug concentration as predictors, adjusted for age and gender (R^2=16.2). ** p-value<0.05. ADA, Anti-drug Antibodies. ADL, Adalimumab.

than ADA titer at w14 (median ΔADA level = -45ng/mL) with only a few being of the neutralizing type (n=1; 4% vs n=3; 11.5%, at bl and w14 respectively). There were no statistically significant associations between ADA titer (at bl or w14) and drug concentrations at w14 and response to ADL (Table 2).

Conclusion: Our results show that even though assays used to detect drug concentration and ADA titer may be influenced by an individual/endogenous immune profile (previous to drug administration), response to ADL does not seem to be significantly affected by ADA titers or ADL concentration.

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Abstract Number: 0587

Increased Prevalence of Cardiac Disorders in Dutch Ankylosing Spondylitis Patients: The CARDAS Study

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The overall mortality rate in ankylosing spondylitis (AS) patients is increased by 60–90% compared with the general population. This higher mortality rate is predominately caused by cardiovascular disease (CVD) comprising both by increased prevalence of cardiac diseases such as valvular heart disease, conduction disturbances and cardiomyopathies as well as atherosclerotic diseases such as myocardial infarctions. However, there is some diversity in the literature and there is a lack of contemporary studies. Therefore, we investigated current prevalences of cardiac disorders in a well characterized cohorts of Dutch patients with AS.

The CARDAS study aims to describe the prevalence of CVD in AS patients in a Dutch cohort.

Methods: We performed a cross-sectional study in consecutive AS patients between 50-75 years. Subjects were recruited from a large rheumatology outpatient clinic (Reade) in Amsterdam, the Netherlands. Patients underwent echocardiography with 2D, spectral and Color Doppler imaging. Diastolic dysfunction was evaluated by an experienced cardiologist based on the AEA/ASE guideline 2009. Furthermore, an ECG, blood sample, surveys and physical examination were performed. Disease activity and function were measured with the BASFI, BASDAI and the ASDAS-CRP.

Table 1. Patient characteristics

	All	50-59 years	60-69 years	70-75 years
N	191			
Men	131 (71%)			
Age (years)	58 (54-65)			
Disease activity				
BASDAI	3.1 (±2,3)			
ASDAS-CRP	2.1 (±1.0)			
BASFI	3.5 (1.6-5.7)			
CVD				
History of CVD*		7.5%	9.4%	19%
Hypertension		45.3%	64.1%	85.7%
Aortic valve regurgitation**		10.4%	12.5%	33.4%
Mitral valve regurgitation**		33%	31.1%	42.9%
Diastolic dysfunction		40.4%	61.9%	89.5%

* Described as angina pectoris, myocardial infarction, stroke and/or peripheral ischemia
** moderate – severe regurgitation.

Results: 191 Consecutive AS patients were included with a median age of 58 years (54-65) of which mostly men (136/191, 71%) (Table 1). The mean disease duration was 34.9 years (± 11.9) The disease activity measures , BASDAI, ASDAS-CRP and BASFI, indicated moderate disease activity and were, respectively 3.1 (±2,3), 2.1 (±1.0) and 3.5 (1.6-5.7). The use of bDMARD's (anti-TNF) was present in 42% of the AS patients. As cardiac manifestations are age related, AS patients were divided in 3 age categories, respectively, 50-59 years, 60-69 years and 70-75 years. Hypertension was diagnosed in respectively 45.3%, 64.1% and 85.7%. History of CVD described as angina pectoris, myocardial infarction, stroke and/or peripheral ischemia were present in respectively 7.5%, 9.4% and 19%. Diastolic dysfunction was present in respectively 40.4%, 61.9% and 89.5% of the AS patients. The diastolic dysfunction present in this population was mainly mild with 60.2% of patients presenting with grade 1 and 39.8% with grade 2 diastolic dysfunction. Moderate to severe aortic regurgitation was present in, respectively 10.4%, 12.5% and 33.4% and moderate to severe mitral valve regurgitation in 33%, 31.3% and 42.9% of the AS patients. These prevalences are substantially increased in comparison to the general Dutch population.

Conclusion: We demonstrated increased prevalences of diastolic dysfunction, aortic valve regurgitation, mitral valve regurgitation and hypertension in Dutch AS patients compared to age matched general population. Although our results suggest mandatory echocardiography screening, this first needs to be established in prospective follow-up studies.

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Abstract Number: 0588

The Gut Enthesis Axis Coming into Focus with the Description of Enriched Entheseal Resident Mucosal Associated Invariant T-cells (MAITs) Capable of IL17A and TNF Production

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SESSION INFORMATION
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Background/Purpose: Mucosal associated invariant T-cells (MAITs) are innate-like T lymphocytes that express a semi-invariant TCR repertoire that are activated by microbial ligands or cytokines including IL-23 and secrete inflammatory cytokines, including IL-17A. MAIT cells are enriched at mucosal surfaces and have been implicated in the pathogenesis of spondyloarthritis (SpA) and inflammatory bowel disease (IBD). Although the human enthesis is not a mucosal surface it is the primary site of inflammation in SpA which has strong association with IBD. The aim of this study was to investigate if a population of MAITs is present at the normal human enthesis thereby supporting the gut-enthesis axis concept.

Methods: Healthy interspinous ligament and spinous process were harvested from patients undergoing elective surgery for the correction of mechanical spinal defects. Entheseal soft tissue (EST) and peri-entheseal bone (PEB) were separated, and cells were harvested by enzymatic and mechanical digestion respectively. The proportion of cells expressing markers consistent with MAITS (CD45+, CD3+, CD161+, TCRVα7.2+) were measured by flow cytometry in EST, PEB and matched blood. Expression of CD69 and CD45RA were examined for phenotypic analysis and IL-17A and TNF production was measured using intracellular flow following in vitro activation with PMA/ionomycin Transcript analysis for inflammatory, immunomodulatory and genes associated with tissue residency was performed on sorted entheseal MAITs and conventional CD8+ T-cells.

Results: As a proportion of total T-cells, MAITs were of approximately 3 fold and 2.5 fold greater abundance in EST and PEB respectively in comparison to matched peripheral blood (both p=0.034). MAITs in entheseal tissue had an overwhelming resident memory phenotype (CD69+, CD45RA-) median 53.2% (range 42.4 – 78.6%) in EST and 54.9% (45.2 - 82.1%) in PEB compared to those from blood 17.7 (6.8 – 69.4). They readily express IL-17A and TNF protein following PMA stimulation and showed higher basal expression of IL-23R (9-fold), RORC (3-fold), TNF (6-fold) and less TGFb (13-fold) and SOCS2 (5-fold). However, expression of transcripts relevant to tissue localisation was not altered in PEB MAITs compared to those from blood.

Conclusion: Healthy human entheseal tissue contains an enriched population of MAITs at a frequency comparable to that reported in the colon. The majority of these cells express a resident memory phenotype suggesting that they are a distinct population residing in entheseal tissue. These observations are potentially relevant to SpA pathogenesis, the observed link between SpA and IBD and may help to explain entheseal pathology following $\alpha 4\beta 7$ integrin inhibition in patients with IBD since MAITs are known to express this integrin receptor.

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Abstract Number: 0589

Smoking, Alcohol Intake and Body Mass Index in Prediction of Disease Activity over Time in Early Axial Spondyloarthritis - Results from the SPondyloArthritis Caught Early (SPACE) Cohort

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

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Background/Purpose: In ankylosing spondylitis (AS), smokers have been found to have both higher disease activity and greater syndesmophyte progression, and a higher body mass index (BMI) has been associated with disease activity in cross sectional studies of both late and early disease. In established AS, alcohol consumption (AC) was as-

Table 1. Differences in ASDAS over time, by baseline life style factors.
Linear mixed effect models.

	MEN		WOMEN	
	Total n and % exposed	Estimated mean difference 1st year (95% CL)	Total n and % exposed	Estimated mean difference 1st year (95% CL)
Age-adjusted				
BMI	n=158		n=157	
Normal (<25)	63%	Ref	67%	Ref
Overweight (25-29.9)	32%	0.08 (-0.19, 0.34)	15%	0.31 (-0.039, 0.65)
Obese (>30)	4%	-0.026 (-0.62, 0.59)	18%	**0.58 (0.26, 0.90)***
Smoking	n=157		n=163	
Never	56%	Ref	64%	Ref
Previous	22%	0.03 (-0.27, 0.33)	25%	**0.30 (0.02, 0.58)****
Current	22%	**0.32 (0.01, 0.63)****	10%	0.17 (-0.24, 0.57)
Alcohol consumption***	n=166		n=171	
None	14%	Ref	30%	Ref
Lowest (0.1-2)	22%	-0.32 (-0.73, 0.10)	32%	-0.06 (-0.36, 0.23)
Middle (3-5)	15%	-0.30 (-0.74, 0.15)	8%	-0.41 (-0.86, 0.04)
Highest (≥6)	27%	-0.20 (-0.60, 0.20)	6%	**-0.54 (-1.04, -0.04)****
Multivariate[1, 2]	n=151		n=150	
BMI				
Normal (<25)	64%	Ref	67%	Ref
Overweight (25-29.9)	32%	0.13 (-0.15, 0.40)	15%	0.32 (-0.01, 0.66)
Obese (>30)	5%	0.01 (-0.62, 0.62)	18%	**0.44 (0.11, 0.77)****
Smoking				
Never	58%	Ref	64%	Ref

sociated with lower disease activity. However, little is known about the longitudinal effect on disease activity of such modifiable life-style factors, and very few studies have been performed in early axial spondylarthritis (axSPA). Our aim was therefore to study the relation of baseline smoking, BMI and AC with disease activity over time in early axSPA.

Methods: Data from the SPondyloArthritis Caught Early cohort, which includes patients with chronic back pain for ≥3 months, ≤2 years and onset < 45 years, were used to predict disease activity, measured as ASDAS, during the first year of follow-up. ASDAS was recorded at baseline (inclusion), after 3 and 12 months. Patients included in the analyses had a definite diagnosis of axSPA (physician's level of confidence regarding SpA-diagnosis ≥7 on a 0-10 scale). Exposures measured at baseline were categorized as follows; BMI (normal < 25, overweight 25-29.9, obese > 30 kg/m2), smoking history (never, previous, current) and AC (none, 1-2, 3-5, ≥6 units of alcohol/week). Differences in ASDAS over 1 year by BMI category, smoking status and AC at baseline were estimated using mixed linear regression models, taking into account repeated measures of ASDAS.

Results: Of the 344 included subjects, the mean age at inclusion was 30 years and 49% were men. ASDAS decreased over the year of study with 0.58 in men and 0.46 in women. Obesity was more common in women whereas smoking and increased AC were more frequent in men (Table 1).

In age-adjusted models obesity in women (compared to normal BMI), but not in men, was associated with on average 0.58 (95% CL: 0.26, 0.90) *higher* ASDAS. The highest category of AC (≥6 units/week, compared to no AC) in women was associated with -0.54 (95% CL: -1.04, -0.04) *lower* ASDAS; and current smoking (compared to never smoking) in men with 0.32 (95% CL: 0.01, 0.63) *higher* ASDAS (Table 1).

In multivariate analyses including age, BMI-category, smoking history and AC the point estimates were overall similar, albeit the difference between current smokers and non-smokers in men did not reach statistical significance (Table 1).

Conclusion: Current smoking, AC and BMI, representing modifiable life style factors, were associated with disease activity over time in patients with early axSPA, with modest estimated differences and different patterns in women and men. Further analyses will explore to what extent residual confounding may explain these associations.

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Abstract Number: 0590

What Is the Impact of MRI on the Performance of the ASAS Classification Criteria in Patients Presenting with Undiagnosed Back Pain?

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SESSION INFORMATION

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Background/Purpose: Classification criteria for axSpA comprise an imaging and a clinical arm, the former requiring radiographic or MRI evidence of sacroiliitis. Several cohorts have reported the performance of the ASAS classification criteria in settings where clinical, radiographic, and MRI features have been simultaneously incorporated into the diagnostic evaluation in arriving at a gold standard for the testing of the criteria, which introduces circularity. We aimed to test the performance of the criteria in a setting where diagnostic evaluation can be conducted sequentially before and after MRI assessment in unselected patients referred with undiagnosed back pain who have presented with acute anterior uveitis (AAU), psoriasis, or colitis to their respective specialists.

Methods: Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis (AAU), or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA and MRI evaluation is ordered per rheumatologist decision. The rheumatologist determines the presence or absence of axial SpA and the degree of confidence in the diagnosis (-10 (definitely not SpA) to +10 (definite SpA)) at 3 sequential stages: 1. After the clinical evaluation; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of MRI evaluation. We calculated the sensitivity and specificity of the ASAS criteria and the component imaging and clinical arms using the stage 2 (pre-MRI) and 3 (post-MRI) diagnostic assessments by the local rheumatologist as gold standard.

Results: A total of 246 patients were recruited, 47.6% being diagnosed with axSpA (61.5% male, age 33.7 years, symptom duration 7.6 years, B27 positive 52.1%), after final diagnostic evaluation. Sensitivity/specificity of the ASAS criteria, imaging arm, clinical arm after stage 2 diagnostic evaluation for the entire cohort (prior to assessment of MRI) were 67.4/85.7%, 39.7/95.2%, 48.9/87.6%, respectively (Table). Sensitivity and specificity were higher in patients diagnosed with a high degree of confidence. For the subset of 146 patients who had MRI evaluation, and therefore had diagnostic evaluation at both stage 2 (pre-MRI) and stage 3 (post-MRI evaluation), there was a substantial enhancement in the sensitivity of the imaging arm (from 23.3% pre-MRI to 44.8% post-MRI) without change in specificity (>90%). However, there was a substantial decrease in specificity of the overall ASAS criteria from 83.9% pre-MRI to 74.7% post-MRI. This was primarily due to a substantial decrease in the specificity of the clinical arm from 85.7% pre-MRI to 77.2% post-MRI.

Conclusion: The clinical arm of the ASAS criteria performed less well after MRI assessment was added to the process of evaluation to enhance diagnostic precision. This could reflect rheumatologist diagnostic 'over-call' based on clinical findings in a population presenting with a higher pre-test probability of axSpA.

Table 1.

Patient Category	Stage of diagnostic evaluation	No of Patients	ASAS criteria		Imaging arm		Clinical arm	
			Sen	Spec	Sen	Spec	Sens	Spec
All patients	2	246	67.4	85.7	39.7	95.2	48.9	87.6
Patients diagnosed with high confidence	2	144	86.4	85.9	65.2	96.2	56.1	87.2
Subset of patients with MRI	2	146	58.9	83.9	23.3	94.6	46.7	85.7
Subset of patients with MRI	3	146	67.2	74.7	44.8	92.4	47.8	77.2
Subset of patients with MRI and high diagnostic confidence	2	111	74.1	82.1	44.4	92.3	51.9	84.6
Subset of patients with MRI and high diagnostic confidence	3	111	80.5	78.6	58.5	91.4	53.7	81.4

Disclosure: W. Maksymowych, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, AbbVie Inc., 2, 5, 8, Abbvie, Amgen, Eli Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, and UCB Pharma], 2, 5, 8, Amgen, 2, 5, 8, Boehringer, 5, 8, Boehringer-Ingelheim, 5, 8, Canadian Research and Education Arthritis, 6, CARE ARTHRITIS, 3, 6, 9, Celgene, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi, 2, 5, 8, Synarc, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5, 8; **R. Carmona**, None; **J. Chan**, Janssen Inc., 8; **J. Yeung**, None; **S. Aydin**, None; **L. Martin**, None; **A. Masetto**, None; **D. Mosher**, None; **O. Ziouzina**, None; **S. Keeling**, None; **S. Rohekar**, None; **R. Dadashova**, None; **J. Paschke**, None; **A. Carapellucci**, None; **R. Lambert**, None.

Abstract Number: 0591

Longitudinal Assessment of MRI of the Sacroiliac Joints in the ASAS Classification Cohort: Evolution of Diagnostic Features and Predictive Utility for Axial Spondyloarthritis

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

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Session Time: 9:00AM–11:00AM

Background/Purpose: Follow up of the ASAS Classification Cohort (CC) indicated a high positive predictive value for the ASAS classification criteria derived from baseline patient and imaging data[1]. Moreover, diagnosis of axSpA was changed by the local rheumatologist in only 11.2% of patients who were available at follow up at 4.4 years. This has raised potential concerns regarding diagnostic ascertainment bias. We aimed to determine the evolution of MRI features of axSpA from baseline to follow up by central reading of scans from this cohort, whether this reflects

Rheumatologist's diagnosis	MRI indicative of axSpA (agreement by ≥ 2 readers)			
	Yes at baseline and yes at follow up (N =48)	Yes at baseline and no at follow up (N = 4)	No at baseline and yes at follow up (N =6)	No at baseline and No at follow up (N = 50)
SpA yes at baseline and follow up (N= 82)	46 (56.1%)	2 (2.4%)	4 (4.9%)	30 (36.6%)
SpA no at baseline and yes at follow up (N =5)	1 (20%)	0 (0%)	1 (20%)	3 (60%)
SpA yes at baseline and no at follow up (N = 4)	1 (25%)	1 (25%)	0 (0%)	2 (50%)
SpA no at baseline and no at follow up (N =17)	0 (0%)	1 (5.9%)	1 (5.9%)	15 (88.2%)

MRI data from at least 2 readers and from the majority (≥5/8) was used to calculate positive and negative predictive values (PPV, NPV)

Table 2

MRI scan at baseline	Rheumatologist Diagnosis of axSpA at follow up n=108			
	Sensitivity	Specificity	PPV(%)	NPV(%)
Active lesions typical of axSpA (any 2 readers)	48.3 (37.4-59.2)	100.0 (83.9-100.0)	100.0	31.8
Active lesions typical of axSpA (majority of readers)	40.2 (29.9-51.3)	100.0 (83.9-100.0)	100.0	28.8
Structural lesions typical of axSpA (any 2 readers)	48.3 (37.4-59.2)	90.48 (69.6-98.9)	95.5	29.7
Structural lesions typical of axSpA (majority of readers)	31.0 (21.5-41.9)	95.2 (76.2-99.9)	96.4	25.0
ASAS positive MRI (any 2 readers)	46.0 (35.2-57.0)	100.0 (83.9-100.0)	100.0	30.9
ASAS positive MRI (majority of readers)	40.23 (29.9-51.3)	100.0 (83.9-100.0)	100.0	28.8
MRI indicative of axSpA (any 2 readers)	56.3 (45.3-66.9)	85.7 (63.7-97.0)	94.2	32.1
MRI indicative of axSpA (majority of readers)	50.6 (39.6-61.5)	100.0 (83.9-100.0)	100.0	32.8

diagnostic assignment by the local rheumatologist, and the predictive utility of baseline MRI considered indicative of axSpA.

Methods: MRI images were available from 108 cases who had MRI performed at baseline and 4.4 years follow up and also had a local rheumatologist diagnosis at both time points. Eight experienced readers from the ASAS MRI group recorded MRI lesions in an eCRF that comprised global assessment (MRI indicative of axSpA: yes or no, active and/or structural lesion typical of axSpA present/absent according to ASAS definitions), whether the features met the criteria for an ASAS positive MRI, and detailed scoring of lesions per SIJ quadrant (SPARCC SIJ quadrantic method). MRI data from at least 2 readers and from the majority (≥5/8) was used to calculate positive and negative predictive values (PPV, NPV).

Results: MRI was considered indicative of axSpA in 52/108 (48.1%) at baseline and in 47/86 (54.7%) diagnosed as axSpA by the rheumatologist. Change in MRI diagnosis was recorded in only 10/108 (9.3%) of cases (4 from yes to no, and 6 from no to yes for axSpA) according to agreement by at least 2 readers (Table 1). Change in MRI diagnosis was recorded in only 3 cases according to a majority of readers. Change in rheumatologist diagnosis was recorded in 9/108 (8.3%), 2 of which had a change in MRI diagnosis. Baseline MRI had very high PPV for follow up diagnosis of axSpA (Table 2).

Conclusion: The lack of change in diagnostic ascertainment of rheumatologists over follow up of the ASAS-CC is supported by the evaluation of MRI scans by central reading. A positive MRI at baseline had very high PPV for a follow up diagnosis of axSpA.

Reference:

1. Sepriano et al. ARD 2016;75:1034-42.

Disclosure: W. Maksymowych, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, AbbVie Inc., 2, 5, 8, Abbvie, Amgen, Eli Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, and UCB Pharma], 2, 5, 8, Amgen, 2, 5, 8, Boehringer, 5, 8, Boehringer-Ingelheim, 5, 8, Canadian Research and Education Arthritis, 6, CARE ARTHRITIS, 3, 6, 9, Celgene, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi, 2, 5, 8, Synarc, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5, 8; **X. Baraliakos**, AbbVie, 2, 4, 5, 8, Biocad, 2, 5, Bristol-Myers Squibb, 2, 4, 5,

8, Celgene, 2, 5, 8, Chugai, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, MSD, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5, 8; **M. de Hooge**, None; **I. Eshed**, None; **S. Juhl Pedersen**, None; **U. Weber**, None; **J. Sieper**, AbbVie, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Novartis, 5, 8; **S. Wichuk**, None; **D. Poddubnyy**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 2, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8; **M. Rudwaleit**, Abbott, 5, AbbVie, 5, 8, BMS, 5, 8, Bristol Myers-Squibb, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Eli Lilly, 5, 8, Eli Lily, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB Pharma, 5, 8; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **R. Landewé**, Abbott, 2, 5, 8, Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8; **J. Paschke**, None; **R. Lambert**, None; **M. Østergaard**, AbbVie, 2, 8, 9, Abbvie, 2, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, UCB, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, 5, 8, Abbvie, Celgene, Centocor, Merck, and Novartis, 2, Abbvie, Celgene, Centocor, Merck, Novartis, 2, BMS, 2, 5, 8, 9, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8.

Abstract Number: 0592

Replacement of Radiographic Sacroilitis by MRI Structural Lesions: What Is the Impact on Classification of Axial Spondyloarthritis in the ASAS Classification Cohort?

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: xClassification of axial spondyloarthritis is based on the application of either an imaging or clinical arm. Radiographic or MRI evidence of sacroiliitis can be applied for the imaging arm. However, it is well-established that reliability for detection of radiographic sacroiliitis is inadequate, especially in early disease, and radiography is insensitive compared to MRI for detection of either active or structural lesions. Active lesions on MRI (MRI-A) are already included as an alternative to radiographic sacroiliitis in the imaging arm. We aimed to assess the impact of replacing radiographic sacroiliitis with MRI structural lesions (MRI-S) typical of axSpA on the number of patients classified as having axSpA in patients with undiagnosed back pain recruited to the ASAS Classification Cohort (ASAS-CC).

Methods: MRI images (STIR and T1-weighted sequences) of the sacroiliac joint (SIJ) enabling assessment of both active and structural lesions were available from 219 cases in the ASAS-CC, and these also had available clinical, laboratory, and radiographic data. Seven central readers from the ASAS-MRI group recorded MRI lesions in an eCRF that included wording of lesions defining active (MRI-A) and structural (MRI-S) lesions typical of axSpA. MRI-A was deemed to be present according to majority agreement (≥4/7) of central readers. MRI-S was deemed to be present according to the majority (majority reader MRI-S) and also according to any 2 central readers (2-reader MRI-S). We calculated the number of patients that were classified differently after replacement of radiographs by MRI-S for overall fulfillment of the ASAS criteria and for the imaging arm.

Results: In total,124 (56.6%) fulfilled the ASAS axSpA criteria based on local reading of radiographic sacroiliitis and central reading of MRI-A. This changed to 126 (57.5%) and 120 (54.8%) patients after replacement of radiographic sacroiliitis by 2-reader and majority reader MRI-S, respectively (Table). 9 (4.1%) and 4 (1.8%) of patients who were not classified as axSpA were then re-classified as axSpA after substitution with 2-reader and majority reader MRI-S, respectively. Conversely, 7 (3.2%) and 8 (3.7%) were re-classified as not axSpA after substitution by 2-reader and majority reader MRI-S, respectively. When fulfillment of the imaging arm was required (irrespective of the clinical arm), the number of patients reclassified from not axSpA to axSpA was 18 (8.2%) by 2-reader MRI-S and 8 (3.7%) by majority reader MRI-S, while 8 (3.7%) and 11 (5.0%) were reclassified from axSpA to not axSpA, after substitution of radiographic sacroiliitis with 2-reader and majority reader MRI-S, respectively.

Conclusion: The number of patients classified as having axSpA does not change substantially when MRI-S replaces radiographic sacroiliitis. However, it is unclear to what degree MRI structural lesions could have affected the final diagnostic ascertainment, the gold standard for assessment of the performance of the ASAS criteria.

Disclosure: W. Maksymowych, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, AbbVie Inc., 2, 5, 8, Abbvie, Amgen, Eli Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, and UCB Pharma], 2, 5, 8, Amgen, 2, 5, 8, Boehringer, 5, 8, Boehringer-Ingelheim, 5, 8,

Table 1

	SpA Classification =Yes No. (%)	SpA Classification=No No. (%)
Radiographic Sacroiliitis + Majority Central Reader MRI Inflammation Positive	124 (56.6%)	95 (43.4%)
Replace Radiographic Sacroiliitis with >2 Central Reader MRI Structural Positive	126 (57.5%)	93 (42.5%)
Replace Radiographic Sacroiliitis with Majority Central Reader MRI Structural Positive	120 (54.8%)	99 (45.2%)

Canadian Research and Education Arthritis, 6, CARE ARTHRITIS, 3, 6, 9, Celgene, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi, 2, 5, 8, Synarc, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5, 8; **P. Machado**, None; **R. Lambert**, None; **X. Baraliakos**, AbbVie, 2, 4, 5, 8, Biocad, 2, 5, Bristol-Myers Squibb, 2, 4, 5, 8, Celgene, 2, 5, 8, Chugai, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, MSD, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5, 8; **M. Østergaard**, AbbVie, 2, 8, 9, Abbvie, 2, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, UCB, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, 5, 8, Abbvie, Celgene, Centocor, Merck, and Novartis, 2, Abbvie, Celgene, Centocor, Merck, Novartis, 2, BMS, 2, 5, 8, 9, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8; **J. Sieper**, AbbVie, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Novartis, 5, 8; **S. Wichuk**, None; **D. Poddubnyy**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 2, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8; **M. Rudwaleit**, Abbott, 5, AbbVie, 5, 8, BMS, 5, 8, Bristol Myers-Squibb, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Eli Lilly, 5, 8, Eli Lily, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB Pharma, 5, 8; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **R. Landewé**, Abbott, 2, 5, 8, Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8; **J. Paschke**, None; **S. Juhl Pedersen**, None; **U. Weber**, None.

Abstract Number: 0593

Performance of the ASAS Classification Criteria Presenting with Undiagnosed Back Pain: Data from the Screening in Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis Cohort

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Classification criteria for axial spondyloarthritis (axSpA) that capture the spectrum of disease present challenges due to the frequency of back pain, the relative infrequency of axSpA, and limited physical and laboratory findings in early disease. Several cohorts have reported the performance of the ASAS classification criteria in settings where patients have been selected for certain features such as the presence of inflammatory back pain and/or short symptom duration. We aimed to test the performance of the ASAS classification criteria in unselected patients with undiagnosed back pain who were referred after first presenting with acute anterior uveitis (AAU), psoriasis, or colitis to their respective specialists and whether performance varied according to the presentation of disease.

Methods: The multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at early detection of axial SpA in patients referred after first presenting with these disorders. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, AAU, or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA and MRI evaluation is ordered per rheumatologist decision. The rheumatologist determines the presence or absence of axial SpA and the degree of confidence in the diagnosis (-10 (definitely not SpA) to +10 (definite SpA)) at 3 consecutive stages: 1. After the clinical evaluation; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of MRI evaluation. Assessment of imaging was conducted by local and central readers. We calculated the sensitivity and specificity of the ASAS criteria and the component imaging and clinical arms using the stage 3 diagnostic assessment by the local rheumatologist as gold standard but using central reads for imaging.

Results: A total of 246 patients were recruited, 47.6% being diagnosed with axSpA (61.5% male, age 33.7 years, symptom duration 7.6 years, B27 positive 52.1%), after stage 3 evaluation. Sensitivity/specificity of the ASAS criteria, imaging arm, clinical arm were 65/82.2%, 36.8/97.7%, 50.4/82.2%, respectively (Table). For patients diagnosed with a high degree of confidence sensitivity/specificity was 73.8/84.5%, 47.5/98.2%, 56.3/84.5%, respectively. Performance varied substantially according to presentation of disease characterized by much higher sensitivity but markedly lower specificity, especially for the clinical arm, in patients presenting with AAU. This was noted even in patients diagnosed with high confidence. The imaging arm had high specificity (>90%) in all patient groups and was at least twice as sensitive in males versus females.

Table 1

Patient Category	Number	ASAS criteria		Imaging arm		Clinical arm	
		Sen	Spec	Sen	Spec	Sens	Spec
All SASPIC patients							
All	246	65	82.2	36.8	97.7	50.4	82.2
High confidence in diagnosis	190	73.8	84.5	47.5	98.2	56.3	84.5
Males	129	68.1	84.2	47.2	98.2	48.6	84.2
Females	117	60	80.6	20	97.2	53.3	80.6
IBD patients							
All	127	51	88.2	31.4	98.7	31.4	88.2
High confidence in diagnosis	106	59.5	88.4	43.2	98.6	32.4	88.4
Males	64	55.2	88.6	44.8	100	24.1	88.6
Females	63	45.5	87.8	13.6	97.6	40.9	87.8
AAU patients							
All	73	91.1	60.7	46.7	92.9	82.2	60.7
High confidence in diagnosis	56	94.1	63.6	52.9	95.5	85.3	63.6
Males	41	92.9	61.5	57.1	92.3	85.7	61.5
Females	32	88.2	60	29.4	93.3	76.5	60
Psoriasis patients							
All	46	42.9	88	28.6	100	28.6	88
High confidence in diagnosis	28	55.6	94.7	44.4	100	44.4	94.7
Males	24	46.7	100	33.3	100	26.7	100
Females	22	33.3	81.3	16.7	100	33.3	81.3

Conclusion: The performance of the ASAS criteria in the SASPIC cohort demonstrated lower sensitivity and specificity when compared to published cohorts, even in patients diagnosed with high confidence. This was characterized by much lower specificity for the clinical arm in patients presenting with AAU and raises the potential for 'diagnostic overcall' in the setting of a perceived high pre-test probability of axSpA.

Disclosure: W. Maksymowych, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, AbbVie Inc., 2, 5, 8, Abbvie, Amgen, Eli Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, and UCB Pharma], 2, 5, 8, Amgen, 2, 5, 8, Boehringer, 5, 8, Boehringer-Ingelheim, 5, 8, Canadian Research and Education Arthritis, 6, CARE ARTHRITIS, 3, 6, 9, Celgene, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi, 2, 5, 8, Synarc, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5, 8; **R. Carmona**, None; **J. Chan**, Janssen Inc., 8; **J. Yeung**, None; **S. Aydin**, None; **L. Martin**, None; **A. Masetto**, None; **D. Mosher**, None; **O. Ziouzina**, None; **S. Keeling**, None; **S. Rohekar**, None; **R. Dadashova**, None; **J. Paschke**, None; **A. Carapellucci**, None; **R. Lambert**, None.

Abstract Number: 0594

Enhanced Performance of the ASAS Classification Criteria by Deletion of Non-Discriminatory Clinical Items: Data from the Screening in Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis Cohort

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Table 1

Patient Category	Number	ASAS criteria		Imaging arm		Clinical arm	
		Sen	Spec	Sen	Spec	Sens	Spec
All SASPIC patients							
All	246	65	82.2	36.8	97.7	50.4	82.2
High confidence in diagnosis	190	73.8	84.5	47.5	98.2	56.3	84.5
Males	129	68.1	84.2	47.2	98.2	48.6	84.2
Females	117	60	80.6	20	97.2	53.3	80.6
IBD patients							
All	127	51	88.2	31.4	98.7	31.4	88.2
High confidence in diagnosis	106	59.5	88.4	43.2	98.6	32.4	88.4
Males	64	55.2	88.6	44.8	100	24.1	88.6
Females	63	45.5	87.8	13.6	97.6	40.9	87.8
AAU patients							
All	73	91.1	60.7	46.7	92.9	82.2	60.7
High confidence in diagnosis	56	94.1	63.6	52.9	95.5	85.3	63.6
Males	41	92.9	61.5	57.1	92.3	85.7	61.5
Females	32	88.2	60	29.4	93.3	76.5	60
Psoriasis patients							
All	46	42.9	88	28.6	100	28.6	88
High confidence in diagnosis	28	55.6	94.7	44.4	100	44.4	94.7
Males	24	46.7	100	33.3	100	26.7	100
Females	22	33.3	81.3	16.7	100	33.3	81.3

Background/Purpose: xThe ASAS classification criteria for axial spondyloarthritis (axSpA) have overall sensitivity/specificity of 82.9%/84.4% but component imaging and clinical arms differ in performance (66.2%/97.3% and 56.6%/83.3%, respectively). We aimed to demonstrate that a data-driven elimination of SpA clinical features that were non-discriminatory in comparisons of patients diagnosed with and without axSpA in a prospective cohort of unselected patients with undiagnosed back pain could enhance the performance of the criteria.

Methods: We used data from the prospective multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study, which is aimed at early detection of axial SpA in patients referred by the respective specialist after first presenting with these disorders. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, AAU, or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA and MRI evaluation is ordered per rheumatologist decision. The rheumatologist determines the presence or absence of axial SpA and the degree of confidence in the diagnosis. Imaging was assessed by central readers. Univariable and multivariable logistic regression analysis was performed to determine which clinical SpA features were/were not discriminatory for the final diagnosis of axSpA. We then compared the sensitivity and specificity of the ASAS criteria with and without these features.

Results: xA total of 246 patients were recruited, 47.6% being diagnosed with axSpA (61.5% male, age 33.7 years, symptom duration 7.6 years, B27 positive 52.1%). The following clinical SpA features were non-discriminatory between axSpA/not axSpA: NSAID response, family history of SpA, heel enthesitis, peripheral arthritis, dactylitis. Specificity of the clinical arm and the overall criteria increased from 82.2% to 86.8% without impacting sensitivity. This effect was particularly noteworthy in patients with lower degree of symptomatology (back pain severity < 5/10, specificity increases from 76.7% to 90.7%), short symptom duration (< 5 years, specificity increases from 78% to 84.7%), and in females (specificity increases from 80.6% to 86.1%).

Conclusion: xIn a prospective cohort with a high pre-test probability of axSpA certain clinical SpA features were not helpful in discriminating a diagnosis of SpA from not-SpA. Deletion of these features from the list of SpA features used in the ASAS classification criteria enhanced the performance of the criteria, especially in female patients and those with early disease.

Disclosure: W. Maksymowych, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, AbbVie Inc., 2, 5, 8, Abbvie, Amgen, Eli Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, and UCB Pharma], 2, 5, 8, Amgen, 2, 5, 8, Boehringer, 5, 8, Boehringer-Ingelheim, 5, 8, Canadian Research and Education Arthritis, 6, CARE ARTHRITIS, 3, 6, 9, Celgene, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi, 2, 5, 8, Synarc, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5, 8; **R. Carmona**, None; **J. Chan**, Janssen Inc., 8; **J. Yeung**, None; **S. Aydin**, None; **L. Martin**, None; **A. Masetto**, None; **D. Mosher**, None; **O. Ziouzina**, None; **S. Keeling**, None; **S. Rohekar**, None; **R. Dadashova**, None; **J. Paschke**, None; **A. Carapellucci**, None; **R. Lambert**, None.

Abstract Number: 0595

What Is the Impact of Discrepancy Between Central and Local Readers in Evaluation of MRI Scans on the Classification of Axial Spondyloarthritis? Data from the ASAS Classification Cohort Study

Walter P. Maksymowych,[1] Susanne Juhl Pedersen,[2] Ulrich Weber,[3] Pedro Machado,[4] Xenofon Baraliakos,[5] Joachim Sieper,[6] Stephanie Wichuk,[7] Denis Poddubnyy,[8] Martin Rudwaleit,[9] Désirée van der Heijde,[10] Robert B.M. Landewé,[11] Joel Paschke,[12] Mikkel Østergaard,[13] and Robert Lambert[7], [1]University of Alberta/CARE ARTHRITIS, Edmonton, AB, Canada, [2]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark, Copenhagen, Hovedstaden, Denmark, [3]Danish Hospital for Rheumatic Diseases, University Hospital of Southern Denmark, Sonderborg, Denmark, [4]University College London, London,

United Kingdom, [5]Rheumatology Department, Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Bochum, Germany, [6]Charité Universitätsmedizin Berlin, Germany, Berlin, Germany, [7]University of Alberta, Edmonton, Canada, [8]Charité - Universitätsmedizin Berlin and German Rheumatism Research Centre, Berlin, Germany, Berlin, Germany, [9]Klinikum Bielefeld, Charité Berlin, Gent University, Bielefeld, Germany, [10]Leiden University Medical Center, Leiden, Netherlands, [11]Amsterdam University Medical Center, Amsterdam, Netherlands, [12]CARE Arthritis, Edmonton, Canada, [13]Copenhagen Center for Arthritis Research, University of Copenhagen, Copenhagen, Denmark

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Active MRI lesions typical of axSpA were reported in 61.6% and 2.2% of axSpA and not-axSpA patients, respectively, from the ASAS classification cohort (ASAS-CC)[1]. Discrepancy between local and central reader evaluation of MRI scans regarding could result in differences in numbers of patients fulfilling the imaging arm of the ASAS classification criteria. But final classification may not be impacted if discrepant patients still fulfill the clinical arm. We aimed to assess the impact of reader discrepancy in detection of active MRI lesions on the number of patients classified as having axSpA in patients recruited to the ASAS-CC.

Methods: MRI images of the sacroiliac joints (SIJs) were available from 253 cases in the ASAS-CC, and these also had clinical and radiographic data. Seven central readers from the ASAS-MRI group recorded MRI lesions in an eCRF that included wording of lesions defining active lesions typical of axSpA in the SIJ (MRI-active) that was exactly the same as in the original ASAS-CC eCRF permitting comparisons between central and local site readers. Active lesions were deemed to be present according to majority agreement (≥4/7) of central readers and also any 2 central readers. We calculated the number of patients that were classified differently after central evaluation for overall fulfilment of the ASAS criteria and for the imaging arm.

Results: Discordance between central and local readers for detection of MRI-active was recorded in 70(27.1%) and 47(18.2%) of cases according to 2-reader and majority (≥4/7) central reader data, respectively (kappa (95%CI) of 0.62(0.52-0.71) and 0.58(0.49-0.67)). With central reading as external standard the false-positive rate for MRI-SI was 47.9% and 33.3% ('local overcall') for 2-reader and majority reader data. False-negative rate was 5.4% and 3.1%, respectively. A total of 159(62.8%) patients fulfilled the ASAS axSpA criteria based on local-reading, and 149(58.9%) and 143(56.5%) patients based on 2-reader and majority central-reading, respectively (Table). 25(9.9%) and 20(7.9%) patients who were classified as axSpA after local reading were no longer classified as axSpA after 2-reader and majority reader central evaluation. 7(2.8%) and 4(1.6%) classified as axSpA after central reading were not after local assessment. When fulfillment of the imaging arm was required (irrespective of the clinical arm), 45(17.8%) and 31(12.3%) cases were classified as axSpA after local MRI inflammation reading but not after 2-reader and majority

Table 1

Impact of Central Vs. Local Reader SIJ MRI Inflammation Assessment on SpA Classification in cases with all clinical, radiographic, and central and local MRI inflammation data available (n=253)		
	SpA Classification=Yes after MRI assessment N(%)	SpA Classification=No after MRI assessment N(%)
Local Reader SIJ MRI Inflammation positive	159 (62.8%)	94 (37.2%)
>2 Central Reader SIJ MRI Inflammation Assessment positive	149 (58.9%)	104 (41.1%)
Majority Central Reader SIJ MRI inflammation Assessment positive	143 (56.5%)	110 (43.5%)

central reading evaluation, and 5(1.9%) and 3(1.2%) cases that were not classified as axSpA after local MRI inflammation reading were classified as axSpA after central reading.

Conclusion: Despite substantial overcall for positive MRI SIJ inflammation by local readers when central readers are considered the reference standard, the number of patients classified as having axSpA did not change substantially. However, it is unclear whether reader discrepancy could have affected the final diagnosis, the gold standard for assessment of the performance of the ASAS criteria. Also, the gap of >10 years between local and central reading has to be taken into account.

Reference:

1. Rudwaleit et al. Ann Rheum Dis 2009;68: 777-83

Disclosure: W. Maksymowych, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, AbbVie Inc., 2, 5, 8, Abbvie, Amgen, Eli Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, and UCB Pharma], 2, 5, 8, Amgen, 2, 5, 8, Boehringer, 5, 8, Boehringer-Ingelheim, 5, 8, Canadian Research and Education Arthritis, 6, CARE ARTHRITIS, 3, 6, 9, Celgene, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi, 2, 5, 8, Synarc, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5, 8; **S. Juhl Pedersen**, None; **U. Weber**, None; **P. Machado**, None; **X. Baraliakos**, AbbVie, 2, 4, 5, 8, Biocad, 2, 5, Bristol-Myers Squibb, 2, 4, 5, 8, Celgene, 2, 5, 8, Chugai, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, MSD, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5, 8; **J. Sieper**, AbbVie, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Novartis, 5, 8; **S. Wichuk**, None; **D. Poddubnyy**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 2, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8; **M. Rudwaleit**, Abbott, 5, AbbVie, 5, 8, BMS, 5, 8, Bristol Myers-Squibb, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Eli Lilly, 5, 8, Eli Lily, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB Pharma, 5, 8; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **R. Landewé**, Abbott, 2, 5, 8, Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8; **J. Paschke**, None; **M. Østergaard**, AbbVie, 2, 8, 9, Abbvie, 2, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, UCB, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, 5, 8, Abbvie, Celgene, Centocor, Merck, and Novartis, 2, Abbvie, Celgene, Centocor, Merck, Novartis, 2, BMS, 2, 5, 8, 9, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8,

Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8; **R. Lambert**, None.

Abstract Number: 0596

Prostaglandin Receptor EP4 Drives Pathogenic Th17 Cell Development in Ankylosing Spondylitis and Is a New Marker of Disease Activity

Anja Meyer,[1] Charlotte Klasen,[1] Pauline Wittekind,[1] Iris Waqué,[1] Schafiq Nabhani,[1] and David Kofler[1], [1]University of Cologne, Cologne, Germany

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Th17 cells are involved in the pathogenesis of ankylosing spondylitis (AS). However, the mechanism underlying enhanced Th17 cell accumulation in AS remains unknown. The prostaglandin E2 receptor EP2/EP4 signaling pathway plays a critical role in the development of autoimmune Th17 cells. Interestingly, recent genome-wide association studies (GWAS) have identified five risk alleles for AS in *PTGER4*, the gene encoding for EP4. The aim of this study was to reveal a possible link between EP4 and disease activity in patients with AS.

Methods: Th17 cells from patients with AS were analyzed for the transcriptional expression of prostaglandin receptor genes by quantitative RT-PCR. Th17 cells from patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and from healthy individuals served as controls. EP4 receptor expression in Th17 cells was assessed *ex vivo*by flow cytometry and by western blot. Functional analysis using EP4 specific agonists was performed to reveal how EP4 regulates Th17 cells.

Results: EP4 is significantly overexpressed in Th17 cells from patients with AS compared to Th17 cells from healthy individuals or patients with RA or PsA. EP4 upregulation is unique to Th17 cells and is not found in other CD4+ T cell subsets. Interestingly, EP4 expression is not increased in Th17 cells from HLA-B27 negative patients with AS. The highest amount of EP4 expression is found in IL-17+/IFNγ+ double positive CD4+ T cells. This is remarkable, because IL-17+/IFNγ+ Th17 cells have been identified previously as pathogenic autoimmune Th17 cells. Specific activation of EP4 drives Th17 cell development and promotes EP4 expression in a positive feedback loop in AS but not in RA or PsA. Mechanistically, EP4 acts by suppressing the RORγt inhibitor FoxO1 and by enhancing STAT3 phosphorylation. As a consequence, the interleukin-23 receptor (IL-23R) is upregulated on Th17 cells. Importantly, increased EP4 expression levels in Th17 cells from AS patients correlate with high disease activity as defined by a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score ≥ 4 (r=0.7591,p=0.0016).

Conclusion: EP4 is a potential marker of disease activity in patients with AS. Aberrant EP4 expression might contribute to pathogenic Th17 cell accumulation and represents a new target for the treatment of AS.

Disclosure: A. Meyer, None; **C. Klasen**, None; **P. Wittekind**, None; **I. Waqué**, None; **S. Nabhani**, None; **D. Kofler**, Chugai Pharmaceutical Co., LTD., 2, Bristol-Myers Squibb, 2.

Abstract Number: 0597

High Prevalence of Sacroiliac Bone Marrow Edema on MRI in Post Partum Women: A Temporary Phenomenom

Thomas Renson,[1] Ann-Sophie De Craemer,[1] Liselotte Deroo,[1] Anaïs Depicker,[1] Manouk de Hooge,[1] Nele Herregods,[1] Lennart Jans,[1] Kristien Roelens,[1] Isabelle Dehaene,[1] Philippe Carron,[1] Filip Van den Bosch,[1] and Dirk Elewaut[1], [1]Ghent University Hospital, Ghent, Belgium

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Magnetic Resonance Imaging (MRI) is a sensitive method for detection of sacroiliitis. However, recently, concerns have been raised about its specificity. In contrast to radiographic spondyloarthritis (SpA), non-radiographic SpA has a more equal sex distribution. Hence, in young women with back pain a broad differential diagnosis has to be considered. In clinical practice, women occasionally present with inflammatory(-like) low back pain, following pregnancy and childbirth. Up until now, little is known regarding the presence of SpA-like MRI lesions in postpartum women. We hypothesized that physical stress on the pelvis during pregnancy may lead to signs of bone marrow edema on MRI.

The objectives of this study are to explore (A) the association between pregnancy and giving birth on the one hand, and the occurrence of MRI lesions compatible with SpA on the other hand; and (B) if these lesions are transient.

Methods: Twenty-five women underwent an MRI of the sacroiliac joints (SIJ) in the first 10 days after vaginal delivery. The scan was repeated after 6 months. Both time points were scored in pairs by 3 trained readers, blinded for time

Table. Number of MRI-SIJ lesions in 25 postpartum women.

	Baseline			6 months		
Inflammatory lesions	Median	IQR	95% CI	Median	IQR	95% CI
SPARCC (/72)	5	1 – 11	1 – 8	0	0 – 1	0 – 1
Capsulitis (/12)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Enthesitis (/12)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
High signal intensity (/12)	0	0 – 4	0 – 3	0	0 – 0	0 – 0
Structural lesions	Median	IQR	95% CI	Median	IQR	95% CI
Erosions (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Fatty lesions (/48)	0	0 – 1	0 – 0	0	0 – 0	0 – 0
Sclerosis (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Partial ankylosis (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Ankylosis (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0

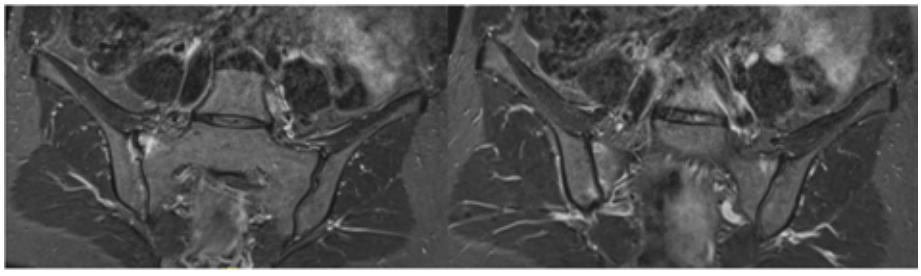

Figure. Baseline MRI T2 short tau inversion recovery (STIR) images of sacroiliac bone marrow edema in a 33-year old postpartum woman.

sequence and subject characteristics. MRI assessment was done on 6 consecutive slices for inflammatory and structural SpA-like lesions; bone marrow edema (BME), capsulitis, enthesitis, high signal intensity in joint space, erosions, fatty lesions, sclerosis and (partial) ankylosis. In addition, the Assessment of SpondyloArthritis international Society (ASAS) definition of a positive MRI-SIJ was applied. MRI reader scores were reported as 2 out of 3 (median) scores.

Results: Twenty out of 25 (80.0%) subjects displayed BME; the median SPARCC score was 5 (IQR 1-11) (see table). One subject was lost to follow-up. After 6 months, 11 out of 24 (45.8%) subjects still showed BME; however, median SPARCC score dropped to 0 (IQR 0-1) ($p = 0.002$). At baseline, 16 out of 25 (64.0%) participants had a positive MRI-SIJ according to the ASAS definition, reducing to 4 out of 24 (16.7%) after 6 months ($p = 0.002$). 75.5% of the baseline lesions were located in the anterior part of the SIJ; 57.3% situated on the iliac side. Structural lesions were rarely detected in this study population (see table).

Conclusion: A very high prevalence of sacroiliac BME on MRI was seen in women immediately postpartum with 64.0% even having a positive MRI for sacroiliitis according to the ASAS definition. A significant decrease in BME was seen over 6 months time, yet a substantial fraction continued to display BME after follow up. History of a recent pregnancy is crucial to take into account when interpreting an MRI-SIJ. In case of a recent pregnancy and clinical suspicion of SpA, it may be wise to postpone MRI-SIJ imaging until at least 6 months after the delivery.

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Abstract Number: 0598

Identification of Potential Risk Factors for Spinal Structural Damage in Chinese Patients with Ankylosing Spondylitis

Weiping Kong,[1] Caroline Jefferies,[2] Tom Learch,[2] Feng Zhu,[1] Nan Zhang,[1] Dier Jin,[1] Yingze Zhang,[1] Qingwen Tao,[1] Xiaoping Yan,[1] Michael Weisman,[3] and Mariko Ishimori[2], [1]China-Japan Friendship Hospital, Beijing, China (People's Republic), [2]Cedars-Sinai Medical Center, Los Angeles, CA, [3]David Geffen School of Medicine at UCLA, Los Angeles, CA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Spinal structural damage can lead to physical dysfunction and decline of spinal mobility in patients with ankylosing spondylitis (AS). Although great progress has been made to identify potential risk factors associated with the severity of spinal structural damage, there is no definite consensus on how many factors are actually involved in its development. To yield more information, we conducted a cross-sectional study in 270 Chinese AS patients, aiming to identify potential risk factors responsible for the severity of spinal structural damage, both individually and in combination.

Methods: In total, 270 AS patients fulfilled the modified New York criteria. Computed tomography (CT) scans and lumbar/cervical X-rays were used to separately assess BASRI-SI, BASRI-hips and modified Stoke Ankylosing Spon-

Table 1. Baseline characteristics of study patients with ankylosing spondylitis

Characteristics	All patients	mSASSS <10	mSASSS ≥10	*p*
Age (years)	32 (26, 40)	30 (24, 37)	36 (31, 49)	<0.001
Gender				0.283
Female	57 (21.1%)	42 (23%)	15 (17.2%)	
Male	213 (78.9%)	141 (77%)	72 (82.8%)	
HLA-B27 (+)				0.868
Negative	26 (9.6%)	18 (9.8%)	8 (9.2%)	
Positive	244 (90.4%)	165 (90.2%)	79 (90.8%)	
Family history of AS				0.255
No	209 (77.4%)	138 (75.4%)	71 (81.6%)	
Yes	61 (22.6%)	45 (24.6%)	16 (18.4%)	
Occupation				0.838
Unemployed	17 (6.3%)	11 (6%)	6 (6.9%)	
mental labor	198 (73.3%)	133 (72.7%)	65 (74.7%)	
Physical labor	55 (20.4%)	39 (21.3%)	16 (18.4%)	
Smoking duration (years)	0 (0, 0)	0 (0, 0)	0 (0, 7)	0.099
Cigarettes per day	0 (0, 0)	0 (0, 0)	0 (0, 5)	0.197
Ever smoking				0.220
No	202 (74.8%)	141 (77%)	61 (70.1%)	
Yes	68 (25.2%)	42 (23%)	26 (29.9%)	
Current smoking				0.151
No	204 (75.6%)	143 (78.1%)	61 (70.1%)	
Yes	66 (24.4%)	40 (21.9%)	26 (29.9%)	
Physical activity				0.660
0	229 (84.8%)	154 (84.2%)	75 (86.2%)	
1	41 (15.2%)	29 (15.8%)	12 (13.8%)	
Duration of symptoms (years)	9 (5, 14)	7 (4, 11)	10 (7, 20)	<0.001
Diagnosis delay (years)	2 (0, 5)	2 (0, 4)	2 (0.500, 8)	0.020
Onset age (years)	22.50 (16, 29)	22 (16, 27.50)	24 (17, 32)	0.047
BMI (kg/m^2)	23.43 (20.24, 25.91)	22.84 (20.13, 25.09)	24.49 (21.48, 27.64)	0.003
Night pain (VAS)	4 (3, 5)	4 (3, 5)	4 (3, 5)	1.175
PGA (VAS)	4 (3, 5)	4 (3, 5)	4 (3, 5)	1.064
ESR (mm/h)	16 (7, 29)	14 (7, 28)	17 (11, 30)	0.110
CRP (mg/dL)	1.195 (0.515, 2.130)	1.090 (0.446, 2.030)	1.360 (0.621, 2.330)	0.195
ASDAS-CRP	1.705 (1.240, 2.120)	1.710 (1.210, 2.140)	1.660 (1.250, 2.110)	1.056
BASDAI	3 (2.200, 3.900)	3 (2.200, 3.900)	2.700 (2.200, 4)	1.668
Sacroiliitis grade	3 (2, 4)	3 (2, 3)	4 (3, 4)	<0.001
Hip involvement				0.001
Negative	136 (62.4%)	102 (70.3%)	34 (46.6%)	
Positive	82 (37.6%)	43 (29.7%)	39 (53.4%)	

Abbreviations: AS, ankylosing spondylitis; HLA-B27, human leukocyte antigen B27; BMI, body mass index; PGA, patient global assessment; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; ASDAS, ankylosing spondylitis disease activity score; BASDAI, bath ankylosing spondylitis disease activity index; VAS, (10 cm) visual analogue scale; mSASSS, modified stoke ankylosing spondylitis spine score. Data are expressed as either count (per cent) or median (interquartile range). The *p* value was calculated by Chi-squared test or Wilcoxon rank-sum (Mann-Whitney) test, where appropriate.

dylitis Spine Score (mSASSS), which were scored by a trained rheumatologist and a musculoskeletal radiologist where the inter-rater reliability (average *kappa*: 87.3%) was excellent. Spinal structural damage was appraised by mSASSS that was binarized at a cutoff of 10. Hip involvement was defined as BASRI-hips >0. Univariate and multivariate logistic regression analyses were done to identify potential risk factors for the severity of spinal structural damage, and nomogram graph was presented to facilitate clinical assessment. Statistical analyses were completed using the STATA software (v14.1) and R language (v3.5.1).

Results: 183 AS patients had mSASSS < 10 (low mSASSS), and 87 patients had mSASSS ≥10 (high mSASSS) (Table 1). Univariate analysis revealed that AS onset age, body mass index (BMI), duration of smoking, duration

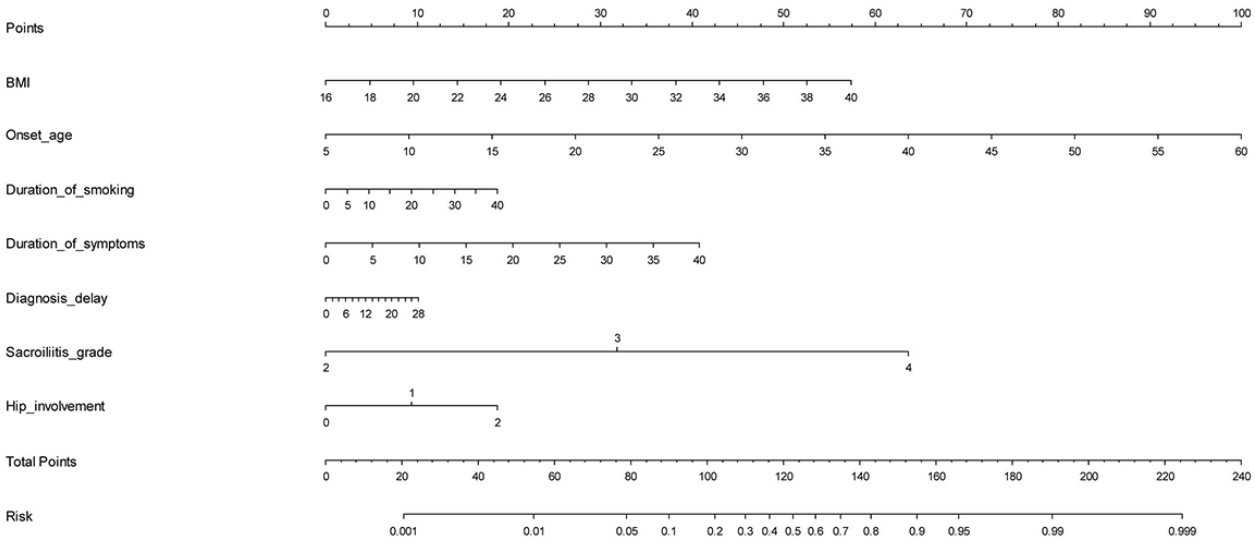
Table 2. Identification of significant risk factors for spinal structural damage

Significant risk factors	Unadjusted model				Adjusted model*			
	OR	95% CI		*p*	OR	95% CI		*p*
Onset age	1.23	1.08	1.40	0.002	1.21	1.03	1.42	0.019
BMI	1.37	1.14	1.66	0.001	1.36	1.12	1.64	0.002
Duration of smoking	1.54	1.06	2.24	0.023	1.59	1.07	2.35	0.021
Duration of symptom	1.69	1.37	2.08	<0.001	1.65	1.33	2.05	<0.001
Diagnosis delay	1.45	1.10	1.90	0.008	1.42	1.07	1.88	0.015
Hip involvement	2.65	1.54	4.56	<0.001	2.63	1.50	4.62	0.001
Sacroiliitis grade	5.01	3.27	7.67	<0.001	5.92	3.67	9.55	<0.001

Abbreviations: BMI, body mass index; OR, odds ratio; 95% CI, 95% confidence interval. *The *p* was adjusted for age, gender and human leukocyte antigen B27.

of symptoms, diagnosis delay, hip involvement and sacroiliitis grade were significantly associated with the risk of having high mSASSS, and all remained significant after adjusting for age, gender and HLA-B27 (all p< 0.05) (Table 2). In further analyses, hip involvement was found to be in significant interaction with BMI and duration of smoking in a graded manner. For instance, relative to patients with low BMI and negative hip involvement, those with high BMI and negative hip involvement, low BMI and positive hip involvement, and high BMI and positive hip involvement had a 1.94-, 3.29- and 5.07-fold increased risk of having high mSASSS (95% confidence interval: 0.84-4.47, 1.37-7.89, and 1.97-13.06, p=0.118, 0.008 and 0.001), respectively. To facilitate clinical assessment, a nomogram graph (Figure 1) based on 7 significant risk factors was generated with decent prediction accuracy (C-index: 0.906 and p< 0.001), and importantly besides sacroiliitis grade, onset age and BMI carried a greater weight than other risk factors.

Figure 1. Nomogram graph for the risk prediction of spinal structural damage using significant risk factors. Abbreciations: BMI, body mass index.



Conclusion: We have identified seven potential risk factors responsible for the severity of spinal structural damage in Chinese AS patients. Importantly, positive hip involvement, in combination with high BMI or long duration of smoking, was associated with a remarkably increased risk of having severe structural damage in spine. Hip involvement was prevalent in our cohort and use of CT may have increased identification of hip findings compared to past studies in which X-rays were reviewed.

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Abstract Number: 0599

Muscle Physical Properties in Young Adult Axial Spondyloarthritis Patients, the MyoSpA Study

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: An important mechanism regarding axial spondyloarthritis (axSpA) susceptibility and progression is the biomechanical concept, suspected from axial myofascial hypertonicity and stiffness in ankylosing spondylitis (AS). This pathway may promote local tissue microtrauma and contribute to immunological activation and subsequent bony fusion or ankylosis. The MyoSpA study tests the novel hypothesis of increased resting lumbar and appendicular (upper and lower limbs) myofascial tone/stiffness in axSpA patients compared to healthy controls (HC).

Methods: A cross-sectional study was conducted on 54 participants (18-50 years), 27 axSpA (according to ASAS criteria, with less than 10 years since symptoms onset) and 27 HC, matched by gender and age.

Muscle physical properties (stiffness, tone and elasticity) was quantified using the MyotonPro device. This myotonometer is a non-invasive device which applies a slight mechanical impulse to the skin via a probe, which is transmitted to the underlying soft tissue and muscle, and resultant oscillations are electronically recorded. Measurements were performed by a single tester, in three different body locations: lower lumbar (erector spinae myofascia at the L3-4 level), upper limbs (extensor digitorium, 5 cm below the elbow) and lower limbs (gastrocnemius 10 cm below

Table: Median (25th-75th percentile) stiffness (Nm) in combined male and female axSpA and control subjects

Variable	Patients *n*=27	Controls *n*=27	*p*-value
Trunk			
Average	246.5(230.5–286.5)	232.50(211.0–293.5)	0.382
Dominant	261.0(232.0–312.0)	241.0 (204.3–303.0)	0.278
Non-Dominant	242.0(219.0–291.0)	232.0 (209.3–288.0)	0.319
Upper Limb			
Average	288.0(266.0–320.0)	293.0(265.0–307.5)	0.598
Dominant	282.0(266.0–334.0)	293.0(254.8–311.8)	0.803
Non-Dominant	283.0(267.0–313.0)	290.0(266.0–313.0)	0.957
Lower Limb			
Average	293.5(277.0–329.5)	289.0(265.0–325.0)	0.749
Dominant	299.0(257.0–349.0)	298.0(271.0–325.0)	0.908
Non-Dominant	295.0(269.0–321.0)	290.0(263.5–314.3)	0.810

knee), on both sides, after 10-minutes prone rest interval. Body composition was measured by octapolar multifrequency bioelectrical impedance analysis (InBody770). Physical activity was assessed by the International Physical Activity Questionnaire (IPAQ). Variables (except age, disease duration, BASDAI, BASFI) are presented as median (inter-quartile range). Non-parametric tests were used to compare groups.

Results: Mean (SD) age of the 27 axSpA patients was 36.8±7.4 years and the 27 HC was 36.3±7.8 (p=0.79), each having 18 males, 9 females. No significant difference occurred between groups in body mass index and physical activity. AxSpA patients had mean (SD) symptoms duration of 6.5±3.2 years, with BASDAI of 2.7±2.3 and BASFI of 0.9±3.1.

AxSpA and HC subjects showed no significant difference in muscle stiffness, tone and elasticity in the lumbar, upper and lower limbs, when the averaged values of combined male and female, right and left measurements were analyzed. AxSpA patients had slightly greater lumbar muscle stiffness [246.5 (230.5–286.5] than HC [232.5 (211.0–293.5], p=0.380. The difference was slightly greater on the dominant side [261.0 (232.0–312.0) vs 241.0 (204.3–303.0), p=0.28]. Gender had no influence on the results.

Conclusion: Young axSpA patients with mainly controlled disease, minor functional repercussion and short disease duration did not show a difference in muscle physical properties compared to HC. Further studies are needed to support the hypothesized biomechanical concept of increased resting lumbar myofascial stiffness in active axSpA patients.

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Abstract Number: 0600

Frequency of Disease Flares Under Long-Term Anti-TNF Therapy in Patients with Early Axial Spondyloarthritis: Results from the Etanercept versus Sulfasalazine in Early Axial Spondyloarthritis Trial (ESTHER)

Fabian Proft,[1] Murat Torgutalp,[2] Anja Weiß,[3] Mikhail Protopopov,[4] Valeria Rios Rodriguez,[5] Hildrun Haibel,[1] Kay-Geert Hermann,[5] Christian Althoff,[5] Olaf Behmer,[6] Joachim Sieper,[1] and Denis Poddubnyy[7], [1]Charité Universitätsmedizin Berlin, Germany, Berlin, Germany, [2]Charité Universitätsmedizin Berlin, Germany and Ankara University Faculty of Medicine, Ankara, Turkey., Berlin, Germany, [3]German Rheumatism Research Center (DRFZ), Berlin, Germany, [4]Charité Universitätsmedizin Berlin, Germany, Berlin, Berlin, Germany, [5]Charité Universitätsmedizin, Berlin, Germany, [6]Pfizer Inc., Berlin, Germany, [7]Charité - Universitätsmedizin Berlin and German Rheumatism Research Centre, Berlin, Germany, Berlin, Germany

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

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Session Time: 9:00AM–11:00AM

Background/Purpose: Disease flares in axial spondyloarthritis (axSpA) might occur even in patients with otherwise stable disease receiving effective anti-inflammatory therapy such as TNF inhibitors. The frequency of disease flares, especially in patients with axSpA receiving long-term stable therapy, and factors associated with flares are not sufficiently investigated. The ASAS group recently developed the first data driven definition of a clinically important worsening (flare) in axSpA based on the ASDAS [1]. Objective of the presented analysis was to assess the frequency of disease flares and to identify factors associated with flares in axSpA patients receiving continuous longterm treatment with a TNF Inhibitor.

Methods: In ESTHER, patients with early axSpA (symptom duration ≤5 years) were treated with ETN (n=40) versus sulfasalazine (n=36) for 48 weeks [2]. After one year all patients were treated continuously with etanercept (n=17 patients temporarily interrupted treatment in the 2nd year to assess time to flare and were then (re-)treated with etanercept, except 4 patients who completed the study in sustained remission) for up to 10 years in total. Only patients who were continuously treated with etanercept for at least 6 months were included in the current analysis. The disease flare was defined as a worsening of the ASDAS by ≥0.9 as compared to the value obtained at the previous visit. Univariate and multivariable cox-regression analyses were performed to analyze the predictors of flares.

Results: Out of 76 patients who entered the study at baseline, 62 patients (n=32 with radiographic (r-) axSpA and n=30 with non-radiographic (nr-) axSpA) fulfilled the criterion of the continuous etanercept treatment. A total of 22 patients (35%) experienced at least one flare over the entire treatment period 10 patients (31.3%) in the r-axSpA and 12 patients (40%) in the nr-axSpA subgroup) - figure. A total of 81 flares occurred (33 and 48 in the r- and nr-axSpA subgroups, respectively) in the 10 years of follow-up. None of the documented disease flares resulted in a direct study withdrawal. The majority of flares occurred within first 4 years of treatment (figure). There were also no statistically significant differences between nr- and r-axSpA in the time until the first flare (p=0.4, Log-rank test). In the multivariable Cox regression analysis, an elevated CRP value (>5mg/l) at baseline, HLA-B27 negativity, a longer symptom duration at study entry, a lower spinal osteitis score and a higher spinal fatty lesion score on MRI at baseline were associated with a higher risk for flares (Table).

Figure. Kaplan-Meier curves indicating time to the first flare and flare free survival propability in patients with early axial spondyloarthritis on stable etanercept treatment

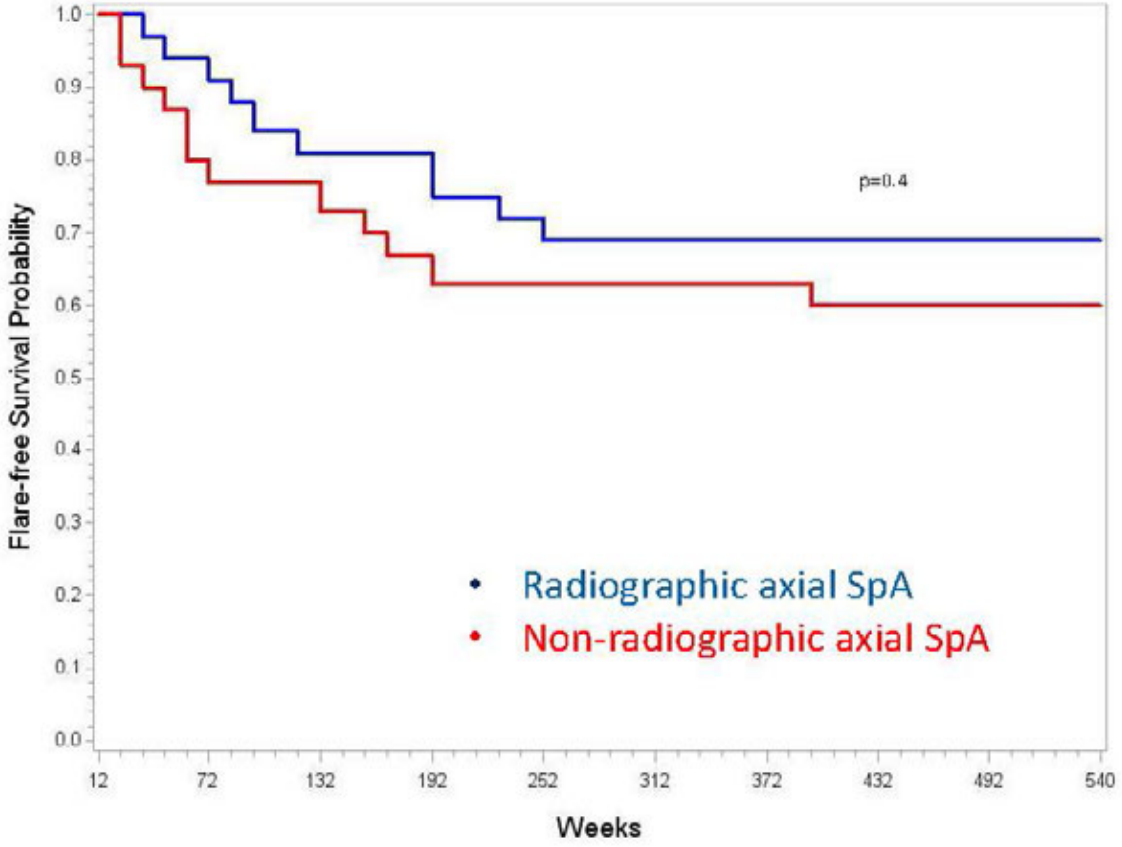

Table: Multivariable Cox-regression analysis of factors associated with flares in early axial spondyloarthritis patients on stable anti-TNF treatment with etanercept.

	Hazard Ratio 95% CI
HLA-B27 negativity	**1.359 (1.08, 1.71)**
CRP positivity (>5mg/l) at baseline	**1.42 (1.01, 2.0)**
Symptom duration at baseline	**1.052 (1.01, 1.1)**
MRI spinal osteitis score at baseline	**0.973 (0.95, 1)**
MRI spinal fatty lesion score at baseline	**1.072 (1.02, 1.12)**

Conclusion: Disease flares according to the ASAS definition of clinically important worsening in axSpA based on ASDAS occurred in approximately one third of patients with early axSpA who received a treatment with the TNF-inhibitor etanercept for up to 10 years without major differences between r- and nr- forms of axSpA. HLA-B27 negativity, elevated CRP at baseline, longer symptom duration with higher fatty lesion and lower osteitis spinal score were associated with a higher risk of flares.

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References:
1. Molto et al. Ann Rheum Dis. 2018 Jan; 77(1):124-127.
2. Song IH, et al. Ann Rheum Dis. 2011 Apr; 70(4):590-596.

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Abstract Number: 0601

Development of an Optimized Online Self-Referral Tool for Early Recognition of Patients with Axial Spondyloarthritis - Data from the OptiRef Study

Fabian Proft,[1] Laura Spiller,[2] Mikhail Protopopov,[3] Valeria Rios Rodriguez,[2] Burkhard Muche,[2] Judith Rademacher,[2] Susanne Lüders,[2] Anne Katrin Weber,[2] Imke Redeker,[4] and Denis Poddubnyy[5], [1]Charité Universitätsmedizin Berlin, Germany, Berlin, Germany, [2]Charité Universitätsmedizin, Berlin, Germany, [3]Charité Universitätsmedizin Berlin, Germany, Berlin, Berlin, Germany, [4]Charité – Universitätsmedizin Berlin and German Rheumatism Research Centre, Berlin, Germany, [5]Charité - Universitätsmedizin Berlin and German Rheumatism Research Centre, Berlin, Germany, Berlin, Germany

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: One of the major reasons for a long diagnostic delay in axial spondyloarthritis (axSpA) is the late referral of patients by primary care physicians dealing with patients with chronic back pain. We developed and implemented an online self-referral tool (www.bechterew-check.de), which gave access to a rheumatological consultation if patients declared suffering from chronic back pain (≥ 3 months) with a symptom onset ≤ 45 years of age, and at least one feature indicative of SpA. In the prospective "Identification of the Optimal Referral Strategy for Early Diagnosis of Axial Spondyloarthritis (OptiRef) Study" we could diagnose axSpA in 19% of the self-referred patients. The objective was to optimize the online-self-referral tool for recognition of patients with high suspicion of axSpA in order to increase the specificity by keeping the high level of sensitivity.

Methods: 181 patients who had fulfilled the online self-referral strategy were included and underwent a standardized rheumatology examination. The final diagnosis of axial SpA / no axial SpA by the rheumatologist served as the gold standard. The performance of all possible combinations of the referral parameters (13 parameters in total including 5 features of inflammatory back pain (IBP) and 8 other SpA features) added to both stem parameters (chronic back pain starting at age of ≤45 years) was tested. In addition, the following pre-specified combinations were evaluated: 1) ≥1 IBP parameter AND ≥1 other SpA parameter, 2) ≥1 IBP parameter OR ≥1 other SpA parameter. For all combinations, a sensitivity, a specificity, positive and negative predictive values (PPV and NPV), as well as a positive and negative

Figure 1: The data-driven optimized self-referral strategy.

1	**Does your back pain last 3 months or longer?**	No □ Yes □
2	**Did your back pain start prior to 45 years of age?**	No □ Yes □
3	**What are the characteristics of your back pain?**	
	• The back pain onset was rather slow and was not related to a trauma	No □ Yes □
	• I suffer from stiffness in my back of 30 minutes or longer upon getting up in the morning	No □ Yes □
	• Movement or exercises (but not rest) improve my back pain	No □ Yes □
	• I wake up sometimes in the night (especially 2nd half) because of back pain	No □ Yes □
	• I have or I had alternating (flipping from side to side) pain in my buttocks	No □ Yes □
4	**Other signs and symptoms which might indicate an inflammatory nature of the back pain:**	
	• I took a nonsteroidal anti-inflammatory drug (such as Diclofenac or Ibuprofen) because of back pain, and pain was completely relieved or was much better after the drug intake	No □ Yes □
	• I have / had joint pain with swelling and/or inflammation in the areas of tendons insertion to the bone (e.g., heels).	No □ Yes □
	• The genetic marker HLA-B27 has been tested in my blood already and the result was „positive"	No □ Yes □
	• I have / had elevated markers of inflammation in the blood (C-reactive protein or erythrocyte sedimentation rate), which are unlikely to be explained by other reasons (such as infections)	No □ Yes □
	• I suffer from psoriasis	No □ Yes □
	• I suffer from inflammatory bowel disease (Crohn's disease or ulcerative colitis)	No □ Yes □
	• I suffer / suffered from (iritis)	No □ Yes □
	• One or several of my direct relatives suffer / suffered from ankylosing spondylitis, psoriasis or inflammatory bowel disease (Crohn's disease or ulcerative colitis)	No □ Yes □
	*The strategy is fulfilled if **1** + **2** + ≥ 2 questions in the **3** + ≥ 1 question in the **4** are answered with yes.*	

Table 1: Performance of self-referral strategies based on combinations of SpA parameters in addition to the stem parameters (chronic back pain starting at age of ≤45 years).

Number of fulfilled criteria (z)*	*Number of patients*	*PPV*	*NPV*	*Sensitivity*	*Specificity*	*LR+*	*LR-*
*1***	*163*	*0.19 (31/163)*		*1.00 (31/31)*			
2	*158*	*0.20 (31/158)*	*1.00 (5/5)*	*1.00 (31/31)*	*0.04 (5/132)*	*1.04*	*0.00*
3	*147*	*0.21 (31/147)*	*1.00 (16/16)*	*1.00 (31/31)*	*0.12 (16/132)*	*1.14*	*0.00*
4	*128*	*0.22 (28/128)*	*0.91 (32/35)*	*0.90 (28/31)*	*0.24 (32/132)*	*1.19*	*0.40*
5	*114*	*0.23 (26/114)*	*0.90 (44/49)*	*0.84 (26/31)*	*0.33 (44/132)*	*1.26*	*0.48*
6	*74*	*0.31 (23/74)*	*0.91 (81/89)*	*0.74 (23/31)*	*0.61 (81/132)*	*1.92*	*0.42*
7	*48*	*0.38 (18/48)*	*0.89 (102/115)*	*0.58 (18/31)*	*0.77 (102/132)*	*2.55*	*0.54*
8	*27*	*0.48 (13/27)*	*0.87 (118/136)*	*0.42 (13/31)*	*0.89 (118/132)*	*3.95*	*0.65*
9	*17*	*0.59 (10/17)*	*0.86 (125/146)*	*0.32 (10/31)*	*0.95 (125/132)*	*6.08*	*0.72*
10	*7*	*0.43 (3/7)*	*0.82 (128/156)*	*0.10 (3/31)*	*0.97 (128/132)*	*3.19*	*0.93*
11	*1*	*1.00 (1/1)*	*0.81 (132/162)*	*0.03 (1/31)*	*1.00 (132/132)*	*-*	*0.97*
12	*1*	*1.00 (1/1)*	*0.81 (132/162)*	*0.03 (1/31)*	*1.00 (132/132)*	*-*	*0.97*
13	*1*	*1.00 (1/1)*	*0.81 (132/162)*	*0.03 (1/31)*	*1.00 (132/132)*	*-*	*0.97*

**Criteria: insidious onset; improving with exercise, no improvement with rest; waking up in the second half of the night; morning stiffness ≥ 30 minutes; alternating buttock pain; good response to NSAIDs; arthritis/enthesitis ever; HLA-B27 positive; uveitis; psoriasis; inflammatory bowel disease; SpA family history; elevated acute phase reactants.*

***The original strategy, reference for the calculation of the performance of all other strategies*

likelihood ratio (LR+ and LR-) were calculated. We targeted the maximal specificity by acceptable sensitivity (defined as ≥90% of the original strategy).

Results: For 163 of the included patients, full data of the online questionnaire as well as of rheumatology examination including the final diagnosis was available. 31 (19%) of them were diagnosed with axial SpA. Raising the threshold of the number of positive parameters (table 1) resulted in a quick drop of the sensitivity. According to the pre-defined selection criterion, only a strategy with any four positive parameters would be acceptable. An analysis of

combined strategies (IBP parameters and/or other SpA parameters) resulted into identification of a strategy with an improved performance: a combination of ≥2 IBP parameters with ≥1 other SpA parameters (in addition to both stem parameters) showed a sensitivity of 90% (28/31), a specificity of 27% (35/132), a PPV of 22% (28/125), a NPV of 92% (35/38), LR+ of 1.23 and LR- of 0.36. Thus, identifying 28 of 31 patients with axSpA would have been possible after the assessment of 125 patients instead of 163.

Conclusion: The data-driven optimized online self-referral tool (figure 1) requires the following parameters to be positive: chronic back pain (≥3 months) plus back pain onset before 45 years of age plus ≥2 IBP parameters plus ≥1 other SpA feature. The performance of this tool should be confirmed in a prospective study.

Disclosure: F. Proft, Abbvie, 5, 8, BMS, 8, MSD, 8, Novartis, 5, 8, Novartis Pharma, 2, Pfizer, 5, 8, Roche, 8, UCB, 5, 8; **L. Spiller**, None; **M. Protopopov**, MSD, 8, Novartis, 5, 8, Pfizer, 8; **V. Rios Rodriguez**, AbbVie, 5, 8, MSD, 5, 8, Novartis, 5, 8; **B. Muche**, None; **J. Rademacher**, None; **S. Lüders**, None; **A. Weber**, None; **I. Redeker**, None; **D. Poddubnyy**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 2, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8.

Abstract Number: 0602

Comparison of Men and Women with Axial Spondyloarthritis in the US-Based Corrona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease that primarily affects the axial skeleton and frequently affects the peripheral joints and entheses. AxSpA encompasses ankylosing spondylitis and nonradiographic axSpA. Sex differences have been described for patient reported outcomes (PROs) in SpA; however, more research is needed to better understand the overall clinical burden of axSpA in women, particularly in the United States. We aim to compare the patient demographics, clinical characteristics, treatment profiles, disease activity, quality of life, and work productivity between men and women with axSpA in the US-based Corrona PsA/SpA Registry.

Methods: This study included patients aged ≥ 18 years with axSpA enrolled in the Corrona PsA/SpA Registry between March 2013 and November 2018. Patients who were concurrently diagnosed with PsA were excluded. Patient demographics, clinical characteristics, treatment profiles, disease activity, quality of life, and work productivity were characterized for all patients with axSpA at enrollment and were compared between men and women using *t* tests or Wilcoxon rank-sum tests for continuous variables and χ^2 or Fisher exact tests for categorical variables.

Table 1. Demographic and Clinical Characteristics and Treatment Profiles in Men and Women With AxSpA at Enrollment*

Characteristic	Patients With AxSpA		*P* Value
	Men (N = 307)	Women (N = 191)	
Age, mean (SD), years	47.3 (13.9)	47.7 (13.5)	0.75
Race, n (%)	n = 302	n = 186	0.08
White	276 (91.4)	172 (92.5)	
Black	3 (1.0)	6 (3.2)	
Other	23 (7.6)	8 (4.3)	
Work status, n (%)			< 0.01
Full time	190 (62.1)	102 (53.7)	
Part time	11 (3.6)	20 (10.5)	
Disabled	49 (16.0)	24 (12.6)	
Retired	38 (12.4)	22 (11.6)	
Other	18 (5.9)	22 (11.6)	
BMI, mean (SD) [n], kg/m^2	29.8 (6.0)	30.0 (8.5)	0.32
BMI (in kg/m^2) categories, n (%)			0.04
Normal/underweight (< 25)	64 (21.5)	60 (31.7)	
Overweight (25 to < 30)	102 (34.3)	54 (28.6)	
Obese (≥ 30)	131 (44.1)	75 (39.7)	
Symptom duration, mean (SD), years	17.6 (12.3)	15.7 (11.6)	0.09
Disease duration, mean (SD), years	10.3 (10.8)	8.2 (9.9)	0.02
HLA-B27 positive test result, n (%)	224 (73.0)	124 (64.9)	0.06
Select comorbidities, n (%)			
Depression	37 (12.1)	49 (25.7)	< 0.01
Fibromyalgia	3 (1.0)	20 (10.5)	< 0.01
Ulcerative colitis	9 (2.9)	13 (6.8)	0.04
Anxiety	7 (2.3)	10 (5.2)	0.08
Prior biologic use, n (%)	89 (29.0)	63 (33.0)	0.35
Number of prior biologics, n (%)			0.62
0	218 (71.0)	128 (67.0)	
1	57 (18.6)	39 (20.4)	
≥ 2	32 (10.4)	24 (12.6)	
Prior csDMARD use, n (%)	41 (13.4)	42 (22.0)	0.01
Prior prednisone use, n (%)	27 (8.8)	30 (15.7)	0.02

AxSpA, axial spondyloarthritis; BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug.
* All values were calculated based on available data, and all variables had < 20% missing data.

Results: Of 498 patients with axSpA who were included in the study, 307 (61.6%) were male and 191 (38.4%) were female. Compared with men, women were less likely to work full time, were more likely to be normal weight/underweight, had a shorter disease duration, and were more likely to have depression, fibromyalgia, and prior csDMARD and prednisone use (**Table 1**; all $P < 0.05$). At enrollment, women with axSpA had a shorter occiput-to-wall distance, but also had worse disease activity compared with men, as reflected by higher BASDAI and BASFI scores, higher enthesitis and tender/swollen joint counts, worse pain and fatigue, worse physical function (HAQ-S) and health state today (EQ VAS), and more severe work and activity impairment (**Table 2**; all $P < 0.05$).

Conclusion: In this US registry of patients with axSpA, women had an increased overall burden of disease compared with men, including higher patient reported symptoms, higher disease activity, and greater work productivity impairment. Women also had lower scores for spinal mobility with increased signs of peripheral arthritis (eg, higher tender/swollen joint and enthesitis counts), suggesting that conventional definitions of axSpA centered around axial symptoms may not be representative of the female population with disease. Improved awareness of sex differences in presentation of axSpA may aid physicians in earlier identification and improved management of the disease.

Table 2. Disease Activity, Quality of Life, and Work Productivity in Men and Women With AxSpA at Enrollment*

Characteristic	Patients With AxSpA		*P* Value
	Men (N = 307)	Women (N = 191)	
ASDAS, mean (SD)	2.6 (1.2)	2.8 (0.9)	0.07
BASDAI (0-10), mean (SD)	4.2 (2.5)	4.9 (2.3)	< 0.01
BASFI (0-10), mean (SD)	3.4 (2.8)	4.1 (2.7)	< 0.01
Lateral lumbar flexion (average of left and right), mean (SD), cm	24.1 (20.1)	23.4 (19.0)	0.76
Occiput to wall, mean (SD), cm	5.8 (7.7)	2.7 (5.0)	< 0.01
Enthesitis, n (%)	62 (20.2)	71 (37.2)	< 0.01
SPARCC Enthesitis Index (1-16)	3.2 (2.4)	4.8 (3.2)	< 0.01
Dactylitis, n (%)	9 (2.9)	3 (1.6)	0.39
Dactylitis count (1-20)	3.4 (3.5)	1.3 (0.6)	0.37
Tender joint count (0-68), mean (SD)	1.8 (4.7)	5.1 (9.6)	< 0.01
Swollen joint count (0-66), mean (SD)	0.6 (2.5)	0.9 (2.2)	0.01
Physician global assessment, mean (SD)	25.7 (23.4)	30.8 (22.2)	< 0.01
Patient pain (VAS 0-100), mean (SD)	45.3 (30.5)	51.6 (27.8)	0.03
Patient fatigue (VAS 0-100), mean (SD)	45.4 (29.1)	53.9 (27.4)	< 0.01
Morning stiffness, n (%)			0.10
< 30 minutes	88 (29.4)	43 (22.6)	
≥ 30 minutes	211 (70.6)	147 (77.4)	
Patient global assessment (VAS 0-100), mean (SD)	52.2 (32.5)	52.5 (33.1)	0.82
HAQ-S (0-3), mean (SD)	0.59 (0.62)	0.82 (0.65)	< 0.01
EQ VAS (0-100), mean (SD)	66.2 (22.2)	61.1 (22.4)	< 0.01
WPAI domains, mean (SD)			
Current employment, n/m (%)	206/304 (67.8)	121/189 (64.0)	0.39
% Work time missed	6.7 (18.4)	7.3 (17.4)	0.33
% Impairment while working	24.9 (23.8)	35.4 (28.5)	< 0.01
% Overall work impairment	28.4 (27.1)	36.4 (28.6)	0.03
% Activity impairment	36.1 (29.7)	45.9 (30.0)	< 0.01

ASDAS, Ankylosing Spondylitis Disease Activity Score; AxSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Functional Index; EQ VAS, EuroQol visual analogue scale; HAQ-S, Health Assessment Questionnaire for the Spondyloarthropathies; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment questionnaire.
* All values were calculated based on available data. All variables had < 20% missing data except ASDAS (available for 302 patients), CRP (available for 320 patients), and ESR (available for 307 patients).

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Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8, Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8; **M. Liu**, Corrona, LLC, 3; **S. Rebello**, Corrona, LLC, 3; **R. McLean**, Corrona, LLC, 3; **B. Dube**, Corrona, LLC, 3; **M. Glynn**, Corrona, LLC, 3; **E. Yi**, Novartis, 3, Novartis Pharmaceuticals Corporation, 3; **Y. Park**, Novartis, 3; **A. Ogdie**, AbbVie, 5, 8, Amgen, 2, 5, 8, BMS, 5, Celgene, 5, 8, Corrona, LLC, 5, Lilly, 5, National Psoriasis Foundation, 2, NIH/NIAMS, 2, Novartis, 2, 5, 7, Pfizer, 2, 5, Rheumatology Research Foundation, 2, Takeda, 5.

Abstract Number: 0603

Are the Modified New York and ASAS Criteria Interchangeable in the Classification of Patients with Spondyloarthritis with Radiographic Sacroiliitis?

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Table 1 Classification of patients with axial spondyloarthritis with radiographic sacroiliitis using the modified New York criteria for the classification of AS, and the ASAS criteria for the classification of radiographic axSpA.

Modified New York criteria for the classification of AS	ASAS criteria for the classification of radiographic axSpA
1. Low back pain and stiffness for at least 3 months, which improves with exercise and is not relieved by rest 2. Limitation of lumbar spine motion in the sagittal and frontal planes 3. Decreased chest expansion, compared to age- and sex-matched controls 4a. Unilateral sacroiliitis grade 3 or 4 4b. Bilateral sacroiliitis grade 2 to 4	1. Back pain ≥3 months 2. Age at onset <45 years 3. Definite radiographic sacroiliitis according to mNY criteria 4. ≥1 SpA feature: – Inflammatory back pain – Arthritis – Enthesitis – Uveitis – Dactylitis – Psoriasis – Crohn's/colitis – Good response to NSAIDs – Family history for SpA – HLA-B27 positive – Elevated CRP (or ESR)
Definite AS if sacroiliitis as described in 4a or 4b and any of the clinical symptoms (1-3)	Definite r-axSpA if fulfilment of 1 and 2, sacroiliitis as described in 3 and at least one of the clinical SpA features as described in 4

Background/Purpose: Patients with axial spondyloarthritis (axSpA) with radiographic sacroiliitis may be classified using the modified New York (mNY) criteria as ankylosing spondylitis and using the more recent ASAS criteria as radiographic axSpA (r-axSpA).

In both the mNY and the ASAS r-axSpA classification sets the radiographic criterion is the same but the additionally required features differ (Table 1). The aim of this study was therefore, to investigate if patients who fulfil the mNY criteria also fulfil the ASAS criteria for r-axSpA and vice-versa.

Methods: Patients diagnosed with axSpA who had back pain > 3 months and definite radiographic sacroiliitis according to the mNY radiographic criterion (#4a or 4b in Table 1), were selected from eight cohorts (ASAS, Esperanza, GESPIC, OASIS, Reuma.pt, SCQM, SPACE, and UCSF axSpA cohort). Subsequently we calculated the percentage of patients who fulfil the ASAS r-axSpA criteria within the group of patients fulfilling the mNY criteria. In six cohorts (all except Esperanza and OASIS) we were also able to calculate the percentage of patients fulfilling the mNY criteria within the group fulfilling the ASAS r-axSpA criteria.

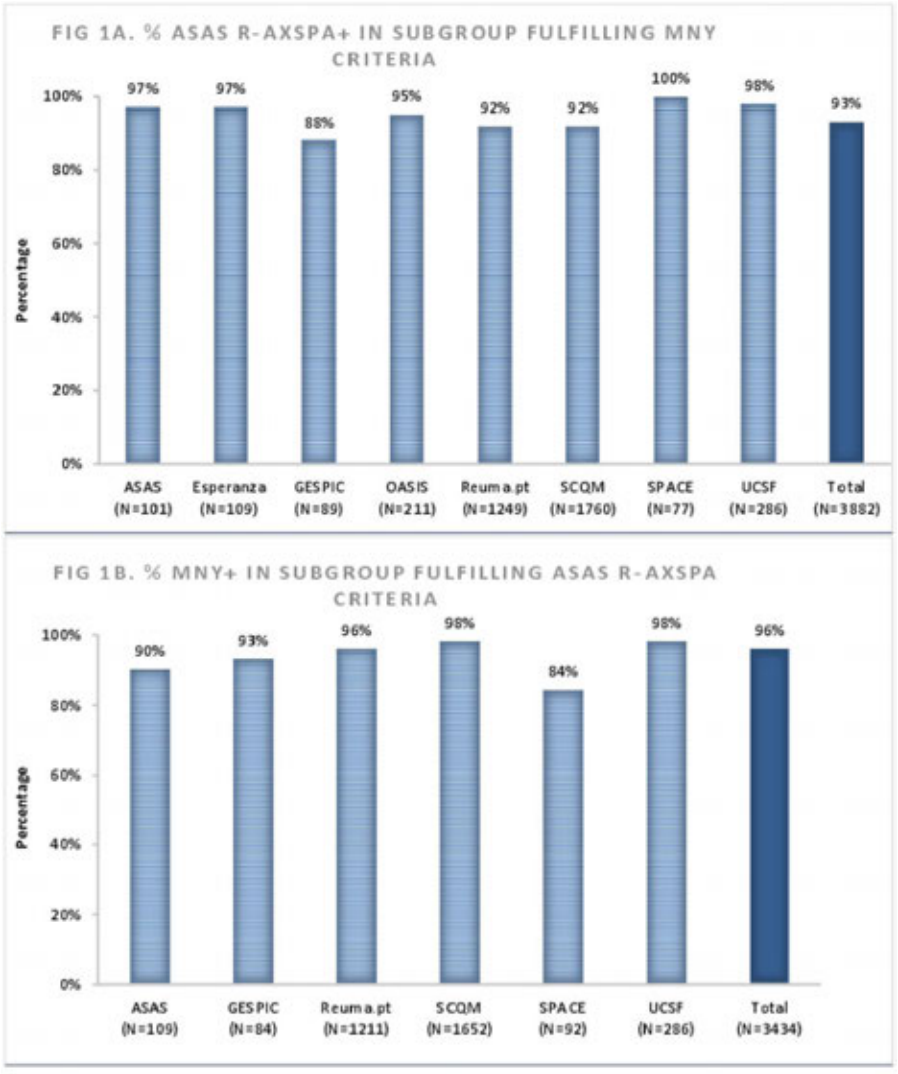

Figure 1: Percentage of patients fulfilling ASAS r-axSpA within subgroup fulfilling mNY criteria (3607/3882 (1a) and percentage of patients fulfilling mNY criteria within subgroup fulfilling ASAS r-axSpA (3300/3434)(1b), per cohort and overall.

Results: Of the 3,882 patients fulfilling the mNY criteria, 93% also fulfilled the ASAS r-axSpA criteria (Figure 1a). Inversely, of the 3,434 patients fulfilling the ASAS r-axSpA criteria, 96% also fulfilled the mNY criteria (Figure 1b). In total, 89% (3607/4041) of patients fulfilled both criteria sets; 7% only the mNY criteria; 3% only the ASAS criteria and 1% neither set.

The main difference between the two criteria sets was caused by reported age at onset of back pain. Out of 275 mNY+ patients not fulfilling the ASAS criteria, 265 (96%) cases were due to the age criterion and 10 (4%) due to the absence of SpA features. The 134 mNY-/ASAS+ patients did not have mobility restriction or IBP but at least one other SpA feature instead.

Conclusion: Agreement between the mNY and ASAS r-axSpA criteria is very high, with mostly the same patients being classified according to both criteria, which supports the interchangeable use of the terms AS and r-axSpA. This has important implications for the axSpA research field, since acknowledging that both criteria sets identify the same patients implies that older literature on AS and newer literature on r-axSpA can be directly compared.

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Abstract Number: 0604

Do Illness Perceptions and Coping Change over Time in Patients Recently Diagnosed with Axial Spondyloarthritis? A 2-Year Follow-Up Study in the SPACE Cohort

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: We have previously shown that in patients with recently diagnosed axial SpA (axSpA), illness perceptions had a negative impact on the relationship between back pain and Health-Related Quality of Life (HRQoL) and work productivity loss (WPL). We investigated if illness perceptions and coping strategies change after axSpA diagnosis.

Methods: Patients recently diagnosed with axSpA and ≥1 follow-up visit (1 year and/or 2 years) in the SPACE-cohort were included in the analysis. Mixed linear models were used to test if illness perceptions (measured by the Revised

Table 1 Overview of illness perceptions and coping strategies measured by the IPQ-R and CORS questionnaires

Label/Dimension	Explanation	Example
Illness perceptions		
Identity	Summed number of experienced symptoms that the patient attributes to his/her illness	Symptoms as *"pain"* or *"fatigue"*
Consequences	Perceived impact of the illness on the patient's life	*"My illness has major consequences on my life"*
Acute/chronic timeline	Perceived likeliness of chronicity of the illness	*"My illness is likely to be permanent/chronic rather than temporary"*
Personal control	Perceived personal control over the illness	*"There is a lot which I can do to control my symptoms"*
Treatment control	Perceived efficacy of treatment	*"My treatment will be effective in curing my illness"*
Illness coherence	Extent to which the patient feels he/she understand the illness	*"My illness is a mystery to me"*
Cyclical timeline	Patient's perceptions of variability of the illness	*"My symptoms come and go in cycles"*
Emotional representation	Experienced negative emotions due to the illness	*"When I think about my illness I get upset/angry/afraid"*
Psychological attributions	Believing that psychological attributions are a possible cause for the illness	*"Stress/worry or my mental attitude e.g. thinking about life negatively "*
Risk factors	Believing that risk factors are a possible cause for the illness	*"Hereditary – it runs in my family"*
Immunity	Believing that immunity is a possible cause for the illness	*"A germ or virus"*
Accident	Believing that accident is a possible cause for the illness	*"Accident or injury"*
Chance	Believing that chance is a possible cause for the illness	*"Chance or bad luck"*
Coping		
Comforting cognitions	Coping with pain by putting pain in perspective	*"I think the pain will decrease in time"*
Decreasing activities	Coping with pain by decreasing activities	*"I stop my activities"*
Diverting attention	Coping with pain by thinking about/focusing on something else	*"I think of pleasant things"*
Optimism	Coping with limitations by being optimistic	*"I try to be optimistic"*
Pacing	Coping with limitations by adapting/lowering the level of activity	*"I take more time for my activities"*
Creative solution seeking	Coping with limitations by searching for creative solutions to cope with limitations in daily life	*"I try to find new ways of getting things done"*
Accepting	Coping with dependence by making efforts to accept the level of dependence	*"I accept my dependence on other people"*
Showing consideration	Coping with dependence by considering other people's feelings	*"I try not to ask too much from any one person"*

CORS, Coping with Rheumatic Stressors; IPQ-R, Revised Illness Perception Questionnaire.

Table 2 Illness perceptions over time in axSpA patients with baseline and/or 1- or 2-years data in the SPACE cohort (n=150)

Dimension	Range	Baseline	Year 1	Year 2	Change per year (B (95%CI))
Identity	0-15				
Age <29 years		4.6 (2.3)	4.6 (2.5)	4.1 (2.0)	-0.3 (-0.5; 0.02)
Age ≥29 years		4.9 (2.6)	5.3 (2.8)	5.1 (2.7)	0.09 (-0.2; 0.4)
Consequences	1-5	2.9 (0.7)	2.8 (0.8)	2.8 (0.9)	-0.09 (-0.2; -0.03)
Timeline (acute/chronic)	1-5				
Age <29 years		3.7 (0.8)	3.7 (0.8)	3.7 (0.8)	0.05 (-0.06; 0.2)
Age ≥29 years		3.6 (0.8)	3.8 (0.8)	4.0 (0.7)	**0.2 (0.08; 0.3)**
Personal control	1-5	3.3 (0.6)	3.3 (0.6)	3.4 (0.6)	0.06 (0.008; 0.1)
Treatment control	1-5	3.5 (0.5)	3.4 (0.6)	3.5 (0.6)	0.01 (-0.04; 0.07)
Illness coherence	1-5	3.3 (0.8)	3.5 (0.8)	3.6 (0.7)	**0.2 (0.1; 0.2)**
Timeline (cyclical)	1-5	3.6 (0.8)	3.6 (0.8)	3.6 (0.8)	-0.04 (-0.1; 0.04)
Emotional representation	1-5	2.7 (0.8)	2.6 (0.8)	2.5 (0.8)	**-0.1 (-0.2; -0.08)**
Possible causes for illness					
Psychological attributions	1-5	2.1 (0.9)	2.1 (0.9)	2.1 (0.9)	-0.005 (-0.06; 0.05)
Risk factors	1-5	2.2 (0.6)	2.2 (0.6)	2.1 (0.6)	-0.01 (-0.06; 0.03)
Immunity	1-5	2.3 (0.8)	2.4 (0.9)	2.3 (0.9)	-0.03 (-0.1; 0.04)
Accident	1-5				
Male		2.3 (1.2)	2.1 (1.1)	2.0 (1.1)	-0.2 (-0.3; -0.04)
Female		1.8 (1.0)	2.1 (1.2)	1.9 (1.1)	0.07 (-0.07; 0.2)
Chance	1-5	3.3 (1.2)	3.2 (1.2)	3.3 (1.2)	-0.02 (-0.1; 0.08)

Results are presented as mean (SD) unless stated otherwise. Changes in illness perceptions were considered to be statistically significant and printed in bold when p<0.002 (p<0.05/21 (illness perceptions and coping strategies combined), correction for multiple testing).

Illness Perception Questionnaire (IPQ-R), **Table 1**) and coping (Coping with Rheumatic Stressors (CORS), **Table 1**) as well as back pain (scale 0-10), HRQoL (physical (PCS) and mental component summary (MCS), scale 0-100, 36-item Short-Form Health Survey (SF-36)), WPL and activity impairment (Work Productivity and Activity Impairment (WPAI, range 0-100%)), changed over time. Results were stratified for gender and age when the interaction term was statistically significant (p< 0.10).

Results: In total, 150 axSpA patients (mean age 30.4 years, 51% female, 65% HLA-B27+) were analysed. At baseline mean back pain (SD) was 4.0 (2.5), PCS was 28.8 (14.0), MCS was 46.6 (13.6), WPL was 34.1% (29.8) and activity

Table 3 Coping strategies over time in axSpA patients with baseline and/or 1- or 2-years data in the SPACE cohort (n=150)

	Range	Baseline	Year 1	Year 2	Change per year (B (95%CI))
Coping with pain					
Comforting cognitions	1-4	2.8 (0.6)	2.9 (0.6)	2.8 (0.6)	0.01 (-0.04; 0.06)
Decreasing activities	1-4	2.1 (0.6)	2.1 (0.6)	2.0 (0.6)	-0.05 (-0.1; -0.008)
Diverting attention	1-4	2.3 (0.6)	2.4 (0.6)	2.4 (0.6)	0.03 (-0.02; 0.07)
Coping with limitations					
Optimism	1-4	2.8 (0.7)	2.9 (0.7)	2.9 (0.7)	0.08 (0.02; 0.1)
Pacing	1-4				
Male		2.1 (0.6)	2.1 (0.6)	2.0 (0.6)	-0.05 (-0.1; 0.006)
Female		2.2 (0.6)	2.3 (0.6)	2.4 (0.6)	0.08 (0.007; 0.2)
Creative solution seeking	1-4				
Male		2.3 (0.6)	2.4 (0.6)	2.3 (0.07)	0.01 (-0.05; 0.07)
Female		2.3 (0.6)	2.4 (0.6)	2.6 (0.06)	**0.1 (0.07; 0.2)**
Coping with dependency					
Accepting	1-4	1.8 (0.6)	1.8 (0.6)	1.7 (0.6)	-0.03 (-0.09; 0.02)
Consideration	1-4	2.7 (0.6)	2.7 (0.6)	2.7 (0.6)	0.004 (-0.05; 0.06)

Results are presented as mean (SD) unless stated otherwise. Changes in coping strategies were considered to be statistically significant and printed in bold when p<0.002 (p<0.05/21 (illness perceptions and coping strategies combined), correction for multiple testing).

impairment was 38.7% (27.9). Over two years, the percentage patients with ASDAS inactive or low disease activity increased from 39% to 68%, back pain (mean change ± SD is -1.5 ± 2.2) and activity impairment (-14.4% ± 27.2) decreased, PCS (11.1 ± 13.3) and WPL (-15.3% ± 28.7) improved statistically significantly (all $p< 0.05$), but MCS did not change (0.7 ± 13.9, $p=0.201$).

Illness perceptions and coping strategies showed little and no clinically meaningful change over time (**Table 2, 3**). Over two years patients remained having negative illness perceptions (which were important in the association between back pain and health outcomes in the previous study). For example, at two years patients strongly believed that their illness had severe consequences ('*consequences*'), they had negative emotions such as feeling upset or having fear towards their illness ('*emotional representation*'), and had strong beliefs in chance or bad luck ('*chance*') being the cause for axSpA.

Patients most often coped with pain by putting pain in perspective ('*comforting cognitions*'), most often coped with limitations by trying to be optimistic ('*optimism*'), and most often coped with dependence of other people by considering feelings of these people ('*consideration*').

Conclusion: Whilst back pain, disease activity, and health outcomes clearly improved over 2 years, illness perceptions about their illness and coping strategies to live with their illness remained remarkably stable in patients recently diagnosed with axSpA.

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Abstract Number: 0605

Macrophage Migration Inhibitory Factor Is a Critical Regulator in a Mouse Model of Spondyloarthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Spondyloarthritis (SpA) is a chronic rheumatic disease characterized by severe inflammation in the spine, peripheral joints, intestine, skin and eyes. Although current treatment modalities including tumor-necrosis-factor (TNF) and interleukin (IL)-17 blockers could control inflammation, up to 40% of SpA patients don't adequately response to any medications or lose their efficacies, resulting in severe pain, increased cardiovascular risk and deteriorating mental health. Macrophage migration inhibitory factor (MIF) is a pleiotropic cytokine that exhibits pro-inflammatory effects. MIF has functions in the regulation of immune responses and has been implicated in various inflammatory conditions. We recently discovered that serum levels of MIF were significantly elevated in Ankylosing Spondylitis (AS) patients compared to healthy controls. However, the specific role of MIF in SpA is largely unknown.

Methods: Curdlan (β-glucan) or MIF-plasmid (mini-circle) treated SKG mice (8-10 weeks) were used as SpA mouse models. The expression of MIF in serum or tissues was measured by ELISA, quantitative PCR (qPCR), western blotting, immunohistochemistry (IHC) and/or immunofluorescence (IF). MIF knockout (KO) SKG mice were generated as MIF deficiency mice. MIF inhibitor (MIF098) was used to block the function of MIF in SpA mouse models to assess the therapeutic or prophylactic effects in a curdlan-treated SpA mouse model. Populations of immunological cells were assessed by flow cytometry. Anti-Gr-1 monoclonal antibody (mAb) or isotype control mAb was used to block the function of polymorphonuclear myeloid-derived suppressor cells (PMN-MDSCs) or monocytic MDSCs (mMDSCs). Clinical scores, histopathology and microCT imaging were used to assess the severity of inflammation in the various tissues of the mouse models.

Results: The expression of MIF and its receptor CD74 were significantly up-regulated in serum, spleen, ileum, sacroiliac and ankle joints of curdlan-treated SKG mice. MIF-overexpressed SKG mice injected with MIF-plasmid remarkably induced major SpA clinical features including colitis, psoriasis and arthritis in the axial and peripheral joints, while MIFKO SKG mice or blocking the function of MIF with MIF inhibitor (MIF098) dramatically suppressed or attenuated these manifestations, with decreased populations of Th17 and increased regulatory T (Treg) cells. We have also identified the cell populations (PMN-MDSCs and mMDSCs) substantially producing MIF in the disease condition. Interestingly, adopted transfer of these cells into non-disease control mice clearly exhibits SpA phenotype including arthritis, blepharitis and psoriasis. Furthermore, blocking the function of those cells with anti-Gr-1 antibody suppresses the SpA phenotype.

Conclusion: These results indicate that MIF is a crucial regulator of inflammation and may be a promising therapeutic target in SpA.

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Abstract Number: 0606

Effectiveness of TNFi After a First Switch in Patients with Early Axial Spondyloarthritis: A Longitudinal Analysis of the DESIR Cohort

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

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Session Time: 9:00AM–11:00AM

Background/Purpose: Contradictory data has been reported on the effectiveness of a second and third line of TNFi in early axial spondyloarthritis (axSpA). The objective of the study was to evaluate the effectiveness of TNFi after a first switch, in real life conditions, over 5 years of follow-up in this population.

Methods: Observational prospective French cohort (DESIR) with 5 years of follow-up, including 708 TNFi-naïve early axSpA patients. Study visits were scheduled every 6 months in the first two years and then yearly up to 5 years. Treatment (TNFi or other) was at the discretion of the treating rheumatologist's. The characteristics of patients who received a second and a third TNFi were compared to those who never switched. Effectiveness of the first, second and third TNFi was firstly defined by their drug survival, estimated by the Kaplan-Meier method, and compared with the log-rank test. Secondly, we evaluated treatment effect of the second TNFi by the probability to reach an ASAS40 response in both groups (second TNFi vs. responders to the first TNFi), after at least 10months of exposure. To overcome prescriptions bias repeatedly occurring over time, we have applied an iterative method based on inverse propensity score (PS) weighting using a marginal structural model, that allows the integration of the repeated weights derived from the propensity score at each visit (i.e the probability to receive the treatment at each visit). The structural model used for this analysis was a PS-weighted cox regression, to estimate the probability to present an ASAS40 response after at least 10months of treatment.

Results: of the 708 patients included in the analysis, 258 (36.4%) patients initiated a first TNFi during the 5y of follow-up. Of these, 127/258 (49.2%) switched to a second TNFi, and among them, 59/127 (46.5%) switched to a third TNFi. Patients who switched to a second or a third TNFi were more frequently older, predominantly females, HLA-B27 negative, with MRI and radiographic sacroiliitis negative, without history of peripheral arthritis, and with higher BASFI and BASDAI scores at baseline of the DESIR cohort (see table). Estimated median drug survival for the first, second

Baseline characteristics	Patients remaining in their first TNFi	Patients switching to a 2nd TNFi	Patients switching to a 3rd TNFi
	N=88	N=127	N=59
Age (years)	33.6(9.4)	35.3(8.7)	35.4(8.5)
Sex (male)	52(59.1)	40(31.5)	17(28.8)
HLA-B27 positive	57(64.8)	62(48.8)	26(44.1)
MRI sacroiliitis positive	46/85(55.1)	39/125(31.2)	16/57(28.1)
Radiographic sacroiliitis positive	27/85(31.8)	17(13.4)	9(15.3)
History of arthritis	31(35.2)	37/125(29.6)	17/58(29.3)
BASDAI (range 0-10)	4.5(1.8)	5.9(1.5)	6.0(1.4)
BASFI (range 0-10)	3.1(2.1)	4.6(2.1)	4.8(2.1)

and third TNFi was 21.7months [95%CI 17.6-33.6], 18.8months [95%CI 15.1-24.4] and 25.0months [95%CI 11.8-NA] respectively. Drug survival was significantly extended for the first TNFi compared to the second one (p=0.004), but no differences were observed between the 2nd and the 3rd TNFi. Identically, when taking into account the time-varying propension to perform a switch, likelihood of an ASAS40 response was lower for the second TNFi than for the first one (HR=2.4[95%CI 1.9-3.0] vs HR=3.3[95%CI 2.9-3.8] respectively), but remained clinically significant.

Conclusion: Our study suggests a lower but clinically significant TNFi effectiveness after a first switch in real-life conditions in early axial spondyloarthritis.

switch

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Abstract Number: 0607

Expansion of Peripheral Cytotoxic T Cells in Co-morbid Inflammatory Bowel Disease and Spondyloarthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: The clinical overlap of axial spondyloarthritis (axSpA) and Crohn's disease (CD) has given rise to the hypothesis that these conditions may share pathophysiologic mechanisms. However, the relationship between each of these diseases and the "overlapping" condition of co-morbid CD and axSpA (OVR) remains unknown. Here, we sought to address this question by an initial unbiased immune profiling in the peripheral blood of individuals with axSpA, CD, and OVR relative to healthy controls (HC) using single-cell RNA sequencing followed by validation of potential cellular populations with flow cytometry.

Methods: Peripheral blood was collected from 71 subjects (18 HC, 26 CD, 17 axSpA, and 10 OVR) and peripheral blood mononuclear cells (PBMCs) isolated. Viable CD45+ PBMCs from two representative male patients in each group were isolated by flow sorting and underwent high-depth single-cell RNA sequencing (10X Genomics). Significance with respect to change in transcript abundance was set at $P < 10^{-6}$. Validation of findings was then performed by flow cytometry using PBMCs from the full cohort of 71 subjects. Flow data was analyzed in FloJo and GraphPad Prism, and significance was determined by Mann-Whitney-U test at $P < 0.05$.

Results: Single cell RNA sequencing demonstrated an expansion of CD27+ Granzyme B+ memory (CD45RA-) T cells in our patients with axSpA and OVR. However, in CD, we observed an expansion of a similar memory T cell population expressing the innate-like T cell transcription factor PLZF, which we hypothesized to be gd T cells. B cell and monocyte populations in all disease groups had increased expression of genes within antigen presentation, inflammasome, and apoptotic pathways. Together, our sequencing data suggested upregulated cytolytic activity in

the peripheral blood of individuals with axSpA, CD, and OVR patients. In order to validate these findings in our larger cohort, we utilized flow cytometry to interrogate the cytotoxic T cell population. We observed an increase in gd T cells in CD relative to HCs ($P < 0.005$). In OVR, we saw a significantly decreased naïve T cell compartment ($P< 0.005$) compared to HC, CD, and axSpA, with a corresponding increase in effector memory (CCR7- CD45RA-) T cells ($P < 0.005$). The proportion of CD4 T cells bearing markers of cytotoxicity (Granzyme B+, NKG2a+) was significantly ($P< 0.05$) increased in OVR compared to HC, CD, and axSpA. The overall proportion of cytotoxic CD4s as fraction of total PBMCs in OVR was 1.3%, more than triple that found in the other groups ($P< 0.05$).

Conclusion: Altogether, our data suggest that the immunologic profile of individuals with OVR are distinct from both CD and axSpA. Specifically, we demonstrate an expansion of cytotoxic T cells in OVR relative to HC, CD, and axSpA, and the absence of the gd T cell expansion seen in CD. Given the association between cytotoxic CD4+ T cells and Th1 responses, these data may indicate a shift away from the Th17 dominant disease process found in axSpA. Future directions will validate these findings in an independent cohort of subjects as well as focus on elucidating the functional relevance of cytotoxic CD4 T cells in the pathophysiology of overlapping CD-axSpA.

Disclosure: A. Lefferts, None; **E. Regner**, None; **A. Stahly**, None; **R. O'Rourke**, None; **K. Jones**, None; **K. Kuhn**, None.

Abstract Number: 0608

Prevalence of Radiographic Entheseal Lesions at the Hip and Pelvic Region in Patients with Ankylosing Spondylitis versus Controls

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesitis is one of the features of ankylosing spondylitis (AS). High prevalence of structural and inflammatory ultrasound lesions of peripheral entheses are found in AS patients. Furthermore, plain radiographs provide good imaging of peripheral enthesopathy at well-defined skeletal sites[1]. There are several entheseal sites at the pelvis and hip region, but little is known about the presence of structural entheseal anomalies at these sites in AS. Our aim was to investigate the prevalence of radiographic entheseal lesions at the hip and pelvic region in patients with AS compared to control subjects.

Methods: The present analysis was performed in 214 patients from the Groningen Leeuwarden Axial SpA (GLAS) cohort study and 100 control subjects. The AS patients were included between November 2004 and December 2010 and had available anteroposterior (AP) pelvis radiographs at baseline. All patients fulfilled the modified New York criteria for AS. AP pelvis radiographs from control subjects matched for age and gender were obtained from the radiology department of the University Medical Center Groningen (UMCG).

Radiographs with blinded sacroiliac joints were randomized and scored by two trained readers. Anomalies with absolute agreement were reported. The entheseal sites scored were: trochanter major, trochanter minor, os ischium, crista iliaca, both left and right side and symphysis pubis. The following 3 anomalies were scored: cortical irregularities/erosions, calcifications and enthesophytes.

Results: Of the 214 AS patients, 148 (69%) were male, mean age was 42.5 ± 11.6 years, 171 (80%) were HLA-B27 positive and median symptom duration was 16 years (IQR 8-24). Patients had active disease with BASDAI 5.6 ± 1.9 and ASDAScrp 3.5 ± 0.9. Reader agreement on the entheseal lesions was overall moderate with Cohen's kappa between 0.42 and 0.78.

Radiographic entheseal lesions at the hip and pelvic region were found in 160 (75%) patients and 58 (58%) controls. In total, 602 lesions were found of which 478 (80%) were present in AS patients. For both groups, the most prevalent lesion was irregularity/erosion (n=333 in 150 (70%) AS patients and n=85 in 50 (50%) controls), followed by enthesophytes (n=129 in 64 (30%) AS patients and n=37 in 21 (21%) controls). In both AS patients and controls, most lesions were found at the os ischii (n=275 in 138 (65%) AS patients and n=97 in 53 (53%) controls).

Conclusion: Radiographic entheseal lesions at the hip and pelvic region are more prevalent in AS patients compared to controls. Irregularities and erosions were most frequently found in both groups, especially at the os ischium. These new findings concerning structural entheseal lesions at the pelvis and hip region contributes to the knowledge of entheseal involvement in AS.

Disclosure: F. Wink, Abbvie, 2, 5, Pfizer, 2, 5, UCB, 2; **T. Diemel**, None; **S. Arends**, Pfizer, 2; **A. Spoorenberg**, Pfizer, 2, 5, Abbvie, 2, 5, UCB, 2.

Abstract Number: 0609

Baseline Characteristics and Natural History of Radiographic versus Non-radiographic Axial Spondyloarthritis: 5 Years Follow-up of the Desir Cohort

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: There is still a debate concerning the concept of non-radiographic (nr-axSpA) axial Spondyloarthritis (e.g. to consider it as a distinct entity from r-axSpA (Ankylosing Spondylitis) or to consider it as the same disease with different phenotypical presentations). This study aims to compare clinical manifestations and burden of disease between r-axSpA and nr-axSpA over 5 years of follow-up in the DESIR cohort.

Methods: Patients from the DESIR cohort with x-ray sacroiliac joints available at baseline and who did not abandon the study because of different diagnosis than axSpA were included. A unilateral rating of "obvious sacroiliitis" according to the local reader (either a radiologist or a rheumatologist) was considered sufficient to be classified as r-axSpA. The incidence of a new episode of peripheral and extra-rheumatological manifestations between r-axSpA vs. nr-axSpA was assessed using incidence/100 person-years, incidence rate ratio and cox regressions adjusted for sex, age and TNF blockers (TNFb) intake. Mean values of c-reactive protein (CRP), patient reported outcomes (PROs) and days of sick leave over 5 years of follow-up were assessed using mixed models with random effects adjusted for sex, age, TNFb intake and baseline values. Disease-modifying drugs (DMARDs) initiation were also evaluated adjusted for CRP mean levels.

Table 1. Prevalence and incidence of peripheral and extra-rheumatological manifestations. *p-value <0.05 between r-axSpA and nr-axSpA

		Prevalence at baseline		Prevalence after 5 years of follow-up		Incidence/100 person-years		
Handling missing data		Without imputation		LOCF and imputed "0" at baseline		LOCF and excluding patients with positive event at baseline		
		Per group	Whole population	Per group	Whole population	Per group	Whole population	Incidence rate ratio (95%CI)
Peripheral arthritis (ever)	r-axSpA	51/185 (27.6%)	183/664 (27.6%)	66/185 (35.7%)	264/669 (39.5%)	2.40	3.70	0.57 (0.33-0.99)*
	nr-axSpA	132/479 (27.6%)		198/484 (40.9%)		4.22		
Peripheral enthesitis (any)	r-axSpA	88/185 (47.6%)*	379/669 (56.7%)	124/185 (67.9%)*	493/669 (73.7%)	9.60	10.54	0.87 (0.58-1.29)
	nr-axSpA	291/484 (60.1%)		369/484 (76.2%)		11.05		
Dactylitis	r-axSpA	25/185 (13.5%)	95/666 (14.3%)	36/185 (19.5%)	146/669 (21.8%)	1.44	1.87	0.70 (0.36-1.37)
	nr-axSpA	70/481 (14.6%)		110/484 (22.7%)		2.03		
Uveitis	r-axSpA	22/185 (12.0%)	62/669 (9.3%)	35/185 (18.9%)*	96/669 (14.3%)	1.65	1.15	1.70 (0.85-3.39)
	nr-axSpA	40/484 (8.3%)		61/484 (12.6%)		0.97		
Inflammatory bowel disease	r-axSpA	14/185 (7.57%)	34/669 (5.1%)	23/185 (12.4%)	60/669 (9.0%)	1.08	0.84	1.45 (0.64-3.25)
	nr-axSpA	20/484 (4.13%)		37/484 (7.6%)		0.75		
Psoriasis	r-axSpA	29/185 (15.67%)	115/669 (17.2%)	46/185 (24.9%)	164/669 (24.5%)	2.30	1.85	1.37 (1.76-2.47)
	nr-axSpA	86/484 (17.77%)		118/484 (24.4%)		1.68		

Table 2. Mixed model with random effects to compare burden of disease over 5 years of follow up. Mean (SD) represent the mean value over 5 years of follow-up.

	Whole population N = 669 mean (SD)	r-axSpA N = 185 mean (SD)	nr-axSpA N = 484 mean (SD)	Crude p-value	p-value adjusted for baseline value	p-value adjusted for age, sex and baseline value	p-value adjusted for TNFb and baseline value	p-value adjusted for age, sex, TNFb and baseline value
BASDAI	36.64 (21.65)	30.91 (20.90)	38.92 (21.52)	**<0.001**	**<0.001**	**0.011**	**0.006**	0.130
BASFI	24.55 (22.03)	20.74 (20.28)	20.06 (22.50)	**0.002**	**0.004**	0.087	**0.018**	0.236
ASDAS	2.24 (0.94)	2.16 (0.96)	2.27 (0.93)	0.072	**0.003**	0.081	**0.028**	0.351
CRP	5.63 (10.22)	7.69 (13.38)	4.80 (8.49)	**<0.001**	**0.001**	**<0.001**	**<0.001**	**<0.001**
SF-36 MCS	43.30 (11.29)	44.66 (11.20)	42.76 (11.28)	**0.016**	0.148	0.447	0.269	0.662
SF-36 PCS	42.26 (9.42)	44.10 (8.59)	41.53 (9.63)	**<0.001**	**0.003**	0.109	**0.011**	0.214
Days of sick leave	21.74 (61.11)	14.88 (45.46)	24.32 (65.87)	**0.009**	0.082	0.462	0.072	0.424

Results: In total 669 patients were included, of whom 185 (27.7%) and 484 (72.3%) were classified as r-axSpA and nr-axSpA, respectively. At baseline, r-axSpA patients showed significant higher prevalence of males (59.5% vs. 41.7%), smokers (44.0% vs. 34.2%), lower prevalence of peripheral enthesitis (47.6% vs. 60.1%) and lower mean age (31.3±8.9 vs. 34.5±8.4 years) than nr-axSpA. Table 1 shows baseline and 5 years-follow up prevalence, as well as the incidence of new cases of peripheral and extra-rheumatological manifestations. Only peripheral arthritis showed significant lower incidence among r-axSpA patients (2.40 vs. 4.22 new cases/100 person-years, incidence rate ratio 0.57 (95%CI 0.33-0.99)). However, adjusting for age, sex and TFNb intake, cox regressions did not show significant differences in the development of peripheral and extra-rheumatological manifestations between the two groups. Crude mixed models (Table 2) showed significant higher disease activity (BASDAI), poorer quality of life (SF-36 questionnaire) and higher mean days of sick leave over time among nr-axSpA patients. However, these differences disappeared when adjusting for confounders (see Table 2). r-axSpA group showed significant higher incidence of TNFb

initiation (14.77 vs. 9.26 new first prescriptions/100 person-years) than nr-axSpA group, with a HR of 1.56 (95%CI 1.17-2.06) adjusted for sex, age and CRP mean levels.

Conclusion: r-axSpA and nr-axSpA patients showed minor differences at baseline. However, they seem to behave similarly over time, since the incidence of peripheral and extra-rheumatological manifestations as well as the burden of disease development remained similar when adjusted for confounders. Only peripheral arthritis seemed to be more incident among nr-axSpA group, while TNFb was most frequently used by r-axSpA patients.

Disclosure: C. López-Medina, None; **A. Moltó**, None; **P. Claudepierre**, Janssen, 8; **M. Dougados**, AbbVie, 2, 5, 8, Amgen, 5, Biogen, 5, BMS, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, Merck, 2, 5, Merck Inc, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 0610

Ankylosing Spondylitis-associated Killer Immunoglobin-like Receptors Are Strongly Expressed on γδ T Cells

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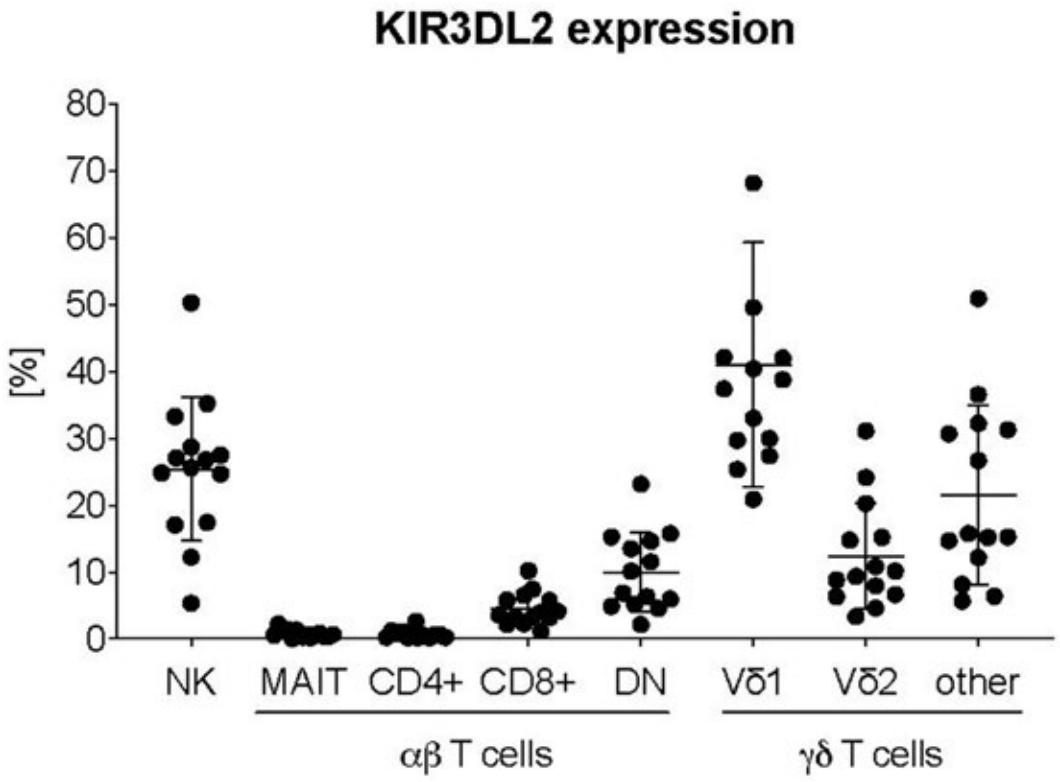
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The mechanism underlying the association between ankylosing spondylitis (AS) and HLA-B27 is still unknown. One of the hypotheses involves the interaction of HLA-B27 homodimers with KIR3DL2 receptors on CD4+ T cells. KIR3DL2 is a member of the killer immunoglobin-like receptor (KIR) family of MHC class I ligands that transmit activating or inhibitory signals to KIR expressing lymphocytes. KIR3DL2 binds to HLA-B27 homodimers whereas KIR3DL1 interacts with native HLA-B27 complexes. Previous work has shown an expansion of KIR3DL2 positive IL-17A producing CD4+ T cells in HLA-B27 positive patients with AS. Multiple other IL-17A producing lymphocyte subsets including γδ T cells have been implicated in AS pathogenesis. The purpose of this study was to further characterize the expression of KIR3DL2 and KIR3DL1 on these lymphocyte subsets.

Methods: Human peripheral blood mononuclear cells (PBMC) were prepared by Ficoll density gradient centrifugation from the blood of healthy individuals. To measure cytokine production, PBMC were stimulated with PMA/ionomycin for 4 hours in the presence of brefeldin A/monensin followed by intracellular staining. In other experiments, PBMC were stimulated with phytohemagglutinin (PHA) for up to 3 days in medium supplemented with IL-2 and IL-7. Cells were analyzed using a 19-parameter flow cytometry panel that distinguishes natural killer (NK) cells, mucosal-associated invariant T (MAIT) cells, CD4+ T cells, CD8+ T cells, CD4-CD8- DN αβ T cells and γδ T cells further subdivided into Vδ1+, Vδ2+ and other γδ T cells. MAIT cells were identified using MR1 tetramers. Lineage markers were combined with antibodies specific for relevant KIRs and cytokines. Flow cytometric analysis was performed using a 5-laser BD LSRFortessa cytometer and FlowJo software.

Results: KIR3DL2 and KIR3DL1 were variably expressed by all lymphocyte subsets analyzed. The highest frequencies of KIR expressing cells were observed for NK and γδ T cells, in particular Vδ1 cells. Only a small fraction of CD4+ T cells stained positive for KIR3DL2 in our cohort of healthy individuals. The highest frequency of IL-17A secreting cells was observed amongst MAIT and CD4+ T cells. When stratified based on KIR3DL2 expression, IL-17A expres-



KIR3DL2 Expression on Lymphocyte Subsets in Peripheral Blood of Healthy Individuals

sion was enriched in KIR3DL2+ cells in most subsets, regardless of whether the blood was from HLA-B27+ or HLA-B27- subjects. γδ and other T cells but not NK cells upregulated KIR3DL2 and KIR3DL1 upon stimulation with PHA in vitro.

Conclusion: AS-associated KIRs (KIR3DL2, KIR3DL1) are strongly expressed on γδ T cells in healthy individuals and further upregulated upon stimulation. Our data suggest that studies testing the KIR hypothesis for the HLA-B27 association of AS should consider a wider spectrum of KIR expressing lymphocytes including γδ T cells.

Disclosure: M. Lefton, None; **N. Sharma**, None; **J. Ermann**, Boehringer Ingelheim, 2, Eli Lilly, 5, Novartis, 5, Pfizer, 2, UCB, 5.

Abstract Number: 0611

Retina of Ankylosing Spondylitis Patients Shows Early Signs of Atherosclerotic Disease in Comparison with Healthy Controls

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
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Background/Purpose: Chronic systemic inflammation in patients with ankylosing spondylitis (AS) contributes to the development of cardiovascular disease (CVD). Early recognition of microvascular changes could improve prevention. The retinal vasculature has been proven to reflect systemic (micro)vascular changes. Narrowing of retinal arterioles, widening of retinal venules and decreased vascular density are associated with coronary artery disease. Furthermore, systemic inflammation was reported to result in wider retinal venules. Remarkably, studies in AS patients are lacking, while the retinal vasculature is easily accessible and could provide an opportunity to recognize preclinical CVD. This study compared the retinal microvasculature of AS patients to healthy controls, and its association with cardiovascular risk.

Methods: Cross-sectional case-control study comparing AS patients with healthy controls from a cohort of the Dutch Twins Register.(1) Inclusion criteria were: age 50-75 years and no history of diabetes mellitus or cerebrovascular disease. AS patients fulfilled the modified New York criteria. Controls with an auto-inflammatory disease were excluded. Consecutive AS patients were recruited from the Rheumatology outpatient clinic of Reade and Amsterdam UMC (VUmc). Controls were selected from the pre-existing EMIF-AD PreClinAD cohort.(1) All subjects underwent Optical Coherence Tomography Angiography (OCTA) and fundus photography, analyzed with Singapore I Vessel Assessment software (Table 1). Data on patient- and disease characteristics, CVD risk factors, medication and lipids were collected. For subjects without a previous CVD, the 10 years cardiovascular comorbidity/mortality risk was calculated (Systematic Coronary Risk Evaluation, SCORE). Data were evaluated with linear regression, correcting for age when comparing patients and controls. The association between the SCORE and ocular parameters was assessed stratified for patients and controls.

Results: In total, 57 AS patients (51% women) and 56 controls (50% women) were included. Both groups differed significantly in mean age (AS: 60±SD6 years; Controls 68±SD4; p< 0.01, Table 2). Fundus photo parameters (Table 1), in particular retinal arteriole and venule diameter, did not differ between patients and controls. However, patients showed significantly lower retinal vessel density (OCTA) compared to controls (age-corrected Beta: -0.53, p=0.046). Only in AS patients, lower retinal vessel density (p=0.02), arteriole fractal dimension; (p=.04) and arteriole diameter (p=.02) were associated with a higher cardiovascular risk (SCORE), but not in controls.

Conclusion: This study did not find differences in arteriolar and venular diameter between AS patients and controls. However, it is the first to report a significantly decreased retinal vessel density in AS patients, which was associated

Table 1 Overview ocular vascular parameters

Fundus photo with Singapore I Vessel Assessment (SIVA) assessment
Central retinal **artery caliber size**
Central retinal **vein caliber size**
Ratio of the central retinal **artery and vein**
Fractal dimension of **arteriolar** network
Fractal dimension of **venular** network
Curvature **tortuosity arterioles**
Curvature **tortuosity venules**
Optical Coherence Tomography Angiography (OCTA)
Vessel density of the macular region

Table 2. Patient characteristics

	Ankylosing Spondylitis (AS) (n = 57)	Control (n=56)	*P*
Gender, women (%)	29 (51)	28 (50)	ns
Age, yrs	60 ±6	68 ±4	<0.01
Smoking currently	11 (19)	2 (4)	0.02
Smoking previously	22 (39)	31 (55)	
Body mass index	26 ±4	26 ±3	ns
Cardiovascular history:			
Hypertension	24 (42)	24 (43)	ns
Dyslipidemia	18 (32)	21 (38)	ns
Coronary disease (PCI)	6 (11)	5 (9)	ns
Peripheral artery disease	1 (2)	3 (5)	ns
SCORE 10 yrs risk morbidity/mortality*	12 ±10	17 ±9	0.01
Current treatment			
NSAIDS	33 (58)	0 (0)	<0.01
TNF inhibitor	26 (74)	0 (0)	<0.01
Cardiovascular medication**	25 (44)	23 (41)	ns
Cholesterol lowering medication	10 (18)	11 (20)	ns
ASs disease characteristics			
Disease duration, yrs with symptoms	36 ±11	.	
HLA-B27 positive	42 (74)	.	
AS disease activity (ASDAS)-score	2.1 ±0.9	.	

Legend: Values are reported as numbers (% of total), mean (±standard deviation, SD) or median (1st and 3rd quartile, Q1-Q3). NSAIDs, nonsteroidal anti-inflammatory drugs; RHI, reactive hyperemia index; TNF inhibitor, Tumor necrosis factor inhibitor. *SCORE applicable/available in AS patients n=38, Control patients n=46. **Medication to control blood pressure or cardiac rhythm

with a higher cardiovascular risk. Therefore, decreased vascular density might be an early sign of preclinical cardiovascular disease in AS patients.

Reference:

1. Konijnenberg E et al. The EMIF-AD PreclinAD study: study design and baseline cohort overview. Alzheimers Res Ther. 2018; 10:75.

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Abstract Number: 0612

Objective Ankylosing Spondylitis Physical Performance Index (ASPI) Is Highly Reliable and Feasible in Chilean Patients

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SESSION INFORMATION

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Background/Purpose: In axial spondyloarthritis (axSpA), preservation of physical functioning is an important treatment goal and is usually assessed with the patient-reported BASFI questionnaire. The Ankylosing Spondylitis Physical performance Index (ASPI) test is the first test that assesses physical functioning in axSpA patients with a performance measure (1). However, the ASPI has only been validated in the Netherlands and the interobserver reliability was never evaluated. This study assessed the reliability (interobserver, test-retest) and feasibility of the ASPI test in axSpA patients in Chile.

Methods: The original Dutch ASPI patient instructions were translated into Spanish through a forward-backward procedure by 4 bilingual speakers (2 native Spanish, 2 native Dutch). Radiographic (r-axSpA) and non-radiographic (nr-axSpA) patients, fulfilling the ASAS classification criteria, ≥18 years old, were eligible for study participation. The ASPI consists of 3 tests: 1) 'picking up 6 pencils one by one', 2) 'putting on socks', and 3) 'getting up from the floor'. (1) For each test the performance time was recorded (ASPI; seconds), as well as the patient-reported test-related pain (numeric rating scale, 0-10) and exertion (Borg-scale, 0-10). For test 2 and 3, the mean of three repetitions was calculated. To assess feasibility the total ASPI duration was recorded from the start of instructions until the end of the last test. At baseline, the ASPI was done twice in all patients, by two observers. Test-retest (intra-observer) reliability was done within 1-3 weeks after baseline. In addition, disease characteristics, current treatment, BASDAI, ASDAS, BASFI, CRP, ESR and spinal mobility (BASMI score) were collected. For reliability analyses intra class correlation

Table 1. Patient characteristics (n = 68)

		T_0 (n = 68)
Gender, women		29 (43)
Private health care, %		29 (43)
Radiographic axSpA		35 (52)
Age, yrs		44 ±12
Disease duration[I], yrs		11 (6-22)
HLA-B27 positive[II] *		33 (49)
Extra-axial manifestations		49 (72)
Current treatment	NSAIDs	43 (63)
	DMARD	32 (47)
	Biologic	27 (40)
BASMI linear score		3.6 (2.8-4.8)
ASDAS-score		2.9 ±1.2
BASDAI score, nrs		5.0 ±2.5
High disease activity[III]		46 (68)
BASFI score, nrs		4.1 ±2.8

Legend: Values are reported as numbers (% of total), mean (±standard deviation, SD) or median (1st and 3d quartile, Q1-Q3). I: years with symptoms. II: 24 (35%) HLA-B27 negative, 11 (16%) unknown. III: ASDAS≥2.1 or, if unavailable, BASDAI≥4.

ASDAS, AS disease activity score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; DMARD, disease modifying anti-rheumatic drug; HLA-B27, Human Leukocyte Antigen B27; NSAIDs, nonsteroidal anti-inflammatory drugs. * Prevalence of HLA-B27 gene in Chile: 2-3%.

Table 2. ASPI test results T0 (baseline) and T1 (retest visit)

	T_0 Observer 1	T_1*[1]
	(n= 68)	(n= 39)
All tests performed, no of patients	56 (82)	32 (82)
≥1 test performed	68 (100)	39 (100)
Duration ASPI-test, minutes	9 ±3	7 ±2
ASPI test overall score		
1] Bending (pick up pencils), patients	66 (97)	38 (97)
ASPI, sec:hs	20:89 (15:69-37:13)	18:59 (15:73-31:41)
Pain, nrs	3 (0-6)	1 (0-5)
Exertion, nrs	4 ±2	3.3 ±2.4
2] Putting on socks, patients	67 (99)	39 (100)
ASPI, sec:hs	14:65 (10:15-21:63)	13:27 (09:38-19:52)
Pain, nrs	1 (0-4)	1 (0-5)
Exertion, nrs	3 ±2	3 ±2
3] Getting up from the floor, patients	62 (91)	33 (85)
ASPI, sec:hs	04:60 (03:70-08:17)	04:76 (03:54-06:34)
Pain, nrs	2 (0-4)	2 (0-5)
Exertion, nrs	3 ±2	3 ±2

Legend: Values are reported as numbers (% of total), mean (±standard deviation, SD) or median (1st and 3rd quartile, Q1-Q3). *: T_1 was performed 7 (7-14) days after T_0. Hs, hundredths; NRS, numeric rating scale; sec, seconds.

Table 3 ASPI interobserver- and test-retest agreement

		ASPI time		Patient experience during ASPI			
				Exertion		Pain	
	n =	ICC	95% CI	ICC	95% CI	Kappa*	95% CI
[1] Picking up pencils							
Interobserver	61	**0.90**	0.85 – 0.94	**0.84**	0.75 – 0.90	**0.73**	0.64 – 0.82
Test-retest	38	**0.89**	0.75 – 0.94	**0.79**	0.63 – 0.88	**0.61**	0.44 – 0.75
[2] Putting on socks							
Interobserver	60	**0.88**	0.81 – 0.93	**0.91**	0.85 – 0.94	**0.81**	0.75 – 0.87
Test-retest	39	**0.90**	0.68 – 0.96	**0.80**	0.65 – 0.89	**0.63**	0.50 – 0.77
[3] Getting up from the floor							
Interobserver	56	**0.98**	0.96 – 0.99	**0.88**	0.81 – 0.93	**0.75**	0.65 – 0.83
Test-retest	33	**0.96**	0.91 – 0.98	**0.78**	0.61 – 0.89	**0.53**	0.33 – 0.71

Legend: Interobserver- and test-retest agreement of the ASPI performance time and pain and exertion during test performance. ICC, Intra-class Correlation Coefficient; CI, confidence interval. *weighted Kappa

coefficients (ICC absolute agreement) or weighted kappa (for nonparametric variables) were reported with 95% confidence intervals (95%CI).

Results: Sixty-eight patients were included (43% female, aged 44 (SD 12) years, 52% r-axSpA; Table 1). Interobserver and test-retest reliability were tested in respectively 61 and 39 patients. At baseline, the mean ASPI duration was 9 (SD 3) minutes, and 82% was capable of performing all tests (Table 2). The ASPI interobserver and test-retest (intra-rater) reliability were respectively good to excellent (ICC 95%CI: 0.81-0.99; Table 3) and moderate to excellent (ICC 95% CI: 0.68 - 0.98), for all tests. The pain and exertion during the ASPI showed lower reliability (poor to good).

Conclusion: This study is the first to perform the ASPI in non-Dutch- and also nr-axSpA patients. Despite high disease activity and differences in treatment access between patients in Chile, the ASPI was highly feasible. Importantly, the ASPI had high interobserver and test-retest reliability. The test-retest reliability was even somewhat higher than

reported previously. Therefore, the ASPI appears appropriate for objective evaluation of physical functioning in Latin American axSpA patients.

Reference:

1. van Weely SF. Objective evaluation of physical functioning after tumor necrosis factor inhibitory therapy in patients with ankylosing spondylitis: a selection of 3 feasible performance-based tests. J Rheumatol. 2015;42(4):623-9.

Disclosure: R. van Bentum, None; **S. Ibáñez Vodnizza**, None; **F. Valenzuela Aldridge**, None; **M. Poblete**, None; **S. van weely**, None; **M. ter Wee**, None; **O. Valenzuela**, None; **I. van der Horst-Bruinsma**, None.

Abstract Number: 0613

Can Fecal Calprotectin Predict Future Development of Inflammatory Bowel Disease in Axial Spondyloarthritis Patients? - TReasure Real-Life Preliminary Data

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Table 1. Demographic and clinical findings according to fecal calprotectin levels in axSpA patients.

Findings	Fecal calprotectin level		p
	<200 µg/g	≥200 µg/g	
Age, year, median (Q1-Q3)	41 (31-49)	48 (39-54)	0.023
BMI, median (Q1-Q3)	26.59 (23.59-28.97)	30.35 (26.3-32.66)	0.005
Sex, female, n (%)	39 (34.2)	7 (30.4)	0.727
Disease duration, year, median (Q1-Q3)	9.4 (4.9-13.9)	8.9 (5.0-16.0)	0.909
BASDAI, median (Q1-Q3)	2.2 (0.9-3.6)	2.3 (1.2-3.6)	0.731
BASFI, median (Q1-Q3)	1.4 (0.4-3.4)	2.2 (0.2-3)	0.823
Patient global-VAS, median (Q1-Q3)	20 (10-40)	35 (20-50)	0.051
Pain-VAS, median (Q1-Q3)	20 (10-40)	25 (10-50)	0.700
Fatigue-VAS, median (Q1-Q3)	20 (10-50)	35 (10-40)	0.494
ASDAS-ESR, median (Q1-Q3)	1.78 (1.31-2.3)	1.51 (1.31-1.82)	0.158
ASDAS-CRP, median (Q1-Q3)	1.72 (1.28-2.37)	1.6 (1.25-1.95)	0.342
ESR, mm/h, median (Q1-Q3)	12 (7-25)	11 (4-18)	0.350
CRP, mg/dL, median (Q1-Q3)	4 (1.14-8)	2.92 (1-4.9)	0.286

Background/Purpose: Inflammatory bowel disease (IBD) is frequently seen in patients with axial spondyloarthritis (axSpA). This study aimed to investigate whether fecal calprotectin levels could predict future development of IBD in axSpA patients.

Methods: This multicenter, prospective observational cohort study used the TReasure database in which web-based registration of rheumatoid arthritis (RA) and SpA patients are being performed in 15 centers across different regions of Turkey. Fecal calprotectin levels were measured in 137 axSpA patients as of September 2018. Fecal calprotectin level ≥200 µg/g was considered significant. All study subjects were evaluated for IBD symptoms (loose defecation, mucous diarrhea, bloody defecation, bloody diarrhea, abdominal pain, obstruction, or pseudo-obstruction). Patients who had previous IBD diagnosis or who used NSAIDs at least 2 weeks before fecal calprotectin measurement were excluded. It was planned to examine patients for IBD by control visits at every 3 months for 1 year. In this paper, preliminary results of the patients were presented.

For axSpA patients, disease activity was evaluated by the ASDAS CRP, BASDAI, *BASFI*, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), visual analog scale (VAS)-pain, VAS-fatigue, and tender and swollen joint count. Moreover, 24 healthy volunteers and 25 RA patients were included as a control group.

Results: This study included 137 axSpA patients (33.6% females) with the median (Q1-Q3) age of 43 years (33-50 years) and median (Q1-Q3) disease duration of 8.9 years (5.0-13.9 years). Among 24 RA patients (79.2% females), the median (Q1-Q3) age was 59 years (48-64 years) and the median (Q1-Q3) disease duration was 10.6 years (8.1-18.6 years). Rheumatoid factor was positive in 79% of the RA patients. The median (Q1-Q3) fecal calprotectin level was 48 µg/g (30-122 µg/g) in axSpA patients. The median fecal calprotectin level was ≥200 µg/g in 23/137 (16.8%) axSpA patients and in 15/24 (62.5%) RA patients. Fecal calprotectin levels were not high in any healthy volunteers. The axSpA patients with calprotectin level of ≥200 µg/g were older [48 years (39-54 years) vs. 41 years (31-49 years); p=0.025] and had higher BMI values [30.3 (26.3-32.7) vs. 26.6 (23.5-29.0); p=0.003]. Disease activity levels of the patients at baseline are given in Table 1; there was no difference regarding fecal calprotectin level. In the axSpA patients, RA patients, and healthy controls, while the rates of abdominal pain were 5.8% (n=8), 16.5% (n=4), and 8% (n=2), respectively and the rates of loose defecation were 5.1% (n=7), 12.5% (n=3), and 4% (n=1), respectively, none of the patients had mucous diarrhea, bloody diarrhea, and obstruction.

Conclusion: In the present study, preliminary results for the fact that whether or not fecal calprotectin levels could predict future development of IBD were presented. Fecal calprotectin levels were higher in 15% of the asymptomatic axSpA patients; the follow-up results of these patients may give information about daily practice.

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Abstract Number: 0614

Tapering of Tumor Necrosis Factor Inhibitor and Healthcare Cost Differences in Patients with Ankylosing Spondylitis: A Retrospective Analysis of Korean National Health Insurance Data

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Tapering of tumor necrosis factor (TNF) inhibitors may be considered in patients with ankylosing spondylitis (AS) with low disease activity. However, there is still a lack of evidence that TNF inhibitors can be safely tapered and maintained with low medical costs. The aim of this study was to analyze the pattern of tapering of each TNF inhibitor and to evaluate the reduction of healthcare costs due to tapering of TNF inhibitors in patients with AS using an insurance claims database.

Methods: Data was obtained from an insurance claims database of the Health Insurance Review & Assessment Service in South Korea. Patients with AS who initiated TNF inhibitors such as etanercept, adalimumab, golimumab, and infliximab between July 1, 2013 to June 30, 2016 were enrolled. Among them, patients treated with TNF inhibitors for more than 2 years were included. Tapering of the TNF inhibitor was defined as a reduction of 50% or more of the recommended dose. We compared the rate of tapering and the time to 50% reduction of recommended dose between each TNF inhibitor. In addition, the implication of tapering on healthcare costs related to AS based on whether patients were subjected to a tapering dose was analyzed.

Table 1. Tapering in patients who persist TNF inhibitor

	2-year of follow-up (n=764)				
	ADL	ETN	GLM	IFX	P-value
	264	145	188	167	
Standard weekly dose (mg)†	20	50	12.5	44.38††	
Tapering					
Percentage of patients, n (%)	58 (21.97)	36 (24.83)	22 (11.70)	20 (11.98)	**0.0028***
Index weekly dose (mg)					
mean (SD)	17.31 (5.25)	37.92 (13.52)	11.22 (1.88)	25.69 (9.75)	
median (IQR)	18.67 (15.56-19.31)	43.75 (24.56-48.28)	11.67 (10.94-12.07)	24.15 (21.54-29.87)	
Reduced weekly dose (%)					
mean (SD)	11.62 (1.89)	30.23 (5.94)	7.16 (0.96)	25.64 (3.72)	
mean percentage (%)	58.10	60.45	57.32	58.35	0.8673*
median (IQR)	10.87 (10.18-14.72)	27.95 (25.44-32.79)	7.16 (6.36-7.57)	24.61 (22.50-27.74)	
Time to tapering (days)					
mean (SD)	365.02 (192.36)	297.44 (219.11)	448.59 (157.14)	380.6 (121.78)	**0.0294****
median (IQR)	377 (169-518)	193 (121.5-482.5)	443 (332-596)	387.5 (256-503)	**0.0224*****

†: Refered from Ministry of Food and Drug Safety drug approval documents, ††: Reflected average weights for Korean; * Chi-square test, ** ANOVA test, *** Kruskal-wallis test, SD: Standard deviation; IQR: Interquartile range

Table 2. AS related healthcare costs associated with tapering in patients who persist TNF inhibitor (Unit: $)

Cost category	Tapering		Non tapering		P-value*
	Adjusted Mean†	(Exponentiated range)	Adjusted Mean†	(Exponentiated range)	
Adalimumab, n	**58**		**206**		
TNF inhibitor costs	12,678	(12,035-13,357)	17,179	(16,565-17,816)	**<0.0001**
Other drug costs	615	(453-835)	642	(520-792)	0.7538
Other medical costs	704	(553-895)	729	(618-862)	0.7394
Total costs	14,026	(13,278-14,815)	18,665	(17,965-19,392)	**<0.0001**
Etanercept, n	**36**		**109**		
TNF inhibitor costs	11,143	(10,326-12,025)	16,441	(15,442-17,505)	**<0.0001**
Other drug costs	671	(435-1,035)	837	(599-1,169)	0.3274
Other medical costs	698	(532-913)	849	(691-1,044)	0.1294
Total costs	12,566	(11,592-13,622)	18,424	(17,247-19,680)	**<0.0001**
Golimumab, n	**22**		**166**		
TNF inhibitor costs	12,386	(11,497-13,343)	16,347	(15,489-17,251)	**<0.0001**
Other drug costs	184	(106-318)	381	(258-560)	**0.0013**
Other medical costs	461	(296-716)	796	(579-1,093)	**0.0019**
Total costs	13,001	(11,896-14,208)	17,651	(16,553-18,821)	**<0.0001**
Infliximab, n	**20**		**147**		
TNF inhibitor costs	8,774	(7,799-9,870)	13,899	(12,991-14,869)	**<0.0001**
Other drug costs	685	(435-1,077)	902	(699-1,164)	0.2252
Other medical costs	687	(500-945)	910	(756-1,094)	0.0365
Total costs	10,207	(9,051-11,511)	15,830	(14,776-16,961)	**<0.0001**

† Adjusted for Age, Sex, CCI; * Using generalized linear models

Results: A total of 1,352 patients were included in the study. Among them, 264 patients were continuously treated with adalimumab, 145 patients with etanercept, 188 patients with golimumab, and 167 patients with infliximab (Table 1). Of these, tapering of TNF inhibitors was more frequently observed in 58 (22.0%) patients on adalimumab and 36 (24.83%) on etanercept compared to 22 (11.7%) on golimumab and 20 (12.0%) on infliximab (p=0.0028). The mean time to 50% reduction was shorter in etanercept (297.4 ± 219.1 days) compared to adalimumab (365.0 ± 192.36 days), golimumab (448.59 ± 157.14 days), and infliximab (380.6 ± 121.78 days) (p=0.0294). The costs of TNF inhibitors was the highest among all AS-related healthcare costs. In addition, tapering significantly reduced AS-related total costs for all TNF inhibitors (Table 2).

Conclusion: TNF inhibitors with short intervals tended to be more frequently tapered in patients with AS. Tapering of TNF inhibitors may also help reduce healthcare costs related to AS.

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Abstract Number: 0615

Effects of NSAIDs and TNF Inhibitors on Cardiovascular Events in Ankylosing Spondylitis: A Systematic Review and Meta-Analysis

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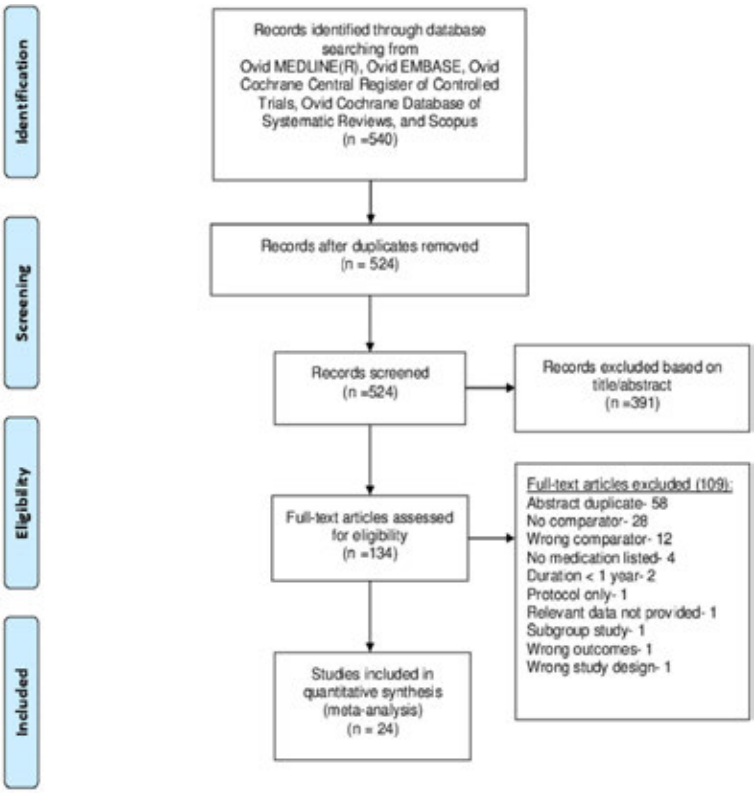

Figure 1. Flow chart describing systematic search and study selection process

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Most studies show a significantly higher risk of myocardial infarction [MI] (odds ratio [OR] = 1.60) and stroke (OR = 1.50) in ankylosing spondylitis (AS) patients. Whether therapies targeted at controlling inflammation may potentially reduce the risk of cardiovascular events (CVE) in AS, is not well understood. While NSAIDs are known to be associated with an increased risk of CVE in the general population, whether the anti-inflammatory effects of NSAIDs reduce or modify CVE risk in AS is controversial. It is also unclear if CVE risk is reduced by TNF inhibitors (TNFi), which has been shown in rheumatoid arthritis (RA). We aimed to perform a systematic review and meta-analysis to explore the association between NSAIDs, TNFi and CVE in AS.

Methods: We conducted a comprehensive search of several databases from inception to January 16, 2019. We included studies of patients with AS treated with NSAIDs, non-biological DMARDs or biologics, and had a control group. Outcomes of interest were all CVEs, myocardial infarction, stroke, congestive heart failure (CHF), and the composite outcome of major adverse cardiac events (MACE). Reported ORs and hazard ratios reported were converted to risk ratios (RR) using validated statistical formulae. Study specific RR were pooled using random-effects model (DerSimonian and Laird). Between-study heterogeneity was assessed using I^2 statistics.

Results: Nine nonrandomized studies from a total of 1,425 studies screened fulfilled the inclusion criteria (Figure 1). In NSAID users as a whole, no increased risk of CVE was noted; however, the risk of cerebrovascular accident (CVA)

Table 1. Baseline characteristics of the included studies

Author, Year	Study Design	AS definition	Events reported (definition)	Follow-up duration (years)	Treatment				Control			
					Drug	N	Female, %	Age, mean (SD)	Drug	N	Female, %	Age, mean (SD)
Essers, 2014	Retrospective, cohort study using Clinical Practice Research Datalink GOLG (CPRD)	Read Codes documented by GP	Incident IHD and acute MI (EMR)	15	COX-2 inhibitors Naproxen Other traditional NSAIDS Any NSAIDS	287 291 692 1233	29.61 29.21 25.72 27.57	-	No NSAIDs	3353 3349 2948 2407	29.88 29.92 30.83 31.03	
Kristensen, 2015	National register-based cohort study (Swedish National patient register)	ICD codes (Majority of patients were diagnosed and treated by rheumatologist)	Atherosclerotic cardiac/cerebrovascular events, congestive heart failure (ICD codes)	4 (2006-2009)	Etoricoxib Celecoxib Nonselective NSAID	1655 858 6292	51.8 51.2	Median 46 (interquartile range 35-57)	No NSAIDs	20217 21014 15580	47.9 48	Median 46 (interquartile range 35-57)
Tsai, 2015	Nationwide case control study (Taiwan National Health Insurance database)	At least 2 AS service claims or ambulatory/ inpatient care for further confirmation	All Incident CVD, CVA, MACE, CHF (ICD-9 codes)	3 (1997-2008 data)	All NSAIDs Non-selective NSAIDs Selective NSAIDs	-	-	-	No NSAIDs	-	-	-
Wu, 2016	Nationwide population-based case-control study (Taiwan National Health Insurance database)	ICD-9 codes	Coronary artery disease (ICD-9 codes)	Prevalent CAD cases (2001-2010)	Celecoxib Etoricoxib Naproxen Diclofenac	198 61 171 579	45.62	55.17 (14.64)	No NSAIDs	510 647 537 129	45.62	55.17 (14.64)
Dubreuil, 2018	Nested case control study UK THIN database	Read codes documented by the GP	Incident MI (first recording of MI read code)	21 (1994-2015)	Current Diclofenac Current naproxen Current other NSAID	22 17 50	30.3	62.76 (11.42)	No NSAIDs	148 153 120	30.3	62.76 (14.12)
Dubreuil (abstract), 2018	Nested case-control study (OptumLabs Data Warehouse)	Diagnostic code- AS dx after at least 6 months of Claims data prior to AS dx	Incident MI (Diagnostic codes)	23 (1994-2017)	NSAID TNFi	1282 ~89	48.9	59.1 (11.9)	No NSAID No TNFi	21967 23160	48.9	59.1 (11.9)
Lee, 2018	Prospective national cohort study (Australian Rheumatology	ICD-10 codes	All CVE (angina, MI, CABG, PCI, stroke/TIA)	15 (2001-2015)	NSAID TNFi	-	-	-	No NSAIDs No TNFi	-	-	-

was significantly lower (RR: 0.58, 95% CI 0.37 – 0.93, I^2=66%). Cox-2 inhibitor use was associated with reduced risk of all CVE (RR: 0.48, 95%CI 0.33 - 0.70, I^2= 0%) and CVA (RR: 0.58, 95% CI 0.37 - 0.93, I^2= 66%). Non selective NSAIDs did not show a significant association with risk of any CVE. There was only 1 study reporting all CVE with TNFi, which showed a slightly higher risk (RR: 1.60, 95%CI 1.05 - 2.41). Meta-analysis of 3 studies of MI specifically did not show a significant association with TNFi (RR: 0.88, 95%CI 0.57 - 1.35, I^2=76%). Only 1 study each reported risk of CHF and MACE, which were both low in all NSAID groups (Table 1). The certainty in evidence in all estimates was low due to the studies being nonrandomized.

Conclusion: This systematic review suggests that Cox-2 inhibitors in AS patients are associated with a lower risk of the composite CVE outcome and CVA, unlike their use in the general population. Similarly, NSAID users as a whole and users of non-selective NSAIDS did not have higher risk of any CVE. No significant association between TNFi and MI was observed. More studies are needed to study the association between TNFi use and CVE in general to evaluate a possible protective role in AS.

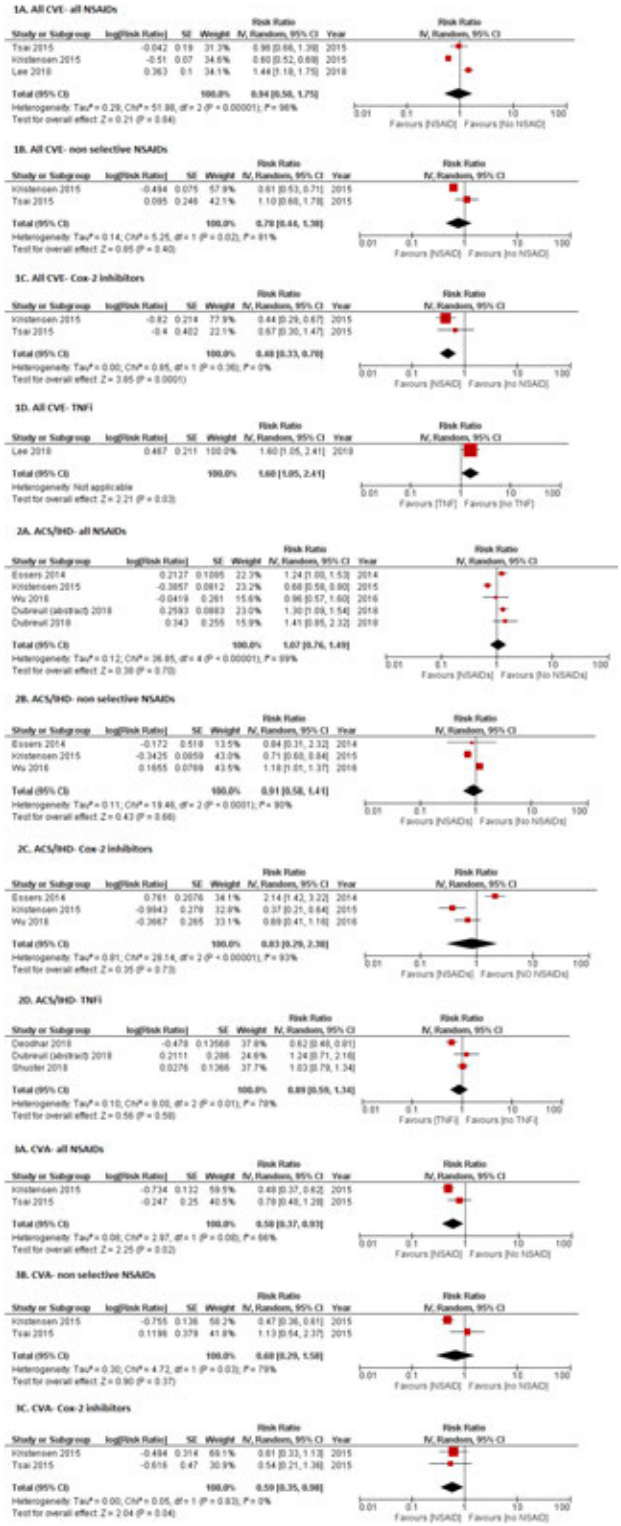

Figure 2. Forest plot of the risk of cardiovascular events with NSAIDs and TNF inhibitors in Ankylosing Spondylitis

Disclosure: P. Karmacharya, None; **R. Shahukhal**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo Bio-Science Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **M. Murad**, None; **P. shrestha**, None; **D. Bekele**, None; **K. Wright**, Pfizer, 2; **J. Davis**, Abbvie, 5, Pfizer, 2, 5, Sanofi Genzyme, 5; **M. Dubreuil**, None.

Abstract Number: 0616

Association of Clinical and Radiographic Phenotype of Axial Spondyloarthritis and Skin Psoriasis: Results from the German Spondyloarthritis Inception Cohort

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Table 1. Association between skin psoriasis and axial spondyloarthritis features.

Parameter (n (%) or mean±SD)	Psoriasis (n=28)	No psoriasis (n=182)	P*
Clinical characteristics and demographics			
Male sex	12 (42.9%)	95 (52.2%)	0.419
Age, BL	39.1 ± 10.7	37.0 ± 10.5	0.278
Age at symptom onset, years	33.9 ± 11.4	33.0 ± 10.8	0.63
Diagnostic delay, years	3.2 ± 2.1	2.6 ± 2.4	0.08
HLA-B27 positivity	16 (57.1%)	150 (82.9%)	**0.004**
Smoking	6 (21.4%)	65 (35.7%)	0.20
Inflammatory back pain, BL	25 (89.3%)	153 (84.1%)	0.58
Family history of SpA	15 (53.6%)	63 (34.6%)	0.06
Peripheral arthritis at baseline	7 (25%)	24 (13.2%)	0.15
Peripheral arthritis ever	16 (57.1%)	58 (31.9%)	**0.01**
Enthesitis at baseline	8 (28.6%)	38 (20.9%)	0.34
Inflammatory bowel disease, ever	1 (3.6%)	3 (1.6%)	0.44
Uveitis, ever	6 (21.4%)	36 (19.8%)	0.80
Disease activity			
BASDAI, BL	5.0 ± 2.2	3.8 ± 2.1	**0.01**
CRP mg/l, BL	10.1 ± 13.1	9.7 ± 15.6	0.84
Functional status			
BASFI, BL	3.8 ± 2.3	2.8 ± 2.3	**0.02**
BASMI, BL	2.1 ± 1.5	1.7 ± 1.7	0.07
Radiographic characteristics			
Fulfillment of the mNY-Criteria, BL	17 (60.7%)	98 (53.8%)	0.55
Sacroiliitis sum score, BL	4.1 ± 2.2	4.1 ± 2.0	0.95
Asymmetric sacroiliitis, BL (difference in by ≥1 sacroiliitis grade between the sides)	2 (7.1%)	17 (9.3%)	1.00
Mean mSASSS, BL	7.4 ± 12.1	3.8 ± 7.5	0.25
At least 1 syndesmophyte, BL	9 (32.1%)	55 (30.2%)	0.84
Treatment			
NSAID intake, BL	17 (60.7%)	123 (67.6%)	0.52
NSAID Index over 2 years of follow-up	43.6 ± 30.9	31.6 ± 27.1	0.06
DMARD intake, BL	16 (57.1%)	45 (24.7%)	**0.001**
TNFi intake over 2 years of follow-up	6 (21.4%)	16 (8.8%)	0.08
CS intake, BL	3 (10.7%)	9 (4.9%)	0.20

* Mann-Whitney U-Test for continuous variables, Fisher exact test for binary variables.

BL – baseline; HLA-B27 - Human leukocyte antigen B27; SpA – spondyloarthritis; BASDAI – Bath Ankylosing Spondylitis Disease Activity Index; CRP - C-reactive protein; BASFI – Bath Ankylosing Spondylitis Functional Index; BASMI – Bath Ankylosing Spondylitis Metrology Index; mNY Criteria – modified New York Criteria for Ankylosing Spondylitis, 1984; mSASSS - modified Stoke Ankylosing Spondylitis Spine Score; NSAID – non-steroid anti-inflammatory drugs, DMARD – disease-modifying anti-rheumatic drugs; TNFi – tumour necrosis factor α inhibitors; CS – corticosteroids.

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriasis is a common feature of axial spondyloarthritis (axSpA) occuring in approximately 10% of patients with axSpA. It has been presumed that such an association may be associated with a particular phenotype of the disease, which has not been extensively investigated so far. The purpose of the study was to analyze the association between clinical phenotype and radiographic progression and skin psoriasis in patients with axSpA.

Methods: Altogether 210 patients with axSpA (115 with radiographic and 95 with non-radiographic axSpA) were included in the analysis. Radiographs of the spine and sacroiliac joints (SIJ) were scored by two readers in a randomly selected order according to the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) and the grading system of the modified New York criteria. A sacroiliitis sum score was calculated as a sum of the grades for the left and right SIJ. Mann-Whitney analysis was performed for group comparisons. A multivariable regression analysis was performed to analyze the influence of of the psoriasis on radiographic progression.

Results: Overall, 28 patients (13.3%) with axSpA had skin psoriasis. Patients with psoriasis were less frequently HLA-B27 positive, had higher anamnestic prevalence of peripheral arthritis (16 (57.1%) vs. 58 (31.9%), p=0.01), higher disease activity (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 5.0 ± 2.2 and 3.8 ± 2.1, respectively, p=0.01) and worse physical function (Bath Ankylosing Spondylitis Functional Index (BASFI) 3.8 ± 2.3 and 2.8 ± 2.3, respectively, p=0.02) They were also more frequently treated with DMARDs. Baseline radiographic characteristics were comparable between the groups (*Table 1*). Radiographic progression was generally comparable between the groups. (*Table 2*). In a multivariable regression analysis (adjusted for the smoking status, sex, NSAID intake, presence of syndesmophytes at the baseline and time-averaged ASDAS), there was no significant association of psoriasis with radiographic progression in the spine (OR 2.93, 95% CI 0.81 to 10.58) or sacroiliac joints (OR 1.98, 95% CI 0.72 to 5.43).

Conclusion: Presence of skin psoriasis in patients with axSpA was associated with HLA-B27 negativity, peripheral arthritis, higher disease activity and worse functional status and did not impact the radiographic progression in axSpA.

Table 2. Association of skin psoriasis with radiographic progression in axial spondyloarthritis after 2 years of follow-up.

Outcome	Psoriasis (n=28)	No psoriasis (n=185)	p*
Spine			
mSASSS change	1.52 ± 4.02	0.61 ± 1.95	0.55
Progression of mSASSS by ≥2 points	6 (21.4%)	24 (13.2%)	0.25
New syndesmophytes or progression of syndesmophytes	7 (25.0%)	26 (14.3%)	0.16
Sacroiliac joints			
Change of the sacroiliitis sum score	0.18 ± 0.63	0.12 ± 0.87	0.71
Progression of sacroiliitis by at least 1 grade in opinion of both readers	3 (10.7%)	23 (12.6%)	1.00

* Mann-Whitney U-Test for continuous variables, Fisher Exact test for binary variables.

mSASSS - modified Stoke Ankylosing Spondylitis Spine Score.

Disclosure: M. Protopopov, MSD, 8, Novartis, 5, 8, Pfizer, 8; **F. Proft**, Abbvie, 5, 8, BMS, 8, MSD, 8, Novartis, 5, 8, Novartis Pharma, 2, Pfizer, 5, 8, Roche, 8, UCB, 5, 8; **J. Sieper**, AbbVie, 5, 8, Eli Lilly and Company, 5, 8, Janssen,

5, 8, Lilly, 5, 8, Merck, 5, 8, Novartis, 5, 8; **H. Haibel**, AbbVie, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8; **M. Rudwaleit**, Abbott, 5, AbbVie, 5, 8, BMS, 5, 8, Bristol Myers-Squibb, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Eli Lilly, 5, 8, Eli Lily, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB Pharma, 5, 8; **D. Poddubnyy**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 2, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8.

Abstract Number: 0617

Peripheral Involvement Is Associated with Less Radiographic Spinal Progression in Patients with Early Axial Spondyloarthritis: Results from the German Spondyloarthritis Inception Cohort

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SESSION INFORMATION
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Background/Purpose: Peripheral involvement (PI), such as arthritis, enthesitis, and dactylitis, is common in patients with axial spondyloarthritis (axSpA); data showing the influence of PI on radiographic progression of axSpA are controversial. The purpose of this study was to analyze the influence of PI on radiographic structural damage in patients with axSpA.

Methods: A total of 210 patients with axSpA (115 with radiographic and 95 with non-radiographic axSpA) were selected for this analysis. Radiographs of the spine were scored by two trained readers in a randomly selected order according to the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). Radiographs of the sacroiliac joint (SIJ) were scored according to the grading system of the modified New York criteria; a sacroiliitis sum score was calculated as a sum of the grades for the left and right SIJ. Mann-Whitney analysis was performed for group comparisons. A multivariable regression analysis was performed to analyze the influence of PI on radiographic spinal progression and progression of radiographic sacroiliitis.

Results: Overall, of the 101 (48.1%) patients with PI (documented history or current presence), 78 had peripheral arthritis, 48 had enthesitis, and 12 had dactylitis. 32 patients had more than 1 periferal manifestation. Patients with PI were older were less frequently human leukocyte antigen (HLA)-B27 positive, compared with patients with no PI (73 (73.0%) vs. 93 (85.3%), p=0.028), more frequently had family history for spondyloarthritis as well as psoriasis, had higher disease activity (time-averaged Ankylosing Spondylitis Disease Activity Score (ASDAS) over 2 years 2.6 ± 0.9 vs. 2.3 ± 0.9; p=0.032), worse physical function, higher exposure to disease modifying anti-rheumatic drugs and lower baseline radiographic sacroiliitis sum score. Patients with a documented history or current presence of PI had lower absolute progression in mSASSS after 2 years than those without (0.28 ± 1.39 vs 1.15 ± 2.9, p=0.045); 7.9% of patients with PI had a progression of mSASSS by ≥2 points compared to 20.2% in patients without PI (p=0.011) - **Table 1.**

Table 1. Characteristics of patients with axial spondyloarthritis with and without peripheral involvement

	Peripheral Involvement (n=101)	**Without Peripheral involvement (n=109)**	**P***
Male sex, n (%)	48 (47.5)	59 (54.1)	0.339
Age at BL, years	39.3 ± 10.5	35.4 ± 10.3	***0.002***
HLA-B27 positivity, n (%)	73 (73.0)	93 (85.3)	***0.028***
Smoking, n (%)	30 (29.7)	41 (37.6)	0.226
Inflammatory back pain BL, n (%)	87 (86.1)	91 (83.5)	0.593
Family history of SpA, n (%)	46 (45.5)	32 (29.4)	***0.015***
Psoriasis ever, n (%)	19 (18.8)	9 (8.3)	***0.025***
Inflammatory bowel disease ever, n (%)	2 (2.0)	2 (1.8)	0.660
Uveitis ever, n (%)	18 (17.8)	24 (22.0)	0.447
BASDAI, BL	4.6 ± 2.1	3.3 ± 1.9	***< 0.001***
Back pain, VAS (0-10)	5.7 ± 2.6	4.9 ± 2.3	***0.044***
CRP mg/l, BL	11.5 ± 19.4	8.1 ± 9.7	0.980
Time-averaged ASDAS over 2 years	2.6 ± 0.9	2.3 ± 0.9	***0.032***
BASFI, BL	3.5 ± 2.3	2.3 ± 2.2	***< 0.001***
BASMI BL, n (%)	1.8 ± 1.5	1.7 ± 1.7	0.242
NSAID intake BL, n (%)	72 (72.3)	67 (61.5)	0.097
NSAID Index over 2 years of follow-up	35.3 ± 29.5	31.3 ± 26.3	0.464
DMARD intake BL, n (%)	39 (38.6)	22 (20.2)	***0.003***
TNFi intake over 2 years of follow-up, n (%)	13 (12.9)	9 (8.3)	0.275
CS intake BL, n (%)	8 (7.9)	4 (3.7)	0.185
Fulfillment of the mNY-Criteria BL, n (%)	50 (49.5)	65 (59.6)	0.141
Sacroiliitis sum score, BL	3.8 ± 1.9	4.4 ± 2.1	***0.026***
Mean mSASSS, BL	3.08 ± 4.59	5.33 ± 10.58	0.783
At least 1 syndesmophyte BL, n (%)	28 (27.7)	36 (33.0)	0.404
mSASSS change score	0.28 ± 1.39	1.15 ± 2.9	***0.045***
Progression of mSASSS by ≥2 points	8 (7.9)	22 (20.2)	***0.011***
Change of the sacroiliitis sum score	0.07 ± 0.89	0.18 ± 0.79	0.433
Progression of sacroiliitis by at least 1 grade in opinion of both readers	11 (10.9)	15 (13.8)	0.528

* Mann-Whitney U-Test for continuous variables, X^2 test for binary variables.

ASDAS – Ankylosing Spondylitis Disease Activity Score; BASDAI – Bath Ankylosing Spondylitis Disease Activity Index; BASFI – Bath Ankylosing Spondylitis Functional Index; BASMI – Bath Ankylosing Spondylitis Metrology Index; BL – baseline; CRP – C-reactive protein; CS – corticosteroids; DMARD – disease-modifying anti-rheumatic drugs; HLA-B27 – human leukocyte antigen B27; mNY Criteria – modified New York Criteria for Ankylosing Spondylitis, 1984; mSASSS – modified Stoke Ankylosing Spondylitis Spine Score; NSAID – non-steroid anti-inflammatory drugs; SpA – spondyloarthritis; TNFi – tumour necrosis factor α inhibitors.

Table 2. Association of peripheral involvement with radiographic progression in axial spondyloarthritis after 2 years of follow-up.

Multivariable linear regression analysis	
Outcome	**β (95 %CI)**
mSASSS change score	**-0.98 (-1.68 to -0.28)***
Change of the sacroiliitis sum score	-0.06 (-0.32 to 0.20)**
Multivariable logistic regression analysis	
Outcome	**Odds ratio (95 %CI)**
Progression of mSASSS by ≥2 points	**0.33 (0.12 to 0.91)***
Progression of sacroiliitis by at least 1 grade in opinion of both readers	0.84 (0.33 to 2.09)**

mSASSS - modified Stoke Ankylosing Spondylitis Spine Score.

*Adjusted for the smoking status, HLA-B27 status, NSAIDs intake, baseline syndesmophytes, and time-averaged ASDAS.

**Adjusted for the smoking status, HLA-B27 status, NSAIDs intake, sacroiliitis sum score at baseline, and time-averaged ASDAS.

In a multivariable regression analysis, presence of PI was associated with a lower mSASSS progression and lower odds for the mSASSS progression by ≥2 points after 2 years: β=-0.98 (95% -1.68 to -0.28) OR=0.33 (95% CI 0.12 to 0.91), respectively - **Table 2**.

Conclusion: Presence of PI is associated with distinct characteristics of SpA including slower radiographic spinal progression which might be explained partly by the numerically lower mSASSS score at baseline.

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Abstract Number: 0618

Factors Associated with Complete Spinal Fusion in Patients with Ankylosing Spondylitis

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SESSION INFORMATION
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Background/Purpose: Most patients with ankylosing spondylitis (AS) do not develop complete spinal fusion. The purpose of this study was to compare patients with complete spinal fusion defined here as having a Modified Stoke Ankylosing Spondylitis Scoring System (mSASSS) of score of 72 (indicating complete fusion of the cervical and lumbar spine) versus those with no syndesmophyte formation (mSASSS=0) adjusted for disease duration.

Methods: Patient meeting modified New York Criteria for AS enrolled in a longitudinal study of outcome were included in this study. All films were scored for the modified Stoke Ankylosing Spondylitis Scoring System by the same musculoskeletal radiologist (TJL). Sociodemographic features, medication utilization, comorbidities, disease activity (BASDAI, ASDAS), functional impairment (BASFI), joint counts, metrology and enthesitis assessment was recorded, and HLA-B typing at baseline and C-reactive protein, and ESR obtained at each study visit. Pelvic, lumbar and cervical spine radiographs were obtained at baseline visit as well as every two years thereafter. Univariable logistic regression models were conducted to evaluate the factors that were associated with complete spinal fusion (mSASSS=72) compared with those with no radiographic stigmata of AS in the lumbar and cervical spine (mSASSS=0) after adjusting for study site and disease duration.

Table 1. Factors Associated with Spinal Fusion Based on Logistic Regression Model

variable	No spinal fusion n=308 (83.02%)	Complete spinal fusion n=63 (16.98%)	†adjusted Odds Ratio (95% CI)	p-value
Male, n(%)	60.7	93.7	**18.4 (4.45, 75.7)**	**<.0001**
Age**, mean(SD)	36.48 (11.11)	59.76 (11.16)	**1.12 (1.07, 1.17)**	**<.0001**
Age at disease onset, mean(SD)	22.57 (8.24)	24.97 (9.49)	**1.12 (1.07, 1.17)**	**<.0001**
HLA-B27 positive, (%)	83.6	84.1	0.52 (0.19, 1.45)	0.2107
Ever smoke at baseline, (%)	34.5	69.8	**2.03 (0.98, 4.22)**	**0.0572**
Current smoke at baseline, (%)	9.56	15.8	2.80 (0.98, 8.00)	0.0544
Race: White, (%)	79.2	76.2	**0.23 (0.09, 0.55)**	**0.0012**
Baseline BASFI, mean(SD)	25.18 (22.64)	58.57 (26.09)	**1.04 (1.03, 1.06)**	**<.0001**
Employed for compensation (%)	43.8	22.2	**0.31 (0.14, 0.71)**	**0.0051**
Family history of AS (%)	20.5	7.27	**0.08 (0.02, 0.35)**	**0.0008**
First available BASDAI, mean(SD)	3.83 (2.46)	4.56 (2.46)	1.08 (0.91, 1.28)	0.3749
First available CRP, mean(SD)	0.73 (1.34)	1.79 (2.58)	**1.45 (1.19, 1.76)**	**0.0002**

†: disease duration was adjusted; * data at the same visit when the last available radiograph data were collected

Results: Of 1253 AS patients meeting modified New York criteria enrolled in a longitudinal study of outcome, 371 had either complete spinal fusion at most recent radiographic assessment(i.e., mSASSS of 72, n=63, of whom only four were women); or no spinal fusion (i.e., mSASSS of 0, n=308). These were included in this statistical analysis. Median Follow-up was 1.92 years (IQR 0,4) (maximum=13 years). Median number of mSASSS sets was 2 (IQR= [1,3]) and mean disease of duration was 17.46 years (SD=12.9). Univariable analysis after adjusting for disease duration (Table 1) showed associations of complete spinal fusion with male gender, nonwhite ethnicity, older age at assessment and at disease onset, a history of smoking, greater functional impairment,not being employed, a negative family history of AS and elevated baseline C-reactive protein.

Conclusion: These data suggest that complete spinal fusion in patients with AS is most highly associated with greater age at disease onset, non-white ethnicity, male gender, as well as with objective (but not subjective) markers of disease activity.

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Abstract Number: 0619

Relation of Therapies for Ankylosing Spondylitis to Risk of Total Hip and Knee Arthroplasty

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SESSION INFORMATION

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Background/Purpose: Ankylosing spondylitis (AS) is an inflammatory arthritis that predominantly affects the axial skeleton, but commonly affects peripheral joints as well. Peripheral joint involvement often leads to total hip arthroplasty (THA) or total knee arthroplasty (TKA) in AS. We evaluated the relation of tumor necrosis factor inhibitors (TNFi) and other therapies in AS relative to nonsteroidal anti-inflammatory drugs (NSAIDs) to the risk of THA/TKA.

Methods: We conducted a nested case control study using 1994-2018 data from the OptumLabs® Data Warehouse, which includes medical and pharmacy claims, laboratory results, and enrollment records for commercial and Medicare Advantage enrollees. The database contains longitudinal health information on enrollees and patients, representing a diverse mixture of ages, ethnicities and geographical regions across the United States. Claims were used to identify patients with AS ages 18-89. Subjects were required to have medical and pharmacy coverage at least 6 months prior to AS diagnosis. Incident THA/TKAs were defined by diagnostic codes. THA or TKA cases were matched to four controls by sex, age (+/- 3 years), AS diagnosis year (+/- 1) and insurance type (private or Medicare). We assessed AS treatment in 6-month period prior to THA or TKA, using categories of NSAID (referent), symptom modifying anti-rheumatic drug (SMARD), and TNFi, either alone or in combination with other therapies. We evaluated the relation of each type of treatment to risk of THA or TKA using conditional logistical regression, with adjustment for age and history of chronic kidney disease, diabetes, liver disease, obesity, and peptic ulcer disease at baseline. Sensitivity analyses included 3-month and 14-month exposure assessment periods and models assessing THA and TKA separately.

Results: Among 22,166 adults with AS meeting eligibility criteria, we identified 539 cases of THA or TKA, and 1568 matched controls. Mean age was 58.9 (SD +/- 11.2) years, and 51.5% were female. Relative to NSAID use, the adjusted OR (aOR) within the 6-month exposure assessment period for TNFi only use was 0.45 (95% CI 0.26-0.78) and the aOR for SMARD only use was 0.49 (95% CI 0.32-0.75; see Table). Associations for other combinations of ther-

Table. Odds of NSAID, SMARD, TNFi or combination treatment within 6 months of THA or TKA among adults with AS

	Cases	Controls	Adjusted OR⁺
NSAID only	399	1012	1.0 (referent)
SMARD only	32	178	**0.49 (0.32-0.75)**
TNFi only	20	110	**0.45 (0.26-0.78)**
NSAID + SMARD	44	149	0.81 (0.55-1.21)
NSAID + TNFi	32	72	1.03 (0.64-1.66)
SMARD + TNFi	<20*	20	0.81 (0.31-2.12)
NSAID + SMARD + TNFi	<20*	27	0.43 (0.16-1.15)

OR: odds ratio; NSAID: nonsteroidal anti-inflammatory drug; TNFi: tumor necrosis factor inhibitor; SMARD: symptom modifying anti-rheumatic drug

⁺Adjusted for age, chronic kidney disease, diabetes, liver disease, obesity, and peptic ulcer disease prior to study eligibility.

*Small cells are suppressed to prevent the possibility of patient identification.

apies were not significant. Sensitivity analyses using 3-month and 14-month exposure assessment periods yielded aORs for TNFi only use of 0.39 (95% CI 0.22-0.69) and 0.44 (95% CI 0.23-0.86), respectively, and for SMARD only use aORs of 0.55 (95% CI 0.35-0.84) and 0.56 (95% CI 0.37-0.84). Results were similar for analyses of THA and TKA individually.

Conclusion: In this large sample of US adults with AS, the use of TNFi only and SMARD only were associated with lower odds of THA and TKA relative to NSAID use alone. Combinations of AS therapies were not associated with lower odds of THA and TKA. SMARD or TNFi therapy appear to have beneficial effects beyond the spine in AS on peripheral joints compared with NSAIDs; however, whether this may reflect benefits of those therapies versus detrimental effects of NSAIDs cannot be discerned.

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Abstract Number: 0620

Arterial Elasticity by 2 Dimensional Circumferential Strain and Beta Stiffness Index in Patients with Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is associated with elevated risk of cardiovascular disease (CVD) and increased mortality. Arterial stiffness is associated with atherosclerosis and CV events. Stiffness can be examined by ultrasound providing β stiffness index and by a more recently developed method, 2 dimensional (D) strain by speckle tracking technique, which measures deformation in more dimensions. The aims were to examine bilateral common carotid arterial (CCA) circumferential 2D strain and β stiffness index and in patients with AS and 1) compare the results with age and sex-matched controls and 2) explore relationships between circumferential strain and β stiffness index with disease related and traditional risk factors for CVD in AS patients.

Methods: A cohort of 149 patients with AS from northern Sweden, mean age 55.3±11.2 years, 102(68.5%) men, 146(98%) HLAB27) were examined with radiographs for modified Stoke Ankylosing Spondylitis Spine Score (mSASSS), BASMI, BASFI, ASDAS-CRP, BASDAI and conventional risk factors of CVD. Circumferential 2D strain and β stiffness index were assessed of bilateral CCAs. Forty-six AS patients and 46 age- and sex-matched controls without hypertension, diabetes or history of myocardial infarction or stroke were compared. Univariate and standard multivariable linear regression analyses were used. Variables with a univariate p-value ≤ 0.1 were considered for the multivariable models.

Results: The mean bilateral circumferential 2D strain was lower in AS patients compared with controls, 7.9±2.6% vs 10.3±1.9%, p< 0.001 whereas the mean bilateral β stiffness index was higher, 13.1±1.6 mmHg/mm vs 12.3±1.3

mmHg/mm, p=0.018. Multivariable linear regression analyses with mean circumferential bilateral 2D strain as dependent variable showed inverse significant associations with age, erythrocyte sedimentation rate, history of anterior uveitis and to be on a csDMARD and/or a bDMARD (R2 0.33) while mean β stiffness index as dependent variable showed significant associations with age (R2 0.22).

Conclusion: Both CCAs 2D strain and β stiffness index differed significantly between AS patients and controls indicating worse subclinical arterial status in AS. The circumferential 2D strain was associated with age and AS related variables while the β stiffness index with age indicating that the methods complement each other. Longitudinal studies are required to investigate the clinical importance of these CV surrogate biomarkers in AS.

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Abstract Number: 0621

The Use of Microbial Flow Cytometry to Analyze the Intestinal and Oral Microbiota

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Background/Purpose: The role of the microbiome in the pathogenesis of autoimmune disorders such as axial spondyloarthritis (SpA) has been well-established through means of describing gross microbial community dysbiosis between healthy controls. However specific mechanisms of how pathogenic bacteria cause disease progression in axial SpA have escaped current research. In this novel project we use flow cytometry to interrogate microbial composition using Quantitative Microbial Profiling (QMP), where we couple flow cytometric microbe counts with 16S rRNA sequencing. We compare QMP to the standard microbial analysis technique, Relative Microbial Profiling (RMP), that does not account for potential inter-sample differences in total microbial load. We also investigate the host-immune response to these microbial communities using the IgA-SEQ technique in which we flow sort and sequence IgA-coated bacteria.

Methods: Fecal samples of healthy controls (n = 23) and axial SpA patients (n = 24) were subjected to QMP through the combination of microbial flow cytometry and 16s rRNA sequencing. Antibiotic use was an exclusion criteria and 12/24 (50%) of the axial SpA patients had exposure to biologics for treatment. Saliva and feces of axial SpA and healthy control patients were subsequently subjected to IgA-SEQ (n = 12-13/group) in which IgA-coated bacteria are sorted and 16s rRNA sequenced to produce an IgA-coating index score for comparison of host immune response. This method identifies targets of the intestinal and oral IgA response in patients with axial SpA. The data was analyzed using the *DADA2* pipeline implemented in R.

Results: For the first time, QMP methods revealed striking quantitative fecal microbial load differences between axial SpA patients and healthy controls, underpinned by a dramatic near log-fold decrease in total microbial concentration as compared to healthy controls ($p < 0.01$). Additionally, IgA-SEQ analysis demonstrated a significantly altered microbiota-specific IgA repertoire between axial SpA patients and healthy controls in both saliva and feces. Of note,

some of the most significantly altered bacterial populations were from the *Lachnospiraceae* family, specifically from the genus *Roseburia*.

Conclusion: Through the use of QMP we identify a number of novel quantitative differences to the composition of the intestinal microbiota in axial SpA patients as compared to healthy controls. We also propose that patients with axial SpA have an altered host immune response to the oral and fecal microbiome that could play a critical role in disease pathogenesis and drive progression. Further research focused on immunogenic microbes, including *L. roseburia* could yield potential treatments to delay or stop disease progression.

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Abstract Number: 0622

Ten-year Atherosclerotic Cardiovascular Disease Risk Scores in Axial Spondyloarthritis versus the General Population: A Cross-sectional Study

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Background/Purpose: Cardiovascular morbidity and mortality are increased in axial spondyloarthritis (axSpA). The 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend high intensity statin therapy for primary prevention for 10-year atherosclerotic cardiovascular disease (ASCVD) risk scores ≥ 7.5%. We conducted a cross-sectional study evaluating the ASCVD risk profile of patients with axSpA compared to the general US population.

Methods: We included adults 18 years and older with AS by the modified New York criteria or non-radiographic axSpA by the ASAS criteria, who were followed longitudinally at two sites. After exclusion of ages outside the range of 40-75 years and patients without available cholesterol measures or blood pressures, 208 axSpA patients were included in the analysis. Other variables of interest were singly imputed using the last observation carried forward to the time of the cholesterol measurements. For general population comparators, we used individuals from the 2009-2014 National Health and Examination Survey (NHANES) cycles, who had available data for ASCVD risk score calculation by the Pooled Cohort Equation. Comparators from NHANES were matched 4:1 to subjects with axSpA on age, sex, and race. We performed descriptive statistics and estimated the prevalence ratio for a 10-year ASCVD risk score ≥7.5% comparing AS and matched NHANES comparators using conditional Poisson regression. We performed the same analysis among the subset of patients with AS (n=158).

Results: Overall, subjects had a mean ± SD age of 54.2 ± 11.4years, 68% were male, and 75% were white. The mean 10-year ASCVD risk score was 6.5 ± 6.9% for those with axSpA and 9.5 ± 10.4% for NHANES comparators.

Table 1. Baseline characteristics, comparing axSpA patients with age-, sex-, race-matched NHANES comparators

Variables	Overall n = 1040	axSpA n = 208	NHANES n = 832
Age, years	54.2 ± 11.4	53.9 ± 10.0	54.3 ± 11.7
Male sex	68%	68%	68%
Race/ethnicity			
White	75%	75%	75%
Black	3%	3%	3%
Hispanic	1%	1%	1%
Other	21%	21%	21%
10-year ASCVD risk score, %	8.9 ± 9.9	6.5 ± 6.9	9.5 ± 10.4
SBP, mm Hg	124.7± 15.9	126.7 ± 15.9	124.2 ± 15.8
Taking hypertensive medication	32%	35%	31%
HDL, mg/dl	51.8 ± 16.1	54.9 ± 16.7	51.0 ± 15.8
Total cholesterol, mg/dl	195.0 ± 42.3	189.8 ± 43.8	196.4 ± 41.8
Taking cholesterol medication	25%	21%	26%
ASCVD risk score ≥7.5%	38%	39%	38%
Diabetes	14%	7%	15%
Current smoker	18%	5%	22%

Abbreviations: axSpA: axial spondyloarthritis; NHANES: National Health and Examination Survey; ASCVD: atherosclerotic cardiovascular disease; HDL: high density lipoprotein; SBP: systolic blood pressure

Compared to those with axSpA, the prevalence of current smoking and diabetes was higher among NHANES comparators. The estimated prevalence ratio for a 10-year ASCVD risk score ≥7.5% comparing those with axSpA and their age-, sex-, and race-matched comparators was 0.94 (95% CI, 0.83-1.05). Similar results were seen among the subset of patients with AS.

Conclusion: In our study, the prevalence of a 10-year ASCVD risk score ≥7.5% was not significantly different comparing patients with axSpA and those drawn from the general population, who were similar in terms of age, sex, and race. The increased CV risk associated with axSpA may be underestimated by this risk score calculation. Although axSpA patients may be at lower CV risk overall due to heterogenous disease severity, similar results were seen among an AS subset. In addition, further interpretation of these findings is limited by the small sample size and lack of information on socioeconomic status. Additional investigation of the performance of ASCVD risk scores in patients with axSpA is needed.

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Abstract Number: 0623

Evaluation of the Early Cervical Structural Changes in Patients with Non-Radiographic Axial Spondyloarthropathy

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

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Background/Purpose: The aim of this double-blind, controlled, cross-sectional study is to compare the cervical vertebral structural changes of the patients with nr-axSpA, AS and control group using the mSASSS and to determine whether the cervical vertebral involvement is more early and more than the lumbar spine in the early period of the axial SpA.

Methods: A total of 205 people, 71 of whom were diagnosed as AS, 68 of whom were nr-axSpA, and 66 of them were control group were included in the study. Demographic data, CRP values, and HLA-B27 results were recorded. BASDAİ, BASFİ, BASMİ, and MASES values were calculated at the evaluation of the patients. The presence of sacroiliitis on pelvic radiography was evaluated according to the mNY criteria. Radiological evaluation of cervical and lumbar lateral radiographs was performed according to the mSASSS system.

Results: In this study, the duration of symptoms was significantly shorter in the nr-axSpA group than in the AS group (p = 0.010). There was a statistically significant difference at total mSASSS between the AS group and the nr-axSpA group (p= 0,038) but not at cervical and lumbar mSASSS (p=0,449, p=0,460). There was a statistically significant correlation between cervical and lumbar mSASSS scores in the AS group (p: 0.038, CC: 0.248), but not in the nr-axSpA group (p: 0,115, CC: 0,194). In AS and nr-axSpA groups, cervical mSASSS scores were higher than lumbar mSASSS scores in the majority of patients (%82,8 and %89,5). Although in the AS group, the cervical and total mSASSS scores were positively correlated with the duration of symptoms (CC:0,255, CC:0,295), there was no correlation in the nr-axSpA group.

Conclusion: Although the duration of the symptoms was shorter in the nr-axSpA group than in the AS group, there was no statistically significant difference between the cervical mSASSSS scores between the AS and nr-axSpA

	AS	Nr-axSpA	Control	p
Male Gender %	%50,7	%39,7	%31,8	0,078
HLA-B27 (+)%	%53,5	%27,9	%4,5	<0,001*
	Mean±SD Median	Mean±SD Median	Mean±SD Median	
Age (year)	38,96±10,29 38(18-59)	39,6±10,67 39,50(18-64)	39.39±11,29 39(19-64)	0,937
Symptom duration (month)	109,86±95,29 96 (1-372)	69,34±67,79 36 (2-240)		0,010*
mSASSS cervical	10,63±6,33 9 (2-36)	8,97±4,33 8 (2-26)	5,12±3,07 5 (0-14)	<0,001*α <0,001*β 0,449 γ
mSASSS lumbar	5,79±8,89 2,5 (0-36)	3,25±4,07 2 (0-19)		0,460
mSASSS total	16,47±13,55 12 (2-72)	12,18±7,18 10 (4-43)		0,038*

*:p<0,05, α: AS cervical mSASSS-control cervical mSASSS, β: nr-axSpA cervical mSASSS-control cervical mSASSS, γ: AS cervical mSASSS-nr-axSpA cervical mSASSS

Basic demographic, clinical and radiological features

	AS	p	nr-axSpA	p
mSASSS lumbar<mSASSS cervical n (%)	58 (%82,85)		60 (%89,5)	
mSASSS lumbar>mSASSS cervical n (%)	9 (%12,85)		5 (%7,46)	
mSASSS lumbar=mSASSS cervical n (%)	3 (%4,28)	<0,001*	2 (%2,98)	<0,001*
Total n	70		67	

mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score, AS: Ankylosing Spondylitis, nr-axSpA: non-radiographic axial spondyloarthritis, *:p<0,05

Intra-group comparison of cervical and lomber mSASSS

	mSASSS cervical-mSASSS lumbar	
	p	CC
AS group	0,038*	0,248*
nr-axSpA group	0,115	0,194

mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score, AS: Ankylosing Spondylitis, nr-axSpA: non-radiographic axial spondyloarthritis, *:p<0,05, CC: correlation coefficient

Correlation analysis of cervical and lumbar mSASSS values

groups. This situation may indicate that cervical vertebral changes occur in the early period of axial spondyloarthropathy. A similar statistical non-significant result was found between lumbar mSASSS scores of AS and nr-axSpA groups although not at total mSASSS.

However, there was a statistically significant correlation between cervical and lumbar mSASSS scores in the AS group and none in the nr-axSpA group. In AS and nr-axSpA group, cervical mSASSS scores were higher than lumbar mSASSS scores in the majority of patients. In contrast to our traditional knowledge, in patients with axial spondyloarthropathy cervical vertebral involvement was more prominent than lumbar vertebral involvement. This results may support our hypothesis that cervical involvement is early and more severe than the lumbar spine in the early period of the axial SpA.

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Abstract Number: 0624

Axial Spondyloarthritis: Knowledge, Screening and Referral Practices Amongst Primary Care Providers

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Background/Purpose: Early recognition is crucial in improving outcomes in patients with axial spondyloarthritis (axSpA). Despite this, there exists long delay between symptom onset and rheumatology diagnosis, with an average

interval of 8 years. Compounding this issue is uncertainty regarding initial axSpA screening and referral practices amongst primary care providers. The purpose of this study was to examine the knowledge, screening and referral practices for suspected axSpA within primary care.

Methods: Primary care physicians (MDs), physiotherapists (PTs), chiropractors (DCs) and nurse practitioners (NPs), licensed and registered with an Ontario regulatory college or professional association, were sent an electronic questionnaire via their respective professional institutions using Survey Monkey™ from September 2017 to September 2018. The questionnaire was developed based on our results from a qualitative study of primary care axSpA screening and referral practices conducted in 2016 and was piloted by ten primary care practitioners to strengthen face and content validity, clarity, relevance and format. The questionnaire addressed: i) knowledge of clinical and investigative features of axSpA; ii) awareness of axSpA screening tools and iii) referral practices for evaluation of suspected axSpA. Univariate statistics were used to address the above objective. All data analyses were conducted on *SAS version 9.4*.

Results: In total there were 276 respondents: MDs (44.5%), DCs (34%), PTs (19%) and NPs (2.4%). 93.1% worked in urban settings. 61.8% indicated > 10 years of primary care experience. In terms of clinical knowledge, the following were considered "very important" when assessing suspected axSpA: morning stiffness lasting > 30 minutes (81.9%); presence of HLA B27 (66.7%); evaluation of acute phase reactants (46.4%) and radiographs (spine and pelvis) (45.3%). Most respondents "never used" or "were not familiar" with axSpA screening tools (80%). The majority of MDs (90.9%) indicated they would "always" or "often" refer to rheumatology. PTs (90.5%) and DCs (88.0%) would "always" or "often" refer back to the patient's MD to facilitate further investigation and/or referral, as they are not legislated to directly refer to medical specialists in the province of Ontario. Travel (28.8%) and prolonged wait times (53.2%) were identified as referral barriers. DCs and PTs indicated legislative issues pertaining to scope of practice as a barrier to assessing patients with suspected axSpA (82.2%, 50.0%, respectively).

Conclusion: The majority of primary care practitioners demonstrate reasonable knowledge of clinical features for suspected axSpA; however there is little awareness of axSpA screening tools. Although the majority of MDs refer their patients with suspected axSpA for rheumatology consultation, prolonged wait times were identified as a substantial barrier. PTs and DCs, who are also first contact healthcare providers, identified barriers to axSpA screening and referral related legislative scope of practice, that if mitigated, could allow for better early detection of axSpA. The results of this study may inform targeted education of primary care practitioners to improve early recognition of axSpA.

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Abstract Number: 0625

Associations of Work-Related Abilities with Disability in Ankylosing Spondylitis

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Background/Purpose: Withdrawal from the workforce is 3.1 times higher in patients with Ankylosing Spondylitis (AS) compared to the general population [Boonen A, et al. 2001]. Functional disability is the most important predictor of total costs in patients with AS [Ward M. 2002]. Age at onset of AS, less formal education, and having physically demanding jobs were significant risk factors for permanent work disability, which had a prevalence of 13% in one AS cohort [Ward M, et al. 2001].

The purpose of our study was to identify factors associated with work disability, including specific work abilities, in patients with AS. We chose to specifically look at trunk strength, and dynamic flexibility because prior research has shown that bending, twisting, and stretching are the occupational activities associated with greater functional limitations and radiographic damage in patients with longstanding AS [Ward M, et al. 2008].

Methods: We included 1115 patients meeting modified New York Criteria from a prospective AS cohort. We used patients' current occupation data reported. Occupations were assigned a code from the Occupational Information Network, the US Department of Labor's job classification database. Each code is associated with a scale ranging from 0-100 that signifies the degree of importance of a particular work ability for that occupation. We used univariable

Table 1: Association of factors with disability based on univariable models (n=1115)

Variable	Not Disabled n=907 (81.35%)	Disabled n=208 (18.65%)	Unadjusted Odds Ratio (95% CI)	p-value
Male sex, n(%)	673 (74.20)	151 (72.60)	0.92 (0.66, 1.29)	0.6347
Age (year), mean(SD)	44.31 (13.97)	48.61 (13.92)	1.02 (1.01, 1.03)	0.0001
Country- Australia, n(%)	70 (7.72)	19 (9.13)	1.20 (0.71, 2.04)	0.4969
White race, n(%)	753 (83.02)	150 (72.12)	0.53 (0.37, 0.75)	0.0003
# years of education, mean(SD)	15.99 (2.95)	14.14 (2.94)	0.81 (0.77, 0.86)	<0.0001
Trunk Strength (1-100), mean(SD)	23.65 (16.39)	30.63 (18.03)	1.02 (1.01, 1.03)	<0.0001
Dynamic Flexibility(1-100), mean(SD)	1.47 (4.74)	2.80 (5.55)	1.04 (1.02, 1.07)	0.0013

Table 2: Association between work-related ability and disability based on a final multivariable logistic regression model

variable	Adjusted Odds Ratio (95% CI)	P-value
Trunk Strength (1-100)	**1.02 (1.004, 1.03)**	**0.0075**
Dynamic Flexibility (1-100)	**0.99 (0.95, 1.02)**	**0.4355**
Age (year)	1.03 (1.02, 1.05)	<.0001
# years of education	0.82 (0.77, 0.87)	<.0001
Country Australia vs. US	0.67 (0.36, 1.23)	0.1909
Sex Male vs. Female	0.83 (0.58, 1.18)	0.2961
Race White vs. other	0.50 (0.34, 0.75)	0.0007

and multivariable logistic regression models to evaluate whether work-related ability that requires trunk strength or dynamic flexibility was associated with self-reported disability.

Results: Our cohort had a mean ± SD age of 45 years, 73.9% were male, 81.0 % were white, and 18.7% reported work disability secondary to AS. In the multivariable model, after controlling for confounders such as demographic characteristics, work activity that required more trunk strength was significantly associated with disability (adjusted OR (aOR) 1.02; 95% CI,1.004-1.03), but no significant association was found between dynamic flexibility and disability (aOR 0.99; 95% CI,0.95-1.02). Older age was also significantly associated with disability (aOR 1.03). Higher education and White race were inversely associated with disability (aOR 0.82 and aOR 0.50, respectively). We did not find any significant effect modification between each variable and trunk strength or dynamic flexibility.

Conclusion: AS patients with occupations requiring higher trunk strength reported significantly higher work disability. Another association included older age. Longer years of education and White race were inversely associated with disability. Disease onset of AS begins when patients are usually in young adulthood; identifying risk factors may identify potential interventions that decrease work disability for AS patients.

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Abstract Number: 0626

Are There Really Differences Between Non-radiographic and Radiographic Axial Spondyloarthritis? Data from the Spanish Atlas

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Session Time: 9:00AM–11:00AM

Background/Purpose: Most research studies support the fact that both, radiographic and non-radiographic axial spondyloarthritis (r-axSpA and nr-axSpA), share similar clinical characteristics and equivalent burden of the disease. However, worldwide data about nr-axSpA entity is limited, and specific research on the subject in Spain is almost non-existent. The purpose of the present study is to describe and compare the characteristics and burden of the disease in patients with r-axSpA and nr-axSpA in Spain.

Table 1. Sociodemographic characteristics and PROs of patients with nr-axSpA (N: 35, unless other specified) and with r-axSpA (N: 645, unless other specified)

Variable	Nr-axSpA (N: 35) mean ± SD or n(%)	r-axSpA (N: 645) mean ± SD or n(%)	p-value
Age (years)	42.1 ± 8.8	45.9 ± 10.9	**0.050***
Gender (female)	32 (91.4)	325 (50.4)	**<0.001***
Education level (University)	17 (48.6)	234(36.3)	ns
Marital status (Married)	20 (57.1)	466 (72.2)	ns
Employment Status (Unemployed)	4 (20.0); N: 20	86 (21.8); N: 395	ns
Diagnostic delay (years)	10.1 ± 8.9; N: 32	8.4 ± 7.6; N: 518	ns
BASDAI (0-10)	5.7 ± 2.1; N: 18	5.7 ± 2.0; N: 400	ns
High BASDAI (≥ 4)	15 (83.3); N: 18	322 (80.5); N: 400	ns
Global Stiffness Index (3-12)	6.5 ± 2.5; N: 24	7.5 ± 2.7; N: 470	ns
Global Limitation Index (0-54)	45.6 ± 10.4	42.2 ± 10.0; N: 570	**0.008***
GHQ-12 (0-12)	7.5 ± 4.9; N: 20	5.7 ± 4.5; N: 454	ns
GHQ-12 (≥ 3)	15 (75.0); N: 20	295 (65.0); N: 454	ns
Anxiety	6 (17.1)	129 (20.0)	ns
Depression	5 (14.3)	95 (14.7)	ns
Visits to rheumatologist in the past 12 months	3.8 ± 4.5	3.8 ± 4.5	ns
Visits to the GP in the past 12 months	8.0 ± 10.7	5.1 ± 13.2	**0.005***
Current use of biologics	7 (20.0)	237 (36.7)	**0.044***

Methods: The Atlas 2017 is an initiative of the Spanish Coordinator of Patient Associations of Spondylarthritis (CEADE) aiming to better understand the reality of the patients suffering from this disease from an integrated approach. During this project, a cross-sectional on-line survey of unselected patients with self-reported axSpA from all geographical regions in Spain was conducted from May 1st to August 15th 2016 by the University of Seville. Participants were recruited through patient organizations. Patients and disease characteristics and reported outcomes were analysed and compared between patients with r-axSpA and patients with nr-axSpA. These included: sociodemographic characteristics, symptoms duration until diagnosis, patient-reported outcomes on disease activity (BASDAI), mental health (GHQ-12), employment status, treatment and healthcare utilization.

Results: In total, 680 axSpA patients participated in the Atlas survey. Mean age was 45.7±10.8 years, 52.5% were female and 36.9% university-educated. Of those, 35 (5.2%) self-reported a diagnosis of nr-axSpA while the rest (94.8%) reported r-axSpA. Compared to r-axSpA patients, those with nr-axSpA were more frequently women (50.4% vs 91.4%, p< 0.001; respectively), had longer diagnostic delay (10.1±8.9 vs 8.4±7.6 years), similar degree of disease activity (BASDAI: 5.7±2.1 vs 5.7±2.0), higher psychological distress (GHQ: 7.5±4.9 vs 5.7±4.) and approximately the same proportion of unemployment (20.0% vs 21.8%) (table 1). In addition, 20.0% of nr-axSpA received biologics vs 36.7% of r-axSpA p=0.044. The number of visits to the rheumatologist in the past 12 months were similar in both groups (3.8±4.5 vs 3.3±3.9), while the visits to the GP were much higher within the nr-axSpA (8.0±10.7 vs 5.1±13.2 p=0.005).

Conclusion: Patients with nr-axSpA were more frequent women and presented younger age, higher diagnostic delay and lower use of biologic therapy compared to axSpA. However, for the overall sociodemographic characteristics, PROs, employment status and healthcare uses, both groups reported similar trends.

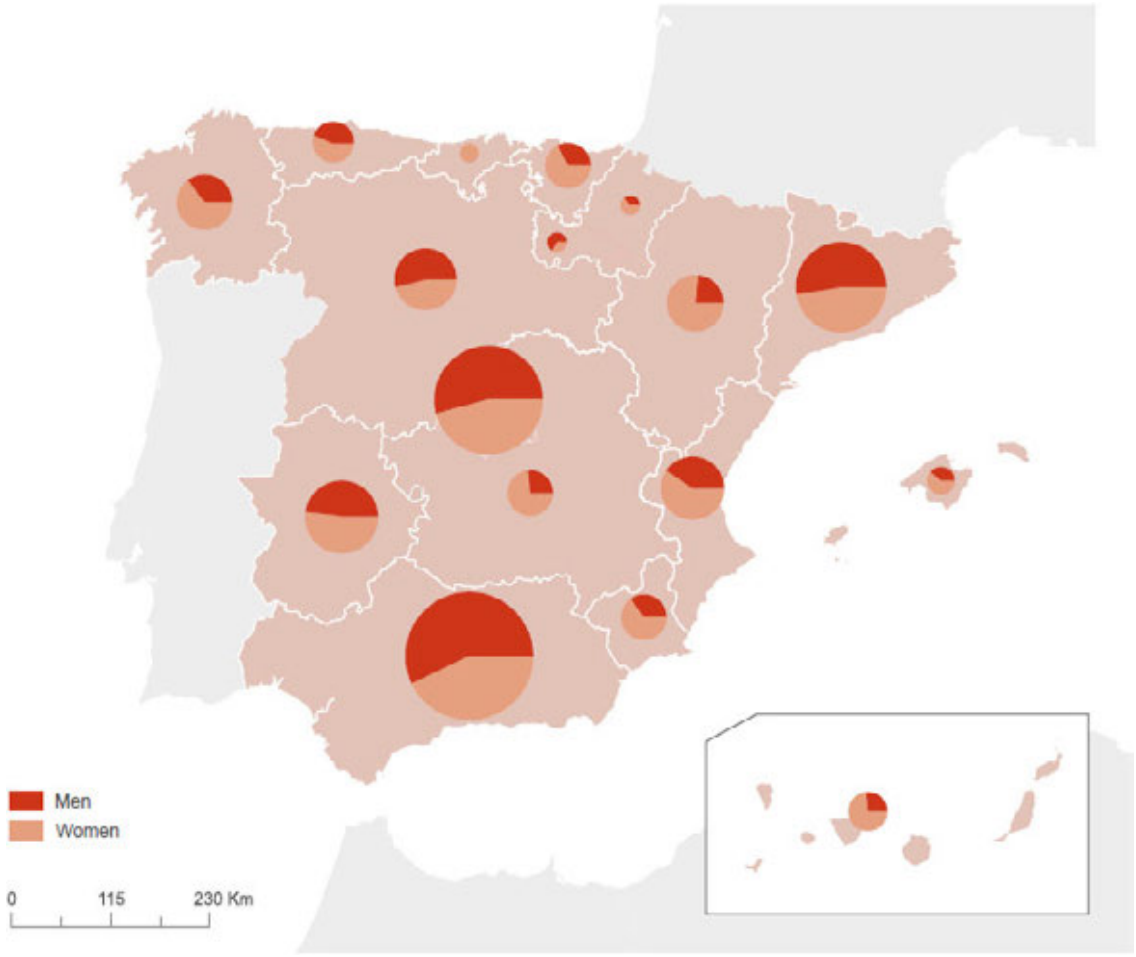

Figure 1. Distribution of patients by Gender and Autonomous Communities

Disclosure: M. Garrido-Cumbrera, None; **J. Gratacós**, None; **E. Collantes**, None; **P. Zarco**, None; **C. Sastre**, Novartis employee, 3; **S. Sanz-Gómez**, None; **V. Navarro-Compán**, AbbVie, 5, 8, Bristol, 8, Bristol, Roche, 8, Eli Lilly and Company, 5, 8, Eli Lilly, Novartis, Abbvie, UCB, MSD, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, Roche, 8, UCB, 5, 8.

Abstract Number: 0627

Metabolomics Screening in Axial Spondyloarthritis: Identifying Potential Biomarkers

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Early intervention in axial spondyloarthritis (axSpA) may prevent pathogenic changes such as bone remodeling and spinal fusion. Unfortunately, early intervention is difficult, as there remains an average 5-10 year gap between onset of symptoms and diagnosis partly due to a lack of diagnostic biomarkers. Currently, diagnosis is based on a combination of clinical features, inflammatory markers, and imaging, as existing biomarkers such as CRP and HLA-B27 are not sensitive/specific enough alone. Ideally, a sensitive and specific biomarker could be used alongside existing tools to lessen the time to diagnosis. We hypothesized that metabolites, which can serve as markers of ongoing cellular functions that are likely altered in axSpA, would reveal a sensitive and specific biomarker that would differentiate axSpA cases from healthy controls.

Methods: Patients were selected from our ongoing mucosal studies cohort in which participants undergo colonic mucosal biopsies alongside blood draw. Healthy controls (n=24) were recruited from the endoscopy schedule while undergoing screening colonoscopies with biopsies and an additional blood draw, while axSpA cases (n=23) were recruited from rheumatology clinics and underwent a flexible sigmoidoscopy with biopsies and blood draw. AxSpA cases met ASAS criteria and had imaging consistent with the diagnosis of axSpA. Blood was drawn at the time of the endoscopy visit, then processed and stored. Collected plasma was analyzed by high-pressure liquid chromatography coupled with mass spectrometry (LC-MS).

Statistical analyses were performed using two-sided t-tests, principle component analysis (PCA), partial least squares discriminant analysis (PLSDA), and Receiver Operating Characteristics (ROC) analysis.

Results: PLSDA analysis showed good separation of groups, chiefly driven by oxalosuccinate and 3-sulfocatechol. Oxalosuccinate and 3-sulfocatechol levels significantly differed between axSpA and healthy controls ($p: < 0.0001$, $p: < 0.0001$). In ROC analysis oxalosuccinate had an area under the curve of 0.962, while 3-sulfocatechol had an AUC of 0.88. Oxalosuccinate alone outperformed any combination of other metabolites in correctly differentiating axSpA cases vs healthy controls, and did not significantly correlate with B27 status, BASDAI, endoscopy type, sex, or medication status.

Conclusion: Significant metabolic differences between axSpA and healthy controls were identified in our study, which may provide insight into the underlying pathophysiology of this disease. Furthermore and most strikingly, oxalosuccinate, a product in the TCA cycle, correctly differentiates axSpA from healthy controls and holds promise as a diagnostic biomarker. More work is needed to validate these results in another cohort and with additional controls as well as investigate the mechanism by which the TCA cycle is impacted in axSpA.

Disclosure: A. Stahly, None; **E. Regner**, None; **A. Lefferts**, None; **B. Brown**, None; **A. D'Alessandro**, None; **K. Kuhn**, None.

Abstract Number: 0628

Pain Perception and Opiate Use Among Patients with Inflammatory Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Pain is the most common symptom among patients with inflammatory arthritis (IA) and residual pain is common in patients IA despite appropriate treatment. Opiate pain medications have been used in the past to assist in managing patients' pain but have increasingly been recognized as potentially harmful medications. The objectives of this study were to a) examine pain perception among patients with RA, PsA, and AS and b) to examine the prevalence and incidence of opiate pain mediation use between 2001-2018 among patients with IA.

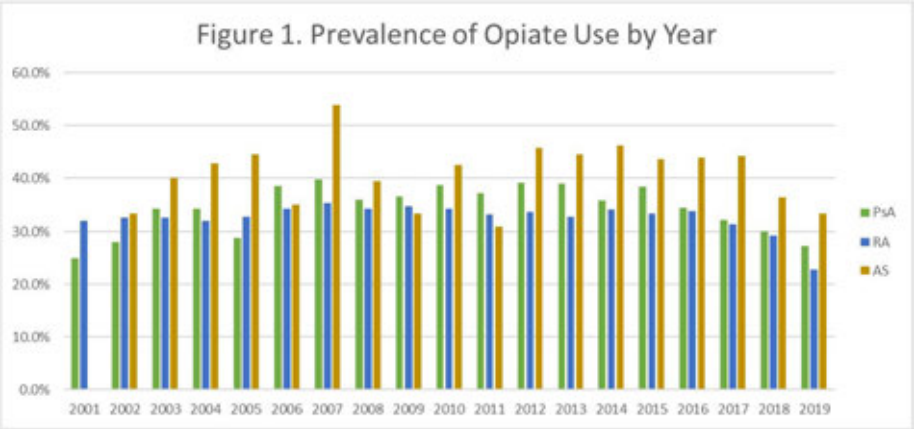
Methods: Using data from Forward/National Data Bank for Rheumatic Diseases between 2001-2018, a cross-sectional study was performed using the most recent visit for patients with AS, PsA, or RA with a rheumatologist confirmed diagnosis. Additionally, a retrospective cohort study was performed in the same cohort to examine time trends in the prevalence and incidence of opiate use. Participants in Forward complete questionnaires every 6 months that include patient reported outcome (PRO) measures such as PROMIS29, a wide spread pain index, and a survey of medications used, including pain medications. Incident opiate use was defined as having no prior report of opiate use in previous questionnaires with at least one completed questionnaire prior to the first report of opiate use. Mean and standard deviations for PRO scores were reported for each group and a Kruskal Wallis test or chi2 test was used to determine whether significant differences existed (for continuous and categorical outcomes respectively).

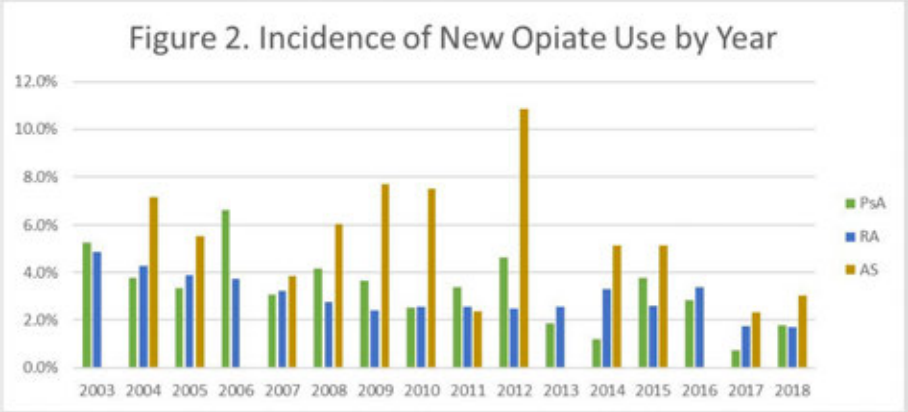
Results: Among those enrolled in Forward, 13,805, 370, and 126 patients with RA, PsA, and AS respectively met eligibility criteria for this study. Patients with RA generally had more follow up time and were older (mean age 64 vs 58 and 50 respectively) and more likely to be female (80% vs 70% and 66% respectively). In general, pain scores (pain numeric rating scale, PROMIS29 pain score, wide spread pain index, Table 1) were statistically similar across the three diseases but numerically higher in AS. Patients with PsA had higher depression scores while patients with AS had higher fatigue scores. While more patients with RA were using non-opioid pain medications at their most recent

Table 1. Demographics and Patient Reported Outcomes Among Patients with RA, PsA, and AS

	RA	PsA	AS	p-value
Number of patients	**13805**	**370**	**126**	
Number of visits (Median, IQR)	8 (3-17)	7 (3-13)	5 (2-10)	<0.001
Sex (F)	10653 (80%)	253 (70%)	80 (66%)	<0.001
Age (Mean(SD)	64.4 (13.5)	58.1 (12.4)	50.5 (13.1)	<0.001
Duration	19.0 (12.2)	16.8 (11.0)	17.9 (13.1)	<0.01
BMI	28.2 (7.1)	31.2 (7.7)	30.2 (7.5)	<0.001
College Education	3,839 (32%)	128 (42%)	42 (50%)	<0.001
Current Smoking	1324 (10%)	32 (9%)	12 (10%)	NS
Comorbidity index (Mean(SD))	2.1 (1.7)	2.1 (1.8)	2.3 (1.9)	NS
Non-opioid	2021 (15%)	37 (10%)	13 (10%)	0.02
NSAID	7015 (51%)	188 (51%)	66 (52%)	NS
Any opioid	4400 (32%)	115 (31%)	49 (39%)	NS
Weak opioid	3584 (26%)	97 (26%)	38 (30%)	NS
Strong opioid	1205 (9%)	32 (9%)	18 (14%)	NS
Wide Spread Pain Index (mean(SD))	5.9 (5.5)	6.1 (5.7)	6.3 (5.1)	NS
Pain scale (0-10)	4.2 (2.8)	4.2 (2.8)	4.7 (2.8)	NS
Patient Global (0-10)	4.3 (2.5)	4.3 (2.5)	4.5 (2.3)	NS
PROMIS 29 Sleep T-Score	51. 4 (9.4)	52.6 (9.4)	52.7 (7.6)	NS
PROMIS 29 Pain T-Score	57.5 (9.1)	59.1 (9.7)	59.8 (9.4)	NS
PROMIS 29 Fatigue T-Score	54.3 (11.5)	54.1 (12.2)	57.7 (11.9)	NS
PROMIS 29 Depression T-Score	48.9 (9.8)	50.1 (9.8)	47.0 (10.3)	NS
PROMIS 29 Anxiety T-Score	49.4 (10.1)	50.0 (9.5)	48.0 (13.3)	NS
PROMIS 29 Physical T-Score	40.8 (9.4)	42.4 (9.1)	41.3 (8.2)	NS

*PROMIS T-scores increase with more of the concept being measured (i.e., more fatigue results in a higher T-score).





survey time point, more patients with AS reported taking an opioid pain medication. In most years, patients with AS were more likely to be taking opioid pain medications and this was statistically significant overall (p=0.01). AS patients also had a higher incidence of new opioid use. In general, for all three diseases, new opiate use has been declining over the past 3 years.

Conclusion: In this study among patients with IA, statistically similar levels of pain, fatigue, sleep, depression and anxiety were reported though AS patients had numerically higher pain scores. Patients with AS received more opioid medications. However, in general, opioid use has been declining in the last three years.

Disclosure: A. Ogdie, Abbvie, 5, 8, Amgen, 2, 5, 8, BMS, 5, Celgene, 5, 8, Corrona, 5, Lilly, 5, Novartis, 2, 5, 7, 8, Pfizer, 2, 5; **S. Pedro**, None; **K. Michaud**, Pfizer, 2, Rheumatology Research Foundation, 2.

Abstract Number: 0629

Gender Differences in Comorbidities and Treatment Utilization Among Ankylosing Spondylitis Patients Initiating a Biologic in a Real-World Setting

Anna Sheahan,[1] Maya Balamane,[1] Edward Lee,[2] and Robert Suruki[1], [1]UCB Pharma, Raleigh, NC, [2]UCB Pharma, Smyrna, GA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To identify opportunities to optimize treatment of AS, an understanding of the treatment approaches and patient characteristics is necessary. This study describes comorbidities, comedications, and biologic treatment patterns, including any gender differences, in AS patients initiating biologics in the real-world setting.

Methods: This retrospective observational study analyzed US commercial claims data (IBM® MarketScan®) from 2012–2017. AS patients newly initiating a biologic (1st claim [index date] and no claims for ≥1 year prior), ≥18 years old, with continuous enrollment in the 12-months preceding (baseline) and following (follow-up) the index date were identified. Diagnoses were based on ICD 9/10 codes. Persistence was defined as treatment with the index biologic with gaps of ≤90 days over 12 months. The following treatment outcomes were also assessed: 110% of the label-recommended dose for ≥30 days (above-label dosing), new biologic initiation within 90 days of discontinuing index biologic (switch), and index biologic cessation (>90 days with no treatment [non-switch discontinuation]). Patients were categorized based on the first event experienced.

Results: A total of 1,526 patients met the inclusion criteria. Women (n=668) were more likely than men (n=858) to have ≥1 claim at baseline for anxiety (17% vs 8%), depression (23% vs 10%), fatigue (29% vs 21%) and fibromyalgia (≥2 codes) (16% vs 6%). At baseline, women were more likely to have ≥1 claim for an opioid (59% vs 50%) or an NSAID (72% vs 67%) and to have claims for ≥2 different NSAIDs (33% vs 23%). The same trend was present in follow-up comparing women to men for opioids (69% vs 63%) and NSAIDs (75% vs 66%). The most common index biologics were adalimumab (52%) and etanercept (31%). Persistence of the index biologic at 12 months was 50% and was lower in women (43%) vs men (55%). The most frequent treatment outcome assessed was non-switch discontinuation (35%), followed by switching (16%) and above label dosing (16%). Among those who discontinued without switching, 14% restarted their index biologic within 6 months. Women were more likely to switch than men (20% vs 13%) and were less likely to be receiving a biologic (index or otherwise) at 12 months (71% vs 78%).

Conclusion: Index biologic treatment included primarily adalimumab and etanercept. The comorbidity and treatment exposures depict a more complex profile for women vs men, which may be important to consider when determining the best approach to disease management. Further real-world studies on treatment patterns are needed to understand factors leading to poor persistence and how best to optimize treatment.

Disclosure: A. Sheahan, UCB Pharma, 1, 3; **M. Balamane**, UCB Pharma, 3; **E. Lee**, UCB Pharma, 1, 3; **R. Suruki**, UCB Pharma, 1, 3.

Abstract Number: 0630

Assessing the Humanistic and Economic Burden of Enthesitis Among Patients with Peripheral and Axial Spondyloarthritis: Results from a Multi-National Real World Survey Database

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesitis is a major source of pain, functional impairment, and reduced health-related quality of life (HRQoL) in spondyloarthritis (SpA) patients; however, limited information is available in the literature regarding the burden associated with enthesitis in this population. This retrospective cohort study assessed the burden associated with enthesitis among patients with peripheral SpA (known as psoriatic arthritis [PsA]) and axial SpA (axSpA) in the real world.

Methods: Data were taken from the Adelphi Spondyloarthritis Disease Specific Programme, which collected information from rheumatologists/dermatologists and their consulting axSpA and PsA patients across Europe, Asia-Pacific, United States, Latin America, and Middle East between 2015 and 2016. Bivariate descriptive analyses were

Table 1. Bivariate analyses: Demographics, clinical characteristics and disease burden for axSpA and PsA patients

Variable	axSpA (n=5,660)*			PsA (n=3,570)*		
Demographics and Clinical characteristics						
	without enthesitis (n=5,154)	with enthesitis (n=506)	P value	without enthesitis (n=3,310)	with enthesitis (n=260)	P value
Current age (mean)	42.6	41.8	0.4506	**48.4**	**46.6**	**0.0364**
Gender, % male	65.5	61.5	0.0704	51.8	49.2	0.4395
Time since diagnosis, years (mean)	4.8	4.4	0.0620	4.8	4.4	0.4301
Pain level at diagnosis [1-10] (mean)	**6.4**	**6.7**	**0.0028**	**5.9**	**6.6**	**<0.0001**
% currently severe (disease severity)	**5.2**	**7.5**	**<0.0001**	**4.3**	**10.0**	**<0.0001**
% currently receiving AT	58.0	59.5	0.1954	**55.8**	**59.9**	**0.0083**
Use of additional pain medication, % yes	**15.4**	**28.2**	**<0.0001**	**13.7**	**22.2**	**0.0118**
Patient Region (%): Americas,EU5, APAC, Turkey & Middle Est	**23.3; 53.7; 11.2; 11.8**	**31.6; 52.4; 10.1; 5.9**	**<0.0001**	**22.1; 51.8; 15.7; 10.5**	**27.3; 48.1; 18.5; 6.2**	**0.0264**
Body Mass Index (mean)	**25.7**	**25.3**	**0.028**	26.4	2.6	0.0610
Charlson Comorbidity Index	0.1	0.1	0.5527	0.1	0.2	0.1832
Outcomes						
	without enthesitis (n=1,214*)	with enthesitis (n=110*)	P value	without enthesitis (n=1,566*)	with enthesitis (n=131*)	P value
Current pain level [1-10], mean	**3.4**	**4.4**	**<0.0001**	**3.1**	**4.4**	**<0.0001**
BASDAI (mean)	**3.5**	**4.8**	**<0.0001**	NA	NA	NA
EQ-5D-3L, mean, currently	**0.74**	**0.68**	**<0.0001**	**0.72**	**0.64**	**0.0002**
SF-36 PCS, mean	**43.9**	**40.4**	**<0.0001**	**44.3**	**41.4**	**0.0004**
SF-36 MCS, mean	**44.7**	**42.1**	**0.0006**	**44.5**	**42.6**	**0.0364**
WPAI-GH, % activity impairment	**33.5**	**45.7**	**<0.0001**	**35.3**	**40.8**	**0.0165**
Number of specialist consultations in last 12 months, mean	**3.8**	**4.7**	**0.0002**	**5.7**	**7.0**	**<0.0001**
High to severe distress, %	**14.8**	**26.2**	**<0.0001**	**16.3**	**28.3**	**0.0001**

P values highlighted in bold indicate statistically significant results; 0.05 is used as the cut-off for significance.
*Sample size varies for some variables due to missing responses.
APAC: Asia Pacific; AT: Advanced treatment; axSpA: axial spondyloarthritis; BASDAI: Bath ankylosing spondylitis disease activity index; EQ-5D-3L: EuroQol five-dimensions three-level; EU5: Germany, France, Spain, Italy and UK; MCS: Mental component score; NA: not applicable; PCS: Physical component score; PsA: Psoriatic arthritis; SF-36: Short-form-36; WPAI-GH: Work productivity and activity impairment - general health.
Advanced treatment includes biologic/biosimilar disease-modifying antirheumatic drugs (DMARDs) e.g. etanercept, adalimumab, and targeted synthetic DMARDs (apremilast).

Table 2. Propensity score matching analyses for axSpA patients

Variable	Without enthesitis (n)	With enthesitis (n)	Coefficient	P value
Current pain level [1-10]	**3.39 (133)**	**4.08 (136)**	**0.7218**	**0.001**
BASDAI	**3.65 (122)**	**4.76 (124)**	**1.1004**	**0.001**
EQ-5D-3L	0.71 (130)	0.69 (133)	-0.0310	0.306
SF-36 PCS	**43.88 (130)**	**40.15 (133)**	**-3.5768**	**<0.001**
SF-36 MCS	43.62 (130)	42.17 (133)	-1.4998	0.240
SF-36 social functioning	**68.75 (130)**	**60.71 (133)**	**-7.7884**	**0.003**
SF-36 physical functioning	**68.08 (130)**	**55.73 (133)**	**-11.9060**	**<0.001**
SF-36 bodily pain	**61.69 (130)**	**53.92 (133)**	**-7.5615**	**0.004**
SF-36 mental health	62.50 (130)	60.19 (133)	-2.4615	0.330
SF-36 role physical	**65.29 (130)**	**57.52 (133)**	**-7.5000**	**0.016**
SF-36 general health	48.66 (130)	44.64 (133)	-3.9846	0.129
SF-36 vitality	52.08 (130)	49.98 (133)	-2.1474	0.359
SF-36 role emotional	**72.05 (130)**	**64.29 (133)**	**-7.6282**	**0.015**
WPAI-GH, % activity impairment	**37.69 (108)**	**46.42 (109)**	**8.4260**	**0.026**
Number of specialist consultations in the last 12 months	**4.48 (128)**	**6.57 (130)**	**2.1016**	**<0.001**

P values highlighted in bold indicate statistically significant results; 0.05 is used as the cut-off for significance. n indicates number of patients in the matched population for a given outcome.
Propensity score analyses matched patients on age, sex, current severity, region, advanced therapy status, body mass index, time since diagnosis, the Charlson Comorbidity Index and use of additional pain medication.
axSpA: axial spondyloarthritis; BASDAI: Bath ankylosing spondylitis disease activity index; EQ-5D-3L: EuroQol five-dimensions three-level; MCS: Mental component score; PCS: Physical component score; SF-36: Short-form-36; WPAI-GH: Work productivity and activity impairment - general health.

Table 3. Propensity score matching analyses for PsA patients

Variable	Without enthesitis (n)	With enthesitis (n)	Coefficient	P value
Current pain level [1-10]	3.80 (76)	4.26 (143)	0.3816	0.204
EQ-5D-3L	0.71 (71)	0.67 (74)	-0.0472	0.325
SF-36 PCS	43.90 (74)	41.96 (77)	-1.9422	0.202
SF-36 MCS	43.74 (74)	42.57 (77)	-1.1759	0.481
SF-36 social functioning	**70.61 (74)**	**62.66 (77)**	**-7.7702**	**0.048**
SF-36 physical functioning	66.88 (74)	59.38 (77)	-7.1021	0.181
SF-36 bodily pain	60.27 (74)	58.62 (77)	-2.0135	0.614
SF-36 mental health	63.24 (74)	62.26 (77)	-0.8277	0.809
SF-36 role physical	67.74 (74)	61.04 (77)	-6.8412	0.093
SF-36 general health	48.47 (74)	47.28 (77)	-1.1993	0.726
SF-36 vitality	52.87 (74)	52.71 (77)	-0.2252	0.947
SF-36 role emotional	69.82 (74)	64.39 (77)	-5.6306	0.220
WPAI-GH, % activity impairment	35.96 (57)	38.45 (58)	1.7544	0.749
Number of specialist consultations in the last 12 months	**6.99 (72)**	**8.86 (74)**	**1.8194**	**0.001**

P values highlighted in bold indicate statistically significant results; 0.05 is used as the cut-off for significance. n indicates number of patients in the matched population for a given outcome.
Propensity score analyses matched patients on age, sex, current severity, region, advanced therapy status, body mass index, time since diagnosis, the Charlson Comorbidity Index and use of additional pain medication.
EQ-5D-3L: EuroQol five-dimensions three-level; MCS: Mental component score; PCS: Physical component score; PsA: Psoriatic arthritis; SF-36: Short-form-36; WPAI-GH: Work productivity and activity impairment – general health.

conducted to describe differences between patients with and without enthesitis, in terms of demographics, clinical characteristics, and humanistic and economic burden as measured by patient-reported pain, HRQoL (EuroQol five-dimensions three-level [EQ-5D-3L] and short-form [SF]-36), healthcare resource utilization (HCRU), and activity impairment (work productivity and activity impairment - general health [WPAI-GH]). Inclusion in the enthesitis group was based on physician reporting clinical enthesitis as one of the symptoms currently present in the patient. Propensity score matching analyses were conducted to compare differences in outcomes between enthesitis and without enthesitis groups, matching patients by demographic and clinical characteristics.

Results: The analysis included data for 5,660 axSpA (with enthesitis: 506 [9%]; without: 5154 [91%]) and 3,570 PsA (with enthesitis: 260 [7%]; without: 3310 [93%]) patients. Bivariate analysis showed a significantly higher proportion

of axSpA and PsA patients with enthesitis currently had severe disease and were more likely to require additional pain medications compared to those without enthesitis (Table 1). Patients with enthesitis experienced significantly higher levels of pain, worse HRQoL, greater activity impairment, with a higher number of specialist consultations in the last 12 months compared to those without enthesitis, in both axSpA and PsA subgroups (Table 1). After adjusting for confounding factors in propensity score analysis, burden in terms of pain, HRQoL, activity impairment, and HCRU was mostly significantly higher in patients with enthesitis vs those without in axSpA (Table 2). PsA patients with enthesitis experienced higher burden compared to those without enthesitis, although most differences were not statistically significant, in part due to low sample size (Table 3).

Conclusion: Results from this multinational real world analysis demonstrate that axSpA and PsA patients with enthesitis experience more disease burden than patients without enthesitis. Treatment regimens with demonstrated efficacy on enthesitis should be considered to improve patient outcomes.

Disclosure: V. Strand, Abbvie, 5, AbbVie, 5, Amgen, 5, Amgen, Abbvie, Bayer, BMS, Boehringer Ingelheim, Celltrion, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, UCB, 5, AstraZeneca, 5, AURA, 8, Bayer, 5, BMS, 5, Boehringer Ingelheim, 5, Celgene, 5, Celltrion, 5, Cleveland Clinic, 8, CORRONA, 5, Crescendo, 5, Crescendo Bioscience, 5, Eli Lilly, 5, EMD Serono, 5, Genentech, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Inmedix, 5, Janssen, 5, Kezar, 5, Lilly, 5, Merck, 5, NACCME, 8, Novartis, 5, Pfizer, 5, Purdue, 8, RA Forum, 8, RAN, 8, Regeneron, 5, Roche, 5, Samsung, 5, Sandoz, 5, Sanofi, 5, Servier, 5, Setpoint, 5, SLRA, 8, UCB, 5, Up to Date, 7, Washington University, 8, WIR, 8, WRA, 8; **A. Deodhar**, AbbVie, 2, 5, 9, Abbvie, 5, 8, Abbvie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, and UCB Pharma, 5, 8, AbbVie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GSK, Galapagos, Janssen, Novartis, Pfizer and UCB, 5, AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Glaxo Smith and Klein, Janssen, Novartis, Pfizer, UCB, 5, Amgen, 5, 8, 9, BMS, 2, 5, 8, BMS, Eli Lilly, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, 2, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, UCB Pharma, 2, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, 8, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, 9, Eli Lilly and Company, 2, 5, Eli Lilly,, 5, Eli Lilly, GSK, Novartis, Pfizer and UCB, 2, Galagagos, 5, Galapagos, 5, 8, 9, Glaxo Smith & Klein, 2, Glaxo Smith & Kline, 2, 5, 8, Glaxo Smith Klein, 5, Glaxo SmithKlein, 2, 5, GlaxoSmithKlein, 2, 5, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, Janssen, 2, 5, 8, 9, Janssen Pharmaceutica, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9; **P. Conaghan**, Abbvie, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, 8, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Eli Lilly, 8, EMD, 5, EMD Serono, 5, EMD Serono Research and Development Institute, Inc., 5, 8, Flexion, 5, 8, Flexion Therapeutics, 5, 8, Galapagos, 5, 8, Glaxo Smith Kline, 5, GlaxoSmithKline, 5, 8, Lilly, 8, Medivir, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Samumed, 5, 8, Serono, 5, Stryker, 5, 8; **I. Gilloteau**, Novartis Pharma AG, 1, 3; **O. Massey**, Adelphi Real World, 3, Janssen Scientific Affairs, LLC, 5; **H. Tian**, Novartis, 3, 4, Novartis Pharmaceuticals Corporations, 1, 3; **A. Yocolly**, Novartis Product Lifecycle Services –NBS, Novartis Global Service Center, 3; **N. Booth**, Adelphi Real World, 3; **R. Alten**, Galapagos, 2, Galapagos NV, 2, Gilead, 2, Gilead Sciences, Inc., 2, Novartis, 2, Pfizer, 2, 8.

Abstract Number: 0631

Recognition of Inflammatory Back Pain by US Healthcare Providers and Barriers to Specialist Referral

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

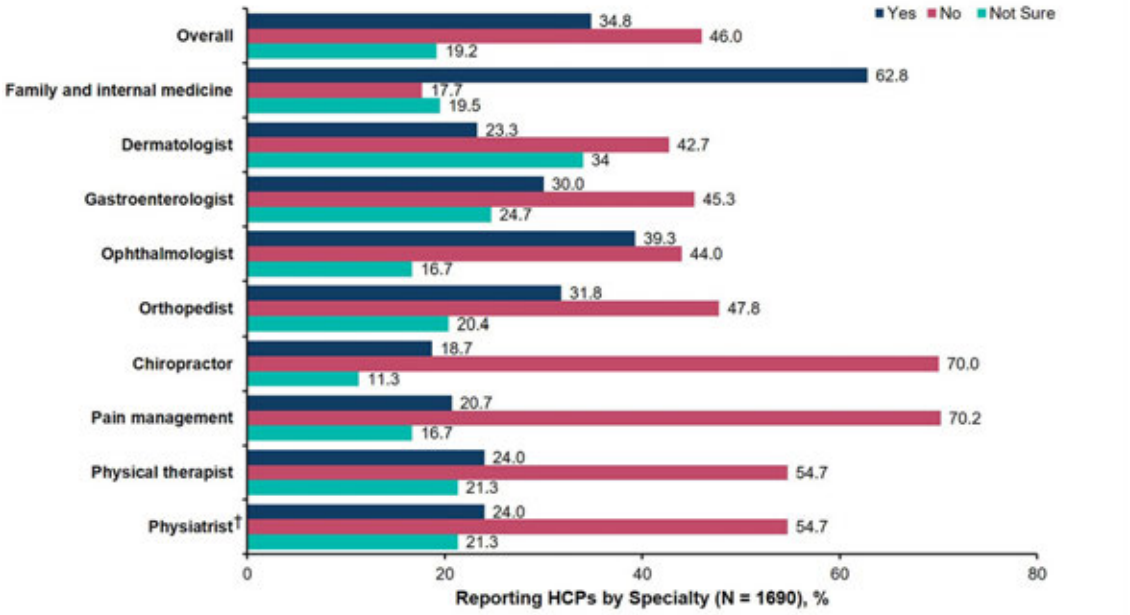
Session Time: 9:00AM–11:00AM

Background/Purpose: Early diagnosis of axial spondyloarthritis (axSpA) in the United States remains challenging due to the high prevalence and nonspecific presentation of chronic back pain treated by non-rheumatology health-care providers (HCPs). We aim to understand the patient referral and follow-up process and barriers to rheumatology referral among patients with putative inflammatory back pain (IBP) suggestive of axSpA.

Methods: Survey content was developed based on concept elicitation interviews with HCPs, and final questionnaires were generated to characterize their patient referral process. The survey was then cognitively tested with HCPs from 10 specialties (family medicine, internal medicine, dermatology, gastroenterology, ophthalmology, orthopedics, chiropractic, pain management, physical therapy, and physiatry), revised, and finalized. HCPs from these 10 specialties were invited to participate in the cross-sectional web-based survey hosted by Survey Sampling International between June 27 and July 20, 2018. HCPs who were currently licensed, actively practicing in the United States, and had referred a patient with suspected IBP (except ophthalmology) or uveitis/iritis (ophthalmology only) within the past 12 months were eligible to participate. Descriptive statistics were used to analyze the data.

Results: Of 2395 HCPs screened, 1690 were eligible and included in our study. Overall, HCPs saw a median of 100 patients with chronic back pain within the past 12 months. HCPs most frequently reported an average time of 3 to 4 months before a patient decided to see them (18.2%), whereas 17.1% reported 1 to 2 years. Overall, almost half of HCPs (46.0%) indicated that their patients had seen other specialists before consulting them; however, 62.8% of primary care HCPs (family and internal medicine) reported that they were the first HCPs seen by their patients (**Figure 1**). Once IBP was suspected, most HCPs (48.5%) would refer the patient after conducting a thorough evaluation, and

Figure 1. Proportion of Treating HCPs Indicating That They Were The First Provider Seen by Patients With Suspected IBP Suggestive of Rheumatic Disease*

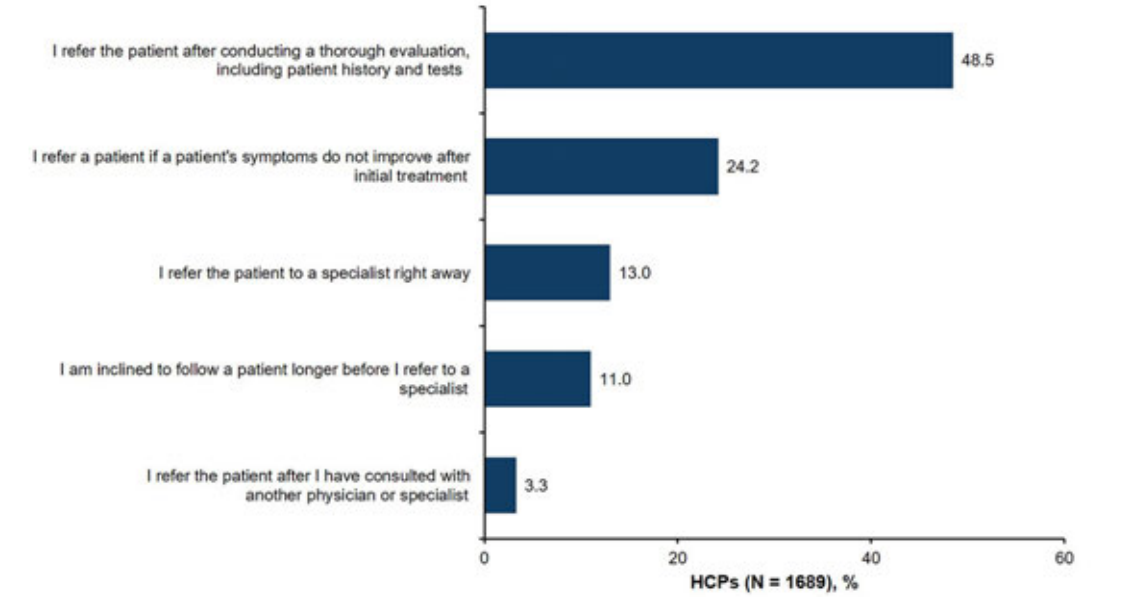


HCP, healthcare provider; IBP, inflammatory back pain.

* The phrase "inflammatory back pain" was used for all specialties except ophthalmology and chiropractic. Ophthalmologists were asked about patients with uveitis who may have "autoimmune rheumatic disease," and chiropractors were asked about patients who may have "inflammatory back pain or back pain due to underlying inflammatory conditions."

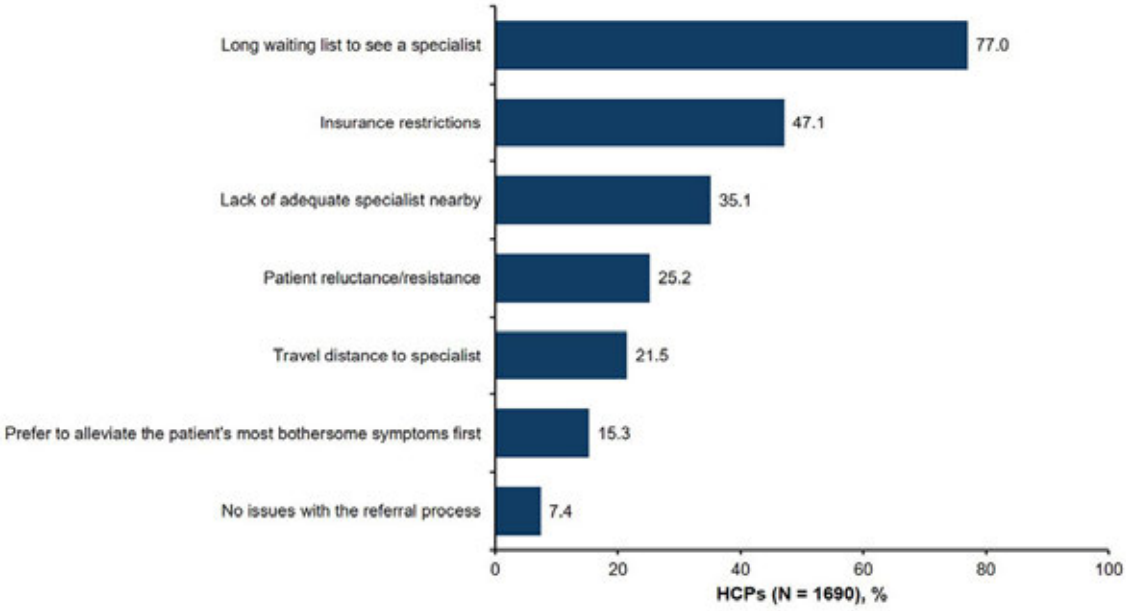
† Specialty category that includes physiatry, rehabilitation, and physical medicine.

Figure 2. Next Course of Action Taken by HCPs After Suspicion of IBP Suggestive of Rheumatic Disease*



HCP, healthcare provider; IBP, inflammatory back pain.
* The phrase "inflammatory back pain" was used for all specialties except ophthalmology and chiropractic. Ophthalmologists were asked about patients with uveitis who may have "autoimmune rheumatic disease," and chiropractors were asked about patients who may have "inflammatory back pain or back pain due to underlying inflammatory conditions."

Figure 3. Barriers Preventing Patients From Promptly Seeing A Specialist



HCP, healthcare provider.

13.0% would refer the patient to a specialist right away (**Figure 2**). Upon referral, 90.2% of HCPs estimated a wait time of up to 2 months for their patient to see a rheumatologist, 9.1% estimated a wait time of 3 to 6 months, and 0.7% estimated a wait time of 7 months to > 1 year; long waiting time (77.0%) and insurance restrictions (47.1%) were the primary reasons that may prevent patients from being able to see a specialist right away (**Figure 3**). Of 1607 HCPs queried, 61.9% ranked the specialist's expertise in treating autoimmune disease as the most important factor influencing their referral.

Conclusion: Nearly two-thirds of primary care HCPs reported that they were the first HCPs consulted by patients with suspected IBP, suggesting that targeted education of primary care HCPs may improve referral rates and yield a timely diagnosis of axSpA. Most HCPs (90.2%) estimated a wait time of up to 2 months for their patient to see a specialist after a referral was made and indicated that the specialist's expertise in autoimmune diseases is the most important factor influencing their referral.

Disclosure: M. Magrey, AbbVie, 2, Abbvie, 2, Abbvie, UCB and Amgen, 2, Amgen, 2, 5, Eli Lilly, 5, Eli Lilly and Company, 5, Eli Lily, Novartis, 5, Novartis, 5, 9, UCB, 2, UCB Pharma, 2; **E. Yi**, Novartis, 3, Novartis Pharmaceuticals Corporation, 3; **D. Wolin**, RTI Health Solutions, 3; **M. Price**, RTI Health Solutions, 3; **C. Chirila**, RTI Health Solutions, 3; **E. Davenport**, RTI Health Solutions, 3; **Y. Park**, Novartis, 3.

Abstract Number: 0632

An Observational Analysis of the Co-existence of Brugada Syndrome in Patients with Spondyloarthritis; A Potentially Important Link

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiac involvement in Spondyloarthritis (SpA) has been recognised as an important determinant of increased comorbidity and mortality due to atherosclerosis, aortitis, aortic regurgitation and ventricular dysfunction. Cardiac conduction abnormalities are commonly noted and may occur prior to symptom onset.

One potential relationship that warrants further study is with Brugada Syndrome (BrS). This is a rare inherited cardiac disorder characterised by disturbances of the conduction system of the heart. The clinical presentation varies from being asymptomatic to syncope and sudden cardiac death (SCD) due to ventricular arrhythmias. BrS can be associated with mutations in the *SCN5A* gene in a fifth of cases, encoding the cardiac sodium channel alpha subunit leading to cardiac conduction defects.

Methods: A database search of patients diagnosed with BrS at one centre was performed. The diagnosis was made in line with international guidelines (1): the presence of a spontaneous or intravenous Ajmaline (class Ia antiarrhythmic) provoked type 1 or 'coved' electrographic (ECG) pattern with J point and ≥2mm concave ST elevation in at least one ECG lead V1/2 recorded from the 4^{th},3^{rd} and/or 2^{nd} intercostal spaces; J point and 'saddleback' ST elevation with a positive T wave in at least one ECG lead V1/2 recorded from the 4th, 3rd and/or 2nd intercostal spaces (type 2/3: depending on degree of J point and ST elevation) if converted to a type 1 through Ajmaline induction. Documented ventricular fibrillation (VF) or polymorphic ventricular tachycardia (VT), syncope, family history of premature SCD and/or type 1 Brugada pattern was supportive. A validated genetic screen was done. All patients who were also under Rheumatology were identified. An interrogation of their medical records was conducted to extract: demographics, diagnosis of SpA, as defined by the Assessment of SpondyloArthritis International Society (ASAS) criteria, other rheumatology diagnoses, and other co-variates.

Patient	Diagnosis	Disease Duration (years)	HLA-B27 status	EAMs*	Drug Therapy	Resting ECG pattern	Additional criteria
1	Axial SpA, peripheral involvement	8	positive	nil	ETA†	Type1	VF Cardiac arrest
2	Peripheral SpA	9	negative	nil	SSZ	Type 2/3	VF Syncope
3	Axial SpA, predominant peripheral involvement	10	negative	psoriasis	MTX	Type 2/3	Sibling death from SADS‡
4	Peripheral SpA	4	positive	psoriasis	MTX	Type 2	Family history SCD
5	Rheumatoid arthritis	13	Not applicable	nil	MTX SSZ	Type 2	Syncope
6	Supraspinatus tendonitis	1	Not applicable	nil	Nil	Type 1	Offspring confirmed BrS with ICD$, syncope

*Extra-articular manifestations† ETA Etanercept ‡Sudden arrhythmic death syndrome: unexplained SCD $ implantable cardiovertor-defibrillator

Results: Of the 600 patients diagnosed with BrS, n=6, were found to have attended Rheumatology. There were 4 females and 2 males with a mean age= 52.1 years (30-71).
The Table shows the main findings.
All patients demonstrated a Type 1 Brugada pattern during the provocation test or spontaneously. All had structurally normal hearts on echocardiography and cardiac MRI at diagnosis. None of the patients had the *SCN5A* mutation. Patients 1 and 2 had an ICD device fitted as a consequence. All were given preventative lifestyle advice in the form of avoidance of excess alcohol, illicit substances, arrhythmogenic drugs, treating fever promptly with anti-pyretics and keeping hydrated.

Conclusion: There appears to be a preponderance of patients with peripheral SpA who have BrS (0.67%) compared to expected Caucasian and SE Asian population frequencies of 0.05% and 0.2% respectively. Half of the cases were HLA-B27 positive. Aside from psoriasis, there were no other EAMs noted. Whether this reflects inflammatory activity or a genetic link is unclear. This analysis highlights a potential important relationship, which requires further study.

Reference:

1.Priori, S.G., et al., Heart Rhythm, 2013. 10(12): p.1932-63

Disclosure: K. Lall, None; **R. Ramsden**, None; **E. Behr**, None; **V. Sandhu**, None.

Abstract Number: 0633

Diagnostic Delay in Spondyloarthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Spondyloarthritis (Spa) is an heterogeneous group of diseases. Diagnostic delay contributes to poor patient outcome. Prompt diagnosis of Spa is the first step towards optimal patient management. The aims of the study were to determinate if there were difference in diagnostic delay of Spa before 2010 vs 2010-2019 and to identify features associated with diagnostic delay more than twelve months.

Methods: Cross-sectional, analytical, multi-center study. Patients older than 18 years, fulfilling ASAS criteria were inclued. Socio-demographic and clinical features, comorbidities and treatments were recorded. Disease activity: patient´s global assessment (GA), physician´s GA; peripheral: joint count (SJC66/TJC68), enthesis evaluation (LEI) and DAS28; axial: BASDAI, ASDAS-ERS, SASDAS-ERS, functional assessment by BASFI. Disability by HAQ; Quality of life by ASQol and global health status by ASAS Health Index. Statistical analysis: descriptive statistics, Mann-Whitney or T-test for continuous variables and Fisher's exact test or Chi^2 for categorical ones, p 0.05 was considered significant. STATA 14.

Results: Two hundred one patients were inclued, 55.7% were males, mean age 48.8 years old (SD 14.3), median evolution time 65 months (IQR 24-132), median BMI 27.3 (IQR 22.7-35.8). More than half had peripheral involvement (53.73%). The 51.74% had enthesitis (*n* 101), 34.33% had dactylitis (*n* 69). Ninety-nine (49.5%) had psoriatic arthritis, 4.98% (*n* 10) inflammatory bowel disease and 13.93% (*n* 28) uveitis. Before 2010: diagnostic delay was longer than after 2010 [median 48 months (IQR 12-84) vs 12 months (IQR 4-24) *p 0.000*]. The greater diagnostic delay was associated to older patients [56 years old (IQR 42-64) vs 47 years old (34-56) *p 0.001*] and more of them loosed their job (*p: 0.001*). Diagnostic delay more than twelve months were associated with more prevalence of hypertension [39.3% vs 18.06% *p: 0.003*], loss of work [43.82 vs 23.61% *p*: 0.006] and use of biologics [58.43% vs 28.89% *p: 0.010*]. We did not find differences in disease activity, disability, quality of life or global health status by ASAS Health Index between both groups.

Conclusion: In recent years we have considerably improved the diagnosis delay of Spa. Even twelve months' delay was associated with loss of work, more comorbidities (hypertension) and greater use of biological treatments. ASAS criteria and the best knowledge of our diseases have contributed to this improvement.

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Abstract Number: 0634

Targeted ^{1}H NMR Based Metabolomics Analysis Revealed Significantly Higher Synovial Phe/Tyr Ratio in Reactive Arthritis and Undifferentiated Spondyloarthropathy

Hafis Muhammed,[1] Dinesh Kumar,[2] Durgesh Dubey,[2] Sandeep Kumar,[3] Smriti Chaurasia,[3] Anupam Guleria,[2] Sanjukta Majumder,[3] Rajeev Singh,[3] Vikas Agarwal,[1] and Ramnath Misra[4], [1]SGPGI, Lucknow, Uttar Pradesh, India, [2]Centre for Biomedical Research, Sanjay Gandhi Post Graduate Institute of Medical Science, Lucknow, Uttar Pradesh, India, [3]Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Post Graduate Institute of Medical Science, Lucknow, Uttar Pradesh, India, [4]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Lucknow, Uttar Pradesh, India

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

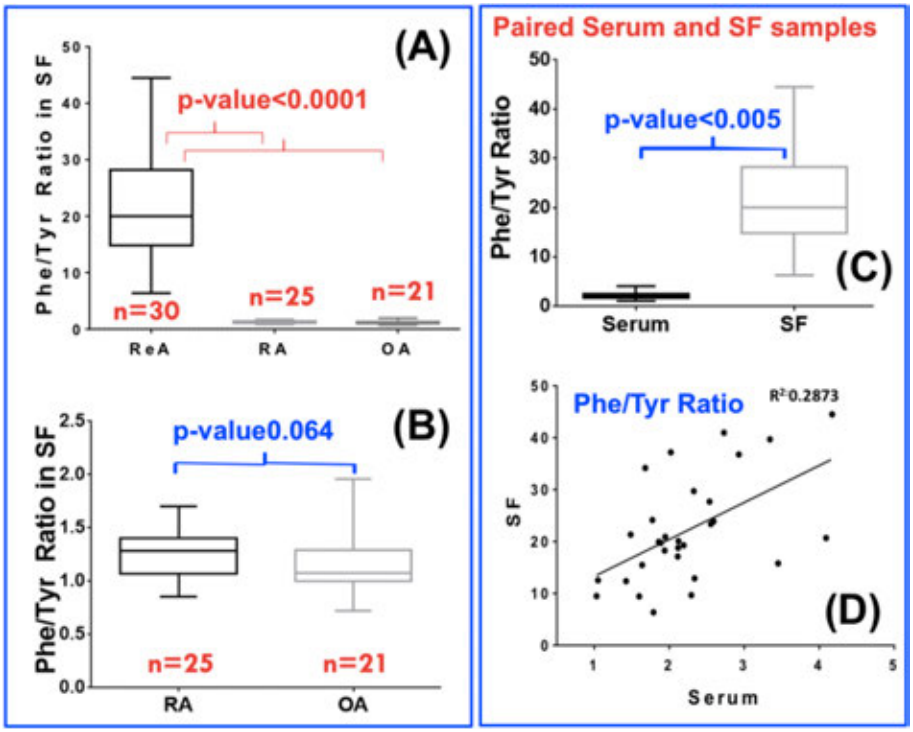
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Elevated phenylalanine-to-tyrosine ratio (Phe/Tyr) is a marker of oxidative stress. We hypothesized that the synovial Phe/Tyr in reactive arthritis is higher than Rheumatoid arthritis(RA) and osteoarthritis(OA). We conducted this study with the objective to compare the synovial Phe/Tyr between ReA/uSpA and RA and OA by NMR spectroscopy

Methods: Paired synovial fluid and serum of 30 patients with ReA/uSpA were collected and analysed using a 1D ^{1}H CPMG NMR spectra recorded on 800 MHz NMR spectrometer equipped with a TCI Cryoprobe (at 300 k). Phenylala-



Synovial Phe/Tyr ratio was significantly higher in ReA/uSpA compared to RA and OA

nine and tyrosine were quantified. Synovial fluid from 25 patients with RA fulfilling ACR classification criteria and 21 patients with OA were taken as inflammatory and non-inflammatory controls.

Results: Synovial Phe/Tyr ratio was significantly higher in ReA/uSpA compared to RA and OA. Synovial Phe/Tyr ratios were comparable in RA and OA patients. Compared to serum, the Phe/Tyr was significantly higher in the SF in ReA/uSpA. The Phe/Tyr was also found to be positively correlated between serum and SF samples with regression coefficient (r^2) of 0.287.

Conclusion: NMR based metabolomics study demonstrates that the synovial Phe/Tyr are specifically elevated in ReA/uSpA.

Disclosure: H. Muhammed, None; **D. Kumar**, None; **D. Dubey**, None; **S. Kumar**, None; **S. Chaurasia**, None; **A. Guleria**, None; **S. Majumder**, None; **R. Singh**, None; **V. Agarwal**, None; **R. Misra**, None.

Abstract Number: 0635

Association Between Radiographic Progression and Cardiovascular Risk in Spondyloarthritis: Data from CoSpaR REGISTRY

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster I: Axial Spondyloarthritis, Clinical Features

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Our objectives are:

1. To analyze the prevalence of comorbidities related to CV risk in a register of patients with spondyloarthritis (CoSpaR).
2. To evaluate if there is an association between structural damage, the presence of atherosclerotic plaques, the endothelial function and the increased CV risk in patients with axSpA.

Methods: Eight-five patients with axSpA from the SpA registry from Cordoba (CoSpaR) were selected for a cross-sectional study. Patients were recruited in a probabilistic and sequential way from a SpA monographic ambulatory, and a complete clinical history, physical examination and a biochemical analysis were performed.

CV risk was evaluated by estimating the SCORE index and assessing the presence of atherosclerotic plaques through carotid ultrasound. The study of endothelial function was performed with laser doppler flowmetry, ana-

Baseline characteristics	Mean (SD) or N(%)
Age (years) (N=85)	44,55±12,22
Sex (males) (N=85)	59 (69,4)
HLA B27 (N=83)	71 (83,5)
axSpA (N=85)	79 (92,9)
Radiographic axSpA (N=77)	63 (74,1)
Psoriasis (N=84)	10 (11,8)
BMI (kg/m^2) (N=80)	26,88± 4,13
Disease duration (years) (N=82)	18,01±13,62
Smokers (N=84)	33 (38,8)
ASDAS-CRP	3,13 ±1,05
ASAS HI (N=82)	4,05 ±3,8
BASDAI (N=84)	3,48 ±2,17
CRP (mg/L) (N=80)	6,64 ±10,86
ESR (mm/h) (N=63)	8,49 ±9,22
Arterial hypertension	16 (18,8)
Diagnosis of hyperlipaemia (N=83)	13 (15,3)

Characteristics related to structural damage and CV risk	Mean (SD) or N(%)
Total mSASSS (N=79)	14,84 ± 18,4
Cervical mSASSS (N=79)	7,27 ± 9,64
Lumbar mSASSS (N=79)	7,72 ± 10,14
Glucose (mg/dL) (N=80)	84,02 ± 14,5
Total Cholesterol (mg/dL) (N=80)	187,84 ± 33,75
HDL-cholesterol (mg/dL) (N=79)	54,92 ± 15,54
LDL-cholesterol (mg/dL) (N=78)	111,96 ± 30,91
Tryglicerides (mg/dL) (N=80)	100,68 ± 65,85
Insuline (N=70)	6,1 ± 4,1
Diabetes Mellitus (N=84)	1 (1,2
Atherosclerotic carotid plaques (N=66)	14 (16,5)
Insuline resistance (N=85)	7 (3,4)
SCORE (N=78) • Low CV risk • Moderate CV risk • High CV risk • Very high CV risk	57 (67,1) 13 (15,3) 4 (4,7) 4 (4,7)

lyzing the response to reactive hyperemia, so as the increase in blood flow occurred after temporary occlusion of blood flow.

Data was collected and analyzed using SPSS v25 program. Independent-samples t test was used to evaluate the association between radiological characteristics and presence of atherosclerotic plaques. The linear lelationship between the variables has been measured by Pearson's linear correlation coefficient. Multiple lineal regression (MLR) was performed to assess the variables potentially associated with increased SCORE. All comparisons were bilateral considering $p \leq 0.05$ as a significant result.

Results: Baseline characteristics are shown in table 1.Characteristics related with radiographic damage and CV risk are shown in table 2. Direct linear relationship was found between the CV risk measured by SCORE index and total, lumbar and cervical mSASSS, and the presence of bone bridges. Analysis of atherosclerotic plaques at the carotid showed that age, disease duration, and variables related to radiographic damage (total mSASSS, cervical spine mSASSS, lumbar spine mSASSS, and bone bridges) were significantly higher in patients with atherosclerotic plaques($p< 0.05$). In addition, mSASSS in cervical spine ($p=0.063$) and age ($p< 0.0001$) were found to be associated with the SCORE index value and were predictors of increased CV risk in MLR analysis. Endothelial function (measured by Laser Doppler measurement of post ischemic reactive hyperemia) correlated inversely ($p< 0,05$) with total and lumbar mSASSS, as shown by the values of hyperemic area after occlusion was released.

Conclusion: The presence of atherosclerotic plaques in patients with axSpA is associated not only with age and disease duration, but also with the degree of radiographic damage present. Age and structural damage predicted the increased risk of CV disease observed in axSpA. Therefore, we have observed that older patients with axSpA and more structural damage, especially in the cervical spine, had a greater risk of CV disease. Endothelial disfunction is also found in patients with axSpA.

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Abstract Number: 0636

Validation and Transcultural Adaptation of the Spanish Version of Brief Index of Lupus Damage (BILD) Questionnaire

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) develop irreversible organ damage as a consequence of disease activity, chronic inflammation, comorbidities and side effects of medications. Quantifying organ damage is relevant in their assessment. Damage is traditionally evaluated by the Systemic Lupus International Collaborating Clinics Damage Index (SLICC-SDI). Two patient-reported damage questionnaires have been validated: Lupus Damage Index Questionnaire (LDIQ) and Brief Index of Lupus Damage (BILD). BILD was developed from the LDIQ. The original English version has better correlation with SLICC-SDI than LDIQ.

Our aim was to perform validation and transcultural adaptation of the BILD questionnaire to Spanish.

Table 1. Correlation between BILD and SLICC-SDI, LupusQol, SLEDAI, patient and physician global VAS.

Variable	Spearman coefficient	P
SLICC SDI total	0.73	<0.001
SLICC SDI, ocular	0.71	<0.001
SLICC SDI, neurophsychiatric	0.85	<0.001
SLICC SDI, renal	0.72	<0.001
SLICC SDI, pulmonary	0.32	0.003
SLICC SDI, cardiovascular	0.40	0.002
SLICC SDI, peripheral vascular	0.45	<0.001
SLICC SDI, gastrointestinal	-0.02	0.804
SLICC SDI, musculoskeletal	0.58	<0.001
SLICC SDI, skin	0.18	0.094
SLICC SDI, premature gonadal failure	0.79	<0.001
SLICC SDI, diabetes	-	-
SLICC SDI, malignancy	1	<0.001
LupusQol total	-0.11	0.298
SLEDAI	0.12	0.271
Patient global VAS (n=49)	-0.01	0.924
Physician global VAS	0.22	0.036

Table 2. Comparison of demographics and clinical characteristics by BILD score cut-off points

BILD score	≤ 3 (n=70)	>3 (n=15)	p
Female sex, *n (%)*	63 (90)	13 (86.7)	0.70
Age, *years mean (SD)*	40.3 (10.8)	49.9 (14)	**0.004**
Disease duration, *years mean (SD)*	10.7 (7.8)	19.6 (9.6)	**0.001**
SLEDAI, *mean (SD)*	1.43 (2.6)	4 (4.6)	**0.004**
Lupus Qol, *mean (SD)*	87.13 (23.2)	89.8 (18.6)	0.67
Physician global VAS, *median (IQR)*	1.5 (0-3)	3 (1-6)	**0.005**
Patient global VAS, *median (IQR)*	2 (1-3)	3 (1-5)	0.22
Number of immunosupressors, *mean (SD)*	1.9 (1.3)	2.5 (1.7)	0.15
Charlson score, *median (IQR)*	1 (1-2)	3 (1-4)	**0.002**

Methods: The original BILD questionnaire in English was translated to Spanish independently by two bilingual physicians and a first intermediate Spanish version was produced. A back translation was performed and compared with the original BILD to assess conceptual equivalence and detect possible misunderstandings. On the basis of this comparison, a final Spanish version was created.

The BILD questionnaire was administered to 85 consecutive SLE patients from 2 Hospitals (one public and the other private). All patients fulfilled ACR 1997/ ACR-SLICC 2012 SLE criteria. Sociodemographic data, Charlson comorbid-

ity index, SLICC-SDI, SLEDAI score, global physician visual analogue scale (VAS) were obtained from each patient. Patients also completed the LupusQol questionnaire and global patient VAS.

We estimated the stability by a test retest method and a Spearman correlation coefficient. Internal consistency was evaluated with the Cronbach alpha coefficient. To evaluate criterion validity, a Spearman correlation coefficient was calculated for SLICC-SDI and BILD total scores and for item-by-item comparison. To asses construct validity we compared patients characteristics and disease variables in 2 cut off points of the BILD score.

The feasibility was obtained by taking into account the percentage of no answered questions and the time required to answer.

Results: We evaluated 85 patients, 89.4% female, mean age 42 years (SD 11.9) with mean disease duration of 12.3 years (SD 8.8). Eighty percent of patients had more than 12 years of education. Fifty-five patients were white, 20 Amerindian, 9 Mestizo y 1 Asian. The mean SLICC-SDI score was 1.14 (SD 1.44) and the mean BILD score was 1.48 (SD 1.84). The test retest method showed a strong correlation with a Spearman coefficient of 0.91 ($p < 0.001$). The Cronbach alpha coefficient was 0.66. The correlation between total scores of BILD and SLICC-SDI and each of its domains is shown in Table 1. Table 2 shows the construct validity analysis. In the multivariate analysis patients in the upper half of BILD scores were more likely to have longer disease duration and higher Charlson score. No incomplete answers were obtained and the mean time to answer was 4 minutes and 13 seconds (SD 1.92).

Conclusion: We demonstrated that the self-reported BILD questionnaire has a strong correlation with SLICC-SDI. In the item by item analysis we found that only the domains of gastrointestinal system and skin had a weak or none correlation with the corresponding SLICC-SDI items.

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Abstract Number: 0637

How Often Should SLE Patients Be Tested for Lupus Anticoagulant?

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE patients with persistent lupus anticoagulant (LAC) have been observed to be at significantly higher risk of thrombosis. A common clinical definition of persistent LAC is to have two confirmed tests for LAC separated in time by at least 12 weeks. The likelihood of identifying a patient with LAC based on this definition depends on the frequency with which it is assessed. The purpose of this analysis is to determine the impact of frequent repeated testing of LAC on patient identification and clinical outcomes.

Methods: LAC was measured repeatedly in patients in a large American clinical cohort of prevalent and incident SLE patients. (51% Caucasian-American, 40% African American) . Patients were defined as LAC positive at a clinic visit if they had a dRVVT of 45 or more seconds, a mixing study, and then a positive confirmatory test. For 20% of the

Table 1. Rates of thromboses in months classified by whether the patient was classified as having LAC based on 5 previous measures, or on all previous measures of LAC

Subgroups of Months	Number of thromboses[1] observed	Rate per 1000 person-months (95% CI)	P-value[2]
No prior persistent LAC	140	1.3 (1.1, 1.6)	
Prior persistent LAC based on first 5 tests.	34	2.5 (1.5, 3.5)	0.018
Prior persistent LAC based on all prior LAC assessments but not classified as positive based only on the first 5 tests	14	1.8 (0.5, 3.1)	0.46

[1] Thromboses were clinical diagnoses of stroke, myocardial infarction, other arterial thromboses, deep venous thromboses, or other venous thromboses.
[2] P-value compares rates to those months with No Prior persistent LAC.

patients, the confirmatory test was missing and these values were imputed using multiple imputation based largely on the value of dRVVT. Persistent lupus anticoagulant was defined as having two consecutive visits with confirmed lupus anticoagulant separated by at least 12 weeks. We determined the number of patients who would be identified as having persistent LAC under two scenarios: 1) if only 5 LAC assessments were made, or 2) if multiple repeated assessments were made. In addition, we determined whether those identified with persistent LAC based on multiple repeat assessments but who were not identified based on only 5 assessments were at increased risk of thrombosis. This was based on discrete survival analysis including followup that occurred after at least 5 LAC assessments was included.

Results: The analysis was based on 36,218 clinical tests of LAC from 1457 different patients who had at least 5 LAC tests. The number of tests per patient ranged from 5 to 74 with a mean of 25. Based on only the first 5 tests per patient, the prevalence of persistent LAC was 11.7%. Based on all the LAC tests, the prevalence of persistent LAC was found to be 15.8%. Table 1 shows the rates of thrombosis in months defined by LAC classification based on all prior tests. In those months that were not preceded by persistent LAC the rate of thrombosis was 1.3 per 1000 person-months. In those months that were preceded by a diagnosis of LAC based on the patient's first 5 LAC tests, the rate of thrombosis was 2.5 per 1000 person-months (p=0.018 relative to months without LAC). In those months that were not classified as having prior persistent LAC based on the patient's first 5 LAC tests, but were classified as having persistent LAC based on all prior LAC tests, the rate of thrombosis was 1.8 per 1000 person months (p=0.46 relative to months without LAC).

Conclusion: 26% of those with persistent LAC are missed if LAC assessment is based only on the first 5 LAC tests. However, those classified as having LAC based on their first 5 tests are at highest risk of thrombosis. This information can inform decision-making related to frequency of LAC testing.

Disclosure: L. Magder, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 0638

Longitudinal Trends for Estimated Glomerular Filtration Rate and Predictors of Change in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To characterize the longitudinal trajectory of estimated glomerular filtration rate (eGFR) in patients with systemic lupus erythematosus (SLE) and identify predictors of change in eGFR trajectory.

Methods: All patients with SLE who participated in a large American Lupus Cohort in or after year 2006 were identified. Patients were followed until death, diagnosis of end-stage renal disease or renal failure, or the last follow-up date, whichever came first. The longitudinal eGFR level of patients were modelled by piecewise linear regression. We evaluated the slope of different line segments. The slopes were classified into declining (≤ -4 mL/min/1.73 m^2 per year), stable (-4 to 4 mL/min/1.73 m^2 per year), and increasing (≥4 mL/min/1.73 m^2 per year) states of eGFR. The transition rate between states and the impact of clinical parameters on transition rate were estimated using Proportional Hazards modeling.

Results: We identified 494 SLE patients with 15,329 clinical visits over time. Two hundred and sixty-one (52.8%) patients were between 40 and 59 years old at the first clinical visit (baseline); 183 (37.0%) were younger than 40 years old; 50 (10.1%) were at or above 60 years old at baseline; 455 (92.1%) patients were female; 267 (54.0%) patients were Caucasian; 185 (37.4%) patients were African American. Their mean SLE disease activity index was 2.7 ± 3.4

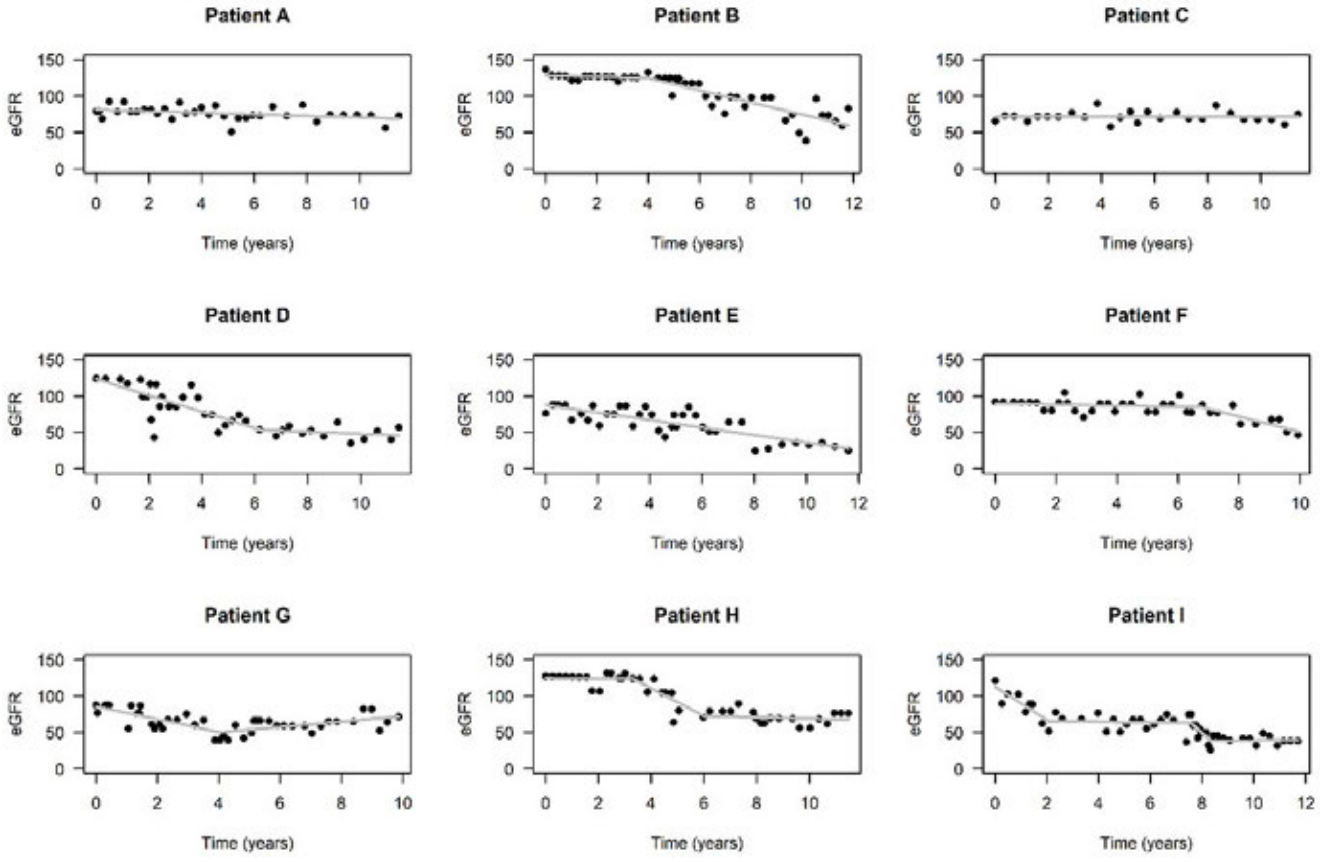

Figure 1. eGFR trajectory of selected patients (Gray line represents the estimated trajectory by piecewise linear regression. Black dot represents the eGFR of the patient in each visit).

Table 1. Univariate and multivariable predictiors of transition from non-declining state to declining state.

Parameters	Univariate analysis		Multivariable analysis	
	Hazard ratio (95% CI)	*P* value	Adjusted hazard ratio (95% CI)	*P* value
Age (years)				
<40	Referent		Referent	
40-59	1.39 (0.85 – 2.28)	0.192	1.19 (0.70 – 2.05)	0.520
≥60	1.80 (1.03 – 3.13)	0.038	1.19 (0.63 – 2.25)	0.591
Male gender	0.40 (0.06 – 2.67)	0.345	0.34 (0.04 – 2.59)	0.298
Race				
Caucasian	Referent		Referent	
African American	0.55 (0.36 – 0.83)	0.004	0.50 (0.31 – 0.81)	0.004
Other	0.88 (0.40 – 1.94)	0.745	0.82 (0.34 – 1.99)	0.667
eGFR (mL/min/1.73 m^2)				
≥90	Referent		Referent	
60-89	2.05 (1.23 – 3.43)	0.006	1.87 (1.09 – 3.20)	0.023
<60	3.36 (1.98 – 5.73)	<0.001	2.72 (1.52 – 4.87)	<0.001
High systolic blood pressure [a]	0.72 (0.43 – 1.22)	0.221	0.68 (0.40 – 1.17)	0.167
High urine protein-to-creatinine ratio [b]	0.85 (0.43 – 1.69)	0.647	0.70 (0.33 – 1.52)	0.368
Detectable anti-dsDNA	0.92 (0.57 – 1.47)	0.717	1.21 (0.71 – 2.07)	0.486
SLEDAI without renal variables	0.95 (0.86 – 1.04)	0.246	0.97 (0.86 – 1.10)	0.672
Low complement component 3	0.95 (0.57 – 1.58)	0.836	0.94 (0.51 – 1.75)	0.851
Low complement component 4	0.93 (0.52 – 1.67)	0.810	1.11 (0.55 – 2.23)	0.772
Low hematocrit [c]	1.30 (0.87 – 1.93)	0.206	1.54 (0.98 – 2.41)	0.061
Use of prednisone	1.55 (1.04 – 2.32)	0.032	1.61 (1.04 – 2.49)	0.032
Use of hydroxychloroquine	0.88 (0.51 – 1.50)	0.631	0.85 (0.49 – 1.49)	0.575
Use of antihypertensive drugs	1.82 (1.10 – 3.00)	0.020	1.37 (0.81 – 2.32)	0.234

[a] High systolic blood pressure was defined as systolic blood pressure ≥140 mmHg.
[b] High urine protein-to-creatinine ratio was defined as urine protein-to-creatinine ratio >0.5.
[c] Low hematocrit was defined as <41% for males and <36% for females.
anti-dsDNA = anti-double stranded DNA, CI = confidence interval, eGFR=estimated glomerular filtration rate, SLEDAI=systemic lupus erythematosus disease activity index.

at baseline. Three hundred and eight (62.3%) patients had an eGFR ≥90 mL/min/1.73 m2 at baseline; 152 (30.8%) had an eGFR between 60 and 89 mL/min/1.73 m2 at baseline; 34 (6.9%) had a baseline eGFR < 60 mL/min/1.73 m2. The eGFR trajectory of selected patients is shown in Figure 1. Of all patients, 34.4% experienced a declining state at some point in their follow-up. In patients with one transition, 43 (40.2%) changed from declining to stable state while 29 (27.1%) changed from stable to declining state. High blood pressure, low C4 and low hematocrit were associated with change from non-declining to declining state (Table 1). High urine protein-to-creatinine ratio also tended to be associated with change from non-declining to declining state. African American patients were less likely to move from declining to non-declining state. Use of prednisone was associated with change from declining to non-declining state (Table 2).

Conclusion: A declining eGFR trajectory is common in SLE patients. High blood pressure and urine protein-to-creatinine ratio, and low C4 and hematocrit are risk factors for transition from stable to declining GFR. Use of prednisone may attenuate the declining eGFR. These findings can help clinicians anticipate changes in GFR trajectory.

Table 2. Univariate and multivariable predictiors of transition from declining to non-declining state.

Parameters	Univariate analysis		Multivariable analysis	
	Hazard ratio (95% CI)	*P* value	Adjusted hazard ratio (95% CI)	*P* value
Age (years)				
<40	Referent		Referent	
40-59	0.51 (0.31 – 0.84)	0.008	0.84 (0.48 – 1.46)	0.536
≥60	0.53 (0.28 – 1.03)	0.061	1.27 (0.58 – 2.76)	0.555
Male gender	0.26 (0.07 – 1.08)	0.064	0.28 (0.07 – 1.14)	0.075
Race				
Caucasian	Referent		Referent	
African American	1.63 (1.01 – 2.62)	0.045	0.99 (0.57 – 1.72)	0.974
Other	1.19 (0.50 – 2.83)	0.697	0.88 (0.36 – 2.16)	0.787
eGFR (mL/min/1.73 m^2)				
≥90	Referent		Referent	
60-89	0.36 (0.21 – 0.65)	<0.001	0.43 (0.23 – 0.78)	0.005
<60	0.27 (0.10 – 0.73)	0.010	0.22 (0.07 – 0.66)	0.007
High systolic blood pressure [a]	1.82 (1.07 – 3.09)	0.028	1.77 (1.01 – 3.12)	0.047
High urine protein-to-creatinine ratio [b]	2.74 (1.40 – 5.33)	0.003	2.07 (1.00 – 4.29)	0.051
Detectable anti-dsDNA	1.84 (1.10 – 3.07)	0.020	0.98 (0.52 – 1.86)	0.963
SLEDAI without renal variables	1.13 (1.05 – 1.23)	0.002	1.02 (0.92 – 1.14)	0.699
Low complement component 3	1.56 (0.88 – 2.75)	0.126	0.83 (0.42 – 1.66)	0.602
Low complement component 4	2.53 (1.49 – 4.30)	<0.001	1.96 (1.02 – 3.77)	0.044
Low hematocrit [c]	2.12 (1.34 – 3.35)	0.001	1.71 (1.02 – 2.86)	0.040
Use of prednisone	1.93 (1.22 – 3.05)	0.005	1.47 (0.90 – 2.40)	0.125
Use of hydroxychloroquine	0.95 (0.51 – 1.76)	0.873	1.09 (0.56 – 2.13)	0.808
Use of antihypertensive drugs	0.81 (0.52 – 1.28)	0.360	0.86 (0.52 – 1.43)	0.555

[a] High systolic blood pressure was defined as systolic blood pressure ≥140 mmHg.
[b] High urine protein-to-creatinine ratio was defined as urine protein-to-creatinine ratio >0.5.
[c] Low hematocrit was defined as <41% for males and <36% for females.
anti-dsDNA = anti-double stranded DNA, CI = confidence interval, eGFR=estimated glomerular filtration rate, SLEDAI=systemic lupus erythematosus disease activity index.

Disclosure: T. Yip, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5; **L. Magder**, None.

Abstract Number: 0639

African-American Risk of Proteinuria After SLE Diagnosis Increases Throughout Thirty Years of Followup

Michelle Petri,[1] and Jessica Li[1], [1]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: African-Americans lupus nephritis is more common than in Caucasians, more severe and more likely to lead to end stage renal disease. We asked whether the difference in frequency was just at the time of SLE diagnosis.

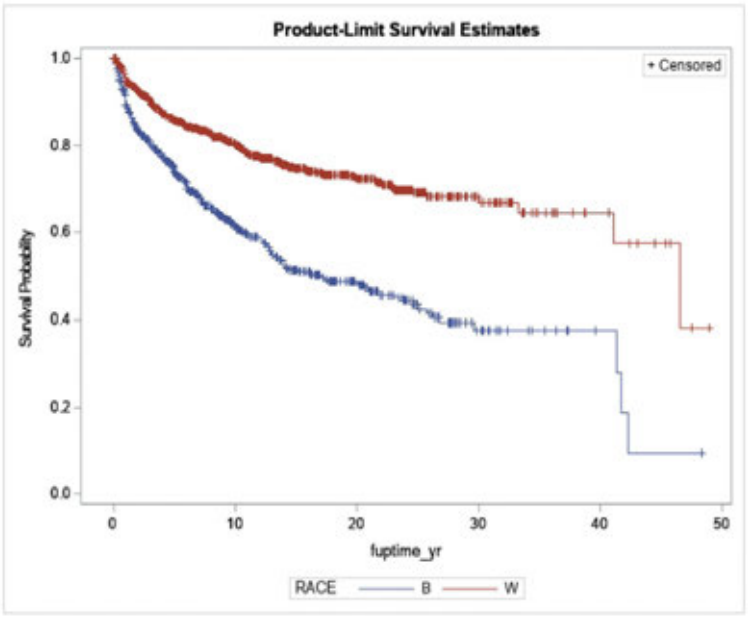

Figure 1 - Time to First Proteinuria for African-Americans (B) and Caucasians (W)

Table 1 - Risk of proteinuria after SLE diagnosis

	Risk of proteinuria after SLE diagnosis (95% CI)[1]		p-value[2]
Risk within:	African American	Caucasian	<0.0001
½ year	4.9% (3.5%, 6.8%)	1.6% (1%, 2.6%)	
1 year	10.5% (8.4%, 13%)	5.4% (4.2%, 6.9%)	
2 years	16.3% (13.8%, 19.3%)	7.6% (6.1%, 9.3%)	
5 years	25.9% (22.7%, 29.4%)	14.3% (12.3%, 16.6%)	
10 years	38.3% (34.5%, 42.4%)	19.6% (17.1%, 22.3%)	
20 years	51.7% (47.2%, 56.4%)	27.4% (24.2%, 30.9%)	
30 years	62.4% (55.7%, 69.2%)	33.1% (28.3%, 38.5%)	
[1] based on Kaplan Meier estimates [2]based on log rank test comparing African American and Caucasian			

Table 2 - Hazard Ratio for Proteinuria After Diagnosis – African-American vs Caucasian

	Unadjusted		Adjusted[1]	
	HR (95% CI)	p-value	HR (95% CI)	p-value
African American	2.19 (1.91, 2.52)	<0.0001	2.14 (1.86, 2.46)	<0.0001
Caucasian	Ref group		Ref group	
[1]adjusted for gender and age at diagnosis				

Methods: 1849 SLE patients were included in this analysis. The patients were 93% female, 39.3% African-American and 60.7% Caucasian. 478 patients (27.2%, 271/997 African-American and 15.6%, 207/1330 Caucasian) who had proteinuria before or at the date of diagnosis (± 1 month) were excluded.

Results: The Kaplan-Meier curve of time to first proteinuria (in those without proteinuria at diagnosis) is shown in Figure 1. The separation between African-Americans and Caucasians starts almost immediately after diagnosis and continues to widen until year 30. Although it appears to level off at year 30, that is likely due to smaller numbers remaining in the cohort. Table 1 shows the estimated risk of proteinuria after diagnosis. The estimated probability of having proteinuria within 5 year is 26% for African-American patients and 14% for Caucasian patients. Risk accumulates even 5 years after diagnosis. Table 2 shows the hazard ratio for proteinuria after diagnosis. The risk of proteinuria is 2.19 times higher among African-American patients compared to Caucasians in the unadjusted model.

After adjustment for age at diagnosis and gender, the risk remains 2.14 higher for African-Americans compared to Caucasians.

Conclusion: The increased risk of lupus nephritis in African-Americans is not limited to diagnosis or even to the first five years after diagnosis. Increased risk is present through 30 years after diagnosis. As these data also show continued risk in Caucasians, monitoring the urine protein/cr at every follow up visit is recommended for all SLE patients.

Disclosure: M. Petri, Eli Lilly and Company, 5, Exagen, 2, 5; **J. Li**, None.

Abstract Number: 0640

Elevated Serum Interleukin-23 Level in Patients with Systemic Lupus Erythematosus Is Associated with Disease Activity, Clinical and Immunological Markers

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SESSION INFORMATION
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Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
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Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a autoimmune disease characterized by deregulated cytokine production. IL-23 bridges innate and adaptive immunity by inducing the differentiation of T cells into pro-inflammatory Th17. We have previously shown that IL-23 is upregulated in SLE patients and lupus prone mice. Besides inducing the generation of Th1, we found that in lupus, IL-23 promotes the generation of T follicular helper cells (Tfh) and inhibits regulatory T cells, thus increasing production of anti-dsDNA antibodies. Aim of this study was to evaluate IL-23 levels and its association with various clinical and laboratory parameters of SLE.

Methods: Serum IL-23 was measured in 56 SLE patients by ELISA (54 females and 2 males; age:42±12years; racial distribution:43% white, 28% African-American,20% Asian, 8% other). Institutional IRB approved the study. Disease activity was measured by SLEDAI (0-34; mean±sem= 6.71±1.02). 55% of patients were on prednisone at a mean dose of 11.09 mg (1–60). Other medications included hydroxychloroquine (67%), mycophenolate mofetil (34%), azathioprine (10%). Two patients were on IV cyclophosphamide, 3 on belimumab, 1 on tacrolimus, 1 on tocilizumab. STATA was used for statistical analyses: non-paired t-test and Pearson's correlation. Multiple linear regression analysis was used to analyze the effect of SLEDAI and medications on IL-23 expression.

Results: IL-23 levels in the serum of SLE patients were significantly higher in patients with active disease as measured by the SLEDAI (r=0.4363, p=0.0008). Correlation persisted even when we excluded the dsDNA and complement components from the SLEDAI, defined as clinical SLEDAI (r=0.3752, p=0.0044). Serum IL-23 was strongly correlated with skin (r=0.2853; p=0.03), renal (r=0.2928; p=0.0286) domains of SLEDAI and arthritis (p=0.03).There was no correlation with neurological manifestations or presence of serositis. IL-23 levels had significant positive correlation with anti-dsDNA (p=0.005) and negative with complement C3 (p=0.0003). We found no relationship between patients' demographics, prior disease manifestations or other autoantibody profile or cytopenias. Of note, SSA+ patients had a non-statistically significant trend for higher IL-23 levels than SSA- patients (p=0.065). Multivariate regression analysis

was used to account for potential confounding effect of medications on the correlation of SLEDAI and IL-23 levels. We found that IL-23 levels strongly correlate with SLEDAI after controlling for dose and type of medications including prednisone dose ($p< 0.001$).

Conclusion: In this cross-sectional analysis of SLE patients we found that IL-23 levels track disease activity and correlate with renal, skin and musculoskeletal manifestations but not with cytopenias or serositis. This is in line with murine data where blocking IL-23 ameliorated both kidney and skin disease. No immunomodulatory medication seems to be affecting IL-23 levels suggesting that current medications used in SLE are not as effective in shutting down the IL-23/IL-17 axis. Furthermore, our data suggest that IL-23 inhibitors may be helpful not only in non-renal SLE, where they are currently being tested, but also in lupus nephritis.

Disclosure: M. Vukelic, None; **A. Laloo**, None; **V. Kyttaris**, exagen diagnostics, 2, Exagen Diagnostics, 2, GSK, 5, gsk, 5, horizon pharma, 5, Horizon Pharma, 5.

Abstract Number: 0641

A Novel Method to Analyze Circulating Immune Complexes Predicts Disease Activity and Severity in Systemic Lupus Erythematosus and Rheumatoid Arthritis

Anders Bengtsson,[1] Helena Tyden,[1] Tiffany Pan,[2] J. Lee Nelson,[3] and **Christian Lood** [2,1]Lund University, Lund, Sweden, [2]University of Washington, Seattle, [3]Fred Hutchinson Cancer Research Center, Seattle

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Circulating immune complexes (IC) are detectable in a variety of systemic inflammatory diseases, including rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), reflecting the autoimmune process, e.g. autoantibodies binding to self-antigens. ICs are main contributors to the disease pathogenesis through engaging FcgR-bearing cells, as well as activating the complement system, mediating inflammation and organ damage, including erosion and nephritis. The main aim of the current study was to explore the clinical utility of analyzing levels of circulating ICs in patients with rheumatic diseases using a novel flow cytometry-based assay developed in our lab.

Methods: Levels of ICs were analyzed by an in-house flow cytometry-based method, analyzing IC binding to FcgRI-IA. Three cross-sectional SLE cohorts (n=92-142), one cross-sectional RA cohort (n=247), and healthy controls (n=100), were analyzed. To determine the capacity of ICs to predict disease flare in SLE, a forth, longitudinal SLE cohort (n=47) was recruited at time-point of low disease activity and followed over three months, with 14 patients remaining in remission, and 33 patients developing worsening of disease. A longitudinal inception RA cohort (n=247), seen for a follow-up a median of 8 years later, was used for predictive analyses. Type I interferon (IFN) activity was analyzed using a cell reporter system (WISH).

Results: Levels of ICs were elevated in SLE as compared to healthy controls ($p< 0.0001$). Whereas only 5% of the healthy controls had elevated levels of ICs, 61% of the SLE patients were positive for ICs, reaching more than 80% in patients with active disease. In contrast, anti-dsDNA antibodies, commonly used to monitor disease activity, were

only detectable in 14% of the patients at time-point of blood draw. Though anti-dsDNA antibodies were associated with active disease (OR=3.5, p< 0.0001), dual positivity for both anti-dsDNA antibodies and ICs further strengthened the association with active disease (OR=5.9., p< 0.0001). Levels of ICs reflected active disease as determined by SLEDAI (r=0.45, p< 0.0001), and were associated with ongoing type I IFN activity (r=0.25, p=0.003), complement activation (r=0.53, p< 0.0001) and active lupus nephritis (p=0.02). Levels of ICs were elevated in patients with a history of nephritis (p=0.002) and anti-dsDNA antibodies (p< 0.0001). In the longitudinal setting, baseline levels of ICs, at time-point of quiescent disease, could predict worsening of disease within three months (OR=4.4, p=0.03). Levels of ICs were elevated also in RA patients (p< 0.0001), though the frequency of patients having circulating ICs was lower as compared to SLE patients (21.7%). Importantly, RA patients with elevated levels of ICs at baseline identified patients developing a severe and erosive disease with joint space narrowing (p< 0.05).

Conclusion: ICs are instrumental in RA and SLE pathogenesis. Analyzing IC levels may facilitate monitoring of disease activity, as well as identify patients at risk of developing flare and/or severe disease, including erosion and nephritis, allowing for early preventive interventions.

Disclosure: A. Bengtsson, None; **H. Tyden**, None; **T. Pan**, None; **J. Nelson**, None; **C. Lood**, None.

Abstract Number: 0642

Complement Deposition C4d on Platelets Is Associated with Vascular Events in Systemic Lupus Erythematosus

Elisabet Svenungsson,[1] Johanna Gustavsson,[2] Giorgia Grosso,[2] Iva Gunnarsson,[2] Bo Nilsson,[3] Anders Larsson,[3] Anders Bengtsson,[4] and **Christian Lood**[5], [1]Division of Rheumatology, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden, [2]Karolinska Institutet, Stockholm, Sweden, [3]Uppsala University, Uppsala, Sweden, [4]Lund University, Lund, Sweden, [5]University of Washington, Seattle

SESSION INFORMATION
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Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
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Background/Purpose: Complement components, including C4d, can be detected on the surface of activated platelets and they have been associated with vascular disease in systemic lupus erythematosus (SLE). In the current study, we investigate whether platelet C4d (PC4d) adds additional value to traditional and known SLE-associated risk factors when identifying SLE patients with vascular disease.

Methods: We included 308 well-characterized SLE patients and 308 matched population controls in a cross-sectional design. Traditional risk factors including age, gender, smoking, hypertension and lupus associated risk factors aPL and glomerular filtration rate measured by MDRD formula were tabulated. PC4d deposition was analyzed using flow cytometry. Values >95% of controls were considered as PC4d positivity (+). Antiphospholipid antibodies (aPL) were determined by Luminex, and the lupus anticoagulant (LA) test was performed by a Dilute Russel Viper Venom Time method.

Results: SLE patients had increased PC4d deposition as compared to population controls (p< 0.0001). 50.3% of SLE patients were PC4d+. In SLE patients, PC4d+ associated with previous vascular events (AVE), specifically with venous and cerebrovascular, but not with ischemic heart events. PC4d was also associated with all investigated aPL

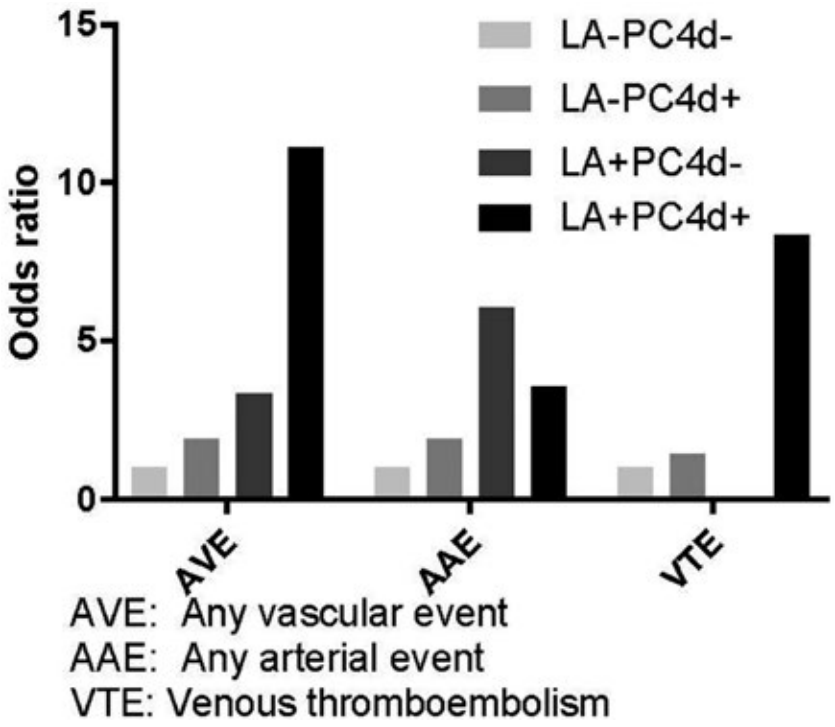

Figure 1. Interaction analysis between lupus anticoagulant and PC4d

Table 1. Multivariable logistic regression model for PC4d and vascular event

Multivariable logistic regression model for Any Vascular Event N=87

	OR	95% CI	P-value
Age/10 years	1.4	1.1-1.8	0.003
Gender female	0.8	0.5-1.4	0.51
Hypertension	1.5	0.8-2.8	0.51
Smoking	1.1	0.5-2.3	0.82
Glomerular filtration rate (MDRD) mL/min	0.9	0.8-1.1	0.24
LA (positive)	4.5	2.1-9.4	<0.0001
PC4d (positivity)	2.4	1.3-4.6	0.006

profiles and the anti-phospholipid syndrome (APS, p< 0.0001). After adjustment for traditional and SLE-associated risk factors that were associated with any vascular event in uni-variable analyses, previous vascular events remained associated with PC4d+ (OR:2.4, 95% CI 1.3-4.5, p=0.006, table). There was furthermore a positive interaction between PC4d+ and LA+ regarding any vascular events (OR:11.1, 95% 5.1-24.3, p< 0.0001, Figure 1) versus patients negative for both PC4d and LA.

Conclusion: PC4d+ is associated with vascular events in SLE, independently of traditional and SLE-associated risk factors. The combination of PC4d+ and LA+ interacted positively and increased the association with vascular events even further. If measurement of both aPL and PC4d can predict vascular events in patients with SLE and/or APS should be evaluated in prospective studies.

Disclosure: E. Svenungsson, None; **J. Gustavsson**, None; **G. Grosso**, None; **I. Gunnarsson**, None; **B. Nilsson**, None; **A. Larsson**, None; **A. Bengtsson**, None; **C. Lood**, None.

Abstract Number: 0643

Association Between Neutrophil to Lymphocyte, Monocyte to Lymphocyte, and Platelet to Lymphocyte Ratios and Lupus Disease Activity and Lupus Nephritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Subjects with Systemic Lupus Erythematosus (SLE) are at elevated risk for end-organ damage. Lupus nephritis continues to be the complication with the highest standardized mortality ratio in SLE, yet clinicians have few tools to identify patients at risk. A complete blood count is a readily available test but little is known about its usefulness in tracking lupus nephritis and activity. In recent years, neutrophil/lymphocyte (NLR), monocyte/lymphocyte (MLR), and platelet/lymphocyte (PLR) ratios have emerged as markers of systemic inflammation. This study sought to evaluate the association between NLR, MLR, and PLR and its individual components and lupus disease activity and lupus nephritis.

Methods: 25 matched healthy controls and 85 patients fulfilling ACR or SLICC criteria for SLE were enrolled in the study and demographics, disease activity, as measured by the Hybrid SLEDAI, medications, and clinical manifestations were recorded. 20 lupus patients included in the study had active lupus nephritis, as defined by proteinuria greater than 500 mg/g creatinine. A complete blood cell count was assessed on all patients and healthy controls. Patients with platelet counts less than 100K or on nonsteroidal anti-inflammatory drugs were excluded from the study.

Results: Overall, SLE patients had a significantly higher PLR (p=0.0001), NLR (p=0.0003), and MLR (p=0.0035) compared to healthy controls. Lymphocyte counts alone negatively associated with SLEDAI (beta=-0.31, p=0.006) but monocyte, neutrophil, or platelet counts did not show a significant association with SLEDAI. All three ratios showed a significant positive association with SLEDAI in linear regression analysis with PLR being a better predictor than lymphocyte counts alone (beta=0.38, p< 0.0001). The associations between PLR or MLR but not NLR and SLEDAI remained significant in a multivariate linear regression model adjusting for age, race, sex, ethnicity, and medications. Specifically, the dose of glucocorticoids did not explain the clinical associations with these cellular ratios. When evaluating active lupus nephritis, PLR (p=0.118) was not significant in a logistic regression and NLR (p=0.007) and MLR (p=0.007) performed equally well. These associations between NLR or MLR and active lupus nephritis persisted in a multivariate logistic regression model adjusting for age, race, sex, ethnicity, and medications. Interestingly, lymphocyte, monocyte, neutrophil, or platelet counts alone did not associate with active lupus nephritis.

Conclusion: These data suggest that by using standard clinical labs to calculate NLR, MLR, and PLR clinicians may be able to better characterize lupus activity and current lupus nephritis.

Disclosure: P. Carlucci, None; **E. Luttrell-Williams**, None; **R. Bhan**, None; **C. Trad**, None; **H. El Bannoudi**, None; **P. Izmirly**, Glaxosmithkline, 5, GSK, 5; **H. Belmont**, None; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **J. Berger**, None.

Abstract Number: 0644

Decreased HVEM Expression in Lupus Patients and Impact of HVEM Knockout Mouse Model of Lupus Suggest a Role for BTLA Signaling in Disease Pathogenesis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: B and T Lymphocyte Attenuator (BTLA; CD272) is an Ig superfamily member and part of a family of checkpoint receptors that negatively regulate immune cell activation. BTLA is primarily expressed on B cells, T cells, and dendritic cells with highest expression on B and plasmacytoid dendritic cells, followed by CD4+ T cells, then lowest expression on myeloid dendritic cells, gamma-delta (gd) and CD8+ T cells (Murphy & Murphy, 2010). The natural ligand for BTLA is the TNF receptor superfamily member, herpes virus entry mediator (HVEM; TNFRSF14) and binding of HVEM to BTLA leads to attenuation of lymphocyte activation (Gonzalez, 2005). In this study we evaluated the role of BTLA and HVEM expression in the pathogenesis of SLE.

Methods: Healthy volunteer PBMCs were evaluated by mass cytometry (CyToF) to establish baseline expression of BTLA and HVEM on human lymphocytes and compared to SLE patient PBMCs (N=5) acquired by a vendor (SanguineBio) during self-reported flare. The role of BTLA signaling in a mouse model of lupus was examined using the BM12 lupus model where donor cells were transferred into the HVEM knockout or C57BL/6J control recipient mice (N=11 and 9, respectively).

Results: High levels of BTLA protein was observed on B cells, CD4+ T cells, CD8+ T cells and plasmacytoid dendritic cells in healthy control PBMCs. HVEM protein levels were lower in SLE patients compared to RA patients and healthy controls, while BTLA levels were similar between SLE and RA and controls. The BM12 lupus model does not generally present with significant kidney involvement. However, the HVEM recipient mice had increased prevalence of kidney disease (50%), as measured by albumin/creatinine ratio (ACR) greater than 300 mg/mg, compared to C57BL/6J control mice (22%).

Conclusion: These studies confirmed that BTLA protein is present on key immune cells linked to the pathogenesis of SLE. Reduced HVEM protein expression in SLE patients in flare compared to RA and healthy donors indicate that SLE is associated with ligand deficiency in the BTLA system. Furthermore, in a preclinical model of lupus using HVEM knockout mice demonstrate that disrupting this signaling system exacerbates disease pathogenesis. These data provide clinical rationale for evaluating a BTLA agonist in SLE. A phase 1 trial with a BTLA agonist antibody in healthy volunteers is in progress.

Disclosure: A. Vendel, Eli Lilly and Company, 1, 3, 4; **K. Griffiths**, Eli Lilly and Company, 3, 4; **A. Rhode-Kurnow**, Eli Lilly and Company, 2; **E. Merriman**, Eli Lilly and Company, 3, 4; **M. Daniels**, Eli Lilly and Company, 1, 3, 4, Eli Lilly and Company, 3, 4; **W. Chang**, Eli Lilly and Company, 1, 3, 4; **C. Ware**, Eli Lilly and Company, 2.

Abstract Number: 0645

Association of Co-positivity for Anti-dsDNA, -Nucleosome, and -Histone Antibodies and Disease Activity in Patients with Lupus Nephritis: Results from the KORNET Registry

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
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Session Time: 9:00AM–11:00AM

Background/Purpose: Recent studies have shown that the simultaneous positivity of anti-double stranded DNA, -nucleosome, and -histone antibodies (3-pos) is prevalent in lupus nephritis (LN) patients compared to non-renal systemic lupus erythematosus (SLE) patients. The aim of this study was to define the clinical, biologic, histopathologic, and prognostic differences according to the simultaneous reactivity to those antibodies in Korean patients with biopsy-proven LN.

Methods: We studied 102 patients who underwent kidney biopsy prior to the start of induction treatment and who were subsequently treated with immunosuppressives and followed-up for more than 12 months. Sociodemographic, clinical, laboratory, and treatment-related data at the time of kidney biopsy and during follow-up were obtained by a review of patients' charts. Antibodies were detected by immunoblot analysis or ELISA at the time of renal biopsy.

Results: Fifty-eight (35.4%) of the total of 102 LN patients had 3-pos. In comparison with non-3-pos patients, the patients with 3-pos showed a higher SLE Disease Activity Index-2000 score (P=0.002), lower lymphocyte level (p=0.004), higher proportion of proteinuria >3.5 g/24 hr (p=0.005), and higher positivity of urinary sediments (p=0.005) at the time of renal biopsy. In the renal histopathologic findings, the patients with 3-pos had more proliferative LN (p=0.015) and also showed more endocapillary hypercellularity, sub-endothelial hyaline deposits, fibrinoid necrosis/karyorrhexis, and cellular crescents in the disease activity index (p=0.016, p=0.045, p=0.002, and p=0.022, respectively), as well as a higher activity score (p=0.011). After a median follow-up of 83.2 months, rapid glomerular filtration rate decline was frequently observed in patients with 3-pos compared to those without (p=0.012).

Conclusion: Our findings suggest that 3-pos is related to severe LN and, furthermore, that patients with 3-pos show a rapid decline of renal function compared to those without.

Disclosure: S. Choi, None; **D. Park**, None; **J. Kang**, None; **H. Xu**, None; **S. Lee**, None.

Abstract Number: 0646

A Meta-Analysis of Anti-Ribosomal P Autoantibodies in Systemic Lupus Erythematosus: A Misunderstood Autoantibody

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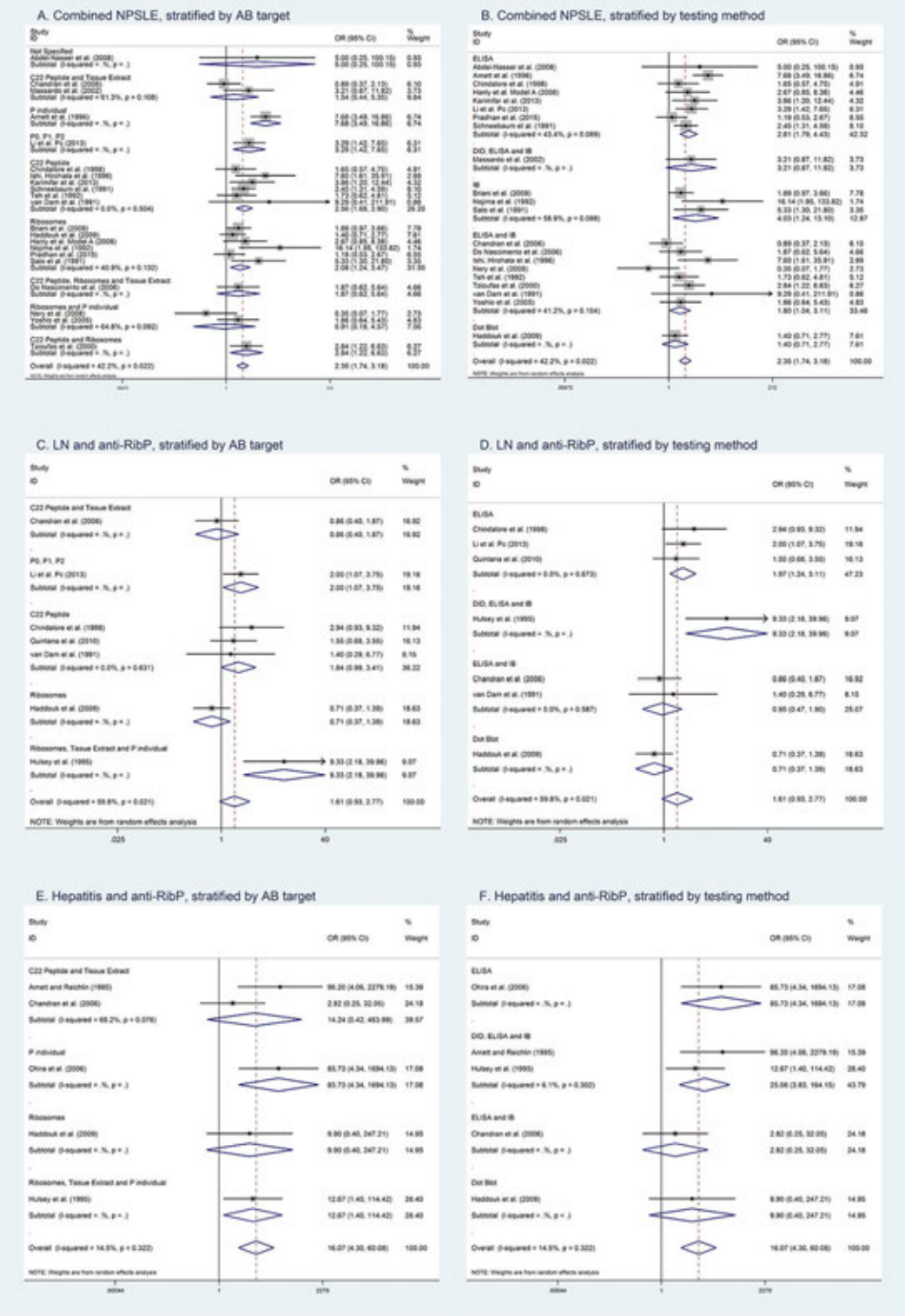

Figure 1. Pooled odds ratios of NPSLE (combined symptoms), lupus nephritis, and lupus hepatitis with anti-ribosomal P antibodies stratified by antigenic target (A, C, E) and testing method (B, D, F). Abbreviations: AB, antigenic target; anti-RibP, anti-ribosomal P; CI, confidence interval; DID, double diffusion; ELISA, enzyme-linked immunosorbent assay; IB, immunoblot; LN, lupus nephritis; NPSLE, neuropsychiatric lupus; OR, odds ratio.

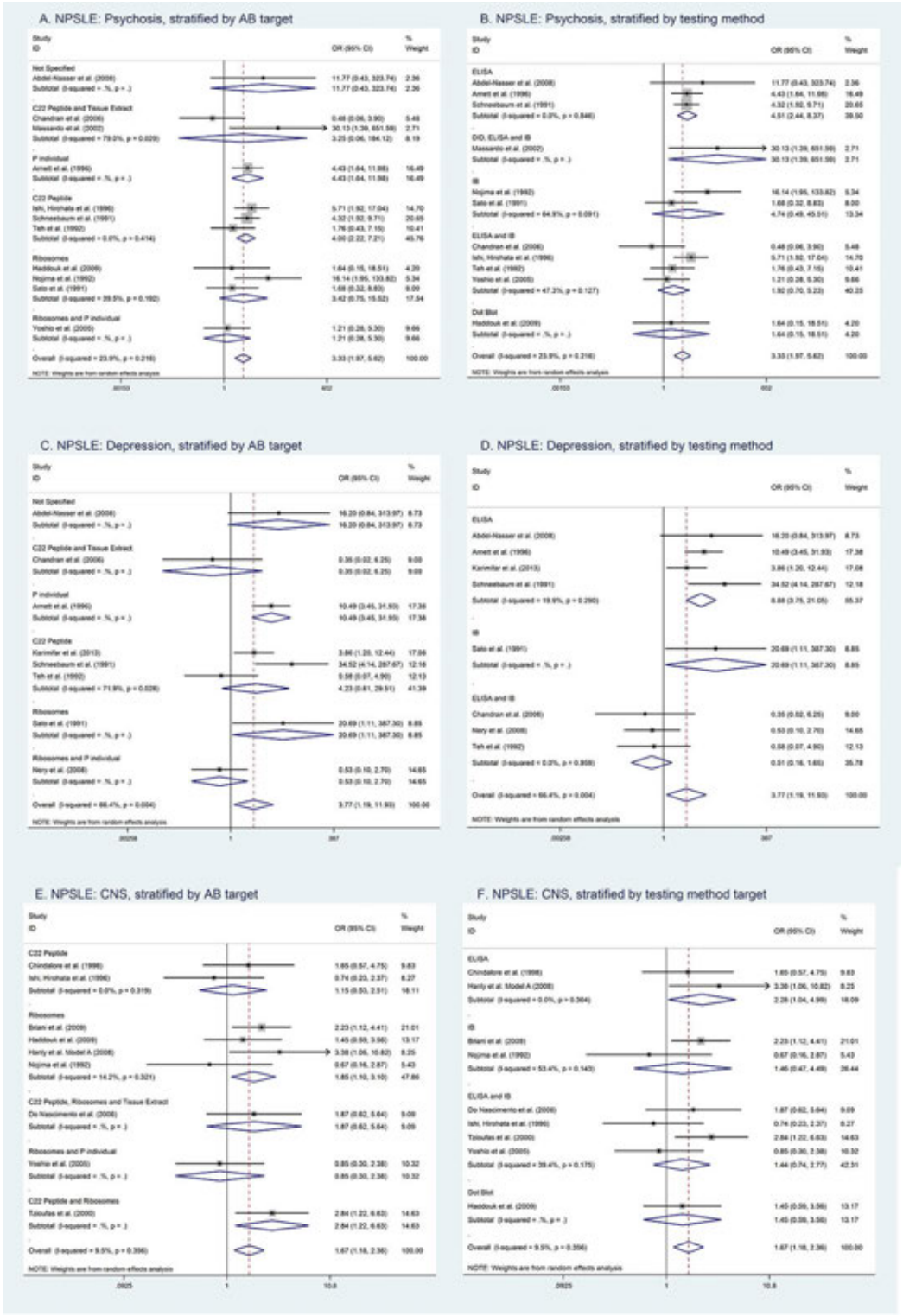

Figure 2. Pooled odds ratios of different symptoms of neuropsychiatric SLE with anti-ribosomal P antibodies stratified by antigenic target (A, C, E) and testing method (B, D, F). Abbreviations: AB, antigenic target; anti-RibP, anti-ribosomal P; CI, confidence interval; DID, double diffusion; ELISA, enzyme-linked immunosorbent assay; IB, immunoblot; LN, lupus nephritis; NPSLE, neuropsychiatric lupus; OR, odds ratio.

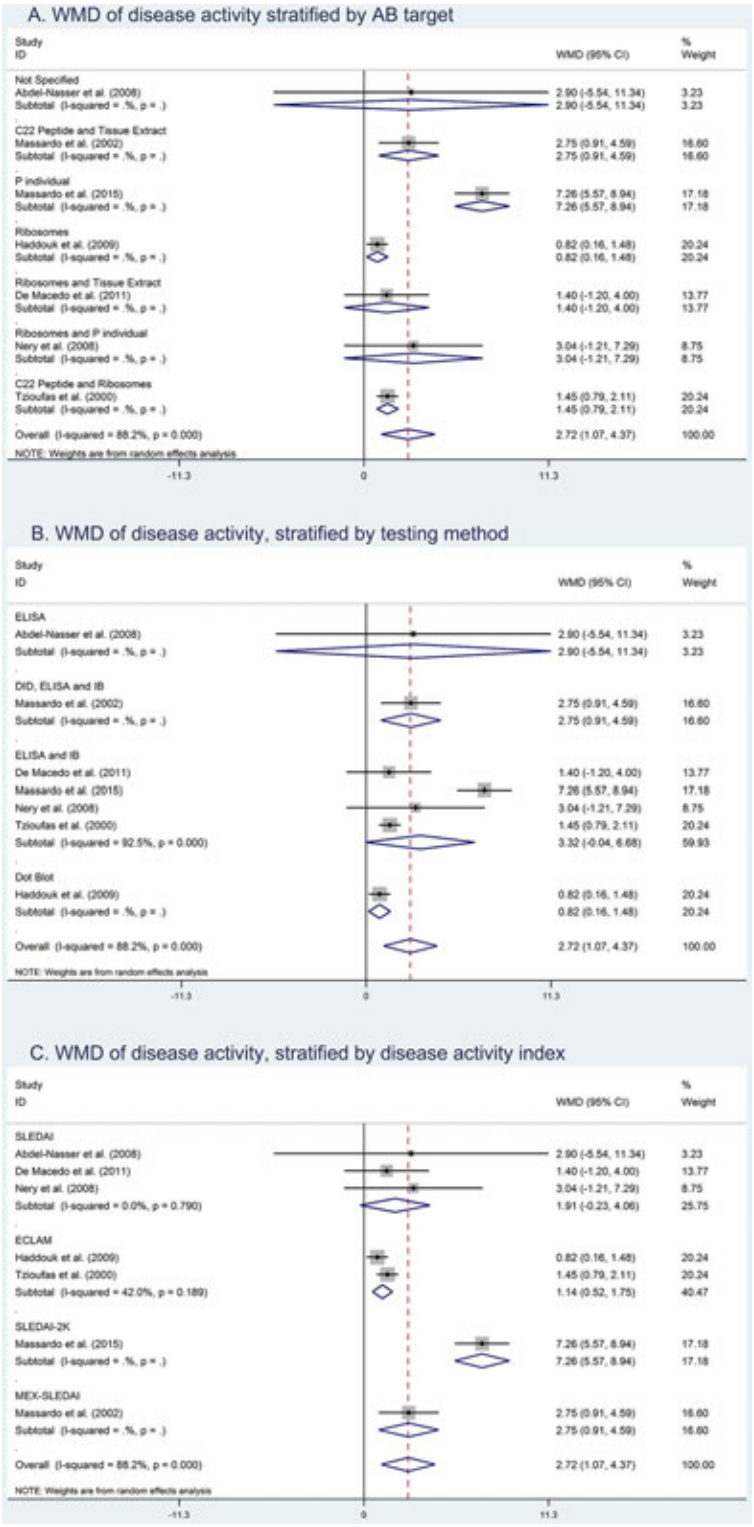

Figure 3. Pooled weighted mean difference of disease activity with anti-ribosomal P antibodies stratified by antigenic target (A), testing method (B), and disease activity index (C). Abbreviations: AB, antigenic target; anti-RibP, anti-ribosomal P; CI, confidence interval; DID, double diffusion; ECLAM, European Consensus Lupus Activity Measurement; ELISA, enzyme-linked immunosorbent assay; IB, immunoblot; LN, lupus nephritis; MEX SLEDAI, Mexican Systemic Lupus Erythematosus Disease Activity Index; NPSLE, neuropsychiatric lupus; OR, odds ratio; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
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Background/Purpose: Anti-ribosomal P (Rib-P) antibodies have become known as a highly specific biomarker for the diagnosis of SLE and potentially a biomarker for neuropsychiatric SLE (NPSLE). However, despite comparable specificity in comparison to other SLE autoantibodies such as anti-Sm and anti-dsDNA, anti-Rib-P has not been included in classification criteria for SLE. One limitation has been the wide variation of immunoassays and antigenic targets used to detect anti-Rib-P. Furthermore, the definition of NPSLE encompasses a broad spectrum of neuropsychiatric symptoms. To clarify the clinical associations in SLE, we performed a systematic review and meta-analysis to compare the different anti-Ribo-P assay platforms, antigenic targets, and specific clinical features of SLE and NPSLE.

Methods: PubMed, EMBASE, and Web of Science databases were searched. Associations with clinical features of SLE with attention to specific neuropsychiatric symptoms, type of immunoassays and antigenic targets were extracted. Data were pooled using random effects methods. Associations were expressed as pooled odds ratio (OR) and forest plots to visualize the results.

Results: Our preliminary search identified 21 studies (n=3128) that reported a pooled OR of anti-Rib-P positivity in NPSLE of 2.36 (95% confidence interval (CI): 1.74-3.18) (Figure 1). When stratified by different symptoms of NPSLE, depression had the highest pooled OR of 3.77 (95% CI: 1.19-11.93), followed by psychosis (OR 3.33 (95% CI: 1.97-5.62)), and then central nervous system (CNS) involvement (OR 1.65 (95% CI: 1.11-2.45)) (Figure 2). There were 7 studies (n=1060) that reported a pooled OR for lupus nephritis (LN) of 1.61 (95%CI: 0.93-2.77) and 5 small studies (n=504) that reported a pooled OR for lupus hepatitis of 16.07 (95% CI: 4.30-60.08). Seven studies reported that anti-Rib-P was associated with increased disease activity, however, we were not able to pool the results because different disease activity scores were used (SLEDAI, ECLAM, SLEDAI 2K or MEX-SLEDAI) (Figure 3). There was significant heterogeneity between studies that was at least partly explained by heterogeneity in antigenic targets (C22 peptide, ribosomes, P0/P1/P2, tissue extract, and P individual) and assays (double diffusion, enzyme-linked immunosorbent assay, immunoblot, and/or dot blot) used for these studies.

Conclusion: The addition of anti-Rib-P may improve the specificity of SLE classification criteria in patients presenting with NPSLE symptoms. Anti-Rib-P was also found to be an important biomarker for lupus hepatitis and potentially disease activity. Heterogeneity between studies in this meta-analysis is explained by different assays and antigenic targets.

Disclosure: M. Choi, None; **R. Brown**, None; **K. Buhler**, None; **M. Mahler**, Inova Diagnostics, 3; **M. Fritzler**, Alexion Canada, 7, BioRad, 5, Dr. Fooke Laboratorien GmbH, 5, Euroimmun GmbH, 5, 7, ImmunoConcepts, 7, Inova Diagnostics, 5, 7, 8, Inova Diagnostics Inc. San diego, CA, 5, Inova Dx, Mikrogen GmbH, 5, Werfen International, 5.

Abstract Number: 0647

Is ANA-status at Disease Inception Associated with Long-term Damage Accrual and Direct and Indirect Health Care Costs in the Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort?

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SESSION INFORMATION

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Background/Purpose: We reported that 7.7% (88/1137) of patients in an international inception cohort were ANA-negative at enrolment (*Arthritis Care Res 2018 doi:1002/acr23712*). There are no data on whether long-term outcomes or health care costs differ between ANA-negative versus ANA-positive patients. We compared damage accrual and costs between those who were ANA-negative versus ANA-positive at disease inception.

Methods: Patients fulfilling the revised ACR SLE Criteria from 33 centres in 11 countries were enrolled within 15 months of diagnosis. ANA at enrolment was detected by indirect immunofluorescence in a single laboratory; a positive ANA was defined as a titre ≥ 1/160. Data were collected annually on disease damage (SLICC/ACR Damage Index, SDI) and health care use (i.e., hospitalizations, medications, dialysis, and selected procedures) and supplemented by data on additional resource use and lost work-force/non-work-force productivity in a patient subset. Primary analyses included partial direct cost estimates based on the major health care components for the full sample. Estimates of complete direct and indirect costs were obtained by assuming that the ratios of total direct to partial direct costs and indirect to partial direct costs were the same for the full sample as for the subset. Health care use was costed using 2018 Canadian prices and lost productivity using Statistics Canada age-and-sex specific wages. The average annual rate of damage accrual and average annual costs over follow up were compared between patients who were ANA-negative versus ANA-positive at enrolment using multivariable regressions, adjusting for age and race/ethnicity.

Results: 1052 of the 1137 patients provided cost data and were included; 76/1052 (7.2%) were ANA-negative at enrolment (Table 1). ANA-negative versus ANA-positive patients were older, more likely to be of Caucasian race/ethnicity, and less likely to be on immunosuppressants or have SLE-associated autoantibodies. Mean follow up of the ANA-negative versus ANA-positive was similar (8.6 years (range 0.8 – 17.8) versus 9.6 years (range 0.6 – 18.5).

Table 1. Demographics and clinical characteristics of ANA-negative versus ANA-positive patients at enrolment in an international Inception cohort**

	ANA-negative n=76	ANA-positive n=976	Difference (95% CI) ANA-negative versus ANA-positive
Demographics			
Age at diagnosis, year, mean	40.2	34.9	5.3 (2.1, 8.4) *
Female, %	92.1	89.7	2.5 (-3.9, 8.8)
Disease duration, months	4.8	5.7	-0.9 (-1.8, 0.1)
Caucasian, %	81.6	52.2	29.4 (20.2, 38.7) *
Nephritis (based on renal biopsy or ACR Criteria) at enrollment, %	30.9	29.5	1.3 (-10.0, 12.7)
# ACR criteria, mean	4.7	4.8	-0.1 (-0.4, 0.1)
SLEDAI-2K score, mean	4.4	5.4	-1.1 (-2.3, 0.2)
Medications, % ever used			
Glucocorticoids	76.3	80.9	-4.6 (-14.5, 5.2)
Antimalarials	65.8	74.0	-8.2 (-19.2, 2.8)
Immunosuppressants	30.3	44.2*	-13.9 (-24.7, -3.1) *
Autoantibodies, %			
dsDNA***, %	13.2	29.4*	-16.2 (-24.3, -8.1) *
PCNA****	2.6%	7.0%	-4.3 (-10.1, 1.5)
Ribosomal-P	5.3%	16.0%	-10.7 (-16.2, -5.2) *
Ro52/TRIM21	21.1%	36.5%	-15.4 (-25.1, -5.8) *
SSA/Ro60	23.7%	47.4%	-23.8 (-33.8, -13.7) *
SSB/La	6.6%	15.8%	-9.2 (-15.2, -3.2) *
Sm	6.6%	25.2%	-18.6 (-24.8, -12.4) *
U1-RNP	10.5%	33.0%	-22.5 (-30.0, -15.0) *

*Denotes values are significantly different between ANA-negative and ANA-positive patients

** ANA at enrolment was detected by indirect immunofluorescence on HEp-2000 substrate (Immunoconcepts, Sacremento, CA) in a single laboratory; a positive ANA was defined as a titre ≥ 1/160.

***Anti-ds DNA was detected by chemiluminescence immunoassay (QUANTA Flash, Inova, San Diego, CA) in a single laboratory; a positive anti-ds DNA was defined as ≥ 70 IU/ml.

****Antibodies to PCNA, ribosomal-P, recombinant Ro52/TRIM21, native SSA/Ro60, SSB/LA, Sm, and U1-RNP were detected using the extractable nuclear antigen (ENA) FIDIS Connective Profile kit 13 addressable laser bead immunoassay (ALBIA, TheraDiag, Paris) in a single laboratory.

In the ANA-negative versus ANA-positive, the average annual rate of damage accrual was 0.10 versus 0.12 units/year; the difference was not significant in the univariable or multivariable analysis. In the ANA-negative versus ANA-positive, the average annual partial direct, complete direct, and indirect costs were significantly less ($2310 (95% CI 897, 3723), $3902 (95% CI 1516, 6287) and $14,620 (95% CI 5680, 23560) versus $4036 (95% CI 3428, 4645), $6818 (95% CI 5790, 7845) and $25,548 (95% CI 21698, 29398)) (Table 2). However, in multivariable analysis, wide CIs precluded definitive conclusions (β-coefficient for ANA-negativity, -$5684, 95% CI -$24258, $12890).

Conclusion: ANA-negative versus ANA-positive SLE patients at disease inception incurred lower costs in univariable analysis, but with adjustment for age and race/ethnicity, no differences could be detected. More research is required to characterize ANA-status over the disease and determine if costs/outcomes are more associated with persistent ANA-negativity/positivity, rather than ANA-status at disease inception.

Table 2. Average annual partial and complete direct and indirect health care costs (2018 Canadian dollars)

	ANA-negative n=76	ANA-positive n=976	Difference (95% CI) ANA-negative versus ANA-positive
Partial direct costs	2310	4037	-1727 (-3243, -210)*
Hospital visits	437	1416	-979 (-1338, -619)*
Medications	1802	1929	-127 (-1551, 1298)
Dialysis	0	616	-616 (-954, -278)*
Select procedures	70	76	-6 (-45, 34)
Complete direct costs	3902	6818	-2916 (-5478, -354)*
Indirect costs	14620	25548	-10928 (-20527, -1328)*
Total costs	18522	32366	-13844 (-26006, -1682)*

*Denotes values are significantly different between ANA-negative and ANA-positive patients

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Abstract Number: 0648

Patients of African Descent Score Higher on Quality of Life Indices Despite Their Known Disease Severity

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus **(**SLE) may have a significant impact on multiple dimensions of quality of life. Patient-reported outcome (PRO) tools may provide valuable insights for clinical trials and treatment decisions in clinical practice. LupusPRO is a disease targeted, patient reported outcome measure designed specifically for patients with SLE. It includes 43 variables of which 30 items are health-related. The SF-36 Health Survey is a widely used, multipurpose, short-form index comprised of 36 items suitable for assessment of all medical conditions. Both instruments are internationally validated and have been correlated to each other in many lupus studies. The aim of this study was to compare SF-36 and LupusPRO scores in a racially and culturally diverse cohort of SLE patients.

Methods: The Cohort for Rheumatic Diseases is a longitudinal real-world study that follows 1,635 patients, including an embedded Lupus Cohort (674 patients who meet ACR classification criteria for SLE). 365 SLE patients completed the LupusPRO questionnaire and SF-36 during the same routine clinical visits between 2011 and 2019. Spearman's rank tests and Kruskal-Wallis methods were used to compare age, race, gender, and year of disease to SF-36 and LupusPRO scores. Linear regression methods were then used to compare LupusPRO and SF-36 scores controlling for these variables.

Table 1: Characteristics of participants (N=367)

Variables	N	(%)
Age, years		
Mean ± SD	45.50	±13.26
Gender		
Female	333	(90.74)
Male	34	(9.26)
Race		
EA	206	(56.13)
AA	83	(22.62)
Others	78	(21.25)
Year of Diseases at Enrollment		
Median(IQR1-IQR3)	14	(6-40)
SF-36		
Median(IQR1-IQR3)	40	(25-60)
Lupus-Pro		
Median(IQR1-IQR3)	70.57	(54.63-84.63)

Table 2: Univariate analyses between SF-36 or Lupus-Pro with other variables

Variables	SF-36		Lupus-Pro	
	Coefficient	p-value	Coefficient	p-value
Age, years	0.01	0.842[a]	-0.00	0.978[a]
Gender	14.42	0.0001[b]	10.91	0.001[b]
Race	36.80	0.0001[b]	65.68	0.0001[b]
Year of Diseases	0.07	0.013[a]	0.03	0.379[a]

[a]From Spearman test results
[b]From Kruskal-Wallis test results

Table 3: Multivariate analyses between SF-36 and Lupus-Pro, controlling for other variables: linear regression

Variables	SF-36	
	Coefficient	p-value
Gender	3.40	0.055
Race		
EA	1	
AA	4.46	0.001
Others	0.92	0.487
Year of Diseases	0.06	0.097
Lupus-Pro	0.62	<0.0001

Results: The patients completed a mean of 3.43 paired results. Subjects were 90% female with a mean age of 45.50 (SD=13.26) years. The population was 56.1% Caucasian, 22.6% African American, and 21.3% Other Race, primarily consisting of American Indian and mixed race. In univariate analysis, results of the PROs were comparable ($p< 0.0001$) (Table 2) and African American patients had higher scores than European Americans ($p=0.001$) (Table 3). The positive correlation between LupusPRO and SF-36 remained in multivariate analysis ($p< 0.0001$) when controlled for race, gender, and year of disease (Table 3).

Conclusion: SF-36 and LupusPRO gave similar results. African American patients have higher scores on both instruments, indicating their report of better functioning and quality of life, despite their known increased disease severity. Both disease-targeted LupusPRO and generic SF-36 tools may be useful for measuring quality of life in SLE studies, but potential cultural and disease impacts on these measures need to be carefully considered.

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Abstract Number: 0649

Potentially Reversible Associations with Fatigue in SLE Patients - Results from a Single-centre Study

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SESSION INFORMATION

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Background/Purpose: Fatigue is the most common symptom in SLE patients with a strong impact on patients' reported quality of life. The cause of fatigue is most likely multifactorial. Previous studies identified possible associations with fatigue with some contradictory results. The aim of this study was to identify additional potentially reversible associations with fatigue to generate a target for future interventions.

Methods: Our study population consisted of 234 consecutively recruited SLE (according to the 1997 ACR criteria) outpatients from our university hospital based lupus reference centre. We analyzed clinical and demographic data from routine visits, laboratory variables, as well as sleeping disorders, disease perception, coping, social activities and health locus of control using validated questionnaires. We captured fatigue using the Fatigue Severity Scale (FSS). A score of ≥ 4 points is considered pathological. To assess depression, we used the German CES-D depression scale (values $\geq 23/60$ points are considered pathological).

Table 1. Potentially reversible associations with fatigue in our cohort of 234 SLE patients, absolute numbers and percentages

Variable	n (%)	FSS ≥ 4 points	FSS < 4 points
Obesity (BMI >30kg/m²)	26/234 (11.1)	15/119 (12.6)	11/115 (9.6)
Signs for depression (ADS-L ≥ 23 points)	59/209 (28.2)	41/110 (37.3)	18/99 (18.2)
Vitamin D deficiency (25-hydroxyvitamin D <30 ng/ml)	73/213 (34.3)	34/107 (31.8)	39/106 (34.0)
Anemia (Hb <11.9 g/dl)	41/234 (17.5)	24/119 (20.2)	17/115 (14.8)
Hypothyroidism (TSH >4,2 µUI/ml)	6/225 (2.6)	4/113 (3.5)	2/112 (1.7)

Results: Our predominantly Caucasian cohort (99.1%) was mostly female (87.6%), with a mean age of 45.3 years (±13.4 [SD]) and a mean disease duration of 16.2 years (±9.5). In our cohort, 50.9% of patients reached a pathological result in the FSS. Depression was significantly associated with fatigue ($p < 0.001$), with 37.5% of patients with fatigue vs. 18.2 % in patients without fatigue showing a clinically relevant CES-D score (mean CES-D score 20.2±9.4 vs. 14.3±8.6). Patients with poor self-assessment of their health condition (including sleeping disorders, pain, disease activity and damage) showed significantly more fatigue ($p < 0.01$). In our gradual regression analysis, reduced social activities exhibited the highest correlation with fatigue (Beta 0.535). Overall, in 71.4 % of our SLE patients, we could identify at least one potentially reversible association for fatigue (shown in table 1).

Conclusion: We observed a high prevalence of depressive disorders in our cohort and a significant correlation of depressive status with fatigue. Therefore, we suggest that psychological wellbeing is assessed in everyday clinical practice and treating physicians should react to patients' needs accordingly. Additionally, obesity, anaemia, hypothyroidism and vitamin D deficiency can easily be assessed. Optimizing these factors represent possible targets in order to improve fatigue in SLE patients.

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Performance of the Proposed American College of Rheumatology/ European League Against Rheumatism Classification Criteria for Systemic Lupus Erythematosus in Korean Patients

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Table 1. Sensitivity, specificity, accuracy, positive predictive value, and negative predictive value, including 95% confidence intervals (in parentheses) of each classification ground

	1997 ACR	2012 SLICC	Proposed ACR/EULAR
Sensitivity	0.955 (0.934-0.971)	0.985 (0.967-0.994)	0.976 (0.957-0.988)
Specificity	0.938 (0.934-0.971)	0.926 (0.908-0.935)	0.917 (0.897-0.929)
Accuracy	0.946 (0.925-0.962)	0.955 (0.938-0.965)	0.946 (0.927-0.959)
PPV	0.938 (0.917-0.954)	0.930 (0.913-0.938)	0.921 (0.903-0.933)
NPV	0.955 (0.979-0.999)	0.984 (0.966-0.994)	0.975 (0.954-0.988)

ACR, American college of rheumatology; EULAR, European League against Rheumatism; NPV, negative predictive value; PPV, positive predictive value; SLICC, Systemic Lupus International Collaborating Clinics

SESSION INFORMATION
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Background/Purpose: To evaluate the performance of the proposed American College of Rheumatology/European League against Rheumatism (ACR/EULAR) classification criteria for systemic lupus erythematosus (SLE) in Korean patients

Methods: We conducted medical chart review study of patients with SLE and defined rheumatic diseases as control group. The clinical diagnosis was used as the gold standard. The classification based on 1997 ACR criteria, 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria and the newly proposed ACR/EULAR criteria were examined with analysis of sensitivity, specificity, accuracy, positive predictive value and negative predicted value.

Results: A total of 335 SLE patients and 337 non-SLE patients were included in the analysis. Non-SLE patients included rheumatoid arthritis (RA) (n=92), anti-phospholipid syndrome (APS) (n=57), mixed connective tissue disease (CTD) (n=52), systemic sclerosis (n=43), primary Sjögren's syndrome (SS) (n=39), undifferentiated CTD (n=28), RA with secondary SS (n=24), dermatomyositis (n=1) and spondyloarthropathy (n=1). The sensitivity of the proposed ACR/EULAR criteria was 97.6% (95% confidence interval (CI), 0.957-0.988) compared with 98.5% (95% CI, 0.967-0.994) for the 2012 SLICC criteria. The specificity for the proposed ACR/EULAR criteria and 2012 SLICC criteria were 91.7% (95% CI, 0.897-0.929) and 92.6% (95% CI, 0.908-0.935), respectively. Eight patients who were classified as SLE with the proposed ACR/EULAR criteria but not with 2012 SLICC criteria, had a tendency of having arthritis domain and highly specific antibody domain which counts for a score of 6. One patient classified as SLE according to the proposed ACR/EULAR criteria had malar rash and arthritis and one patient had serositis, leukopenia and fever (constitutional domain). Three APS patients who were classified as SLE according to the 2012 SLICC criteria did not meet the proposed ACR/EULAR criteria due to the entry criterion of positive anti-nuclear antibody. The ACR/EULAR score $\geq$ 12 rather than a score $\geq$ 10, resulted in higher specificity, positive predictive value, and accuracy and higher sensitivity than 1997 ACR criteria.

Conclusion: The proposed ACR/EULAR criteria for SLE had comparable performance in respect of diagnostic accuracy, sensitivity and specificity in this Korean population of SLE and other rheumatic diseases. However, the proposed criteria could not reach higher specificity than 2012 SLICC criteria.

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Abstract Number: 0651

Predictors of Renal Damage in Systemic Lupus Erythematosus Patients from Latin America

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis and renal damage are serious complications in patients with SLE. Proteinuria < 0.8 g/24 hours at 12 months has proven to be a good predictor of long-term renal outcome. The aim of this study is to identify the predictors of renal damage in Latin American SLE patients.

Methods: Patients with lupus nephritis from a multiethnic, multinational, multicenter cohort were included in this study. Lupus nephritis was defined clinically (proteinuria greater than 0.5 g/day on two or more occasions or the presence of red cell casts) or histologically (renal biopsy compatible with lupus nephritis histopathology class II-V according to the World Health Organization). The following time-dependent variables were considered as possible predictors of renal damage: proteinuria, low complement, anti-dsDNA, red cell casts, creatinine level, hypertension, the renal component of the SLEDAI, prednisone dose, immunosuppressive drugs use, and antimalarial use. The following baseline variables were also included: gender, age at nephritis diagnosis, residence rural or urban, ethnic group and socioeconomic status (SES). Proteinuria was assessed at baseline and after 12 months, to determine if early response (proteinuria < 0.8 g/d within 12 months since the diagnosis of lupus nephritis) is protective of renal damage occurrence in SLE patients; renal damage was defined as an increase of at least one point in the renal domain of the SLICC/ACR damage index. Univariable and multivariable Cox regression models using a backward selection method with alpha-level to stay in the model set at 0.05 were performed.

Table 1. Predictors of renal damage. Univariable and multivariable models.

	Univariable HR (CI95%)	p value	Multivariable HR (CI95%)	p value
Age at nephritis diagnosis	0.99 (0.97-1.01)	0.195		
Gender (male)	1.84 (1.14-2.98)	0.013	1.93 (1.18-3.15)	<0.001
Residence (urban)	0.70 (0.339-1.43)	0.321		
Ethnicity				
Caucasian	Ref.			
Mestizo	1.64 (1.09-2.47)	0.017		
African Latin-American	1.34 (0.72-2.48)	0.357		
Others	1.19 (0.42-3.34)	0.745		
SES				
High	Ref.			
Medium	2.08 (0.63-6.87)	0.228	2.57 (0.77-8.55)	0.124
Low	3.57 (1.13-11.28)	0.030	3.945 (1.24-12.57)	0.020
Early treatment response	0.54 (0.33-0.87)	0.012	0.60 (0.37-0.99)	0.043
Proteinuria	1.20 (0.69-2.10)	0.512		
Low complement	1.33 (0.91-1.93)	0.138		
Anti-dsDNA	1.09 (0.76-1.57)	0.652		
Red cell casts	1.79 (1.24-2.59)	0.002		
Creatinine level	1.13 (1.06-1.21)	<0.001		
Hypertension	2.30 (1.54-3.44)	<0.001	1.85 (1.223-2.81)	0.003
Renal component of SLEDAI	1.91 (1.31-2.80)	<0.001	1.77 (1.19-2.61)	0.004
Prednisone dose	0.91 (0.63-1.32)	0.627		
Immunosuppressive drugs use	1.92 (1.31-2.82)	<0.001		
Antimalarial use	0.45 (0.29-0.72)	<0.001	0.48 (0.29-0.76)	0.002

SES: Socioeconomic status. Early treatment response: proteinuria <0.8 g/d within 12 months since the diagnosis of lupus nephritis.

Results: Four hundred and ninety patients were included; 89.4% of them (n = 438) were female, with a median age at SLE diagnosis of 26.4 IQR (19.0-36.0) years and median age at nephritis diagnosis of 27.5 (20.3-37.4) with a median follow-up after nephritis diagnosis of 3.9 (2.0-5.6) years. At baseline, the median creatinine was 0.9 (0.7-1.1) mg/dl. One-hundred and twenty patients (24.5%) accrued renal damage during their follow-up.

Early response to treatment (as defined) (HR 0.604), and antimalarial use (HR 0.477) were protective of the occurrence of renal damage whereas male gender (HR 1.930), low socioeconomic status (HR 3.945), hypertension (HR 1.854) and the renal component of the SLEDAI (HR 1.768) were risk factors for renal damage occurrence. Univariable and multivariable models are depicted in table 1.

Conclusion: Early response and antimalarial use were protective of renal damage occurrence, while male gender, hypertension, low socioeconomic status, higher renal domain of SLEDAI were risk factors for its occurrence in SLE patients. Strict control of modifiable risk factors such as early proteinuria response, antimalarial use and hypertension control, is therefore strongly recommended for patients with lupus nephritis to minimize damage.

Disclosure: C. Reátegui-Sokolova, None; **M. Ugarte-Gil**, None; **G. Harvey**, None; **G. Pons-Estel**, None; **R. Quintana**, None; **L. Catoggio**, None; **E. Soriano**, Abbvie, 2, 5, 8, ABBVIE, 2, 5, 8, AbbVie, 2, 5, 8, Amber, 8, Amgen, 5, 8, AMGEN, 5, 8, BMS, 8, BRISTOL, 8, Bristol MS, 8, BRISTOL MYERS SQUIBB, 8, Bristol-Myers Squibb, 8, eli lilly, 5, 8, Genzyme, 8, GENZYME, 8, GLAXO, 2, Glaxo, 2, glaxosmithkline, 2, GlaxoSmithKline, 2, GSK, 2, Janssen, 8, Lilly, 5, 8, LILLY, 5, 8, Novartis, 2, 5, 8, NOVARTIS, 2, 5, 8, PFIZER, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, 8, Roche, 2, 8, ROCHE, 2, 8, Sandoz, 5, SANDOZ, 5, Sanofi, 5, SANOFI, 5, SANOPHY, 5, UCB, 8; **M. Garcia**, None; **V. Saurit**, None; **F. Caeiro**, None; **E. Bonfa**, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #305068/2014-8), 2, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4 and #2010/10749-0), 2; **N. da**

Silva, None; **E. Sato**, None; **G. Vasquez**, None; **L. Massardo**, None; **O. Neira**, None; **M. Cardiel**, None; **I. Garcia De-La Torre**, None; **M. Amigo**, None; **M. Guibert-Toledano**, None; **M. Portela-Hernandez**, None; **R. Chacon-Diaz**, None; **G. Alarcón**, None; **B. Pons-Estel**, None.

Abstract Number: 0652

Clinical Relevance According to Staining Patterns and Titers of Antinuclear Antibody

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Immunofluorescent antinuclear antibody (ANA) test using HEp-2 cells still plays an important role in the diagnosis of autoimmune diseases. The aim of this study was to investigate the clinical relevance of ANA according to titers and patterns.

Methods: We identified patients who were newly positive in the ANA test between December 2010 to November 2016, and collected data such as, diagnosis, ANA titer and pattern, and specific autoantibody test results.

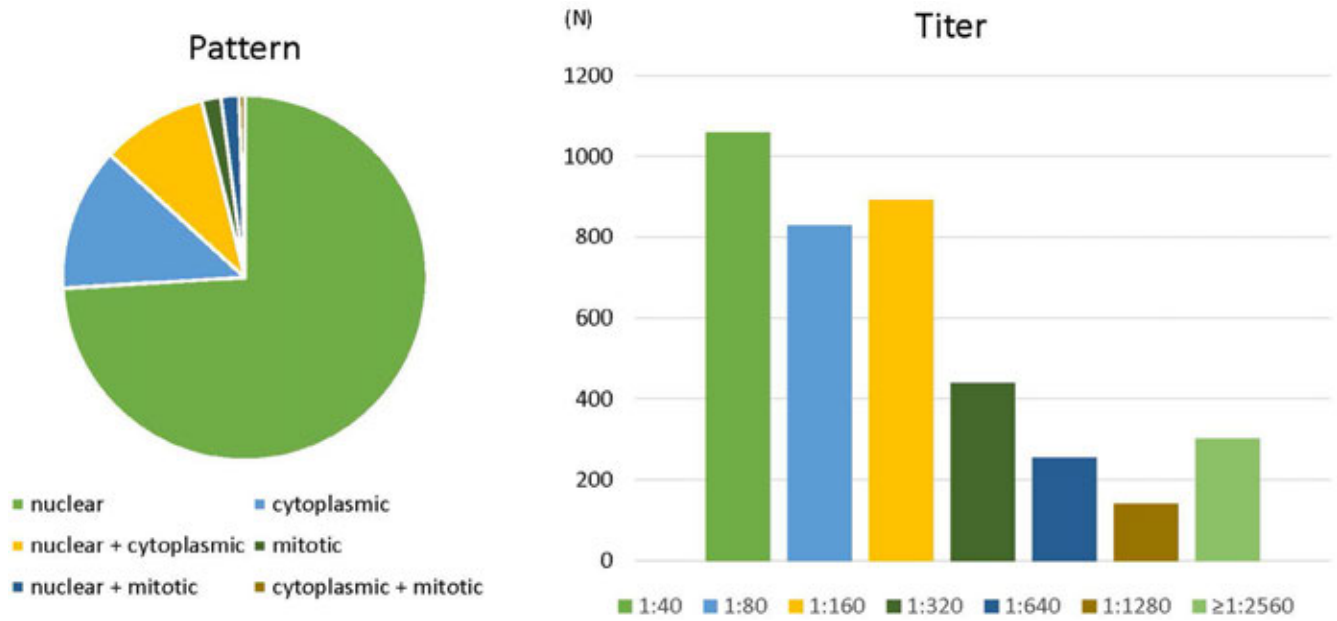

Figure 1. Patient distribution by ANA titer and pattern.

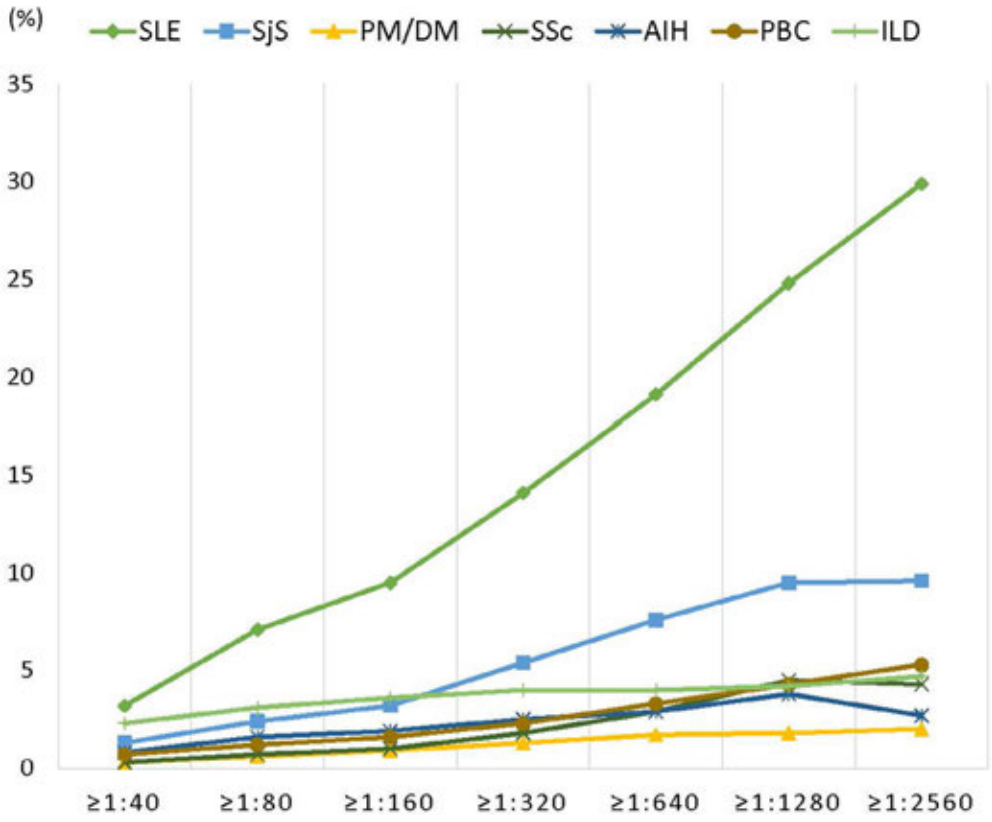

Figure 2. Disease prevalence according to ANA titer

Results: In total, 7591 patients were included in this study. The average age was 51 (interquartile range (IQR): 35-63) years, and 69.4% were women. Figure 1 showed the patient distribution by ANA titer and pattern. The diseases with a difference in prevalence according to ANA titer were systemic lupus erythematosus (SLE), Sjögren syndrome (SjS), polymyositis/dermatomyositis (PM/DM), systemic sclerosis (SSc), autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), liver cirrhosis, hemolytic anemia, immune thrombocytopenic purpura, interstitial lung disease (ILD), chronic obstructive pulmonary disease/bronchiectasis (COPD/BE), cerebrovascular accident, and crystal induced arthropathy (CIA). A multivariable analysis was conducted to determine whether ANA titer was an independent factor. As a result, diseases with increased prevalence with increasing ANA titer were SLE, SjS, PM/DM, SSc, AIH, PBC, and ILD, and the opposite result showed in COPD/BE and CIA (Figure 2).

SLE was the most prevalent in patients with mixed pattern of nuclear and cytoplasmic (6.4% in ≥1:40, 40% in ≥1:2560). SjS and SSc showed the same results (SjS: 1.9% in ≥1:40, 10% in ≥1:2560, SSc: 0.5% in ≥1:40, 6.7% in ≥1:2560). The prevalence of PM/DM, AIH, PBC and ILD was highest in mixed pattern of nuclear and cytoplasmic in all patients, but it was highest in cytoplasmic pattern from 1:160 or more of ANA titer.

Conclusion: SLE, SjS, PM/DM, SSc, AIH, PBC and ILD were the diseases in which ANA titer independently affected disease prevalence. Patients with mixed pattern of nuclear and cytoplasmic had a higher prevalence of SLE, SjS and SSc than purely nuclear pattern. It is necessary to note that the cytoplasmic pattern is accompanied by the nuclear pattern in the ANA test.

Disclosure: M. Seo, None; **J. Yeo**, None; **H. Ryu**, None; **H. Choi**, None; **H. Baek**, None.

Abstract Number: 0653

Newly Diagnosed Lupus Nephritis in Elderly Predicts Good Renal Outcome: A Distinct Disease Subset from Young-onset Lupus Nephritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Elderly-onset SLE is recognized to be benign disease entity with a favorable nature course. Although late-onset lupus nephritis (LN), long interval between onset of SLE and diagnosis of LN is associated with poor renal outcome, little information has been available in newly diagnosed LN in the elderly. The purpose of this study is to compare renal prognosis and clinical characteristics between elderly-onset and young-onset LN.

Figure 1

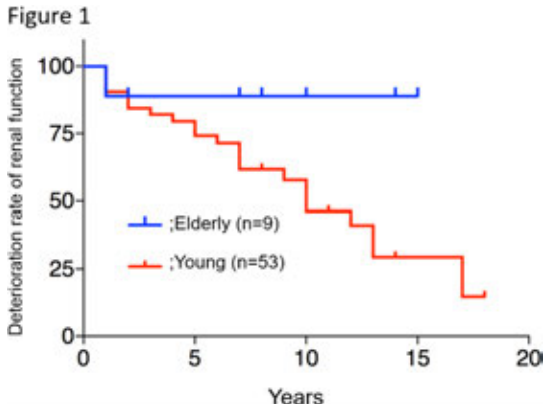
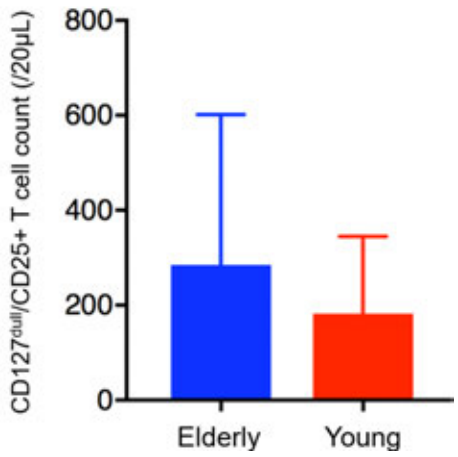


Figure 2



Methods: We reviewed SLE patients with LN from 2000 to 2018 in our hospital. LN was defined as biopsy-proven LN or persistent proteinuria (more than 0.5 g/gCr or ≥3+ for more than 3 months). Patients were classified into two groups based on disease onset: young-onset LN (< 50 years old) and elderly-onset LN (≥50 years old). Deterioration of renal function (more than 30% eGFR decline from baseline) and circulating regulatory T (Treg) cell counts were compared by fluorescence-activated cell sorting (FACS) analysis using anti-CD3, 4, 25, 127 antibodies between them.

Results: Fifty-three patients with young-onset LN and 9 with elderly-onset LN were evaluated. Baseline eGFR was significantly lower in patients with elderly-onset LN than young-onset LN (63.3±19.0 vs 93.4±23.5 ml/min, p< 0.01). There was no significant difference in baseline SLEDAI (16 vs 16, p=0.33), observational periods (8 vs 10, p=0.47), maximum dose of prednisolone (p=0.42), percentage of IVCY use (p=0.15) and MMF use (p=0.46) between the two groups. Cumulative deterioration rate of renal function tended to be lower in the elderly than young-onset LN (p=0.10, Figure 1). A higher tendency of peripheral Treg (CD3+/CD4+/CD25+/CD127dull) counts by FACS analysis was observed in the elderly than young-onset LN (p=0.60, Figure 2).

Conclusion: This study suggests that elderly-onset LN may have better renal prognosis than young-onset LN. Increasing number of peripheral Treg in the elderly-onset LN indicate that alteration of immune system by aging may influence the results. Adequate sample size and a longer period of observation may be required to verify the results.

Disclosure: K. Hiramoto, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **H. Hanaoka**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **J. Kikuchi**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **S. Saito**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **H. Takei**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **T. Oshige**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **N. Seki**, Mitsubishi Tanabe Pharma Corporation, 3; **H. Tsujimoto**, Mitsubishi Tanabe Pharma Corporation, 3; **Y. Kaneko**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **T. Takeuchi**, Mitsubishi Tanabe Pharma Co., 2, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8.

Abstract Number: 0654

Applying Systemic Lupus International Collaborating Clinics (SLICC) and Provisional ACR/EULAR Systemic Lupus Erythematosus Classification Criteria in a Cohort of Patients with Undifferentiated Connective Tissue Disease

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Undifferentiated Connective Tissue Disease (UCTD) describes the clinical scenario where a patient demonstrates characteristics of a connective tissue disease but does not meet criteria for a defined CTD. The CTD that is most frequently implicated with UCTD is systemic lupus erythematosus (SLE). In recent years, new classification criteria for SLE have been developed. This study investigates the reclassification of UCTD patients using newly proposed SLE criteria.

Methods: Patients were identified within the Rheumatology and Arthritis Investigational Network (RAIN) database at the University of Nebraska Medical Center. Medical records of all patients were reviewed to confirm fulfillment of

Table 1. Disease features at time of diagnosis of UCTD by fulfillment of SLICC SLE criteria.

	All Patients	UCTD	SLE	p-value
Number of Patients (%)	129 (100)	111 (86.0)	18 (14.0)	
Acute Cutaneous Lupus (%)	28 (21.7)	24 (21.6)	4 (22.2)	1.00
Chronic Cutaneous Lupus (%)	3 (2.3)	3 (2.7)	0	1.00
Oral Ulcers (%)	18 (14.0)	14 (12.6)	4 (22.2)	0.28
Non-scarring Alopecia (%)	15 (11.6)	10 (9.0)	5 (27.8)	0.04
Arthritis (%)	40 (31.0)	33 (29.7)	7 (38.9)	0.43
Serositis (%)	8 (6.2)	7 (6.31)	1 (5.6)	1.00
Renal Involvement (%)	2 (1.6)	0	2 (11.1)	0.02
Neurologic Involvement (%)	0	0	0	N/A
Hemolytic Anemia (%)	0	0	0	N/A
Leukopenia (%)	9 (7.0)	3 (2.7)	6 (33.3)	<0.001
Thrombocytopenia (%)	5 (3.9)	1 (0.9)	4 (22.2)	0.001
ANA (%)	129 (100)	111 (100.0)	18 (100.0)	1.00
Anti-dsDNA (%)	29 (22.5)	18 (16.2)	11 (61.1)	<0.001
Anti-Smith (%)	1 (0.8)	1 (0.9)	0	1.00
Antiphospholipid Antibodies* (%)	12 (9.3)	9 (8.1)	3 (16.7)	0.37
Low Complement (%)	30 (23.3)	15 (13.5)	15 (83.3)	<0.001
Direct Coombs' Test (%)	0	0	0	N/A

Comparison made between group reclassified as SLE and group not reclassified according to SLICC criteria. Disease features were evaluated according to the definition provided by the SLICC criteria. *Includes anticardiolipin, lupus anticoagulant, anti-β2-glycoprotein

Table 2. Disease features at time of diagnosis of UCTD by fulfillment of ACR/EULAR SLE criteria.

	All Patients	UCTD	SLE	p-value
Number of Patients, n	129 (100)	103 (79.8)	26 (20.2)	
Acute Cutaneous Lupus (%)	24 (18.6)	19 (18.5)	5 (19.2)	1.00
Subacute Cutaneous Lupus (%)	4 (3.1)	4 (3.9)	0	0.58
Chronic Cutaneous Lupus (%)	1 (0.8)	0	1 (3.9)	0.20
Oral Ulcers (%)	18 (14.0)	17 (16.5)	1 (3.9)	0.12
Non-scarring Alopecia (%)	15 (11.6)	11 (10.7)	4 (15.38)	0.50
Arthritis (%)	41 (31.8)	26 (25.2)	15 (57.7)	0.004
Serositis (%)	7 (5.4)	4 (3.9)	3 (11.5)	0.15
Renal Involvement (%)	2 (1.55)	0	2 (7.7)	0.04
Neurologic Involvement (%)	0	0	0	N/A
Hemolytic Anemia (%)	0	0	0	N/A
Leukopenia (%)	9 (7.0)	4 (3.9)	5 (19.2)	0.02
Thrombocytopenia (%)	5 (3.9)	0	5 (19.2)	<0.001
ANA (%)	129 (100)	103 (100.0)	29 (100.0)	1.00
Anti-dsDNA (%)	29 (22.5)	12 (11.6)	17 (65.4)	<0.001
Anti-Smith (%)	1 (0.8)	1 (1.0)	0	N/A
Antiphospholipid Antibodies* (%)	12 (9.3)	9 (8.7)	3 (11.5)	0.71
Low C3 or C4 (%)	30 (23.3)	17 (16.5)	13 (50.0)	0.001
Low C3 & C4 (%)	12 (9.3)	4 (3.9)	8 (30.8)	<0.001
Direct Coombs' Test (%)	0	0	0	N/A

Comparison made between group reclassified as SLE and group not reclassified according to ACR/EULAR criteria. Disease features were evaluated according to the definition provided by the ACR/EULAR criteria. *Includes anticardiolipin, lupus anticoagulant, anti-β2-glycoprotein

proposed classification criteria for UCTD: positive ANA, signs and symptoms of a CTD but not fulfilling the criteria for a defined CTD, and a disease duration of at least one year, including early UCTD. Characteristics at the time of diagnosis with UCTD were collected through medical record review and managed using the REDCap electronic data capture tool. The SLICC and ACR/EULAR criteria for SLE were applied at the time of diagnosis with UCTD. We then compared the proportion of patients reclassified as SLE according to these criteria as well as the specific disease features associated with reclassification as SLE.

Results: A total of 129 patients were included in the study. The majority of patients were female and white (90.7%), and the mean (SD) age at UCTD diagnosis was 43.5 (13.9). When applying the SLICC criteria, 18 patients (14.0%) were reclassified as SLE while 26 patients (20.2%) were reclassified using the ACR/EULAR criteria. Disease features which were associated with reclassification for both SLICC (**Table 1**) and ACR/EULAR criteria (**Table 2**) were renal involvement, leukopenia, thrombocytopenia, anti-dsDNA antibody, and hypocomplementemia. Non-scarring alopecia was associated with reclassification as SLE only under the SLICC criteria while the presence of arthritis was associated with reclassification as SLE under the ACR/EULAR criteria.

Conclusion: Both the SLICC and ACR/EULAR criteria exhibit increased sensitivity for SLE classification. The only disease feature associated with reclassification under the ACR/EULAR criteria but not the SLICC criteria was the presence of arthritis. Because arthritis is weighted heavily in this criteria (6 out of 10 points), it will reclassify many patients with this frequent manifestation as SLE.

Disclosure: K. Drehmel, None; **A. Erickson**, None; **B. England**, None; **M. Hearth-Holmes**, None.

Abstract Number: 0655

Assessing Perceptions, Barriers, and Preferences to Exercise in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular disease is a significant cause of mortality in patients with SLE. High levels of fatigue are also reported in patients with SLE and negatively impact quality of life. Physical activity is associated with improvements in both cardiovascular disease and fatigue, but trials of exercise interventions involve activities that may not be feasible or sustainable outside the formal setting of a study. Our objective is to understand the perceptions, attitudes, barriers and preferences to exercise in patients with SLE.

Methods: Patients ≥18 years old with SLE seen in the Lupus Clinic at McMaster University Medical Centre were invited to complete a short questionnaire during their routine clinic appointments. This questionnaire, adapted from an exercise questionnaire validated in an osteoporosis population, contained four sections: 1) patient characteristics, 2) perceptions and attitudes towards exercise, 3) perceived barriers to exercise, and 4) preferences to performing exercise.

Results: Respondents included 49 females and 6 males (mean (SD) age 39 (12.9) years), of whom 32 worked full-time, 9 worked part-time and 14 were not employed. Almost half (n=25, 45%) reported caring for children or family

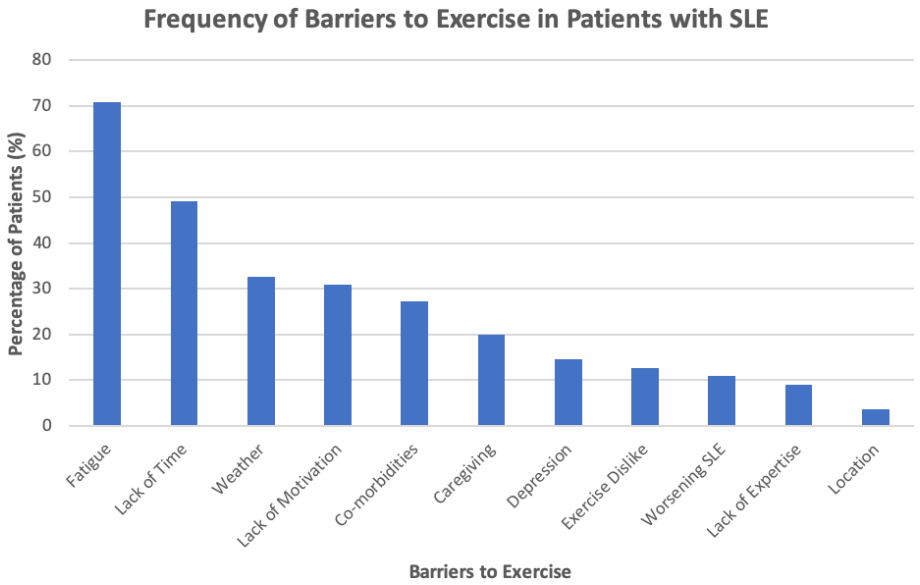

Figure 1. Frequency of barriers to exercise in patients with SLE. The x-axis indicates the barriers to exercise cited by patients. The y-axis depicts the percentage of respondents who cited each barrier. The most frequently cited barriers include fatigue, lack of time, weather, and lack of motivation.

members. Most patients (89%, n=49) reported having barriers to exercise. Those most frequently reported (**Figure 1**) included fatigue (n=39, 71%), lack of time (n=27, 49%), weather conditions (n=18, 33%), and lack of motivation (n=17, 31%). About 87% (n=48) of respondents were willing to change their daily routine to include more exercise. Walking was the most preferred exercise (n=43, 78%), followed by strengthening exercises (n=41, 75%) and flexibility exercises (n=28, 51%). After performing vigorous exercise, 49% (n=27) of patients thought they would feel better compared to when they do not exercise while 18% (n=10) thought they would feel the same and 33% (n=18) thought they would feel worse. After performing moderate exercise, 64% (n=35) of patients reported feeling better, 27% (n=15) reported feeling the same, and 9% (n=5) reported feeling worse.

Conclusion: The majority of our patients were female of child-rearing years. Many were employed full-time and were primary caregivers, which may explain fatigue and time being the most commonly reported barriers to exercise. Walking was overwhelmingly the most preferred type of exercise. Most patients found moderate exercise to be beneficial, while a sizeable minority thought vigorous activity would be detrimental. Most patients expressed willingness to incorporate more physical activity into their daily routine. There is a need for a feasible exercise regimen that considers barriers and personal preferences in patients with SLE.

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Serum Albumin as a Long-term Predictor of Renal Evolution in Lupus Nephritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: End-stage renal disease (ESRD) develops in 10-30% of patients with lupus nephritis (LN) despite standard treatment. A biomarker with excellent sensitivity and specificity to predict the evolution of LN would determine the intensity and duration of treatment as a primary end point in clinical trials. It was shown that proteinuria at 12 months has a sensitivity of 71% and specificity of 75% to predict renal outcomes at 7 years. There is evidence that serum albumin could predict renal evolution, the basis of this premise is the clinical observation that, despite proteinuria, preserved serum albumin is associated with sustained renal function. The objective of this study is to evaluate the association between baseline serum albumin and at 12 months with renal evolution at two years.

Methods: Cross-sectional, retrospective study in patients with SLE (SLICC 2012) with LN staged by biopsy, between January/2015 to January/2019. The levels of serum albumin, complement, urinary sediment and proteinuria were evaluated at diagnosis and at 12 months. An adverse renal outcome (ARO) was defined as the doubling of baseline serum creatinine, or creatinine >4 mg/dL if the initial one was >2.5 mg/dL, ESRD requiring hemodialysis (HD) therapy or transplantation. ROC curve analysis was performed for albumin value below 3 g/dL as cut value. Patients had to have at least one additional follow-up visit 24 months after diagnosis.

Results: We included 62 patients, 87% women with a mean age of 32 years (SD +/- 11). FAN positive in all patients. Anti-DNA 63%, Anti-Sm 24%, Anti-Ro 37%. ACL IgM 5%, IgG 6.7%. B2-IgM glycoprotein 5%, IgG 8.3%. LA 10%. Hypocomplementemia 89% (C3 63%, C4 89%). LN: II 16%; III 26%; IV 45%; V 11%; VI 2%. 54% of patients with LN received pulses of steroids. Induction therapy: CFD 61%, RTX 6.5% and MMF 25%. Maintenance therapy: MMF 70%, AZA 20%. They received HCQ 96.7%.

At the diagnosis of LN: proteinuria 4.3 g/day (SD +/- 3), serum albumin 3.4 g/dL (SD +/- 0.9 CI 95% 2.6-4.2); serum albumin at 12 months 4.2 g/dL (SD +/- 0.57 IC 95% 3.7-4.6). Basal hypoalbuminemia association with ARO p = 0.44 (creatinine increase: p = 0.45, ESRD p = 0.43, HD p = 0.93). Hypoalbuminemia at 12 months with ARO p = 0.003 (Creatinine increase p = 0.007, ESRD p = 0.001, HD p = 0.61). A ROC curve is made taking albumin values less than 3 g/dL as a cut-off value AUC = 0.77 p = 0.001; sensitivity 61% and specificity 93%.

Conclusion: We found an association between the level of serum albumin at 12 months and renal evolution at two years, so it should be taken into account as it is a quick, easy and cheap study. Hypoalbuminemia has a moderate sensitivity and good specificity to predict poor renal evolution. The association between serum albumin at diagnosis and renal evolution was not significant. Prospective studies in large cohorts are necessary to validate this association, investigate causality and its usefulness in monitoring and therapeutic decisions.

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Abstract Number: 0657

Performance of the "Do You Know What I Mean" Questionnaire in the Assessment of Disease Knowledge in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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Background/Purpose: 'Do you know what I mean?' is a self-reported questionnaire developed to assess disease knowledge level in Systemic lupus erythematosus (SLE) patients. It is a 27-item true/false questionnaire based on disease outcomes, complications and treatment. The aim of this study was to validate this questionnaire in a cohort of patients with SLE, to assess the level of knowledge of the disease and its association with disease characteristics.

Methods: Multicenter, observational, cross-sectional, descriptive and analytical study. Consecutive patients ≥ 18 years old with SLE (ACR 97 and SLICC 2012) were included. Sociodemographic variables, disease characteristics and those that could influence the level of knowledge were recorded: level of instruction; age at onset and disease duration; hospitalizations associated with SLE; proximity to SLE (defined as past or current contact with a relative, friend or partner with SLE); and educational exposure (use of internet or social networks, or participation in support groups). The questionnaire was filled out by all the patients. Statistical analysis: Sociodemographic and disease characteristics were described. Cronbach´s alpha and test-retest reliability were determined. For each question, median and interquartile range (IQR) of correct, incorrect and missing answers were recorded. All the comparisons were made with Student's T test, Chi2 and Fisher's exact test or Spearman correlation.

Results: A total of 277 SLE patients from 14 centers were included: 89% women, mean age 38.7 years (SD 13). Mean age at SLE onset was 28.7 years (SD 12.5) and median disease duration was 96 months (IQR 36-168). Sixty

five percent of patients reported hospitalizations due to SLE and 23% proximity to SLE. Forty percent of patients had high school level education. Twenty three percent reported educational exposure to SLE: 71% searched information on social networks, 52% on the internet and only 19% attended informative meetings. Cronbach's alpha was 0.73, no redundant questions were detected and test-retest reliability was 0.78. Median of correct answers was 18 (IQR 15-20) and of incorrect ones 5 (IQR 3-7). An earlier age at disease onset was associated with higher number of correct answers ($p < 0.0001$). In addition, a higher level of education and educational exposure to SLE were associated with higher knowledge level ($p=0.0012$). Individual question analysis showed that 55% to 77% of patients do not consider SLE as a cardiovascular risk factor or as a cause of death; however, 93% recognized that physical activity could improve bone and heart health. Sixteen to 36% of patients gave incorrect answers in questions regarding glucocorticoid-related adverse effects and between 11% and 50% reported that they didn't know the answer.

Conclusion: 'Do you know what I mean?' proved to be a valid and reliable questionnaire in patients with SLE. In addition, this study showed that the areas of highest lack of knowledge were those associated with cardiovascular impact of the disease and glucocorticoid-related adverse effects. We believe that the use of this questionnaire could be useful as a guide of educational strategies in patients with SLE, in order to improve adherence to treatment and prognosis.

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Disentangling Connective Tissue Diseases: Overlaps and Disparities in Clinical Diagnosis, Classification Criteria and Autoantibodies – Results from the Lupus Extended Autoimmune Phenotype Study

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Background/Purpose: Connective tissue diseases (CTDs) are a heterogeneous group of diseases with overlapping clinical features and shared immunopathology. In routine practice, a clinician diagnosis is often made without direct

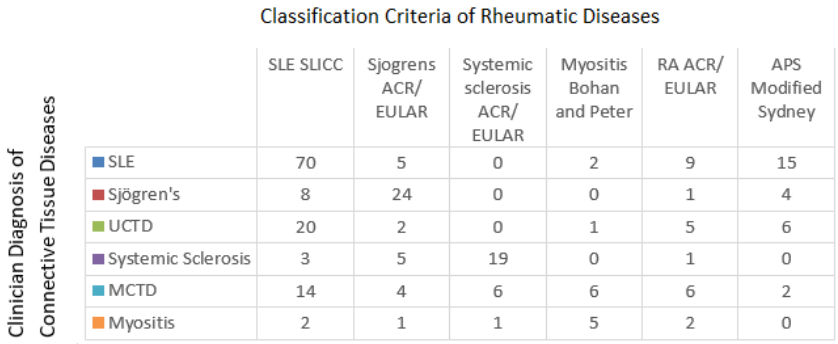

Figure 1. Patients Meeting Classification Criteria for Rheumatic Diseases According to Clinician Diagnosis of CTD

reference to classification criteria however meeting classification criteria is important when recruiting to studies and trials and in accessing medicines. We aimed to assess whether patients clinically diagnosed with a CTD met the relevant classification criteria and describe their clinical manifestations and immunological profile. Secondly, we applied accepted classification criteria to each individual patient.

Methods: Adult patients were recruited with one or more clinical feature suggestive of a CTD and one or more antibody within the antinuclear spectrum. Patients were initially grouped according to clinician diagnosis and we described their clinical features and immunological profile. Patients were then reviewed and classified, where appropriate, using SLICC SLE 2012 criteria, ACR/EULAR 2016 Sjögren's syndrome criteria, ACR/EULAR 2013 Systemic Sclerosis (SSc) criteria, the Bohan and Peter 1975 Myositis criteria, Rheumatoid Arthritis (RA) 2010 ACR/ EULAR criteria and Antiphospholipid syndrome (APS) -Modified Sydney criteria, 2006.

Results: We recruited 249 patients from May 2014-April 2019. Of these, 227 (91.2%) were female with a mean (SD) age of 48.5 (13.0) years. By clinician diagnosis, 86 (34.5%) had SLE, 35 (14.1%) had Sjögren's syndrome, 58 (23.3%) had UCTD, 26 (10.4%) had SSc, 32 (12.9%) had Mixed Connective Tissue Disease (MCTD) and 12 (4.8%) had myositis. Disease duration was shortest in patients with UCTD and myositis (median 3 years), and longest in SLE (median 10 years).

Patients from each clinician diagnosed disease group met SLICC SLE criteria including 20 (34.5%) UCTD and 14 (43.8%) MCTD patients (Fig 1). SLICC/SLE mucocutaneous criteria (including ulcers, alopecia and cutaneous lesions) and arthritis were prevalent across all diseases, affecting 83 (96.5%) SLE patients, 20 (57.1%) of Sjögren's syndrome, 45 (77.6%) UCTD, 12 (46.2%) SSc, 29 (90.6%) MCTD and 6 (50%) myositis patients. In contrast, deep organ involvement (such as renal, neurological and serositis) satisfying SLICC SLE criteria, were mostly observed in SLE patients.

	SLE N (%)	**Sjögren's** N (%)	**UCTD** N (%)	**Systemic Sclerosis** N (%)	**MCTD** N (%)	**Myositis** N (%)
	N=86	N=35	N=58	N=26	N=32	N=12
Low C3 or C4	43 (50)	9 (25.7)	10 (17.2)	4 (15.4)	9 (28.1)	2 (16.7)
anti-dsDNA	40 (46.5)	8 (22.9)	11 (19)	0	3 (9.4)	1 (8.3)
anti-Sm	17 (20)	2 (5.7)	3 (5.2)	1 (3.9)	9 (28.1)	0
anti-RNP	24 (27.9)	4 (11.4)	9 (15.5)	1 (3.9)	16 (50)	0
anti-Ro	26 (30.2)	24 (68.6)	11 (19)	2 (7.7)	8 (25)	4 (33.3)
anti-La	12 (14.0)	14 (40)	10 (17.2)	0	2 (6.3)	0
anti-Ro or anti-La	29 (33.7)	26 (74.3)	18 (31)	2 (7.7)	8 (25)	4 (33.3)
anti-Jo	0	1 (2.9)	1 (1.7)	0	0	4 (33.3)
anti-Chromatin	26 (30.2)	3 (8.6)	6 (10.3)	1 (3.9)	15 (46.9)	0
anti-Centromere	0	0	3 (5.2)	14 (53.9)	2 (6.3)	0
anti-Scl70	3 (3.5)	0	1 (1.7)	2 (7.7)	2 (6.3)	0
Rheumatoid factor	12 (14.0)	8 (22.9)	12 (20.7)	5 (19.2)	13 (40.6)	1 (8.3)

Figure 2. Immunology and Auto-Antibody Profiles Across Rheumatic Diseases According to Clinician Diagnosis of CTD

Anti-dsDNA antibodies were found in 22.9% of Sjögren's patients and 19% of UCTD patients (Fig 2). Anti-centromere antibodies had a high specificity for SSc. In contrast, other auto-antibodies were prevalent across a number of CTDs, in particular rheumatoid factor and low complement were observed in all conditions.

Conclusion: Within this CTD cohort, patients met classification criteria for CTDs other than the diagnosis given by the treating clinician and the autoantibody spectrum observed showed significant overlaps across diagnostic and classification subsets. Of note a high proportion of UCTD and MCTD patients fulfil criteria for other CTDs. Our study suggests that CTD patients are likely to have overlapping clinical and immunological phenotypes and they need to be continually reassessed for new or evolving clinical features.

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Abstract Number: 0659

Diminished Memory B-cells in Systemic Lupus Erythematosus Patients with Low Disease Activity

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SESSION INFORMATION
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Background/Purpose: B-cells play a pivotal role in the initiation and perpetuation of systemic lupus erythematosus (SLE). Recently, it has been demonstrated that in active SLE patients, the peripheral blood is enriched in $CD27^{+}IgD^{-}$ post-switched memory B-cells. The aim of our study was to delineate the B-cell repertoire of SLE patients with low disease activity (SLEDAI – 2K ≤4).

Methods: Peripheral blood samples from 42 patients suffering from SLE (mean±SD; age 42±13 years, 88% females, disease duration 10.9±7 years) and 74 age-matched healthy controls (HC; age 46±17 years, 80% female) were drawn over 2 years. All SLE patients were in remission or with low disease activity (SLEDAI of 2.0±1.7) achieved with different therapies, e.g. rituximab (RTX), cyclophosphamide, hydroxychloroquine or mycophenolate. B-cells were characterized using $CD19^{-}$, $CD20^{-}$, $CD5^{-}$, $CD27^{-}$ antibodies and grouped in naïve ($IgD^{+}27^{-}$), non-switched memory (IgD^{+}, $CD27^{+}$), memory (IgD^{-}, $CD27^{+}$), B1 ($CD5^{+}27^{-}$) and MBL-like ($CD5^{++}$) B-cells. A quantitative flow cytometric bead-based assay (QuantiBRITE PE kit from Becton Dickinson) was used for the estimation of CD19 antibodies bound per cell. All cytometric measurements were performed using a standardized BD LSR Fortessa platform.

Results: SLE patients had significantly higher B1 type B-cells in comparison with HC (median±SE, 16.8±2.1% vs. 9.9±0.7%; p=0.001). In addition, naïve and MBL type B-cells were significantly more frequent (p< 0.005) in patients

with SLE than in HC (77.2±3.6% vs. 61.6±1.4%; 0.3±0.1 vs.0.2±0.1; respectively). In contrast, memory and marginal zone B-cells were significantly reduced (p=0.001) in SLE patients with low disease activity (10.2±1.8% vs.16.6±1.0%; 2.9±0.9% vs. 9.9±0.7%; respectively). Interestingly, also non-switched memory B-cells were significantly lower in SLE patients compared to HC (2.1±0.7% vs. 6.5±0.5%; p< 0.0001). No significant difference was seen for the number of CD19 molecules on the surface of B-cells of SLE patients or HC (7432±449 vs. 7900±225; respectively). In addition, the percentage of CD86+ B-cells capable of activating T-cells were similar between SLE patients and HC (9.3±1.1% vs.8.4 ± 0.4%; p =0.421).

Conclusion: Patients with low SLE activity show an increase of naïve and inactive B-cells. This is true for patients treated successfully with RTX, cyclophosphamide and also for SLE patients treated with mycophenolate and hydroxychloroquine.

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Abstract Number: 0660

Antiphospholipid Syndrome (APS) in Systemic Lupus Erythematosus (SLE) Leads to a More Severe Disease

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SESSION INFORMATION

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Background/Purpose: Antiphospholipid antibodies (aPL) have been associated with organ damage and certain features in SLE patients. Our aim was to investigate the differences between SLE patients according to the presence of aPL and/or clinical antiphospholipid syndrome (APS).

Methods: Patients from the RELESSER-T registry were included. RELESSER-T is a multicenter, hospital-based registry, with retrospective cross-sectional collection of data from a large representative sample of adult non-selected patients with SLE attending Spanish rheumatology services from the public national health system.

Table 1. Main clinical and demographic characteristics of the studied groups.

	SLE, n =2283 (%)	SLE APS, n=552 (%)	SLE aPL, n=816 (%)	*p*
Female sex	2075 (90.9)	486 (88)	737 (90.3%)	0.127
Age, mean±SD (yr)	47.0±15.1	48.6±14.4	45.1±14.2	<0.001
Disease duration, mean±SD (mo)	141.5±100.7	157.5±110.5	135.3±92.7	0.006
Tobacco use: • Current • Former	335 (16.3) 494 (24.1)	97 (18.9) 124 (24.1)	119 (16.4) 184 (25.3)	0.637
High blood pressure	647 (28.6)	224 (40.8)	190 (23.5)	<0.001
Dyslipidemia	664 (30.3)	226 (42.0)	211 (26.8)	<0.001
Diabetes	114 (5.1)	43 (7.9)	22 (2.8)	0.001
Cutaneous manifestations	1700 (74.4)	378 (68.1)	591 (72.3)	0.011
Joint symptoms	1784 (78)	421 (75.9)	626 (76.6)	0.455
Respiratory manifestations	568 (24.8)	185 (33.3)	189 (23.1)	<0.001
Cardiac manifestations	397 (17,4)	147 (26,5)	122 (14,9)	<0.001
Renal manifestations	859 (37.6)	258 (46.5)	287 (35.1)	<0.001
Neuropsychiatric manifestations	348 (15.2)	153 (27.6)	124 (15.2)	<0.001
Ophthalmological manifestations	77 (3.4)	40 (7.2)	39 (4.8)	<0.001
Positive anti DNA antibodies	1599 (71.5)	436 (80.8)	584 (73.9)	<0.001
Hypocomplementemia	1716 (76.7)	441 (82.4)	628 (78)	0.017

Results: We included 3651 SLE patients and 1368 were positive for aPL. Overall 2283 patients were classified as SLE no aPL, 552 as SLE-APS and 816 as SLE-aPL. Demographic data, clinical and laboratory features in the different groups are showed in Table 1. Regarding cardiovascular risk factors, SLE-APS patients had higher rates of hypertension, dyslipidemia and diabetes ($p \leq 0.001$). SLE-APS patients showed higher rates of neuropsychiatric, cardiac, pulmonary, renal and ophthalmological manifestations than the other groups ($p < 0.001$) (Table 1). In accordance with a more severe clinical profile, higher frequency of anti-DNA antibodies were observed in the SLE-APS group comparing with SLE ($p < 0.001$). SLE APS patients presented more damage accrual with higher values in SLICC (1.9±2.2 in SLE APS, 0.9±1.4 in SLE aPL and 1.1±1.6, $p < 0.001$) and Katz indexes (3±1.8 in SLE APS, 2.7±1.7 in SLE aPL and 2.6±1.6 in SLE no aPL, $p < 0.001$). In line with a more severe disease, mortality rate was higher in SLE APS patients ($p < 0.001$).

Conclusion: SLE-APS patients show a more severe clinical profile with higher frequency of major organ involvement and more damage accrual than SLE-aPL and SLE no APL.

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Abstract Number: 0661

Association of Serum and Urine Levels of TWEAK, MCP-1 and NGAL with Disease Activity in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: TWEAK, MCP-1 and NGAL, mediators in pathogenesis of systemic lupus erythematosus (SLE), are proinflammatory cytokines/chemokines that are thought as potential biomarkers reflecting disease activity. In this study, we aimed to investigate the association of serum (s) and urine (u) levels of TWEAK, MCP-1 and NGAL with disease activity in both renal and non-renal SLE.

Methods: Thirty active patients with SLE (15 renal and 15 non-renal) were recruited. Disease activity was determined using SLE Disease Activity Index (SELENA-SLEDAI) and British Isles Lupus Assessment Group (BILAG)-2004 index. Thirty-one inactive patients with SLE (16 renal and 15 non-renal), 14 patients with ANCA-associated vasculitis (AAV) all of whom had active renal involvement and 20 healthy volunteers were selected as control groups. In patients with AAV, disease activity was evaluated using Birmingham Vasculitis Activity Score (BVAS) v3. Serum and urine levels of TWEAK, MCP-1 and NGAL were tested using ELISA.

Results: Sixty-one SLE patients, 51 (83.6%) of whom were female, with a median disease duration of 83 (23.5-135) months and a median age of 35 (27-47.5) were included in the study. Serum and urine levels of TWEAK and NGAL were significantly higher in the active SLE group compared with the inactive SLE (n=31) group (sTWEAK: p=0.005; uTWEAK: p=0.026; sNGAL: p< 0.001; uNGAL: p=0.002); whilst no significant differences regarding serum and urine MCP-1 levels were observed (p=0.189 and p=0.106). uTWEAK (p=0.237), sMCP-1 (p=0.141), uMCP-1 (p=0.206), sNGAL (p=0.419) and uNGAL (p=0.443) levels did not differ between patients with active LN and non-renal active SLE; yet levels of sTWEAK were higher in patients with active LN (p=0.006). There were no differences between active LN and renal active AAV. Levels of all biomarkers were correlated with SLEDAI (sTWEAK: p=0.001; uTWEAK: p=0.006; sMCP-1: p=0.049; uMCP-1: p=0.014; sNGAL: p< 0.001; uNGAL: p=0.002).

Conclusion: sTWEAK, uTWEAK, sNGAL and uNGAL are significant biomarkers showing disease activity in SLE. However, our results implicate that these biomarkers may not be specific for SLE, and can be elevated in patients with active renal involvement of AAV. sTWEAK may be of use for discriminating active nephritis from non-renal active disease in SLE. Further studies are awaited to confirm these results (This study was funded by Istanbul University with the project number TTU-2017-24738 and Turkish Society for Rheumatology).

Disclosure: S. MIRIOGLU, None; **S. CINAR**, None; **H. Yazici**, None; **A. Gül**, None; **L. Öcal**, None; **M. Inanc**, None; **B. Artim-Esen**, None.

Abstract Number: 0662

Utility of a Mobile Phone Based Application to Collect Patient-Reported Outcome Information from People Living with Systemic Lupus Erythematosus

Brooke Williams,[1] Bridget Muckian,[1] Claire Dykas,[2] Christine Peschken,[3] Richard Furie,[4] Elena Massarotti,[5] Vanja sikirica,[6] Steven Gilbert,[7] Martin Hodge,[7] and Peter Lipsky[8], [1]AMPEL BioSolutions, Charlottesville, VA, [2]AmpelBioSolutions, Charlottesville, VA, [3]University of Manitoba, Winnepeg, Canada, [4]Northwell Health, Great Neck, NY, [5]Brigham and Women's Hospital/Harvard Medical School, Boston, MA, [6]Pfizer, Boston, MA, [7]Pfizer, Boston, [8]AMPEL BioSolutions, LLC, Charlottesville, VA

SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Patient Reported Outcomes (PROs) can provide important data about the impact of a disease on an individual and/or the quality of the response to medication. However, in most circumstances, PRO information is collected only intermittently and usually at the point of care or treatment. The development of mobile technology to collect PRO data electronically (ePRO) provided the opportunity to acquire this information more frequently, in real time, and in the person's normal environment. The objective of the research was to develop a smart phone application (app) and test its utility to collect ePRO information in people with systemic lupus erythematosus (SLE).

Methods: A smart phone app was developed that collects data from a number of PRO instruments, including FACIT-F (fatigue), SF-36 (health-related quality of life) and patient global assessment (PtGA). People living with SLE were involved in the initial development and evaluation of the acceptability of the app. To test to utility of this app, a multicenter clinical study (VALUE, NCT03142711) was carried out in collaboration with people with SLE, in whom ePRO information was collected with the app daily (PtGA) or weekly (FACIT-F and SF-36) in the person's environment and also with the app and a paper form monthly at the clinical site. Demographic information, compliance and intra-class

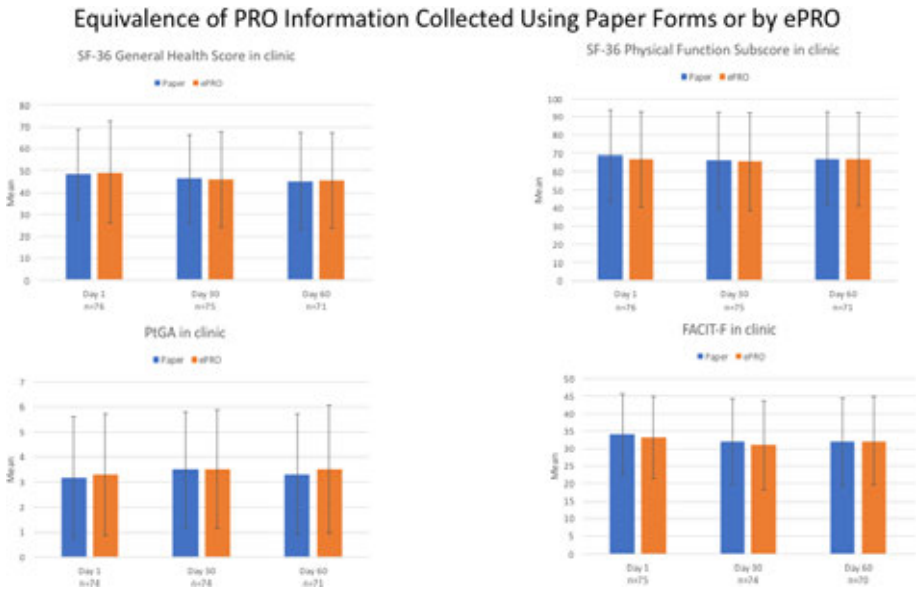

Figure 1

correlation coefficients between information collected with the app and using a paper form at the clinical site were assessed.

Results: Of the 80 people enrolled in this study, 91.3% were women; 57.5%, 16.3% and 17.5% identified themselves as of European, African or Asian ancestry, respectively. The mean age was 42.6 years and the mean duration of education was 15.6 years. Overall compliance with completing the ePRO instruments with the app at the scheduled time was 88%. To determine the consistency of information collected with the app, PRO instruments were completed on three occasions: a) in standard fashion using a paper form and b) using the app, separated by an interruption at the clinical site. The mean (SD) PtGA, FACIT-F and SF-36 Physical Functioning and General Health scores at baseline, month 1 and month 2 using the app and paper forms were similar (Figure 1). The Intraclass Correlation Coefficient (ICC) and 90%CI were 0.97 (0.96-0.98), 0.96 (0.94-0.07) and 0.95(0.93-0.97) at the three time points, respectively for the PtGA; 0.94(0.91-0.96), 0.96(0.95-0.98) and 0.96(0.94-0.97), respectively for the FACIT-F instrument; and , 0.96(0.94-0.97), 0.94(0.91-0.96) and 0.96 (0.94-0.97) for the 3 time points, respectively for the SF-36 Physical Functioning score.

Conclusion: Compliance with completion of ePROs using a mobile app was high and the content collected with the app conformed with that collected using a paper form. Since compliance with the use of a mobile app to collect ePRO information and the consistency of the information obtained compared to that obtained using a paper form were high, the app affords the potential opportunity to acquire frequent and highly reliable information about the impact of disease and response to medication in individuals with SLE.

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Abstract Number: 0663

Peripheral Blood Toll Like Receptor 7 Expression and Serum Interferon Lambda 1 Levels in Systemic Lupus Erythematosus and Their Relation to Disease Activity and Lupus Nephritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
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Background/Purpose: Toll-like receptor 7 (TLR7) can sense single-stranded RNA with subsequent induction of different interferon (IFN) types including IFN lambda (IFNL) and may contribute to the development of autoimmune diseases. The present work was designed to investigate the potential role of TLR7 and IFNL1 in systemic lupus erythematosus (SLE) and their relation to disease activity and development of lupus nephritis (LN).

Methods: Thirty patients with SLE (15 patients without LN and 15 patients with LN) and 15 healthy subjects were enrolled in the study. Disease activity was assessed using the SLE disease activity index (SLEDAI). Antinuclear antibody (ANA) and anti-double stranded DNA antibodies (anti-dsDNA) titer were assayed. TLR7 expression on

peripheral blood CD14+ monocytes was studied by color flow cytometry and the absolute number of CD14+ TLR7+ cells was calculated. Quantification of IFNL1 levels in serum was determined using enzyme-linked immunosorbant assay. Renal function was assessed by estimating serum creatinine, estimated glomerular filtration rate (eGFR) and urinary albumin to creatinine (UAC) ratio. Erythrocyte sedimentation rate (ESR), serum high-sensitivity C-reactive protein (hsCRP) and serum complement 3 and 4 (C3 and C4 respectively) were quantified. Renal biopsy was performed to patients with LN and classified according to the international society of nephrology/renal pathology society.

Results: The number of peripheral blood CD14+ TLR7+ monocytes and serum IFNL1 levels showed significant increases in patients with and without LN compared with healthy controls and in patients with LN compared with those without LN ($P < 0.001$). Changes in TLR7 expression and IFNL1 production in peripheral blood were positively correlated ($P < 0.001$) and both showed positive correlations with SLEDAI score, ANA and anti-dsDNA titers, serum creatinine, UAC ratio, ESR, serum hsCRP levels and renal activity index and inverse correlations with eGFR and serum C3 and C4 levels in SLE patients ($P < 0.05$). By plotting receiver operating characteristics (ROC) curve, the sensitivity and specificity of the number of peripheral blood CD14+ TLR7+ monocytes in discriminating SLE patients with and without LN were higher than those of serum IFNL1 levels (100% and 93.33% respectively, area under the curve (AUC) = 0.996 vs. 86.7% and 40% respectively, AUC = 0.687).

Conclusion: Activation of TLR7/IFNL1 pathway may play an important role in the pathogenesis of SLE in relation to disease activity and development of LN and could be a potential therapeutic target for the treatment of SLE and LN.

Disclosure: H. ElAggan, None; **N. Farahat**, None; **M. Sakr**, None; **S. Tawfik**, None.

Abstract Number: 0664

Myxovirus Resistance Protein a Is a Useful Additional Histological Marker for Cutaneous Lupus Erythematosus

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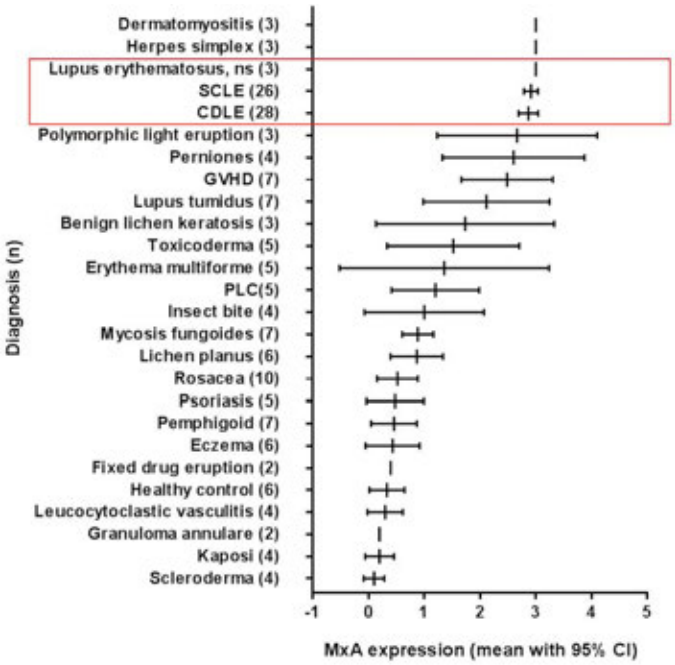
Background/Purpose: Cutaneous lupus erythematosus (CLE) is a heterogeneous auto-inflammatory skin disease, that is driven to a great extent by interferon (IFN) type I[1], and is characterized by superficial and deep perivascular and periadnexal infiltration of lymphocytes as well as interface dermatitis. Unfortunately, no specific histological marker for CLE is currently available.

Methods: 163 skin biopsy specimens were collected from the local pathology database. Various conditions (eg. CLE, dermatomyositis, rosacea, psoriasis, graft versus host disease, scleroderma) were selected, provided that clinical diagnosis matched with histological diagnosis. Herpes simplex lesions were used as positive controls. Skin sections were incubated with anti-MxA (R&D systems, AF7946). Consecutively, rabbit anti goat-HRP conjugate (Dako, 0449) was added and sections were stained with diaminobenzidine.



Abbreviations: ns = not specified, SCLE = subacute cutaneous lupus erythematosus, CDLE = chronic discoid lupus erythematosus, GVHD = graft versus host disease, PLC = pityriasis lichenoides chronica.

Figure 1. Myxovirus resistance protein A expression in various skin diseases. Abbreviations: ns = not specified, SCLE = subacute cutaneous lupus erythematosus, CDLE = chronic discoid lupus erythematosus, GVHD = graft versus host disease, PLC = pityriasis lichenoides chronica.

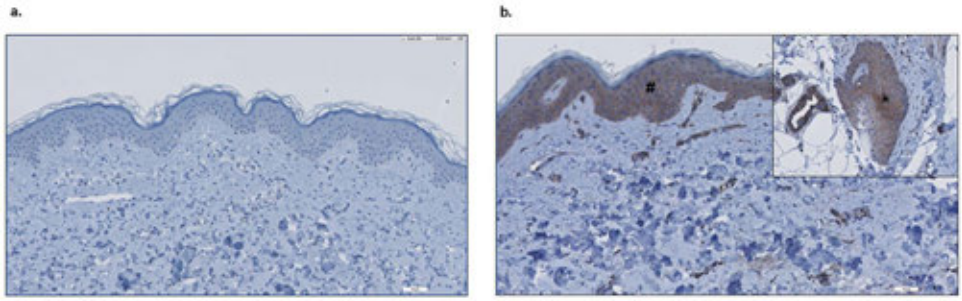


Figure 2. MxA staining in skin biopsies of (a) healthy control and (b) cutaneous lupus erythematosus with MxA expression in epidermis (#), endothelium (->) and adnexa (*)

The expression of MxA was scored semi-quantitatively by 2 researchers in respectively epidermis, dermal structures, fibroblasts, infiltrates, and endothelium (0 for no expression, 1 for moderate expression, 2 for mediate expression, and 3 for strong expression). Mean scores were calculated based on cumulative expression divided by the number of assessable skin parts.

Results: MxA staining was strongly positive in both epidermis, dermal structures, infiltrate, and endothelium in nearly all lesional CLE skin sections (except lupus tumidus), as well as in dermatomyositis (see figure 1), which is also an IFN-driven autoimmune disease. Although most other inflammatory skin diseases did show no or a low expression of MxA. In some conditions, like perniones and graft versus host disease, high expression could be found, but this was less consistent compared to CLE.

Conclusion: MxA is strongly expressed in CLE skin, and therefore is useful as additional diagnostic histological marker, expectedly resulting in restriction of misdiagnosis and treatment delay. The high expression found in skin biopsies from graft versus host disease and perniones, suggests that IFN type I plays a role in the pathogenesis of these conditions.

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Abstract Number: 0665

Utility of Repeat Renal Biopsies in Patients with Lupus Nephritis in Western Australia

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SESSION INFORMATION
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Background/Purpose: The role of repeat renal biopsy (RRBx) in lupus nephritis (LN) to guide treatment or predict prognosis is not fully understood. We assessed the association between histopathological changes and clinical outcomes across renal biopsies.

Methods: A retrospective cohort study of 99 patients with biopsy confirmed lupus nephritis (LN), and 39 (39.4%) patients [mean age 29.2 ± 11.0 years; 89.7% female] who had at least one RRBx (median of 2 renal biopsies; interquartile range: 2, 3) for evaluation of persistent/current symptoms. Renal specimens were assessed by ISN classification (Class I and II grouped as mild disease, Class III + IV as proliferative disease, and Class V as membranous proliferative disease), NIH Activity (0-24) and Chronicity (0-12) indices and immunofluorescence findings (0-3) with data on clinical characteristics, serology, medication, disease activity (Systemic Lupus Erythematosus Disease Activity Index - 2K (SLEDAI-2K)), organ damage (SLICC Damage Index (SDI)) at biopsy recorded. Study endpoints included the doubling of serum creatinine, requirement for renal replacement therapy (RRT), and mortality.

Outcomes were assessed comparatively across biopsy events with non-parametric and Chi-square tests; and, logistic regression quantified the odds of study endpoints.

Results: Compared to patients without repeated biopsies; at the initial biopsy, RRBx patients were younger (29 vs 36 years, p=0.026) and, more likely to be lymphopenic (79.5% vs 60.0%, p=0.04) and had “Full house IF findings” (89.5% vs 62.2%, p=0.03). Patients had similar median proteinuria level (300 vs 257, p=0.70) and SLEDAI scores (13 vs 12, p=0.19). RRBx (n=39) occurred 2.95 years (IQR 1.20, 6.10) after the index biopsy; and, clinical characteristics, laboratory levels and SLEDAI scores were similar to the index biopsy data. Class switching occurred in 9 (23%) patients; with Class worsening in 6 and improvement in 3 (p=0.04). NIH Activity Index was not significantly different from the index biopsy; however, Glomerular Sclerosis (0 vs 1), Interstitial Fibrosis (0 vs 1),

and the NIH Chronicity Index (1 vs 2) had worsened at the repeat biopsy, all p< 0.01. Increasing Cellular Crescents increased the odds of RRT [OR 1.7 (95%CI: 1.0, 2.8) p=0.049], and the doubling of serum creatinine at last follow-up [OR 2.0 (95%CI 1.0, 4.00), p=0.05]. Increasing NIH Chronicity Index increased the odds of doubling of creatinine at last follow-up [OR 3.6 (95%CI 1.1, 12.3), p=0.04]. There was no impact of histological findings on repeat biopsy on mortality.

Conclusion: Patients with LN with a RRBx showed low rates of ISN Class switching within 3 years, and NIH Activity Index remained unchanged across biopsies; suggesting that repeat biopsies had little impact on disease management. In contrast, NIH Chronicity Index scores were increased and associated with worse renal outcome.

Disclosure: W. Raymond, None; **A. Kang**, None; **D. Wong**, None; **A. Chakera**, None; **J. Nossent**, None.

Abstract Number: 0666

Sensitivity to Change of the Patient Reported Outcomes Measurement Information System (PROMIS) Computerized Adaptive Test (CAT) Measures in a Single Canadian Lupus Cohort

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SESSION INFORMATION
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Background/Purpose: Patient-reported outcomes (PROs) measures are a key component of the care of patients with systemic lupus erythematosus (SLE). The Patient Reported Outcomes Measurement Information System (PROMIS) computerized adaptive test (CAT) is a recently developed PRO instrument that has not yet been well studied in SLE. This study seeks to examine the sensitivity to change of PROMIS CAT compared to patient-reported anchors within a cohort of adult SLE patients.

Methods: All consecutive adult (≥18 years old) English-speaking patients with SLE and visiting the Toronto Lupus Clinic between July-September 2018 were approached to participate. Patients completed PROMIS CAT during their clinical visit assessing 14 domains. 89 patients completed PROMIS CAT at baseline and at 3-month follow-up. At 3 months, the generic anchor question "Compared to when you started the study, how have you been during the last 48 hours? (responses: same, worse,)" was asked to identify two subsets of patients, those with improved vs worsened symptoms at 3 months. Similar domain-specific anchor questions were asked at 3 months, with responses graded from -7 (greatest worsening) to +7 (greatest improvement), and 0 representing no change. For domain-specific anchors, patients were deemed to have improved if they graded >1, and worsened if < -1. Responsiveness was evaluated using standardized response means (SRM), with higher SRM values reflecting greater sensitivity to change (0.3-0.5 low, 0.5-0.8 moderate, >0.8 high). SRMs for each domain were determined with respect to the generic as well as domain-specific anchors. We hypothesized that domains demonstrate worsening and improvement in concordance with the anchors.

Table 1. Patient characteristics of entire cohort (n=89)

Characteristic		
Mean age at 3 month visit (years)	48.3 ± 13.6	
Mean SLE duration at 3 month visit (years)	20.2 ± 12.5	
Female	82 (92.1%)	
Ethnicity	Black	11 (12.4%)
	Caucasian	57 (64.0%)
	Chinese	11 (12.4%)
	Others	10 (11.2%)
Education	< Grade 8	1 (1.1%)
	Grade 8	2 (2.3%)
	High school graduate	16 (18.4%)
	College	28 (32.2%)
	University	40 (46.0%)

Table 2. Baseline patient characteristics of groups with improved vs worsened symptoms (based on generic anchor question)

Characteristic	**Improvement of symptoms (n=19)**	**Worsening of symptoms (n=13)**
Mean age at 3-month visit (years)	48.3 ± 15.3	50.2 ± 14.8
Mean SLE duration at 3-month visit (years)	19.5 ± 13.5	22.2 ± 13.9
Female	18 (94.7%)	13 (100%)
Ethnicity		
Black	3 (15.8%)	1 (7.7%)
Caucasian	11 (57.9%)	10 (76.9%)
Chinese	3 (15.8%)	2 (15.4%)
Other	2 (10.5%)	0 (0%)
Education		
< Grade 8	0 (0%)	0 (0%)
Grade 8	1 (5.3%)	0 (0%)
High school graduate	3 (15.8%)	5 (41.7%)
College	6 (31.6%)	5 (41.7%)
University	9 (47.4%)	2 (16.7%)
PROMIS domains	Mean ± SD	Mean ± SD
Physical Function	42.8 ± 7.6	38.2 ± 9.0
Mobility	44.1 ± 10.7	40.2 ± 11.6
Pain Behaviour	54.7 ± 10.2	58.8 ± 8.0
Pain Interference	58.2 ± 9.7	60.0 ± 10.2
Participation in social roles	45.5 ± 8.2	43.6 ± 10.0
Satisfaction in social roles	47.4 ± 12.2	43.9 ± 12.9
Fatigue	59.7 ± 9.3	62.7 ± 12.9
Sleep disturbance	56.7 ± 8.3	60.3 ± 11.2
Sleep related impairment	57.9 ± 9.6	61.8 ± 11.0
Anger	53.0 ± 8.3	53.6 ± 7.3
Anxiety	57.6 ± 9.2	56.5 ± 9.2
Depression	53.0 ± 6.6	56.2 ± 9.1
Cognitive function abilities	44.5 ± 9.5	41.7 ± 6.9
General cognitive function	45.8 ± 9.3	42.3 ± 8.5

PROMIS domains have population mean ± SD = 50 ± 10.

Results: Patient characteristics are in **Table 1**. **Table 2** contains the baseline characteristics of the subsets of patients with improvement and worsening at follow-up.

With respect to the general anchor, of 14 PROMIS domains, 8 demonstrated moderate SRMs: mobility, pain behaviour, pain interference, participation in social roles, fatigue, anxiety, depression, and cognitive function abilities (**Table 3**).

For domain-specific anchors (**Table 3**), only 3 domains (pain behaviour, pain interference, depression) demonstrated moderate SRMs. Only 1 domain (satisfaction in social roles) had a high SRM. SRM were overall larger with the generic anchor compared to domain-specific anchor.

Table 3. Standard response means comparing baseline and 3-month follow-up in patient subsets with improved vs worsened symptoms.

	Generic anchor		Domain-specific anchor	
Domains	**Improvement of symptoms (n=19)**	**Worsening of symptoms (n=13)**	**Improvement of symptoms (n=29)**	**Worsening of symptoms (n=14)**
Physical Function	0.14	0.02	0.27*	-0.18*
Mobility	0.23	-0.52	0.06	-0.37
Pain Behaviour	0.09	0.66	0.06	0.55
Pain Interference	-0.77	0.66	-0.29	0.68
Participation in social roles	0.75	-0.42	0.32	-0.43
Satisfaction in social roles	0.38	-0.33	-0.10	-0.95
Fatigue	-0.64	0.30	-0.28	-0.11
Sleep disturbance	-0.12	-0.03	0.02	0.10
Sleep related impairment	-0.14	-0.03	-0.06	0.03
Anger	-0.45	0.19	-0.12	0.42
Anxiety	-0.51	0.42	-0.25	0.26
Depression	-0.20	0.66	-0.20	0.53
Cognitive function abilities	0.65	-0.49	-0.01	-0.49
General cognitive function	0.33	0.20	-	-

*n=28 for improved; n=13 for worsened for domain-specific physical function
SRM 0.3-0.5 = low, 0.5-0.8 = moderate, >0.8 = high

Notice that for each of 13 Anchor questions, the answers and their corresponding scores are:
0 = "No change"
1 = "Almost the same, hardly any better at all"
2 = "A little better"
3 = "Somewhat better"
4 = "Moderately better"
5 = "A good deal better"
6 = "A great deal better"
7 = "A very great deal better"
-**1** = "Almost the same, hardly any worse at all"
-**2** = "A little worse"
-**3** = "Somewhat worse"
-**4** = "Moderately worse"
-**5** = "A good deal worse"
-**6** = "A great deal worse"
-**7** = "A very great deal worse";

Conclusion: Out of 14 PROMIS domains, 8 were sensitive to change at 3-month follow-up when compared to a generic anchor question. In contrast, for domain-specific anchors, only 4 domains were sensitive to change at 3-month follow-up, of which one had not been sensitive in the generic anchor analysis. This highlights the importance of using appropriate anchor questions when assessing responsiveness. Focusing on patients with more significant reported changes (+/- 4-7 on anchors) may yield larger SRMS. This requires a larger sample size and currently cannot be performed. Further work is needed to evaluate the utility of PROMIS CAT measures in the care of lupus patients as well as to determine minimal clinically important differences.

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Abstract Number: 0667

The PROMIS-29 as a Measure of Type 1 and 2 SLE Activity

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SESSION INFORMATION
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Background/Purpose: We have developed a new conceptual model that characterizes lupus into subtypes based on physician- and patient-reported measures: **Type 1** is assessed by the rheumatologist and incorporates immunologic activity and organ involvement; **Type 2** is based on patient report of fatigue, myalgia, mood disturbance, and perceived cognitive dysfunction. We have previously defined Type 2 symptoms based on the ACR's Fibromyalgia Severity Score (FSS), and here we seek to assess the impact of Type 1 and 2 SLE activity on the NIH's Patient-Reported Outcomes Measurement Information System (PROMIS) measures.

Methods: Data on physician- and patient-reported measures of disease activity were collected on women with SLE enrolled in a prospective registry at a single academic center from 2018-2019. Patients were classified as having Type

Table 1. Median PROMIS measure T-score by lupus subtype. A score of 50 corresponds to the US population mean, and a score difference of 5 (half standard deviation) is clinically significant.

	LOW TYPE 2 SLE ACTIVITY		HIGH TYPE 2 SLE ACTIVITY		
MEDIAN (IQR)	Minimal SLE Activity	Type 1 SLE Activity	Type 2 SLE Activity	Mixed SLE Activity	p-value
HIGH SCORE IS WORST:					
PAIN INTERFERENCE	52.4 (41.6-55.7)	59.5 (53.0-61.3)	63.1 (61.3-66.7)	64.1 (61.3-69.9)	<0.0001
FATIGUE	51.0 (46.0-58.6)	56.6 (51.0-62.1)	64.8 (62.7-71.5)	69.0 (60.9-75.8)	<0.0001
SLEEP DISTURBANCE	55.7 (53.3-58.7)	56.4 (54.4-58.3)	56.4 (53.9-59.0)	56.0 (54.5-59.0)	0.8
HIGH SCORE IS BEST:					
PHYSICAL FUNCTIONING	45.7 (39.8-57.0)	41.5 (37.2-46.8)	35.0 (32.1-38.8)	36.3 (34.4-38.4)	<0.0001
SOCIAL HEALTH	51.8 (48.0-64.2)	48.8 (44.2-54.5)	40.3 (37.2-44.2)	41.8 (32.0-44.2)	<0.0001

1 SLE activity (SLEDAI ≥6, clinical SLEDAI ≥4, or active nephritis), Type 2 SLE activity (FSS >10), Mixed (both Type 1 and Type 2 SLE activity), or minimal (neither Type 1 or Type 2 SLE activity). We compared the PROMIS composite measures of pain interference, physical functioning, sleep disturbance, fatigue, and ability to participate in social roles and activities between groups using the Wilcoxon rank-sum test. A PROMIS score of 50 is the national average, and a score difference of 5 (half standard deviation) is clinically significant.

Results: Data were collected from 116 women with SLE of whom 63% were African American with an average age 43. Compared to the US general population, patients with either Mixed or Type 2 SLE activity have moderately worse scores (1-2 standard deviation difference), while patients with Type 1 SLE activity alone have only mildly worse scores (< 1 standard deviation difference) in physical functioning, ability to participate in social roles and activities, fatigue, and pain interference. Patients with Minimal SLE activity were the least limited by pain, suffered from less interference with physical and social functioning, and their scores were not clinically significantly different (within a half standard deviation) from the general population. Despite the large differences in fatigue, all SLE groups reported similar degrees of mild sleep disturbance (Table 1).

Conclusion: The presence or absence of Type 2 symptoms was the primary determinant of PROMIS scores in pain, physical functioning, fatigue, and social well-being. This analysis demonstrates that multiple domains of the PROMIS-29 correspond to the Type 1 and 2 SLE model and may be useful in measuring levels of Type 1 and 2 SLE activity. Next steps include identifying and validating the optimal PROMIS domains that can be used to determine current Type 2 SLE activity.

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Abstract Number: 0668

Lack of Uptake of Prophylactic Human Papilloma Virus (HPV) Vaccination Among Women with Systemic Lupus Erythematosus (SLE) in the Detroit, MI Area, a High Risk Population

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SESSION INFORMATION
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Background/Purpose: Women with SLE are at increased risk for cervical neoplasia likely because of infection with high risk (HR) HPV and thus should be considered for HPV vaccination. We previously showed quadrivalent human papillomavirus (qHPV) vaccine to be safe and immunogenic in women with SLE. We sought to determine the frequency of HRHPV infection and uptake of HPV vaccination in the female outpatient lupus population. The qHPV vaccine was approved for use in 2006 for women ages 9-26 years.

Methods: We conducted a retrospective chart review of women ages 16-70 years, with an ICD-10 diagnosis of SLE, seen in the Internal Medicine, Family Medicine, OB/Gyn and Rheumatology clinics associated with a large teaching hospital in Detroit, Michigan during the period 10/2015 to 2/2019. After obtaining IRB approval, data were collected

Table 1. Comparison for Women HRHPV+ vs. HRHPV- (N=45 tested)

	HPV + (n=6)	HPV – (n=39)	p-value
Age in years (mean ± s.d.)	40.0 ± 8.3	47.4 ± 10.7	0.11
Race (n, %)			- -
White	1 (7.7%)	12 (92.3%)	
Black	5 (16.7%)	25 (83.3%)	
Other	0 (0%)	2 (100%)	
Smoke Exposure (n, %)			- -
Current	0 (0%)	7 (100%)	
Former	1 (14.3%)	6 (85.7%)	
Never	5 (16.1%)	26 (83.9%)	

on demographic and clinical characteristics. Data were analyzed using Student's t-test, analysis of variance followed by multiple pairwise comparisons using the Bonferroni correction of the p-value.

Results: We collected data on 118 women, mean age 44.5 ± 11.6 years, 40.7% Caucasian (48/119), 50% Black (59/118) and 9.3% other/unknown race (10/118). Current smoking was reported by 17.1% (20/117), with 26.5% being former smokers (31/117) and 56.4% never smokers (66/117). HRHPV testing was performed in 45 (38.1%) of these women; six were positive (13.3%). There were no significant differences in test results by age, race or smoking status (Table 1). Black women (50.8%) were more likely to be tested than Caucasians (27.1%) or other races (18.2%), p=0.02. Only 4.3% of the study group were vaccinated (5/117). Of the 112 women who were eligible to receive an HPV vaccine, 38.4% (43/112) were tested for HRHPV with 5 being positive. Of the 5 that were vaccinated, only one woman had testing for HRHPV and this female was positive for HRHPV.

Conclusion: Despite the fact that HPV related cervical disease and neoplasia are increased in women with SLE, the frequency of testing for HRHPV testing is low (38.4%) and vaccination rate even lower (4.3%) in our region. This highlights the importance of the need for monitoring for HRHPV and including HPV vaccination as part of general health care in this vulnerable population. Promoting awareness of this problem with primary care doctors and the lupus community would improve uptake of prophylactic HPV vaccination and be beneficial to gynecologic health in women with SLE.

Disclosure: J. Dhar, None; **L. Saravolatz**, None; **S. Szpunar**, None.

Abstract Number: 0669

Complement Activation in Probable Systemic Lupus Erythematosus (pSLE) May Predict Progression to SLE Defined by Fulfillment of ACR Classification Criteria

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Background/Purpose: We reported (R*amsey-Goldman et al., Arthritis Rheumatol 2018: 70 [suppl 10])* that cell-bound complement activation products (CB-CAPs) and a multi-analyte assay panel with algorithm (MAP) are positive more frequently than standard immunological markers in patients with probable systemic lupus erythematosus (pSLE) who fulfilled 3 ACR criteria. We followed pSLE prospectively to evaluate whether CB-CAPs and MAP positivity at enrollment predict transition to classifiable SLE by fulfillment of a fourth ACR criterion.

Methods: pSLE were followed prospectively at academic lupus centers and clinical and laboratory data were collected. Biomarkers were measured at every visit. CB-CAPs - C4d bound to erythrocytes (EC4d) and B-cells (BC4d) - were measured by quantitative flow cytometry and expressed as mean fluorescent intensity (MFI). Serum C3 and C4 and autoantibodies were measured by turbidimetry and ELISA, respectively. Anti-dsDNA positivity was confirmed by immunofluorescence (IFA) with *Crithidia Luciliae*. MAP was evaluated as previously described (Dervieux T, et al. *J Immunol Methods* 2017) and consists of an algorithm which utilizes CB-CAPs and autoantibodies. A MAP score >0.1 is considered positive, the higher the number (to 3.5) the greater the likelihood of SLE. For this study, decision analysis with Youden index showed that MAP >0.8 and EC4d >20 MFI reflected the optimal cutoff. Data were analyzed by Fisher's exact test and Kaplan-Meier with log-rank test and Cox proportional hazards model for time to fulfillment of a fourth ACR criterion, expressed as hazard ratios.

Results: Of the 92 pSLE enrolled, 69 had 1 follow up visit 9-18 months after enrollment (average±SD = 12.4±1.7 months; median = 12 months). The time to acquire the 4th ACR criterion was estimated by the investigators at the follow up visit. Twenty pSLE (29%) fulfilled a fourth ACR criterion during this time. SLICC fulfillment at enrollment did not predict fulfillment of ACR criteria (p =0.27). Eight of the 20 (40%) pSLE who transitioned to classifiable SLE by ACR criteria had MAP >0.8 at enrollment while 8/48 (17%) non-transitioned patients had MAP > 0.8 at enrollment (p =0.06). Patients with MAP >0.8 at enrollment fulfilled ACR criteria with a hazard ratio (HR) =3.11 within 18 months (p < 0.01 by log-rank test). HR of MAP was higher than other individual biomarkers, although anti-dsDNA and EC4d >20 MFI were of borderline significance (Table).

Conclusion: Complement activation as detected by MAP >0.8 at enrollment may predict disease evolution of pSLE into classifiable SLE by ACR criteria better than anti-dsDNA and low serum complement.

	HR	95% CI	p value
Low C3 and/or C4	1.93	0.44-8.53	0.375
Anti-dsDNA (IFA)	2.97	0.98-8.99	0.043
Positive CB-CAPs (EC4d and/or BC4d)	1.66	0.67-4.09	0.275
EC4d >20 MFI	2.61	0.99-6.88	0.053
MAP >0.8	3.11	1.26-7.69	0.010

Hazard ratio (HR) of biomarkers in predicting fulfillment of a fourth ACR classification criterion by 18 months in the pSLE population. Data of 69 follow-up visits (n = 68 for MAP) that occurred 9 to 18 months after enrollment were analyzed. CB-CAPs: cell-bound complement activation products; MAP: multianalyte assay panel with algorithm; HR: hazard ratio; CI: confidence intervals.

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Abstract Number: 0670

Association Between Ambient Air Pollutant Exposures and Childhood-Onset Systemic Lupus Erythematosus: A 12-Year Population-Based Cohort Study in Taiwan

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SESSION INFORMATION
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Background/Purpose: Air pollutants exposure has been linked to inducing oxidative stress, pulmonary and systemic inflammation. We hypothesized that long-term exposure to air pollution would be associated with childhood-onset systemic lupus erythematosus (cSLE).

Methods: We collected data from the Taiwan National health insurance research database and linked these data to the Taiwan Air Quality-Monitoring Database. Children < 18 years old, identified from January 1st, 2000, were followed-up until the first diagnosis of cSLE was made or December 31st, 2012. The daily average air pollutant concentrations, including particulate matter (PM2.5) and total hydrocarbons (THC), were categorized into four quartile-

Table 1. Baseline demographics and exposure of air pollutants in Taiwan children, 2000-2012

N=244607		n	%
Gender	Boys	126734	51.8
	Girls	117873	48.2
Age, years	mean, SD	6.09	2.99
Urbanization level	1 (highest)	81894	33.5
	2	77950	31.9
	3	46364	19.0
	4 (lowest)	38399	15.7
Exposure of air pollutants			
$PM_{2.5}$ level (daily average, μ g/m3)	mean, SD	36.8	8.16
THC level (daily average, ppm)	mean, SD	2.42	0.23
Outcome			
Systemic lupus erythematosus	Yes	394	0.16
Follow-up time, years	mean, SD	11.2	2.32

The urbanization level was categorized by the population density of the residential area into 4 levels, with level 1 as the most urbanized and level 4 as the least urbanized.
PM, particulate matter; PM2.5, particles with aerodynamic diameter < 2.5 μm; THC, total hydrocarbons; SD, standard deviation

Table 2. Baseline urbanization level among quartiles of daily average concentration of air pollutants in Taiwan children, 2000-2012

Air pollutant Concentration	Quartile 1 (Q1) (lowest)	Quartile 2 (Q2)	Quartile 3 (Q3)	Quartile 4 (Q4) (highest)	*p-value
N=244607	n (%)	n (%)	n (%)	n (%)	
Particulate matter (PM2.5)					<0.001
Urbanization level					
1 (highest)	19547 (46.2)	24598 (41.7)	21523 (28.7)	16226 (23.8)	
2	7586 (17.9)	16989 (28.8)	27379 (36.5)	25996 (38.1)	
3	6889 (16.3)	9828 (28.8)	11993 (16.0)	17654 (25.9)	
4 (lowest)	8301 (19.6)	7644 (12.9)	14106 (18.8)	8348 (12.2)	
Total hydrocarbons (THC)					<0.001
Urbanization level					
1 (highest)	18880 (28.2)	11292 (22.7)	27324 (34.3)	24398 (50.6)	
2	16322 (24.4)	19580 (39.4)	27636 (34.6)	14412 (29.9)	
3	15493 (23.2)	7905 (15.9)	16466 (20.6)	6500 (13.5)	
4 (lowest)	16155 (24.2)	10971 (22.1)	8351 (10.5)	2922 (6.06)	

*Chi-square test
The urbanization level was categorized by the population density of the residential area into 4 levels, with level 1 as the most urbanized and level 4 as the least urbanized.
The daily average air pollutant concentrations were categorized into 4 groups based on quartiles for each air pollutant.

Table 3. The risk of systemic lupus erythematosus in children exposed to various air pollutants stratified by quartile of daily average concentration in Cox proportional hazard regression

	IR	cHR (95%CI)	aHR† (95%CI)
Particulate matter (PM2.5)			
1st Quartile	4.7	Reference group	Reference group
2nd Quartile	14.1	2.97 (1.88, 4.69)*	2.74 (1.74, 4.33)*
3rd Quartile	13.5	2.86 (1.82, 4.47)*	2.65 (1.69, 4.15)*
4th Quartile	21.9	4.61 (2.98, 7.13)*	4.23 (2.74, 6.55)*
Total hydrocarbons (THC)			
1st Quartile	9.5	Reference group	Reference group
2nd Quartile	8.6	0.91 (0.63, 1.30)	0.93 (0.65, 1.33)
3rd Quartile	16.2	1.75 (1.32, 2.31)*	1.82 (1.36, 2.42)*
4th Quartile	26.1	2.87 (2.16, 3.82)*	3.03 (2.25, 4.09)*

IR, incidence rate (per 100,000 person-years)
cHR, crude hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval
The daily average air pollutant concentrations were categorized into 4 groups based on quartiles for each air pollutant.
†Adjusted HR, adjusted for age, sex, monthly income, and urbanization level
*** p<0.001**

based groups (Q1-Q4). We measured the incidence rate, hazard ratios (HRs) and 95% confidence intervals for cSLE stratified by the quartiles of air pollutant concentration using Cox proportional hazards models, adjusted for age, sex, monthly income, and urbanization.

Results: A total of 394 children (0.16%) were diagnosed with SLE. The incidence rate for SLE increased with $PM_{2.5}$ and THC exposure concentration, from 4.7 (Q1) to 21.9 (Q4) and 9.5 (Q1) to 26.1 (Q4) per 100,000 person-years, respectively. Compared with those exposed to the concentrations in Q1 level, the adjusted HR for SLE increased with the $PM_{2.5}$ and THC exposure concentrations from 2.74 to 4.23 and 0.93 to 3.03, respectively.

Conclusion: The present study provides evidence that long-term ambient air pollutant exposures are risk factors of the development of cSLE.

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Abstract Number: 0671

Peripheral Nervous System Disease in Systemic Lupus Erythematosus: Results from an International, Inception Cohort Study

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SESSION INFORMATION

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Background/Purpose: Although there is a large body of work on central nervous system (CNS) disease in SLE patients, involvement of the peripheral nervous system (PNS) is less well established. The objective of our study was to determine the frequency, clinical characteristics, associations and outcomes in different types of PNS disease in a prospective, multi-ethnic/racial, inception cohort study of SLE patients.

Methods: Patients were evaluated annually for 19 neuropsychiatric (NP) events, including seven types of PNS disease using standardized case definitions. Attribution models were used to determine if the PNS events were due to SLE or other causes. SLE disease activity (SLEDAI-2K), organ damage (SLICC/ACR damage index), autoantibodies, patient (SF-36) and physician (Likert score) assessment of outcomes were measured. Statistical analyses included time to event and linear regressions as appropriate.

Results: Of 1,827 SLE patients enrolled, 88.8% were female and 48.8% Caucasian. The mean ± SD age was 35.1 ± 13.3 years, disease duration at enrollment was 5.6 ± 4.2 months and follow-up was 7.6 ± 4.6 years. There were 161 PNS events in 139/1,827 (7.6%) patients. The predominant events were peripheral neuropathy [66/161 (41.0%)], mononeuropathy [44/161 (27.3%)] and cranial neuropathy [39/161 (24.2%)] and the remaining 4 types of PNS disease accounted for only 12/161 (7.5%) events. The majority of PNS events [118/161 (73.3%)] in 104/139 (74.8%) patients were attributed to SLE. Multivariable Cox regression [HR, (95%CI)] indicated a negative association with Asian race/ethnicity [0.42 (0.19, 0.93)] and a positive association with other concurrent NP events attributed to SLE [2.74 (1.49, 5.03)]. By physician assessment, the majority of neuropathies resolved or improved over time. Multivariable analysis indicated that a longer time to resolution was associated with recurrent PNS events [0.38 (0.16, 0.90)], older age at SLE diagnosis [0.76 (0.60, 0.98)], higher SLEDAI-2K scores excluding NP variables [0.71 (0.51, 0.99)] and peripheral neuropathy [0.45 (0.25, 0.82)]. Patients with neuropathy reported significantly lower SF-36 physical and mental component summary scores compared to patients without NP events. Resolution was associated with improvements in SF-36 physical component summary scores that were both clinically and statistically ($p< 0.01$) significant in patients with peripheral neuropathy (mean change: +8.74) and mononeuropathy (mean change: +9.27).

Conclusion: PNS disease is a manifestation of NPSLE and has a significant negative impact on health related quality of life. The outcome is favourable for most patients, but several factors associated with longer time to resolution were identified.

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Abstract Number: 0672

Mouse SLE Studies Do Not Describe Human SLE

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SESSION INFORMATION
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Background/Purpose: Although mouse models of systemic lupus erythematosus (SLE) are useful proxies for human illness, they are heterogeneous, and publications about mouse SLE may not sufficiently emphasize differences between animals and humans with SLE. We examined recent literature to compare the criteria used to label mice as having SLE to phenotypes of human SLE.

Methods: Using "lupus AND animal NOT (review OR systematic review OR meta-analysis)" as the search terms, and filtering for full-text availability and English, we systematically reviewed studies published between July 3, 2013

Table 1: Mouse Models Used in 693 Animal Systemic Lupus Erythematosus Studies, Between July 3, 2013 - July 3, 2018

Mouse Models	N (%)
Spontaneous Models	440 (63)
- MRL/*lpr*	231 (33)
- NZB/WF1	134 (19)
- B6.*Sle123*	22 (3)
- NZM (2328/2410)	9 (1)
- MRL/*lpr* + NZB/W F1	8 (1)
- MRL/*lpr* + B6.Sle	4 (1)
- Others	32 (5)
Transgenic / Knockout	137 (20)
Induced Models	69 (10)
- Pristane	35* (5)
- ALD – DNA	7 (1)
- Nephrotoxic serum	4 (1)
- Others	23 (3)
Combinations of mouse models	44 (6)
- Transgenic / Knockout + Induced	21 (3)
- Spontaneous + Induced	12 (2)
- Spontaneous + Transgenic / Knockout	10 (1)
- Spontaneous + Induced + Transgenic / Knockout	1
N/A	3

ALD-DNA: activated lymphocyte-derived DNA; ***:** 1 with imiquimod

and July 3, 2018, excluding review articles, papers from journals with impact factor (IF) < 2, and non-mouse animal studies. We recorded main mouse model groups (spontaneous, induced, transgenic/knockout, or combinations), sub-groups (MRL/lpr, NZB/W F1, pristane), and gender for each study; how lupus was defined in the model (clinical manifestations, immunohistochemistry, and serology); and how and when authors defined clinical and serological disease onset (< 8 weeks, 8-16weeks, >16weeks). Additionally, asked whether the title of the article easily informed the reader whether the study was of animals or humans.

Results: Of 1572 articles identified, 693 were suitable for analysis. Table 1 presents mouse models used in 693 animal SLE studies. Four hundred forty (63%) used models of spontaneous heritable SLE (243 [35%] MRL/lpr and 147 [21%] NZB/W F1); 69 (10%) used induced models, of which 35 (5%) were pristane-induced; 138 (20%) used transgenic/knockout models; and 44 (6%) used combinations of models. Determinants of diagnosis, as shown in Table 2, were anti-DNA antibody and/or ANA autoantibody in 58% of studies, proteinuria in 41%, both serology and proteinuria in 32%, and immunohistochemistry in 72%. Of the latter, 500 (63%) included renal pathology. Other criteria included behavioral tests in 2%, skin manifestations in 2%, and arthritis in 1%. Only 64% of papers defined time of clinical and/or biological onset of illness (< 8 weeks, 4%; 8-16 weeks, 28%; >16 weeks 32%; not indicated, 36%), and only 30% defined time of serological onset (< 8 weeks, 3%; 8-16 weeks, 14%; >16 weeks, 14%; not indicated,

Table 2: Definition of Systemic Lupus Erythematosus in Mouse Studies, Between July 3, 2013 - July 3, 2018

Disease Manifestations	N (%)
Clinical/Serological	**693**
- Proteinuria*	62** (9)
- Proteinuria + serology	220*** (32)
- Anti-dsDNA and/or ANA	399$^{\text{Þ}}$ (58)
> Anti-dsDNA + ANA$^{\delta}$	72 (10)
> Anti-RNP / anti-Sm	31 (4)
> Anti-histone	24 (3)
- Body weight	18 (3)
- Behavioral tests	16 (2)
- Anti-chromatin	15 (2)
- Skin findings	16 (2)
- Blood pressure	10 (1)
- Experimental autoimmune encephalomyelitis	9 (1)
- aPL	7 (1)
- Arthritis	6 (1)
- Alopecia	1
- N/A	161 (23)
Immunohistochemistry	**500 (72)**
- Kidney$^{\phi}$ + other organs	434 (63)
White Blood Cell Studies	503 (73)

*: only; **: 54 with kidney biopsy; ***: anti-dsDNA: 175, ANA: 14, both: 31; Þ: ANA only: 43 (14 with proteinuria), anti-DNA only: 283 (175 with proteinuria); δ: 31 with proteinuria and other serologies, ϕ: kidney only: 348 (50%)

Table 3: Disease Onset Comparison by Systemic Lupus Erythematosus Models in Mouse Studies, Between July 3, 2013 - July 3, 2018

N: 646	Spontaneous (440)	Induced (69)	Transgenic/ Knockout (137)	p
Biological Onset				
<8 weeks	21 (%5)	3 (4%)	2 (1%)	0.23
8-16 weeks	122 (28%)	17 (25%)	42 (31%)	0.64
>16 weeks	160 (36%)	26 (38%)	19 (14%)	***0.000****
N/A	137 (31%)	23 (33%)	74 (54%)	***0.000***
Serological Onset				
<8 weeks	13 (3%)	3 (4%)	1 (1%)	0.24
8-16 weeks	62 (14%)	11 (16%)	15 (11%)	0.54
>16 weeks	68 (15%)	13 (19%)	7 (5%)	***0.003**$^{\delta}$*
N/A	297 (68%)	42 (61%)	114 (83%)	***0.000**$^{\phi}$*

*: spontaneous vs transgenic/knockout p: 0.000; induced vs transgenic/knockout p: 0.001
**: spontaneous vs transgenic/knockout p: 0.000; induced vs transgenic/knockout p: 0.009
δ: spontaneous vs transgenic/knockout p: 0.006; induced vs transgenic/knockout p: 0.02
ϕ: spontaneous vs transgenic/knockout p: 0.001; induced vs transgenic/knockout p: 0.003

70%). Table 3 compares disease onset, clinical, biological, and serological definitions of the mouse model groups, excluding studies that used combinations of these models. Seventy-one percent of papers' titles mentioned SLE; but in only 38% of those, and 44% of all papers, did the titles indicate that the study concerned animal rather than human SLE.

Conclusion: Publications about mouse SLE use the term SLE in ways that do not easily translate to human SLE. SLE is defined by histopathology in most mouse studies and by autoantibodies in slightly more than half. Many studies do not define sex, age of onset, or disease activity of diagnosed animals. While mouse models play an important role in understanding human lupus, the different criteria used to define mouse and human lupus may mislead readers seeking information about SLE who are unfamiliar with details of mouse models.

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Abstract Number: 0673

Clinical Characteristics of Lymphadenopathy in Systemic Lupus Erythematous: A Case Control Study from a Tertiary Care Center

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SESSION INFORMATION
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Background/Purpose: While lymphadenopathy and/or lymphadenitis (LAD) is considered a relatively common clinical finding in SLE patients, its clinical significance is poorly understood. Previous studies described the prevalence of lymphadenopathy, but not the prognostic significance and/or characteristic serologic associations. We report the prevalence, type of LAD, and the phenotypical profile of SLE patients who develop this manifestation over the course of their disease.

Methods: We conducted a retrospective case series analysis on 220 SLE patients enrolled at Beth Israel Deaconess Medical Center Lupus Cohort in 2008-2019 comparing patients with and without LAD. Patients were recruited from the Rheumatology clinic and eligible to participate if they met 1994 ACR SLE criteria and provided informed consent. Data on LAD was obtained from physical exam documentation and/or imaging reports. When available, pathology samples were reviewed from tissue obtained during routine clinical care. The study was IRB approved. Statistical analysis: Chi-square Test and Fisher's exact test were used for categorical variables using VassarStats.

Results: In our cohort, 13% (28/220) of patients developed LAD, a significantly lower proportion than previously reported (Dubois et al, JAMA 1964). LAD typically was a presenting and/or early manifestation occurring within the 12 months of diagnosis for most patients (82%) and typically predicted more active clinical course. The mean duration of time since SLE diagnosis for all patients was 15.2 years. Within the LAD group, 19 patients underwent lymph node biopsy as part of their workup. The predominant pathology patterns were necrotizing (26%), reactive (47%), and proliferative (16%) lymphadenitis. Of note, one biopsy revealed Non-Hodgkin lymphoma, one patient had sequential biopsies with initial reactive hyperplasia followed by diffuse large B cell lymphoma on a deeper pelvic node, and one biopsy was non diagnostic. We then asked whether the disease phenotype was different between the LAD group and the non-LAD group. Patients with LAD were more likely than non-LAD patients to have fever (OR 5.4, p=< 0.0001) nephritis (OR 1.7, p=0.1897), splenomegaly (OR 22.9, p=0.0076), and leukopenia (OR 2.0, p=0.0969). LAD patients also had more serologically active disease than non-LAD patients; specifically LAD patients were more likely to have positive Smith (OR 4.18, p=0.005), RNP (OR 4.05, p=0.0087), and SSB (OR 2.41, p=0.0424) as well as hypocomplementemia (C3 OR 4.80, p=0.0051; C4 OR 4.03, p=0.0039).

Conclusion: In our cohort, lymphadenopathy was an uncommon SLE manifestation. Interestingly, necrotizing LAD, which is often associated with infection, was relatively prevalent in our cohort. Our data suggest that patients with lymphadenopathy are more likely to have constitutional symptoms, cytopenias, and splenomegaly as well as increased auto-antibodies and hypocomplementemia. These symptoms can be seen with lymphomas and two patients were ultimately found to have lymphoma (DLBCL and NHL). These patients developed LAD either within 12 months or after more than 10 years of SLE diagnosis. This suggests that biopsy is warranted in SLE patients with LAD at any point in their disease course.

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Abstract Number: 0674

Affordability Concerns Prevalent Among Patients with Systemic Lupus Erythematosus (SLE)

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Table DeQuattro Affordability concerns prevalent among patients with systemic lupus erythematosus 5.23.19

Mean (adjusted[1]) patient-reported outcomes of activity, damage, depression and physical function, by affordability concerns, 259 CLUES respondents.

	SLAQ (Activity)	BILD (Damage)	PHQ (Depression)	PROMISPF (Physical Function)
No Affordability Concerns	5.7 (4.0-7.4)	1.5 (1.0-2.0)	3.5 (2.2-4.8)	50.8 (48.6-53.0)
Affordability Concerns	9.5 (8.6-10.4)*	2.1 (1.8-2.4)*	6.4 (5.7-7.1)*	46.6 (45.4-47.8)*

SLAQ -Systemic Lupus Activity Questionnaire; BILD - Brief Index of Lupus Damage; PHQ - Patient Health Questionnaire depression scale; PROMIS PF – Patient-Reported Outcomes Measurement Information System Physical Function. Greater SLAQ, BILD and PHQ denote worse outcomes. Lesser PROMISPF scores denote worse outcomes.

Cells are means (95% confidence intervals)

[1]Adjusted for age, sex, race/ethnicity, disease onset, education level, job status, insurance status

*p<0.05

SESSION INFORMATION
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Background/Purpose: Among rheumatologic conditions, SLE is associated with very high healthcare and out of pocket costs. Little is known about patients' concerns regarding costs of care. We analyzed patterns of patient perceptions of affordability of care and medication costs and explored associations with disease measures in SLE.

Methods: Data derive from the California Lupus Epidemiology Study (CLUES), a diverse population-based cohort of individuals with SLE. As part of an extensive interview, 259 participants answered 2 questions about affordability of care (at diagnosis [recalled] and at present) and 6 questions about medication costs (Is paying for your lupus medicines financially difficult?; Have you ever: taken less medicine; delayed filling a prescription; asked about lower cost medicine; bought medicine out of the country; applied for patient assistance program?). These 8 items were combined to describe "affordability concerns." We compared prevalence of affordability concerns by race/ethnicity and socioeconomic status and examined associations with patient reported measures in linear regression models [with and without adjustment for age, gender, age of diagnosis, race/ethnicity, income below poverty, education (no bachelor's degree vs bachelor's), insurance (private vs public) and employment].

Results: Concern about affordability of care at diagnosis (56%) and at present (53%) were greater than concerns about medication costs (25%). Most patients with SLE (77% of 259 respondents) reported at least one affordability concern. There were no differences in affordability concerns by race/ethnicity, either at diagnosis or at present. Affordability concerns were most prevalent among those with public insurance (83% vs 70%, p< 0.01), an education

below a college degree (88% vs 66%, p< 0.01) and income below the poverty level (98% vs 70%, p< 0.01). Individuals with affordability concerns had worse patient-reported scores of disease activity, damage, depression and physical function than non-concerned peers, even controlling for sociodemographic factors (Table).

Conclusion: Most people with SLE are concerned about cost of treatment among individuals with SLE both at diagnosis and over time. Concern about affordability is associated with poorer patient-reported outcomes. Our findings support strategies to proactively assess affordability concerns and develop resources that focus on mitigating cost of care for this population.

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Clinical and Serological Lupus Activity Before and After Developing End Stage Renal Disease

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Background/Purpose: SLE disease activity tends to diminish after the development of end stage renal disease (ESRD)[1, 2]. Nonetheless, some patients continue to show signs of active disease and experience flares after ESRD[3]. To date, little is known about the evolution of SLE-related symptoms pre and post ESRD. Whether specific symptoms abate after ESRD or a shift towards different manifestations occurs deserves further study. Prompt identification of subtler SLE manifestations is further complicated by a trend towards poor rheumatology follow once ESRD develops. SLE manifestations post-ESRD may be underdiagnosed and undertreated contributing to increased morbidity and mortality. Therefore, the objective of this study was to analyzed the different clinical manifestations and serological markers of SLE disease activity before and after ESRD development.

Methods: We performed a retrospective chart review of SLE patients with ESRD at a tertiary care center between the years of 2010 and 2017. SLE was defined by ACR and/or SLICC criteria. SLE ESRD patients were included if they had at least one visit with rheumatology, nephrology, or primary care pre- and post-ESRD. SLE-related symptoms and serologic markers of disease activity were identified from chart review before and after ESRD onset.

Results: Fifty-eight patients were included. Twenty-five patients had a least one clinical non-renal criteria documented pre-ESRD. Of them, 14 achieved complete clinical remission post-ESRD. Post-ESRD, cytopenias persisted in 49 of the 55 patients who were cytopenic pre-ESRD. Arthritis persisted in 3 of the 13 patients who had arthritis pre-ESRD. Of the 37 patients with hypocomplementemia pre-ESRD, 29 remained hypocomplementemic post-ESRD. Twenty-nine had elevated dsDNA pre-ESRD, of them, dsDNA remained elevated in 16 patients post-ESRD. Six

patients developed at least one new clinical criteria post-ESRD. Three patients developed low complement and 5 developed elevated dsDNA post-ESRD.

Conclusion: Lupus activity may diminish after ESRD onset. However, many patients experience persistent disease activity. New arthritis, low complements and elevated dsDNA may develop after ESRD. Limited evaluation and documentation of disease activity by non-rheumatology providers may have resulted in under-reporting of SLE signs and symptoms on this study. SLE ESRD patients should be carefully evaluated for subtle signs of active SLE.

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Abstract Number: 0676

Cluster Profiling of Patients in a Real-World Data Set with Systemic Lupus Erythematosus and Their Associated Treatments

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Background/Purpose: Previous systemic lupus erythematosus (SLE) studies have identified potential clusters of SLE clinical manifestations.

To describe the presentation of SLE across different cohorts of patients and describe standard of care within clusters.

Methods: Cross-sectional study of 263 rheumatologists in the US and EU5. Data were collected from the Adelphi Real World 2015 Lupus Disease Specific Programme. Physicians completed patient record forms (PRFs) for the next 5 patients consulting with SLE; these patients completed patient self-completion (PSC) forms describing how SLE affected them. PRFs data include patient's characteristics and management history. PSCs focused on similar data collection, including patient reported outcome measures on the humanistic burden. Principal-component factor analysis reduced 39 unique SLE symptoms to 8 factors. These factors were used as covariates in latent class cluster analysis to provide discrete cohorts of patients. Chi-squared and Kruskal-Wallis tests compared patient outcomes across clusters.

Table 1 Cluster analysis

		Clusters				
Factors, n (%)	Overall (n=1376)	1 (n=325)	2 (n=743)	3 (n=143)	4 (n=165)	p-value
Joint	956 (69.5)	0	729 (98.1)	62 (43.4)	165 (100.0)	<0.0001
Haematological	289 (21.0)	17 (5.2)	112 (15.1)	48 (33.6)	112 (67.9)	<0.0001
Constitutional/Mental	413 (30.0)	11 (3.4)	251 (33.8)	14 (9.8)	137 (83.0)	<0.0001
Skin	688 (50.0)	69 (21.2)	389 (52.4)	81 (56.6)	149 (90.3)	<0.0001
Circulatory	71 (5.2)	0	0	39 (27.3)	32 (19.4)	<0.0001
Cardiovascular	130 (9.4)	0	0	68 (47.6)	62 (37.6)	<0.0001
Renal	297 (21.6)	18 (5.5)	146 (19.7)	48 (33.6)	85 (51.5)	<0.0001
Muscular	268 (19.5)	6 (1.8)	109 (14.7)	38 (26.6)	115 (69.7)	<0.0001

Results: Data were extracted from 1376 PRFs. Factor analysis resulted in 8 clusters of concurrent symptoms; joint, haematological, constitutional/mental health, skin, circulatory, cardiovascular, renal, and muscular symptoms respectively. The four-cluster solution was selected. Cluster 1 displayed the lowest symptom burden, characterised by low skin involvement. Cluster 2 is characterised by joint and skin involvement. Cluster 3 & 4 had a high frequency of all factors, with cardiovascular involvement high in cluster 3 and renal/constitutional involvement high in cluster 4 (table 1). Significant between-cluster differences were observed when comparing clinical and humanistic outcomes; physician/patient satisfaction were greatest in cluster 1 (physician satisfied 94.2% vs. 2: 90.8%, 3: 85.2%, 4: 74.4%, $p< 0.0001$; patient 94.7% vs. 2: 93.9%, 3: 91.5%, 4: 79.2%, $p< 0.0001$), whilst disease progression (deteriorating slowly 2.5% vs. 2: 12.9%, 3: 9.8%, 4: 25.5%, $p< 0.0001$) and flaring in the last 12 months (flared 30.0% vs. 2: 54.8%, 3: 62.2%, 4: 70.8%, $p< 0.0001$) differed significantly with worst outcomes seen in cluster 4. Significant differences were also observed between clusters in relation to treatment proportions; anti-malarials (highest cluster 1: 70.5%), biologic DMARD (highest cluster 3: 17.5%), glucocorticoid and immunosuppressants (highest cluster 4: 85.5%, 74.5%).

Conclusion: This study adds to the evidence demonstrating the heterogenous nature of SLE experienced within distinct patient clusters. Significant proportions of SLE patients experience high symptom burden and low levels of satisfaction. Additional analysis to understand limited biologic use in more severe patients is needed.

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Abstract Number: 0677

Performance of Montreal Cognitive Assessment (MoCA) in Screening for Cognitive Impairment in Patients with Lupus Compared to the Neuropsychological Battery

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Cognitive impairment (CI) is a common neuropsychological manifestation of Systemic Lupus Erythematosus (SLE) with a prevalence of 38% [95% confidence interval: 33,43%]. Previous studies, have reported promising results on the utility of the Montreal Cognitive Assessment (MoCA) as a screening tool for CI in SLE compared to a comprehensive neuropsychological battery (CNB). The aim of this study was to assess the utility of

Table 1. Characteristics of patients (n=276)

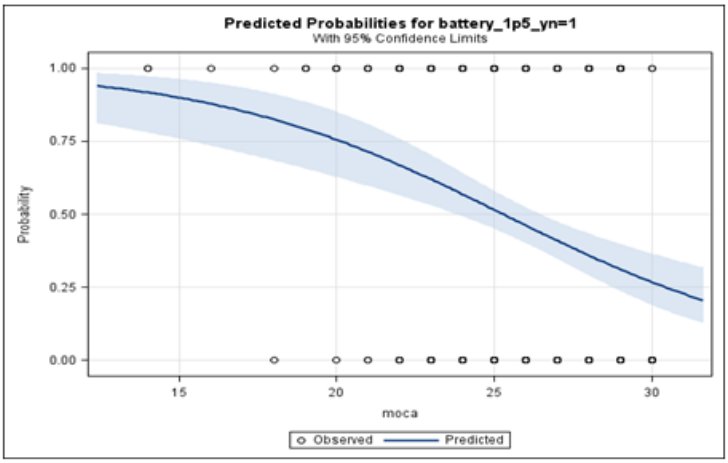
Age	
18-29	58 (21.0%)
30-39	76 (27.5%)
40-49	64 (23.2%)
50-59	54 (19.6%)
60-65	24 (8.7%)
Race	
Caucasian	153 (57.7%)
Black	54 (20.4%)
Chinese	25 (9.4%)
Other	33 (12.5%)
Level of Education	
University	112 (41.8%)
College	98 (36.6%)
High School	48 (17.9%)
Grade 8	10 (3.7%)

the MoCA as a screening test for the detection of CI using a comprehensive NB as the gold standard for classification of cases.

Methods: From 2016 to 2019, 276 consecutive consenting adult SLE patients (excluding those with learning disabilities, and less than semi-fluent English language skills were administered the MoCA followed by a CNB. The MoCA, ranging from 0-30, was designed to screen for Mild Cognitive Impairment (MCI) in dementia a score of ≥26 considered above the threshold for MCI. In this study, patients were classified as having CI if they had a z-score of ≤-1.5 in ≥2 domains of the 6 domains of CNB, and otherwise non-CI. Descriptive statistics and two-by-two contingency tables with a MoCA cut-off score of 26 were applied to determine its sensitivity (Se) and specificity (Sp) to CI. The Se, Sp, positive predictive value (PPV) and negative predictive value (NPV) were evaluated. Additionally, a **discriminant function analysis** was applied to assess the ability of the MoCA to differentiate between CI, undetermined CI (one domain with a z-score of ≤-1.5) and non-CI patients.

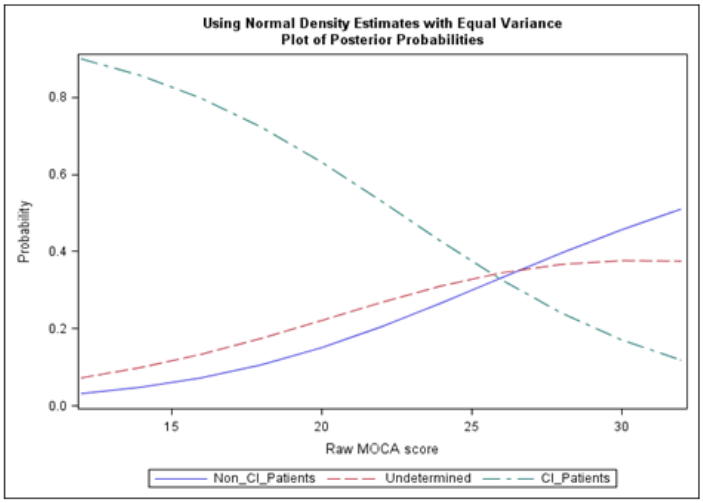
Results: 276 SLE patients were enrolled; 89.5% were females and the mean age was 41.2 ± 12.2 years at enrolment, and mean SLE duration of 14.1 ± 10.1 years (demographics in **Table 1**). Based on the CNB, 129 patients (47%) had CI, 85 (31%) had undetermined CI, and 62 (22%) were non-CI patients.

Figure 1. The Predicted probability of having CI by MoCA scores (n=276)



Even with the highest MoCA score, 30, there was 25% predicted probability of being CI.

Figure 2. The probability of belonging to three CI groups at each MoCA scores (n=276)



The three groups (CI, undetermined-CI and non-CI) overlap around the MoCA scores 25 to 27, indicating poor discriminative ability of MoCA.

CI was not accurately predicted by MoCA with an area under curve (AUC) of 65% [95% Confidence interval: 0.59, 0.72]. The *cut-off* **of 26** yielded Se, Sp, PPV and NPV of 50%, 70%, 59% and 61%, respectively.

There was a 25% predicted probability of CI with the highest score (30) on the MoCA **(Figure 1).** Although the MoCA cut-off score of 27 reached a sensitivity of 80%, the specificity was very low at 45%.

Based on the discriminant function analysis, the misclassification rates in the 3 categories (CI, undetermined-CI and non-CI) were 50%, 83%, and 44%, respectively. All three categories overlapped between the scores 25 to 27 (**Figure 2**). Thus, the MoCA had low ability to accurately identify CI status.

Conclusion: This analysis does not provide sufficient evidence to recommend MoCA as a screen for CI in SLE compared to a CNB. There was a low predicted probability of having CI with a low MoCA score and a relatively high predicted probability of having CI with a high MoCA score.

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Abstract Number: 0678

Performance of the EULAR/ACR 2019 Classification Criteria for Systemic Lupus Erythematosus in Men, Diverse Ethnicities, and Early Disease

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Winfried Graninger,[30] Bernadette Halda-Kiss,[31] Sarfaraz Hasni,[32] Peter Izmirly,[33] Michelle Jung,[26] Gabor Kumanovics,[31] Xavier Mariette,[34] Ivan Padjen,[23] Jose Maria Pego-Reigosa,[35] Juanita Romero-Diaz,[36] Iñigo Rua Figueroa,[37] Raphaèle Seror,[24] Georg Stummvoll,[10] Yoshiya Tanaka,[38] Maria Tektonidou,[39] Carlos Vasconcelos,[40] Edward Vital,[41] Daniel Wallace,[42] Sule Yavuz,[43] Raymond Naden,[44] Thomas Dörner,[45] and Sindhu R. Johnson[46], [1]Division of Rheumatology, Department of Medicine III, University Medical Center & Faculty of Medicine Carl Gustav Carus, TU Dresden, Dresden, Germany, [2]Department of Rheumatology and Hiller Research Unit of Rheumatology, UKD, Heinrich-Heine University, Düsseldorf, Germany, [3]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [4]University of California at San Francisco and VA Medical Center, San Francisco, CA, [5]University of Athens, Athens, Greece, [6]Vasculitis and Lupus Clinic, Addenbrooke's Hospital, University of Cambridge, Cambridge, United Kingdom, [7]Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC, [8]Rheumatology Unit, Department of clinical and experimental medicine, University of Pisa, Pisa, Italy, [9]Northwestern University, Chicago, IL, [10]Medical University of Vienna, Vienna, Austria, [11]UCSF, San Francisco, [12]Feinstein Institutes for Medical Research, Manhasset, [13]Copenhagen Lupus and Vasculitis Clinic, Copenhagen, Denmark, [14]University of Michigan, Ann Arbor, MI, [15]Autoimmune Diseases Unit, Hospital Universitario Cruces, Barakaldo, Spain, [16]Policlinic for Rheumatology & Hiller Research Centre for Rheumatology, Heinrich-Heine-University Duesseldorf, Düsseldorf, Germany, [17]University Health Network, University of Toronto, Toronto, ON, Canada, [18]University of Crete, Rheumatology, Clinical Immunology and Allergy Unit, Heraklion, Greece, [19]University of Schleswig-Holstein at Kiel, and Charité – Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Kiel, Germany, [20]University Medical Center and Faculty of Medicine TU Dresden, Dresden, Germany, [21]Azienda Ospedaliero Universitaria Pisana, University of Pisa, Pisa, Italy, [22]Brigham and Women's Hospital, Div. of Rheumatology, Immunology and Allergy, Boston, MA, [23]UHC Zagreb and University of Zagreb School of Medicine, Zagreb, Croatia, [24]Université Paris Sud, Hôpitaux Universitaires Paris-Sud, AP-HP, INSERM UMR 1184, Le Kremlin-Bicêtre, France, [25]University of Hong Kong, Hong Kong, Hong Kong, [26]University of Calgary, Calgary, AB, Canada, [27]Hospital for Special Surgery, New York, NY, [28]Dept. of Rheumatology and Immunology, University of Pécs, Pécs, Hungary, [29]University and Azienda Ospedaliera of Padova, Padova, Italy, [30]Medical University of Graz, Graz, Austria, [31]University of Pécs, Pécs, Hungary, [32]NIAMS, National Institutes of Health, Bethesda, MD, [33]NYU School of Medicine, New York, [34]Center for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique – Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, Le Kremlin-Bicêtre, Université Paris Sud, INSERM, Paris, France, [35]Complexo Hospitalario Universitario, Vigo, Spain, [36]Instituto Nacional de Ciencias Medicas y Nutricion Salvador, Zubiran Vasco de Quiroga, Mexico City, Mexico, [37]Hospital Doctor Negrin, Las Palmas, [38]University of Occupational and Environmental Health Japan, Kitakyushu, Japan, [39]First Department of Internal Medicine, National and Kapodistrian University of Athens, Athens, Greece, [40]University of Porto, UMIB Abel Salazar Biomedical Sciences Institute, Porto, Portugal, [41]University of Leeds, Leeds, United Kingdom, [42]Cedars-Sinai Medical Center/University California at Los Angeles, Los Angeles, CA, [43]Uppsala University, Istanbul, Turkey, [44]McMaster University, Hamilton, ON, Canada, [45]Charite Universitätsmedizin Berlin and DRFZ, Berlin, Germany, [46]Toronto Scleroderma Program, Department of Medicine, Toronto Western and Mount Sinai Hospitals, University of Toronto, Toronto, Canada

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The EULAR/ACR 2019 Classification Criteria for SLE have been validated in an international cohort of 696 SLE patients and 574 non-SLE patients with a sensitivity of 96.1% and a specificity of 93.4%. We comparatively evaluated the performance characteristics of the SLE classification systems in subsets of the validation cohort with regard to gender, race/ethnicity, and disease duration.

Methods: 21 SLE expert centers from 16 countries submitted up to 100 SLE cases and 100 SLE mimicking controls each, using a standardized form without knowledge of the new criteria system to form the validation cohort. Cases and control diagnosis (SLE or not SLE) were independently verified by 3 SLE experts. The EULAR/ACR 2019 classification criteria validation cohort consisted of female (n=1,098) and male (n=172) patients; Asian (n=118), Black (n=68), Hispanic (n=124) and White (n=941) patients; and patients with an SLE duration of less than 1 year (n=34), 1-3 years (n=196), 3-5 years (n=157), and 5 or more years (n=879). Sensitivity and specificity with 95% confidence intervals (CI) were estimated for the EULAR-ACR 2019 criteria, the SLICC 2012 criteria and the ACR 1997 criteria.

	n	EULAR/ACR 2019 Criteria		ACR 1997 Criteria		SLICC 2012 Criteria	
		Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Full cohort	**1,270**	**0.96**	**0.93**	**0.83**	**0.93**	**0.97**	**0.84**
95% CI		0.95-0.98	0.91-0.95	0.80-0.85	0.91-0.95	0.95-0.98	0.80-0.87
Gender							
Women	1,098	0.97	0.94	0.83	0.93	0.97	0.82
Men	172	0.93	0.96	0.78	0.94	0.94	0.90
Race/ Ethnicity							
Asian	118	0.97	0.91	0.77	0.93	0.99	0.91
Black	68	0.98	1.00	0.82	1.00	0.98	0.92
Hispanic	124	1.00	0.96	0.86	0.96	1.00	0.78
White	941	0.95	0.94	0.83	0.93	0.96	0.83
Disease duration							
< 1 year	34	0.89	0.92	0.56	0.92	0.89	0.92
1 to <3 yrs	196	0.97	0.96	0.81	0.95	0.98	0.88
3 to <5 yrs	157	0.96	0.99	0.81	0.94	0.91	0.89
≥5 years	879	0.96	0.93	0.84	0.93	0.97	0.81

Table 1

Results: As shown in Table 1, most of the point estimates for sensitivity and specificity in subsets lay within the 95% confidence intervals of the sensitivity and specificity of the EULAR/ACR 2019 criteria validation. In particular, sensitivity and specificity for all race/ethnicity groups were within the confidence intervals or even higher. Formally, the sensitivity was slightly lower for male patients, corresponding to a higher specificity, but the male 95% confidence intervals (0.86-0.98 for sensitivity, 0.90-0.99 for specificity) overlapped with those of the full cohort. Sensitivity appeared independent of disease duration at least from year 1 on, with all 95% confidence intervals overlapping (for the first year after diagnosis 0.52-1.00 for sensitivity, 0.69-0.97 for specificity).

Conclusion: The point estimates of sensitivity and specificity suggest that the EULAR/ACR 2019 SLE classification criteria perform well in diverse race/ethnicity groups, in men and in early disease. These results now need to be independently validated in larger groups of African American/Black, Asian, and Hispanic patients, male patients and in early disease.

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Abstract Number: 0679

Longitudinal Changes in Manifestations of SLE

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Our group has developed a conceptual model to categorize SLE manifestations into two dimensions termed Type 1 and Type 2. Type 1 SLE consists of active inflammatory manifestations like arthritis, nephritis, and rashes, and Type 2 SLE includes symptoms of fatigue, myalgia, mood disturbance, and cognitive dysfunction. SLE is characterized by waxing and waning of Type 1 inflammatory features considered to be disease activity. To advance lupus symptom characterization, we assessed whether Type 2 symptoms fluctuate over time.

Methods: SLE patients meeting SLICC criteria with ≥2 visits at a university rheumatology clinic between January 2018 and May 2019 were included. At each visit, SLEDAI was measured and patients completed the ACR FM Diagnostic Criteria. The FM severity score (FSS) is the sum of the widespread pain (0-19) and symptom severity scores (0-12). Patients were classified as having Type 1 SLE manifestations (SLEDAI ≥6, clinical SLEDAI ≥4, or active nephritis), Type 2 SLE symptoms (FSS >10), Mixed (both Type 1 and Type 2), or Minimal (neither Type 1 or Type 2). A clinically significant change in SLEDAI and FSS was defined as a +/- 2-point change between two visits for either of these measures. Changes in Type 1 and Type 2 severity between the two visits were estimated using simple statistics.

Results: 84 patients were included in the analysis (mean age 42 years, mean duration of SLE 14 years, 95% female, 65% African American, 56% with history of lupus nephritis). The average time between visits was 19 weeks (range: 4-34). At the first visit, 17% of patients were classified as Type 1, 12% as Type 2, 25% as Mixed, and 46% as Minimal.

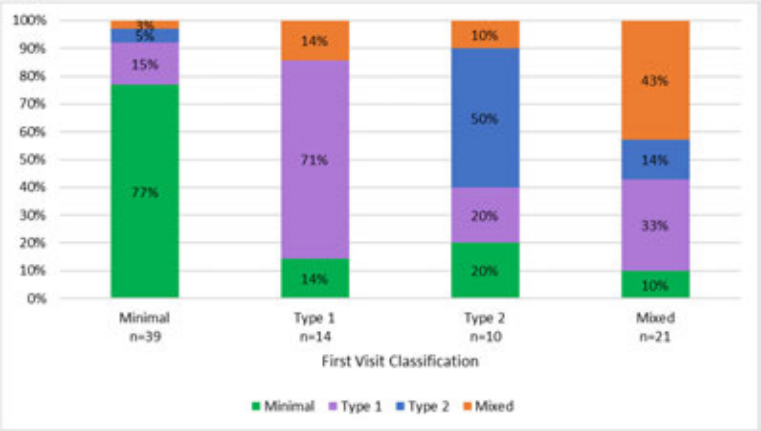

Figure 1. Change in Type 1 and Type 2 SLE Classification Between Visits. The bars represent the distribution of patient symptoms at Visit 2 for each Visit 1 classification group.

Figure 2. Change in Fibromyalgia Severity Score and SLEDAI between visits.

In patients with Minimal or Type 1 SLE at Visit 1, 8-14% experienced active Type 2 symptoms at Visit 2 (Figure 1). In comparison, for patients with Type 2 or Mixed SLE at Visit 1, approximately 40% were no longer classified as having active Type 2 symptoms at Visit 2.

Overall, 44% of patients had an improved FSS at Visit 2 and 30% had improvement in SLEDAI (Figure 2). Type 2 symptoms fluctuated in all patient groups between visits. Type 2 SLE symptoms worsened in 21% of Minimal and 36% of Type 1 SLE patients. Interestingly, patients with Mixed activity appeared to have a greater improvement in FSS (81%) compared to patients with only Type 2 SLE activity (50%). When specific Type 2 symptoms were explored, 78% of patients who reported moderate or severe fatigue at Visit 1 continued to have moderate or severe fatigue at Visit 2, whereas only 16% of patients without fatigue at Visit 1 experienced fatigue at Visit 2. Fatigue was more prevalent and persistent in patients classified as Type 2 and Mixed at Visit 1. Improvements were seen in cognitive dysfunction, muscle weakness, and muscle pain, with approximately 40% of patients reporting improvement in symptoms at Visit 2.

Conclusion: Our findings suggest that, similar to Type 1 features, Type 2 symptoms vary over time, with almost half of the patients in the analysis having an improvement in FSS between visits. Future studies are needed to determine Type 2 fluctuations over a longer follow-up period, as well as to identify treatment approaches to improve Type 2 symptoms.

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Abstract Number: 0680

Patients Who Do Not Fulfill the 2018 EULAR/ACR Criteria for Systemic Lupus Erythematosus Accrue Less Damage: Data from a Multicenter, Multiethnic US Cohort

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SESSION INFORMATION
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Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
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Session Time: 9:00AM–11:00AM

Background/Purpose: The 2018 EULAR/ACR Criteria for the classification of patients with systemic lupus erythematosus (SLE) were proposed in order to improve the sensitivity and specificity of the previously published SLE criteria. In addition to its sensitivity and specificity, it is important to know if those patients who would not be classified as having SLE according to these criteria have a different prognosis than those who continue to be classified as SLE. The aim of this study was to determine the difference in damage accrual in patients who achieved or not these new criteria.

Methods: Patients from a well-defined multicenter, multiethnic US lupus cohort were included. For this cohort, SLE was defined using the 1982/1997 ACR criteria. For these analyses, we compared those patients who achieved the 2018 EULAR/ACR criteria any time during the follow-up to those who did not. The predefined outcome was the last SLICC/ACR damage index (SDI). Possible confounders included were age, gender, race/ethnicity, poverty, disease duration at baseline, baseline SLAM, baseline SDI, antimalarial, glucocorticoids and immunosuppressive drugs use

Table 1 Impact of achieving or not the 2018 EULAR/ACR criteria on the damage accrual

Parameter	Estimate	Standard Error	p value
Intercept	-1.6924	0.2224	<0.0001
Not achieving the 2018 EULAR/ACR criteria	-0.3773	0.1416	0.0077
Age at baseline	0.0174	0.0037	<0.0001
Ethnicity			
Hispanic (Texas)	0.9339	0.1740	<0.0001
African-American	0.9513	0.1592	<0.0001
Caucasian	0.5969	0.1661	0.0003
Puerto Rican	Referent		
SLAM at baseline	0.0562	0.0084	<0.0001
Poverty	0.1785	0.0946	0.0593
Disease duration at baseline	0.1439	0.0327	<.0001
Immunosuppressive drugs at baseline	0.3626	0.1125	0.0013

at baseline. Univariable and multivariable negative binomial regression models were performed; adjustment model was based on a forward selection process. An alternative analyses was performed in order to evaluated the impact of being classified earlier, at the same time or later with the 2018 EULAR/ACR criteria.

Results: Ninety-eight out of 640 patients never achieved the 2018 EULAR/ACR criteria. The 98 patients were older and less likely to be Hispanic or African American than those who did achieve the criteria. There was no difference in mean baseline SDI among the patients who did not achieve the criteria (0.6±1.2) compared to those who achieved the criteria (0.8 ± 1.2, p=0.3580). Conversely, the mean SDI at last visit was lower for those who never achieved the criteria (1.2±1.7 vs. 2.0±2.3, p=0.0004). In the final adjusted model (Table 1), the SDI score at last visit was 31% lower for those not achieving the criteria (p=0.0077). There were not differences on damage accrual if the patients were classified earlier, at the same time or later with the 2018 EULAR/ACR criteria (data not shown).

Conclusion: In our cohort, those who did not achieve the 2018 EULAR/ACR criteria accrued less damage, suggesting that these criteria could allow us to identify a subset of patients with more severe disease than previous criteria.

Disclosure: M. Ugarte-Gil, None; **G. Pons-Estel**, None; **L. Vilá**, None; **R. Griffin**, None; **G. Alarcón**, None.

Abstract Number: 0681

Evaluation of the Lupus Foundation of America - Rapid Evaluation of Activity in Lupus (LFA-REAL) Clinician Reported Outcome (ClinRO) and Patient Reported Outcome (PRO) in a Primarily Mestizo Population

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Table 1: Correlations between different disease activity measures

	Range	Mean (SD)	LFA-REAL ClinRO R (p value)	LFA-REAL PRO R (p value)	PGA R (p value)	SLEDAI-2K R (p value)	Clinical SLEDAI-2K R (p value)
LFA-REAL ClinRO	0-1400	23.8 (34.3)	X	0.192 (0.012)	0.693 (<0.001)	0.688 (<0.001)	0.705 (<0.001)
LFA-REAL PRO	0-1200	239.6 (187.7)	0.192 (0.012)	X	0.301 (<0.001)	0.161 (0.037)	0.167 (0.030)
PGA	0-100	10.0 (14.2)	0.693 (<0.001)	0.301 (<0.001)	X	0.488 (<0.001)	0.546 (<0.001)
SLEDAI-2K	0-51	2.4 (3.4)	0.688 (<0.001)	0.161 (0.037)	0.488 (<0.001)	X	0.952 (<0.001)
Clinical SLEDAI-2K	0-47	1.7 (3.0)	0.705 (<0.001)	0.167 (0.030)	0.546 (<0.001)	0.952 (<0.001)	X

SD: Standard deviation

SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: There are several instruments to measure disease activity in patients with systemic lupus erythematosus (SLE); however, none of them are able to capture all possible clinical events/manifestations. The LFA-REAL ClinRO has been proposed in order to address this problem as it allows the clinician to evaluate every possible manifestation of SLE. Additionally, the LFA-REAL PRO includes a comprehensive patient-reported disease activity measure. The aim of this study was to determine the correlation between both, the LFA-REAL ClinRO and the LFA-REAL PRO, with other disease activity measures.

Methods: A cross-sectional analyses of patients from a single-center cohort was performed. Disease activity measures included were LFA-REAL ClinRO (0-1400), LFA-REAL PRO (0-1200), SLEDAI-2K, clinical SLEDAI-2K and Physician Global Assessment (PGA, 0-100). The correlation between these indices were evaluated with the Pearson correlation. As an alternative analysis, the correlation between the corresponding domains of LFA-REAL PRO and LFA-REAL ClinRO were examined.

Results: One-hundred and sixty-nine patients with SLE, with a mean age of 45.8 (SD: 14.2), 156 (92.3%) were female. The mean (SD) LFA-REAL ClinRO was 23.8 (34.3), the LFA-REAL PRO was 239.6 (187.7), the PGA was 10.0 (14.2), the SLEDAI-2K was 2.4 (3.4) and the clinical SLEDAI-2K was 1.7 (3.0), the SDI was 1.7 (1.5). LFA-REAL ClinRO correlated with LFA-REAL PRO (R=0.192; p=0.012), PGA (R=0.693, p< 0.001), SLEDAI-2K (R=0.688, p< 0.001) and clinical SLEDAI-2K (R=0.705, p< 0.001); the LFA-REAL PRO correlated with PGA (R=0.301, p< 0.001), SLEDAI-2K (R=0.161, p=0.037) and clinical SLEDAI-2K (R=0.167, p=0.030). The correlations between these disease activity measures are depicted in table 1. Additionally, the LFA-REAL PRO rash correlated with the LFA-REAL ClinRO global mucocutaneous involvement (R=0.154, p=0.046) and with the LFA-REAL ClinRO rash (R=0.245, p=0.001); the LFA-REAL PRO global articular correlated with the LFA-REAL ClinRO global musculoskeletal involvement (R=0.346, p< 0.001).

Conclusion: The LFA-REAL ClinRO and the LFA-REAL PRO had a good correlation with other physician-based disease activity measures. These measures need to be evaluated in other cohorts in order to determine their real value for the monitoring of SLE patients.

Disclosure: M. Ugarte-Gil, None; **R. Gamboa-Cárdenas**, None; **C. Reátegui-Sokolova**, None; **V. Pimentel-Quiroz**, None; **P. Zeña-Huancas**, None; **M. Medina**, None; **C. Elera-Fitzcarrald**, None; **S. García**, None; **L. Gil**, None; **E. Noriega**, None; **C. Pastor-Asurza**, None; **Z. Rodríguez-Bellido**, None; **J. Merrill**, Xencor, 2; **A. Askanase**, Xencor, 2; **G. Alarcón**, None; **R. Perich-Campos**, None.

Abstract Number: 0682

Correlation Between the Lupus Foundation of America - Rapid Evaluation of Activity in Lupus (LFA-REAL) Patient Reported Outcome (PRO) and Health-Related Quality of Life (HRQoL) and Other PROs in a Primarily Mestizo Population

Manuel Ugarte-Gil,[1] Rocío-V. Gamboa-Cárdenas,[2] Victor Pimentel-Quiroz,[3] Cristina Reátegui-Sokolova,[4] Paola Zeña-Huancas,[2] Mariela Medina,[2] Claudia Elera-Fitzcarrald,[1] Luciana Gil,[2] Samira García,[4] Francisco Zevallos,[4] Cesar Pastor-Asurza,[4] Zoila Rodríguez-Bellido,[2] Anca Askanase,[5] Joan Merrill,[6] Graciela Alarcón,[7] and Risto Perich-Campos[2],
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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Table 1: Correlation between LFA-REAL PRO and HRQoL, Fatigue and Work Productivity Impairment*

	Mean (SD)	LFA-REAL PRO	
		R	p-value
LupusQoL			
Physical health	69.4 (22.7)	-0.578	<0.001
Pain	71.1 (24.0)	-0.684	<0.001
Planning	74.0 (25.1)	-0.622	<0.001
Intimate relationship	41.0 (47.2)	-0.237	0.002
Burden to others	57.0 (30.5)	-0.407	<0.001
Emotional health	67.6 (24.9)	-0.466	<0.001
Body image	56.1 (36.0)	-0.261	0.001
Fatigue	65.6 (24.4)	-0.553	<0.001
SF-36			
Physical health	64.3 (25.1)	-0.574	<0.001
Role physical	43.6 (43.7)	-0.544	<0.001
Bodily pain	58.1 (25.4)	-0.712	<0.001
Global health	47.5 (20.2)	-0.558	<0.001
Vitality	55.1 (18.3)	-0.567	<0.001
Social functioning	62.3 (24.3)	-0.573	<0.001
Role emotional	46.9 (43.0)	-0.466	<0.001
Mental health	61.2 (18.4)	-0.504	<0.001
PCS	53.7 (22.1)	-0.700	<0.001
MCS	54.5 (21.0)	-0.618	<0.001
FACIT	33.2 (10.5)	-0.698	<0.001
WPAI-SLE			
Absenteism	3.8 (9.0)	0.173	0.109
Presenteism	28.7 (27.4)	0.544	<0.001
Work productivity impairment	30.8 (28.1)	0.545	<0.001
Activity impairment	36.1 (29.9)	0.626	<0.001

*Range for all scales is 0-100 except for the FACIT which is 0-52.

Background/Purpose: Disease activity in systemic lupus erythematosus (SLE) is understood differently by patients and physicians; furthermore, there are no reliable measures for patients to assess their levels of disease activity. The LFA-REAL PRO has been proposed for addressing this void, and it is expected to correlate with HRQoL and with other PROs. The aim of this study was to determine the correlations between LFA-REAL PRO and HRQoL, fatigue and work disability.

Methods: A cross-sectional analyses of patients from a single-center cohort was performed. The disease activity measure included was the LFA-REAL PRO (0-1200); PROs included were LupusQoL (with its eight domains), SF-36 (with its eight domains and two main subcomponents), FACIT (as a measure of fatigue) and WPAI (as a measure of work productivity impairment). For the LFA-REAL PRO and WPAI, the higher the scores, the worse the disease activity and the more impaired the patient is; for the SF-36, LupusQoL and FACIT is the opposite. The correlation between these indices was evaluated with Pearson correlations.

Results: One-hundred and sixty-nine patients with SLE, with a mean age of 45.8 (SD: 14.2), 156 (92.3%) were female. The mean (SD) the LFA-REAL PRO was 239.6 (187.7), the Physical Component Summary SF-36 was 53.7 (22.1) and the Mental Component Summary SF-36 was 54.6 (21.0). The mean value of the components of the LupusQoL ranged between 41.0 and 69.4. The FACIT was 33.2 (10.5), the percentage of overall work productivity impairment was 30.8 (28.1) and of activity impairment was 36.1 (29.9). LFA-REAL PRO correlated with all domains of LupusQoL, SF-36, FACIT and WPAI, with the exception of absenteeism.

Conclusion: The LFA-REAL PRO correlates with several measures of HRQoL and other outcomes relevant to lupus patients like fatigue and work disability, suggesting that this index could be useful in monitoring them.

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Abstract Number: 0683

Biologic Differences Between Type 1 and 2 Lupus

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: The manifestations of systemic lupus erythematosus (SLE) can be divided into categories according to a recently proposed model: a category of classic active autoimmune-driven manifestations that cause organ damage (Type 1) and a second category of fatigue, myalgia, mood disturbance, and cognitive dysfunction (Type 2); whereas Type 1 signs are treated with immunosuppression, Type 2 symptoms remain resistant to immuno-

Table 1. Clinical characteristics of women with Type 1 or Type 2 lupus.

	Type 1 Lupus N=10	Type 2 Lupus N=10	p-value
Female	10	10	
Ancestry: Black #	8	5	0.14
Hispanic #	1	0	0.50
Age *mean (SD), years*	35.9 (11.0) Range: 21-58	48.5 (11.4) Range: 33-71	0.02
Duration of SLE *mean (SD), years*	14 (6.7) Range: 1-22	21 (6.9) Range: 13-34	0.05
History of Lupus Nephritis #	9	2	0.003
Current Type 1 Lupus Activity:			
Proteinuria #	6	0	0.005
Positive dsDNA #	5	0	0.02
Low complement #	7	0	0.002
SLEDAI *mean (SD)*	9.7 (4.2) Range: 6-18	0	<0.001
Current Type 2 Lupus Activity: *mean (SD)*			
Total Areas of Pain	0.8 (1.8) Range: 0-6	9.1 (3.9) Range: 3-15	<0.001
Symptom Severity Score	1.9 (1.4) Range: 0-4	5.7 (1.6) Range: 3-8	<0.001
Fibromyalgia Severity Score	2.7 (2.4) Range: 0-8	13.8 (4.3) Range: 10-21	<0.001
Patient-reported Lupus Activity (10=worst) *mean (SD)*	2.9 (2.4) Range: 0-8	4.8 (2.7) Range: 1-10	0.12
Current medications #			
Hydroxychloroquine	9	9	0.78
Prednisone	7 Dose Range: 5-40mg	2 Dose Range: 5-7.5mg	0.04
Immunosuppression	8 [1]	4 [3]	0.09
Medications for Type 2 symptoms	4 [2]	10 [4]	0.005

Medications in patients with Type 1 lupus activity:

[1] Immunosuppression: mycophenolate (6), cyclophosphamide (1), azathioprine (1), belimumab (1)

[2] Type 2 medications: amitriptyline (3), gabapentin (1), pregabalin (1), venlafaxine (1), mirtazapine (1)

Medications in patients with Type 2 lupus activity:

[3] Immunosuppression: Leflunomide (2), methotrexate (1), adalimumab (1)

[4] Type 2 medications: duloxetine (5), gabapentin (4), trazodone(3), cyclobenzaprine (2), zolpidem (2), pregabalin (1), amitriptyline (1), venlafaxine (1), milnacipran (1), buproprion (1), tramadol (1), baclofen (1), melatonin (1), tizanidine (1).

suppression. Distinguishing between Type 1 and 2 SLE can be challenging, especially for the non-rheumatologist. We sought to determine whether transcriptomic differences distinguish between these categories of lupus.

Methods: Using a book-ended approach to avoid clinical overlap in the populations, we identified two cohorts of women with lupus. The first consisted of 10 women with Type 1 disease, defined by a SLEDAI ≥6 and a fibromyalgia severity score (FSS) < 9. A second cohort of 10 women had Type 2 lupus with a SLEDAI of 0 and an FSS > 9. Whole blood was collected in PAXgene Blood RNA tubes and whole transcriptome RNA sequencing was performed. Hierarchical clustering and limma differential expression (DE) analysis were used to compare women of African heritage in the Type 1 and Type 2 cohorts to limit heterogeneity by race. Gene set variation analysis (GSVA) was carried out on all Type 1 and Type 2 lupus patients using modules of co-expressed genes obtained from DE analysis. Clinical characteristics were compared by Fisher's Exact test.

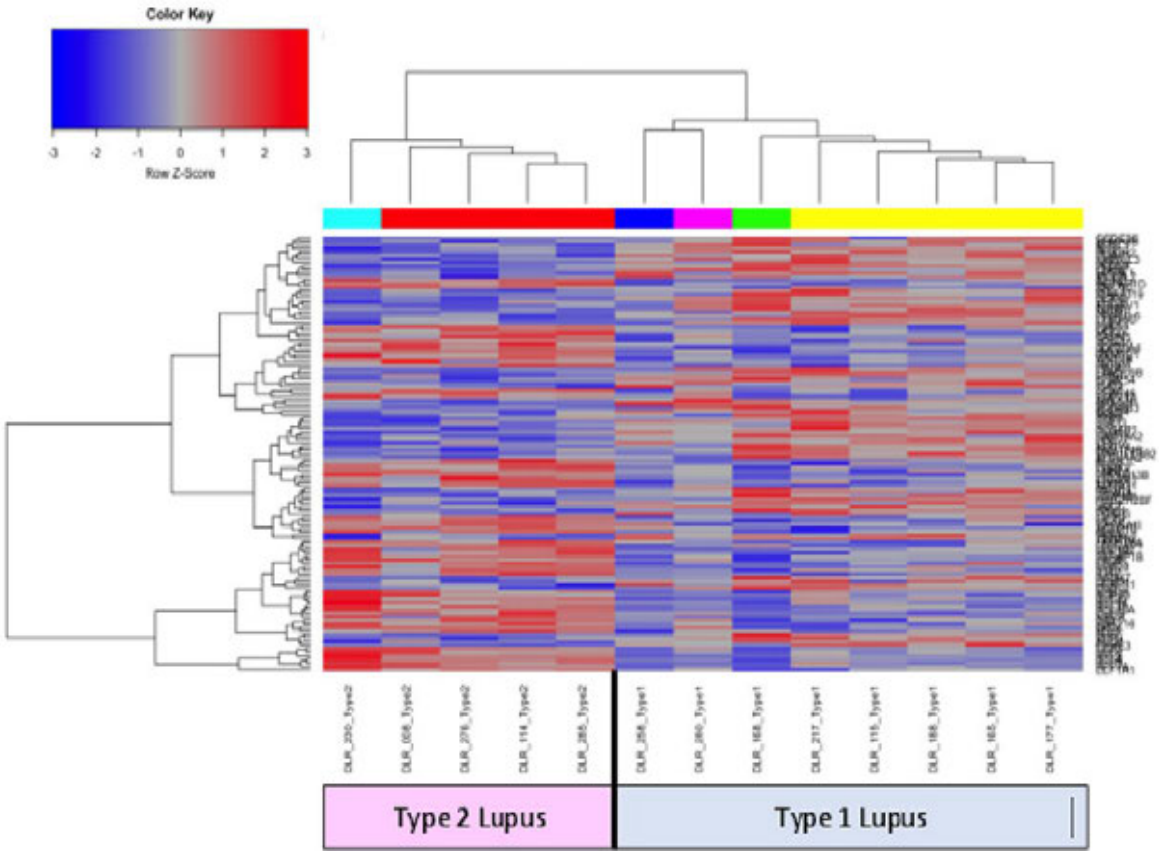

Figure 1. Heat map of differential expressed gene between Type 1 and Type 2 African American women with lupus.

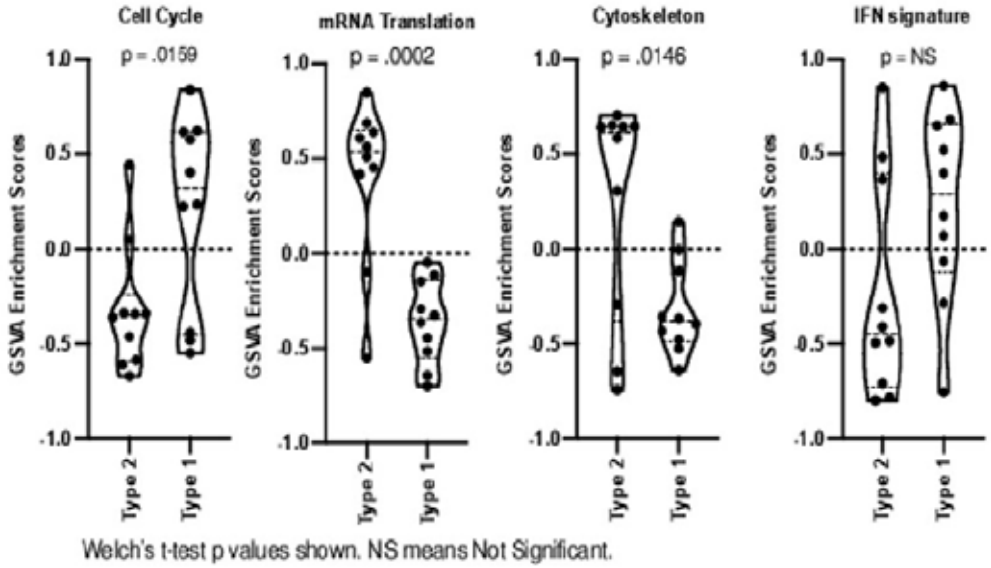

Figure 2. Enrichment of gene modules by GSVA in women with Type 1 and Type 2 lupus.

Results: Women with symptomatic Type 1 lupus were younger and had a shorter disease duration; most had prior and current nephritis; 5 had elevated dsDNA antibodies, and 7 had low complement (Table 1). The average SLEDAI was 9.8 (range 6-18). Of women with Type 2 lupus, 20% had a history of lupus nephritis and none had current proteinuria. Women with Type 2 lupus had more areas of pain, symptoms of fatigue, brain fog, and non-restorative sleep.

Interestingly, the patient assessment of lupus activity did not differ between the groups. The large majority of women in both groups were taking hydroxychloroquine. More women with Type 1 lupus took immunosuppressants and corticosteroids whereas more women with Type 2 lupus took medications for pain and depression.

DE analysis determined distinct hierarchical clustering between Type 1 and Type 2 lupus (Figure 1). Biologically-informed gene clustering identified transcripts for interferon signature genes, low density granulocytes, cell cycle genes, and *SDC1*, a marker of plasma cells, as increased in Type I lupus; transcripts associated with mRNA translation and the cytoskeleton were increased in Type 2 lupus. GSVA using these signatures demonstrated that the cell cycle signature was significantly ($p < .05$) enriched in Type 1 lupus and mRNA translation and the cytoskeleton were significantly ($p < .05$) enriched in Type 2 lupus (Figure 2).

Conclusion: Our new conceptual model characterizes lupus in terms of two categories: Type 1, with immunologic activity and organ involvement, and Type 2, with minimal immunologic activity but debilitating chronic symptoms. Transcriptomic analysis provides evidence that these categories are biologically distinct and can be distinguished by uniquely aberrant molecular pathways.

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Abstract Number: 0684

Clinical Biomarkers at Renal Flare Are Associated with Histologic Changes in Repeat Renal Biopsy in Patients with Biopsy-proven Lupus Nephritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Renal flares are common during treatment of biopsy-proven lupus nephritis (LN). However, it is unknown whether biopsy should be repeated in the event of renal flare. This study aimed to reveal the clinical biomarkers which predict the histologic changes in the repeat renal biopsy during renal flare.

Methods: We evaluated all patients with biopsy-proven LN who underwent repeat renal biopsies at the time of renal flare in Seoul National University Hospital between 2004 and 2018. Renal flare is indicated by an increase in proteinuria, serum creatinine or abnormal urinary sediments. Clinical lupus biomarkers included serum C3/C4, anti-dsDNA antibody level at the time of repeat biopsy. Histologic changes were defined as 1) histologic switch to other ISN/RPS class or alternative pathology, 2) active inflammation (activity index ≥ 7, presence of cellular crescents, interstitial inflammation) and 3) chronic damage (chronicity index ≥ 5, tubular atrophy or interstitial fibrosis). Associations between clinical biomarkers and histologic changes were examined using univariate and multivariate logistic regression analysis adjusting for potential confounding factors.

Table 1. Histologic switch in repeat renal biopsy

	Repeat biopsy			
	Proliferative*	Pure non-proliferative†	Class VI	Alternative pathology‡
Reference biopsy				
Proliferative	42	0	4	2
Pure non-proliferative	1	1	0	0

*Proliferative class included ISN/RPS class III, IV, III+V or IV+V.
†Pure non-proliferative class included ISN/RPS class II or V.
‡Alternative pathology: diabetes nephropathy (n=1), minimal change disease (n=1).

Results: We analyzed 50 pairs of repeat renal biopsy from 46 LN patients with two or more biopsies. The median age was 26 [IQR 18-32] years at reference biopsy and 32 [27-40.7] years at repeat biopsy. 84% was female and the median duration between biopsies was 5.9 years. Of the 50 cases of repeat biopsies, ISN/RPS class switch or alternative pathology was observed in 22 (44%) cases. 6 (12.5%) cases showed histologic switch from proliferative to class VI or alternative pathology, but no pure non-proliferative class. Pure non-proliferative class in the reference biopsy was rare (4%). Low C3 (adjusted odds ratio, 0.04; 95% CI, 0.002 to 0.41; *P*=0.02) or increased anti-dsDNA antibody (adjusted odds ratio, 0.10; 95% CI, 0.009 to 0.96; *P*=0.05) was associated with lower conversion rates of proliferative to class VI or alternative pathology at renal flare. In addition, low C3 was associated with higher activity index (adjusted odds ratio, 19.83; 95% CI, 2.05 to 191.57; *P*=0.01) and presence of cellular crescent (adjusted odds ratio, 10.73; 95% CI, 1.11 to 104.04; *P*=0.04), while serum creatinine was associated with advanced tubulointerstitial damage at renal flare (adjusted odds ratio, 2.62; 95% CI, 1.25 to 5.46; *P*=0.04).

Conclusion: Low C3 at renal flare is associated with the retention of proliferative class and active glomerular inflammation at renal flare in patients with originally proliferative LN. These results support C3 as a surrogate marker to distinguish active LN from change to class VI or alternative pathology at renal flare. Hence, it will be helpful for making decisions about repeat renal biopsy or immunosuppressive therapy.

Disclosure: M. Kim, None; **H. Lee**, None; **Y. Song**, Astellas Pharma, Inc., 9; **E. Lee**, Seoul National University Hospital, 3.

Abstract Number: 0685

Neutrophil Lymphocyte Ratio as a Marker for Immune Complex-Driven Inflammation in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
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Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
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Background/Purpose: Neutrophils play a crucial role in pathogenesis of systemic lupus erythematosus (SLE). Recently, neutrophil to lymphocyte ratio (NLR) has been studied as a biomarker for various rheumatic diseases including

in SLE. The aim of the current study was to evaluate if NLR reflects underlying pathogenetic mechanisms including reactions driven by immune complex (IC) in SLE.

Methods: Clinical information including peripheral blood cell counts, SLE disease activity index (SLEDAI), autoantibody (autoAb) profiles, complement levels, and treatment were collected for 104 SLE patients through the University of Washington (UW) Lupus Repository. Univariate and multivariate linear regression analyses were performed to determine associations between NLR and these variables, including clinical SLEDAI (calculated by subtracting any score for anti-dsDNA and complement from total SLEDAI). A second SLE cohort (n=143), recruited from Lund University (LU), Sweden, was included to investigate associations between NLR and immunological and inflammatory markers, serum type I interferon (IFN) activity as measured by a reporter cell system, and neutrophil subpopulations. For theses analyses, high NLR was defined as above 90th percentile of healthy individuals, and Mann-Whitney U test and logistic regression analyses were performed.

Results: In the first cohort from UW, log-transformed NLR levels were significantly associated with clinical SLEDAI, anti-dsDNA, number of autoAbs, C3, C4, and prednisone dose in univariate analyses. In multivariate analyses, anti-dsDNA remained significantly associated with NLR (β= 0.3, p = 0.003) after controlling for age, gender, clinical SLEDAI, and prednisone dose. Among anti-DNA positive patients, NLR was independently associated with low C3 (β= 0.3, p = 0.02). In the second cohort from LU, high NLR correlated with increased circulating immune complexes (p=0.02) and downstream type I IFN activity (OR=2.3, p=0.04). Lastly, we observed a strong association between high NLR and elevated levels of the serum neutrophil activation marker, S100A8/A9 (p=0.001), and enrichment for low-density granulocytes (LDGs, p=0.001), a neutrophil subset known to be pathogenic in SLE patients.

Conclusion: Our findings support an association in SLE patients between NLR and markers of IC-driven inflammation, including anti-dsDNA, low C3, and type I IFN activity. Additionally, high NLR may reflect abnormal production of immature LDGs, known to promote inflammation and organ damage. Further studies are needed to determine the significance and underlying mechanisms of elevated NLR in SLE.

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Abstract Number: 0686

Association Between the Soluble Terminal Complement Complex C5b-9 (sC5b-9) and Signs of Active Kidney Disease in a Swiss SLE Cohort

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SESSION INFORMATION
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Background/Purpose: There is a lack of reliable biomarkers for disease activity in SLE. While C3a, an anaphylatoxin generated during of complement activation, could be predictive for disease flares, a possible role of the soluble terminal complement complex, sC5b-9, in active SLE has yet to be elucidated. It's proinflammatory effects on a number of cells types, e.g. glomerular mesangial cells and synovial fibroblasts, have been described.

Objectives: To study whether the sC5b-9 is associated with clinical disease activity in SLE and to compare it with C3 and C4, well characterized in active disease, and the split product C3a, in addition to laboratory parameters of standard of care.

Methods: *Study population and design*

Patients included into the Swiss SLE Cohort Study (SSCS, from St. Gallen centre fulfilling the ACR criteria at inclusion), were entered consecutively into a prospective observational study (Oct. 2015 - Dec. 2017). The following were determined at two clinical visits, at least 6 months apart, and compared with 18 healthy controls:

- clinical disease activity by clinical examination, SELENA-SLEDAI, and by SLICC-Damage, SF-36, PGA, and FACIT
- C3a and sC5b-9 by ELISA,
- a spectrum of routine laboratory of standard routine care

Table 1. Patient characteristics at inclusion in 127 patients with systemic lupus erythematosus

	All
No. (%)†	254 (100)
Female sex, no. (%)	208 (82)
Age, mean ± SD, years	51 ± 17
Disease duration, median [IQR], years	5.8 [3.5-9.1]
Overlap-syndromes, no. (%)‡	24 (9)
Disease activity	
LLDAS, no. (%)	222 (87)
SLEDAI >0, no. (%)	124 (49)
SLEDAI >0, mean ± SD	4.2 ± 3.1
ACR criteria at baseline,	
Arthritis, no. (%)	152 (60)
Haematological disorder, no. (%)	144 (57)
Photosensitivity rash, no. (%)	120 (47)
Oral ulcers, no. (%)	86 (34)
Malar rash, no. (%)	72 (28)
Discoid rash, no. (%)	48 (19)
Pleuritis, no. (%)	44 (17)
Renal disorder, no. (%)	40 (16)
Pericarditis, no. (%)	28 (11)
Psychosis, no. (%)	8 (3)
Seizures, no. (%)	4 (2)
ANA positive, no. (%)	254 (100)
anti-APL positive, no. (%)	126 (50)
anti-dsDNA positive, no. (%)	102 (40)
anti-Sm positive, no. (%)	16 (6)

† two samples (one per time point) per patient; ‡Overlap-syndromes: dermatomyositis (N=1), polymyositis (N=1), rheumatoid arthritis (N=1), systemic sclerosis (N=9). Standard deviation (SD); interquartile range [IQR]. LLDAS = Lupus Low Disease Activity State; anti-APL, anti-phospholipid antibodies

Statistics

Correlation analyses were performed calculating nonparametric Spearman rank correlation coefficients. Independent associations of continuous and categorical variables were studied by analysis of covariance (ANCOVA) models, using the general linear model approach.

Results: The disposition at inclusion of our 127 patients is shown in table 1, with 87% of patients in Lupus Low Disease Activity State and 49% with a SELENA-SLEDAI > 0.

There were significant association/correlations (univariate analyses) between:

- sC5b-9 and haematuria ($p < 0.001$)
- sC5b-9 and glomerular dysmorphic erythrocytes ($r=0.139$, $p=0.020$)
- dsDNA ab and sC5b-9 ($r=0.221$, $p < 0.001$) with IgG ($r=0.421$, $p \leq 0.001$)

There were further correlations between:

- C3a with sC5b-9 ($r=0.299$, $p \leq 0.001$), C3a with C3 ($r=0.318$, $p=0.01$), and C3a with C4 ($r=0.137$, $p=0.02$)

Sensitivities/specificities (with regard to haematuria or increased glomerular erythrocytes) were 75/63% or 64/62% for sC5b-9, 8/68%, or 27/69% for C3, and 8/84% or 18/84% for C4, respectively.

Of note, Immunoglobulin G (IgG) levels were associated with SELENA-SLEDAI ($F=4.94$, $p=0.027$) in a multivariate model after adaptation for age, gender, CRP, ESR, ANA titre, dsDNA antibody value, complement factor C3 and C4.

A significant association of C3a with routine laboratory parameters of standard of care, and of sC5b-9 with overall disease activity or other components of the SLEDAI, could not be detected.

Conclusion: Soluble C5b-9, elevated in our cohort concomitant to urinary signs of renal manifestation, may contribute to the pathogenesis in SLE and be a useful marker of active renal disease.

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Abstract Number: 0687

CCP Autoantibody Positive SLE Patients Show Unique Enrichments in SLE Criteria and Autoantibody Biomarkers That Vary by Race

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SESSION INFORMATION
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Background/Purpose: Anti-cyclic citrullinated peptide (anti-CCP) antibodies are a hallmark of RA but are widely distributed in other autoimmune diseases. Although SLE is well characterized as a complex autoimmune disease eliciting a broad spectrum of autoantibodies, the significance of CCP antibodies in SLE patients (pts) remains poorly understood. This study evaluated the prevalence of anti-CCP antibodies in pts with SLE and their associations with demographic characteristics, clinical history, and other autoantibodies.

Methods: SLE patients pts (n=499) consented for research in the Oklahoma Cohort for Rheumatic Diseases were tested for anti-CCP by ELISA. Demographic information, clinical characteristics, and autoantibody profiles were extracted from medical records. Clinical features of pts who had ever tested positive for anti-CCP antibodies were compared to those who consistently tested negative for anti-CCP antibodies. Variables were analyzed using Fisher's exact test.

Results: In 499 pts meeting ACR classification criteria for SLE 12% (61) were anti-CCP positive. Malar rash was the only classification criterion significantly less frequent in the CCP+ SLE group (CCP+: 44% vs CCP-: 58%, $p < 0.05$). Anti-nuclear antibody positivity did not vary between these groups. Anti-CCP antibodies were not more common in any racial subgroup including African American (AA), Native American (NA), and European American (EA) pts. Subsetting by race into AA, EA, and NA subgroups revealed significant enrichment of serositis criteria in the AA CCP+ subgroup compared to the CCP+ EA and CCP+ NA subgroups. In the CCP- subgroups, EA subjects were enriched for malar rash compared to the CCP- AA subgroup and enriched for photosensitivity compared to the CCP- AA and CCP- NA subgroups. The CCP- AA subgroup was significantly enriched for renal criteria compared to the CCP- EA subgroup and enriched for immunologic criteria compared to the CCP- EA and CCP- NA subgroups. In both the CCP+ and CCP- AA subgroups, discoid rash was enriched compared to the EA and NA subgroups and anti-Sm positivity was enriched compared to the EA subgroups. Among the CCP- subgroups, SS-B (La) was enriched in the NA subgroup compared to the AA subgroup and Cent B was enriched in the NA subgroup compared to the AA and EA subgroups. All RNP autoantibodies were enriched in the CCP- AA subgroup, but not the CCP+ AA subgroup.

Conclusion: Race contributes to variations in the frequency of ACR criteria and antinuclear autoantibodies which were observed between the CCP+ and CCP- SLE patients.

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Comparison of the Physicians' Clinical Diagnosis and the EULAR/ACR Classification Criteria for Systemic Lupus Erythematosus in a Multiethnic Cohort

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Background/Purpose: Diagnosis and classification of patients as having systemic lupus erythematosus (SLE) is critical in daily clinical practice as well as for clinical trials and observational studies. The objective of this study was to identify whether patients would be classified earlier using the 2018 EULAR/ACR criteria than the physicians' diagnosis and what items may help for the earlier diagnosis in a multiethnic lupus cohort.

Methods: Patients from a Latin American, multiethnic, multicenter cohort were included. For these analyses, the 2018 EULAR/ACR items were evaluated to determine which clinical manifestations and/or laboratory parameters could be of help to attain an earlier classification of patients. Categorical variables were compared using Chi-square. A p-value of 0.05 was set as the level of statistical significance. The statistical analyses were performed using SAS software version 9.4.

Table 1. Characteristics at the time of EULAR/ACR -based classification in GLADEL cohort patients classified at the same time, earlier, or later than based on the physicians' diagnosis.

EULAR/ACR criteria, Items	EULAR/ACR classification earlier, %	EULAR/ACR classification at the same time, %	EULAR/ACR classification later, %	p-value*
	n=177 (18.1%)	n=483 (49.3%)	n=319 (32.6%)	
CLINICAL				
Fever	67.2	62.3	65.2	0.452
Acute Cutaneous	66.7	67.7	68.0	0.952
Subacute Cutaneous Lupus	3.4	4.8	4.1	0.724
Discoid Lupus	12.4	11.0	10.7	0.825
Oral Ulcers	41.8	44.9	44.8	0.756
Nonscarring alopecia	63.8	66.3	60.5	0.252
Synovitis	85.9	82.0	83.7	0.479
Seizures	10.7	10.1	9.4	0.886
Psychosis	6.8	6.6	9.4	0.315
Delirium	NA	NA	NA	NA
Acute pericarditis	17.0	17.4	14.7	0.598
Serositis	32.2	32.3	27.9	0.381
Thrombocytopenia	26.6	24.6	23.2	0.704
Autoimmune hemolysis	11.9	16.2	10.7	0.065
Leucopenia	57.1	53.4	60.2	0.163
Proteinuria	47.5	46.0	50.5	0.456
Renal Biopsy II or V	6.2	6.8	10,0	0.177
Renal Biopsy III or IV	17.0	18.8	20.4	0.643
IMMUNOLOGIC				
aCL>40 or LAC (+)	37.9	34.8	43.6	0.043
Low C3 or C4	51.4	61.9	58.6	0.052
Low C3 and C4	36.2	47.6	42.6	0.027
Anti-Smith	22.6	29.4	23.5	0.085
Anti-dsDNA	65.5	69.2	64.6	0.363
* Estimated from a Chi-square test				

Results: One thousand forty-seven patients out of 1480 were analyzed. Of them, 979 patients fulfilled the 2018 EULAR/ACR criteria and 68 patients did not. Of those who fulfilled the 2018 EULAR/ACR criteria, the mean (±SD) age at diagnosis was 28.0 (12.5) years; 10.6% were African-Latin Americans, 38.5% Mestizos, 48.9% Caucasians, and 2.0% others. A total of 177 (18.1%) patients achieved the 2018 EULAR/ACR criteria earlier, 483 (49.3%) at the same time and 319 (32.6%) did it later. So considering patients diagnosed later (n=319) and those that could not be included (n=68), the 2018 EULAR/ACR criteria recognized as lupus at the same time or earlier, only about two-thirds [660/1047 (63%)] of the patients diagnosed by expert physicians. Patients who accrued the 2018 EULAR/ACR later were more likely to have positive anticardiolipin antibodies and/or the lupus anticoagulant; low complement levels were not uniformly distributed among the three groups but a clear pattern did not emerge. No differences were found in the clinical items of the criteria.

Conclusion: When the 2018 EULAR/ACR set of criteria were compared to the judgment of expert physicians no clinical or laboratory variable was found to allow earlier classification of lupus except for the presence of aPL antibodies which were more frequent among those diagnosed later. As compared with the physician's clinical diagnosis, the new criteria do not seem to have a good performance for the early classification of lupus patients in this real-life scenario in a multiethnic cohort. To our knowledge this is the first independent comparison of the new proposed criteria for SLE and the gold standard diagnostic method, that is the physician's diagnosis.

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Patterns of High Disease Activity Status and Outcomes in Systemic Lupus Erythematosus

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Background/Purpose: High Disease Activity Status (HDAS), defined as ever attainment of SLEDAI-2k of 10 or greater, may be a useful indicator of overall disease severity in systemic lupus erythematosus. The natural history and disease course following episodes of HDAS has not been previously described.

Methods: Using prospectively collected data from the Australian Lupus Registry and Biobank, we examined the patterns and consequences of HDAS. A HDAS episode (until resolution) was defined as the interval from first visit with a

Table 1. Odds ratio of damage accrual is dependent of the number of HDAS episodes.

Number of HDAS episodes	OR	95% CI	p-value
0	1	-	-
1	1.51	0.81-2.84	0.24
2	4.12	2.06-8.23	<0.001
3	6.24	2.15-18.13	<0.001
4	14.98	1.63-137.48	0.01
5 or more	18.72	2.13-164.49	0.003

recorded SLEDAI -2K≥10, to the time when patient achieved Low Lupus Disease Activity State (LLDAS)[1]. Recurrent HDAS was defined as patients who had at least 2 visits with SLEDAI-2k≥10 that were at least 2 months apart. Persistent HDAS was defined as a subset of recurrent HDAS patients in whom SLEDAI-2k was ≥10 at consecutive visits. The associations of these time course patterns with clinical outcomes were analysed.

Results: Data on 286 patients followed for 4.5 +/- 3.3 years were studied. A total of 128 patients had at least one visit that met the criteria for HDAS, accounting for 254 HDAS episodes. The duration of HDAS episodes was variable (median 133 days, IQR 70-245 days), and were significantly longer in patients entering an HDAS episode with SLEDAI-2K > 10 compared to those entering the HDAS episode with SLEDAI-2K = 10 (p=0.003, unpaired heteroscedactic t-test). Accordingly, the likelihood of an HDAS episode lasting > 12 months was 1.89 (95% CI 1.03-3.46, p=0.04) if starting SLEDAI was >10 compared to =10. The number of HDAS episodes increased the odds of damage accrual, with an odds ratio for increased SLICC damage of 4.12 (p< 0.001) if the patient experienced 2 episodes during the observed period (Table 1).

Most HDAS patients had recurrent HDAS (95/128, 74%). Forty-four patients fulfilled the definition of persistent HDAS. Compared to patients who never experienced HDAS, the risk of damage accrual was markedly increased in recurrent HDAS patients, with an OR 3.1 (95% CI 1.82-5.32, p< 0.001). Persistent HDAS patients have the highest risk of damage accrual with an OR 7.13 (95% CI 3.45-15.62, p< 0.001).

Conclusion: HDAS is a clinically relevant SLE disease severity measure, but its disease course can be highly variable. The risk of damage accrual increased progressively according to exposure to HDAS. Patients with persistent HDAS are at the highest risk of damage accrual.

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Urinary MRP8/14, an Endogenous Toll-Like Receptor 4 Ligand, Reflects Renal Disease Activity in Lupus Nephritis: A Cross-Sectional and Longitudinal Assessment

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Table1. Baseline characteristics of SLE patients in the three categories

	Active Nephritis (AN)	Active Non-Renal (ANR)	Inactive Disease (ID)
Number	32	10	10
F:M	3:29	10	10
Median age (yrs)	26 (18 – 47)	27 (20 – 53)	25 (19 – 52)
rSLEDAI	8 (4 – 16)	0 (0)	0 (0)
SLEDAI	18 (6 – 26)	8 (5 – 19)	2 (0 – 4)
C3 (g/L)	0.705 (0.186 - 1.935)	1.132 (0.599 – 2.134)	1.132 (0.599 – 2.134)
C4 (g/L)	0.187 (0.049 - 1.32)	0.119 (0.049 – 0.231)	0.119 (0.049 – 0.231)
Anti-ds DNA (IU/ml)	373.66 (17.11 - >800)	580.14 (11.32 – >800)	56.16 (1.2 – 633.3)
U_{Pr}/U_{Cr} ratio	2.79 (0.52 – 9.95)	0.12 (0.04 – 0.5)	0.1 (0.03 – 0.5)
Serum Creatinine (mg/dl)	0.9 (0.3 – 2.8)	0.8 (0.6 – 1.2)	0.8 (0.4 – 1.2)
Serum MRP8/14 (ng/ml)	8634.5 (678.5 – 110970.6)	4780.5 (1588 – 44994.4)	3940 (1843-36920)*
$U_{MRP8/14}/U_{Cr}$ (x 100 ng/mg)	44.64 (5.68 – 1288.93)	11.67 (0.03 – 183.57)*	4.38 (1.46 – 43.19)***

p-value *= <0.05 & ***=<0.001 as compared to AN group

Table 2. Change in different disease activity parameters, serum and normalized urinary MRP8/14 in the active nephritis group with treatment over 1 year

	Baseline	3 months	6 months	9 months	12 months
Number	32	29	26	22	16
rSLEDAI	8 (4 – 16)	0 (0 – 16)	0 (0 – 4)	0 (0 – 8)	0 (0 – 8)
SLEDAI	18 (6 – 26)	2 (0 – 18)	2 (0 – 6)	2 (0 – 8)	2 (0 – 12)
C3 (g/L)	0.705 (0.186 - 1.935)	1.054 (0.175 – 1.929)	1.15 (0.604 – 2.87)	0.831 (0.126 – 1.926)	1.196 (0.361 – 2.014)
C4 (g/L)	0.187 (0.049 - 1.32)	0.233 (0.049 – 0.474)	0.227 (0.049 – 0.656)	0.126 (0.05 – 0.478)	0.154 (0.053 – 0.543)
Anti-ds DNA (IU/ml)	373.66 (17.11 - >800)	58.21 (6.98 – 608.05)	73.57 (17.42 – 590.27)	171.52 (27 – 931.19)	231.95 (10 – 1049.04)
U_{Pr}/U_{Cr} ratio	2.79 (0.52 – 9.95)	0.96 (0 – 14.73)	0.75 (0.02 – 8.3)	0.76 (0.04 – 6.5)	0.72 (0.03 – 8.52)
Serum Creatinine (mg/dl)	0.9 (0.3 – 2.8)	0.8 (0 – 3.2)	0.8 (0.4 – 1.7)	0.84 (0.3 – 1.3)	0.8 (0.5 – 1.2)
Serum MRP8/14 (ng/ml)	8634.5 (678.5 – 110970.6)	8047 (1445 – 59000)	4851 (1618 – 15860) **	4929.5 (1707 – 18890)**	4048 (1716 – 43605.92)*
$U_{MRP8/14}/U_{Cr}$ (x 100 ng/mg)	44.64 (5.68 – 1288.93)	16.26 (0.43 – 351.09)	11.34 (1.17 – 345.3)***	15.01 (0.28 – 88.5)***	19.73 (1.5 – 292.02)***

p-value *= <0.05, **=<0.01 & ***=<0.001 as compared to baseline values

Background/Purpose: Monocytes/macrophages are the most abundant cells infiltrating the glomeruli and in the active urinary sediment of patients with Lupus Nephritis (LN).[1] These cells also have relative abundance of Toll Like Receptor 4 (TLR4) as compared to other white blood cells.[2] Therefore MRP8/14 (Calprotectin), an endogenous

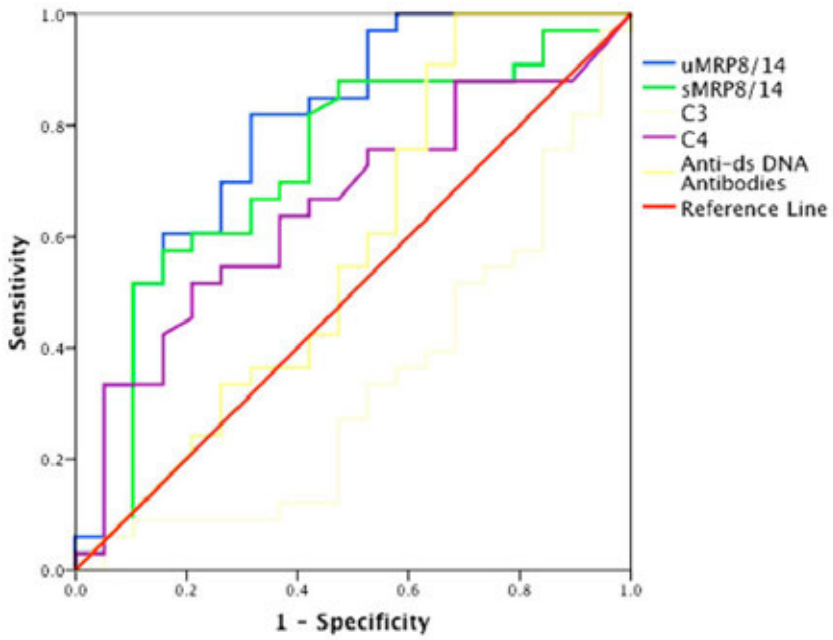

Figure 1. ROC analysis at baseline for conventional disease activity parameters and serum and urinary MRP8/14 levels

TLR4 ligand, could be responsible for their activation in LN and may serve as a biomarker of renal disease activity in urine.

Methods: SLE patients with active nephritis (AN), active disease without nephritis (active non-renal; ANR) and inactive disease (ID) were enrolled. Disease activity was assessed using SLEDAI and renal SLEDAI (rSLEDAI). Patients in AN group were treated according to the ACR 2012 guidelines and followed up every 3 months for 1 year. AN disease was defined as SLEDAI ≥5 with rSLEDAI ≥4, ANR was defined as SLEDAI ≥5 with rSLEDAI =0 and ID was defined as SLEDAI ≤4 with rSLEDAI =0. Urine and serum samples were collected at baseline for all patients and at every 3 months for 1 year in AN group. Urine samples from 10 healthy subjects (HC) and 10 patients of rheumatoid arthritis (RA) served as controls. Serum MRP8/14 (sMRP8/14) and urinary MRP8/14 (uMRP8/14) were measured using commercially available ELISA kits (BioLegend, San Diego, CA, USA) and urinary values were normalized for creatinine excretion. Variables are expressed as median (range) and non-parametric tests were used for analysis. A p-value < 0.05 was considered significant.

Results: A total of 52 SLE patients (F:M = 49:3) were enrolled. Among these, 32 were in AN category whereas 10 patients each were enrolled in ANR and ID categories. Complete response rates at 3, 6, 9 and 12 months were 24%, 42%, 50% and 50% respectively and 3 patients expired at 3 months because of high disease activity. At baseline, normalized uMRP8/14 (ng/mg of creatinine) was significantly higher in AN group [4464 (569-128894)] as compared to ANR [1167 (4-18357)], ID [438 (147-4320)], HC [1348 (3-2726)] and RA [339 (6-11519)] (p-value < 0.05) groups. At baseline, uMRP8/14 showed good correlation with urinary protein:creatinine ratio (r=0.55; p-value< 0.001), rSLEDAI (r=0.5, p-value < 0.001) and SLEDAI (r=0.3, p-value < 0.001) but not with sMRP8/14 (r=0.25). Baseline uMRP8/14 but not sMRP8/14 could differentiate between AN and ANR groups (Table 1) and on ROC analysis, uMRP8/14 (AUC=0.8) performed better than sMRP8/14 (AUC=0.72), C3 (AUC=0.67), C4 (AUC=0.35) and anti-ds DNA antibodies (AUC=0.58) (Figure 1). On follow-up of AN patients, with a reduction in disease activity, uMRP8/14 also decreased significantly at 6,9 and 12 months visits as compared to baseline (p-value < 0.05) (Table 2). sMRP8/14 also decreased significantly at 6 and 9 months but had an erratic and irregular trend. uMRP8/14 also showed a rise before conventional markers in 6 patients who relapsed within 1 year of follow-up requiring change of therapy.

Conclusion: uMRP8/14 is a potential biomarker of LN disease activity. In patients with active SLE, it helps differentiate between patients with and without renal involvement. It correlates with renal disease activity and has a potential to predict relapse of LN.

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Disclosure: R. Gupta, None; **D. Mitra**, None; **S. Rani**, None.

Abstract Number: 0691

Adjusted GAPSS in Systemic Lupus Erythematosus Patients in Argentina

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SESSION INFORMATION
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Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
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Background/Purpose: Assessment of risk both for pregnancy morbidity and thrombosis in the presence of antiphospholipid antibodies (aPL) is still a challenge. The Global Antiphospholipid Syndrome Score (GAPSS) takes into account the aPL profile (criteria and non-criteria), the conventional cardiovascular risk factors and the autoinmune antibody profile. An adjusted model of the score (aGAPSS) suggests that the score is able to stratify patients for their rate of events making it widely applicable in daily clinical practice. The aim was to evaluate the aGAPSS in an external multicentric cohort of Systemic Lupus Erythematous (SLE) patients in Argentina.

Methods: SLE patients from seven Rheumatologist centers were included. Traditional cardiovascular risk factors as Arterial Hypertension (AH), diabetes, smoking, obesity and hyperlipidemia were collected, as well as immobilization, surgery, pregnancy and contraceptive pills/ Hormonal Replacement Therapy (HRT). Immunological tests: antinuclear antibodies (ANA), anti-DNA, anti-Ro, anti-La, anti-RNP, anti-Sm and anti-phospholipid antibodies (Lupus Anticoagulant (LA), anti-cardiolipin (aCL) and β 2 Glycoprotein I (β2GPI) were evaluated. Received treatment: hydroxychloroquine, low doses of aspirin and oral anticoagulants. The score aGAPSS was calculated in each patient by adding together the points corresponding to the risk factors: 1 for AH, 3 for dyslipidemia, 4 for LA and B2GPI and 5 for aCL Score ranges from 0 to 17. Quantitative data were presented as a mean (SD) and were compared by using the t-test, analysis of variance (ANOVA) or the non-parametric Mann- Whitney test. A 95% confidence interval (CI) was selected and a p value< 0.05 was considered significant. The discriminative ability of the aGAPSS was calculated by

Table 1. Associated factors with thrombotic events.

Table 1. Associated factors with thrombotic events.

Variables	Event n (%)	No Event n (%)	p-value
Female Sex	108 (93.1)	150 (88.2)	0.17
Diabetes	6 (5.2)	5 (2.9)	0.33
Obesity	20 (17.2)	24 (14.1)	0.47
Smoking	18 (15.5)	19 (11.2)	0.28
Immobilization	7 (6)	2 (1.2)	0.021
Surgery	15 (12.9)	9 (5.3)	0.022
Contraceptive pills/ HRT	5 (4.3)	7 (4.1)	0.93
Cancer History	3 (2.6)	4 (2.4)	0.90
Pregnancy	5 (4.3)	1 (0.6)	0.031
LAC+	42 (36.2)	37 (21.8)	0.007
Anti- Cardiolipin +	47 (40.5)	37 (21.8)	0.001
Anti- Beta2 GPI +	22 (19)	24 (14.1)	0.27
Arterial Hypertension	36 (31)	35 (20.6)	0.04
Dyslipemia	15 (12.9)	24 (14.1)	0.77
Triple + antibodies	12 (10.3)	15 (8.8)	0.66
ANA +	107 (92.2)	160 (94.1)	0.53
Anti-DNA +	49 (42.2)	91 (53.5)	0.06
Anti- Sm +	29 (25)	66 (38.8)	0.015
Anti-RNP +	30 (25.9)	52 (30.6)	0.38
Anti- Ro +	43 (37.1)	75 (44.1)	0.23
Anti- La +	16 (13.8)	22 (12.9)	0.83
Low dose Aspirin	39 (33.6)	45 (26.5)	0.19
Hydroxychloroquine	108 (93.1)	160 (94.1)	0.72

measuring the area under the receiver operating characteristic curve (AUC). Multivariate logistic regression analysis was accomplished to examine the impact of multiple cardiovascular risk factors and laboratory parameters on the occurrence of thrombosis.

Results: Two-hundred eighty-six SLE patients were included (90.2% women, mean age at SLE diagnosis of 31.8 years (SD±12.3). One-hundred and sixteen patients (40.6%) presented thrombotic/ pregnancy complications. Fifty-four patients (18.9%) presented at least one thrombotic episode (64 events; 34 arterial and 30 venous thrombosis). Table 1 shows associated factors with thrombotic/ obstetrical events. Multivariate logistic regression analysis showed that aCL [OR 2.1 (CI 95% 1.15-3.9); p 0.016] and anti-Sm [OR 0.45 (CI95% 0.25-0.8); p 0.006] antibodies were independent risk factors for thrombotic events. Mean aGAPSS was significantly higher in patients who experienced a thrombotic event compared with those without [4.9 (SD±4.4) versus 3.1 (SD± 4.3); p 0.009]. The AUC showed that aGAPSS ≥4 presented the best diagnostic accuracy (0.63 p 0.03 IC95% 0.57- 0.70) with 61.2% sensibility and 62.9% specificity. The aGAPSS ≥4 was independently associated with thrombotic events OR 1.89 (CI 95% 1.89-3.85); p 0.013.

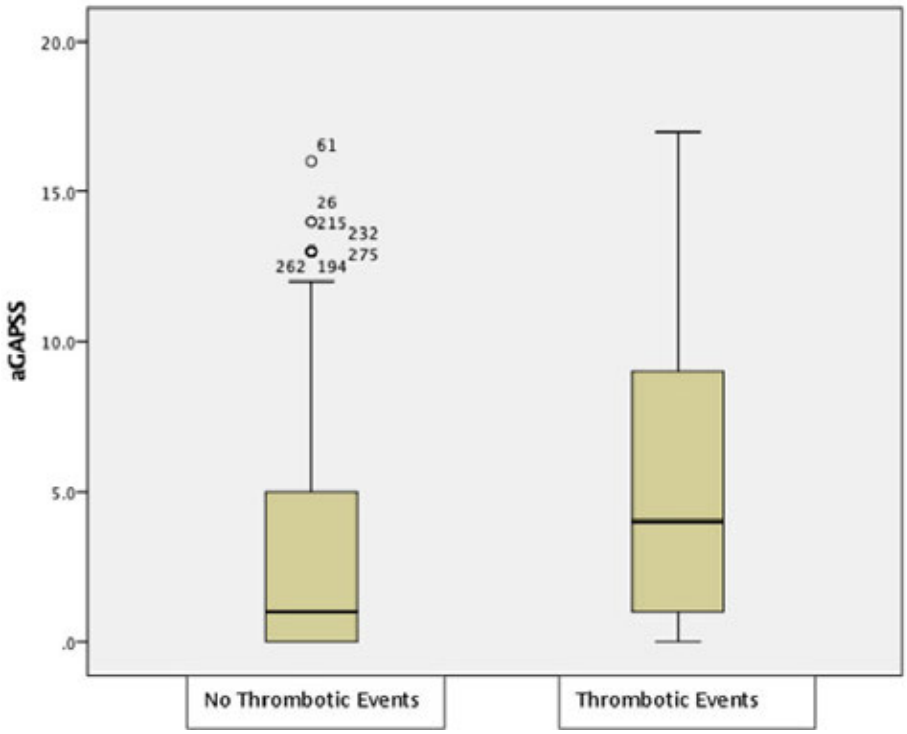

Figure Distribution of aGAPSS in SLE patients.

Conclusion: aGAPSS was significantly higher in patients who experienced a thrombotic event compared with those without. This score is a simple tool to use in SLE patients in daily practice.

Disclosure: L. Garcia, None; **M. Martire**, None; **S. Velloso**, None; **F. Savy**, None; **F. Arizpe**, None; **N. Garcia**, None; **A. Testi**, None; **C. Pena**, None; **D. Capelusnik**, None; **C. Isnardi**, None; **V. Collado**, None; **M. Rodriguez**, None; **C. Pisoni**, None; **S. Mazza**, None; **Y. Soria Curi**, None; **A. Seewald**, None; **M. de la Torre**, None; **M. Garcia**, None.

Abstract Number: 0692

Correlation of Urinary Soluble CD163 Levels with Clinicopathological Features in Lupus Nephritis: Its Role as a Potential Biomarker

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Background/Purpose: Lupus nephritis (LN), is seen in 30-50% patients with SLE and 5-10% patients progress to end-stage renal disease. The clinical disease activity indices do not reliably predict the renal histological activity. Hence, biopsy is still the gold standard to help in treatment decisions and prognosis assessment.

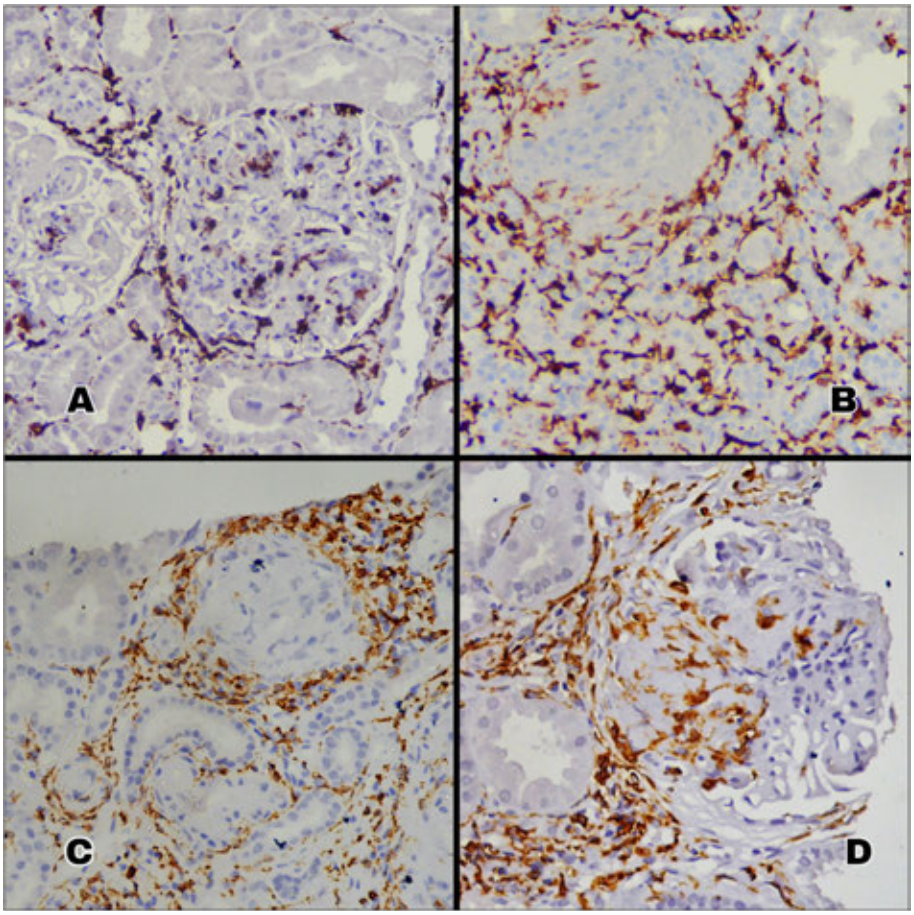

Figure 1. CD163 positive cells in renal biopsies at different sites

Soluble CD163 (sCD163), receptor shed from the alternatively activated macrophage (M2) has been recently found to be a potential urinary biomarker of active LN. To explore further, we studied the urinary sCD163 levels and CD163 positive cells in renal biopsies and studied their correlation with histological features.

Methods: SLE patients undergoing renal biopsy for LN were enrolled. The clinical data regarding disease activity and other parameters was collected. Pre-biopsy urine sample was collected and cell free supernatant was stored at -80C till analysis. Urinary sCD163 (uCD163) was measured by ELISA and the values were normalized to urinary creatinine excretion. 10 healthy control (HC) urine samples were also tested for comparison. The renal biopsies were classified according to the ISN-RPS classification. Activity index (AI) and chronicity index (CI) were calculated using modified NIH scoring system. Immunohistochemistry (IHC) for CD163 positive macrophages was done. Statistical analysis was done using SPSSv20.0

Results: Forty SLE patients with active LN were enrolled [37 females, median age 27 years (12-56)]. All patients had active disease [median SLEDAI 16 (6-43), renal SLEDAI 8 (4-16)]. Among 40 patients, 1 had class II LN, 11 had class III, 26 had class IV and 2 had class V nephritis. The median AI was 8 (1-15) and CI was 2 (0-8).

Urinary sCD163 levels were higher in proliferative LN as compared to healthy controls.[49.6 ug/mg of creatinine (3.6-451) versus 4.2 ug/mg of creatinine (0.7-12) in HC; $p< 0.001$] and showed significant correlation with biopsy activity index ($r=0.50$; p-value < 0.001), presence and frequency of subendothelial hyaline deposits ($r=0.39$; p-value < 0.05) and karyorrhexis ($r=0.42$; p-value < 0.01). They also correlated with the percentage of glomeruli with endocapillary hypercellularity ($r=0.39$; p-value < 0.01). The average number of CD163 positive cells/glomerulus was 7.8 (0-18). The

positive association of uCD163 with activity Index was supported by the localization of CD163+ macrophages in the areas of interstitial inflammation, tubulointerstitial damage and glomeruli with proliferative lesions (Figure 1).

Renal SLEDAI (r=0.46, p-value < 0.01), serum creatinine (r=0.531; p-value < 0.001) and serum total protein (r=-0.34; p-value< 0.05) significantly correlated with chronicity index. The CD163 positive cells were seen along periglomerular fibrosis and around sclerosed glomeruli, though uCD163 levels did not correlate with chronicity index.

Conclusion: Urinary CD163 is a good marker of active LN and correlates with histological activity. CD163+ macrophages are localized to areas of activity as well as chronicity and may contribute to pathogenesis of LN.

Disclosure: S. Venkataraman, None; **A. Singh**, None; **M. Murari**, None; **V. Agrawal**, None; **A. Aggarwal**, None; **R. Pandey**, None.

Abstract Number: 0693

Hair Chemicals and Systemic Lupus Erythematosus: A Case-Control Study

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Background/Purpose: Systemic lupus erythematosus (SLE) is a complex chronic autoimmune disease of unknown etiology. Previous studies of beauty products as potential triggers of SLE development have shown conflicting results. Our study evaluates the use of hair chemicals in patients with SLE and controls and the relationship of use with disease severity among patients.

Methods: Data was obtained from an ongoing longitudinal registry of patients with SLE and non-SLE population-matched controls at a single center. Participants seen over a 12 year period. Information on demographics, medical history, social history, types of hair chemicals used, and SLE characteristics (if applicable) was gathered from in-person interviews. Chart review and telephone follow-up was done for missing values. Disease damage was determined by SLICC/ACR Damage Index ("damage present" if score ≥1). Males and children were excluded from the study population. "Cutaneous lupus" includes SLE patients with documented malar rash, discoid rash, photo-

Table 1. Group Characteristics

Characteristics	SLE n = 359	Controls n = 175	p-value
Current age (mean years ± sd)	48.5±15.6	51.5±16.9	<0.01
African American (%)	70.2	70.3	0.98 (NS)
Insured, any (%)	95.0	93.7	0.56 (NS)
High school graduate (%) (adults)	90.3	88.8	0.61 (NS)
Any hair chemical usage (%)	65.5	49.7	<0.01

Table 2. Disease Characteristics

Disease Characteristics	Hair Chemical Users with SLE n = 235	Non-Users with SLE n = 124	p-value
African American (%)	79.8	55.7	<0.01
Age of SLE diagnosis (years +/- sd)	31.0 ± 13.5	30.8 ± 13.9	0.84 (NS)
History of cutaneous manifesations (%)	85.0	76.7	0.10 (NS)
History of lupus nephritis (%)	45.6	43.3	0.71 (NS)
History of hematologic manifestations (%)	60.2	54.9	0.40 (NS)
Any damage by SLICC-DI (%)	57.9	58.1	0.97 (NS)

sensitivity, and/or alopecia. Pearson's chi-squared testing was performed for categorical measures and two-sample t-tests were performed for continuous measures. Significance was set at alpha = 0.05.

Results: A total of 359 female SLE patients and 175 female controls were included, Table 1. Hair chemical use was more frequent in self-identified black patients (p< 0.01). Patients with SLE were significantly more likely to use hair chemicals compared to controls (65.5% vs. 49.7%, p< 0.01), specifically with higher proportions of patients using hair relaxers/straighteners (p=0.91), hair dyes (p=0.07), and permanent wave products (p=0.23). SLE damage did not differ among patients who use hair chemicals compared to non-users (p=0.97), Table 2. A higher percentage of hair chemical users had cutaneous manifestations, but was not statistically significant (p=0.10)

Conclusion: In conclusion, we found that hair chemical use among females was significantly higher in patients with SLE compared to controls, especially hair dyes. These results provide a basis to look further in to hair chemical use and its relation to autoimmunity. Ongoing analyses are examining the timing and duration of hair chemical use and the development of autoimmunity.

Disclosure: J. English, None; **T. Faith**, None; **D. Wilson**, None; **D. Kamen**, None.

Abstract Number: 0694

Body Mass Index at Time of Diagnosis Is Predictive of Future Disease Activity in SLE

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Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
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Background/Purpose: Obesity is more common in patients with SLE compared to the general population. The prevalence of obesity among SLE patients is between 28 and 50 percent. We previously demonstrated an inverse correlation between body mass index and disease activity in systemic lupus, even after adjusting for prednisone dose. The question of whether these findings were epiphenomena related to disease activity itself remained unanswered. We thus hypothesized that the BMI at cohort entry was predictive of future disease activity.

Methods: 2406 patients in a prospective SLE cohort had their weight assessed at each visit. Patients were categorized into five predetermined groups based on weight: low (BMI< 20 kg/m2), normal weight (reference, BMI 20-24.9 kg/m2), overweight (25-29.9 kg/m2), obese (BMI 30-34.9 kg/m2), and severely obese (BMI >35 kg/m2). Disease activity was characterized on the basis of SLE Disease Activity Index (SLEDAI) scores; for each BMI category we created an Adjusted Mean SLEDAI score. This involved calculating the area under the curve of SLEDAI scores over time. The area under the curve between each two visits was the average of the SLEDAI values at those two visits multiplied by the length of time between the two visits. All the calculated areas were then summed and divided by the total length of the time period. The adjusted mean SLEDAI had the same units as SLEDAI. The adjusted mean SLEDAI has been shown to be a valid measure of SLE activity. To calculate adjusted mean of SLEDAI over time, we only included patients attending the clinic at 3 month intervals for a minimum of 3 visits. 1896 patients were included in the analysis. 1763 (93.0%) were females. Majority (53.0%) were Caucasians, 39.0% African American. To determine whether BMI at cohort entry was predictive of future disease activity, we compared the categorized BMI at cohort entry with the adjusted mean SLEDAI by pairwise t test and ANOVA test. Data were adjusted for prednisone use at cohort entry.

Results: SLEDAI (adjusted mean) by Body Mass Index at baseline visit

BMI	N (%)	SLEDAI Mean (SD)	P value*
Low (Reference)	183 (9.7)	2.9 (2.2)	REF
Normal	655 (34.5)	2.7 (2.4)	0.1912
Overweight	531 (28)	2.5 (2.1)	0.0328
Obese	290 (15.3)	2.6 (2.1)	0.0464
Severely Obese	237 (12.5)	2.5 (2.1)	0.0755

* p-values adjusted for prednisone dose (as a continuous variable) at cohort entry

Conclusion: Body weight at cohort entry was predictive of future disease activity. Overweight and obese patients had a significantly lower adjusted mean SLEDAI over time (P< 0.05). This analysis adds further support to the existence of an obesity paradox in SLE.

Disclosure: G. Stojan, None; **J. Li**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 0695

Environmental and Atmospheric Factors in Systemic Lupus Erythematosus: A Regression Analysis

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SESSION INFORMATION
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Background/Purpose: Understanding the role of environmental exposures in the development of SLE and their association with SLE activity may help identify modifiable risk factors and potential etiological mechanisms. We hypothesized that changes in fine particulate matter (PM2.5) concentration, ozone concentration, temperature, resultant wind, relative humidity, and barometric pressure are predictive of organ specific flares in lupus.

Methods: 1628 patients who fulfill 4 of the 11 ACR or SLICC classification criteria for SLE were included in the analysis. The data ranged from 1999 to 2017. Maximum distance between visits was 110 days with 1 month time aggregation units. Disease activity was expressed as Physician Global Estimate (PGA), taken at every patient visit. A flare was defined as a PGA score increase of 1 point or more compared to the previous visit. Environmental and atmospheric data was obtained from the EPA, including PM2.5 and ozone concentration, temperature, residual wind, relative humidity, and barometric pressure. The average values of each factor 10 days prior to patient visit was calculated. Univariate and multivariate models were built in order to study the association of these variables with lupus disease activity. The models were adjusted for age, sex, income, racial distribution, and rural vs. urban patient residence. Multivariate logistic regression was used to identify significant determinants associated with lupus flares. Regression was performed for each organ flare outcome. Regression inference was based on generalized estimating equations (GEE) to account for the time repeated outcomes.

Results: Rash, serositis, hematologic, and joint flares were statistically significantly associated ($p< 0.0.5$) with an increase in temperature in univariate and multivariate analysis. Renal flares were negatively associated with increases in temperature ($p< 0.05$) in both univariate and multivariate analysis. Renal flares were negatively associated with increases in ozone concentration ($p< 0.05$) in univariate and multivariate analysis. Joint ($p< 0.001$), neurologic ($p< 0.001$), renal ($p< 0.01$), hematologic ($p< 0.05$), and pulmonary ($p< 0.001$) flares were directly associated with residual wind in univariate and multivariate analysis. Humidity was significantly associated with joint ($p< 0.001$), and serositis ($p< 0.05$) flares in univariate and multivariate analysis. Barometric pressure had no significant associations. PM2.5 concentration was significantly associated with rash ($p< 0.001$), joints ($p< 0.001$), serositis ($p< 0.001$), and hematologic flares ($p< 0.001$) in univariate and multivariate analysis.

Conclusion: There is a strong association between changes in atmospheric and environmental variables 10 days prior to patient visit and organ specific lupus activity at the visit. No environmental or atmospheric factor had a general association with all organ specific lupus flares. These data could add an important aspect to lupus trials, the outcomes of which may be affected by so far unrecognized environmental factors, and ultimately it could allow predictive modelling of lupus flares which would revolutionize the approach to treatment.

Disclosure: G. Stojan, None; **F. Curriero**, None; **A. Kvit**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 0696

The Performance of a Renal Activity Index in Lupus Nephritis in Induction Therapy

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

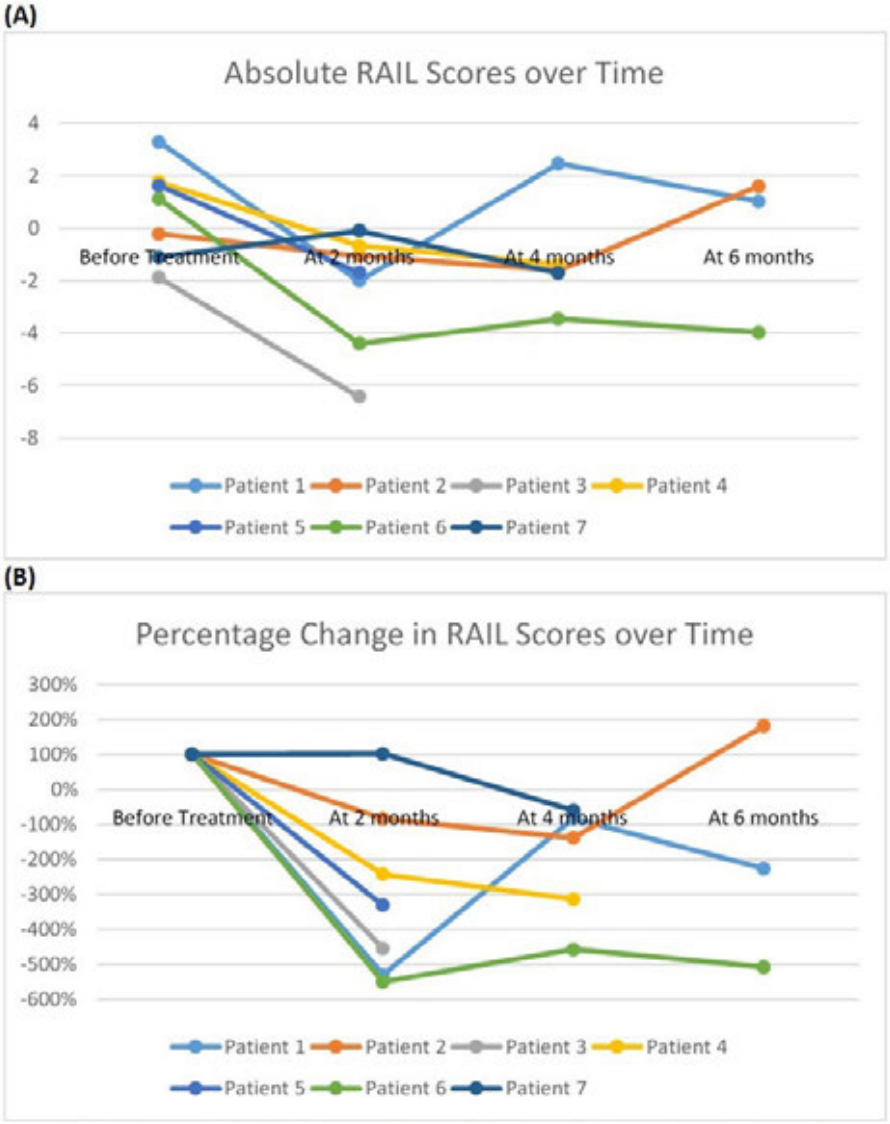

Figure 1. Changes in the RAIL score from baseline, at 2 months, at 4 months and at 6 months in 7 patients with LN: (A) Absolute RAIL scores over 6 months, (B) Percentage change of RAIL scores over 6 months.

Background/Purpose: Lupus nephritis (LN) is associated with high morbidity and mortality. Current standard tools to monitor LN are suboptimal compared to the invasive renal biopsy. The *Renal Activity Index In Lupus* (RAIL) considers the urine concentrations of 6 biomarkers (neutrophil gelatinase-associated lipocalin, ceruloplasmin, monocyte chemoattractant protein-1, adiponectin, hemopexin, kidney injury molecule-1) and has been shown to reflect histologic activity with 92% accuracy. Biomarkers part of his score have also demonstrated changes that predicted response to LN therapy at least 3 months earlier. We aimed to study the changes in the RAIL score in relation to induction treatment in LN.

Methods: Urine samples were collected from active LN patients prior to induction treatment for LN and serially afterwards, coinciding with clinical visits. Luminex Bead Multiplex Assay was used for the analyses of urine biomarkers included in the RAIL. RAIL scores were calculated per the defined algorithm for each urine sample[1]. Serial data collected between 0 and 6 months post LN diagnosis included LN histologic class as per

the International Society of Nephrology (ISN)/Renal Pathology Society (RPS), renal SLE disease activity index (rSLEDAI) score, and type of therapy.

Results: At the time of the analysis, data from 6 active LN patients were collected longitudinally. Patients were all females and all had class IV LN per the ISN/RPS. All patients were started on intravenous (IV) methylprednisolone and cyclophosphamide (CYC) therapy. All but one patient completed 6 doses of monthly CYC before switching to oral mycophenolate mofetil therapy. The RAIL scores for the 6 patients ranged between -1.8 and 3.3. All patients had reductions in their RAIL score at 4 months period (mean absolute decline of 4.3 points; Figure 1A, mean % decline of 211%; Figure 1B). Among 3 with longer follow-up information, all but 2 patients maintained a decline of RAIL scores below the baseline. Patient 1 is known to have medication non-adherence. At 4 months Patient 1 had a prominent rise in RAIL score after which repeat renal biopsy showed persistently high activity of LN leading to commencement of Rituximab therapy. Patient 2 had only 3 monthly doses of CYC. All rSLEDAI scores decreased between baseline and the 6 months interval, except for Patient 2.

Conclusion: RAIL scores show overall improvement from baseline with LN induction therapy. Lack of improvement was associated with flare of disease. Additional data points and a larger study sample are required to study the ability of the RAIL score to reflect clinical improvement of LN. As with other biomarkers, biologic variability creates a variable distribution across patients, therefore it is important to analyze the relative change in the score over time.

Disclosure: N. Aljaberi, None; **Q. Ma**, None; **T. Hennard**, None; **A. Mathur**, None; **H. Brunner**, ., 2, 5, 8, AbbVie, 5, AstraZeneca, 5, Bayer, 5, Bristol-Myers Squibb, 2, 5, EMD Serono, 5, Genentech, 2, 5, 8, GlaxoSmithKline, 5, Janssen, 5, Lilly, 5, Novartis, 5, 8, Pfizer, 2, 5, R-Pharm, 5, Sanofi, 5, UCB, 5.

Abstract Number: 0697

Differing Opinions on Clinical Research Between Healthcare Providers and Lupus Patients

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis

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Table 1. Knowledge Questions. Primary care providers (MDs, DOs, PAs, NPs) and lupus patients were asked the same questions on the topics of: 1) triggers of SLE, 2) racial differences in lupus, and 3) elements of informed consent. All scores improved after the educational program.

	Provider			Patient			Provider-Patient	
	Pre	Post	Pre-Post	Pre	Post	Pre-Post	Pre	Post
SLE Triggers	45%	89%	**<0.0001**	47%	88%	**<0.0001**	0.8554	>0.9999
Racial Differences in Lupus	62%	93%	**<0.0001**	65%	86%	**0.0200**	0.7063	0.2200
Elements of Informed Consent	82%	92%	0.1000	49%	73%	**0.0020**	**0.0001**	**0.0098**

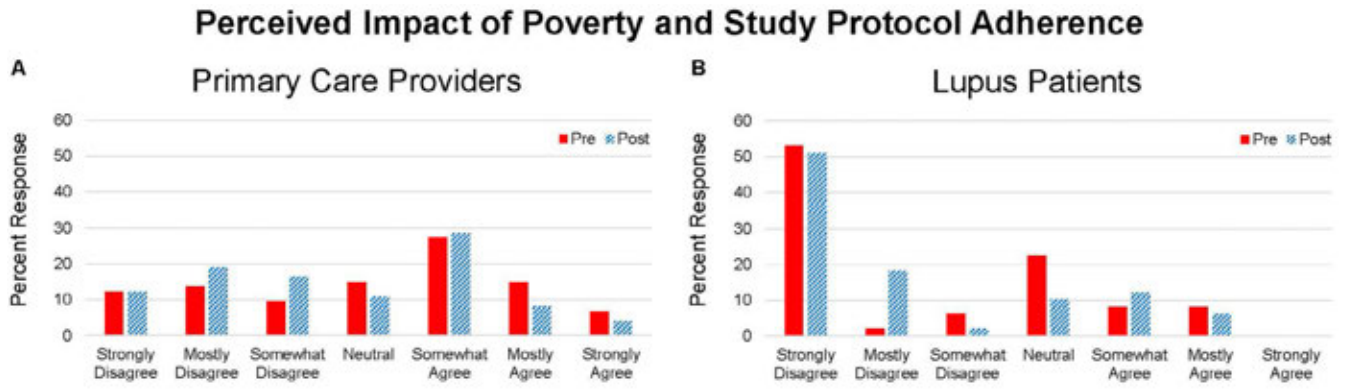

Figure 1. A & B. Mixed responses were obtained from primary care providers (A) when asked whether they believe poverty might reduce protocol adherence in clinical trials. Patients (B) were less likely to agree that poverty reduced protocol adherence both before the program ($p<0.0001$) and after the program ($p<0.0001$) when compared to providers. Providers shifted towards disagreement after completing the educational program ($p=0.02$).

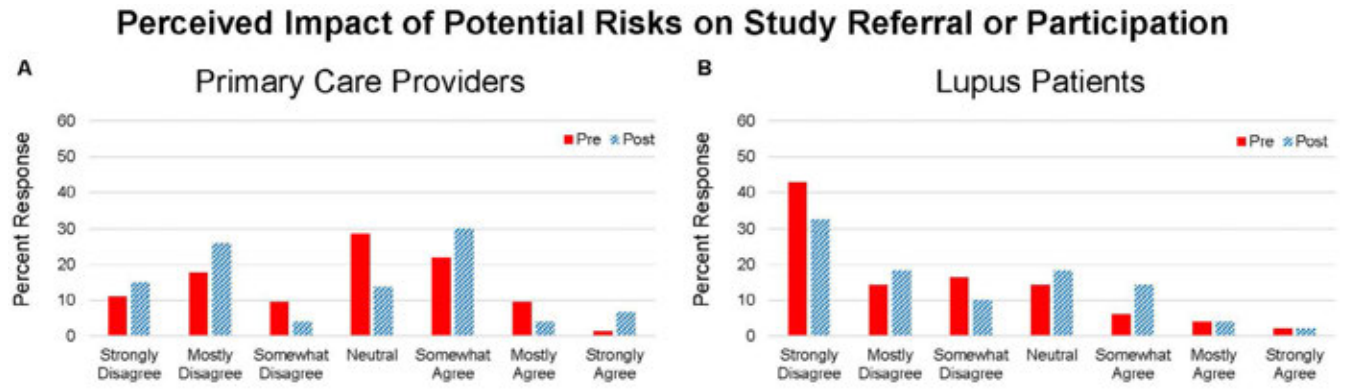

Figure 2 A & B. Significant differences in responses between providers and patients were noted before the program ($p<0.0001$) and after the program ($p=0.02$) with providers more concerned than patients about potential risks in clinical trials. Following the program patients shifted slightly towards more concern about risks and providers slightly less, neither of these changes were significant

Background/Purpose: Although SLE disproportionately affects minority racial groups, this population is significantly under-represented in clinical trials, increasing risk for underpowered, incorrect conclusions in race-based subgroup analyses. The decision to participate in clinical research is complex. Primary care providers (PCPs) have the ability to inform their patients about research and refer to specialists who participate in clinical trials. We evaluated knowledge of SLE and thoughts about clinical research participation with both PCPs and lupus patients.

Methods: Lupus patients and PCPs completed a pre-test consisting of knowledge and belief questions prior to engaging in an educational program about lupus, clinical research, and human subjects' protections. As part of the post-test, the same set of questions were repeated. Knowledge questions were analyzed by Fisher's exact test or McNemar's test for between group and within group comparisons. Belief questions (Likert scale ratings) were analyzed by Mann-Whitney or Wilcoxon matched pairs for between group and within group comparisons.

Results: 73 providers and 49 lupus patients completed the questionnaires and program. Knowledge topics included 1) triggers of SLE, 2) racial differences in lupus, and 3) elements of informed consent. On the pre-test there were differences between groups in scoring of the informed consent question (PCP 82% correct and patient 49%, $p=0.0001$). On the post-test the patients' scores improved (PCP 92% and patient 73%, $p=0.0098$). The education program resulted in improvement in all knowledge scores for PCPs and patients (Table 1). Points of view about clinical trials

included questions about the impact of differing racial background between provider and patient, education level of study participants, risks of trial participation, and effect of poverty on protocol compliance – the latter two resulted in the greatest incongruence (Figure 1 and 2).

Conclusion: Concepts about race, education, and poverty may impact interactions between clinicians and patients that could inhibit referral to clinical trial centers and clinical trial participation. We found that some providers may hold a belief that indigent patients are poor candidates for clinical trials. Despite a shift away from this opinion following an educational program, providers remained much more likely to retain this point of view compared to lupus patients. Further effort to optimize conditions for clinical trial access to all patients is needed. This work may benefit from better understanding of the barriers that have led to underrepresentation of minority patients.

Disclosure: C. Arriens, AstraZeneca, 5, BMS, 2, 5, Exagen, 2, GSK, 2, 5; **D. Forciea**, None; **J. James**, Abbvie, 5, Janssen, 5, Progentec, 2, Progentec Diagnostics, Inc., 2, Xencor, 2, Xencor, Inc., 2; **J. Merrill**, Abbvie, 5, Amgen, 5, Astellas, 5, AstraZeneca, 5, BMS, 2, 5, Celgene, 5, EMD Serono, 5, GSK, 2, 5, Idorsia, 5, ILTOO, 5, Immupharma, 5, Incyte, 5, Janssen, 5, Lilly, 5, Remegen, 5, Servier, 5, Xencor, Inc., 2.

Abstract Number: 0698

Measurement of Type I IFNα Production at the mRNA Level and Its Potential Use as a Biomarker in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
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Background/Purpose: Gene expression studies have previously demonstrated increased Type I interferon α (IFN) inducible genes in peripheral blood mononuclear cells of systemic lupus erythematosus (SLE) patients as compared to controls. Prior studies also showed increased IFNα gene expression is associated with markers of disease activity, both by disease activity scores and serological markers (Kennedy et al, 2015 and Kirou et al 2005). Despite the success of large phase II trials of anti-IFN therapies in patients with SLE, phase III trials were reportedly negative. Identifying the optimal biomarker in order to target the appropriate population of SLE patients to receive anti-IFN therapy remains elusive and a critical goal. Rather than using IFNα inducible genes as biomarkers, we investigated IFNα subtype expression in SLE patients versus healthy controls. We also evaluated associations of IFNα subtype expression in SLE patients with disease-related characteristics and clinical phenotype.

Methods: Patients were recruited from Beth Israel Deaconess Medical Center and the protocol was approved by our institution's IRB. We obtained serum samples from 26 patients and 4 controls. Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) of interferon α subtypes (1, 2, 4, 5, 6, 7, 8, 10, 14, 16, 17, 21) and β-actin mRNA were done using the Inexsia/Amplikine platform (PBL InterferonSource, Piscataway, NJ). For each mRNA/cDNA in the sample, the fluorescence threshold cycle (Ct) during the amplification reaction was identified. The Dct was then calculated for each interferon α subtype mRNA by subtracting its Ct from the β-actin Ct ($Dct_{\text{interferon α subtype}} = Ct_{\text{actin}} - Ct_{\text{interferon α subtype}}$). Statistical analyses were done using SPSS. Between group differences were analyzed with independent samples t-test. Multiple linear regression analyses were conducted to evaluate for independent associations between

IFNα expression, SLEDAI, autoantibodies, markers of disease activity and clinical phenotypes. Follow up correlational analyses were done using Pearson's correlation.

Results: Analyses revealed that Type I IFN α2 mRNA expression in patients' peripheral blood mononuclear cells was elevated as compared to controls (p = 0.02, t= -2.65). No other subtypes demonstrated between group differences. Type I IFN α2 mRNA expression in patients trended towards correlating with disease activity as measured by SLEDAI scores (p =0.07, F= 4.2). There was also a trend found for a correlation between IFN α2 expression and lupus nephritis (R=.48, p=.067). No serological markers of disease activity or autoantibodies were significantly associated with IFN α2 expression.

Conclusion: Prior studies and clinical trials investigating IFNα in SLE used surrogate markers to deduce IFNα production. We propose that direct measurement of IFNα production at the mRNA level is feasible and can potentially be used as a biomarker for guiding anti-IFNα therapy in patients with SLE.

Disclosure: I. Abeles, None; **V. Kyttaris**, exagen diagnostics, 2, Exagen Diagnostics, 2, GSK, 5, gsk, 5, horizon pharma, 5, Horizon Pharma, 5.

Abstract Number: 0699

Revising the SLEDAI-2K to Include Additional Constitutional Symptoms to More Accurately Assess Lupus Disease Activity

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
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Background/Purpose: The SLEDAI-2K, a widely-used measure for disease activity, does not incorporate symptoms such as weight loss, lymphadenopathy (LAD) or fatigue which may limit accurate assessment of disease activity. Another instrument, the Physician Global Assessment (PGA), derives from physician perception of overall disease activity. Our primary objective was to determine whether the addition of weight loss, LAD, and fatigue to the SLEDAI-2K improves the accuracy of disease activity assessment as measured by the PGA.

Methods: A revised SLEDAI (SLED-R) was created that substituted the "Fever" descriptor with a new "Constitutional" descriptor that included the original fever > 38 °C plus weight loss of more than 5%, lymphadenopathy ≥ 0.5 cm (categorized 0.5cm-1cm or ≥1cm), and/or fatigue (defined as fatigue limiting activities of daily living ≥ 50% of the time) in the preceding 28 days (excluding Fibromyalgia or other known causes). In order to preserve integrity of the original SLEDAI (SLED-O) scoring, total points for the new descriptor remained 1. A total of 414 SLED-O and SLED-R scores were prospectively collected from 163 SLE subjects in the Rheumatology clinics at Northwell Health. Concomitant PGA and Patient Global Assessment (PtGA) scores were also collected (Table 2). The primary analysis was a Steiger's test to compare correlation coefficients obtained using a Spearman's Rank correlations test between SLED-O vs. PGA and SLED-R vs. PGA. Similar analyses were performed comparing SLED-O and SLED-R to the PtGA.

Results: Demographic data is presented descriptively (Table 1); PGA, SLED-O and SLED-R were collected on all subjects, PtGA were collected on 390. The new Constitutional descriptor was scored in 45 of the 414 SLEDAIs collected; among these, fatigue scored in 20, LAD scored in 23 (> 1 cm in 9, 0.5 -1 cm in 14), weight loss in 1 and fever in 5. The original descriptor, Fever alone, was scored in 3 in contrast to an additional 42 that scored with the new Constitutional descriptor. The correlation between PGA and SLED-R (R 0.790, p< 0.00) is significantly greater than the correlation between SLED-O and PGA (R 0.784, p< 0.00), (p=0.048, Steiger's test). Significance was lost if either fatigue or LAD was removed from the new descriptor (Table 3). The correlation between PtGA and SLED-R (R 0.436, p< 0.00) is significantly greater than the correlation between SLED-O and PtGA (R 0.417, p< 0.00), (p< 0.00, Steiger's test).

Conclusion: Expansion of the Fever descriptor to include other constitutional symptoms, both subjective (fatigue) and objective (LAD, fever, weight loss), resulted in higher SLEDAI scores in 10.86% of this cohort. This was driven by both fatigue and LAD and removal of either negated the significance, suggesting that both measures contribute. Importantly, the addition of more constitutional signs/symptoms improved the SLEDAI correlations with PGA, suggesting increased accuracy of the revised SLEDAI. Further clinical studies would be needed to assess the applicability of the SLED-R as a tool in guiding therapeutic changes and long-term outcomes in SLE patients.

Table 1. Subject Characteristics, n=163	
Age	mean +/- SD: 42.6 +/- 13.5 range: 19-80
Sex	
Female	147 (90.2%)
Male	16 (9.8%)
Ethnicity	
Hispanic/Latino	47 (28.8%)
Not Hispanic/Latino	116 (71.2%)
Race	
Black	62 (38%)
White	46 (28.2%)
Asian	13 (8%)
Other	42 (25.8%)

Table 2. Subject Evaluations	
Original SLEDAI (SLED-O), n=414	median +/- IQR: 2.0 +/- 5 range: 0-32
Revised SLEDAI (SLED-R), n=414	median +/- IQR: 2.0 +/- 5 range: 0-32
SLED-R with Constitutional Descriptors Scored, n=45	mean +/- IQR: 6.6 +/- 4.8 range: 1-21
Physician Global Assessment (PGA), n=414	median +/- IQR: 0.3 +/- 0.9 range: 0-2.8
Patient Global Assessment (PtGA), n=390	median +/- IQR: 1.4 +/- 4.0 range: 0-10

Table 3. Correlations between the Revised SLEDAI (SLED-R), Original SLEDAI (SLED-O) and PGA

SLED-R	Correlation with PGA	Correlation with SLED-O	Steiger's Test
SLED-R, complete	R 0.790, p<0.00	R 0.995, p<0.00	p=0.048
With fatigue removed	R 0.782, p<0.00	R 0.997, p<0.00	p=0.339
With lymphadenopathy removed	R 0.792, p<0.00	R 0.998, p<0.00	p=0.294

Disclosure: B. Shah, None; **E. Anderson**, None; **M. Mackay**, None; **C. Aranow**, EMD Serrono, 2, GlaxoSmithKline, 2, Janssen, 2, Takeda, 2, UCB, Inc, 2, Xencor, 2; **M. Sansone**, None; **J. Hong**, None.

Abstract Number: 0700

Sleep Quality Among Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Poor sleep quality is a frequent concern among patients with systemic lupus erythematosus (SLE) and contributes to fatigue and other comorbidities. This study investigates the prevalence of poor sleep quality among patients with SLE and the relationship between sleep quality and SLE-related medication use.

Methods: Patients with SLE participating in a longitudinal observational study at a single academic center were invited by email to complete a web-based sleep questionnaire and medication inventory. The Pittsburg Sleep Quality Index (PSQI), a self-reported validated questionnaire ascertaining sleep habits over the past month, was the metric chosen for measuring sleep quality and was scored using the PSQI scoring algorithm. Demographics, medical history including classification criteria for SLE and SLE disease damage scores were obtained from the existing research registry for each participant. Pearson's chi-squared testing was performed for categorical measures and two-sample t-tests were performed for continuous measures. Significance was set at alpha = 0.05.

Results: Of the 142 patients that completed the Pittsburg Sleep Quality Index (PSQI), 99% were female and 86% were African American. The mean PSQI score was 11.98 +/- sd 3.63 with a minimum score of 4 and maximum of 20 out of a possible 21. Higher PSQI scores (corresponding to worse sleep quality) were significantly associated with getting less than 7 hours of sleep ($p< 0.01$), taking sleep medications at least weekly ($p< 0.01$), and having a diagnosis of obstructive sleep apnea ($p< 0.01$), but there was no significant difference found between patients based on age, race, history of lupus nephritis or accumulated disease damage by SLICC-DI. Having a poor PSQI score was not associated with prednisone dose ($p= 0.09$), however taking greater than 7mg of prednisone daily was inversely correlated to the number of hours patients slept per night ($p< 0.01$). Mean number of hours per sleep per night was 5.7 +/- sd 1.5, despite a mean of 8.0 +/- sd 2.0 hours spent in bed. 42.3% of patients reported taking medications for sleep at least once a week.

Conclusion: In this study of patients with SLE, we found a high prevalence of poor quality sleep and a mean of less than 6 hours of sleep/24 hours despite an average of 2 additional hours spent in bed. Although we did not find SLE-specific predictors of poor sleep quality, the overall sleep habits of the patients reflect a critical need to address sleep with patients and work toward interventions for improvement of sleep quality.

Disclosure: A. Schwab, None; **D. Kamen**, None.

Abstract Number: 0701

Association of Cumulative Urinary Podocyte Number and Urinary Podocalyxin with Long-term Renal Prognosis in Lupus Nephritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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Background/Purpose: Podocytes, glomerular visceral epithelial cells, function as molecular sieve not to filter high molecular weight proteins such as albumin and globulins. Various immunological insults damage podocyte to cause detachment from capillary wall in lupus nephritis, leading to reduced podocyte number per glomeruli, glomerulosclerosis, and end stage kidney disease, because podocytes are unable to proliferate and regenerate itself. Therefore, we hypothesized that more podocyte loss or more podocyte damage in a certain period relates to poor renal outcome. It was recently reported that urinary podocyte number (U-Pod) and urinary podocalyxin (U-PCX) were related to podocyte injury in lupus nephritis. We conducted the longitudinal study to clarify the association of accumulated U-Pod and U-PCX with long-term renal prognosis.

Methods: U-Pod were determined by counting PCX-positive cells in sediments from urine samples. U-PCX were measured by sandwich ELISA, normalized to urine creatinine levels. All patients were diagnosed as lupus nephritis with fulfilment of 1997 ACR classification of systemic lupus erythematosus and renal biopsy, and recruited between January 2011 and February 2015 (ISN/RPS Classification III: 2 patients, III+V: 3 patients, IV: 12 patients, IV+V: 7 patients, V: 1 patients). U-Pod, U-PCX, and eGFR were obtained around the treatment start, and at 1, 3, 6 and 12 months (mo) after treatment. eGFR was additionally obtained 5 years after treatment. Cumulative U-Pod (c-U-Pod) and (c-U-PCX) were generated by the summations of values measured at all 5 time points as above. U-Pod and U-PCX were compared between eGFR decliner and non-decliner (eGFR after 5 years – eGFR after 6 months). Correlation of c-U-Pod and c-U-PCX with the change of eGFR was analyzed. Statistical analysis was done with Mann-Whitney U test and Spearman correlation. $p < 0.05$ was defined as statistical significance. Each value was described as median and interquartile range.

Results: In this study, 10 eGFR decliner and 15 eGFR non-decliner were obtained. Both of c-U-Pod and c-U-PCX were not significantly different between eGFR decliner and eGFR non-decliner (c-U-Pod cells/mgCr, decliner: 3.18, 0.69-7.43, non-decliner: 5.93, 1.73-13.78, p=0.40, c-U-PCX mg/gCr, decliner: 911.1, 561.2-1401.0, non-decliner: 985.6, 396.6-1785.0, p=0.76). There was no significant correlation of c-U-Pod and c-U-PCX with long-term (4 years and 6 months) eGFR change (c-U-Pod: r 0.32, p=0.14, c-U-PCX: r 0.18, p=0.39).

Conclusion: c-U-Pod and c-U-PCX were not significantly associated with long-term eGFR change. Podocyte loss could not solely explain long-term renal prognosis.

Disclosure: H. Kajiyama, None; **H. Ikeuchi**, None; **J. Suwa**, None; **D. Ikuma**, None; **H. Kurosawa**, None; **Y. Hirayama**, None; **M. Hara**, None; **Y. Nojima**, None; **K. Hiromura**, None; **T. Mimura**, None.

Abstract Number: 0702

Seasonality of Cutaneous and Systemic Flares in Adults and Children in the Einstein Lupus Cohort

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Background/Purpose: Ultra violet light (UV) exposure has been implicated as a major contributor to pathogenesis and flares in lupus. While some studies have looked at the association between seasons (as proxy for sun exposure) and cutaneous or systemic flares in lupus patients, results are mixed and few include racially diverse cohorts. Our objectives were to study whether a seasonal relationship exists with cutaneous and systemic lupus flares in a racially and ethnically diverse cohort of pediatric and adult lupus patients.

Methods: We retrospectively analyzed consecutive study visits from 2002-2019 of adult and pediatric lupus patients enrolled in the Einstein Lupus Cohort at Montefiore Medical Center in Bronx, NY. We defined cutaneous flare by SELENA SLEDAI inflammatory rash, and systemic flare as SLEDAI ≥ 4. Mixed-effects regression models were used to determine whether cutaneous or systemic flares were associated with season adjusting for race/ethnicity and sex as potential confounders and accounting for repeated measures for each patient. We examined the relationship in a second model including average UV index (UVI) in New York City for the month preceding study visits, to account for the expected lag between UV exposure and onset of symptoms.

Results: We examined 2,351 patient visits for 704 individual patients. Our patients were 87% female; 36% were Black non-Hispanic, 47% were Hispanic and 3% were white non-Hispanic. Among all visits, 9% were associated with new inflammatory rash. Looking at cutaneous disease in a mixed effects model, to account for repeated measures from the same patient, we found that summer (July-Sept) was significantly associated with cutaneous flare compared to winter (Jan-Mar); results remained significant when we adjusted for race/ethnicity and sex (OR 1.8, [95% CI 1.0-3.1], p=0.04). Once adjusting for the previous month's UVI there was no longer an association between summer and cutaneous flare. There was no association between season and systemic flare (OR 1.0 [95% CI 0.7-1.4], p=0.9). However, a bi-modal distribution of systemic flare rates was observed (1st peak in Mar/April, 2nd peak in July-Oct). In an adjusted mixed-effect model with sex, race/ethnicity and previous month's UVI included, Mar/April and Jul-Oct were both still significantly associated with systemic flare compared to other months: Mar/April (OR 2.0 [95% CI 1.4-2.9], p< 0.001), Jul-Oct (OR 2.9 [95% CI 1.7-4.7], p< 0.001).

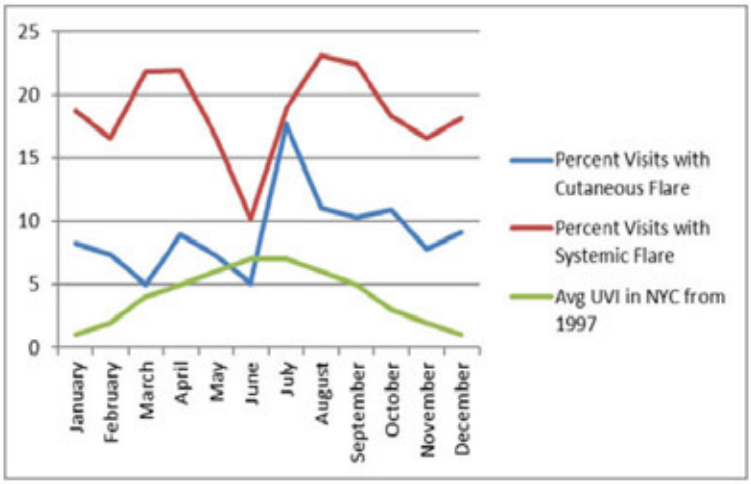

Figure 1. Percent visits with cutaneous or systemic flares across calendar months

Conclusion: We found as association between cutaneous flare and summer in a racially and ethnically diverse cohort of patients with SLE, a relationship that appears to be mostly explained by the previous month's UVI. Though we found no association between systemic flare and season, a bimodal relationship was observed in systemic flares with peak rates in early spring and again in summer through early fall. These two peak periods were associated with systemic activity even while accounting for previous month's UVI. Further epidemiologic studies examining other potential exposures that vary with season may help elucidate triggers that help explain this relationship.

Disclosure: T. Tanner, None; **D. Wahezi**, None; **I. Agalliu**, None; **C. Putterman**, None; **A. Broder**, None; **N. Jordan**, None; **D. Maldonado Andujar**, None; **T. Rubinstein**, None.

Abstract Number: 0703

Prior Knowledge Feature Reduction Improves Performance in a Machine Learning Model of Systemic Lupus Erythematosus Flare Status Using Serum Proteomics

Nimisha Schneider,[1] and Andrew Thompson[1], [1]PatientsLikeMe, Cambridge

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic auto-immune condition characterized by systemic inflammation that can exacerbate (flare) unpredictably, causing widespread organ damage. Identification of SLE flares, particularly at an early stage, remains a challenge for rheumatologists because many flare symptoms mimic those of other conditions but is critical in order to resolve systemic inflammation and spare patients unnecessary treatment if their symptoms are not SLE-related.

Methods: We use a machine-learning approach to classify patient-reported flare status from proteomic measurements in serum from a cohort of 144 individuals with SLE. Proteomic measurements collected from serum samples were inputed to a logistic regression model. The cohort was split 70-30% into training and test sets; 5 fold cross validation was performed within the training set to select hyperparameters. Performance in the test set is reported as area under the receiver operating characterisic curve as an average from 100 test-training split iterations.

Results: We find improvement in the performance of a logistic regression model of patient-reported flare status when the substrate feature pool is reduced from the full proteomic panel of 900 proteins to a 6-protein panel of cytokines selected through curation of peer-reviewed biomedical literature. Use of this prior knowledge protein panel as input to the learning algorithm boosts performance from AUC=0.66 using the full panel to AUC=0.83 using the 6-feature selected panel.

Conclusion: Our results point to a critical role for prior experimental knowledge of molecular disease drivers in creating accurate mathematical, molecular models with diagnostic potential.

Disclosure: N. Schneider, PatientsLikeMe, Inc., 3, PatientsLikeMe, Inc., 3; **A. Thompson**, PatientsLikeMe, Inc., 3.

Abstract Number: 0704

Improving Patient-Centered Care by Utilizing Lupus Wellness Program

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SESSION INFORMATION
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Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
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Background/Purpose: Although the mortality rate of lupus has decreased with improvement of treatment options, it remains high compared to non-SLE mortality. The factors that contribute to this increased mortality are heterogonous including both disease and patient related factors. Several studies have shown the discordance between physician and patient agendas regarding SLE care. Physicians have a greater focus on screening for and treating SLE-related organ involvement, whereas patients are often more concerned with symptoms of burden which often leads to frustration on both sides. This disparity in priorities, along with diminishing time availability of the physician for patient counseling and overall poor health literacy of patients have significantly affected treatment efficacy and adherence. The Lupus Wellness Program aims to serve as an intervention to bridge the care gap.

Methods: SLE patients participated in a Lupus Wellness Program in which they met with a rheumatology nurse practitioner in a one-to-one session every 2 to 12 weeks (depending on preference and availability of the patient) for a total of about 4 sessions. The program followed a curriculum with written information and materials given to the participants at each visit. Forty-seven patients with lupus completed the program. All patients were given a pre-program and post-program knowledge assessment. We measured cardiovascular risk factors (blood pressure, inflammatory markers such as ESR and CRP, prednisone dosage and bodyweight) of the patient 1 year

before starting the program and 1 year after the completion of the program. We also compared health practices over the last 5 years of the participants of the program (intervention group) to a control group of lupus patients who had not participated in the lupus program. Our outcome measurements were 1)rate of flu vaccination, 2) rate of pneumonia vaccinations, 3) cholesterol screening and 4) access to MyChart (patient portal to electronic medical record).

Results: Our study indicates that lupus patients who completed the Lupus Wellness Program had about 80% improvement in knowledge assessment between their pre and post program assessments. Patients who participated in the program within the first 3 years after their diagnosis of lupus tended to have greater improvements in their knowledge assessment compared to those who started the program 4 or more years after diagnosis. Participants had better control in blood pressure and inflammation markers and used less amount of prednisone, but less changes on body weight, as compared to before the intervention. Compared to non-participants, participants of the program received more PNA and Flu vaccinations, and signed up to use MyChart more often.

Conclusion: Our study indicates that usage of an individualized educational program for lupus patients may serve as valuable tool to help to improve long term health outcomes in this population, especially when implemented early on in the disease course. With the increasing demand and decreasing time availability of rheumatology physicians, an advanced practice provider may serve as valuable asset to bridge the gap in patient care.

Disclosure: J. Renaldi, None; **F. Koumpouras**, None; **L. Buckley**, None; **M. Dong**, None.

Abstract Number: 0705

A Tale of Three Cohorts: SLE Criteria in Developed vs Developing Countries

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE diagnostic criteria are important for reliable epidemiologic data. The prevalence of SLE in West Africa is falsely low due to barriers including limited access to both resource and labor-intensive diagnostic testing. Recently, the ACR and EULAR have proposed a weighted classification tool which is thought to improve diagnostic sensitivity and specificity compared to the established ACR and SLICC criteria. Here we aim to investigate the performance of each classification criteria in two West African cohorts--Korle bu Teaching Hospital, Accra Ghana (GH); and Lagos University Teaching Hospital, Lagos, Nigeria (N)--compared to an NYU Langone-African American (AA) cohort.

Methods: We collected data on a total of 355 SLE patients: AA: n=151, GH: n=110, and N: n=94, diagnosed by expert clinicians. Clinical information including demographics, SLE criteria, SLEDAI scores, SLICC damage indexes,

vital signs, and laboratory values as available was obtained at the initial patient encounter. Longitudinal data was collected over the course of at least 1 year at 6 month intervals during routine clinical visits. Where necessary, clinical charts were retrospectively reviewed, and the proportion of patients in each cohort meeting ACR, SLICC and the ACR/EULAR classification criteria was calculated.

Results: The demographics per cohort were as follows: Age (in yrs): AA=43.1, GH=32.4yrs, N=35.5; percent female: AA=90, GH=100, N=97; Mean SLE disease duration (yrs): AA=14.3, GH=2.2, N=4.4. In each cohort, the percentage of patients meeting ACR, SLICC, and ACR/EULAR criteria were AA=96%, 96%, and 95%; GH=85%, 84%, 62%; N=90%, 87%, 61%. This discrepancy was largely due to missing laboratory data particularly with regard to immunologic and hematologic studies. ANA was missing in 0% of the AA cohort, 26% of the GH cohort, and 33% of the N cohort respectively. Compared to the GH and N cohorts, the reference AA cohort was more likely to meet ACR, SLICC, and ACR/EULAR criteria with likelihood ratios (LR) of GH=10.2 $p< 0.001$ and N=3.0 p=0.08; GH=11.5, $p< 0.001$ and N=6.3, p=0.01; and GH=46.1 $P< 0.001$ and N=44.9, $p< 0.001$ respectively. On average, the mean number of ACR/EULAR points by cohort was AA: 26.1±11.8, GH: 21.3±8.1, and N: 19.0±6.2. While the ANA entry criteria greatly diminished the new ACR/EULAR diagnostic utility in the GH and N cohorts, the weighted point system performed better than either of the ACR or SLICC criteria with 96% of the AA cohort, 92%of the GH, and 95% of the N cohort meeting criteria (LR: AA vs GH=1.9, p=0.2; AA vs N=0.23, p=0.6).

Conclusion: Due to a relative lack of resources, supportive laboratory assays including an ANA may be more difficult to attain in developing nations. SLE is a clinical syndrome that may be efficiently diagnosed using the new weighted ACR/EULAR criteria. The entry criteria of ANA 1:80 greatly diminished the diagnostic utility of this classification system in the Ghanaian and Nigerian cohorts compared to the African American cohort. Clinical trials should consider offering wide ANA testing to cohorts in the developing world.

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Abstract Number: 0706

Neuronal BC RNAs: Systemic Lupus Erythematosus Autoantibodies Cause Dendritic Transport Impairments

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical Poster I: Epidemiology & Pathogenesis – ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In systemic lupus erythematosus (SLE), autoantibodies are often directed against nucleic acids or their binding proteins. Regulatory Brain-specific Cytoplasmic (BC) RNAs operate as translational regulators at neuronal synapses. BC RNAs are transported to synapto-dendritic sites of function by heterogeneous nuclear ribonucleoprotein A2 (hnRNP A2). Dysregulation of BC RNA control has been associated with cognitive impairment and epilepsy. Here we hypothesize that transport-specifying structural motifs in BC RNAs can become targets of autoimmune reactivity in neuropsychiatric SLE.

Methods: We collected sera from 69 patients diagnosed with SLE. Sera from non-SLE human (n = 38) subjects were collected as follows: healthy subjects (HS), patients with rheumatoid arthritis (RA), and patients with multiple sclerosis (MS). IgG was purified from sera using Protein A/G and Protein G spin columns (Nab Spin Kit, Thermo Fisher Scientific). BC RNA transcripts were generated by in vitro transcription (Promega). RNA-protein interactions were analyzed by electrophoretic mobility shift assays (EMSAs). Microinjection transport analysis was performed with sympathetic neurons in primary**.** BALB/c mice were used for in situ hybridization. Quantitative and statistical analysis was performed with Prism (Graphpad) and SPSS Statistics.

Results: Autoantibodies against BC RNAs (anti-BC abs) were detected in a subset of lupus patient sera. Strength of SLE anti-BC autoimmune reactivity and occurrence of neuropsychiatric manifestations correlated strongly (Spearman's $r_s = 0.89$, $P < 0.0001$, $n = 69$). Anti-BC abs were not detected in sera from RA or MS patients or in sera from HS. RNA transport experiments were performed as follows. Following preincubation with IgGs, radiolabeled BC RNAs were injected into sympathetic neurons in primary culture. Preincubation with SLE IgG SLE, but not with non-SLE IgG, significantly reduced dendritic delivery of BC RNAs (one-way ANOVA, $P < 0.0001$). In a second set of experiments, we bath-applied IgGs to sympathetic neurons in culture prior to microinjection of BC RNAs. Bath application of SLE IgG, but not of non-SLE IgG, resulted in significantly reduced dendritic targeting of BC RNAs ($P < 0.0001$). In vivo experiments showed that SLE IgG, but not non-SLE IgG, prevented endogenous BC1 RNA from localizing to pyramidal cell dendrites in hippocampal CA1 (Dunnett's test stratum pyramidale vs. strata oriens and radiatum: $P < 0.0001$). SLE anti-BC abs were specifically directed at BC RNA structural motifs that serve as dendritic targeting elements (DTEs). Interaction of SLE anti-BC abs with such motifs caused displacement of RNA transport factor hnRNP A2 from BC RNAs. As a result, SLE anti-BC abs significantly reduced BC RNA dendritic targeting.

Conclusion: Our findings demonstrate that lupus anti-BC abs effectively compete with hnRNP A2 for DTE access and significantly diminish BC RNA delivery to synapto-dendritic destination sites. Lack of BC RNA causes phenotypic abnormalities including cognitive impairment and epileptogenic responses. The combined data indicate a role of anti-BC RNA autoimmunity in SLE and its neuropsychiatric manifestations.

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Abstract Number: 0707

Severity and Evolution over Time of Gastro-Intestinal Involvement in Patients with Systemic Sclerosis in Two Large and Independent Cohorts

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In systemic sclerosis (SSc), the gastro-intestinal tract (GIT) is reported to be the most affected organ after the skin. GIT involvement is associated with high morbidity and mortality. Identifying patients with pro-

Baseline characteristics LUMC and OUH cohort

	LUMC	OUH
Demographic	n=456	n=380
Female, n(%)	336 (81)	307 (81)
Age, mean (SD)	55 (14)	56 (13)
Disease duration RP, median (IQR)	9.8 (3.3-19.8)	8.4 (3.3-15.5)
Disease duration nonRP, median (IQR)	3.8 (1.1-10.2)	4.3 (1.8-8.8)
Smoking, ever n (%)	245 (55)	122 (45)
Organ involvement		
DcSSc, n(%)	88 (21)	84 (22)
mRSS, median (SD)	4 (2-7)	4 (2-11)
Puffy fingers, n(%)	142 (34)	87 (23)
Sclerodactylie, n(%)	251 (60)	240 (63)
DLCO% < 60% of pred, n (%)	134 (32)	100 (29)
FVC% < 70% of pred, n(%)	36 (9)	26 (8)
ILD on HRCT, n(%)	92 (20)	120 (32)
PAH, n(%)	19 (4)	34 (9)
Autoantibodies		
Anti RNA p III, n(%)	21 (5)	37 (10)
Anti-centromere, n(%)	177 (39)	208 (55)
Anti-topoisomerase, n(%)	113 (25)	48 (13)

Table 1. Baseline characteristics. RP= Raynaud Phenomenon, dcSSc=diffuse cutaneous systemic sclerosis, mRSS=modified Rodnan Skin Score, DLCO= single-breath diffusing lung capacity for carbon monoxide FVC= forced vital capacity ILD=interstitial lung disease, HRCT= high resolution computed tomography, PAH= pulmonary arterial hypertension, anti-RNA p III= anti-RNA polymerase III,

gressive GIT involvement could help tailor disease management and allow earlier access to appropriate treatments for patients at risk; as well as facilitate inclusion of patients in clinical trials. The aim of this study was to evaluate the severity and evolution over time of GIT involvement in SSc patients measured by the UCLA GIT 2.0 questionnaire (UCLA GIT score) and assess predictive factors for progression of GIT involvement in two large and independent SSc cohorts.

Methods: All SSc patients fulfilling the American College of Rheumatology (ACR 2013) criteria followed at the Leiden University Medical Centre (LUMC) or Oslo University Hospital (OUH) between 2013-2018 were included. Clinical and demographic features were collected and GIT involvement assessed by the UCLA GIT score at baseline and annually up to 5 years. Progression of GIT involvement was determined for total GIT and each subdomain using the minimal clinical important difference (MCID, Khanna et al. 2011). Univariable and multivariable logistic regression were used to identify baseline variables associated with baseline GIT involvement. Linear mixed-effect regression analysis models

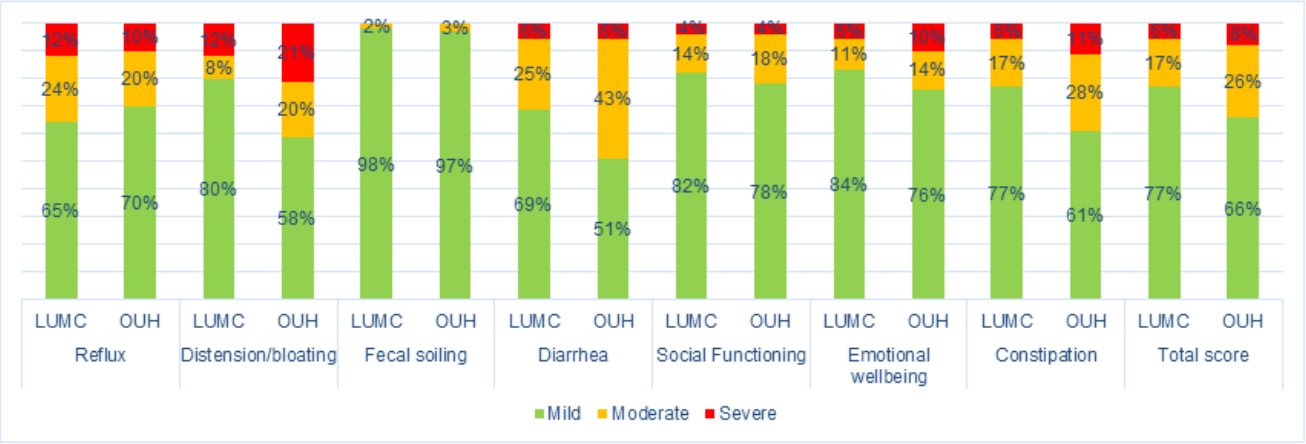

Figure 1. Gastro-intestinal involvement severity per subdomain at baseline in both cohorts.

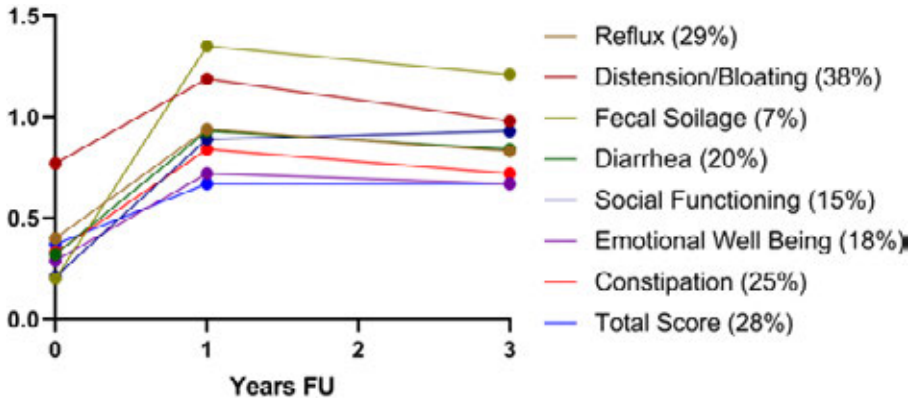

Figure 2. Mean score of the GIT subdomains at baseline, after 1 year and after 3 years of follow-up measured in patients who met the MCID per subdomain. Percentage indicates amount of patients meeting the MCID after 1 year on each subdomain.

were used to assess changes in UCLA GIT scores over time, to control for repeated measurements and to identify predictive factors associated with any change in UCLA GIT score during the observation period.

Results: In total 834 SSc patients were included (LUMC n=456, OUH n=380), of these 536 (64%) had at least one year, and 270 (32%) had at least three year of follow-up. The majority was female (81%) and median disease duration since non-Raynaud was 4.1 years (Table 1). The severity of GIT involvement was similar in both cohorts with 6% (LUMC) and 8% (OUH) patients with severe GIT involvement (Figure 1). Disease duration since onset non-Raynaud (OR 1.03 CI 1.01-1.06), smoking (OR 2.30 CI 1.1-5.0) and anti-centromere antibody (ACA; OR 1.84 CI 0.9-3.9)) were significantly associated with severity of GIT involvement at baseline. Evaluation of GIT progression during the first year showed progression for total GIT score in 28%, with clear variation between the subdomains (Figure 2). In the mixed-effect models, predictive factors for progression of GIT involvement over the observation period were time from onset non-Raynaud, female gender and ACA. Treatment with calcium channel blockers (CCB) was protective for severe GI involvement and for progression

Conclusion: These data from two large and independent SSc cohorts provide novel and important insights regarding the frequency, severity and course of GIT involvement in patients with SSc. We show that assessing GIT involvement using the UCLA GIT subdomains identifies more patients with relevant GIT progression than using the total score. ACA and female gender were identified as the strongest predictors for progression and interestingly CCB treatment was protective.

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Abstract Number: 0708

Improvement and Stabilization of Lung Function in Patients with SSc-ILD Treated with Nintedanib vs Placebo in a Randomized, Placebo-Controlled Phase III Trial: Proportions of Patients with FVC Changes Using Cutoffs Previously Proposed to Define Minimally Clinically Important Differences

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Mean change in forced vital capacity percent predicted (FVC %pred) is a common endpoint in the assessment of treatment-related outcomes in patients with interstitial lung disease (ILD), including those with systemic sclerosis-associated ILD (SSc-ILD). However, it is important to determine the extent to which changes in FVC %pred for individual patients are clinically meaningful. In a previous analysis of two large randomized trials of cyclophosphamide versus placebo (Scleroderma Lung Study [SLS]-I) or versus mycophenolate mofetil (SLS-II) in patients with SSc-ILD, improvement in FVC %pred of ≥3% or deterioration of –3.3% were estimated to be the minimal clinically important differences (MCIDs) associated with statistically significant improvements or worsening in patient-reported outcomes, computer-assisted extent of fibrosis and total ILD (Kafaja et al. Am J Resp Crit Care Med 2018; 197:646–52). A Phase III randomized trial (SENSCIS®, NCT02597933) compared nintedanib 150 mg twice daily with placebo in patients with SSc-ILD, with the primary endpoint the annual rate of decline of FVC. In this analysis, we have assessed the proportions of patients with improvement, and stabilization or deterioration of disease after 1 year of treatment, according to the MCIDs established by Kafaja et al.

Methods: The SENSCIS® trial was a randomized, double-blind, placebo-controlled, parallel group trial conducted in 32 countries. Patients with SSc-ILD, defined as ≥10% lung fibrosis with a baseline FVC ≥40% predicted and DL_{co} of 30–89% predicted, were randomized 1:1 to receive oral nintedanib 150 mg twice daily or placebo. Background stable mycophenolate or methotrexate therapy was permitted. Spirometry (read and analyzed centrally) was conducted over 52 weeks. In this responder analysis, individual changes in FVC %pred from baseline at Week 52 were defined according to MCIDs defined for SLS-I and SLS-II as improvement (≥3% increase), stabilization (change between 3% and –3.3%) or deterioration (at least –3.3%).

Results: A total of 575 patients were included in the analysis, and baseline characteristics were comparable between treatment groups. An improvement in FVC %pred of ≥3% was observed after 52 weeks in 66/287 (23%) patients treated with nintedanib, and 43/288 (15%) who received placebo (OR 1.69; 95% CI 1.11–2.59; P=0.014) (Table). Significantly more patients in the nintedanib arm also experienced either an improvement or stabilization (66% vs 56%;

Minimal clinically importance difference in FVC %pred, n (%)	Nintedanib 150 mg twice daily n=287	Placebo n=288	OR (95% CI)	P-value (exploratory)
Improvement (increase ≥3%)	66 (23)	43 (15)	1.69 (1.11–2.59)	0.014
Improvement (≥3%) or stabilization (change between 3% and –3.3%)	190 (66)	162 (56)	1.52 (1.08–2.13)	0.015
Deterioration (decline ≥–3.3%)	97 (34)	126 (44)	0.66 (0.47–0.92)	0.015

OR 1.52; 95% CI 1.08–2.13; P=0.015) and significantly fewer patients in the nintedanib arm experienced deterioration (34% vs 44%; OR 0.66; 95% CI 0.47–0.92; P=0.015).

Conclusion: In patients with SSc-ILD, more patients treated with nintedanib than placebo experienced improvement in FVC %pred, and more experienced stabilization or improvement in FVC %pred, while fewer experienced deterioration, applying thresholds of clinical meaningfulness established in SLS-I and II, which included a similar patient population.

Minimal clinically importance difference in FVC Table

Number of patients who met or exceeded the MCID (from SLS I and II) for improvement, stabilization or deterioration in lung function over 52 weeks in patients with SSc-ILD participating in the SENSCIS® trial.

Disclosure: Y. Allanore, Actelion, 2, 5, Alpine, 2, 5, Bayer, 2, 5, BMS, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 2, 5, Genentech Roche, 2, 5, Inventiva, 2, 5, Italfarmaco, 2, 5, Sanofi, 2, 5, Servier, 2, 5; **D. Khanna**, Acceleron, 5, 8, Acceleron Pharma, 5, Actelion, 5, 8, Actelion Pharmaceuticals, 5, Astra Zeneca, 5, Bayer, 2, 5, 8, Behring, 5, Blade, 5, Blade Therapeutics, 5, 8, Blade therapeutics, 5, BMS, 2, 5, 8, Boehringer Ingelham, 5, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Celegene, 5, Celgene, 5, 8, ChemomAB, 5, ChemomAb, 5, CiviBioPharma, Inc., 3, Corbus, 5, Corobus, 5, Corpus, 5, CSL Behring, 5, 8, Curizon, 5, Curzion, 5, Cytori, 5, 8, Eicos, 4, Eicos Sciences, 4, Eicos Sciences, Inc, 4, Eicos Sciences, Inc/ CiviBioPharma, Inc, 1, 4, Eicos Sciences, Inc/ CiviBioPharma, Inc., 1, Eicos, Inc, 4, Eicos, Inc., 5, 8, Eicos, INC., 4, Galapagos, 5, Genentech, 5, Genentech/Roche, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 2, 5, Mitsubishi Tanabe Pharma, 5, Mitsubishi Tanabe Pharma Dev America, 5, Mitsubishi Tanabe Pharma Development America, 5, Mitsubishi Tanabi, 5, NIH K24 and R01, 2, NIH / NIAMS K24 AR-063120, 2, NIH/NIAMS R01& K24, 2, Pfizer, 2, 5, Sanofi, 5, Sanofi Aventis, 5, Sanofi-Aventis, 5, 8, Sanofi-Aventis/Genzyme, 5, UCB, 5, UCB Pharma, 5; **E. Volkmann**, Boehringer Ingelheim, 5, Boehringer-Ingelheim, 5, Pfizer, 1, 4; **C. Stock**, Boehringer Ingelheim, 3; **M. Gahlemann**, Boehringer Ingelheim, 3; **N. Schoof**, Boehringer Ingelheim International GmbH, 3; **O. Distler**, A. Menarini, 5, Abbvie, Acceleron, 5, Acceleron Pharma, 5, Actelion, 2, 5, 8, Actelion Pharmaceuticals, 2, 5, 8, 9, Amgen, 5, AnaMar, 2, 5, Bayer, 2, 5, 8, 9, Biogen Idec, 2, 5, Blade Therapeutics, 5, Boehringer Ingelheim, 2, 5, 8, 9, Catenion, 5, 9, ChemomAb, 2, 5, ChemomAB, 5, CSL Behring, 5, Ergonex, 5, espeRare Foundation, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 5, GSK, 2, 5, Holds Patent mir-29 for the treatment of systemic sclerosis, 9, Inventiva, 2, 5, iQvia, 5, Italfarmaco, 2, 5, Italfarmco, 5, Lilly, 2, 5, med, 5, 8, medac, 5, Medac, 2, 5, MedImmune, 2, 5, Medscape, 5, 8, 9, Menarini, 8, Mepha, 8, Mitsubishi Tanabe, 2, 5, Mitsubishi Tanabe Pharma, 2, 5, MSD, 5, 8, Novartis, 2, 5, 8, 9, Patent, 9, Patent issued, 9, Pfizer, 2, 5, 8, Pharmacyclics, 2, 5, Roche, 5, 8, 9, Sanofi, 2, 5, Sinoxa, 2, 5, Target Bio Science, 5, Target BioScience, 5, UCB, 2, 5, 9, UCB in the area of potential treatments of scleroderma and its complications, 2, 5; **T. Maher**, Boehringer Ingelheim, 5, 8.

Abstract Number: 0709

Structural Abnormalities of the Optic Nerve Head and Retinal Nerve Fiber Layer Using Optical Coherence Tomography in Patients with Systemic Sclerosis

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SESSION INFORMATION
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Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
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Background/Purpose: Vascular dysfunction, characterized by vasospasm and endothelial activation, represents a central and early event in systemic sclerosis (SSc). Ocular vasospasm may induce optic nerve head (ONH) damage and have been involved in the pathogenesis of glaucoma, especially normal-tension glaucoma (NTG). Swept-source optical coherence tomography (OCT) is a high-resolution noninvasive imaging method for the quantitative assessment of the ONH and retinal nerve fiber layer (RNFL) structure changes, which are affected in glaucoma. The present study aimed to investigate the presence of structural abnormalities associated with NTG in SSc patients using OCT. In addition, we evaluated the correlations between OCT parameters and nailfold capillaroscopy and measures of digital blood flow using laser Doppler imaging in SSc patients.

Methods: In this cross-sectional study, patients with SSc (2013 ACR/EULAR classification criteria) and age- and sex-matched controls were included. All participants underwent complete ophthalmological examination, including visual acuity, intraocular pressure, slit-lamp biomicroscopy, gonioscopy and visual field examination. The following parameters were measured using high-speed swept-source OCT (SS-OCT, DRI OCT, Topcon, Tokyo, Japan); mean and sectoral RNFL thickness, sectoral and global macular RNFL thickness, macular ganglion cell layer (GCL), GCL + inner plexiform layer (IPL), RNFL+GCL+IPL thickness and ONH morphology. Furthermore, nailfold capillaroscopy (NFC) and the measurement of the digital blood flow of the second to fifth fingers of the non-dominant hand using Laser Doppler imaging before and after cold stimulus were performed in all patients.

Results: A total of 23 eyes of 23 controls (mean age 55.0 ± 9.2 years), and 40 eyes of 40 SSc patients (mean age 51.9 ± 11.2 years) were evaluated. The mean RNFL was of 104.28 ±11.99 µm in SSc patients and of 108.70 ± 12.14 µm in controls (p=0.19). SSc patients showed a thinner temporal RNFL compared with the controls (63.23 ± 11.74 µm versus 83.35 ± 20.19 µm, respectively; p=0.001). The other parameters were similar between the two groups. In SSc patients, the disease duration showed an inverse correlation with the superior RNFL thickness (p=0.01), and the macular RNFL thickness in the outer nasal (p = 0.04), inner inferior (p=0.04) and inner nasal (p=0.04) areas. There was also a significant inverse correlation between the disease duration and the total and superior GCL+IPL thickness (p=0.04, p=0.04, respectively). Laser Doppler imaging measurements did not show significant correlation with OCT parameters. There was an inverse correlation between the avascular score in NFC and the vertical cup/disco ratio (p=0.012) and a positive correlation with the central macular and the fovea thickness segments (p=0.037, p=0.006, respectively).

Conclusion: The significantly thinner temporal RNFL, but not ONH abnormalities observed in patients with SSc, suggest the presence of early structural damage that may result in ganglion cell damage. Further prospective studies with higher number of patients are necessary to better understand the impact of structural RNFL damage in SSc.

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Abstract Number: 0710

Relationship Between High-Resolution Computer Tomography and FVC% Predicted for Classification of Pulmonary Hypertension in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary arterial hypertension (PAH) is one of the leading causes of mortality in scleroderma-spectrum disorders (SSc). FVC% has been used to differentiate Group 1 (PAH) vs. Group 3 (PH due to chronic lung diseases) in different trials and cohorts. The objective of the current analysis was to assess the relationship between the degree of lung disease on high-resolution computed tomography (HRCT, gold standard) vs. FVC% in identifying those with PH due to Group 1 vs. Group 3 PH.

Methods: In this single center retrospective analysis, 268 patients with SSc who had right heart catheterizations (RHCs) at a tertiary center in US were included. HRCTs were reviewed by 2 thoracic radiologists who assessed the degree of total lung involvement in increments of 10% to up to 30% or > 30% lung involvement, and if there was concomitant emphysema. If emphysema was present, it was classified as mild, moderate, or severe. Chronic lung disease was defined as HRCT showing > 20% total lung involvement due to ILD; or if the total lung involvement due to ILD was 10-20% but the patient had concomitant moderate-to-severe emphysema. Each HRCT was categorized based on FVC% performed closest to the RHC into < 70% or ≥ 70%. Sensitivities and specificities were calculated .

Results: Of 268 RHCs, 57 had Group 1 and 36 had Group 3 PH based on the updated hemodynamic definition of pulmonary hypertension[1], as proposed by the 6th World Symposium on Pulmonary Hypertension[2]. In 75 of 93 patients with Group 1 or 3 PH, we had available HRCT data and 54 were reviewed by thoracic radiologists. Of 75 HRCTs, 34 (45%) patients had moderate-to-severe lung disease (based on the definition above), 20 had mild disease, and 21 did not have any ILD and/or significant emphysema. When we included all HRCTs, FVC% had a sensitivity

Table 1. Relationship between HRCTs and FVC% in the Whole Cohort

(N = 75)

FVC %, N(%)	HRCT consistent with moderate to severe chronic lung disease (N = 34)	HRCT- normal or mild chronic lung disease (N = 41)
FVC < 70%, 51 (68%)	25 (74%)	26 (63%)
FVC ≥ 70 %, 24 (32%)	9 (26%)	15 (37%)
	Sensitivity 74% 95% CI (59%, 88%)	Specificity 37% 95% CI (22%, 51%)

Table 2. Relationship between HRCTs and FVC% in those with ILD Involvement on HRCT (N = 54)

FVC %, N(%)	HRCT consistent with moderate to severe chronic lung disease (N = 34)	HRCT- mild chronic lung disease (N = 20)
FVC < 70%, 35 (65%)	25 (74%)	10 (50%)
FVC ≥ 70 %, 19 (35%)	9 (26%)	10 (50%)
	Sensitivity 74% 95% CI (59%, 88%)	Specificity 50% 95% CI (28%, 72%)

of 74% (95% CI (59%, 88%)) and specificity of 37% ((95% CI (22%, 51%)) Table 1). When we excluded those with normal HRCTs, FVC% had a sensitivity of 74% (95% CI (59%, 88%)) and specificity of 50% (95% CI (28%, 72%)) when compared to FVC% (Table 2).

Conclusion: FVC% misclassifies a large number of patients into Group 1 vs. Group 3 PH as it may be influenced by other SSc-related disease processes. Future studies should incorporate the degree of HRCT involvement to differentiate between the 2 groups.

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Abstract Number: 0711

Ultrasound Evaluation of the Hands in Patients with Systemic Sclerosis: Osteophytosis Is a Major Contributor to Tender Joints

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
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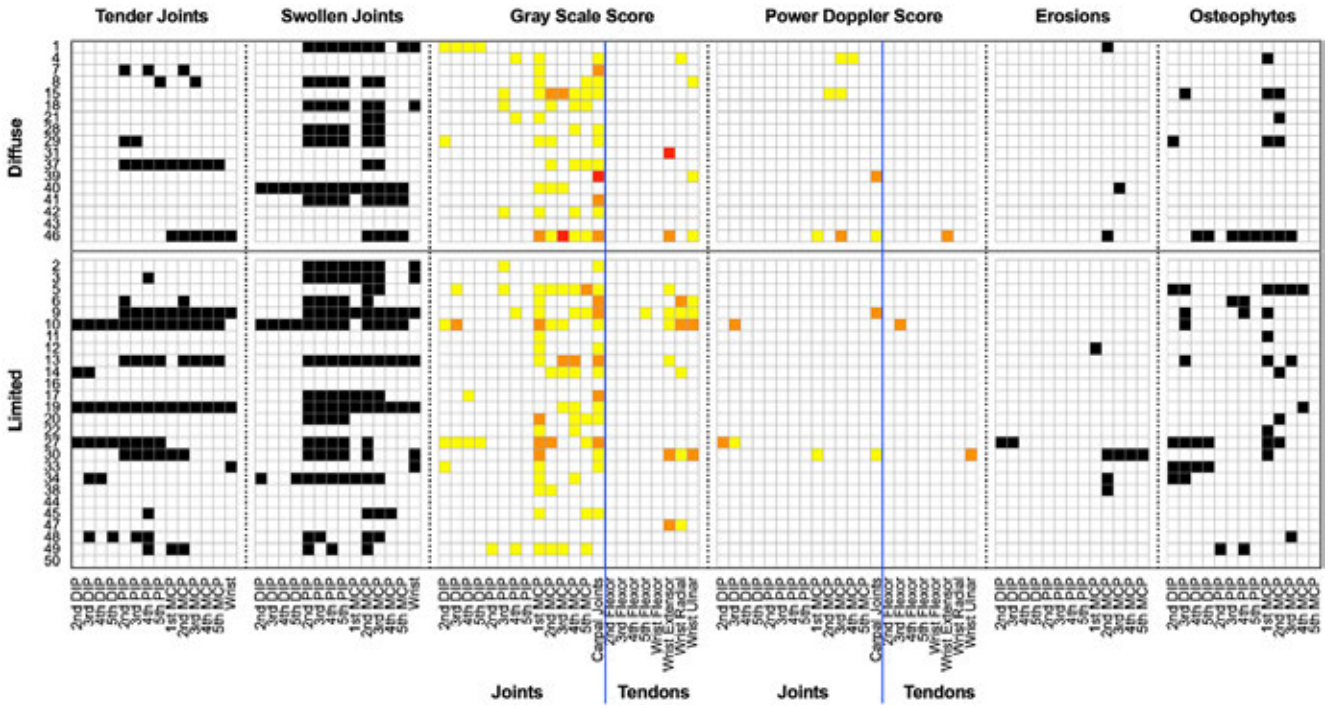
Background/Purpose: Systemic Sclerosis (SSc) is a progressive fibrotic and vascular disease with peripheral manifestations including arthritis, tendinopathy, sclerodactyly, contractures, calcinosis, acroosteolysis, and vascular disease which can lead to significant pain, deformity, and functional impairment. Tender joints (TJs) and swollen joints

Figure 1. Heat map of ultrasound and clinical examination findings



Rows corresponds to an individual patients. Black = present, white = absent or 0, yellow = 1, orange = 2, red = 3.

(SJs) are frequently encountered in SSc, but identifying their exact cause remains challenging. Prior studies have suggested inflammatory arthritis is present in anywhere from 25% to 49% of SSc patients. We sought to use ultrasound (US) to evaluate the prevalence of inflammatory arthritis and other joint and soft tissue pathology and to assess for associations with presence of TJs and SJs.

Methods: Patients meeting ACR/EULAR classification criteria for SSc were prospectively evaluated by US of the hands and wrists. Bilateral B-mode and power doppler exams of the joints and tendons were rated on a semiquantitative scoring system (0-3) for both gray scale (GS, a marker of synovial hypertrophy) and power doppler (PD, a mark-

Table 1. Ultrasound, clinical, and X-ray features.

Ultrasound Features	**n = 43**
Highest GS score, n (%)	
GS 0	6(14)
GS 1	21 (49)
GS 2-3	16 (37)
Highest PD score, n (%)	
PD 0	35 (81)
PD 1-3	8 (19)
ER (1 or more, excludes wrist), n (%)	8 (19)
OS (1 or more, excludes wrist), n (%)	21 (49)
Median nerve area, mean (±SD) mm^2	12.1 (3.7)
UAO, n patients (%)	16 (37)
Clinical and X-ray Features	
Contractures, n patients (%)	22 (51)
Ulcers, n patients (%)	7 (16)
MRSS, total, mean (± SD)	10.2 (8.2)
MRSS, fingers, hands, arms, mean (± SD)	2.2 (1.7)
Calcinosis, n patients (%)	15 (35)

GS = gray scale, PD = power doppler, ER = erosions, OS = osteophytes, UAO = ulnar artery occlusion, MRSS = modified Rodnan skin score.

Table 2. Concordance and correlations of severity between gray scale and clinical and ultrasound findings.		
	Gray Scale (GS)	
	κ*	ρ† (p)
Tender Joints (TJs)	0.72 (0.69, 0.76)	0.47 (0.001)
Swollen Joints (SJs)	0.52 (0.47, 0.57)	0.32 (0.04)
Osteophytes (OS)	0.88 (0.86, 0.90)	0.59 (<0.001)
Power Doppler (PD)	0.85 (0.83, 0.88)	0.55 (0.001)
Erosions (ER)	0.87 (0.85, 0.89)	0.17 (0.26)

GS = gray scale, TJs = tender joints, SJs = swollen joints, OS = osteophytes, PD = power doppler, ER = erosions. Since multiple GS, PD, ER, and OS measurements were recorded per joint region, single scores corresponding to the highest values observed in the region were recorded. *κ value = chance-corrected Cohen's Kappa statistic (GS and PD scores were transformed into binary variables 0 versus 1-3). †ρ = Spearman correlation coefficient using severity scores (severity scores calculated by summing individual joint region scores).

er of hyperemia and active inflammation). Studies were scored blindly by 3 experienced sonographers using OMERACT consensus guidelines. US also evaluated for erosions (ER), osteophytes (OS), ulnar artery occlusion (UAO), and median nerve cross sectional area. TJs, SJs, modified Rodnan skin score (MRSS), contractures, and ulcerations were assessed clinically. Concordance between US features and TJs and SJs was assessed using chance-corrected Cohen's Kappa statistic. Severity scores for GS, PD, OS, ER, TJs and SJs for each patient were obtained by summation. Correlations between the severity of TJs and SJs and US features were assessed by Spearman's rank correlation.

Results: 43 SSc patients (17 diffuse, mean age 58 ± 13.5) were evaluated by US. GS = 2-3 in at least one joint or tendon was seen in 16 (37%) of patients and PD > 0 in at least one joint or tendon was observed in 8 (19%) of patients (Table 1). TJs and SJs did not correlate with median nerve cross sectional area, UAO, calcinosis, digital ulcers, MRSS, or contractures. GS had higher concordance with and severity correlated more strongly with TJs than SJs. Both OS and PD severity strongly correlated with GS severity (Table 2). Of the 37 SSc patients with positive GS findings, PD and OS were seen in 22% and 54% of patients, respectively. Of the 19 patients with TJs, PD and OS were seen in 26% and 74% of patients, respectively.

Conclusion: US revealed a relatively low prevalence of active inflammatory arthritis of 19% as noted by infrequent PD findings. A majority of patients with GS and TJs were found to have OS while PD was less frequent, suggesting US findings of synovial hypertrophy and clinical TJs may be better explained by osteophytosis rather than active inflammatory arthritis.

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Abstract Number: 0712

Safety and Tolerability of Nintedanib in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease in the SENSCIS Trial: Subgroup Analysis Based on Demographic Characteristics

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SESSION INFORMATION

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Table 1. Adverse events in subgroups by age and gender

	Age <65 years		Age ≥65 years		Female		Male	
	Nintedanib (n=224)	Placebo (n=229)	Nintedanib (n=64)	Placebo (n=59)	Nintedanib (n=221)	Placebo (n=212)	Nintedanib (n=67)	Placebo (n=76)
Diarrhea	167 (74.6)	74 (32.3)	51 (79.7)	17 (28.8)	165 (74.7)	66 (31.1)	53 (79.1)	25 (32.9)
Nausea	71 (31.7)	34 (14.8)	20 (31.3)	5 (8.5)	78 (35.3)	29 (13.7)	13 (19.4)	10 (13.2)
Vomiting	53 (23.7)	24 (10.5)	18 (28.1)	6 (10.2)	62 (28.1)	19 (9.0)	9 (13.4)	11 (14.5)
Skin ulcer	42 (18.8)	45 (19.7)	11 (17.2)	5 (8.5)	42 (19.0)	37 (17.5)	11 (16.4)	13 (17.1)
Nasopharyngitis	28 (12.5)	39 (17.0)	8 (12.5)	10 (16.9)	27 (12.2)	36 (17.0)	9 (13.4)	13 (17.1)
Cough	26 (11.6)	42 (18.3)	8 (12.5)	10 (16.9)	23 (10.4)	37 (17.5)	11 (16.4)	15 (19.7)
Weight decreased	22 (9.8)	9 (3.9)	12 (18.8)	3 (5.1)	27 (12.2)	7 (3.3)	7 (10.4)	5 (6.6)
Decreased appetite	15 (6.7)	10 (4.4)	12 (18.8)	2 (3.4)	19 (8.6)	9 (4.2)	8 (11.9)	3 (3.9)
Upper respiratory tract infection	28 (12.5)	32 (14.0)	5 (7.8)	3 (5.1)	26 (11.8)	27 (12.7)	7 (10.4)	8 (10.5)
Liver test abnormalities	29 (12.9)	8 (3.5)	11 (17.2)	1 (1.7)	34 (15.4)	6 (2.8)	6 (9.0)	3 (3.9)
Adverse events leading to treatment discontinuation	33 (14.7)	16 (7.0)	13 (20.3)	9 (15.3)	37 (16.7)	18 (8.5)	9 (13.4)	7 (9.2)
Serious adverse events	53 (23.7)	47 (20.5)	16 (25.0)	15 (25.4)	47 (21.3)	43 (20.3)	22 (32.8)	19 (25.0)

Data shown are n (%) of patients with ≥1 such event. Adverse events are listed by preferred term in the Medical Dictionary for Regulatory Activities (MedDRA) except for liver test abnormalities, which were based on the standardized MedDRA query "liver related investigations, signs and symptoms" (broad definition). The adverse events shown are those reported in >15% of patients and >5 patients in any of the subgroups shown. Serious adverse events were defined as events that resulted in death, were life-threatening, resulted in hospitalization or prolongation of hospitalization, resulted in persistent or clinically significant disability or incapacity, were a congenital anomaly or birth defect, or were deemed to be serious for any other reason.

Table 2. Adverse events in subgroups by race and weight

	White		Asian		Black/African-American		Weight ≤65 kg		Weight >65 kg	
	Nintedanib (n=201)	Placebo (n=186)	Nintedanib (n=62)	Placebo (n=81)	Nintedanib (n=20)	Placebo (n=16)	Nintedanib (n=120)	Placebo (n=117)	Nintedanib (n=168)	Placebo (n=171)
Diarrhea	146 (72.6)	62 (33.3)	50 (80.6)	23 (28.4)	17 (85.0)	3 (18.8)	86 (71.7)	29 (24.8)	132 (78.6)	62 (36.3)
Nausea	73 (36.3)	31 (16.7)	13 (21.0)	6 (7.4)	5 (25.0)	0	33 (27.5)	16 (13.7)	58 (34.5)	23 (13.5)
Vomiting	52 (25.9)	25 (13.4)	13 (21.0)	3 (3.7)	6 (30.0)	0	26 (21.7)	12 (10.3)	45 (26.8)	18 (10.5)
Skin ulcer	33 (16.4)	35 (18.8)	15 (24.2)	11 (13.6)	5 (25.0)	2 (12.5)	31 (25.8)	23 (19.7)	22 (13.1)	27 (15.8)
Nasopharyngitis	26 (12.9)	31 (16.7)	10 (16.1)	16 (19.8)	0	0	13 (10.8)	24 (20.5)	23 (13.7)	25 (14.6)
Cough	26 (12.9)	40 (21.5)	4 (6.5)	9 (11.1)	4 (20.0)	2 (12.5)	8 (6.7)	22 (18.8)	26 (15.5)	30 (17.5)
Weight decreased	25 (12.4)	9 (4.8)	8 (12.9)	2 (2.5)	1 (5.0)	1 (6.3)	15 (12.5)	5 (4.3)	19 (11.3)	7 (4.1)
Decreased appetite	17 (8.5)	9 (4.8)	9 (14.5)	2 (2.5)	1 (5.0)	0	11 (9.2)	4 (3.4)	16 (9.5)	8 (4.7)
Upper respiratory tract infection	21 (10.4)	21 (11.3)	10 (16.1)	11 (13.6)	1 (5.0)	2 (12.5)	12 (10.0)	13 (11.1)	21 (12.5)	22 (12.9)
Liver test abnormalities	25 (12.4)	6 (3.2)	12 (19.4)	3 (3.7)	3 (15.0)	0	16 (13.3)	6 (5.1)	24 (14.3)	3 (1.8)
Adverse events leading to treatment discontinuation	33 (16.4)	17 (9.1)	9 (14.5)	5 (6.2)	3 (15.0)	3 (18.8)	25 (20.8)	12 (10.3)	21 (12.5)	13 (7.6)
Serious adverse events	45 (22.4)	43 (23.1)	16 (25.8)	12 (14.8)	8 (40.0)	7 (43.8)	29 (24.2)	26 (22.2)	40 (23.8)	36 (21.1)

Data shown are n (%) of patients with ≥1 such event. Adverse events are listed by preferred term in the Medical Dictionary for Regulatory Activities (MedDRA) except for liver test abnormalities, which were based on the standardized MedDRA query "liver related investigations, signs and symptoms" (broad definition). The adverse events shown are those reported in >15% of patients and >5 patients in any of the subgroups shown. Serious adverse events were defined as events that resulted in death, were life-threatening, resulted in hospitalization or prolongation of hospitalization, resulted in persistent or clinically significant disability or incapacity, were a congenital anomaly or birth defect, or were deemed to be serious for any other reason.

Background/Purpose: In the SENSCIS trial in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD), the adverse events associated with nintedanib were manageable for most patients and characterized mainly by gastrointestinal events. We assessed the safety and tolerability of nintedanib in subgroups defined based on demographic characteristics at baseline.

Methods: Adverse events that occurred over 52 weeks of treatment, irrespective of causality, were assessed in subgroups of patients by age (< 65, ≥65 years), gender, race (White, Asian, Black/African-American) and weight (≤65, >65 kg) at baseline. Descriptive analyses, based on comparing the proportions of patients who had adverse events across subgroups, were performed in subjects who received ≥1 dose of trial drug.

Results: A total of 576 patients received trial drug (288 nintedanib; 288 placebo). At baseline, mean (SD) age was 54.0 (12.2) years and weight was 69.7 (15.9) kg. The majority of patients were female (75.2%) and white (67.2%). The adverse event profile of nintedanib, and the proportions of patients with adverse events leading to treatment discontinuation, were generally similar across subgroups defined by age, gender, race, and weight (Tables 1 and 2). Diarrhea was the most frequently reported adverse event with nintedanib in all the subgroups. Decreased appetite and decreased weight were reported more frequently in nintedanib-treated patients aged ≥65 years than < 65 years. Nausea and vomiting were reported more frequently in female than male patients treated with nintedanib. Liver test abnormalities were reported more frequently in nintedanib-treated patients who were female, aged ≥65 years, or Asian. Premature treatment discontinuations were more common in patients who were female, aged ≥65 years, or had a weight < 65kg.The number of Black/African-American patients was too small to allow conclusions to be drawn about adverse events in this subgroup.

Conclusion: The safety and tolerability profile of nintedanib in patients with SSc-ILD was generally consistent across subgroups of patients defined by age, gender, race and weight. A management plan based on the recommendations given in clinical trials may help patients to manage the most common adverse events associated with nintedanib therapy.

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von Wangenheim, Boehringer Ingelheim, 3; **M. Gahlemann**, Boehringer Ingelheim, 3; **V. Kohlbrenner**, Boehringer Ingelheim, 3; **M. Alves**, Boehringer Ingelheim, 3; **E. Clerisme-Beaty**, Boehringer Ingelheim, 3; **A. Azuma**, Asahikasei Pharma Co., 5, 9, Boehringer Ingelheim, 5, 9, Shionogi & Co., Ltd, 5, 9, Taiho Pharmaceutical Co., Ltd, 5, 9.

Abstract Number: 0713

NEMO Score in Nailfold Videocapillaroscopy Is a Good Tool to Assess Both Steady State Levels and Overtime Changes of Disease Activity in Patients with Systemic Sclerosis: A Comparison with Both the Composite EScSG and EUSTAR Indices for This Disease Status Entity

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Session Time: 9:00AM–11:00AM

Background/Purpose: We previously demonstrated that NEMO score, i.e., the cumulative number of microhaemorrhages (MHEs) and microthrombosis (MTs) observed in nailfold videocapillaroscopy (NVC), was a good indicator of the steady state level of disease activity (DA) in patients with SSc when the European Scleroderma Study Group (EScSG) index was taken as gold standard. *Aim of the study*. To verify whether the NEMO score could be *(i)* a valid tool to assess DA, even when the modified European Scleroderma Trials and Research (EUSTAR) index was considered as comparator; *(ii)* a sensitive method to capture the overtime changes of DA.

Methods: NEMO score, EScSG and EUSTAR indices were assessed at baseline (T0) and after a follow up of 6-12 months (T1) in a cohort of 98 patients affected by SSc according to ACR/EULAR 2013 criteria (48 with limited and 50 with diffuse SSc). It was preliminarily established that at least 50% of SSc patients should be active at enrolment time (score ≥3, according to the EScSG DA index). The area under the curve (AUC) of the receiver operating characteristic (ROC) curve was calculated to measure the sensitivity and specificity of NEMO score in classifying patients with predefined level of DA (≥ 3.0 and ≥ 2.5 scores for EScSG and EUSTAR indices, respectively). To assess overtime changes of DA, the differences (Δ) between T0 and T1 values of NEMO score, EScSG and EUSTAR indices were calculated and compared to each other.

Results: NEMO score values were very closely correlated with the corresponding values of both EScSG and EUSTAR indices at T0 and T1 observations [$p < 0.0001$ in all cases with the exception of the correlation with EScSG values at T1 ($p < 0.03$)]. Values of the two composite DA indices were also strictly related to each other either at T0 or T1 observations ($p < 0.0001$). NEMO score showed a very good performance in classifying patients with predefined level of DA. AUCs of ROC curve analysis were 0.91 and 0.88 considering the respective predefined levels of EScSG and EUSTAR indices as standard measures of significant levels of DA ($p < 0.0001$ in both cases). Δ values of NEMO score were significantly correlated with the corresponding values of both EScSG and EUSTAR indices. Weighted Cohen's k level of agreement between Δ values of NEMO score and those of EScSG and EUSTAR indices was moderate (0.55 and 0.60, respectively), but close to the level of good agreement (>0.60).

Conclusion: NEMO score confirms to be a feasible, non-invasive and valid tool to assess steady state levels and overtime changes of DA in patients with SSc. Thus, this NVC evaluation can represent an alternative or complementary method to measure this disease status entity in this disorder.

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Abstract Number: 0714

Characteristics of Patients with Systemic Sclerosis in the Rheumatology Informatics System for Effectiveness (RISE) Registry

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SS), is characterized by fibrosis of the skin and internal organs and vasculopathy with relatively high morbidity and mortality. Given the rarity of the disease, studying epidemiology, treatment and natural history is challenging without large patient cohorts. We conducted a cross-sectional study to understand the prevalence, disease characteristics, demographics, and treatment patterns ofSS patients using the Rheumatology Informatics System for Effectiveness (RISE) EHR-based registry.

Methods: Between 2015 and 2017, we identified patients who had at least one physician diagnosis code of SS (M34.x or M34.xx) and aged 18 years or older at the first encounter. The demographics included age, gender, race, region, and body mass index (BMI). We identified relevant comorbidities that associated with scleroderma including other autoimmune diseases, interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH). In addition we evaluated relevant medications including prednisone, immunomodulation, calcium channel blockers (CCB), phosphodiesterase type 5 (PDE 5) inhibitors, endothelin receptor antagonists (ERA), proton pump inhibitors (PPIs), H2 blockers, angiotension-converting enzyme inhibitors (ACEIs), angiotensin II receptor antagonist (ARBs) and opioids. We identified comorbidities associated with scleroderma using ICD 9/10 diagnosis codes, and identified medications using prescriptions or associated procedures. We also evaluated the patients' characteristics across different practice sites.

Results: We identified 12,057 scleroderma patients who had >=1 physician diagnosis in RISE 2015-2017, representing 210 separate sites. After limiting to patients who were 18 year or older, 10,286 patients were eligible for the analysis. The majority of SS patients were female (88.5%) and white (56.8), with average age of 59.6 (SD: 13.8) years. 11% and 12% of patients had a diagnosis codes for ILD and PAH, respectively. Among all eligible patients, 24.5% ever had prednisone, 42% had immunomodulation, 33% had CCB, 9.1% had PDE5, 3.2% have ERAs, 42.7% had PPIs, 10.7% had ACEI, 8.2% had ARBs, and 16.1% had opioids. Only 25 sites reported orders for pulmonary function testing (PFTs) with the proportion of patients undergoing these ranging between 4 and 90% per site.

Conclusion: The RISE registry serves as one of the largest patient cohorts for systemic sclerosis. It is comprised largely of patients from community practices, identified by rheumatologists. The demographics and identified treat-

ments may differ from other academic cohorts but potentially better represents management of patients seen in a general practice. PFT use varies significantly amongst practices, however this finding may be more a reflection of how the registry captures this data and where these tests are performed which is a limitation of this cohort. Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

Disclosure: A. Shah, Beohringer-Ingelheim, 2, Bristol-Myers Squibb, 2, Reata, 2; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **Y. Lee**, Cigna Corp, 1, Eli Lilly, 2, 5, Eli Lilly and Company, 2, Express Scripts, 4, Pfizer, 2; **F. Xie**, None; **L. Chen**, None; **H. Yun**, BMS, 2, Bristol-Myers Squibb, 2, Pfizer, 2.

Abstract Number: 0715

Imaging Technique (R)evolution to Measure the Digital Microcirculatory Flow in Systemic Sclerosis: A Systematic Review

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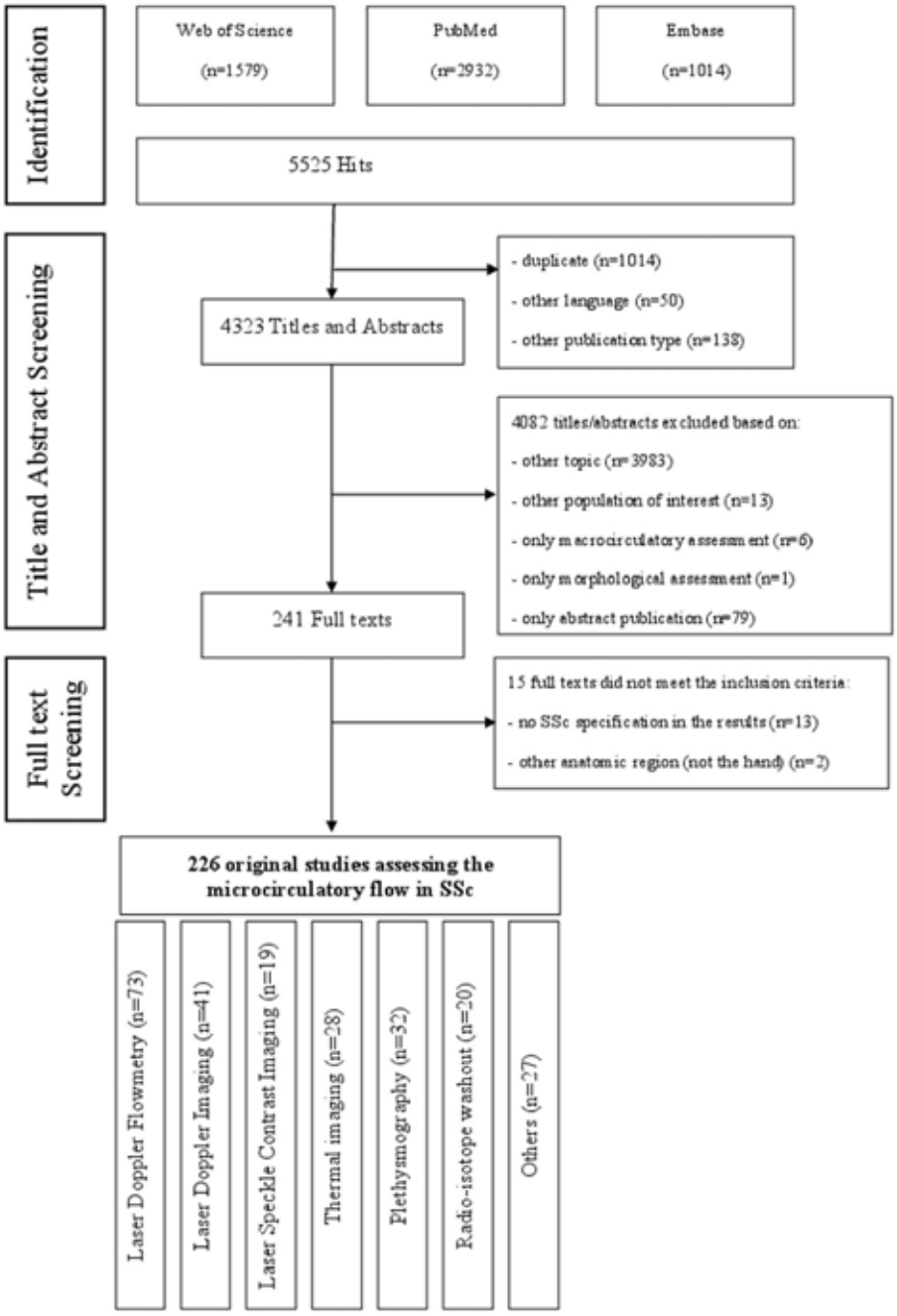
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a chronic, auto-immune disease characterised by a widespread vasculopathy. There is a high need to obtain validated outcome measures for use in clinical and research setting. The last decades numerous techniques have been developed to quantify the microcirculatory flow in the hands of patients with SSc-related digital vasculopathy. The aim of this study is to give a time related overview of the different techniques used to assess the microcirculatory flow in SSc.

Methods: A systematic search was done on the 21st of January 2019 by two reviewers in PubMed, Embase and Web of Science to detect all original studies assessing the microcirculatory flow in SSc patients. Studies including only the morphological aspects of the microcirculation were excluded. The resulting publications were sorted in the following groups: radio-isotope techniques, plethysmography, infrared thermal imaging, laser doppler flowmetry (LDF), laser doppler imaging (LDI) and laser speckle contrast imaging (LSCI). A time dependent evolution in publication rate per technique was evaluated.

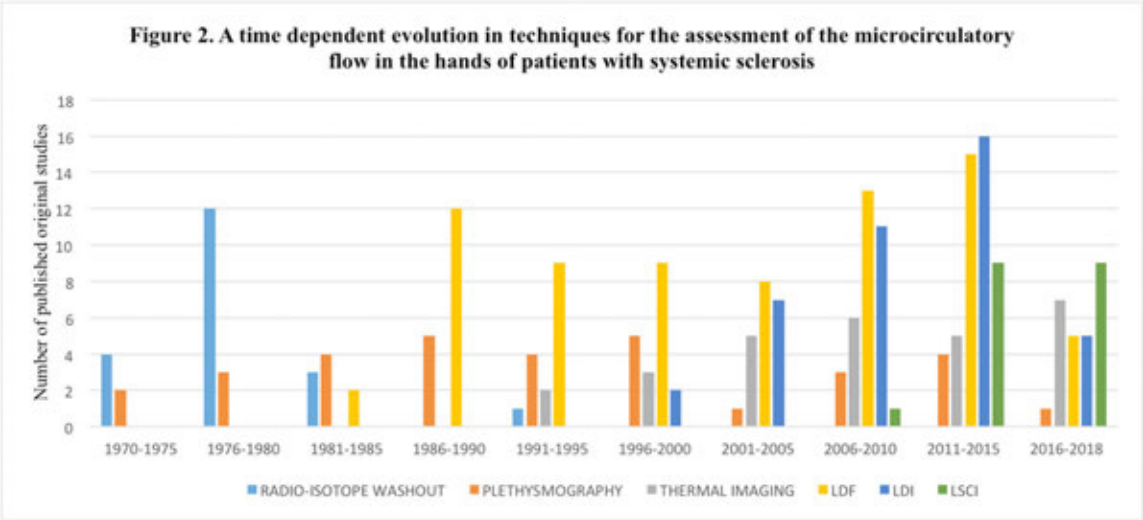
Results: The systematic literature search resulted in 4323 hits. After title and abstract screening 241 original studies were retained. Finally, 15 more full texts were excluded because there were no details of their results on SSc or the region of interest was different (fig 1). The majority of the publications reported on LDF (n=73), though in the last decade emerging techniques are LDI (n=41) and LSCI (n=19). There is a peak in publication rates between 2011 and 2015,

Figure 1. Flowchart of search strategy and results from 1970-2019



especially concerning the laser doppler based techniques. Infrared thermal imaging was steadily investigated in the past 20 years. LSCI is the last upcoming technique with publication rates that are growing in comparison to other techniques (fig 2). Photoacoustic imaging and optical microangiography are two related novel techniques, which are in the pipeline to assess the microcirculatory flow in SSc patients.

Conclusion: This systematic review reveals in a visual way the change in publication rates per technique, and indirectly the change in ongoing investigations concerning the objective quantification of the microcirculatory flow in SSc. The results are in favor of the LSCI technique, which is increasingly being used compared to other techniques.



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Disclosure: K. Melsens, None; **A. Vanhaecke**, None; **W. Van Eenoo**, None; **M. Cutolo**, Boehringer, Actelion, Celgene, Bristol-Mayer Squibb, 2; **V. Smith**, None.

Abstract Number: 0716

Looking for a "Very Early" Nailfold Capillaroscopic Pattern: Specific Alterations of Nailfold Capillaries May Precede the Validated Scleroderma-Patterns in Systemic Sclerosis Patients

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SESSION INFORMATION
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The purpose of this pilot study is to identify, in a cohort of Systemic Sclerosis (SSc) patients, a "very early" nailfold videocapillaroscopy (NVC) pattern able to predict the evolution to the already defined NVC scleroderma-patterns (early (E), active (A), late (L), scleroderma-like (SL)).

Methods: We selected NVC images from 273 patients affected by SSc (according to 2013 ACR criteria) presenting one of the validated NVC scleroderma-patterns [1]: 81 had an "E" pattern, 84 an "A" pattern, 92 a "L" pattern, 16 a "SL" pattern. Among the 273 SSc patients, 54 had a NVC analysis performed before the development of the "E" scleroderma-pattern; thus, we enrolled them for an accurate study of time of evolution and capillaroscopic characteristics. A detailed pilot study of NVC features was initially random performed on 10 of the 54 patients selected. Since we have previously demonstrated that capillary diameter over 30 μm is an independent predictor for development of SSc associated secondary Raynaud's phenomenon (SRP) [2], the analysis included the number and the limbs diameters (arterial, venous, and apical) of capillaries with a diameter over 30 μm, together with the total number of capillaries and microhemorrhages, in 16 images per subject.

Results: The average time of evolution in a scleroderma-pattern was 4 years: 31 (57%) patients developed an "E" scleroderma-pattern in the following 3 years; over longer time, 6 (11%) patients evolved in "A" pattern in 4 years and 3 (6%) patients in "L" NVC pattern in 5 years; 14 (26%) patients developed a "Scleroderma-like" pattern in 4 years. All the 54 SSc patients (100%) showed enlarged capillaries with an average diameter over 30 μm in their previous NVC. The detailed pilot morphological study conducted on 10 patients at last non-specific NVC analysis revealed an average total number of capillaries of 8.6/mm. Capillaries with a diameter over 30 μm were 2.66 (31%); among these, the mean value diameter of the most dilated capillary was 35.74 μm (arterial 33.34 μm, apical 43.94 μm, venous 30 μm). The mean value for microhemorrhages was 0.6/mm. The mean number of capillaries reduced from 8.6±0.8 to 6.9±2.2/mm (p=0.01) during follow-up (4 years).

Conclusion: Present pilot study demonstrates for the first time that, before developing a validated NVC scleroderma-pattern, all SSc patients enrolled present a significant increase of nailfold capillary diameter over 30 μm at NVC. Together with the total number of dilated capillaries, the subsequent reduction in total number of capillaries (as shown at follow up) and the presence of microhemorrhages, it lets to identify a "Very Early" scleroderma pattern, able to intercept patients with SRP at higher risk of evolution in a validated SSc NVC pattern. A larger sample of patients is under investigations.

Reference:

1. Cutolo et al. J Rheumatol 2000;27:155-60; 2.Trombetta et al. J Rheumatol 2016;43:599-606.

Disclosure: M. Pendolino, None; **C. Pizzorni**, None; **S. Paolino**, None; **V. Tomatis**, None; **E. Alessandri**, None; **A. Sulli**, None; **F. Goegan**, None; **V. Smith**, None; **M. Cutolo**, Boehringer, Actelion, Celgene, Bristol-Mayer Squibb, 2.

Abstract Number: 0717

Dental Health in Systemic Sclerosis Patients Risk Factors and Comorbidities

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a rare multisystemic autoimmune disease characterized by microvascular damage and progressive fibrosis of skin and internal organs. Global oral health in SSc may depend by skin fibrosis of oral facial region or masticatory apparatus and quality of bone that is sustaining dentition (1). Trabecular Bone Score (TBS) analysis provides an indirect measurement of microarchitecture and get information about bone quality in several rheumatic diseases such as SSc (2).

Objectives: The aim of the study was to evaluate the most frequent dental/oral alterations in a cohort of SSc patients and the relationship between dental loose and quality of bone evaluated by TBS.

Methods: 32 patients, fulfilling the ACR/EULAR 2013 criteria for SSc underwent a dual-energy X-ray absorptiometry scan (DXA) to evaluate bone mineral density and TBS. All patient performed a standard questionnaire regarding dental health

Results: Patients were 5 men (16%), 27 women (84%), mean age 60.3+8.7 years, disease duration from the first Raynaud symptoms was 13.2+4.5 years. All patients came from urban environment: 65.6% affected by limited SSc (lSSc) and 34.4% by diffuse SSc (dSSc). Most of patients were taking immunosoppressive drugs (MTX 15%, MMF 32%, previous cyclophosfamide treatment 25%, cyclosporine 13%, RTX 6%) and 28 % were treated with only symptomatic drugs (i.e. vasodilators). Nobody was treated with bone antiresorptive drugs (bisphosphonates). Smokers were 19%.

The most frequent oral/dental alterations observed were: oral ulcers 31.3%; painful gums 46.8%; bleeding gums 37.5%; loos teeth 56.3%; dentures 66%; halitosis 46,8%; xerostomia 53.1 (sicca syndrome); swollen gums 25%; receding gums 59%; dental caries 65.6%; cewing issues 28.1%; microstomia 46.9%. The clinical evaluation looking at risk factors found: gastrointestinal involvement with dysmotility and disfagia (31%) and “claw hand” with difficult handgrip and related limited teeth brushing (19%). Most of patients (67%) presented low bone mass and osteopenia, only one case was diagnosed as true osteoporosis. Of note, no statistically differences in TBS were reported between patients with or without dental loose (1.276±0.08 vs 1.19±0.08 P=0.70).

Conclusion: SSc is associated with poor dental health with high prevalence of dental loose. Bone quality assessed by TBS do not seems to influence the unstable dentition and teeth loose; most probably the mechanism is related to ischemic bone area induced by microangiopathy as recently reported in literature (3).

Reference:

1. Jung S et al. Oral Dis. 2017;23(4):424–439. **2**. Ruaro B, et al. Clin Rheumatol. 2018 Nov;37(11):3057-3062. **3.** Puzio A et al. Adv Clin Exp Med 2019;28(4):547-554

Disclosure: S. Paolino, None; **F. Cattelan**, None; **S. Carlotta**, None; **A. Sulli**, None; **A. Casabella**, None; **C. Pizzorni**, None; **M. Cutolo**, Boehringer, Actelion, Celgene, Bristol-Mayer Squibb, 2.

Abstract Number: 0718

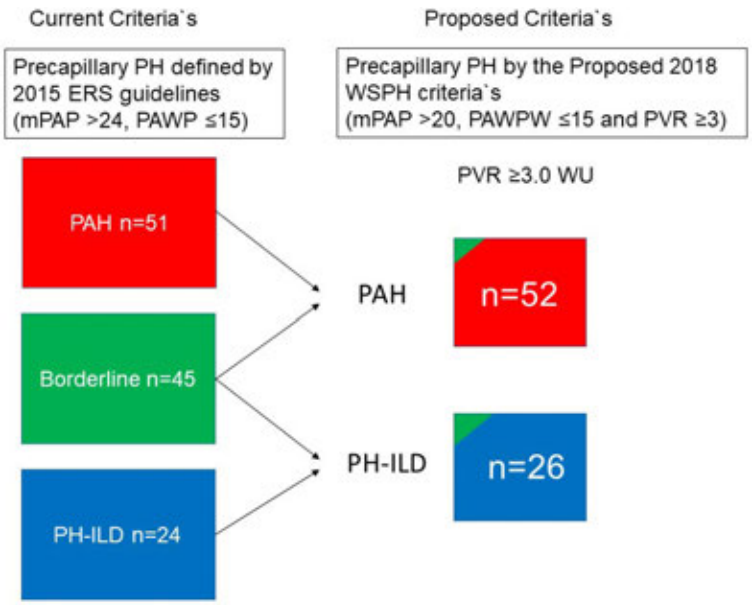
Diagnosing Pulmonary Hypertension Using the Proposed 6th World Symposium on Pulmonary Hypertensions New Definitions

Håvard Fretheim,[1] Øyvind Midtvedt,[2] Torhild Garen,[2] Arne Kristian Andreassen,[2] Einar Gude,[2] Øyvind Molberg,[3] and Anna Maria Hoffmann-Vold[4], [1]Oslo University Hospital, Oslo, [2]Oslo University Hospital, Oslo, Norway, [3]University Hospital Oslo, Oslo, Norway, [4]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, Oslo, Norway

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Pre-capillary pulmonary hypertension (PH) is a feared complication in patients with systemic sclerosis (SSc) and is associated with high mortality despite new treatment options. Pre-capillary PH is diagnosed by right heart catheterization (RHC) with mean pulmonary artery pressure (mPAP) ≥25 mmHg and a pulmonary artery wedge pressure (PAWP) of ≤15 mmHg. The 6th World Symposium on Pulmonary Hypertension proposed new definitions for pre-capillary PH, lowering the mPAP value to ≥ 21 mmHg and including pulmonary vascular resistance (PVR) ≥3.0 Wood Units (WU). The aim of this study was to explore the impact on prevalence of PH in an SSc cohort by applying the new definitions.

Methods: All SSc patients from the Oslo University Hospital SSc cohort who had performed at least one RHC (n=191) were included. We used data from the first RHC with mPAP ≥ 21 mmHg when available. Using the current pre-capillary PH definitions, PH was defined as mPAP ≥25 mmHg and PAWP ≤ 15 mmHg. Borderline PH was defined as mPAP 21-24mmHg. Pulmonary arterial hypertension (PAH) and PH due to interstitial lung disease (ILD) were defined as pre-capillary PH in absence or presence of ILD on high resolution CT scan with < / >10 % pulmonary fibrosis, respectively. Secondly, the newly proposed haemodynamic definitions for pre-capillary PH including mPAP ≥ 21 mmHg, PAWP ≤15 mmHg and PVR ≥3 WU were applied.



Results: Of the 191 SSc patients, 150/191 (79%) were female, 143/191 (75%) had limited cutaneous SSc and 85/191 (45%) were anti-centromere antibody positive. Mean age of the patients was 57 years and mean time from SSc diagnosis to PH diagnosis was 6 years. Using the current PH criteria 51/191 (27%) SSc patients were diagnosed with PAH, 36/191(19%) patients with PH-ILD and 45 (24%) patients with borderline PH. Using the newly proposed definitions the frequency of PAH and PH-ILD changed as shown in Figure 1. 24 patients had an mPAP ≥ 21 mmHg and a PVR value 2.0-2.9 WU. The mean mPAP in these 24 patients was 23.8 mmHg, the mean PAWP 10.1 mmHg, 20/26 (77%) were female and 16/26 (62%) were anti-centromere antibody positive.

Conclusion: Lowering the mPAP to ≥ 21 mmHg and including PVR ≥ 3.0 WU did not substantially change the PH prevalence in our cohort due to the PVR cut-off value. We still need more knowledge about the long-term outcome of SSc patients with pre-capillary PH when changing definitions for pre-capillary PH. Also, it will be important to decide how and when to treat these patients.

Disclosure: H. Fretheim, GSK, 9, Actelion, 9; **Ø. Midtvedt**, ACHIM, 4; **T. Garen**, None; **A. Andreassen**, Actelion, 8; **E. Gude**, Actelion, 8; **Ø. Molberg**, None; **A. Hoffmann-Vold**, Actelion, 5, 8, Boehringer Ingelheim, 2, 5, 8, GSK, 5, 8.

Abstract Number: 0719

Distinct Characteristics of the Gut Microbiome of Patients with Systemic Sclerosis and Small Intestinal Bacterial Overgrowth

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The gastrointestinal tract (GIT) is commonly involved in SSc with up to 98% of patients reporting GIT manifestations. Small intestinal bacterial overgrowth (SIBO) is more prevalent in patients with SSc than the general population, but little is known about the relationship between SIBO and SSc. To better understand the gut microbiota of patients with SSc, we compared fecal bacterial compositions of SSc patients to a healthy cohort. We additionally examined differences in the gut microbiota of SSc patients with or without SIBO and inflammatory seromarkers.

Methods: Adults with SSc (ACR/EULAR criteria) were assessed as having SIBO (SIBO+) or no SIBO (SIBO-) using an H_2/CH_4 breath test. GIT symptoms were assessed using the UCLA SCTC GIT 2.0 questionnaire. To analyze microbiome composition, DNA was isolated from fecal samples of individual patients, and 16S rRNA gene was amplified and sequenced with Illumina technique. The gut microbiota of patients with SSc was compared to controls with no history of autoimmune disease and GIT symptoms. Additional analyses were conducted according to the presence/absence of anti-centromere antibody (ACA) and antibodies against topoisomerase I (Scl-70) in patients with SSc. Microbiome B-diversity of SIBO+ and SIBO- patients was compared using Bray Curtis dissimilarity matrix.

Results: Of 25 SSc patients (mean (SD) age = 56.4 (11.2) years, 96% female), 13 (52%) tested SIBO+, 19 (76%) ACA+, 4 (16%) anti-Scl70+ and 2 (8%) were seronegative. The healthy cohort consisted of 20 participants (mean (SD) age = 33.1 (13.5) years, 70% female). After correcting for multiple comparisons and the effect of age differences, the composition of microbiota in SSc patients was significantly different from healthy controls; notably, patients with SSc

Table 1: Bacterial genera with significantly different relative abundances in SSc patients compared to a healthy cohort. Age-adjusted and corrected for multiple comparisons.

		% of total bacteria Median (IQR)		Q-value
		SSc	Healthy	
SSc > Healthy	Bacteria|Bacteroidetes|bacteroida|Bacteroidales|Odoribacteraceae|Odoribacter	0.23 (0.28)	0.01 (0.02)	0.003
	Bacteria|Proteobacteria|Deltaproteobacteria|Desulfovibrionales|Desulfovibrionaceae|Bilophila	0.07 (0.15)	<0.00 (0.01)	0.002
	Bacteria|Firmicutes|Clostridia|Clostridiales|Lachnospiraceae|Lachnospira	2.17 (4.25)	0.49 (0.74)	0.005
Healthy > SSc	Bacteria|Firmicutes|Erysipelotrichi|Erysipelotrichales|Erysipelotrichaceae	0.20 (0.68)	0.86 (1.33)	0.007
	Bacteria|Firmicutes|Clostridia|Clostridiales|Lachnospiraceae|Coprococcus	0.15 (0.51)	0.69 (0.74)	0.006
	Bacteria|Actinobacteria|Actinobacteria|Actinomycetales|Actinomycetaceae|Actinomyces	<0.00 (0.01)	0.01 (0.02)	0.012
	Bacteria|Actinobacteria|Coriobacteria|Coriobacteriales|Coriobacteriaceae|Adlercreutzia	0.06 (0.11)	0.14 (0.19)	0.012
	Bacteria|Firmicutes|Bacili|Lactobacillales|Streptococcaceae|Lactococcus	<0.00 (0.01)	0.02 (0.04)	0.013
	Bacteria|Firmicutes|Clostridia|Clostridiales|Lachnospiraceae|Pseudobutyrivibrio	1.60 (2.74)	3.69 (9.42)	0.011

Q-value represents p-value corrected for multiple comparisons.

had increased abundance of Odoribacter, Bilophila and Lachnospira species ($p < 0.05$) and decreased abundance of Erysipelotrichaceae, Adlercreutzia, Lactococcus, and Pseudobutyrivibrio species ($p < 0.05$) (Table 1). Compared to SIBO- patients, SIBO+ patients had significantly higher bacterial richness (Chao1 and observed species) and diversity (Shannon diversity index) (Figure 1). Although SIBO+ and SIBO- patients did not have significantly different microbiome compositions, SIBO+ ACA+ SSc patients had significantly higher abundance of Rikenellaceae species in comparison to SIBO- ACA+ SSc patients. SIBO- patients reported significantly more reflux [SIBO+ mean SD 0.59 (0.56), SIBO- 1.31 (0.59), $p < 0.01$], while SIBO+ patients experienced more (but $p > 0.05$) soilage [SIBO+ 0.62 (0.87), SIBO- 0.18 (0.40)] and diarrhea [SIBO+ 0.62 (0.46), SIBO- 0.36 (0.45)].

Conclusion: The current study is the first to examine the relationship between SIBO and SSc on a bacterial level and found notable differences between the microbiota composition of SIBO+ and SIBO- SSc patients. These differences

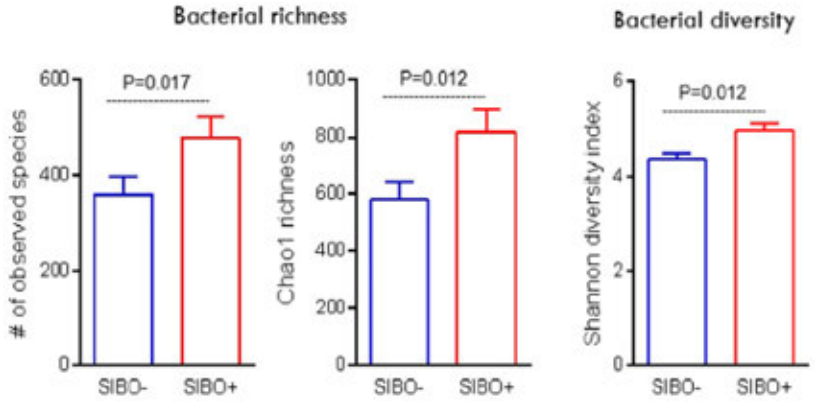

Figure 1. SIBO+ SSc patients had significantly greater bacterial richness and diversity than SIBO- patients.

in gut microbiota appeared to affect the presentation of GIT symptoms. The increased microbiota richness and diversity of SIBO+ patients may exacerbate inflammatory disease activity, and the effects of SIBO on SSc progression and response to treatment warrant further exploration.

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Abstract Number: 0720

Baseline Subject Demographics and Disease Characteristics in a Phase 3 Study of Safety and Efficacy of Lenabasum in Diffuse Cutaneous Systemic Sclerosis

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SESSION INFORMATION
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Table 1. Baseline Demographics and Disease Characteristics (Blinded)

Characteristic at First Dose	Mean (SD) or %		
	Disease duration		
	0 to ≤ 6 years	0 to ≤ 3 years	> 3 to ≤ 6 years
	N = 364 (100%)	N = 241 (66%)	N = 123 (34%)
Years of age	51 ± 13.0	51 ± 12.6	49 ± 13.54
Female	77%	78%	81%
Caucasian Asian Black Other Not stated	64% 23% 5%	Need	Need
Any immunosuppressive drug ≥ 2 immunosuppressive drugs Mycophenolate Corticosteroids Methotrexate Other	77% 35% 48% 25% 23% 27%	78% 38% 48% 29% 26% 26%	75% 28% 48% 16% 14% 29%
Modified Rodnan Skin Score Physician Global Assessment Patient Global Assessment HAQ-DI with aids/devices Forced vital capacity % predicted	22.4 ± 8.2 5.4 ± 1.6 4.9 ± 2.1 1.1 ± 0.76 80.0 ± 17.0	22.2 ± 8.9 5.4 ± 1.6 5.0 ± 2.1 1.1 ± 0.77 81.4 ± 16.3	22.8 ± 6.8 5.4 ± 1.5 4.8 ± 2.2 1.1 ± 0.74 77.1 ± 17.9

Background/Purpose: We report the baseline characteristics of a large cohort of diffuse cutaneous systemic sclerosis (dcSSc) patients enrolled in a Phase 3 trial of lenabasum, a preferential cannabinoid receptor type 2 agonist. Treatment with lenabasum, a cannabinoid receptor type 2 agonist, was safe and well-tolerated in a prior Phase 2 study in dcSSc patients and associated with improvements in ACR Combined Response Index in diffuse cutaneous Systemic Sclerosis (CRISS) score and multiple secondary efficacy outcomes.

Methods: The RESOLVE-1 Phase 3 study was designed with input from Principal Investigators, other study investigators, and regulatory authorities in the US, EU, and Japan. An important intent of the design was to have eligibility criteria that allow testing of efficacy and safety of lenabasum in an inclusive group of dcSSc subjects to maximize relevance to patients in current practice. The study is ongoing and remains blinded.

Results: Primary efficacy outcome is the ACR CRISS score at 12 months, comparing lenabasum 20 mg BID to placebo. Key inclusion criteria are males and females ≥ 18 years of age with dcSSc and disease duration ≤ 6 years who are on stable standard of care medicines, with immunosuppressive mediations allowed. Exceptions are concomitant treatment with > 10 mg per day prednisone or equivalent is disallowed and mRSS needs to be ≥ 15 if disease duration is > 3 to ≤ 6 years. The study enrolled 364 subjects over 15 months who received ≥ 1 dose of study drug at 77 sites in 13 countries in North America (n = 139), Europe (n = 109), and Israel (n = 37), and Asia-Pacific (n = 79), with last subject first visit on May 1, 2019. Baseline characteristics as shown in Table 1. The majority were middle-aged, female, and white, and 77% were on immunosuppressive drugs. Mycophenolate/mycophenolic acid used in 48% of subjects, and 35% of subjects took ≥ 2 concurrent immunosuppressive drugs (max = 4 concurrent). Subjects with disease duration ≤ 3 years and > 3 to ≤ 6 years had similar demographics and disease characteristics, except a lower proportion of the subjects with longer disease duration were on methotrexate (p = 0.041, Chi-square), low dose corticosteroids (p = 0.006, Chi-square), or multiple immunosuppressive medications (p = 0.055, Chi-square). Subjects with longer disease duration also had slightly lower FVC % predicted (p = 0.018, t-test).

Conclusion: This is the first Phase 3 study to use ACR CRISS as the primary efficacy outcome, a composite outcome of multiple clinically relevant measures of SSc, and the largest interventional study to date in diffuse cutaneous SSc. Benefits of having inclusive eligibility criteria are that they facilitated timely full enrollment and will make the study population representative of real-world practice, if trial is positive. This study provides a template for Phase 3 dcSSc trials and will give valuable information on outcome with routine care as well as test efficacy of lenabasum.

Disclosure: R. Spiera, Actelion, BIPI, 2, Chemocentryx, 2, 5, Corbus Pharmaceuticals, 2, Cytori, 2, EMD Serono, Evidera, Formation Biologics, 2, Genentech, Genentech/Roche, 2, 5, Glaxosmithkline, 2, 5, InflaRx, InterMune, Janssen, 5, Litmus, Novartis, PPD/GSK, Sanofi, 2, 5; **N. Dgetluck**, Corbus Pharmaceuticals, 3, 4; **B. Bloom**, Corbus Pharmaceuticals, 3, 4; **B. White**, Corbus Pharmaceuticals, 1, 3, 4, 6; **C. Denton**, Actelion, 5, Actelion Pharmaceuticals, 5, Actelion, GlaxoSmithKline, Bayer, Sanofi, Inventiva, Boehringer Ingelheim, Roche, Bristol Myers Squibb, CSL Behring, UCB, Leadiant Biosciences, 5, Bayer, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Corbus Pharmaceuticals, 5, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, Leadiant Biosciences, 2, 5, Inventiva, 5, Pfizer, 5, Roche, 5, Sanofi, 5, UCB, 5.

Abstract Number: 0721

Ultrasound Measurement of the Nail Bed Matrix Thickness as a Useful Marker for Scleroderma-Related Interstitial Lung Disease

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Background/Purpose: Lung involvement is the leading cause of death in systemic sclerosis (SSc) (1). Pulmonary function tests (PFTs) and chest high-resolution CT scan (HRCT) are used to confirm this common complication.

We performed high resolution musculoskeletal (MSK) ultrasound of the nailbed to assess digital clubbing and attempted to correlate with the presence of scleroderma-related interstitial lung disease (SSc-ILD).

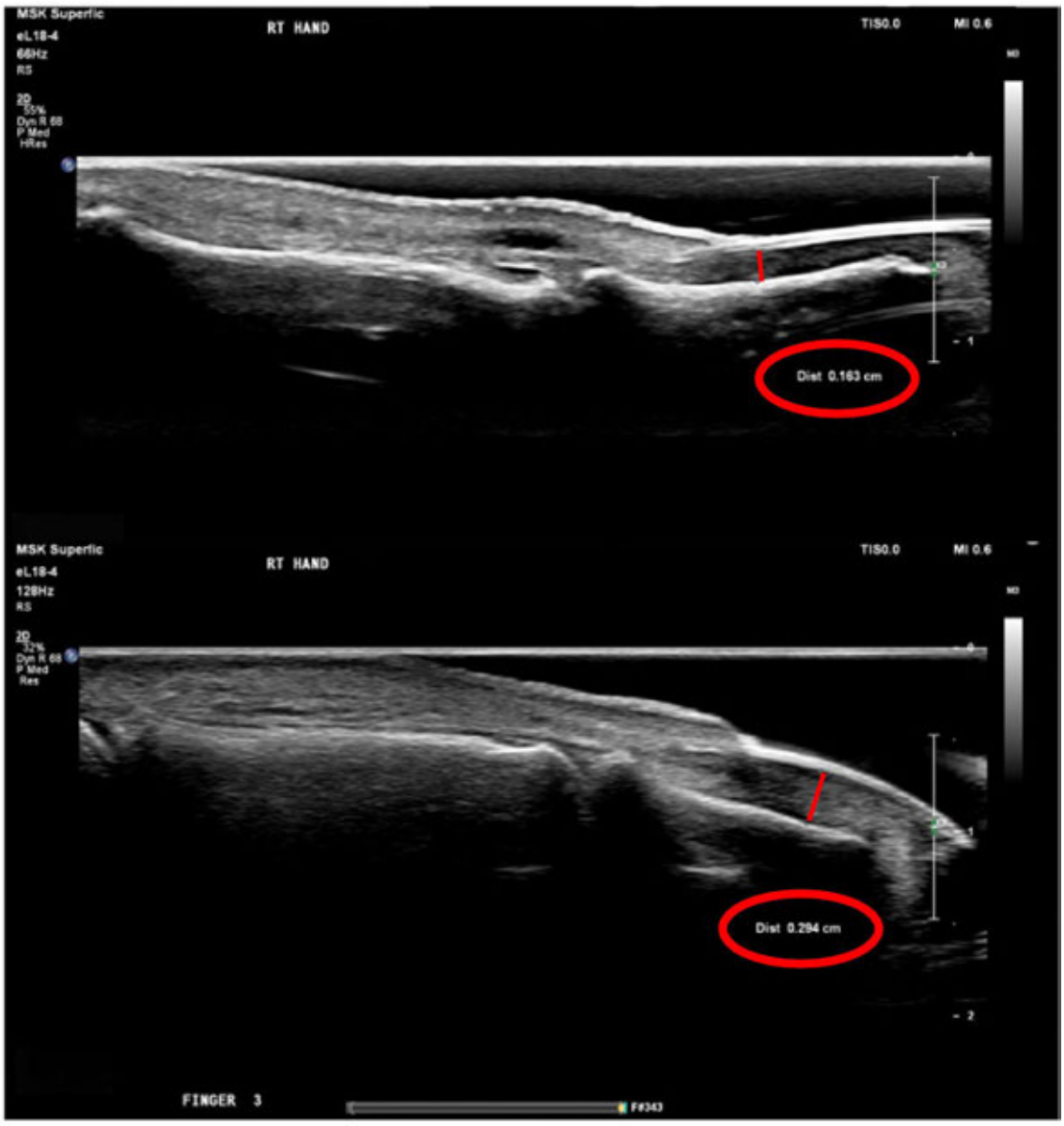

Figure 1. Ultrasound 2D Mode (long axis view) of the third finger's distal phalanx in two SSc subjects with normal (top) and abnormal (bottom) nail bed matrix thickness (NBMT). Red line represents the NBMT, measured distance between volar plate of the nail and dorsal surface of the distal phalanx bone.

Table 1: Clinical characteristics and NBMT measurements in control population and SSc patients with and without ILD

	Controls N=18	SSc (No ILD) N=12 (SD)	SSc (ILD) N=17 (SD)	p value
Disease duration in years, mean (SD)		9.3 (9.2)	10.2 (7.8)	NS
Age, mean (SD)	50.4 (17.4)	45.8 (16.3)	57.9 (14.8)	0.136
Sex, n (%)				0.105
Female	18(100%)	10(62.5%)	13 (76.5%)	
Male	0	2 (16.6%)	4 (23.5%)	
Race, n (%)				0.127
Caucasian	11 (61.1%)	11(91.7%)	13 (76.5%)	
African American	4 (22.2%)	1 (8.3%)	3 (17.6%)	
Other	3 (16.6%)		1 (5.9%)	
Ethnicity, n (%)				0.632
Hispanic	1 (5.5%)	2 (16.7%)	2 (11.8%)	
Non-Hispanic	17(94.5%)	10 (83.3%)	15 (88.2%)	
Mean NBMT levels (in mm) (SD)				
1-st finger	1.94 (0.51)	1.95 (0.25)	2.17 (0.40)	0.197
2-nd finger	1.64 (0.34)	1.86 (0.20)	2.09 (0.49)	**0.005**
3-rd finger	1.77 (0.25)	1.89 (0.25)	2.25 (0.52)	**0.001**
4-th finger	1.61 (0.35)	1.76(0.37)	2.09 (0.53)	**0.006**
5-th finger	1.39 (0.40)	1.36(0.29)	1.65 (0.45)	0.086
Average for five fingers	1.65 (0.36)	1.76 (0.22)	2.05 (0.44)	**0.007**

SD – standard deviation from mean value; NS – not significant differences; p value<0.05 was statistically significant (ANOVA)

Table 2: Subgroup analysis of PFTs in SSc patients with normal and increased NBMT

PFT parameters*	SSc patient with normal NBMT n=14 Mean (SD)	SSc patient with increased NBMT n=16 Mean (SD)	p value
%TLC	84.9 (19.6)	79.0 (19.4)	0.440
%FVC	90.2 (21.0)	79.6 (15.4)	0.120
%DLCo	69.7 (20.9)	53.7 (18.0)	**0.035**

*TLC - total lung capacity, FVC - forced vital capacity, DLCO - diffusing capacity for carbon monoxide; SD-standard deviation p-value <0.05 was statistically significant (by ANOVA)

Since Hippocratic times, digital clubbing has been described in patients with hypertrophic osteoarthropathy (2), associated with many chronic illnesses such as cardiovascular and pulmonary diseases (3). Digital clubbing is associated with abnormal proliferation of skin and periosteal tissues of the fingertips characterized by periostosis of

tubular bones, uniform swelling of soft tissues of the terminal phalanx and increased nail-to-nail bed angle (4). The increased nail bed matrix thickening (NBMT) is associated with digital clubbing, normal reported 1.7+/-0.18mm (5). Our hypothesis is that measurement of the NBMT by MSK Ultrasound can be an effective marker for clinically significant SSc-ILD.

Methods: In this IRB-approved study, we evaluated the dominant hand of 47 subjects by MSK ultrasound. Twenty-nine patients met the 2013 ACT criteria for SSc (6) and were divided into 2 subgroups (Group 2A with ILD and Group 2B without ILD). Eighteen subjects served as the age-matched control group (group 1, no SSc). Using the Phillips Epiq 5, all subjects underwent MSK ultrasound of the dominant hand utilizing linear high frequency probe with 2-22 MHz frequency. The NBMT of all 5 fingers were examined and 235 nail beds were recorded. SSc-ILD was confirmed by HRCT associated with restrictive pattern on PFTs. We used ANOVA testing to calculate differences between groups and a p-value < 0.05 was statistically significant.

Results: Table 1 shows a significantly higher NBMT for the 2nd, 3rd and 4th fingers in the SSc lung cohort, and interdigital analysis determined that the 3rd finger NBMT had the highest NBMT between the fingers. The mean cutoff value for normal NBMT in the 3rd finger was less than 2.27mm. The PFT parameters of SSc cohort (Table 2) showed a trend towards increased NBMT in those with SSc-ILD, although only %DLCo was significant in our small cohort.

Conclusion: Our study suggests common mechanisms that may be responsible for digital clubbing in SSc resulting from chronic local tissue hypoxia due to chronic lung disease (7). This is readily visible by MSK ultrasound, often before it is evident on physical exam and may be a predictor of more clinically significant pulmonary disease. We found that a NBMT greater than 2.27mm in the 3rd finger was associated with presence of SSc-ILD. Larger studies are needed to verify our findings.

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Disclosure: M. Sidor, None; **R. Zuckerman**, None; **N. Schlesinger**, amgen, 2, horizon pharma, 5, IFM Therapeutics, 5, Mallinckrodt Pharmaceuticals, 5, Novartis, 5, olatec, 5, pfizer, 2, Selecta Biosciences, 5; **R. Sussman**, None; **H. Sabahath**, None; **V. Hsu**, None.

Abstract Number: 0722

The Lymphangiogenetic Factor VEGF-C and Its Receptor VEGFR-3 Are Associated with Pulmonary Arterial Hypertension in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary arterial hypertension (PAH) is a major complication in systemic sclerosis (SSc) and is characterized by abnormalities in vascular pathways. In murine models of PAH increased lymphangiogensis has been shown in lung tissue by elevated vascular endothelial growth factor receptor 3 (VEGFR-3) expression, which is a known lymphatic marker. The ligand acting through VEGFR-3 is vascular endothelial growth factor C (VEGF-C), a major growth factor in the lymphatic vessels under physiological conditions. We have shown that VEGF-C is down-regulated in SSc patients and aim to assess the characteristics of VEGF-C and its receptor VEGFR-3 in SSc patients, and investigate the VEGF-C/VEGFR-3 axis in SSc-PAH.

Table 1. Longitudinal clinical and demographic data.

	OUH Identification cohort			USZ Validation cohort		Healthy controls
	Total (n=457)	PAH (n=47)	No PH (n=57)	Total (n=95)	PAH (n=21)	HC (n=68)
Age at disease onset, yrs	51.8 (15.3)	58.1 (3.0)	50.9 (1.6)	50.1 (15.8)	44.4 (4.0)	n.a.
Time from onset to PAH, yrs	n.a.	6.8 (1.6)	n.a.	n.a	9.8 (3.4)	n.a.
Females, no (%)	383 (83.8)	38 (77.5)	46 (85.3)	74 (77.9)	18 (85.7)	46.0 (67.6)
Deceased, no (%)	112 (21.3)	24 (60.0)	17 (22.7)	n.a.	n.a.	n.a.
Limited cutaneous SSc, no (%)	354 (77.5)	43 (89.5)	40 (77.3)	65 (80.2)	13 (72.2)	n.a.
Anti-Centromere Ab, no (%)	249 (54.4)	28 (70.0)	43 (56.8)	34 (39.5)	12 (57.1)	n.a.
Mean VEGF-C level, ng/ml (SE)	2.10 (0.04)	1.80 (0.12)	2.12 (0.10)	1.33 (0.09)	1.05 (0.13)	2.89 (0.12)
Mean VEGFR-3 level, ng/ml (SE)	1.57 (0.18)	2.29 (0.79)	1.67 (0.56)	0.81 (0.19)	0.66 (0.23)	0.50 (0.06)

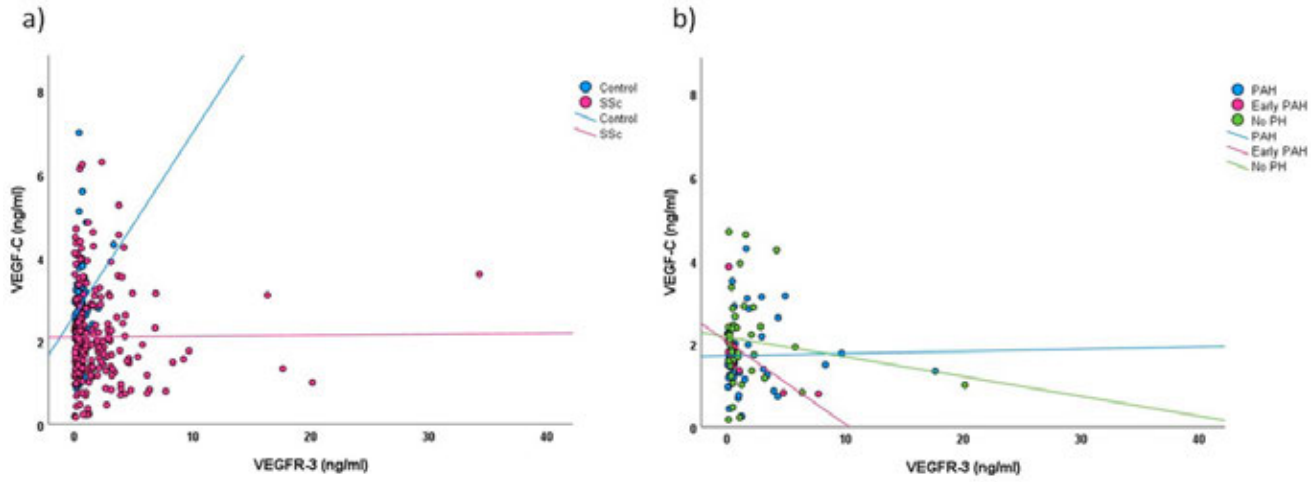

Figure 1. Correlation between VEGF-C and VEGFR-3 levels in a) Systemic sclerosis patients and healthy controls, and b) PH-patients in OUS and USZ cohorts combined.

Methods: Sera samples from the SSc cohorts at Oslo University Hospital (n=457, identification cohort) and Zurich University Hospital (n=95, validation cohort), as well as age and gender matched healthy controls (n=68) were included in the study, and analyzed for soluble VEGF-C and VEGFR-3 levels by Luminex kits from Millipore. SSc patients with clinically suspect PH were referred to right heart catheterization (RHC). Mean pulmonary arterial pressure (mPAP) ≥21 mmHg in the absence of significant interstitial lung disease and a PVR ≥ 3 Wood Units (WU) was defined as PAH, whereas PVR < 3 WU was defined as early PAH. Descriptive statistics were performed and correlations were calculated by non-parametric Spearman's rho analysis.

Results: The demographics and clinical data of SSc patients were similar in the Oslo identification and Zurich validation cohorts (Table 1), and were assembled for further analysis. Serum levels of VEGF-C were significantly lower in SSc patients than in healthy controls (2.1±0.04 ng/ml vs. 2.9±0.12 ng/ml, p< 0.001), while serum levels of VEGFR-3 were significantly higher in SSc compared to healthy controls (1.8±0.20 ng/ml vs. 0.5±0.06 ng/ml, p=0.001) in both cohorts. A total of 238 (43.1%) patients were assessed by RHC. Patients with post-capillary (n=51), PH-ILD (n=32) and early PH-ILD (n=6) were excluded, while the remaining 149 RHC verified patients were included in the investigation of VEGF-C and VEGFR-3 serum levels; including 68 patients with PAH, 22 with early PAH and 59 with no PH. Correlation of VEGF-C and VEGFR-3 were weak in SSc patients and healthy controls (r=0.1, p=0.150 vs. r=0.3*, p=0.020), and the difference between the correlation coefficients were not significant (p=0.083). The correlation between VEGF-C and VEGFR-3 in SSc cases having RHC findings of PAH and no PH were also weak (r=0.3*, p=0.034 vs. r=-0.1, p=0.337) with no significant difference between the correlation coefficients (p=0.057). Notably, the correlation in early PAH subjects were strong (-0.8*, p=0.001), and there was a significant difference between the correlation coefficients of early PAH and PAH (p=0.001) and early PAH and no PH groups (p=0.003) (Figure 1).

Conclusion: VEGF-C and its receptor VEGFR-3 is associated with SSc, and the observed skewing of VEGF-C/VEGFR-3 ratios in early and established PAH indicates dysregulation of the VEGF-C/VEGFR-3 axis during development of PAH.

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Abstract Number: 0723

Diagnosis of Systemic Sclerosis: How and When

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Systemic sclerosis (SSc) is a heterogeneous disease regarding its clinical expression, evolution and forms of presentation. In spite of the lack of a disease modifying therapy, there are effective treatment options to control complications such as pulmonary arterial hypertension (PAH), interstitial lung disease (ILD) or digital ulcers (DU). Early diagnosis is crucial and allows the physician to start these treatments as soon as possible. Our objetive is to study the main clinical manifestations that lead to diagnosis of SSc, the delay of the diagnosis after the beginning of the first symptom, and to analyze the role of the different clinical features in the diagnosis.

Methods: A retrospective and descriptive study was conducted, which included patients with SSc from our Rheumatology Department. Clinical data and specific autoantibodies profile (ACA, Scl-70, RNP) were recorded, paying special attention to the clinical manifestations that led to diagnosis. We classified them in eight categories: secondary Raynaud's phenomenon (SRP), digital ischemia or DU, musculoskeletal symptoms, skin induration, ILD, PAH, specific autoantibodies detection, and others. The date of starting of Raynaud's phenomenon (RP), of the first non-Raynaud symptom and the date when the diagnosis was established were registered. Analysis were conducted using STATA.

Results: The sample included 149 patients with SSc, meeting the 2013 ACR/EULAR criteria. RP appeared several years prior to the diagnosis (median of 3 years, IQR 0-8), and typically before the first non-Raynaud symptom. 141 out of 149 patients (94,6%) presented RP prior to the diagnosis. However, SRP was the manifestation that led to diagnosis in only 42/149 patients (41,6%), followed by skin induration (18,1%) and DU (12,7%). Surprisingly, 30/149 patients (20,1%) were diagnosed after the appearance of severe complications such as DU, ILD or PAH. Most patients started symptoms related to SSc several years before diagnosis (details in Table 1). 40/48 patients (83%) that were diagnosed due to SRP, presented abnormalities in nailfold capillaroscopy as well as specific autoantibodies (Table 2). Presenting telangiectasia, calcinosis, ILD or PAH was not associated with an early diagnosis, nor was ACA, Scl-70 or RNP positivity.

Table 1. Signs and symptoms that led to the diagnosis of SSc. n (%) are shown.

Clinical manifestation that leads to diagnosis	Patients	Years from first symptom to diagnosis	Years from Raynaud's phenomenon to diagnosis
	n (%)	median (IQR)	median (IQR)
Raynaud's Phenomenon	62 (41,6)	3 (1-10)	3 (1-9)
Skin induration	27 (18,1)	1 (0-4)	1 (0-4)
Digital Ischemia/UD	19 (12,7)	2 (0-12)	2 (0-12)
Musculoskeletal symptoms	18 (12,1)	3 (0-6)	3,5 (0-6)
ILD	8 (5,3)	2,5 (1-4)	3 (0-4)
Specific autoantibodies	6 (4)	5,5 (4-9)	3 (0-9)
Others	6 (4)	5,5 (0-10)	5,5, (0-10)
PAH	3 (2)	35 (20-35)	35 (20-35)

Table 2. Frequency of positive antibodies (%) in patients with RP and abnormal capillaroscopy.

Patients with Raynaud's Phenomenon	n (%)
With abnormal capillaroscopy	48/59 (81)
...and only ACA+	36 (75)
...and only anti Scl-70+	3 (6,2)
...and only anti-RNP+	2 (4,1)
... and ACA+ and/or Scl70+ and/or anti-RNP+	40 (83,3)
... without autoantibodies	8 (16,6)

Conclusion: One out of five patients with SSc was diagnosed after the onset of complications. The study of RP by capillaroscopy and specific antibodies allows to reach the diagnosis of early SSc in up to 83% of patients. Early referral of patients with RP to the Rheumatologist and a multidisciplinary management of complications would improve the diagnosis of this potentially serious disease.

Disclosure: C. Sobrino, None; **C. De la Puente**, None.

Abstract Number: 0724

Biomechanical Properties of Skin for Assessment of Scleroderma: A Systemic Review

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

Background/Purpose: Skin involvement is one of the early features of scleroderma and an important predictor of internal organ involvement and mortality. Skin fibrosis alters the normal dermal architecture and compromises biomechanical skin properties. Therefore, biomechanical parameters can not only provide quantitative assessment of the disease severity, but also help physicians monitor disease progression. However, no systemic review has summarized recent findings about the role of biomechanics in the assessment of scleroderma. This systemic review evaluates the effectiveness of biomechanical tools in diagnosing and tracking skin diseases for patients with scleroderma.

Methods: A comprehensive search of PubMed/Medline and Cochrane databases was performed until May, 2019. In addition, a manual search was conducted in which reference lists of selected articles were screened to include relevant ones. Several related synonyms were used, including biomechanics, scleroderma and assessment. Selection criteria included studies that were comprised of participants with either limited cutaneous (lcSSc) or diffuse cutaneous systemic sclerosis (dcSSc), with a sample size greater than 20, and investigated at least one biomechanical property of the skin.

Results: 46 relevant studies were identified and 12 articles were eligible to be included in this review, with a total of 212 participants. The techniques developed for quantitative measurements of skin properties included durometer (2 articles), indentation (2 articles), suction method (3 articles), surface wave technique (2 articles), ultrasound (1 article), atomic force microscopy (1 article) and photoacoustic elastic tomography (1 article). All studies reported at least one skin biomechanical property that was significantly different in patients with scleroderma compared to normal controls. The skin of patients with scleroderma was found to have decreased extensibility ($p< 0.05$), increased stiffness ($p< 0.03$), and decreased skin viscoelasticity ($p < 0.03$ in patients with dcSSc). Besides, skin sclerosis was associated with smaller difference in viscoelasticity among different anatomic sites ($p < 0.05$). One study reported that some anatomic sites of patients already showed significantly different biomechanical properties ($p < 0.05$), even with a modified Rodnan score of 0, suggesting that biomechanical measurements could be helpful for diagnosis at early stages and might provide more sensitive assessment of disease progression.

Conclusion: Current evidence suggests that biomechanical properties of the skin can be used as a marker for diagnosis and monitoring of disease progression in scleroderma. Compared to the modified Rodnan skin score, they may

provide a more objective, reliable and sensitive way to evaluate skin disease. Rigorous and large-scale randomized control trials are warranted to further assess the clinical value of tracking skin biomechanical properties in patients with scleroderma.

Disclosure: P. Ni, None; **L. Garibyan**, None; **R. Anderson**, None.

Abstract Number: 0725

Amniotic Membrane Dressings Provide an Effective Treatment for Systemic Sclerosis Digital Ulcers

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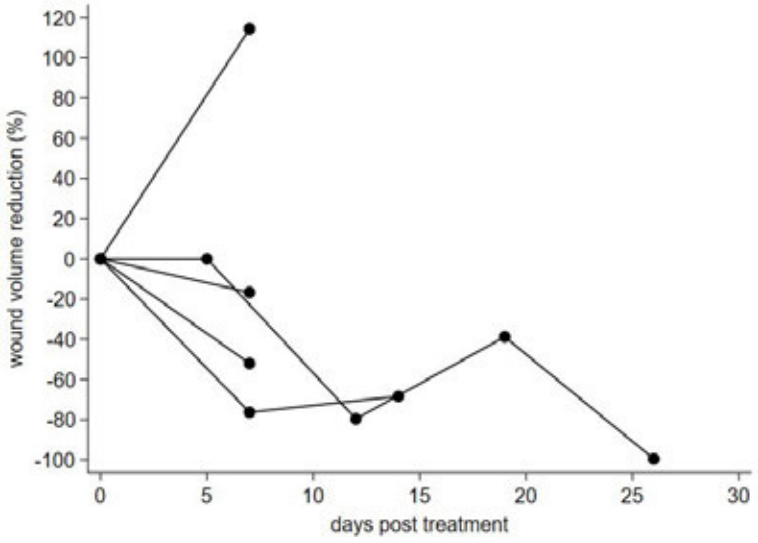
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc)-related digital ulcers are a major burden for patients. The purpose of this study was to assess the effectiveness of amnion membrane treatments on healing rate as determined by manual and ultrasound weekly measurements.

Methods: SSc patients that met 2013 ACR/EULAR classification criteria and presented to clinic with a digital ulcer between 02/2019-05/2019 were consented to participate. Consented participants were asked to complete a Raynaud's Condition Score (RCS), Hand Mobility in Scleroderma (HAMIS), Scleroderma Health Assessment Disability Questionnaire (HAQ-DI), and return every 5-7 days for a wound nurse's visit until complete healing. All patients received education on wound care management including assessment, cleaning, and dressing. The volume of the wound was calculated and change in volume was tracked over time at the time of wound care.



Wound volume change with amniotic membrane dressing

Results: During the two-month study period, 15 SSc patients with a DU were approached for consent at the time of their routine SSc care visit. Two patients refused consent due to perceived burden of participation. Of the 13 consented patients, nine patients subsequently withdrew due to burden of participation; length questionnaires and driving to wound care were the most common reported reasons. Five patients had at least two formal measurements of their DU during wound care. Three patients did not return to wound care after the first follow-up visit due to complete healing reported. The demographics of the 5 SSc patients that returned for care included three female; four white patients; three limited cutaneous SSc, with a mean age of 62 (SD 11). The duration from first non-RP symptom of SSc was 5.8 years (SD 4). Wound volume (length x width x depth) ranged from 3 to 182 mm^3. Two wounds (3 mm^3 and 9 mm^3) healed completely after one application and these patients did not return to wound care. One wound (39.2 mm^3) was over a joint contracture and traumatic in origin increased in volume at follow-up measurement. The change in wound volume of these 5 wounds over time after amnion dressing was applied is shown in **Figure 1**. None of these SSc wound patients completed all questionnaires.

Conclusion: Assessments of SSc-related DU healing must minimize patient burden; the appropriate number of questionnaires used for assessment must be carefully assessed in the study design of this outcome, and remote wound monitoring should be considered. DU healing can be measured effectively by weekly ultrasound that estimates wound volume. Amnion membrane dressings are effective for wound healing in this patient population, especially for wounds that are vascular in origin.

Disclosure: T. Frech, None; **J. Pierce**, None; **G. Stoddard**, None; **C. McNeill**, None; **M. Radic**, None; **J. Reems**, None.

Abstract Number: 0726

Digital Blood Perfusion Differences Between Black Africans and Caucasians with Systemic Sclerosis

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SESSION INFORMATION
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Background/Purpose: Microvascular dysfunction is a prominent feature in SSc. Laser speckle contrast analysis (LASCA) has been shown to be a reliable tool to quantify skin blood perfusion (BP) in SSc (1,2). Patients of African descent have a more severe disease burden than their European counterparts (3). Data are lacking on race/ethnic related differences in peripheral BP measured by LASCA in SSc. The objective of this study was to assess and compare BP at the level of fingertips between black Africans and Caucasians.

Methods: Forty black Africans and 29 Caucasian consenting patients fulfilling 2013 ACR/EULAR classification criteria for SSc were enrolled at 2 different geographic sites. Cutaneous BP in the hands was assessed by LASCA, calculating flows in regions of interest created at the 2-5 volar and dorsal fingertips (4). Standardized protocols for instrumental, environmental and patient conditions were applied at both study sites (1). Median BP was reported as perfusion units (PU).

Table 1. Digital blood perfusion between black Africans and Caucasians with systemic sclerosis

	Median volar fingertip blood perfusion (PU)		
Variable	Black Africans (n=40)	Caucasians (n=29)	p-value
Females	58.73 (n=35)	131.89 (n=23)	0.001
Males	59.40 (n=5)	133.28 (n=6)	0.018
Disease duration > 5 years	55.48 (n=23)	138.82 (n=10)	0.003
LcSSc	65.64 (n=13)	135.13 (n=24)	0.026
DcSSc	55.48 (n=23)	98.18 (n=5)	0.031
Skin score fingers none/mild	53.86 (n=22)	76.62 (n=12)	0.061
Skin score fingers moderate/severe	62.52 (n=18)	138.37 (n=12)	0.000
Anti-centromere+	139.03 (n=2)	124.85 (n=5)	1.000
Anti-topoisomerase 1+	57.44 (n=6)	130.04 (n=14)	0.008
Calcinosis	52.51 (n=6)	93.78 (n=1)	0.617
Current DU and/or Pits	54.17 (n=24)	201.74 (n=6)	0.001
Pits	54.17 (n=24)	199.86 (n=5)	0.002
Vasodilator CCB	58.73 (n=39)	199.86 (n=11)	0.001

PU: perfusion units; DU: digital ulcers; CCB: calcium channel blocker

Digital blood perfusion between black Africans and Caucasians with systemic sclerosis>

Results: With respect to demographic and clinical characteristics, the significant differences between the 2 cohorts were that blacks were younger (mean age 48.5±9.9 vs 55.5±12.3 years, p=0.01), had a longer disease duration (mean 9.2±7.1 vs 5.8±6 years, p=0.04), a greater proportion of the diffuse cutaneous disease (67.5% vs 17.2%, p< 0.001), and were more likely to be on vasodilator calcium channel blocker therapy (97.5% vs 37.9%, p< 0.0001), compared to Caucasians. In both groups the median BP values were significantly higher for the volar fingertips compared to dorsal fingertips (Blacks: 59.07 vs. 37.39 PU, p=0.0002; Caucasians: 131.89 vs. 96.64 PU, p=0.03). Table 1 shows the univariate analysis comparing the groups with respect to demographics, disease subsets, autoantibodies and selected clinical features in relation to volar fingertip BP measured by LASCA. Overall, the average BP was significantly lower in blacks compared to Caucasians (59.07 vs. 131.89, p=0.0001). Multivariable analysis showed that when using Caucasian females as the referent group, black females and males has significantly lower digital BP (t= -3.86, p< 0.0001; t= -2.93, p=0.005, respectively), with black females showing the lowest BP.

Conclusion: This study shows better BP at the volar fingertips compared to the dorsal fingertips in both groups. We found several differences in digital BP between blacks and Caucasians with SSc. Caucasian females had the best BP and black females had the most impaired digital BP. These racial differences in peripheral BP warrant further investigation of possible ethnic differences in endothelial function.

References:

1. Lambrecht V, et al. Ann Rheum Dis 2016; 75: 1263-64.
2. Cutolo M, et al. Autoimmunity Reviews 2018; 17: 775-80.
3. Morgan ND, et al. Medicine 2017; 96 (51). 4) Ruaro B, et al. Ann Rheum Dis 2014; 73: 1181-85

Disclosure: C. Ickinger, None; **V. Lambrecht**, None; **E. Musenge**, None; **M. Tikly**, None; **M. Cutolo**, Boehringer, Actelion, Celgene, Bristol-Mayer Squibb, 2; **V. Smith**, None.

Abstract Number: 0727

Mortality and Morbidity in Scleroderma Renal Crisis: A Systematic Literature Review

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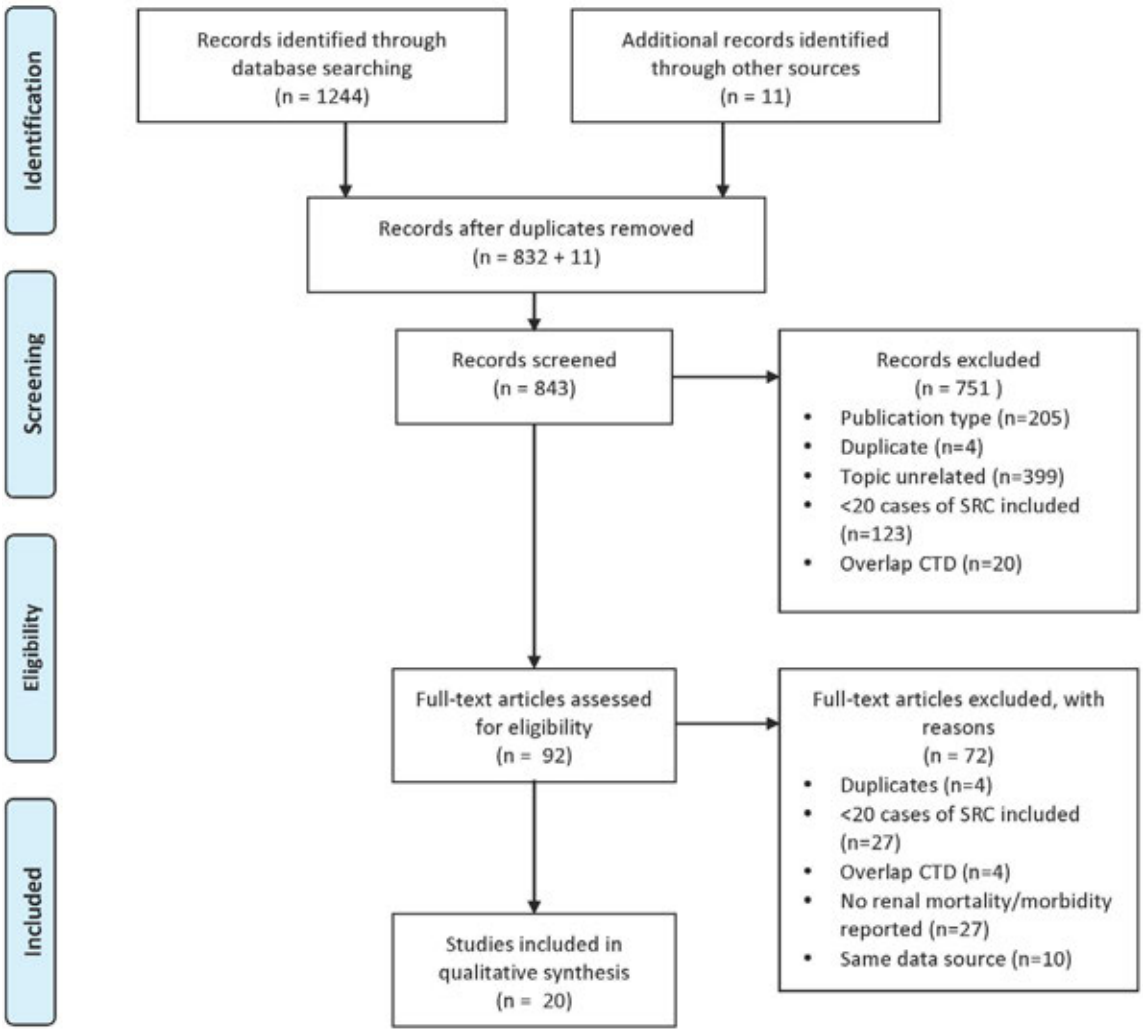
Figure 1 Flow Diagram



Search Results: Studies identified from search strategy with reasons for exclusions.

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

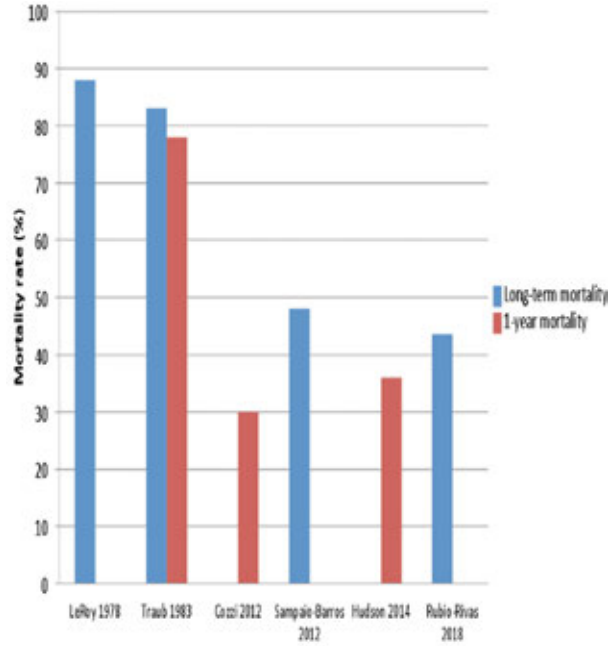


Figure 2. Mortality in scleroderma renal crisis and trends over time

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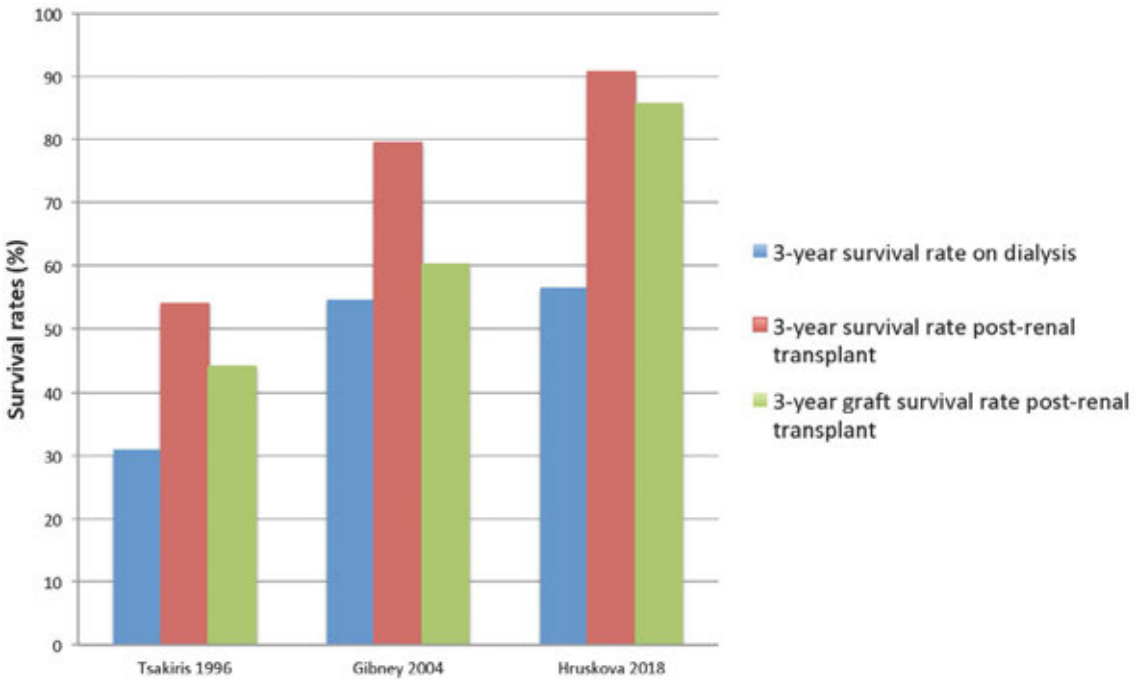

Figure 3. 3-year outcomes in SSc-end stage renal disease

Figure 3. 3-year outcomes in scleroderma end stage renal disease.

Background/Purpose: The introduction of angiotensin converting enzyme (ACE) inhibitors in the early 1970s resulted in marked improvement in clinical outcomes of scleroderma renal crisis (SRC).Despite the undisputed improvement in outcomes of SRC since the availability of ACE inhibitors, estimates of mortality and morbidity vary considerably. The objective of this study was to systematically review the mortality and morbidity associated with SRC and to determine temporal trends.

Methods: We searched Medline, EMBASE and the Cochrane Database of Systematic Reviews from database inception to January 15, 2019. Bibliographies of selected articles were hand-searched for additional references. Data were extracted using a standardized extraction form. Study quality was assessed using the Newcastle-Ottawa scale. Results were analyzed qualitatively.

Results: Twenty studies with 14,059 SSc subjects, of which 854 had SRC and 4095 had SSc-associated end stage renal disease (SSc-ESRD), met inclusion criteria. Study quality was generally moderate. Cumulative mortality in the post-angiotensin converting enzyme (ACE) inhibitor era was approximately 20% at 6 months, 30-36% at 1 year, 19%-40% at 3 years and almost 50% at 10 years from SRC onset. Although the introduction of ACE inhibitors in the early 1970s resulted in a 50% improvement in SRC mortality, there was no further improvement thereafter. SRC mortality rates were proportionally higher than mortality rates associated with other SSc organ involvement. The rate of permanent dialysis after SRC in the post-ACE inhibitor era ranged from 19-40%. Three to 17% of SSc patients underwent renal transplant. Survival was better in patients post-renal transplant (54-91%) compared to those on dialysis (31-56%). Graft survival improved over time and appeared similar to that of patients with other types of ESRD.

Conclusion: SRC mortality and morbidity remain high. Novel treatments are required to improve outcomes of SRC.

Disclosure: H. Kim, None; **F. Lefebvre**, None; **S. Hoa**, None; **M. Hudson**, None.

Abstract Number: 0728

Nailfold Videocapillaroscopy Patterns and Digital Occlusive Arterial Disease on Laser Doppler Flowmetry Strongly Predicts the Diagnosis of Systemic Sclerosis and Other Connective Tissue Diseases

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SESSION INFORMATION
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Background/Purpose: Vasculopathy is a key feature of systemic sclerosis (SSc), a chronic autoimmune disease associated with widespread fibrosis and internal organ dysfunction. While structural abnormalities of the microcirculation are best seen on nailfold videocapillaroscopy (NVC), laser doppler flowmetry (LDF) with a thermal challenge is a highly accurate, safe, and noninvasive means to detect digital occlusive arterial disease (DOAD) with a sensitivity

Table. Sensitivity, specificity, positive and negative predictive values of nailfold videocapillaroscopy (NVC) alone and in association with digital occlusive arterial disease (DOAD) on laser doppler flowmetry (LDF) in predicting systemic sclerosis (SSc) and connective tissue disaeses (CTDs)

Outcome	Predictor	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
SSc (ACR/EULAR 2013 criteria)	Abnormal NVC alone	0.94 (0.81-0.98)	0.65 (0.57-0.72)	0.37 (0.32-0.43)	0.98 (0.93-0.99)
	Abnormal NVC or DOAD	0.94 (0.81-0.98)	0.61 (0.53-0.68)	0.35 (0.30-0.40)	0.98 (0.92-0.99)
	SSc NVC pattern	0.93 (0.77-0.98)	0.76 (0.68-0.83)	0.46 (0.38-0.54)	0.98 (0.93-0.99)
	SSc NVC pattern + DOAD	0.54 (0.36-0.70)	0.98 (0.93-0.99)	0.83 (0.61-0.94)	0.91 (0.87-0.94)
VEDOSS	Abnormal NVC alone	0.87 (0.77-0.93)	0.76 (0.68-0.83)	0.67 (0.59-0.74)	0.91 (0.85-0.95)
	Abnormal NVC or DOAD	0.87 (0.77-0.93)	0.71 (0.63-0.79)	0.63 (0.56-0.69)	0.91 (0.84-0.95)
	SSc NVC pattern	0.84 (0.73-0.92)	0.91 (0.84-0.95)	0.84 (0.74-0.91)	0.91 (0.85-0.95)
	SSc NVC pattern + DOAD	0.30 (0.20-0.43)	0.99 (0.95-1)	0.94 (0.70-0.99)	0.72 (0.68-0.75)
Any CTD (clinical diagnosis)	Abnormal NVC alone	0.62 (0.51-0.71)	0.68 (0.58-0.76)	0.64 (0.56-0.71)	0.66 (0.59-0.72)
	Abnormal NVC or DOAD	0.64 (0.53-0.73)	0.64 (0.54-0.72)	0.62 (0.54-0.69)	0.66 (0.58-0.72)
	SSc NVC pattern	0.56 (0.45-0.66)	0.84 (0.74-0.90)	0.77 (0.66-0.85)	0.66 (0.59-0.71)
	SSc NVC pattern + DOAD	0.23 (0.15-0.33)	1.00 (0.95-1)	1.00 (0.71-0.98)	0.57 (0.53-0.60)

CI=Confidence Interval

and specificity of >90% (1).We reviewed NVC patterns and DOAD on LDF in a cohort of patients referred to our NVC clinic for evaluation of Raynaud's or suspected connective tissue disease (CTD), their correlation, and their predictive value in diagnosing SSc or any CTD.

Methods: Medical records of patients that underwent NVC and LDF at our institution between 1/1/2017 and 3/31/2019 were retrospectively reviewed. NVC results were classified as normal or abnormal (non-specific or SSc specific pattern- early, active or late). Presence or absence of DOAD on LDF was abstracted. Clinical diagnosis of CTDs and fulfilment of ACR/EULAR 2013 SSc classification criteria and Very early diagnosis of Systemic sclerosis (VEDOSS) criteria was ascertained.

Results: 190 patients (mean age 46 ± 15 yrs, 81% females, 93% white) underwent NVC and LDF during the study period. NVC was normal in 102 (54%) patients and abnormal in 88 (Non-specific 31[35%], SSc pattern 57[65%]).

On LDF with thermal challenge, 78% of patients had vasospasm and DOAD was noted in 30 (16%) patients. Among 30 patients with DOAD, a CTD was diagnosed in 24 (80%), of which 17 (57%) met SSc criteria.

Among the 30 patients with DOAD, 24 (80%) had abnormal NVC patterns with SSc NVC pattern in 18 (60%) (3 early, 8 active and 7 late). Among the 160 patients without DOAD, 93 (58%) did not have any CTD and NVC was normal in 96 (60%) of the patients.

SSc NVC pattern was strongly predictive of meeting VEDOSS (positive predictive value (PPV):84%) and diagnosis of CTDs (PPV: 77%). Addition of DOAD to SSc NVC pattern increased the likelihood of meeting SSc criteria (PPV increased from 46% to 83%), diagnosis of CTDs (PPV increased from 77% to 100%) and slightly improved fulfillment of VEDOSS.

Having normal NVC was associated with very low likelihood of SSc diagnosis (negative predictive value (NPV): 98%) and VEDOSS (NPV: 91%), but did not help significantly in exclusion of other CTDs (NPV: 66%). Using a composite predictor of abnormal NVC or DOAD did not significantly change the NPV for excluding SSc or CTDs, compared to NVC alone (Table).

Conclusion: Our study suggests that the presence of DOAD on LDF in patients with RP and/or suspected CTD is strongly associated with presence of an underlying CTD, particularly SSc. Patients with DOAD and SSc, are more likely to have an 'active or late' SSc pattern on NVC rather than 'early'. A SSc pattern NVC in combination with DOAD is very strongly predictive of an underlying CTD, with SSc in >80% cases. A normal NVC virtually excludes the presence of SSc, but not other CTDs. Adding LDF to NVC, can further increase the predictive value of NVC alone for CTD diagnosis.

Reference:

1. Mahe G et al. J Vasc Surg. 2014 Apr;59(4):1051-1057.e1.

Disclosure: Y. Radwan, None; **T. Gunderson**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **D. Liedl**, None; **A. Hinze**, None; **K. Warrington**, Eli Lilly, 2, GlaxoSmithKline, 2, roche, 2, 8, Roche, 2, 5, 8, Sanofi, 5, sanofi, 5; **P. Wennberg**, None; **A. Makol**, None.

Abstract Number: 0729

Modelled Patient Level Skin Score Trajectory Predicts Risk of Death or Major Organ-Based Complications in Diffuse Cutaneous Systemic Sclerosis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session (Sunday)
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Background/Purpose: For most patients with diffuse cutaneous systemic sclerosis (dcSSc), skin thickness improves over time, especially with background immunosuppressive treatment. This has reduced confidence in group level skin score (mRss) change as a meaningful endpoint in clinical trials that may not convincingly demonstrate greater improvement in active treatment arms compared to control. Nevertheless, skin thickening contributes significantly to dcSSc morbidity. We explore the association between skin change over time and outcomes in a cohort of early dcSSc patients.

Methods: DcSSc subjects with at least one mRss assessment within the first 5 years from onset were included. Observed change in mRss between first assessment and 12(±2) months follow-up was calculated and categorised as improvement, if there was a decline by ≥ 5 units or 25%; worsening, if we observed increase by ≥ 5 units or

Table 1. Multivariable mixed effect model for change in mRss over time

	β	95% CI		p-value
Time (years, centred at 12 months)	-3.75	-4.80	-2.69	<0.001
Time (years, centred at 12 months)^2	0.36	0.10	0.62	0.006
Constant	25.01	23.90	26.13	<0.001
Random-effect parameters				
SD Time (years, centred at 12 months)	6.66	5.64	7.85	
SD Time (years, centred at 12 months)^2	1.42	1.16	1.75	
SD Constant	9.04	8.15	10.04	
Correlation (Time, Time^2)	-0.92	-0.95	-0.88	
Correlation (Time, Constant)	-0.30	-0.45	-0.13	
Correlation (Time^2, Constant)	0.05	-0.16	0.27	
Residual SD	4.82	4.57	5.08	

Table 2. Associations between time to death or organ complication development and mRss

mRss trajectory	HR	95% CIs		p-value
Death				
Intercept	1.080	1.038	1.123	<0.001
Slope	1.040	1.007	1.075	0.017
Intercept*time (years)	0.9954	0.9912	0.9995	0.029
Clinically-significant pulmonary fibrosis				
Slope	1.035	1.001	1.070	0.045
Pulmonary hypertension				
Slope	1.069	1.002	1.140	0.042
Scleroderma renal crisis				
Slope	0.751	0.599	0.942	0.013
Slope^2	0.300	0.101	0.885	0.029

25% and stable, if change was within 5 units and 25%. Random effect models were fitted to evaluate continuous changes in mRss over time. Model-predicted individual patient intercept and slope were used to assess association between absolute mRss at baseline (12 months from onset), mRss change and time to death or development of organ disease.

Results: Of the 467 patients, 106 (22.7%) were male and mean age of disease onset was 45.5 (SD 13.2) years. Most frequent autoantibodies were anti-topoisomerase I antibody (ATA) in 141 (30.2%) and anti-RNA polymerase antibodies (ARA) in 140 (30.0%) of the subjects. Other antibodies included anti-U3RNP in 32 (6.9%), anti-PmScl in 21 (4.5%) and 73 (15.6%) of the subjects were ANA positive, but ENA negative (ANA+ENA-). In 94 patients (20.1%) mRss was assessed once, while 278 (59.5%) had three or more mRss assessments.

Average mRss at 12 months from onset was estimated to be 25 and there was consistent decline over subsequent years, which slowed down with longer disease duration (3.4, 2.7, 1.9 and 1.2 units at years 2, 3, 4 and 5). As previously shown, there was a weak negative correlation between mRss at 12 months and subsequent change (correlation coefficient -0.3), suggesting higher initial mRss associates with greater subsequent decline (Table 1).

Of the 147 patients who had two mRss assessments within 12(±2) months, only 12.9% had worsening mRss, 34.7% had improvement and the majority (52.4%) experienced very little change. Both higher intercept and higher slope predicted increased risk of death with 8% increase in hazard for every unit higher baseline mRss

and 4% increase for every unit higher change per year (Table 2). Pulmonary fibrosis and pulmonary hypertension development associated with higher change in mRss, but not with baseline absolute mRss values (3.5% and 7% increase in the hazard respectively for one unit higher mRss change over 12 months). It appeared that higher slope associated with lower hazard of scleroderma renal crisis, while we found no associations between skin and cardiac SSc.

Conclusion: Skin changes over the initial 5 years of disease vary between patients. At a group level there is an improvement, however, for individual patients slower improvement or deterioration in skin predicts increased risk of pulmonary complications and higher mortality rates.

Disclosure: S. Nihtyanova, Daiichi Sankyo, 3; **E. Derrett-Smith**, None; **C. Fonseca**, None; **V. Ong**, None; **C. Denton**, Actelion, 5, Actelion Pharmaceuticals, 5, Actelion, GlaxoSmithKline, Bayer, Sanofi, Inventiva, Boehringer Ingelheim, Roche, Bristol Myers Squibb, CSL Behring, UCB, Leadiant Biosciences, 5, Bayer, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Corbus Pharmaceuticals, 5, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, Leadiant Biosciences, 2, 5, Inventiva, 5, Pfizer, 5, Roche, 5, Sanofi, 5, UCB, 5.

Abstract Number: 0730

Energy Levels: An Overlooked Element in Patient Assessment in Scleroderma

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Scleroderma (SSc) is a debilitating multi-system chronic disease which directly affects patient related Quality of Life. We wanted to identify how the patient interprets their inability to work and get their perspective on energy levels during daily activities. We hypothesized that there are abnormal constitutional symptoms in SSc patients (i.e. energy levels, sleep quality and time to feeling fatigued) which may directly affect patient productivity.

Objective:

- To assess the proportion of SSc patients with abnormal energy levels, sleep and with early fatigue.
- To evaluate the relation between energy levels and sleep quality, time to fatigue, pain visual analogue scale (VAS), Pt global VAS, MD global VAS.

Methods: Eighty -five SSc patients meeting the ACR/EULAR 2013 SSc criteria were recruited from Pacific Arthritis Scleroderma Clinic. Laboratory and clinical data were obtained from charts for statistical correlations. Data were cross-sectional and were from the first clinical record available, usually the first clinical visit.

Table 1: demographics and pt characteristics of Scleroderma patients

variable	Mean(SD), number (%)
Age	55.7(13.2)
Sex, females	76 (89 %)
mRSS	7 (7.5)
ILD	37 (43%)
PAH	14(16 %)
HgB	12.2 (1.2)
Pt Global VAS	4 (2.4)
MD global	4(1.6)
Pain VAS	3(2.8)

Table 2: Number (%) of patient in each category of Energy level, sleep and time to fatigue

	Good	Ok	Fair	poor
Energy	31 (36%)	6 (7%)	24(28%)	24(28 %)
Sleep	31(36%)	15 (17%)	11(12%)	26 (31%)
Time to fatigue	(9.5-≥12hrs) 25(29%)	6.5-9hrs 18 (21%)	3.5-6hrs 12(14%)	(0-3hrs) 29 (34%)

Energy levels were assessed by the question “how is your energy?” and Sleep was ascertained as: ” How well do you sleep?” or “How is your sleep?” For these questions, answers were categorical: “Good” (0), “OK” (1), “Fair”(2) or” Low”(3).

Fatigue was ascertained as “How long after you get up ,do you start to get tired or fatigued?”. Answers were in hours, including 0 for fatigued immediately upon awakening to 12+(maximum); responses were in 0.5-hour increments. Regression modelling used energy levels as the dependent variable and time to fatigue , sleep quality, pain VAS, pt global, MD global as independent variables.

Results: The 85 SSc patients’ characteristics were as follows: mean age 55 (13%), female 76 ILD (37), mean MRSS 7 (±7.5) Table 1. Energy levels were fair-poor in more than 50%, while significantly shortened time to fatigue (< =3 hrs) occurred in 29(34%)) . Sleep quality was only fair-poor in 37/85(43%) Table 2. Regression model identified fatigue, sleep , pain VAS, patient global and MD as strong predictors of Energy levels in SSc pts (p =0.0001, 0.0001, 0.009,0.0001 and 0.0001 respectively).

Conclusion: Energy levels among other constitutional symptoms (ie, sleep and fatigue) are significantly altered in SSc patients, more care is to be given to address possible causes , assessment tools and to improve management plans.

Disclosure: Y. Suliman, None; **S. Kafaja**, None; **M. Alemam**, None; **D. Furst**, Actelion, 2, 5, Actelion Pharmaceuticals, 2, 5, Amgen, 2, 5, BMS, 2, 5, CME, 5, 8, Corbus, 2, 5, Galapagos, 2, 5, Galapogos Novartis, 5, GlaxoSmithKline, 2, GSK, 2, 5, NIH, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche/Genentech, 2, 5, Sanofi, 2, 5.

Abstract Number: 0731

A Systemic Review of Factors Associated with Systemic Sclerosis-associated Pulmonary Arterial Hypertension (SSc-PAH)

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary arterial hypertension (PAH) in systemic sclerosis (SSc) is a lethal complication affecting approximately 8-15% of patients. Screening methods including echocardiography and pulmonary function tests exist to triage patients for definitive diagnosis by right heart catheterization. Improving our understanding of SSc-PAH associated risk factors could help stratify high-risk patients for regular screening.

Methods: A systematic review was performed in SCOPUS, Medline, EMBASE, Web of Science, and the Cochrane Library from their inception to February 22, 2019. Terms included phrases related to pulmonary arterial hypertension, systemic sclerosis, and prevalence. Studies were included if they reported on the frequency of a risk/association factor related to SSc-PAH. Studies were included if they determined PAH with right heart catheterization, compared SSc patients with and without PAH, and had sample size larger than 20.

Results: The search found 2654 articles of which, 984 were duplicates and 1578 were excluded due to irrelevant title. After the remaining 92 were screened, 37 articles met eligibility criteria. Forty-three risk/association factors for SSc-PAH were identified and placed into seven categories. The most frequently mentioned categories included: patient characteristics, pulmonary physiology, antibody profiles, and genetics/epigenetics factors. In contrast, biomarkers and other labs featured the fewest distinct risk factors. Specific risk factors found for patients were lowered

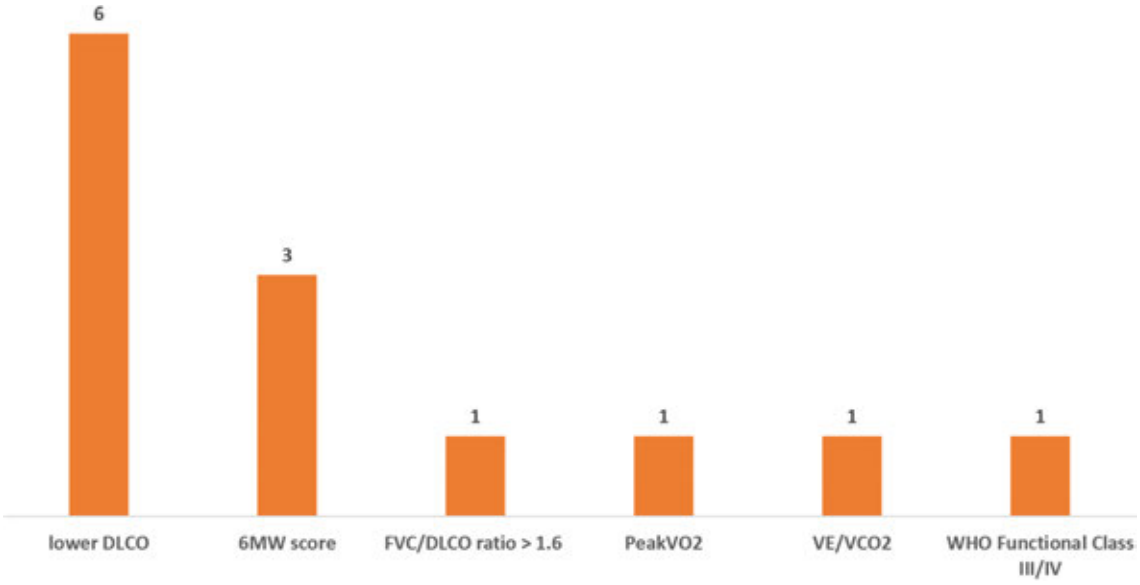

Figure 1. Pulmonary physiology measurements related to literature reported SSc-PAH

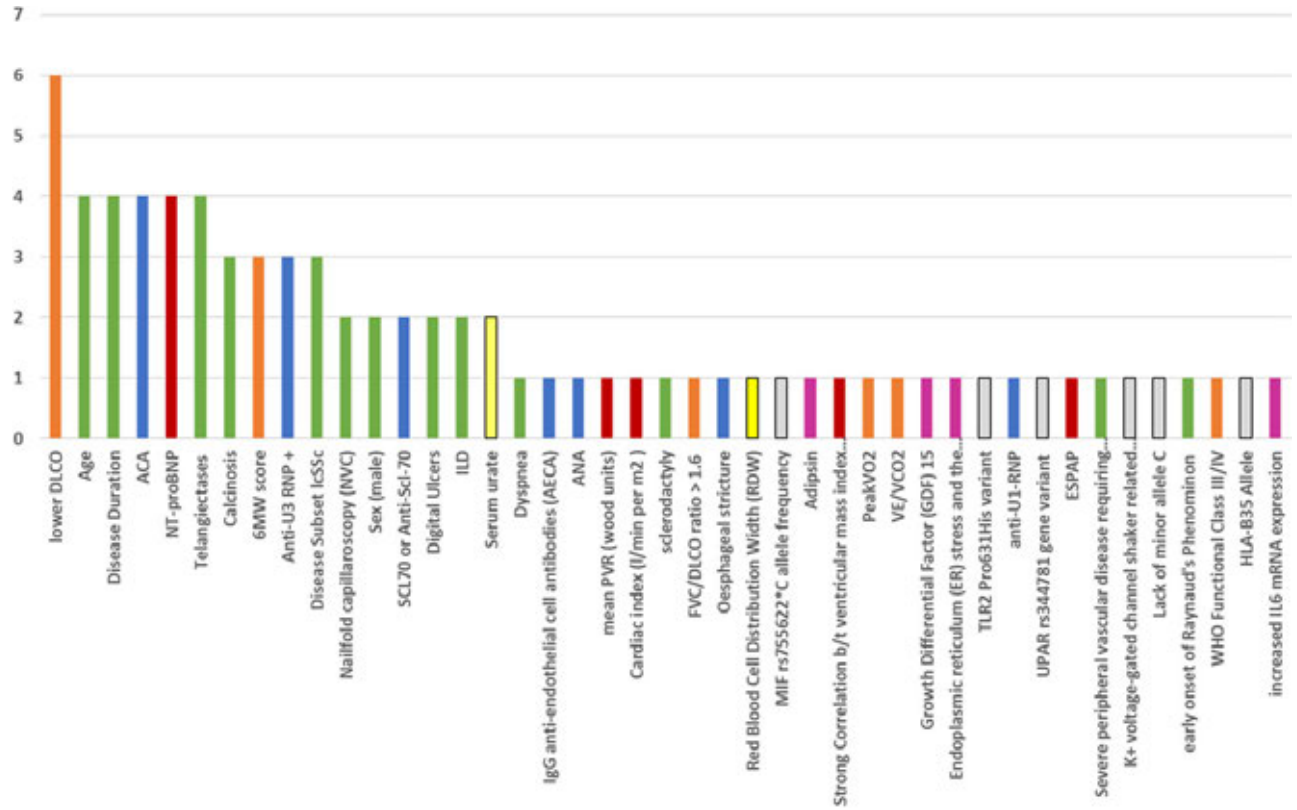

Fig. 2 All clinical parameters associated with SSc_PAH as reported in the literature

diffusing capacity of the lungs for carbon monoxide, older age, and longer disease duration among others. Interstitial lung disease and anti-centromere antibody (ACA) were also frequently associated (Figure 1 and 2).

Conclusion: Presence of ILD, ACA, older age, and disease duration are consistently identified risk factors in PAH-SSc. Risk factors for SSc-PAH such as limited-SSc, ACA, older age, longer disease duration and presence of ILD may enrich screening programs. Patterns in genotypes and antibody profiles are inconsistent and requires further validation. Understanding these risk factors may give insight into which patients will need further screening but some risks are associated with Class I PAH (ex. ACA) and others with Class III (ILD, hypoxia) which may be why risk factors are inconsistent in the literature.

Disclosure: Y. Jiang, None; **M. Turk**, None; **J. Pope**, AbbVie, 5, Abbvie, 5, Actelion, 5, Actellion, 5, Amgen, 2, 5, AstraZeneca, 2, Astra-Zeneca, 2, Bayer, 2, 5, BMS, 2, 5, Eicos Sciences, 5, Eli Lilly & Company, 5, Eli Lilly and Company, 5, EMERALD, 5, Emerald, 5, Genzyme, 5, Janssen, 5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8.

Abstract Number: 0732

Risk of Heart Valve Disease in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I

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Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiac valve involvement in patients with Systemic Sclerosis (SSc) is uncommon, except for tricuspid regurgitation associated with pulmonary hypertension, and data regarding its frequency is inconsistent. Our objective was to estimate incidence rate of moderate to severe valvular disease in patients with SSc compared with controls.

Methods: We included patients with SSc diagnosis (ACR 2013 criteria) belonging to our health management organization (HMO) and followed by our unit from january 1st 2000 to december 31th 2017. Each patient with SSc was

	Patients with Systemic Sclerosis (n=127)	Controls (n= 497)	p
Female, n (%)	122 (96.1)	477 (95.9)	0.96
Follow-up time, in years, median (IQR)	10.7 (6.4-14.7)	11.3 (6.6-14.6)	0.81
Age at the las cardiac ultrasound, years (SD)	68.6 (14.7)	68.2 (16.6)	0.81
N° of cardiac ultrasound performed, median (IQR)	2 (1-3)	4 (2-8)	< 0.001
Arterial hypertension, n (%, 95% CI)	69 (54.3, 45.6-62.8)	343 (69.0, 64.8-72.9)	0.002
Diabetes, n (%, 95% CI)	2 (1.6, 0.4-6.1)	44 (8.9, 6.7-11.7)	0.005
Dyslipidemia, n (%, 95% IC)	46 (36.2, 28.3-44.9)	255 (51.3, 46.9-55.7)	0.002
Ever smoke , n (%, 95% CI)	32 (25.2, 18.4-33.5)	113 (22.8, 19.3-26.7)	0.06
Coronary disease, n (%, 95% CI)	7 (5.5, 2.6-11.1)	35 (7.0, 5.1-9.7)	0.54
Chronic renal failure, n (%, 95% CI)	14 (11.0, 6.6-17.8)	45 (9.1, 6.8-11.9)	0.51
Stroke, n (%, 95% CI)	6 (4.7, 2.1-10.2)	24 (4.8, 3.3-7.1)	0.96
Past rheumatic fever, n (%, 95% CI)	1 (0.8, 0.1-5.4)	2 (0.4, 0.1-1.6)	0.58
BMI, median (IQR)	24 (21.0-26.2)	27.2 (24.0-30.9)	< 0.001
Moderate-severe aortic regurgitation, Incidence rate, 100 patients-year (95% CI)	1.4 (0.1-2.1)	1.1 (0.8-1.4)	0.16
Moderate-severe aortic stenosis, Incidence rate, 100 patients-year (95% CI)	1.1 (0.7-1.8)	0.3 (0.2-0.5)	**< 0.001**
Moderate-severe mitral regurgitation, Incidence rate, 100 patients-year (95% CI)	1.9 (1.3-2.7)	0.9 (0.7-1.2)	**0.001**
Moderate-severe mitral stenosis Incidence rate, 100 patients-year (95% CI)	0.2 (0.08-0.7)	0.06 (0.02-0.17)	0.06
Moderate-severe pulmonary regurgitation, Incidence rate, 100 patients-year (95% CI)	0	0.02 (0.003-0.13)	0.40
Moderate-severe tricuspid regurgitation, Incidence rate, 100 patients-year (95% CI)	1.9 (1.3-2.7)	0.4 (0.3-0.6)	**< 0.001**
Aortic sclerosis, Incidence rate, 100 patients-year (95% CI)	6.7 (5.9-7.5)	5.1 (4.7-5.5)	**0.02**
Mitral sclerosis, Incidence rate, 100 patients-year (95% CI)	2.3 (1.7-3.1)	0.9 (0.7-1.2)	**< 0.001**
Aortic calcification, Incidence rate, 100 patients-year (95% CI)	2.1 (1.5-2.9)	0.9 (0.7-1.2)	**< 0.001**
Mitral calcification, Incidence rate, 100 patients-year (95% CI)	2.9 (2.2-3.8)	1.6 (1.3-1.9)	**0.001**
Pulmonary hypertension, by cardiac ultrasound (PSP* > 40 mmHg), n (%, 95% CI)	29 (22.8, 16.3-30.9)	22 (4.4, 2.9-6.6)	**< 0.001**
Valvular surgery, Incidence rate, 100 patients-year (95% CI)	0.4 (0.2-0.9)	0,1 (0.05-0.3)	**0.03**

*PSP: pulmonary artery systolic pressure

Risk of Heart Valve Disease in Systemic Sclerosis.

matched by age and sex with 3 to 4 controls of our HMO with at least 1 cardiac ultrasound performed during the study period. Subjects were followed until: a) their death, b) the end of the study, c) they voluntarily left the HMO. Electronic medical records were reviewed, demographic and disease characteristics were collected and incidence rates of valve involvement were calculated for each valve (moderate/severe valvular disease, valve calcification and valve sclerosis) and compared between SSc and controls.

Results: 127 patients with SSc (108 with limited and 18 with diffuse SSc; 96.1% females; 18.4% Scl-70 positive and 67.2% anti centromere positive) and 497 controls were included. Patients with SSC had significantly more incidence of aortic stenosis (1.1 vs 0.3 per 100 patients-year, $p < 0.001$), mitral regurgitation (1.9 vs 0.9 per 100 patients-year, $p = 0.001$) and tricuspid regurgitation (1.9 vs 0.4 per 100 patients-year, $p < 0.001$) than controls. Valvular surgery was significantly more frequent in SSc than controls (0.4 vs 0.1 per 100 patients-year, $p = 0.03$). Aortic sclerosis (6.7 per 100 patients-year), aortic calcification (2.1 per 100 patients-year), mitral sclerosis (2.3 per 100 patients-year) and mitral calcification (2.9 per 100 patients-year) were also more frequent in SSc patients than controls ($p < 0.05$ for all comparisons).

Conclusion: We found significant higher incidence rates of aortic stenosis, mitral regurgitation and tricuspid regurgitation in SSc patients compared to their matched controls. Patients with SSc also required more valvular surgery. Moreover, aortic and mitral valves sclerosis and calcification were found more often in SSc patient's echocardiographies than in controls.

Disclosure: R. Alvarado, None; **M. Scolnik**, Abbvie, 8, ABBVIE, 8, Bristol, 8, BRISTOL, 8, Bristol-Myers, 8, Bristol-Myers Squibb, 8, Glaxo, 8, GLAXO, 8, Lilly, 8, LILLY, 8, Pfizer, 8, PFIZER, 8, Pfizer Inc, 8, Roche, 8, ROCHE, 8; **N. Marin Zucaro**, None; **G. Alle**, None; **M. Trasante Borches**, None; **L. Catoggio**, None; **E. Soriano**, Abbvie, 2, 5, 8, ABBVIE, 2, 5, 8, AbbVie, 2, 5, 8, Amber, 8, Amgen, 5, 8, AMGEN, 5, 8, BMS, 8, BRISTOL, 8, Bristol MS, 8, BRISTOL MYERS SQUIBB, 8, Bristol-Myers Squibb, 8, eli lilly, 5, 8, Genzyme, 8, GENZYME, 8, GLAXO, 2, Glaxo, 2, glaxosmithkline, 2, GlaxoSmithKline, 2, GSK, 2, Janssen, 8, Lilly, 5, 8, LILLY, 5, 8, Novartis, 2, 5, 8, NOVARTIS, 2, 5, 8, PFIZER, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, 8, Roche, 2, 8, ROCHE, 2, 8, Sandoz, 5, SANDOZ, 5, Sanofi, 5, SANOFI, 5, SANOPHY, 5, UCB, 8.

Abstract Number: 0733

Vonoprazan, a Novel Potassium-competitive Acid Blocker, for Treatment of Proton Pump Inhibitor-resistant Reflux Esophagitis in Patients with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Esophageal involvement is one of the most frequent organ manifestations in patients with systemic sclerosis (SSc). Gastroesophageal reflux disease (GERD) is associated with reflux esophagitis, resulting in

impaired quality of life and increased risk for esophageal stricture and cancer. Continuous use of proton pump inhibitors (PPIs) is recommended as the primary treatment for SSc-associated GERD and leads relief of the symptoms. However, some patients experience reflux esophagitis refractory to the maximum dose of conventional PPIs. Vonoprazan is a novel potassium-competitive acid blocker, and is shown to have several advantages over conventional PPIs, including long duration of acid suppression. Several clinical trials have consistently demonstrated superiority of vonoprazan over conventional PPIs in terms of achieving healing of mucosal breaks and maintaining the healing. The present study investigated the efficacy of vonoprazan for treating PPI-resistant reflux esophagitis in SSc patients.

Methods: This study enrolled SSc patients with PPI-resistant reflux esophagitis, who were selected from SSc database of Nippon Medical School Hospital, composing of 228 patients who visited our clinic after August of 2014. Patients eligible for this study included i) fulfillment of 2013 ACR/EURAR classification criteria for SSc; ii) reflux esophagitis proved by endoscopy on treatment of PPIs; iii) medication switch from PPIs to vonoprazan; and iv) endoscopic and patient-reported outcome evaluations available before and after switch to vonoprazan. Vonoprazan was started orally at a dosage of 20mg or 10mg daily, and the dosage was adjusted if necessary. Reflux esophagitis was graded using Los Angeles (LA) classification, and patient-reported outcomes were assessed using a frequency scale for the symptoms of GERD (FSSG) questionnaire. Safety was also evaluated by retrospective chart review.

Results: Of 13 patients with endoscopy-confirmed reflux esophagitis resistant to PPI treatment, PPIs were switched to vonoprazan in 12 patients. Complete before-and-after data were available in 7 patients, and follow-up evaluations were conducted after an interval of 3.4 ± 2.7 months. All the patients were female, mean age at study entry was 62 ± 13 years, mean disease duration from non-Raynaud's symptom was 13 ± 8 years. Baseline LA classification was A in one, B in 3, C in 2, and D in one, but follow-up endoscopic evaluation revealed that reflux esophagitis was completely healed in 6 of 7 (86%) patients after switching to vonoprazan. Total FSSG score significantly improved from 18.4 ± 9.9 to 11.3 ± 14.2 ($P = 0.04$). The acid reflux component of the FSSG score improved significantly (12.0 ± 6.2 to 7.0 ± 7.9; $P = 0.03$), whereas the dysmotility component did not change (6.4 ± 4.7 to 4.3 ± 6.6). Vonoprazan has been continuously used for 18.7 ± 9.4 months without any adverse events. One patient had vonoprazan-resistant reflux esophagitis based on lack of improvement of the endoscopic findings, but symptomatic improvement was somewhat observed by the FSSG score.

Conclusion: This pilot study suggests that vonoprazan is beneficial for PPI-resistant reflux esophagitis in patients with SSc. A randomized clinical trial is warranted.

Disclosure: Y. Shirai, Actelion, 8, Bayer, 8, Boehringer-Ingelheim, 8, Mochida Pharma, 8, Nippon Shinyaku, 8, Pfizer, 8; **N. Kawami**, Takeda, 8, Otsuka Pharmaceutical, 8; **K. Iwakiri**, Takeda, 2, 8, Otsuka Pharmaceutical, 2, 8; **M. Kuwana**, Abbvie, 2, 8, Actelion, 2, 8, Actelion Pharmaceuticals, 2, 8, Astellas, 2, 8, Bayer, 5, Boehringer Ingelheim, 5, Boehringer-Ingelheim, 5, Chugai, 2, 5, 8, Corbus, 5, CSL Behring, 5, CSL Berling, 5, Eisai, 2, 8, Eli Lilly, 2, Janssen, 8, Japan Blood Products Organization, 8, MBL, 7, 8, Ono, 2, 8, Pfizer, 2, Reata, 5, Tanabe-Mitsubishi, 2, 8.

Abstract Number: 0734

Risk Assessment in Connective Tissue Disease Associated Pulmonary Arterial Hypertension

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SESSION INFORMATION
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Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
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Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary arterial hypertension (PAH) still holds a poor prognosis in patients with connective tissue diseases (CTD), especially those with systemic sclerosis (SSc). A variety of pulmonary vasodilators are currently available, but treatment regimen should be optimized based on risk for poor outcomes in individual patients. The 2015 ESC/ERS guidelines recommended the use of risk assessment based on variables to predict prognosis. The simplified version of the risk assessment using 6 variables that stratify the patients into low, intermediate, and high risk groups has been validated in large cohorts of PAH patients. However, utility of this risk stratification strategy in patients with CTD-PAH has not been established. The present study evaluated risk stratification approaches in patients with CTD-PAH using our database.

Methods: This study enrolled 61 consecutive patients who were diagnosed as having CTD-PAH at Keio University Hospital between 2000 and 2014 and Nippon Medical School Hospital between 2014 and 2019. All clinical information had been prospectively recorded on the database. Six variables, including WHO functional class (WHO-FC), 6 minutes walking distance, BNP/NT-proBNP, right atrial pressure, cardiac index (CI), and mixed venous oxygen saturation at PAH diagnosis were used to categorize the patients into 3 risk groups. The cut-off values and the risk grading were determined according to the 2015 ESC/ERS guidelines. Survival curves were obtained using Kaplan-Meier method and cumulative survival rates were compared by log-rank test.

Results: Baseline characteristics of the enrolled patients included 98% female, age at PAH diagnosis of 51 ± 18, 64% WHO-FC III/IV, and mean pulmonary arterial pressure of 45 ± 10 mmHg. Underlying CTDs were SSc in 33%, systemic lupus erythematosus in 30%, mixed connective tissue disease in 13%, and primary Sjogren's syndrome in 15%. Risk stratification using the standard approach failed to stratify cumulative survival rates in 3 risk groups (Figure 1). When individual variables were used to stratify patients into 3 risk groups, survival rates were significantly different between patients with low risk and intermediate or high risk judged based on WHO-FC (P = 0.016 and 0.011), and between patients with low or intermediate risk and high risk judged based on CI (P = 0.009 and 0.018). Therefore, we modified the original stratification approach by weighting WHO-FC and CI for dividing the patients into the risk groups. Specifically, risk was judged to be low if WHO-FC was I or II, and high if CI was < 2.0 L/min/m2, regardless of

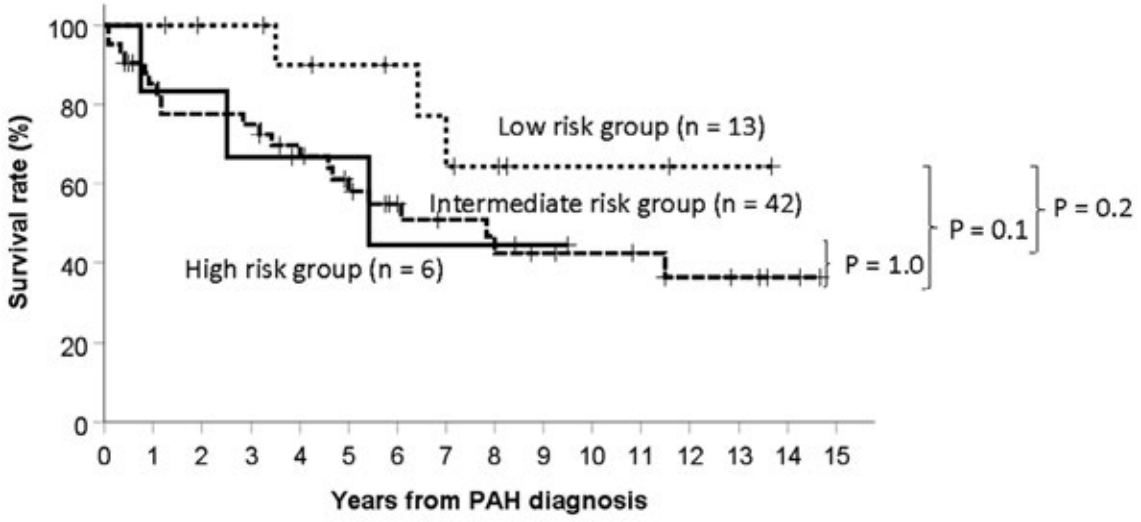

Figure 1 The standard approach

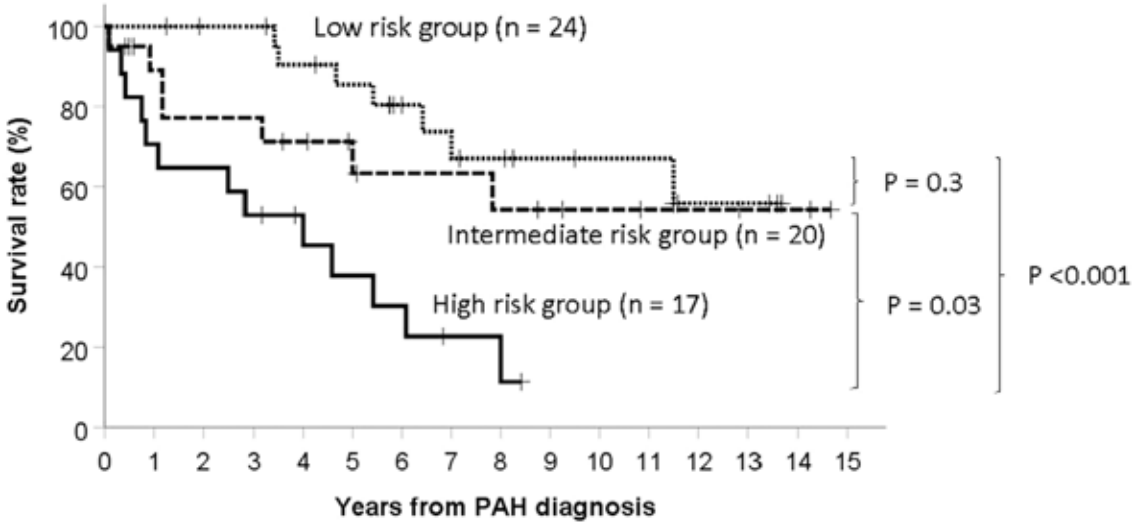

Figure 2. The modified approach by weighting WHO functional class and cardiac index

the risk of other variables. The modified version successfully separated survival curves of 3 risk groups, and survival rates were significantly different between high risk group and low or intermediate risk group ($P < 0.001$ and 0.025) (Figure 2). Principally concordant results were observed in SSc-PAH sub-population.

Conclusion: The simplified 2015 ESC/ERS PAH risk stratification using 6 variables at baseline failed to predict prognosis of patients with CTD-PAH accurately. The modified approach weighting WHO-FC and CI might be useful to discriminate survival rates among risk groups, but it should be verified using independent patient cohorts.

Disclosure: Y. Shirai, Actelion, 8, Bayer, 8, Boehringer-Ingelheim, 8, Mochida Pharma, 8, Nippon Shinyaku, 8, Pfizer, 8; **H. Yasuoka**, None; **Y. Tamura**, Actelion, 2, 5, 8, GSK, 2, 8, Mochida Pharma, 2, 8, Nippon Shinyaku, 2, 8, Bayer, 2, 8, Daiichi Sankyo Pharma, 2, 8, Pfizer, 2, Astellas, 2, Boehringer-Ingelheim, 8, TEIJIN Pharma, 8; **M. Kuwana**, Abbvie, 2, 8, Actelion, 2, 8, Actelion Pharmaceuticals, 2, 8, Astellas, 2, 8, Bayer, 5, Boehringer Ingelheim, 5, Boehringer-Ingelheim, 5, Chugai, 2, 5, 8, Corbus, 5, CSL Behring, 5, CSL Berling, 5, Eisai, 2, 8, Eli Lilly, 2, Janssen, 8, Japan Blood Products Organization, 8, MBL, 7, 8, Ono, 2, 8, Pfizer, 2, Reata, 5, Tanabe-Mitsubishi, 2, 8.

Abstract Number: 0735

The Relationship Between Gastrointestinal Symptoms and Severity and Whole Gut Transit in Patients with Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Table 1. Objective GI Involvement in SSc Using the Whole Gut Transit Study

Region of the gut	WGT in SSc (n=63)	WGT in normal controls (n=18)	P-value
Esophagus			
Abnormal, n (%)	39/62 (63%)	2/17 (12%)	**<0.001**
Esophageal Transit Time (sec)	28 (11-30)	10 (8-12)	**0.004**
Esophageal % emptying at 10 sec, median (IQR)	80 (62-88)	92 (86-93)	**<0.001**
Stomach			
- ***Abnormal liquid +/- solid transit***	27/63 (43%)	1/18 (11%)	**0.013**
- ***Liquid***			
Abnormal, n (%)	13/63 (21%)	1/18 (6%)	0.175
Delayed T1/2 (min)	18 (12-22)	16 (11-20)	0.229
Solid			
Abnormal, n (%)	11/61 (18)	1/18 (6)	0.278
% emptying at 2 hours, median (IQR)	61 (46-78)	84 (65-87)	**0.003**
% emptying at 4 hours, median (IQR)	95 (89-98)	98 (97-99)	**<0.001**
Small bowel			
Abnormal, n (%)	10/61 (16%)	1/18 (6%)	0.440
Transit time, median (IQR)	70 (58-82)	72 (62-77)	0.678
Colon			
Abnormal	37/62 (60%)	7/18 (39%)	0.119
Percent colonic emptying at 72 hours, median (IQR)	44 (0-86)	84 (60-94)	**0.008**

Normal ranges: Esophageal transit time (ETT) = >15 seconds; Escophageal emptying at 10 sec= = 83%; liquid emptying = at 1 hour <39%, or at 2 hours <78%; Delayed liquid T1/2 >74 min solid emptying 2 hrs = 40%; solid emptying 4 hrs = 90%; small bowel transit time at 6 hrs <50%; colonic transit time at 72 hrs <67%

Background/Purpose: The gastrointestinal (GI) tract is the most commonly affected internal organ system in systemic sclerosis (SSc), resulting in significant morbidity and mortality. Several studies that objectively evaluated GI tract dysfunction and abnormal transit in SSc have shown that such abnormalities associate inconsistently with clinical symptoms and severity, resulting in challenges related to diagnosis, risk stratification, and therapeutic inter-

Table 2. Pearson Correlation Table between Whole Gut Transit Study and GI Symptoms (UCLA GIT 2.0)

	GIT Reflux	GIT Dist/Bloat	GIT Soilage	GIT Diarrhea	GIT Social	GIT Emotional	GIT Constipation	GIT total score
Esophageal transit time Esoph 10s	-0.20	0.11	0.06	-0.11	0.01	0.01	0.14	-0.12
Stomach 1hr	-0.11	-0.23	0.03	-0.02	-0.04	-0.17	0.01	-0.17
Stomach 2hr	-0.20	**-0.34**	0.02	-0.16	-0.18	-0.19	-0.11	-0.24
Stomach 4hr	-0.09	-0.07	0.12	-0.02	-0.13	-0.12	-0.12	-0.04
Small bowel	-0.22	-0.18	-0.17	**-0.26**	**-0.29**	-0.24	-0.07	**-0.29**
Large bowel	0.02	0.01	-0.11	**0.31**	0.05	-0.15	0.08	0.03

ventions. We sought to determine whether clinical symptoms associate with objective evidence of GI dysmotility in SSc, and to determine how patterns of abnormal transit fit with existing GI symptom and severity scales in the field of scleroderma.

Methods: Patients with SSc and GI symptoms were recruited from clinic in the Johns Hopkins Scleroderma Center. Patients completed the UCLA GIT 2.0 survey, were assessed by the Medsger GI severity score, and underwent a nuclear medicine-based whole gut transit (WGT) study. The association between patient GI symptoms, GI severity, and characteristics of abnormal transit in each region of the GI tract were compared, and the association between areas of abnormal transit and GI severity was also examined.

Results: WGT scintigraphy was performed on 63 SSc patients with active GI symptoms and 18 healthy controls. In the cohort, the average age was 58.4 years, with 84.1% being female and 80.6% being Caucasian. Median disease duration was 10 years, and 27.1% had diffuse cutaneous disease. Approximately 60% of SSc patients had more than one abnormal region on WGT studies. SSc patients were more likely to have delayed esophageal transit time [28% vs. 10%; p=0.004], delayed esophageal percentage emptying at 10 seconds [80% vs 92%; p=< 0.001], delayed gastric emptying at both 2 hours [61% vs. 84%; p=0.003] and 4 hours [95% vs. 98%; p< 0.001], and delayed colonic emptying at 72 hours [44% vs. 84%; p=0.008] compared to healthy controls (Table 1). Evaluating the association between Medsger GI severity scores (MGISS) and WGT results, patients with MGISS of 2 had slower esophageal transit and more gastroparesis compared to other Medsger groups. Patients with pseudo-obstruction and/or malabsorption (MGISS=3) were significantly more likely to have severe colonic delay (p< 0.05). Patients requiring total parenteral nutrition (MGISS=4) were significantly more likely to have small bowel dysmotility (p< 0.05). When comparing symptoms assessed by the UCLA GIT 2.0 with WGT measurements, symptoms of distention and bloating were inversely associated with percent gastric emptying at 2 hours (r=-0.34; p=0.011), and symptoms of diarrhea were positively associated with higher colonic transit times (r=0.031; p=0.026) (Table 2).

Conclusion: WGT provides a non-invasive assessment of bowel dysfunction and defines specific anatomical areas that associate with clinical symptoms and GI severity. This has implications not only in enhancing our understanding of symptom etiology, but also to guide therapy. These results are exciting in the face of known challenges in capturing objective pathology in SSc GI disease, and determining the association with active GI symptoms and outcome measures.

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Abstract Number: 0736

Reduced Circulating Levels of Inorganic Pyrophosphate Are Associated with Ectopic Calcification in Scleroderma Spectrum Disorders

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SESSION INFORMATION

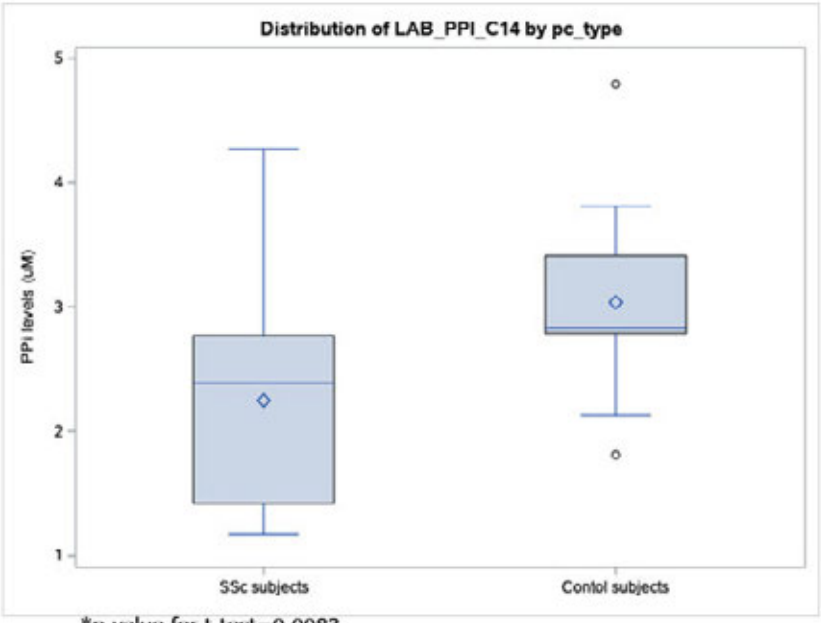
Session Date: Sunday, November 10, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Figure 1. Mean PPi levels by SSc groups (controls and SSc subjects)



*p-value for t-test=0.0083

Table 1. Mean PPi levels by SSc groups

	Unadjusted*		Sex-adjusted**	
	Mean	95% CI	Mean	95% CI
Control	3.04	2.61 – 3.46	2.63	2.11 – 3.15
SSc (no calcinosis)	2.08	1.51 – 2.65	1.93	1.39 – 2.47
SSc (calcinosis)	2.05	1.38 – 2.73	1.84	1.19 – 2.49

* p-for group difference= 0.0137
** p-for group difference= 0.0734

Background/Purpose: Calcinosis cutis due to ectopic mineralization is a common and disabling complication of systemic sclerosis (SSc) that has poorly understood pathogenesis and no effective treatment. Inorganic pyrophosphate (PPi) is a key regulator of ectopic mineralization acting by inhibiting hydroxyapatite crystal growth (1,2). Ectopic mineralization has been attributed to low PPi levels in several genetic disorders such as pseudoxanthoma elasticum, generalized arterial calcification of infancy, and arterial calcification due to CD73 deficiency (3). Herein, we sought to test the hypothesis that reduced plasma PPi levels may be associated with SSc and play a pathogenic role in calcinosis.

Methods: Subjects meeting the 2013 ACR criteria for SSc (4) and age-matched controls without SSc were recruited from Rheumatology outpatient clinics for this IRB-approved study. Calcinosis was confirmed either by clinical criteria or by imaging. Levels of PPi in platelet-free plasma were measured by enzymatic reaction using ^{14}C-labeled uridine-diphosphoglucose as substrate (5). Student T-test was used to compare mean PPi levels between control and SSc groups and linear regression to compare means between the 3 groups (control, SS-calcinosis and SSc-no calcinosis) with adjustment of potential confounders.

Results: We studied 33 subjects (19 control and 14 SSc, 5 of whom had SSc-calcinosis). In the SSc cohort, 60% had limited cutaneous SSc, as did 4 of 5 subjects with SSc-calcinosis. The mean disease duration (from non-Raynaud symptoms) was 18.7 (SD 8.7) years in SSc-calcinosis and 10.3 (SD 7.4) years in SSc-no calcinosis groups.

Figure 1 shows that the SSc cohort had significantly lower plasma levels of PPi (mean=2.25 uM vs 3.04uM, p=0.0083) compared to the control group (see Table 1, p for group difference= 0.0137). After adjusting for sex, the highest mean PPi levels were seen in the control group and the lowest in the SSc-calcinosis group.

Conclusion: Our findings indicate PPi levels are significantly reduced in SSc patients with calcinosis. The results suggest that PPi deficiency may be due to genetic or environmental influences that may be important in the pathophysiology of calcinosis, and could serve as a biomarker of the ectopic mineralization process. Larger clinical studies to confirm our findings are warranted.

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Abstract Number: 0737

The MUC5B Promoter Variant Does Not Predict Outcomes in Systemic Sclerosis-related Interstitial Lung Disease

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SESSION INFORMATION
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Background/Purpose: Interstitial lung disease (ILD) affects the majority of patients with systemic sclerosis (SSc). The disease course of ILD varies among SSc patients and no reliable clinical or biological parameters consistently predict outcomes. We investigated whether the presence of a gain-of-function MUC5B promoter polymorphism, previously shown to be strongly associated with idiopathic pulmonary fibrosis and rheumatoid arthritis-related ILD predicted response to immunosuppression with cyclophosphamide (CYC) and mycophenolate (MMF) in SSc-ILD.

Methods: 142 patients in Scleroderma Lung Study (SLS) II (Tashkin et al. Lancet Resp Med 2016) were randomized to receive either MMF for 2 years or oral CYC for 1 year followed by 1 year of placebo. Presence of ground glass opacity was a requirement for enrollment. Genotyping of the MUC5B rs35705950 single nucleotide polymorphism was performed using TaqMan Genotyping Assaysin all patients with an available DNA sample. The forced vital capacity (FVC) and the diffusing capacity for carbon monoxide (DLCO) were measured every 3 months. Quantitaive Lung fibrosis (QLF) and Quantitative

Table 1. Linear regression analyses evaluating the relationship between the presence of the MUC5B promoter variant and change in radiographic fibrosis.

1A. Outcome: QLF-WL at 24 months

Parameter	Estimate	Standard Error	t Value	P-Value
Intercept	2.255139320	1.05689633	2.13	0.0357
MUC5B presence	-1.842087825	1.10086179	-1.67	0.0979
QLF-WL Baseline	0.815676811	0.06047437	13.49	<.0001
CYC arm	0.121978419	0.85470740	0.14	0.8868
MMF arm	0.000000000	.	.	.
Caucasian	-0.335065965	0.99599846	-0.34	0.7374

1B. Outcome: QLF-ZM at 24 months

Parameter	Estimate	Standard Error	t Value	P-Value
Intercept	5.987430209	2.82982883	2.12	0.0372
MUC5B presence	-2.278872568	2.92898686	-0.78	0.4387
QLF-ZM Baseline	0.936594917	0.05377281	17.42	<.0001
CYC arm	-0.528627291	2.27171403	-0.23	0.8165
MMF arm	0.000000000	.	.	.
Caucasian	-2.539803728	2.66775191	-0.95	0.3437

1C. Outcome: QILD-WL at 24 months

Parameter	Estimate	Standard Error	t Value	P-Value
Intercept	3.045143406	2.67220691	1.14	0.2576
MUC5B presence	-2.333839575	2.36647746	-0.99	0.3268
QILD-WL Baseline	0.805585776	0.06830329	11.79	<.0001
CYC arm	1.365380101	1.83945368	0.74	0.4599
MMF arm	0.000000000	.	.	.
Caucasian	0.069880494	2.11895742	0.03	0.9738

1D. Outcome: QILD-ZM at 24 months

Parameter	Estimate	Standard Error	t Value	P-Value
Intercept	0.397806993	4.30606699	0.09	0.9266
MUC5B presence	-2.087144802	3.31622549	-0.63	0.5308
QILD-ZM Baseline	0.972417103	0.05982617	16.25	<.0001
CYC arm	0.102744235	2.56950723	0.04	0.9682
MMF arm	0.000000000	.	.	.
Caucasian	0.967680055	3.03414005	0.32	0.7505

ILD (QILD) scores for whole lung (WL) and zone of maximum involvement (ZM) were measured at baseline and 24 months. Linear regression models with the outcomes of change in radiographic fibrosis and ILD scores at 24 months were created to investigate the relationship between the presence of the MUC5B variant and SSc-ILD progression.

Results: Among 128 SLS II participants, 23 (18%) possessed at least one copy of the MUC5B rs35705950 minor allele. There were no significant differences in the baseline characteristics between SSc-ILD patients with and without this variant with respect to age, sex, %diffuse disease, disease duration, FVC, DLCO, radiographic extent of fibrosis, nor the presence of honeycombing on high resolution computed tomography. Similar to available data from the general population, this variant was rare among African Americans (4%) in our cohort. The presence of this MUC5B variant was not significantly associated with the change of QLF-ZM, QLF-WL, QILD-ZM, QILD-WL scores at 24 months, even after adjusting for baseline extent of fibrosis, treatment arm, and race (Table 1). In addition, using a joint model analysis with the covariates of FVC, treatment arm, race and a time trend, the presence of the MUC5B variant did not predict the course of the FVC%-predicted.

Conclusion: Among SSc-ILD patients with ground glass opacity on imaging who received treatment with CYC or MMF in a rigorously-conducted clinical trial, the presence of MUC5B rs35705950 minor allele did not predict ILD disease progression. Future studies are needed to further investigate how the presence of this variant affects outcomes in other SSc populations.

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Abstract Number: 0738

Systemic Sclerosis Myocarditis Has Unique Clinical, Histological and Prognostic Features: Comparative Analysis Between Patients with Endomyocardial Biopsy-proven Myocarditis

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

Background/Purpose: Myocarditis is a life-threatening inflammatory disease increasingly reported in Systemic Sclerosis(SSc); the histological, clinical and prognostic features of SSc-myocardits have not been elucidated yet. We aimed to evaluate clinical, histological and prognostic features of SSc-myocarditis compared to patients with endomyocardial biopsy(EBM)-proven virus-negative myocarditis(VNM).

Table 1. Demographic and clinical characteristics of our cohort.

SSc patients (12)	
Females, n (%)	11 (91.7)
Age (years), mean ± SD	49.3 ± 14.2
Disease duration (months), mean ± SD	47.6 ± 18.3
Diffuse cutaneous disease, n (%)	7 (58.3)
Anti-Scl70, n (%)	8 (66.7)
Anti-centromere, n (%)	4 (33.)
Clinical onset	
Subclinical onset, n (%)	6 (50.0)
Heart failure, n (%)	3 (25)
Ventricular arrhythmias, n (%)	2 (16.7)
Chest pain, n (%)	1 (8.3)
Cardiac deaths, n (%)	6 (50)*
Patients with i-VNLM (12)	
Age (years), mean ± SD	47.7 ± 10.8
Clinical onset	
Subclinical onset, n (%)	2 (16.7)
Heart failure, n (%)	0 (0)
Ventricular arrhythmias, n (%)	7 (58.3)
Chest pain, n (%)	3 (25)
Cardiac deaths, n (%)	0 (0)
Patients with a-VNLM (8)	
Age (years), mean ± SD	48.4 ± 16.3
Systemic Lupus Erythematosus, n (%)	3 (37.5)
Anti-synthetase syndrome, n (%)	2 (25.0)
Anti-phospholipid syndrome, n (%)	1 (12.5)
Undifferentiated connective tissue disease, n (%)	1 (12.5)
Eosinofilic granulomatosis with polyangiitis, n (%)	1 (12.5)
Clinical onset	
Subclinical onset, n (%)	6 (75)
Heart failure, n (%)	0 (0)
Ventricular arrhythmias, n (%)	2 (25.0)
Chest pain, n (%)	0 (0)
Cardiac deaths, n (%)	0 (0)

*SSc= systemic sclerosis, classified according to ACR/EULAR 2013 classification criteria; VNLM=virus negative lymphocytic myocarditis; i-VNLM= isolated VNLM; a-VNLM= VNLM in the course of systemic immune-mediated diseases other than SSc; SD= standard deviation; n= number; *3 patients died suddenly do to fatal arrhythmias, 3 patients died for congestive heart failure.*

Methods: we enrolled 12 SSc patients with EBM-proven myocarditis(SSc-VNM), 12 patients with isolated VNLM(i-VNM) and 8 patients with VNLM in the context of other systemic autoimmune diseases(a-VNM), matched by age, gender and cardiovascular risk profile. On EMB, VNM was classified as acute, chronic and subacute, and the degree of fibrosis was scored as 0=absent,1=mild;2=moderate;3=severe. Clinical data, cardiac enzymes, echocardiogram, 24h-ECG-Holter and cardiac magnetic resonance(CMR), were obtained at baseline and at 3, 6 and 12 months, then during follow-up as clinically needed. Myocarditis-related complications(cardiac death, end-stage heart failure[HF], malignant arrhythmias or need for ICD-implantation) were recorded during a 1-year follow-up. Non parametric tests were used.

Results: clinical and demographic characteristics of our cohorts are represented in Table1. Clinical presentation did not statically differ between the 3 groups(p=ns), although dyspnoea class was significantly higher at presentation in SSc-VNLM patients compared to i-VNLM and a-VNLM (median 2 vs 0,p=0.047) and we found HF only in SSc-VNLM(25%). At CMR, myocardial oedema was more frequent in i-VNLM and a-VNLM, compared to SSc-VNLM(75% and 75% vs 8.3%,p=0.002), whereas late gadolinium enhancement(LGE) was present in all SSc-VNLM patients and in the majority of i-VNLM(87.5%) and a-VNLM(83.3%) patients(p=0.457). Levels of troponin T and NT-proBNP, left ventricular ejection fraction and number of ventricular ectopic beats on 24h-Holter did not differ between groups(p=ns). On EBM, acute myocarditis was diagnosed in 50% of both i-VNLM and SSc-VNLM patients, compared to 12.5% of a-VNLM patients(p=0.178); chronic myocarditis was diagnosed in 25% of both i-VNLM and SSc-VNLM patients, compared to 12.5% in a-VNLM patients(p=0.758), while subacute myocarditis was almost statically significantly more frequent in i-VNLM(75%), as compared to a-VNLM and SSc-VNLM patients(25% for both,p=0.063). The mean fibrosis score was significantly higher in SSc-VNLM patients(1.5±1.08) compared to a-VNLM(0.87±0.35) and

i-VNLM(0.58±0.52)(p=0.046). As about the clinical outcome, the number of patients who died during follow-up due to cardiac complications (sudden cardiac death and HF) was significantly higher in SSc-VNLM patients(6 patients,50%), as compared to a-VNLM(0%) and i-VNLM(1 patient,8.3%)(p=0.006). Arrhythmic complications and need for ICD implantation were comparable between groups(25% and 8.3% in SSc-VNLM, 25% and 12.5% in a-VNLM, and 33.3% and 33.3% in i-VNLM,p=ns).

Conclusion: SSc-related myocarditis tends to present more frequently with HF and a higher dyspnoea class and to show higher degrees of fibrosis on EBM. These peculiar features are paralleled by a worst cardiac prognosis.

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Abstract Number: 0739

Does Digital Thermal Monitoring Correlate to Specific Nailfold Videocapillaroscopy Abnormalities?

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Background/Purpose: The fingers have specialized structural and functional features for thermoregulation, and are the most common areas of Raynaud's phenomenon (RP) in systemic sclerosis (SSc). Nailfold videocapillaroscopy (NVC) is the gold standard for quantification of vascular abnormalities in SSc-RP. Digital thermal monitoring (DTM) of vascular reactivity assesses Doppler ultrasound hyperemic, low frequency, blood velocity of radial artery and fingertip vascular function. In this study, we investigated the correlation of NVC patterns and DTM variables in SSc patients.

Methods: Patients enrolled in a single center SSc (2013 ACR/EULAR Classification Criteria) registry who had NVC and DTM performed at a time standard care visit were included in this analysis. The SSc clinical features were recorded. DTM of both hands was obtained during 5 min stabilization, 5 min cuff inflation to 50 mm Hg greater than systolic blood pressure, and 5 min deflation using an automated, operator-independent protocol (VENDYS, Endothelix Inc., Houston, TX). Thermal changes during a 5 min arm-cuff induced reactive hyperemia test were monitored continuously in the fingertip of both the occluded and non-occluded arms using VENDYS software. Dual channel temperature data were simultaneously recorded at a 1 Hz sampling rate. Temperature rebound is defined as temperature prior to cuff inflation subtracted from temperature maximum after cuff relief. Temperature rebound area under the curve is provided as a single value of DTM. Vascular reactivity index (VRI) was calculated on adjusted temperature rebound. NVC was performed to classify the patients into one of the three main patterns of SSc microangiopathy ("early", "active", "late"). The following parameters were analyzed in eight fingers of the hands (excluding thumbs): number of

capillaries/mm, number of enlarged and giant capillaries, microhemorrhages, and avascular score. Statistical evaluation was performed by non-parametric tests to assess the correlation of NVC and DTM variables.

Results: Thirty-one SSc subjects with interpretable NVC and DTM performed on the same day were included in the study. Thirty subjects were female (91%) and mean age ± SD was 58 ± 12 yrs. Mean duration from first non-RP symptom of SSc was 10.8 ± 8 yrs. VRI was progressively higher in SSc patients with the 'early', 'active' and 'late' NVC patterns of microangiopathy ($p< 0.0001$, Kruskal-Wallis test). There was a significant negative correlation between VRI and microhemorrhages score ($r=-0.363$, $p=0.044$, Spearman's rank correlation). There was no correlation between VRI and other NVC parameters (data not show).

Conclusion: Correlation of NVC patterns and microhemorrhages parameter with VRI seen in this non-invasive study warrants further research. The lack of complete correlation between functional and morphological microvascular abnormalities, measured by DTM and NVC, suggests each of these tools has a place in the evaluation of microangiopathy aspects in SSc patients and complement each other.

Disclosure: M. Radic, None; **R. Overbury**, None; **T. Frech**, None.

Abstract Number: 0740

Rituximab Rescue Therapy in Patients with Systemic Sclerosis or Other Connective Tissue Diseases and Refractory Interstitial Lung Disease

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
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Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a common and life-threatening organ manifestation of patients with various connective tissue diseases (CTDs), and with systemic sclerosis and anti-synthetase syndromes, in particular. B cell depletion with rituximab (RTX) is used as an off-label rescue therapy in patients with CTD-ILD progressing despite conventional immunosuppression. The purpose of this study was to systematically evaluate the outcome of such RTX rescue therapy in our center.

Methods: For the years 2009 through 2018, a monocentric historical prospective chart review was performed on all patients with RTX treatment for interstitial lung disease and a connective tissue disease. Patients were identified by systematically screening documentation of all CTD patients treated for ILD on the Rheumatology ward and of all patients with systemic sclerosis (SSc), poly- or dermatomyositis, mixed connective tissue disease (MCTD) and Sjögren's syndrome for patients with ILD and treated with rituximab. All patients were followed until the end of 2018, death, or loss of follow-up (n=1). ILD was confirmed by both high resolution CT imaging and pulmonary function tests (PFT) with forced vital capacity (FVC) and/or total lung capacity (TLC) and/or corrected diffusion capacity for carbon monoxide (DLCOc) < 80% of predicted value. Mean changes in %FVC (n=18), %TLC (n=20) and %DLCOc (n=17) to baseline were compared between 2-12 months before (pre-RTX) and 2-12 months after (post-RTX) the initial RTX administration. Paired t-test and Wilcoxon matched pairs signed rank test were used as appropriate.

Results: A total 21 patients were identified, of whom 15 and 2 patients met the ACR/EULAR criteria for SSc and primary Sjögren's syndrome (SjS), respectively, and 4 patients the EULAR/ACR criteria for polymyositis (PM). Patients received RTX at a median of 13 [IQR 5-49] months after the ILD diagnosis. The median follow-up after initial RTX treatment was 2.1 (0.1-9.8) years. The baseline median FVC was 63.2% [IQR 52.9-78.2%], mean±SD TLC 72.1±17.3% and mean±SD DLCOc 38.4±18.3%. Before RTX administration, patients had received a median of 2 (1-4) other immunosuppressive therapies, including cyclophosphamide in n=14 patients. In contrast to a mean decline of -6.4±11.8% in FVC and -3.2±8.5% in TLC in the pre-RTX interval, paired analysis of PFT data showed a mean improvement of +5.2±9% in FVC ($p< 0.01$) and of +2.6±8.1% in TLC ($p=0.04$) post-RTX. No significant improvement in DLCOc was seen (pre-RTX -2.8% [IQR -12.2-0.8%], post-RTX -1.8% [IQR -3.3-11.1%]). A total of five of the 21 RTX-treated patients died. One SSc patient died of non-small-cell-lung cancer with brain metastases, diagnosed 1.5 years after last RTX treatment. One patient with SSc developed pneumonia after the first RTX administration and died in septic shock. Two other SSc patients (one with sigmoid cancer) died of right heart failure due to pulmonary embolism 1 and 7 months after last RTX administration. The death of one patient with PM was reported due to an unspecified malignancy.

Conclusion: Our monocentric experience is in line with stabilization of lung function in CTD patients undergoing RTX rescue therapy for severe, refractory ILD, and in SSc, in particular.

Disclosure: M. Benad, None; **D. Koschel**, Roche, 8; **K. Herrmann**, None; **K. Wiefel**, None; **A. Kleymann**, None; **M. Aringer**, Abbvie, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, 8, BMS, 5, 8, Boehringer Ingelheim, 5, 8, Bristol-Myers Squibb, 5, 8, Chugai, 5, 8, Hexal, 8, HEXAL, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, Sanofi-Aventis, 5, 8, UCB, 8.

Abstract Number: 0741

Vascular Damage Is Less Present in an Early Inception Cohort in Takayasu's Arteritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica
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Session Time: 9:00AM–11:00AM

Background/Purpose: There is only retrospective and very limited data for the long term prognosis of Takayasu's Arteritis (TAK), a rare large-vessel vasculitis. In this study, we aimed to present the preliminary results of a Takayasu Inception Cohort settled for long term, prospective follow-up of only newly-diagnosed patients with TAK.

Methods: Patients fullfilling the American College of Rheumatology 1990 criteria for TAK and diagnosed in the last 12 months were included to the study. Patients' data were recorded in an electronic database of an international "Takayasu's Arteritis Registry" requiring baseline and at least annual visits. Data is compared with an historical Turkish cohort previously published (*Bıçakçıgil, et al, 2009).*

Results: The study included 170 patients (age: 38.5±13.1 years, F/M: 143/27) with TAK from 15 tertiary Rheumatology centers in Turkey. The mean symptom duration of patients was 5.2 years at diagnosis. According to the angiographic classification, 68.2% of the study group had type I and only 18.3% had type V disease. When we

Table 1: Clinical characteristics of Inception and Retrospective Cohorts from Turkey

	Inception Cohort (n=170)	Retrospective Cohort (*Bicakcigil, et al*) (n=248)
Constitutional symptoms	115/165(69.6%)	163/248/ (66%)
Limb claudication	87/131(66.4%)	119/248 (48%)
Carotidynia	31/130 (18.2%)	-
Pulseless	45/130(34.6 %)	218/248 (88%)
Musculoskeletal manifestations	90/163 (52.9%)	104/248 (42%)
Mucocutaneous manifestations	30/162 (17.6%)	22/248 (8.8%)
Respiratory manifestations	47/163 (28.8%)	22/184 (12%)
Neurologic manifestations	69/163 (40.6%)	156/248 (63%)
Cardiac involvement	64/146 (43.8 %)	141/248 (57%)
Ophthalmologic involvement	27/166 (16.2%)	57/248 (36%)

compared our results to our retrospective cohort (previously published by Turkish Takayasu Arteritis Study Group), constitutional symptoms (115/165= 69.6% vs 66%) and limb claudication (87/131= 66.4% vs 48%) were observed to be more frequent, whereas pulselessness (45/130=34.6 %vs 88%) was less in the inception cohort.(Table 1) Carotidynia was present only in the inception cohort. Similarly, mucocutaneous symptoms also seem to be a feature of newly-diagnosed disease (30/162=18.5% vs 8.8%). Regarding comorbidities at diagnosis, the rate of dyslipidemia was 17.6 (30/165)%, diabetes mellitus 15.1(25/165)%, smoking 20 (34/164)% and obesity (BMI >30) 14 (22/157)% among TAK patients. All patients were given oral corticosteroid (CS) therapy (0.5-1 mg/kg) at diagnosis, 17 patients (17/170=10%) also having CS pulses. In addition to CSs, 86 patients (50.6 %) were given methotrexate, 31patients (18.2%) azathioprine, 6 (3.5%) cyclophosphomide, 12 patients (7.1%)leflunamide, 2(1.2%) patients mycophenolate mofetil and 5(2.9%) patients biologics at disease-onset(2 tocilizumab, 2 infliximab, 1 adalimumab). Biologic agents were chosen for 7 patients (7/32) at last vizit(1 adalimumab, 4 tosiluzumab, 2 infliximab). Seventy-three patients (42.9%) had follow-up > 3 months. Remission was observed 78% of patients. At least one relaps was observed 40% of these patients. Mortality rate was 4.1% (3/73 patients) during a mean 25.7 months follow-up.

Conclusion: Our results suggest that, in an inception cohort, signs and symptoms of 'systemic inflammation' is more prominent in newly-diagnosed TAK patients, whereas vascular extent and damage accumulates during the disease course. The long term follow-up of our inception cohort shows that 40% of patients relapse within 2 years after diagnosis in spite of IS treatments.

Disclosure: F. Alibaz-Oner, None.

Abstract Number: 0742

Polymyalgia Rheumatica: New Therapeutic Strategy Based on Low Dose Metrotexate Plus Local Infiltration with Corticosteroids

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Polymyalgia rheumatic (PMR) is a common rheumatic inflammatory disease in the elderly. Glucocorticoids (GC) are the therapeutic mainstay in PMR but induce significant toxicity in this population. Methotrexate (MTX) has demonstrated efficacy as a steroid sparing agent in two randomized clinical trials but has not been studied as first line therapy. Our objetive is to evaluate the efficacy and safety of first-line MTX plus initial and on demand local GC infiltrations without oral GC.

Methods: In a single-center prospective observational study, 26 patients with newly diagnosed PMR (EULAR/ACR criteria) who had not received oral GC, were treated with MTX plus initial and on demand shoulder infiltrations with 40 mg triamcinolone acetonide for 24 months. At each visit (at one month and on a quarterly basis) patient 100 mm VAS pain for shoulders and hips, morning stiffness duration and HAQ were recorded. Remission was defined as absence of reported pain and morning stiffness and normalization of acute phase reactants (APR). After two years of treatment, MTX was withdrawn and patients were followed-up for additional 14±4 months. The primary end point was the rate of PMR remission at 6 months. Secondary outcomes were toxicity, remission at 24 months and relapses after MTX withdrawal.

Results: 26 patients were included. Three patients did not complete the study due to prostate cancer, an asthmatic episode requiring high dose GC, or MTX intolerance. These 23 patients (57% female) had a mean age of 74±8 years and a mean disease duration of 110±55 days. Initial weekly MTX dose was 5 mg in 14 patients and 7,5 mg in 9, and further increased according to efficacy/toxicity. Only 5 patients required more than 10 mg and the mean dose was 9±3 mg. Mean time until remission was 2.7±1.9 months. Other measures of efficacy are shown in Table 1. The mean number of GC infiltrations along the 24 months was 1.4±0.7 per shoulder. During the first 24 months, 5 patients had relapses that resolved with MTX dose increase and/or GC shoulder infiltration. MTX was well tolerated in all but one patient initially excluded due to digestive intolerance. Side effects included one alopecia, one mild thrombopenia, one diabetes onset, and one respiratory infection, but none required MTX suspension. None suffered osteoporotic fractures. In 20 of the 23 patients, MTX was stopped after 24 months, and after 14±4 months of follow-up no relapses were observed.

	Baseline	Month 6	*p value*	Month 24	*p value*
mVAS shoulders	7,87 (0-6)	0,57 (0-6)	*p=0,000**	0,74 (0-4)	*p=0,000**
mVAS hips	6,39 (3-9)	0,61 (0-5)	*p=0,000**	0 (0-0)	*p=0,000**
Morning stiffness (min)	90 (60-120)	0 (0-90)	*p=0,000**	0 (0-0)	*p=0,000**
mHAQ	2.2 (1-3)	0.3 (0-2.1)	*p=0,000**	0 (0-0.4)	*p=0,000**
Abnormal CPR	22 (97)	3 (13)	*p=0,000***	0 (0)	*p=0,000***
Abnormal VSG	21 (91)	2 (9)	*p=0,000***	0 (0)	*p=0,000***

*Wilcoxon rank test, **McNemar test.

Conclusion: Low dose methotrexate is effective as initial therapy for PMR in combination with a very limited exposure to local GC infiltrations. Randomized controlled trials are warranted to confirm this observation that may significantly reduce GC side effects in this population

Disclosure: M. Retuerto, None; **P. Fernández-Dapica**, None; **P. Lavilla**, None; **F. Lozano**, None; **M. Vallejo**, None; **J. Pablos**, None.

Abstract Number: 0743

Association Between Acute-phase Reactants, interleukin-6(IL6), Tumor Necrosis Factor-a(TNFa) and Disease Activity in Takayasu's Arteritis During Follow-up with Repeated Evaluation of Vascular Imaging Manifestations

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica

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Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the laboratory indicators of disease activity during follow-up of Takayasu's arteritis(TAK).

Methods: Electronic data of 588 patients with TAK enrolled in the Chinese Registry for Systemic Vasculitis (CRSV) from 2013 to April 30 of 2019 were exported for analysis. Disease activity was judged with clinical manifestations, BVAS and VDI scoring, laboratory results and vascular imaging including Doppler and/or CTA by a senior rheumatologist in each visit. Records of visit with repeated vascular imaging examinations were collected,and erythrocyte sedimentation rate(ESR), the serum levels of high sensitive C-reactive protein(hsCRP), interleukin-6(IL6), and tumor necrosis factor-a(TNFa) of these patients in each visit were analyzed for the association with disease activity by logistic regression.

Table 1 Univariate and multivariate logistic regression analysis of ESR, hsCRP, IL6 and TNFα with TAK disease activity

Variations in equation	Total		After correction of age		After correction of gender		After correction of disease duration		Exclude patients with medication of TNFα or IL-6 inhibitor and/or pregnancy	
	P-value	Expectancy(95%CI)	*P*-value	Expectancy(95%CI)	*P*-value	Expectancy(95%CI)	*P*-value	Expectancy(95%CI)	*P*-value	Expectancy(95%CI)
Log_{10}ESR	<0.001	7.69 (5.55, 10.65)	<0.001	7.70 (5.56, 10.66)	<0.001	7.69 (5.55, 10.65)	<0.001	7.69 (5.55, 10.65)	<0.001	7.88 (5.48, 11.32)
Log_{10}hsCRP	<0.001	4.65 (3.81, 5.66)	<0.001	4.67 (3.83, 5.70)	<0.001	4.65 (3.81, 5.67)	<0.001	4.65 (3.81, 5.67)	<0.001	4.94 (3.96, 6.16)
Log_{10}IL6	<0.001	8.78 (6.00, 12.84)	<0.001	8.83 (6.03, 12.92)	<0.001	8.71 (5.95, 12.75)	<0.001	8.80 (6.02, 12.87)	<0.001	12.68 (8.09, 19.87)
TNFα(2)	0.001	1.50 (1.17, 1.93)	0.001	1.51 (1.17, 1.93)	0.001	1.50 (1.17, 1.93)	0.001	1.50 (1.17, 1.93)	0.006	1.46 (1.11, 1.90)
Log_{10}ESR	0.02	1.69 (1.07, 2.68)	0.03	1.68 (1.06, 2.65)	0.02	1.70 (1.07, 2.69)	0.03	1.68 (1.07, 2.66)	0.05	1.64 (0.99, 2.69)
Log_{10}hsCRP	<0.001	2.53 (1.92, 3.34)	<0.001	2.56 (1.94, 3.39)	<0.001	2.55 (1.93, 3.37)	<0.001	2.54 (1.92, 3.35)	<0.001	2.49 (1.82, 3.41)
Log_{10}IL6	<0.001	3.72 (2.42, 5.72)	<0.001	3.72 (2.42, 5.71)	<0.001	3.67 (2.39, 5.64)	<0.001	3.74 (2.43, 5.74)	<0.001	4.05 (2.37, 6.91)
TNFα(2)	0.19	1.22 (0.91, 1.65)	0.17	1.23 (0.91, 1.66)	0.18	1.23 (0.91, 1.66)	0.19	1.22 (0.91, 1.65)	0.24	1.21 (0.88, 1.66)

Results: 1483 records of visit were collected. After transformation, log_{10}ESR, log_{10}hsCRP and log_{10}IL6 were found to be distributed normally. Due to the non-normal distribution pattern, TNFa was stratified into 2 groups by the upper normal range in healthy people(< 8.1pg/ml).In univariate logistic regression analysis, log_{10}ESR, log_{10}hsCRP, log_{10}IL6 and TNFa were strongly associated with the disease activity respectively. But in multivariate logistic regression analysis, the association between TNFa and disease activity disappeared. After correction of age, gender or disease duration, the result of logistic regression analysis were similar.After exclusion of records from the patients with medication of TNFa and/or IL6 inhibitors, and the patients with pregnancy during follow-up, the results of univariate logistic regression analysis were similar, but in multivariate analysis association between log_{10}ESR and disease activity disappeared.(Table 1)

Conclusion: Repeated vascular imaging examination in each follow-up visit combined with other clinical evaluation methods had proved the reliability for using ESR, hsCRP, IL6 and TNFa as indicator in evaluation of disease activity in patients with TAK. The effect of hsCRP and IL6 may be stronger than ESR and TNFa.

Disclosure: J. LI, None; **Y. Yang**, None; **Y. WANG**, None; **J. Zhao**, None; **M. Li**, None; **X. Tian**, None; **X. Zeng**, None.

Abstract Number: 0744

Are Hematologic Indexes Helpful in the Diagnosis and Prognosis of Polymyalgia Rheumatica?

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica
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Session Time: 9:00AM–11:00AM

Background/Purpose: Recently, the use of hematologic indexes as markers of systemic inflammation has been reported in oncological, cardiovascular and rheumatic diseases. Only 2 studies evaluated their role in polymyalgia rheumatica (PMR).

Our objective was to primarily compare the levels of neutrophil- (NLR), monocyte- (MLR), eosinophil- (ELR), basophil- (BLR) and platelet to lymphocyte ratio (PLR) in PMR and control patients without inflammatory conditions and, secondarily, to evaluate their use as prognostic markers in PMR.

Table 1. Age, gender and laboratory date of both populations

	PMR (n=63)	Controls (n=101)
Age, *years mean (SD)*	76.7 (7.6)	73.2 (6.9)
Gender, *M/F*	21/42	17/84
WBC, *10^9/L mean (SD)*	8.48 (2.37)	6.51 (1.57)
Neutrophil count, *10^9/L mean (SD)*	5.35 (1.86)	3.73 (1.21)
Lymphocyte count, *10^9/L mean (SD)*	2.11 (0.81)	2 (0.55)
Monocyte count, *10^9/L mean (SD)*	0.72 (0.25)	0.53 (0.18)
Eosinophil count, *10^9/L mean (SD)*	0.23 (0.24)	0.21 (0.16)
Basophil count, *10^9/L mean (SD)*	0.03 (0.02)	0.03 (0.02)
Platelets count, *10^9/L mean (SD)*	284.02 (82.41)	249.09 (55.22)

Table 2. Characteristics of PMR patients

N	63
Age, *years mean (SD)*	76.7 (7.6)
Gender, *M/F*	21/42
Charlson comorbidity index, *median (IQR)*	4 (3-5)
Duration of symptoms before diagnosis, *months, median (IQR)*	2 (1-6)
Initial dose of corticosteroids, *mg/d, mean (SD)*	16.6 (4.5)
Duration of treatment, *months, median (IQR)*	15.7 (10.5-27.8)
Duration of follow up, *months, median (IQR)*	18.1 (10.5-35.3)
Relapses, *n (%)*	22 (34.9)
Recurrences, *n (%)*	11 (17.5)
Use of methotrexate, *n (%)*	24 (38.1)

Table 3. Comparison of NLR in PMR patients based on relapses, recurrences and use of methotrexate

		NLR	p
Relapses	yes	2.33 (0.77)	0.07
	no	3 (1.59)	
Recurrences	yes	2.55 (1.02)	0.57
	no	2.81 (1.46)	
Use of MTX	yes	2.54 (0.92)	0.3
	no	2.91 (1.60)	

Methods: This retrospective case control study included 63 patients with PMR and 101 patients without inflammatory conditions who attended our Hospital. Clinical data and blood cell counts at diagnosis (prior to start treatment) were obtained from medical records and laboratory reports.

We compared the indexes of both groups at diagnosis by a Student's t test and sequentially performed a subgroup analysis in PMR patients in order to determinate the utility of the indexes to evaluate prognosis, relapses and recurrences. We also analyzed the use of methotrexate as a marker of more severe disease. A correlation with inflammatory markers using Student's t test and Pearson correlation coefficient was performed

Results: Age, gender and laboratory data of PMR and control patients are shown in Table 1. The control group included patients with osteoarthritis (78,2%), fibromyalgia (9.9%) and others soft tissue non inflammatory conditions (11.9%). NLR and MLR levels were significantly higher in PMR patients than controls (NLR 2.77 vs 1.99, $p < 0.001$ and MLR 0.37 vs 0.27, $p < 0.001$). All the other indexes did not differ between populations. Clinical characteristics of PMR patients are shown in Table 2. The median time of follow up of PMR patients was 24.1 months (IQR 10.5-35.3). When evaluating this subgroup of patients, neither NLR nor MLR were associated with relapses, recurrences or need of methotrexate during follow up. Results shown in table 3. No correlation was found between both indexes and the duration of symptoms before diagnosis and duration of glucocorticoid treatment. The median erythrocyte sedimentation rate (ESR) was 41.5 mm/hr (19 – 62) and C reactive protein (CRP) level was 2.48 mg/L (0.54 – 3.38) at diagnosis. We found a poor correlation between NLR and MLR and ESR and CRP levels. Fourteen PMR patients (22.2%) had normal values of ESR and CRP. However, the treating physician considered the diagnosis on a clinical basis and started treatment accordingly. When comparing NLR and MLR levels, there were no differences between this group and control patients; on the other hand, a significant difference was found with PMR patients who presented with high levels of acute phase reactants.

Conclusion: NLR and MLR levels were significantly higher in PMR patients than controls. Baseline indexes did not correlate adequately with acute phase reactants and they were not able to predict a poor outcome in PMR.

Disclosure: M. de la Torre, None; **C. Pisoni**, None.

Abstract Number: 0745

Cardiac Involvements Are Related to Poor Prognosis in Patients with Takayasu's Arteritis in China

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Table 1. Echocardiographic values in patients with Takayasu arteritis in different groups.

	Total N=198	Normal N=55	Mild N=97	Severe N=46	P value
Cardiovascular values					
Aortic foot diameter (mm, median, IQR)	31(28-34)	29(27-32)	31(29-34)	32.5(30-36)	<0.001
Pulmonary artery pressure (mm, median, IQR)	32(28-35)	30(26.5-33)	31(28-35)	39(32-53)	<0.001
Atrioventricular values					
LA diameter (mm, median, IQR)	34.5(31.8-39)	32(30-34)	35(32-39)	40(35-42.8)	<0.001
LV end-systolic diameter (mm, median, IQR)	29(27-33)	27(26-29)	30(28-32)	35.5(28.3-45)	<0.001
LV end-diastolic diameter (mm, median, IQR)	46.5(43-51.3)	44(41.8-46.3)	47(43.3-50)	54(44.3-60)	<0.001
Septal thickness (mm, median, IQR)	9(8-11)	8(8-9)	10(9-11)	11(9-12)	<0.001
Ejection fraction (%)	66(61-69)	68(66-69.3)	65(62-68)	60(48-66.5)	<0.001

IQR indicates interquartile range; LA, left atrial; and LV, left ventricle.

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Table 2. Comparison of clinical features at baseline among different groups.

Characteristic	Normal (n=55)	Mild (n=97)	Severe (n=46)	P value
Demographics				
Sex, n(%)				0.455
Female	40(72.7%)	77(79.4%)	38(82.6%)	
Male	15(27.3%)	20(20.6%)	8(17.4%)	
Age at onset, year, median(IQR)	26(21-32)	34(24.5-47)	44.5(33-56)	<0.001
Duration of disease at first UCG, months, median(IQR)	10(2-40)	17(2-61)	24.5(9.5-96.3)	0.066
Numano angiographic classification, n(%)				0.859
Type I	15(27.3%)	22(22.7%)	10(21.7%)	
Type IIa	-	1(1%)	1(2.2%)	
Type IIb	6(10.9%)	15(15.5%)	4(8.7%)	
Type III	5(9.1%)	5(5.2%)	3(6.5%)	
Type IV	6(10.9%)	11(11.3%)	3(6.5%)	
Type V	23(41.8%)	43(44.3%)	25(54.3%)	
Symptoms, n(%)				
Chest distress	1(1.8%)	20(20.6%)	41(89.1%)	<0.001

Continued on next page

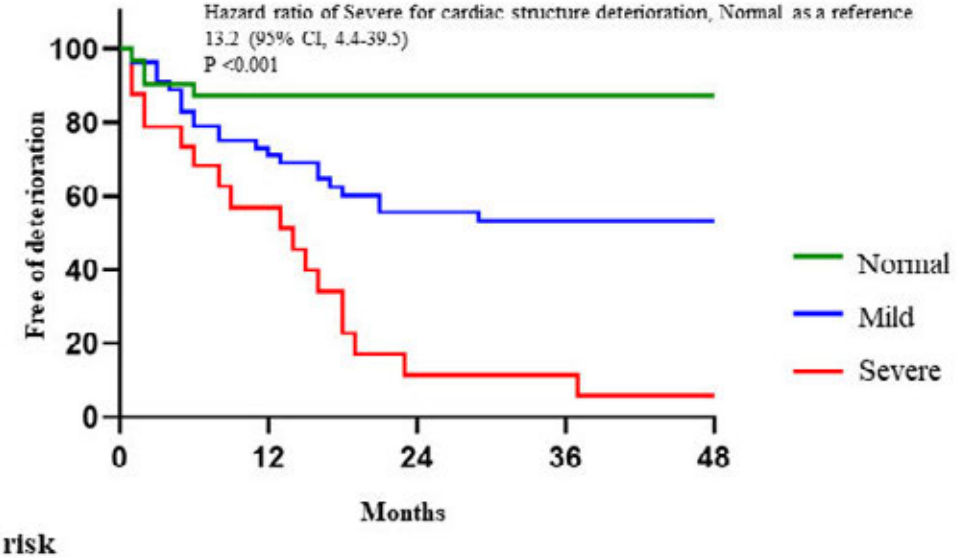
Background/Purpose: Heart involvements are closely associated with prognosis in patients with Takayasu's arteritis (TA). This study was aimed to assess the long-term adverse outcomes of cardiac structure and function and their underlying risk factors in TA.

Methods: One hundred and ninety-eight patients, diagnosed as TA, at the Department of Rheumatology, Zhongshan Hospital from January 2012 to December 2017 were recruited in the present study. Patients were divided into normal, mild and severe groups based on the severity of cardiac structure and function impairment. Data, including demographics, clinical characteristics, treatment at baseline, and cardiac outcomes during long-term follow-up were collected.

Results: 60.1% (119/198) patients exhibited heart involvement on echocardiography. 70.6% (84/119) and 79.8% (95/119) cases showed pathological valvular and atrioventricular abnormalities, respectively. The median follow-up duration of patients with heart involvement was 14.25 (8.47-24.92) months, and more than two echocardiography were performed. 3 cases of death were noted. That onset age (p=0.005) and baseline interleukin-6 level (p= 0.031)

Survival curve indicating the deterioration rate of cardiac structure in three groups.

	No. of events / No. of patients	1-year rate of deterioration (95% CI) %	2-year rate of deterioration (95% CI) %
Normal	4/31	2.1 (1.1-3.2)	2.1 (1.1-3.2)
Mild	23/57	11.3 (9.9-12.7)	28.3 (26.2-30.5)
Severe	19/30	20.0 (16.5-23.5)	69.2 (65.0-73.4)



No. at risk

Normal	31	27	27	27	27
Mild	57	42	35	34	34
Severe	30	20	12	12	11

were risk factors for the deterioration of cardiac structure. Using normal group as a reference, the risk of worsening cardiac structure (p< 0.001) and function (p< 0.001) was greatest in the severe group, with hazard ratios (HRs) of 13.2 (95% CI, 4.4–39.5) and 52.6 (95% CI, 6.8–403.9)respectively, which mostly occurred within 2 years after onset.

Conclusion: The prognosis of TA patients with severe cardiac structure and function impairment is relatively poor, particularly during the first 2 years after onset.

Disclosure: Y. Wang, None; **L. Ma**, None; **Y. Yan**, None; **Y. Sun**, None; **Y. Wang**, None; **X. Dai**, None; **Z. Ji**, None; **L. Ma**, None; **H. Chen**, None; **L. Jiang**, None.

Abstract Number: 0746

Childhood-Onset Takayasu's Arteritis (TAK) Is Clinically More Active, However Has Similar Cumulative Damage Compared to Adult-Onset TAK

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Childhood-onset Takayasu's Arteritis (TAK) may differ in presentation, clinical manifestations and treatment, as previously shown[1]. We aimed to compare the clinical manifestations, vascular involvement patterns, activity, damage and treatments used in childhood- and adult-onset TAK patients.

Methods: Patients from two cohorts of TAK from two tertiary-care centers in Turkey were retrospectively studied. Patients of the adult clinic were also classified as childhood-onset if they were diagnosed before the age of 18. Clinical presentation, angiographic data and treatment regimens were reviewed from clinical charts. The activity was determined by Indian Takayasu Clinical Activity Score (ITAS) on the first visit. Takayasu Arteritis Damage Score (TADS) and Vasculitis Damage Index (VDI) were employed to document the damage.

Results: Twenty four childhood-onset and 121 adult-onset TAK patients were included in the analysis (**Table 1**). In the basal visits, claudication of the arms [74 (62.2%) vs. 5 (20.8%), p< 0.001], carotidynia [19 (16%) vs. 0, p= 0.043], subclavian bruit [63 (58%) vs. 8 (35%), p= 0.044] and the loss of radial pulse [63 (57.8%) vs. 8 (34.8%), p= 0.044] were more common in adult-onset patients. In contrast, ischemic abdominal pain [5 (21%) vs. 8 (7%), p= 0.07], renal [9 (39%) vs. 15 (14%), p= 0.014] and abdominal bruits [11 (48%) vs. 9 (8%), p< 0.001] were more common in childhood-onset patients. Angiographic distribution of the involved vessels is shown in **Table 2**. Median ITAS score on the first visit was 15 (IQR: 10) for pediatric-onset and 13 (IQR: 6) for adult-onset cases (p=0.57). Medical treatment and surgical/interventional modalities are shown in **Table 3**. Median TADS score was 8 (IQR: 8) and 8 (IQR: 4) for pediatric and adult cases, respectively (p=0.91). Median VDI of the pediatric cases were slightly lower [4 (IQR:3) vs. 5 (IQR:3), p: 0.037]. Four of the adult patients and none of the pediatric patients died during follow-up. At least one episode of remission was achieved in 12 (50%) of pediatric cases and 91 (75%)

of adults (p=0.013). Among patients who had information regarding activity status, 12 (50%) of pediatric cases, and 88 (82%) of the adults were in remission at the last visit.

Conclusion: In childhood-onset TAK, the involvement of the aorta was more common, whereas the upper extremity was relatively spared as evidenced by symptoms and imaging. Remission was harder to achieve in pediatric cases,

Table 1. Demographics, clinical characteristics and angiographic classification of childhood-onset and adult-onset TAK patients

	Pediatric (n = 24)	Adult (n = 121)
Female	21 (87.5)	108 (89.3)
Age at Symptom Onset, Median (IQR) years	14 (6.3)	30 (19.5)
Age at Diagnosis, Median (IQR) years	14.15 (6)	34 (22)
Delay in Diagnosis, Median (IQR) months	3 (9)	12 (53)*
Follow-Up Duration, Median (IQR) months	53 (115)	69 (67)
Angiographic Classification		
1	1 (4.2)	43 (36.1)
2	3 (12.5)	14 (11.8)
3	4 (16.7)	0
4	5 (20.8)	3 (2.5)
5	11 (45.8)	59 (49.6)

Values represent the number (%) of the patients unless indicated otherwise.
IQR: Interquartile range
*p<0.001

Table 2. Distribution of angiographic abnormalities (DSA, MRA or CTA)

Angiographic Abnormality	Pediatric (%)	Adult (%)	p
Ascending Aorta	6 (25)	14 (12.1)	0.113
Descending Aorta	14 (58.3)	16 (13.8)	<0.001
Abdominal Aorta	15 (62.5)	27 (23.3)	<0.001
Any part of the Aorta	19 (79.2)	38 (32.8)	<0.001
Carotid	11 (45.8)	70 (60.3)	0.190
Subclavian	12 (50)	96 (82.8)	0.001
Mesenteric	14 (58.3)	30 (25.9)	0.002
Renal Artery	12 (50)	35 (30.2)	0.061
Distal Arm	0	16 (13.8)	0.074
Distal Leg	0	7 (6)	0.603
Coronary	1 (4.2)	12 (10.3)	0.468
Intracranial	1 (4.2)	1 (0.9)	0.314
Iliofemoral	5 (20.8)	14 (12.1)	0.322
Pulm Artery	1 (4.2)	5 (4.3)	0.975
Vertebral	5 (20.8)	29 (25)	0.665

Table 3. Comparison of medical and surgical treatments in childhood- and adult-onset patients

	Pediatric	Adult	p
MEDICAL			
Pulse Steroid n (%)	8 (36.4)	10 (9)	0.002
Oral Steroid mg (%)	24 (100)	104 (93.7)	0.352
Cumulative Steroid Dose, Median (IQR) grs	10.1 (6.48)	7.4 (8.45)	0.093
Cyclophosphamide	12 (50)	10 (9)	<0.001
Any Biologic Treatment* n (%)	11 (47.8)	14 (12.6)	<0.001
Tocilizumab n (%)	8 (33.3)	4 (3.6)	<0.001
Anti-TNF n (%)	3 (13)	13 (12)	0.858
INTERVENTION*			
Any Intervention Before Diagnosis	0	24 (22.4)	0.007
Any Intervention After Diagnosis	9 (37.5)	20 (18.2)	0.037

* Includes stent procedures, baloon angioplasty and surgery
Values represent the number (%) of the patients unless indicated otherwise.
IQR: Interquartile range

and they were treated with more biologic agents. Although more surgeries were also required, the cumulative damage seemed similar in both groups.

References:

1. Sahin, S. et al. Childhood–onset Takayasu arteritis: A 15-year experience from a tertiary referral center. *Int J Rheum Dis*. 2019; 22: 132– 139.

Disclosure: M. Karabacak, None; **S. Kaymaz-Tahra**, None; **S. Sahin**, AbbVie, 2; **M. Yıldız**, None; **A. Adrovic**, AbbVie, 2; **K. Barut**, AbbVie, 2; **H. Direskeneli**, None; **O. Kasapcopur**, AbbVie, 2; **F. Alibaz-Oner**, None.

Abstract Number: 0747

Detrimental Factors Affecting the First-year Clinical Response in Korean Patients with Polymyalgia Rheumatica

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Polymyalgia rheumatica (PMR) is a chronic inflammatory disease in which patients respond well to glucocorticoids (GCs). However, a number of patients experience a flare in the course of tapering GCs. We aimed to elucidate the negative factors that hinder the early clinical response in PMR patients.

Methods: Electronic medical records of 85 PMR patients between Jan 2011 and Dec 2017 were reviewed in second and tertiary centers. We analyzed the clinical and laboratory data at diagnosis (baseline), then at follow-up visits of these subjects. The tapering schedule of GC was determined by the attending rheumatologist. Patients were classified into subjects with a good versus poor clinical response mainly based on the daily GC (prednisolone or its equivalent) dose at the end of the year. Logistic regression analysis was performed to assess the factors related to an unfavorable response in our subjects.

Results: The mean age of PMR patients was 70.7 years with mean disease duration of 38.9 months, and 60% patients (51/85) were females. The mean dose of daily GC at the end of the year was 5.7 mg; 61.2% of patients tapered GC to less than 5 mg/day. The patients with hip pain or restricted range of hip motion at diagnosis showed a good clinical response (p = 0.002). In contrast, the presence of peripheral arthritis at diagnosis was associated with a poor clinical response to GCs (p = 0.002). A multivariable logistic regression analysis revealed that absence of hip involvement [hazard ratio (HR); 0.179, 95% confidence interval (CI); 0.053-0.600, p = 0.005], presence of peripheral arthritis [HR; 4.099 (1.412-11.900), p = 0.009] and concurrent diabetes mellitus (HR; 3.524, 95% CI; 1.064-11.672, p = 0.039) at diagnosis were independently associated with a poor clinical response during the first year of treatment.

Conclusion: Our study demonstrates that PMR patients with peripheral arthritis or diabetes mellitus, and those without hip involvement are prone to a poor first-year clinical response to treatment.

References:

1. Albrecht K, Huscher D, Buttgereit F, et al. Long termglucocorticoid treatment in patients with polymyalgia rheumatica, giant cell arteritis, or both diseases: results from a national rheumatology database. Rheumatol Int. 2018; 38: 569–577.
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Disclosure: Y. Oh, None; **S. Jung**, None; **B. Choi**, None; **K. Shin**, None.

Abstract Number: 0748

Takayasu Arteritis and Sacroiliitis: A Case Control Study in 28 Patients of a Single Italian Center

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SESSION INFORMATION
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A lot of clinical case descriptions about spondyloarthropathy in TAK patients were reported. Recently, a paper about an increased incidence of spondyloarthropathy in TAK patients (Guzel Esen S., Joint Bone Spine 2019 in press) was published. The diagnosis of sacroiliitis may be performed by X-ray, CT or MRI. CT findings of sacroiliitis are: contour irregularities, joint space alterations, joint erosion, subcondral bone changes (osteoporosis or sclerosis), enthesitis, ankylosis. Patients with Takayasu Arteritis (TAK) performe routinely FDG-CT-PET for monitoring disease activity. The aim of this study is to understand if there are an increased association of sacroiliitis in TAK patients in our monocentric cohort.

Methods: We collected retrospectively imaging data (CT) from 28 patients affected by TAK and 28 controls undergoing FDG-PET-CT scan in our center. Controls were selected among patients who performed FDG-PET-CT in our Nuclear Medicine Unit, excluding patients with bone tumors, tumors with bone metastasis and thyroid cancers. The majority of controls were affected by lymphoma in a complete remission. Controls and patients were matched for sex and age. An expert rheumatologist read the CT scans of sacroiliac joints.

Results: No patients and no controls demonstrated FDG-uptake in sacroiliac joints.

In the control group, we detected sacroiliac sclerosis in two cases: one due to a degenerative changes and another to a sacroiliitis (1/28, 4%).

In the TAK group four patients presented CT alterations suggestive for sacroiliitis: bilateral erosions in one case, a bilateral sclerosis in one case, a mono lateral sclerosis in two cases (4/28,14%). One of these patients complained an inflammatory back pain.

Conclusion: In our cohort of TAK patients we demonstrated an increased prevalence of sacroiliitis, diagnosed by CT scan. Only one patient of TAK group reported an inflammatory back pain, while three patients had only radiological signs of previous sacroiliitis. This reinforce the need to look for spondyloarthropathy in TAK patients even if asymptomatic.

Disclosure: P. Toniati, None; **F. Regola**, None; **F. Franceschini**, None; **G. Bosio**, None; **A. Tincani**, None.

Abstract Number: 0749

Childhood Takayasu Arteritis: Characteristics and Outcomes of a Mexican Cohort

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SESSION INFORMATION
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Takayasu arteritis (TA) is a large vessel vasculitis that affects aorta and its main branches. Despite being the third most common vasculitis in childhood, it still rare and data are scarce in the literature. Diagnosis may be delayed due to its non-specific manifestations. Early diagnosis and treatment are essential due to its high morbidity and mortality in these patients.

Methods: A descriptive single-center study of pediatric patients that met the EULAR/PRINTO/PReS criteria for childhood TA (cTA) between January 2000 and April 2019. Demographic data, time to diagnosis, clinical features, laboratory markers, imaging features, extension according to the Numano classification and treatment were documented. Disease activity was retrospectively assessed at the time of diagnosis by Paediatric Vasculitis Activity Score (PVAS). Damage was assessed by Paediatric Vasculitis Damage Index (PVDI) at last follow-up.

Results: Ten patients were included. Demographic data and main features are shown in table 1. Non-specific symptoms were the predominant ones at presentation (90%) followed by more specific manifestations in most cases. In our population, there is a tendency to present extensive vascular disease (Numano V in 50%). Most frequently involved vessels are shown in table 2. All patients were active at the time of their recruitment in our institution (documented by clinical and laboratory findings or by positron emission tomography). Nevertheless, only 40% of them had acute phase reactants elevation (ESR 30% and CRP 30%), which suggests that these analytes do not always correlate with cTA activity. Medical treatment included: glucocorticoids (100%), methotrexate (80%), azathioprine (20%), biological therapy (20%) and others (mycophenolic acid and cyclophosphamide). Six patients (60%) required interventional treatment, five of them (50%) endovascular intervention with stenting. Arteries that required interventional treatment (Stenting) are shown in table 3. Thoracic and abdominal aorta were the more frequently arteries that required surgical replacement with stenting. Two patients required intra-stent balloon angioplasty; one of them required this procedure 3 times. In the first time with placement of a non-medicated stent in one renal artery and twice more placement of medicated stents in both renal arteries because stent restenosis (intra-stent stenting in one side). One patient was treated with balloon angioplasty in both renal arteries and abdominal aorta without stenting. Only three patients (30%) required a surgical procedure. Mortality was 10%, after non-coronary Valsalva sinus plasty with supra-coronary replacement of ascending aorta).

Table 1. Demographic data and main features	
Characteristic	**Patients (n=10)**
Median age at diagnosis	10.4 years (1 a 16)
Female gender	9 (90%)
Median time between onset of symptoms and diagnosis	17.6 months (1 – 36)
Comorbidities	
Chronic kidney disease	2 (20%)
Juvenile idiopathic arthritis	1 (10%)
Symptoms at diagnosis	
Non-specific symptoms	9 (90%)
Headache	3 (30%)
Dyspnea	2 (20%)
Unintentional weight loss	2 (20%)
Findings on clinical exam	
Decreased / absent pulse	8 (80%)
Arterial Hypertension	8 (80%)
Blood pressure discrepancy	7 (70%)
Bruits over large arteries	6 (60%)
Acute phase reactant elevation at diagnosis	4 (40%)
Median PVAS at diagnosis	13.9 (6-27)
Median PVDI at last follow-up	3.6 (1-6)
Classification according to Numano	
V	5 (50%)
IV	2 (20%)
III	1 (10%)
I	1 (10%)
IIa	1 (10%)

Abbreviations: *PVAS*: PAEDIATRIC VASCULITIS ACTIVITY SCORE; *PVDI*:PAEDIATRIC VASCULITIS DAMAGE INDEX

Table 2. Arterial Vessel involvement (CT/MR)		
Artery	**At diagnosis**	**Last follow-up**
Supra-aortic vessels	5 (50%)	5 (50%)
Carotid	3 (30%)	3 (30%)
Vertebral	4 (40%)	5 (50%)
Subclavian	3 (30%)	4 (40%)
Ascending aorta	2 (20%)	2 (20%)
Aortic arch	0	1 (10%)
Thoracic aorta	3 (30%)	3 (30%)
Abdominal aorta	5 (50%)	7 (70%)
Renal	6 (60%)	6 (60%)
Iliac	2 (20%)	3 (30%)
Superior mesenteric	3 (30%)	3 (30%)
Celiac trunk	1 (10%)	2 (20%)
Pulmonary	1 (10%)	2 (20%)

Conclusion: In our cohort, cTA tends to present with extensive vascular disease, associated in most of the cases with nonspecific symptoms. The percentage of acute phase reactants elevation was less than 50% despite having detected cTA activity in 100% of patients at diagnosis, so thorough exploration is essential. Mortality was related to a surgical complication (part of the treatment) and not to the activity of vasculitis.

Table 3. Arteries that required interventional treatment (Stenting)

Artery	Patients (N=6)
Abdominal aorta	2
Thoracic aorta	2
Right subclavian	1
Left subclavian	1
Right common carotid	1
Left common carotid	1
Right renal	1
Left renal	1

Disclosure: G. Valero-Gaona, None; **E. Faugier-Fuentes**, None; **A. Vargas Guerrero**, None.

Abstract Number: 0750

Extravascular Inflammatory Manifestations of Takayasu Arteritis in a Monocentric Cohort

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SESSION INFORMATION
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Background/Purpose: Takayasu arteritis (TAK) is an inflammatory disease which primarily affects large vessels. However, as a systemic disease, the spectrum of its manifestations is not limited to the arterial wall.

Methods: Data records of TAK patients diagnosed according to the 1990 ACR criteria and followed-up at our Large Vessel Vasculitis Clinic were reviewed. Any significant inflammatory/autoimmune comorbidity and family history for inflammatory/autoimmune disease were considered. For each comorbidity, temporal correlation with TAK diagnosis was assessed. Need for biological therapy for TAK control, as an indirect measure of TAK aggressiveness, was evaluated. Non-parametric statistic tests were used.

Results: In our cohort of 128 TAK patients, 46 patients (35.9%) were identified as having an inflammatory/autoimmune comorbidity, for a total of 64 comorbidities (14 patients experienced >1 comorbidity). Comorbidities were classified into 6 categories: systemic inflammatory diseases (11 patients, 14.3%); gastro-intestinal (6 patients, 7.8%), articular (7 patients, 9.1%), ocular (13 patients, 16.9%) and muco-cutaneous (25 patients, 32.5%) involvement; miscellaneous (autoimmune hepatitis, retroperitoneal fibrosis). In 33 cases (51.6%) the comorbidity onset preceded, in 25 (39%) followed and in 6 (9.4%) was synchronous with TAK diagnosis (Table 1). In 25 patients (54.3%) use of a biological therapy to control TAK activity was needed (versus 35.4% in TAK patients without comorbidities, p = 0.042). Having a comorbidity increased the risk for the introduction of a biologic therapy, odds ratio=2.176 (1.042-4.541). Of

	DISEASE	N° OF CASES	ANTECEDENT TO TAK DIAGNOSIS	SUBSEQUENT TO TAK DIAGNOSIS	SYNCHRONOUS WITH TAK DIAGNOSIS	NEED FOR BIOLOGICAL THERAPY
AUTO-INFLAMMATORY	Pericarditis	4	3	0	1	3
	Relapsing Polychondritis	4	4	0	0	3
	Sarcoidosis	3	0	1	2	1
	TOT.	**11**	**7**	**1**	**3**	**7 (63.7 %)**
GUT	Ulcerative Rectocolitis	3	2	1	0	2
	Crohn Disease	1	1	0	0	1
	Undifferentiated Colitis	1	1	0	0	1
	Celiac Disease	1	0	1	0	0
	TOT.	**6**	**4**	**2**	**0**	**4 (66.7 %)**
ARTICULAR	Psoriatic Arthritis	4	0	4	0	3
	Enteropathic Arthritis	2	0	2	0	2
	Seronegative Rheumatoid Arthritis	1	1	0	0	1
	TOT.	**7**	**1**	**6**	**0**	**6 (85.7 %)**
EYE	Scleritis	6	3	3	0	4
	Anterior Uveitis	3	2	1	0	1
	Posterior Uveitis	1	0	1	0	0
	Optic Neuritis	2	2	0	0	1
	Serpiginous Choroiditis	1	1	0	0	0
	TOT.	**13**	**8**	**5**	**0**	**6 (46.2 %)**
SKIN/MUCOSA	Erythema Nodosum	18	8	8	2	10
	Chronic Urticaria	4	3	1	0	3
	Chronic Recurrent Oral Aphthous Ulcers	2	1	1	0	2
	Skin Psoriasis	1	1	0	0	0
	TOT.	**25**	**13**	**10**	**2**	**15 (60%)**
MISCELLANEOUS	Retroperitoneal fibrosis	1	0	0	1	0
	Autoimmune Hepatitis	1	0	1	0	0
		64 (46 patients)	**33 (51.6%)**	**25 (39%)**	**6 (9.4%)**	**38 (25 patients)**

Prevalence and characteristics of inflammatory/autoimmune extravascular comorbidities in a cohort of 128 patients with Takayasu arteritis (TAK), temporal correlation with TAK diagnosis, and need for biological therapy.

the 128 TAK patients, 17 (13.3%) had a positive family history for inflammatory or autoimmune diseases (8 psoriasis, 5 rheumatoid arthritis, 3 inflammatory bowel disease, 1 sarcoidosis).

Conclusion: In TAK patients, extravascular involvement is a common finding and usually precedes the vascular involvement (the only significant exception is represented by inflammatory arthritis). Inflammatory and autoimmune extravascular comorbidities seem to be associated with a significant higher burden of vascular inflammation, as inferred by the higher rate of biological therapies use in these TAK patients.

Disclosure: E. Baldissera, Sobi, 8, Sanofi, 5, Roche, 8, Pfizer, 8, Novartis, 8, Abbvie, 8, Alfa-sigma, 8; **A. Tomelleri**, None; **S. Sartorelli**, None; **C. Campochiaro**, GSK, 8, GSK, SOBI, Pfizer, 5, 8, Pfizer, 8, SOBI, 5; **L. Dagna**, Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI., 5, 8.

Abstract Number: 0751

Pregnancy Outcome in Patients with Takayasu Arteritis: The Results of Turkish Takayasu Study Group

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Takayasu's arteritis (TAK) is a large vessel vasculitis of the young women in their reproductive age. According to our previous report from single center TAK pregnancies may have a favorable outcome. On the other hand, pregnancy outcomes were worse in the French TAK cohort. Herein, we reported fetal and maternal complications of pregnancy in a larger group of Turkish TAK patients.

Methods: A total of 68 TAK patients, followed by Turkish Takayasu Study Group in 7 tertiary centers and diagnosed according to the 1990 ACR criteria were consecutively assessed for pregnancy and newborn outcome. Pregnancies were divided into 2 groups as pre-diagnosis (pre-d) and post-diagnosis (post-d) pregnancies and compared to feto-maternal complications (FMC) such as hypertension (HT), preeclampsia-eclampsia, abortion, prematurity, low birth weight. Post-d pregnancies were also divided into 2 groups according to FMC development status and baseline demographic data and TAK clinical characteristics were compared between groups.

Results: The mean age of the patients who received 167 pregnancy data retrospectively was 43±12.1 years. 42 (25.1%) of these pregnancies developed after the onset of the disease. FMC rate was higher in the post-d pregnancies than in the pre-d pregnancies [15 (35.7%), 20 (15.7%); p = 0.006]. FMC are shown in Table 1. Maternal heart failure, cardiovascular event or death was not observed in any pregnancy. Disease characteristics of patients with post-d pregnancies according to FMC development are seen in Table 2. None of the patients was smoker and had cardiovascular events.

Conclusion: The most common maternal complications of TAK patients are associated with HT. It was observed that TAK negatively affected the fetal outcomes of pregnancies however the majority of the pregnancies were found as successful in our cohort.

Table 1. Fetomaternal complications in pre-d and post-d pregnancies (IUGR: Intrauterine growth retardation)

	Pre-d pregnancies	Post-d pregnancies	
	n: 127 (%)	n: 40 (%)	p
Maternal complications			
Hypertension-new	0	2 (5)	0.061
Hypertension-worsening	0	8 (20)	0.000
Preeclampsia/eclampsia	0	1 (2.5)	0.249
Fetal complications			
Abortion	13 (10.2)	4 (10)	0.616
Prematurity	2 (1.5)	2 (5)	0.258
Low birth weight	2 (1.5)	2 (5)	0.153
IUGR	1 (0.7)	0	0.751
Fetal anomaly	0	1 (2.5)	0.249
Fetal death	2 (1.5)	0	0.564

Table 2. Disease characteristics of patients with post-d pregnancies according to FMC development (SS: Standard deviation)

	FMC +, n:15 (%)	FMC -, n:27 (%)	p
Age (Mean±SD)	27.1±4.5	26.7±4.7	0.695
Hypertension	4 (26.6)	11 (40.7)	0.285
Cardiac valvular disease	3 (20)	10 (37)	0.215
Cerebrovascular event	1 (6.6)	2 (7.4)	0.713
Renal artery involvement	9 (60)	8 (29.6)	0.056

Disclosure: N. Alpay-Kanitez, None; **S. Kaymaz-Tahra**, None; **A. Yazici**, None; **A. Cefle**, None; **M. Kara**, None; **H. Yarkan-Tugsal**, None; **O. Gercik**, None; **S. Akar**, Abbvie, 2, 5, Amgen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5; **F. Onen**, Tofacitinib (Pfizer), 8; **K. Aksu**, None; **G. Keser**, None; **C. Bes**, None; **S. Kamalı**, None; **F. Alibaz-Oner**, None; **H. Direskeneli**, None.

Abstract Number: 0752

Drug Retention and Discontinuation Reasons Between Seven Biologics in Patients with Takayasu Arteritis

Corrado Campochiaro,[1] Alessandro Tomelleri,[2] Silvia Sartorelli,[3] Giulio Cavalli,[2] De Luca Giacomo,[4] Elena Baldissera,[2] and Lorenzo Dagna[2], [1]Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR), IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, Italy, [2]Unit of Immunology, Rheumatology, Allergy and Rare Diseases. IRCCS San Raffaele Hospital. Vita-Salute San Raffaele University, Milan, Italy, [3]Vita-Salute San Raffaele University, IRCCS San Raffaele Hospital, Milan, Italy, [4]Unit of Immunology, Rheumatology, Allergy and Rare Diseases, IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, Italy, Milan, Italy

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica

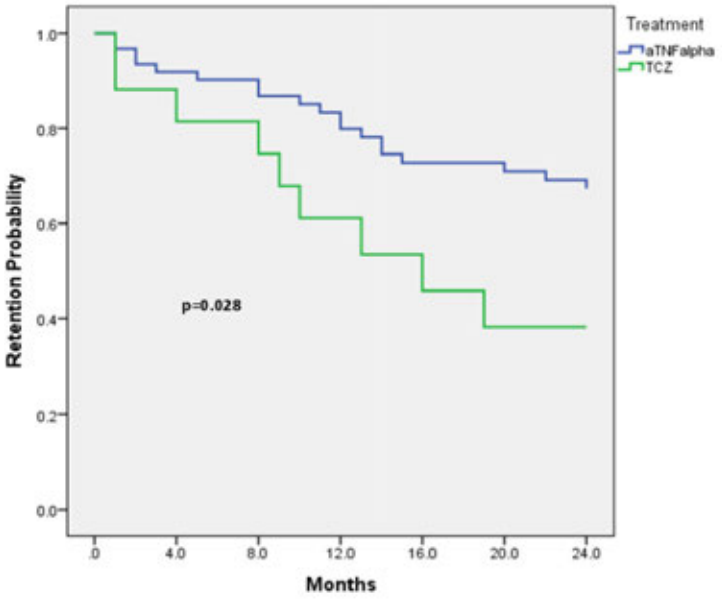
Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Takayasu's arteritis (TA) is a large vessel vasculitis affecting mainly young women. Biologic agents are currently use to treat refractory TA patients but no data are available on drug retention rate (DRR) of biologic disease-modifying anti-rheumatic drugs (bDMARDs) TA patients. We retrospectively investigated DRR and reasons for discontinuation of seven bDMARDs in TA patients in a real-world setting.

Methods: TA patients followed-up in our Centre fulfilling the 1990 ACR criteria and treated with ≥1 bDMARD were selected. Data about disease duration, number of bDMARDs, reasons for bDMARDs discontinuation, concomitant conventional synthetic (cs)DMARDs were collected. Survival curves were examined by the Kaplan-Meier method

Figure 1. Kaplan-Meier curves comparing Takayasu patients treated with anti-TNFalpha (infliximab, adalimumab, golimumab) and with tocilizumab at 24 months.



Number of subjects at risk (%)

aTNF	61 (100%)	56 (92%)	53 (87%)	47 (77%)	43 (70%)	42 (69%)	41 (67%)
TCZ	17 (100%)	14 (82%)	13 (76%)	10 (59%)	8 (47%)	7 (41%)	7 (41%)

and compared using a stratified log-rank test. 24-month DRR was calculated. Hazard ratio (HR) for concomitant csDMARDs and for previous bDMARDs was evaluated. A comparative sub-analysis between anti-TNFα drugs and tocilizumab was performed.

Results: We identified 50 patients and 86 bDMARD-courses. Patients characteristics are summerized in Table 1. No significant differences were observed in age and disease duration between the seven groups (data not shown). Infliximab was the most frequent first-line bDMARD (78.6%). At bDMARDs initiation, all patients were on prednisone (mean dose, 13.5±10.3 mg/day) and 85.2% on concomitant csDMARD therapy. 43% of treatment courses were stopped by 24 months. Golimumab had the highest DRR (71.4%), followed by infliximab (69%), adalimumab (56.3%), abatacept (50%), tocilizumab (41.1%), anakinra (0%) and rituximab (0%), p=0.016. Concomitant csDMARDs therapy showed positive effects on DRR (HR=2.87, 95% CI=1.19-6.92, p=0.019). Anti-TNFα drugs had significantly higher DRR compared to tocilizumab (67.2% vs 41.1%, p=0.028), see Figure 1. Even in these subgroups, csDMARDs showed positive effects on DRR (HR=3.79, 95% CI=1.49-9.6, p=0.005).

Conclusion: Anti-TNFα agents had the highest DRR overall and a higher DRR in a head-to-head comparison with tocilizumab. Concomitant csDMARDs had a significant positive effect on bDMARDs DRR.

Table 1. Clinical characteristics at initiation of seven biologic agents in Takayasu arteritis.

ABT, abatacept; ADA, adalimumab; ANK, anakinra; AZA, azathioprine; bDMARD, biologic disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; GOL, golimumab; IFX, infliximab; MMF, mycophenolate-mofetil; MTX, methotrexate; PDN, prednisone; RTX, rituximab; SSZ, sulfasalazine; TCZ, tocilizumab.

	ABT (n=2)	ADA (n=12)	ANK (n=4)	GOL (n=7)	IFX (n=42)	RTX (n=2)	TCZ (n=17)	P-value
Mean age (years)	38.5 ± 2.1	33.8 ± 9.1	44 ± 13.9	43.6 ± 15.2	39.0 ± 13.1	34.5 ± 4.9	39.8 ± 11.6	0.533
Female sex	2 (100%)	11 (91.7%)	3 (75%)	7 (100%)	37 (88.1%)	2 (100%)	16 (94.1%)	0.780
Mean disease duration (months)	139 ± 43.8	113 ± 109.4	246 ± 203.1	115.4 ± 71.3	89.1 ± 91.2	96 ± 84.9	152.5 ± 118.8	0.176
Mean n° of previous bDMARDs	4.5 ± 0.7	0.9 ± 1.5	2.3 ± 1	2.1 ± 2	0.2 ± 0.5	2.5 ± 0.7	1.3 ± 1.2	**<0.001**
Mean PDN dosage (mg)	13.8 ± 5.3	14.4 ± 7.7	18.1 ± 12.5	17.9 ± 15.6	15 ± 11.3	21.3 ± 15.9	9.6 ± 5.1	0.301
Concomitant csDMARD	1 (50%)	11 (91.7%)	2 (50%)	6 (85.7%)	38 (90.5%)	1 (50%)	15 (88.2%)	0.940
MTX	1	8	2	4	28	1	9	
AZA	0	2	0	0	7	0	3	
Sirolimus	0	0	0	1	2	0	2	
MMF	0	1	0	1	1	0	0	
SSZ	0	0	0	0	0	0	1	

Disclosure: C. Campochiaro, GSK, 8, GSK, SOBI, Pfizer, 5, 8, Pfizer, 8, SOBI, 5; **A. Tomelleri**, None; **S. Sartorelli**, None; **G. Cavalli**, SOBI, Novartis, Pfizer, 5, 8; **D. Giacomo**, GSK, 8, Pfitzer, 8, SOBI, 5, SOBI, Novartis, SOBI, Pfizer, 5, 8; **E. Baldissera**, Sobi, 8, Sanofi, 5, Roche, 8, Pfizer, 8, Novartis, 8, Abbvie, 8, Alfa-sigma, 8; **L. Dagna**, Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI., 5, 8.

Abstract Number: 0753

Initial Clinical Presentation Is Associated with Outcome in Takayasu's Arteritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The natural history of Takayasu's arteritis (TAK) remains poorly characterized. A "triphasic" pattern of disease has been proposed where constitutional symptoms precede vascular inflammation and subsequent vascular damage. However, this pattern is often not seen, and there is wide variability in the initial features of disease, including asymptomatic patients diagnosed based on incidental findings on vascular examination or imaging. This study aimed to characterize patients with Takayasu's arteritis based on the presenting features of disease in association with clinical outcomes.

Methods: An observational cohort of patients with TAK was prospectively recruited. All patients fulfilled the 1990 ACR Classification Criteria for TAK. Patients were divided into four categories based on initial presentation as follows: 1) asymptomatic, 2) nonspecific constitutional symptoms alone, 3) vascular inflammation (defined as carotidynia), and 4) vascular ischemia [defined as a symptom secondary to arterial damage (i.e limb claudication, stroke, etc.)]. Group status was studied in association with demographics, diagnostic delay, acute phase reactant levels, relapse

Table. Clinical Characteristics of Patients with Takayasu's Arteritis Grouped by Initial Clinical Presentation

	Asymptomatic* n = 9	Constitutional n = 10	Carotidynia n = 8	Vascular Ischemia n = 34	P value
Gender *(%, female)*	8 (89)	6 (60)	7 (88)	30 (80)	0.18
Race					
Caucasian	3 (33)	7 (70)	7 (88)	23 (68)	
African American	3 (33)	1 (10)	0 (0)	2 (6)	0.19
Asian	3 (33)	1 (10)	1 (12)	5 (15)	
Other	0 (0)	1 (10)	0 (0)	4 (12)	
Ethnicity					
Hispanic	0 (0)	1 (10)	1 (12)	5 (15)	0.67
Not Hispanic	9 (100)	9 (90)	7 (88)	29 (85)	
Age *(years, median, IQR)*					
Symptom onset	28 (21-36.5)	21 (15-32.5)	18.5 (15-29.5)	23 (14.5-34)	0.56
Diagnosis	28 (21- 36.5)	21.5 (15.3-39.5)	19 (15.3-31.5)	28 (17-35.5)	0.68
Disease duration	4.6 (2.7-14.1)	4.6 (3.0-8.7)	5.5 (2.2-8.3)	7.5 (2.4-15.6)	0.77
Elevated ACP	2 (22)	10 (100)	7 (88)	10 (29)	<0.01
Treatment Received					
No treatment	3 (33)	0 (0)	0 (0)	0 (0)	<0.01
Corticosteroids	5 (56)	10 (100)	8 (100)	32 (94)	<0.01
DMARD	5 (56)	10 (100)	8 (100)	34 (100)	<0.01
Biologic	2 (22)	7 (70)	7 (88)	18 (53)	0.04
>1 Biologic	1 (13)	3 (30)	5 (63)	5 (15)	0.02
Relapse	3 (33)	5 (50)	8 (100)	21 (62)	0.03
Recurrent pharyngitis	0 (0)	1 (10)	5 (63)	2 (6)	<0.01
Co-existing chronic disease**	5 (56)	0 (0)	1 (13)	8 (24)	0.03

ACP: acute phase reactants

*6 patients diagnosed after discovery of an abnormal physical examination finding and 3 patients diagnosed from an incidental imaging finding

** Inflammatory bowel disease (n=3), Ankylosing spondylitis (n=2), Juvenile Idiopathic Arthritis (n=2), Sarcoidosis (n=2), Tuberculosis (n=4), HIV (n=1)

rate, treatment received, a history of antecedent pharyngitis, and presence of chronic inflammatory co-morbidities. Differences among groups were assessed by chi square test and Kruskal-Wallis test as appropriate.

Results: 61 patients with TAK were studied, with a median disease duration of 6 years (Table). Most patients reported vascular symptoms as the first feature of disease. Eight patients (13%) presented with carotidynia, and 34 patients (56%) presented with an ischemic vascular event. Ten patients (16%) presented with nonspecific constitutional symptoms alone, and nine patients (15%) were asymptomatic at presentation. Initial presentation was not associated with gender, race, ethnicity, or age. Elevated acute phase reactants were most frequent in the group presenting with constitutional symptoms (100%) and carotidynia (88%) ($p< 0.01$). The group presenting with carotidynia had the most frequent relapses, with 100% of patients relapsing at some point in their disease course ($p=0.03$). This group was the most frequently refractory to treatment with corticosteroids and DMARDS; biologic therapy was required in 88% patients ($p=0.04$) and >1 biologic was required in 63% patients ($p=0.02$). Many patients in the group with nonspecific constitutional symptoms also had refractory disease with 70% patients requiring biologic therapy and 30% requiring >1 biologic. Antecedent pharyngitis was seen in five of the eight patients (63%) presenting with carotidynia ($p< 0.01$). Co-existing chronic inflammatory disease was most frequently seen in the patients who were asymptomatic at disease diagnosis ($p=0.03$).

Conclusion: There is heterogeneity in clinical presentation at time of diagnosis in TAK, and patients do not necessarily progress sequentially through multiple phases of the disease. Initial clinical presentation may dictate future disease trajectory and inform treatment response, risk for relapse, and potential causal factors.

Disclosure: K. Quinn, None; **K. Gribbons**, None; **E. Novakovich**, None; **P. Grayson**, None.

Abstract Number: 0754

Dynamic Distribution and Phenotype Shift from M1 to M2 of Macrophages in Vascular Lesions of Naïve and Treated Patients with Takayasu Arteritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Takayasu arteritis (TA) is a chronic inflammatory disease characterized by arterial vascular fibrosis. Type I (M1) and type II (M2) macrophages play very important roles in the development of TA, and monocyte chemotactic protein-1 (MCP-1) has also been implicated in TA. However, the roles and interactions of these three factors with each other and with the current therapeutic agents for TA are unclear. Therefore, in the current study, we investigated the M1 and M2 profile in the vascular tissue of TA patients and detected the concentration of monocyte chemotactic protein-1 (MCP-1) in vascular tissue and peripheral blood before and after treatment.

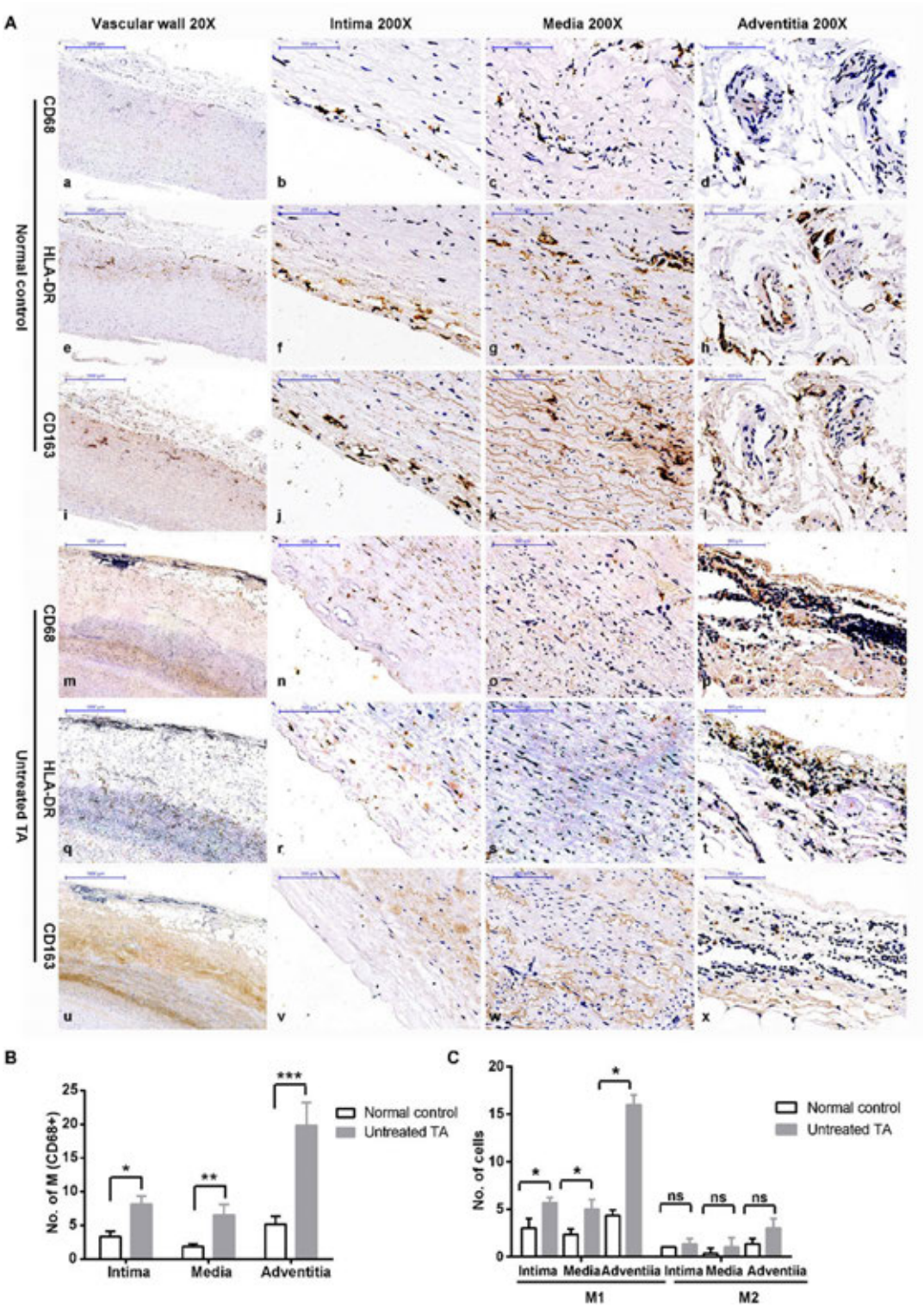

Figure 1. Distribution and phenotype of macrophages in untreated vascular tissue (inflammatory stage)

Methods: This study included 8 untreated TA patients, 7 treated patients and 4 controls who provided vascular tissue specimens, as well as 38 treatment-naïve patients and 28 healthy controls who provided their serum samples before and after treatment (only 19 TA samples were obtained after treatment). The treatment strategy was prednisone combined with immunosuppressants. Immunohistochemical staining for M1 and M2 markers and MCP-1

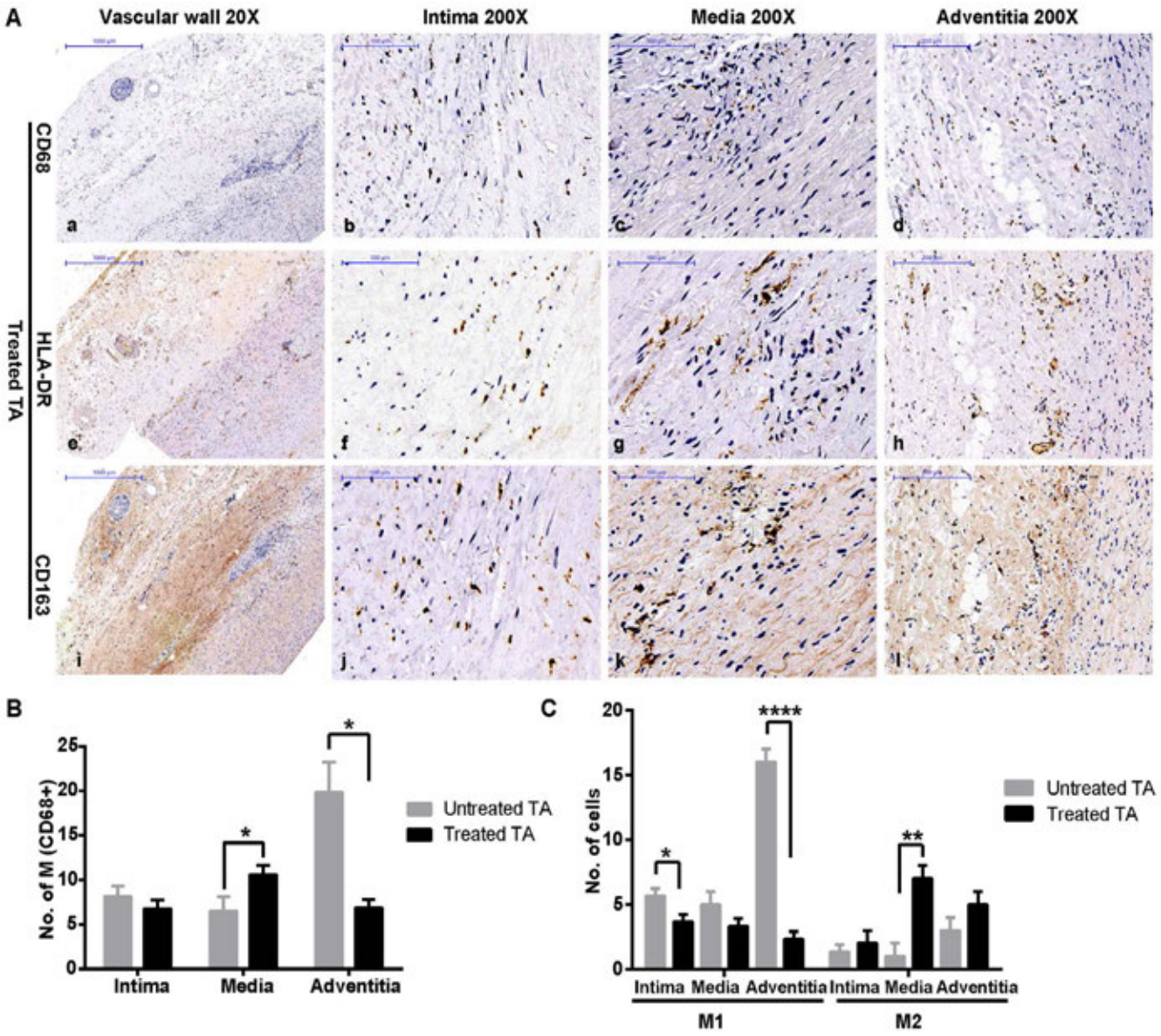

Figure 2. Distribution and phenotype of macrophages in treated vascular tissue (fibrotic stage)

was performed in the vascular tissue samples. The serum level of MCP-1 was detected by ELISA. Disease activity was evaluated by the Kerr activity score.

Results: M1 macrophages were more prominent in the acute (pro-inflammatory) stage of TA and in naïve patients, while M2 macrophages were more prominent in the chronic (pro-fibrotic) stage and in treated patients. This pattern was also observed in MCP-1 expression. Macrophages and MCP-1 showed increased levels in vascular tissue (mainly in the adventitia), along with an increase in peripheral MCP-1, in the treatment-naïve patients. In contrast, in the patients who had received 6 months of treatment, both the macrophage and MCP-1 (vascular adventitia and peripheral) levels were decreased. In the vascular media from treated patients, an increase in MCP-1 levels and M2 infiltration was observed. Furthermore, peripheral MCP-1 was correlated Kerr activity score (Rho = 0.50, P = 0.002) and peripheral IL-6 levels (Ro = 0.55, P < 0.001).

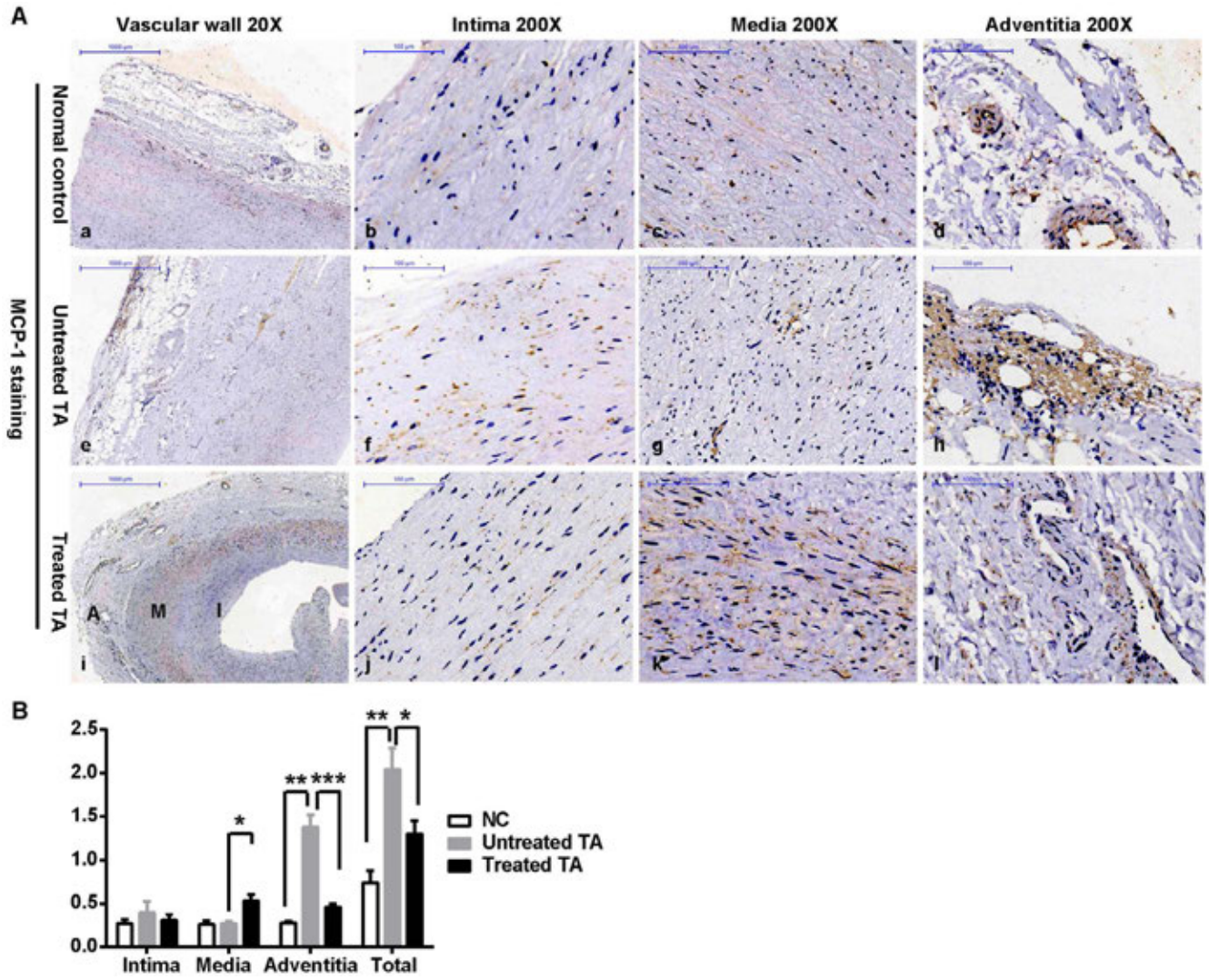

Figure 3. MCP-1 expression in normal aorta, untreated TA aorta and treated TA artery

Conclusion: In the vascular wall, M1 and M2 distribution is dynamic and is closely associated with MCP-1 expression, which is increased in the serum and vascular tissue of TA patients. The current treatment strategies do not target M2 infiltration, as a result of which fibrosis is aggravated. Thus, more efficacious treatment strategies that target both M1 and M2 should be used. Further, the serum level of MCP-1 may prove to be a useful indicator of disease stage and treatment efficacy in the future.

Disclosure: X. Kong, None; **M. Xu**, None; **X. Cui**, None; **L. Ma**, None; **H. Chen**, None; **L. Ma**, None; **L. Jiang**, None.

Abstract Number: 0755

A Novel Diagnostic Algorithm for Polymyalgia Rheumatica Using Three Musculoskeletal Sites on Whole Body PET/CT

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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Background/Purpose: PMR is associated with a pattern of abnormal ^{18}F-Fluorodeoxyglucose (^{18}F-FDG) uptake on whole body PET/CT that is increasingly recognised to correlate anatomically with inflammation of extracapsular structures.(1) The aim of this study was to evaluate the sensitivity and specificity of PET/CT findings in PMR including novel involvement at the posteromedial knee and develop a representative diagnostic scoring algorithm utilising results from a minimum number of musculoskeletal sites.

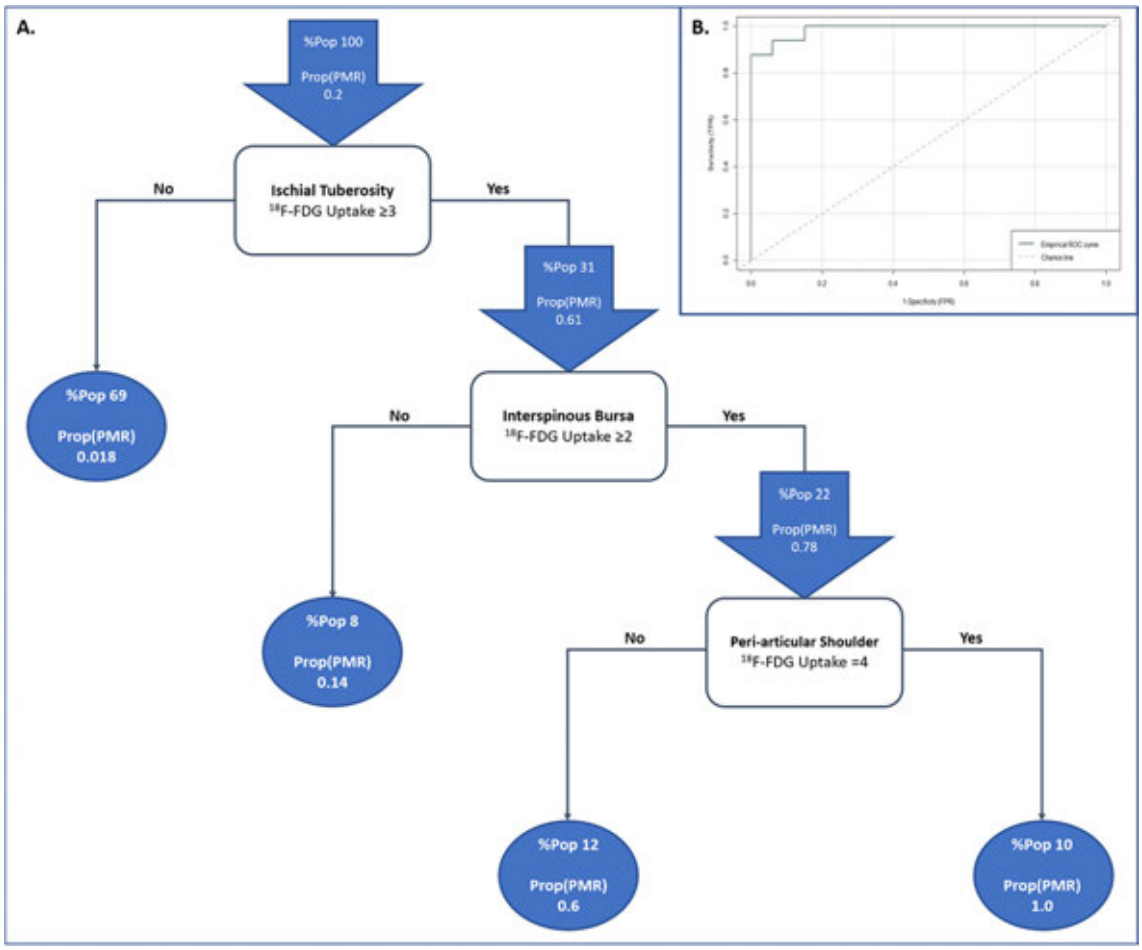


Figure 1. A – A diagnostic algorithm for PMR utilising Meller scores at three musculoskeletal sites. %Pop represents the percentage of the total study population with this abnormal finding. Prop(PMR) represents the proportion of PMR cases in that subset; B – ROC curve for the diagnostic algorithm (AUC 0.987; sensitivity 93.9%, specificity 93.9%).

Table 1. Incidence, mean Meller score and mean SUVmax for cases compared with controls. Results for continuous variables are reported as mean ± standard deviation.

Musculoskeletal Site	^{18}F-FDG Uptake ≥1 Cases (n=33)	^{18}F-FDG Uptake ≥1 Controls (n=132)	Mean Meller Score Cases	Mean Meller Score Controls	p-value	Mean SUV_{max} Cases	Mean SUV_{max} Controls	p-value
Peri-articular Shoulder	32 (97.0%)	103 (78.0%)	3.5±0.8	2.1±0.9	0.0001	3.4±1.3	2.2±0.9	0.0001
Interspinous Bursa	30 (90.9%)	23 (17.4%)	3.1±1.0	1.3±0.6	0.0001	2.9±1.5	1.7±1.1	0.0001
Peri-articular Hip	32 (97.0%)	81 (61.4%)	3.3±0.9	1.9±0.8	0.0001	3.4±1.8	2.0±0.7	0.0001
Trochanteric Bursa	33 (100%)	98 (75.4%) (n=130)	3.1±0.8	2.0±0.7	0.0001	2.5±0.9	2.1±0.8	0.005
Adjacent to Ischial Tuberosities	33 (100%)	77 (58.3%)	3.7±0.5	1.8±0.8	0.0001	3.6±1.4	2.0±0.7	0.0001
Posteromedial Knee	24 (72.7%) (n=32)	25 (19.8%) (n=126)	2.7±1.1	1.3±0.6	0.0001	2.7±1.0	1.4±0.7	0.0001

Table 2. AUC, sensitivity and specificity for PMR diagnosis of abnormal findings at different musculoskeletal sites and their combinations.

Musculoskeletal Site	AUC	Sensitivity	Specificity
Peri-articular Shoulder	0.898	81.8%	90.9%
Interspinous Bursa (Int Bursa)	0.959	100.0%	82.6%
Peri-articular Hip	0.888	75.8%	95.4%
Trochanteric Bursa	0.901	97.0%	79.5%
Adjacent to Ischial Tuberosities (Ischial Tub)	0.980	93.9%	96.2%
Posteromedial Knee (Post Knee)	0.940	100.0%	80.3%
Peri-articular Shoulder + Int Bursa	0.941	84.8%	96.2%
Peri-articular Shoulder + Ischial Tub	0.962	93.9%	91.7%
Peri-articular Shoulder + Post Knee	0.930	93.9%	83.3%
Int Bursa + Ischial Tub	0.971	93.9%	93.9%
Int Bursa + Post Knee	0.959	93.9%	85.6%
Ischial Tub + Post Knee	0.976	93.9%	92.4%
Peri-articular Shoulder + Int Bursa + Ischial Tub	0.964	93.9%	97.0%
Peri-articular Shoulder + Ischial Tub + Post Knee	0.965	93.9%	91.7%
Int Bursa + Ischial Tub + Post Knee	0.971	93.9%	92.4%

Methods: Steroid-naïve patients with newly diagnosed PMR (2012 EULAR/ACR classification criteria) were prospectively recruited. Participants with giant cell arteritis were excluded. A whole body ^{18}F-FDG PET/CT scan from skull vertex to toes was performed at baseline. Each PMR case was age- and sex-matched to four consecutive historic PET/CT controls, with relevant data pertaining to scan indication, underlying diagnosis and medical history extracted from the clinical record. Qualitative (Meller score) and semi-quantitative scoring (standardised uptake value maximum [SUVmax]) of abnormal ^{18}F-FDG uptake at 21 musculoskeletal sites was undertaken for cases and controls. Results were compared using the Mann-Whitney U test, a p-value < 0.05 being considered statistically significant. Receiver operating characteristics (ROC) curves were generated for abnormal findings at each musculoskeletal site, along with calculation of the area under the curve (AUC), sensitivity and specificity.

Results: 33 cases met the inclusion criteria and were matched to 132 controls. Mean age was 68.6±7.4 years for cases cf. 68.2±7.3 for controls, and 54.5% of patients were male. Mean EULAR/ACR score was 5.2±0.6 for the PMR group, with median CRP 49 (32 – 65) and ESR 41.5 (24.6 – 64.4). The predominant indication for whole body PET/CT in the controls was malignancy (47.0%). 43/132 controls (32.6%) had a history of a rheumatic condition including 9 (6.8%) with an inflammatory arthritis. Table 1 summarizes the incidence of abnormal findings on whole body PET/CT in cases compared with controls. Individual musculoskeletal sites proved insufficient for diagnostic purposes, however ^{18}F-FDG uptake at the peri-articular shoulder in combination with interspinous bursa and adjacent to the ischial tuberosities achieved a sensitivity of 93.9% and specificity of 97% (Table 2). A diagnostic algorithm utilising scores at

each of these 3 musculoskeletal sites is depicted in Figure 1 (AUC 0.987; sensitivity 93.9%, specificity 93.9%). When tested on the study population, none of the controls were misdiagnosed with PMR.

Conclusion: The combination of abnormal ^{18}F-FDG uptake at the peri-articular shoulder, interspinous bursa and adjacent to the ischial tuberosities on whole body PET/CT is highly sensitive and specific for a diagnosis of PMR.

Reference:

1.Owen CE, Poon AMT, Lee ST, Yap LP, Zwar RB, McMenamin CM, et al. Fusion of positron emission tomography/computed tomography with magnetic resonance imaging reveals hamstring peritendonitis in polymyalgia rheumatica. Rheumatology. 2018;57(2):345-53.

Disclosure: C. Owen, None; **A. Poon**, None; **V. Yang**, None; **C. McMaster**, None; **S. Lee**, None; **D. Liew**, None; **J. Leung**, None; **A. Scott**, None; **R. Buchanan**, None.

Abstract Number: 0756

A Volar Pattern of ^{18}F-Fluorodeoxyglucose Uptake at the Hand on Whole Body PET/CT Predicts Glucocorticoid-Responsive Disease in Polymyalgia Rheumatica

Claire Owen,[1] Aurora Poon,[1] Sze Ting Lee,[1] Chris McMaster,[1] Jessica Leung,[1] David Liew,[1] Andrew Scott,[1] and Russell Buchanan[1], [1]Austin Health, Heidelberg, Victoria, Australia

Site	Frequency of ^{18}F-FDG Uptake ≥2	Frequency of ^{18}F-FDG Uptake ≥3	Mean Ref. Score	Mean SUV_{max}
Shoulder:				
• Peri-articular	34 (97.1%)	27 (79.4%)	3.4±0.9	3.3±1.3
• GH Joint	24 (68.6%)	8 (22.8%)	2.0±1.0	1.9±1.0
Hip:				
• Peri-articular	33 (94.3%)	25 (71.4%)	3.2±1.0	3.3±1.8
• Hip Joint	20 (57.1%)	8 (22.8%)	1.9±1.0	1.8±1.1
Trochanteric Bursa	34 (97.1%)	23 (65.7%)	3.0±0.8	2.4±0.9
Adjacent to Ischial Tuberosities	34 (97.1%)	32 (91.4%)	3.6±0.7	3.5±1.4
Interspinous Bursa	31 (88.6%)	22 (62.8%)	3.0±1.1	2.8±1.6
Knee: (n=34)	27 (79.4%)			
• Posteromedial	25 (73.5%)	19 (55.9%)	2.6±1.1	2.7±1.0
• Joint	18 (82.9%)	12 (35.3%)	2.0±1.3	2.7±1.0
Wrist/Hand: (n=34)	24 (68.6%)			
• Wrist Joint	17 (50.0%)	10 (29.4%)	1.8±1.1	1.8±1.1
• Volar Hand	12 (35.3%)	9 (25.7%)	1.7±1.1	2.4±1.0

Table 1. Analysis of abnormal 18F-FDG uptake on whole body PET/CT. Results for continuous variables are reported as mean ± standard deviation. Categorical variables are represented as proportions (percentages).

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica

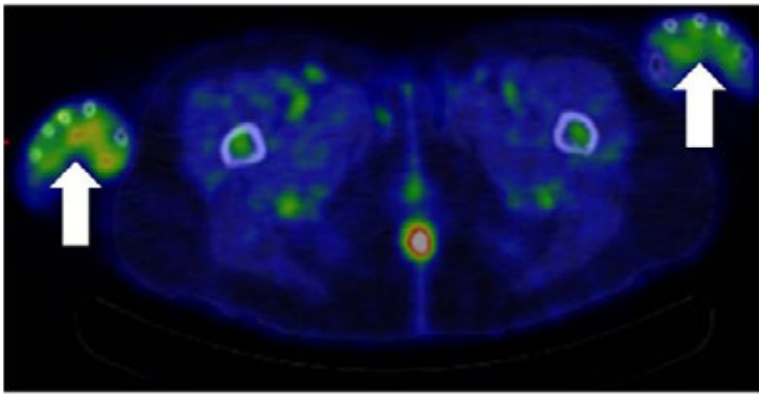
Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Almost half of all patients diagnosed with PMR require a protracted duration of glucocorticoid therapy due to relapsing disease.(1) On whole body PET/CT, PMR possesses a distinctive pattern of abnormal ^{18}F-fluorodeoxyglucose (^{18}F-FDG) uptake, however the prognostic potential of this test is unknown. The aim of this study was to characterise ^{18}F-FDG uptake on whole body PET/CT and investigate its ability to predict relapsing PMR.

Methods: Steroid-naïve patients with newly diagnosed PMR (2012 EULAR/ACR Classification Criteria) were prospectively recruited. Participants with GCA were excluded. Disease activity (PMR-Activity Score [PMR-AS]) was assessed and whole body PET/CT including dedicated hand views undertaken prior to the commencement of a standardised weaning course of prednisolone (BSR Guideline). PMR-AS was recalculated at weeks 4, 8, 16, 24, 32 and 46. Relapse was defined by a PMR-AS score of ≥9.35 in a patient who had achieved clinical remission (PMR-AS < 9.35) or an increase in PMR-AS by ≥6.6 if the participant had been previously responding to treatment (PMR-AS ≥9.35 but falling between successive visits). Qualitative (Meller score) and semi-quantitative (standardised uptake value maximum [SUVmax]) scoring of 21

Figure 1. A novel pattern of volar 18F-FDG uptake at the hand on whole body PET/CT.



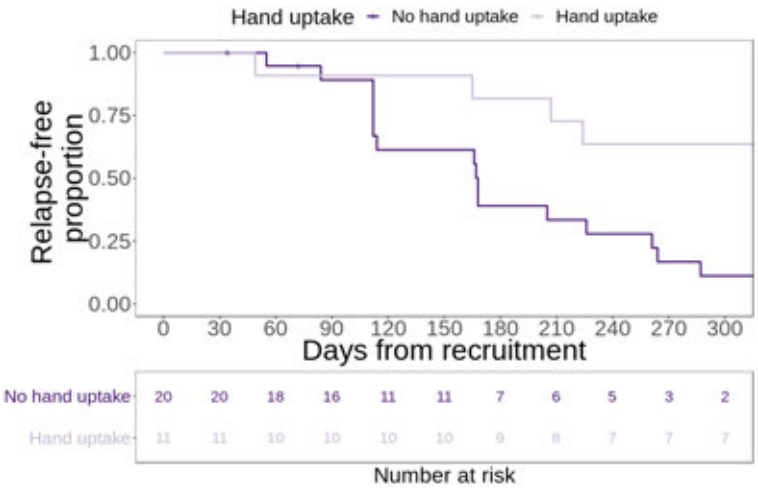


Figure 2. Kaplan-Meier plot demonstrating the relationship between the presence or absence of volar hand 18F-FDG uptake and time to first relapse.

musculoskeletal sites on whole body PET/CT was performed by two experienced nuclear medicine physicians, with any difference in opinion resolved by consensus. The Cox proportional-hazards model investigated the relationship between relapse and 18F-FDG uptake, with a p-value < 0.05 representing statistical significance.

Results: 35 patients met the inclusion criteria. Mean age was 69.5±7.15 years and 19/35 (54.3%) were male. Findings on whole body PET/CT are presented in Table 1, with a peri-articular pattern of abnormal ^{18}F-FDG uptake predominating at the shoulder and hip. A high frequency of knee (79.4%) as well as wrist and/or hand involvement (68.6%) was appreciated, including a novel pattern of volar ^{18}F-FDG uptake (Figure 1). Longitudinal PMR-AS data was available for 32 participants, 25 (78%) of whom relapsed during follow-up. Figure 2 depicts the statistically significant relationship identified between the presence of volar hand ^{18}F-FDG uptake and later time to first relapse/no relapse (HR 0.25 [0.09 – 0.71], p=0.004).

Conclusion: A novel pattern of volar ^{18}F-FDG uptake at the hand was associated with glucocorticoid-responsive disease in a prospective cohort of newly diagnosed PMR patients.

Reference:

1. Kremers HM, Reinalda MS, Crowson CS, Zinsmeister AR, Hunder GG, Gabriel SE. Relapse in a population based cohort of patients with polymyalgia rheumatica. J Rheumatol. 2005;32(1):65-73.

Disclosure: C. Owen, None; **A. Poon**, None; **S. Lee**, None; **C. McMaster**, None; **J. Leung**, None; **D. Liew**, None; **A. Scott**, None; **R. Buchanan**, None.

Abstract Number: 0757

Long-term Clinical Course and Outcomes of 2013 Patients with Takayasu Arteritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Takayasu arteritis (TAK) occurs at a young age and has a long-term clinical course. Progression of arterial stenosis or dilatation leads to organ dysfunction. To provide information for improvement of the treatment strategies, we surveyed the treatments, complications, damages, and activities of daily living in the long-term clinical course of TAK, using the data of 2013 patients from the national registry of Japan.

Methods: Data of 211 newly registered and 2584 continuously registered patients were obtained from the case report forms for TAK in the year 2013 from the national registry. We excluded cases with inconsistent data and age of onset >60 years, leaving 76 newly registered and 1937 continuously registered patients. The patients were analyzed by stratification into four groups: 1) new and 2) disease duration < 5 years, 3) 5–20 years, and 4) >20

Table 1. Long-term clinical course of 2013 patients with Takayasu arteritis

Disease duration	New	<5 years	5-20 years	>20 years
Glucocorticoid	65 / 73 (89.0%)	244 / 267 (91.4%)	574 / 743 (77.3%)	434 / 855 (50.8%)
Mean PSL dose (mg)	34.4 (n = 63)	13.6 (n = 240)	7.8 (n = 553)	5.7 (n = 420)
Immunosuppressant	11 / 70 (15.7%)	114 / 260 (43.8%)	201 / 713 (28.2%)	58 / 801 (7.2%)
Mean ESR (mmHg)	73.3 (n = 63)	18.6 (n = 188)	18.5 (n = 466)	21.1 (n = 506)
Mean CRP (mg/dL)	6.7 (n = 76)	0.8 (n = 261)	0.5 (n = 717)	0.6 (n = 817)
Fever	51 / 76 (67.1%)	82 / 273 (30.0%)	83 / 766 (10.8%)	37 / 898 (4.1%)
Brain ischemia	8 / 75 (10.7%)	17 / 271 (6.3%)	52 / 758 (6.9%)	142 / 882 (16.1%)
Blindness	0 / 76 (0.0%)	0 / 273 (0.0%)	3 / 766 (0.4%)	16 / 898 (1.8%)
Aortic regurgitation	17 / 72 (23.6%)	59 / 264 (22.3%)	226 / 716 (31.6%)	392 / 843 (46.5%)
Aortic aneurysm	9 / 76 (11.8%)	24 / 271 (8.9%)	91 / 758 (12.0%)	132 / 877 (15.1%)
Ischemic heart disease	2 / 75 (2.7%)	12 / 271 (4.4%)	46 / 762 (6.0%)	168 / 886 (19.0%)

n=76, 273, 766, and 898 (New, <5 years, 5-20 years, 20 years<). Items with missing data have smaller numbers. PSL, prednisolone.

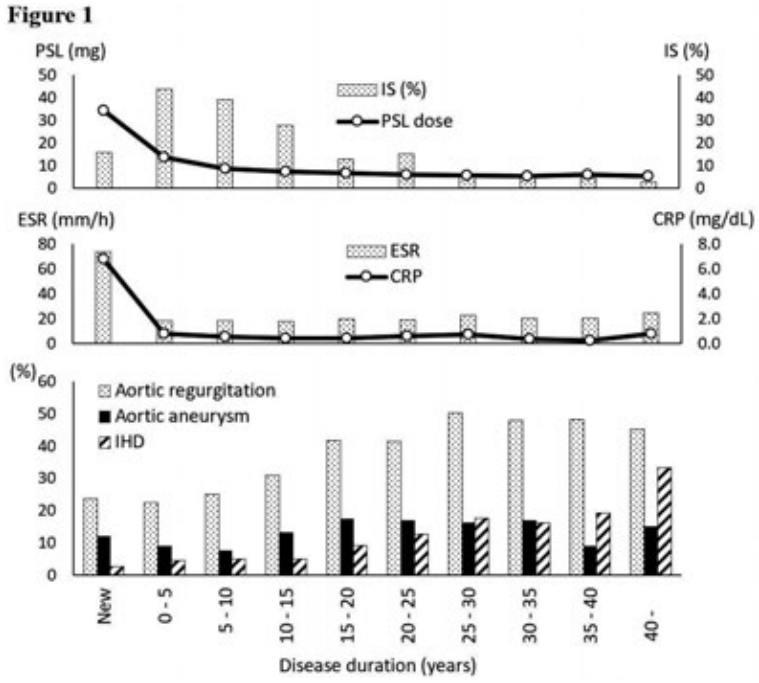

Figure 1. Long-term clinical trends of Takayasu arteritis. We stratified 2013 patients by disease duration divided into 5-year intervals and plotted the mean values or percentages of clinical items. IHD, ischemic heart disease; IS, immunosuppressant; PSL, prednisolone.

years (n=76, 273, 766, and 898; mean current age=34, 35, 46, and 62 years; female ratio=84%, 85%, 86%, and 95%, respectively).

Results: The mean prednisolone dose was lower in patients with longer disease duration: (new, < 5 years, 5-20 years, >20 years = 34, 14, 8, and 6 mg/day, respectively) (**Table 1**). Immunosuppressants (IS) were used in 44% of patients after initiation of glucocorticoid (GC). The frequencies of fever (67%, 30%, 11%, and 4%, respectively) and CRP levels (6.7, 0.8, 0.5, and 0.6 mg/dL, respectively) were also lower in patients with longer disease duration. Conversely, the frequencies of aortic regurgitation (24%, 22%, 32%, and 47%, respectively), aortic aneurysm (12%, 9%, 12%, and 15%, respectively), ischemic heart disease (3%, 4%, 6%, and 19%, respectively), and blindness (0%, 0%, 0.4%, and 1.8%, respectively) tended to be higher in patients with longer disease duration (**Fig. 1**). The percentage of patients with severe disease (Class IV + V) (20%, 10%, 13%, and 22%, respectively) was high at onset, decreased

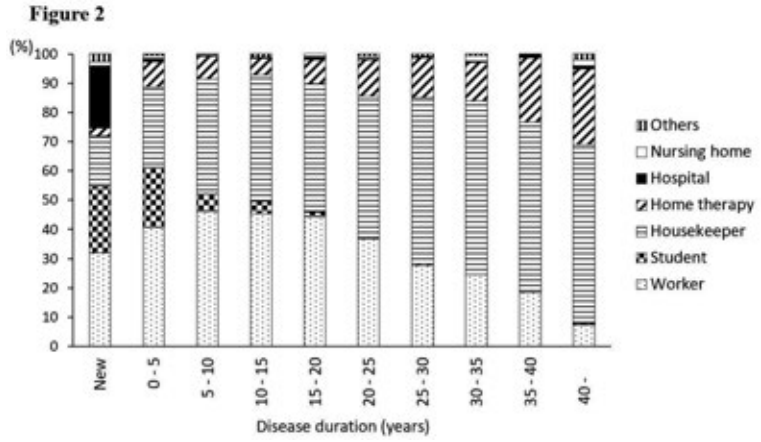

Figure 2. Social situation of 1963 patients with Takayasu arteritis. We stratified 1963 patients with available data by disease duration divided into 5-year intervals and calculated the percentage of each item.

after initiation of therapy, and showed an increasing tendency depending on disease duration. The percentage of workers was < 50% irrespective of disease duration (**Fig. 2**).

Conclusion: In this cohort, treatments with GC (initially medium dose) and IS (approximately 40%) were suggested to improve the disease activity of TAK. However, the frequency of complications and damages showed an increasing tendency depending on disease duration, leading to a limited social role.

Disclosure: H. Yoshifuji, Astellas Pharma, 2, Chugai Pharmaceutical, 8; **H. Uchida**, Kawanishi Holdings, 9, Chugai pharmaceutical, 9, Boehringer Ingelheim, 9, MSD, 9; **Y. Nakaoka**, Chugai pharmaceutical, 2, 8, Actelion pharmaceuticals, 8, Nippon Shinyaku, 8, Bayer Yakuhin, 2, 8, Astellas Pharma, 8, Novartis, 8, MSD, 2, 8, Daiichi-Sankyo, 2, Takeda Pharmaceutical, 2, Otsuka Pharmaceutical, 2, Pfizer, 2, Mitsubishi Tanabe Pharma, 2; **T. Sugihara**, Ayumi Pharmaceutical, 9, Ayumi Pharmaceutical Corporation, 2, Chugai Pharmaceutical, 9, Chugai Pharmaceutical Co., Ltd., 2, CSL Behring, 9, CSL Behring K.K., 2, Japan Blood Products Organization, 2, 9, UCB Japan, 9, UCB Japan Co. Ltd., 2; **M. Isobe**, Chugai pharmaceutical, 8, Daiichi Sankyo, 2, 8, Otsuka Pharmaceutical, 2, 8, Teijin pharma, 2, Mitsubishi Tanabe Pharma, 2, Ono Pharmaceutical, 2; **M. Harigai**, AbbVie Japan GK, 2, 8, Ayumi Pharmaceutical Co. Ltd., 2, Bristol Meyers Squib, 2, 5, 8, Bristol-Myers Squibb Co. Ltd, 2, 5, 8, Chugai Pharmaceutical Co. Ltd., 2, 5, 8, Chugai Pharmaceutical Co., Ltd., 2, 5, 8, Eisai Co. Ltd., 2, Eisai Co., Ltd., 2, Eli Lilly, 5, 8, Mitsubishi Tanabe Pharma Co., 2, Mitsubishi Tanabe Pharma Corp., 2, Nippon Kayaku Co. Ltd., 2, Taisho Toyama Pharmaceutical Co. Ltd., 2, Takeda Pharmaceutical Co., 2, Takeda Pharmaceutical Co., Ltd., 2, Teijin Pharma Ltd., 2, 8, Teijin Pharma, Ltd., 2, 8.

Abstract Number: 0758

Interleukin-6 May Predict Disease Relapse During Long-term Follow-up in Takayasu's Arteritis in a Han Chinese Population

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the role of interleukin-6 (IL-6) in predictinglong-term disease prognosis for Takayasu's arteritis (TA).

Methods: Thirty-one patients diagnosed with TA between January 2012 and December 2013 were enrolled. The baseline IL-6 levels were detected in all, and a 5-year follow-up was suggested. Data including clinical presentations, laboratory indices, treatments, and radiological images during the 5-year follow-up were recorded. The value of IL-6 in predicting disease relapse and imaging progression was analyzed.

Results: Patients were divided into three groups according to baseline serum IL-6 levels: low group (≤8.8 pg/mL, n=13); medium group (8.9–18.9 pg/mL, n=9); and high group (≥19.0 ng/mL, n=9). Patients in the high and medium group had higher disease activity than those in the low group ($p< 0.01$). Baseline IL-6 levels were correlated with luminal stenosis ($p< 0.05$), although no significant correlations with long-term imaging progression were observed. Patients with more than 2 episodes of disease relapses were more commonly seen in the medium and high groups ($p=0.03$). Multivariate Cox proportional hazard regression analysis indicated that medium and high IL-6 levels were both positive predictors for disease relapse (medium group: HR 8.26, 95%CI 0.67–53.44, $p=0.072$; high group: HR 14.77, 95%CI 1.09–92.31, $p=0.041$) in TA. Goodness-of-fit test further confirmed the value of high levels of IL-6 in predicting disease relapse ($R=0.71$, $R2=0.57$, $p=0.06$).

Conclusion: IL-6 is a valuable predictor of TA disease relapse during long-term follow-up. Thus, treatments targeted at IL-6 pathways may reduce disease relapse and have better long-term prognostic effects for TA patients.

Disclosure: Y. Sun, None; **K. Xiufang**, None; **L. Jiang**, None.

Abstract Number: 0759

Polymyalgia Rheumatica Patients with and Without Elevated Baseline Acute Phase Reactants: Distinct Subgroups of Polymyalgia Rheumatica?

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic signs of inflammation such as raised CRP or ESR are a classical feature of PMR, but some patients present with normal acute phase reactants (APR).[1,2] It is not known whether these patients represent milder forms of PMR, whether their disease is not yet fully expressed, or whether they represent another disease entirely. We will explore baseline differences in demographics and clinical characteristics in PMR patients with and without elevated APR to evaluate whether they are distinct subgroups of PMR.

Methods: We conducted a retrospective cohort study of newly diagnosed PMR patients (clinical diagnosis) who visited our outpatient clinic between April 2012 and September 2017. Patient with concomitant inflammatory rheumatic disease were excluded. Data on patient-, disease,- and treatment characteristics were extracted from the electronic health record. Descriptive statistics were used [mean (SD), median (p25-p75) or n (%) as appropriate], and differences between patients with normal versus high APR(CRP >10 mg/L and/or ESR >30mm/hour) were tested using Fischer's exact test for categorical data, t-test for normally and Wilcoxon test for non-normally distributed data.

Table 1. Baseline characteristics of patients with normal versus elevated APR

Characteristic	Normal APR (N= 62; 14%)	Elevated APR (N= 392; 86%)
Female (%)	32 (52)	218 (56)
Age in years at diagnosis (SD)	66.0 (7.5)	66.6 (8.9)
History of previous PMR (%)	10 (16)	32 (8)
Weeks with PMR symptoms before diagnosis (IQR)*	**13 (7-20)**	**10 (6-16)**
Neckpain (%)	27 (44)	175 (45)
Bilateral shoulderpain/stiffness (%) No shoulderpain/stiffness (%)	57 (93) 2 (3)	361 (92) 20 (5)
Bilateral hippain/stiffness (%) No hippain/stiffness (%)	55 (87) 7 (11)	327 (83) 51 (13)
Both bilateral shoulder- and hippain/stiffness (%)	52 (84)	310 (79)
Peripheral arthritis (%) * Dubious (%)	**1 (2)** 4 (6)	**35 (9)** 32 (8)
Distal swelling pitting edema (%)	1 (2)	11 (3)
Systemic symptoms (%) ‡	27 (44)	172 (44)
ESR (IQR)	19 (12-25)	42 (31-53)
CRP (IQR)**	5 (2-7)	34 (21-57)
Anemia (%)*	**8 (17)**	**132 (43)**
Morning stiffness>45 min (%)	29 (73)	206 (68)
Rheumatoid factor present (%) *** Anti-CCP present (%)***	4 (11) 0 (0)	34 (13) 3 (1)
Osteoarthritis (%)	22 (35)	163 (42)
Hypercholesterolemia (%)	10 (16)	86 (22)
Diabetes mellitus (%)	4 (6)	52 (13)
Hypertension (%)	25 (40)	145 (37)
Thyroid disease (%)	2 (3)	38 (10)
Ischemic heart disease (%)****	5 (8)	40 (10)
Other cardiovascular disease (%) *****	4 (6)	39 (10)
Oral GC only (%) Oral GC + MP i.m. 120 mg (%) MP i.m. only (%)	38 (61) 20 (32) 4 (6)	281 (72) 105 (27) 6 (2)
Starting dose oral GC in mg (IQR) ¤	15 (15-20)	15 (15-20)

* Significant with appropriate test at alpha level 0.05

‡Fever, night sweats, weight loss, anorexia

**N=46 in normal APR group; N= 358 in elevated APR group

***Rheumatoid factor: N= 36 versus N= 257; anti-CCP: N= 33 versus N= 242

**** Angina pectoris, myocardial infarction

***** Cardiovascular disease: cerebrovascular event, peripheral arterial disease, heart failure, thrombosis

¤ N=42 in normal APR group; N= 339 in elevated APR group

Results: 454 patients were included (table 1). Sixty-two patients had normal, and 392 had elevated APR. Fewer patients with normal APR had peripheral arthritis (2 versus 9 %; p=0.044) and anemia at diagnosis (17 versus 43%; p=0.001). Furthermore, patients had a longer median duration of symptoms before diagnosis (13 versus 10 weeks; p=0.02) and were more likely to have a history of PMR (16 versus 8 %;p=0.057). Patients with normal APR had a shorter median time to referral general practitioner due to GC-free remission (552 versus 693 days; n= 36 versus 160; p=0.023). In both groups flares occurred more often between 12-24 versus < 12 months compared to the first 12 months (35 versus 13%; p=0.001 and 30 versus 20%; p=0.010 in normal and elevated APR group respectively). Fewer patients with normal APR were prescribed methotrexate; 3 versus 12%; p=0.046).

Conclusion: The results of this cohort suggest that patients with normal APR are a somewhat milder subset of PMR patients and have a better prognosis. However, flare risk does not differ from APR positive patients.

Table 2. Follow-up (FU) characteristics of patients with normal versus elevated APR (FU)

Characteristic	Normal APR (N= 62; 14%)	Elevated APR (N= 392; 86%)
Insufficient response to GC at 4 weeks (%)* **	16 (26)	83 (21)
Referral back to general practitioner in GC-free remission (%)*	**36 (58)**	**160 (41)**
Median time in days to referral in patients referred back to GP (IQR)*	**552 (430-758)**	**693 (511-993)**
Proportion of GC-free remission **		
12 m FU (%)	14 (23)	111 (29)
24 m FU (%)	25 (52)	136 (44)
Total patients with flares during FU (%)	36 (58)	254 (65)
1 flare (%)	15 (24)	124 (32)
2 flares (%)	7 (11)	61 (16)
3 or more flares (%)	14 (23)	68 (17)
Flares during FU		
<12 months (%)	8 (13)	77 (20)
12-24 months‡ (%)	**21 (35)**	**114 (30)**
Median time in days to first flare in patients who flared (IQR)	289 (132-477)	276 (164-451)
DMARD‡‡		
Methotrexate (%)*	**2 (3)**	**48 (12)**
Azathioprine (%)	0	8 (2)
TCZ (%)	0	1 (0)
Other (%) ‡‡‡	0	12 (3)
Osteoarthritis (%)	10 (16)	94 (24)
Rheumatoid arthritis (%)	2 (3)	21 (5)
Giant cell arteritis (%)	1 (2)	7 (2)
Malignancy** (%)**	0	13 (3)
Death (%)	0	1

* significant with appropriate tests at alpha level 0.05
** Normal APR at 12 months n= 61 and at 24 months n= 48, elevated APR n=380; and at 24 months n =309
*** Remission defined by rheumatologist (clinical judgement)
****Types of malignancy: bladder cancer (2), renal cell carcinoma, ovarian cancer, grawitz tumor, leukemia, skin tumor, squamous cell carcinoma, choleduchus carcinoma
‡ Total patients who flared at 12-24 months was significantly higher than total patients who flared before 12 months, in both normal and elevated APR group
‡‡ Reason for prescribing disease modifying drugs (DMARD) in elevated APR: ineffectiveness GC: methotrexate (MTX) 23, azathioprine (AZA) 6 ; tocilizumab (TCZ) 1; adverse events GC: MTX 4, ineffectiveness and adverse events GC: MTX 7, AZA 3, other disease: MTX 4
‡‡‡ Hydroxochloroquine, sulfasalazine, etanercept and adalimumab were prescribed in 8 patients due to other diseases than PMR; leflunomide in 3 patients due to ineffectiveness GC in PMR and failure on MTX

Disclosure: D. Marsman, None; **A. van der Maas**, None; **A. den Broeder**, AbbVie, 9, Amgen, 8, Biogen, 9, BMS, 8, Boehringer Ingelheim, 8, Cellgene, 9, Fresenius, 8, Roche, 9; **N. den Broeder**, None; **N. Boers**, None; **F. van den Hoogen**, AbbVie, 5, Actelion, 2, Amgen, 8, Biogen, 5, BMS, 2, Boehringer Ingelheim, 5, Celgene, 5, Celltrion Healthcare, 5, 8, Corbus, 8, Eli Lily, 2, Janssen, 8, Mundipharma, 5, Novartis, 5, Pfizer, 2, Roche, 8, Sandoz, 8, Sanofi Genzyme, 5.

Abstract Number: 0760

Prescribing Methotrexate in Polymyalgia Rheumatica: A Missed Opportunity?

Diane Marsman,[1] Aatke van der Maas,[1] Nathan den Broeder,[1] Thomas Bolhuis,[1] Nadine Boers,[2] Alfons den Broeder,[1] and Frank van den Hoogen[1], [1]Sint Maartenskliniek, Nijmegen, Netherlands, [2]Sint Maartenskliniek, Nijmegen

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with polymyalgia rheumatica (PMR) and giant cell arthritis (GCA) constitute approximately 20% of diseases chronically treated with glucocorticoids (GC) with a daily dose of 7.5 mg or more,[1] and GC-related adverse events (AE) are reported in up to 65% of PMR patients.[2] Additionally, 50% of secondary care patients are not able to discontinue their GC treatment, emphasizing the need for GC-sparing agents.[3] The recent guidelines on management of PMR recommend early introduction of methotrexate (MTX), especially in patients at risk for worse prognosis such as female gender, high erythrocyte sedimentation rate (ESR) and peripheral arthritis at

Table 1. Baseline, follow-up and treatment characteristics

Characteristic	Patients (N total = 454)
Female (%)	250 (55)
Age, years(SD)*	66.5 (8.7)
Weeks with PMR symptoms before diagnosis (IQR)**	10 (6-16)
Both bilateral shoulder- and hippain/stiffness (%)	362 (80)
Peripheral arthritis (%)	36 (8)
Systemic symptoms*** (%)	199 (44)
ESR in mm/hour (IQR)	37 (26-51)
CRP in mg/ l (IQR)	30 (15-54)
Rheumatoid factor present****(%) Anti-CCP present**** (%)	38 (8) 3 (1)
Starting dose oral GC in mg (IQR)	15 (15-20)
Total patients with flares during FU (%) 1 flare (%) 2 flares (%) 3 or more flares (%)	290 (64) 139 (31) 68 (15) 83 (18)
Methotrexate total (%) PMR total (%) Rheumatoid arthritis (%) Giant cell arthritis (%)	65 (14) 52 (11) 9 (2) 4 (1)
Other DMARDs in PMR[‡] (%) Azathioprine (%) Leflunomide (%) TCZ (%)	8 (2) 5 (1) 3 (1) 1 (0)
Reason for prescribing MTX in PMR Ineffectiveness GC (%) Adverse events GC[‡‡] (%) Both ineffectiveness and adverse events GC (%) Unknown (%)	 24 (46) 4 (8) 11 (21) 13 (25)
Mean time in days to MTX introduction in PMR patients (SD)	535 (353)
MTX start dose in PMR patients in mg 10 (%) 15 (%) 20 (%) 25 (%)	 5 (10) 24 (46) 8 (15) 15 (29)
Route of GC administration in PMR patients with MTX Oral (%) Intramuscular (%)	 43 (83) 4 (8)
Mean oral GC-dose at introduction MTX in mg (SD)	8.9 (5.5)
Mean intramuscular GC dose at MTX in mg (SD)	95 (38)
MTX introduction in PMR 0-1 flare (%) MTX introduction in PMR 2 flares (%) MTX introduction in PMR >3 flares (%)	18 (35) 14 (27) 20 (38)

*SD= Standard deviation

**IQR = Interquartile range

***Fever, night sweats, weight loss, anorexia

****Rheumatoid factor: N= 293; anti-CCP: N= 275

‡Reason for prescribing in PMR: azathioprine (AZA) : all due to ineffectiveness GC. Leflunomide: all due to ineffectiveness GC in PMR and failure on MTX. Tocilizumab (TCZ) 1; adverse events GC

‡‡ GC-related adverse events described: Cushingoid face, hair loss, hot flashes, brittle skin, stomach ache, dizziness, weight gain, cataract, osteoporosis

diagnosis.[4] However, evidence regarding MTX use in daily clinical practice is limited.[4] Therefore our aim is to assess MTX treatment in GC dependent PMR patients in a large Dutch rheumatology clinic.

Methods: This is a retrospective cohort study of newly diagnosed PMR patients (clinical diagnosis) who visited our rheumatology clinic between April 2012 and September 2017. Patients with concomitant active inflammatory rheumatic disease were excluded. Data on patient, disease and treatment characteristics were extracted from the electronic health records. Descriptive statistics were used as appropriate.

Results: Baseline, follow-up and treatment characteristics of the 454 included patients are described in table 1. MTX was prescribed in 52/454 (11%) PMR patients while 33% of patients had two or more flares during follow-up. Other disease modifying anti-rheumatic drugs (DMARDs) were prescribed in 2% of patients. Reasons for prescribing MTX were GC ineffectiveness in 46%, GC adverse events in 8%, both GC ineffectiveness and adverse events in 21% and unknown in 25% of patients. Mean time to MTX introduction was 535 days (SD 353) and the starting MTX dose was 10mg in 10%, 15 mg in 46%, 20mg in 15% and 25mg in 29% of PMR patients respectively. Of the PMR patients treated with MTX, 83% was on oral GC (mean dose was 8.9mg, SD 5.5mg) and 8% on intramuscular GC (mean dose 95mg per approximately one month, SD38mg). At the start of MTX treatment, 38% of patients had experienced three or more flares, 27% two flares and 35% one flare.

Conclusion: Early introduction of concomitant MTX early in GC dependent PMR is limited in our rheumatology clinic. Several interventions can be conceived to enhance follow-up to (inter)national guidelines on management of PMR.

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Disclosure: D. Marsman, None; **A. van der Maas**, None; **N. den Broeder**, None; **T. Bolhuis**, None; **N. Boers**, None; **A. den Broeder**, AbbVie, 9, Amgen, 8, Biogen, 9, BMS, 8, Boehringer Ingelheim, 8, Cellgene, 9, Fresenius, 8, Roche, 9; **F. van den Hoogen**, AbbVie, 5, Actelion, 2, Amgen, 8, Biogen, 5, BMS, 2, Boehringer Ingelheim, 5, Celgene, 5, Celltrion Healthcare, 5, 8, Corbus, 8, Eli Lily, 2, Janssen, 8, Mundipharma, 5, Novartis, 5, Pfizer, 2, Roche, 8, Sandoz, 8, Sanofi Genzyme, 5.

Abstract Number: 0761

Polymyalgia Rheumatica: Winter Is Coming

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

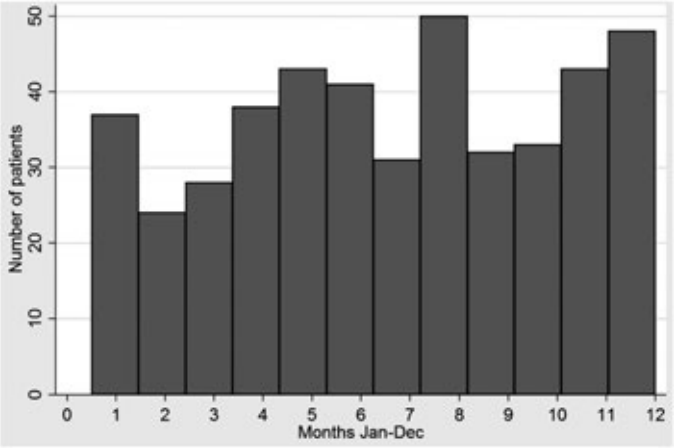

Figure 1. Onset of PMR Symptoms

Table 1. Baseline characteristics of PMR patients (n=448)

Characteristic	
Female (%)	247 (55)
Age in years at diagnosis (SD)	66 (8.6)
History of previous PMR (%)	41 (9)
PMR symptoms before diagnosis in weeks (IQR)	10 (6-16)
Neck pain (%)	205 (46)
Bilateral shoulder pain /stiffness (%)	412 (91)
Bilateral hip pain/stiffness (%)	380 (85)
Both bilateral shoulder- and hippain/stiffness (%)	359 (80)
Morning stiffness>45 min (%)	233 (52)
Peripheral arthritis (%) **Dubious (%)**	35 (8) 34 (8)
Systemic symptoms* (%)	199 (44)
Concurrent infection at diagnosis (%)	33 (7)
Elevated ESR mm/hour and / or CRP mg/l	309 (87)
ESR in mm/hour(IQR)	37 (26-51)
CRP in mg/l (IQR)	30 (15-54)
Anemia (%)	135 (30)
Rheumatoid factor present (%)** **Anti-CCP present** (%)**	38 (8) 3 (2)

*Fever, night sweats, weight loss, anorexia
** ESR n= 428 and CRP n=396
***Rheumatoid factor: N= 293; anti-CCP: N= 275

Background/Purpose: The cause for polymyalgia rheumatic (PMR) is currently unknown. Disease onset may be triggered by a combination of genetic predisposition and environmental factors such as infection.[1] In different regions of Denmark a simultaneous peak incidence of giant cell arthritis and PMR occurred together with epidemics of Myco-

plasma pneumoniae, Chlamydophila pneumoniae and Parvovirus B19.[1] A seasonal epidemics pattern for PMR would be supporting evidence for an infectious cause.[1] However, the current evidence of seasonal effect on the occurrence and disease severity of PMR is limited and show conflicting results.[2,3] We therefore aim to evaluate whether there is a seasonal effect on the risk of developing PMR in the Netherlands.

Methods: We retrospectively collected data on patient-, disease,- and treatment characteristics from newly diagnosed PMR patients (clinical diagnosis) who visited our outpatient clinic during April 2012 and September 2017. Exclusion criteria was other concomitant inflammatory rheumatic disease. Based on the onset of PMR (start symptoms, not time of diagnosis) patients were grouped per month. Descriptive statistics were used [mean (SD), median (p25-p75) or n (%) as appropriate]. The Chi square goodness of fit test was used to determine whether the incidence of onset of symptoms was different between months of the year.

Results: In total 448 patients were included and 55 % were female and mean age was 66 years. Other baseline characteristics are described in table 1. The chi-square goodness of fit test to determine whether there was a peak incidence in months was p=0.06. As shown in figure 1 the incidence of onset PMR symptoms is higher in December-January, April through June with a peak in August. The April-June peaks coincides with incidence peaks of Mycoplasma pneumoniae infections and possibly Parvovirus B19 in spring and summer, The December-January peak coincides with Parvovirus B19 infections.[4,5]

Conclusion: No definitive seasonal effect was found on risk of developing PMR, although a bimodal seasonal pattern compatible with the proposed respiratory infections is suggested.

Disclosure: D. Marsman, None; **A. van der Maas**, None; **A. den Broeder**, AbbVie, 9, Amgen, 8, Biogen, 9, BMS, 8, Boehringer Ingelheim, 8, Cellgene, 9, Fresenius, 8, Roche, 9; **F. van den Hoogen**, AbbVie, 5, Actelion, 2, Amgen, 8, Biogen, 5, BMS, 2, Boehringer Ingelheim, 5, Celgene, 5, Celltrion Healthcare, 5, 8, Corbus, 8, Eli Lily, 2, Janssen, 8, Mundipharma, 5, Novartis, 5, Pfizer, 2, Roche, 8, Sandoz, 8, Sanofi Genzyme, 5; **N. den Broeder**, None; **N. Boers**, None.

Abstract Number: 0762

Are There Any Identifiable Triggers in Polymyalgia Rheumatica? A Matched-Control Study

Mayra Tobar Jaramillo,[1] Victor Santos Andrade,[2] Marina Scolnik,[3] Luciano Fernando Lo Giudice,[4] John Jaramillo Gallego,[5] Valeria Scaglioni,[5] and Enrique Soriano[6], [1]Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires, Argentina, Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina, [2]Rheumatology Section, Internal Medicine Service, Fundacion Valle de lili, Colombia, Cali, Valle del Cauca, Colombia, [3]Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires, Argentina, Ciudad Autonoma de Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina, [4]Hospital Italiano de Buenos Aires, Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina, [5]Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires, Argentina, Ciudad Autónoma de Buenos Aires, Argentina, [6]Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires, Argentina., Buenos Aires, Buenos Aires, Argentina

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Table 1. PMR patients and controls characteristics in the year previous to index date

	PMR patients (n=169)	Controls (n=169)	P value
Females, n (%)	135 (79.9)	135 (79.9)	1
Hypertension, n (%, 95% CI)	68 (40.2, 33.1-47.8)	68 (40.2, 33.1-47.8)	1
Dyslipidemia, n (%, 95% CI)	34 (20.1, 14.7-26.9)	21 (12.4, 8.2-18.4)	0.06
Diabetes, n (%, 95% CI)	9 (5.3, 2.8-9.9)	12 (7.1, 4.1-12.1)	0.49
Obesity, n (%, 95% CI)	19 (11.2, 7.3-16.9)	20 (11.8, 7.7-16.7)	0.86
Statin initiation, n (%, 95% CI)	17 (10.1, 6.3-15.6)	9 (5.3, 2.8- 9.9)	0.10
Any vaccine received and recorded, n (%, 95% CI)	31 (18.3, 13.2-24.9)	24 (14.2, 9.7-20.4)	0.30
Infections requiring antibiotics or ambulatory consultation, n (%, 95% CI)	25 (18.3, 13.2-24.9)	18 (10.6, 6.8-16.3)	0.25
Infections requiring hospitalization, n (%, 95% CI)	4 (2.4, 0.9-6.2)	2 (1.2, 0.3-4.6)	0.41
Surgery, n (%, 95% CI)	7 (4.1, 1.9-8.5)	6 (3.6, 1.6-7.7)	0.78
Cardiovascular event, n (%, 95% CI)	2 (1.2, 0.3-4.6)	1 (0.6, 0.1-4.1)	0.56

Background/Purpose: As many other rheumatologic diseases, pathogenesis of Polymyalgia Rheumatica (PMR) is not well understood. Genetic factors seem to play a role. Some studies have suggested a seasonal variation, indicating a possible infectious trigger; others have shown and association with statins initiation. Our objective was to compare PMR patients with matched controls in order to identify possible triggers in the year previous to PMR development.

Methods: PMR patients (fulfilling ACR 2012 criteria) belonging to a Health Management Organization (HMO) of a tertiary university hospital were matched 1:1 by gender and date of birth with controls belonging to the same HMO. Date of PMR diagnosis was considered as the index date for patients and their correspondent control. Electronic medical records were manually reviewed and data on infections, hospitalizations, surgeries, vaccines and starting of statins in the year previous to the index date were recorded for both PMR patients and controls and compared between them. For PMR patients, season where disease symptoms started was also analyzed.

Table 2. PMR patients' characteristics

	PMR patients (n=169)
Females, n (%)	135 (79.9)
Age at diagnosis, years, mean (SD)	79.5 (6.1)
Erythrosedimentation rate at diagnosis, mm/h, mean (SD)	54.0 (24.1)
Shoulder girdle pain, n (%, 95% CI)	91.1 (85.7-94.6)
Pelvic girdle pain, n (%, 95% CI)	84.0 (77.6-88.8)
Arthritis, n (%, 95% CI)	60 (35.5, 28.6-43.0)
Initial dose of meprednisone, mean (SD)	9.3 (5.4)
Duration of corticosteroid treatment, median (IQR)	21 (13-33)
PMR symptoms starting in summer, n (%, 95% CI)	50 (29.6, 23.1-36.9)
PMR symptoms starting in autumn, n (%, 95% CI)	50 (29.6, 23.1-36.9)
PMR symptoms starting in winter, n (%, 95% CI)	42 (24.8, 18.9-31.9)
PMR symptoms starting in spring, n (%, 95% CI)	27 (15.9, 11.1-22.4)

Results: 169 PMR patients and 169 controls were included. 79.9 % were females. Age at PMR diagnosis was 79.5 years (SD 6.1). No differences were found between PMR patients and controls regarding infections, hospitalizations, vaccines, surgeries or statin initiation in the year previous to PMR diagnosis (table 1). PMR symptoms started in summer in 50 patients (29.6%, 95% CI: 23.1-36.9), in autumn in 50 (29.6%, 95% CI: 23.1-36.9), winter in 42 (24.8%, 95% CI: 18.9-31.9) and spring in 27 (15.9%, 95% CI: 11.1- 22.4) (Table 2).

Conclusion: We didn't find an identifiable trigger for the development of PMR when analyzing the year previous to diagnosis comparing to matched controls. No seasonal pattern was clearly seen.

Disclosure: M. Tobar Jaramillo, None; **V. Santos Andrade**, None; **M. Scolnik**, Abbvie, 8, ABBVIE, 8, Bristol, 8, BRISTOL, 8, Bristol-Myers, 8, Bristol-Myers Squibb, 8, Glaxo, 8, GLAXO, 8, Lilly, 8, LILLY, 8, Pfizer, 8, PFIZER, 8, Pfizer Inc, 8, Roche, 8, ROCHE, 8; **L. Lo Giudice**, None; **J. Jaramillo Gallego**, None; **V. Scaglioni**, None; **E. Soriano**, Abbvie, 2, 5, 8, ABBVIE, 2, 5, 8, AbbVie, 2, 5, 8, Amber, 8, Amgen, 5, 8, AMGEN, 5, 8, BMS, 8, BRISTOL, 8, Bristol MS, 8, BRISTOL MYERS SQUIBB, 8, Bristol-Myers Squibb, 8, eli lilly, 5, 8, Genzyme, 8, GENZYME, 8, GLAXO, 2, Glaxo, 2, glaxosmithkline, 2, GlaxoSmithKline, 2, GSK, 2, Janssen, 8, Lilly, 5, 8, LILLY, 5, 8, Novartis, 2, 5, 8, NOVARTIS, 2, 5, 8, PFIZER, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, 8, Roche, 2, 8, ROCHE, 2, 8, Sandoz, 5, SANDOZ, 5, Sanofi, 5, SANOFI, 5, SANOPHY, 5, UCB, 8.

Abstract Number: 0763

Treatment Efficacy Evaluation of Leflunomide by Regulating Macrophages in Takayasu Arteritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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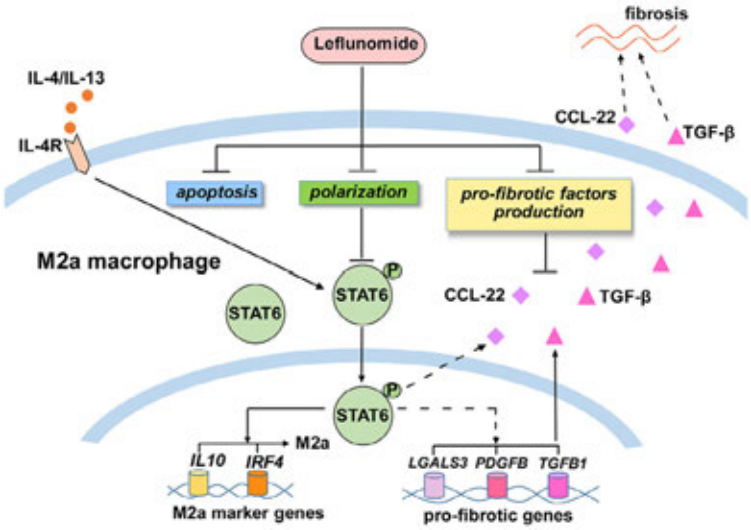
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the efficacy and safety of leflunomide (LEF) for active Chinese Takayasu Arteritis (TA) patients in induction therapy compared with cyclophosphamide (CYC) and in long-term treatment with comparison between new-onset patients and refractory patients who were ineffective or recurrent after CYC treatment. The mechanism of LEF on improving the inflammatory fibrosis in TA by regulating M2 macrophages were also explored.

Methods: Based on the East China TA cohort, a total of 131 patients with active TA who were treated with LEF or CYC were enrolled. The patients were all followed up for 6 months. Their epidemiological data, clinical performance, laboratory data and imaging data at baseline and follow-up were collected for comparison of the efficacy and safety of LEF and CYC. Multivariate analysis was used to compare the response rate of the two groups of patients after 6 months of treatment. Propensity-score matching (PSM) was used to correct the baseline data of the two groups. Fifty-six of patients treated with LEF were further analyzed for their response to treatment after 6 months and 12 months. Among them, 41 patients were treated with LEF since initial visit, and 15 patients were replaced with leflunomide after treatment with CYC. Peripheral blood monocytes of sixteen TA patients were treated with LEF. The ratio of M1/M2 and the apoptosis of M2 were detected by Flow cytometry. The supernatant level of cytokines and chemok-



Leflunomide could regulate the number and function of M2a cells in Takayasu's arteritis through multiple targets, including restriction of M2a polarization by inhibiting STAT6 phosphorylation and reducing expression of IL-10 and IRF4, promotion of apoptosis, inhibition of profibrotic genes expression, as well as reduction of production of profibrotic chemokines. Through these functions, leflunomide could prohibit the involvement of M2a in vascular remodeling.

ines secreted by M2a macrophages were detected by ELISA. The relative expression of profibrotic cytokines mRNA in M2a were detected by real-time PCR. Western Blot was used to measure the phosphorylation of Stat6.

Results: Patients in the LEF group were younger and had higher erythrocyte sedimentation rate (ESR) compared with CYC group. After 6 months of treatment, the clinical remission rate of LEF group was not inferior to CYC group. The overall clinical remission rate of patients treatment with LEF was 67.9% after 6 months of treatment, and 55.4% after 12 months. The level of ESR, C-reactive protein (CRP) and NIH scores decreased significantly after 12 months of LEF treatment. Patients who reacted as resistance to CYC achieved clinical remission in more than half of them after 6 and 12 months of LEF therapy. In addition, during the 12-month follow-up, most patients treated with LEF had well drug tolerance and a low incidence of adverse reactions. LEF could inhibite M2 polarization by curtailing STAT6 phosphorylation. LEF could also promote apoptosis of M2 and reduce the release of M2-derived CCL22 as well as the expression of profibrotic cytokines including CCL22 and TGF-β in M2.

Conclusion: LEF has comparable efficacy to CYC for induction of remission in active TA. Treatment with LEF in TA can achieve clinical remission in a short period of time, and maintain long-term stability of the disease, especially for refractory patients. LEF presents safety for women of childbearing age, and can be used for long-term treatment of patients with TA. LEF could reduce vascular fibrosis potential by down-regulating number and function of M2, which, eventually, could alleviate inflammatory fibrosis of aortic lesions in TA patients.

Disclosure: X. Cui, None; **X. Dai**, None; **X. Kong**, None; **R. Chen**, None; **L. Ma**, None; **Y. Sun**, None; **L. Jiang**, None.

Abstract Number: 0764

The Clinical and Angiographic Features of Chinese Takayasu's Arteritis Patients: A Cohort Study of 591 Patients in 6 Years

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the clinical and angiographic features of 591 Chinese Takayasu's arteritis (TAK) patients

Methods: Clinical and angiographic findings of 591 Chinese TAK patients enrolled in the Chinese Registry for Systemic Vasculitis (CRSV) from 2013 to October 31 of 2018 were collected. The vascular involvement were analyzed by Dendrogram using Ward Linkage.

Results: Clinical manifestations included Systemic manifestation in 66.2%, mucocutaneous abnormalities in 15.2% , sign and symptoms of peripheral vessels in 92.9%(as showed in Figure 1), abnormalities of central nervous system in 57.2%(56 patients suffered from stroke), vision loss in 11.2%,hypertension in 46.1% and abnormalities of renal

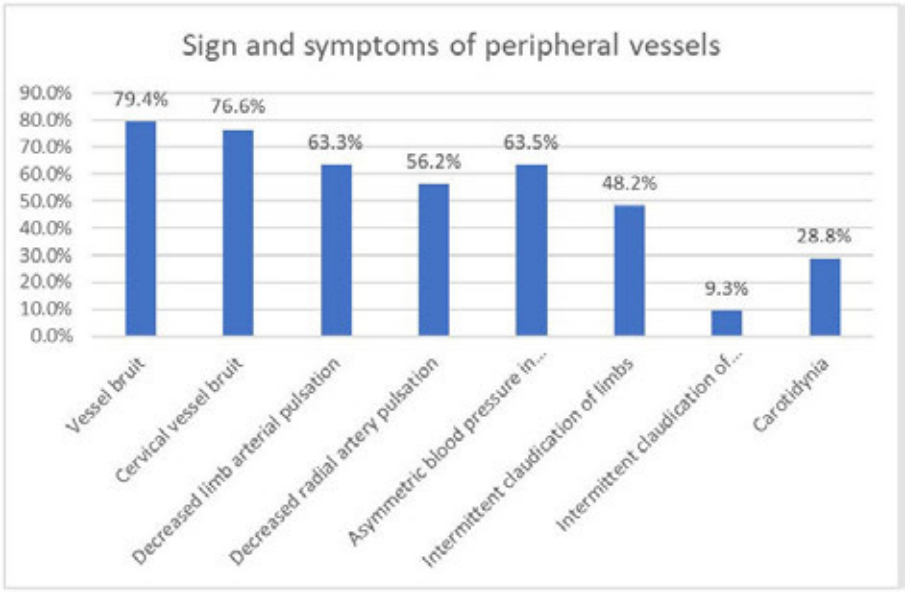

Figure 1. Sign and symptoms of peripheral vessels.

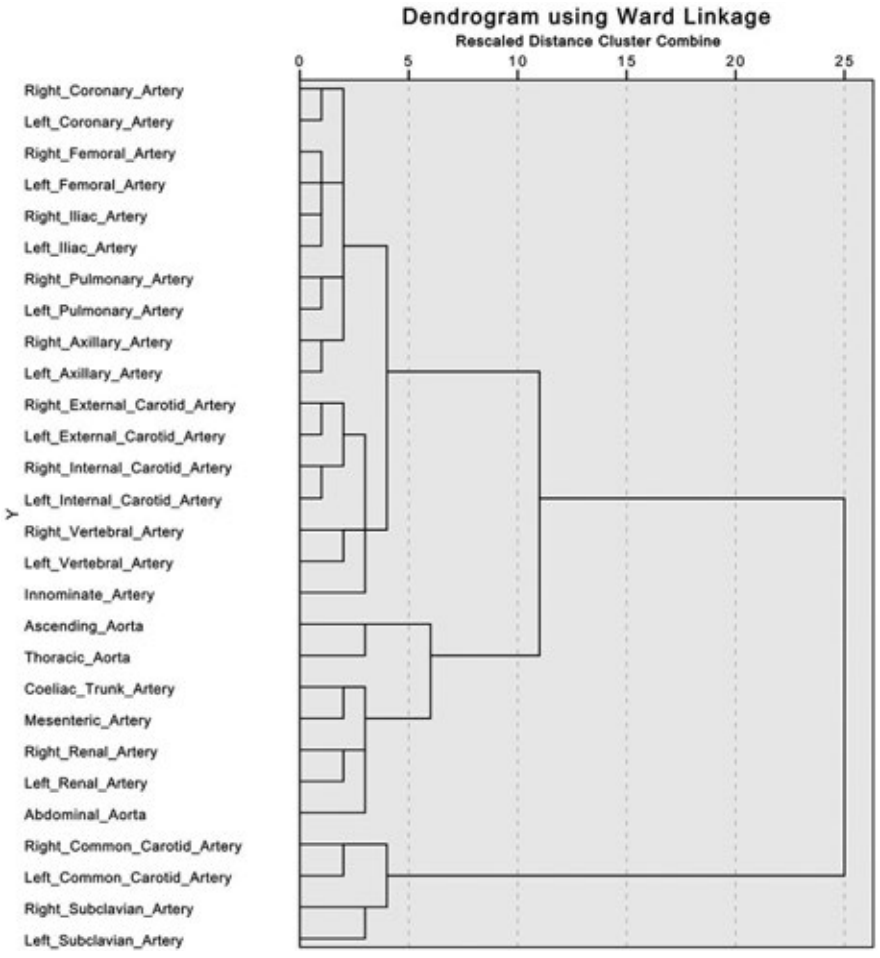

Figure 2. The clustering analysis of arterial involvement.

arteries in 35.5% of the patients. Meanwhile,28.1% of patients underwent angioplasty during the course of disease. The clustering analysis of arterial involvement was showed in figure 2.

Conclusion: The clinical and angiographic findings of TAK patients in China were different to those reported from other countries. We should pay more attention to the uniqueness of Chinese patients with Takayasu arteritis.

Disclosure: Y. Yang, None; **J. Li**, None; **X. Tian**, None; **X. Zeng**, None.

Abstract Number: 0765

Application of Different Sets of Classification/diagnostic Criteria for Polymyalgia Rheumatica: Single Center Study of 100 Patients

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SESSION INFORMATION
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Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Polymyalgia rheumatica (PMR) diagnosis is based on clinical and analytical features characterized by shoulder and pelvic girdle pain associated with elevated acute phase reactants. Traditionally, Bird et al. and Chuang et al. criteria have been used for establishing PMR diagnosis. In 2012 an international working group developed new European League Against Rheumatism (EULAR)/American Collegue of Rheumatology (ACR) classification criteria for PMR. Purpose: a) To compare the performance of Bird et al., Chuang et al. and 2012 EULAR/ACR classification criteria for PMR in a single-center study. b) To describe the characteristics of the patients excluded by these criteria.

Methods: We included 100 patients with new-onset PMR who were consecutively diagnosed over a 7-year period in a referral center by experienced rheumatologists. PMR diagnosis was confirmed during a prospective 24-month follow-up after excluding other mimicking conditions. Rheumatoid factor (RF) and anticitrullinated protein antibodies (ACPA) were determined in all patients. Subjects were classified by each of the three different criteria.

Results: We studied 100 patients (61 women/39 men); mean age 67.1 ± 10.2 years. 96% of the patients fulfilled Bird et. al criteria, 94% fulfilled Chuang et al. criteria and 84% of the patients fulfilled 2012 EULAR/ACR criteria (TABLE 1, 2 and 3). We assessed the characteristics of the 16 patients who did not fulfilled 2012 EULAR/ACR criteria: 6 of them were under 50 years of age (range age 43-48 years). Another 10 patients did not complain of pain/stiffness in the shoulder girdle at any time. However, they presented a predominance of inflammatory pelvic girdle pain and elevated acute phase reactants.

Conclusion: In our single-center experience we found that 2012 EULAR/ACR criteria classified most of our patients. However, patients who presented predominant pelvic girdle affection and those who were under 50 years old despite showing all the rest of clinical and analytical required items were excluded. Some of these patients fulfilled Bird and/or Chuang criteria.

TABLE 1. 2012 ACR/EULAR CLASSIFICATION CRITERIA

Age at onset ≥ 50 years (required)	94/100	94%
Bilateral shoulder aching (required)	89/100	89%
Abnormal CRP and/or ESR (required)	96/100	96%
Morning stiffness duration > 45 min (2 points)	54/100	54%
Hip pain or limited range of motion (1 point)	90/100	90%
Absence of RF or ACPA (2 points)	100/100	100%
Absence of other joint involvement (1 point)	95/100	95%
Required for classification: score of 4 or more	**84/100**	**84%**

TABLE 2. CHUANG ET AL. CRITERIA (1982)

Age at onset ≥ 50 years (required)	94/100	94%
ESR ≥ 40 mm/hr	96/100	96%
Bilateral aching for ≥ 1 month involving two of the following areas:		
- Neck	47/100	47%
- Shoulders or proximal regions of the arms	89/100	89%
- Hips or proximal aspects of the thighs	90/100	90%
Exclusion of all other diagnosis of mimicking entities	100/100	100%
All criteria are required for classification	**94/100**	**94%**

TABLE 3. BIRD/WOOD CRITERIA (1979)

Age at onset > 65 years	59/100	59%
ESR > 40 mm/hr	96/100	96%
Bilateral shoulder pain/stiffness	89/100	89%
Duration onset < 2 weeks	77/100	77%
Stiffness > 1 h	54/100	54%
Depression and/or weight loss	16/100	16%
Bilateral upper arm tenderness	89/100	89%
Probable: 3 or more	**96/100**	**96%**

Disclosure: D. Prieto-Pena, None; **M. Calderón-Goercke**, None; **I. Gonzalez-Mazon**, None; **J. Martín-Varillas**, None; **L. Sanchez-Bilbao**, None; **B. Atienza-Mateo**, None; **M. González-Gay**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 2, 5, EliLilly, 2, 5, Jansen, 2, Janssen, 2, MSD, 2, 5, 8, Novartis, 2, 5, Pfizer, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, Sobi, 5, 8; **R. Blanco**, None.

Abstract Number: 0766

Predictors of Long-term Therapy with Glucocorticoid in Polymyalgia Rheumatica

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical symptoms of polymyalgia rheumatica (PMR) are improved by low-dose glucocorticoids (GC), but relapses and long-term GC therapy are common. 2015 EULAR/ACR recommendations suggest early introduction of methotrexate (MTX) in addition to GC, particularly in patients at a high risk for relapse and/or prolonged therapy. However, risk factors for prolonged therapy are not clear yet. We investigated predictive factors which corresponded to the long-term GC therapy.

Methods: This was a retrospective study in a single general hospital in Japan. We reviewed the medical records of 96 Japanese patients with PMR between April 2011 and May 2019. Diagnosis of PMR was based on Bird's criteria or 2012 EULAR/ACR Classification Criteria. All patients were treated with prednisolone (PSL) according to the BSR and BHPR guidelines. Patients treated with MTX and accompanied by the giant cell arteritis were excluded from this study. Relapse was defined as the reappearance of symptoms associated with elevated C-reactive protein (CRP) levels in patients receiving GC. Remission was defined as the absence of clinical symptoms and normal CRP with discontinuation of GC. We compared the clinical findings, laboratory data at baseline and clinical course between those who achieved remission within 2 years (early-remission group; n=38) and those who required GC therapy for more than 2 years (long-therapy group; n=16). Comparisons between groups was made using Student's t-test and chi-square test (IBM SSPE statistics version 25).

Results: 54/96 (56%) were women. The mean age at diagnosis was 75 (SD 16.0). As of May 2019, 46 patients have achieved a remission, 32 were undergoing treatment, and 18 have transferred to other hospitals or died (Table 1). The median duration of GC therapy of patients who have achieved remission was 18.5 months. Remission was achieved

Table 1 Summary of patients with diagnosis with PMR

		Duration of GC therapy	
		less than 2 years	more than 2 years
Remission	n=46	38	8
Under treatment	n=32	26	6
Changing hospital or death	n=18	16	2
Patients included in the analysis		Early-remission n=38	Long-treatment n=16

PMR, polymyalgia rheumatica; GC, glucocorticoid

Table 2 Clinical findings in patients of 2 groups

Demographic, clinical, and laboratory findings at diagnosis		Early-remission n=38			Long-therapy n=16			p
Woman	n (%)	17	(44.7	)	9	(56.3	)	0.4
Age: years	mean (SD)	74.4	(8.05	)	75.1	(4.25	)	0.7
Body weight, kg	mean (SD)	56	(11.23	)	51	(9.9	)	0.1
Body mass index, kg/m2	mean (SD)	22.8	(4.10	)	20.2	(3.08	)	0.02
Fever	n (%)	10	(26.3	)	7	(43.8	)	0.2
Body weight loss	n (%)	12	(31.6	)	7	(43.8	)	0.4
Peripheral edema	n (%)	15	(39.5	)	7	(43.8	)	0.8
Serum C-reactive protein, mg/dL	mean (SD)	6.5	(4.09	)	9.5	(4.26	)	0.02
Serum albumin, mg/dL	mean (SD)	3.2	(0.49	)	3.3	(0.60	)	0.7
Lymphocyte, %	mean (SD)	17.8	(6.78	)	12.4	(4.01	)	<0.01
Treatment and clinical course								
Starting dose of PSL: mg/day	mean (SD)	12.4	(4.21	)	14.5	(4.10	)	0.1
mg/kg/day	mean (SD)	0.24	(0.085	)	0.29	(0.087	)	0.04
Mean duration of GC treatment	month (SD)	14.4	(4.69	)	46.2	(19.75	)	<0.01
Relapse: times	mean (SD)	0.4	(0.72	)	2.9	(1.86	)	<0.01
Relapse till 6 months	n (%)	3	(7.9	)	7	(73.8	)	<0.01

PSL, predonisolone; GC, glucocorticoid; SD, standard deviation

Table 2. Clinical findings in patients of 2 groups

in 16% (11/69) after one-year GC therapy, and 70% (38/54) after two-year GC therapy. There were no differences in sex, age, and or clinical features at diagnosis. Body-mass index and lymphocyte% were lower, and CRP was significantly higher in the long-therapy group (Table 2). Multivariate logistic regression analysis showed that history of relapse till 6 months was a significant predictor of long-term GC therapy (odds ratio, 9.07; 95%CI 1.949-42.248).

Conclusion: According to GCs therapy guidelines, the remission rate in our hospital is not low. However, some patients need the long-term therapy for more than 2 years. We might consider additional MTX therapy in patients who experience a relapse during the first six months.

Disclosure: A. Aoki, None; **H. Kobayashi**, None; **H. Oka**, None.

Abstract Number: 0767

Outcome Measures in Large-Vessel Vasculitis: Relationships Between Patient, Physician, Imaging, and Laboratory-Based Domains

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Takayasu's Arteritis & Polymyalgia Rheumatica

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Large-vessel vasculitis (LVV) is characterized by inflammation of the aorta and its major branches. The most common forms of LVV include giant cell arteritis (GCA) and Takayasu's arteritis (TAK). No standardized set of outcome measures currently exist to evaluate treatment response in patients with LVV. Various outcome domains have been proposed for LVV, including patient-reported outcomes (PROs), physician assessment of disease activity, vascular imaging, and laboratory assessment. However, data examining the relationships between these domains is limited. The objective of the current study was to assess the relationship structure between patient, physician, imaging, and laboratory-based outcome measure domains in patients with LVV.

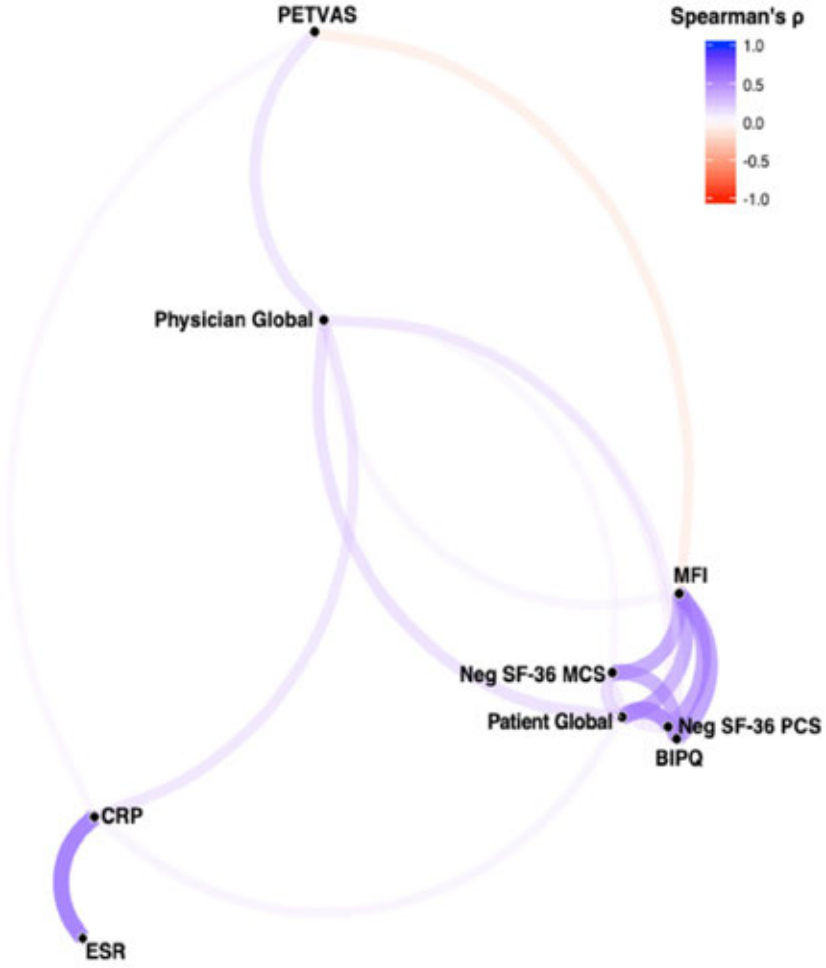

Figure. Correlation network of outcome measure domains in patients with LVV. Correlation network of the significant Spearman ρ correlation coefficients ($p<0.05$) between outcome measures created using the R package corrr. Color and thickness of the edges between nodes indicates the strength of the correlation. Nodes for each outcome measure are clustered in space using multidimensional scaling of the absolute values of the correlations, such that outcome measures with the highest overall magnitude of correlation with each other are closer in space. For ease of visualization, the SF-36 PCS and MCS measures were multiplied by -1 so that a higher score would indicate a worse outcome. MFI= Multidimensional fatigue inventory; BIPQ= brief illness perception questionnaire; Neg SF-36 PCS= negatively transformed 36-item short form health survey physical component summary score; Neg SF-36 MCS= negatively transformed 36-item short form health survey mental component summary score; CRP= c-reactive protein; ESR= erythrocyte sedimentation rate; PETVAS= qualitative score of vascular FDG-PET activity.

Methods: Patients fulfilling the ACR 1990 criteria for the classification of TAK or the modified ACR 1990 criteria for the classification of GCA were recruited into a prospective, observational cohort. Assessments within the following domains were independently recorded: patient-reported outcomes [multi-dimensional fatigue inventory (MFI); patient global assessment (PtGlobal); 36-item short form health survey (SF-36); brief-illness perception questionnaire (BIPQ)], physician global assessment (PhGlobal), acute-phase reactants (CRP, ESR), and imaging assessment (PET-VAS, a qualitative score of vascular FDG-PET activity). To visualize the relationship between domains, Spearman's correlation network analysis was performed. This analysis enables visualization of the strength and directionality of correlations and clusters variables most correlated to one another. Change over time in outcome measures was compared using the Wilcoxon signed rank test in patients with a change in clinical status from active disease (PhGlobal >0) to remission (PhGlobal=0) or from remission to active disease. Multivariable nominal logistic regression was performed to determine the outcome measures associated with clinically active disease.

Results: Analyses were performed on 112 patients (GCA=56, TAK=56), over 296 visits, with a median follow-up interval of 6 months. Correlation network analysis revealed outcome measures clustered independently and by specific domain (**Figure**). PhGlobal was centrally linked to all other domains, but correlations were modest (ρ=0.12 – 0.31, $p < 0.05$). All four PROs strongly correlated with each other (ρ=0.35-0.60, $p < 0.0001$). PROs were not correlated with PETVAS and only PtGlobal correlated with CRP (ρ=0.16, $p< 0.01$). Patients whose clinical assessment changed from active disease to remission (n=29) had corresponding significant decrease in ESR, CRP, and PETVAS at the remission visit. Patients whose clinical assessment changed from remission to active disease (n=11) had corresponding significant increase in CRP and PtGlobal at the active visit. PETVAS, CRP, and PtGlobal were independently associated with clinically active disease in regression analyses.

Conclusion: Measures of disease assessment in large-vessel vasculitis consist of independent, yet complementary domains, supporting the need to develop multidimensional and/or composite outcome measures, or a standard set of measures covering all domains.

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Abstract Number: 0768

Angiographic Patterns and Changes in Arterial Lesions in Patients with Behcet's Disease

Su Jin Choi,[1] So Hye Nam,[1] Jung Sun Lee,[1] Doo-Ho Lim,[2] Ji Seon Oh,[3] Seokchan Hong,[1] Yong-Gil Kim,[1] Chang-Keun Lee,[1] and Bin Yoo[1], [1]Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea, [2]Division of Rheumatology, Department of Internal Medicine, Ulsan University Hospital, Ulsan, Republic of Korea, [3]Department of Biomedical Informatics, Asan Medical Center, Seoul, Korea, Seoul, Republic of Korea

SESSION INFORMATION

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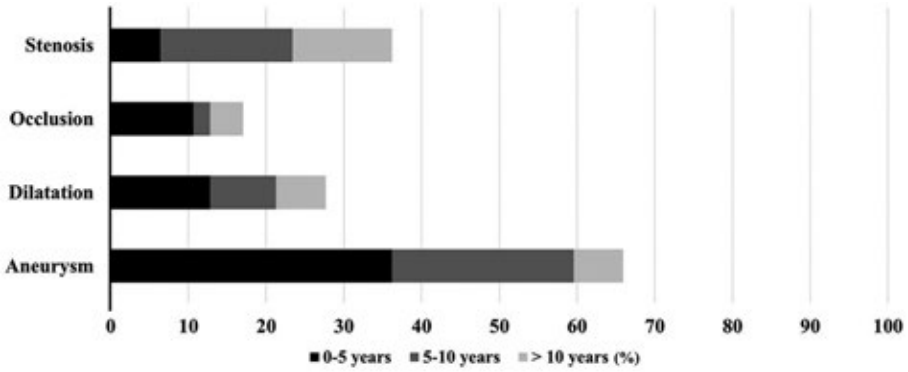

Figure 1. Pattern of arterial lesions in BD patients according to the symptom onset (n = 47).

Background/Purpose: Arterial involvement is a manifestation of systemic vasculitis in Behçet's disease (BD). Changes to BD arterial lesions over time can help predict patient prognosis. Few reports have been published, however, on arterial lesion during time courses in BD patients. We evaluated the angiographic patterns and changes to arterial lesions in BD patients.

Methods: We retrospectively reviewed BD patients with arterial lesions from January 1995 to December 2015. Arterial lesion patterns were categorized as stenosis, occlusion, dilatation, or aneurysm. Patients were divided into three groups by length of time (0-5 years, 5-10 years, and >10 years) of symptom duration before BD with arterial involvement diagnosis. Progression of arterial lesions was assessed by follow-up imaging. The Cox proportional hazards model was used to evaluate hazard ratios (HR) with a 95% confidence interval (CI) for arterial lesion progression.

Results: For 45 BD patients with arterial involvement, 99 total arterial lesions were observed as follows: stenosis (n = 27), occlusion (n = 9), dilatation (n = 19), and aneurysm (n = 44). Aneurysm was the most common angiographic lesion in 17 patients (36.2%), whereas only 3 patients (6.4%) had stenosis within five years of symptom onset (Figure 1). In patients with a symptom duration of 10 years or more, however, stenosis (n = 6, 12.8%) was most frequently observed, followed by aneurysm (n = 3, 6.4%). In 23 patients who underwent follow-up imaging (median 5.7 [IQR 2.8-7.5] years), 11 new lesions were detected in 8 patients (8/23; 34.8%) as follows: stenosis (n = 5), occlusion (n = 0), dilatation (n = 1), and aneurysm (n = 5). One of the 14 stenoses progressed to occlusion, and 2 of the 12 dilated lesions progressed to aneurysm. In multivariable analyses, arterial lesion progression was significantly associated with hypertension (HR 4.26, 95% CI 1.08-16.87, p = 0.039) and arterial involvement in a lower extremity (HR 5.44, 95% CI 1.09-27.10, p = 0.039).

Conclusion: In BD with arterial involvement, aneurysm was most often observed in early stages (symptom duration ≤ 5 years), while stenosis was more often observed during later stages (symptom duration > 10 years). Hypertension and arterial involvement in a lower extremity were found to be risk factors for arterial lesion progression.

Disclosure: S. Choi, None; **S. Nam**, None; **J. Lee**, None; **D. Lim**, None; **J. Oh**, None; **S. Hong**, None; **Y. Kim**, None; **C. Lee**, None; **B. Yoo**, None.

Abstract Number: 0769

Damage in Takayasu's Arteritis Is Associated with Age at Symptom-onset, Disease-duration and Corticosteroid Dose but Not Relapse in Routine Follow-up

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SESSION INFORMATION
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Background/Purpose: As a large-vessel vasculitis of young-age group, Takayasu's arteritis (TAK) have a high morbidity and mortality caused by the disease or treatments such as corticosteroids. In this study we aimed to evaluate the damage in our Takayasu's arteritis patients by using Vasculitis Damage Index (VDI) and Takayasu's Arteritis Damage Score (TADS).

Methods: Takayasu arteritis patients fullfilling the ACR 1990 criteria and had >6 months follow-up were enrolled in this single-center study retrospectively. Data was collected from patients charts. TADS and VDI scores at diagnosis and at the end of the follow-up were evaluated and compared with baseline damage. Variables associated with damage scores were evaluated.

Figure1. Patient numbers with disease and treatment-related damage items at last visit

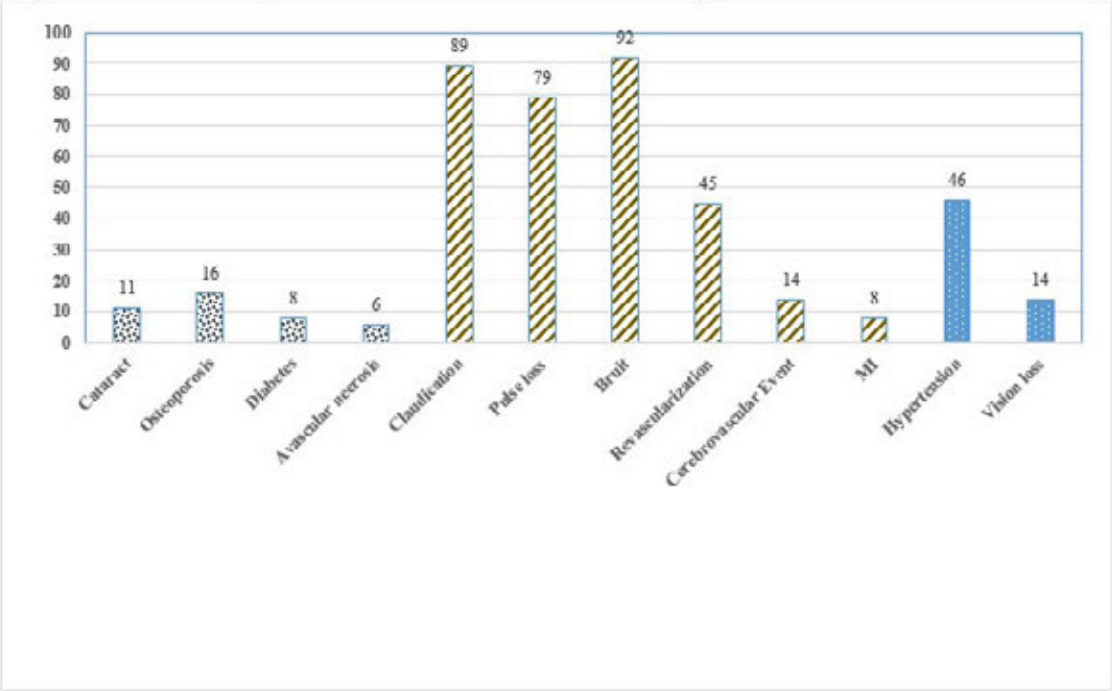

Table1. Variables associated with damage scores

	Univariable analysis		Multivariable analysis*	
	OR (95% CI)	p value	OR(95% CI)	p value
VDI score ≥5				
Female sex	1.09 (0.31-3.83)	0.88	-	-
Age at symptom onset, years	1.04 (1.01-1.07)	**0.011**	1.06 (1.02-1.10)	**0.005**
Cumulative steroid dose, g	1.12 (1.03-1.22)	**0.007**	1.17 (1.06-1.29)	**0.002**
Disease duration, months	1.00 (0.99-1.01)	**0.09**	1.00 (0.99-1.01)	0.17
Any relapse	0.94 (0.44-2.01)	0.88	-	-
Number of relapses	1.11 (0.73-1.71)	0.60	-	-
TADS score ≥8				
Female sex	0.64 (0.17-2.33)	0.50	-	-
Age at symptom onset, years	1.04 (1.00-1.07)	0.016	1.04 (1.01-1.07)	**0.009**
Cumulative steroid dose, g	1.04 (0.98-1.11)	0.17	1.05 (0.98-1.12)	0.12
Disease duration, months	1.00 (0.99-1.01)	0.08	1.00 (1.00-1.01)	**0.039**
Any relapse	1.11 (0.52-2.37)	0.77	-	-
Number of relapses	0.98(0.65-1.49)	0.95	-	-

**Only variables with a p value of 0.2 in univariable analysis were involved in multivariable analysis*

Results: One-hundred fourteen patients (F/M: 101/13) were included in the study. The mean age at diagnosis, median symptom duration at baseline visit and mean follow-up duration were 35.3±13.3 years, 12 (0-360) months and 76.9 ± 51.4 months, respectively. Median VDI score was 4 (1-8) and median TADS score was 7 (1-15) at baseline assessment. At the end of the follow-up median VDI score was 5.0 (1-17) and median TADS score was 8.0 (1-19). Median ΔTADS was 1 (0-9) and ΔVDI was 1 (0-11). The median number of disease-related items were higher in TADS scoring (8 items vs 4 items). At least 1 new corticosteroid-related damage item occured in 35 patients (31%) (Figure 1). Age at symptom onset and cumulative CS doses were predictor factors for higher VDI score (≥5) in multivariate logistic regression analysis. Also age at symptom onset and disease duration were associated with increase in TADS (≥8). Gender and any relapse or number of relapses were not found to be associated with damage scores (Table 1).

Conclusion: In Takayasu arteritis, detecting the disease- and treatment-related part of damage must be considered while monitoring the disease. VDI seems to be predominantly evaluating the treatment-related damage, whereas TADS provides more detailed information on disease-related damage. Older age at symptom onset, disease duration and cumulative CS dose were associated with higher damage scores. Interestingly, the relapse frequency did not influence the damage level in our routine-follow-up of TAK patients.

Disclosure: S. Kaymaz-Tahra, None; **F. Alibaz-Oner**, None; **H. Direskeneli**, None.

Abstract Number: 0770

Involvement of Iliofemoral and Axillary Arteries in PET-CT May Be Associated with Atherosclerotic Risk Factors in Takayasu's Arteritis

Sema Kaymaz-Tahra,[1] Salih Ozguven,[2] Ali Ugur Unal,[3] Fatma Alibaz-Oner,[4] Tunc Ones,[2] Tanju Yusuf Erdil,[2] and Haner Direskeneli[5], [1]Marmara University School of Medicine, Division of Rheumatology, Istanbul, Istanbul, Turkey, [2]Marmara University Faculty of Medicine, Nuclear Medicine, Istanbul, Turkey, [3]Marmara University Faculty of Medicine, Rheumatology, Istanbul, Turkey, [4]Marmara University Faculty of Medicine,Department of Rheumatology,Istanbul,Turkey, Istanbul, Turkey, [5]Marmara University, School of Medicine, Division of Rheumatology, Istanbul, Turkey

SESSION INFORMATION

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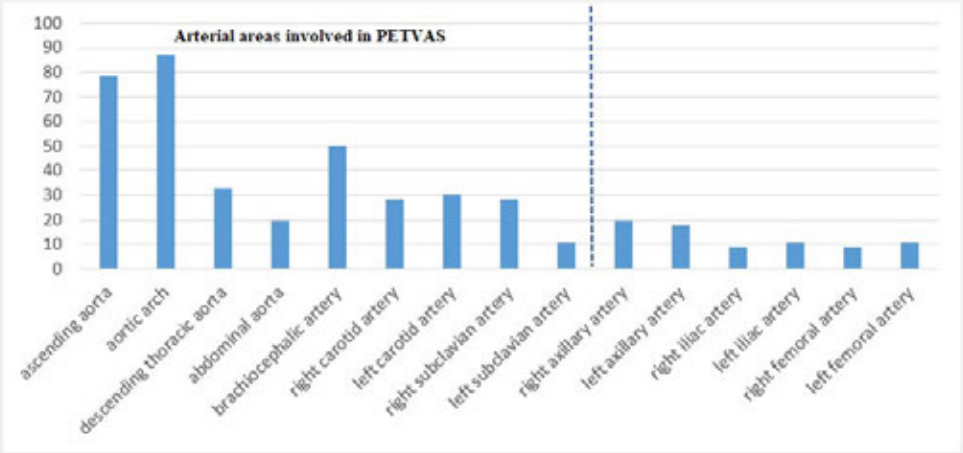
Background/Purpose: FDG-PET-CT is recommended as one of the imaging modalities for the diagnosis and monitoring of primary large-vessel vasculitis (LVV), such as Takayasu's arteritis (TAK). Interpretation of FDG uptake is based on the principle of determining the inflammatory metabolic activity in the vessel wall in LVV. However, vascular uptake due to atherosclerosis may be a contributing factor in PET-CT assessment. In this study we aimed to evaluate the characteristics of patients with and without involvement of arteries other than the 9 arteries used for assessing PET Vascular Activity Score (PETVAS), which is developed to determine LVV activity in most-commonly involved arterial areas.

Methods: Patients fulfilling ACR1990 classification criteria for TAK and underwent PET-CT imaging were evaluated retrospectively. Demographic and clinical data were collected from patients' charts. Traditional cardiovascular risk factors: diabetes, hypertension, hyperlipidemia, smoking history and body mass index (BMI) were evaluated. Nine arterial areas used for assessing PETVAS were ascending aorta, aortic arch, descending aorta, abdominal aorta, right and left carotid arteries, innominate artery, right and left subclavian arteries, as originally suggested. Bilateral axillary arteries and iliofemoral arteries were evaluated as atypical (extra-PETVAS) involvement.

Table1. Cardiovascular risk factors in patients with and without atypical arterial involvement

	Patients with involvement in only PETVAS arteries (n=21)	Patients with atypical arterial involvement (n=10)	p value
Age, years	33.8±9.6	51.3±16.6	**0.008**
Diabetes, n (%)	1 (5)	1 (10)	0.57
Hypertension, n (%)	7 (35)	6 (60)	0.25
Hyperlipidemia, n (%)	3 (15)	5 (50)	0.07
Smoking, n (%)	5 (25)	6 (60)	0.10
BMI, kg/m²	22.8±3.6	23.1±3.9	0.72

Figure 1. Distribution of vascular FDG uptake in Takayasu's arteritis patients



Results: 46 imagings of 34 patients (F/M:28/6) were evaluated. Mean disease duration was 9.3 ±6.5 years and mean age was 40.5± 15.1 years. In the majority of patients aortic arch (87%) was involved followed by ascending aorta (78%) and brachiocephalic artery (50%)(Figure 1). At least one arterial area was involved in 43 images. In 28% of these imagings (12/43), a PET involvement of an artery other than the arteries used for assessing PETVAS, were observed. The mean age of this group was higher than the rest of the group (51.0±16.6 vs 35.8±11.9 years, p=0.01). The number of involved arterial areas (8.5±4.0 vs 3.2±1.5, p=0.000) and total PETVAS scores (10 (2-27) vs 4 (1-17), p=0.013) were higher in atypical arterial involvement group. These patients were also more likely to have the cardiovascular risk factors (Table 1). Patients who had at least 2 cardiovascular risk factors had atypical arterial involvement more frequently (60% (6/10) vs 19% (4/21), p=0.03).

Conclusion: Patients with atypical arterial involvements in PET-CT may have increased atherosclerotic risk factors. These patients had more extended arterial involvement, implying that chronic vascular inflammation may be enhanced by atherosclerosis. Our results suggest that anti-atherosclerotic approaches should be implemented more vigourously in TAK patients.

Disclosure: S. Kaymaz-Tahra, None; **S. Ozguven**, None; **A. Unal**, None; **F. Alibaz-Oner**, None; **T. Ones**, None; **T. Erdil**, None; **H. Direskeneli**, None.

Abstract Number: 0771

Von Willebrand Factor Is Localized in the Extravascular Tissue of Patients with Juvenile Scleroderma

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Von Willebrand Factor (VWF) is a glycoprotein synthesized in endothelial cells and megakaryocytes that has an essential role in primary hemostasis. There is increasing evidence indicating that VWF is involved in inflammation and may play a role in the pathogenesis of fibrosing and cutaneous inflammatory conditions. Our objective was to study the role of VWF in the pathogenesis of skin manifestations of patients with Juvenile Scleroderma (JScl) compared to those with Juvenile Dermatomyositis (JDM). We hypothesize that patients with JScl have increased VWF expression in the extravascular tissue as compared to those with JDM. Since JScl patients have increased collagen deposition in the subcutaneous matrix, and VWF binds collagen, we also hypothesize that VWF colocalize with collagen in the subcutaneous matrix

Methods: We examined 11 skin biopsies from 4 patients with systemic sclerosis (SSc), 3 with localized scleroderma (LS) and 4 with JDM. Double immunofluorescence staining was performed in each tissue with antibodies against vWF and collagens type I and III. DAPI (4′, 6-diamidino-2-phenylindole) was also used for counterstaining of inflammatory cells. Tissue staining patterns were compared between groups

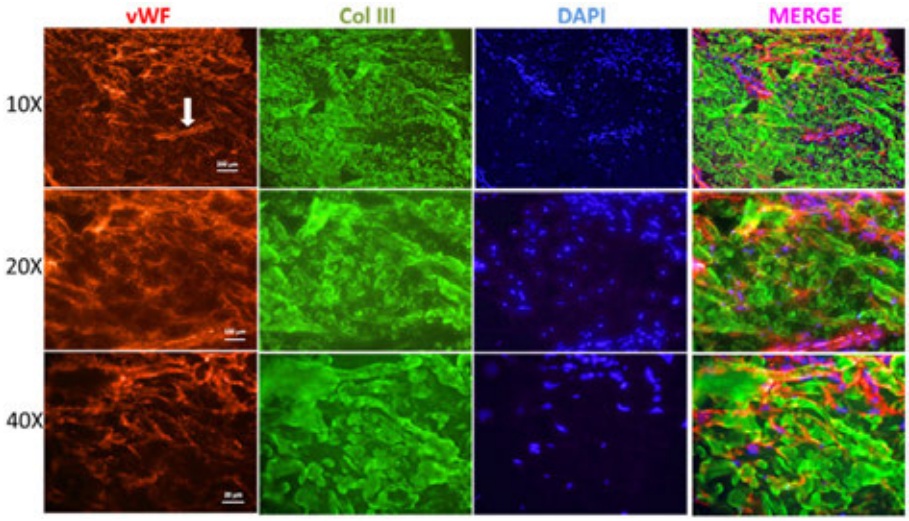

Figure 1. Double Immunofluorescence staining for VWF and collagen III in the skin of a patient with diffuse SSc. Cuts of the reticular dermis are shown at different magnifications. There is evidence of increased collagen expression (green) throughout the reticular dermis that diffusely co-localize with increased expression of VWF (red). Vessels (arrow) stain at higher intensity due to the presence of VWF in the subendothelium. There is also a superficial and deep perivascular inflammatory cell infiltrate (blue) co-localizing with VWF in areas of higher VWF expression.

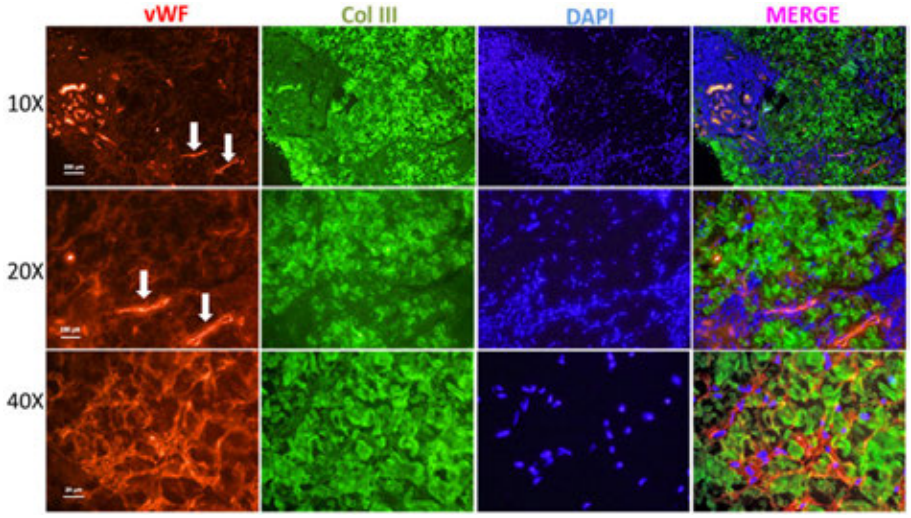

Figure 2. Double Immunofluorescence staining for VWF and collagen III in the skin of a patient with LS. Cuts of the reticular dermis are shown at different magnifications. There is increased collagen expression (green) that co-localizes with VWF (red). Vessels (arrow) stain at higher intensity due to the presence of VWF in the subendothelium. Superficial and deep perivascular, and interstitial inflammatory cell infiltrate is also found (blue) co-localizing with VWF in areas of higher VWF expression.

Results: Biopsies were obtained from the upper extremity of 10 females and the lower extremity of 1 male. Mean age and median disease duration from the first presenting symptom at time of biopsy was 8.8 years (SD 4.5) and 7 months (IQR 3-8), respectively. Seven patients had elevated levels of VWF in serum around time of biopsy (median 221%, IQR 101-282). All but 1 biopsy was performed prior to initiation of immunosuppressive therapy. Immunofluorescence staining showed a superficial and deep perivascular inflammatory cell infiltrate that co-localized with VWF in all tissues. There was expression of VWF in the extravascular tissue of patients with JScl co-localizing with collagen III in the reticular dermis (Figures 1 and 2). In comparison, VWF expression did not co-localize with collagen in the dermis of patients with JDM (Figure 3). Patients with SSc had higher expression of VWF as compared to patients with LS

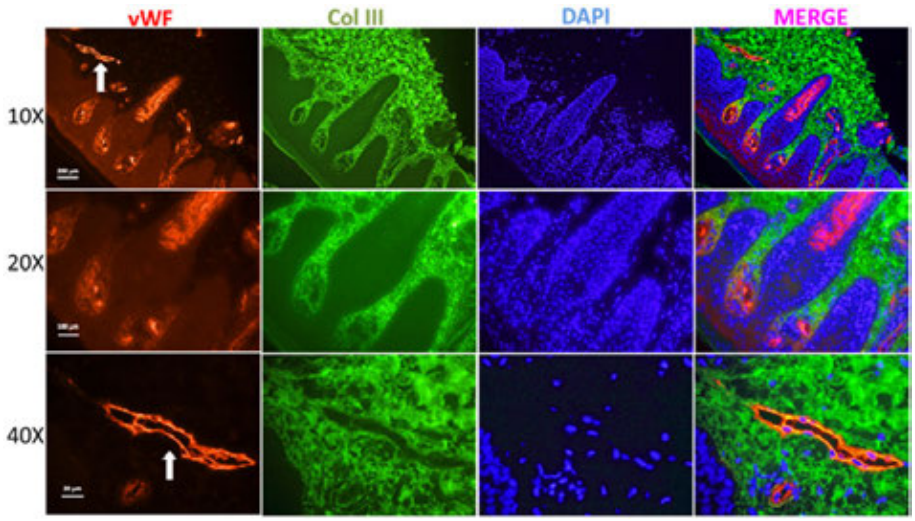

Figure 3. Double Immunofluorescence staining for VWF and collagen III in the skin of a patient with JDM. Cuts of the reticular and papillary dermis are shown at different magnifications. Expression of collagen III (green) is seen in the reticular dermis without co-localizing with VWF (red). Vessels (arrow) stain at higher intensity due to the presence of VWF in the subendothelium. There is an inflammatory infiltrate at the dermal papillae and at the periphery of the vessels that co-localizes with VWF.

Conclusion: VWF may participate in the pathogenesis of cutaneous inflammatory conditions. We have demonstrated that VWF co-localizes with cellular inflammatory infiltrates in the perivascular areas and in the dermis of patients with JScl and JDM. We additionally speculate that VWF may participate in the pathogenesis of fibrosing skin diseases based on evidence of increased extravascular expression in the tissue of patients with JScl (vs. JDM), and its co-localization with collagen. VWF expression intensity in the dermis of JScl patients may relate to extent of disease (SSc vs. LS)

Disclosure: N. Vasquez-Canizares, None; **B. Agarwal**, None; **T. Rubinstein**, None; **D. Wahezi**, None; **M. Reyes Gil**, None.

Abstract Number: 0772

The Study of the Novel G87V Mutation in the *TNFRSF1A* Gene Identified in a Family with TNF Receptor-Associated Periodic Syndrome (TRAPS)

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

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Background/Purpose: TNF Receptor-Associated Periodic Syndrome (TRAPS) is one of the autoinflammatory diseases. TRAPS is caused by heterozygous mutations in *the TNFRSF1A* gene. Although more than 100 *TNFRSF1A* mutations have been reported, only a few mutations such as T79M have been shown as TRAPS mutations. Previous studies suggested that mutant TNFR1 accumulates in the endoplasmic reticulum (ER), resulting in inflammatory responses owing to excessive ER stress. Reflecting the mechanism, the cell surface expression of T79M TNFR1 has been previously shown to be decreased. Recently, we have identified two TRAPS patients with a novel G87V mutation. In this study, we examined the effects of the novel G87V mutation using a cell model by comparing with the T79M mutation and low-penetrant mutations (R121Q, T90I).

Methods: Wild-type (WT) or mutant *TNFRSF1A* (G87V, T79M, R121Q, T90I) constructs were transfected into HEK-293 cells. The cell surface and intracellular expression levels were determined by flow cytometry. To examine the effect of G87V mutation in the patients, we measured the mitochondrial reactive oxygen species (ROS) in the peripheral blood mononuclear cells (PBMCs) of the patients and healthy donors. To evaluate the susceptibility to various inflammatory stimuli, PBMCs from TRAPS patients and healthy donors were treated with Toll-like receptor (TLR) ligands. Cytokine and chemokine profiles in the supernatant were determined by the Milliplex Human Cytokine/chemokine magnetic bead premixed 29-plex kit.

Results: The cell surface expression of TNFR1 was decreased in the G87V and T79M mutant cells compared to WT TNFR1-transfected cells. In contrast, the R92Q and T90I mutations did not suppress the cell surface expression of TNFR1. Mitochondrial ROS levels were increased in both monocytes and lymphocytes from TRAPS patients compared to those in cells from healthy individuals. In cytokine assay, PBMCs from the TRAPS patients tended to produce a larger amount of IL-6 in response to a low concentration (0.1 ng/ml) of LPS (TRAPS patient 1973.0 ± 923.4 pg/ml vs. healthy individual 46.9 ± 25.2 pg/ml). FSL-1 (TLR2/6 ligand) stimulation enhanced IL-8 production in the TRAPS PBMCs compared to that in control PBMCs (TRAPS patient 6604.8 ± 1325.0 pg/ml vs. healthy individual 3777.2 ± 2104.2 pg/ml, $p< 0.05$). Additionally, we found increased production of GM-CSF in response to LPS in the TRAPS PBMCs (TRAPS patient 45.6 ± 21.4 pg/ml vs. healthy individual 17.4 ± 10.9 pg/ml, $p< 0.05$). However, the secretion of IL-1α, IL-1β, and TNF in the TRAPS PBMCs was not increased.

Conclusion: The G87V TNFR1 was not expressed on the cell surface, similar to the pathogenic T79M mutation. The TLR2/6 ligand and cytokines (IL-8 and GM-CSF) are suggested to be involved in the pathophysiological mechanism underlying TRAPS. Our findings obtained from patients harboring unique mutations provide novel insight for better understanding of the inflammatory responses of TRAPS.

Disclosure: S. Tsuji, Chugai Pharmaceutical Co., Ltd., 2, Glaxo Smith Kline K.K., 2; **H. Matsuzaki**, None; **M. Iseki**, None; **A. Nagasu**, Chugai Pharmaceutical Co., Ltd., 2, Glaxo Smith Kline K.K., 2; **H. Hirano**, Chugai Pharmaceutical Co., Ltd., 2, Glaxo Smith Kline K.K., 2; **K. Ishihara**, None; **N. Ueda**, None; **Y. Honda**, None; **T. Horiuchi**, None; **R. Nishikomori**, None; **Y. Morita**, Chugai Pharmaceutical Co., Ltd., 2, Glaxo Smith Kline K.K., 2; **T. Mukai**, Chugai Pharmaceutical Co., Ltd., 2, Glaxo Smith Kline K.K., 2.

Abstract Number: 0773

Chondrocytes Influence Fibroblast-like Synoviocytes from Patients with Juvenile Idiopathic Arthritis, Through the Abrogation of TGFβ Signaling, to Delay Cell Differentiation and Maturation

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SESSION INFORMATION

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Background/Purpose: Progression of Juvenile Idiopathic Arthritis (JIA) can lead to growth disturbances in affected joints. Fibroblast-like synoviocytes (FLS) play a key role in the pathogenesis of JIA; however, the mechanisms of communication between FLS and growth plate chondrocytes is not well described. We have previously shown that JIA FLS overexpress BMP4, which promotes chondrocyte hypertrophy during endochondral bone formation (EBF) [1,2]. We examined the influence of chondrocytes (Ch) on diseased FLS to establish a possible mechanism for the bony overgrowth seen in JIA.

Methods: RNA was collected from three control FLS (CFLS) and JIA FLS (JFLS) cell lines cultured in their respective media at 6 and 24 hours. Concurrently, RNA was collected from three CFLS and JFLS cell lines cultured in conditioned media from Ch (CFLS-Ch and JFLS-Ch). Clariom S microarray was performed and log ratios of fold change over time calculated using linear expression.

Results: JFLS favor TGFβ signaling via an increase in Smad2 expression over BMP related genes (BMPR1a and BMP2) when compared to CFLS (Fig 1A). When exposed to chondrocyte-conditioned media, CFLS-Ch downregulate BMP-related genes (Smad5, Smad7, BMPR1b, BMP2, and GDF5) compared to untreated CFLS (Fig 1B). TGFβ-induced gene is significantly downregulated in JFLS-Ch compared to untreated JFLS (Fig 1C). Untreated JFLS overexpress genes related to proliferating/prehypertrophic chondrocytes (MMP9, MMP12, PCNA) than genes expressed during hypertrophy (VEGFA and SPP1) (Fig 2A). Both CFLS-Ch and JFLS-Ch express genes of chondroprogenitor

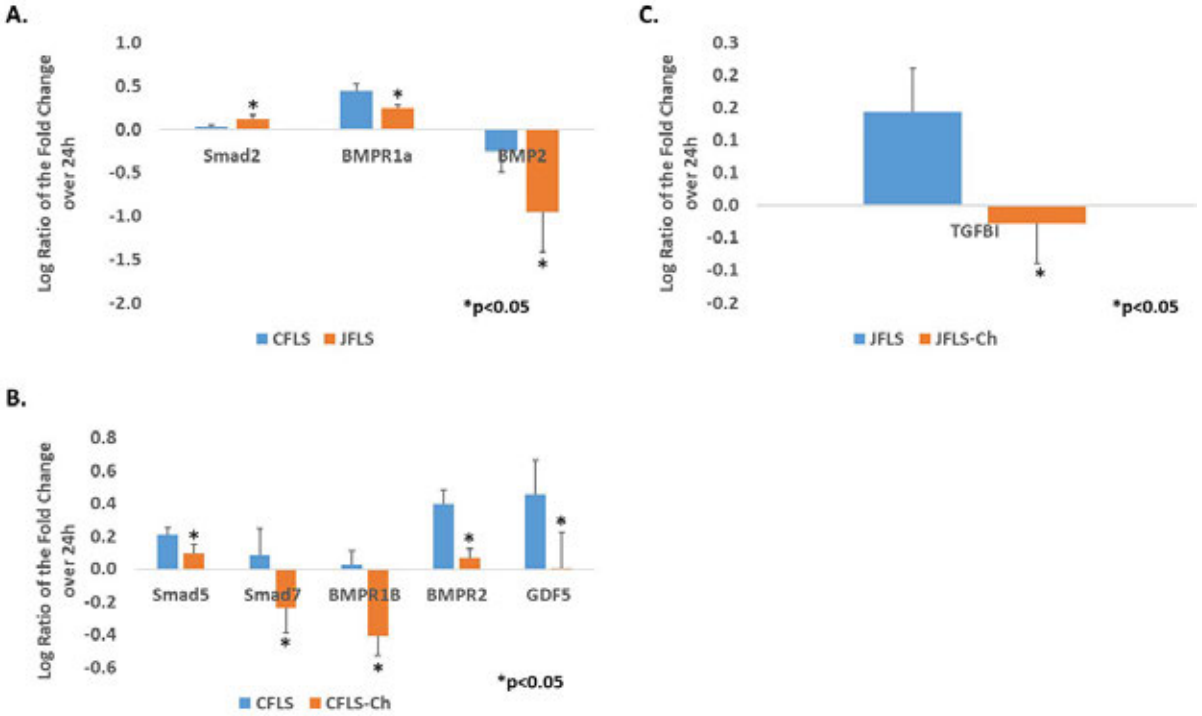

Figure 1. Log ratio of fold change in gene expression of TGFbeta/BMP genes over 24 hours. A. untreated control FLS (CFLS) and JIA FLS (JFLS). B. untreated CFLS compared to CFLS exposed to chondrocyte conditioned media (CFLS-Ch). C. untreated JFLS compared to JFLS exposed to chondrocyte conditioned media (JFLS-Ch) (*p-value<0.05)

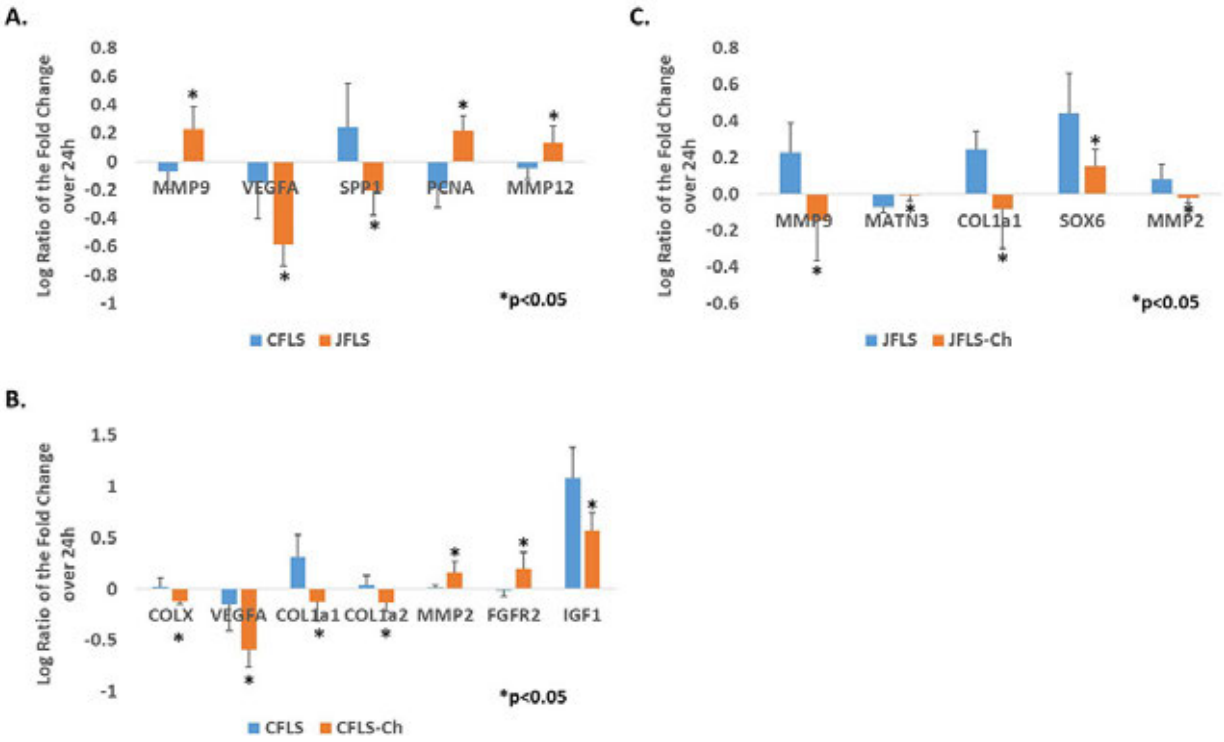

Figure 2. Log ratio of fold change in gene expression of cell differentiation/maturation over 24 hours. A. untreated control FLS (CFLS) and JIA FLS (JFLS). B. untreated CFLS compared to CFLS exposed to chondrocyte conditioned media (CFLS-Ch). C. untreated JFLS compared to JFLS exposed to chondrocyte conditioned media (JFLS-Ch) (*p-value<0.05)

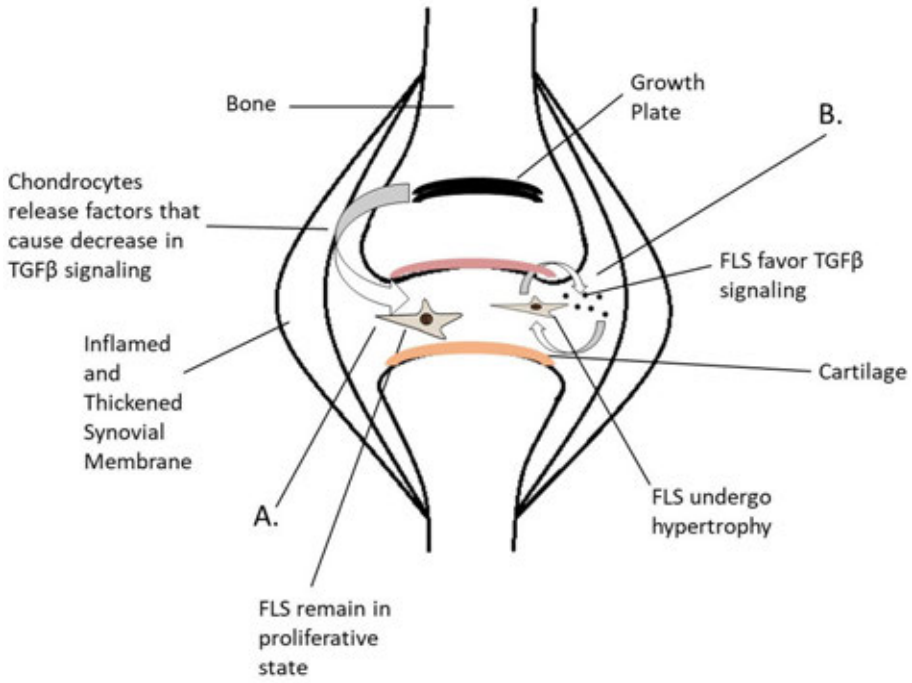

Figure 3. Ch delay JFLS maturation. A. Ch influence JFLS to downregulate TGFβ-related gene expression, causing these cells to remain in an undifferentiated, proliferative state. B. JFLS, without the influence of Ch, favor TGFβ signaling and express genes related to hypertrophy, suggesting these cells play a central role in bony overgrowth.

cells (MMP2, FGFR2 in CFLS and MATN3 in JFLS) as opposed to genes of prehypertrophic/hypertrophic Ch (COLX, VEGFA, COL1, IGF1 in CFLS and MMP9, COL1, SOX6, MMP2 in JFLS) (Fig 2B and 2C).

Conclusion: While untreated JFLS favor TGFβ signaling via increases in Smad2 expression, JFLS-Ch have a reduction in TGFβ signaling through TGFBI, a gene induced by TGFβ ligands with a role in EBF and Ch maturation [3]. Ch influencing JFLS to abrogate TGFβ signaling leads JFLS-Ch to express markers of chondroprogenitor cells as opposed to markers that promote chondrocyte hypertrophy. Ch may have mechanisms to prevent JFLS from influencing the growth plate Ch to undergo EBF. Untreated JFLS express genes related to chondrocyte hypertrophy and proliferation, suggesting that JFLS may play a direct role in the growth discrepancies seen in JIA (Fig 3).

References:

1. Brescia, A.C., et al., *The role of transforming growth factor beta signaling in fibroblast-like synoviocytes from patients with oligoarticular juvenile idiopathic arthritis: dysregulation of transforming growth factor beta signaling, including overexpression of bone morphogenetic protein 4, may lead to a chondrocyte phenotype and may contribute to bony hypertrophy.* Arthritis Rheumatol. **66**(5): p. 1352-62.
2. Chen, G., Deng, C., & Li, Y. *TGF-β and BMP Signaling in Osteoblast Differentiation and Bone Formation.* International Journal of Biological Sciences*.* **8**(2), 272-288.
3. Lee, JM, et al., *Tgfbi deficiency leads to a reduction in skeletal size and degradation of the bone matrix.* Calcif Tissue Int. (1):56-64.

Disclosure: M. Simonds, None; **A. Schlefman**, None; **S. McCahan**, None; **K. Sullivan**, None; **C. Rose**, None; **A. Brescia**, None.

Abstract Number: 0774

Identical T Cell Clones Identified over Time in the Joints of Oligoarticular Juvenile Idiopathic Arthritis Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Oligoarticular juvenile idiopathic arthritis (oligo JIA) is characterized by arthritis in a few joints (fewer than 5) with recurrent flares of inflammation, often in the same joint distribution. The mechanisms driving site-specific inflammation in oligo JIA remain unknown. Previous evaluations of the T cell receptor beta (TCRB) repertoire in oligo JIA patients revealed clonotypic expansion among $CD4^+$ effector and regulatory T cell populations obtained from the synovial fluid (SF). We aimed to further delineate the dynamics of the T cell repertoire in the arthritic joints of oligo JIA patients longitudinally.

Methods: SF samples were collected from 3 oligo JIA patients, defined by ILAR criteria, at 2 timepoints. Serial samples were taken from the same affected joint in a given patient. Peripheral blood (PB) from 7 healthy donors was also collected. DNA was extracted from sorted regulatory ($CD4^+CD25^+CD127^{lo}$, Treg), effector ($CD4^+CD25^-$, Teff), and $CD8^+$ T cells. The TCRB complementarity determining region 3 (CDR3) was amplified by multiplex PCR and sequenced using the Illumina HiSeq platform (Adaptive Biotechnologies). Data was analyzed with VDJtools 1.2.1 and R 3.5.1.

Results: 3 oligo JIA patients (1 male and 2 females) with an average age of 6.4 years were studied. SF was collected from the knee joint in all cases. At baseline (T1), no patient was treated with immunosuppressive medications; however, at the second timepoint (T2), all were taking disease-modifying antirheumatic drugs. The SF sample at T2 was on average 17.3 months after the sample at T1. The SF Treg, Teff, and $CD8^+$ TCRB repertoires were more clonal than those of the respective T cell population in the PB of controls. There was no substantial variation over time in the clonality of Treg, Teff, and $CD8^+$ T cell populations from serial SF samples. In an individual patient, there was overlap in the amino acid sequences of the TCRB CDR3 at T1 and T2: on average, 18%, 19% and 8% of the clonotypes were the same at T1 and T2, respectively for Treg, Teff, and $CD8^+$ T cell repertoires. TCR clones that reoccurred over time tended to be more clonally expanded than TCR clones that occurred at only one timepoint, with frequencies of shared clones being 2-, 3-, and 5-fold larger on average, respectively in Treg, Teff and CD8+ T cells. Sharing of clones across patients was identified more frequently in Treg and $CD8^+$ T cell than Teff cells.

Conclusion: Flares of arthritis in oligo JIA were characterized by resurgence of the same TCR clones longitudinally. There was also sharing of TCR clonotypes in Treg and $CD8^+$ T cells across oligo JIA patients. These findings suggest that pathogenic clones, potentially recognizing similar antigens, may persist in the joints of oligo JIA patients and drive disease over time. While recurring clones may be recruited to the joint with each flare, the extent of repertoire overlap suggests a resident phenotype. Further work is ongoing to characterize the physicochemical properties of shared and clonally expanded clones, and to determine whether they are resident in the affected joints.

Disclosure: A. Jule, None; **K. Hoyt**, None; **M. Chang**, None; **F. Dedeoglu**, None; **M. Hazen**, None; **P. Nigrovic**, None; **L. Henderson**, None.

Abstract Number: 0775

Cutaneous Gene Expression Signatures in Juvenile Myositis Reveal a Prominent IFN Signature in Lesional Skin

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever
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Background/Purpose: Skin inflammation can herald systemic disease manifestations and disease chronicity in juvenile myositis (JM), yet we lack an understanding of the pathogenic mechanisms driving skin inflammation in JM. The objectives of this study were to 1) define transcriptional signatures and biological networks in JM lesional skin, and 2) identify key genes and pathways that differentiate skin disease in JM from childhood-onset SLE (cSLE).

Methods: With IRB approval, we identified JM and cSLE patients who had a skin biopsy performed at either the University of Michigan or Lurie Children's Hospital of Chicago and verified diagnosis through chart review of clinical

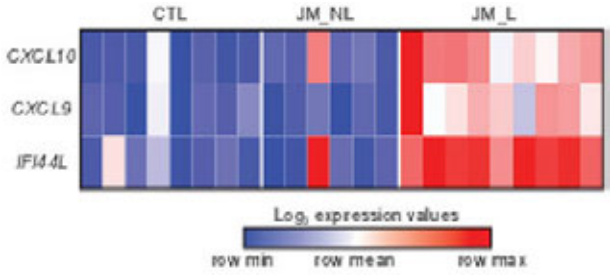

Figure 1. Top three differentially expressed genes in JM lesional skin compared to control and JM non-lesional skin

findings, labs, imaging and histopathology. We then isolated RNA from formalin-fixed, paraffin-embedded (FFPE) skin biopsy samples of 15 JM (9 lesional, 6 non-lesional), 7 cSLE and 8 control patients (CTL; samples from uninvolved skin removed with nevi excision). Following RNA isolation, we performed microarray analysis using Affymetrix ST 2.1 arrays and significance analysis of microarrays (SAM) to determine differentially expressed genes (DEGs; q-value ≤ 5%) between patient groups, comparing JM lesional (JM_L), JM non-lesional (JM_NL), cSLE and CTL. We utilized Ingenuity Pathway Analysis (IPA) to highlight enriched biological pathways and Genomatix Pathway System (GePS) to characterize regulated genes within biological networks.

Results: In the JM cohort, 2 patients had amyopathic disease, and 2 lacked characteristic skin findings of Gottron's papules, with the remaining patients having a classical JDM presentation. Principal component analysis demonstrated that the 2 patients without characteristic skin findings of JDM clustered with other JM_L patients. Comparison of JM_L to CTL skin revealed 221 DEGs, with all but one upregulated in JM_L. The majority of upregulated genes in JM_L were IFN-sensitive, with *CXCL10*, *CXCL9* and *IFI44L* representing the top three DEGs (FC = 23.2, 13.3, 13.0, q-value = < 0.0001) **(Figure 1)**. IPA revealed IFN signaling as the top canonical pathway and also showed upregulation of antigen presentation, pattern recognition receptors, communication between innate and adaptive immune cells, T cell signaling, the complement system and dendritic cell maturation. The top predicted upstream regulator was IFN alpha (p-value = 7.91×10^{-88}). JM_NL skin had a strikingly different transcriptional signature, both lacking a prominent IFN signal and with downregulation of multiple genes and pathways, including oxidative phosphorylation and protein ubiquitination. JM_L skin shared a highly similar gene expression pattern with cSLE. There were only 28 unique DEGs in JM_L compared to cSLE, whereas cSLE skin had 722 unique DEGs compared to JM_L. Of note, cSLE skin uniquely demonstrated increased expression of IFN gamma relative to CTL.

Conclusion: JM lesional skin demonstrates a striking IFN signature similar to that previously reported in muscle and peripheral blood. Although JM skin has few unique DEGs when compared to cSLE, a lack of upregulated genes specific to cSLE skin may distinguish JM. The origin of the IFN signature in JM skin and its association with clinical phenotype and response to therapy remains to be established.

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Abstract Number: 0776

Genetic Signatures Support Inflammation Driven Fibrosis in Localized Scleroderma

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Background/Purpose: Localized scleroderma (LS) is a progressive autoimmune disease of the skin and underlying tissue that is characterized by an initial inflammatory infiltration which is followed by fibrosis and collagen deposition. When left unchecked LS causes significant functional disability and disfigurement, especially in developing children. Histopathologic review of LS skin biopsies typically shows a stronger inflammatory or fibrotic pattern depending on disease stage. Our goal was to determine the transcriptome within inflammatory vs. fibrotic tissue to identify potential molecular targets using RNA sequencing (RNAseq) compared to histology scoring of inflammatory infiltrates vs. collagen deposition/fibrosis. Differentially expressed genes (DEGs) in LS patients were compared to skin histopathological features to determine correlation.

Methods: RNAseq was performed on paraffin-embedded skin (n=15 LS, n=2 pediatric healthy) using the Illumina HTS and TrueSeq Access library preparation. Paired-end RNAseq data was aligned using STAR and analyzed for DEGs using DESeq2. Genes were analyzed using DEG cutoffs of log fold change > ±2.0, adjusted $p < 0.05$, and a false discovery rate (FDR) cutoff of < 0.05 for Ingenuity Pathway Analysis (IPA) and enrichment software (GSEA©). Skin biopsies were reviewed by 2 blinded pathologists who determined 3 areas of inflammatory infiltrate per skin layer (papillary dermis, upper and lower reticular dermis) and counted total inflammatory cells (lymphocytes and plasma cells) per infiltrate, which determined a categorical inflammation score. Similar scoring was also developed for fibrosis, where 3 areas were chosen per skin layer and 3 measurements of collagen bundle thickness were taken. The average of these measurements was used for fibrotic scoring. Spearman's correlation between genes of interest and histology scoring was performed using GraphPad Prism.

Results: The degree of inflammatory cell infiltrate significantly correlated with both inflammatory (IFNγ, immunoglobulin, and T-cell activation, rs > ±0.5, $p < 0.01$) and fibrotic (IL-12 mediated signaling, and DNA damage response) (rs > ±0.5, $p < 0.05$) genes (Table 1). Collagen thickness did not correlate with typical fibrotic genes, but did correlate (rs > ±0.4, $p < 0.05$) with upregulated inflammatory genes, such as those associated with interferon signaling and T-cell activation (Table 1). Further support of IFN-related signaling, T lymphocyte activation, and cytokine production was demonstrated with IPA.

Conclusion: The identified immune pathways and genes corresponding with the LS skin inflammatory infiltrate indicate a unique genetic signature present during active disease with moderate-severe lymphoplasmacytic infiltrate and collagen thickness. This may indicate that fibrosis occurring in later stages of LS is an inflammation-driven process. Further investigation into the relationship and functions of these genes is underway and will aid in advancing treatment options for LS patients.

Table 1: Correlation Between Histology Features and Differentially Expressed Genes		
Total Inflammatory Cell Correlation	**r_s**	**p**
Inflammatory Genes		
CXCL9	0.62	0.0085
CXCL10	0.68	0.0026
CXCL11	0.83	<0.0001
IGHG1	0.74	0.0007
IGHG3	0.75	0.0005
IGHM	0.65	0.0046
AGER	0.61	0.0095
KLRC4-KLRK1	0.76	0.0004
TNC	0.69	0.0021
ELANE	-0.65	0.0049
Fibrotic Genes		
EOMES	0.59	0.0222
DPP4	0.61	0.0178
PCNA	0.56	0.0310
MDM2	0.79	0.0008
TP53INP1	0.88	<0.0001
USP14	0.53	0.0454
Average Collagen Thickness Correlation	**r_s**	**p**
Inflammatory Genes		
MX1	0.49	0.045
IFI27	0.55	0.023
OAS3	0.49	0.045
PIM1	0.50	0.038
PTX3	-0.51	0.036
TNFSF9	0.57	0.021
P2RX7	0.50	0.043
SERPINB8	0.49	0.047
Fibrotic Genes		
	Not Significant	Not Significant

Disclosure: C. Schutt, None; **E. Mirizio**, None; **C. Salgado**, None; **M. Reyes-Mugica**, None; **K. Schollaert**, None; **K. Torok**, None.

Abstract Number: 0777

Interferon Response Gene Expression Differs in Whole Blood, Peripheral Blood Mononuclear Cells, Monocytes, Dendritic Cells, Neutrophils, and Skin Tissue in Patients with the Autoinflammatory Interferonopathies, CANDLE and SAVI

Jacob Mitchell,[1] Sara Alehashemi,[2] Bernadette Marrero,[3] Yan Huang,[4] Lena Bichell,[5] Gina Montealegre Sanchez,[1] Raphaela Goldbach-Mansky,[2] and Adriana de Jesus[1], [1]Translational Autoinflammatory Disease Section/NIAID/NIH, Bethesda, [2]Translational Autoinflammatory Diseases Section/NIAID/NIH, Bethesda, MD, [3]Computational Systems Biology Section/NIAID/NIH, Bethesda, [4]Translational Autoinflammatory Disease Section/NIAID/NIH, Bethesda, MD, [5]Translational Autoinflammatory Diseases Section/NIAID/NIH, Bethesda

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The disease progression of patients (pts.) with type-I interferon (IFN)-mediated diseases undergoing treatment with JAK1 and JAK2 inhibitors is monitored in part by measuring the transcription of a 28 IFN response gene (IRG) signature in whole blood with Nanostring technology, a 28-gene standardized IFN score is calculated. We sought to determine differences in 28-gene standardized IFN scores and in the patterns of IRG signatures among peripheral blood mononuclear cells (PBMCs), isolated monocytes, dendritic cells, neutrophils, and skin biopsies in the Type-I IFN-mediated diseases CANDLE (chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperatures) and SAVI (STING-associated vasculopathy with onset in infancy) compared to whole blood IRG signatures.

Methods: RNA was extracted from pt. and healthy control whole blood, PBMCs, monocytes, neutrophils, dendritic cells (DC), and skin biopsies. After cells isolation by Ficoll (PBMC), CD14 (monocytes) or CD123 (DC) magnetic bead isolation and density gradient separation with red blood cell lysis (neutrophils), RNA was extracted. Transcript counts for 28 IRGs and 4 additional genes were measured with a NanoString instrument, normalized based on the expression of 4 housekeeping genes in the sample, and scored as the sum of the 28-genes' z-scores compared to expression in the same cells or tissues in a cohort of healthy controls.

Results: Both CANDLE (n=4) and SAVI (n=5) patients have significantly greater 28-gene standardized IFN scores in whole blood, PBMCs than healthy controls (n=10). Higher IFN scores were seen in SAVI PBMCs as compared to SAVI whole blood, while CANDLE PBMC IFN scores were not different compared to CANDLE whole blood.SAVI PBMCs had significantly higher 28-gene IFN scores than CANDLE PBMCs (2003 ±2301 vs. 352.3 ±285.5, p=0.0082). In addition, SAVI PBMCs transcribed higher levels of *IFNA2* (7068 ±14434 vs. 3.158 ±0.657) and *IFNB1*(8452±16468 vs. 2.119 ±0.619) than PBMCs from CANDLE pts., corroborating RNAseq data that demonstrates highest Type-I IFN expression in the monocytes followed by dendritic cells of SAVI pts. One family of 3 patients with SAVI who had a novel STING missense variant had very elevated IFN scores in their PBMCs, while their whole blood IFN score was not considered to be elevated. Nanostring performed on RNA from skin tissue from 3 CANDLE and 3 SAVI pts. demonstrated a distinct distribution of the 28 IRGs in comparison with whole blood, with a relatively higher contribution of *CXCL10*to the 28-gene IFN score.

Conclusion: High expression of Type-I IFNs and IRGs in the PBMCs of SAVI pts. may demonstrate the role of myeloid cells in the amplification of constitutive IFN signaling in SAVI. In addition, pts. with a SAVI phenotype but a negative IRG signature in whole blood may only have an IRG signature in the PBMC fraction. Differences in IRG transcription profiles demonstrate that responses to IFN signaling are not uniform among cell subsets in different Type-I IFN-mediated diseases.

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Disclosure: J. Mitchell, None; **S. Alehashemi**, None; **B. Marrero**, None; **Y. Huang**, None; **L. Bichell**, None; **G. Montealegre Sanchez**, None; **R. Goldbach-Mansky**, None; **A. de Jesus**, None.

Abstract Number: 0778

Multiple Genetic Diagnoses in a Cohort of Patients with Cryopyrin Associated Periodic Syndrome (CAPS)

Sofia Torreggiani,[1] Megha Garg,[2] Sara Alehashemi,[3] Kim johnson,[1] Jenna Wade,[4] Lena Bichell,[4] Magdalena Walkiewicz,[5] Adriana de Jesus,[6] and Raphaela Goldbach-Mansky[3], [1]Translational and Autoinflammatory Diseases Section/NIAID/NIH, Bethesda, MD, [2]Rochester Regional Health, Rochester, NY, [3]Translational Autoinflammatory Diseases Section/NIAID/NIH, Bethesda, MD, [4]Translational Autoinflammatory Diseases Section/NIAID/NIH, Bethesda, [5]Division of Intramural Research (DIR)/NIAID/NIH, Bethesda, MD, [6]Translation Autoinflammatory Diseases Section/NIAID/NIH, Silver Spring, MD

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

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Session Time: 9:00AM–11:00AM

Background/Purpose: Cryopyrin associated periodic syndrome (CAPS) is an autosomal dominant autoinflammatory disease caused by mutations in *NLRP3*. CAPS comprises 3 clinical phenotypes of increasing severity: familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), neonatal onset multisystem inflammatory disease (NOMID). CAPS is characterized by early onset systemic inflammation and neutrophilic urticaria (NOMID, MWS, FCAS), cochlear inflammation with hearing loss (NOMID, MWS), and central nervous system inflammation (NOMID). Although all patients had clinical features of CAPS, we aimed to identify additional Mendelian diagnoses that may explain phenotypic variability not attributable to CAPS.

Methods: CAPS patients and their parents, when available, had whole exome sequencing (WES) performed at the NIAID Centralized Sequencing Initiative (CENSEQ). Chromosomal microarray analysis (CMA) was performed in selected cases. Patients were evaluated for investigation of clinical phenotypic features not associated with CAPS.

Results: Of the 11 CAPS patients analyzed, 4 (36.4%) had a Mendelian genetic diagnosis in addition to CAPS. **Patient 1** is a 10-year-old female with a somatic mutation in *NLRP3* (p.G307C, ~15% mosaicism) and classic NOMID manifestations responsive to anti-IL-1 therapy. She was noted to have developmental delay, upslanting palpebral fissures and sparse eyebrows, which were explained by CMA findings compatible with 12q21.2q22 deletion syndrome (1). **Patient 2** is a 10-year-old female with a germline *NLRP3* mutation (p.E304K), clinical features of FCAS/MWS and response to anti IL-1. She presented clinodactyly, scoliosis, and broad great toes. Height was between the 5th and 10th percentile. WES revealed a novel heterozygous variant in *NPR2* (p.M1?), gene associated with autosomal dominant epiphyseal chondrodysplasia (OMIM#615923). **Patient 3** is an 8-year-old female with a

germline *NLRP3* mutation (p.N479K) and a NOMID phenotype, treated with anakinra with resolution of inflammation but no benefit on growth. She presented brachydactyly, a round face and a broad nasal bridge. WES showed a novel heterozygous variant in *FBN1* (p.L2626V), gene associated with several musculoskeletal syndromes, including Marfan syndrome (OMIM#154700), geleophysic dysplasia 2 (OMIM#614185) and Weill-Marchesani syndrome (OMIM#608328). **Patient 4** is a 19-year-old male with a germline mutation in *NLRP3* (p.G326E) and a clinical picture of NOMID, requiring high doses of canakinumab. WES showed a novel heterozygous variant (p.M274R) in *NLRC4* (OMIM#616050).

Conclusion: Of 11 CAPS patients with pathogenic *NLRP3* mutation, 4 had a secondary genetic diagnosis, which explained clinical features that were not attributable to CAPS. Our data suggest that further genetic testing should be considered to explain "phenotypic variability".

Reference:

1. Oliveira R, Pereira C, Melo JB, Mesquita S, Venâncio M, Carreira IM, Saraiva J. 12q21.2q22 deletion: a new patient. Am J Med Genet A. 2015 Aug;167A(8):1877-83.

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Disclosure: S. Torreggiani, None; **M. Garg**, None; **S. Alehashemi**, None; **K. johnson**, None; **J. Wade**, None; **L. Bichell**, None; **M. Walkiewicz**, None; **A. de Jesus**, None; **R. Goldbach-Mansky**, None.

Abstract Number: 0779

The Juvenile Idiopathic Arthritis-Associated IL2RA Haplotype Contains an Intronic Enhancer Whose Function Is Diminished by JIA-Associated Genetic Variants

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: *IL2RA* has been identified as a JIA-associated risk locus using both candidate gene and genetic fine mapping approaches. However, numerous gene expression studies comparing children with active JIA to healthy control children have failed to identify *IL2RA* as a differentially expressed gene. Furthermore, the SNPs used to identify *IL2RA* lie within the first intron of the *IL2RA* gene, not its promoter or coding regions. The risk haplotype is marked by prominent H3K4me1/H3K27ac histone marks, suggesting that genetic risk may be mediated through enhancer function. We therefore sought to confirm whether this region is a functional enhancer and whether the enhancer operates in lymphoid cells, myeloid cells, or both. We also examined the effects of genetic variants on enhancer function at the *IL2RA* locus.

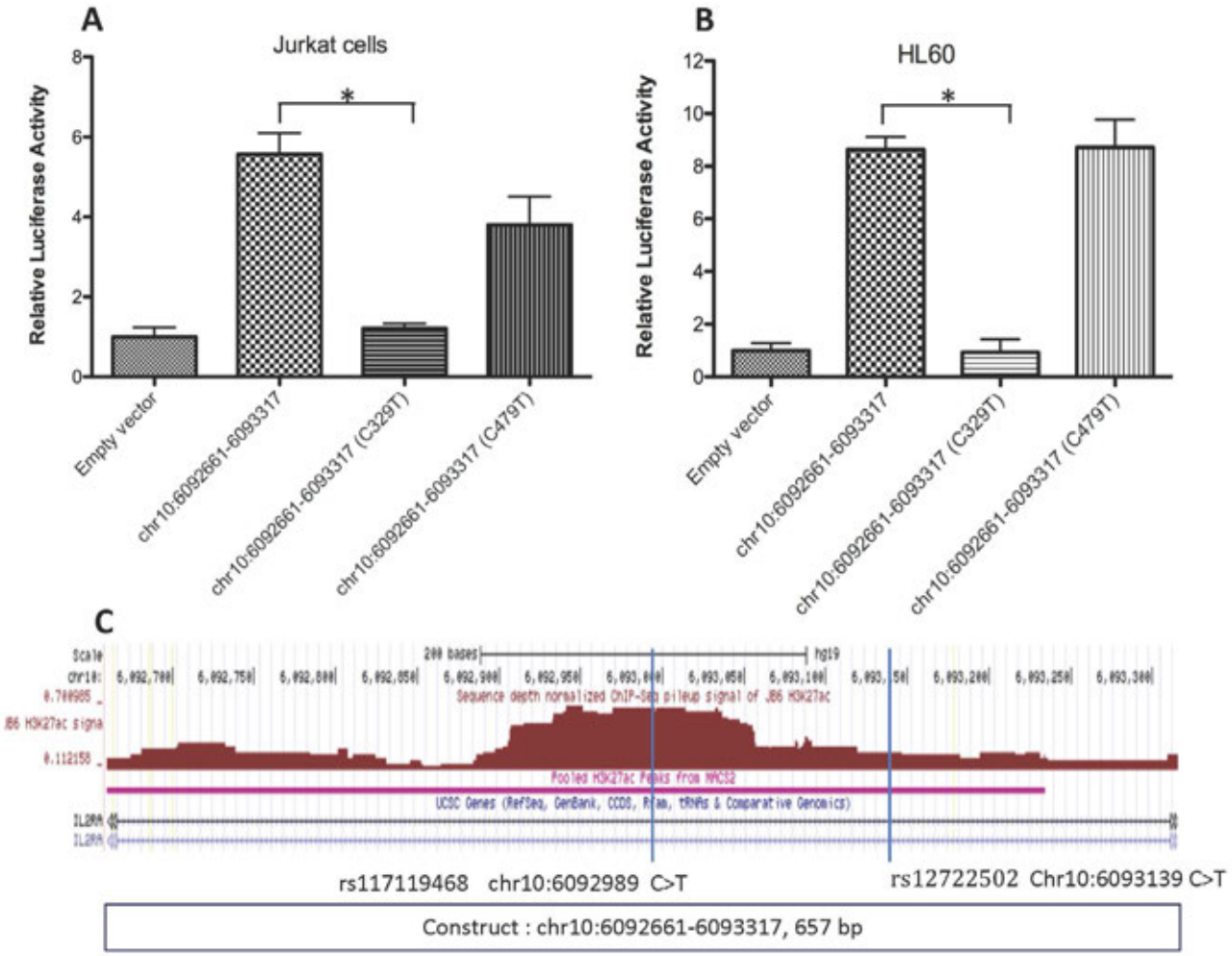

Figure 1. Effects of genetic variants

Methods: We used the pGL4 reporter system to query enhancer effects across a 1,000 bp region within the first intron of the IL2RA gene marked by H3K4me1 and H3K27ac histone marks in both CD4+ T cells and neutrophils. This region is within the linkage disequilbrium block that includes the SNPs used on both candidate gene and genetic fine mapping studies that identified IL2RA as a JIA risk locus. The pGL3 vector contains a minimal SV40 promoter that is, by itself, inefficient at driving luciferase function. We tiled three 500 bp constructs across the region of interest and cloned these constructs into pGL3 vectors, which were then transfected into Jurkat T cells and myeloid HL60. Cells were incubated for 24 hr, after which luciferase production was assessed using standard methods. We repeated these same experiments using constructs containing genetic variants (rs117119468 C- >T and rs12722502 C- >T) that we identified in children with JIA using whole genome sequencing.

Results: Within the H3K4me1/H3K27ac-marked region within the first intron of IL2RA, we observed enhancer activity across a 657 bp region from chr10:6092661 to chr10:6093317 in both Jurkat T cells and HL60 myeloid cells. The reporter constructs enhanced luciferase activity by 5-8 fold in Jurkat T cells (compared with a control vector that contained only the minimal SV40 promoter and the luciferase gene) and 4-6 fold in HL60 cells. A construct carrying a sequence within the first intron of the IL2R Agene that was not marked by the H3K4me1/H23K27ac histone

signature showed no enhancement of luciferase expression compared to background. Constructs containing the JIA-associated rs117119468 C- >T allele abolished the enhancer activity within the IL2R Alocus, while the construct containing the rs12722502 C- >T allele reduced luciferase activity by 30%.

Conclusion: The JIA-associated risk locus, *IL2RA*, contains an intronic enhancer that is active in both lymphoid and myeloid cells. JIA-associated genetic variants identified by WGS attenuate or abolish enhancer activity at this locus. These findings demonstrate the importance of assessing the non-coding functions of JIA risk loci, even where the coding function a specific gene might be plausibly implicated. Our findings also underline the potential importance of rare genetic variants, which may have stronger biological effects than GWAS SNPs, in complex traits like JIA.

Disclosure: K. Jiang, None; **Y. Park**, None; **T. Evan**, None; **T. Liu**, None; **J. Jarvis**, None.

Abstract Number: 0780

Changes in MiR-17-92 Cluster Expression Link Systemic Juvenile Idiopathic Arthritis, Monocyte-to-Macrophage Differentiation, and Interferon Regulation

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: MicroRNAs (miRNAs) are small noncoding RNAs which post-transcriptionally regulate gene expression. The miR-17-92 cluster is well characterized; its overexpression has been found to serve a major oncogenic role in the targeting and downregulation of tumor-suppressive pathways. Our previous work identified several members of the cluster with significantly higher levels in monocytes from patients with active Systemic Juvenile Idiopathic Arthritis (SJIA), a chronic inflammatory disease of childhood. Children with SJIA are at risk for life-threatening complications including Macrophage Activation Syndrome (MAS), an episode of overwhelming inflammation driven by IFNɣ. The objectives of this study were to characterize the regulation of the miR-17-92 cluster, define key targets, and determine the cluster's role in inflammation and SJIA.

Methods: MiRNA levels were examined in THP-1 cells and primary human monocytes over the course of the monocyte to monocyte-derived macrophage (MDM) transition. MiR-17, miR-19a, and miR-20a were overexpressed in CD14+ monocytes for 2 days. Transcriptional profiles were performed using Ampliseq Transcriptome and the Ion Torrent S5 system and analyzed using AltAnalyze. Potential targets of the miR-17-92 cluster were then validated via dual-luciferase reporter assay.

Results: Neither blood monocytes nor fully differentiated THP-1 cells showed significant changes in miR-17-92 levels under standard polarization conditions, including M1, M2a, and M2b conditions, or IL-6 and IL-10 stimulation. The most sizable changes in miR-17-92 levels were found during monocyte to macrophage transition. Interestingly, primary monocytes showed increases in miR-17-92 levels within the first 48 hours of differentiation towards MDM similar to that seen in SJIA monocytes. In contrast, both PMA-differentiated THP1 cells and fully differentiated MDMs showed decreased miR-17-92 compared to undifferentiated monocytic cells. MiR-17-92 was overexpressed

in primary monocytes to model these early transition changes. Genome-wide transcriptional profiling showed an upregulation of genes involved in Type I and II Interferon pathways, including response to interferon-alpha (adjusted p=2.71x10-12) and interferon-gamma (adjusted p=7.81x10-9). Analysis of genes significantly downregulated by miR-17, miR-19a, or miR-20a identified several putative and previously validated miR-17-92 cluster targets, including ATG5, IFRD2, JAK1, PPARG, and PTPN2 which have interferon-regulatory functions. Dual-luciferase reporter assay experiments support that these genes are direct targets of miR-17, miR-19a, and/or miR-20a.

Conclusion: MiR-17-92 demonstrates initial increase followed by subsequent decrease in human monocyte to macrophage differentiation. Overexpression of miR-17-92 upregulates Type I and II interferon pathway genes, and these miRNAs target multiple genes involved in regulating interferon signaling and/or inflammatory response. Taken together, miR-17-92 overexpression in SJIA monocytes may suggest a more differentiated phenotype, and contribute to IFNɣ sensitivity and risk for MAS.

Disclosure: D. Takellapti, None; **X. Niu**, None; **T. Do**, None; **G. Schulert**, Novartis, 5, 8.

Abstract Number: 0781

Is down Syndrome Associated Arthritis (DA) a Distinct Disease from Juvenile Idiopathic Arthritis (JIA)?

Charlene Foley,[1] Achilleas Floudas,[2] Sharon Ansboro,[2] Mary Canavan,[2] Monika Biniecka,[2] Emma Jane MacDermott,[3] Ronan Mullan,[4] Gerry Wilson,[5] Ursula Fearon,[6] and Orla Killeen[7], [1]Great Ormond Street Hospital, London, Ireland, [2]TBSI, Dublin, Ireland, [3]OLCHC, Dublin, Ireland, [4]Tallaght Hospital, Dublin, Ireland, [5]UCD, Dublin, Ireland, [6]TBSI, Dublin, [7]National Centre for Paediatric Rheumatology (NCPR), Our Lady's Children's Hospital Crumlin (OLCHC), Dublin, Ireland

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: Poster Session (Sunday)
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Background/Purpose: Down syndrome associated Arthritis (DA) is 20 times more common than JIA. It is an erosive, polyarticular RF negative arthritis with predominance in the small joints of the hands and wrists. Little is known about the underlying mechanisms that drive DA pathogenesis. We hypothesise that it is a distinct disease from its closest ILAR subtype, polyarticular RF negative JIA (pRF-JIA) given the differences observed in the clinical phenotypes.

Our aims were to compare B cell subsets and T cell cytokine profiles in peripheral blood mononuclear cells (PBMCs); and synovial membrane immunohistochemistry and synovial fibroblast cell (SFC) functionality in children with DA and the ILAR subtype pRF-JIA. We also looked to see if known pRF-JIA susceptibility loci, *HLA-DQB1/HLA-DQA2* (rs7775055) and *PTPN22* (rs6679677) were present in children with DA.

Methods: Multicolour flow cytometry and FlowJo and SPICE software were used to analyse B cell subsets and T cell cytokine expression (IL17a, GMCSF, IFNγ, TNFα) in PBMCs from children with pRF-JIA, DA, T21 and HC, (n = 10 / gp).

Synovial tissue was obtained through ultrasound guided biopsy (DA n = 3; pRF-JIA n = 4) and analysed by immunohistochemistry for CD3 (T cells), CD20 (B cells) and CD68 (macrophages). Vascularity and lining layer hyperplasia were also scored.

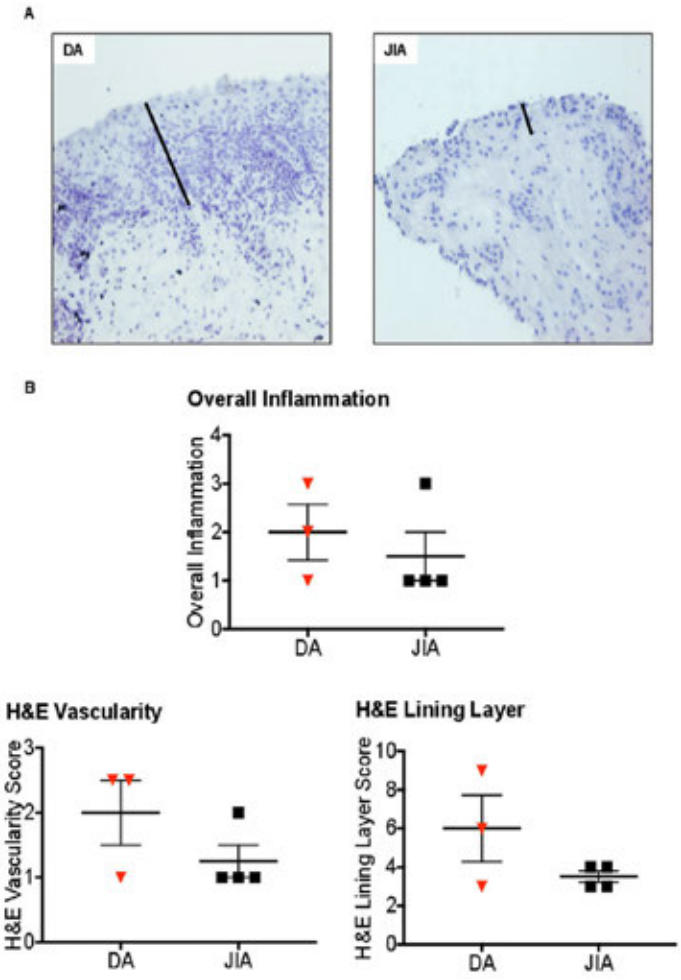
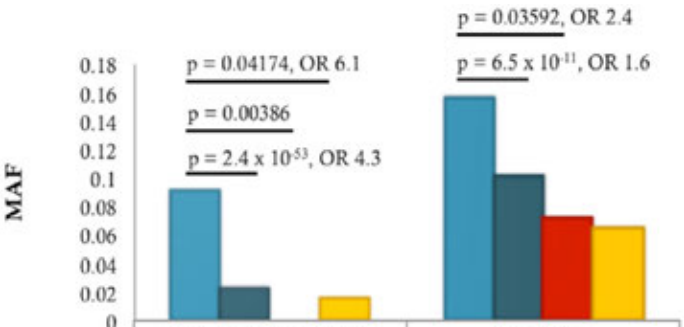


Figure 1. H&E staining of synovial tissue from children with DA and JIA, scored for global inflammation, vascularity and lining layer thickness A. Representative images of synovial tissue from the knee joint of a child with DA and JIA. The black line denotes lining layer. B. Two independent observers performed scoring. Graphs depict results for global inflammation and vascularity, with a score range of 0-3. Lining layer thickness was scored by number of cells thick. Sample size was DA n = 3 and JIA n = 4. Original magnification used was 20 X. Data are presented as mean ± SEM.

DA-SFC and pRF-JIA-SFC migration was assessed by wound repair scratch assays; invasion by Biocoat Matrigel™ Invasion Chambers; and bioenergetic activity using the XFe96-Flux-analyser where oxidative phosphorylation and glycolysis were quantified. Real-time PCR assessed glycolytic gene expression.

The team at the Arthritis Research UK Centre for Genetics and Genomics (Manchester) performed genotyping and analysis of rs7775055 and rs6679677 in DNA from children with pRF-JIA (n = 732), DA (n = 42), T21 (n = 31) and HC (n = 9196).

Results: Flow cytometry analysis revealed that children with DA had a significantly lower number of circulating CD19+CD20+ B cells when compared to children with pRF-JIA and HC. However, they had a greater proportion of memory B cells (CD27+) when compared to children with T21. T cell IFNγ and TNFα production was significantly greater in DA compared to pRF-JIA and HC. Greater T cell polyfunctionality was also observed in children with DA compared to all three comparison groups.



	HLA-DQB1/DQA2	PTPN22
JIA MAF	0.09085	0.1557
HC MAF	0.02251	0.1013
DA MAF	0	0.07143
T21 MAF	0.01613	0.06452

Figure 2. Comparison of MAF for HLA-DQB1/HLA-DQA2 (rs7775055) and PTPN22 (rs6679677) Comparable to the literature, the MAF for HLA-DQB1/HLA-DQA2 (rs7775055) in JIA is significantly greater than HC (p=2.4 x 10-53, OR 4.3). When compared to HC, both T21 and DA have a lower MAF. Results for these cohorts are significantly lower when compared to JIA MAF (p=0.04174 and p=0.00386 respectively). Similarly, for PTPN22 (rs6679677), MAF in JIA is significantly greater than HC (p=6.5 x 10-11, OR 1.6). Again, in both the T21 and DA cohort, MAF is lower compared to HC. DA MAF is significantly lower than JIA MAF (p=0.03592, OR 2.4) for this JIA susceptibility locus.

DA synovial tissue demonstrated greater lining layer hyperplasia (**figure 1**). Median cell thickness in DA was 6 (3-9 cells), compared to 2 (2-4 cells) in pRF-JIA. There was also increased vascularity and inflammatory cell infiltration in DA compared to pRF-JIA.

DA-SFC showed greater migratory and invasive capacity, and increased basal metabolic activity and metabolic gene expression when compared to pRF-JIA-SFC.

The MAF (minor allele frequency) for the pRF-JIA associated variants rs7775055 and rs6679677 were not similar in DA. The minor allele of rs7775055 was absent in DA (p = 0.004). The rs6679677 MAF was significantly different between DA and pRF-JIA, p = 0.036 (**figure 2**).

Conclusion: Significant differences were observed in the immune, histological and genetic profiles of DA and its closest ILAR subtype, pRF-JIA. These differences may help explain the erosive phenotype observed in DA and suggest it may be a distinct disease from JIA.

Disclosure: C. Foley, None; **A. Floudas**, None; **S. Ansboro**, None; **M. Canavan**, None; **M. Biniecka**, None; **E. MacDermott**, None; **R. Mullan**, None; **G. Wilson**, None; **U. Fearon**, None; **O. Killeen**, None.

Abstract Number: 0782

Oligoarticular Juvenile Idiopathic Arthritis Displayed Increased Expression of Co-Inhibitory Receptors Without Signs of T-Cell Exhaustion

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever
Session Type: Poster Session (Sunday)
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Background/Purpose: Activated T cells are involved in the pathogenesis of the synovitis in oligoarticular Juvenile Idiopathic Arthritis (o-JIA). T cell activation is counter-balanced via co-inhibitory receptors (co-IRs) such as CTLA-4, PD-1, LAG-3, and TIM-3. Here we identify the role of co-IRs in the pathogenesis of o-JIA.

Methods: Paired synovial fluid (SF) and plasma, PBMCs and SFMCs, were obtained from o-JIA patients together with clinical data (n=14). Plasma from healthy controls (HC, n=14) and paired SF and plasma from 5 children requiring arthroscopy for non-inflammatory orthopaedic problems (OC, n=5) served as controls. Soluble levels of co-IRs were measured by ELISA and their cellular expression by flow cytometry. Spontaneously differentiated fibroblast-like synoviocytes (FLS) from SFMCs were co-cultured with autologous PBMCs/SFMCs and used as an *ex-vivo* disease models. Functional effects of co-IRs were evaluated via blocking them with checkpoint inhibitors in these *ex-vivo* disease models.

Results: o-JIA patients had increased soluble levels (Figure 1A) and CD3+CD4+CD45RO+ T cell surface expressions of sPD-1, sLAG-3, sTIM-3, but not sCTLA-4 in SF compared with plasma (Figure 1B). Plasma and SF levels of sLAG-3 and TIM-3, but not sPD-1 levels were higher in o-JIA patients compared with controls. (Figure 1A) None of the soluble co-IR levels correlated with disease activity. As CD4 T cell exhaustion is an outcome of continued antigen presentation, we examined if MHC-class II expression was present on these FLS. FLS expressed nearly no MHC-class II molecules in monocultures, but this was readily detected when co-cultured with PBMCs and SFMCs together with an increased Monocyte Chemoattractant Protein-1 (MCP-1) production. (Figure 2A) Only anti-LAG3 antibodies significantly increased the MCP-1 production in PBMC monocultures and FLS+PBMC co-cultures. (Figure 2B) PBMCs and SFMCs produced significantly higher levels of IFN-ɣ after CD3/CD28 activation ($p < 0.001$), but they were not affected by the addition of antibody towards the other checkpoint inhibitors.

Conclusion: This is the first report studying the effects of different co-IRs in o-JIA. Both the soluble levels and the surface expressions of co-IRs were higher at the site of inflammation in o-JIA. SFMCs and PBMCs of o-JIA patients are not exhausted, based on their ability to respond to CD3/CD28 activation. This is opposite to what has been shown in adult inflammatory arthritis. Co-cultures of autologous FLSs and PBMCs/SFMCs may serve as an *ex-vivo* arthritis model to perform functional analysis. LAG-3 might play a role in o-JIA pathogenesis and maybe a potential therapeutic option.

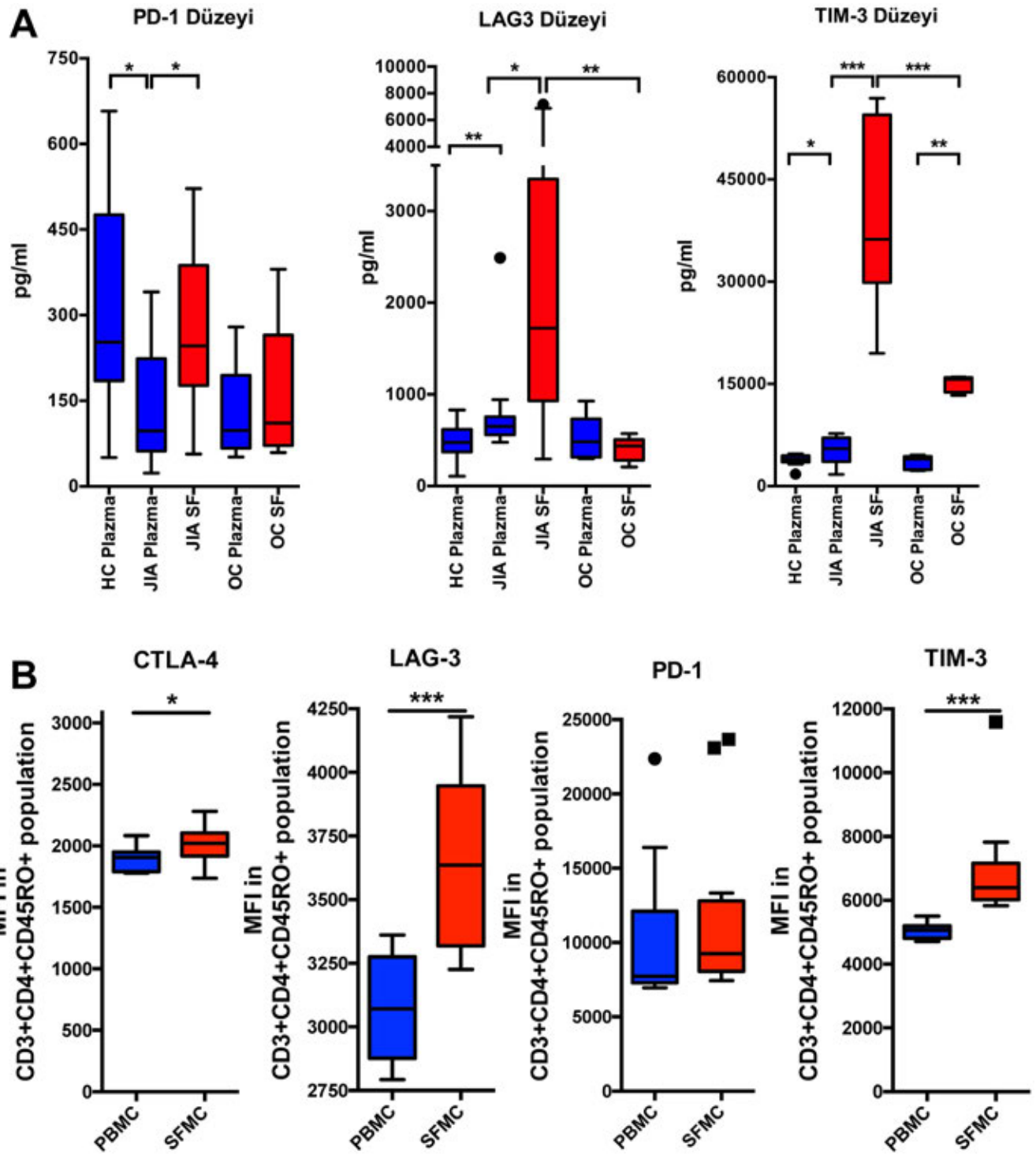

Figure 1. A. Soluble Levels of Co-inhibitor Receptors In Oligoarticular JIA (n=14), Non-inflammatory Juvenile Orthopaedic Controls (n=5) And Healthy Controls (n=14) In Plasma and SF B. Surface expressions of Co-inhibitor Receptors In JIA PBMC and SFMCs (n=12) (HC: Healthy Control, OC: Non-Inflammatory Juvenile Orthopedic Controls, JIA: Juvenile Idiopathic Arthritis, SF: synovial fluid, PBMC: Peripheral Blood Mononuclear Cells; SFMC: Synovial Fluid Mononuclear Cells, MFI: Median Fluorescence Intensity, sPD-1: soluble Programmed Death-1, sLAG-3: soluble Lymphocyte Activation Gene 3, sTIM-3: soluble T cell Immunoglobulin Mucin 3, CTLA-4: Cytotoxic T-Lymphocyte associated Antigen 4; Boxes indicate median and IQR, whiskers indicate 10th–90th percentiles*p<0.05; **p<0.01; ***p<0.001)

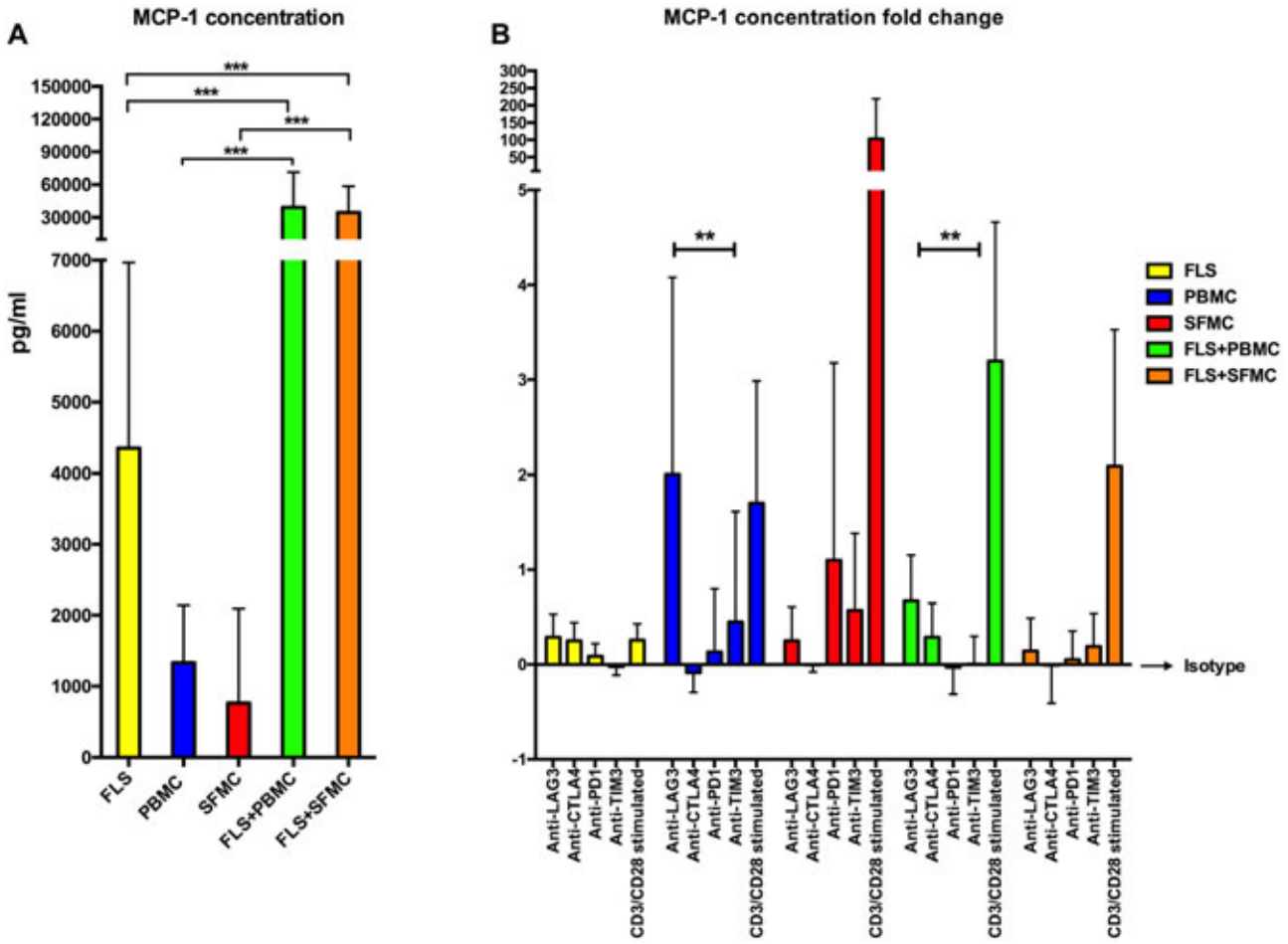

Figure 2. MCP-1 levels in the co-culture supernatants of ex vivo arthritis model (n=7). A. Spontaneous production of MCP-1 in ex-vivo arthritis model (***p<0.001). B. MCP-1 production after addition of neutralizing antibodies against CTLA-4, PD-1, LAG-3, TIM-3, expressed as mean fold change to isotype control (**p<0.01). (FLS: Fibroblast-Like Synoviocytes PBMC: Peripheral Blood Mononuclear Cells; SFMC: Synovial Fluid Mononuclear Cell; MCP-1: Monocyte Chemoattractant Protein-1 Cells CTLA-4: Cytotoxic T-Lymphocyte associated Antigen 4, PD-1: Programmed Death-1, LAG-3: Lymphocyte Activation Gene 3, TIM-3: T cell Immunoglobulin Mucin 3)

Disclosure: E. Sag, AbbVie, 2; **S. Demir**, None; **M. Nielsen**, None; **M. Hvid**, None; **E. Turhan**, None; **Y. Bilginer**, AbbVie, 2; **S. Ozen**, Enzyvant, 8; **B. Deleuran**, None.

Abstract Number: 0783

Differences in Chromatin Architecture in Treatment Naïve Pediatric Lupus Patients

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex disease likely triggered by gene-environment interactions. We have shown that most of the SLE-associated haplotypes encompass genomic regions enriched for epigenetic marks associated with enhancer function in neutrophils, and T/B cells, suggesting that genetic risk is exerted through altered gene regulation. Data remain scarce on how epigenetic variance contributes to disease risk in pediatric SLE. We aim to identify differences in epigenetically-regulated chromatin architecture in treatment-naïve pediatric lupus (pSLE) patients compared to healthy children.

Methods: We used the assay for transposase-accessible chromatin-sequencing (ATACseq) to survey open chromatin in 8 treatment-naïve pSLE patients and 5 healthy children (HC). We investigated whether regions of open chromatin unique to pSLE patients might demonstrate enrichment for specific transcriptional regulators, using standard computational approaches to identify unique peaks and a false discovery rate of < 0.05.

Results: The mean age of onset was 13.75 (range 7-17) years in pSLE patients; 3 out of 8 patients were male. pSLE patients were 50% African American, 38% Caucasian, and 12% Asian, with all but 1 patient identifying Hispanic. The mean SLEDAI was 12.8 (range 6-24). Differential peak analysis identified 30139 uniquely accessible sites in pSLE patients. Further analyses of these open regions revealed that 46-60% of the peaks seen only in pSLE patients are located more than 100kb from the nearest transcription start site, implying that many transcription factors (TFs) may be acting on distal enhancers to regulate transcription. Differentially accessible regions (DARs) were enriched for enhancer marks H3K4me2, H3K4me3, and H3K27ac, and contained 42 TFs that may be accessible in pSLE patients but not HC. Variant calling within DARs found 3864 genes belonging to 129 different biologic processes, most notably cellular activation in immune response, regulation of cell proliferation, and cellular responses to external stimuli (e.g., interferon).

Conclusion: Over 50% of DARs identified in pSLE patients are located far from their nearest transcription start sites, and appear to be enriched for several enhancer histone marks, implying that TF binding sites are poised for activation. Pathways of significance analyses identified immunologic pathways important in the pro-inflammatory response. Thus, patterns of chromatin accessibility suggest important roles for chromatin regulators in treatment-naïve pSLE.

Disclosure: J. Hui-Yuen, None; **F. Jenkins**, None; **K. Jiang**, None; **S. Malkiel**, None; **B. Diamond**, GSK, 5, Jansen, 5, Lilly, 5; **J. Jarvis**, None.

Abstract Number: 0784

Application of Systems Biology-Based *In Silico* Tools for Optimal Treatment Strategy Identification in Still's Disease

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic JIA (sJIA) and Adult Onset Still's Disease may represent a disease continuum[1] of the same autoinflammatory disorder, Still's Disease. Current challenges in its management include the complex disease clinical phenotypes (systemic/rheumatic symptoms) and the absence of optimal treatment guidelines. Several efforts are being made to identify the best targeted strategy to take advantage of the "window of opportunity" and prevent complications and damage[2]. Systems biology-based methods are becoming reliable tools to understand the molecular effects of drugs in complex clinical settings. In this study, we constructed *in silico* models to explore and compare the mode of action (MoA) in Still's Disease of current biologicals, anakinra (ANA), canakinumab (CAN) and tocilizumab (TCZ), in addition to non-biological drugs such as corticosteroids and methotrexate, aiming to advance towards an optimal treatment approach.

Methods: Therapeutic Performance Mapping System was used to create Still's Disease pathophysiology and drug MoA models. Drugs' efficacies were compared using artificial neuronal networks, and detailed MoA of IL-1β and IL-6 blockers was modeled using sampling methods. Available expression data in sJIA patients was used for model validation (GSE80060, GSE21521, GSE8361, GSE7753, GSE76492).

Results: The models reflected human physiology (>90% accuracy) and Still's Disease pathophysiology (Figure 1A). Biologicals were found more efficient than non-biologicals (Table 1). IL-1 blockers behaved similarly (CAN as IL-1β-specific blocker was used for further analyses) and presented an innate immune system-centered mechanism, while TCZ acted over the adaptive immune system. A detailed evaluation of the MoA of CAN and TCZ on the innate immune system showed some well-known proteins (Figure 1B) differentially modulated. While CAN inhibits NF-κB, CXCL8 and S100A9 more effectively, CD64 (FCGR1A) is preferentially inhibited by TCZ. The CAN and TCZ MoA models reproduced 67% of the information obtained from expression data (Figure 2).

Conclusion: The created *in silico* Still's Disease models reproduce known clinical and molecular findings, which render them a good tool for future patient profiling, biomarker identification and treatment strategy designing. According to the models, the biologicals tested for proof-of-concept purposes provide a more pathophysiology-directed MoA than non-biological drugs, and are similarly effective on both systemic and rheumatic disease features. IL-1 blockers, specifically CAN, might be more efficient than TCZ in initial autoinflammatory/systemic phases of Still's Disease that is dominated by innate immune dysregulation. Key innate immune mediators are hereby proposed to explain the differences observed between CAN and TCZ MoA. Our systems biology data may thus support the development of therapeutic strategies fostering early intervention with CAN during the window of opportunity to prevent the development of destructive chronic arthritis and treatment- or disease-associated complications long-term.

References:

1. Luthi F, et al. Clin Exp Rheumatol. 2002.
2. Nigrovich PA, et al. Arth Rheum. 2014.

Disclosure: C. Segu-Verges, None; **M. Coma**, None; **C. Kessel**, None; **S. Smeets**, Novartis, 1, 3; **D. Foell**, Novartis, Pfizer, Roche/Chugai, Sobi, 2, 5, 8; **A. Aldea**, None.

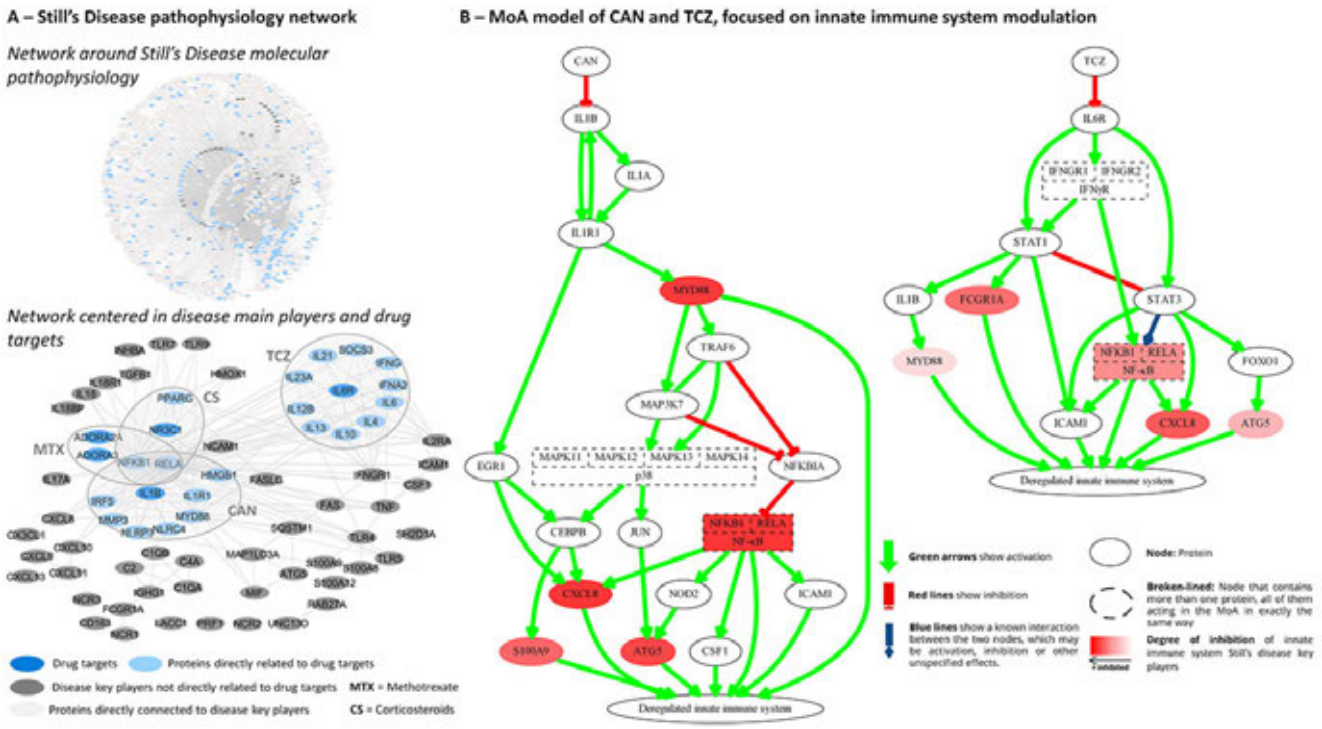

Figure 1. Systems biology-based models. Network A.1) around Still's Disease molecular pathophysiology; and A.2) centered in disease main players, and their relationship to drug targets. B) Model of MoA of CAN and TCZ, focused on innate immune system modulation.

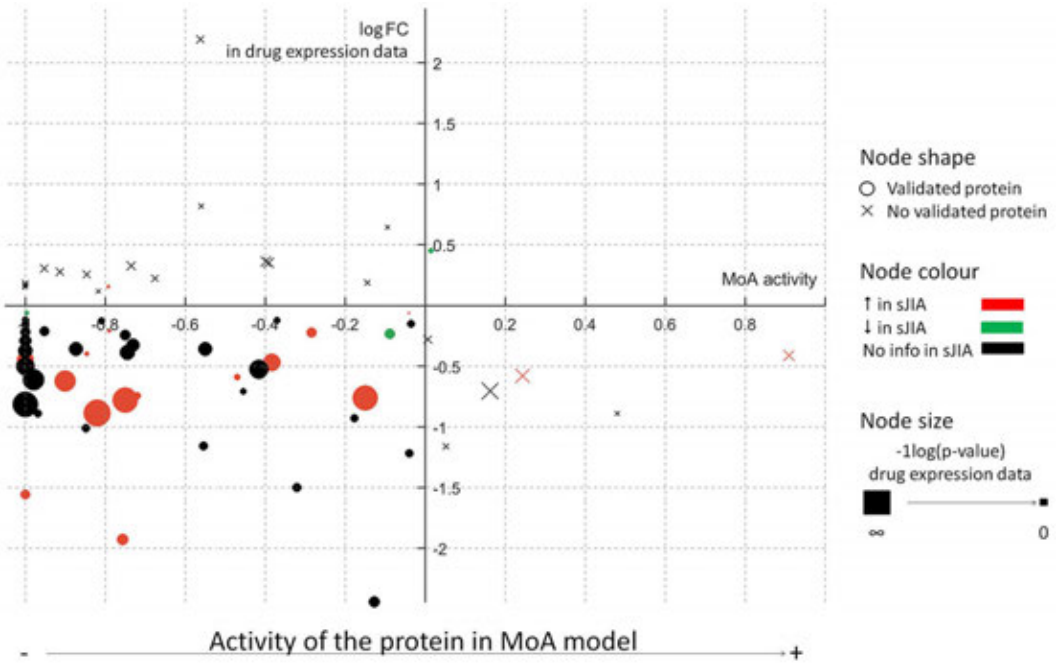

Figure 2. MoA models validation with expression data. Both sJIA vs. control (shown in nodes color) and treated vs. non-treated sJIA patients with CAN or TCZ (Y axis and node size) expression data has been used for comparison to model protein values (X axis). Proteins validated by either sJIA vs. control or treated vs. non-treated expression data are shown as circles, while crosses represent not validated proteins – most of the validated proteins fall on the third quadrant, i.e., their expression is downregulated by the drugs and the MoA model predict downregulation in their activation.

Table 1. Summary of artificial neuronal network results, divided on global Still's Disease evaluation, per patient profile and per immune system component.

Drug information		Artificial neuronal network efficacy evaluation					
		Still's Disease molecular definition			Immune system components		
Drug type	Drug Name	Still's Disease	Systemic profile	Rheumatic profile	Innate immune system deregulation	Adaptive immune system T-cell response activation	Adaptive immune system Immunoregulation
Biologicals	Anakinra	High	High	High	Medium-High	Medium	Low
	Canakinumab	High	High	High	Medium-High	Low	Low
	Tocilizumab	High	High	High	Medium	Medium-High	Medium
Non-Biologicals	Methotrexate	Low	Low	Low	Low	Low	Low
	Prednisone	Medium-High	Medium-High	Medium-High	Medium-High	Medium	Medium

* Categories indicate the probability of true relationship between the drugs and the conditions evaluated according to the predictive models
High if p-value<0.05; Medium-High if p-value<0.15; Medium if p-value<0.25 and Low if p-value>0.25

Abstract Number: 0785

Predictors of Response to Tumour Necrosis Factor - α Inhibitors (TNFi) in Juvenile Idiopathic Arthritis (JIA): A Single-center Experience

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Biologics have transformed the treatment of Juvenile idiopathic arthritis (JIA) and escalation to Tumour Necrosis Factor - α inhibitors (TNFi) after failure of methotrexate (MTX) was enshrined as NHS standard practice in National Institute of Clinical Excellence guidelines in 2002. The aim of our study was to explore the clinical response to first TNFi including duration on treatment before discontinuation due to loss of efficacy (secondary failure), clinical remission or side-effects. We looked at six sub-types of JIA. Group A consisted of subtypes of JIA with polyarticular course of disease encompassing Seropositive and Seronegative polyarticular JIA (SPPJIA, SNPJIA) and Extended oligoarticular JIA (EOJIA). The other groups were Persistent oligoarticular JIA (PO JIA), Psoriatic arthritis (Ps JIA) and Enthesitis-related arthritis (ERA). We excluded Systemic and undifferentiated JIA as we wanted to focus on the response to TNFi.

Methods: This was a retrospective, single centered, observational real-life study of the cohort of patients with JIA at UCLH (University College London Hospitals). We took a single data extract from our clinical database in January 2019. We included patients diagnosed with JIA (fulfilling International League of Associations for Rheumatology criteria) starting on TNFi from October 2012 (database inception) to December 2018. All had at least six months of follow-up since the introduction of the TNFi to 2018. The patients remaining on TNFi 6 months after initiation were defined as responders in accordance with national guidelines (NHS England stipulate that TNFi must be stopped if there is a failure to respond after 6 months). IBM statistics 2017 SPSS and Prism 8 for macOS was used for data analysis.

Results: We initially included a total of 328 JIA patients. Ten were excluded (5 missing data, 3 with treatment duration < 6 month, 2 malignancies). The baseline characteristics of the 318 patients are presented in **table 1**. Overall, the

response rate was 61% (195/318) (**Graph 1 a**). Of the 195 responders, 77 (39.5%) eventually stopped their treatment (**Graph 1 b**).Of these 45 (60%) had secondary failure due to inefficacy, 21 (27%) were in remission and 10 (13%) due to an adverse reaction.

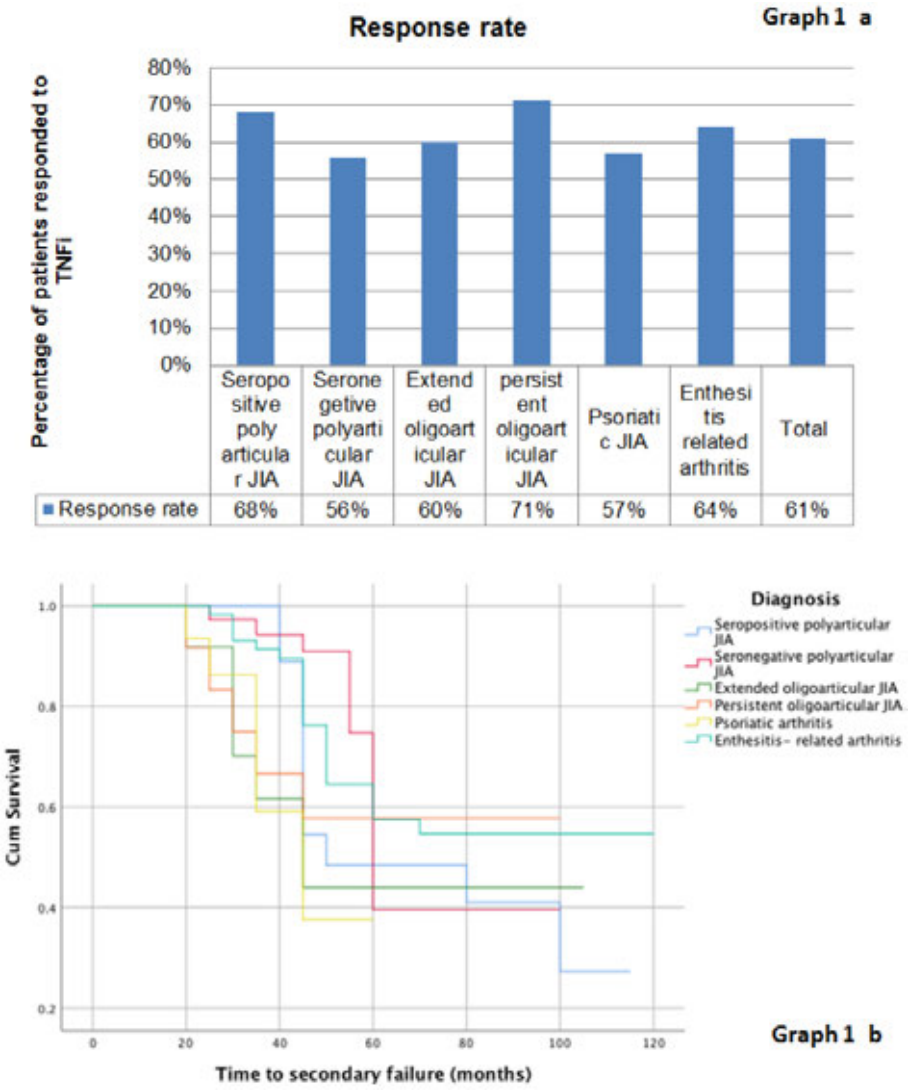
Unlike other studies, there was no significant correlation between age of disease onset and treatment response (**graph 2 a**). Group A showed significantly better response if treatment was started earlier (**graph 2 b**). However, this was not demonstrated in other subtypes. Group A only demonstrated a better response if on MTX (**graph 2 c**). There was no significant difference among the other subtypes. A higher basal metabolic index (BMI) was associated with poorer response to TNFi in Ps JIA group (**graph 2 d**). A higher baseline C-reactive protein (CRP) was associated with better response to TNFi for ERA (**graph 2 e**). In Ps JIA a good response to TNFi was associated with a significantly lower Erythrocyte sedimentation rate (ESR) (**graph 2 f**) at initial presentation.

Conclusion: We found that a good response to TNFi treatment in patients with JIA was associated with

1. Polyarticular course disease (group A) - Early start of treatment, concomitant use of MTX.
2. Ps JIA: Lower BMI, Lower ESR.
3. ERA: Higher CRP.

Characteristics	Group A			Persistent oligo articular JIA (n=17)	Psoriatic arthritis (n=30)	Enthesitis-related arthritis (n=99)
	Seropositive Polyarticular JIA (n=37)	Seronegative Polyarticular JIA (n=72)	Extended oligo articular JIA (n=63)			
Female, n (%)	37 (100%)	42 (58%)	47 (75%)	10 (71%)	17 (57%)	20 (20%)
Age of disease onset, years	11.6 (9.8-12.2)	10.9 (8.1-11.9)	8.3 (6.1-10.3)	9.1 (8.5-11.3)	10.5(8.0-11.6)	10.6 (8.5-13.9)
Duration of disease when start on TNFi, months	8.0 (5.6-16)	15.8 (11-19)	24.4 (17.8-42.4)	18.4 (14.5-22.4)	15.8 (14.5-22.4)	15.2 (13.8-25.6)
Baseline BMI	24.2 (22.5-25.4)	23.4 (21-24.5)	22.9 (21.3-24.1)	24.5 (22.6-26.8)	25.7 (22.3-27.8)	24.9 (22.7-26)
Concomitant Methotrexate at baseline, n (%)	29 (78%)	50 (69%)	45 (71%)	14 (82%)	20 (67%)	76 (77%)
Baseline ESR, mm	15.6 (7.5-20.3)	20.3 (13.2-23.2)	14.2 (8.5-17.8)	5.5-8.5 (3-15)	29.7 (16-40.3)	27.1 (21-34)
Baseline CRP, mg/L (normal range 0-5 mg/L)	10.2(6.1-15.2)	9.1 (4.3-11)	7.1 (4.8-8.9)	4 (2-8)	11 (7.8-14.7)	17.2 (10.2-25.3)
Numbers are medians (interquartile ranges) unless otherwise stated. BMI: Body mass index, csDMARDs: conventional synthetic disease modifying anti-Rheumatic drugs, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein						

Table 1. Baseline characteristics of the Juvenile idiopathic arthritis (JIA) patients



Graph 1 (a,b). 1a - Response rate of initial TNFi and the; 1b - TNFi efficacy maintenance curve (Kaplan –Meier curve).

Disclosure: M. Shipa, None; **A. Madenidou**, None; **v. Choida**, None; **A. Radziszewska**, None; **c. fisher**, None; **c. ciurtin**, None; **m. Leandro**, None; **D. Sen**, None.

Abstract Number: 0786

Distinguishing S100 Proteins and Cytokine Levels Between Active and Inactive Uveitis in Children with Juvenile Idiopathic Arthritis

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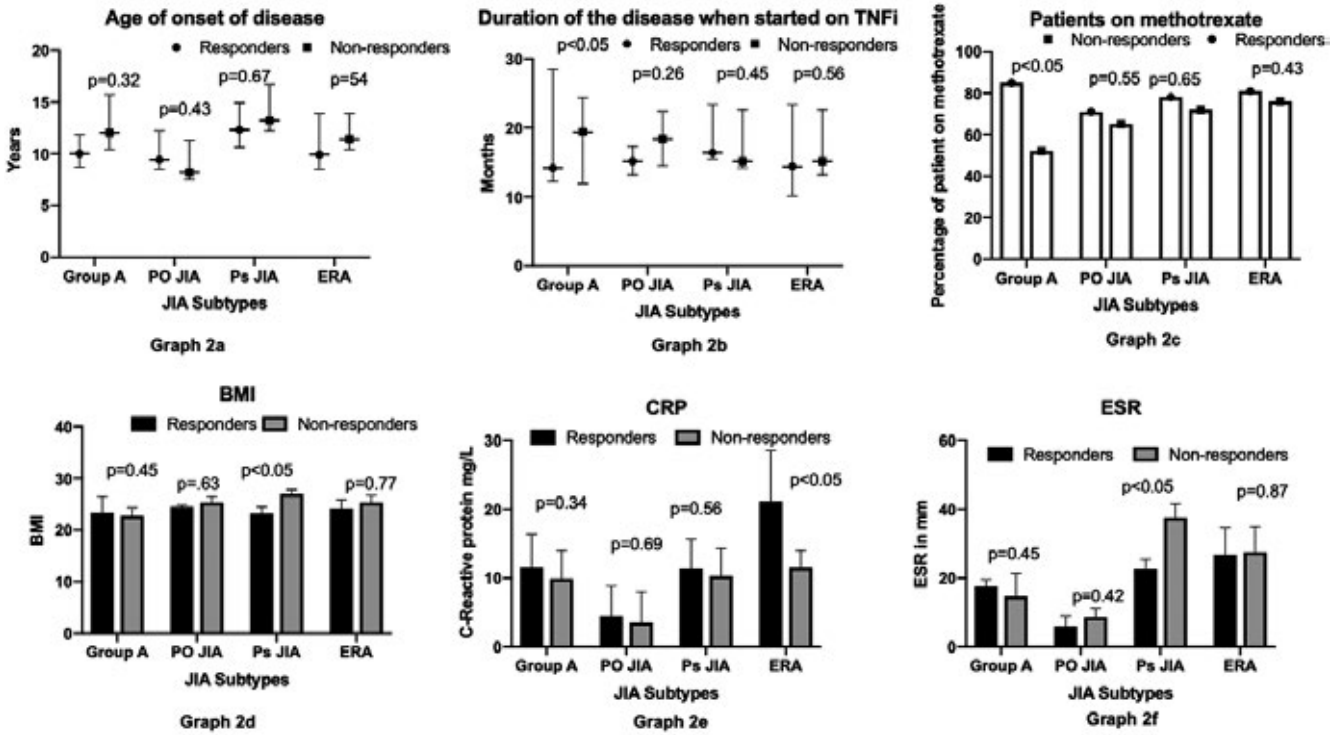

Graph 2 (a-f). Response of different subtypes of JIA on various baseline characteristics; a (age of onset), b (Duration of disease), c (concomitant methotrexate), d (Basal metabolic index/BMI), e (C - reactive protein in mg/L), f (Erythrocyte sedimentation rate in mm)

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Uveitis occurs in 10-20% of children with Juvenile Idiopathic Arthritis (JIA) and is typically asymptomatic. Ocular complications occur in 50% of children, (i.e. cataracts, vision loss). Even after uveitis is controlled, risk of disease exacerbation still exists. Therefore, frequent ophthalmic screening and monitoring is important for detection and management of JIA-associated uveitis (JIA-U). Potential objective measures of ocular inflammation are S100 proteins, cytokines, and chemokines that have been identified as biomarkers in aqueous humor. However, aqueous humor collection is invasive. Measuring the same biomarkers in tears, would be a less invasive approach. Our objective is to determine whether S100 proteins, cytokines, and chemokine levels differ in tears of JIA-U children with active or inactive uveitis.

Methods: Tears were collected using Schirmer strips from children ≥5 years old with JIA-U (n=20) and pediatric healthy controls (n=20) during routine clinic visit. S100A8, A9, and A12 were measured by ELISA, and IL-18, IL-8, IP-10, MCP-1, RANTES, and sICAM-1 by Luminex assays. Levels were compared between JIA-U children and healthy controls and between JIA-U children with active and inactive uveitis.

Results: S100 proteins, cytokines and most chemokines levels were similar in JIA-U compared to controls. However, differences were observed between JIA-U patients with active and inactive uveitis. Patients with active uveitis had significantly higher levels of tear S100A12 as compared to inactive uveitis (mean 27,722 pg/ML [SE

1.3] vs. 5,937pg/ML [SE 1.3], p=0.0001). Similar increased levels in active uveitis as compared to inactive uveitis for IL-8 (73 pg/ML [SE 1.3] vs. 37 pg/ML [SE 1.1], p = 0.026) and sICAM-1 (15,823 pg/ML [SE 1.2] vs. 8,778 pg/ML [SE 1.6], p=0.004)

Conclusion: Identifying uveitis biomarkers using tears would provide a noninvasive and objective method of detecting and monitoring uveitis. Our results indicate that S100A12, IL-8 and sICAM-1 from tears could be utilized as potential biomarkers for distinguishing inactive and active uveitis. This suggests that neutrophils may play a role in the pathogenesis of anterior uveitis which has been reported in an animal model of acute anterior uveitis.

Disclosure: J. Rodriguez-Smith, None; **V. Utz**, Retrophin, 2; **S. Thornton**, None; **G. Schulert**, Novartis, 5, 8; **A. Kauffman**, 1800 contacts and alcon, 5; **A. Sproles**, None; **N. Mwase**, None; **T. Hennard**, None; **A. Grom**, AB2 Bio Ltd, 2, 5, AB2Bio, 2, 5, Children's Hospital Medical Center, 3, Novartis, 2, 5, Novartis Pharmaceuticals Corporation, 2, 5, Novartis Pharmaceuticals Corporations, 5, NovImmune, 2, 5, Novimmune, 2, 5; **M. Altaye**, None; **G. Holland**, None; **S. Angeles-Han**, None.

Abstract Number: 0787

Complement Protein Levels Reflect Disease Activity in Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: There is an increasing body of evidence that inadequately controlled activation of complement factors leading to either overactivity or deficiency may be involved in the pathogenesis of some autoimmune diseases. However, the role of the complement system in juvenile idiopathic arthritis (JIA)is still not fully elucidated. The aims of this study were to determine the serum levels of the lectin pathway proteins early in the disease course and 17 years after disease onset and to correlate the protein levels to markers of disease activity in participants from a population-based Nordic JIA cohort. Additionally, we aimed to assess the predictive value of lectin pathway proteins with respect to remission status.

Methods: A population-based cohort study of consecutive cases of JIA with a disease onset from 1997-2000 from defined geographical areas of Finland, Sweden, Norway and Denmark with 17 years of follow-up was performed. Clinical characteristics were registered and H-ficolin, M-ficolin, MASP-1, MASP-3, MBL and CL-K1 levels in serum were analyzed.

Results: In total, 293 patients with JIA and available blood samples were included (mean age 23.7 ± 4.4 years; mean follow-up 17.2 ± 1.7 years). Further clinical characteristics of the participants at the 17-year follow-up are reported in Table 1.Concentrations of the lectin proteins in serum were higher at baseline compared to the levels 17 years after disease onset ($p \leq 0.006$, n=164). At baseline, the highest level of M-ficolin was observed in systemic JIA, which was significantly higher than in the oligoarticular persistent (p=0.024), polyarticular RF neg (p=0.048), ERA (p=0.02) and the undifferentiated categories (p=0.014) (Figure 1). Conversely, MASP-1 levels at baseline were significantly lower for the systemic group compared to the oligoarticular persistent (p=0.03) and the undifferentiated categories (p=0.019).

Further, high M-ficolin levels at baseline and at 17-year follow-up were correlated to high levels of ESR (Table 2). In contrast, high MASP-1 and MASP-3 tended to correlate to low ESR. CL-K1 showed a negative correlation to JADAS71 at baseline.

None of the protein levels had prognostic abilities with respect to remission or inactive disease status 17 years after disease onset.

Table 1 Clinical characteristics of participants in the Nordic JIA cohort at the 17-year follow-up visit.

	Total cohort N= 293
Females, n (%)	208 (71.0)
Age at onset, y*	6.5±4.1
Age at follow-up, y*	23.7 ±4.4
Disease duration, y*	17.2 ±1.7
ANA positive, n (%)	89 (30.4)
HLA-B27 positive, n (%)	66 (22.5)
CRP >10 mg/L, n (%)	16 (5.4)
ESR >20 mm/h, n (%)	18 (6.1)
Active joint count, median (IQR)	0 (0–0)
Cumulative joints, median (IQR)	8(4-15)
JADAS71≤1, n (%)	126 (43.0)
Systemic JIA	13 (4.4%)
Oligoarticular persistent	66 (22.5%)
Oligoarticular extended	55 (18.8%)
Polyarticular RF negative	53 (18.1%)
Polyarticular RF positive	5 (1.7%)
Psoriatic	19 (6.5%)
Enthesitis-related arthritis	33 (11.3%)
Undifferentiated	49 (16.7%)

y* = Mean in years ±SD, IQR= 1st-3rd interquartile range, ANA= Antinuclear antibodies, HLA-B27= Human leukocyte antigen B27, CRP= C-reactive Protein, ESR= Erythrocyte sedimentation rate, IQR= 1st-3rd interquartile range, JADAS71= Juvenile Arthritis Disease Activity Score of 71 joints, RF = Rheumatoid factor.

Table 2 Correlation between disease activity and lectin levels at baseline and 17-years of follow-up.

	BASELINE#(n=238)			17-YEAR FOLLOW-UP (n=293)		
	ESR	JADAS71	Cum joints	ESR	JADAS71	Cum joints
MBL	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
H-ficolin	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
M-ficolin	r=0.23 p<0.01	N.S.	N.S.	r=0.20 p<0.01	N.S.	N.S.
CL-K1	N.S.	r=−0.16 p=0.05	N.S.	r=−0.13 p=0.05	N.S.	N.S.
MASP-1	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.
MASP3	N.S.	N.S.	r=−0.13 p=0.04	N.S.	N.S.	N.S.

Only results with a p≤0.05 are listed. N.S= non-significant. #: Baseline was 6 months (-1/+2 months) after disease onset. ESR= erythrocytes sedimentation rate at baseline, JADAS71= juvenile arthritis disease activity score of 71 joints; cum joints= cumulative joint count; MASP= MBL-associated serine proteases; MBL= mannan-binding lectin; CL-K1= collectin kidney, r= Spearman's rho.

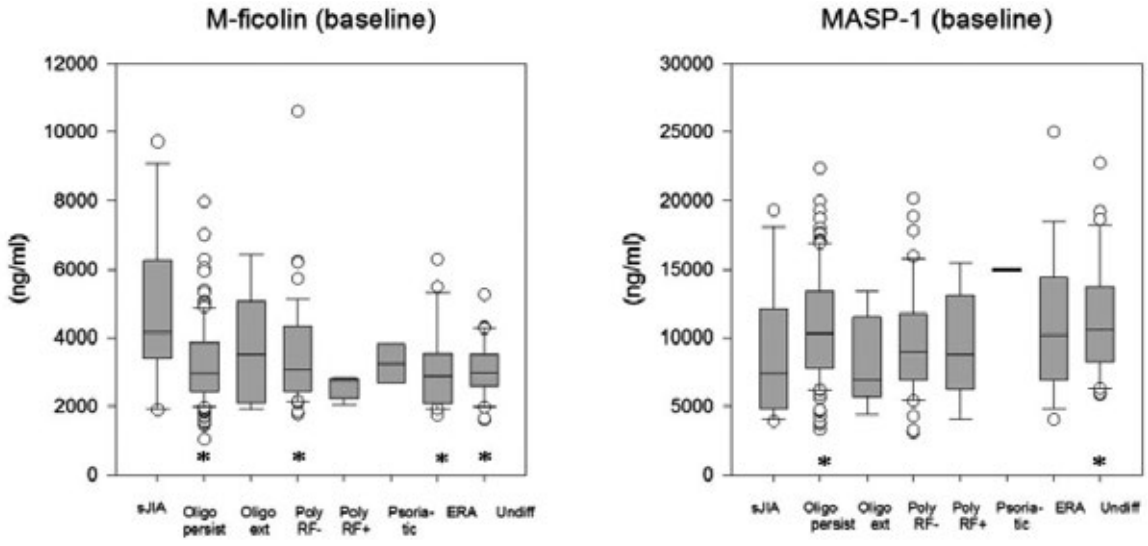

Figure 1 Distribution of M-ficolin (a) and MASP-1 (b) levels at baseline among the different JIA categories. * indicate p<0.05 when comparing to the level of systemic JIA (sJIA). Boxes indicate 25–75 percentile (IQR); a line in all boxes indicate medians; whiskers indicate upper adjacent values; small circles are outliers.

Conclusion: We hypothesize that increased serum M-ficolin levels are associated with higher disease activity in JIA and further, the results indicate that MASP-1, MASP-3 and CL-K1 negatively correlated to markers of inflammation.

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Abstract Number: 0788

Type I Interferon Score and Interferon Induced Mediators CXCL10 and Neopterin Are Correlated with Disease Activity in Juvenile Dermatomyositis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Interferons (IFNs) seem to play an important role in the pathogenesis of juvenile dermatomyositis (JDM). Our group previously reported that expression of both type I and type II IFN related genes is increased in muscle biopsies of JDM patients and correlates with histological and clinical features of the disease. The aim of this study was to investigate expression of interferon regulated genes (IRGs), as well as serum levels of two type I and type II IFN induced chemokines (CXCL9, CXCL10) and neopterin in peripheral blood of JDM patients and to assess their correlations with clinical and laboratory findings.

Methods: We collected 189 blood samples from 39 JDM patients at different time points during follow-up. In 11 patients we obtained the first blood sample at time of muscle biopsy. We measured expression of type I IRGs (IFI27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1), IFNg and type II IRGs (CXCL9, CIITA, IDO1) by quantitative PCR (qPCR) and calculated a type I and type II IFN score for muscle and blood samples; serum levels of CXCL9, CXCL10 and neopterin were analyzed by ELISA. Ten healthy subjects were used as controls (HC). At each visit, the following clinical data were recorded: physician's global assessment (PGA) of disease activity VAS (Visual Analogue Scale), cutaneous VAS, Cutaneous Assessment Tool (CAT) activity score, Childhood Myositis Assessment Score (CMAS), serum levels of creatine phosphokinase (CK, IU/l), presence of myositis specific or myositis associated antibodies (MSA/MAA), prednisone (or equivalent) dose (mg/kg/daily), ongoing immunosuppressive medications.

Results: Serum levels of CXCL9 where significantly correlated with muscle expression of IFNg and type II IFN score. The correlation of CXCL10 levels with muscle type I and type II IFN score was weaker. Muscle expression of CXCL9 and CXCL10 correlated with serum levels of these chemokines. Type I IFN score in blood of JDM patients was increased compared to HC and significantly correlated with PGA, cutaneous VAS, CAT activity score. Serum levels of CXCL9 and CXCL10 were significantly higher in JDM patients compared to HC. MSA positive JDM patients showed higher levels of CXCL9 and CXCL10 compared to MSA negative patients. CXCL10 levels were correlated with PGA

and CMAS, but not with cutaneous disease activity. CXCL9 showed no significant association with the evaluated clinical features. Neopterin levels were significantly correlated with PGA, cutaneous VAS, CAT activity score and CMAS.

Conclusion: Our findings indicate that expression of IRGs, measured as type I IFN score, and serum levels of CXCL10 and neopterin reflect specific features of disease activity in JDM, supporting their role as valuable disease biomarkers.

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Abstract Number: 0789

DNASE1L3 Variant in Hypocomplementemic Urticarial Vasculitis Syndrome Identifies a Different Clinical Phenotype

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SESSION INFORMATION
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Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever
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Background/Purpose: Hypocomplementemic urticarial vasculitis syndrome (HUVS) is a rare disease characterized by persistent urticarial lesions and hypocomplementemia associated with systemic features involving musculoskeletal, pulmonary, renal and gastrointestinal systems. Systemic lupus erythematosus (SLE) develops in >50% of patients with HUVS, although the pathogenesis is unknown.

Methods: We describe 6 paediatric patients with HUVS, three of whom carry a homozygous variant of *DNASE1L3* and present a peculiar clinical phenotype. A Targeted Resequencing using a panel including genes already known to be mainly associated to Interferonopathies Lupus-like (*DNASE1*, *DNASE2*, *DNASE1L3*, *TREX1*) on the Illumina NextSeq® platform was performed. All variants identified were confirmed by Sanger sequencing and, when possible, family members were tested to study the segregation of identified variants. We applied in silico studies only to variants with an allelic frequency ≤1%.

Results: All patients described are Caucasian and 3 of them are female. Two patients presented at onset with extended cutaneous manifestation, joints and abdominal involvement with cholecystitis. They did not develop renal or pulmonary involvement. In contrast, the other four patients presented a more severe disease. All of them developed renal involvement (from microhaematuria up to nephrotic syndrome) with renal biopsy showing mesangial glomerulonephritis in three patients and pauci-immune glomerulonephritis (ANCA negative) in one. Moreover, two of them developed also pulmonary vasculitis (Table 1). A homozygous *DNASE1L3* variant (c.290_291delCA) was identified

Table 1. Patients' clinical characteristics

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6
Age at onset	9 y 6/12	3 y 10/12	9y 5/12	14y 3/12	3y 6/12	3y 1/12
Joints	Yes	Yes	Yes	No	Yes	Yes
Ocular	No	Yes	No	No	No	No
Abdominal	Yes	Yes	Yes	No	Yes	Yes
Pulmonary	No	Yes	Yes	No	No	No
Renal	Yes	Yes	Yes	Yes	No	No
Antibody anti-C1q	+	+	+	+	+	+
Anti-dsDNA	absent	absent	absent	absent	absent	absent
C3 (nv 90-180 mg/dl)	57	63	52	57	19	57
C4 (nv 10-40 mg/dl)	7	6	2	7	1	1
DNASE1L3 variant	+	+	Ongoing	+	-	-

in three of these patients. All of them were treated with glucocorticoid and dapsone at onset. Cyclophosphamide, mycophenolate mofetil and azathioprine were used in patients with renal involvement. None of them developed SLE.

Conclusion: HUVS is very rare disease in childhood. Approximately 50% of HUVS patients develop SLE. Genetic susceptibility to SLE is recognized and *DNASE1L3*-related SLE have been reported. Özçakar et al. have described 5 children from two families with HUVS who carry the same variant on *DNASE1L3* that we report here (1). Our patients confirm that variant in *DNASE1L3* can cause HUVS and support the hypothesis that this variant is responsible of a more severe phenotype with major organ involvement (renal and pulmonary). Patients with HUVS need to be followed very strictly for the risk to develop SLE. Presence of variant in *DNASE1L3* can identify patients with more severe disease and high risk to develop major organ involvement. These patients need more aggressive and possibly life-long immunosuppressive treatment.

Reference:

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Disclosure: M. Ranalli, None; **C. Passarelli**, None; **V. Messia**, None; **M. Pardeo**, None; **E. Sacco**, None; **A. Insalaco**, None; **M. Vivarelli**, None; **F. De Benedetti**, AbbVie, 2, BMS, 2, Novartis, 2, Novartis, Novimmune, Hoffmann- La Roche, SOBI, AbbVie, Pfizer, 2, Novimmune, 2, Pfizer, 2, Roche, 2, Sanofi, 2, Sobi, 2, Swedish Orphan Biovitrum, 2, UCB, 2; **C. Bracaglia**, None.

Abstract Number: 0790

Can High ANA Titre Combined with Clinical Features Predict Developing Autoimmune Conditions in Children?

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Antinuclear antibodies (ANA) are autoantibodies that recognise cellular antigens found predominantly in the cell nucleus. They are associated with numerous autoimmune diseases such as systemic lupus erythematosus (SLE), but may also be found in infectious diseases, malignancies and apparently healthy individuals.

ANA is routinely requested as part of an initial work-up for autoimmune conditions. The titre of ANA required before a sample is considered "positive" varies between laboratories and is dependent on factors such as the technique used. In healthy children (5-18%), ANA titres of 1/80 to 1/320 have been reported. Over time a proportion will decrease in titre or disappear. However, some may persist raising concerns about the possibility of autoimmune disease in evolution. A prospective study of healthy children with positive ANA found that children who developed autoimmune disease had clinical features at presentation that were suspicious for such an outcome. Therefore, the usefulness of a positive ANA result for diagnosing autoimmune conditions is limited without clinical correlation.

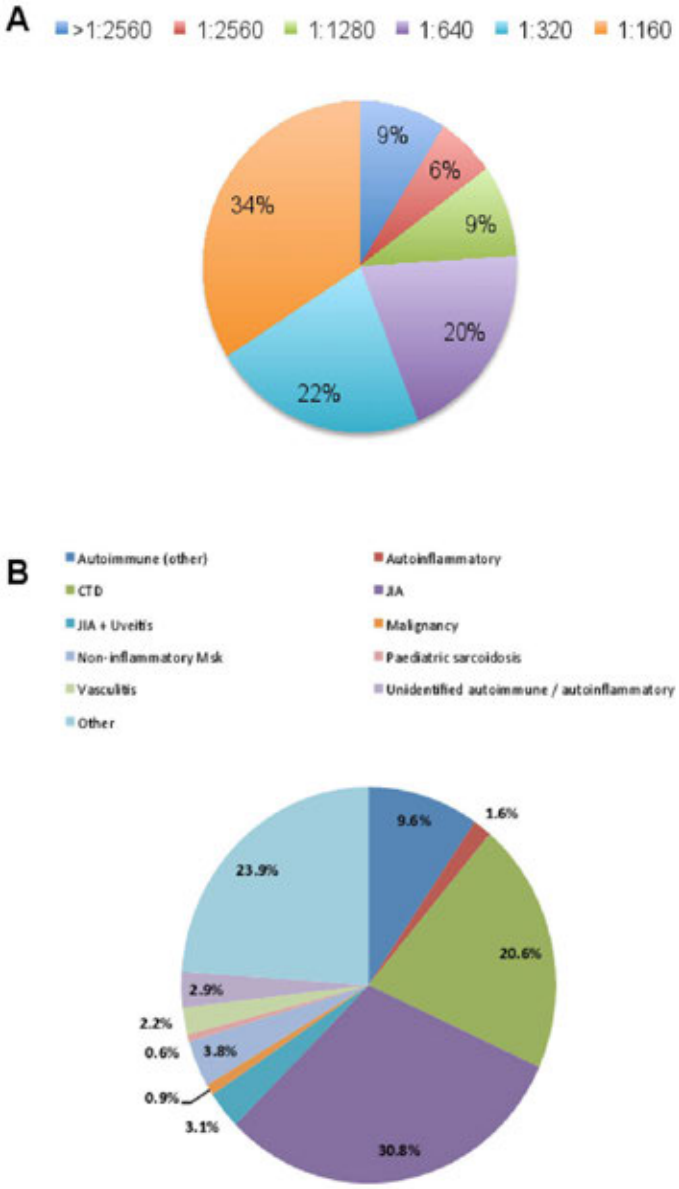

Figure 1. Percentage of each ANA titre observed in our cohort. B. Range of diagnoses observed in children with positive ANA results at presentation.

Our aim was to assess whether high ANA titre and clinical features at first presentation could predict final diagnosis

Methods: Single centre (Great Ormond Street Hospital for Children GOSH), retrospective study. The immunology laboratory at GOSH provided a list of positive ANA results (using indirect immunofluorescence) reported by their laboratory from January 2013 to July 2018. Results were filtered to exclude duplicate results for the same patient, creating a list of patients with ANA titre results from their first contact with our hospital. A retrospective chart review

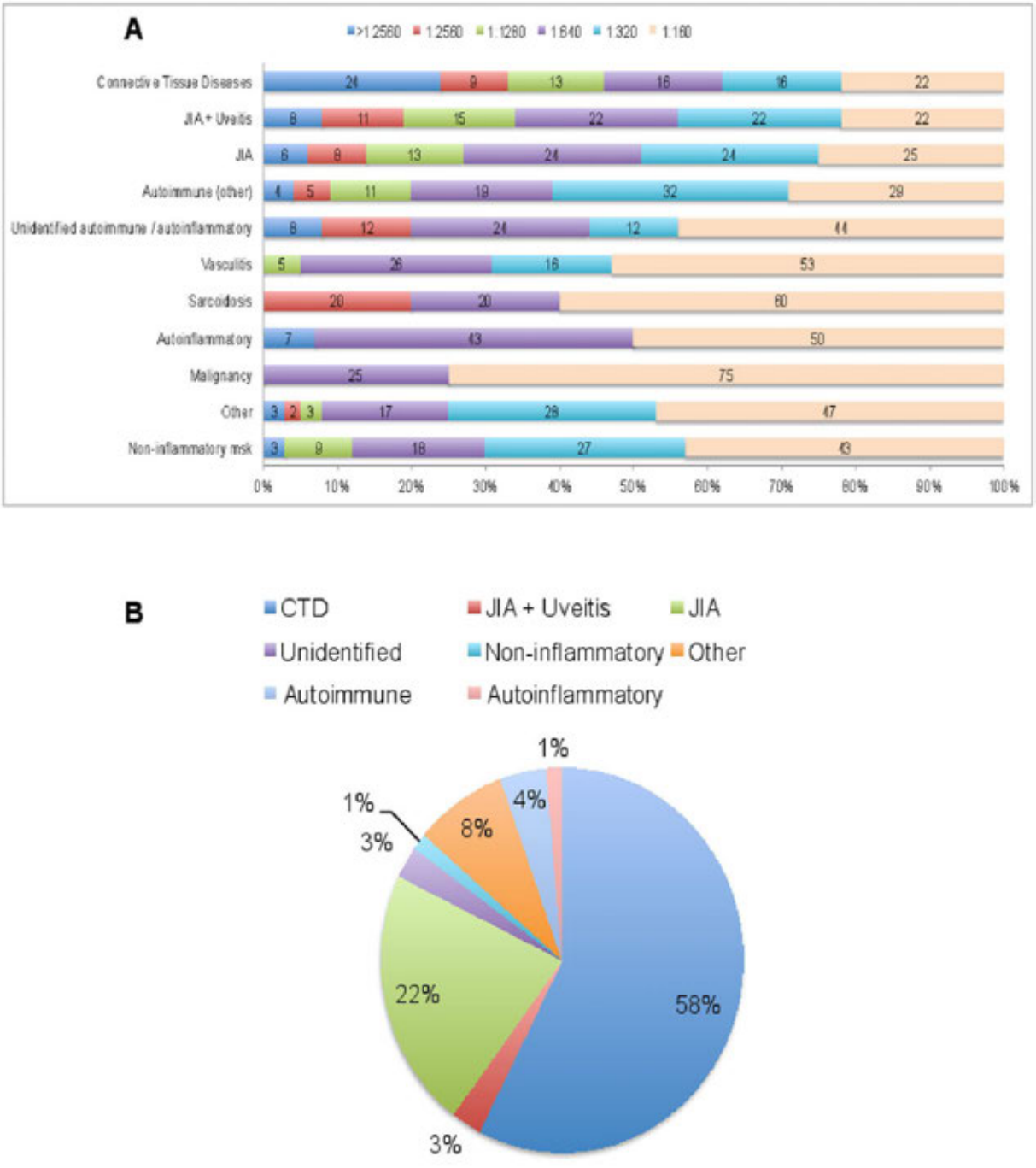

Figure 2. Bar chart displays the percentage of each diagnostic cohort that had each ANA titre. B. Pie chart for ANA titre >1:2560 showing the percentage of each diagnostic cohort that had this high titre. Over 50% of those with an ANA titre >1:2560 at presentation were diagnosed with a connective tissue disease (CTD)

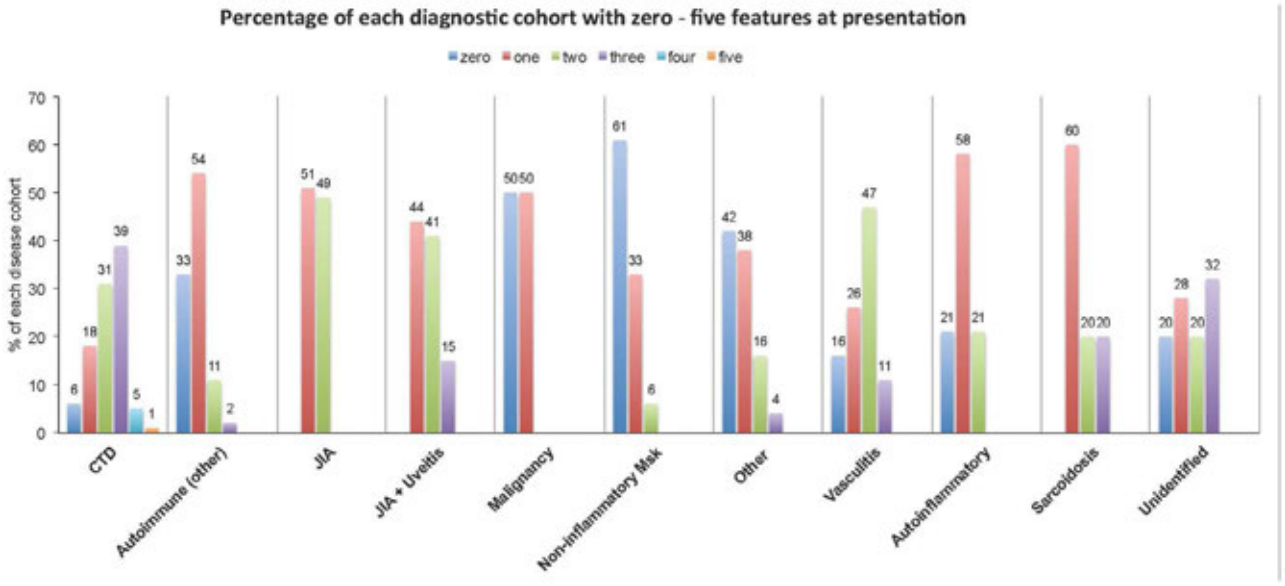

Figure 3. Bar chart depicting the number of clinical features children presented with depending on final diagnosis. Children diagnosed with a connective tissue disease (CTD) presented with 2 or more clinical features in 76% of cases, compared to only 6% of the non-inflammatory cohort.

was performed to ascertain presence or absence of clinical features at presentation under the following titles, arthritis, skin involvement, eyes, CNS involvement and raynaud's. We then reviewed the last clinical contact to document confirmed diagnosis and grouped these into 11 categories such as Connective Tissue Disease (CTD), JIA and so on.

Results: We performed a retrospective chart review on 1354 children (67% female; median age 7.5 years (0.1-17.5); median follow-up 4.8 years (0-18)) with positive ANA results (titres 1/160, 1/320, 1/640, 1/1280, 1/2560 and >1/2560). Figure 1A summarises the ANA titres observed in our cohort, and 1B the range of final diagnoses made. Figure 2A reports ANA titres at first presentation in relation to final diagnosis. A titre of 1/640 or above was most commonly seen (>50%) in children with an autoimmune rheumatology condition (JIA, JIA and uveitis or a CTD). In fact, children with the highest titre (>1:2560) were significantly more likely to be diagnosed with one of these conditions (figure 2B). Finally, we looked at the number of presenting features and correlated with final diagnosis (figure 3). Those diagnosed with a CTD were most likely to present with 2-5 clinical features (chi square $p< 0.0001$).

Conclusion: This study suggests that, patients presenting with higher ANA titres and a combination of clinical features at presentation should be assessed systemically and followed-up as they may have increased risk of an autoimmune rheumatological diagnosis.

Disclosure: O. Kul Cinar, None; **C. Foley**, None; **A. Al-Hussain**, None; **K. Gilmour**, None; **M. Buckland**, None; **M. Al-Obaidi**, None.

Abstract Number: 0791

Closing the Seronegative Gap in Pediatric Localized Scleroderma and Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

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Background/Purpose: It has become increasingly recognized that extra-cutaneous manifestations, such as musculoskeletal and neurologic involvement, are common in pediatric patients with localized scleroderma (LS). We previously demonstrated that the presence of certain autoantibodies (Aab) is associated with deep tissue and internal

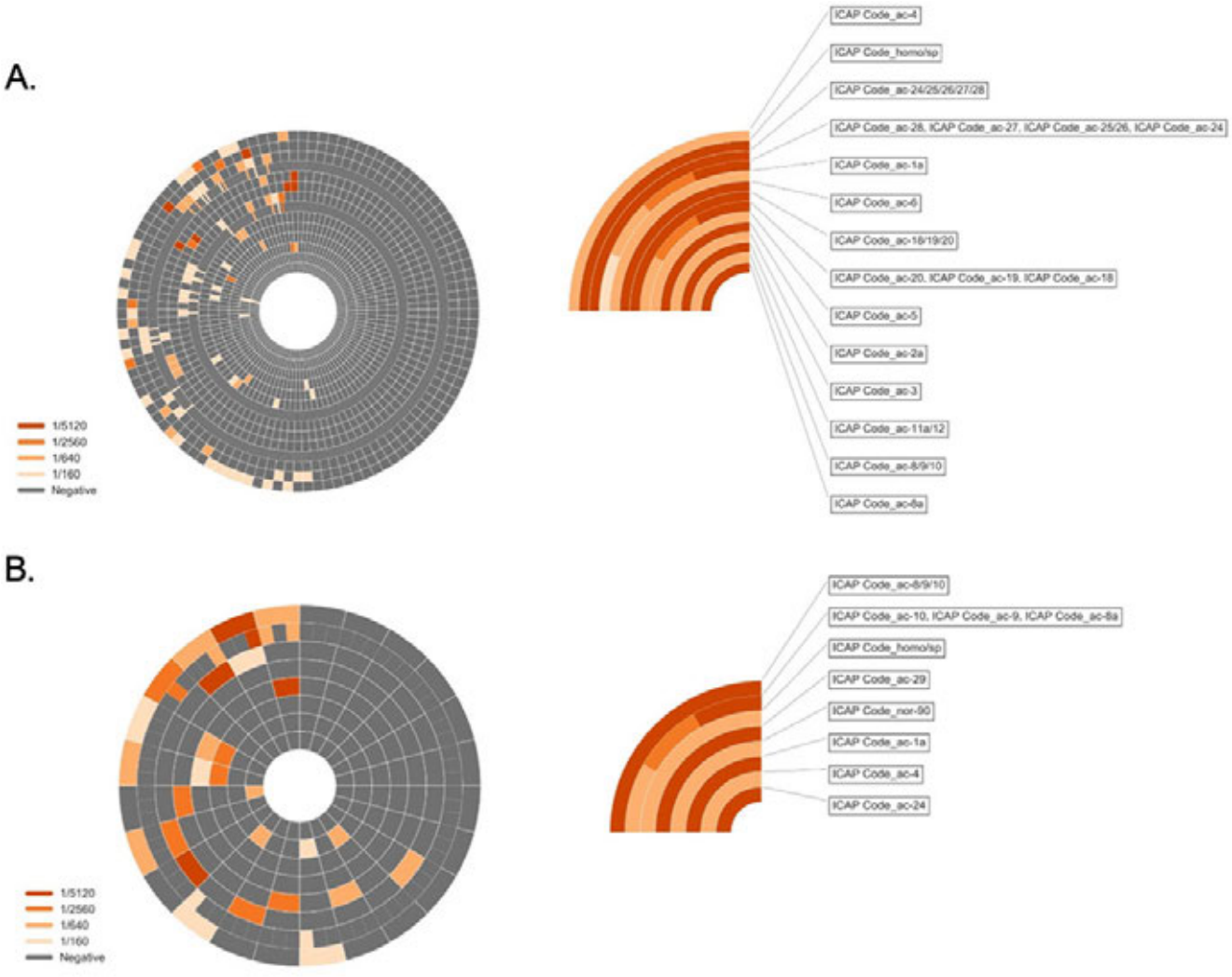

Figure 1. Circular heat maps for anti-nuclear antibody indirect immunofluorescence patterns in localized scleroderma (A) and systemic sclerosis (B) pediatric patients using the international consensus on ANA patterns (ICAP) nomenclature (www.anapatterns.org).

organ involvement compared to pediatric healthy controls. In this study, a wider screening Aab array was used in a study to compare pediatric LS to pediatric systemic sclerosis (SSc).

Methods: A total of 133 pediatric patients (n=109 LS and 24 SSc) were included. Sera was tested for antinuclear antibodies (ANA) using indirect immunofluorescence (IIF) on HEp-2 cells (Inova Diagnostics, San Diego, CA) where a titre of equal to or greater than 1/80 was considered to be positive. Circular heat maps were generated to compare the frequency of ANA patterns in each group. The international consensus on ANA patterns (ICAP, www.anapatterns.org) nomenclature was used to denote ANA IIF pattern nomenclature.

Results: A total of 59/109 (54%) LS patients and 16/24 (67%) SSc patients were ANA positive. LS had the greatest number of distinct ANA patterns (n=11) compared to SSc (n=7) (Figure 1). AC-4 (nuclear speckled) was the most common pattern (23/109, 21%) while AC-8/9/10 (nucleolar) was the least common in LS (2/109, 2%). The opposite was true for SSc where AC-8/9/10 (9/24, 38%) was the most common and AC-4 was uncommon (3/24, 13%). Other ANA IIF patterns such as AC-2 (dense fine speckles) (4/109, 4%) and AC-24 (centrosome) (8/109, 7%) were seen in LS, but was absent or rare in SSc.

Conclusion: Pediatric SSc had higher frequency of ANA positivity compared to pediatric LS, as clinically expected, but not by a high margin. Interestingly, patients with LS had more heterogeneous expression of ANA patterns, including patterns that are rarely seen in SSc such as AC-24 (centrosome). Furthermore, since the centrosome is in the cytoplasm, the centrosome pattern would not be reported by laboratories that only report nuclear IIF patterns as a positive ANA. Therefore, an ANA test that includes nuclear, cytoplasmic, and mitotic patterns should be considered as the screening test in patients with scleroderma, especially LS.

Disclosure: M. Choi, None; **E. Mirizio**, None; **F. Quinteros**, None; **K. Buhler**, None; **M. Fritzler**, Alexion Canada, 7, BioRad, 5, Dr. Fooke Laboratorien GmbH, 5, Euroimmun GmbH, 5, 7, ImmunoConcepts, 7, Inova Diagnostics, 5, 7, 8, Inova Diagnostics Inc. San diego, CA, 5, Inova Dx, Mikrogen GmbH, 5, Werfen International, 5; **K. Torok**, None.

Abstract Number: 0792

Speckle Tracking Echocardiography, a Sensitive Tool to Detect Early Cardiac Dysfunctions in Juvenile Systemic Sclerosis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Juvenile Systemic Sclerosis (JSSc) is a rare connective tissue disease in which cardiac involvement is burdened by high morbidity and mortality. The traditional cardiac imaging techniques seem to be partially appropriate to assess the subclinical course of the disease. In adult-onset SSc, the Speckle Tracking Echocardiography (STE), was shown to be able to identify regional ventricular dysfunctions also in early stages of [1,2]. Aim of our study was to assess the role of STE of the right and left ventricle in order to identify early ventricular dysfunctions in JSSc.

Methods: Consecutive patients with JSSc [3], followed at our Pediatric Rheumatology Center, were periodically evaluated by the cardiology team. For each patient, information on demographic and clinical data, autoantibody profile and treatment were collected. Cardiac investigations, performed at least three times, at baseline (T0), 18 months (T18) and 36 months (T36) included: electrocardiography, conventional echocardiography, STE with assessment of left ventricular global longitudinal strain (GLS) (n.v. < -19%) and right ventricular longitudinal strain (RVLS) (n.v. < -25 %). The course of cardiac involvement during the follow-up was correlated with the overall disease severity, measured by the Juvenile Systemic Sclerosis Severity Score (J4S)[4].

Results: 18 JSSc patients, 12 (67%) females, entered the study (Table 1). ANA were positive in 17 patients (94%), 6 (33%) were anti Scl-70+. At T0, EKG was abnormal in 3 patients, EF was reduced in one survivor to cardiopulmonary arrest (EF=53.8%), the GLS was abnormal in 3 patients, only one with concomitant reduced EF and clinical history of cardiac involvement. A significant correlation between GLS and J4S at T0 was found (r=0.595; p=0.012) (Figure 1). The RVLS resulted abnormal in 5 patients with significant correlation with GLS (r=0.693; p=0.002). At T18, EF remained relatively stable while at T36 it decreased in 7/9 patients, with a mean value of 62.2% (p=0.09). GLS also worsened (from -21.6% to -18.2%; p=0.01). As for treatment, at baseline, none of the patients with pathological GLS was assuming calcium channel blockers (CCB), while all of those taking CCB during follow up had normal GLS. GLS

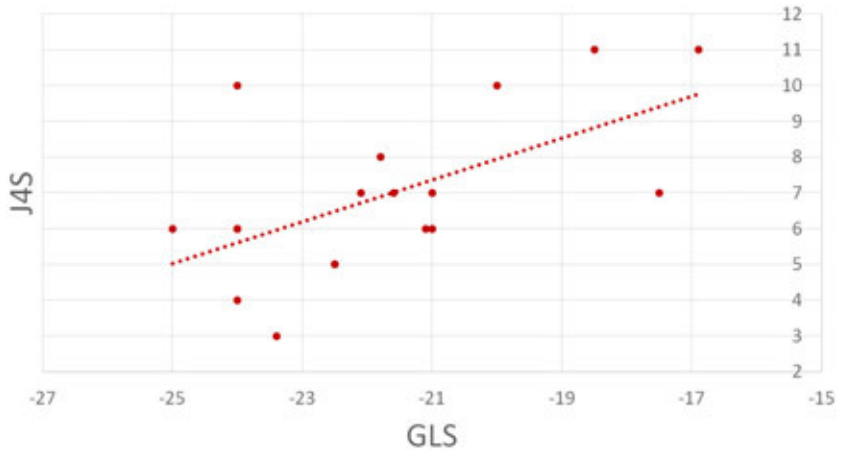

Figure 1. Correlation between J4S and GLS

Table 1 Clinical characteristics of the patients	T0 no.18	T18 no.9	T36 no.9
Sex F (%)	12 (67%)	5 (55%)	5 (55%)
Age (years)	12.3 ± 4.2	13.9 ± 3.4	15.1 ± 4.3
Age at onset (years)	7.8 ± 3	9.5 ± 2.7	9.5 ± 2.7
Disease duration (years)	4.5 ± 3.7	4.4 ± 1.5	5.8 ± 1.2
J4S	6.9 ± 2.3	6.4 ± 2.5	5.8 ± 3.7
mRSS	10.4 ± 9	8.3 ± 6.2	6.5 ± 4.8
Raynaud Phenomenon (% positive)	11 (61.1%)	7 (77.7%)	4 (44.4%)
Lung Involvement (% positive)	9 (50%)	3 (33.3%)	2 (22.2%)
GI Involvement (% positive)	15 (83%)	9 (100%)	7 (77.7%)
Musculoskeletal Symptoms (% positive)	10 (55%)	3 (33.3%)	3 (33.3%)

at baseline showed a significant correlation with the disease severity, measured by J4S (p=0.012). The same was observed for the RVLS (p=0.02).

Conclusion: STE is more sensitive than standard echo to evaluate the cardiac involvement in JSSc. Over time, we observed a gradual worsening of GLS, sign of a progressive left ventricular dysfunction, that was not identified by EF. It is possible that the coronary microvascular damage compromises the subendocardial fibers function which are more sensitive to ischemia and whose contractility is well assessed by GLS [5].

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Disclosure: G. Civieri, None; **B. Castaldi**, None; **G. Martini**, None; **A. Meneghel**, None; **O. Milanesi**, None; **F. Zulian**, None.

Abstract Number: 0793

Rituximab for Rapidly Progressive Juvenile Systemic Sclerosis: A Proof-of-concept Study in Four Patients

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Background/Purpose: Juvenile Systemic Sclerosis (JSSc) is a rare multi-systemic disease characterized by fibrous changes of the skin and internal organs [1]. Patients with "rapidly progressive" SSc present with rapid development of skin induration and life threatening organ involvement, leading to poor prognosis [2, 3]. Recently, Rituximab (RTX), a monoclonal antibody against the CD20 antigen on B cells, has shown to be a promising therapy for adult patients with SSc [4, 5]. We present our experience with four pediatric patients with rapidly progressive JSSc treated with RTX.

Methods: Data on clinical, laboratory and instrumental parameters were collected from four patients with rapidly progressive JSSc treated with RTX for at least one year. Data were recorded at baseline and every 6 months after initiation of therapy. All patients underwent i.v. RTX therapy with four cycles (375 mg/m^2 every 2 weeks), at 3 months intervals. Low dose oral prednisone and mycophenolate mofetil (MMF, 500 mg/m^2/day) were administered between RTX pulses. Skin changes were assessed by mRSS, changes on muscles involvement by CMAS. Variations on BMI, pulmonary function tests (FVC, FEV1, DLCO) and cardiac involvement (LVEF, LVEDV, GLS) were expressed as % change from baseline. J4S was used to assess the overall disease severity [6].

Results: Four JSSc patients (3M, 1F), aged 8-17 years, entered the study (Table 1). Three patients presented with prevalent cardiac involvement. One patient (no.3) presented with severe pulmonary involvement. After one year RTX treatment, all patients showed significant decreased of number/duration of Raynaud Phenomenon attacks and cutaneous involvement. Prior RTX treatment, 2 patients needed an implantable cardioverter defibrillator (ICD) because of episodes of severe ventricular tachycardia (VT). After 12 months of therapy one patient presented improvement LVEF (+19%) and J4S, the other showed a global cardiac improvement (LVEF +37%, LVEDV -18%) and J4S. Both underwent a second year-long treatment with RTX with stabilization of internal organs' involvement. Case 3 showed a significant improvement of the respiratory function (FVC +46%, FEV1 +33%, DLCO +30%) with decreased J4S. Case 4 improved her arrhythmia and muscle strength (CMAS +17%). No major RTX-related side effects were reported.

Conclusion: Rapidly progressive JSSc still carries a high mortality rate. To the best of our knowledge this is the first series of patients with JSSc successfully treated with RTX. Our experience, although in a small cohort, confirms the beneficial effect of this therapy on the life-threatening internal organ involvement, particularly on cardiac function.

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Table 1. Clinical characteristics of the JSSc patients treated with Rituximab

Patient	Sex	Age at onset*	Age at diagnosis *	Age at RTX*	Disease duration pre-RTX*	Organ involvement	ANA (ENA)	Previous DMARD	RTX-related side effects	Follow up duration*
no.1 (LG)	M	6.8	7.8	7.9	1.1	V, Sk, MS, GI, **P**	1:640	no	no	1,1
no.2 (BG)	M	10.7	14.6	14.6	3.9	V, Sk, GI, **Ca**	1:640 (SCL-70)	no	diarrhea	2
no.3 (VO)	M	15.4	15.9	17.4	2.1	V, Sk, GI, **Ca**	1:1280 (RNA pol III)	no	skin rash low-grade fever	2
no.4 (SA)	F	11.5	11.8	17.1	5.6	V, Sk, MS, GI, **P, Ca**	1:640 (SCL-70)	CYC	flushing	1

Legend: V: vascular involvement; Sk: involvement; MS: Musculo-skeletal involvement; GI: Gastrointestinal involvement; P: Pulmonary involvement; Ca: Cardiac involvement; RTX: rituximab; CYC: cyclophosphamide *years, months

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Abstract Number: 0794

Mycophenolate Mofetil for the Treatment of Severe or Methotrexate-refractory Juvenile Localized Scleroderma

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile Localized Scleroderma (JLS), includes a number of conditions characterized by skin thickening with varying degree of severity. Many patients, particularly those with the linear subtype, develop deformities and joint limitation or, as in scleroderma of head/face, functional and cosmetic problems as well as involvement of eyes and brain [1]. Although represents the first-line treatment for JLS [2], for some patients Methotrexate (MTX) is ineffective or not well tolerated. We investigated the safety and efficacy of mycophenolate mofetil (MMF) in a cohort of patients with severe or MTX-refractory JLS.

Methods: Consecutive JLS patients with severe or MTX-refractory followed at our Pediatric Rheumatology Unit were treated with MMF at doses varying from 600-1200 mg/m2/day bid. The disease was defined as active by the appearance of new lesions or increasing size of pre-existing ones, clinical signs of active inflammation, such as erythema, and/or by detection of disease activity by thermography when the affected area was more than 0.5°C warmer than the contralateral side or the surrounding skin depending on the site of the lesion itself. Outcome was defined as active disease (A), clinical remission on medication (CRM) (inactive disease for at least 6 consecutive months ON treatment) and Clinical Remission (CR) (inactive disease for at least 24 consecutive months OFF treatment).

Results: Twenty one patients (9M, 12F) entered the study. The JLS clinical subtypes [3] were circumscribed (C) morphea (2 pts), generalized morphea (GM) (1), linear scleroderma limbs (LSL) (5), linear scleroderma head/face (LSHF) (4), pansclerotic morphea (PM) (3), mixed subtype (MiX) (6). The age at onset of the disease was 8.2 yrs (range 0–14), disease duration at diagnosis was 10 months (range 0–3 years). Before starting MMF, 19 patients have been treated with MTX and low dose corticosteroids oral in 13 pts, IV pulse in 6. In this group, MMF was started because of MTX lost efficacy (10) or relapse after MTX withdrawal (9). In one patient MMF was started because of MTX-related anaphylaxis and one patient with linear head/face congenital scleroderma with cerebral involvement. After 7.4 year follow up (range 2-14.7) CRM was present in 8 patients (38%) and sustained CR in 8 (38%). Five patients (24%) (1 PM, 2 LSHF, 2 MiX) have still active disease despite MMF.

Conclusion: MMF is effective in severe and/or MTX-refractory JLS and generally well tolerated. Our study, although with the limits of being small-sized and retrospective, confirms that MMF represents a valid alternative to MTX, particularly in severe cases, when extracutaneous manifestations are present, or as complementary to MTX, when it loses efficacy. Further controlled studies are needed to confirm these data or to proof its efficacy as first line treatment of JLS.

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Abstract Number: 0795

Is the Presentation and Severity Different of the Juvenile Diffuse and Limited Subtype Systemic Sclerosis? Results of Juvenile Scleroderma Inception Cohort

Ivan Foeldvari,[1] Jens Klotsche,[2] Ozgur Kasapcopur,[3] Amra Adrovic,[4] Kathryn Torok,[5] Valda Stanevicha,[6] Maria Teresa Terreri,[7] Flavio Sztajnbok,[8] Ekaterina Alexeeva,[9] Jordi Antón,[10] Brian Feldman,[11] Maria Katsicas,[12] Vanessa Smith,[13] Tadej Avcin,[14] Rolando Cimaz,[15] Mikhail Kostik,[16] Thomas Lehman,[17] Walter Sifuentes-Giraldo,[18] Natalia Vasquez-Canizares,[19] Simone Appenzeller,[20] Mahesh Janarthanan,[21] Monika Moll,[22] Dana Nemcova,[23] Maria José Santos,[24] Dieneke Schonenberg,[25] Christina Battagliotti,[26] Lillemor Berntson,[27] Blanca Bica,[28] Juergen Brunner,[29] Patricia Costa Reis,[30] Despina Eleftheriou,[31] Liora Harel,[32] Gerd Horneff,[33] Tilmann Kallinich,[34] Dragana Lazarevic,[35] Kirsten Minden,[36] Susan Nielsen,[37] Farzana Nuruzzaman,[38] Anjali Patwardhan,[39] Yosef Uziel,[40] Daniela Kaiser,[41] and Nicola Helmus[1], [1]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, Germany, [2]German Rheumatism Research Center, Berlin, Germany, [3]Department of Pediatric Rheumatology, Istanbul University-Cerrahpasa,[4]Cerrahpaşa Tıp Fakültesi, Istanbul, Turkey, [5]UPMC Children's Hospital of Pittsburgh, Pittsburgh, [6]Riga Stradins University, Riga, Latvia, [7]Pediatric Rheumatology Unit, Universidade Federal de São Paulo, São Paulo, Brazil, [8]Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, [9]National Medical Research Center of Children`s Health, Moscow, Russia, [10]Hospital Sant Joan de Déu, Barcelona, Spain, [11]University of Toronto & The Hospital for Sick Children, Toronto, ON, Canada, [12]Hospital de Pediatria, Buenos Aires, Argentina, [13]Dept. of Rheumatology, Ghent University Hospital, Ghent, Belgium; Dept. of Internal Medicine, Ghent University, Ghent, Belgium; Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center (IRC), Ghent, Belgium, Gent, Belgium, [14]Ljubljana University Medical Centre, Ljubljana, Slovenia, [15]University Hospital Meyer, Florence, Italy, [16]Saint-Petersburg State Pediatric Medical University, Saint-Petersburg, Russia, [17]Hospital for Special Surgery, New York, [18]Hospital Universitario Ramón y Cajal, Madrid, Spain, [19]Children's Hospital at Montefiore, Bronx NY, [20]UNICAMP Universidade Estadual de Campinas, Sao Paulo, Brazil, [21]Sri Ramachandra University, Chennai, India, [22]University of Tuebingen, Tuebingen, Germany, [23]General University Hospital, Prague, Czech Republic, [24]Rheumatology department, Hospital Garcia de Orta, Almada, Portugal, [25]Amsterdam UMC, Amsterdam, Netherlands, [26]Children's Hospital Dr. Orlando Alassia, Santa Fee, Argentina, [27]Uppsala University Hospital, Uppsala, Sweden, [28]Hospital Universitário Clementino Fraga Filho (HUCFF/UFRJ), Rio de Janeiro, Brazil, [29]Tirol Kliniken, Innsbruck, Austria, [30]Hospital de Santa Maria, Lisbon, Portugal, [31]Great Ormond Street Hospital, London, United Kingdom, [32]Tel Aviv University, Tel Aviv, Israel, [33]Asklepios Clinic Sankt Augustin, Sankt Augustin, Germany, [34]Charite, Berlin, Germany, [35]KC Niš, Niš, Serbia, [36]German Rheumatism Research Center and Charité University Medicine, Berlin, Germany, [37]Department of Pediatrics, Rigshospitalet, Copenhagen University Hospital, [38]Stony Brook Children's Hospital, Stony Brook, NY, [39]University of Missouri, Columbia, [40]Meir Medical Center, Kfar Saba, Israel, [41]Luzerner Kantonsspital | Kinderspital, Luzern, Switzerland

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

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Background/Purpose: Juvenile systemic scleroderma (jSSc) is an orphan disease with an estimated prevalence of 1 in 1 000 000 children. In the adult systemic scleroderma population there are large differences regarding organ pattern and severity between diffuse and limited subtypes.

Methods: We reviewed all patients of juvenile scleroderma inception cohort (jSScC) at the time of inclusion till 15th May 2019. The jSScC is a cohort, where patients, who fulfill the adult 2013 classification criteria , are age under 18 at the time of inclusion and developed the first non-Raynaud before the age of 16 years are included.

Results: 131 patients were included, 72.5% with diffuse subtype. 75% females in the diffuse (djSSc) and 71% in the limited subtype(ljSSc). 86% of patients were Caucasian. Mean age of onset of Raynauds was 9.7 years in the djSSc and 10.7 years in the ljSSc (p=0.8). Mean age of onset of the non-Raynauds was 9.9 years in the djSSc and 11.2 years in the ljSSc (p=0.7). Mean disease duration at time of inclusion was 3.4 years in the djSSc and 2.4 years in the ljSSc There was no significant difference in the ANA, anti-Scl-70 and anticentromere positivity. The mean modified skin score was significantly higher in the djSSc (17.3 compared 7.1, (p=0.3)). They were significantly more teleangiectasia in the djSSc group (39% compared to 19% (p=0.003)). Cardiac involvement was significantly higher in the ljSSc group (19% compared to 3% (p=0.005) There was no significant difference in the proportion of ILD, pulmonary hypertension, gastrointestinal involvement and renal involvement. No renal hypertension was observed. There was significantly more muscle weakness observed in the ljSSc group (38% compared to 17% (p=0.029)). There was no significant difference regarding number of joints with contractions. Physician rated disease activity (40 compared to 29, on 100 mm VAS scale (p=0.013)) and disease damage (37 compared 18, on a 100 mm VAS scale (p< 0.001)) was significantly higher in the djSSc. This significant difference was not found in rating of patients of disease damage and activity.

Conclusion: ljSSc and djSSc seems to be more similar than in adult patient with these subtypes, although physician rating of disease activity and damage found the djSSc more severe.

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Under Detection of Interstitial Lung Disease in Juvenile Systemic Sclerosis (jSSc) Utilizing Pulmonary Function Tests: Results from the Juvenile Scleroderma Inception Cohort

Ivan Foeldvari,[1] Bernd Hinrichs,[2] Kathryn Torok,[3] Maria José Santos,[4] Ozgur Kasapcopur,[5] Amra Adrovic,[6] Valda Stanevicha,[7] Flavio Sztajnbok,[8] Maria Teresa Terreri,[9] Ekaterina Alexeeva,[10] Jordi Antón,[11] Maria Katsicas,[12] Vanessa Smith,[13] Tadej Avcin,[14] Rolando Cimaz,[15] Mikhail Kostik,[16] Thomas Lehman,[17] Walter Sifuentes-Giraldo,[18] Simone Appenzeller,[19] Mahesh Janarthanan,[20] Monika Moll,[21] Dana Nemcova,[22] Dieneke Schonenberg,[23] Christina Battagliotti,[24] Lillemor Berntson,[25] Blanca Bica,[26] Juergen Brunner,[27] Patricia Costa Reis,[28] Despina Eleftheriou,[29] Liora Harel,[30] Gerd Horneff,[31] Tilmann Kallinich,[32] Dragana Lazarevic,[33] Kirsten Minden,[34] Susan Nielsen,[35] Farzana Nuruzzaman,[36] Anjali Patwardhan,[37] Yosef Uziel,[38] and Nicola Helmus[1], [1]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, Germany, [2]Asklepios Klinik Nord - Heidberg, Hamburg, Germany, [3]UPMC Children's Hospital of Pittsburgh, Pittsburgh, [4]Rheumatology department, Hospital Garcia de Orta, Almada, Portugal, [5]Department of Pediatric Rheumatology, Istanbul University-Cerrahpasa, Istanbul, Turkey, Istanbul, Turkey, [6]Cerrahpaşa Tıp Fakültesi, Istanbul, Turkey, [7]Riga Stradins University, Riga, Latvia, [8]Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, [9]Pediatric Rheumatology Unit, Universidade Federal de São Paulo, São Paulo, Brazil, [10]National Medical Research Center of Children`s Health, Moscow, Russia, [11]Hospital Sant Joan de Déu, Barcelona, Spain, [12]Hospital de Pediatria, Buenos Aires, Argentina, [13]Dept. of Rheumatology, Ghent University Hospital, Ghent, Belgium; Dept. of Internal Medicine, Ghent University, Ghent, Belgium; Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center (IRC), Ghent, Belgium, Gent, Belgium, [14]Ljubljana University Medical Centre, Ljubljana, Slovenia, [15]University Hospital Meyer, Florence, Italy, [16]Saint-Petersburg State Pediatric Medical University, Saint-Petersburg, Russia, [17]Hospital for Special Surgery, New York, [18]Hospital Universitario Ramón y Cajal, Madrid, Spain, [19]UNICAMP Universidade Estadual de Campinas, Sao Paulo, Brazil, [20]Sri Ramachandra University, Chennai, India, [21]University of Tuebingen, Tuebingen, Germany, [22]General University Hospital, Prague, Czech Republic, [23]Amsterdam UMC, Amsterdam, Netherlands, [24]Children's Hospital Dr. Orlando Alassia, Santa Fee, Argentina, [25]Uppsala University Hospital, Uppsala, Sweden, [26]Hospital Universitário Clementino Fraga Filho (HUCFF/UFRJ), Rio de Janeiro, Brazil, [27]Tirol Kliniken, Innsbruck, Austria, [28]Hospital de Santa Maria, Lisbon, Portugal, [29]Great Ormond Street Hospital, London, United Kingdom, [30]Tel Aviv University, Tel Aviv, Israel, [31]Asklepios Clinic Sankt Augustin, Sankt Augustin, Germany, [32]Charite, Berlin, Germany, [33]KC Niš, Niš, Serbia, [34]German Rheumatism Research Center and Charité University Medicine, Berlin, Germany, [35]Department of Pediatrics, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark., Copenhavn, Denmark, [36]Stony Brook Children's Hospital, Stony Brook, NY, [37]University of Missouri, Columbia, [38]Meir Medical Center, Kfar Saba, Israel

SESSION INFORMATION

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Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

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Background/Purpose: Juvenile systemic sclerosis(jSSc) is an orphan disease with a prevalence in around 3 in a million children [1]. Pulmonary involvement in jSSc occurs in approximately 40 % in the inception cohort [2]. Traditionally in jSSc, pulmonary function testing (PFT) with FVC and DLCO are used for screening and computed tomography (HRCT) was more reserved for those with abnormal PFTs. More recently, it has become apparent that PFTs might not be sensitive enough for detecting ILD in children.

Methods: Utilizing a prospective international juvenile systemic scleroderma cohort (JSScC) [2], to determine if pulmonary screening with FVC and DLCO is sufficient enough to assess the presence of interstitial lung disease in comparison to CT evaluation.

The JSScC cohort database was queried for available patients with recorded PFT parameters and HRCT performed to determine sensitivity of PFTs detecting disease process.

Table 1. Diagnostic test properties of FVC as a test for ILD detection.

	Disease + (ILD Yes on HRCT)	Disease – (ILD No on HRCT)	Total
Test + (FVC <80%)	a) True positive = 13	c) False positive = 7	a+c =20 (+Test)
Test – (FVC>80%)	b) False negative = 20	d) True negative = 27	b+d =47 (-Test)
Total	a +b = 33 (+Disease)	c+d = 34 (- Disease)	

Results: Of 129 patients in the jSScC, 67 patients had both CT imaging and an FVC reading from PFTs for direct comparison. DLCO readings were also captured but not in as many patients with tandem HRCT (n =55 DCLO and HRCT scan). Therefore, initial analyses focused on the sensitivity, specificity and accuracy of the FVC value from the PFTs to capture the diagnosis of interstitial lung disease as determined by HRCT. Table 1 presents these diagnostic test evaluations for the FVC. Overall, 49% of the patients had ILD determined by HRCT, with 60% of patients having normal FVC (>80%) with positive HRCT findings, and 24% of patients having normal DLCO (> 80%) with positive HRCT findings. Fourteen percent (n = 3/21) of patients with both FVC and DLCO values within the normal range had a positive HRCT finding.

Conclusion: The sensitivity of the FVC in the JSScC cohort in detecting ILD was only 39%. Relying on PFTs alone for screening for ILD in juvenile systemic sclerosis would have missed the detection of ILD in almost 2/3 of the sample cohort, supporting the use of HRCT for detection of ILD in children with SSc. In addition, the cut off utilized, of less than 80% of predicted FVC or DLCO could be too low for pediatric patients to exclude beginning ILD. This pilot data needs confirmation in a larger patient population.

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Abstract Number: 0797

Characteristics of Coexisting Localized Scleroderma and Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Localized scleroderma (LS), including morphea and linear scleroderma, is an autoimmune disease where excessive collagen deposits underneath the skin lead to thickening, scarring, and fibrosis. Often limited to the skin, affecting only the outer layer and subcutaneous tissues, this disease may be one manifestation of a diffuse systemic inflammatory process. LS coexisting with juvenile idiopathic arthritis (JIA) is less well-described but has been reported in as many as 20% in a recent cohort of 53 LS patients. Herein, we describe a cohort of 8 children with both LS and JIA. The objective of this study is to determine the characteristics of JIA in children with LS and response to treatment regimens.

Methods: A retrospective chart review was completed on patients less than 19 years of age who were diagnosed with either morphea or linear scleroderma at a single institution from 2004-2018. Patients were identified using ICD-9 and ICD-10 diagnostic codes. Records were reviewed for additional diagnostic codes, exams, and laboratory findings confirming coexisting JIA.

Results: A total of 87 patients with a diagnosis of either morphea or linear or circumscribed scleroderma were identified. Eight (9%) also had coexisting JIA per diagnostic codes with active arthritis as documented by a pediatric rheumatologist. Median age of initial rheumatic disease diagnosis was 7.5 years. A majority of patients with both LS and JIA were female (62.5%). Half of the patients (n=4, 50%) had LS lesions over arthritic joints. JIA subtype varied widely with 3 (37.5%) patients with rheumatoid factor (RF) negative polyarticular JIA, 2 (25%) patients with oligoarticular JIA, 2 (25%) patients with psoriatic JIA, and 1 (12.5%) with enthesitis-related JIA. The timing of onset of LS and JIA also varied widely. Three (37.5%) patients had LS lesions preceding the appearance of clinical arthritis on exam, and three (37.5%) patients had arthritis before the appearance of LS. Two (25%) patients had both LS and arthritis at time of diagnosis. Two (25%) of the 8 patients had a positive ANA screen, both less than or equal to 1:320 with negative extractable nuclear antigen panels. All patients received methotrexate (MTX) during their disease course with only three (37.5%) receiving systemic steroids during treatment. All 8 patients had resolution of LS lesions. With respect to active joint count, 1 patient achieved remission on MTX alone, and 1 patient achieved remission on MTX and a tumor-necrosis factor inhibitor (TNFi). Six of the 8 patients had active arthritis on combination MTX and TNFi therapy.

Conclusion: In this cohort of pediatric patients with LS, 9% had coexisting JIA, which is lower than the 20% reported in previous studies. The characteristics of this cohort who had both LS and JIA varied widely. Presence of autoantibodies, including ANA titer, was inconsistent. All patients received MTX initially with resolution of LS lesions. However, the majority failed to respond to MTX and TNFi combination therapy and continued to have active arthritis. These results suggest that JIA coexisting with LS may be less likely to respond to traditional JIA therapies.

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Abstract Number: 0798

Development of Large Vessel Vasculitis Including Aortitis in a Patient with Deficiency of the IL-1 Receptor Antagonist (DIRA) Points to Converging Roles of IL-1 and TNF in Vascular Pathogenesis Recapitulating Findings from a Murine Model

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Deficiency of interleukin-1-receptor antagonist (DIRA) is a rare autoinflammatory disease caused by autosomal recessive loss of function mutations in *IL1RN* and characterized by early-onset generalized pustulosis, aseptic multifocal osteomyelitis, and elevation of acute-phase reactants. In a DIRA mouse model, aortitis can develop in a TNF-α dependent manner, no DIRA patients with large vessel vasculitis have previously been reported.

Methods: We performed clinical, genetic and radiographic evaluation of a patient with DIRA who developed an intra-cranial hemorrhage on anakinra treatment and had persistent low-grade elevation of acute phase reactants. We performed including whole exome sequencing and PET CT.

Results: A Puerto Rican patient previously reported with a homozygous 175-kb deletion and multiple comorbidities including severe bone deformities, developmental delay, generalized hypotonia at birth, pyoderma gangrenosum, developed a left intra-cranial hemorrhage at age 12. Follow-up work up of potential pathogenic causes revealed right-sided carotiditis and aortitis on PET CT images. Vascular findings were associated with carotid stenosis and an ascending aortic aneurism. Vascular abnormalities occurred while on optimal doses of anakinra (3.33 ±1.82 mg/kg/day) but persistently elevated inflammatory markers(CRP 5.41 ±3.08 mg/L and ESR 21.40 ±13.99 mm/hr). No other patient with DIRA was diagnosed with large vessel. vasculitis. While IL-1 receptor antagonist (*Il-1ra)* knock out (KO) murine models are prone to the development of vascular diseases, different genetic backgrounds modify vascular inflammation and injury. *Il1ra* KO on a C57BL/6J background is associated with intima damage and the development of atherosclerosis and *Il1ra* KO BALB/c mice develop aortitis that is responsive to TNF inhibition. Insights into the murine model suggested addition of TNF inhibitor after failure of increased doses of anakinra and steroids in achieving disease control. Acute phase reactants normalized after treatment with infliximab. Genetic analyses of rare variants that may contribute to the development af large vessel vasculitis are ongoing.

Conclusion: The development of large vessel vasculitis including carotitis and aortitis in a patient with DIRA who responds to combination therapy of IL-1 and TNF inhibition suggests a role of TNF in the development of large vessel vasculitis and may provide insights into pathways that may shed light on the pathogenesis of other forms of large vessel vasculitis. Strict monitoring of adverse events is required given the increased risk for opportunistic infections.

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Abstract Number: 0799

Application of the Autoinflammatory Disease Activity Index (ADDI) to a Cohort of Patients in a Tertiary Hospital

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoinflammatory diseases (AIDs) cause chronic systemic inflammation that can damage multiple organs. Recently, the ADDI index has been developed and validated in the four most common monogenic AIDs, Cryopyrin-associated Periodic Syndrome (CAPS), Familial Mediterranean Fever (FMF), Mevalonate Kinase Deficiency (MKD) and Tumor Necrosis Factor Receptor-associated Periodic Fever Syndrome (TRAPS). The use of ADDI index could also be of great value in other AIDs. We sought to assess the application of ADDI in patients with the four most common monogenic diseases and other AIDs. To accomplish this objective a detailed cohort of patients with different AIDs is presented.

Methods: All patients with AIDs followed in the Pediatric Rheumatology Unit from Hospital Universitari Vall d'Hebron were identified. A cross- sectional, descriptive study was performed applying ADDI by two pediatric rheumatologists (EM, ML). CRP mg/dl, amyloid protein (AP) mg/L, ESR mm/h and protein/creatinine rate (mg/g Cr) were performed at the moment ADDI was applied. Disease duration and current treatment were assessed. The continuous variables are presented as mean and standard deviation (mean ± SD) and categorical variables are presented by percentages. Kappa (k) coefficient was calculated. Differences between two groups (sex and GC intake) was compared using Student's t-test and a significance level of < 0.05 was considered.

Results: A total of 41 patients with AIDs were included, 61% were female, with a median age of 20 ± 11.9 years at inclusion. Disease duration was 11 ± 8.2 years. AIDs included were 11 patients with FMF (26.8%), TRAPS n=4 (9.8%), MKD n=3 (7.3%), CAPS n= 2 (4,9%), Blau syndrome n= 7 (17.1%), SAVI syndrome n=3 (7.3%), CRMO n=4 (9.8%), PFAPA n=2 (4.9%), APLAID n=1 (2.4%), Stickler syndrome n=1 (2.4%), and 3 unknown AIDs with genetic test negative n=3 (7.3%). Current treatment is variable among patients, 6 (15.8%) are taking DMARDs, 9 (23.7%) Colchicine, 8 (21.1%) Anakinra, 13 anti-TNF therapy (34.2%), 1 (2.6%) Ruxolitinib and 1 (2.6%) Abatacept. Only 6 patients were receiving steroids with mean prednisone dose of 7.5 mg/day. The global ADDI mean score was 2.3 ± 2.2. No differences were found between gender and ADDI (male 2.19, female 1.9, P= 0.68). Musculoskeletal domain (MSK) shown the highest score with 1.02, followed by the ocular domain with 0.42. The patient with APLAID syndrome had the highest score of 6 followed by Blau syndrome with 4.71. FMF has the lowest score with 0.83. Patients with GC intake had a highest ADDI score than patients without GC treatment (3.7 vs 1.63 P=0.0018). Laboratory test results were mean ESR 27.2 ± 26.7mm/h, CRP 0.7 ± 1.3 mg/dl, AP 13.9 ± 18.6mg/L. Proteinuria was present in 2 patients with mean 286.5 ± 246.1mg/g. The k statistic showed an excellent agreement between two rheumatologist (k=0.98, P< 0.001). EM and ML applied ADDI in 5-10 minutes average.

Conclusion: ADDI is a feasible index suitable to measure damage in a single patient. In our cohort the mean ADDI index was low and MSK has the highest score. GC intake was associated with a higher ADDI score. Knowing the difficulties of applying an unified index for all diseases, ADDI may be supportive in other AIDs and longitudinal cohorts.

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Cryopyrin-Associated Periodic Syndrome in Korea: 19 Years of Experience

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Background/Purpose: Cryopyrin-associated periodic syndrome (CAPS) is rare auto-inflammatory disorder characterized by recurrent episodes fever with variable manifestation of systemic inflammation such as urticarial skin rash, joint destruction, sensorineural hearing loss (SNHL) and neurologic problems. It includes familial cold auto-inflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal onset multisystem inflammatory disease (NOMID). Pathogenic variants in NLRP3 are thought to be responsible for most cases of CAPS by excessive production of interleukin (IL)-1β.

Methods: Patients with diagnosis of CAPS who visited Seoul National University Children's Hospital from January 2000 to December 2018 were eligible for inclusion. Retrospective analysis was performed by review of medical records. Clinical information on symptoms and signs, inflammatory markers, pure tone audiometries, simple radiographs of joints, ophthalmoscopies, and other relevant data were collected. Molecular analysis for NLRP3 was performed by Sanger sequencing. Finally, clinical response to recombinant non-glycosylated human IL-1 receptor antagonist (anakinra) was determined by comparing symptoms and signs and changes in test results before and after the treatment.

Results: Sixteen patients were identified (11 NOMID, 3 FCAS, 2 MWS). Total of 112 person years were followed. Most consistent symptoms were fever and rash, present in all cases followed by joint symptoms (n=15), SNHL (n=9). Screening pure tone audiometry revealed high frequency hearing loss in 67% (4/6) of patients with normal hearing, including one FCAS patient. Eleven patients had onset within 1 week after birth, three patients within 3 months. Most common initial diagnoses were milk allergy (n=5), juvenile idiopathic arthritis (n=4), and neonatal sepsis (n=3). Diagnostic delay was common, ranging from 1 month to 17 years (median = 22 months). Pathogenic variation in NLRP3 gene was confirmed in fifteen patients. Anakinra was started for fifteen patients. All patients on anakinra had marked reduction of fever and rash, and 57.5% (5/8) of patients with SNHL had improved or maintained stable hearing. Three of five patients with high frequency hearing loss had improved or maintained stable hearing threshold at 8KHz. Five of eight patients with joint destruction restored normal joint anatomy. Mean initial anakinra dose was 1.19mg/kg/day,

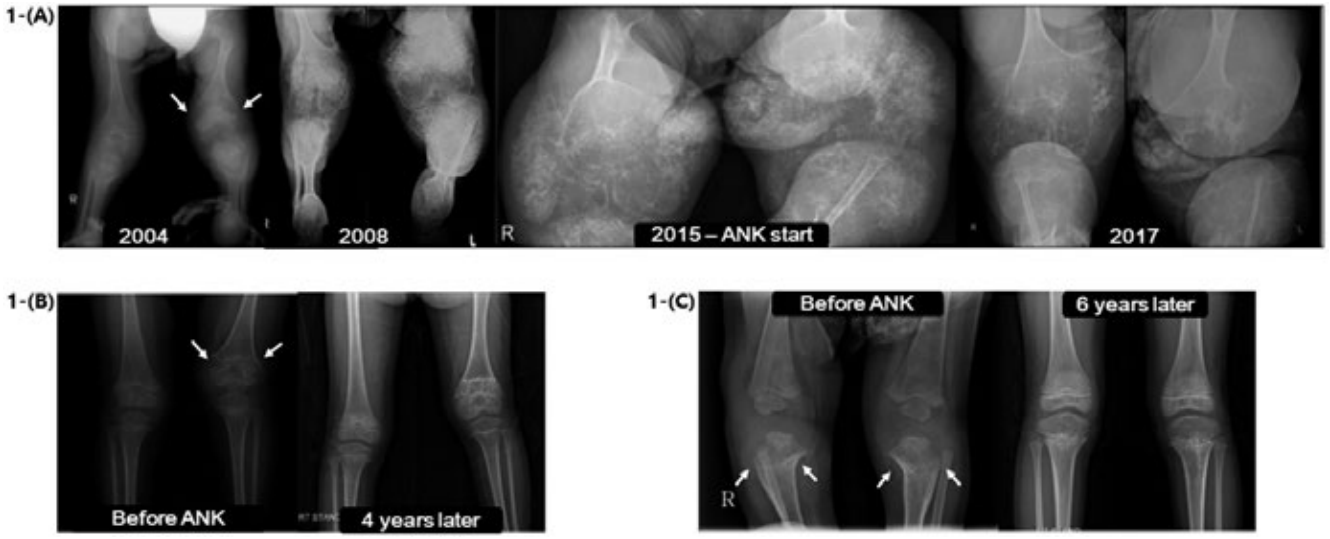

Figure 1. Simple radiographs of knee joint. White arrows indicate metaphyseal fraying and cupping and widening of the growth plate. 1-(a). Patient 2 with irreversible hip, knee, and ankle joint destruction. This patient started treatment with Anakinra (ANK) 14 years after diagnosis. 1-(b). Patient 10 with asymmetric distal femur involvement. This patient developed limb length discrepancy despite treatment. 1-(c). Patient 6 who restored normal joint anatomy after use of anakinra 10 months after diagnosis.

and mean final anakinra dose was 2.02mg/kg/day. Most common reason for dose escalation was relapsing clinical symptoms such as fever and rash. One patient with SNHL and one patient with high frequency hearing loss experienced improvement of hearing only after dose escalation. The most common adverse events were injection site erythema and infection.

Conclusion: This study represents the largest cohort of CAPS patients in Korea. High index of suspicion and early intervention with anakinra is crucial to prevent potentially devastating outcomes. In addition this study suggest regular audiometry is necessary and hearing problem maybe the most sensitive factor to determine anakinra dose.

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Abstract Number: 0801

Preliminary Analysis of Hearing Loss in a Neonatal-Onset Multisystem Inflammatory Disease (NOMID) Cohort Followed over a Mean of 10 Years: Normal Hearing at Baseline and Early Treatment with Anakinra Area Associated with Maintenance of Normal Hearing

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

DEMOGRAPHICS		NOMID N=39
	Age at diagnosis *Median (range) years*	7 (1-28)
	Gender *(%)*	Female (59)
	Ethnicity *%White (%Hispanic)*	64 (10)
Genetic Diagnosis	*NLRP3 mutations*	33 Germline 6 Gonosomal mosaicism
Follow up duration	*Years* *Median (range)*	10 (4-17)
Age at treatment initiation	*Years* *Median (range)*	7 (1-28)
CLINICAL CHARACTERISTICS AT BASELINE		
	ESR mm/h *Median (range)*	57 (11-143)
	CRP mg/L *Median (range)*	57 (13-157)
	Cochlear enhancement on MRI (%)	28 (72)
CLINICAL CHARACTERISTICS FOLLOW UP*		
	ESR mm/h *Median (range)*	8 (2-31)
	CRP mg/L *Median (range)*	1.3 (<0.1-20)
	Cochlear enhancement on MRI (%)	16 (41)

Table 1. Patient characteristics CRP (0-4.99 mg/L), ESR (0-42 mm/h) *6 patients had disease flare, with high CRP/normal ESR in follow up

Background/Purpose: Neonatal-onset multisystem inflammatory disease (NOMID), caused by gain-of-function mutation in the NLRP3 inflammasome, presents with systemic inflammation, rash, eye inflammation, aseptic meningitis and sensorineural hearing loss. We assessed hearing loss progression in NOMID patients on anakinra treatment over median of 10 years.

Methods: 39 patients (23 female, median age at baseline 7y) were followed (median 10y) after starting therapy with IL-1 blocker Anakinra (table 1). All patients were on continuous therapy with dose adjustment for weight gain and disease flare (1). First audiograms obtained at the time of treatment initiation (or when able to cooperate) were compared to an audiogram obtained after a median of 10 (4 to 17) years on treatment. Pure-tone averages at 500, 1000, 2000, 4000 Hz (4F-PTA) and high frequency air conduction averages for 6000, 8000 Hz (HF-PTA) were calculated. For the current analysis, the first and last audiograms were compared. Normal hearing is defined as hearing threshold < 20 dB, mild hearing loss 20 to 40 dB, moderate loss 40 to 70 dB and severe loss is hearing threshold greater than 70 dB, 4F-PTA and HF-PTA were separately assessed. A change from one category to another (using 4F-PTA) was consideredPresence of cochlear enhancement was obtained from reports of 1.8 mm sections, contrast-enhanced FLAIR-MRI through the inner ear. The association between hearing loss progression and age at start of treatment, as well as presence of cochlear enhancement in last MRI was assessed using Fisher's exact test.

Results: Inflammatory markers normalized in 33 (85%) but cochlear enhancement persisted in 16 patients (41%) on treatment. At baseline, 34 (44%) ears had normal hearing on the 4F-PTA, only 28 (36%) ears had normal hearing on HF-PTA (figure 1).

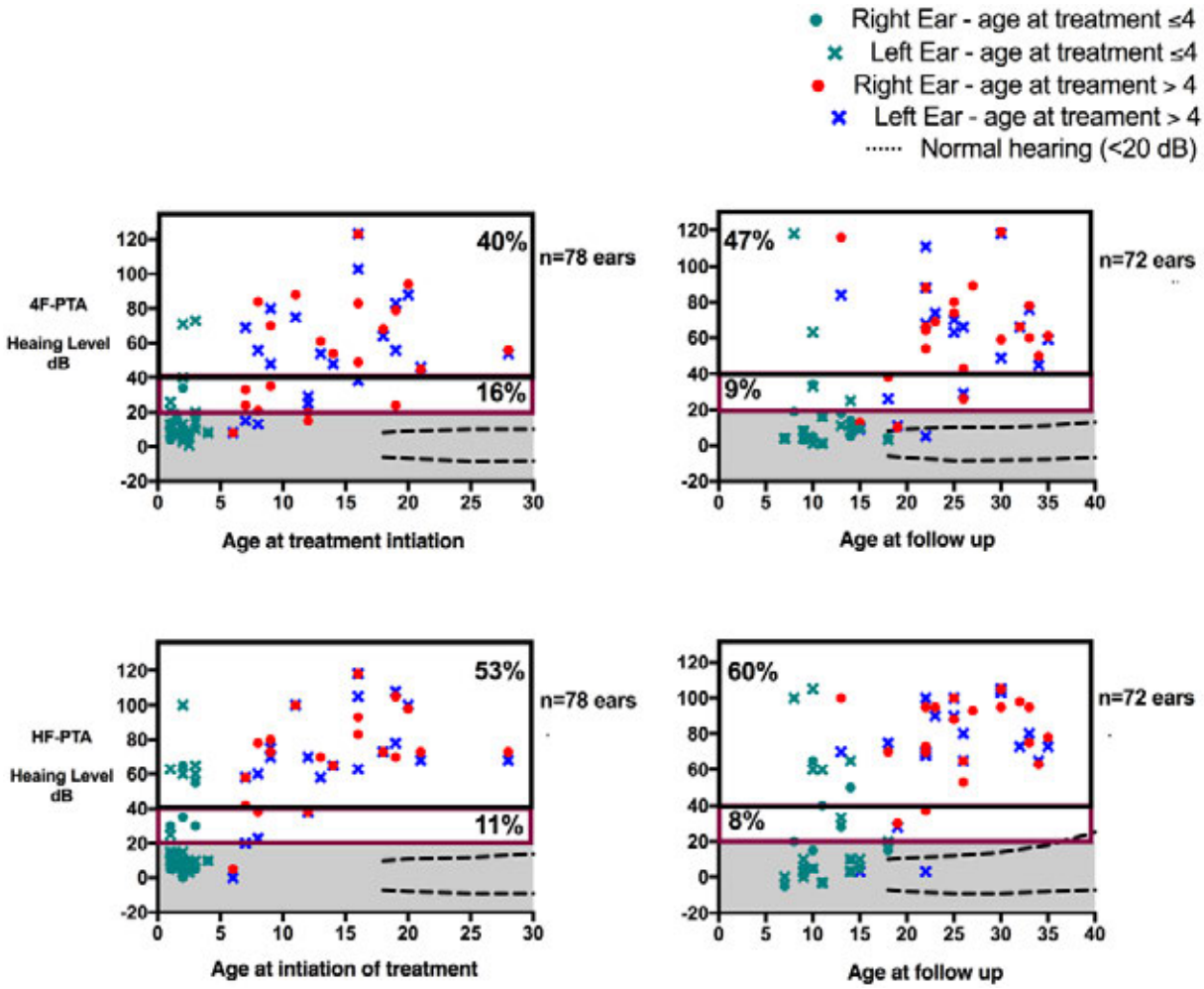

Figure 1. Ears with normal, mild and moderate to severe hearing loss at baseline and 10-year follow up are graphed separately based on values of 4F-PTA (500, 1000, 2000, 4000 Hz) (upper panels) and high frequency HF- PTA (6000, 8000 Hz) (lower panels). Normal hearing is defined as thresholds <20 dB, mild hearing loss is defined as 20 to 40 dB, and moderate to severe hearing loss is defined as hearing thresholds greater than 40 dB. From 14 patients who had normal hearing at baseline in both ears and were treated age 4 or younger, 13 retained hearing in follow up (green color). Dashed lines denote the 5th and 95th-percentile of age-matched normative thresholds from the International Organization for Standardization ISO 7029. As typically seen in sensorineural hearing loss progression of hearing loss is first seen in the HF-PTA before present in 4FT-PTA.

14 patients had normal hearing at baseline (36%); 13 (93%) started treatment at age 4y or younger, eleven of these retained normal hearing at follow up (median follow up 8y, range 4 to 15). Hearing worsened over time in 18 of 56 ears (32%) from 13 patients who had hearing loss at baseline. At last follow up, 2 patients had received cochlear implants for the past 5 and 10 years and 2 years respectively. All patients with progressive hearing loss were treated after age 4 (p = 0.0002). More ears with progressive hearing loss had cochlear enhancement at the time of the last MRI (p = 0.001) (Figure 2).

Conclusion: Progression of hearing loss was prevented in patients starting IL-1 blocking treatment at age of 4 or younger and had normal hearing at baseline. Hearing loss, when present at baseline, typically progressed over time on treatment and was first detected with the HF-PTA. Persistent inner ear enhancement on FLAIR MRI was associated with progressive hearing and suggest the use of FLAIR MRI to monitor inner ear inflammation. Our data points to the need of early treatment in maintaining normal hearing in patients with NOMID.

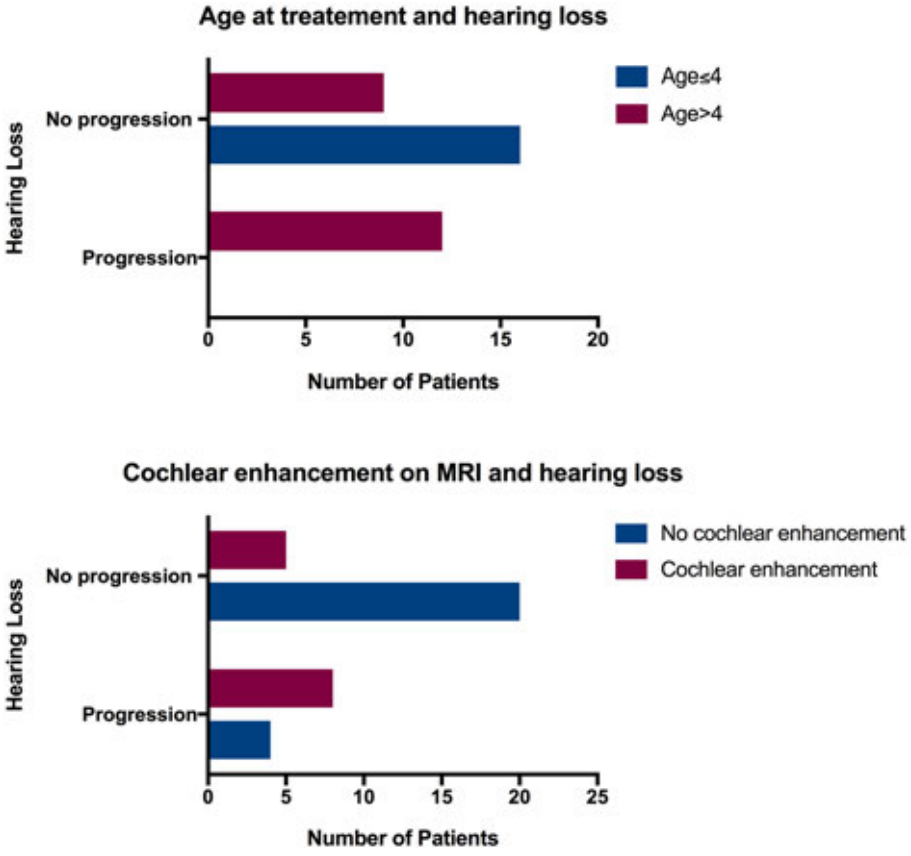

Figure 2. 37 patients had audiogram in follow up: Hearing loss was not observed in patients who started treatment at age <4y who had normal hearing at baseline. Hearing loss progressed in 13 patients who had hearing loss at baseline. All were treated after age 4 (upper panel). In ears with progressive hearing loss, cochlear enhancement was present in 66.8% of ears compared to 20% of hear that had no progressive hearing loss (p = 0.001).

Reference:

Sibley, et al. "Sustained response and prevention of damage progression in NOMID treated with anakinra: three-and five-year outcomes." Arthritis & Rheumatism (2012)

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Abstract Number: 0802

Canakinumab Improves Patient-Reported Outcomes in Patients with Recurrent Fever Syndromes: Results from a Phase 3 Trial

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SESSION INFORMATION

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Background/Purpose: Recurrent fever syndromes have a significant impact on health-related quality of life (HRQoL).[1] Canakinumab (CAN) has demonstrated efficacy and safety in patients with colchicine-resistant familial Mediterranean fever (crFMF), hyper-immunoglobulin D syndrome/mevalonate kinase deficiency (HIDS/MKD) and tumor necrosis factor receptor-associated periodic syndrome (TRAPS) in the pivotal phase 3, CLUSTER trial (NCT02059291).[2] However, the published data on impact of CAN on the HRQoL, work/school and social life of these patients are limited. To evaluate the effect of CAN on HRQoL, work/school and social life of patients in the 3 disease cohorts (crFMF, HIDS/MKD, and TRAPS) in a double blinded randomized Phase 3 trial (CLUSTER).

Methods: The detailed study design was reported previously.[2] The HRQoL of patients treated with CAN who met the primary endpoint of the CLUSTER trial2 was assessed at Baseline (BL), Week 17 (Wk17) and Week 41 (Wk41). HRQoL was also assessed in all patients (those initially randomized to CAN, those randomized to placebo who subsequently switched to CAN and those who did not switch to CAN). Outcomes measures were the Child Health Questionnaire (CHQ)-PF50 psychosocial (PsS) and physical (PhS) component summary scores (children >5–< 18 years), Short-Form health survey (SF-12) physical component summary (PCS) and mental component summary (MCS; adults ≥18 years) scores. An increase from baseline of 2, 5, and 8 points in the CHQ-PF50 PsS and PhS corresponds to a small, moderate and large treatment effect, respectively. Functional impairment related to work/school, social life and family life/home responsibilities was assessed by Sheehan Disability Scale (SDS) with a score of 5 or higher being associated with significant impairment.

HRQoL outcomes in patients who met the primary endpoint

Outcome measures	crFMF			HIDS/MKD			TRAPS		
Median scores	**BL**	**Week 17**	**Week 41**	**BL**	**Week 17**	**Week 41**	**BL**	**Week 17**	**Week 41**
CHQ-PF50 PsS	41.4 (n=8)	52.9 (n=8)	51.3 (n=7)	47.1 (n=8)	53.1 (n=8)	51.1 (n=6)	50.5 (n=5)	56.7 (n=5)	49.2 (n=4)
CHQ-PF50 PhS	27.5 (n=8)	47.6 (n=8)	52.8 (n=7)	33.7 (n=8)	48.6 (n=8)	43.7 (n=6)	30.8 (n=5)	50.9 (n=5)	47.8 (n=4)
SF-12 MCS	36.7 (n=10)	47.9 (n=10)	50.4 (n=9)	40.9 (n=4)	47.2 (n=4)	43.6 (n=4)	42.2 (n=5)	45.9 (n=5)	48.3 (n=4)
SF-12 PCS	38.5 (n=10)	50.5 (n=10)	52.7 (n=9)	27.9 (n=4)	50.9 (n=4)	51.0 (n=4)	34.8 (n=5)	51.4 (n=5)	45.5 (n=4)
SDS GFI	15.0 (n=18)	3.0 (n=15)	3.0 (n=14)	13.0 (n=13)	3.5 (n=10)	3.0 (n=11)	17.0 (n=10)	9.5 (n=6)	8.0 (n=7)
SDS, social life	5.0 (n=18)	1.0 (n=16)	1.0 (n=16)	6.0 (n=14)	1.0 (n=11)	1.0 (n=12)	5.0 (n=11)	3.0 (n=10)	2.5 (n=8)

BL, baseline; CHQ, Child Health Questionnaire; GFI, global functional impairment; HRQoL, health-related quality of life; MCS, mental component summary; PCS, physical component summary; PhS, physical summary score; PsS, psychosocial component summary; SF-12, Short form health survey; SDS, Sheehan Disability Scale. n= number of patients evaluated for HRQoL

Table 1

HRQoL outcomes in overall patients									
Outcome measures	**crFMF**			**HIDS/MKD**			**TRAPS**		
Median scores	**BL**	**Week 17**	**Week 41**	**BL**	**Week 17**	**Week 41**	**BL**	**Week 17**	**Week 41**
CHQ-PF50 PsS	42.6 (n=24)	53.4 (n=24)	51.1 (n=22)	45.6 (n=38)	49.7 (n=38)	52.6 (n=31)	47.2 (n=19)	52.2 (n=17)	52.7 (n=13)
CHQ-PF50 PhS	27.2 (n=24)	48.9 (n=24)	50.0 (n=22)	26.4 (n=38)	36.8 (n=38)	46.6 (n=31)	29.3 (n=19)	49.2 (n=17)	48.9 (n=13)
SF-12 MCS	41.8 (n=33)	44.0 (n=31)	50.0 (n=28)	45.8 (n=15)	51.6 (n=15)	51.0 (n=15)	42.2 (n=17)	46.4 (n=17)	51.5 (n=15)
SF-12 PCS	37.9 (n=33)	47.8 (n=31)	49.5 (n=28)	33.8 (n=15)	54.8 (n=15)	54.0 (n=15)	34.8 (n=17)	41.8 (n=17)	44.2 (n=15)
SDS GFI	18.0 (n=55)	6.0 (n=47)	2.0 (n=43)	16.0 (n=61)	7.0 (n=46)	5.0 (n=49)	15.5 (n=36)	4.0 (n=27)	7.0 (n=27)
SDS, social life	6.0 (n=59)	1.5 (n=54)	1.0 (n=52)	6.0 (n=65)	2.0 (n=53)	1.0 (n=55)	5.0 (n=41)	1.5 (n=36)	2.0 (n=34)

BL, baseline; CHQ, Child Health Questionnaire; GFI, global functional impairment; HRQoL, health-related quality of life; MCS, mental component summary; PCS, physical component summary; PhS, physical summary score; PsS, psychosocial component summary; SF-12, Short form health survey; SDS, Sheehan Disability Scale. n= number of patients evaluated for HRQoL

Table 2

Results: Out of 181 patients, 90 (31 crFMF, 37 HIDS/MKD, and 22 TRAPS) were randomized to CAN treatment and 91 to placebo. Patients in all 3 cohorts showed a high impairment of HRQoL at baseline. In patients who met the primary endpoint, CAN was shown to improve CHQ-PF50 PsS and PhS; SF-12 MCS and PCS; and SDS scores, from baseline to Wk 17, which was maintained at Wk 41 **(Table 1)**. The improvement in HRQoL was also observed in all patients treated with CAN, and was sustained through Wk 41 **(Table 2)**.

Conclusion: Treatment with canakinumab led to sustained improvement of HRQoL, work/school and social life in patients with crFMF, HIDS/MKD and TRAPS.

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1. Sahin et al. *Eur Rev Med Pharmacol Sci*. 2013;17:958–963.
2. De Benedetti et al. *NEJM* 2018;378:1908–1990.

Disclosure: H. Lachmann, Novartis, SOBI, 5; **B. Lauwerys**, None; **P. Miettunen**, None; **T. Kallinich**, None; **A. Jansson**, None; **I. Rosner**, None; **R. Manna**, None; **S. Murias**, None; **S. Savic**, Novartis, SOBI, 2, 5; **S. Smeets**, Novartis, 1, 3; **F. De Benedetti**, AbbVie, 2, BMS, 2, Novartis, 2, Novartis, Novimmune, Hoffmann- La Roche, SOBI, AbbVie, Pfizer, 2, Novimmune, 2, Pfizer, 2, Roche, 2, Sanofi, 2, Sobi, 2, Swedish Orphan Biovitrum, 2, UCB, 2; **A. Simon**, None.

Abstract Number: 0803

Hepatitis a Virus Vaccination in Autoinflammatory Diseases Under Canakinumab and Tocilizumab Treatment

Kenan Barut,[1] Amra Adrovic,[2] Sezgin Sahin,[3] Mehmet Yıldız,[2] Oya Koker,[2] Gamze Yalcin,[2] Omer Faruk Beser,[4] Bekir Kocazeybek,[5] Pelin Yuksel,[5] and **Ozgur Kasapcopur**[6], [1]Department of Pediatric Rheumatology, Cerrahpasa Medical School, Istanbul University-Cerrahpasa, Istanbul, Turkey, İstanbul, Istanbul, Turkey, [2]Department of Pediatric Rheumatology, Istanbul University Cerrahpasa, Istanbul, Istanbul, Turkey, [3]Department of Pediatric Rheumatology, Cerrahpasa Medical School, Istanbul University-Cerrahpasa, Istanbul, Turkey, Istanbul, Istanbul, Turkey, [4]Department of Pediatrics, Okmeydani Education and Training Hospital, Istanbul, Istanbul, Turkey, [5]Department of Microbiology, Istanbul University Cerrahpasa, Istanbul, Istanbul, Turkey, [6]Department of Pediatric Rheumatology, Istanbul University-Cerrahpasa, Istanbul, Turkey, Istanbul, Turkey

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever

Session Type: Poster Session (Sunday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune, autoinflammatory mechanism and drugs used in treatment increase the risk of liver disease in patients with chronic rheumatic diseases. Hepatitis A vaccine is a highly effective vaccine that prevents both the formation and spread of clinical hepatitis. In childhood chronic rheumatic diseases, vaccination is of great importance. The risk of various infections increases with the immunosuppressive effect of both the disease and the drugs.Therefore, vaccination of these diseases is of high importance for the prevention of infectious diseases. Studies on the efficacy and safety of vaccines in autoimmune and autoinflammatory diseases are limited. The aim of this study was to investigate the efficacy and safety of hepatitis A vaccine in patients with autoinflammatory disease on anti-interleukin 1 and 6 treatment.

Methods: This study was carried out in Pediatric Rheumatology outpatient clinic and general paediatric outpatient clinic. A total of 39 patients with autoinflammatory diseases on anti IL-1 and IL-6 therapy were initially evaluated but 25 of them were excluded due to anti-HAV IgG positivity. At the end, 24 patients with autoinflammatory diseases on anti IL-1, anti IL-6 therapy and 39 healthy participants who were seronegative for hepatitis A received two doses of the hepatitis A vaccine in a 0 and 6 month schedule. Hepatitis A virus (HAV) IgG antibodies were measured before vaccination and one month after last dose of the vaccine. Anti-HAV IgG titer as S/ CO;1.1, IU/L was considered positive and protective.

Results: Total 24 patients with autoinflammatory condition and 39 healthy controls were included in the study. Among patients with diagnosis of autoinflammatory disease, 19 were Systemic juvenile idiopathic arthritis (SJİA) and 5 were Cryopyrin-associated periodic syndromes (CAPS) patients. The mean age was 14.1±3.7 and 12.2±3.3 years respectively. Canakinumab was used in 15 (62.5%) and tocilizumab in 9 (37.5%) all patients. Among all SJİA patients, 10 (52.6%) were treated with canakinumab and 9(47.4%) were treated with tocilizumab. All patients with CAPS (n: 5) were using canakinumab. Among SJIA cases, 15(75%) were also using methotrexate and 14(70%) prednisolone. Anti-HAV IgG concentrations were measured one month after the last dose of hepatitis A vaccine. There was statistically significant difference between patients with autoinflammatory condition and healthy controls regarding the anti-HAV IgG titer (mean 5.3±1.5 IU/L) versus (10.5±7 IU/L) $p< 0.05$. The rate of anti-HAV IgG seropositivity (cut-off 1.1 IU/L) in autoinflammatory disease (24/24 (100%) was significantly different comparing to healthy controls (33/39, 84.6%) ($p=0.04$). There was no disease flare of disease nor the adverse event detected in any patients after vaccination.

Conclusion: Anti-HAV IgG seroconversion was detected in patients with autoinflammatory disease on anti-IL1 and anti - IL6 therapy 1 month after the last dose of hepatitis A vaccine. The response to vaccine did not differ between healthy children and patients with autoinflammatory disease under canakinumab and tocilizumab. In this study hepatitis A vaccine was found to be safe in autoinflammatory diseases with canakinumab and tocilizumab treatment.

Disclosure: K. Barut, AbbVie, 2; **A. Adrovic**, None; **S. Sahin**, AbbVie, 2; **M. Yıldız**, None; **O. Koker**, None; **G. Yalcin**, None; **O. Beser**, None; **B. Kocazeybek**, None; **P. Yuksel**, None; **O. Kasapcopur**, AbbVie, 2.

Abstract Number: 0804

STING-associated Vasculopathy with Onset in Infancy (SAVI Syndrome) Can Mimic Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Pediatric Rheumatology – ePoster I: Basic Science, Biomarkers, & Sclerodermic Fever – ARP
Session Type: Poster Session (Sunday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Gain-of-function mutations in TMEM173 encoding STING (Stimulator of Interferon Genes) underlie a novel type I INF termed SAVI syndrome. It is characterized by a vasculopathy that can affect skin, lungs and joints and can simulate Juvenile Idiopathic Arthritis (JIA).

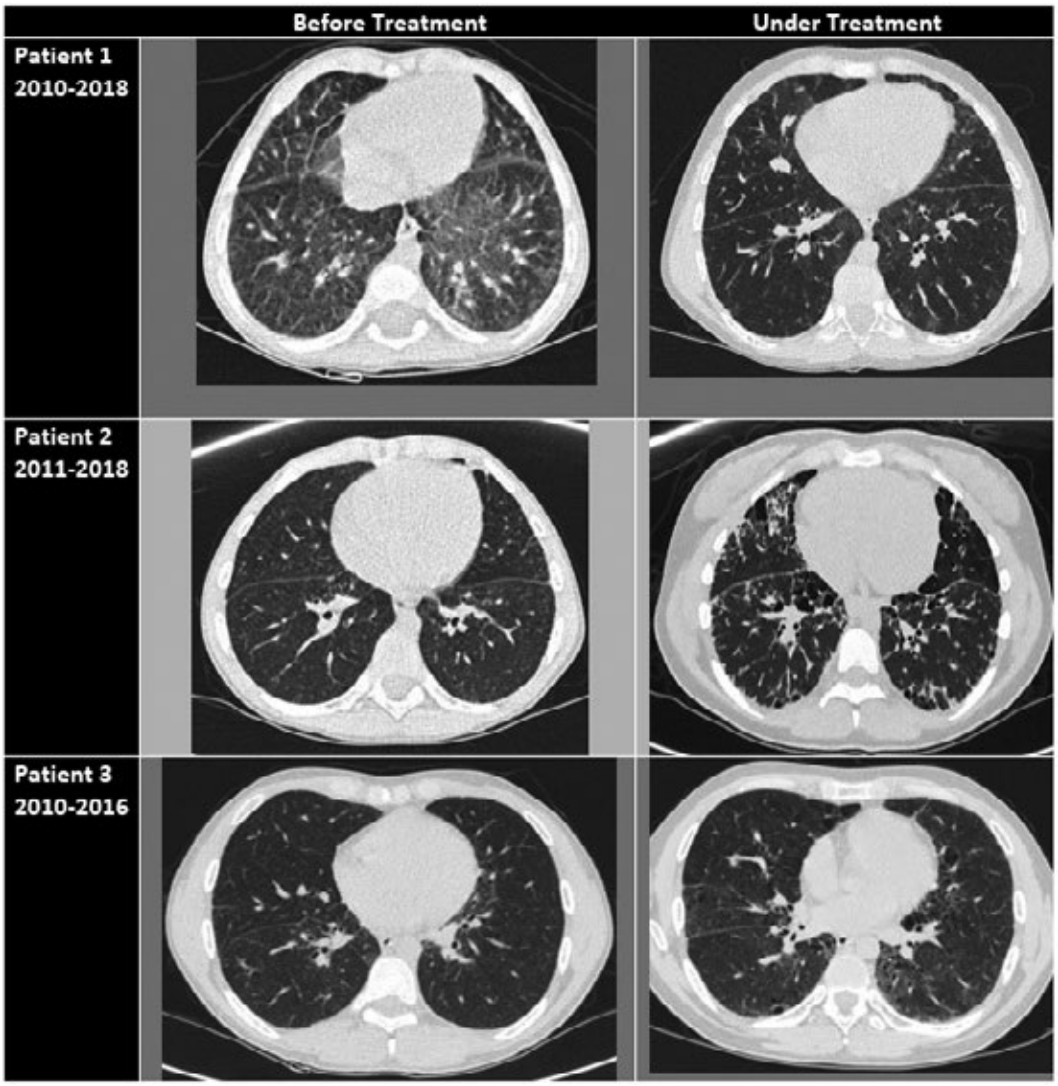
Objectives: To describe a detailed cohort of patients with SAVI syndrome and highlight the similarity of the phenotype with JIA.

Methods: 3 patients diagnosed with SAVI syndrome from the Hospital Universitari Vall d'Hebron were recruited. Written informed parental consent was obtained for the use of clinical data and pictures reported. Detailed clinical data is described.

Results: Patient 1, an 11-year-old boy, was identified to carry a de novo c.461A >G mutation in TMEM173. He presented at 1st month of life with bronchial infection and skin vasculitis lesions in acral zones and arthritis. Fever was not reported. High-resolution computed tomography (HRCT) of the lungs identified a nonspecific interstitial pneumonia (NSIP) and a lung biopsy (LB) showed lymphoid hyperplasia. Rheumatoid factor (RF), ACPA antibodies and antinuclear antibodies (ANA) were also positive. Immunosuppressive (IS) treatments were given without any response (table 1). At the age of 6 years Ruxolitinib (RX) with an improvement of skin disease and lung function and the arthritis was well controlled. Patient 2, a 17-year-old girl, was identified to carry a de novo c.463G >A mutation in TMEM173. She presented at the age of 3 with a severe polyarthritis. No fever, skin or respiratory symptoms were reported at the beginning of the disease. Lab tests were positive for RF and ACPA antibodies. She was diagnosed with pJIA and few months later she reported dyspnoea. HRCT showed NSIP and lymphoid interstitial pneumopathy was found at the LB. RX was initiated at the age of 17 years but fibrosis was established and she has been included to lung transplant (LT). Patient 3, a 29-year-old man, was recently diagnosed with a de novo c.463G >A mutation in TMEM173. He presented at the age of 7 years with polyarthritis. Lab test was positive for RF, ACPA, and ANA. With the diagnosis of pJIA he received IS treatments with no response. Due to

	Patient 1	Patient 2	Patient 3
Gender	Male	Female	Male
Race	Caucasian	Caucasian	Caucasian
First symptom	Skin	Joints	Joints
Age of first manifestation (months)	2	43	90
Age at diagnosis (years old)	6	17	22
TMEM 173 location	Exon 5	Exon 5	Exon 5
HGVS sequence name	c.461A>G	c.463G>A	c.463G>A
HGVS protein name	p.(Asn154Ser)	p.(Val155Met)	p.(Val155Met)
Febrile syndrome (present/absence)	No	No	No
Acute Phase Reactants (present/absence)	Yes	Yes	Yes
Joint involvement (present/absence)	Yes	Yes	Yes
Cutaneous Vasculitis (present/absence)	Yes	No	No
ANA (titter)	1/320	1/320	1/320
Rheumatoid Factor (positive/negative)	Positive	Positive	Positive
ACPA antibodies (titter)	>250	>250	>250
FVC (% predicted)	1,29L (81%)	0,95L (26%)	3.25 L(78%)
FEV1 (% predicted)	1,21L (89,6%)	0,95L (29,3%)	2.2(62,7%)
TLC (% predicted)	2,24L (97,9%)	2,01 (45,4%)	4,21 (75%)
DLCO (% predicted)	1,23 (58,4%)	N.F.	2,73 (25%)
6MWT ((distance in meters, Worst O2-saturation at exercise)	340m, 98%	165m, 86%	420m, 87%
Interstitial Lung Disease(present/absence)	Yes	Yes	Yes
Pulmonary hypertension(present/absence)	No	Yes	Yes
Glucocorticoids (received/not received)	Yes	Yes	Yes
Methotrexate (received/not received)	No	Yes	Yes
Leflunomide (received/not received)	No	Yes	No
Calcineurin inh. (received/not received)	Yes	No	No
Hidroxycloroquine (received/not received)	Yes	No	No
Azathioprine (received/not received)	Yes	No	Yes
Mycophenolate (received/not received)	Yes	Yes	No
Anakinra (received/not received)	Yes	No	No
Rituximab (received/not received)	No	Yes	No
IGIV (received/not received)	Yes	Yes	No
Tocilizumab (received/not received)	Yes	Yes	No
Abatacept (received/not received)	No	Yes	No
Etanercept (received/not received)	No	Yes	Yes
Adalimumab (received/not received)	No	Yes	No
Ruxolitinib (received/not received)	Yes	Yes	Yes
Permanent Oxygen Therapy	No	Yes	Yes
Listed for lung transplantation	No	Yes	Yes

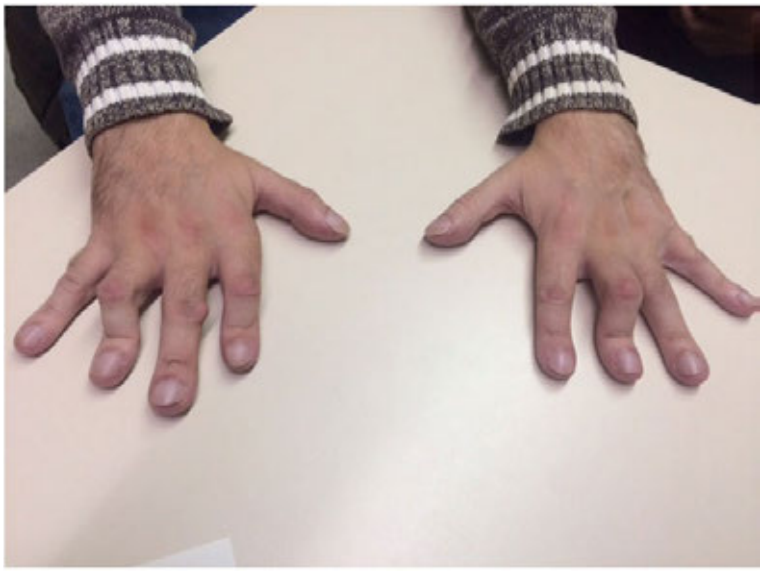
TABLE 1
Demographic, clinical, analytical, lung function and previous and current treatment



HRCT- Evolution of the Interstitial Lung Disease

recurrent bronchial infections a HRCT was performed showing an ILD and NSIP. SAVI syndrome was suspected and genetic test was performed with positive result. RX was initiated but compliance was not good. He is also being evaluated for LT.

Conclusion: SAVI syndrome is a rare monogenic autoinflammatory disease with few cases reported in the literature. Patient 2 and 3, in contrast with patient 1, had a different mutation (table 1), also severe articular and lung manifestations with no skin involvement. Furthermore, lab tests were positive for RF and ACPA and were misdiagnosed as JIA so genetic test was performed later in the follow-up. Being aware of the distinct phenotype of the disease could help the clinicians reassess the patients with these presentations that not respond well to conventional treatments.



Patient 3

Disclosure: J. Tandaipan, None; **M. Lopez Corbeto**, None; **E. Moreno Ruzafa**, None.

Abstract Number: 0805

Risk of Cardiovascular Disease in SLE Is Significant Early and Highlights Racial Disparities

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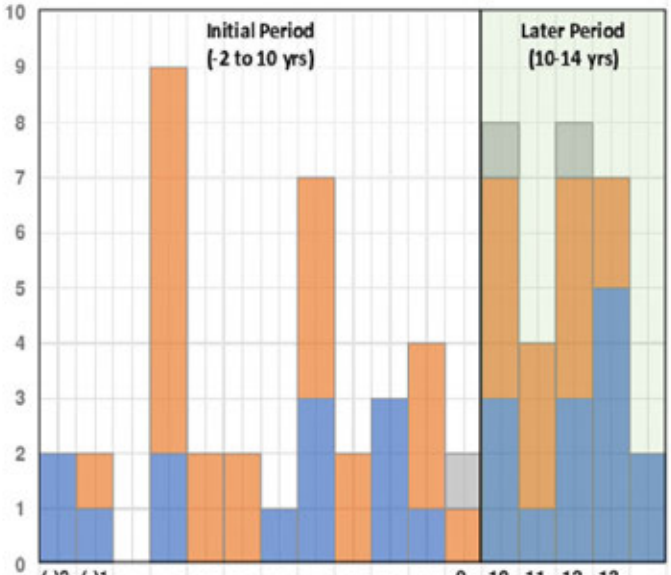
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Plenary I
Session Type: Plenary Session I
Session Time: 11:00AM–12:30PM

Background/Purpose: SLE is an independent risk factor for premature cardiovascular disease (CVD) and afflicts African Americans (AA's) 3 times more than whites. Two predominantly white cohorts have challenged the paradigm that CVD is a predominantly late complication of SLE. This study measured the risk of CVD events and predictors in a population-based incident cohort comprised mostly of AA's over a 14-year period, starting from 2 years before diagnosis.

Methods: The Georgia Lupus Registry (GLR) is a population-based registry of SLE patients from Atlanta, Georgia. Incident SLE patients in 2002-04 met ≥4 ACR SLE criteria or 3 criteria with a final diagnosis of SLE by their board-certified rheumatologist. CVD events or CVD deaths included ischemic heart disease, cerebrovascular accident, transient ischemic attack and peripheral vascular disease as adjudicated using published guidelines. Patients were matched to the Georgia Hospital Discharge Database and National Death Index from 2000-13. CVD-related hospitalizations and deaths were classified by the first three admission or cause of death codes. Predictors of CVD events during this period were examined using Cox proportional hazards model.

Figure 1. Cardiovascular Disease Events 2 Years Before SLE Diagnosis up to 14 Years After SLE Diagnosis



	(-)2-(-)1 yrs	(-)1 - 0 yrs	0-1 yrs	1-2 yrs	2-3 yrs	3-4 yrs	4-5 yrs	5-6 yrs	6-7 yrs	7-8 yrs	8-9 yrs	9-10 yrs	10-11 yrs	11-12 yrs	12-13 yrs	13-14 yrs	>14 yrs
Number of PVD events		0	0	0	0	0	0	0	0	0	0	1	1	0	1	0	0
Number of CVA & TIA events		1	0	7	2	2	0	4	2	0	3	1	4	3	4	2	0
Number of IHD events	2	1	0	2	0	0	1	3	0	3	1	0	3	1	3	5	2

**PVD = Peripheral Vascular Disease, CVA = Cerebrovascular Accident, TIA = Transient Ischemic Attack, IHD = Ischemic Heart Disease*

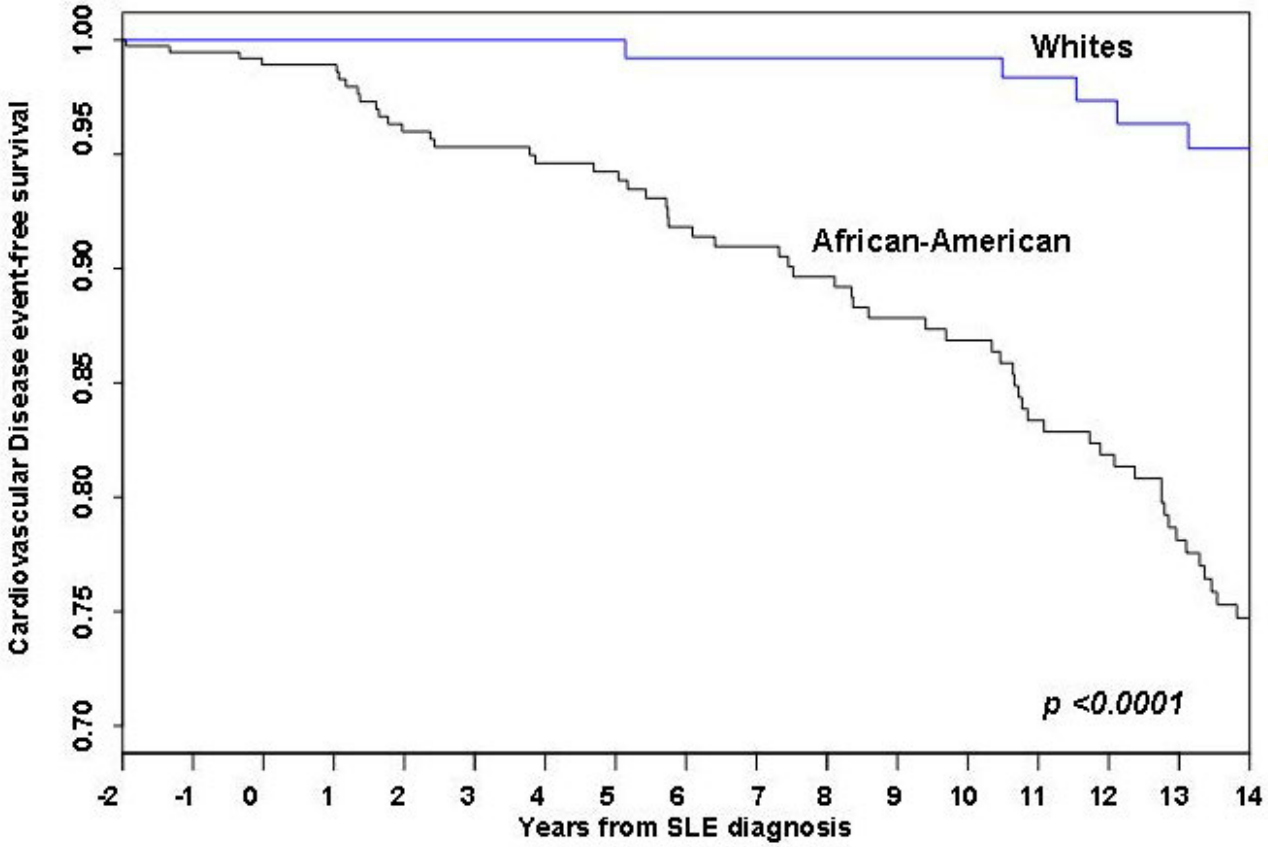
Table 1. Predictors of CVD events in Incident SLE Cohort (n=336)

Variables	Adjusted Hazard Ratio (95% CI)	p value
Age <19 yrs	ref	ref
Age 19 - <35 yrs	0.7 (0.2-1.9)	0.5
Age 35 - <50 yrs	1.8 (0.7-5.0)	0.2
Age 50 - <65 yrs	1.2 (0.4-3.8)	0.8
Age ≥65 yrs	**7.9 (2.2-29)**	**0.002**
Male	ref	ref
Female	1.4 (0.7-3.0)	0.4
Non African-American Race	ref	ref
African-American Race	**6.4 (2.4-17.5)**	**0.0003**
No Discoid rash	ref	ref
Discoid Rash	**3.2 (1.5-6.8)**	**0.003**
No Immunological criteria	ref	ref
Immunological criteria	**2.1 (1.01-4.4)**	**0.046**
No ESRD or Lupus Nephritis	ref	ref
ESRD or Lupus Nephritis	1.8 (0.95-3.3)	0.08

**ACR Criteria with p<0.1 on univariable analysis included in Multivariable Cox Proportional Hazards Model; ESRD=end stage renal disease*

Results: Among 336 incident SLE patients, 87% were females, 75% were AA and mean age at SLE diagnosis was 40 ± 17 years. Overall, we found 31 CVD-related events and 5 CVD-related deaths from 2 years before until 10 years after SLE diagnosis and 26 CVD-related events and 1 CVD-related death from 10-14 years after SLE diagnosis. There

Figure 2. Cardiovascular Disease Event-Free Survival Stratified By Race in SLE cohort



were two CVD events which occurred >14 years after SLE diagnosis. The mean ages at SLE diagnosis and the first CVD event during 12-years of follow up starting 2 years before SLE diagnosis were 46 and 48 years, respectively, with 91% of events in females and 75% in AA. The mean ages of SLE diagnosis and first CVD event in the period 10-14 years after diagnosis were 38 and 52 years, respectively, with 70% of events in females and 76% in AA. CVD event probability is shown in Figure 1 with 22% experiencing any CVD event and the highest number of events occurring 1-2 years after SLE diagnosis. AA race predicted a 6-fold higher risk of a CVD event during the follow-up period (Adjusted HR 6.4, 95% CI 2.4-17.5; Table 1). CVD event rates in AA's were 18-fold higher during the initial 10 years starting 2 years before SLE diagnosis (Adjusted HR 18, 95% CI 2.2-141; data not shown). Other predictors were discoid lupus (Adjusted HR 3.2, 95% CI 1.5-6.8), age >65 years (Adjusted HR 7.9, 95% CI 2.2-29), and presence of immunological criteria (Adjusted HR 2.1, 95% CI 1.01-4.4) (Table 1). The stratified Cox proportional hazard model show significantly accelerated CVD events in AA compared to whites ($p< 0.0001$) (Figure 2).

Conclusion: We found significant CVD events peaking 1-2 years after SLE diagnosis, supporting other observations but now in a predominantly AA population-based cohort. AA race was the strongest predictor of CVD events in SLE. Future CVD prevention efforts should target such populations to reduce racial disparities, particularly around the period of SLE diagnosis.

Disclosure: S. Garg, None; **C. Bartels**, Pfizer, 2, Pfizer Independent Grants for Learning and Change, 2; **C. Drenkard**, None; **G. Bao**, None; **S. Lim**, None.

Abstract Number: 0806

A Randomized, Controlled Trial of Rituximab versus Azathioprine After Induction of Remission with Rituximab for Patients with ANCA-associated Vasculitis and Relapsing Disease

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Plenary I
Session Type: Plenary Session I
Session Time: 11:00AM–12:30PM

Background/Purpose: Rituximab is an effective therapy for induction of remission in ANCA-associated vasculitis (AAV). However, the effect of rituximab is not sustained, and relapse rates are high, especially in patients with a history of relapse. The RITAZAREM trial (ClinicalTrials.gov identifier: NCT01697267) is an international, multi-center, open-labelled, randomized, controlled trial of patients with AAV with relapsing disease comparing the efficacy, after induction of remission with rituximab, of two relapse-prevention strategies: repeat dose rituximab or daily oral azathioprine.

Methods: Patients with AAV were recruited at time of relapse and received induction therapy with rituximab and glucocorticoids. If remission was achieved by month 4, patients were randomized in a 1:1 ratio to receive either rituximab (1000 mg every 4 months for 5 doses) or azathioprine (2 mg/kg/day) as maintenance therapy. Patients were followed for a minimum of 36 months, with the primary outcome being time to disease relapse. The formal hypothesis testing plan initially considers the hazard ratio for relapse across all time periods. If, and only if this global test is significant at a 5% level then the hazard ratios during the treatment period and the follow-up periods are considered separately.

Results: 190 patients were enrolled and 170 randomized at 4 months (85 to rituximab; 85 to azathioprine). The data are complete on all patients up to at least month 24. Median age was 59 years (range 19-89), with a prior disease duration of 5.3 years (0.4-38.5). 123/170 (72%) patients had a history of testing positive for anti-proteinase 3 ANCA; 47/170 (28%) for myeloperoxidase ANCA; 104/170 (61%) were enrolled having suffered a major relapse, and 48/170 (28%) received a pre-specified higher dose glucocorticoid induction regimen (Table 1). Rituximab was superior to azathioprine in preventing disease relapse with a preliminary overall hazard ratio (HR) estimate of 0.36 (95% CI 0.23-0.57, $p < 0.001$) and a during-treatment HR estimate of 0.30 (95% CI 0.15-0.60, $p< 0.001$) (Figure 1). After adjustment, none of the randomization stratification covariates (ANCA type, glucocorticoid induction regimen, or relapse severity) had a significant differential effect on the primary outcome. By 24 months after entry, 20 months after randomization, 11/85 (13%) patients in the rituximab group had experienced a relapse compared to 32/85 (38%) patients in the azathioprine group. In the rituximab group 2/11 (18%) relapses were classified as major, compared to 12/32 (38%) in the azathioprine group. 19/85 (22%) patients in the rituximab group and 31/85 (36%) patients in the azathioprine group experienced at least one severe adverse event (SAE). 25/85 (29%) and 42/85 (49%) patients in the rituximab group developed hypogammaglobulinaemia (IgG < 5g/l) and non-severe infections respectively, compared to 21/85 (25%) and 41/85 (48%) in the azathioprine group.

Conclusion: In the RITAZAREM trial, following induction of remission with rituximab, rituximab was superior to azathioprine for preventing disease relapse in patients with AAV with a prior history of relapse. There were no new major safety signals for use of these medications in this population.

Table 1: Baseline characteristics of patients enrolled in RITAZAREM trial

	Rituximab (N=85)	Azathioprine (N=85)	Total (N=170)
Age, years: median (range)	57 (18-89)	61 (27-83)	59 (18-89)
Female, number (%)	42 (49.4%)	44 (51.8%)	86 (50.6%)
Disease duration, years: median (range)	5.8 (0.4-38.5)	4.9 (0.4-25.8)	5.3 (0.4-38.5)
Prior cyclophosphamide therapy			
Number of patients (%)	67/85 (78.8%)	66/85 (77.6%)	133/170 (78.2%)
Cumulative dose, grams (g): median (range)	7.1 g (0.2-301)	12 g (1.0-146)	10 g (0.2-301)
Prior rituximab therapy			
Number (%) patient	33/85 (38.8%)	27/85 (31.8%)	60/170 (35.3%)
Cumulative dose, grams (g): median (range)	3.2 g (2.0-16.0)	5.4 g (1.5-14.0)	3.9 g (1.5-16.0)
Glucocorticoid induction regimen			
1mg/kg/day starting dose	24/85 (28.2%)	24/85 (28.2%)	48/170 (28.2%)
0.5mg/kg/day starting dose	61/85 (71.8%)	61/85 (71.8%)	122/170 (71.8%)
ANCA type			
Anti-proteinase 3	61/85 (71.8%)	62/85 (72.9%)	123/170 (72.4%)
Anti-myeloperoxidase	24/85 (28.2%)	23/85 (27.1%)	47/170 (27.6%)
Relapse type upon entry into trial			
Severe	52/85 (61.2%)	52/85 (61.2%)	104/170 (61.2%)
Non-severe	33/85 (38.8%)	33/85 (38.8%)	66/170 (38.8%)

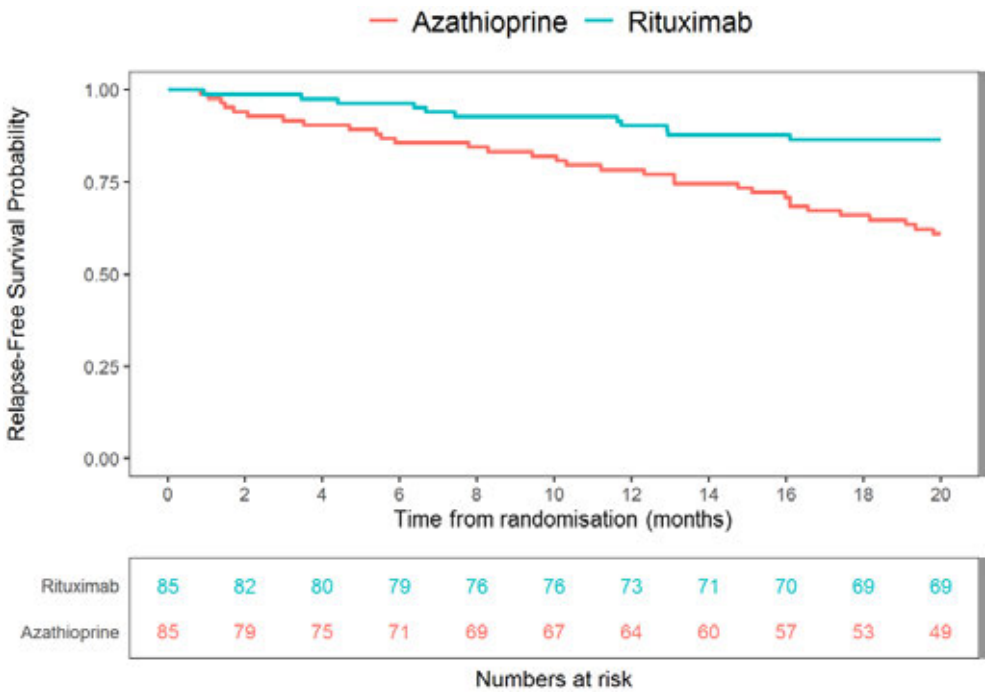


Figure 1. Relapse-free survival in RITAZAREM trial: rituximab versus azathioprine

Disclosure: R. Smith, Roche, 2, 8, Sanofi, 2, Medimmune, 2; **D. Jayne**, Astra Zeneca, 5, Boehringer-Ingelheim, 5, Celgene, 5, ChemoCentryx, 2, 5, GSK, 2, 5, Infla-Rx, 5, InflaRx GmbH, 5, Insmed, 5, Roche Genetech, 2, Sanofi Genzyme, 2, Takeda, 5; **P. Merkel**, AbbVie, 5, AstraZeneca, 2, 5, Biogen, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 5, GlaxoSmithKline, 2, 5, InflaRx, 5, Imsmed, 5, Jannsen, 5, Kiniksa, 5, Kypha, 2, TerumoBCT, 2.

Abstract Number: 0807

Guselkumab, an Anti-interleukin-23p19 Monoclonal Antibody, in Patients with Active Psoriatic Arthritis Who Were Biologic-Naïve or Prior TNFα Inhibitor-Treated: Week 24 Results of a Phase 3, Randomized, Double-blind, Placebo-controlled Study

Atul Deodhar,[1] Philip Helliwell,[2] Wolf-Henning Boencke,[3] Elizabeth Hsia,[4] Alexa Kollmeier,[5] Ramanand Subramanian,[5] Xie Xu,[5] Shihong Sheng,[5] Bei Zhou,[5] and Christopher Ritchlin[6], [1]Oregon Health & Science University, Portland, OR, [2]University of Leeds, Leeds, United Kingdom, [3]Geneva Univ Hospitals, Geneva, Switzerland, [4]Janssen Research & Development, LLC/University of Pennsylvania, Spring House/Philadelphia, PA, [5]Janssen Research & Development, LLC, Spring House, PA, [6]Division of Allergy, Immunology and Rheumatology, Center for Musculoskeletal Research, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA, Rochester, NY

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Plenary I
Session Type: Plenary Session I
Session Time: 11:00AM–12:30PM

Background/Purpose: Guselkumab (GUS), an anti-interleukin-23p19 monoclonal antibody, is approved to treat PsO. We evaluated GUS efficacy and safety in a Phase 3, double-blind, PBO-controlled trial in pts with active PsA who were biologic-naïve or prior TNFα inhibitor (TNFi)-treated (DISCOVER-1).

Methods: Adults with active PsA (≥3 swollen+≥3 tender joints; CRP ≥0.3mg/dL) despite standard therapies (eg, non-biologic DMARDs, apremilast, or NSAIDs) were eligible. Approx. 30% of pts previously could have received or have had inadequate response to 1-2 TNFi. Pts were randomized 1:1:1, stratified by Week [W] 0 DMARD use [Y/N] and prior TNFi use (Y/N), to GUS 100mg Q4W; GUS 100mg at W0, W4, Q8W (Q8W); or PBO. Concomitant stable use of select non-biologic DMARDs, oral corticosteroids, and NSAIDs was allowed. At W16, pts with < 5% improvement in tender+swollen joints could initiate or increase the dose of permitted medications while continuing study treatment. The primary endpoint was ACR20 at W24. Major secondary endpoints included: Investigator's Global Assessment (IGA) PsO response (IGA=0/1 + ≥2-grade reduction) at W24 in pts with ≥3% BSA PsO & IGA ≥2 at W0; changes in DAS28-CRP, HAQ-DI and SF-36 PCS scores and ACR50/70 response at W24; and ACR20/50 response at W16. As preplanned, enthesitis or dactylitis data were pooled with those from the companion Phase 3 GUS in PsA study (DISCOVER-2; to be reported elsewhere). Due to regional health authority differences in regulatory requirements for multiplicity control, two multiplicity control procedures were prespecified (Global and US). Results of statistical testing via US procedures are presented. Unadjusted (nominal) p-values are provided for other endpoints (Table). Adverse events (AEs) through W24 are reported.

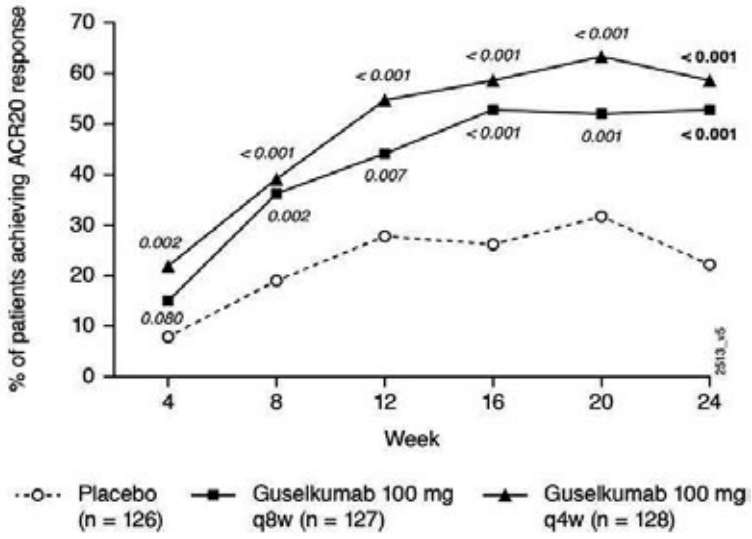
Results: 381 pts were treated and analyzed; baseline characteristics were consistent with moderate-to-severe disease (mean BSA involved with PsO: 13.4%, pts with IGA=3-4: 42.5%; mean swollen/tender joint counts: 9.8/19.3). Significantly more pts receiving GUS Q4W (58.6%) and Q8W (52.8%) vs PBO (22.2%, both p< 0.001) achieved ACR20 response at W24 (Figure). Consistent response rates were observed in the subgroups of pts with or without prior TNFi use (Table). Significantly greater improvements in HAQ-DI and SF-36 PCS scores were seen in GUS- vs PBO-treated pts from W0 to W24. Among 249 pts with ≥3% BSA PsO and IGA ≥2 at W0, significantly more GUS- vs PBO-treated pts achieved IGA response. Higher proportions of pts achieved ACR20 response at W16, ACR50 response at W16/24, ACR70 response at W24, and PASI75/90/100 responses at W24. More GUS Q4W- or Q8W- vs PBO-treated pts achieved MDA response at W24 (Table). Serious AEs, serious infections, and death occurred in 9/381 (2.4%), 2/381 (0.5%), and 1/381 (0.3%) pts, respectively.

Table. Clinical Efficacy for DISCOVER-1, a Randomized, Placebo-controlled, Phase 3 Study of GUS in Pts with Active PsA Who Were Biologic-Naïve or Prior TNFi-Treated

	GUS 100 mg Q4W (N=128)	GUS 100 mg Q8W (N=127)	Matching PBO (N=126)
Endpoints controlled for multiplicity in the US procedure			
Primary endpoint			
ACR20 at W24, n (%)	75 (58.6%)	67 (52.8%)	28 (22.2%)
[Diff vs PBO (95% CI)]	*[36.4 (25.3, 47.4)]*	*[30.6 (19.4, 41.9)]*	
P value[1]	*<0.001*	*<0.001*	
Major secondary endpoints			
IGA 0/1 and ≥2-grade decrease at W24,[2] n/N (%)	67/89 (75.3%)	47/82 (57.3%)	12/78 (15.4%)
[Diff vs PBO (95% CI)]	*[60.0 (48.3, 71.8)]*	*[42.0 (28.9, 55.1)]*	
P value	*<0.001*	*<0.001*	
HAQ-DI at W24, LSmean (95% CI) change	-0.380 (-0.462, -0.298)	-0.311 (-0.393, -0.230)	-0.085 (-0.168, -0.003)
[LSMean diff vs PBO(95% CI)]	*[-0.295 (-0.405, -0.184)]*	*[-0.226 (-0.336, -0.115)]*	
P value[1]	*<0.001*	*<0.001*	
SF-36 PCS at W24, LSmean (95% CI) change	6.87 (5.60, 8.14)	6.10 (4.83, 7.37)	1.96 (0.69, 3.24)
[LSMean diff vs PBO(95% CI)]	*[4.91 (3.19, 6.63)]*	*[4.14 (2.42, 5.85)]*	
P value[1]	*<0.001*	*<0.001*	
Endpoints not controlled for multiplicity in the US procedure			
ACR20 at W24 in TNFi-experienced pts, n/N (%)	22/38 (57.9%)	23/41 (56.1%)	7/39 (17.9%)
[Diff vs PBO (95% CI)]	*[40.0 (20.8, 59.2)]*	*[38.5 (19.3, 57.7)]*	
ACR20 at W24 in TNFi-naive pts, n/N (%)	53/90 (58.9%)	44/86 (51.2%)	21/87 (24.1%)
[Diff vs PBO (95% CI)]	*[34.8 (21.2, 48.3)]*	*[27.0 (13.2, 40.8)]*	
ACR20 at W16, n (%)	75 (58.6%)	67 (52.8%)	33 (26.2%)
[Diff vs PBO (95% CI)]	*[32.4 (21.1, 43.7)]*	*[26.6 (15.2, 38.1)]*	
Unadjusted[3] *P value*	*<0.001*	*<0.001*	
ACR50 at W24, n (%)	47 (36.7%)	38 (29.9%)	11 (8.7%)
[Diff vs PBO (95% CI)]	*[28.0 (18.4, 37.6)]*	*[21.4 (12.1, 30.7)]*	
Unadjusted[3] *P value*	*<0.001*	*<0.001*	
ACR50 at W16, n (%)	34 (26.6%)	28 (22.0%)	16 (12.7%)
[Diff vs PBO (95% CI)]	*[13.9 (4.4, 23.4)]*	*[9.4 (0.3, 18.5)]*	
Unadjusted[3] *P value*	*0.006*	*0.050*	
ACR70 at W24, n (%)	26 (20.3%)	15 (11.8%)	7 (5.6%)
[Diff vs PBO (95% CI)]	*[14.8 (6.9, 22.7)]*	*[6.4 (-0.3, 13.1)]*	
Unadjusted[3] *P value*	*<0.001*	*0.069*	
DAS28-CRP at W24, LSmean (95% CI) change	-1.61 (-1.80, -1.42)	-1.43 (-1.61, -1.24)	-0.70 (-0.89, -0.51)
[LSMean diff vs PBO(95% CI)]	*[-0.91 (-1.16, -0.66]*	*[-0.73 (-0.98, -0.48)]*	
Unadjusted[3] *P value*	*<0.001*	*<0.001*	
PASI75[4] **at W24,** n/N (%)	77/89 (86.5%)	62/82 (75.6%)	11/78 (14.1%)
[Diff vs PBO (95% CI)]	*[72.6 (62.3, 82.8)]*	*[61.7 (49.8, 73.7)]*	
Unadjusted[3] *P value*	*<0.001*	*<0.001*	
PASI90[4] **at W24,** n/N (%)	56/89 (62.9%)	41/82 (50.0%)	9/78 (11.5%)
[Diff vs PBO (95% CI)]	*[51.7 (39.7, 63.7)]*	*[38.6 (25.8, 51.4)]*	
Unadjusted[3] *P value*	*<0.001*	*<0.001*	
PASI100[4] **at W24,** n/N (%)	40/89 (44.9%)	21/82 (25.6%)	5/78 (6.4%)
[Diff vs PBO (95% CI)]	*[38.9 (27.5, 50.3)]*	*[19.9 (9.6, 30.2)]*	
Unadjusted[3] *P value*	*<0.001*	*<0.001*	
SF-36 MCS at W24, LSmean (95% CI) change	3.59 (2.16, 5.02)	3.20 (1.78, 4.63)	2.37 (0.93, 3.81)
[LSMean diff vs PBO(95% CI)]	*[1.22 (-0.72, 3.15)]*	*[0.83 (-1.10, 2.77)]*	
Unadjusted*[3] *P value	***0.217***	***0.397***	

Conclusion: In pts with active PsA who were biologic-naïve or had been treated with TNFi, both GUS Q4W and Q8W demonstrated efficacy for joint and skin symptoms, physical function, and quality of life relative to PBO. Observed AEs were consistent with GUS safety established in PsO.

Disclosure: A. Deodhar, AbbVie, 2, 5, 9, Abbvie, 5, 8, Abbvie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, and UCB Pharma, 5, 8, AbbVie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GSK, Galapagos, Janssen, Novartis, Pfizer and UCB, 5, AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers



italicized p values are unadjusted
bolded p values are adjusted

Figure. ACR20 response over time.

Table. Clinical Efficacy for DISCOVER-1, a Randomized, Placebo-controlled, Phase 3 Study of GUS in Pts with Active PsA Who Were Biologic-Naïve or Prior TNFi-Treated

	GUS 100 mg Q4W (N=128)	GUS 100 mg Q8W (N=127)	Matching PBO (N=126)
MDA at W24, n (%)	39 (30.5%)	30 (23.6%)	14 (11.1%)
[Diff vs PBO (95% CI)]	*[19.3 (9.7, 28.9)]*	*[12.7 (3.6, 21.7)]*	
Unadjusted[3] P value	*<0.001*	*0.008*	

Pts meeting treatment-failure criteria were considered nonresponders for binary endpoints and as having no improvement from baseline for continuous endpoints. Missing data were imputed as nonresponders for binary endpoints; multiple imputation was used to impute missing data for continuous endpoints. Treatment difference for binary endpoints was assessed via Cochran-Mantel-Haenszel test stratified by baseline use of non-biologic DMARDs (yes/no) and prior exposure to anti-TNFα agents (yes/no). Treatment difference for continuous endpoints was assessed via an analysis of covariance model.

[1] In the US procedure, the overall Type I error of the treatment comparisons of both doses versus placebo for the primary and the 3 selected major secondary endpoints, representing a total of 8 hypotheses, was controlled at a significance level of ≤0.05.

[2] Assessed in pts with ≥3% BSA PsO and IGA score ≥2 at W0.

[3] Unadjusted (nominal) p values are not controlled for multiplicity and descriptive/supportive only; no statistical significance should be implied.

Squibb, Eli Lilly, Glaxo Smith and Klein, Janssen, Novartis, Pfizer, UCB, 5, Amgen, 5, 8, 9, BMS, 2, 5, 8, BMS, Eli Lilly, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, 2, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, UCB Pharma, 2, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, 8, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, 9, Eli Lilly and Company, 2, 5, Eli Lilly,, 5, Eli Lilly, GSK, Novartis, Pfizer and UCB, 2, Galagagos, 5, Galapagos, 5, 8, 9, Glaxo Smith & Klein, 2, Glaxo Smith & Kline, 2, 5, 8, Glaxo Smith Klein, 5, Glaxo SmithKlein, 2, 5, GlaxoSmithKlein, 2, 5, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, Janssen, 2, 5, 8, 9, Janssen Pharmaceutica, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9; **P. Helliwell**, AbbVie, 2, 8, Amgen, 8, Celgen, 8, Celgene, 8, Galapagos, 8, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, Pfizer, 8, Pfizer Inc, 8, UCB, 8; **W. Boencke**, Janssen Research & Development, LLC, 2; **E. Hsia**, Janssen Research & Development, LLC, 3; **A. Kollmeier**, Janssen Research & Development, LLC, 3; **R. Subramanian**, Janssen Research & Development, LLC, 3; **X. Xu**, Janssen Research & Development, LLC, 3; **S. Sheng**, Janssen Research & Development, LLC, 3; **B. Zhou**, Janssen Research & Development, LLC, 3; **C. Ritchlin**, AbbVie, 2, 5, 9, Amgen, 2, 5, BMS, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Lilly, 5, Novartis, 5, Pfizer, 2, Pfizer Inc, 5, UCB, 2, 5.

Abstract Number: 0808

Long-Term Outcome of Tocilizumab for Patients with Giant Cell Arteritis: Results from Part 2 of a Randomized Controlled Phase 3 Trial

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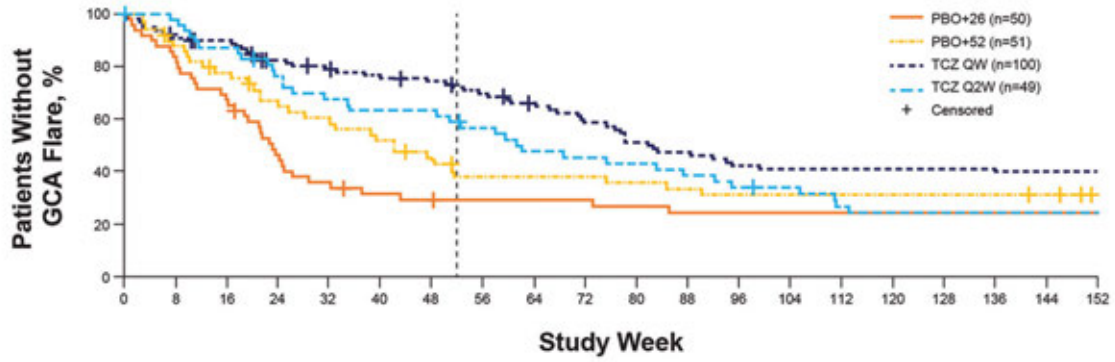
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Plenary I
Session Type: Plenary Session I
Session Time: 11:00AM–12:30PM

Background/Purpose: Tocilizumab (TCZ) 162 mg administered subcutaneously weekly (QW) or every-other-week (Q2W) plus 26-wk prednisone tapering resulted in higher rates of sustained glucocorticoid (GC)–free remission in patients with giant cell arteritis (GCA) than placebo plus 26-wk (PBO+26) or 52-wk (PBO+52) prednisone tapering in the 52-wk, double-blind, randomized controlled GiACTA trial.[1] The objective of this analysis was to determine long-term safety and explore maintenance of efficacy in GCA patients in a 2-year long-term extension (part 2) of this trial.

Methods: At the end of the double-blind period, patients in clinical remission (CR) were instructed to stop double-blind TCZ treatment upon entering part 2. CR was defined as absence of flare per investigator assessment without requirement for normalization of CRP < 1 mg/dL. GCA therapy, which could include initiation/termination of open-label TCZ and/or GC, was administered at investigator's discretion per disease status. Outcomes included maintenance of CR (no flare during part 2), flare, time to first flare, treatments received, cumulative GC dose, and safety. Treatment groups refer to originally assigned treatment (PBO or TCZ).

Results: Among 250 patients treated in the double-blind period, 215 entered part 2 and 197 (92%) completed 3 years in the trial. Among the 81 TCZ QW and 36 TCZ Q2W patients in CR at wk 52, 38 (47%) and 13 (36%) patients, respectively, maintained CR during part 2. Of these 51 original TCZ patients, 33 (65%) were treatment-free (no TCZ or GC treatment), which was higher than the treatment-free proportion of original PBO patients who maintained CR in part 2 (17/38; 45%). Median time to first flare while not receiving TCZ was longer for patients in the original TCZ groups (TCZ QW, 575 days; TCZ Q2W, 428 days) than for patients in the original PBO groups (PBO+26, 162 days; PBO+52, 295 days); TCZ QW patients remained flare-free the longest (Figure 1). Retreatment with TCZ (with or without GC) for flare was effective for restoring CR in part 2. Cumulative GC dose over the 3 years was lowest in the TCZ QW group (median dose [mg/day]: TCZ QW, 2647; TCZ Q2W, 3782; PBO+26, 5248; PBO+52, 5323). Rates of serious adverse events per 100 patient-years over 3 years (double-blind period + part 2) were comparable for patients who never received TCZ (23.2) and those who did receive ≥1 dose of TCZ (25.4), and rates of serious infections were 4.6 and 3.5 per 100 patient-years, respectively. Additional results will be presented for original PBO patients.

Figure 1. Kaplan-Meier plot of time to first flare over 3 years (double-blind and part 2 periods; ITT population).



No. of Patients

PBO+26	50	45	41	35	33	28	22	18	17	15	14	13	13	12	12	12	12	12	12	11	11	11	10	10	10	10	10	10	10	10	10	10	10	10	10
PBO+52	50	47	43	40	37	34	31	29	28	26	24	21	20	16	16	16	16	16	16	15	15	15	14	13	13	13	13	13	13	13	13	13	13	13	12	11	9
TCZ QW	100	93	88	85	85	79	75	72	70	68	66	65	64	60	58	55	53	50	47	46	41	38	38	36	34	33	33	33	33	33	33	33	33	33	32	32	32	32
TCZ Q2W	49	47	46	41	41	39	35	32	31	29	29	29	29	27	25	23	21	21	20	19	19	18	17	17	15	14	14	13	11	10	10	10	10	10	10	10	10	10

Patients never in remission were censored at day 1. Patients who withdrew were censored from the time of withdrawal. Dashed line indicates start of part 2.

Conclusion: Nearly half of patients treated with TCZ QW maintained CR for the entirety of part 2, but flares still occurred in the remaining patients once they discontinued TCZ treatment. Among patients who maintained CR in part 2, higher proportions of those originally assigned to TCZ were treatment-free compared with those originally assigned to PBO. Retreatment with TCZ restored CR in patients who experienced flare. Cumulative GC dose over 3 years was lower in patients originally assigned to TCZ than in those originally assigned to PBO. No new safety signals were observed with TCZ exposure in GCA patients during the 3-year study.

Reference:

1. Stone JH et al. *N Engl J Med* 2017;377:317-328.

Disclosure: J. Stone, Genentech, 2, 5, Roche, 2, 5, Xencor, 2, 5; **M. Bao**, Genentech, 1, 3, Genentech, Inc., 3, Roche, 4; **J. Han**, Genentech, 1, 3, Genentech, Inc., 3; **M. Aringer**, Abbvie, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, 8, BMS, 5, 8, Boehringer Ingelheim, 5, 8, Bristol-Myers Squibb, 5, 8, Chugai, 5, 8, Hexal, 8, HEXAL, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, Sanofi-Aventis, 5, 8, UCB, 8; **D. Blockmans**, None; **E. Brouwer**, Roche, 5, 8; **M. Cid**, Roche, 9; **B. Dasgupta**, Abbvie, 2, BMS, 5, GSK, 5, Roche, 2, 5, 8, Roche Chugai, 5, 8, Sanofi, 2, 5, Sanofi Aventis, 5, Sanofi-Aventis, 5; **J. Rech**, AbbVie, 8, Biogen, 8, BMS, 5, 8, Celgene, 5, 8, Chugai, 5, MSD, 8, Novartis, 5, 8, Roche, 5; **C. Salvarani**, None; **R. Spiera**, BMS, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, ChemoCentryx, 2, 5, Chemocentryx, 2, Corbus, 2, CSL Behring, 5, Cytori, 2, Formation Biologics, 2, Genentech, Inc., 2, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, GSK, 2, 5, Hoffman-La Roche Ltd, 2, Janssen, 5, Mitsubishi, 5, Roche, 2, Roche Genetech, 2, 5, Roche/Genetech, 2, 5, Roche-Genentech, 2, 5, Roche-Genetech, 2, 5, Sanofi, 5, Sanofi-Aventis, 5; **S. Unizony**, Genentech, Inc., 2.

Abstract Number: 0809

TNF-α Drives Progressive Obliterative Pulmonary Vascular Disease and Represents a Novel Model of Connective-Tissue Disease Associated Pulmonary Arterial Hypertension (CTD-PAH)

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Plenary I
Session Type: Plenary Session I
Session Time: 11:00AM–12:30PM

Background/Purpose: Pulmonary arterial hypertension (PAH) is a severe cardiopulmonary disease characterized by an obliterative vasculopathy and vascular remodeling, right heart hypertrophy, and premature death. Connective tissue disease associated PAH (CTD-PAH) is common in scleroderma, and other autoimmune diseases, which have poor clinical outcomes. Recently, it has been shown that female human TNF-transgenic (TNF-Tg) mice die by 6-months from cardiopulmonary disease. Thus, we aimed to formally characterize this pathophysiology and assess its potential as a model of CTD-PAH.

Methods: Histologic analysis and immunofluorescent (IF) staining was performed on female TNF-Tg (3647 line) and wild type (WT) mice to characterize the pulmonary vascular and right ventricular pathology. Mice ($n \geq 4$) underwent: right heart catheterization to assess hemodynamics, or barium-perfused micro-CT to assess vascular morphology, or gas chromatography. Lungs from TNF-Tg/WT bone marrow chimeric mice, and anti-TNF vs. placebo treated TNF-Tg mice were assessed ($n \geq 3$). RNA sequencing was performed on lung tissue, and bioinformatic techniques were applied to compare TNF-Tg mouse lungs to publicly available human normal and CTD-PAH transcriptomic data.

Results: Female TNF-Tg mice display a progressive pulmonary vasculopathy beginning at 3 months of age manifested by vascular collagen deposition, enlarged pulmonary arteries, attenuation of distal arterioles, and vascular occlusion, which closely resemble CTD-PAH pathologically (Fig 1A-C). Hemodynamic assessment demonstrated a significantly increased right ventricular systolic pressure of 83.7± 10.3 mmHg vs. 25.7 ± 0.4 mmHg in TNF-Tg vs. WT mice (Fig 1D), making this one of the most robust models of murine PAH ever reported. μCT analysis confirmed pruning of the vascular tree (Fig 1H), and TNF-Tg mice had reduced gas exchange (Fig 1G). Increased aSMA IF staining in TNF-Tg lungs corresponded to proliferation (Ki-67+), and loss of von Willebrand factor positive (vWF+) vessels over time. We also observed an increase in $aSMA^{+}vWF^{+}$ cells (Fig 1, E, F, I), implicating endothelial-mesenchymal transition in this process. By 4 months of age, TNF-Tg mice display remarkable right ventricular hypertrophy, and transcriptional evidence of RV dysregulation (Fig 2A-G). Bone marrow chimera experiments revealed that mesenchymal cells, and not bone-marrow derived cells, are necessary to drive this process (Fig 2H), while anti-TNF therapy halted the progression of PAH pathology (Fig 2I). Human SSc-PAH lungs display increased TNF-a staining (Fig 3A), and human microarray data demonstrated a prominent TNF signature that can distinguish PAH from control lungs (Fig 3B). Comparison of gene expression between TNF-Tg lungs and CTD-PAH lungs showed significant similarities in expression patterns and clustering (Fig 3C) with enrichment in pathway overlaps including angiogenesis, Notch signaling, apoptosis, and VEGF signaling (Fig 3D).

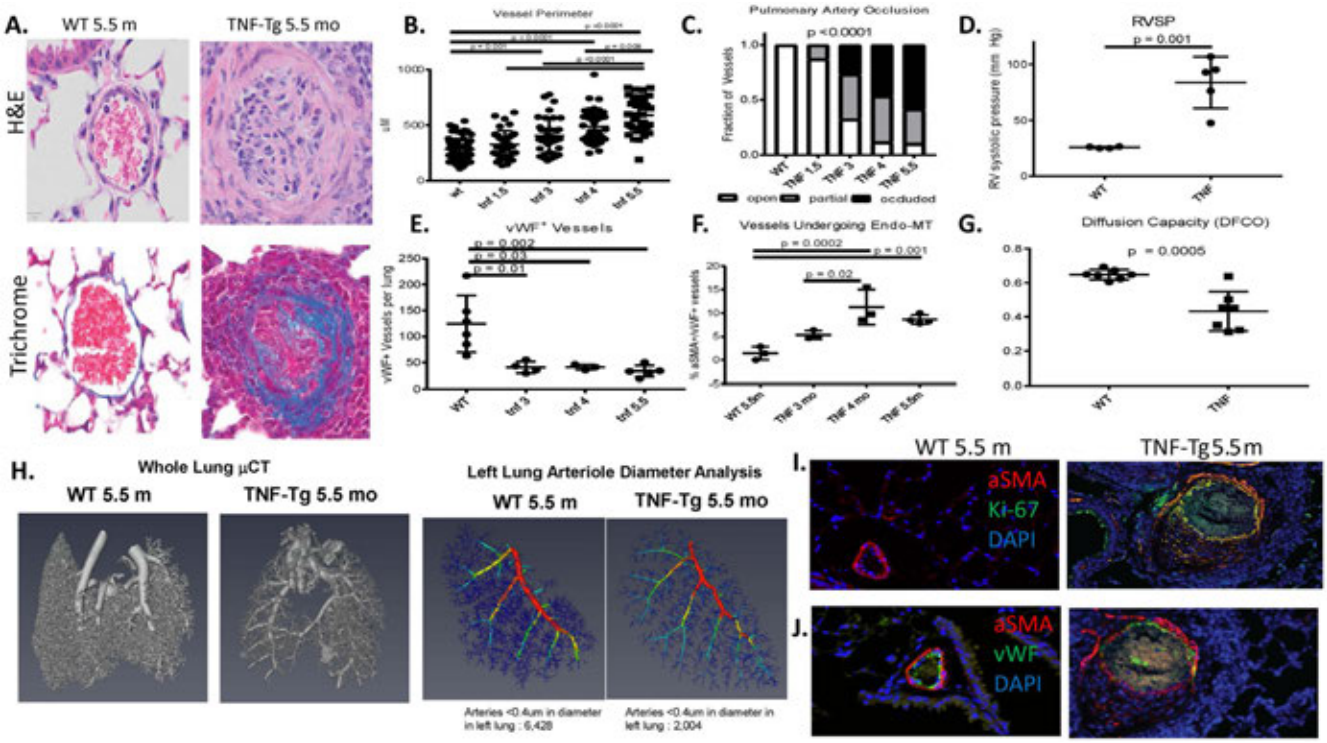


Figure 1. Characterization of pulmonary vascular abnormalities in TNF-transgenic (TNF-Tg) mice. A. Histologic evaluation of TNF-Tg pulmonary arterioles revealed intimal proliferation and vascular occlusion associated with vascular collagen deposition (Top, H&E, Bottom, Masson's Trichrome, 20x). B. Pulmonary arteriole size begins to increase at 3 months of age and becomes progressively larger over time. WT indicates 5.5 month old WT mice for this and all subsequent figures. C. Pulmonary arteries were progressively occluded in the TNF-Tg mice with over 90% of vessels showing at least partial occlusion by 4 months of age. D. Right heart catheterization of TNF-Tg mice demonstrate evidence of severe pulmonary arterial hypertension with increased right ventricular systolic pressure (RVSP) of 83.7± 10.3 mmHg vs. 25.7 ± 0.4 mmHg in TNF-Tg vs. WT mice. E. Number of arterioles in each mouse lung was counted on sections stained for von Willebrand factor (vWF) and there was substantial vessel loss by 3 months of age. F. Quantification of vessels immunofluorescently labeled double positive for both vWF and aSMA indicated that there is a progressive increase in endothelial-mesenchymal transition in TNF-Tg mice. G. TNF-Tg mice have impaired gas exchange as shown by gas chromatography for diffusion of carbon monoxide (DFCO). H. 3D reconstruction of micro-CT scans of barium perfused TNF-Tg and WT lungs demonstrates substantial pruning of the vascular tree with loss of distal arterioles in the TNF-Tg mouse (left, whole lung reconstruction, right, tree structure diagram used for quantification of arteriole size in left lung). I. Double immunostaining for aSMA and proliferation marker Ki-67 demonstrate co-localization in TNF-Tg mice indicating smooth cell proliferation not seen in WT mice. J. Double immunostaining for aSMA and vWF demonstrates co-localization of a subset of cells indicative of the presence of endo-MT in these lesions.

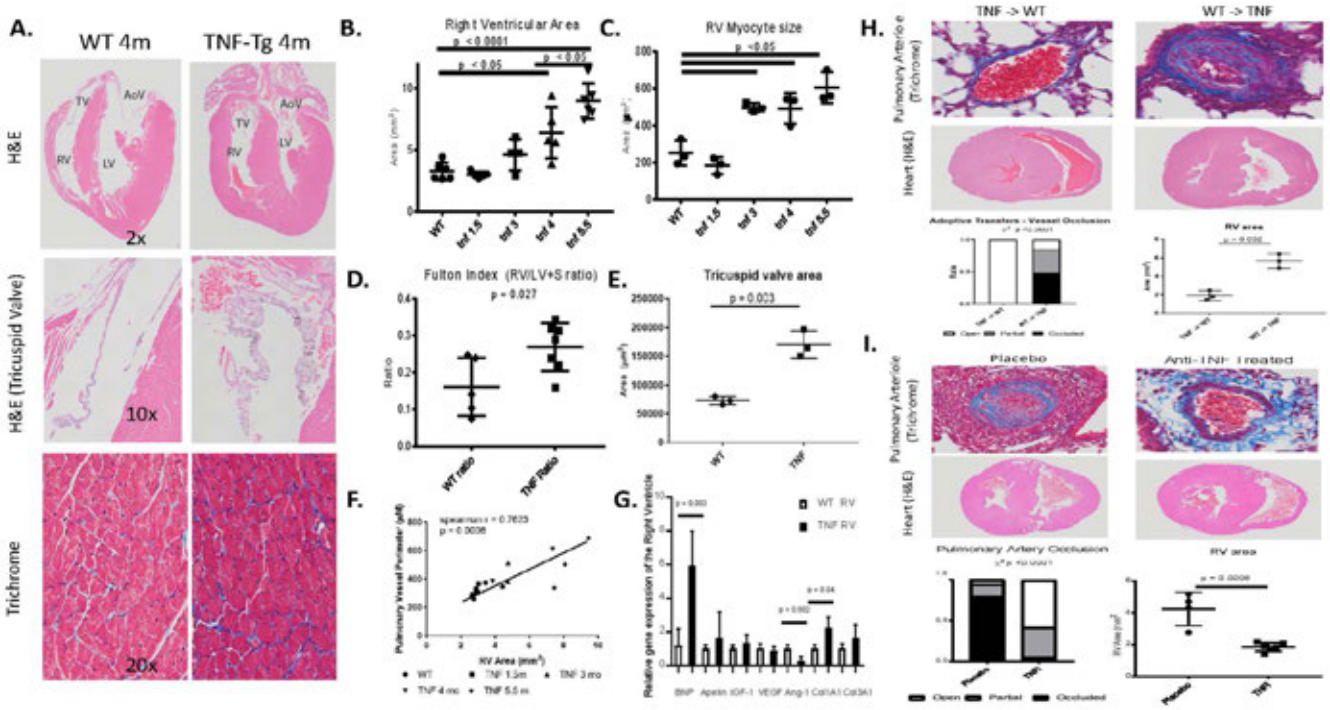
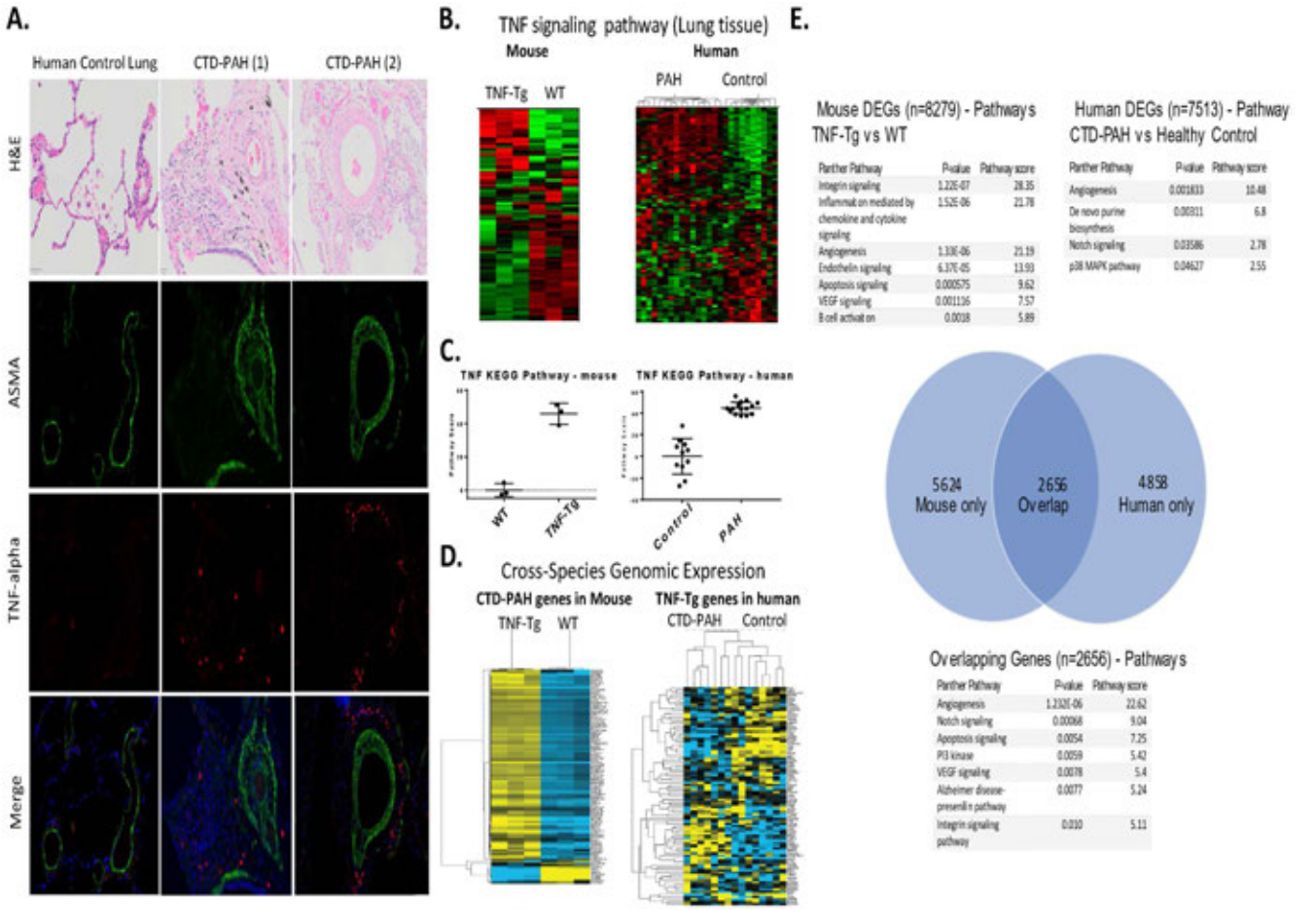


Figure 2. Right ventricular dysfunction in TNF-Tg mice. A. Right ventricular hypertrophy (top, H&E, 2x), tricuspid valve enlargement (middle, H&E, 10x) and myocyte hypertrophy and collagen deposition (bottom, Masson's trichrome, 20x) seen in 4 mo old TNF-Tg hearts compared to WT. B. Histomorphometry revealed progressive increase in RV size over time. C. Histomorphometry revealed progressive increase in RV myocyte size over time. D. Assessment of cardiac weight as measured by the Fulton index (RV/RV+LV+septum) demonstrates abnormal RV weight indicative of RV pathology in 4 mo old TNF-Tg and WT mice. E. Increase in tricuspid valve area in 4 month old TNF-Tg mice. F. RV area is significantly positively associated with pulmonary artery size. G. qPCR of RVs for genes previously shown to be abnormal in RV dysfunction demonstrate significant increases in B natriuretic peptide (BNP) and collagen 1A1 and decrease in angiopoietin-1 in TNF-Tg mice compared to WT, all genes relative expression were normalized to GAPDH. H. Bone marrow chimera experiments revealed that WT mice given TNF-Tg bone marrow at 6 weeks of age did not develop pulmonary or cardiac evidence of PAH at 5 months of age while TNF-Tg mice given WT bone marrow still developed the pathology indicating that mesenchymal rather than bone-marrow derived cells are responsible for the pathology. I. Treatment of TNF-Tg mice with anti-TNF therapy or placebo (CNTO12 and CNTO151, respectively, 10 mg/kg given weekly intraperitoneally from 3 months to 4.5 months of age) demonstrated a lack of progression of pulmonary vascular lesions and no significant right heart pathology after treatment with anti-TNF therapy while placebo animals developed severe PAH.



pah acr abstract figures korman et al 3

Figure 3. TNF expression and other relevant pathways overlap in human CTD-PAH and TNF-Tg mice. A. Immunostaining for aSMA and TNF-alpha in lung biopsies from CTD-PAH patients (n=2, representative of n=5) and normal lung (n=1 representative of n=2) demonstrate that CTD-PAH patients have a significant TNF+ infiltrate in the area surrounding vessels with aSMA proliferation not seen in control individuals. B. RNA sequencing of mouse lungs reveals that the TNF KEGG pathway can distinguish TNF-Tg and WT mice (n=3 per group) by hierarchical clustering (left heatmap, red = increased expression, green = decreased expression) and that the same TNF KEGG pathway in human lungs was able to distinguish patients with PAH of multiple etiologies (n=15) from control lungs (n=11) in publicly available microarray data (GSE113439, right heatmap), C. Condensed TNF pathway scores show significant differences between cases and controls (left, mouse, right, human). D. Top 100 differentially expressed genes from mouse and human PAH lungs are sufficient to distinguish PAH across species (left, top 100 CTD-PAH genes in mouse lung samples, right, top 100 TNF-Tg genes in human lung samples). E. Pathway analysis of human and mouse PAH show substantial overlaps. Over one third (n = 2656) of genes differentially expressed ($p<0.05$ in one species) showed overlap between species. Top pathways in overlapping genes included angiogenesis, notch signaling, apoptosis, and PI3 kinase signaling.

Conclusion: The TNF-Tg mouse represents a novel model of CTD-PAH which recapitulates nearly all key features of the disease and can serve as a valuable tool to better study and test potential CTD-PAH therapeutics.

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Abstract Number: 0810

Small Vessel Vasculitis Syndrome with Autoinflammation Caused by *De Novo* Mutations in LYN Kinase

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SESSION INFORMATION

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Session Title: Pediatric Rheumatology – Basic Science

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Lyn kinase is a member of the Src family of non-receptor tyrosine-protein kinases that modifies signals from various cell surface receptors and regulates innate and adaptive immune responses in myeloid cells, B cells and non-hematopoietic cells. We describe two unrelated patients, with de novo Lyn kinase (LYN) mutations, whose disease sheds light on the pathogenesis of neutrophilic small vessel vasculitis.

Methods: The patients were assessed clinically, immunological parameters, trio whole exome sequencing (WES) and pathogenic studies of the disease-causing *LYN* mutations were investigated in transfection studies and in patients' cells. Cytokine and chemokine panels were measured in patient's serum and monocyte culture supernatants; neutrophil function was assessed.

Results: Both patients presented with perinatal onset of neutrophilic small vessel vasculitis and systemic inflammation including hepatosplenomegaly, periorbital erythema, colitis and epididymitis. Low titer autoantibodies (ANA, anti-Sm, anti-SSA, anti-phospholipids and anti-mitochondrial) and vanishing bile duct disease and liver fibrosis were present in one patient. Both patients had a de novo mutation in Lyn kinase (LYN) (c.1524C >G, p.Y508* and c.1523A >T, p.Y508F). One patient responded to a TNF inhibitor alone, the other patient required combination with the src kinase inhibitor, dasatinib. Patients B cells had constitutive phosphorylation of LYN and downstream kinases (CD19, BTK, CD22, PLCg2) by flow cytometry. Skin biopsy sowed capillaritis with myeloperoxidase (MPO)+ neutrophils attached to small vessel walls. LYN was expressed neutrophils and upregulated in endothelial cells of capillaries with and without vasculitis, but not in endothelial cells of larger vessels. Markers of patient neutrophils had constitutively and stimulated increased expression of activated CD11b (granulocyte adhesion marker), CD64 (FC-receptor), and CD63 (marker of primary granule release) compared to normal controls. However, response to higher doses of chemoattractants was blunted in patient compared to control neutrophils. On dasatinib, bridging fibrosis and FibroScan measurements improved and RNA-seq from 3 liver biopsies showed progressive decrease in gene expression pathways related to wound healing and fibrosis. On dasatinib monotherapy, patient monocytes exhibited constitutive

activation of proinflammatory cytokines including TNF-a, G-CSF, IL-6, MIP-1a and MIP-1b, which was mitigated with combination therapy with src-kinase and TNF inhibitors.

Conclusion: Lyn tyrosine kinase mutations at Tyr508 lead to GOF and an autoinflammatory syndrome characterized by skin vasculitis, colitis, variable liver fibrosis and autoantibody production that sheds light on the role of neutrophil and endothelial cell activation in the pathogenesis of small vessel vasculitis and illustrates a therapeutic role for TNF inhibition alone or in combination with dasatinib.

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Abstract Number: 0811

Monomethyl Fumarate as a Novel Therapy for Macrophage Activation Syndrome: Mechanism of Action in an Animal Model

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SESSION INFORMATION
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Session Title: Pediatric Rheumatology – Basic Science
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Macrophage activation syndrome (MAS) is a deadly systemic inflammatory condition marked by an increase in enzymes of iron metabolism including ferritin and heme-oxygenase 1 (HO-1). Since HO-1 has been implicated in anti-inflammatory pathways, we reasoned that drugs that increase HO-1 activity may work to decrease disease activity in MAS. Dimethyl fumarate is an FDA approved drug for the treatment of inflammatory lesions in multiple sclerosis; its active metabolite monomethyl fumarate (MmF) has been shown to increase HO-1 activity. We therefore tested whether MMF could ameliorate MAS in a murine a model of the disease, and to determine its mechanism of action.

Methods: MAS was induced in mice using the well standardized TLR9-MAS protocol. MmF was injected i.p. at a dose of 45 mg/kg twice daily, DMSO injections were used as control. Organs were measured for weight, serum cytokines were measured by ELISA, cellular populations by flow cytometry, and complete blood counts were performed to assess disease activity. C57BL/6 mice were used for all experiments, HO-1 floxed mice bred to LysM-Cre mice (HO-$1^{\Delta Mac}$) were used in experiments to test the role of HO-1. HO-1 levels were examined by western blotting. Statistical testing was performed using Student's T-test or by 2-way ANOVA as appropriate.

Results: HO-1 is upregulated by TLR9 stimulation and is required for the majority of IL-10 induced by TLR9 in vitro and in vivo. Loss of HO-1 by monocytes and macrophages in the HO-$1^{\Delta Mac}$ mouse did result in lower IL-10 in TLR9-MAS, but did not significantly affect any of the disease parameters. Treatment with MmF increased HO-1 expression in splenic and peritoneal macrophages. Treatment with MmF during TLR9-MAS significantly improved anemia and

splenomegaly, and increased serum IL-10 levels while decreasing IFNγ and IL-12 levels. This improvement was significantly, but only partially dependent on HO-1 expression in the monocyte/macrophage compartment as HO-1$^{\Delta Mac}$ mice were not as protected by MmF therapy as wild type mice during TLR9-MAS.

Conclusion: MmF was effective in reducing a number of disease activity parameters of TLR9-MAS. Furthermore, decreases of the known disease driving cytokines IL-12 and IFNγ were profound. These changes were accompanied an increase in IL-10. We also show that HO-1 plays an important role in regulating IL-10 levels in inflammation, that MmF can increase HO-1 levels, and that the beneficial effects of MmF are partially dependent on HO-1 in the monocyte/macrophage compartment. These results suggest that the parent compound, the FDA approved drug dimethyl fumarate, should be considered in future investigations of MAS therapy, and that pharmacologic manipulation of the HO-1/IL-10 axis may be an important target for future MAS therapies.

Disclosure: C. Biswas, None; **T. Burn**, None; **N. Chu**, None; **E. Behrens**, None.

Abstract Number: 0812

Sex Differences in Autoimmunity and Cardiovascular Risk Could Be Associated with Altered Treg Phenotype and Lipoprotein Metabolism

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SESSION INFORMATION
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Session Title: Pediatric Rheumatology – Basic Science
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Males and females have altered immune responses resulting in variation in autoimmune risk. Sex differences exist in the frequency and activity of immune-cell subsets but mechanisms underlying sexual dimorphism remain unknown. Our previous work identified a link between immune cell function and lipid metabolism. We hypothesised that sex hormones could influence immune cell differentiation via changes in lipid metabolism and this could be altered in autoimmune diseases such as juvenile-onset systemic lupus erythematosus (JSLE) that emerges during puberty and has a strong female prevalence.

Methods: Flow cytometry and qPCR were used to measure metabolic marker expression on 44 immune cell subsets from 39 teenage healthy controls (HCs, 17 male, 22 female, mean age 19), 35 age matched JSLE patients (12 male, 23 female, mean age 19), pre puberty HCs (10 males and 10 females, mean age 8) and individuals with gender dysphoria undergoing cross-sex hormone therapy (10 biologic males and 10 biologic females). Analysis of metabolic biomarkers including lipoprotein composition was performed on matching serum using nuclear magnetic resonance.

Results: HC responder (Tresp) and regulatory (Treg) T-cell subsets displayed the strongest immune profile differences by sex with significantly increased Tregs (p= 0.036) and reduced Tresp (p= 0.001) frequencies in males compared to females. HC Male Tregs had an increased suppressive capacity, IL-4 production (p= 0.019) (supported by increased GATA-3 expression) and plasma membrane glycosphingolipid (GSL) expression (p= 0.038) compared to Tregs from HC females. GSL changes were mirrored by increased expression of GSL synthesis enzyme UGCG (p= 0.042) in male Tregs, suggesting a sex-specific alteration in lipid metabolism related to Treg function.

Metabolomic lipoprotein analysis of matching serum revealed that teenage HC males had significantly reduced atheroprotective high density lipoprotein subsets and increased atherogenic very low density lipoprotein (VLDL) subsets compared to HC females. These differences were not observed pre-puberty but were induced appropriately by sex hormone treatment in gender dysphoria individuals; suggesting that sex hormones regulate lipid metabolism in vivo.

VLDL subsets from HC males were preferentially enriched with triglycerides and correlated positively with activated Treg subsets compared to VLDL from HC females where no such relationship was seen. Furthermore, Tregs cultured with VLDL isolated from either HC males or females recapitulated the male and female Treg phenotype respectively. Strikingly, sex differences in Treg frequency, phenotype, lipid metabolism and serum lipoproteins were lost in patients with JSLE. This loss of sexual dimorphism in JSLE patients involved the development of a more atherogenic metabolomic profile and pro-inflammatory T-cell phenotype in females.

Conclusion: Potential defects in sex hormone signalling in patients with JSLE may lead to a loss of differential male/female lipid taxonomy. Defective lipoprotein metabolism in JSLE could alter immune cell plasma membrane lipids and immune cell function and contribute to increased cardiovascular risk in female JSLE patients.

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Abstract Number: 0813

Monocyte and Macrophage Transcriptional Phenotypes in Systemic Juvenile Idiopathic Arthritis Reveal TRIM8 as a Mediator of IFNγ Hyperresponsiveness and Risk for Macrophage Activation Syndrome

Grant Schulert,[1] Thuy Do,[1] Sanjeev Dhakal,[1] Ndate Fall,[2] Mario Medvedovich,[3] Sherry Thornton,[1] Nathan salomonis,[2] and Alexei A. Grom[1], [1]Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]University of Cincinnati College of Medicine, Cincinnati, OH

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Pediatric Rheumatology – Basic Science
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Systemic juvenile idiopathic arthritis (SJIA) is a severe and distinct subtype of childhood arthritis. Children with SJIA are at risk for macrophage activation syndrome (MAS), a life-threatening episode of hyperinflammation driven by interferon-gamma (IFNγ). Previous work has suggested that monocytes in SJIA display hyperresponsiveness to IFNγ, but the molecular basis of this remains unclear. The objective of this study is to identify monocyte and macrophage polarization phenotypes including features of interferon response.

Methods: Bulk RNA-sequencing (RNA-seq) was performed on purified monocytes from 26 patients with SJIA without overt MAS. In addition, single-cell RNA-seq was performed on isolated bone marrow macrophages (BMM). THP-1 monocytic cells were transfected with TRIM8-specific small-interfering RNA (siRNA) prior to stimulation with IFNγ.

Results: Bulk RNA-seq of purified SJIA monocytes revealed marked transcriptional changes between cells from patients with high vs low serum ferritin levels including upregulated gene pathways Response to External Stimulus ($p=2.73x10^{-17}$) Defense Response ($p=2.66x10^{-14}$), and Inflammatory Response ($p=1.95x10^{-11}$). When comparing the

SJIA monocyte signature to well-characterized polarization phenotypes, we identified little evidence of IFNγ-induced signature but substantial overlap with multiple polarization states, reflecting either a mixed phenotype or multiple distinct cell populations. Interestingly, among the most highly upregulated genes in SJIA monocytes was tripartite motif containing 8 (TRIM8), an E3 ubiquitin-ligase involved in activation of IFNγ through promoting degradation of the suppressor of cytokine signaling 1 (SOCS1). Elevated TRIM8 expression was found in monocytes from both active and inactive SJIA patients, with the highest levels in those with subclinical MAS (n=3). Furthermore, we utilized scRNA-seq to determine gene expression profiles of BMM from a patient with subclinical MAS. This single cell approach identified a distinct subpopulation of BMM which exhibited markedly altered transcriptional profiles, with the most significantly upregulated pathways being cellular response to IFNγ (p=1.35e-14), endocytic vesicle membranes (p=8.44E-14), and phagosome (p=2.98e-9). These BMM also showed significantly increased expression of TRIM8 (6.4-fold), IFNAR1 (10.5-fold), and IFNGR2 (13.8-fold). To confirm the role of TRIM8 in augmenting macrophage responses to IFNγ, TRIM8 expression was knocked-down in THP-1 using siRNA. TRIM8 knock-down macrophages showed significant reductions in both early (4 hour) and late (24-48 hours) response to IFNγ, as determined by production of CXCL9, a biomarker for MAS activity in both mouse models and patients.

Conclusion: Peripheral monocytes in SJIA display markers of multiple polarization states, while during MAS BMM demonstrate a clear IFNγ response phenotype. TRIM8 is highly expressed in both monocytes and macrophages in SJIA, and in vitro knockdown of TRIM8 reduces macrophage IFNγ response. These data provide a molecular mechanism for monocyte hyperresponsiveness to IFNγ in SJIA, as well as a novel therapeutic target for MAS.

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Abstract Number: 0814

Interferon Signature and Cytokine Patterns Define Novel Autoinflammatory Diseases

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SESSION INFORMATION

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Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Undifferentiated systemic autoinflammatory diseases (USAID) present diagnostic and therapeutic challenges. Cytokine dysregulation may identify disease groups that respond to targeted treatments. IFN-signaling blocking treatments in patients with high IFN signature and novel treatments for macrophage activation syndrome (MAS) may benefit patients without a genetic diagnosis. An integrated screening approach of patients with USAIDs that included assessment of an IFN signature and serum cytokines followed by genomic evaluation led to the identification of novel disease subsets that present with an IFN signature.

Methods: We evaluated 66 patients with USAID. Using a Nanostring assay, a 28-gene IFN score of selected interferon response genes (IRGs) was calculated. RNA-seq of matched samples was used for the correlation between RNA-seq and Nanostring for the validation of a 4-gene NF-kB Nanostring subscore. Serum levels of 48 analytes were determined by a multiplex cytokine assay and high IL-18 levels were reanalyzed by ELISA. Whole exome sequencing (WES) and/or whole genome sequencing (WGS) was performed in 61 of the 66 patients.

Results: Of the 66 patients, 36 (55%) had elevated interferon response gene signatures (IRS). Neutrophilic panniculitis (40% vs 0%) basal ganglia calcifications (46% vs. 0%), interstitial lung disease (47% vs 5%) and myositis (60% vs 10%) were significantly higher in pts with elevated IRS. Eight pts with pulmonary alveolar proteinosis (PAP) had highly-elevated IL-18 serum levels and recurrent macrophage activation syndrome (MAS). Of 11 patients with low IFN score elevation, CANDLE-like panniculitis and progressive cytopenias 2 were compound heterozygous for novel *LRBA* mutations, 3 males harbor novel splice variants in *IKBKG*/NEMO, and 6 patients have de novo frameshift mutations in *SAMD9L.* Of 13 patients with highly elevated IRS and CANDLE-, SAVI- or Aicardi-Goutières-Syndrome (AGS)-like phenotypes, 5 pts had each a mutation in either *SAMHD1, TREX1, PSMB8 or PSMG2*. Two patients had anti-MDA5-positive juvenile dermatomyositis, and 7 could not be further characterized. Different patterns of interferon-response-gene (IRG) elevation with a higher relative expression of 4 IRGs with NF-kB binding sites assessed referred to as 4- NF-kB/24-STAT1 ratio distinguished patients with *LRBA, IKBKG*/*NEMO* and *SAMD9L* mutations from the autoinflammatory interferonopathies CANDLE, SAVI and AGS and suggested proportionally increased concomitant NF-kB signaling in LRBA deficiency and NEMO-NDAS.

Conclusion: IRS elevation, characteristic cytokine elevations and clinical features identified 3 novel diseases, IL-18-mediated PAP and recurrent MAS (IL-18PAP-MAS), NEMOD5-associated autoinflammatory syndrome (NDAS), and SAMD9L-associated autoinflammatory disease (SAAD), thus expanding the diagnostic armamentarium in assessing patients with USAIDs, and pointing to novel pathways regulating interferon-response-gene-expression.

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Abstract Number: 0815

Expression Profiling of Genes in Rheumatoid Fibroblast-like Synoviocytes Regulated by Fas Ligand Using cDNA Microarray Analysis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis I
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Fas ligand (FasL) is a member of tumor necrosis factor superfamily (TNFSF6) and reported to contribute to synovial hyperplasia of rheumatoid arthritis (RA). Apoptosis through Fas/FasL pathway of RA synovial cells was inhibited by pro-inflammatory cytokines present within the synovium. We previously reported that decoy receptor 3 overexpressed in rheumatoid synovial fibroblasts (RA-FLS) stimulated by TNFα protects the cells from Fas-induced apoptosis. In this study, we investigated the gene expression profiles regulated by FasL in RA-FLS to reveal how FasL is involved in the pathogenesis of RA.

Methods: Primary cultured RA-FLS were incubated with either 1000 ng/ml of recombinant human FasL protein or phosphate buffered saline as unstimulated control diluted with Opti-MEM reduced serum medium for 12h. Gene expressions were detected by microarray assay (Human Genome U133 Plus 2.0, GeneChip® 3' Expression Array; Thermo Fisher Scientific).

Results: Microarray data analysis revealed that FasL up-regulated or down-regulated the expression of various genes in RA-FLS. The most up-regulated 3 genes by FasL were dual specificity phosphatase 6 (DUSP6; fold change, 34.6), epiregulin (EREG; fold change, 29.2) and interleukin11 (IL-11; fold change, 25.3). DUSP6 regulates CD4+ T-cell activation and differentiation by inhibiting the T-cell receptor-dependent extracellular signal-regulated kinases 1 and 2 activations. EREG is increased in patients with RA and associated with the development of cytokine-induced arthritis. IL-11 regulates the growth and development of hematopoietic stem cells and decreases the pro-inflammatory cytokines and nitric oxide productions. The most down-regulated 3 genes by FasL were angiopoietin-like 7 (ANGPTL7; fold change, 11.6), protein inhibitor of activated STAT2 (PIAS2; fold change, 11.3) and growth differentiation factor 5 (GDF5; fold change, 11.1). ANGPTL7 is pro-angiogenic factor and promotes pro-inflammatory responses through the P38 signaling pathway. PIAS proteins inhibit the activated STAT and are involved in the pathogenesis of RA. GDF5 is associated with joint destruction of patients with OA and RA. The function of regulated genes included transcriptional activator activity, positive regulation of metabolic process, positive regulation of cellular metabolic process, positive regulation of macromolecule metabolic process, positive regulation of nitrogen compound metabolic process, regulation of phosphorylation, positive regulation of biological process, regulation of phosphate metabolic process, regulation of MAPK cascade, and regulation of multicellular organismal process.

Conclusion: FasL regulates the expression of various genes in RA-FLS. FasL may affect the pathogenesis of RA by regulating gene expression of RA-FLS.

Disclosure: K. Fukuda, None; **Y. Miura**, None; **S. Hayashi**, None; **T. Maeda**, None; **R. Kuroda**, None.

Abstract Number: 0816

The Long Non-coding RNA HOTAIR Regulates BMP2 and Wnt Pathways in Synovial Fibroblasts

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Etiology & Pathogenesis I

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Mechanisms involved in joint patterning of rheumatic diseases remain unknown. The long non-coding RNA HOTAIR is exclusively expressed in synovial fibroblasts (SF) from lower extremity joints. HOTAIR is known to be an important regulator of the epigenetic landscape by modulating H3K27me3 and H3K4me1 marks. Here, we analysed the function of HOTAIR in SF.

Methods: HOTAIR was silenced in knee SF from osteoarthritis (OA) patients by GapmeRs. ChIP-sequencing of H3K27me3 marks (Illumina HiSeq 2500) and RNA-sequencing (NovaSeq 6000) were performed in GapHOTAIR- and control-transfected SF at 48h after transfection (n=3). Enriched pathways and protein interactions were analyzed using DAVID and STRING networks, respectively. Regulated genes were confirmed by real-time PCR in SF from OA and rheumatoid arthritis (RA) patients (n=8) and changes after cycloheximide adjunction (10ug/ml 6h and 24h) were evaluated (n=3). Signaling pathways were studied by Western blotting (n=5). Effect of HOTAIR silencing on the canonical Wnt pathway was assessed using TOP/FOP reporter system (n=4). The expression of HOTAIR was studied after stimulation with TNF-α in SF (n=17) and correlated with TNF-α-expression in synovial tissues from RA patients (knee and ankle) (n=7).

Results: ChIP-sequencing showed 3225 loci, which lost H3K27me3 marks in HOTAIR silenced SF. Transcription of the genes at 492 of these loci was up-regulated in SF transfected with GapHOTAIR. Pathway enrichment showed that these transcripts were mainly involved in cancer, apoptosis and Wnt signaling. Among them, we confirmed the overexpression of BMP2 (1.7±0.5-fold; $p< 0.01$) and CTNNB1 (beta-catenin) (1.5±0.5-fold; $p< 0.01$) and showed a down-regulation of other genes belonging to the Wnt pathway (LGR5 ($p=0.02$), GSK3β ($p=0.03$) and a trend for LRP6 ($p=0.06$)). Blocking translation by adding cycloheximide did not change BMP2 and CTNNB1 expression, confirming a direct effect of HOTAIR on these genes, whereas the effect on other Wnt genes was indirect. The repressor of Wnt pathway SFRP1 was significantly enriched for H3K27me3 marks in controls as compared to GapHOTAIR SF, but its transcription was not changed in GapHOTAIR SF. The regulation of the canonical-Wnt pathway was confirmed by the TOP/FOP system by 1.8±0.2-fold decrease in Wnt activation after HOTAIR silencing ($p=0.01$). BMP2 regulation was mediated by non-canonical pathway through ERK1/2 phosphorylation ($p=0.01$). TNF-α stimulation led to a 2.1±0.3 decrease in HOTAIR expression in SF ($p< 0.0001$) and was inversely correlated with HOTAIR in the RA synovium ($r=-0.79$; $p< 0.05$).

Conclusion: HOTAIR regulates the non-canonical BMP2 and the canonical Wnt pathway by epigenetic and transcriptional mechanisms. Downregulation of HOTAIR during inflammation might influence the phenotype of chronic arthritis in joints of the lower extremities with implications for disease severity and therapy.

Disclosure: M. Elhai, None; **R. Micheroli**, None; **M. Frank-Bertoncelj**, Kurt und Senta Herrmann Foundation, 2, Promedica Foundation, 2; **K. Klein**, None; **O. Distler**, A. Menarini, 5, Abbvie, Acceleron, 5, Acceleron Pharma, 5, Actelion, 2, 5, 8, Actelion Pharmaceuticals, 2, 5, 8, 9, Amgen, 5, AnaMar, 2, 5, Bayer, 2, 5, 8, 9, Biogen Idec, 2, 5, Blade Therapeutics, 5, Boehringer Ingelheim, 2, 5, 8, 9, Catenion, 5, 9, ChemomAb, 2, 5, ChemomAB, 5, CSL Behring, 5, Ergonex, 5, espeRare Foundation, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 5, GSK, 2, 5, Holds Patent mir-29 for the treatment of systemic sclerosis, 9, Inventiva, 2, 5, iQvia, 5, Italfarmaco, 2, 5, Italfarmco, 5, Lilly, 2, 5, med, 5, 8, medac, 5, Medac, 2, 5, MedImmune, 2, 5, Medscape, 5, 8, 9, Menarini, 8, Mepha, 8, Mitsubishi Tanabe, 2, 5, Mitsubishi Tanabe Pharma, 2, 5, MSD, 5, 8, Novartis, 2, 5, 8, 9, Patent, 9, Patent issued, 9, Pfizer, 2, 5, 8, Pharmacyclics, 2, 5, Roche, 5, 8, 9, Sanofi, 2, 5, Sinoxa, 2, 5, Target Bio Science, 5, Target BioScience, 5, UCB, 2, 5, 9, UCB in the area of potential treatments of scleroderma and its complications, 2, 5; **C. Ospelt**, Kurt und Senta Herrmann Foundation, 2, Promedica Foundation, 2.

Abstract Number: 0817

Enhanced Expression of mRNA for TAK1 in CD34+ Cells of the Bone Marrow in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis I
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by synovial hyperplasia, consisting of type A macrophage-like synoviocytes and type B fibroblast-like synoviocytes (FLS). We have previously demonstrated that bone marrow (BM) CD34+ cells from RA patients have abnormal capacities to respond to tumor necrosis factor-α (TNF-α) and to differentiate into FLS, playing an important role in the pathogenesis of RA. However, the mechanism of the abnormal responses to TNF-α of BM CD34+ cells has been unclear. Of note, transforming growth factor β activated kinase 1 (TAK1) has been shown to be activated in the inflammatory signal transduction pathways in response to IL-1β, TNF-α or toll-like receptor stimulation. Moreover, it has been disclosed that intraarticular administration of siRNA for TAK1 inhibited the development of collagen-induced arthritis in mice. It

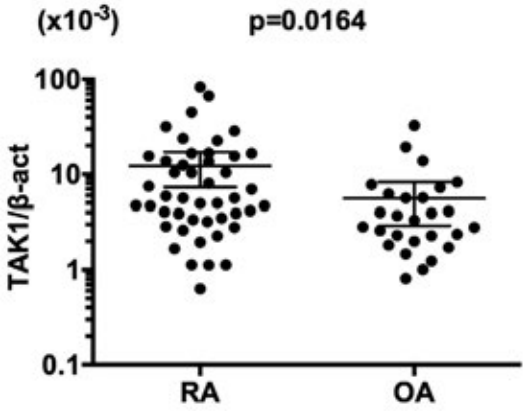

Figure 1. The expression of mRNA for TAK1 in bone marrow CD34+ cells in RA patients and in OA patients

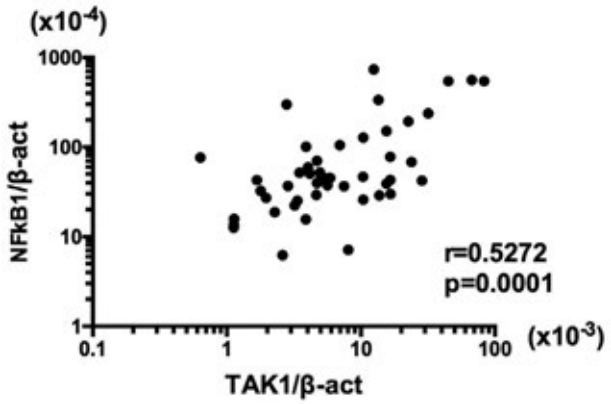

Figure 2. The correlation of the expression of TAK1 mRNA with that of NFκB1 (p50) mRNA in bone marrow CD34+ cells in RA patients

is thus possible that aberrant expression of TAK1 in BM CD34+ cells might lead to their abnormal responses to TNF-α resulting in enhanced differentiation into FLS. The current study therefore examined the mRNA expression of TAK1 in BM CD34+ cells from RA patients.

Methods: BM samples were obtained from 47 patients with RA (6 males and 41 females: mean age 58.8 years) and 27 patients with OA (2 males and 25 females: mean age 70.4 years), who gave informed consent, during joint operations via aspiration from iliac crest. CD34+ cells were purified from the BM mononuclear cells by positive selection with magnetic beads. The expression of mRNA for TAK1 was examined by quantitative reverse transcription PCR. The results are shown as the ratio of the copy numbers to those of β-actin mRNA.

Results: The expression of mRNA for TAK1 was significantly higher in RA BM CD34+ cells than OA BM CD34+ cells (Figure 1). The mRNA expression levels of TAK1 were not correlated with serum C-reactive protein (r=0.08316, p=0.5784) or with treatment regimens with or without methotrexate or glucocorticoids. TAK1 mRNA expression was significantly correlated with NFκB1 mRNA expression in RA BM CD34+ cells (Figure 2). Finally, TNF-α enhanced NFκB1 mRNA expression, but not TAK1 mRNA expression, in BM CD34+ cells from normal individuals.

Conclusion: These results indicate that the enhanced expression of TAK1 mRNA in BM CD34+ cells plays a pivotal role in the pathogenesis of RA through upregulation of differentiation of FLS. Moreover, the data have also disclosed that the upregulation of TAK1 mRNA expression might lead to the increased expression of NFκB1 mRNA in BM CD34+ cells, but not vice versa, consistently with the position of TAK1 upstream of mitogen-activated protein kinases and the IkB kinase complex in signaling cascades. It is thus confirmed that TAK1 might be a good therapeutic target in RA.

Disclosure: S. Hirohata, None; **T. Nagai**, None; **T. Tomita**, None; **H. Yoshikawa**, None.

Abstract Number: 0818

Semaphorins: From Angiogenesis to Inflammation in Rheumatoid Arthritis

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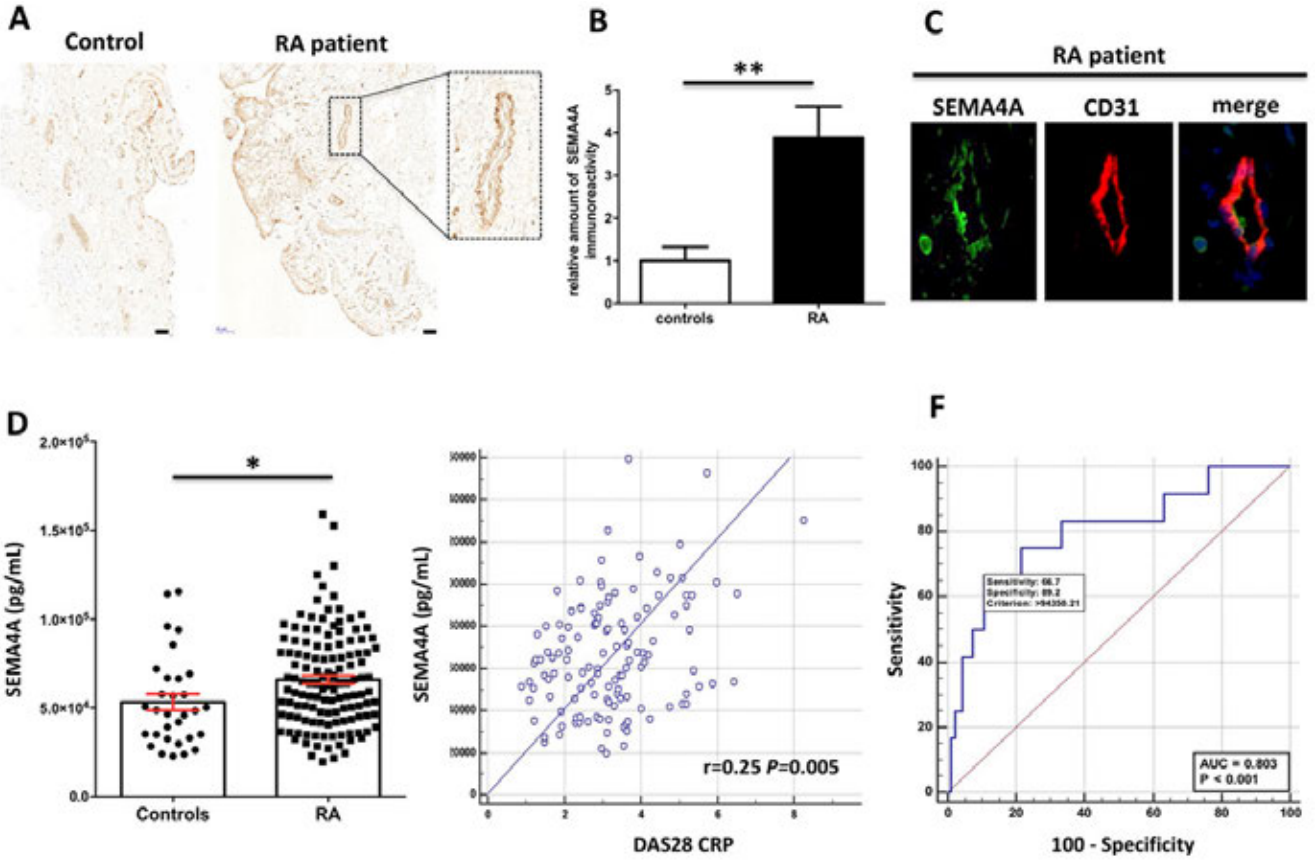
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis I
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Synovial neoangiogenesis is an early and crucial event to promote the development of the hyperplasic proliferative pathologic synovium in rheumatoid arthritis (RA). A recent microarray analysis revealed a differential expression of semaphorin family in RA endothelial cells (ECs), which is known to contribute to angiogenesis and inflammation. Our aim was to study the potential implication of semaphorins in RA pathogenesis.

Methods: mRNA levels of class 3 and 4 Semaphorins (SEMA) SEMA3A, SEMA3E, SEMA4A and SEMA4E, as well as their receptors PlexinD1 (PLXND1) and Neuropillin-1 (NRP1), were measured by real-time quantitative PCR in RA (n=15) and control (n=15) ECs. Protein expression of these 4 semaphorins and their receptors was evaluated in ECs of 10 RA patients and controls by western blot, and in the synovial tissue of 10 RA patients and 5 controls by immunohistochemistry and immunofluorescence. Serum concentrations of these 4 semaphorins were measured by sandwich ELISA in a cohort of 130 patients with RA (85% women, mean age: 58 ± 12 years and mean disease duration: 11 ± 12 years) and 30 age- (56 ± 10 years) and sex- (82% women) matched controls.



A-C, Overexpression of SEMA4A in the synovial tissue of patients with rheumatoid arthritis (RA) compred to healthy controls. A, Representative images synovial sections stained for SEMA4A (scale bar 100μm). B, amount of immunoreactivity quantified with the image J software (n=5 for each). C, D Double labeling for SEMA4A and CD31 showing the expression of SEMA4A in synovial vessels. D, Increased circulating SEMA4A levels in the serum of patients with RA (n=130) as compared to healthy controls (n=30). E, correlation between SEMA4A serum levels and the disease activity score (DAS)-28 CRP. F, ROC curve illustrating the diagnostic value of SEMA4A to identify patients patients with high disease activity. *p<0.05, ** p<0.01.

Results: ResultsSEMA4A, PLXND1 and NRP1 mRNA and protein levels were markedly increased in RA ECs. The expression of SEMA4A (Figure 1A-B), SEMA3A, SEMA3E, PLXND1 and NRP1 was strikingly increased in the synovial tissue of RA patients. Confocal microscopy with double labeling for CD31 confirmed the prominent endothelial expression of these class 3 and 4 semaphorins and their receptors (Figure 1C). Serum levels of SEMA4A (Figure 1D) and SEMA3E were significantly increased in patients with RA compared to controls. Conversely, SEMA3A serum levels were strikingly lower in patients with RA compared to controls. SEMA4A (Figure 1E), SEMA3A, SEMA3E and SEMA4D serum levels correlated with markers of joint and systemic inflammation (swollen joint count, ESR, CRP, synovial vascularization assessed by power Doppler), validated composite score measuring disease activity (DAS28 and DAS28-CRP) as well as circulating proangiogenic markers (VEGF, Tie2, VCAM-1, IL-8). The diagnostic value of SEMA4A to identify patients with an "inflammatory profile" (DAS28 >3.2, CRP >10 mg/L and increased power Doppler global arthritis score) was defined by an area under curve (AUC) of 0.80 (P< 0.001) (Figure 1F). In the 52/130 patients (40%) in remission or with low disease activity defined by a DAS28< 3.2, defined by the persistence of synovial hyperemia detected on at least one joint, SEMA4A and SEMA4D detected residual infraclinical disease activity with an AUC of 0.70 (P=0.008 and P=0.012, respectively).

Conclusion: Gene expression profiling of ECs identified semaphorins as potential biomarkers and therapeutic candidates in RA. Class 3 and 4 semaphorins are overexpressed in ECs, synovial vessels and the serum of patients with RA. They also correlated with validated markers of inflammation and angiogenesis. Thus, semaphorins might be novel and appealing EC-derived inflammatory and proangiogenic targets in RA.

Disclosure: J. Avouac, Pfizer, 2, 8; **S. Pezet**, None; **E. Vandebeuque**, None; **Y. Allanore**, None.

Abstract Number: 0819

The Long Noncoding RNA HOTTIP Regulates Cell Cycle and Inflammatory Response in Hand Synovial Fibroblasts

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Etiology & Pathogenesis I
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Previously we showed that the long noncoding RNA (lncRNA) HOTTIP is exclusively expressed in synovial fibroblasts (SF) from distal joints, such as small joints of hands and feet, which exhibit prominent proliferative and chemotactic activities (Frank-Bertoncelj, *et al*. Nat Commun, 2017). Our objective was to explore the role of HOTTIP in shaping the function of hand SF in arthritis.

Methods: We silenced the lncRNA HOTTIP in hand SF using LNA GapmeRs (100 nM, 48h). We conducted RNA-sequencing (n=2) and confirmed RNA-sequencing data with qPCR in a larger cohort of hand SF from RA patients (n=6). Protein-protein interaction analysis of RNA-sequencing data was performed using STRING. Protein levels of IL8 (n=4) and MMP3 (n=6) in cell supernatants were measured by ELISA. Cyclin dependent kinase inhibitor p21 (n=4) was detected by Western blot. Proliferation (n=3) was measured in vitro using the BrdU assay. Apoptosis and necro-

sis (n=6) were determined with Real time-Glo annexin V apoptosis and necrosis assay. Significance was defined as $p< 0.05$ measured by one-sample t-test or paired t-test.

Results: STRING analysis of RNA sequencing data showed changes in cell cycle, inflammatory response and integrin pathways after silencing of HOTTIP in hand SF. We confirmed the significant downregulation of transcripts involved in mitotic cell cycle (NCAPG, TUBGCP5, TADA3, ASPM, ZWILCH, CDC27, BUB1, GPSM2 and CDK6), significantly increased transcript and protein expression of the cyclin-dependent kinase inhibitor p21 and significantly less proliferation in HOTTIP silenced hand SF. No difference in apoptosis and necrosis was observed between HOTTIP and control silenced hand SF. Furthermore, silencing of HOTTIP resulted in significant upregulation of transcripts involved in inflammatory and immune response pathways (IL8, IL12A, IL17C, CXCL3, MMP3 and TNFAIP3) and significantly increased protein levels of IL8 and MMP3. Silencing of HOTTIP also significantly altered gene expression of different types of integrins (ITGA3, ITGB1, ITGB5, ITGB7 and ITGA2B) that play a role in adhesion and organization of newly synthesized extracellular matrix. Stimulation of hand SF with TNFα and IL6/IL6R resulted in significant decrease of HOTTIP expression.

Conclusion: Distal-specific expression of HOTTIP could support enhanced proliferative properties in hand SF. In inflammatory conditions, reduced levels of HOTTIP might shape a location-specific inflammatory response with joint-specific changes in cytokine and chemokine expression, cell adhesion and cell-to-extracellular matrix interactions.

Disclosure: M. Frank-Bertoncelj, Kurt und Senta Herrmann Foundation, 2, Promedica Foundation, 2; **T. Kuret**, EULAR Scientific Bursary, 2, IUBMB Wood-Whelan Fellowship, 2, Swiss-European Mobility Programme (SEMP) Scholarship, 2, Slovenian Research Agency, 2; **A. Županič**, EULAR Scientific Bursary, 2; **S. Sodin-Semrl**, None; **O. Distler**, A. Menarini, 5, Abbvie, Acceleron, 5, Acceleron Pharma, 5, Actelion, 2, 5, 8, Actelion Pharmaceuticals, 2, 5, 8, 9, Amgen, 5, AnaMar, 2, 5, Bayer, 2, 5, 8, 9, Biogen Idec, 2, 5, Blade Therapeutics, 5, Boehringer Ingelheim, 2, 5, 8, 9, Catenion, 5, 9, ChemomAb, 2, 5, ChemomAB, 5, CSL Behring, 5, Ergonex, 5, espeRare Foundation, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 5, GSK, 2, 5, Holds Patent mir-29 for the treatment of systemic sclerosis, 9, Inventiva, 2, 5, iQvia, 5, Italfarmaco, 2, 5, Italfarmco, 5, Lilly, 2, 5, med, 5, 8, medac, 5, Medac, 2, 5, MedImmune, 2, 5, Medscape, 5, 8, 9, Menarini, 8, Mepha, 8, Mitsubishi Tanabe, 2, 5, Mitsubishi Tanabe Pharma, 2, 5, MSD, 5, 8, Novartis, 2, 5, 8, 9, Patent, 9, Patent issued, 9, Pfizer, 2, 5, 8, Pharmacyclics, 2, 5, Roche, 5, 8, 9, Sanofi, 2, 5, Sinoxa, 2, 5, Target Bio Science, 5, Target BioScience, 5, UCB, 2, 5, 9, UCB in the area of potential treatments of scleroderma and its complications, 2, 5; **C. Ospelt**, Kurt und Senta Herrmann Foundation, 2, Promedica Foundation, 2.

Abstract Number: 0820

Diurnal Stability of Transcriptional Profiles in Rheumatoid Arthritis

Louise Bennett,[1] Fraser Morton,[1] George Fragoulis,[1] Caron Paterson,[1] Dominic Rimmer,[2] Gary Semple,[3] Alison Young,[3] Jagtar S Nijjar,[4] Michael Barrett,[5] Stefan Siebert,[1] Duncan Porter,[5] Carl Goodyear,[6] and Iain McInnes[1], [1]Institute of Infection, Immunity & Inflammation, University of Glasgow, Glasgow, United Kingdom, [2]Clinical Research Facility, NHS Greater Glasgow and Clyde, Glasgow, United Kingdom, [3]Clinical Research Facility, NHS Greater Glasgow and Clyde, Glasgow, [4]Department of Medicine, University of Cambridge, Cambridge, United Kingdom, [5]Institute of Infection, Immunity & Inflammation, University of Glasgow, Glasgow, [6]University of Glasgow, Glasgow, United Kingdom

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Etiology & Pathogenesis I

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Our understanding of disease pathogenesis in Rheumatoid Arthritis (RA) is rapidly expanding with the advent of 'Omics' techniques. Importantly, current analysis takes into account many clinical covariates such as gender and age, however there are no studies to date that have systematically examined the impact that the timing of sample acquisition has on transcriptional profiles. This is a fundamental covariate given the real-world clinical setting of samples acquisition. Moreover, within day variation in RA symptoms are characteristic of disease (e.g. early morning stiffness). Herein, we evaluated the diurnal variation in transcriptomic profiles in 10 RA patients.

Methods: Whole blood was drawn into Paxgene tubes from 10 RA patients over the course of one day (8am, 9am, 11am, 1pm and 3pm), and stored at -80°C. RNA was extracted using the Paxgene Blood miRNA kit and libraries prepared for RNA-Seq using the Illumina TruSeq Stranded Total RNA Ribo-Zero H/M/R Gold kit. RNA-seq was performed and data analysed using the likelihood ratio test in the DESeq2 R package to identify any genes that showed a change in expression across the different time points. The genes identified as being differentially expressed and having a fold change greater than 1.5 between any two time points in the RNA-Seq analysis were clustered to identify patterns of expression. Gene ontology enrichment analysis as well as pathway over-representation analysis using the Reactome database was performed.

Results: RNA-Seq analysis identified 395 genes with a fold change of 1.5 or greater that were differentially expressed between the timepoints. Cluster analysis of these genes identified four patterns of expression. Two of the expression clusters (utilising 86 or 149 genes respectively) showed a decrease in transcripts throughout the day, figure 1. Notably, the gene ontology terms associated with the clusters were; neutrophil activation, myeloid and leucocyte migration, neutrophil degranulation, figure 2a. Furthermore, Reactome Pathways Analysis highlighted; interleukin-33 signalling, interleukin-10 signalling, and interleukin-1 family signalling as over-represented in the clusters. All of which are commensurate with increased immune activation in the morning. In comparison, the other two expression

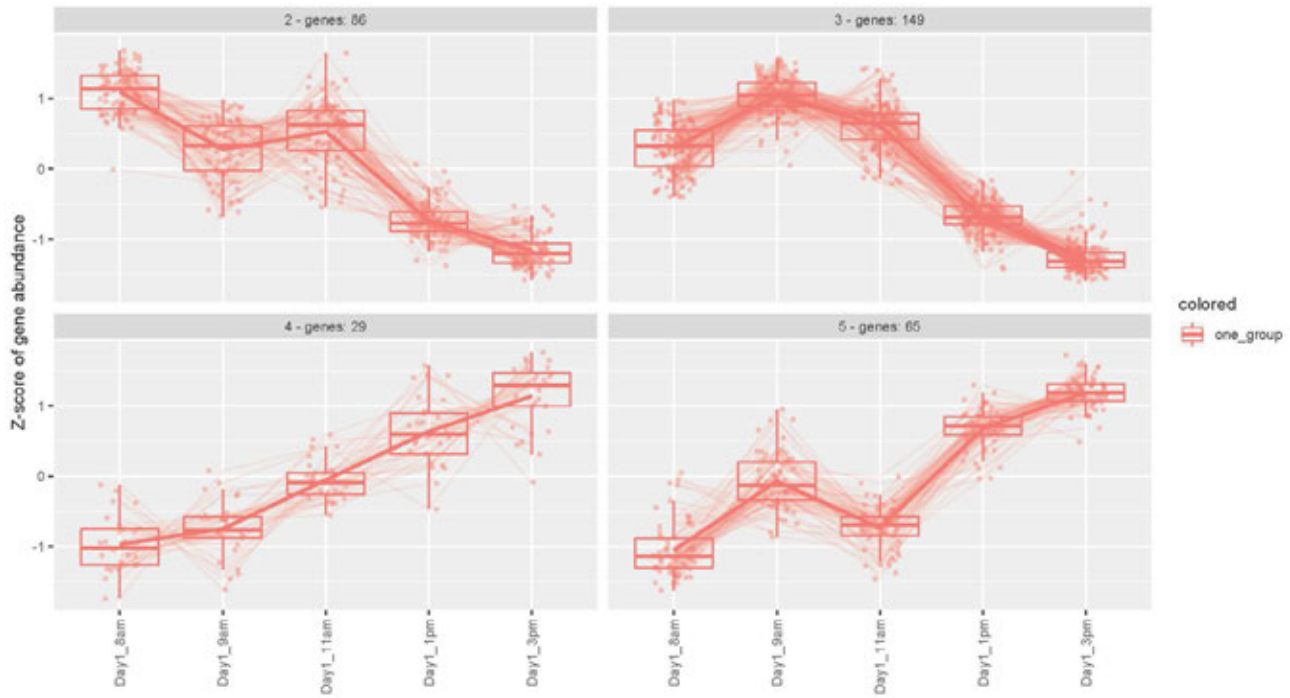
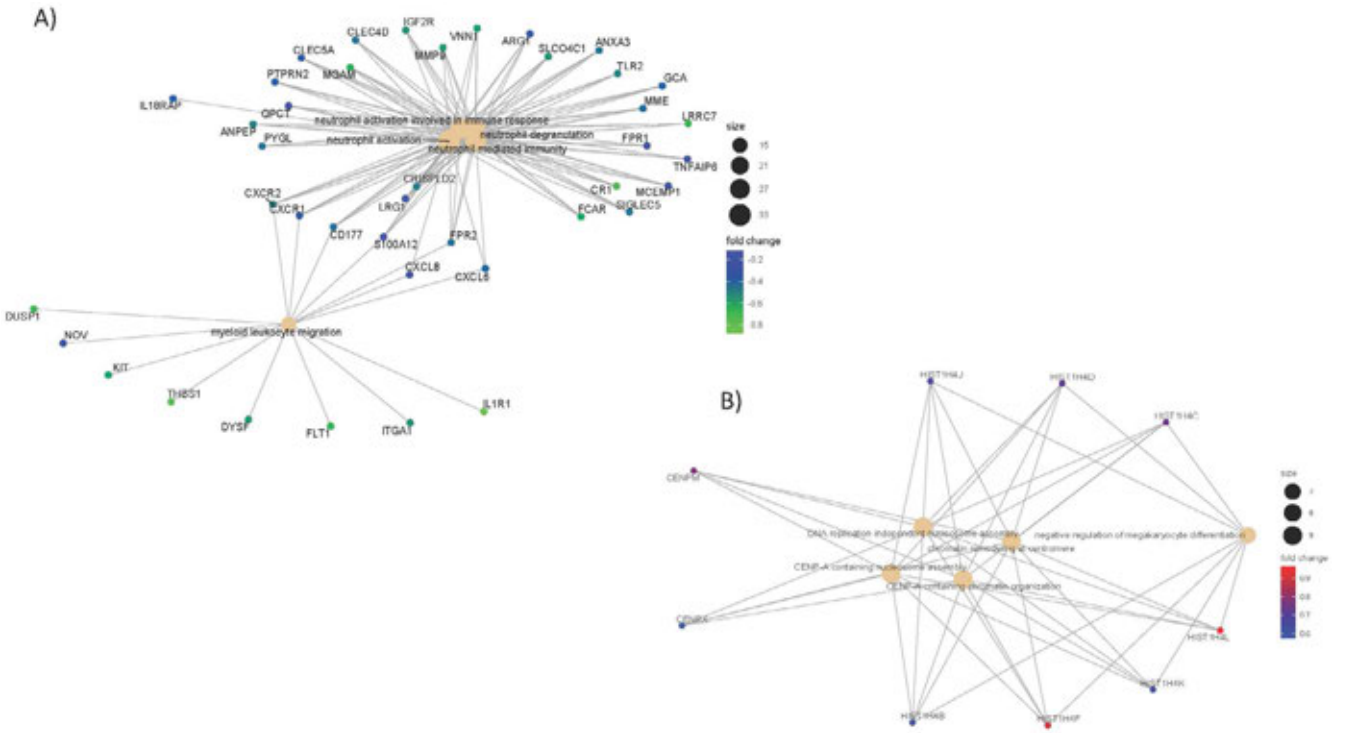


Figure 1. Clustering of genes with similar expressions patterns – The figure shows the detected patterns of expression within the differentially expressed genes having a fold change greater than 1.5. The z-score of gene abundance represents the number of standard deviations the expression at a time point is away from the overall mean.



Figures 2a and 2b show the relationships between the genes from the cluster analysis and the enriched categories from the gene ontology analysis. Figure 2a show the genes from clusters 2 and 3 where there is an association with immune system function, and figure 2b, containing the genes from clusters 4 and 5, which were associated with DNA replication and processing. The fold changes displayed are log2 transformed and are between the 8am and 3pm time points.

clusters (utilising 29 and 65 gene respectively) increased during the day, figure 1. These clusters were associated with DNA replication and processing pathways and gene ontology terms, figure 2b.

Conclusion: Our results clearly demonstrate that timing of sample collection has a significant impact on the transcription profile of circulating cells and should therefore be accommodated within biomarker studies. Moreover, alterations were observed across rather fundamental biological pathways that may inform disease pathogenesis studies in future.

Disclosure: L. Bennett, None; **F. Morton**, None; **G. Fragoulis**, None; **C. Paterson**, None; **D. Rimmer**, None; **G. Semple**, None; **A. Young**, None; **J. Nijjar**, None; **M. Barrett**, None; **S. Siebert**, Abbvie, 2, 5, 8, AbbVie, 2, 5, BMS, 2, Boehringer Ingelheim, 2, 5, 8, Celgene, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8; **D. Porter**, None; **C. Goodyear**, Celgene, 2, AstraZeneca, 2, 5, MedAnnex, 2, 5, UCB, 2, Jannsen, 2; **I. McInnes**, Abbott, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, Roche., 2, 8, Abbvie, 5, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Astra Zeneca, 2, 5, AstraZeneca, 5, BI, 2, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 5, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Leo, 5, Lilly, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 0821

Trends in Incidence and Prevalence of Osteoarthritis in the United Kingdom: Findings from the Clinical Practice Research Datalink (CPRD)

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health I: Risk Factors & Outcomes for Rheumatic Diseases

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Osteoarthritis (OA) is by far the most common arthritis.(1) However, its chronological trend in the United Kingdom (UK) is not known. We aimed to explore the trend in both incidence and prevalence of OA among adults aged 20 years or more in the UK during the period 1997-2017 using a large nationally representative primary care database.

Methods: The UK Clinical Practice Research Datalink (CPRD), comprising data on 17 million patients, was used for this study (2). We estimated the incidence and prevalence of general practitioner (GP) diagnosed OA (both overall

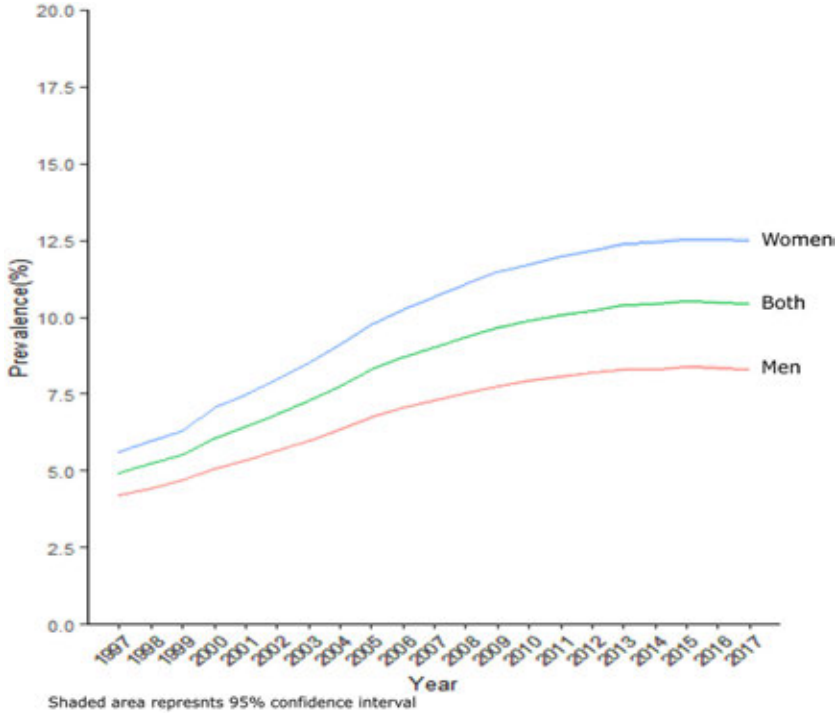

Figure 1. Trends of standardized prevalence of GP diagnosed OA in the UK 1997-2017 For men and women- Age standardized; Both- Age and sex standardized

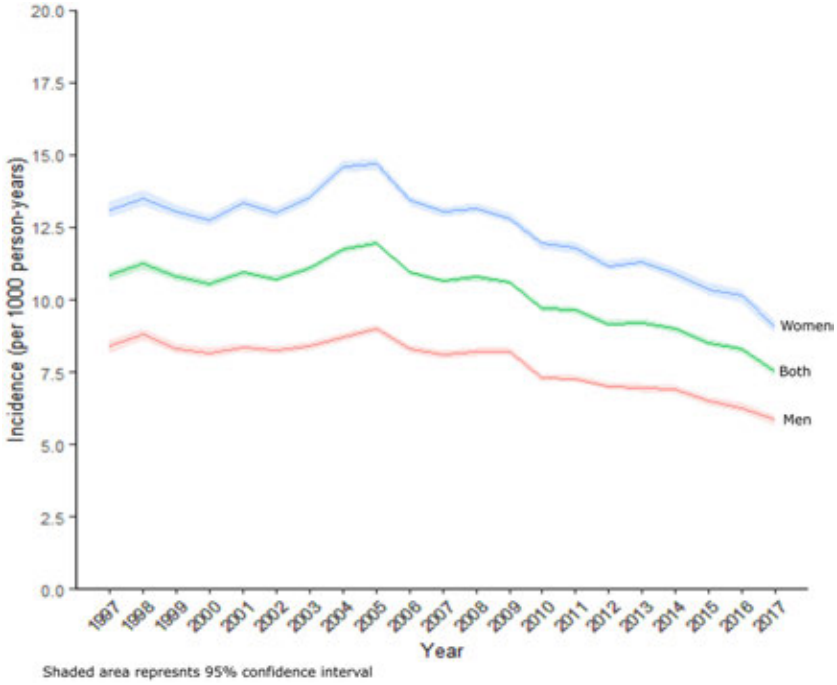

Figure 2. Trends in standardized incidence of GP diagnosed OA in the UK (1997-2017) For men and women- Age standardized; Both- Age and sex standardized

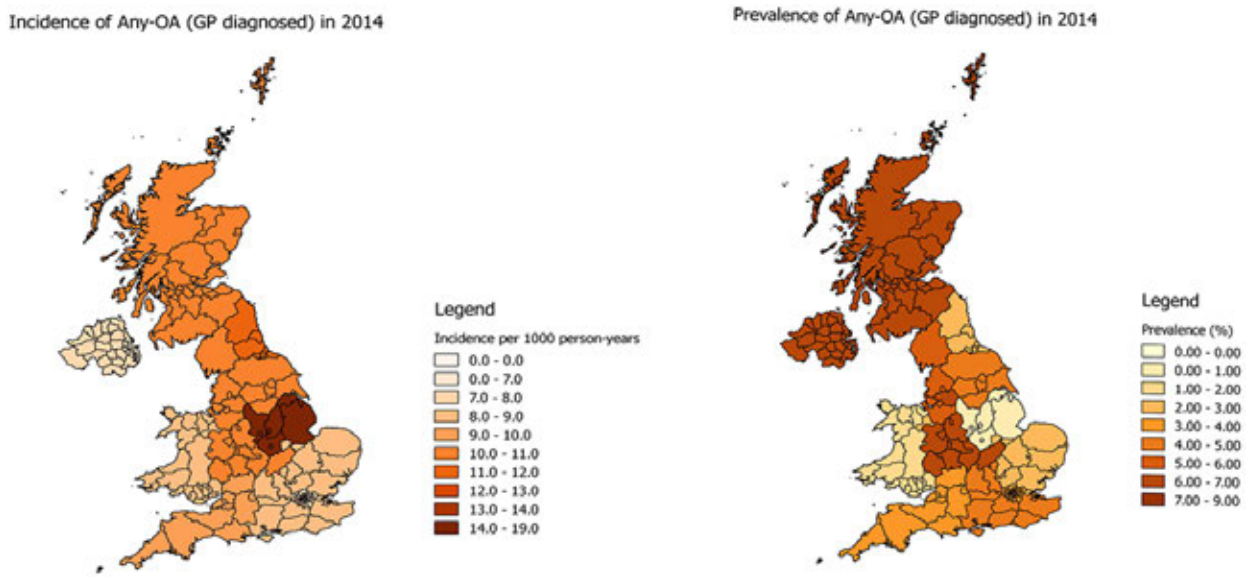

Figure 3. Prevalence and incidence of GP-diagnosed OA in different regions of the UK in 2014 The contribution from East Midlands region to the CPRD-GOLD database used in the study was nearly zero, which did not allow to have whole country representation for the year 2017.

and joint-specific: hip, knee, ankle/foot, wrist/hand and unspecified site) which was age-sex standardized using 2017 UK mid-year population. Joinpoint analysis was performed to identify the trend points. Geographical distribution was mapped according to the different regions in the UK. The data used for the study is recorded by the GPs in UK, and nearly 100% patients would have met the ACR classification criteria.

Results: During the year 1997-2017, 608,350 incident OA cases aged ≥20 years were recorded. In 2017, the standardized prevalence of GP-diagnosed OA for any joint in both sexes was 10.44% (95% CI 10.39%-10.49%), 12.49%; 95% CI 12.41%-12.56%) in women and 8.28% (95%CI 8.22%-8.35%) in men. The prevalence recorded according to body site was unspecified joint (7.32%), knee (2.76%), hip (1.17%), wrist/hand (0.52%) and foot/ankle (0.29%). The prevalence of any-OA increased from 4.9% in 1997 to 10.4% in 2017 with average annual percentage increase of 3.9% (95% CI 3.5-4.2%). (Figure-1) The standardised incidence of any OA in both sexes in 2017 was 7.5 per 1000 person-years (95% CI 7.4-7.6 per 1000 person-years), 9.0 per 1000 person-years (95% CI 8.8-9.2 per 1000 person-years) in women and 5.8 per 1000 person-years (95% CI 5.7-6.0 per 1000 person-years) in men. In 2017, the incidence recorded in joints was: unspecified site OA (5.2 per 1000 person-years), followed by knee (2.3 per 1000 person-years), hip (1.1 per 1000 person-years), wrist/hand (0.68 per 1000 person-years) and foot/ankle (0.19 per 1000 person-years) OA. The incidence of any OA decreased from 10.8 per 1000 person-years (95% CI 10.7-11.0 per 1000 person-years) in 1997 to 7.5 per 1000 person-years (95% CI 7.4-7.6 1000 person-years) in 2017 with an average annual percentage reduction of -1.7% (95%CI -2.6 to -0.8). (Figure-2) The prevalence and incidence varied across the UK, with the northern region had higher OA prevalence and incidence compared to the rest of the UK in 2014 with few exceptions. (Figure-3)

Conclusion: In the UK approximately one in 10 adults have clinically diagnosed OA. The knee is the commonest recorded site for OA that results in GP consultation. While the prevalence has increased, incidence has decreased in this population in the past 20 years. Further research is needed to understand these changes.

Reference:

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Abstract Number: 0822

Cigarette Smoking Is a Risk Factor for ANCA-Associated Vasculitis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health I: Risk Factors & Outcomes for Rheumatic Diseases
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: ANCA-associated vasculitis (AAV) is a systemic small vessel vasculitis of unclear etiology associated with excess morbidity and mortality compared to the general population. Environmental exposures (e.g.

asbestos) have been associated with AAV but the effect of cigarette smoking on disease risk is unclear. Previous studies suggest that smoking is associated with an increased risk of AAV relapse and its effect may vary according to age and disease manifestation. However, these findings were based on studies with relatively small sample size. We performed a large case-control study to examine the association of cigarette smoking, a potentially modifiable factor, with the risk of AAV.

Methods: The Partners AAV (PAAV) Cohort is a consecutive inception cohort established at Partners HealthCare, a large hospital system in New England. All cases are PR3- or MPO-ANCA+. Eosinophilic granulomatosis with polyangiitis cases were excluded. For each AAV case, we randomly selected 3 controls from participants in the Partners HealthCare Biobank who completed a smoking questionnaire (N=30,536) and with no diagnosis of AAV and matched

	AAV	Control	Odds Ratio (95% CI)
Overall			
Never	219 (46%)	823 (58%)	Ref
Former	211 (45%)	533 (38%)	1.58 (1.25-2.00)
Current	43 (9%)	63 (4%)	2.70 (1.76-4.14)
Male			
Never	81 (42%)	343 (60%)	Ref
Former	95 (49%)	212 (37%)	2.14 (1.46-3.13)
Current	16 (8%)	21 (4%)	3.62 (1.73-7.55)
Female			
Never	138 (49%)	480 (57%)	Ref
Former	116 (41%)	321 (38%)	1.29 (0.95-1.75)
Current	27 (10%)	42 (5%)	2.30 (1.35-3.90)
PR3-ANCA+			
Never	86 (52%)	290 (59%)	Ref
Former	64 (39%)	173 (35%)	1.31 (0.87-1.99)
Current	14 (9%)	29 (6%)	1.71 (0.84-3.47)
MPO-ANCA+			
Never	133 (43%)	533 (58%)	Ref
Former	147 (48%)	360 (39%)	1.73 (1.29-2.30)
Current	29 (9%)	34 (4%)	3.54 (2.05-6.10)
HEENT			
Never	108 (50%)	392 (60%)	Ref
Former	91 (42%)	223 (34%)	1.58 (1.11-2.26)
Current	17 (8%)	33 (5%)	1.95 (1.01-3.74)
Pulmonary			
Never	84 (43%)	350 (60%)	Ref
Former	95 (49%)	201 (35%)	2.20 (1.51-3.19)
Current	15 (8%)	31 (5%)	2.14 (1.09-4.23)
Renal			
Never	132 (43%)	514 (56%)	Ref
Former	151 (50%)	360 (39%)	1.76 (1.32-2.36)
Current	21 (7%)	38 (4%)	2.28 (1.28-4.06)
Care Established at Partners Prior to Diagnosis			
Never	67 (39%)	271 (53%)	Ref
Former	87 (51%)	216 (42%)	1.76 (1.19-2.62)
Current	16 (9%)	23 (5%)	3.15 (1.51-6.56)
Care Established at Partners After the Diagnosis			
Never	152 (50%)	552 (61%)	Ref
Former	124 (41%)	316 (35%)	1.49 (1.11-2.00)
Current	27 (9%)	40 (4%)	2.51 (1.48-4.26)
Cases Diagnosed Before 1/1/2010			
Never	105 (46%)	389 (57%)	Ref
Former	101 (45%)	261 (38%)	1.48 (1.06-2.07)
Current	20 (9%)	28 (4%)	2.70 (1.45-5.02)
Cases Diagnosed After 1/1/2010			
Never	114 (46%)	434 (59%)	Ref
Former	110 (45%)	272 (37%)	1.68 (1.20-2.36)
Current	23 (9%)	35 (5%)	2.71 (1.50-4.89)

by sex, race, and age (± 2 years) at the index date (i.e., treatment initiation). Smoking status at the index date was extracted from the electronic medical record and categorized into three groups: never, former, current. We examined the association between cigarette smoking and the odds of AAV using conditional logistic regression. We performed stratified analyses to verify the robustness of the findings.

Results: We identified 473 AAV cases and 1,419 controls whose data on smoking status were available (mean age: 59 (±16) years; women: 59%, white: 84%). The majority (65%) of cases were MPO-ANCA+ and 64% had any baseline renal involvement. There was a greater proportion of current and former smokers among AAV cases (Current=43 [9%], Former=211 [45%]) than in the control group (Current=63 [4%], Former=533 [38%]). The multivariable adjusted odds ratios for AAV were 1.58 (95% CI: 1.25-2.00) for former cigarette smoking and 2.70 (95% CI 1.76-4.14) for current cigarette smoking as compared with non-smoking (Table 1). When the proportion of ever-smokers was compared with that of never smokers, we found a similar association (1.72 [95% CI: 1.37-2.15]). These associations persisted in stratified analyses by sex, ANCA type, and organ involvement though they did not reach statistical significance in the PR3-ANCA+ subgroup. When we further matched cases and controls by education level, our findings were unchanged. When we stratified by index date and whether or not a case had established care in Partners ≥ 1 year prior to the index date, our findings were unchanged.

Conclusion: In this large case-control study, being a current or former smoker was strongly associated with an increased risk of AAV, especially MPO-ANCA+ AAV. The precise biological mechanism underlying this association remains to be elucidated but may be related to cell apoptosis and necrosis, and/or oxidative endothelial stress. These findings suggest that cigarette smoking may be a modifiable risk factor for AAV. Additional studies are warranted to confirm these findings.

The Association of Cigarette Smoking with the Risk of ANCA-Associated Vasculitis

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Disclosure: G. McDermott, None; **X. Fu**, None; **J. Stone**, Genentech, 2, 5, Roche, 2, 5, Xencor, 2, 5; **Y. Zhang**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5; **Z. Wallace**, National Institute of Arthritis, Musculoskeletal, and Skin Diseases, 2, Rheumatology Research Foundation, 2.

Abstract Number: 0823

The Risk of Venous Thromboembolism in Patients with Psoriatic Disease and Rheumatoid Arthritis, a Population-based Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health I: Risk Factors & Outcomes for Rheumatic Diseases
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Venous thromboembolism (VTE, which includes pulmonary embolism [PE] and deep vein thrombosis [DVT]) is associated with increased morbidity and mortality. Previous studies have shown an increased

	PSD	Non-PSD	RA	Non-RA
VTE	N=109608	N= 109771	N = 89346	N = 177859
Cases, N	1091	863	3555	4421
Incidence Rate/1000 Person-Years	1.19	0.97	3.95	2.39
Age-, Sex-, Entry Time-Matched Cox HR (95% CI)	1.25 (1.14-1.36)	1	1.76 (1.67-1.85)	1
*Fully-Adjusted Cox HR (95% CI)	1.12 (1.03-1.23)	1	1.46 (1.38-1.55)	1
PE	N=110005	110046	N = 89346	N = 177859
Cases, N	547	443	1412	1747
Incidence Rate/1000 Person-Years	0.59	0.50	1.55	0.94
Age-, Sex-, Entry Time-Matched Cox HR (95% CI)	1.22 (1.08-1.38)	1	1.81 (1.67-1.95)	1
*Fully-Adjusted Cox HR (95% CI)	1.12 (0.98-1.27)	1	1.48 (1.35-1.62)	1
DVT	N=109811	N= 109944	N = 89346	N = 177859
Cases, N	734	568	2575	3258
Incidence Rate/1000 Person-Years	0.80	0.64	2.85	1.76
Age-, Sex-, Entry Time-Matched Cox HR (95% CI)	1.27 (1.14-1.42)	1	1.73 (1.63-1.83)	1
*Fully-Adjusted Cox HR (95% CI)	1.13 (1.01-1.26)	1	1.45 1.36-1.55)	1
*Adjusted for obesity, alcoholism, hypertension, sepsis, varicosed vein, inflammatory bowel disease, trauma, fractures, surgery, charlson comorbidity index), medication use (glucocorticoids, hormone replacement therapy, aspirin, cox-2 inhibitors), and healthcare utilization (number of outpatient and inpatient visits				

Table1. Relative risk of incident VTE, PE and DVT according to PSD and RA status.Values are HR (95% CI).

risk of VTE in patients with psoriatic disease (PsD, which includes psoriasis and psoriatic arthritis) and rheumatoid arthritis (RA), two of the most prevalent inflammatory arthritis. However, population-based data using incident cohorts of PsD and RA are limited. Our objective was to estimate the risk of VTE, PE and DVT among patients with newly diagnosed PsD and RA compared with the general population.

Methods: We conducted a matched cohort analysis for PsD and RA separately. Our data included all outpatient and inpatient visits from Jan 1990 until Mar 2015 and all dispensed medication from Sept 1995 to Mar 2015 in the province of British Columbia. Incident PsD and RA patients were identified using previously validated algorithms and were matched with non-PsD (1:1) and non-RA (1:2) individuals randomly selected from the general population based on age, sex and entry cohort time. Patients should have at least a 7-year run-in period in order to consider the case as incident. Incident VTE was defined using ICD codes plus a dispensation of an oral anticoagulant. We calculated incidence rate ratio (IRRs), as well as age-, sex-, and entry-time-matched and multivariable hazard ratios (HRs) for the

	PSD			RA		
Variable	VTE HR (95% CI)	PE HR (95% CI)	DVT HR (95% CI)	VTE HR (95% CI)	PE HR (95% CI)	DVT HR (95% CI)
<1 year	1.36 (1.03-1.79)	1.14 (0.77-1.68)	1.49 (1.06-2.09)	2.16 (1.80-2.59)	2.35 (1.74-3.18)	1.89 (1.52-2.35)
<2 years	1.32 (1.08-1.61)	1.24 (0.93-1.65)	1.33 (1.05-1.69)	1.92 (1.69-2.20)	2.01 (1.63-2.48)	1.80 (1.54-2.11)
<3 years	1.30 (1.10-1.54)	1.34 (1.05-1.70)	1.31 (1.06-1.61)	1.77 (1.59-1.98)	1.78 (1.50-2.13)	1.70 (1.49-1.94)
<4 years	1.28 (1.10-1.48)	1.29 (1.05-1.59)	1.29 (1.07-1.55)	1.68 (1.52-1.85)	1.56 (1.34-1.82)	1.67 (1.48-1.87)
<5 years	1.28 (1.12-1.47)	1.31 (1.08-1.58)	1.28 (1.09-1.52)	1.65 (1.51-1.80)	1.57 (1.36-1.81)	1.62 (1.45-1.80)

Table2 Age- and sex-adjusted relative risk for VTE, PE, and DVT in PSD and RA according to follow up period. Values are HR (95% CI).

risk of VTE, PE, and DVT adjusting for potential confounders. To test the robustness of our results, we performed two sensitivity analyses. First, to estimate the effect of unmeasured confounders, we included a simulated unmeasured confounder into our model. Second, we accounted for the competing risk of death via the subdistribution proportional hazards model.

Results: Cohorts included 110,323 individuals with incident PsD (51% female, mean age 47 yrs) and 89,346 individuals with incident RA (66% female, mean age 59 yrs). Of those at risk of incident events, 1,091 and 3,555 developed VTE, 547 and 1412 developed PE, 734 and 2,575 developed DVT, respectively (incidence rates= 1.19 and 3.95 for VTE, 0.59 and 1.55 for PE, 0.80 and 2.85 for DVT per 1000 person-years, respectively). Compared with the corresponding non-PsD and non-RA cohorts the age-, sex-, and entry-time-matched HRs for VTE, PE and DVT were 1.25 and 1.76, 1.22 and 1.81, 1.27 and 1.73, respectively ($P< 0.05$ for all). After further adjustment for baseline characteristics, the HRs remained significant except for PE in the PsD cohort. The risks were greatest within the first year after diagnosis and progressively attenuated with time except for PE in the PsD cohort. HRs remained significant after accounting for the competing risk of death for all outcomes in both PsD and RA cohorts. The results also remained significant at values of 20% prevalence in the RA cohort and OR of 1.3 for the association between the unmeasured confounder and all outcomes, but not in the PsD cohort.

Conclusion: Patients with PsD and RA have an increased risk of VTE (12% and 46%), PE (12% and 48%) and DVT (13% and 45%). The risk of VTE peaked in the first year after diagnosis and decreased with time thereafter. These findings support the need of increased monitoring of VTE complications in patients with PsD or RA.

Disclosure: L. Li, None; **N. Lu**, None; **E. Sayre**, None; **H. Xie**, None; **D. Lacaille**, None; **J. Esdaile**, None; **J. Avina-Zubieta**, None.

Abstract Number: 0824

Results from a Randomized Controlled Trial of the Safety of the Live Varicella Vaccine in TNF-Treated Patients

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Epidemiology & Public Health I: Risk Factors & Outcomes for Rheumatic Diseases

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: There has been minimal evaluation of the safety of live virus vaccines in patients receiving biologic therapies who may be immunocompromised. The Varicella Zoster Vaccine (VERVE) study is a blinded, 1:1 randomized placebo-controlled trial of the live attenuated zoster vaccine (ZV) in patients receiving TNF inhibitors (TNFi) to evaluate safety and immunogenicity.

Methods: Eligible participants: at least 50 years of age, current users of TNFi for any indication, and no prior ZV. Safety follow-up occurred over 6 weeks (the FDA-specified risk window for vaccine-related infection, were it to occur). Suspected cases of varicella infection or shingles had clinical assessment, PCR collection (with subtyping to differentiate wild-type vs. vaccine [Oka]-related infection), and digital photographs. Review was conducted under oversight of an NIH-appointed Data Safety Monitoring Board. Serum and PBMCs were collected at baseline and week 6 to assess ZV-related immunity, with safety follow-up through 6 months, at which time participants were unmasked to treatment arm.

Results: Recruitment closed in December 2018, with 617 randomized participants recruited at 33 centers: mean (SD) age 62.4 (7.5) years, 66.9% female, 87.2% white, 8.8% AA, 4.4% Hispanic. Most common TNFi indications: rheumatoid arthritis (59.6%), psoriatic arthritis (24.5%); TNFi medication at baseline: adalimumab (32.7%), infliximab (31.3%), etanercept (21.2%), golimumab (9.1%), certolizumab (5.7%). Concomitant therapies included background methotrexate (48.0%), and oral glucocorticoids (10.5%). Through week 6, there were zero cases of confirmed disseminated or local varicella infection, either wild type or vaccine strain, yielding an upper bound of the 95% confidence interval for vaccine-related varicella infection of < 1%. A total of 8 rashes were swabbed for varicella PCR; none were positive, and no clinically adjudicated varicella or shingles reactivation cases were observed through week 6. VERVE will close to blinded follow up in Summer 2019 and immunologic effectiveness of ZV will be reported in the full cohort in November 2019.

Conclusion: The randomized VERVE trial comprised of more than 600 patients receiving TNFi for multiple indications observed no cases of vaccine-related varicella infection or reactivation in the 6-week risk period following live zoster vaccination. This trial informs safety concerns of use of live virus vaccines in this population.

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Abstract Number: 0825

Systemic Sclerosis Deaths at Younger Ages Have Decreased over the past Five Decades

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health I: Risk Factors & Outcomes for Rheumatic Diseases
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Patients with systemic sclerosis (SSc) can die prematurely of disease-associated complications. Over the past 2 decades, several advances in the treatment of SSc-associated complications may have affected SSc outcomes. For example, the two-year survival of patients with SSc-associated pulmonary arterial hypertension has improved from 47% to 71% with the availability of prostanoids. The influence of these advances on long-term SSc mortality in the general population remains unknown. Here, we tested the hypothesis that death from SSc is decreasing at younger ages over time.

Methods: This is a population-based study using a national mortality database of all U.S. residents, 1968 through 2015. First, we calculated the proportions of deaths for SSc and for all other causes (non-SSc) by age groups for each year from 1968 through 2015 and performed joinpoint trend analysis to estimate annual percent change (APC) and average APC (AAPC) in the proportion of deaths by age. Second, we calculated age-standardized mortality rate (ASMR) for SSc and non-SSc causes and ratio of SSc-ASMR to non-SSc-ASMR by age groups for each year from 1968 through 2015 and performed joinpoint trend analysis to estimate APC and AAPC for these measures by age groups.

Results: From 1968 through 2015, SSc was recorded as the underlying cause of death in 46,798 deaths. In 1968, 23.4% of all SSc deaths as compared to 13.5% of non-SSc deaths occurred at a younger (≤44 years) age group ($p< 0.001$, Chi-square test). In this age group, the proportion of annual deaths decreased more for SSc than for non-SSc causes: from 23.4% in 1968 to 5.7% in 2015 at an AAPC of -2.2% (95% CI, -2.4% to -2.0%) for SSc, and from 13.5% to 6.9% at an AAPC of -1.5% (95% CI, -1.9% to -1.1%) for non-SSc. Thus, in 2015, the proportion of SSc and non-

SSc deaths in ≤44 year age group was no longer significantly different. The percent of deaths in the 45-54 year age group also decreased more for SSc than for non-SSc over the 48-year period, but no statistical change was noted in the 55-64 year age group. However, in ≥65 year age group, the proportion of SSc deaths increased more for SSc than for non-SSc causes, indicating that SSc patients were dying later in life. Consistent with this observation, ASMR for SSc decreased from 1.0 (95% CI, 0.8-1.2) in 1968 to 0.4 (95% CI, 0.3-0.5) per million persons in 2015, a cumulative decrease of 60% at an AAPC of -1.9% (95% CI, -2.5% to -1.2%) in ≤44 year age group. The ratio of SSc-ASMR to non-SSc-ASMR also decreased in this age group (cumulative, -20%; AAPC -0.3%).

Conclusion: Mortality for SSc has steadily decreased in younger ages. Young individuals with SSc now make up the same proportion of deaths as those without SSc.

Disclosure: E. Yen, None; **D. Singh**, None; **R. Singh**, None.

Abstract Number: 0826

Immune-Mediated Inflammatory Diseases (IMID) Collectively Rank Among the Leading Causes of Death

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health I: Risk Factors & Outcomes for Rheumatic Diseases
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Almost every organ system can be affected by primary immune-mediated diseases characterized by inflammation and therapeutic response to immune-suppressive or anti-inflammatory drugs. These diseases can be collectively referred to as immune-mediated inflammatory diseases (IMID). Many rheumatic diseases can be categorized as IMIDs. Since IMIDs are purported to have shared pathogenic mechanisms, it would be important to understand their burden of disease together. Our goals are to determine 1) the burden of IMID deaths relative to the leading causes of death published by the Centers for Disease Control and Prevention (CDC) and 2) the mortality trends of top 15 individual IMIDs.

Methods: We compiled 43 IMIDs with a reported prevalence of >1 per 100,000 population, and obtained death counts for each of them using the CDC-WONDER database. We then calculated their crude death rates, pooled death counts of the 15 IMIDs with the highest crude death rates, and ranked the pooled IMID death counts among the CDC's official leading-causes-of-death ranklist for eleven age groups. Next, we calculated the annual age-standardized mortality rate (ASMR) for the top 15 individual IMIDs from 1999 to 2017. Lastly, we performed joinpoint trend analysis of the annual ASMRs for these 15 IMIDs.

Results: 371,154 deaths were attributed to the top 15 IMIDs in 5 years from 2013 to 2017. Of these deaths, IMIDs were recorded as the underlying cause in 202,430 deaths and as the contributing cause in 168,724 deaths. These IMID deaths (underlying + contributing) ranked 6th to 9th for all age groups among the leading causes of death. When only the underlying cause of death was considered, IMID ranked among the top 15 for all age groups and 7th to 9th in 15 to 64 year age groups. Among IMIDs, primary interstitial lung disease, multiple sclerosis, and type 1 diabe-

tes had the highest ASMRs in 2017 followed by rheumatic diseases including rheumatoid arthritis, lupus, systemic sclerosis, and systemic vasculitis, which ranked in the top 10. Joinpoint trend analysis showed that annual mortality rates for most IMIDs including rheumatoid arthritis, lupus, systemic sclerosis, systemic vasculitis, type 1 diabetes, myocarditis, primary biliary cirrhosis, and idiopathic thrombocytopenic purpura have decreased from 1999 to 2017, but have increased or unchanged for a few IMIDs including primary interstitial lung disease, multiple sclerosis, and myasthenia gravis.

Conclusion: Ranking of IMID among the top ten leading causes of death emphasizes the high burden of diseases characterized by inflammation. These data further highlight that IMID is a major public health problem. Similar to various forms of cancer, various IMIDs should be considered as a collective disease entity. The recognition of IMID as a leading cause of death may influence healthcare prioritization and research funding, which may help to reduce their disease burden.

Disclosure: M. Wu, None; **E. Yen**, None; **R. Singh**, None.

Abstract Number: 0827

A Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of Bedtime Sublingual Cyclobenzaprine (TNX-102 SL) for the Treatment of Fibromyalgia (FM): Evidence for a Broad Spectrum of Activity on the FM Syndrome

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Fibromyalgia & Other Clinical Pain Syndromes
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Background/Purpose: Fibromyalgia (FM) is characterized by chronic widespread pain, unrefreshing sleep, fatigue, and cognitive complaints. TNX-102 SL* is a sublingual (SL) formulation of cyclobenzaprine (CBP) that is rapidly absorbed and bypasses first-pass metabolism, providing for unique pharmacokinetics of the parent CBP and long-lived metabolite norcyclobenzaprine that previous studies have suggested lead to improvements in overall sleep quality. This may lead to improvements in pain and other somatic complaints by a mechanism distinct from existing FM therapies. This Phase 3 double-blind, randomized, placebo-controlled, multicenter trial (AFFIRM Study) evaluated safety and efficacy of a 2.8 mg dose of TNX-102 SL 2.8 mg in FM.

Methods: A total of 519 patients meeting ACR 2010 FM criteria were enrolled across 35 centers in a 12-week trial. Patients were randomized 1:1 to receive TNX-102 SL 2.8 mg (N=262) or placebo (N=257). Primary efficacy endpoint was a responder analysis of patients who reported ≥30% reduction in daily diary pain from baseline to endpoint. Secondary outcome measures included analyses of diary mean pain and sleep ratings, Fibromyalgia Impact Questionnaire (FIQ-R), Patient Global Impression of Change (PGIC), and PROMIS Sleep Disturbance (SD) scales.

Results: The study did not achieve statistical significance on the primary efficacy endpoint (TNX-102 SL, 28.6% responders v. placebo 22.6% responders; OR 1.41 [0.94-2.10], P=0.095). TNX-102 SL did show significant effects on pain over placebo when analyzed by other standard approaches including: 30% responder analysis with BOCF/LOCF imputation (P=0.012); 50% responder analysis with BOCF alone (P=0.035); and MMRM of mean change from baseline (P< 0.001). TNX-102 SL 2.8 mg improved FIQ-R total score: -13.7 compared to -7.5 for placebo (P< 0.001). PGIC responder rate v. placebo: 23.7% v. 16.3% (P=0.038). Measures of sleep quality improved including PROMIS SD: -8.0 v. -4.7 (P< 0.001); daily diary: 1.8 v. -1.0 (P< 0.001). Systemic adverse events (AEs) were infrequent, with the only AE reported in ≥5% of TNX-102 SL-treated patients of fatigue (5.7% v. 2.3% in placebo).The most common AEs were local oral events: transient oral hypoaesthesia (40.1% v. 0.8% in placebo), glossodynia (9.2% v. 1.6% in placebo), paresthesia oral (7.6% v. 1.2% in placebo), product taste abnormal (6.1% v. 0.8% in placebo). A total of 77.5% of TNX-102 SL-treated patients completed the study compared with 86.4% on placebo.

Conclusion: Bedtime TNX-102 SL 2.8 mg, although failing to achieve statistical significance on the 30% pain responder analysis primary outcome, had clinically meaningful effects on pain and sleep by several other measures. Moreover, there were robust effects of TNX-102 SL at 2.8 mg on the broad array of measures of FM symptoms and function, fatigue, and particularly on measures of sleep quality, the hypothesized mechanism of TNX-102 SL in FM. Post-study analyses suggest that a higher dose of TNX-102 SL may be needed to meaningfully improve pain symptoms in a greater percentage of treated patients.

*TNX-102 SL is an Investigational New Drug and has not been approved for any indication.

Disclosure: G. Sullivan, Tonix Pharmaceuticals Inc, 1, 3, 4, 6; **R. Gendreau**, Tonix Pharmaceuticals Inc, 5; **J. Gendreau**, Tonix Pharmaceuticals Inc, 3, 5; **A. Peters**, Tonix Pharmaceuticals Inc, 3, 4; **P. Peters**, Tonix Pharmaceuticals Inc, 3, 4; **S. Lederman**, Tonix Pharmaceuticals Inc, 1, 3, 4, 6.

Abstract Number: 0828

A Path Model Analysis of the Cognitive Determinants of Physical Activity Among Patients with Fibromyalgia (FM)

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SESSION INFORMATION
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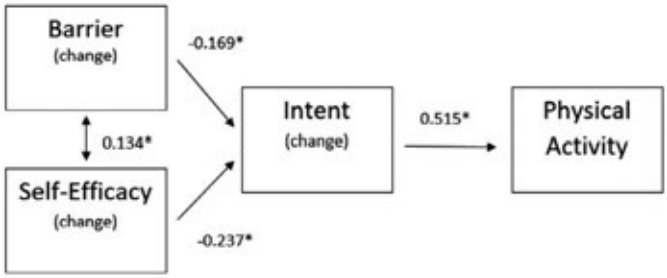
Background/Purpose: In individuals with FM, regular participation in physical activity (PA) is associated with improvement of symptoms, daily physical functioning, and overall well-being. Given the importance but also the challenges associated with the initiation and maintenance of physical activity, it is imperative that therapeutic targets are identified to increase and maintain moderate level of PA.

Methods: This is a secondary data analysis of a 36-week randomized clinical trial to promote PA among patients with FM. Participants were randomized to 1 of 2 treatment arms: 6 phone-based motivational interviewing (MI) sessions or an equal number of FM self-management instructions.

Table 1. Bivariate associations between changes in cognitive variables and physical activity groups

	Group 1 ≥10 MET hours/week increment and maintained (n=27)	Group 2 ≥10 MET hours/week increment followed by decline (n=68)	Group 3 Did not achieve ≥10 MET hours/week increment (n=75)	adjusted p-values
Exercise self-efficacy	-0.79 (0.34)	-0.06 (0.21)	0.68 (0.21)	0.0009
Perceived benefits	0.27 (1.44)	0.40 (0.91)	2.66 (0.89)	0.2654
Perceived barriers	0.91 (0.80)	1.65 (0.51)	-0.81 (0.49)	0.0022
Intention	-1.06 (0.26)	-0.40 (0.16)	0.52 (0.16)	< 0.0001



Changes in CHAMPS, a validated self-report measure of PA, were analyzed at each assessment period (baseline to week 12; week 12 to week 24; and week 24 to week 36). Based on CHAMPS, sustained PA was defined as an increase in moderate-vigorous PA (MVPA) of at least 10 MET h/week for ≥ 12 weeks. Using this threshold, three PA groups were defined based on subjects who: (Group 1) achieved a minimum increase of 10 metabolic equivalent (MET) hours/week that was subsequently sustained for at least 12 weeks; (Group 2) achieved a minimum increase of 10 MET hours/week that was not sustained for at least 12 weeks; and (Group 3) did not achieve an increase of at least 10 MET hour/week from baseline. Primary independent variables were baseline to week 36 changes in exercise self-efficacy, perceived benefits of PA, perceived barriers of PA, and intention to engage in MVPA. Initial analyses were performed using ANCOVA models to determine the association between cognitive variables and physical activity groups, adjusted for baseline values, and were performed using SAS v9.4. Controlling for treatment group assignment, path analyses were performed using M plus v7.31.

Results: For exercise self-efficacy, group 1 reported the largest improvement in exercise self-efficacy followed by group 2, and no improvement in group 3. For perceived barriers, groups 1 and 2 reported reductions in perceived barriers, while group 3 reported increased perceived barriers. For intention, groups 1 and 2 reported greater intention to engage in MVPA, while group 3 reported less intention. Change in perceived benefits were not significantly different among the 3 PA groups.

As shown in Figure 1 below, changes in perceived barriers and exercise self-efficacy influence intention to engage in PA, which in turn impacts changes in in the volume of PA. Perceived benefits of PA was not associated with either intention nor with physical activity. About 77% of the variance related to PA is explained by the model below.

Conclusion: When designing programs to promote PA in persons with FM, improving self-efficacy and resolving perceived barriers to exercise should be considered important therapeutic goals. Increasing awareness on the benefits of PA; however, may not elicit the desired PA behavior change.

Disclosure: D. Ang, None; **A. Kaleth**, None; **W. Bush**, None.

Abstract Number: 0829

Dietary Intake Does Not Explain Microbiome Alterations or Symptom Severity in Fibromyalgia

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Session Title: Fibromyalgia & Other Clinical Pain Syndromes
Session Type: ACR Abstract Session
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Background/Purpose: We have recently reported significant alterations in gut microbiome compositionin women with fibromyalgia (FM). As gut microbiome is affected by diet, differences in nutritional intake may have accounted for these alterations. Furthermore, there are some reports of selected dietary interventions impacting symptoms of FM. FM patients also frequently try various dietary regimens for symptom relief. The aim of this study was to examine the diet of women with FM compared to healthy controls, and to explore possible associations between the intake of certain nutrients, symptoms severity and gut microbiome composition.

Methods: The study population comprised 77 women with FM (by validated 2016 FM criteria) and 79 controls (household contacts, 1st degree relatives, other controls) Measures included: demographics, comorbidities, polysymptomatic distress scale and quality of life (FIQ). Dietary intake was assessed using the NIH Automated Self-Administered 24-hour recall, following dietician instruction and completion of three-day dietary recall. Datasets with at least two complete days were retained (n=146) and daily nutrient averages were calculated. Under-reporters were excluded from analysis. The Healthy Eating Index (HEI-2015) was calculated to assess diet quality. Intake of micro- and macro-nutrients was correlated with clinical measures of FM using Spearman's coefficient, and significance was adjusted for multiple comparisons. The gut microbiome was assessed by 16S and whole genome sequencing of stool samples.

Results: There were no differences in demographic and anthropometric characteristics among groups. Significant differences were observed in the abundance of 72 bacterial taxa of the gut microbiome between individuals with FM and controls. Energy and macronutrient intake (total and relative) and overall diet quality score were not different among patients and controls (Table 1). In addition, vitamin, mineral, different fatty acids, alcohol, caffeine, sugar and fiber intakes did not differ among groups; Normalised daily intake of micro- and macro-nutrients showed no significant correlation with demographic and anthropometric measures, disease specific measures, or with the quantities of gut microbiome bacterial taxa differentially abundant in FM.

Conclusion: The gut microbiome of FM patients differed significantly from controls, but without differences in dietary intake. Furthermore macro- and micro-nutrient intake was not correlated with clinical indices of FM, including pain intensity, fatigue, cognitive symptoms and sleep problems. Objective measures of nutrient status, when applicable, would be required to confirm these observations. These data suggest that reported dietary differences between patients and controls are unlikely to explain the differences in gut microbiome or the clinical phenotype of of FM, and add to the emerging body of evidence of a gut-brain axis.

Disclosure: A. minerbi, None; **S. Chevalier**, None; **A. Anjarkouchian**, None; **A. Moyen**, None; **Y. Shir**, None; **M. Fitzcharles**, None.

	FM (72)	First degree relatives (11)	Household members (18)	Unrelated controls (43)
Energy (kcal)	1940 ± 460	1936 ± 322	2180 ± 552	2008 ± 600
Energy (kcal/kg)	28 ± 11	24 ± 5*	34 ± 11	31 ± 12
Protein (g)	76 ± 25	83 ± 24	89 ± 31	81 ± 24
Protein (g/kg)	1.1 ± 0.5	1.1 ± 0.4	1.4 ± 0.6	1.2 ± 0.4
Protein (% of E)	16 ± 4	17 ± 4	16 ± 4	15 ± 3
Carbohydrates (% of E)	47 ± 10	48 ± 6	46 ± 5	49 ± 9
Lipids (% of E)	36 ± 7	35 ± 5	37 ± 5	35 ± 7

Table 1. Daily average intakes of macronutrients. Mean ± SD. Asterisk indicates difference from household members group, p<0.05 ANOVA and Games-Howell post-hoc test.

Abstract Number: 0830

The Efficacy of Non-Pharmacological Interventions for Fibromyalgia: A Systematic Review with Meta-Analysis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Fibromyalgia & Other Clinical Pain Syndromes

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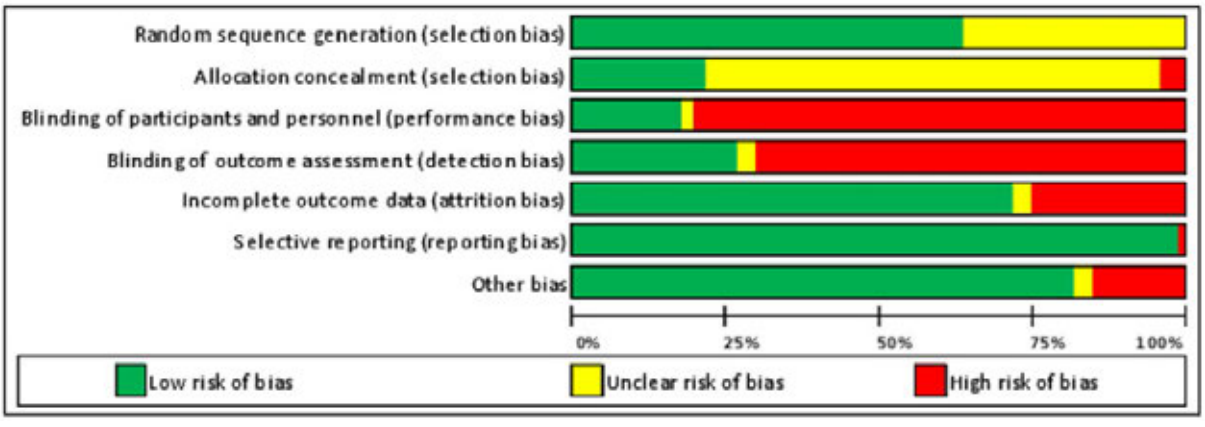

Figure 1. Risk of bias assessment

Interventions	FIQ	Pain	Fatigue	Sleep	Depression
Acupuncture	**-0.59 (-0.99, -0.19)** -1.18 (-2.46, 0.11)*	**-0.64 (-0.96, -0.31)** **-1.08 (-1.79, -0.36)***	**-0.41 (-0.80, -0.01)** **-0.50 (-0.90, -0.10)***	-0.30 (-0.69, 0.10) 1.95 (-2.29, 6.19)*	-0.23 (-0.63, 0.16) -0.63 (-1.46, 0.20)*
Balneotherapy	**-1.13 (-1.64, -0.61)**	**-1.29 (-2.00, -0.58)**	**-0.43 (-0.81, -0.05)**	-0.00 (-0.62, 0.61)	**-0.68 (-1.23, -0.13)**
Biofeedback	**-0.92 (-1.68, -0.17)**	-0.42 (-1.18, 0.33)	-0.09 (-0.54, 0.36)	-	-
Cupping	0.07 (-0.33, 0.47)*	-0.09 (-0.49, 0.32)*	0.06 (-0.34, 0.46)*	-0.20 (-0.60, 0.21)*	-
Education	-0.15 (-0.38, 0.08)	-0.18 (-0.41, 0.05)	**-0.31 (-0.55, -0.06)**	-0.25 (-0.61, 0.11)	-0.08 (-0.35, 0.20)
Electrotherapy	-0.97 (-3.10, 1.15) **-0.88 (-1.54, -0.23)***	-0.73 (-1.97, 0.51) -0.22 (-0.86, 0.42)*	**-1.04 (-2.07, -0.01)***	**-0.77 (-1.32, -0.21)** **-0.97 (-1.51, -0.43)***	**-0.88 (-1.46, -0.29)***
Exercise	**-0.67 (-0.89, -0.45)**	**-0.84 (-1.13, -0.55)**	**-0.88 (-1.39, -0.37)**	**-0.55 (-1.04, -0.06)**	**-0.55 (-0.82, -0.28)**
Homeopathy	**-0.80 (-1.49, -0.12)**	**-0.73 (-1.41, -0.05)**	**-0.69 (-1.36, -0.01)** -0.19 (-0.69, 0.31)*	**-0.91 (-1.60, -0.22)**	-0.15 (-0.81, 0.51) **-0.56 (-1.07, -0.06)***
HOT	-	**-2.22 (-2.93, -1.51)**	-	-	-
Magnetotherapy	**-0.69 (-1.28, -0.10)***	**-0.89 (-1.74, -0.04)***	**-2.61 (-3.70, -1.52)***	**-1.00 (-1.83, -0.16)***	-0.11 (-0.64, 0.41)*
Manual therapy	-0.31 (-0.84, 0.22)	**-0.86 (-1.32, -0.41)**	-0.44 (-1.02, 0.13)	0.10 (-1.22, 1.41)	-0.32 (-0.96, 0.32)
Massage	**-1.08 (-1.90, -0.26)**	**-0.76 (-1.32, -0.19)**	**-1.09 (-1.56, -0.63)**	**-0.79 (-1.23, -0.34)**	-0.73 (-1.83, 0.37)
Material of cloth	-3.25 (-8.27, 1.77)*	-2.89 (-6.82, 1.04)*	**-5.97 (-7.29, -4.65)***	**-8.94 (-10.8, -7.07)***	**-3.36 (-4.23, -2.49)***
MDT	**-0.41 (-0.79, -0.03)**	**-1.33 (-2.16, -0.49)**	-0.58 (-1.22, 0.06)	**-1.15 (-2.11, -0.18)**	**-1.26 (-2.06, -0.45)**
Music	-0.32 (-0.74, 0.10)	-0.58 (-1.24, 0.07)	-0.11 (-0.72, 0.50)	-	**-0.54 (-0.92, -0.15)**
Nutritional S.	-0.31 (-1.13, 0.50)*	-0.29 (-0.69, 0.11)*	**-0.41 (-0.77, -0.05)***	**-0.43 (-0.79, -0.06)***	-0.04 (-0.99, 0.90)*
Psychological T.	**-0.33 (-0.65, -0.02)**	**-0.44 (-0.59, -0.28)**	-0.20 (-0.53, 0.12)	-0.42 (-0.86, 0.02)	**-0.35 (-0.52, -0.17)**
tDCS	**-0.74 (-0.99, -0.48)***	-0.45 (-1.18, 0.27) **-0.84 (-1.21, -0.47)***	**--0.73 (-1.28, -0.19)***	**-0.57 (-0.96, -0.17)***	**-1.07 (-1.84, -0.30)** **-0.32 (-0.52, -0.13)***
WBV	-0.21 (-0.79, 0.37)	-	-	-	-
Weight loss	**-0.54 (-0.98, -0.11)**	-	-	**-0.66 (-1.11, -0.22)**	**-0.68 (-1.13, -0.24)**

FIQ: Fibromyalgia Impact Questionnaire, HOT: Hyperbaric Oxygen Therapy, MDT: Multidisciplinary Treatment, S: Supplement, T: Treatment, tDCS: Transcranial direct current stimulation, WBV: Whole Body Vibration

*: showing studies comparing with placebo. Text in bold shows significant values. Negative SMD favours treatment group.

Table 1. Effect size – Intervention versus non-intervention (usual care or placebo*): FIQ, pain, fatigue, sleep, depression

Background/Purpose: Non-pharmacological interventions are recommended as first-line treatment for fibromyalgia (FM)1. However, the evidence base supporting this has not been updated comprehensively, and the recent EULAR guideline was only based on a review of systematic reviews. The objective of this study was to assess the efficacy of non-pharmacological interventions on disease specific quality of life (FM Impact Questionnaire (FIQ)), pain, fatigue, sleep and depression in fibromyalgia.

Methods: MEDLINE, EMBASE, AMED, PsychINFO, CINAHL, Web of Science were systematically searched from their dates of inception until September 2018. In addition, the first 100 articles on Google Scholar were included. Randomised controlled trials (RCTs) comparing any non-pharmacological intervention versus usual care, no treatment, waiting list or placebo in patients with FM aged >16 years were included without language restriction. FIQ was the primary outcome of interest. Standardised mean difference (SMD) and 95% confidence interval (CI) were calculated using random effects model. The risk of bias was evaluated using modified Cochrane's tool.

Results: 16,251 studies were identified, and 148 RCTs (n=9,598) met all inclusion criteria. 89% patients in the included studies met ACR's 1990, 2010 or 2016 diagnostic criteria for FM. 109 studies (n=7,677) compared active treatment to usual care, waiting list or no treatment; and 39 (n=1,921) compared treatment with placebo or sham treatment. In total, 20 non-pharmacological interventions were evaluated. 52% trials had sample size < 50, and were at high risk of bias, especially on blinding (Fig 1).

Exercise (pooled for any type of exercise) was the only intervention associated with significant improvements for all five outcomes [FIQ (SMD=-0.67; 95% CI -0.89, -0.45), pain (-0.84; 95% CI -1.13, -0.55), fatigue (-0.88; 95%

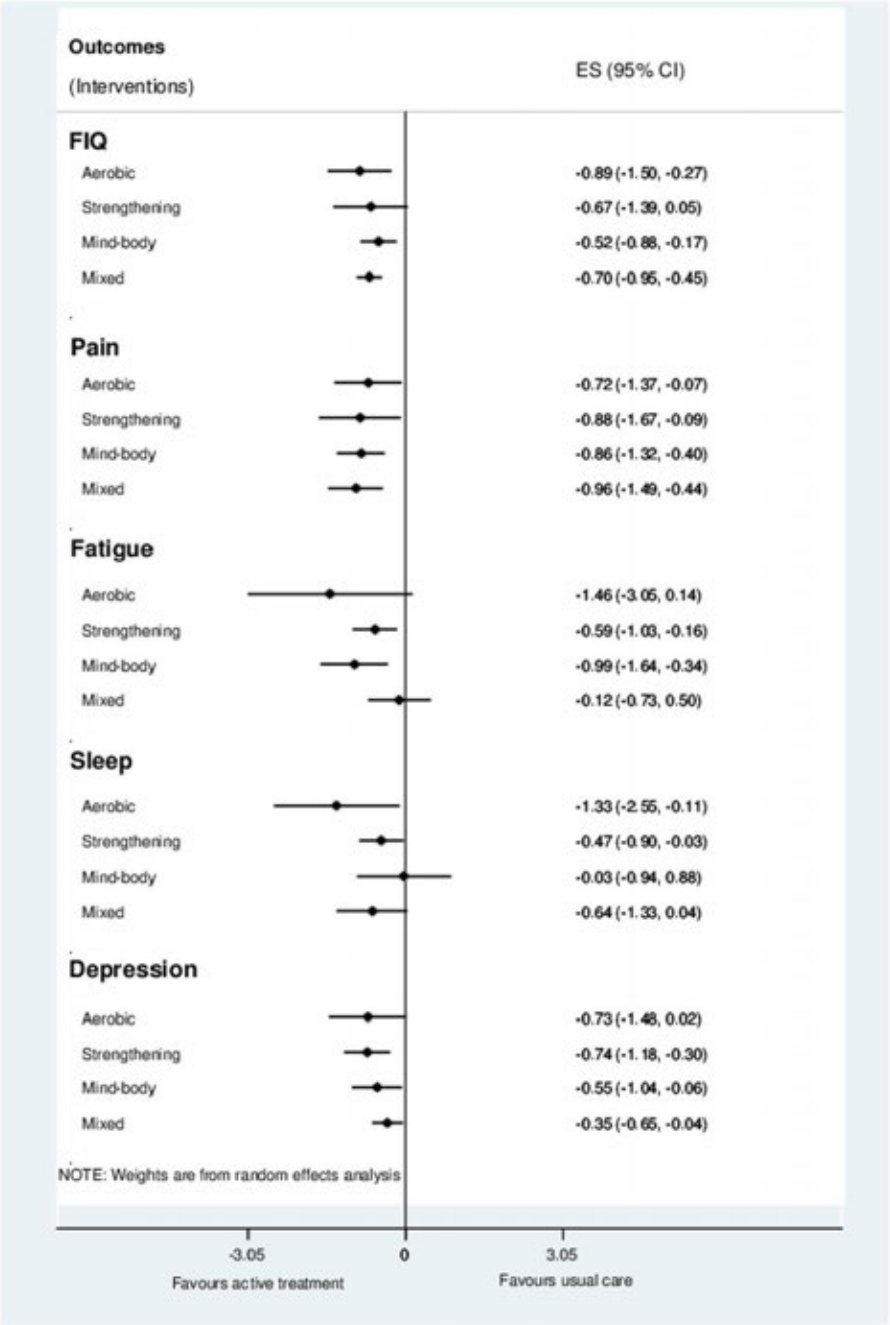

Figure 2. Effect size – Exercise types versus usual care: FIQ, pain, fatigue, sleep, depression

CI -1.39, -0.37), sleep (-0.55; 95% CI -1.04, -0.06) and depression (-0.55; 95% CI -0.82, -0.28)]. Psychological treatments including cognitive behavioural therapy and mindfulness were significantly more efficacious than usual care for FIQ, pain and depression but showed no improvement for fatigue and sleep (Table 1). All exercise types were effective at relieving pain (Fig 2). Mind body and strengthening exercises were effective at improving fatigue, while aerobic and strengthening exercises were effective at improving sleep. However, aerobic exercise had greater magnitude of effect on sleep than strengthening exercise. All exercise types except for aerobic exercise improved depression.

Conclusion: Non-pharmacological interventions are beneficial for FM. Exercise appears to be the most promising non-pharmacological intervention for relieving FM symptoms, although different exercise types benefit different outcomes. This suggests that different types of exercise should be prescribed to patients depending on their predominant symptoms.

Reference:

1. Macfarlane, G.J., Kronisch, C., Dean, L.E., Atzeni, F., Häuser, W., Fluß, E., Choy, E., Kosek, E., Amris, K., Branco, J. and Dincer, F., 2017. EULAR revised recommendations for the management of fibromyalgia. *Annals of the rheumatic diseases*, *76*(2), pp.318-328.

Disclosure: B. Kundakci, None; **J. Kaur**, None; **S. Goh**, None; **M. Hall**, None; **M. Doherty**, None; **W. Zhang**, None; **A. Abhishek**, None.

Abstract Number: 0831

Maintaining Musculoskeletal Health: A Randomized Controlled Prevention Trial Amongst People at High Risk of Developing Chronic Widespread Pain

Gary Macfarlane,[1] Marcus Beasley,[1] Neil Scott,[1] Gordon Prescott,[2] Paul McNamee,[1] John McBeth,[3] Gareth Jones,[1] Neil Basu,[4] Phil Hannaford,[1] Phil Keeley,[5] and Karina Lovell[6], [1]University of Aberdeen, Aberdeen, United Kingdom, [2]University of Central Lancashire, Preston, United Kingdom, [3]Versus Arthritis Centre for Epidemiology, Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Sciences, School of Biological Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, United Kingdom, Manchester, United Kingdom, [4]University of Glasgow, Glasgow, United Kingdom, [5]University of Huddersfield, Huddersfield, United Kingdom, [6]University of Manchester, Manchester, United Kingdom

SESSION INFORMATION
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Session Type: ACR Abstract Session
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Background/Purpose: Cognitive behaviour therapy (CBT) is effective in the management of fibromyalgia (and its characteristic feature Chronic Widespread Pain (CWP). CBT is recommended in all recent major fibromyalgia management guidelines. From large-scale epidemiological studies prediction models are available which identify groups at high-risk of developing CWP. We now test whether it is possible to prevent onset of CWP and/or change factors associated with its onset.

Methods: A randomized controlled trial of CBT delivered by telephone plus usual care (tCBT) was tested against usual care alone (UC). Eligible adults aged at least 25 years were identified by a survey of persons registered with sixteen general practices across Scotland. Respondents reporting regional pain (not CWP) for which they had recently consulted their GP and at least 2 items from a previously validated “high risk” profile (Somatic Symptom Scale, Sleep Problem Scale, Illness Behaviour Scale) were invited to participate. tCBT was delivered across 6 sessions over 8 weeks with booster sessions 3 and 6 months after treatment start. Primary outcome was CWP at 12 months. Secondary outcomes were risk profile measures: fatigue (Chalder Fatigue Scale), Patient Global Impression of Change (PGIC: 7 categories), psychological distress (General Health Questionnaire) and quality of life (EQ-5D-5L) also at 12

months. Analysis used logistic, ordinal logistic or linear regression depending on outcome variable type; expressed as an effect size with 95% confidence interval.

Results: 1002 people were randomized, with equal numbers assigned to each arm of the trial: 59% of participants were female, with a median age of 59 (range 25-91) years. 66% of tCBT participants completed treatment and 83% of all participants provided follow-up data at 12 months. There was no difference in the proportion with CWP at 12 months (tCBT 18.0% v. UC 17.5%). There were improvements (all favouring tCBT) in Illness Behaviour Score (mean difference (md) -0.83; -1.55,-0.11), Sleep Problem Scale (md -0.90; -1.45,-0.36), psychological distress (Odds Ratio (OR) $_{\text{per category}}$ 0.65; 0.50, 0.85), EQ-5D-5L (md 0.024; 0.009, 0.039), Chalder Fatigue Scale (md -1.05;-1.66,-0.44) and PGIC (OR $_{\text{per category}}$ 0.51;0.39,0.67). Specifically 30.2% of those receiving tCBT reported their health as much or very much better, compared to 17.3% of those receiving UC.

Conclusion: This first-ever large-scale trial of prevention, aimed at persons at high risk, has shown tCBT does not change the likelihood of CWP onset but does improve the underlying risk profile for developing the condition as well as improving distress , fatigue and quality of life. Those receiving tCBT were, 12 months later, significantly more like to consider their health was better. This trial provides evidence for extending the group of people considered to benefit from CBT.

Disclosure: G. Macfarlane, Celgene, 2; **M. Beasley**, None; **N. Scott**, None; **G. Prescott**, None; **P. McNamee**, None; **J. McBeth**, None; **G. Jones**, Celgene, 2; **N. Basu**, None; **P. Hannaford**, None; **P. Keeley**, None; **K. Lovell**, None.

Abstract Number: 0832

Diagnosis of Fibromyalgia: Comparison of AAPT and ACR Criteria

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Time: 2:30PM–4:00PM

Background/Purpose: In recent years, the diagnostic criteria for fibromyalgia (FM) have been reviewed multiple times, up to the publication of the provisional criteria of the ACR in their 2016 revision [1]. In 2018, a revised FM diagnosis was proposed by the ACTION-APS Pain Taxonomy (AAPT) [2], requiring for the diagnosis the presence of multisite pain (MSP), defined as 6 or more painful sites of a total of 9 possible sites, plus moderate to severe sleep poblems or fatigue.

The purpose of this work was to compare the diagnostic characteristics of the different sets of criteria.

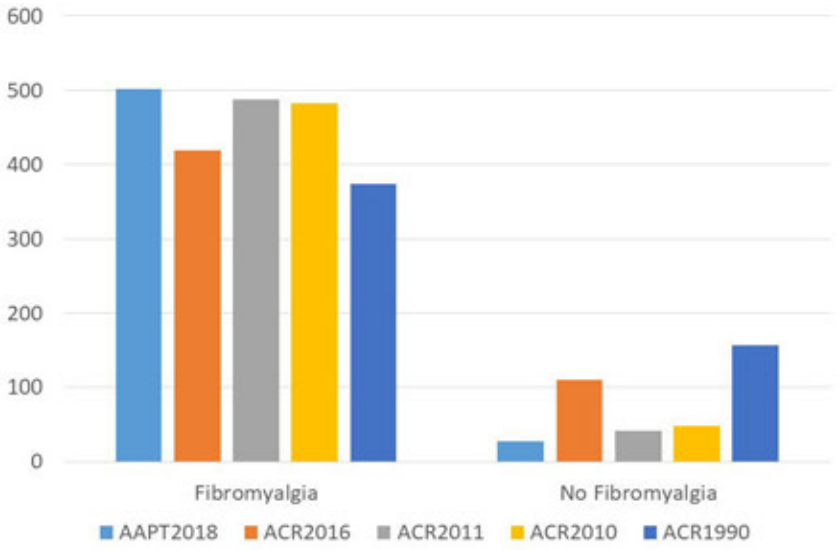
Methods: The study population consisted of 530 patients (481 F, 49 M, mean age 47.9 ± 11.7 yrs) referred for fibromyalgia. All patients underwent a complete clinical workout, including the compilation of multiple questionnaires addressing the different domains of fibromyalgia. All patients were classified according to the newly proposed criteria and to the different sets of ACR criteria, including the 1990 criteria based only on tender points count, and the revised 2010 criteria with 2011 and 2016 revisions. Statistical analysis were performed with SPSS software, and parametric and non parametric methods were used as appropriate.

Results: Overall, FM was diagnosed in 95% of patients (503/530) by AAPT criteria; for ACR criteria, a diagnosis of FM was made in 79 % (420/530), 92% (488/539), 91% (482/530), and 71% (374/530) respectively by 2016, 2011, 2010 and 1990 criteria. The overall agreement (k statistics) between AAPT and the four sets of ACR criteria, although statistically significant $p < 0.001$ in all cases), was at best moderate (0.120, 0.472, 0.428, and 0.324 respectively). In particular, comparing AAPT and ACR2016 criteria, there were 89 discrepant cases, mostly diagnoses of FM by AAPT not confirmed by ACR2016 criteria (AAPT+/ACR2016-, N=83; AAPT-/ACR2016+, N=6). Overall, AAPT+/ACR2016- cases showed a moderate pain level (average 5.89±2.4 on a 0-10 NRS scale) and 82% was characterized by mild to moderate severity according to Polysymptomatic Distress Scale (value < 12).

Conclusion: Our results confirm that the diagnosis of fibromyalgia by the newly proposed AAPT diagnostic criteria is not completely coincident with ACR criteria. Fibromyalgia will be diagnosed more frequently by the new criteria. Further analysis is necessary to fully clarify the real extent of the proposed changes.

References:

1. Wolfe F, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016 Dec;46(3):319-329.
2. Arnold LM, et al. AAPT Diagnostic Criteria for Fibromyalgia. J Pain. 2018 Nov 16. pii: S1526-5900(18)30832-0.



Classification of 530 patients according to the different sets of criteria

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Abstract Number: 0833

Effect of a Mobile App to Monitor Patient Reported Outcomes in Rheumatoid Arthritis: A Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes I: Patient Reported Outcomes

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Treat to target (TTT) is an effective strategy to improve outcomes in rheumatoid arthritis (RA). However, barriers to TTT include frequent clinic visits, poor access to rheumatologists, and poor patient acceptance of treatment escalation. Mobile technology may provide a solution by enabling collection of patient-reported outcomes (PROs) between clinic visits. The objectives of this study were to examine the effects of a mobile application (app) to monitor PROs on: 1) patient satisfaction and 2) disease activity in RA.

Methods: We conducted a 6-month randomized controlled trial of an app + population manager vs. population manager alone in 191 RA patients. Participants in the app group were prompted to answer daily questionnaires on disease activity, function, pain, fatigue, sleep, and mood, using an app. Both groups were assigned a population manager who spoke with participants on the telephone at 6 and 18 weeks. Population managers also communicated with participants in the app group if responses to the daily assessments indicated a sustained increase in disease activity. The analysis followed an intent-to-treat principle. Missing data were imputed using last observation carried forward. To address the aim of improving patient satisfaction, the main outcomes were the global satisfaction score from the Treatment Satisfaction Questionnaire for Medication (TSQM) and the Perceived Efficacy in Patient-Physician Interactions (PEPPI) score. To address the aim of decreasing disease activity, the primary outcome was the Clinical Disease Activity Index (CDAI). Treatment effects were estimated with repeated measures analyses (baseline, 3-month, 6-month), using bootstrapped quantile regression models, adjusted for age, sex, and race.

Results: Of the 191 participants, 156 (82%) were women. 29% were at least 65 years old. Baseline global TSQM and PEPPI scores were high, with a median of 83.3 (interquartile range [IQR] 66.7-100) and 50 (IQR 47-50), respectively (Table). The median baseline CDAI was 8 (IQR 4-14), indicating low disease activity. After 6 months, median TSQM scores were 83.3 (IQR 66.7-100) in both groups, and median PEPPI scores were 50 (IQR 47-50) in the app group and 50 (IQR 48-50) in the no app group (Figure). Median 6-month CDAI scores were 8 (IQR 4-14) in the app group vs. 10 (IQR 3-16) in the no app group. Quantile regression analyses indicated no group (app vs. no app) differences at 6-months in medians of: TSQM β 0.00, 95% confidence interval [CI] -9.18, 9.18; PEPPI β 0.00, 95% CI -0.16, 0.16; and CDAI β -0.50, 95% CI -3.82, 2.82. Adherence with the app was over 75% during the 6-month follow-up.

Conclusion: A mobile app designed to collect PRO data on RA symptoms did not improve patient satisfaction or disease activity. However, baseline satisfaction scores were high and disease activity was low, suggesting ceiling and floor effects. Adherence with the app was strong. Future studies are needed to determine: a) if the app would be

Table. Baseline characteristics of trial participants.

Characteristic	Mobile app + Population Manager (N = 100)	Population Manager Alone (N = 91)	Overall Study Cohort (N = 191)
Sex, n (%)			
Female	83 (83.0%)	73 (80.2%)	156 (81.7%)
Male	17 (17.0%)	18 (19.8%)	35 (18.3%)
Age, n (%)			
<45 years	28 (28.0%)	21 (23.1%)	49 (25.7%)
45-65 years	43 (43.0%)	44 (48.4%)	87 (45.6%)
≥ 65 years	29 (29.0%)	26 (28.6%)	55 (28.8%)
Race, n (%)			
White	86 (86.0%)	79 (86.8%)	165 (86.4%)
Non-white	14 (14.0%)	12 (13.2%)	26 (13.2%)
Education, n (%)			
High school or below	22 (22.0%)	19 (20.9%)	41 (21.5%)
College	47 (47.0%)	52 (57.1%)	99 (51.8%)
Post college	31 (31.0%)	20 (22.0%)	51 (26.7%)
Treatment Satisfaction Questionnaire for Medication (TSQM), median (IQR)	83.3 (66.7 - 100)	83.3 (66.7 - 100)	83.3 (66.7 - 100)
Perceived Efficacy in Patient-Physician Interactions (PEPPI), median (IQR)	50 (48 - 50)	50 (46 - 50)	50 (47 - 50)
Clinical Disease Activity Index (CDAI), median (IQR)	8.5 (3.5 - 14)	8 (4 - 14)	8 (4 - 14)

*IQR, interquartile range

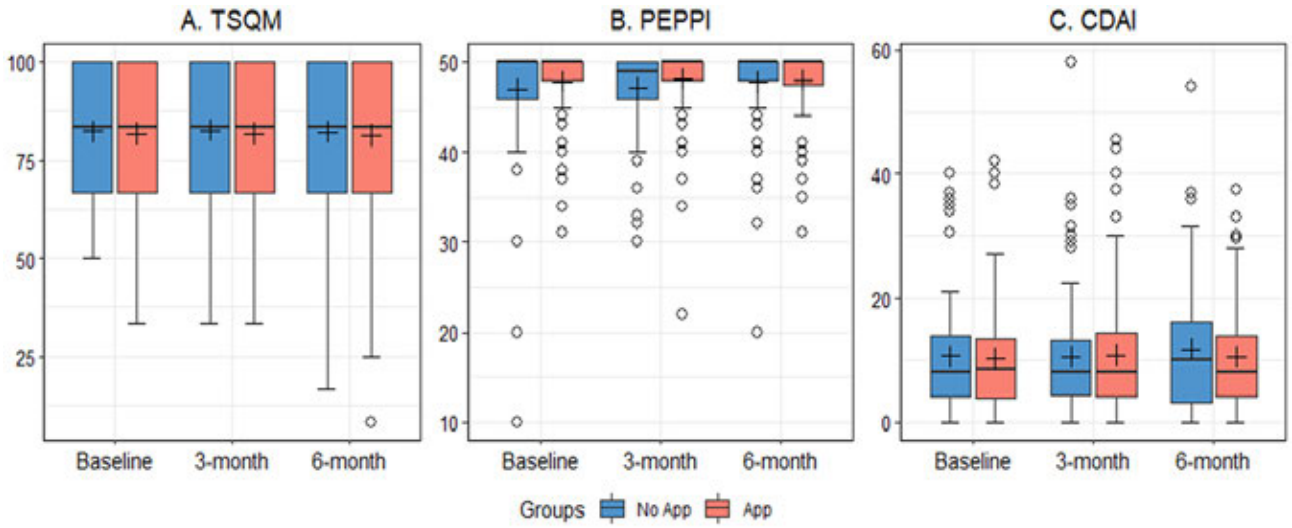

Figure. A. Primary outcomes of Treatment Satisfaction Questionnaire for Medication (TSQM), B. Perceived Efficacy in Patient-Provider Interactions (PEPPI), and C. Clinical Disease Activity Index (CDAI) by intervention group and visits. The horizontal line within each box indicates the median; the top and bottom of the boxes indicates the interquartile range (IQR); and the whiskers represent the minimum and maximum observations within the lower and upper fences (1.5 x IQR). The plus sign represents the mean.

beneficial in a population with lower baseline satisfaction and/or more disease activity, and b) if improvements in the app (e.g., voice-enabled system, personalized frequency of data collection) would enhance efficacy.

Disclosure: Y. Lee, Cigna Corp, 1, Eli Lilly, 2, 5, Eli Lilly and Company, 2, Express Scripts, 4, Pfizer, 2; **F. Lu**, None; **J. Colls**, None; **M. Murray**, None; **D. Suh**, None; **J. Song**, None; **J. Lee**, None; **D. Dunlop**, None; **D. Solomon**, AbbVie, 2, Abbvie, 2, Amgen, 2, AstraZeneca, 2, Corrona, 2, Genentech, 2, Janssen, 2, Lilly, 2, Pfizer, 2.

Abstract Number: 0834

Implementing Patient-Reported Outcome Measures in Clinical Care: Rheumatologist Perspectives on Opportunities and Challenges

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes I: Patient Reported Outcomes

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: There is growing interest in the implementation of patient-reported outcome measures (PROMs) in clinical rheumatology to promote patient-centered care and to meet the mandates of value-based health care initiatives. While studies suggest that patients support the routine measurement of patient-reported outcomes in clinical care, the views of rheumatologists are unknown. Understanding rheumatologists' perspectives on the potential utility and challenges of using PROMs at the point of care is critical to the successful clinical implementation of PROMs. The objective of this study was to investigate rheumatologists' views on the benefits of and barriers to utilizing PROMs in clinical care, with a specific focus on patients with systemic lupus erythematosus (SLE).

Methods: Structured interviews were conducted with academically affiliated clinical rheumatologists. Interviews were audio-recorded and transcribed verbatim. De-identified transcripts were uploaded into Dedoose™ Version

Table 1. Uses and Benefits of Patient-Reported Outcome Measures (PROMs) in Clinical Care

Contribute to Clinical Impression	
	"Do I use it clinically? I guess it becomes part of the equation in your brain. But do I specifically do something based on only that result? No... you talk to the patient, you examine the patient, you have a plan in your mind and that's high numbers over there that just supports what you are thinking if the patient is coming with a flare." [R3]
	"I use the information in combination with my clinical observation and impression of the patient because sometimes there's discrepancies." [R4]
	"You have to put it in the clinical context for sure but I think it's just another way to sort of fill that out. And I think it's just when somebody's really sick it's obvious. Quality of life is poor and all that stuff. Like that's a no brainer. But I think, you know, that maybe is only like ten to fifteen percent of the patients and the rest of the patients are a continuum of doing okay. Like doing okay well, and you know, actually not doing so well. And sometimes depending on people's coping mechanisms, you might have a misguided sense of really what their quality of life is." [R1]
- Identify Patient Perspective	"There are patients who have mild connective tissue disease or lupus but who really are suffering much more than other patients. I think that it's important to know that. That is some of the information that you get." [R2]
	"The other role it could play would be in a situation where you think the disease isn't that active and then there's enough things that are legitimately inflammatory that you realize you're just wrong about it. Because I think when a patient is upbeat and cheerful they sometimes don't seem that sick. But when you realize they're very fatigued; they can't get out of bed for two hours; they can't do this, that or the other thing. You're like hmm, maybe I'm not right about that or maybe they're not right about that." [R1]
- Identify Red Flags	"If I saw an outline or a number suddenly that was much lower or much higher, I'd probably ask them about it. So it would be a prompt for me to check into it." [R10]
	"I will glance at it when I go in. If I see something that I find surprising, I will raise it with a patient." [R2]
- "Biomarker"	"In some patients if you see a trend where some of these more subjective features tend to happen when their disease is more active. You can perhaps understand that in that patient that could be an actual marker of impending flare." [R12]
	"I think all of these things are useful in context. So if there is an idea that these – that a particular measure reflects disease activity in some kind of measurable standard way, then yeah, it would be really helpful to have some measure of that." [R5]
Set the Agenda	
	"It helps you focus because every patient's different. So when you go in the room, you're focusing on the things the patients care about because I think you don't always know what that is. And it's obvious sometimes when the patient still looks unhappy that you haven't hit on the right thing. So this way you can just get to the important stuff." [R1]
	"To have the information gathered for you, it just allows you to hone in on what seems to be most important for that particular patient." [R2]
- Save Time	"It would actually help you save time because it would show you some things that otherwise maybe wouldn't come out until the end of the visit." [R10]
	"I think that this kind of thing can save a little bit of time because we're all so constrained in terms of the amount of time we have for our encounters with patients. It provides you with an at-a-glance idea of how the patient perceives

Table 2. Challenges of Implementing Patient-Reported Outcome Measures (PROMs) in Clinical Care

No Added Value	
	"After 20 years of experience, you kind of know what's going on in five minutes ... Like many times we get the picture and we don't ask all the questions that we really need to ask if you are a resident." [R3]
	"I think I get to the same questions without doing it in a formal way... I think I get to the point, the questions that I need to ask for patient care and I think of [PROMs] more as for studies." [R15]
	"I don't feel like it adds to what I'm going to do for the patient beyond the things that I do." [R10]
	"I'm not always sure that it adds more to just asking people how they're doing and whether things are good or bad, or what their problems are. So I'm not always convinced there's an additive effect there." [R6]
Physician Culture Change	
	"I think sometimes people who are maybe a little skeptical about patient-reported outcomes think that the people who promulgate them are suggesting that they don't know how to talk to patients. They don't know how to get the right information and therefore this is fixing you not being a very good doctor." [R7]
	"If you're adding time, and you're adding logistical headaches, and you're adding all of these things to all the stuff that a physician has to do to get through a visit, then there has to be some good coming out of it. I think convincing people of the value of this stuff is sort of where you can get them to be interested in using it for patient care." [R15]
	"It's very difficult to change their culture or how physicians practice, or before practicing, just to bring something new to patient care." [R3]
	"I think the doctor has to be a believer as well because a lot of doctors may walk in the room thinking they know what to do, but they may not... some doctors may not think it's really that important and others may think, oh, this is really going to change what I offer the patient today." [R13]
Time Constraints/ Competing Priorities	
	"It doesn't mean that you don't think it's important, but you have to focus on what you think is medically the most important. I think that's why these other things, they just don't get addressed because of lack of time, lack of resources." [R2]
	"The doctor feels like they just barely have enough time to address all the other important issues, which the patient may not think that's important at the time; it's always the main issue here." [R14]
Score Interpretation	
	"I see it in the chart there in front of me. I have no clue what that means for a patient. So, to me asking them how are you doing is so much more than what those numbers say. And I have people that check nine every time and I don't – it's like all right. Well, for ten years they've been checking nine and it's fibromyalgia." [R10]
	"Unfortunately it's the people with lupus that's kind of not severe that you most want a score like this, where it works the least well because they're the people who you're like eh, is it all fibro-y stuff going on here?" [R6]
	"Absent context there's no kind of anchoring for it. It can be very high in that different people give very disparate answers based on – I don't know – all kinds of reasons." [R5]
Lack of Effective Interventions	

8.2.14 web application for qualitative data analysis. Two authors (SK and AL) reviewed a subset of transcripts to construct a preliminary codebook which was iteratively updated to include emergent themes as additional transcripts were coded. The final codebook was applied using a comparison and consensus approach. Thematic analysis was used to identify the main benefits and barriers of the use of PROMs in clinical care.

Results: Interviewees consisted of 15 attending rheumatologists affiliated with two academic medical centers in two states, and included 8 women (53%) and 7 men (47%). Subjects reported a median of 15 years in practice (range 5 to 43), with 53% reporting a specific interest in SLE. Rheumatologists identified several uses and benefits of implementing PROMs in clinical care (Table 1), including contributing to the clinical impression by providing the patient perspective, and promoting agenda setting by uncovering "the unspoken questions." Interviewees noted PROMs could support treatment planning by enabling longitudinal tracking, identifying avenues for intervention, and providing a mechanism for asynchronous care and population management. They noted significant benefits of PROMs in building patient-physician relationships and facilitating patient engagement. However, they also identified several barriers to integrating PROMs in clinical care (Table 2), highlighting physician buy-in and culture change as significant

challenges beyond logistical considerations. They further underscored the lack of effective interventions and resources for addressing the domains of most interest to patients.

Conclusion: Rheumatologists identified multiple mechanisms through which PROMs could augment the care of SLE, but also noted several obstacles to implementation in clinical settings, questioning the added value of PROMs and the limited availability of interventions to improve patient-centered outcomes. Programs seeking to successfully integrate PROMs to enhance patient-centered care and meet quality benchmarks must prioritize physician buy-in and training, and provide resources to address the outcomes that are measured.

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Abstract Number: 0835

High Baseline Patient's Compared with Evaluator's Global Assessment Is Associated with Lower Retention and Remission Rates of First TNF Inhibitor in Psoriatic Arthritis Patients - Data from the EuroSpA Research Collaboration Network

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes I: Patient Reported Outcomes

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Discordance between baseline patient's and evaluator's global assessment of disease activity is common[1] and may reduce the likelihood of remission following tumor necrosis factor inhibitor (TNFi) treatment in patients with psoriatic arthritis (PsA).[2] However, the impact of such discordance on retention rates of TNFi in PsA patients remains unexplored. Hence, the aim of this study was to explore the impact of discordance, defined as patient's minus evaluator's global assessment (ΔPEG), on retention rates and remission rates (DAS28(3)CRP (without patient's global) and DAS28(4)CRP (including patient's global)) in PsA patients initiating their first TNFi treatment. We used pooled data from the European Spondyloarthritis Research Collaboration Network (EuroSpA).

Methods: TNFi naïve PsA patients from 11 European registries in EuroSpA were included. Kaplan-Meier analyses were used to estimate TNFi retention rates after 6/12/24 months, with comparison between baseline ΔPEG quartiles using the log rank test, stratified by gender. Remission rates were compared between different ΔPEG quartiles with Chi-square test, stratified by gender.

Results: A total of 5855 PsA patients were included. Mean (SD) age for women (n=2988) / men (n=2867) were 49.3 (12.5) / 47.4 (11.7) years, disease duration 6.6 (7.3) / 6.7 (7.2) years, median (25-75 percentiles) baseline ΔPEG 17 (0-38) / 10 (0-30) mm. Retention rates and DAS28(4)CRP but not DAS28(3)CRP remission rates were lower for higher quartiles of baseline ΔPEG (table, figure).

TNFi retention rates	TNFi retention rates (%, 95%CI) according to baseline patient's minus evaluator's global assessment (ΔPEG) quartiles									
	Women (n=2988)					Men (n=2867)				
	1st quartile (-100 to 0) (n=815)	2nd quartile (1 to 17) (n=694)	3rd quartile (18 to 38) (n=739)	4th quartile (39 to 100) (n=740)	p value	1st quartile (-100 to -1) (n=648)	2nd quartile (0 to 9) (n=683)	3rd quartile (10 to 30) (n=865)	4th quartile (31 to 100) (n=671)	p value
6 months	87% (85-90%)	85% (82-88%)	81% (78-84%)	74% (71-77%)	<0.001	93% (91-95%)	93% (91-95%)	92% (90-93%)	86% (83-89%)	<0.001
12 months	79% (76-82%)	76% (73-79%)	70% (67-74%)	61% (57-65%)	<0.001	88% (85-90%)	86% (84-89%)	83% (80-85%)	78% (75-81%)	<0.001
24 months	69% (66-72%)	69% (65-72%)	61% (57-65%)	52% (48-56%)	<0.001	77% (74-81%)	79% (76-82%)	74% (71-78%)	69% (66-73%)	<0.001
DAS28(4)CRP remission (<2.6)	Proportions, % (95%CI), of patients in DAS28(4)CRP remission according to baseline patient's minus evaluator's global assessment (ΔPEG) quartiles									
	Women					Men				
	1st quartile (-100 to 0)	2nd quartile (1 to 17)	3rd quartile (18 to 38)	4th quartile (39 to 100)	p value	1st quartile (-100 to -1)	2nd quartile (0 to 9)	3rd quartile (10 to 30)	4th quartile (31 to 100)	p value
6 months	51% (47-56%)	48% (44-53%)	39% (34-43%)	36% (32-41%)	<0.001	63% (58-68%)	67% (63-71%)	59% (55-63%)	59% (54-63%)	0.04
12 months	53% (48-57%)	53% (48-58%)	43% (38-47%)	38% (33-43%)	<0.001	68% (58-68%)	69% (63-71%)	63% (55-63%)	65% (54-63%)	0.21
24 months	58% (53-63%)	58% (52-63%)	47% (42-53%)	37% (32-43%)	<0.001	69% (64-74%)	72% (67-77%)	64% (59-69%)	60% (55-66%)	0.007
DAS28(3)CRP remission (<2.6)	Proportions, % (95%CI), of patients in DAS28(3)CRP remission according to baseline patient's minus evaluator's global assessment (ΔPEG) quartiles									
	Women					Men				
	1st quartile (-100 to 0)	2nd quartile (1 to 17)	3rd quartile (18 to 38)	4th quartile (39 to 100)	p value	1st quartile (-100 to -1)	2nd quartile (0 to 9)	3rd quartile (10 to 30)	4th quartile (31 to 100)	p value
6 months	52% (48-57%)	53% (48-57%)	47% (43-52%)	48% (43-52%)	0.19	65% (60-70%)	69% (64-73%)	64% (60-68%)	68% (64-73%)	0.28
12 months	54% (50-59%)	57% (52-61%)	53% (48-57%)	50% (45-55%)	0.30	70% (66-75%)	72% (67-76%)	69% (65-73%)	72% (68-76%)	0.77
24 months	61% (56-66%)	60% (55-65%)	55% (50-60%)	52% (46-57%)	0.04	74% (69-79%)	76% (71-80%)	70% (66-74%)	73% (69-78%)	0.32

Table. Retention and remission rates of first TNFi in PsA patients.

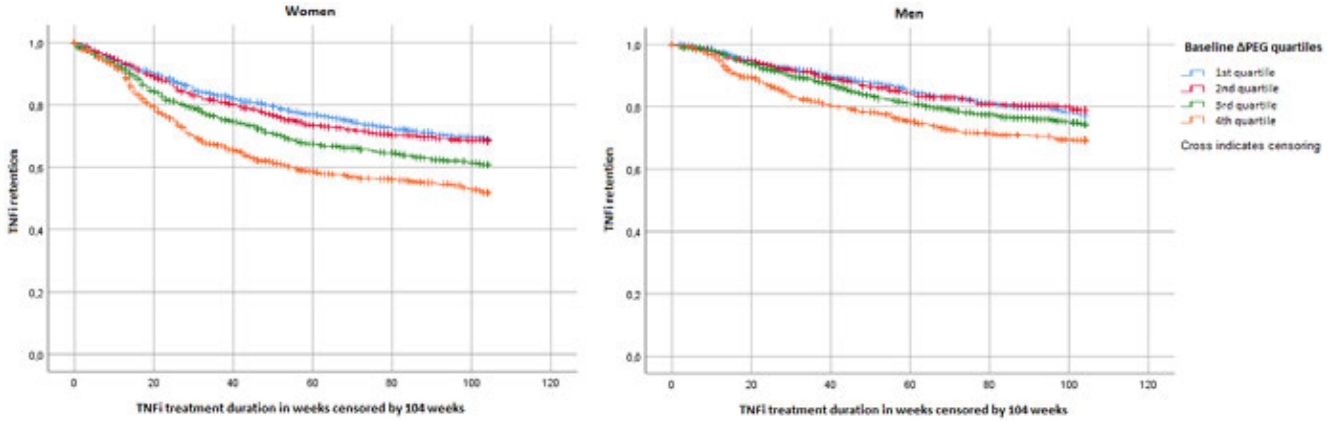

Figure 1. Retention rates of first TNFi across ΔPEG quartiles, censored by 104 weeks.

Conclusion: High baseline discordance (ΔPEG) was associated with lower TNFi retention rates and with lower DAS28(4)CRP remission rates, but not DAS28(3)CRP remission rates, after 6, 12 and 24 months' follow-up in both male and female PsA patients. The choice of remission criteria in the follow-up of PsA patients may affect important treatment decisions, and may be of particular impact in patients with high baseline ΔPEG.

Disclosure: B. Michelsen, Novartis, 2, 5; **L. Midtbøll Ørnbjerg**, Novartis, 2; **H. Mann**, None; **T. Kvien**, AbbVie, 2, 8, Biogen, 5, 8, Biogen, Egis, Eli Lilly, Hikma, Mylan, Novartis/Sandoz, Oktal, Hospira/Pfizer, Sanofi and UCB, 5, BMS, 8, Celltrion, 8, Egis, 5, 8, Eli Lilly, 5, 8, Hikma, 5, 8, Hospira/Pfizer, 2, 5, 8, MSD, 2, 8, Mylan, 5, 8, Novartis, 8, Novartis/Sandoz, 5, 8, Oktal, 5, 8, Orion Pharma, 8, Roche, 2, 8, Sandoz, 8, Sanofi, 5, 8, UCB, 5, 8; **M. Nissen**, Abbvie, Celgene, Lilly, MSD, Novartis, Pfizer, 5, 8; **M. Santos**, AbbVie, 8, Biogen, 8, Novartis, 8, Pfizer, 8, Roche, 8; **D. Nordström**, AbbVie, 5, 8, BMS, 5, 8, Celgene, 5, 8, Lilly, 5, 8, MSD, 2, 4, 8, Novartis, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, UCB, 5, 8; **L. Jacobsson**, None; **Z. Rotar**, AbbVie, 9, Amgen, 5, 8, Eli-Lilly, 9, MSD, 5, Novartis, 9, Pfizer, 9, Sanofi, 5; **B. Gudbjornsson**, Actavis, 8, Amgen, 8, Novartis, 8, Pfizer, 8; **S. Koca**, None; **C. Codreanu**, AbbVie, 5, 8, Egis, 5, 8, Eli-Lilly, 5, 8, Ewopharma, 5, 8, Mylan, 5, 8, Novartis/Sandoz, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8; **M. Pombo-Suarez**, None; **I. van der Horst-Bruinsma**, AbbVie, 2, 5, 8, Bristol Myers-Squibb, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB Pharma, 2, 5, 8; **A. Loft**, None; **K. Pavelka**, AbbVie, 8, Abbvie, 5, 8, Amgen, 5, 8, BMS, 8, Egis, 5, 8, Lilly, 5, 8, MSD, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 8; **E. Kristianslund**, None; **B. Moeller**, AbbVie, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Merck, 2, 8, Novartis, 2, 8, Pfizer, 2, 8, UCB, 2, 9; **E. Vieira-Sousa**, None; **A. Hokkanen**, None; **U. Lindström**, None; **M. Tomsic**, None; **T. Love**, None; **A. Tufan**, None; **R. IONESCU**, Abbvie, 5, 8, Amgen, 5, 8, Alpha Sigma, 5, 8, BMS, 5, 8, Ewopharma, 5, 8, Lilly, 5, 8, Mylan, 5, 8, Novartis, 5, 8, MSD, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Roche, 5, 8, Sandoz, 5, 8; **C. Sánchez-Piedra**, None; **M. van de Sande**, None; **G. Macfarlane**, Celgene, 2; **F. Iannone**, AbbVie, 5, 8, BMS, 5, 8, Janssen, 5, 8, lilly, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **L. Hyldstrup**, Novartis, 2; **M. Østergaard**, AbbVie, 2, 8, 9, Abbvie, 2, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, UCB, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, 5, 8, Abbvie, Celgene, Centocor, Merck, and Novartis, 2, Abbvie, Celgene, Centocor, Merck, Novartis, 2, BMS, 2, 5, 8, 9, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8; **M. Lund Hetland**, Abbvie, 2, AbbVie, 2, Biogen, 2, BMS, 2, CellTrion, 2, 9, MSD, 2, Novartis, 2, Orion, 2, Pfizer, 2, Samsung, 2, UCB, 2.

Abstract Number: 0836

Patient-Reported Outcomes from a Randomised, Open-Label, Parallel-Group Study Evaluating Ixekizumab versus Adalimumab in Patients with PsA Who Are Biologic DMARD Naïve: 24-Week Results

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes I: Patient Reported Outcomes

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Therapeutic options for patients with PsA are increasing but data directly comparing biologics are limited. The multicentre, open-label SPIRIT-H2H trial (NCT03151551) evaluated the efficacy and safety of ixekizumab (IXE) vs adalimumab (ADA) over a 52-week treatment period in biologic DMARD-naïve patients with active PsA. This analysis directly compared the effects of IXE vs ADA on patient-reported outcomes (PROs) and health-related quality of life (HRQoL) after 24 weeks' treatment in SPIRIT-H2H.

Methods: All patients fulfilled the Classification Criteria for Psoriatic Arthritis (CASPAR). Patients were randomised (1:1) to 52 weeks of IXE (160 mg week 0, then 80 mg every 2 weeks [Q2W] to week 12 and Q4W thereafter for patients with moderate-to-severe plaque psoriasis [PsO] or 160 mg week 0, then 80 mg Q4W for other patients) or ADA (80 mg week 0 then 40 mg Q2W from week 1 for patients with moderate-to-severe PsO or 40 mg week 0 then 40 mg Q2W for other patients). The primary objective was to assess the superiority of IXE vs ADA by comparing the proportion of patients achieving a simultaneous improvement of ≥50% in ACR criteria (ACR50) and 100% in Psoriasis Area Severity Index score (PASI100) at week 24. A number of PROs and HRQoL were evaluated (see Table). PRO changes from baseline to week 24 were analysed using analysis of covariance models with modified baseline observation carried forward imputation. Treatment satisfaction was assessed using the Treatment Satisfaction Questionnaire. Logistic regressions with non-responder imputation in the intent-to-treat population were used to evaluate results.

Results: A total of 566 patients were randomised to IXE or ADA; of these 82% of patients did not have moderate-to-severe PsO. Baseline characteristics were generally balanced between the two treatment groups. The percentage of patients simultaneously achieving ACR50 and PASI100 responses at week 24 was statistically superior for IXE vs ADA (36% vs 28%; $p< 0.05$). All PRO and HRQoL outcomes (Table) significantly improved from baseline in both treatment groups ($p< .001$ for all). Treatment with IXE was associated with a statistically significantly greater improvement in itch, Short form-36 Health Survey scores, Role-emotional and Dermatology Life Quality Index (DLQI) scores vs ADA (seen as early as week 4 for itch and DLQI improvement). For patients' overall satisfaction with treatment, 62.5% of IXE and 59.7% of ADA recipients were mostly satisfied. Both biologics had acceptable safety and tolerability.

Conclusion: In bDMARD-naïve patients with active PsA and PsO, IXE showed superior efficacy compared to ADA based on simultaneous achievement of ACR50 and PASI100 responses at week 24. Both biologics significantly improved HRQoL and other PROs. Greater improvements in PROs related to PsO were observed for IXE- compared to ADA-treated patients.

Table. PROs and HRQoL at baseline and least square mean change from baseline at week 24

Endpoint	IXE (N=283)		ADA (N=283)	
	Baseline	Change at wk 24	Baseline	Change at wk 24
Patient Global Assessment of Disease Activity VAS	62.39	-36.80	65.19	-35.48
Fatigue NRS	5.87	-2.66	6.46	-2.58
Pain VAS	59.66	-31.77	62.35	-31.50
Health Assessment Questionnaire–Disability Index	1.20	-.63	1.27	-.57
European Quality of Life 5-Dimensions VAS	54.06	19.59	54.21	17.04
SF-36				
Physical Component Summary	36.80	9.90	36.12	9.04
Mental Component Summary	45.40	4.52	44.85	3.81
Physical functioning	45.32	26.25	44.34	22.50
Role-physical	47.17	22.16	44.13	19.17
Bodily pain	39.22	26.59	37.68	24.07
General health	45.45	14.23	44.28	13.73
Vitality	44.06	15.33	41.99	15.60
Social functioning	61.47	17.47	60.28	15.21
Role-emotional	65.23	14.64*	63.49	10.84
Mental health	60.59	10.47	59.93	8.94
Itch NRS	5.54	-3.66*	5.68	-3.14
DLQI	9.77	-7.60**	9.82	-6.26

*p<.05, **p<.001 vs ADA.
Baseline mean scores are presented for PROs and HRQoL endpoints. Overall treatment satisfaction results are presented as percentage of patients.
ADA, adalimumab; DLQI, Dermatology Life Quality Index; IXE, ixekizumab; NRS, Numeric Rating Scale; SF-36, 36-item Short Form Health Survey; VAS, Visual Analogue Scale; wk, week

Disclosure: F. Van den Bosch, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, Bristol-Myers Squibb, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sanofi and UCB, 5, 8, ABBVIE, CELGENE, ELI LILLY, GALAPAGOS, MERCK, NOVARTIS, PFIZER, VCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **L. Kristensen**, UCB, 2, 8, Biogen, 2, 8, Janssen pharmaceuticals, 2, 8, Novartis, 2, 8, Pfizer, 8, AbbVie, 8, Amgen, 8, Bristol-Myers Squibb, 8, MSD, 8, Eli Lilly and Company, 8; **D. McGonagle**, AbbVie, 9, Abbvie, 2, 8, BMS, 9, Celgene, 2, 8, 9, Janssen, 2, 8, Johnson & Johnson, 9, Lilly, 2, 8, MSD, 9, Novartis, 2, 8, 9, Pfizer, 2, 8, 9, UCB, 8, 9; **M. Rossini**, Abiogen, 5, Biogen, 5, Eli Lilly, 5, 8, Novartis, 5, UCB, 5; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **C. Sapin**, Eli Lilly and Company, 3, 4; **G. Meszaros**, Eli Lilly and Company, 3, 4; **J. Merola**, AbbVie, 2, 5, 8, Aclaris, 2, 5, Almirall, 2, 5, Amgen, 5, Biogen, 2, 5, Biogen Idec, 2, 5, Biogen IDEC, 5, Brigham and Women's Hospital, Harvard, 3, Burrage Capital Management Boston Advisory Board, 6, Celgene, 2, 5, Dermavant, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 5, GlaxoSmithKline, 5, GSK, 2, 5, Incyte, 2, 5, Janssen, 2, 5, Leo Pharma, 2, 5, Lilly, 5, Merck, 5, Merck Research Laboratories, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Regeneron, 5, Samumed, 2, 5, Sanofi, 5, Sanofi Regeneron, 2, 5, Science 37, 5, Sun Pharma, 2, 5, UCB, 2, 5.

Abstract Number: 0837

Does Discordance Between Baseline Patient's and Evaluator's Global Assessment of Disease Activity Impact Retention and Remission Rates of a First TNF Inhibitor in Patients with Axial Spondyloarthritis? Data from the EuroSpA Research Collaboration Network

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes I: Patient Reported Outcomes

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Discordance between baseline patient's and evaluator's global assessment of disease activity is common.[1] However, the impact of such discordance on retention and remission rates of TNF inhibitor (TNFi) therapy in axial spondyloarthritis (axSpA) patients remains unexplored. Hence, the aim of this study was to assess the impact of baseline discordance, defined as "patient's minus evaluator's global assessment of disease activity" (ΔPEG), on retention and remission rates of a first TNFi in axSpA patients across Europe.

TNFi retention rates	Retention rates (%, 95%CI) across different baseline patient's minus evaluator's global assessment (ΔPEG) quartiles									
	Women (n=3639)					Men (n=5374				
	1st quartile (-100 to 2) (n=908)	2nd quartile (3 to 20) (n=915)	3rd quartile (21 to 42) (n=907)	4th quartile (43 to 100) (n=909)	p value	1st quartile (-100 to -1) (n=1220)	2nd quartile (0 to 15) (n=1487)	3rd quartile (16 to 37) (n=1338)	4th quartile (38 to 100) (n=1329)	p value
6 months	88% (86-90%)	84% (82-87%)	78% (75-81%)	76% (73-79%)	<0.001	94% (92-95%)	91% (89-92%)	89% (88-91%)	87% (85-89%)	<0.001
12 months	81% (78-84%)	74% (71-77%)	67% (64-70%)	64% (61-68%)	<0.001	88% (86-90%)	86% (84-88%)	83% (81-85%)	79% (77-82%)	<0.001
24 months	75% (72-78%)	64% (61-67%)	60% (57-64%)	55% (52-59%)	<0.001	83% (81-86%)	80% (77-82%)	75% (72-77%)	72% (69-75%)	<0.001
ASDAS<1.3	Proportions, % (95%CI), of patients achieving ASDAS<1.3 at follow-up compared across different baseline ΔPEG quartiles									
	Women					Men				
	1st quartile (-100 to 2)	2nd quartile (3 to 20)	3rd quartile (21 to 42)	4th quartile (43 to 100)	p value	1st quartile (-100 to -1)	2nd quartile (0 to 15)	3rd quartile (16 to 37)	4th quartile (38 to 100)	p value
6 months	28% (23-33%)	24% (19-28%)	23% (18-27%)	17% (14-21%)	0.005	40% (36-45%)	41% (36-45%)	34% (30-38%)	31% (27-35%)	<0.001
12 months	27% (22-33%)	23% (18-29%)	23% (18-29%)	15% (12-19%)	0.002	41% (37-46%)	41% (37-46%)	33% (28-37%)	31% (27-35%)	<0.001
24 months	29% (23-35%)	24% (18-30%)	27% (21-33%)	16% (11-20%)	0.002	45% (40-50%)	41% (36-45%)	39% (33- 44%)	31% (27-35%)	<0.001
BASDAI≤2	Proportions, % (95%CI), of patients achieving BASDAI≤2 at follow-up compared across different baseline ΔPEG quartiles									
	Women					Men				
	1st quartile (-100 to 2)	2nd quartile (3 to 20)	3rd quartile (21 to 42)	4th quartile (43 to 100)	p value	1st quartile (-100 to -1)	2nd quartile (0 to 15)	3rd quartile (16 to 37)	4th quartile (38 to 100)	p value
6 months	45% (40-49%)	32% (28-36%)	28% (24-32%)	26% (23-30%)	<0.001	60% (56-63%)	51% (48-54%)	46% (42-49%)	42% (38-45%)	<0.001
12 months	47% (42-51%)	34% (30-38%)	30% (26-35%)	26% (23-30%)	<0.001	61% (57-64%)	53% (50-56%)	45% (41-48%)	43% (40-47%)	<0.001
24 months	49% (44-54%)	35% (31-40%)	31% (27-36%)	22% (18-26%)	<0.001	62% (58-66%)	56% (52-59%)	46% (42-50%)	42% (38-46%)	<0.001

Table. Retention and remission rates of first TNFi in axSpA patients.

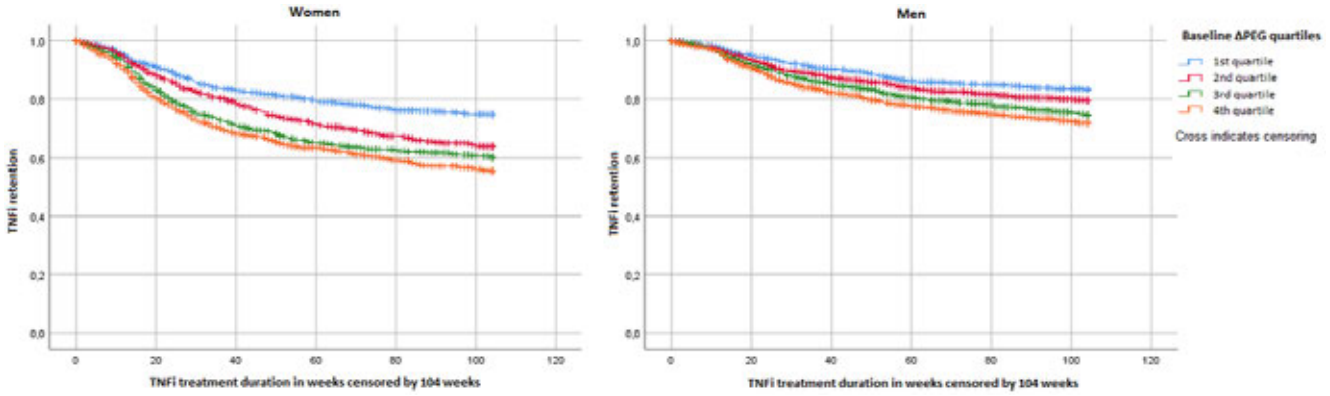

Figure. TNFi retention rate across ΔPEG quartiles, censored by 104 weeks.

Methods: AxSpA patients from 10 European registries participating in the European Spondyloarthritis Research Collaboration Network (EuroSpA) were included. Retention rates after 6/12/24 months' treatment with first TNFi were assessed with Kaplan-Meier analyses, with comparison between baseline ΔPEG quartiles with log rank test, stratified by gender. Proportions of patients in BASDAI remission (≤2) and ASDAS inactive disease (< 1.3) after 6/12/24 months for different ΔPEG quartiles were compared with Chi-square test, stratified by gender.

Results: A total of 9013 axSpA patients were included. Mean (SD) age for women (n=3639)/men (n=5374) were 42.7(12.0)/41.7(12.0) years, disease duration 5.1(7.4)/6.9(8.7) years, median (25-75 percentiles) baseline ΔPEG 20(3-42)/15(0-37) mm. TNFi retention rates and proportions of patients achieving BASDAI≤2 and ASDAS< 1.3 after 6/12/24 months were lower for higher quartiles of ΔPEG (table, figure).

Conclusion: In patients receiving their first TNFi, high baseline patient's compared with evaluator's global assessment is negatively associated with retention rates as well as proportions of patients achieving BASDAI remission and ASDAS inactive disease after 6, 12 as well as 24 months follow-up, both in female and male axSpA patients. TNFi retention rates were lower for women than for men at all timepoints.

Disclosure: B. Michelsen, Novartis, 2, 5; **L. Midtbøll Ørnbjerg**, Novartis, 2; **A. Loft**, None; **T. Kvien**, AbbVie, 2, 8, Biogen, 5, 8, Biogen, Egis, Eli Lilly, Hikma, Mylan, Novartis/Sandoz, Oktal, Hospira/Pfizer, Sanofi and UCB, 5, BMS, 8, Celltrion, 8, Egis, 5, 8, Eli Lilly, 5, 8, Hikma, 5, 8, Hospira/Pfizer, 2, 5, 8, MSD, 2, 8, Mylan, 5, 8, Novartis, 8, Novartis/Sandoz, 5, 8, Oktal, 5, 8, Orion Pharma, 8, Roche, 2, 8, Sandoz, 8, Sanofi, 5, 8, UCB, 5, 8; **A. Ciurea**, AbbVie, 5, Celgene, 5, Eli Lilly, 5, Janssen-Cilag, 5, MSD, 5, Novartis, 5, Pfizer, 5, UCB, 5; **H. Mann**, None; **K. Eklund**, None; **A. Yazici**, None; **M. Santos**, AbbVie, 8, Biogen, 8, Novartis, 8, Pfizer, 8, Roche, 8; **J. Askling**, AbbVie, 2, BMS, 2, Lilly, 2, MSD, 2, Pfizer, 2, Roche, 2, Samsung Bioepis, 2, UCB, 2; **Z. Rotar**, AbbVie, 9, Amgen, 5, 8, Eli-Lilly, 9, MSD, 5, Novartis, 9, Pfizer, 9, Sanofi, 5; **B. Gudbjornsson**, Actavis, 8, Amgen, 8, Novartis, 8, Pfizer, 8; **M. Pombo-Suarez**, None; **C. Codreanu**, AbbVie, 5, 8, Egis, 5, 8, Eli-Lilly, 5, 8, Ewopharma, 5, 8, Mylan, 5, 8, Novartis/Sandoz, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8; **I. van der Horst-Bruinsma**, AbbVie, 2, 5, 8, Bristol Myers-Squibb, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB Pharma, 2, 5, 8; **E. Kristianslund**, None; **M. Nissen**, Abbvie, Celgene, Lilly, MSD, Novartis, Pfizer, 5, 8; **K. Pavelka**, AbbVie, 8, Abbvie, 5, 8, Amgen, 5, 8, BMS, 8, Egis, 5, 8, Lilly, 5, 8, MSD, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 8; **N. Trokovic**, None; **N. Inanc**, None; **E. Vieira-Sousa**, None; **D. DiGuiseppe**, None; **M. Tomsic**, None; **A. Geirsson**, None; **R. IONESCU**, Abbvie, 5, 8, Amgen, 5, 8, Alpha Sigma, 5, 8, BMS, 5, 8, Ewopharma, 5, 8, Lilly, 5, 8, Mylan, 5, 8, Novartis, 5, 8, MSD, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Roche, 5, 8, Sandoz, 5, 8; **M. van de Sande**, None; **F. Iannone**, AbbVie, 5, 8, BMS, 5, 8, Janssen, 5, 8, lilly, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **C. Sánchez-Piedra**, None; **G. Jones**, Celgene, 2; **L. Hyldstrup**, Novartis, 2; **M. Lund Hetland**, Abbvie, 2, AbbVie, 2, Biogen, 2, BMS, 2, CellTrion, 2, 9, MSD, 2, Novartis, 2, Orion, 2, Pfizer, 2, Samsung, 2, UCB, 2; **M. Østergaard**, AbbVie, 2, 8, 9, Abbvie, 2, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, UCB, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, 5, 8, Abbvie, Celgene, Centocor, Merck, and Novartis, 2, Abbvie, Celgene, Centocor, Merck, Novartis, 2, BMS, 2, 5, 8, 9, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8.

Abstract Number: 0838

Are PROMIS Measures Associated with Minimal Disease Activity in Psoriatic Arthritis?

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes I: Patient Reported Outcomes

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Patient-reported outcomes (PROs) are an important part of clinical decision making and are frequently used in combination with objective measures of disease activity and physicians' clinical assessment to help guide treatment decisions. Discrepancies between PROs and clinical measures of disease activity can lead to over-treated or under-treated disease and patient dissatisfaction. We sought to examine the correlation between minimal disease activity (MDA) with PROs as measured by the NIH Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health (GH) questionnaire, and assess the effect of demographics, psoriatic arthritis related comorbidities, and number of comorbidities on PROMIS GH and MDA status.

Methods: A cross-sectional study was performed within Psoriatic Arthritis Research Consortium (PARC), a cohort of adult psoriatic arthritis patients meeting CASPAR criteria enrolled between 2016-2019. PARC is a longitudinal observational cohort study conducted at four institutions in the United States. The mean differences of PROMIS Physical, Mental and Fatigue T-scores between patients in MDA compared to those not in MDA were compared using the two sample t-tests. Correlations between MDA scores (0-7 criteria met) and PROMIS Physical, Mental and Fatigue T-scores were calculated using Spearman rank correlation. Higher T-scores on PROMIS measures mean 'more' of that concept for PROMIS Physical and Mental domains. Logistic regression model was used to evaluate contribution of additional covariates on MDA, including age, gender, hypertension, dyslipidemia, BMI, diabetes, smoking and number of comorbidities (Table 2). The odds ratios and 95% confidence intervals were presented. Multiple imputation was performed to impute missing data points. Data analysis was performed in SAS software (Version 9.4; Cary, NC).

		Non-remission (N=106)		Remission (N=129)		
Factor	Total (N=235)	N	Statistics	N	Statistics	p-value
PROMIS Physical Tscore	43.7 ± 9.0	106	38.2 ± 7.0	129	48.1 ± 8.0	*<0.001*[a]
PROMIS Mental Tscore	47.4 ± 10.5	106	42.7 ± 10.1	129	51.2 ± 9.3	*<0.001*[a]
PROMIS Fatigue Tscore	55.3 ± 10.3	105	59.8 ± 8.6	123	51.4 ± 10.1	*<0.001*[a]

Statistics presented as Mean± SD.
p-values: a=t-test.

Table 1. Comparison of PROMIS domains between MDA and non-MDA patients

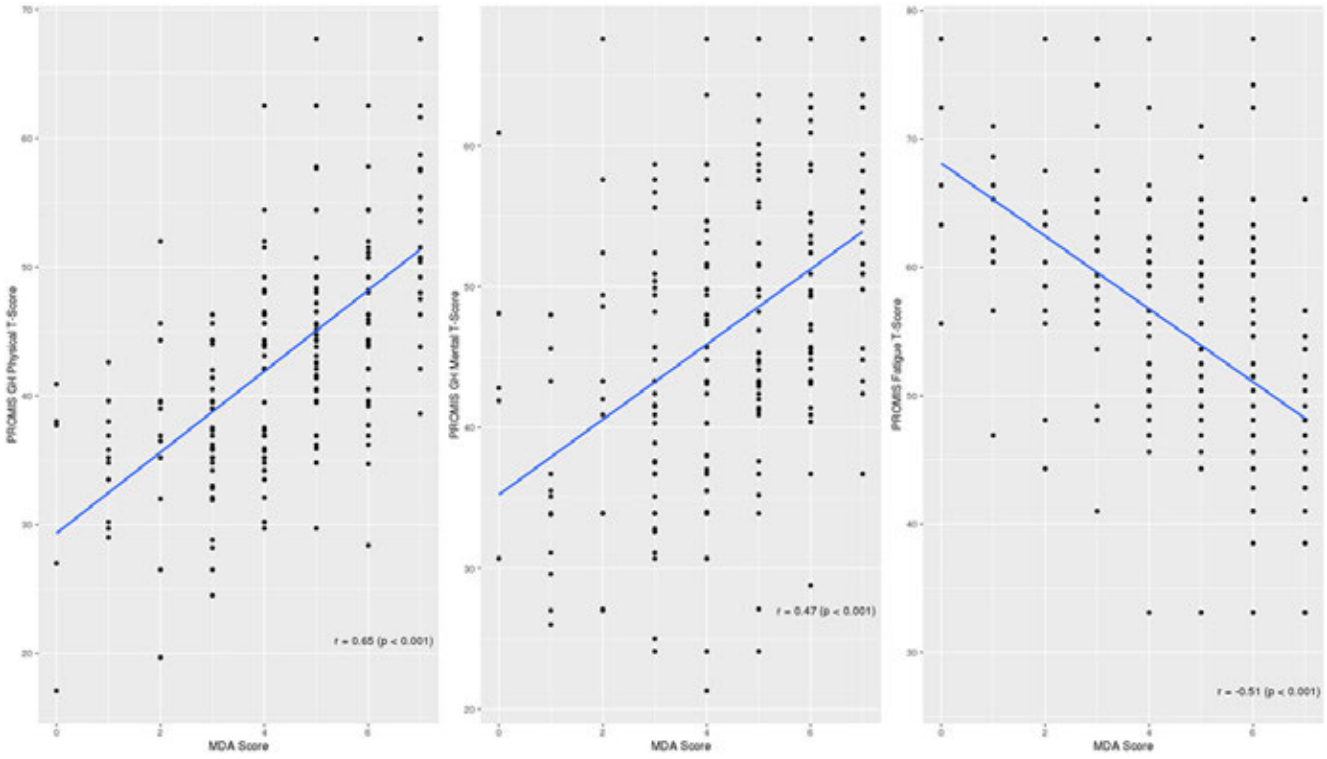

Figure 1. Scatterplot of MDA and PROMIS Physical, Mental and Fatigue Domains

Results: 235 patients (50% female, mean age 51±13.9) were included. 129 were in MDA and 106 were not in MDA. Patients in MDA had significantly higher PROMIS Physical, Mental and improved Fatigue T-scores compared to non-MDA patients (Table 1; $p< 0.001$). There was a positive correlation between MDA scores and PROMIS scores in Physical and Mental domains; correlation was strongest for PROMIS Physical T-score (Figure 1; $r=0.65$, $p< 0.001$). There was a moderate correlation between MDA and PROMIS Fatigue T-score (Figure 1; $r=-0.51$, $p< 0.001$). In the univariate analysis, there was a statistically significant association between hypertension and number of comorbidities with MDA status (Table 2). However, this effect was not observed in the multivariate analysis.

Conclusion: Achieving MDA was associated with a positive effect on patients' physical, mental and fatigue domains, irrespective of their demographics or PsA comorbidities. However, patients with a greater number of comorbidities were less likely to be in MDA. In this study, the PROMIS Physical domain had a higher correlation with MDA scores compared to the Mental domain and PROMIS Fatigue. PROMIS measures may be a useful tool in assessing disease activity from the patient's perspective.

Acknowledgement: Funded by NIH/NIAMS R01 AR072363

Factor	Total (N=235)	Non-remission (N=106)		Remission (N=129)		p-value
		n	Statistics	n	Statistics	
Age	50.8±13.9	106	51.4±13.0	129	50.3±14.6	0.54[a]
BMI	29.6±6.8	96	30.1±7.2	118	29.3±6.5	0.36[a]
Gender		102		129		0.12[c]
. Male	113(48.9)		44(43.1)		69(53.5)	
. Female	118(51.1)		58(56.9)		60(46.5)	
HTN		101		125		***0.008***[c]
. No	212(93.8)		90(89.1)		122(97.6)	
. Yes	14(6.2)		11(10.9)		3(2.4)	
Dyslipidemia		101		125		0.49[c]
. No	213(94.2)		94(93.1)		119(95.2)	
. Yes	13(5.8)		7(6.9)		6(4.8)	
DM		101		125		0.25[d]
. No	219(96.9)		96(95.0)		123(98.4)	
. Yes	7(3.1)		5(5.0)		2(1.6)	
Smoking		77		109		0.91[c]
. Never	75(40.3)		31(40.3)		44(40.4)	
. Yes	22(11.8)		10(13.0)		12(11.0)	
. No	89(47.8)		36(46.8)		53(48.6)	
Other comorbidities		101		125		***0.028***[c]
. 0	165(73.0)		65(64.4)		100(80.0)	
. 1-3	37(16.4)		21(20.8)		16(12.8)	
. >3	24(10.6)		15(14.9)		9(7.2)	

Statistics presented as Mean ± SD, N (column %).
p-values: a=ANOVA, c=Pearson's chi-square test, d=Fisher's Exact test.

Table 2. Univariate association between MDA and different covariates

Disclosure: J. Yedimenko, None; **Y. Jin**, None; **A. Ogdie**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Takeda, 5, Amgen, 2, 4, 5, 8, Amgen to Forward National Databank, 2, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 4, 5, 8, Corrona, 5, CORRONA, 5, From Noavrtis to husband, 7, Lilly, 5, Lily, 5, Novartis, 2, 5, 7, Novartis to UPenn, 2, Novartis, Pfizer, 2, Pfizer, 2, 5, Pfizer Inc, 2, 5, Pfizer to UPenn, 2; **J. Walsh**, AbbVie, 2, 5, ABBVIE, NOVARTIS, LILLY, AMGEN, UCB, 5, Amgen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, PFIZER, ABBVIE, 2, UCB, 5; **J. Scher**, Amgen, 5, Bristol-Myers Squibb, 5, Janssen, 5, Novartis, 2, 5, Pfizer, 2, UCB, 5; **S. Reddy**, Novartis, 5, Pfizer, 8, UCB, Amgen, 5, Abbvie, 5; **M. Husni**, Abbvie, 5, AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, Regeneron, Sanofi-Genzyme, UCB, 5, Abbvie, Amgen, Janssen, Novartis, Lilly, Regeneron, Pfizer and UCB, 5, Bristol-Myers Squibb, 5, Eli Lilly, 5, Genentech, 5, Janssen, 5, Janssen Research & Development, LLC, 2, 3, Novartis, 5, PASE questionnaires, 7, Pfizer, 5, Sanofi-Genzyme, 5, UCB, 5.

Abstract Number: 0839

Disease Activity, Cytokine Profiles, and the Risk of Incident Diabetes in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes I: Pulmonary & Other Comorbidities

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Rheumatoid arthritis is associated with a higher risk of diabetes mellitus (DM) and cardiovascular disease. While disproportional obesity and visceral fat accumulation may contribute to a higher incidence of DM, the systemic inflammatory disease may directly lead to insulin resistance and promote the development of cardiometabolic disease. Our aim was to evaluate associations between disease activity (including evaluation of specific cytokines and chemokines) among veterans with RA and determine independent associations with incident DM incidence in a longitudinal cohort.

Methods: Participants were enrollees in a multicenter, longitudinal observational cohort of US veterans with RA. Baseline demographics, comorbidities, body mass index (BMI), ACPA status, disease activity (DAS28-CRP), and active therapies were derived from query of the electronic medical record and registry data. Therapies and disease activity were assessed as time-varying covariates in initial models. Seventeen cytokines and chemokines were measured in banked serum obtained at the time of enrollment in a subset of partiipants using a bead-based multiplex

	Incident Diabetes N=1,918 P-Y=9,055 years Events: 239	
	HR (95% CI)	P value
Age (per 1 yr)	1.03 (1.02, 1.03)	<0.001
Female	0.58 (0.42, 0.80)	0.001
White	0.68 (0.5, 0.83)	<0.001
Current Smoking	0.96 (0.75, 1.26)	0.78
BMI Category		
<20 kg/m^2	0.72 (0.30, 1.83)	0.52
20-25 kg/m^2	Reference	–
25-30 kg/m^2	0.98 (0.62, 1.54)	0.93
30-35 kg/m^2	1.69 (1.26, 2.25)	<0.001
>35 kg/m^2	2.09 (1.16, 3.76)	0.02
DAS28(CRP)		
Remission	Reference	–
Low	1.14 (0.80, 1.62)	0.48
Moderate	1.18 (0.93, 1.49)	0.18
High	1.69 (1.23, 2.32)	0.001
ACPA Positive	0.91 (0.75, 1.11)	0.25
Methotrexate	0.92 (0.72, 1.17)	0.50
TNFi	0.60 (0.522, 0.69)	<0.001
Prednisone	0.94 (0.70, 1.26)	0.69
Hydroxychloroquine	0.82 (0.67, 1.00)	0.053

Table 1. Association between clinical factors and the risk of incident diabetes. Disease activity and medications evaluated as time-varying covariates.

	Incident Diabetes N=1,314 P-Y=8,189 Events: 235	
MIP-1β	HR (95% CI)	p
1	1 (reference	
2	0.88 (0.48, 1.60)	0.68
3	1.35 (0.96 ,1.90)	0.08
4	1.55 (0.94, 2.55)	0.09
	Test for trend	(0.001)
Interleulkin-8		
1	1 (reference)	–
2	1.41 (0.95, 2.08)	0.09
3	1.59 (1.19, 2.12)	0.002
4	1.66 (1.16, 2.40)	0.006
	Test for trend	(0.006)
Adjusted for age, sex, white race, smoking, baseline BMI, and baseline use of methotrexate, TNFi, and prednisone.		

Table 2. Cox proportional hazards models assessing associations between quartile of MIP-1β and IL-8 and incident diabetes (2 separate models).

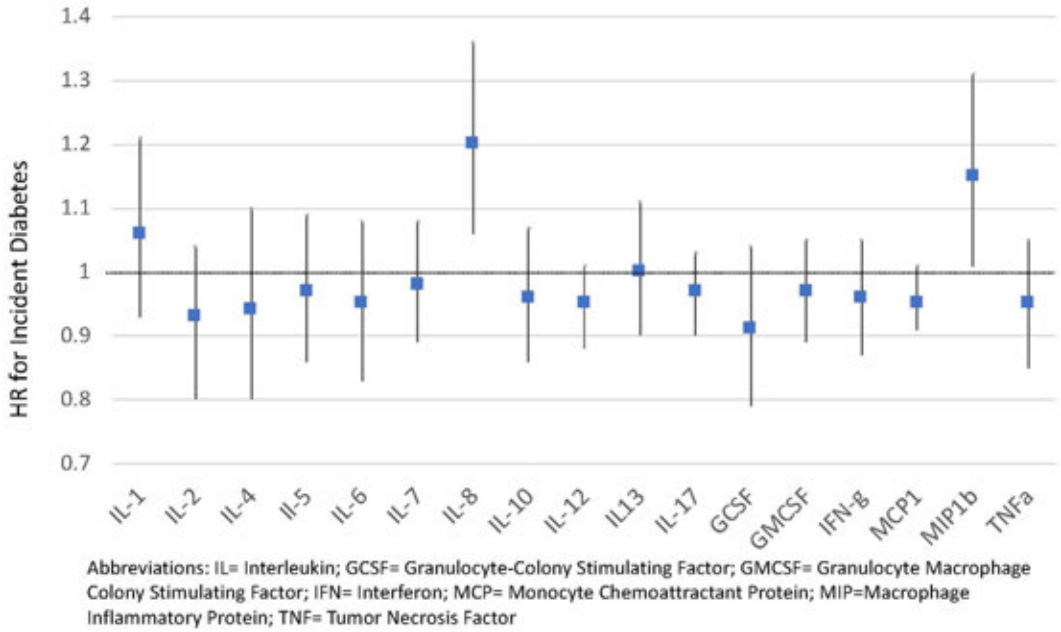

Figure. Hazard ratios for the risk of incident diabetes among rheumatoid arthritis patients by individual cytokine concentrations (per 1 SD) adjusting for age, sex, race, current smoking, baseline body mass index, and baseline medication use (each represents a separate model).

assay. Cytokine/chemokine values were log-adjusted and standardized (all values are per 1 SD). Incident DM was defined as the presence of a new diagnosis code at any time in follow-up (following at least 12 months of follow up without a code). Multivariable Cox proportional hazards models evaluated associations between clinical factors and incident DM. Independent associations between specific cytokines and chemokines were assessed adjusting for age, sex, race, smoking, and medication use at baseline.

Results: Among 1,918 RA patients without prevalent DM, there were 239 cases of incident DM over 9,055 person-years of follow-up. Patients with high disease activity, obese BMI, older age, male sex, and non-white race were at the greatest risk for incident DM (Table 1). Those using TNFi were at significantly lower risk. In models adjusting for demographics, smoking, and baseline medication use, two chemokines evaluated were significantly associated with the incidence of DM (per 1 SD). These were Macrophage Inhibitory Protein (MIP)-1b [HR 1.20 (95% CI 1.04, 1.39) p=0.01] and Interleukin(IL)-8 [HR 1.16 (95% CI 1.02, 1.33) p=0.02] (Figure). Higher quartiles of MIP-1b and IL-8 were associated with incident DM in a dose-dependent manner (Table 2). These associations were not attenuated with adjustment for DAS28-CRP.

Conclusion: Older age, male sex, higher disease activity, greater BMI, and elevated levels of the chemokines MIP-1b and IL-8 are associated with incident DM in veterans with RA. Notably, levels of IL-1, TNF-a, and IL-6 were not significantly associated with incident DM in this population although TNFi use was predictive of future DM. Future study may help to determine if other targeted treatments in at-risk individuals could help to prevent the development of DM in patients with RA.

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Abstract Number: 0840

Trajectory of Multimorbidity in Rheumatoid Arthritis in a U.S. Commercial Insurance Claims Database from 2006-2015

Bryant England,[1] Punyasha Roul,[2] Fang Yu,[2] Harlan Sayles,[2] Kaleb Michaud,[2] Fenglong Xie,[3] Jeffrey Curtis,[4] and Ted Mikuls[5], [1]VA Nebraska-Western IA Health Care System & University of Nebraska Medical Center, Omaha, [2]University of Nebraska Medical Center, Omaha, NE, [3]University of Alabama at Birmingham, Birmingham, [4]University of Alabama at Birmingham, Birmingham, AL, [5]VA Nebraska-Western IA Health Care System & University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes I: Pulmonary & Other Comorbidities
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Multimorbidity, the presence of multiple chronic conditions, predisposes individuals to disability and premature mortality. RA is well known to be associated with select chronic conditions, but the timing of onset of multimorbidity and the rate of accruing additional conditions is not well established. We aimed to determine the trajectory of multimorbidity in RA compared to the general population.

Methods: We assembled RA cohorts within Truven MarketScan database from 1/2006-9/2015 using ≥2 ICD-9 codes for RA, a rheumatologist diagnosis, and DMARD use. Incident RA was identified using validated algorithms for claims data that required at least 12 months of observable time with medical and pharmacy coverage (observability) without RA diagnostic codes or DMARDs (Curtis et al. AC&R, 2018). RA subjects were matched 1:1 to non-RA subjects on age, sex, and calendar year. Chronic conditions were identified from observability to the end of follow-up (censoring at disenrollment or end of study period) using ICD-9 codes for 48 chronic conditions identified in systematic reviews of multimorbidity. Conditions occurring on or before the date fulfilling the RA algorithm (or equivalent date for non-RA) were considered prevalent. Multimorbidity was defined as having ≥2 chronic conditions (not including RA) and multimorbidity burden was defined by the number of conditions present. Cross-sectional prevalence and burden of

Table 1. Prevalence of chronic conditions in rheumatoid arthritis (RA) vs. non-RA subjects.

Condition	RA (n=139402) N (%)	Non-RA (n=139402) N (%)	Odds Ratio (95% CI)*
Most prevalent conditions in RA subjects*			
Hypertension	27376 (19.6)	20438 (14.7)	1.51 (1.48, 1.54)
Chronic back pain	20140 (14.5)	10266 (7.4)	2.24 (2.18, 2.30)
Osteoarthritis	19281 (13.8)	4754 (3.4)	5.17 (4.98, 5.36)
Non-inflammatory gynecologic disorders***	12954 (12.2)	11349 (10.6)	1.17 (1.13, 1.20)
Hyperlipidemia	15100 (10.8)	12183 (8.7)	1.30 (1.27, 1.34)
Diabetes, uncomplicated	10085 (7.2)	8268 (5.9)	1.25 (1.21, 1.29)
Hypothyroid	7305 (5.2)	4213 (3.0)	1.81 (1.74, 1.88)
Fibromyalgia	6595 (4.7)	1219 (0.9)	5.90 (5.53, 6.29)
Anemia	6154 (4.4)	2513 (1.8)	2.56 (2.44, 2.69)
Gastroesophageal reflux disease	5731 (4.1)	3058 (2.2)	1.94 (1.86, 2.03)

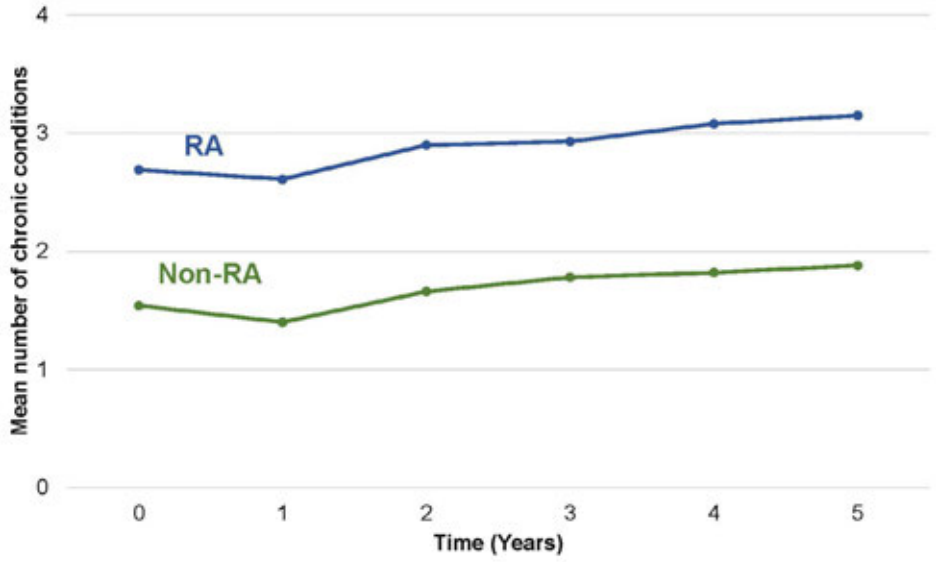
*Conditional odds ratios accounting for matching on age, sex, calendar year
**Ten most prevalent conditions in RA subjects are shown
***Among females only

multimorbidity in all RA vs. non-RA was determined using conditional logistic and negative binomial regression. The trajectory of multimorbidity over time in incident RA vs. non-RA was assessed using generalized estimating equations with an interaction term between RA status and year of follow-up.

Results: A total of 139,403 RA subjects (overall cohort) were matched to 139,403 non-RA subjects. This included a subcohort of 30,764 incident RA subjects. Mean (SD) age was 54.1 (13.4) years with 76.5% female. Time from observability to index date was 1.2 (1.8) years in the overall group and 3.2 (1.9) years in the incident subcohort. In the overall cohort, multimorbidity was present in 34.2% of RA subjects vs. 21.3% of non-RA (OR 2.30, 95% CI 2.26-2.35, $p< 0.001$). Multimorbidity burden was significantly higher in RA vs. non-RA (ratio of conditions 1.67, 95% CI 1.65-1.69, $p< 0.001$). Of the 48 chronic conditions examined, 42 were overrepresented (Table 1). In the incident subcohort, multimorbidity frequency was higher in RA subjects throughout follow-up (OR 2.75, 95% CI 2.66-2.84). Similarly, multimorbidity burden was higher in incident RA than non-RA at baseline and throughout follow-up (Figure 1; ratio of conditions 1.76, 95% CI 1.73-1.79). The rate of accruing chronic conditions was not higher in incident RA than non-RA (ratio of accruing conditions per year 0.99, 95% CI 0.98-1.00, $p=0.06$).

Conclusion: In a large, national, commercial claims database, we found the odds of multimorbidity were 2.3-fold higher in RA compared to the general population. Trajectory analyses in those with new onset disease suggest the heightened risk of multimorbidity in RA occurs early in the disease course or may even precede RA onset.

Figure 1. Mean chronic conditions over time in incident rheumatoid arthritis (RA) vs. non-RA.



N RA	30764	24641	15669	9773	5734	3294
N Non-RA	30764	22419	13387	8481	5342	3201

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Abstract Number: 0841

Elevation of Anti-Citrullinated Protein Antibodies Prior to Rheumatoid Arthritis Onset and Risks for Developing Chronic Obstructive Pulmonary Disease or Asthma

Alessandra Zaccardelli,[1] Xinyi Liu,[1] Julia Ford,[1] Jing Cui,[1] Bing Lu,[1] Su H. Chu,[2] Peter Schur,[1] Cameron Speyer,[1] Karen Costenbader,[1] William Robinson,[3] Jeremy Sokolove,[4] Elizabeth Karlson,[1] Carlos Camargo,[5] and Jeffrey Sparks[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [3]Stanford University, Stanford, CA, [4]AbbVie Immunology Clinical Development, Redwood City, [5]Massachusetts General Hospital, Boston, MA

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes I: Pulmonary & Other Comorbidities

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Elevation of anti-citrullinated protein antibodies (ACPA) precedes clinical rheumatoid arthritis (RA) diagnosis by years and may originate at inflamed mucosa, including airways. Damage from chronic inflammation may pre-dispose individuals with ACPA elevation to developing obstructive airway diseases, such as chronic obstructive pulmonary disease (COPD) and asthma, prior to or after clinical RA onset. Therefore, we investigated the association between elevated ACPA in blood banked prior to clinical RA diagnosis and risks for developing COPD or asthma.

Methods: We performed a cohort study among women who donated blood for research purposes in the Nurses' Health Studies to investigate whether pre-RA elevated ACPA was associated with development of COPD or asthma. RA cases met 1987 ACR or 2010 ACR/EULAR criteria and were each matched to 3 controls by age and menopausal factors at date of RA diagnosis (index date). Pre-RA ACPA elevation among RA cases was defined as: elevation (>5 units/mL) on 2nd generation commercial assay for cyclic citrullinated peptide or elevation (>99th percentile of the control distribution) of autoantibodies to ≥2 different citrullinated proteins on a research assay measuring autoantibodies targeting specific citrullinated protein epitopes. Incident COPD or asthma occurring after date of blood draw was determined using biennial questionnaires. Covariates, including smoking pack-years, were assessed by questionnaires. Cox regression estimated HRs for incident COPD and asthma in separate analyses. In all analyses (**Figure**), the date of blood draw was the baseline, and RA cases (by pre-RA ACPA status) were compared to their matched controls, excluding prevalent respiratory disease at blood draw. We performed a secondary analysis restricting follow-up to time between blood draw and index date to investigate the pre-RA/index period.

Results: We measured ACPA on a total of 1,125 women (283 pre-RA cases and 842 matched controls). Blood was banked mean 9.7 years (SD 5.8) prior to index date and mean age at blood draw was 51.4 years (SD 7.9). There were 59 RA cases (20.8%) with elevated ACPA in pre-RA blood. Pre-RA ACPA+ RA was associated with incident COPD occurring after blood draw (multivariable HR 3.06, 95%CI 1.34, 7.00) compared to their matched controls (**Table 1**). Pre-RA ACPA+ RA had a HR for asthma of 1.76 (95%CI 0.72, 4.26), similar to the association of Pre-RA ACPA- RA with asthma (HR 1.64, 95%CI 1.04, 2.58) (**Table 2**). When restricting follow-up to the pre-RA/index period, pre-RA ACPA+ RA was strongly associated with increased COPD risk (HR 10.84, 95%CI 1.13, 104.08), but asthma had similar results to the primary analysis (all RA: HR 1.69, 95%CI 1.00-2.86).

Conclusion: Women with elevated ACPA before RA diagnosis had increased risk for developing COPD, particularly just before RA presentation, suggesting lung damage accrues prior to clinical RA onset. Women who were later diagnosed with RA were more likely to report new-onset asthma than matched controls, regardless of pre-RA ACPA

Table 1. Hazard ratios for incident chronic obstructive pulmonary disease occurring after blood draw date, comparing RA cases by pre-RA ACPA status to their matched controls among women in the Nurses' Health Studies who donated blood and had ACPA tested for research purposes (n=1,125).

	Incident COPD cases/person-years	HR (95%CI) adjusted for matching factors*	Multivariable** HR (95%CI)
All RA (n=283)	36/5,147	**1.61 (1.08, 2.40)**	1.39 (0.93, 3.10)
Matched controls (n=842)	71/16,342	1.00 (Ref)	1.00 (Ref)
Pre-RA ACPA+ RA (n=59)	13/1,030	**3.02 (1.42, 6.43)**	**3.06 (1.34, 7.00)**
Matched controls (n=176)	14/3,375	1.00 (Ref)	1.00 (Ref)
Pre-RA ACPA- RA (n=224)	23/4,117	1.27 (0.78, 2.06)	1.09 (0.66, 1.78)
Matched controls (n=666)	57/12,967	1.00 (Ref)	1.00 (Ref)

*Cases and controls were matched by age at index date, time from blood draw to index date, cohort, menopausal status, and postmenopausal hormone use.

**Additionally adjusted for smoking (continuous pack-years), body mass index (continuous, kg/m^2), median household income (quartile with missing indicator), and asthma (yes/no)

ACPA, anti-citrullinated protein antibodies; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; RA, rheumatoid arthritis.

Table 2. Hazard ratios for incident asthma after blood draw date, comparing RA cases by pre-RA ACPA status to their matched controls among women in the Nurses' Health Studies who donated blood and had ACPA tested for research purposes (n=951, excluding prevalent asthma at baseline).

	Incident asthma cases/person-years	HR (95%CI) adjusted for matching factors*	Multivariable** HR (95%CI)
All RA (n=252)	39/4,667	**1.72 (1.16, 2.56)**	**1.65 (1.11, 2.46)**
Matched controls (n=699)	66/13,698	1.00 (Ref)	1.00 (Ref)
Pre-RA ACPA+ RA (n=49)	8/890	1.71 (0.72, 4.07)	1.76 (0.72, 4.26)
Matched controls (n=136)	14/2,660	1.00 (Ref)	1.00 (Ref)
Pre-RA ACPA- RA (n=203)	31/3,777	**1.73 (1.11, 2.70)**	**1.64 (1.04, 2.58)**
Matched controls (n=563)	52/11,039	1.00 (Ref)	1.00 (Ref)

*Cases and controls were matched by age at index date, time from blood draw to index date, cohort, menopausal status, and postmenopausal hormone use.
**Additionally adjusted for smoking (continuous pack-years), body mass index (continuous, kg/m^2), median household income (quartile with missing indicator)

ACPA, anti-citrullinated protein antibodies; CI, confidence interval; HR, hazard ratio; RA, rheumatoid arthritis.

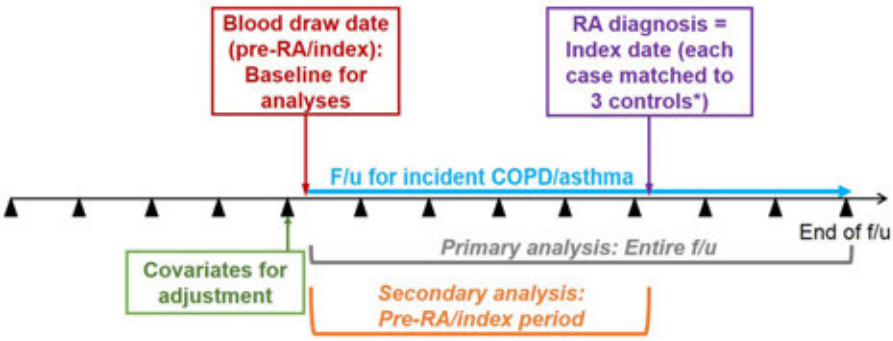

Figure. Study design for cohort study investigating pre-RA ACPA status and risk for incident chronic obstructive pulmonary disease or asthma. ACPA, anti-citrullinated protein antibodies; RA, rheumatoid arthritis.

status. These findings provide evidence for the hypothesis that chronic airway inflammation may contribute to both RA development and respiratory outcomes beyond the effect of smoking.

Disclosure: A. Zaccardelli, None; **X. Liu**, None; **J. Ford**, None; **J. Cui**, None; **B. Lu**, None; **S. Chu**, None; **P. Schur**, None; **C. Speyer**, None; **K. Costenbader**, Astra-Zeneca, 2, Glaxo Smith Kline, 2, Janssen Scientific Affairs, LLC, 2, Lupus Foundation of America, 2, Lupus Research Alliance, 2, Merck, 2; **W. Robinson**, None; **J. Sokolove**, AbbVie, 3, 4; **E. Karlson**, None; **C. Camargo**, None; **J. Sparks**, None.

Abstract Number: 0842

Mortality Ratio and Risk Factors in CT Confirmed Rheumatoid Arthritis Related Lung Disease: UIP, Pleural Effusion and the Time of Diagnosis of Rheumatoid Arthritis - Lung Disease

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes I: Pulmonary & Other Comorbidities

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: The frequency of pulmonary involvement in rheumatoid arthritis varies between 7-35%. The most important cause of death in RA patients is lung disease in UIP pattern. The aim of this study was to determine the mortality and associated factors in RA- related lung disease (RA-LD) patients followed up in a single tertiary center.

Table 1. Demographic,clinical characteristics and computed tomography findings of patients

	Death (+) (n=40)	Death (-) (n=116)	P	Multivariate
Sex (M/F)	23/27	35/81	0.78	1,18 (0,3-4,2)
Age at the diagnosis of RA ,years	61.4 (11,7)	53.5 (11,7)	<0.001	
Age at diagnosis of ILD ,years	66.0 (9.7)	61.6 (9.5)	0.014	
<3 years between RA and ILD diagnosis (%)	18/32(56,3)	26/101(25,7)	0.001	4.34 (1.27-14.8)
BMI (kg/m²)	26.4 (4)	28.5 (4,9)	0.03	
Smoking (ever) (%)	16/34 (47)	51/97 (52,5)	0.58	
RF + (%)	34/35 (97,1)	101/114 (88,5)	0.13	
RF titer ,IU/ml	1119 (1370)	471 (768)	0.01	
Anti-CCP + (%)	11/12 (91,6)	51/74 (68,9)	0.1	
Anti-CCP titer, ru/ml	335 (358)	273 (553)	0,7	
Anemia (%)	34/40 (%85)	80/116 (68,9)	0.1	0,6 (0,1-3,2)
Shortness of breath (%)	77	31	<0.001	
Crackles on physical examination (%)	92	51	<0.001	
Signs of ILD in lung x-ray (%)	96	70	0.005	
Pattern of lung involvement n (%)			<0.001	
UIP	35 (87)	54 (47)		10.33 (2.46-43.42)
NSIP	4 (10)	47 (41)		
AD	1 (3)	15 (12)		
Lung CT findings n (%)				
Ground glass appearance	35 (88)	84 (72)	0.053	
Bronchiectasis	36 (90)	60 (48)	<0.001	
Interseptal thickening	22 (55)	31(27)	0.001	
Reticular densities	38 (95)	89 (77)	0.01	
Honeycombing	32 (80)	42 (36)	<0.001	
Pleural effusion n (%)	9 (23)	9 (8)	0.02	14.4 (2.4-84.6)
Rheumatoid nodule n (%)	13 (33)	56 (49)	0.07	

Data was shown as mean (SD)

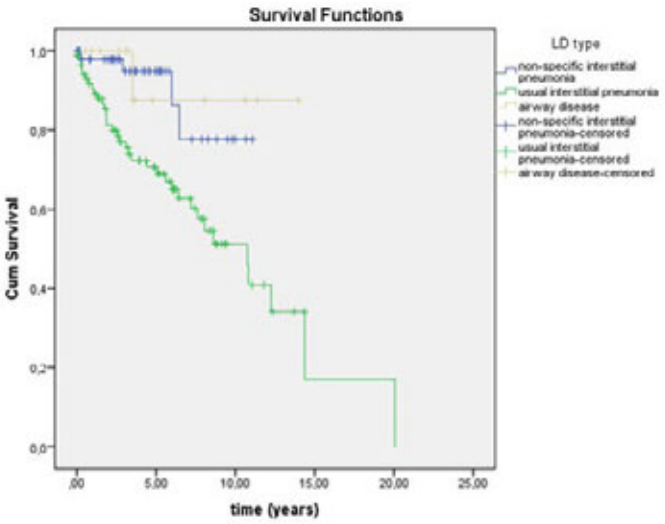

Figure 1. Kaplan-meier survival analysis of different RA-LD patterns

Methods: During January 2010 and March 2019, 826 RA patients had lung computerized tomography in Hacettepe University. Three radiologists re-evaluated lung CTs and 156/826 (18.8%) patients with RA-LD were included in the final analysis. Overall, 104 patients (%66.7) had at least one control lung CT. Lung CT findings were classified as UIP, NSIP and isolated airway disease (AD). Demographic, clinical, laboratory and therapeutic data was collected. Information on death of patients was obtained either by chart review of through the national death registration database. Factors related to mortality were analyzed with univariate and multivariate analysis; Kaplan-Meier plots were used for survival analysis.

Results: Totally, 156 patients (30.8% male) were included in the study. The mean (SD) follow-up duration was 129 (90) months for RA, and 53.8 (45) months for RA-ILD. Eighty-nine patients had UIP (57.0%), 51 (32.7%) had NSIP and 16 (10.2%) had AD pattern. 40/157 (25.6%) patients died during the follow-up period. The mean age of death was 70.7 years (10). The mean follow-up duration was 4.4 (4,4) years for the patient who had died, and 4.7 (3,5) years for the living patients. Presence of crackles was higher in the patients who died (34/37 [%92] vs 50/98 [51%], $p < 0.001$). Initial lung functions were similar (FVC: 85% (24.5) vs 82% (19), FEV1: 91% (22.4) vs 84% (20.5) however, patients who had died had lower lung volumes at last control visit (FVC: 57.1% (16.7) vs 91.0% (22.3), $p < 0.001$, FEV1: 61.0% (17.4) vs 87.0% (23.4), $p = 0.001$). Mortality was higher in patients with UIP (log-rank: 0.004) (figure 1). Among the treatments used, only the history of methotrexate and cyclophosphamide use were related with mortality (methotrexate 24 (60%) vs. 95 (81.9%) $p = 0.005$, steroid 39 (97.5%) vs 112 (96.6%) $p = 0.7$, leflunomide 29 (%) 72.5) vs 90 (77.6%) $p = 0.5$, sulfasalazine 18 (45%) vs 70 (60.3%) $p = 0.09$, hydroxychloroquine 30 (75%) vs 101 (87%, 1) $p = 0.07$, azathioprine 7 (17.5%) vs 10 (8.6%) $p = 0.14$, cyclophosphamide 10 (25%) vs 7 (6%) $p = 0.002$, pulse steroid 8 (20%) vs 3 (2.6%) $p = 0.001$, taking any biological treatment 16 (40%) vs 53 (45.7%) $p = 0.53$, Anti TNF 6 (15%) vs 32 (% 27.6) $p = 0.11$, abatacept 1 (2.5%) vs 11 (9.5%) $p=0.29$, rituximab 14 (35%) vs 24 (20.7%) $p=0.06$). Relationship between mortality and other parameters is shown in the table 1. UIP pattern, pleural effusion and the shorter time interval (< 3 years) between the diagnosis of RA and RA-LD were independent predictors of mortality in multivariate analysis (Table 1).

Conclusion: In our study, for RA-LD mortality, UIP pattern is usual suspected risk factor and pleural effusion, shorter time-interval between diagnosis RA and RA-LD are newly defined strong predictors. These risk factors may be used in the early risk stratification in the management of RA-LD routine practice.

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Abstract Number: 0843

High Lung Attenuation Measured with Quantitative Densitometry as a Surrogate Marker for Interstitial Lung Disease in RA: Association with Anti-CCP, Smoking, and Absence of Shared Epitope

Michail Alevizos,[1] Sonye Danoff,[2] Dimitrios Pappas,[1] David Lederer,[3] Cheilonda Johnson,[4] Elana Bernstein,[5] Joan Bathon,[5] and Jon Giles[5], [1]Division of Rheumatology, Columbia University, New York, [2]Division of Pulmonary & Critical Care Medicine, Johns Hopkins University, Baltimore, [3]Division of Pulmonary & Critical Care Medicine, Columbia University, New York, [4]Division of Pulmonary & Critical Care Medicine, University of Pennsylvania, Philadelphia, [5]Division of Rheumatology, Columbia University, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes I: Pulmonary & Other Comorbidities

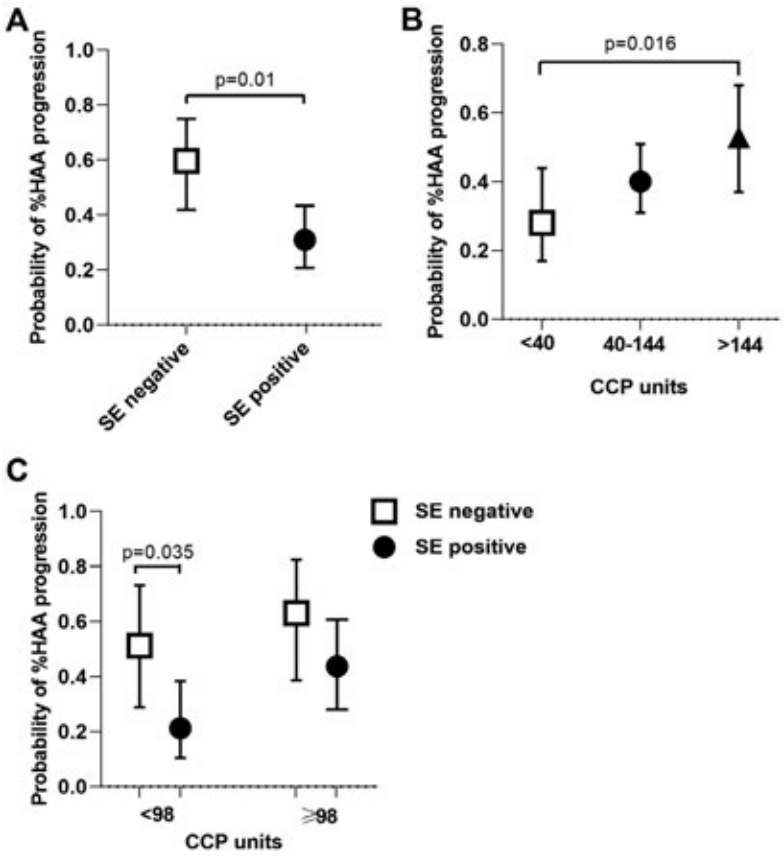
Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Risk factors for rheumatoid arthritis-associated interstitial lung disease (RA-ILD), a significant cause of morbidity and mortality, are poorly understood. RA-ILD detection is limited by the poor inter- and intra- observer variability on computed tomography (CT) scans, especially in early disease or when quantification of lung parenchyma involvement is attempted. Quantitative densitometry uses a computerized algorithm to measure the density of lung parenchyma, expressed as the proportion of the volume of high attenuation [percent high attenuation areas (%HAA)]. We sought to identify demographic and RA disease-specific risk factors for %HAA progression (increased by ≥ 10% from baseline %HAA).

Methods: RA patients enrolled in a prospective cohort study of cardiovascular disease underwent cardiac CT scans at baseline, pulmonary function testing and pulmonary symptom questionnaire at visit 2 (an average of 18 months post-baseline). A subset of patients underwent repeat cardiac CT scans at visit 3 (an average of 38 months post-baseline). Baseline scans were read by an expert pulmonary radiologist for ILD features. Baseline and V3 scans were assessed with quantitative densitometry, with %HAA calculated. Logistic regression was used to model the association of RA characteristics with strata of %HAA.

Results: A total of 193 patients had CT densitometry assessed at V1 [mean age=59 years; 61% female; median RA duration=8 years; %HAA=2.3-18.8 % of the lung parenchyma; 36% had evidence of ILD (predominantly mild) on expert read, 60% of whom were symptomatic]. Compared with subjects in the low %HAA stratum, subjects in the high %HAA stratum had a greater number of pack-years of smoking, a higher BMI, and a higher fibrosis score based on expert evaluation. A greater proportion were ever smokers, had shortness of breath on exertion on visit 2, a restrictive pattern on pulmonary function tests on visit 2, and a lower FVC on visit 2. After adjustment, higher BMI, anti-CCP ≥ 200 units, and a greater number of pack-years of smoking were each significantly associated with increased %HAA (≥10 % of the lung) at baseline visit, while male sex had a protective role against %HAA. For the subgroup of n=107 patients with repeat CT densitometry at V3, %HAA remained stable in 26%, decreased in 35%, and progressed in 39% of subjects. After adjustment, shared epitope was inversely associated with %HAA progression in the follow-up period (Figure A). Higher anti-CCP was significantly associated with %HAA progression in the follow-up period



(Figure B). The protective effect of shared epitope against HAA progression was statistically significant in patients in the low anti-CCP stratum (Figure C).

Conclusion: These prospective data provide evidence that anti-CCP, smoking, and absence of shared epitope are contributors to RA-ILD and could allow for early diagnosis and management of this serious complication of RA. Our findings on the negative effect of shared epitope are congruent with recently published data that have revealed strong association of a non-HLA gene (MUC5B promoter variant) with RA-ILD.

Adjusted means and 95% CIs depicted. Adjusted for pack-years of smoking, anti-CCP units, shared epitope, and baseline %HAA.

Disclosure: M. Alevizos, None; **S. Danoff**, None; **D. Pappas**, None; **D. Lederer**, None; **C. Johnson**, None; **E. Bernstein**, None; **J. Bathon**, None; **J. Giles**, Eli Lilly & Company, 5, Pfizer Inc, 2.

Abstract Number: 0844

Impact of Glucocorticoid Tapering on Markers of Bone Metabolism in Patients with Rheumatoid Arthritis Who Achieved Low Disease Activity or Remission on Tocilizumab: Exploratory Analysis from a Randomized Controlled Trial

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes I: Pulmonary & Other Comorbidities
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

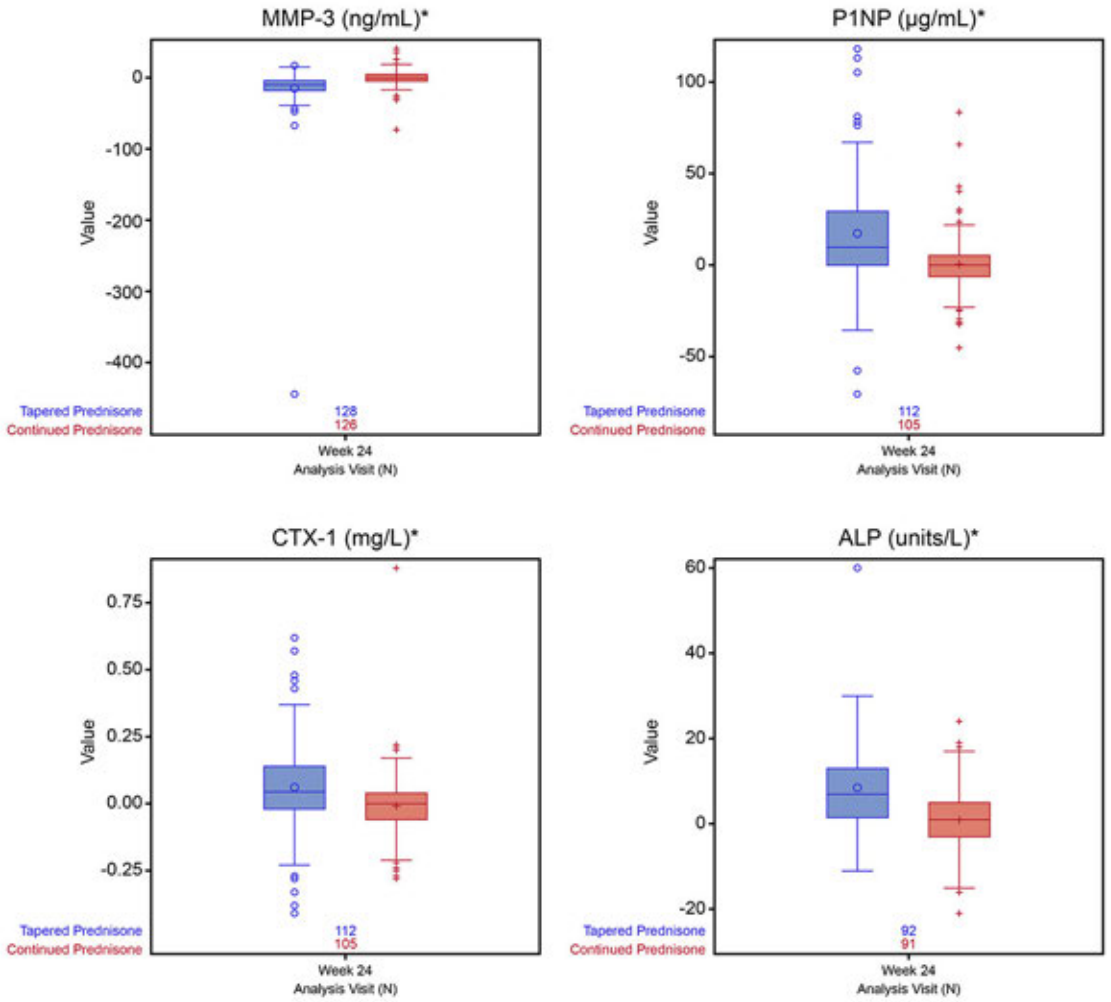
Background/Purpose: Glucocorticoids (GCs) directly impact bone metabolism via increased bone resorption and inhibited bone formation[1]; hence, systemic fracture risk increases with daily and cumulative GC doses.[2] However, many patients with established rheumatoid arthritis (RA) receive long-term treatment with GCs to suppress inflammation, which confers some benefit in delaying bone erosion.[3] This exploratory analysis of the SEMIRA (Steroid EliMination In RA) study[4] compared changes in markers of bone and cartilage metabolism in RA with low disease activity (LDA) or remission on tocilizumab (TCZ) + GC ± conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) who received either slow GC tapering (GC-taper) or continuation (5 mg; GC-5mg).

Methods: Patients (diagnosed per revised 1987 ACR criteria) had at least stable LDA (DAS28-ESR ≤3.2) for ≥4 weeks, were receiving a stable prednisone regimen (5 mg/day) + TCZ ± csDMARDs for ≥4 weeks, and received TCZ + GCs (prednisone equivalent 5-15 mg/day) for ≥6 months before randomization. Patients were randomly assigned to GC-5mg (n=128) or GC-taper (n=131; starting at 4 mg/day with 1-mg reduction every 4 weeks to 0 mg/day at weeks 16-24) for 24 weeks, during which TCZ ± csDMARDs remained stable. Change between baseline (BL) and week 24 in serum levels of markers of bone and cartilage metabolism—including N-terminal propeptide of type 1 collagen (P1NP), C-terminal telopeptide of type 1 collagen (CTX1), alkaline phosphatase (ALP), matrix metalloproteinase 3 (MMP3), calcium, phosphorus, and albumin—were exploratory outcomes. Within-group and between-group changes from baseline were evaluated by Wilcoxon paired rank test and Wilcoxon signed rank test, respectively.

Results: Figure 1 shows changes from BL to week 24 in bone and cartilage biomarkers. MMP3 (marker of cartilage degradation) was reduced at week 24 in the GC-taper group compared with GC-5mg. Change from BL at week 24 in P1NP (bone formation) and CTX1 (bone resorption) favored the GC-taper arm, with P1NP increasing relatively more than CTX1 (44% and 24%, respectively, compared with GC-5mg), indicating net anabolism. The increase in ALP from BL to week 24 was greater for the GC-taper arm than for the GC-5mg arm, suggesting neomineralization. There was no difference in the change from BL to week 24 in calcium, phosphorus, or albumin (not shown).

Conclusion: The findings of this biochemical marker analysis suggest that withdrawal from GC after achievement of LDA or remission with TCZ results in increased bone remodeling, with a trend toward an anabolic window and reduced cartilage degradation. Given that it could take a year to recover from increased fracture risk after cessation of GC therapy,[5] our results offer further insight on the reversible risk of systemic harm to noninflamed bone versus benefits for inflamed joints in the context of LDA or remission.

Figure 1. Box plots of change from baseline to week 24 in biomarkers of bone metabolism observed values



ALP, alkaline phosphatase; CTX-1, C-terminal telopeptide of type 1 collagen; MMP-3, matrix metalloproteinase 3; P1NP, N-terminal propeptide of type 1 collagen
*p<0.001 for tapered prednisone vs continued prednisone based on Wilcoxon signed rank test

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Abstract Number: 0845

Comparison of Rituximab-Associated Hypogammaglobulinemia Rates in Patients with Systemic Rheumatologic Conditions

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Treatments I: Safety and Outcomes
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Rituximab (RTX) is used in a wide variety of rheumatic disease. Emerging guidelines suggest measuring immunoglobulins (Ig) at pre-treatment screening and prior to repeat cycles of RTX. The association between hypogammaglobulinemia and infection post RTX has been evaluated in rheumatoid arthritis (RA) trials; however, there is limited data comparing total IgG levels across different diseases. We aim to compare the rate of hypogammaglobulinemia across RA, ANCA-associated vasculitis (AAV), and connective tissue disease (CTD) patients in a cohort at a tertiary university-based medical center. We hypothesized that baseline clinical and laboratory data will allow for risk prediction of hypogammaglobulinemia and infection rates in these patients.

Methods: Medical records of all RA, AAV, and CTD patients treated with RTX in an academic center from 2002 to 2019 were retrospectively reviewed. Baseline data at initiation of RTX, including clinical diagnosis, demographics, DMARD exposure, glucocorticoid (GC) dose, total serum IgG (normal range 0.7 to 1.6 g/dL) and disease activity were assessed. We defined GC exposure between the two Ig measurements, as an average daily prednisone dose: high (20mg or more), medium (11-19mg), or low (10mg or less). Analysis was performed using STATA. Group comparisons were done using chi square for categorical data and T-test for continuous variables.

Results: We screened 302 patients with rheumatologic conditions who were treated with RTX; of these, 165 patients received RTX for RA, AAV or a CTD. 58 of 165 patients had documented IgG levels pre and post treatment with RTX and 14/58 developed new onset hypogammaglobulinemia post RTX. Rates of hypogammaglobulinemia were significantly higher in AAV than in CTD patients (42.1% vs. 16.7%, p:0.014), despite similar cumulative exposure to RTX. The rate of hypogammaglobulinemia post RTX was trending higher in patients with AAV compared to RA (42.1% vs. 23.5%, p:0.24) despite AAV patients having lower cumulative exposure to RTX than RA patients (3.3+/-0.3g vs. 6.3+/-1.9g, p=0.1). GC exposure was greater in GPA versus RA ($p< 0.001$) and CTD (p=0.003) patients. Both RA and CTD patients were more likely to have prior exposure to conventional DMARD (cDMARD) versus AAV patients (p=0.005). RA patients had a higher likelihood of prior exposure to biologics versus AAV patients ($p< 0.001$). GPA patients were younger than CTD and RA groups. There was no observed difference in the infection rate among the groups.

Conclusion: AAV patients were more likely to develop hypogammaglobulinemia than RA and CTD patients. We identified high GC exposure as a potential risk factor for hypogammaglobulinemia. Age, cDMARD, and biologic exposure were not associated with increased risk of hypogammaglobulinemia. Reassuringly, infection rate was not increased in the AAV group, potentially reflecting use of prophylactic antibiotics. Limitations include low utilization of quantitative IgG measurements with repeat cycles of RTX in our center. Additional multicenter studies are needed to determine the true risk of low total IgG levels on rates of clinically significant infections, particularly in patients with AAV and high cumulative GC dose.

Disclosure: S. Wade, None; **V. Kyttaris**, exagen diagnostics, 2, Exagen Diagnostics, 2, GSK, 5, gsk, 5, horizon pharma, 5, Horizon Pharma, 5.

Abstract Number: 0846

MACE and VTE Across Multiple Upadacitinib Studies in Rheumatoid Arthritis: Integrated Analysis from the SELECT Phase 3 Clinical Program

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SESSION INFORMATION

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Session Title: RA – Treatments I: Safety and Outcomes

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Patients (pts) with RA have an approximate 2-fold increased risk of cardiovascular (CV) morbidity and mortality and of venous thromboembolic events (VTE)[1,2]. Among RA pts, the rates of major adverse CV events (MACE) and VTE were 0.3 – 0.7 incidences per 100 patient-years (PY)[3] and 0.3 – 0.8 events per 100 PY[4], respectively. Treatment of RA with Janus Kinase (JAK) inhibitors is known to increase lipid levels[5] along with mild, variable impacts on platelet counts[5,6], however these changes have not been linked to a CV[7] or VTE[8] risk, respectively.

Assess the rates of MACE and VTE from the integrated safety database of the Phase 3 clinical program of Upadacitinib (UPA), an oral, potent, reversible, JAK1-selective inhibitor, in pts with moderately to severely active RA.

Table. Adjudicated MACE and VTEs in patients treated with UPA, PBO and active controls

				UPA All Phase 3 Long-term	
	PBO Pooled N=1042, PYS=256.8, E/100 PY (95% CI)	MTX, Pooled[a] N=530, PYS=368.7, E/100PY (95% CI)	ADA 40 mg EOW N=579, PYS=467.8, E/100PY (95% CI)	UPA 15 mg QD N=2630, PYS=2655.1 E/100PY (95% CI)	UPA 30 mg QD N=1204, PYS=1365.0 E/100PY (95% CI)
Any MACE (adjudicated)	1.2 (0.2, 3.4)	0.5 (0.1, 2.0)	0.4 (0.1, 1.5)	0.6 (0.4, 1.0)	1.0 (0.5, 1.6)
CV death[b]	0.4 (0, 2.2)	0.3 (0.0, 1.5)	0.2 (0.0, 1.2)	0.3 (0.1, 0.5)	0.4 (0.1, 0.9)
Non-fatal MI	0.8 (0.1, 2.8)	0 (0.0, 1.0)	0 (0.0, 0.8)	0.2 (0.1, 0.5)	0.4 (0.1, 0.9)
Non-fatal stroke	0.0 (0, 1.4)	0.3 (0.0, 1.5)	0.2 (0.0, 1.2)	0.2 (0.0, 0.4)	0.2 (0.0, 0.6)
Any VTE (adjudicated)	0.4 (0.0, 2.2)	0.5 (0.1, 2.0)	1.1 (0.3, 2.5)	0.6 (0.3, 1.0)	0.3 (0.1, 0.8)
Deep Vein Thrombosis (DVT) alone	0.0 (0.0, 1.4)	0.3 (0.0, 1.5)	0.2 (0.0, 1.2)	0.3 (0.1, 0.6)	0.2 (0.0, 0.6)
Pulmonary Embolism (PE) alone	0.4 (0.0, 2.2)	0.5 (0.1, 2.0)	0.9 (0.2, 2.2)	0.5 (0.2, 0.8)[c]	0.1 (0.0, 0.5)
DVT and PE (Concurrent)	0.0 (0.0, 1.4)	0.3 (0.0 1.5)	0 (0.0, 0.8)	0.2 (0.0, 0.4)	<0.1 (0.0, 0.4)
Deaths due to DVT/PE	0.0 (0.0, 1.4)	0 (0.0, 1.0)	0 (0.0, 0.8)	<0.1 (0.0, 0.2)[c]	0 (0.0, 0.3)

[a]Includes patients on MTX monotherapy censored at time of rescue to combination therapy (either to UPA + MTX or addition of csDMARD); [b]Deaths are only treatment-emergent; [c]includes 1 fatal PE event: 55-year-old female with history of obesity, diabetes and hypertension developed PE after prolonged driving.
MACE was defined as CV death, non-fatal MI, and non-fatal stroke. VTE was defined as deep vein thrombosis and pulmonary embolism.
ADA, adalimumab, AE, adverse events; DVT, Deep Vein Thrombosis; E, events; EOW, every other week; MACE, major adverse cardiovascular events; MTX, methotrexate; PBO, placebo; PY, patient years; QD, once-daily; SAE, serious adverse events; TEAEs, treatment-emergent AEs; UPA, upadacitinib; VTE, venous thromboembolic events.

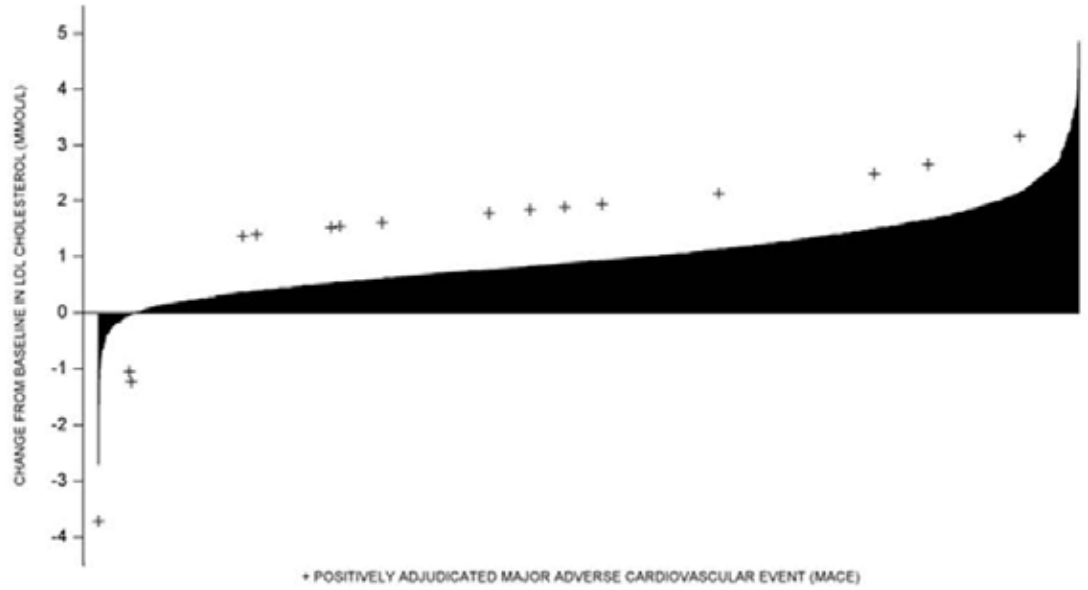
Methods: Treatment-emergent adverse events of MACE and VTE from 5 pivotal, randomized, blinded, Phase 3 trials of UPA 15 mg QD (all 5 trials) or 30 mg QD (4 trials) in RA pts were summarized into the integrated placebo (PBO), MTX, ADA 40 mg, UPA 15 mg and UPA 30 mg treatment groups. Data are presented as exposure adjusted event rates (EAERs, E/100 PY). All suspected MACE and VTEs were adjudicated by an external, independent, CV adjudication committee.

Results: Across trials, 3834 pts received ≥1 dose of UPA 15 mg (n=2630) or 30 mg (n=1204) with no option to switch doses (exposure =4020.1 PY), 1042 pts received PBO (256.8 PY), 530 pts received MTX (368.7 PY) and 579 pts received ADA 40 mg (467.8 PY). History of prior CV events (2-3%) and VTEs (4-7%) were comparable across groups.

The EAERs of MACE and VTE in the UPA groups were comparable to PBO, MTX and ADA **(Table).** Approximately 40% of MACE events and 1 pulmonary embolism event (UPA 15 mg) were fatal. All pts with a MACE or VTE event had ≥1 CV risk factor (hypertension, diabetes, dyslipidemia) or ≥1 VTE risk factor (prior history of thrombotic event, obesity, or hypertension) at baseline, respectively.

Though treatment with UPA increased the levels of low- and high-density lipoprotein cholesterol (LDL-C and HDL-C), their ratio remained constant over time. Analysis of data showed no association of LDL-C increases and MACE occurrences **(Figure)**. In both UPA groups, neither a dose-response nor a pattern of time-to-VTE-onset (23 to 1127 days of UPA) was observed. Slight decreases in mean platelet count from baseline were observed.

Figure: Adjudicated MACE events in patients with varying ΔBL in LDL-C



Note: the above plot of adjudicated MACE events is from the long-term exposure of the UPA 15 mg arm.
MACE is defined as CV death, non-fatal MI and non-fatal stroke;
CV, cardiovascular; LDL-C, Low density Lipid-Cholesterol, MACE, major adverse cardiovascular events; MI, myocardial infarction; UPA, upadacitinib; QD, once-daily.

Conclusion: EAERs of adjudicated MACE and VTE with UPA were comparable with MTX and ADA and consistent with reported background rates in the RA population. Similar to other JAK inhibitors, UPA increased the levels of lipids. However, no association between lipid levels and MACE could be established.

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Abstract Number: 0847

Safety Profile of Baricitinib for the Treatment of Rheumatoid Arthritis up to 7 Years: An Updated Integrated Safety Analysis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Treatments I: Safety and Outcomes

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Table. Safety Summary

	Placebo-controlled (to Week 24)			2-4-mg extended		All-Bari-RA
	Placebo (N=1215)	Bari 2-mg (N=479)	Bari 4-mg (N=1142)	Bari 2-mg (N=479)	Bari 4-mg (N=479)	All Bari RA (N=3770)
Exposure						
Total patient-years	450.8	185.8	471.8	675.6	698.6	10127
Median duration, days	166	168	169	257	342	1115
Longest exposure, days	235	197	211	1805	2520	2520
≥1 AE, n (EAIR)						
TEAE	748 (165.9)	316 (170.1)	803 (170.2)	378 (55.9)	417 (59.7)	3332 (32.9)
Serious adverse event including death	54 (12.0)	18 (9.7)	58 (12.3)	62 (9.2)	84 (12.0)	786 (7.8)
Temporary interruption due to AE	98 (21.7)	50 (26.9)	117 (24.8)	108 (16.0)	118 (16.9)	1111 (11.02)
Permanent discontinuation due to AE	37 (8.2)	20 (10.8)	50 (10.6)	39 (5.7)	59 (8.3)	426 (4.2)
Death, n (IR)	2 (0.4)	0	3 (0.6)	1 (0.2)	4 (0.6)	44 (0.4)
Malignancy, n (IR)						
Malignancy excluding NMSC						
As treated	2 (0.4)	1 (0.5)	2 (0.4)	3 (0.4)	10 (1.4)	85 (0.8)
As randomized				12 (0.8)	14 (1.0)	
Lymphoma	0	0	0	0	1 (0.1)	8 (0.1)
NMSC	1 (0.2)	0	3 (0.6)	2 (0.3)	8 (1.1)	37 (0.4)
Infections, n (IR)						
Serious infection	19 (4.1)	8 (4.2)	19 (4.0)	21 (3.1)	32 (4.6)	283 (2.8)
Herpes zoster	4 (0.9)	6 (3.1)	18 (3.8)*	18 (2.7)	27 (3.9)	323 (3.3)
Tuberculosis	0	0	1 (0.2)	0	7 (0.5)	15 (0.2)
Opportunistic infection including MD HZ[a]	2 (0.5)	0	4 (0.9)	2 (0.3)	3 (0.4)	52 (0.5)
Adverse cardiovascular events of special interest, n (IR)						
Major adverse cardiovascular events	2 (0.5)	0	3 (0.7)	2 (0.3)	2 (0.3)	51 (0.5)
DVT/PE	0	0	6 (1.3)	4 (0.6)	4 (0.6)	49 (0.5)
DVT	0	0	3 (0.6)	4 (0.6)	2 (0.3)	35 (0.4)
PE	0	0	3 (0.6)	1 (0.2)	2 (0.3)	24 (0.2)
Gastrointestinal perforations, n (EAIR)	0	0	0	0	1 (0.1)	4 (0.04)

*$P<0.05$ Bari 4-mg vs placebo.
[a]No statistical comparisons were performed.
AE=adverse event; Bari=baricitinib; DVT=deep vein thrombosis; EAIR=exposure-adjusted incidence rate; IR=incidence rate; NMSC=non-melanoma skin cancer; PE=pulmonary embolism; TE=treatment-emergent.

Background/Purpose: Baricitinib (bari), an oral, selective inhibitor of Janus kinase (JAK) 1 and 2, is used to treat moderately to severely active RA in adults. The objective of the study was to update bari's safety profile with data from an additional Phase 3 trial and ongoing long-term extension (LTE) study.

Methods: Long-term safety of once-daily bari was evaluated in the All-Bari-RA dataset: all patients exposed to any bari dose from 9 randomized trials (5 Phase 3, 3 Phase 2, 1 Phase 1b) and 1 LTE (data to 13-Feb-2018). Placebo comparisons were evaluated to Week 24 from 7 Phase 2/3 trials: patients randomized to placebo, bari 2-mg, or 4-mg, with censoring at rescue/treatment switch. Dose responses were evaluated in the 2/4-mg extended dataset from 4 Phase 2/3 trials: patients randomized to 2- or 4-mg, LTE data included; data censored at rescue/dose change (as-treated

analysis) and, due to latent period for malignancy, analyzed without censoring (as-randomized analysis). Incidence rates (IRs) per 100 patient-years were calculated.

Results: A total of 3770 patients received bari (10,127 patient-years); maximum exposure was 7 years (Table). No significant differences were seen for bari 4-mg versus placebo in adverse events leading to permanent drug discontinuation, death, malignancy, serious infection, or major adverse cardiovascular events. Herpes zoster incidence rate (IR) was significantly higher for bari 4-mg versus placebo (3.8 vs 0.9) and numerically higher for bari 2-mg (3.1). IRs for deep vein thrombosis/pulmonary embolism were numerically higher in bari 4-mg versus placebo; IRs were similar in 2/4-mg-extended dataset. Malignancy (excluding non-melanoma skin cancer) IRs were 0.8 (2-mg) and 1.0 (4-mg; as-randomized analysis). Fewer than 1% of patients discontinued due to abnormal laboratory results.

Conclusion: In this updated integrated analysis of patients with active RA exposed to bari for up to 7 years, across safety topics, bari maintained a safety profile similar to that previously reported[1] and acceptable in the context of demonstrated efficacy.

Reference:

1. Smolen JS et al. J Rheumatol. 2019;46:7-18.

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Abstract Number: 0848

Risk of Serious Infection with Long-Term Use of Low-Dose Glucocorticoids in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

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Session Title: RA – Treatments I: Safety and Outcomes

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: As many as 30-40% of patients with RA remain on long term glucocorticoids. Infection risk with higher dose glucocorticoids is well known, but evidence on risk with low dose therapy is mixed. We aimed to assess infection risk with low-dose, long-term glucocorticoid use by studying patients on stable DMARD therapy.

Methods: Using Medicare claims data from 2006-2015, we evaluated RA patients (2 diagnoses ≥7 days apart) who initiated MTX or a biologic/targeted synthetic DMARD (tsDMARD) and remained on therapy for >180 days (no gaps > 90 days and no new biologic/tsDMARDs). Patients with other autoimmune rheumatic diseases, cancer, or HIV were excluded. The baseline period included the 180 days prior to the DMARD course initiation and the first 180 days of treatment (Figure 1). Average glucocorticoid dose in prednisone equivalents was calculated in the final 90 days of the baseline period and updated at each subsequent 90-day interval, categorizing as none, ≤5mg, 5-10mg, or >10mg/day. Cox models evaluated associations between glucocorticoid dose and time to the first serious infection (diagnoses from any position in hospital discharge diagnoses, positive predictive value >80%), clustering to account for patients contributing > 1 treatment episode. Patients were censored at end of the DMARD course, end of enrollment, 9/30/2015, death, or 90 days after a change in glucocorticoid dose category. Covariates were balanced across glucocorticoid dose categories using propensity score-based inverse probability weights. Predicted 1-year incidence of infection was calculated from weighted models.

Results: We identified 244,833 treatment episodes (56% methotrexate and 44% biologic/tsDMARD) among 170,357 unique patients meeting inclusion and exclusion criteria. At baseline 47% of patients were receiving glucocorticoids (Table 1). There were 20,630 serious infections with overall crude incidence of 11.0/100 person-years, most fre-

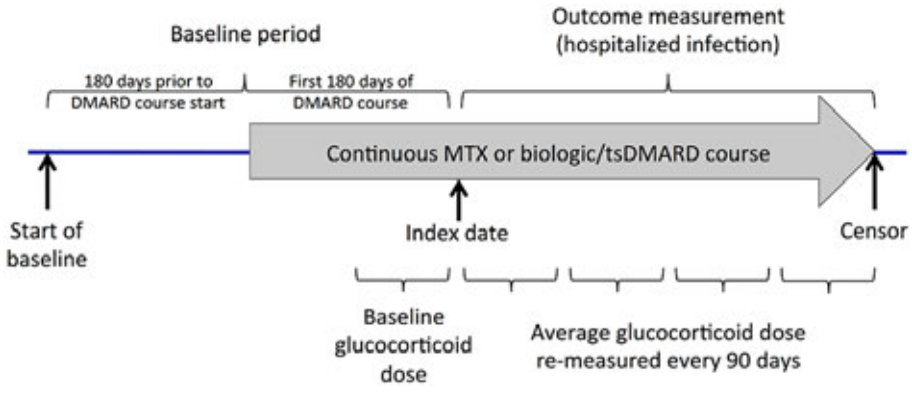

Figure 1. Study Design

Table 1: Select cohort characteristics

	Baseline glucocorticoid dose				Total
	None	≤5mg/day	5-10mg/day	>10mg/day	
N, treatment episodes	130556	75517	30782	7978	244833
Female	106611 (81.7%)	61353 (81.2%)	23558 (76.5%)	5785 (72.5%)	197307 (80.6%)
Age, years	68.6 +/- 11.8	69.6 +/- 11.5	68.1 +/- 11.8	65.1 +/- 12.7	68.7 +/- 11.8
White	92181 (70.6%)	54219 (71.8%)	22169 (72.0%)	5855 (73.4%)	174424 (71.2%)
DMARD Treatment					
Methotrexate*	72708 (55.7%)	43011 (57.0%)	17078 (55.5%)	4184 (52.4%)	136981 (55.9%)
Abatacept	10707 (8.2%)	7085 (9.4%)	3097 (10.1%)	725 (9.1%)	21614 (8.8%)
Adalimumab	10413 (8.0%)	5383 (7.1%)	2267 (7.4%)	678 (8.5%)	18741 (7.7%)
Certolizumab	2828 (2.2%)	1459 (1.9%)	694 (2.3%)	161 (2.0%)	5142 (2.1%)
Etanercept	13822 (10.6%)	6637 (8.8%)	2549 (8.3%)	729 (9.1%)	23737 (9.7%)
Golimumab	2018 (1.5%)	1185 (1.6%)	502 (1.6%)	147 (1.8%)	3852 (1.6%)
Infliximab	13271 (10.2%)	7541 (10.0%)	3042 (9.9%)	867 (10.9%)	24721 (10.1%)
Rituximab	709 (0.5%)	340 (0.5%)	177 (0.6%)	77 (1.0%)	1303 (0.5%)
Tocilizumab	2944 (2.3%)	2183 (2.9%)	1060 (3.4%)	311 (3.9%)	6498 (2.7%)
Tofacitinib	1136 (0.9%)	693 (0.9%)	316 (1.0%)	99 (1.2%)	2244 (0.9%)
Prior biologics	40955 (31.4%)	26158 (34.6%)	11915 (38.7%)	3318 (41.6%)	82346 (33.6%)
Diabetes	22546 (17.3%)	12545 (16.6%)	5665 (18.4%)	1742 (21.8%)	42498 (17.4%)
COPD	11492 (8.8%)	9027 (12.0%)	4505 (14.6%)	1618 (20.3%)	26642 (10.9%)
Charlson Score	2 [0-3]	2 [0-4]	2 [0-4]	2 [0-5]	2 [0-4]
Hospitalized infection past year	9768 (7.5%)	7795 (10.3%)	4261 (13.8%)	1493 (18.7%)	23317 (9.5%)

N (%) or mean +/- standard deviation shown.
* Methotrexate = methotrexate without a biologic or targeted synthetic DMARD

Table 2: Association between glucocorticoid use and serious infection

			Serious Infection		
	N	Person-years	N (incidence/ 100 person-years)	Unadjusted HR (95% CI)	Propensity Adjusted HR (95% CI)
Glucocorticoid dose					
None	130556	125705	10652 (8.4)	Reference	Reference
≤5mg/day	75517	46983	6433 (12.7)	1.55 (1.50-1.60)	1.37 (1.32-1.41)
>5-10mg/day	30782	12585	2741 (21.7)	2.33 (2.23-2.44)	1.92 (1.83-2.01)
>10mg/day	7978	2702	894 (33.1)	3.47 (3.24-3.73)	2.78 (2.57-3.01)

Hazard ratios (HR) from Cox models. Propensity score adjusted analyses performed using stabilized inverse probability weights to balance covariates across treatment groups. Covariates included in propensity score models: age (categorized), female, race, year, disability, dual Medicare/Medicaid eligibility, quintiles of zip code based median household income, DMARD type, number previous biologics, diabetes, hypertension, COPD, asthma, cerebrovascular disease, obesity, congestive heart failure, coronary artery disease, myocardial infarction, peptic ulcer disease, extra-articular RA, anemia, chronic kidney disease, end-stage renal disease, depression, chronic pain, Charlson score, influenza vaccine past year, pneumococcal or zoster vaccine (ever), hospitalized infection past year, use of durable medical equipment, skilled nursing facility stay.

quently urinary infection, pneumonia, bacteremia/septicemia, and skin/soft tissue infection. Glucocorticoids were associated with an increased rate of serious infections with significant risk even at ≤5mg/day [HR 1.37 (1.32-1.41)] (Table 2). Predicted 1-year incidence of infection from propensity weighted models was 12.5% (95% CI 12.2-12.9) for ≤5mg, 17.2% (16.5-17.9) for 5-10mg, and 23.9% (22.3-25.6) for >10mg vs. 9.3% with no glucocorticoids. Results

were similar in sensitivity analyses requiring a primary diagnosis of infection, excluding patients with prior serious infection, and stratifying by MTX vs. biologic/tsDMARD use. Results remained significant in analyses that did not censor with glucocorticoid dose changes (37% of censoring events in the main analysis).

Conclusion: Among older RA patients stable on MTX or biologic/tsDMARDs, long term use of glucocorticoids is associated with a significant increase in the risk of serious infections even at doses ≤5mg/day. The magnitude of risk with ≤5mg/day is similar to that observed with biologics in other studies. Although the influence of disease activity could not be directly assessed, these results support recommendations to limit long term glucocorticoid use in RA.

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Abstract Number: 0849

Risk of Malignancies Associated with Biologics in Rheumatoid Arthritis: Analysis of a National Claim Database

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SESSION INFORMATION
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Session Title: RA – Treatments I: Safety and Outcomes
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Our objectives were to estimate and compare the incidence rate of malignancies between biologic and csDMARD-treated RA patients.

Methods: We conducted an historical cohort study within our national claim database that prospectively records individual health resource use of 86% of the French population (65 million inhabitants). RA adult patients were identified based on ICD-10 code (M05 or M06) between 2007-2016. Patients with previouscancer history were excluded.

Treatment exposures were incident first use of any treatment: csDMARD (methotrexate, leflunomide, sulfasalazine, azathioprine, hydroxychloroquine) or biologics (anti-TNF, rituximab, abatacept, tocilizumab, ustekinumab, anakinra). To identify incident treatment periods, a one year period prior our period of analysis was analysed; only patients that

Type of malignancies	HR csDMARD (ref) vs. all biologics	p value
All malignancies	0.92 [0.80;1.05]	p=0.224
Solid cancer (excluding non melanoma skin cancer)	0.90 [0.78;1.05]	p=0.182
Lymphoma	1.00 [0.55;1.835]	p=0.992
Other hematologic malignancies	0.85 [0.43;1.67]	p=0.636

Table 1. Risk of cancer of biologics compared to csDMARD in RA patients

did not receive any treatment during this period were included. .Exposure definition was considered with a 90-day latency after treatment initiation and a 180-day remanence period after drug discontinuation.

To compare the risk of malignancies between csDMARD and biologics treated patients, a dynamically propensity score (including age, sexe, year of first occurrence of RA code, date of treatment initiation, number of previous DMARDs, Charlson comorbidity index, diagnosis of tobacco and/or alcohol-associated disorders, number of hospitalisations for RA, cumulative corticosteroid dose) was constructed using pooled logistic regression. Hazard Ratios (HRs) for risk of cancer were estimated using Cox proportional hazards model after dynamically propensity score matching. Exposure was considered as a time-dependent variable. Sensitivity analyses are ongoing to assess the robustness of our results.

Results: Between 2007 and 2016, 83 706 RA patients exposed to csDMARD (n=63837) and/or biologics (n=19869) were identified. After propensity score matching, analyses were conducted on 19687 patients in each group (mean age: 51 ±14 yrs; female: 74.6%). Malignancies occurred in 435 patients exposed to biologics and 357 patients exposed to csDMARD,

The HR for overall risk of malignancies, risk of solid cancer (excluding non-melanoma skin cancer), lymphoma, and other hematologic malignancies did not differ significantly between csDMARD and all biologics analysed together (table). Regarding organ specific cancer, no difference was observed, except for risk of prostate cancer in men that occurred significantly less frequently in biologic treated patients (HR: 0.47 [0.29;0.76], p=0.003).

Conclusion: Using a large nationwide healthcare database, representative of the French population, the overall risk of malignancies and the risk of organ-specific cancers and hematologic malignancies in biologic treated RA patients did not differ from that of patients treated with csDMARD. Except for prostate cancer in men, which occurred less frequently in biologics treated patients. The reason of this difference remains unclear, but could be linked to a high frequency of screening before introducing biologic.

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Abstract Number: 0850

Safety of Synthetic and Biological DMARDs: A Systematic Literature Review Informing the 2019 Update of the EULAR Recommendations for Management of Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: To assess the most recent safety-data of synthetic (s) and biological (b)DMARDs to inform the 2019 update of the EULAR recommendations for the management of RA.

Methods: Observational studies comparing any DMARD with another intervention for the management of patients with RA were identified by searches in MEDLINE, Embase and Cochrane (time-window: 2016-2019). Interventions included any bDMARD, csDMARD, tsDMARD or glucocorticoids. A comparator group was required for the study to be included. All safety outcomes were included. Observational studies were chosen because they better reflect routine clinical care. For treatments still without registry data, randomized controlled trials (RCTs) and long-term extensions (LTEs) thereof were used to extract safety data. Risk of bias was assessed according to the Hayden's tool for observational studies and Cochrane Collaboration's tool for RCTs.

Results: Of 3,886 articles screened, 42 observational studies fulfilled the inclusion criteria, with 16 focusing on the risk of infections, 8 on cancer, 10 on major cardiovascular events (MACE), 3 on lower intestinal perforations (LIP), 5 on withdrawals due to adverse events and 2 on immunological reactions. Studies were heterogeneous precluding meta-analysis. Two studies showed an increased risk of serious infections (SI) with bDMARDs compared to csDMARDs (aIRR: 3.1-3.9). In 9 studies, 4 at low risk of bias, the risk of SI was not different between bDMARDs, with one also showing no difference between tofacitinib and TNFi (Table 1). Two studies (high risk of bias) showed no difference in the risk of infection by herpes zoster across bDMARDs, but in one, an increased risk for tofacitinib compared to abatacept was reported. Five studies (4 at low risk of bias) showed no increased risk of cancer for bDMARDs compared to csDMARDs; and 2 (at low risk of bias) no difference between bDMARDs. The risk of MACE did not differ between bDMARDs and csDMARD (3 studies, 1 at low risk of bias) and also comparing different bDMARDs (4 studies, 1 at low risk of bias). An increased risk of LIP was found for tocilizumab compared to csDMARDs (1 study, low risk of bias) and to TNFi (2 studies, high risk of bias). In total, 57 manuscripts reported safety data from RCTs/LTEs, 21 evaluating biosimilars, 18 bDMARDs and 18 tsDMARDs. Overall, no unexpected safety outcomes were found, except for the possible increased risk of venous thromboembolism (VTE) with tsDMARDs (Table 2). This signal prompted FDA/EMA to issue warnings to avoid baricitinib 4mg (not 2mg) and tofacitinib 10 mg bid (not 5mg bid) in patients with risk factors for VTE.

Table 1. Serious infections in patients on bDMARDs or tsDMARDs (observational studies)

Study ID	Registry	Intervention	Control	aHR (i vs c)	Risk of Bias
Serious infections					
Carrara 2019 Clin Exp Rheumatol	RECORD	ADA	ETA	1.4 (1.0; 2.0)	High
		IFX		1.0 (0.6; 1.6)	
		CZP		1.3 (0.5; 3.6)	
		GOL		1.1 (0.4; 3.2)	
		ABA		**0.3 (0.1; 0.8)**	
		RTX		1.0 (0.5; 1.9)	
		TCZ		1.2 (0.6; 2.6)	
Cecconi 2018 J Clin Rheumatol	BIOBADABRASIL	ADA	IFX	**aIRR: 0.5 (0.4; 0.8)**	Moderate
		ETA		aIRR: 0.8 (0.6; 1.2)	
Grøn 2019 Ann Rheum Dis	DANBIO and ARTIS	ABA	RTX	aIRR: 0.9 (0.7; 1.1)	Low
		TCZ		aIRR: 0.8 (0.6; 1.0)	
Harrold 2018 Arthritis Res Ther	CORRONA	CZP	Other TNFi	aIRR: 1.3 (0.8; 1.9)	Low
Machado 2018 Arthritis Res Ther	Claims database	TNFi	Non-TNFi	1.1 (1.0; 1.4)	High
		TOFA		1.5 (0.9; 2.6)	
Mori 2017 PLoS One	SARABA	IFX	ETA	1.5 (0.8; 3.0)	Moderate
		ADA		1.7 (0.9; 3.3)	
		ABA		1.1 (0.6; 2.2)	
		TCZ		1.0 (0.6; 1.9)	
Pawar 2019 Ann Rheum Dis	Claims database	TCZ	TNFi	1.1 (1.0; 1.2)	High
		ABA		1.4 (1.2; 1.6)	
Rutherford 2018 Ann Rheum Dis	BSRBR-RA	IFX	ETA	0.9 (0.8; 1.0)	Low
		ADA		1.0 (0.9; 1.1)	
		RTX		0.9 (0.8; 1.0)	
		TCZ		**1.2 (1.0; 1.5)**	
		CZP		**0.8 (0.6; 1.0)**	
Silva-Fernández 2018 Rheumatology (Oxford)	BSRBR-RA	RTX	TNFi	1.0 (0.7; 1.4)	Low

Conclusion: Data obtained by this SLR are aligned with previous evidence; they show a slightly increased risk of SI with bDMARDs compared to csDMARDs and no difference between bDMARDs. The overall risk of cancer and MACE was not increased with bDMARDs compared with csDMARDs. The risk of LIP with tocilizumab and VTE with tsDMARDs needs further evaluation.

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Table 2. Venous thromboembolism in patients on tsDMARDs (randomized controlled trials)

Study ID (trial)	Follow-up	Intervention	N	VTE (%)	Risk of bias
Placebo-controlled trials					
Burmester 2018 Lancet (SELECT-NEXT)	12	PBO	221	0 (0)	low
		UPA 15 QD	221	0 (0)	
		UPA 30 QD	219	0 (0)	
Dougados 2017 Ann Rheum Dis (RA-BUILD)	24	PBO	228	0 (0.0)	low
		BAR 2 QD	229	0 (0.0)	
		BAR 4 QD	227	1 (0.4)*	
Genovese 2018 Lancet (SELECT-BEYOND)	24	PBO	169	0 (0)	low
		UPA 15 QD	164	3 (1.8)†	
		UPA 30 QD	165	1 (0.6)‡	
Head-to-Head trials					
Fleischmann 2017 Arthritis Rheumatol (RA-BEGIN)	52	MTX Q1W mono	210	1 (0.5)¥	low
		BAR 4 QD mono	159	0 (0.0)	
		BAR 4 QD + MTX Q1W	215	0 (0.0)	
Taylor 2017 N Engl J Med (RA-BEAM)	52	BAR 4 QD	487	1 (0.2)£	low
		ADA 40 Q2W	330	0 (0.0)	

* Pulmonary embolism. † One case of pulmonary embolism occurred during the 12-week PBO-controlled phase and 2 cases (one with concomitant deep venous thrombosis) between week 12 and week 24 in patients who switched from PBO to UPA15 (2/72=2.8%); ‡ One case of pulmonary embolism in a patient who switched from PBO to UPA30 after week 12; ¥ Death by pulmonary thromboembolism; £ Thrombophlebitis; QD, once daily; Q1W, once a week; mono, monotherapy.

Company, 5, UCB, 5, 8, UCB Pharma, 5; **M. Dougados**, AbbVie, 2, 5, 8, Amgen, 5, Biogen, 5, BMS, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, Merck, 2, 5, Merck Inc, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8; **R. Van Vollenhoven**, Abbvie, 5, 8, Astra-Zeneca, 5, 8, Biotest, 5, 8, BMS, 2, 5, 8, Celgene, 5, 8, GSK, 2, 5, 8, Janssen, 5, 8, Lilly, 2, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 2, 5, 8; **I. McInnes**, None; **J. Bijlsma**, Lilly, 8, Roche, 2, 8; **G. Burmester**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma., 5, 8, AbbVie Inc., 5, 8, BMS, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Merck Shar & Dohme, 5, 8, MSD, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche, Sanofi-Genzyme, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Union Chimique Belge, 2, 5, 8; **M. de Wit**, Abbvie, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen-Cilag, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8; **L. Falzon**, None; **R. Landewé**, Abbott, 2, 5, 8, Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8.

Abstract Number: 0851

Association Between Bone Marrow Edema and Structural Progression in the Same Quadrant in Axial Spondyloarthritis – 5-year Data from the DESIR Cohort

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical I: Imaging in Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: The overall presence of inflammation in the MRI-SIJ is associated with overall 5-year radiographic damage in patients with axSpA. But we do not know if a bone marrow edema (BME) lesion leads to a structural lesion at the same place (i.e. in the same quadrant). This study aims to investigate the association between BME and structural progression in the same quadrant of the SIJ, over time.

Methods: Patients from the DESIR cohort (early axSpA according to the rheumatologist) with ≥2 consecutive MRI-SIJ (out of baseline, 2 and 5 years), were included. Each image was independently scored by 3 trained central readers blinded to chronological order. BME was considered present in a time point if detected in ≥1/6 slices in each of the 8 quadrants. The prevalence of BME (yes/no) and structural lesions (sclerosis, erosions, fatty lesions and ankylosis;

Table 1- Prevalence of different imaging lesions* per Quadrant – at BL and 5 years

Baseline (n=197)					
Left side	BME - %	Sclerosis - %	Erosions - %	Fatty lesion - %	Ankylosis - %
Q1	14.2	4.1	23.4	9.6	1.5
Q2	12.7	0	4.1	12.7	1.5
Q3	11.7	0	1.5	7.6	2.2
Q4	14.7	2.5	13.7	10.7	2.2
Right side	BME - %	Sclerosis - %	Erosions - %	Fatty lesion - %	Ankylosis - %
Q1	13.7	3.1	19.8	3.6	0.5
Q2	13.7	0	6.1	14.2	0.5
Q3	10.7	0	1.5	8.1	1.5
Q4	16.2	1.0	11.7	7.1	1.5
At 5 years (n=136)					
Left side	BME - %	Sclerosis - %	Erosions - %	Fatty lesion - %	Ankylosis - %
Q1	7.9	5.0	28.1	13.7	2.9
Q2	11.5	0	5.8	18.7	2.9
Q3	6.5	0	2.9	18.0	2.9
Q4	10.8	1.4	13.0	13.7	2.9
Right side	BME - %	Sclerosis - %	Erosions - %	Fatty lesion - %	Ankylosis - %
Q1	11.8	3.6	25.9	8.6	2.2
Q2	14.0	0	7.2	20.9	2.2
Q3	7.4	0	5.8	15.1	5.0
Q4	11.0	1.4	12.2	10.1	5.0

* Agreement between ≥ 2 out of the 3 readers. Q= quadrant; BME: Bone Marrow Edema

Table 2 – Longitudinal association between BME and structural outcomes in the same quadrant over 5 years

Outcome	Binomial GEE - OR [95% CI][a]
Sclerosis	**1.7 (1.0;3.2)**
Erosion	**2.0 (1.5;2.5)**
Fatty	**1.7 (1.2;2.5)**
Ankylosis	*(not convergent)*

[a]: Multilevel (reader, time, side, quadrant) with auto-regression and adjusted for the following variables: age, gender, ASDAS, treatment (NSAIDs, steroids, csDMARDs, and TNFi) and reader. ASDAS and treatment are time-lagged

all yes/no) defined, per quadrant, by the agreement of ≥2 out of 3 readers, was described at BL and at 5 years. The longitudinal association between BME and each of the structural lesions in the same quadrant was tested in time-lagged multilevel Generalized Estimating Equation (GEE) models with autoregression (i.e. adjusted for the structural lesion in the previous time point) and adjusting for clinical variables selected a priori on clinical grounds (age, gender, disease activity and treatment).

Results: In total, 197 patients were included (age 34 (SD 9) years, 48% male and 61% HLA-B27 positive). While BME and fatty lesions were evenly distributed across quadrants, erosions and sclerosis occurred preferably in the iliac side (i.e. Q1 and Q4) (Table 1). The prevalence of BME decreased over time (baseline range: 11%-16%; 5-year range: 7%-14%), while erosions (baseline: 2%-23%; 5-year: 3%-28%) and especially fatty lesions (baseline: 4%-14%; 5-year: 9%-21%) increased. Ankylosis and sclerosis were rare in this early axSpA cohort. In the multivariable models, BME was longitudinally associated with sclerosis (OR:1.7 (95% CI: 1.0;3.2)), erosions (2.0 (1.5;2.5)) and fatty lesions (1.7 (1.1;2.5)) (Table 2). The possible association with ankylosis could not be tested due to too low number of lesions.

Conclusion: In patients with early axSpA, inflammation in one SIJ quadrant leads to structural damage in the same quadrant. This finding reinforces the pathophysiological implications of inflammation in axSpA.

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Abstract Number: 0852

Ileal but Not Colonic Inflammation Is Linked to Fatty Lesions on MRI of the Sacroiliac Joints in Spondyloarthritis Patients

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical I: Imaging in Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Gut and joint inflammation in spondyloarthritis (SpA) are closely intertwined. About 50% of axial SpA patients display microscopic signs of inflammation in ileum and/or colon, a risk factor to develop Crohn's disease over time. It is currently not known if presence of microscopic gut inflammation in new onset SpA is associated with more structural lesions on magnetic resonance imaging of the sacroiliac joints (MRI-SIJ) and whether these lesions relate to the localization of gut inflammation. This study aims to assess whether structural lesions on MRI-SIJ (A) are associated with microscopic gut inflammation in SpA patients and (B) are preferably related to colon or ileum inflammation in case of gut involvement.

Methods: We analyzed baseline information from a patient cohort with a new diagnosis of SpA (expert opinion). Included patients fulfill the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axial or peripheral SpA. MRI-SIJ was scored by 3 readers, blinded for subject characteristics. Six consecutive slices were assessed for structural lesions: sclerosis, erosions, fatty lesions and (partial) ankylosis. MRI sum scores were analyzed as 2 out of 3 (median) scores. Colon and ileum biopsies were evaluated for microscopic signs of inflammation. The effect of gut inflammation (colon and/or ileum) on MRI-SIJ lesions was investigated by generalized linear models (GLM), adjusted for age and gender and stratified for the SpA phenotype.

Results: By January 2019, baseline data were available on 105 patients (95 axial and 10 peripheral SpA). Gut inflammation was present in 35 patients (17 ileum, 8 colon, 10 both). Table 1 shows the slope (β_1) of the GLMs for erosions, fatty lesions, sclerosis and (partial) ankylosis and the p-value for the SpA phenotype as an interaction term. Erosions, sclerosis, nor ankylosis show a significant association with gut inflammation in general. If present, colon inflammation has no significant relationship with each individual structural lesion. In contrast, presence of ileum inflammation was associated with an increase in the number of fatty lesions by 0,68 (95%CI 0,04 – 1,38). All results are independent of the SpA phenotype (p > 0,05).

Structural lesion	Gut inflammation	β_1	95% CI	p-value	p-value interaction term*
Erosions	Colon and/or ileum	0,02	(-0,39 – 0,45)	0,92	0,53
	Colon	-0,08	(-0,56 – 0,45)	0,75	0,50
	Ileum	-0,01	(-0,47 – 0,46)	0,94	0,66
Fatty lesions	Colon and/or ileum	0,38	(-0,23 – 1,04)	0,22	0,61
	Colon	-0,54	(-1,28 – 0,30)	0,16	0,94
	Ileum	**0,68**	**(0,04 – 1,38)**	**0,04**	0,88
Sclerosis	Colon and/or ileum	-0,19	(-0,60 – 0,23)	0,35	0,81
	Colon	0,05	(-0,45 – 0,60)	0,84	0,60
	Ileum	-0,27	(-0,68 – 0,17)	0,22	0,62
(Partial) Ankylosis	Colon and/or ileum	-0,38	(-1,14 – 0,44)	0,35	0,41
	Colon	-0,40	(-1,33 – 0,76)	0,45	0,60
	Ileum	-0,24	(-1,05 – 0,68)	0,58	0,40

Conclusion: Ileal but not colonic inflammatory gut lesions are linked to more fatty lesions on MRI-SIJ in newly diagnosed SpA patients. Baseline microscopic gut inflammation was not associated with erosions, sclerosis nor ankylosis. These data support the concept that microscopic gut inflammation, especially ileal inflammation, is associated with more severe axial inflammation in SpA.

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Table 1. Association between MRI–SIJ structural lesions and gut inflammation in SpA patients. *SpA subtype (axial versus peripheral SpA) as an interaction term.

Abstract Number: 0853

Two-Year Progression of Facet Joint Ankylosis on Whole Spine Low-Dose CT in Patients with Radiographic Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019

Table 1: Facet joint ankylosis prevalence, interreader reliability and progression in patients with r-axSpA with at least one syndesmophyte

	Reader 1 mean (SD) *range*	Reader 2 mean (SD) *range*	ICC (95% CI) (average)	SDC
Whole spine excluding C5-T2 *max score 38*				
Baseline	7.3 (10) 0 - 34	9.4 (10.9) 0 - 37	0.93 (0.87-0.96)	
Follow-up	7.8 (9.7) 0 - 34	10.3 (10.9) 0 - 34	0.91 (0.82-0.95)	
Change score	1.0 (2.8) -8.4 - 11.9	1.1 (2.6) -4.2 - 11.2	0.56 (0.22-0.75)	2
Cervical excluding C5-T1 *max score 6*				
Baseline	0.9 (1.8) 0 - 6	1.1 (2) 0 - 6	0.84 (0.73-0.90)	
Follow-up	0.7 (1.6) 0 - 6	1.2 (1.9) 0 - 6	0.72 (0.52-0.84)	
Change score	0.0 (0.4) -2 - 1	0.0 (0.4) -2- 1.2	0.91 (0.83-0.95)	0.2
Thoracic excluding T1-T2 *max score 22*				
Baseline	5.4 (7.4) 0 - 22	6.5 (7.6) 0 - 22	0.91 (0.85-0.95)	
Follow-up	6.0 (7.2) 0 - 22	7.3 (7.9) 0 - 22	0.90 (0.82-0.94)	
Change score	0.9 (2.5) -8.8 - 7	0.9 (2.3) -4.4 - 11	0.56 (0.21-0.75)	2.7
Lumbar *max score 10*				
Baseline	1.0 (2.5) 0 - 10	1.8 (3.1) 0 - 10	0.81 (0.67-0.89)	
Follow-up	1.1 (2.5) 0 - 10	1.8 (3) 0 - 10	0.85 (0.73-0.92)	
Change score	0.0 (0.8) -2 - 3	0.2 (0.9) -2 - 5	0.10 (-0.58-0.48)	1.1

Baseline and follow-up: N=52 (reader 1), N=53 (reader 2); whole spine change score: N=50 (r1), N=52 (r2), N=50 (ICC); cervical segment change score: N=44 (r1), N=45 (r2), N=40 (ICC), thoracic segment change score: N=50 (r1), N=52 (r2), N=50 (ICC); lumbar segment change score: N=51 (r1), N=52 (r2), N=51 (ICC)

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical I: Imaging in Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Inflammation and new bone formation in the axial skeleton are characteristic features of radiographic axial spondyloarthritis (r-axSpA). Facet joints are frequently involved in r-axSpA but rather difficult to visualize on conventional radiography (CR). However, we have recently shown that low-dose CT (ldCT) can be used to assess facet joint ankylosis in the whole spine, except for the cervicothoracic junction, in patients with r-axSpA. We now aimed to study progression of facet joint ankylosis over two years in patients with r-axSpA.

Methods: In an observational cohort, r-axSpA patients with syndesmophytes on ≥1 but no more than 75% of spinal levels of the cervical and lumbar segments on CR and ≥1 inflammatory lesion on spinal MRI underwent whole spine ldCT (about 4 mSv) with repeated ldCT after 2 years. Paired ldCTs were independently assessed by 2 trained readers, blinded to chronology. Left and right facet joints of all levels between C2 and S1, with the exception of the levels between C5 and T2, were scored as ankylosis present (1) or absent (0). Interreader reliability was assessed with intraclass correlation coefficients (ICCs) (two-way average, absolute agreement) and smallest detectable change (SDC). Status scores were calculated for baseline and follow-up. Change scores of the whole spine and per segment were calculated if < 25% of the joint scores were missing. Remaining missing scores were imputed with the mean segment change score. For each reader, progression was calculated as the proportion of patients with change score >0. For the average score of the readers, progression was given as change score >0.5 and >SDC as well as net progression,

Table 2: Number of r-axSpA patients with progression of facet joint ankylosis over 2-year follow-up

		Reader 1 N(%)	**Reader 2 N(%)**
Whole spine change >0		15/50 (30%)	22/52 (42%)
Cervical segment change >0		2/44 (4%)	3/45 (7%)
Thoracic segment change >0		15/50 (30%)	17/52 (33%)
Lumbar segment change >0		3/51 (6%)	6/52 (12%)
	SDC	**Average of 2 readers N(%)**	
Whole spine			
Change >0.5	2	24/50 (54%)	
Change >SDC		13/50 (26%)	
Net progression		21/50 (42%)	
Cervical segment			
Change >0.5	0.2	1/40 (2.5%)	
Change >SDC		3/40 (7.5%)	
Net progression		0/40 (0%)	
Thoracic segment			
Change >0.5	2.7	23/50 (48%)	
Change >SDC		7/50 (14%)	
Net progression		21/50 (42%)	
Lumbar segment			
Change >0.5	1.1	5/51 (13.7%)	
Change >SDC		4/51 (7.8%)	
Net progression		3/51 (5.9%)	

Whole spine: N=50 (r1), N=52 (r2), N=50 (average 2 readers)
Cervical segment: N=44 (r1), N=45 (r2), N=40 (average 2 readers)
Thoracic segment: N=50 (r1), N=52 (r2), N=50 (average 2 readers)
Lumbar segment: N=51 (r1), N=52 (r2), N=51 (average 2 readers)

defined as the number of patients with change score >0.5 minus the number of patients with change score < -0.5 divided by the total number of patients.

Results: Baseline and 2-year follow up ldCT were available in 53 patients with r-axSpA (mean age 48.3, 85% male, 79% HLA-B27+). Interreader reliability for status scores was good to excellent. For change scores this was poor to excellent (table 1). SDCs were relatively low (tables 1 and 2). The proportion of patients with progression is given in table 2. Most changes were seen in the thoracic spine (tables 1 and 2).

Conclusion: Over two years, a fair number of patients had progression of facet joint ankylosis with most progression occurring in the thoracic spine. These results show that using whole spine ldCT, progression of facet joint ankylosis can provide useful information on new bone formation in r-axSpA patients.

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Abstract Number: 0854

Do Smoking and Socio-economic Factors Independently Influence Imaging Outcomes in Axial Spondyloarthritis? Five-year Data from the DESIR Cohort

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical I: Imaging in Axial Spondyloarthritis & Psoriatic Arthritis

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Session Time: 2:30PM–4:00PM

Background/Purpose: Smoking and systemic inflammation have been shown to independently associate with radiographic spinal progression in patients with axSpA. Evidence suggests that certain socioeconomic (SE) factors (e.g. physically demanding jobs) may modify these associations.The study investigates the relationship between smoking and imaging outcomes (SI joints, spine, MRI and radiographs) over time in axSpA, to assess if SE factors first modify and if not, confound, such a relationship.

Methods: Patients with axSpA from the DESIR cohort who fulfil the ASAS axSpA classification criteria were included. Four imaging continuous outcomes (X-ray spine [mSASSS, range 0-72]; X-ray SIJs modified New York grading [mNY, 0-8]; MRI-Spine [SPARCC, range 0-414] and MRI-SIJ [SPARCC, range 0-72]) have been scored by 3 central readers independently (average score used) in one session, blinded for time order (baseline, 2 and 5 years). Smoking was tested as a binary variable: smoking status since last visit. SE variables were: age, gender, ethnicity (Caucasian vs other), job type based on 'collar' (blue [manual labour work] vs white [office-based work]); educational status (low vs high [university]); marital status (married vs not) and parental (number of children) status. Potential interactions between smoking and SE factors were first investigated and, if statistically ($p< 0.15$) and clinically relevant, models were stratified. The effect of smoking on imaging outcomes was assessed in multivariable time-varying models using generalized estimating equations adjusted for other possible confounders.

Results: In total, 425 axSpA patients were included: 225 [53%] male, 167 [40%] smokers and 287 [68%] blue collar. The mean baseline (SD) MRI-SIJ SPARCC was 4.67 (7.85), MRI-spine SPARCC: 2.73 (7.95)); mSASSS: 0.39(1.66); mNY: 1.70(1.84)). A significant interaction was found between smoking and job type with MRI-SIJ inflammation as the outcome ($p=0.031$) as well as with mNY grading ($p=0.096$). Similarly, educational status also proved to modify the association between smoking and MRI-SIJ inflammation ($p=0.026$). In the multivariable models, smoking was significantly associated with more MRI-SIJ inflammation over 5 years of follow-up but only in patients with a blue-collar job (β [95% CI]: 3.35 [0.54,6.17]) (table). Results were similar in the low education stratum (β [95% CI]: 2.69 [0.48, 4.91]. Smoking was not significantly associated with any of the other imaging outcomes over time. Male gender was positively associated with MRI-SIJ inflammation regardless of job type, and also with MRI-Spine inflammation and structural damage although only for blue-collar patients in the case of SIJ damage.

Conclusion: There is a strong association between smoking and MRI-SIJ inflammation over time in axSpA patients with blue collar job type or low education, irrespective of other socio-economic factors, systemic inflammation and

Table. (Time-varying) relationship between smoking and imaging outcomes across all patients or in strata according to type of job.

OUTCOME	MRI-SIJ (SPARCC)		mNY-SIJs		MRI-Spine (SPARCC)	mSASSS-Spine
STRATA	EVER BLUE COLLAR	NEVER BLUE COLLAR	EVER BLUE COLLAR	NEVER BLUE COLLAR	ALL PATIENTS	ALL PATIENTS
	β Coefficient (95% CI)	β Coefficient (95% CI)	β Coefficient (95% CI)	β Coefficient (95% CI)	β Coefficient (95% CI)	β Coefficient (95% CI)
Model numbers	N=64	N=198	N=85	N=209	N=381	N=403
Smoking (vs not)	**3.35(0.54,6.17)**	0.47(-1.08,2.02)	0.43(-0.04,0.90)	0.05(-0.08,0.18)	1.32(-0.04,2.67)	0.49(-0.11,1.08)
Age	-0.16(-0.34,0.01)	-0.10, -0.20,-0.00)	-0.00(-0.05,0.04)	0.01(-0.01,-0.02)	0.07(-0.03,0.17)	**0.06(0.02,0.10)**
Gender (M vs F)	**3.95(0.89,7.01)**	**1.61(0.24,2.98)**	**1.38(0.56,2.20)**	0.59(0.05,1.07)	**2.48(1.34,3.62)**	**0.55(0.04,1.06)**
Married (vs not)	-3.45(-9.38,2.49)^	-0.60(-2.15,0.96)				
CRP abnormal at visit (vs not)	**8.09(2.97,13.20)**	**3.03(0.98,5.09)**			**4.18(2.13,6.23)**	
NSAID score (last 6months)			0.00(-0.00,0.00) ^	-0.00(-0.00,0.00)		-0.00(-0.00,0.00) ^
csDMARD use last 6m (vs no)	**-4.43(-7.47,-1.39)**	**-2.15(-3.46,-0.84)**	**-0.35(-0.60,-0.10)**	0.01(-0.07,0.10)	**-2.46(-3.58,-1.34)**	
TNF use					**-1.46(-2.64,-0.28)**	
Presence of uveitis					**-1.81(-2.91,-0.72)**	

Other independent variables tested in models included HLA B27 status, all SE variables of interest, ASDAS or BASDAI, presence of psoriasis, inflammatory bowel disease and peripheral arthritis. ^Indicates confounding effect on the association between smoking and the outcome.

treatment. These findings suggest a possible role for mechanical stress (seen with manual jobs) amplifying the effect of smoking on axial inflammation in axSpA. No significant relationship was found between smoking and spinal inflammation or axial damage, possibly also due to the limited imaging changes in this cohort.

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Abstract Number: 0855

Which Magnetic Resonance Imaging Lesions of the Sacroiliac Joints Are of Diagnostic Value for Axial Spondyloarthritis?

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Classification of patients as having axial spondyloarthritis (axSpA) by the imaging arm of the ASAS criteria relies partly on the detection of bone marrow edema (BME) suspicious of SpA on magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ). Fatty lesions (FL) and erosions on SIJ-MRI have been suggested to be genuinely related to SpA in the context of interpretation of a 'positive' MRI in case of doubtful BME cases (1). We evaluated the role of different SIJ-MRI lesions for diagnosing axSpA in daily routine practice.

Methods: Consecutive patients with chronic back pain (duration >3 months) starting before age 45 and clinical suspicion of axSpA underwent a complete diagnostic workup including SIJ-MRI. All clinical, laboratory and imaging data

Lesion type	Sensitivity	Specificity	OR	95% CI	p-value
BME	72.5%	63.3%	4.6	2.8-7.5	0.001
BME + any chronic lesion	71.8%	72.8%	16.0	7.5-34.0	0.001
FL	56.5%	89.3%	10.9	6.0-19.8	0.001
Erosion	59.5%	88.8%	11.6	6.4-21.0	0.001
Sclerosis	81.7%	43.2%	3.4	2.0-5.8	0.001
Ankylosis	12.2%	99.4%	23.4	3.1-178.7	0.002
BME+FL	36.6%	95.3%	11.6	5.3-25.7	0.001
BME+Erosion	48.9%	94.1%	15.2	7.4-31.4	0.001
BME+Sclerosis	64.1%	75.1%			0.001
BME+Ankylosis	5.3%	99.4%	9.5	1.2-78.1	0.036

Table 1. Odds ratios for MRI lesions and combinations used for diagnosing axSpA.

	Lesion type	axSpA	non-SpA	p-value
Mean±SD	Total score	14.8±10.8	2.7±3.4	p<0.001
	BME (0-24)	3.3±3.6	0.8±1.3	
	FL (0-24)	5.2±6.8	0.5±1.9	
	Erosions (0-24)	4.5±5.4	0.4±1.4	
Median	Sclerosis or Ankylosis (0-2)	0	0	--

Table 2. Mean/median Berlin SIJ scores ± standard deviation for inflammatory and chronic lesions.

were available to experienced rheumatologists for diagnosing axSpA or not (non-SpA). In parallel, two experienced readers, blinded to all patients´ information and diagnosis, evaluated the MRIs and made a 'diagnostic judgement' based only on imaging features. In addition, radiologists quantitatively assessed MRIs for BME (Berlin Score), FL, erosions, sclerosis and ankylosis.

Results: A total of 300 consecutive patients were recruited. AxSpA was diagnosed by the rheumatologists in 131 patients (43.7%) with mean age of 34.5±7.2 years, 73% HLA-B27+, mean symptom duration 58.6±69.5 months, vs. 169 non-SpA patients with mean age of 34.5±7.4 years, 21.3% HLA-B27+, mean symptom duration 33.9±45.1 months. The ASAS classification criteria were fulfilled by 99/131 patients diagnosed with axSpA (75.6%) vs. 70/169 patients diagnosed vs. non-SpA non-SpA (41.4%).

In 97/162 patients, rheumatologists and radiologists agreed on a diagnosis of axSpA and in the same number (97/162) there was agreement for non-SpA (overall agreement: 86.3%). However, 34/131 (28.1%) patients were diagnosed with axSpA by rheumatologists but not by radiologists.

According to radiologists, BME alone was critical for diagnosis in only 7/97 patients (7.2%) with axSpA as agreed by both, rheumatologists and radiologists, in contrast to chronic lesions alone (30/97, 30.9%) or the combination of both lesion types (60/97, 61.9%).

While the sensitivity of BME for diagnosing axSpA did not change, the specificity improved when chronic lesions were also present (Tab.1). In addition, based on rheumatologists´ diagnosis, the respective odds ratio (OR) for identifying axSpA by MRI was higher when chronic lesions were present (Tab.1). MRI scores were significantly higher in axSpA vs. non-SpA patients, indicating that axSpA is associated with deeper BME or chronic lesions (Tab.2).

Conclusion: The combination of structural changes and BME lesions as assessed by MRI performed best in the process of identifying axSpA in consecutive patients in a real-life setting. The discrepancy in diagnosis between rheumatologists and radiologists reflects the increasing insecurity of including only BME of SIJ as the major criterium for diagnosing axSpA.

Reference:

1. Lambert R et al. Ann Rheum Dis 2016

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Abstract Number: 0856

MRI of the Sacroiliac Joints in Athletes: Do Semi-axial Slices Added to Standard Semi-coronal Scans Facilitate Recognition of Non-specific Bone Marrow Edema?

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical I: Imaging in Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Low grade bone marrow edema (BME) on magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ) is challenging the discrimination between patients with early axial spondyloarthritis (SpA) and mechanical back pain. In our previous analysis, recreational and elite athletes had on average 3-4 SIJ quadrants with BME, and 30-41% met the Assessment of SpondyloArthritis international Society (ASAS) definition of active sacroiliitis [1]. Potential conditions simulating SIJ BME such as vascular partial volume effect or anatomical SIJ variants could not be explored due to standard semi-coronal MRI scans only. Our goals by assessing combined semi-axial and semi-coronal SIJ MRI scans in 2 cohorts of young athletes were to explore the frequency and topography of non-specific BME by 2 perpendicular MRI planes, its association with 4 constitutional SIJ features, and potential limitation of false positive assignments of ASAS-defined sacroiliitis by standard semi-coronal scans alone.

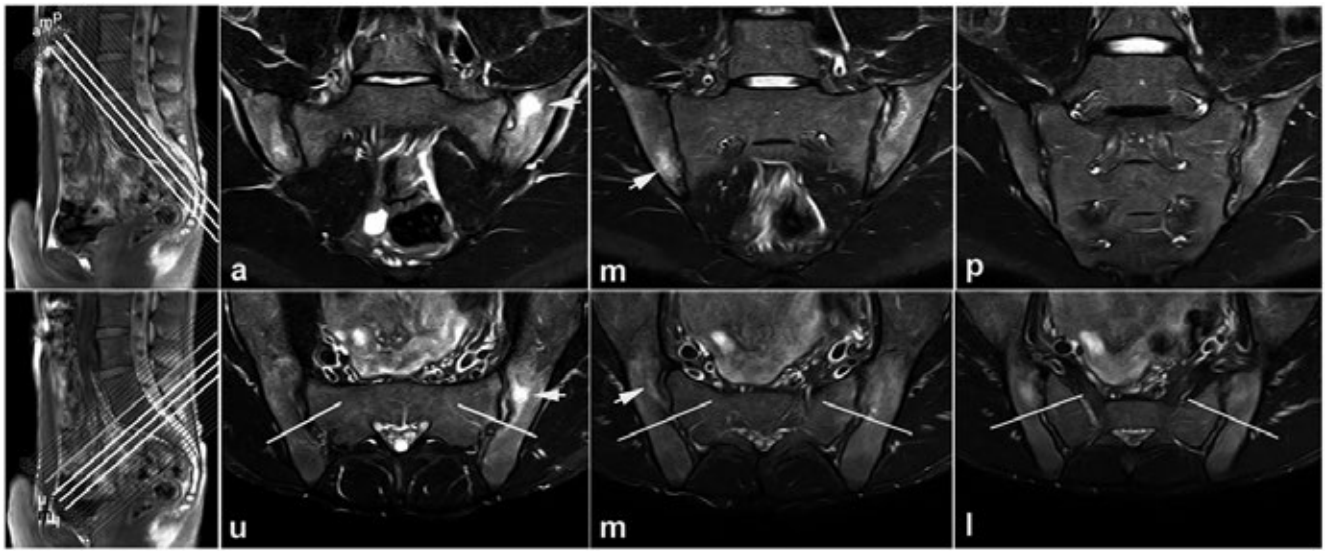

Figure 1. SIJ MRI with semi-coronal (upper row) and semi-axial (lower row) scans. Scout lines on the left panel visualize the orientation of the 2 perpendicular planes. Arrows indicate subchondral BME in corresponding anatomic location on both planes in a patient with axial SpA.

Table 1

	Runners before running (n=20)	Runners after running (n=20)	Ice-hockey players (n=22)
BME			
BME on 2 planes: n (%)	5 (25.0)	5 (25.0)	6 (27.3)
BME on semi-coronal plane[1]: n (%)	7 (35.0)	6 (30.0)	9 (40.9)
BME on 2 planes and BME on semi-coronal plane[1]: n (%)	4 (20.0)	4 (20.0)	4 (18.2)
BME on 2 planes but not on semi-coronal plane[1]: n (%)	1 (5.0)	1 (5.0)	2 (9.1)
BME on semi-coronal plane[1] but not on 2 planes: n (%)	3 (15.0)	2 (10.0)	5 (22.7)
Constitutional sacroiliac joint feature			
≥1 sacroiliac joint feature: n (%)	6 (30.0)	4 (20.0)	8 (36.4)
≥2 sacroiliac joint features: n (%)	0	0	1 (4.5)
Vascular partial volume effect: n (%)	2 (10.0)	1 (5.0)	4 (18.2)
Deep iliac ligament insertion: n (%)	3 (15.0)	2 (10.0)	2 (9.1)
Fluid-filled bone cyst: n (%)	0	0	2 (9.1)
Lumbosacral transitional anomaly: n (%)	1 (5.0)	1 (5.0)	1 (4.5)

Table 1. Frequency of sacroiliac joint BME on 2 perpendicular MRI planes versus on standard semi-coronal scans fulfilling the ASAS definition of active sacroiliitis, and frequency of BME associated with 4 constitutional sacroiliac joint features. n (%): number of subjects (percentage) showing a given feature as concordantly reported by ≥2/3 readers.

Methods: Combined semi-axial and semi-coronal SIJ MRI scans of 20 recreational runners before/after running and 22 elite ice-hockey players were evaluated by 3 blinded readers for BME and its association with 4 constitutional SIJ features: vascular partial volume effect, deep iliac ligament insertion, fluid-filled bone cyst, and lumbosacral transitional anomaly. Scans of TNF-treated SpA patients served to mask readers. Pre-test reader agreement for BME on semi-axial scans was calculated by single measure, absolute agreement intraclass correlation coefficient (ICC). We analysed distribution and topography of BME and associated constitutional SIJ features across 8 anatomical SIJ regions (upper/lower ilium/sacrum, subdivided in anterior/posterior slices) descriptively, as concordantly recorded by ≥2/3 readers on both MRI planes. BME confirmed on both scans was compared with previous evaluation of semi-coronal MRI alone which met the ASAS definition for active sacroiliitis.

Results: ICC agreement among 3 readers for semi-axial SIJ BME was 0.86 (0.72-0.95). Perpendicular semi-axial and semi-coronal MRI scans confirmed SIJ BME consistently in 25% and 27% of athletes, preferentially in the anterior upper sacrum. BME associated with 4 constitutional SIJ features was observed in 20-36% of athletes, clustering in the posterior lower ilium. The proportion of ASAS-positive sacroiliitis recorded on semi-coronal plane alone decreased by 30-50% upon amending semi-axial scans (from 30-35% to 20% in runners, from 41% to 18% in ice-hockey players).

Conclusion: Semi-axial combined with standard semi-coronal scans in MRI protocols for sacroiliitis facilitated recognition of non-specific BME, which clustered in the posterior lower ilium in association with constitutional SIJ features, and in the anterior upper sacrum. The proportion of false-positive ASAS assignments of sacroiliitis recorded on semi-coronal plane alone could be substantially reduced by amending semi-axial scans.

Reference:

1. Weber U et al. Arthritis Rheum 2018;70:736.

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Abstract Number: 0857

Mesenchymal Stem Cell Therapy Induces FLT3L and CD1c$^+$ Dendritic Cells in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION
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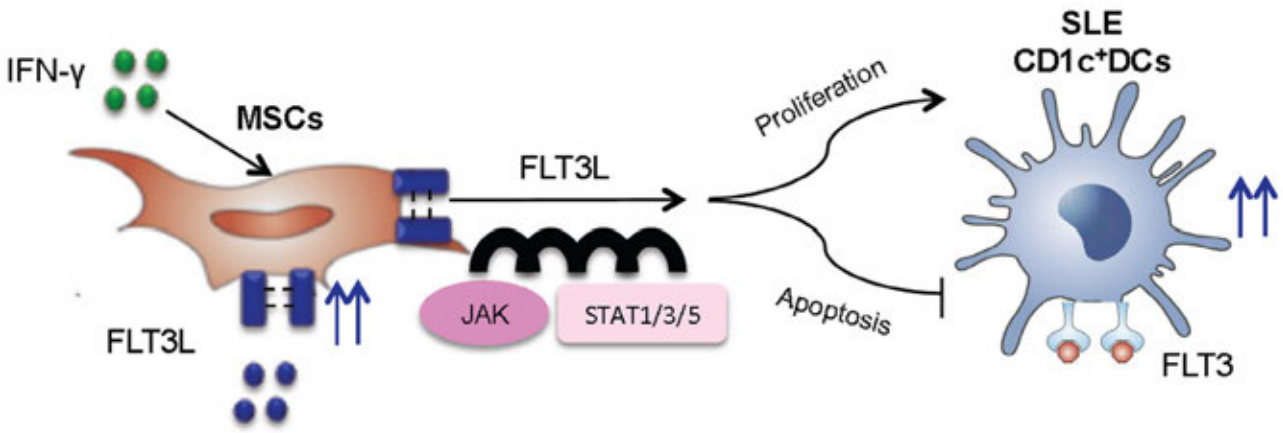
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Allogeneic mesenchymal stem cells (MSCs) exhibit immunoregulatory function in human autoimmune diseases such as systemic lupus erythematosus (SLE), but the underlying mechanisms remain incompletely understood.



Methods: Totally, 166 SLE patients and 78 healthy subjects were included in this study. Tolerogenic DCs were isolated as Lin(CD3/19/56/14)$^-$ HLA DR$^+$CD11c$^+$CD1c$^+$ from peripheral blood mononuclear cells (PBMCs). Level of tolerogenic DCs was determined by flow cytometry, and serum concentration of FLT3L was assessed by ELISA from healthy controls and SLE patients. Twenty-one SLE patients were given MSCs infusions. We compared the number and function of tolerogenic DCs, as well as serum FLT3L before and after MSCs transplantation. PBMCs from SLE patients were collected and co-cultured with MSCs, to detect the number and function of tolerogenic DCs. The level of FLT3L in the supernatant solution was analyzed. FLT3L siRNA was added to the co-culture system, and the level of tolerogenic DCs was detected.

Results: Here we show that the number of peripheral tolerogenic CD1c$^+$ dendritic cells (DCs) and the levels of serum FLT3L are significantly decreased in SLE patients especially with lupus nephritis, compared to healthy controls. Transplantation of allogeneic umbilical cord-derived MSCs (UC-MSCs) significantly up-regulates peripheral blood CD1c$^+$DCs and serum FLT3L. Mechanistically, UC-MSCs express FLT3L that binds to FLT3 on CD1c$^+$DCs to promote the proliferation and inhibit the apoptosis of tolerogenic CD1c$^+$DCs. Conversely, reduction of FLT3L with small interfering RNA in MSCs abolishes the up-regulation of tolerogenic CD1c$^+$DCs in lupus patients treated with MSCs. Interferon-γ induces FLT3L expression in UC-MSCs through JAK/STAT signaling pathway.

Conclusion: In summary, allogeneic MSCs might suppress inflammation in lupus through up-regulating tolerogenic DCs.

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Abstract Number: 0858

Adverse Events of Special Interest, SLE Medication Utilization, Hospitalizations, and Organ Damage: Results from a Phase 4, Randomized, Double-Blind, Placebo-Controlled, 52-week Study of Belimumab in Adults with Active, Autoantibody-Positive SLE

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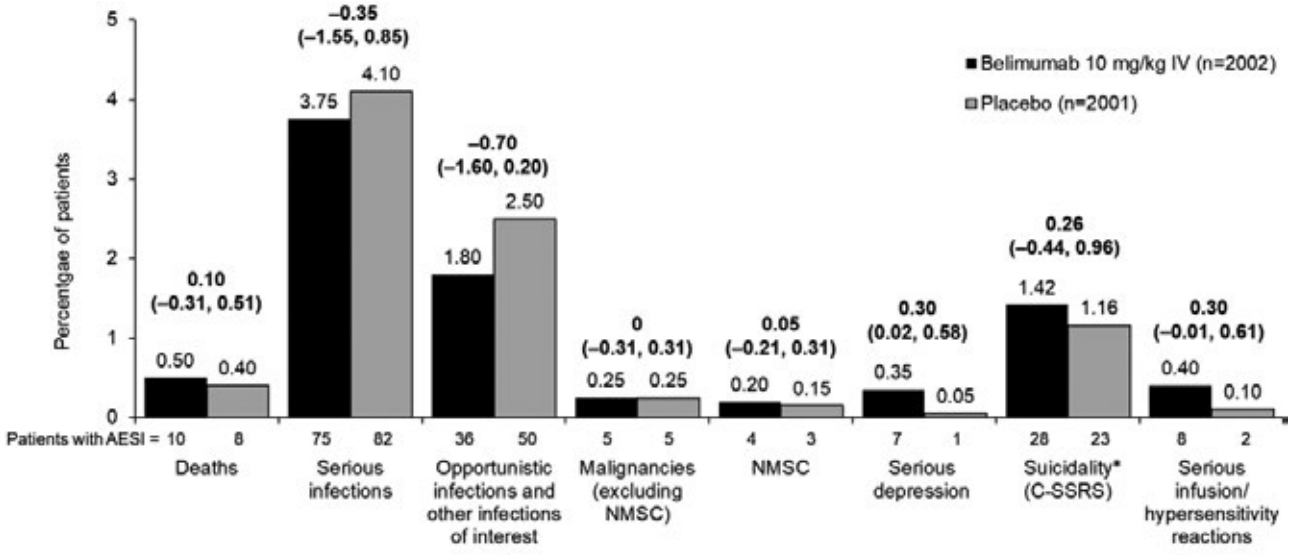
Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM



*Treatment-emergent suicidal ideation/behavior; belimumab: n=1972, placebo: n=1986.
Difference in % (95% CI) vs placebo displayed above bars. One patient was randomized to placebo but incorrectly received belimumab for >50% of doses, so is included in the belimumab arm for safety analyses (as-treated population).
CI, confidence interval; C-SSRS, Columbia-Suicide Severity Rating Scale; NMSC, non-melanoma skin cancer.

Figure. Prespecified AESI endpoints in the BASE study (on-treatment period: as-treated population)

Background/Purpose: Belimumab (BEL), approved in active, autoantibody-positive SLE, has demonstrated a positive efficacy/safety profile while suggesting potential for steroid sparing and reduced organ damage accrual. BASE, a placebo-controlled study, evaluated all-cause mortality and adverse events of special interest (AESIs), and limited efficacy endpoints.

Methods: Adults who met ACR SLE criteria were randomized (1:1) to monthly BEL 10 mg/kg IV or placebo (PBO) plus standard of care for 48 weeks. There was no minimum disease activity required or exclusions for psychiatric conditions, and no protocol mandated corticosteroid (CS) taper or assessment of change in disease activity. For primary endpoints of mortality and AESIs (reported previously), differences in rates (95% CI) were assessed vs PBO on-treatment (first to last dose +28 days). Serious suicidal ideation/behavior and self-injury events on-treatment, and C-SSRS suicidal ideation/behavior on-study (first dose to end of Week 52 follow up) were assessed (differences calculated *post hoc*). Percentages of patients with baseline CS dose >7.5 mg/day whose dose to treat SLE reduced by ≥25% to ≤7.5 mg/day (Weeks 40−52), SLE immunomodulator use (baseline vs treatment completion), study hospitalizations, and organ damage accrual (Week 52), were assessed.

Results: Baseline demographics and disease activity/characteristics were similar between groups. All-cause mortality was also similar (**Figure**); most deaths were due to infections (9 [0.45%] BEL, 3 [0.15%] PBO). On-study deaths occurred in 13 (0.65%) BEL and 22 (1.10%) PBO patients (difference [95% CI]: –0.45 [–1.03, 0.13]). Rates of on-treatment AESIs were similar, except for serious depression and serious infusion/hypersensitivity reactions (**Figure**).

On-treatment serious suicidal ideation/behavior and self-injury sponsor-adjudicated events occurred in 15 (0.75%) BEL and 5 (0.25%) PBO patients (difference [95% CI]: 0.50 [0.06, 0.94]); on-study suicidal ideation/behavior (C-SSRS) occurred in 48 (2.43%) BEL and 39 (1.96%) PBO patients (difference [95% CI]: 0.47 [–0.44, 1.38]). There were no suicide-related deaths.

Efficacy endpoints were assessed in those receiving ≥1 dose (intent-to-treat; 2001 BEL, 2002 PBO). More BEL vs PBO patients had a SLE CS dose reduction (**Table**). SLE immunomodulator use did not change vs baseline. Hospitalizations were similar between groups. BEL impact on organ damage, if any, was minimal.

Conclusion: In the largest, double-blind, placebo-controlled SLE study to date, on-treatment all-cause mortality, infection, and malignancy AESI rates were similar between BEL and PBO; imbalances were observed in serious depression, serious suicidal ideation/behavior and self-injury events, and serious infusion/hypersensitivity reactions. BEL reduced SLE CS use in high-dose patients; the effect was small and without supporting parallel disease activity measures. There was no change in SLE immunomodulator use, no differences in hospitalizations, and organ damage impact was minimal, as in other BEL studies.

n/N (%)	Placebo (n=2002)	Belimumab 10 mg/kg IV (n=2001)	Odds ratio vs PBO (95% CI)
Corticosteroid (to treat SLE) dose reduction of ≥25% to ≤7.5 mg/day during Weeks 40–52*	160/990 (16.2)	196/986 (19.9)	1.30 (1.03, 1.65); p=0.0284
SLE immunomodulatory agents†			
Baseline	813/1646 (49.4)	830/1655 (50.2)	NA
Treatment completion	810/1646 (49.2)	808/1655 (48.8)	NA
Hospitalized during the study	221/2002 (11.0)	208/2001 (10.4)	NA
Patients with organ damage (SLICC/ACR Damage index; SDI) worsening‡	52/1631 (3.2)	45/1630 (2.8)	0.87 (0.58, 1.31); p=0.5033

*Of those receiving >7.5 mg/day at baseline (prednisone equivalent); †in treatment completers; ‡in treatment completers with an assessment at baseline and Week 52. ITT, intent-to-treat; NA, not assessed.

Table. Efficacy endpoints in the BASE study (ITT population)

We acknowledge the BASE participants and Study Group. Study funding: GSK. Medical writing support: Louisa McKay, PhD, Fishawack Indicia Ltd, UK (funded by GSK).

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Abstract Number: 0859

Long-term Outcome of a Randomized Controlled Trial Comparing Tacrolimus with Mycophenolate Mofetil as Induction Therapy of Severe Lupus Nephritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical I: Clinical Trials
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: To report the 10-year outcome of patients with lupus nephritis (LN) treated with combined prednisolone with mycophenolate mofetil (MMF) or tacrolimus (TAC) as induction in a randomized controlled trial (RCT).

Methods: Patients with active LN were randomized to receive MMF (2-3g/day) (N=76) or TAC (0.1-0.06mg/kg/day) (N=74) in combination with high-dose prednisolone (0.6mg/kg/day for 6-8 weeks and tapered) as induction therapy between 2005 and 2012. Complete renal (CR) or good partial renal responders were switched to azathioprine (AZA) (2mg/kg/day) for maintenance. We hereby report the 10-year outcomes of the patients in terms of renal flares (proteinuric/nephritic), renal function decline (drop in eGFR by ≥30% from baseline), development of chronic kidney disease (CKD) stage 4/5 (eGFR< 30ml/min) and mortality. Factors affecting renal prognosis were studied by Cox regression analysis. Renal parameters (urine P/Cr ratio [uPCr], eGFR) at different time points from 6 to 24 months were studied for their predictive value of a poor renal prognosis by ROC analysis.

Results: 150 patients (92% women) were studied (age 35.5±12.8 years, ISN/RPS class III±V 36%; IVG/S±V 46%; pure V 19%, activity and chronicity score 8.2±3.4 and 2.6±1.6, respectively). At entry, 67% patients had eGFR< 90ml/min. The rate of CR at 6m was 59% in MMF and 62% in the TAC group (p=0.71). Maintenance AZA was given to 79% patients. After a follow-up of 118.2±42 months, proteinuric and nephritic renal flares occurred in 34% and 37% of

patients treated with MMF and 53% and 30% in those treated with TAC, respectively. There was a total of 77 renal flares in 43 (57%) MMF-treated patients (0.11/patient-year) and 92 renal flares in 46 (62%) patients treated with TAC (0.12/patient-year; p=0.44). The cumulative risk of renal flare in patients treated with MMF/AZA was 28% at 3 years, 42% at 5 years and 58% at 10 years, whereas the corresponding figures for those treated with TAC/AZA was 32% at 3 years, 53% in 5 years and 66% in 10 years (p=0.43). Time to first renal flare was 70.4±47.1 months in MMF group and 65.2 ±50 months in the TAC group (p=0.61). The cumulative incidence of a composite outcome of eGFR decline by ≥30%, development of CKD stage 4/5 or death at 5 and 10 years was 24% and 33%, respectively, in patients treated with MMF, and 17% and 33%, respectively, in those treated with TAC (p=0.90). Factors significantly associated with this outcome were first time lupus nephritis (HR 0.26[0.11-0.59]; p=0.001), uPCR at 6m (HR 1.33[1.02-1.76]; p=0.04) and eGFR at 6m (HR 0.98[0.97-0.997]; p=0.02). ROC analysis demonstrated that an eGFR cut-off of 80ml/min (AUC 0.70; sensitivity 0.64, specificity 0.66) and uPCR cut-off of 0.75 (AUC 0.73; sensitivity 0.69, specificity 0.74) at month 18 best predicted CKD stage 4/5 or decline of eGFR by ≥30%.

Conclusion: Long-term data of our RCT showed that TAC remained non-inferior to MMF as induction therapy of LN in terms of renal flares, renal function decline and mortality. Relapsed renal disease, lower eGFR and more proteinuria post-induction therapy were associated with a poorer outcome. An uPCR ≤0.75 and eGFR of >80ml/min at 18 months best predicted a better outcome at 10 years, and should be considered as a target for induction/consolidation therapy.

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Abstract Number: 0860

Efficacy of Belimumab in Patients of Black Race with Systemic Lupus Erythematosus and High Disease Activity or Renal Manifestations

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SESSION INFORMATION
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Session Title: SLE – Clinical I: Clinical Trials
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Background/Purpose: Black patients have more severe SLE and more frequent lupus nephritis vs other racial groups. Efficacy and safety of intravenous (IV) belimumab was demonstrated in three Phase 3 SLE studies; few black patients were included, limiting subgroup analyses. The EMBRACE study assessed efficacy and safety of IV belimumab plus standard of care (SoC) in black patients with SLE. Primary and key secondary endpoints have been presented;[1] here we focus on efficacy in patients with high disease activity (HDA) and renal manifestations.

Methods: EMBRACE (NCT01632241; GSK study 115471) is a multicenter, double-blind, placebo-controlled trial in patients of self-identified black race, ≥18 years, with active SLE by ACR criteria at screening. Patients were randomized (2:1) to receive monthly belimumab 10 mg/kg IV or placebo, plus SoC. The primary endpoint was the difference in modified SLE Responder Index (SRI-S2K) response rates between belimumab and placebo. SRI-S2K incorporates the SLEDAI-2K (S2K) proteinuria definition (>0.5 mg/24 h) rather than the SELENA-SLEDAI (SS) version (>0.5 mg/24-h

increase). A response is defined as ≥4-point reduction in S2K, no worsening [increase < 0.3] in Physician's Global Assessment, and no new BILAG A/2 B domain scores. SRI response (SS proteinuria scoring) at Week 52 was a key secondary endpoint. Subgroup analyses of SRI-S2K and SRI in patients with HDA (anti-dsDNA antibody positive, hypocomplementemia, or high SS-S2K scores [SS with S2K proteinuria scoring]) at baseline were performed. Other endpoints included time to renal flare, change from baseline in SS-S2K renal domain, and in proteinuria, over 52 weeks.

Results: No significant differences were seen in the mITT population (N=448) for SRI-S2K (**Table**). Among patients meeting HDA definitions at baseline, greater proportions were SRI-S2K responders at Week 52 with belimumab vs placebo; in the high anti-dsDNA group, the difference numerically favored belimumab. Similar results were observed with the SRI.

Belimumab patients (mITT) had a 46% lower risk of a renal flare vs placebo (hazard ratio [95% CI]: 0.54 [0.21, 1.36]; p=0.1880). Among those with baseline renal involvement measured by SS-S2K, numerically more belimumab patients experienced improvements in this domain at Week 52 vs placebo (23/55 [41.8%] vs 7/34 [20.6%]). Among those without baseline renal involvement measured by SS-S2K, the percentage worsening at Week 52 was low for both groups (placebo: 9/115 [7.8%], belimumab: 15/244 [6.1%]). In patients with baseline proteinuria >0.5 g/24 h, median (interquartile range) percentage reduction at Week 52 was numerically greater with belimumab (-65.3% [-81.1, -38.8%], n=38) vs placebo (-32.9% [-76.6, 36.3%], n=23; p=0.0558); more of these patients experienced proteinuria normalization (values ≤0.5 g/24 h) with belimumab (16/38 [42.1%]) vs placebo (6/23 [26.1%]) at Week 52. No new safety concerns were identified.

Conclusion: Black patients with SLE and HDA demonstrate benefits with belimumab vs placebo, with reductions in disease activity and SLEDAI renal domain scores.

Reference:

1. D'Cruz D et al *Lupus Sci Med* 2019;6.

	SRI-S2K response rate (n [%])		OR (95% CI) vs placebo
	Placebo (n=149)	Belimumab 10 mg/kg IV (n=299)	
Total mITT population (n=149 vs 298)	62 (41.6)	145 (48.7)	1.40 (0.93, 2.11) p=0.1068
SS-S2K score at baseline			
Score: ≥10 (n=93 vs 158)	38 (40.9)	83 (52.5)	1.76 (1.03, 3.00) **p=0.0384**
Score: ≤9 (n=56 vs 140)	24 (42.9)	62 (44.3)	0.97 (0.51, 1.85) p=0.9198
Anti-dsDNA at baseline			
Anti-dsDNA ≥30 IU/mL (n=99 vs 181)	36 (36.4)	84 (46.4)	1.60 (0.95, 2.68) p=0.0743
Anti-dsDNA <30 IU/mL (n=50 vs 117)	26 (52.0)	61 (52.1)	1.05 (0.52, 2.11) p=0.8892
C3 and/or C4 at baseline			
Low C3 or C4 (n=57 vs 108)	14 (24.6)	51 (47.2)	3.00 (1.45, 6.23) **p=0.0031**
Without low C3 or C4 (n=92 vs 190)	48 (52.2)	94 (49.5)	0.92 (0.55, 1.54) p=0.7554
C3/C4 and anti-dsDNA at baseline			
Low C3 or C4 and anti-dsDNA ≥30 IU/mL (n=50 vs 91)	12 (24.0)	41 (45.1)	3.00 (1.35, 6.68) **p=0.0072**
Without C3 or C4 and anti-dsDNA ≥30 IU/mL (n=99 vs 207)	50 (50.5)	104 (50.2)	1.01 (0.62, 1.66) p=0.9556

C, complement; CI, confidence interval; dsDNA, double-stranded DNA; mITT, modified intent-to-treat; OR, odds ratio

Table. Efficacy in patients meeting HDA definitions at baseline: SRI-S2K response (primary endpoint) at Week 52 subgroup analyses

Study funding: GSK. Medical writing support: Louisa McKay, PhD, Fishawack Indicia Ltd, UK (funded by GSK).

Disclosure: L. Sergio Guedes Barbosa, None; **A. Saxena**, AstraZeneca, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, GlaxoSmithKline, 5, GSK, 5; **E. Ginzler**, Ablynx, 5, Aurinia, 2, Genentech, 2, GlaxoSmithKline, 2, Guidepoint Global Gerson Lerman Group, 5, Janssen, 5; **R. Furie**, Biogen, 5, GlaxoSmithKline, 2, 5, UCB Pharma, 2, 5; **D. D'Cruz**, AstraZeneca, Bristol-Myers Squibb, 2, 5, Eli Lilly, Eli Lily, 2, 5, GlaxoSmithKline, 2, 5, Human Genome Sciences, 5, Idorsia, Merck Serono, 2, 5, Pfizer, Roche, 5, TEVA, 2, 5; **S. Burriss**, GlaxoSmithKline, 1, 3; **J. Gilbride**, GlaxoSmithKline, 1, 3; **M. Miller**, GlaxoSmithKline, 1, 3; **J. Groark**, GlaxoSmithKline, 1, 3; **D. Roth**, GlaxoSmithKline, 1, 3, 4; **B. Ji**, GlaxoSmithKline, 1, 3, 4.

Abstract Number: 0861

Cutaneous Lupus Erythematosus Disease Area & Severity Index (CLASI) Demonstrates Thresholds for Detection of Treatment Response in a Phase-2, Placebo-Controlled Trial of Ustekinumab in SLE

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SESSION INFORMATION
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Session Title: SLE – Clinical I: Clinical Trials
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Ustekinumab (UST), an anti-IL-12/23 p40 monoclonal antibody, showed significantly greater improvement at week (wk) 24 compared with placebo (PBO) in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) response (≥4-point improvement from baseline, BL) in a Phase 2 study.[1] Post hoc analysis revealed more UST than PBO patients (pts) achieving ≥50% improvement in total Cutaneous Lupus Erythematosus Disease Area & Severity Index (CLASI) activity score. Harmonization of measures of disease activity and improvement in SLE trials is important since the same clinical manifestations are defined differently among various assessment indices. Here, we examine the relationships of CLASI activity responses to SLEDAI-2K (S2K) mucocutaneous disease responses.

Methods: This phase 2 study enrolled adults with active SLE (S2K ≥6, ≥1 BILAG A and/or ≥2 BILAG B scores) despite standard of care therapy. Pts (n=102) were randomized (3:2) to UST IV ~6 mg/kg or PBO at wk 0, followed by SC injections of UST 90 mg or PBO every 8 wks beginning at wk 8, both added to standard of care. The S2K index, used in this analysis, measures complete improvement from BL. S2K Responder Index-50 (S2K RI-50) evaluates partial improvement and was used to assess partial (≥50%) improvement in S2K rash. CLASI rash was defined as the sum of erythema and scale/hypertrophy score. Independent adjudication of SLE assessments was performed to ensure medical plausibility and consistency of SLE disease activity scores in conjunction with all relevant pt data. In post hoc analysis, improvement in CLASI total activity score at wk 24 was calculated using increasing thresholds of BL disease activity and various cut points of improvement to define treatment response.

Results: Complete improvement from BL in rash was concordant between CLASI and S2K (correlation coefficients ≥0.997, Table 1). There was less agreement between CLASI and S2K RI-50 when assessing partial improvement

Table 1. CLASI Activity Scores Compared with SLEDAI-2K Activity

24-Week Improvement	Treatment	Activity Measure % (n/N*)		Correlation Coefficient **
		CLASI Rash†	SLEDAI-2K Rash‡	
100%	Placebo	30.8% (8/26)	30.8% (8/26)	1.0000
	Ustekinumab	28.9% (13/45)	31.1% (14/45)	0.9997
≥50%	Placebo	38.5% (10/26)	50.0% (13/26)	0.9996
	Ustekinumab	60.0% (27/45)	51.1% (23/45)	0.8693
		CLASI Mucosal Ulcer	SLEDAI-2K Mucosal Ulcer	
100%	Placebo	66.7% (8/12)	69.2% (9/13)	1.0000
	Ustekinumab	89.5% (17/19)	89.5% (17/19)	1.0000

*N=Evaluated populations with baseline SLEDAI rash present, total CLASI activity score >0, and CLASI rash or mucosal ulcer activity scores >0 in analyses of subcomponents;
**Correlation coefficients were calculated using tetrachoric correlation; †CLASI Rash = sum of erythema and scale/hypertrophy measure; ‡The SLEDAI-2K index was used to assess 100% improvement from baseline in SLEDAI-2K rash. SLEDAI-2K Responder Index-50 (S2K RI-50), was used to assess partial improvement (≥50% but less than 100% improvement) from baseline in SLEDAI-2K rash based on the percentage of body surface area involved.

in rash. A treatment difference (UST vs PBO) in the proportion of pts achieving partial improvement in rash was observed for CLASI (60% UST vs PBO 38.5%), but not S2K RI-50 (51.1% UST vs 50% PBO) (Table 1). Complete improvement from BL in mucosal ulceration was congruent between CLASI and S2K (correlation coefficient=1). Both instruments demonstrated greater proportions of responders to UST compared with PBO (Table 1). Treatment differences between UST and PBO in achievement of ≥20%, ≥35%, and ≥50% improvement from BL in total CLASI activity score were noteworthy at various thresholds of BL disease activity (Table 2).

Conclusion: CLASI was able to demonstrate partial improvement in active mucocutaneous disease that was not captured by S2K RI-50. A treatment effect favoring UST vs PBO was observed across a range of thresholds of BL CLASI activity and various cut points used to define improvement, which have previously been shown to be clinically meaningful.[2] While these findings are based on a limited sample size and duration of therapy, the results will be confirmed in an ongoing Phase 3 clinical trial of UST in SLE (NCT03517722).

References:

1. Van Vollenhoven *Lancet*. 2018;392:1330.
2. Chakka S. J Invest Dermatol 139: S101 (abstract #587), 2019.

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Abstract Number: 0862

First Use of Cenerimod, a Selective sphingosine-1-phosphate 1 ($S1P_1$) Receptor Modulator, for the Treatment of Systemic Lupus Erythematosus: A Double-Blind, Randomised, Placebo-Controlled, Phase II, Proof-of-Concept Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical I: Clinical Trials
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Aberrantly activated T- and B-lymphocytes play a major pathophysiological role in SLE. Cenerimod, a potent, selective sphingosine-1-phosphate 1 receptor modulator, blocks the egress of lymphocytes from lymphoid organs, thereby reducing their availability, thus providing rationale for development. The study investigated the effect of cenerimod on circulating lymphocytes, disease activity, safety and pharmacokinetics in SLE patients.

Methods: This study was conducted in two parts, separated by a safety review. Patients with SLEDAI-2K score ≥2 points for mucocutaneous or musculoskeletal manifestations and positive serum test for ANA or anti-dsDNA antibodies were randomised evenly in Part A to cenerimod 0.5, 1, or 2 mg or placebo once daily (QD) and 3:1 in Part B to cenerimod 4 mg or placebo QD and treated for 12 weeks. Predefined Day 1 safety assessments included heart rate (HR) monitoring and hourly 12-lead ECG monitoring (pre dose, to 6 hours post-dose). Endpoints included treatment-emergent adverse events (TEAEs), changes in total lymphocyte count, SLEDAI-2K score (modified [mSLEDAI] to exclude leucopoenia), biomarker anti-dsDNA antibody and pharmacokinetic assessments. All 67 patients (A: 49; B: 18) met at least 4 ACR criteria in the past, 70% had 4 to 11 ACR criteria ongoing at screening. Mean (SD) mSLEDAI-2K was 7.7 (±3.1) at baseline.

Table 2. Treatment Differences in Achievement of Partial Improvement in Total CLASI Activity Score at Various Thresholds of Baseline Disease Activity

Activity Measure	Improvement Threshold	Placebo % (n/N*)	Ustekinumab % (n/N*)	Difference % (UST vs PBO)
CLASI Total	≥20%	54.8 (17/31)	74.5 (38/51)	19.7
Activity Score	≥35%	41.9 (13/31)	60.8 (31/51)	18.9
Baseline >0	≥50%	41.9 (13/31)	54.9 (28/51)	13.0
CLASI Total	≥20%	58.8 (10/17)	71.9 (23/32)	13.1
Activity Score	≥35%	35.3 (6/17)	62.5 (20/32)	27.2
Baseline ≥4	≥50%	35.3 (6/17)	53.1 (17/32)	17.8
CLASI Total	≥20%	53.8 (7/13)	72.0 (18/25)	18.2
Activity Score	≥35%	30.8 (4/13)	60.0 (15/25)	29.2
Baseline ≥6	≥50%	30.8 (4/13)	52.0 (13/25)	21.2
CLASI Total	≥20%	58.3 (7/12)	70.6 (12/17)	12.3
Activity Score	≥35%	33.3 (4/12)	58.8 (10/17)	25.5
Baseline ≥8	≥50%	33.3 (4/12)	47.1 (8/17)	13.8

*N=Evaluated populations with baseline total CLASI activity score >0, ≥4, ≥6, ≥8 based on post hoc analyses. Values for subjects meeting treatment failure criteria were set to missing from the point of treatment failure forward

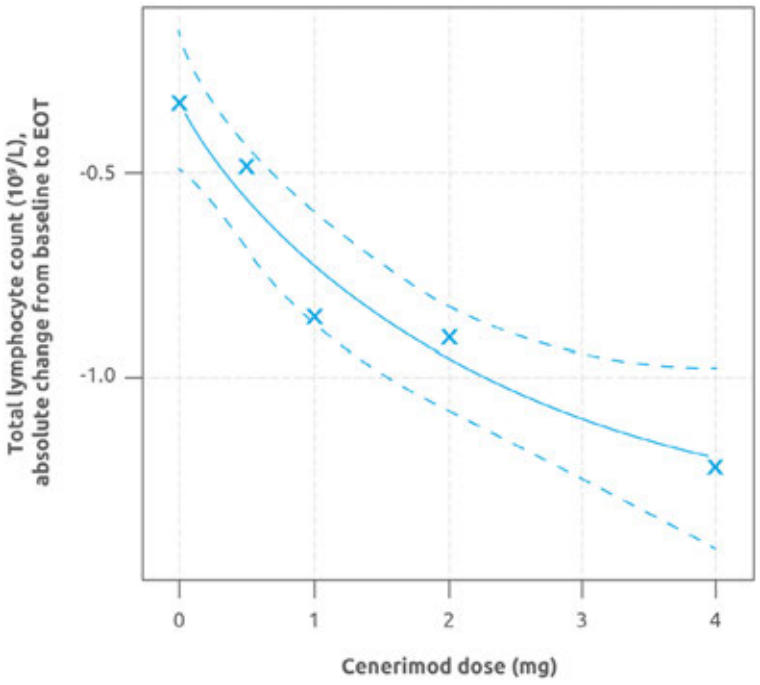

Figure 1. Estimation of dose-response relationship for absolute change from baseline to end of treatment. The MCP-Mod approach was performed for each of the five considered dose-response models. Plot shows the maximum effect (Emax) curve, with 95% CI (dashed lines), related to the model with the highest t-statistic. CI, confidence intervals; EOT, end of treatment; MCP-Mod, Multiple Comparison Procedure and Modelling.

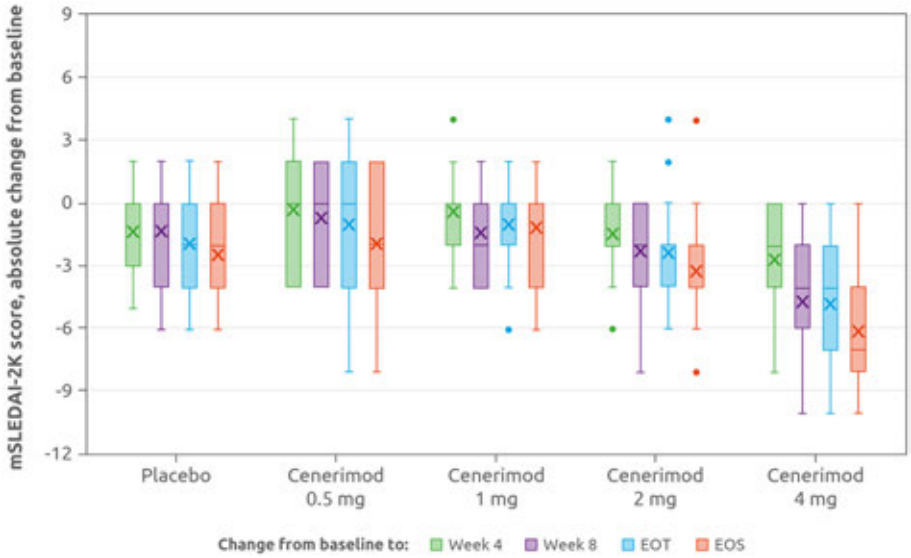

Figure 2. Absolute change from baseline in mSLEDAI-2K score. Box and whisker plot indicates the interquartile range (box), upper and lower 1.5 interquartile range (whiskers), mean and median (cross and horizontal line, respectively, within the box), and outliers at least above or below 1.5 times the interquartile range (dots). mSLEDAI-2K modified to exclude leucopoenia. EOS, end of study; EOT, end of treatment; mSLEDAI-2K, modified SLE Disease Activity Index-2000.

Results: Part A included 49 patients (12:12:13:12 receiving cenerimod 0.5, 1, 2 mg or placebo); Part B included 18 (13 cenerimod 4 mg; 5 placebo). Cenerimod dose-dependently reduced total lymphocyte count from baseline to end of treatment (EOT; $p< 0.001$; Figure 1). In pairwise comparisons, cenerimod 1, 2, and 4 mg significantly decreased lymphocytes versus placebo (all $p< 0.001$). Exploratory analyses indicated clinical and biological improvement with

cenerimod 4 mg with an estimated mean treatment effect on change from baseline to EOT in mSLEDAI-2K score of –2.420 (p=0.0306; Figure 2), and a decrease in anti-dsDNA of –28.80 U/mL (p=0.0146) compared with placebo. All treatment groups reported similar and non-dose-related rates of TEAEs (cenerimod 0.5: 41.7%; 1: 41.7%; 2: 46.2%; 4 mg: 38.5%; and placebo: 58.8%). After the first dose, cenerimod induced minimal, transient and dose-dependent decreases in HR; no patient had an HR < 40 bpm at any time post baseline. Small decreases in pulmonary function, not dose-related, were observed in cenerimod-treated patients at EOT. Cenerimod did not increase blood pressure or show any effects on laboratory variables. Trough plasma concentrations revealed steady-state conditions were reached after 4–8 weeks of QD dosing and dose-proportionality was observed.

Conclusion: Cenerimod has the potential to be a new therapeutic approach for patients with SLE and has shown to date an acceptable efficacy and safety profile with minimal, non-clinically relevant cardiovascular effects. These results warrant further evaluation in a larger study over a longer treatment duration. A Phase IIb, randomised dose-finding study was initiated in December 2018 to evaluate efficacy and safety of cenerimod in addition to background therapy in moderate-to-severe SLE (NCT03742037).

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Abstract Number: 0863

Tofacitinib in Early Diffuse Cutaneous Systemic Sclerosis— Results of Phase I/II Investigator-Initiated, Double-Blind Randomized Placebo-Controlled Trial

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorder – Clinical I: Therapeutics & Outcomes
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Tofacitinib (TOFA) is a potent pan inhibitor of the Janus Kinase (JAK) family of kinases with a high degree of selectivity against JAK1 and JAK3 more than TYK2 or JAK2. This Phase I/II trial assessed the safety of TOFA 5 mg twice a day versus placebo (PLA) in diffuse cutaneous systemic sclerosis (dcSSc; clinicaltrials.gov NCT03274076).

Methods: A 6-month, 2 center, double-blind, randomized placebo-controlled trial was conducted between November 2017 and August 2018. Participants were randomized to either TOFA or matching PLA. Key inclusion criteria included dcSSc with disease duration of ≤ 60 months (defined as first non–Raynaud phenomenon) and modified Rodnan skin score (mRSS) ≥ 10 and ≤ 45 units. Background stable immunosuppressive therapies were allowed and varicella-zoster vaccine was required (unless previously received). Open label therapy was offered at Month 6. Primary outcome included the proportion of participants who experience Grade 3 or higher adverse events (AEs) using the

NIH guidance: Common Terminology Criteria for Adverse Events (CTCAE v4.03[1]) that occur at or before Month 6. Efficacy end points include mRSS, Health Assessment Questionnaire-Disability Index (HAQ-DI), patient and physician global assessments, and the ACR composite measure: Combined Response Index in Systemic Sclerosis (CRISS) [2]. The current abstract provides results from the double blind phase of the trial.

Results: 15 participants were randomized (2:1; 10 to TOFA and 5 to PLA) and formed the mITT group; 10 (100%) and 4 (80%) completed the 6-month treatment period in TOFA and PLA groups, respectively. Thirteen (13) of 15 participants were on stable daily doses of mycophenolate mofetil (mean dose=1700 mg; N=12) or weekly methotrexate (dose = 25 mg, N=1). Both the active and placebo group had 1 participant on methotrexate, leaving 8 of the TOFA participants on background mycophenolate as well as 3 in the PLA group. At baseline, mean/median age was 50.3/50.0 years, 66.7% were female, mean/median disease duration was 2.1/ 2.0 years, mean/median mRSS was 23.3/23.0, and mean/median HAQ-DI was 0.98/0.88. TOFA was well tolerated with no Grade 3 or higher AE's before or at month 6. There were comparable AEs and AEs of special interest between treatments with no serious AEs or deaths in the trial. There were trends in efficacy favoring TOFA vs. PLA at month 6, including mRSS and ACR CRISS.

Outcome at or before Month 6	Tofacitinib N=10	Placebo N=5
Number of Grade 3 of higher AE's	0	0
Number of Grade 2[1] of higher AE's	14	10
Number of treatment emergent AE's	21	12
Infections and Infestations	4	1
Gastrointestinal Disorders	4	1
General Disorders	1	4
Musculoskeletal and Connective Tissue Disorders	1	3
Skin and subcutaneous Disorder	3	0
Investigations	2	1
Respiratory, Thoracic, and Mediastinal Disorders	2	0
Nervous System Disorders	2	0
Cardiac Disorders	1	1
Renal and Urinary Disorders	0	1

Table 1. Safety outcomes during the double blind phase of the trial

Outcome at Month 6	Tofacitinib N=10	Placebo N=5	P-value
*ΔmRSS, 0-51, mean/median**	-5.8, -6.0	-2.3, -3.0	0.42
*ΔPatient Global Assessment, 0-10, mean/median **	0.0, 0.0	-2.8, -1.5	0.06
*ΔPhysician Global Assessment, 0-10, mean/median **	-1.6, -1.5	0.5, 0.5	0.04
*ΔHAQ-DI, mean/median **	-0.11, -0.06	0.06, 0.13	0.35
*ACR CRISS index, median**	0.30	0.10	0.68

*Two-sample t-tests (Kruskal-Wallis Test), Δ= change

Table 2. Efficacy measures during the double blind phase of the trial

Conclusion: In participants with dcSSc, TOFA was well tolerated with manageable AEs, with no Grade 3 or higher AEs, no SAEs and there were trends in improvement of clinical outcome measures. This study supports further evaluation of TOFA in dcSSc.

References:

1. CTCAE v4.03 https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf

2. Khanna D, et al. Arthritis Rheum 2016.

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Disclosure: D. Khanna, Acceleron, 5, Actelion, 5, Bayer, 2, 5, Blade Therapeutics, 5, BMS, 2, 5, Boehringer Ingelheim, 5, Celegene, 5, ChemomAB, 5, Corubus, 5, CSL Behring, 5, Curzion, 5, Cytori, 5, Eicos, Inc, 4, Genentech, 5, GSK, 5, Horizon, 2, Mitsubishi Tanabe Pharma Development America, 5, Pfizer, 2, Sanofi-Aventis, 5, UCB, 5; **E. Bush**, None; **V. Nagaraja**, None; **A. Koenig**, Pfizer, 1, 4, 9, CSL Behring, 3; **P. Khanna**, Horizon, 5, Sobi, 5; **A. Young**, None; **J. Moore**, None; **D. Fox**, None; **R. Lafyatis**, PRISM Biolab, 2, MERCK, 5, Bristol-Myers Squibb, 5, Regeneron, 2, Elpidera, 2, Kiniksa, 2, Biocon, 5, UCB, 5, Formation, 5, Sanofi, 5, Genentech / Roche, 5.

Abstract Number: 0864

Change in Scleroderma Skin Histology Correlates with the Combined Response Index in Systemic Sclerosis (CRISS) in Patients with Early, Diffuse Cutaneous Systemic Sclerosis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorder – Clinical I: Therapeutics & Outcomes
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: The Combined Response Index in Systemic Sclerosis (CRISS) is a composite outcome measure provisionally endorsed by the American College of Rheumatology for use in systemic sclerosis (SSc) clinical trials. In two early, diffuse SSc trials, skin histologic change within patients was evaluated at baseline and 52-weeks. The purpose of this study is to determine if change in skin histologic severity correlates with CRISS.

Methods: Paired baseline and 52-week post-treatment clinical data and forearm skin histology were examined from patient specimens in the Nilotinib (n=6) and Belimumab (n=18) trials. During these trials, a dermatopathologist (CM), blinded to clinical response, evaluated global histologic severity (pathologist overall impression on hematoxylin and eosin stain), infiltrate intensity, collagen density, and alpha-smooth muscle actin (aSMA) and CD34 staining intensity on a semi-quantitative scale (0-3), and measured thickness (epidermis to subcutis) and follicle count. The validation of these methods is presented separately. CRISS was calculated using 52-week change in physician and patient global assessment (0-10), % predicted forced vital capacity (FVC), health assessment questionnaire disability index (HAQ-DI), and modified Rodnan skin score (MRSS). Patients were assessed for criteria that renders CRISS score zero (scleroderma renal crisis, FVC decline >15% predicted, new heart failure, or new pulmonary arterial hypertension treatment). Wilcoxon rank sum or Kruskal-Wallis tests were performed to evaluate differences in CRISS according to histologic change. Spearman correlation was used to evaluate the correlation between histologic change and CRISS.

Results: 24 diffuse SSc patients contributed baseline and 52-week biopsies. Most were female (79%) and Caucasian (75%) with median [IQR] disease duration of 0.9 [0.6, 1.2] years. 54% were RNA polymerase III positive. Baseline

Table 1. Histologic change and Composite Response Index in Systemic Sclerosis (CRISS) at 52-weeks in 24 patients with diffuse cutaneous systemic sclerosis

Histologic Variable	Median [IQR] CRISS	p-value
Global Histologic Severity		0.02
Worse (n=6)	0.34 [0.00, 0.82]	
Stable (n=3)	1.00 [0.28, 1.00]	
Improved (n=15)	1.00 [0.84, 1.00]	
CD34 Staining Intensity		0.01
Decreased or Stable* (n=4)	0.34 [0.00, 0.69]	
Increased (n=20)	1.00 [0.83, 1.00]	
aSMA Staining Intensity		0.08
Decreased (n=13)	0.55 [0.27, 0.96]	
Stable (n=4)	0.55 [0.21, 0.84]	
Increased (n=7)	0.77 [0.00, 0.90]	
Collagen Density		0.08
Decreased (n=15)	0.77 [0.27, 0.97]	
Stable (n=4)	0.51 [0.05, 0.96]	
Increased (n=5)	0.00 [0.00, 0.68]	
Follicle Count		0.83
Decreased (n=7)	0.90 [0.68, 0.99]	
Stable (n=9)	0.55 [0.09, 0.91]	
Increased (n=8)	0.02 [0.01, 0.66]	
Infiltrate Intensity		0.47
Decreased (n=11)	0.55 [0.02, 0.92]	
Stable (n=8)	0.76 [0.22, 0.95]	
Increased (n=5)	0.00 [0.00, 0.96]	
Thickness		0.54
Decreased (n=9)	0.89 [0.42, 0.96]	
Stable (n=3)	0.55 [0.00, 0.68]	
Increased (n=12)	0.29 [0.01, 0.93]	

Legend: aSMA=alpha-smooth muscle actin. *Only 1 paired sample demonstrated decreased CD34 staining intensity; therefore, decreased and stable CD34 pairs were combined for analysis.

Table 2. Correlation between 52-week histologic change and the Composite Response Index in Systemic Sclerosis (CRISS) in 24 patients with diffuse cutaneous systemic sclerosis		
Histology Response Score and CRISS	**Spearman's Correlation Coefficient**	**p-value**
Global Histologic Severity	-0.52	0.01
CD34 Staining Intensity	0.53	0.01
Alpha-Smooth Muscle Actin Staining Intensity	-0.44	0.03
Collagen Density	-0.44	0.03
Follicle Count	-0.09	0.66
Infiltrate Intensity	-0.09	0.69
Thickness (μm, epidermis to subcutis)	-0.20	0.35

median [IQR] MRSS was 24 [22, 29] and physician global assessment was 5.8 [5.0, 6.8]. Mean (SD) patient global assessment was 3.2 (2.53) and HAQ-DI was 0.85 (0.59). Interstitial lung disease was present in 7 of 24 (29%). Mean (SD) baseline % predicted FVC was 86 (16). Median [IQR] CRISS was 0.93 [0.47, 1.00].

Treatment response, measured by median CRISS, was higher (improved) in those with decreased global histologic severity (p=0.02) and increased CD34 staining intensity (p=0.01) (Table 1). CRISS correlated negatively with change (decreased, stable, or increased) in global histologic severity (r=-0.52, p=0.01), aSMA staining intensity (r=-0.44, p=0.03), and collagen density (r=-0.44, p=0.03), and correlated positively with change in CD34 staining intensity (r=0.53, p=0.01) (Table 2).

Conclusion: Improved CRISS is associated with decreased global histologic severity, aSMA staining intensity, and collagen density, and increased CD34 staining intensity, suggesting these histologic features are treatment responsive and provide clinically meaningful information. Median CRISS in those with global histologic worsening was below the threshold of 0.6 that defines CRISS improvement in SSc trials. Future work may determine if baseline histologic features predict clinical response, measured by CRISS.

Disclosure: K. Showalter, None; **R. Spiera**, BMS, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, Chemo-Centryx, 2, 5, Chemocentryx, 2, Corbus, 2, CSL Behring, 5, Cytori, 2, Formation Biologics, 2, Genentech, Inc., 2, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, GSK, 2, 5, Hoffman-La Roche Ltd, 2, Janssen, 5, Mitsubishi, 5, Roche, 2, Roche Genetech, 2, 5, Roche/Genetech, 2, 5, Roche-Genentech, 2, 5, Roche-Genetech, 2, 5, Sanofi, 5, Sanofi-Aventis, 5; **D. Orange**, None; **C. Magro**, None; **Y. Zhang**, None; **J. Finik**, None; **J. Gordon**, Corbus, 2, Corbus Pharmaceuticals, 2, Cumberland, 2, Cumberland Pharmaceuticals, 2, Elcos, 2.

Abstract Number: 0865

Safety and Efficacy of Lenabasum at 21 Months in an Open-Label Extension of a Phase 2 Study in Diffuse Cutaneous Systemic Sclerosis Subjects

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Systemic Sclerosis & Related Disorder – Clinical I: Therapeutics & Outcomes

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses and limits fibrosis in animal models of SSc. Lenabasum had acceptable safety and tolerability, and improved efficacy outcomes in the 16-week, double-blinded, randomized, placebo-controlled Part A of Phase 2 trial JBT101-SSc-001 (NCT02465437) in dcSSc subjects. The purpose of this study is to provide long-term open-label safety and efficacy data in study JBT101-SSc-001.

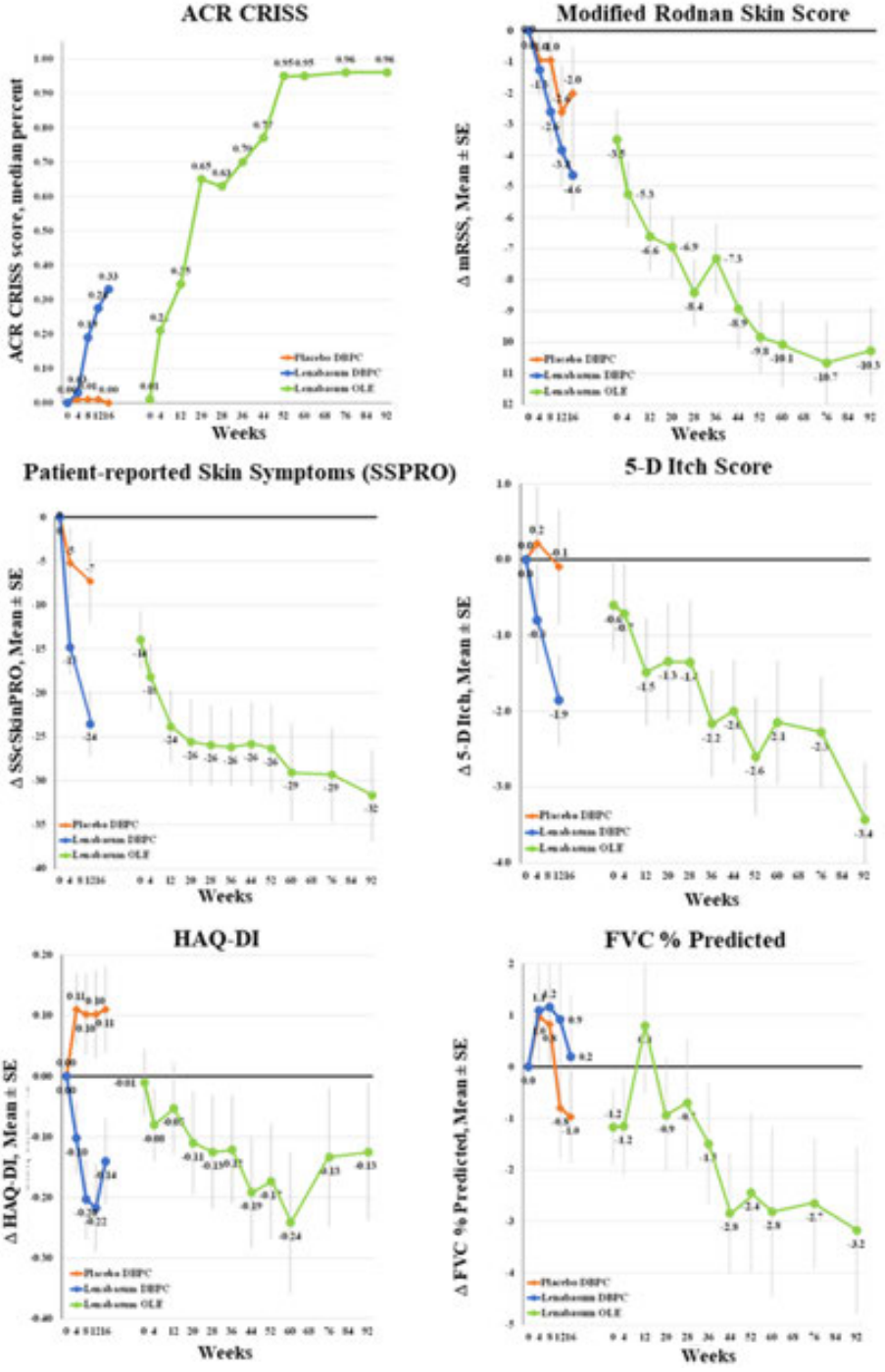
Methods: Subjects who completed Part A were eligible to receive oral lenabasum 20 mg BID in an open-label extension (OLE) that assessed safety and efficacy at 4 weeks, then every 8 weeks.

Results: 36/38 (95%) eligible subjects enrolled in the OLE. At data cut in March 2019, 29/36 (81%) patients remained in the OLE and had completed at least Week 92 in the study. Four subjects withdrew consent, 2 subjects withdrew due to AEs unrelated to lenabasum (tendonitis and scleroderma renal crisis), and 1 subject withdrew for other reasons. At Week 92, 35 (97%) subjects experienced at least 1 AE, with 249 total AEs. Seven (19%) subjects had ≥ 1 AE considered related to lenabasum in the OLE and 3 had AEs judged to be probably or definitely related to lenabasum: 1 had mild fatigue, 1 had a moderate skin ulcer and moderate lymph node pain, and 1 had mild disturbance in attention and mild lethargy and moderate feeling abnormal. Most subjects experienced AEs that were mild (n = 6, 17%) to moderate (n = 23, 64%) in maximum severity. Six (17%) had severe AEs and 1 (3%) had a life-threating AE of renal crisis associated with high-dose steroids. AEs in ≥ 10% of subjects were: upper respiratory tract infection (n = 11, 31%); skin ulcer, urinary tract infection, and arthralgia (each n = 6, 17%); and diarrhea, nasopharyngitis, and cough (each n = 4, 11%). Dizziness and fatigue occurred in 3 (8.3%) subjects each.

Improvement was seen in multiple physician- and patient-reported efficacy outcomes; selected outcomes are shown in Figure 1. Compared to study start, the CRISS median score (primary efficacy outcome) was 0.96 (0.43 IQR) at Week 92 and mRSS declined by mean (SD) = -10.3 (7.2) points. Health Assessment Questionnaire-Disability Index, Physician Global Assessment, Patient Global Assessment, skin symptoms, itch, and multiple PROMIS-29 domains also improved. FVC % predicted decreased 3.2% from study start.

Conclusion: Lenabasum continues to have a favorable safety and tolerability profile in the OLE of the Phase 2 trial JBT101-SSc-001 with no serious AEs or study discontinuations related to lenabasum. Efficacy out-

Figure 1. Change from Baseline in Selected Efficacy Outcomes in OLE



comes show stable improvement from about 1 year in the OLE or continued improvement in some cases. Background therapy, natural history of the disease, and open-label dosing limit what can be definitely contributed to lenabasum.

Disclosure: R. Spiera, Actelion, BIPI, 2, Chemocentryx, 2, 5, Corbus Pharmaceuticals, 2, Cytori, 2, EMD Serono, Evidera, Formation Biologics, 2, Genentech, Genentech/Roche, 2, 5, Glaxosmithkline, 2, 5, InflaRx, InterMune, Janssen, 5, Litmus, Novartis, PPD/GSK, Sanofi, 2, 5; **L. Hummers**, Boehringer Ingelheim, 2, 5, Boehringer-Ingelheim, 2, 5, Corbus, 2, Corbus Pharmacueticals, 2, CSL Behring, 5, Cumberland, 2, Cumberland Pharmaceuticals, 2, Cytori, 2, Cytori Therapeutics, 2, GlaxoSmithKline, 2; **L. Chung**, Boehringer-Ingelheim, 5, Eicos, 5, Reata, 5, Mitsubishi Tanabe, 5, BMS, 5; **T. Frech**, None; **R. Domsic**, Boehringer Ingelheim, 5, Boehringer-Ingelheim, 5, Eicos, 5, EICOS Sciences Inc, 5; **V. Hsu**, None; **D. Furst**, Actelion, 2, 5, Actelion Pharmaceuticals, 2, 5, Amgen, 2, 5, BMS, 2, 5, CME, 5, 8, Corbus, 2, 5, Galapagos, 2, 5, Galapogos Novartis, 5, GlaxoSmithKline, 2, GSK, 2, 5, NIH, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche/Genentech, 2, 5, Sanofi, 2, 5; **J. Gordon**, Corbus, 2, Corbus Pharmaceuticals, 2, Cumberland, 2, Cumberland Pharmaceuticals, 2, Elcos, 2; **M. Myers**, None; **R. Simms**, None; **E. Lee**, Corbus Pharmaceuticals, 3; **S. Constantine**, Corbus Pharmaceuticals, 1, 3, 4; **N. Dgetluck**, Corbus Pharmaceuticals, 3, 4; **B. Bloom**, Corbus Pharmaceuticals, 3, 4; **B. White**, Corbus Pharmaceuticals, 1, 3, 4, 6.

Abstract Number: 0866

Evaluation of the Highly Selective Endothelin a Receptor Antagonist Zibotentan in Systemic Sclerosis Associated Chronic Kidney Disease

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorder – Clinical I: Therapeutics & Outcomes
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Systemic sclerosis (SSc) causes scleroderma renal crisis (SRC) and chronic kidney disease (CKD). A previous open label trial of bosentan suggested possible benefit for CKD following SRC [1]. Here we report the results of a placebo-controlled trial of zibotentan, a highly selective endothelin A receptor antagonist, in SSc associated CKD.

Methods: ZEBRA-1 was a double-blind randomised placebo-controlled trial in SSc with CKD (eGFR 45-60 ml/min) comparing oral zibotentan 10 mg/day and placebo over 26 weeks with final safety assessment at 52 weeks (Clinical Trials NCT02047708). Efficacy was assessed by eGFR with safety a key secondary endpoint. Candidate urinary molecular markers of SSc-associated CKD were measured. Variables were compared by non-parametric Mann-Whitney U test. Pharmacokinetics (PK) were explored in ZEBRA-1 and an additional single escalating dose PK substudy (ZEBRA-2) undertaken in patients (n=8) on haemodialysis.

Results: 16 patients consented to enter ZEBRA-1. There were 3 screen failures due to renal function being ineligible on re-testing. 7 patients received placebo and 6 zibotentan. Baseline renal function was well matched between treatment groups (median eGFR in placebo 51 (44-58); zibotentan 50.5 (49-59)). Renal function was equal at 26 weeks

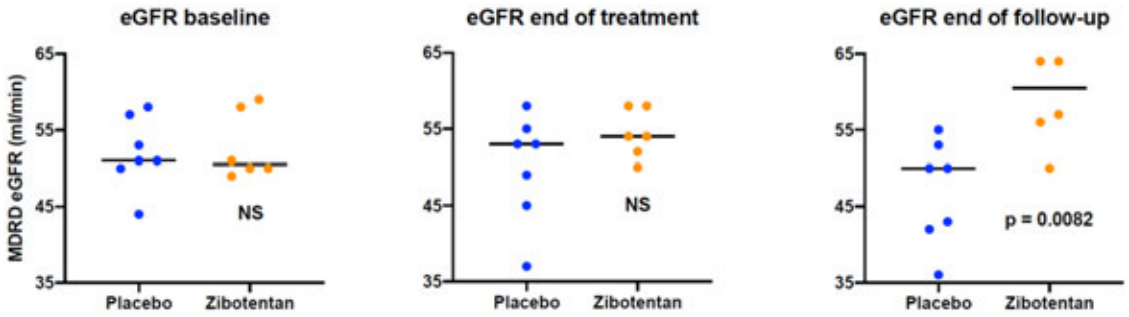

Figure 1. Impact of zibotentan or placebo on eGFR at baseline, 26 and 52 weeks

(placebo 53 (37-58); zibotentan 54 (50-58)) but eGFR significantly improved in the active treatment group at 52 weeks (placebo 50 (36-55) zibotentan 60.5 (50-74), p=0.0082) (see **Figure 1**).

Our previous work identified elevated urinary MCP-1: creatinine ratio as a marker of SSc-CKD [2]. Interestingly, levels declined on zibotentan but not in placebo. Thus, median baseline urinary MCP1/creatinine (pg/mg/L) was 7.1 (5.2-21.9) in placebo arm and 5.4 (3.1-28.9) for zibotentan, increased to 8.8 (6.3-33.5) at 26 weeks on placebo and reduced to 4.4 (2.9-11.2) on zibotentan. At 52 weeks MCP-1/creatinine for placebo arm was 7.5 (6.4-15.8) and was significantly lower at 4.5 (4.1-6.0; p=0.0095) after zibotentan.

There were 46 reported adverse events (AE) (26 placebo and 20 active treatment) in ZEBRA-1 in 11 patients (6 placebo and 5 zibotentan). Of the 46 reported AE, 6 were serious (3 in each arm). PK confirmed zibotentan levels within therapeutic range in ZEBRA-1 and suggested feasible dose regimen for dialysis patients (ZEBRA-2).

Conclusion: This is the first placebo-controlled interventional trial in renal SSc. Zibotentan was generally well tolerated. Compared with placebo, zibotentan treatment over 26 weeks was associated with improved eGFR at 52 weeks and fall in urinary MCP1:creatinine, a candidate marker for SSc kidney disease. Whilst preliminary, these results suggest targeting endothelin A in SSc associated CKD may be beneficial.

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Abstract Number: 0867

Safety and Efficacy of B-cell Depletion with Rituximab for the Treatment of Systemic Sclerosis-associated Pulmonary Arterial Hypertension in a Multi-center NIH Clinical Trial

Mark Nicolls,[1] David Badesch,[2] Lorinda Chung,[3] Robyn Domsic,[4] Thomas Medsger,[5] Ashley Pinckney,[6] Lynette Keyes-Elstein,[6] Carla D'Aveta,[6] Meagan Spychala,[6] R James White,[7] Paul Hassoun,[8] Fernando Torres,[9] Jerry Molitor,[10] Dinesh Khanna,[11] Holden Maeker,[12] Beverly Welch,[13] Ellen Goldmuntz,[14] Roham Zamanian,[1] and On Behalf of ASC01 Investigators[15], [1]Stanford University, Stanford, [2]University of Colorado, Denver, [3]Stanford University, Palo Alto, CA, [4]University of Pittsburgh, Pittsburgh, PA, [5]University of Pittsburgh, Pittsburgh, [6]Rho Federal Systems, Durham, [7]University of Rochester, Rochester, NY, [8]Johns Hopkins School of Medicine, Baltimore, [9]UT Southwestern, Dallas, [10]University of Minnesota, University of Minnesota, [11]Department of Medicine, University of Michigan, Ann Arbor, Michigan, USA, Ann Arbor, [12]Stanford, Stanford, [13]National Institute of Allergy and Infectious Diseases, NIH, Bethesda, [14]NIAID, Washington, DC, [15]---, USA

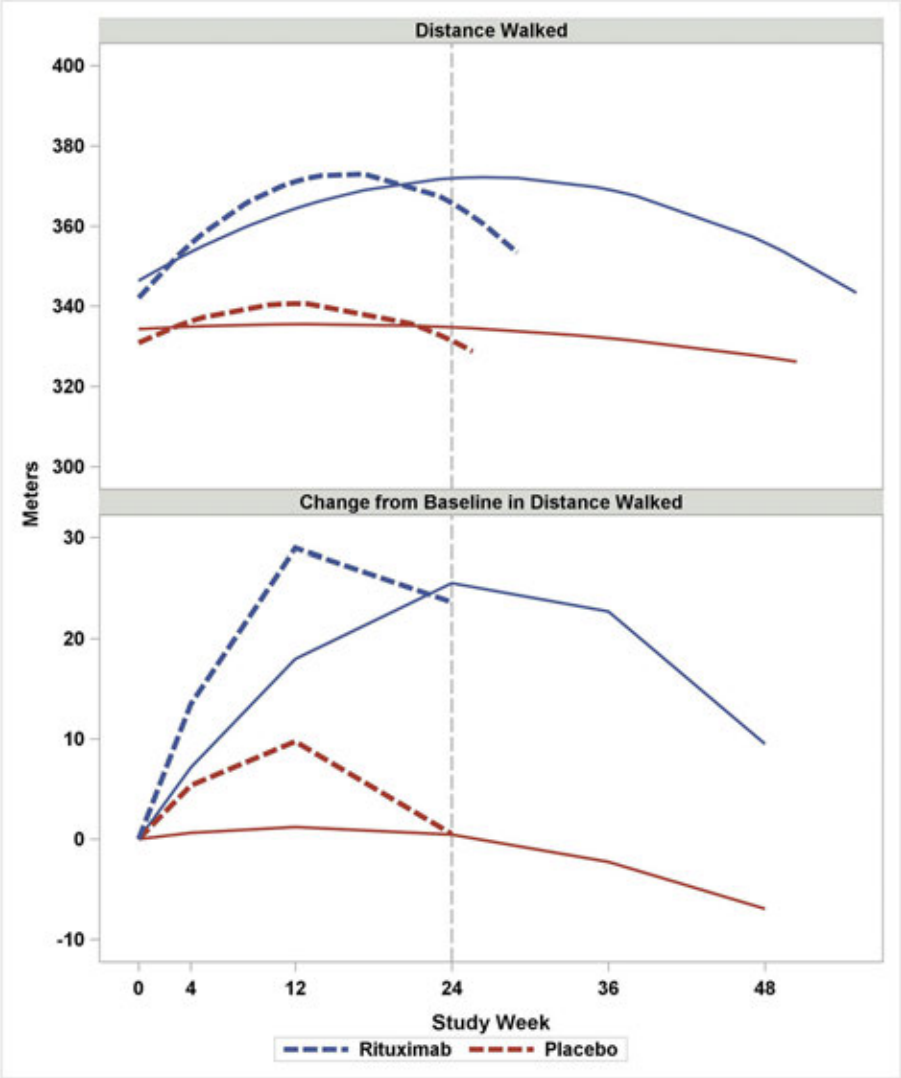
SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Systemic Sclerosis & Related Disorder – Clinical I: Therapeutics & Outcomes

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM



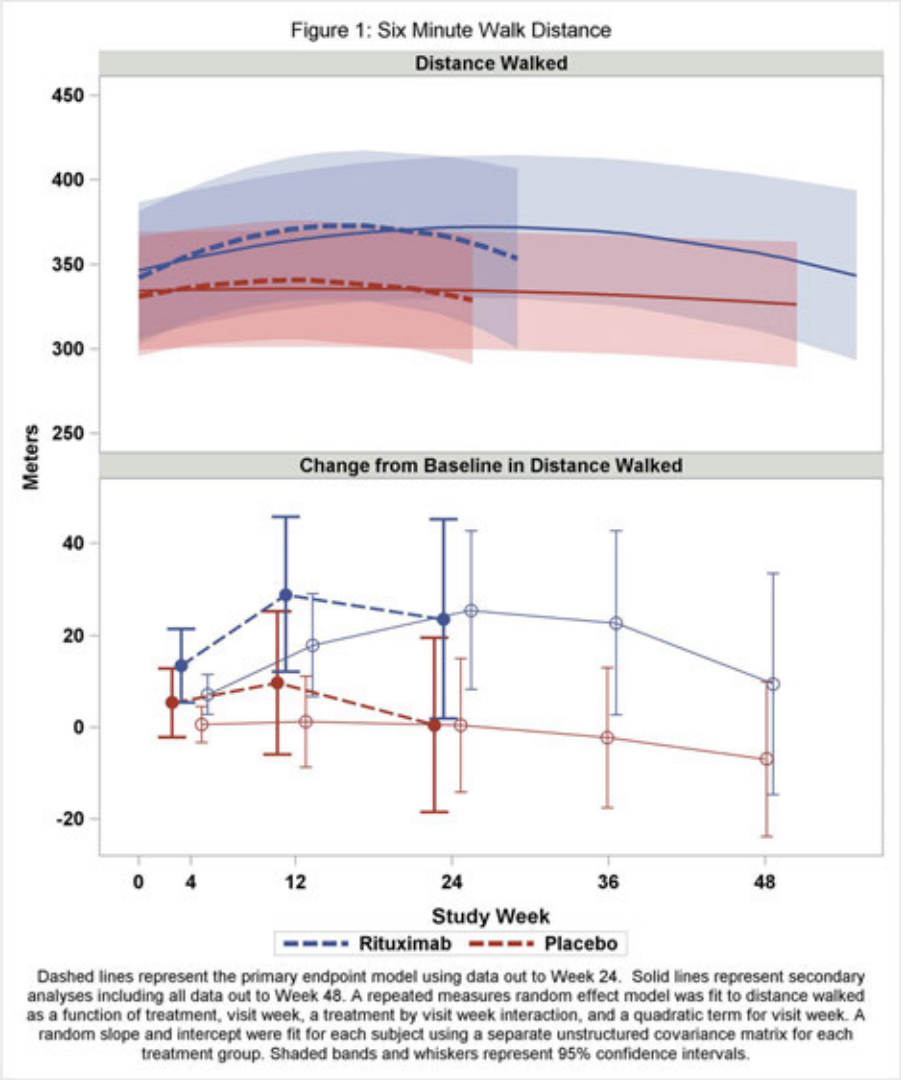


FIGURE 1. 6MWD Secondary Analysis Results. Top panel shows model-based longitudinal trends total distance walked in meters over time for both treatment groups. Lower panel shows the change in distance walked compared to baseline estimated from the model.

Background/Purpose: Pulmonary arterial hypertension (PAH) is a life-threatening complication of systemic sclerosis (SSc). Pre-clinical and clinical data have strongly implicated immune dysregulation and B cell activation in the pathogenesis of both SSc and PAH. While standard PAH therapies are approved for SSc-PAH, ongoing immune injury to the pulmonary vasculature is not routinely addressed. Consequently, we sought to determine whether B cell depletion with rituximab (Rx) could be effective in SSc-PAH.

Methods: We conducted a Phase II, randomized, double-blind, placebo-controlled multi-center clinical trial sponsored by the Autoimmunity Centers of Excellence, NIH. SSc-PAH patients on a stable standard PAH therapy without significant interstitial lung or renal disease were eligible. Dosing was two 1000 mg Rx infusions, 14 days apart. In this under-powered proof-of-concept study, multiple endpoints were evaluated to explore the potential for clinical benefit. The primary endpoint was change in 6-minute walk distance (6MWD) at 24 weeks. Key secondary efficacy endpoints included change in 6MWD at other time points, pulmonary vascular resistance (PVR), and time to change or addition of PAH medications, which were expected to remain unchanged until week 24 per protocol. A secondary objective of the study was to evaluate the safety profile of Rx in this population.

Table 1: Primary and Secondary Endpoints
Population: Modified Intention-to-Treat[1]

	Rituximab (n=27)	Placebo (n=27)	p-value
Primary Endpoint			
Change from Baseline in SMWT (meters)[2], mean (SE)			
Week 24	23.6 (11.05)	0.5 (9.71)	0.12
Secondary Endpoints:			
Change from Baseline in SMWT (meters)[3], mean (SE)			
Week 24	25.5 (8.79)	0.4 (7.43)	*
Week 48	9.5 (12.35)	-7.0 (8.63)	
Change from Baseline in PVR at Week 24 (dyes/sec/cm^5), mean (SD)	-39.0 (28.85)	7.2 (48.51)	
Change or Addition of PAH Medications, % Probability[4]			
By Week 12	11%	0%	
By Week 24	11%	15%	
By Week 36	28%	41%	
By Week 48	28%	41%	

* The p-value = 0.03 for this treatment group comparison. For all other secondary endpoints, the p-values for treatment group comparisons were >0.05.

1. The modified intention-to-treat population includes all eligible subjects who initiated treatment.
2. Model uses all data through Week 24 for estimates.
3. Model uses all data through Week 48 for estimates.
4. The probabilities are estimated from Kaplan-Meier curves for time-to-change or addition of PAH medications.

TABLE 2. Summary of Adverse Events

Results: Between 2010-2018, 57 participants (29 Rx, 28 placebo (Pc)) were randomized; 91% female, mean age = 58(SD 9.1) years, 90% limited SSc, mean duration of SSc-PAH = 1.8(SD 1.2) years. In the primary longitudinal analysis using data through week 24, 6MWD trended towards improvement after Rx relative to Pc but did not reach statistical significance (23.6±11.1m Rx, 0.5±9.7m Pc, p=0.12, Fig 1). A pre-specified secondary analysis, which included 6MWD data through week 48, demonstrated improvement at week 24 (25.5±8.8m Rx, 0.4±7.4m Pc, p=0.03, Figure 1), that was lost by week 48(9.5±12.4m Rx, -7.0±8.6m Pc, p=0.28). The probability of change or addition of PAH therapies after week 24 was lower in the Rx group (28% Rx, 41% Pc at weeks 38 and 48, Table 1). Changes in PVR at Week 24 were highly variable, but on average Rx fared better (mean(SD): -39 (28.9) Rx, 7.2(48.5) Pc, Table 1). Rx was well-tolerated with no unexpected adverse events or hypersensitivity reactions (Table 2). The number of adverse events, including infections, was similar in both treatment groups. A total of 4 deaths occurred in this at-risk cohort (3 in Rx, 1 in Pc); none of these deaths were directly attributed to Rx.

Conclusion: This is the first controlled trial examining the role of immunotherapy for SSc-PAH. Adjuvant B cell depletion therapy is a potentially effective and safe treatment for SSc-PAH. Our analyses uncovered potential benefits, despite being under-powered, and offer hope that targeted immunotherapy may be a promising approach. These results suggest repeat dosing of Rx after 24 weeks in responsive SSc-PAH patients. These results suggest that B cell-mediated injury contributes to ongoing pulmonary vascular disease in SSc-PAH and warrants further st udy.

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Abstract Number: 0868

The Effect of Atorvastatin on Microvascular Endothelial Function and Raynaud Phenomenon in Early Diffuse Scleroderma: Results of the "Tamer"' Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Systemic Sclerosis & Related Disorder – Clinical I: Therapeutics & Outcomes
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Statins have pleiotropic effects felt to influence in their beneficial cardiovascular effects. These include increased nitric oxide production and improved endothelial function, modulation of inflammation, and inhibition of overproduction of matrix components. Prior studies have been conflicting regarding the efficacy of statin therapy for Raynaud phenomenon (RP) in systemic sclerosis (SSc). However, these studies enrolled patients of wide disease duration and likely advanced vasculopathy. We hypothesized that there may be a window of opportunity; statin use in the early disease stages may benefit microvascular endothelial function and improve RP symptoms.

Methods: We performed an investigator-initiated, double-blind, randomized, placebo-controlled trial of atorvastatin 40 mg once daily vs placebo x 16 weeks (1:1 randomization). Patients were 18-70 years with early diffuse SSc, defined as < 3 years of SSc symptoms and RP. RP medications were stable ≥4 weeks. Patients were excluded if they had: diabetes, cardiovascular disease, were current smokers or used phosphodiesterase-5 inhibitors, recent prostacyclin therapy or prior sympathectomy. The primary outcome was improvement in microvascular endothelial function measured by reactive hyperemia index (RHI) using the EndoPAT™ system. Secondary outcomes included change in macrovascular endothelial function by brachial flow-mediated (FMD) dilation, and RP severity using the Raynaud condition score (RCS) and visual analog scale (RP-VAS). Given the sample size non-parametric analysis was performed to compare outcome measures between therapy groups.

Results: Twenty-four patients were randomized. One patient was diagnosed with pulmonary hypertension and withdrawn before 16 weeks. Baseline characteristics are in Table 1. Although randomized, the atorvastatin group had significantly lower RHI scores (worse endothelial function) and higher RCS and RP-VAS scores,

Table 1: Baseline characteristics of the TAMER study population			
	Atorvastatin n=10	Placebo n=14	p-value
Age at enrollment (years)	50±13.9	55.7 ± 7.3	0.27
Female	9 (90%)	10 (71%)	0.27
Ethnicity			0.41
Caucasian, non-Hispanic	7 (78%)	13 (93%)	
African-American	1 (11%)	1 (7%)	
Asian	1 (11%)	0	
History of hyperlipidemia	4 (40%)	2 (14%)	0.19
History of hypertension	1 (10%)	7 (60%)	**0.04**
Family History of early CVD	1 (10%)	1 (7%)	0.80
Obesity (BMI > 30)	2 (20%)	6 (43%	0.24
DISEASE CHARACTERISTICS			
Disease Duration (years)	1.54 ± 0.60	2.20 ± 0.76	**0.04**
Mean modified Rodnan skin score	18.9 ±9.6	22.8 ± 8.9	0.33
Digital pitting scar	4 (40%)	4 (29%)	0.31
Digital ulcers	0	1 (7%)	--
Fibrosis on chest imaging	3 (30%)	5 (36%	0.77
Gastrointestinal involvement	6 (60%)	8 (57%)	0.89
VASCULAR MEASURES			
Raynaud Condition Score (median, IQR)	5.0 (3.0, 7.5)	2.0 (1.0, 4.0)	0.49
RP VAS (median, IQR)	4.5 (2.0, 7.5)	1.5 (0.5, 3.0)	0.08
Mean EndoPAT RHI score (SD)	1.36 ± 0.36	1.85 ± 1.2)	**0.05**
Median % Peak Flow Mediated Dilation (IQR)	6.27 (6.75)	5.26 (5.19)	0.53

Table 2: Change in Raynaud phenomenon symptoms at 16 weeks			
	Atorvastatin	Placebo	p-value
Median change (IQR) in RCS	-2.0 (-2.0, 0)	0.0 (-1.0, 1.0)	0.12
Median change (IQR) in RP VAS	0.5 (-1.5, 6.0)	0.0 (-1.0, 1.5)	0.38

suggesting overall worse peripheral vascular disease. In those treated with atorvastatin, 60% (6/10) improved their RHI, compared to 29% (4/14) in the placebo group (p=0.12). There was no difference in change in peak FMD% between groups. The RCS decreased 2 points in the statin group compared to no change in the placebo (p=0.12; Table 2).

Conclusion: The results show a non-significant improvement in microvascular endothelial function measured by EndoPAT and RCS scores with the treatment of atorvastatin. This is encouraging given the small number of patients enrolled into the trial (original power calculations based on 30 patients) and the random assignment of a statin therapy group with significantly worse endothelial function and RP activity at baseline. Future studies of statins in early disease should be considered

Disclosure: R. Domsic, Boehringer Ingelheim, 5, Boehringer-Ingelheim, 5, Eicos, 5, EICOS Sciences Inc, 5; **M. Laffoon**, None; **B. Goundappa**, None; **T. Medsger**, None; **R. Lafyatis**, None; **S. Wisniewski**, None.

Abstract Number: 0869

Clinical Manifestations of Patients with Eosinophilic Granulomatosis with Polyangiitis in a Large North American Cohort

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SESSION INFORMATION
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Session Title: Vasculitis – ANCA-Associated I
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare, systemic necrotizing small-vessel vasculitis, with only a few published North American series. This project aimed to describe main clinical characteristics, treatment patterns, and outcomes of patients with EGPA enrolled in the Vasculitis Clinical Research Consortium (VCRC).

Methods: Retrospective analysis of patients with EGPA participating in the VCRC Longitudinal Study (LS) or One-Time DNA (OT) collection from 2003-2019. Patients were at least 18 years old at enrollment and fulfilled the modified American College of Rheumatology 1990 criteria. Main demographics, time of onset of asthma to diagnosis, main organ involvement, ANCA status, type of treatments received since diagnosis, relapses, and deaths were analyzed. Patient subsets were compared according to ANCA status and use of cyclophosphamide (CYC).

Results: 354 patients (277 LS; 77 OT) were included; 309 (87.3%) were white, 20 (5.7%) Asian, and 7 (2%) Black or African American; male/female ratio was 145/209. Mean age at diagnosis and enrollment was 50.0 (±14.2) and 53.5 (±13.6) years, respectively; 246 (69.5%) had a diagnosis of asthma prior to the diagnosis of EGPA, for a mean of 8.6 (±12.2) years; 329 (92.9%) were eventually diagnosed with asthma. Of those tested for ANCA, 38.9% were positive, mostly with MPO-ANCA (86.2%). Main manifestations at diagnosis, and over the entire course of the disease (until last study visit), are listed in **Table 1**. With a mean follow-up from diagnosis of 7.0 (±6.2) years, 49.4% of patients had at least one relapse, with 35.7% of the 277 VCRC-LS patients relapsing post-enrollment. Characteristics of these first relapses post-enrollment included active asthma (35%), other lung disease (46%), ear/nose/throat (39%), cardiac (9%), skin manifestations (8%), and/or neuropathy (18%). Eleven (4%) of the VCRC-LS patients died after a mean of 4.7 (±2.5) years post-diagnosis (2 myocardial infarctions, 1 intestinal perforation, 1 metastatic cancer, 7 unknown). In the VCRC-LS, 115 (41.5%) patients received CYC at some point in their disease, 29 (10.5%) rituximab, 25 (9.0%) mepolizumab, 145 (52.4%) azathioprine, 109 (39.4%) methotrexate, and 25 (9%) mycophenolate mofetil. ANCA-positive patients had more kidney and neurologic involvement and a higher mortality, but less lung or cardiac manifestations (**Table 2**). Patients who received CYC had more cardiac and neurologic manifestations. At last study visit, 221 (79.8%) patients were off glucocorticoids (GC), but only 8 (2.9%) have been off systemic GC and immunosuppressant medications for >2 years during their follow-up.

Clinical manifestation	At diagnosis	Cumulative manifestations
Constitutional symptoms	207 (58.5%)	290 (81.9%)
Weight loss	83 (23.7%)	106 (29.9%)
Fatigue	178 (50.7%)	256 (72.3%)
Arthralgias	93 (26.5%)	140 (39.6%)
Myalgias	64 (18.2%)	91 (25.7%)
Ear/Nose/Throat	201 (56.8%)	292 (82.5%)
Nasal polyposis	123 (35.0%)	177 (50.0%)
Sinus involvement	188 (53.6%)	273 (77.1%)
Lung	196 (55.4%)	296 (83.6%)
Asthma	246 (69.5%)	329 (92.9%)
Pulmonary infiltrate	138 (39.3%)	205 (57.9%)
Alveolar hemorrhage	12 (3.4%)	21 (5.9%)
Nodules or cavities	23 (6.6%)	43 (12.2%)
Pleural effusion	24 (6.8%)	35 (9.9%)
Cutaneous	68 (19.2%)	106 (29.9%)
Purpura	54 (15.4%)	88 (24.9%)
Ulcer	8 (2.3%)	14 (4.0%)
Gangrene	3 (0.9%)	4 (1.1%)
Nodules	15 (4.3%)	26 (78.3%)
Neurological	151 (42.7%)	214 (60.5%)
Stroke	2 (0.6%)	5 (2.0%)
Sensory neuropathy	126 (35.9%)	181 (51.1%)
Mononeuritis multiplex	81 (23.1%)	116 (32.8%)
Cardiovascular	51 (14.4%)	75 (21.2%)
Pericarditis	22 (6.3%)	35 (9.9%)
Myocarditis	42 (12.0%)	57 (16.1%)
Gastrointestinal	11 (3.1%)	22 (6.2%)
Colitis	6 (1.7%)	15 (4.2%)
Mesenteric ischemia	5 (1.4%)	7 (2.0%)
Renal	16 (4.5%)	36 (10.2%)
Proteinuria	13 (3.7%)	22 (6.2%)
Hematuria	13 (3.7%)	29 (8.2%)
Elevated serum creatinine	10 (2.9%)	18 (5.1%)

Table 1. Clinical manifestations of 354 patients with eosinophilic granulomatosis with polyangiitis

Main characteristic / manifestation	All N=354	ANCA-Positive N=123	ANCA-Negative N=193	P	All* N=277	Use of CYC N=115	No use of CYC N=162	P
Female	189 (59.8%)	61 (49.6%)	128 (66.3%)	<0.01	157 (56.7%)	52 (45.2%)	105 (64.8%)	<0.01
ANCA-positive					98 (40.2%)	46 (45.5%)	52 (36.4%)	0.15
Constitutional symptoms	265 (83.9%)	107 (87.0%)	158 (81.9%)	0.23	231 (83.4%)	99 (86.1%)	132 (81.5%)	0.31
Ear/Nose/Throat	264 (83.5%)	98 (79.7%)	166 (86.0%)	0.14	226 (81.6%)	90 (78.3%)	136 (84.0%)	0.23
Lung	263 (83.2%)	93 (75.6%)	170 (88.1%)	<0.01	232 (83.8%)	89 (77.4%)	143 (88.3%)	0.02
Cardiac	63 (19.9%)	16 (13.0%)	47 (24.4%)	0.01	66 (23.8%)	38 (33.0%)	28 (17.3%)	<0.01
Neurological	199 (63.0%)	90 (72.2%)	109 (56.5%)	<0.01	171 (61.7%)	85 (73.9%)	86 (53.1%)	<0.01
Renal	31 (9.8%)	20 (16.3%)	11 (5.7%)	<0.01	26 (9.4%)	15 (13.0%)	11 (6.8%)	0.08
Gastrointestinal	20 (6.3%)	4 (3.3%)	16 (8.3%)	0.07	18 (6.5%)	8 (7.0%)	10 (6.2%)	0.79
Cutaneous	94 (29.8%)	41 (33.3%)	53 (27.5%)	0.27	89 (32.1%)	39 (33.9%)	50 (30.9%)	0.59
Cyclophosphamide use	101 (41.4%)	46 (46.9%)	55 (37.7%)	0.15				
Relapse	158 (50.0%)	64 (52.0%)	94 (48.7%)	0.56	174 (62.8%)	66 (57.4%)	108 (66.7%)	0.12
Death	10 (3.2%)	7 (5.7%)	3 (1.6%)	0.04	11 (4.0%)	5 (4.4%)	6 (3.7%)	0.79
Off oral glucocorticoid and immunosuppressant	5 (1.6%)	3 (2.4%)	2 (1.04%)	0.33	8 (2.6%)	3 (2.6%)	5 (3.1%)	0.82

*Data from patients within Vasculitis Clinical Research Consortium Longitudinal Study only.
ANCA: Anti-neutrophil cytoplasmic antibody; CYC: cyclophosphamide

Table 2. Main clinical manifestations at any point in disease course of 354 patients with eosinophilic granulomatosis with polyangiitis, according to ANCA status and use of cyclophosphamide

Conclusion: This first detailed analysis of the large VCRC cohort of patients with EGPA highlights the broad range of clinical manifestations seen in this disease and confirms that some clinical manifestations differ based on ANCA status, and that relapse rates are high. The extremely low number of patients able to stop GC and other immunosuppressant medications strongly supports the need for more effective treatments and identification of disease subsets to better tailor treatments.

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Abstract Number: 0870

Off-Label Use of Biotherapies to Treat Relapsing And/or Refractory Eosinophilic Granulomatosis with Polyangiitis (Churg–Strauss)

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SESSION INFORMATION
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Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA; formerly Churg–Strauss syndrome), is characterized by small-vessel necrotizing vasculitis, and blood and tissue eosinophilia in asthmatic individuals. Glucocorticoids (GCs) usually control EGPA, but vasculitis relapses and GC-dependent asthma are frequent, as are long-term adverse events, leading to potential biotherapy use. We examined off-label biological therapy use for relapsing/refractory EGPA.

Methods: This retrospective European collaborative study included patients with EGPA, meeting the ACR criteria and/or Chapel Hill Consensus Conference definitions. Treatment efficacy and safety were recorded. Remission was defined as the absence of asthma, sinonasal and vasculitis manifestations with ≤5 mg/day of prednisone, and partial response as the absence of manifestations but requiring 6–10 mg/day of prednisone.

Results: Among the147 patients (74 men, 73 women; median age 52 years) included, 63 (43%) received rituximab (RTX), 51 (35%) mepolizumab (MEPO), at monthly respective doses of 100 mg or 300 mg for 29 (57%) and 22 (43%), and 33 (22%) omalizumab (OMA). Previous treatments were: GCs for all, azathioprine (68%), cyclophosphamide (40%), methotrexate (29%) or mycophenolate mofetil (15%).

At inclusion, median (interquartile range) BVAS in the RTX, OMA and MEPO groups, respectively, were 8.5 (5-13), 2 (2-5) and 2 (2-6). In the RTX-treated patients, median BVAS fell to 1 (0-4.5) at 6 and 0 (0-2) ay 12 months.A Median GCs dose decreased to 7.5 (5-10) at 6 months and 12 months. Overall, remissions, partial responses, therapeutic failure and stop for adverse event, respectively, were noted in 49%, 24%, 24% and 3% for RTX recipients. Remission was observed in 57% of ANCA-positive patients compared to 42% in ANCA-negative patients.

To treat GC-dependent asthma, MEPO had a much better GCs-sparing effect than OMA, and a better overall response. Remissions, partial responses, therapeutic failure and stop for adverse event, respectively, were noted in 15%, 33%, 48% and 4% for OMA recipients and 78%, 10%, 8% and 4% for MEPO recipients.Finally, no obvious difference was noted between patients receiving MEPO 100 mg and those 300 mg monthly, in terms of GC-sparing effect and overall response.

Sixteen (25%) patients stopped RTX: 2 for adverse events, and 14 for refractory disease. Also, 17 (27%) experienced adverse events, mainly severe infections. Seventeen (52%) stopped OMA: 1 for severe infusion reaction, and 16 for refractory disease. Four (12%) patients receiving OMA experienced mild to moderate adverse events. Three (6%) patients stopped MEPO: 2 for adverse events (one severe infusion reaction and one because of paraesthesia), and 1 for pregnancy. Eleven (22%) patients receiving MEPO experienced mild to moderate adverse events, mainly asthenia.

Conclusion: These results suggest that RTX could be effective for 50% of patients with EGPA vasculitis relapses, with an acceptable safety profile. MEPO is highly effective with a good GCs-sparing effect and safety profile in patients with GCs-dependant asthma, and 100 mg monthly seems to be an acceptable dose at first-line.

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Abstract Number: 0871

ANCA-Associated Vasculitis Management in the United States: Data from the RISE Registry

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Background/Purpose: The management of ANCA-associated vasculitis (AAV) evolved substantially in recent years because of evidence supporting the efficacy of various treatment regimens. As such, treatment approaches may vary across physicians. Understanding current practice can guide the design of pragmatic trials, inform cost-effectiveness research, and establish benchmarks. We sought to identify AAV treatment patterns in the US, especially outside of referral centers.

Methods: AAV patients seen in practices participating in the Rheumatology Informatics System for Efficacy (RISE) registry between January 1st, 2015 and December 31st, 2017 were included. AAV was defined as ≥ physician visit-associated 2 ICD-10 codes for AAV (M31.1, M31.31, M31.7, M30.1) ≥ 3 months apart and prescription/administration for rituximab (RTX), cyclophosphamide (CYC), azathioprine (AZA), methotrexate (MTX), mycophenolate mofetil (MMF), or glucocorticoids 3 months before or up to 6 months after the first ICD-10 code. New or flaring AAV cases were identified based on encounter codes for New/Consult visit; medications prescribed within 3 months of the 1st ICD-10 diagnosis code were assumed to be for "induction therapy." Demographic and prescription trends were assessed overall and across US regions. This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

Results: 1,462 patients fulfilled the AAV case definition; 259 (18%) were new cases (**Table 1**). GPA was more common (1,097, 75%) than MPA (235, 16%) or EGPA (139, 10%). The mean age at the initial visit was 59.8 (±15.3) and 864 (59%) were female. Most visits occurred in the South (658, 45%) followed by the Mid-West (470, 32%), West (174, 12%), and Northeast (122, 8%). During the study period, patients had a median of 3 (IQR 0, 9) rheumatology clinician visits and an average follow-up of 579 days (IQR 328, 715). Among new patients, the most common induction regimens (**Table 2**) were RTX (80, 31%) followed by MTX (48, 19%). CYC was used in 11 (4%) cases. Among all patients (new and follow-up), the most common initially prescribed medication was a glucocorticoid (531, 36%), followed by MTX (290, 20%), RTX (286, 20%), and/or AZA (242, 17%); the most commonly prescribed medication at the end of follow-up was a glucocorticoid (684, 46.8%), followed by RTX (434, 30%), MTX (345, 24%), AZA (315, 22%), and/or MMF (170, 12%). Prescription trends were similar across regions.

Conclusion: This is among the first US studies to evaluate demographic and management patterns of AAV outside of major referral centers. The demographics of AAV patients in RISE are similar to those of other AAV cohorts. There was wide variation in management at different time points in care but these variations were similar across regions. Though RTX and CYC are considered non-inferior to one another, there was minimal CYC use. Glucocorticoids, RTX, and MTX were the most commonly prescribed medication throughout AAV care. Despite the superiority of RTX over

	Overall	Northeast	South	Mid-West	West	Unknown
N	1,462	122	658	470	174	38
Age (Years, Mean, SD)	59.8 (15.3)	60.7 (16.2)	59.5 (15.4)	59.9 (15.3)	59.3 (14.4)	61.0 (14.9)
Female (N, %)	864 (59.1%)	67 (54.9%)	396 (60.2%)	283 (60.2%)	98 (56.3)	20 (52.6%)
Race						
White	824 (56.4%)	90 (73.8%)	359 (54.6%)	255 (54.3%)	93 (53.5%)	27 (71.1%)
Black	44 (3.0%)	3 (2.5%)	31 (4.7%)	9 (1.9%)	1 (0.6%)	0 (0%)
Other	594 (40.6%)	29 (23.8%)	268 (40.7%)	206 (43.8%)	80 (46.0%)	11 (28.9%)
Hispanic (N, %)	130 (8.9%)	3 (2.5%)	90 (13.7%)	12 (2.6%)	23 (13.2%)	2 (5.3%)
No of Encounters (Median, IQR)	3 (0, 9)	4.5 (1, 13)	4 (0, 11)	2 (0, 6)	4 (1, 8)	4.5 (0, 11)
Follow-up (Days, Median, IQR)	579 (328, 715)	507 (287, 729)	573 (324, 713)	594 (336, 714)	595 (357, 720)	623 (344, 779)
AAV Type						
GPA	1, 097 (75.0%)	93 (76.2%)	505 (76.8%)	333 (70.9%)	134 (77.0%)	32 (84.2%)
MPA	235 (16.1%)	16 (13.1%)	101 (15.4%)	90 (19.2%)	26 (14.9%)	2 (5.3%)
EGPA	139 (9.5%)	13 (10.7%)	57 (8.7%)	49 (10.4%)	16 (9.2%)	4 (10.5%)
New Visit	259 (17.7%)	18 (14.8%)	124 (18.8%)	76 (16.2%)	33 (19.0%)	8 (21.1%)

Table 1. Demographics of AAV Subjects in RISE Registry (2015-2017)

	Overall	Northeast	South	Mid-West	West	Unknown
Induction Regimens	259	18	124	76	33	8
Rituximab	80 (30.9%)	4 (22.2%)	37 (29.8%)	25 (32.9%)	12 (36.4%)	2 (25.0%)
Cyclophosphamide	11 (4.3%)	1 (5.6%)	4 (3.2%)	3 (4.0%)	1 (3.0%)	2 (25.0%)
Rituximab & Cyclophosphamide	8 (3.1%)	1 (5.6%)	5 (4.0%)	1 (1.3%)	1 (3.0%)	0 (0%)
Methotrexate	48 (18.5%)	2 (11.1%)	24 (19.4%)	17 (22.4%)	4 (12.1%)	1 (12.5%)
Mycophenolate Mofetil	18 (7.0%)	0 (0%)	11 (8.9%)	4 (5.3%)	3 (9.1%)	0 (0%)
Other & Combinations	34 (13.1%)	4 (22.2%)	15 (12.1%)	8 (10.5%)	4 (12.1%)	3 (37.5%)
None Associated with Visit	60 (23.2%)	6 (33.3%)	28 (22.6%)	18 (23.7%)	8 (24.2%)	0 (0%)
First Prescription	1,462	122	658	470	174	38
Rituximab	286 (19.6%)	34 (27.9%)	141 (21.4%)	77 (16.4%)	27 (15.5%)	7 (18.4%)
Cyclophosphamide	30 (2.1%)	1 (0.8%)	11 (1.7%)	12 (2.6%)	5 (2.9%)	1 (2.6%)
Methotrexate	290 (19.8%)	18 (14.8%)	125 (19.0%)	110 (23.4%)	34 (19.5%)	3 (7.9%)
Azathioprine	242 (16.6%)	16 (13.1%)	99 (15.1%)	81 (17.2%)	40 (23.0%)	6 (15.8%)
Mycophenolate mofetil	123 (8.4%)	5 (4.1%)	60 (9.1%)	32 (6.8%)	26 (14.9%)	0 (0%)
Glucocorticoid	531 (36.3%)	48 (39.3%)	244 (37.1%)	169 (36.0%)	49 (28.2%)	21 (55.3%)
Last Prescription	1,462	122	658	470	174	38
Rituximab	434 (29.7%)	46 (37.7%)	213 (32.4%)	125 (26.6%)	40 (23.0%)	10 (26.3%)
Cyclophosphamide	19 (1.3%)	0 (0%)	10 (1.5%)	5 (1.1%)	4 (2.3%)	0 (0%)
Methotrexate	345 (23.6%)	22 (18.0%)	149 (22.6%)	125 (26.6%)	41 (23.6%)	8 (21.1%)
Azathioprine	315 (21.6%)	22 (18.0%)	129 (19.6%)	104 (22.1%)	50 (28.7%)	10 (26.3%)
Mycophenolate mofetil	170 (11.6%)	10 (8.2%)	78 (11.9%)	48 (10.2%)	29 (16.7%)	5 (13.2%)
Glucocorticoid	684 (46.8%)	48 (39.3%)	309 (50.0%)	210 (44.7%)	98 (56.3%)	19 (50.0%)

Table 2. AAV Treatment in RISE Registry (2015-2017)

AZA for maintenance of remission in AAV, AZA use was common. Future studies should characterize the severity of AAV cases in RISE and evaluate patient and provider treatment preferences and practice variability.

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Granulomatosis with Polyangiitis Sustained Remission Off-Therapy: Data from the French Vasculitis Study Group Registry

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SESSION INFORMATION

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Background/Purpose: Data on granulomatosis with polyangiitis (GPA) sustained remission off-therapy (SROT) are limited and it is unknown whether disease characteristics or treatment regimen may affect it. This study aimed to assess SROT of GPA patients from the French Vasculitis Study Group registry, and identify factors associated with its occurrence and durability during follow-up.

Methods: GPA had to satisfy the 1990 ACR classification criteria and/or revised Chapel Hill Nomenclature for study inclusion. SROT was defined as remission (BVAS=0) without glucocorticoids (GC) or immunosuppressants (IS), the latter for ≥6 months (ie 2 consecutive visits). SROT and its duration were extracted from the database. Data from patients with 3-, 5- and 10-year SROT were analyzed. Baseline characteristics of patients with 3-year GPA SROT were compared to those of registry GPA patients with available data at 3 years but not in SROT (controls), and 3-year SROT achieving 5-year SROT vs those who relapsed between 3 & 5 years. Patients with 3-year GPA SROT follow-up +7 years were analyzed according to maintained SROT or not.

Results: Among 795 database patients with new-onset GPA, 259 achieved at least 1 SROT at some time during their disease, after a median [IQR] of 36 [28–63] months post-diagnosis. The first SROT lasted a median of 14 [I8-32] months. Among 202 of those patients who had follow-up, 73 (36%) remained in SROT for a median follow-up of 34 [14-45] months post-SROT. Among 434 (54%) patients followed for ≥3 years post-diagnosis, 82% had received GC and cyclophosphamide induction therapy. At 3 years post-diagnosis, 92 (21%) patients in SROT were compared to 342 (79%) controls who had relapsed or were still taking GC or IS. Patients achieving 3-year SROT vs controls, respectively, had more frequently received intravenous cyclophosphamide as induction therapy (89% vs 77%, P=0.01), with a higher median number of infusions (7.5 vs 6; P=0.05); no other clinical or biological baseline difference was found. Among those 92 3-year SROT patients, 74 had ≥2 years of additional follow-up: 46 (62%) attained 5-year SROT and 28 (38%) had relapsed after a mean follow-up of 13 months. Baseline clinical and biological characteristics of patients achieving 5-year SROT did not differ from those of 3-year SROT patients who relapsed. Among those 92 3-year SROT patients, 16 had ≥7 additional years of follow-up: 6 (38%) achieved 10-year SROT, ie 8% of 75 GPA with available data at 10 years, and 10 (63%) had relapsed a mean 35 ± 28 months after achieving 3-year SROT.

Conclusion: Only 8% of GPA patients achieved 10-year SROT after conventional induction and maintenance therapies. No baseline clinical or biological characteristics helped distinguish patients achieving or maintaining SROT and

those who relapsed. However, patients achieving 3-year SROT had received more intensive induction therapy than those who relapsed or were still on GC or IS at 3 years.

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Abstract Number: 0873

Survival After Lung Transplantation in Adults with Primary Systemic Vasculitides: Analysis of the United Network of Organ Sharing (UNOS) Database

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Background/Purpose: Pulmonary involvement, including pulmonary vascular disease and interstitial lung disease can be an important cause of morbidity and even mortality in patients with primary systemic vasculitides (PSV). Outcomes of lung transplantation (LTx), a potentially life-saving intervention for patients with advanced pulmonary disease in patients with underlying autoimmune conditions including systemic sclerosis (SSc) and connective tissue disease-related ILD (CTD-ILD) are comparable to those of patients without underlying autoimmune conditions. Outcomes of LTx in patients with PSV have not been reported other than descriptively in scattered case reports. The aim of this study is to describe survival after transplantation in patients with PSV undergoing LTx and compare that to survival in LTx patients with SSc and non-CTD-ILD.

Methods: We conducted a retrospective cohort study of adult who underwent LTx in the United States between January 1996 and May 2018. Data was provided by UNOS, a non-profit organization that records data on all solid organ transplants performed in the US. Subjects from the thoracic transplant databases were included if they were at least 18 years of age and had diagnostic codes for PSV. Diagnosis of PSV included: Takayasu's arteritis (TAK), Granulomatosis with Polyangiitis (GPA), Eosinophilic Granulomatosis with Polyangiitis (EGPA) and Microscopic Polyangiitis (MPA). Age (within a 5-year range) and sex-matched controls undergoing LTx were identified for 2 other groups of transplanted patients: 1) Patients with a primary diagnosis of SSc and 2) Patients with a diagnosis of ILD (not CTD-ILD) and selected in a 1:1:1 ratio. We compared patient survival using Kaplan-Meier estimates and a Kruskal-Wallis test.

Results: 23 patients with PSV were identified in the thoracic transplant database. Of these, 2 patients underwent heart transplant (1 EGPA, 1 TAK) and 1 patient with diagnosis of GPA had a lung and heart transplant. 20 patients with a diagnosis of PSV were listed only for LTx, of those only 15 underwent LTx. 73% were male, with a median age 43 years and 73% were white (Table 1). GPA was the most common diagnosis (73%) (Table 2). Except for 1 patient with a diagnosis of TAK, all patients underwent LTx after May 4, 2005 (implementation of Lung Allocation Score). Patients with a diagnosis of PSV and SSc had a longer duration on waiting list compared to ILD patients ($p = 0.04$). Otherwise, there were no significant differences among baseline recipient characteristics between groups. Patients with PSV and

Table 1. Characteristics of Recipients with diagnosis of Primary vasculitis (PSV), Systemic Sclerosis (SSc) and Interstitial Lung Disease (ILD) and patient survival time after lung transplantation

Recipient Characteristic	PSV N = 15	SSc N = 12	ILD N = 16	p-value
Age, median (IQR)	43.0 (32.0-58.0)	45.0 (33.5-53.0)	46.0 (33.0-60.5)	0.71
Sex, n (%)				0.93
Female	4 (27%)	4 (33%)	5 (31%)	
Male	11 (73%)	8 (67%)	11 (69%)	
Race, n (%)				0.13
White	11 (73%)	9 (75%)	10 (63%)	
Black	1 (7%)	3 (25%)	5 (31%)	
Hispanic	3 (20%)	0 (0%)	0 (0%)	
Asian	0 (0%)	0 (0%)	1 (6%)	
BMI, mean (SD)	24.0 (4.0)	24.2 (3.0)	25.7 (4.84)	0.45
Pulmonary artery systolic pressure, median (IQR), mmHg	38.0 (27.0-53.0)	42.0 (37.5-49.0)	43.0 (32.5-52.0)	0.54
Pulmonary artery mean pressure, median (IQR), mmHg	25.0 (16.0-38.5)	28.0 (24.0-31.5)	29.0 (20.5-34.0)	0.73
FVC % predicted, median (IQR)	25.5 (21.0-39.0)	34.50 (26.5-39.0)	37.0 (28.0-50.0)	0.13
Serum Creatine, median (IQR), mg/dl	0.9 (0.7-1.3)	0.7 (0.7-0.8)	0.8 (0.7-1.1)	0.16
History of diabetes, n (%)	1 (7%)	0 (0%)	3 (13%)	0.35
History of malignancy, n (%)	0 (0%)	0 (0%)	1 (5%)	0.42
History of smoking, n (%)	3 (21%)	5 (45%)	4 (25%)	0.38
ECMO at listing	1 (5%)	0 (0%)	1 (6%)	0.40
O2 requirement, median (IQR), l/min	3.0 (1.0-6.0)	4.5 (3.0-6.5)	5.0 (3.0-10.0)	0.27
Bilateral transplant, n (%)	10 (77%)	10 (83%)	13 (81%)	0.92
Total days on waiting list, median (IQR)	63.0 (17.0-237.0)	80.0 (28.5-290.5)	28.5 (6.0-72.5)	0.44
Lung allocation score, median (IQR)	44.41 (35.3-48.2)	80.0 (28.5-290.5)	28.5 (6.0-72.5)	0.04
Day of follow-up, median (IQR)	1,407.0 (460.0-2,173.0)	1,222.0 (237.0-1963.5)	364.0 (156.5-580.0)	0.04
No. of deaths	4	5	6	
Person-years	3.85	3.35	1.00	0.04

BMI = Body mass index; FVC = Forced vital capacity; ECMO = Extracorporeal Membrane Oxygenation; O2 = oxygen.

SSc had a longer survival time compared to ILD (p = .040) (Figure 1). There were no differences in survival or cause of death between PSV diagnoses.

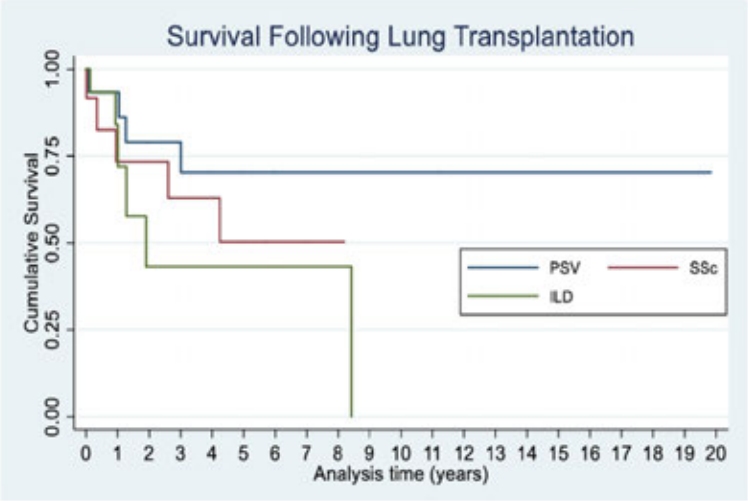
Conclusion: To our knowledge, this is the first analysis reporting outcomes of patients with PSV undergoing LTx. PSV remains a rare context for LTx. There were no significant differences in patient survival time between PSV and SSc. Although this study has limitations, in particular small sample size, our data suggest that lung transplantation in patients with PSV achieved comparable outcomes to those in patients with SSc and better than ILD patients and should be considered a therapeutic option in this patient population.

Table 2. Outcomes of Lung transplantation by PSV diagnosis

	GPA N = 11	EGPA N = 1	TAK N = 2	Other N = 1	p-value
Days of follow-up, median (IRQ), days	1,407.0 (460.0 - 1803.0)	703.0 (703.0 - 703.0)	3,639.0 (30.0 - 7,248.0)	2,173.0 (2,173.0 - 2,173.0)	0.74
Decedents, n (%)	3 (27%)	0 (0%)	1 (50%)	0 (0%)	0.76
Cause of death, n (%)					0.79
Unknown	1 (9%)	0 (0%)	0 (0%)	0 (0%)	
Acute rejection	1 (9%)	0 (0%)	0 (0%)	0 (0%)	
Graft infection	1 (9%)	0 (0%)	0 (0%)	0 (0%)	
Cardiac arrest	0 (0%)	0 (0%)	1 (50%)	0 (0%)	

GPA = Granulomatosis with Polyangiitis; EGPA = Eosinophilic Granulomatosis with Polyangiitis; TAK = Takayasu arteritis.

Figure 1. Kaplan-Meier Survival Curve for adults with diagnosis of PSV, SSc and ILD following lung transplantation



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Abstract Number: 0874

Comparative Analysis Between ANCA-associated Interstitial Lung Disease and Interstitial Pneumonitis with Autoimmune Features

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – ANCA-Associated I

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Table 1: Baseline characteristics of ANCA-associated ILD and IPAF groups with respect to demographic, serologic and pulmonary physiology data.

	ANCA (n=52)	IPAF (n-101)	P-value
Demographic, n (%)			
Female	31 (59.6)	59 (58.4)	0.89
Age, mean (SD)	63.2 (13.3)	62.7 (11.9)	0.80
Race			0.70
Caucasian	38 (73.1)	76 (75.3)	
African-American	11 (21.2)	19 (18.8)	
Asian	3 (5.7)	4 (3.9)	
Hispanic/ Latino	0	2 (1.9)	
Serologies, n (%)			
ANA positivity[1]	44 (84.6)	85 (85)	0.95
ANA, median (IQR)	640 (160-2560)	640 (320-2560)	0.58
Anti-CCP[2]	4 (8.3)	5 (5.4)	0.51
Rheumatoid factor[3]	14 (28)	20 (21.1)	0.35
Anti-dsDNA[4]	3 (6)	1 (1.0)	0.078
Anti-RNP[2]	7 (14.9)	5 (5.3)	0.055
Anti-SS-A[2]	12 (24)	24 (24.2)	0.97
Anti-SS-B[2]	3 (6.3)	3 (3.0)	0.36
anti-Jo-1[2]	1 (2.1)	1 (1.1)	0.65
Other anti-synthetase ab[2]	4 (18.2)	4 (10.8)	0.43
Anti-Scl-70[5]	3 (7.1)	2 (2.2)	0.16
anti-Smith[2]	3 (6.8)	1 (1.1)	0.065
PFTs, % predicted, mean (SD)[6]			
BMI, mean (SD)[7]	30.2 (7.5)	30.2 (6.3)	0.97
TLC	69.1 (16.9)	70 (18.0)	0.65
FVC	64.4 (18.6)	64.4 (18.7)	0.98
FEV1	73 (21.3)	75 (22.4)	0.51
DLCO	51.7 (13.3)	50.4 (22.7)	0.74

[1]ANA positivity defined as ANA IF assay ≥80 titer; [2]Antibody positivity defined as ≥20 U; [3]Rheumatoid factor positivity defined as ≥14 IU/ mL; [4]Anti-ds-DNA positivity defined as ≥10 titer; [5]Anti-Scl-70 positivity defined as ≥1U.
[6]Pulmonary functional tests percentage of predicted value for age, gender, race/ethnicity, height, and weight.
[7]Body mass index, kg/m^2

Background/Purpose: Anti-neutrophil cytoplasmic antibodies (ANCA) have been identified in patients who have pneumonia without a diagnosis of ANCA-associated vasculitis (AAV). These patients are presently categorized as having idiopathic pulmonary fibrosis (IPF). Recent criteria categorize patients with features of autoimmunity but without a defined connective tissue disease as having interstitial pneumonitis with autoimmune features (IPAF). However, these criteria do not include ANCA. Growing evidence suggests that patients with ILD and ANCA may present differently from those with ILD in the setting of AAV or IPF.

Methods: We performed a retrospective case-cohort study of ANCA-associated ILD and randomly selected age and gender-matched controls with IPAF. Both groups were followed at the University of Chicago (1/2005 - 10/2018). Data on autoimmune serologies, baseline high-resolution CT scan using CALIPER (Computer-Aided Lung Informatics for Pathology Evaluation and Rating) parameters, baseline and longitudinal pulmonary functional tests (PFTs), vital status and lung transplant were collected from the electronic medical records. Variable comparisons utilized the Student's t-test or chi-squared, while panel data was evaluated with mixed-effect modeling. Survival analysis was computed using Cox regression models and the Kaplan-Meier estimator. (IRB#18-03349; #14163-A).

Results: In the study population (ANCA-associated ILD, n=52; IPAF, n=101), the mean age at ILD diagnosis was 63yrs, and 59% were women. Compared to white subjects, racial/ethnic minorities had lower TLC%, FVC%, FEV1%, and DLCO% (P=0.004, 0.003, 0.011, and 0.08 respectively). Groups were otherwise comparable with respect to race (Table 1). The prevalence of other autoimmune antibodies appeared greater in ANCA-associated ILD compared to IPAF, however these differences were not statistically significant (Table 1). Baseline and longitudinal PFTs were similar between both groups. Patients with ANCA-associated ILD had greater honeycombing in central portions of the lower lobes, and the central region of the left middle lobe (Table 2). ANCA positivity was not predictive of mortality (Figure 1), whereas total lung vessel volume, older age, non-White race, and lower DLCO% (P=0.043, < 0.001, 0.008, 0.054 respectively) were associated with mortality.

Table 2: Comparison between ANCA-associated ILD and IPAF groups with respect to CALIPER-derived parameters.

	ANCA (n=40)	IPAF (n=82)	P-value
CALIPER, mean (SD)[1]			
Total Lung			
Mild air-trapping	594.0 (853.5)	735.3 (985.8)	0.44
Moderate air-trapping	12.2 (19.6)	37.5 (121.2)	0.19
Severe air-trapping	24.3 (146.6)	5.2 (19)	0.25
Ground glass opacity	706.3 (26)	754.2 (551.8)	0.63
Honeycombing	64.9 (322.6)	7.1 (19.6)	0.11
Reticulation	168.8 (171.5)	143.6 (101.9)	0.31
Vessel volume	258.2 (542.3)	178.5 (71.6)	0.19
Left-middle central lobe			
Severe air-trapping	$5.2x10^{-3}(1.2x10^{-2})$	$5.3x10^{-2}(0.2)$	0.022
Right-lower central lobe			
Honeycombing	1.3 (4.7)	0.4 (0.8)	0.075
Left-lower central lobe			
Honeycombing	1.0 (2.7)	0.3 (0.7)	0.033

[1]CALIPER data described in the volumetric unit voxel.

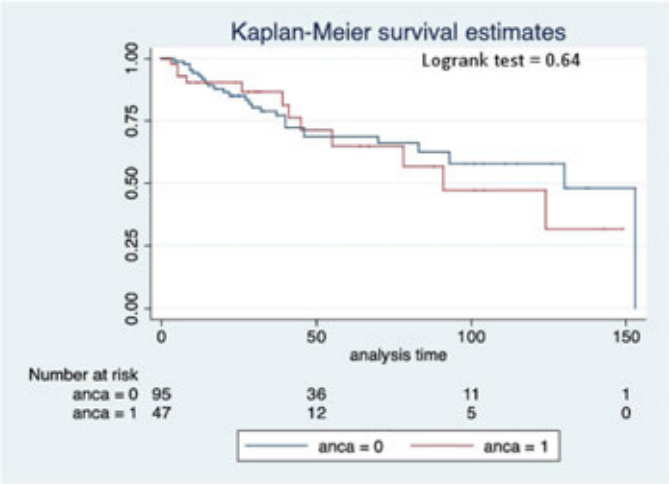

Figure 1: Kaplan-Meyer estimator of survival functions of ANCA- associated ILD and IPAF groups.

Conclusion: This is the largest US study comparing ANCA-associated ILD to IPAF. Our results suggest that these groups are similar, and these findings may argue in favor of adding ANCA to the IPAF criteria. Our radiographic data also suggests that ANCA-associated ILD may be driven by inhaled antigens and airway inflammation, leading to centrilobular fibrosis.

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Abstract Number: 0875

Effect of the Dr. Bart Application on Healthcare Use and Clinical Outcomes in People with Osteoarthritis of the Knee And/or Hip in the Netherlands; A Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: New Approaches to Old Diseases
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Self-management is of paramount importance in non-surgical treatment of knee/hip osteoarthritis (OA). Modern technologies offer the possibility to support self-management 24/7. We developed an e-self-management application (dr. Bart app) for people with knee/hip OA. A central element of the dr. Bart app is that the app proposes a selection of 72 preformulated goals to induce health behaviors based on the 'tiny habits method'[1]. The primary objective of this RCT was to evaluate the short term effects (3 & 6 months) of the use of the dr. Bart app (ad libitum), compared to usual care, on the number of secondary health care consultations in people with knee/hip

OA in the Netherlands. Secondary objectives were to study the effectiveness on clinical outcomes attributable to dr. Bart app.

Methods: A randomized controlled design involving participants ≥50 years with self-reported knee and/or hip OA, randomly allocated to the dr. Bart app or usual care. Participants were recruited from the community through advertisements in local newspapers and social media campaigns. In Figure 1 the theoretical framework of the dr. Bart app is presented. Participants received online questionnaires at baseline and after 3 and 6 months of follow-up. The primary outcome was the number of consultations in secondary health care due to OA in the knee/hip in the past six months. Secondary outcome measures were self-management behavior, pain, symptoms, functional limitations, physical activity, quality of life, and illness perceptions. Data were analyzed using negative binomial regression or linear mixed models, as appropriate, corrected for baseline, main OA-location (knee or hip), and interaction between treatment group and time.

Results: In total 427 eligible participants were allocated to either the dr. Bart group (n=214) or usual care (n=213). Mean age of the participants was 62.1 (SD 7.3) years, with the majority being female (72%) and having symptoms predominantly in their knee(s) (73%). Response rates for the follow-up questionnaires were 75.4% and 69.3% at 3 and 6 months, respectively. With respect to the number of consultations in secondary health care we found a non-significant incidence rate ratio (1.20 (95% CI: 0.67; 2.19)) between the dr. Bart app group and the usual care group. We found a positive overall treatment effect of the dr. Bart app on symptoms (2.6 (95% CI: 0.4; 4.9)), pain (3.5 (95% CI: 0.9; 6.0)) and, activities of daily living (2.9 (95% CI: 0.2; 5.6)), see Table 1. We found non-significant differences between groups for self-management behavior, physical activity, health-related quality of life and illness perceptions.

Conclusion: The dr. Bart app did not reduce the number of secondary health care consultations compared to usual care. However, we found positive effects attributable to the dr. Bart app on pain, symptoms, activities of daily living and functioning in sport and recreation in people with knee/hip OA, suggesting that the dr. Bart app has potential to positively influence health in people with knee/hip OA.

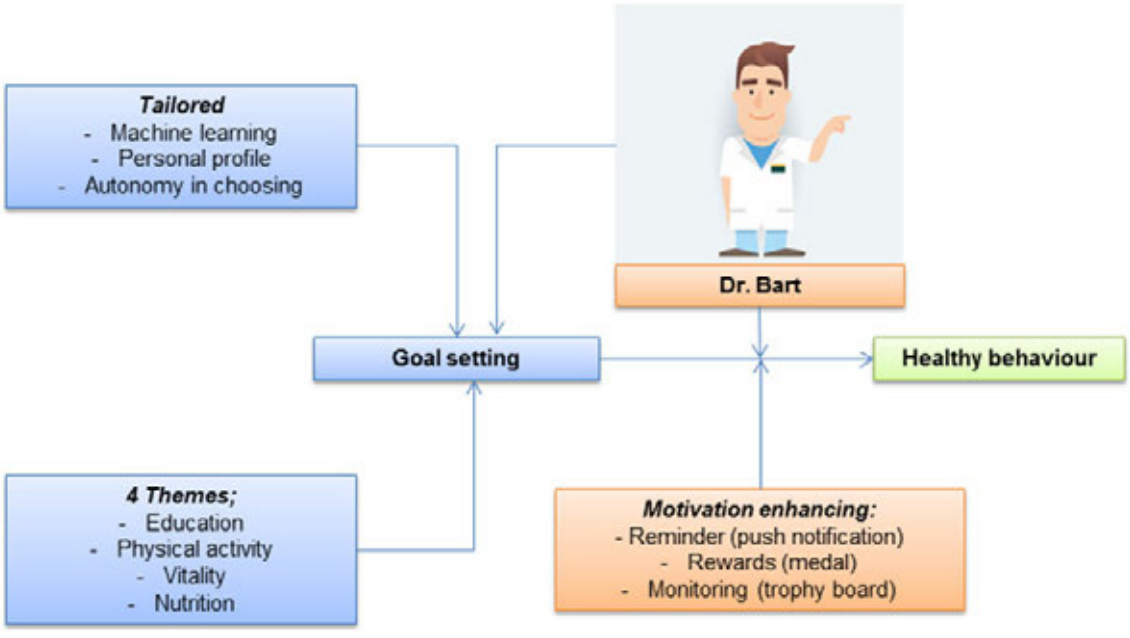

Figure 1. Theoretical framework of the dr. Bart app.

Measures	Treatment effects of dr. Bart app		
	Δ3 months§∞ (95 % CI)	Δ6 months§∞ (95 % CI)	Δ overall§ (95 % CI)
Number of consultations in secondary health care †	1.05 (0.55; 2.02)	1.32 (0.89; 2.87)	1.20 (0.67; 2.16)
KOOS/HOOS			
- Symptoms	1.5 (-1.2;4.1)	2.6 (-0.4; 5.6)	2.6 (0.4; 4.9)*
- Pain	3.1 (0.2; 5.9)*	0.9 (-2.0; 3.8)	3.5 (0.9; 6.0)*
- Activities of daily living	2.5 (-0.7; 5.7)	0.9(-2.6; 4.4)	2.9 (0.2; 5.6)*
- Functioning in sport and recreation	-1.7 (-6.4; 2.9)	7.7 (2.7; 12.7)*	1.9 (-2.0; 5.9)

Table 1. Overall treatment effect and treatment effects at 3 and 6 months of the dr. Bart app. * Indicates p-value < 0.05 † Reported as incidence rate ratio §Adjusted for baseline value, treatment group and main OA-location (knee/hip) ∞ Adjusted for time, and interaction between treatment group and time Abbreviations: KOOS; Knee Injury and Osteoarthritis Outcome Score; HOOS; Hip Disability and Osteoarthritis Outcome Score.

Reference :

1. Fogg GJ: A behavior model for persuasive design. In: *Proceedings of the 4th international Conference on Persuasive Technology: 2009: ACM; 2009: 40.*

Disclosure: T. Pelle, None; **K. Bevers**, None; **J. van der Palen**, None; **F. van den Hoogen**, AbbVie, 5, Actelion, 2, Amgen, 8, Biogen, 5, BMS, 2, Boehringer Ingelheim, 5, Celgene, 5, Celltrion Healthcare, 5, 8, Corbus, 8, Eli Lily, 2, Janssen, 8, Mundipharma, 5, Novartis, 5, Pfizer, 2, Roche, 8, Sandoz, 8, Sanofi Genzyme, 5; **C. van den Ende**, None.

Abstract Number: 0876

"When You Read This, You Really Feel Old!" Perspectives of Young People with Inflammatory Arthritis on Patient Reported Outcome Measures from a European Qualitative Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: New Approaches to Old Diseases
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Although patient-reported outcome measures (PROMs) are extensively used in clinical practice and research, it is unclear whether the most commonly used instruments adequately cover the perspective of young people with chronic inflammatory arthritis. This study was undertaken to investigate whether the aspects important to young people with inflammatory arthritis are sufficiently covered by the PROMs that are widely used in clinical practice and research.

Methods: A qualitative, multicentre focus group interview study was conducted in Austria, Croatia, Italy and the Netherlands in order to inform a EULAR-funded taskforce. Three groups of young people (aged 18-35 years) with either (1) rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA) and Still's disease, (2) psoriatic arthritis (PsA), or (3) axial spondyloarthritis (SpA) were interviewed at each centre. The interview guide was based on the WHO International Classification of Functioning, Disability and Health (ICF) to comprehensively cover all aspects of functioning in daily life [1]. It also included questions on the perspectives and views of the participants on selected PROMs (Pain scales, Patient Global Assessment [PGA], FACIT Fatigue Scale, The Health Assessment Questionnaire [HAQ]/Bath Ankylosing Spondylitis Functional Index [BASFI], and The 36-Item Short Form Health Survey [SF-36]). All interviews

Table. Overview of higher-level concepts and related quotes

Higher-level concepts	Quotes
Relevant issues for young people are not covered by widely used PROMs	*My appearance has never been brought up for discussion, but it impacts my teaching, my sex life, [...].* (male, 30, PsA)
Information, transparency and clarity regarding the purpose of PROMs are often missing	*Honestly, I have often thought that we should fill all those questionnaires to keep us quiet and to avoid that we will freak out!* (female, 27, PsA) *I do not understand the meaning. Why does the doctor care if I can wash my hair? Who will wash it instead? It is a stupid question!* (female, 27, PsA)
The individual life situation of a patient adds essential importance to the results of PROMs	*In my opinion it is problematic to estimate disease activity for today. With my medication, or without? At the moment, I am feeling fine, but it won't be like that without any medication, I guess. And that makes scoring a bit difficult.* (female, 27, PsA)
The scoring on a rating scale sometimes differs from the current health situation	*I am just putting my line anywhere and think – that's fine. (female, 27, PsA)* *I always score very low, like a 1, 2, or 3. which might look very harmless to the doctor. I often ask myself whether I should score worse, to get recognized.* (male, 30, PsA)
Certain PROMs were seen as outdated	*When you read this, you really feel old! (female, 21, RA)* *I think 'working on your computer' or 'typing' or something could be included. I mean how often do we still use a pen and pencil all day long? It should be a little more up to date.* (female, 25, PsA)
PROMs focusing on symptoms and physical function only, do not comprehensively cover patients' experiences	*I think it is also important what you [as an individual] need. Not only the physical part, but also the mental part, so how are you feeling. I think that is important too.* (male, 22, SpA)
The use of new technologies for data acquisition was suggested by some young patients	*Sometimes I do not want to answer with a whole story. [...] but I can also do that questionnaire [HAQ] digitally at my hospital. That is nice!* (female, 25, PsA)

were conducted by trained local investigators, audio-recorded, transcribed verbatim, and analysed using a modified form of 'meaning condensation' [2]. During a face-to-face meeting of the task-force members, the concepts were reformulated and organized into a scheme of higher and lower-level concepts.

Results: Thematic saturation was reached after 12 focus groups with 53 participants (21 with RA/JIA/Still's, 15 with SpA, 17 with PsA; 72% female, mean age 28, SD±5), resulting in 18 hours and 22 minutes of recorded time and 269 pages of transcript. The analysis revealed aspects of functioning in daily life important to young people with inflammatory arthritis which were mentioned in all countries. Furthermore, 55 concepts emerged with regard to PROMs and were summarized into seven higher-level concepts. The table depicts these higher-level concepts including quotes from the interviews.

Conclusion: The evaluation of young patients' perspectives should probably reach beyond the topics/aspects covered in the most commonly used PROMs. Accordingly, tailoring the assessments to specific needs of young people should be considered.

References:

1. WHO, International classification of functioning, disability and health: ICF. 2001: Geneva: World Health Organization.
2. Stamm, T.A., et al., Concepts of functioning and health important to people with systemic sclerosis: a qualitative study in four European countries. Ann Rheum Dis, 2011. 70(6): p. 1074-9.

Disclosure: E. Mosor, None; **P. Studenic**, None; **A. Alunno**, None; **I. Padjen**, None; **W. Olsder**, None; **S. Ramiro**, AbbVie, 5, 8, Eli Lilly, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8; **I. Bini**, None; **N. Caeyers**, None; **L. Gossec**, Abbvie, 5, AbbVie, 5, Abbvie, Biogen, BMS, Celgene, Lilly, Novartis, Pfizer, SAnofi-Aventis, UCB, 5, Amgen, 5, Biogen, 5, BMS, 2, 5, Celgene, 5, Celgene Corporation, 2, Janssen, 5, Lilly, 2, 5, MSD, 5, Nordic Pharma, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 5, Sanofi-Aventis, 5, UCB, 5; **M. Kouloumas**, None; **E. Nikiphorou**, AbbVie, 8, Celltrion, 5, 6, Eli Lilly, 8, Eli Lilly and Company, 8, Gilead, 5, 6, Pfizer, 8, Sanofi, 5, 8; **S. Stones**, None; **T. Wilhelmer**, None; **T. Stamm**, Janssen, 8, MSD, 8, Novartis, 8, Roche, 2, 8.

Abstract Number: 0877

Rheumatoid Arthritis Patients' Perspectives on Tapering of Biologics: A Qualitative Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: New Approaches to Old Diseases
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Tapering of biologics is now recommended in the management of people with RA in sustained remission.[1] Clinical studies have shown some RA patients can successfully taper their biologic without significant increases in disease activity or radiographic progression. However, little is known of RA patients' perspectives about the possibility of tapering their biologic. This study sought to identify factors that may influence RA patients' decision to taper their biologic.

Methods: Patients meeting the 2010 ACR/EULAR classification criteria for RA and currently taking biologics were eligible to participate in focus groups or individual interviews. Patients with any level of disease activity were included to allow exploration of a wide range of perspectives and to avoid exclusion of potentially valuable insights. All interviews and focus group discussions were audio recorded and transcribed verbatim. Transcripts were coded using an established approach to thematic analysis[2] to determine themes relating to patients' decision about tapering biologics.

Results: 128 eligible patients were invited, 76 declined or did not respond and 7 were unavailable. 45 participants were involved in either 1 of 6 focus groups (n=43) or an in-depth individual interview (n=2). Around two-thirds of participants were receiving biologics via infusion and the remaining were self-injecting. Five themes were identified: fear of the uncertainty of outcomes, prioritizing quality of life over the risk of adverse effects, relief from medication burden, healthcare system support, and preference for involvement in decision-making. Participants had strong concerns that tapering their biologic might lead to periods of uncontrolled disease activity leading to joint damage. Their desire for better quality of life outweighed the concern of adverse effects associated with long-term biologic use. Nevertheless, participants recognized a lower frequency of administration would provide convenience in some aspects of daily life. Prompt reinitiation of biologics and consultation with the rheumatology team if flares occur when tapering are crucial from the perspective of the participants. Furthermore, participants would prefer to make the decision to taper biologics together with their rheumatologist.

Conclusion: Concerns of uncontrolled disease and receiving access to treatment when disease flares are among the key issues that need to be addressed when planning tapering protocols. Tool to aid shared decision making may facilitate the exchange of information, improve patients' knowledge and understanding of the benefits and risks involved in tapering their biologic leading to greater acceptance of tapering.

Reference:

1. Smolen et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017;76(6):960-977
2. Braun et al. Using thematic analysis in psychology. *Qualitative Research in Psychology.* 2006;3(1):77-101

Disclosure: J. Chan, None; **L. Stamp**, None; **N. Liebergreen**, None; **H. Ndukwe**, None; **C. Marra**, None; **G. Treharne**, None.

Abstract Number: 0878

The Association of Serum Magnesium with Chondrocalcinosis and Osteoarthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: New Approaches to Old Diseases
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Table: Cross-sectional and Longitudinal association of serum magnesium level with radiographic and symptomatic chondrocalcinosis and osteoarthritis	
Cross-sectional	**Adjusted** OR (95% CI)**
	Prevalent Radiographic chondrocalcinosis (N=985)
Serum Magnesium (mEq/L)	0.70 (0.52, 0.95)
	Prevalent Symptomatic chondrocalcinosis (N=985)
Serum Magnesium (mEq/L)	0.63 (0.35, 1.15)
	Prevalent Radiographic osteoarthritis (N=985)
Serum Magnesium (mEq/L)	0.94 (0.82, 1.08)
Longitudinal	**Adjusted** HR (95% CI)**
	Incident Radiographic chondrocalcinosis (N=772)
Serum Magnesium (mEq/L)	0.87 (0.66, 1.17)
	Incident Symptomatic chondrocalcinosis N=(830)
Serum Magnesium (mEq/L)	0.60 (0.43, 0.84)
	Incident Radiographic osteoarthritis (N=606)
Serum Magnesium (mEq/L)	0.99 (0.87, 1.16)
	Incident Symptomatic osteoarthritis (N=893)
Serum Magnesium (mEq/L)	0.95 (0.84, 1.07)
Adjusted for age, sex, BMI Odds and Hazard ratios are per SD increase in Magnesium	

Background/Purpose: High serum magnesium (Mg) may have anti-inflammatory effects and prevents the release of extracellular pyrophosphate, inhibiting CPP deposition. Cross-sectional data has linked low serum Mg levels with radiographic chondrocalcinosis (CC) but there is a paucity of longitudinal studies and an absence of studies of symptomatic CC. Since osteoarthritis (OA) and CC often co-exist and have other common risk factors, we evaluated the relation of serum Mg levels to prevalence and risk of 4 outcomes, radiographic CC, symptomatic CC, radiographic knee OA, and symptomatic knee OA in a large cohort of community dwelling older adults.

Methods: For each of the 4 outcomes we performed a nested case-control study within the Multicenter Osteoarthritis (MOST) study, a NIH-funded longitudinal cohort of persons with or at risk of knee OA. Serum Mg level (mEq/L) was measured (AU480, Beckman Coulter Inc., Brea CA 92821) at baseline. For each outcome, we excluded those who, at baseline had the outcome. Our outcomes from baseline through 60 month follow-up were incident (new onset) radiographic OA (KL-grade ≥2 in either or both knees), symptomatic OA (radiographic OA with frequent knee pain in the same knee), radiographic CC (presence of CC in either or both knees) and symptomatic CC (radiographic CC with frequent knee pain in the same knee). To examine cross sectional baseline associations for each outcome, we took subjects selected for Mg assessment for the other outcomes and evaluated the association of serum Mg (per SD increase) to prevalent radiographic OA, radiographic and symptomatic CC using logistic regression. Using each case control sample, we then examined the longitudinal association of baseline serum Mg to incident radiographic

OA, symptomatic OA, radiographic and symptomatic CC using Cox proportional hazards regression. All analyses were adjusted for age, sex, and BMI.

Results: Among 985 participants (mean age 62 yrs, 59% women and mean BMI 29.9 kg/, mean Mg levels 1.89 mEq/L) , the prevalence was 324 radiographic OA, 47 radiographic CC and 11 symptomatic CC. In **cross-sectional analyses (see table)**, serum Mg was not associated with prevalence of radiographic OA (per standard deviation of Mg, OR=0.94, 95% CI 0.82, 1.08) but was modestly associated with radiographic CC (OR=0.70, 95% CI 0.52, 0.95) and symptomatic CC (OR= 0.63, 95% CI 0.35, 1.15).

Incidence of radiographic OA occurred in 250 of 606 persons; 336 of 893 had incident symptomatic OA; 46 of 772 had incident radiographic CC; 33 of 830 had incident symptomatic CC. In **longitudinal analyses**, higher baseline serum Mg levels were not associated with risk of incident radiographic OA (HR=0.99, 95% CI 0.87, 1.16), symptomatic OA (HR 0.95, 95% CI 0.84, 1.07) or radiographic CC (HR=0.87, 95%CI 0.66, 1.17) but were associated with risk of symptomatic CC (HR= 0.60, 95% CI 0.43, 0.84).

Conclusion: Higher serum magnesium levels were associated with a lower risk of symptomatic CC but not with radiographic CC, radiographic OA, or symptomatic OA. The association of Mg with incident symptomatic CC has important clinical implications and is consistent with cross sectional studies but is based on small numbers and needs replication.

Disclosure: D. Misra, None; **X. Sun**, None; **M. Nevitt**, None; **B. Lewis**, None; **J. Torner**, None; **T. Neogi**, MerckSerono, 5, Novartis, 5; **A. Lichtenstein**, None; **N. Matthan**, None; **D. Felson**, None.

Abstract Number: 0879

Evaluation of Marijuana and Cannabidiol Use in the Rheumatologic Population from a Patient and Clinician Perspective: A Survey-Based Study

Heather Goodwin,[1] **Ali Porter**,[1] Melinda Edwards,[1] and Bonita Libman[1], [1]The University of Vermont Medical Center, Burlington, VT

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: New Approaches to Old Diseases
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: To evaluate use of marijuana (MJ) and cannabidiol (CBD) as described by rheumatology patients at an academic medical center in Vermont, and to describe beliefs and practices of rheumatology clinicians regarding patient use of MJ and CBD in the United States.

Methods: A paper survey was distributed to adult patients during routine rheumatology clinic visits at the University of Vermont Medical Center between November 2018 and February 2019. A second survey was developed using Research Electronic Data Capture (RedCap) software and was disseminated via email to clinicians identified from the American College of Rheumatology membership list. Descriptive statistics were used to assess responses.

Results: A total of 419 patient surveys were collected with 148 (35.3%) reporting current use of MJ and/or CBD. Of those 148 patients, 42% were using both MJ and CBD, 36% only CBD, and 22% only MJ. RAPID3 scores of users

were collected; 52% as high severity, 40% moderate, 36% low, and 21% near remission. Worsening disease severity influenced patient use (Wald $\chi 2$ (3) =15.3, p =0.0165). Over half (51%) agreed they were able to decrease use of pain medication when MJ or CBD was used. The average self-reported pain on a 0-10 scale before and after use of MJ and/or CBD was 6.9 and 4.4 respectively.

Nearly half of clinician respondents disagreed that MJ (45.2%; n = 106) or CBD (37.4%; n = 105) should be recommended as medical therapy for patients with rheumatologic disorders. Of those practicing in states where MJ is legal for medical and recreational use, 52.9% agreed that they were comfortable addressing questions surrounding use vs. 33.3% in states where MJ is illegal, although this was not statistically significant. Many disagreed that opioid and NSAID use decreases with marijuana use (33.9% and 40.9% respectively), this was similar for CBD (32.2% and 34.8% respectively).

Conclusion: Patient and clinician perceptions are dissimilar regarding benefits of MJ and CBD use, especially around pain medication requirements. Worsening disease severity influences probability of use. Surrounding laws likely impact clinician perception and comfort with medical use. Additional research is needed to better understand the benefits and risks of MJ and CBD use in the rheumatologic patient population.

Disclosure: H. Goodwin, None; **A. Porter**, None; **M. Edwards**, Amgen, 8; **B. Libman**, None.

Abstract Number: 0880

Diseased Lupus Nephritis Kidneys Serve as a Primary Site of Systemic Autoimmune Development

Matthew Woodruff,[1] Christopher Tipton,[1] Jennifer Hom,[1] and Iñaki Sanz[1], [1]Emory University, Atlanta, GA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Lupus nephritis (LN) is an autoimmune destruction of the kidney glomeruli and loss of kidney function affecting almost half of lupus patients. Although the disease is classified and treated based on accumulated glomerular damage and proliferative lesions, it has been shown that tubulointerstitial inflammation deeper in the organ is a better predictor of long-term renal viability. Autoimmune B cells have been identified as an important mediator of this inflammation, and recent work has identified interesting transcriptional maturation of these cells upon tissue engraftment. Here, we examine other critical properties of these cells that remain yet unexplored.

Methods: Kidney biopsies and matched blood from patients with Class II, III, or IV (+/- V) LN were obtained and processed for next-generation B cell receptor sequencing. The resulting B cell repertoire was analyzed to understand the properties of kidney B cells (KBCs), and their relationship to established compartments in the blood.

Results: Through repertoire sequencing and analysis, we report a highly dynamic B cell environment hallmarked by *in situ* development of kidney-derived B cell (KBC) lineages from naive-like precursors. These KBC lineages are capable of class switching, undergo extensive division, and display levels of somatic hypermutation not seen even in the memory autoimmune B cell compartment in the blood. Importantly, these highly selected B cell lineages are not restricted to the kidney following maturation, and can be identified in the blood of patients years after initial expansion in the kidney. Finally, biopsies of patients during acute onset of LN versus patients with a longer LN history

reveal distinct phases of humoral development within the renal environment that is not captured by current disease classification systems, and may be relevant to disease treatment.

Conclusion: Through these data we draw the surprising conclusion that rather than serving as a target of autoimmune attack, the renal environment serves as a primary site of humoral autoimmune development. This development is progressive by nature, and the early phase of disease onset may represent a distinct therapeutic opportunity for aggressive B cell directed intervention. Additionally, these data may help explain mixed results when applying B cell directed therapies towards these patients. In all, this study reveals a dynamic, progressive, and pervasive humoral immune component in the renal environment in every LN patient assessed to-date, and highlights a surprising gap between traditional histological classification of the disease and the underlying immune status.

Disclosure: M. Woodruff, None; **C. Tipton**, None; **J. Hom**, None; **I. Sanz**, None.

Abstract Number: 0881

Auto-antibodies Targeting Components of Sarcolemma Repair: A Pathogenic Mechanism in Human Inflammatory Myopathies

Kevin McElhanon,[1] Ana Capati,[2] Nicholas Young,[3] Brian Paleo,[2] Eric Beck,[2] Zarife Sahenk,[4] Rohit Aggarwal,[5] Chester Oddis,[5] Noah Weisleder,[1] and Wael Jarjour[6], [1]Dorothy M. Davis Heart and Lung Research Institute & Dept. of Physiology & Cell Biology, The Ohio State University Wexner Medical Center, Columbus, OH, [2]The Ohio State University Wexner Medical Center, Columbus, OH, [3]The Ohio State University Wexner Medical Center, Division of Immunology and Rheumatology, Columbus, OH, [4]Nationwide Children's Hospital, Columbus, OH, [5]University of Pittsburgh Medical Center, Pittsburgh, PA, [6]Ohio State College of Medicine, Columbus, OH

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) represent a group of disorders causing chronic inflammation and significant damage to skeletal muscle due to an unchecked autoimmune response. Two mouse models of IIM have recently provided new insights into the pathogenesis of the disease. The synaptotagmin VII null (Syt VII$^{-/-}$) mouse is characterized by defects in membrane resealing and presents with a mild form of myositis at 2 months of age. A more robust model of IIM combines knock-out of Syt VII with a FoxP3 mutation resulting in a mouse with impaired membrane resealing and regulatory T-cell deficiency. Tripartite motif (TRIM) proteins are another family that has a critical role in membrane repair. Here, we explore the presence of a pathogenic mechanism involving sarcolemma repair that is responsible for initiation and/or propagation of muscle inflammation.

Methods: Autoantibodies directed to TRIM family protein members were examined by immunoblotting and/or ELISA. Membrane repair was monitored *ex vivo* using an established assay where the membrane of individual muscle fibers of intact skeletal muscle bundles were injured using an infrared multi-photon laser. Confocal live cell imaging was used to record entry of FM4-64 dye, which only fluoresces once it enters the cell. To examine membrane fragility, mouse skeletal muscle was collected from wild type mice or RAG1$^{-/-}$ mice adoptively transferred with lymph node preparations from either Syt VII$^{-/-}$/FoxP3$^{-/Y}$ mice or FoxP3$^{-/Y}$. Tissue was analyzed by immunohistochemistry for evidence of inflammation and tissue injury.

Results: We have established by direct ELISA that auto-antibodies against TRIM72, a critical protein involved in sarcolemmal membrane repair, is elevated in IIM patient sera. We show, for the first time, that a deficiency in T-regulatory

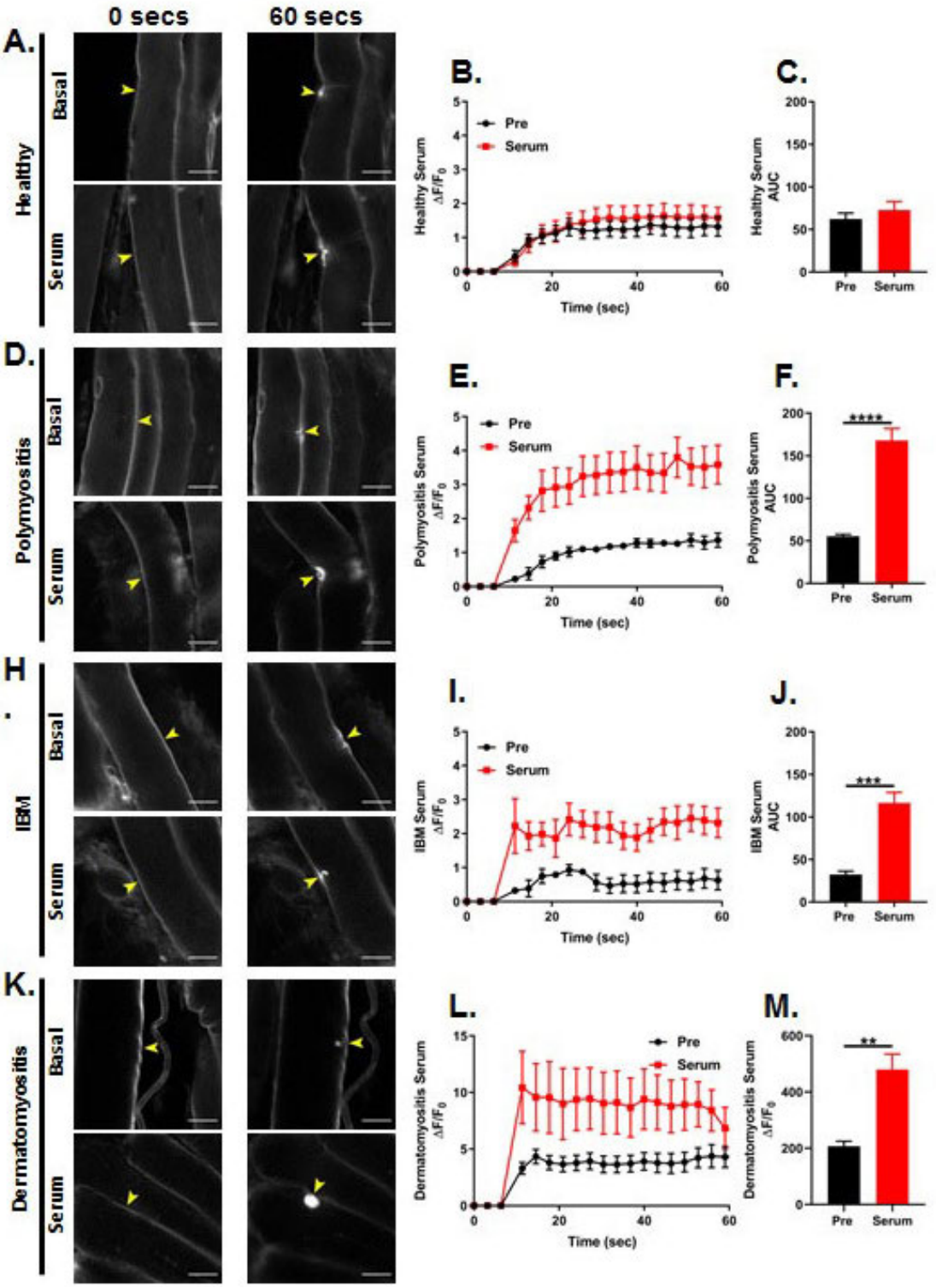

Figure. Myositis patient sera positive for TRIM72 autoantibodies compromises sarcolemmal repair in healthy skeletal muscle.

cells is not sufficient to induce sarcolemma fragility, however, purified antibodies against critical proteins that facilitate the sarcolemma repair process are sufficient to reduce membrane repair capacity. We also demonstrate that sarcolemma integrity is reduced in distal skeletal muscle in the absence of inflammation in our novel murine model of IIM. Moreover, we find that exogenous delivery of IIM (dermatomyositis, inclusion body myositis and polymyositis) patient

serum containing antibodies to TRIM72 can compromise sarcolemma resealing in healthy skeletal muscle in an *ex vivo* laser injury assay (see figure).

Conclusion: These findings represent a novel mechanism in IIM whereby decreased sarcolemma integrity induces a vicious cycle of aberrant antigen presentation that directly contributes to the pathophysiology of idiopathic immune myopathies.

Myositis patient sera positive for TRIM72 autoantibodies compromises sarcolemmal repair in healthy skeletal muscle.

Disclosure: K. McElhanon, None; **A. Capati**, None; **N. Young**, None; **B. Paleo**, None; **E. Beck**, None; **Z. Sahenk**, None; **R. Aggarwal**, Bristol Myers-Squibb, 2, 5, Pfizer, 2, Genentech, 2, Momenta, 2, Mallinckrodt, 2, 5, Octapharma, 5, CSL Behring, 5, AstraZeneca, 5, Corbus, 5, Kezar, 5; **C. Oddis**, None; **N. Weisleder**, None; **W. Jarjour**, None.

Abstract Number: 0882

Serum Anti-Vimentin Autoantibodies May Uniquely Predict Response to Therapy in Lupus Nephritis

Andrew Kinloch,[1] Matthew Cascino,[2] Jian Dai,[3] Rene Bermea,[1] Kichul Ko,[1] Margaret Vesselits,[4] Maureen Legendre,[5] Michael Okoreeh,[1] David Markovitz,[5] Leonard Dragone,[6] Michael Townsend,[3] and Marcus Clark[1], [1]University of Chicago, Chicago, IL, [2]Genentech, Inc., San Fransisco, CA, [3]Genentech, San Fransisco, CA, [4]University of Chicago, Chicago, [5]University of Michigan, Ann Arbor, MI, [6]UCSF, San Fransisco, CA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Tubulointerstitial inflammation (TII) in lupus nephritis (LN) is associated with a worse prognosis. Vimentin, a cytoplasmic antigen, is commonly targeted by *in situ* activated B-cells in TII. The prognostic im-

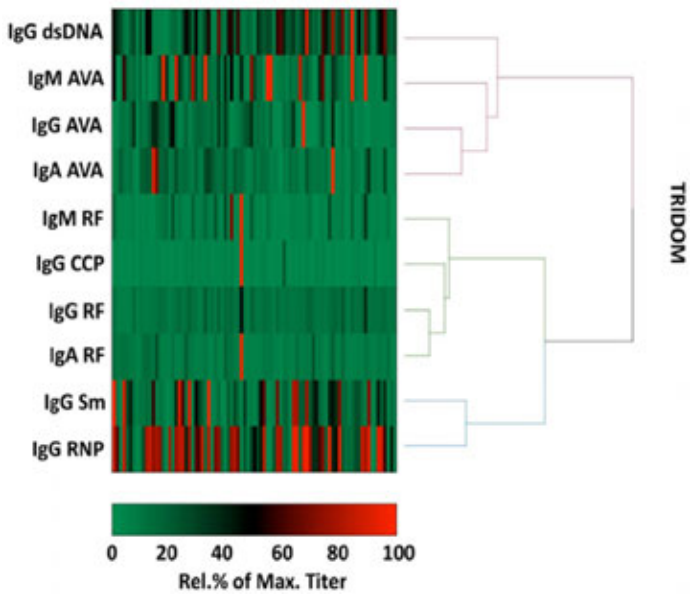

Figure 1. Heat Map and Hierarchical Clustering of autoantibody titers in serum samples from the cross-sectional mixed lupus cohort "TRIDOM"

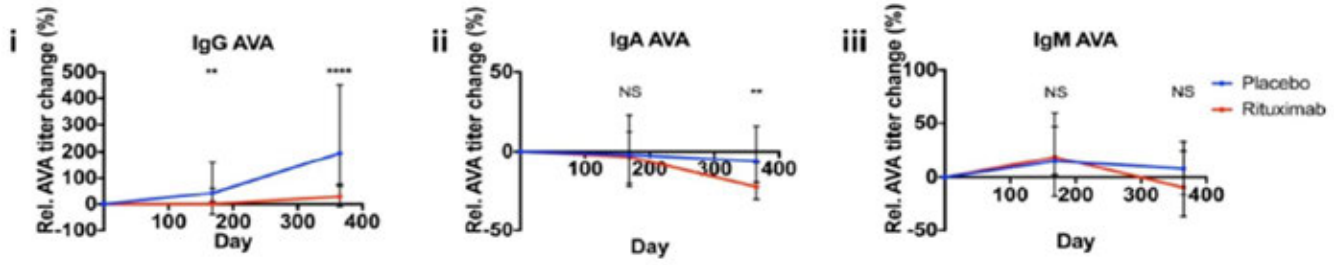

Figure 2. Difference between (i) IgG-, (ii) IgA- and (iii) IgM AVA by median relative titer change (as a percentage of serum titer at trial baseline) in LUNAR trial enrolled proliferative nephritis patients receiving MMF in the presence of rituximab or placebo

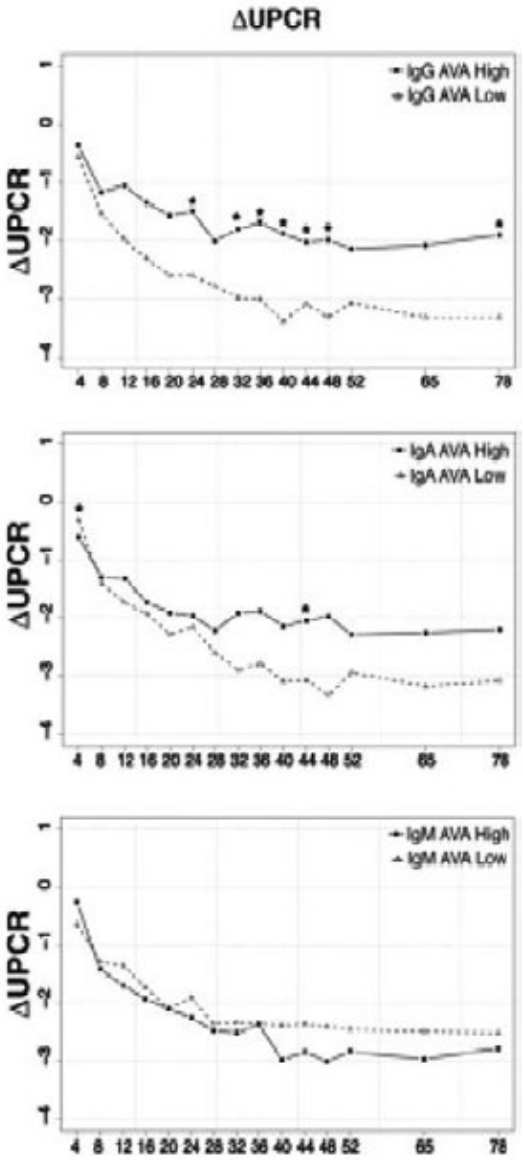

Figure 3. Change in Urine Protein to Creatinine Ratio from baseline in LUNAR patients. Patients from both treatment groups were pooled and subsequently stratified by having the indicated AVA isotype titer above or below total patient median titer at trial baseline.

portance of high serum anti-vimentin antibodies (AVAs) in LN and their relationship with common lupus autoantibody specificities is unknown. We investigated associations between AVA isotypes, other autoantibodies, and response to mycophenolate mofetil in the presence or absence of rituximab.

Methods: An inhouse AVA ELISA was developed using human vimentin as substrate (over expressed in, and purified from the inclusion bodies of, E.coli). Serum from a cross-sectional cohort of 99 lupus patients (22% LN, from the Translational Research Inititative in the Department of Medicine, "TRIDOM") was titrated for IgG-, IgA- and IgM-AVAs, lupus- associated, and RA-associated autoantibodies, and titers subjected to hierarchical clustering. Serum from baseline, 26 and 52 weeks from 131 proliferative LN patients enrolled in the LUNAR trial was analysed for a more exhaustive range of lupus associated antibodies and evaluated for associations with longitudinal laboratory parameters up to week 78.

Results: In TRIDOM, hierarchical clustering analysis revealed AVAs and IgG anti-dsDNA clustered together, whereas AVAs clustered away from anti-Sm, anti-RNP, and RA-associated autoantibodies. In LUNAR at baseline, AVAs correlated weakly with anti-dsDNA and more strongly with anti-cardiolipin titers. IgG anti-dsDNA titers were reduced in both treatment groups, but more profoundly in patients receiving rituximab. In contrast, IgG AVAs increased in both treatment groups from baseline to week 52 (median fold increase of 195% in the absence vs 28% in the presence of rituximab) while titers of IgM and IgA AVAs did not increase over time. Over 78 weeks a reduction in proteinuria was observed for each treatment group, as reported previously at 52 weeks. However, less reduction in proteinuria was observed for patients with baseline high titers of IgG AVA ($p< 0.0001$ for overall effect; mean difference in change of UPCR between high and low groups at week 78 = 1.42 g/g) and IgA AVA ($p=0.0069$; mean difference: 0.88 g/g). In comparison, baseline IgM AVA status was not associated with subsequent difference in change of UPCR ($p=0.75$).

Conclusion: AVAs, especially IgG AVAs, are unique in distribution and response to therapy compared to other commonly measured autoantibody specificities in lupus. Furthermore, high-titer IgG AVAs identify LN patients resistant to conventional therapies. AVAs may represent a new class of prognostic autoantibodies.

Disclosure: A. Kinloch, None; **M. Cascino**, Genentech, 3, Genentech, Inc., 3; **J. Dai**, Genentech, 3; **R. Bermea**, None; **K. Ko**, None; **M. Vesselits**, None; **M. Legendre**, None; **M. Okoreeh**, None; **D. Markovitz**, None; **L. Dragone**, None; **M. Townsend**, Genentech, 3; **M. Clark**, None.

Abstract Number: 0883

B Cell-specific MyD88 Regulates Pathology After Disease Onset in Murine Lupus

Jeremy Tilstra,[1] Minjung Kim,[1] Claire Leibler,[1] and Mark Shlomchik[1], [1]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease defined by immune dysregulation, antibody formation, followed by end-organ damage. MyD88 is a central immune adaptor protein that regulates disease pathogenesis in SLE that acts downstream of the Toll-like receptors, well known mediators of disease in SLE. Several components of the MyD88/TLR signaling pathway have been identified as risk alleles in SLE patients, including TLR7, TLR8, TLR9, IRAK1, IRAK4, OPN, and ACP1. Previously, we showed that global and B

cell-specific MyD88-deficient mice exhibited ameliorated disease, including reduced organ damage and suppressed autoantibody formation. Whether MyD88 regulates only disease initiation or contributes to disease perpetuation after onset of symptoms is unclear. By defining the role of MyD88 in SLE pathogenesis, we will be able to determine if MyD88 is a potential therapeutic target for SLE patients.

Methods: Lupus prone (MRL.*Fas*^{lpr}) mice develop autoantibodies, proteinuria, dermatitis, and glomerulonephritis, with disease onset occurring between 9-11 weeks of age. In order to study the therapeutic potential of MyD88 suppression, we used lupus prone (MRL.*Fas*^{lpr}) mice in which B cell-specific depletion of MyD88 is induced by tamoxifen (hCD20-Tam Cre, Myd88^{floxed}) while both Cre negative littermates and hCD20-Tam Cre^{+} Myd88 sufficient mice were used as a comparator groups. For all groups, tamoxifen was orally administered biweekly starting after disease onset (12 weeks of age). Cell specific deletion was assessed using cell sorting and qPCR of genomic DNA. Mice were analyzed for disease pathology at 19 and 21 weeks of age for females and males respectively. Analysis included proteinuria, renal histology for both interstitial and histologic disease, dermatitis, autoantibody production, and immune cell activation. Survival analysis was performed on female mice.

Results: MRL.*Fas*^{lpr} mice with induced B cell-specific deletion of MyD88 (Tam,B-MyD88$^{fl/fl}$) exhibited a significant survival advantage over control mice ($p< 0.05$) with reduced kidney histologic disease, including both glomerulonephritis ($p< 0.01$) and interstitial inflammation ($p< 0.01$). Additionally, Tam,B-MyD88$^{fl/fl}$ mice had reduced autoantibody formation as assessed by ANA immunofluorescence and ELISA. The B cell compartment was altered in these mice with no change in the percentage of total B cells, but vastly reduced ABC formation (defined as CD19^{+},CD11c^{+}, CD11b^{+}) ($p< 0.005$) and reduced total number of plasmablasts (CD19^{int}, CD138^{+}, CD44^{+})

Conclusion: These experiments suggest that there is a continued role for MyD88 signaling in B cells throughout the course of disease in MRL.*Fas*^{lpr} lupus prone mice, rather than simply disease initiation. Numerous genetic deletions have resulted in suppressed disease onset in lupus models, but herein, we observed disease amelioration after disease onset. This portends that targeting MyD88 or its upstream activators may be a viable therapeutic option in SLE.

Disclosure: J. Tilstra, None; **M. Kim**, None; **C. Leibler**, None; **M. Shlomchik**, None.

Abstract Number: 0884

Interferon-Alpha Disrupts Multiple B Cell Tolerance Mechanisms in 3H9 Mice

Dario Ferri,[1] Yuriy Baglaenko,[2] Kieran Manion,[3] Carolina Munoz-Grajales,[4] and **Joan Wither**[5], [1]University Health Network, Toronto, ON, Canada, [2]Brigham Woman's Hospital, Boston, [3]Krembil Research Institute, Toronto, ON, Canada, [4]University Health Network, Toronto, Canada, [5]University Health Network, Krembil Research Institute, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Interferon-alpha (IFNα) is elevated in Systemic Lupus Erythematosus (SLE) and is thought to play a central role in its pathogenesis. Amongst IFNα's many effects on the immune system are direct effects on B cells, leading to enhanced B cell signaling and survival. It also plays a major role in the induction of B cell activating factor (BAFF). While past studies have explored the effects BAFF on B cell tolerance, little work has focused on how

IFNα directly affects this process. We hypothesize that elevated levels of IFNα directly contribute to the breach of B cell tolerance in SLE. To address this question, we used an adenoviral vector that expresses mouse IFNα (mDEF201) to induce sustained elevations of serum IFNα in the 3H9 mouse model of B cell tolerance.

Methods: 6-8 week old 3H9 mice, which contain a knock-in Ig heavy chain derived from a DNA-specific hybridoma, were injected IV with 10^7 PFU of Ad-mIFNα (mDEF201) or Ad-dl70-3 (empty vector). At 2 weeks post-treatment immune cell populations in the spleen and bone marrow were examined by flow cytometry, and anti-DNA antibody production was measured by ELISA. Serum levels of IFNα were quantified by ELISA and IFN-induced gene expression was assessed by qRT-PCR.

Results: Mice administered mDEF201 had elevated serum levels of IFNα and increased mRNA expression of several IFN-inducible genes. Elevated IFNα was associated with a marked increase in the levels of anti-ss/dsDNA autoantibodies, signifying a breach of B cell tolerance. Consistent with this idea, mDEF201 infected mice displayed several abnormalities suggestive of altered B cell homeostasis, including increased numbers of mature follicular/marginal zone B cells, increased frequencies of activated B cells, age-associated B cells (ABC), germinal center B cells, and $CD138^+$ plasma cells. These changes occurred in the setting of minimal changes to the T cell compartment. In the bone marrow, infected mice demonstrated reduced receptor editing, consistent with impaired tolerance induction. To assess the effect of IFNα on B cell anergy, the fate of $Ig\lambda1^+$ expressing B cells, a well-characterized dsDNA-reactive anergic B cell population, was examined. $Ig\lambda1^+$ B cells demonstrated several features of impaired anergy such as enhanced selection in to the mature B cell follicular compartment, increased levels of activation markers, and increased germinal center recruitment; however, anti-dsDNA $Ig\lambda1^+$ levels were not increased, suggesting only a partial breach of anergy. To determine whether altered B cell tolerance in infected mice was due to a direct effect of IFNα on B cells, 3H9 mice with B cell-specific knockout of IFNAR were produced. In these mice several of the IFNα-induced changes were reversed, such as enhanced B cell selection into the follicular, marginal zone, and ABC populations, enhanced B cell activation, and elevated levels of anti-dsDNA antibodies, highlighting the important role of IFNα-B cell interactions in these results.

Conclusion: These data indicate that IFNα may be a major contributing factor to the breach B cell tolerance in SLE through direct effects on autoreactive B cells that impact multiple mechanisms of tolerance, leading to enhanced B cell activation, generation of ABCs and autoantibody production.

Disclosure: D. Ferri, None; **Y. Baglaenko**, None; **K. Manion**, None; **C. Munoz-Grajales**, None; **J. Wither**, None.

Abstract Number: 0885

TLR9 Signaling in HCV-Associated Atypical Memory B Cells Triggers Th1 and Rheumatoid Factor Autoantibody Responses

Chloé Comarmond,[1] Valerie Lorin,[2] Cindy Marques,[1] Anna Maciejewski-Duval,[1] Nizar Joher,[2] Cyril Planchais,[2] Maxime Touzot,[3] Thierry Hieu,[2] Valentin Quiniou,[1] Anne Desbois,[4] Michelle Rosenzwajg,[1] David Klatzmann,[1] Patrice Cacoub,[5] Hugo Mouquet,[2] and David Saadoun[5], [1]Assistance Publique des Hopitaux de Paris, PARIS, France, [2]Institut Pasteur, PARIS, France, [3]Institut Curie, Paris, France, [4]GHPS, Paris, France, [5]AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Department of Internal Medicine and Clinical Immunology, F-75013, Paris, France, Paris, France

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Hepatitis C virus (HCV) infection contributes to the development of autoimmune disorders such as cryoglobulinemia vasculitis (CV). However, it remains unclear why only some HCV-infected individuals develop CV. HCV-CV is characterized by expansions of anergic $CD19^{+}CD27^{+}CD21^{low/-}$ atypical memory B cells (AtM). Here, we report the mechanisms by which AtM participate to HCV-associated autoimmunity.

Methods: Phenotype and function of peripheral AtM were studied by multi-color flow cytometry and co-culture assays with effector T cells and regulatory T cells in twenty chronically HCV-CV patients, 10 chronically HCV-infected patients without CV and 8 healthy donors. We performed gene expression profile analysis of AtM stimulated or not by TLR9. Immunoglobulin gene repertoire of AtM were analyzed after single B cell FACS sorting and expression-cloning of antibodies. Antibody reactivities of AtM were studied by ELISA.

Results: We show $Tbet^{+}CD11c^{+}CD27^{+}CD21^{-}$ AtM B-cell expansions in HCV-CV patients as compared to HCV controls without CV. TLR9 activation of AtM induces a specific transcriptional signature centered on TNFα overexpression, and an enhanced secretion of TNFα and rheumatoid factor-type IgMs in HCV-CV patients. AtM stimulated through TLR9 promote type 1 effector T-cell activation and reduce the proliferation of $CD4^{+}CD25^{hi}CD127^{-/low}FoxP3^{+}$ regulatory T cells. AtM expansions display intraclonal diversity with immunoglogulin features of antigen-driven maturation. AtM-derived IgM monoclonal antibodies do not react against ubiquitous autoantigens or HCV antigens including NS3 and E2 proteins. Rather, AtM-derived antibodies target unique epitopes on the human IgG Fc region and possess rheumatoid factor activity.

Conclusion: Our data strongly suggest a central role for TLR9 activation of AtM in driving HCV-CV autoimmunity through rheumatoid factors production and type 1 T-cell response.

Disclosure: C. Comarmond, None; **V. Lorin**, None; **C. Marques**, None; **A. Maciejewski-Duval**, None; **N. Joher**, None; **C. Planchais**, None; **M. Touzot**, None; **T. Hieu**, None; **V. Quiniou**, None; **A. Desbois**, None; **M. Rosenzwajg**, None; **D. Klatzmann**, None; **P. Cacoub**, Abbvie, 5, AstraZeneca, 5, Bristol meyer squibb, 5, Gilead, 5, Glaxo Smith Kline, 5, Janssen, 5, Merck Sharp Dohme, 5, Roche, 5, Servier, 5, Vifor, 5; **H. Mouquet**, None; **D. Saadoun**, Abbvie, 5, AstraZeneca, 5, Bristol meyer squibb, 5, Gilead, 5, Glaxo Smith Kline, 5, Roche, 5, Servier, 5.

Abstract Number: 0886

Mesenchymal Stem Cell Senescence Alleviates Their Chondrogenic and Seno-Suppressive Properties, Contributing to Osteoarthritis Development

Olivier Malaise,[1] Yassin Tachikart,[2] Michael Constantinides,[2] Marcus Mumme,[3] Daniele Noel,[2] Jing Wang,[4] Christian Jorgensen,[2] and Jean-Marc brondello[2], [1]GIGA Research, CHU and University of Liège, Liège, Belgium, [2]IRMB, INSERM U1183, University of Montpellier, Montpellier, France, [3]University Hospital of Basel, Basel, Switzerland, [4]INM, INSERM U1050, University of Montpellier, Montpeller, France

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Tissue accumulation of $p16^{INK4A}$-positive senescent cells is associated with age-related disorders such as osteoarthritis (OA). These senescent cells induce a tissue loss of function through a particular secretory phenotype called SASP (senescence-associated secretory phenotype). Links between OA onset and cellular

senescence remain poorly detailed. We wanted to determine the presence of articular senescent cells in *in vivo* OA mouse models and study the involvement of mesenchymal stem cells (MSC) senescence in OA pathogenesis.

Methods: Wild-type mice C57BL/6, SAMP8/R1 (senescence accelerated mouse-prone and resistant), transgenic *p16*$^{INK4A\ +/Luc}$and *p16*$^{INK4ALuc/Luc}$were used. Experimental OA was induced by intraarticular injections of collagenase (CIOA).

Results: (1) CIOA was induced in senescence-driven luciferase transgenic mice. Under CCD camera, a peak in luminescence was detected revealing the presence of senescent cells in the joint. Remarkably, articular senescence also contributes to OA: mice deficient in p16INK4a, a main senescence-driving known cell cycle inhibitor, were partially protected against CIOA. These results were confirmed in C57Bl/6 mice after CIOA by showing an increase in gene expression for senescence in the synovial tissue. (2) MSCs found in synovial, cartilage, fat pad and bone marrow participate in joint homeostasis. Because MSC are at the root of OA development, we hypothesize that cellular senescence onset in these progenitors would be a possible etiological factor for OA. We stablished an in vitro p16^{INK4A}-induced senescence model on human MSC: their intrinsic properties (self-renewing and chondrogenesis) are altered when senescent. In co-culture conditions with chondrocytes from OA patients, senescent MSC lost their extrinsic chondroprotective properties. (3) To in vivo challenge these findings, we rely on the mouse model of accelerated senescence SAMP8, which develop spontaneous OA at the age of 6 months with cartilage degradation, synovial hypertrophy, osteophytosis and subchondral bone remodelingassociated to meniscal calcification (micro-tomography). Isolated MSC from these mice express senescence (p16^{INK4a}, p21^{waf1}, MMP13, TGF-β1). Intra-articular injection of these isolated SAMP8-derived MSC compared to SAMR1-derived control MSC, in young wid-type C57Bl/6 mice, was suffisant by its own, to induce significant articular cartilage degradation (OA score of 12.2 ± 1.5 vs 6.1 ± 3.5 for SAMP8 and SAMR1 MSC respectively. $p < 0.05$).

Conclusion: p16^{INK4A}-induced cellular senescence in MSC played a causative role in cartilage loss of function and OA pathogeny. *In vitro*, senescent MSC show altered intrinsic and extrinsic supportive tissue functions.*In vivo*, intra-articular injection of senescent MSC induced cartilage degradation. Specific targeting of such deleterious senescent cells could be an innovating and promising treatment in OA.

Disclosure: O. Malaise, None; **Y. Tachikart**, None; **M. Constantinides**, None; **M. Mumme**, None; **D. Noel**, None; **J. Wang**, None; **C. Jorgensen**, None; **J. brondello**, None.

Abstract Number: 0887

Critical Role of the Cholinergic System Involvement in Osteoarthritis

Alice Courties,[1] Ariane Do,[1] Sarah Leite,[2] Audrey Pigenet,[2] Morgane Belle,[3] Geoffroy Nourissat,[4] Alain Sautet,[5] Alain Chedotal,[3] Uwe Maskos,[6] Francis Berenbaum,[7] and Jérémie Sellam[1], [1]Service de Rhumatologie, AP-HP Hôpital Saint-Antoine, Sorbonne Université, INSERM, Centre de Recherche Saint-Antoine, Paris, France, Paris, France, [2]Sorbonne Université, INSERM, Centre de Recherche Saint-Antoine, Paris, France, Paris, France, [3]Sorbonne Université, INSERM, CNRS, Institut de la Vision, Paris, France, Paris, France, [4]Chirurgie orthopédique, Clinique Maussins, Groupe Ramsay générale de santé, 67 rue de Romainville, 75019, Paris, Paris, France, [5]Chirurgie orthopédique, AP-HP Hôpital Saint-Antoine, Paris, Paris, France, [6]Unité de neurobiologie intégrative des systèmes cholinergiques, CNRS UMR 3571, Institut Pasteur, Paris, Paris, France, [7]Sorbonne Université-Inserm CDR Saint-Antoine, AP-HP, Paris, France

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: The efferent vagus nerve can regulate inflammation via its principal neurotransmitter acetylcholine (ACh), a concept referred as the 'cholinergic anti-inflammatory pathway'. ACh interacts with members of the nicotinic acetylcholine receptor (Chrna) family, in particular with the alpha7 subunit (Chrna7), which is expressed not only by neurons but also by other cells involved in inflammation.

We aimed to decipher the roles of the non-neuronal and neuronal cholinergic systems in osteoarthritis (OA).

Methods: To explore the presence of neuronal cholinergic fibers in the joints, we used a whole joint immunolabeling protocol after 3Disco clearing. We evaluated the coexpression of peripherin (nerve marker) and choline acetyltransferase (cholinergic marker) in human bone-cartilage samples, from OA patients undergoing knee arthroplasty.

To explore the role of the non-neuronal cholinergic pathway, primary cultures of human OA chondrocytes and of WT and KO Chrna7$^{-/-}$ murine osteoblasts (OB) and chondrocytes were performed. The expressions of the molecular partners of Ach metabolism and of the cholinergic nicotinic receptors were assessed. *In vitro*, WT and Chrna7$^{-/-}$ chondrocytes and OB were treated with IL1b for 24h. In order to study the role of nicotinic receptors in cell activation, chondrocytes and OB were pretreated with nicotine at 1; 10 or 100 μM. We quantified the production of interleukin-6 (IL6) and metalloproteinase (MMP) along with RANK-ligand for OB by ELISA.

To induce OA, medial meniscus destabilization (DMM) of the knee was performed on 12-week-old WT and Chrna7 $^{-/-}$ mice and histological OARSI scoring was compared after 8 weeks between both genotypes.

Results: Cholinergic fibers were present in subchondral bone of all 3 OA joints explants analyzed coming from 3 different patients (Fig 1). Human OA and murine chondrocytes as well as murine OB express the whole machinery needed for the synthesis, transport and degradation of Ach. All these cells express nicotinic subunits a 4, 5, 6, 7 and β4. IL1β stimulation induced a significant increased production of IL6 and MMPs by WT and Chrna7-/- chondrocytes. Nicotine pretreatment counteracted this effect (decrease of 65% for IL6, 64% for MMP3 with nicotine 10μM, n=5; $p < 0.05$). Conversely to what happened in WT, nicotine had no effect on Chrna7-/- chondrocytes supporting a predominant role of this receptor in chondrocyte activation. In OB, stimulation of nicotinic receptors decreased the production of IL6, MMP3 and RANK-L induced by IL1β in the same manner in WT and Chrna7-/- OB, meaning that other subunits

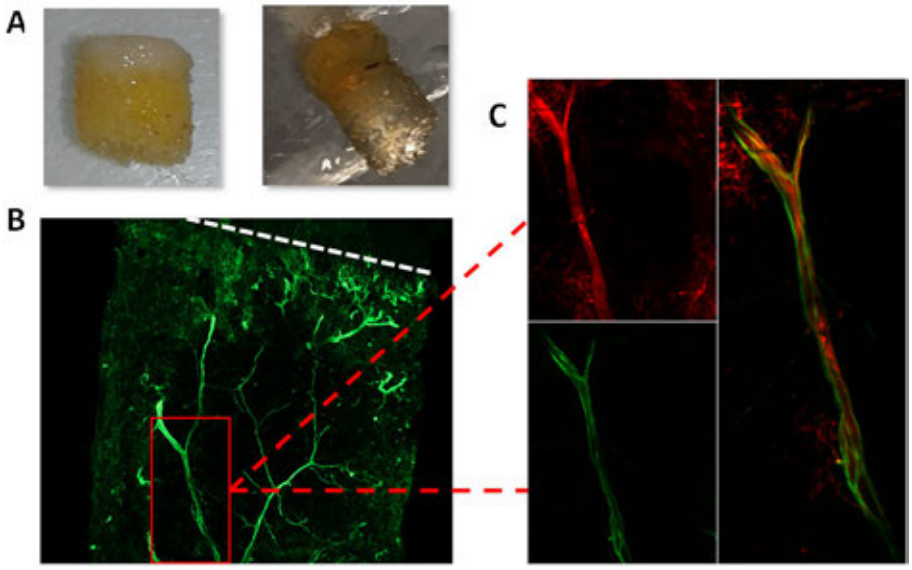

Figure 1. A: Osteoarthritic human bone and cartilage sample before and after 3DISCO clearing protocol, B and C: 3D in toto immunofluorescence of peripherin (nerve marker) in green and of ChAT (cholinergic nerve fiber) in red with colocalization of their expressions.

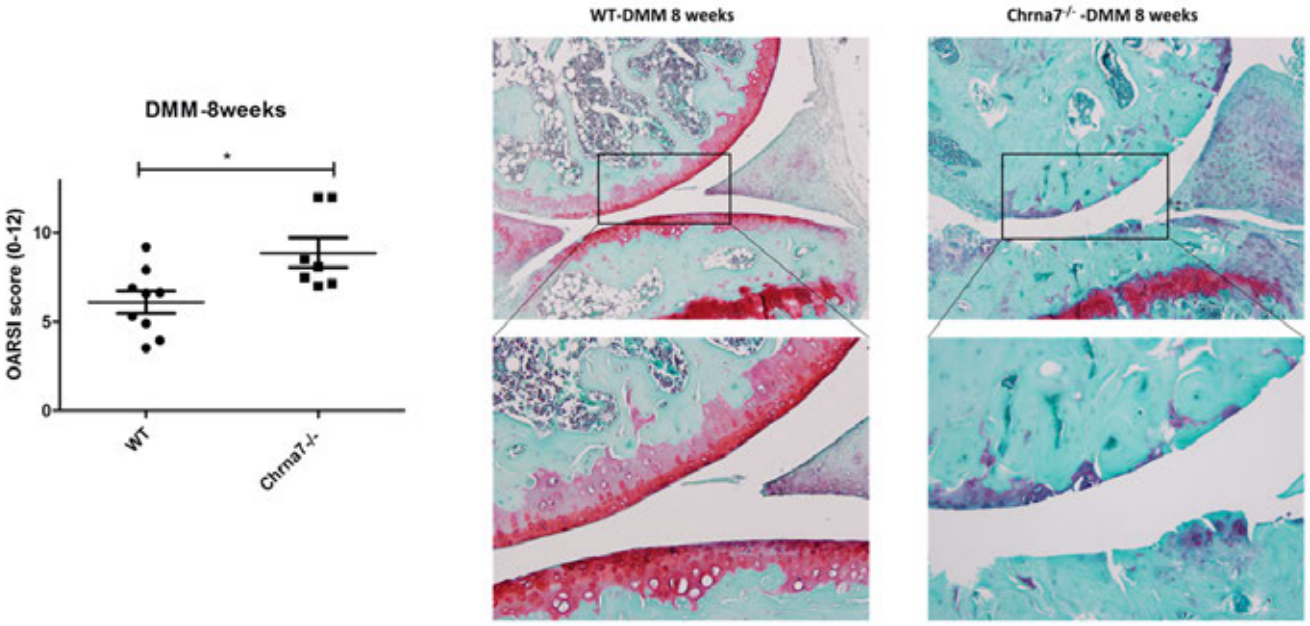

Figure 2. Chrna7 gene deletion is associated with more severe post-traumatic murine OA Left : OARSI score of the sum of femoral condyle and tibial plateau (0-12, 12 being the worst) between WT (n=9) and Chrna7 -/- (n=7) mice 8 weeks after the DMM,*p<0.05; Right : Representative SafraninO/fast green stained sections of the right knee 8 weeks after DMM in WT and Chnra7 -/- mice

than a7 are involved in OB activation. After DMM, Chrna7 -/- mice displayed significantly more OA lesions than their WT counterparts with a mean±SD OARSI score of 8.9±0.82 for Chrna7 -/- and 6.1±0.6 for WT (Fig 2).

Conclusion: Neuronal and non-neuronal cholinergic systems are present in murine and human joints. The activation of nicotinic receptors displays anti-inflammatory, anti-catabolic and antiresorptive properties on bone and cartilage. In chondrocytes this protective effect is mediated by the Chrna7 suggesting that activating the cholinergic system could be a new therapeutic target in OA.

Disclosure: A. Courties, None; **A. Do**, None; **S. Leite**, None; **A. Pigenet**, None; **M. Belle**, None; **G. Nourissat**, None; **A. Sautet**, None; **A. Chedotal**, None; **U. Maskos**, None; **F. Berenbaum**, 4P Pharma, 2; **J. Sellam**, Janssen, 8.

Abstract Number: 0888

Mitochondrial DNA Impact on Joint Degeneration Process Using DMM OA and Spontaneous Aging Conplastic Mice Models

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Osteoarthritis & Joint Biology – Basic Science

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Accumulated data indicated that osteoarthritis has a strong genetic component with a prevalent role of mitochondria and mtDNA variations. In the present work, we aimed to study the influence of the mtDNA variation in the joint deterioration in aging-related and surgically-induced OA in mice with the same nuclear genome but different mtDNA variants (named conplastic mice).

Methods: Conplastic mice (BL/6^{NZB}) strain was developed with the C57BL/6JOlaHsd nuclear genome and the NZB/OlaHsd mtDNA to compare with the original C57BL/6JOlaHsd strain (BL/6^{C57}).

In the spontaneous aging-related OA model, mice were kept under normal conditions and sacrificed at 25, 75 and 90 weeks of age. Hind knee joints from BL/6^{NZB} mice as well as from BL/6^{C57} mice were processed and cut into coronal sections for histological analysis. All sections were stained with Hematoxylin-Eosine and Safranin O-fast green and graded using a Mankin scoring system. Cartilage expression of markers of autophagy like LC3 and metalloproteinases like MMP-13 were also analyzed by immunohistochemistry. The surgical OA model was induced in 17 months old BL/6^{C57} and BL/6^{NZB} mice by transection of the medial meniscotibial ligament (DMM model) of the hind left knee joint. The right knee joint was used as sham surgery. The animals were euthanized 8 weeks later. Both hind knees were processed and cut into sagittal sections and examined for histopathological changes (OARSI scoring system, subchondral bone changes).

Results: In the aging model, conplastic mice BL/6^{NZB} presented reduced cartilage Mankin score at 25 (p=0.0317), 75 (p=0.0087) and 90 (p=0.0484) weeks compared with mice of the original strain BL/6^{C57} at the same age. Specifically, we showed a reduced score in both femoral condyle (FC) and tibial plateau (TP) of BL/6^{NZB} mice that reached the statistical significance at 25 (FC: p=0.0317; TP: p=0.0079) and 75 weeks (FC: p=0.0411; TP: p=0.0238). These results were accompanied with more expression of LC3 in cartilage from BL/6^{NZB} mice at 75 and 90 weeks when compared with cartilage from BL/6^{C57} at the same age. Difference in MMP13 cartilage expression between the two mice strains were also found. In the surgical OA model, we found that joints from BL/6^{NZB} mice presented a reduced OARSI score compared with BL/6^{C57} (p=0.018) in both femoral condyle and tibial plateau. We also observed less subchondral bone changes in BL/6^{NZB} mice compared with BL/6^{C57} mice (p=0.035).

Conclusion: This study demonstrates that mtDNA genetic manipulation improve both spontaneous joint aging and joint degradation in a conplastic aging animal model and in a surgically-induced OA conplastic mice respectively. BL/6^{NZB} conplastic mice develop less severe spontaneous joint aging and OA compared with the original strain BL/6^{C57}. These results support the hypothesis that mtDNA background has a role in the process of joint damage, suggesting a potential role of mtDNA as a novel therapeutic target in OA.

Disclosure: M. Scotece, None; **I. Rego-Pérez**, None; **A. Lechuga-Vieco**, None; **M. Jiménez Gómez**, None; **P. Filgueira-Fernández**, None; **J. Enriquez**, None; **F. Blanco**, None.

Abstract Number: 0889

Identification of Genetic Variants Associated with Erosive Hand Osteoarthritis Using Pedigrees from a State-Wide Population-Based Cohort

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Erosive osteoarthritis (EOA) of the hand is a characterized radiographically with centrally-located interphalangeal joint erosions, and clinically by its rapid onset, rapid rate of progression, and potential for substantial disability and deformity. Although an association between a single nucleotide polymorphism in the interleukin-1β gene has been demonstrated for EOA in a small case-control study, it remains unclear whether this condition has a genetic basis and there remains a lack of understanding of the underlying pathophysiology. Our purpose was to determine whether EOA clusters in families, which would suggest a genetic etiologic contribution. Secondarily, we performed genomic analyses on one high-risk family with EOA to identify candidate genes that have a significant contribution to the onset and progression of EOA.

Methods: EOA patients were identified by ICD-10 code (M15.4), then mapped to pedigrees using methods developed by the Utah Population Database (UPDB). The UPDB is a collection of >10 million individuals in multigenerational pedigrees dating back to the late 1700's which are linked to >30 million medical records. High-risk families with excess clustering of EOA were identified using the Familial Standardized Incidence Ratio (FSIR) threshold of ≥ 2.0. The magnitude of familial risk was calculated using relative risk from Cox regression models to determine the relative risk of EOA in related individuals using a ratio of 1:10 affected individuals to controls. Genomic analyses were performed as previously reported.

Results: We identified 231 unrelated high-risk pedigrees with an FSIR ≥ 2.0 (top pedigrees illustrated in Table 1). Of the 580 affected individuals within these pedigrees, mean age at diagnosis was 66 ± 11.0 years and 80.1% were female. The relative risk of developing EOA was significantly elevated in first-degree relatives (RR 30.51; 95% confidence interval 3.3 – 282.4; p = 0.0026). Genomic analyses in one EOA family consisting of two distantly related affected individuals and one unaffected sibling (Figure 1) identified a rare coding variant in the procollagen galactosyltransferase *COLGALT1* (Arg326Cys, AF - 0.00009) (Figure 2).

Conclusion: Our finding of excess familial clustering of hand EOA patients indicates a significant genetic contribution to the etiology of the disease. Although functional testing is still underway, we have identified a coding variant

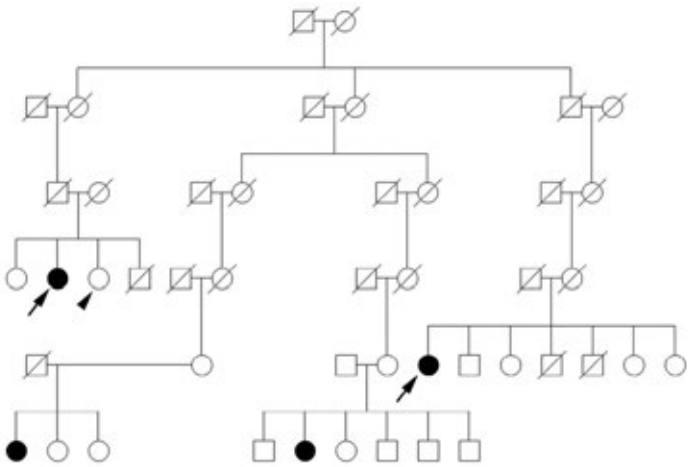

Figure 1 - EOA family #1 pedigree. EOA segregates as an apparent autosomal dominant trait. Arrows marks the affected individuals used for genomic analyses. Arrowhead marks the unaffected individual used for genomic analyses.

Table 1 - High-Risk Pedigrees with Excess Familial Clustering of Erosive Osteoarthritis of the Hand

Founder Number and Birth Year	Descendants	Number of Affected Living Individuals	FSIR	p-value
1 - 1795	29645	8	4.3	< 0.05
2 - 1774	49184	8	2.6	< 0.05
3 - 1744	52482	8	2.2	< 0.05
5 - 1710	38036	8	3.0	< 0.05
4 - 1758	34100	7	3.6	< 0.05
6 - 1762	6592	6	20.2	< 0.05
7 - 1768	7130	4	18.4	< 0.05
8 - 1794	7121	4	12.8	< 0.05
9 - 1721	7140	4	12.8	< 0.05
10 - 1815	1437	3	33.6	< 0.05

Abbreviations: FSIR = familial standardized incidence ratio.

associated with EOA – namely *COLGALT1*, a gene involved with glycosylation of hydroxylated lysines in procollagen.[6] These results, and those to be gained through whole-exome sequencing of additional identified high-risk pedigrees, may lead to an improved understanding of EOA pathophysiology.

Disclosure: N. Kazmers, None; **K. Novak**, None; **Z. Yu**, None; **T. Barker**, None; **T. Abraham**, None; **R. Romero**, None; **M. Jurynec**, None.

Abstract Number: 0890

Adenosine A2A Receptor Signaling Activates FoxO1 and FoxO3 and Promotes Cartilage Autophagy

Benjamin Friedman,[1] Carmen Corciulo,[2] Cristina Castro-Rivera,[2] and Bruce Cronstein[2], [1]Department of Medicine, Division of Rheumatology NYUSoM, NYC, [2]NYU Langone, New York

SESSION INFORMATION

Session Date: Sunday, November 10, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Osteoarthritis (OA) is a debilitating and costly condition caused by loss of articular cartilage secondary to chondrocyte dysfunction. Autophagy is a homeostatic pathway that is upregulated in cellular stress and it is decreased in OA. Recent work demonstrates that the Forkhead transcription factors FoxO1 and FoxO3 regulate chondrocyte autophagy and their deficiency leads to the development of OA. We have previously reported that A2ARKO mice develop severe OA and rats with post-traumatic OA (PTOA) have lower OARSI scores when treated with liposomal preparations of adenosine by activating A2AR (Corciulo, et al NComms, 2017).

Methods: Active (non-phos FoxO) and inactive (Akt-phos FoxO) levels were evaluated in the human TC28α2 chondrocyte cell line by IF and WB after stimulation with the A2AR agonist CGS21680 (CGS, 1mM) +/- A2AR antagonist ZM241385 (ZM, 1mM) at 30 min. Autophagy proteins p62/SQTSM1, Gabarapl1, Beclin-1 and apoptosis proteins p53 and caspase 3 were analyzed by IF and WB at 1h. An *in vivo* obesity OA mouse model treated with joint injections of liposomal-CGS or lipo-adenosine was assessed by IHC for FoxO1/3 or phos-FoxO1/3, p62, Gabarapl1, and Beclin-1.

Results: FoxO1/3 both translocated to the nucleus in TC28α2 cells 30m post-CGS, while phos-FoxO1/3 translocated to the cytoplasm; these changes were all reversed with ZM pre-treatment. Total cellular FoxO1 increased significantly after A2AR activation by WB (1.6±0.08 vs 1.0±0.08, p< 0.001, n=4) and FoxO3 levels trended up (2.0±0.7 vs 1.0±0.3, p=0.11, n=3). There was p62 reduction in TC28α2 cells over a 3-hour time course (0.74±0.17 vs 1.0±0.24, p=0.01, n=3), which indicates active autophagy as p62 is degraded with the cargo. However, in the presence of 25μM hydroxychloroquine (HCQ) to inhibit autophagosome-lysosome fusion, there was a clear increase in p62 levels in A2AR-stimulated chondrocytes (78±7% vs 9±1.4% cells, p=0.003, n=3) consistent with increased autophagic flux. Similarly, autophagosome-associated Gabarapl1 and upstream regulator Beclin-1 formed punctate autophagy nucleation complexes after CGS treatment. While autophagy is generally pro-survival, it can be associated with apoptosis. We found that A2AR-stimulated autophagy was associated with decreased p53 level by WB at 1h (0.66±0.12 vs 1.0±0.11, p=0.02, n=3) and a visible reduction of p53 and caspase 3 by IF. The in vitro results were reflected by in vivo experiments from obese mouse knee joints, in which we observed an increase in cellular levels and nuclear localization of FoxO1/3 with a concomitant decrease in phos-FoxO1 in mice treated with the A2AR agonist. Similar to our in vitro results, the treated obese mice joints displayed decreased p62 and increase in Gabarapl1 and Beclin-1.

Conclusion: These results demonstrate that A2AR stimulation increases activation and nuclear localization of FoxO1 and FoxO3 and promotes an increase in autophagic flux without increasing apoptosis *in vitro*. More importantly, similar changes were observed *in vivo* in a murine model of obesity-induced OA. These findings provide a mechanism by which A2AR stimulation maintains chondrocyte homeostasis and reduces OA.

Disclosure: B. Friedman, None; **C. Corciulo**, Regenosine, Inc., 4; **C. Castro-Rivera**, None; **B. Cronstein**, AstraZeneca, 5, CanFite Biopharmaceuticals, 4, Horizon Pharmaceuticals, 5, Regenosine, Inc., 4.

Abstract Number: 0891

Lorecivivint (SM04690), a Potential Disease-Modifying Osteoarthritis Drug, Inhibits CLK2 and DYRK1A, Novel Molecular Regulators of Wnt Signaling, Chondrogenesis, and Inflammation

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: In the synovial joint, Wnt pathway upregulation contributes to osteoarthritis (OA) by increasing osteocyte differentiation, cartilage thinning, and inflammation. Lorecivivint (LOR; SM04690), a novel small molecule, has previously demonstrated potential OA disease-modifying effects through Wnt pathway inhibition *in vitro*

and *in vivo*. These studies sought to elucidate the novel mechanism of action for LOR on Wnt pathway inhibition, chondrocyte differentiation, and anti-inflammation.

Methods: Wnt pathway activity was measured using a cell-based TCF/LEF luciferase reporter in SW480 colon cancer cells. A kinome screen (318 kinases) was performed. The effects of LOR on protein phosphorylation of serine and arginine rich splicing factors (SRSF proteins), Sirt1, and FoxO1 in hMSCs, chondrocytes, and synovial fibroblasts were measured by Western blot. The effects of LOR and siRNA knockdown (KD) on chondrogenic and Wnt pathway gene expression were measured by NanoString gene expression panels and effects on LPS-induced inflammatory cytokines (IL-6, IL-8, TNF-α) in BEAS-2B cells were measured by qPCR and ELISA. *In vivo*, the pharmacodynamic effects of LOR were evaluated in monosodium iodoacetate injection-induced and anterior cruciate ligament transection with partial medial meniscectomy rat knee OA models in which a single intra-articular LOR (0.1 µg, 0.3 µg, 1.0 µg) or vehicle injection was administered. Cartilage was isolated at Day 10 and 35; phosphorylation and expression of SRSF proteins, Sirt1, FoxO1, STAT3, and NF-κB were measured by Western blot.

Results: LOR was a potent (EC50=11nM) inhibitor of Wnt signaling. CDC-like kinases (CLKs) and dual-specificity tyrosine kinase (DYRK1A) were identified as molecular targets of LOR. In hMSCs and chondrocytes, compared to DMSO, LOR potently inhibited CLK-mediated phosphorylation of SRSF proteins. LOR also inhibited DYRK1A-mediated Sirt1 and FoxO1 phosphorylation, thus increasing total and nuclear FoxO1 levels. Compared to siRNA control, DYRK1A/CLK2 dual KD increased expression of chondrogenic genes (COL2A1, ACAN, COMP, CD44 [all $P < 0.05$]). Compared to siRNA control, CLK2 and DYRK1A KDs each inhibited Wnt pathway genes (AXIN2, TCF7, TCF4, LRP5, FZD6, FZD7, PITX2 [all $P < 0.05$]) with no effects on β-catenin levels. In synovial fibroblasts, compared to DMSO, LOR decreased phosphorylation of NF-kB and STAT3. In BEAS-2B cells, compared to siRNA control, DYRK1A KD inhibited inflammatory cytokine production (IL-6, IL-8, TNF-α [all $P < 0.05$]) while DYRK1A/CLK2 dual KD enhanced anti-inflammatory effects of DYRK1A KD. In cartilage from rat OA models, compared to vehicle, LOR inhibited phosphorylation of SRSF proteins, Sirt1, FoxO1, and STAT3 as well as expression of NF-κB.

Conclusion: Inhibition of nuclear kinases CLK2 and DYRK1A leads to effects on the Wnt pathway, chondrocytes, and inflammation **(Image)**. This dual mechanism of LOR potentially modifies OA through increased chondrocyte differentiation and function and benefits symptoms through anti-inflammatory activity. Human trials are ongoing.

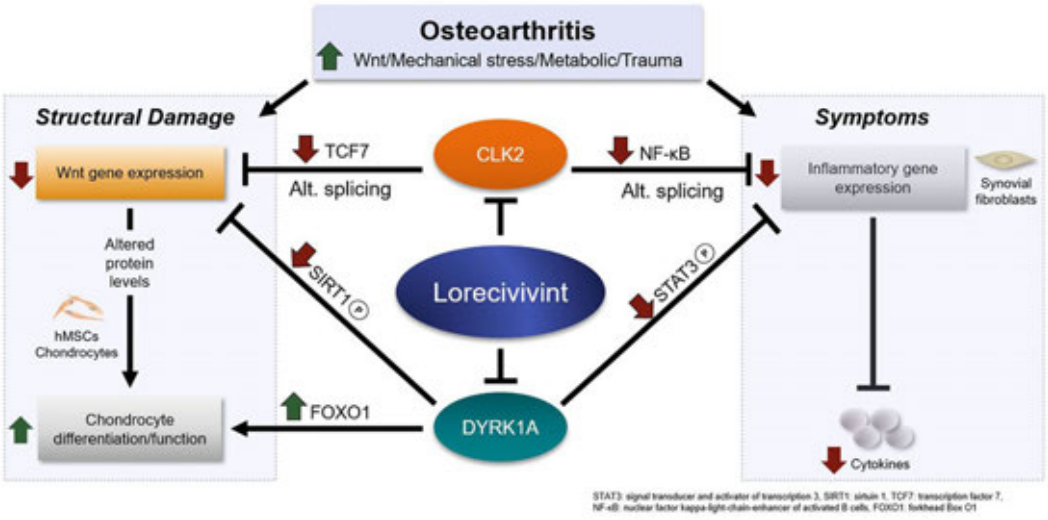

Image: Schematic representation of lorecivivint's proposed mechanism of action via CLK2 and DYRK1A inhibition in OA

Disclosure: V. Deshmukh, Samumed, LLC, 1, 3; **A. O'Green**, Samumed, LLC, 1, 3; **C. Bossard**, Samumed, LLC, 1, 3; **T. Seo**, Samumed, LLC, 1, 3; **L. Lamangan**, Samumed, LLC, 1, 3; **M. Ibanez**, Samumed, LLC, 1, 3; **A. Ghias**, Samumed, LLC, 1, 3; **C. Lai**, Samumed, LLC, 1, 3; **L. Do**, Samumed, LLC, 1, 3; **S. Cho**, Samumed, LLC, 1, 3; **J. Cahiwat**, Samumed, LLC, 1, 3; **K. Chiu**, Samumed, LLC, 1, 3; **M. Pedraza**, Samumed, LLC, 1, 3; **Y. Yazici**, Samumed, LLC, 1, 3, 4, 6.

Abstract Number: 0892

Adverse Childhood Experiences Are Associated with Systemic Lupus Erythematosus in a Clinical Population from Bronx, New York

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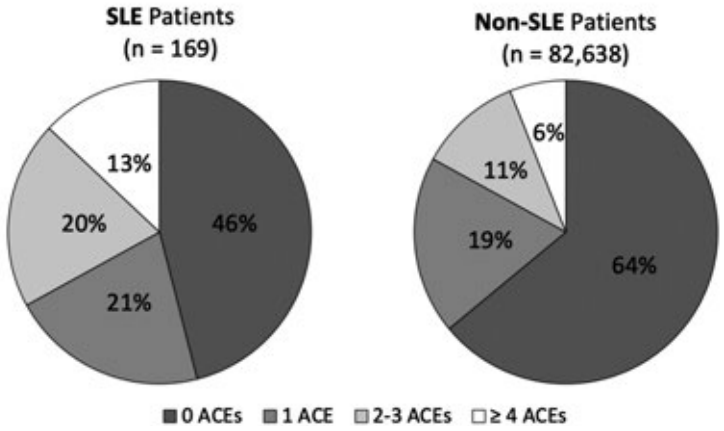
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health II: SLE
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Adverse Childhood Experiences (ACEs), which can result in chronic stress, are associated with autoimmune diseases in adulthood and arthritis in childhood. Recently ACEs were found to be associated with worse health outcomes as reported by adults with SLE in a dose-dependent manner. However, an association between ACEs and the diagnosis of SLE has not yet been demonstrated in either adult-onset or childhood-onset SLE. We aimed to determine whether ACEs are associated with SLE by examining ACE screens from patients with childhood- and adult-onset SLE compared to patients without SLE from Bronx, New York. We hypothesized that ACEs would be more common among patients with childhood-onset SLE and adult-onset SLE than those without SLE.

Methods: Using Clinical Looking Glass, a web-based software tool developed at a large, urban medical center in the Bronx, NY that allows for the extraction of patient data, we examined cross-sectional data on SLE diagnoses and ACE screenings administered at outpatient primary care and subspecialty clinics. Patients with SLE diagnoses were initially identified by billing diagnosis codes and validated by chart review to determine that they met either ACR or SLICC SLE classification criteria. We compared demographics using Pearson's chi-square for categorical variables and the Kruskal-Wallis test for nonparametric data. We examined ACE score as a categorical variable (0, 1, 2-3, $\geq$4) between patients with and without SLE. Multinomial logistic regression models were constructed to assess for associations between categorical ACE score and the presence of childhood-onset SLE or adult-onset SLE compared to no SLE, while adjusting for potential confounders (age, sex, race/ethnicity, and socioeconomic status).

Results: Our study included 169 SLE and 82,638 non-SLE patients. Age, sex, and race/ethnicity were significantly different between the two groups ($p< 0.001$), while socioeconomic status was not ($p=0.39$). The prevalence of any ACE in the SLE group was 54% vs 36% in non-SLE patients ($p< 0.001$). Overall, patients with SLE had higher ACE scores than patients without (Figure 1). Adjusted multinomial logistic regression revealed that ACEs at the levels of 2-3 and >4 were significantly associated with both childhood-onset and adult-onset SLE when compared to non-SLE patients. Further, there was a graded dose-response within the childhood-onset SLE group as the degree of ACE burden increased from 1 ACE, to 2-3 ACEs, and to >4 ACEs (Table 1).

Figure 1. ACE Burden in SLE vs non-SLE from Bronx, New York



Conclusion: Similar to prior studies of arthritis and other autoimmune diseases, this study found an association

Table 1. Multinomial Regression Model for Adverse Childhood Experience (ACE) Burden Among Patients with and without Childhood-onset Systemic Lupus Erythematosus (cSLE)

	Unadjusted model			Adjusted model*		
	OR	95% CI	p value	aOR	95% CI	p value
0 ACEs	-	-	-	-	-	-
1 ACE	1.9	1.0, 3.5	0.05	1.6	0.8, 3.0	0.19
2-3 ACEs	2.5	1.2, 5.0	0.01	**2.3**	**1.1, 4.6**	**0.03**
≥4 ACEs	2.7	1.2, 6.2	0.02	**2.6**	**1.1, 6.1**	**0.03**

*Adjusted for age, sex, race/ethnicity, and socioeconomic status

between ACEs and SLE. This relationship is evident in both childhood-onset SLE and adult-onset SLE in this cohort from Bronx, NY, where social and economic disadvantage may place patients at a higher risk of developing ACEs. Understanding an association between ACEs and SLE development may elucidate biopsychosocial mechanisms for the disease. Further prospective studies should examine how ACEs impact disease development, activity, and damage.

Disclosure: R. Valdovinos, None; **N. Brown**, None; **M. Germán**, None; **Q. Gao**, None; **K. Brathwaite**, None; **K. Reidy**, None; **D. Wahezi**, None; **C. Putterman**, Equillium, 5, Equillium, Inc, 2, 5, Exagen, 2; **R. Stein**, None; **T. Rubinstein**, None.

Abstract Number: 0893

The Presence of Extractable Nuclear Antigens (ENA) Antibodies in a Large Population-based Cohort from the Netherlands and Their Association with Known Risk Factors for Systemic Lupus Erythematosus and Primary Sjögren Syndrome

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health II: SLE
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Previous studies have demonstrated that years before clinical onset of auto-immune diseases, auto-antibodies can already be present. However, it is also known that some individuals can have these auto-antibodies and will never develop an auto-immune disease. So far, little information is available on the presence of antibodies to extractable nuclear antigens (anti-ENA) in the general population in relation to the risk of developing an auto-immune disease, with special interest for Systemic Lupus Erythematosus (SLE) and primary Sjögren Syndrome (pSS).

Objectives: To estimate the prevalence of anti-ENA and their association with the presence of known risk factors for SLE and pSS in the general Dutch population.

Methods: Lifelines is a prospective population-based cohort study in the Netherlands. Cross-sectional data from 40,135 participants were analyzed. The detection of anti-ENA was performed using the ENA-CTD (connective tissue disease) screen on the Phadia-250 analyzer with a ratio >1.0 considered positive. An extensive questionnaire was taken on demographic and clinical information (e.g. early musculoskeletal symptoms). Furthermore, some general blood parameters were available. SLE and pSS were defined by a combination of self-reported SLE or pSS, specific medication use and visiting a medical specialist within the last year. Characteristics were compared between 3 groups: SLE/pSS patients, anti-ENA positive, and anti-ENA negative participants.

Results: Of the total 40,135 consecutive individuals, 41 were detected as having defined SLE or pSS of whom 49% were anti-ENA positive. SLE/pSS patients were older and more often female. Of the remaining individuals (40,094), 1089 (2.7%) were found anti-ENA positive. Anti-ENA positivity was significantly associated with older age, female gender and joint stiffness compared to anti-ENA-negative participants. Interestingly, levels of haemoglobin, leucocytes and lymphocytes were significantly decreased in anti-ENA-positive participants compared to anti-ENA-negative participants. SLE/pSS participants had even significantly lower haemoglobin and reported even more joint stiffness then anti-ENA positive individuals. Lower lymphocyte levels, gender and older age appear as significantly independent predictors of anti-ENA positivity and also for being defined SLE/pSS. Of the anti-ENA positive individuals, 2.3% were positive for anti-dsDNA as well as anti-SSA. These individuals showed significantly lower lymphocyte-, leukocyte-, neutrophilic granulocyte- and monocyte levels compared to other anti-ENA positive participants.

Conclusion: In this large population-based study, the prevalence of anti-ENA-positivity was 2.8% for the total group and 2.7% when excluding patients with SLE or pSS. Older age, female gender, joint complaints and lower levels of hemoglobin, leucocytes and lymphocytes were more frequently present in anti-ENA-positive participants. Longitudinal studies are performed up to 15 years to investigate which individuals might develop SLE or pSS to be able to develop prediction models.

Disclosure: P. Yntema-Eckenhaussen, None; **S. Arends**, None; **E. Brouwer**, Roche, 5, 8; **C. Roozendaal**, None; **H. Bootsma**, Bristol-Myers Squibb, 2, 5, 8, GlaxoSmithKline, 2, 5, HarmonicSS, 2, MedImmune, 2, 5, Medimmune, 5, Novartis, 5, 8, Roche, 2, 5, UCB, 2, 5, Union Chimique Belge, 5; **J. Westra**, None; **K. de Leeuw**, None.

Abstract Number: 0894

Frequency, Severity and Costs of Flares Increase with Disease Severity in Newly Diagnosed Systematic Lupus Erythematous: A Real-World Cohort Study, United States, 2004–2015

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health II: SLE
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: We evaluated the real-world frequency and severity of flares and associated costs 1 year post diagnosis in a US cohort with newly diagnosed SLE.

Methods: Adult patients with newly diagnosed SLE were identified using linked Truven Health MarketScan® commercial claims data and IQVIA's GE Centricity electronic medical record (EMR) database between January 1, 2005 and December 31, 2014. Patients were required to have no prior SLE or lupus nephritis diagnosis during 1 year prior to index date (diagnosis) and ≥1 year of continuous enrollment pre- and post-index date.

Disease severity and flare severity were classified as mild, moderate, or severe during 1 year post diagnosis using a claims-based algorithm, which combined SLE diagnosis, disease activity/SLE-related conditions (eg, end-stage renal disease as severe), medications (eg, oral corticosteroids [CS] ≥60 mg/day as severe), and health service use (eg, hospitalizations, emergency department visits), supplemented with EMRs (1). We evaluated the frequency and severity of flares by SLE severity during the first year post diagnosis. Annualized flare rates and all-cause costs 30, 60, and 90 days after a SLE flare were calculated using 2017 US dollars.

Results: Of 2,227 patients included in this analysis, the average age was 50.2 years; 90.6% were female and 54.4% white. In total, 26.3% (586) of patients were categorized as having mild, 51.0% (1,135) moderate, and 22.7% (506) severe SLE. Prescribed treatments included CS (76.1%), hydroxychloroquine (59.7%), methotrexate (14.7%), and biologics (2.7%).

The annualized flare rate among all SLE patients during the year post diagnosis was 3.45 (SD 1.90) flares. Annualized flare rates increased with disease severity: mild SLE, 2.23 (1.63); moderate SLE, 3.74 (1.73); severe SLE, 4.19 (1.89); $P < 0.0001$ (**Figure 1**). Patients with mild SLE did not experience severe flares. A total of 95.1% of all patients with

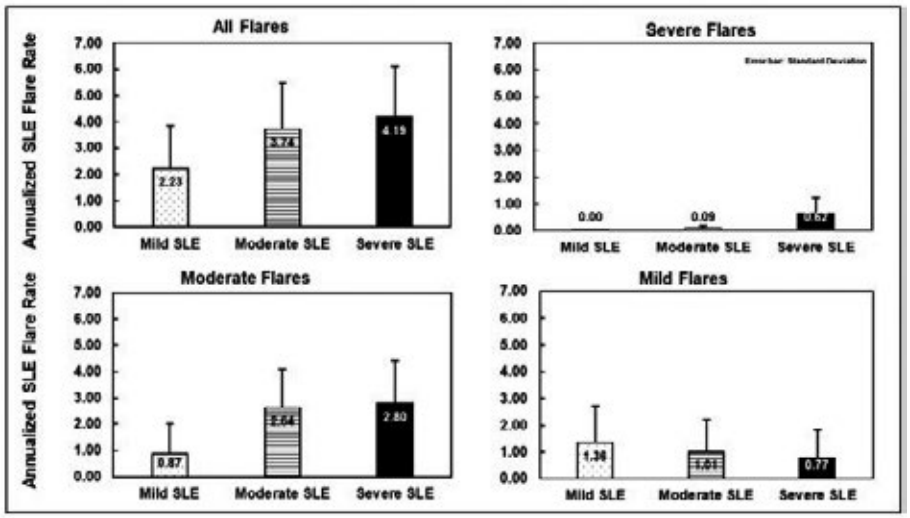

Figure 1. Annualized SLE Flare Rates (Mild, Moderate, and Severe) by SLE Disease Severity among Newly Diagnosed Patients During First Year of Diagnosis, United States 2005–2014

SLE had ≥1 flare, whereas 67.0% experienced 3 or more flares. The proportion of patients who experienced ≥3 flares increased with disease severity (42.0% mild, 74.5% moderate, and 79.6% severe SLE; $P< 0.0001$).

During the initial 30 days after a flare, the total mean all-cause cost of care was $3,884 (SD $12,178), and by flare severity was mild flare $1,672 ($4,566), moderate flare $3,831 ($11,552), and severe flare $16,856 ($29,001); $P< 0.0001$ (**Figure 2**). Health care costs following severe flares was 10.1-fold higher compared with mild flares and 4.4-fold higher for moderate flares compared with mild flares. Health care costs continued to increase 60 and 90 days after a flare with increasing flare severity. Inpatient costs were the primary driver of health care cost after a severe flare.

Conclusion: The frequency and severity of flares in patients with SLE increases with disease severity and with an associated significant increase in health care costs. Health care costs continue to increase substantially well into 90 days after a flare. Preventing the occurrence of flares, or reducing the rate and duration of flares, has potential to reduce SLE health care costs and reduce disease progression.

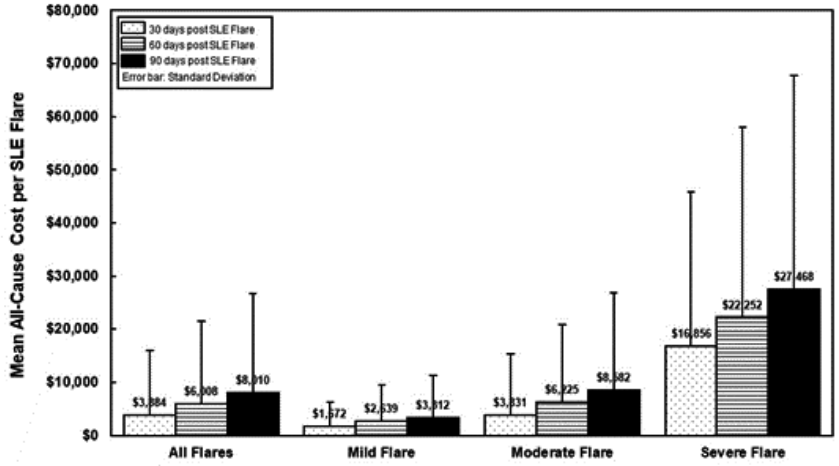

Figure 2. Mean All-Cause Costs Per Flare after SLE Flares (30, 60, and 90 days) During First Year of Diagnosis, United States 2005–2014

Reference:

1. Garris C, et al. *J Med Econ*. 2013;16:667–677.

Disclosure: M. Jiang, AstraZeneca, 3; **B. Desta**, AstraZeneca, 3; **A. Near**, IQVIA, 3; **X. Wang**, AstraZeneca, 3; **E. Hammond**, AstraZeneca, 3.

Abstract Number: 0895

A Spatial-temporal Analysis of Organ-specific Lupus Flares in Relation to Fine Particulate Matter Pollution and Temperature

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health II: SLE
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: We performed a spatial-time cluster analysis of the Hopkins Lupus Cohort with the goal of identifying potential clusters of SLE organ specific flares and their relation to temperature changes and fine particulate matter pollution (PM2.5).

Methods: 1628 patients who fulfilled the SLICC classification criteria for SLE and who had recorded home addresses were included in the analysis. Disease activity was expressed as the Lupus Activity Index. Assessment of rash, joint involvement, serositis, neurologic, pulmonary, renal, and hematologic activity was quantified on a 0-3 VAS. An organ specific flare was defined as an increase in visual analogue scale (VAS) of 1 point or more compared to the previous visit. Daily fine particulate matter pollution (PM2.5) data measured in micrograms per cubic meter and temperature measured in degrees Fahrenheit were collected at various monitoring stations in the eastern United States and obtained from the Environmental Protection Agency. The nearest monitoring station for each patient at each visit date was determined, and the average PM2.5 concentration and temperature ten days prior to clinic visit was calculated. Both univariate and multivariate Generalized Estimating Equations (GEE) logistic regression models with an exchangeable correlation structure were built to study the association of individual (age, sex, ethnicity) and environmental (PM2.5, temperature) variables with the seven different outlined types of lupus disease activity. Spatiotemporal cluster detection was conducted using the SaTScan software. One month long minimum time intervals were considered for this analysis, and spatially overlapping clusters were allowed as long as the overlapping cluster did not contain the centroid of the cluster that was already there. Regression models were used for adjustment and included age, sex, and race, as well as PM2.5 and temperature.

Results: Three statistically significant ($p< 0.05$) unadjusted clusters were identified for joint flares, four rash flare clusters, one hematologic flare cluster, four neurologic flare clusters, three serositis flare clusters, four renal flare clusters, and five pulmonary flare clusters. Most of the identified clusters changed in significance, temporal, or spatial extent after adjusting for temperature, PM2.5 concentration, and individual covariates.

Conclusion: We describe the first space-time clusters of lupus organ-specific disease activity. Seasonal, as well as multi-year cluster patterns were identified, differing in extent and location for the various organ-specific flare types.

Many of the identified clusters changed in significance, temporal, or spatial extent after adjusting for environmental or individual covariates. Further study focusing on each individual lupus organ-specific activity will be required to better understand the driving forces behind these observed changes. The proposed spatial temporal analytical methods could lay the foundation for a new approach in the discovery of potential environmental and atmospheric factors and their role in the etiopathogenesis of lupus

Disclosure: G. Stojan, None; **A. Kvit**, None; **F. Curriero**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 0896

Hydroxychloroquine Use and Cardiovascular Events Among Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health II: SLE
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Hydroxychloroquine (HCQ) is near-universally recommended for patients with SLE and is often used in the treatment of RA. Use of HCQ has been associated with reductions in hyperlipidemia, hyperglycemia, and hypercoagulability, which are established risk factors for cardiovascular-metabolic endpoints. We aimed to determine the potential temporal association between HCQ use and cardiovascular (CV) events among patients with SLE or RA.

Methods: We conducted a nested case-control study within a combined inception cohort of SLE and RA using an administrative health database including the entire population in the province of British Columbia, Canada. We identified cases with incident CV events, including non-fatal or fatal myocardial infarction (MI), stroke/transient ischemic attack (TIA), or venous thromboembolism (VTE) (e.g., deep vein thrombosis and pulmonary embolism), as defined by ICD codes. For each case, we identified up to three controls with SLE or RA matched on age, sex, and disease. HCQ exposure was categorized by the time between the last HCQ prescription date covered and the index date as remote (>365 days), recent (30-365 days) current (< 30 days), or never used.We used conditional logistic regression to assess the association between current use of HCQ or recent discontinuation of HCQ and the risks of incident combined CV events, MI, stroke/TIA, and VTE relative to remote HCQ use. Fully adjusted models included age, sex, SLE vs. RA, Charlson comorbidity index, chronic kidney disease, glucocorticoids, other DMARDs, cardiovascular medication use, and healthcare utilization assessed at the time of SLE or RA diagnosis.

Results: We identified 532 SLE cases matched with 1,249 SLE controls and 9,736 RA cases matched with 28,720 RA controls. The mean age at index date was 74 years. The majority were female (64% of cases and controls) (**Table 1**). Adjusted odd ratios (ORs) for combined CV events relative to the remote users were 0.83 (95% CI: 0.73, 0.93) for current users and 1.08 (95% CI: 0.91, 1.29) for subjects who recently discontinued HCQ (**Table 2**). HCQ non-users had the same risk of combined CV events as remote users (OR 0.99 [95% CI: 0.90, 1.08]).

Table 1. Characteristics of SLE and RA Cases with Cardiovascular Events and Matched Controls

Variable	Cases (n=10,268)	Controls (n=29,969)
Age (mean, SD)	74 (13)	74 (13)
Sex (% female)	63.6	63.7
Systemic Lupus Erythematosus (n)	532	1249
Rheumatoid Arthritis (n)	9736	28720
Charlson comorbidity index, mean (SD)	1.20 (1.21)	1.04 (1.03)
Chronic Kidney Disease (%)	14.3	11.8
Medications (%)		
Glucocorticoids	32.0	27.0
Cardiovascular medications	53.6	42.9
Other DMARDs	15.9	14.3
Healthcare Utilization, mean (SD)		
Number of hospitalizations	0.6 (1.1)	0.4 (0.8)
Number of outpatient visits	27.2 (19.7)	22.4 (15.5)

DMARDs, disease-modifying anti-rheumatic drugs. Includes azathioprine, methotrexate, mycophenolate, leflunomide, cyclosporine, cyclophosphamide, penicillamine, chlorambucil, minocycline, and gold.
Cardiovascular medications include anti-hypertensives, cardiac glycosides, diuretics, anti-arrhythmics, nitrates, and anticoagulants.

Table 2. Hydroxychloroquine Use and Cardiovascular Events According to Hydroxychloroquine Exposure Status

	Cases, N	Controls, N	Odds Ratio (95% CI)	Adjusted* Odds Ratio (95% CI)
Combined CV Events				
Remote HCQ Users	784	2097	1.0 (reference)	1.0 (reference)
Recent HCQ users	228	543	1.10 (0.93-1.30)	1.08 (0.91-1.29)
Current HCQ users	715	2101	0.88 (0.79-0.99)	0.83 (0.73-0.93)
HCQ non-users	8461	25197	0.88 (0.81-0.96)	0.99 (0.90-1.08)
Myocardial Infarction				
Remote HCQ Users	351	909	1.0 (reference)	1.0 (reference)
Recent HCQ users	103	242	1.09 (0.84-1.42)	1.09 (0.84-1.43)
Current HCQ users	333	927	0.92 (0.77-1.10)	0.86 (0.72-1.04)
HCQ non-users	3742	11227	0.86 (0.75-0.98)	0.95 (0.83-1.09)
Stroke/TIA				
Remote HCQ Users	314	881	1.0 (reference)	1.0 (reference)
Recent HCQ users	86	217	1.11 (0.83-1.46)	1.09 (0.82-1.45)
Current HCQ users	273	856	0.91 (0.75-1.10)	0.84 (0.69-1.02)
HCQ non-users	3636	10707	0.97 (0.84-1.11)	1.03 (0.89-1.18)
Venous Thromboembolism				
Remote HCQ Users	119	307	1.0 (reference)	1.0 (reference)
Recent HCQ users	39	84	1.21 (0.78-1.88)	1.06 (0.68-1.67)
Current HCQ users	109	318	0.89 (0.65-1.21)	0.73 (0.53-1.00)
HCQ non-users	1083	3263	0.86 (0.68-1.08)	0.92 (0.73-1.17)

*Additionally adjusted for Charlson comorbidity index, chronic kidney disease, glucocorticoid use, DMARD use, and cardiovascular medication use.

Conclusion: In this nested case-control study within an incident SLE/RA cohort, we found a 17% reduced risk of incident CV events overall associated with current HCQ use. We also identified trends towards reduced risks of MI, Stroke/TIA, and VTE associated with current HCQ use. By leveraging remote users as the comparison group, we reduced the potential for confounding by indication. These findings suggest a preventative benefit of HCQ use in reducing CV disease among patients with SLE and RA.

Disclosure: A. Jorge, None; **N. Lu**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5; **J. Esdaile**, None; **D. Lacaille**, None; **J. Avina-Zubieta**, None.

Abstract Number: 0897

Mortality Rates After Coronary Revascularization Procedures Among Systemic Lupus Erythematosus Compared to Diabetes Mellitus and General Population Medicaid Patients

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Epidemiology & Public Health II: SLE
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Despite similar myocardial infarction risks in SLE and diabetes mellitus (DM) patients, individuals with SLE enrolled in Medicaid had substantially higher rates of coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) compared to age- and sex-matched DM patients. However, little is known about mortality after coronary revascularization procedures in SLE versus DM and general population patients and we hypothesized that SLE patients would have poorer outcomes. We evaluated 30-day mortality rates following coronary revascularization procedures among SLE compared to DM and general population patients enrolled in Medicaid.

Methods: We utilized Medicaid Analytic eXtract (MAX) data, containing billing claims from 29 most populated U.S. states (2007-2010) and identified adults aged ≥18-65 years with prevalent SLE or DM (≥3 ICD-9 codes, each ≥30 days apart) and >6 months enrollment prior to 3rd code, and patients without SLE or DM ("general population"). Among those in each cohort undergoing first CABG or PCI, we calculated post-procedure 30-day mortality rates (MRs) and mortality rate ratios (MRRs) per 1,000 person-years, with 95% confidence intervals (95% CIs) com-

Table. 30-day Mortality Rates and Adjusted Risks following Coronary Revascularization Procedures (Coronary Artery Bypass Graft and/or Percutaneous Coronary Intervention) in Systemic Lupus Erythematosus (SLE), Diabetes Mellitus (DM), and General Population (Non-SLE/Non-DM) Medicaid patients (2007-2010)

	Systemic Lupus Erythematosus N=40,212	Diabetes Mellitus N=80,424	General Population N=160,848
Patients who underwent Coronary Revascularization Procedures, N (%)	608 (1.51)	1185 (1.47)	628 (0.39)
Age at Procedure, Mean (SD)	43.59 (12.62)	49.07 (10.19)	51.82 (9.31)
Female, N (%)	539 (88.65)	1059 (89.37)	536 (85.35)
Black, N (%)	310 (50.99)	365 (30.80)	159 (25.32)
Deaths within 30 days Procedure, N (%*)	18 (2.96)	21 (1.77)	---
Person-years follow-up after Procedure, Mean (SD)	0.08 (0.02)	0.08 (0.01)	---
30-day MR* (95% CI)	351.35 (221.36-557.67)	210.87 (137.49-323.42)	189.54 (101.98-352.27)
Reference: General Population			
30-day MRR**[A] (95%CI)	**1.85 (1.31-2.63)**	1.11 (0.79-1.56)	1.0 (ref)
OR for death***[A] (95% CI)	1.93 (0.85-4.42)	0.91 (0.42-1.99)	1.0 (ref)
Reference: Diabetes Mellitus			
30-day MRR**[B] (95% CI)	**1.67 (1.25-2.21)**	1.0 (ref)	0.90 (0.64-1.26)
OR for death***[B] (95% CI)	**2.13 (1.09-4.13)**	1.0 (ref)	1.10 (0.50-2.50)

*MR = mortality rate, per 1,000 person years, **MRR= unadjusted mortality rate ratio
***OR=odds ratio for death within 30 days of coronary revascularization, adjusted for age (continuous), sex, race/ethnicity, Charlson score
[A]General population reference group
[B]Diabetes mellitus reference group
SD= standard deviation
---event cell sizes and follow-up suppressed given Federal reporting guidelines

pared to the DM and general populations separately. We used multivariable logistic regression models, adjusting for age, sex, race/ethnicity and Charlson index, to calculate odds ratios (OR) and 95% CIs, for 30-day mortality post-coronary revascularization procedures in the SLE compared to the DM and general population cohorts separately.

Results: Among 40,212 SLE patients, we identified 608 (1.51%) coronary revascularization procedures; among 80,424 prevalent DM, we identified 1185 (1.47%), and among 160,848 general population patients, there were 628 (0.39%) over similar follow-up periods in each group (approximately 1.7 years). Demographics and deaths within 30 days are shown in **Table**. Mean age at procedure was youngest in SLE patients and proportion of Black patients was highest in SLE. SLE patients had the highest 30-day post-revascularization mortality rate (351.35 [95% CI 221.36-557.67]) per 1,000 person years of observation, compared to DM (MRR 1.67 [95%CI 1.25-2.21]) and the general population (MRR 1.85 [1.31-2.63]). After multivariable adjustment, the odds of death within 30 days of coronary revascularization procedure were doubled in SLE compared to DM (OR 2.13 [95%CI 1.09-4.13]); a similar but non-significant trend was seen for SLE compared to general population (OR 1.93 [95%CI 0.85-4.42]).

Conclusion: SLE patients had 1.7 times higher 30-day mortality rates post-coronary revascularization compared to DM and general population patients, despite being on average much younger at procedure. After adjusting for demographics and comorbid index, SLE patients were twice as likely to die within 30-days of coronary revascularization procedure as DM patients. Future studies accounting for healthcare utilization, the complexity and indications of the procedures performed, SLE and cardiac disease severity, and investigating causes of post-procedure deaths are required.

Disclosure: M. Barbhaiya, None; **S. Chen**, None; **C. Feldman**, None; **H. Guan**, None; **B. Everett**, Amgen, 5, FDA, 5, NIDDK, 5, Novartis, 2, 5, Roche Diagnostics, 2, 5; **K. Costenbader**, Astra-Zeneca, 2, Glaxo Smith Kline, 2, Janssen Scientific Affairs, LLC, 2, Lupus Foundation of America, 2, Lupus Research Alliance, 2, Merck, 2.

Abstract Number: 0898

Ultrasound Demonstrates Rapid Reduction of Crystal Depositions During a Treat-to-target Approach in Gout Patients: Two-year Results from a Longitudinal, Observational Study (NOR-GOUT)

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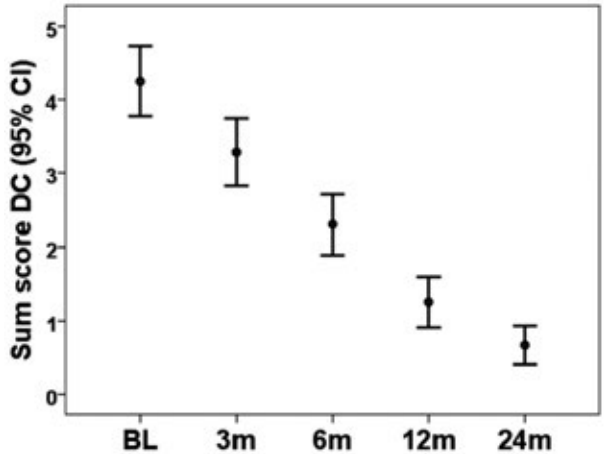
Background/Purpose: Ultrasound is sensitive for detecting depositions of uric monosodium urate (MSU) crystals and is included in the ACR/EULAR classification criteria for gout. The OMERACT ultrasound group has developed

	Baseline (n=207) Mean (SD)	3 months (n=187) Mean (SD)	6 months (n=181) Mean (SD)	12 months (n=166) Mean (SD)	24 months (n=103) Mean (SD)
DC sum score	4.3 (3.5)	3.3 (3.2)**	2.3 (2.8)**	1.3 (2.2)**	0.7 (1.3)**
Tophi sum score	6.3 (6.3)	5.9 (5.8)	4.9 (5.8)**	3.8 (5.0)**	2.8 (4.1)**
Aggregates sum score	9.2 (5.4)	8.6 (5.2)*	7.6 (4.9)**	6.6 (5.0)**	5.7 (4.7)**
Total sum score (DC, tophi and aggregates)	19.8 (13.6)	17.8 (12.7)**	14.7 (12.1)**	11.7 (11.1)**	9.2 (9.1)**

*=p<0.05, **=p<0.001)



definitions for elementary lesions in gout including the double contour (DC) sign (depositions of crystals on the surface of cartilage), tophus (larger hypo-echoic aggregation of crystals, usually well delineated) and aggregates (small hyper-echoic deposits). The present objective was to explore by ultrasound the longitudinal change of MSU depositions during a treat-to-target (T2T) approach with urate lowering therapy (ULT) in patients with gout.

Methods: In a prospective observational study, patients with crystal-proven gout were included if they presented after a recent gout flare and had increased serum urate levels (>360 μmol/L). The T2T approach focused on ULT and increasing drug doses with monthly follow-up until the treatment target was met (< 360 μmol/L, or < 300 μmol/L if clinical tophi), and no scheduled visits between 12 and 24 months. An extensive ultrasound assessment was performed (GE E9 machine, grey scale 15MHz) at baseline and after 3, 6, 12 and 24 months to assess MSU depositons (DC, tophi and aggregates) with bilateral assessment of radiocarpal joint, MCP 2, insertion of triceps and quadriceps, proximal and distal patellar and the Achilles tendon, cartilage of distal femur (maximal flexed knee), the talar cartilage of tibiotalar joint and MTP 1 joint. The degree of elementary lesions was semi-quantitatively scored 0-3 (0=none, 1=possible, 2=certain, 3=major deposits). Total sum scores of DC, tophi and aggregates separately as well as all lesions combined were calculated at each visit. Changes from baseline were explored by paired samples T-test.

Results: 207 patients were included at baseline (94.3% men, mean (SD) age 56.3 (13.7) years, disease duration 7.9 (7.7) years). The mean (SD) serum urate level decreased from 496 (81) μmol/L at baseline to 332 (75) μmol/L at 24 months. The treatment target was met in 87% at 12 months and in 76% at 24 months. Sum scores of MSU depositions decreased over 24 months (table) and the numeric decrease was most pronounced for DC (figure). At baseline/24 months the percentages of patients with no presence of DC sign was 7%/70%, no tophi; 7%/27% and no aggregates 1%/7%. Of patients having DC at baseline, 62% had no detected DC at 24 months, for tophi the corresponding percentages was 20, and for aggregates 6.

Conclusion: This study shows that most of the patients reached the target during T2T lowering therapy, and that this was followed by a major reduction of the ultrasound detected MSU depositions, especially DC.

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Abstract Number: 0899

Lack of Effect of Tart Cherry Concentrate Dose on Serum Urate in People with Gout

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Background/Purpose: In small studies, cherries and cherry concentrate have been suggested to reduce serum urate and gout flares. The aims of this study were to determine the magnitude of the effect of tart cherry concentrate on serum urate in people with gout, the most effective dose of tart cherry concentrate in lowering serum urate, and adverse effects with tart cherry concentrate.

Methods: Fifty people with gout as defined by ARA preliminary classification criteria for gout AND a serum urate >6mg/dl (0.36mmol/l) were recruited. People with type 2 diabetes and those receiving diuretics were excluded. Half the participants were already receiving allopurinol and half were on no urate lowering therapy at the time of recruitment, and participants in each of these blocks were randomised into 5 Cherryvite montmorency tart cherry juice concentrate groups: placebo, 7.5mls twice daily, 15mls twice daily, 22.5mls twice daily and 30mls twice daily for 28 days. Participants were commenced on tart cherry concentrate and blood samples were taken at baseline, the 1, 3, and 5 hours post cherry and then day 1, 3, 7, 14, 21 and 28. Urine anthocyanin concentrations were determined by HPLC as a measure of compliance at before any cherry concentrate day 0 and 28. AUC for serum urate was calculated over the 28-day study period.

Table: Effect of cherry concentrate

	Placebo			7.5mls			15mls			22.5mls			30mls		
	Day 0	Day 28	Change	Day 0	Day 28	Change	Day 0	Day 28	Change	Day 0	Day 28	Change	Day 0	Day 28	Change
Serum urate (mmol/l)	0.47 (0.08)	0.47 (0.12)	0.00 (0.06	0.43 (0.05)	0.40 (0.08)	-0.01 (0.08)	0.44 (0.05)	0.44 (0.10)	0.00 (0.06)	0.45 (0.09)	0.44 (0.12)	-0.01 (0.05)	0.43 (0.08)	0.42 (0.08)	-0.02 (0.02)
Creatinine (umol/l)	99.3 (15.7)	103.5 (21.1)	4.2 (11.1)	93.8 (13.2)	97.1 (16.5)	-0.8 (8.1)	94.7 (7.8)	98 (9.7)	3.3 (4.7)	94.5 (8.7)	93.2 (8.7)	-1.4 (10.9)	91.8 (9.2)	94.5 (9.1)	2.7 (7.8)
eGFR (ml/min/1.7m^2)	72.3 (12.7)	69.5 (14.1)	-2.8 (6.7)	73.1 (16.3)	71.8 (16.8)	1.125 (6.1)	73.2 (10.2)	70.4 (10.3)	-2.8 (4.1)	75 (15.8)	75.6 (13.4)	0.7 (8.2)	79 (13.5)	76.1 (11.6)	-2.9 (7.6)
HBA1C	37.6 (9.1)	36.5 (8.2)	-1.1 (4.0)	36.1 (7.3)	36.5 (9.4)	0.5 (4.0)	40.3 (13.5)	39.7 (12.4)	-0.6 (5.0)	33.6 (4.4)	34.2 (5.3)	0.7 (3.3)	33.3 (4.6)	34.5 (4.5)	1.2 (2.9)
Urine anthocyanins	2482 (2441)	10039 (12662)	7557 (11443)	3899 (5085)	17018 (20696)	12631 (22431)	1213 (1866)	17509 (26534)	16417 (26254)	1258 (2723)	11266 (10002)	10008 (10916)	2217 (2445)	15619 (15668)	13662 (15303)
Gout flares	0.5 (0.5)	0.4 (0.5)	-0.1 (0.6)	0.4 (0.5)	0.6 (0.5)	0.1 (0.8)	0.2 (0.4)	0.4 (0.5)	0.2 (0.6)	0.4 (0.5)	0.6 (0.5)	0.1 (0.6)	0.0 (0.0)	0.4 (0.5)	0.4 (0.5)

Data are mean (SD)

Results: Cherry concentrate dose had no significant effect on reduction in serum urate AUC over the 28-day study period. There was no influence of cherry concentrate on the urate lowering effect of allopurinol. There was no effect of cherry concentrate dose on change in urinary anthocyanin between day 0 and day 28 (table). However, those receiving allopurinol had significantly greater increases in urinary anthocyanins (p< 001). Cherry concentrate dose had no significant effect on urinary urate excretion as measured by Simkin Index (p=0.53) or fractional excretion of urate (p=0.32). There were 24 adverse events over the 28 day period with only one (hyperglycaemia) considered possibly related to cherry concentrate. There was no significant effect of cherry concentrate on change in HbA1c (p=0.68) or weight (p=0.80) over the 28 days. There was no effect of cherry concentrate on the frequency of gout flares over the 28-day study period p=0.76) (table).

Conclusion: Tart cherry concentrate had no effect on serum urate or urine urate excretion over 28 days. Reassuringly there were few adverse events. If there is an effect of cherry concentrate on gout flares over a longer time period it is not likely to be mediated by reduction in serum urate.

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Abstract Number: 0900

Serum Urate Lowering with Allopurinol Improves Endothelial Function in Young Adults

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Background/Purpose: An effect of serum urate on vascular endothelium has been postulated as a mechanism for its association with hypertension and cardiovascular disease. Prior studies in this area have produced conflicting

	Mean or frequency
Age (years)	27.7± 7.0
Gender Male Female	 49 (64%) 28 (36%)
Race/Ethnicity African American Not African American	 30 (39%) 47 (61%)
Serum urate at baseline Male Female	 6.3 ± 0.9 mg/dL 4.9 ± 0.9 mg/dL
Blood pressure at enrollment Mean Systolic (mmHg) Mean Diastolic (mmHg)	 133.8 ± 10.2 84.1 ± 9.2
FMD at baseline (%)	9.9 ± 4.1
Highly sensitive C-reactive protein at baseline (mg/L) (n=79)	3.8 ± 4.7

Table 1. Baseline characteristics of participants who completed FMD testing (n =77)

Outcomes	Placebo			Allopurinol			p for change in FMD
	Pretreatment	End of Placebo phase	p	Pretreatment	End of Allopurinol phase	p	
FMD (%)	9.9 (4.3)	9.8 (4.3)	0.76	9.9 (5.1)	12.9 (5.4)	<0.0001	
Change in FMD (%)		-0.1 (3.6)			2.9 (4.5)		<0.0001

Table 2. Endothelial function measured as flow mediated dilation (FMD) percent change during placebo and allopurinol administration phases

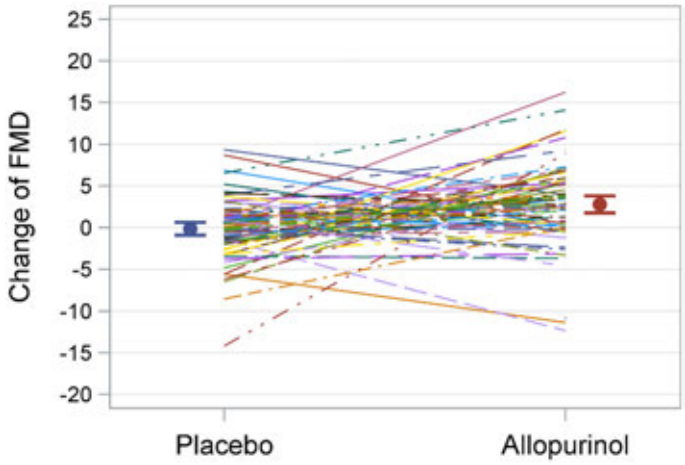

Figure. Change in endothelial function measured as flow mediated dilation (FMD) percent change during placebo and allopurinol administration phases

results. We sought to test the hypothesis that serum urate reduction with allopurinol would lead to improvements in endothelial function in young adults with pre-hypertension.

Methods: Single center, double-blinded, crossover trial in which participants were randomly assigned to allopurinol (300 daily mg) and placebo for a period of 4 weeks, separated by a 2-4 week washout. Adults ages 18-40 with base-

line systolic blood pressure (SBP) ≥ 120 and < 160 mm Hg or diastolic blood pressure ≥ 80 and < 100 mm Hg, and serum urate ≥ 5.0 mg/dL for men or ≥ 4.0 mg/dL for women were enrolled. Key exclusion criteria included chronic kidney disease, gout, or use of urate-lowering therapies. Endothelial function was assessed with flow-mediated dilation (FMD) testing of the brachial artery using high-resolution ultrasound at four study time points: 1) first baseline, 2) post-allopurinol or placebo treatment, 3) second baseline post-washout, and 4) post-placebo or allopurinol treatment. High-sensitive C-reactive protein (hs-CRP) was measured at the same study points as FMD. Safety assessments were conducted as part of the study.

Results: Of the 99 randomized main study participants, 77 completed all FMD testing (Table 1). Among these 77 participants, serum urate decreased by 1.40 + 1.19 mg/dL during the allopurinol period ($p< 0.0001$) and by a (non-significant) 0.06 + 0.76 mg/dL while taking placebo. The percent change in FMD was highly significant ($p< 0.001$) during the period assigned to allopurinol (2.9 ± 4.5) versus during the period assigned to placebo (-0.1 ± 3.6)(Table 2 and Figure). Changes in serum urate and FMD were highly correlated (Pearson r = -0.31, p =0.005). Improvements in FMD measurements while taking allopurinol were seen across all studied participant subgroups (younger and older, men and women, African-American and non-African-American, higher categories of serum urate, higher blood pressure at baseline visits). There were no changes from baseline in hs-CRP levels after the allopurinol or placebo phases. No allopurinol hypersensitivity events or other serious adverse events were observed.

Conclusion: Urate-lowering therapy with allopurinol in young adults led to significant improvements in endothelial function when compared with placebo while there was no observed effect on hs-CRP levels.

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Abstract Number: 0901

Sensitivity of Dual-Energy CT, Ultrasound, and X-Ray for Pseudogout: A Pilot Study

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SESSION INFORMATION
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Background/Purpose: Advanced imaging modalities such as ultrasound (US) and dual-energy CT (DECT) can help diagnose crystalline arthritis. DECT is a highly sensitive and specific modality to detect gout and has not been well studied in pseudogout. We compared the sensitivity of DECT, US, and x-ray (XR) in pseudogout.

Table 1. Performance of DECT, ultrasound and x-ray in pseudogout

	DECT volume >0.40 cm^3	DECT volume >0.01 cm^3	Ultrasound	X-ray
Sensitivity (95% CI) in the aspirated joint	90% (62-100%)	100% (74-100%)	100% (74-100%)	70% (41-92%)
Prevalence (95% CI) in the standardized joint	20% (4-49%)	90% (62-100%)	80% (51-96%)	30% (9-59%)

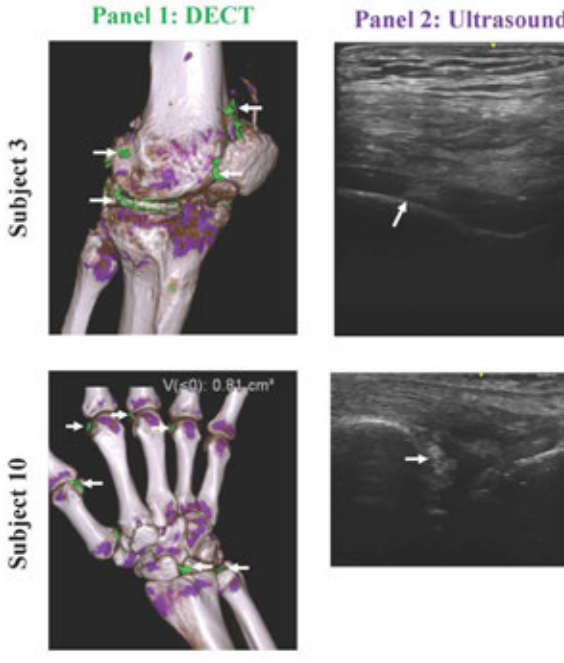

Figure 1. DECT, ultrasound, and x-ray images of an aspirated knee (top row) and wrist (bottom row), each with synovial fluid CPP crystals. Imaging abnormalities are indicated with white arrows.

Panel 1: DECT. 3D volume-rendered technique reconstructed DECT images using Siemens CT *syngo.*via CPPD software package. CPP deposits are shown in green.

Panel 2: Ultrasound. Calcific deposits in the femoral hyaline cartilage (top row) and TFCC (bottom row)

Panel 3: X-ray. Chondrocalcinosis in the meniscus and intercondylar notch (top row) and in the intercarpal joints, radiocarpal joint, and TFCC (bottom row)

Methods: We prospectively enrolled patients with crystal-proven pseudogout in a pilot study at a tertiary care center, 3/2018-11/2018. Eligible patients were 18 years old with acute monoarthritis, joint aspiration, and synovial fluid calcium pyrophosphate (CPP) crystals identified via polarized microscopy. Patients with both monosodium urate and CPP crystals were excluded. Subjects underwent DECT, US, and XR of the aspirated joint and a standardized joint (right wrist). A musculoskeletal radiologist interpreted all images; a rheumatologist trained in US additionally interpreted US images and consensus was reached for each scan. DECT images were post-processed using Siemens syngo. via software, applying color-coded overlay indicating volume and location of CPP deposits. DECT was defined as positive if color-coded overlay consistent with CPP was present. We excluded artifacts in nail beds, skin, motion or beam hardening, and deposits < 1 mm. We considered two volume thresholds (cm^3) for a positive DECT scan after inspecting the data: >0.40 cm^3 and >0.01 cm^3. Ultrasound was defined as positive if hyperechoic deposits in hyaline cartilage, fibrocartilage, or tendon were observed. X-ray was defined as positive if chondrocalcinosis was observed in hyaline cartilage or fibrocartilage. We calculated the sensitivity of a positive scan in the aspirated joint (reference standard: synovial fluid CPP crystals) and prevalence in the standardized joint.

Results: Ten patients enrolled a mean (SD) of 17 (9) days after joint aspiration. Mean age was 73 (10) years and 40% were female. The knee was aspirated in 8/10 and the wrist was aspirated in 2/10. Six subjects received intra-articular

steroids before enrollment. In the aspirated joint, sensitivity (95% confidence interval) was 90% (62-100%) for DECT volume >0.40 cm^3, and 100% (74-100%) for DECT volume >0.01 cm^3; 100% (74-100%) for US; and 70% (41-92%) for XR (**Table 1**). In the standardized joint, DECT was positive in 20% (4-49%) for volume >0.40 cm^3, and 90% (62-100%) for volume >0.01 cm^3. XR chondrocalcinosis was present in 30% (9-59%) and US was positive in 80% (51-96%) of wrists. Representative images from an aspirated knee and wrist are presented in **Figure1**.

Conclusion: DECT and US had high sensitivity for pseudogout using synovial fluid CPP crystal analysis as the reference standard. Larger studies testing the sensitivity and specificity of DECT in pseudogout vs. other types of arthritis and establishing a volume threshold are needed.

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Abstract Number: 0902

The Effects of a Low-Fat, Mediterranean, or Low-Carbohydrate Diet on Serum Urate

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Background/Purpose: Gout and hyperuricemia are associated with cardiometabolic comorbidities and increased risk of premature mortality. Often, low-purine (i.e., low-protein) diets are recommended for patients with gout, based on epidemiologic studies linking purine intake and risk of incident gout and gout flares. However, such a diet could potentially lead to higher intake of foods rich in refined carbohydrates and trans fat, which could worsen the cardiometabolic comorbidities of gout. Conversely, diets that promote weight loss, such as Mediterranean and low-carbohydrate diets, could improve cardiovascular risk factors and may also reduce serum urate (SU) by improving insulin resistance, thereby enhancing urate excretion. However, clinical trial data on the effect of dietary interventions on SU are scarce. Thus, the objective of this study was to determine the effects of three established weight loss diets (i. low-fat restricted calorie; ii. Mediterranean restricted calorie; iii. low-carbohydrate non-restricted calorie) on SU levels by conducting a post-hoc analysis of the Dietary Intervention Randomized Controlled Trial (DIRECT) study.

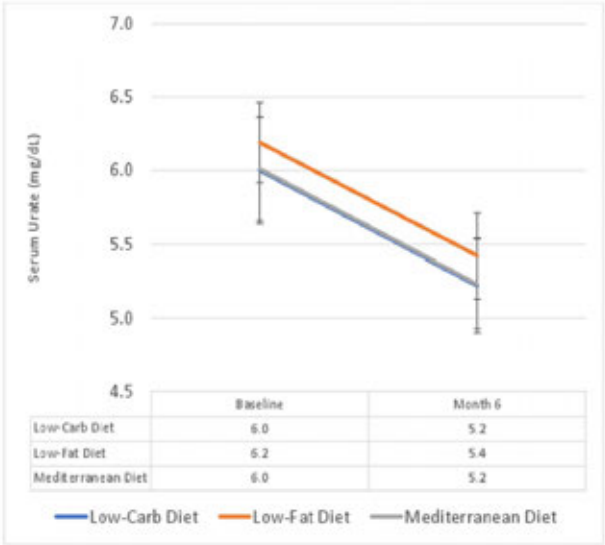
Methods: The DIRECT study included men and women age 40-65 with a body mass index (BMI) of at least 27 kg/m^2 or a diagnosis of either type 2 diabetes or coronary heart disease (regardless of BMI). Participants were randomly assigned to one of three weight loss diets: i. low-fat restricted calorie; ii. Mediterranean restricted calorie; iii. low-carbohydrate non-restricted calorie. We measured SU levels at baseline and 6 months using stored samples from the study from 232 trial participants. The primary outcome of this ancillary analysis was the change in SU from baseline among the three diet groups.

Table 1: Baseline Characteristics of Study Participants

Baseline Characteristics*	Low-Fat Diet (n=84)	Mediterranean Diet (n=75)	Low-Carbohydrate Diet (n=73)
Age, years	50.8 ± 6.5	52.6 ± 6.2	51.2 ± 6.2
Male, N (%)	72 (85.7)	65 (86.7)	66 (90.4)
SUA, mg/dL	6.2 ± 1.3	6.0 ± 1.5	6.0 ± 1.5
SU ≥ 7 mg/dL, N (%)	22 (26.2)	17 (22.7)	18 (24.7)
BMI, kg/m^2	30.5 ± 3.1	30.1 ± 3.3	30.7 ± 3.5
Weight, kg	90.8 ± 12.2	87.7 ± 12.1	91.3 ± 14.6
Diabetes, N (%)	10 (11.9)	11 (14.7)	12 (16.4)
Coronary heart disease, N (%)	27 (32.1)	36 (48.0)	20 (27.8)
Blood pressure, mm Hg			
Systolic	129.8 ± 12.6	131.3 ± 16.4	129.3 ± 14.3
Diastolic	79.0 ± 8.8	80.0 ± 10.2	77.5 ± 8.1
Lipid profile			
HDL, mg/dL	38.4 ± 9.7	40.2 ± 9.8	37.2 ± 8.8
Triglycerides, mg/dL	155.9 ± 62.5	168.5 ± 65.1	171.9 ± 84.8
Total cholesterol : HDL ratio	5.2 ± 1.4	5.3 ± 1.4	5.6 ± 1.5
GFR, ml/minute/1.73 m^2	96.4 ± 23.6	92.6 ± 18.7	99.2 ± 21.8
HOMA-IR	2.8 ± 1.9	3.4 ± 2.7	3.4 ± 3.2

*Unless indicated otherwise, values are the mean ± standard deviation.
Abbreviations: SU – serum urate; BMI – body mass index; HDL – high-density lipoprotein; GFR – glomerular filtration rate; HOMA-IR – homeostasis model assessment of insulin resistance.

Figure 1: Overall Serum Urate Response According to Diet Group

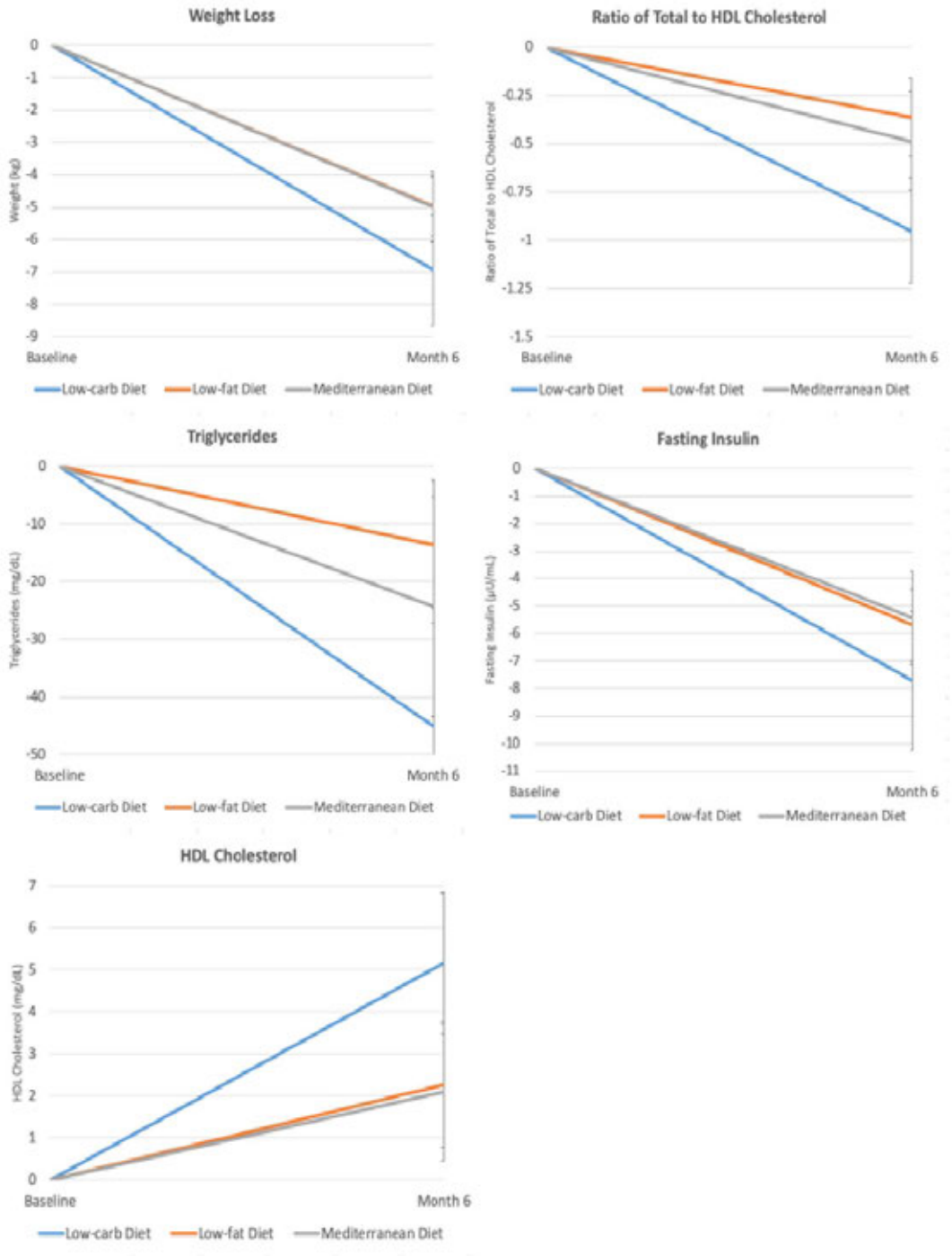


Results: Baseline characteristics were well-balanced between the three groups (Table 1). All three diets significantly reduced SU levels by 0.8 mg/dL each over 6 months (all p for within-group comparison < 0.001 and p >0.98 for between-group comparisons) (Figure 1). This urate-lowering effect was most pronounced among those with baseline hyperuricemia (i.e., SU 7mg/dL). The mean SU decrease was 1.9 mg/dL for the low-fat group, 2.0 mg/dL for the Mediterranean group, and 2.5 mg/dL for the low-carbohydrate group. The relative reduction in the ratio of total cholesterol to high-density lipoprotein cholesterol was 16.9% in the low-carbohydrate group and 7.0% in the low-fat

group (p=0.01). BMI, blood pressure, cholesterol profile, triglycerides, and insulin levels also improved significantly in all three groups (Figure 2), with more prominent improvement in the low-carbohydrate group, particularly lipid profiles.

Conclusion: Low-fat restricted calorie, Mediterranean restricted calorie, and low-carbohydrate non-restricted calorie diets can all lower SU levels, although the effect size is smaller than that of a typical urate-lowering drug. Cardio-

Figure 2: Weight Loss and Cardiovascular Risk Factors Among Those with Baseline Hyperuricemia



vascular risk factors improved consistently across all three diets, whereas it remains unclear whether urate-lowering drugs have similar benefits. Thus, dietary interventions aimed at weight loss could be a useful adjunctive tool to modestly lower SU levels and improve the cardiovascular risk factors associated with hyperuricemia.

Disclosure: C. Yokose, None; **S. Rai**, None; **N. Lu**, None; **N. McCormick**, None; **G. Curhan**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5.

Abstract Number: 0903

Prevalence of Atopic Features in Classic Autoinflammatory Diseases

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease I: Expanding the Spectrum of Clinical Features in Rheumatological Disorders

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Autoinflammatory diseases (AIDs), often caused by single gene mutations, are disorders in which aberrant activation of innate immune cells causes uncontrolled systemic inflammation. Because many autoinflammatory mediators negatively regulate of allergic/atopic cytokines, patients with AIDs are thought to be at low risk of developing atopy. However, the prevalence of atopy in the AIDs is not established.

Methods: We conducted a retrospective chart review of patients enrolled on protocol 94-HG-0105 “Genetics and Pathophysiology of Familial Mediterranean Fever and Related Disorders”. All patients had a molecular diagnosis (Sanger sequencing) of familial Mediterranean fever (FMF); cryopyrin-associated periodic syndrome (CAPS); tumor necrosis factor-associated periodic syndrome (TRAPS); deficiency of adenosine deaminase 2 (DADA2), hyper-IgD syndrome (HIDS); pyogenic arthritis, pyoderma gangrenosum, and acne (PAPA); or haploinsufficiency of A20 (HA20). Atopic features were defined as serum IgE > 100 kU/L, absolute eosinophil count (AEC) > 500, true (non-neutrophilic) urticaria, asthma, atopic dermatitis, or food allergy. Severe atopic features were defined as serum IgE > 500, AEC > 1500, anaphylaxis (excluding medication-induced), recurrent angioedema, multiple food allergies, or eosinophilic gastrointestinal disease (EGID). Comparator laboratory data (IgE, AEC) were obtained from theNational Health and Nutrition Examination Survey (NHANES). Comparator data on food allergy, asthma, atopic dermatitis, angioedema, anaphylaxis, and EGID were obtained from US population-based studies (National Health Interview Survey, Behavioral Risk Factor Surveillance System, National Opinion Research Center, US commercial healthcare databases). Comparator data on urticaria and angioedema, which had not been studied in US populations, were obtained from European population-based studies (surveys and national registries).

Results: Atopic features are shown in Table 1, and severe atopic features are shown in Table 2. Clinical features of atopy were less prevalent in AIDs than in the general population except for asthma, which was observed in CAPS, PAPA, and HA20. Of the AIDs, FMF, TRAPS, and HIDS had the lowest prevalence of atopy. With regards to lab features of atopy, AIDs had a low prevalence of elevated IgE, whereas mild eosinophilia was highly prevalent in CAPS, PAPA, and HA20. Severe atopy was rare in all the AIDs, with rates lower than those seen in the general population for all features except eosinophilia. Severe eosinophilia (AEC > 1500) was seen in CAPS and PAPA, and EGID was a prominent component of intestinal inflammation in one HA20 patient.

Disease (total patients)	IgE>500	AEC>1500	Recurrent angioedema	Anaphylaxis	EGID	Multiple food allergies
FMF (99)	0.0%	1.0%	0.0%	0.0%	0.0%	0.0%
CAPS (76)	7.9%	7.9%	0.0%	3.9%	0.0%	2.6%
HIDS (33)	0.0%	0.0%	0.0%	3.0%	0.0%	0.0%
PAPA (15)	0.0%	6.7%	0.0%	0.0%	0.0%	0.0%
TRAPS (44)	0.0%	0.0%	0.0%	2.3%	0.0%	2.3%
HA20 (12)	0.0%	0.0%	0.0%	0.0%	8.3%	0.0%
DADA2 (38)	0.0%	0.0%	0.0%	2.6%	0.0%	0.0%
Adult general population (prevalence)	7.3%	0.2%	<0.1%(*8*)	0.05-2%(*9*)	<0.1%(*10*)	4.9%(*2*)
Pediatric general population (prevalence)	8.1%	0.4%	<0.1%(*8*)	0.05-0.5%(*9*)	<0.1%(*10*)	2.4%(*6*)

Table 2. Prevalence of severe atopic features in patients with autoinflammatory disease confirmed by genetic testing, and comparison data in the general population. IgE= total serum IgE (international units/mL); AEC= absolute eosinophil count (103/μL); EGID= eosinophilic gastrointestinal disease; FMF= familial Mediterranean fever; CAPS= cryopyrin-associated periodic syndrome; TRAPS= tumor necrosis factor-associated periodic syndrome; DADA2= deficiency of adenosine deaminase 2; HIDS= hyper-IgD syndrome; PAPA= pyogenic arthritis, pyoderma gangrenosum, and acne; HA20= haploinsufficiency of A20.

Conclusion: Most clinical features associated with atopy are rare in AIDs, as is elevated IgE, and the presence of severe atopy in an AID should prompt further investigation. However, both mild and severe eosinophilia are seen at a higher prevalence in CAPS, PAPA, and HA20, suggesting that *NLRP3*, *PSTPIP1*, and *TNFAIP3*mutations may alter eosinophil biology. Further studies are needed to determine the significance, disease associations, and treatment associations of eosinophilia in these diseases.

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Disclosure: B. Dizon, None; **H. komarow**, None; **D. Stone**, None; **P. Hoffmann**, None; **A. Jones**, None; **T. Romeo**, None; **K. Barron**, None; **I. Aksentijevich**, None; **D. Kastner**, None; **A. Ombrello**, None; **J. Milner**, None; **D. Schwartz**, None.

Abstract Number: 0904

Bone Manifestations in Gaucher Disease: A Monocentric Study of 128 Patients

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SESSION INFORMATION

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Session Title: Miscellaneous Rheumatic & Inflammatory Disease I: Expanding the Spectrum of Clinical Features in Rheumatological Disorders

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Gaucher disease (GD) is a rare lysosomal storage disorder caused by mutations in the glucocerebrosidase gene, leading to defective lysosomal acid β-glucosidase. Its incidence ranges between 0.4 and 5.8 for 100,000 inhabitants. GD patients may present splenomegaly, hepatomegaly, cytopenia, and/or skeletal disease. Bone manifestations (BM) include acute or chronic bone pain, risk of pathologic fractures (PF), epiphyseal avascular necrosis (AVN), bone infarcts and/or decreased bone mineral density. We aimed to describe BM at baseline and during follow-up in a large cohort of GD patients.

Methods: We conducted a monocentric retrospective study of GD patients followed in a French referral center for lysosomal disorders and enrolled in the French Gaucher Disease Registry. Their demographical and clinical characteristics at diagnosis, and their treatments, clinical bone manifestations and imaging during follow-up were collected.

Results: A total of 128 GD patients (123 GD type 1 and 5 GD type 3) were followed up for a median [interquartile range] of 24.7 [12.9–34.3] years. Male/female ratio was 0.9. Genotype was N370S/N370S for 22 (17.1%), N370S/other for 77 (60.2%), and other/unknown for 29 (22.7%) patients. Median age at GD diagnosis was 19.2 [9.1–29.2] years. BM were the first GD symptom for 11 (8.6%) patients. At GD diagnosis, 31 (28.2%) had chronic bone pain, and 16 (12.5%) had acute bone crisis. During follow-up, 98 (76.6%) had clinical BM. Thirty (23.5%) patients had had at least one episode of epiphyseal AVN, including 14 (10.9%) with multiple AVN. Of the 52 AVN episodes, 33 (63.5%) involved femoral head, 6 (11.5%) humeral head, 6 (11.5%) knees, and 8 (15.4%) other joints. Diaphyseal or metaphyseal bone infarcts occurred in 32 (25.0%) patients, including 12 (9.4%) with multiple bone infarcts. Of the 50 episodes of bone infarcts, femoral diaphysis was involved in 18 (36%) cases, tibia in 13 (26%), pelvis in 6 (12%) and humerus in 3 (6%). PF occurred in 38 (29.7%) patients: 25 had a unique PF, whereas 13 had ≥2 PFs. On the 66 PF, 25 (37.9%) were located on upper limbs, 19 (28.8%) on lower limbs, and 15 (22.7%) were vertebral fractures. Of the 77 patients with available bone X-rays, 48 (62.3%) were pathologic, showing Erlenmeyer flask deformity in 28 (36.4%) cases, osteopenia in 18 (23.4%) and/or osteolytic lesions in18 (23.4%). Evidence of bone marrow infiltration was present for at least 62 (52.1%) of the 119 patients with available magnetic resonance imaging. Of the 66 patients with available bone densitometry during follow-up, 29 (43.9%) had osteopenia with T-score between -1 and -2.5, and 11 (16.7%) had osteoporosis with T-score < -2.5. In 2019, 118 (92.2%) were alive. Among them, 106 (89.8%) are currently treated with imiglucerase (n=54), velaglucerase (n=31), or eliglustat (n=21).

Conclusion: This retrospective monocentric study of 128 patients followed up in a GD referal center during a median of 25 years provides useful information on bone involvement in GD, which occurs in a large majority of GD patients.

Disclosure: Y. Nguyen, None; **J. Stirnemann**, None; **M. Bengherbia**, None; **K. Yousfi**, None; **D. Hamroun**, None; **W. Allaham**, None; **B. Fantin**, None; **N. Belmatoug**, None.

Abstract Number: 0905

A Third of Relapsing Polychondritis Patients with Ear Involvement at Presentation Had Airway Involvement at the Last Follow-up with a High Mortality Rate

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease I: Expanding the Spectrum of Clinical Features in Rheumatological Disorders

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: We have reported that 239 patients with relapsing polychondritis (RP) were divided into three subgroups, namely patients with airway involvement (A subgroup, 20% of 239 patients), patients with ear involvement (E subgroup, 49%), and patients with both airway and ear involvement (B subgroup, 29%) (Medicine. 2018; 97(42): e12837.). Each subgroup exhibited characteristic clinical features. Patients in A subgroup and patients in E subgroup were characterized by saddle nose deformity and central nervous system (CNS) disorders, respectively. Patients in B subgroup had clinical characteristics of progressive and long disease course. We suggested that the disease progressed from A and E subgroups to B subgroup.

Methods: In the current study, we compared organ involvement at disease onset with that at the last follow-up to assess whether the disease progressed from A and E subgroups to B subgroup in patients with RP. We measured serum matrix metalloproteinase-3 (MMP3) concentrations of 32 samples obtained from newly recruited RP patients.

Results: At the first visit, patients had airway involvement (namely A subgroup at disease onset, 18% of 239 patients), ear involvement (E subgroup at disease onset, 56%), both airway and ear involvement (B subgroup at disease onset, 1.7%), eye involvement (7.1%), inner ear dysfunction (3.8%), arthritis (2.9%), CNS involvement (2.5%), nasal chondritis (1.3%), and skin involvement (0.84%). 34% of RP patients in E subgroup at disease onset developed airway involvement by the last follow-up (mean follow-up, 6.0 years) with a significantly higher mortality rate (13%) compared with those without airway involvement (2.3%). Cumulative incidence of CNS involvement was 12% (28 patients) in this study and encephalitis and meningitis were the most frequent manifestations (12 patients, 5.0%). Encephalitis/meningitis occurred before the onset of obvious chondritis in 6 patients (2.5%). In another cohort of RP patients, serum MMP3 concentrations were significantly higher in B subgroup (n=13) than those in A subgroup (n=7) and E subgroup (n=12).

Conclusion: RP patients with disease progression from E subgroup to B subgroup had higher mortality than those remaining in E subgroup at the last follow-up. Caution should be exercised in the diagnosis of CNS involvement in RP patients because of the varying clinical course at disease onset. Although the further study is necessary, MMP3 in RP patients may aggravate the inflammatory response of chondrocytes and promote overlapping organ involvement.

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Abstract Number: 0906

Sarcoidosis as a Systemic Disease. Clinical and Epidemiological Characterization of Systemic Phenotype in 1521 Patients

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SESSION INFORMATION

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Session Title: Miscellaneous Rheumatic & Inflammatory Disease I: Expanding the Spectrum of Clinical Features in Rheumatological Disorders

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Session Time: 4:30PM–6:00PM

Background/Purpose: To characterize the main epidemiological, clinical and radiological features at presentation of sarcoidosis in a large multicenter cohort from Southern Europe.

Methods: In January 2016, the Autoimmune Diseases Study Group (GEAS-SEMI) created a national registry (SARCOGEAS) of patients with sarcoidosis. Sarcoidosis was diagnosed in agreement with the criteria proposed by the American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) 1999 statement on sarcoidosis. Organ involvement was retrospectively determined in each patient at the time of diagnosis using the 2014 WASOG organ assessment instrument. Ethnicity was defined according to the FDA classification.

Results: The cohort consisted of 1521 patients (81% biopsy-proven), including 877 (58%) women and 644 (42%) men, with a mean age at diagnosis of 47.4 ± 15.2 years; 234 (15%) patients were born outside Spain. With respect to the FDA ethnic classification, 1370 (90%) patients were classified as White, 80 (5%) as Hispanic, 47 (3%) as Black/African American and 24 (2%) as Asian. Thoracic involvement was present at diagnosis in 1409 (92%) patients,

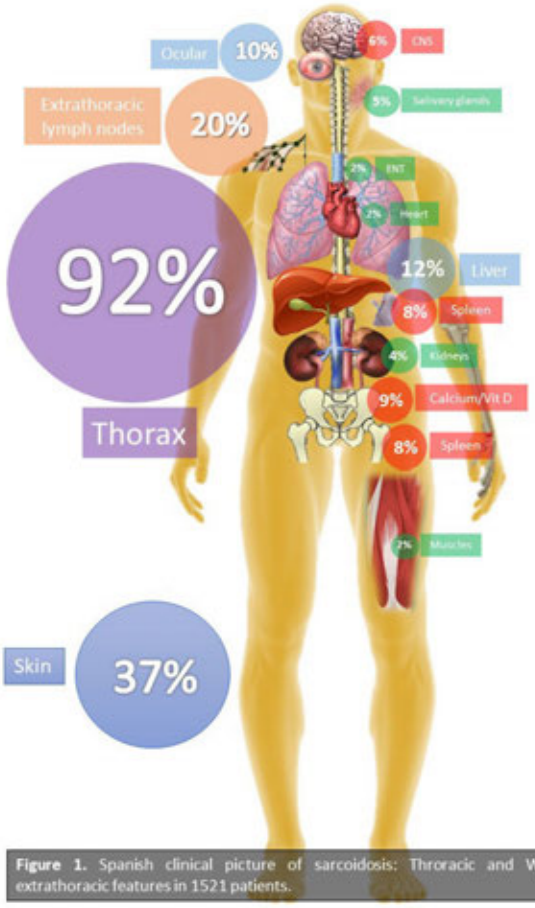

Figure 1. Spanish clinical picture of sarcoidosis: Thoracic and WASOG extrathoracic features in 1521 patients.

including 427 (29%) patients presenting with stage I, 619 (41%) with stage II, 288 (19%) with stage III and 53 (3%) presenting with stage IV. Extrathoracic disease was reported in 1096 (72%), and systemic disease (defined as at least 2 extrathoracic organs involved) in 523 (34%). According to the WASOG classification, the most frequently reported extrathoracic involvements at diagnosis were cutaneous in 558 (37%) patients, extrathoracic lymph nodes in 309 (20%), liver involvement in 189 (12%) and ocular involvement in 156 (10%) (**Figure**). Potentially life-threatening WASOG involvements were reported in frequencies less than 10%, including neurological involvement in 98 (6%) patients, kidney involvement in 58 (4%) or cardiac involvement in 30 (2%). Need for systemic therapy was required in 756 (50%) and aggressiveness of therapy in 124 (8%). Therapeutic approaches at diagnosis included the use of oral glucocorticosteroids in 731 (49%) patients, immunosuppressive agents in 118 (8%) and biological agents in 22 (1.5%).

Conclusion: This is one of the largest series of sarcoidosis reported out of the US, predominantly composed by White patients in nearly 90% of cases. Clinical presentation is dominated by adenopathies (both thoracic and extrathoracic) and cutaneous features (erythema nodosum), with lower frequencies in the main extrathoracic involvements. However, extrathoracic disease was reported in 3 out of 4 patients, and one third of patients presented with at least 2 different extrathoracic organs involved. These findings underline the systemic clinical expression of sarcoidosis, being mandatory a multidisciplinary management of the disease.

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Abstract Number: 0907

Musculoskeletal Sarcoidosis: Characterization and Clinical Expression of 129 Patients with Granulomatous Infiltration of Bones And/or Muscles

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease I: Expanding the Spectrum of Clinical Features in Rheumatological Disorders

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: To analyze the prevalence and characteristics of musculoskeletal sarcoidosis in a large nationwide multicenter cohort.

Methods: In January 2016, the Autoimmune Diseases Study Group (GEAS-SEMI) created a national registry (SARCOGEAS) of patients with sarcoidosis. Sarcoidosis was diagnosed in agreement with the criteria proposed by the American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) 1999 statement on sarcoidosis. Musculoskeletal involvement was characterized according to the 2014 WASOG organ assessment instrument, which is defined as the direct infiltrative granulomatous involvement affecting joints, bones, tendons and/or muscles (demonstrated either by imaging techniques or biopsy).

Results: Among 1521 patients included in the Registry at May 31, 2019, there were 129 (8.5%) that fulfilled the WASOG criteria for musculoskeletal sarcoidosis (72 women and 53 men, mean age at diagnosis of 45.4 years): 108 (7.1%) presented with osseous involvement and 21 (1.4%) presented with muscular sarcoidosis. Among patients presenting with osseous sarcoidosis, 24 presented typical radiological features of osseous granulomatous infiltration, 6 presented dactylitis, 25 nodular tenosynovitis and 56 asymptomatic osseous involvement demonstrated by PET/MRI: Among patients with muscular sarcoidosis, 5 presented with asymptomatic muscular involvement demonstrated by PET/MRI, 2 with palpable muscle masses, and the remaining 14 with biological/histopathological evidence of muscular involvement. In comparison with patients without musculoskeletal infiltrative involvement, those presenting with musculoskeletal sarcoidosis were predominantly White patients (96% vs 89%, p=0.025), had more frequently an acute onset of the disease (28% vs 18%, p=0.02), a higher frequency of systemic sarcoidosis (defined as the involvement of at least 2 different extrathoracic organs, 82% vs 30%, p< 0.001), a higher frequency of skin involvement (60% vs 35%, p< 0.001) and a higher frequency of need for therapy (64% vs 48%, p=0.001), including both glucocorticosteroids (61% vs 48%, p=0.007) and immunosuppressive agents (16% vs 7%, p=0.003).

Conclusion: Sarcoid musculoskeletal infiltration affects around 9% of patients with sarcoidosis, in most cases presenting as asymptomatic bone/muscular involvement demonstrated by PET, MRI and/or biopsy. These patients present with a very active systemic phenotypic profile, especially including cutaneous features, and required a more intensive systemic therapeutic approach.

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Abstract Number: 0908

Epidemiology and Presentation of Sarcoidosis with and Without HIV Infection

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SESSION INFORMATION

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Background/Purpose: Sarcoidosis and HIV are thought of as antithetical, one driven by excess, the other by deficiency, of CD4+ T-cells. However, case reports and series describe comorbid sarcoidosis and HIV. To date, there has been no controlled comparison of the incidence and presentation of sarcoidosis in persons with and without HIV infection.

Methods: Patients were selected from the Veterans Administration Cohort Study, a longitudinal cohort of veterans with HIV and age, sex and race-matched uninfected comparators. Among those with at least one ICD code for sarcoidosis, chart review was conducted to confirm incident or prevalent sarcoidosis. Cases where sarcoidosis developed before HIV were excluded from analysis. Incident cases (other than Stage I pulmonary sarcoidosis) were required to have tissue diagnosis and compatible clinical presentation with exclusion of reasonable alternative diagnoses; prevalent cases required documentation of diagnosis only. Organ involvement and immunosuppressive therapy were recorded for one year following the date of biopsy.

Results: Among 1,610 patients with at least one ICD code for sarcoidosis, 875 (54%) had prevalent sarcoidosis and 332 (21%) had incident sarcoidosis. After excluding 9 cases in which sarcoidosis developed before HIV and all prevalent cases, incidence of sarcoidosis among patients living with (N=56,470) and without (N=116,130) HIV was 0.9 (95% CI: 0.7-1.2), versus 1.5 (95% CI: 1.3-1.7) per 10,000 person-years. Uninfected individuals developed sarcoidosis more frequently than those with HIV (rate ratio 1.6 (95% CI: 1.2-2.1)). In those with HIV, sarcoidosis was diagnosed

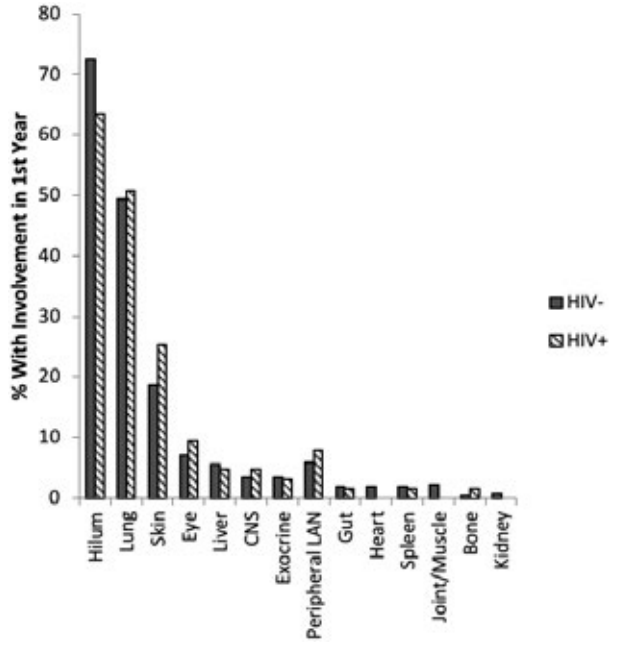

Figure 1 Frequency of Organ Involvement in First Year of Sarcoidosis, in Patients With or Without HIV. CNS=central nervous system. LAN=lymphadenopathy.

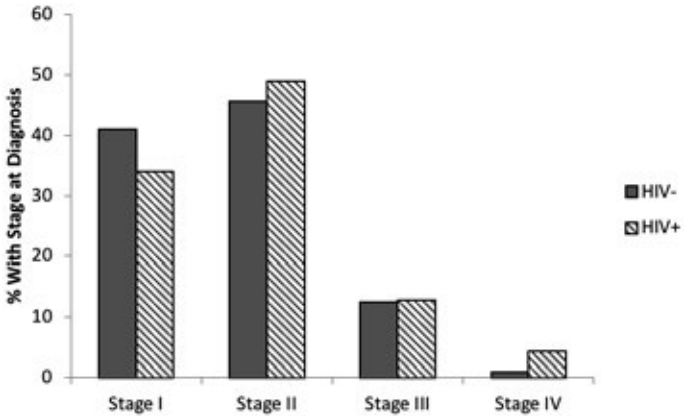

Figure 2. Stage of Pulmonary Sarcoidosis at Diagnosis

a median of 8.0 years after HIV diagnosis (3.3-15.4). At diagnosis, median CD4 count was 420 cells/mm^3 (268-530) and 56% of patients had a viral load < 500 copies/mL. Organ involvement and stage of pulmonary involvement (Figure 1, Figure 2), treatment with systemic glucocorticoids (37% vs 36%, p=0.93) and total dose of prednisone over one year (2195 vs 1800 mg, p=0.97) were all similar by HIV status. Use of steroid-sparing immunosuppressants (methotrexate, hydroxychloroquine, azathioprine and calcineurin inhibitors) tended to be less common in those with HIV (4.8% vs 10.4%, p=0.17).

Conclusion: Compared to those with HIV, those without were 60% more likely to develop sarcoidosis. Most patients with HIV and incident sarcoidosis had CD4 counts over 200, while just over half were virally suppressed. While presentation was similar, as was the use and total dose of oral glucocorticoids, use of steroid-sparing regimens tended to be less common among those with HIV.

Disclosure: J. Hanberg, None; **L. Fraenkel**, None; **A. Justice**, None.

Abstract Number: 0909

Is Long-term High-intensity Strength Training Beneficial or Harmful for Knee Osteoarthritis Patients? The Strength Training and Arthritis Trial (START)

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SESSION INFORMATION
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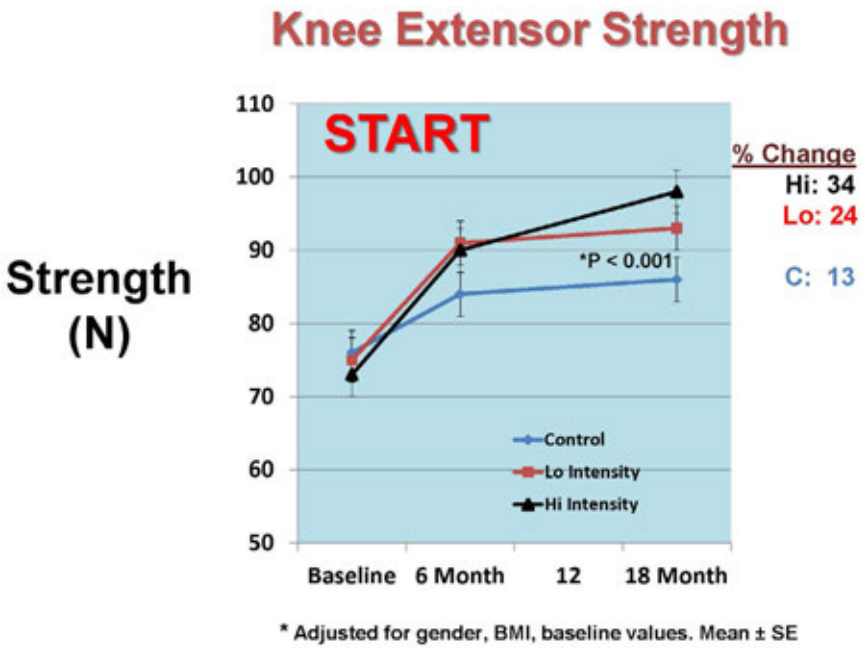
Background/Purpose: Few have studied long-term high-intensity strength training in knee osteoarthritis (OA) patients due to the unsubstantiated belief that it might exacerbate OA symptoms. Our purpose was to determine whether high-intensity strength training would improve mechanistic and clinical outcomes compared to low-intensity strength training and attention control.

Methods: Single-blind, 18-month, 3-arm randomized clinical trial conducted between September 2011 and August 2017. The strength training interventions were center-based. Participants were 377 community-dwelling adults (age ≥ 55 years) with a body mass index of 20-45 kg/m^2 (mean = 31.4 kg/m^2) with pain and mild to moderate radiographic



Figures 1-2. Baseline and 6- and 18-month follow-up knee extensor and knee flexor strength for the high and low intensity strength training and control groups.

Table 1. Mean (95%CI) adjusted (baseline value, gender, BMI) outcomes at baseline and 18-month follow-up by group.							
	Control		Low Intensity		High Intensity		
	Baseline	18 months	Baseline	18 months	Baseline	18 months	P
WOMAC Pain (0-20)	7.2	4.8	7.4	4.5	7.0	5.1	0.22
95% CI		4.3,5.4		3.9, 5.0		4.6,5.6	
Comp Force (Newtons)	2261	2493	2325	2455	2338	2492	0.90
95% CI		2362,2625		2324,2586		2362,2621	
6 minute walk (m)	490	512	479	504	466	507	0.76
95% CI		497,526		491,518		494,521	
WOMAC Function (0-68)	25.0	16.3	26.6	14.8	25.5	17.7	0.06
95% CI		14.5,18.1		13.1,16.6		16.0,19.4	
IL-6 (pg/ml)	3.21	2.89	3.08	3.62	3.54	3.10	0.37
95% CI		2.13,3.65		2.89,4.35		2.34,3.85	
BMI (kg/m^2)	31.7	31.1	31.2	31.1	31.3	31.0	0.95
95% CI		30.7,31.4		30.7,31.4		30.6,31.3	
Self-Efficacy (0-100)	90.5	80.1	91.1	91.0	90.2	90.2	<0.001
95% CI		76.5,83.6		87.5,94.5		86.8,93.6	
Thigh Muscle Vol (cm^3)	661	670	685	679	662	673	0.65
95% CI		655,685		664,694		657,687	
Joint Space Width (mm)	3.02	2.75	3.05	2.79	3.13	2.93	0.13
95% CI		2.62,2.88		2.66,2.92		2.80,3.06	

START outcome table ACR Table 1. Mean (95% CI) baseline and 18-month follow-up data for the high and low intensity strength training and control groups.

knee OA. Randomization was to either high-intensity strength training (75-90% 1RM), low-intensity strength training (30-40% 1RM), or attention control (healthy living classes). Primary outcomes were knee pain and knee-joint compressive forces during walking. Secondary outcomes included additional clinical measures of disease severity (e.g., function, mobility), radiographic progression by joint space narrowing, thigh muscle volume, knee extensor and knee flexor strength, inflammatory biomarkers, and self-efficacy. All primary statistical analyses used an intention-to-treat method.

Results: At 18 months, 320 (85%) participants completed the study. Knee pain and knee compressive forces were similar between the groups. Knee extension and flexion strength were significantly greater in the two strength-training groups (Figures 1 and 2). Self-reported function, 6-minute walk distance, BMI, IL-6, thigh muscle volume, and joint space width were similar across groups. Self-efficacy was greater in the two strength-training groups compared to the control group (Table 1). The two strength-training groups and the attention control group met the OARSI responder criteria of clinically important reductions in pain (between 27-39%) and improvements in function (between 31-44%) with no statistical differences between groups.

Conclusion: The significant improvements in knee strength in the two strength-training groups relative to the control group did not result in significantly better reductions in pain and knee joint loads, or improvements in function. This was due, in part, to the clinically important improvements in pain and function in the control group of between 33-35%. These results indicate that long-term high-intensity strength training for knee OA patients is a well-tolerated non-pharmacologic intervention that increases knee extensor and flexor strength, significantly improves self-efficacy, and does not exacerbate knee pain or disease progression relative to low-intensity strength training or attention control. An attention control with a focus on healthy living and living with OA, however, is just as effective as high- and low-intensity strength training in improving most clinical and mechanistic outcomes.

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Abstract Number: 0910

Is There Any Role for Opioids in the Management of OA?

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
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Background/Purpose: Opioids have long been prescribed for chronic pain conditions, including osteoarthritis (OA). Although the safety of opioids has been questioned, there is little information about their temporal efficacy. Additionally, differences in overall efficacy and safety between strong versus weak opioid classes have not been clearly delineated. We conducted meta-analyses of pain and function at 2, 4, 8, and 12 weeks and analyzed relevant safety outcomes for all opioids, as well as strong versus weak opioids.

Methods: We searched MEDLINE and the Cochrane Database from inception to April 2019 and actively sought unpublished data. Placebo-controlled RCTs assessing the efficacy and/or safety of FDA-approved opioids in patients with knee and/or hip OA were included. We excluded studies using enriched enrollment or double-dummy design involving non-oral treatments. Screening and data extraction were undertaken by two reviewers. We calculated standardized mean differences and risk ratios with 95% confidence intervals. Study quality was assessed using Cochrane risk of bias tool. Random effects meta-analyses were performed, and heterogeneity assessed using the I^2 statistic. Subgroup analyses of strong and weak opioids were conducted for pain at every time point, and for safety outcomes. Meta-regression was performed to assess the impact of dosage (morphine equivalency) on pain relief.

Results: The included 23 RCTs comprised 11,402 participants. 64% were female. The mean age ranged from 54 to 67 years; mean BMI from 28 to 34 kg/m^2. All trials were of moderate quality with potential attrition bias being the primary methodological concern. Overall, opioids demonstrated small, statistically significant benefits on pain at each time point ranging from -0.28 to -0.19 (Figure 1); similarly small, statistically significant effects were observed with respect to function at 2, 4, and 12 weeks ranging from -0.26 to -0.16. Opioids had no impact on quality of life or depression; participants who received opioids reported significantly higher quality of sleep. We found that strong opioids had consistently smaller benefits on pain than weak opioids (Figure 1). Meta-regression revealed that opioid dosage (morphine equivalency) has no impact on pain relief (p=0.09) (Figure 2). Methodological bias (selection, attrition) may contribute to the poor performance of strong opioids, or perhaps a pharmacodynamic classification of “strong” has been incorrectly equated with the clinical efficacy of these drugs. Strong opioids showed a safety profile consistently worse than weak opioids, particularly with respect to drug withdrawal symptoms (2.78 [1.41, 5.49] versus 1.06 [0.19, 5.80]) and discontinuations due to adverse events (5.47 [4.63, 6.47] versus 2.77 [2.26, 3.39]).

Conclusion: Overall, opioids demonstrate only small benefits on pain and function from 2 to 12 weeks of treatment and contribute no measurable benefit to QOL or depression versus placebo. Strong opioids demonstrated consistently worse pain relief, with greater risk of any safety outcome than weak opioids. In light of this evidence, clinicians and policy makers should reconsider the utility of strong opioids in the management of OA.

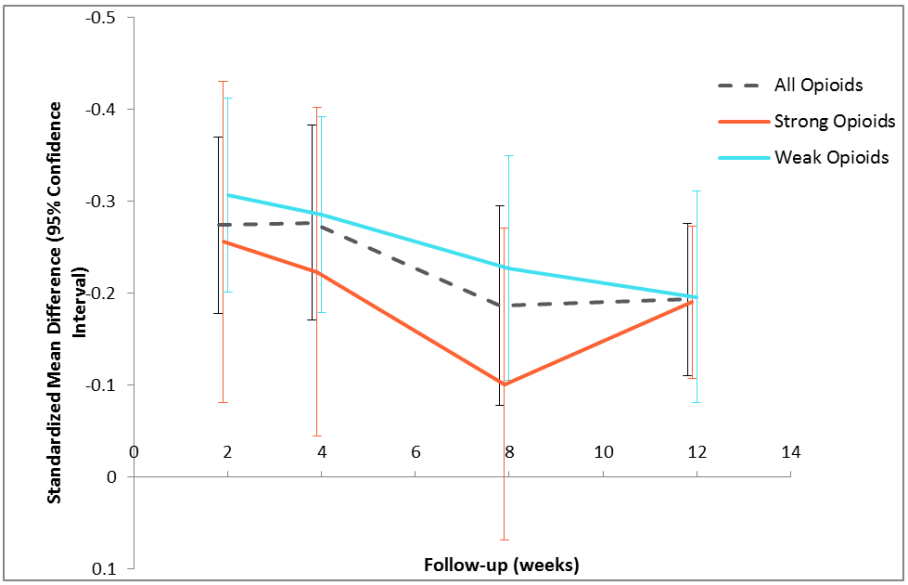

Figure 1. Differences in Pain Trajectory Based on Opioid Strength

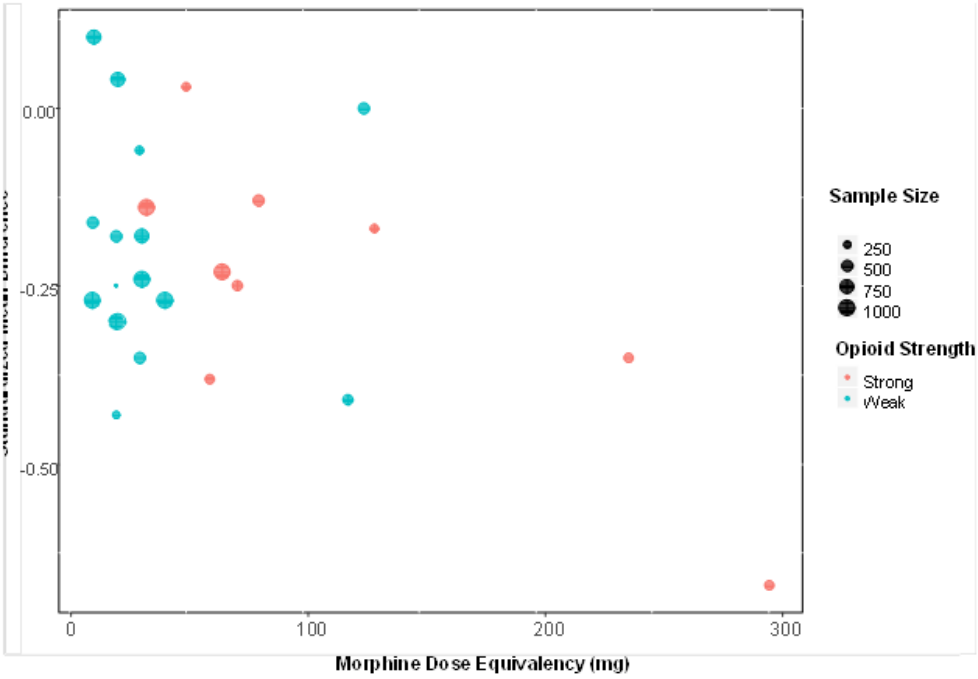

Figure 2. Meta-Regression of Effects of Strong and Weak Opioids on Pain, based on Morphine Dose Equivalency

Disclosure: M. Osani, None; **S. Lohmander**, Pfizer, 8, Roche, 5, GSK, 5, Johnson & Johnson, 5, Galapagos, 5, Regeneron, 5; **R. Bannuru**, None.

Abstract Number: 0911

Perfusion in Bone Marrow Lesions Assessed on Dynamic Contrast-enhanced MRI and Its Association with Pain in Knee Osteoarthritis: A Cross-sectional Study

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SESSION INFORMATION
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Session Time: 4:30PM–6:00PM

Background/Purpose: In osteoarthritis (OA) structural changes are only weakly associated with pain. The reason for this discrepancy remains unknown and the exact cause of knee pain in OA is still unclear which makes the target of treatment difficult. Bone marrow lesions (BMLs) and cysts are hallmarks of knee OA changes on MRI but studies investigating the association between BML and pain show conflicting results. Our objective was to evaluate the association between pain and perfusion in BMLs assessed on static- and dynamic contrast enhanced (DCE)-MRI in patients with knee OA in a cross-sectional setting.

Methods: MRI was performed at enrolment in the LOSEIT trial (ClinicalTrials.gov NCT02905864) studying persons with overweight/obesity and knee OA. BMLs with and without subchondral cystes were assessed across the whole knee using both DCE-MRI analysed with DYNAMIKA® (Image Analysis Group, LTD, London) and non-CE-MRI scored according to the MRI Osteoarthritis Knee Score (MOAKS) and correlated to pain using the Knee injury and Osteoarthritis Outcome Score (KOOS).

Results: Data were available from 107 participants, 64% women, 89% had radiologically verified OA (KLG 2 or 3). The participants had a mean age of 60.8 years, a mean BMI of 34.5 kg/m2, a mean KOOS pain of 63.7 (0-100 scale),

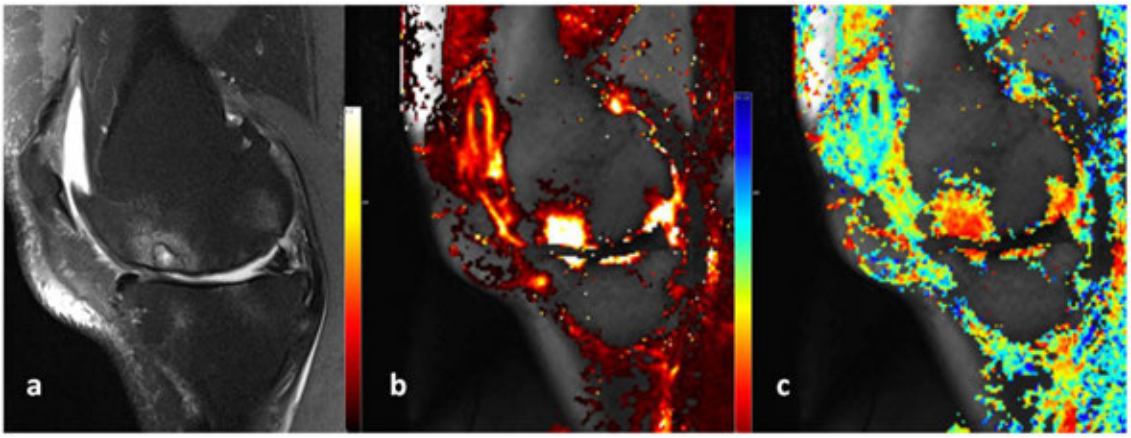

Figure. 1 Bone marrow lesion with cyst in knee with OA. a) non-CE-MRI b) DCE-MRI Initial rate of enhancement (IRE) c) DCE-MRI Time To Peak (TTP).

and a mean BML sum score of 6.5 (0-45 scale). For BMLs containing subchondral cysts the heuristic perfusion variable Time To Peak (TTP) showed a statistically significant correlation with KOOS Pain (r=0.40; p=0.002) meaning that higher and faster perfusion leading to earlier TTP in BMLs containing subchondral cysts is correlated to more knee pain. DCE-MRI parameters in BMLs without cysts and MOAKS BML scores were not correlated to KOOS pain.

Conclusion: In this study, we found that the perfusion variable TTP from DYNAMIKA® on DCE-MRI data in BMLs containing subchondral cysts was associated with the severity of knee pain in patients with knee OA. Thus DCE-MRI has the potential to separate and study different pain phenotypes of knee OA.

Disclosure: C. Daugaard, None; **R. Riis**, None; **E. Bandak**, None; **J. Nybing**, None; **S. Hangaard**, None; **H. Gudbergsen**, None; **M. Henriksen**, Thuasne Group, 6; **H. Bliddal**, None; **M. Boesen**, Image Analysis LTD, 1, UCB, 5, Abbvie, 5, Eli Lilly, 5, Novartis, 5, Glenmark, 5, Pfizer, 5, Astra Zeneca, 5, Esaote, 9.

Abstract Number: 0912

Co-morbidities Associated with Discordance Between Structural Severity and Pain in Osteoarthritis: Implications for Clinical Trial Design in OA – a Post-Hoc Analysis of Data from Two Randomized Controlled Trials

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Osteoarthritis – Clinical I: Innovations
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Development of new disease-modifying drugs in osteoarthritis (DMOADs) has proven difficult and is complicated by heterogeneous study populations and insensitive endpoints of structural change, symptomatic benefit, and discordances between structural disease severity and reported symptoms. In such trials, counterintuitively, mild structural disease may be associated with severe symptoms and vice versa. The reasons for this discordance are unknown, and research to uncover factors potentially distorting the perceived severity of symptoms is needed to better characterize the clinical relevance of structural improvement, if any, in DMOAD trials. Psychological conditions including anxiety and depressive disorders (ADD) as well as concurrent pain conditions are known to affect pain sensitivity and perception, and as common co-morbidities of osteoarthritis (OA), these conditions may partly explain the observed discordance between structure and symptoms, and if established, exclusion of patients with such co-morbidities in DMOAD trials could potentially improve the understanding of structural benefit in a clinical context.

	Spearman's r	P-value
Anxiety-depression group	-0.05	0.55
Anxiety-depression controls	-0.21	0.01*
Back pain group	-0.01	0.93
Back pain controls	-0.13	0.02*

Table 1. Associations between WOMAC pain JSW (in red) and other baseline covariates

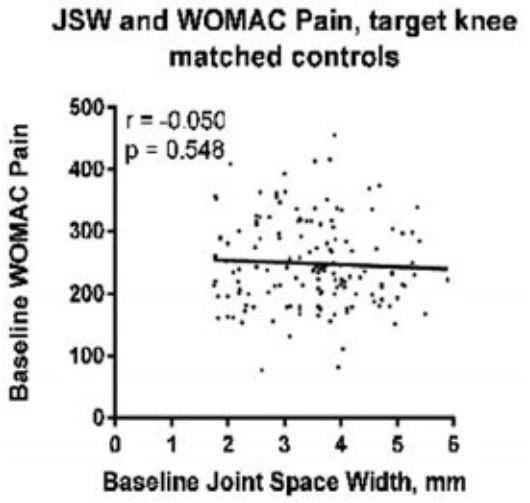

Figure 1. Linear correlations between WOMAC pain and JSW in ADD group, with Spearman's R reported

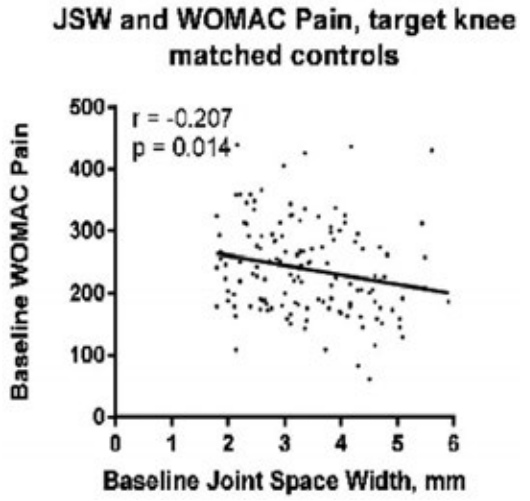

Figure 2. Linear correlations between WOMAC pain and JSW in ADD controls, with Spearman's R reported

The purpose of this analysis was to investigate the impact of ADD and back pain (BP) on the association between structural features of OA and the patient-reported pain.

Methods: Baseline data from two phase 3 clinical trials investigating oral salmon calcitonin in OA, NCT00486434 and NCT00704847 (total N=2206), was analyzed in a post-hoc cross-sectional analysis. Patients with self-reported depression, anxiety, post-traumatic stress syndrome (PTSD), either present or previous, were selected and compared with a control group, matched by sex, age, BMI and Kellgren Lawrence (KL) grade. The correlations between Joint-Space Width (JSW), and the WOMAC Pain Score were plotted for the ADD group and ADD controls, and Spearman's correlation analysis was performed for both ADD and BP groups.

Results: In the ADD group, 149 patients had AD in medical history of which 123 were ongoing at baseline. In the BP group, 333 patients had BP in medical history of which 322 were ongoing at baseline. The study groups of ADD, BP and respective matched controls (MC) were highly similar in terms of age, sex, BMI, JSW, KL-grade and WOMAC pain.

Associations between pain and JSW

Referring to table 1, no correlation was found in the ADD and BP group between JSW and WOMAC pain. In the respective MC groups, statistically significant correlations (MC for ADD: R= -0.21, p = 0.01, and MC for BP: R=-0.13, p=0.02) was found between JSW and pain indicating that lower JSW was associated with higher pain in the control groups but not in the ADD or BP groups. The univariate linear relationship between JSW and pain in the ADD and MC groups are illustrated in Figure 1 and 2.

Conclusion: A marked structure-symptoms discordance was found in OA patients with ADD and BP, while a statistically significant correlation was seen in matched controls without ADD or BP. The results suggest that exclusion of trial patients with anxiety and depression and/or back pain in medical history may improve the accuracy of pain reporting in clinical OA trials.

Disclosure: J. Bjerre-Bastos, Nordic Bioscience Clinical Development, 3; **I. Byrjalsen**, Nordic Bioscience, 3, Nordic Bioscience Clinical Development, 3; **M. Karsdal**, Nordic Biosceince, 1, 3, Nordic Bioscience, 1, 2, 3, 4, 5; **J. Andersen**, Nordic Bioscience, 1, 3, Nordic Bioscience Clinical Development, 3; **A. Bihlet**, Nordic Bioscience, 1, 3, Nordic Bioscience Clinical Development, 3.

Abstract Number: 0913

Depression as a Moderator of Analgesic Effectiveness in Knee Osteoarthritis

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SESSION INFORMATION
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Background/Purpose: Depression often accompanies knee osteoarthritis (OA), exacerbating the severity and persistence of pain, and may negatively affect clinical outcomes associated with analgesic treatment. This study evaluated whether depression moderates (Figure 1) the effectiveness of analgesics on knee pain severity in knee OA.

Methods: Eligible participants (n=1,477) were identified from the Osteoarthritis Initiative and were not using analgesics (acetaminophen, non-steroidal anti-inflammatory drugs, or opioids) at baseline (time *t*) and had radiographic disease (Kellgren-Lawrence [K-L] grade 2, 3, or 4) at the first annual follow-up visit (time *t*+1). Analgesic initiation and utilization was assessed at the first three annual follow-up visits (time *t*+1, time *t*+2, time *t*+3), and depression was evaluated concurrent to analgesic use with the Center for Epidemiological Studies Depression (CES-D) scale and corresponding screening threshold (CES-D score ≥ 16). Knee pain severity from the second to the fourth annual follow-up visit (time *t*+2, time *t*+3, time *t*+4) was measured with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scale (rescaled range = 0-100). Time-invariant and time-varying confounders measured at time *t* and time *t*+1, time *t*+2, and time *t+3* were age, sex, race, education, marital status, employment, health insurance, smoking, alcohol consumption, Charlson comorbidity index, and symptomatic knee OA status; and K-L grade, body mass index, physical performance, knee injuries, knee injections, and WOMAC pain score, respectively. Structural nested mean models appropriate for evaluating time-varying effect moderation were implemented using an inverse-probability-of-treatment-weighting regression-with-residuals approach.

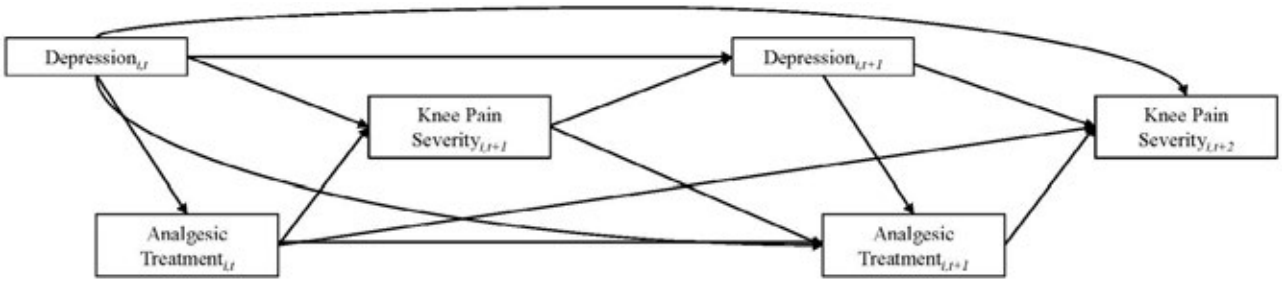

Figure 1. Directed acyclic graph illustrating the hypothesized causal relationships between analgesic treatment, depression, and knee pain severity. Subscripts *i* and *t* refer to the ith participant at time point t, respectively.

Table 1. Moderated intermediate causal effects (treated versus untreated) of analgesic treatment on knee pain severity in depressed and non-depressed participants with radiographic knee OA.

Treatment Interval	Pain Assessment	Depressed (β, 95% CI)		Non-Depressed (β, 95% CI)		Difference (β, 95% CI)	
Y1	Y2-Y4	-0.42	(-7.56, 6.72)	0.12	(-2.11, 2.34)	-0.54	(-8.04, 6.98)
Y2	Y3-Y4	-1.57	(-12.89, 9.74)	-1.16	(-3.48, 1.16)	-0.41	(-11.96, 11.14)
Y3	Y4	**-15.51**	**(-26.13, -4.89)**	0.76	(-1.67, 3.18)	**-16.27**	**(-27.12, -5.42)**
Y1-Y2	Y2-Y4	-1.99	(-16.74, 12.76)	-1.05	(-4.18, 2.09)	-0.94	(-16.03, 14.14)
Y1-Y3	Y2-Y4	-17.50	(-36.33, 1.33)	-0.29	(-4.03, 3.45)	-17.21	(-36.50, 2.07)

Y1: Year 1; Y2: Year 2; Y3: Year 3; Y4: Year 4; Y1-Y2: Year 1 to Year 2; Y1-Y3: Year 1 to Year 3; Y2-Y4: Year 2 to Year 4; Y3-Y4: Year 3 to Year 4.

Results: In non-depressed participants, analgesic treatment at years one, two, and three had minimal effect (Table 1) on knee pain severity at years two, three, and four, respectively, and time-specific associations ranged from -1.16 (95% CI: -3.48, 1.16) to 0.76 (95% CI: -1.67, 3.18). Moreover, persistent use of analgesics did not increase the magnitude of the treatment effect in non-depressed participants. By contrast, time-specific treatment effects in depressed participants increased during follow-up from -0.42 (95% CI: -7.56, 6.72) to -15.51 (95% CI: -26.13, -4.89), and the association between year three analgesic use and year four knee pain severity was statistically significant. The magnitude of the associations increased with persistent analgesic use in depressed participants, primarily due to significant effect moderation concerning year three analgesic use, where the subsequent difference in treatment effect between depressed and non-depressed participants was -16.27 (95% CI: -27.12, -5.42).

Conclusion: Findings indicate a statistically and clinically significant greater one-year treatment effect of analgesic use that lowered knee pain severity in persons with knee OA and depression. Thus, OA patients with depression may derive more benefit from analgesic treatment for chronic knee pain than non-depressed patients, perhaps because their pain is undertreated.

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Abstract Number: 0914

The Effects of Vitamin D and Marine Omega-3 Fatty Acid Supplementation on Chronic Knee Pain in Older U.S. Adults

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Osteoarthritis – Clinical I: Innovations

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

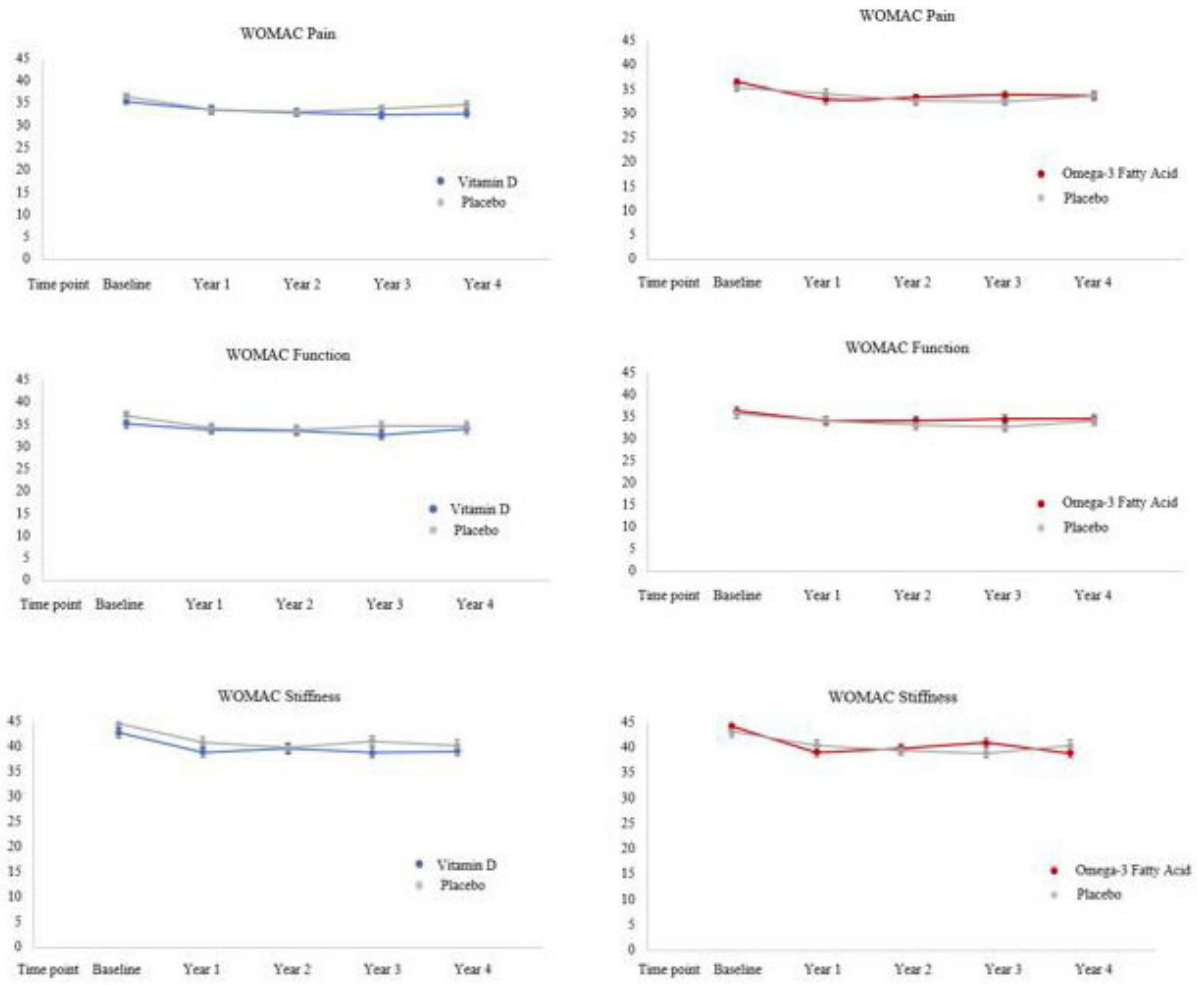

Figure 1. Repeated measure analyses of WOMAC scores over time for Vitamin D and Omega- 3 Fatty acid versus placebo with censoring for total knee replacement adjusted for age, sex, and other treatment group respectively, among subjects followed in the Knee Pain Subcohort of the VITAL trial (n=1398)

Background/Purpose: Chronic knee pain from osteoarthritis (OA) is frequent in the older adult population. Prior trials have had conflicting results concerning vitamin D's therapeutic effects, and no large trials have investigated the potential benefits of marine omega-3 fatty acids (n-3 FA) for chronic knee pain. We investigated the effects of vitamin D and n-3 FA supplementation on knee pain in a large clinical trial of older adults.

Methods: The double-blind, placebo-controlled VITamin D and OmegA-3 TriaL (VITAL) randomized 25,871 U.S. adults (women ≥ age 55, men ≥ age 50) in a 2-by-2 factorial design to supplementation with vitamin D (2000 IU/day) and/or n-3 FA (1 gm/day). Prior to randomization, we identified a subgroup of 1430 eligible participants reporting frequent, chronic knee pain and provided additional annual knee pain questionnaires. Analyses included 1398 participants who returned ≥ 1 questionnaire. Questionnaires assessed self-reported pain and functional status with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at baseline and annually over 5-years of follow-up. For the primary intention-to-treat analysis, we used a repeated measures model to assess the effect of treatment on measures of WOMAC over follow-up, after adjustment for age, sex, and the other treatment arm. Analyses were censored for total knee replacement (TKR). The time by treatment interaction term was used to assess change in WOMAC between randomized groups. In secondary analyses, differences in rates of TKR between treatment groups and placebo were assessed using Cox regression. Reduction in use of daily pain medications (non-steroidal anti-inflammatory and stronger pain medications such as opiates) comparing treatment groups and placebo was ascertained using chi square analysis.

Results: Participants' mean age was 68 years (SD= 7) and 66% were female. Baseline characteristics were well balanced. In a validation study, 400 participants were randomly selected for record review; of the 226 records received, 92% were confirmed to have knee OA. Over 5-years of follow-up, WOMAC Pain did not differ between vitamin D and placebo or n-3 FA and placebo at any time point. The time by treatment interactions were not statistically significant for either treatment arm (p interaction vitamin D = 0.41, p interaction n-3 FA = 0.77). Similarly, we did not observe clinically or statistically significant differences in WOMAC Function and Stiffness between randomized groups at any time point or over time. (Figure 1) TKR was reported by 140 participants in the vitamin D arm and 156 in placebo; 146 reported TKR in the n-3 FA and 150 in placebo. The hazard ratios for incident TKR in the vitamin D and n-3 FA arms were 0. 97 (95% CI 0.77, 1.22) and 0.99 (95% CI 0.79, 1.24) respectively in comparison to placebo after adjustment for age and sex. Among the daily pain medication users at baseline, there were no significant differences in frequency of pain medication use at last available follow-up between vitamin D and placebo and n-3 FA and placebo.

Conclusion: Neither Vitamin D nor n-3 FA supplementation for up to 5 years improved knee pain, stiffness or function, rate of TKR, or pain medication use in older adults with frequent, chronic knee pain.

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Abstract Number: 0915

Development and Initial Validation of the Systemic JADAS, a New Composite Disease Activity Score for Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Pediatric Rheumatology – Clinical I: Systemic JIA

Session Type: ACR Abstract Session

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Background/Purpose: The Juvenile Arthritis Disease Activity Score (JADAS) has gained increasing popularity for the measurement of the level of disease activity in patients with juvenile idiopathic arthritis (JIA). However, so far the JADAS has been validated only in children with the non-systemic categories of JIA. The objective of our study has been to develop and validate the systemic JADAS (sJADAS), a new version of the JADAS specific to systemic JIA (sJIA).

Methods: The sJADAS is made up by adding a fifth item, named Systemic Manifestation Score (SMS), to the four items included in the original tool (physician global assessment of disease activity, parent/patient global assessment of well-being, active joint count and erythrocyte sedimentation rate). The SMS ranges from 0 to 10 and is aimed to quantify the activity of systemic features. The sJADAS score ranges from 0 to 50. The validation sample included patients with definite and possible/probable sJIA with active systemic manifestations, which should comprise fever, who were assessed at baseline and then at a subsequent visit, 2 weeks to 3 months after initial evaluation. Validation procedures included assessment of concurrent, construct and discriminant validity, internal consistency and responsiveness to clinical change.

Main disease activity features and values of composite disease activity scores of patients with systemic juvenile idiopathic arthritis at study entry and at second visit.

	Baseline (No.)		Second visit	
	No		No	
Physician global assessment	160	7.5 (6 - 9)	157	1 (0 - 3.5)
No swollen joints	161	3 (0-7)	157	0 (0 - 1)
No tender joints	158	4 (1 - 11)	154	0 (0 - 1)
No joints with limited range of motion	158	3 (1 - 8)	157	0 (0 - 0)
No active joints	161	4 (1 - 10)	157	0 (0 – 2)
White blood cell count, $\times 10^9$/liter	161	15 (9.64 - 20)	161	11.255 (7840 - 15000)
Neutrophil count, $\times 10^9$/liter	159	8770 (4895 - 14200)	159	6186 (3995 - 8960)
Hemoglobin, g/dl	162	10.1 (8.9 - 11.1)	162	11.8 (10.6 - 12.8)
Platelet count, $\times 10^9$/liter	161	468 (349 - 575)	161	354500 (271 - 450)
Ferritin, ng/ml	152	874 (284 - 2956)	152	161 (60 - 330)
Erythrocyte sedimentation rate, mm/hour	160	65 (40 - 95)	160	18 (7 - 36)
C-reactive protein, mg/dl	153	13.9 (7.9 - 24.3)	153	1 (0.3 - 4.8)
Fibrinogen, gm/liter	98	518 (350 - 637)	98	264.5 (199 - 374)
sJADAS10	160	28.2 (22.6 - 34.9)	156	6.5 (1.8 - 12.3)
JADAS10	160	23.3 (17.3 - 28.5)	157	6 (1 - 10.5)
cJADAS10	160	18.5 (13.3 - 24.3)	157	4 (0.5 - 9)
DAS28	157	5 (3.9 – 6.1)	151	2.4 (1.7 – 3.3)
CDAI	157	18.5 (14.0 – 28.0)	156	4.0 (0.5 – 9.5)
Systemic Manifestation Score	158	5 (4 - 7)	156	0 (0 - 2)

Data are the median (interquartile range)

Results: A total of 163 patients, 86.9% (n=139) with definite sJIA and 13.1% (n=21) with possible/probable sJIA, assessed at disease onset (n=91; 55.8%) or at time of a disease flare (n=72; 44.2%) were enrolled in 57 centers in 10 countries from February 2017 to December 2018. Median age at disease onset was 4.9 years (interquartile range, IQR 2.6–7.9) and median age at study entry was 6.4 years (IQR 3.7–10.8). Median disease duration from onset to study entry was 0.2 years (IQR 0.1–1.9). Median sJADAS at baseline visit was 28.2 (IQR 22.8–34.9), while median JADAS10 and clinical JADAS10 (cJADAS10) were respectively 23.3 (IQR 17.3–28.5) and 18.5 (IQR 13.3-24.3). sJADAS correlated strongly with JADAS10 (rs=0.98), cJADAS10 (rs=0.91), DAS28 (rs=0.83) and CDAI (rs=0.83); moderately with functional ability scales (JAFS and CHAQ) (rs=0.69; rs=0.62) and total score (rs=0.56) and physical (rs=0.59) and psychosocial (rs=0.38) subscale scores of the health-related quality of life tool (PRQL) and with pain VAS (rs=0.58); mildly with CRP (rs=0.40). sJADAS discriminated well between patients with or without morning stiffness ($p< 0.0001$), with different levels of disease activity defined by the physician ($p< 0.0001$) and with different degrees of pain ($p< 0.0001$). Internal consistency was good (Cronbach's alpha=0.635) and comparable to that of JADAS10 (Cronbach's alpha=0.595). Responsiveness to change, measured on all patients (SRM=2.21) and on patients classified as improved at second visit (SRM=2.59) was strong and superior to that of JADAS10 (SRM=1.97 and 2.28, respectively).

Conclusion: The sJADAS was found to be a valid instrument for the assessment of disease activity in sJIA. This score is feasible and easily applicable in standard clinical practice, which should result in its widespread acceptance and use. The good responsiveness to clinical change indicates that the sJADAS is suitable to assess therapeutic response in sJIA clinical trials.

Concurrent validity (baseline values).

Correlation between sJADAS and:	Spearman' r [N]
JADAS10	0.98 [n=160]
cJADAS	0.91 [n=160]
DAS 28	0.83 [n=155]
CDAI	0.83 [n=157]

Convergent validity (baseline values).

Correlation between sJADAS and:	Spearman' r [N]
CRP	0.40 [n=151]
JAFS	0.69 [n=157]
Parent Pain VAS	0.58 [n=158]
HRQL	0.56 [n=150]
Physical sub-score HRQL	0.59 [n=150]
Psychosocial sub-score HRQL	0.38 [n=150]
CHAQ	0.62 [n=119]

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Abstract Number: 0916

Development and Initial Validation of the MS Score for Diagnosis of Macrophage Activation Syndrome in Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION

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Session Title: Pediatric Rheumatology – Clinical I: Systemic JIA

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Background/Purpose: Macrophage activation syndrome (MAS) is the most severe complication of systemic juvenile idiopathic arthritis (sJIA) and its adult equivalent, adult-onset Still's disease (AOSD). Because MAS can follow a rapidly fatal course, its prompt recognition and immediate therapeutic intervention are critical. An international collaborative effort has recently led to the publication of the 2016 classification criteria for MAS in sJIA. However these criteria are intended to serve for classification purposes and not as diagnostic tool. The aim of this study was to develop and validate a diagnostic score for timely detection of MAS in patients with sJIA

Table 1.

	β-coefficient	95% Confidence Interval
Central nervous system (CNS) involvement	2.44	1.26; 3.65
Hemorrhagic manifestations	1.54	0.00; 3.05
Active arthritis	-1.30	-2.05; 0.00
Platelet count (PLT), x 10^9/liter	-0.003	-0.005; -0.001
Lactic dehydrogenase (LDH), U/liter	0.001	0.0002; 0.002
Fibrinogen, mg/dl	-0.004	-0.006; -0.002
Ferritin, ng/ml	0.0001	0.00; 0.0002

Calculation of the MS score = CNS involvement*2.44 + hemorrhagic manifestations*1.54 + arthritis*(-1.30) + PLT count*(-0.003) + LDH*0.001 + fibrinogen*(-0.004) + ferritin*0.0001

In a febrile patient with known or suspected systemic juvenile idiopathic arthritis, the diagnosis of MAS should be considered if the MS score is ≥ -2.1

The area under the curve of the model is 0.95. For clinical variables (CNS involvement, hemorrhagic manifestations, active arthritis), a score of 1 or 0 is placed in the formula, depending on whether the variable is present or absent, respectively. For laboratory variables, the observed value in the above-mentioned unit are included.

Methods: The clinical and laboratory features of 362 patients with sJIA-associated MAS and 404 patients with active sJIA without evidence of MAS were collected in a multinational collaborative project. Eighty percent of the study population was used to develop the score and the remaining 20% constituted the validation sample. A Bayesian Model Averaging approach was used to assess the role of each clinical and laboratory variable in the diagnosis of MAS and to obtain the coefficients of selected variables. Variables with an inclusion probability greater than 0.80 composed the final score, named MAS/sJIA (MS) score, which resulted from the linear combination of the values of each variable multiplied by their coefficients. The cutoff that best discriminated MAS from active sJIA was calculated by means of receiver operating characteristic (ROC) curve analysis. Score performance was evaluated in both developmental and validation samples

Results: The 7 variables included in the MS score (central nervous system dysfunction, hemorrhagic manifestations, active arthritis, platelet count, fibrinogen, lactate dehydrogenase and ferritin) are presented in Table 1 together with their coefficients and with the MS score calculation formula. The final score ranges from -8.4 to 41.8. A cut-off value > -2.1 revealed the best performance in discriminating MAS from active sJIA, with a sensitivity (SE) of 0.85, a specificity (SP) of 0.95, area under the curve of 0.95 and a kappa value of 0.80. The good performance of the MS score was confirmed in the validation sample (SE 0.89, SP 0.99, AUC 0.97, kappa 0.87)

Conclusion: The MS score is a powerful and feasible tool that may assist practitioners inmaking a timely diagnosis of MAS in patients with sJIA. Future assessments at the bedside could be enhanced and made easier by developing a phone/web application. Considering that sJIA and AOSD are nowadays thought to be part of the same disease spectrum, the MS score might be also useful in timely recognition of MAS in patients with AOSD. The MS score deserves validation in a prospective cohort of patients with sJIA-associated MAS

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Abstract Number: 0917

Systemic Juvenile Idiopathic Arthritis-Lung Disease: Characterization and Risk Factors

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Background/Purpose: Systemic Juvenile Idiopathic Arthritis (SJIA) is associated with a recently recognized albeit poorly defined and characterized lung disease (LD). Our objective is to describe clinical characteristics, risk factors, histopathologic and immunologic features of SJIA-associated LD (SJIA-LD).

Methods: This was a prospective cohort study; patients were identified upon lung disease detection or referral to Cincinnati Children's Hospital for consultation or second opinion. This study was approved by the Institutional Review Board, and written informed consent was obtained from all patients and/or their legal guardians. Clinical data was abstracted from medical records, and epidemiologic, cellular, biochemical, genomic analysis, and transcriptional profiling analyses were performed.

Results: Twenty-two patients with SJIA-LD have been evaluated since 2010. Typical radiographic findings included diffuse ground-glass opacities, subpleural reticulation, peribronchovascular and/or septal thickening, and lymphadenopathy. Pathologic findings included patchy but extensive lymphoplasmacytic infiltrates and mixed features of pulmonary alveolar proteinosis (PAP) and endogenous lipoid pneumonia (ELP). Compared to SJIA patients without LD, children with SJIA-LD were younger at SJIA diagnosis, had prior episodes of macrophage activation syndrome (MAS), have had adverse reactions to biologic therapy, and have higher serum IL-18. PAP is classically associated with primary or secondary dysfunction of alveolar macrophages leading to accumulation of pulmonary surfactant in alveolar spaces. However, SJIA-LD patients lacked genetic, serologic, or functional evidence of GM-CSF pathway dysfunction typical of primary familial or autoimmune PAP. Additionally, bronchoalveolar lavage (BAL) rarely demonstrated proteinaceous material and had less lipid-laden macrophages than seen in primary PAP. Instead, SJIA-LD BAL fluid contained elevated levels of IL-18 and IFNγ-induced chemokines CXCL9-10. Finally, multiplex transcriptional profiling of SJIA-LD lung tissue identified upregulated type II interferon and T-cell activation networks, including a STAT1 transcriptional network. Two of the most highly upregulated non-HLA genes were *CXCL10* (9-fold increase) and *CXCL9* (7-fold increase), IFN-induced chemokines whose serum levels are strongly associated with MAS. This signature was also present in SJIA-LD lung tissue sections lacking substantial histopathological findings, suggesting it may precede and may even drive lung pathology. Taken together, this gene expression analysis supports significant IFNγ-induced pulmonary inflammation in children with SJIA-LD.

Conclusion: Pulmonary disease in SJIA has distinct clinical and immunologic features and represents an uncharacterized inflammatory lung disease. MAS may constitute a risk factor for SJIA-LD development. Both BAL cytokine analysis and gene expression profiling of lung tissue revealed substantial inflammation including elevated IL-18, IFNγ pathway activation and T cell function.

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Abstract Number: 0918

Multiplex Serum Analysis Identifies Potential Biomarkers of Systemic Juvenile Idiopathic Arthritis, Macrophage Activation Syndrome, and Associated Pulmonary Alveolar Proteinosis: Evidence for Independently-regulated Hyperinflammatory and Eosinophilic Inflammation

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SESSION INFORMATION

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Background/Purpose: Recent experiences suggest a disturbing epidemic of digital clubbing and insidious, Pulmonary Alveolar Proteinosis (PAP)-like lung disease occurring in patients with Systemic Juvenile Idiopathic Arthritis (SJIA-PAP). Many SJIA-PAP patients also suffer from prior and/or concomitant Macrophage Activation Syndrome (MAS) and most have been exposed to IL-1 and/or IL-6 inhibition. Though variable, many SJIA-PAP patients progress to pulmonary hypertension, respiratory failure, and death. To improve diagnostic screening and pathogenic understanding of SJIA-PAP, we undertook a near-proteomic serum analysis in SJIA-PAP and related controls.

Methods: We measured 1311 distinct analytes in 162 serum samples from a cohort of patients with SJIA-PAP (n=11), inactive sJIA/MAS (30, including two NLRC4-MAS), active SJIA (24), active MAS (12, including two NLRC4-MAS), autoimmune/genetic PAP (14), Neonatal-Onset Multisystem Inflammatory Disease (5), STING-associated Vasculopathy of Infancy with interstitial lung disease (4), and healthy controls (21). Targets were measured using Slow Off-rate Modified Aptamers (SOMAmers), augmented by selected Luminex-based measurements. We used a linear regression model (Limma) to identify relationships with individual diseases.

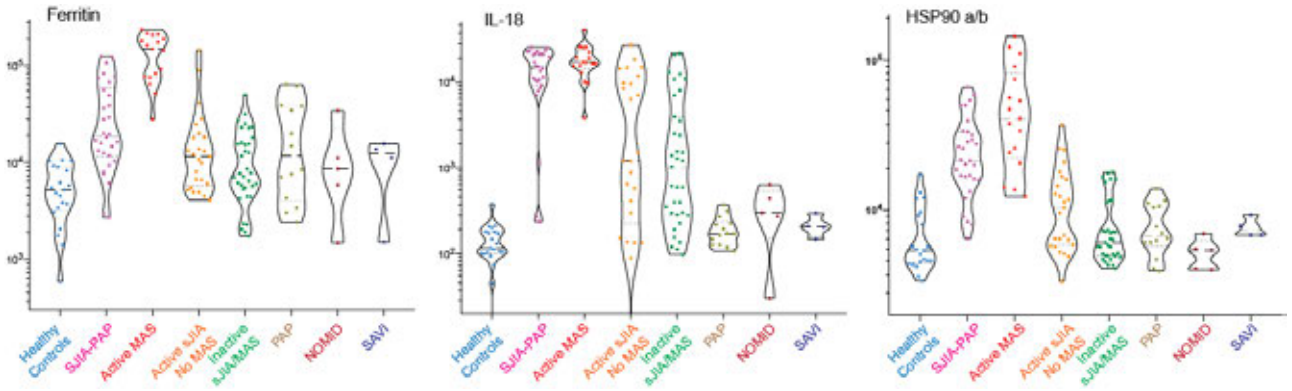

Figure 1. Violin plots of MAS-associated protein targets in the indicated patient groups.

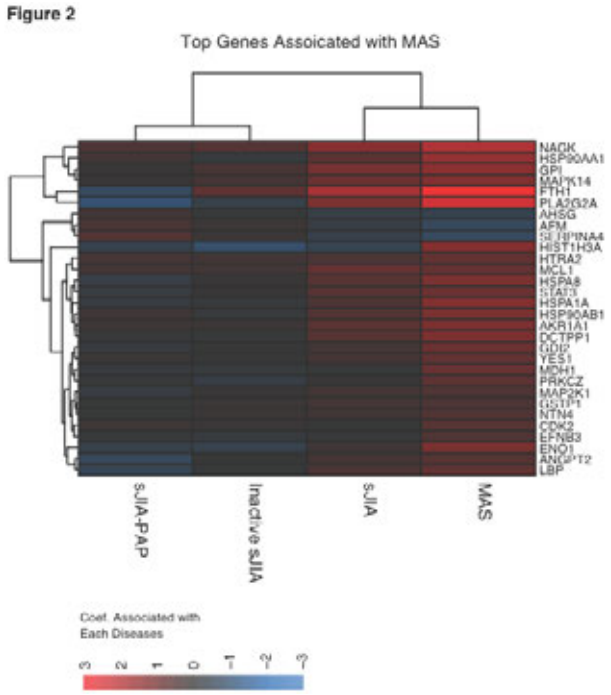

Figure 2. Top 30 targets (FDR<0.05) associated with MAS. Color represents the coefficients for each target under each condition, as determined by limma.

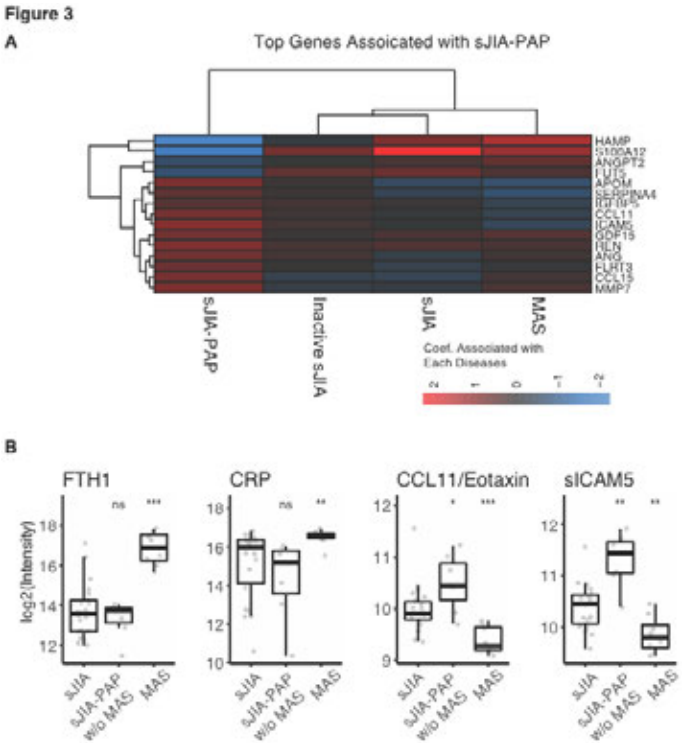

Figure 3. An SJIA-PAP signature is independent of the MAS signature. A) Top 15 targets (FDR < 0.2) associated with lung disease. B) Expression of four targets in SJIA, SJIA-PAP w/o MAS (those SJIA-PAP patients without CRP and ferritin elevation), and active MAS.

Results: Biomarkers canonically associated with SJIA and MAS (e.g. CRP, S100 proteins, ferritin, IL-18) supported the validity of pre-analysis groupings (Fig. 1). Novel, MAS-specific biomarkers suggested targetable cell death (heat-shock proteins) and metabolic (glycolytic enzyme) pathways (Fig. 2). Analytes elevated in SJIA-PAP but not inactive

SJIA, active SJIA, or active MAS (e.g. sICAM-5 & MMP7) suggest lung-intrinsic macrophage activity and may aid in screening or monitoring SJIA-PAP. About half the SJIA-PAP samples demonstrated MAS-like features despite the absence of overt MAS, while the other half displayed relatively low CRP and ferritin levels (Fig 3B), lacked prominent elements of the sJIA/MAS signature (e.g., S100, heat-shock proteins), but had elevated IL-18. Lung disease in these patients was not resolved, and they expressed an sJIA-PAP signature (Fig 3B) that did not correlate with the MAS signature, suggesting distinct regulation of MAS and SJIA-PAP.

Conclusion: This massively-multiplexed serum analysis identified novel targets and pathways in MAS, and suggested an eosinophilic feature in SJIA-PAP patients. High MAS activity was frequently observed despite the absence of overt MAS, but was not required to maintain SJIA-PAP inflammation. Though these data require prospective validation, they provide mechanistic insights into SJIA, MAS, and the development of SJIA-PAP and may provide candidate biomarkers with which to better diagnose and monitor these disorders.

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Abstract Number: 0919

Free Interlukin-18: A New Promising Biomarker for Systemic Juvenile Idiopathic Arthritis and Macrophage Activation Syndrome

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Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) is a childhood arthritis with features of autoinflammation, and is associated with high risk of macrophage activation syndrome (MAS). IL-18 has been increasingly shown to have key roles in linking sJIA and MAS, in particular due to an imbalance between IL-18 and its natural inhibitor IL-18 binding protein (IL-18 BP). Therefore, we hypothesized that free(unbound) IL-18, rather than total IL-18, might be a more accurate biomarker for sJIA disease activity and emerging MAS.

Methods: Serum samples were obtained from 43 established sJIA patients, free and total IL-18 (pg/ml), CXCL9, and S100 protein levels were determined. Free IL-18 levels were compared between patients with regards to clinical and laboratory features, including disease activity, history of MAS, and other emerging biomarkers for sJIA and MAS.

Results: Median free IL-18 level for the cohort was 2.03 pg/ml (IQR: 0-35.68). Free IL-18 levels were significantly higher in patients with active disease (median 25.96, IQR 16.89-66.52) compared to those with clinically inactive disease (CID) (0, IQR -1.29-7.79; p=0.0002). Likewise, those with history of MAS had significantly higher free IL-18

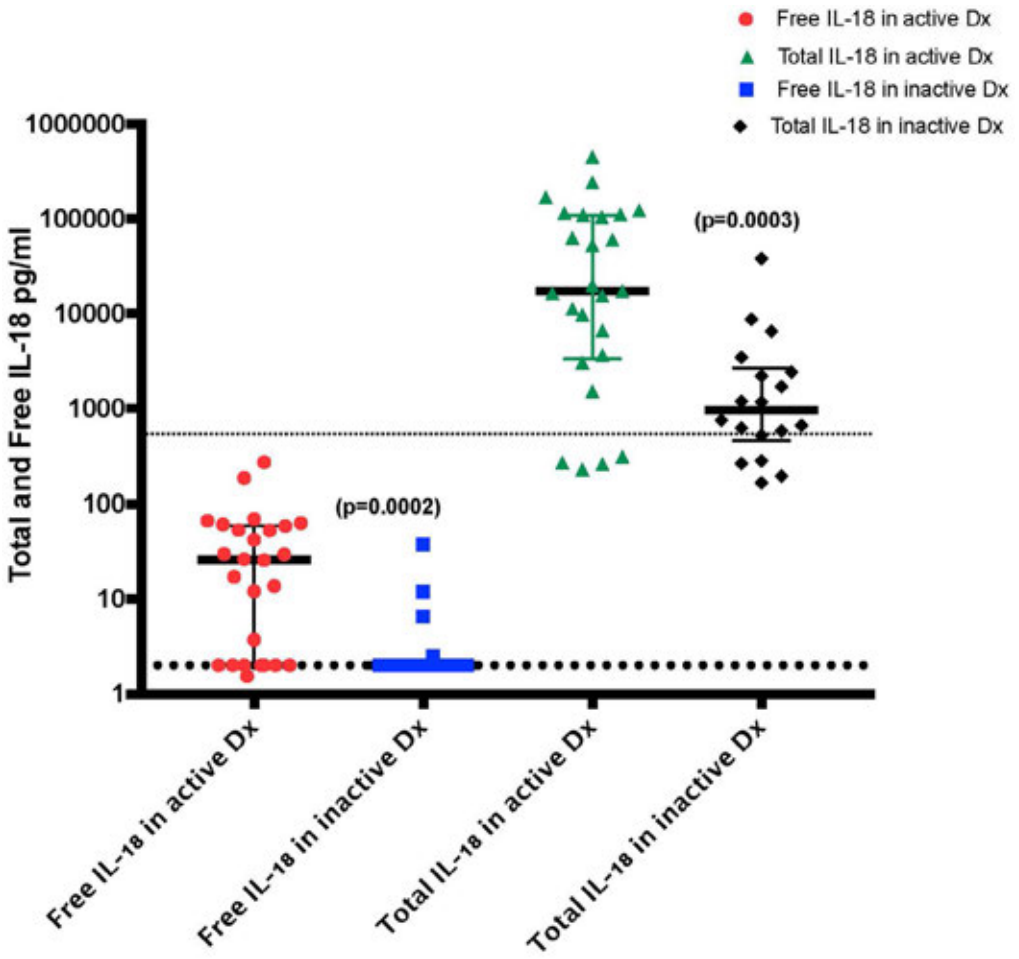

Figure (1). Free and total IL-18 levels in patients with active and inactive disease. Horizontal Lines represent upper limit normal for free (0 pg/ml) and total IL-18 (540 pg/ml).

levels (29.55, IQR 16.14-67.51) when compared to those without MAS history (0, IQR -0.29-15.07; p=< 0.0001).Of note, Patients with active disease and history of MAS had higher free IL-18 than in patients with active disease and no history of MAS (0=0.01). Patients with fever, arthritis, systemic features or elevated inflammatory markers (ESR/CRP) had significantly higher free IL-18 levels (p= 0.001, 0.318,0.0003 and < 0.0001, respectively). Notably, free IL-18 levels were undetectable in the majority (78%) of patients with CID. This is in marked contrast to total IL-18, where a majority (83%) of CID still had high levels (median 956.5, IQR 458-2682, upper limit normal 540 pg/ml) (Figure 1).

Free IL-18 performed well as a biomarker for disease activity with AUC of 81% (p=0.0006). There was a strong correlation between free and total IL-18 levels (r=0.87, p< 0.0001)), with sustained significance when restricted to patients with only active disease or CID (r=0.81 and 0.73 respectively). Correlation was moderate with CXCL9 (r=0.57, p< 0.0001)), S100A8/9 (r=0.50, p=0.0022)) and S100 A12 (r=0.38, p=0.0228)). Interestingly, correlations between free IL-18 and S100 A8/9 and A12 were stronger in patients with active disease (r=0.68 and 0.58), but weak and statistically insignificant for patients in CID.

Conclusion: Free IL-18 levels were significantly higher in sJIA patients with active disease, fever, systemic features and arthritis. Levels were undetectable in the majority of patients with CID. Free IL-18 correlated well with other disease biomarkers particularly when disease was active, indicating that free IL-18 is a promising new sensitive biomarker for sJIA disease activity. It also supports the role of IL-18/IL-18 BP imbalance in the pathogenesis of sJIA and MAS.

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Abstract Number: 0920

Adenosine Deaminase 2 as a Circulating Biomarker of Macrophage Activation Syndrome

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Background/Purpose: Macrophage activation syndrome (MAS) is a life-threatening complication of systemic juvenile idiopathic arthritis (sJIA) characterized by a vicious cycle of immune cell activation and dysregulated cytokine production that can result in multi-organ failure. Unambiguous biomarkers of MAS are needed to facilitate prompt diagnosis and treatment, as well as to inform the understanding of disease pathogenesis.

Methods: Adenosine deaminase 2 (ADA2) activity was quantified in peripheral blood using an established spectrophotometric assay in healthy children and in children with a range of inflammatory diseases. Sources of ADA2 and triggers for its release were explored using cytokine stimulation of peripheral blood mononuclear cells, flow cytometry, and confocal microscopy of MAS bone marrow.

Results: We established normal levels of peripheral blood ADA2 levels in 175 healthy children and compared these values with Kawasaki disease (KD; n = 25), systemic lupus erythematosus (SLE; n = 13), juvenile dermatomyositis (JDM; n = 13) and multiple forms of juvenile idiopathic arthritis (JIA; n = 120). Aside from mild elevation in some patients with SLE and JDM, levels of ADA2 levels above the upper limit of normal were largely restricted to sJIA patients with clinically diagnosed MAS (**Figure 1**). In two independent sJIA cohorts, ADA2 activity beyond the upper limit of normal effectively distinguished MAS from active sJIA without MAS, with combined sensitivity = 86% and specificity = 93%. Longitudinal analysis of several patients with sJIA/MAS showed normalization of ADA2 levels with resolution of MAS. In sJIA patients, ADA2 levels correlated closely with other biomarkers of MAS including ferritin, interleukin (IL)-18, and the interferon (IFN)-γ-inducible chemokine CXCL9. In peripheral blood mononuclear cells, ADA2 was strongly induced by IL-12, IL-18 and IFN-γ. Monocytes were the primary ADA2 source in peripheral blood, with hemophagocytes a prominent source of ADA2 in MAS bone marrow as assessed by confocal microscopy.

Conclusion: ADA2 in the peripheral blood is a sensitive and specific biomarker of MAS, reflecting the activation status of monocytes, macrophages, and potentially hemophagocytes. In patients with active sJIA, ADA2 activity

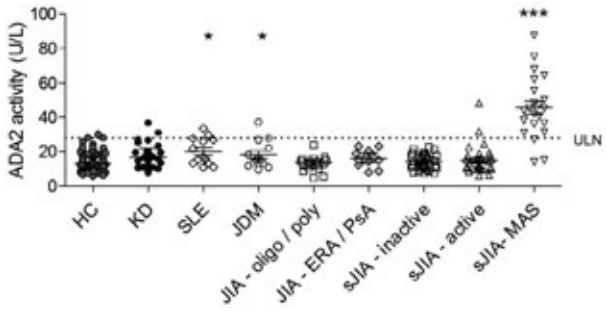

Figure 1. Peripheral ADA2 activity in healthy children and patients with childhood inflammatory diseases. HC, healthy control; KD, Kawasaki disease; SLE, systemic lupus erythematosus; JDM, juvenile dermatomyositis; JIA, juvenile idiopathic arthritis; ERA, enthesitis-related arthritis; PsA, psoriatic arthritis; MAS, macrophage activation syndrome; ULN, upper limit of normal; * $p < 0.01$, *** $p < 0.0001$

beyond the upper limit of normal represents strong evidence for concomitant MAS and could potentially help guide clinical care.

Disclosure: P. Lee, None; **G. Schulert**, Novartis, 5, 8; **S. Canna**, AB2 Bio Ltd, 5, AB2Bio, Ltd, 8, Novartis, 5, 8; **Y. Huang**, None; **J. Sundel**, None; **M. Son**, None; **L. Henderson**, None; **P. Nigrovic**, None; **J. Newburger**, None; **F. Dedeoglu**, None; **M. Lo**, None; **E. Meidan**, None; **Y. Li**, None; **O. Halyabar**, None; **M. Chang**, None; **K. Hoyt**, None; **T. Do**, None; **R. Sundel**, None; **R. Blaustein**, None.

Abstract Number: 0921

Indicators of Actionable Levels of Atherosclerosis in RA Patients Who Appear to Have Low or Intermediate Atherosclerotic Cardiovascular Risk Based on Standard Risk Algorithms

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Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: In the general population, statins reduces atherosclerotic cardiovascular disease (ASCVD) events in those with a computed tomography (CT)-assessed coronary artery calcium (CAC) score ≥100 units, regardless of background level of predicted ASCVD risk. Since general ASCVD risk models underperform in RA, we sought to identify RA-specific clinical indicators of an actionable level of CAC [i.e. CAC ≥100 (aICAC)] to distinguish those seemingly at lower ASCVD risk who would benefit from CAC screening and/or ASCVD prevention.

Methods: Data were pooled from 4 cohorts of RA patients and a cohort of non-RA controls who all underwent CT-assessed CAC calculated using the Agatston method. Those on statins or with prior known CVD were excluded. Predictors of aICAC were modeled using logistic regression for those with low (< 5%) and intermediate (5-15%) ASCVD risk based on the ACC/AHA 10-year risk equation. The number needed to screen (NNS) with CT to identify an individual with aICAC was assessed before and after classifying patients according to ASCVD strata-specific predicted probabilities.

Table. Actionable Level of CAC (alCAC) and Number Needed to Screen (NNS) with Computed Tomography (CT) to Detect alCAC According to Strata of the American College of Cardiology/American Heart Association (ACC/AHA) 10-year Hard ASCVD Event Risk Score*

ASCVD Score	Number of RA patients	% with alCAC	OR_{adj} RA vs. Control**	p-value	RA-NNS	Control-NNS
All	546	24.2%	2.50	<0.001	n=4	n=8
< 5%	310	8.7%	2.51	0.001	n=12	n=36
5 – 14.99%	148	33.1%	2.19	<0.001	n=3	n=7
≥ 15%	88	63.6%	3.51	<0.001	n=2	n=3

* alCAC = Agatston CAC Score ≥ 100 units

** Adjusted for age, gender, race/ethnicity, body mass index, traditional CVD risk factors, NSAID use, and aspirin use

Results: A total of 546 RA patients and 5,279 non-RA controls were studied. The majority (57%) of the RA group had an ASCVD risk score< 5% and 27% had risk between 5-15%. alCAC was observed in n=132 (24%) of the RA group, and 58% of the total alCAC for the RA cohort was contained within the two lower ASCVD risk groups, including 20% in the group with an ASCVD score < 5%. The adjusted odds of alCAC was greater in the RA vs. control groups for all strata of ASCVD risk (Table), and the NNS was lower in RA for each stratum. In the low ASCVD risk RA group, alCAC was associated significantly and independently with higher age, ever smoking, lower BMI (particularly among ever smokers), antihypertensive use, very low and high LDL-C, aspirin use, RA duration (particularly among those not treated with biologics), and higher DAS28 score. The AUC-ROC for these indicators was 0.921 (95% CI 0.858, 0.984) and was significantly higher than modeling the ASCVD score alone (AUC=0.657; p-value for model comparison< 0.001). A different set of indicators of alCAC was present for those with ASCVD risk between 5-15% [male gender, waist circumference, current smoking (particularly among those with a normal BMI), antihypertensive use, and non-use of methotrexate]. The AUC-ROC for these indicators was 0.776 (95% CI 0.694, 0.857) and was significantly higher than modeling the ASCVD score alone (AUC=0.605; p-value for model comparison=0.004). Taking only those in the 4th quartile of predicted probability from each ASCVD risk stratum identified 67% of the seemingly low/intermediate ASCVD risk RA patients with alCAC (NNS=3), including all but n=4 in the low risk group. Taking the 3rd and 4th quartiles identified 80% with an alCAC (NNS=3), including all in the low risk group.

Conclusion: Using ASCVD strata-specific prediction models, clinical characteristics that included RA features were able to distinguish a large proportion of the seemingly lower ASCVD risk RA patients with alCAC who would benefit from additional screening and/or aggressive preventive treatment. External validation is warranted in order to apply this approach to clinical practice.

Disclosure: J. Giles, None; **C. Chung**, NIH grant RC2GM092618 from NIGMS/OD, 2, NIH grant U01HG004603 from NHGRI/NIGMS, 2, NIH: R01GM126535 and R01 bridge award, 2, Rheumatology Research Foundation K-supplement, 2, Vanderbilt National Center for Advancing Translational Science grant 2UL1 TR000445-06 from NCATS/NIH, 2; **M. Wasko**, None; **A. Kao**, None; **A. Oeser**, None; **C. Stein**, None; **J. Bathon**, None.

Abstract Number: 0922

Improved Incidence of Cardiovascular Disease in Patients with Incident Rheumatoid Arthritis in 2000s: A Population-Based Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes II: Cardiovascular Comorbidities

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

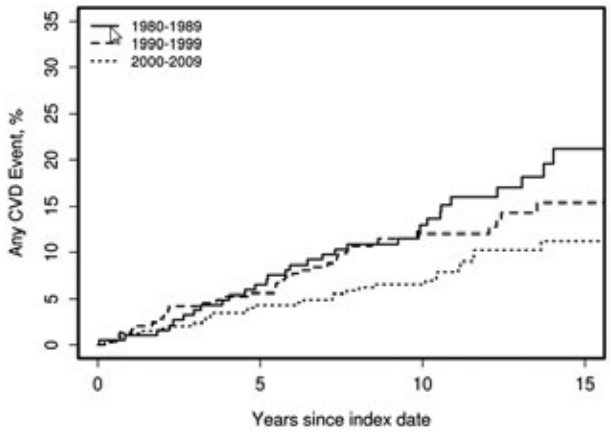

Figure. Cumulative incidence of any CVD event in patients with RA by decade of RA incidence

Background/Purpose: Increased burden of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) as compared to the general population is well recognized. Several studies suggested reduced CVD mortality in RA in recent decades. Longitudinal studies on trends in occurrence of CVD events in RA patients over time are lacking. To address this gap in knowledge, we evaluated trends in incidence of CVD in patients with incident RA in 1980-2009.

Methods: We studied patients with incident RA (age ≥18 years, 1987 ACR criteria met in 1980-2009) followed until death, migration out of the region, or 12/31/2016. Follow-up of each decade was truncated to make the length of follow-up comparable (i.e., the 1980–89 cohort was truncated at December 31, 1996, the 1990–99 cohort was truncated at December 31, 2006 and the 2000–09 cohort was truncated at December 31, 2016). Incident CVD events included myocardial infarction (MI), stroke (ischemic or hemorrhagic), coronary heart disease (CHD) death and first occurrence of any of these. Patients with CVD events prior to RA incidence date were excluded. Cox proportional hazards models were used to compare incident CVD events by decade, adjusting for age and sex. Cumulative incidence of CVD events adjusted for death from other causes was calculated.

Results: The study included 906 patients with incident RA (mean age 55.9 years; 69% female). There were 201, 299 and 406 patients in 1980-89, 1990-99 and 2000-09, respectively. During median follow-up of 10.6, 10.4 and 10.2 years per decade of RA incidence, CVD events occurred in 31, 38, and 31 patients. Patients with incident RA in 2000–09 had markedly lower cumulative incidence of any CVD events than patients diagnosed in 1990s and 1980s (Figure). Hazard ratios (HR) for any CVD events demonstrated a temporal reduction in CVD events among patients with incident RA in 2000s compared with incident RA in 1980s (HR: 0.52; 95% confidence interval (CI): 0.32-0.86) and a reduction compared with incident RA in 1990s (HR: 0.65; 95% CI: 0.40-1.05).

Conclusion: The incidence of major CVD events in RA declined markedly over time. These findings may reflect increased awareness, improved primary CVD prevention and better RA disease management in recent years. More studies are needed to understand the determinants and implications of these data.

Disclosure: E. Myasoedova, Pfizer, 2; **J. Davis**, Abbvie, 5, Pfizer, 2, 5, Sanofi Genzyme, 5; **V. Roger**, None; **S. Achenbach**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2.

Abstract Number: 0923

First Cardiovascular Event in Rheumatoid Arthritis: Do Patients with Venous Thromboembolism Have a Different Risk Profile Than Patients with Atherosclerotic Cardiovascular Disease?

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes II: Cardiovascular Comorbidities
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Chronic inflammation is linked to increased risk of cardiovascular disease (CVD) in RA that may manifest as venous thromboembolism (VTE) or atherosclerotic CVD (ASCVD). VTE is a potentially fatal condition that has been an increasing concern due to recent associations with the use of JAK inhibitors. However, our knowledge is limited about what factors determine VTE development in patients with RA, and if these risk factors are different than the ones for atherosclerotic CVD (ASCVD). We performed a cohort study aiming to assess risk factors favoring VTE over ASCVD in patients with RA.

Methods: RA patients participating in FORWARD, The National Databank for Rheumatic Diseases, from 1998 through 2018 were assessed for incident nonfatal or fatal unprovoked VTE (deep venous thrombosis and pulmonary emboli not associated with active cancer, recent surgery, hospitalization, fracture, pregnancy) and ASCVD (myocardial infarction and stroke) validated from hospital/death records. Patients with prior VTE/ASCVD and active cancer were excluded. Event rates were calculated, and the risk factors for VTE and ASCVD were determined separately using Cox proportional hazards compared to patients who had no history of VTE and ASCVD.

Results: Of 31,366 RA patients, we identified 539 first unprovoked VTE and 1,648 first ASCVD events during median (IQR) 4 (1.5-7) years of follow-up. The crude incidence rates per 1,000 patient-years (95% CI) were 0.34 (0.31-0.37) for VTE and 1.57 (1.51-1.63) for ASCVD. Baseline characteristics of patients by the CVD type are presented in *Table 1*. Patients with VTE were significantly more obese than patients with ASCVD but not different in terms of the history of prior cancer, fracture and traditional CV risk factors (diabetes [DM], hypertension [HT], and smoking). The multivariable models showed that older age, being male, having more comorbidities, history of fracture, worse HAQ scores, moderate/high disease activity and glucocorticoid use were associated with both increased VTE and ASCVD risks (*Table 2*). However, age and gender were stronger risk factors for ASCVD than for VTE and history of prior fracture and glucocorticoid use were stronger risk factors for VTE than for ASCVD. Traditional CV risk factors, DM and HT increased only ASCVD risk. Obesity had opposite effects on VTE and ASCVD risks: increased VTE risk (HR [95% CI], 1.46 [1.13-1.87]) and decreased ASCVD risk (HR [95% CI], 0.58 [0.50-0.68]) while underweight (HR [95% CI], 1.51 [1.13-2.02]) increased ASCVD risk. Hydroxycholoroquine use was found to be associated with a lower risk of VTE and ASCVD (*Table 2*).

Conclusion: With different risk magnitudes, VTE and ASCVD share common risk factors representing RA disease severity including disability, high disease activity and glucocorticoid use. The main difference in risk factors for these CV events is the traditional CV risk factors; DM and HT increase ASCVD risk and obesity increases VTE risk with a paradoxical effect on ASCVD. Being obese and having a prior fracture may be promoting immobilization and hence

Variables	RA without VTE or ASCVD, N=29,179	RA with VTE as first CVD, N=539	RA with ASCVD as first CVD, N=1,648	P value for VTE vs. ASCVD
Age, years	58.9 (13.6)†	66.5 (12.0)	71.8 (10.3)	**<0.001**
Female, %	82.2‡	79.4	71.4	**<0.001**
Caucasian, %	94.6‡	93.5	97.5	**<0.001**
RA duration, years	15.4 (11.1)†	19.6 (13.0)	19.4 (13.5)	0.843
BMI, kg/m^2	28.5 (6.4)†	30.4 (7.8)	27.0 (5.6)	**<0.001**
Obesity, %	28.8†	40.6	24.0	**<0.001**
Exercise, %	9.4†	8.0	14.1	**0.002**
RDCI (0-9)	1.8 (0.6)†	2.7 (1.8)	2.2 (1.6)	**<0.001**
Ever-smoked, %	40.8‡	43.4	46.5	0.206
Diabetes, %	9.8†	17.4	15.3	0.235
Hypertension, %	28.5†	49.4	47.3	0.432
Pulmonary disease, %	6.0†	13.4¶	11.8	0.356
Prior fracture, %	2.4†	10.1	7.7	0.189
Prior cancer, %	7.6†	15.7	15.0	0.737
HAQ disability (0-3)	1.1 (0.7)†	1.4 (0.7)	1.4 (0.8)	0.661
PAS (0-10)	4.0 (2.3)†	4.6 (2.1)	4.5 (2.3)	0.697
Glucocorticoid current, %	33.7†	50.9	46.2	0.063
Glucocorticoid ever, %	71.8†	84.9	79.5	**0.006**
MTX, %	47.6†	49.4	48.5	0.743
Hydroxychloroquine, %	20.3†	17.9	15.1	0.123
TNFi, %	30.2†	36.5	33.2	0.161
Other b/tsDMARDs, %	8.9†	11.9	3.9	**<0.001**
NSAIDs, %	49.0†	38.2	43.8	**0.023**

Table 1. Characteristics of patients who did not have any CVD or who developed a VTE or ASCVD as the first CVD at the time of the event*

Variables	aHR (95% CI) for VTE vs. no CVD	aHR (95% CI) for ASCVD vs. no CVD
Age groups		
<45 years	Reference	Reference
45-64 years	**1.58 (1.02-2.43)**	**3.01 (1.87-4.86)**
≥65 years	**2.30 (1.43-3.69)**	**7.85 (4.82-12.80)**
Male	**1.36 (1.06-1.73)**	**1.76 (1.53-2.03)**
Caucasian	0.94 (0.66-1.34)	1.20 (0.96-1.46)
RA duration, years	1.00 (0.99-1.01)	1.00 (0.99-1.00)
BMI in WHO categories		
Underweight	0.64 (0.26-1.58)	**1.51 (1.13-2.02)**
Normal weight	Reference	Reference
Overweight	1.03 (0.80-1.33)	**0.74 (0.64-0.84)**
Obese	**1.46 (1.13-1.87)**	**0.58 (0.50-0.68)**
Exercise	1.04 (0.92-1.17)	1.19 (1.00-1.20)
RDCI	**1.21 (1.14-1.30)**	**1.12 (1.07-1.17)**
Ever-smoked	0.90 (0.74-1.08)	1.05 (0.94-1.18)
Diabetes	0.97 (0.75-1.25)	**1.35 (1.15-1.59)**
Hypertension	1.18 (0.8-1.43)	**1.20 (1.06-1.35)**
Pulmonary disease	0.94 (0.71-1.26)	0.98 (0.81-1.19)
Prior fracture	**1.59 (1.37-1.84)**	**1.17 (1.04-1.33)**
Prior cancer	1.12 (0.86-1.45)	1.07 (0.90-1.26)
HAQ disability (0-3)	**1.21 (1.03-1.42)**	**1.28 (1.16-1.42)**
Moderate/high disease activity vs. Remission/low disease activity¶	**1.29 (1.05-1.57)**	**1.30 (1.16-1.47)**
Medication use		

Table 2. Multivariable associations with VTE and ASCVD in patients with RA*

VTE. These risk factors can be helpful in individual risk assessment, particularly in the availability of JAK inhibitors that may increase VTE risk.

Disclosure: G. Ozen, None; **S. Pedro**, None; **R. Schumacher**, None; **T. Simon**, Bristol-Myers Squibb, 3; **K. Michaud**, FORWARD, The National Databank for Rheumatic Diseases, 3, Pfizer, 2, Pfizer & Rheumatology Research Foundation, 2, Rheumatology Research Foundation, 2, University of Nebraska Medical Center, 3.

Abstract Number: 0924

Highly-sensitive Cardiac Troponin-I and Beta-2-Glycoprotein-I IgA Antibodies Inform the Utility of Screening and Follow-up Non-invasive Coronary Atherosclerosis Evaluation and Optimize Cardiovascular Risk Assessment in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes II: Cardiovascular Comorbidities

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: We recently reported that highly-sensitive cardiac troponin-I (hs-cTnI) associates with occult coronary atherosclerosis burden and cardiovascular event (CVE) risk in rheumatoid arthritis (RA). We further showed that IgA antibodies against beta2-glycoprotein-1 (a-b2GPI-IgA) contribute to higher coronary artery calcium (CAC) and accelerated plaque and CAC progression in RA. It is unclear when to proceed with coronary atherosclerosis evaluation in asymptomatic RA patients and whether such an assessment should be repeated in the future. We here explored whether either biomarker alone or their combination best predicted plaque or CAC presence on an initial coronary CT angiogram (CCTA); we then interrogated whether either biomarker predicted progression to extensive or obstructive plaque on a follow-up evaluation

Methods: One hundred fifty RA patients underwent a baseline CCTA; 101 had repeat evaluation within 83±3.6 months. Hs-cTnI and a-b2GPI IgAwere assessed at baseline; the latter were confirmed 12 weeks later, if positive. Extensive plaque was defined as >5 coronary segments withplaque, or stenosis score >5, or CAC >100.The diagnostic accuracy of Framingham D'Agostino cardiac risk score (FRSDA) alone vs. hs-cTnI or a-b2GPI-IgA sequentially

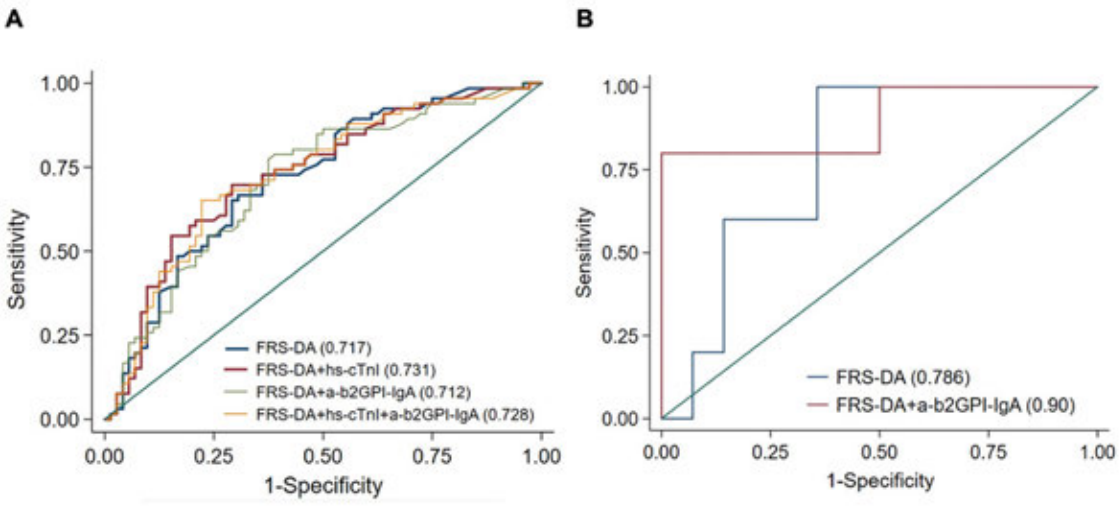

Figure 1. (A) Diagnostic accuracy for prediction of occult coronary plaque at baseline. Framingham D'Agostino (FRSDA) alone is the baseline model followed by addition of hs-cTnI or a-b2GPI-IgA individually or combined. **(B)** Diagnostic accuracy for progression from non-obstructive and non-extensive plaque at baseline to obstructive or extensive atherosclerosis at follow-up.

or combined for plaque or CAC at baseline was evaluated as area under the curve (AUC). Improvement in prediction accuracy between constructs was further assessed as integrated discrimination improvement (IDI). Similar AUC and IDI constructs were evaluated for transition to obstructive or extensive atherosclerosis at follow-up in patients with baseline plaque.

Results: High hs-cTnI added to FRSDA increased AUC from 0.717 to 0.731 (Figure 1A) and improved prediction for baseline plaque [IDI=0.041 (SE)=0.017, p=0.015]. In contrast, a-b2GPI-IgA did not [0.005 (0.006), p=0.47] and the combination offered no added benefit to the hs-cTnI model alone. Similar observations were made for baseline CAC. Hs-cTnI alone did not independently predict CAC change (β=0.084, p=0.215) whereas a-b2GPI-IgA presence did (β=0.235, p=0.001). High hs-cTnI predicted greater CAC change in a-b2GPI-IgA positive patients but not in negative ones [p-interaction= 0.034, estimated marginal mean difference (IQR)=0.36 (0.12-0.59), p=0.003]. Addition of a-b2GPI-IgA to FRSDA in patients with prevalent non-extensive non-obstructive plaque increased AUC from 0.785 to 0.900 (Figure 1B) and significantly improved the prediction for development of obstructive or extensive atherosclerosis at follow-up [0.387, (0.13), p=0.003].

Conclusion: High hs-cTnI significantly and independently improved the risk of baseline plaque presence and may trigger an initial non-invasive coronary atherosclerosis evaluation. A-b2GPI-IgA presence may justify a follow-up evaluation in patients with non-extensive, non-obstructive plaque at baseline.

Disclosure: G. Karpouzas, Bristol Meyer Squibb, 8, bristol Meyer Squibb, 8, Bristol-Meyer-Squibb, 8, Pfizer, 2, 9, pfizer, 2, Sanofi, 5, 8; **S. Ormseth**, None; **E. Hernandez**, None; **M. Budoff**, None.

Abstract Number: 0925

Incidence of Dementia and Association with Cardiovascular Disease and Risk Factors in Rheumatoid Arthritis – Analysis of a National Claims Database

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes II: Cardiovascular Comorbidities
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Session Time: 4:30PM–6:00PM

Background/Purpose: Inflammation has been thought to be a risk factor for cognitive impairment and dementia. RA, an autoimmune inflammatory disorder is associated with a high risk of cardiovascular disease (CVD) as a result of underlying inflammation, However, it is unknown if RA patients at risk of CVD are similarly at higher risk of developing dementia. The objective of this study was to describe the incidence of dementia among patients with RA older than 40 years, and to compare the risk of incident dementia between those with known CVD and those without CVD, with and without traditional CVD risk factors.

Methods: We conducted a longitudinal analysis, using Centers for Medicare and Medicaid claims (CMS) data from 2006-2014. To be included, patients had to be continuously enrolled throughout 2006 (12 months calendar year of fee for service), > 40 years old, eligible for Medicare parts A, B and D, and without a diagnosis of dementia in 2006. RA

Table 1. Characteristics of Patients with RA Older than 40 Years of Age without Dementia Stratified by History of Cardiovascular Disease (CVD) and Traditional CVD Risk Factors

Characteristic	Prevalent CVD N = 9487 (12.5%)		No prevalent CVD, but with CVD risk factors N = 47096 (62.3%)		No prevalent CVD or CVD risk factors N = 19051 (25.2%)		p-value
	N	%	N	%	N	%	
Age Categories							<0.0001
40 to 54	481	5.07	3955	8.40	3195	16.77	
55 to 64	1065	11.23	6574	13.96	3060	16.06	
65 to 74	3529	37.20	20556	46.65	7759	40.7.	
75 plus	4412	46.51	16011	34.00	5037	26.44	
Female	7261	76.54	38619	82.00	15275	80.18	<0.0001
Race							≤0.0001
White	7380	77.79	36858	78.26	16035	84.17	
Black	1087	11.46	5001	10.62	1177	6.18	
Hispanic	810	8.54	4036	8.57	1351	7.09	
Other	209	2.20	1199	2.55	488	2.56	
Charlson-Deyo score							<0.0001
1	241	2.54	23682	50.28	15300	80.31	
2	2652	27.95	15480	32.87	3368	17.68	
≥ 3	6587	69.43	7934	16.85	383	2.01	

CVD = cardiovascular disease; Prevalent CVD as defined by ICD-9-CM codes for myocardial infarction, heart failure, stroke, or CVD procedures (coronary artery bypass grafting, percutaneous coronary intervention, or carotid endarterectomy); CVD risk factors included diabetes, hyperlipidemia, hypertension, and obesity in 2006 defined by ICD-9-CM codes.

was defined as: two RA diagnoses (ICD-9-CM 714.xx) by a rheumatologist > 7 and < 365 days apart and or at least one diagnosis of RA and least 1 prescription for a DMARD. Incident dementia was defined as: 2 outpatient claims for dementia (ICD-9-CM codes for 290.xx, 294.1x, or 331.xx) at least 40 days apart in 2007 or later. Prevalent CVD was defined by ICD-9-CM codes for myocardial infarction, heart failure, stroke, or CVD procedures (coronary artery bypass grafting, percutaneous coronary intervention, or carotid endarterectomy) in 2006. CVD risk factors were defined by ICD-9-CM codes for diabetes, hyperlipidemia, hypertension, and obesity in 2006. Age-adjusted incidence rates (IR) were estimated using Poisson models. Age- and sex-adjusted Cox proportional hazard models (HR) were used to compare risk of incident dementia in 3 groups of RA patients; 1) with prevalent CVD 2) without CVD but with CVD risk factors, and 3) no prevalent CVD events nor CVD risk factors.

Results: There were 79,957 RA patients in the study sample; 80.8% were female, and 79.6% were white (Table 1). The prevalence of dementia was 2.36% (n = 1,887). After removing RA patients with prevalent dementia in 2006, 75,634 remained. Between 2007-2014, there were 9,835 (13%) cases of incident dementia (Table 1). The age-adjusted IR of dementia was 25.6 (95% CI 24.3 – 26.9) per 1000 person-years for those with prevalent CVD, 17.5 (95% CI 17.1 – 18.1) per 1000 person-years for those with CVD risk factors, and 15.2 (95% CI 14.59-16.00) in patients with neither (Table 2). The age- and sex-adjusted HR for incident dementia was 2.1 (95% CI 1.9 - 2.2) in those with prevalent CVD and 1.2 (95% CI 1.1 - 1.2) in those without prevalent CVD with presence of any CVD risk factor compared to those without CVD and or CVD risk factors.

Table 2. Incident Rates of Dementia Between Year 2007-2014 in Patients with RA Stratified by History of Cardiovascular Disease (CVD) and Presence of CVD Risk Factor during Calendar Year 2006 (Baseline)

	N	Number of patients with incident dementia	Mean number of years of followup	Crude Rate per 1000 person years	Age Adjusted Incident rate per 1000	Age and Gender Adjusted Hazard Ratios (95% CI)
Prevalent CVD	9,487	1,717	4.78	37.86	25.60 (24.32 - 26.93)	2.08 (1.94 - 2.21)
No prevalent CVD, but with CVD risk factor	47,096	6,218	5.94	22.22	17.55 (17.05 - 18.06)	1.18 (1.12 - 1.24)
No prevalent CVD or CVD risk factors	19,051	1,900	6.13	16.26	15.28 (14.59 - 16.00)	Reference

CVD = cardiovascular disease; Prevalent CVD as defined by ICD-9-CM codes for myocardial infarction, heart failure, stroke, or CVD procedures (coronary artery bypass grafting, percutaneous coronary intervention, or carotid endarterectomy); CVD risk factors included diabetes, hyperlipidemia, hypertension, and obesity in 2006 defined by ICD-9-CM codes.

Conclusion: The incidence of dementia in patients with RA was as high or higher than previous reports from the general population. The presence of CVD in patients with RA increases the risk for incident dementia 2-fold when compared to patients with RA without CVD or CVD risk factors. Our study suggests that in patients with RA, increasing risk for CVD may also be associated with an increased risk for dementia. Further studies comparing patients with and without RA are needed to clarify this association.

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Abstract Number: 0926

Methotrexate Is Associated with Reduced Cardiovascular Risk in Rheumatoid Arthritis Independent of Disease Activity Modification

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SESSION INFORMATION

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Session Title: RA – Diagnosis, Manifestations, & Outcomes II: Cardiovascular Comorbidities

Session Type: ACR Abstract Session

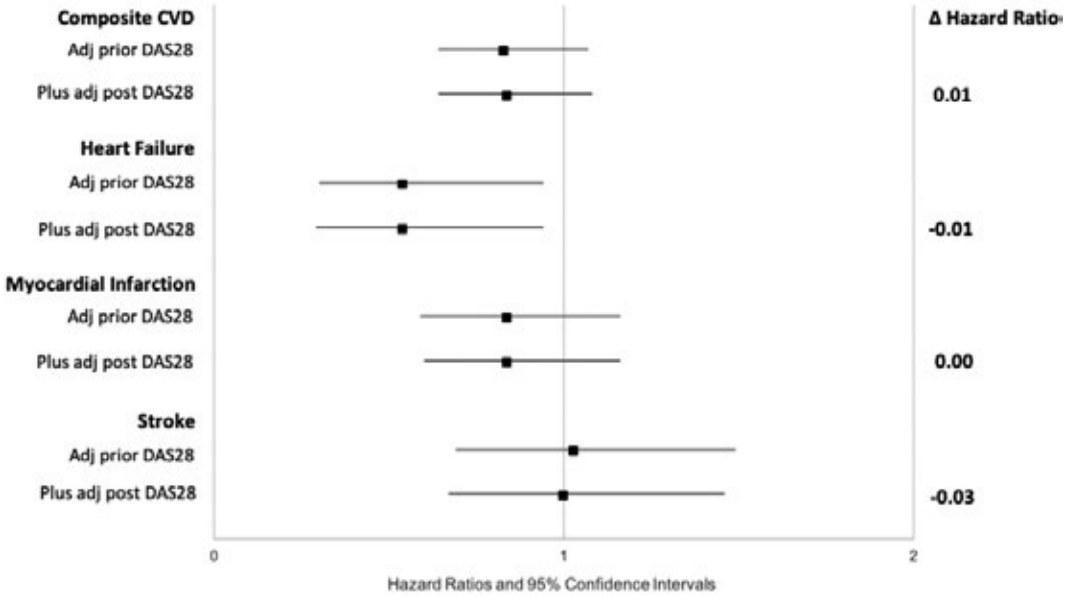
Session Time: 4:30PM–6:00PM

Table. Marginal structural models examining associations of time-varying methotrexate use with incident cardiovascular events in rheumatoid arthritis‡

Event category	HR (95% CI)	p-value
Composite CVD	**0.72 (0.56-0.91)**	**0.006**
Heart failure	0.40 (0.23-0.67)	0.001
Myocardial infarction*	0.78 (0.53-1.13)	0.19
Stroke	0.76 (0.41-1.43)	0.40

‡ Marginal structural models included baseline sex, race, smoking status, hypertension, hyperlipidemia, diabetes, chronic kidney disease, liver disease, previous CVD, statin use, and RA duration. Age, BMI, aspirin and NSAID use, DMARD exposure (non-methotrexate conventional DMARDs, biologic DMARDs, and prednisone), and DAS28 were used from the current and prior visit.
* Myocardial infarction includes coronary revascularization (percutaneous coronary intervention, coronary bypass)
Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio

Figure. Effect of Rheumatoid Arthritis Disease Activity Modulation as a Mediator of Cardiovascular Risk Reduction with Methotrexate use in Rheumatoid Arthritis



Forest plots illustrating the association of time-varying MTX use with incident cardiovascular events in rheumatoid arthritis patients. Sequential multivariable cox models include pre-MTX disease activity (Adj prior DAS28) and post-MTX disease activity (Plus adj post DAS28).

Background/Purpose: Rheumatoid arthritis (RA) patients are at increased risk of cardiovascular disease (CVD). Methotrexate (MTX), a mainstay in the treatment of RA, appears to mitigate this risk. However, prior studies have been limited in their ability to account for the effects of disease activity and examine the mechanisms that account for CVD risk reduction. We aimed to determine whether the association of MTX with reduced CVD risk was related to modulation of disease activity or direct effects.

Methods: We observed participants in a prospective, multicenter cohort of US Veterans with RA for incident CVD events from 4/2005 to 4/2015. CVD events were defined as a composite of acute myocardial infarction (AMI), coronary revascularization, stroke, and hospitalization for heart failure (CHF). These were identified using diagnostic and procedure codes from inpatient and outpatient encounters (validated by medical record review) and the National Death Index. Demographics, traditional CVD risk factors, comorbidities (including hypertension, hyperlipidemia, diabetes, chronic kidney disease, liver disease, and prior CVD), as well as aspirin, statin, and NSAID use were assessed using registry and administrative data. MTX (and other DMARD/prednisone) exposure was defined at each visit by linking to pharmacy dispensing data,

including a 90-day grace period upon discontinuation. To reduce confounding by disease activity, we used marginal structural models incorporating disease activity from the prior visit into the propensity to receive MTX to determine the overall association of MTX with CVD events. To examine whether the association of MTX use with CVD was mediated through disease activity, we used sequential Cox models including post-MTX disease activity.

Results: RA patients (n=2168) were predominantly older (mean age 64 years), male (90%), frequent smokers (80% current/former), seropositive (79% RF, 78% anti-CCP), with moderate baseline disease activity (mean DAS28 3.7). The incidence of composite CVD events (n=401) was lower in MTX exposed patients (33.8/1000 person-years) vs. MTX non-exposed patients (40.7/1000 person-years). Using marginal structural models to account for disease activity at the prior visit, MTX use was associated with reduced risk of composite CVD events (HR 0.72, 95% CI 0.55-0.89) and CHF (HR 0.40, 95% CI 0.23-0.67), with a trend toward reduced risk of AMI and stroke (**Table**). In sequential multivariable Cox models to assess direct and indirect effects, adjustment for post-MTX disease activity did not significantly alter the association of MTX use with composite or individual CVD events (range ΔHR -0.03 to 0.01, **Figure**).

Conclusion: In a multicenter RA cohort, MTX use was associated with a 30% reduced risk of composite CVD events and a 60% reduced risk of CHF hospitalizations. The protective effect of MTX was independent of other factors including treatment-related changes in disease activity, suggesting that additional mechanisms mediate CVD risk reduction with MTX in RA. This should be considered when selecting DMARD therapy regimens in RA patients.

Disclosure: T. Johnson, None; **J. Baker**, Bristol-Myers Squibb, 2, 5, Burns-White LLC, 5; **P. Roul**, None; **H. Sayles**, None; **G. Cannon**, Amgen, 2; **B. Sauer**, Amgen, 2; **T. Mikuls**, BMS, 2, Horizon, 2; **B. England**, None.

Abstract Number: 0927

Efficacy and Safety of Filgotinib for Patients with Rheumatoid Arthritis Naïve to Methotrexate Therapy: FINCH3 Primary Outcome Results

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SESSION INFORMATION
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Background/Purpose: Filgotinib (FIL), an orally administered, potent, selective inhibitor of Janus kinase 1 (JAK1), has shown good efficacy and was well tolerated for treatment of rheumatoid arthritis (RA). The objective of this study is to compare efficacy and safety of FIL with and without methotrexate (MTX) in patients with RA who were naïve to MTX therapy.

Methods: This phase 3, double-blind, active-controlled study randomized patients with moderately to severely active RA (2:1:1:2) to FIL 200mg daily + MTX weekly (up to 20mg), FIL 100mg + MTX, FIL 200mg (+placebo [PBO]), or MTX (+PBO) for up to 52 weeks; results through week 24 are presented. Primary efficacy endpoint was proportion of patients achieving ACR20 response at week 24; additional assessments included ACR50 and ACR70 responses;

Table 1. Efficacy Outcomes at Week 24[a]

	FIL 200 mg + MTX (N = 416)	FIL 100 mg + MTX (N = 207)	FIL 200 mg Monotherapy (N = 210)	MTX Monotherapy (N = 416)
ACR20, %	81.0***	80.2*	78.1	71.4
ACR50, %	61.5***	57.0**	58.1**#	45.7
ACR70, %	43.8***	40.1***	40.0***#	26.0
DAS28-CRP ≤ 3.2, %	68.8***#	62.8***#	60.0***#	46.2
DAS28-CRP < 2.6, %	54.1***	42.5***	42.4***#	29.1
mTSS, mean change from BL	0.20	0.22	−0.04**#	0.52
HAQ-DI, mean change from BL	−0.94***	−0.90**	−0.89**#	−0.79
SF-36 PCS, mean change from BL	12.3***#	11.1*#	10.4	9.7
FACIT-Fatigue, mean change from BL	10.6	11.4	10.2	10.1

[a]All patients who were randomized and received at least 1 dose of study drug were included in efficacy analyses.
*P<0.05 vs MTX monotherapy; **P<0.01 vs MTX monotherapy; ***P<0.001 vs MTX monotherapy; #Comparison not adjusted for multiplicity.
ACR20/50/70, 20%/50%/70% improvement in American College of Rheumatology criteria; BL, baseline; DAS28-CRP, Disease Activity Score based in 28 joints with C-reactive protein; FACIT, Functional Assessment of Chronic Illness Therapy; FIL, filgotinib; HAQ-DI, Health Assessment Questionnaire Disability Index; mTSS, modified total Sharp score; MTX, methotrexate; PBO, placebo; SF-36 PCS, Short-Form 36 Physical Component Summary.

Table 2. Safety Events of Interest through Week 24

Patients with event, n (%)	FIL 200 mg + MTX (N = 416)	FIL 100 mg + MTX (N = 207)	FIL 200 mg Monotherapy (N = 210)	MTX Monotherapy (N = 416)
Serious AEs	17 (4.1)	5 (2.4)	10 (4.8)	12 (2.9)
Serious infections	4 (1.0)	2 (1.0)	3 (1.4)	4 (1.0)
Herpes zoster	2 (0.5)	1 (0.5)	1 (0.5)	2 (0.5)
Adjudicated MACEs	2 (0.5)	0	1 (0.5)	2 (0.5)
Venous thrombotic events	0	0	0	1 (0.2)
Malignancies	0	0	0	1 (0.2)
Deaths	1 (0.2)[a]	0	0	0

[a]Cause of death was lupus myocardiopathy.
AE, adverse event; MACE, major adverse cardiovascular event

DAS28-CRP score ≤3.2 and < 2.6, and changes in van der Heijde mTSS, HAQ-DI, SF-36 PCS, and FACIT-Fatigue. Safety endpoints included types and rates of adverse events (AEs). Logistic regression adjusting for stratification factors with nonresponder imputation was used for treatment comparisons for ACR response and other binary endpoints. Mixed-effect model adjusting for baseline value, stratification factors, treatment, visit, and treatment by visit interaction as fixed effects with observed cases was used for continuous endpoints.

Results: Of 1,252 randomized patients, 1,249 received study drug (416 FIL 200mg+MTX; 207 FIL 100mg+MTX; 210 FIL 200mg monotherapy; 416 MTX monotherapy) and were analyzed; 1,130 completed week 24. Most (76.9%) were female; mean time since RA diagnosis was 2.2 years (median 0.4 years); mean (standard deviation [SD]) DAS28-CRP was 5.7 (1.0); and 35.9% were using oral steroids at baseline. At week 24, significantly more patients in the FIL 200mg+MTX (81.0%; P< 0.001) and FIL 100mg+MTX (80.2%; P< 0.05) arms achieved an ACR20 response compared to MTX monotherapy (71.4%)(Table 1). Compared to MTX monotherapy, more patients receiving FIL with or without MTX achieved ACR50 and ACR70 responses, DAS28-CRP < 2.6 and ≤3.2, and reported improvements in SF-36 PCS (Table 1). The onset of activity was rapid, with significantly more patients achieving ACR50 and DAS28-CRP < 2.6 with FIL than MTX at week 2. The FIL safety profile was consistent with prior studies through week 24 (Table 2).

Conclusion: The JAK1 inhibitor FIL in combination with MTX led to significant improvements in RA signs and symptoms, physical function, and patient-reported outcomes compared to MTX alone and was well tolerated in patients with early active RA naïve to MTX. Clinically meaningful response to FIL occurred as early as 2 weeks after treatment initiation.

Disclosure: R. Westhovens, Celltrion, 5, 8, 9, Celltrion, Inc., 2, 5, Galapagos, 5, 8, Galapagos NV, 5, 9, Galapagos/Gilead, 2, 5, Gilead Sciences, Inc., 5, 8, 9; **W. Rigby**, Abbvie, 5, AbbVie, 5, BMS, 5, Bristol-Myers Squibb, 5, Gilead Sciences, Inc., 5, Pfizer, 5, Roche, 5; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **D. Ching**, AbbVie, 5; **B. Bartok**, Gilead Sciences, Inc., 3, 4; **F. Matzkies**, Gilead Sciences, Inc., 1, 3, 4; **Z. Yin**, Gilead Sciences, Inc., 3, 4; **Y. Guo**, Gilead Sciences, Inc., 3, 4; **C. Tasset**, Galapagos, 1, 3, Galapagos NV, 3, 4; **J. Sundy**, Gilead Sciences, Inc., 3, 4; **N. Mozaffarian**, Gilead Sciences, Inc., 1, Glenmark Pharmaceuticals, 3; **O. Messina**, None; **R. Landewé**, Abbott, 2, 5, 8, Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8; **T. Atsumi**, AbbVie, 5, 8, Abbvie, 5, 8, Asahi Kasei Pharma Corporation, 8, Astellas Pharma, 8, 9, Astellas Pharma Inc, 8, AstraZeneca, 5, AstraZeneca plc, 5, 8, Bayer Yakuhin, 8, Bayer Yakuhin, Ltd., 8, Bristol-Myers Squibb, 8, 9, Chugai Pharmaceutical Co Ltd, 8, Chugai Pharmaceutical Co., 8, 9, Daiichi Sankyo, 8, 9, Daiichi Sankyo Co Ltd, 8, Eisai Co., Ltd, 8, Eli Lilly and Company, 8, 9, Eli Lilly Japan KK, 8, Elsai Co Ltd, 8, Gilead Sciences, 8, Gilead Sciences, Inc., 8, MEDICAL & BIOLOGICAL LABORATORIES CO., 5, Medical and Biological Laboratories Co Ltd, 5, Mitsubishi Tanabe Pharma, 8, 9, Nippon Shinyaku Co., 8, Novartis, 5, Novartis Pharma KK, 5, Ono Pharmaceutical, 5, ONO Pharmaceutical Co Ltd, 5, Otsuka Pharmaceutical, 8, Pfizer, 5, 9, Pfizer Inc, 5, 8, Sanofi, 9, Takeda Pharmaceutical Company, 8, Takeda Pharmaceuticals, 8; **G. Burmester**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma., 5, 8, AbbVie Inc., 5, 8, BMS, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Merck Shar & Dohme, 5, 8, MSD, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche, Sanofi-Genzyme, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Union Chimique Belge, 2, 5, 8.

Abstract Number: 0928

Monotherapy with Upadacitinib in MTX-naïve Patients with Rheumatoid Arthritis: Results at 48 Weeks

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: RA – Treatments II: Novel Treatments for RA

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Background/Purpose: Upadacitinib (UPA), a JAK1-selective inhibitor, was efficacious as monotherapy upto 24 weeks (wks) in MTX-naive patients (pts) with active RA.[1]

To assess safety and efficacy of UPA through 48 wks in an ongoing extension of the ph 3 SELECT-EARLY RCT.

Methods: SELECT-EARLY had a 48-wk double-blind active comparator-controlled period. Pts were initially randomized to monotherapy (mono) with UPA 15 or 30 mg or MTX (titrated up to Wk8). Rescue therapy was offered if pts met the following: (1) From Wk 12-24, pts without ≥20% improvement from BL (Δ) in both TJC and SJC at 2 consecutive visits continued blinded study drug with optimized background RA medications. (2) At Wk26, pts with CDAI ≤2.8 continued their original study drug; in pts with CDAI >2.8 and < 20% Δ in TJC and SJC, for those on MTX, UPA15/30mg was added; for those on UPA15/30mg, MTX was added. For pts with CDAI >2.8 but ≥20%Δ in TJC and SJC, background medications were optimized. Background csDMARDs could be initiated after Wk26. After Wk48, pts could continue in a long-term extension. Efficacy data up to the Wk48 visit are reported based on initial randomized treatment. For binary non-radiographic endpoints, NRI was used for missing data and rescue handling; for continuous non- radiographic endpoints, LOCF was used for rescue handling. Radiographic analyses are based on linear extrapolation for missing data imputation and rescue handling. Adverse events (AE) per 100 pt yrs (PY) are summarized up to a cut-off date of Aug 16 2018.

Table 1. Efficacy Endpoints at Week 48

	MTX N=314	UPA 15 MG N=317	UPA 30 MG N=314
ACR20, %	57	74***	75***
ACR50,%	43	63***	68***
ACR70,%	29	51***	53***
DAS28-CRP LDA (≤3.2), %	39	59***	66***
DAS28-CRP <2.6, %	29	49***	53***
CDAI LDA, (≤10), %	43	60***	64***
CDAI REM, (≤2.8), %	17	33***	40***
Boolean REM, %	13	28***	33***
Change in HAQ-DI	-0.74	-0.96***	-1.04***
Change in FACIT-F	8.5	10.1#	11.6***
Change in mTSS§	1.00	0.03***	0.14***

Results are based on NRI (binary endpoints), LOCF for rescue (change in HAQ-DI, FACIT-F), or linear extrapolation (change in mTSS); ***, p<.001 vs MTX; #p=.058;
Boolean REM: TJC ≤1, SJC ≤1, CRP ≤1 mg/dl, PGA ≤1 (0–10 scale)
§mTSS from 2nd reading session of radiographs at Wk48

Table 2. Treatment emergent adverse event (AE) summary; E/100PY in Patients on monotherapy (censored at time of change to combination exposure of UPA+MTX/csDMARD)

	MTX MONO N=314, PYS=314.4	UPA 15 MONO N=317 PY=343.1	UPA 30 MONO N=314 PY=336.7
Any Adverse Event	303.1	345.4	358.2
Serious AE	11.8	14.3	15.4
AE Leading To D/C Of Study Drug	8.9	11.4	10.7
Serious Infection	2.9	4.1	5.0
Herpes Zoster[ǂ]	1.3	6.4	4.8
Hepatic disorder[¥]	19.7	18.7	15.7
Any Malignancy (excluding NMSC)[γ]	1.0	1.2	0.6
MACE (adjudicated)[δ]	0.6	0.9	1.2
VTE (adjudicated)[§]	0.6	0	0.3
Deaths[†]	0.3	1.2	1.8

[ǂ]Herpes zoster: most involved a single dermatome and were non-serious. No cases of CNS involvement.
[¥]Hepatic disorders: majority were asymptomatic transaminase elevations,
[γ]Malignancies excl NMSC: MTX: 1 malignant neoplasm of ovary, 1 pt with gall bladder adenocarcinoma and hepatic cancer;
UPA15: 1 malignant neoplasm progression, 1 metastatic malignant melanoma, 1 squamous cell carcinoma of lung, 1 uterine carcinoma in situ;
UPA30: 1 cervix cell carcinoma, 1 uterine cancer
[δ]MACE (includes cardiovascular [CV] death, non-fatal Myocardial infarction [MI], non-fatal stroke): MTX:1 CV death, 1 non-fatal stroke; UPA15: 1 CV death, 1 pt had 2 adjudicated events: a non-fatal MI, followed by CV death (due to hypoxic encephalopathy, not MI); UPA30:3 CV deaths, 1 non-fatal MI
[§]VTE: MTX: 1 pt with PE, 1 pt with DVT and PE; UPA30: 1 DVT
[†]Deaths (includes non-treatment emergent [NTE] deaths): MTX: 1 due to acute MI; UPA15: 2 due to MI (1 was NTE), 1 due to malignant melanoma and malignant neoplasm (NTE), 1 non-CV death; UPA30: 1 due to pneumonia /sepsis, 1 fatal MI, 2 CV deaths, 1 due to peritonitis, 1 CV death due to other causes (NTE); 1 death due to meningitis was reported on combination of UPA30+csDMARDs

References:

1. van Vollenhoven R et al. Arthritis Rheumatol. 2018;70 (supp10):

Results: Of 945 pts randomized and treated, 747(79%) completed Wk48 treatment, 163 (17.2%) discontinued (D/C) study drug prior to Wk48, 35 pts (4%) had not completed the Wk48 treatment as of this analysis. Primary reasons for D/C were AEs for 62 pts (6.5%), and lack of efficacy in 20 pts (2.1%). At Wk26, UPA15/30 was added for 37 (12%) of pts on MTX; MTX was added for 19 (6%) and 9 (3%) of pts on UPA15 and UPA30, respectively. Cumulative exposures to MTX mono, UPA15 mono and UPA30 mono were 314.4, 343.1 and 336.7 PYs, respectively. Through Wk48, pts on UPA15 and 30 vs MTX continued to have significantly greater improvements in clinical, functional and pt-reported outcomes (except FACIT-F for UPA15, p=.058 vs MTX) (Table 1). At Wk 48, CDAI Remission (REM) was achieved by 33% and 40% of pts on UPA15 and 30 respectively vs 17% on MTX; 28% and 33% vs 13% achieved Boolean REM. At Wk48, ΔmTSS were significantly less on UPA15 and UPA30 vs MTX. The safety profile of UPA15 and UPA30 mono was generally similar to MTX, except for total AEs and herpes zoster, which were higher with UPA15 and 30 vs MTX (Table 2). There were 11 deaths (including 3 non-treatment emergent deaths) due to varied causes.

Conclusion: UPA15 and 30 monotherapy continued to show significant improvements in RA signs and symptoms and inhibition of structural damage vs MTX through 48 wks. Only a small proportion of pts required MTX addition to UPA mono at Wk26 to achieve and maintain response. The safety profile based on all exposure remained consistent with ph 2 and 3 RCTs in RA, although an integrated safety analysis of UPA across the full ph 3 RA program will provide a more comprehensive understanding of the benefit:risk profile of UPA in RA.

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Abstract Number: 0929

Efficacy and Safety of Fenebrutinib, a BTK Inhibitor, Compared to Placebo in Rheumatoid Arthritis Patients with Active Disease Despite TNF Inhibitor Treatment: Randomized, Double Blind, Phase 2 Study

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SESSION INFORMATION
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Background/Purpose: Fenebrutinib (GDC-0853, FEN) is an orally administered, highly selective, non-covalent, and reversible small molecule inhibitor of Bruton's Tyrosine Kinase (BTK).[1] We report the efficacy and safety of FEN compared with placebo (PBO) in combination with background methotrexate (MTX) in patients with rheumatoid arthritis (RA) and an inadequate response to tumor necrosis factor (TNF-IR), identified as a population with existing unmet medical need.

Methods: This multicenter, randomized, double-blind Phase 2 study included two cohorts of patients with moderate-to-severe RA: cohort 1 (MTX-IR patients) and cohort 2 (TNF-IR patients). Primary (cohort 1) and key secondary (cohorts 1 and 2) endpoints were a 50% improvement in the American College of Rheumatology scores (ACR50) at Week

Table 1. Efficacy endpoints for TNF-IR patients

Week 12 Response	PBO (*n*=50)*	FEN 200 mg QD (*n*=48)*
ACR50		
Responders, *n* (%)	6 (12)	12 (25)
95% CI (%)	(3, 21)	(13, 37)
P value vs. PBO**	-	0.0717
ACR20		
Responders, *n* (%)	12 (24)	28 (58)
95% CI (%)	(12, 36)	(44, 72)
P value vs. PBO	-	0.0001
ACR70		
Responders, *n* (%)	2 (4)	7 (15)
95% CI (%)	(0, 9)	(5, 25)
P value vs. PBO	-	0.0983
DAS28-CRP		
Patients, *n*	43	47
Change from baseline, mean	-1.43	-2.26
P value vs. PBO		0.0001
CRP (mg/dL)		
Patients, *n*	44	47
Change from baseline, mean (Standard Deviation)	-0.56 (2.75)	-1.55 (2.35)
ESR (mm/h)		
Patients, *n*	45	47
Change from baseline, mean (Standard Deviation)	-8.29 (21.91)	-18.68 (20.50)
HAQ-DI score		
Patients, *n*	43	44
Change from baseline, mean (Standard Deviation)	-0.30 (0.62)	-0.53 (0.61)

*Intent-to-treat population **Pre-specified alpha = 0.2

12, with pre-specified alpha of 0.2. Patients in cohort 2 (TNF-IR) were randomized to PBO and to FEN 200 mg BID arms for 12 weeks with the continuation of background MTX dose; the safety and efficacy results for this cohort are reported here (cohort 1 data has been reported previously[2]).

Results: Demographics and disease characteristics for the TNF-IR cohort were balanced in the PBO (*n*=49) and FEN (*n*=49) arms with mean age of 55 and 51 years, respectively, and 76% female patients/arm. Median duration of RA disease was 8.7 years (PBO) and 7.2 years (FEN). The mean baseline doses for MTX were 16.6 mg (PBO) and 15.7 mg (FEN). Corticosteroid mean doses were 8.3 and 7.5 mg prednisone-equivalents in the 33% and 39% of patients using corticosteroids in the PBO and FEN arms at baseline, respectively. Baseline mean values for DAS28-CRP and HAQ-DI were similar (6.0 and 5.9, and 1.76 and 1.45, respectively) for PBO and FEN arms. The majority of patients in the PBO (90%) and FEN (98%) arms completed the 12-week study. ACR20/50/70 responses (**Table 1**) were greater for FEN versus PBO and generally increased over time, with plateau of ACR50 after W8 for all patients. ACR50 response at W12 was greater for FEN (25% vs 12%, *p*-value=0.07 [pre-specified type-1 error rate=0.20 two sided]). At W12, DAS28-CRP decreased by -1.43 (PBO) and -2.26 (FEN) from baseline. More patients in the PBO arm (45%) than in the FEN arm (22%) reported at least one AE; no serious AEs were reported. There were 37 AEs in the PBO arm and 22 AEs in the FEN arm (including one case of herpes zoster), with one AE (worsening RA) leading to treatment

withdrawal in the PBO group. No deaths or malignancies were reported. There were no clinically significant changes in hematology or immunoglobulin parameters. In two patients treated with FEN, Grade 3 chemistry abnormalities were observed (low phosphorous, high uric acid). No Grade 4 or 5 abnormalities were reported. Although no Grade 3 creatinine elevations were observed, there was an increased mean change from baseline in creatinine in the FEN arm (5.1 µmol/L) in comparison to PBO arm (-0.4 µmol/L) at W12.

Conclusion: FEN demonstrated higher efficacy rates across disease activity measures vs. PBO at W12 in the TNF-IR population. The safety profile of FEN in this population is acceptable.

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Neurostimulation for Treatment of Drug Refractory Rheumatoid Arthritis: A First-in-Human Study Using a Novel Vagus Nerve Stimulator

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SESSION INFORMATION
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Session Title: RA – Treatments II: Novel Treatments for RA
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Session Time: 4:30PM–6:00PM

Background/Purpose: The inflammatory reflex is an endogenous neuroimmune circuit that helps regulate innate and adaptive immunity (Annu. Rev. Immunol. 2012; 30:313). Activation of this reflex by electrical vagus nerve stimulation (VNS) reduced systemic inflammation and disease activity in a 17 patient rheumatoid arthritis (RA) proof-of-concept study using a reprogrammed epilepsy stimulator (PNAS 2016; 113(29):8284). Here we report on the safety and efficacy of a novel miniaturized neurostimulator, the "MicroRegulator" (MR), in a first-in-human, double-blind pilot study of VNS in multi-drug refractory RA patients.

Methods: The MR was implanted on the left vagus nerve in 14 patients with active RA and prior insufficient response to ≥2 bDMARDS or JAK inhibitors with ≥2 different modes of action; all patients remained on a stable background of MTX (n=12) or HCQ. Three weeks after implantation, the first 3 subjects were stimulated 1 min QD and, following safety review board approval, the remaining 11 patients were implanted with the MR and ran-

domized to 1 min: sham, QD, or QID VNS for 12 weeks (primary endpoint; PE). Patients, rheumatologists, joint assessors and monitors were fully blinded to treatment arm. Patients randomized to sham had their devices activated after the PE was reached. The pharmacodynamic response to VNS was assessed in blood using cytokine production in an ex-vivo bioassay (TruCulture). Clinical efficacy was measured by DAS28-CRP and CDAI responses and by wrist MRI (RAMRIS OMERACT). Vagus nerve activity (tone) was extracted from heart rate variability assessments of Holter-captured ECG.

Results: 14 patients were enrolled (mean prior bDMARDs = 4.8, mean DAS28-CRP= 5.94). Implantation and stimulation were generally well tolerated. There were no device or treatment-related SAEs and 2 notable surgery related adverse events (left vocal cord paralysis, Horner's syndrome) that resolved without clinically significant sequelae. Confirming activation of the inflammatory reflex, the pharmacodynamic response of VNS was observed in both actively stimulated groups with >30% decrease from baseline in bioassay levels of IL-1β, IL-6, and TNF-α at PE, with minimal change in the sham group. Mean DAS28-CRP change at PE was: combined QD= -1.34, QID= 0.38, Sham= 0.16. Of QD stimulated patients, 4/6 had a EULAR good or moderate response vs. 1/4 QID and 0/4 shams. Both DAS28 and CDAI response was achieved by 5/10 actively stimulated patients at PE, with 2 in DAS28 remission. MRI inflammation measures did not change by PE. RAMRIS erosion scores correlated with EULAR response (change in responders = -2.2 vs. 2.4 in non-responders). Mean vagal tone in the stimulated patients was increased 2.75-fold relative to sham stimulated patients.

Conclusion: The novel MR device and stimulation was well tolerated independent of the two surgery-related events. MR associated VNS reduced signs and symptoms of RA in a meaningful number of highly drug-refractory patients. No clinical improvement was observed in the sham group. These initial pilot data support the use of the MR for QD VNS in a larger blinded sham-controlled study in patients who have failed biologics or targeted oral therapies as a novel approach for treatment of RA.

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Abstract Number: 0931

Ultra-Low Doses of Rituximab for Retreatment of RA: A Randomized Controlled Non-Inferiority Trial

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SESSION INFORMATION

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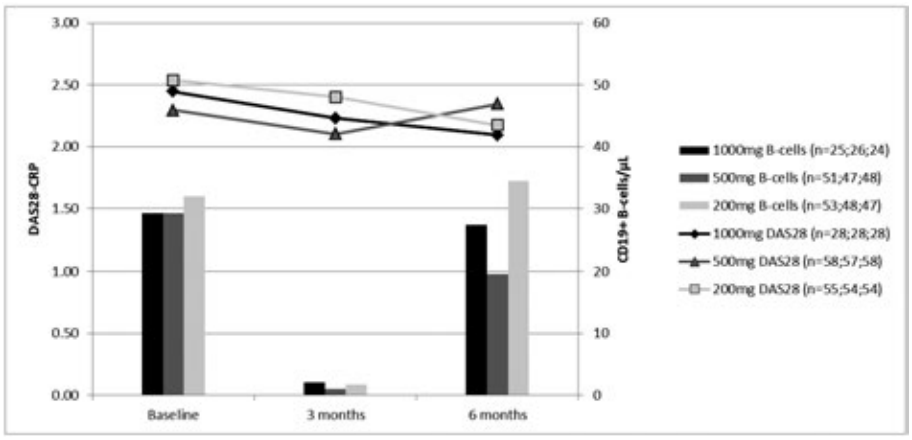
Background/Purpose: Rituximab is an effective treatment for patients with RA. 1000mg (1×1000mg or 2×500mg) has similar six-month efficacy as the registered dose of 2×1000mg.(1) Based on several case reports and a case series even lower doses might be sufficient for maintenance treatment, potentially improving safety and decreasing costs.(2) The objective of this study was to compare effectiveness of rituximab retreatment with ultra-low doses (1×500mg or 1×200mg) to standard low dose (1×1000mg).

Methods: A six-month double-blind randomized controlled non-inferiority trial (REDO study (3)) was performed in five centers in the Netherlands. Patients with rheumatoid arthritis responding well to rituximab (based on DAS28-CRP< 2.9 or clinical judgement) were randomized (1:2:2) to 1×1000mg, 1×500mg or 1×200mg rituximab respectively. DAS28-CRP and peripheral CD19+ B-cells were measured at baseline, three and six months. Primary analysis (per protocol with last observation carried forward (LOCF)) consisted of a hierarchical testing procedure comparing ultra-low doses (1×500mg at three and six months, then 1×200mg at three and six months) to 1×1000mg using a non-inferiority margin of 0.6 (on DAS28-CRP). DAS28-CRP change of study groups was compared using linear regression,

1a. Baseline characteristics (mean (sd) or n (%))				
	1000mg (n=29)	500mg (n=58)	200mg (n=55)	Total (n=142)
Age	63.8 (9.0)	64.0 (10.9)	64.2 (12.2)	64.0 (11.0)
Female	18 (62%)	37 (64%)	40 (73%)	95 (67%)
ACR1987/2010 positive	27 (93%)	57 (98%)	52 (95%)	136 (96%)
Disease duration in years	17.1 (11.1)	14.9 (10.7)	13.5 (7.2)	14.8 (9.6)
RF/ACPA positive	27 (93%)	54 (93%)	49 (89%)	130 (92%)
Duration of RTX use (years)	4.0 (2.8)	3.3 (2.7)	4.0 (2.4)	3.7 (2.6)
Concomitant csDMARD	20 (69%)	35 (60%)	32 (58%)	87 (61%)
Concomitant oral prednisone	4 (14%)	9 (16%)	9 (19%)	22 (15%)
1b. Flares, co-medication and (S)AEs during follow-up (n (%))				
Patients with flare(s)	3 (10%)	14 (24%)	10 (18%)	27 (19%)
Extra 1000mg RTX received*	0 (0%)	2 (3%)	2 (4%)	4 (3%)
Patients with ia gc injection(s)	2 (7%)	1 (2%)	4 (7%)	7 (5%)
Patients with im gc injection(s)	4 (14%)	7 (12%)	16 (29%)	27 (19%)
Patients with SAE(s)	3 (10%)	6 (10%)	4 (7%)	13 (9%)
Infections/patient years	1.24 (18/14.57)	0.52 (15/28.95)	0.55 (15/27.49)	0.68 (48/71.01)

*2 patients with regular RTX accidently given a few days before study end (protocol violation) not included
ia: intra-articular; im: intramuscular; gc: glucocorticoid; RTX: rituximab; SAE: serious adverse event.

Table 1



adjusted for baseline DAS28-CRP, RF/ACPA status and concomitant csDMARD use. Intention-to-treat (ITT) analyses were done similarly (including all cases without LOCF).

Results: The projected inclusion was met (n=142, table 1a). In both ultra-low dose groups two patients received an extra dose of 1000mg rituximab due to a flare. The 500mg dose was non-inferior to 1000mg at three months (-0.07 (95% CI -0.41 to 0.27)), but not at six months (0.29 (95% CI -0.08 to 0.65). The 200mg dose was non-inferior to 1000mg at both time points. Because of our pre-defined hierarchical testing, non-inferiority could not formally be inferred for the 200mg dose. ITT analyses showed non-inferiority for all comparisons. Mean DAS28-CRP scores remained low in all groups throughout the study, and B-cell counts decreased similarly at three months (figure 1). The incidence density of infections was lower in the 500mg group (rate ratio 0.42 (95% CI 0.21 to 0.83, p=0.01)) and in the 200mg group (rate ratio 0.44 (95% CI 0.22 to 0.88, p=0.02)) compared to the 1000mg group (table 1b).

Conclusion: Non-inferiority of retreatment with 1×500mg or 1×200mg rituximab versus 1×1000mg after 6 months could not formally be established. However, ultra-low doses appear similarly effective in the majority of RA patients, judged by non-inferiority of ITT analyses, DAS28-CRP course over time and B-cell results, with a better safety profile and possibly slightly more co-medication.

References:

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2. Shenoy et al. Arthritis Rheumatol. 2015;67(suppl 10).
3. den Broeder et al. Trials. 2017;30;18(1):403

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Abstract Number: 0932

Efficacy and Safety of E6011, an Anti-Fractalkine Monoclonal Antibody, in MTX-IR Patients with Rheumatoid Arthritis

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SESSION INFORMATION

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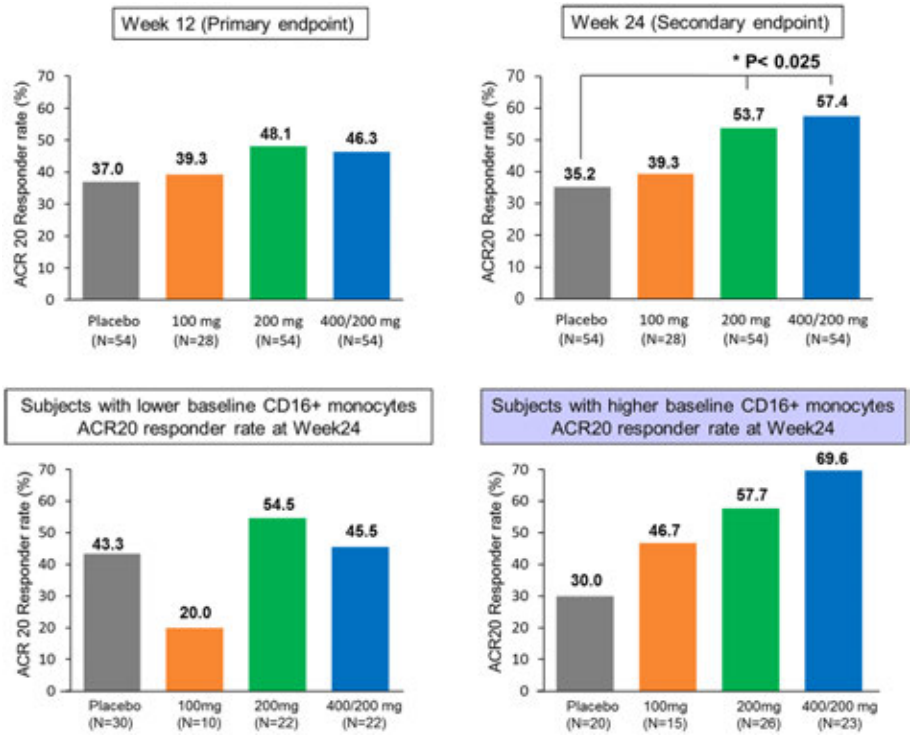
Session Time: 4:30PM–6:00PM

Background/Purpose: Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to dual actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1. We have conducted clinical trials of E6011, a novel humanized anti-FKN monoclonal antibody, for patients with rheumatoid arthritis (RA) in Japan[1]. This is the report of efficacy and safety results of E6011 from a Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group comparison study in RA patients inadequately responding to MTX (NCT02960438)

Methods: During the 24-week double-blind period, patients with moderately to severely active RA of inadequate response to MTX were randomly assigned to E6011 100 mg, 200 mg, 400/200 mg, or placebo groups at a 1:2:2:2 ratio. In the E6011 100 mg, 200 mg, and placebo groups, subjects received 100 mg, 200 mg, or placebo at Weeks 0, 1, 2, and every 2 weeks subsequently. In the E6011 400/200 mg group, subjects received 400 mg at Weeks 0, 1, 2, 4, 6, 8, 10 and then 200 mg every 2 weeks subsequently.

Results: A total of 190 subjects (54 in the placebo group, 28 in the 100 mg group, 54 in the 200 mg group, 54 in the 400/200 mg group) received study drug. Of the 190 subjects, 169 completed and 21 discontinued study treatment prematurely during the 24-week double-blind period. The ACR20 response rate at Week 12 (non-responder imputation), the primary endpoint, was 37.0% in the placebo group, 39.3% in the 100 mg group, 48.1% in the 200 mg group, and 46.3% in the 400/200 mg group (not statistically significant), and statistically significant difference from placebo in ACR20 response rate was found in the 200 mg and 400/200 mg groups at Week 24 (35.2% for placebo, 39.3% for 100 mg, 53.7% for 200 mg, 57.4% for 400/200 mg). In addition, we focused on CD16+ monocytes which highly expressing FKN receptor/CX3CR1 as a blood biomarker that linked to the clinical response to E6011. The whole patient population was divided into 2 groups according to the median value of baseline CD16+ monocyte percentage (Median: 10.35%). Much clearer ACR20 response was observed in a dose dependent manner in the subjects who showed higher baseline CD16+ monocytes over the median at Week 24 (NRI) (30.0% for placebo, 46.7% for 100 mg, 57.7% for 200 mg, and 69.6% for 400/200 mg) although such fashion was obscure in the subjects below the median value. This study explored the effect on progression of joint destruction by mTSS, a clear signal that E6011 suppressed the progression of joint destruction was not detected. Adverse events that occurred in ≥5% of subjects in any E6011 group were nasopharyngitis, upper respiratory tract infection, stomatitis, bronchitis, back pain, pharyngitis, and dental caries. As a results, E6011 was well tolerated with no notable safety concerns at doses of 100, 200, and 400/200 mg when administered subcutaneously for 24 weeks.



Conclusion: E6011 provided clinical improvements with a good safety profile in RA patients with inadequately responding to MTX. Especially, a higher efficacy of E6011 was suggested in patients with higher baseline CD16+ monocytes (%). This is the world-first evidence suggesting that a novel approach to target FKN/CX3CR1 interaction could be beneficial for RA.

Disclosure: Y. Tanaka, Abbvie, 8, AbbVie, 5, 8, Asahi-kasei, 2, Asahi-Kasei, 2, Asahi-kasei, BMS, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Ono, Pfizer, Sanofi, Takeda, UCB, 2, Astellas, 8, Astellas Pharma, 9, Astellas Pharma, Inc., 2, 3, 5, 8, 9, Astellas, BMS, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi-Tanabe, Pfizer, Sanofic, UCB, YL Biologics, 8, BMS, 2, 5, 8, Bristol-Myers, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Daiichi-Sankyo, 2, 8, Daiichi-Sankyo, Astellas, Eli Lilly, Chugai, Sanofi, Abbvie, Pfizer, YL Biologics, Bristol-Myers, 8, Eisai, 2, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 8, Genzyme, 5, Glaxo-Smithkline, UCB, Mitsubishi-Tanabe, Novartis, Eisai, Takeda, Janssen, Asahi-kasei, 8, Janssen, 8, Mitsubishi-Tanabe, 2, 8, Mitsubishi-Tanabe, Bristol-Myers, Eisai, Chugai, Takeda, Abbvie, Astellas, Daiichi-Sankyo, Ono, MSD, Taisho-Toyama., 2, Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, 2, Novartis, 8, Ono, 2, Pfizer, 5, 8, Pfizer Inc, 8, Roche, 5, Sanofi, 2, Takeda, 2, 8, Teijin, 8, UCB, 2, YL Biologics, 8; **T. Takeuchi**, AbbVie, 2, 5, 8, AbbVie GK, 2, 9, Asahi Kasei, 2, Asahikasei, 2, Asahikasei Pharma Corp., 2, Astellas, 2, 8, 9, Astellas Pharma Inc, 2, Astellas Pharma, Inc., 2, 5, 8, 9, Astra Zeneca, 2, AstraZeneca, 8, AYUMI, 2, 9, AYUMI Pharmaceutical Corporation, 2, BMS, 2, 8, Boehringer-ingelheim, 9, Bristol–Myers K.K., 9, Bristol-Myers, 2, Bristol-Myers Squibb, 8, Chugai, 2, 8, 9, Chugai Pharmaceutical Co, Ltd., 2, Daiichi Sankyo, 2, 8, 9, Daiichi Sankyo Co., Ltd., 2, Eisai, 2, 5, 8, 9, Eisai Co., Ltd., 2, Eli Lilly, 2, 8, Eli Lilly Japan, 9, Gilead Sciences, Inc., 9, GlaxoSmithKline K.K, 9, GSK, 8, Janssen, 2, 8, Janssen Pharmaceutical K.K, 9, Mitsubishi Tanabe, 2, 9, Mitsubishi Tanabe Pharma Co., 2, Mitsubishi-Tanabe Pharma Corp, 2, 8, 9, Nippon Kayaku, 2, Nipponkayaku, 2, 9, Nipponkayaku Co.Ltd., 2, Novartis, 2, 8, Novartis Pharma K.K, 2, 9, Novartis Pharma K.K., 2, Pfizer, 2, 8, Pfizer Japan, 2, 9, Pfizer Japan Inc., 2, Sanofi, 8, Sanofi K.K, 9, Shionogi & Co., 2, Shionogi & Co., LTD., 2, Taiho, 2, 8, 9, Taisho, 9, Taisho Toyama, 2, 8, Takahashi Industrial and Economic Research Foundation, 2, Takeda, 2, 8, Takeda Pharmaceutical Co., Ltd., 2, Teijin, 2, 8, UCB, 8, 9, UCB Japan, 9; **H. Yamanaka**, Teijin Pharma Limited, 5; **T. Nanki**, Eisai Co., Ltd., 2, 5, 8, Takeda Pharmaceutical Co., 8, Teijin Pharma Ltd., 2, 8, Eli Lilly Japan K.K., 2, 8, Bristol-Myers K.K., AbbVie GK., 2, Ono Pharmaceutical Co., Ltd., 2, 8, Novartis Pharma K.K., 2, 8, Asahikasei Phar-

ma Corp., 2, 5, 8, Mitsubishi-Tanabe Pharma Co., 2, 8, Chugai Pharmaceutical Co., 2, 5, 8, Astellas Pharma Inc., 2, 8, Ayumi Pharmaceutical Corporation, 2, 8, Pfizer Japan Inc., 2, 8, Daiichi Sankyo Co., Ltd., 2, Shionogi & Co., Ltd., 2, Sanofi K.K., 2, Nippon Kayaku Co., Ltd., 2, 8, Yutoku Pharmaceutical Ind. Co., Ltd., 2, UCB Japan Co., Ltd., 2, 5, Nihon Pharmaceutical Co., Ltd., 2, Bayer Yakuhin, Ltd., 2, Janssen Pharmaceutical K.K., 8, AbbVie GK, 8, Boehringer Ingelheim, 8; **H. Umehara**, None; **N. Yasuda**, KAN Research Institute, Inc., 3; **F. Tago**, Eisai Co., Ltd., 3; **Y. Kitahara**, Eisai Co., Ltd., 1, 3; **M. Kawakubo**, Eisai Co., Ltd., 1, 3; **K. Torii**, Eisai Co., Ltd., 1, 3; **S. Hojo**, Eisai Co., Ltd., 3; **T. Kawano**, KAN Research Institute, Inc., 3; **T. Imai**, KAN Research Institute, Inc., 3.

Abstract Number: 0933

Tumor Necrosis Factor Inhibitors Slow Radiologic Progression in Patients with Ankylosing Spondylitis: 18-year Longitudinal Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical II: Axial Spondyloarthritis Treatment
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: It is difficult to evaluate the role of TNF inhibitor therapy in slowing the radiologic progression in patients with ankylosing spondylitis (AS) because of frequent changes in disease activity and medication. In addition, the role of TNF inhibitors in slowing the radiologic progression was underestimated because most patients starting TNF inhibitors were in a high inflammatory state. Therefore, an analysis of time varying compounders such as disease activity is essential. The aim of this study was to investigate whether long-term treatment with TNF inhibitors can reduce radiographic progression in patients with AS using an 18-year longitudinal cohort data.

Methods: Of the 1,280 patients who followed for 18 years in single center cohort, data of 328 patients treated with TNF inhibitors were included. For each patient who received TNF inhibitors, the time interval was categorized based on the patient's TNF inhibitor status ('on the TNF inhibitors' and 'off the TNF inhibitors' intervals). The data were analyzed using the Modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS), erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and imputed at each time point by linear interpolation. We obtained 2315 intervals (1,063 intervals 'on the TNF inhibitors' and 1,252 intervals 'off the TNF inhibitors') from 328 patients with computable intervals. A multivariable linear regression with compound symmetry correlation structure within each patient was performed using a generalized estimating equation for rate of change in mSASSS (per year) as the outcome, and with ESR, CRP, and BASDAI as the time-varying covariate. A marginal structural model for inverse probability of treatment weighting (MSM with IPTW) was constructed to evaluate the underestimated effect of TNF inhibitors.

Results: The rate of mSASSS significantly decreased with the use of TNF inhibitors (b=-0.054, p=0.023 in the multivariable model) (Table 1). The adjusted rate of mSASSS with multivariable analysis was 0.916 per year during 'on the TNF inhibitors' and 0.970 per year during 'off the TNF inhibitors' period when the other covariates were fixed at their

Table 1. Association between mSASSS and covariates.

Independent variable	Univariate model				Multivariable model			
	Beta Estimate	95% CI LB	UB	P-value	Beta Estimate	95% CI LB	UB	P-value
Age at baseline	0.017	0.005	0.028	0.004	0.013	-0.001	0.027	0.067
Sex	-0.416	-0.715	-0.117	0.006	-0.564	-0.887	-0.242	0.001
HLA-B27	0.584	0.048	1.121	0.033				
Eye involvement	0.434	0.143	0.725	0.003	0.425	0.128	0.722	0.005
Peripheral involvement	-0.215	-0.511	0.081	0.155	-0.174	-0.474	0.126	0.255
ESR at start (log)	0.128	0.050	0.206	0.001	0.200	0.094	0.305	0.000
CRP at start (log)	0.045	-0.091	0.181	0.520				
BASDAI at start (sqrt)	-0.100	-0.245	0.044	0.173	-0.226	-0.408	-0.044	0.015
NSAIDs	-0.079	-0.209	0.051	0.235				
Steroids	0.134	-0.283	0.552	0.529				
cDMARDs	-0.335	-0.538	-0.133	0.001	-0.237	-0.494	0.020	0.070
TNF inhibitors	-0.054	-0.099	-0.009	0.017	-0.054	-0.101	-0.007	0.023

Table 2. Original data and data with Inverse Probability of Treatment Weighting

Covariates	Original Data			Data with IPTW		
	Off the TNF inhibitors	On the TNF inhibitors	SMD	Off the TNF inhibitors	On the TNF inhibitors	SMD*
Age (mean(sd))	32.59 (8.68)	32.68 (8.70)	0.010	33.20 (9.17)	32.97 (8.91)	0.025
Sex (female count (%))	101 (10.6)	120 (10.7)	0.004	88.2 (10.5)	107.0 (10.9)	0.011
Uveitis (yes count (%))	466 (48.8)	547 (48.8)	0.002	444.8 (53.1)	504.1 (51.2)	0.037
Peripheral Involvement (yes count (%))	538 (56.4)	628 (56.0)	0.009	508.6 (60.7)	580.8 (59.0)	0.034
ESR at start (log, mean(sd))	2.30 (1.08)	2.51 (1.17)	0.190	2.42 (1.14)	2.51 (1.19)	0.071
CRP at start (log, mean(sd))	0.02 (0.47)	0.17 (0.64)	0.274	0.13 (0.62)	0.19 (0.66)	0.083
cDMARDs (yes count (%))	27 (2.8)	55 (4.9)	0.108	41.6 (5.0)	52.8 (5.4)	0.018
NSAIDs (yes count (%))	101 (10.6)	305 (27.2)	0.434	158.9 (19.0)	204.8 (20.8)	0.046
Steroids (yes count (%))	16 (1.7)	17 (1.5)	0.013	35.2 (4.2)	16.3 (1.7)	0.152
BASDAI at start (sqrt, mean(sd))	2.90 (1.92)	3.90 (2.69)	0.429	3.35 (2.28)	3.86 (2.77)	0.199
Previous mSASSS rate (mean(sd))	20.03 (20.08)	19.46 (19.97)	0.028	20.97 (20.15)	20.18 (20.33)	0.039

*standardized mean difference

mean values. However, the role of TNF inhibitors was underestimated on the rate of mSASSS because ESR and CRP at the start of interval were significantly higher in 'on the TNF inhibitors intervals (b=-5.946, $p< 0.001$ and b=0.412, $p< 0.001$, respectively). To eliminate the effects of confounding variables such as ESR and CRP on the mSASSS, we

created a pseudo-population using an IPTW. (Table 2) The rate of mSASSS showed a greater decrease with the use of TNF inhibitors (b=-0.111, p< 0.001) than in the multivariable regression model. The adjusted rate of mSASSS was 0.848 per year during 'on the TNF inhibitors' and 0.959 per year during 'off the TNF inhibitors' intervals.

Conclusion: TNF inhibitor treatment significantly slowed radiologic progression when compared to other therapies. In addition, the effect of TNF inhibitors on radiological progress has been previously underestimated.

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Abstract Number: 0934

Predictors of Survival of Secukinumab Treatment in a Multicenter Cohort of 556 Spondylarthritis

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical II: Axial Spondyloarthritis Treatment

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Secukinumab (SEC) is an interleukin-17 inhibitor used to treat patients with axial spondylarthritis (axSpA) and psoriatic arthritis (PsA). Drug survival is often used as a proxy for treatment effectiveness and safety. We aim to assess SEC survival in routine clinical practice and to identify survival predictors associated.

Methods: We conducted a retrospective, longitudinal, observational, multicentric study including all patients with axSpA or PsA who received at least 1 injection of SEC between July 2016 and April 2019. We collected demographic and clinical characteristics, onset date, initial dosage and dosage modification of SEC, previous biologic Disease-modifying antirheumatic drugs (bDMARDs) and concomitant treatments. We classified the reason of discontinua-

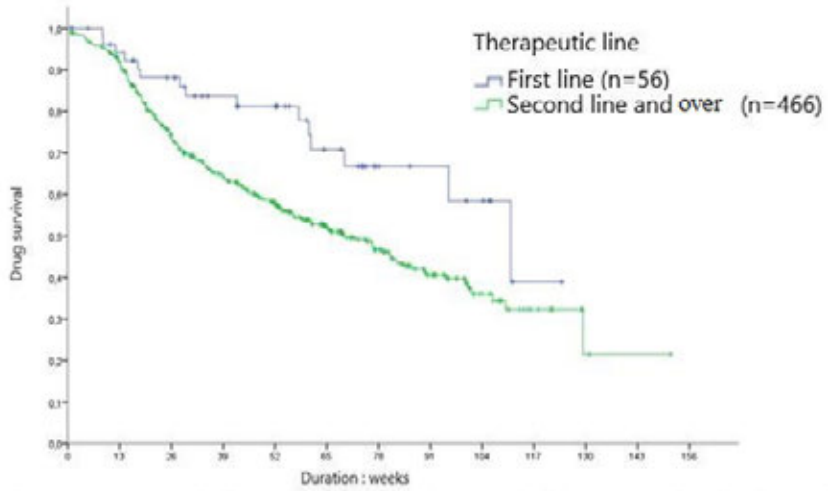

Figure 1 : Drug survival according to the therapeutic line among the whole population

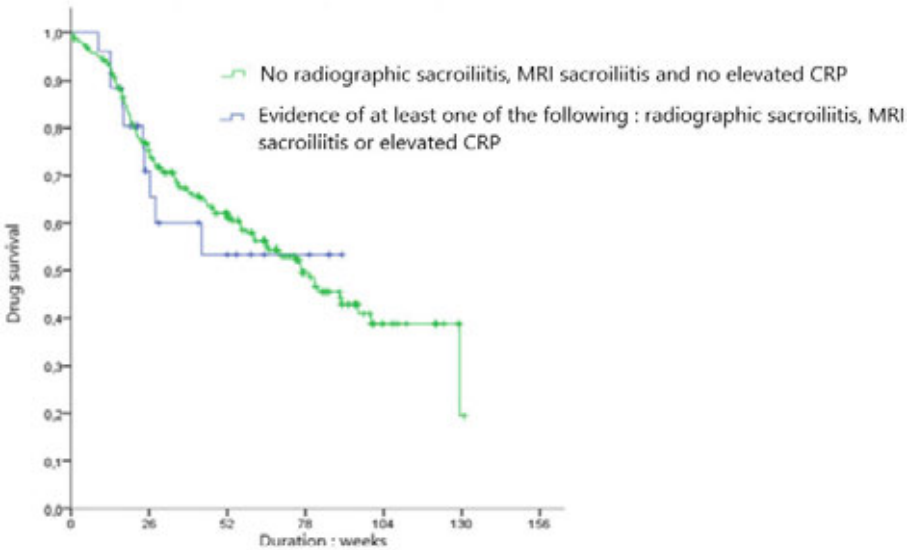

Figure 2 : Drug survival according to imaging and CRP status among the axSpA population

tion in lack of effectiveness, adverse events and others. Potential predictors evaluated were baseline age, gender, smoking status, previous bDMARDs and concomitant treatment. Among the axSpA cohort, evidence of radiographic sacroiliitis, MRI sacroiliitis or elevated CRP were also assessed as potential predictors. Drug survival was analyzed by the Kaplan-Meier method and differences of survival between groups was assessed by log-rank test.

Results: The main characteristics of the 556 patients (pts) included were the following: 338 (61%) axSpA , 183 (33%) PsA, 324 (58%) female, mean age 47 +/- 12 years, 221 (40%) smokers,160 (29%) radiographic sacroiliitis, 238 (43%) MRI sacroiliitis, 206 (37%) elevated CRP, 239 (43%) HLA B27 positive, mean BASDAI 48,9 +/-27%. SEC was associated to methotrexate (MTX) in 140 pts (25%) and was the first line bDMARD in 56 patients (10%).

The median drug survival (MDS) of SEC was 76 weeks (w) (interquartile range [65-88]). At 52w, 245 pts (60%) SpA were still treated with SEC. Among reasons of discontinuation, 172 (68%) pts discontinued SEC for lack of effectiveness, 46 (18%) for adverse events and 13 (5.1%) for others.

First line SEC administration was associated with a longer survival versus second line and more: 111w [83-138] vs 69w [57-81] (p=0.01) (figure 1). MDS was not significantly different according to gender, disease, MTX combo, elevated CRP, axSpA vs PsA and smoking status.

Among the axSpA pts, absence of radiographic or MRI sacroiliitis and normal CRP did not modify significantly SEC survival (p=0.85) (figure2).

Conclusion: In routine clinical practice, SEC median survival was 76 weeks. Fist line administration was associated with improved SEC retention. Lack of effectiveness was the most common reason of discontinuation.

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Abstract Number: 0935

Reduction of Anterior Uveitis Flares in Patients with Axial Spondyloarthritis Following 1 Year of Treatment with Certolizumab Pegol: 48-Week Interim Results from a 96-Week Open-Label Study

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical II: Axial Spondyloarthritis Treatment

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Acute anterior uveitis (AAU), inflammation of the anterior uveal tract, is the most common extraarticular manifestation in patients (pts) with axial spondyloarthritis (axSpA), reported by up to 40% of pts.[1]

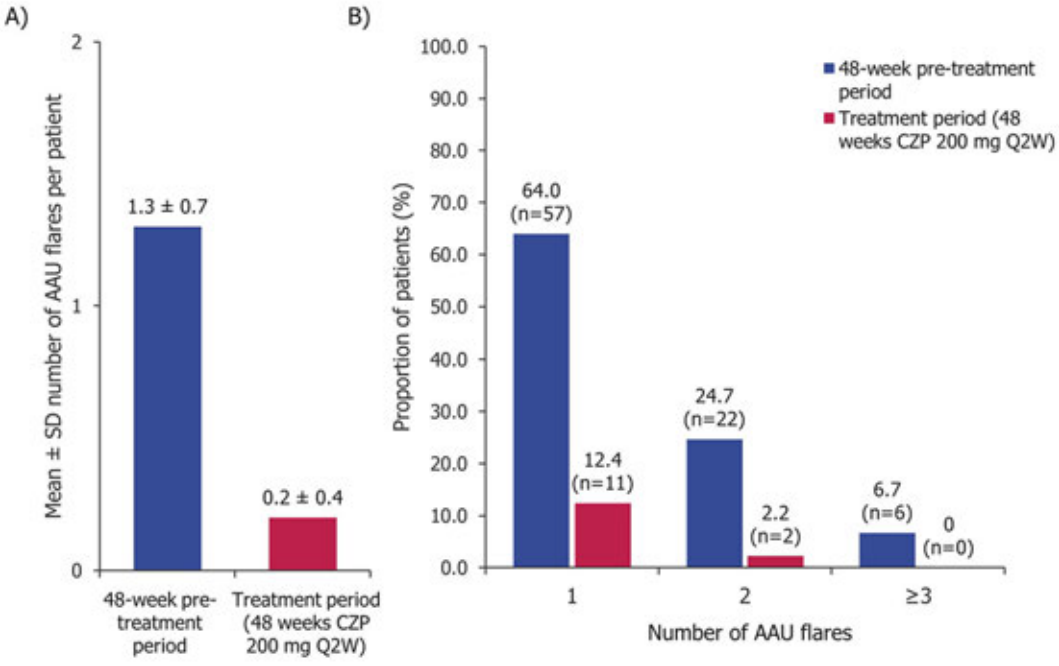
Uveitis is associated with a significant clinical burden; common symptoms include blurred vision, photophobia and pain.[2] Previous studies have shown that anti-TNFs can reduce the incidence of AAU flares in pts with radiographic axSpA (ankylosing spondylitis),[3,4,5] but few have focused on pts across the full axSpA spectrum. The aim of the C-VIEW study was to analyze the impact of certolizumab pegol (CZP) treatment on AAU flares in pts with active axSpA (radiographic and non-radiographic) and a recent history of AAU.

Table: Baseline characteristics of patients in C-VIEW

	CZP 200 mg Q2W (N=89)
Age (years), mean ± SD	46.5 ± 11.2
Male, n (%)	56 (62.9)
Racial group, n (%)	
Caucasian	87 (97.8)
Other	2 (2.2)
Diagnosis, n (%)	
Radiographic axSpA	75 (84.3)
Non-radiographic axSpA	14 (15.7)
Duration of axSpA (years), mean ± SD	8.6 ± 8.4
Time since onset of first uveitis flare (years), mean ± SD	9.9 ± 9.0
ASDAS, mean ± SD	3.5 ± 0.9
BASDAI, mean ± SD	6.5 ± 1.5

ASDAS: Ankylosing Spondylitis Disease Activity Score; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CZP: certolizumab pegol; Q2W: every 2 weeks; SD: standard deviation.

Figure: (A) Mean number of AAU flares experienced by patients in C-VIEW and (B) proportion of patients experiencing 1, 2 or ≥3 AAU flares



AAU: acute anterior uveitis; CZP: certolizumab pegol; Q2W: every 2 weeks; SD: standard deviation.

Methods: C-VIEW (NCT03020992) is an ongoing multicenter, open-label, phase 4 study. Pts had active axSpA according to the Assessment of SpondyloArthritis international Society (ASAS) classification criteria, a history of recurrent AAU (≥2 AAU flares in total and ≥1 AAU flare in the year prior to study entry), were HLA-B27 positive, and were eligible for anti-TNF treatment (active axSpA, previous failure of ≥2 NSAIDs, biologic naïve or had failed at most one anti-TNF). Pts received CZP 400 mg at Weeks (Wks) 0/2/4, then 200 mg every 2 wks through 96 wks. The primary variable was the incidence of AAU flares compared to historic rates. A pre-specified interim analysis compared AAU incidence in the 48 wks prior to CZP treatment initiation with the 48 wks of treatment, using Poisson regression adjusted for possible within-patient correlations, with period (pre- and post-baseline) and axSpA disease duration as covariates. Incidence rates (IR) were calculated based on the number of cases per pts at risk over 48 weeks. Observed data are reported.

Results: Of 115 enrolled pts, 89 initiated CZP treatment and 85 completed Wk 48. Baseline characteristics are shown in the **Table**. The 48-wk interim analysis revealed significantly fewer AAU flares per pt during CZP treatment compared to before treatment (**Figure**; Poisson-adjusted IR: 0.2 vs 1.5, $p< 0.001$). The number of pts experiencing 1 and ≥2 AAU flares (64.0% and 31.5%, respectively) was substantially reduced during CZP treatment (12.4% and 2.2%). In the 13 patients who had AAU flares both pre- and post-baseline, the mean duration of AAU flares was also reduced during CZP treatment from 97.4 to 58.4 days. After 48 wks CZP, pts' disease activity had improved substantially (mean ± SD Ankylosing Spondylitis Disease Activity Score [ASDAS]: 2.0 ± 0.9; BASDAI: 3.3 ± 2.1), with 31.4% of pts achieving ASAS partial remission and 29.1% ASDAS major improvement. No new safety signals were identified.

Conclusion: In this open-label study, we found a significant reduction in the AAU flare rate in axSpA pts with a history of recurrent AAU during the first 48 wks of CZP treatment. Pts also experienced significant improvement in axSpA disease activity during CZP treatment.

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Abstract Number: 0936

Earlier Treatment of Non-Radiographic Axial Spondyloarthritis with Certolizumab Pegol Results in Improved Clinical and Patient-Reported Outcomes

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical II: Axial Spondyloarthritis Treatment

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Session Time: 4:30PM–6:00PM

Table: Clinical and patient-reported outcomes in patients treated with PBO or CZP stratified by symptom duration

		CZP (n=159)		PBO (n=158)	
	Wk	Symptom duration: < 5 yrs (n=80)	Symptom duration: ≥ 5 yrs (n=79)	Symptom duration: < 5 yrs (n=77)	Symptom duration: ≥ 5 yrs (n=81)
ASDAS-MI	**12**	46.3 (37)	24.1 (19)	9.1 (7)	3.7 (3)
% (n)	**52**	55.0 (44)	39.2 (31)	7.8 (6)	6.2 (5)
ASAS40	**12**	58.8 (47)	36.7 (29)	11.7 (9)	11.1 (9)
% (n)	**52**	65.0 (52)	48.1 (38)	18.2 (14)	13.6 (11)
BASDAI	**0**	6.7 (1.3; 80)	7.0 (1.5; 79)	6.9 (1.3; 77)	6.7 (1.3; 81)
Mean (SD; n)	**12**	3.4 (2.1; 79)	4.5 (2.2; 78)	5.8 (2.1; 77)	5.6 (2.1; 81)
	52	2.8 (2.3; 79)	3.7 (2.5; 78)	5.5 (2.4; 77)	5.4 (2.2; 81)
Nocturnal spinal pain	**0**	6.2 (2.7; 80)	7.1 (1.8; 78)	6.4 (2.2; 77)	6.8 (2.0; 81)
Mean (SD; n)	**12**	2.8 (2.7; 79)	4.1 (2.5; 78)	5.5 (2.6; 77)	5.6 (2.5; 81)
	52	2.2 (2.7; 79)	3.2 (2.7; 78)	5.2 (2.7; 77)	5.7 (2.9; 81)
Fatigue [a]	**0**	7.1 (1.5; 80)	7.2 (1.7; 79)	7.3 (1.3; 77)	7.2 (1.4; 81)
Mean (SD; n)	**12**	3.8 (2.2; 79)	4.9 (2.4; 78)	6.1 (2.1; 77)	6.1 (2.3; 81)
	52	3.3 (2.7; 79)	4.1 (2.7; 78)	5.9 (2.3; 77)	6.0 (2.4; 81)
Morning stiffness [b]	**0**	6.7 (1.9; 80)	7.2 (1.7; 79)	6.8 (1.8; 77)	6.6 (1.8; 81)
Mean (SD; n)	**12**	2.9 (2.3; 79)	4.3 (2.2; 78)	5.7 (2.6; 77)	5.4 (2.2; 81)
	52	2.2 (2.3; 79)	3.6 (2.4; 78)	5.3 (2.8; 77)	5.1 (2.4; 81)
SF-36 PCS	**0**	35.0 (7.1; 80)	34.2 (7.0; 77)	34.0 (6.8; 77)	33.5 (7.2; 80)
Mean (SD; n)	**12**	44.3 (8.4; 79)	40.9 (8.4; 78)	35.8 (7.3; 76)	36.0 (8.4; 81)
	52	47.6 (8.9; 79)	42.1 (9.4; 78)	37.3 (8.2; 76)	36.7 (8.3; 81)
SF-36 MCS	**0**	41.7 (11.0; 80)	42.3 (11.0; 77)	41.7 (9.3; 77)	40.6 (10.8; 80)
Mean (SD; n)	**12**	47.7 (9.5; 79)	45.2 (11.4; 78)	42.6 (10.6; 76)	43.7 (11.1; 81)
	52	47.1 (10.5; 79)	47.3 (11.2; 78)	41.9 (11.9; 76)	43.4 (11.0; 81)

Missing values were imputed using double-blind last observation carried forward or, for ASDAS-MI and ASAS40, considered to be non-response. [a] BASDAI Q1; [b] Average of BASDAI Q5 and Q6. ASAS40: Assessment in SpondyloArthritis international Society 40% response; ASDAS-MI: Ankylosing Spondylitis Disease Activity Score – Major Improvement; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CZP: certolizumab pegol; MCS: mental component summary; PBO: placebo; PCS: physical component summary; SD: standard deviation; SF-36: 36-Item Short Form Survey (SF-36); wk: week; yrs: years.

Background/Purpose: Patients (pts) with axial spondyloarthritis (axSpA) often experience delayed diagnosis, which can lead to treatment delay. However, there are indications that earlier treatment with anti-TNFs can lead to a greater clinical response. Certolizumab pegol (CZP) has been shown to improve the signs and symptoms of non-radiographic (nr)-axSpA.[1] However, it is not known if earlier CZP treatment has a greater impact on efficacy in nr-axSpA. Here we report clinical and pt-reported outcomes in pts with active nr-axSpA treated with CZP or placebo (PBO) over 52 weeks (wks) stratified by their symptom duration.

Methods: C-axSpAnd (NCT02552212) is a 3-year, phase 3, multicenter study including a 52-wk double-blind, PBO-controlled period (completed).1 Pts had previous inadequate response to ≥ 2 NSAIDs and were randomized 1:1 to PBO or CZP (400 mg at Wks 0/2/4, then 200 mg every 2 wks). This post-hoc analysis reports outcomes at Wk 12 and Wk 52 in pts stratified by their baseline symptom duration (< 5 and ≥ 5 years; key clinical outcomes also reported for < 3 and ≥ 3 years). Outcomes included: Ankylosing Spondylitis Disease Activity Score – Major Improvement (ASDAS-MI), Assessment in SpondyloArthritis international Society 40% response (ASAS40), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), nocturnal spinal pain, fatigue (BASDAI Q1), morning stiffness (average of BASDAI Q5 and Q6), and the 36-Item Short Form Survey (SF-36) physical and mental component summary (PCS/MCS). Subjects with missing values or values observed after discontinuing double-blind study treatment were considered as non-responders for binary measures or, for quantitative measures, had the last observation from double-blind treatment carried forward.

Results: Of 317 recruited pts, 159 were randomized to CZP, and 158 to PBO. The median (range) baseline (BL) symptom duration was 4.9 (1.0–41.9) years for CZP-treated pts and 5.2 (1.1–38.2) years for PBO pts. 50.3% (80/159) CZP pts and 48.7% (77/158) PBO pts had a symptom duration < 5 years. At Wks 12 and 52, ASDAS-MI and ASAS40 responder rates, and improvements in BASDAI, nocturnal spinal pain, fatigue, morning stiffness and SF-36 PCS were substantially better among CZP-treated pts with shorter symptom duration (< 5 years at BL) vs longer symptom duration (**Table**). Amongst PBO pts, responses were low and there was no consistent trend in outcomes by symptom duration (**Table**). Similarly, using a cut-off of 3 years, responder rates for ASDAS-MI and ASAS40 were greater in CZP-treated pts with shorter symptom duration: at Wk 52, 56.4% (31/55) and 42.3% (44/104) of pts with < 3 and ≥ 3 years symptom duration achieved ASDAS-MI, respectively, while 65.5% (36/55) and 51.9% (54/104) achieved ASAS40.

Conclusion: In this post-hoc analysis, CZP-treated nr-axSpA pts with shorter symptom duration (< 5 vs ≥ 5 years) showed greater improvements across signs and symptoms of disease and in quality of life. To our knowledge, this is the first report indicating that early CZP treatment for nr-axSpA may be beneficial to pts.

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Abstract Number: 0937

Dual Neutralization of IL-17A and IL-17F with Bimekizumab in Patients with Active Ankylosing Spondylitis: 48-Week Efficacy and Safety Results from a Phase 2b, Randomized, Blinded, Placebo-Controlled, Dose-Ranging Study

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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Session Time: 4:30PM–6:00PM

Background/Purpose: The monoclonal antibody bimekizumab potently and selectively neutralizes both IL-17A and IL-17F. We report the 48-week efficacy and safety of bimekizumab in patients (pts) with active ankylosing spondylitis (AS; NCT02963506). The positive primary endpoint (Assessment in SpondyloArthritis International Society [ASAS] 40 response rate at Week 12) was previously reported.[1]

Methods: Eligible pts with active AS (Bath AS Disease Activity Index [BASDAI] ≥4; spinal pain ≥4 [0–10]) who fulfilled the modified New York criteria (central reading) with inadequate response/intolerance to NSAIDs were randomized 1:1:1:1:1 to subcutaneous (sc) bimekizumab 16 mg, 64 mg, 160 mg, 320 mg, or placebo every 4 weeks, for 12 weeks

(double-blind period). Subsequently, pts in the 16 mg, 64 mg, and placebo groups were re-randomized 1:1 to sc bimekizumab 160 mg or 320 mg every 4 weeks through Week 48; dosing in the original 160 mg and 320 mg groups was unchanged through Week 48 (dose-blind period). Efficacy endpoints included ASAS20, ASAS40, ASAS5/6, ASAS partial remission, and AS Disease Activity Score with C-reactive Protein (ASDAS-CRP) to Week 48; data presented for all pts who began the dose-blind period and received ≥1 dose of study drug. Non-responder imputation accounted for missing binary scores; multiple imputation accounted for missing continuous values.

Results: Of 303 randomized pts, 265 (87.5%) completed the 48-week treatment period. Pts (mean [SD] age 42.2 [11.8] years; males 84.5%; median [range] time from first symptoms 12.3 [0.2–47.2] years; mean [SD] BASDAI 6.5 [1.4]; mean [SD] total spinal pain 7.1 [1.7]; HLA-B27 positive 89.1%; prior anti-TNF therapy 11.2%) had similar baseline characteristics across treatment groups.

At Week 12, significantly more bimekizumab-treated pts vs placebo achieved ASAS40 (16 mg 29.5%; 64 mg 42.6%; 160 mg 46.7%; 320 mg 45.9%; placebo 13.3%; $p< 0.05$, all doses). ASAS40 response rates increased to Week 24 and were maintained to Week 48 (35.5–64.0%; Table 1). Improvements observed at Week 12 in other efficacy endpoints were sustained to Week 48: ASAS20 51.9–80.0%, ASAS5/6 41.9–80.0%, ASAS partial remission 20.6–34.4% (Table 1). At Week 12, mean improvement from baseline in ASDAS-CRP scores were from –0.3 to –1.7; scores improved further from baseline and were maintained to Week 48: from –1.6 to –2.0 (Table 1).

During the 48-week treatment period, treatment-emergent adverse events (TEAEs) were reported by 235/303 (77.6%) pts; 20/303 (6.6%) discontinued due to TEAEs (safety set; Table 2). One death (cardiac arrest, 160 mg group, double-blind period) was judged unrelated to study drug by the investigator. Most commonly reported TEAEs were nasopharyngitis, bronchitis, and pharyngitis. Irritable bowel disease was reported by 4/303 (1.3%) pts; no TEAEs of suicidal ideation were reported. Serious infections were reported by 4/303 (1.3%) pts (Table 2). $p< 0.05$

Table 1. Efficacy results at Week 48, presented by treatment groups during the dose-blind period (dose-blind set[a])

	Placebo→ BKZ 160 mg n=24	Placebo→ BKZ 320 mg n=34	BKZ 16→ 160 mg n=31	BKZ 16→ 320 mg n=27	BKZ 64→ 160 mg n=34	BKZ 64→ 320 mg n=25	BKZ 160→ 160 mg n=58	BKZ 320→ 320 mg n=61
ASAS40 response,[b] n (%)	13 (54.2)	18 (50.0)	11 (35.5)	11 (40.7)	19 (55.9)	16 (64.0)	34 (58.6)	38 (62.3)
ASAS20 response,[b] n (%)	17 (70.8)	22 (61.1)	17 (54.8)	14 (51.9)	25 (73.5)	20 (80.0)	45 (77.6)	46 (75.4)
ASAS5/6 response,[b] n (%)	15 (62.5)	16 (44.4)	13 (41.9)	13 (48.1)	21 (61.8)	20 (80.0)	37 (63.8)	40 (65.6)
ASAS partial remission,[b] n (%)	8 (33.3)	8 (22.2)	4 (12.9)	8 (29.6)	7 (20.6)	7 (28.0)	17 (29.3)	21 (34.4)
ASDAS-CRP,[c] change from baseline, mean (SD)	–1.7 (0.9)	–1.8 (0.9)	–1.6 (1.1)	–1.6 (0.9)	–2.0 (1.1)	–2.0 (1.0)	–1.8 (1.0)	–2.0 (0.9)

[a]Dose-blind set: all patients who began the dose-blind period and received at least 1 dose of study drug in that period

[b]Non-responder imputation accounted for missing ASAS values

[c]Multiple imputation accounted for missing ASDAS-CRP values

ASAS, Assessment in SpondyloArthritis International Society; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score-C-reactive protein; BKZ, bimekizumab; SD, standard deviation

Table 1. Efficacy results at Week 48, presented by treatment groups during the dose-blind period (dose-blind set)

Table 2. Overview of incidence of treatment-emergent adverse events, most frequently reported treatment-emergent adverse events, and TEAEs of interest during the treatment period (safety set[a])			
	BKZ 160 mg n=149	BKZ 320 mg n=150	All BKZ N=303[b]
Any TEAE, n (%)	103 (69.1)	122 (81.3)	235 (77.6)
Drug-related TEAEs, n (%)	48 (32.2)	54 (36.0)	110 (36.3)
Serious TEAEs, n (%)	5 (3.4)	6 (4.0)	13 (4.3)
Discontinuations due to TEAEs, n (%)	7 (4.7)	10 (6.7)	20 (6.6)
Deaths, n (%)	1 (0.7)	0	1 (0.3)
TEAEs reported by ≥5% in any treatment group, n (%)			
Nasopharyngitis	13 (8.7)	19 (12.7)	34 (11.2)
Bronchitis	4 (2.7)	12 (8.0)	18 (5.9)
Pharyngitis	11 (7.4)	7 (4.7)	18 (5.9)
Upper respiratory tract infection	5 (3.4)	11 (7.3)	17 (5.6)
Oral candidiasis	8 (5.4)	8 (5.3)	16 (5.3)
Oral fungal infection	8 (5.4)	6 (4.0)	14 (4.6)
TEAEs of interest, n (%)			
IBD[c]	1 (0.7)	2 (1.3)	4 (1.3)[d]
Opportunistic infections	0	0	1 (0.3)[e]
Depressive disorders	0	0	1 (0.3)
Serious TEAEs of infection	3 (2.0)	1 (0.7)	4 (1.3)
Suicidal ideation and behavior[f]	0	0	0

[a]Safety set: all randomized patients who received at least 1 dose of study drug

[b]The all BKZ group included 5 patients who received BKZ in the double-blind period but did not receive BKZ 160 mg or 320 mg: 2 patients in the 16 mg group and 2 patients in the 64 mg group discontinued before re-randomization; 1 patient in the 16 mg group did not start the dose-blind period. In addition, 1 patient received doses of 160 mg and 320 mg in error and was therefore included in both the 160 mg and 320 mg groups, but only once in the all-BKZ group

[c]IBD was defined as the higher-level MedDRA term of non-infective colitis; including both incident cases and disease flares

[d]One patient reported IBD while receiving bimekizumab 16 mg during the double-blind period

[e]This patient reported an opportunistic infection of Herpes zoster while receiving bimekizumab 16 mg during the double-blind period

[f]Suicidal ideation as measured by the electronic Columbia Suicide Severity Rating Scale (eCSSRS) was reported by 2 patients at baseline, 3 patients at Week 1, 1 patient at Week 8, and by no patients for the remainder of the 48-week treatment period (dose-blind set). No suicidal behavior as measured by the eCSSRS was reported throughout the 48-week treatment period

BKZ, bimekizumab; IBD, irritable bowel disease; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event

Table 2. Overview of incidence of treatment-emergent adverse events, most frequently reported treatment-emergent adverse events, and TEAEs of interest during the treatment period (safety set) BKZ 160 mg

Conclusion: Following positive results at Week 12,[1] this Phase 2b study demonstrated the sustained efficacy of bimekizumab in pts with active AS to Week 48. Bimekizumab was generally well tolerated and no new or unexpected safety findings were identified.

References:

1. van der Heijde ARD 2018;77(Suppl.2):A70

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Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **L. Gensler**, AbbVie, 2, 5, Abbvie, 2, 9, Amgen, 2, Amgen, AbbVie and Novartis, 2, Center for Disease Control, 8, Division of Vaccine Injury Compensation, 8, Eli Lilly, 5, 9, Eli Lilly and Company, 9, Galapagos, 5, 9, Galapagos, Janssen, Eli Lilly, Novartis, Pfizer, and UCB, 5, Janssen, 5, 9, Novartis, 2, 5, 9, Pfizer, 2, 9, Spondylitis Association of America, 6, Spondyloarthritis Research and Treatment Network (SPARTAN), 6, UCB, 2, 5, 9, UCB Pharma, 2, 9; **A. Deodhar**, AbbVie, 2, 5, 9, Abbvie, 5, 8, Abbvie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, and UCB Pharma, 5, 8, AbbVie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GSK, Galapagos, Janssen, Novartis, Pfizer and UCB, 5, AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Glaxo Smith and Klein, Janssen, Novartis, Pfizer, UCB, 5, Amgen, 5, 8, 9, BMS, 2, 5, 8, BMS, Eli Lilly, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, 2, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, UCB Pharma, 2, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, 8, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, 9, Eli Lilly and Company, 2, 5, Eli Lilly,, 5, Eli Lilly, GSK, Novartis, Pfizer and UCB, 2, Galagagos, 5, Galapagos, 5, 8, 9, Glaxo Smith & Klein, 2, Glaxo Smith & Kline, 2, 5, 8, Glaxo Smith Klein, 5, Glaxo SmithKlein, 2, 5, GlaxoSmithKlein, 2, 5, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, Janssen, 2, 5, 8, 9, Janssen Pharmaceutica, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9; **X. Baraliakos**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, BMS, 2, 5, 8, 9, Bristol-Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, 9, Chugai, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Lilly, 2, 8, 9, Merck, 2, 5, 8, MSD, 2, 5, 8, 9, Novartis, 2, 5, 8, 9, Novatis, 2, 5, 8, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9, UCB Pharma, 2, 5, 8, Werfen, 2, 5, 8; **D. Poddubnyy**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 2, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8; **A. Kivitz**, AbbVie, 5, Amgen, 1, 4, 5, Boehringer Ingeleheim, 5, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 5, 8, Flexion Therapeutics, 8, Genzyme, 5, 8, Gilead, 1, 4, 5, Gilead Sciences, Inc., 4, Horizon, 8, Janssen, 5, Janssen Research & Development, LLC, 2, Merck, 8, Novartis, 1, 4, 8, Pfizer, 1, 4, 5, 8, Regeneron, 1, 5, 8, Sanofi, 1, 4, 5, 8, Sun Pharma, 5, SUN Pharma Advanced Research, 5, UCB, 5; **M. Oortgiesen**, UCB Pharma, 3, 4; **D. Baeten**, UCB Pharma, 3, 4; **N. Goldammer**, UCB Pharma, 3, 4; **J. Coarse**, UCB, 3, UCB Pharma, 3, 4; **M. Farmer**, UCB Pharma, 3, 4; **M. Dougados**, AbbVie, 2, 5, 8, Amgen, 5, Biogen, 5, BMS, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, Merck, 2, 5, Merck Inc, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 0938

TNF Inhibitors Reduce Spinal Radiographic Progression in Axial Spondyloarthritis by Mechanisms Associated with but Also Independent of Disease Activity

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical II: Axial Spondyloarthritis Treatment

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

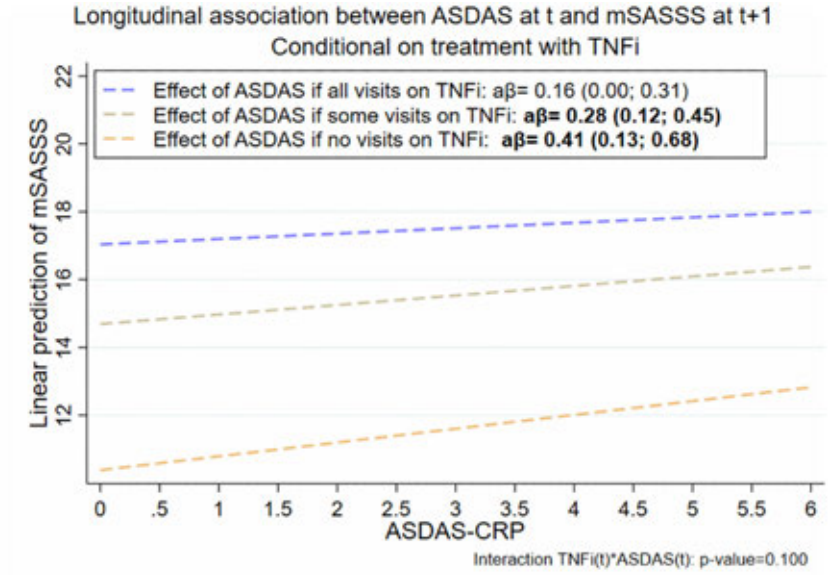

Figure. Longitudinal effect of ASDAS at the beginning of each 2-year interval on mSASSS 2 years later conditional on TNFi treatment group (multivariable linear GEE model with autoregression adjusted for symptom duration, gender, HLA-B27 and number of previous TNFi).

Background/Purpose: Recent observational data suggest that TNFi reduce spinal radiographic progression in radiographic axial spondyloarthritis (r-axSpA) mostly by inhibiting disease activity[1]. Yet, resolution on the controversial effect of TNFi on structural progression is yet to be achieved. We aimed to investigate whether in r-axSpA TNFi have an indirect (through ASDAS) and/or direct effect on spinal radiographic progression.

Methods: Patients (pts) with axial spondyloarthritis (axSpA) fulfilling the modified New York criteria (mNY) were included in this prospective, observational cohort (ALBERTA FORCAST). Clinical and imaging data were collected at baseline and every 2 years up to 10 years of follow-up. Radiographs of the spine were independently scored by 2 central readers and one adjudicator (if disagreement), with known chronological order but blinded to clinical data, using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The indirect effect of TNFi on mSASSS progression was evaluated by testing the interaction between TNFi and ASDAS at the start of each 2-year interval (t). If significant ($p< 0.15$) the association between ASDAS at t and mSASSS at the end of the interval (t+1) was assessed in 3 groups of exposure to TNFi: i. treatment in all visits; ii. treatment in some visits and iii. Never treated. The direct effect of TNFi on mSASSS progression was evaluated by testing the association between TNFi at t and mSASSS at t+1 (adjusting for ASDAS at t). Multivariable GEE models adjusted for mSASSS at t (autoregression) and for a set of potential confounders defined a priori on clinical grounds (Figure). In a sensitivity analysis, the direct effect of TNFi was also tested after adjusting for a propensity score (PS), to take confounding by indication into account.

Results: In total, 314 pts were included [74% males, mean symptom duration 17.8 (SD 11.7) years, 83% HLA-B27 positive and 7% previously treated with ≥1 TNFi]. The interaction between ASDAS and TNFi at t was significant (p=0.10). A gradient was seen for the effect of ASDAS at t on mSASSS at t+1, which was more than 2 times higher in patients never treated with TNFi (β (95% CI): 0.41 (0.13; 0.68) compared to those always treated [β (95% CI): 0.16 (0.00; 0.31)] (Figure), showing that treatment with TNFi diminishes the effect of ASDAS on mSASSS. In addition to the indirect effect, TNFi also directly associated with less mSASSS progression: Pts receiving TNFi at t had on average 0.87 mSASSS-units less on t+1 compared to those not treated [β (95% CI): -0.85 (-1.35; -0.35)] and this was noted independently of ASDAS. Importantly, this effect remained significant after PS-adjustment [β (95% CI): -0.80 (-1.37; -0.22)].

Conclusion: This data indicates that treatment with TNFi limits spinal radiographic progression in pts with r-axSpA only partially by decreasing disease activity. A direct effect of TNFi in reducing mSASSS progression, and independent of ASDAS inflammation, is also seen suggesting that other mechanisms also contribute to structural modification by TNFi.

Disclosure: A. Sepriano, None; **S. Ramiro**, AbbVie, 5, 8, Eli Lilly, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8; **S. Wichuk**, None; **P. Chiowchanwisawakit**, None; **T. MacCosham**, None; **J. Paschke**, None; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **R. Landewé**, Abbott, 2, 5, 8, Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8; **W. Maksymowych**, Abbvie, 2, 5, 8, Boehringer, 5, 8, Celgene, 5, 8, Galapagos, 5, 8, Lilly, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 5, 8.

Abstract Number: 0939

A Phase II Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Obinutuzumab or Placebo in Combination with Mycophenolate Mofetil in Patients with Active Class III or IV Lupus Nephritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical III: Clinical Trials II
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Randomized trials in lupus nephritis (LN) of type I anti-CD20 monoclonal antibodies failed to demonstrate superiority over standard of care alone. NOBILITY (NCT02550652) is a Phase II, randomized, double-

Table 1. Response Rates at Week 52

	Obinutuzumab + MMF N = 63	Placebo + MMF N = 62	Difference, % (80% CI)	*P* Value
CRR, n (%)	22 (34.9)	14 (22.6)	12.3 (2.1 to 22.6)	0.1145
Overall response (CRR or PRR), n (%)	35 (55.6)	22 (35.5)	20.1 (8.9 to 31.3)	0.0246
mCRR, n (%)	25 (39.7)	16 (25.8)	13.9 (3.2 to 24.5)	0.0900

CRR, complete renal response; mCRR, modified CRR, which excluded the urinary sediment criterion; MMF, mycophenolate mofetil; PRR, partial renal response.

Table 2. Adverse Events Through Week 52

	Obinutuzumab + MMF N = 63	Placebo + MMF N = 62
AEs, n (%)	55 (87.3)	52 (83.9)
Serious AEs, n (%)	9 (14.3)	13 (21.0)
Deaths, n (%)	0	2 (3.2)
Serious infection, n (%)	1 (1.6)	8 (12.9)
Infusion-related reaction, n (%)	10 (15.9)	6 (9.7)

AE, adverse event; MMF, mycophenolate mofetil.

blind, placebo (PBO)-controlled study designed to test the hypothesis that enhanced B-cell depletion with the type II anti-CD20 monoclonal antibody obinutuzumab (OBI) will result in improved responses in proliferative LN.

Methods: 125 patients with biopsy-proven ISN/RPS 2003 Class III or IV LN within 6 months and urine protein to creatinine ratio (UPCR) > 1 on a 24-hour collection were randomized to receive OBI 1000 mg or PBO infusions on days 1, 15, 168, and 182 with safety and efficacy assessments through week 104. All patients received mycophenolate mofetil (MMF) and corticosteroids; a corticosteroid taper was mandatory. The primary endpoint was complete renal response (CRR) at week 52, defined as achievement of UPCR < 0.5, normal serum creatinine not increased by > 15% from baseline, and urine RBCs < 10/hpf without RBC casts. Key secondary endpoints were achievement of overall (complete or partial) renal response (ORR), modified CRR without urinary sediment, and improvements in serologic markers of activity. Peripheral B cells were measured using high sensitivity flow cytometry (HSFC). The prespecified alpha level was 0.2.

Results: At baseline, mean UPCR was 3.1 g/g and mean serum creatinine was 0.84 mg/dL. The primary endpoint, CRR at week 52, was achieved by 34.9% of patients in the OBI group and 22.6% in the PBO group (12.3% delta; 80% CI 2.1% to 22.6%; $P = 0.115$). 55.6% of patients in the OBI group and 35.5% in the PBO group achieved ORR at week 52 (20.1% delta; 80% CI 8.9% to 31.3%; $P = 0.025$). 91% of patients in the OBI group had no detectable peripheral B cells by HSFC at day 28. Significant improvements in anti-dsDNA titers and C3 and C4 levels were observed with OBI compared with PBO. There were no unexpected safety findings. OBI was not associated with increased rates of serious adverse events (14.3% vs. 21.0%) or serious infections (1.6% vs. 12.9%) compared with PBO. Infusion-related reactions were more common with OBI (15.9% vs. 9.7%) and were generally mild. Two deaths occurred prior to week 52, both in the PBO group.

Conclusion: NOBILITY met its primary and key secondary efficacy endpoints. At one year, OBI resulted in increased complete and partial renal responses compared with placebo when added to MMF and corticosteroids for the treatment of proliferative LN. OBI was not associated with increases in rates of serious adverse events or serious infections. Forthcoming data through week 104 will permit further assessment of the longer term safety and efficacy of OBI in proliferative LN.

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Abstract Number: 0940

Response to Placebo in Randomized Clinical Trials with Biologics in Non-renal, Non-neuropsychiatric Systemic Lupus Erythematosus: A Systematic Review and Pooled Analysis

Konstantinos Tselios,[1] Laura Wakani,[2] Dafna Gladman,[3] Jiandong Su,[4] and Murray Urowitz[4], [1]University Health Network, University of Toronto, Toronto, Canada, [2]University Health Network, Toronto, Canada, [3]Toronto Western Hospital, Toronto, Canada, Toronto, ON, Canada, [4]University Health Network, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: SLE – Clinical III: Clinical Trials II
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Most randomized controlled trials (RCTs) with biologic medicines in systemic lupus erythematosus (SLE) failed to reach their respective end-points with the rates of the response to placebo (plus standard of care treatment) being unexpectedly high. The aim of this systematic review was to quantify the response to placebo for different end-points in the RCTs in non-renal, non-neuropsychiatric lupus patients.

Response rates at 48-52 weeks for placebo-treated patients from 12 RCTs in non-renal, non-neuropsychiatric SLE

Outcome	Patients (responders/all)	Response rate (%)	Range of response (%)
Primary end-point*	940/2621	33.5	17.5-48.6
SRI-4	910/2319	39.2	32.3-48.4
SRI-5	345/1240	27.8	20.4-39.3
SRI-6	334/1240	26.9	18.9-37.4
BICLA	238/722	33	25.7-36.1
Patients reducing prednisone to ≤7.5mg/day	141/919	15.3	12-26.6
Normalization of anti-dsDNA antibodies	142/1829	7.8	6-9.7
Normalization of C3	375/1829	20.5	14-22
Normalization of C4	177/1074	16.5	7.7-21.9

*As defined by each study
SRI-4: SLE Responder Index 4 (reduction of ≥4 in SLEDAI-2K, no worsening in PGA, no new A or two new B scores in the British Isles Lupus Assessment Group, BILAG)
SRI-5: as above with ≥5 reduction in SLEDAI-2K
SRI-6: as above with ≥6 reduction in SLEDAI-2K
BICLA: (BILAG-based Combined Lupus Assessment) improvement from baseline in the BILAG-2004 score, no worsening in SLEDAI-2K and PGA, no unpermitted changes in concomitant medications

Methods: The Pubmed database was searched from 2000 to April 2019 for phase II/III RCTs that assessed the efficacy and safety of biologic drugs in human non-renal, non-neuropsychiatric SLE at 48 or 52 weeks after randomization. Data on efficacy (primary and secondary end-points) and safety (serious adverse events, serious infections, malignancies and deaths) of the placebo-treated patients were collected in a pre-established data retrieval form. Descriptive statistics were used.

Results: Twelve RCTs (n=7940 in total) were included. Patients who received placebo (n=2621) were mostly females (2460, 93.9%) and Caucasians (1621, 61.8%) with a mean age of 39.7±12.2 years and mean disease duration of 6.5±6.8 years. Their initial SLE Disease Activity Index 2000 (SLEDAI-2K) was 10.3±3.7 whereas 1278/2096 (61%) were positive for anti-dsDNA antibodies, 881/2039 (43.2%) had low C3 and 772/2039 (37.9%) low C4 at randomization. Their standard of care (SOC) treatment included glucocorticosteroids in 2128/2464 (86.4%) [mean dose 11.5±7.9mg/day, prednisone >7.5mg/day in 1062/1917, 55.4%], antimalarials in 1619/2376 (68.1%) and immunosuppressives in 1067/2376 (44.9%) (509 azathioprine, 369 methotrexate, 270 mycophenolate). There were no significant differences regarding demographics, clinical manifestations and treatment between placebo-treated patients and individuals in the active arms of most RCTs. The response rates of the placebo-treated patients for the different end-points are shown in the table.

The mean reduction in SLEDAI-2K (n=1267) was 4.05 (range 3.3-4.8) and in the Physician Global Assessment (PGA, 0-100 scale, n=1554) 19.9 (range 11.7-23.8). The sample size in 10 studies was calculated with an expectation of an average 15% difference between the active drug and placebo (range 12-20%) in achieving the primary end-point; the actual difference was 9% on average (range 1.2-17.9%). Regarding safety, there were 449/2621 (17.1%) serious adverse events with 105/1899 (5.5%) serious infections, 6/1310 (0.5%) malignancies and 17/2621 (0.65%) deaths.

Conclusion: One third of the patients treated with placebo plus SOC achieved their respective primary end-points in RCTs with biologics in non-renal, non-neuropsychiatric SLE. The response rate was even higher for certain end-points, such as the SRI-4, while it decreased with more stringent end-points. It is possible that certain patient characteristics (prevalent cases with a long disease duration at enrollment and unspecified phase of the disease course i.e. recent or chronic, persistent flare at randomization) and study design (use of glucocorticosteroids and immunosuppressives, stringency of the outcomes) influence the response to placebo.

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Abstract Number: 0941

Treatment of Lupus Nephritis with anti-CD20 Followed by Anti-BAFF: Impact on B Cell Reconstitution, B Cell Subsets, and Autoreactivity

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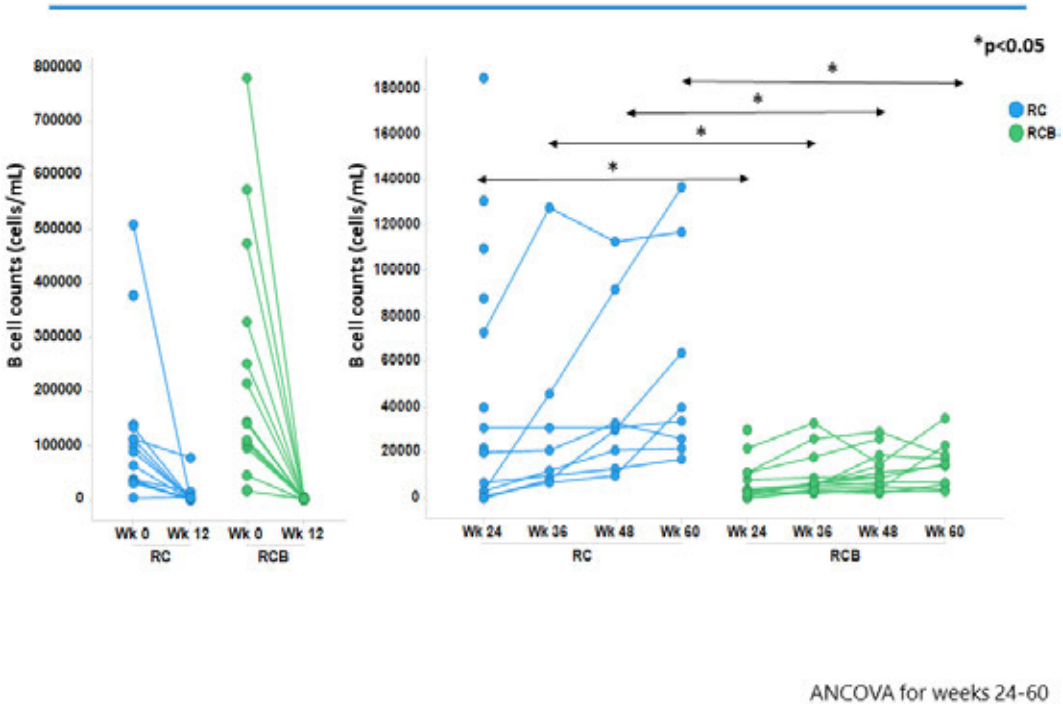

Figure 1. B cell counts in Per Protocol Sample

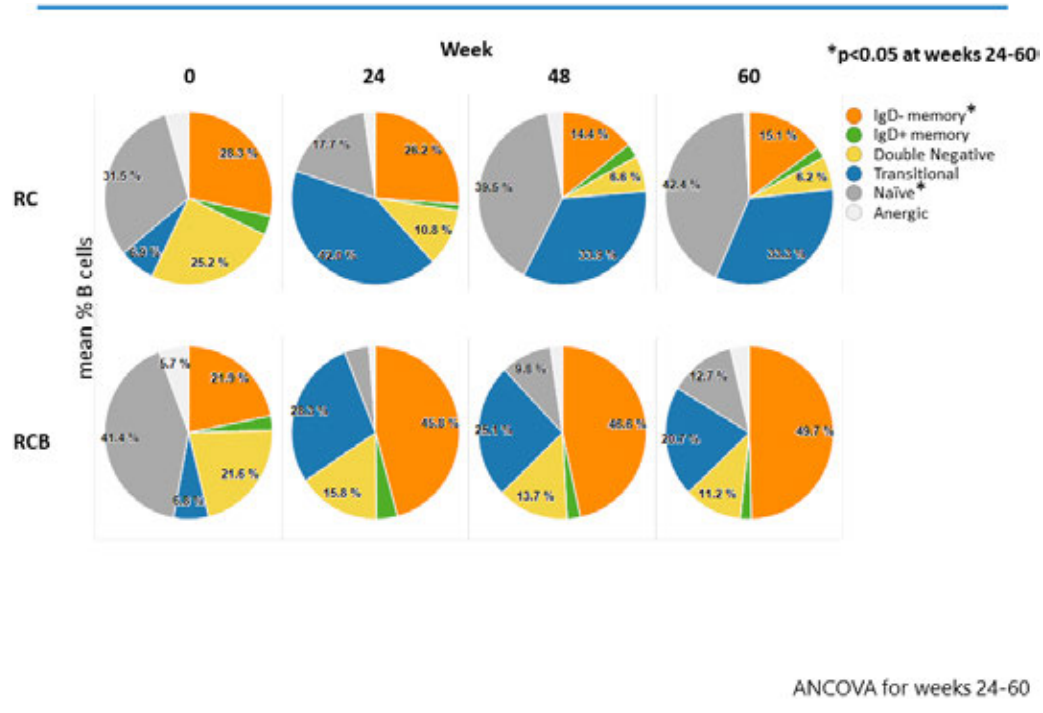

Figure 2. Relative Proportions of B Cell Subpopulations Differ Between RC v. RCB Subjects in Per Protocol Sample

Background/Purpose: Despite the relevance of B cells in lupus, two clinical trials of anti-CD20 failed to meet primary endpoints in patients with lupus and lupus nephritis (LN). One explanation is that after treatment with anti-CD20, BAFF levels are elevated, which may favor survival and expansion of pathogenic autoreactive B cells. The CALIBRATE study (NCT 02260934) was designed to determine whether addition of anti-BAFF (belimumab) could enhance the clinical and biological effects of anti-CD20 (rituximab), and to assess safety of the combination.

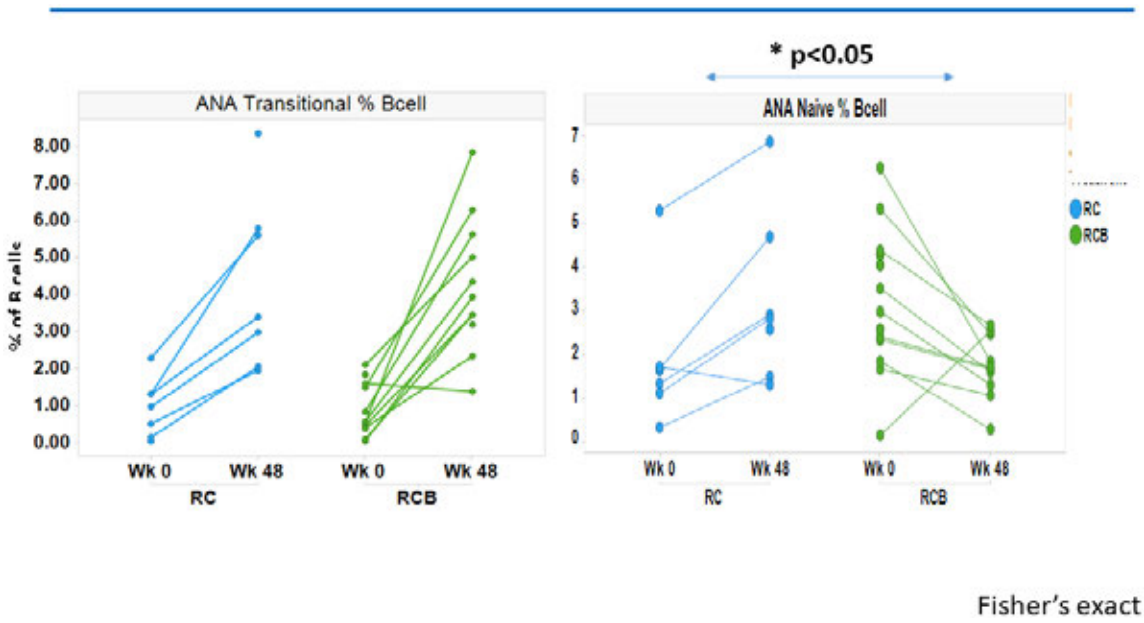

Figure 3. Proportions of ANA+ transitional and Naïve B cells in RC v. RCB Subjects in Per Protocol Sample

Methods: Forty-three patients with active LN despite conventional treatment were enrolled in a prospective randomized open-label trial that compared two regimens. All subjects received iv rituximab (1000 mg), CYC (750 mg), and methylprednisolone (100 mg) at wks 0 and 2, followed by 40 mg/d prednisone with taper to 10 mg/d by wk 12. At wk 4, subjects were randomized to belimumab (10 mg/kg iv at wks 4, 6, 8 and then every 4 wks) plus prednisone (RCB, n=21) or prednisone alone (RC, n=22) to wk 48. After wk 48, patients received only prednisone. Complete response (CR) was defined as: (i) urine protein:creatinine ratio (UPCR) < 0.5; (ii) eGFR ≥ 120 or, if < 120, eGFR >80% of screening; and (iii) prednisone dose of 10 mg/d. Partial response (PR) differed only in the UPCR criterion (>50% reduction). B cell populations and autoreactive B cells (ANA+ B cells) from peripheral blood were analyzed in Per Protocol (PP) samples as previously described (Arthritis Rheum 2016;68:2210) at wk 0, 24, 48 and 60

Results: B cell depletion occurred in both groups by wk 12. Partial reconstitution was observed in the RC group by wk 24 compared to the RCB group. B cells counts in the RCB group remained lower at wk 60, 12 wks after belimumab was discontinued (Figure 1). In both groups, the proportion of transitional B cells was increased compared to baseline at all time points. Proportions of naïve B cells decreased and switched memory B cells increased in the RCB group compared to the RC group, and these differences persisted after belimumab was discontinued (Figure 2). In both groups, the proportion of ANA^+ transitional cells in the B cell compartment was increased at wk 48. In contrast, the proportion of ANA^+ naive cells was increased in the RC group and decreased in the RCB group (Figure 3).

At wk 48, CR was 38% in the RCB group and 32% in the RC group; overall response (CR+PR) was 52% in the RCB group compared to 41% in the RC group (*p*-ns). Five subjects in the RC group and 2 in the RCB group experienced grade 3 or higher infectious adverse events, and all resolved. At wk 48, in PP patients, median IgG levels remained within the normal range in both groups. Resolution of hypocomplementemia and positive anti-DNA antibody status was not statistically different between groups.

Conclusion: Treatment with anti-BAFF following anti-CD20 was not associated with increased risk of infections or adverse events. The sequential treatment impaired B cell reconstitution, altered proportions of B cell subpopulations, and decreased the relative proportion of autoreactive ANA^+ naïve cells in circulating B cells. In this phase 2a study, addition of anti-BAFF did not significantly improve clinical outcome.

Disclosure: Y. Atisha Fregoso, None; **S. Malkiel**, None; **K. Harris**, None; **S. Kanaparthi**, None; **M. Byron**, None; **L. Ding**, None; **D. Smilek**, None; **D. Wofsy**, Celgene, 5, Genentech, 5, GlaxoSmithKline, Lilly, 5, Novartis, Principia, 5; **M. Dall'Era**, Biogen,, 5, Genentech, 5, Janssen Pharmaceuticals, 5, Kezar Life Sciences, 2, Pfizer, 5; **C. Aranow**, EMD Serrono, 2, GlaxoSmithKline, 2, Janssen, 2, Takeda, 2, UCB, Inc, 2, Xencor, 2; **B. Diamond**, GSK, 5, Jansen, 5, Lilly, 5.

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A Randomized Prospective Trial to Assess the Clinical Utility of Multianalyte Assay with Complement Activation Products in Diagnosing Systemic Lupus Erythematosus

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Background/Purpose: Cell-Bound Complement Activation Products (CB-CAPs) in multianalyte assay panel (MAP) is a diagnostic immunology laboratory test with established clinical validity in distinguishing systemic lupus erythematosus (SLE) from other rheumatic diseases. The Clinical Laboratory Assessment and Recommendation (CARE) for Lupus study was designed to evaluate the clinical utility of this testing method in diagnosing SLE.

Methods: CARE for Lupus was a multicentered, randomized, and prospective study that enrolled patients evaluated for a suspicion of SLE by board certified rheumatologists (within three months of referral). At baseline, all patients presented with an history of antinuclear antibody positivity and were randomized (1:1) to standard diagnostic laboratory testing (SDLT, all ordered at the discretion of the rheumatologist) or to CB-CAPs/MAP testing, which reports a two-tiered index test result and has 80% sensitivity and 86% specificity for SLE. The primary end-point was based on the change in the physician likelihood of SLE on a 5-point Likert scale collected before and after testing (at 4 and 12-weeks). Changes in pharmacological treatment based on laboratory results were assessed in both arms. Statistical analysis consisted of Wilcoxon and Fisher's Exact tests.

Results: A total of 145 subjects were enrolled at 32 sites and randomized to SDLT arm (n=73 subjects, mean [SEM] age=48±2 years, 94% females) and CB-CAPs/MAP arm (n=72 subjects, 50±2 years, 93% females). Positivity rate for CB-CAPs/MAP was similar in the 2 groups (15.1% in SDLT arm vs. 12.5% in CB-CAPs/MAP arm, p=0.65). At enrollment (pre-test), likelihood of SLE in SDLT and CB-CAPs/MAP arms was similar (**Table**). At the 4 weeks follow-up visit, patients randomized to the CB-CAPs/MAP testing arm presented with greater decrease in the likelihood of SLE than those randomized to the SDLT arm (p=0.027) and these differences remained significant at the 12-week follow-up visit (p=0.025) (**Table**). We observed a significantly greater decrease in the likelihood of SLE (decrease ≥1 point from enrollment) in the group of patients randomized to CB-CAPs/MAP testing arm (40/72, 56%) compared to the SDLT

Table. Physician reported likelihood of SLE pre-test and post-test.
Results are expressed as mean ± SEM at each study visit and change from enrollment (in brackets).

	Pre-test (enrollment)	Post-test at 4-weeks	Post-test at 12-weeks
SDLT arm N=73	1.46±0.06	1.23±0.08 [-0.19±0.07]	1.11±0.10 [-0.31±0.10]
CB-CAPs/MAP testing arm N=72	1.42±0.05	1.01±0.10 [-0.44±0.10]	0.84±0.10 [-0.61±0.10]

Table. Physician reported likelihood of SLE pre-test and post-test. Results are expressed as mean ± SEM at each study visit and change from enrollment (in brackets).

arm (27/73, 37%) (difference= 19%; p=0.031) at 12 weeks. In the group of patients randomized to the CB-CAPs/MAP testing, two-tiered test results associated significantly with initiation of prednisone (50% Tier-1 positive and 14% Tier-2 positive vs. 3% Tier-2 negative, p=0.034) and a similar trend was observed in the initiation of hydroxychloroquine (HCQ) (50% Tier-1 positive and 29% Tier-2 positive vs. 11% Tier-2 negative, p=0.112). Initiation of prednisone and HCQ also associated with two-tiered positive test results in the group of patients randomized to SDLT (blinded group) (p=0.020 and p=0.054, respectively).

Conclusion: The decrease in the likelihood of SLE in both study arms following testing is consistent with the low prevalence of the disease. CB-CAPs/MAP was more effective than SDLT in allowing the physician to determine that SLE is an unlikely diagnosis. In addition, positive CB-CAPs/MAP test results impacted treatment management.

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A Phase 1b/2a Trial of Tofacitinib, an Oral Janus Kinase Inhibitor, in Systemic Lupus Erythematosus

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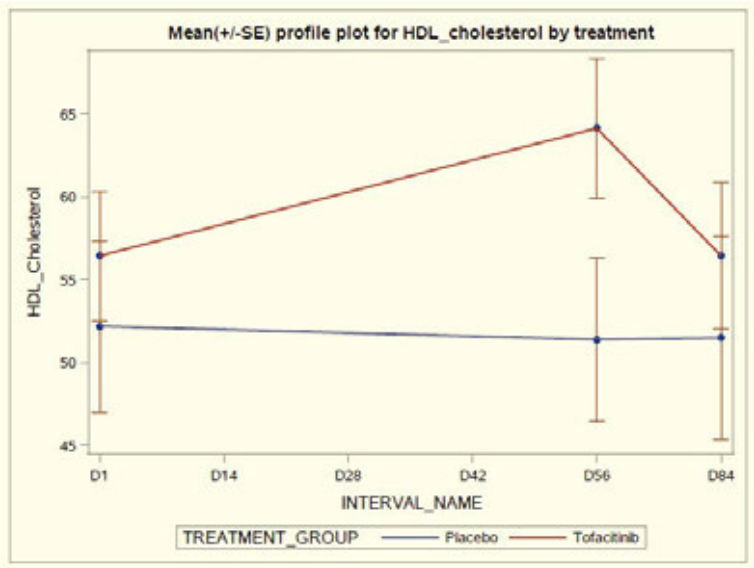
	Tofacitinib	Placebo
Age (Years)		
Median(Range)	48.5(23-75)	41(18-56)
Gender, N (%)		
Female	17 (85%)	9 (90%)
Male	3 (15%)	1 (10%)
SLEDAI		
Mean ± SD	4.5±2.4	5.0±1.4
Disease Duration		
Mean ± SD	13.2±11.5	13.0±11.0

Demographics Table

Adverse events by severity observed by treatment group			
	Tofacitinib N=43	Placebo N=28	Total N=71
Mild	32(74.4%)	23(82.1%)	55(77.5%)
Moderate	11(25.6%)	3(10.7%)	14(19.7%)
Severe	0(0%)	2(7.1%)	2(2.8%)

Adverse Events



Significant Increase(p=0.0006) in HDLc Number and Particle Size in Treatment group at Day 56

Background/Purpose: A pharmacologic intervention that modulates JAK/STAT signaling pathways represents a novel approach for the treatment of Systemic Lupus Erythematosus (SLE). In animal models of SLE, tofacitinib improved clinical features, immune dysregulation and vascular dysfunction. The *STAT4* risk allele is associated with higher risk of severe manifestations in SLE. We hypothesized that immune modulation in response to JAK/STAT inhibition would differ between SLE subjects that carry or not carry the *STAT4* risk allele.

Methods: We conducted a phase 1b/2a randomized, double-blind, placebo-controlled clinical trial of oral tofacitinib, 5 mg twice daily, in 30 SLE subjects (2:1 drug to placebo ratio) with mild to moderate disease activity, stratified by

the presence or absence of *STAT4* risk allele. Study duration was 84 days, with 56 days of active treatment followed by 28 days of off drug period. In addition to recording adverse events (AEs), lipoprotein profile, non-invasive vascular function studies, immuno-phenotyping, and gene expression studies were performed at various time points.

Results: Tofacitinib was well tolerated with no worsening of SLE disease activity, and no severe AEs, opportunistic infections or liver function abnormalities. No thromboembolic events were observed in this short duration trial. A total of 43 AEs (mostly mild respiratory infections) occurred in the treated group compared to 28 AEs in placebo. There was a significant increase in HDL-C and HDL particle size in tofacitinib-treated patients at day 56 accompanied by significant improvements in plasma protein lecithin: cholesterol acyltransferase (LCAT) concentration and cholesterol efflux capacity. Arterial stiffness decreased in the tofacitinib-treated group but not in the placebo-treated group. The type I Interferon gene signature, circulating levels of low- density granulocytes and neutrophil extracellular traps significantly decreased in the tofacitinib treated group compared to the placebo group by the end of treatment, accompanied by significant decreases in pSTAT phosphorylation of different immune cells. Various T cell activation and checkpoint markers significantly decreased in tofacitinib treated individuals and this was modulated by presence or absence of *STAT4* risk allele.

Conclusion: In a short-term trial, tofacitinib was well tolerated in SLE subjects with mild-moderate disease activity. Use of tofacitinib resulted in improvements in innate and adaptive immune dysregulation and lipoprotein phenotype and function. This study also points to the potential utility of including genetic data in clinical trials to advance precision medicine. Long-term studies are needed to determine the efficacy of tofacitinib in the various manifestations of SLE including cardiovascular risk.

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Efficacy and Safety of Dapirolizumab Pegol in Patients with Moderately to Severely Active Systemic Lupus Erythematosus: A Randomized, Placebo-Controlled Study

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Table A: Baseline demographics and disease characteristics

Mean (SD), unless otherwise stated	SOC + PBO (N=43)	SOC + DZP 6 mg/kg (N=43)	SOC + DZP 24 mg/kg (N=44)	SOC + DZP 45 mg/kg (N=46)
Patient demographics				
Age, years	42.7 (12.5)	40.5 (11.7)	42.6 (10.5)	39.0 (13.1)
Female, n (%)	39 (90.7)	40 (93.0)	39 (88.6)	42 (91.3)
BMI, kg/m^2	25.6 (4.2)	26.1 (5.0)	26.0 (4.4)	25.3 (4.8)
Disease characteristics				
Time since diagnosis, years, median (min–max)	5.4 (0.1–30.0)	5.0 (0.2–27.8)	5.1 (0.3–27.0)	8.2 (0.3–25.0)
BILAG 2004 total score	18.6 (3.7)	19.1 (4.1)	18.6 (3.9)	19.8 (5.5)
SLEDAI-2K total score [a]	10.7 (3.4)	11.4 (2.4)	9.9 (2.5)	11.1 (3.4)
ANA ≥1:80, n (%)	43 (100.0)	41 (95.3)	42 (95.5)	41 (89.1)
anti-dsDNA >10 iU, n (%)	17 (39.5)	24 (55.8)	18 (40.9)	21 (45.7)
Low C3 or C4, n (%)	23 (53.5)	25 (58.1)	26 (59.1)	26 (56.5)
Medications at screening				
Corticosteroids, n (%)	38 (88.4)	40 (93.0)	39 (88.6)	36 (78.3)
Dose, mg/day, median (min–max)	10.0 (0.0–40.0)	10.0 (0.0–25.0)	10.0 (0.0–25.0)	10.0 (0.0–30.0)
≥10 mg/day, n (%)	27 (62.8)	28 (65.1)	24 (54.5)	24 (52.2)
Immunosuppressants, n (%)	22 (51.2)	25 (58.1)	25 (56.8)	26 (56.5)
Antimalarials, n (%)	29 (67.4)	30 (69.8)	33 (75.0)	28 (60.9)

[a] SLEDAI-2K total score calculated using anti-dsDNA positive if >10 iU. ANA: antinuclear antibody; BILAG: British Isles Lupus Assessment Group; BMI: body mass index; C3/4: complement C3/C4; DZP: dapirolizumab pegol; PBO: placebo; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000; SOC: standard of care.

Background/Purpose: Dapirolizumab pegol (DZP) is a polyethylene glycol-conjugated Fab' fragment, which targets CD40 ligand and is in development for the treatment of systemic lupus erythematosus (SLE). The primary objective was to establish a dose-response relationship for DZP using prespecified models. Other objectives were to compare the safety and efficacy of DZP to standard of care (SOC) treatment, and to assess the durability of response after study drug withdrawal.

Methods: This phase 2b study (NCT02804763) consisted of a 24-week double-blind (DB), placebo (PBO)-controlled period (study drug plus SOC), followed by a 24-week observational period (SOC only). Patients were randomized 1:1:1:1 to SOC+PBO or SOC+intravenous DZP (6/24/45 mg/kg) every 4 weeks to Week 24. The primary objective was measured at Week 24, and other objectives throughout the study.

Adults with SLE (SLICC classification criteria) and moderate to severe disease activity (SLEDAI-2K score ≥6 and ≥1 BILAG A or ≥2 BILAG B domain scores), receiving stable doses of corticosteroids (CS; ≤40 mg/day prednisone-equivalent) and/or antimalarials and/or immunosuppressants, were eligible. Patients receiving CS ≥10 mg/day were required to start tapering within 4 weeks of first study drug infusion. Patients with stable lupus nephritis were permitted entry.

Table B: Immunologic and clinical outcomes

Mean change from baseline, unless otherwise stated	SOC + PBO (N=43)		SOC + DZP 6 mg/kg (N=43)		SOC + DZP 24 mg/kg (N=44)		SOC + DZP 45 mg/kg (N=46)	
Week:	24	48	24	48	24	48	24	48
Immunologic outcomes								
Anti-dsDNA antibodies (iU/mL), median % change from baseline [a]	-18.4	**2.0**	-43.3	**-24.5**	-55.7	**-9.2**	-52.4	**-26.2**
Complement C3 (mg/L) [b]	34.1	**-20.6**	57.8	**13.3**	98.1	**88.7**	123.8	**35.9**
Complement C4 (mg/L) [b]	2.9	**-3.5**	26.2	**28.1**	15.5	**13.9**	42.0	**6.8**
Anti-phospholipid antibodies [c]								
Anti-β2 glycoprotein IgG (U/mL)	2.9	**-13.2**	-4.7	**-0.6**	-3.9	**4.4**	-13.6	**-4.5**
Anti-β2 glycoprotein IgM (U/mL)	-4.1	**-7.2**	-16.6	**-9.9**	-9.4	**-7.3**	-11.7	**-1.0**
Anti-cardiolipin IgG (GPL U)	2.8	**-17.8**	-1.8	**2.5**	-11.0	**-7.4**	-15.7	**-2.2**
Anti-cardiolipin IgM (MPL U)	0.6	**-2.0**	-13.5	**-7.3**	-5.3	**-4.1**	-14.2	**2.6**
Clinical outcomes								
BICLA responder rate, % (Δ/OR vs PBO), *mNRI* [d]	37.2 (N/A)	**25.6 (N/A)**	48.8 (11.6/1.6)	**37.2 (11.6/1.7)**	54.5 (17.3/2.0)	**36.4 (10.8/1.7)**	52.2 (15.0/1.9)	**39.1 (13.5/1.9)**
BILAG improvement, %, *mNRI* [e]	37.2	**27.9**	48.8	**51.2**	63.6	**52.3**	60.9	**56.5**
SRI-4 responder rate, % (Δ/OR vs PBO), *mNRI* [d]	51.2 (N/A)	**37.2 (N/A)**	67.4 (16.3/2.0)	**53.5 (16.3/2.0)**	50.0 (-1.2/1.0)	**40.9 (3.7/1.2)**	63.0 (11.9/1.6)	**52.2 (15.0/1.9)**
PGA	-27.0	**-29.6**	-31.7	**-32.2**	-32.2	**-34.7**	-28.0	**-29.7**
SLEDAI-2K	-4.2	**-4.1**	-5.0	**-5.6**	-5.1	**-5.3**	-5.3	**-5.4**
Cumulative no. BILAG severe flares [f]	7	**12**	4	**12**	0	**5**	1	**5**

Observed case data, unless otherwise specified. [a] In patients with anti-dsDNA >10 iU at baseline, measured using the Farr assay; [b] In patients with C3 or C4 below the lower limit of normal at baseline; [c] In patients who tested positive for each antibody at baseline; [d] Decreases at Week 48 are due to intervention with escape treatment; [e] Defined as all Grade As improved to B, C, or D, and all Grade Bs improved to C or D, and no worsening in other organ systems with Grade C, D, or E at baseline (worsening is defined as ≥1 new A or ≥2 new Bs); [f] BILAG severe flare: a new BILAG 2004 Grade A since the previous visit in any system, due to individual items that are new or worse qualifying for the Grade A. Δ: difference vs placebo; mNRI: modified non-responder imputation; OR: odds ratio vs placebo; PGA: physician's global assessment; SRI: SLE Responder Index.

Clinical outcomes were analyzed in patients who received ≥1 full dose of study medication and had ≥1 post-baseline efficacy measurement. Safety and immunologic outcomes were analyzed in patients who received ≥1 dose of study medication (any dose).

Results: Of 182 randomized patients, 178 (97.8%) completed the DB period to Week 24 (including 167 [91.8%] on study drug), and 164 (90.1%) completed the observational period to Week 48. Baseline demographics were similar across groups **(Table A)**. At Week 24, all DZP groups showed numerically greater improvements in immunological and clinical outcomes vs PBO **(Table B)**. Following study drug withdrawal, immunologic parameters generally worsened and returned towards baseline. Whereas SLEDAI and PGA stabilized across treatment groups after study drug withdrawal **(Table B)**, BICLA and SRI-4 response rates declined, mostly due to interventions with escape medicines during this period, which automatically led to non-responder status. As none of the prespecified dose-response models fit the Week 24 BICLA responder rates with statistical significance ($p< 0.05$), the primary objective was not met. Rates of treatment-emergent adverse events (TEAEs) and serious TEAEs were generally balanced across treatment groups **(Table C)**. Four thromboembolic TEAEs were observed during the DB period: one in the 24 mg/kg DZP group and three in PBO.

Table C: Safety outcomes

n (%) [ER per 100 patient-years]	SOC + PBO (N=45)	SOC + DZP 6 mg/kg (N=45)	SOC + DZP 24 mg/kg (N=45)	SOC + DZP 45 mg/kg (N=47)
Mean duration of exposure (days)	***216.7***	***224.0***	***215.6***	***212.1***
Any TEAE	28 (62.2) [90]	29 (64.4) [130]	35 (77.8) [116]	34 (72.3) [84]
Infections and Infestations	15 (33.3) [21]	21 (46.7) [43]	26 (57.8) [40]	22 (46.8) [29]
Infusion reactions	0	0	0	1 (2.1) [1]
Thromboembolic events	3 (6.7)	0	1 (2.2)	0
Serious TEAEs	5 (11.1) [6]	2 (4.4) [2]	4 (8.9) [4]	5 (10.6) [6]
Study discontinuation due to TEAEs	1 (2.2) [1]	0	0	0
Permanent withdrawal of study drug due to TEAEs	4 (8.9) [4]	0	2 (4.4) [2]	2 (4.3) [2]
Severe TEAEs	3 (6.7) [4]	1 (2.2) [1]	3 (6.7) [3]	7 (14.9) [8]
Deaths	0	0	0	0

TEAEs were those with onset at the time of, or after, the first dose of study drug, until 12 weeks after the last dose. Patients who withdrew from the study early (during the DB Treatment Period) entered a Safety Follow-Up Period, which ended 12 weeks after the final dose of study drug. DZP: dapirolizumab pegol; ER: event rate; PBO: placebo; TEAE: treatment-emergent adverse event; SOC: standard of care.

Conclusion: DZP-treated patients showed consistent improvements in disease activity across all doses. Upon study drug withdrawal, immunologic parameters returned to baseline levels, whilst clinical outcomes such as SLEDAI and PGA stabilized. None of the prespecified dose-response models could be selected; thus, the primary endpoint was not met. DZP was generally well-tolerated. The potential clinical benefit of DZP warrants investigation in a larger stu dy.

Disclosure: R. Furie, Biogen, 5, GlaxoSmithKline, 2, 5, UCB Pharma, 2, 5; **I. Bruce**, Astra Zenica, 5, AstraZeneca, 5, Eli Lilly, 5, 8, Genzyme Sanofi, 2, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, 8, ILTOO, 5, Iltoo, 5, MedImmune, 5, 8, Medimmune, 5, Merck Serono, 5, 8, Merk Serono, 5, Roche, 5, 8, Sanofi Genzyme, 2, UCB, 2, 5, 8, UCB Pharma, 5, 8; **T. Dörner**, AbbVie, 5, Celgene, 5, Eli Lilly and Company, 5, 8, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Novartis Pharma AG, 5, Roche, 5, 8, Samsung, 5, 8, Sanofi, 2, UCB, 5, UCB Pharma, 2, 5; **M. Leon**, None; **P. Leszczyński**, None; **M. Urowitz**, Janssen Research & Development, LLC, 2, UCB Pharma, 9; **B. Haier**, UCB Pharma, 3, 4; **C. Brittain**, UCB Pharma, 3, 4; **J. Liu**, Biogen, 3, 4; **C. Barbey**, Biogen, 3, 4; **C. Stach**, UCB Pharma, 3, 4.

Abstract Number: 0945

Comparison of Clinical Manifestations in IgG4 Related Disease Patients with/without Aortitis/Periaortitis and Periarteritis: A Prospective Cohort Study of 587 Patients with IgG4-RD Disease

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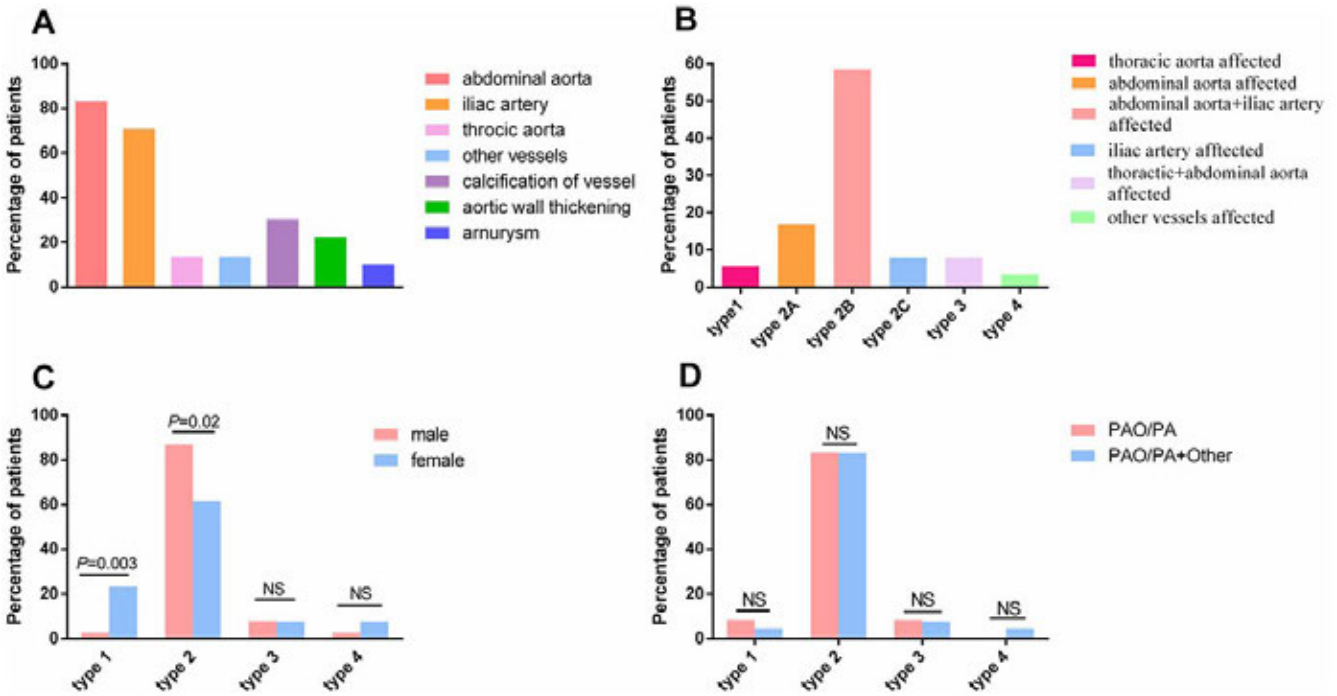
SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders I: Miscellaneous Disorders
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: We aimed to clarify the clinical features of IgG4-related disease (IgG4-RD) with/without aortitis/periaortitis and periarteritis (PAO/PA), and evaluate the treatment efficacy of patients with PAO/PA.

Methods: A total of 587 IgG4-RD patients with a follow up time of more than 6 months were enrolled in this study. The distribution of IgG4 related PAO/PA was classified into four types: type 1, thoracic aorta affected; type 2a, abdominal aorta affected, type 2b, abdominal aorta and iliac artery affected, type 2c, iliac artery affected; type 3, thoracic and abdominal aorta affected; type 4, other artery affected. The demographic data, clinical characteristics, laboratory parameters and treatment efficacy of enrolled patients were analyzed.

Results: Of 587 IgG4-RD patients, 89 (15.2%) had PAO/PA. The age of PAO/PA patients was 58.3 ± 11.1 years, and there was a male dominance(85.4%, 76 male patients). The percentage of vessels affected in IgG4 related PAO/PA was as follows: the abdominal aorta affected was 83.1%, the iliac artery affected was 70.8%, the thoracic aorta affected was 13.5% and the other vessels were affected. The most prevalent type of PAO/PA was type 2B, with 74 (83.1%) patients, followed by type 2A, type 2C, type 3 and type 1. Compared with patients without PAO/PA, patients with PAO/PA had higher percentage of back pain, and abdominal pain, the percentage of dacryoadenitis/ sialadenitis and paranasal sinus affected was lower. ESR and hsCRP was higher in patients with PAO/PA, whereas serum IgG4 and T-IgE levels were lower compared with patients without PAO/PA. After treatment with glucocorticoid and immunosuppressants, patients IgG4-RD RI, ESR, hsCRP, serum IgG4 and T-IgE levels decreased significantly. 44 (38.2%) patients achieved a remission with the reduction of abnormal soft tissues more than 70%, 39 (43.8%) with a reduction of 31%-70%, and 16 (18.0%) patients with a reduction of less than 30%.



Vessels affected of IgG4-RD patients with PAO/PA Figure 1A represented vessels affected of patients with PAO/PA. Figure 1B represented the distribution of IgG4 related PAO/PA. figure 1C and 1D represented the comparison of vessel distribution between male and female patients, PAO/PA merely and PAO/PA respectively

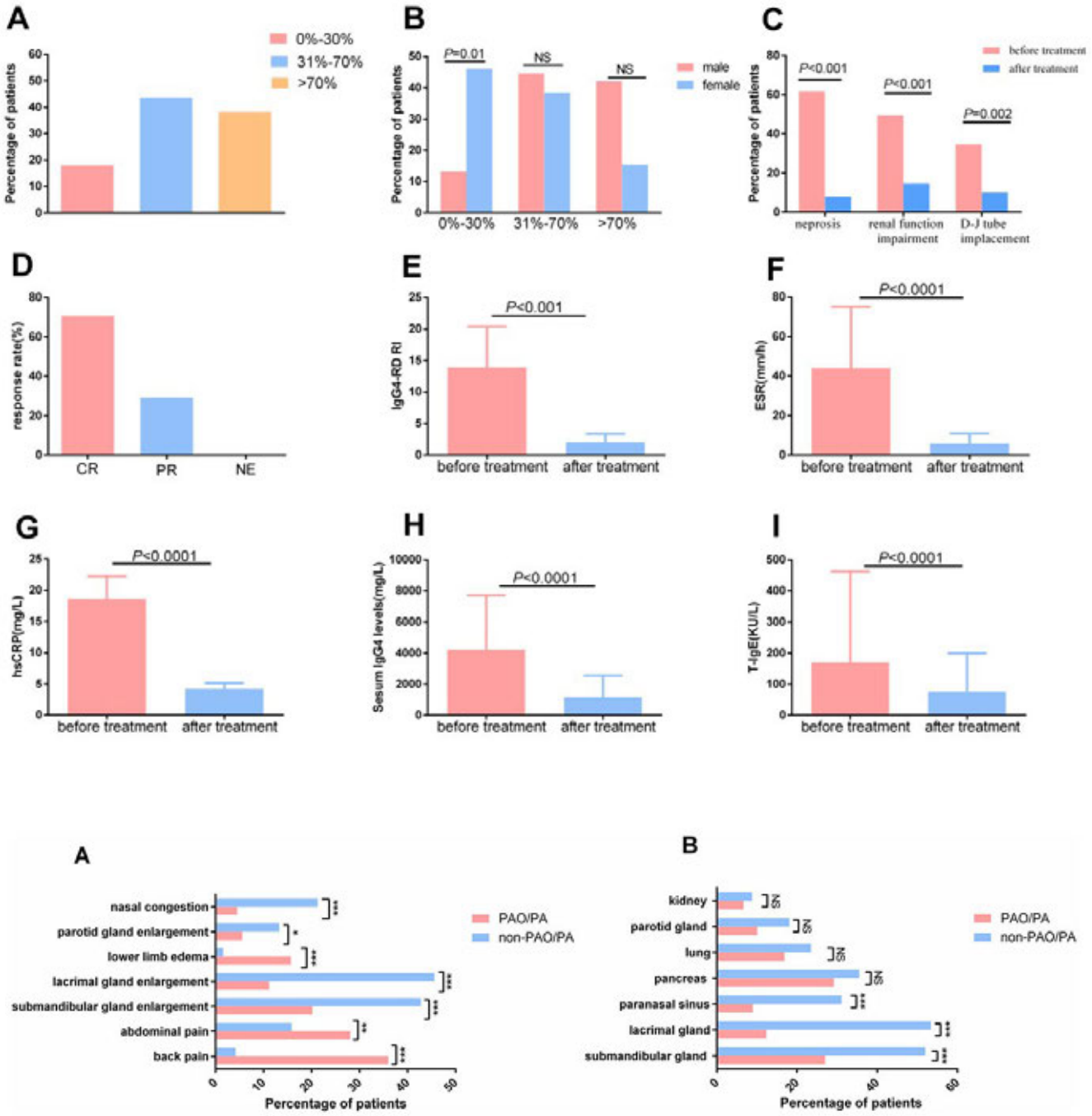


Figure 3 Onset symptoms and organs affected of patients with/without PAO/PA Figure 3A and figure 3B represented onset symptoms and organs affected of IgG4-RD with PAO/PA. * represented P<0.05, *** represented P<0.001.

and without active major organ involvement. The primary efficacy endpoint was area under the curve for the number of OU over 12 weeks (AUC_{Wk0-12}). Clinical improvement of OU was evaluated by assessments of OU pain (100 mm visual analogue scale) and measures of disease activity and QoL. Disease activity measures included the Behçet's Syndrome Activity Score (BSAS) and Behçet's Disease Current Activity Index Form (BDCAF; including 3 components: Behçet's Disease Current Activity Index, Patient's Perception of Disease Activity, Clinician's Overall Perception of Disease Activity). QoL assessments included the Behçet's Disease QoL (BDQoL) score and the 36-item Short-Form Health Survey version 2 (SF-36v2), consisting of the Physical and Mental Component Summary (PCS and MCS) scores and Physical Functioning domain (PF) score. An analysis of covariance model was used to analyze the prima-

Conclusion: The most common affected vessel in patients with PAO/PA was abdominal aorta, and type 2b was the predominant distribution of PAO/PA. Patients with PAO/PA had lower percentage of allergy history, dacryoadenitis/sialadenitis and paranasal sinus affected, lower serum IgG4 levels, T-IgE, higher IgG4-RD RI, ESR and hsCRP than patients without PAO/PA.

Disclosure: L. Peng, None; **W. Zhang**, None; **P. Zhang**, None.

Abstract Number: 0946

Improvements in Disease Activity and Quality of Life for up to 64 Weeks in Patients with Behçet's Syndrome: Results from a Phase III Study

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders I: Miscellaneous Disorders

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Behçet's syndrome is a chronic, multi-system inflammatory disorder characterized by painful, recurrent oral ulcers (OU) that can impair quality of life (QoL). Apremilast (APR), an oral phosphodiesterase 4 inhibitor, demonstrated efficacy in the treatment of OU of Behçet's syndrome in a phase III, multicenter, randomized, double-blind, placebo (PBO)-controlled study (RELIEF). We report short- and long-term results from RELIEF for the efficacy of APR treatment on QoL and physical function for up to 64 weeks.

Methods: A total of 207 patients were randomized (1:1) to APR 30 mg twice daily (APR 30 BID) or PBO twice daily for a 12-week PBO-controlled phase, followed by a 52-week active treatment extension. Eligible patients were ≥18 years old, had active Behçet's syndrome, with ≥3 OU at randomization or ≥2 OU at screening and randomization

Changes From Baseline at Week 12 and Week 64

	Week 12*			Week 64†	
	PBO	APR 30 BID	*P* Value	PBO/ APR 30 BID	APR 30 BID
BDQoL, mean change (SD)	−0.5 (0.7)	−3.5 (0.7)	0.0003	−3.41 (6.6)	−3.57 (6.6)
SF-36v2 PCS, mean change (SD)	0.9 (0.8)	3.1 (0.8)	0.0204	3.3 (9.1)	3.4 (7.9)
SF-36v2 MCS, mean change (SD)	−0.7 (0.9)	4.6 (0.9)	<0.0001	1.9 (10.5)	5.4 (11.1)
SF-36v2 PF, mean change (SD)	0.04 (0.9)	2.9 (0.9)	0.0060	2.5 (10.1)	3.4 (10.2)

Intent-to-treat population.

*Last-observation-carried-forward analysis; least-squares mean is shown for Week 12. †Data as observed. For SF-36v2, a higher score indicates better functioning and a positive change from baseline indicates improvement. For BDQoL, a lower BDQoL score indicates better QoL and a negative change from baseline indicates improvement.

ry endpoint and change from baseline in BDQoL score and SF-36v2 PCS, MCS and PF scores at Week 12. Data at Week 64 are as observed.

Results: The primary efficacy endpoint of AUCWk0-12 for the number of OU was significantly lower in APR 30 BID vs PBO patients ($P< 0.0001$); improvement in the number of OU and OU pain was sustained in patients continuing APR 30 BID treatment for up to 64 weeks and emerged in patients switched from PBO to APR 30 BID for Weeks 12 to 64. Significant improvements were observed with APR 30 BID vs PBO in mean change from baseline at Week 12 in BSAS ($P< 0.0001$), BDCAF components ($P\leq0.0335$), and BDQoL score ($P=0.0003$). The improvements in BSAS, BDCAF, and BDQoL outcomes were maintained in patients continuing APR 30 BID treatment for up to 64 weeks, and comparable effects were observed at Week 64 among patients who switched from PBO to APR 30 BID. Significant improvements were also observed in mean change from baseline at Week 12 in SF-36v2 PCS ($P=0.0204$), MCS ($P< 0.0001$), and PF ($P=0.0060$) scores in APR 30 BID vs PBO patients. These effects in SF-36v2 scores were also maintained at Week 64 among patients initially randomized to APR 30 BID, and the improvements were generally similar among patients who switched from PBO to APR 30 BID (Table).

Conclusion: Patients with active Behçet's syndrome treated with APR 30 BID vs PBO experienced significant reductions in OU and clinically meaningful improvements at Week 12 in disease activity and QoL. Improvements were sustained at Week 64 in patients continuing APR treatment.

Disclosure: G. Hatemi, Abbvie, Mustafa Nevzet, UCB, 8, Bayer, Eli Lilly, 5, BMS, Celgene Corporation, Silk Road Therapeutics, 2, Silk Road Therapeutics, 2; **A. Mahr**, Celgene, 8, Chugai Pharma France, 8, Roche, 8, Roche, Chugai, 8; **M. Takeno**, Celgene Corporation, 5, Mitsubishi-Tanabe, 8; **D. Kim**, None; **M. Melikoglu**, None; **S. Cheng**, Celgene Corporation, 3; **S. McCue**, Celgene Corporation, 3; **M. Paris**, Celgene Corporation, 3; **M. Chen**, Celgene Corporation, 3; **Y. Yazici**, BMS, Celgene Corporation, Genentech, and Sanofi, 5, BMS, Celgene Corporation, Genetech,

Figure 2A represented the reduction of soft tissues around PAO/PA. figure 2B represented the comparison of soft tissues reduction of PAO/PA between male and female patients. Figure 2C was the recovery of nephrosis, renal function and D-J tube implacement of patients before and after treatment. Figure 2D represented the remission rate of patients with PAO/PA. figure 2E to 2I represented IgG4-RD RI, ESR, hsCRP, serum IgG4 and T-IgE respectively before and after treatment.

Sanofi, 5.

Abstract Number: 0947

TNF Inhibitor Treatment and Dramatic Stroke Risk Reduction in Patients with Deficiency of Adenosine Deaminase 2

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders I: Miscellaneous Disorders

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Deficiency of adenosine deaminase 2 (DADA2) is an autosomal recessive disease caused by biallelic loss-of-function mutations in the *ADA2* gene . Over 60 pathogenic mutations have been identified in all domains of the resultant protein, adenosine deaminase 2 (ADA2). ADA2 is an endothelial cell growth factor and promotes M2 macrophage differentiation, leading to a chronic inflammatory state. Known manifestations of ADA2 deficiency include recurrent fevers, immunodeficiency, livedo racemosa, polyarteritis nodosa, and early-onset stroke – many of which may worsen with acute or recurrent disease flares. An earlier study by our group demonstrated a reduced risk of recurrent strokes in 15 patients with DADA2 secondary to anti-tumor necrosis factor (TNF) treatment. The purpose of this abstract is to provide additional stroke data before and after initiation of anti-TNF treatment on a larger cohort since the initial publication.

Methods: A single center study evaluated 49 patients with molecularly diagnosed pathogenic mutations in ADA2. Medical records were manually reviewed. Stroke incidences were only included if reported as confirmed by imaging. Patients were subdivided by past incidence of stroke and initiation of anti-TNF treatment such as etanercept, adalimumab, golimumab, or infliximab. Cumulative duration of the disease was calculated for each patient before and after initiation of anti-TNF treatment, i.e. time since birth and time to present record, respectively.

Results: Of the 49 patient cohort, 24 had documented histories of strokes, all of which are currently on anti-TNF treatment. The median age of first stroke was 5.0 years (range, 0.48 to 21) with a median of 2 strokes per patient (range, 1 to 10). Before initialization of anti-TNF treatment, the patients had a cumulative disease duration of 8,997

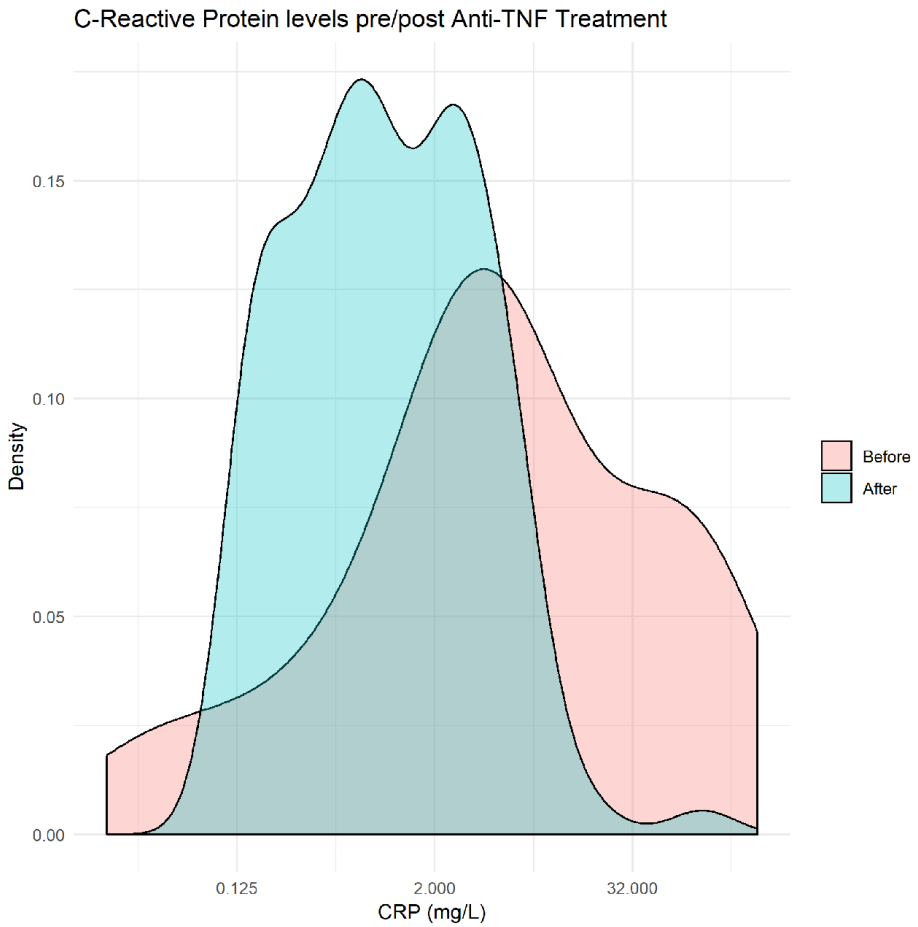

Figure 1: CRP level in patients with history of early-onset stroke before and after starting anti-tnf treatment, n = 24. Before treatment the average CRP level was 24.7 mg/L (median, 4.72) with a standard deviation of 42.7 mg/L. After starting anti-tnf treatment average CRP was 2.72 mg/ (median, 1.00) with a standard deviation of 8.36 mg/L.

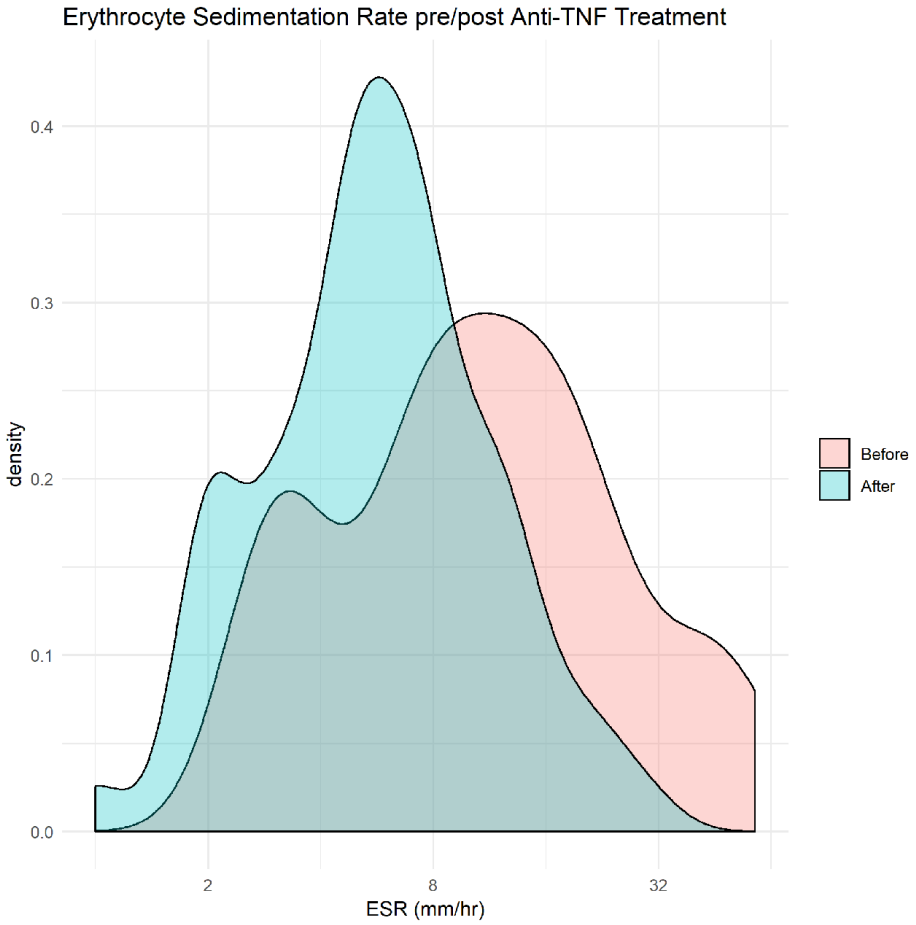

Figure 2: ESR level in patients with history of early-onset stroke before and after starting anti-tnf treatment, n = 24. Before treatment the average ESR was 15.1 mm/hr (median, 11.0) with a standard deviation of 13.8 mg/L. After anti-tnf treatment average ESR was 7.06 mm/hr (median, 5.50) with a standard deviation of 5.31 mm/hr.

patient months and a cumulative total of 69 strokes. After the initiation of anti-TNF treatment there have been no reported strokes over a period of 2,024 patient-months with a median duration of 56 months (range, 1.7 to 153) ($p < 0.001$).

Conclusion: Patients with DADA2 have a high risk for early-onset strokes. In a cohort of 49 patients with DADA2, 24 patients with history of stroke have all began anti-TNF treatment. Thus far these patients have experienced no recurrent strokes over a cumulative period of 2,024 patient months. This suggests anti-TNF treatment plays a key role in the reduction of strokes in patients with DADA2. Aside from stroke reduction, we have seen a normalization in key lab values such as CRP (Figure 1), ESR (Figure 2), Hgb and HCT which indicates an overall decrease in inflammation. Other lab indicators such as neutropenia and red cell aplasia remain variable or unchanged, suggesting additional targeted therapy may further benefit DADA2 patients.

Disclosure: R. Laird, None; **P. Hoffmann**, None; **K. Barron**, None; **D. Stone**, None; **M. Nehrebecky**, None; **A. Jones**, None; **T. Romeo**, None; **C. Toro**, None; **A. Soldatos**, None; **C. Cudrici**, None; **D. Kastner**, None; **A. Ombrello**, None.

Abstract Number: 0948

Relapsing Cryoglobulinemic Vasculitis Following Successful HCV Eradication by Interferon-Free Direct Acting Antivirals, an International Multicenter Study

Mohamed Tharwat Hegazy,[1] Ahmed Fayed,[1] Tarek El Shabony,[1] Marcella Visentini,[2] David Saadoun,[3] Patrice Cacoub,[3] and Gaafar Ragab[1], [1]Cairo University, Cairo, Egypt, Cairo, Egypt, [2]Sapienza University of Rome, Rome, Italy, Rome, Italy, [3]AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Department of Internal Medicine and Clinical Immunology, F-75013, Paris, France, Paris, France

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

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Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Interferon-free Direct Acting Antiviral (DAA) combinations proved to be effective for the treatment of HCV induced Cryoglobulinemic Vasculitis (HCV-Cryovas). Some reports showed relapses of HCV-Cryovas despite a sustained viral response (SVR) after DAA. Possible explanations for such relapses included the persistence of few copies of HCV-RNA in liver cells, macrophages, or lymphocytes, or the persistence of pathogenic B-cell clones. The scale and features of these relapses are not fully appreciated. Our aim was to follow HCV-Cryovas patients treated with DAAs for a longer period and to assess Cryovas relapsers clinically and serologically

Methods: We studied a total of 1019 HCV-Cryovas patients who fulfilled the validated 2014 classification criteria. All cases received DAA treatment protocols. They represented the collective registries of the following 4 centers: 1- Nephrology unit, Internal Medicine Department, Cairo University, Egypt, 2- Rheumatology and clinical Immunology unit, Internal Medicine Department, Cairo University, Egypt, 3- Department of Internal Medicine and Clinical Immunology, National Reference Center for Autoimmune Systemic Rare Diseases, Hopital La Pitié Salpêtrière, Paris, France, 4- Referral Centre for Mixed Cryoglobulinemia, Department of Translational and Precision Medicine, Sapienza University of Rome, Rome, Italy. We excluded cases with hepatitis B or HIV, as well as cases that received IFN-based protocols. From 2015 to 2019, patients received the following DAA protocols: Sofosbuvir + either Simeprevir, Daclatasvir, Ledipasvir or Ribavirin. They all achieved a sustained viral response (SVR). They were followed over 24 months after viral eradication. Cases with cutaneous or renal relapses were additionally assessed by skin and/ or renal biopsies. Clinical relapse was reported when there was purpura, arthralgia/arthritis, neuropathy, or nephropathy. Serological relapses were considered if Cryoglobulins >1.5%, elevated rheumatoid factor (RF) or consumed complement 4 (C4) are detected. Acute interstitial nephritis in renal biopsy means lymphocytic or mononuclear inflammatory interstitial infiltrate. Vasculitis in renal biopsy would be either cryoglobulinemic-type or polyarteritisnodosa-type

Results: All 1019 HCV-Cryovas patients achieved SVR and showed partial or complete clinical and serological responses of Cryovas at the end of DAA treatment (EOT). A total of 116/1019 (11.38%) cases showed evidence of both clinical and serological Cryovas relapses **(Table 1)**, while 7/1019 (0.7%) cases only showed evidence of serological Cryovas relapse. All 123/1019 (12.07%) Cryovas relapsers remained negative for HCV by PCR. Overall, 98 cases of the relapsers had renal manifestations and 95 cases had a renal biopsy **(Table 2)**; 102 patients had purpura and 95 of them had a skin biopsy **(Table 3)**.

Conclusion: In our multicenter international study, after a follow-up period of 24 months and despite a SVR post-DAA, we report a 12.07% relapse rate of HCV-Cryovas. Close observation and longer follow-up studies, as well as,

Clinical Manifestations of the HCV Cryovas Relapsers	Number (%)
Purpura	102/116 (87.9%)
Renal	98/116 (84.4%)
Peripheral neuropathy	88/116 (75.8%)
Arthralgia/arthritis	8/116 (6.9%)
Lymphoma	3/116 (2.5%)
Skin ulcers	3/116 (2.5%)

Table 1: Clinical Manifestations of HCV Cryovas Relapsers.

Renal Pathology of HCV-Cryovas Relapsers	Number (%)
Membrano-Proliferative glomerulonephritis (GN)	43/95 (45.3%)
Membranous nephropathy	17/95 (17.9%)
Focal segmental glomerulosclerosis (FSGS)	2/95 (2.1%)
Crescentic GN	33/95 (34.7%)
Acute interstitial nephritis	56/95 (58.9%)
Thrombotic microangiopathy	37//95 (38.9%)
Vasculitis	40/95 (42.1%)
Arterial intimal fibrosis	25/95 (26.3%)

Table 2: Renal pathology.

Skin Pathology	Number (%)
Fibrinoid necrosis	95/95 (100%)
Endothelial cell swelling and thickening of the blood vessel wall	95/95 (100%)
Infiltration of the blood vessel wall with neutrophils and nuclear dust	77/95 (81.1%)
Extravasation of erythrocytes	89/95 (93.7%)
Intracapillary hyaline thrombi	51/95 (53.7%)

Table 3: Skin pathology.

deeper investigations of the immune system are needed to better understand the underlying mechanism of Cryovas relapse after HCV viral eradication

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Disclosure: M. Tharwat Hegazy, None; **A. Fayed**, None; **T. El Shabony**, None; **M. Visentini**, None; **D. Saadoun**, Abbvie, 5, AstraZeneca, 5, Bristol meyer squibb, 5, Gilead, 5, Glaxo Smith Kline, 5, Roche, 5, Servier, 5; **P. Cacoub**, Abbvie, 5, AstraZeneca, 5, Bristol meyer squibb, 5, Gilead, 5, Glaxo Smith Kline, 5, Janssen, 5, Merck Sharp Dohme, 5, Roche, 5, Servier, 5, Vifor, 5; **G. Ragab**, None.

Abstract Number: 0949

Assessment of Femoral Vein Wall Thickness with Doppler Ultrasound Can Be a Diagnostic Tool for Behcet's Disease

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SESSION INFORMATION

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Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Behcet's disease(BD) is a uniqe systemic vasculitis mainly involving venous vessels in contrast to other systemic vasculitides. Diagnosing BD is a challenge, especially in countries with a low prevalence. International Study Group Criteria, accepted to as diagnostic, has low sensitivity, especially in early cases when major organ involvement such as uveitis or deep vein thrombosis(DVT) presents alone. Pathergy (skin prick) test, the only specific diagnostic tool, has quite a low positivity. We recently published a controlled study of assessing venous wall thickness(VWT) as a surrogate marker of venous disease in BD with doppler ultrasound (US) and observed a very sensitive and specific VWT in male BD patients. The common femoral vein(CFV) thickness measurement, as the primary site of US with the cut-off values > 0.48-0.49 mm, had a high area under the receiver operating characteristic curve(>0.8) with sensitivity and specificity of around 80% (1). In this study, we aimed to investigate the diagnostic performance of CVF thickness measurement in BD including females comparing with multiple control disease groups.

Table 1: Venous Wall Measurements of Lower Extremity in Study Groups

	Behcet's Disease (n=110)	Healthy Controls (n=47)	Systemic Vasculitis (n=21)	Venous Insufficiency (n=28)	Anti-phospholipid Syndrome with DVT (n=29)
Age (years)	33.5 ± 6	30.1 ± 5	33.3 ± 7	36.7 ± 6	38.3± 9
Gender, male n (%)	89 (81)	40 (85)	12 (58)	13 (46)	9 (65)
Body Mass Index, kg/m2	25.5 ± 4	24 ± 2	23.8 ± 3.5	27.7 ± 4	27.2 ± 7
Right CFV Thickness (mm)	0.79 ± 0.3	0.34 ± 0.1	0.34 ± 0.15	0.38± 0.1	0.48 ± 0.15
Left CFV Thickness (mm)	0.78 ± 0.3	0.3 ± 0.1	0.36 ± 0.14	0.38 ± 0.2	0.48 ± 0.15

CFV: Common Femoral vein, DVT:Deep Venous Thrombosis

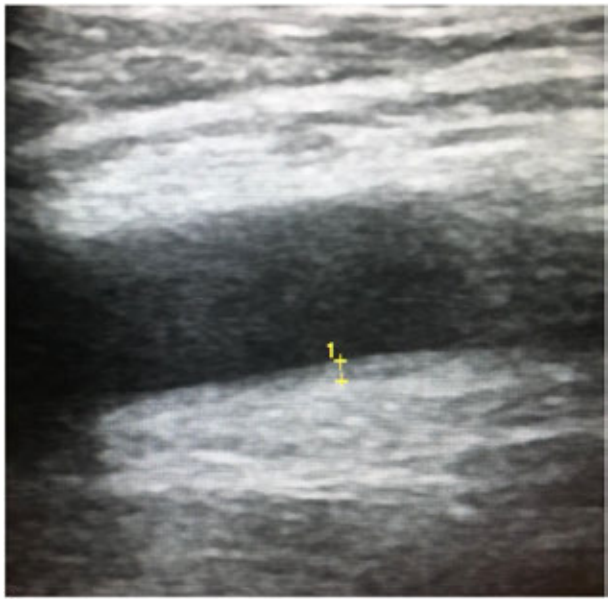

Figure 1. Measurement of common femoral vein thickness

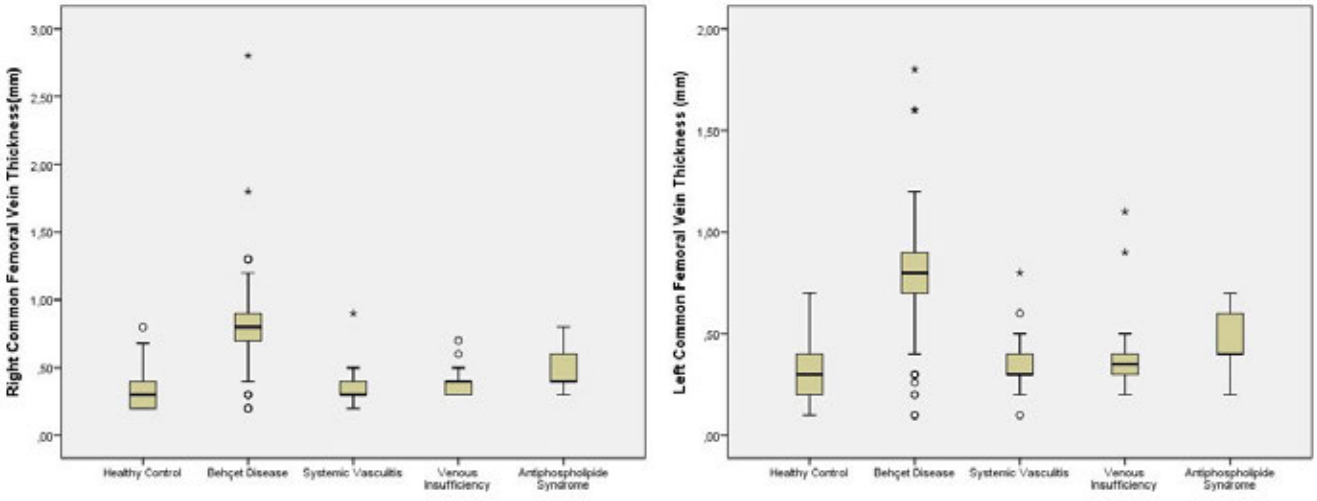

Figure 2. Distribution of common femoral vein thickness in study groups

Methods: One hundred-ten patients with BD, 47 healthy controls (HC), 21 patients with systemic vasculitides, 28 patients with venous insufficiency, 29 patients with antiphospholipid syndrome(APS) having DVT history, were included the study. Behcet's Syndrome Activity Score(BSAS) was used to assess disease activity. Bilateral CFV thickness was measured with US by an experienced radiologist blinded to cases(Figure 1).

Results: Bilateral CFV thickness was significantly higher in BD compared to all comparative groups ($p< 0.001$ for all)(Table 1 and Figure 2). No correlations were present between CFV thickness and both BSAS and CRP levels ($p >0.05$ for all). In only 2 (8%) patients with venous insufficiency and 2 (10%) patients with systemic vasculitis, bilateral CVF thickness was higher than the cut- off values. Interestingly, APS was the only control group with positivity, in 12 (41%) patients with APS, bilateral CFV thickness was higher than the cut-offs. There was no difference between male vs female BD patients regarding CVF thickness (right CFV:0.78±0.3 mm vs 0.79±0.1 mm,$p=0.96$, left CFV:0.78±0.3 vs 0.81±0.1, $p=0.80$). Although a higher CVF thickness tendency was observed in VBD, no statistically significant

difference was present between BD patients with (n=40) and without (n=58) vascular involvement (right CFV:0.82±0.3 mm vs 0.75±0.3 mm, p=0.122, left CFV:0.84 ± 0.3 vs 0.76±0.3, p=0.165).

Conclusion: Increased CFV thickness is present in BD patients, independent of vascular involvement. We also found that CFV thickness is a distinctive feature of BD, rarely present in other inflammatory/vascular diseases such as ankylosing spondylitis (previously shown), systemic vasculitides and venous insufficiency (except APS with DVT). CFV thicknesses are easily and reliably measured by Doppler US. We, therefore, suggest that assessment of CFV can be a diagnostic tool for Behcet's disease with a good sensitivity and specificity to differentiate BD from similar disorders.

Reference

1. Alibaz-Oner et al. Clinical Rheumatology (2019) 38:1447–51.

Disclosure: F. Alibaz-Oner, None; **R. ERGELEN**, None; **Y. YILDIZ**, None; **A. Yazici**, None; **A. MUTIS**, None; **Z. ERTURK**, None; **M. ALDAG**, None; **A. Cefle**, None; **B. Artim-Esen**, None; **G. MUMCU**, None; **T. ERGUN**, None; **H. Direskeneli**, None.

Abstract Number: 0950

Low-Dose IL-2 Effectively Restored Decreased Regulatory T Cells in Patients with Behcet's Disease

Xiao-qing Liu,[1] Xiaojie Liu,[2] Nalin Lai,[3] Ting Cheng,[1] Chong Gao,[4] and Xiao-feng Li[1], [1]The Second Hospital of Shanxi Medical University, Taiyuan, China (People's Republic), [2]Taiyuan University of Technology, Taiyuan, China (People's Republic), [3]Shanxi Medical University, Taiyuan, China (People's Republic), [4]Brigham and Women's Hospital, Harvard Medical School, Boston

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders I: Miscellaneous Disorders
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Behcet's disease (BD) is a chronic multisystemic disease characterized by muco-cutaneous and ocular manifestations, with central nervous system, vascular and/or gastro-intestinal involvement. Several studies have shown that immune mechanisms play an important role in the development of the disease and limited options of therapeutic medicines for BD. Low dose IL-2 has been reported to selectively promote the expansion of Treg. This study aimed to investigate the significance of Treg cells in the pathogenesis and the effect of low dose IL-2 on BD.

Methods: Absolute number of CD4+CD25+FOXP3+Treg, CD4+IL17+T (Th17) and other subsets in peripheral blood (PB) from 173 patients with BD and 90 healthy donors were characterized by flow cytometry combined with an internal microsphere counting standard. Thirty-nine patients were treated with daily subcutaneous injections of 0.5 million IU of human IL-2 for five consecutive days, and then its effects on lymphocyte subpopulations in PB were analyzed.

Results: There was a significant disturbance in lymphocyte subpopulations mainly manifested as the decreased level of Tregs compared with the health controls (median:22.32 cells/ul VS median:33.12 cells/ul, $P< 0.001$) and it was correlated negatively with BDCAF, ESR and CRP ($P < 0.01$), suggesting an important role of Tregs in sustained high disease activity. While no major difference in the absolute counts of circulating Th17 cells between patients with BD and health control. Accordingly, the ratios of Th17/Treg in patients with BD (median:0.38) were significantly higher

than those of health control (median:0.21). Moreover, low dose IL-2 effectively increased the number of Tregs ($P < 0.001$) and re-balance the ratio of Th17 and Tregs, leading to clinic symptom partly remission in a rapid way without observed side effects.There was a significant disturbance in lymphocyte subpopulations mainly manifested as the decreased level of Tregs compared with the health controls (median:22.32 cells/ul VS median:33.12 cells/ul, $P< 0.001$) and it was correlated negatively with BDCAF, ESR and CRP ($P < 0.01$), suggesting an important role of Tregs in sustained high disease activity. While no major difference in the absolute counts of circulating Th17 cells between patients with BD and health control. Accordingly, the ratios of Th17/Treg in patients with BD (median:0.38) were significantly higher than those of health control (median:0.21). Moreover, low dose IL-2 effectively increased the number of Tregs ($P < 0.001$) and re-balance the ratio of Th17 and Tregs, leading to clinic symptom partly remission in a rapid way without observed side effects.

Conclusion: Absolute decrease of PB Tregs in patients with BD was associated with disease activity ,which might be the major reason for imbalance of Th17/Tregs. It is speculated that BD is an autoimmune disease triggered by the defect of immunotolerance. More importantly, low-dose IL-2 proposes a selective biological treatment strategy by restoring immune tolerance and promoting rapidly remission.

Disclosure: X. Liu, None; **X. Liu**, None; **N. Lai**, None; **T. Cheng**, None; **C. Gao**, None; **X. Li**, None.

Abstract Number: 0951

Avoidable Acute Care Use for Vaccine-Preventable Illnesses Among Medicaid Beneficiaries with Lupus: Demographic and Healthcare Utilization Differences

Candace Feldman,[1] Chang Xu,[1] and Karen Costenbader[1], [1]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research I: Clinical Perspectives
Session Type: ACR/ARP Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Nearly 25% of patients with SLE are hospitalized each year often for outcomes that may have been avoided if patients had received sustained, high quality outpatient care. A recent Delphi panel defined SLE-specific adverse outcomes that may result in avoidable acute care use (emergency department [ED] visits or hospitalizations) and included 7 vaccine-preventable illnesses. We used U.S. nationwide data from a vulnerable SLE population to describe the burden of acute care use for these illnesses and to examine demographic and healthcare utilization predictors.

Methods: Using claims data from Medicaid (public insurance for low income individuals) from 29 U.S. states (2000-2010), we identified adults (18-65 years) with prevalent SLE (≥3 ICD-9 codes 710.0 separated by ≥30 days). We required 12 months of enrollment prior to the first code (index date) to identify baseline comorbidities, vaccine uptake, and healthcare utilization. We defined avoidable acute care use for vaccine-preventable illnesses as discharge diagnosis codes from ED visits or hospitalizations for influenza, pneumococcal disease, meningococcal disease, herpes zoster, high-grade cervical dysplasia/cervical cancer, and hepatitis B, after the index date. We estimated the incidence rate (IR) of acute care use for vaccine-preventable illnesses and used Cox regression to assess risk (HR, 95% CI) of first acute care visit for vaccine-preventable illnesses by baseline demographics and healthcare use, adjusting for vaccinations, SLE-related comorbidities and medications.

Table 1: Incidence rates of acute care use* for vaccine-preventable illnesses among Medicaid beneficiaries with SLE (N=46,075)				
	Number of patients	Person-years	Incidence Rate per 1,000 person-years (95% CI)	Percent of events in patients without vaccine claims**
Composite of vaccine-preventable illnesses†	1340	195,960	6.8 (6.5-7.2)	93%
Herpes zoster	490	199,382	2.5 (2.2-2.7)	97%
Influenza	412	199,669	2.1 (1.9-2.3)	95%
Pneumococcal disease	325	200,283	1.6 (1.4-1.8)	NR
Hepatitis B	91	201,340	0.5 (0.4-0.5)	100%
High-grade cervical dysplasia/Cervical cancer	58	190,321	0.3 (0.2-0.4)	100%
Meningococcal disease	26	201,444	0.1 (0-0.1)	100%
*Acute care use includes emergency department visits or hospitalizations †31 SLE patients had more than one vaccine-preventable illness but were included once in the composite measure **Vaccine claims during the 12-month baseline period NR= In accordance with CMS policies, cell sizes >0 and <11 are not reported; percent of events among patients who received pneumococcal vaccine is within this range				

Table 1 Vaccine Prevent Illness ACR

Results: We identified 46,075 Medicaid beneficiaries with SLE with mean follow-up of 4 (SD 3) years. The mean age was 39 (SD 12) and 93% were female, 40% were black, 38% white, 13% Hispanic, 2% Asian. Vaccine uptake during the 12-month baseline period included: 3,331 (7.2%) receiving the influenza vaccine, 1,020 (2.2%) shingles, 551 (1.2%) pneumococcal, 290 (0.63%) hepatitis B, 91 (0.2%) human papillomavirus, and 17 (0.04%) meningitis. The incidence rate of acute care use for vaccine-preventable illnesses was 6.8 per 1,000 person-years; most were herpes zoster, influenza or pneumococcal disease (**Table 1**). 93% of events occurred in patients who had not received baseline vaccinations. In adjusted analyses, we observed a higher risk of acute care use for vaccine-preventable illnesses among black patients, in the Midwest and South, and among patients with more baseline ED visits and hospitalizations (**Table 2**). Greater outpatient visits were associated with a dose-response reduction in acute care use, with >30% reduced risk (HR 0.69, 95% CI 0.56-0.74) comparing >10 visits to none.

Conclusion: Claims for vaccinations in this nationwide, vulnerable population of SLE patients were rare, likely reflecting a combination of underreporting and low uptake. As expected, patients with vaccine claims had minimal acute care use for vaccine-preventable illnesses. Greater outpatient use was associated with significantly reduced risk of ED visits and hospitalizations for vaccine-preventable illnesses suggesting that established, consistent outpatient care with optimal SLE monitoring and management, and access to preventive care, can reduce avoidable acute care use.

Table 2: Multivariable Cox regression model for first episode of acute care use for vaccine-preventable illnesses by demographic factors and baseline healthcare utilization among Medicaid beneficiaries with SLE (N=46,075)	
Variables	**Hazard ratio (95% Confidence Interval)**
Age category *(ref=51-65 years)*	
18-34 years	1.13 (0.96-1.33)
35-50 years	1.08 (0.93-1.26)
Male *(ref=Female)*	1.11 (0.87-1.42)
Race/ethnicity *(ref=White)*	
Black	**1.18 (1.05-1.35)**
Asian	1.25 (0.88-1.79)
Hispanic	1.01 (0.84-1.2)
American Indian/Alaska Native	1.23 (0.74-2.03)
More than one race	1.30 (0.98-1.74)
Geographic region *(ref=Northeast)*	
Midwest	**1.24 (1.04-1.48)**
South	**1.28 (1.09-1.49)**
West	1.17 (0.98-1.39)
Outpatient visits *(ref=0)*	
1-5 visits	0.90 (0.75-1.06)
6-10 visits	**0.77 (0.63-0.93)**
>10 visits	**0.69 (0.56 -0.74)**
Hospitalization *(ref=0)*	**1.64 (1.46-1.85)**
Emergency department visits *(ref=0)*	
1-5 visits	**1.70 (1.49-1.94)**
>5 visits	**2.95 (2.42-3.59)**
Model also adjusted for calendar year, SLE risk adjustment index, number of medications at index date, medication use (glucocorticoids, immunosuppressants, hydroxychloroquine), vaccinations and Pap smear during the 12-month baseline period; bolded values are statistically significant (p<0.05)	

Table 2 Avoidable vaccine abstract

Disclosure: C. Feldman, None; **C. Xu**, None; **K. Costenbader**, Astra-Zeneca, 2, Glaxo Smith Kline, 2, Janssen Scientific Affairs, LLC, 2, Lupus Foundation of America, 2, Lupus Research Alliance, 2, Merck, 2.

Abstract Number: 0952

Rate of Thirty-Day Readmissions in Systemic Lupus Erythematosus Rivals Congestive Heart Failure and Exceeds the General Medicare Population

Ann Chodara,[1] Xing Wang,[1] Fangfang Shi,[1] Shivani Garg,[1] Ryan Powell,[1] Maria Schletzbaum,[1] Ann Sheehy,[1] Amy Kind,[1] and Christie Bartels[1], [1]University of Wisconsin School of Medicine and Public Health, Madison, WI

SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Health Services Research I: Clinical Perspectives

Session Type: ACR/ARP Abstract Session

Session Time: 4:30PM–6:00PM

Table 1. Baseline characteristics of Medicare admissions with SLE, CHF and overall

		Overall n=1,389,522	SLE n=10,868	CHF n=345,628	p*
Patient Variables					
Age at hospitalization (mean, SD)		73.4 (13.6)	59.9 (16.7)	76.9 (12.0)	
Age at admission	18-33	1%	9%	<1%	<0.001
	34-49	5%	20%	3%	
	50-64	14%	26%	12%	
	65-79	46%	34%	41%	
	≥80	34%	11%	45%	
Gender	Female	57%	89%	54%	<0.001
Race	White	82%	62%	81%	<0.001
	Black	12%	29%	14%	
	Asian	1%	1%	1%	
	Native American	1%	1%	1%	
	Other/Unknown	1%	2%	1%	
	Hispanic	2%	5%	2%	
Medicaid ever		30%	46%	31%	<0.001
Medicare enrollment reason	Disability	32%	65%	30%	<0.001
	ESRD	3%	15%	4%	<0.001
Prior hospitalization in last 12 mos		37%	48%	49%	<0.001
Rural-Urban	Urban	84%	87%	83%	<0.001
RUCA codes	Large City/Town	8%	7%	8%	
	Small Rural	5%	3%	5%	
	Isolated	4%	2%	4%	
ADI Disadvantage Quintile	1-20	17%	14%	16%	<0.001
	21-40	21%	18%	20%	
	41-60	22%	21%	22%	
	61-80	22%	23%	23%	
	81-100	18%	23%	20%	
CHF		40%	41%	93%	<0.001
COPD		45%	47%	63%	<0.001
Diabetes mellitus		36%	30%	48%	<0.001
Chronic kidney/ESRD		7%	20%	11%	<0.001
Hospital Variables					
Discharge volume	Highest	34%	39%	34%	<0.001
	Middle	33%	34%	33%	
	Lowest	33%	27%	33%	
Medical school affiliation		49%	55%	49%	<0.001
Outcome Events					
Readmissions		18%	24%	24%	<0.001

**P values calculated using t-test or chi-square test comparing SLE to CHF. Abbreviations: ESRD = end-stage renal disease, RUCA = rural urban commuting area, ADI = area deprivation index, CHF = congestive heart failure, COPD = chronic obstructive pulmonary disorder*

Table 2. Hazard ratios (HR) of 30 day readmissions in SLE and CHF

	Unadjusted HR, 95% CI	p	Adjusted HR, 95% CI	p
Overall	ref	<0.0001	Ref	<0.0001
CHF	1.539 (1.538, 1.540)		1.190 (1.190, 1.191)	
SLE	1.528 (1.527, 1.529)		1.192 (1.192, 1.192)	

Table 3. Hazard ratios (HR) for 30-day readmission in SLE

		Unadjusted HR, 95% CI	Adjusted HR, 95% CI
Age at admission	18-33	Ref	**Ref**
	34-49	0.686 (0.686, 0.686)	0.809 (0.809, 0.810)
	50-64	0.499 (0.499, 0.499)	0.601 (0.601, 0.601)
	65-79	0.451 (0.451, 0.451)	0.623 (0.623, 0.623)
	≥80	0.413 (0.413, 0.413)	0.573 (0.573, 0.573)
Gender	Female	0.951 (0.950, 0.953)	0.949 (0.949, 0.949)
Race/Ethnicity	White	Ref	Ref
	Black	1.553 (1.553, 1.553)	**1.067** (1.067, 1.067)
	Asian	0.827 (0.826, 0.827)	0.673 (0.673, 0.673)
	Native American	1.625 (1.624, 1.627)	**1.224** (1.224, 1.224)
	Other/Unknown	1.341 (1.341, 1.341)	0.929 (0.929, 0.929)
	Hispanic	1.293 (1.293, 1.294)	0.870 (0.870, 0.870)
Medicaid ever		1.451 (1.451, 1.451)	**1.052** (1.052, 1.052)
Prior hosp <12 mos		2.032 (2.032, 2.032)	**1.535** (1.535, 1.535)
ADI disadvantage	1-20 (least)	Ref	Ref
	21-40	0.868 (0.868, 0.869)	0.857 (0.857, 0.857)
	41-60	1.096 (1.096, 1.096)	0.987 (0.987, 0.987)
	61-80	1.110 (1.110, 1.110)	0.965 (0.965, 0.966)
	81-100 (most)	1.190 (1.190, 1.190)	0.937 (0.937, 0.937)
CHF		1.750 (1.749, 1.750)	**1.388** (1.388, 1.388)
COPD		1.400 (1.400, 1.400)	**1.224** (1.224, 1.224)
Diabetes mellitus		1.261 (1.261, 1.261)	**1.065** (1.065, 1.065)
Chronic kidney/ESRD		1.952 (1.952, 1.952)	**1.397** (1.397, 1.397)
Discharge volume	Highest	Ref	Ref
	Middle	1.011 (1.011, 1.011)	**1.020** (1.020, 1.020)
	Lowest	0.865 (0.865, 0.865)	0.907 (0.907, 0.907)
Medical school affiliation		1.089 (1.088, 1.090)	0.988 (0.988, 0.988)

Abbreviations: ESRD = end-stage renal disease, CHF = chronic heart failure, COPD= chronic obstructive pulmonary disease, ADI = Area Deprivation Index

Background/Purpose: Medicare measures readmissions within 30 days of hospitalization across several conditions as a marker of care quality. While not currently a reporting condition, in systemic lupus erythematosus (SLE) observed 30-day readmission rates range from 17-27%, rivaling reportable conditions such as congestive heart failure (CHF). No controlled studies thus far have performed such between-condition comparisons. Using a nationwide

Medicare cohort, we compared adjusted readmission rates among SLE, CHF, and the general Medicare population, and assessed relationships between patient and hospital factors and 30-day readmissions in SLE with the goal of identifying targets for readmission prevention measures.

Methods: Using claims data from a 20% random US national Medicare sample, we identified all patients with inpatient hospitalizations in 2014 to compare risk of 30-day readmission among patients with SLE to those with CHF and the general Medicare population. Inclusion required age of at least 18 years old, live discharge, and at least 12 months of continuous Medicare part A and B coverage prior to index admission. Baseline patient and hospital covariates included age, sex, race, ethnicity, Medicaid, baseline year comorbidity, prior hospitalization, hospital volume, medical school affiliation, and area deprivation index (ADI)–a measure of neighborhood disadvantage from patients' census block group. Analysis used multivariable Cox proportional-hazards regression clustered by patient to find adjusted hazard ratios (HRs) of 30-day readmission among patients with SLE compared to those with CHF and the general Medicare population.

Results: The SLE cohort (n=10,868) was younger by nearly 20 years and predominantly female. They were twice as likely to be Black, on Medicaid or disabled, and had nearly four-fold higher ESRD as compared to CHF or general Medicare (Table 1). The 30-day readmission rate of 24% was identical for SLE and CHF, and significantly higher than the general Medicare cohort rate of 18%. Patients with CHF and SLE had similarly elevated hazard ratios for readmission (HR 1.190, 95% CI 1.190, 1.191 and HR 1.192, 95% CI 1.192, 1.192, respectively; Table 2), compared to patients without either condition. Among patients with SLE, readmission risk was highest in the 18-33 age group (Table 3). Higher readmission risk was also observed in SLE patients who were Black, Native American, hospitalized within the past year, and who had comorbidities including CHF, COPD, and ESRD. Dual Medicaid status predicted slightly increased risk, and hospital factors were more modestly predictive. Overall, primary diagnoses for readmissions did not significantly differ between groups.

Conclusion: 30-day readmission rates in SLE are as high as those in CHF, with readmissions impacting one in four hospitalized SLE patients. Transitional care programs, Medicare policies, and other efforts designed to reduce readmissions should consider focusing on SLE, a high risk group for readmissions that is currently not widely recognized as such. Existing interventions should particularly target SLE patients who are younger, with ESRD or prior hospitalization.

Disclosure: A. Chodara, None; **X. Wang**, None; **F. Shi**, None; **S. Garg**, None; **R. Powell**, None; **M. Schletzbaum**, None; **A. Sheehy**, None; **A. Kind**, None; **C. Bartels**, Pfizer, 2, Pfizer Independent Grants for Learning and Change, 2.

Abstract Number: 0953

Treatment Patterns and Persistency Following the First Biologic DMARD in Patients with Rheumatoid Arthritis: Real-World Analysis of 2012–2016 US Medicare Data

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SESSION INFORMATION

Session Date: Sunday, November 10, 2019

Session Title: Health Services Research I: Clinical Perspectives

Session Type: ACR/ARP Abstract Session

Session Time: 4:30PM–6:00PM

Table. Patient Baseline Demographic Characteristics

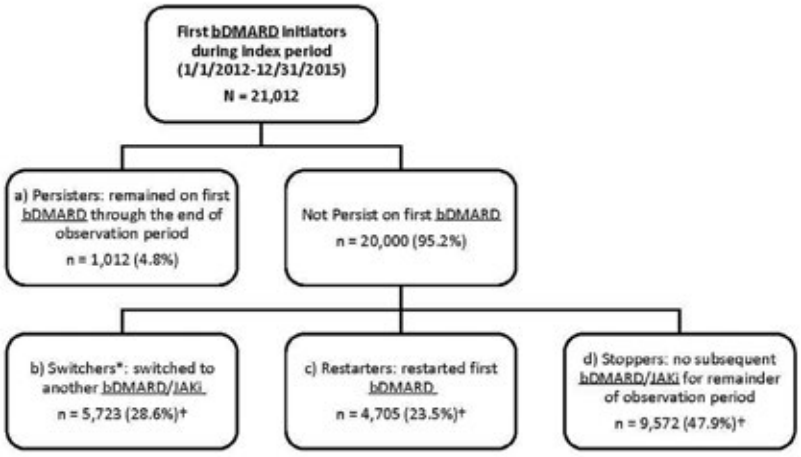
Characteristic	Overall bDMARD initiators	Persisters	Non-Persisters			
			All	Switchers	Restarters	Stoppers
N (row %)	21,012 (100%)	1,012 (4.8%)	20,000 (95.2%)	5,723 (27.2%)	4,705 (22.4%)	9,572 (45.6%)
Demographics						
Age, years, mean±SD; median [IQR]	66.0±10.9 66.1 [61.6,72.1]	67.2±8.1 66.4 [65.0, 71.1]	65.9±11.0 66.0 [61.3, 72.2]	64.0±11.0 65.4 [58.7, 70.1]	65.3±11.2 65.7 [60.7, 71.6]	67.3±10.6 66.8 [63.6, 73.8]
Female, n (%)	16,673 (79.4%)	727 (71.8%)	15,949 (79.8%)	4,652 (81.3%)	3,765 (80.0%)	7,532 (78.7%)
Race/ethnicity, n (%)						
White	16,945 (80.6%)	855 (84.5%)	16,090 (80.5%)	4,586 (80.1%)	3,724 (79.2%)	7,780 (81.3%)
Black	2,242 (10.7%)	100 (9.9%)	2,142 (10.7%)	602 (10.5%)	565 (12.0%)	975 (10.2%)
Others	1,825 (8.7%)	57 (5.6%)	1,768 (8.8%)	535 (9.4%)	416 (8.8%)	817 (8.4%)
Payer Type, n (%)						
Medicare only	16,348 (77.8%)	918 (90.7%)	15,430 (77.2%)	4,169 (72.9%)	3,691 (78.5%)	7,570 (79.1%)
Medicare/Medicaid dual	4,664 (22.2%)	94 (9.3%)	4,570 (22.9%)	1,554 (27.2%)	1,014 (21.6%)	2,002 (20.9%)
Follow-up Duration in Study, months, mean±SD; median [IQR]	31.8±15.4 30.9 [20.0,45.2]	33.3±14.1 33.1 [20.8, 45.7]	31.8±15.5 30.9 [20.0, 45.2]	35.4±15.2 35.5 [23.1, 47.7]	33.9±15.1 33.7 [22.4,46.5]	28.6±15.2 26.0 [17.0,40.4]
Censored follow-up						
Died before 12/31/2016	1,531 (7.3%)	15 (1.5%)	1,516 (7.6%)	275 (4.8%)	249 (5.3%)	992 (10.4%)
Lost Medicare before 12/31/2016	4,021 (19.1%)	55 (5.4%)	3,966 (19.8%)	991 (17.3%)	960 (20.4%)	2,015 (21.1%)

bDMARD, biologic DMARD; IQR, interquartile range; SD, standard deviation.

Background/Purpose: In RA patients not meeting treat-to-target goals despite treatment with a biologic (b)DMARD, ACR guidelines[1] recommend using other targeted immunomodulators (TIM): TNF-α inhibitor (TNFi), non-TNFi biologic (b)DMARDs, or a Janus kinase inhibitor (JAKi). Understanding treatment disposition and persistency can help optimize next treatment selection among Medicare recipients who initiated first bDMARD. We described treatment patterns and persistency in Medicare RA patients on first bDMARD.

Methods: In 20% sample of Medicare fee-for-service beneficiaries, the study population comprised RA patients (≥1 RA claims + ≥1 DMARD claims) who initiated (index date) their first bDMARD between 01/2012 and 12/2015 (no bDMARD use ≥12 months pre-index), without cancer or non-RA autoimmune disease. Subsequent treatment patterns were described during a follow-up period ending 12/2016, with censoring at death or end of Medicare coverage. Patients were grouped as Persisters (persisted on their first bDMARD) or Non-Persisters (did not persist), the latter being divided into Switchers (switched to another TIM), Restarters (restarted the first bDMARD after a gap), and Stoppers (stopped TIMs altogether). Persistency loss was estimated through Kaplan-Meier time-to-event analysis, with the event being discontinuation or first gap in initial bDMARD coverage exceeding 60 days past next-refill due date. Persistency was estimated for all patients and stratified by Non-Persisters, and then further by Switchers, Restarters, Stoppers.

Figure 1. Patient Disposition



*Switchers: 1291 patients switched to another bDMARD/JAKi before completing all prescribed days of their first bDMARD (medication possession), with 762 switching within 30 days prior to end of first bDMARD medication possession
†Percentages shown are within the 20,000 Non-Persisters. The estimates as a percent of N=21,012 first bDMARD initiators: Switchers 27.2%, Restarters 22.4%, and Stoppers 45.6%
bDMARD, biologic DMARD; JAKi, Janus kinase inhibitor.

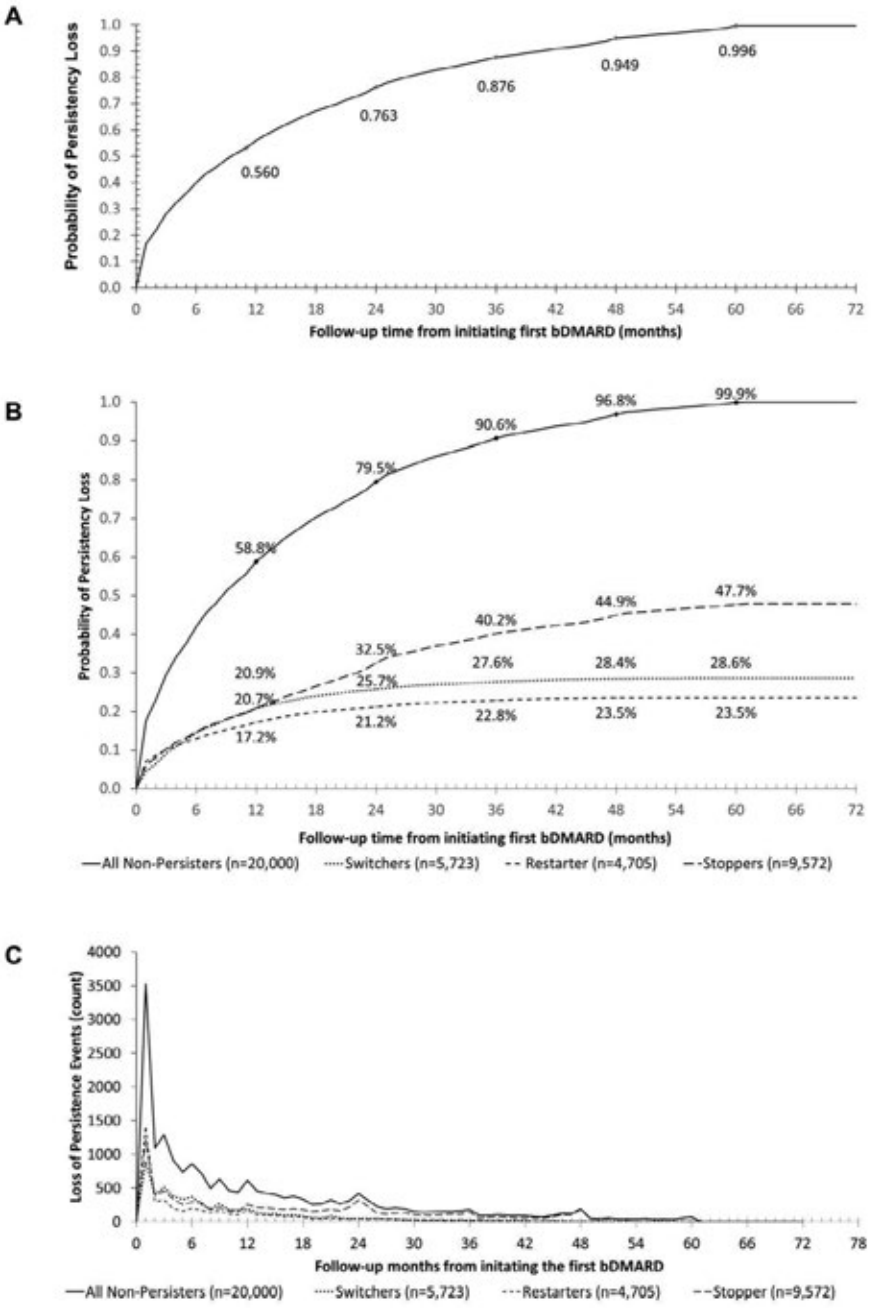
Results: The sample of 10,314,539 enrollees contained 154,311 RA patients, including 21,012 patients initiating bDMARD (52% intravenous, 48% subcutaneous): 79% female with mean age 66 years (Table). The sample consisted of 1,012 (4.8%) Persisters, 5,723 (27.2%) Switchers, 4,705 (22.4%) Restarters, and 9,572 (45.6%) Stoppers (Figure 1). Among all bDMARD initiators, 22.0% lost persistency by month 2 and 56.0% by month 12 (Figure 2a). Within Non-Persisters, the probability of losing persistency at month 12 was 58.9% overall, 72.4% for Switchers, 73.0% for Restarters, and 43.8% for Stoppers (Figure 2b). Among Non-Persisters, incident events peaked at months 1, 3, 6, 9, 12, 24, 36, 48, and 60; with contributions to persistency loss similar for all groups until month 12, after which Stoppers largely drove ongoing loss of persistency (Figure 2b, c).

Conclusion: After initiating their first bDMARD, Medicare beneficiaries with RA experienced substantial treatment interruptions, demonstrating deviations from the standard treatment-escalation approach described in the ACR guidelines. Over half the patients lost persistency on first bDMARD by year 1. Moreover, almost half of those who lost persistency on first bDMARD remained off TIM therapy altogether, suggesting a substantial unmet need for treatment in this patient population that warrants further investigation.

References:

1. Singh JA, et al. Arthritis Rheumatol 2016;68:1-26.

Figure 2. Persistency loss on the first bDMARD. A) Probability of losing persistency (among all first bDMARD initiators, N = 21,012); B) Cumulative incidence of loss of persistency on first bDMARD among Non-Persisters and by disposition; C) Incident Loss of Persistency.



Disclosure: R. Dore, AbbVie, 2, 5, 8, AbbVie, Inc., 5, 8, 9, Abbvie, Inc., 2, 5, 8, Amgen, 2, 5, 8, 9, Biogen, 2, 9, Gilead Science, 2, 5, Gilead Sciences, Inc., 2, 5, 9, Lilly, 2, 5, 8, 9, Novartis, 2, 5, 9, Pfizer, 2, 8, 9, Radius, 8, Regeneron, 8, Sanofi, 8, UCB, 2, 8, 9, VCB, 8; **L. Chang**, Gilead Science, 9, Gilead Sciences, Inc., 1, 3, Lilly, 9; **Y. Ji**, None; **S. Li**, None; **J. Antonova**, Gilead Science, 1, 3, Gilead Sciences, Inc., 1, 3; **M. Genovese**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 9, Astellas, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck Serono, 2, 5, Galapagos, 2, 5, Galapagos NV, 2, 5, 9, Genentech/Roche, 2, 5, Gilead, 2, 5, Gilead Science, 9, Gilead Sciences, Inc., 2, 5, 9, GSK, 5, Lilly, 2, 5, 9, Novartis, 2, 5, Pfizer, 2, 5, 9, Pfizer Inc, 2, 5, Pfizer, Inc., 9, Pzier, 9, RPharm, 5, Sanofi Genzyme, 2, 5, Vertex, 2, 5.

Abstract Number: 0954

Physical Therapy and Opioid Use in Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research I: Clinical Perspectives
Session Type: ACR/ARP Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Knee osteoarthritis (OA) is a leading cause of chronic pain in older adults. Physical therapy (PT) decreases OA pain and consequently may reduce burden of opioid use in this population. The purpose of this study was to investigate the associations of type, dose, and timing of PT with utilization of opioids following PT in individuals with incident knee OA who had used opioids in the past or were opioid naïve, using data from a large claims database.

Methods: We conducted a cohort study using 2000-2014 data from the OptumLabs® Data Warehouse (OLDW), a longitudinal, real-world dataset with de-identified administrative claims and electronic health record (EHR) data. We included adults between the ages of 40-89, who after ≥ 6 months of claims data, had a knee OA diagnosis using ICD9 codes, the date of which we defined as the index date. We excluded individuals with OA-related surgeries, knee injuries, PT, cancer, or rheumatoid arthritis within 6 months prior to index date. Only persons who received PT within 12 months of the index date and who had at least 1 year of follow-up after the first PT episode of care were included. The first PT episode of care was considered to start with an initial PT evaluation followed by at least one treatment session, and was considered to end if there was a 4-week period with no PT claim or if a second evaluation was recorded. We studied several PT exposures including dose (number of sessions), timing and active versus passive modality (Table 1). The outcome was any opioid use in the 12 months after the end of the PT episode of care. Opioid use was defined as at least 2 filled prescriptions of opioids commonly used for musculoskeletal pain. Combinations of opioids with medications commonly used for cough, nasal congestion, and headache were excluded. We conducted the analyses in individuals who had used opioids prior to PT ("opioid experienced") and those who had not used opioids prior to PT ("opioid naïve"). Covariates included age, hyperlipidemia, diabetes, and overweight/obesity. Adjusted odds (aOR) of receiving opioids were assessed (Table 1) using logistic regression.

Exposure	Definition	Modeling	Reference category
Dose of PT	Number of PT sessions on unique dates within the first PT episode of care	1-5 sessions, 6-12 sessions, > 12 sessions	1-5 sessions
Timing of PT	Time between knee OA diagnosis and start of first PT episode of care	<3 months, 3-<6 months, 6-<9 months, 9-<12 months	<3 months
Active vs. passive PT	Active PT defined as only active PT treatment codes (e.g. therapeutic exercise, gait retraining, etc.); passive PT = passive treatment codes (e.g. ultrasound, hot pack, manual therapy, etc.).	Active (only active or active ≥ passive), passive (only passive or passive > active)	Passive

Table 1. Exposure definitions

Variables		Opioid Experienced			Opioid Naïve		
		Subjects	Opioid Use	aOR	Subjects	Opioid Use	aOR
Total		32,324	18,901 (58.5%)		39,302	6,092 (15.5%)	
Physical Therapy Dose (# sessions)	1-5	46.9%	65.6%	REF	55.9%	16.9%	REF
	6-12	30.1%	55.3%	0.65 (0.62, 0.69)	31.6%	13.8%	0.79 (0.74, 0.84)
	>12	23.0%	48.1%	0.49 (0.47, 0.52	12.5%	13.6%	0.77 (0.70, 0.84)
Physical Therapy Timing (Months)	<3	49.5%	57.8%	REF	72.0%	14.9%	REF
	3-<6	25.1%	57.3%	0.98 (0.93, 1.04)	13.3%	18.0%	1.26 (1.17, 1.37)
	6-<9	14.5%	60.2%	1.10 (1.03, 1.17)	8.3%	16.5%	1.14 (1.03, 1.26)
	9-<12	10.9%	62.1%	1.20 (1.11, 1.29)	6.3%	16.2%	1.11 (1.00, 1.25)
Active vs. Passive Physical Therapy	Passive	25.8%	61.2%	REF	26.5%	15.6%	REF
	Active	74.2%	57.5%	0.86 (0.82, 0.91)	73.5%	15.5%	1.00 (0.94, 1.06)

Table 2. Prevalence of exposure and outcomes among opioid experienced and naïve individuals

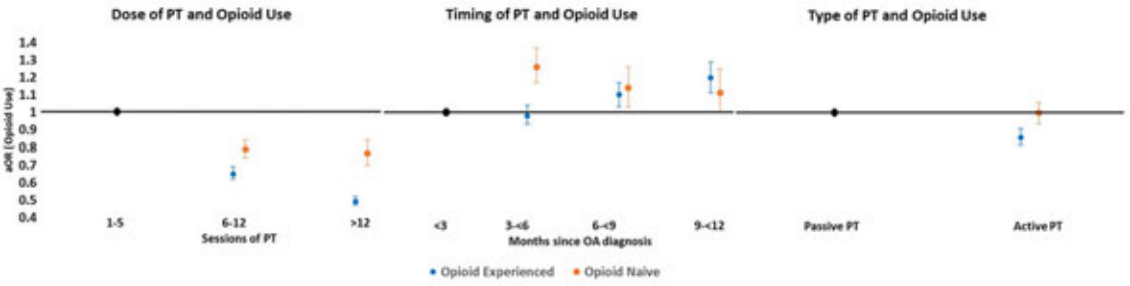

Figure 1. Adjusted odds ratios of opioid use among opioid experienced and naïve individuals

Results: We included 32,324 opioid experienced (age=60.9±10.3 years; 61.5% female) and 39,302 opioid naïve individuals (age=62.6±11.2 years; 66.0% female) (Table 2). Among both opioid experienced and opioid naïve individuals, more than 5 sessions of PT and early PT after knee OA diagnosis (vs. > 6 months) were associated with reduced odds of opioid use (Table 2, Figure 1). Among opioid naïve individuals, receiving PT >3 months after diagnosis vs. earlier was related with increase odds of opioid use (Table 2, Figure 1). Receiving active PT (vs. passive PT) was associated with reduced odds of further opioid use in opioid experienced individuals but not in the opioid naïve group (Table 2, Figure 1).

Conclusion: PT provided earlier after OA diagnosis, more than 5 sessions of PT, and use of active PT interventions may reduce opioid use in people with knee OA. These results provide guidance on optimal dosage, timing, and type of PT interventions that might be effective at reducing opioid use in this population.

Disclosure: D. Kumar, None; **C. Peloquin**, None; **A. Stokes**, None; **L. Marinko**, None; **J. Camarinos**, None; **D. Felson**, None; **M. Dubreuil**, None.

Abstract Number: 0955

Adherence to Statin Therapy in Rheumatoid Arthritis Patients: A Population-Based Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research I: Clinical Perspectives
Session Type: ACR/ARP Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Cardiovascular diseases (CVD) are increased in RA and lead to premature mortality. Statins are effective at preventing incidence of, and mortality from, CVD; yet, adherence can be problematic. The objective of this study was to assess adherence to statin therapy in a population-based cohort of rheumatoid arthritis (RA) patients compared to the general population, and to identify the predictors of statin discontinuation in the RA cohort.

Methods: A population-based cohort study using administrative health data was conducted on all incident RA patients in the Province, identified using physician billing data and previously published criteria, and general population controls matched (2:1) on age, sex and calendar year. The study included all individuals who initiated a statin for the first time between January 1997 and December 2009, with follow-up until December 2014. Statin discontinuation was defined as a gap in medication dispensing of ≥4 months. The primary outcome was survival time from statin initiation until first discontinuation , and the secondary outcome was the proportion of days covered (PDC) of medication, calculated only during courses of active statin use (i.e., excluding periods of statin discontinuation), which represents the percentage of the time when a medication is taken as prescribed. A multivariable Cox proportional hazards models was used to identify the predictors of statin discontinuation in the RA sample only.

Results: The sample includes 4845 incident RA patients who were incident statin users, and 9204 individuals from the general population, providing 16728 and 34351 PY of follow-up, resp. 82.4% of the RA and 80.2% of the general population cohorts had at least one discontinuation; and 42.2% of RA and 40.2% of the general population permanently discontinued statin therapy during follow-up. Figure 1 shows that survival on statin (time to first statin discontinuation) was slightly lower for RA than general population ($p < 0.001$). Median survival was 2.29 years for RA patients and 2.64 years (for controls. Incidence rate of discontinuation was 23.87 per 100PY for RA and 21.48 per 100PY for the general population, yielding an incidence rate ratio (IRR) of 1.11; 95% CI, 1.07 – 1.16. Adherence [Mean (SD) PDC] during treatment courses was 92.9 (9.3)% in RA patients and 92.7 (9.4)% among controls. Significant pre-

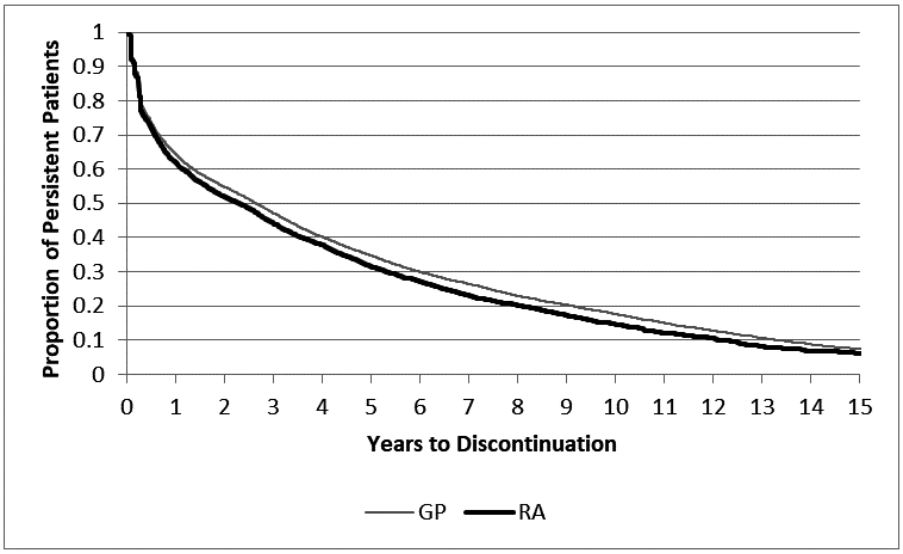


Figure 1. Kaplan Meier survival curves modelling time from incident statin therapy to first discontinuation in rheumatoid arthritis patients and general population. P value <0.001 determined by log-rank test.

Table 1. Multivariable Cox Proportional Hazards Model estimating risk of discontinuation of statin therapy in RA patients.

	Adjusted HR (95% CI) [1]	p value [5]
Age, per 10 year increase	1.01 (0.98-1.04)	0.560
Female	1.05 (0.98-1.12)	0.151
Rural	0.97 (0.90-1.05)	0.493
Income Quintile		
- 2 vs 1	0.95 (0.86-1.04)	0.247
- 3 vs 1	0.92 (0.84-1.01)	0.087
- 4 vs 1	0.85 (0.77-0.94)	0.001
- 5 vs 1	0.83 (0.75-0.92)	<0.001
Diabetes Mellitus [3]	1.05 (0.96-1.14)	0.281
Previous MI [4]	0.86 (0.78-0.95)	0.002
Previous CVA [4]	0.94 (0.84-1.04)	0.234
Depression [3]	1.14 (1.03-1.26)	0.011
CVD medication use [3]	0.88 (0.82-0.94)	<0.001
Number of daily medications, per unit increase [3]	0.96 (0.95-0.97)	<0.001
Charlson comorbidity score, per unit increase [3]	1.01 (0.98-1.04)	0.428
DMARD categories [2,3]:		
- 2 vs 1	0.83 (0.73-0.95)	0.005
- 3 vs 1	0.97 (0.86-1.10)	0.671
- 4 vs 1	1.05 (0.79-1.38)	0.750
- 5 vs 1	1.21 (0.94-1.56)	0.142
RA-related medical visits, per visit increase [3]	1.01 (0.99-1.02)	0.295
Glucocorticoid use [3]	1.08 (0.99-1.19)	0.098
RA-related orthopedic procedure [4]	0.96 (0.87-1.06)	0.401

[1] *Adjusted HR's from a combined multivariable model. HR = hazard ratio; 95% CI = 95% confidence interval; RA = rheumatoid arthritis; MI = myocardial infarction; CVA = cerebrovascular accident; CVD = cardiovascular disease; DMARD = disease-modifying antirheumatic drug.*

[2] *DMARD categories: 1 = no DMARD use; 2 = antimalarial drugs, sulfasalazine; 3 = methotrexate, intramuscular gold; 4 = leflunomide, cyclosporine A, azathioprine, cyclophosphamide, chlorambucil, or mycophenolate mofetil; and 5 = biologics.*

[3] *Evaluated over the 1 year preceding statin initiation.*

[4] *Evaluated prior to statin initiation since 1990 (earliest available data).*

[5] *P value for Chi-square test.*

dictors of statin discontinuation in RA included number of daily medications; use of CVD medications; previous MI; higher income; and depression (Table 1).

Conclusion: Findings from our population-based study indicate that RA patients and the general population both frequently discontinue statin therapy, but have high adherence during periods of statin use. Rates of statin discontinuation were slightly higher in RA patients, despite an increased risk of CVD. Risk of discontinuation was lower in RA patients with a higher number of daily meds, use of cardiovascular meds, prior MI, and higher income, and was higher in patients with depression. These results emphasize the importance of discussing adherence.

Disclosure: T. Hahn, None; **E. Sayre**, None; **M. Goycochea-Robles**, None; **D. Lacaille**, None.

Abstract Number: 0956

The Impact of Psychiatric Comorbidity on Health Care Utilization and Preventive Health Care in Rheumatoid Arthritis: A Population Based Study

Carol Hitchon,[1] Charles Bernstein,[1] James Bolton,[1] Renée El-Gabalawy,[1] John Fisk,[2] Alan Katz,[1] Lisa Lix,[3] James Marriott,[1] Scott Patten,[4] Christine Peschken,[3] Jitender Sareen,[1] Alexander Singer,[1] Randy Walld,[1] and Ruth Ann Marrie[1], [1]University of Manitoba, Winnipeg, MB, Canada, [2]Dalhousie University, Halifax, NS, Canada, [3]University of Manitoba, Winnipeg, Canada, [4]University of Calgary, Calgary, AB, Canada

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Health Services Research I: Clinical Perspectives
Session Type: ACR/ARP Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Psychiatric comorbidity is increased in rheumatoid arthritis (RA) and may complicate medical care, increasing the risk of adverse health outcomes and health care utilization (HCU). We describe the impact of psychiatric comorbidity in RA on HCU (ambulatory care visits, hospitalizations, number of hospital days, prescription drugs) including recommended preventive health care (influenza vaccination, pap and mammogram tests).

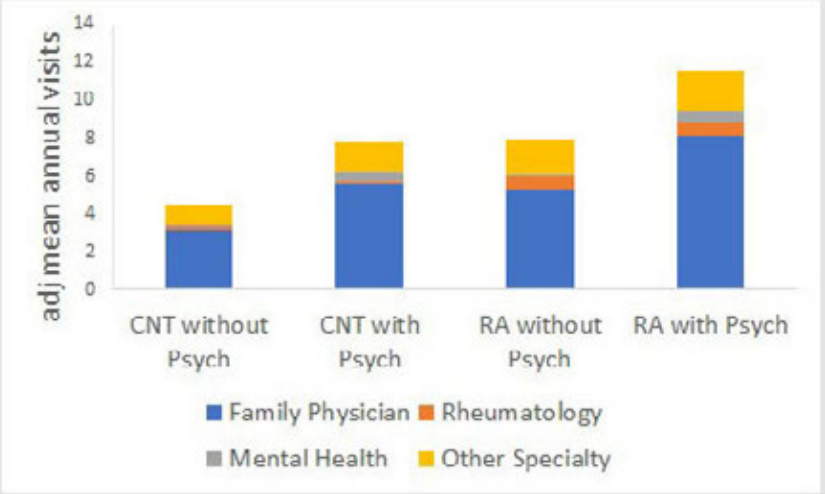
Methods: We accessed administrative health data (1984-2016) from a region with near universal health coverage and identified a prevalent cohort with diagnosed RA (n=16975). We matched each RA case on age and sex with up to 5 controls (CNT) with no RA diagnosis (n= 84756). Psychiatric morbidities including depression, anxiety and bipolar disorder (PsyMb) were identified in RA cases and CNT. Annual rates of ambulatory care visits [mean visits (SD)/person], all-cause hospitalization (%), days of hospitalization [(mean days (SD)/hospitalization], total prescribed drugs (mean (SD)/person), influenza vaccination (%), pap tests (%), and mammograms (%), were age and sex-standardized to the 2010 Canadian population. Ambulatory care visits were categorized by provider (family physician [FP], rheumatologist, mental health specialist, other specialist). We compared rates of HCU and preventive care amongst four groups (CNT, CNT+PsyMb, RA, RA+PsyMb) using generalized linear models adjusted for age, sex, rural vs urban residence, income quintile, total comorbidities (assessed by John Hopkins Aggregated Diagnostic Groups), DMARD prescription, and RA-specific procedures (e.g. arthroplasty). Rates and percentages are reported with 95% confidence intervals (CI). We tested whether PsyMB and RA had additive or synergistic effects on HCU or preventive care.

Results: Most RA patients were female (72%) and urban residents (59%). Mean age at diagnosis was 54(SD:16) years. Mean follow-up duration was 13(SD:9) years. After adjustment, compared to RA without PsyMb, those RA with PsyMb had an additional 3.7 (95%CI: 3.5-3.9, p< 0.0001) ambulatory visits/year, 2.3% (95%CI: 1.8-2.8; p< 0.0001) increased hospitalization, 0.7 (95%CI: 0.5-0.95 p< 0.0001) more hospital days/admission and were prescribed 2.3 (95%CI 2.2-2.5; p< 0.0001) more drugs (Table). RA+PsyMb had increased ambulatory care visits for all providers particularly FPs [additional 2.9 FP visits/year (2.8, 3.0); interaction between RA, Psych and provider p< 0.0001] (Figure). Overall rates of preventive care in RA were 34% for influenza vaccination, 38.3% for mammograms and 43.3% for pap tests when indicated. RA+PsyMb had increased influenza vaccinations (5.5%; 4.8-6.2%, p< 0.0001) and screening mammograms (4.7%; 3.7-5.7%, p< 0.0001) but not pap tests (0.2%; -1-0.06%, p=0.6). No interactive effects were significant for influenza vaccination or mammogram preventive measures between RA and RA+PsyMb (Table).

Conclusion: Psychiatric comorbidity increases health care utilization among those with RA, particularly for FP visits. Increased contact with care providers may contribute to higher rates of some preventative care such as vaccination, but overall preventive care rates remained suboptimal.

Group	Ambulatory visits Mean (95% CI)	Number drugs Mean (95% CI)	Hospitalization % (95%CI)	Hospital days Mean (95% CI)	Influenza vaccine % (95%CI)	Pap test % (95%CI)	Mammogram % (95%CI)
CNT	5.3 (5.3,5.3)	3.3 (3.3, 3.4)	10.2 (10.1, 10.3)	2.2 (2.1, 2.2)	22.4 (22.2, 22.6)	41.0 (40.7, 41.3)	34.1 (33.8, 34.5)
PsyMb	8.3 (8.3-8.4)	5.0 (5.0, 5.1)	13.2 (13,0, 13.3)	2.6 (2.6, 2.7)	27.9 (27.6, 28.2)	42.0 (41.7, 42.3)	39.2 (38.8, 39.6)
RA	7.9 (7.8, 8.0)	6.3 (6.2, 6.4)	15.6 (15.3, 15.9	3.0 (2.9, 3.1)	26.2 (25.7, 26.7)	41.4 (40.7, 42.0)	33.0 (32.1, 33.6)
RA + PsyMb	11.6 (11.4-11.8)	8.6 (8.5, 8.7)	17.9 (17.5, 18.4)	3.72 (3.5,3.9)	31.7 (31.1, 32.3)	41.2 (40.1, 41.8)	37.6 (36.7, 38.4)
Interaction RA + PsyMb	<0.0001	<0.0001	0.013	0.005	0.98	0.006	0.44

Annual health care utilization and preventive care per person adjusted for covariates



Ambulatory care visits by provider adjusted for covariates

Disclosure: C. Hitchon, Pfizer, 2, UCB Canada, 2; **C. Bernstein**, Abbvie Canada, 5, 9, Ferring Canada, 5, 8, Janssen Canada, 5, 9, Pfizer Canada, 5, Shire Canada, 5, 8, 9, Takeda Canada, 5, Mylan Pharmaceuticals, 5, Medrontic Canada, 8; **J. Bolton**, None; **R. El-Gabalawy**, None; **J. Fisk**, None; **A. Katz**, None; **L. Lix**, None; **J. Marriott**, Biogen, 2, Idec, 2, Roche, 2; **S. Patten**, None; **C. Peschken**, Astra Zeneca, 2, Celgene, 2, Janssen, 2; **J. Sareen**, None; **A. Singer**, IBM, 2, Calian, 2; **R. Walld**, None; **R. Marrie**, None.

Abstract Number: 0957

Alterations in Cholesterol Homeostasis Regulate Autoimmunity/Age-associated B Cells

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Age-associated B cells (ABCs) are a novel B cell subset, which expands with age in non-autoimmune mice but accumulates prematurely in autoimmune-prone strains. ABCs exhibit unique phenotypic and functional characteristics. In addition to classical B cell markers, ABCs also express myeloid markers such as CD11c. ABC differentiation depends on T-bet and is promoted by TLR7 stimulation and cytokines like IFN-g and IL-21. While ABCs have been proposed to play a key role in the development of autoimmune diseases, the mechanisms regulating ABC formation and function are poorly understood. The SWEF proteins are a small family of proteins that includes SWAP-70 and its homolog DEF6, a recently identified risk variant for human SLE. The lack of SWEF proteins leads to the spontaneous development of a lupus-like syndrome, which, similarly to human SLE, preferentially occurs in females. We have recently shown that ABC formation is enhanced in SWEF-deficient mice (=DKO mice). Given that alterations in cholesterol homeostasis can promote autoimmunity, here we have investigated whether the accumulation and/or function of ABCs in SWEF-deficient mice could be affected by changes in the expression of the LDL receptor (LDLR) and/or a High Cholesterol Diet (HCD).

Methods: We have generated DKO mice, which also lack the LDLR (LDLRKO-DKOs), to assess the effects of metabolic dysregulation on the development of autoimmunity in DKO mice. Mice were fed either chow or a HCD. T_{FH} cells, ABCs, germinal center B cells (GCBs), and plasma cells (PCs), were analyzed in the spleens of DKO females and males, LDLRKO-DKO females and males and control mice (WT, LDLRKO females and males) by FACS. To monitor the severity of the lupus phenotype, autoantibody levels were tested by ELISAs and end-organ inflammation was assessed by histology.

Results: As compared to wt mice, DKO mice exhibit an accumulation of T_{FH} cells, ABCs, GCBs, and PCs (F >M). DKO female mice with a concomitant deletion of the LDLR (LDLRKO-DKOs) fed a chow diet displayed a similar expansion of ABCs, GCBs, and PCs to DKO female mice. As compared to DKO females, LDLRKO-DKO females on a chow diet however displayed increased focal chronic inflammation of skeletal muscles and joints. Feeding a HCD to LDLRKO-DKO female mice did not substantially affect the expansion of ABCs, GCBs, and PCs. Interestingly, as compared to DKO males on a chow diet, DKO males fed a HCD exhibited a marked increase in ABCs, GCBs, and PCs, which was associated with an increased production of autoantibodies. LDLRKO-DKO males on either a chow or a HCD exhibited an increase in PCs and a more variable increase in ABCs and GCBs.

Conclusion: ABCs accumulate to a similar manner in female DKO mice irrespective of the concomitant absence of the LDLR. Lack of the LDLR in DKO female mice, however, leads to increased tissue inflammation. A HCD can pro-

mote marked expansion of ABCs in DKO male mice and promote the production of autoantibodies. Thus, alterations in cholesterol homeostasis can affect ABC accumulation and other autoimmune parameters in a sex-specific manner.

Disclosure: Z. Chen, None; **M. Manni**, None; **D. Flores-Castro**, None; **T. Pannellini**, None; **A. Pernis**, Kadmon pharmaceutical, 2.

Abstract Number: 0958

Identification of IFN-γ-producing Effector B Cells in Humans: Their Relevance to the Pathogenesis of Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: B Cell Biology & Targets In Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune, multi-systemic disease that potentially affects any organ in the body. Clinical efficacy of B cell-targeting therapy underscores a crucial role of the antibody (Ab)-independent functions of B cells in the pathogenesis of SLE. Among such functions, cytokine production by B cells has recently gained much attention. The type 2 interferon IFN-γ is a key cytokine involved in SLE and produced by a variety of immune cells, however it remains somewhat elusive whether human B cells have potential to produce this cytokine. Here, we have sought to identify IFN-γ-producing B cells in humans and investigate their role in the pathogenesis of SLE.

Methods: B cell subsets from peripheral blood (PB) from healthy controls (HC) and patients with SLE were enriched by cell sorting, stimulated with $CD4^+$ T cell-related cytokines and subjected to the analysis of IFN-γ expression at both mRNA and protein levels. To check whether IFN-γ-producing B cells can be induced by $CD4^+$ T cells, we co-cultured B cells with $CD4^+$ T cell subsets. To determine the functional impacts of IFN-γ-producing B cells on $CD4^+$ T cells, B cells from patients with SLE were co-cultured with $CD4^+$ T cells. In addition, we thoroughly analyzed the surface markers of IFN-γ-producing B cells in HCPB and investigated whether this unique B cell subset coexists with $CD4^+$ T cell subsets in the effusion of SLE patients with pleuritis.

Results: Among a panel of $CD4^+$ T cell-related cytokines, IFN-γ and IL-21 significantly facilitated the generation of IFN-γ-producing B cells particularly from switched-memory (IgD^-CD27^+) B cells.In the presence of anti-BCR/CD40L with IFN-γ and IL-21 which mimics stimulation of B cells by follicular helper $CD4^+$ type 1 cells (Tfh1 cells), the $CXCR3^+$ fraction of switched-memory B cells strongly produced IFN-γ. Consistent with this, circulating Tfh1 cells from HCPB induced IFN-γ production from $CXCR3^+$ switched-memory B cells. IFN-γ-producing B cells were enriched in the $CD226^+PD\text{-}1^+$ fraction. The frequency of $CXCR3^+$ switched-memory B cells was higher in patients with SLE than HC. Intriguingly, under Tfh1 conditions $CXCR3^+$ switched-memory B cells from patients with SLE further accelerated IFN-γ production from $CD4^+$ T cells. In the effusion of SLE patients with pleuritis, Tfh1 cells were the predominant Tfh subset and $CD226^+PD\text{-}1^+CXCR3^+$ switched-memory B cells produced high amounts of IFN-γ.

Conclusion: Together, these findings clearly suggest the existence of IFN-γ-producing effector B cells in humans that are involved in the pathogenesis of SLE via closely interacting with $CD4^+$ T cells.

Disclosure: K. Higashioka, None; **M. Ayano**, None; **Y. Kimoto**, None; **H. Mitoma**, None; **M. Akahoshi**, None; **Y. Arinobu**, None; **K. Akashi**, None; **T. Horiuchi**, None; **H. Niiro**, None.

Abstract Number: 0959

A Novel Image Analysis Program, "CytoSkaler", Demonstrates That Anti-Vimentin Antibody Affinity Maturation in Lupus Tubulointerstitial Nephritis Also Results in More Selective Antigen Targeting

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: B Cell Biology & Targets In Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Vimentin is a dominant target of B-cells selected in lupus tubulointerstial inflammation (TII), a predictor of renal failure. The origins of anti-vimentin antibodies (AVA) are unknown. Technologies quantifying specific antigenic targeting do not exist. **Objectives**:$_1$ Characterize reactivities of germline BCR precursors of TII AVAs; $_2$ Develop software to quantify mAb reactivity with subcellular regions of cultured cells and tissue; $_3$ Quantify selectivity of mAbs for vimentin vs other cellular antigens; $_4$ Determine somatic hypermutations (SHMs) influential in Vimentin selectivity.

Methods: 10 human IgG1 AVA mAbs (from 6 TII patients) in selected (sel) and germ-line reverted (rev) forms, and 21 mAbs from naïve healthy B-cells were generated. Recombinant human vimentin (native and citrullinated) reactivity was assayed by ELISA. HEp-2 cells were co-stained with TII AVAs (sel and rev) and subcellular markers (nuclear [Hoechst], vimentin [mAb V9] and cytoplasm [mAb eno-1]), and imaged by multicolor immunofluorescence laser scanning confocal microscopy. Single amino acid variants of TII mAbs "PB4" (n=16) and "PB5" (n=11), representing single SHM reversions were also assayed. Lupus TII tissue was co-stained with novel FLAG-tagged variants of PB4 and PB5 (sel and rev). Mean pixel intensity (MPI) was a measure of magnitude of human mAb reactivity. Vimentin selectivity was quantified by co-variance of binding (Pearson Correlation coefficient of MPI with anti-vimentin channel), or ratio of MPI of vimentin positive : other respective subcellular region. A machine learned software ("CytoSkaler") was developed to identify individual cultured cells, and subcellular areas, allowing measurement of human mAb reactivities (MPIs) with subcellular regions. CytoSkaler was also used for quantifying reactivity with subcellular regions of TII tissue.

Results: 9/10 reverted TII AVA mAbs had reduced vimentin reactivities by ELISA, comparable to those of naïve healthy B-cell derived mAbs. All TII mAbs had lower reactivities with citrullinated antigen. CytoSkaler yielded highly accurate cell segmentation estimations (accuracy =0.97, intersection of union =0.96), allowing high throughput quantification of human mAb reactivities with subcellular regions. Typically, CytoSkaler demonstrated progression from low magnitude, broad cellular reactivity at germline, to high preference, and magnitude of reactivity, for vimentin positive regions following affinity maturation (i.e "PB4"). MAb PB5 was unique, maturing from a germline precursor with a speckled nuclear pattern and purified histone reactivity. Staining patterns observed with TII tissue using Flag-

PB4 and -PB5 matched those generated with HEp-2 cells. Reactivity of PB4 with vimentin was due to a combination of multiple SHMs. In PB5, S36D reversion was responsible for nuclear (Histone) reactivity and G55D lost vimentin reactivity.

Conclusion: From low reactivities comparable to naïve healthy B-cells, or Histone reactivity, TII AVAs gain both affinity and selectivity for vimentin. We have developed image analysis software for quantifying mAb selectivity for candidate antigens, and a flag human IgG1 mAb construct enabling analysis of human tissue rich in IgG.

Disclosure: A. Kinloch, None; **A. Mohsin**, None; **Y. Asano**, None; **C. Henry**, None; **N. Mor Vaknin**, None; **M. Legendre**, None; **P. Wilson**, None; **D. Markovitz**, None; **M. Clark**, None.

Abstract Number: 0960

Autoantibodies in Rheumatoid Arthritis Target Citrulline-Containing and Native Epitopes from Conformationally Disordered Regions of Proteins

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: B Cell Biology & Targets In Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-citrullinated protein antibodies (ACPAs) and rheumatoid factor (RF) are the main diagnostic and pathologic autoantibodies in rheumatoid arthritis. However, autoantibodies develop against proteins with other post-translational modifications, such as homocitrullination, as well as against various native proteins without obvious unifying characteristics of the antigens. Moreover, some rheumatoid arthritis patients generate only RF or only ACPAs (as detected by the anti-cyclic citrullinated peptide (CCP) test) and some produce neither. We have a poor understanding of the autoantibody repertoire in these patients. Our objective was to broadly evaluate autoantibody binding in seronegative and seropositive rheumatoid arthritis to identify general and novel features of autoantibody reactivity.

Methods: An array was created with 172,828 overlapping peptides derived from 122 proteins citrullinated in the rheumatoid joint including variants with arginines or lysines replaced with citrullines or homocitrullines, respectively. IgG and IgM binding to peptides was compared for CCP+RF+, CCP+RF-, CCP-RF+, and CCP-RF- rheumatoid arthritis versus controls. Highly bound peptides were analyzed for amino acid patterns and predictors of structural disorder. Published synovial fluid citrullinomes were also analyzed for amino acid patterns.

Results: Broadly, CCP+RF+ subjects had very high and CCP+RF- and CCP-RF+ subjects had modest citrulline-specific IgG binding. All rheumatoid arthritis groups had low homocitrulline-specific IgG binding and CCP+RF+ subjects had high IgG binding to native peptides. CCP-RF- subjects had very little antibody binding in general. By far, the highest IgG binding in rheumatoid arthritis was to citrulline-containing peptides, irrespective of protein identity, especially if the citrulline was adjacent to glycine or serine. Citrullinated arginines in the rheumatoid joint were also frequently next to glycine and serine. The most highly bound citrulline-containing and native peptides had multiple features predictive of conformational disorder.

Conclusion: In general, we observed a continuum of autoantibody binding in rheumatoid arthritis with a very high amount of binding in CCP+RF+ subjects, modest binding in CCP+RF- and CCP-RF+ subjects, and very little binding in CCP-RF- subjects. Further, citrulline, particularly next to serine or glycine, is a major driver of autoantibody reactivity in rheumatoid arthritis, likely due in part to frequent *in vivo* citrullination of arginine next to serine or glycine. Finally, structural disorder may be a newly discovered feature that drives rheumatoid arthritis autoantibodies.

Disclosure: Z. Zheng, None; **L. Fahmy**, None; **A. Bridges**, None; **M. Newton**, None; **M. Shelef**, None.

Abstract Number: 0961

Microenvironment in Systemic Sclerosis Provides a Protective Niche for Tissue-resident B Cells During B Cell Depletion Therapy with Anti-CD20 Antibody

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: B Cell Biology & Targets In Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: B cell depletion therapy with anti-CD20 antibody rituximab has emerged as a potential treatment for systemic sclerosis (SSc). Rituximab, which has been used to treat B cell malignancies and some autoimmune diseases, efficiently depletes circulating B cells. Tissue-resident B cells, on the other hand, have been shown to be more difficult to deplete, posing a therapeutic challenge. Resistance of tissue-resident B cells to rituximab has been associated with the inflammatory microenvironment in malignancy and autoimmunity, where B cell survival is promoted by various cytokines and chemokines. Among these survival factors, the following two have received much attention: CXCL12, a chemokine essential for the B cell niche in bone marrow, and B cell activating factor (BAFF), a cytokine promoting the survival of autoreactive B cells. In this study, we investigated the role of microenvironment on tissue-resident B cells during B cell depletion therapy with anti-CD20 antibody in SSc.

Methods: Bleomycin (BLM)-induced SSc model mice were treated with anti-CD20 antibody. AMD 3100, an antagonist of the CXCL12 receptor CXCR4, was used to block CXCL12. Anti-BAFF antibody was used to block BAFF. B cell depletion was assessed by flow cytometry in bone marrow, spleen, lymph nodes, lungs, and peripheral blood. Skin and lung fibrosis was evaluated histopathologically. CXCL12 and BAFF expression was quantified by qRT-PCR and immunofluorescence staining.

Results: While anti-CD20 antibody efficiently depleted circulating B cells and attenuated skin and lung fibrosis, a fraction of $CD20^+$ B cells persisted in spleen, lymph nodes, and lungs of BLM-induced SSc model mice, contrasting with efficient depletion of tissue-resident B cells in control mice. Residual B cells showed increased expression of CXCR4. CXCL12 and BAFF expression was increased in skin and lungs of BLM-induced SSc model mice. Co-administration of anti-CD20 antibody with AMD3100 or anti-BAFF antibody enhanced the depletion of tissue-resident B cells. Furthermore, these combination therapies achieved greater attenuation of fibrosis in BLM-induced SSc model mice compared with anti-CD20 monotherapy.

Conclusion: SSc microenvironment provides a protective niche for tissue-resident B cells against anti-CD20 antibody. B cell survival factors like CXCL12 and BAFF are potential therapeutic targets that enhance the efficacy of B cell depletion therapy in SSc.

Disclosure: A. Kuzumi, None; **A. Yoshizaki**, None; **T. Fukasawa**, None; **S. Ebata**, None; **Y. Asano**, None; **S. Sato**, None.

Abstract Number: 0962

The Presence of Circulating $CD19^{+}CD21^{lo}$ cells Predicts the Presence of Interstitial Lung Disease in Patients with Systemic Sclerosis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Table 1. Patient Demographics		
	SSc Patients (n=40)	Healthy Controls (n=21)
Average Age	61.7 ± 13.4	49.3 ± 11.3
Female Gender	30 (75%)	16/21 (76.2%)
Race		
Caucasian	32 (80%)	19/21 (90.4%)
African American	5 (12.5%)	1/21 (4.8%)
Other	3 (7.5%)	1/21 (4.8%)
Average Disease Duration	11.4 ± 10.3	
Cutaneous Involvement		
Limited	28 (70%)	
Diffuse	12 (30%)	
Interstitial Lung disease	26 (65%)	
Average %FVC (n=24)	69.5% ± 22.9%	
Average %DLCO (n=22)	48.9% ± 24.7%	
Pulmonary Hypertension	17 (43%)	
Serologic Status		
+ANA (n=30)	28/30 (93%)	
Anti-centromere (n=30)	10/30 (33%)	
Anti-Scl70 (n=24)	9/24 (38%)	
Anti-RNApolymerase III (n=13)	2/13 (15%)	
Therapy at enrollment		
Cytotoxic DMARD therapy	12 (30%)	
Non-cytotoxic therapy	10 (25%)	
No therapy	18 (45%)	
Meets 2013 Classification Criteria	40 (100%)	

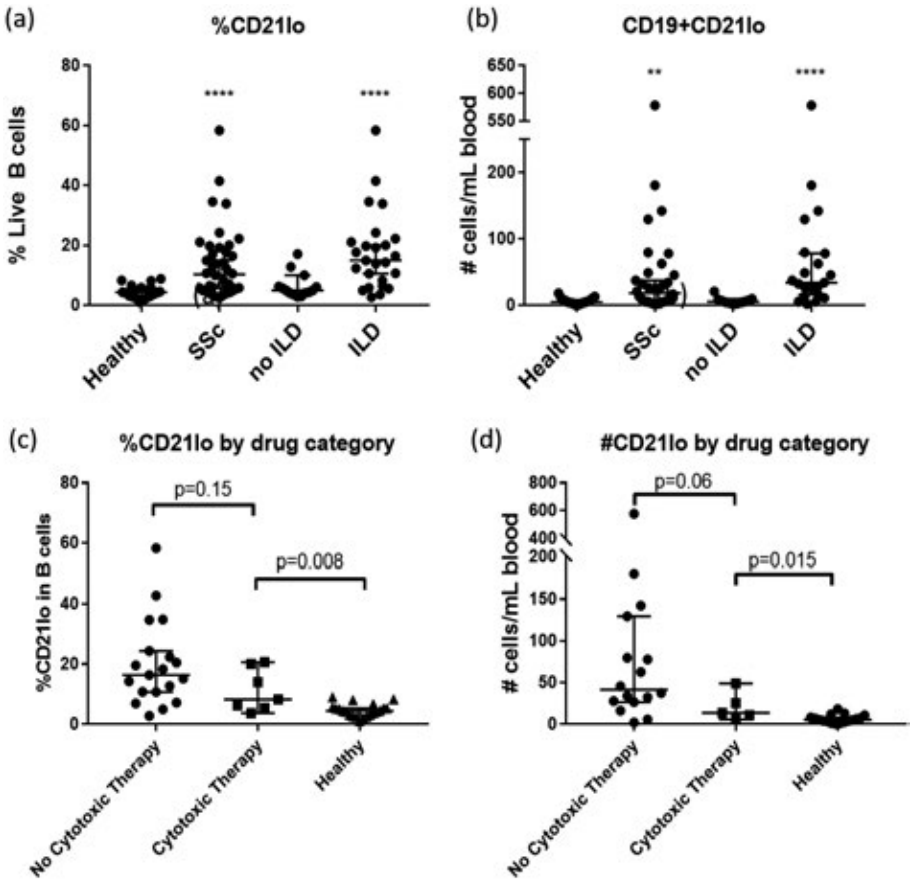

Figure 1. Only patients with SSc-ILD have an increase frequency (a) and absolute number (b) circulating $CD19^{+}CD21^{lo}$ cells; SSc patents without ILD have no difference in $CD19^{=}CD21^{lo}$ cells compared to healthy controls. (C-D) Patients who are treated with cytotoxic therapy (e.g. MMF/AZA) have a trend towards normalization for this cell population. ** p<0.01, ****p<0.0001

Background/Purpose: Systemic sclerosis (SSc) is a severe systemic disease characterized by fibrosis of the skin and visceral organs. While protein biomarkers of lung damage, e.g. krebs von den lungen-6 and surfactant protein D (SPD) have been reported in SSc-ILD, no immunologic predictors of SSc-ILD have been reported. CD21lo B lymphocytes have been implicated as autoimmune-prone cells. We evaluated the relationship of these cells to clinical phenotype in patients with SSc.

Methods: Cryopreserved peripheral blood mononuclear cells (PBMCs) were stored as part of the MYSTIC cohort (VUMC IRB 141415). Detailed clinical phenotyping, including extent of cutaneous involvement and serologic status, was performed at the time of patient enrollment. All patients met the 2013 ACR classification criteria for SSc. The presence of interstitial lung disease was defined as FVC< 79% predicted, isolated DLCO< 79% predicted in the absence of pulmonary hypertension, or radiographic fibrosis on CT scan. PBMCs were thawed and subjected to mass cytometry to investigate B cell phenotypes in patients with SSc (n=40) versus healthy controls (n=21). Data was analyzed with biaxial gating and correlated to clinical phenotypes. Statistical significance was determined using Mann-Whitney U-tests.

Results: Basic demographics are shown in table 1. Patients with SSc-ILD have a higher percentage of CD19+CD-21lo cells compared to patients without interstitial lung disease (15.0% versus 5.0%, p=0.0004); there is no increased

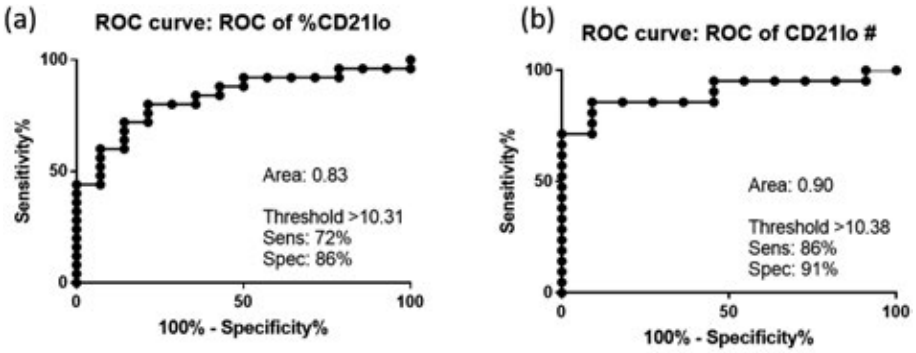

Figure 2. ROC curves showing the correlation of (a) percent and (b) absolute number of circulating $CD19^{+}CD21^{lo}$ cells with SSc-ILD

CD19+CD21lo frequency for patients with SSc without ILD compared to healthy controls (5.0% v. 4.4%, p=0.22). Similarly, the absolute number of circulating CD19+CD21lo cells is increased for SSc-ILD compared to SSc without ILD or healthy controls (34.0 v. 5.59 v. 5.09 cells/mL, p< 0.0001) (Figure 1A-B). There was no correlation between CD19+CD21lo cells and extent of cutaneous involvement of serologic status. For the subset of patients with ILD treated with mycophenolate mofetil or azathioprine (n=7), there was a trend towards normalization of their CD19+CD-21lo frequency (8.2% v. 16.4%, p=0.15) compared to those not treated with these medications (n=19). This trend was even stronger when considering the absolute number of circulating CD19+CD21lo cells for treated versus untreated patients (13.6 v. 41.4 cells/mL, p=0.06) (Figure 1C-D). An ROC curve was generated to predict the presence of ILD. A threshold of 10.3% circulating CD19+CD21lo cells had sensitivity of 76%, specificity of 86%, and AUC 0.87. A threshold of 10.4 cells/mL had a sensitivity of 86%, specificity of 91%, and AUC of 0.90 (Figure 2).

Conclusion: This single center study demonstrated the presence of circulating $CD19^{+}CD21^{lo}$ cells is highly predictive of SSc-ILD. The frequency and absolute number of circulating cells seems to decrease with treatment of ILD. These findings will need to be confirmed in a second large cohort.

Disclosure: E. Wilfong, None; **J. Young-Glazer**, None; **E. Rizzi**, None; **R. Dudenhofer**, None; **L. Crofford**, None; **P. Kendall**, None.

Abstract Number: 0963

Alterations of Memory and Naive B Cell Subsets Associate with Reduced IFNα and TNFRII in ANA+ Healthy Individuals

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SESSION INFORMATION
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Background/Purpose: Loss of systemic self-tolerance leading to anti-nuclear autoantibody (ANAs) by B cells is a hallmark of SLE. However, up to 20% of healthy female individuals are also ANA+, and most will never develop clin-

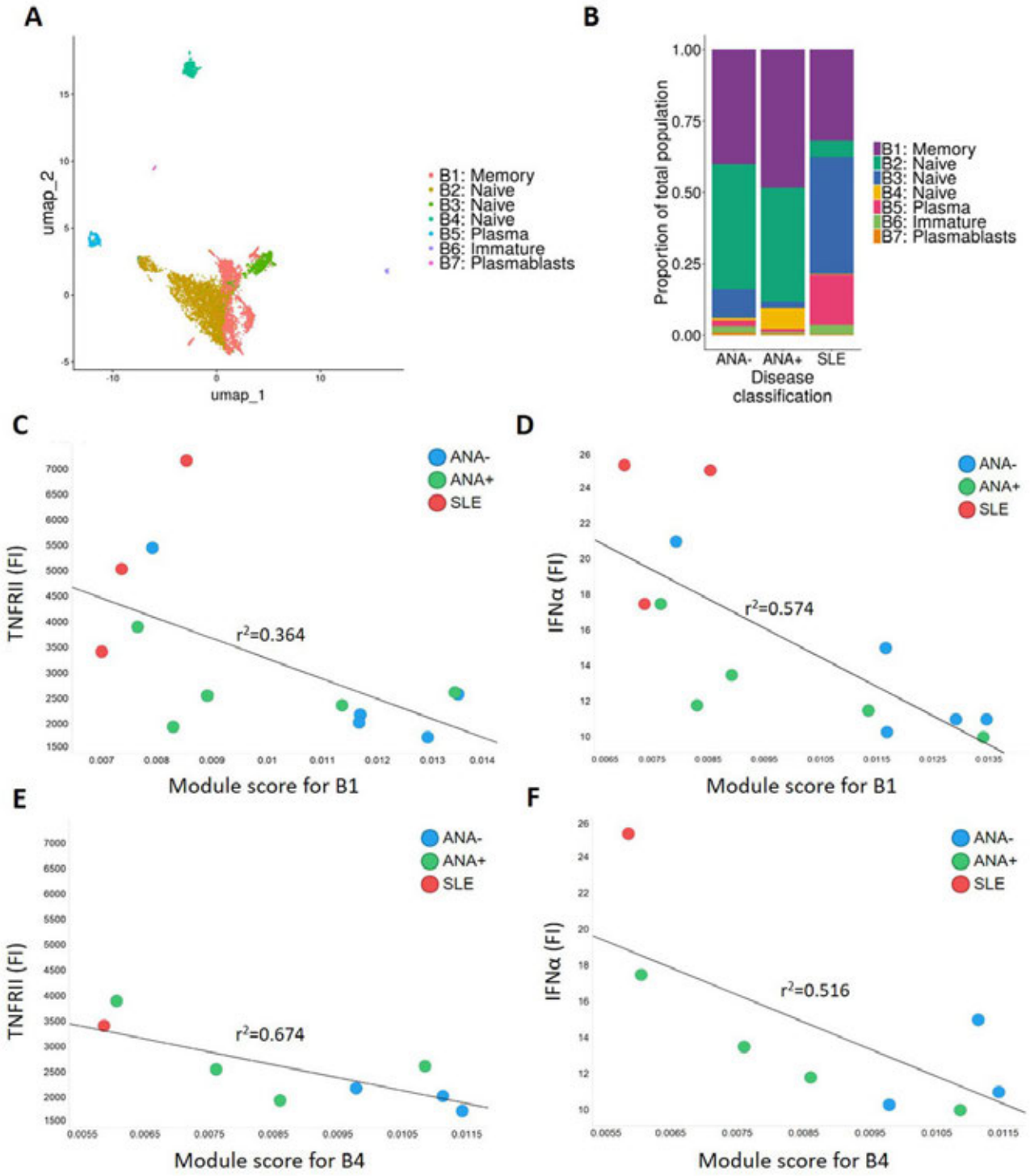

Figure 1. African American ANA+ B cell populations negatively correlate with pro-inflammatory cytokines. A. Visualization of B cell subpopulations by UMAP of scRNA-seq data. B. Proportion of cells from each disease classification in each B cell cluster reveals differences is constituent subpopulations. C. Linear regression of plasma TNFRII fluorescent intensity (FI) with TNFRII/p53/apoptosis/death-receptor signaling - related gene module score for memory B cells (cluster B1). D. Linear regression of plasma IFNα fluorescent intensity (FI) with TNFRII/p53/apoptosis/death-receptor signaling - related gene module score for memory B cells (cluster B1). E. Linear regression of plasma TNFRII fluorescent intensity (FI) with TNFRII/p53/apoptosis/death-receptor signaling - related gene module score for naive B cells (cluster B4). F. Linear regression of plasma IFNα fluorescent intensity (FI) with TNFRII/p53/apoptosis/death-receptor signaling - related gene module score for naive B cells (cluster B4).

ical autoimmune disease. The B cell pathways involved in autoimmune progression and regulation of healthy ANA+ individuals is unknown.

Methods: Peripheral blood mononuclear cells (PBMCs) from African American ANA- (n=6), ANA+ healthy individuals (n=6) and SLE (n=6) subjects were sorted for CD3-CD19+ B cells by flow cytometry and RNA was isolated for next-generation sequencing. Differential gene expression, Weighted Gene Correlation Network Analysis and pathway analysis were used to identify differences in pathways and upstream regulators. scRNA-sequencing of B cells from PBMCs were used to determine frequencies and identify differential gene signatures in specific B cells subsets. Plasma soluble mediators were assessed by xMAP multiplex arrays and used for linear regression analyses.

Results: Pathway analysis of total B cells in ANA+ healthy individuals revealed unique pathway modules with elevated eigengene scores associated with p53 signaling (p=0.000275), TNFRII signaling (p=0.0000699), apoptosis (p=0.00399) and death receptor signaling (p=0.00902) compared to ANA- controls and SLE patients. Using scRNA-seq analysis, seven distinct B cell populations among all subjects were identified using a community detection algorithm and visualized using Uniform Manifold Approximation Projection. The proportion of total B cells within each cluster varied by disease status. A unique cluster of $CD69^{low}$ naïve B cells was more prevalent in ANA+ healthy subjects, memory B cells also trended higher in ANA+ healthy individuals, while SLE patients were characterized by higher frequencies of plasma cells and $CD69^{high}$ naïve B cells. Gene expression signatures of p53/TNFRII, apoptosis, and death receptor signaling were elevated in all B cell subsets of ANA+ healthy individuals (Figure 1A-B). In ANA+ healthy individuals, the elevated gene expression signatures in memory B cells correlated negatively with plasma IFNα (p=0.0027), IL-15 (p=0.011), IP-10 (p=0.027), IL-10 (0.025), TNFRII (p=0.029), and IL-23 (p=0.038) levels, and negatively in $CD69^{low}$ naïve B cells with IFNα (p=0.012) and TNFRII (p=0.045) levels (Figure 1C-F). SLE patients exhibited higher plasma levels of multiple cytokines including IFNα and associated mediators, TNFRII, IL-10, BLyS and Th1/2/17 associated mediators ($p< 0.05$).

Conclusion: ANA+ healthy individuals have enhanced gene expression in B cell pathways that drive apoptosis and cell cycle suppression, which may regulate autoreactive T cell activation, and proliferation, and subsequent clinical autoimmune pathogenesis. This provides clues into potential targets for prevention of clinical autoimmunity.

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Abstract Number: 0964

Identifying Jo-1-Specific B Cells in the Primary Immune Repertoire in Idiopathic Inflammatory Myopathies

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Table 1

	Healthy Controls n=4	Jo-1 (-) Inflammatory Myopathy n=4	Jo-1 (+) Inflammatory Myopathy n=10
Age, years (SD)	55.3 (15.8)	55.8 (15.4)	55.5 (10.1)
Gender, N (%)			
-- Male	2 (50)	1 (25)	3 (30)
-- Female	2 (50)	3 (75)	7 (70)
Ethnicity, N (%)			
-- Caucasian	4 (100)	4 (100)	8 (80)
-- Afr. American	0 (0)	0 (0)	2 (20)
Disease Duration, years (SD)	--	2.0 (2.1)	10.5 (8.4)
Disease Severity, N (%)			
-- Stable		2 (50)	6 (60)
-- Active	--	2 (50)	1 (10)
-- Life threatening		0 (0)	3 (30)
Recruitment Location, N (%)			
-- Outpatient		3 (75)	7 (70)
-- Inpatient	--	1 (25)	1 (10)
-- ICU		0 (0)	2 (20)

Table 1. Demographics of patients and healthy volunteers included in study. Four healthy controls, 4 patients with non-Jo-1 inflammatory myopathy patients (one each with anti-Tif1-gamma, anti-Mi-2, anti-EJ, and anti-PL-7 antibodies), and 10 patients with anti-Jo-1 antibodies as determined by clinical testing. Demographics and clinical information were collected from the electronic medical record at the time of enrollment. Disease severity was defined as stable if the patient's primary rheumatologist or pulmonologist did not discuss changing medications at the time of enrollment and "active" if immunosuppression was increased. Disease activity was determined to be "life threatening" if the patient was admitted to the hospital due to their rheumatologic illness, was receiving pulse steroids, and was receiving an increase in immunosuppression.

Figure 1

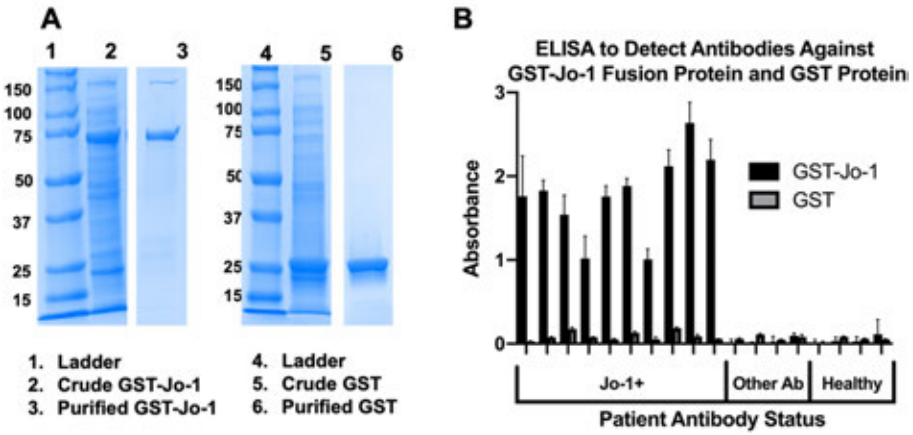

Figure 1. ELISA detects anti-Jo-1 specific antibody in the sera of patients with clinical laboratory confirmed cases of Jo-1 associated disease. (A) Glutathione S-transferase (GST) and GST-Jo-1 were expressed in bacteria and purified. Samples were run on SDS-page gels and Coomassie blue staining confirmed purity of protein samples. (B) ELISA performed against purified GST-Jo-1 fusion protein (black) and purified GST protein (gray). Patient sera were diluted 1:1000 and applied to plates coated with purified GST-Jo-1 or GST proteins. Our ELISA successfully discriminates between Jo-1-positive and Jo-1-negative sera. The Jo-1-positive patient sera react against GST-Jo-1 fusion protein but not against GST alone, demonstrating that the antibodies are specific for the Jo-1 protein.

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are systemic autoimmune diseases traditionally classified as dermatomyositis or polymyositis, but these disorders are increasingly defined by the presence of myositis-specific and myositis-associated antibodies. Anti-Jo-1 autoantibodies recognize histidyl tRNA synthetase

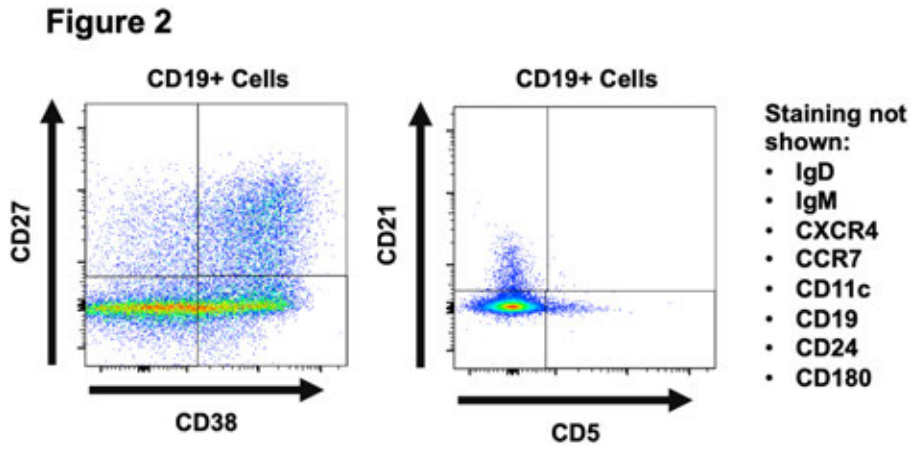

Figure 2. Representative flow cytometry data. Cryopreserved PBMCs from a known Jo-1 positive patient were thawed and stimulated in vitro. After 6 days of stimulation, cell culture supernatants were screened for the presence of anti-Jo-1 antibodies. Equal numbers of Jo-1 positive and Jo-1 negative screened wells were phenotyped using flow cytometry. Representative data for a Jo-1 positive well are shown above amongst CD19+ cells.

and are frequently found in these patients. In addition to producing antibody, B cells present antigen to T cells, a function that is independent of antibody production. Jo-1-specific B cells have not been previously characterized. To develop targeted therapies for IIM, we must first understand the etiology of autoreactive B cells in this disease. We hypothesize that anti-Jo-1 B cells will exhibit features of memory B cells and show evidence of somatic hypermutation and antigen-driven selection.

Methods: We enrolled 10 patients that were anti-Jo-1 autoantibody positive by clinical testing at our university medical center (Table 1). Antigen-specific B lymphocytes are typically rare in the repertoire and the B cell receptor is not automatically secreted as antibody, making detection of specificity difficult. To overcome these challenges, we polyclonally stimulated peripheral blood mononuclear cells (PBMCs) from IIM patients to drive *in vitro* B cell differentiation into antibody-secreting cells and developed a high throughput ELISA to screen and identify wells containing Jo-1 antibody-secreting cells. We applied flow cytometry phenotyping of wells that were positive or negative for anti-Jo-1 B to investigate their expression of twelve B cell phenotypic markers.

Results: Using recombinant Jo-1 protein, our ELISA successfully distinguished the presence or absence of anti-Jo-1 antibodies in clinically validated patient sera (Figure 1). Stimulation of human PBMC resulted in detection of IgG in the supernatants of all wells. A proportion of these wells were positive for anti-Jo-1 IgG autoantibody with an estimated frequency of approximately 0.01% of the total B cell repertoire, a frequency that is comparable to previously reported tetanus toxoid B cells in vaccinated individuals. We also detected a residual population of anti-Jo-1 B cells in a patient who previously received rituximab. B cell subsets differentially expressed CD24, CD27, CD38, IgM, and IgD following polyclonal stimulation. Differences in CXCR4 and CCR7 expression were also observed in different B cell subsets identified in these cultures.

Conclusion: This is the first demonstration of anti-Jo-1 B cells in the primary immune repertoire of patients with IIM, including those who have previously received rituximab. Flow phenotypic analysis suggests that differences in B cell subset distribution of anti-Jo-1 B cells can be assessed using our methods. These data provide the first critical steps towards understanding anti-Jo-1 B cell biology in patients with IIM to enable their future tracking as clinical disease and therapeutic response biomarkers.

Disclosure: J. Young-Glazer, None; **E. Wilfong**, None; **P. Kendall**, None; **R. Bonami**, None; **L. Crofford**, None.

Abstract Number: 0965

Discovery of DWP212525, a Potent JAK3 and BTK Dual Target Inhibitor for the Treatment of Autoimmune Diseases

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SESSION INFORMATION
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Background/Purpose: Janus Kinase (JAK) and Bruton's tyrosine kinase (BTK) play critical roles in activation and function of T cells and B cells. Dysregulation of this process has been known to cause various immune-related diseases. Tofacitinib, a JAK inhibitor, was originally developed as a JAK3 inhibitor but it showed limited selectivity against JAK1 and JAK2. Although Tofacitinib has proved therapeutic effects in RA, serious side effects such as anemia and neutropenia have been frequently reported. Meanwhile, existing BTK inhibitors have insufficient clinical efficacy, which creates higher demands for treatment with improved efficacy. DWP212525 is a novel and selective JAK3 and BTK inhibitor which may have synergistic effects for the treatment of rheumatoid arthritis and other inflammatory diseases such as pemphigus vulgaris (PV).

Methods: Inhibition of JAK3 and BTK enzyme activity and selectivity against Cys-family kinase group were evaluated by a series of biochemical assays. Cellular activity for target phosphorylation in human T and B cells were measured by Phospho-STAT5 or phospho-BTK cellular kit. BCR dependent CD69 expressions were determined in hPBMC. To measure BTK occupancy, mouse spleen was extracted at several time points up to 24 hours after receiving an oral administration of DWP212525. Occupancy was quantified by the number of unbound BTK in ELISA-based assay using biotinylated-DWP212525, which binds to free active site of target after oral administration of DWP212525. Furthermore, the efficacy of DWP212525 was investigated in the mouse collagen-induced arthritis (CIA) model and mouse PV model, in comparison with selective BTK inhibitor.

Results: We developed a novel and potent dual target inhibitor, DWP212525, with JAK3 IC_{50} value of 0.2 nM and BTK IC_{50} value of 1.5 nM. More importantly, DWP212525 is highly selective against JAK3 and BTK, yet has low affinity toward JAK1, JAK2 and EGFR. DWP212525 shows successful inhibition of BCR-dependent CD69 expression in B cells (IC_{50} value of 132nM). *In vivo*, oral administration of low-dose DWP212525 (1mg/kg) showed more than 80% BTK occupancy in mouse splenocytes. Interestingly, the plasma concentration of DWP212525 rapidly decreased, but high rate of BTK occupancy was maintained for up to 24 hours. In mouse CIA model, we observed a dose-dependent improvement of arthritis symptoms in the group treated with DWP212525. The ED_{50} value of DWP212525 is 0.8 mg/kg. In mouse PV model, DWP212525 alleviated the severity of disease index score prevented body weight loss and confirmed that the survival rate was higher than the positive control group treated with a BTK inhibitor and the vehicle group at the end of the 32-day oral administration after the induction of the disease.

Conclusion: We developed a novel, highly potent, and selective covalent inhibitor of JAK3 and BTK, DWP212525. We demonstrated that DWP212525 has potent *in vitro* and *in vivo* pharmacological activities compared to Tofacitinib and existing selective BTK inhibitor. These results suggest that DWP212525 can be more effective due to the addition of JAK3 inhibition than selective BTK inhibitor for the treatment of various autoimmune diseases, including RA and PV.

Disclosure: Y. Shin, None; **J. Jung**, None; **E. Kim**, None; **S. IM**, None; **S. Jun**, None; **N. Kim**, None; **S. Jeong**, None; **H. Hyun**, None; **J. Park**, None.

Abstract Number: 0966

Minimal Residual Autoimmunity After Rituximab in ANCA-associated Vasculitis Patients

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Background/Purpose: Background: B-cell depletion with rituximab (RTX) is an effective treatment for ANCA-associated vasculitis (AAV) patients. Repeated RTX upon B-cell repopulation or return of ANCAs improved therapeutic efficacy, which indicates the presence of minimal residual autoimmunity (MRA) after RTX. Therefore, this study aimed to perform in-depth phenotypic and functional analyses of B and plasma cells after RTX in AAV.

Methods: EuroFlow-based highly sensitive flow cytometry (HSFC) was used during longitudinal follow-up of RTX-treated AAV patients (n=12). To investigate MRA in the memory B-cell compartment after RTX, peripheral blood mononuclear cells (PBMCs) were stimulated with CpG, IL-2 and IL-21 *in vitro* to induce plasma cells (PCs) and ANCA-IgG and -IgM were measured in these supernatants and in paired serum samples by ELISA.

Results: By employing HSFC we demonstrated that 12 weeks after RTX, low but significant numbers of circulating $CD19^+$ B cells ($0.21*10^6$ cells/L) could still be detected (reduction of -99.7%). While naïve B-cells, memory B-cells and $CD20^+$ plasmablasts (PB) were rapidly depleted, $CD20^-$ PCs were reduced slower and depleted incompletely. Residual $CD20^-$ PCs were $0.05*10^6$ cells/L (-95.8% from baseline), whereof 57% were mature $CD138^+$ PCs. Early repopulation at 12 weeks was dominated by $CD20^-CD138^-$ PCs, followed by $CD20^+$ PBs at 24 weeks while memory and naïve B cells remained suppressed. Simultaneously, serum ANCA IgG, IgM and IgA, produced by autoreactive PCs, decreased but did not disappear after RTX. Interestingly, 24 weeks after RTX, serum anti-MPO IgM increased in 3/4 patients, which associated with repopulating $CD20^+$ PBs. This suggested remaining autoreactive B cells despite RTX treatment, which was further studied by *in vitro* PBMC cultures. In these supernatants both anti-MPO-IgG and -IgM were detected at baseline, whereas anti-MPO IgG disappeared after RTX, in contrast to anti-MPO IgM, which was detected 24 weeks after RTX.

Conclusion: RTX results in a strong but not complete B cell depletion. In-depth analysis demonstrated that both ANCA-producing PCs and ANCA-memory B cells can be detected after RTX, indicating residual B-cell autoimmunity in AAV patients. Further identification of MRA could be worthwhile for guiding personalized treatment in AAV patients.

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Abstract Number: 0967

Bruton's Tyrosine Kinase (BTK) Pathway Is Active in Synovium at Various Stages of Rheumatoid Arthritis Disease Progression

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SESSION INFORMATION
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Background/Purpose: Bruton's tyrosine kinase (BTK), a TEC family non-receptor kinase, is expressed in B cells and myeloid cells. BTK relays signaling downstream of B cell receptor (BCR) and toll-like receptors (TLR) in B cells, whereas in myeloid cells, it mediates activating Fcg receptor and TLR signal transduction. Given the importance of these cell types in autoimmune pathogenesis, inhibition of BTK pathway is expected to provide an effective strategy for the treatment of rheumatoid arthritis (RA). However, the activity status of the BTK pathway in RA synovium and at various stages of RA disease progression has not been addressed.

Methods: RNA-Seq expression profiling was used to examine the expression of *BTK* in synovial tissue samples from healthy, osteoarthritis (OA), seropositive arthralgia, early RA and established RA subjects. Immunohistochemistry was performed to determine the expression of BTK protein in healthy, OA and RA synovial tissue biopsies. BTK-responsive gene signatures were generated from vehicle or BTK inhibitor-treated and activated human B cells and monocytes. Gene Set Variation Analysis (GSVA) was employed to assess the status of BTK signaling by interrogating BTK in vitro B cell and monocyte gene signatures against expression profiles of synovial tissues from various stages of RA disease progression.

Results: We demonstrate that the expression of *BTK* was significantly increased in arthralgia, early RA and established RA, compared to healthy and OA synovial tissue samples. In addition, RA patients showed increased cytoplasmic BTK protein expression in the synovium when compared to their healthy and OA counterparts, and the protein was restricted to synovial immune cell infiltrates. GSVA revealed that anti-IgM-responsive genes in naïve B cells were significantly enriched in synovial tissues from various stages of RA disease progression, whereas immune complex (HSA and anti-HSA complex)-responsive genes in monocytes showed enrichment only in established RA synovial tissue samples, demonstrating differential involvement of B cells and monocytes in arthralgia and early disease vs., established RA. In accordance with these observations, BTK gene signatures from activated B cells showed enrichment in synovial tissue samples during RA disease progression, while BTK monocyte gene signatures showed enrichment only in established RA synovium.

Conclusion: Taken together, these data suggest that BTK pathway is active in synovium during RA disease progression, and BTK inhibitors may show efficacy not only for the treatment of RA but also in halting the progression of the disease to established RA.

Disclosure: S. Nagpal, Janssen Research & Development, 3, Janssen Research, Johnson&Johnson, 1, 3, 4, Johnson & Johnson, 1, 4; **Q. Song**, Janssen Research, Johnson&Johnson, 1, 3, 4; **M. Loza**, Janssen Research & Development, LLC, 3; **Y. Chen**, Johnson & Johnson, 1, 3, 4; **X. Yin**, Janssen Research, Johnson&Johnson, 1, 3, 4; **L. Cheng**, Johnson & Johnson, 1, 3, 4; **M. Huber**, Johnson & Johnson, 1, 3, 4; **F. Baribaud**, Janssen Research & Development, LLC, 3; **F. Shen**, Janssen Research, Johnson&Johnson, 1, 3, 4; **N. Rao**, Janssen Research & Development, 3, Johnson & Johnson, 1, 3, 4.

Abstract Number: 0968

Circulating PR3-Specific B Cells in Patients with Active ANCA-Associated Vasculitis

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SESSION INFORMATION

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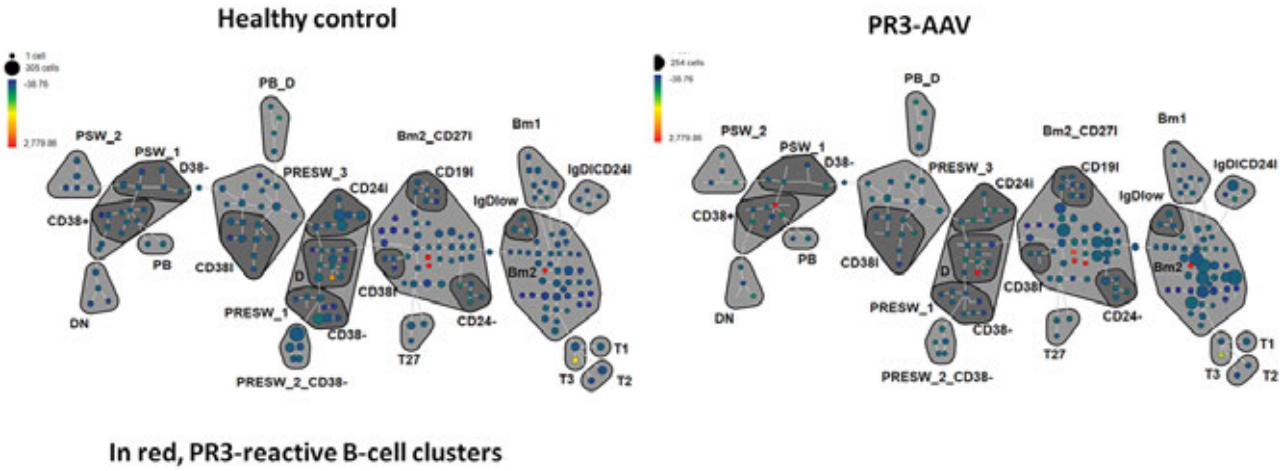
Background/Purpose: We previously developed a method to recognize proteinase 3 (PR3)-specific B cells by flow cytometry. We reported that, in a small number of subjects, the proportion of PR3-specific B cells was higher in patients with PR3-ANCA-associated vasculitis (AAV) compared to healthy controls (HCs) (Cornec et al, J Autoimmunity 2017). The objectives of this study were to replicate our previous findings on a larger number of subjects, including anti-myeloperoxidase (MPO)-AAV patients as disease controls, and to study the association of PR3-specific B cell proportions with clinical and biological features in patients with PR3-AAV.

Methods: We analyzed samples from 161 patients who participated in the RAVE trial, including 110 patients with PR3-AAV and 51patients with MPO-AAV, as well as 27 HCs. We measured the proportion of PR3-specific B cells and subsets among cryopreserved PBMCs using a multi-color flow cytometry panel including CD19, IgD, CD27, CD38, CD24, and biotinylated PR3. SPADE (Spanning-tree Progression Analysis of Density-normalized Events) algorithm was used for the unsupervised clustering of flow cytometry data, based on the level of expression of each of the 6 markers on each cell.

Results: The proportion of PR3-specific B cells was higher in patients with PR3-AAV and MPO-AAV (median [25-75% interquartile range]: 2.82% [2.35-3.74] and 2.87 [2.15-3.84], respectively) compared to HCs (1.51 [1.25-1.73], both $p< 0.001$), while they did not differ substantially between PR3-AAV and MPO-AAV ($p=0.517$). We observed a significant shift towards a more mature phenotype of these PR3-specific B cells in patients with PR3-AAV compared to MPO-AAV and HCs, as represented by a higher proportion of PR3-specific B cells among the unswitched memory B-cell subsets (IgD+CD27+; 6.14% [4.27-8.74] versus 4.47% [3.11-6.87] versus 2.89% [2.19-4.23], $p< 0.01$ for all comparisons), switched memory B-cell subsets (IgD-CD27+; 2.98% [1.67-5.00] versus 2.1% [1.38-3.09] versus 1.19% [0.96-1.60], $p< 0.001$ for all comparisons), and double negative B-cell subsets (IgD-CD27-; 2.23% [1.54-3.76] versus 1.44% [0.83-2.53] versus 0.80% [0.00-1.34], $p< 0.01$ for all comparisons). In patients with PR3-AAV, no associations between PR3-specific B cell proportion and age, sex, new diagnosis vs relapsing disease, or disease activity (BVAS/WG) was observed. The SPADE clustering resulted in the definition of 200 distinct subsets detectable in each sample with variable proportions, and showed a strong segregation of patients and HCs, and PR3-AAV and MPO-AAV patients. A cluster belonging to the switched memory subset was PR3-reactive only in PR3-AAV (figure).



SPADE analysis of B-cell subsets. PR3-reactive subsets are represented in red. One post-switch memory B-cell subset is PR3-reactive only in PR3-AAV patients.

Conclusion: Circulating PR3-specific B cells can be detected in the peripheral blood. The proportion of PR3-specific B cells was higher in patients than in HCs. Interestingly, PR3-specific B cell repartition is shifted towards a memory phenotype in PR3-AAV patients. Further studies are ongoing to characterize the dynamics of the PR3-specific B cells after therapy, and to understand the differences of these autoreactive B cells between patients with PR3-AAV and HCs.

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Abstract Number: 0969

ß-adrenergic Receptor Activation: A Way to Enhance CD4 T Cell Suppression by Improving Regulatory B Cell Function

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SESSION INFORMATION

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Background/Purpose: 1. Rheumatoid arthritis (RA) is an autoimmune disease in which next to other cell populations CD4 T cells play a crucial role. It has been shown that catecholamines provided by the sympathetic nervous system (SNS) ameliorate the development and course of arthritis by increasing the production of the anti-inflammatory cytokine IL-10 in regulatory B cells (Bregs). In the current study, we investigated whether Bregs have the ability to produce catecholamines and how such a production is regulated. Moreover, we tested which adrenergic receptor activation is important to improve the Bregs function to evaluate if an additional adrenergic receptor stimulus can enhance the suppression of CD4 T cells.

Methods: In *in vitro* experiments on activated murine B cells or B cells and splenocytes from collagen-induced arthritis (CIA) mice, modulation of Bregs and their effect on CD4 T cells proliferation were investigated. The production and release of catecholamines were analyzed in naïve, IgM, CpG or IgM/CpG activated B cells after 4h and 24h by FACS. For analysis of CD4 T cell suppression pre-inactivated or pre-activated B cells and CD3/CD28 activated splenocytes from immunized mice were cocultured for 48h and 72 h. CD4 T cell proliferation as well as the expression of PDL-1 and Fas-L on B cells was monitored by FACS. The IL-10 production from B cells was directly measured in the cells by intracellular FACS staining or in the supernatant of B cell cultures by ELISA.

Results: Catecholamines are not only provided by the SNS but are produced by the B cells themselves. Analysis of B cells by FACS showed a raised production of catecholamines after short time exposure to different B cell activation stimuli (Control vs. IgM, n=6, n.s.; Control vs. CpG, n=6, p***< 0,0002; Control vs. IgM/CpG, n= 6, p****< 0,0001). Long time activation of B cells, on the other hand, leads to release of produced catecholamines (Control vs. IgM, n=4, p**< 0,0029; Control vs. CpG, n=4, p****< 0,0001; Control vs. IgM/CpG, n= 4, p****< 0,0001). This hints to a time and context dependent production and release of catecholamines. Furthermore, FACS analysis showed that CpG-activated Bregs have the ability to suppress CD4 T cells (Control vs. CpG, n= 11, p****< 0,0001). Increased suppression of CD4 T cells was observed after addition of norepinephrine or isoproterenol, ADR beta agonists, to CpG-activated Bregs (CpG vs. CpG/NE, n=11, p*=0,0343; CpG vs. CpG/Iso, n=11, p***=0,0009). This higher suppression of CD4 T cells correlates with enhanced IL-10 production by Bregs (CpG vs. CpG+Iso, n=8, % rel. to control ~40%, p**=0,0045; CpG vs. CpG+NE, n=8, % rel. to control ~16%, p**=0,0012).

Conclusion: In conclusion, our data suggest that ß-adrenergic receptor activation by catecholamines or synthethic receptor agonists in addition to a BCR/TLR9 stimulus is associated with an increase of the anti-inflammatory potential of regulatory B cells to suppress CD4 T cells. This could be a strategy to modulate Bregs for therapeutic purposes in RA.

Disclosure: N. Honke, None; **B. Opgenoorth**, None; **M. Schneider**, None; **G. Pongratz**, None.

Abstract Number: 0970

New-onset ANCA-associated Vasculitis Is Associated with Significant Phenotypic B Cell Dysfunction

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SESSION INFORMATION

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Figure 1. B cell phenotype in ANCA-associated vasculitis compared to healthy controls

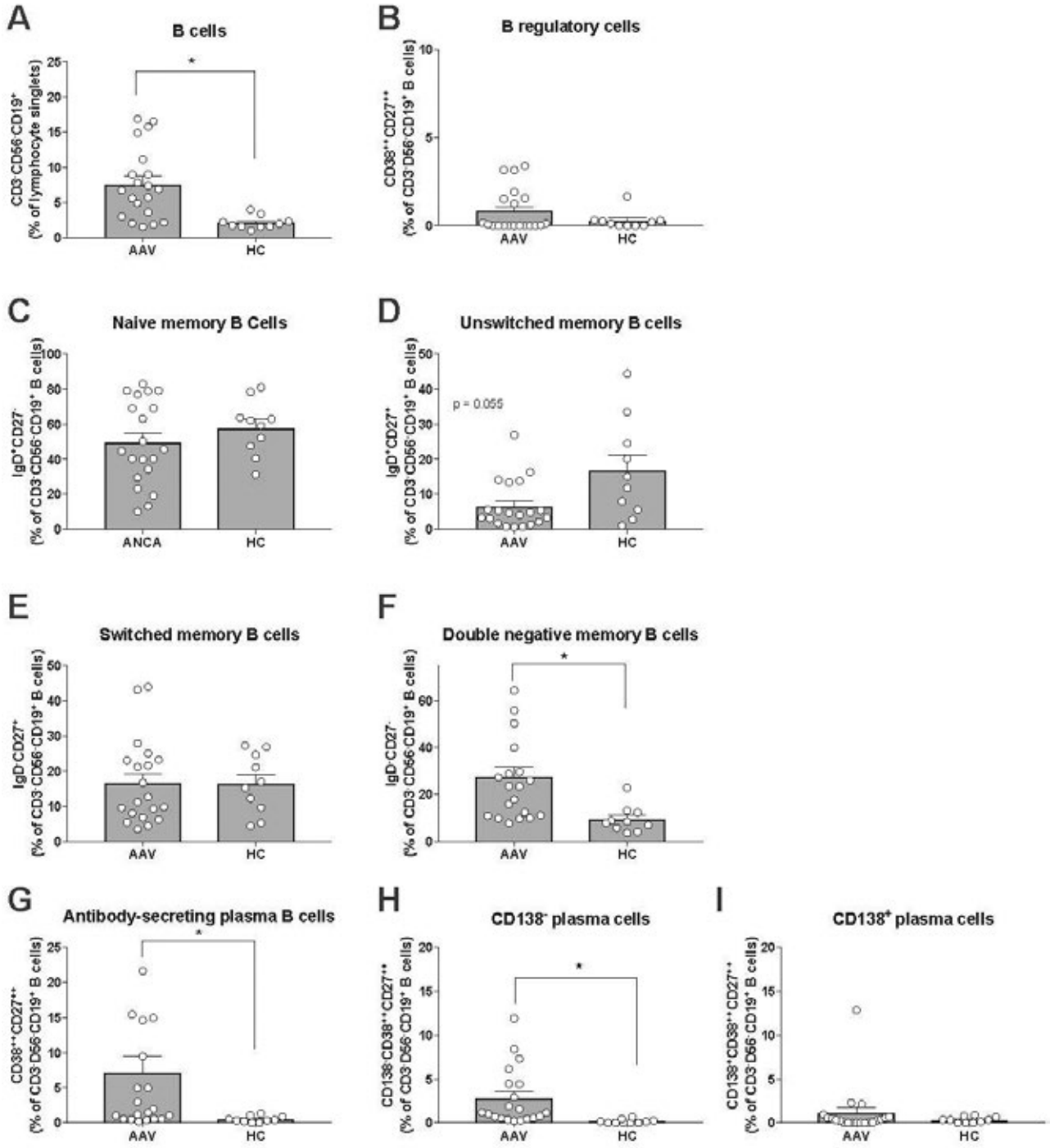

Figure 1. Percentages of CD3-CD56-CD19+ B cells (A) and CD25 hi CD71hi B regulatory cells (B) in ANCA-associated vasculitis patients (AAV, n=20) and healthy controls (HC, n=10). Percentages of B memory cell subpopulations: IgD+CD27- naive, IgD+CD27+ unswitched, IgD-CD27+ switched, and IgD-CD27- double negative (C-F). Percentages of CD38hiCD27hi plasma cells with expression of CD138- and CD138+ (G-I). *p<0.05.

Background/Purpose: ANCA-associated vasculitis (AAV) is characterized by the production of auto-antibodies and can be treated with rituximab, a B cell-depleting agent. Despite this, limited data are available characterizing the B cell dysfunction associated with AAV.

Methods: We performed comprehensive flow-cytometric analyses of major cell markers of B cell function in 20 patients with new diagnosis of AAV with renal involvement and 10 healthy controls (HC). Peripheral blood samples were taken at clinical onset prior to treatment initiation for AAV patients. We measured CD25 ^{hi} CD71^{hi} B regulatory cells; subpopulations of memory B cells, including IgD^{+}CD27^{-} naive, IgD^{+}CD27^{+} unswitched, IgD^{-}CD27^{+} switched, and IgD^{-} CD27^{-} double negative; and CD38^{hi}CD27^{hi} plasma cells and their expression of CD138.

Results: We found significantly increased percentages of of CD3^{-}CD56^{-}CD19^{+} B cells in AAV patients compared to HC (**Fig. 1A**). We did not find a significant difference in CD25 ^{hi} CD71^{hi} B regulatory cells between AAV and HC (**Fig. 1B**). AAV patients had increased frequency of double negative IgD^{-}CD27^{-} memory B cells but no difference in the naïve, switched, or unswitched memory B cell subpopulations (**Fig. 1C-F**). We found significantly higher levels of CD38^{hi}CD27^{hi} plasma cells in AAV patients, with greater CD138^{-} but no difference in CD138^{+} expression between groups (**Fig. G-I**).

Conclusion: Patients with new diagnosis AAV display a unique phenotype of B cell dysfunction that is characterized by an increase in the double negative (DN) memory B cell population, which has been implicated in other autoimmune diseases, and an increase in plasma cells, suggesting persistent antibody production. We did not demonstrate a difference in B regulatory cells, a departure from previously published results that may be explained by our study of early disease activity.

Disclosure: E. Chan, None; **S. Hartzell**, None; **L. Anderson**, None; **C. Cantarelli**, None; **C. Guglielmo**, None; **I. Tassiulas**, None; **S. Andrighetto**, None; **A. Angeletti**, None; **J. Manrique Escola**, None; **P. Cravedi**, None.

Abstract Number: 0971

B Cell ROCK1 Promotes Germinal Center Responses and Is Required for Optimal Humoral Immunity

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Rho GTPases, such as RhoA, have emerged as important regulators of lymphocyte biology owing to their ability to be rapidly activated downstream of a broad range of signals. Two of the major effectors of RhoA signaling are the Rho Kinases (ROCKs), ROCK1 and ROCK2, a pair of serine-threonine kinases that have been previously implicated in the control of cell adhesion, migration, proliferation/survival, and gene expression. Despite the fundamental reliance of T and B cells on these processes, the precise involvement of the ROCKs in lymphocyte

biology is yet to be elucidated. Here, we investigate the contribution of ROCK1 to B cell development and differentiation following immunization with a T-dependent antigen.

Methods: To assess the roles of B cell ROCK1 in T cell-dependent responses, mice with B cell-specific deletions of ROCK1 (CD23-Cre.*Rock1*$^{flox/flox}$ and Cγ-Cre.*Rock1*$^{flox/flox}$ mice) were immunized with a T-dependent antigen. *Rock-1*$^{flox/flox}$ mice were also immunized as a control for this study. The differentiation of germinal center (GC) B cells and plasmablast/plasma cells (PB/PCs) was monitored by FACS at various timepoints following immunization. Total and antigen-specific antibody responses were also assessed by ELISA. The molecular mechanisms employed by ROCK1 to promote B cell differentiation were further examined by FACS-sorting B cell populations from spleens of immunized mice followed by RNA-sequencing analyses.

Results: We found that ROCK1 is expressed and activated in splenic B cells. Mice with B cell-specific deletion of ROCK1 showed marked reductions in total and antigen-specific antibody responses following immunization. These decreased humoral responses corresponded with impaired formation and maintenance of antigen-specific GC B cells and PB/PCs following immunization in the ROCK1-deficient mice. Through next generation sequencing, we have furthermore identified a ROCK1-regulated transcriptional program that supports the phenotype of GC B cells.

Conclusion: Our study demonstrates that ROCK1 is activated in B cells and is required for the optimal development of mature B cell populations at baseline and for efficient GC responses following immunization. These findings thus uncover previously unknown B cell-specific roles for ROCK1 in promoting humoral responses and suggests that targeting ROCK1 activity may provide therapeutic benefit for the treatment of diseases marked by aberrant B cell responses.

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Abstract Number: 0972

Disease Severity Is Linked to an Increase in Autoantibody Diversity in IgG4-related Disease

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Background/Purpose: The oligoclonal expansion in IgG4-related disease (IgG4-RD) of both plasmablasts and tissue-infiltrating CD4+ cytotoxic T lymphocytes, the identification of specific auto-antigens as B cell targets, and the consistent clinical responsiveness to B cell depletion all support the possibility that this disorder is an autoimmune disease in which adaptive immune responses contribute to the associated tissue fibrosis. Since 2015, four different auto-antigens have been described as potential triggers for IgG4-RD: prohibitin, annexin A11, laminin 511-E8 and galectin-3. However, validation of these findings using external patient cohorts and characterization of the relationship between these specific auto-antigens has yet to be achieved.

Methods: Autoantibody responses against prohibitin, annexin A11 and laminin 511-E8 were measured by ELISA among a clinically diverse cohort of IgG4-RD patients (n = 100). Idiopathic pulmonary fibrosis (IPF) plasma samples (n = 50) were used as a disease control and age- and sex-matched healthy donor plasma samples (n = 50) as healthy controls. We clustered our cohort into subsets of patients according to their number of autoantibody responses (no responses, 1 response, and ≥ 2 responses) and compared clinical parameters among these groups.

Results: The frequencies of IgG4 autoantibody responses against prohibitin (10%), annexin A11 (12%), and laminin 511-E8 (7%) were not significantly different from those of controls. Patients with pancreatobiliary disease did not enrich for annexin A11 or laminin 511-E8 autoantibodies. A portion of the cohort (n = 86) had been analyzed previously at our center for anti-galectin-3 antibody responses with 25 (29%) having IgG4 anti-galectin-3 antibodies. Among these 86 subjects, 32 (37%) had IgG4 antibodies to at least one of the 4 auto-antigens and 12 (14%) showed reactivity to ≥ 2 of the tested antigens. The subset of patients with ≥ 2 autoantibodies had higher total IgG1, IgG2, IgG4, and C-reactive protein levels; were more commonly hypocomplementemic; and were more likely to have visceral organ involvement.

Conclusion: Antibodies against prohibitin, annexin A11, and laminin 511-E8 were found in only a small portion of patients with IgG4-RD. A subset of IgG4-RD patients, however, had IgG4 antibodies against ≥ 2 autoantigens. Patients with antibodies against ≥ 2 autoantigens present with robust IgG subclass elevations, complement consumption, and visceral organ involvement. This broader break in immunological tolerance in IgG4-RD was associated with more severe disease. (Supported by NIH U19 AI 110495 and UM1 AI144295)

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Abstract Number: 0973

Serum IgG4 Concentrations Differ According to Race and Sex

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Elevated IgG4 concentrations are used to support a diagnosis of IgG4-related disease (IgG4-RD). IgG4 concentrations are reported to be higher in male IgG4-RD patients than in female patients and higher in Asian patients than in non-Asian patients. Similar observations have been made in studies of other immunoglobulin concentrations but were limited by relying on small cohorts with similar conditions/exposures or by excluding certain races. There are scarce data on demographic differences in IgG4 concentrations. We assessed IgG4 concentration differences according to sex and race in a large cohort with demographic diversity.

Methods: The Partners Research Patient Data Registry (RPDR) was queried to identify patients who had ≥ one IgG subclass concentrations measured between January 1, 1989 and March 15, 2018 within the Partners HealthCare Network. Immunoglobulin (Ig) concentration test results, sex, date of birth, self-reported race, billing ZIP code (to

	Race			Sex		
	Asian (N = 302)	**Black (N=611)**	**White (N= 11,673)**	**Female (N=7,917)**	**Male (N=4,934)**	**Overall (N = 12,851)**
Male*	143 (47.4%)	222 (36.3%)	4,470 (38.7%)	--	4,934	4,934 (38.4%)
Race						
White	--	--	11673	7,203 (91.0%)	4,470 (90.6%)	11,673 (90.8%)
Black	--	611	--	389 (4.9%)	222 (4.5%)	611 (4.8%)
Asian	302	--	--	159 (2.0%)	143 (2.9%)	302 (2.4%)
Other	--	--	--	166 (2.1%)	99 (2.0%)	265 (2.1%)
Age (years) at first test	51.6 (18.2)	55.0 (18.3)	52.8 (16.5)	54.9 (17.9)	54.3 (18.9)	54.7 (18.2)
Number of tests per subject	3.4 (7.7)	3.4 (7.3)	4.5 (10.8)	3.8 (8.8)	5.1 (12.8)	4.3 (10.5)

*Results presented as N (%) or mean (SD)

Cohort Characteristics

	Race			Sex		
	Asian	**Black**	**White**	**Female**	**Male**	**Overall**
IgG4 Concentration	140.4 (408.1)	53.6 (103.1)	41.6 (89.9)*	37.4 (75.2)	56.3 (148.5)*	44.6 (109.7)
Unadjusted (β)	+98.8*	+11.9*	0.0 (Ref)	-18.9*	0.0 (Ref)	--
Age, Sex, Race-Adjusted (β)^	+97.9*	+12.8*	0.0 (Ref)	-18.2*	0.0 (Ref)	--
Age, Sex, Race, SES-Adjusted (β)†	+20.5*	+8.6*	0.0 (Ref)	-5.0*	0.0 (Ref)	--
> Upper Limit of Normal (N, %)	75 (24.8%)	73 (12.0%)	819 (7.0%)*	483 (6.1%)	517 (10.5%)*	1,000 (7.8%)
Unadjusted (OR, 95% CI)	4.4 (3.3-5.7)*	1.8 (1.4-2.3)*	1.0 (Ref)	0.6 (0.5-0.6)*	1.0 (Ref)	--
Age, Sex, Race-Adjusted (OR, 95% CI)‡	4.3 (3.3-5.7)*	1.9 (1.4-2.4)*	1.0 (Ref)	0.6 (0.5-0.6)*	1.0 (Ref)	--
Age, Sex, Race, SES-Adjusted (OR, 95% CI)	4.4 (3.4-5.8)*	1.8 (1.4-2.4)*	1.0 (Ref)	0.6 (0.5-0.6)*	1.0 (Ref)	--

* $p < 0.05$; †Multivariate quantile regression; ^Linear regression; ‡Logistic regression

Unadjusted and Multivariate-Adjusted Differences in IgG4 Concentrations According to Sex and Race

	Race			Sex	
Ig Class	**Asian**	**Black**	**White**	**Female**	**Male**
IgG (mg/dL)	+356.3*	+517.6*	0.0 (Reference)	+10.7	0.0 (Reference)
IgG1 (mg/dL)	+189.7*	+345.6*	0.0 (Reference)	+5.8	0.0 (Reference)
IgG2 (mg/dL)	+189.7*	+80.1*	0.0 (Reference)	-1.7	0.0 (Reference)
IgG3 (mg/dL)	+21.1*	+36.1*	0.0 (Reference)	+0.7	0.0 (Reference)
IgA (mg/dL)	+62.1*	+103.4*	0.0 (Reference)	-18.3*	0.0 (Reference)
IgE (mg/dL)	+172.8	+488.9*	0.0 (Reference)	-122.0*	0.0 (Reference)
IgM (IU/mL)	0.0	-2.5	0.0 (Reference)	+19.3*	0.0 (Reference)

* $p < 0.05$

Multivariate-Adjusted Differences in IgG, IgA, IgE, and IgM Concentrations According to Sex and Race

estimate socioeconomic status [SES]), and diagnostic billing codes (to determine clinical indication for testing) were extracted. The distributions of IgG4 concentrations were compared across race and sex categories using t-tests and ANOVA tests, as appropriate. Multivariate-adjusted differences in IgG4 concentrations and the proportion of subjects with results above the reference range across race and sex subgroups were estimated using linear and logistic regression, respectively.

Results: Of the 12,851 subjects, the mean age was 54.7 (±18.3) years, 7,917 (62%) were female, 11,673 (91%) were White, 611 (5%) were Black, and 302 (2%) were Asian (Table 1). Asian and Black subjects, compared to White subjects, had higher IgG4 concentrations (mean 140.4 and 53.6 vs. 41.6 mg/dL, $p< 0.001$) and more often had IgG4

concentrations above the ULN (24.8% and 12.0% vs. 7.0%; p< 0.001). In age- and sex-adjusted analyses, Asian subjects had over a 4-fold higher odds (aOR 4.3, 95% CI 3.3-5.7) and Black subjects had a2-fold higher odds (aOR 1.9, 95% CI 1.4-2.4) of having an IgG4 above the ULN than White subjects. Males had higher IgG4 concentrations than females (mean 56.3 vs. 37.4 mg/dL, p< 0.001) and more often had IgG4 concentrations above the upper limit of normal (ULN) than females (10.5% vs 6.1%, p< 0.001; Table 2). In age- and race-adjusted analyses, females were 40% less likely than males to have an IgG4 above the ULN (aOR 0.6, 95% CI 0.5-0.6). These differences persisted but were attenuated after adjustment for SES (Table 2). Our findings were similar when we stratified according to clinical indication. Similar observations were made when evaluating IgG, IgG1, IgG2, IgG3, IgA, and IgE concentrations (Table 3).

Conclusion: IgG4 concentrations differ according to race and sex and reflect similar differences observed in other Ig concentrations. These similarities suggest that a non-specific activation of Ig-producing B cells by environmental or genetic factors is responsible for these observations. These results have implications both for the interpretation of IgG4 concentration testing for the diagnosis of IgG4-RD and for the use of Ig concentrations in other clinical settings and research.

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Abstract Number: 0974

Bruton's Tyrosine Kinase (BTK) Inhibitors and Autoimmune Disease: Making Sense of BTK Inhibitor Specificity Profiles and Recent Clinical Trial Successes and Failures

Garth Ringheim,[1] Matthew Wampole,[1] and Kinsi Oberoi[1], [1]Clarivate Analytics, Philadelphia, PA

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Background/Purpose: Clinical development of BTK/Tec family kinase inhibitors for treating autoimmune diseases has lagged that of their successful application in oncology. The lack of selective BTK inhibitors to date has partly limited progress in developing drugs that target BTK for autoimmune diseases, where the tenant is held that long term therapy in nonlife threatening diseases necessitates minimizing off-target effects. Autoimmune diseases, however, often demonstrate alterations in multiple immune cell types and signaling pathways, making it difficult to decipher which of these factors are causal and to what degree. The objective of this study was to perform a meta-analysis on available BTK inhibitor pre-clinical and clinical data to develop guidelines and predictors of successful therapeutic applications in autoimmune diseases.

Methods: Biochemical and functional data were collected and analyzed for BTK inhibitors in clinical development from public data sources and Clarivate Analytics database content using a repertoire of programs and services including PubMed, Web of Science, Cortellis Intelligence, Cortellis Integrity, Metacore, Metabase, OFF-X, and CBDD. Development candidates were assessed and categorized for their target specificity profiles, signaling pathways, immunocyte functions, biomarkers, and their reported biological activities in clinical trials.

Results: BTK inhibitor profiles showed remarkably similar specificity profiles within the Tec family kinase group of enzymes. Some differences, however, were observed in T-, B-, and macrophage cell associated enzymes across development candidates that were inconsistent with functional effects, suggesting additional mechanism of action participation. Clinical trial failures in rheumatoid arthritis despite BTK inhibition and effects on B cell biomarkers suggest insufficiency of BTK inhibition as well as off-target pathways associated with those drugs. In contrast, enzymes involved in pathways targeting antibody and T cell activities showed correlation with clinical trial success in diseases where these processes are implicated, including multiple sclerosis and pemphigus vulgarus. Overlap of these disease mechanisms and additional biological pathways associated with lupus strongly suggest a future therapeutic application in this yet to be validate clinical indication.

Conclusion: Current BTK inhibitors in development for autoimmune diseases demonstrate significant lack of specificity with similar patterns of off-target enzyme activities. Some specificity differences, however, were evident. Overall, similarities and differences in specificity showed strong correlation with most reported immunocyte functions, but inconsistencies were evident in some activities that challenge current ascribed functional assumptions for BTK inhibitors. Meta-analysis of BTK inhibitor specificity profiles validated by current clinical trials demonstrate the potential for the collective use of data to understand autoimmune disease pathology and to enhance efficiency in disease indication selection for drugs in clinical development.

Disclosure: G. Ringheim, None; **M. Wampole**, None; **K. Oberoi**, None.

Abstract Number: 0975

Functional Impairment of Mitf and the MiT Transcription Factor Family Dysregulates B Cell Activation and Function

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Background/Purpose: Autoreactive B cells are central in the development of many autoimmune diseases, such as systemic lupus erythematosus (SLE), and are normally eliminated or inactivated by B cell tolerance mechanisms. Our lab developed a mouse model, called TDN-B, whereby inhibition of the *microphthalmia* transcription factor (MITF) and its family members, TFE3, TFEB, and TFEC occurs specifically in B cells. Prior work showed that B cell homeostasis and tolerance were compromised in this model, as evidenced by splenomegaly, elevated autoantibody titers, and altered B cell compartments. Further, this model worsened SLE-like disease when superimposed on an SLE-susceptible genetic background (B6.lpr), driving accelerated mortality, production of pathologic autoantibodies, and hastened renal disease. To define the signaling pathways regulated by Mitf and the MiT family that could explain their involvement in B cell tolerance, the presented work evaluated the TDN-B model, and a genetic model in which Mitf was not expressed in any cell type ($Mitf^{mi\text{-}vga9}$).

Methods: B cell and T cell subsets were characterized by flow cytometry of bone marrow and spleen, serum immunoglobulin and autoantibody serum titers were quantified by ELISA, in-vitro isolated B cell cytokine secretion was

quantified by Luminex, B cell and T cell organization within splenic follicles was visualized through wide-field and confocal microscopy, and comprehensive investigation of mRNA expression in ex-vivo B cells was defined through RNA sequencing. All experiments compared TDN-B, Mitf$^{mi\text{-}vga9}$, and wildtype mice.

Results: Both TDN-B and Mitf$^{mi\text{-}vga9}$ mice showed increased serum rheumatoid factor, splenomegaly, increased numbers of splenocytes, and disorganization of splenic follicles. Uniquely, Mitf$^{mi\text{-}vga9}$ mice, with Mitf absent in all cells, showed increased serum levels of IgG anti-dsDNA, increased splenic germinal center (GC) B cells, and increased splenic plasma cells (PCs). While increased splenic GC B cells and PCs were not observed in TDN-B mice, increased numbers of pre-B/immature B cells and PCs were observed in the bone marrow. RNA sequencing of ex-vivo B cells showed that in both models, upregulated mRNA pools were significantly enriched for genes with roles in GC growth and/or regulation. Further, pathways related to regulation of cell cycle, MHCII antigen presentation, and cytokine signaling were all significantly enriched for in mRNA from both Mitf$^{mi\text{-}vga9}$ and TDN-B B cells. Additional experiments in Mitf$^{mi\text{-}vga9}$ mice uniquely demonstrated increased numbers of B cells with surface expression of activation markers (CD69, CD25) and antigen presentation molecules (MHCII, CD86), and that B cells in culture had increased secretion of TNF-alpha after LPS stimulation.

Conclusion: These data demonstrate that the functional impairment of Mitf and the MiT transcription factor family results in a breach of B cell tolerance that is coincident with cellular and molecular changes, which lead to dysregulation of B cell activation, antigen presentation, cytokine secretion, germinal center organization, plasma cell differentiation, and autoantibody production. The underlying mechanisms responsible for these effects are under investigation.

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Abstract Number: 0976

Identification of Novel Genes Associated with Dysregulation of B Cells in Patients with Primary Sjögren's Syndrome

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SESSION INFORMATION

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Background/Purpose: Dysregulation of B cells play a critical role in the pathogenesis of primary Sjögren's syndrome (pSS). Long non-coding RNAs (lncRNAs), which have become the focus of studies on autoimmune diseases, may contribute to the pathogenesis of pSS through multiple signal transduction pathways. However, no study focuses on the effects of dysregulation of the transcriptomes, including lncRNAs, of B cells on the pathogenesis of pSS. The aim of this study was to identify the molecular mechanism of dysregulation of B cell subpopulations of pSS at the transcriptome level.

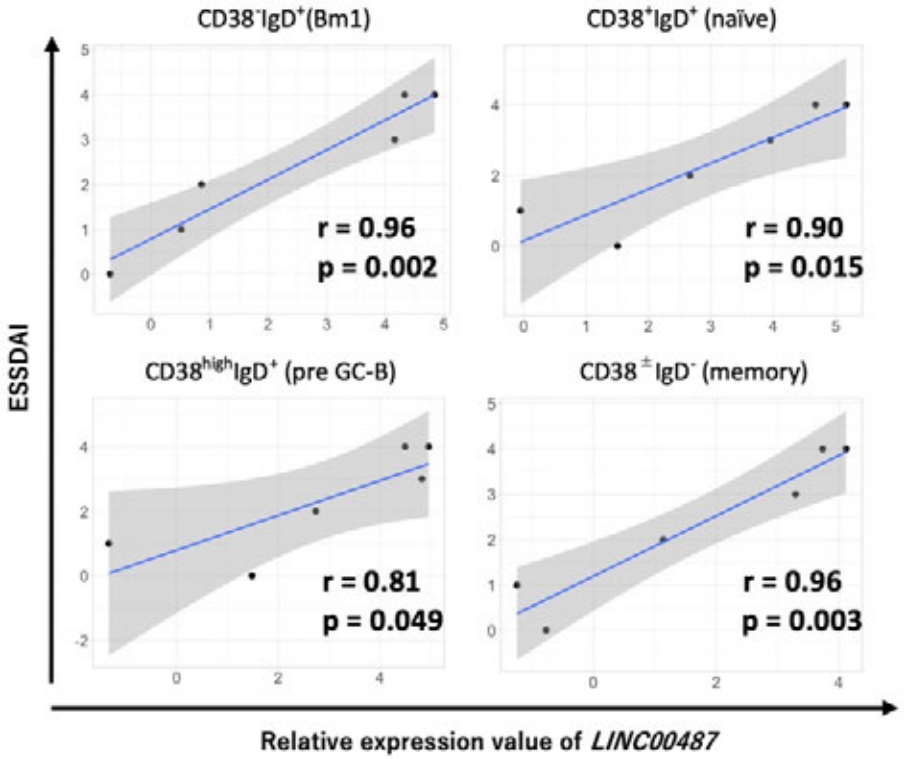

Figure 1. Scatter plot of disease activity score and relative expression level of LINC00487 in CD38-IgD+ (Bm1), CD38+IgD+ (naïve), CD38highIgD+ (pre GC-B) and CD38±IgD- (memory) subset of patients with primary Sjögren's syndrome.

Methods: We enrolled patients with pSS (n=6) and healthy controls (HC) (n=6). Peripheral B cells acquired from these subjects were separated by cell sorting into four subsets: $CD38^{-}IgD^{+}$ (Bm1), $CD38^{+}IgD^{+}$ (naïve B cells), $CD38^{high}IgD^{+}$ (pre-germinal centre B cells), and $CD38^{\pm l}gD^{-}$ (memory B cells). Total RNA was extracted, and gene expression was measured using microarrays. We conducted a bioinformatics analysis to identify differentially expressed genes (DEGs) and weighted gene co-expression network analysis (WGCNA) to identify pSS-associated signalling pathways. We validated gene expression levels in $CD19^{+}$ B cells of patients with pSS (n=7) and HC (n=7) in other cohorts by quantitative PCR (qPCR).

Results: Using principal component and clustering analyses, we found that transcript expression patterns depended on cell type rather than clinical condition (pSS or HC). DEGs analysis identified *LINC00487* as significantly upregulated in all B cell subsets as well as HLA and interferon signature genes. Moreover, the normalized intensity value of *LINC00487* significantly correlated with the disease activity score in all pSS B cell subsets (Figure 1). An in vitro study using human B cell lines revealed that the expression of *LINC00487* was strongly induced by IFNα. In validation cohort using qPCR, expression of *LINC00487* in $CD19^{+}$ B cells of patients with pSS tended to upregulate compared with HC, although it was not significant (relative expression levels of *LINC00487*/GDH; 0.00227 vs 0.00025, p = 0.12). Further, expression of *LINC00487* was significantly correlated with interferon stimulated gene, *interferon induced protein 44 like* (*IFI44L*). WGCNA revealed six clusters associated with the B cell subpopulation of pSS. Further, genes that encode components of the B cell receptor (BCR) signaling pathway were identified as intramodule hub genes such as *IKZF3* and *HRK*. *SOX4*, which may be targeted by several microRNAs identified in upstream analysis, was identified as an inter-module hub gene (Figure 2).

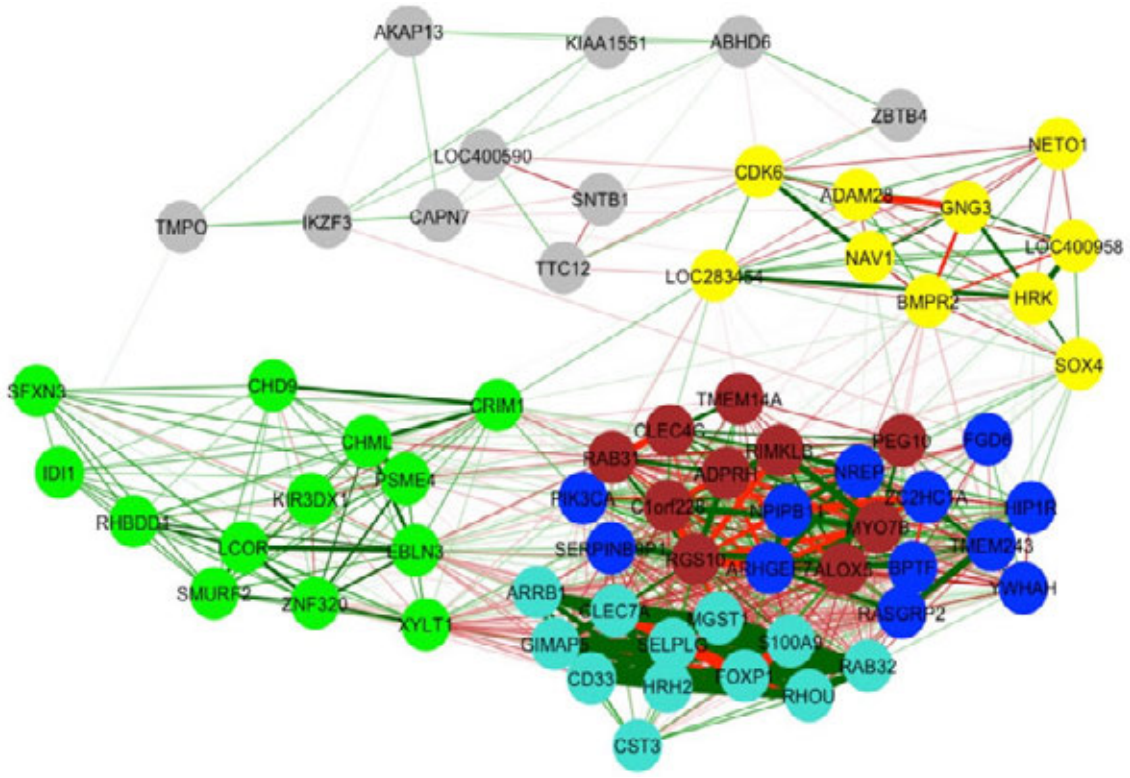

Figure 2. Associativity of intra- and inter-modular hub genes in B cells of pSS. Node-color corresponds with module-color. Green-coded edge means positive correlation and red-coded edge means negative correlation, respectively. The width of edge reflects absolute weight of correlation.

Conclusion: Our transcriptome analysis revealed key genes involved in the molecular dysregulation of B cell subpopulations associated with pSS. This knowledge contributes to our understandings of the pathogenesis of pSS.

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Abstract Number: 0977

Conditional Deletion of MKL1 Inhibits Osteoclast Formation and Bone Erosions in Collagen Induced Arthritis Mice

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SESSION INFORMATION
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Background/Purpose: Excessively osteoclasts (OCs) activation play an essential role in bone erosions in rheumatoid arthritis (RA). Thus, controlling OCs would be an effective strategy to prevent pathological bone resorption. OCs originate from the hematopoietic monocyte-macrophage lineage. We previously showed that MKL1 is high expressed in macrophages and is indispensable for TNFα induced proinflammatory transcription in macrophages. Here, we explored the effect of MKL1 on OCs differentiation and function and examined its role on bone resorption during inflammatory arthritis.

Methods: OCs differenation and function were assayed by TRAP staining and pit formation assay. Bone erosions in collagen induced arthritis mice (CIA) was analyzed by histopathology and MicroCT. RNA-seq was used to detect the potential mechanism that involved in OCs formation after conditional deletion of MKL1 in macrophages.

Results: The multinucleated osteoclast formation in vitro was impaired in bone marrow cells isolated from the KO mice compared with those from wild-type mice (WT). OCs related genes expression included TRAP and CTSK were significantly down-regulated in KO mice. Targeted ablation of MKL1 in macrophages resulted in decreased OCs numbers in bone marrow and increased bone mass in KO mice. In contrast, no effect on T cells, B cells and monocyte numbers in bone marrow. Deletion of MKL1 mice showed the mild bone resorption after subcutaneously injecting of LPS on calvariae compared with WT mice. In a CIA model , KO mice exhibited the delayed arthritis onset, mild arthritis score, lower synovial inflammatory cell infiltration and decreased bone erosion, as compared with WT mice. RNA-seq indicated that OCs derived from mice with macrophage MKL1-deficient mice had an increased Rho kinase and IFN signaling pathway.

Conclusion: Our data suggested that MKL1 plays an important role in regulation osteoclast formation and bone erosions in CIA mice.

Disclosure: W. Tan, None; **A. Luo**, None; **Y. Xu**, None; **S. Lin**, None; **M. Zhang**, None; **F. Wang**, None.

Abstract Number: 0978

Light Mediated Therapeutics in Arthritis

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Background/Purpose: Rheumatoid arthritis (RA) therapies are constrained by the failure to deliver sufficient quantities of drug to the inflamed site, systemic side effects, and the inability for the patient to self-direct therapeutics in a site-targeted fashion. To address this, we have conjugated anti-inflammatory drugs to the light-responsive fluorophore Cy5, anchored to vitamin B12. These photocleavable drug-conjugates can be loaded into red blood cells (RBCs) and released only after laser light activation. *In vitro* studies have shown RBC-B12-Cy5-dexamethasone successfully induced nuclear migration of the glucocorticoid receptor after laser light photocleavage. We believe this system can be used in the treatment of RA, where externally and selectively applied laser to joints can trigger photocleavage of anti-inflammatories internally loaded into RBCs to the targeted site.

Methods: Collagen Antibody Induced Arthritis (CAIA) was induced in 45 DBA1J mice. Arthritis was measured by a blinded observer with a clinical disease score index, and mice were randomized to 3 groups after symptom onset: RBC-B12-Cy5-dexamethasone (RBC-DEX), RBC-Cy5 (negative control), intraperitoneal dexamethasone (IP-DEX; positive control). Hypotonic solution was used to create a porous membrane in murine RBCs for drug uptake, followed by isotonic solution to close the pores and trap the phototherapeutic inside until photo-release. The RBC-DEX group received RBCs (90% hematocrit, 100μL) loaded with B12-Cy5-dexamethasone (approx. 0.0065 mg) intravenously. The RBC-Cy5 control group received RBCs internally loaded with only B12-Cy5. Intravenous injections were given one time at symptom onset for both RBC-DEX and RBC-Cy5. The IP-DEX group received 0.5mg/kg daily until a clinical score of 0 in the arthritic paw receiving laser. Laser (635 nm, 3 mW) was applied to one affected joint for 5 minutes immediately following i.v. or i.p. injection (based on group assignment) and each day until termination. There were no adverse reactions from laser application.

Results: RBC-DEX and IP-DEX produce significant improvement in clinical arthritis compared to the control RBC-Cy5 (p=0.0007, p=0.0002 respectively), but do not significantly differ from each other (p=0.6) (Fig. 1). The RBC-DEX

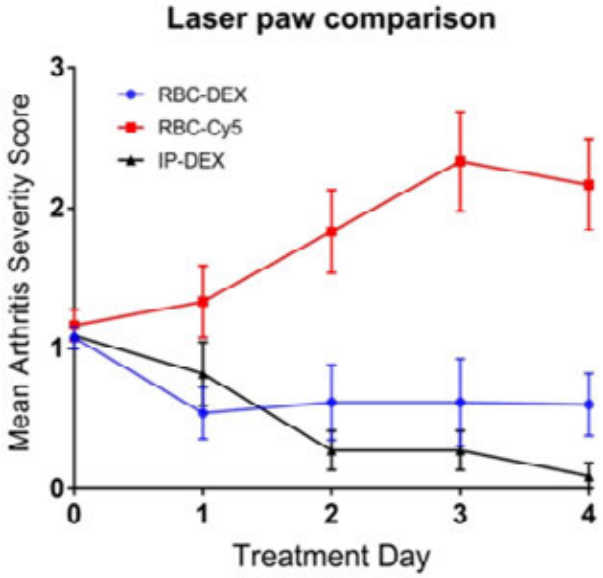

Figure 1. Assessment of mean arthritis severity score after treatment. Across 3 groups: p<0.0001*. RBC-Cy5 vs. IP-DEX: p=0.0002* RBC-DEX vs. IP-DEX: p=0.6 RBC-DEX vs. RBC-Cy5: p=0.0007*

group received on average 80% less dexamethasone as compared to the IP-DEX treatment group, without significantly different results.

Conclusion: RBC-DEX is an effective CAIA treatment compared to negative control and is as effective as the positive drug control using a substantially lower dose of dexamethasone. This warrants further study into the parameters that are required for selective release of RBC-DEX in arthritis treatment.

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Abstract Number: 0979

Platelet Derived Growth Factor Receptor Alpha (PDGFRα) Blockade Inhibits Arthritis in Mice

Bhanupriya Madarampalli,[1] Paul Panipinto,[1] Erica Chow,[1] Kendahl Sugai,[1] Fanqi Shi,[1] and Erika Noss[1], [1]University of Washington, Seattle, WA

SESSION INFORMATION
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Background/Purpose: The interplay between infiltrating immune cells and activated joint stromal cells drives inflammation, cartilage destruction, and bone erosion in rheumatoid arthritis (RA). Among joint cells, fibroblasts amplify inflammation and erode cartilage. Identifying anti-fibroblast therapies to combine with approved drugs targeting the systemic immune response has the potential to improve clinical efficacy without substantially increasing immunosuppressive risk. Based on prior studies showing PDGFRα expression is upregulated in RA synovium and stimulates fibroblast proliferation and matrix invasion *in vitro, w*e propose that targeting platelet-derived growth factor receptor-alpha (PDGFRα) will block synovial fibroblast-mediated inflammation and cartilage erosion, promoting translation of a new anti-PDGFRα biologic for sarcoma treatment to autoimmune arthritis.

Methods: PDGFR expression in human primary synovial fibroblasts was determined by quantitative reverse transcription-polymerase chain reaction (qRT-PCR) and flow cytometry analysis. Matrix metalloproteinase (MMP)-3 release was quantified by ELISA. Role of PDGFRα *in vivo* was tested using the serum transfer arthritis model. PDGFRα-expressing cell populations in arthritic KxB/N mice synovium were analyzed by flow cytometry after *ex vivo* enzymatic digestion. Since PDGFRα genetic silencing is embryonically lethal, PDGFRα conditional knock out (KO) mice were developed by breeding floxed PDGFRα (*B6.Cg-PDGFRatm8SorEiJ*) mice with a strain expressing tamoxifen-inducible cre-recombinase under control of the ubiquitin promoter (*B6.Cg-Tg(UBC-cre/ERT2)1Ejb/1J)*. Commercially available anti-PDGFRα antibodies were used to prevent arthritis.

Results: *In vitro* cultured human synovial fibroblasts expressed higher levels of PDGFRα, compared to the related receptor, PDGFRβ, by qPCR analysis. Although both PDGFRα and PDGFRβ activation increased synovial fibroblast proliferation *in vitro*, only PDGFRα activation through its specific ligand, PDGF-AA, acted synergistically with TNF-α to increase production of MMP-3, a known biomarker of RA joint damage. PDGFRα KO mice developed less arthritis and histologic damage compared to littermate controls in the serum transfer arthritis model. A pilot antibody treatment experiment also showed that antibodies directed against PDGFRα prevented arthritis development. By flow cytometry, most synovial CD45-CD31- mesenchymal (fibroblast) cells in inflamed KxB/N mice synovium strongly

expressed PDGFRα and PDGFRβ. However, PDGFRα was more selectively expressed by fibroblasts, with PDGFRβ also expressed on populations of immune and endothelial cells.

Conclusion: These *in vitro* and *in vivo* studies support a role of PDGFRα in regulating synovial fibroblast-mediated pathology, indicating that blocking PDGFRα may be a new treatment strategy in inflammatory arthritis. Further investigation of the role of PDGFRα in arthritis development is expected to support translation of a new anti-PDGFRα cancer monoclonal antibody into arthritis treatment.

Disclosure: B. Madarampalli, None; **P. Panipinto**, None; **E. Chow**, None; **K. Sugai**, None; **F. Shi**, None; **E. Noss**, None.

Abstract Number: 0980

Sema3B Expression Is Reduced in Rheumatoid Arthritis Patients and Has a Protective Role in a Murine Model of Arthritis

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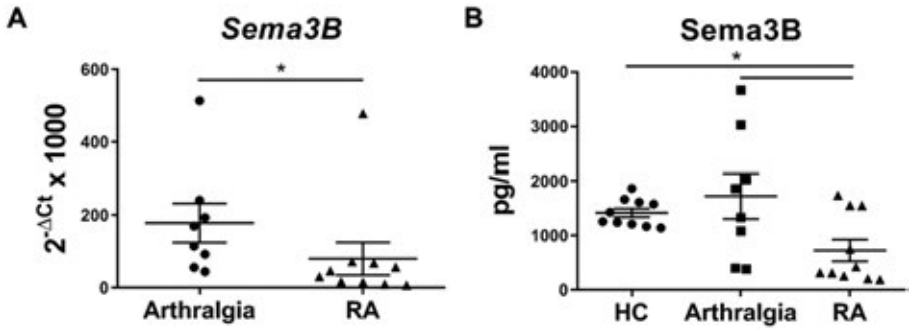
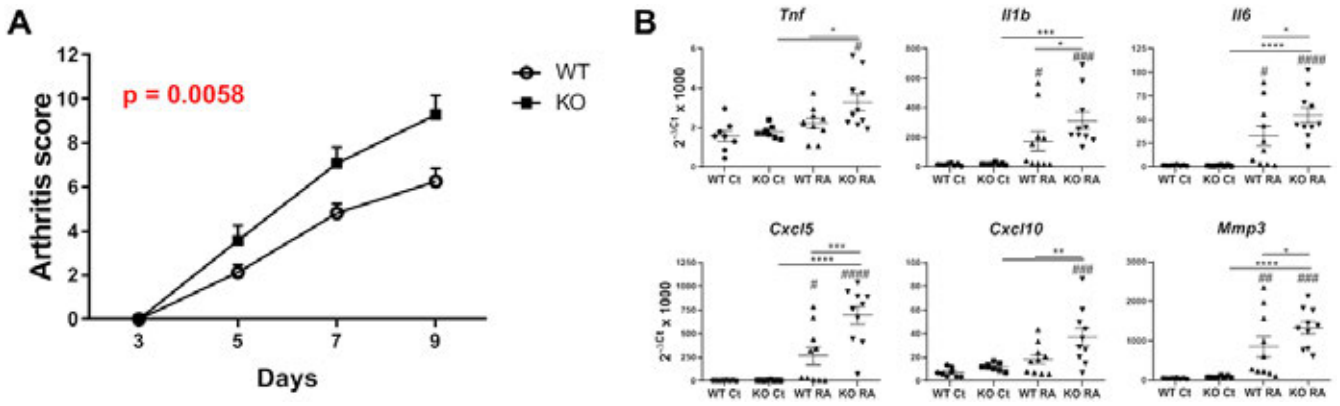
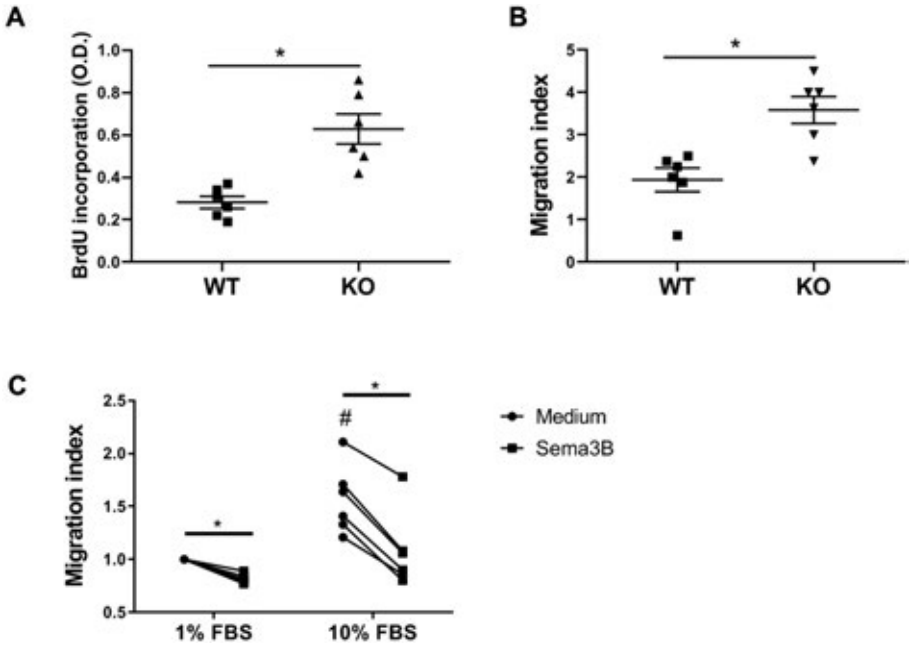
Background/Purpose: The semaphorin family is a large group of proteins initially described in axon guidance. However, semaphorins also play a role in other processes involved in rheumatoid arthritis (RA) such as the regulation of



A-B. Sema3B mRNA and protein levels in the synovial tissue (A) and serum (B) of RA and arthralgia patients. Data is presented as a scatter plot, where each point represents an individual patient. * $p<0.05$.



(A) Daily global arthritic scores of WT and Sema3B deficient (KO) mice. (B) mRNA expression of inflammatory mediators in the forepaws of control and arthritic WT or Sema3B KO mice. Data is presented as a scatter plot, where each point represents an individual mouse. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ and **** $p < 0.0001$. # $p < 0.05$, ## $p < 0.01$, ### $p < 0.001$ and #### $p < 0.0001$ compared to WT control mice.



A-B. Proliferation (A) and migration (B) of mFLS from WT and Sema3B-deficient (KO) mice in the presence or absence of 10% FBS for 24 h. Data is shown as BrdU incorporation (A) or migration index (B) and presented as a scatter plot, where each point represents an individual mouse. C. Migration of mFLS stimulated with Sema3B (100 ng/ml) in the presence or absence of 10% FBS for24 h. Data is shown as migration index and presented as connected dots. * $p < 0.05$ compared to medium 1% FBS.

immunity, angiogenesis, apoptosis and cell migration and invasion. Previously we demonstrated that semaphorin 3B (Sema3B) expression is reduced in the synovial tissue and synovial fluid of RA compared to undifferentiated arthritis patients and reduces the invasive capacity of RA fibroblast like synoviocytes (FLS). Here, we validated initial findings in an independent cohort of patients and determined the role of Sema3B in an *in vivo* model of arthritis

Methods: Sema3B expression in healthy control (HC, n=10), RA (n=10) and arthralgia patient (n=8) synovial tissue and serum was determined by qPCR and ELISA. Arthritis was induced in wild type (WT) and Sema3B-deficient mice (Sema3B KO) mice (n=10 for both) by intraperitoneal injection of 100 ml of K/BxN serum on day 0 and day 2. Mice were sacrificed on day 9 after serum transfer. mRNA expression in total joints and murine fibroblast-like synociocytes

(mFLS) was determined by qPCR. mFLS proliferation and migration were determined using BrdU and wound closure assays, respectively.

Results: mRNA levels of Sema3B were significantly lower in the synovial tissue of RA patients compared to arthralgia patient (p=0.0205). Importantly, serum levels of Sema3B were also reduced in RA patients compared to HC and arthralgia patients (p=0.034 and p=0.0241, respectively) The clinical severity of serum-induced arthritis was significantly higher in Sema3B KO mice compared to WT mice (p=0.0015). This was associated with a higher joint and mFLS expression of the inflammatory mediators IL-1β, TNF, IL-6, CXCL-5 and CXCL-10 and the matrix metalloproteinases MMP-2 and MMP-3 (p-values ranging between $p< 0.05$ and $p< 0.001$). Functional experiments demonstrated a significantly higher proliferation and migration capacity (p=0.034 and p=0.0313, respectively) in the mFLS from Sema3B KO compared to WT mice. Importantly, the administration of recombinant mouse Sema3B abrogated the enhanced migratory capacity of Sema3B KO mFLS (p=0.044).

Conclusion: Our data confirm our previous results demonstrating that Sema3B expression is reduced early in RA onset and provide evidence that Sema3B has a protective role in a mouse model of arthritis. Therefore, Sema3B administration could be a novel therapeutic strategy for the treatment of RA.

Disclosure: A. Igea, None; **T. Carvalheiro**, None; **B. Malvar Fernandez**, None; **A. Rodriguez-Trillo**, None; **T. McGarry**, None; **C. Conde**, None; **D. Veale**, Health Beacon, 1; **U. Fearon**, None; **A. Gonzalez**, None; **T. Radstake**, None; **K. Reedquist**, None; **S. Garcia**, None.

Abstract Number: 0981

Adipocytokines and Obesity in the Context of Rheumatoid and Osteoarthritis Mouse Models

Hani Manfred Sauermilch,[1] Marie-Lisa Hülser,[1] Carina Schreiyäck,[1] Yubin Luo,[2] Aline Bozec,[2] Georg Schett,[3] Ulf Müller-Ladner,[4] and Elena Neumann[5], [1]Dept. of Rheumatology and Clinical Immunology, Campus Kerckhoff, Justus-Liebig-University Giessen, Germany, Giessen, Germany, [2]Department Clinic of Medicine 3 - Immunology and Rheumatology, University of Erlangen-Nürnberg, Erlangen, Germany, Erlangen, Germany, [3]Department of Internal Medicine 3, Friedrich Alexander University Erlangen-Nuremberg, Erlangen, Germany, [4]Justus Liebig University Gießen, Department of Rheumatology and Clinical Immunology, Campus Kerckhoff, Bad Nauheim, Germany, Gießen, Hessen, Germany, [5]Justus Liebig University Gießen, Department of Rheumatology and Clinical Immunology, Campus Kerckhoff, Bad Nauheim, Germany, Giessen, Hessen, Germany

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Background/Purpose: Adipocytokines are bioactive factors mainly produced by adipose tissue and exert many important effects on energy homeostasis as well as immune responses. Osteoarthritis (OA) is one of the most common degenerative joint diseases whereas rheumatoid arthritis (RA) is a chronic autoimmune joint disease. To evaluate the role of adipokines and obesity in the setting of both diseases at different time points, we combined an obesity model (high-fat diet, HFD) with a model for OA (DMM, destabilization of the medial meniscus) and RA (collagen induced arthritis, CIA).

Methods: The DMM model was performed in C57Bl/6 mice fed with HFD or ND (normal diet) prior to OA induction. In the CIA model, DBA/1Rj mice were fed with the same diets for 12 (DMM) and 6 (CIA) weeks prior to CIA induction.

Mice were sacrificed to collect histological as well as serological data after 4, 6 and 8 weeks (DMM model) or after 4, 5.5 and 7 weeks (CIA model) after arthritis induction. Histological scoring for arthritis induction (both models) and assessment of a clinical score for the CIA model was performed. Serum concentrations of CRP, the adipokines adiponectin, leptin and visfatin were measured. Immunohistochemical stainings were performed to evaluate local adipokine distribution in the joints. Diet-induced systemic changes were analyzed using a fatty liver score and evaluation of crown-like structures (CLS) in adipose tissue.

Results: Induction of OA/ RA was successfully established in an HFD setting, shown by the histological joint destruction and the increased fatty liver score and bodyweight, respectively. In DMM, the number of CLS were significantly higher in the HFD group (0.2 ± 0.16, n=7) compared to the ND group (5.2 ± 0.98, n=8). However, CIA induction increased the number of CLS in HFD (2.77 ± 1.07, n=6) and especially in ND animals (8.14 ± 0.23, n=5) compared to healthy ND mice (0.45 ± 0.03, n=4) and healthy HFD mice (2.57 ± 0.53, n=4) without CIA induction. With regard to healthy animals, CRP serum levels were significantly increased in mice after CIA induction. Interestingly, CIA and DMM induction decreased systemic leptin levels significantly which could not be observed in the local leptin distribution in the joints (CIA).

Conclusion: Our data show that OA is deteriorated by HFD, similar to observations in humans. Histological CIA scoring showed no significant difference in CIA severity under HFD or ND. The high numbers of CLS in CIA animals with ND and the strong reduction of serum leptin levels in CIA animals with HFD indicates that CIA onset and severity are mainly obesity independent while OA (DMM) appears to be influenced by obesity. Interestingly, systemic and local adipokine concentrations did not match in DMM as well as the CIA model. This data suggests a time-dependent adipokine expression and segregation of local and systemic adipokine effects in the context of RA and OA.

Disclosure: H. Sauermilch, None; **M. Hülser**, None; **C. Schreiyäck**, None; **Y. Luo**, None; **A. Bozec**, None; **G. Schett**, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, 8, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, UCB, 5, BMS, Celgene, GSK, Lilly, Novartis, 2; **U. Müller-Ladner**, None; **E. Neumann**, None.

Abstract Number: 0982

A Novel Role for Nod2 in Controlling Autoantibody Production and Arthritis in SKG Mice

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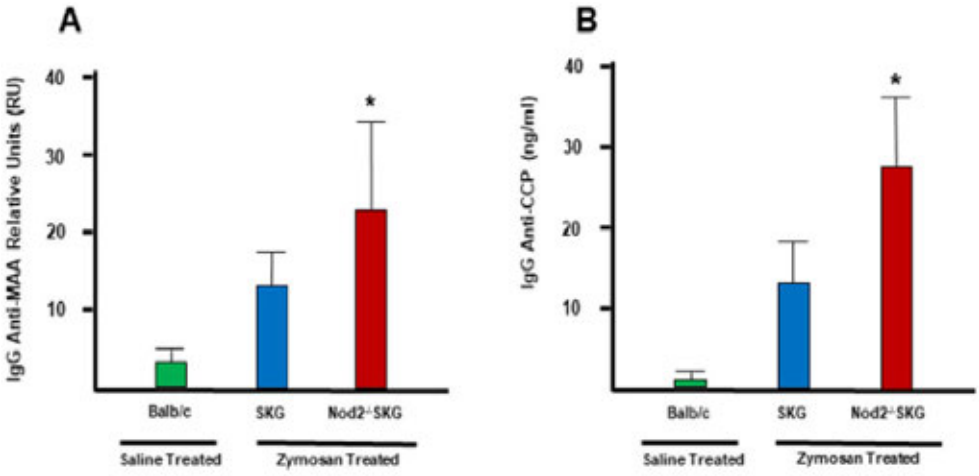
Background/Purpose: Rheumatoid arthritis (RA) is a systemic inflammatory disease that manifests in a chronic and debilitating polyarthritis. Although the etiology of RA is unknown pathogenic autoreactive T cells and autoantibodies including anti-CCP and anti- malondialdehyde-acetaldehyde (MAA) are thought to contribute to disease pathogenesis. Our recent studies identified the microbial sensor Nod2 as a critical genetic determinant in controlling the Th17-response and arthritis severity in SKG mice (Napier RJ et al. J Immunol 2018). However, whether Nod2 also contrib-



Increased concentrations of serum anti-CCP and anti-MAA autoantibodies at 8 weeks post zymosan exposure in Nod2-/-SKG, zymosan-exposed SKG and saline treated Balb/c mice. IgG anti-MAA (A) and IgG anti-CCP (B) antibody concentrations were significantly elevated in Nod2-/-SKG zymosan treated mice as compared to SKG zymosan treated mice ($p = 0.0111$ for CCP; and, $p = 0.0223$ for MAA) and sham treated Balb/c mice ($p = 0.0371$ for CCP; and, $p = 0.0430$ for MAA). No significant differences were observed in the concentrations of anti-CCP or anti-MAA antibodies between the SKG zymosan treated mice and the saline treated Balb/c mice.

utes to autoantibody production in SKG mice is unknown. The purpose of this study was to extend our understanding of the protective mechanisms by which Nod2 controls arthritis in SKG mice to humoral immunity.

Methods: Balb/c, SKG and Nod2$^{-/-}$SKG mice (6-8 wk age) were housed under specific pathogen-free conditions. Arthritis was induced by i.p. injection of 1.5 mg zymosan (Sigma-Aldrich) vs. saline (sham control). Serum IgG anti-CCP and anti-MAA antibodies were measured by ELISA 8 weeks later. Clinical arthritis for each paw was graded (0–4) in masked fashion. T cells (CD4$^+$ and CD8$^+$) were isolated from joint synovial fluid and evaluated (#T cells/ml) by flow cytometry.

Results: Nod2$^{-/-}$SKG mice had significantly increased concentrations of serum anti-CCP and anti-MAA autoantibodies at 8 weeks post zymosan exposure compared to zymosan-exposed SKG ($p = 0.0111$ for CCP; and, $p = 0.0223$ for MAA) and sham treated Balb/c mice ($p = 0.0371$ for CCP; and, $p = 0.0430$ for MAA), the latter group demonstrating only negligible autoantibody reactivity. While there were increased concentrations of anti-CCP and anti-MAA antibodies in SKG mice exposed to zymosan compared to saline exposed Balb/c mice, they were not significantly higher ($p = 0.080$ for CCP; and, $p = 0.111$ for MAA). Comparisons with previously reported data (Napier et al.) showed serum anti-CCP and anti-MAA concentrations were increased in conjunction with arthritis scores in SKG and Nod2$^{-/-}$SKG mice stimulated with zymosan. Likewise, we observed similar increases anti-CCP and anti-MAA concentrations that were associated with the total number of CD4$^+$ T cells present in the synovial fluid collected from SKG and Nod2$^{-/-}$ SKG mice stimulated with zymosan.

Conclusion: These data suggest a previously unprecedented role for Nod2 in suppressing autoreactive B cell responses in the SKG arthritis model. Increased autoantibody concentrations correlated with increased synovial T cell responses and more severe arthritis. Understanding the mechanisms and consequences of enhanced autoantibody production in Nod2-deficient SKG mice will contribute to our understanding of the pathophysiology of RA. Moreover, arthritis resulting from Nod2 deficiency in SKG mice renders a disease model that is characterized by enhancements in both T cell responses and humoral immunity, suggesting that the Nod2$^{-/-}$SKG mice might provide a highly relevant system for modeling RA.

Increased concentrations of serum anti-CCP and anti-MAA autoantibodies at 8 weeks post zymosan exposure in Nod2-/-SKG, zymosan-exposed SKG and saline treated Balb/c mice. IgG anti-MAA (A) and IgG anti-CCP (B) anti-

body concentrations were significantly elevated in Nod2-/-SKG zymosan treated mice as compared to SKG zymosan treated mice (p = 0.0111 for CCP; and, p = 0.0223 for MAA) and sham treated Balb/c mice (p = 0.0371 for CCP; and, p = 0.0430 for MAA). No significant differences were observed in the concentrations of anti-CCP or anti-MAA antibodies between the SKG zymosan treated mice and the saline treated Balb/c mice.

Disclosure: R. Napier, None; **E. Vance**, None; **J. O'Dell**, None; **J. Poole**, None; **B. England**, None; **M. Duryee**, None; **T. Mikuls**, BMS, 2, Horizon, 2; **H. Rosenzweig**, None; **G. Thiele**, None.

Abstract Number: 0983

Fecal Transfer from Mice on High or Low Magnesium Diets Confers Arthritis Protection

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Background/Purpose: Magnesium (Mg) plays a key role in the immune response. We have previously demonstrated that alterations in the Mg balance by increasing or decreasing the Mg daily intake significantly protected mice in Collagen Induced Arthritis and KRN serum-induced arthritis. The effect correlated with reduced number of Th17 T cells and increased number of FoxP3$^+$ Treg cells, as well as with a significant reduction in the amounts of Segmented filamentous bacteria (SFB) and a significant increase in the amounts of *Bacteroides fragilis (*BFR). In this study, we hypothesized that the gut microbiota changes induced by dietary Mg modifications could account for the arthritis protective effect induced by the diet.

Methods: Donor mice (C57BL/6; Taconic) were placed on a low (50 ppm), regular (500 ppm) or high Mg diet (2800 ppm) for 14 days. Fecal samples were obtained on days 14 and 15, homogenized in water (30 mg of fecal pellet in 400 ml) and filtered. Recipient mice (C57BL/6; Taconic) were treated with an antibiotic cocktail containing Metronidazol (140 mg/Kg), Neomycin (140 mg/Kg) and Vancomycin (10 mg/Kg) for 5 days and allowed to recover for 2 days. Recipient mice receiving a regular 500ppm diet were then gavaged daily from day 0 to day 5 with fecal material from the donor mice and arthritis was induced by injecting 100 ml of arthritogenic serum from KRN mice on days 3 and 5. The animals were scored daily for

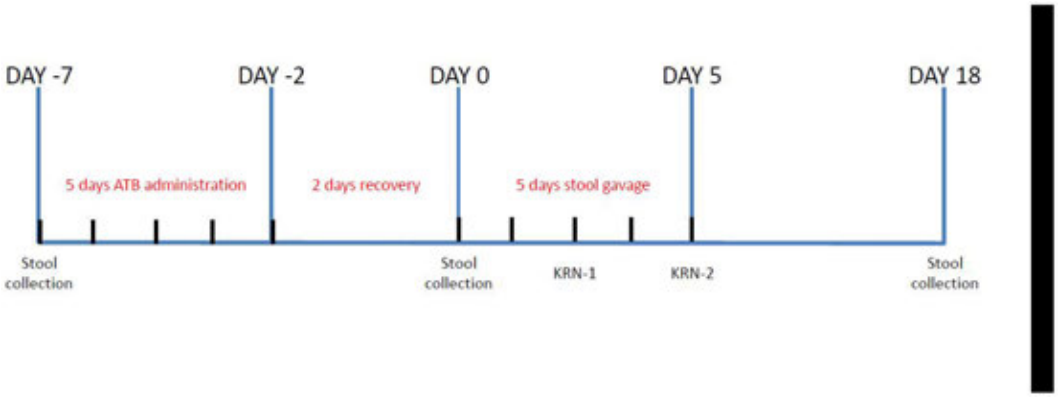

Figure 1. Timing of the stool collection, antibiotic (ATB) administration, stool collection and arthritis induction with KRN serum transfer (KRN-1= first dose; KRN-2=second dose) from day -7 to day 18.

15 days. Fecal samples were collected before antibiotics treatment (day -7), after antibiotic treatment but before the fecal transfer (day 0) and at endpoint (day 18). Genomic DNA was extracted and the levels of the commensal bacteria BFR and SFB determined by qPCR. Tissues were also collected for histology and flow cytometry analysis.

Results: Antibiotic treatment for 5 days eliminated SFB and BFR content in all groups (stool qPCR day 0). Fecal transfers were completed without problems. Recipient groups receiving fecal transfer from either the low or high Mg diet donor mice had a significant 50% reduction in maximum arthritis severity scores ($p< 0.05$) and a nearly 30% increase in FoxP3+ Treg and Tr1+ compared with recipients of fecal transfer from the regular Mg diet mice.

Conclusion: This study provides evidence suggesting that the high and low Mg diets reduce arthritis severity and increase numbers of FoxP3+ Tregs via the modulation of the intestinal microbiome and that stools from these mice can transfer these protective phenotypes into recipient mice. Therefore, targeting Mg homeostasis with dietary modifications has the potential to become a new tool to modify the intestinal microbiome to treat autoimmune disorders such as arthritis.

Disclosure: T. Laragione, None; **C. Harris**, None; **P. Gulko**, None.

Abstract Number: 0984

Important Role of CD11c^{+} Cells in Inflammatory Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Animal Models Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Dendritic cells (DCs) are important antigen presenting cells (APCs) and therefore they play an important role in bridging the innate and the adaptive immune response. DCs can be divided in different subsets with specific functions. As powerful APCs, DCs are thought to play an important role in the induction of autoimmune diseases such as rheumatoid arthritis. However, the active role of DCs in joint inflammation is not known yet.

Methods: We analyzed histological sections of K/BxN serum transfer arthritis as well as hTNFtg arthritis for the presence of CD11c+ cells by immunohistochemistry. We used CD11c-diphteria toxin receptor (DTR) transgenic mice. K/BxN serum transfer arthritis was induced, and mice were given either DT or PBS or in wt and BARF3 deficient mice. In addition CD11c DTR mice were crossed into hTNFtg animals and also received either DT or PBS. The severity of arthritis was determined clinically and histologically.

Results: Both CD8+CD11c+ and CD11b+CD11c+, can be found in synovial tissue in TNF driven arthritis. Upon depletion of CD11c+ cells clinical signs of K/BxN serum transfer arthritis were significantly reduced. Histological analysis found reduced synovial inflammation after the depletion of CD11c+ cells in K/BxN arthritis. In addition, local bone destruction and the number of osteoclasts was also significantly reduced. In addition to K/BxN arthritis, we found that also in TNF-driven arthritis depletion of CD11c+ cells led to a striking reduction of synovial inflammation and a complete depletion of osteoclasts.

Conclusion: These data show that in addition to initiating an adaptive immune response, CD11c+ dendritic cells, are also involved in innate effector mechanisms of inflammatory arthritis. Especially CD11b+CD11c+ and monocyte derived inflammatory seem to play a role in inflammatory arthritis, suggesting that they could be an important therapeutic target.

Disclosure: A. Puchner, None; **E. Simader**, None; **V. Saferding**, None; **G. Kroenke**, None; **R. Pfeifle**, None; **D. Aletaha**, AbbVie, 2, 5, 8, AbbVie, Janssen, Lilly, Novartis, Pfizer, and Roche, 5, AbbVie, Merck Sharp and Dohme, and Roche., 2, Amgen, 5, 8, Bristol-Myers Squibb, 8, Bristol-Myers Squibb, Celgene, Merck Sharp and Dohme, and UCB, 8, Celgene, 5, 8, Janssen, 5, Lilly, 5, 8, Medac, 5, 8, Merck, 5, 8, Merck Sharp and Dohme, 2, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, Sandoz, 5, 8, Sanofi/Genzyme, 5, 8, UCB, 8; **J. Smolen**, AbbVie, Amgen, Astra-Zeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, 8, AbbVie, Eli Lilly, Janssen, MSD, Pfizer, Roche, 2, ILTOO, Janssen, Medimmune, MSD, Novartis, Pfizer, Roche, Samsung, Sanofi, UCB, 8; **S. Blueml**, None.

Abstract Number: 0985

Inhibition of Calcium/calmodulin-dependent Protein Kinase IV in Rheumatoid Arthritis: Dual Effect on Th17 Cell Activation and Osteoclastogenesis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: CD4 $^{+}$ T cells are important in the pathogenesis of rheumatoid arthritis (RA), and therapies targeting the differentiation of osteoclasts are attracting attention. Calcium/calmodulin-dependent protein kinase IV (CaMK4) is a molecule involved in T cell activation and osteoclast differentiation, but the role of CaMK4 in T cells and osteoclasts in RA remains unclear.

Objective: We investigated the role of calcium/calmodulin-dependent protein kinase IV (CaMK4) in the expression of joint injury in rheumatoid arthritis (RA).

Methods: Mice subjected to collagen-induced arthritis (CIA) were treated with KN-93, a CaMK4 inhibitor, and the clinical score was evaluated by micro-computed tomography (μ-CT) and histology. The effect of CaMK4 inhibition on inflammatory cytokines and humoral immune response was also examined. *CAMK4* gene expression was measured in $CD4^{+}$ T cells from healthy controls and patients with active RA. $CD4^{+}$ cells were isolated from RA patients to determine the effect of KN-93 on T cell differentiation. We also isolated $CD14^{+}$ cells from RA patients to investigate osteoclast differentiation.

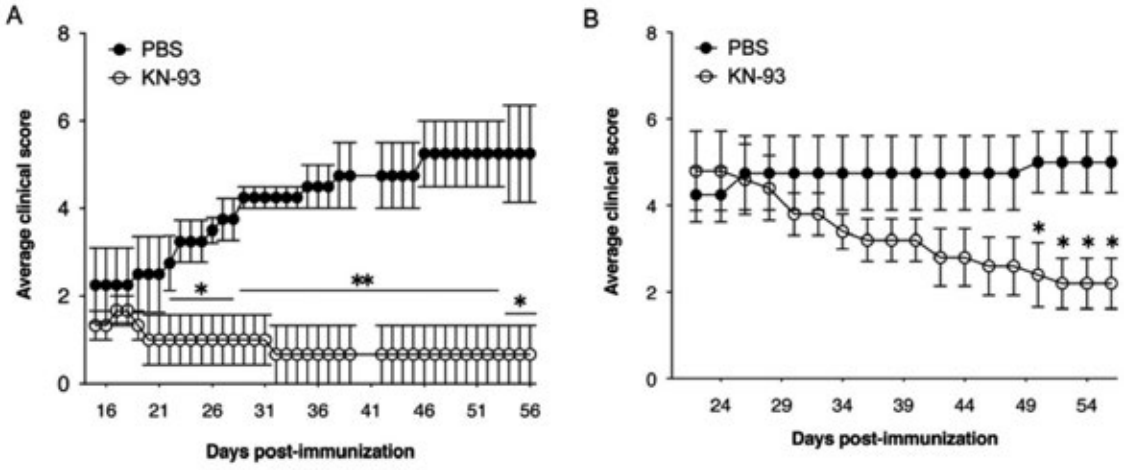

Figure 1. Administration of CaMK4 inhibitor, KN-93, attenuates the development of CIA in mice. Mean clinical scores of CIA in mice treated with KN-93 or PBS prior to the onset of disease (n = 5 per group) (A) and after established disease (n = 5 per group) (B) *p < 0.05; mean ± SEM.

Results: Treatment of CIA mice with KN-93 reduced significantly the arthritis clinical score and joint destruction as evaluated by μ-CT and histology. Further analysis revealed that CaMK4 inhibition in CIA mice suppressed the production of inflammatory cytokines including IL-6, IL-17, G-CSF, and MCP-1. Expression of *CAMK4* was significantly higher in $CD4^+$ T cells from patients with RA compared with cells from healthy controls. CaMK4 inhibition mitigated IL-17 production by $CD4^+$ cells from patients with RA. The number of *in vitro* differentiated osteoclasts from $CD14^+$ cells from RA patients was significantly decreased in the presence of the CaMK4 inhibitor.

Conclusion: The present study provides evidence that CaMK4 inhibition ameliorates CIA by suppressing the production of Th17 cell-related cytokines. At the translational level, we demonstrate that CaMK4 is increased in $CD4^+$ T cells from patients with active RA and that CaMK4 inhibition results in the decreased levels of osteoclast differentiation. Taken together, our findings indicate that CaMK4 inhibitors represent potential therapeutic agents in the treatment of patients with RA.

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Abstract Number: 0986

Tofacitinib Enhanced Cerebral Brain-derived Neurotrophic Factor Levelsin a Rat Model of Rheumatoid Arthritis

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SESSION INFORMATION

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Session Title: RA – Animal Models Poster

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

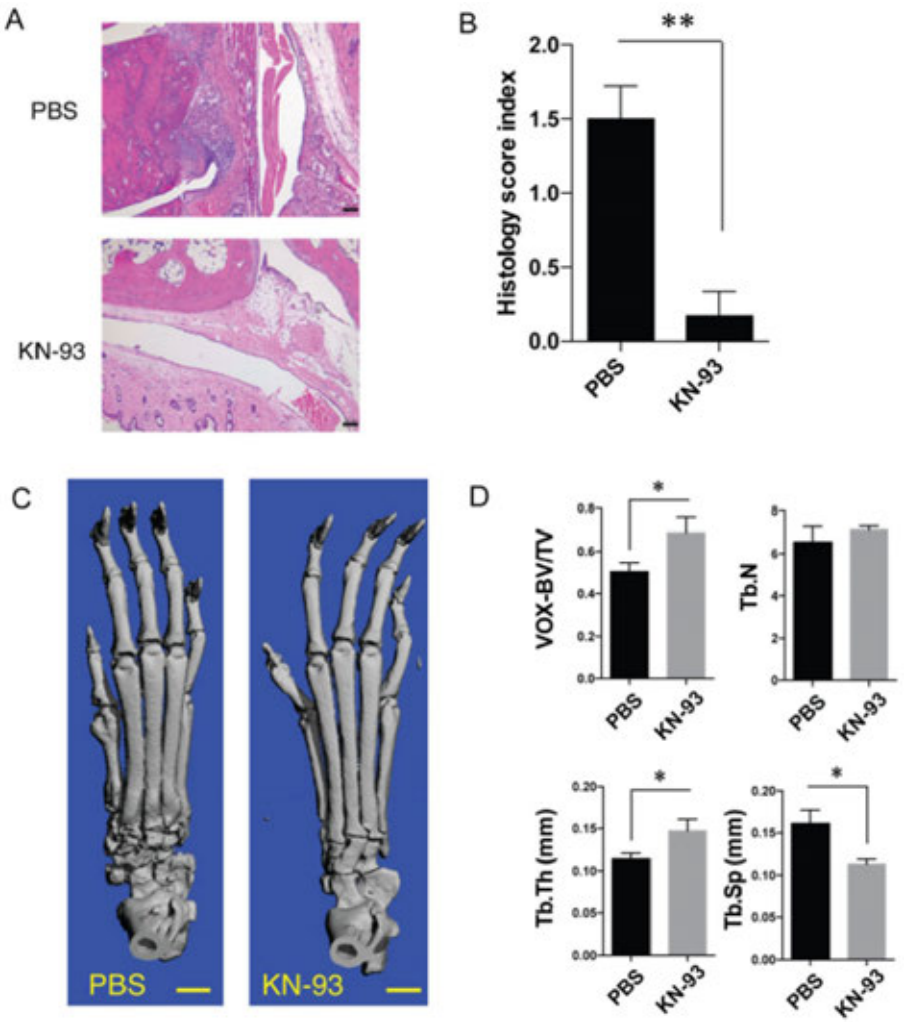

Figure 2. Preventive effect of KN-93 on joint damage in CIA mice. (A) Representative hematoxylin and eosin staining of the ankle joints of KN-93 or PBS-treated mice with CIA. Scale bars represent 100 μm. (B) Pathology scores of each group were calculated and expressed as mean ± SEM (n=4). * p< 0.05. (C) Microfocal computed tomographic images showing the dorsal surface reconstruction of the hind paws of PBS-treated (left) and KN-93 treated (right) mice. (D) Bone volume fraction (BV/TV), trabecular number (Tb.N), trabecular thickness (Tb.Th), and trabecular spacing (Tb.Sp) in mice treated with PBS or KN-93. Data represent mean and SEM, *p < 0.05.

Background/Purpose: Cognitive dysfunction including depression-like symptoms is a frequent comorbidity of rheumatoid arthritis (RA). Recently, rats with adjuvant-induced arthritis (AIA) were found to exhibit reduced levels of brain-derived neurotrophic factor (BDNF), a neurotrophin largely involved in neuroplasticity, learning, memory and cognitive abilities, in cognition-related brain regions[1]. Tofacitinib, an inhibitor of JAK3 and JAK1, has a great effect on RA activity, but whether it might improve cognition is unknown. To answer this question, the present study investigated the effect of Tofacitinib on brain BDNF levels and depression-like symptoms in AIA rats.

Methods: AIA was induced by injection of *Mycobacterium butyricum* in the tail of male Lewis rats. A group of rats without arthritis served as controls. At the first signs of arthritis, AIA received Tofacitinib (10 mg/kg twice daily, s.c.) or saline (Vehicle). Arthritis score was daily evaluated and a radiographic score was attributed to hind paws at the end of the treatment period. After 21 days of treatment, BDNF levels were measured in two brain regions involved in cog-

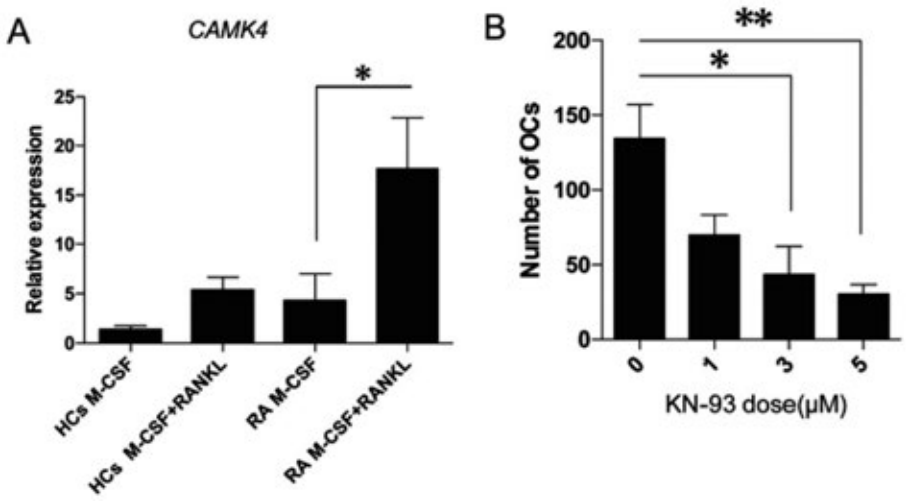

Figure 3. CaMK4 expression is involved in the osteoclastogenesis of RA (A) CAMK4 mRNA expression in CD14+ monocytes from patients with RA or HCs determined by qPCR. (* p< 0.05; median with interquartile range). (B) Active RA patients had significantly lower numbers of osteoclasts in the presence of KN-93 (* p< 0.05, ** p < 0.01; mean ± SD; n = 4). (C)

nition (prefrontal cortex and hippocampus) using western blot analysis. Anhedonia as a core symptom of depression was assessed from the sugar preference test before and during (3 times) treatment.

Results: As compared to controls, AIA resulted in depression-like symptoms from day 6 to 28 post-immunization. These symptoms coincided with a significant decrease in BDNF levels in the prefrontal cortex (-46%, p< 0.001) but not in the hippocampus (-5%, n.s.). BDNF levels were higher in Tofacitinib-AIA rats than vehicle-AIA rats either in the prefrontal cortex (+20%, p< 0.05) or hippocampus (+132%, p< 0.001). By contrast, anhedonia did not differ between Vehicle- and Tofacitinib-AIA rats.

Conclusion: The present data showed that Tofacitinib increased cerebral BDNF levels in AIA rats whatever the cognition-related structure considered, but with a stronger effect in the hippocampus than in the prefrontal cortex. However, the positive effect of Tofacitinib on BDNF did not translate into reduced anhedonia. Further studies are needed to identify the BDNF-dependent cognitive functions that are improved by Tofacitinib in RA.

Reference

1. Pedard M, Demougeot C, Prati C, Marie C. Brain-derived neurotrophic factor in adjuvant-induced arthritis in rats. Relationship with inflammation and endothelial dysfunction. *Progress in Neuropsychopharmacology & Biological Psychiatry, 2018, 82:249-254*.

Disclosure: A. Quirié, None; **C. PRATI**, None; **D. WENDLING**, None; **P. Totoson**, None; **C. Demougeot**, None; **C. Marie**, None.

Abstract Number: 0987

Anti-citrullinated Protein Antibodies Induce Subclinical Inflammation, Bone Loss and Pain in Mice

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Background/Purpose: Autoantibodies against citrullinated proteins (ACPAs) could be associated with bone loss, pain and tenosynovitis prior to disease onset in human rheumatoid arthritis (RA) and induce bone loss and pain when injected in mice. We aimed to investigate if transfer of human ACPAs into mice could induce tenosynovitis and/or subclinical inflammation.

Methods: Monoclonal ACPA (1325:04C03 and 1325:01B09) and control (1362:01E02) antibodies (mAbs) were generated from synovial plasma or memory B cells of RA patients. 2mg of combination of monoclonal ACPAs or control antibody were injected in BALB/c female mice (12-16 Weeks). Pain-like behavior was monitored by measuring mechanical hypersensitivity using von Frey filaments every 3 days and estimation by up-down Dixon method. Bone mineral density was measured by micro-CT. Using specially designed mobilization casts, dedicated mouse MRI coils, and gadolinium enhanced contrast medium, the hind limbs of these mice were scanned and evaluated for any signs of soft tissue joint inflammation. The MRI images were scored for the presence of synovial thickening, effusion and tendon inflammatory changes by 3 readers in a blinded manner.

Results: ACPAs (1325:04C03 and 1325:01B09) induced significantly more pronounced pain-like behavior (lasting for at least 4 weeks) and reduction of the trabecular bone thickness in the hind limbs, whereas no such effect was seen with the control monclonals generated in the same way as the monoclonal ACPAs. While no macroscopic sign of joint inflammation could be detected, MRI data shows sub-clinical joint inflammatory changes (such as perfusion of contrast in tendons, soft tissues and joints) in mice injected with ACPAs but not in those injected with control mAb. Using a semiquantitative score for the degree of inflammatory changes (0- Within normal range, 1-Mild, 2- Moderate and 3- Severe) we were able to show that ACPA induced mild to moderate inflammatory changes affecting tendon thickness, joint effusion and soft tissue enhancements, in contrast to control antibody or Saline injected mice which was within normal range (figure 1 below).

Conclusion: We show that ACPA induces pain-like behavior, bone loss and sub-clinical inflammation in mice, a model that mimics the pre-clinical state of ACPA positive RA

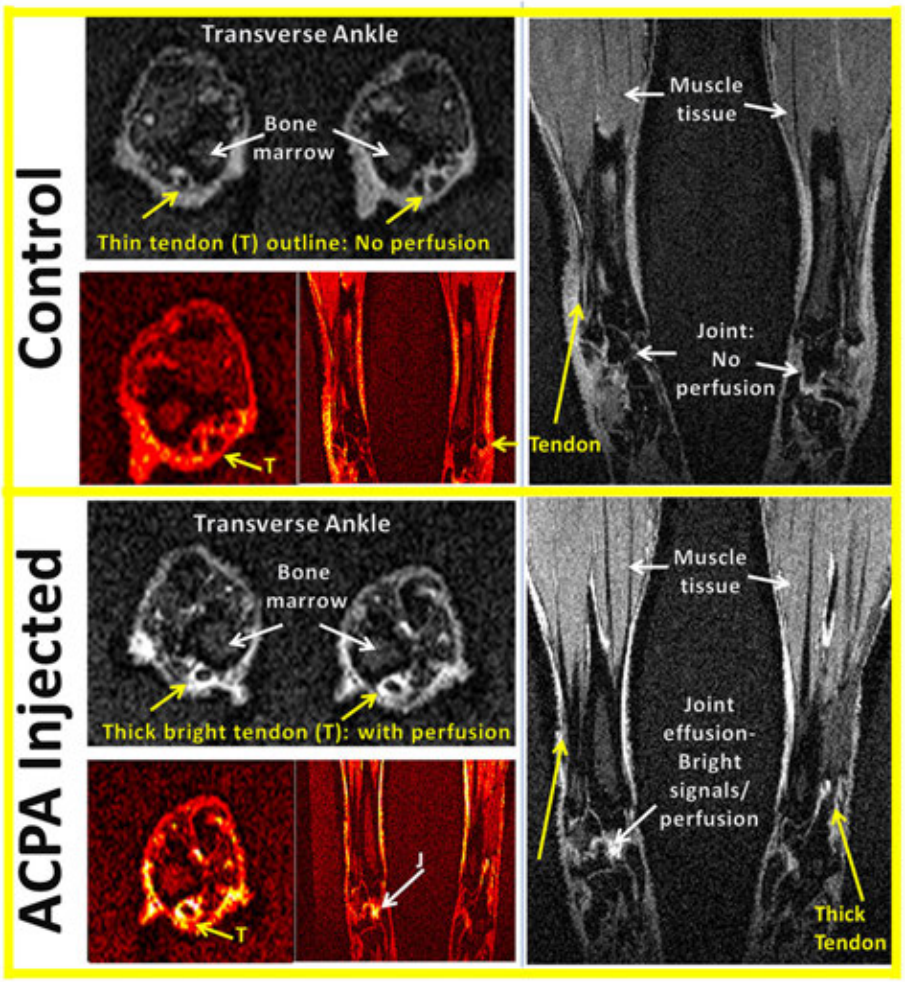

Figure 1. Representative MRI image showing the ACPA induced sub-clinical changes in the joints of the mice

Disclosure: A. Krishnamurthy, None; **Y. Kisten**, None; **A. Circiumaru**, None; **K. Sandor**, None; **K. Sakurabas**, None; **G. Wigerblad**, None; **P. Damberg**, None; **H. Wähämaa**, None; **P. Jarvolli**, None; **V. Malmström**, None; **L. Klareskog**, BMS, 2, Janssen, 2, Pfizer, 2; **C. Svensson**, None; **J. Jimenez Andrade**, None; **B. Rethi**, None; **A. Catrina**, None.

Abstract Number: 0988

Translational Imaging of Treatment Effects for a Novel Anti-TNF-Steroid Antibody Drug Conjugate in a Rat Model of Rheumatoid Arthritis

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is an inflammatory joint disease of autoimmune etiology. If insufficiently treated, RA leads to joint damage and irreversible disability. Although there is no cure, remission is possible with biological and synthetic disease-modifying antirheumatic drugs (DMARDs). Steroid treatment is highly efficacious in many autoimmune diseases, but significant side effects prevent their chronic use. With current treatment options many patients still do not achieve remission, thus prompting the need for improved therapeutics. An antibody drug conjugate (ADC) has been developed that combines TNF inhibition via the antibody with selective delivery of glucocorticoid into inflammatory cells, allowing disease inhibition while preventing the steroid side effects. In this study we evaluated longitudinal *in vivo* treatment effects of this anti-TNF-steroid ADC in the rat collagen-induced arthritis (CIA) model by multimodal translational imaging.

Methods: Inflammatory arthritis was induced in female Lewis rats by immunization with bovine type II collagen in incomplete Freund's adjuvant (IFA) on days 0 and 6. Rats were treated starting at peak inflammation on day 17 with either 10 mg/kg anti-TNF-steroid ADC, ip, qw; 10 mg/kg unconjugated anti-TNF mAb, ip, qw; or 3 mg/kg of the steroid payload po, qd; for three weeks. Paw swelling was assessed by measuring hindlimb volumes with a plethysmometer. Longitudinal *in vivo* magnetic resonance (MR) and X-ray micro-computed tomography (μCT) imaging of the hindlimb were used to monitor pathological changes in soft tissues and in bones, respectively, from day 0 before treatment to day 42. Rats were sacrificed on day 42 for histopathological assessment of hindlimb pathology including pannus and bone remodeling. In addition, *ex vivo* μCT was performed on hindlimb samples collected at the study endpoint (day 42).

Results: T2-weighted (T2W) images revealed that treatment with anti-TNF-steroid ADC for one week reduced joint tissue edema, while anti-TNF mAb elicited only a modest reduction. To further explore these changes in T2W contrast, we employed a histogram-based approach to divide the tibia-talus-tarsal hindlimb region into two compartments based on the T2W images. Anti-TNF-steroid ADC displayed superior treatment effects in both compartments as compared to anti-TNF mAb. Treatment effects in preserving bone integrity were evaluated by quantifying bone density, roughness, volume, and surface area with μCT. Three weeks of treatment with anti-TNF-steroid ADC significantly protected bone from damage indicated by an increased high-density bone volume and reduced surface area and roughness relative to the control. Both *in vivo* MRI and μCT and *ex vivo* μCT metrics corresponded well with histologic evaluation at the study endpoint (day 42).

Conclusion: These results demonstrate improved treatment efficacy of the anti-TNF-steroid ADC showing both resolution of inflammation as well as preservation of bone integrity when compared to anti-TNF mAb treatment alone. The quantitative imaging metrics were sensitive to treatment effects and may serve as biomarkers in a clinical trial.

Disclosure: B. Hooker, AbbVie, 3; **X. Zhang**, AbbVie, 3; **T. Cole**, AbbVie, 3; **A. Tovcimak**, AbbVie, 3; **S. Bryant**, Abbvie, 3, AbbVie, 3; **L. Phillips**, AbbVie, 3, Abbvie, 3; **D. Blanchard**, AbbVie, 3; **D. Wooten**, AbbVie, 3; **Q. Guo**, AbbVie, 3; **M. Ruzek**, AbbVie, 3; **A. Hobson**, AbbVie, 3, Abbvie, 3; **M. McPherson**, Abbvie, 3, AbbVie, 3; **R. Stoffel**, AbbVie, 3, Abbvie, 3; **W. Waegell**, AbbVie, 3, Abbvie, 3; **Y. Luo**, AbbVie, 3.

Abstract Number: 0989

Lineage Tracing of Murine Lymphatic Smooth Muscle Cells to Determine the Role of the Lymphatic System in Inflammatory Arthritis

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Background/Purpose: Dysfunction of lymphatic vessel contraction has been implicated in inflammatory arthritis progression and arthritic flare in murine models. Previous studies have demonstrated that tumor necrosis factor transgenic (TNF-Tg) mouse models of rheumatoid arthritis (RA) have notable ultrastructural damage to lymphatic smooth muscle cells (LSMCs).[1] As inflammatory arthritis progresses, LSMC contractions initially increase in frequency and the lymph node expands followed by a complete loss of LSMC contractions and lymph node collapse in severe disease states.[2] Effective treatment of inflammatory arthritis in TNF-Tg mice is associated with recovery of LSMCs and lymphatic vessel contractions.[1] As this regenerative process is critical for joint homeostasis and RA remission, elusive information on LSMC progenitors is needed. To address this, we tested the hypothesis that LSMCs are derived from the same stem cell pathway as vascular smooth muscle cells (VSMCs), which includes early mesenchymal expression of Paired Related Homeobox 1 (Prrx1) and subsequently differentiated Neural-Glial Antigen 2 (NG2) cell markers.[3,4,5]

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2. Bouta et al. 2018. *Nature Reviews Rheumatology*. 14(2):94-106.
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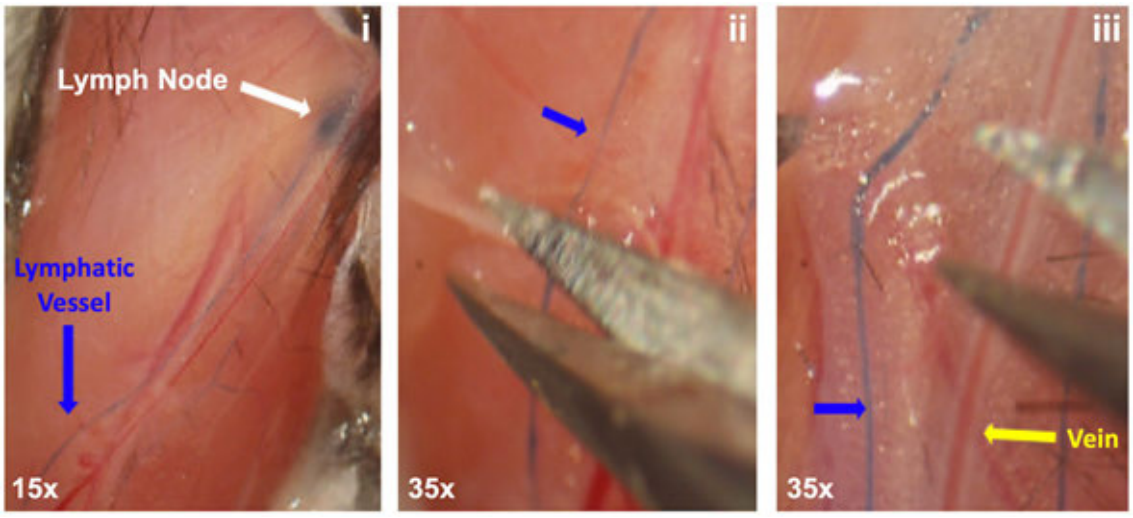
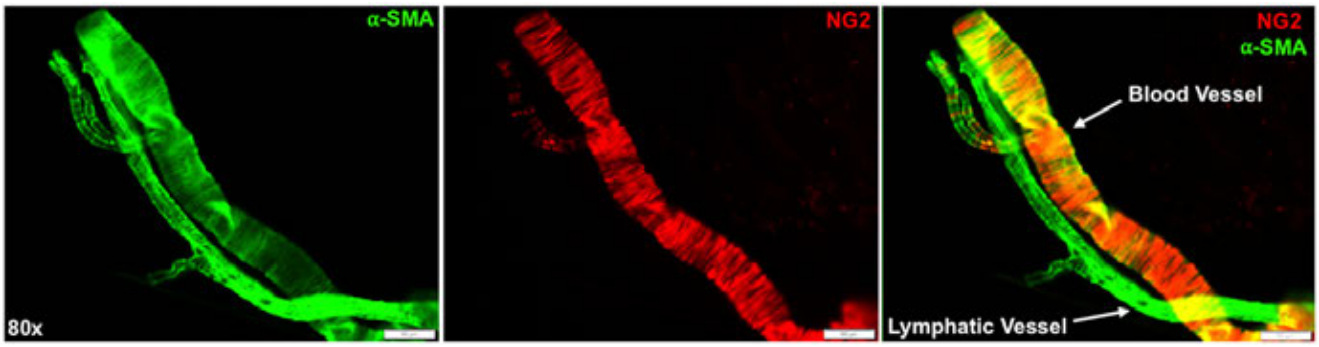
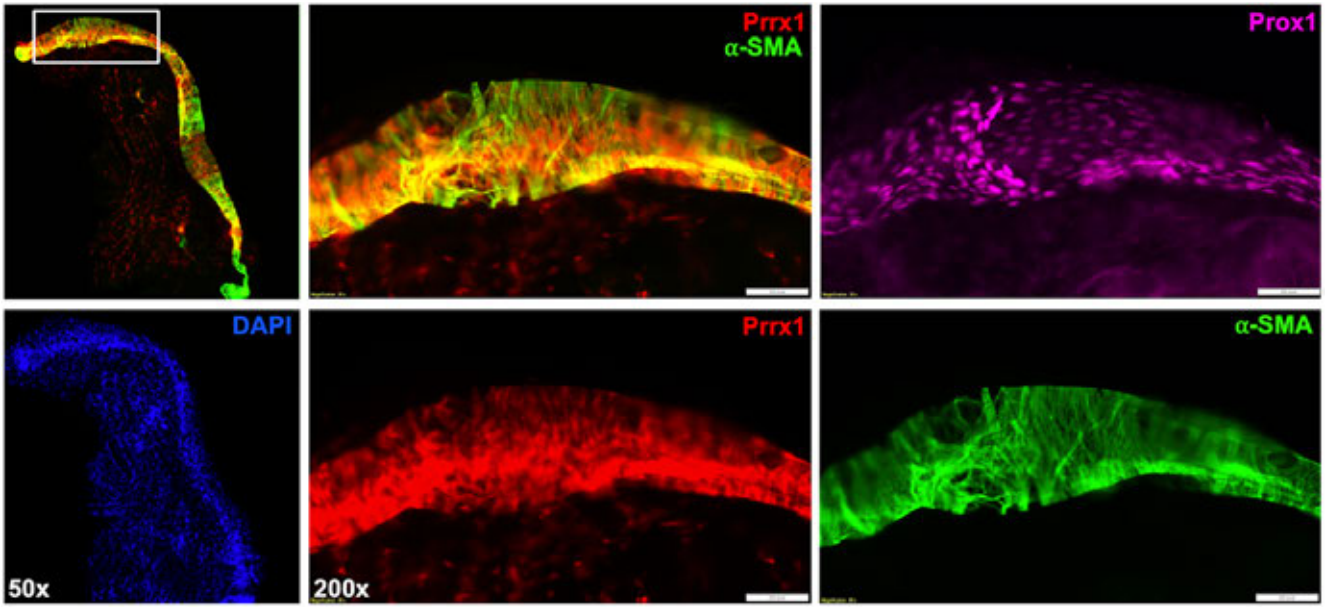
Methods: All animal studies were performed on IACUC approved protocols. We harvested the popliteal lymphatic vessels and saphenous vein from Prrx1-Cre and NG2-CreER^{T2} x Rosa26-Ai9 mice via micro-dissection of the sura. For the procedure, the mice were anesthetized, and 2% Evan's Blue dye was injected into their footpads to locate the lymphatic vessels. Induction of the NG2-CreER^{T2} was achieved with 0.1 mg/g of tamoxifen administered intraperitoneal on 4 consecutive days starting at post-natal day 10. All cohorts were sacrificed at post-natal day 20. To



Micro-dissection of popliteal lymphatic vessels from the sura. Mice were anesthetized and injected with 2% Evan's Blue dye into their footpad. With the dye, micro-dissections of the popliteal lymphatic vessels can be performed after opening the sural surface of the leg. (i) The length of the lymphatic vessel can be seen in blue (blue arrow in all panels) traveling to the popliteal lymph node (white arrow). (ii) Incisions were made on the anterolateral border of the lymphatic vessel to release it from the fat pad. (iii) The lymphatic vessel was then cut away from the saphenous vein (yellow arrow) and removed.



Post-natal lymphatic smooth muscle cells are not NG2 derived. The vessels were dissected from Ai9+/- x NG2-CreERT2 +/- (NG2-Cre+) mice at post-natal day 20. The NG2-Cre+ mice were all administered 0.1 mg/g of tamoxifen intraperitoneal for 4 days starting at post-natal day 10 to induce the Cre system in NG2+ cells. The NG2-Cre+ LSMCs have no red fluorescent protein unlike the VSMCs, which show notable red fluorescence of NG2+ VSMCs that co-localizes with α-SMA.



Post-natal lymphatic smooth muscle cells have Prrx1 heritage. The vessels were dissected from Ai9+/- x Prrx1-Cre +/- (Prrx1-Cre+) mice at post-natal day 20. The Prrx1-Cre+ mice constitutively expressed tdTomato via the Cre system in Prrx1+ cells without induction with tamoxifen. The Prrx1-Cre+ LSMCs have notable red fluorescent protein just as VSMCs (not shown) that co-localizes with the α-SMA. This novel finding demonstrates that LSMCs are of Prrx1 origin, similar to VSMCs, but the LSMC lineage diverges prior to the expression of NG2.

identify the lymphatic vessel, we used immunofluorescent staining for Prospero Homeobox Protein 1 (Prox1) – a lymphatic endothelial cell specific transcription factor. We visualized the LSMCs and VSMCs through immunofluorescent staining for Alpha-Smooth Muscle Actin (αSMA) to determine if Prrx1+ or NG2+ SMCs co-localized with αSMA via multicolor immunofluorescent microscopy.

Results: Our findings demonstrate that Prox1+/αSMA+ LSMCs are Prrx1 derived, but are NG2 negative. The LSMCs from NG2-CreER^{T2} x Rosa26-Ai9 mice were devoid of red fluorescence, while the LSMCs from Prrx1-Cre x Rosa26-Ai9 mice showed notable red fluorescence that co-localized with αSMA. Thus, LSMCs originate from an unknown progenitor cell pathway that is similar to, yet importantly unique from, that of the vascular system.

Conclusion: LSMCs are derived from Prrx1+ mesenchyme similar to VSMCs, but diverge before expression of NG2. They are also not derived from Paired Box Protein 7 (Pax7)+ satellite cells (data not shown). Future work elucidating the LSMC lineage could yield insights for targeted therapies for diseases with lymphatic involvement, such as inflammatory arthritis.

Micro-dissection of popliteal lymphatic vessels from the sura. Mice were anesthetized and injected with 2% Evan's Blue dye into their footpad. With the dye, micro-dissections of the popliteal lymphatic vessels can be performed after opening the sural surface of the leg. (i) The length of the lymphatic vessel can be seen in blue (blue arrow in all panels) traveling to the popliteal lymph node (white arrow). (ii) Incisions were made on the anterolateral border of the lymphatic vessel to release it from the fat pad. (iii) The lymphatic vessel was then cut away from the saphenous vein (yellow arrow) and removed.

Post-natal lymphatic smooth muscle cells are not NG2 derived. The vessels were dissected from Ai9+/- x NG2-CreERT2 +/- (NG2-Cre+) mice at post-natal day 20. The NG2-Cre+ mice were all administered 0.1 mg/g of tamoxifen intraperitoneal for 4 days starting at post-natal day 10 to induce the Cre system in NG2+ cells. The NG2-Cre+ LSMCs have no red fluorescent protein unlike the VSMCs, which show notable red fluorescence of NG2+ VSMCs that co-localizes with α-SMA.

Post-natal lymphatic smooth muscle cells have Prrx1 heritage. The vessels were dissected from Ai9+/- x Prrx1-Cre +/- (Prrx1-Cre+) mice at post-natal day 20. The Prrx1-Cre+ mice constitutively expressed tdTomato via the Cre system in Prrx1+ cells without induction with tamoxifen. The Prrx1-Cre+ LSMCs have notable red fluorescent protein just as VSMCs (not shown) that co-localizes with the α-SMA. This novel finding demonstrates that LSMCs are of Prrx1 origin, similar to VSMCs, but the LSMC lineage diverges prior to the expression of NG2.

Disclosure: H. Kenney, None; **R. Bell**, None; **E. Schwarz**, None.

Abstract Number: 0990

Development of a Novel Anti TNF-Steroid Antibody Drug Conjugate That Shows Promising Efficacy at Doses That Avoid Steroid Side Effects in a Mouse Model of Rheumatoid Arthritis

Wendy Waegell,[1] Christian Goess,[2] Robert Stoffel,[1] Michael McPherson,[1] Adrian Hobson,[1] Suzanne Mathieu,[2] Lucy Phillips,[1] and Shaughn Bryant[1], [1]AbbVie, Worcester, [2]Abbvie bioresearch Center, Worcester, MA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Animal Models Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: TNF-inhibitors are a well established therapy for autoimmune diseases including rheumatoid arthritis, Crohn's disease, psoriasis and ankylosing spondylitis but they have limited efficacy in some patients. Corticosteroid treatment is highly effective in autoimmunity but prolonged use at efficacious doses is contraindicated by significant side effects. We have developed a plasma stable antibody drug conjugate (ADC) that has steroid molecules linked to an anti-TNF a mAb. This ADC is targeted to TNF-a expressing inflammatory cells and internalized to cellular lysosomes. Once in the lysosome the ADC is digested and delivers steroid molecules into the cell. This significantly reduces the efficacious steroid dose to below levels that induce undesired side effects. In an acute in vivo model, contact hypersensitivity in C57BL/6 mice, we have shown that an anti-TNF-steroid ADC can significantly

inhibit the inflammatory response with a minimal effect on the steroid biomarkers, corticosterone and P1NP. Additionally, in a mouse model of rheumatoid arthritis, collagen induced arthritis (mCIA), we have demonstrated that a single therapeutic treatment with an anti-TNF-steroid ADC is able to completely inhibit disease for a greater than 30 days, while anti-TNF mAb only partially inhibits disease.

Methods: To evaluate whether the anti-TNF-ADC can reverse joint damage in mCIA we modified the mCIA model so that treatment was initiated 7 days after disease onset.

Results: To evaluate whether the anti-TNF-ADC can reverse joint damage in mCIA we modified the model so that treatment was initiated 7 days after disease onset. At this time there is significant pannus invasion as well as bone and cartilage destruction in the tarsal region of the ankle joint in these mice. We demonstrate that anti-TNF-steroid ADC treatment, after established disease, appears to heal the joints of previously arthritic mice when compared to a group of satellite animals sacrificed 7 days after disease onset. The tarsal joints from these mice were evaluated using micro computed tomography and by histologic evaluation. Restoration of normal joint architecture was seen in at least 40% of mice with TNF-steroid ADC treatment that was not seen with either an isotype control ADC or with the anti-TNF mAb alone.

Conclusion: These promising results suggest that a steroid targeted to cells involved in joint destruction via TNF binding has the potential to achieve not only lasting remission but also repair of the arthritic joints in RA patients, while sparing patients from steroid induced side effects.

Disclosure: W. Waegell, AbbVie, 3, Abbvie, 3; **C. Goess**, Abbvie, 3; **R. Stoffel**, AbbVie, 3, Abbvie, 3; **M. McPherson**, Abbvie, 3, AbbVie, 3; **A. Hobson**, AbbVie, 3, Abbvie, 3; **S. Mathieu**, Abbvie, 3; **L. Phillips**, AbbVie, 3, Abbvie, 3; **S. Bryant**, Abbvie, 3, AbbVie, 3.

Abstract Number: 0991

Identification of Citrullinated Peptide Specific T-cells in Humanized Mice Immunized with Citrullinated Peptides

Matthew McElwee,[1] Thamotharampillai Dileepan,[1] and Marc Jenkins[1], [1]University of Minnesota, Minneapolis, MN

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Animal Models Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Seropositive rheumatoid arthritis (RA) is a T-cell mediated disease that is characterized by the presence of antibodies to proteins that have undergone the post-translational conversion of arginine to citrulline. Certain HLA-DR major histocompatibility complex class II (MHCII) molecules, for example HLA-DRB1*0401 are closely associated with the development of seropositive RA. These molecules prefer to bind peptides with citrulline not arginine in the P4 position. Thus, citrullination of arginine can create peptides that bind to HLA-DRB1*0401 molecules better than the un-citrullinated versions. These citrullinated peptide:HLA-DRB1*0401 complexes may form neoantigens that activate T-cells with specific T-cell receptors. Indeed, such cells have been identified in patients with RA. In this study, we investigated the correlation between the reported binding affinity of citrullinated peptides to HLA-DRB1*0401 molecules (Ting et al.) and the number of T-cells that recognize these complexes after immunization with citrullinated peptide in transgenic mice expressing HLA-DRB1*0401 molecules.

Methods: Mice expressing HLA-DRB*0401 were immunized with 100 mg of one of eleven citrullinated peptides. The citrullinated peptides tested all had a citrulline at the P4 position and were from human proteins known to have citrullinated antibodies raised against them in RA. These proteins were: collagen intermediate layer protein (2 peptides), fibrinogen (2 peptides), vimentin (3 peptides), LL37 (1 peptide), a-enolase (1 peptide), and aggrecan (2 peptides). Ten days after immunization, citrullinated peptide:HLA-DRB1*0401 tetramers were used to identify specific T-cells in secondary lymphoid organs by flow cytometry.

Results: There was a wide range in the number of citrullinated peptide:HLA-DRB1*0401 tetramer-binding cells isolated from immunized mice (43-5557). The peptide that generated the lowest number of tetramer-binding cells was from human aggrecan 89-103 (Cit95) and the highest number was from human fibrinogen 69-81 (Cit74). When analyzing all peptides, there was a significant correlation between the affinity of the peptide for HLA-DRB1*0401 and the log10 number of citrullinated peptide:MHC tetramer positive cells identified after immunization (R squared 0.454, $p< 0.03$)

Conclusion: Immunization with citrullinated peptides with higher binding affinity to an RA-associated MHCII molecule stimulated a greater number of specific T-cells. These results provide further evidence that citrullination enhances T cell immunogenicity by improving the capacity of peptides to bind MHCII molecules.

Disclosure: M. McElwee, None; **T. Dileepan**, None; **M. Jenkins**, None.

Abstract Number: 0992

Identification of CJ-15314, a Novel Highly Selective JAK1 Inhibitor, for the Treatment of Rheumatoid Arthritis

So Young Ki,[1] Dongkyu Kim,[1] Juhyun Lee,[1] Byoung Seok Moon,[1] and Shin-Young Ryu[1], [1]CJ Healthcare, Icheon-si, Republic of Korea

SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Janus kinases (JAKs) play critical roles in mediating various cytokine signaling. First-generation non-selective JAK inhibitors such as tofacitinib and baricitinib are widely used for rheumatoid arthritis (RA). However, safety concerns such as anemia, thrombosis, and infection are raised for these therapeutics primarily linked with insufficient selectivity for JAK subfamily. The second-generation selective JAK1 inhibitor, filgotinib, exhibits a better safety profile, but testicular toxicity issue remains to be resolved. In the present study, we demonstrate that CJ-15314, a novel highly selective JAK1 inhibitor, exhibits robust efficacy in RA animal models with a preferable safety profile.

Methods: Biochemical, cell-based, human whole blood assay were performed to determine the inhibition potency and selectivity for JAK subfamily kinases. In vivo efficacy was evaluated in rat adjuvant-induced arthritis (rAIA) and collagen-induced arthritis (rCIA) models following oral administration (q.d.) for 2 weeks. A 2-weeks rat repeated dose toxicity study was performed to directly compare the toxicity between CJ-15314 and filgotinib.

Results: In biochemical analysis, CJ-15314 inhibited the JAK kinase family in a concentration - dependent manner, and the IC_{50} value of JAK1 was 3.8 nM, showing 18 fold more highly selectivity over JAK2 and 83 fold over JAK 3.

Accordingly, in human whole blood assays, CJ-15314 is 11 fold more potent against IL6-induced pSTAT1 inhibition through JAK1 (IC_{50} value: 70 nM) than GM-CSF-induced pSTAT5 inhibition (JAK2) whereas bricitinib and filgotinib exhibited only 2-fold and 7 fold respectively. In an in vivo efficacy model, CJ-15314 inhibited disease severity scores in a dose dependent manner. In the rAIA model, relative to vehicle-treated animals, CJ-15314 at 30 mg/kg showed 95.3% decrease in disease activity score, 51.2% in figotinib at 30 mg/kg, baricitinib at 10 mg/kg showed 97.7%. CJ-15314 showed superior anti-arthritic efficacy than filgotinib and similar efficacy to baricitinib. Although baricitinib induced a significant decrease in hematocrit, RBC, and reticulocyte count, CJ-15314 minimally affected anemia-related parameters at end of the 2-week treatment. In the rats CIA model, like 10 mg/kg of bricitinib, 30 mg/kg of CJ-15314 also had a similar effect, with a significant reduction in histopathological scores and plasma IL-1 beta level. In an acute 5-day repeated dose study in mice, CJ-15314 demonstrates relatively low responses to drug-induced platelet counts increase in 10, 30, 90 mg/kg treated groups compared with that of other JAK inhibitors, suggesting a low risk of thrombosis due to inhibition of peripheral thrombopoietin signal. In a rat 2 weeks repeated dose toxicity study, CJ-15314 exhibited a preferable safety profile, whereas tubular atrophy and luminal cell debris were observed testis and epididymis for filgotinib-treated groups.

Conclusion: CJ-15314 is a highly selective JAK1 inhibitor, demonstrates robust efficacy in RA animal models, exhibits differentiated toxicity profiles.

Disclosure: S. Ki, None; **D. Kim**, None; **J. Lee**, None; **B. Moon**, None; **S. Ryu**, None.

Abstract Number: 0993

pH-Sensitive Nanoformulated Triptolide as a Targeted Therapeutic Strategy for Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Animal Models Poster

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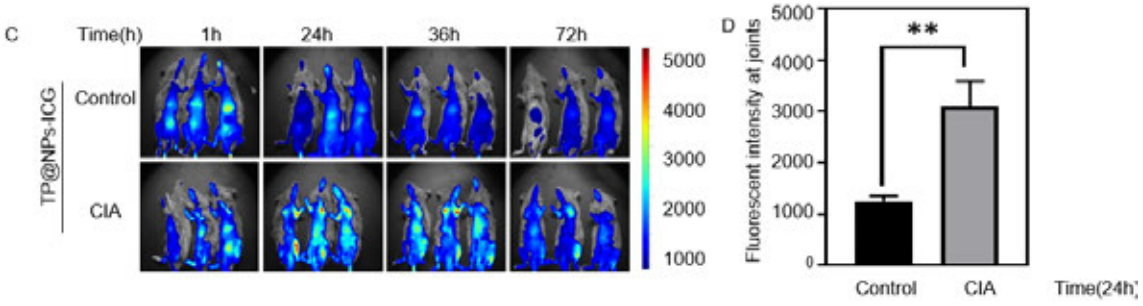
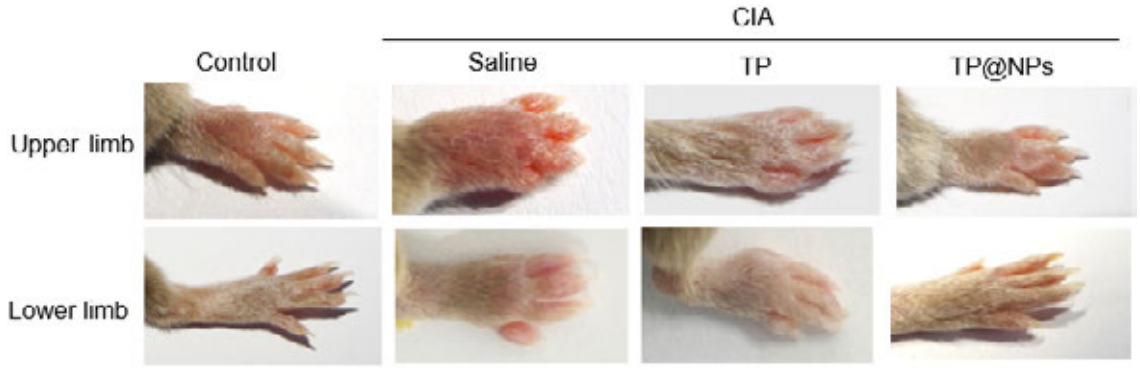


To observe drug targeting and release in vivo, we applied small animal in vivo imaging technology to detect the enrichment efficiency and retention time of TP@NPs in arthritis mice. After injection of TP@ NPs-ICG, the fluorescence intensity in the joint of CIA mice was higher, which was the most obvious at 24 hours. The fluorescence of normal mice was not enriched in the joints.



The results suggested that the Model+TP@NPs group, as well as the control group had no obvious swelling and deformity of the claws on the mices. In addition, compared with Model+Saline group, free TP group was improved, but its curative effect was far less than that of Model+TP@NPs group.

Background/Purpose: The best packaging of holistic therapy for Rheumatoid arthritis (RA) will involve two components: a potent anti-inflammatory therapeutic and a rationally designed drug delivery vehicle to enrich the target site concentration and sustained release of the drug. The natural product, triptolide (TP), which is an effective anti-inflammatory compound, has been used for RA in clinical. However, the potential clinical application of triptolide is limited due to its poor solubility and high toxicity. Drug delivery systems responding to inflammatory acidic pH environment can be constructed by using nanomaterials as carriers combined with TP. Through targeting and nano-drug sustained release, the toxic and side effects of drugs can be reduced and therapeutic effects can be improved.

Methods: The effects of TP@NPs on cell survival, apoptosis and ROS production were detected in RAW264.7 cells. NPs group and saline group were used as control group, TP@NPs group and free TP component of the same amount of TP were given high and low doses (0.15mg/kg/3 days and 0.075mg/kg/3 days) to treat collagen induced arthritis mice for 30 days. ABOG staining,TRAP staining and micro-CT were used to observe bone destruction. HE staining and biochemical indexes of liver and kidney (ALT, AST, CRE, BUN) were used to observe drug toxicity.

Results: Compared with TP, TP@NPs could effectively improve the survival rate of RAW264.7 cells($P< 0.05$).The apoptosis rate of TP was 26.6±8.052, while that of TP@NPs was 1.693 ±0.1617 ($P< 0.01$).The proportion of ROS produced by TP was 10.97±0.5774, which was reduced to 3.68±0.51 by TP @NPs ($P< 0.01$). Q-PCR showed that TP@NPs and TP had the similar effect on inhibiting inflammation in vitro ($P >0.05$). In vivo study, the serum AST ($n=5$, $P=0.0083$), ALT ($n=5$, $P=0.0013$), CRE ($n=5$, $P=0.0069$) and BUN ($n=5$, $P=0.0312$) in TP@NPs (containing high dose TP) treated CIA mice were significantly lower than those in high dose TP group. HE staining showed histomorphological abnormalities of liver, kidney and spleen in high dose TP treated CIA mice, while the structure of those organs in TP@NPs (containing high dose TP) group maintained normal. Furthermore, the score of CIA mice ($n=10$, $P< 0.05$), and the serum level of IL-1β, IL-6 and TNF-α($n=5$, $P< 0.05$) of TP@NPs (containing low dose TP) group were lower than low dose TP group. ABOG and TRAP staining and micro-CT showed that TP@NPs (containing low dose TP) effectively reduce the destruction of articular cartilage, synovial hyperplasia and osteoclast production ($n=10$, $P< 0.05$), and the loss of talus bone mass (0.95±0.1108 VS 1.133 ±0.09074 $n=9$, $P=0.007$). In vivo imaging showed that TP@NPs was able to target inflammatory joints of CIA mice, but not normal mice (the fluorescence intensity was 1247 ± 108.2, $n=3$, 12 limbs VS 3093 ± 496.4, $n=3$, 12 limbs) at 24 h.

Conclusion: The nano-drug can achieve the sustained release of TP, maintain a good blood concentration, improve water solubility, improve the efficacy, reduce toxic side effects, and can be candidate therapy for RA.

To observe drug targeting and release in vivo, we applied small animal in vivo imaging technology to detect the enrichment efficiency and retention time of TP@NPs in arthritis mice. After injection of TP@ NPs-ICG, the fluorescence intensity in the joint of CIA mice was higher, which was the most obvious at 24 hours. The fluorescence of normal mice was not enriched in the joints.

The results suggested that the Model+TP@NPs group, as well as the control group had no obvious swelling and deformity of the claws on the mices. In addition, compared with Model+Saline group, free TP group was improved, but its curative effect was far less than that of Model+TP@NPs group.

Disclosure: L. Yang, None; **J. JianQiu**, None; **X. Hao**, None; **H. HaiHui**, None; **H. Tong**, None; **Z. WeiAn**, None; **L. QianQian**, None.

Abstract Number: 0994

Increased Antibody and T-cell Responses Following Treatment of Collagen-Induced Arthritis in C57Bl/6 Mice with Organic Dust Inhalants

Michael Duryee,[1] Jill Poole,[1] Amy Nelson,[1] Katherine Janike,[1] Kathryn Rentfro,[1] Lynell Klassen,[1] James O'Dell,[2] Bryant England,[3] Geoffrey Thiele,[2] and Ted Mikuls[2], [1]University of Nebraska Medical Center, Omaha, NE, [2]VA Nebraska-Western IA Health Care System & University of Nebraska Medical Center, Omaha, NE, [3]VA Nebraska-Western IA Health Care System & University of Nebraska Medical Center, Omaha

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Animal Models Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Increasing evidence suggests that inhalant exposures, such as tobacco smoke or silica, are implicated in the initiation of autoimmunity leading to rheumatoid arthritis (RA). To further study the relationship between inhalant lung injury and RA-related autoimmunity, a mouse model of collagen induced arthritis was subjected to inhalation of organic dust extract (ODE) and disease-specific autoantibody and T cell responses were measured.

Methods: Male C57BL/6 mice were injected with chicken collagen type II plus Freund's complete adjuvant (CIA) or saline on day 1 and 21. ODE or saline was instilled by intranasal inhalation daily for 5 weeks. Groups are identified as: 1) Sham (saline injection + saline inhalation), 2) ODE, 3) CIA, and 4) ODE + CIA. At 5 weeks, IgG antibody to malondialdehyde-acetaldehyde (MAA) and anti-citrullinated protein antibody (ACPA) were measured in serum. T-cell proliferation assays were performed by IFN-γ ELISPOT using human serum albumin (HSA) that was either MAA modified or citrullinated (CIT) as the stimulating antigen.

Results: Serum IgG anti-MAA antibody concentrations were significantly increased ($p < 0.0001$) in ODE + CIA mice compared to all other groups Figure (A). In contrast, ACPA concentrations were significantly lower ($p < 0.0001$) in CIA + ODE mice compared to CIA alone with the former group demonstrating autoantibody concentrations similar to sham and ODE mice (B). T-cell proliferations against HSA-MAA were significantly increased in both CIA ($p < 0.0001$) and CIA + ODE ($p < 0.01$) mice compared to sham and ODE, yet neither of these differed significantly from each other (C). In contrast, T cell proliferations were significantly decreased ($p < 0.01$) in the CIA + ODE group compared to CIA alone when HSA-CIT was used as the stimulating antigen (D).

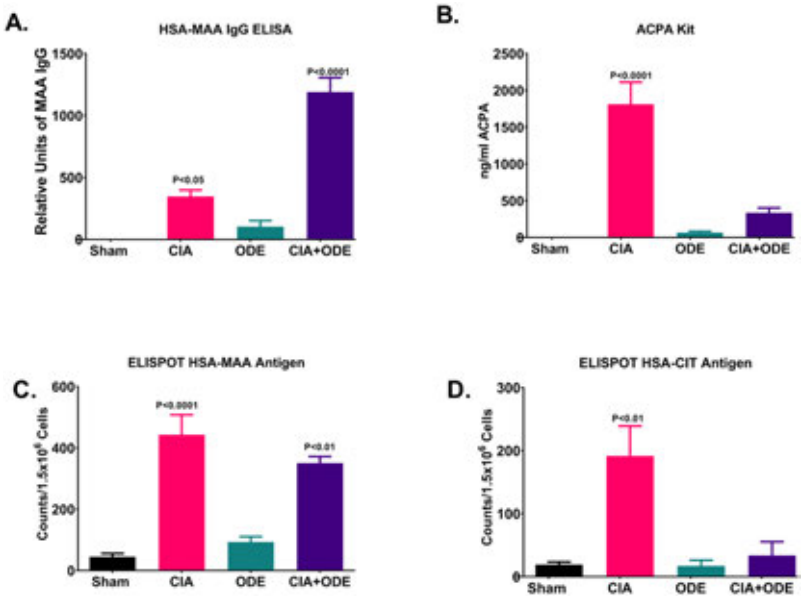


Figure 1. Increased Antibody and T-cells Response to MAA Modified Antigens in C57bl/6 Treated with Sham, CIA, ODE, or ODE+CIA. (A) Serum anti-MAA antibody (CIA p<0.05 vs. sham or ODE; CIA+ODE p<0.0001 vs. all other groups). (B) Serum ACPA (CIA p<0.0001 vs. all other groups; p=NS for all other comparisons). (C) T-cell proliferation to HSA-MAA (CIA p<0.0001 vs. sham or ODE; CIA+ODE p<0.01 vs. sham or ODE; p=NS for CIA vs. CIA+ODE). (D) T-cell proliferation to HSA-CIT (CIA p<0.01 vs. all other groups). N=10 mice per group.

Conclusion: Increased anti-MAA antibody and decreased ACPA concentrations in the ODE + CIA treated group compared to CIA alone suggests a shift in autoimmune response when arthritis prone mice are exposed to inhalant injury. Although mechanisms underpinning these "shifts" require further investigation, an increase in proliferating T-cells to MAA and a simultaneous decrease to citrullinated antigen suggests that inhalant injury may reduce immune responses to disease-specific antigen (citrullinated antigen) at the expense of enhanced responses to a more ubiquitous autoantigen (MAA-modified antigen). This novel animal model that incorporates CIA and inhalant injury, has the potential of providing much needed insight into the complex interplay between mucosal injury and autoimmunity that characterizes RA.

Disclosure: M. Duryee, None; **J. Poole**, None; **A. Nelson**, None; **K. Janike**, None; **K. Rentfro**, None; **L. Klassen**, None; **J. O'Dell**, None; **B. England**, None; **G. Thiele**, None; **T. Mikuls**, BMS, 2, Horizon, 2.

Abstract Number: 0995

Inhibition of Endoplasmic Reticulum Stress Using 4-phenylbutyric Acid Ameliorates the Severity of Collagen-induced Arthritis in Mice via Attenuation of Proliferation and Inflammatory Responses of Synovial Fibroblasts

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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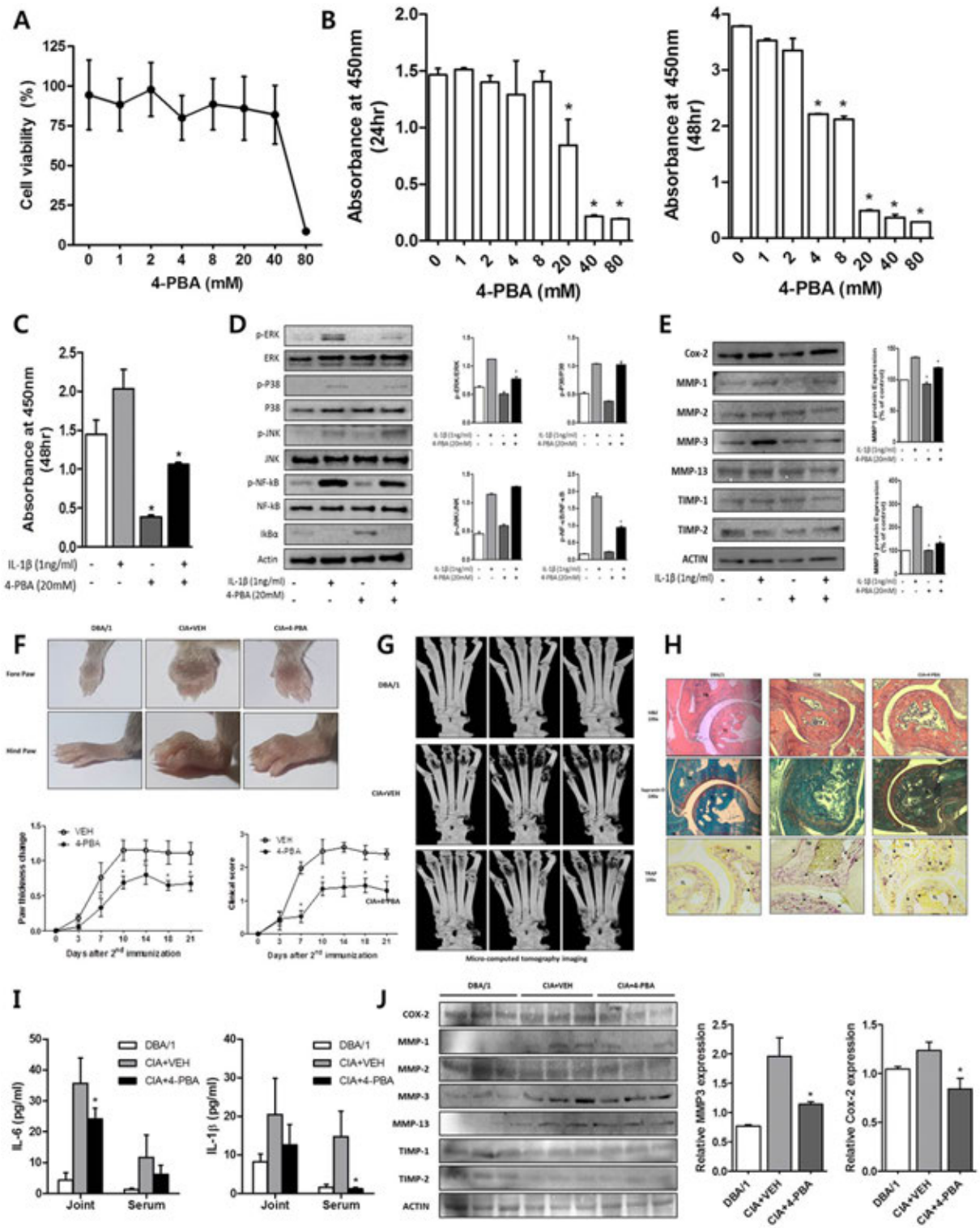

Background/Purpose: Several studies have recently revealed the pathological role of endoplasmic reticulum (ER) stress in the pathogenesis of inflammatory diseases. In addition, 4-phenylbutyric acid (4-PBA) was shown to exert potent pharmacological effects, including anti-inflammatory properties, via inhibition of ER stress. However, it is not known whether 4-PBA attenuates the severity of rheumatoid arthritis, which is most the common inflammatory arthritis.

The purpose of the present study was to investigate the effect of ER stress inhibition by 4-PBA on interleukin-1β-induced proliferation and the inflammatory response of rheumatoid synovial fibroblasts (RASFs) and determine whether the inhibition of ER stress by 4-PBA ameliorated experimentally induced arthritis. The potential underlying mechanisms of the therapeutic efficacy of 4-PBA were also investigated.

Methods: The proliferation of RASFs and expression of matrix metalloproteinases were evaluated in the presence of IL-1β with or without 4-PBA. The effect of 4-PBA on the phosphorylation of MAPK and the activation of NF-kB in IL-1β-stimulated RASFs was assessed. In an in vivo study, the effects of 4-PBA were investigated using DBA/1 mice with collagen-induced arthritis (CIA). Assessments of paw thickness, clinical score, micro-computed tomography imaging, histology of tibiotalar joints, and the inflammatory cytokine levels of joints extracts and serum were used to determine the therapeutic effect of 4-PBA.

Results: In vitro, 4-PBA inhibited the proliferation and expression of IL-1β-stimulated RASFs and matrix metalloproteinases (MMP-1 and MMP-3) through the suppression of both the phosphorylation of MAPKs and NF-kB in IL-1β-stimulated RASFs. The intraperitoneal administration of 4-PBA markedly attenuated the severity of arthritis in CIA mice. 4-PBA treatment ameliorated joint swelling, the degree of bone erosion and destruction, and decreased the level of inflammatory cytokines (IL-6 and IL-1β) and matrix metalloproteinases (MMP-3 and Cox-2). Furthermore, remarkable improvements in histopathological findings occurred in 4-PBA-treated mice.

Conclusion: These findings suggested that 4-PBA could attenuate the severity of arthritis in CIA mice through partially blocking the phosphorylation of MAPKs and the activation of NF-κB in RASFs. Thus, through the inhibition of ER stress, 4-PBA may be a potent agent for the treatment of RA.

Disclosure: W. Yoo, None; **Y. Choi**, None; **E. Lee**, None; **C. Lee**, None; **M. Lee**, None.

Abstract Number: 0996

The Role of Flip in Differentiation and Survival of Synovial Tissue Resident Macrophages

Qi Huang,[1] Renee Doyle,[1] Shang-Yang Chen,[2] Alexander Misharin,[3] Deborah Winter,[4] and Richard Pope[5],
[1]Northwestern University Feinberg School of Medicine, Chicago, IL, [2]Northwestern University, Chicago, [3]Northwestern University Feinberg School of Medicine, chicago, [4]Northwestern University Feinberg School of Medicine, Division of Rheumatology, Chicago, [5]Northwestern University Feinberg School of Medicine, Division of Rheumatology, chicago, IL

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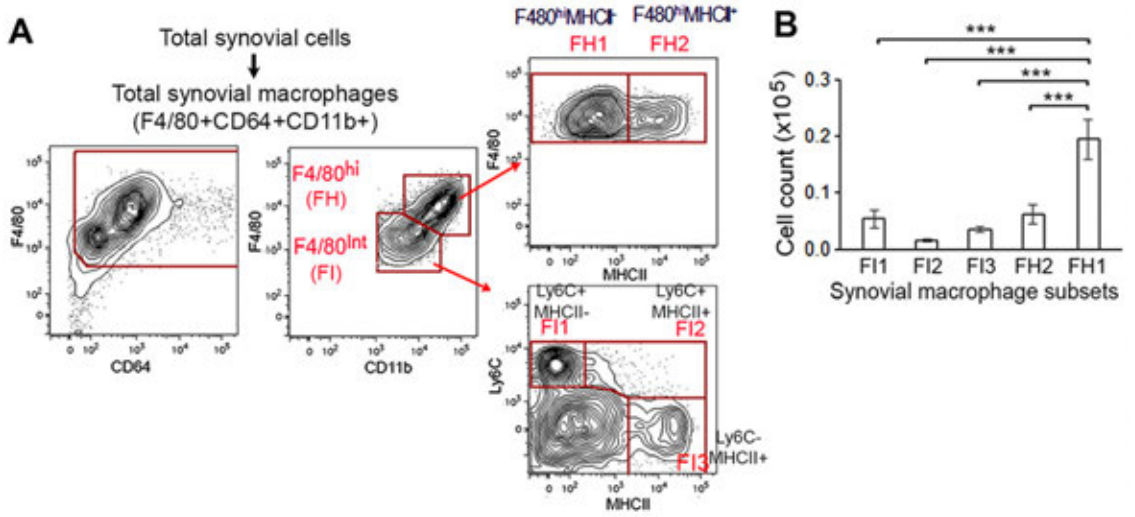
Session Time: 9:00AM–11:00AM

Background/Purpose: We previously identified that under homeostatic conditions Flip was necessary for macrophage (MΦ) survival. The mechanisms responsible for the differentiation of monocyte-derived MΦs into anti-

Figure 1.



Synovial tissue macrophage subsets during homeostasis

inflammatory tissue-resident MΦs (TRMs), under chronic inflammatory conditions, is not known. Earlier studies demonstrated that under homeostatic conditions, efferocytosis is important in maintaining MΦ tissue residency. The purpose of this study was to define synovial TRMs and the role of Flip in MΦ differentiation during chronic inflammation.

Methods: The HUPO arthritis model was established employing mice with *Flip* depleted in CD11c^{+} cells. HUPO arthritis, which begins spontaneously after 4 weeks of age, was evaluated by clinical scoring and histology. Synovial tissue MΦ subsets were defined by flow cytometry and proliferation by BrdU incorporation. Transcriptional profiles for each subset was documented by RNAseq. Monocyte-derived MΦs in joint tissue were identified following bone marrow reconstitution and parabiosis.

Results: We identified the F4/80^{hi}MHCII^{-}Ly6C^{-} subset (FH1) as the population of TRMs, dominant among the 5 subsets of synovial MΦs during homeostasis (Fig 1). Genes that are upregulated in the TRMs have tissue-specific functions such as for MΦ maturation and maintenance of homeostasis. The wild type FH1 and FH2 (F4/80^{hi} MHCII^{+}Ly6C^{-}) subsets are maintained at a slow self-renewing rate and not replenished by circulating monocytes. The *cflar* (Flip) expression is high in F4/80^{hi} MΦs, and targeted deletion of *Flip* in the *Flip$^{f/f}$ CD11c^{cre}* HUPO mice results in a marked reduction of the FH1 population, while the FH2 subset is greatly increased. The percent of the FH1 subset inversely correlated with arthritis severity and granulocyte infiltration. Parabiosis experiments demonstrated both HUPO and control monocytes differentiated into FH2 MΦs in HUPO recipients, while only the control MΦs were able to differentiate into FH1 cells. This inability of HUPO monocytes to differentiate from FH2 to FH1 MΦs was not due to increased MΦ apoptosis. The reduced Flip did not result in increased apoptosis was associated with a reduction of pro-apoptotic, and an increase of anti-apoptotic signaling molecules. Further, the HUPO FH2 MΦs demonstrated a reduction of genes and their coding proteins such as Cfs1r (CD115), Tgfbr2, and Mrc1 (CD206), which are associated with tissue residency and efferocytosis. In addition, genes important for MΦ functions and phagocytic clearance of apoptotic cells, such as *Timd4* and *CD163* were reduced in the HUPO FH1 and FH2 subsets.

Conclusion: These observations suggest that under homeostatic conditions, efferocytosis maintains the dominance of the FH1 population as TRMs. In contrast, apoptosis is reduced, and all populations of MΦs, except FH1, are increased under HUPO chronic inflammatory conditions. FH2 MΦs deficient in Flip survive, but are not capable of

differentiation into anti-inflammatory TRMs. These observations provide novel insights into the role of MΦs in the initiation and progression rheumatoid arthritis.

Disclosure: Q. Huang, None; **R. Doyle**, None; **S. Chen**, None; **A. Misharin**, None; **D. Winter**, None; **R. Pope**, None.

Abstract Number: 0997

Stromal Cell-derived DCSTAMP Coordinates Cell Migration and Osteoclast Activation in TNF-driven Murine Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Animal Models Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: DC-STAMP is a transmembrane protein involved in the fusion of mononuclear osteoclasts and essential for the formation of fully functional multinucleated osteoclasts (OCs). Recently we found impaired accumulation of macrophages in the inflamed synovium, and a correlation between reduced bone resorption and the area occupied by $TRAP^+$OCs in bones of $DCSTAMP^{+/+}$TNF Tg mice. Interestingly, serum concentration of murine TNF and MCP-1, a macrophage attracting chemokine, was lower in DCS-$STAMP^{-/-}$TNF Tg mice than TNF Tg mice. These results suggested that impaired bone erosion in DC-$STAMP^{-/-}$TNF Tg mice may result from defective attraction of immune cells to the joints. Thus, we examined both the mechanism and type of cells involved in the progression of TNF-driven inflammatory arthritis in the presence or absence of DCSTAMP.

Methods: C57BL/6 mice were irradiated and reconstituted with $1X10^7CD45.2^+$TNF Tg and $1X10^7CD45.1^+DCSTAMP^{-/-}$ bone marrow cells. Six weeks after bone marrow transfer, mice were i.p injected, at days 0 and 3, with 150 ml of serum from NOD.KRN mice. $CD45.2^+$and $CD45.1^+$cells were enumerated by flow cytometry or immunofluorescence. To elucidate whether DCSTAMP on stromal cells participates in bone resorption, we generated reciprocal chimeric mice, using WT, $DCSTAMP^{-/-}$, TNF Tg, $DCSTAMP^{-/-}$TNF Tg mice as recipients or donors of BM cells, and measured bone density by mCT scan. Migration of bone marrow cells isolated from WT, $DCSTAMP^{-/-}$, TNF Tg and $DCSTAMP^{-/-}$ TNF Tg mice was tested by chemotaxis assays using conditioned media from stromal cells activated with TNF. mRNA expression of inflammatory cytokines by macrophages activated with IL-4 or LPS/IFNgwas quantitated with qPCR.

Results: Enumeration of congenic cells by flow cytometry in 50:50 bone marrow chimeras showedthat 77% ±1.5 and 70% ±1 of $CD45.1^+$DC-$STAMP^{-/-}$cells accumulated in popliteallymph nodes and spleen, respectively; but they were absent in the inflamed synovium. In contrast, $CD45.2^+$ TNF-producing cells were significantly increased in the synovium of mice with acute arthritis. Moreover, polarized macrophages of DC-$STAMP^{-/-}$and DC-$STAMP^{-/-}$ TNF Tg mice had a significantly lower expression of TNF ($p = 0.004$), IL1b ($p = 0.02$) and iNOS ($p = 0.001$) and higher IL10 expression ($p = 0.04$). We also found that bone volume in mice expressing DC-STAMP on the stromal or hematopoietic cells increased 2-fold in femur ($p = 0.05$) and 2.5-fold in tibia ($p=0.04$), compared with mice expressing TNF in both stromal and hematopoietic cells. Interestingly, $DCSTAMP^{-/-}$stromal cells activated with mouse or human TNF had lower expression of MCP1 ($p = 0.002$), CX3CL1 ($p = 0.001$), IL-1b ($p = 0.03$) and MMP9 than WT stromal cells. *In vitro* chemotaxis assay using supernatant collected from WT stromal cells showed a 28-fold decrease in migration

of monocytes from DCSTAMP$^{-/-}$(p = 0.02) and DCSTAMP$^{-/-}$ TNF mice (p = 0.01). These monocytes also had 4-fold decrease (p = 0.01) in the migration towards supernatant from DC-STAMP$^{-/-}$stromal cells.

Conclusion: Our data reveal an unexpected role for stromal cell-derived DC-STAMP in the modulation of migration and pathogenic polarization of monocytes into inflamed arthritic joints.

Disclosure: M. Garcia-Hernandez, None; **J. Rangel-Moreno**, None; **B. Korman**, None; **A. Paine**, None; **N. Huertas**, None; **C. Ritchlin**, None.

Abstract Number: 0998

Stimulation of Splenic Neurovascular Bundle Protect Mice from Developing Collagen-induced Arthritis

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SESSION INFORMATION
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Background/Purpose: Vagus nerve (VN) stimulation has shown the potential to improve the disease development in animal models of arthritis and in patients with RA. However, the VN can affect respiratory, cardiovascular, and gastro-intestinal physiology. The splenic nerve (SpN) has been confirmed to be the principal effector nerve for the VN-mediated immune control. Here we tested efficiency of stimulating the nerve plexus around the splenic artery on acute LPS-induced inflammation and collagen-induced arthritis (CIA) in mice and compared it to VN stimulation (VNS) and anti-TNF treatment.

Methods: In an acute LPS mouse model, mice were implanted on the SpN or VN. After recovery from surgery, LPS was injected and splenic nerve stimulation (SNS) or VNS was applied in conscious mice. TNF and norepinephrine (NE) were measured after 90 min. Next, SNS was evaluated in CIA. CIA was induced in DBA1/J mice by immunization with bovine type II collagen at days 0 and 21. At day 11, mice were implanted with micro-cuff electrode (CorTec) onto the SpN or VN. From day 16 to day 45, VNS and SNS were applied as rectangular charged-balanced biphasic pulses with 650 μA pulse amplitude, 200 μs pulse width at 10 Hz frequency for 2 min 1 or 6 times a day using a Plexon stimulator. Alternatively, mice were treated 3 times/week from day 16 to 45 with 10mg/kg anti-TNF (etanercept) i.p. In curative settings, SNS was applied 6 times a day when mice scored positive for 3 consecutive days. Clinical arthritis was determined by visual examination of swelling and redness of the paws and measurement of paw thickness. Sham mice were undergoing the same procedure but did not receive stimulation.

Results: Stimulating the splenic nerve resulted in an increase of NE (by >100%) in the spleen, as well as a significant reduction in LPS-induced TNF (~50%). This effect was comparable to VNS. In CIA in mice all sham animals developed arthritis, compared to 14% following 6 times per day SNS ($p < 0.001$). In contrast, 85% of the animals developed arthritis ($p = 0.35$) when SNS was applied only once a day. However, in both stimulated groups a significant decrease in clinical scores and paw thickness was observed compared to unstimulated group ($p < 0.01$ and $p < 0.05$, respectively). Interestingly, SNS treatment inhibited CIA to the same extend as VNS. Moreover, the same electrical parameters dramatically decreased arterial blood pressure during VNS stimulation, which was not the case for

SNS. While etanercept treatment reduced clinical scores ($p < 0.001$) an immediate rebound in clinical score was seen following cessation of treatment, while mice with SNS were still partially protected 35 days after treatment discontinuation ($p = 0.013$, compared to sham). Finally, when SNS was applied as a therapeutic treatment, clinical scores were significantly reduced ($p < 0.001$). Analysis of the cells within the spleen after SNS demonstrated a reduction of inflammatory monocytes that correlated with an improvement in clinical scores.

Conclusion: These studies demonstrate that SNS affect the immune cells in the spleen, suppresses pro-inflammatory cytokine production, and reduces clinical symptoms in CIA providing compelling scientific rationale and pre-clinical evidence for the use of splenic neuromodulation in treating RA.

Disclosure: T. Simon, None; **C. Panzolini**, None; **J. Lavergne**, None; **A. Srihar**, Galvani, 3; **M. Vervoordeldonk**, Galvani, 3; **n. Glaichenhaus**, None; **P. Blancou**, None.

Abstract Number: 0999

Targeted Drug Delivery Using a Novel Joint-homing Peptide for Arthritis Therapy

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Animal Models Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic debilitating autoimmune disease characterized by inflammation of the synovial tissue of the joints, which if not controlled early and adequately, may cause severe joint damage and deformity. There are many potent anti-arthritic drugs, which are given orally or by injection, and their prolonged use is associated with many adverse reactions. This is attributable in part to the widespread distribution of the drugs, exposing healthy organs to those drugs. Thus, there is a need for targeted drug delivery methods to direct the drugs primarily to the inflamed joints.

Methods: We developed a peptide-directed liposomal drug delivery system to deliver dexamethasone (DEX) to arthritic joints of rats with adjuvant-induced (AA) arthritis. The peptide ART-2 shows preferential homing to inflamed joints when injected intravenously. Therefore, we exploited this attribute of peptide ART-2 to guide the DEX-entrapping liposomes to arthritic joints. Arthritic rats were treated with test or control liposomes, or free drug after the onset of disease and the severity of arthritis was monitored regularly thereafter. Sera of these rats were tested for assessment of toxicity to liver, kidney, and pancreas.

Results: ART-2-DEX liposomes, when injected intravenously into arthritic rats after the onset of arthritis, were more effective in suppressing disease progression than control-DEX liposomes lacking ART-2 or free DEX at an equivalent dose of this drug. Furthermore, despite increased efficacy, the toxicity profile of ART-2-DEX liposomes was comparable to that of control liposomes or free DEX, thereby resulting in enhanced therapeutic index of DEX therapy.

Conclusion: Our results furnish a proof-of concept for the use of a novel joint-homing peptide for targeted delivery of drugs including biologics or small molecule compounds to arthritic joints with enhanced efficacy and reduced

systemic exposure. This targeted therapy platform may be suitable for use in RA patients. (Supported by VA Merit Review I01 BX002424, NIH R01AT004321, and RRF.)

Disclosure: R. Meka, None; **S. Venkatesha**, None; **B. Acharya**, None; **K. Moudgil**, None.

Abstract Number: 1000

RKIP, as an Upstream Regulator of Intracellular Signaling, Exerts Anti-arthritic Effect in Fibroblast-like Synoviocyte and Collagen-induced Arthritis

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

Background/Purpose: Nuclear factor-kappaB (NF-kappaB) and extracellular-signal-regulated kinase (ERK) have been implicated as a therapeutic target for the treatment of rheumatoid arthritis (RA). Raf kinase inhibitory protein (RKIP), as an upstream regulator for NF-kB and ERK pathways, has been widely explored in the field of cancer. However, the effect of RKIP in RA have not yet been elucidated. Thus, the purpose of this study was to investigate whether RKIP might have anti-arthritic effects.

Methods: The adenovirus containing RKIP complementary DNA (Ad-RKIP) or RKIP shRNA (Ad-shRKIP) were used in fibroblast-like synoviocytes (FLS) of RA patients and mouse models of collagen-induced arthritis (CIA) and K/BxN serum transfer arthritis. Quantitative real-time PCR, phospho-protein array analysis, immunohistochemistry, ELISA, western blotting, TRAP and safranin-O staining, migration and invasion assay were used.

Results: The expression of RKIP were significantly decreased in synovial tissue and FLS of RA compared to osteoarthritis (OA). Ad-RKIP suppressed invasion and migration, chemokine production, and matrix metalloproteinase secretion induced by cytokines (IL 1ß, LPS, TNF α, and TGF ß) in RA FLS. Additionally, RKIP negatively regulated the Raf/MEK/ERK and NF-κB pathway in RA FLS. CIA and K/BxN serum transfer arthritic mice, which were injected with Ad-shRKIP, showed earlier development and exacerbation of arthritis. However, Ad-RKIP treated CIA mice had a lower cumulative incidence and less severe arthritis, based on radiologic and histopathologic findings, and inflammatory cytokine levels, than control virus-injected mice.

Conclusion: These results suggest that using RKIP to block the NF-kappaB and the Raf/MEK/ERK pathway in RA reduce both the inflammatory response and the joint destruction. Thus, RKIP may have therapeutic potential in the prevention and treatment of RA.

Disclosure: S. Lee, None; **H. Noh**, None; **Y. Cheon**, None.

Abstract Number: 1001

Oral Collagen Type V Supplementation Inhibits Cartilage Degeneration in Experimental Arthritis

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SESSION INFORMATION
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Background/Purpose: It is known that collagen V (col V) can generate autoimmunity when exposed. In contrast, induction of tolerance with col V supplementation is able to protect affected tissues in autoimmune diseases. In an earlier study, we found that Col V oral supplementation reduced synovial inflammation in experimental arthritis but its action in cartilage is not known. To verify the action of oral Col V supplementation on cartilage in an experimental model of induced arthritis (IA).

Methods: Thirty 3 months-old male *Lewis* rats with weight of 220–240g were used. Arthritis was induced by intra-articular infiltration of 500μg of mBSA emulsified in complete Freund's adjuvant (10μl) at days zero, 7 and 14. Oral Col V (isolated from bovine placenta) supplementation (500μg/300μl / day / 30 days) was daily performed until 30 days' euthanasia in 10 animals (IA-Col V group). The other 10 did not receive oral Col V (IA group). Five rats received intra-articular saline (Sal group) and 5 received only oral Col V (Col V). Morphological and histomorphometric analyses were performed after Safranin-O/Fast Green, immunofluorescence and immunohistochemistry staining with *Image-Pro Plus6.0 software*. Serum IL-1β, TNFα, IL-17, IL-10 and anti-Col V were measured. All the animals received human care in compliance with the *Guide for the Care and Use of Laboratory Animals*, published by the US National Institutes of Health. Ethics in Committee Research for Animal Studies approval number 295/12.

Results: In the IA-Col V group, cartilage showed neither cracks, nor chondrocyte organization, and the growth line was preserved compared to the IA group. There was no reduction in chondrocytes number in the IA-col V group (39.86±1.79 vs 25.35±4.62, p< 0.009), cartilage thickness (78.73±7.27 vs 52.52±5.74, p< 0.03), proteoglycans content (76.82±9.31 vs 25.45±1.23%, p< 0.0036), type II collagen content (76.99±1,339 vs 39.13±5,618 p< 0.0001) and apoptosis (21.85±6.92 vs 71.69±10.46) compared to the IA group. In addition, there was lower serum expression in the IA-col V group of IL-1β (4.28±4.75 vs 21.96±2.29, p< 0.0001), TNFα (1.70 ± 0.51 vs 1.76 ± 0.39, p< 0.0001), IL-17 (2.19±0.50 vs 27.24±10.65, p< 0.0001) and IL-10 (0.13±0.03 vs 27.95±17.11, p< 0.0001) compared to the IA group. Furthermore, the IA group presented serum anti-collagen V. The results of the Sal and Col V groups were similar to those of the IA-Col V group for every parameter.

Conclusion: The oral collagen V supplementation avoided the degradation of cartilage in an experimental arthritis model and may represent a new therapeutic option for this condition.

Disclosure: L. Silveira, None; **J. Rodrigues**, None; **S. Atayde**, None; **S. Catanozi**, None; **A. dos Santos Filho**, None; **V. Capelozzi**, None; **R. Fuller**, None; **A. Velosa**, None; **W. Teodoro**, None.

Abstract Number: 1002

Beneficial Effect of Angiotensin Receptor Blocker in a Spondyloarthritis Animal Model

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
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Background/Purpose: Non-steroidal anti-inflammatory drugs (NSAIDs) have been shown to be efficacious in the treatment of the signs and symptoms of spondyloarthritis (SpA). However, NSAIDs have a variety of side effects on gastrointestinal tract, kidney, and cardiovascular system. Angiotensin II (AT II) mediates several pro-inflammatory responses by signaling through AT type I receptor (AT1R). The recruitment of circulating inflammatory cells to the endothelium and subendothelial space is an early step in the inflammatory response. Ang II can also trigger Toll-like receptor 4 activation in various cell types, which stimulates the innate immunity. In addition, it has been reported that Ang II drives colonic mucosal inflammation by promoting intestinal epithelial cell apoptosis and mucosal TH17 responses in colitis development.

The purpose of this study is to investigate the benefits of angiotensin receptor blocker (ARB) on the bony overgrowth and the bowel inflammation in a SpA animal model.

Methods: ZAP-70W163C–mutant (SKG) mice were housed under specific pathogen free conditions. All of the mice were injected intraperitoneally with 1,3-glucan (curdlan). Mice were treated with ARB and/or naproxen (NXN). Clini-

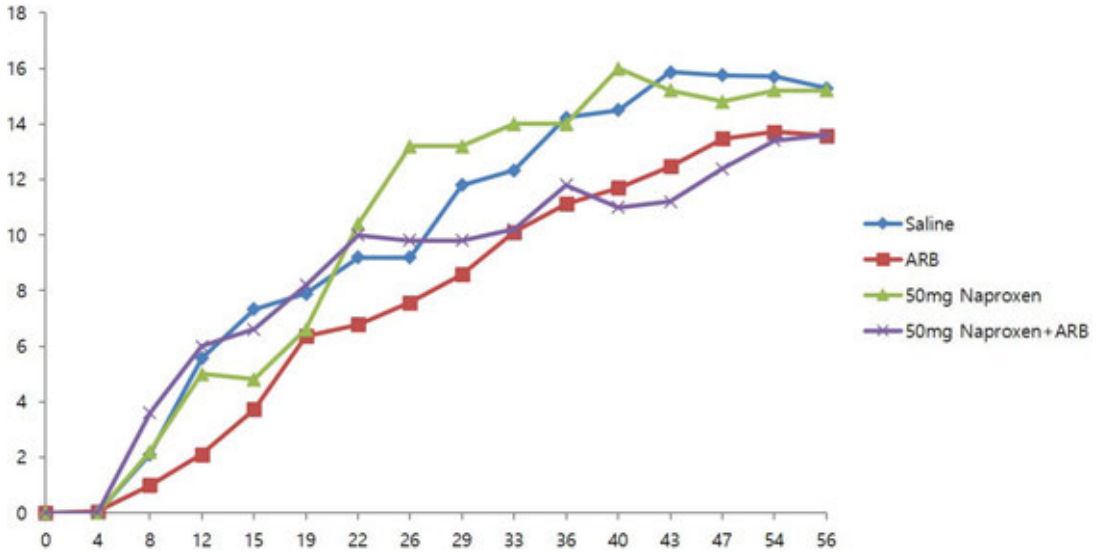

Figure 1. Peripheral Arthritis in SKG.

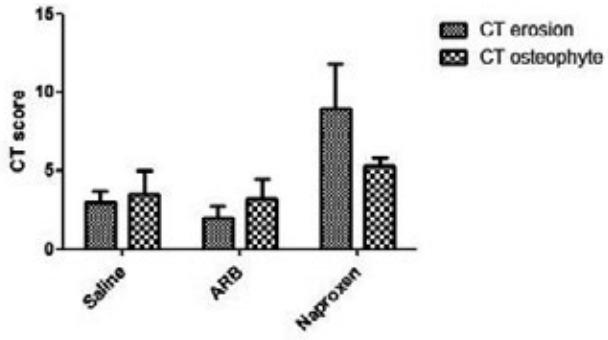

Figure 2. Bone morphology in SKG.

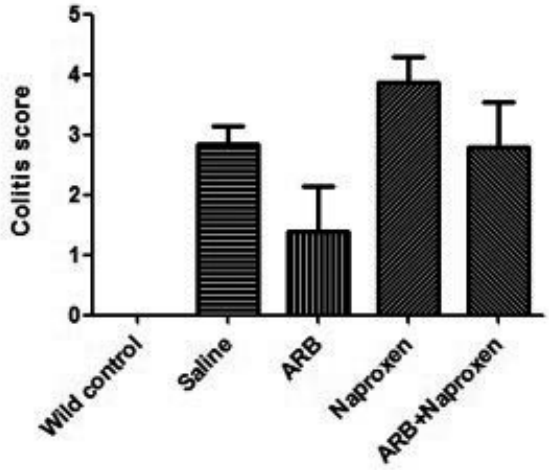

Figure 3. Intestinal inflammation in SKG.

cal manifestations were scored and the expression of inflammatory molecules were examined. Arthritis, spondylitis, and ileitis were assessed histologically at 8-week experimental end points. A bone mineral density tests (BMD) were conducted as well.

Results: ARB treatments lowered the morphology scores (MS), but NXN did not (Fig 1). The expression of myeloperoxidase was decreased in peripheral and axial joints by ARB but not by NXN, which might be caused by decreased expression of TNF-α, IL-17, IL-22, and IL-23.

The development of erosion and osteophyte was inhibited by ARB, while increased by NXN in bone CTs (Fig 2). ARB decreased the expression of BMP2, RUNX2, and osterix.

Next, we investigated the effect of ARB and NXN on ileitis of the SKG mice. ARB improved ileitis, but NXN significantly aggravated the ileitis which was partially restored on the combination therapy with ARB (Fig 3). In addition, we analyzed the results on BMDs in SKG mice depending on the treatment groups. Both ARB and NXN improved BMDs.

Conclusion: These results indicate that ARB has beneficial effects on the arthritis, ileitis, and osteoporosis in a SpA mice model. Further clinical studies are warranted.

Disclosure: S. Shim, None; **J. Choi**, None; **J. Kim**, None; **C. Park**, None.

Abstract Number: 1003

TNF Inhibitors Improves Arterial Stiffness with Cs DMARDs-resistant Active Psoriatic Arthritis: A Cohort Extended Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
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Background/Purpose: Background/ Patients with psoriatic arthritis (PsA) have an increased cardiovascular (CV) risk. We should have strategies for primary cardiovascular prevention in PsA[1)]. But there is no evidence of CV risk management and arterial stiffness about Tumor necrotic factor (TNF) inhibitors in patients with PsA.

Objective/ To examine the effect of TNF inhibitors on arterial stiffness in conventional synthetic (cs) DMARDs resistant PsA patients in a cohort study design.

Methods: Sixty eight PSA and patients with moderate to severe active disease despite cs DMARDs treatment (disease activity score: DAPSA2) score >14) were received TNF inhibitors plus cs DMARDs. All patients have no previous history of CV. Arterial stiffness was assessed with cardio-ankle vascular index (CAVI, modified pulse wave velocity(PWV)) and augmentation index corrected for a heart rate of 75 beats per minute (AIx@75) at baseline and 24 weeks follow-up. Clinical data were collected at regular visits. CAVI is very similar to pulse wave velocity (PWV), and CAVI measures arterial wall stiffness independent of blood pressure and it is superior to brachial ankle PWV as an index of arterial stiffness.

Results: 58 PsA patients(28 patients adalimumab, and 30 patients infliximabrespectively) were completed this study, Treatment with TNF inhibitors(10.88 ± 1.86 and 9.46 ± 1.14 %; p = 0.006), attenuated the CAVI significantly from baseline to 24 weeks follow up. Treatment with TNF inhibitors (36.4 ± 8.6, 32.1 ± 3.8 %; p = 0.008) attenuated the Aix@75 significantly from baseline to 24 weeks follow up. DAPSA score improved significantly from baseline to 24 weeks(17.45 ± 6.33, 5.44 ± 3.43: p=0.01). There are no significant differences among biologics about CAVI and Aix@75. Surprisingly, improvement of CAVI and AIx@75 were not correlated disease activity at 24 weeks of biologics treatment (CAVI: p=0.91, AIx@75: p=0.88). TNF inhibitors improves arterial stiffness independently of its effects on disease activity, since even in high disease activity (8 cases; DAPSA score >28) is halted.

Conclusion: These findings suggest that combination therapy, TNF inhibitors with cs DMARDs not only reduced PsA disease activity but also limited vascular damage in patients with cs DMARDS resistant active PsA.

Disclosure: K. Kume, None; **k. amano**, None; **t. kanazawa**, None; **s. yamada**, None; **k. hatta**, None.

Abstract Number: 1004

Genetic Ablation of γδTCR Inhibits IL-23-induced Neutrophilia and Attenuates Epidermal Hyperplasia, Synovitis, Onycholysis and Enthesitis Associated with Psoriatic Arthritis

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SESSION INFORMATION
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Background/Purpose: γδ T cells are non-conventional lymphocytes that straddle between innate and adaptive immunity. Although γδ T cells have been implicated in psoriatic arthritis, the exact mechanisms that govern pathogenicity remain elusive.

Methods: To investigate the roles of γδ T cells in eliciting psoriatic arthritis-like pathology, we performed *in vivo* gene transfer of IL-23 (minicircle DNA) in B10.RIII (WT) and/or $TCR^{\delta-/-}$ mice. qRT-PCR, RNAseq, Western blot, flow cytometry, ELISA, H&E and immunofluorescence staining were used to analyze the phenotype of WT and transgenic mice in this study.

Results: Herein, we show that IL-23 MC gene transfer induces SCART scavenger receptors 1/2 surface marker of adult γδ T cells and a population of $CD11b^{+}LY6G^{+}$ associated with synovitis and epidermal hyperplasia in joint and skin tissues respectively which is accompanied with onycholysis and enthesitis hallmark pathologic features of human PsA. We observed a profound neutrophil inflammatory infiltrate in the synovium, epidermis, nail bed, and enthesis in IL-23 gene transfer WT mice, which were absent in $TCR^{\delta-/-}$ mice. Furthermore, our data demonstrate that absence of γδ T cells was associated with an attenuation of inflammatory gene expression as well as expression of neutrophil markers which mechanistically correlated with a reduction of IL-17A and a marked increase of the anti-inflammatory cytokine IL-27.

Conclusion: Collectively, our data demonstrate that γδ T cells are critical components in pathogenesis of IL-23-induced psoriatic arthritis like disease, suggesting that γδ T cells could be potentially targeted for treatment of the rheumatic diseases.

Disclosure: C. Nguyen, None; **T. Chan**, None; **I. Tagkopoulos**, None; **M. Eberl**, None; **I. Adamopoulos**, None.

Abstract Number: 1005

Tendon T-cell Interactions as Drivers of Chronicity in Spondyloarthritis

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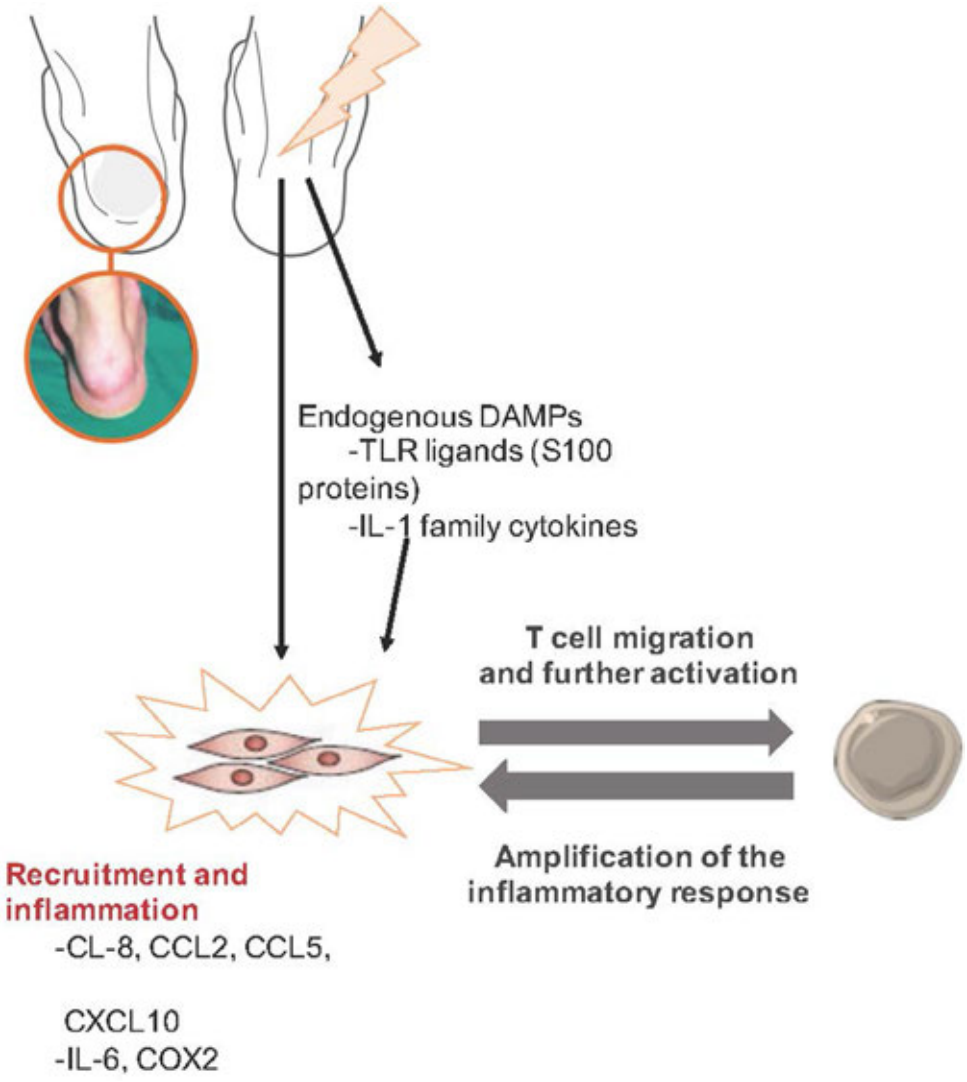
Background/Purpose: Emerging evidence supports the concept that stromal cell functions extend beyond maintenance of tissue architecture, exerting a key role in choreographing immune responses and thereby defining disease persistence. Accordingly, as enthesitis is a hallmark of spondyloarthropaties (SpA), we propose an interplay between tendon stromal cells (tenocytes) and the adaptive immune system (T cells) in the development of a chronic inflammatory response in SpA.

We aimed to assess the effect of tendon stromal cells (tenocytes) on T cell migration and activation and the impact of these activated T cells on the stroma.

Methods: Tenocytes were explanted from tissue obtained from anterior cruciate ligament (ACL) reconstructions. The effect of damage on tenocytes after stimulation with conditioned media from tendon explants or IL-1ß was evaluated



Proposed mechanisms driving T cell/stromal tendon activation in SpA.

by qPCR. A transwell membrane system was used to test the impact of conditioned media from tenocytes on T cell migration. T cells and tenocytes were co-cultured with or without the presence of a transwell membrane to quantify T cell activation (CD69 by FACS and IFN-γ by ELISA). Changes in gene expression on tenocytes after co-culture with activated T cells were analysed by qPCR.

Results: In the presence of damage, tenocytes upregulated inflammatory mediators (IL-6, COX2), chemokines (CCL2, CCL5, CXCL10, CXCL12) and adhesion molecules (ICAM-1). Conditioned media, particularly after stimulation with IL-1ß, from tenocytes induced T cell migration. Co-cultures of tenocytes and T cells resulted in activation of T cells that was contact dependant. In turn, these activated T cells upregulated the production of inflammatory mediators in tenocytes and increased the COL3/COL1 ratio.

Conclusion: Our results support a role of the tendon stromal compartment in the development and maintenance of an inflammatory response in SpA. Following damage, tendon stromal cells are able to induce the recruitment of T cells, that once enter the tissue interact with the stroma and get further activated. These activated T cells promote an upregulation of inflammatory cytokines and chemokines from the stromal compartment, creating a positive feedback loop that amplifies and maintains this inflammatory response.

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Abstract Number: 1006

Vaspin rs35262691 Is Associated with Atherosclerotic Disease in Axial Spondyloarthritis Patients

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Table 1. Association between vaspin rs35262691 polymorphism and presence/absence of carotid plaques in patients with axSpA.

Genotype/Allele	Presence of carotid plaques (%)	Absence of carotid plaques (%)	OR [95% CI]	p
TT	23.1	35.8	1 (Reference)	-
TC	51.9	47.1	**1.92 [0.99-3.71]**	**0.052**
CC	25.0	17.1	**4.90 [2.12-11.37]**	**<0.001**
T	49.1	59.3	1 (Reference)	-
C	50.9	40.7	**2.08 [1.40-3.09]**	**<0.001**

p values adjusted by sex, age at the time of the study and traditional cardiovascular risk factors (hypertension, dyslipidemia, obesity, smoking habit).
CI: Confidence interval; OR: odds ratio.

Background/Purpose: Vaspin is a novel adipokine with insulin-sensitizing functions that exerts anti-inflammatory actions[1,2]. It has been associated with cardiovascular (CV) disease, CV risk factors and inflammation in the general population and in chronic inflammatory conditions different from axial SpA (axSpA)[2-4]. In particular, it has been suggested that vaspin may act as a compensatory mechanism for inflammation and CV disease[1,3]. This could be relevant for axSpA, given the high incidence of CV disease (mainly due to accelerated atherosclerosis) exhibited by these patients[5,6], which turns this comorbidity into a matter of major concern among rheumatologists. However, data on the role of vaspin regarding surrogate markers of atherosclerosis in the context of axSpA is scarce. For this reason, we aimed to evaluate the implication of vaspin in subclinical atherosclerosis in axSpA at the genetic and protein level.

Methods: This study included 385 patients that fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA[7]. Clinical data was retrieved from medical records. Carotid US was performed to evaluate the presence of subclinical atherosclerosis (carotid plaques and abnormal carotid intima-media thickness [cIMT] values). 3 polymorphisms of *vaspin* (rs2236242, rs35262691 and rs7159023), previously associated with CV risk factors and/or reported as functional gene variants, were genotyped by TaqMan probes. Serum vaspin levels were assessed by ELISA. Statistical analysis was performed using STATA® v. 11.1, adjusting the results by potential confounding factors.

Results: We disclosed that the C allele of rs35262691 conferred a higher risk of developing carotid plaques in axSpA ($p< 0.05$)(Table 1). Regarding serum vaspin levels, even if they showed no statistically significant association with carotid plaques or cIMT values, these values positively correlated with factors associated with high CV risk such as systolic blood pressure ($p=0.02$) and waist circumference ($p=0.03$). Furthermore, serum vaspin levels were significantly higher in female patients than in males ($p< 0.001$).

Conclusion: Our results show for the first time that *vaspin* rs35262691 polymorphism is associated with carotid plaques in axSpA. The relevance of this molecule in the atherosclerotic process is further demonstrated by the relationship between serum levels and CV risk factors. All these data support a key role of vaspin in atherosclerosis in axSpA.

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Abstract Number: 1007

Memory ex-Th17 Cells Contribute to Synovial Inflammation in Spondyloarthritis

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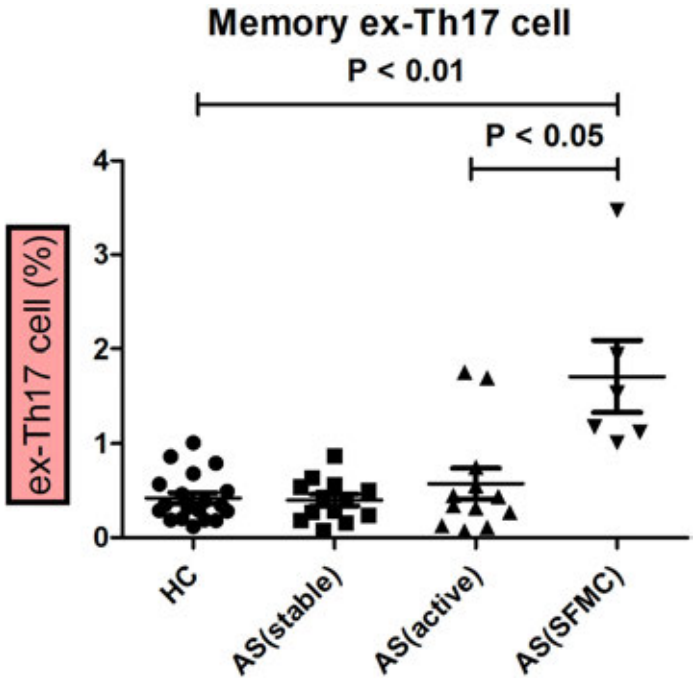
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Spondyloarthritis (SpA) is characterized by inflammation of the synovium. An increase in the number of Th17cells in SpA has been reported. However, it is known that Th17 cells exhibit considerable plasticity, at sites of autoimmune inflammation. Th17 cells can switch to become IL-17 and IFN-r producing ex-Th17 cells. The aim of this study was to investigate the human ex-Th17 cells in synovial fluid at the site of the inflammation in SpA.

Methods: The samples of peripheral blood mononuclear cells (PBMC) and synovial fluid mononuclear cells (SFMC) samples were obtained from SpA patients, and age- and sex-matched Healthy controls(HCs). Cells were surface stained with anti–CD4-Pacific Blue, anti-Fixable Viability Dye-eFluor780, anti-CD45RO-PE. Cells were intracellular stained with antibodies against IFN-r (FITC) / IL-17 (APC) and analyzed. Intracellular cytokine staining, samples were pre-stimulated with 100 ng/ml PMA and 1UM ionomycin in the presence of Golgi-plug for 4 h. For STAT3 Phosflow, Cells were harvested, fixed, and permeabilized using appropriate buffers (Cytofix Fixation Buffer and Phosflow Perm Buffer III) at the time points indicated. The anti-phospho-STAT3 Tyr705-PE Abs were used. The Levels of cytokines in the serum or synovial fluid were assessed using Magnetic Luminex Assay. Statistical analysis was performed using Prism 5.0 Software (GraphPad Software, San Diego, USA). A $p < 0.05$ was considered statistically significant.



Results: Memory CD4 T cells present in the PBMC and SFMC of patients with SpA, as well as in the PBMC of HCs, were analyzed for the production of IFN-r and IL-17A. We observed a increase of ex-Th17 cells in the synovium from patients with SpA compared to the PBMC from HCs. The proportion of memory ex-Th17 was higher in SpA arthritis patients (mean±SD, 1.70±0.92 %) than in healthy controls (0.42±0.25 %) (*P< 0.01)* (Figure 1). Because the cytokine milieu regulates the immune cells function, we measured the inflammatory cytokines in the synovial fluid. Among the cytokines, synovial IL-6 levels were significantly higher in SpA patients(13357±4984 pg/ml) than those in Osteoarthritis (207±146 pg/ml) or serum in HCs (37.87±56.11 pg/ml) ($P < 0.001$).

We next evaluated IL-6 and pSTAT3 expression. Significantly higher levels of IL-6 and pSTAT3 transcripts were detected in arthritis patients when compared with SpA without arthritis, or normal controls. PBMC from AS patients were cultured in the presence of different concentrations of IL-6 (10, 20, 50, 100, or 500ng/ml), in the absence of exogenous IL-23 and TGF. IL-6 was sufficiently inducing significant ex-Th17 expansion. Ex vivo targeting of ex-Th17 cells with the IL-6 inhibitor significantly decreased the production of IL-17 as well as IFN-r cytokines in synovial cells.

Conclusion: We showed that pathogenic ex-Th17 cells accumulated in the joints of SpA patients. Ex-Th17 cell is dependent on the cytokine milieu with IL-6. They may play a pathogenic role at sites of inflammation, suggesting that the IL-6/STAT-3 axis is functioning in arthritis patients with SpA.

Disclosure: S. Jin, None; **P. Park**, None; **J. Kang**, None; **D. Park**, None; **T. Kim**, None.

Abstract Number: 1008

C-X-C Motif Chemokine 10 (CXCL10) as a Transcriptomic Biomarker of Psoriatic Arthritis Susceptibility

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: We previously identified CXCL10, NOTCH2NL, HAT1, and SETD2 as differentially expressed between psoriasis arthritis (PsA) and psoriasis patients without arthritis (PsC). This study aimed to validate these findings and determine their expression in leukocyte subsets in psoriatic disease.

Methods: Prospectively followed psoriasis patients without arthritis (PsC) were assessed yearly by rheumatologists for the presence of PsA. *CXCL10, CXCR3, NOTCH2NL, HAT1,* and *SETD2* mRNA levels were measured in whole blood from 39 patients with early PsA (< 2 years disease duration), 38 PsC (>10 years disease duration) and 39 healthy controls (HCs) as well as in T-cells (CD3+), monocytes (CD14+), and NK cells (CD56+) from PsA (n=25), PsC (n=23) and HCs (n=15). Gene expression was compared between groups using Mann-Whitney U tests.

Results: *CXCL10* expression was elevated in PsA compared to PsC (2.4-fold, p=0.071) and HC (1.9-fold, p=0.407), although this was not statistically significant. Within T cells, *CXCL10* was increased in PsA patients compared to HC (Figure 1; 4.9-fold, p< 0.01). *CXCL10* expression was higher in monocytes as compared to T-cells (6.7-fold, p< 0.001) and NK cells (5.0-fold, p< 0.001) in all study subjects combined. *CXCR3, HAT1* and *SETD2* were higher in T cells (233.7-fold, 3.2-fold and 2.9-fold, respectively) and NK cells (168.2-fold, 2.3-fold and 2.6-fold, respectively) compared to monocytes (p< 0.001). Expression of *NOTCH2NL* was increased in T cells compared to monocytes (1.9-fold; p< 0.001).

Conclusion: Gene expression differences were identified in psoriatic disease that could provide insight into their role in driving the development of PsA and aid in developing targeted treatments.

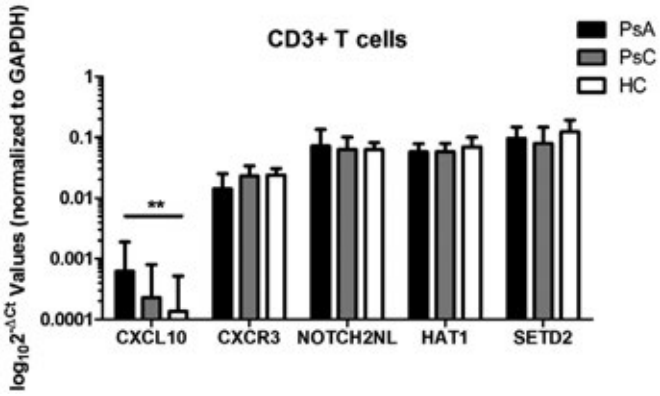

Figure 1. Bar graph depicting gene expression of CXCL10, CXCR3, NOTCH2NL, HAT1 and SETD2 in PsA (n=25), PsC (n=23) and HC (n=15) in CD3+ T cells from human whole blood. CXCL10 expression in T cells was significantly higher in PsA patients compared to HC. ** indicates p<0.01.

Disclosure: F. Abji, None; **A. Muntyanu**, None; **R. Pollock**, None; **R. Machhar**, None; **J. Ye**, None; **V. Chandran**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, GSI, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5.

Abstract Number: 1009

PDE4 Inhibition Could Improve Endothelial and Adipose Tissue Dysfunction Associated with Psoriatic Arthritis, Key Processes in Cardiovascular Disease

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

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Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is the rheumatic disease most associated with metabolic disorders, including obesity and metabolic syndrome, where inflammation is a determinant key factor, increasing the risk of cardiovascular disease. Thus, searching a therapeutic strategy that could target both inflammation and metabolic complications is of great interest to reduce cardiovascular risk in these patients. **Objectives:** 1) To analyze the effect of Apremilast in the adipocytokine pattern, metabolic syndrome components and endothelial dysfunction in patients with PsA and metabolic syndrome (MetSyn). 2) To explore the *in vitro* effects of PDE4 inhibition in the endothelial function and adipocyte biology in the PsA context.

Methods: Human study: Twelve PsA patients diagnosed with MetSyn were given apremilast 30 mg twice daily for 6 months. Microvascular endothelial function was measured through post occlusive hyperemia using Laser-Doppler. The levels of cytokines, inflammatory and oxidative stress markers, endothelial adhesion molecules and adipokines were analyzed on serum and peripheral mononuclear blood cells (PMBCs) by ELISA and RT-PCR. **Treatment of adipocytes and endothelial cells with serum from PsA patients and apremilast:** 3T3L1-differentiated adipocytes and HUVECs were treated with serum 10% of PsA patients and HDs alone or with apremilast (10 mM) for 24h. The expression of adipokines (leptin, adiponectin, visfatin and resistin), adhesion molecules (e-Selectin, VCAM, ICAM), genes involved in inflammation (TNF-a, IL-1b, IL-8 and IL-6), lipid metabolism (DGAT, PLIN, HSL, GLP-1 and PPAR-g), insulin signalling (IRS-1, IRS-2 and GLUT-4) and oxidative stress (SOD-1) was analysed by RT-PCR and western blot.

Results: After 6 months of treatment, Apremilast significantly reduced BMI index, insulin resistance state and levels of complement C3, inflammation, and levels of ApoB. Microvascular endothelial dysfunction was significantly restored shown by an increase of the peak flow and hyperaemia area and decreased adhesion and inflammatory molecules in serum. Altered serum adipokines profile was minimized. mRNA expression levels of inflammatory, adhesion and migration molecules and adipokines were modulated in PMBCs from PsA patients after 6 months with apremilast.

In vitro treatment of endothelial cells with apremilast significantly reduced the expression of adhesion molecules, genes involved in proliferation, adipocytokines and oxidative molecules induced by the serum of PsA patients.

In vitro treatment of adipocytes with apremilast decreased the high levels of leptin, visfatin and resistin induced by PsA serum. In addition, levels of genes involved in lypolisis, adipogenesis and insulin signalling were modulated, favoring an improvement of the insulin resistance induced by PsA serum.

Conclusions: Our *in vivo* and *in vitro* studies suggest that apremilast might reduce IR, inflammation and endothelial dysfunction, parameters strongly involved in cardiovascular disease, by directly targeting adipose tissue and endothelial cells.

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Disclosure: I. Arias de la Rosa, None; **C. Torres-Granados**, None; **M. Abalos-Aguilera**, None; **I. Gomez-Garcia**, None; **R. Guzman-Ruiz**, None; **M. Malagon**, None; **C. Perez-Sanchez**, None; **A. Patiño-Trives**, None; **M. Luque-Tevar**, None; **A. Ibañez-Costa**, None; **A. Escudero**, None; **E. Collantes-Estevez**, None; **C. Lopez-Pedrera**, None; **M. Lopez-Montilla**, None; **N. Barbarroja**, None.

Abstract Number: 1010

IL-17A Induces Distinct Functional Differences Between Two Novel Mesenchymal Stem Cell Populations Identified at the Human Enthesis

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SESSION INFORMATION
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Background/Purpose: Ankylosing spondylitis (AS) is associated with entheseal inflammation and new bone formation. Resident populations of lymphocytes have been identified at the enthesis that on stimulation with IL-23 produce pro-inflammatory cytokines including IL-17A and IL-22 (1) which drive inflammation and may also influence osteogenesis. Surprisingly, enthesis resident mesenchymal stem cells (MSCs) have not been phenotypically or functionally characterised.

To determine if human entheseal tissue harbours a population of MSCs and to investigate the effect of spondyloarthritis associated pro-inflammatory cytokines on MSC osteogenesis and adipogenesis.

Methods: Samples from healthy spinous process and interspinous ligament (10 male, 10 female, median age = 49) were divided into entheseal soft tissue (EST) and peri-entheseal bone (PEB) (1) and enzymatically digested. MSCs content was assessed using a CFU-F assay. Flow cytometry was used to examine expression of MSCs specific markers in plastic adherent cultures. Following osteogenic, chondrogenic and adipogenic inductions, osteogenesis was qualitatively assessed by alkaline phosphatase and alizarin red staining and quantitatively by measurement of calcium accumulation. Chondrogenesis and adipogenesis were assessed using glycosaminoglycan assay and Oil

Red O staining respectively. Osteogenic and adipogenic cultures were also supplemented with IL-17A (50ng/ml), IL-22 (10ng/ml) or TNF-α (1ng/ml) to determine the effect of these cytokines on adipogenesis and osteogenesis.

Results: As a proportion of total cellularity EST developed approximately 5 fold more CFU-F than matched PEB ($p< 0.0001$). Cultured cells were overwhelmingly positive for expression of MSC markers CD73, CD90, CD105 (median 98.66% range: 87.69-98.7%) and negative for CD14, CD19, CD45 and HLA-DR (median 0.34% range: 0-2.53%) however some CD34 expression was noted particularly in EST cultures (median 3.74% range: 0-29%). Both populations were capable of tri-lineage differentiation, although PEB MSCs had 2.75-fold greater osteogenic ($p< 0.05$) and -4.4-fold adipogenic ($p< 0.05$) potential than matched EST MSCs. Calcium accumulation was significantly lower for PEB MSCs when exposed to any cytokine ($p< 0.05$), though addition of IL-17A to EST MSCs significantly increased calcium accumulation by 1.5-fold ($p< 0.05$). Addition of IL-17A or TNF-α significantly decreased lipid accumulation for EST MSCs ($p< 0.05$).

Conclusion: Both the EST and PEB contain cells that meet the ISCT criteria defining MSCs. However, MSCs from these sources are functionally distinct in terms of their differentiation potential and response to inflammatory cytokines. IL-17A is capable of enhancing osteogenesis and impairing lipid accumulation in entheseal soft tissue MSCs. These findings are potentially important in explaining the altered bone and fat phenotype observed in AS as the aberrant new bone formation arises in this tissue.

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Abstract Number: 1011

Single Cell RNA Sequencing of Patients with Psoriatic Disease

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Delayed diagnosis of psoriatic arthritis (PsA) can lead to poor clinical outcomes. A large proportion of PsA patients remain undiagnosed due to a lack of robust biomarkers. Gene expression analysis at single peripheral blood mononuclear cell (PBMC) resolution may help to identify novel cells and RNA signatures present in PsA compared to psoriasis patients without arthritis (PsC).

Table 1. Number of clusters identified in each sample.

Sample	PsA1	PsA2	PsA3	PsC1	PsC2	PsC3
# Clusters	9	8	7	7	12	10

Table 2. Top 5 differentially expressed genes across selected cell types.

Cell Type	Gene	Fold Change PsA vs PsC	Adj P Val
Myeloid dendritic cells	JUP	1.365355	6.84E-47
	MT-ND3	1.226618	5.64E-40
	LYZ	1.231937	2.88E-39
	MT-CO3	1.213961	1.84E-32
	MNDA	1.20201	2.68E-31
NK cells	RPL28	0.704756	7.48E-68
	RPS2	0.774634	1.05E-34
	RPLP0	0.763298	1.57E-30
	RPS5	0.783851	2.11E-29
	RPL8	0.802218	8.90E-28
T Cells	RPS4Y1	1.784758	4.30E-43
	IL32	0.668177	4.97E-35
	HLA-C	1.280377	3.18E-33
	MT-CO3	1.278838	5.16E-33
	ERAP2	0.771176	2.95E-16
Cytotoxic T cells	TRBV4-2	3.029385	7.28E-29
	TRGV2	1.966839	7.38E-23
	TRGV4	0.559101	2.38E-22
	RPL8	0.809835	1.10E-20
	TNFAIP3	1.354977	3.84E-06
T helper cells	MT-ND3	1.301365	3.25E-23
	RPS26	1.526976	9.33E-21
	MT-ATP8	1.367316	8.43E-14
	RPS9	1.433772	1.44E-11
	RPSA	1.191029	5.10E-09
FCGR3A+ monocytes	JUP	1.572302	1.57E-18
	IFITM3	1.563526	3.54E-11
	TNF	0.573474	1.43E-10
	DUSP1	0.666042	2.31E-10
	LILRA6	1.238221	1.77E-05

Methods: PBMCs were isolated from 3 patients with early PsA (< 2 years) and 3 PsC patients matched for age, sex, and psoriasis duration. All patients were treatment naïve. Single cells were isolated using the droplet-based Chromium platform (10X Genomics) and cDNA libraries were sequenced on an Illumina HiSeq 4000. Data were processed in CELLRANGER and secondary analysis performed using R packages. Poor quality cells were filtered out based on high percentage of mitochondrial content, number of genes expressed and library size. Data were normalized by

scran normalization and unsupervised graph-based clustering of cells was performed using a K-nearest neighbor algorithm. Cell types were inferred using immune marker genes and computed cluster markers.

Results: PsA patients were 2/3 male, median age 65 (range 53-75) years, median active joint count 3 (0-7), and median psoriasis area and severity index (PASI) score of 1.4 (0.4-3.1). PsC patients were 2/3 male, age 64 (56-75) years, PASI score 2.8 (0.3-8.7). After quality control and filtering, high quality expression profiles were obtained from 7350 and 7022 cells from PsA and PsC patients, respectively. The number of clusters identified in each sample is shown in Table 1. Sample PsA2 had unique clusters of monocytes and CD34+ cells, whereas PsC2 had a unique cluster of plasmacytoid dendritic cells. The remaining clusters were evident in all patients and consisted of T cells, B cells, macrophages, NK cells and myeloid dendritic cells. Differential expression analysis of PsA compared to PsC patients revealed several differences (shown in Table 2). In myeloid dendritic cells significant upregulation of genes such as *JUP* (junction plakoglobin/gamma catenin, fold change[FC]=1.36, adj.p=$6.8x10^{-47}$) and *LYZ* (lysozyme, FC=1.23, adj.p=$2.9x10^{-39}$) was found. T cells showed significant downregulation of *IL32* (interleukin 32, FC=0.66, adj.p=$5.0x10^{-35}$), *ERAP2* (endoplasmic reticulum aminopeptidase 2, FC=0.77, adj.p=$3.0x10^{-16}$), and upregulation of *HLA-C* (human leukocyte antigen C, FC=1.28, adj.p=$3.2x10^{-33}$). FCGR3A+ monocytes showed a significant upregulation of *IFITM3* (interferon induced transmembrane protein 3, FC=1.56, adj.p=$3.5x10^{-11}$) and *LILRA6* (leukocyte immunoglobulin-like receptor A6, FC=1.23, adj.p=$1.8x10^{-5}$). Cytotoxic T cells showed upregulation of *TRBV4-2* (T cell receptor beta variable 4-2, FC=3.02, adj.p=$7.3x10^{-29}$) and *TNFAIP3* (TNF alpha induced protein 3, FC=1.35, adj.p=$3.8x10^{-6}$). Natural killer cells and naïve T helper cells showed significant downregulation of several ribosomal proteins in PsA compared to PsC patients.

Conclusion: The data show novel insights into gene expression differences in different cell populations that might help in differentiating PsA from PsC.

Disclosure: R. Machhar, None; **K. Liang**, None; **R. Pollock**, None; **D. Gladman**, None.

Abstract Number: 1012

Apremilast Inhibits Immune Cells Support of Inflammatory Osteoclastogenesis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: PsA is associated with bone erosion and inflammation-induced bone loss. This process is mediated by osteoclasts, and modulated by inflammatory cytokines (*i.e.* TNF, IL-1, IL-6, IL-17, and GM-CSF) from immune and stromal cells. Apremilast (APR; a selective phosphodiesterase 4 inhibitor) has known efficacy in PsA, and decreases pro-inflammatory mediators. Although published data indirectly suggest a positive impact of APR on inflammatory-driven bone loss in PsA, data is lacking with regard to the impact on osteoclast generation and activity.

Methods: Osteoclasts were differentiated from primary human $CD14^+$ blood monocytes (derived from PsA patients and healthy controls (HC)) with M-CSF, sub-optimal level of RANKL, plus additional inflammatory-associated stimuli. In brief, osteoclastogenesis was undertaken in the presence of: *(i)* TNF, *(ii)* Supernatants from activated Peripheral

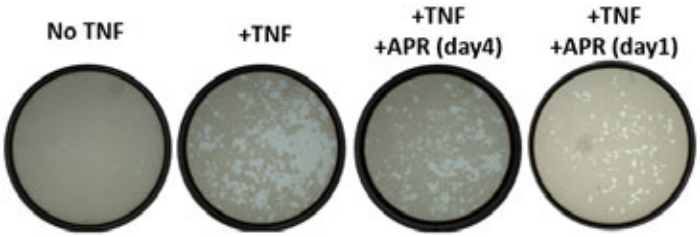

Figure 1. Impact of apremilast on osteoclast resorptive activity. Osteoclastogenesis was driven by TNF. CD14+ precursor where treated at monocyte stage (day1) or pre-osteoclast stage (day4). Resorption plates from a PsA patient representative of 5 experiments in PsA patients and HC.

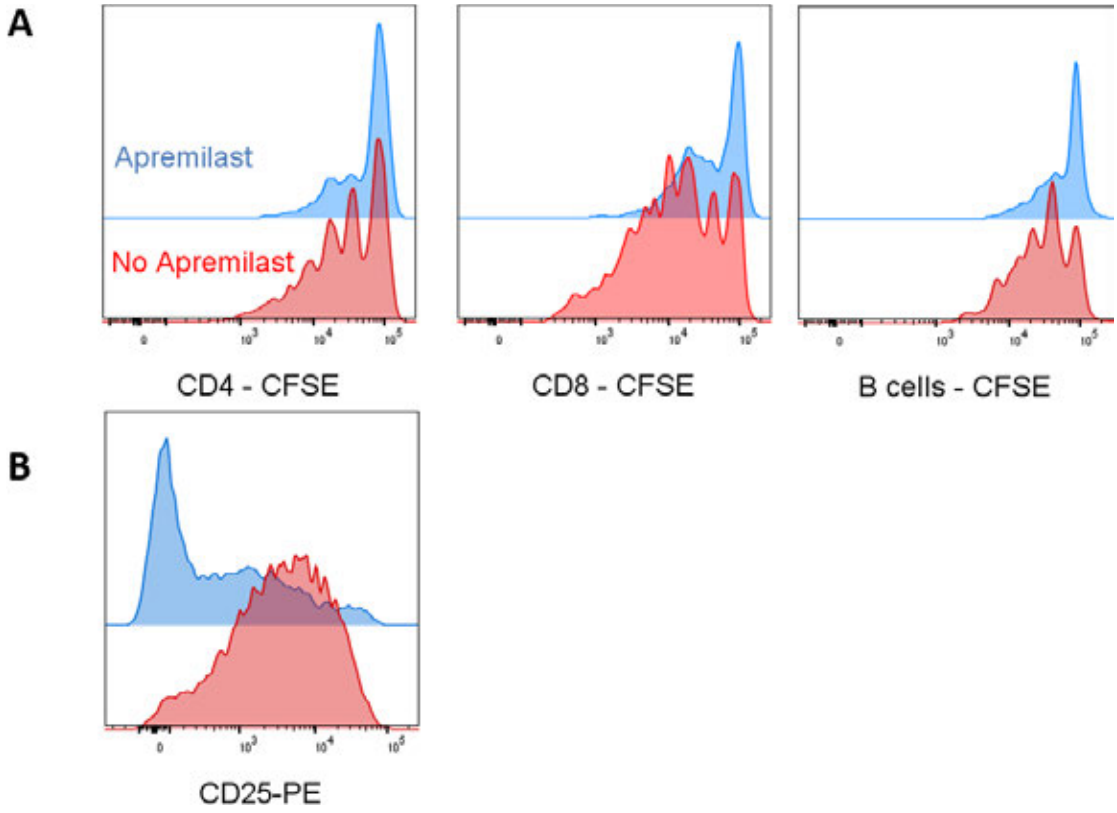

Figure 2. Impact of apremilast on PBMC proliferation and activation. PBMC were activated for 3 days with anti-CD3/CD28/CD2 beads +/- apremilast. (A) Proliferation of T cells and B cells (CFSE uptake) and (B) lymphocytes activation (CD25 membrane expression) were assessed by flow cytometry. FACS plots representative of 3 experiments in HC.

Blood Mononuclear Cells (PBMC) treated with or without APR, *(iii)* Co-culture with activated PBMC, pre-treated with or without APR. Mature osteoclasts were enumerated (Tartrate-Resistant Acid Phosphatase staining/microscopy) and assessed for resorptive activity (Osteo Assay Surface/microscopy). The direct impact of APR on lymphocytes proliferation and activation was also assessed via flow cytometry and cytokines assay.

Results: APR significantly decreased TNF-enhanced osteoclastogenesis and osteolytic activity in both PsA and HC samples *(Figure 1)*. Notably, APR had a dramatic impact on the ability of monocytic precursors to respond to osteoclastogenic signals, but was also able to substantially modulate the capacity of pre-osteoclast to respond to the same signals.

The treatment of activated PBMCs with APR markedly reduced lymphocytes proliferation (CD4, CD8, B cells), and activation (CD25 membrane expression; TNF, IL-17A, M-CSF, IL-2 production in supernatants) *(Figure 2)*. This mod-

ulation resulted in a decrease in the capacity of either PBMC condition media or PBMC coculture-driven osteoclastogenesis.

Conclusion: Phosphodiesterase 4 targeting by APR inhibits *in vitro* inflammation-driven osteoclastogenesis. Our study supports the hypothesis that this therapeutic approach can modulate bone integrity in inflammatory condition such as PsA.

Disclosure: Y. Degboe, Celgene, 2; **F. Sunzini**, None; **I. McInnes**, Abbott, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, Roche., 2, 8, Abbvie, 5, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Astra Zeneca, 2, 5, AstraZeneca, 5, BI, 2, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 5, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Leo, 5, Lilly, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8; **C. Goodyear**, Celgene, 2, AstraZeneca, 2, 5, MedAnnex, 2, 5, UCB, 2, Jannsen, 2.

Abstract Number: 1013

Effects of Anti-TNF on MiR Expression in Monocytes and CD4$^+$ T-Lymphocytes in Spondyloarthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: TNFα inhibitors are an effective treatment for many inflammatory diseases. However, their mechanism of action is more complicated than just blocking the targeted cytokine. MicroRNAs are important post-translational regulators of gene expression and their expression has been found deregulated in rheumatic diseases such as rheumatoid arthritis or spondyloarthritis. The general goal of this work is to investigate changes in miR expression in monocytes and CD4+ T-lymphocytes from patients with axial spondyloarthritis during anti-TNF treatment.

Methods: Sixty-eight patients with axial spondyloarthritis were enrolled in the study. Among these patients, 63 fulfilled the 2009 ASAS classification criteria (imaging arm) with sacro-iliitis on X-rays (n= 47) or objective signs of inflammation on MRI (n=16) and 72% were HLA-B27 positive. All patients were naïve for biologic treatments at baseline and had an active disease (mean BASDAI score of 49 +/- 19 and mean ASDAS score of 3+/-1) requiring the initiation of a TNFα inhibitor (Etanercept 41, Adalimumab 17, Golimumab 10). Mean CRP at baseline was 12.5 +/-18. At 3 months, the BASDAI response rate was 59%. Blood sample were collected at baseline (M0) and 3 months (M3) after the initiation of the treatment. Monocytes and CD4$^+$ T-lymphocytes were isolated from peripheral blood mononuclear cells and 372 miR were investigated by qPCR. A paired Wilcoxon signed-rank test was used to explore differential expression of miRs between M0 and M3.

Results: Pair-wise comparison of miR level before and 3 months after anti-TNF treatment identified 35 differentially expressed (DE) miRs in circulating CD4+ T lymphocytes and 53 DE miRs in monocytes (false discovery rate < 5%). Eighteen miRs were commonly deregulated in both cell types, among which 12 were upregulated and 6 were down-regulated after treatment. Strikingly, we found DE miRs before and after treatment in patients with good response

to TNF inhibitors while there was little or no DE miRs in non-responders according to BASDAI response criteria. Differentially expressed miRs were not correlated to the CRP levels or to the variation of the CRP between 0 and 3 months. Also, in patients with negative CRP at baseline, we found DE miRs (nominal p-value < 5%) suggesting that the modulation of miRs was not only reflecting a better inflammation control.

Conclusion: This work demonstrates that TNF inhibitors might at least partially act by modulating miR expression, especially in patients who respond well to treatment.

Disclosure: O. Fogel, None; **M. Fagny**, None; **E. Roche**, None; **N. Sigrist**, None; **J. Deleuze**, None; **M. Dougados**, AbbVie, 2, 5, 8, Amgen, 5, Biogen, 5, BMS, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, Merck, 2, 5, Merck Inc, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8; **C. Miceli-Richard**, Abbott, Bristol-Myers Squibb, Merck, Pfizer, Roche, Schering-Plough, and Wyeth, 8, Abbvie, 2, 5, AbbVie, Bristol-Myers Squibb, Novartis, Merck, Pfizer, and Wyeth, 2, Biogen, 2, BMS, 5, MSD, 2, Novartis, 2, 5, Pfizer, 2, Pfizer, Roche, UCB, Wyeth, and Merck, 5, UCB, 2; **J. Tost**, None.

Abstract Number: 1014

Regulatory Role of IL-23 and Its Receptor System in Spondyloarthritis and Its Therapeutic Relevance in anti-IL-17 Failure Patients

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Here we hypothesized that (i) IL-23/IL-23R system more specifically the specific IL-23p19 subunit mediated signaling system regulates expansion/maintenance and functional maturation in respect to production of the signature cytokines of Th17 cells (IL-17 and IL-22) in psoriatic arthritis (PsA) and ankylosing spondylitis (AS) and that (ii) a high affinity humanized IgG1/j monoclonal antibody that binds to the p19 subunit of IL-23 such as tildrakizumab will block IL-23 induced JAK/STAT signaling system and inhibit expansion/maintenance and functional maturation of the effector Th17 cells in PsA and AS.

Methods: PsA and AS patients with an active disease not on DMARDS/biologics were recruited in this study. Mononuclear cells from peripheral blood (PBMC) and synovial fluid (SFMC) of age/sex matched PsA patients (n=10), PBMCs from AS patients (n=10) and normal individuals (n=10) were isolated. Magnetically selected $CD3^+$ T cells (10^6 cells/ml) were activated with anti-human CD3/CD28 cocktail+rIL-23. Activated $CD3^+$ T cells were cultured with and without tildrakizumab (120 pM). To identify the activated memory $CD4^+CD11a^+CD45RO^+IL\text{-}17^+$ T cells and $CD4^+CD11a^+CD45RO^+IL\text{-}22^+$ T cells Hi-D FACS studies were performed (FACSFusion Aria); the % of cell population and the MFI were analyzed by using Flow Jo software. Anti-proliferative effect of tildrakizumab on PBMCs and SFMCs was assessed by MTT and CFSE dilution assays. Immunoblot assays were done on lysates of the cultured $CD3^+$T cells to identify Jak2/p-Jak2, Tyk2/p-Tyk2, stat3/p-stat3, and RORγt.

Results: (i). In PBMCs/SFMCs of PsA and AS patients rIL-23 induced marked upregulation of IL-17A and IL-22 in the memory T cells (CD11a+CD45RO+); tildrakizumab inhibited rIL-23 induced IL-17 and IL-22 expression in CD4+ memory T cells, more specifically we noticed with tildrakizumab there was marked reduction of CD4+CD11a+CD45RO+IL-17+

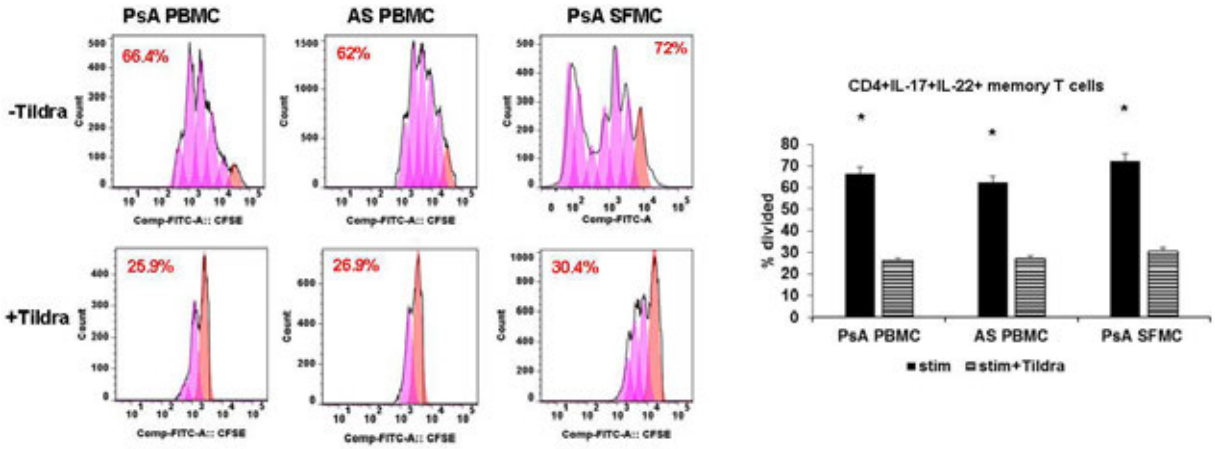

Figure 1. Recombinant IL-23 induces proliferation of CD4+IL-17+IL-22 memory T cells and that can be blocked by tildrakizumab, a monoclonal antibody that binds to the p19 subunit of IL-23. PBMCs of PsA (n=10), AS (n=10), OA (n=10) and SFMCs of PsA (n=5), OA (n=5) were stained with 5μM CFSE and then incubated in the presence or absence of tildrakizumab prior to stimulation with CD3/CD28+rIL-23. HI-D FACS studies were performed to identify live CD3+CD4+CD11a+CD45RO+IL-17+IL-22+ T cells. Cells pre-treated with tildrakizumab had significant reduction of proliferation of IL-17+IL-22+ memory T cells (p<.01).

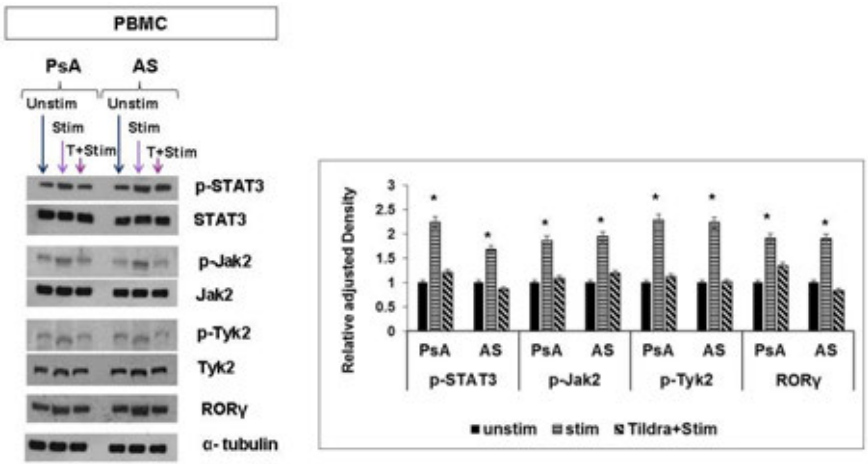

Figure 2. In activated PBMC T cells of psoriatic arthritis (PsA) and ankylosing spondylitis (AS) rIL-23 induced JAK/STAT signaling system and activation of RORγt the master transcription factor for IL-17 and IL-22; and these phosphorylation events could be inhibited by tildrakizumab (p<0.001). Unstim= Unstimulated; Stim= Stimulated, T+ Stim= tildrakizumab + Stimulated.

T cells and CD4+CD11a+CD45RO+IL-22+ T cells (p< .01)) (ii) tildrakizumab significantly inhibited proliferation of these CD4+IL-17+ memory T cells and CD4+IL-22+ (Fig 1) (iii) Immunoblot assays demonstrated PsA/AS activated CD3+ T cells treated with tildrakizumab had decreased expression of phospho-STAT3/Jak2/Tyk2/RORgt by two-folds (p< 0.001) compared to CD3+ T cells not treated with tildrakizumab (Fig 2).

Conclusion: Marked upregulation of IL-23 at the disease sites of PsA and AS is well established. rIL-23 activated sorted pathological $CD3^{+}$ T cells in PsA and AS induced proliferation of CD4+IL-17+IL-22+ memory T cells and up-regulations of IL-17A and IL-22 (by ELISA) and tildrakizumab inhibited all these outcomes significantly. We noticed in secukinumab treated PsA patients (n=10) those who had pretreatment higher levels of IL-22 did not respond to secukinumab. This suggests that by blocking the IL-23R an additional therapeutic advantage can happen because of its inhibition of both IL-17 and Il-22. Putting together here we have provided the (i) proof of concept about IL-23p19 induced immune dysregulations in PsA and AS (ii) the potentials of p19 targeted therapy for PsA and AS (iii) a prospect for a choice of anti-IL23p19 therapy in anti-IL-17 resistant patients.

Disclosure: S. Raychaudhuri, AbbVie, 2, Amgen, 5, Janssen, 2, 5, Lilly, 5, Novartis, 2, 5, Pfizer, 2, 5, Pfizer Inc, 2, Sun Pharma, 2; **S. Raychaudhuri**, Sun Pharmaceutical Industries Limited, 2.

Abstract Number: 1015

Evidence for Substantial Immune Activation in Asymptomatic ANA Positive Individuals

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Etiology & Pathogenesis Poster I

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic autoimmune rheumatic diseases (SARD) including Sjogren's Disease (SjD), Systemic Sclerosis (SSc) and Systemic Lupus Erythematosus (SLE) are characterized by the production of anti-nuclear antibodies (ANA) and are associated with considerable morbidity and/or mortality. ANA production can also be seen in ~20% healthy women, only a small subset of which will eventually progress to a SARD diagnosis. Although pro-inflammatory cytokines including TNFα and IL-6 are only increased in symptomatic patients, some of the cellular immune changes associated with SARD are also seen in ANA^+ non-symptomatic (ANA^+ NS) individuals. In order to better understand the immunologic changes that lead to SARD progression, we used flow cytometry to investigate a variety of innate and adaptive immune populations in ANA^+ NS as compared to healthy controls (HC) and SARD patients.

Methods: Consenting ANA^+ (IF ≥ 1:160) participants were recruited through the clinic and classified as ANA^+ NS (n = 38), ANA^+ with symptoms but lacking sufficient criteria for SARD diagnosis (UCTD, n=42) or early SARD (SLE, n=5, SSc, n=2). SARD diagnosis and classification was assessed according to the 1997 ACR criteria for SLE and the 2013 ACR-EULAR criteria for SSc. All SARD patients were within 2 years of diagnosis and not taking DMARDs (hydroxychloroquine allowed) or prednisone. ANA^- HC (n= 14) were also recruited. Peripheral blood mononuclear cells (PMBCs) were isolated and stained with fluorochrome labeled antibodies to identify immune cell populations via flow cytometry.

Results: Several of the immunologic changes previously reported for SARD patients were also seen in ANA^+ NS and UCTD. These included: increased proportions of plasma cells and plasmablasts; a trend to increased transitional B cells, activated class-switch memory B cells, activated memory Tfh and Tph cells; and a trend towards decreased proportions class-switched memory B cells. Contrary to initial reports that T regulatory (T_{reg}) cells are decreased in SARD, these cells were increased in ANA^+ NS and UCTD groups with similar changes seen for the SARD patients. However, a subset of regulatory cells, CD8 T_{reg} were markedly decreased in ANA^+ NS and UCTD patients, suggesting a potential functional role for these cells in regulating autoimmunity. Monocytes and myeloid dendritic cells are increased in SARD patients and have been shown to produce pro-inflammatory cytokines. These populations were also significantly increased in ANA^+ NS and to a lesser extent in UCTD patients, as compared to HC. In contrast, no changes were seen in the proportion of plasmacytoid dendritic cells in ANA^+ NS and UCTD patients.

Conclusion: Several of the immune changes in ANA$^+$ NS individuals appear to parallel those seen in SARD patients, indicating that there is substantial immune activation even in asymptomatic ANA$^+$ individuals. These findings argue that the differences between ANA$^+$ NS and SARD patients may result from altered function rather than altered proportions of these populations.

Disclosure: E. Van Lieshout, None; **D. Bonilla**, None; **Z. Touma**, None; **A. Bookman**, None; **L. Hiraki**, None; **Z. Ahmad**, None; **S. Johnson**, Bayer, 2, Boehringer Ingelheim, 2, 5, Corbus, 2, Ikaria, 5, Roche, 2; **E. Silverman**, None; **J. Wither**, None.

Abstract Number: 1016

Identification of Differentially Expressed Genes and Signaling Pathways in Systemic Lupus Erythematosus by Integrated Bioinformatics Analysis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a common autoimmune disease. The occurrence and development of SLE is a result of multiple factors, but its exact pathogenesis has not been fully elucidated.

Methods: Here, we used bioinformatics to analyze and identify the key pathogenic genes of SLE and to reveal the underlying pathogenic molecular mechanism.

Results: The expression profiles of GDS4185, GDS4888, GDS4889 and GDS4890 were downloaded from the Gene Expression Omnibus (GEO) database, which contained 99 samples, including 42 cases of SLE samples and 57 cases of normal samples. The four microarray datasets were integrated to get differentially expressed genes (DEGs). The gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichments of DEGs were operated by DAVID and KOBAS online calculuses, respectively. The protein–protein interaction (PPI) networks of the DEGs were created from the STRING database. A total of 839 DEGs were extracted from the four GEO datasets, of which 289 genes were upregulated and 550 genes were downregulated. GO analysis indicated that the biological functions of DEGs focused primarily on response to virus, type I interferon signaling pathway and cellular protein metabolic process. The main cellular components include perinuclear region of cytoplasm, focal adhesion and cell-cell adherens junction. The molecular functions include protein binding, double-stranded RNA binding and actin filament binding. KEGG pathway analysis showed that these DEGs were mainly involved in the Osteoclast differentiation, HTLV-I infection, Measles, FoxO signaling pathway, Herpes simplex infection, Primary immunodeficiency and Jak-STAT signaling pathway. The 14 most closely related genes among DEGs were identified from the PPI network.The 14 genes are: HERC5, TP53, CDC20, GNB2, GNB4, PPP2R1A, GNAI2, PMCH, SOCS3, HERC6, STAT1, SOCS1, ISG15, IFIT3.

Conclusion: This research suggests that screening for DEGs and pathways in SLE using integrated bioinformatics methods could help us realize the molecular mechanism underlying the development of SLE, be of clinical implication for the early diagnosis and prevention of SLE, and afford reliable targets for the treatment of SLE.

Disclosure: W. Liu, None; **Y. Wu**, None; **W. Zhao**, None.

Abstract Number: 1017

The Integration of Genetic Data, Molecular Pathway Analysis and Differential Expression to Delineate the Impact of Ancestral Differences on Lupus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multi-organ autoimmune disorder with a prominent genetic component. Evidence has shown that individuals of African-Ancestry (AA) experience the disease more severely and with an increased co-morbidity burden compared to European-Ancestry (EA) populations. However, the relationship between genetics, molecular pathways, and disease severity has not been fully delineated. Here, we examined AA and EA SLE-associated single nucleotide polymorphisms (SNPs) and linked them via expression quantitative trait loci (eQTL) across multiple tissues to genes with altered expression (E-Genes). Putative EA and AA E-Gene signatures were coupled with SLE differential expression (DE) datasets and upstream regulators to map candidate molecular pathways. Together, these genetic and gene expression analyses enable a better understanding of how the identified SNPs could contribute to aberrant immune function as well as the influence of ancestry on the genetic basis of SLE.

Methods: A previous SLE Immunochip study (Langefeld et al., 2017) identified SNPs significantly associated with SLE in AA (2,970 cases; 2,452 controls) and EA (6,748 cases; 11,516 controls) cohorts. eQTL mapping identified E-Genes from SLE SNPs and their ancestry-specific SNP proxies (based on linkage disequilibrium) via the GTEx database. For both ancestral groups, E-Gene lists were examined for the significant enrichment of gene ontogeny (GO) terms, canonical IPA® (Qiagen) pathways and BIG-C™ categories. Next, we analyzed the gene expression profiles of predicted E-Genes across multiple SLE DE datasets, including those from blood and multiple tissues. Differential expressed genes (DEGs) were identified and subjected to pathway analysis with IPA®, clustering using MCODE and visualization in Cytoscape with the ClusterMaker2 plugin. Drug candidates targeting E-Genes, DEGs and upstream regulators (UPRs) were identified using CLUE, IPA® and STITCH.

Results: A total of 908 Immunochip SNPs were mapped to 252 eQTLs and coupled to 760 E-Genes (207 in EAs, 30 in AAs, 523 shared; Figure 1A). Shared E-Genes were highly enriched in interferon signaling, whereas EA E-Genes were associated with nucleotide degradation and AA E-Genes were linked to multiple biosynthesis and intracellular signaling pathways (e.g., retinol biosynthesis and AMPK signaling). Protein-protein interaction (PPI) networks of clustered EA, AA and shared E-Genes illustrate the high degree of ancestral overlap evident within each E-Gene set (Figure 1B). Clustering analysis of all DE E-Genes and IPA-predicted UPRs highlight disease-associated pathways that are both shared and ancestry-specific. Drug candidate comparison identified a total of 115 drugs targeting EA, AA and shared E-Genes and their molecular pathways.

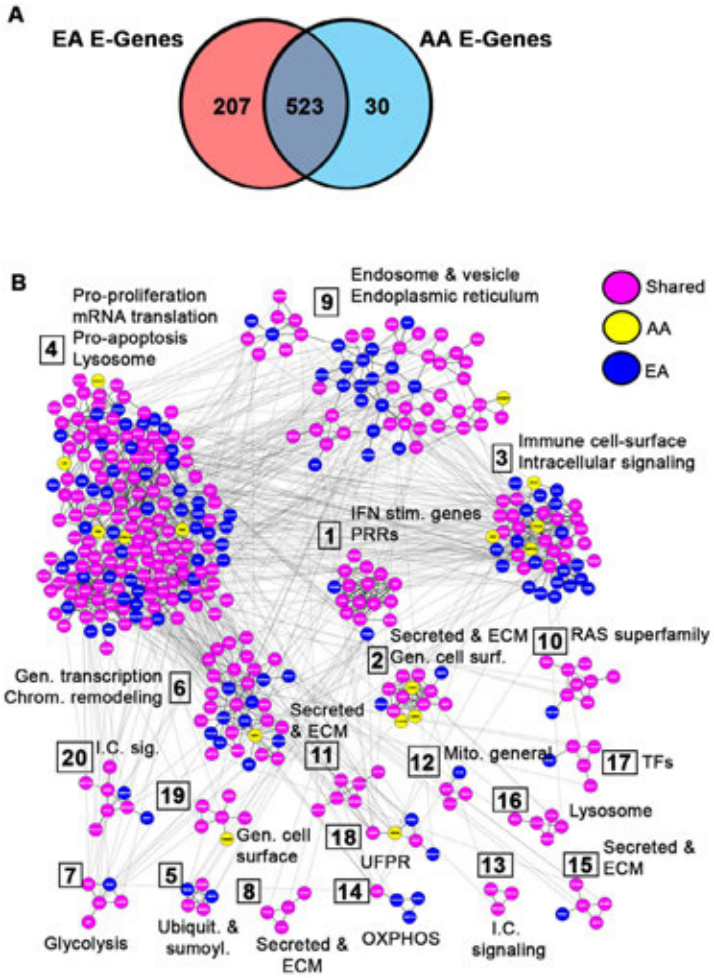

Figure 1. (A) Venn of E-Gene overlap. (B) Cytoscape visualization of E-Gene PPI networks using MCODE clustering. Significant BIG-C functional categories for individual modules are listed.

Conclusion: Using a bioinformatics-based approach that utilizes pathway analysis and gene expression data, we were able to discover novel ancestry-dependent and ancestry-agnostic candidate causal targets in SLE and couple those with drug discovery tools to identify new therapies with the potential to impact disease processes within and across specific populations.

Disclosure: K. Owen, None; **B. Aidukaitis**, None; **A. Labonte**, None; **M. Catalina**, None; **P. Bachali**, None; **N. Geraci**, None; **M. Marion**, None; **H. Ainsworth**, None; **k. Zimmerman**, None; **T. Howard**, None; **C. Langefeld**, None; **P. Lipsky**, Horizon, 5, Janssen Research & Development, LLC, 2; **A. Grammer**, None.

Abstract Number: 1018

Renal Single Cell Genomics Links Type II Interferon and Lupus Nephritis in African-Americans

Andrea Fava,[1] Yuji Zhang,[2] Jill Buyon,[3] Chaim Putterman,[4] Nir Hacohen,[5] Arnon Arazi,[5] Celine Berthier,[6] Deepak Rao,[7] Michael Brenner,[8] David Wofsy,[9] Anne Davidson,[10] Mathias Kretzler,[11] David Hildeman,[12] E. Steve Woodle,[12] Betty Diamond,[10] Thomas Tuschl,[13] Evan Der,[14] Hemant Suryawanshi,[13] H. Michael Belmont,[15] Peter Izmirly,[16] Robert Clancy,[16] The Accelerating Medicines Partnership,[17] and Michelle Petri[18], [1]Johns Hopkins University, Baltimore, [2]University of Maryland, Baltimore, [3]NYU School of Medicine, New York, [4]Albert Einstein College of Medicine, New York, NY, [5]Broad Institute, Cambridge, [6]University of Michigan, Ann Arbor, MI, [7]Brigham and Women's Hospital,

Boston, MA, [8]Brigham and Women's Hospital, Boston, [9]UCSF, San Francisco, [10]Feinstein Institutes for Medical Research, Manhasset, [11]University of Michigan, Ann Arbor, [12]University of Cincinnati, Cincinnati, [13]Rockefeller Research Laboratories, New York, [14]Albert Einstein College of Medicine, New York, [15]New York University School of Medicine, Ney York, [16]New York University School of Medicine, New York, [17]Multiple Organizations, USA, [18]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Compared to Caucasian, African-American ethnicity is associated with a higher risk of developing systemic lupus erythematosus, lupus nephritis, high-risk histological features, resistance to treatment, and mortality. In phase 1 of the Accelerating Medicines Partnership (AMP), we used single-cell genomics to identify ethnicity associated features.

Methods: Single cell RNA sequencing was performed on renal biopsies obtained for clinical purpose; one pipeline applying CEL-Seq2 in a leukocyte enriched sample and the other Fluidigm C1 800 in an agnostic approach to dissociated renal cells. Differential abundance of cell populations was determined using a logistic mixed model. Then, the differential expression profile was determined for each cell cluster and interpreted using pathway enrichment analysis.

Results: Samples from 19 African-American and 20 Caucasian patients were obtained. We identified 30 cell clusters. Type I and II interferon inducible genes were upregulated in most cell populations. A cluster of T cells with exceptionally high interferon signature was found to be increased in African-Americans (OR 4.8). Macrophages and DC4-like dendritic cells were instead less abundant (OR 0.3). In African-Americans, type I and II interferon response pathways were enriched in several cell types including T cells, B cells, plasma cells, and activated monocytes. The majority of the differentially expressed genes was specifically inducible by type II interferon. In addition, while there was no local expression of type I interferons, interferon gamma was abundantly expressed by infiltrating NK and CD8 T cells.

Conclusion: African-American patients with lupus nephritis have a stronger interferon response pathway activation, especially type II. Our findings suggest an intrinsic biological factor underlying the outcome gap and highlight the role of interferon gamma in lupus nephritis, implicating this pathway as a potential therapeutic target in SLE. Further work in Phase 2 of AMP is being pursued to validate and extend these findings.

Disclosure: A. Fava, None; **Y. Zhang**, None; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **C. Putterman**, Equillium, 5, Equillium, Inc, 2, 5, Exagen, 2; **N. Hacohen**, Neon Therapeutics, 1, 8; **A. Arazi**, None; **C. Berthier**, None; **D. Rao**, Janssen, 5, Merck, 2, Pfizer, 5; **M. Brenner**, None; **D. Wofsy**, Celgene, 5, Genentech, 5, GlaxoSmith-Kline, Lilly, 5, Novartis, Principia, 5; **A. Davidson**, None; **M. Kretzler**, None; **D. Hildeman**, None; **E. Woodle**, None; **B. Diamond**, GSK, 5, Jansen, 5, Lilly, 5; **T. Tuschl**, None; **E. Der**, None; **H. Suryawanshi**, None; **H. Belmont**, None; **P. Izmirly**, Glaxosmithkline, 5, GSK, 5; **R. Clancy**, None; **T. Accelerating Medicines Partnership**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 1019

Type I Interferon Levels Vary with Regional Ancestry in European-derived SLE Cohorts

Justine Shum,[1] Yogita Ghodke-Puranik,[2] Regine Tipon,[2] Jessica Dorschner,[3] Danielle Vsetecka,[3] Shreyasee Amin,[4] Ashima Makol,[5] Floranne Ernste,[4] Thomas Osborn,[5] Kevin Moder,[3] Vaidehi Chowdhary,[3] Uma Thanarajasingam,[6] Vilija Oke,[7] Iva Gunnarsson,[7] Agneta Zickert,[7] Maria Zervou,[8] Elisabet Svenungsson,[9] George Goulielmos,[8] and Timothy Niewold[2], [1]NYU School of Medicine, New York, [2]Colton Center for Autoimmunity, NYU School of Medicine, New York, [3]Mayo Clinic, Rochester, [4]Mayo Clinic Rochester, Rochester, MN, [5]Mayo Clinic Minnesota, rochester, MN, [6]Mayo Clinic, Rochester, MN, [7]Karolinska Institutet, Stockholm, Sweden, [8]University of Crete, Crete, Greece, [9]Division of Rheumatology, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden

SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Session Time: 9:00AM–11:00AM

Background/Purpose: Type I interferon (IFN) is an important mediator in the pathogenesis of systemic lupus erythematosus. Serum type I IFN levels clearly vary between SLE patients of different continental ancestral backgrounds, with levels being highest in African-American SLE patients. It is not known whether this diversity is also present within continental ancestral groups. In this study, we examine regional differences between European populations and use ancestry informative markers (AIMs) to assess for Northern versus Southern European admixture in a European-American cohort, and to correlate proportional regional European ancestry with serum type I IFN activity.

Methods: We studied type I IFN levels in European ancestry SLE patient cohorts from Sweden, Crete and the United States. Patients all met the ACR classification criteria for SLE. Serum IFN-a activity was determined using a WISH cell reporter assay. In the United States cohort, a validated set of European American ancestry informative markers (AIMs) designed to distinguish northwest and southeast European ancestry was used to assess for proportional Northern versus Southern European ancestry. Principal component analysis (PCA) was performed to infer population structure.

Results: The Swedish cohort had the highest type I IFN levels, while the US cohort was intermediate, and the lowest IFN levels were detected in the Crete cohort. The US subjects are a mix of Northern and Southern European ancestry by self-report, so we genotyped 297 ancestry informative markers in the 366 US SLE patients with self-reported European American ancestry. In this group, circulating type I IFN levels were correlated with three of the top five principal components derived from the AIMs considered in aggregate using Fisher's method for the combination of p-values across the three components ($p = 0.024$). Given that these components segregate northern versus southern European ancestry, this finding in the US cohort supports the concept that type I IFN levels vary according to regional genetic ancestry within Europe.

Conclusion: In this study, we demonstrate that variations in type I IFN levels correlate with regional ancestry within Europe in European-derived cohorts of SLE patients, further supporting the heterogeneity in type I IFN pathway activation in SLE patients of different ancestral backgrounds.

Disclosure: J. Shum, None; **Y. Ghodke-Puranik**, None; **R. Tipon**, None; **J. Dorschner**, None; **D. Vsetecka**, None; **S. Amin**, None; **A. Makol**, None; **F. Ernste**, None; **T. Osborn**, None; **K. Moder**, None; **V. Chowdhary**, None; **U. Thanarajasingam**, None; **V. Oke**, None; **I. Gunnarsson**, None; **A. Zickert**, None; **M. Zervou**, None; **E. Svenungsson**, None; **G. Goulielmos**, None; **T. Niewold**, None.

Abstract Number: 1020

NLRP12 Regulates Interferon-α Expression and Is a Biomarker for Disease Activity of Systemic Lupus Erythematosus

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

Background/Purpose: Systemic lupus erythematous (SLE) is a systemic autoimmune disease with diverse etiological factors. It was well recognized that interferon (IFN) signature did the perpetration on the progress of this disease. NLRP12 (NOD-like receptor family (NLR) pyrin domain containing 12) is a pyrin containing NLR protein that we had linked its new biological function to the cross-regulation of Toll like receptor (TLRs) and Rig-I like receptor (RIG-I) pathways. NLPR12 acts as an innate immune check-point in regulating type I IFNs expression during TLRs and RIG-I activation. Therefore, we aimed to investigate the underline molecular mechanism of NLRP12 regulation and its significance in SLE patients.

Methods: PBMCs were collected from 60 SLE patients and 20 healthy donors for analysis of *NLRP12* and IFN-α (*IFNA)* gene expression by RT-QPCR. PBMCs were applied for Chromatin immuneprecipitation (ChIP) assay and electrical mobility shift assay (EMSA) to determine the putative transcription factor that regulates *NLRP12* expression. An involvement of epigenetic regulation of *NLRP12* expression in SLE patients was also analyzed.

Results: We found that *NLRP12* expression was significantly lower in PBMC isolated from SLE patients compared to healthy donors. The inverse correlation was observed in *NLRP12* and *IFNA* gene expression as well as *NLRP12* expression and amount of double-stranded DNA autoantibody in SLE patients. Interestingly, *NLRP12* expression was gradually restored to the normal level after treatments in the patients. Results from Chlp and EMSA analysis indicated potential transcription factors (TFs) regulating *NLRP12* promoter activity, thus lead to transcriptional suppression of *NLRP12* in SLE PBMC.

Conclusion: In this study, expression level of *NLRP12* has been demonstrated to be a biomarker of disease activity in SLE patients. Mechanistically, a specific transcription factor regulating *NLRP12* expression in SLE PBMC is in accord with the same TF that suppresses *NLRP12* expression in type I IFN treated-monocyte. This finding may offer clues and an explanation for SLE patients with type I IFN signature.

Disclosure: M. Chen, None; **Y. Tsao**, None; **S. Chen**, None.

Abstract Number: 1021

Anti-IFNAR Treatment Does Not Reverse Neuropsychiatric Disease in MRL/*lpr* Lupus Mice

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SESSION INFORMATION
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Session Title: SLE – Etiology & Pathogenesis Poster I
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Background/Purpose: Many systemic lupus erythematosus patients display a type I interferon (IFN) signature, and IFNα levels and gene signatures have been positively correlated with disease severity. Previous studies blocking the type I IFN pathway systemically in lupus models have seen some beneficial effects in attenuating both systemic and renal disease. However, its effects on the neuropsychiatric manifestations have yet to be assessed, even though therapeutic administration of IFNα has been associated with induction of depression, a common manifestation in NPSLE patients. Our aim was to investigate whether disrupting the type I IFN pathway systemically would attenuate the development of murine neuropsychiatric lupus.

Methods: Female MRL/*lpr* mice were administered an anti-IFNAR antibody (MAR1-5A3; MedImmune, Gaithersburg, MD) or an IgG isotype control antibody (1A7, IgG1) intraperitoneally 3 times weekly for 12 weeks starting at 4-5 weeks of age. Depression-like behavior was assessed at 8-9 weeks of age using the Porsolt swim test. Cognitive dysfunction was assessed at the end of treatment at 16-17 weeks of age, using the object placement (OP) and object recognition (OR) tests, which evaluates spatial and recognition memory, respectively. Brain tissue was analyzed by histology and by immunofluorescent staining for $B220^+$ and $CD3^+$ cells, as well as albumin and IgG deposition in the brain parenchyma to determine brain barrier integrity.

Results: No significant differences were seen between the anti-IFNAR and control treated mice when assessing for depression-like behavior (p=0.32) or cognitive dysfunction (OP: $x^2(1) = 0.54$, $p = 0.46$; OR: $x^2(1) = 0.002$, $p = 0.96$). Anti-IFNAR treatment also did not significantly improve cellular infiltration, as evident by hematoxylin and eosin staining and infiltrate composition comparing $B220^+$ and $CD3^+$ cell counts. Staining for albumin and IgG leakage in the brain parenchyma also showed similar brain barrier integrity between the groups. RNA expression level of CXCL10, a known interferon-stimulated gene, were significantly different in the spleen ($p = 0.023$) and the choroid plexus ($p = 0.0088$), suggesting that the pathway was inhibited in the choroid plexus with systemic delivery of the antibody.

Conclusion: Surprisingly, our results showed no improvement in neuropsychiatric disease in the MRL/*lpr* mouse model and suggest that the role of IFNAR signaling in the pathogenesis of neuropsychiatric lupus continues to need to be carefully assessed.

Disclosure: M. Huang, None; **A. Stock**, None; **E. Mike**, None; **R. Kolbeck**, MedImmune, 3, 6; **C. Putterman**, Equillium, 5, Equillium, Inc, 2, 5, Exagen, 2.

Abstract Number: 1022

Single Cell Transcriptome Analysis of Circulating Plasmacytoid Dendritic Cells and Switched Memory B-cells in SLE Patients Reveals Transcriptional Subsets Within the Classical Cell Lineages

Amrutesh Puranik,[1] Yogita Ghodke-Puranik,[2] Regine Tipon,[2] Mark Jensen,[1] Auroni Gupta,[3] Jacqueline Paredes,[3] Uma Sankaramanchi,[4] Ilona Nln,[3] Amit Saxena,[5] H. Michael Belmont,[6] Peter Izmirly,[7] Robert Clancy,[7] Jill Buyon,[5] and Timothy Niewold[2], [1]Colton Center for Autoimmunity, NYU School of Medicine, New York, NY, [2]Colton Center for Autoimmunity, NYU School of Medicine, New York, [3]Colton Center for Autoimmunity, NYU School of Medicine, ny, [4]Colton Center for Autoimmunity, NYU Langone Medical Center, NY, [5]New York University School of Medicine, New York, NY, [6]New York University School of Medicine, Ney York, [7]New York University School of Medicine, New York

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
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Session Time: 9:00AM–11:00AM

Background/Purpose: Both plasmacytoid dendritic cells (pDCs) and switched memory B cells (SMBCs) are considered to be key effector cells in systemic lupus erythematosus. It seems likely that within these classical cell lineages, additional diversity of function will exist that will contribute to disease pathogenesis. To explore this question, we performed single-cell RNA sequencing in pDCs and SMBCs from SLE patients and controls to assess gene expression patterns and cellular sub-groupings within these lineages.

Methods: pDCs and SMBCs from SLE patients (n=10) and Healthy controls (n=5) were purified by magnetic separation. For deep sequencing, we used the Fluidigm C1 HT system with 800 capture site chips to capture single cells. Single cell capture was verified by direct visualization using the Array Scan system, allowing us to remove empty wells and wells with multiple cells. After quality control and adaptor trimming, the data was analyzed using SeqGeq software. pDCs and SMBCs were clustered using UMAP and pseudo-time analysis was performed using the Monocle program. Type I IFN activity in SLE plasma was measured using reporter cell assay.

Results: A total of 2774 pDCs and 2578 SMBCs from SLE and healthy controls passed the quality control and were used for further analysis. In pDCs, we observed unique clusters for patients with high interferon, low interferon, and controls, indicating that the IFN response is a major determinant of overall gene expression patterns in SLE patient pDCs. IFN signature in pDCs correlated with circulating type I IFN activity in the SLE patients measured at the same time. Other genes upregulated in pDCs included the type I interferon regulator AXL and MACC1. The SMBCs were heterogeneous in patients and controls, and in contrast to the pDCs, the overall clustering pattern was independent of the IFN score. SMBC clusters were predominantly defined by genes indicating cellular activation or proliferation such as HLA-DRs and CREB1, or genes associated with nucleic acid processing such as DNASE1 and SNORD3B-1.

Conclusion: We find distinct clusters of cells defined transcriptionally within the pDC and SMBC lineages, and the transcripts which define these subgroups differ between cell lineages. Type I IFN induced transcripts are important to pDC diversity, while in SMBCs transcripts related to cellular activation and nucleic acid processing are critical markers of transcriptional heterogeneity.

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Abstract Number: 1023

Neutrophils Are an Important Source of Microparticles in Lupus and Asymptomatic ANA$^+$ Individuals

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SESSION INFORMATION
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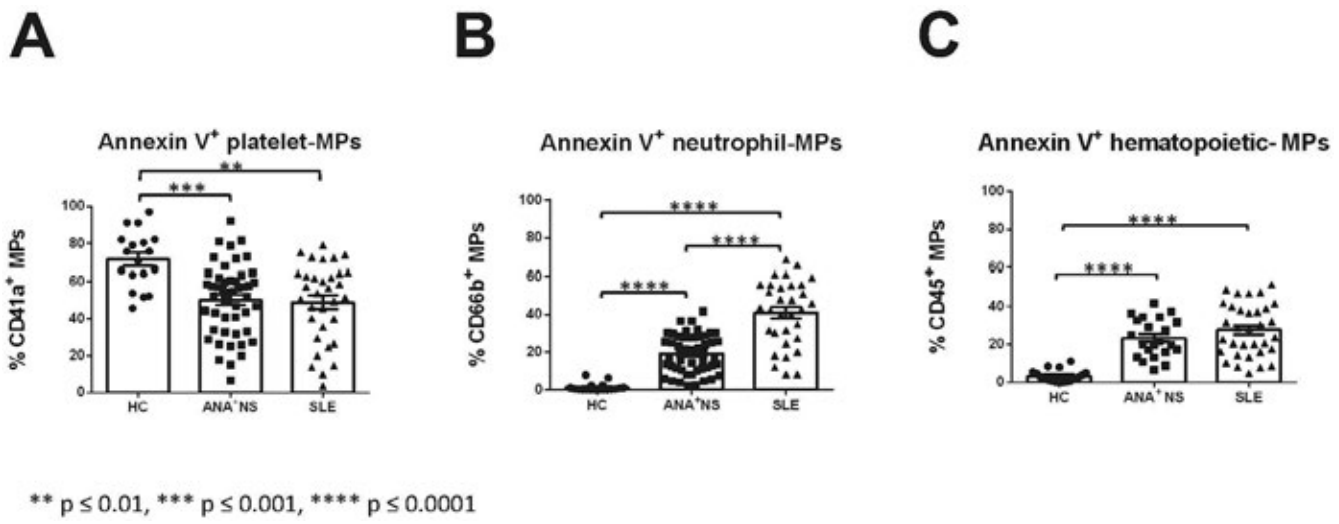
Background/Purpose: Apoptotic microparticles (MPs) in the circulation of systemic lupus erythematosus (SLE) patients are enriched for nucleic acids and complexed with IgG (MP-IC), as compared with those from healthy controls (HC). These MPs have been shown to activate monocytes, suggesting that they are an important stimulus for production of pro-inflammatory factors in SLE. We previously presented data showing that nucleic acid-enriched IgG-complexed MPs are also increased in asymptomatic anti-nuclear antibody (ANA) positive individuals (ANA^+NS), in the absence of elevated levels of pro-inflammatory factors. Although platelets represent the main source of MPs in healthy individuals, endothelial- and neutrophil-derived MPs are also found in SLE. In this study, we examined the origin of MPs in ANA^+NS.

Methods: Flow cytometry was used to examine the number, origin, nucleic acid content, and IgG binding of peripheral blood Annexin V^+MPs in ANA^-HC (n=18), ANA^+NS (≥1:160 by IF, n=48), and SLE patients (n=33). MP nucleic acid content was determined by staining with Syto13 and the MP cell source by staining with antibodies against CD41a (Platelets), CD105 (endothelium), CD45 (hematopoietic cells), CD14 (monocytes), CD66b (neutrophils), CD19 (B cells), CD3 (T cells), and CD235a (erythrocytes).

Results: Consistent with published work and with our previous data, SLE patients had increased levels of MPs and MP-ICs that contained higher levels of nucleic acids, as compared to ANA^- HC. A subset of ANA^+NS had similar elevations in the amount of IgG coating their MPs and nucleic acid content to those seen in SLE. As expected, the majority of the MPs obtained from HC exhibited platelet markers (**Figure A**). Notably, in ANA^+NS individuals and SLE patients the proportion of Annexin V^+ platelet-MPs was reduced compared to HC (**Figure A**) and there were increased proportions of Annexin V^+ $CD66b^+$MPs (apoptotic neutrophils-MPs) and $CD45^+$MPs (hematopoietic) **(Figure B and**



C). However, the proportion of neutrophil-MPs was significantly higher in SLE than in ANA$^+$NS (**Figure B)**. There were non-statistically significant trends to higher CD14$^+$MPs (monocytes-MPs) and endothelial MPs in ANA$^+$ NS. There were no CD19, CD3, or CD235a positive MPs detected.

Conclusion: Apoptotic and/or activated neutrophils and hematopoietic cells are a significant source of auto-antigenic MPs in both ANA$^+$NS individuals and SLE patients. However, neutrophil apoptosis/activation appears to be more prominent in SLE patients, raising the possibility that it contributes to the pro-inflammatory process that discriminates symptomatic and asymptomatic ANA$^+$individuals.

Disclosure: C. Muñoz-Grajales, None; **D. Bonilla**, None; **E. Silverman**, None; **S. Johnson**, Bayer, 2, Boehringer Ingelheim, 2, 5, Corbus, 2, Ikaria, 5, Roche, 2; **A. Bookman**, None; **Z. Touma**, Janssen Research & Development, LLC, 2, Janssen Scientific Affairs, LLC, 2; **Z. Ahmad**, None; **L. Hiraki**, None; **J. Wither**, None.

Abstract Number: 1024

Lysosome Defects in SLE Promote the Accumulation of Nuclear Antigens on the Surface of Hematopoietic Cells

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Background/Purpose: Impaired clearance of cell debris allows nuclear self-antigens such as DNA to accumulate, bind autoreactive IgG and form immune complexes (IgG-ICs) in SLE. We recently reported that multiple models of lupus-prone mice harbor defects in lysosome acidification. Reduced acidification diminishes the degradation of IgG-ICs and induces their recycling back to the plasma membrane. This perpetuates FcγR signal transduction which in turn further impairs lysosome function, and promotes BAFF secretion. The sustained presence of IgG-ICs in the endocytic pathway causes phagolysosome membrane permeability allowing IgG-ICs to enter the cytosol, activating Type I IFN and inducing pyroptosis. In this study, we translate our murine findings and assess whether lysosomal defects and surface accumulation of DNA-containing ICs are evident in active vs inactive SLE patients.

Methods: We enrolled ANA positive active or inactive SLE patients (SLEDAI ≥ 6, or ≤ 5 meeting 2012 SLICC criteria) and seropositive (RF/CCP) active rheumatoid arthritis (RA) patients (2010 ACR criteria and DAS28 >5.1). Healthy controls (HCs) were enrolled from a platelet donation center.

The levels of surface-bound antigen (DNA or CCP) from circulating hematopoietic cells (monocytes, dendritic cells, T and B cells), in SLE, RA and HC were analyzed by flow cytometry. Lysosomal pH was measured using ratiometric flow cytometry from whole blood cells treated with exogenous IgG-ICs. Lysosomal pH changes were normalized to cells treated with Concanamycin A, an inhibitor of lysosome acidification.

Results: We measured relative lysosome pH in blood monocytes and B cells from 18 active and 16 inactive SLE patients with 16 HCs. Among active SLE patients, 67% of monocytes and 50% of B cells showed defective pH changes

Table 1. Lysosomal pH Changes in SLE patients.

	Time points			Healthy Mean +SD	# of patients	Total # of Patients analyzed	%
CD14+	T30			0.84			
		Active patients	above Healthy Mean+SD		16	18	88.89
			below Healthy Mean+SD		2	18	11.11
		Inactive Patients	above Healthy Mean+SD		11	16	68.75
			below Healthy Mean+SD		5	16	31.25
	T60			0.85			
		Active patients	above Healthy Mean+SD		12	18	66.67
			below Healthy Mean+SD		6	18	33.33
		Inactive Patients	above Healthy Mean+SD		1	16	6.25
			below Healthy Mean+SD		15	16	93.75
CD19+	T30			0.975			
		Active patients	above Healthy Mean+SD		8	18	44.44
			below Healthy Mean+SD		10	18	55.56
		Inactive Patients	above Healthy Mean+SD		1	16	6.25
			below Healthy Mean+SD		15	16	93.75
	T60			0.97			
		Active patients	above Healthy Mean+SD		9	18	50.00
			below Healthy Mean+SD		9	18	50.00
		Inactive Patients	above Healthy Mean+SD		2	16	12.50
			below Healthy Mean+SD		14	16	87.50

Table 2. Crosssectional study of the level of surface bound DNA on hematopoietic cells from lupus patients.

		SLE				RA	
		Active SLEDAI ≥ 6	Inactive SLEDAI ≤ 5	HC	*p* compared to HC	RA patients	HC
CD19+	N	57	52	109		8	5
	Surface DNA (MFI)	22.94	11.53	4.99	0.000000161	1.47	1.08
	Surface DNA (Fold over HC)	4.60	2.31	1.00		1.36	1.00
CD3+		51.00	47.00	98.00		8.00	5.00
	Surface DNA (MFI)	4.57	2.70	3.00	0.0490	1.10	1.00
	Surface DNA (Fold over HC)	1.52	0.90	1.00		1.10	1.00
CD14+		57.00	51.00	109.00		8.00	5.00
	Surface DNA (MFI)	13.49	12.99	9.64	0.0217	6.31	3.45
	Surface DNA (Fold over HC)	1.40	1.35	1.00		1.83	1.00
CD14-CD19-CD11chi		29.00	19.00	46.00		8.00	5.00
	Surface DNA (MFI)	24.99	17.17	12.65	0.0273	12.97	17.95
	Surface DNA (Fold over HC)	1.98	1.36	1.00		0.72	1.00

at 60 min (relative pH greater than mean+SD of HC). Of inactive SLE patients, only 6% of monocytes and 13% of B cells showed defective lysosomal acidification (Table 1).

To define whether altered lysosome function promoted accumulation of IgG-ICs, we measured surface DNA levels in 57 active and 51 inactive patients and 109 HCs. We found a significant increase in surface DNA on B cells (4.6 fold) and dendritic cells (2.0 fold), but not on T cells (1.5 fold) or monocytes (1.4 fold) in active SLE vs. HC. Levels of surface DNA on B cells were significantly higher in active versus inactive patients (Table 2). Conversely, 14 active RA patients did not show elevated surface DNA or CCP on any cell type.

Conclusion: We show that monocytes and B cells from active, but not inactive, SLE patients exhibit significantly diminished lysosome function, and that B cells and DCs accumulate surface DNA. The lower level of antigen on monocytes may reflect migration of activated monocytes from blood, because in mice, we also observed that blood monocytes do not exhibit high levels of surface nuclear antigens unlike splenic macrophages from the same animal. The mechanisms underlying accumulation of nuclear antigen on T cells remain unclear. Last, elevated levels of nuclear antigens were not present on active RA controls, suggesting that the defect is driven by mechanisms unique to lupus.

Disclosure: S. Kang, None; **J. Rogers**, None; **S. Sheikh**, GSK, 5; **M. Clowse**, GSK, 2, UCB, 5; **L. Criscione-Schreiber**, None; **B. Vilen**, None.

Abstract Number: 1025

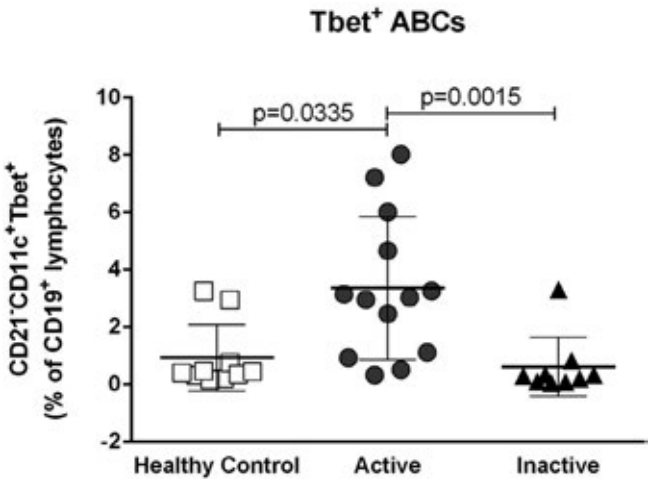
Dynamic Changes During SLE Flare Implicate Age-Associated B Cells and Altered T Follicular and Peripheral Helper Cell Responses in Disease Activity

Kieran Manion,[1] Zahi Touma,[2] Dennisse Bonilla,[2] Dafna Gladman,[3] Murray Urowitz,[2] and Joan Wither[4], [1]Krembil Research Institute, Toronto, ON, Canada, [2]University Health Network, University of Toronto, Toronto, ON, Canada, [3]Krembil Research Institute, U of Toronto, Toronto, ON, Canada, [4]University Health Network, Krembil Research Institute, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is a chronic autoimmune disorder in which periods of relative disease inactivity are punctuated by flares that present with increased inflammation and tissue damage. The current literature suggests that this enhanced disease activity is linked to immune cell subsets involved in ANA production, including T follicular (T_{fh}) and peripheral helper (T_{ph}) cells, plasma cells, and age-associated B cells (ABCs); however, it is largely unknown how these and other immune subsets differ between flare and inactive disease, particularly in individual patients followed longitudinally.

Methods: 12 healthy controls (HC), 23 SLE patients with flare (Active) and 9 inactive SLE patients (Inactive) were recruited. All patients had a diagnosis of SLE based on the 1997 ACR criteria. Active patients had to be within 1 month of flare onset (defined as a clinical SLEDAI-2K≥0 requiring a change in therapy) and agree to follow-up assessments at 6 and 12 months. Inactive patients had to be inactive for ≥1 year (clinical SLEDAI-2K=0) and be on ≤10mg prednisone at recruitment. Peripheral blood mononuclear cells (PBMCs) were isolated over a Ficoll gradient within 3 hrs of collection, stained with fluorescent antibodies for immune cell subsets, and examined by flow cytometry. Statisti-

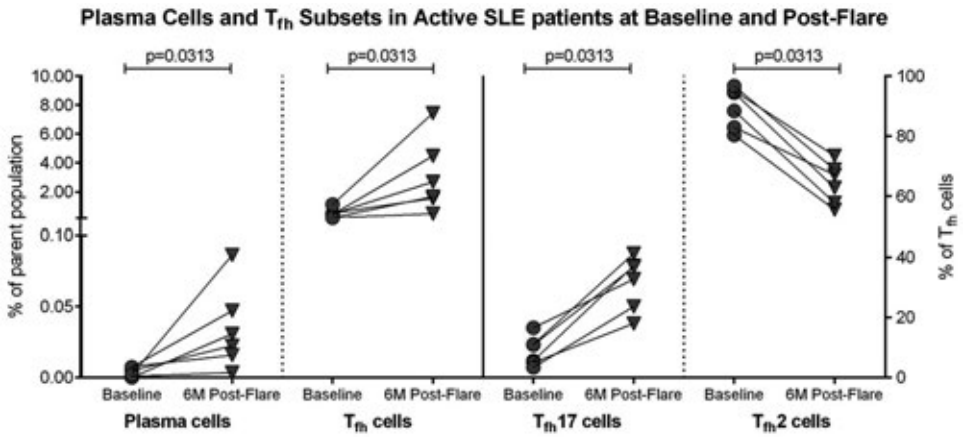


Tbet+ age-associated B cells (ABCs; CD19+CD21-CD11c+Tbet+) are significantly elevated in SLE patients experiencing a flare as compared to healthy controls or inactive SLE patients.

cal significance was determined using Kruskal-Wallis tests to compare HC, active and inactive SLE groups, Wilcoxon matched-pairs signed rank tests to compare baseline and follow-up visits, and Spearman tests for correlation.

Results: While active and inactive patients had increased proportions of T_{ph} cells ($CD4^+PD1^{hi}CXCR5^-$) compared to HC, only a small subset of patients in either group had elevated levels of plasma cells ($CD19^{lo}CD27^{hi}CD38^+CD138^+$), plasmablasts ($CD19^{lo}CD27^{hi}CD38^+CD138^-$) and activated memory T_{fh} cells ($CD4^+PD1^{hi}CXCR5^{hi}$), with no differences between the two groups. In contrast, active patients had significantly more ABCs ($CD19^+CD21^-CD11c^+Tbet^+$) than inactive patients or HC and this correlated significantly with T_{ph} cells (r=0.6909, p=0.0226). Interestingly, at their 6-month follow-up visit, active patients showed significant increases in T_{fh} and plasma cells, and trends to increased $CD86^+$ B and T_{ph} cells, despite improvements in their SLEDAI-2K. These findings suggest that activated T and B cells may be depleted from the blood during flares, possibly as a result of tissue recruitment. Notably, increases in activated memory T_{fh} cells post-flare were predominantly due to increases in the $T_{fh}17$ subset, while the $T_{fh}2$ subset was significantly decreased.

Conclusion: Our results show that while T_{ph} cells and ABCs are elevated in active SLE, plasma cells and activated T_{fh} cells may be depleted from the peripheral blood during acute flare and return to the blood post-flare, reflecting



Left Y-axis: Plasma cells (CD19loCD27hiCD38+CD138+) and T follicular helper cells (Tfh; CD4+PD1hiCXCR5hi) are significantly elevated in the blood of SLE patients at 6-months post-flare compared with baseline. Right Y-axis: Tfh17 cells (CD4+PD1hiCXCR5hiCXCR3-CCR6+) are significantly elevated in SLE patients 6-months post-flare compared with baseline, while Tfh2 cells (CD4+PD1hiCXCR5hiCXCR3-CCR6-) show a significant decrease.

recruitment to and subsequent release from tissues. These findings highlight the importance of longitudinal studies in individuals with active SLE.

Disclosure: K. Manion, None; **Z. Touma**, Janssen Research & Development, LLC, 2, Janssen Scientific Affairs, LLC, 2; **D. Bonilla**, None; **D. Gladman**, None; **M. Urowitz**, Janssen Research & Development, LLC, 2, UCB Pharma, 9; **J. Wither**, None.

Abstract Number: 1026

Interferon Lambda Promotes Age-Associated B Cells

Jennifer Barnas,[1] Nida Meednu,[1] Andrew McDavid,[1] Jennifer Albrecht,[1] Christopher Richardson,[1] R. John Looney,[2] and Jennifer Anolik[1], [1]University of Rochester Medical Center, Rochester, NY, [2]University of Rochester Medical Center, Rochester

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Age-associated B cells (ABC), defined as CD11c+ T-bet+ or CD11c+CD21-, represent a subset of B lymphocytes that are increased in systemic lupus erythematosus (SLE) patients. ABC are posited to differentiate into autoreactive plasma cells in autoimmune disease. We and others reported that this population is found within the naïve and memory B cell compartments, but are most expanded in the IgD- CD27- CD24- CD21- (DN2) B cell subset. Using flow cytometry, we have previously shown that DN2, T-bet+, and CD11c+CD21- peripheral blood B cells correlate with interferon lambda (IFN-λ) serum levels, and numbers of ABC increase with SLE disease activity. An interferon stimulated gene (ISG) expression profile is found in many cell types in SLE, including B cells, and interferon is thought to be important to lupus pathogenesis. IFN-λ is known to generate an IFN signature similar to that of IFN alpha in epithelial cells, but few studies address IFN-λ effects on B cells. We hypothesized IFN-λ contributes to the gene expression profile seen in SLE and impacts B lymphocytes.

Methods: Human peripheral blood from healthy donors (n=6) or SLE (n=8) patients meeting ACR criteria were stained for CD11c, CD19, CD14, CD27 and IgD then flow sorted into CD14+ (monocytes), CD27- IgD- CD19+ (DN B cells), or CD27-IgD+ CD19+ (naïve B cells) populations and their RNA isolated for RNA-Seq transcriptomic analysis. B cells were cultured with IL-21, anti-Ig, R848 and BAFF to generate ABC-like cells *in vitro* with no IFN, interferon gamma (IFN-γ), IFN-λ1 or both for RNA isolation (4 hours) or flow cytometry (7 days). TBX21 (T-bet) and IFIT1 (an ISG) expression was measured by qRT-PCR. Cells were stained for CD3, CD11c, CD19, CD21, CD27, CD38, IgD and T-bet.

Results: Of the CD19+ cells used for transcriptional analysis, 5.2±3.0% of healthy donors and 9.6±7.9% of SLE B cells were CD11c+ as detected during the flow cytometry sort. Using RNA-Seq transcriptional analysis, IFN-λ receptor (IFNLR1) was expressed in B cells but was absent from monocytes. Expression in naïve B cells was 40 counts/million reads for healthy and 53 counts/million in SLE. The DN compartment had higher IFNLR1 expression with 66 counts/million in healthy and 131 counts/million in SLE. IFN-λ1 induced expression of IFIT1 *in vitro* suggesting that the IFN-λ receptor is indeed functional in B cells. When B cells were cultured in the presence of IFN-γ, TBX21 expression was strongly induced. IFN- λ1 could not be substituted for IFN-γ for the generation of CD11c+ CD21- cells as measured by flow cytometry or TBX21 expression at the RNA level. However, the combination of IFN-γ and IFN-λ1 resulted in an increased percentage of CD11c+ CD21- B cells at 7 days.

Conclusion: ABC are most represented in the DN2 B cell compartment. The DN2 B cells have the highest level of expression of IFNLR1. IFNLR1 is functional on B cells as ISG expression is increased when stimulated with IFN-λ1.

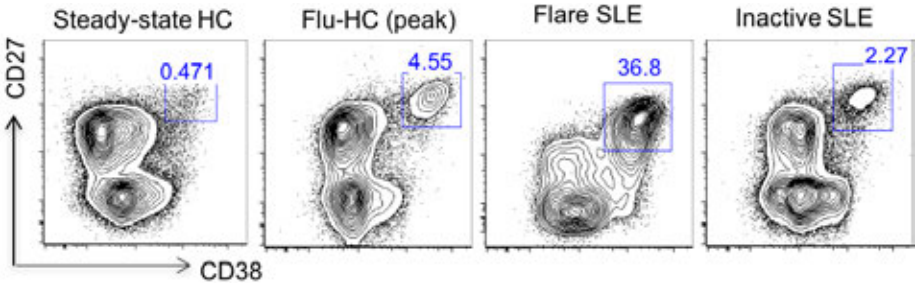
Studies are ongoing to determine if IFN-λ1 has differential effects on different B cell compartments, alters B cell differentiation pathways including generation of autoreactive plasma cells (PC), or enhances ABC and PC survival, thus potentiating SLE disease pathogenesis.

Disclosure: J. Barnas, Rheumatology Research Foundation, 2; **N. Meednu**, None; **A. McDavid**, None; **J. Albrecht**, None; **C. Richardson**, None; **R. Looney**, None; **J. Anolik**, None.

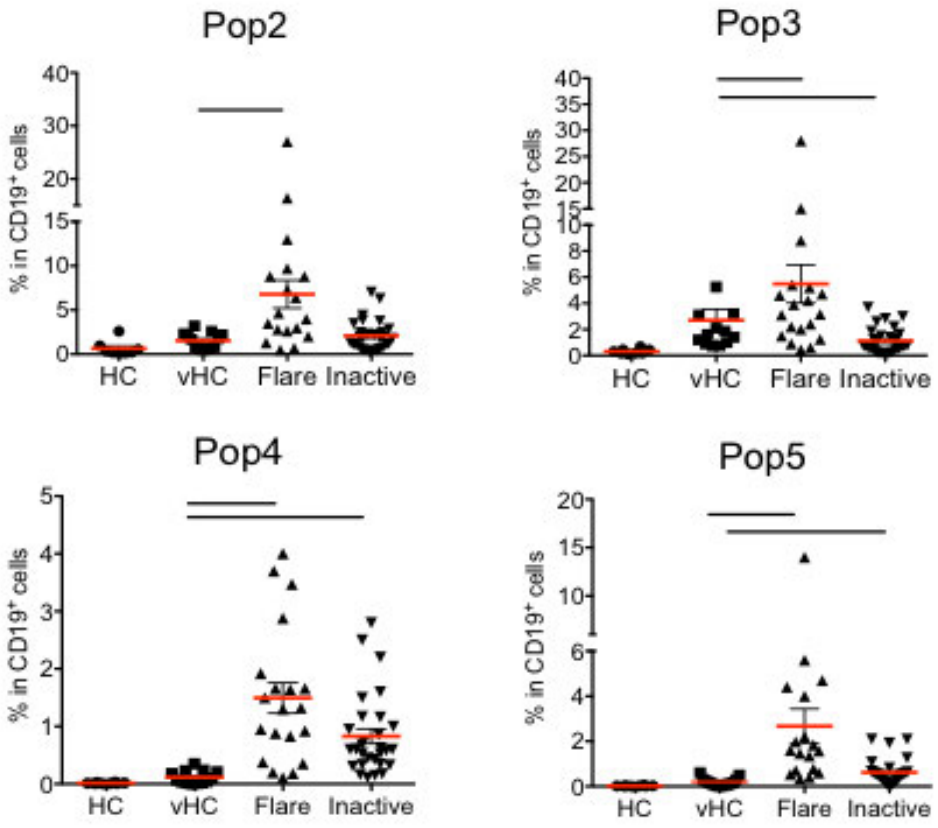
Abstract Number: 1027

Characterization of Antibody Secreting Cells in Patients with Active Systemic Lupus Erythematosus

Weirong Chen,[1] Sohee Hong,[2] Christopher Tipton,[1] Jennifer Hom,[1] Fabliha Anam,[3] Eun-Hyung Lee,[1] and Iñaki Sanz[1], [1]Emory University, Atlanta, GA, [2]Emory Univeristy, Atlanta, [3]Emory University, Atlanta



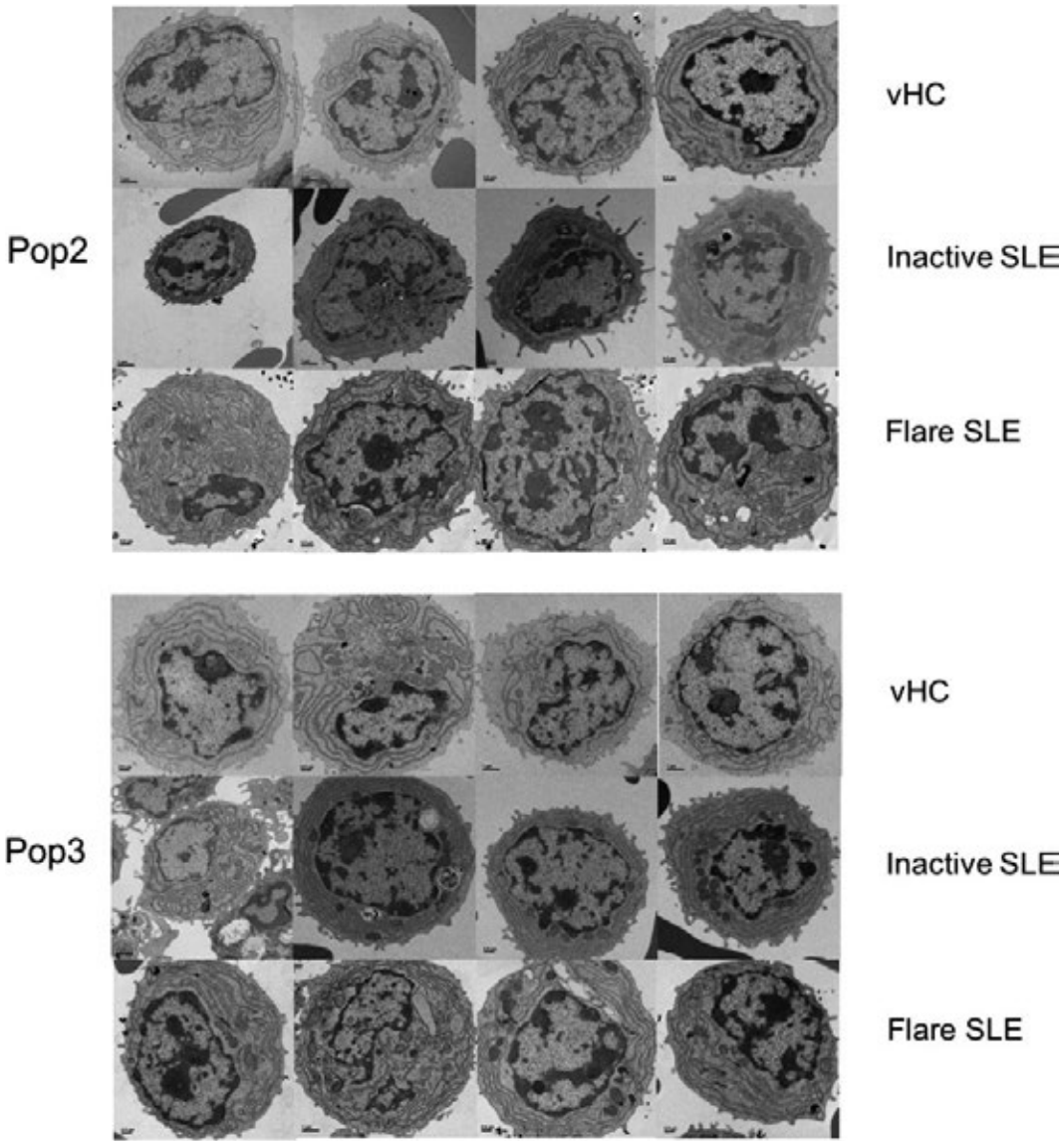
Rise of the circulating antibody-secreting cells in SLE patients during flare.



All ASC subsets are markedly increased in flaring SLE patients.

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a severe systemic autoimmune disease in which multiple autoantibodies against nuclear, cytoplasmic and cell surface auto-antigens are produced by antibody secreting cells (ASCs). In the non-disease state, the frequency of circulating ASCs in total B cells is extremely low, and increases in a tightly regulated manner following immunization or infection. However, during active SLE, ASCs are dysregulated and exhibit a dramatic increase in the circulation. Indeed, the frequency of ASCs in the peripheral blood is correlated with disease activity, as measured by the SLEDAI scoring system. Despite their clinical significance, the subsets, morphology, and molecular phenotypes of circulating ASCs in SLE remain largely unknown.



Ultra structural morphology of ASC subsets from SLE patients and healthy subjects.

Methods: Healthy subjects received the vaccination against influenza virus were recruited and peripheral blood from healthy controls was obtained at the steady state or at the peak of antibody secreting response after vaccination (day

6-7). Patients with SLE fulfilled four or more criteria of the modified American College of Rheumatology classification were recruited and evaluated by expert rheumatologists for disease status.

Results: In this study, peripheral ASC were divided into 4 subsets based on the surface expression of the CD19 and CD138: CD19+CD138- (pop2), CD19+CD138+ (pop3), CD19-CD138- (pop4), and CD19-CD138+ (pop5). CD19+ subsets, and to a larger extent, CD19- subsets, were markedly increased in active SLE patients compared to healthy controls post flu-vaccination. Besides, electron microscopy showed ultrastructural changes in the circulating ASCs subsets from active SLE patients relative to those from vaccinated healthy controls, including a condensed nucleus, enhanced endoplasmic reticulum volume, increased numbers of mitochondria, and presence of autophagosomes, features resembling those of bone marrow plasma cells. Interestingly, phenotypic characterization of circulating ASCs suggested that those from active SLE patients had significantly elevated expression of CXCR4, receptors for homing and survival in the bone marrow, compared to healthy controls post vaccination. Furthermore, next generation sequencing was used to analyze the clonality and connectivity between circulating ASC subsets from active SLE patients. In most flare SLE patients, we observed highly polyclonal repertoire and clonal relatedness in all ASC subsets.

Conclusion: Together, these data show that, during flare SLE, ASCs dramatically increase and undergo morphological changes and CXCR4 upregulation, indicating their potential of bone marrow homing and becoming long-lived plasma cells.

Disclosure: W. Chen, None; **S. Hong**, None; **C. Tipton**, None; **J. Hom**, None; **F. Anam**, None; **E. Lee**, None; **I. Sanz**, None.

Abstract Number: 1028

Lupus Auto-antibodies Act as Positive Allosteric Modulators at GluN2A-containing NMDA Receptors to Induce Excitotoxicity and Spatial Memory Deficits

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with Systemic lupus erythematosus (SLE) experience various peripheral and central nervous system manifestations including spatial memory impairment. A subset of auto-antibodies (DNRAbs) cross-react with the GluN2A and GluN2B subunits of the NMDA receptor (NMDAR). The underlying subunit specificity for DNRAbs to mediate SLE neuropathological effects are currently unknown. Here, we characterize the specific subunit effects of DNRAbs on NMDA receptors.

Methods: We employ whole-cell and single-channel patch clamp electrophysiology to study the mechanism of potentiating NMDAR currents by DNRAbs. We employ primary neuronal cell cultures, pharmacology, and ICC to test for subunit-specific NMDAR antagonists to block DNRAb-mediated cell death. We employ transgenic animals to selectively knock out NMDAR subunits for immunohistochemistry, microglia assessment, *in vivo* place field recordings, and spatial memory behavior testing.

Results: We find that these DNRAbs act as positive allosteric modulators on NMDARs with GluN2A-containing NMDARs, even those containing a single GluN2A subunit, exhibiting a much greater sensitivity to DNRAbs than those with exclusively GluN2B. Accordingly, GluN2A-specific antagonists provide greater protection from DNRAb-mediated neuronal cell death than GluN2B antagonists. Using transgenic mice to perturb expression of either GluN2A or GluN2B in vivo, we find that DNRAb-mediated disruption of spatial memory characterized by early neuronal cell death and subsequent microglia-dependent pathologies requires GluN2A-containing NMDARs. Finally, spatial memory defects resulting from aberrant hippocampal place fields affected by DNRAbs require GluN2A-containing NMDARs as well.

Conclusion: Our results indicate that GluN2A is the primary subunit that drives DNRAb-mediated NMDAR potentiation, and SLE cognitive/spatial memory defects. Thus, GluN2A-specific antagonists or negative allosteric modulators are strong candidates to treat SLE patients with nervous system dysfunction.

Disclosure: K. Chan, None; **J. Nestor**, None; **T. Huerta**, None; **C. Kowal**, None; **P. Huerta**, None; **B. Volpe**, None; **B. Diamond**, GSK, 5, Jansen, 5, Lilly, 5; **L. Wollmuth**, None.

Abstract Number: 1029

Epstein-Barr Virus Interleukin 10 in SLE Pathogenesis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease characterized by periods of elevated and suppressed disease activity. Epstein Barr Virus (EBV) has been associated with SLE. EBV maintains latency in infected B cells and shows intermittent reactivation. Response to EBV can lead to loss of tolerance to lupus autoantigen Ro/SS-A by molecular mimicry and epitope spreading. Elevated levels of EBV Viral capsid antigen (VCA) and Early Antigen (EA) IgG, which are indirect measures of viral reactivation, increase the probability of transitioning to SLE in unaffected family members, which underscores the importance of EBV reactivation in SLE autoimmune responses. Viral IL10 (vIL10), an EBV lytic protein, is a homolog of interleukin 10, and we showed increased plasma vIL-10 in SLE patients compared to controls. In this study we aimed to understand the importance of vIL-10 in SLE clinical disease progression.

Methods: Plasma from 28 SLE patients with varying disease activity and 19 matched healthy unrelated controls were concentrated and vIL10 detected by western blotting and normalized to pooled control sera. Plasma cytokines were measured by xMAP assays. EBV EA IgG were measured by ELISA. Transcriptional co-expression signature module scores were calculated from Illumina Beadchip Microarray gene expression data for 29 immune pathway related modules.

Results: The levels of vIL-10 correlated with EA IgG ($r=0.4468$, $p=0.0044$). vIL-10 and EA IgG correlated with IFN gene expression module score ($r=0.604$, $p=0.006$, $r=0.588$, $p=0.003$, respectively). vIL10 levels additionally correlated with IFNβ, IFNg, and B cell modules. vIL-10 levels were independent of steroid, hydroxychloroquine, or immunosuppressant use or SLE disease activity. vIL-10 levels were significantly higher in patients that were Ro positive compared to Ro negative patients ($p=0.0365$). We did not observe any differences in vIL-10 levels between patients based

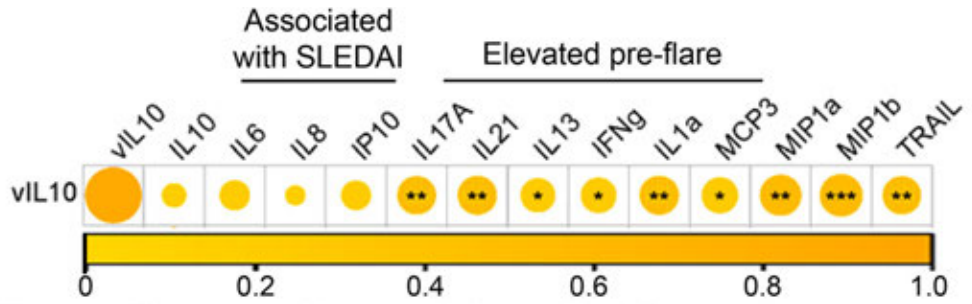

Figure 1. Plasma cytokine correlations with vIL10. Plasma cytokines were measured by xMAP assays. vIL10 measured as in Fig 1. Spearman rho were calculated and correlogram was generated in R. Color represents direction and size represents strength of correlation. *p<0.05, **p<0.01, *** p<0.001. IL-6, IL-8 and IP10 correlate with disease activity scores, while IL-17, IL-21, IL-13, IFNγ, IL1α, MCP3 are elevated pre-flare.

on dsDNA or RNP antibody positivity, nor based upon clinical ACR classification criteria. There was significant positive correlation between vIL10 levels and plasma cytokines, including: MIP1 α (r=0.5264, p=0.0020), MIP1β (r=0.5620, p=0.0008), TRAIL (r=0.4501, p=0.0097), and IL-17A (r=0.4543, p= 0.009), IL-21 (r=0.4659, p=0.0072), IFNg (r=0.3834, p=0.0303), IL-1 α (r=0.4710, p=0.0065), MCP3 (r=0.3994, p=0.0235), and IL-13 (r=0.3604, p=0.0427), which are cytokines that are elevated in SLE patient plasma prior to a flare (Figure 1). The levels of vIL-10 did not correlate with IL-6, IL-8, or IP-10 that are associated with disease activity.

Conclusion: The correlation of vIL-10 levels with B cell and anti-viral and gene expression modules supports increased EBV reactivation. The correlation of vIL-10 with cytokines elevated pre-flare suggests that increased reactivation followed by increased vIL-10 preceding a flare may initiate an inflammatory cascade that culminates in a flare. An increased vIL-10 level in Ro+ patients suggests that distinct pathways may regulate autoimmune response in patients based on autoantibody specificities.

Disclosure: N. Jog, None; **W. DeJager**, None; **J. Guthridge**, DxTerity, 2; **J. James**, Abbvie, 5, Janssen, 5, Progentec, 2, Progentec Diagnostics, Inc., 2, Xencor, 2, Xencor, Inc., 2.

Abstract Number: 1030

DNA Methylation Changes Are Associated with Particulate Matter 2.5 Exposure in SLE Patients

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with heterogeneous clinical manifestations. Epigenetic changes, including DNA methylation, have been implicated in SLE; specifically, differenc-

Table 1. Differentially methylated CpG sites by PM2.5 exposure.

probeID	logFC	P-Value	FDR P-value	Hypo/Hyper	Chr	Position	Gene	Location	Island
cg06073535	-0.048	1.34E-09	0.001	Hypo	11	733406			N_Shore
cg01232185	-0.026	8.46E-09	0.0032	Hypo	11	43425992	*TTC17*	Body	
cg16065769	-0.034	1.54E-08	0.0038	Hypo	4	52903163	*SGCB*	Body	N_Shore
cg00347818	-0.02	3.49E-08	0.0047	Hypo	8	130692530	*CCDC26*	TSS200	
cg01109289	-0.032	3.87E-08	0.0047	Hypo	2	100206998	*AFF3*	Body	N_Shelf
cg08848269	-0.03	4.36E-08	0.0047	Hypo	1	39282666			N_Shore
cg21550295	-0.019	3.82E-08	0.0047	Hypo	7	128551923	*KCP*	TSS1500	S_Shore
cg14164044	0.02	5.62E-08	0.0053	Hyper	15	89952135			N_Shore
cg13938257	-0.024	1.81E-07	0.015	Hypo	12	59175690			
cg10541663	-0.028	2.33E-07	0.0175	Hypo	3	177528511			
cg21617903	-0.028	2.66E-07	0.0181	Hypo	3	11599713	*VGLL4*	3'UTR	
cg05448114	-0.03	3.36E-07	0.021	Hypo	6	2993082			S_Shelf
cg13592817	-0.028	4.37E-07	0.0252	Hypo	1	205017182	*CNTN2*	5'UTR	
cg09976670	-0.029	5.03E-07	0.0269	Hypo	1	5934941	*NPHP4*	Body	N_Shelf
cg00235070	-0.026	9.00E-07	0.0412	Hypo	9	128098957	*GAPVD1*	Body	
cg12764611	-0.023	9.36E-07	0.0412	Hypo	6	90635163			
cg14450543	-0.023	8.28E-07	0.0412	Hypo	7	33871304			

Table 2. Differentially methylated region by PM2.5 exposure.

Location	Value	P-Value	FWER	Hypo/Hyper	Gene
chr12: 10563947-10564015	-0.11	5.30E-06	0.04	Hypo	*KLRC3*

es in methylation have been associated with auto-antibody and lupus nephritis status. A prior study showed that closer residential proximity to highways was associated with hypomethylation of 3 CpG sites in the *UBE2U* gene in SLE patients.

Methods: In this study, we examine the association of particular matter 2.5 ($PM_{2.5}$) levels on the day of blood draw with DNA methylation in a cohort of SLE patients from the California Lupus Epidemiology Study (CLUES). All subjects satisfy the ACR criteria for SLE. $PM_{2.5}$ levels were estimated by Sonoma Technology from air pollution concentrations based on geocoded residential locations. DNA methylation was measured using the Illumina HumanMethylationEPIC BeadChip for 271 unique subjects of White, Hispanic, African American, and Asian ethnicities. Noob background subtraction with dye-bias correction as well as quantile normalization were conducted in *minfi*. CpG sites with high detection p-values, cross-reactive probes, and CpG sites potentially measuring SNPs were removed for a total of 748,793 CpG sites for analysis. We first conducted an analysis for differentially methylated position (DMPs) using *limma* linear models with empirical Bayes variance shrinkage, adjusting for age, sex, current smoking status, current medication use, estimated cell-type proportions from *ReFACTor*, and genetic ancestry. We then conducted an analysis of differentially methylated regions (DMRs) using *bumphunter*. Given the previous findings in the *UBE2U* gene, we also conducted a candidate DMP analysis for the 21 CpG sites on the EPIC chip which map to *UBE2U.*

Results: Concentrations of $PM_{2.5}$ fell between 1.8 and 25.9 μg/m3 (SD = 3.3) with all subjects' exposure classified as either "Good" or "Moderate" according to the Air Quality Index (AQI). Preliminary results showed 17 DMPs (after FDR correction) associated with $PM_{2.5}$ exposure, 16 of which were hypomethylated. These CpG sites mapped to genes including *TTC17, SGCB, CCDC26, AFF3, KCP, VGLL4, CNTN2, NPHP4, and GAPVD1.* One region located 900bp upstream of *KLRC3* was significantly differentially methylated after FDR correction. No CpG sites in *UBE2U* reached statistical significance.

Conclusion: These results suggest for the first time that there is differential methylation with increased $PM_{2.5}$ exposure in SLE patients.

Disclosure: O. Solomon, None; **C. Lanata**, None; **M. Dall'Era**, Biogen,, 5, Genentech, 5, Janssen Pharmaceuticals, 5, Kezar Life Sciences, 2, Pfizer, 5; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2; **P. Katz**, None; **L. Trupin**, None; **K. Taylor**, None; **J. Nititham**, None; **B. Rhead**, None; **L. Criswell**, None; **L. Barcellos**, None.

Abstract Number: 1031

Expanded Circulating Peripheral Helper T Cells Are Associated with B Cell Differentiation in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoreactive T-B cell interactions in lymphoid tissue have been thought to play a crucial role in the autoantibody production in systemic lupus erythematosus (SLE). These $CD4^+$T cells are known as follicular helper T (T_{FH}) cells expressing CXCR5, a chemokine receptor promoting cell migration to B cell follicles. Recently, a new population of 'peripheral helper' T (T_{PH}) cells that help B cell responses has been discovered in synovium of patients with rheumatoid arthritis. Like T_{FH} cells, T_{PH} cells express ICOS and PD-1, but these cells lack CXCR5. Previously we reported that circulating T_{PH} cells are increased in SLE and their activated status was associated with the disease activity. Here we assessed whether T_{PH} cells contribute to autoantibody production by B cells in SLE.

Methods: Peripheral blood mononuclear cells collected from SLE patients and healthy individuals were analyzed for T and B cell subsets by flow cytometry. T_{PH} cells were identified as $CD3^+CD4^+CD45RA^-CXCR5^-$ cells with a high expression of PD-1. The production of IL-21 by T_{PH} cells stimulated with phorbol 12-myristate 13-acetate (PMA) and ionomycin was assessed by intracellular cytokine staining and flow cytometry. To assess functional roles of T_{PH} cells in B cell maturation and antibody production, T cell populations (T_{PH}, T_{FH}, and $CXCR5^-PD\text{-}1^-$memory $CD4^+$T cells)and switched memory B ($CD19^+CD27^+IgD^-$) cells were sorted from PBMC using magnetic bead selection and a FACS Aria sorter. Sorted T cell populations and autologous B cells were co-cultured and stimulated with lipopolysaccharide (LPS) and staphylococcus enterotoxin B (SEB) for 7 days. Plasmablast differentiation was assessed by flow cytometry. Antibody levels in culture supernatants were measured by ELISA.

Results: Activated T_{PH} cells were positively correlated with SLEDAI and anti-DNA antibody titers, and were negatively correlated with serum complement levels and lymphocyte counts. The frequency of activated T_{PH} cells was correlated with that of plasmablasts and activated switched memory B cells. Lupus T_{PH} cells had the capacity to produce IL-21, a pivotal cytokine for B cell and plasma cell differentiation, as much as T_{FH} cells. T_{PH} cells from lupus patients induced B cell differentiation into plasmablasts and promoted antibody production in T-B cell co-cultures.

Conclusion: Our data demonstrate that the increased frequency and activated status of T_{PH} cells are associated with the disease activity as well as enhanced B cell responses in SLE, and T_{PH} cells provide B cell help. $CD4^+ICOS^+PD\text{-}1^+$cells and plasma cells were reported to be present in the nephritic kidneys and associated with active disease in SLE. These data indicate the contribution of T_{PH} cells to autoantibody production in aberrant lymphoid organs and the involvement of extra-follicular T-B cell interactions in the pathogenesis of SLE.

Disclosure: A. Makiyama, None; **A. Chiba**, None; **D. Noto**, None; **G. Murayama**, None; **T. Mizuno**, None; **T. Kuga**, None; **K. Yamaji**, ASAHI KASEI PHARMA, 2, Astellas pharma, 2, 8, bristol myers, 8, Chugai Pharma, 2, Janssen Pharma, 8, Mitsubishi-Tanabe Pharma, 2, 8, Sanofi Pharma, 8, Takeda Pharma, 2; **N. Tamura**, AbbVie GK, 8, AbbVie pharma, 8, ASAHI KASEI MEDICAL, 2, ASAHI KASEI PHARMA, 2, astellas pharma, 2, 8, Astellas Pharma Inc., 2, 8, AYUMI PHARMA, 2, AYUMI Pharmaceutical Corporation, 2, bristol myers, 8, Bristol-Myers Squibb, 8, Chugai Phamaceutical Co. Ltd., 2, Chugai Pharma, 2, Eisai Co., Ltd., 2, Eisai Pharama, 2, Janssen Pharma, 8, Janssen Pharmaceutical K.K., 8, Mitsubishi Tanabe Pharma Corporation, 2, 8, Mitsubishi-Tanabe Pharma, 2, 8, Sanofi K.K., 8, Sanofi Pharma, 8, Takeda Pharma, 2, Takeda Pharmaceutical Company Ltd., 2; **S. Miyake**, Bristol myers squibb, 2, Bristol-Myers Squibb, 2, Pfizer, 2, Pfizer Japan Inc., 2, Taiho pharmaceutical, 8, TAIHO PHARMACEUTICAL CO., LTD., 8.

Abstract Number: 1032

Lipocalin-2 Exacerbates Lupus Nephritis by Promoting Th1 Cell Differentiation

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Kidney involvement is a major concern in systemic lupus erythematosus (SLE). Lipocalin-2 (LCN2) has been indicated as a potential marker of the presence and severity of lupus nephritis (LN), but the role of increased LCN2 in LN and the underlying molecular mechanisms remain unclear.

Methods: LCN2 expression in naïve $CD4^+$ T cells of SLE patients was evaluated by real-time PCR (RT-PCR). LCN2 expression in renal biopsy samples from patients with lupus nephritis was detected by immunohistochemical staining. To investigate the production of LCN2 in lupus mice during progression of LN, LCN2 expression in PBMCs and naïve $CD4^+$ T cells were measured by RT-PCR, mRNA and protein levels of LCN2 in kidneys were measured by qPCR and western blot respectively at different stages of disease. To investigate whether increased LCN2 levels contribute to the development of LN, the MRL/*lpr* mice received intraperitoneal injection of anti-LCN2 antibody or recombinant LCN2. Pristane was injected to induce lupus in WT and *LCN2*-/- mice. At the end of the experiment, the renal pathology, proteinuria, spleen index were evaluated. The frequency of T lymphocyte subpopulations in spleen, lymph node and kidney was analyzed by flow cytometry. To further investigate whether LCN2 regulates Th1 differentiation, MACS-sorted WT and *LCN2*-/- naïve $CD4^+$ T cells were differentiated into Th1 cells under specific skewing condition.

Results: Here we report that the levels of LCN2 in peripheral blood and renal tissue are highly increased in LN patients and mouse models. Elevated LCN2 in $CD4^+$ T cells promote IFN-γ overexpression through upregulating

STAT4 phosphorylation. Both genetic depletion of LCN2 in pristane-induced mice or inhibition of LCN2 by injection of anti-LCN2 antibody in MRL/*lpr* mice greatly improve nephritis. The frequency of splenic or renal Th1 cells reduces in proportion to LN disease acitivity. Furthermore, administration of LCN2 exacerbates the disease with significantly higher renal activity scores accompanied by increased Th1 cells. Importantly, circulating Th1 cells and IFN-γ levels are markedly increased in LN patients, and these changes are associated with increased LCN2 levels.

Conclusion: Collectively, our findings demonstrate LCN2 is a regulator of Th1 which could be a therapeutic target for the treatment of LN.

Disclosure: W. Chen, None; **L. Sun**, None.

Abstract Number: 1033

Mass Cytometric Immunophenotyping Highlights a Dysregulated T cell-B Cell Axis in Patients with New-onset Lupus

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SESSION INFORMATION

Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The immune cell subsets most altered early in SLE disease course remain unclear. Defining abnormalities in lymphocyte populations in patients with new-onset SLE may reveal pathways that are fundamental drivers of the autoimmune response in SLE. Mass cytometry provides a powerful method to broadly assess immune cell phenotypes in samples from patients and may reveal immune cell subsets that are most prominently altered in SLE patients compared to controls.

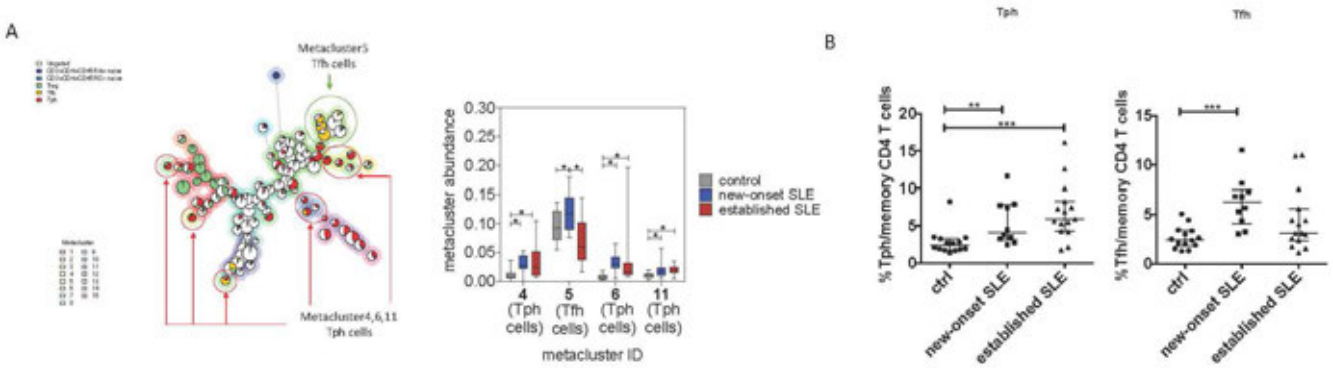

Figure 1. Expanded PD-1hi CXCR5- Tph cells and PD-1hi CXCR5+ Tfh cells in blood of new-onset SLE patients. A. FlowSOM analysis of CD45RO+ CD4+ T cells shows an increased abundance of T cell metaclusters 4,5,6,11. Metaclusters 4,6,11 are PD-1hi CXCR5- cells. Metacluster 5 is PD-1hi CXCR5+ cells. *Student's t-test p<0.05. B. Quantification of Tph cells (PD-1hi CXCR5-) and Tfh cells (PD-1hi CXCR5+) cells by biaxial gating. * p<0.05, ** p<0.01, *** p<0.001 by Mann-Whitney U test.

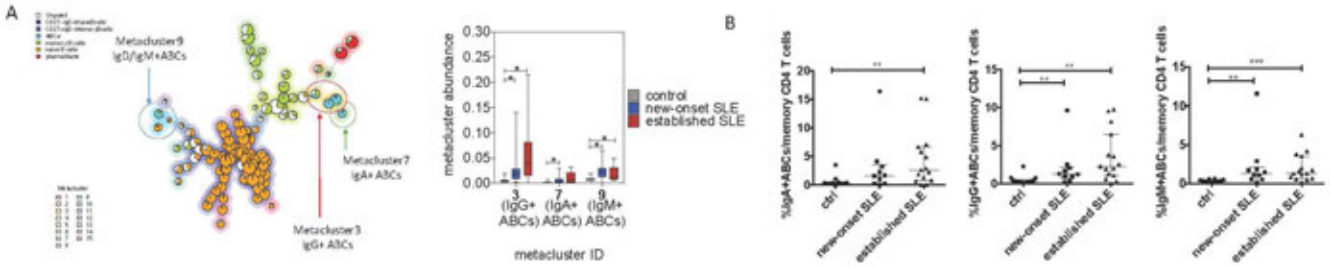

Figure 2. Expanded CD11c+ ABCs in the blood of new-onset and established SLE patients. A. FlowSOM analysis of total B cells shows an increased abundance of B cell metaclusters 3,7 and 9. Metacluster 3 is IgG+ ABCs. Metacluster 7 is IgA+ ABCs. Metacluster 9 is IgM+ ABCs. *Student's t-test p<0.05. B. Quantification of IgG+, IgA+, and IgM+ ABCs by biaxial gating. * p<0.05, ** p<0.01, *** p<0.001 by by Mann-Whitney U test.

Methods: We used two 39-marker mass cytometry panels (a T cell panel and B cell panel) to evaluate CD4+ T cells and B cells in cryopreserved peripheral blood mononuclear cells from patients with new-onset SLE (diagnosis within 6 months, n=10), compared to patients with established SLE (n=15), and non-inflammatory controls (n=14). All SLE patients met the 1997 ACR classification criteria for SLE. New-onset SLE patients were naïve to immunosuppressive therapy; hydroxychloroquine and prednisone ≤ 10mg/day were permitted. Established SLE patients were on a range of treatments. We used FlowSOM to define and quantify metaclusters of memory CD4+ T cells and B cells based on their 39-parameter characterization. We used Student's t-test to identify significantly altered metaclusters in SLE patients ($p< 0.05$). Expanded cell populations were confirmed by biaxial gating.

Results: We identified 15 metaclusters (i.e. cell populations) of memory CD4+ T cells by FlowSOM. Of these, 4 T cell metaclusters were significantly increased in new-onset SLE patients compared to healthy controls (Figure 1). Three of these 4 metaclusters were also increased in established SLE patients. Analysis of marker expression on these cell populations revealed that all 4 populations displayed high expression of PD-1 and ICOS. One of the populations also expressed CXCR5, consistent T follicular helper (Tfh) cells, while the other 3 lacked CXCR5, consistent with T peripheral helper (Tph) cells, a CXCR5- B cell-helper T cell population initially identified in RA joints. Biaxial gating confirmed a significant expansion of both Tph cells (2.0-fold, p=0.034) and Tfh cells (2.4-fold, p=0.001) in new-onset SLE patients. In the analysis of B cells by FlowSOM, we identified 3/15 B cell metaclusters significantly expanded in new-onset SLE patients (Figure 2). Cells in all 3 of these metaclusters showed a CD11c+ Tbet+ CD21- phenotype consistent with age-associated B cells (ABCs). The 3 metaclusters were distinguished by expression of distinct immunoglobulin isotypes representing IgM+, IgG+, and IgA+ ABCs. Across all patient groups, the frequency of Tph cells was positively correlated with the frequency of ABCs (r=0.34,p=0.036), including both IgG+ and IgM+ ABCs, and with the frequency of Tfh cells (r=0.44,p=0.005). Tph cells, but not Tfh cells, also showed a negative association with serum complement C3 levels (r=-0.51,p=0.017), a marker of disease activity in SLE.

Conclusion: Broad immunophenotyping analyses highlight marked expansion of Tph cells, Tfh cells, and ABCs are prominent features of the immune dysregulation in patients with new-onset, immunosuppressant-naïve SLE. These cells may be involved in the early phases of the pathologic autoimmune response in SLE.

Disclosure: Y. Cao, None; **S. Alves**, Merck, 3; **C. Sinnette**, None; **C. Speyer**, None; **G. Keras**, None; **Y. Qu**, Merck, 3; **J. Keegan**, None; **J. Lederer**, None; **D. Rao**, Janssen, 5, Merck, 2, Pfizer, 5; **K. Costenbader**, Astra-Zeneca, 2, Glaxo Smith Kline, 2, Janssen Scientific Affairs, LLC, 2, Lupus Foundation of America, 2, Lupus Research Alliance, 2, Merck, 2.

Abstract Number: 1034

Circulating MicroRNAs as Potential Biomarkers for Monitoring the Response to *In Vivo* Treatment with Rituximab in Systemic Lupus Erythematosus

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Recent studies have highlighted the potential role of microRNAs (miRNAs) as diagnostic and prognostic biomarkers in Systemic Lupus Erythematosus (SLE). While Rituximab (RTX) represents an important therapeutic option, identifying those patients who might benefit from this approach is still an unmet clinical need. This study aimed to analyze the circulating miRNAs profile in SLE patients' serum and the modulatory effect of RTX.

Methods: Twenty-seven healthy donors (HDs) and 25 SLE patients were recruited. SLE patients were clinically and serologically evaluated at baseline and after 3-month RTX treatment (375 mg/sq weekly / 4 weeks). Clinical assessment included changes in disease activity, using the SLE Disease Activity Index 2000 (SLEDAI-2K) and complete serological evaluation. Whole miRNome profile of serum samples was performed in an exploratory cohort of HDs and SLE patients before and after RTX therapy. The functional classification and target gene prediction of altered miRNAs was interrogated by Ingenuity Pathway Analysis software (IPA), which allowed us to select a set of miRNAs whose expression was validated by qPCR in the whole cohorts of patients and HDs. Changes in the levels of potential inflammatory mediators modulated by these miRNAs was also evaluated by multiplex assay.

Results: After 3-month RTX therapy, active SLE patients (SLEDAI-2K=9,5) showed a significant reduction in disease activity (SLEDAI-2K=1,5) along with reduced acute phase reactants (CRP and ESR) levels, and anti-dsDNA titers. miRNome profile showed altered expression of 153 miRNAs in SLE at baseline when compared to HDs (cut-off: 2-fold change): 142 increased and 11 reduced. Among those, the expression of 121 out of 153 (79%) miRNAs were reverted by *in vivo* treatment with RTX. The functional classification of these miRNAs revealed their association with clinical features of the SLE physiopathology such as inflammatory response, renal and haematological disease, connective tissue disorders and neurological, cardiovascular and dermatological disease, among others.

By using IPA analysis, we identified a panel of 5 microRNAs (miR-149-3p, 125b-5p, 199a-5p, 106b-3p 124-3p) that showed potential targets molecules comprising key pro-inflammatory cytokines and immune receptors, along with a high number of molecules that control intracellular pathways associated with inflammatory and autoimmune pro-

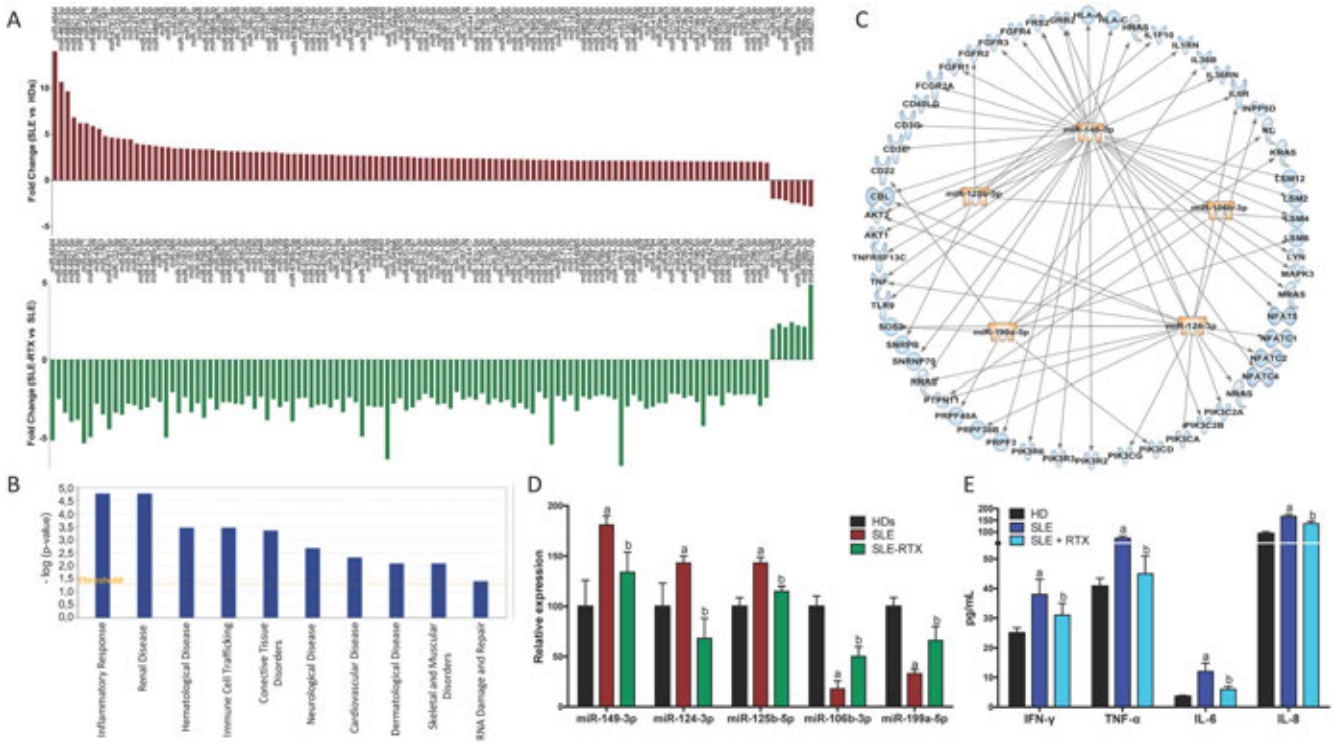

Figure 1. Autoimmunity Review-v1.

cesses. The altered expression of these selected miRNAs in SLE patients' serum vs HD was further validated in the entire cohort, along with the effect of RTX in the reversion of those levels.

Accordingly, the reestablishment of the altered circulating miRNA profile of SLE patients was accompanied by the downregulation of a set of pro-inflammatory cytokines found elevated in SLE serum, including IFNg, TNFa, IL6 and IL8.

Conclusion: Our overall data support the role of specific miRNAs as biomarkers for monitoring the response to B-depletion treatment in SLE, allowing an early identification of those patients who could benefit more from this therapy, and ultimately leading to a more tailored approach.

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Abstract Number: 1035

Examining the Transcriptional Impact of Liganded ERα in the Inflammatory Milieu of Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Etiology & Pathogenesis Poster I

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) disproportionally affects females (9:1) over males. Despite significant research effort, the exact mechanisms behind this compelling sex bias are undefined. Our prior studies demonstrate a significant role for estrogen receptor alpha (ERα) mediated inflammation in the pathogenesis of disease. NZM2410 lupus prone mice, expressing a truncated ERα functional knockout, survived longer and had significantly reduced renal disease. Yet, a complete knockout of ERα was not protective, suggesting the truncated isoform may be protective with the full-length gene necessary for disease.

Methods: Our goal is to identify the molecular mechanisms utilized by liganded ERα in regulating the inflammatory milieu. To understand ERα function, transient transfections of full length ERα and a shortened isoform ERα46 (lacking the AF-1 activation domain and similar to the functional knockout) were performed in MDA-MB-231 cells, which lack ERα and mRNA of inflammatory cytokines and cellular proliferation markers examined. Additionally, we identified ERα associated target genes and determined differences in their expression in B cells isolated from female African American (AA) lupus patients with an average age of 45.5 years and matched healthy controls.

Results: Transfection results indicate that both ERα46 reduces ERα66 driven mRNA expression of IL-1β one hour after stimulation with a TLR4 agonist. Similar results were also obtained for the cellular proliferation and survival markers MAPK14 and KLF4. Interestingly, an additive increase in expression was seen for TFF1, another cellular proliferation marker one hour after stimulation. RNA-seq analysis indicates that 60% of ERα associated target genes were differentially expressed between patients and controls. The majority of these genes (82%) were upregulated in lupus patients compared to controls. Genes with increased expression were included TLRs, NFκB related transcription factors and IL-1β.

Conclusion: These results further support a role for ERα in the pathogenesis of SLE. Future goals include utilizing high throughput sequencing technology to examine the transcriptional impact of liganded ERα in B cells of African American pediatric lupus patients.

Disclosure: M. Lennard Richard, None; **M. Cunningham**, None; **B. Tsao**, None; **G. Gilkeson**, None.

Abstract Number: 1036

RNA Sequencing of PBMCs Reveals Estrogen-Mediated Upregulation of Micro-RNA Processing Machinery

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Etiology & Pathogenesis Poster I

Session Type: Poster Session (Monday)

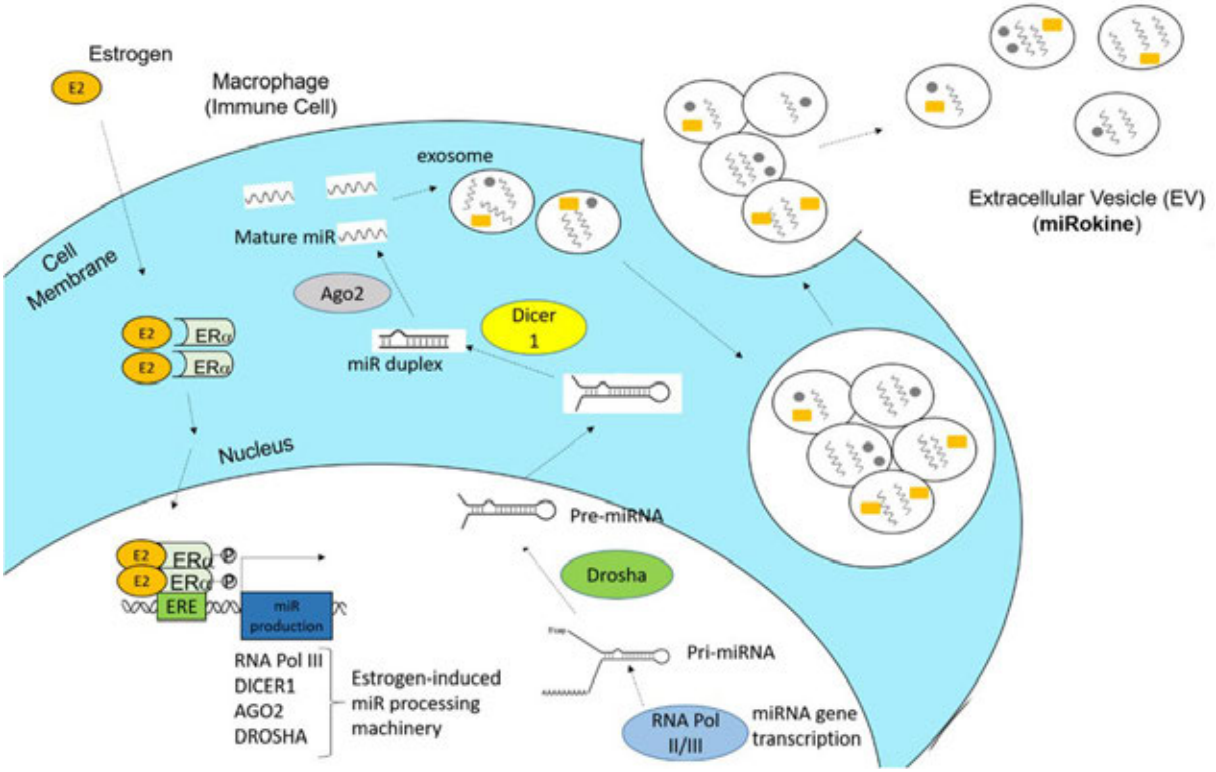
Session Time: 9:00AM–11:00AM

Background/Purpose: Studies examining intracellular micro-RNA (miR) expression in PBMCs of patients with Systemic Lupus Erythematous (SLE) have identified distinct disease-associated changes in expression. We have previously demonstrated that estrogen lowers the threshold of immune cell activation to a greater extent in females and leads to significantly enhanced toll-like receptor (TLR)7 and TLR8 expression. Moreover, our studies have also shown enhanced estrogenic responses in PBMCs from SLE patients compared to healthy controls. Furthermore, our recent data demonstrates estrogen-mediated upregulation of extracellular vesicle (EV) production via enhanced TLR8 expression in THP-1 cell lines and unique miR signatures in EVs isolated from SLE patient plasma and urine. The overall objective of the current study is to identify novel estrogen-regulated mRNAs and miRs that may be responsible, in part, for the unique miR signatures observed in EVs from SLE patients.

Methods: Our cohort for this study consisted of five post-adolescent, premenopausal, female donors. Human PBMCs were isolated from whole blood and cultured in hormone free conditions before stimulation with 10 nM of 17β-estradiol (estrogen; E2) for 24 hr. E2-treated samples were compared to untreated controls for each donor. RNA was isolated from cell lysates and RNA libraries were prepared for RNA-sequencing (RNAseq). Global RNA reads were analyzed and cross-referenced with a sequencing database (miRBase) of known miRs and mRNAs. Results for mRNA and miR data were analyzed collectively on Ingenuity Pathway Analysis (IPA) software.

Results: Analysis of our RNAseq data by IPA revealed the predicted upregulation of estrogen-dependent breast cancer signaling by canonical pathway overlay and estrogen receptor upregulation by overlap upstream analysis. Additionally, further analysis identified upregulated pathways that included several involved in miR transcription and processing. Specifically, argonaute-2 (AGO2) had an IPA overlap p-value of 0.006, which resulted from upregulation of AGO2 expression by 1.3-fold ($p < 0.01$) with E2 treatment and significant downregulation of FOS, miR-127, miR-34, and miR-27. Moreover, Dicer1 (Ribonuclease III) was also stimulated 1.3-fold ($p < 0.01$) with E2 and an IPA overlap p-value of 0.001 was observed that resulted from miR-34, miR-196, and miR-218 suppression. Also, RNA polymerase III ($p < 0.01$) and Drosha RNase III ($p < 0.01$) were found to be signafigantly induced with estrogen treatment.

Conclusion: Our data reveal a potential mechanism of estrogen-mediated miR production and pathogenic inflammation via EV signaling in SLE. In this model, estrogen would enter an immune cell, dimerize with estrogen receptor (ER) α, translocate to the nucleus, and promote the expression of miR processing machinery, including RNA polymerase III, Dicer1, AGO2, and Drosha. The resulting miRs can then be packaged along with other proteins and secreted in EVs as



Schematic of our proposed mechanism of estrogen-mediated micro-RNA production and inflammation via extracellular vesicle signaling in lupus.

extracellular signaling regulators (miRokines) that can be taken up by recipient immune cells to induce an inflammatory cascade.

Disclosure: N. Young, None; **K. Jablonski**, None; **I. Okafor**, None; **E. Schwarz**, None; **P. Harb**, None; **C. Henry**, None; **L. Wu**, None; **W. Jarjour**, None.

Abstract Number: 1037

Urinary C3d Is a Good Marker for Monitoring Treatment Response After 3 Months of Induction Treatment in Patients with Biopsy Proven Lupus Nephritis

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SESSION INFORMATION
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Session Title: SLE – Etiology & Pathogenesis Poster I
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Session Time: 9:00AM–11:00AM

Background/Purpose: Complement activation is one of the important pathogenic features of lupus nephritis and low serum complements are conventionally used to monitor disease activity in lupus Earlier we have shown that urinary C3d correlates with renal disease activity in a cross sectional study(1). In this study we sought to explore whether urine C3d correates with renal disease activity after 3 months of immunosuppressive therapy.

Methods: 37 consecutive patients of SLE who fulfilled SLE SLICC 2012 classification criteria seen between – through – month and year were included in the study of which 18 (M:F-1:17) patients were biopsy proven active nephritis (AN) (defined if there was urinary protein 1 g/day or 0.5g/day and sediment abnormalities (urine RBC or WBC count >5/hpf) or increased serum creatinine), 4(M:F-1:3) were inactive nephritis(IN), 5(All females) were non nephritis(NN) and 10(all females) were age and sex matched healthy controls . Plasma and urine samples were collected for all the patients and stored at -80. Repeat samples were taken for active nephritis patients on 3 months follow up. Clinical parameters were noted and serum C3,C4 and antiDsdna was obtained. SLEDAI and renal SLEDAI was calculated. Urine C3d was analysed using commercially available ELISA Kit and the values were normalized to creatinine excretion(pg/mg).

All statistical analysis was done using SPSS ver 23.

Results: Twelve patients achieved remission or low disease activity at 3 months. In these 12 patients the median Urinary C3d significantly decreased from 800.43 pg/mg(IQR- 115.32-1517.52) to 50.34 pg/mg, (28.43-756.17) after 3 months of treatment(p-0.01). This could be due to increase in C3d values on follow up in 6 patients in whom proteinuria was persistent and there was no response to treatment. The Area under curve(AUC) for differentiating active nephritis from inactive nephritis was 0.926 (SE- SE-0.064, 95%CI- O.8012-0.99, p- 0.009). The AUC for differentiating active nephritis from extra renal lupus was 0.647 (SE-0.117 95%CI-0.419-0.875, p -0.009) and from healthy controls was 0.906 (SE-0.061, 95%CI- 0.7872-0.99, p-0.001). There was a significant correlation of Urine C3d values with Urine protein to creatinine ratio(r-0.458, p-0.002) but no correlation was seen with serum C3, C4, antidsdna , SLEDAI and rSLEDAI.

Conclusion: Urinary C3d levels can be used to differentiate active renal from inactive renal disease and extra renal involvement. Decrease in urinary levels on follow up makes it a useful biomarker to monitor treatment. Lack of correlation with serum C3 points towards renal generation of C3d and hence an added biomarker in our current repertoire.

Reference:

1. Negi VS, Aggarwal AM, Dayal RA, Naik SI, Misra RA. Complement degradation product C3d in urine: marker of lupus nephritis.

Disclosure: S. Ganguly, None; **S. Majumder**, None; **H. Muhammed**, None; **A. Aggarwal**, None; **R. Misra**, None.

Abstract Number: 1038

Distinct Cell-bound Complement Activation Signatures Are Observed in Patients with Systemic Lupus Erythematosus

Rebecca Schriefer,[1] Gabriel Arguelles,[1] John Atkinson,[1] Dennis Hourcade,[1] and **Alfred Kim** [1], [1]Washington University School of Medicine, Saint Louis, MO

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Cell-bound complement activation products (CB-CAPs) have previously been shown to associate with SLE disease activity, but only a small fraction of total CB-CAPs has been examined. Leveraging mass cytometry, we have developed and validated a panel capable of comprehensively characterizing the types and quantities of CB-CAPs and complement receptors on human PBMCs. In this pilot study, we sought to characterize the types and amounts of CB-CAPs observed in flaring and inactive SLE and identify SLE patient stratifications based on CB-CAPs signatures.

Methods: Six paired PBMC samples from flaring and remission consented patients with 1997 ACR or 2012 SLICC classified SLE were obtained from the Washington University Lupus Clinic. Mass-tag barcoded PBMCs were stained using a validated set of 30 antibodies to cell surface markers, various CB-CAPs, and complement receptors. Stained PBMCs were run on a Helios-upgraded CyTOF2 mass cytometer, and data analyzed in Cytobank (viSNE, FlowSOM).

Results: We found that in flaring subjects, B cells possessed the greatest load of CB-CAPs compared to T cell and macrophages. Most CB-CAPs markers were absent in the paired remission samples. Evidence of classical, alternative, and common pathway activation was observed on these SLE B cells and can be categorized into six broad metaclusters. Five of the metaclusters possessed both classical and alternative pathway activation markers but differed in how completely the common pathway was activated, including 25% of B cells that did not activate C5 at all despite C3 activation. The fifth metacluster possessed only alternative and common pathway activation markers. B cell subsets of virtually every type could be found in each metacluster, with the exception of plasma cells which were devoid of any complement activation markers.

Conclusion: These data represent the first attempt to stratify SLE patients based off of CB-CAP signatures. B cells from flaring subjects broadly possess CB-CAPs, and all B cell subsets with exception of plasma cells are subject to complement activation. Subjects in remission were essentially devoid of CB-CAPs. We observed six distinct CB-CAPs signatures, with differences in the extent of classical, alternative, and common pathway activation defining these signatures. Our data may have important implications for how CB-CAPs biomarkers are best used in the clinic and clinical trials. Additionally, identification of CAPS signatures may inform investigators about which complement targets are best suited for specific individuals.

Disclosure: R. Schriefer, None; **G. Arguelles**, None; **J. Atkinson**, Kypha, Inc., 5, Compliment Corporation, 5, Gemini Therapeutics, 5, Celidex Therapeutics, 5, Clinical Pharmacy Services, 5, CDMI, 5, Omeros Corporation, 5, Achillion Pharmaceuticals, 5, True North Therapeutics, 5, BioMarin Pharmaceutical, 5, Annexon Biosciences, 5, AdMiRx, 5; **D. Hourcade**, None; **A. Kim**, Exagen Diagnostics, Inc., 5, 8, Exagen Diagnotics, Inc., 5, 8, GlaxoSmithKline, 2, 5, 8, Kypha, Inc, 2, Kypha, Inc., 2.

Abstract Number: 1039

Molecular Profiling Identifies Immunologic Subgroups and Informs Mechanism of Action of Baricitinib in SLE

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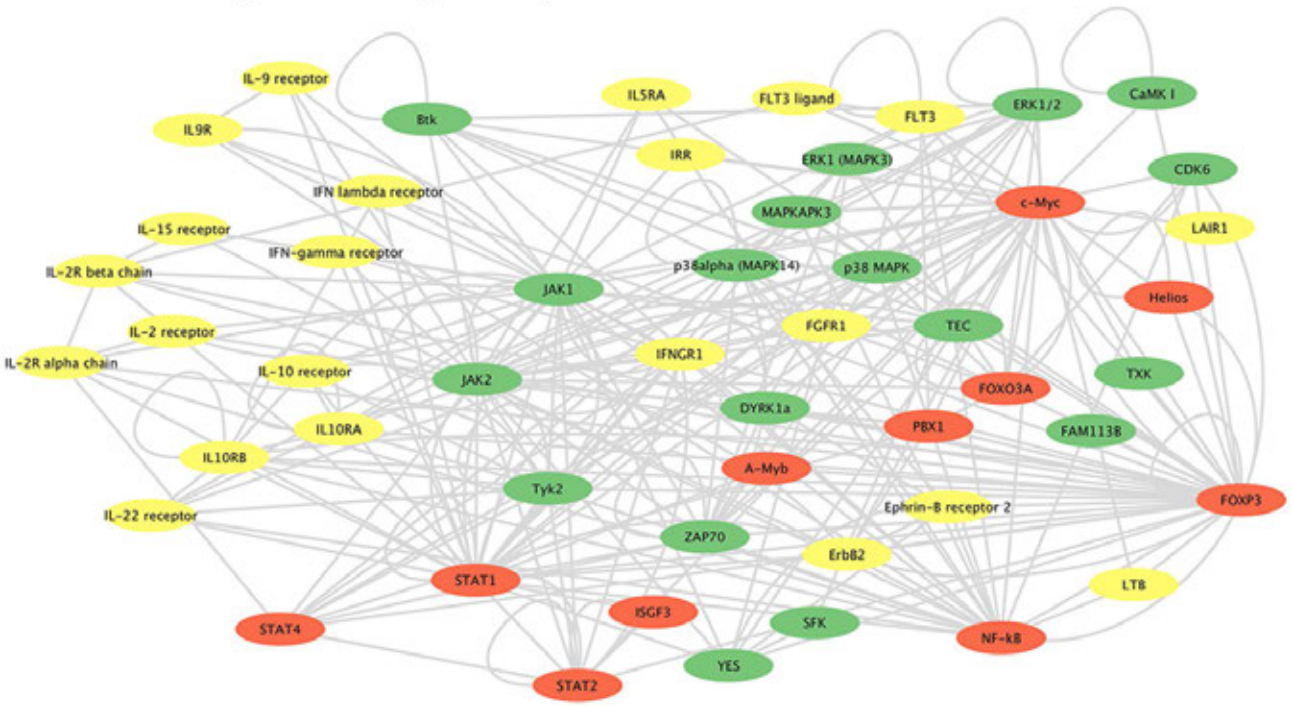
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Etiology & Pathogenesis Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Baricitinib is an oral selective Janus kinase (JAK) 1 and JAK2 inhibitor. In the Phase II, 24-week, randomized, placebo-controlled, double-blind study JAHH (NCT02708095), once-daily baricitinib resulted in significant clinical improvements in patients with active SLE receiving standard background therapy, compared with placebo.[1] We characterized the molecular and cellular immune pathways impacted by baricitinib in SLE.

Methods: A total of 314 patients were randomized 1:1:1 to receive once-daily placebo, baricitinib 2-mg, or baricitinib 4-mg for 24 weeks in study JAHH. Patients were 18 years of age or older, had a diagnosis of SLE, and had active disease involving skin or joints. Whole blood samples were obtained from patients in JAHH at baseline and weeks 2, 4, 12, and 24, and cellular and serologic immune biomarkers were measured using flow cytometry and immunochemistry assays. RNA was isolated from whole blood and analyzed using Affymetrix HTA2.0 array and quantitative PCR. Data were summarized to transcript level and analyzed using a mixed effects model on a log2 transformed response with multiplicity correction. Clinical and immunologic characteristics were compared between subgroups defined using molecular profiling.

Results: At baseline, the IFN signature negatively correlated with complement (C) 3 and C4, and positively correlated with serum immunoglobulin (Ig) G, anti-dsDNA, anti-Sm, anti-RNP, anti-Ro 52/SSA, anti-Ro 60/SSA, and anti-La/SSB in patients with active SLE. These correlations constituted a distinctive subgroup, or endotype. Serum autoantibodies and complement were not altered by baricitinib treatment, suggesting that the mechanism of action of baricitinib in SLE may be primarily through an anti-inflammatory effect. Gene expression profiling demon-

Figure. Gene network analysis of pharmacologically-induced changes in gene expression in response to treatment with baricitinib 4-mg at week 12 compared with placebo



strated that there was an elevation of *STAT1, STAT2,* and multiple IFN responsive genes at baseline in patients with SLE. Statistical and gene network analysis demonstrated that baricitinib treatment reduced the expression of functionally interconnected genes involved in SLE including *STAT1*, *STAT2*, and *STAT4*, and multiple IFN responsive genes (Figure).

Conclusion: Baricitinib treatment reduced the expression of *STAT1*, *STAT2*, and IFN responsive genes in patients with SLE. Gene network analysis revealed that baricitinib treatment reduced the expression of a network of genes associated with JAK/STAT pathways, cytokine signaling, and SLE pathogenesis, suggesting that baricitinib effects may be mediated through pharmacologic impact on multiple immune pathways.

Reference:

1. Wallace DJ et al. *Lancet*. 2018;392:222-231.

Gene network analysis of genes changed based on baricitinib's inhibition of JAK1 and JAK2 signaling and the most significantly baricitinib-induced changed genes, regardless of mechanism. The analysis includes genes changed with baricitinib 4-mg at week 12 compared with placebo. The genes included were identified by two Methods 1) the 50 genes most significantly changed with baricitinib-treatment and 2) genes that interact with JAK1 or JAK2 via transcriptional regulation or phosphorylation as defined by the curated MetaBase (www.clarivate.com) database and had an adjusted P value < 0.05. In order to graphically show the interactions, these genes, along with STAT1, STAT2, JAK1, JAK2, and TYK2 were queried against the known interactions in MetaBase, and kinases (green), ligands/receptors (yellow), and transcription factors (red) with known interactions were connected and displayed using cytoscape (cytoscape.org); genes that were not directly connected to this network or were in other categories are not shown.

Disclosure: T. Dörner, AbbVie, 5, Celgene, 5, Eli Lilly and Company, 5, 8, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Novartis Pharma AG, 5, Roche, 5, 8, Samsung, 5, 8, Sanofi, 2, UCB, 5, UCB Pharma, 2, 5; **Y. Tanaka**, Abbvie, 8, AbbVie, 5, 8, Asahi-kasei, 2, Asahi-Kasei, 2, Asahi-kasei, BMS, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Ono, Pfizer, Sanofi, Takeda, UCB, 2, Astellas, 8, Astellas Pharma, 9, Astellas Pharma, Inc., 2, 3, 5, 8, 9, Astellas, BMS, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi-Tanabe, Pfizer, Sanofic, UCB, YL Biologics, 8, BMS, 2, 5, 8, Bristol-Myers, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Daiichi-Sankyo, 2, 8, Daiichi-Sankyo, Astellas, Eli Lilly, Chugai, Sanofi, Abbvie, Pfizer, YL Biologics, Bristol-Myers, 8, Eisai, 2, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 8, Genzyme, 5, Glaxo-Smithkline, UCB, Mitsubishi-Tanabe, Novartis, Eisai, Takeda, Janssen, Asahi-kasei, 8, Janssen, 8, Mitsubishi-Tanabe, 2, 8, Mitsubishi-Tanabe, Bristol-Myers, Eisai, Chugai, Takeda, Abbvie, Astellas, Daiichi-Sankyo, Ono, MSD, Taisho-Toyama., 2, Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, 2, Novartis, 8, Ono, 2, Pfizer, 5, 8, Pfizer Inc, 8, Roche, 5, Sanofi, 2, Takeda, 2, 8, Teijin, 8, UCB, 2, YL Biologics, 8; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5; **J. Smolen**, AbbVie, 2, 5, 8, Abbvie, 2, 5, Amgen, 5, 8, AstraZeneca, 2, 5, 8, Astra-Zeneca, 5, Astro, 5, 8, BMS, 5, Celgene, 5, 8, Celltrion, 5, Celtrion, 5, 8, Chugai, 5, Eli Lilly and Company, 2, 5, Gilead, 5, GlaxoSmithKline, 5, 8, ILTOO, 5, 8, ILTOO Janssen, 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Medimmune, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, Novartis- Sandoz, 5, Novartis-Sandoz, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 5, Roche, 2, 5, Roche;, 2, 5, 8, Samsung, 5, 8, Sanofi, 5, 8, Sanofi-Aventis, 5, UCB, 5, 8; **D. Wallace**, Amgen, 5, 9, Eli Lilly and Co, 9, Eli Lilly and Company, 5, EMD Merck Serono, 5, EMD Serono, 9, Pfizer, 5, 9; **E. Dow**, Eli Lilly and Company, 1, 3; **D. Fantini**, Eli Lilly and Company, 1, 3; **R. Higgs**, Eli Lilly and Company, 1, 3; **G. Rocha**, Eli Lilly and Company, 1, 3; **B. Crowe**, Eli Lilly and Company, 1, 3; **R. Benschop**, Eli Lilly and Company, 1, 3; **A. Abel**, Eli Lilly and Company, 1, 3; **N. Byers**, Eli Lilly and Company, 1, 3; **M. Silk**, Eli Lilly and Company, 1, 3; **S. de Bono**, Eli Lilly and Company, 1, 3; **R. Hoffman**, Eli Lilly and Company, 1, 3.

Abstract Number: 1040

Proposition of a Novel Animal Model of Systemic Sclerosis Induced by Type V Collagen in C57BL/6 Mice Reproducing Fibrosis, Vasculopathy and Autoimmunity

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: A better knowledge of the mechanisms and biomarkers of skin and lung damage in systemic sclerosis (SSc) related fibrosis remain a challenge. Our aim was to characterize serological and vascular manifestations, functional and histopathological features of skin and lung in the purpose of establishing a novel SSc murine model induced by Collagen V immunization.

Methods: Female C57BL/6 mice (n=19, IMU-COLV) were subcutaneously immunized with two doses of Col V (150μg) emulsified in complete Freund adjuvant, followed by two intramuscular boosters. The control group (n=19) did not receive Col V. After 120 days, respiratory mechanics, serum autoantibodies and vascular manifestations were examined. The skin and lung inflammatory process and the collagen gene/protein expression were analyzed.

Results: After immunization, the skin of the animals presented increased thickness (28.59±1.79 vs. 22.84±0.82; p=0.0132), epidermal rectification, decreased papillary dermis, and appendages atrophy, also showing increased deposition of collagen III (20.05±2.20 vs. 11.65±1.29; p=0.0147) and collagen V (3.65±0.47 vs. 1.05±0.18; p=0.011) fibers, and increased gene expression of COL5A1 (3,15±0,80 vs. 0,90±0,32; p=0,0316) and COL5A2 (2,10±0,24 vs. 0,56±0,24; p=0,0401). Vascular changes included endothelial cell activity and apoptosis by increased expression of VEGF (21.1±1.55 vs. 6.88±0.19; p< 0,004), endothelin-1 (10.20±0.81 vs. 2.35±0.44, p< 0,0022) and caspase-3 (21.21±1.34 vs. 8.26±0.29, p=0,0007), coinciding with increased gene expression of endothelin-1 (2,02±0,32 vs. 0,78±0,07; p=0,0351), VEGF (2.26±0.37 vs. 0.97±0.11; p=0.0019) and caspase-3 (1.99±0.17 vs. 0.92±0.10; p< 001). Immunized animals presented lung dysfunction characterized by increased tissue elastance and remodeling of parenchyma by non-specific interstitial pneumonia and vascular sclerosis. Compared to controls, immunization promoted increase of total collagen (6.95±0.42 vs. 5.33±0.31, p=0,0071), collagen I (25.90±3.31 vs. 5.57±0.59; p=0.003) and V (18.53±1.05 vs. 7.53±0.41; p< 0.0001) fibers in lung parenchyma, coinciding with COL1A1 (2.34±0.40 vs. 0.85±0.12; p=0.0070), COL1A2 (2.39±0.23 vs. 1.30±0.06; p=0.0016), COL5A1 (1.80±0.32 vs. 0.97±0.13; p=0.0379) and COL5A2 (1.56±0.18 vs. 0.93±0.10; p=0.014) gene expression. Anti-collagen III (0,15±0,006 vs. 0,09±0,005; p=0,0001) and IV (1,369±0,005 vs. 0,15±0,044; p< 0,0001) and antinuclear antibodies (ANA) (p=0,001) were detected in sera from IMU-COLV.

Conclusion: We demonstrated that cutaneous, vascular and pulmonary remodeling are mimicked by type V collagen-induced SSc mice model, thus representing a suitable preclinical model to study the mechanisms and therapeutic approaches in SSc.

Disclosure: W. Teodoro, None; **A. Velosa**, None; **Z. Queiroz**, None; **L. Araujo**, None; **S. Catanozi**, None; **A. dos Santos Filho**, None; **C. Bueno**, None; **M. Vendramini**, None; **S. Fernezlian**, None; **E. Eher**, None; **J. Tomaz de Miranda**, None; **F. Lopes**, None; **S. Pasoto**, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2; **P. Sampaio-Barros**, None; **V. Capelozzi**, None.

Abstract Number: 1041

Computational Methods for Drug Repositioning of Systemic Sclerosis Using Gene Fold-Change and Network Analyses

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical trials with systemic sclerosis (SSc) patients have yet to lead to an FDA approved treatment. We have adopted a gene fold-change analysis called "IDEA" to compare cell lines from the CMAP 2.0 database with biopsies of SSc patients. Using IDEA, we can identify perturbagens that induce a genetic signature in cell lines to be more comparable with healthy controls than SSc patients. We have also created correlation networks with patient cohort gene expression data. Head nodes within these networks may be targetable via perturbagens, disrupting genes highly correlated with the SSc disease phenotype. Here, we use this method to identify several potential perturbagens that may modulate the SSc phenotype.

Methods: Raw .cel files were downloaded from CMAP 2.0, processed with RMA, quantile normalized and fit to a multichip linear model. Probes are collapsed at average intensity while gene fold-change is the ratio of treatment to control intensities followed by a $\log_2$-transformation. The data is then processed for use with the BASE algorithm. A t-test (Bonferroni corrected) is calculated to determine which perturbagens have a gene signature most similar to healthy controls when compared to either the Inflammatory or Fibroproliferative SSc patient subsets. Patient cohort data is run through WGCNA using a signed network. Modules that correlate highly with patient subsets are chosen to create their respective correlation networks.

Results: Using two independent microarray datasets, we found four overlapping perturbagens that affect the inflammatory subset and fourteen that affect the fibroproliferative subset. Using drug set enrichment analysis (DSEA), we were able to classify which drugs are more highly enriched in cell signaling pathways and immune system pathways. PI3K-inhibitors and an immunosuppressive highly regulate these pathways. WGCNA was used to create correlation networks based on genes most associated with patient gene expression subtypes. The top hub nodes for the inflammatory network were MS4A6A, CD93 and HLA-DMA, while the fibroproliferative network had IKBKG (fig. 1). These hubs and their associated genes may be key gene expression hubs to target with for intervention.

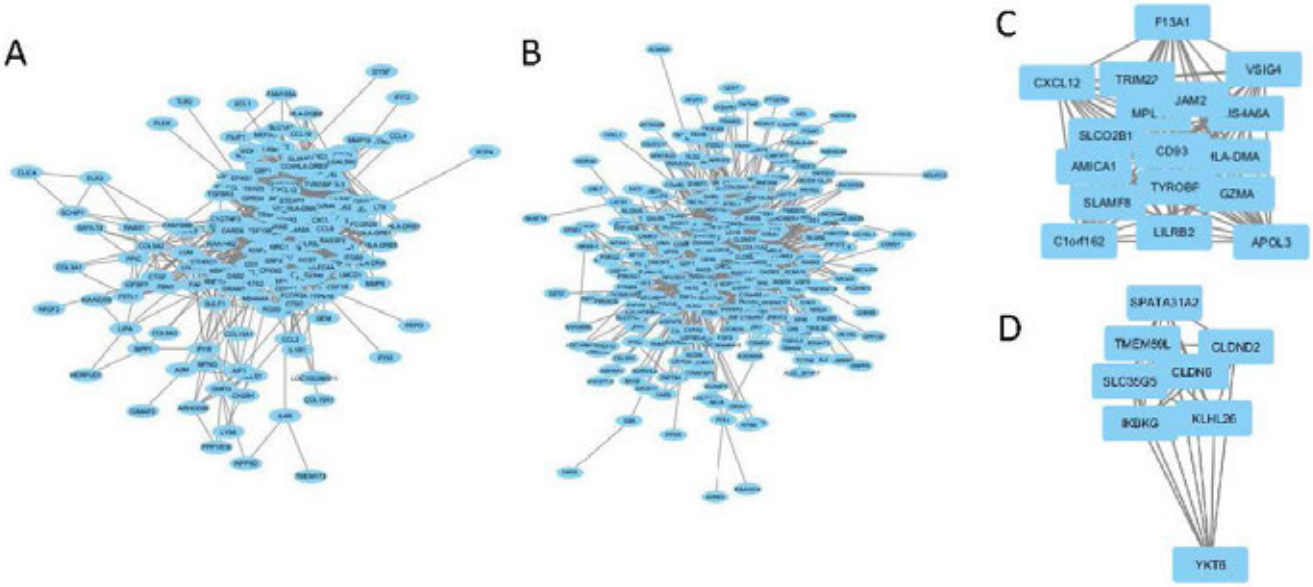

Figure 1. A) Left – Highest correlated modules with the Inflammatory subset of patients as a correlation network. B) Highest correlated modules with the Fibroproliferative subset of patients as a correlation network. C) Nodes with the highest degrees from the inflammatory network. D) Nodes with the highest degrees from the Fibroproliferative network.

Conclusion: We have identified a wide range of perturbagens ranging in mechanism of action, from anti-inflammatories to anti-psychotics and anti-biotics as potential therapeutic perturbagens of interest to further test. These perturbagens have been shown to genetically modulate the molecular pathways dysregulated in SSc, opening a different avenue towards treating the disease.

Disclosure: D. Popovich, None; **M. Whitfield**, None; **Y. Wang**, None; **G. Cai**, None; **M. Huang**, None.

Abstract Number: 1042

Thy-1 (CD90) as a Novel Marker for Tracking *in Vivo* Skin Fibrosis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Thy-1 (CD90) is a cell surface marker which is found primarily on fibroblasts and whose expression has previously been shown to correlate with pathologic subsets of fibroblasts. SSc patients have been shown to have increased circulating levels of Thy-1 and increased Thy-1 staining in skin. Assessment of fibrosis in animal models is usually limited by the need for histologic and biochemical assays to determine the course of collagen dep-

osition, ASMA expression, and other characteristic findings. We used a Thy-1-YFP reporter mouse to assess whether expression of Thy-1 can serve as a surrogate for fibrosis in vivo using the bleomycin induced skin fibrosis model.

Methods: Thy-1-YFP mice were injected with intradermal bleomycin over a time-course with 0 to 10 injections and were imaged on an IVIS spectrum in vivo fluorescent imaging system three times per week for up to 35 days. 3 mice per time point were assessed histologically and biochemically at 0, 3, 8, 14, 16, 21, 28, and 35 day time points. Skin was assessed for presence of YFP+ cells using fluorescent microscopy, for dermal thickness, for biochemical assessments of fibrosis, and for fibrogenic gene expression.

Results: SSc patients have increased Thy-1 expression in skin and this correlates with collagen and other fibrogenic gene expression and the modified Rodnan skin score (MRSS). Thy-1-YFP mice had no baseline skin Thy-1 fluorescence and began to display epi-fluorescence which was localized to the areas surrounding intradermal bleomycin injections. This was statistically increased by IVIS at day 10 and then progressively increased until 21 days at which point it began to dissipate. This pattern correlated closely with both dermal thickness and expression of fibrotic genes. Fluorescence microscopy confirmed that YFP positive cells were restricted to dermal cells with spindle-shaped fibroblast morphology.

Conclusion: Thy-1 is differentially expressed in SSc skin and correlates with extent of skin disease. In bleomycin-induced fibrosis, Thy-1-YFP mice demonstrated inducible expression with bleomycin and were useful for quantitatively tracking fibrosis progression using in vivo fluorescent imaging. Fluorescent intensity measured in vivo correlated with histologic and biochemical outcomes of fibrosis measured terminally. This system is able to track fibrosis in vivo and will allow for dynamic assessment of fibrosis over time in treatment trials to assess onset and resolution of fibrosis without requiring large numbers of experimental animals. Further studies should further assess the pathophysiologic role of Thy-1 in SSc skin fibrosis.

Disclosure: B. Korman, None; **A. Paine**, None; **S. Duemmel**, None; **M. Nuzzo**, None; **C. Ritchlin**, AbbVie, 2, 5, 9, Amgen, 2, 5, BMS, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Lilly, 5, Novartis, 5, Pfizer, 2, Pfizer Inc, 5, UCB, 2, 5.

Abstract Number: 1043

The Metabolic Intermediate Alpha-Ketoglutarate Suppresses the TGFβ-driven Profibrotic Responses of Dermal Fibroblasts

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Metabolic perturbations are emerging as drivers of fibroblast activation in fibrosis. Transcriptomic analyses have shown the enrichment of glycolysis and suppression of tricarboxylic acid (TCA) cycle in fibrotic human skin, which could favor the development of skin fibrosis (Zhao et.al Nat Metab 2019). Here we explored, whether TGFβ can induce metabolic alterations in dermal fibroblasts (DF) and whether dimethyl alpha-ketoglutarate (αKG), the key TCA metabolite, can influence the TGFβ-driven profibrotic responses in DF.

Methods: Human DF from healthy controls (HC, n=3-7) and patients with systemic sclerosis (SSc, n=4-8) were treated with TGFβ and/or αKG (6 mM). Apoptosis was measured with flow cytometry using Annexin V assay. Overall metabolic activity was assessed by the Alamar blue assay. Gene expression was analyzed by qPCR. Protein amounts (fibronectin, αSMA) were measured with Western blot. Contractile properties of DF were assessed by gel contraction assay. Significance ($p< 0.05$) was determined by one sample t test or ANOVA with Tukey's correction for multiple comparisons.

Results: The basal mRNA expression of genes involved in metabolism, e.g. *GPI*, *ACO1* and *SUCLA*, differed between DF from HC and SSc patients ($p< 0.05$). TGFβ increased the overall metabolic activity of DF (p=0.01, mean x-fold±SD 1.22±1.2 above background) as assessed by the Alamar blue assay and significantly ($p< 0.05$) upregulated mRNA levels of the core components of glucose uptake and glycolysis (*GLUT1, PGK1, PGAM1, ENO*), the TCA cycle (*SUCLA, MDH*) and glutaminolysis (*SLC1A5, GLS1, GOT2*). The mRNA expression of *HIF1α*, a major inducer of metabolic reprogramming, was enhanced (Fig. 1, p=0.0001, x-fold 3.2±1.6), whereas the mRNA expression of *PGC1α*, the central regulator of mitochondrial biogenesis and cellular energy metabolism, was strongly suppressed (Fig. 1, $p< 0.0001$, x-fold 0.2±0.2). αKG reversed the TGFβ-driven upregulation of HIF1α (Fig. 1, p=0.06, x-fold 1.4±0.3) but had no effect on the TGFβ-driven suppression of PGC1α mRNA (Fig. 1). Furthermore, αKG significantly repressed the TGFβ-driven secretion of fibronectin into cell culture supernatants (p=0.047, normalized O.D. TGFβ+αKG 0.5±0.1 vs. TGFβ 1.2±0.6) and diminished the TGFβ-induced production of *αSMA* mRNA (p=0.07, x-fold TGFβ+αKG 2.1±1.2 vs. TGFβ 8.2±4.7) and protein (p=0.02, normalized O.D. TGFβ+αKG 0.34±0.38 vs. TGFβ 3.1±2.3). αKG reduced the contractile capacity of TGFβ-stimulated DF (p=0.003, no contraction in TGFβ+αKG–treated DF vs. 67.1±5.4% in TGFβ-stimulated DF). Apoptosis was not enhanced in TGFβ ± αKG–treated DF.

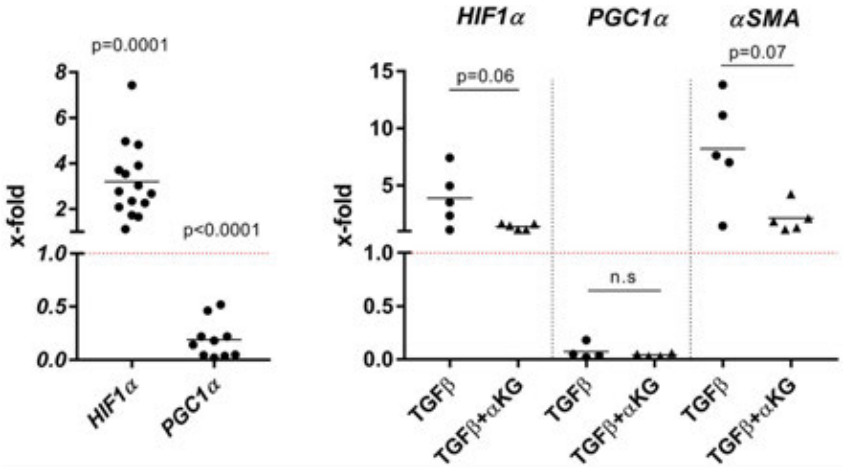

Figure 1. Gene expression analysis of HIF1a, PGC1a and aSMA in dermal fibroblasts stimulated with TGFb in the presence or absence of alpha-ketoglutarate (aKG). The results are shown as x-fold change of normalized gene expression vs. untreated cells (set to 1, as denoted with red line).

Conclusion: TGFβ alters the expression of central metabolic regulators and increases the overall metabolic rate in DF, whereas αKG suppresses the TGFβ-driven profibrotic responses in DF. This suggests that metabolism is intimately linked to the fibrotic processes in skin. Targeting perturbed metabolism could offer novel anti-fibrotic strategies in SSc.

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Abstract Number: 1044

TGF-β Isoforms Modulate the RNA Cargo of Extracellular Vesicles (Exosomes) Isolated from Cultured Normal Human Lung Microvascular Endothelial Cells: A Mechanistic Link Between Endothelial Cell Dysfunction and the Establishment of a Profibrotic Phenotype in SSc?

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Background/Purpose: Extracellular vesicles (EV) are a diverse assortment of lipid bilayer-bound vesicles of various sizes and origin. Exosomes are a subset of EV arising from multivesicular bodies released into the extracellular space and into the circulation that contain various macromolecules including numerous microRNA (miRNA) and proteins. EV can mediate intercellular communication by fusing and releasing their macromolecular contents into target cells. The mechanism of the establishment and progression of a profibrotic phenotype in Systemic Sclerosis (SSc) is not currently well understood. Microvascular damage is considered an early event in SSc pathogenesis and EV produced by damaged microvascular endothelial cells may represent an important component in the initiation and progression of SSc. Here, we characterized the miRNA content of EV isolated from cultured normal human lung microvascular endothelial cells (HLMVEC) treated with TGF-β1, TGF-β2, or TGF-β3 to determine the specific influence of the TGF-β isoforms on the RNA content of HLMVEC.

Methods: Commercially obtained normal HLMVEC were treated with 10 ng/ml of TGF-β1, TGF-β2, or TGF-β3 in FBS-free media. Culture media was isolated from duplicate wells after 72h and EV were isolated by resin-based purification. Total EV RNA was isolated and RNA sequencing (RNA-seq) was performed by 50bp paired-end RNA-seq at 10-20 million reads per sample and aligned to the reference genome (hg19). Differential analysis of RNA content was performed by comparing each treatment group to untreated cells using OASIS 2.0. Gene set enrichment and pathway analysis of miRNA targets was performed employing the MirPath v3.0. Differential expression of selected EV RNA was verified by qPCR.

Results: Treatment of cultured normal HLMVEC with TGF-β isoforms altered the RNA contents of EV isolated from these cells. In addition to changes in miRNA content, marked differences in the amounts and identity of other classes of small RNA such as piRNA were induced upon treatment with the TGF-β isoforms. Analysis of EV miRNA targets indicated extracellular matrix (ECM)-receptor interactions, proteoglycans, ECM components and TGF-β signaling were among the most significantly targeted pathways.

Conclusion: Despite similarities in structure and sequence, TGF-β protein isoforms result in distinct populations of HLMVEC-derived EV. The pattern of upregulated and downregulated EV miRNA from TGF-β1- and TGF-β3-treated HLMVEC show considerable overlap compared with TGF-β2-treated HLMVEC. However, each TGF-β isoform mediated distinct patterns and levels of EV small RNA species. Pathway analysis revealed that numerous pathways are regulated by all three isoforms although the individual genes affected and the magnitude of the changes produced differed for each specific TGF-β isoform. The pathways targeted indicate that EV miRNA could affect target cells by altering the pathways involved in extracellular matrix synthesis, potentially inducing a profibrotic phenotype in target cells. This mechanism may explain the extension of SSc-associated pathological alterations from afftected to normal tissues.

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Myocardial Involvement in SSc: Key Role of $Lin^{-}gp38^{+}$ Stromal Cells in the Onset of Fibrosis and Defects of the Conduction System

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Background/Purpose: Cardiac fibrosis is a known complication of SSc, associated with increased mortality. During fibrogenesis, fibroblasts differentiate into myofibroblasts and secrete excessive extracellular matrix proteins. Here,

we aim to identify the role of a specific fibroblast subset in fibrogenesis and defects of the cardiac electrophysiology in the Fra2 transgenic (tg) mouse model.

Methods: Cardiac function of Fra2 tg and Rag2$^{-/-}$ Fra2 tg mice was assessed by echocardiography, ECG and radiotelemetry. Hearts were analysed by immunohistochemistry (IHC) and IF. The myocardial fibroblast subset represented by stromal (Ter119$^-$CD45$^-$CD31$^-$, hereafter Lin$^-$) gp38$^+$ cells, was sorted and cultured. The phenotype was evaluated by qPCR, α-smooth muscle actin (αSMA) and stress fibre IF, secreted collagens and contraction assay. Proliferation and apoptosis were measured by BrdU incorporation and Caspase 3/7 activity.

Results: Fra2 tg mice displayed increased ejection fraction (p=0.02) and fractional shortening (p=0.02) with decreased left ventricle end-diameter and end-volume in systole (p=0.006, p=0.008) and in diastole (p=0.007, p=0.008) in echocardiography. ECG in conscious mice revealed lower heart rate (HR) (WT 741 ± 33 BPM, tg 644 ± 37 BPM, p< 0.0001) and prolonged QRS, ST and QTc parameters (p=0.001, p=0.01, p=0.01), which may predispose to arrhythmias. Continuous ECG measured by radiotelemetry showed the presence of atrioventricular (AV) blocks that correlated with phenotype severity score (R=0.9, p=0.02). Fibrosis might be responsible for these changes by separating myocardial bundles, causing improper conduction. Indeed, the myocardium of Fra2 tg mice uncovered mild inflammation and interstitial fibrosis with higher expression of collagen- (p=0.03, n=7) and periostin-expressing cells (p=0.001, n=7), increased number of αSMA+ myofibroblasts as well as Lin-gp38+ cells compared to WT mice (1.4% ± 1.4, n=15 and Fra-2 tg: 6% ± 4.5, n=14, p=0.001). Importantly, the majority of myocardial Fra-2 tg gp38+ cells co-expressed αSMA, collagen, ADAM12 and periostin, indicating a myofibroblast-like phenotype. Finally, gp38 expression correlated with collagen deposition (R=0.9, p< 0.0001) measured by Sirius Red staining. In vitro, sorted Lin-gp38+ cells isolated from Fra2 tg mice showed increased αSMA total protein and αSMA fibres that co-localized with stress fibres, resulting in a faster and stronger contraction capability of Fra2 tg cells (p< 0.0001, n=3). Proliferation of Fra2 tg cells was increased compared to WT cells (p=0.007, n=5), while apoptosis was unchanged (p=0.335, n=5). Rag2-/-Fra2 tg mice showed no myocardial fibrosis or Lin-gp38+ cell expansion. ECG parameters of Rag2-/-Fra2 tg mice did not differ from control mice, indicating that inflammation is necessary to acquire the Fra2-driven fibrotic phenotype and defects in the conduction system.

Conclusion: Fra2 overexpression and inflammation drive the differentiation of fibroblasts into myofibroblasts, leading to cardiac fibrosis and defects of the conduction system. This mechanism might be a therapeutic target for SSc patients with disorders of the cardiac conduction system.

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Abstract Number: 1046

The Effect of Nintedanib versus Mycopheolate Mofetil in the FRA2 Mouse Model of Systemic Sclerosis Associated Interstitial Lung Disease

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Background/Purpose: Interstitial lung disease (ILD) is a key driver of mortality in patients with systemic sclerosis (SSc). In lack of approved treatment it constitutes a high unmet medical need. Nintedanib is approved for the treatment of idiopathic pulmonary fibrosis. A recently completed Phase III clinical trial including patients with SSc-ILD (SENSCIS®) showed that nintedanib slows the loss of pulmonary function by 44% in patients with SSc-ILD relative to placebo, as measured by annual rate of decline in FVC over 52 weeks. Mycophenolate mofetil (MMF), an immunosuppressant acting on T and B lymphocytes is used in the clinical practice to treat patients with SSc.

Aim: To compare the activity of nintedanib and MMF in transgenic (tg) FRA2 mice a model of SSc-ILD

Methods: FRA2 mice at an age of 9 weeks were treated with MMF at 100 or 150 mg/kg qd or nintedanib 50 mg/kg bid and were sacrificed at an age of 16 weeks. Histological changes of pulmonary fibrosis were quantified by Ashcroft Scoring. In addition, whole lung sections were stained with Sirius Red and fibrotic area was determined using ImageJ. The amount of collagen protein in skin samples was determined via hydroxyproline assay. The degree of luminal occlusion of pulmonary arteries was examined histologically. The percentage of proliferating vascular smooth muscle cells was evaluated by triple staining for DAPI (nuclear staining), Ki67 (proliferation marker) and SM22. The percentage of apoptotic endothelial cells in the skin of mice was determined by double staining for CD31 (endothelial cells) and caspase 3 (apoptosis).

Results: Nintedanib effectively ameliorated pulmonary fibrosis in FRA2 tg mice and reduced the fibrotic area, the Ashcroft scores and the hydroxyproline content as compared to vehicle-treated FRA2 tg mice. In contrast, treatment of FRA2 tg mice with MMF at doses of 100 mg/kg or 150 mg/kg qd had only mild antifibrotic effects that did not yield statistically significant effects across the three different outcomes.

Treatment with nintedanib also ameliorated remodeling of the pulmonary arteries and significantly reduced the number of occluded pulmonary vessels, the number of proliferating vascular smooth muscle cells and the number of apoptotic endothelial cells. No effect on the remodeling of pulmonary arteries was observed with MMF.

Conclusion: In the FRA2 mouse model of SSc-ILD nintedanib ameliorates pulmonary fibrosis, proliferation of pulmonary vascular smooth muscle cells and apoptosis of microvascular endothelial cells. In contrast, MMF has minor effects on pulmonary fibrosis and no effects on vascular manifestations.

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BMS, 2, Boehringer Ingelheim, 2, 5, Bristol-Myers Squibb, 2, Celgene, 2, 5, Galapagos, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, JB Therapeutics, 5, medac, 5, Medac, 5, Novartis, 2, Pfizer, 5, RedX, 2, RuiYi, 5, Sanofi, 2, Sanofi-Aventis, 2, UCB, 2, 5; **L. Wollin**, Boehringer Ingelheim, 3.

Abstract Number: 1047

CXCL4-L1 Levels Are Elevated in Systemic Sclerosis Patients and Correlate with Pulmonary Arterial Hypertension and Capillaroscopic Indices of Vascular Damage

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Background/Purpose: Recent findings have implicated CXCL4 in the pathogenesis of systemic sclerosis (SSc), while also indicating a potential role of this chemokine as a biomarker in SSc. Herein, we examined whether plasma levels of CXCL4-L1, a non-allelic variant of CXCL4, which displays a constitutive pathway of secretion by platelets and smooth muscle cells and is a stronger inhibitor of angiogenesis compared to CXCL4, differ between SSc patients and healthy controls. Furthermore, we investigated if CXCL4-L1 levels correlate with clinical and capillaroscopy features of SSc patients.

Methods: CXCL4 plasma levels were measured by ELISA in 94 SSc patients, 5 patients with very early diagnosis of SSc (VEDOSS) and 74 healthy controls. CXCL4-L1 plasma levels were measured by ELISA in 68 of 94 SSc patients, 9 VEDOSS patients and 58 of 74 healthy controls. Nailfold Video Capillaroscopy (NVC) and clinical data were collected from all patients. To compare levels of expression of CXCL4-L1 mRNA in peripheral blood mononuclear cells (PBMCs) between SSc patients with and without pulmonary arterial hypertension (PAH) and healthy controls we used information from the publicly available online microaray dataset GSE33463. Comparisons were performed using the Mann-Whitney U-test.

Results: Plasma levels of CXCL4 were significantly higher in SSc patients (mean±SD= 62.84 ± 82.32ng/ml) compared to controls (mean±SD= 32.67 ± 33.48ng/ml, p=0.0004) and correlated significantly with smocking (B=51.74, p=0.024) and presence of interstitial lung disease on high resolution computed tomography of the chest (B=33.47, p=0.042), after adjustment for age and gender. CXCL4-L1 plasma levels were increased in SSc patients (mean±SD=205.54±199.39pg/ml), compared to both VEDOSS patients (mean±SD=75.67±51.00 pg/ml, p=0.0158) and controls (mean±SD=82.29±114.88pg/ml, p< 0.0001) and correlated significantly with capillaroscopic parameters [dilatation score, (B=116.3, p=0.007), micohemorrhages score, (B=185.87, p=0.012)]. After correction for age and gender correlation with microhemorrhages score remained marginally significant (B=146.26, p=0.063). In terms of

mRNA expression CXCL4-L1 was increased in PBMCs of SSc patients compared to controls, as well as in PBMCs of SSc patients with PAH compared to SSc patients without PAH.

Conclusion: CXCL4-L1, an angiogenesis inhibitor, is increased in the peripheral blood of SSc patients both at the mRNA and protein levels. Correlation of CXCL4-L1 levels with capillaroscopic indices and PAH in these patients suggest that further prospective studies should examine whether CXCL4-L1 may serve as biomarker for vascular damage in SSc.

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Clonally Expanded CD4+ Cytotoxic T Cells, Endothelial Cell Apoptosis and the Pathogenesis of Early Systemic Sclerosis

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Background/Purpose: The CD4+ T cell subset driving the pathogenesis of systemic sclerosis (SSc) remains poorly understood. Many different CD4+ T cell subsets have been implicated, but previous studies on SSc have typically not used quantitative multi-color approaches on tissue biopsies. We have previously reported on the expansion of CD4+ cytotoxic T lymphocytes (CD4+CTLs) in the blood of SSc patients. Furthermore, CD4+CTLs are implicated in the pathogenesis of another autoimmune fibrotic disease, IgG4-related disease. We sought to quantify CD4+CTLs and other CD4+ T cell subsets in untreated SSc tissues from patients with diffuse cutaneous SSc (dcSSc).

Methods: Multi-color immunofluorescence was used to quantify CD4+ T cell subsets in 350 skin sections of thirty-five patients with early dcSSc enrolled in the ASSET trial (placebo-controlled trial of abatacept vs. placebo in early dcSSc, clinicaltrials.gov NCT02161406). Paired blood samples from 18 of these patients, along with 9 additional SSc blood samples recruited through the Massachusetts General Hospital (MGH), were used to quantify frequencies of, examine the TCR repertoire and explore the transcriptomes of circulating CD4+CTLs. All patient samples from the ASSET trial and 6 of 9 of the subjects recruited through the MGH were untreated at the time of collection. Twenty age-matched healthy donors and 19 non-fibrotic sarcoidosis patient samples were used as blood controls, while 10 skin samples from healthy donors were used as tissue controls.

Results: CD4+CTLs were expanded in the blood of SSc patients, showed marked clonal-restriction by TCR repertoire analysis and the magnitude of expansion correlated with the degree of tissue fibrosis. The transcriptomes of CD4+ CTLs from SSc patients enriched for gene sets suggesting enhanced metabolic activity, cell survival, and

conditioning by both type 1 and type 2 interferons. Quantitative multi-color immunofluorescence revealed that T_{H1}, T_{H2}, and T_{FH} cells are relatively rare populations in SSc tissues, comparable to those observed in normal skin, whereas CD4+CTLs are prominent and represent the most abundant CD4+ T cell subset in most dcSSc skin biopsies. Many of these cells synthesized IL-1β suggesting that they have been reactivated in tissues. We observed and quantified prominent activated caspase-3 staining, particularly in endothelial cells, and many endothelial cells upregulated MHC class II molecules in dcSSc skin biopsies.

Conclusion: The low abundance of infiltrating T_{H1}, T_{H2}, and T_{FH} cells in the skin of SSc subjects suggests that these CD4+ T cells are unlikely to be of pathogenic significance in this disease. In contrast, activated, clonally-expanded and tissue infiltrating CD4+CTLs likely drive the pathogenesis of SSc. The prominent accumulation of apoptotic HLA class II expressing endothelial cells in the lesions of these patients suggests that recurring immune mediated endothelial cell apoptosis may contribute to tissue damage and remodeling in this fibrotic disease. (Supported by Autoimmune Centers of Excellence awards from the NIAID to SP, DK, DF and JS)

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Abstract Number: 1049

Induction of a Profibrotic Phenotype in Normal Dermal Fibroblasts by Expression of PIM1 Kinase and Demonstration of Antifibrotic Effects of Inhibition of PIM Kinases in Systemic Sclerosis Dermal Fibroblasts

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Background/Purpose: There is an urgent unmet need for effective therapeutic approaches for Systemic Sclerosis (SSc), a systemic autoimmune disease characterized by progressive fibrosis of skin and multiple internal organs and

severe microvascular alterations. The molecular mechanisms responsible for the fibrotic process in SSc have not been fully identified, although numerous recent studies have demonstrated a crucial role of various protein kinases in the development of tissue fibrotic reactions. Here we examined the role of a novel group of kinases in the activation of fibrotic phenotype in SSc dermal fibroblasts.

PIM (Proviral Integration Moloney virus) family of serine/threonine protein kinases consists of three members PIM1, PIM2 and PIM3 that promote growth factor-independent proliferation of numerous cell types by phosphorylating a range of cellular proteins. Both PIM1 and PIM2 kinase are involved in the control of cell growth, differentiation and apoptosis. PIM kinases do not have an identified regulatory domain, therefore once transcribed they are constitutively active. Recent crystallography studies revealed that, unlike other kinases, PIM1 and PIM2 possess a hinge region which creates a unique binding pocket for ATP, thus offering a target for an increasing number of potent small-molecule PIM kinase inhibitors such as the novel PIM1/2 Kinase inhibitor VI we studied here.

Methods: PIM1 levels were assessed by Western blot analysis of cell lysates from confluent dermal fibroblasts obtained from skin biopsies from the leading edge of forearm lesions of patients with diffuse SSc of recent onset and from healthy donors. SSc dermal fibroblasts were grown in culture and treated with the PIM1/2 kinase inhibitor. Western blot analysis of cell lysates were performed to examine the effects of the PIM1/2 inhibitor employing specific antibodies for PIM1, αSMA, and housekeeping protein. Media from cell cultures were collected and Western blots for collagen type I and fibronectin were performed. Activation of PIM1 endogenous gene expression in normal fibroblasts was performed employing lentiviral CRISPR activation plasmid particles. Control cells were transduced with control lentiviral particles.

Results: SSc dermal fibroblasts displayed marked elevation of PIM1 levels in comparison with normal fibroblasts (>2-Fold). PIM1/2 kinase inhibitor treatment of cultured SSc dermal fibroblasts did not cause morphological changes or detectable cytotoxicity at the concentrations employed, however, the levels of type I collagen and fibronectin production were markedly decreased as a result of PIM1/2 activity inhibition. Lentiviral overexpression of PIM1 in normal dermal fibroblasts resulted in a remarkable upregulation of the expression and production of numerous profibrotic proteins including collagen type I, αSMA and fibronectin.

Conclusion: The results indicate that PIM1 plays an important role in the molecular mechanisms responsible for the exaggerated fibrotic process in SSc. Thus, inhibition of PIM kinases provides a novel therapeutic target for the development of potent antifibrotic drugs for SSc and other fibrotic disorders.

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Abstract Number: 1050

Genome-Wide DNA Methylation Signatures in Classical Monocytes from African Ancestry Patients with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a rare, fibrotic autoimmune disorder characterized by cutaneous and visceral fibrosis, immune dysregulation, and vasculopathy. It disproportionately affects individuals of African ancestry (AA) who, despite the higher disease severity, are dramatically underrepresented in research. Monocytes show heightened activation in SSc, and in AA relative to European ancestry individuals. Monocytes are thus a good target tissue for elucidating disease mechanisms. In this study, we sought to identify differentially methylated loci associated with SSc in classical monocytes from AA patients.

Methods: We profiled DNA methylation patterns on FACS-isolated classical monocytes (CD14++CD16-) from 12 female AA SSc cases and 12 female AA controls using Illumina's MethylationEPIC BeadChip. All patients met the 2013 ACR/EULAR classification criteria for SSc. After QC and data normalization, a linear mixed model analysis was computed to examine DNA methylation differences between patients and controls, including disease status as a random effect and the first two principal components as fixed effects. The best model was selected based off on the QQ plot. Associated CpGs identified as significant were used to identify the closest gene and then those genes were analyzed for common pathways and functions.

Results: In addition to CpGs near several pseudogenes, top differentially methylated CpGs (P< 10E-05) included those near the cilia and flagellar motility *CFAP44* gene, the T-cell surface glycoprotein *CD5*, the ubiquitin ligase *TRIM4*, the angiopoietin *ANGPTL4*, the DNA repair *FANCC*, the synthetase *OAS3*, and the transporter *SLC41A2*. The top genes have known immune, angiogenic, and transcription regulation roles.

Conclusion: These data support a role for DNA methylation differences in mediating sustained monocyte activation and susceptibility to SSc in AA. Many of the differentially methylated genes comprise pseudogenes and non-coding RNA genes, supporting a contribution of dysregulated regulatory elements to disease. Although DNA methylation studies in skin fibroblasts revealed an enrichment of extracellular matrix and focal adhesion genes, our results in monocytes support a dysregulation of genes involved in immune processes, which is consistent with gene expression studies in different peripheral blood subsets. Collectively, these results support the need to understand the regulatory architecture of SSc in different cell types and in individuals of different ancestries.

Disclosure: P. Allen, None; **J. Wirth**, None; **N. Wilson**, None; **J. Oates**, None; **M. Cunningham**, None; **D. Absher**, None; **P. Ramos**, None.

Abstract Number: 1051

Identification of Differential Chromatin Accessibility Using ATAC-seq in a Novel 3D Tissue Culture System of Systemic Sclerosis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
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Background/Purpose: Although the majority of SSc research has focused on differential gene expression, recent studies havedemonstrated that non-coding epigenetic changes in chromatin accessibility are likely play a key role

in SSc biology. In this study we developed a system for analyzing differentially accessible regulatory regions in SSc-derived cell lines using Assay for Transposase Accessible Chromatin with sequencing (ATAC-seq) in a novel 3D *in vitro* skin-like tissue model.

Methods: SSc and healthy control (HC) dermal fibroblast (FB) lines were isolated and expanded from skin biopsies. All patients met 2013 ACR/EULAR criteria for SSc.FBs were seeded in transwell chambers and cultured for 5 weeks to obtain self-assembled stromal (SAS) tissues in a simple 3D tissue model that recapitulates SSc biology. ATAC-seq was performed on both monolayer/2D fibroblast cultures and 3D tissues following tissue dissociation. ATAC-seq libraries were sequenced. Paired end reads were aligned to the hg19 reference genome and 300bp peaks were called in ZINBA. Data underwent quality control analyses and unsupervised hierarchal clustering. Genomic location of peaks was determined using ChIPseeker. The integrative genomics viewer (IGV) was used to analyze the genomic context of specific differentially accessible regions.

Results: ATAC-seq libraries contained a large number of reads (~30 million) and had comparable accessibility profiles to standard data sets (Fig. 1A-D). SSc FBs contained significantly more open chromatin (Fig. 1E) and the percentage of peaks within distal/intergenic regions was significantly higher than in HC FBs (Fig. 1F). In unsupervised hierarchal clustering of the top 50 differential 300bp peaks in both 2D and 3D tissues, SSc and HC tissues clustered by disease state. A differentially accessible region of significant interest was identified in both 2D and 3D individual heatmaps as well as a combined 2D/3D heatmap in which it was the only genomic peak which distinguished between SSc and HC samples (Fig. 1G). This region falls within an intron of a gene on chromosome 8 and contains a putative enhancer predicted to contain a binding site for the transcription factor STAT3.

Conclusion: We were able to produce high quality data from both 2D and 3D cultures. Preliminary analysis of ATAC-seq data demonstrates that SSc fibroblasts maintain a distinct chromatin accessibility profile as compared to HC fibroblasts, characterized by increased global accessibility. The majority of these differentially accessibility peaks reside in genomic regions commonly associated with regulatory elements. Additionally, we were able to identify a region of significant interest containing a putative enhancer region and predicted binding site for STAT3, a transcription factor known to be dysregulated in SSc.

Disclosure: T. Wheeler, None; **J. Chen**, None; **D. Toledo**, None; **B. Mehta**, None; **Y. Wang**, None; **M. Brown**, None; **R. Bhandari**, None; **M. Huang**, None.

Abstract Number: 1052

The PPAR Agonist Lanifibranor Protects Against Right Ventricular Hypertrophy in a Mouse Model of Systemic Sclerosis Associated Pulmonary Hypertension

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

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Background/Purpose: The TβRIIΔk-fib transgenic mouse model of systemic sclerosis (SSc) develops constitutive structural vasculopathy with vessel wall fibrosis and is susceptible to pulmonary hypertension (PH) induced by the VEGF receptor inhibitor SU5416. This model of SSc-PH results from pulmonary endothelial cell (EC) injury leading to endoluminal EC proliferation. The pan-peroxisome proliferator-activated receptor (PPAR) agonist Lanifibranor has recently been tested in a phase II clinical trial in SSc, and PPAR nuclear receptors are reported to have beneficial effects on haemodynamics in human PH. We have explored the effect of lanifibranor on TβRIIΔk-fib mice receiving SU5416 to trigger PH.

Methods: 8-12 week old TβRIIΔk-fib mice (n=33) and littermate sex-matched WT mice (n=29) were administered one of two doses of lanifibranor (30 mg/kg- low dose- or 100 mg/kg- high dose) or vehicle administered by daily oral gavage for 23 days. On day 2 a single 50mg/kg dose of SU5416 in carboxymethylcellulose vehicle was administered by intraperitoneal injection. Right (RVSP) and left ventricular (MABP) pressures and Fulton index were measured on terminally anaesthetised mice according to local protocols. Histological and immunohistochemical assessment of pulmonary and cardiac tissue was performed.

Results: As expected, no significant differences in MABP were seen across groups. All mice had some elevation of RVSP compared to published baseline pressures in this model due to administration of SU5416 in all groups. TG mice treated with vehicle developed elevated RVSP compared to WT mice in the vehicle groups consistent with previous studies [1]. TG mice treated with high dose lanifibranor demonstrated generally higher RVSP than those treated with vehicle or low dose lanifibranor, for instance: mean RVSP TG-SU-100 35.89 ±4.1; TG-SU vehicle 29.0±2.7; $p < 0.05$) with some values exceptionally high (54 mmHg; 49 mmHg; figure 1). Increased endothelial cell proliferation within pulmonary vessels for mice receiving lanifibranor was identified as the likely cause using Ki-67 immunohistochemistry staining. Despite the elevation in RVSP in those mice treated with lanifibranor at high dose, there was no significant increase in RV mass when compared to other groups (for instance, RV/LV+S in TG-SU-100 0.24±0.007; WT-SU-100 0.24±0.005; not significant; figure 2).

Conclusion: Treatment with high dose lanifibranor exacerbated SU5416-induced pulmonary hypertension in the TβRIIΔk-fib mouse model of SSc without resultant increases in RV mass according to Fulton index. Mechanistically, we propose that agonism of different PPAR isoforms in the pulmonary circulation results in exaggerated EC proliferation after SU5416 leading to paradoxical worsening of PH, but protection from the right ventricular hypertrophy that occurred

Figure 1: Right ventricular systolic pressure following Lanifibranor administration

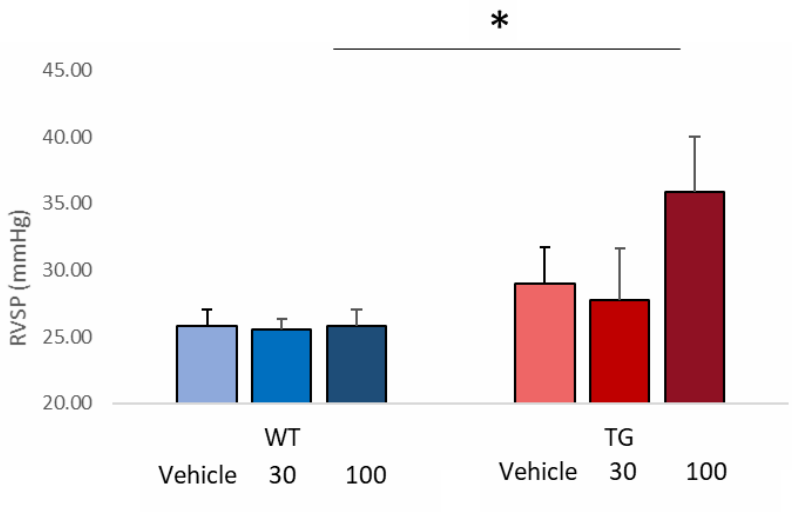
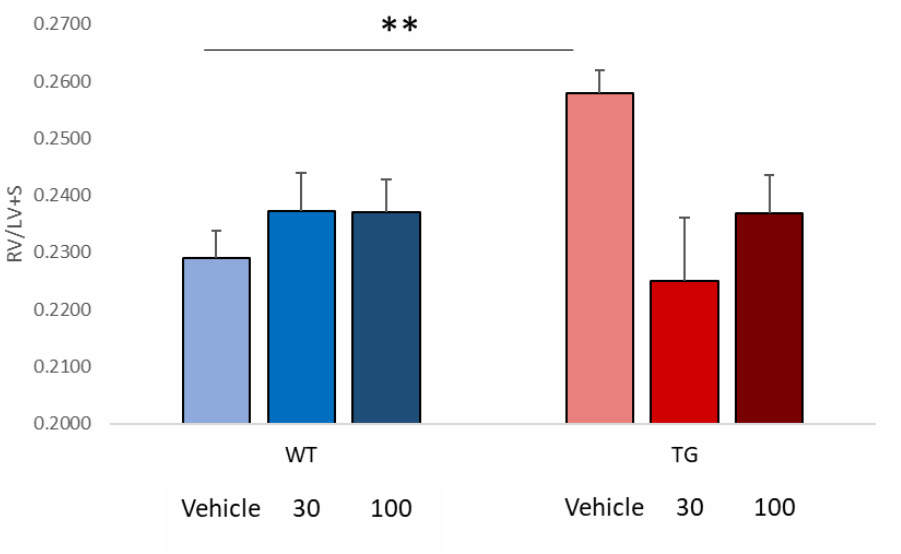


Figure 2: Fulton index following Lanifibranor administration



*p<0.05, **p<0.01

in control mice. Thus, the right ventricular outcomes in our study suggest that there might be protection against RV dilatation and hypertrophy in other forms of murine PH and in human PAH that may positively impact on clinical outcome.

Reference:

1. Derrett-Smith et al, Arthritis Rheum. 2013; 65:2928-39.

Disclosure: E. Derrett-Smith, None; **K. Clark**, None; **S. Xu**, None; **D. Abraham**, UCB, 2; **O. Lacombe**, Inventiva, 3; **P. Broqua**, Inventiva, 3; **J. Junien**, Inventiva, 3; **I. Konstantinova**, Inventiva, 3; **C. Denton**, Actelion, 5, Actelion Pharmaceuticals, 5, Actelion, GlaxoSmithKline, Bayer, Sanofi, Inventiva, Boehringer Ingelheim, Roche, Bristol Myers Squibb, CSL Behring, UCB, Leadiant Biosciences, 5, Bayer, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Corbus Pharmaceuticals, 5, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, Leadiant Biosciences, 2, 5, Inventiva, 5, Pfizer, 5, Roche, 5, Sanofi, 5, UCB, 5.

Abstract Number: 1053

Parallel Analysis of Systemic Sclerosis and Keloidal Morphea Skin Biopsies Delineates the Hallmark Profibrotic Gene Expression Profile for Scleroderma in Vivo

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

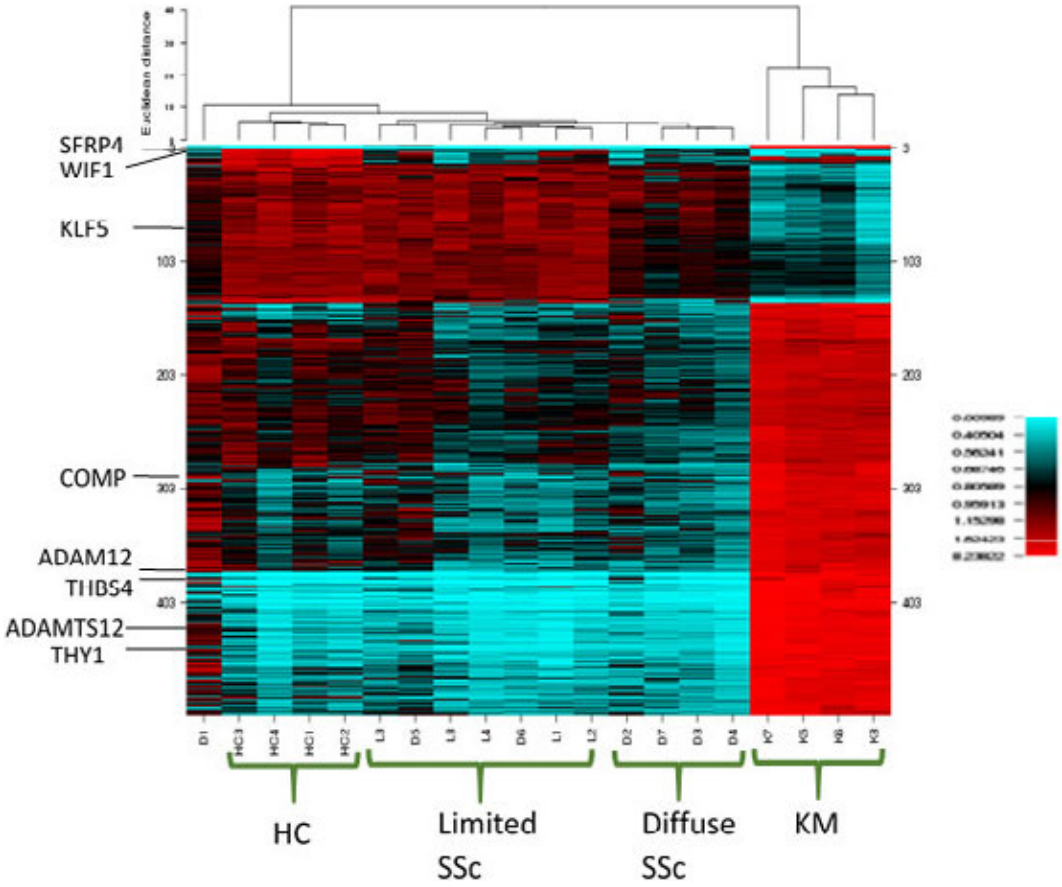

Figure 1. Unsupervised hierarchical clustering of differentially genes across scleroderma spectrum confirms potential utility of these genes in subset classification. Key: HC (healthy control), KM (keloidal morphea)

Table 1. Sample scleroderma genes showing altered expression in keloidal morphea and systemic sclerosis.

		Fold change compared HC			
Gene list	HC- raw	LcSSc	DcSSc	keloid morphea	p
ADAM12	107.75	1.76	3.03	239.27	<0.001
THBS4	7.78	0.78	4.84	39.6	<0.001
SFRP4	14.6	1.27	4.62	48.13	<0.001
COMP	26.07	1.58	3.01	34.84	<0.001
FBN2	84.00	1.32	1.53	30.81	<0.001
COL1A1	55151.75	0.68	1.58	19.29	<0.001
TGFB3	783.25	0.92	1.20	12.00	<0.001
WISP1	486.25	0.54	0.89	11.45	<0.001
ADAMTS12	10.3	1.21	1.85	11.21	<0.001
THY1	43.9	1.23	1.87	9.85	<0.001
KLF5	487.01	0.85	0.73	0.37	<0.001
WIF1	86.87	0.36	0.27	0.01	<0.001

Background/Purpose: We have examined whole skin biopsy gene expression by RNAseq in a rare subgroup of scleroderma with both systemic sclerosis (SSc) and concurrent keloidal morphea (KM). We hypothesised that this subtype of localised scleroderma would provide exceptional insight into fibroblast activation in vivo relevant to skin fibrosis in systemic sclerosis and suggest new potential molecular markers for classification.

Methods: 4mm skin biopsies were taken from forearm skin of SSc cases classified as limited (lcSSc) (n=5) or diffuse (dcSSc) (n=7). All patients met ACR/EULAR criteria for classification of SSc. In 4 cases there was concurrent KM and

4mm skin were also taken from these lesions. Control biopsies were taken from forearm skin of healthy individuals (HC) (n=4). Whole genome expression analysis was performed by RNAseq. Data were normalised and scaled. Gene expression analysis was undertaken and differentially expressed genes were compared across the clinical subgroups using ANOVA with Benjamini-Hochberg post-hoc correction. The 500 most differentially expressed genes were identified, and unsupervised clustering was performed using CIMminer (Bethesda, Maryland, USA). Integration of the candidate genes from ANOVA, and principal component analysis (PCA) was carried out to identify instructive genes for a molecular classifier.

Results: RNAseq identified over 13000 expressed genes. PCA discriminated 4 unique clusters, with keloidal morphea and HCs being the most distinct. PC1 accounted for 33% and PC2 for 22% of variation. Initial analysis identified over 3000 significantly different genes expressed by paired analysis. The 500 most significantly differentially expressed genes (all with $p < 0.001$) were selected. Unsupervised hierarchical clustering of gene expression based on these results, showed clear clustering of the keloidal morphea group, and the HCs. The majority of lcSSc and dcSSc patients clustered to their patient subgroups (Figure 1). Correlation between ANOVA and PCA results highlighted 100 key genes shared across both analysis results. These included genes upregulated in SSc: SFRP4, THY1, COMP, ADAM12, THBS4, ADAMTS12 (table 1) and others with lower expression than in HC: WIF1, KLF5. These include several implicated in pathogenesis or included in recent candidate biomarkers for skin disease in SSc.

Conclusion: We show the high value of RNAseq and the unique strength using skin biopsies from SSc with concurrent keloidal morphea, histologically characterised by dense fibro-proliferation, to define profibrotic genes relevant to SSc. This provides powerful insight into pathogenesis and candidate molecular markers for classification across the scleroderma spectrum.

Disclosure: K. Clark, None; **C. Campochiaro**, None; **N. Gak**, None; **E. Derrett-Smith**, None; **C. Denton**, Actelion, 5, Actelion Pharmaceuticals, 5, Actelion, GlaxoSmithKline, Bayer, Sanofi, Inventiva, Boehringer Ingelheim, Roche, Bristol Myers Squibb, CSL Behring, UCB, Leadiant Biosciences, 5, Bayer, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Corbus Pharmaceuticals, 5, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, Leadiant Biosciences, 2, 5, Inventiva, 5, Pfizer, 5, Roche, 5, Sanofi, 5, UCB, 5.

Abstract Number: 1054

Analysis of Serum Markers Across the Scleroderma Spectrum Shows Subset and Stage Specific Profiles of Fibrogenesis

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SESSION INFORMATION
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Background/Purpose: Systemic sclerosis (SSc) is characterised by autoimmunity, fibrosis and vasculopathy. There is striking heterogeneity in skin fibrosis that is likely to reflect the balance between pro- and anti-fibrotic pathways underlying spontaneous regression of skin fibrosis in late stage diffuse SSc. We have studied potential serum markers

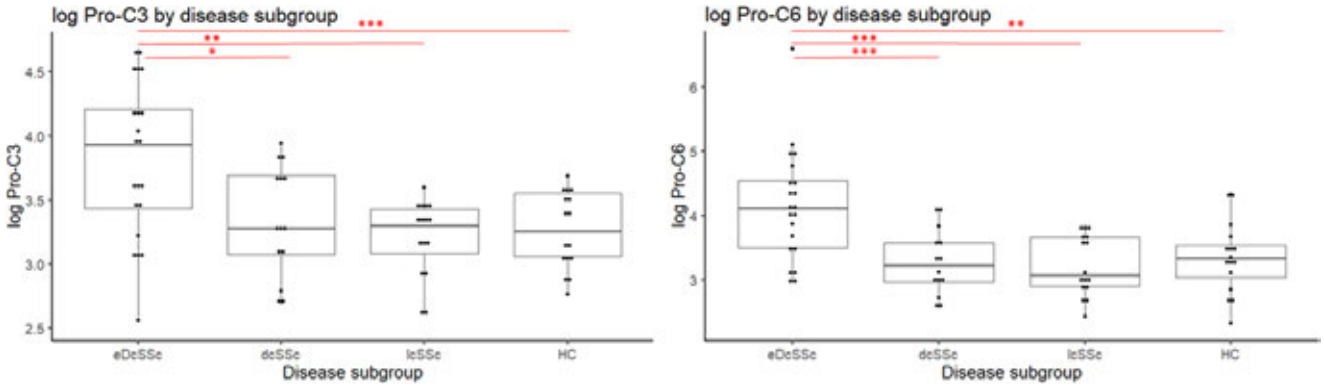

Figure 1. Box plots to show the difference in expression of a) logPro-C3, and b) logPro- C6 in different subgroups in SSc and healthy controls. Significance on subgroup analysis indicated by * p<0.05, **p<0.01, ***p<0.001.

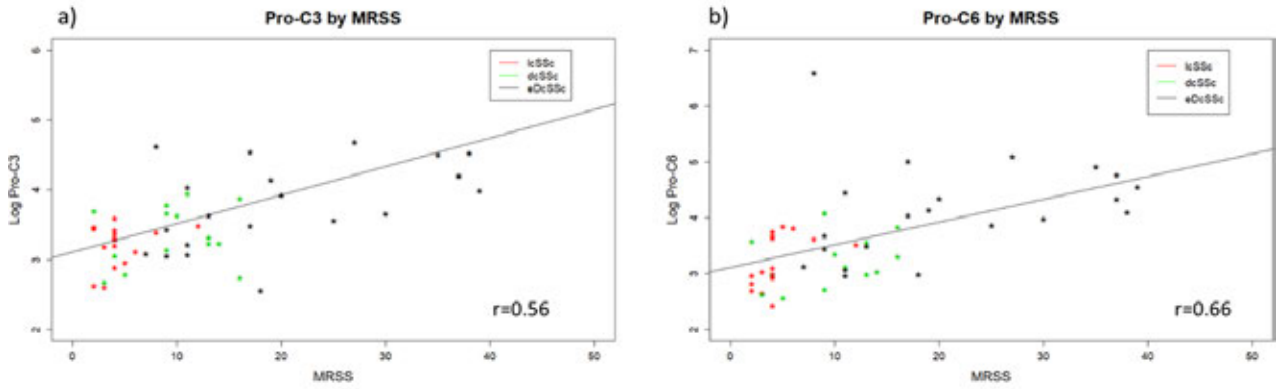

Figure 2. Graph demonstrating significant Pearson correlation between MRSS and a) logPro C3 and b) logPro C6. Colours represent the different patient subgroups (red = lcSSc, green = established dcSSc, black= early dcSSc.

of profibrotic activity in SSc, with a view to understanding their relationship with progression of fibrosis as measured by the modified Rodnan skin score (MRSS) to better define cases likely to respond to fibrosis-targeted therapies.

Methods: We prospectively recruited a cohort of well characterised patients (the BIOPSY cohort) from across the scleroderma spectrum. In total 67 patients had adequate serum and plasma samples to be included in the analysis (21 early diffuse disease (dcSSc) (< 5 years disease duration), 14 established dcSSc, 16 limited SSc (lcSSc), 16 healthy controls (HC)). MRSS was recorded at the time of sample collection. Standard and novel measures of serum

Table 1. Table to show the median results for each subgroup as expressed in log2 format, and the p value for the ANOVA across all subgroups.

	Median result (log2)				ANOVA
	early dcSSc	established dcSSc	LcSSc	HC	p value
Pro-C3	3.93	3.28	3.30	3.25	<0.001
Pro-C6	4.10	3.21	3.07	3.33	<0.001
PIIINP	3.79	3.13	2.94	2.82	<0.001
OSM	4.48	4.01	3.78	3.41	0.01
IL6	0.90	-0.57	0.07	-1.17	0.001
MCP1	8.67	8.60	8.57	7.86	<0.001
C3M	3.56	3.32	3.54	3.44	0.15
C4M2	5.04	4.60	4.84	4.77	0.41
C6M	4.61	4.46	4.47	4.56	0.23
C7m	3.19	2.16	3.11	2.90	0.11
P4NP7S	8.01	7.89	8.17	8.03	0.08
P1NP	5.69	5.57	5.30	5.78	0.25

or plasma markers were undertaken by immunoassay (20 in total) reflecting extracellular matrix (ECM) turnover or cytokine drivers of fibrosis, and analysed at the same time point to reduce any batch effect.

Results: Our results confirmed that 13 analytes showed significant differences in concentration by subgroup using one-way ANOVA. Markers of collagen synthesis were significantly different between the subgroups (Pro-C6, Pro-C3, PIIINP) (Figure 1), while markers of collagen degradation were not significantly altered (C3M, C6M, C4M2, C7M) (Table 1). This difference was most significant between the early dcSSc subgroup compared with the other subgroups (Student t-test with Bonferroni correction). There was significant upregulation of IL-6, MCP-1, and oncostatin M in SSc compared to HC. Consistent with other reports the ELF score, originally validated in liver fibrosis, was significantly higher in the SSc patient cohort. There were significant correlations between several candidate profibrotic serum markers and MRSS: Pro-C3, Pro C6, PIIINP, and IL6 (all $p< 0.01$) (Figure 2).

Conclusion: Our results show the utility of extended patient cohorts to delineate fundamental biology in SSc. We identify key pro-fibrotic molecular markers upregulated in SSc and correlated these to extent of skin fibrosis. Markers of collagen III and collagen VI synthesis are particularly raised, especially in the early stages of the disease. We did not find any significant difference between SSc subgroups and healthy controls for markers of collagen degradation. These promising cross-sectional data suggest that therapies targeting drivers of fibrosis are most likely to show benefit for skin in early dcSSc. This will be further explored longitudinally in the BIOPSY cohort.

Disclosure: K. Clark, None; **C. Campochiaro**, None; **K. Nevin**, GlaxoSmithKline, 3; **E. Csomor**, GlaxoSmithKline, 3; **N. Galwey**, GlaxoSmithKline, 3; **M. Morse**, GlaxoSmithKline, 3; **N. Wisniacki**, GlaxoSmithKline, 3; **S. Flint**, GlaxoSmithKline, 1, 3; **V. Ong**, None; **E. Derrett-Smith**, None; **C. Denton**, Actelion, 5, Actelion Pharmaceuticals, 5, Actelion, GlaxoSmithKline, Bayer, Sanofi, Inventiva, Boehringer Ingelheim, Roche, Bristol Myers Squibb, CSL Behring, UCB, Leadiant Biosciences, 5, Bayer, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Corbus Pharmaceuticals, 5, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, Leadiant Biosciences, 2, 5, Inventiva, 5, Pfizer, 5, Roche, 5, Sanofi, 5, UCB, 5.

Abstract Number: 1055

Proteomic and Transcriptomic Analysis of Human Eosinophilic Fasciitis Fibroblasts

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Background/Purpose: Eosinophilic fasciitis (EF) is a rare scleroderma-like disorder with less than 200 cases reported. Due to the rarity of the disease, data regarding its pathophysiology are lacking. Herein we aimed at studying the transcriptome and the proteome of EF fibroblasts.

Methods: Skin fibroblasts from EF patients (n=4), systemic sclerosis (SSc) patients (n=4), and healthy controls (HC) (n=4), were cultured and harvested for transcriptomic and proteomic analysis. Analyses were performed using next

generation sequencing and label-free quantification, respectfully. Functional analyses were performed using Ingenuity Pathway Analysis and Panther softwares.

Results: Five hundred and nine genes involved in 14 biological processes (BP) and 199 pathways were differentially expressed between EF and control groups. Among them, the circadian clock system (CCS) ($p=1.70\ 10^{-9}$), the plasminogen-activating cascade (PAC) ($p=3.82\ 10^{-5}$), the FGF signalling pathway ($p=1.15\ 10^{-4}$), and the integrin signalling pathway ($p=1.33\ 10^{-3}$) were overrepresented. When comparing EF to HC genes, Panther showed overrepresented down-regulated pathway including CCS ($p=1.71\ 10^{-12}$), and overrepresented up-regulated pathways such as flavin biosynthesis, ($p=9.22\ 10^{-4}$), PAC ($p=1.19\ 10^{-6}$), de novo purine biosynthesis ($p=1.63\ 10^{-3}$), FGF signalling pathway ($p=1.47\ 10^{-3}$) and integrin signalling pathway ($p=9.14\ 10^{-4}$). When comparing EF to SSc genes Panther showed overrepresented down-regulated CCS ($p=2.51\ 10^{-4}$).

Two hundred and twenty four proteins involved in 10 BP and 126 pathways were differentially expressed between EF and control groups. When comparing EF to HC proteins, Panther showed specific overrepresented up-regulated biological processes such as vesicle-mediated transport ($p=4.66\ 10^{-5}$) and intracellular protein transport ($p=1.24\ 10^{-4}$), and overrepresented up-regulated pathways such as 5-hydroxytryptamine degradation (5-HTD) ($p=1.56\ 10^{-4}$) and overrepresented down-regulated pathways such as heterotrimeric G-protein signalling pathways-rod outer segment photo-transduction (HTGSP) ($p=1.24\ 10^{-4}$). When comparing EF to SSc proteins, Panther showed specific overrepresented down-regulated biological processes such as 5-HTD ($p=4.48\ 10^{-4}$), and overrepresented down-regulated pathways such as HTGSP ($p=1.98\ 10^{-4}$), and ubiquitin proteasome pathway ($p=1.05\ 10^{-3}$).

Conclusion: This work described the transcriptome and the proteome of EF fibroblasts and highlighted significant specificities of EF fibroblasts when compared to HC and SSc.

Disclosure: B. Chaigne, None; **C. Fernandez**, None; **M. le Gall**, None; **P. Chafey**, None; **B. Saintpierre**, None; **V. Salnot**, None; **F. Guillonneau**, None; **C. Le Jeunne**, None; **L. Mouthon**, None.

Abstract Number: 1056

Profibrotic Macrophage Activation in Systemic Sclerosis Is Dependent on the Mechanosensing MRTF-A Pathway

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SESSION INFORMATION
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Background/Purpose: An M2-like alternative activation state of macrophages has been linked to the pathogenesis of several fibrotic disorders, including systemic sclerosis (SSc). MRTF-A is an essential mechanosensing transcription factor involved in cellular responses to stiff fibrotic tissue, but its role in controlling macrophage polarisation is unknown. However, genome database profiling identifies the promoter region of the interleukin 13 receptor gene, IL13Rα1, critical to M2 polarisation, as a target of MRTF-A.

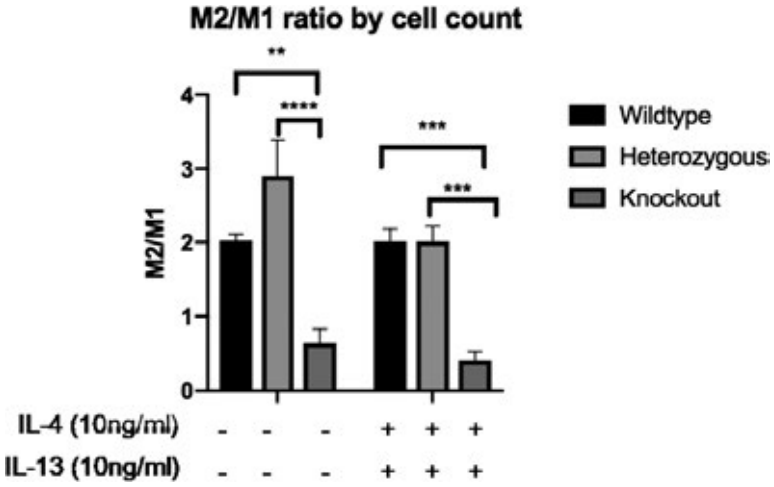

Figure 1. Bone marrow derived macrophages from MRTF-A knockout, heterozygous and wild type mice were cultured on 50kPa Softwell gels with or without cytokine stimulation with IL-4 and IL-13 combined, used to polarise the cells. Morphologic analysis was used to identify M2-like elongated cells or else more rounded M1-like morphology. In the KO cells cytokine treatment failed to induce the M2-like morphology (**p=0.0011, ***p=0.0008, ****p<0.0001).

Methods: MRTF-A knockout (KO) and wild type (WT) control mice, were subject to excisional wound healing and *ex vivo* polarisation of bone marrow-derived macrophages, in order to model M2-responses. Peripheral blood mononuclear cells from SSc patients (N=9) were cultured in M-CSF (4ng/ml) for 7 days to derive M2-like human macrophages. 50kPa Softwell gels were used to reproduce the effect of stiff tissue microenvironments. Morphology (elongated M2-like, round M1-like), and gene expression by qPCR were used to profile the macrophage activation state (IFNγ for M1-like, Arg1 and CD206 M2-like, IL13Rα1 predicted MRTF-A responsive, and IL-4R, predicted non-responsive). Secreted TGFb was assayed by ELISA. CCG-257081 (CCG) (10μM), an MRTF-A pathway inhibitor, was used to block MRTF-A.

Results: In mice, MRTF-A WT (2.02±0.086, mean±SEM) and MRTF-A Het macrophages (2.24±0.716) exhibited significantly higher M2/M1 cell morphology ratio compared to MRTF-A KO macrophages (0.640±0.193) (p=0.0373 and p=0.0165 respectively)(see figure below). Excisional wound repair was also delayed (day 7, WT 47.7±13.9, KO 98.6±19.3, p< 0.037; day 11, WT 3.3 ±1.1, KO 27.4 ± 4.1 p< 0.011, % basal wound area). SSc macrophages showed M2-like activation signature under basal conditions (high Arg1, CD206, M2-morphology), partially reversed by CCG, reducing CD206 (basal 9.16 ± 4.26, CCG treated 1.79±0.98, p=0.0039), supressing the elongated M2-like morphology (SSc basal 4.04, ±0.74, cells per field, CCG treated 0.46±0.18, P=0.0017), and inhibiting the secretion of TGFβ (SSc basal 7.0± 4.9 pg/ml, CCG treated 0.0±1.7 P=0.039). The M1-like inflammatory marker IFNγ was increased by CCG treatment consistent with repolarisation (SSc basal 2.02±0.54, CCG treated 10.4±3.6, p=0.0039). As a direct target of MRTF-A, IL13Rα, was decreased by CCG (21.5±3.39) compared to control (83.2±19.9, p=0.0252), and in mice KO macrophages showed decreased IL13Rα1:IL4R ratio, indicating a pathway selective effect. However, paradoxical elevation of Arg1 in some SSc cells following CCG treatment (SSc basal 7.11±2.89, CCG treated 19.19±8.31, p=0.027), and induction of Arg1 in KO mouse macrophages by polarising cytokines, indicates that not all M2-like responses were affected.

Conclusion: Additional to a pivotal role in myofibroblast function, loss of MRTF-A results in reduced IL-13Rα1 and attenuated cytoskeletal changes associated with M2-like polarisation. Experiments using the CCG-257081 inhibitor in human macrophages support this model, and indicate possible therapeutic potential in inhibiting the MRTF-A mechanosensing pathway by targeting IL4/13.

Disclosure: T. Lim, None; **K. Krogmannova**, None; **S. Xu**, None; **B. Ahmed Abdi**, None; **D. Abraham**, UCB, 2; **C. Denton**, Actelion, 5, Actelion Pharmaceuticals, 5, Actelion, GlaxoSmithKline, Bayer, Sanofi, Inventiva,

Boehringer Ingelheim, Roche, Bristol Myers Squibb, CSL Behring, UCB, Leadiant Biosciences, 5, Bayer, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Corbus Pharmaceuticals, 5, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, Leadiant Biosciences, 2, 5, Inventiva, 5, Pfizer, 5, Roche, 5, Sanofi, 5, UCB, 5; **R. Stratton**, None.

Abstract Number: 1057

Dissecting the Cellular Mechanism of Prostacyclin Analog Iloprost in Reversing Vascular Dysfunction in Scleroderma

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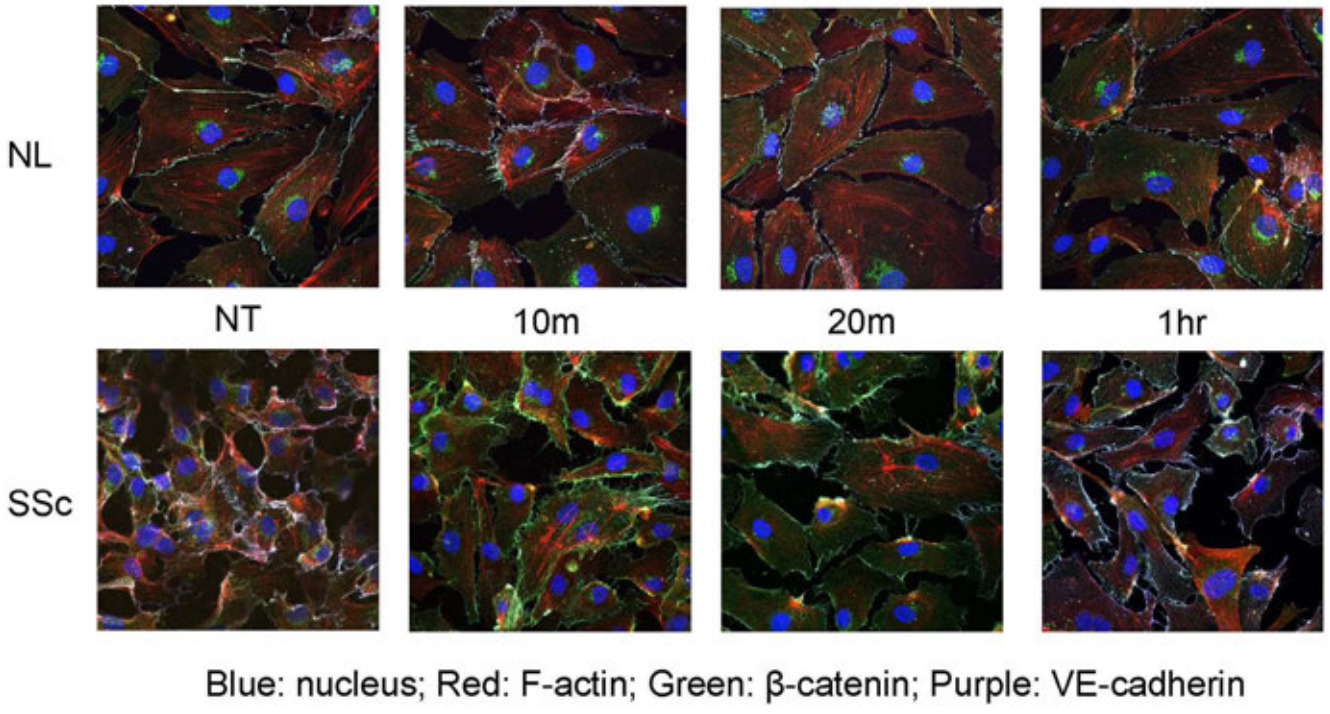
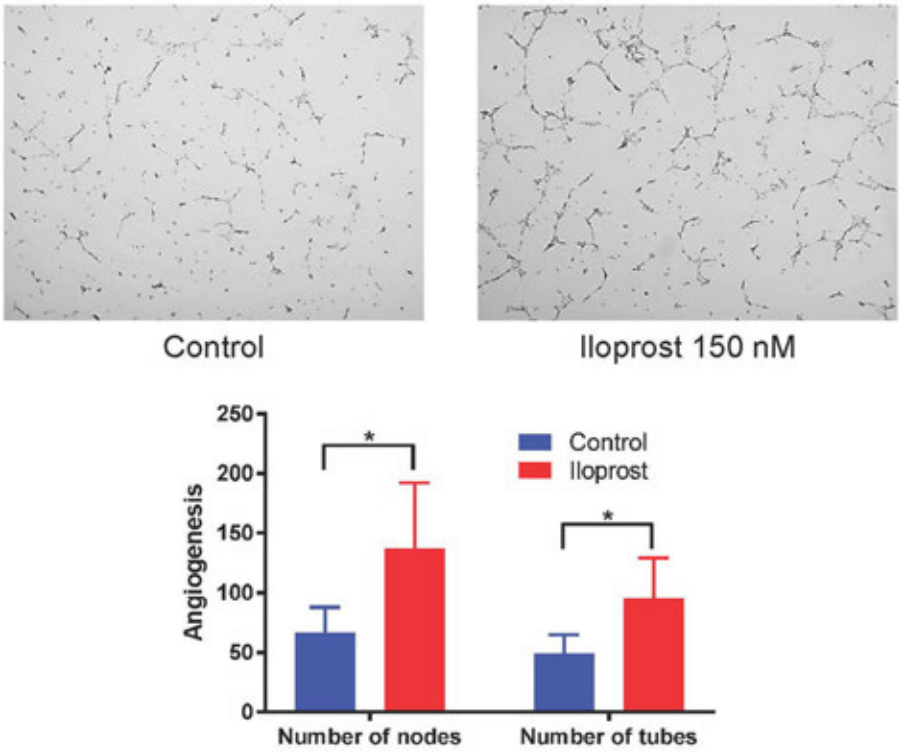
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Iloprost improves Raynaud's phenomenon and digital ulcers in scleroderma (SSc) patients. This is hypothesized to reflect anti-platelet and vasodilatory effects. Different trials and cohorts have reported efficacy of Iloprost for 4-8 weeks [1] despite a short half-life (0.57hr; [2]). Adherens junctions, which are formed by clustering of VE-cadherin on neighboring endothelial cells (ECs), regulate numerous endothelial properties, including cell morphology, signaling and phenotype [3]. When junctions are disrupted, VE-cadherin and β-catenin are disengaged from



Immunofluorescence staining of VE-Cadherin (purple), beta-catenin (green), F-actin (red) after Iloprost incubation in normal and SSc endothelial cells.



Iloprost significantly increased tubulogenesis in SSc endothelial cells.

the cell membrane and can contribute to vascular dysfunction and endothelial to mesenchymal transition (Endo-MT). We hypothesized that vascular dysfunction in SSc reflects disruption of EC adherens junctions and that the vascular protective effect of Iloprost is mediated by strengthening of these junctions in SSc ECs.

Methods: Dermal ECs were isolated from biopsies of healthy subjects and SSc patients. ECs were treated with Iloprost (150nM) for various times. Visualization of cellular localization of VE-cadherin, β-catenin, and F-actin was done by immunofluorescence. Tubulogenesis was examined using Matrigel in vitro tube formation assay. Inhibition of VE-cadherin clustering was achieved by a function blocking antibody. Cell proliferation was assessed by BrdU incorporation. Cell migration was examined using Incucyte imaging. Endo-MT was induced by treating healthy ECs with TGFβ for 72 hrs. Gene expression was determined by qPCR. Plasma VE-cadherin was determined using ELISA. T-tests were used to compare differences between groups, and $P < 0.05$ considered significant.

Results: Cell staining demonstrated disruption of adherens junctions and disorganized F-actin filaments in SSc compared to normal ECs. When stimulated with Iloprost, there was a significant increase in VE-cadherin and β-catenin clustering at cell junctions up to 1 hour of incubation in both normal and SSc ECs. However, F-actin organization in SSc ECs was still distorted (Fig 1). Iloprost treatment increased EC tubulogenesis in both normal and SSc ECs (Fig 2). This effect was inhibited by a neutralizing antibody to VE-cadherin. Iloprost had minimal effect on EC proliferation. In normal ECs, TGFβ induced Endo-MT with upregulation of *ACTA2*, *S100A4*, and *SNAI1*, and downregulation of *PECAM1*, *CDH5*, and *FLI1*. This process was blocked by Iloprost co-incubation; Iloprost normalized the expression of all genes except for *FLI1*. Similar results were observed in SSc ECs treated with Iloprost for 72 hrs (Table 1). Plasma level of VE-cadherin was significantly elevated in SSc compared to healthy controls.

Table 1. Gene expression after Iloprost treatment in SSc ECs (mean ± S.D.)	
Gene	**Expression fold change (n=2 patient pairs)**
COL1A1	0.22 ± 0.30
ACTA2	0.36 ± 0.16
S100A4	0.29 ± 0.07
CDH5	2.32 ± 1.34
PECAM1	6.08 ± 2.95
SNAI1	0.18 ± 0.26
FLI1	0.79 ± 0.50

Conclusion: Our data suggests that long lasting beneficial effects of Iloprost may stem from its ability to stabilize endothelial adherens junctions, increasing EC tubulogenesis, and inhibiting Endo-MT. These results provide a mechanistic basis that supports the use of Iloprost in treating SSc patients with Raynaud's phenomenon and digital ulcers.

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2. Hildebrand, M., Eur J Clin Pharmacol, 1997. **53**(1): p. 51-6.
3. Flavahan, N.A., J Cardiovasc Pharmacol, 2017. **69**(5): p. 248-263.

Disclosure: P. Tsou, None; **N. Flavahan**, None; **D. Khanna**, Acceleron, 5, Actelion, 5, Bayer, 2, 5, Blade Therapeutics, 5, BMS, 2, 5, Boehringer Ingelheim, 5, Celegene, 5, ChemomAB, 5, Corubus, 5, CSL Behring, 5, Curzion, 5, Cytori, 5, Eicos, Inc, 4, Genentech, 5, GSK, 5, Horizon, 2, Mitsubishi Tanabe Pharma Development America, 5, Pfizer, 2, Sanofi-Aventis, 5, UCB, 5.

Abstract Number: 1058

Inhibition of Histone Readers Bromodomain and Extraterminal Domain Proteins Alleviates Scleroderma Fibrosis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Epigenetic regulation, including histone acetylation, plays an important role in scleroderma (SSc) fibrosis. The binding of the bromodomain and extra-terminal domain proteins (BRDs) to acetylated histone residues is critical for gene transcription. It has been shown that BRD inhibitor JQ1 prevents fibrosis in various tissues. However, the involvement of BRDs in SSc fibrosis has not been examined. This study sought to determine the expression and functions of BRDs in SSc fibroblasts. We hypothesize that modulating BRDs by JQ1 will alleviate SSc fibrosis.

Methods: Dermal fibroblasts were isolated from biopsies from healthy subjects or patients with diffuse cutaneous SSc (dcSSc). Fibroblasts were treated with JQ1 (0.01-22μM) for 48 hours. Knockdown of BRD2, BRD3, or BRD4 was achieved by siRNA transfection. Gene expression was determined by qPCR. A scratch wound assay and gel contraction assay were used to evaluate fibroblast function. Cell proliferation was assessed by ki67 immunofluorescence, BrdU incorporation, as well as Incucyte imaging. The *in vivo* anti-fibrotic efficacy of JQ1 was determined in a bleomycin-induced skin fibrosis mouse model. A t-test was used to compare differences between groups, and a p-value of < 0.05 was considered significant.

Results: BRD inhibitor JQ1 dose-dependently downregulated pro-fibrotic genes including *ACTA2*, *COL1A1, and CTGF* in dcSSc fibroblasts. It also downregulated *BRD4* but upregulated *BRD2*. In addition, JQ1 treatment inhibited cell migration, proliferation, and gel contraction mediated by dcSSc fibroblasts. Daily administration of JQ1 (50mg/kg) in mice prevented bleomycin-induced skin fibrosis. The expression of *BRD2*, *BRD3*, and *BRD4* were similar in fibroblasts from healthy controls and dcSSc patients. To determine which BRD is involved in the anti-fibrotic effect of JQ1, we knocked down BRD2, BRD3, or BRD4 in dcSSc fibroblasts. Surprisingly, knockdown of BRD2, 3, or 4 had minimal effect on cell proliferation. BRD4 knockdown in dcSSc fibroblasts resulted in down-regulation of *ACTA2* and *COL1A1* and relaxed gel contraction. In contrast, BRD2 knockdown led to upregulation of *COL1A1* while it had no effect on gel contraction.

Conclusion: BRD modulation by JQ1 showed promising anti-fibrotic effects both *in vitro* and *in vivo*. JQ1 decreased profibrotic gene expression in dcSSc fibroblasts, and inhibited cell migration, proliferation, and gel contraction, which are the three manifestations of dcSSc fibroblasts. Our results suggested that BRD4 is pro-fibrotic while BRD2 might be anti-fibrotic. We believe that BRD modulators have the potential of becoming therapeutics for SSc patients in the future. These results also revealed the specific involvement of BRD2 and BRD4 in SSc fibrosis.

Disclosure: S. Vichaikul, None; **P. Campbell**, None; **M. Amin**, None; **J. Ruth**, None; **D. Rohraff**, None; **D. Fox**, None; **D. Khanna**, Acceleron, 5, Actelion, 5, Bayer, 2, 5, Blade Therapeutics, 5, BMS, 2, 5, Boehringer Ingelheim, 5, Celegene, 5, ChemomAB, 5, Corubus, 5, CSL Behring, 5, Curzion, 5, Cytori, 5, Eicos, Inc, 4, Genentech, 5, GSK, 5, Horizon, 2, Mitsubishi Tanabe Pharma Development America, 5, Pfizer, 2, Sanofi-Aventis, 5, UCB, 5; **A. Sawalha**, None; **P. Tsou**, None.

Abstract Number: 1059

BDCA2 Targeting of Human Plasmacytoid Dendritic Cells via CBS004 Reverts Dependent IFN Activation and Tissue Fibrosis in vitro and in vivo

Rebecca Ross,[1] Clarissa Corinaldesi,[2] Gemma Migneco,[3] Yasser El-Sherbiny,[4] Steve Holmes,[5] Jörg Distler,[6] Clive McKimmie,[7] and Francesco Del Galdo[8], [1]Univesristy of Leeds, Leeds, England, United Kingdom, [2]University of Leeds, Leeds, England, United Kingdom, [3]University of Leeds, Leeds, United Arab Emirates, [4]University of Nottingham, Nottingham, United Kingdom, [5]Capella Bioscience, london, United Kingdom, [6]Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, Erlangen, Germany, [7]University of Leeds, Leeds, United Kingdom, [8]University of Leeds and LTHT NIHR Biomedical Research Centre, Leeds, United Kingdom

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Human plasmacytoid dendritic cells (pDCs) have been implicated in the pathogenesis of Systemic Sclerosis (SSc) through their ability to infiltrate the skin and secrete interferons (IFN), interleukin-6 (IL-6) and other proinflammatory chemokines directly, or through type-I IFN response of resident cells. Blood dendritic cell antigen 2 (BDCA-2) is a human-specific pDC-type II C-type lectin that potently inhibits IFN secretion. Here we determined the effects of CBS004, a novel monoclonal antibody against BDCA-2, on Toll-like receptor (TLR)-induced transcriptome and IFN secretion in pDCs from healthy volunteers (HV) or patients with SSc in vitro, and tested its effect on two different xeno-transplant mouse models of human pDC dependent tissue inflammation and fibrosis.

Methods: Peripheral blood mononuclear cells (PBMCs) were collected from 26 SSc patients and 16 HV. IFN secretion were evaluated by ELISA. TLR7-9 stimulation was induced by Imiquimod or ODN. pDCs were isolated by magnetic cell sorting. Full transcriptome was analysed by RNA-sequencing. For the xenotransplant models, NOD/SCID mice were injected in the tail vein with $25x10^4$human pDCs, 12 h after topical application of Imiquimod for the inflammation model, and along bleomycin skin injections in the fibrotic model. CBS004 was delivered by intraperitoneal injection at 5 mg/kg. Harvested skin was analysed by FACS for human pDC infiltration, by real-time PCR using a mouse type-I IFN response array (Qiagen) and by histology for dermal thickness.

Results: PBMCs from SSc patients spontaneously produced higher levels of IFN-I compared to HV ex vivo (206.7±23.4 vs. 43.4±6.8 pg/ml, P< 0.0001). CBS004 significantly inhibited basal levels of IFN-I in 83% of SSc samples. TLR9 stimulation of SSc PBMCs induced >30-fold increase in IFN-I secretion (7167±4377 pg/ml), which was completely abrogated by treatment with CBS004 (209±40.5 pg/ml, P< 0.001). RNA-seq analysis of human pDCs stimulated with TLR-9 agonist revealed 168 Differentially Expressed Genes (DEGs, FDR < 1%) mapping to IFN, JAK/STAT, IL-6, NF-kB and angiogenesis pathways. Pretreatment with CBS004 prevented upregulation of most DEGs, which drove an expression profile similar to non-stimulated pDCs. In the xenotransplant model, tail vein injection of pDC resulted in detection of human pDCs in the skin (0.3%) with at least 2-fold upregulation of 35/74 mouse type-I IFN response genes including Ccl2, 4, 5 and Cxcl10, Ifit1, 2 and 3, Mx1 and 2, Oas1, Tlr7, 8 and 9 compared to imiquimod treatment alone (P< 0.005). Mice receiving IP injection of CBS004 had a 3-fold reduction in infiltrating pDCs (0.1%) and suppression of 85% of the type-I IFN response genes upregulated by pDC injection (Anova P< 0.01). In the bleomycin model, pDC injection significantly increased dermal thickness (30%, P< 0.01), which was completely prevented by CBS004 treatment.

Conclusion: Our study demonstrates that BDCA-2 targeting with CBS004 mAb may block both the spontaneous and TLR dependent pDC driven IFN activation in Scleroderma. Further, we show that BDCA2 targeting with CBS004 can revert human pDC driven tissue inflammation and fibrosis in two distinct human pDC xenotransplant mouse models.

Disclosure: R. Ross, None; **C. Corinaldesi**, None; **G. Migneco**, None; **Y. El-Sherbiny**, None; **S. Holmes**, Capella Biosciences, 3; **J. Distler**, 4D Science, 4, Actelion, 5, Actelion Pharmaceuticals, 5, Active Biotech, 2, 5, AnaMar, 2, 5, Array Biopharma, 2, aTyr, 2, Bayer, 2, 5, BMS, 2, Boehringer Ingelheim, 2, 5, Bristol-Myers Squibb, 2, Celgene, 2, 5, Galapagos, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, JB Therapeutics, 5, medac, 5, Medac, 5, Novartis, 2, Pfizer, 5, RedX, 2, RuiYi, 5, Sanofi, 2, Sanofi-Aventis, 2, UCB, 2, 5; **C. McKimmie**, Capella Biosciences, 2; **F. Del Galdo**, AstraZeneca, 5, 8, GSK, 5, 8, Boehringer-Ingelheim, 5, 8, Actelion, 5, 8, Capella Biosciences, 2, 5, Chemomab, 2, 5.

Abstract Number: 1060

The Diversity and Community Metrics of the Esophageal Microbiome of SSc Patients

Monica Espinoza,[1] Bhaven Mehta,[2] Yue Wang,[3] Aileen Hoffman,[4] Kathleen Aren,[5] Mary Carns,[6] Noelle Kosarek,[2] Tammara Wood,[3] Monique Hinchcliff,[7] and Michael Whitfield[8], [1]Dartmouth College, Hanover, NH, [2]Dartmouth College, Hanover, [3]Geisel School of Medicine at Dartmouth, Hanover, NH, [4]Northwestern University, Chicago, [5]Northwestern.edu, Chicago, [6]Northwestern University, Hanover, [7]Yale University, Section of Rheumatology, Allergy and Immunology, New Haven, CT, [8]Geisel School of Medicine at Dartmouth College, Biomedical Data Science at Dartmouth College, Hanover

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is an autoimmune disease characterized by fibrosis and inflammation. Multiple organ systems are affected including the skin, gastrointestinal tract, vasculature, and lungs (Katsumoto, Whitfield, & Connolly, 2011). Gene expression analyses have identified four distinct molecular subtypes (inflammatory, fibroproliferative, normal-like, and limited) despite the heterogenous presentation of the disease. Microbial dysbiosis has been implicated previously in SSc skin and lower GI tract, (Arron et al., 2014; Volkmann, 2017), but

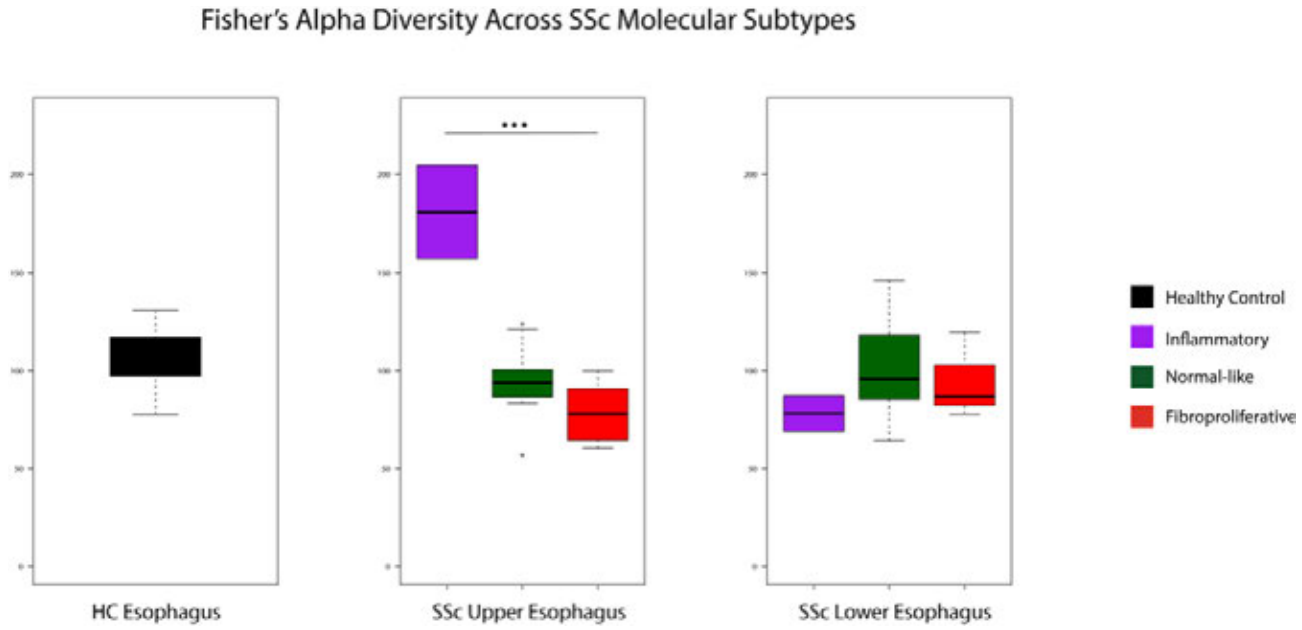

Figure 1. Alpha Diversities by molecular subtype across esophageal sites.

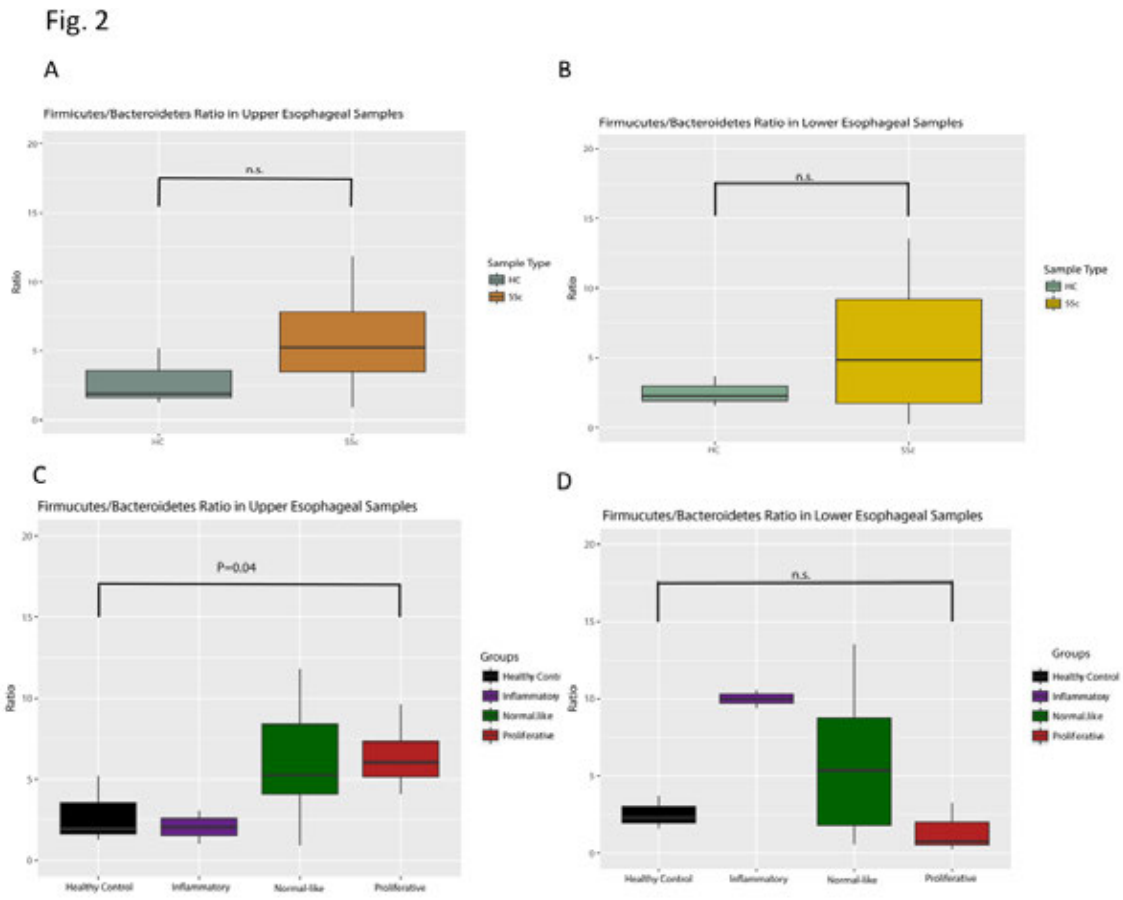

Figure 2. Firmicutes to Bacteroidetes ratios for healthy controls versus SSc patient samples in the upper esophagus, (A) the lower esophagus, (B), the upper esophagus stratified by molecular subtype (C), and the lower esophagus stratified by molecular subtype (D).

Fig.3

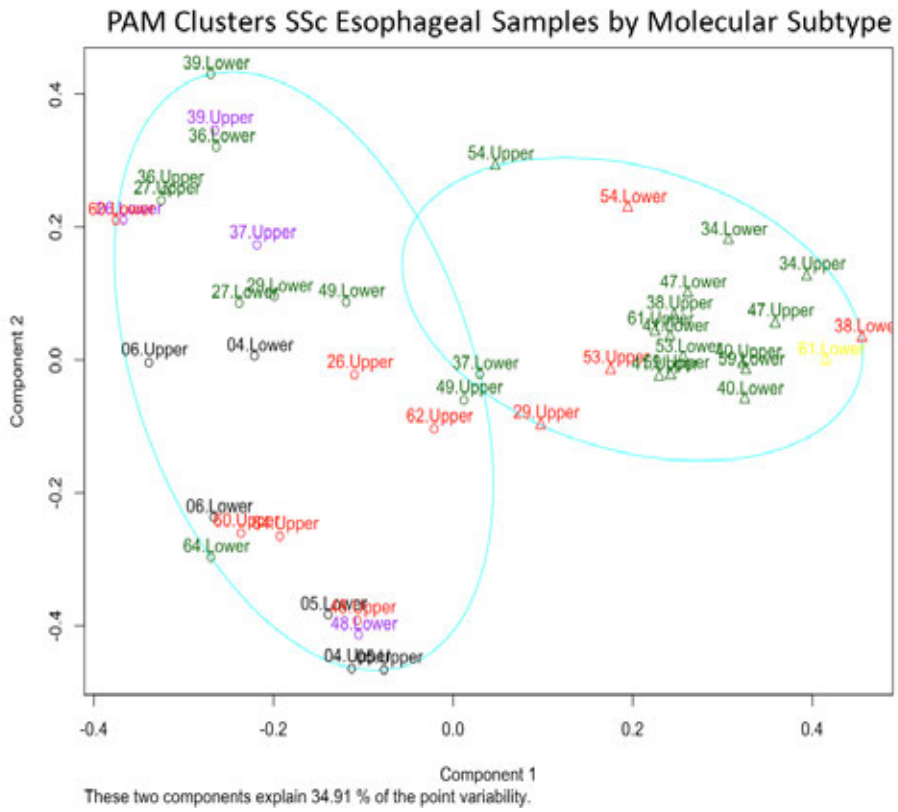

Figure 3. Partition Around Medoids (PAM) clustering of SSc patient esophageal samples based on metagenomic features remaining after filtration and normalization.

no esophageal characterization has been completed. This study characterizes the esophageal microbiome of SSc patients and explores patterns in microbial profiles.

Methods: RNA sequencing was completed on 20 SSc patient and 3 healthy control samples. Sequencing reads were run through Integrated Metagenomic Sequence Analysis (IMSA) to extract non-human microbial reads remaining after initial BLAST to the h19 NCBI human genome. Remaining reads were BLAST to the NCBI nt nucleotide database and taxonomic information was acquired using NCBI taxonomy lookup tool. Non-spurious hits were removed, and samples were rarefied to the lowest read count. Metrics such as the alpha diversity and Firmicutes/Bacteroidetes Ratio, which is associated with gut inflammatory diseases, were calculated. Partition Around Medoids (PAM) clustering based on k clusters was conducted on metagenomic features to group individuals into microbiome enterotypes.

Results: The alpha diversity of SSc samples was lower than that of control samples across the upper and lower esophagus (Wilcoxon Signed-Rank Test, n.s). When parsed by esophageal site and molecular subtype, the alpha diversity was higher in inflammatory samples of the upper esophagus (Kruskal-Wallis Test, $p < 0.05$) and slightly elevated in normal-like and fibroproliferative samples of the lower esophagus (Fig. 1). Concurrent with differences in alpha Diversity, the Firmicutes to Bacteroidetes ratio was elevated in patient samples when compared to healthy controls (Fig. 2A and 2B). When stratified by SSc molecular subtype, Firmicutes/Bacteroidetes ratios were higher in SSc upper esophageal samples which call to the normal-like and fibroproliferative subtypes, and higher in SSc lower esophageal inflammatory and normal-like samples (Fig. 2C and 2D; Kruskal-Wallis test $p < 0.05$ and n.s., respectively). Samples clustered to two groups irrespective of site, and there is a significant association between molecular subtype and cluster membership (Fig. 3; Fisher's Exact Test, $p < 0.05$).

Conclusion: There are patterns and differences in microbial diversity and membership that distinguish SSc and healthy controls, and SSc samples across molecular type. Several of these associations are statistically significant and affirm a potential association between the microbiome and SSc pathogenesis. Work investigating specific microbial membership and gene expression associations are motivated by these findings.

Disclosure: M. Espinoza, None; **B. Mehta**, None; **Y. Wang**, None; **A. Hoffman**, None; **K. Aren**, None; **M. Carns**, None; **N. Kosarek**, None; **T. Wood**, None; **M. Hinchcliff**, None; **M. Whitfield**, None.

Abstract Number: 1061

PI3K-Akt Pathway Plays a Crucial Role in Production of Collagen in Fli1 Deficient Condition and Its Inhibitor Has the Therapeutic Potential in Treating Fibrosis

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SESSION INFORMATION
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Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
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Background/Purpose: Systemic sclerosis (SSc) is a connective tissue disease characterized by fibrosis of the skin and internal organs. Previous studies have shown that dermal fibroblast in patients with SSc frequently shows decreased levels of Fli1 due to hypermethylation. We aimed to clarify the mechanisms underlying the regulation of Fli1 gene of fibrosis using Fli1 deficient cells and mice generated by the CRISPR/Cas9-mediated gene edition.

Methods: Fli1-deficient fibroblast cell line (Fli1ΔNIH3T3 cells) and mice ($Fli1^{+/-}$ mice) were generated by CRISPR/Cas9 system using paired guide RNAs specific for mouse Fli1 and a nickase Cas9 that reduces off-target problem. NIH3T3 cells were transfected with a lentiCRISPR v2 vector and then selected by puromycin. We evaluated collagen and profibrotic cytokine production in the absence of Fli1 by mRNA level. To reveal the mechanism for induction of collagen in Fli1ΔNIH3T3 cells, we treated the cells with various antibodies and inhibitors and performed RNA-sequencing. In order to estimate in vivo efficacy of LY294002 derivative on fibrotic disease, we utilized bleomycin-induced lung fibrosis with $Fli1^{+/-}$ mice and treated with LY294002 derivative by intra-peritoneal injection 3 times and evaluated lung fibrosis by histology, collagen content, and Ashcraft scores. We also evaluated the ex vivo effect of candidate drug using skin fibroblasts from patients with SSc.

Results: Fli1ΔNIH3T3 cells were found to have pro-fibrotic characteristics such as increased expression of COL1A1, COL1A2 as well as increased expression of TGF-b1, CTGF, IL-6, FN, and ACTA2. Antibody neutralization of TGF-β1 and IL-6 didn't inhibited collagen synthesis in Fli1ΔNIH3T3 cells. In addition, whereas MAPK inhibitors of Erk U0126, JNK SP600125, p38 SB20358 failed to suppress the increased collagen production, Nintedanib, a triple kinase inhibitor of VEGFR, FGFR, and PDGFR partially inhibited collagen synthesis. Surprisingly, a phosphoinositide 3-kinases (PI3K) inhibitor, LY294002, which also has inhibitory activity against bromodomain-containing protein (BRD) 2, 3 and 4, had a major inhibitory effect on COL1A2 mRNA expression, suggesting the PI3K-Akt and bromodomain pathways have a major pro-fibrotic role in Fli1ΔNIH3T3 cells. This correlated with the fact that, p-Akt expression was increased in Fli1ΔNIH3T3 cells. In addition, a low toxicity LY294002 derivative also inhibited collagen synthesis in Fli1ΔNIH3T3, confirming PI3K and BRD4 dual inhibition was most effective to reduce COL1A2 production. Furthermore, analyses

of RNA-seq revealed several molecules to induce collagen via PI3K-Akt pathway. Finally, LY294002 derivative treatment significantly ameliorated lung fibrosis as evaluated by Masson Trichrome staining, decreased collagen accumulation in the lung and Ashcroft clinical scores. In both normal and SSc fibroblasts, COL1A2 mRNA were significantly inhibited by LY294002 derivative.

Conclusion: Lack of Fli1 expression activates the molecule that induces collagen accumulation through PI3K-Akt and bromodomain pathway. PI3K and BRD4 dual inhibitor showed therapeutic potential in treating fibrosis.

Disclosure: Y. Ota, None; **A. Kitani**, None; **W. Strober**, None.

Abstract Number: 1062

Lymphocyte Subset Abnormalities in Early Diffuse Cutaneous Systemic Sclerosis

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SESSION INFORMATION
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Background/Purpose: A variety of abnormalities in lymphocyte surface markers and functional subsets have been described in patients with systemic sclerosis (SSc), but conflicting results abound, and these studies often examined patients with heterogeneous disease duration, clinical phenotype, exposure to immunosuppressive agents, and degree of organ involvement. We studied a clinically homogeneous group of 88 early diffuse cutaneous SSc patients who had not received immunosuppressive drugs and 25 matched healthy controls.

Methods: The SSc patients were participants in the ASSET study, a placebo-controlled blinded trial of abatacept in SSc. Lymphocyte subsets were enumerated by multi-parameter flow cytometry of peripheral blood mononuclear cells at the baseline visit. Production of the cytokines IL-4 and IL-17 was measured by intracellular flow cytometry following T cell activation in overnight cultures.

Results: SSc patients had increased percentages of CD4+ T cells and B cells, but a lower percentage of CD8+ T cells compared to healthy control subjects. The CD4+CD28-negative population was expanded in SSc, in the CD4 subset. The number of CD40 ligand+ cells was expanded in the SSc patients ($p=0.003$), but another T cell activation marker CD69, did not show increased expression on SSc T cells. A notable expansion of CD319+ T cells was seen among the CD4+ cells, where they are barely detectable in healthy subjects (2.96% versus 0.8%, $p< 0.001$). These CD4+CD319+ (SLAM-F7+) cells are cytotoxic and oligoclonal, and were recently shown to be a dominant T cell population in perivascular lymphocytic infiltrates in SSc skin. Frequencies of IL-4+ cells did not differ between SSc and

controls, but expansion of IL-17 producing (2.38% versus 0.82%, p=0.007) and dual IL-4/IL-17 producing (1.16% versus 0.24%, p=0.023) cells was observed in SSc. Numbers of regulatory, and peripheral helper T cells were similar in SSc and control groups.

Conclusion: In this carefully selected group of early diffuse SSc patients, analysis of immune cell parameters has identified abnormalities that likely reflect disease pathogenesis and that are candidate biomarkers for sub-classification and targeted treatment of early diffuse SSc.

Disclosure: D. Fox, None; **S. Lundy**, None; **M. Whitfield**, BMS, 5, Boehringer Ingelheim, 5, Corbus Pharmaceuticals, 5, Third Rock Ventures, 5, Celdara Medical LLC, 2, 5, 7, 9; **V. Berrocal**, None; **P. Campbell**, None; **S. Rasmussen**, None; **R. Ohara**, None; **A. Stinson**, None; **E. Wiewiora**, None; **C. Spino**, Eicos, Inc., 5; **E. Bush**, None; **D. Furst**, Actelion, 2, 5, Actelion Pharmaceuticals, 2, 5, Amgen, 2, 5, BMS, 2, 5, CME, 5, 8, Corbus, 2, 5, Galapagos, 2, 5, Galapogos Novartis, 5, GlaxoSmithKline, 2, GSK, 2, 5, NIH, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche/Genentech, 2, 5, Sanofi, 2, 5; **S. Pillai**, Abpro, 6; **D. Khanna**, Acceleron, 5, Actelion, 5, Bayer, 2, 5, Blade Therapeutics, 5, BMS, 2, 5, Boehringer Ingelheim, 5, Celegene, 5, ChemomAB, 5, Corubus, 5, CSL Behring, 5, Curzion, 5, Cytori, 5, Eicos, Inc, 4, Genentech, 5, GSK, 5, Horizon, 2, Mitsubishi Tanabe Pharma Development America, 5, Pfizer, 2, Sanofi-Aventis, 5, UCB, 5.

Abstract Number: 1063

Effects of Abatacept on T Regulatory Cells in Early Diffuse Systemic Sclerosis

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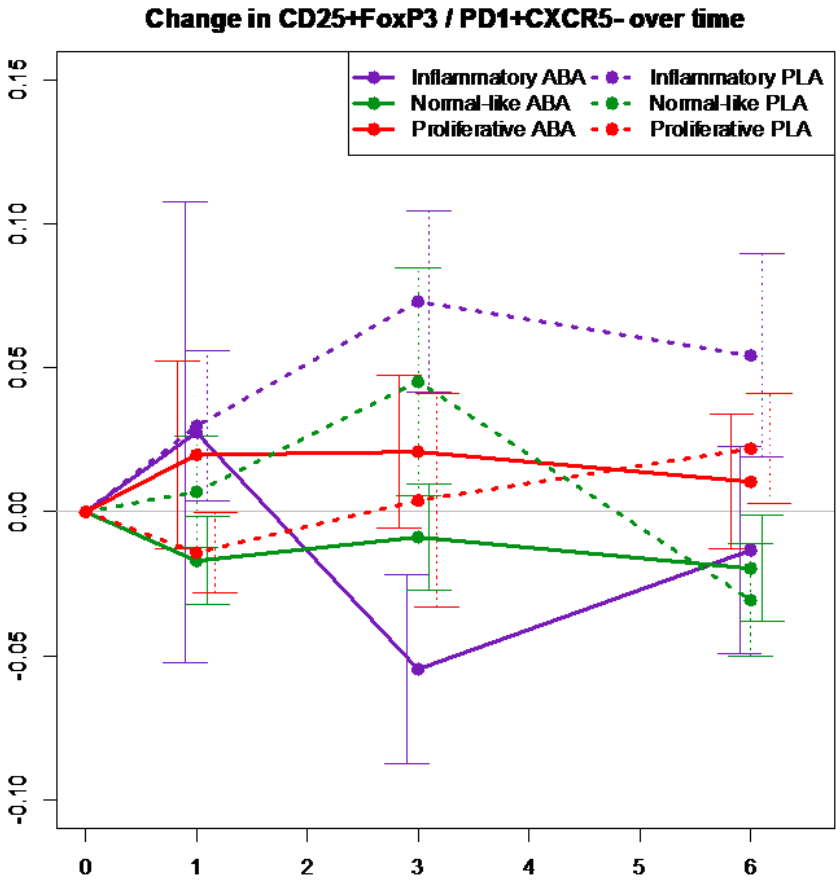
Background/Purpose: Background: In a randomized controlled trial of abatacept in early diffuse systemic sclerosis (Khanna D, et al ACR 2018), we observed early clinical flares (< 2 months into treatment with study drug) in 5 of 88 patients, including 4 renal crisis and one early pulmonary deterioration. Four of these patients (3 renal crisis and pulmonary decline) were receiving abatacept. Early depletion of regulatory T cells (Tregs) was recently observed in a study of abatacept for multiple sclerosis (Glatigny et al, J Immunol, 2019:1373-82). We asked whether depletion of Tregs occurred early in SSc patients treated with abatacept, and whether this could be linked to concurrent clinical deterioration.

Methods: We used multi-parameter flow cytometry to enumerate Tregs and other lymphocyte subsets, such as T peripheral helper cells (Tph) at times 0, 1, 3 and 6 months of the ASSET study. We stratified patients, according to their



pattern of gene expression on baseline skin biopsies, into three predefined distinct subgroups, termed inflammatory, fibroproliferative and normal-like.

Results: The SSc patients who experienced serious early clinical deterioration were all in the inflammatory gene expression subgroup. The numbers of Tregs did not differ at baseline comparing SSc patients (4.7% of CD4+) versus controls (4.14%, p = 0.235), and was not lower in the inflammatory subgroup at baseline (5%), compared with fibro-proliferative (4.29%) or normal-like (4.78%) subgroups (p values not significant comparing these subgroups to each other). With abatacept treatment the Treg number progressively fell in the inflammatory subgroup from month 0 to 3 (p=0.02 at 1 month, 0.0009 at 3 months, 0.02 at 6 months). At 3 months placebo-treated inflammatory subgroup patients had a mean 6.42% Tregs within CD4+ cells compared to 2.49% in abatacept-treated patients. In the normal-like group there was a Treg reduction in the abatacept-treated patients at 3 months (p=0.03). In the fibro-proliferative group Tregs rose in both placebo and abatacept-treated patients (p not significant). We also noticed that changes of Tregs and Tph cells tended to correlate negatively with each other in the inflammatory group patients early during abatacept treatment (r = -0.38, month 0 to 1), compared to patients who received placebo (r = +0.52) and those who received abatacept in the other 2 gene expression subgroups. We created a novel parameter, the ratio of Treg/Tph cells, to further assess immune cell imbalance that might occur with abatacept treatment in early SSc. This ratio declined sharply early during abatacept treatment (p = 0.007 at 3 months)(Figure 1), and the change was primarily driven by patients in the inflammatory subgroup.

Conclusion: Stratification of SSc patients into predefined subgroups based on skin biopsy gene expression predicts which patients are at risk for early flares on abatacept. A proposed mechanism for such flares involves Treg depletion and early Treg/Teffector cell imbalance. Although clinical benefit appears in these patients by 6-12 months, initial treatment may require agents other than or in addition to abatacept. This needs to be further confirmed in other ongoing trials of abatacept.

Disclosure: D. Fox, None; **M. Whitfield**, BMS, 5, Boehringer Ingelheim, 5, Corbus Pharmaceuticals, 5, Third Rock Ventures, 5, Celdara Medical LLC, 2, 5, 7, 9; **V. Berrocal**, None; **S. Lundy**, None; **P. Campbell**, None; **S. Rasmussen**, None; **R. Ohara**, None; **A. Stinson**, None; **E. Wiewiora**, None; **C. Spino**, Eicos, Inc., 5; **E. Bush**, None; **D. Furst**, Actelion, 5, Amgen, 5, BMS, 5, Corbus, 5, Galapagos Novartis, 5, Pfizer, 5, GSK, 5, Novartis, 5, Sanofi, 5, Roche/Genentech, 5, CME, 5; **S. Pillai**, Abpro, 6; **D. Khanna**, Acceleron, 5, Actelion, 5, Bayer, 2, 5, Blade Therapeutics, 5, BMS, 2, 5, Boehringer Ingelheim, 5, Celegene, 5, ChemomAB, 5, Corubus, 5, CSL Behring, 5, Curzion, 5, Cytori, 5, Eicos, Inc, 4, Genentech, 5, GSK, 5, Horizon, 2, Mitsubishi Tanabe Pharma Development America, 5, Pfizer, 2, Sanofi-Aventis, 5, UCB, 5.

Abstract Number: 1064

CD123$^+$ Plasmacytoid Dendritic Cells from Systemic Sclerosis Patients Are Susceptible to the Cytotoxic Activity of Tagraxofusp, a CD123-Targeted Therapy

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SESSION INFORMATION
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Background/Purpose: Tagraxofusp is a novel targeted therapy directed to the interleukin-3 receptor (CD123). Tagraxofusp is comprised of human IL-3 recombinantly fused to a truncated diphtheria toxin (DT) payload engineered such that IL-3 replaces the native DT receptor-binding domain. In this way, the IL-3 domain of tagraxofusp directs the cytotoxic DT payload to cells expressing CD123. Upon internalization, tagraxofusp irreversibly inhibits protein synthesis and induces apoptosis of the target cell.

Tagraxofusp was recently approved by the FDA for the treatment of patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN), a malignancy derived from the plasmacytoid dendritic cell (pDC) precursor. pDCs are immune cells that express CD123, secrete IFN-α, and play a role in inflammation and disease pathogenesis observed in systemic sclerosis (SSc) patients[1,2]. Therapeutic depletion of pDCs or attenuation of pDC function may represent a novel approach to treating SSc patients.

Methods: Patients fulfilled the 2013 ACR/EULAR classification criteria for SSc[3]. PBMCs from either SSc patients or healthy volunteers (HV) were prepared using Ficoll-Paque density gradient from fresh blood. pDCs were isolated from PBMCs as previously described and used to enrich the frequency of pDCs in an additional draw of PBMCs[4]. pDC-enriched PBMCs (3-6% pDCs) were cultured at $2x10^5$ cells per well in the presence or absence of CpG-274 (0.5 μM) to activate pDCs and then incubated with tagraxofusp (0.01-100 ng/ml, 0.17 pM-1.7 nM) at 37°C, 5% CO_2, and 95% humidity. After 24 h of culture, pDC survival was assessed by flow cytometry (CD14-, CD3- BDCA4+ CD123+), and supernatants were collected for cytokine quantification by a multiplexed Luminex assay. Changes in gene expression were measured by PCR on 10 μg cDNA, and calculated based on relative threshold cycle and expression of a ubiquitin housekeeping gene.

Results: Tagraxofusp was cytotoxic towards pDCs from both HV (n=5) and SSc donors (n=5) to a similar extent. The ED_{50} of tagraxofusp in pDCs from HV and SSc was 4.3 and 3.2 ng/ml (74.4 and 55.4 pM), respectively; no effect was observed on B or T cells across the tagraxofusp dose range tested (Fig.1A). Tagraxofusp-mediated pDC depletion

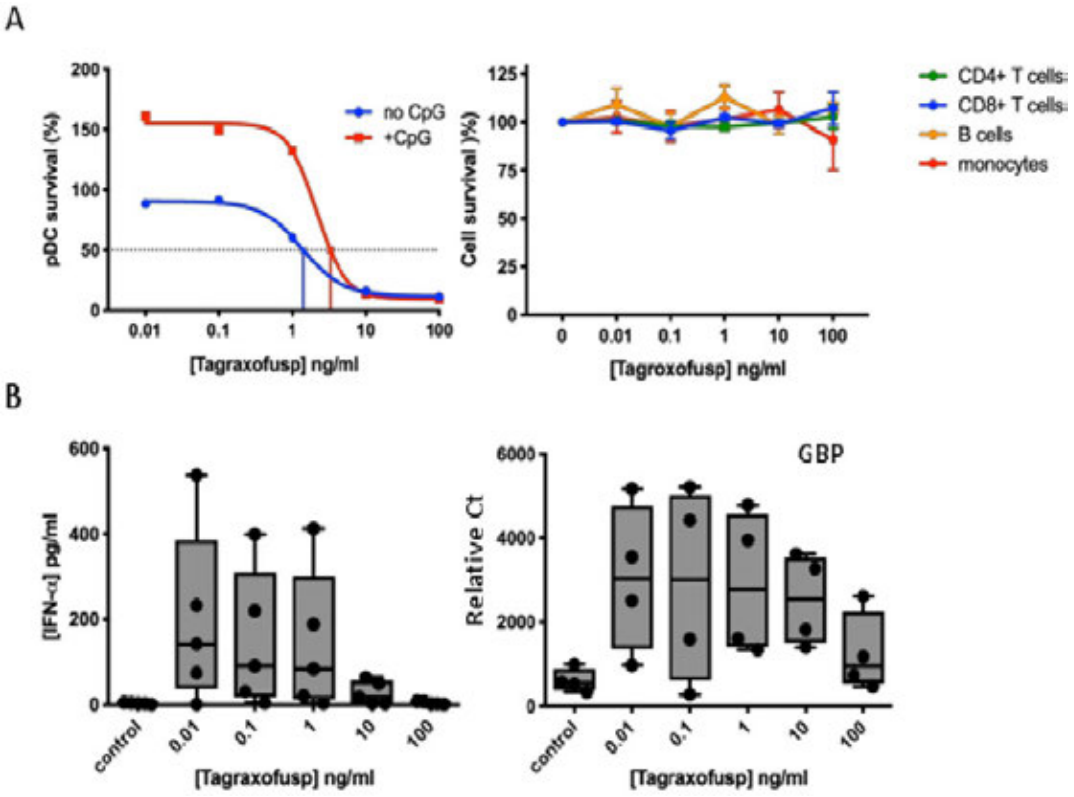

Figure 1. SSc pDC survival following 24 h incubation with tagraxofusp demonstrating a similar ED50 in both CpG-stimulated (red) and unstimulated (blue) pDCs (n=5) but no effect on B/T cells or monocytes (A). Concurrent with the decline in pDC survival, reductions in CpG-induced IFN-a production and expression of the IFN-a-induced gene, GBP, were observed (B).

was further accompanied by a 68-fold reduction in secreted IFN-α and a 3-fold downregulation of GBP, a type 1 IFN-induced gene (Fig. 1B).

Conclusion: Tagraxofusp is a novel CD123-targeted therapy that is cytotoxic towards pDCs from SSc patients. These data present a novel approach of targeting pDCs in the treatment of SSc, and a clinical trial is under design.

Disclosure: R. Lindsay, Stemline Therapeutics, 1, 3; **J. Chen**, Stemline Therapeutics, 1, 3; **R. Spiera**, BMS, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, ChemoCentryx, 2, 5, Chemocentryx, 2, Corbus, 2, CSL Behring, 5, Cytori, 2, Formation Biologics, 2, Genentech, Inc., 2, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, GSK, 2, 5, Hoffman-La Roche Ltd, 2, Janssen, 5, Mitsubishi, 5, Roche, 2, Roche Genetech, 2, 5, Roche/Genetech, 2, 5, Roche-Genentech, 2, 5, Roche-Genetech, 2, 5, Sanofi, 5, Sanofi-Aventis, 5; **J. Gordon**, Corbus, 2, Corbus Pharmaceuticals, 2, Cumberland, 2, Cumberland Pharmaceuticals, 2, Elcos, 2; **M. Ah Kioon**, Stemline Therapeutics, 2; **F. Barrat**, Stemline Therapeutics, 2; **C. Brooks**, Stemline Therpeutics, 1, 3.

Abstract Number: 1065

Aberrant Expression Levels of Soluble Co-inhibitory Receptors Linked to Disease Activity in Systemic Sclerosis

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SESSION INFORMATION

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Background/Purpose: Emerging evidence suggests dysregulated T cell activation in systemic sclerosis (SSc). Co-inhibitory-receptors such as TIM-3, PD-1 and LAG-3 are key factors in immune homeostasis and autoimmunity. These receptors regulate T-cell responses by inhibiting effector T-cell activation directly by affecting antigen presentation. Soluble forms of these molecules are generated by proteolytic cleavage of membrane-bound proteins. We evaluate the potential role of these soluble co-inhibitory markers in SSc and their impact on disease outcomes in diffuse SSc (dcSSc).

Methods: sPD-1, sLAG-3 and sTIM-3 were measured in sera from 35 patients with dcSSc and 26 healthy controls. All patients had disease duration of less than 5 years. Modified Rodnan skin sore (mRss) varied between 8-39, mean 22. Correlation with key clinical parameters including possible effect of disease modifying agents (DMARDs: methotrexate, mycophenolate mofetil and prednisolone) was determined. Patient characteristics are summarised in **Table 1**.

Results: For sPD-1, compared to healthy controls with below detection levels, the mean level was increased (136pg/ml) among dcSSc patients. There was no association between sPD-1 and organ involvement or autoantibodies. Comparison of sPD-1 levels in patients on DMARDs with those without treatment demonstrated significant effect of

Table 1. SSc cohort characteristics

	n	%
Male	12	34.29
Age (years), mean(SD)	51.5 (13.7)	
Age onset (years), mean(SD)	49.7 (13.5)	
Disease duration (months), mean(SD)	22.2 (11.6)	
Overlap	7	20
Organ disease		
Pulmonary fibrosis	11	31.43
Cardiac SSc	2	5.71
Scleroderma renal crisis	5	14.29
Gut involvement	14	40
Digital ulcers	6	17.14
Tendon friction rubs	6	17.14
Antibodies		
Anti-RNA polymerase	18	51.43
Anti-Topoisomerase I	13	37.14
Anti-U3RNP	1	2.86
Treatment		
CYC	2	5.71
MMF	16	45.71
MTX	5	14.29
Pred	9	25.71

immunosuppressive therapies, with mean sPD-1 95.1 pg/ml among patients on DMARD compared to 216.7 pg/ml among those on no treatment (p=0.02).sPD-1 demonstrated association with ESR (Spearman's rho=0.3505, p=0.03), but not CRP. There was association between sPD-1 and mRss (Spearman's rho=0.3759, p=0.04) and FVC (Spearman's rho=0.3722, p=0.04). Mean sLAG-3levels were significantly lower among dcSSc patients (394.6 pg/ml) vs healthy controls (740.8 pg/ml, p< 0.05). sLAG-3 was inversely associated with disease duration (Spearman's rho =-0.3438, p=0.04). There was a trend for association between sLAG-3and mRss, with higher levels of sLAG-3 seen in patients with higher skin score (Spearman's rho =0.3304, p=0.06),and between sLAG-3levels and presence of tendon friction rubs (TFR) (mean sLAG-3366.3 ng/ml among patient without TFR and 531.5 ng/ml among those with TFR, p=0.08). There was highly significant difference in the sTIM-3 levels between healthy controls (mean 4721.9 ng/ml) and dcSSc patients (8728.0 ng/ml, p< 0.05). There was a trend for association between anti-Scl70 (ATA) positivity and sTIM-3 levels (7579.5 ng/ml in ATA+ vs 9406.6 ng/ml in ATA- patients, p=0.09). Hb levels showed significant association with sTIM-3, with higher Hb levels associated with lower sTIM-3 levels (Spearman's rho =-0.4018, p=0.02). There was a weak association between platelet count and sTIM-3 (Spearman's rho =0.3267, p=0.06).

Conclusion: Our data show that soluble co-inhibitors are differentially expressed in early dcSSc and correlate with key clinical features. Although they may be selectively affected by some immunosuppressive therapies, this may reflect pathway dysregulation and may provide serological markers for evaluation of disease activity and severity in diffuse SSc.

Disclosure: V. Ong, None; **S. Nihtyanova**, None; **D. Abraham**, UCB, 2; **M. Aspari**, None; **C. Denton**, Actelion, 5, Actelion Pharmaceuticals, 5, Actelion, GlaxoSmithKline, Bayer, Sanofi, Inventiva, Boehringer Ingelheim, Roche, Bristol Myers Squibb, CSL Behring, UCB, Leadiant Biosciences, 5, Bayer, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Corbus Pharmaceuticals, 5, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, Leadiant Biosciences, 2, 5, Inventiva, 5, Pfizer, 5, Roche, 5, Sanofi, 5, UCB, 5; **B. Deleuran**, None.

Abstract Number: 1066

Dysregulated IL-6 Dependent Dermal Adenosine Signaling via Adenosine A2A Receptor May Drive Fibrosis in Systemic Sclerosis

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Background/Purpose: Altered generation of adenosine from extracellular nucleotides by ectonucleotidases may orchestrate chronic injury responses and promote fibrosis via the adenosine A2A receptor (ADORA2A). We have explored perturbed adenosine signaling pathways and potential links with fibroblast activation in early stage diffuse scleroderma (SSc).

Methods: Dermal fibroblasts were cultured from diffuse SSc (n=15) and healthy controls (n=5). RNA-Seq explored expression of enzymes involved in degradation of adenosine (adenosine deaminase [ADA] and adenosine kinase [AK]), ectonucleotidases(CD39, CD73) and adenosine receptors.Production of key profibrotic mediators (collagen α1[Col1], alpha smooth muscle actin [αSMA] and connective tissue growth factor [CTGF]) was analysed by western

blot of cell lysates in response to adenosine receptor agonist 5'-N-ethylcarboxamidoadenosine (NECA), A2A adenosine agonist (CGS-21680), A2A adenosine antagonist (ZM241385) and polyethylene glycol conjugated recombinant bovine ADA[PEG-rADA] (EZN 2279- elapegademase). Cell migration was assessed at 48h using scratch wound assay and contraction of fibroblast populated 3D collagen gel lattices at 24h.

Results: ADA transcript was increased (1.85-fold, p=0.01, n=12) in SSc fibroblasts (SScF) compared to normal fibroblasts (NF, n=5). In contrast, no significant difference in AK expression (0.79-fold, p=0.19) was observed. ADORA2A was significantly lower in SScF compared to NF (0.33 fold, p=0.04) and CD73 expression reduced in SScF compared to NF (0.61-fold, p=0.004). SScF produced higher levels of Col1 than NF (11.54±2.66 vs 22.07±1.57, p=0.02, n=3). Whilst there was no significant increase in Col1 in response to EZN2279 (9.24±1.18, p=0.2) or ZM241385 (8.95±1.55, p=0.17) in NF, there was with CGS-21680 (1.86 fold, p=0.04). In contrast, there was a smaller induction in Col1 in SScF with CGS-21680 (1.34 fold, p=0.02). The increase in Col1 in SScF was attenuated with EZN2279 and ZM241385 to similar extent (0.56 fold and 0.55 fold respectively, p< 0.05). Analogous response was observed for both αSMA and CTGF. Migratory capacity was enhanced with CGS-21680 in NF (62.83±4.80 vs 45.73±4.86 p< 0.05, n=3) and in SScF (31.17±3.62 vs 25.06±2.01, p< 0.05, n=3). In SScF, this was abrogated with EZN2279 and ZM241385 (56.29±6.26 and 52.32±4.33 respectively, p< 0.05). Gel contraction was induced by CGS-21680 in SScF (120.56±21.19 vs 78.77±6.91, p< 0.05,n=3) compared to NF (196.01±20.87 vs 133.82±19.46, p=0.06,n=3). In SScF, induction of contractile activity was further attenuated with EZN2279 and ZM241385 (189.83±16.44 and 181.02±13.18 respectively, p< 0.05). When stimulated with NECA, increased IL-6 was detected in media of fibroblasts (NF, n=3) (3.09±1.04 vs 14.18±1.56, p< 0.05) and this was attenuated with both EZN2279 and ZM241385 (3.88±0.99 and 3.03±1.10 respectively, p< 0.05).

Conclusion: These data suggest adenosinergic signalling is profibrotic and altered in SSc and that an ADORA2A-IL6 dependent loop may contribute to fibrosis. This may have therapeutic relevance for SSc.

Disclosure: C. Denton, Actelion, 5, Actelion Pharmaceuticals, 5, Actelion, GlaxoSmithKline, Bayer, Sanofi, Inventiva, Boehringer Ingelheim, Roche, Bristol Myers Squibb, CSL Behring, UCB, Leadiant Biosciences, 5, Bayer, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Corbus Pharmaceuticals, 5, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, Leadiant Biosciences, 2, 5, Inventiva, 5, Pfizer, 5, Roche, 5, Sanofi, 5, UCB, 5; **S. Xu**, None; **S. Verma**, Leadiant Biosciences, 3; **V. Ong**, None.

Abstract Number: 1067

Identification of miRNAs in Systemic Sclerosis Based on Activity and Network Analysis

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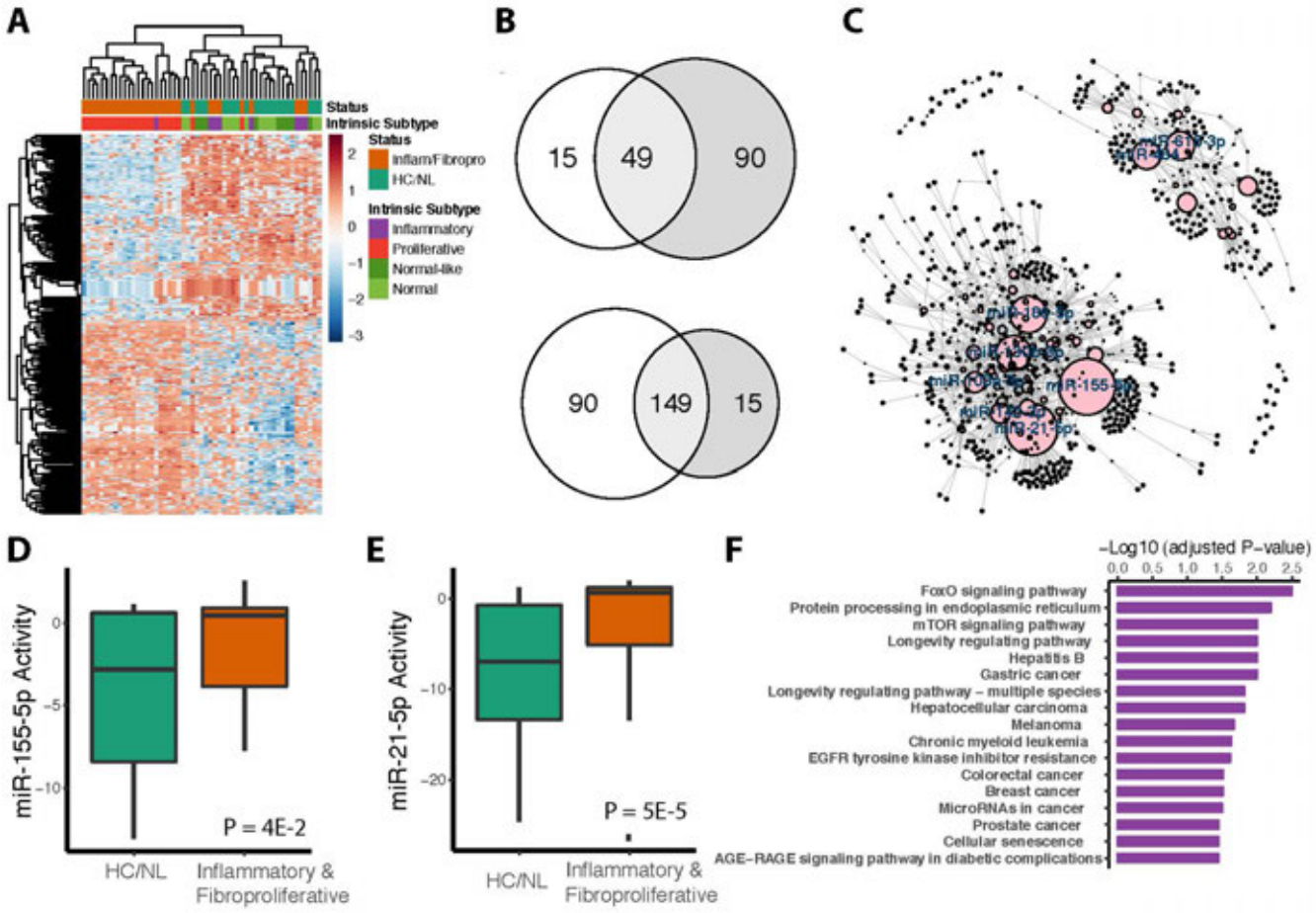

Figure 1. The identification of miRNA in SSc based on activity and network analysis. (A) Heatmap of miRNAs with differential activity in Milano dataset. (B) Venn diagram plot of miRNAs with the consistent direction within datasets. (C) miRNA-target network using miRNAs with differntial activity and targets. (D) and (E): Boxplot for miR-155-5p and miR-21-5p activity in Milano dataset. (F) Enriched pathways of miR-155-5p targets.

Background/Purpose: Systemic sclerosis (SSc; scleroderma) is a rare, heterogenous autoimmune disease characterized by skin fibrosis, vasculopathy and internal organ involvement. SSc patients can be divided into four intrinsic gene expression subtypes: inflammatory, fibroproliferative, limited and normal-like. The expression and activity of miRNAs, non-coding RNAs that post-transcriptionally regulate gene expression, have not been comprehensively characterized across the intrinsic gene expression subsets. We investigated the regulation and activity of miRNAs across the SSc subsets, developed a miRNA-target network, and experimentally validated a key hub of the network.

Methods: Gene expression profiles were downloaded for two patient cohorts, Milano et al. (GSE9285; 75 samples) and Assassi et al. (GSE58095; 102 samples). miRNA-target interactions (MTIs) were collected from miRTarBase; the activity of each miRNA is based on the expression of its target genes. The BASE algorithm was used to generate the miRNA regulatory activity scores for each miRNA in each sample. A Wilcoxon rank sum test was used to identify miRNAs with differential activity in inflammatory and fibroproliferative SSc samples. A miR-seq was performed on 8 SSc and 4 healthy control skin samples to validate findings. Targets strongly inhibited by cognate miRNAs were used to create the MTI network by calculating their negative correlation. The R package “igraph” was used for visualization and topological analysis of the network. Centrality measures

were used to determine the node importance. For the most essential miRNAs, target genes were ranked and functionally annotated by pathway enrichment analysis using g:Profiler. miRNAs knockdowns in primary human SSc-differentiated macrophages were used to validate *in-silico* analyses.

Results: We identified a total of 198 miRNAs that were consistently differentially activated in both datasets (149 miRNAs were upregulated, and 49 miRNAs were downregulated). 1534 target genes were connected to these miRNAs in the network. Topological measurements of the network revealed that miR-155-5p and miR-21-5p had the broadest influence throughout the network. Both miR-155-5p and miR-21-5p showed consistently high activity in inflammatory and fibroproliferative SSc samples, and were highly expressed by miR-seq. MiR-155-5p has 92 target genes in this network that are significantly enriched in pathways that regulate inflammation and macrophage activation including the FoxO signaling pathway, which has been shown to mediate the prevention of autoimmunity.

Conclusion: We identified a list of miRNAs that show differential activity in SSc samples. MiR-155-5p and miR-21-5p were the most central in the regulatory network topologically, and have significantly higher activity and expression in inflammatory and fibroproliferative SSc samples. Over-activation of miR-155-5p leads to the loss of pathways associated with inhibition of autoimmune disease and proliferation of muscle cells.

Disclosure: Y. Yuan, None; **Y. Wang**, None; **P. Pioli**, None; **M. Whitfield**, None.

Abstract Number: 1068

Classical Monocytes from African Ancestry Patients with Systemic Sclerosis Show Transcription and Energy Regulation Gene Expression Signatures

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a rare autoimmune disorder characterized by immune dysregulation, cutaneous and visceral fibrosis, and vasculopathy. It disproportionately affects African ancestry (AA) individuals who, despite the higher disease severity, are dramatically underrepresented in research. Monocytes show heightened activation in SSc, and in AA relative to European ancestry individuals. Monocytes are thus a good target tissue for elucidating disease mechanisms. In this study, we sought to characterize differential gene expression of classical monocytes in SSc patients and unaffected controls of African ancestry.

Methods: Classical monocytes (CD14++CD16-) were FACS-isolated from 17 female AA SSc cases and 18 female AA controls. All patients met the 2013 ACR/EULAR classification criteria for SSc, most (72%) presenting with diffuse cutaneous SSc. Total RNA was used to prepare RNA-Seq libraries using Illumina's TruSeq RNA Exome kit. Upon sequencing on an Illumina HiSeq2500 instrument, data was analyzed by Rosalind, with a HyperScale architecture developed by OnRamp BioInformatics. Specifically, individual sample reads were aligned to the hg19 reference genome using STAR and quantified using HTseq. Differential expression analysis was implemented using DESeq2 and functional enrichment analysis was performed using Advaita iPathway Guide.

Results: A total of 743 genes showed differential expression (FDR P-value < 0.4). The top differentially expressed genes (P < E-04) include the collagen *COL9A2* gene, the protein phosphatase *PPP1R14B*, the tubulin *TUBB4B*, the kinase-binding *AKAP1*, the ubiquitin ligase *RNF146*, the heparanase *HPSE*, the nuclear factor NF-Kappa-B activator *TRAF3IP2*, and the chromatin regulator *SMARCA4.* The SSc monocyte transcriptome showed an enrichment of genes in the AMPK signaling pathway, genes involved in chromatin organization, transcription factor binding, and glycogen storage diseases. The top upstream regulator is the MAPK11 kinase.

Conclusion: Unlike what has been reported in different peripheral blood subsets in EA patients, our results show a weaker upregulation of genes involved in immune and inflammatory processes in monocytes from AA patients. Instead, our study reveals an upregulation of genes involved in cellular processes associated with transcription and energy regulation in SSc patients, consistent with an increased metabolic rate of these myeloid cells in SSc. These results support the increasing awareness that metabolic reprogramming has important roles in mediating immune and vascular responses. Collectively, these results support the need to understand the regulatory architecture of SSc in different cell types and in individuals of different ancestries.

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Abstract Number: 1069

$CD4^+$ T Helper Cell Populations with High PD-1 Expression Are Expanded in Systemic Sclerosis

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SESSION INFORMATION
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Background/Purpose: Systemic sclerosis (SSc) is an autoimmune disease characterized by tissue fibrosis, vascular injury, and autoantibody production. $CXCR5^+$ $PD\text{-}1^+$ T follicular helper (Tfh) cells, which are T cells specialized to help B cells, are expanded in the circulation of SSc patients and may contribute to both immune activation and fibrotic organ damage. Emerging evidence supports the existence of a wider range of B cell-helper T cells characterized by high expression of PD-1 including $PD\text{-}1^{hi}$ $CXCR5^-$ T peripheral helper (Tph) cells, which are dramatically expanded in the joints of RA patients and in the circulation of SLE patients. Here, we have evaluated the frequency of $PD\text{-}1^{hi}$ $CD4^+$ T cell subsets in a well-characterized cohort of SSc patients.

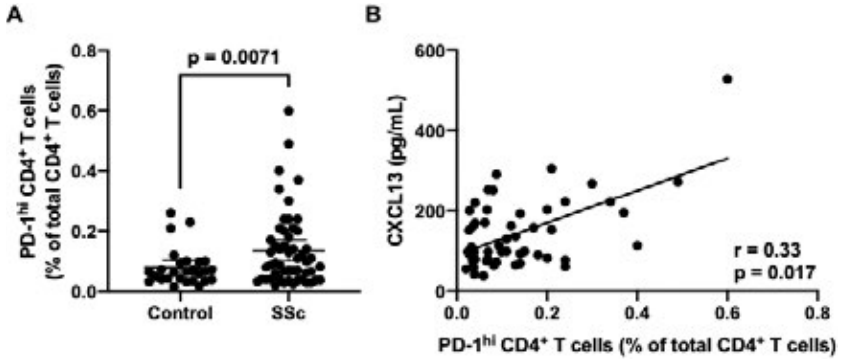

Figure 1. Expanded PD-1hi CD4+ T cell population in SSc patients. A) Percentage of PD-1hi CD4+ T cells among total CD4+ T cells in PBMCs from SSc and control patients by flow cytometry. B) Correlation between frequency of PD-1hi CD4+ T cells and CXCL13 levels as measured by ELISA with Spearman statistics.

Methods: Peripheral blood mononuclear cells (PBMCs) were collected from 101 SSc patients fulfilling the 2013 ACR/EULAR SSc classification criteria and 33 healthy controls. A comprehensive set of demographic and clinical characteristics was obtained at the time of enrollment including data on organ involvement, disease severity, autoantibody profile, pulmonary and cardiac functional status, and medications. Flow cytometry analysis was performed on PBMCs using an antibody panel designed to identify specific $CD4^+$ T cell subsets. Serum cytokine levels were measured by ELISA.

Results: Using strict gating on cells with very high PD-1 expression, we observed that the frequency of PD-1^{hi} $CD4^+$ T cells among total $CD4^+$ T cells was significantly increased in SSc patients compared to healthy controls (0.136% vs. 0.078%, p = 0.0071; Figure 1A). The PD-1^{hi} $CD4^+$ population contains two distinct B cell-helper T cell subsets: $CXCR5^+$ Tfh cells and $CXCR5^-$ Tph cells. Strict gating on $CXCR5^-$ cells indicated that PD-1^{hi} $CXCR5^-$ Tph cells were also increased in SSc samples (p = 0.011). PD-1^{hi} $CD4^+$ T cell populations are the major source of the B cell chemoattractant CXCL13, and we observed a positive correlation between PD-1^{hi} $CD4^+$ T cell frequency and serum CXCL13 concentration in SSc patients (Spearman r = 0.33, p=0.017; Figure 1B). To evaluate clinical associations with PD-1^{hi} $CD4^+$ T cell frequency, we stratified SSc patients based on high (≥ 0.20%) or low (≤ 0.05%) PD-1^{hi} $CD4^+$ T cell frequency. We found that 58% (7/12) of patients with high PD-1^{hi} $CD4^+$ T cell numbers had interstitial lung disease (ILD) compared to 27% (4/15) of patients with low PD-1^{hi} $CD4^+$ T cell numbers.

Conclusion: Our study shows that the frequency of PD-1^{hi} $CD4^+$ T cells, including PD-1^{hi} $CXCR5^-$ Tph cells, is significantly increased in SSc patients. Preliminary analyses suggest a relationship between PD-1^{hi} $CD4^+$ T cell frequency and SSc-ILD. These findings support a potential role for B cell-helper T cells including Tph cells in the autoimmune pathology of SSc.

Disclosure: A. Mueller, None; **A. Fava**, None; **D. Rao**, Janssen, 5, Merck, 2, Pfizer, 5; **F. Boin**, None.

Abstract Number: 1070

Cytokine Signatures Differentiate Systemic Sclerosis Patients at High versus Low Risk for Pulmonary Arterial Hypertension

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SESSION INFORMATION

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Background/Purpose: Pulmonary arterial hypertension (PAH) affects approximately 10% of patients with systemic sclerosis (SSc) and is a leading cause of death. Screening algorithms using clinical parameters have been developed to identify patients at high risk for PAH who should undergo confirmatory right heart catheterization (RHC). We sought to identify serum cytokines that might be useful in risk stratification of SSc patients for this potentially fatal complication.

Table 1. Baseline demographics and clinical characteristics of patient groups.

	Healthy n=20	PAH n=81	High Risk n=71	Low Risk n=10
Age, mean (std) (n)	59.7 (8.9) (20)	58 (11.3) (79)	60.1 (10.8) (71)	52.3 (10.7) (10)
Sex				
Female	15 (75)	59 (74.68)	62 (87.32)	9 (90)
Male	5 (25)	20 (25.32)	9 (12.68)	1 (10)
Race				
Asian/Pacific Islander		1 (1.27)	1 (1.41)	3 (30)
Black		12 (15.19)	2 (2.82)	0
Caucasian		64 (81.01)	60 (84.51)	3 (30)
Hispanic		2 (2.53)	5 (7.04)	3 (30)
Native American		0	2 (2.82)	0
Other Ethnic Origin		0	1 (1.41)	1 (10)
SSc Subtype				
Diffuse		20 (25)	15 (21.13)	5 (50)
Limited		57 (71.25)	54 (76.06)	5 (50)
Unclassified		3 (3.75)	2 (2.82)	
Antibody				
Mixed or other		15 (18.99)	13 (18.57)	0
Scl 70		13 (16.46)	15 (21.43)	2 (20)
U1RNP		3 (3.8)	1 (1.43)	0
Anticentromere		20 (25.32)	15 (21.43)	6 (60)
Isolated Nucleolar		20 (25.32)	13 (18.57)	0
Negative		3 (3.8)	9 (12.86)	2 (20)
RNA polymerase II		5 (6.33)	4 (5.71)	0
FVC, median (range) (n)		71.2 (27.1 - 104.8) (69)	85.2 (32.5 - 130.6) (64)	96 (84 - 112) (10)
DLCO, median (range) (n)		37 (9.9 - 90.7) (67)	50.4 (10.1 - 94.2) (60)	98.5 (80 - 128) (10)
RVSP, median (range) (n)		50.5 (17 - 120) (68)	38.5 (23 - 80) (60)	28 (18 - 35) (7)

Table 1. Baseline demographics and clinical characteristics of patient groups. PAH=pulmonary arterial hypertension; std=standard deviation; FVC=forced vital capacity; DLCO=diffusion capacity for carbon monoxide; SSc=systemic sclerosis.

Methods: Subjects were enrolled in the Pulmonary Hypertension Assessment and Recognition of Outcomes in Scleroderma (PHAROS), a multi-center prospective registry that includes SSc patients with 1) incident PAH based on RHC; 2) at high risk for PAH. High risk patients had a diffusion capacity for carbon monoxide (DLCO) < 55% predicted with a forced vital capacity (FVC) of >70% predicted, FVC/DLCO ratio >1.6, or right ventricular systolic pressure (RVSP) ≥40 mmHg on echocardiography. Low risk patients were enrolled at Stanford and had a DLCO ≥ 80%, FVC ≥ 80%, and RVSP ≤35mmHg or normal echocardiogram if no measurable tricuspid regurgitant jet was observed. Serum was available from 71 high risk patients, 81 incident PAH patients, 10 low risk patients, and 20 healthy controls (HC). A custom 14-plex array was used for cytokine analysis. Samples were normalized by background correction and removed if correlation between technical replicates was < 0.8. Cytokine expression was compared between patient groups by principal component analysis and Tukey's test result. A multiple hypotheses corrected p-value < 0.05 was considered significant.

Results: Baseline characteristics of each patient group are described in Table 1. Two cytokines (sVCAM-1 and PDGF-BB) were removed from further analysis due to low correlation on replicate testing. Principle component analysis showed unique clustering for each patient group (Figure 1). We found that there was a significant difference in cytokine expression in at least one group comparison for every cytokine. Overall, there was very little difference in cytokine expression comparing high risk and PAH patient groups; however, these groups had substantially different cytokine profiles compared to low risk patients. In particular, low expression of PAI-1, EGF, BDNF, and sICAM-1 differentiated the low risk group from the high risk and PAH groups, as well as from HC. Higher levels of RANTES and IL-12p40 differentiated the three SSc groups from HC (Figure 2).

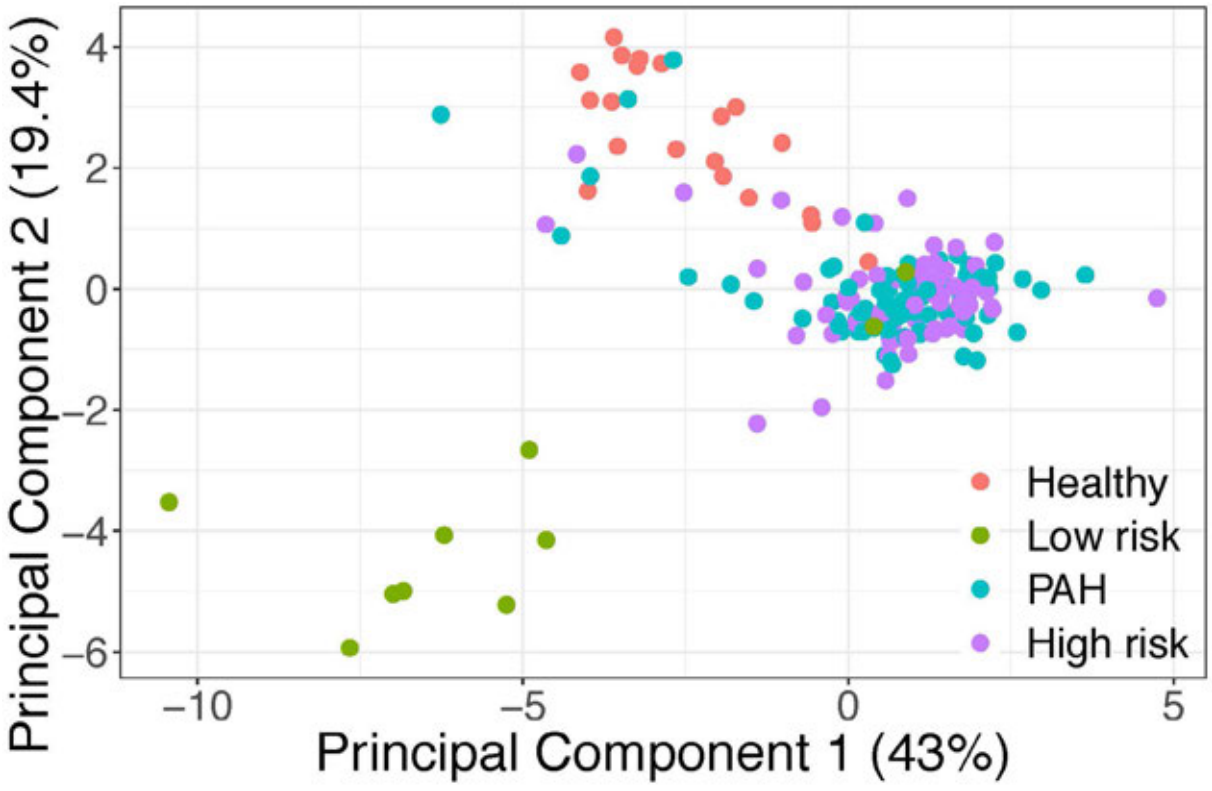

Figure 1. Principal component analysis of 14-plex cytokine array data distinguished different patient groups. Healthy controls and low risk SSC patients were different from SSc patients with PAH or at high risk of developing PAH.

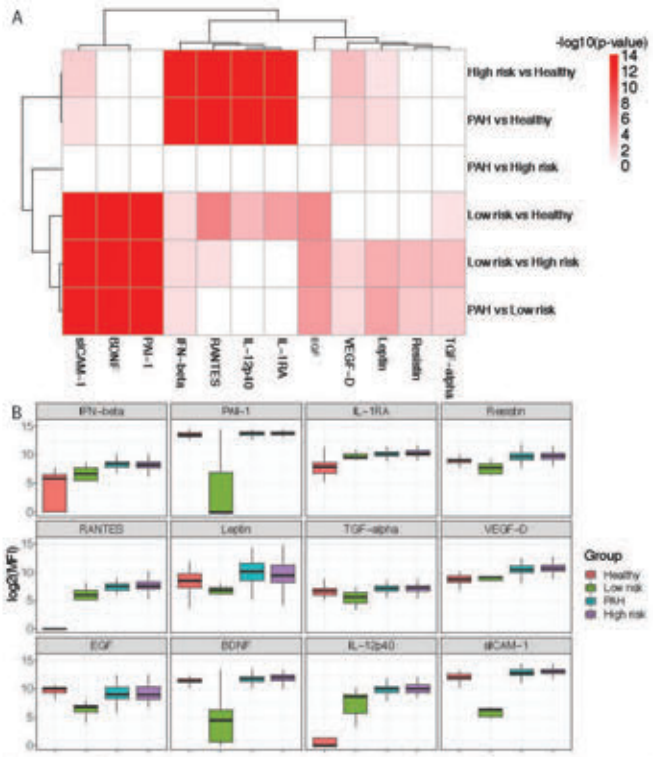

Figure 2. (A) Multiple hypotheses corrected p-values for each antigen in every pairwise comparison using Tukey's test. Every antigen was significantly different in at least one comparison. No antigen was significantly different between SSc patients at high risk of PAH or with PAH. (B) Boxplots of expression of each significant antigen in each of the four groups. Boxes represent inter-quartiles (25% and 75% percentile), and whiskers represent maximum and minimum values.

Conclusion: These data suggest that cytokine profiles can identify SSc patients who are at high risk for PAH. However, high risk and PAH patients had very similar cytokine profiles, suggesting that these patients are on a disease continuum. Our results need to be validated in an independent cohort of SSc patients.

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Abstract Number: 1071

A Common Transcriptional Signature Is Present in Circulating Classical Monocytes and Skin Macrophages in Systemic Sclerosis

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SESSION INFORMATION

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Background/Purpose: The etiology and pathogenesis of systemic sclerosis (SSc) are poorly understood; however, an increasing body of evidence supports an early inflammatory phase that precedes fibrosis. Circulating monocytes likely play a critical role in SSc progression through secretion of pro-inflammatory molecules and as precursors of macrophages that can reorganize the extracellular matrix (ECM) to leading to the development of end-organ fibrosis. Here we evaluate the transcriptional similarities between circulating classical monocytes and macrophages present in the skin of SSc patients.

Methods: Classical monocytes (CMo) were sorted using multiparameter fluorescence-activated cell sorting (FACS) from early diffuse cutaneous (dc) SSc sample blood obtained through the Prospective Registry of Early Systemic Sclerosis (PRESS) cohort. Bulk RNA-seq was performed, and transcriptional profiles were analyzed along with age-, sex-, and ethnicity-matched controls. Additionally, $CD45^+$ immune cells, as well as $CD31^+$ endothelial cells were FACS-sorted from skin biopsies of one SSc patient and one control patient and prepared for single-cell RNA-seq.

Results: There was an expansion in the skin macrophages from 36 cells in the control sample to 67 cells in the patient sample but no significant difference in the quantity (as a percent of total CD45+ cells) of circulating CMo ($p=0.134$) between controls and SSc patients. The differentially expressed genes in the circulating CMo were identified using DESeq2. Of the 152 significantly up-regulated genes (DESeq2, $p< 0.05$, Log2 Fold change in expression >1) observed in the circulating CMo population and the 290 up-regulated genes (Log2 Fold change in expression >1) found in the skin macrophage cluster compared to their respective controls, we find 23 genes in common ($p< 1.23x10\text{-}8$, hypergeometric distribution test). These shared genes are involved in processes that include 'inflammatory response' ($p< 6.56x10\text{-}4$, IL10, IL8, IL1B, CXCR4), 'regulation of mononuclear cell proliferation' ($p< 7.65x10\text{-}5$, IL1B, IL10, MNDA, PNP), 'dendritic cell migration' ($p< 5.07x10\text{-}4$, GPR183, CXCR4), 'cytokine-mediated signaling pathway' ($p< 1.68x10\text{-}5$, IL10, VEGF, CXCR4, IFI6), 'negative regulation of epithelial cell proliferation' ($p< 4.45x10\text{-}4$, RGCC, THBS1, EREG), 'regulation of endothelial cell proliferation' ($p< 4.02x10\text{-}5$, VEGFA, IL10, RGCC, THBS1).

Conclusion: These data indicate that a common transcriptional signature exists between circulating classical monocytes and macrophages present in the skin of SSc patients, potentially suggesting that macrophage-specific pathways that have gone awry at the site of fibrosis can be detected in a circulating precursor population. Future studies will focus on interrogating the penetrance of this gene signature by cross-referencing blood monocyte and skin

macrophage transcriptional profiles from the same patient to determine whether this signature in circulating classical monocytes correlates with the severity of skin fibrosis and/or serves as a predictive marker of disease.

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Abstract Number: 1072

CCR2^{+} Circulating Monocytes Contribute to the Survival of ADSC in Bleomycin-Induced Skin Fibrosis

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SESSION INFORMATION
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Background/Purpose: Monocytes and monocyte-derived cells play a crucial role during homeostasis and also during the development of various inflammatory diseases including skin fibrosis. Ly6C^{hi} inflammatory monocytes formed in the bone marrow enter the circulation as mature C-C Chemokine Receptor 2 (CCR2^{+}) cells and exert their function by their ability to differentiate into macrophages and other myeloid cell types in the peripheral tissues. Our lab previously showed upregulation of monocytes and monocyte derived macrophages followed by loss of adipose-derived stromal cells (ADSC) in bleomycin-induced skin fibrosis. CCR2 is implicated to have a pathogenic role in multiple fibrosis models. Here, we hypothesized that CCR2^{+} monocytes that infiltrate the skin following bleomycin treatment play an important role in modulating ADSC maintenance and bleomycin-induced skin fibrosis changes.

Methods: C57BL/6J wild type (WT) and CCR2 knockout (CCR2KO) mice were injected with either PBS (control) or 100ug of bleomycin subcutaneously on the lower back skin for indicated time periods. Skin was assessed for cellular changes by flow cytometry and for fibrotic changes by H&E staining followed by dermal and dermal white adipose tissue (DWAT) thickness measurements.

Results: Consistent with the idea that monocyte accumulation in skin is dependent on CCR2 and that the macrophages are monocyte-derived, we observed a robust increase in monocytes and monocyte-derived macrophages in WT but not CCR2KO mice at day 21 after bleomycin treatment. Contrary to expectations, however, while bleomycin-treated WT mice showed ~55% reduction in ADSC numbers compared to PBS control, CCR2KO mice under the same conditions showed further severity in ADSC loss (~80% reduction). CCR2 KO mice also showed increased dermal thickness without further loss of DWAT compared to bleomycin-treated WT mice. These results suggest a role for CCR2^{+} cells, potentially monocytes and monocyte-derived macrophages, in maintaining ADSC numbers and limiting fibrosis in bleomycin-induced skin fibrosis.

Conclusion: Our results thus far suggest a protective role for CCR2, potentially by mediating the accumulation of monocytes and macrophages and maintaining ADSC numbers during bleomycin-induced skin fibrosis. Further stud-

ies will focus on establishing the role of CCR2-dependent monocytes versus CCR2 on other cell populations as well as on understanding the mechanism by which CCR2 regulates ADSC populations. These results could thus help in better understanding and therapeutic targeting of the disease.

Disclosure: M. Chalasani, None; **L. Kim**, None; **T. Lu**, None.

Abstract Number: 1073

Identification of Distinct Pro-Fibrotic Monocyte and Macrophage Subsets in Systemic Sclerosis

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Background/Purpose: Chronic inflammation may modulate the balance of classical, intermediate and non-classical monocyte subsets (defined by CD14/CD16 expression)[1]. Monocytes are heterogeneous and subsets can be further delineated by examining expression of other cellular markers such as CD163, a haemoglobin-scavenging receptor which is associated with resolving inflammation and fibrosis. Systemic sclerosis (SSc) is a chronic autoimmune disease and a prototype for studying how the immune system regulates fibrosis[2]. The aim of this study is to characterise monocyte/macrophage subsets, and their function in SSc.

Methods: Blood samples from healthy donors and SSc patients were collected for serum, leukocyte and monocyte isolation. Leukocytes were stained with CD14, CD16 and CD163 antibodies for FACS analysis. Monocytes were iso-

Table 1. Key demographic features of SSc cohort.

Experiment		Healthy control	SSc
FACS	n	9	10
	Age (years)	56.7±14.3	50.7±5.7
	No. of women	7	8
	No. of dcSSc	-	10
	Disease duration ≤ 5 years	-	10
ELISA of supernatant	n	13	27
	Age (years)	60.6±16.7	52.1±13.0
	No. of women	6	26
	No. of dcSSc	-	27
	Disease duration ≤ 5 years	-	15
	> 5 years	-	12
ELISA of serum	n	32	42
	Age (years)	55.4±18.5	52.7±12.2
	No. of women	26	36
	No. of dcSSc	-	38
	Disease duration ≤ 5 years	-	30
	> 5 years	-	12

lated by negative selection and Ficoll separation of blood and cultured for 7 days into macrophages. Soluble CD163 levels were measured by ELISA. Macrophage supernatants were applied to scratch-wounded healthy skin fibroblast monolayers and fibroblast-populated collagen gels, to assess their effect on fibroblast migration and contraction, respectively. Mann-Whitney U tests, 2-tailed unpaired t-tests, Spearman's Rank and linear regression were used for statistical analysis.

Results: In our cohort of SSc patients (Table 1), we found two-fold more circulating $CD163^{+}CD14^{lo}CD16^{hi}$ non-classical monocytes (6.02±0.8 $x10^{3}$ cells/mL), than in healthy controls (2.69±1.0 $x10^{3}$ cells/mL), p=0.026. Accordingly, we observed significantly higher levels of soluble CD163 in SSc sera (682ng/mL) than in healthy control sera (587ng/mL), Mann Whitney U=413, p=0.010. Higher levels of soluble CD163/total protein were detected in supernatants of SSc macrophage cultures (9.96 $x10^{-3}$) compared to those of healthy controls (7.76 $x10^{-3}$), Mann Whitney U=77, p=0.005. There were no associations between sera or supernatant CD163 levels and clinical parameters such as disease duration, modified Rodnan skin score and lung fibrosis.

Fibroblasts treated with SSc macrophage media migrated faster (n=2, rate of closure 2.9% wound area/hour, R^2=0.90) into the scratch wound area of monolayers than those treated with healthy control media (n=2, rate of closure 1.7% wound area/hour, R^2=0.82), p=0.017. SSc macrophage supernatant promoted fibroblast contraction as indicated by the lower weight of fibroblast-populated collagen gels cultured in SSc macrophage supernatant (n=5, 110.7±8.6 mg) compared to those in healthy control supernatant (n=2, 153.6±6.8 mg), p=0.035.

Conclusion: Our data suggests that the increased frequency of systemic $CD163^{+}$ non-classical monocytes corresponds with upregulation of soluble CD163 in SSc. Parallel to this, the paracrine macrophage-fibroblast crosstalk is supportive of the micro-environment in promoting fibrosis. Thus, modulating both the systemic and local effects of non-classical monocytes mediated by CD163 may have therapeutic relevance in targeting fibrosis in SSc.

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1. Ziegler-Heitbrock L *et al,* Blood. 2010;116(16):e74-80.
2. Toledo DM, Pioli PA. Curr Rheumatol Rep. 2019;21(7):31.

Disclosure: A. Tam, None; **L. Reinke-Breen**, Bristol-Myers Squibb, 3; **G. Trujillo**, Bristol-Myers Squibb, 3; **S. Xu**, None; **C. Denton**, Actelion, 5, Actelion Pharmaceuticals, 5, Actelion, GlaxoSmithKline, Bayer, Sanofi, Inventiva, Boehringer Ingelheim, Roche, Bristol Myers Squibb, CSL Behring, UCB, Leadiant Biosciences, 5, Bayer, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Corbus Pharmaceuticals, 5, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, Leadiant Biosciences, 2, 5, Inventiva, 5, Pfizer, 5, Roche, 5, Sanofi, 5, UCB, 5; **D. Abraham**, UCB, 2; **G. Jarai**, Bristol-Myers Squibb, 3; **V. Ong**, None.

Abstract Number: 1074

Epigenetic Regulation-Mediated Reduction in the Expression of Prostacyclin Receptor and Prostacyclin Synthase in Scleroderma Skin, Vascular Smooth Muscle Cells, and Microvascular Endothelial Cells

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Progressive functional and structural vascular disorder is one of the hallmark features of Systemic Sclerosis (Scleroderma, SSc). Vascular dysfunction lead to dysregulated vascular tone control and activation of vascular smooth muscle cells (vSMCs) resulting in enhanced vasospasm and intimal hyperplasia. It is believed that vascular dysfunction results from imbalance in endothelial signals with increase vasoconstrictors and defective release of vasodilators and vSMCs inhibitors. In this study, we examine the expression levels of prostacyclin synthase (PTGIS) and prostacyclin receptor (IP) in normal and SSc skin, microvascular endothelial cells (MVECs) and vSMCs. We also investigated the effects of the DNA methyltransferase inhibitor 5-Aza-2′-deoxycytidine (Aza), and the histone deacetylase inhibiter trichostatin (TSA) on PTGIS and IP gene expression in SSc and normal MVECs and vSMCs.

Methods: MVECs and vSMCs were isolated from SSc patients' skin and matched healthy subjects. The mRNA and protein expression levels of IP and PTGIS were measured by qPCR and Western blot analysis (WB). In addition, epigenetic inhibitors were added to cell cultures to assess the role of epigenetic regulation on IP and PTGIS expression levels. MVECs and VSMCs were treated with Aza at 5uM for 5 days and TSA at 100nM for 1 day, and mRNA and protein expression levels were measured.

Results: The mRNA expression levels of PTGIS and IP were significantly downregulated in SSc-skin to 0.183-fold ± 0.03 for PTGIS ($P< 0.01$) and to 0.54-fold ± 0.06 for IP ($P< 0.01$), compared to control skin. The mRNA expression levels of PTGIS and IP were also decreased in SSc-vSMCs, compared to control (to 0.29-fold ± 0.04, $P< 0.01$ for PTGIS; to 0.46-fold ± 0.06 for IP, $P< 0.01$). WB analysis demonstrated similar reduction on the protein levels in SSc -vSMCs. Addition of Aza and TSA resulted in increased expression of IP and PTGIS to almost normal levels in SSc-vSMCs. SSc-MVECs also exhibited lower expression levels of PTGIS than control MVECs at both mRNA level (0.214-fold ± 0.03, $P< 0.01$) and protein level (0.49-fold ± 0.05, $P< 0.05$). The addition of Aza and TSA corrected the reduced mRNA and protein expression levels of PTGIS in SSc-MVECs.

Conclusion: These data demonstrate a defective prostacyclin (PGI2)-IP pathway in MVECs and vSMCs from SSc patients. This defect may contribute to the vascular dysfunction observed in SSc by decreasing the vasodilatory PGI2/IP signaling pathway, resulting in enhanced vasospasm and vascular remodeling. The addition of Aza and TSA corrected the reduced PTGIS and IP expression levels, suggesting an epigenetic regulation. Augmenting IP and PTGIS expression, either independent of or combined with the use of PGI2 analogues, may be an important new therapeutic strategy for SSc.

Disclosure: Y. Wang, None; **n. Altorok**, None; **B. Kahaleh**, None.

Abstract Number: 1075

The Impact of Race on Birth Outcomes Among Women with Autoimmune Rheumatic Diseases

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune rheumatic diseases (ARDs) are associated with adverse pregnancy outcomes (APOs). There are only a small number of studies that have looked at the association of race with APOs, especially in women of Asian race/ethnicity. Black race has been associated with worse APOs in women with ARDs when compared to Non-Hispanic White populations in a small number of studies. The aim of our study is to evaluate the impact of race and rheumatic disease on birth outcomes including preterm birth (PTB), congenital anomalies, low birth weight (LBW), and small for gestational age (SGA) in a large multiethnic cohort of women.

Table 1: Effect of race on pregnancy outcomes in singleton births of women 18 years and older with ARD in California from 2007 to 2012

Race	Asian		Black		Hispanic		White
	OR	95% CI	OR	95% CI	OR	95% CI	
ARD				*Preterm birth*			
Any [A]	1.63*	1.36-1.96	2.09*	1.72-2.53	1.33*	1.16-1.52	REF
SLE	1.71*	1.31-2.24	1.85*	1.39-2.45	1.54*	1.24-1.91	REF
RA	1.24	0.82-1.89	2.49*	1.70-3.65	0.97	0.75-1.26	REF
				Small for gestational age			
Any [A]	2.33*	1.92-2.83	2.34*	1.89-2.89	1.40*	1.20-1.62	REF
SLE	2.13*	1.59-2.86	1.91*	1.39-2.63	1.44*	1.13-1.84	REF
RA	2.44*	1.61-3.69	2.16*	1.40-3.34	1.44*	1.09-1.91	REF
				Low birth weight			
Any [A]	1.89*	1.55-2.30	2.36*	1.92-2.89	1.63*	1.41-1.89	REF
SLE	1.96*	1.48-2.61	2.13*	1.59-2.87	1.88*	1.50-2.35	REF
RA	1.69*	1.09-2.64	2.68*	1.76-4.09	1.19	0.89-1.60	REF
				Premature rupture of membranes			
Any [A]	1.07	0.73-1.56	1.53*	1.04-2.24	1.06	0.82-1.38	REF
SLE	1.52	0.89-2.59	1.76*	1.02-3.05	1.37	0.89-2.11	REF
RA	0.40	0.14-1.12	1.50	0.73-3.08	0.89	0.57-1.37	REF

Models adjusted for maternal age, education, insurance and parity

ARD = autoimmune rheumatic disease, OR = odd's ratio, CI = confidence interval, SLE = systemic lupus erythematous, RA = rheumatoid arthritis, REF = reference

[A] SLE, RA, antiphospholipid syndrome, psoriatic arthritis, ankylosing spondylitis, JIA

* p≤0.05

Methods: Birth records linked to hospital discharge data of singleton births in California from 2007 to 2012 were leveraged for a retrospective cohort study including women at least 18 years old diagnosed with ARD. International classification of diseases, ninth revision codes were used to identify women with ARD, as well as PTB, LBW, SGA and congenital anomalies among infants. Race/ethnicity was abstracted from birth record data. The odds of PTB, LBW, SGA and congenital anomalies were estimated in separate logistic regression models and models were adjusted for maternal age, education, insurance and parity.

Results: Among women with an ARD diagnosis (rheumatoid arthritis, systemic lupus erythematosus, antiphospholipid syndrome, psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis) who met our eligibility criteria, Black women had a two-fold increased odds of PTB when compared to Non-Hispanic White women (OR 2.09, 95% CI 1.72-2.53). Additionally, Asian (OR 1.63, 95% CI 1.35-1.96) and Hispanic (OR 1.33, 95% CI 1.16-1.52) women were also more likely to give birth preterm. In women with RA, increased OR of PTB was only significant in Black women compared to Non-Hispanic White women. The odds of SGA were significantly increased for Asian (OR 2.33, 95% CI 1.92-2.83), Black (OR 2.24, 95% CI 1.89-2.89) and Hispanic women with any ARD compared with Non-Hispanic White women and remained significant for those with RA and SLE. Among women with any diagnosis of an ARD, race was not significantly associated with premature rupture of membranes except for Black women (OR 1.53, 95% CI 1.04-2.24).

Conclusion: Our findings support previous work that among women with an ARD diagnosis, minority race is a risk factor for adverse pregnancy outcomes including PTB and SGA. Although the etiology of this increased risk is not fully understood socioeconomic and genetic contributions have been proposed in prior work. Our study is the first study with a large group of women with Asian race/ethnicity and found that this group, along with Hispanic and Black women, have an increased risk of adverse pregnancy outcomes when compared with Non-Hispanic White women. Asian, Black, and Hispanic women with ARDs should undergo increased monitoring during pregnancies.

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Abstract Number: 1076

Incidence of Non-serious Infections Among Live Born Infants Born to Mothers Who Used Biologic Medications During Pregnancy for the Treatment of Autoimmune Diseases

Christina Chambers,[1] Yunjun Luo,[2] Diana L. Johnson,[2] Kenneth Lyons Jones,[2] and Ronghui Xu[2], [1]University of California San Diego, La Jolla, [2]University of California, San Diego, La Jolla

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In infants whose mothers were treated with biologic therapies during pregnancy, there has been a theoretical concern regarding potential risk of infections. Several recent reports have not noted significant increased risks for serious infections; however, there are limited data on less serious infections. Methods

The Organization of Teratology Information Specialists MotherToBaby Pregnancy Studies recruited pregnant women in the U.S. or Canada who with or without an autoimmune condition who were or were not taking a biologic medica-

Table 1: Effect of race on pregnancy outcomes in singleton births of women 18 years and older with ARD in California from 2007 to 2012

Race	Asian		Black		Hispanic		White
	OR	95% CI	OR	95% CI	OR	95% CI	
ARD				*Preterm birth*			
Any[A]	1.630*	1.357-1.959	2.090*	1.724-2.534	1.329*	1.164-1.517	REF
SLE	1.714*	1.311-2.241	1.846*	1.391-2.451	1.540*	1.245-1.906	REF
RA	1.245	0.818-1.894	2.494*	1.705-3.648	0.974	0.752-1.262	REF
				Small for gestational age			
Any[A]	2.334*	1.923-2.834	2.338*	1.888-2.895	1.396*	1.199-1.625	REF
SLE	2.130*	1.588-2.857	1.909*	1.388-2.626	1.442*	1.128-1.844	REF
RA	2.437*	1.611-3.686	2.163*	1.402-3.337	1.441*	1.088-1.909	REF
				Low birth weight			
Any[A]	1.888*	1.550-2.300	2.356*	1.918-2.894	1.635*	1.417-1.887	REF
SLE	1.964*	1.479-2.609	2.137*	1.589-2.873	1.879*	1.498-2.355	REF
RA	1.693*	1.086-2.639	2.684*	1.763-4.086	1.194	0.892-1.598	REF
				Premature rupture of membranes			
Any[A]	1.067	0.729-1.561	1.529*	1.045-2.236	1.064	0.820-1.380	REF
SLE	1.518	0.891-2.586	1.762*	1.019-3.047	1.370	0.890-2.110	REF
RA	0.400	0.142-1.123	1.503	0.734-3.078	0.886	0.571-1.373	REF

Models adjusted for maternal age, education, insurance and parity

ARD = autoimmune rheumatic disease, OR = odd's ratio, CI = confidence interval, SLE = systemic lupus erythematous, RA = rheumatoid arthritis

[A] SLE, RA, antiphospholipid syndrome, psoriatic arthritis, ankylosing spondylitis, JIA

* p≤0.05

tion. Live born infants were followed by maternal interview and pediatric records to approximately one year of life. Any use in pregnancy, and gestational timing of biologic medication were examined as predictors of any non-serious infections reported by the mother or the pediatrician in the infant. Non-serious infections were defined as infections not requiring hospitalization, e.g., common cold, otitis media, influenza, or urinary tract infection. Odds ratios (OR) and adjusted odds ratios (aOR) accounting for maternal use of systemic corticosteroids and their 95% Confidence Intervals (CI) were computed using the generalized estimating equation (GEE) approach.

Results: Between 2004 and 2017, 1,513 live born infants were born to women enrolled in the study. Of these, 768 were born to mothers who had used a biologic medication anytime in pregnancy, 311 to mothers with autoimmune diseases who used no biologic medication in pregnancy, and 434 to women with no chronic health conditions. Overall, 423/768 (55.1%) of mothers who used a biologic anytime in pregnancy had an infant with at least one non-serious infection compared to 152/311 (48.9%) in the autoimmune-disease unexposed group (aOR 1.28, 95% CI 0.98, 1.68). 276/492 or 56.1% of infants born to women who used a biologic anytime in the third trimester had a non-serious infection compared to autoimmune-disease unexposed (aOR 1.32, 95% CI 0.99, 1.78). Similarly elevated but non-significant aORs were found regardless of how late in gestation the last dose of biologic medication was taken. In contrast, infants born to mothers who used biologics anytime in pregnancy were consistently more likely to have non-serious infections compared to infants born to women without autoimmune diseases (179/434 or 41.2%); ORs 1.73 to 2.32).

Conclusion: Use of biologic medications anytime during pregnancy or in the third trimester was not associated with a significant increased risk of non-serious infections in infants when compared to infants born to women with the same underlying diseases but no biologic treatment, after accounting for use of systemic steroids. In contrast, a ~2-fold increase in non-serious infections was seen with biologic use in comparison to infants born to women without autoimmune diseases. It is possible that there was bias in documentation of more mild infections in infants born to women with autoimmune diseases compared to those without. Nevertheless, these data are generally reassuring to women with autoimmune diseases who require treatment with biologics during any part or all of pregnancy.

Disclosure: C. Chambers, AbbVie, 2, Amgen Inc., 2, Apotex, 2, Barr Laboratories, Inc., 2, Bristol-Myers Squibb, 2, Celgene, 2, GlaxoSmithKline, 2, Janssen Pharmaceuticals, 2, Kali Laboratories, Inc., 2, Pfizer, Inc., 2, Hoffman La Roche-Genentech, 2, Sandoz Pharmaceuticals, 2, Genzyme Sanofi-Aventis, 2, Takeda Pharmaceutical Company Limited, 2, UCB, USA, 2, Gerber Foundation, 2, Teva Pharmaceutical Industries Ltd., 2; **Y. Luo**, None; **D. Johnson**, None; **K. Lyons Jones**, AbbVie, 2, Amgen Inc., 2, Apotex, 2, Barr Laboratories, Inc., 2, Bristol-Myers Squibb, 2, Celgene, 2, GlaxoSmithKline, 2, Janssen Pharmaceuticals, 2, Kali Laboratories, Inc., 2, Pfizer, Inc., 2, Hoffman La Roche-Genentech, 2, Sandoz Pharmaceuticals, 2, Genzyme Sanofi-Aventis, 2, Takeda Pharmaceutical Company Limited, 2, Teva Pharmaceutical Industries Ltd., 2, UCB, USA, 2; **R. Xu**, AbbVie, 2, Amgen Inc., 2, Apotex, 2, Barr Laboratories, Inc., 2, Bristol-Myers Squibb, 2, Celgene, 2, GlaxoSmithKline, 2, Janssen Pharmaceuticals, 2, Kali Laboratories, Inc., 2, Pfizer, Inc., 2, Hoffman La Roche-Genentech, 2, Sandoz Pharmaceuticals, 2, Genzyme Sanofi-Aventis, 2, Takeda Pharmaceutical Company Limited, 2, Teva Pharmaceutical Industries Ltd., 2, UCB, USA, 2.

Abstract Number: 1077

Mediation of Adverse Pregnancy Outcomes in Autoimmune Conditions by Pregnancy Complications

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune conditions are associated with an increased risk of adverse pregnancy complications and outcomes, suggesting that pregnancy complications may mediate the excess risk. We performed a causal mediation analysis to quantify the mediated effects of autoimmune conditions on adverse pregnancy outcomes.

Table 1. Effect decomposition of the influence of rheumatoid arthritis and potential mediators on adverse pregnancy outcomes in 3 million live births in the state of California

	Total effect[a]		Direct effect[b]		Indirect effect[c]		Proportion
Mediator	aRR	95% CI	aRR	95% CI	aRR	95% CI	mediated[d]
			Preterm Birth				
Preeclampsia/hypertension	1.97	(1.78, 2.17)	1.77	(1.60, 1.96)	1.11	(1.08, 1.13)	20.4%
Gestational diabetes	1.98	(1.80, 2.19)	1.96	(1.78, 2.17)	1.01	(1.00, 1.02)	2.2%
Infection in pregnancy	1.99	(1.81, 2.20)	1.92	(1.74, 2.12)	1.04	(1.03, 1.05)	7.4%
			Cesarean Delivery				
Preeclampsia/hypertension	1.22	(1.15, 1.29)	1.19	(1.12, 1.26)	1.02	(1.02, 1.03)	13.3%
Gestational diabetes	1.23	(1.16, 1.30)	1.22	(1.15, 1.29)	1.01	(1.00, 1.01)	3.0%
Infection in pregnancy	1.23	(1.16, 1.30)	1.22	(1.15, 1.29)	1.01	(1.01, 1.01)	3.6%
			Small for Gestational Age				
Preeclampsia/hypertension *	1.53	(1.37, 1.73)	1.49	(1.33, 1.66)	1.03	(1.01, 1.05)	8.3%
Gestational diabetes	1.53	(1.37, 1.73)	1.53	(1.38, 1.71)	0.99	(0.99, 0.99)	3.0%
Infection in pregnancy	1.53	(1.37, 1.73)	1.52	(1.36, 1.69)	1.01	(1.00, 1.01)	1.5%

Models adjusted for race/ethnicity, maternal age, insurance provider, maternal education, overweight/obesity, and smoking

[a]Effect of rheumatoid arthritis on adverse pregnancy outcomes

[b]Effect of rheumatoid arthritis on adverse pregnancy outcomes that is not mediated by each pregnancy complication

[c]Effect of rheumatoid arthritis on adverse pregnancy outcomes mediated by each pregnancy complication

[d]Proportion of effect of rheumatoid arthritis on adverse pregnancy outcomes mediated by each pregnancy complication

*modeled with interaction term between exposure and mediator

Table 2. Effect decomposition of the influence of systemic lupus erythematosus and potential mediators on adverse pregnancy outcomes in 3 million live births in the state of California

Mediator	Total effect[a] aRR	95% CI	Direct effect[b] aRR	95% CI	Indirect effect[c] aRR	95% CI	Proportion mediated[d]
			Preterm Birth				
Preeclampsia/hypertension	3.09	(2.87, 3.32)	2.46	(2.29, 2.63)	1.25	(1.23, 1.28)	30.2%
Gestational diabetes	3.12	(2.91, 3.35)	3.10	(2.89, 3.32)	1.00	(1.00, 1.01)	1.0%
Infection in pregnancy	3.11	(2.91, 3.34)	2.96	(2.76, 3.18)	1.05	(1.04, 1.05)	7.0%
			Cesarean Delivery				
Preeclampsia/hypertension	1.40	(1.33, 1.47)	1.32	(1.26, 1.39)	1.06	(1.05, 1.06)	18.9%
Gestational diabetes*	1.41	(1.35, 1.48)	1.41	(1.34, 1.48)	1.00	(1.00, 1.00)	0.5%
Infection in pregnancy	1.40	(1.34, 1.48)	1.39	(1.32, 1.46)	1.01	(1.01, 1.01)	3.1%
			Small for Gestational Age				
Preeclampsia/hypertension*	1.89	(1.74, 2.06)	1.73	(1.59. 1.09)	1.09	(1.05, 1.13)	17.6%
Gestational diabetes	1.91	(1.76, 2.06)	1.91	(1.76, 2.07)	0.99	(0.99, 0.99)	0.0%
Infection in pregnancy	1.89	(1.76, 2.07)	1.89	(1.74, 2.05)	1.01	(1.01, 1.01)	1.4%

Models adjusted for race/ethnicity, maternal age, insurance provider, maternal education, overweight/obesity, and smoking

[a]Effect of systemic lupus erythematosus on adverse pregnancy outcomes

[b]Effect of systemic lupus erythematosus on adverse pregnancy outcomes that is not mediated by each pregnancy complication

[c]Effect of systemic lupus erythematosus on adverse pregnancy outcomes mediated by each pregnancy complication

[d]Proportion of effect of systemic lupus erythematosus on adverse pregnancy outcomes mediated by each pregnancy complication

*modeled with interaction term between exposure and mediator

Methods: We queried a retrospective California birth cohort created from linked birth certificates and hospital discharge summaries. From 2,963,888 births, we identified women with rheumatoid arthritis, systemic lupus erythematosus, psoriasis and inflammatory bowel disease. Pregnancy complications included preeclampsia/hypertension, gestational diabetes and infection in pregnancy. Adverse pregnancy outcomes were preterm birth, cesarean delivery and small for gestational age. We performed a causal mediation analysis to estimate the total effects of each autoimmune condition and adverse pregnancy outcome, and the indirect effects of each pregnancy complication.

Results: Each autoimmune condition was associated with an increased risk of all adverse pregnancy outcomes (Tables 1-3, inflammatory bowel disease not shown), except psoriasis and small for gestational age. The strongest mediator was preeclampsia/hypertension, accounting for 20-30% of the excess risk of preterm births and 10-15% of excess cesarean deliveries in all autoimmune conditions except IBD. Gestational diabetes and infections generally accounted for < 10% of excess adverse pregnancy outcomes. Of the four autoimmune conditions, selected pregnancy complications mediated the least amount of adverse pregnancy outcomes among women with inflammatory bowel disease (not shown).

Conclusion: We found evidence that some excess risk of adverse pregnancy outcomes is mediated through pregnancy complications, particularly preeclampsia/hypertension. Quantifying excess risk and associated pathways provides insight into the underlying etiologies of adverse pregnancy outcomes and can inform intervention strategies.

Table 3. Effect decomposition of the influence of psoriasis and potential mediators on adverse pregnancy outcomes in 3 million live births in the state of California

	Total effect[a]		Direct effect[b]		Indirect effect[c]		Proportion
Mediator	aRR	95% CI	aRR	95% CI	aRR	95% CI	mediated[d]
Preterm birth							
Preeclampsia/hypertension*	1.46	(1.22, 1.76)	1.31	(1.08, 1.58)	1.11	(1.05, 1.18)	32.9%
Gestational diabetes	1.48	(1.25, 1.78)	1.44	(1.19, 1.74)	1.03	(1.00, 1.06)	8.9%
Infection in pregnancy*	1.49	(1.25, 1.79)	1.41	(1.18, 1.70)	1.06	(1.01, 1.11)	15.9%
Cesarean Delivery							
Preeclampsia/hypertension	1.22	(1.11, 1.33)	1.19	(1.09, 1.31)	1.02	(1.01, 1.03)	11.8%
Gestational diabetes	1.22	(1.12, 1.34)	1.21	(1.10, 1.32)	1.01	(1.01, 1.02)	7.3%
Infection in pregnancy	1.22	(1.12, 1.34)	1.22	(1.12, 1.33)	1.01	(1.00, 1.01)	3.3%
Small for Gestational Age[e]							

Models adjusted for race/ethnicity, maternal age, insurance provider, maternal education, overweight/obesity, and smoking

[a]Effect of psoriasis on adverse pregnancy outcomes

[b]Effect of psoriasis on adverse pregnancy outcomes that is not mediated by each pregnancy complication

[c]Effect of psoriasis on adverse pregnancy outcomes mediated by each pregnancy complication

[d]Proportion of effect of psoriasis on adverse pregnancy outcomes mediated by each pregnancy complication

[e]Total effects observed between psoriasis and small for gestational age were null (aRR 1.00, 95% CI 0.81, 1.24); no mediation performed

*modeled with interaction term between exposure and mediator

Disclosure: C. Chambers, AbbVie, 2, Amgen Inc., 2, Apotex, 2, Barr Laboratories, Inc., 2, Bristol-Myers Squibb, 2, Celgene, 2, GlaxoSmithKline, 2, Janssen Pharmaceuticals, 2, Kali Laboratories, Inc., 2, Pfizer, Inc., 2, Hoffman La Roche-Genentech, 2, Sandoz Pharmaceuticals, 2, Genzyme Sanofi-Aventis, 2, Takeda Pharmaceutical Company Limited, 2, UCB, USA, 2, Gerber Foundation, 2, Teva Pharmaceutical Industries Ltd., 2; **G. Bandoli**, None; **N. Singh**, None; **J. Strouse**, None; **R. Baer**, None; **B. Donovan**, None; **S. Feuer**, None; **N. Nidey**, None; **K. Ryckman**, None; **L. Jelliffe-Pawlowski**, None.

Abstract Number: 1078

Cardiovascular Risk Awareness in Patients with Rheumatic Diseases: A Case-Control Study

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SESSION INFORMATION

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Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular diseases are among the most common comorbidities in patients with rheumatic diseases (RD) and leads them to an overall increase of mortality in comparison to the general population. Risk reduction can be reached through different strategies that control traditional cardiovascular risk (CVR) factors. In order to start lifestyle changes it is necessary an adequate knowledge of the disease and its consequences. Furthermore, patients who perceive themselves at a higher risk of developing CVD are more likely to make changes. The precaution adoption process model (PAPM) is a self-applied questionnaire useful to evaluate the knowledge of cardiovascular risk and outlines the actions that have been taken by each patient. Therefore, the objective was to assess the awareness of their CVR in patients with/without rheumatic diseases.Methods

A cross-sectional, observational, single center study was designed. Patients were recruited at a community educational healthcare conference. Population was divided into two groups; case group, with the following RD: RA, SLE, SS, AS, Scleroderma, PsA and DM, and a control group with subjects without RD. After clinical history, subjects were asked

Table 1. Demographic Characteristics

	Case (n=140)	Control (n=134)	*p*
Female*	126 (77.6)	104 (90)	**0.005**
Age**	54 (46-64)	57.5 (44-65)	0.330
BMI**	26.6 (23.8-29.8)	27.4 (24.4-30.2)	0.346
Systolic Arterial Pressure**	121 (113-133)	125 (112-139)	0.395
Diastolic Arterial Pressure**	78 (72-84)	78 (71-86.5)	0.860
Active smoking*	9 (6.7)	11 (8.6)	0.567
Sedentary*	77 (57)	64 (50.4)	0.281
Family history of CVD*	57 (43.2)	54 (43.5)	0.953
Arterial hypertension*	30 (21.7)	37 (28.2)	0.218
T2DM*	11 (8.3)	23 (17.7)	**0.023**
Dyslipidemia*	34 (25.8)	49 (38.6)	**0.027**
Myocardial infarction*	2 (1.5)	4 (3.1)	0.373
Stroke*	1 (0.7)	3 (2.3)	0.285
Kidney disease*	5 (3.8)	6 (4.8)	0.689

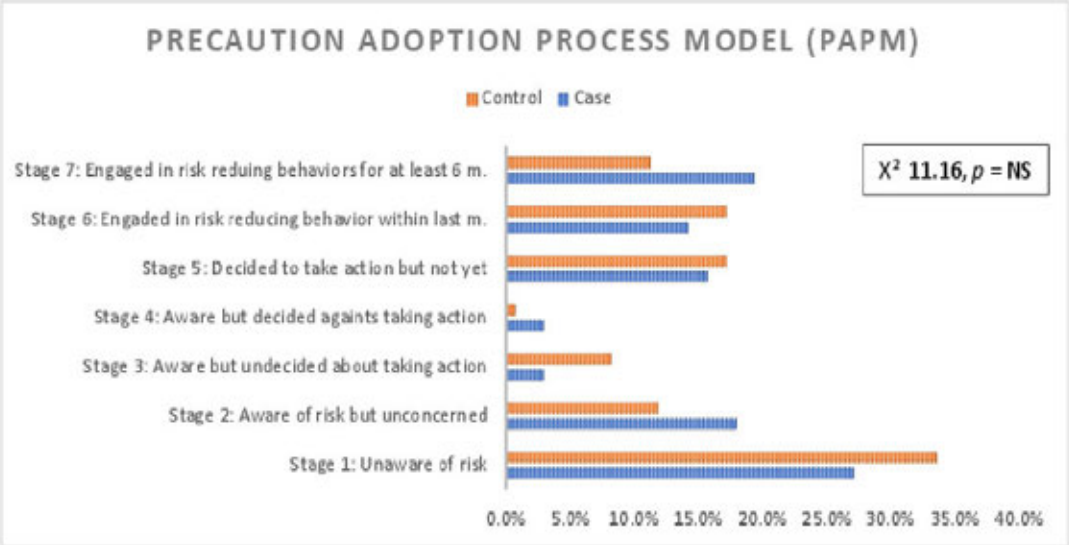
*-variable reported as: n (%), **-variable reported as: median (q25-q75), BMI: body mass index

Table 2. Source of CVR information

	Case (n=140)	Control (n=134)	*p*
None*	45 (32.1)	43 (32.1)	0.723
Doctor*	44 (31.4)	35 (26.1)	
Television*	13 (9.3)	12 (9)	
Magazine*	3 (2.1)	3 (2.2)	
Internet*	14 (10)	15 (11.2)	
Books*	0	1 (0.7)	
More than one*	7 (5)	12 (8.9)	
No answer*	14 (10)	13 (9.7)	

*-variable reported as: n (%)

Table 3 Precaution Adoption Process Model (PAPM)



if they considered themselves at a higher risk of having CVD and PAPM was used to stratify the stage assigned. Frequencies (%) and median values (q25-q75) were used for descriptive analysis and Chi Square test for comparisons.

Results: A total of 274 patients were included. Demographic characteristics are in table 1. CVD risk perception as a binary variable was 56.1% and 47.8% in the case and the control groups, respectively (p= 0.167). Women and subjects with complete university education showed more awareness. According to PAPM scale, most of the patients located themselves in stage 1 (27.1% vs 33.6% in case vs control groups; p= NS), which means they are unaware of their augmented CVR (Figure 1). In the subjects with RD, 66.5% have not made any changes to reduce their risk while 71.6 % of the controls neither. In the control and case group having hypertension makes them prone to start actions to reduce their CVR with an OR of 2.9 (95% CI 1.3-6.6, p=0.007) and OR 2.4 (95% CI 1.0-5.6, p=0.029), respectively. Only 31.4% of the case group received CVR advice from physician, as compared to 26.1% in control group (table 2).

Conclusion: Even though patients with RD have an increased CVR due to the inflammatory condition and coexistence of traditional CVR factors, most of the individuals perceived it the same as control group. Therefore, these could explain the lack of initiative to start actions to reduce their CVR. According to EULAR recommendations the rheumatologist is the one responsible and they should commit to give a better education.

Disclosure: D. Galarza-Delgado, None; **I. Colunga-Pedraza**, None; **J. Azpiri-Lopez**, None; **K. Cuellar-Calderon**, None; **I. Reynosa-Silva**, None; **M. Castro-Gonzalez**, None; **C. Martinez-Flores**, None.

Abstract Number: 1079

Assessing Psoriatic Arthritis Treatment Trends and Patient Journeys Between 2012 and 2018

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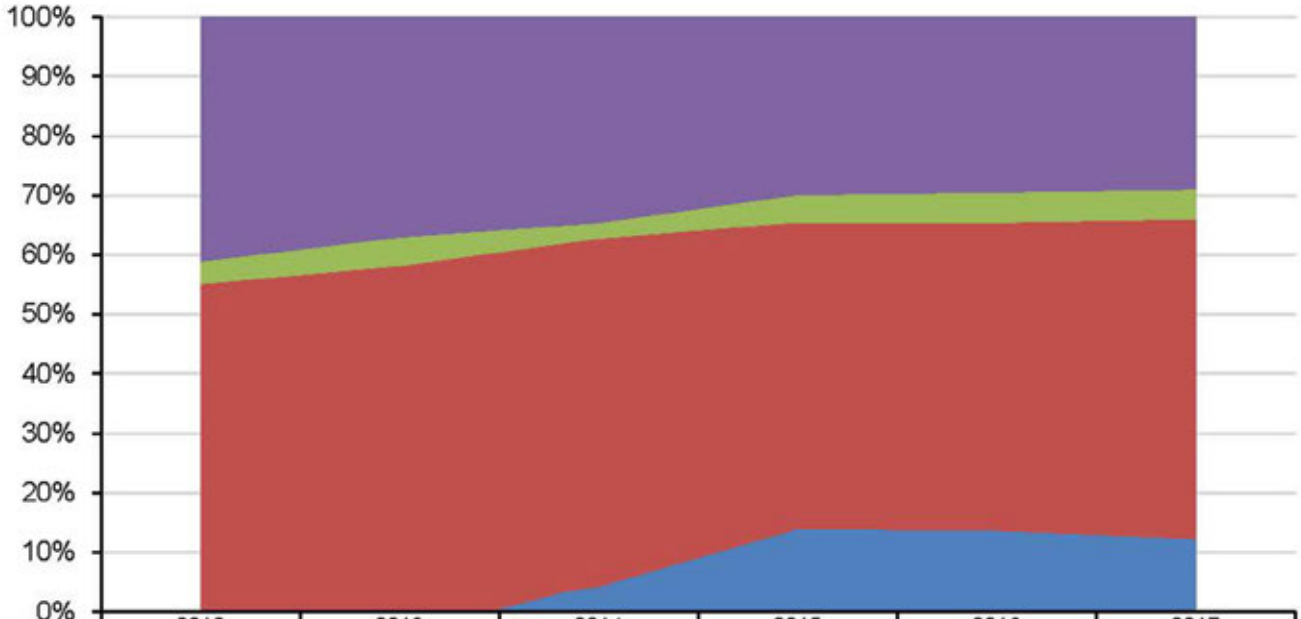
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Figure 1. Frequency of First-Line Regimens Over Time



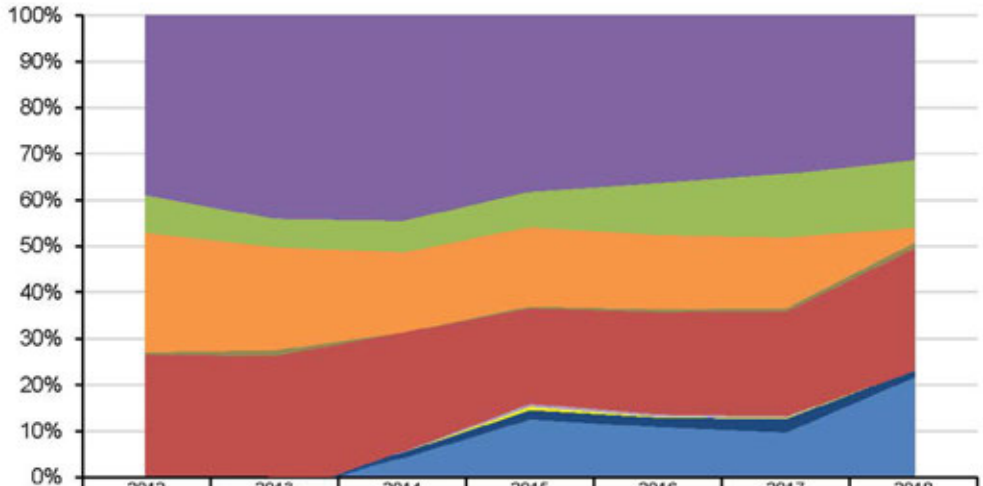
	2012	2013	2014	2015	2016	2017
TNF	41.08	37.01	34.58	29.85	29.46	28.98
IL	3.75	4.8	2.61	4.62	5.08	4.96
cDMARD	55.17	58.19	58.62	51.59	51.81	53.79
APR	0	0	4.2	13.95	13.66	12.27

Background/Purpose: Many new PsA treatments have emerged without clear guidelines on which therapy to use initially. We describe PsA treatment trends and patient journeys between 2012 and 2018.

Methods: Adult PsA patients were selected if they initiated any therapy (index date) with an oral conventional DMARD (cDMARD; cyclosporine, methotrexate, sulfasalazine, leflunomide, azathioprine, gold, hydroxychloroquine), apremilast (APR), TNF inhibitor (adalimumab, certolizumab, etanercept, golimumab, infliximab), or IL inhibitor (ixekizumab, secukinumab, ustekinumab) from January 1, 2012, to June 30, 2017. Selected patients had ≥12 months pre- and post-index continuous enrollment in the IBM Watson Health MarketScan® Commercial and Medicare Supplemental Database and no history of biologic-indicated autoimmune conditions (ie, diagnosis of rheumatoid arthritis or IBD) or cancer in the pre- or post-index period. Treatment patterns were assessed until end of follow-up. Concluding a line of therapy was defined as discontinuation (>90-day lapse in therapy) or switch to a new line of PsA therapy (cDMARD, APR, TNF, or IL), whichever occurred first. Patients switching to a new line of therapy or restarting the previous therapy after discontinuation were categorized. Initiating or switching to combination therapy was defined as ≥2 new agents within 14 days, or adding a new agent on current therapy with ≥60 days' supply overlap. Patient characteristics, first- and second-line PsA agent use, and frequency of treatment sequences were summarized by years and first-line drug categories.

Results: A total of 5,135 PsA patients (cDMARD: n=2,821 APR: n=341, TNF: n=1,756, IL: n=217) were included. Mean age was 48 (SD 11.9) years and 52.3% were female. Mean age was similar among treatment groups, whereas the cDMARD and APR groups had more female patients. Mean length of follow-up was 1,017 (SD 514) days. First-line oral cDMARD and IL use remained consistent from 2012 to 2017. First-line APR use increased

Figure 2. Frequency of Second-Line Regimens Over Time



	2012	2013	2014	2015	2016	2017	2018
TNF	38.76	43.76	44.24	37.93	36.08	34.07	31.13
IL	9.13	6.13	6.84	7.62	11.26	13.81	14.57
cDMARD + TNF	25.84	22.41	17.36	17.18	16.02	15.29	3.32
cDMARD + IL	0.48	1.27	0	0.49	0.72	0.75	1.32
cDMARD	26.79	26.43	25.88	20.58	22.08	22.65	26.49
APR + TNF	0	0	0.34	0.97	0.72	0.55	0
APR + IL	0	0	0	0.65	0.14	0.18	0
APR + cDMARD	0	0	1	1.78	1.88	2.76	1.32
APR	0	0	4.34	12.8	11.11	9.94	21.85

Table 1. Top 5 Patient Treatment Journeys Over Time

2012	%	2017	%
TNF → Still on Therapy	19.21	cDMARD → Discontinuation → None	14.36
cDMARD → Discontinuation → None	16.37	TNF → Still on Therapy	10.97
cDMARD → Still on Therapy	15.37	cDMARD → Still on Therapy	8.88
TNF → Discontinuation → None	11.52	TNF → Discontinuation → None	6.79
cDMARD → Switch → cDMARD, TNF → Still on Therapy	5.22	Apremilast → Still on Therapy	4.96

over time since its FDA approval in 2014, while TNF use decreased (Figure 1). At end of follow-up, a larger proportion of first-line APR patients remained on therapy (27.9%) vs cDMARD (11.8%), TNF (22.5%), and IL (23.5%). Among those who ended first-line therapy, treatment patterns were as follows: APR had the highest rate of sustainability as staying first line (not progressing to second-line therapy) after discontinuation (30.9%), followed by cDMARD (24.6%), TNF (19.3%), and IL (16.3%). Oral cDMARDs had the highest rate of switching (61.4%), followed by TNF (56.7%), APR (52.0%), and IL (44.0%). IL had the most restart after discontinuation (39.8%), followed by TNF (24.0%), APR (17.1%), and cDMARD (14.0%). Second-line cDMARD use was maintained throughout the study period. Second-line APR and IL use increased while TNF and cDMARD + TNF combination use decreased (Figure 2). Differences in the most frequent 12-month patient treatment journeys were observed during the study period (Table 1).

Conclusion: APR as first- and second-line treatment increased while TNF use decreased during the study period. cDMARD use remained consistent and IL therapy use increased second line. Introduction of newer PsA agents has impacted the treatment paradigm.

Disclosure: M. Husni, Abbvie, 5, AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, Regeneron, Sanofi-Genzyme, UCB, 5, Abbvie, Amgen, Janssen, Novartis, Lilly, Regeneron, Pfizer and UCB, 5, Bristol-Myers Squibb, 5, Eli Lilly, 5, Genentech, 5, Janssen, 5, Janssen Research & Development, LLC, 2, 3, Novartis, 5, PASE questionnaires, 7, Pfizer, 5, Sanofi-Genzyme, 5, UCB, 5; **B. Ung**, Celgene Corporation, 3; **S. Richter**, Celgene Corporation, 3; **C. Pelletier**, Celgene Corporation, 3; **M. Tian**, Celgene Corporation, 3.

Abstract Number: 1080

Biosimilar Etanercept Use in Rheumatoid Arthritis, Ankylosing Spondylitis, and Psoriatic Arthritis: The RHUMADATA® Registry Experience

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Table 1. Baseline characteristics according to the initial treatment.

Characteristic	boETA (n=59)	bsETA (n=48)
Female sex (%)	44 (74.6%)	34 (70.8%)
Age at treatment initiation (years), mean (SD)	53.9 ± 14.2	57.5 ± 14.4
Disease duration at treatment initiation (years), mean (SD)	8.0 ± 8.7	10.3 ± 10.9
Age-adjusted CCI score, mean (SD)	2.6 ± 1.5	3.0 ± 1.6
DAS28-ESR at baseline, mean (SD)	4.2 ± 1.1	3.8 ± 2.1
Drugs in use at treatment initiation		
Methotrexate (MTX)	40 (67.8%)	28 (58.3%)
Hydroxychloroquine	38 (64.4%)	30 (62.5%)
Sulfasalazine	6 (10.2%)	8 (16.7%)
Leflunomide	1 (1.7%)	2 (4.2%)
Glucocorticoid	25 (42.4%)	12 (25.0%)
MTX starting dose (mg)	22.0 ± 3.5	19.0 ± 5.2
Previous treatment (%)		
Synthetic DMARDs	37 (62.7)	24 (50)
Adalimumab	2 (3.4)	0 (0.0)
Abatacept	7 (11.9)	1 (2.1)
Anakinra	1 (1.7)	0 (0.0)
Certolizumab	4 (6.8)	2 (4.2)
Etanercept	0 (0.0)	11 (22.9)
Infliximab	1 (1.7)	0 (0.0)
Rituximab	0 (0.0)	2 (4.2)
Tocilizumab	4 (6.8)	1 (2.1)
Tofacitinib	3 (5.1)	5 (10.4)
Sarilumab	0 (0.0)	1 (2.1)

CCI: Charlson comorbidity index; DAS28-ESR: Disease Activity Score - erythrocyte sedimentation rate.

Background/Purpose: Biosimilars hold the potential to improve access to needed therapies at a reduced cost. In Canada, biosimilar etanercept (bsETA-Brenzys® and Erelzi®) were recently approved for rheumatoid arthritis (RA) and other rheumatologic conditions; however, comparisons of patterns of use of biosimilar with its originator product (boETA-Enbrel®) are scarce. Our objective was to describe the recent use of bsETA and boETA in patients with RA, ankylosing spondylitis (AS), and psoriatic arthritis (PsA).

Methods: Data from patients initiating bsETA (either biologic-naïve users, patient transitioning from boETA, swappers and switchers from other biologic agents) were extracted from RHUMADATA®, a practice-based registry (14 Quebec rheumatologists) for the period of January 2015 to November 2018. For comparison purposes, we identified patients initiating/switching/swapping to the boETA product in the same period. We obtained baseline demographics and clinical data for all patients. Therapy persistence in bsETA versus boETA initiators was compared using Kaplan-Meier methods and adjusted hazard ratios (HR). Our hazard models adjusted for age, sex, disease duration, methotrexate (MTX) dose at baseline, and comorbidities (Charlson comorbidity index).

Results: We studied 48 patients initiating bsETA (including 37 etanercept-naïve patients) and 59 patients initiating boETA. Sex distribution, age, comorbidities and disease duration (at etanercept initiation) were similar between groups (Table 1). Use of MTX and/or other conventional synthetic DMARD (csDMARDs) at etanercept initiation was also similar between groups; however, patients in the boETA group started with a significant higher dose of MTX (22.0 ± 3.5mg) when compared to bsETA users (19.0 ± 5.2mg, p=0.011). Persistence on therapy was similar in both groups (Figure 1): after 12 months, 75% of originator etanercept versus 84% of biosimilar etanercept initiators remained on their initial treatment. Adjusting for baseline age, sex, disease duration, methotrexate dose at baseline, and comorbidities, the adjusted HR for therapy persistence in biosimilar etanercept versus originator etanercept group was 2.05 (95% CI 0.83, 5.04).

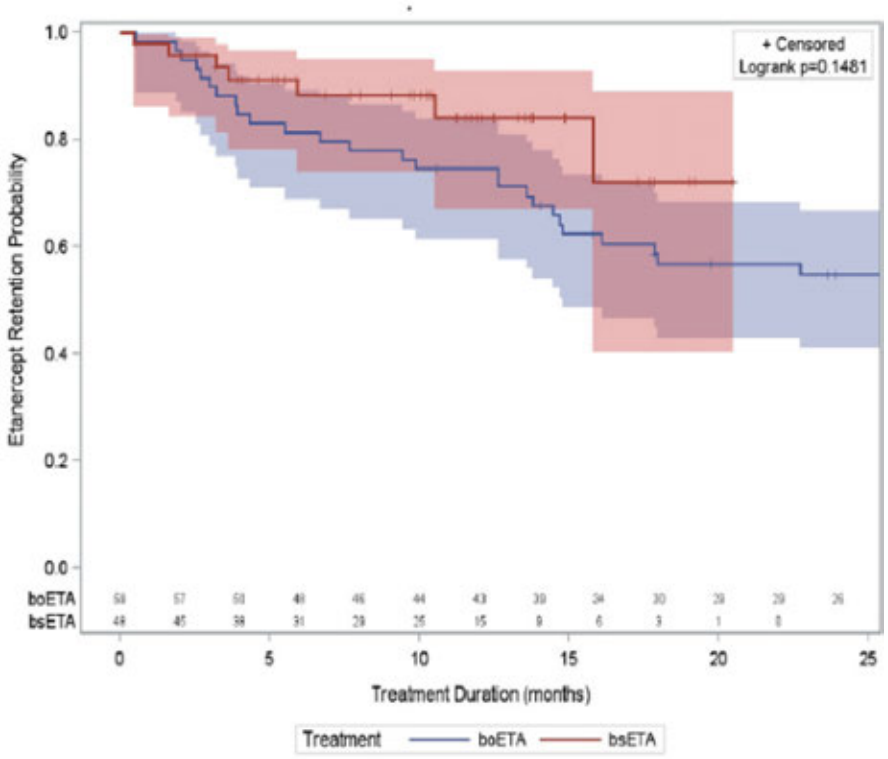

Figure 1. Kaplan Meier survival curves for therapy persistence per treatment group of a) boETA, and b bsETA.

Conclusion: Patients initiating bsETA or boETA were similar in terms of age, disease duration, disease activity, and comorbidities. We were unable to identify clear differences in treatment persistence between the two groups; a strong trend for greater persistence with biosimilar versus originator may be related to residual confounding (e.g.: disease activity). Further work is ongoing to study outcomes in a larger, multicentre group of patients.

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Abstract Number: 1081

Characteristics of Patients with Seropositive or Seronegative Rheumatoid Arthritis, Psoriatic Arthritis, or Axial Spondyloarthritis: Data from the US-Based Corrona Rheumatoid Arthritis and Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registries

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA) share many clinical features but are differentiated by key clinical and molecular characteristics. Patients with RA are often seropositive (S+) for rheumatoid factor (RF) or anti-cyclic citrullinated peptide (CCP) antibodies, whereas those with PsA or axSpA are usually seronegative (S–) for these antibodies. Limited data are available comparing patients with S+ and S– RA, and few studies have compared disease burden across patients with S+ RA, S– RA, PsA, and axSpA. We compared clinical and disease characteristics among these 4 groups in the Corrona RA and PsA/SpA Registries.

Methods: Adult patients with RA enrolled in the Corrona RA Registry and those with PsA or axSpA enrolled in the Corrona PsA/SpA Registry between March 2013 and February 2019 were included. Patients with RA must have had nonmissing RF and anti-CCP values at enrollment and were classified as S+ (RF or anti-CCP $\geq$ 20 U/mL) or S– (RF and anti-CCP $<$ 20 U/mL). Patient demographics, clinical characteristics, and disease activity and patient-reported outcome (PRO) measures collected at registry enrollment were compared between patients with S+ RA vs S– RA, PsA, or axSpA using *t* or Wilcoxon rank-sum tests for continuous variables and χ^2 or Fisher exact tests for categorical variables.

Results: A total of 4827 patients with S+ RA, 1959 with S– RA, 3001 with PsA, and 512 with axSpA were included. Patients with S– RA had a higher prevalence of comorbidities than those with S+ RA, including fibromyalgia (13.1%

Table 1. Demographics and Clinical Characteristics of Patients With Seropositive RA, Seronegative RA, PsA, and AxSpA at Enrollment

Characteristic	S+ RA (N = 4827)	S− RA (N = 1959)	PsA (N = 3001)	AxSpA (N = 512)
Age, mean (SD), years	58.5 (13.5)	59.2 (13.8)*	54.0 (13.2)*	47.4 (13.8)*
Female, n (%)	3651 (75.7)	1503 (76.8)	1604 (53.9)*	198 (39.1)*
Race, n (%)				
White	4191 (87.4)	1797 (92.1)†	2752 (94.1)†	457 (91.8)†
Black	295 (6.2)	64 (3.3)†	21 (0.7)†	9 (1.8)†
Asian	88 (1.8)	20 (1.0)†	59 (2.0)†	15 (3.0)†
Pacific Islander	13 (0.3)	6 (0.3)†	24 (0.8)†	4 (0.8)†
Mixed race	46 (1.0)	21 (1.1)†	31 (1.1)†	8 (1.6)†
Other	161 (3.4)	44 (2.3)†	39 (1.3)†	5 (1.0)†
Work status, n (%)				
Full time	1815 (38.2)	664 (34.3)†	1586 (53.5)†	298 (58.8)†
Part time	398 (8.4)	161 (8.3)†	251 (8.5)†	32 (6.3)†
Disabled	583 (12.3)	241 (12.5)†	291 (9.8)†	74 (14.6)†
Retired	1550 (32.6)	727 (37.6)†	637 (21.5)†	62 (12.2)†
Other	407 (8.6)	142 (7.3)†	201 (6.8)†	41 (8.1)†
BMI, n (%)				
Normal/Underweight (< 25 kg/m^2)	1279 (26.9)	438 (22.5)†	484 (16.5)†	126 (25.2)
Overweight (25 to < 30 kg/m^2)	1432 (30.1)	585 (30.1)†	862 (29.4)†	158 (31.6)
Obese (≥ 30 kg/m^2)	2052 (43.1)	920 (47.3)†	1587 (54.1)†	216 (43.2)
Anti-CCP, mean (SD), U/mL	23.6 (21.3)	13.5 (8.4)*	–	–
RF, mean (SD), U/mL	183.1 (484.1)	9.4 (5.5)*	–	–
Symptom duration, mean (SD), years	8.6 (10.5)	8.1 (10.1)	11.1 (10.3)*	16.7 (12.0)*
Disease duration, mean (SD), years	6.9 (9.4)	5.7 (8.2)*	7.8 (8.5)*	9.4 (10.5)*
Comorbidities, n (%)				
Cardiovascular disease	511 (10.6)	246 (12.6)*	349 (11.6)	52 (10.2)
Depression	850 (17.6)	444 (22.7)*	462 (15.4)*	86 (16.8)
Diabetes mellitus	578 (12.0)	275 (14.0)*	441 (14.7)*	36 (7.0)*
Any cancer (excluding NMSC)	442 (9.2)	221 (11.3)*	225 (7.5)*	21 (4.1)*
Serious infections	248 (5.1)	110 (5.6)	192 (6.4)*	35 (6.8)
Hypertension	1844 (38.2)	844 (43.1)*	1157 (38.6)	168 (32.8)*
Hyperlipidemia	1097 (22.7)	537 (27.4)*	709 (23.6)	77 (15.0)*
Metabolic syndrome	438 (9.1)	217 (11.1)*	279 (9.3)	20 (3.9)*
Psoriasis	86 (1.8)	47 (2.4)	2555 (85.1)*	30 (5.9)*
Fibromyalgia	283 (5.9)	257 (13.1)*	170 (5.7)	25 (4.9)

AxSpA, axial spondyloarthritis; BMI, body mass index; NMSC, nonmelanoma skin cancer; PsA, psoriatic arthritis; RA, rheumatoid arthritis; S+, seropositive; S−, seronegative.
* $P < 0.05$ for comparison between patients with S− RA, PsA, and axSpA vs those with S+ RA.
† $P < 0.05$ for comparison of overall distribution across categories between patients with S− RA, PsA, and axSpA vs those with S+ RA.

vs 5.9%) and depression (22.7% vs 17.6%) (**Table 1**). Patients with axSpA had a lower prevalence of comorbidities than those with S+ RA; there was no clear trend in prevalence of comorbidities between patients with PsA and S+ RA. Overall biologic and prednisone use were comparable between patients with S+ and S− RA, whereas patients with PsA or axSpA had more biologic use and less prednisone use than those with S+ RA (**Table 2**). Prior csDMARD use was higher among patients with S− RA and lower among patients with axSpA than those with S+ RA; current csDMARD use was comparable between patients with S+ and S− RA but lower among those with PsA or axSpA. Patients with S+ RA had higher swollen joint counts, ESR, and CRP levels than those with S− RA, PsA, or axSpA,

Table 2. Prior and Current Treatment Use Among Patients With Seropositive RA, Seronegative RA, PsA, and AxSpA at Enrollment

Characteristic	S+ RA (N = 4827)	S− RA (N = 1959)	PsA (N = 3001)	AxSpA (N = 512)
History of prior medication use, n (%)				
Biologics	1007 (20.9)	400 (20.4)	928 (30.9)*	157 (30.7)*
No. of prior biologics				
0	3820 (79.1)	1559 (79.6)	2073 (69.1)†	355 (69.3)†
1	555 (11.5)	212 (10.8)	545 (18.2)†	100 (19.5)†
≥ 2	452 (9.4)	188 (9.6)	383 (12.8)†	57 (11.1)†
csDMARDs	1320 (27.3)	662 (33.8)*	867 (28.9)	83 (16.2)*
No. of prior csDMARDs				
0	3507 (72.7)	1297 (66.2)†	2134 (71.1)†	429 (83.8)†
1	884 (18.3)	435 (22.2)†	675 (22.5)†	64 (12.5)†
≥ 2	436 (9.0)	227 (11.6)†	192 (6.4)†	19 (3.7)†
Prednisone	1901 (39.4)	807 (41.2)	430 (14.3)*	59 (11.5)*
Current medication use, n (%)				
Biologic	1636 (33.9)	654 (33.4)	1812 (60.4)*	356 (69.5)*
tsDMARD	175 (3.6)	54 (2.8)	203 (6.8)*	0 (0)*
csDMARD	3980 (82.5)	1627 (83.1)	1524 (50.8)*	110 (21.5)*
Prednisone	1527 (31.6)	580 (29.6)	213 (7.1)*	27 (5.3)*

AxSpA, axial spondyloarthritis; csDMARD, conventional synthetic disease-modifying antirheumatic drug; PsA, psoriatic arthritis; RA, rheumatoid arthritis; S+, seropositive; S−, seronegative; TNFi, tumor necrosis factor inhibitor; tsDMARD, targeted synthetic antirheumatic drug.
* $P < 0.05$ for comparison between patients with S− RA, PsA, and axSpA vs those with S+ RA.
† $P < 0.05$ for comparison of overall distribution across categories between patients with S− RA, PsA, and axSpA vs those with S+ RA.

Table 3. Disease Activity and Patient-Reported Outcome Measures of Patients With Seropositive RA, Seronegative RA, PsA, and AxSpA at Enrollment

Characteristic*	S+ RA (N = 4827)	S− RA (N = 1959)	PsA (N = 3001)	AxSpA (N = 512)
Tender joint count (0-28)	4.6 (6.1)	4.4 (6.0)	3.1 (5.2)†	2.0 (4.8)†
Swollen joint count (0-28)	3.8 (5.1)	2.9 (4.3)†	1.7 (3.1)†	0.5 (1.1)†
CDAI	14.6 (13.4)	13.4 (11.9)	10.7 (9.8)†	11.7 (5.0)
Physician global assessment of arthritis	25.5 (22.7)	22.7 (20.9)†	20.2 (21.4)†	28.3 (23.1)†
CRP, mg/L	13.6 (36.4)	10.9 (24.6)†	8.6 (19.0)†	9.7 (20.5)†
ESR, mm/h	23.2 (21.3)	18.5 (18.0)†	17.4 (16.7)†	15.1 (17.8)†
Patient-reported pain (VAS 0-100)	39.2 (30.0)	41.1 (28.8)†	38.7 (29.6)	48.4 (29.5)†
Patient-reported fatigue (VAS 0-100)	42.1 (31.3)	43.5 (31.5)	41.5 (29.6)	48.7 (28.5)†
Patient global assessment of arthritis (VAS 0-100)	36.6 (28.3)	37.9 (27.4)	39.7 (29.8)†	52.3 (32.1)†
Morning stiffness, n (%)				
< 30 min	1850 (38.7)	712 (36.6)	1020 (35.0)‡	132 (26.3)‡
≥ 30 min	2934 (61.3)	1234 (63.4)	1891 (65.0)‡	369 (73.7)‡
HAQ (0-3)	0.9 (0.7)	0.9 (0.7)	0.7 (0.7)†	0.7 (0.6)†
EQ-5D (0-1)	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)†

AxSpA, axial spondyloarthritis; CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; EQ-5D, EuroQol 5 dimensions; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; PsA, psoriatic arthritis; RA, rheumatoid arthritis; S+, seropositive; S−, seronegative; VAS, visual analog scale.
* Data are presented as mean (SD) unless otherwise indicated.
† $P < 0.05$ for comparison between patients with S− RA, PsA, and axSpA vs those with S+ RA.
‡ $P < 0.05$ for comparison of overall distribution across categories between patients with S− RA, PsA, and axSpA vs those with S+ RA.

and higher tender joint counts than those with PsA and axSpA (**Table 3**). Patients with S+ RA had a higher mean physician global assessment score than those with S– RA or PsA but lower than those with axSpA. Patients with S+ RA had a mean patient global assessment score comparable with that of patients with S– RA but lower than those with PsA or axSpA.

Conclusion: Patients with S– RA had a higher comorbidity burden but similar treatment profiles and PRO scores compared with those with S+ RA. Patients with PsA or axSpA had more biologic use and worse PRO scores than those with S+ RA. These results demonstrate the differences in disease manifestations of patients with these diseases. Further studies are needed to identify factors that differentiate these disease groups, particularly regarding therapeutic response.

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Abstract Number: 1082

Cancer Risk in Patients with Ankylosing Spondylitis: A Nationwide Population-based Dynamic Cohort Study from Korea

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

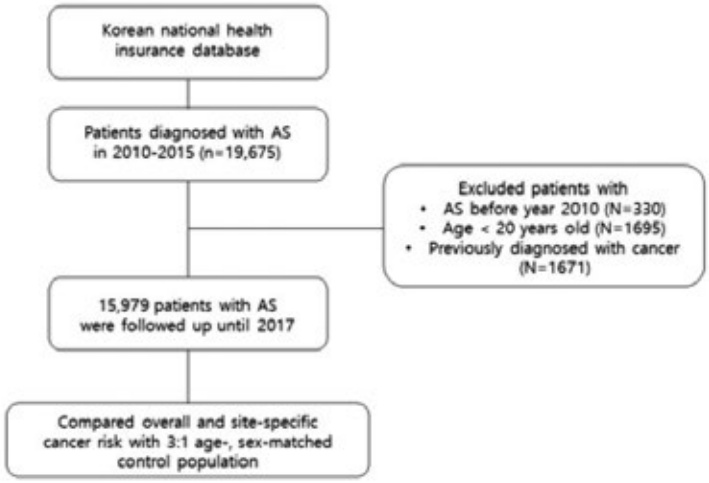
Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study is to determine the risk of overall malignancy and site-specific cancer in ankylosing spondylitis (AS) patients compared with patients without AS in Korea.

Methods: The study utilized the National Health Information Database managed by National Health Insurance Service in Korea. The data from national health screening programs, data related to medical care institutions and a registry of cancer and rare/severe intractable diseases were also included. Patients diagnosed as AS (International Classification of Diseases, 10th revision codes M45.0 and code V140 used in Korea for severe intractable diseases) between 2010 and 2015 were extracted. Of these, patients with a history of cancer during the washout period from 2008 to 2009 were excluded. For the control cohort, an age- and sex-matched population without AS was randomly extracted at a control-to-case ratio of 3:1. The incidence rates for overall and specific cancers were calculated per

Figure 1. Flowchart of the study process



AS, ankylosing spondylitis

1000 person-years. Multivariate Cox regression model was used to evaluate the risk for malignancies. Results presented as hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: A total of 15,979 patients with AS and 47,937 matched controls were included for analysis. The prevalence of diabetes mellitus, hypertension and dyslipidemia which are well known risk factors for cancer were statistically high in AS patients (5.76% vs 4.84%, 16.66% vs 12.34%, 11.3% vs 7.99%, respectively) [$p < 0.0001$, $p< 0.001$ and $p < 0.0001$. respectively]). Cancer was diagnosed in 311 patients (1.95%) and 931 patients (1.94%) in the AS group and age- and sex-matched control group, respectively. After adjusting age, sex, diabetes mellitus, hypertension, dyslipidemia, regions and income status, patients with AS showed higher risk for lymphoma (HR, 3.052; 95% CI, 1.446-6.446), leukemia (HR, 2.322; 95% CI, 0.911-5.914) and multiple myeloma (HR 2.829; 95% CI, 1.16-6.901). The risk of solid cancers was not different between the two groups.

Conclusion: In this nationwide population-based study in Korea, AS patients were associated with increased risk of hematologic malignancies. Further research is needed to determine the relationship between AS and these malignancies.

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Abstract Number: 1083

Patient Reported Outcomes over Time in 25,988 Axial Spondyloarthritis Patients Initiating Treatment with 1st, 2nd or 3rd TNF Inhibitor in Clinical Practice – Is PRO Remission Achieved? Results from the EuroSpA Collaboration

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Gary Macfarlane,[27] Cecilie Heegaard Brahe,[28] Merete Lund Hetland,[1] and Mikkel Østergaard[29], [1]DANBIO and Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Centre of Head and Orthopaedics, Rigshospitalet, Copenhagen, Denmark, [2]Karolinska Institutet, Stockholm, Sweden, [3]Department of Rheumatology, Aarhus University Hospital., Aarhus, Denmark, [4]University Hospital Geneva, Geneva, Switzerland, [5]Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Prague, Czech Republic, Prague 2, Czech Republic, [6]TURKBIO registry and Marmara University School of Medicin, Division of Rheumatology, Istanbul, Turkey, [7]Department of Emergency and Transplantation , Rheumatology Unit, University Hospital of Bari, Bari, Italy., Bari, Italy, [8]Diakonhjemmet Hospital, Dept. of Rheumatology, Oslo, Norway, [9]Department of Medicine, ROB-FIN, Helsinki University Hospital and Helsinki University, Helsinki, Finland., Helsinki, Finland, [10]Rheumatology department, Hospital Garcia de Orta, Almada, Portugal, [11]Center of Rheumatic Diseases, University of Medicine and Pharmacy, Bucharest, Romania., Bucharest, Romania, [12]Unit Research, Spanish Society of Rheumatology, Madrid, Spain, [13]UMC LJUBLJANA, DPT. OF RHEUMATOLOGY, LJUBLJANA, Slovenia, [14]Centre for Rheumatology Research, Landspitali and Faculty of Medicine, University of Iceland, Reykjavik, Iceland, [15]Amsterdam University Medical Center, Amsterdam, Netherlands, [16]University of Gothenburg, Gothenburg, Sweden, [17]University Hospital Zürich, Zürich, Switzerland, [18]TURKBIO registry and Bilim University School of Medicin, Division of Rheumatology, Istanbul, Turkey, [19]Fondazione Policlinico Gemelli-Università Cattolica del Sacro Cuore, Rome, Italy, [20]Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway., Oslo, Norway, [21]Helsinki University Hospital, Helsinki, Finland, [22]Centro Hospitalar Baixo Vouga | iBemed, University of Aveiro, Aveiro, Portugal, [23]SPITALUL CLINIC SFANTA MARIA, Bucharest, [24]Research Unit, Spanish Society of Rheumatology, Madrid, Spain, [25]Department of Rheumatology, University Medical Centre, Ljubjana, Slovenia, [26]Centre for Rheumatology Research, University Hospital and Faculty of Medicine, Reykjavik, Iceland, [27]University of Aberdeen, Aberdeen, United Kingdom, [28]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet Glostrup, Denmark, Copenhagen, Denmark, [29]Copenhagen Center for Arthritis Research, University of Copenhagen, Copenhagen, Denmark

Table 1: Baseline characteristics of pooled axSpA cohort at 1st, 2nd and 3rd TNFi start

	1st TNFI (n = 25988)		2nd TNFi (n = 8294)		3rd TNFi (n = 2842)	
	Available data, n	Median (IQR) or percentage	Available data, n	Median (IQR) or percentage	Available data, n	Median (IQR) or percentage
Age, years	25988	41 (33-51)	8294	43 (35-53)	2842	44 (36-53)
Male	25988	60%	8294	55%	2842	52%
HLA-B27	12618	72%	4041	68%	1920	67%
Time since diagnosis, years	17491	3 (1-9)	5294	5 (2-11)	1777	6 (3-13)
TNFi drug	25988		8294		2842	
Adalimumab		29%		32%		28%
Certolizumab		3%		5%		7%
Etanercept		26%		33%		24%
Golimumab		13%		17%		21%
Infliximab		29%		13%		20%
ASDAS, units	8508	3.6 (2.9-4.3)	2827	3.3 (2.5-4.0)	1097	3.3 (2.5-4.0)
Pain, mm	16672	65 (45-80)	5181	61 (40-78)	1866	65 (44-80)
Global, mm	17203	66 (47-80)	5282	62 (40-80)	1889	67 (46-80)
BASDAI, mm	15668	59 (43-72)	4696	56 (37-71)	1699	59 (40-74)
BASFI, mm	12667	46 (26-65)	4068	44 (23-65)	1523	47 (27-70)
Fatigue, mm	10579	69 (49-80)	3864	65 (41-80)	1476	70 (46-83)

Data are as observed. HLA-B27: Human Leukocyte Antigen B27; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; TNFi: Tumour Necrosis Factor inhibitor; ASDAS: Ankylosing Spondylitis Disease Activity Index.

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment effectiveness in patients with axial spondylarthritis (axSpA) is evaluated by a combination of objective markers of disease activity and patient reported outcomes (PROs), e.g. pain, physical function, fatigue and global scores. Development in PROs over time in patients, who initiate treatment with their 1st, 2nd or 3rd Tumour Necrosis Factor inhibitor (TNFi) in routine practice is limited. Hence, the aim of this study was to investigate PROs at baseline, 6 and 12 months in axSpA patients who initiate their 1st, 2nd or 3rd TNFi in clinical practice: their distribution, changes from baseline and heterogeneity across registries.

Table 2: PROs after 6, 12 and 24 months of TNFi treatment in the pooled AxSpA cohort

	1st TNFi			2nd TNFi			3rd TNFi		
	6 months	12 months	24 months	6 months	12 months	24 months	6 months	12 months	24 months
Pain, mm	22 (9-47)	20 (8-43)	20 (7-40)	32 (14-58)	30 (12-56)	30 (10-51)	40 (20-61)	40 (20-65)	39 (19-60)
Global, mm	25 (10-50)	21 (10-45)	20 (9-42)	35 (15-60)	31 (14-56)	30 (11-54)	40 (20-64)	40 (20-66)	40 (20-60)
BASDAI, mm	24 (10-43)	21 (9-40)	20 (8-38)	32 (15-53)	31 (14-51)	28 (12-49)	40 (20-59)	39 (20-60)	38 (20-57)
BASFI, mm	20 (6-41)	17 (5-38)	16 (4-36)	27 (9-51))	25 (9-47)	22 (7-45)	35 (15-57)	34 (14-56)	34 (15-55)
Fatigue, mm	30 (10-56)	30 (10-54)	29 (10-52)	40 (18-68)	40 (18-65)	38 (15-62)	50 (25-71)	50 (24-71)	50 (24-71)
Changes in PROs from baseline to 6, 12 and 24 months									
	0-6 months	0-12 months	0-24 months	0-6 months	0-12 months	0-24 months	0-6 months	0-12 months	0-24 months
Pain, mm	-30 (-52; -10)	-32 (-55; -10)	-32 (-55; -10)	-18 (-40; 0)	- 19 (-40; -1)	-19 (-41; 0)	-18 (-38; -1)	- 15 (-40; 0)	-18 (-41; -1)
Global, mm	-30 (-50; -10)	- 31 (-54; -10)	-32 (-54; -10)	-18 (-40; 0)	-19 (-40; 0)	-18 (-41; 0)	-18 (-38; 0)	-17 (-38; 0)	-20 (-39; 0)
BASDAI, mm	-28 (-46; -11)	-30 (-48; -12)	-31 (-49; -13)	-15 (-31; -2)	-15 (-32; -7)	-16 (-33; 2)	-14 (-29; -1)	-13 (-30; 0)	-16 (-33; -1)
BASFI, mm	-18 (-34; -5)	-20 (-36; -6)	-21 (-38; -7)	-8 (-22; 0)	-9 (-24; 0)	-10 (-26; 0)	-8 (-21; 1)	-8 (-21; 0)	-11 (-24; 0)
Fatigue, mm	-25 (-50; -5)	-26 (-50; -5)	-25 (-50; -5)	-14 (-35; 0)	-12 (-33; 0)	-11 (-35; 2)	-13 (-30; 0)	-10 (-30; 1)	-13 (-33; 1)
PRO remission rates (%) at 6, 12 and 24 months									
	1st TNFi			2nd TNFi			3rd TNFi		
	Crude* 6/12/24		LUNDEX adjusted**	Crude*		LUNDEX adjusted**	Crude*		LUNDEX adjusted**
Pain ≤ 20	49/51/53		41/35/27	36/38/40		27/22/17	27/28/29		20/17/12
Global ≤ 20	46/50/51		38/35/26	34/36/39		26/21/16	25/27/28		19/16/11
BASDAI ≤ 20	45/49/50		37/34/26	33/34/38		25/20/16	26/26/27		20/15/11
BASFI ≤ 20	52/55/57		43/39/29	41/44/48		31/26/20	32/33/32		24/19/12
Fatigue ≤ 20	40/43/43		33/30/22	31/31/33		23/18/14	22/24/23		17/14/9

Data are as observed. Percentage of available data varied from 10-82%. Values are median (Inter Quartile Range (IQR)) unless otherwise stated. PRO: Patient reported outcome; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; TNFi: Tumour Necrosis Factor inhibitor.

*Crude value: the fraction of patients in PRO remission of those still on drug with available data at 6, 12 and 24 months. Percentage of available data varied from 35to 90%.

** LUNDEX-adjusted: Crude value adjusted for drug retention.

Methods: Pooled data on axSpA patients from 14 European registries participating in the EuroSpA Research Collaboration were analysed (1). Patients were included if they had been followed in the registry from initiation of the 1st TNFi. PROs included scores for pain, disease activity (global and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)), physical function (Bath Ankylosing Spondylitis Functional Index (BASFI)) and fatigue, all captured with Visual Analogue Scales 0-100 mm (VAS). The distribution of PROs at 6, 12 and 24 months after TNFi start and the changes from baseline to 6, 12 and 24 months were investigated with descriptive statistics. PRO remission rates were defined as the proportion of patients achieving a state of pain score ≤20 mm, global score 20 mm, BASDAI ≤20 mm, BASFI ≤20 mm and fatigue score ≤20 mm. Crude and LUNDEX-adjusted (2) PRO remission rates were assessed for the pooled cohort and the individual countries.

Results: Of the 25,988 axSpA patients, who initiated 1st TNFi, 8,294 patients switched to a 2nd TNFi, while 2,842 patients subsequently switched to a 3rd TNFi. Baseline characteristics of the study cohort are shown in Table 1. The 6, 12 and 24 month PRO status and changes in PROs for 1st, 2nd and 3rd TNFi in the pooled cohort are summarized in Table 2. For the 1st, 2nd and 3rd TNFi, median PROs after 6 months ranged from 20mm to 30mm, 27mm to 40mm and 35mm to 50mm, respectively. Similarly, median decreases in PROs from baseline to 6 months ranged from 18 to 30mm, 8 to 18mm and 8 to 18mm for the 1st, 2nd and 3rd TNFi. In the overall cohort 6 month LUNDEX-adjusted PRO remission rates varied from 33% to 41%, 23% to 33% and 17% to 24% for the 1st, 2nd and 3rd TNFi, respectively (Table 2). In the individual registries, LUNDEX-adjusted 6 months PRO remission rates for the 1st TNFi ranged from 32% to 51%, 24% to 50%, 28% to 48%, 32% to 51% and 21% to 47% for pain, global, BASDAI, BASFI and fatigue scores, respectively.

Conclusion: Overall, one-third of patients in a very large observational cohort achieved a state of PRO remission after 6 months of treatment with their first TNFi with considerable variation in PRO remission rates between registries.

As expected, improvements in PROs and PRO remission rates were lower in those who received a 2nd or 3rd TNFi, reflecting confounding by indication (i.e. selection of non-responders and more severe cases).

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2. Kristensen et al. Arthritis Rheumatol, 2006, 54(2), p:600-6

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Yilmaz, Janssen, 8, Pfizer, 8, Novartis, 8; **E. Gremese**, AbbVie, 5, 8, BMS, 5, 8, Celgene, 5, 8, Janssen, 5, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **E. Kristianslund**, None; **A. Hokkanen**, None; **A. Barcelos**, Bene, 8, MSD, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Eli-Lilly, 5; **R. IONESCU**, Abbvie, 5, 8, Amgen, 5, 8, Alpha Sigma, 5, 8, BMS, 5, 8, Ewopharma, 5, 8, Lilly, 5, 8, Mylan, 5, 8, Novartis, 5, 8, MSD, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Roche, 5, 8, Sandoz, 5, 8; **C. Sánchez-Piedra**, None; **M. Tomsic**, None; **A. Geirsson**, None; **M. van de Sande**, Novartis, 2, 5, AbbVie, 5, Janssen, 2, Eli Lilly, 2; **G. Macfarlane**, Celgene, 2; **C. Heegaard Brahe**, Novartis, 2; **M. Lund Hetland**, Abbvie, 2, AbbVie, 2, Biogen, 2, BMS, 2, CellTrion, 2, 9, MSD, 2, Novartis, 2, Orion, 2, Pfizer, 2, Samsung, 2, UCB, 2; **M. Østergaard**, AbbVie, 2, 8, 9, Abbvie, 2, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, UCB, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, 5, 8, Abbvie, Celgene, Centocor, Merck, and Novartis, 2, Abbvie, Celgene, Centocor, Merck, Novartis, 2, BMS, 2, 5, 8, 9, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8.

Abstract Number: 1084

Predicting ASDAS Inactive Disease After 6 Months of TNFi Treatment in Bio-Naive Axial Spondyloarthritis Patients Treated in Clinical Practice – Results from the EuroSpA Collaboration

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor necrosis factor inhibitors (TNFi) have vastly improved prognosis in patients with axial spondyloarthritis (axSpA). However, many patients treated with TNFi still fail to achieve a treatment target of remission. Hence, the aim of this study was to construct and validate a prediction model for achievement of Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease (< 1.3) in bio-naive axSpA patients after 6 months of TNFi treatment.

Methods: Of the 14 registries in the EuroSpA Collaboration (1), 10 collected data on ASDAS and patients with a 6 months follow-up visit (time window 3-9 months) with registration of variables needed for ASDAS calculation constituted the study cohort. The study cohort was split by dividing 50% of patients from each individual registry into a derivation and validation cohort. Logistic regression analyses were used to identify conventional clinical variables (marked with bold in Table 1) associated with ASDAS < 1.3 at follow-up in the derivation cohort. Missing covariate data were imputed with Multiple Imputation with Chained Equations. Variables with a p-value < 0.25 in univariate analyses were included in the initial multivariable model. A priori it was decided to adjust for age, gender and country. Purposeful selection guided removal of variables from the multivariable model. Model fit was tested in the validation cohort by area under the Receiver Operating Curve (ROC) and misclassification error.

Results: Of the 25,988 axSpA patients in the EuroSpA database who started their 1st TNFi 7,396 had a relevant follow-up visit with registration of variables needed for ASDAS calculation. The study cohort had slightly higher

Table 1: Baseline characteristics

	Patients with assessment of ASDAS at follow-up (n=7,396)		Patients without assessment of ASDAS at follow-up (n= 18,592)	
	No. of patients with available data, n	Median (IQR) or percentage	No. of patients with available data, n	Median (IQR) or percentage
Age, years	7,396	41 (32 - 50)	18,592	42 (33 - 51)
Male	7,396	59.5 %	18,592	60.2 %
HLA-B27 positive	4,251	71.6 %	8,367	70.8%
Concomitant csDMARD	6,952	32.3 %	16,793	30.9 %
Time since diagnosis, years	5,136	2 (1 - 8)	12,346	3 (1 - 9)
Current smoking	6,283	25.2 %	14,356	23.4 %
Treatment	7,396		18,592	
Infliximab		26.0 %		29.5 %
Etanercept		21.9 %		27.4 %
Adalimumab		28.0 %		29.7 %
Certolizumab		4.5 %		3.0 %
Golimumab		19.6 %		10.4 %
Year of treatment	7,396		18,592	
Start 2015-2017		46.5 %		21.2 %
Start 2012-2014		34.5 %		21.1 %
Start 2009-2011		12.8 %		25.9 %
Start before 2009		6.2 %		31.8 %
CRP, mg/L	6,311	11 (4 - 24)	13,529	8 (3 - 21)
ASDAS, units	5,565	3.63 (3 – 4.3)	2,583	3.44 (2.66 - 4.16)
BASDAI, mm	6,044	60 (46 - 73)	9,624	58 (42 - 71)
BASFI, mm	5,334	46 (27 - 66)	7,333	45 (35 - 65)
VAS Pain, mm	5,678	70 (50 - 80)	10,994	62 (41 - 78)
VAS Global, mm	6,373	70 (50 - 80)	10,830	62 (42 - 80)
VAS Fatigue, mm	4,649	70 (51 - 83)	5,930	65 (41.2 - 80)
Physician Global, mm	3,698	42 (20 - 63.8)	7,219	40 (25 - 60)

Data are as observed, median (IQR) or percentage; HLA-B27: Human leukocyte antigen B27; csDMARD: conventional synthetic Disease Modifying Anti Rheumatic Drug; CRP: C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Index; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; VAS: visual analogue scale

Table 2. Multivariate models for prediction of ASDAS inactive disease at 6 months by baseline variables in derivation cohort

	Initial model			Final model		
	Odds ratio	**95 % CI**	**p-value**	**Odds ratio**	**95 % CI**	**p-value**
Intercept	4.659	(2.835, 7.657)	<0.0001	4.266	(2.625, 6.934)	<0.0001
Time since diagnosis	1.003	(0.988, 1.018)	0.7187			
HLA-B27 (Positive)	1.476	(1.120, 1.945)	0.0049	1.458	(1.112, 1.912)	0.0055
Smoking status (Past)	0.898	(0.731, 1.104)	0.3057			
Smoking status (Current)	0.859	(0.692, 1.068)	0.1703			
Year of treatment (Start 2012-2014)	0.869	(0.725, 1.042)	0.1288	0.859	(0.719, 1.026)	0.0935
Year of treatment (Start 2009-2011)	0.758	(0.580, 0.991)	0.0426	0.756	(0.580, 0.986)	0.0039
Year of treatment (Start before 2009)	0.515	(0.328, 0.809)	0.0040	0.518	(0.330, 0.813)	0.0042
CRP, mg/L (10-30)	1.219	(1.008, 1.475)	0.0409	1.206	(0.998, 1.456)	0.0524
CRP, mg/L (>30)	1.081	(0.842, 1.389)	0.5391	1.059	(0.829, 1.353)	0.6469
BASDAI	0.991	(0.984, 0.998)	0.0152	0.991	(0.984, 0.998)	0.0077
BASFI	0.983	(0.978, 0.989)	<0.0001	0.982	(0.977, 0.987)	<0.0001
VAS Pain	0.997	(0.990, 1.004)	0.3636			
VAS Global	1.002	(0.996, 1.009)	0.5336			
VAS Fatigue	0.997	(0.991, 1.002)	0.2277	0.996	(0.991, 1.001)	0.1084
Physician Global	0.998	(0.993, 1.003)	0.3951			

Reference: never smoking, start of treatment 2015-2017, C-Reactive Protein (CRP)<=10.
ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; VAS: Visual Analogue Scale

disease activity at baseline than the patients without follow-up ASDAS assessment (Table 1). At 6 months, 2,203 patients (29.8%) of patients were in ASDAS inactive disease. Based on univariate analyses, all tested variables except concomitant csDMARDs were included in the initial multivariate model. During model fitting, time since diagnosis, smoking, VAS pain, VAS Global and Physician global were excluded. The final model demonstrated that HLA-B27 positivity, treatment start after 2015, moderately elevated CRP, low baseline BASDAI, low BASFI and low fatigue scores increased the probability of ASDAS inactive disease at 6 months (Table 2). The regression coefficients of the model were used to derive a prediction index for each patient in the validation cohort, determining their predicted probability of ASDAS inactive disease at 6 months. The ability of the model to correctly predict ASDAS inactive disease using different cut-offs for predicted probability are shown with the ROC (see Figure 1). The fit was deemed reasonable (median area under the curve 0.74, misclassification error 0.26).

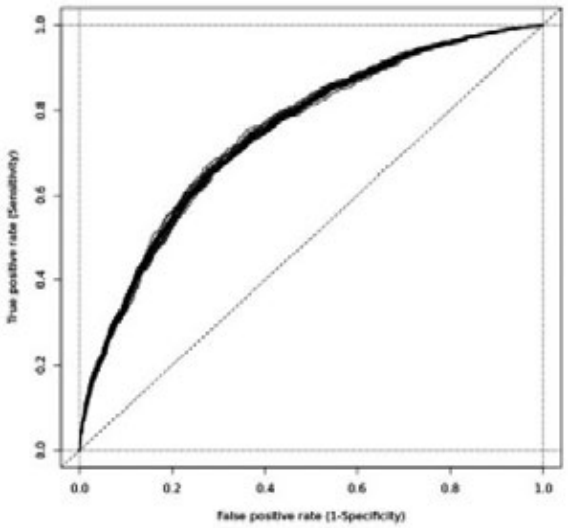

Figure 1: Receiver Operating Curves in the validation cohort (20 imputed datasets)

Conclusion: A clinical prediction model for ASDAS inactive disease after 6 months of TNFi treatment was constructed correctly identifying 3 out of 4 patients as responders/non-responders. Future studies should investigate the potential of improving the model by addition of imaging and soluble biomarkers.

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Reference:

1. Brahe et al. *Arthritis Rheumatol.*2018;70 (suppl 10).

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Abstract Number: 1085

Probiotic Use and Psoriatic Arthritis Disease Activity

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Probiotics have been hypothesized to mediate inflammation through gut microbiome modulation, and growing evidence has suggested that our intestinal gut microbiome may play a role in the development

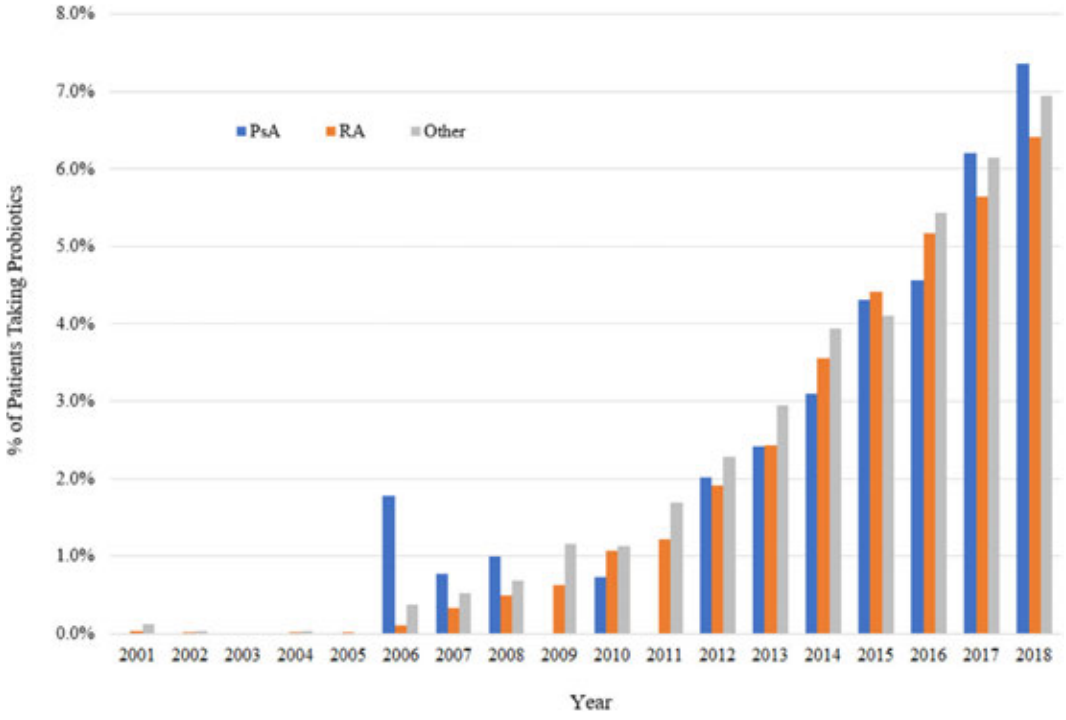

Figure 1. Probiotic use over time by primary rheumatic disease diagnosis in FORWARD. Average N per year was 5 for psoriatic arthritis, 137 for RA, and 81 for Other.

Table 1. Baseline demographic and clinical characteristics of patients by primary diagnosis at enrollment.

	PsA (n = 782)			RA (n = 34378)			
Characteristic	Probiotic user (n = 29)	Nonuser (n = 753)	*p*	Probiotic user (n = 1019)	Nonuser (n = 33091)	*p*	*p* (users, PsA vs RA)
Probiotic use baseline, %	0.9	--	--	0.7	--	--	0.51
Probiotic use ever, %	3.7	--	--	3.0	--	--	0.24
Age, years	55.30 ± 12.22	53.19 ± 12.34	0.37	59.19 ± 11.75	58.43 ± 13.53	0.08	0.08
Female, %	86.2	70.0	0.06	93.4	79.4	**< 0.001**	0.13
Caucasian, %	96.2	91.5	0.72	94.2	86.0	**< 0.001**	1
Education, years	14.92 ± 2.23	14.52 ± 2.21	0.36	14.35 ± 2.40	13.33 ± 2.87	**< 0.001**	0.23
Household income, US$1,000	61.96 ± 34.81	61.42 ± 33.75	0.93	61.25 ± 34.43	49.28 ± 32.45	**< 0.001**	0.91
RDCI, 0-9	2.17 ± 1.28	1.80 ± 1.60	0.22	1.87 ± 1.65	1.70 ± 1.54	**< 0.001**	0.33
Turmeric use, %	3.4	0.7	0.20	2.2	0.3	**< 0.001**	0.48
Fish oil use, %	34.5	8.6	**< 0.001**	16.0	4.7	**< 0.001**	**0.02**
Vitamin D use, %	20.7	10.2	0.11	17.4	6.9	**< 0.001**	0.62
DMARD use, %	51.7	58.6	0.57	76.5	74.4	0.13	**< 0.01**
NSAID use, %	62.1	49.7	0.26	52.6	55.8	**0.04**	0.35
PPI use, %	41.4	26.8	0.09	33.8	22.7	**< 0.001**	0.43
Pain VAS, 0-10	5.07 ± 3.03	4.09 ± 2.84	0.07	4.01 ± 2.74	4.15 ± 2.85	0.12	**0.04**
SF-36 PCS, 0-100	35.26 ± 10.94	38.45 ± 11.29	0.15	36.52 ± 10.76	36.24 ± 10.83	0.44	0.55
SF-36 MCS, 0-100	43.99 ± 12.55	46.57 ± 11.70	0.26	48.85 ± 11.19	47.77 ± 11.87	**< 0.01**	**0.03**
HAQ-II, 0-3	4.08 ± 2.42	3.48 ± 2.29	0.18	3.78 ± 2.18	3.93 ± 2.27	0.09	0.49
PAS-II, 0-10	1.00 ± 0.65	0.79 ± 0.65	0.09	1.00 ± 0.66	1.03 ± 0.68	0.26	0.99

Table 2. Demographic and clinical characteristics of patients by diagnosis following propensity score matching.

	PsA (n = 49)				RA (n = 1462)			
Characteristic	Probiotic user (n = 25)	Nonuser (n = 24)	*p*	StdDiff	Probiotic user (n = 755)	Nonuser (n = 707)	*p*	StdDiff
Age, years	58.54 ± 12.95	57.04 ± 10.00	0.65	0.13	64.13 ± 13.10	63.96 ± 12.18	0.79	0.01
Female, %	84.0	83.3	1	0.02	93.8	92.2	0.26	0.06
Caucasian, %	96.0	100	1	0.29	94.8	93.8	0.43	0.04
Education, years	14.88 ± 2.26	15.08 ± 1.67	0.72	0.10	14.54 ± 2.22	14.59 ± 2.18	0.65	0.02
Household income, US$1,000	64.20 ± 38.04	75.42 ± 42.55	0.34	0.28	62.68 ± 38.14	64.33 ± 38.71	0.41	0.04
RDCI, 0-9	2.28 ± 1.46	1.75 ± 1.45	0.21	0.36	2.47 ± 1.75	2.56 ± 1.85	0.34	0.05
Turmeric use, %	4.0	4.2	1	0.01	7.8	5.7	0.12	0.08
Fish oil use, %	40.0	45.8	0.78	0.12	25.6	24.8	0.76	0.02
Vitamin D use, %	20.0	37.5	0.22	0.39	23.8	25.2	0.58	0.03
DMARD use, %	52.0	45.8	0.78	0.12	68.3	68.0	0.91	0.01
NSAID use, %	64.0	54.2	0.57	0.20	39.5	41.2	0.52	<0.01
PPI use, %	36.0	50.0	0.39	0.29	37.7	36.9	0.75	0.02
Pain VAS, 0-10	4.78 ± 3.09	3.00 ± 2.58	**0.03**	-	3.92 ± 2.72	3.97 ± 2.87	0.77	-
SF-36 PCS, 0-100	33.11 ± 11.50	40.82 ± 11.03	**0.04**	-	36.08 ± 11.54	36.68 ± 10.97	0.36	-
SF-36 MCS, 0-100	45.67 ± 12.64	49.05 ± 9.92	0.34	-	48.91 ± 11.39	47.95 ± 11.63	0.14	-
HAQ-II, 0-3	0.98 ± 0.73	0.75 ± 0.73	0.27	-	1.03 ± 0.69	1.05 ± 0.70	0.75	-
PAS-II, 0-10	4.20 ± 2.58	3.03 ± 2.20	0.10	-	3.73 ± 2.20	3.78 ± 2.28	0.71	-

or persistence of spondyloarthritis. This has become understood to some degree among patients who frequently ask about the possible role of probiotics in PsA. The objective of this study was to evaluate associations between probiotic use and patient-reported outcomes in patients with psoriatic arthritis (PsA).

Methods: We examined probiotic use among patients with PsA in FORWARD, The National Databank for Rheumatic Diseases. Patients with rheumatoid arthritis (RA) acted as a comparison group, and patients with dual diagnoses were excluded. The prevalence of probiotic use was determined for each calendar year since the earliest report on record in the databank. Patients who reported probiotic use in at least one encounter were classified as probiotic users. For comparisons made between probiotic users and nonusers, we used propensity score matching to balance confounders. Descriptive statistics were calculated for patient demographics, clinical characteristics, and five outcomes of interest (PAS-II, HAQ-II, pain VAS, SF-36 PCS, and SF-36 MCS). Significance was assessed with Student's t-tests and Fisher's exact tests as appropriate. Paired t-tests were utilized to assess differences in outcomes before and after probiotic use in the PsA cohort.

Results: Probiotic use has increased in recent years, from less than 1% prior to 2006 to approximately 7% of FORWARD patients reporting probiotic use in 2018 (Figure 1). Of the 782 PsA and 34,378 RA patients included in the study, 3.7% and 3.0% reported probiotic use at some point, respectively. In the RA cohort, probiotic users are more likely than nonusers to be female, be Caucasian, have more education, have a higher income, have a higher comorbidity index, use PPIs, and use other supplements in addition to probiotics. Probiotic users and nonusers in the PsA cohort generally follow these same trends, but the differences do not reach statistical significance except in the case of fish oil use (Table 1). After propensity score matching, probiotic users with PsA had significantly lower SF-36 PCS scores and significantly higher pain VAS scores than nonusers with PsA (Table 2). In the paired comparison of probiotic users with PsA before initiating probiotic use and after probiotic exposure, there were no statistically significant differences in any of the five outcomes.

Conclusion: We found increasing probiotic use reported by patients with PsA. In this observational study, we found no significant changes in patient function scores before and after initiation of a probiotic. Prospective studies are needed to examine whether probiotics affect disease activity and function in patients with PsA. Given the difference noted in pain scores between probiotic users and nonusers with PsA, patients who take probiotics may have higher baseline pain levels.

Disclosure: M. Grinnell, None; **K. Wipfler**, Option Care, 3; **A. Ogdie**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Takeda, 5, Amgen, 2, 4, 5, 8, Amgen to Forward National Databank, 2, BMS, 5, Bristol-Myers

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Abstract Number: 1086

Psoriatic Arthritis - Epidemiology, Incidence Rate in Psoriasis Patients, Comorbidity Profiles and Risk Factor Analysis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Background/Purpose: Psoriasis (PsO) is a systemic inflammatory disease accompanied by comorbidities such as depression, cardiovascular diseases or metabolic syndrome. Approximately 10 - 27% of PsO patients develop psoriatic arthritis (PsA), a rheumatologic comorbidity of PsO. Due to increased impairment of working ability and risk of a potential destructive disease course of PsA, early diagnosis and therapeutic intervention are crucial for optimal patient care. This analysis on German health claims data was conducted to determine the rate of development of PsA in PsO patients over 4 years. Furthermore, comorbidity profiles of PsO patients with and without concomitant PsA were compared as well as potential risk factors for the development of PsA were assessed.

Methods: This was a non-interventional retrospective analysis of anonymized insurance health claims data using a subset of the Institute of Applied Health Research Berlin (InGef) database, which was observable between 2012 and 2017. The database contained 2.9 million subjects stratified by age and gender based on the population structure of Germany as reported by the German Federal Statistical Office DeStatis. Continuously insured individuals were identified by ICD-10 GM version 2019 codes (L40.0: psoriasis vulgaris, L40.5: psoriatic arthritis). Risk factors for the development of PsA in Pso patients were determined by conditional logistic regression analysis in sex- and age-matched populations.

Results: The cumulative percentage of patients with incident PsO developing PsA (PsO-PsA) over 4 years was 3% with a mean time to diagnosis of PsA of 1.5 years. Patients developing PsA were on average approx. 5 years younger than patients not developing PsA within 4 years. Although both patient groups displayed a similar spectrum of comorbidities with a high frequency of diseases associated to metabolic syndrome, unspecific arthritic symptoms were distinctly more frequent in PsO-PsA patients. However, only 4% of patients with PsO and 43% of patients with concomitant PsA consulted ambulatory rheumatologists. PsO patients diagnosed with “acute rheumatism” (odds ratio: 2.93, 95% CI=1.01-2.99; p= < 0.001) or “pain in unspecific joints” (odds ratio: 1.74, 95% CI=1.76-4.86; p= 0.047) showed an increased risk to develop PsA later on. Specific arthritic symptoms such as “Bouchard’s nodes” and “Heberden’s nodes”, on the other hand, did not confer a higher risk for development of PsA

Conclusion: The lower mean age of PsO–PsA patients and the mean time to PsA diagnosis of only 1.5 years show that PsA development can already start early after PsO diagnosis reinforcing the need for early involvement of rheumatologists in the medical care of PsO patients. The small percentage of patients with or without concomitant PsA presented to rheumatologists suggests that the majority of PsO patients with concomitant PsA were not under specialized rheumatologic care and patients with existing PsO might profit from intensified rheumatologic screening. The identified risk factors for the development of PsA, "acute rheumatism" and "pain in unspecific joints", confirm previous findings that PsA diagnosis is preceded by unspecific arthritic symptoms.

Disclosure: J. Rech, AbbVie, 8, Biogen, 8, BMS, 5, 8, Celgene, 5, 8, Chugai, 5, MSD, 8, Novartis, 5, 8, Roche, 5; **M. Sticherling**, Abbvie, 5, 8, 9, Celgene, 5, 8, 9, Janssen Cilag, 5, 8, 9, Lilly, 5, Pfizer, 5, 8, 9, Sanofi, 5, 9, UCB, 5, GSK, 9, MSD, 5, 8, Mundipharma, 5, Novartis, 5, 8, 9, Amgen, 5, 9, Leo Pharma, 5, 8, 9, Regeneron, 9; **M. Biermann**, Novartis Pharma GmbH, 3; **B. Häberle**, Novartis Pharma GmbH, 3; **M. Reinhardt**, Novartis Pharma GmbH, 3.

Abstract Number: 1087

Golimumab Improves Work Productivity and Activity and Quality of Life in Patients with Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA): Final Results from a Non-Interventional Study in Germany (GO-ART)

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SESSION INFORMATION
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Background/Purpose: Golimumab (GLM) has shown its efficacy and tolerability in various randomized clinical trials. Systemic data for GLM regarding health-economic parameters in daily clinical practice are essential not only for pharmaceutical companies but also for cost-benefit analyses in Germany.

This prospective NIS was designed to evaluate the impact of GLM therapy on work productivity and activity as well as Quality of Life (QoL) in patients with RA, AS or PsA in Germany under routine settings over an observation period of 12 months, plus an additional voluntary extension period of 12 months (total 24 months) to collect long-term data on health economic parameters.

Methods: GO-ART was an observational prospective study on patients with RA, AS or PsA (biologic-naïve and biologic-experienced) who started treatment with GLM at 63 sites of Germany.

The primary endpoint was the change in work productivity/activity impairment as measured by Work Productivity and Activity Impairment (WPAI) questionnaire from baseline, measured primarily at month 3 and secondarily at months 6, 12 and 24.

As secondary endpoint the change in quality of life (RAQoL for RA patients, ASQoL for AS patients and NAPPA-QoL for PsA patients) was assessed.

Table 1:

WPAI - Changes in the 4 domain scores from baseline to Months 3, 12 and 24 (mITTe)

Timepoint	Statistics	Total work productivity impairment	Absenteeism	Presenteeism	Activity impairment
RA patients (mITTe: N=158)					
V0 (baseline)	N	108	135	113	154
	Mean	46.8	11.9	46.0	50.9
	SD	27.60	30.80	27.76	28.36
Change in scores:					
	N	78	110	83	133
V0 - V1 (Month 3)	Mean	-11.3	-5.8	-12.5	-13.9
(primary endpoint)	SD	23.77	29.37	23.00	26.77
	p-value	<0.0001[a]	0.0429[b]	<0.0001[b]	<0.0001[b]
V0 – V3 (Month 12)	N	67	89	75	114
	Mean	-13.2	-8.8	-12.7	-15.2
	SD	23.40	35.51	22.08	24.23
	p-value	<0.0001[a]	0.0128[b]	<0.0001[b]	<0.0001[b]
V0 – V6 (Month 24)	N	43	55	45	67
	Mean	-13.7	-7.8	-12.2	-18.4
	SD	25.84	30.73	26.10	26.32
	p-value	0.0012[a]	0.0647[b]	0.0030[a]	<0.0001[a]
PsA patients (mITTe: N=157)					
V0 (baseline)	N	114	137	115	153
	Mean	35.0	12.9	33.4	43.2
	SD	27.77	30.87	26.42	28.45
Change in scores:					
V0 - V1 (Month 3)	N	81	109	85	128
(primary endpoint)	Mean	-13.8	-4.9	-15.4	-17.4
	SD	25.02	28.33	25.98	30.44
	p-value	<0.0001[a]	0.0449[b]	<0.0001[b]	<0.0001[b]
V0 – V3 (Month 12)	N	77	99	80	118
	Mean	-10.6	-4.6	-12.7	-18.3
	SD	30.40	30.62	27.82	30.28
	p-value	0.0046[b]	0.2028[b]	0.0001[b]	<0.0001[a]
V0 – V6 (Month 24)	N	39	48	41	63
	Mean	-9.5	-1.9	-16.5	-23.4
	SD	28.99	31.56	26.84	31.36
	p-value	0.0472[a]	0.6084[b]	0.0003[a]	<0.0001[a]
AS patients (mITTe: N=176)					
V0 (baseline)	N	136	160	142	177
	Mean	48.2	14.0	45.9	52.1
	SD	28.08	29.55	26.74	25.87
Change in scores:					
V0 - V1 (Month 3)	N	104	135	111	162
(primary endpoint)	Mean	-16.9	-8.9	-15.8	-18.3
	SD	26.62	30.73	24.66	26.43
	p-value	<0.0001[b]	0.0001[b]	<0.0001[b]	<0.0001[b]
V0 – V3 (Month 12)	N	93	120	100	130
	Mean	-16.8	-6.1	-16.1	-22.8
	SD	31.92	31.46	30.45	28.77
	p-value	<0.0001[a]	0.0141[b]	<0.0001[a]	<0.0001[a]
V0 – V6 (Month 24)	N	46	64	50	72
	Mean	-24.7	-14.1	-22.0	-28.3
	SD	32.71	33.29	28.64	29.79
	p-value	<0.0001[a]	0.0002[b]	<0.0001[a]	<0.0001[b]

AS = Ankylosing Spondylitis; PsA = Psoriatic Arthritis; RA = Rheumatoid Arthritis
WPAI = Work Productivity and Activity Impairment
Total work productivity impairment = Overall impairment estimate calculated by an algorithm of absenteeism and presenteeism.
Absenteeism = Percentage of work time missed because of patient's health problem in the past 7 days.
Presenteeism = Percentage of impairment experienced while at work in the past 7 days because of patient's health problem.
Activity impairment = Percentage of impairment in daily activities because of patient's health problem in the past 7 days

[a] *t-test;* [b] *Wilcoxon Signed rank test*

Results: 748 patients (RA=250, PsA=249, AS=249) started GLM therapy. The primary efficacy endpoint was analyzed in the modified intention-to-treat (mITT) subset of 493 patients (RA=158, PsA=157, AS=178) with full-time or part-time employment at baseline (mITTe). A total of 348 patients entered the additional 12-month observation period, of which 303 completed the 24-month assessment.

By 3 months after initiation of Golimumab treatment, a marked improvement was seen in all 4 WPAI domain scores ("absenteeism" (time off work), "presenteeism" (on-the-job productivity), "total work productivity impairment" (TWPI), and "activity impairment") in daily living because of patient's health problems related to RA, PsA or AS, as shown in Table 1 (all p-values < 0.05).

The statistically significant improvements in the mean WPAI domain scores were maintained over the 24-month observation period in all 3 indications with a higher treatment effect regarding “activity impairment” and “presenteeism” compared to “absenteeism” (Table 1).

Quality of life improved significantly ($p< 0.0001$) from baseline at month 3, 6, 12 and 24 in patients with RA (RAQoL), AS (ASQoL) and PsA (NAPPA-QoL) based on questionnaire data of 237 RA patients (RA-miTT), 228 AS patients (AS-mITT) and 235 PsA patients (PsA-mITT) indicating a clinically relevant improvement.

Conclusion: Treatment with GLM provided sustained improvement in WPAI and QoL in patients with RA, PsA and AS over the observational period of 24 months.

All scores of the WPAI showed a significant ($p< 0.05$) reduction in mean score values in each indication.

GLM leads to an improvement of work productivity and daily activities in patients already within the first 3 months of treatment.

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Abstract Number: 1088

Does Drug Effectiveness of 2nd and 3rd TNF Inhibitors in Patients with Psoriatic Arthritis Depend on the Reason for Withdrawal from the Previous Treatment? – Results from the EuroSpA Research Collaboration

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SESSION INFORMATION

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Background/Purpose: Tumour necrosis factor inhibitors (TNFi) are efficacious in patients with psoriatic arthritis (PsA), but some patients switch to a different TNFi because of adverse events (AE) or lack of effect (LOE). The EuroSpA Collaboration has previously demonstrated a 1-year retention rate of 77% and 6 months LUNDEX adjusted

Table: Baseline characteristics, retention and remission rates of PsA patients initiating 2nd and 3rd TNFi overall and stratified by reason for withdrawal from the previous TNFi (AE or LOE).

	2nd TNFi (n=4971)*		3rd TNFi (n=1768)**	
	Baseline characteristics			
Age, years	50(41-58)		51(42-59)	
Male	42%		38%	
Concomitant/prior csDMARD	54% / 82%		53% / 86%	
Disease duration, years	5(2-11)		7(4-13)	
First TNFi drug Infliximab/ Etanercept / Adalimumab / Certolizumab / Golimumab	12% / 38% / 34% / 4% / 13%		18% / 28% / 29% / 5% / 20%	
DAS28	4(3.1-4.9)		4.1(3.2-5)	
DAPSA28	24.6(15.2-37)		25.3(16.3-38.6)	
	Retention rates			
6 months (95% CI)	80% (78-81%)		78 % (76-80%)	
12 months (95% CI)	69% (67-70%)		66 % (64-68%)	
24 months (95% CI)	60% (59-61%)		56 % (53-58%)	
	Initiating 2nd TNFi because of AE on 1st TNFi	Initiating 2nd TNFi because of LOE on 1st TNFi	Initiating 3rd TNFi because of AE on 1st TNFi	Initiating 3rd TNFi because of LOE on 1st TNFi
6 months (95% CI)	76% (73-79%)	78% (77-80%)	75% (71-80%)	76% (73-79%)
12 months (95% CI)	66% (64-69%)	65% (64-67%)	65% (60-71%)	63% (59-66%)
24 months (95% CI)	58% (55-61)	56% (54-58%)	55% (50-61%)	51% (48-55%)
	Remission rates			
	LUNDEX adjusted ***		LUNDEX adjusted ***	
DAS28 remission at 6 / 12 / 24 months	35% / 29% / 23%		27% / 22% / 18%	
DAPSA28 remission at 6 / 12 / 24 months	14% / 11% / 9%		10% / 9% / 7%	
	Initiating 2nd TNFi because of AE on 1st TNFi	Initiating 2nd TNFi because of LOE on 1st TNFi	Initiating 3rd TNFi because of AE on 1st TNFi	Initiating 3rd TNFi because of LOE on 1st TNFi
	LUNDEX adjusted ***			
DAS28 remission at 6 / 12 / 24 months	34% / 30% / 23%	31% / 26% / 20%	26% / 25% / 21%	26% / 20% / 18%
DAPSA28 remission at 6 / 12 / 24 months	13% / 10% / 10%	11% / 9% / 8%	9% / 7% / 9%	9% / 8% / 6%

*Data are observed. median (IQR) or percentages; csDMARD: conventional synthetic Disease Modifying Anti Rheumatic Drug; TNFi: tumor necrosis factor inhibitor; DAS28: Disease Activity Score 28 joint-count; DAPSA28: Disease Activity index for Psoriatic Arthritis 28 joint-count; *number of patients with available data varied from n=2904-4971; **number of patients with available data varied from n=1035-1768; ***LUNDEX adjusted: crude rates adjusted for drug retention*

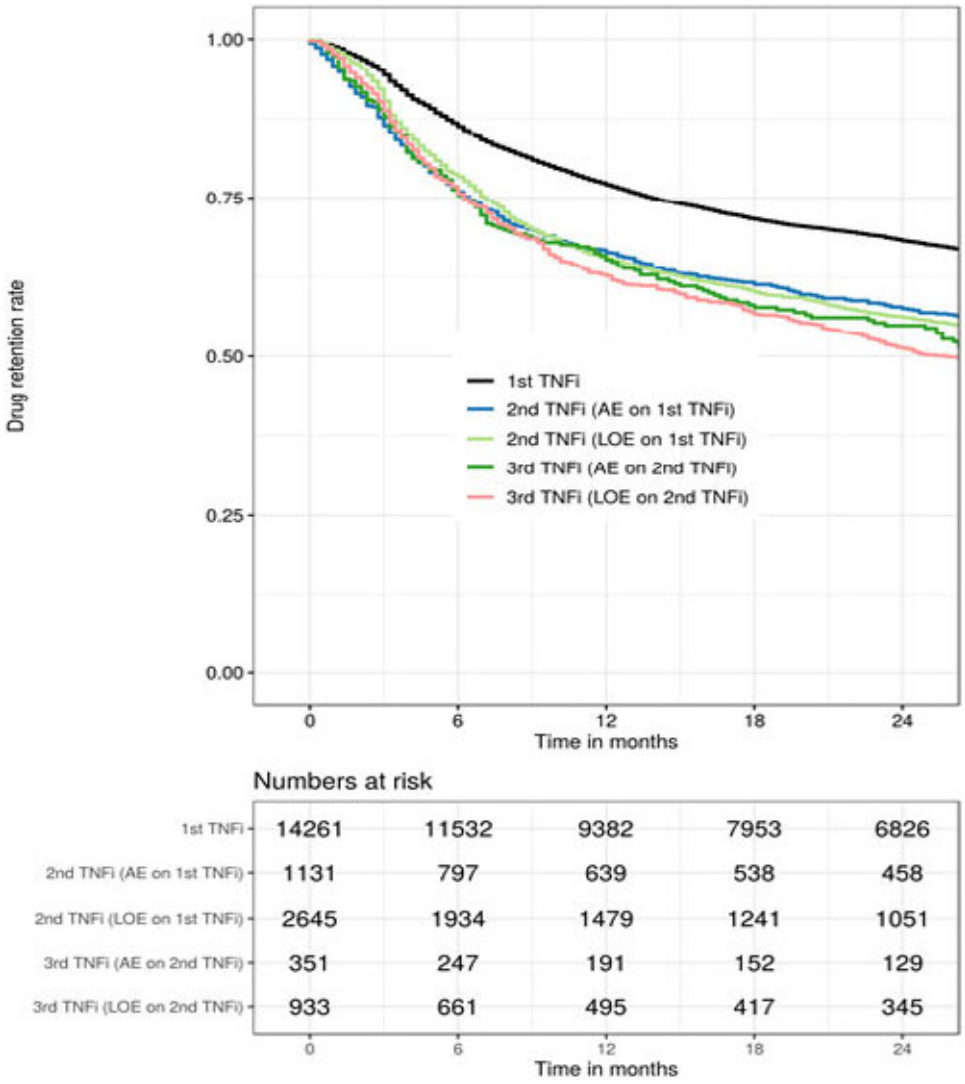

Figure: Kaplan-Meier curves (top) showing drug retention rates up to 24 months for 1st TNFi*, for 2nd (AE or LOE on 1st TNFi) and 3rd TNFi (AE or LOE on 2nd TNFi). The table (bottom) shows the number of patients who were still being treated at the corresponding time points
*previously reported

28-joint count Disease Activity Score (DAS28) remission rates of 45%[1] in patients with PsA initiating the first TNFi treatment. Little is known about the effectiveness of switching to a second and third TNFi in patients with PsA.

We aim to investigate retention and remission rates at 6, 12 and 24 months in patients with PsA initiating the 2nd and 3rd TNFi in clinical practice across Europe. Secondly, to investigate whether the outcomes are associated with the reason for withdrawal (AE or LOE) from the previous TNFi-treatment.

Methods: Prospectively collected data on PsA patients in routine care from 12 European registries were pooled. Kaplan-Meier estimation was used to investigate TNFi retention rates. LUNDEX adjusted[2] remission rates were calculated for DAS28< 2.6 and 28 joint Disease Activity index for Psoriatic Arthritis (DAPSA28) ≤4. Group comparisons were performed by Chi-square test.

Results: A total of 4971 patients initiating their 2nd TNFi and 1768 patients initiating their 3rd TNFi were included. Baseline characteristics are shown in the Table.

The overall retention rates for 2nd and 3rd TNFi at 12 months were 69% (67-70%) and 66% (64-68%), (2nd vs 3rd p=0.053), respectively (Figure). Corresponding retention rates for the individual registries ranged from 48-100% and 49-91%, respectively. If patients had stopped the 1st TNFi due to AE or LOE, 12-month retention rates for the 2nd TNFi treatment were 66% and 65%, respectively. In patients who stopped the 2nd TNFi due to AE or LOE, 12-month retention rates for the 3rd TNFi treatment were 65% and 63%, respectively.

For the 2nd and 3rd TNFi, 6 months LUNDEX adjusted DAS28 remission rates were 35% and 27% (p< 0.001), respectively, and for DAPSA28 remission 14% and 10% (p=0.008) (Table).

Conclusion: The EuroSpA Collaboration demonstrated decreasing retention and remission rates with increasing number of previous TNFi, although with only minor difference between 2nd and 3rd. Patients who had withdrawn from the previous TNFi due to LOE had retention rates and remission rates similar to those who had withdrawn due to AE.

Acknowledgement: Novartis Pharma AG and IQVIA for supporting the EuroSpA collaboration.

References:

1. Brahe et al. ACR 2018
2. Arthritis Rheum, 2006, 54(2), p:600-6

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Abstract Number: 1089

Causes of Death in ANCA-Associated Vasculitis According to ANCA Type

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Survival has improved in ANCA-associated vasculitis (AAV) with evolving management strategies, but patients remain at an increased risk of death compared to the general population. Contemporary data regarding cause of death in AAV remain scarce and although growing appreciation of differences between patients with different ANCA types exists, no analysis has evaluated causes of death among patients with ANCA directed against myeloperoxidase (i.e., MPO-ANCA) as opposed to proteinase-3 (PR3-ANCA). We evaluated overall causes of death in a contemporary inception cohort of AAV patients, stratifying the analysis according to ANCA type.

Methods: We identified a consecutive inception cohort of patients newly-diagnosed with AAV evaluated between 2002 and 2017 in the Partners HealthCare System in Boston and determined vital status through the National Death Index. Cause of death was extracted from death certificates and organized using a validated schema that clusters diagnoses into clinically meaningful categories, such as cardiovascular disease (CVD), infection, malignancy, renal disease, and non-infectious respiratory disease based on ICD-9 or ICD-10 codes. We determined cumulative incidence

Table 1. Baseline Characteristics of the Partners ANCA-Associated Vasculitis Cohort

	Overall	MPO-ANCA+	PR3-ANCA+
N	484	313	171
Demographics			
Age (Mean, SD)	58.2 (17.3)	61.9 (15.8)	51.5 (18.1)
Male (N, %)	196 (40.5)	120 (38.3)	76 (44.4)
White	395 (81.6)	251 (80.2)	144 (84.2)
*Smoking Status**			
Never	229 (47.3)	137 (43.8)	92 (53.8)
Former	211 (43.6)	147 (47.0)	64 (37.4)
Current	43 (8.9)	29 (9.3)	14 (8.2)
Baseline Comorbidities			
Diabetes Mellitus	69 (14.4)	49 (15.7)	20 (12.0)
Hypertension	220 (48.8)	161 (55.1)	59 (37.1)
Hyperlipidemia	114 (24.3)	89 (29.1)	25 (15.3)
Baseline Disease Features			
BVAS/WG (Median, IQR)	4.0 (3.0, 6.0)	4.0 (3.0, 5.0)	5.0 (3.0, 7.0)
HEENT Involvement	223 (46.1)	111 (35.5)	112 (65.5)
Pulmonary Involvement	198 (40.9)	113 (36.1)	85 (49.7)
Renal Involvement	311 (64.3)	208 (66.5)	103 (60.2)
End-Stage Renal Disease	82 (16.9)	59 (18.9)	23 (13.5)
Initial Treatment†			
Cyclophosphamide	223 (46.1)	145 (46.3)	78 (45.6)
Rituximab	189 (39.1)	127 (40.6)	62 (36.3)
Other	72 (14.9)	41 (13.1)	31 (18.1)

*One patient had unknown smoking status; †All patients received glucocorticoids as part of their initial treatment;

Table 2. Standardized Mortality Rates in the Partners ANCA-Associated Vasculitis Cohort

	Overall	MPO-ANCA+	PR3-ANCA+
N	463	296	167
Total Patient-Years (PY)	3,270	1,956	1,314
All-Cause Mortality			
Observed / Expected Deaths	104 / 45	80 / 31	24 / 24
Observed Mortality Rate (95% CI)	36.4 (29.9-42.9)	46.5 (37.0-56.1)	21.3 (13.4-29.2)
Standardized Mortality Ratio	2.3 (1.9-2.8)	2.6 (2.1-3.2)	1.8 (1.2-2.7)
Cardiovascular Mortality			
Observed / Expected Deaths	19 / 8	17 / 6	2 / 2
Observed Mortality Rate (95% CI)	7.3 (4.4-10.3)	11.2 (6.5-15.9)	1.5 (0-3.6)
Standardized Mortality Ratio	2.3 (1.5-3.6)	3.0 (1.8-4.8)	1.7 (0.4-8.1)
Infection Mortality			
Observed / Expected Deaths	12 / 1	10 / 1	2 / 0
Observed Mortality Rate (95% CI)	4.0 (1.8-6.1)	5.1 (1.9-8.3)	2.3 (0-4.9)
Standardized Mortality Ratio	13.9 (7.9-24.5)	16.4 (8.8-30.6)	6.5 (1.6-26.3)
Cancer Mortality†			
Observed / Expected Deaths	20 / 7	14 / 5	6 / 2
Observed Mortality Rate (95% CI)	6.7 (3.9-9.5)	7.7 (3.8-11.5)	5.3 (1.4-9.3)
Standardized Mortality Ratio	2.7 (1.8-4.2)	2.7 (1.6-4.6)	3.7 (1.5-9.5)
Respiratory Mortality			
Observed / Expected Deaths	7 / 4	6 / 3	1 / 1
Observed Mortality Rate (95% CI)	2.4 (0.8-4.1)	3.6 (0.9-6.2)	0.8 (0-2.3)
Standardized Mortality Ratio	2.0 (0.9-4.2)	2.4 (1.1-5.4)	0.9 (0.1-6.4)
Renal Mortality			
Observed / Expected Deaths	4 / 1	3 / 1	1 / 0
Observed Mortality Rate (95% CI)	1.5 (0.2-2.9)	2.0 (0.0-4.0)	0.8 (0-2.3)
Standardized Mortality Ratio	4.3 (1.6-11.3)	4.5 (1.4-13.9)	2.5 (0.3-17.6)

*Restricted to ages 15-85 years old to estimate expected deaths; †Most common cancers included bronchus/lung cancer (n=9) and gastrointestinal cancer (n=6)

of overall and cause-specific mortality and standardized mortality ratios (SMR) compared to the general population. We compared MPO-ANCA+ and PR3-ANCA+ cases using Cox regression models.

Results: The study population consisted of 484 patients with a mean age of 58 years at diagnosis (**Table 1**). 40% were male, 65% were MPO-ANCA+, and 65% had renal involvement. The median baseline BVAS/WG was 4.0. During 3,385 person-years (PY) of follow-up, 130 patients died, yielding a mortality rate of 38.4/1,000 PY and a SMR of 2.3 (95% CI: 1.9-2.8). The most common cause of death was CVD (10-year cumulative incidence 7.1%), followed by malignancy (5.9%) and infection (4.1%). Of the common causes of death, the SMR for death due to infection was greatest for both MPO- and PR3-ANCA cases (16.4 [95% CI: 8.8-30.6] and 6.5 [95% CI: 1.6-26.3], respectively). MPO-ANCA patients had a significantly elevated SMR for death due to CVD (3.0 [95% CI: 1.8-4.8]), respiratory disease (2.4 [95% CI: 1.1-5.4]), and renal disease (4.5 [95% CI: 1.4-13.9]); however, these causes were not significant among PR3-ANCA+ patients (**Table 2**). In contrast, PR3-ANCA+ subjects had a greater SMR for malignancy-associated mortality than MPO-ANCA+ subjects (3.7 [95% CI: 1.5-9.5] vs 2.7 [95% CI: 1.6-4.6]). MPO- and PR3-ANCA cases had similar risk of all-cause mortality (aHR 1.3 [95% CI: 0.8-1.9], p=0.2). However, MPO-ANCA+ cases had a higher risk of CV death (HR 4.52 [95% CI: 1.00-20.33], p=0.049) compared to those who were PR3-ANCA+ (**Figure 1**).

Conclusion: The premature mortality risk in AAV is explained by CVD, infection, malignancy, and renal death. CVD is the most common cause of death but the largest excess mortality risk in AAV is associated with infection. MPO-ANCA+ subjects are at higher risk of CVD death than PR3-ANCA+ subjects. Our findings highlight the importance

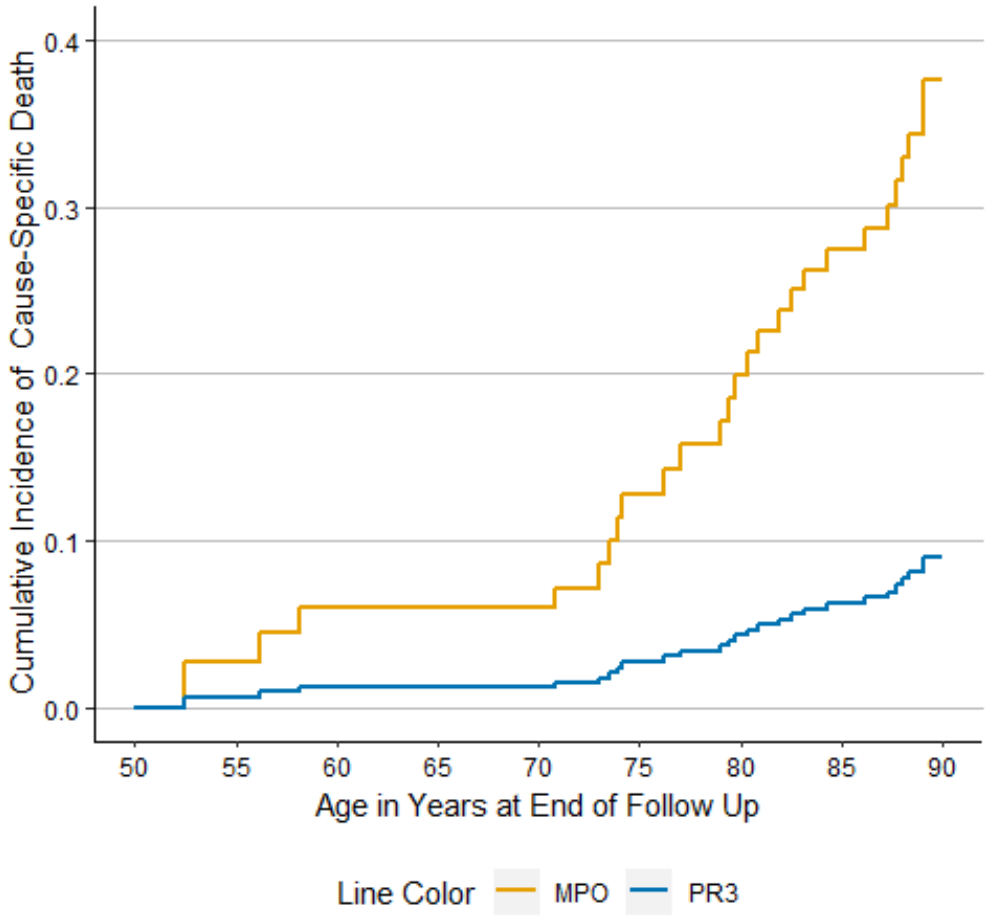

Figure 1. Cumulative Incidence of CVD-Specific Mortality in MPO- vs PR3-ANCA+ ANCA-Associated Vasculitis

of CVD as a cause of death, especially for MPO-ANCA+ subjects, but also emphasize the importance of infections, malignancies, renal failure, and respiratory issues to excess mortality in AAV.

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Abstract Number: 1090

Identification of a Distinct Intestinal Behçet's Disease Cluster in Japan: A Nationwide Retrospective Observational Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

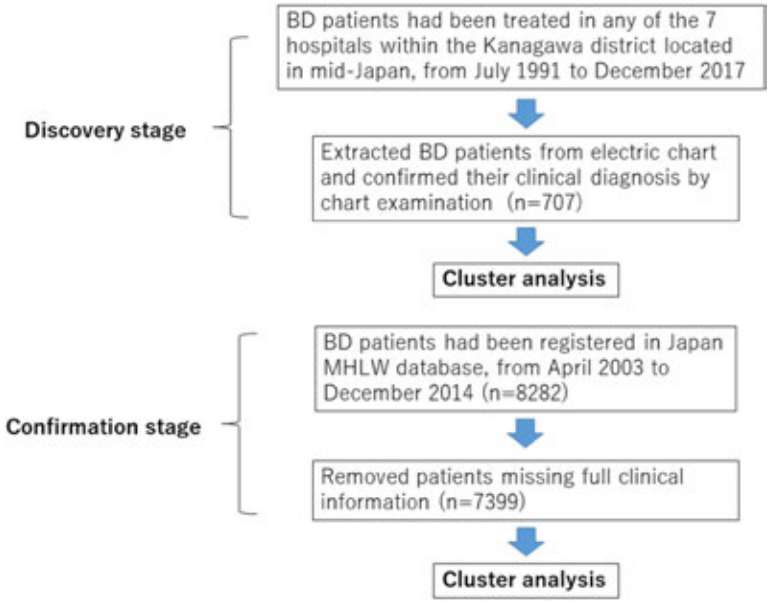
Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Background: Behçet's disease (BD) patients with poor prognoses must be identified to receive individualized care. This study aimed to identify a subgroup of BD patients with distinct clinical manifestations.

Methods: Design: This was a retrospective study of regional and nationwide registries.

Setting: This study was performed in Japan.



Flow diagram of BD patients participating in the study

Table 1. Characteristics of the cluster with BD patients in YCU registry

Characteristics	Total (n=707)	Cluster 1 (n=164)	Cluster 2 (n=168)	Cluster 3 (n=207)	Cluster 4 (n=168)	P
Male, n (%)	301 (42.6)	40 (24.4)	71 (42.3)	85 (41.1)	105 (62.5)	<0.001
Age at onset (years, mean ± SD)	37.0 ± 12.7	37.3 ± 12.2	36.9 ± 14.9	34.2 ± 10.5	40.1 ± 12.7	<0.001
Observation period (years, mean ± SD)	13.4 ± 11.6	16. 3± 12.1	13.1 ± 12.1	13.9 ± 11.9	10.3 ± 9.6	<0.001
Family history of BD, n (%)	22 (3.1)	2 (1.2)	9 (5.4)	10 (4.8)	1 (0.6)	0.016
Oral ulcer, n (%)	699 (98.9)	164 (100)	166 (98.8)	205 (99.0)	164 (97.6)	0.233
Skin involvement, n (%)	623 (88.1)	164 (100)	165 (98.2)	201 (97.1)	93 (55.4)	<0.001
Eye involvement, n (%)	393 (55.6)	78 (47.6)	48 (28.6)	118 (57.0)	149 (88.7)	<0.001
Genital ulcer, n (%)	482(68.2)	164 (100)	98 (58.3)	183 (88.4)	37 (22.0)	<0.001
Arthritis, n (%)	369 (52.2)	164 (100)	104 (61.9)	27 (13.0)	74 (44.0)	<0.001
Gastrointestinal involvement, n (%)	123 (17.4)	0 (0.0)	107 (63.7)	7 (3.4)	9 (5.4)	<0.001
Vascular involvement, n (%)	56 (7.9)	0 (0.0)	53 (31.5)	1 (0.5)	2 (1.2)	<0.001
Neurological involvement, n (%)	69 (9.8)	0 (0.0)	1 (0.6)	65 (31.4)	3 (1.8)	<0.001
Pathergy test, n (%)	79/178(44.4)	27/66 (40.9)	11/28 (39.3)	27/50 (54.0)	14/34 (41.2)	0.452
HLA-B*51, n (%)	220/471 (46.7)	58/114 (50.9)	35/100 (35.0)	77/148 (52.0)	50/109 (45.9)	0.046
Fulfilling ISG criteria, n (%)	583 (82.5)	164 (100)	108 (64.3)	196 (94.7)	115 (68.5)	<0.001
Fulfilling ITR-ICBD criteria, n (%)	654 (92.5)	164 (100)	123 (73.2)	205 (99.0)	162 (96.4)	<0.001
Fulfilling Japanese criteria, n (%)*	657 (92.9)	164 (100)	134 (79.8)	203 (98.1)	156 (92.9)	<0.001
Colchicine, n (%)	398/555 (71.7)	73/115 (63.5)	93/118 (78.8)	127/185 (68.6)	105/137 (76.6)	0.026
Glucocorticoids, n (%)	253/555 (45.6)	40/115 (34.8)	76/118 (64.4)	88/185 (47.6)	49/137 (35.8)	<0.001
Maximum dose of PSL (mg/day, mean ± SD)	11.8 ± 17.6	5.6 ± 11.1	17.2 ± 18.9	14.3 ± 20.3	8.9 ± 15.0	<0.001
mPSL pulse therapy, n (%)	37/555 (6.7)	2/115 (1.7)	8/118 (6.8)	22/185 (11.9)	5/137 (3.6)	0.002
Immunosuppressants, n (%)	213/555 (38.4)	17/115 (14.8)	77/118 (65.3)	67/185 (36.2)	52/137 (38.0)	<0.001
Biologics, n (%)	99 (14.0)	9 (5.5)	26/168 (15.5)	28 (13.5)	36 (21.4)	<0.001
Period from the diagnosis to Biologics administration (years, mean ± SD)	89 (12.6)	4.8 ± 6.9	6.7 ± 10.4	9.6 ± 9.2	2.8 ± 4.3	0.002
Smoking, n (%)	243/488 (49.8)	40/99 (40.4)	47/112 (42.0)	80/154 (51.9)	76/123 (61.8)	0.003

ISG = International Study Group for Behçet's Disease.
ITR-ICBD = International Team for the Revision of the International Criteria for Behçet's Disease.
*Behçet's Disease Research Committee, Ministry Health, Welfare, and Labour, Japan.
PSL = Prednisolone
mPSL = Methylprednisolone

Table 2. Characteristics of the cluster with BD patients in Japan MHLW registry

Characteristics	Total (n=7399)	Cluster A (n=3734)	Cluster B (n=1011)	Cluster C (n=2654)	P
Male, n (%)	3036 (41.0)	1903 (51.0)	466 (46.1)	667 (25.1)	<0.001
Age at onset (years, mean ± SD)	36. 6± 14.2	36.9 ± 13.9	41.1 ± 18.0	34.5 ± 12.5	<0.001
Observation period (years, mean ± SD)	4.0 ± 8.43	5.0 ± 9.6	3.5 ± 8.7	2.9 ± 6.6	<0.001
Oral ulcer, n (%)	6929 (93.6)	3386 (90.7)	889 (87.9)	2654 (100)	<0.001
Skin involvement, n (%)	5990 (81.0)	2777 (74.4)	559 (55.3)	2654 (100)	<0.001
Eye involvement, n (%)	2600 (35.1)	2496 (66.8)	104 (10.3)	0 (0.0)	<0.001
Genital ulcer, n (%)	4607 (62.3)	1537 (41.2)	416 (41.1)	2654 (100)	<0.001
Arthritis, n (%)	3612 (48.8)	1714 (45.9)	414 (40.9)	1484 (54.9)	<0.001
Gastrointestinal involvement, n (%)	994 (13.4)	3 (0.1)	991 (98.0)	0 (0.0)	<0.001
Vascular involvement, n (%)	161 (2.2)	161 (4.3)	0 (0.0)	0 (0.0)	<0.001
Neurological involvement, n (%)	381 (5.1)	381 (10.2)	0 (0.0)	0 (0.0)	<0.001
Pathergy test, n (%)	1502/4654 (32.3)	728/2347 (31.0)	210/629 (33.4)	564/1678 (33.6)	0.181
HLA-B*51, n (%)	1522/3388 (44.9)	908/1816 (50.0)	153/452 (33.8)	461/1120 (41.2)	<0.001
Fulfilling ISG criteria, n (%)	5432 (73.4)	2377 (63.7)	402 (39.8)	2653 (99.9)	<0.001
Fulfilling ITR-ICBD criteria, n (%)	6104 (82.5)	2946 (78.9)	505 (50.0)	2653 (99.9)	<0.001
Colchicine, n (%)	3224 (43.6)	1648 (44.1)	437 (43.2)	1139 (42.9)	0.608
Glucocorticoids, n (%)	2587 (35.0)	1300 (34.8)	381 (37.7)	906 (34.1)	0.127
Immunosuppressants, n (%)	628 (8.5)	314 (8.4)	83 (8.2)	231 (8.7)	0.865

MHLW = Ministry of Health, Welfare, and Labour, Japan.
ISG = International Study Group for Behçet's Disease.
ITR-ICBD = International Team for the Revision of the International Criteria for Behçet's Disease.

Patients: A total of 707 patients registered to the Yokohama City University (YCU) regional BD registry between 1990 and 2017, and 7,399 newly registered BD patients to the Japanese MHLW database between 2003 and 2014, were included.

Measurements: For the discovery stage, YCU registry data on the clinical phenotype of BD, drug use, and HLA-B51 status were obtained. For the confirmation stage, a nationwide registry, including clinical phenotype of BD patients registered < 1 year after BD diagnosis, drug use, and HLA-B51 status, was used. Hierarchical cluster analysis of clinical phenotype and HLA-B51 positivity was independently performed on both populations.

Results: Four different clusters were identified from the YCU registry. Cluster 2 showed higher rates of gastrointestinal (GI) involvement, steroid use, and immunosuppressants, and lower rates of ocular disease, International Study Group criteria fulfillment, and HLA-B51 positivity. A similar GI cluster was identified in the Japan MHLW registry. The evolutional analysis revealed increased rates of the GI cluster in the last 30 years

Conclusion: Clustering analysis identified a distinct GI cluster associated with atypical and severe BD clinical symptoms that are increasing in Japan.

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Abstract Number: 1091

Risk of Preterm Birth by Timing of Lupus Diagnosis Among Women in the Georgia Lupus Registry

Meghan Angley,[1] Penelope P. Howards,[1] Cristina Drenkard,[1] and S Sam Lim[1], [1]Emory University, Atlanta, GA

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Women with systemic lupus erythematosus (SLE) are at a greater risk of having a preterm birth than the general population. Most studies examine preterm births in women with SLE only after they have been diagnosed with SLE, but it has been established that both symptoms and immune abnormalities can appear years before a clinical diagnosis of SLE is made.

Methods: The Georgia Lupus Registry (GLR) is a population-based registry of individuals with SLE in 2002-2004 in Atlanta, Georgia. The GLR was matched to Georgia Birth Certificates from 1994-2013. Births were categorized by timing before and after diagnosis (≥3 years before, 0-3 years before, 0-3 years after and ≥3 years after). Risks of pre-

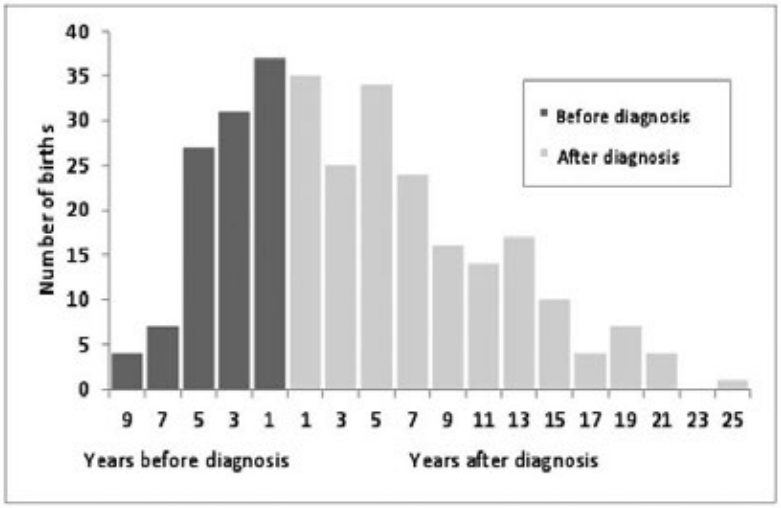

Figure 1. Distribution of births by timing of SLE diagnosis

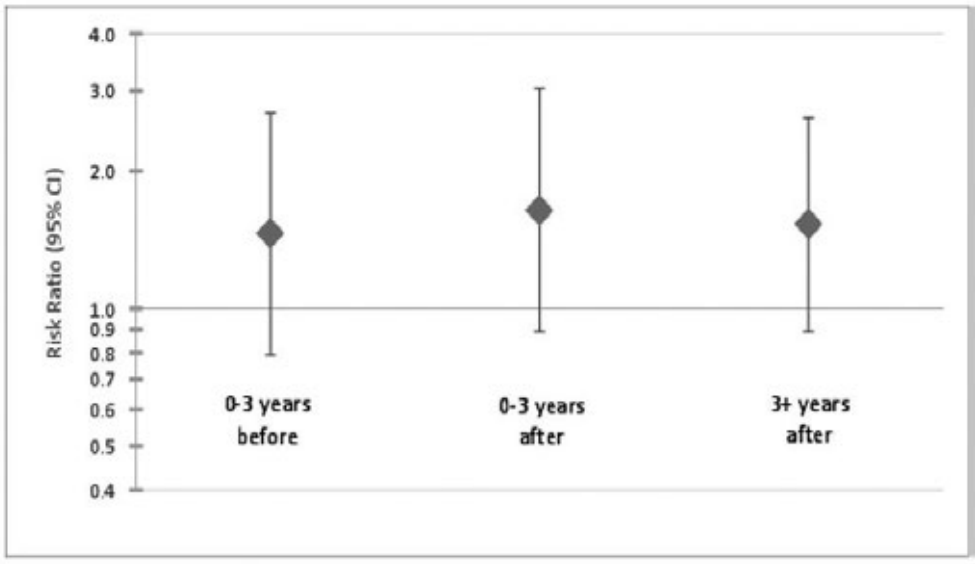

Figure 2. Adjusted risk ratio of preterm birth by timing of SLE diagnosis, compared to births occurring 3+ years before SLE diagnosis

term birth (delivery < 37 weeks of gestation) were calculated. Log-risk models with generalized estimating equations accounted for multiple deliveries in the same woman. Only singleton births were analyzed.

Results: In 189 women, 297 singleton births were identified; 80% were to African American and 18% to white women, and 125 births occurred before and 172 births occurred after diagnosis (see figure 1). For births occurring ≥3 years before, 0-3 years before, 0-3 years after and ≥3 years after, the risks of preterm birth were 19%, 29%, 34% and 33%, respectively. Compared to women who gave birth ≥3 years before, women who gave birth 0-3 years before had slightly elevated risk of preterm birth (risk ratio [RR]: 1.46, 95% confidence interval [CI]: 0.79, 2.68), as did women who gave birth 0-3 years after (RR: 1.64, 95% CI: 0.89, 3.04) and women who gave birth ≥3 years after (RR: 1.53, 95% CI: 0.89, 2.62) (see figure 2). Analyses controlled for parity, age and race.

Conclusion: The risk of preterm birth is also increased preceding SLE diagnosis, although lower than that after diagnosis. This suggests late diagnosis of SLE or that immunologic and other factors may impact birth outcomes years before clinical disease.

Disclosure: M. Angley, None; **P. Howards**, None; **C. Drenkard**, None; **S. Lim**, None.

Abstract Number: 1092

Efficacy and Safety of Dose Adjustment Based on Patients' Body Size in Low Dose Intravenous CYC Treatment for Rheumatic Diseases

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Intravenous (IV) CYC in combination with glucocorticoids is a widely used induction therapy for severe cases of rheumatic diseases such as SLE, SSc, DM and ANCA-associated vasculitis. The dosage of Euro-lupus low dose regimen (six pulses of IV CYC biweekly at a fixed dose of 500 mg), which is one of the standard regimens, does not take account of body size. The fixed dose of 500 mg is equivalent to approximately 300 mg/m^2 or less per body surface area (BSA) for average sized European patients, but it can be more than 300 mg/m^2 per BSA for patients with smaller physiques. In this study, we evaluated the efficacy and safety of dose adjustment based on patients' body size in low dose IV CYC treatment for rheumatic diseases.

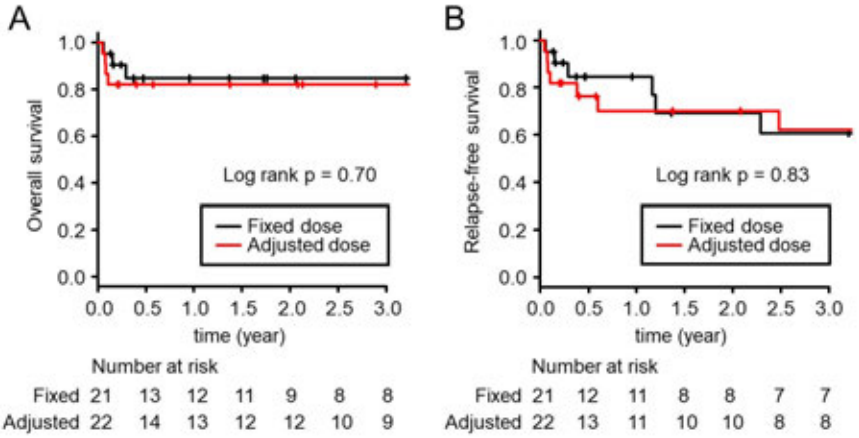
Methods: In this retrospective cohort study, we analyzed consecutive patients with rheumatic diseases, consisting of SLE, SSc, DM and ANCA-associated vasculitis, who received IV CYC therapy at the rheumatology department of the Kyoto Prefectural University of Medicine in Japan between 2008 and 2019. Patients with a creatinine clearance less than 10 mL/min were excluded. We compared clinical outcomes and adverse events in patients receiving doses above and below 300 mg/m^2 for BSA. All data were presented as median [interquartile range (IQR)] or absolute number (percentage). In comparing two groups, we used the Mann–Whitney U test (for continuous variables) or Fisher's exact test (for categorical variables). The Kaplan–Meier curves were compared using the log rank test. Any p value < .05 was considered statistically significant.

Table 1. Baseline characteristics and treatment details of patients

Factor	Adjusted dose group (n=22)	Fixed dose group (n=21)	p value
Rheumatic disease			**<0.001**
SLE	8	3	
SSc	1	2	
DM	4	15	
ANCA-associated vasculitis	9	1	
Age, years, median (IQR)	54.0 (43.5, 66.0)	61.0 (49.8, 66.8)	0.503
Sex, female, n (%)	13 (56)	13 (59)	1
Body height, cm, median (IQR)	159.8 (153.6, 167.5)	158.8 (154.3, 164.1)	0.928
Body weight, kg, median (IQR)	51.2 (46.5, 63.1)	52.8 (48.7, 54.3)	0.919
Body surface area (Du bois), median (IQR)	1.51 (1.47, 1.62)	1.52 (1.47, 1.61)	0.892
CCr			0.108
<10, n (%)	0 (0)	0 (0)	
10~50, n (%)	4 (17)	0 (0)	
50<, n (%)	18 (83)	21 (100)	
Initial prednisolone dose, mg/kg, median (IQR)	0.96 (0.83, 1.21)	0.91 (0.79, 1.05)	0.617
Glucocorticoid pulse therapy, n (%)	14 (61)	7 (32)	0.075
IV CYC dosage, mg/body, median (IQR)	300 (300, 345)	500 (500, 500)	**<0.001**
IV CYC dosage, mg/kg, median (IQR)	5.9 (5.5, 7.4)	10 (9.3, 11.2)	**<0.001**
IV CYC dosage, mg/m^2, median (IQR)	203 (195, 238)	340 (319, 355)	**<0.001**
Times of IV CYC, median (IQR)	4 (2, 6)	4.5 (2.3, 6.8)	0.714
Cumulative dose of CYC, mg, median (IQR)	1200 (810, 2100)	2500 (1413, 3695)	**0.017**

Adjusted dose group = patients who received IV CYC treatment less than 300mg/m2 for BSA (adjusted for body size).
Fixed dose group = patients who received IV CYC treatment more than 300 mg/m2 for BSA (fixed dose of 500mg).
IQR, interquartile range; CCr, creatinine clearance; IV, intravenous.

Figure 1. Kaplan-Meier curves for overall survival and relapse-free survival of patients



Results: We identified 43 patients (SLE = 11, SSc = 3, DM = 19, ANCA-associated vasculitis = 10), all of whom met the ACR classification criteria. Among them, 22 received IV CYC treatment less than 300mg/m^2 for BSA as "adjusted" low dose treatment considering body size, and 21 received more than 300mg/m^2 for BSA as "fixed" low dose treatment. There was no difference between the two groups as age, gender, height, weight and body surface area (Table 1). Although there were differences in underlying rheumatic diseases, the dosage of initial prednisolone was similar between the two groups. There was no difference in the frequency of IV CYC administration, but the median dose for IV CYC was lower in the adjusted dose group than in the fixed dose group (300 mg/body vs 500 mg/body, respectively, $p < 0.001$), and the median cumulative dose was also lower in the adjusted dose group (1200 mg vs

2500 mg, respectively, p = 0.017). Between the two groups, there was no difference in overall survival or relapse-free survival (Figure 1).

Conclusion: Our data indicates that adjusted low dose IV CYC biweekly treatment (less than 300 mg/m^2 for BSA) may have equal clinical efficacy and better safety compared to fixed low dose treatment. This dose adjustment of low dose IV CYC treatment based on patients' body size would be beneficial as an effective and safe remission induction therapy for rheumatic diseases.

Disclosure: A. Hirano, None; **T. Kida**, None; **A. Kasahara**, None; **A. Sakashita**, None; **T. Sagawa**, None; **S. Kaneshita**, None; **T. Inoue**, None; **K. Fujioka**, None; **W. Fujii**, None; **M. Wada**, None; **M. Kohno**, None; **Y. Kawahito**, Asahi Kasei, 2, Pfizer, 2, Takeda, 2.

Abstract Number: 1093

The US Prevalence of Inflammatory Bowel Disease and Associated Axial Pain: Data from the National Health & Nutrition Examination Survey (NHANES)

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Table 1 . US Diagnosed Inflammatory Bowel Disease Prevalence and Demographics

	NHANES 2009-10 (N=5,105)				NHANES II (N=13,730)		
	All IBD		Ulcerative Colitis		Ulcerative Colitis		UC Difference
	Cases	% (SE)	Cases	% (SE)	Cases	% (SE)	*p-value*
Overall Prevalence	62	1.2 (0.2)	53	1.0 (0.2)	144	1.0 (0.1)	n.s.
Age 20-49 years	23	0.9 (0.2)	18	0.7 (0.2)	39	0.7 (0.1)	n.s
Age 50-69 years	39	1.8 (0.4)	35	1.4 (0.4)	105	1.6 (0.2)	n.s.
Men	23	1.1 (0.2)	19	0.9 (0.2)	38	0.5 (0.1)	n.s.
Women	39	1.4 (0.3)	34	1.1 (0.3)	106	1.5 (0.2)	n.s
Mexican-American	17	1.6 (0.3)	15	1.4 (0.2)	ndc	ndc	ndc
Non-Hispanic-White	29	1.4 (0.2)	23	1.1 (0.3)	140	1.1 (0.1)	n.s.
Non-Hispanic Black	7	0.8*	6	0.7*	4	0.5*	*

Abbreviations: NHANES: National Health & Nutrition Examination Survey; IBD= Inflammatory Bowel Disease; UC= Ulcerative Colitis; SE=standard error; n.s.= non significant; ndc=no data collected; All IBD= Ulcerative Colitis and Crohn's Disease; UC Difference: significance value for t-test of Ulcerative Colitis prevalences NHANES 2009-10 vs. NHANES II.
Notes: Overall prevalence is for US adults ages 20-69 years; *variance estimate not reliable, SE not shown.

Background/Purpose: Associations between ulcerative colitis (UC) and Crohn's disease, known together as inflammatory bowel disease (IBD), with axial pain, inflammatory back pain (IBP) and spondyloarthritis (SpA) are well described but vary among studies. This study presents previously unreported nationally representative data from the US health surveys NHANES 2009-10 and NHANES II (1976-80) comparing axial pain rates in those with and without IBD.

Methods: NHANES 2009-10 and NHANES II questionnaires asked patients about history of clinician diagnosed UC (both) or Crohn's (NHANES 2009-10 only), gastrointestinal symptoms, medical care and IBD comorbidities. Both surveys asked questions about the timing and anatomical distribution of axial pain of at least 3 months and history of clinician-diagnosed arthritis. NHANES 2009-10 also asked questions about pain quality to estimate IBP prevalence (Calin, ESSG, Rudwaleit et al. criteria). Statistical analysis used SAS™ 9.4 using survey design variables and sample weights to produce nationally representative estimates.

Results: Data for 5105 participants in NHANES 2009-10 and 13,730 in NHANES II ages 20-69 was analyzed. Overall, IBD prevalence in NHANES 2009-10 was 1.2 % (95% CI 1.0-1.4%); UC prevalence was 1.0% (95% CI 0.8-1.2%). UC prevalence in NHANES II was 1.0% (95% CI 0.8-1.2%). In NHANES II, UC rates were higher at ages 50-69 than at ages 20-49 ($p< 0.01$), and higher among women than men ($p< 0.01$). (Table 1) In NHANES 2009-10, 69% of IBD cases (Crohn's or UC) had colonoscopy at diagnosis; 60% had recent gastrointestinal symptoms; 30% had been hospitalized in the previous year or had prior transfusions; and 21% had IBD comorbidities (uveitis, ankylosing spondylitis, colon cancer, osteoporosis).

Figure 1. illustrates NHANES 2009-2010 subjects with at least 3 months of back pain. IBD cases were more likely to have pain onset older than 45 years (40.0% vs 26.2%), rest or sleep pain (42.9% versus 27.3%), and pain on awakening (90.5% vs 58.0%).

Figure 2. reveals prevalence of axial pain in IBD patients from both surveys. Prevalence rates of axial pain for at least 3 months were non-significantly increased among IBD cases in NHANES 2009-10 (27.8% vs 19.2%), and increased among UC cases in NHANES II (22.3% vs. 7.8%; $p< 0.01$). Amor Criteria axial pain (axial pain plus pain at night or AM stiffness) was increased among UC cases in the NHANES II data (21.3% vs 7.4%, $p< 0.01$), as was clinician-diagnosed arthritis (38.5% vs 20.7%, $p< 0.01$). IBP and SpA analysis in NHANES 2009-2010 was limited due to

Figure 1. Inflammatory Back Pain Indicator Variable Frequencies in the NHANES 2009-10 Survey

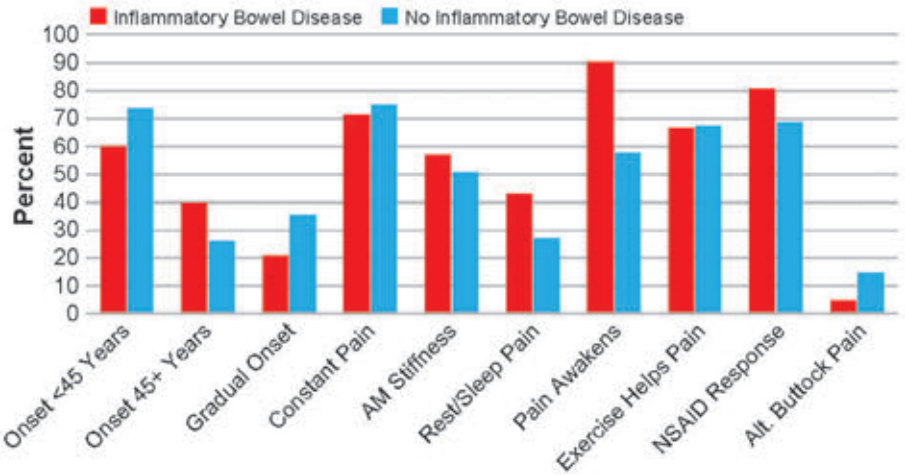
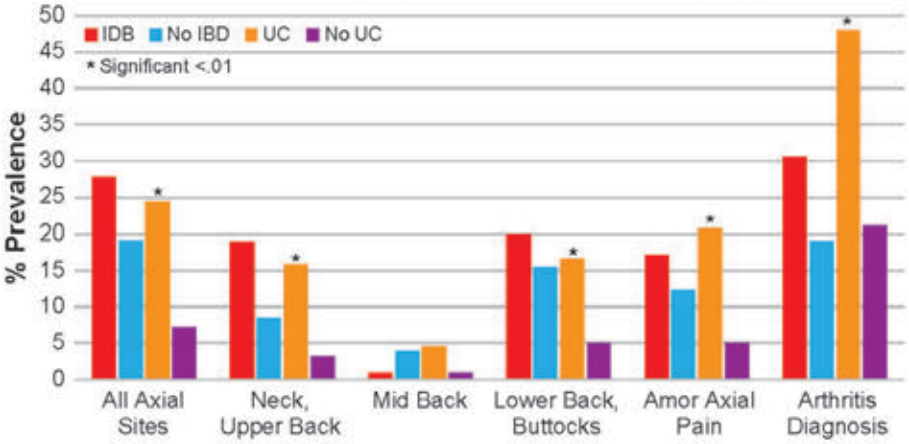


Figure 2. Prevalence of Axial Pain in Diagnosed Inflammatory Bowel Disease (IDB) & Ulcerative Colitis (UC)



Axial Pain 3 or More Months by Site & Diagnosis of Arthritis
IBD Data: NHANES 2009-10; UC Data: NHANES 1976-80

sample size so statistical testing wasn't performed, however, the unadjusted overall IBP and SpA estimates for IBD cases was 9.7% and 10% respectively, vs. 7.2% and 1.8% of controls.

Conclusion: Prevalences of UC in these two nationally representative population surveys were consistent at 1% of the general population, similar to previous surveys. This suggests stable UC prevalence and recognition rates between the 2 survey time periods. Chronic axial pain history was seen in almost 25% of IBD and UC cases and arthritis diagnosis rates were increased. IBD-axial pain was more likely to have an older age at onset and to occur with sleep or rest. Studies with larger sample sizes are required to estimate IBP and SpA rates in IBD.

Disclosure: O. Stens, None; **C. Dillon**, None; **F. Miller**, aTyr Pharma, 9, Biogen, 9, Hope Pharmaceuticals, 9, Idera Pharmaceuticals, 9, MedImmune, 9, Momenta Pharmaceuticals, 9; **M. Weisman**, AbbVie, 9, Boehringer Ingelheim, 9, Eli Lilly, 5, Lilly, 5, 9, Novartis, 5, Paul Hastings, 9, SetPoint Medical, 9, Takeda, 9, Tharpe & Howell LLP, 9, UCB, 5.

Abstract Number: 1094

EULAR Points to Consider for the Development, Evaluation and Implementation of Mobile Health Applications for Self-management in Patients with Rheumatic and Musculoskeletal Diseases

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SESSION INFORMATION

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Background/Purpose: In the expanding era of e-health, a wide range of mobile health applications (apps) have become available to enable people with rheumatic and musculoskeletal diseases (RMDs) to better self-manage their health. However, guidance on the development and evaluation of such apps is lacking. The objective of this EULAR task force was to establish points to consider (PtC) for the development, evaluation and implementation of apps for self-management of RMDs.

Methods: A systematic literature review of app content and development strategies was conducted, followed by a qualitative study with six patients and an online survey of people living with RMDs (n=394). Based on these data and expert opinion, the PtC were formulated in a face-to-face meeting in November 2018 by a multidisciplinary TF panel of experts, including patients, from 10 countries. The level of agreement among the panel in regard to each PtC was established by anonymous online voting.

Results: Three overarching principles and 10 PtC were formulated (Table). Out of the 10 PtC, three were related to patient safety (1,5,6), considered as a critical issue by the panel, along with accuracy of information provided by apps. Three were related to relevance of the content and functionalities (2,7,9) and the importance of apps being tailored to the individual needs of people with RMDs. The requirement for transparency around app developers and funding sources (3,4), along with involvement of relevant health professionals were also raised. Ease of app access across ages and abilities was highlighted (8), in addition to considering the cost-benefit of apps from the outset (10). The level of agreement was high (Table).

Table. The 10 Points to Consider.

	Points to consider	Level of agreement mean (SD)
1.	The information content in self-management Apps should be up to date, scientifically justifiable, user-acceptable and evidence-based where applicable.	9.8 (0.4)
2.	Apps should be relevant and tailored to the individual needs of people with RMDs.	9.7 (0.5)
3.	The design, development and validation of a self-management App should involve people with RMDs and relevant health care providers.	9.8 (0.6)
4.	There should be transparency on an Apps' developer, funding source, content validation process, version updates and data ownership.	9.9 (0.3)
5.	Data collection as part of an App must adhere to all applicable regulatory frameworks, particularly data protection.	9.9 (0.3)
6.	Apps must not result in physical or emotional harm to people with RMDs.	9.3 (1)
7.	Apps could facilitate patient-health care provider communication and contribute to electronic health records or research.	9.4 (0.9)
8.	App design should consider accessibility of people with RMDs across ages and abilities.	9.4 (0.9)
9.	If a social network is an important component of an App, structures should be in place to ensure appropriate content moderation.	9.5 (0.6)
10.	The rheumatology community should consider the cost-benefit balance of Apps before its endorsement and/or its promotion.	8.9 (1.3)

Conclusion: These PtC provide guidance on important aspects that should be considered for the development of new apps, the quality assessment of existing apps, as well as for further development of existing apps.As part of the dissemination phase, these PtC will be shared with a larger group of health professionals, patients and app developers and for wider consensus.

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Abstract Number: 1095

The Role of Immunosuppressive Therapy in the Development of Atherosclerotic Cardiovascular Disease in Patients with Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
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Background/Purpose: There is accumulating evidence demonstrating an increased prevalence of atherosclerotic cardiovascular disease (ASCVD) among the psoriatic arthritis (PsA) population. Yet, the relationship between immunosuppressive therapies and the development of ASCVD remains unclear. This study was undertaken to investigate the ASCVD risk among PsA patients and its relationship with systemic immunosuppressive therapies, including tumor necrosis factor alpha (TNF-α) inhibitors and methotrexate (MTX).

Methods: A multicenter retrospective cohort study involving the Veterans Affairs Hospitals in Long Beach (LBVA) and Greater Los Angeles (GLAVA) was performed. PsA patients from both sites (n=189) were evaluated against controls (n=99) without autoimmune diseases. The groups were matched on age, sex, race, BMI, smoking exposure, and ASCVD risk factors (hypertension, diabetes, and hyperlipidemia). Their ASCVD risk was evaluated using the American College of Cardiology/American Heart Association's (ACC/AHA) ASCVD risk score. The odds ratio (OR) for developing any ASCVD event, myocardial infarctions (MI), congestive heart failure (CHF), and cerebral vascular accidents (CVA) were calculated. Additionally, the OR for CHF in the PsA patients was analyzed in relation to their exposure to TNF-α inhibitors, MTX, and concomitant use of TNF-α inhibitors with MTX, with exposure defined as use of therapy ≥ 12 months.

Results: PsA and controls ACC/AHA ASCVD risk scores of 21.5% and 17.1% (p=0.005). PsA patients twice the risk for developing any ASCVD event (OR 1.9; 95% CI 1.10 to 3.35). CHF (OR 3.4; 95% CI 1.27 to 9.1) was the most likely event to develop when compared to CVA (OR 1.33; 95% CI 0.50 to 3.55) and MI (OR 1.28; 95% CI 0.69 to 2.23). The risk of developing CHF is increased in PsA patients exposed to MTX (OR 4.7; 95% CI 1.24 to 17.77) relative to TNF-α inhibitors (OR 3.42; 95% CI 1.00 to 11.05). Meanwhile, PsA patients exposed to concomitant TNF-α inhibitors with MTX had decreased risk for developing CHF (OR 1.91; 95% CI 1.26 to 12.10) when compared to the overall PsA cohort in this study, and the subgroups of PsA patients exposed to either TNF-α inhibitors or MTX alone.

Conclusion: PsA patients have an increased risk for developing ASCVD, in particular CHF. Exposure to either MTX or TNF-α inhibitor individually does not confer a protective role against CHF. However, combining the use of MTX with TNF-α inhibitor therapy decreases the risk of developing CHF relative to the overall PsA cohort and those receiving monotherapy with MTX or TNF-α inhibitor therapy alone. This suggests that the two therapies work together to attenuate adverse myocardial remodeling and offer a beneficial role against the development of CHF in PsA patients.

Disclosure: L. Truong, None; **N. Ridolfi**, None; **E. Chen**, None; **M. wong**, None.

Abstract Number: 1096

Learning the Relationships Between Psoriatic Arthritis and a Patient's History of Musculoskeletal Symptoms from Electronic Health Records Using Bayesian Networks

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SESSION INFORMATION
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Background/Purpose: Electronic health records (EHRs) from large health care systems provide access to rich and comprehensive patient-specific information from many sources consisting of heterogeneous data types. The unique

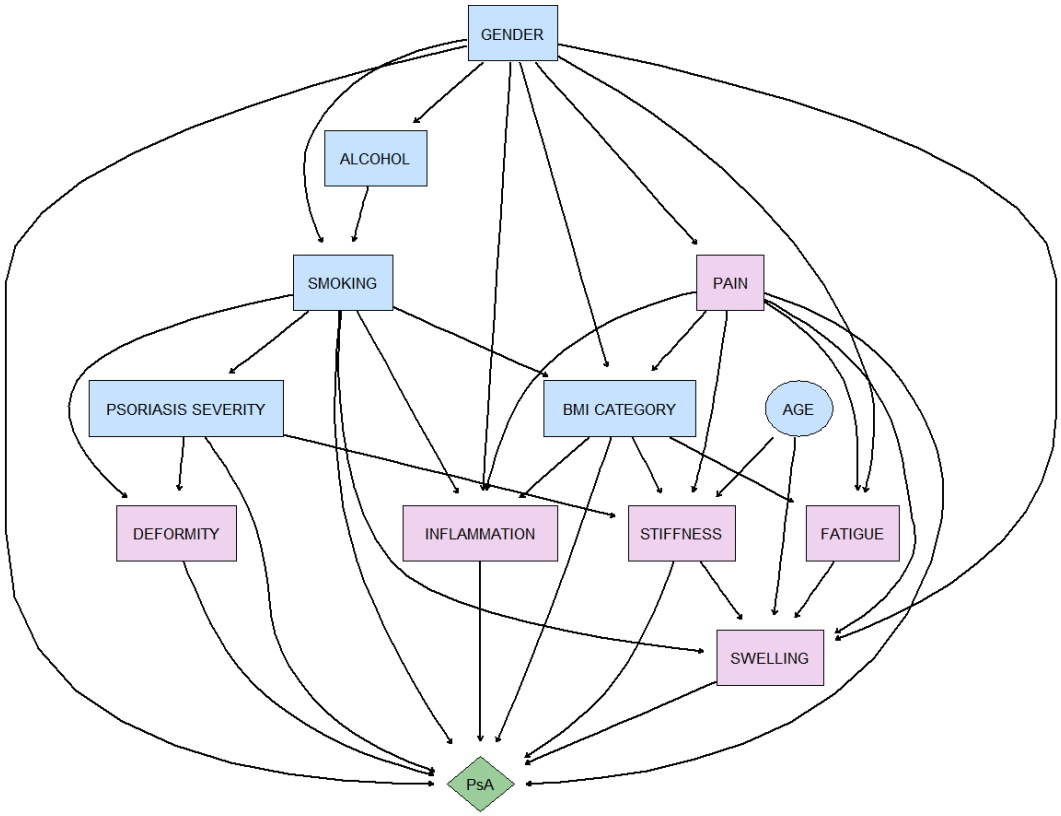

Figure. Graphical model of a Bayesian network built using EHR data to predict the development of PsA in people with psoriasis and to gain insight into the psoriasis population at increased risk of PsA. The figure includes the structure of MSK symptoms (coloured purple), grouped into one of six categories and defined in terms of counts over the study period, in addition to baseline demographic variables (coloured blue). In particular, nodes represent input variables and edges represent conditional dependencies between the variables. Continuous and discrete variables are indicated by elliptical and rectangular nodes, respectively. Nodes are defined as follows: GENDER sex of the patient (male or female); ALCOHOL baseline drinking status of the patient (non-drinker, ex-drinker or current drinker); SMOKING baseline smoking status of the patient (non-smoker, ex-smoker or current smoker); PSORIASIS SEVERITY severity of psoriasis (mild or severe); BMI baseline body mass index of patient; AGE baseline age of the patient (years); PAIN MSK symptoms associated with pain (143 medcodes); DEFORMITY MSK symptoms associated with a deformity or derangement (6 medcodes); INFLAMMATION MSK symptoms associated with inflammation (96 medcodes); STIFFNESS MSK symptoms associated with stiffness (64 medcodes); FATIGUE MSK symptoms associated with fatigue (34 medcodes); SWELLING MSK symptoms associated with swelling (36 medcodes).

features and challenges of EHR data, including missing information and non-linear interactions, require novel statistical approaches for analyses. Bayesian Networks (BNs) provide a relatively new method of representing uncertain relationships among variables and here we explore their ability to learn the structure of MSK symptoms related to the development of PsA in people with psoriasis.

Methods: Incident cases of psoriasis were identified between 1998 and 2015 from the UK Clinical Research Practice Datalink (CPRD). MSK symptoms occurring during the study period were identified based on medcodes and were checked by a physician to eliminate redundant MSK symptoms. Baseline demographics for gender, age, body mass index (BMI), psoriasis severity, alcohol use and smoking status were also extracted. The BN structure was composed using a combination of expert knowledge and data-oriented modeling with several methods compared to obtain a BN structure which best described the relationships between the variables. Bayesian inference was used to compute the posterior distribution of network weights, which quantify the strength of these relationships. The BN model was evaluated using well-established performance metrics.

Results: Over one million MSK symptoms were extracted for the 90,189 incident cases of psoriasis identified, of which 1409 developed PsA. These consisted of 379 unique medcodes which were concatenated into one of six categories (pain, deformity, inflammation, stiffness, swelling or fatigue). The graphical representation of the BN structure in Figure 1 shows widespread probabilistic associations between the 12 variables included in the modelling. Nine were identified as direct predecessors of PsA. While the remaining three variables did not influence the PsA directly, they did influence PsA through their respective child nodes. For example, age and fatigue influence PsA through their common child node, swelling. Our BN was 81% accurate in predicting the development of PsA in a validation set. The AUC for this predictive model was 0.85 (95% confidence interval (CI): 0.83-0.87), translating into 81% sensitivity and 89% specificity.

Conclusion: The presented BN model considers the demographics and MSK symptoms of people with psoriasis and can be used as a useful method to predict the development of PsA with reasonable accuracy. It provides useful information to clinicians, such as the probabilistic relations among variables of interests that associate with individuals at increased risk of developing PsA. In addition to offering both modelling flexibility and statistical validity, our technique seamlessly handles missing data and offers the opportunity to combine findings from the medical literature with clinical judgement to shape the model. Important improvements and future developments to the BN model would a) broaden the MSK symptom categories and b) extend the variable set by including addition EHR data such as tests, prescriptions and referrals.

Disclosure: A. Green, None; **T. Smith**, None; **N. McHugh**, None.

Abstract Number: 1097

Trends in NSAIDs and Opioids Among Patients with SLE: A Population-based Study

Lingyi Li,[1] Na Lu,[1] Jacek Kopec,[2] John Esdaile,[3] Hui Xie,[4] and J. Antonio Avina-Zubieta[2], [1]Arthritis Research Canada, Vancouver, BC, Canada, [2]Arthritis Research Canada and the University of British Columbia, Vancouver, BC, Canada, [3]Arthritis Research Canada and the University of British Columbia, Richmond, BC, Canada, [4]Arthritis Research Canada and Simon Fraser University, Vancouver, BC, Canada

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

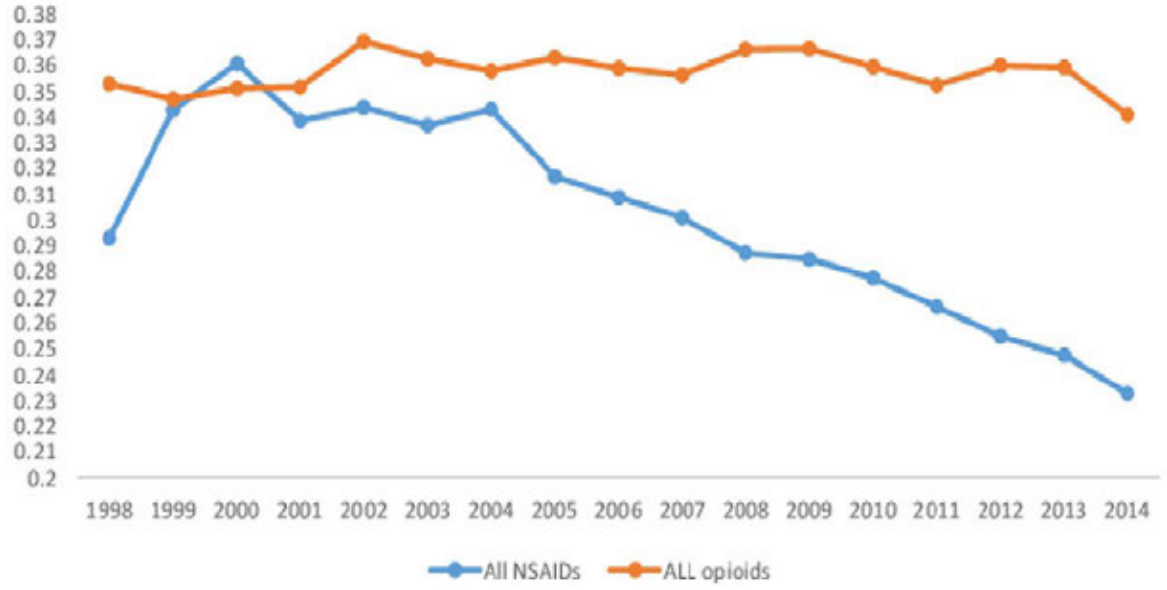

Figure 1. Trends of prescriptions for NSAIDs and opioids among patients with prevalent SLE in an entire province of Canada, 1998-2014

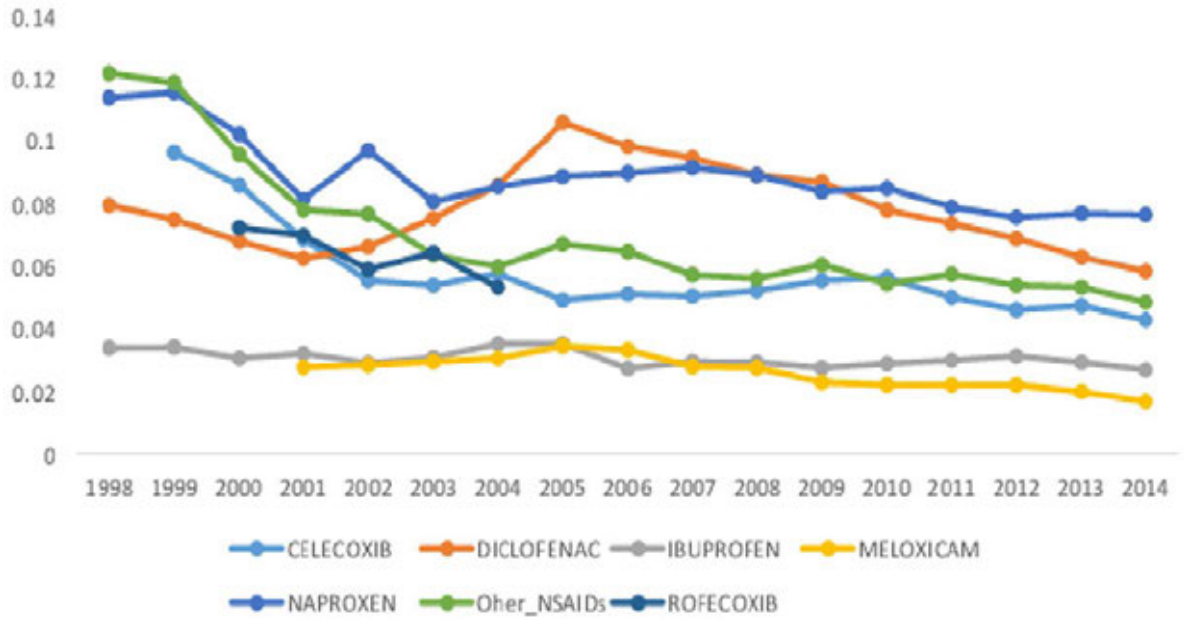

Figure 2. Prescriptions for NSAIDs in patients with prevalent SLE in an entire province of Canada, 1998-2014

Background/Purpose: Non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are prescribed for the management of pain among patients with rheumatic diseases including systemic lupus erythematosus (SLE). However, both types of medication can be associated with serious side effects. For example, increased mortality has been reported among people who use opioids. Our purpose in this study was to describe the trends in prescribing of NSAIDs (including coxibs) and opioids among patients with SLE in the general population.

Methods: We use a population-based administrative database that included all prescriptions for persons aged 20+ processed by pharmacies in the entire province, between 1998 and 2014, linked to diagnostic codes for visits to phy-

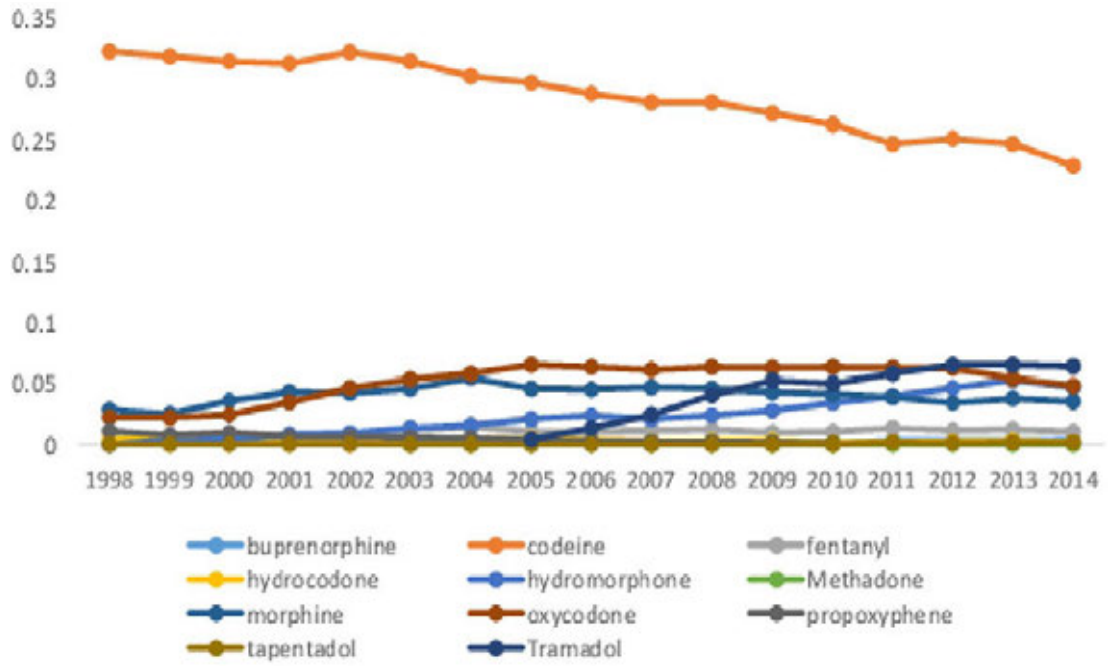

Figure 3. Prescriptions for opioids in patients with prevalent SLE in an entire province of Canada, 1998-2014

sicians and hospitalizations. We identified all prevalent cases of SLE, defined as at least 2 codes at least 2 months apart within 2 years. We identified all prevalent prescriptions for each NSAID and opioid available in the province and calculated the proportion of people receiving NSAID or opioid medication.

Results: Between 1998 and 2014, the proportion of SLE patients with an NSAID prescription declined from 29.2% to 23.2% (Figure 1). For most NSAIDs (Figure 2), prescriptions declined aggressively as of 2004 and were relatively stable until 2014, with the exception of diclofenac, which increased substantially from 2001 to 2005 and decreased afterwards. In 2014, the most common NSAID was naproxen (7.7%) followed by diclofenac (5.8%), celecoxib (4.3%), ibuprofen (2.7%) and meloxicam (1.7%). For opioids (Figure 1), the overall trend was relatively flat from 1998 to 2014, with 35.3% in 1998 to 34.1% in 2014. Codeine was by far the most commonly prescribed opioid throughout the study period, but declined from 32.2% of prevalent SLE patients in 1998 to 22.8% in 2014 (Figure 3). Tramadol increased steadily from its introduction in 2005 and has been the second most common opioid since 2012, reaching 6.4% in 2014. Prescriptions for oxycodone started to decline around 2011 and reached 4.8% in 2014, whereas those for hydromorphone steadily increased (4.7% in 2014). Morphine increased slightly from 1998, reaching 5.5% in 2004, then declined thereafter. Other opioids were rarely prescribed in patients with SLE.

Conclusion: There have been important changes in the pattern of prescribing analgesics in our province during the study period. Declines in NSAIDs may have been compensated by increased prescriptions for some opioids. This is likely to change as new guidelines discourage the long-term use of opioids as a consequence of the current opioid crisis.

Disclosure: L. Li, None; **N. Lu**, None; **J. Kopec**, None; **J. Esdaile**, None; **H. Xie**, None; **J. Avina-Zubieta**, None.

Abstract Number: 1098

Epidemiology and Mortality of SLE (Systemic Lupus Erythematosus) in Hungary Based on a Nationwide Retrospective Claims Database Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

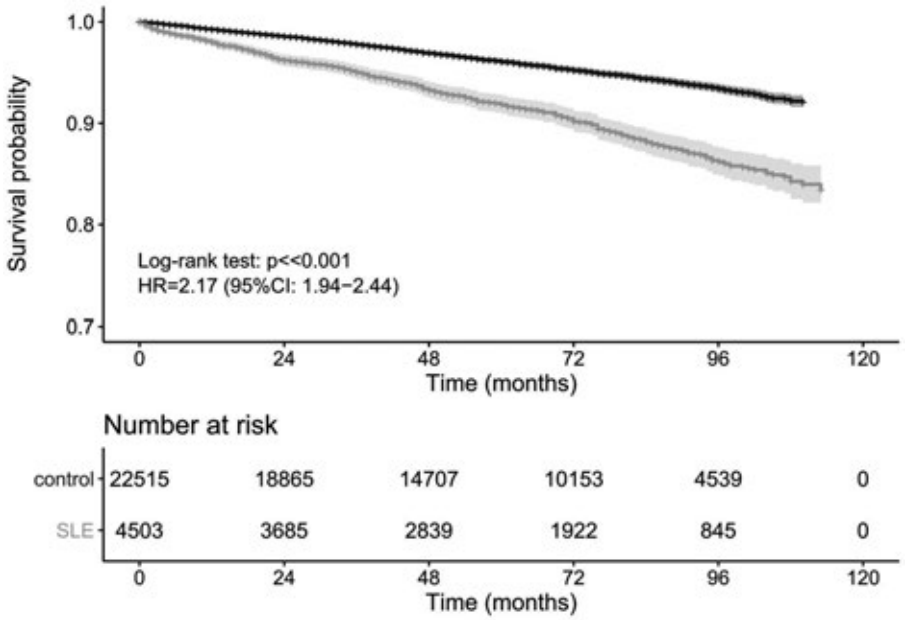
Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: There is little evidence in Hungary on the real incidence, prevalence and mortality of systemic lupus erythematosus (SLE) that is based on a robust estimate from real world data. Claims data-based evidence on the SMR of SLE patients from other countries shows great variance.

Objectives: The aims of this study were to provide robust estimates on the incidence, prevalence and population-controlled mortality of patients with SLE in Hungary.

Methods: Study design and description of data source: This was a non-interventional, retrospective study based on historical real-world data from the database of the National Health Insurance Fund of Hungary (NHIF). This database provides detailed data on the inpatient and outpatient care and prescription purchases of SLE patients covering the full population of Hungary. The analysis will be limited to data collected between 1st January 2008 and 30th June 2017.



Kaplan-Meier estimation of overall survival of SLE patients and matched controls in Group A, comparison using log-rank test

Methods: Patients with minimum 2 SLE ICD codes were included from the database (prevalent patients). Two study groups were created. A wider one consisting of all incident SLE patients (group A) and a subgroup that only contains those who received some form of relevant therapy in the first 6 months from diagnosis (group B).

Baseline demographic characteristics and mortality were described. Mortality was analysed using standardized mortality ratio (SMR) compared to the general population of Hungary. The overall survival (OS) from SLE diagnosis date was estimated using the Kaplan-Meier method and was compared to the survival of a matched sample of the general population using a log-rank test.

Results: In total 7.888 prevalent patients were identified in the database. In group A 4.503 patients were included, 2.582 patients were in group B. Women had an overwhelming majority in both groups (85%). Median age of patients at the time of diagnosis were 46 and 47 years in group A and group B respectively. In group A the yearly incidence decreased from 624 patients in 2008 to 373 patients in 2016, whereas the incidence in group B was more stable, varying between 224 and 336 patients during the same period. In total 12% and 10% of patients had died in the study period in group A and group B respectively. SMR was 1,63 (95% CI 1,43 - 1,83) and 2,09 (95% CI 1,80 - 2,39) in group A and B respectively. Overall survival was significantly worse ($p< < 0,001$) in both groups compared to the general population, HR=2,17 (95% CI 1,94 - 2,44) in group A and HR=2,75 (95% CI 2,38 - 3,17) in group B.

Discussion: Definition of SLE prevalence and incidence are in line with literature for other claims data studies. Results on SLE prevalence and incidence are also similar to the published data. There is a significant excess mortality due to SLE; the level of excess mortality is underestimated.

Conclusion: This full-populational database study showed that despite that a wide range of therapeutic option are available for patients suffering for SLE, the mortality and survival compared to the general population is significantly worse for these patients. Therefore, new innovative therapies are needed to improve these aspects of SLE.

Disclosure: M. Kedves, None; **F. Kósa**, Janssen, 3; **P. Takács**, Janssen, 3, 4; **P. Kunovszki**, Janssen, 3; **J. Lofland**, Janssen Scientific Affairs, LLC, 3; **G. Nagy**, None.

Abstract Number: 1099

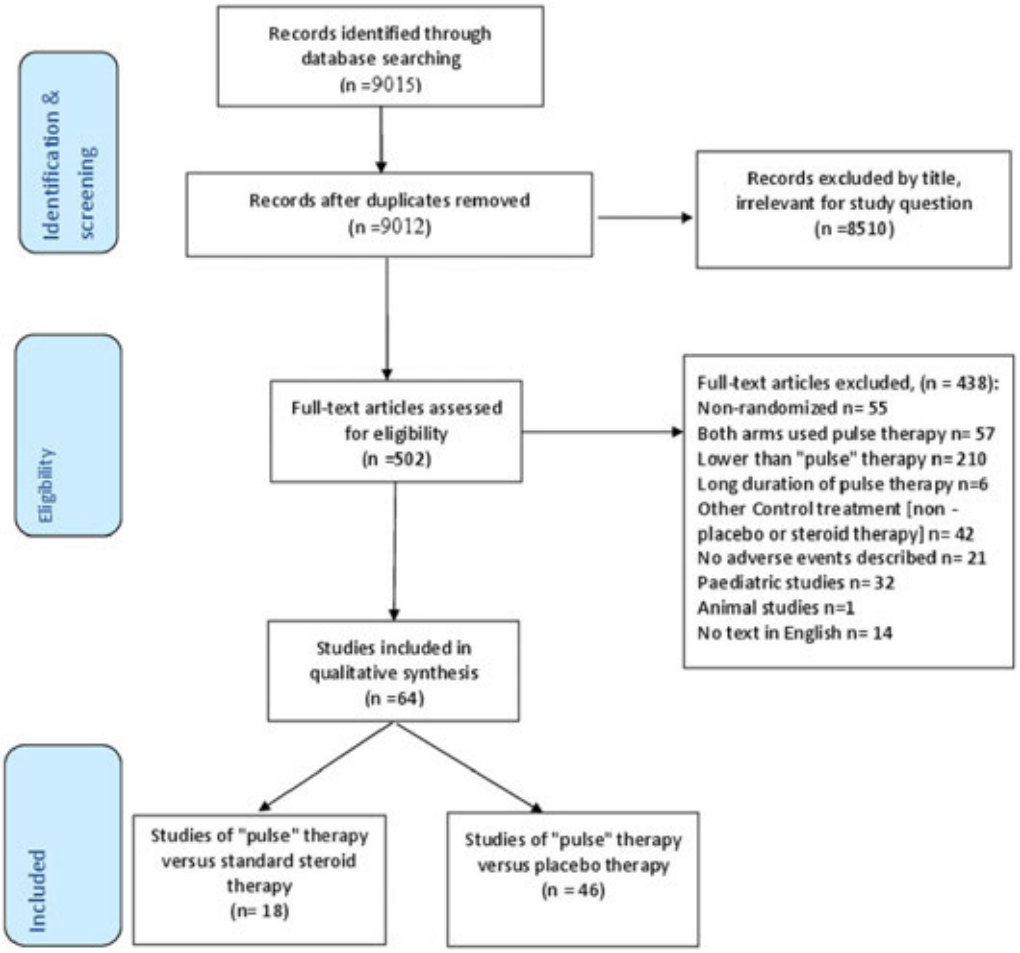
The Safety of Pulse Therapy- Systematic Review and Meta-analysis

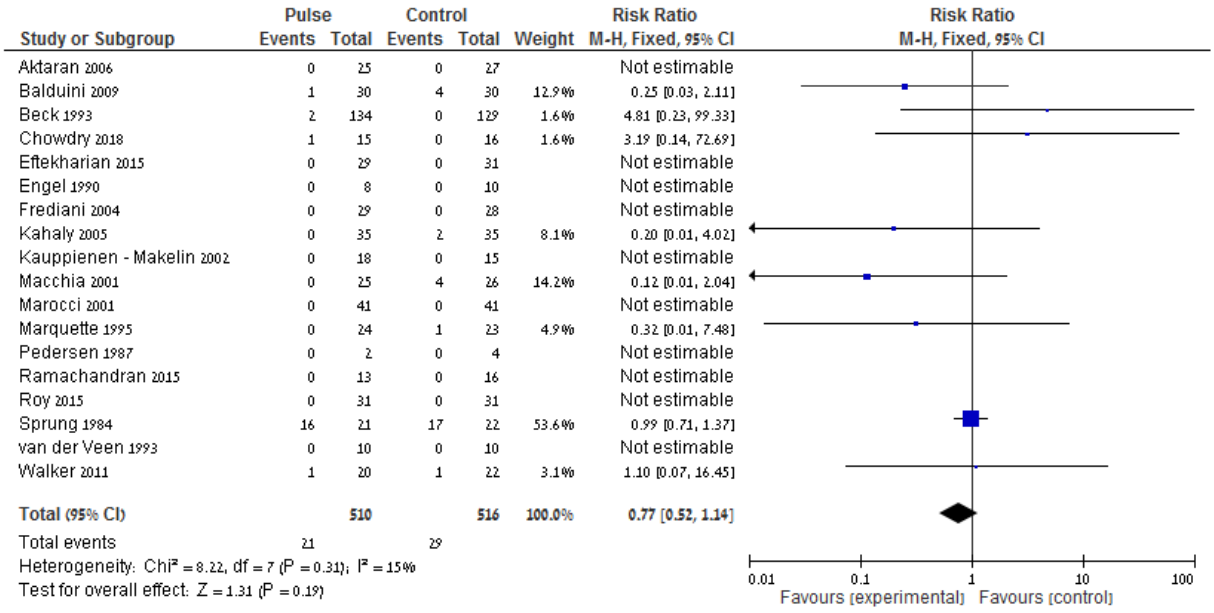
Yonatan Edel,[1] Tomer Avni,[1] Yair Molad,[2] daniel Shepshelovich,[1] Shelley Reich,[1] Benaya Rozen-zvi,[1] Michal elbaz,[3] leonard leibovici,[3] and Anat Gafter-Gvili[1], [1]Rabin Medical Center, petach tikva, HaMerkaz, Israel, [2]Rabin Medical Center, Beilinson Hospital, and Tel Aviv University, Petach Tikva, HaMerkaz, Israel, [3]rabin Medical Center, petach tikva, Israel

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

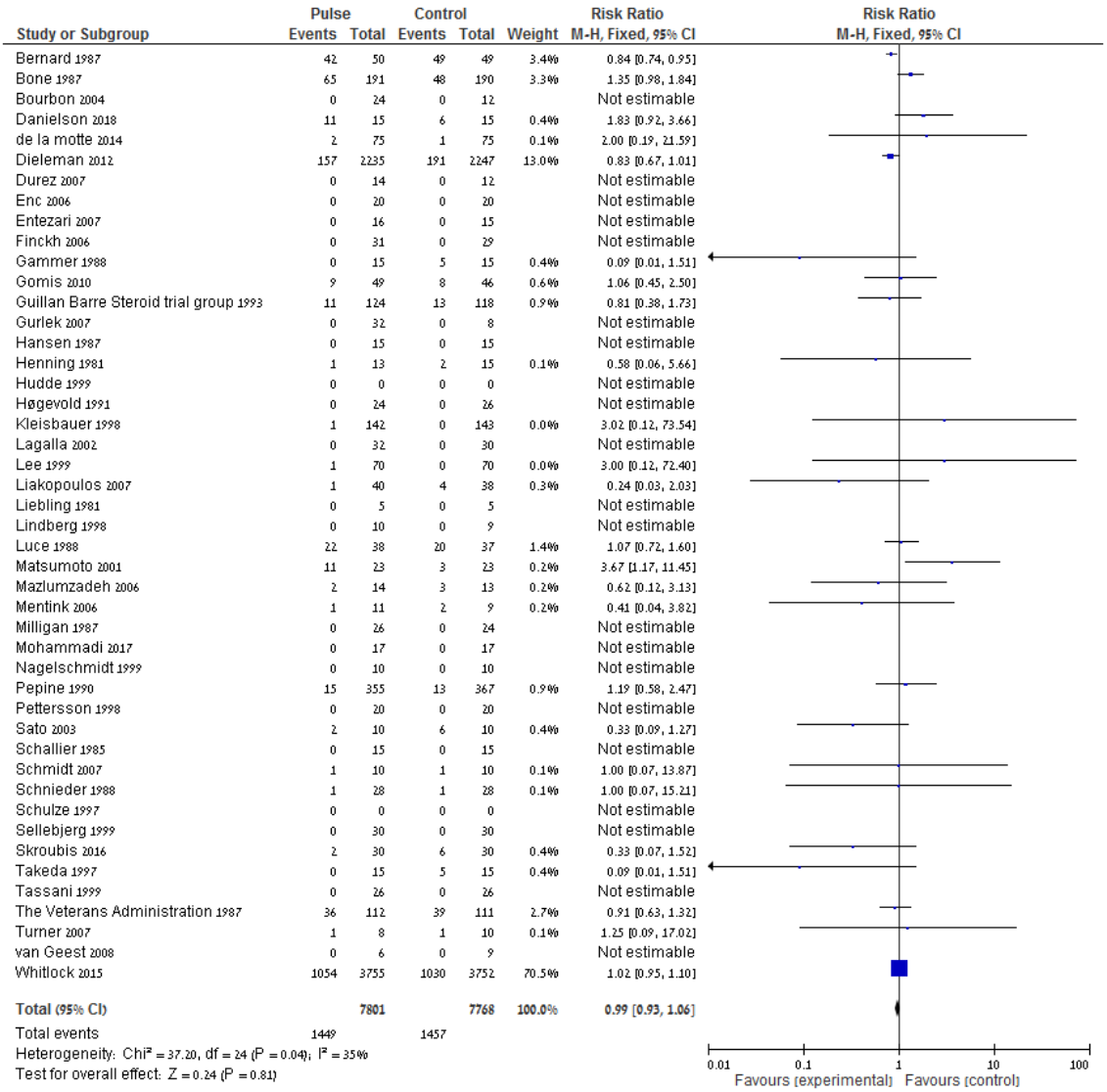
Background/Purpose: Very high dose (or pulse) glucocorticoid treatment is widely used for autoimmune, inflammatory, infectious and other conditions. We aimed to amass all available evidence from randomized controlled trials regarding the safety of pulse steroids therapy, in order to establish its safety

Figure 1: PRISMA study flow chart





Primary outcome: SAEs, pulse steroids vs. oral therapy



Primary outcome: SAEs, pulse steroids vs. placebo / no therapy.

Methods: Systematic review and meta-analysis of all randomized controlled trials comparing pulse steroids to oral steroids or to placebo/no treatment. All electronic databases up to 12/2018 were reviewed. Risk ratios (RR) with 95% (CI) for differences between pulse steroids and comparator were pooled (when RR < 1 denotes less risk with pulse steroids) using a fixed effect meta-analysis. The primary outcome was occurrence of severe adverse events (SAEs). Secondary outcomes included any adverse events (AEs), AEs requiring discontinuation, AEs per system involved and all-cause mortality. Sensitivity analysis was based on the methodology, design, and follow up time. Subgroup analysis was based on comparator, dosage of pulse steroids, treated condition and system involved

Results: A total of 64 trials were included: 18 trials which compared pulse steroids to oral steroids and 46 trials which compared pulse steroids to placebo / no intervention. Pulse steroids was not associated with increased risk for SAEs for both comparators: RR 0.77 (95% CI 0.52-1.14), and RR 0.99 (95% CI 0.93-1.06), respectively. Sensitivity analysis based on adequate allocation concealment and use of a valid AE grading did not alter the results. Subgroup analysis revealed no increased risk of specific SAEs or AEs with pulse steroids compared to oral steroids

Conclusion: Pulse steroids was not associated with an increase risk of SAEs and should be regarded as safe

Disclosure: Y. Edel, None; **T. Avni**, None; **Y. Molad**, None; **d. Shepshelovich**, None; **s. Reich**, None; **B. Rozen-zvi**, None; **M. elbaz**, None; **I. leibovici**, None; **A. Gafter-Gvili**, None.

Abstract Number: 1100

Opioid Overdose Hospitalizations in Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis

Christine Anastasiou,[1] Jing Li,[1] Laura Trupin,[2] Gabriela Schmajuk,[3] and Jinoos Yazdany[1], [1]UCSF Division of Rheumatology, San Francisco, CA, [2]University of California, San Francisco, San Francisco, CA, [3]UCSF, SFVAMC Division of Rheumatology, San Francisco, CA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Individuals with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) often suffer from both acute and chronic pain, and the prevalence of opioid medication use among persons with RA has been estimated at 16%[1]. Because of the risk of overdose among opioid users, we sought to investigate opioid overdose-related hospitalizations among patients with SLE and RA in comparison to the rest of the population.

Methods: We used the National Inpatient Sample (NIS), which after weighting provides annual estimates for more than 35 million hospitalizations in the US. Analysis was limited to individuals without missing relevant variables hospitalized in 2016. Admissions with opioid overdose were identified based on these ICD-10-CM codes: T40.0-40.4, T40.6, X42.x, X62.x or Y12.x, which could be included as the primary reason for admission or one of up to 30 causes. SLE and RA were also captured in ICD-10-CM codes (M32.1x, M32.8, M32.9 and M05.x, M06.0x, M06.2x, M06.8x, M06.9, M08.x respectively); patients with codes for both conditions were classified as SLE. We compared the proportion of opioid overdose admissions among patients with SLE, RA, and neither condition using chi-squared tests. We used Poisson regression to model admissions due to opioid overdose as a function of disease (SLE, RA, or neither), controlling for demographics (age, sex, race) and socioeconomic status (SES) characteristics (health insurance and residence in a low-income ZIP code). All analyses accounted for the complex sampling design of the NIS.

Results: Among 33,207,455 hospitalizations in 2016 included in the analysis, 512,740 (1.5%) were of patients with RA and 147,480 (0.44%) with SLE. A higher proportion of hospitalizations were due to opioid overdose as a primary cause among patients with RA (0.23%) or SLE (0.34%), in comparison to patients with neither condition (0.17%; $p < 0.01$). Including all diagnoses of opioid overdose increased the proportions to 1.46% for patients with RA, 1.50% for SLE, and 0.85% for those with neither condition, and the differences were still significant ($p < 0.01$). After accounting

Table. Opioid overdose admissions among patients with RA or SLE compared to admissions among those with neither condition, adjusted for demographics and SES characteristics.* National Inpatient Survey 2016.

	Opioid overdose as primary diagnosis	Opioid overdose as any diagnosis
Disease group	Adjusted relative risk (95% CI)	Adjusted relative risk (95% CI)
SLE	2.44 (1.99, 2.98)	1.83 (1.67, 2.01)
RA	1.47 (1.30, 1.67)	1.44 (1.37, 1.52)
Neither condition	Ref	Ref

*Results from Poisson regression model, adjusting for age, sex, race, residence in a low-income ZIP code, and health insurance.

for demographic and SES characteristics of the hospitalized patients, both RA and SLE were associated with higher relative risks of opioid overdose hospitalizations compared to patients with neither condition, either as a primary diagnosis or any diagnosis. SLE was associated with a higher relative risk of opioid overdose hospitalization compared to RA (Table).

Conclusion: RA and SLE were associated with a 1.5 to 2-fold higher risk of opioid overdose hospitalization compared to the general population. Local and national overdose intervention programs should consider targeting RA and SLE individuals as at potentially increased risk for opioid overdose.

Reference:

1. Lee YC, Kremer J, Guan H, Greenberg J, Solomon DH. Chronic Opioid Use in Rheumatoid Arthritis: Prevalence and Predictors. *Arthritis Rheumatol*. 2019 May;71(5):670-677.

Disclosure: C. Anastasiou, None; **J. Li**, None; **L. Trupin**, None; **G. Schmajuk**, None; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2.

Abstract Number: 1101

Development of an Algorithm to Identify Sjögren's Syndrome Patients in the French National Healthcare Claims Database

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjogren's syndrome (SS) is a chronic autoimmune disease, consisting of primary SS (pSS) when it presents alone and secondary or associated SS when accompanied by other connective tissue diseases. Prevalence of primary SS ranges between 10 and 90 cases per 100,000 people in Europe. However, there is a lack of efficient algorithm that can be used in claim-based database to identify SS patients. Our objective was to establish an algorithm that can be used to identify SS patients by using a sub-sample of the French healthcare database claim.

Methods: Potential SS cases were identified based on ICD-10 codes (M35.0) when used for SS-related hospitalization or chronic disease status allowing full expenditure reimbursement codage, from 2005 to 2016. Reimbursements of at least one drug of interest, number of specialist prescriptions, reimbursement of Schirmer's test, procedures on salivary gland and research of antinuclear antibody were identified as variables of interest to build an algorithm. Patients having at least exclusion criteria of pSS ACR-EULAR classification criteria were excluded. Patients with associated code of rheumatoid arthritis, juvenile arthritis, ankylosing spondylitis, systemic lupus erythematosus, systemic sclerosis and other overlap syndromes, based on ICD-10 codes or biological therapy reimbursements, were classified as secondary SS. The onset of the disease was identified as the first occurrence of ICD-10 M35.0. A cross-validation was performed by using a logistic regression to estimate the accuracy of 15 different "diagnosis" algorithms.

Results: Among the 447 potential SS patients identified, 44 were excluded, 267 patients were classified as pSS and as 136 secondary SS. The most efficient algorithm to identify pSS (with an accuracy of 0.94) was: ICD code of SS + at least 2 prescriptions of at least one of the drugs of interest in 4 years before, or the 4 years after the first occurrence of the ICD code of SS. For secondary SS, the best algorithm (with an accuracy of 0.89) was: ICD code of SS + at least 2 prescriptions by a rheumatologist or an internal medicine physician both before and after the first occurrence of the ICD code of SS. With these algorithms, estimated prevalences were 29.5 per 100,000 for pSS and 8.30 per 100,000 for secondary SS in 2016.

Conclusion: Using a sub-sample of the French healthcare claims database, we developed, two algorithms to efficiently identify primary and secondary SS patients. Further analysis is planned to estimate at national-level prevalence and incidence of SS in France and analyze healthcare consumption. In addition, these algorithms can potentially be adapted for claims data in other countries.

Disclosure: V. Devauchelle Pensec, Bristol_myers Squibb, 2, CHUGAI, 2, Chugai Pharma France, 8, Roche, 2; **L. Chiche**, None; **J. Zhuo**, Bristol-Myers Squibb, 1, 3; **I. Lavrard**, Bristol-Myers Squibb, 1, Bristol-Myers Squibb, 3; **G. Desjeux**, E-health Services Sanoïa, 3; **R. Seror**, Bristol-Myers Squibb, 5, GlaxoSmithKline, 5, UCB, 5, Lilly, 5, Pfizer, 5.

Abstract Number: 1102

Estimate of Prevalence of Secondary Distal Renal Tubular Acidosis Among Patients with Sjogren's Syndrome and Systemic Lupus Erythematosus in a US Population with Employer-Sponsored Health Insurance

Gary Bryant,[1] Linda Law,[2] and Josephine Li-McLeod[3], [1]University of Minnesota Medical School, Minneapolis, MN, [2]Advicenne, Cincinnati, OH, [3]Stratevi, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Distal renal tubular acidosis (dRTA) involves impairment in the distal tubule, leading to insufficient renal acid secretion, which can result in metabolic acidosis, hypokalemia, nephrolithiasis, nephrocalcinosis and bone demineralization. While primary dRTA is caused by genetic factors, and additionally associated with poor growth and deafness, secondary dRTA may result from autoimmune disorders, such as Sjögren's syndrome or systemic lupus erythematosus (SLE), which also attack the distal tubule. Some medications are also associated with secondary dRTA. While secondary dRTA is a rare disease, US prevalence may be under-reported. This analysis utilizes administrative claims data to estimate the prevalence of secondary dRTA among patients with Sjogren's syndrome or SLE in a US employer-sponsored insurance (ESI) population.

Methods: Utilizing the Truven MarketScan® Commercial and Medicare Supplemental Databases from Jan 1, 2016–Dec 31, 2016, secondary dRTA patients were identified using the following criteria: at least 1 inpatient or ≥2 outpatient claims ≥30 days apart for Sjögren's syndrome (ICD-10-CM: M35.0x) or SLE (ICD-10-CM: M32.xx) or acidosis (ICD-10-CM: E87.2). To further delineate the sample, patients were also required either to have a claim for an alkalinizing agent or have a diagnosis of other disorders resulting from impaired renal tubular function (ICD-10-CM: N25.89). MarketScan Commercial Insurance Weights were then applied to project the sample to the total US ESI population.

Results: A total of 100,680 patients with ICD-10-CM diagnosis code of Sjögren's syndrome, SLE, or Acidosis were identified in the 2016 Marketscan database. Of these, 1,125 were prescribed an alkalinizing agent or had a diagnosis code of impaired renal tubular function. Applying the insurance weights to the 1,125 identified sample, this projected to an estimated 6,716 secondary dRTA patients, which extrapolates to an estimated secondary dRTA patient prevalence rate of 3.88 per 100,000 in the 2016 US ESI population.

Conclusion: The ability to unequivocally identify secondary dRTA patients based on a diagnostic code is limited. This approach used claims data to provisionally identify and estimate the prevalence of secondary dRTA patients in the US ESI population. According to the Kaiser Foundation, ESI represents 49% of the total US population. Further research is needed to validate this approach to effectively identify and characterize the treatment experiences of dRTA patients.

Disclosure: G. Bryant, Advicenne, 5; **L. Law**, Advicenne, 3; **J. Li-McLeod**, Advicenne, 5.

Abstract Number: 1103

Prevalence of Diagnosed Systemic Lupus Erythematosus (SLE), Patient Healthcare Utilization and Characteristics by Major Health Insurance Types in the US

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: One study estimated that between 161,000 and 322,000 people in the US had definite or probable SLE, based on data from the period of 1965-1973. We aimed to provide current US estimates of SLE prevalence by major health insurance types and describe patient healthcare utilization and characteristics.

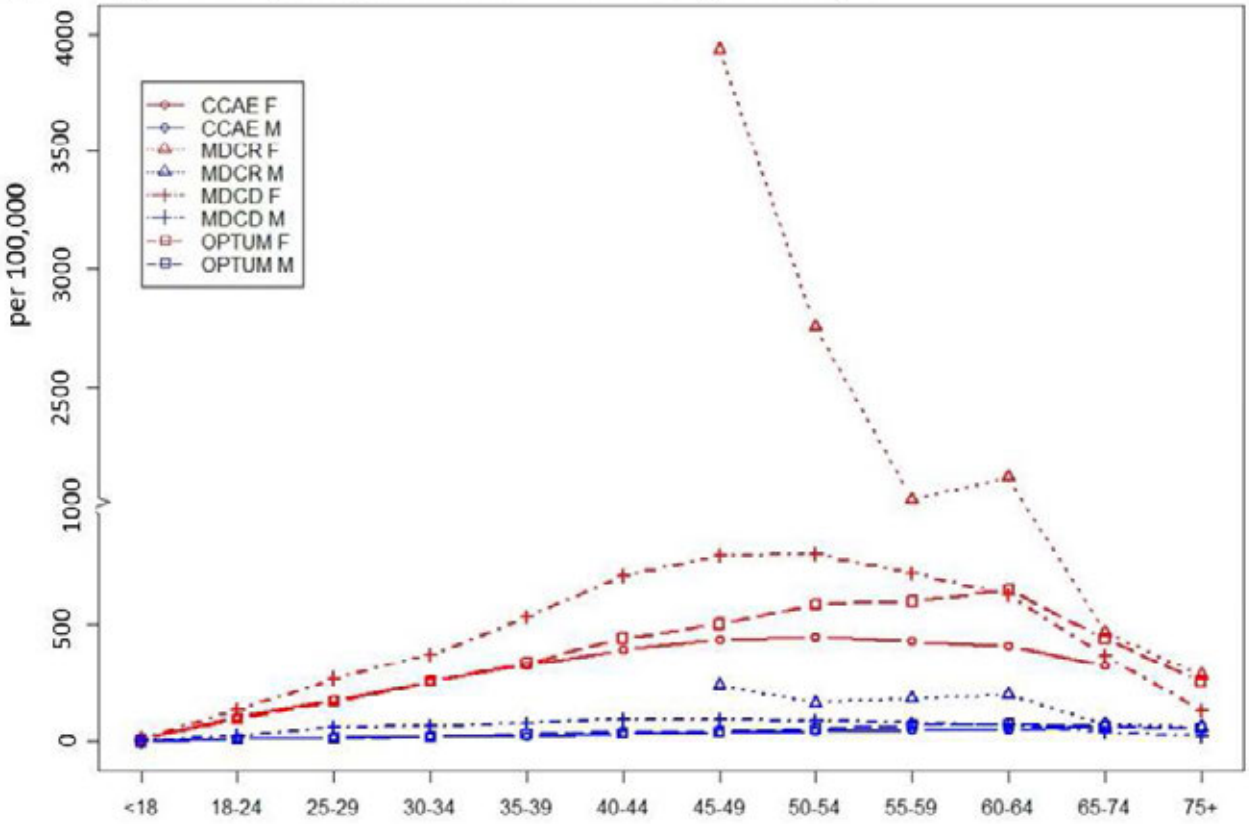
Methods: We used 4 large US health insurance claims databases converted to the OMOP Common Data Model: IBM MarketScan® Commercial (CCAE), IBM MarketScan® Medicare Supplemental (MDCR), IBM MarketScan® Multi-state Medicaid (MDCD), and Optum Clinformatics® Data Mart Databases. In each database, age and sex-specific SLE prevalence was estimated for calendar year 2016.

Numerator for prevalence estimates included individuals with ≥1 SLE diagnosis or ≥1 belimumab prescription in 2016, and met the following before or in 2016:

(1) ≥3 SLE diagnoses (ICD-10 M32.10, or ICD-9 710.0) spanning ≥ 60 days; or
(2) ≥1 belimumab infusion/injection and ≥2 SLE diagnoses; or
(3) ≥1 inpatient SLE diagnosis and ≥1 dispensed prescription for systemic corticosteroids, antimalarials, or immunomodulators commonly used in SLE treatment.

Denominator included individuals enrolled for the entire year of 2016.

Figure 1. Age-, and sex-specific prevalence of SLE in the 4 study databases, 2016



Projection of prevalent SLE cases (rounded in thousands) in the US was based on prevalence estimates from each database and US census data by insurance types.

Results: Figure 1 shows the prevalence in females was consistently higher than males across all age groups, ranging from 4- to 23-fold. The highest prevalence in women and men aged 45-64 was observed for those in Medicare who qualify based on disability status. The estimated number of prevalent SLE cases actively treated under commercial (including Medicare supplemental) or Medicaid plans is 450,000 (=285,000+66,000+99,000) to 521,000 (=422,000+99,000) (Table 1). Overall healthcare utilization including hospitalizations for infections appeared highest (despite lowest mean age) in Medicaid (Table 1). Comorbidities were common across multiple organ systems in SLE patients, including renal failure/dialysis. SLE medications most commonly dispensed were systemic corticosteroids and anti-malarial drugs; < 5% of the SLE patients had claims for anti-inflammatory biologic agents.

Conclusion: Estimates of both prevalence proportion and number of civilian SLE cases based on 2016 US data demonstrate a considerable increase over the last three decades, yet likely underestimate the true public health burden which would include persons undiagnosed or not actively seeking healthcare under the insurance plans contributing to our analysis.

CCAE, IBM MarketScan® Commercial Claims ; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental; Optum, Optum Clinformatics® Data Mart; M: male; F: female

CCAE, IBM MarketScan® Commercial Claims ; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental; Optum, Optum Clinformatics® Data Mart; SD, standard deviation

Table 1. Descriptions of patients with prevalent SLE and their healthcare utilization across 4 US databases, 2016

	CCAE	MDCR	OPTUM	MDCD
Total N	28,846	4,281	23,877	15,096
Projection to the US Health insurance sector	Commercial, age <65	Medicare& Supplemental, age ≥65	Commercial, all ages	Medicaid, all ages
Number of patients with SLE	285,000	66,000	422,000	99,000
Women, n (%)	26,476 (91.8)	3,759 (87.8)	21,568 (90.3)	13,979 (92.6)
Mean age (SD), years	47 (12)	72 (7)	56 (15)	45 (15)
Number of visits, median (interquartile range)				
for any healthcare encounter	17 (10-30)	25 (15-41)	20 (11-35)	25 (13-49)
with SLE diagnosis	4 (2-7)	3 (2-5)	4 (2-7)	4 (2-8)
Number of patients with ≥1 hospitalization, n (%)	4,374 (15.2)	1,185 (27.7)	4,510 (18.9)	5,044 (33.4)
Length of stay, days				
Median (interquartile range)	3 (2-6)	4 (2-8)	4 (2-6)	4 (2-6)
Co-morbidities, n (%)				
Renal diseases	5,018 (17.4)	1,177 (27.5)	6,089 (25.5)	4,328 (28.7)
Renal dialysis/failure	2,429 (8.4)	902 (21.1)	3,970 (16.6)	2,781 (18.4)
Cardiovascular diseases				
Hypertension	10,191 (35.3)	2,999 (70.1)	11,457 (48.0)	5,218 (34.6)
Ischemic heart disease	1,031 (3.6)	545 (12.7)	2,186 (9.2)	1,433 (9.5)
Heart failure	903 (3.1)	638 (14.9)	2,275 (9.5)	2,047 (13.6)
Rheumatic heart disease	483 (1.7)	236 (5.5)	799 (3.4)	537 (3.6)
Cerebral vascular diseases	1,052 (3.7)	484 (11.3)	1,747 (7.3)	1,409 (9.3)
Neuropsychiatric conditions				
Headache (recorded on claims)	4,043 (14.0)	512 (12.0)	3,804 (15.9)	3,897 (25.8)
Psychosis	444 (1.5)	272 (6.4)	990 (4.2)	1,004 (6.7)
Epilepsy/Seizure	1,050 (3.6)	144 (3.4)	1,336 (5.6)	1,800 (11.9)
Depression	4,112 (14.3)	698 (16.3)	4,782 (20.0)	3,284 (21.8)
Cutaneous manifestations				
Cutaneous lupus	4,452 (15.4)	683 (16.0)	4,133 (17.3)	3,136 (20.8)
Dermatosis and dermatitis	3,977 (13.8)	683 (16.0)	3,412 (14.3)	2,184 (14.5)
Infections	8,778 (30.4)	1,450 (33.9)	7,955 (33.3)	6,405 (42.4)
Hospitalized infections	1,543 (5.4)	472 (11.0)	1,847 (7.7)	2,168 (14.4)
Musculoskeletal comorbidities				
Inflammatory Polyarthropathies	6,711 (23.3)	1,238 (28.9)	7,403 (31.0)	3,688 (24.4)
Spondylopathies	3,050 (10.6)	874 (20.4)	3,999 (16.8)	2,337 (15.5)
Osteoarthritis	7,257 (25.2)	2,251 (52.6)	9,360 (39.2)	5,145 (34.1)
Osteoporosis	2,351 (8.2)	1,056 (24.7)	4,051 (17.0)	1,257 (8.3)
Medication use (any), n (%)				
Anti-malarials	18,129 (62.8)	2,275 (53.1)	12,411 (52.0)	5,324 (35.3)
Systemic corticosteroids	18,518 (64.2)	2,768 (64.7)	14,619 (61.2)	9,255 (61.3)
Non-biologic disease modifying drugs	5,906 (20.5)	660 (15.4)	3,904 (16.4)	2,423 (16.1)
Biologics	1,286 (4.5)	139 (3.2)	818 (3.4)	480 (3.2)

Disclosure: Y. Wang, Janssen Pharmaceutical R&D, LLC, 3, 4; **L. Hester**, Janssen Pharmaceutical R&D, LLC, 3, 4; **J. Lofland**, Janssen Scientific Affairs, LLC, 3; **S. Rose**, Janssen Research & Development, LLC, 3; **C. Karyekar**, Abbott, 3, BMS, 3, Janssen, 1, 3, Janssen Scientific Affairs, LLC, 3, Novartis, 3; **D. Kern**, Janssen Pharmaceutical R&D, LLC, 3, 4; **M. Blacketer**, Janssen Pharmaceutical R&D, LLC, 3, 4; **K. Davis**, Janssen Pharmaceutical R&D, LLC, 3, 4; **K. Shields-Tuttle**, Janssen Pharmaceutical R&D, LLC, 3, 4.

Abstract Number: 1104

Heritability and Familial Risk of Systemic Lupus Erythematosus in Sweden: A Population-based Case-control Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies examining the relative risk (RR) associated with having a first degree relative (FDR) with systemic lupus erythematosus (SLE) were small and few investigated different proband-relative relationships nor stratified by proband characteristics, which is likely important when studying a heterogenous disease such as SLE. Our goal was to estimate the familial RR and heritability of SLE stratified by age at onset, sex and kinship in a large population-based sample.

Methods: We conducted a case-control-family study using Swedish nationwide registers. Proband SLE cases were identified from the National Patient Register using ICD codes for SLE (≥2 visits, ≥1 in specialist care (internal medicine, pediatrics, rheumatology, dermatology, nephrology); 1971-2016; n=8801). Lupus nephritis was defined using ICD codes for lupus-related kidney disease (ICD-10 N00-N06, N16.2, N16.4, N16.8, N17-N19, N26, M32.1) Proband controls were matched to each case 5:1 on age, sex and residential location. FDRs and half siblings were identified from the Multi-Generation Register and SLE in relatives was identified the same way as for cases. Conditional logistic regression models estimated RRs for SLE associated with having an FDR with SLE. Models were stratified by age at onset, sex of the proband/relative, and lupus nephritis. Robust variance estimates were used to calculate 95% confidence intervals (95%CI) to account for correlated data. Heritability was estimated using tetrachoric correlations among first degree relatives and prevalence estimates for our population.

	Cases	Controls	RR (95%CI)
	N exposed/N total	N exposed/N total	
First degree relatives			
Number of relatives			
≥1 relative	442/8801	182/36208	11.1 (9.3, 13.3)
≥2 relatives	34/8801	4/36208	39.8 (14.1, 112.4)
Kinship*			
Parents	153/12144	73/53133	9.3 (6.1, 14.1)
Full Siblings	183/10082	50/44502	17.9 (3.1, 101.9)
Offspring	141/13918	62/61358	10.4 (4.6, 23.7)
Age at inclusion*			
<18 y	37/415	7/1870	23.7 (11.0, 53.6)
18-39 y	166/2375	49/10102	16.5 (11.8, 23.2)
40-64 y	174/3867	87/16298	9.2 (7.1, 12.0)
>64 y	65/2144	29/7938	7.2 (4.7, 10.8)
Sex of Proband/Relative*			
Female/Female	308/6775	126/28356	11.2 (9.0, 14.0)
Female/Male	51/6692	27/28143	9.0 (5.5, 14.7)
Male/Female	52/1309	24/5432	9.4 (5.8, 15.5)
Male/Male	32/1299	5/5383	32.0 (11.3, 90.8)
Lupus Nephritis*			
Yes	149/2965	60/12427	11.7 (8.6, 15.9)
No	293/5836	122/23770	10.9 (8.8, 13.5)
Second degree relatives*			
Half siblings	16/3466	7/3634	2.6 (0.5, 13.3)

* Probands can contribute more than one observation, therefore adjusted for autocorrelation from family clustering using robust variance estimates

Results: 5% of proband cases had ≥1 relative with SLE compared to 0.5% of controls. The RR for SLE associated with having ≥1 FDR with SLE was 11.1 (95%CI 9.3, 13.3; Table). The RR was higher if ≥2 FDRs had SLE (39.8; 95%CI 14.1, 112.4) and lower if a half sibling had SLE (RR 2.6; 95%CI 0.5, 13.3). RRs were higher for SLE diagnosed at a younger age (< 18y RR 23.7; 95%CI 11.0, 53.6) and in male proband/male relative kinships (RR 32.0; 95%CI 11.3, 90.8), although this was based on small numbers. There was no considerable difference in the association when stratified by lupus nephritis status. Heritability was 61% (95%CI 58, 64).

Conclusion: Having a first degree relative with SLE is associated with an 11-fold increased risk of SLE, making it a very strong risk factor for the disease. The risk is highest for pediatric SLE and decreases with increasing age at diagnosis. There were no large differences in risk by lupus nephritis phenotype, kinship, or sex. The male proband-male relative association was the highest, although this was based on small numbers. 61% of the phenotypic variance of SLE is attributable to genetic factors.

Relative risk of SLE associated with having relatives diagnosed with systemic lupus erythematosus (SLE) overall and stratified by age at inclusion, sex of the proband, sex of the relative and lupus nephritis phenotype.

Disclosure: E. Arkema, None; **M. Rossides**, None; **C. Sjöwall**, None; **E. Svenungsson**, None; **J. Simard**, None.

Abstract Number: 1105

Relationships Among Cognitive Emotion Regulation, Body Image, Family and Marital Function and Quality of Life in Chinese Female Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: At present, there are few researches on cognitive emotional regulation, body image, family and marital function, and life quality of female patients with systemic lupus erythematosus (SLE) in China. The aim of this study is to explore the relationships of these factors, and to build a path equation model among these factors.

Methods: Participants in the study included 242 female patients with SLE from three hospitals of China. The questionnaires contained demographic information sheet, SLE Disease Activity Index (SLEDAI), Lupus Quality of Life (LupusQoL), Cognitive Emotion Regulation Questionnaire (CERQ), Body Image Lupus Scale (BILS), Family and Marital Functioning Measures (FFM and MFM). Statistical Methods included descriptive analysis, correlation analysis, one-way ANOVA, multiple linear regression, and path equation modeling analysis.

Results: We identified non-adaptive strategies score was negatively correlated with the total score of life quality (r=-0.589, P< 0.05). The score of body image (r=0.466, P< 0.05) and the total score of family and marital function (r=0.562, P< 0.05) were both positively correlated with the total score of life quality. Adaptive strategies score was positively correlated with the total score of family and marital function (r=0.149, P< 0.05), and non-adaptive strate-

gies score was negatively correlated with the body image score (r=-0.313, P< 0.05) and the total score of family and marital function (r=-0.476, P< 0.05). The body image score was positively correlated with the total score of family and marital function (r=0.285, P< 0.05). Moreover, path equation model showed that adaptive strategies had direct positive effect on family and marital function (β=0.227, P=0.000); non-adaptive strategies had direct negative effect on body image (β=-0.231, P=0.001), family and marital function (β=-0.494, P=0.000), and quality of life (β=-0.358, P=0.000); SLEDAI scores had direct negative effect on body image (β=-0.140, P=0.041), family and marital function (β=-0.263, P=0.000), and quality of life (β=-0.363, P=0.000); family and marital function had direct positive effect on body image (β=0.116, P=0.030) and quality of life (β=0.171, P=0.000); body image had direct positive effect on quality of life (β=0.201, P=0.000).

Conclusion: Our results prove that in female SLE patients, non-adaptive strategies lead to low quality of life; and the better the body image and family and marital function, the higher the quality of life. In addition, body image and family and marital function have direct positive effect on quality of life; cognitive emotion regulation styles have direct and/or indirect effect on quality of life. Body image and family and marital function, as mediated variables, can mediate the relationship between cognitive emotion regulation styles and quality of life.

Disclosure: H. Zhang, None; **L. Li**, None; **M. Chen**, None; **Q. Zhang**, None.

Abstract Number: 1106

Systemic Lupus Erythematosus and Sjögren's Syndrome in the Agricultural Health Study: Lower Risk Associated with Childhood Farm Residence and Raising Livestock

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Prior research suggests that growing up on a farm and contact with livestock may confer protection against developing systemic autoimmune diseases, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). We examined associations between SLE and a related disease, Sjögren's syndrome (SS), with childhood and adult farm experience and potential exposures to livestock for licensed pesticide applicators and their spouses in the Agricultural Health Study (AHS).

Methods: Cohort participants were enrolled in 1993-1997 in North Carolina and Iowa and followed through 2015; Lupus (mostly SLE) and SS cases were identified based on self-report and classified as "confirmed" by medical records or "clinical" based on reported use of disease-specific anti-rheumatic drugs. Our analysis sample included 214 participants with confirmed or clinical SLE/SS, with 107 incident cases (N=45 confirmed SLE or lupus with DMARD use, with or without SS, 34 primary SS, and 20 SS with RA), and a comparison group of participants (n=54,205) who did not report a systemic autoimmune disease. Farming exposures were self-reported at enrollment, while data on childhood farm animal contact were collected from 68% of the sample during follow-up. We estimated odds ratios (OR) and 95% Confidence Intervals (CI) using logistic regression models adjusted for age, sex and state for cases, overall and stratified by sex, and in sensitivity analyses excluding RA.

Results: Cases were more likely to be female (83% versus 48% of non-cases; age-adjusted OR=5.3; 95%CI 3.7, 7.6), especially for prevalent (88% female; OR=7.8; 95%CI 4.4, 13.9) and less so for incident cases (77% female; age-adj OR=3.9; 95%CI 2.5, 6.2). Childhood farm residence (at least half the time up to age 18) was inversely associated with risk of becoming a case, overall, (OR=0.46; 95%CI 0.31, 0.69) and in models limited to women (OR=0.59; 95%CI 0.39, 0.91). Incident cases were less likely to live or work on a farm that raised livestock as well as crops compared with those who only raised crops, though the association was not statistically significant (OR=0.72; 95%CI 0.48, 1.09, p=0.12). Among women, however, incident cases were significantly less likely to live or work on a farm that raised 500 or more livestock animals (OR=0.50;95%CI 0.27, 0.92), with inverse associations also seen for women on farms raising hogs, field corn, and hay (all with $p< 0.05$).

Conclusion: These preliminary results support the idea that exposures related to childhood farm residence and livestock farming may decrease susceptibility to developing SLE and SS. While our analyses are limited by the low frequency of SLE/SS in the cohort, especially in men, they are consistent with prior findings for RA in female spouses in the AHS. Further analyses will explore associations of SLE/SS with other agricultural exposures, including pesticides.

Disclosure: C. Parks, None; **S. Long**, None; **L. Beane-Freeman**, None; **H. Jonathan**, None; **S. Dale**, None.

Abstract Number: 1107

Are Rheumatologists Correctly Identifying and Controlling Traditional Cardiovascular Risk Factors?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Epidemiology & Public Health Poster II: Spondyloarthritis & Connective Tissue Disease
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic systemic inflammation generated by rheumatic diseases (RD) is related to the increased cardiovascular risk (CVR) in this population. However, the coexistence of traditional CVR factors such as diabetes, hypertension, obesity, smoking, and dyslipidemia, further increases CVR burden. Through an adequate control of this factors, CVR can be decreased. But to achieve this, primary care physicians and rheumatologists should be aware of how relevant it is to make frequent cardiovascular assessment to RD patients. Therefore, the aim of this study is to determine the prevalence of underdiagnosis and inefficient treatment of traditional cardiovascular risk factors in RD patients.

Methods: An observational, retrospective study of patients between 30 and 75 years with rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus and ankylosing spondylitis. Patient information was obtained from March 2018 to April 2019 through the REPAIR® software, an electronic records database used at the rheumatology clinic at a University Hospital in northeastern Mexico. Exclusion criteria: previous atherosclerotic cardiovascular disease, overlap syndromes, diabetes, or pregnancy. Evaluation included history of lifestyle, comorbidities, use of corticoids, blood pressure, anthropometry and fasting glucose measures. Framingham-Body Mass Index (FRS-BMI) was used to calculate their predicted CVR to 10 years.

Results: A total of 451 patients were recruited, 90.2% were women, with a median age of 52 years (43-59). In this population, 80.2% of the patients had at least one CVR factor; the presence of traditional CVR factors according to

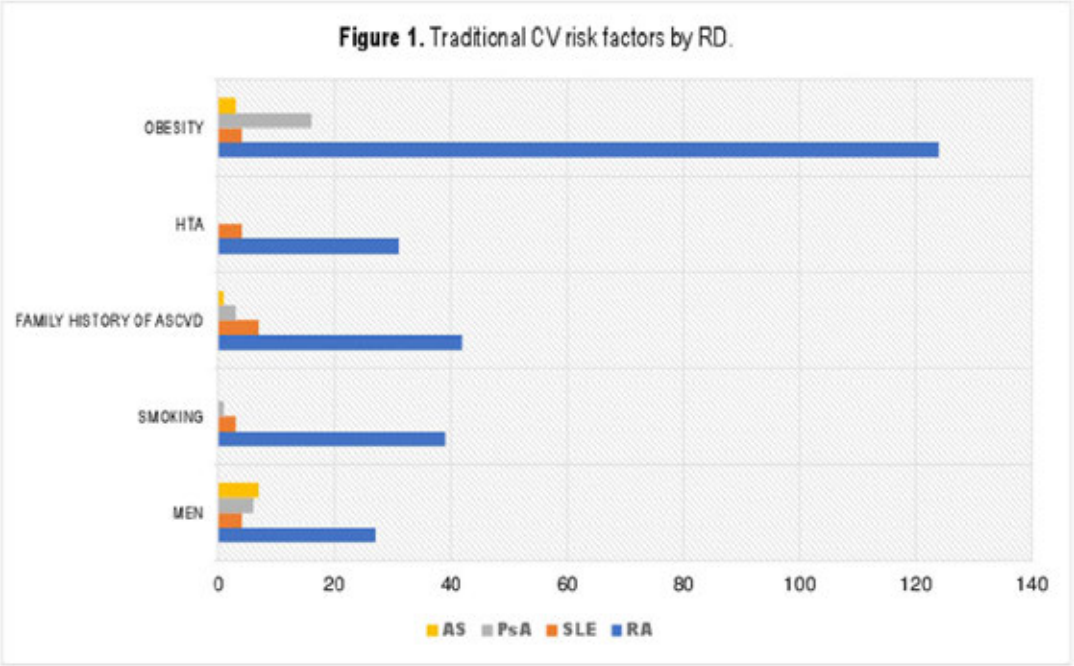

Table 1. Demographic characteristics.	
	n=451
Men, n (%)	44 (9.8)
Active smoking, n (%)	43 (9.5)
Hypertension, n (%)	35 (7.8)
Rheumatoid arthritis, n (%)	365 (80.9)
Psoriatic arthritis, n (%)	14 (3.1)
Systemic lupus erythematosus, n (%)	62 (13.7)
Ankylosing spondylitis, n (%)	10 (2.2)
Corticosteroid use, n (%)	136 (30.2)
Fasting glucose, mg/dL, median (p25-p75)	91 (84-99)
FRS-BMI score, median (p25-p75)	4.9 (2.8-8.1)

RD is shown in Figure 1. Other population characteristics are in Table 1. More than half of the patients were not in their ideal weight, 37.2% being diagnosed as overweight and 32.8% with obesity. Out of the patients with no previous diagnosis of hypertension (n=416, 92.2%), 25.96% had elevated or high blood pressure levels. From the patients that previously had hypertension, 65.7% did not have an adequate control of their blood pressure, even though they were on pharmacological treatment. History of dyslipidemia was found in 4.9% of patients. Half of them arrived at consultation with a recent lipid profile, having a median LDL of 133.5 (109-158) mg/dL, not meeting target levels. Even though no diabetic patients were included, 22.8% of the patients had hyperglycemia. According to FRS-BMI, 82% of the patients had a low CVR, 13.7% moderate risk, and 4.2% had a high CVR.

Conclusion: This study suggests that traditional CVR factors are underdiagnosed and insufficiently treated in RD patients. The previous is alarming, because 80.2% of the patients have at least one CVR factor, and they could highly benefit from its adequate control. Besides having a RD and at least one traditional CVR factor, 17.9% of the patients had a moderate or high CVR according to FRS-BMI. Rheumatologists should become more aware of the increased CVR in RD patients, and make CV assessment a part of their routine.

Disclosure: D. Galarza-Delgado, None; **J. Azpiri-Lopez**, None; **I. Colunga-Pedraza**, None; **I. Hernández-Galarza**, None; **I. Reynosa-Silva**, None; **K. Cuellar-Calderon**, None; **M. Castro-Gonzalez**, None; **C. Martinez-Flores**, None.

Abstract Number: 1108

Mobile Apps in Rheumatology: Review and Analysis Using the Mobile App Rating Scale (MARS)

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Health Services Research Poster II – ACR/ARP

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Mobile applications promise to facilitate the life of patients as well as physicians. In routine practice, however, rheumatology apps are largely unknown and little is known about their quality and safety. The aim of this study was to provide an overview of the mobile rheumatology applications currently available in the German App Stores, to evaluate the app quality using the Mobile App Rating Scale (MARS) and compile brief, ready to-use descriptions for patients as well as rheumatologists.

Methods: The German Google Play and Apple App Stores were systematically searched to identify German Rheumatology mobile applications addressing patients as well as physicians. App quality was assessed independently using MARS by in total 8 physicians, 4 using Android and 4 using iOS smartphones. The MARS score is based on a 5-point Likert scale in four sections with multiple items: engagement (5 items), functionality (4 items), aesthetics (3 items), and information quality (7 items). In addition, there is a "subjective" section consisting of 4 items. Apps were randomly assigned so that 4 apps were rated by all raters and the remaining apps were rated by two Android and two iOS users. Furthermore, brief app descriptions including app developers, app categories and features were compiled to inform potential users and developers.

Table 1: MARS and App Store ratings of included apps

App	MARS[a] score, median (range)	iOS raters, N	Android raters, N	MARS[a] section scores, median (range)					Google Play Store ratings[b], mean (N)	iTunes Store ratings[b], mean (N)
				Aestethics	Engagement	Functionality	Information	Subjective quality		
Rheuma-Auszeit	4.19 (3.92 - 4.55)	4	4	4.33 (4.00 - 5.00)	3.50 (2.40 - 4.00)	4.75 (4.50 - 5.00)	4.00 (3.50 - 5.00)	3.38 (2.50 - 3.75)	4.4 (40)	4.4 (7)
Meditorium	4.11 (3.10 - 4.51)	2	2	3.67 (3.00 - 4.00)	4.00 (1.40 - 4.20)	4.88 (4.00 - 5.00)	4.00 (3.80 - 4.83)	4.12 (1.00 - 4.50)	4.6 (263)	4.7 (97)
RheumaGuide	4.00 (2.82 - 4.13)	2	2	4.00 (1.00 - 5.00)	3.10 (2.00 - 3.40)	4.38 (4.00 - 5.00)	4.35 (3.29 - 4.50)	3.38 (2.75 - 4.00)	4.0 (4)	na[c]
ASAS App	3.94 (3.70 - 4.01)	2	2	4.17 (2.00 - 4.33)	2.50 (2.20 - 3.20)	4.75 (4.75 - 5.00)	4.42 (4.33 - 4.83)	3.38 (2.50 - 4.25)	4.4 (25)	5.0 (1)
RheumaLive	3.93 (3.60 - 4.47)	2	2	4.17 (3.67 - 4.67)	3.40 (3.00 - 4.20)	5.00 (3.75 - 5.00)	3.50 (3.00 - 4.33)	3.25 (3.00 - 3.75)	3.8 (5)	5.0 (2)
Pain Companion	3.88 (3.60 - 4.17)	2	2	4.00 (3.33 - 4.67)	4.20 (3.80 - 4.20)	3.88 (3.25 - 4.00)	3.67 (3.50 - 3.83)	2.38 (1.25 - 2.75)	4.1 (378)	3.4 (20)
MyTherapy	3.87 (3.55 - 4.35)	2	2	4.17 (4.00 - 4.67)	3.90 (3.80 - 4.20)	4.62 (4.25 - 5.00)	2.80 (1.00 - 4.67)	3.25 (2.00 - 4.00)	4.7 (24.408)	4.8 (1.450)
Psoriapp	3.85 (3.31 - 4.33)	4	4	4.33 (3.00 - 5.00)	3.00 (2.20 - 3.80)	4.25 (3.25 - 4.50)	3.90 (3.20 - 4.80)	2.38 (1.75 - 4.25)	na[d]	na[d]
Rheumatologie visuell	3.84 (3.55 - 3.84)	2	1	3.00 (2.67 - 3.67)	3.20 (2.60 - 3.60)	4.50 (3.75 - 4.50)	4.60 (4.17 - 4.67)	4.00 (3.50 - 4.75)	3.0 (2)	na[c]
AxSpaLive	3.60 (3.20 - 4.28)	2	2	3.83 (3.67 - 4.67)	3.10 (2.80 - 3.80)	4.38 (3.50 - 5.00)	3.83 (1.00 - 4.00)	3.00 (2.50 - 4.00)	3.0 (3)	5.0 (1)
PsALive	3.60 (3.20 - 3.78)	2	2	3.67 (3.00 - 4.00)	3.10 (2.80 - 3.60)	4.25 (3.50 - 5.00)	4.00 (1.00 - 4.00)	3.00 (2.50 - 3.50)	1.5 (2)	5.0 (1)
Lupuslog	3.57 (2.65 - 4.59)	4	4	4.17 (2.00 - 5.00)	3.10 (2.40 - 4.20)	3.88 (3.00 - 5.00)	3.37 (2.50 - 4.17)	2.62 (1.50 - 4.00)	4.5 (11)	4.0 (1)
Rheuma Edu	3.55 (3.44 - 4.17)	2	1	4.33 (4.00 - 4.33)	4.20 (2.60 - 4.20)	5.00 (4.00 - 5.00)	2.83 (1.00 - 3.17)	3.00 (2.00 - 3.00)	2.8 (5)	na[c]
ANCA-Assoziierte Vaskulitiden	3.49 (2.95 - 4.33)	2	2	3.00 (2.00 - 4.33)	3.60 (2.20 - 3.80)	3.75 (3.25 - 4.50)	4.23 (3.17 - 4.67)	3.25 (2.00 - 4.00)	4.0 (6)	na[c]
RheumaBuddy	3.44 (2.88 - 3.95)	4	4	3.50 (2.33 - 4.67)	3.10 (2.60 - 3.40)	3.75 (2.50 - 4.25)	3.75 (3.17 - 4.80)	2.12 (1.00 - 4.25)	4.0 (34)	5.0 (1)
Rheumatologie app	2.81 (2.76 - 3.87)	1	2	2.67 (2.00 - 4.33)	3.00 (2.80 - 3.40)	3.25 (2.25 - 3.75)	3.33 (3.00 - 4.00)	2.00 (1.25 - 3.00)	3.0 (4)	2.3 (3)

[a]Mobile App Rating Scale

[b]App Store ratings retrieved on April 21st 2019

[c]No App Store ratings available

[d]App not found in App Store as of April 21st 2019

Results: In total 128 and 63 apps were identified in the German Google Play and Apple App Stores, respectively. After removing doublets and only including apps that were available in both stores 28 apps remained, of which 16 final apps met the inclusion criteria, which were: (1) German language; (2) availability in both app stores; (3) targeting patients or physicians as users, and (4) clearly including rheumatology or rheumatic diseases as subject matter. Exclusion criteria were: (1) congress apps (2) company apps with advertisements. 9 apps addressed patients, 7 apps addressed physicians. No clinical studies to support the effectiveness and safety of these apps could be found. Pharmaceutical companies were the main developers of two apps. Rheuma-Auszeit, was the only app mainly developed by a patient organization. This app, had the highest overall MARS score (4.19/5). 3/9 patient apps featured validated questionnaires. The median overall MARS score was 3.85/5 ranging from 2.81/5 to 4.19/5. One patient targeted app and one physician targeted app had a MARS score >4/5. No significant gender or platform (iOS/Android) differences could be observed.

Conclusion: This is the first study, which systematically identified and evaluated mobile applications in rheumatology for patients as well as physicians available in German App Stores. We found a lack of supporting clinical studies, use of validated questionnaires and involvement of academic developers. Overall app quality was very heterogeneous. To create high-quality apps a closer cooperation lead by patients and physicians is vital.

Disclosure: J. Knitza, None; **K. Tascilar**, None; **E. Messner**, None; **M. Meyer**, None; **D. Vossen**, None; **A. Pulla**, None; **P. Bosch**, None; **J. Kittler**, None; **A. Kleyer**, None; **P. Sewerin**, AbbVie, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Celgene, 2, 5, 8, Chugai, 2, 5, 8, Hexal, 5, 8, Janssen-Cilag, 2, 5, 8, Lilly, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, Sanofi-Genzyme, 5, 8, Swedish Orphan Biovitrum, 5, 8, UCB, 2, 5, 8; **J. Mucke**, None; **I. Haase**, None; **D. Simon**, None; **M. Krusche**, None.

Abstract Number: 1109

Development of Smart-phone Spondyloarthritis Management System and Real-world Study of Chinese Patients with Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Health Services Research Poster II – ACR/ARP
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: We developed a multipurpose digital platform, Smart-phone SpondyloArthritis Management System (SpAMS), based on two of the most important objectives: 1) for patients: to activate patient engagement and provide education about disease self-management and 2) for clinicians and researchers: to provide a new source of real-world data for the scientific community by collecting questionnaire data, physical measurements, and images with comprehensive clinical follow-ups.

Methods: SpAMS was designed for patients with axial SpA, including AS and nonradiographic axial SpA (nr-axSpA), and open to the public by being embedded in the WeChat social media application (Figure 1). The project was launched in August 2015, beta-tested in January 2016 with rheumatologist and a small group of patients, and finally released in April 2016. Patients diagnosed with axial SpA in the Chinese People's Liberation Army (PLA) General Hospital were recruited consecutively in the Chinese Ankylosing Spondylitis Prospective Imaging Cohort (CASPIC). Demographic and clinical data were collected through SpAMS. All data were pseudonymised for analysis and matched by generation time and unique anonymous identifiers.

Results: Between April 2016 and February 2019, 27,628 WeChat social media users all over China subscribed to our WeChat service account and received weekly notifications about SpA disease management strategies. In the last 30 days alone, a total of 50,028 users read those management strategies 85,261 times (Figure 2), and this figure has remained stable over the past 6 months. The most-read articles concern exercise and lifestyle. There were 7,158 subscribers who logged into our system and registered as patients with axial SpA. Of them, 1,684 had face-to-face clinic visits at the Chinese PLA General Hospital (Figure 3). In total, 1,426 patients with axial SpA were enrolled in the

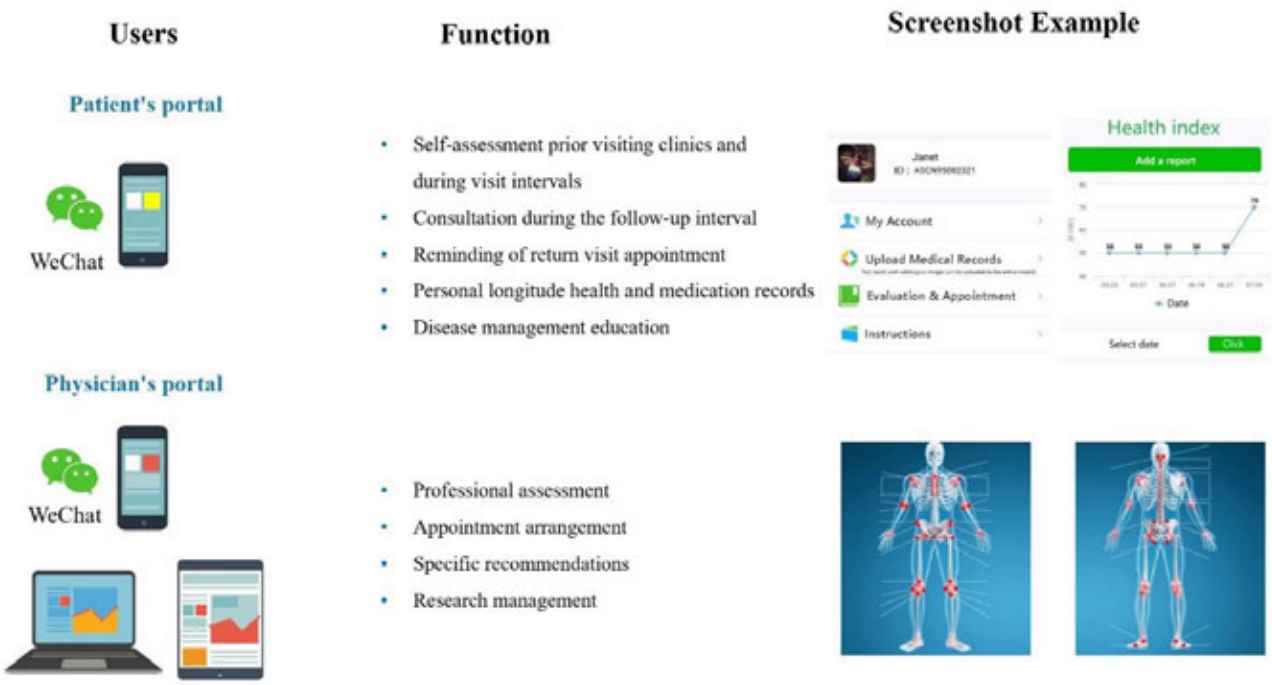

Figure 1. Patient's and Physician's portal in SpAMS.

Figure 2. Pageview of SpA disease management strategies in the last 30 days.

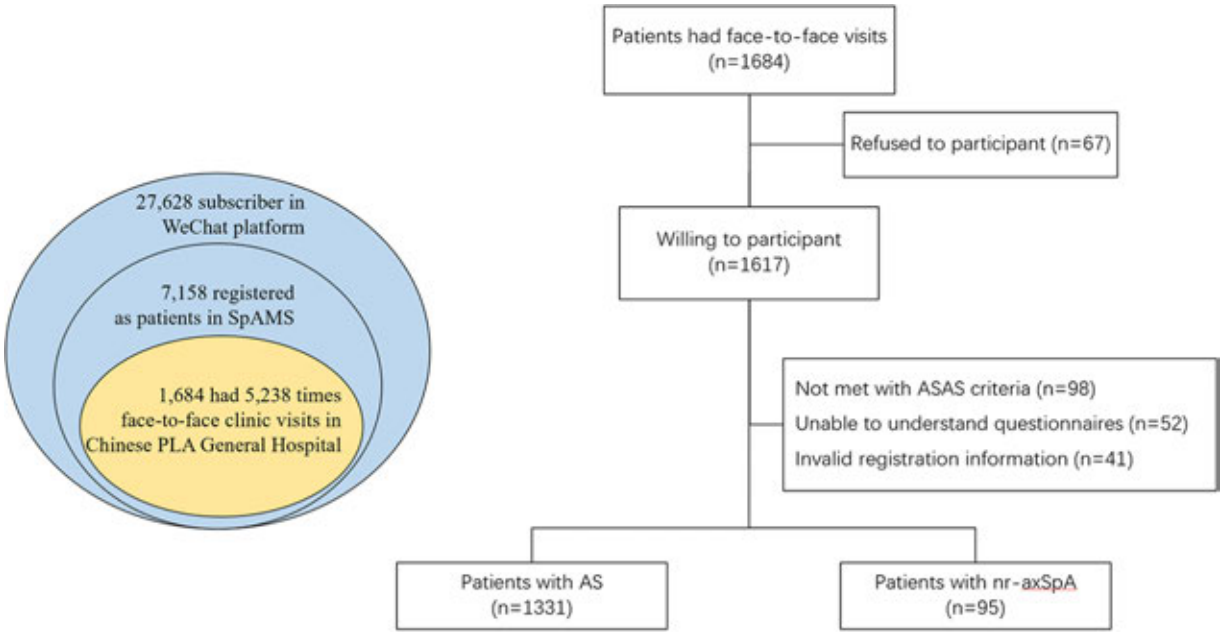

Figure 3. Defining the cohort samples.

cohort (AS = 1331 and nr-axSpA = 95). To date, 4,659 patient-reported assessments (mean 3.9, range 1 to 21) and 3,304 physician-reported assessments (mean 2.8, range 1 to 11) have been collected.

Conclusion: SpAMS is a disease management tool that can help patients with AS perform self-management and provide clinic data to clinicians.

Disclosure: X. Ji, None; **J. Zhu**, None; **J. Zhang**, None; **F. Huang**, None.

Abstract Number: 1110

Expanding Access to Research Using Tele-Health: Lupus and Informatics Feasibility Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Health Services Research Poster II – ACR/ARP
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Session Time: 9:00AM–11:00AM

Background/Purpose: Participating in clinical research can be burdensome for subjects due to time and travel barriers, particularly among underserved, rural, and/or chronic disease bearing populations such as systemic lupus erythematosus (SLE). Telemedicine offers one way to overcome these barriers by providing tele-research visits. Doxy.me is a platform which facilitates these types of visits with its tele-consent functionality. However, diverging from the traditional in-person informed consent methodology could unduly influence subjects' willingness to participate, reduce their comprehension of their study and associated risks or benefits. This poses an ethical concern that warrants exploration prior to widespread implementation. In this study, we examined the impact of tele-consent on measures of consent quality as compared to in-person consenting procedures.

Methods: Assessments of perceived decision-making control (Decision Making Control Index, DMCI), consent quality (Quality of Informed Consent, QuIC), and health literacy (Short Assessment of Health Literacy – English Version) were integrated into an ongoing observational study. This study enrolls African American patients with SLE and healthy controls over the age of 18, many of whom are of Gullah Geechee heritage. Subjects were invited to participate in tele-consent and associated assessments at their in-person observational study visit. Willing subjects were randomized to tele-consent or standard in-person consent, followed by consent assessments. An independent samples t-test was used to compare mean outcome scores and age, whereas the chi-squared test was used for categorical demographic variables.

Results: Twenty-five subjects have completed the study, 12 of whom were randomized to tele-consent. There were no significant differences in age (mean 49 ± 15.39), sex (96% female), or health literacy scores (mean 16.7 ± 2.14, out of 18). The study sample is entirely African American, possesses health insurance, and 52% are diagnosed with SLE. Two tele-consent subjects were unable to complete their tele-consent encounters. One failure was due to a software issue while the other failed due to subject usability problems. Outcome measures did not vary significantly between groups; for tele-consent and standard consent the QuIC part A scores were 95.0 and 92.9 respectively ($p = 6.83$) out of 100, whereas the Part B scores were 4.9 and 4.8 respectively ($p = 0.851$) out of 5. Similarly, scores on the DMCI were 51.2 and 50.8 ($p = 0.974$) out of 54.

Conclusion: The lack of statistically significant differences in outcome measures is promising for the validity of tele-consent. However, two tele-consent failures, one of which was due to the software, were encountered. A larger sample size will provide greater surety in these results and determine if failures may be a significant barrier to implementation. Tele-consenting is a novel methodology to increase recruitment and retention of under-served and hard to reach populations in minimally invasive studies. Trials may benefit from partnering with external laboratories or satellite clinics to facilitate more complex research visits while maintaining a reduction in travel burden for participants.

Disclosure: T. Faith, None; **J. Obeid**, None; **K. Simpson**, None; **D. Kamen**, None.

Abstract Number: 1111

Lupus Teledematology: A Pilot Project to Evaluate the Plausibility of a Rapid Access Dermatology Service for Lupus Patients

Richard Antbring,[1] Malvina Cunningham,[2] Richard Bull,[2] Angela Pakozdi,[1] Ravindra Rajakariar,[1] Myles Lewis,[1] Andrea Cove-Smith,[1] and Debasish Pyne[3], [1]Barts Health Lupus Centre, London, United Kingdom, [2]Barts Health NHS Trust, London, United Kingdom, [3]Barts Lupus Centre, London, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Health Services Research Poster II – ACR/ARP

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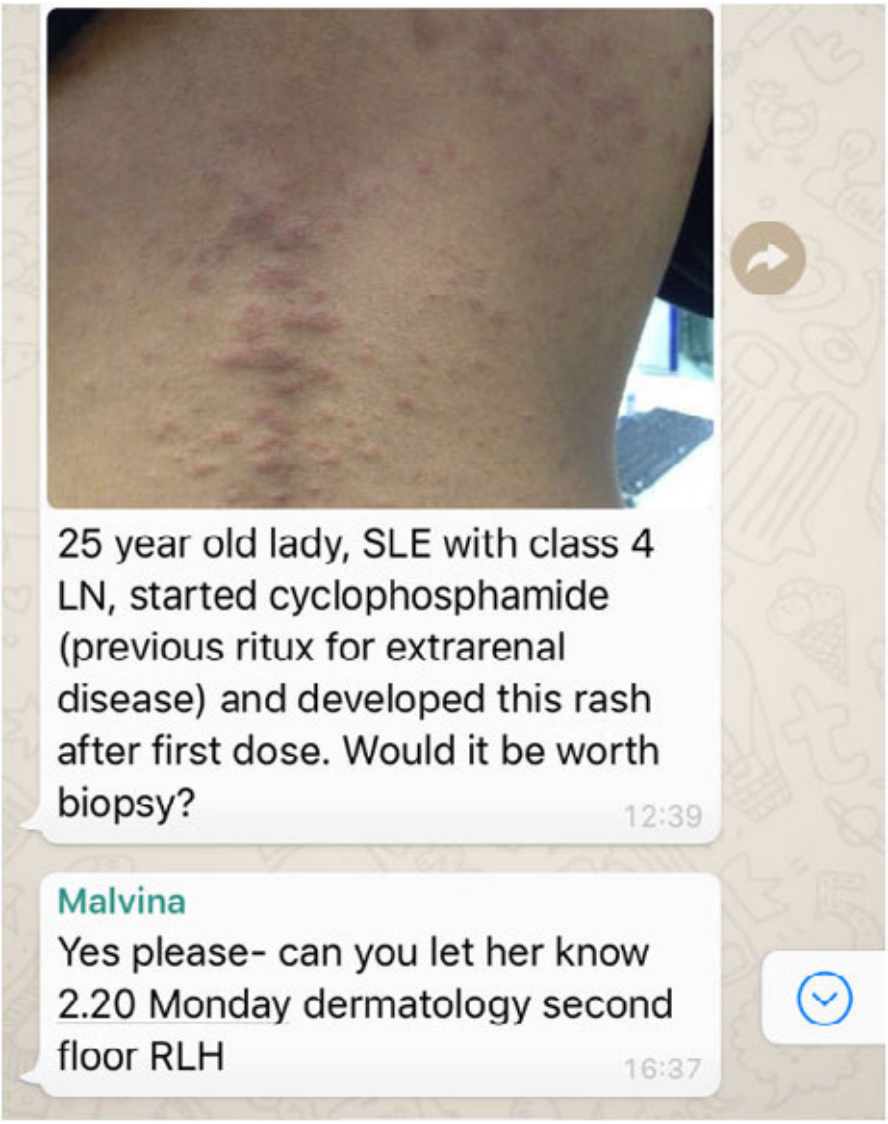
Background/Purpose: Clinicians have been increasingly using social media sites professionally. Platforms such as WhatsApp ® could be a potentially effective tool in teledermatology for rapid diagnosis and/or triage.



Cutaneous disease is a common manifestation of lupus but patients may also develop rashes not directly attributable to the disease and hence the importance of accurate diagnosis and management. In this study we introduced and service evaluated a WhatsApp® lupus telederm platform for diagnosis and management of cutaneous lesions in lupus patients attending clinic at an inner city Lupus Centre.

Methods: A WhatsApp ® group was created comprising all clinicians involved in the running of lupus clinics within the centre and included 2 senior dermatologists. Lupus patients who presented with skin lesions which posed diagnostic or management uncertainty were consented for lesion photography. Images were uploaded to WhatsApp ® along with relevant but brief clinical history. Patient confidentiality was protected by avoiding upload of any patient identifiable data. Dermatologist responses were collated and effectiveness of the service for patients was analysed.

Results: 1-year retrospective data from WhatsApp ® was evaluated. Images from 27 lupus patients had been uploaded for advice. Dermatologist advice could be categorised as either 1. Diagnosis and treatment advice (18 patients) (*example - image1*) or 2. Advice to refer to emergency dermatology clinic for further clinical evaluation (*example*

– *image 2*) (9 patients). Patients in category 1 received a diagnosis and treatment institution within 48 hours. Those in category 2 were seen in dermatology clinic within 11 days where 7 underwent skin biopsy with subsequent diagnosis. The average time of a dermatologist to respond to queries was 1.1 days.

Conclusion: Our pilot project demonstrates that WhatsApp ® is an effective teledermatology platform for lupus patients with skin lesions allowing prompt evaluation and management.

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Abstract Number: 1112

Rheumatologists' Opinions and Use of Telemedicine in the Southwestern U.S

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Health Services Research Poster II – ACR/ARP
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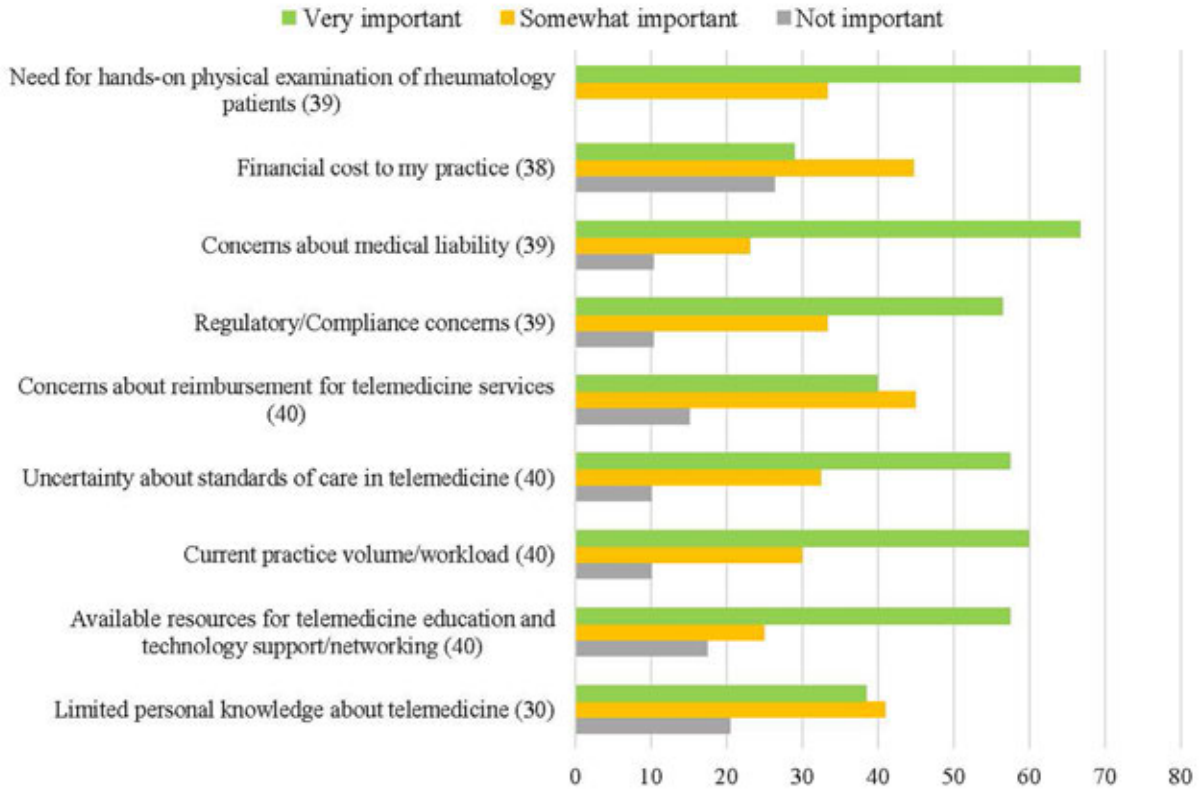
Background/Purpose: Telemedicine (TM) is increasingly employed in chronic disease management and can reduce barriers in access to care. In the Southwestern U.S., where there is a disproportionate shortage of rheumatologists, TM may be one tool to improve access to rheumatology care. While use of TM in rheumatology is growing, the nature of rheumatology patient evaluations presents unique challenges to this modality of care. We sought to understand the attitudes of rheumatologists in the Southwestern U.S. towards the use of TM in caring for patients with rheumatic diseases.

Methods: We surveyed a convenience sample of rheumatology providers attending the 19th Annual Rheumatic Diseases Conference in Santa Fe, NM. Respondents completed paper questionnaires in which we collected general provider information, and assessed use of and familiarity with TM, general attitudes towards TM, and perceived barriers to its use. All respondents were anonymous. Simple counts of provider responses are reported here.

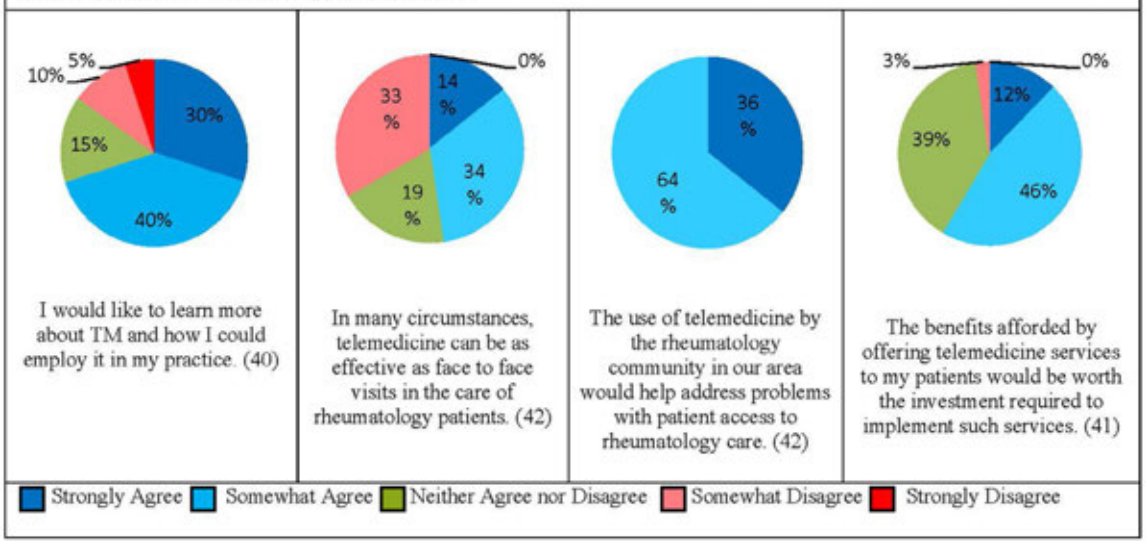
Results: A total of 42 participants completed our survey: 39 were actively practicing rheumatology (31 physicians and 8 physician assistants or nurse practitioners). 32.5% of providers were part of independent small group or solo practices, 37.5% were employed by multispecialty or hospital-affiliated groups, and 25% practiced in academic centers. 22 providers practiced in NM, followed by TX (9) and CO (5), and three were from non-Southwestern states. All but two providers (neither from NM) were practicing in underserved areas. Four providers from NM and CO reported practicing TM. Of those not using TM, 60.5% had considered providing TM services, while 17% had considered implementing TM services, but ultimately decided not to. Among possible barriers to TM, current practice volume/workload, concerns about medical liability, and the need for hands-on physical exam for rheumatology patients were rated as "very important" factors in provider willingness to use TM (60%, 66.7%, and 66.7% of providers, respectively). All respondents either somewhat (64.3%) or strongly (35%) agreed that TM use by rheumatologists would help address problems with access to rheumatology care. Over half of providers also cited the following factors as very important barriers to TM use: available resources for TM education and technology support/networking (57.5%); uncertainty about standards of care in TM (57.5%); and regulatory/compliance concerns (56.4%). Most providers were

Figure 1: Rheumatology Provider Rating of Importance of Potential Barriers to TM and Effects on Willingness to Provide TM Services.



X axis represents percentage of providers rating each barrier as "very important", "somewhat important", or "not important". Numbers of respondents to each item in parentheses.

Figure 2: Provider Agreement with Statements about Telemedicine.
Numbers of respondents to each statement in parentheses



either neutral toward (39%) or somewhat agreed (46.3%) with the statement that the benefits afforded to patients by offering TM would be worth the investments required to implement these services.

Conclusion: While a majority of surveyed rheumatology providers in our area have considered using TM and generally agree that it would improve access to care, few have employed it in their practices. Current provider workload, and uncertainties surrounding practice logistics and adequate patient assessment represent important barriers to TM use. Increased educational efforts in TM technology, regional support for TM infrastructure, and further study and dissemination of patient care tools and standards of care may increase rheumatologist use of TM.

Disclosure: K. Reiter, None.

Abstract Number: 1113

Improving Healthcare Quality and Reducing Cost via Online Interaction for Chinese Patients with Rheumatic Diseases Based on Smart System of Disease Management (SSDM) Mobile Tool

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SESSION INFORMATION

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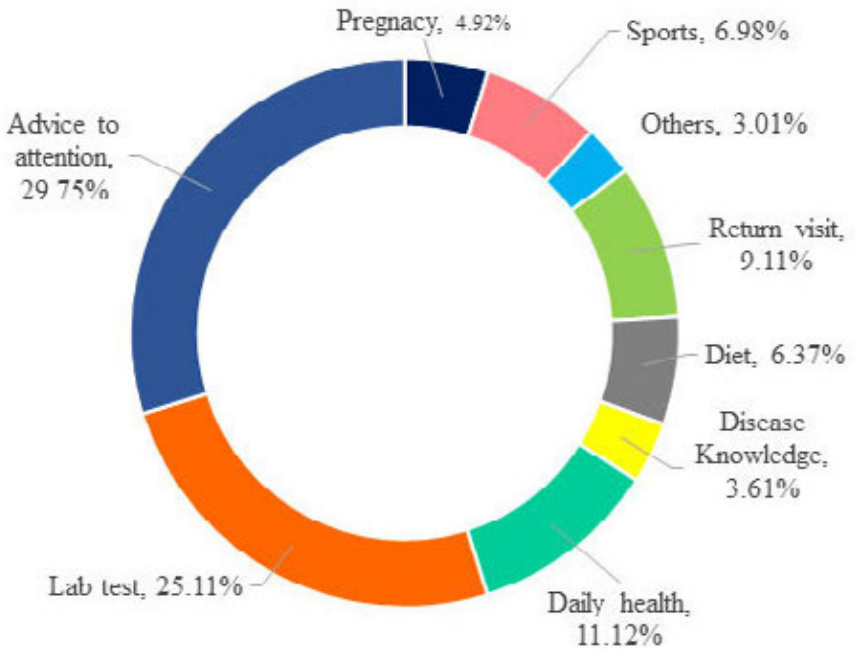
Background/Purpose: Without efficient primary medical care and follow-up system in China, patients can choose any hospital or doctor they like in seeking medical care. As a result, most patients rush to large hospitals. Once patients left those clinics, no follow up data is available. Surveys show that over 40% of patients were unnecessary

Figure1. The distribution diagram of question type.

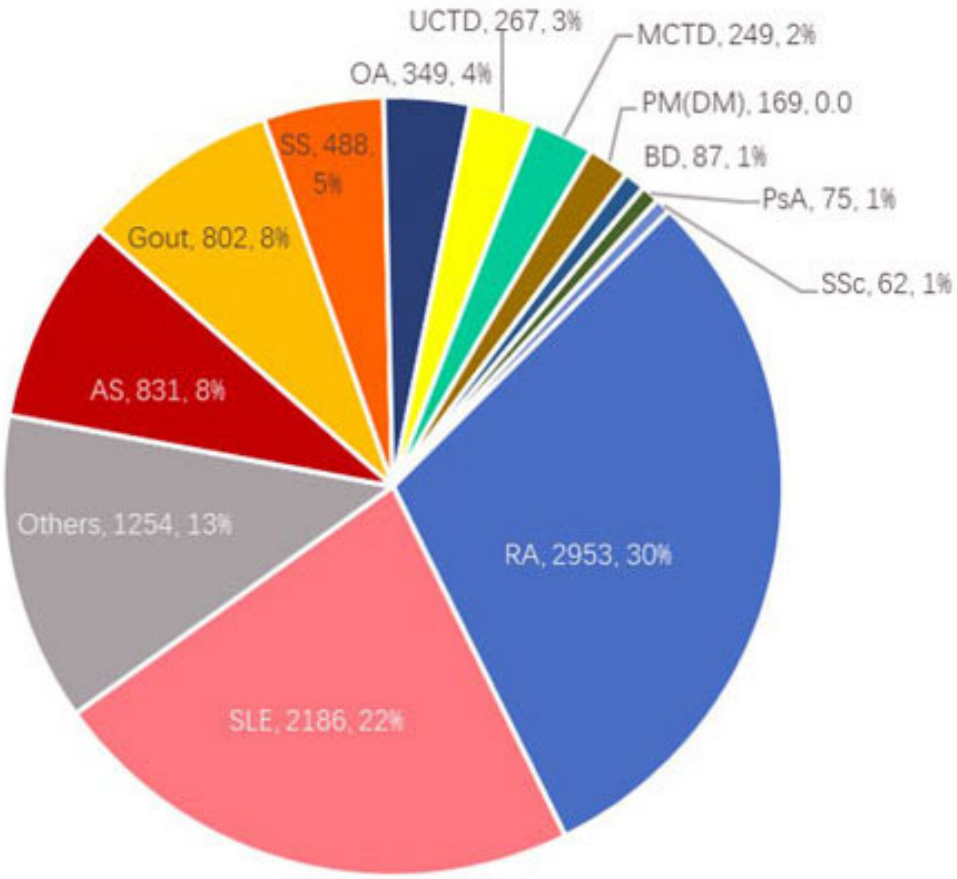


to go to hospital, only need advices from physician. SSDM is a series of APPs for diseases management, which strengthens the interaction between physicians and patients based on valuable data. Our previous study showed that patients could master the SSDM and perform self-management after training.The purpose of this study is to evaluate the feasibility and benefit of improving medical economics and disease activity outcomes in rheumatic patients through online consultation based on SSDM by rheumatologist.

Methods: The rheumatologists implemented the education and training programs on patients in clinic and assisted the patients in downloading the SSDM mobile application. The SSDM includes doctors' and patients' interfaces. The patients' terminal includes serial self-assessments (DAS28, SLEDAI, HAQ), medication management, adverse events and lab data records. After data entry, the data synchronizes to the mobile of the authorized doctor. On the basis of these data, the rheumatologists can accept the request from their follow-up patients and practice consultation through SSDM in the form of text or voice.

Results: From Feb 2015 to May 2019, 729 rheumatologists supplied 9,044 patients (RA 32.7%, SLE 23.7%, AS 9.2%, gout 8.9%, Sjogren syndrome 5.4%, OA 3.9% and other 16.3%) with 13,507 consultations. The diagrams of question type (Figure1) and disease profile (Figure2) were shown in figures. The consulting fee ranged from RMB 0 to 500 yuan (USD: RMB =1: 6.81) each in average of 78.10 ± 45.12 yuan, which matched the registration fee in hospital. The total fee for consultations was 958,584 RMB. 39% patients received online consultation are living in different cities from the rheumatologists. If the patients seek medical care in hospital, in addition to the registration fees and medical expenses, the mean opportunity cost of transportation, accommodation, and lost wages was 874.40 ± 505.21 (200 - 2,800) RMB. The total cost for all patients would have been 11,810,576 RMB, which is 12.3 times more compared with the cost of online consultation. Among 2,913 RA and 1,879 SLE patients with repeat self-evaluations who were followed up for over 90 days, the treat-to-target rate improved from 42.10% to 58.47% (DAS28< =3.2) and from 44.81% to 62.10% (SLEDAI< =4), respectively. Survey shows that satisfaction rate with the consultations is 100%.

Figure2. The diagrams of disease profile.



Conclusion: Through online disease management and consultations using SSDM, Chinese patients with rheumatic diseases enjoy good quality of medical care at lower cost with high satisfaction. Armed with data science, SSDM may supply the rest of world with an option for reshaping the healthcare system.

Disclosure: H. Wei, None; **A. Huang**, None; **L. Luo**, None; **F. Wang**, None; **Q. Li**, None; **H. Zhang**, None; **Y. Wang**, None; **P. Ji**, None; **Y. Zhao**, None; **L. Shen**, None; **Z. Wang**, None; **F. Wei**, None; **T. Xie**, None; **X. Wang**, None; **H. Guo**, None; **Q. Shu**, None; **X. Liu**, None; **R. Du**, None; **A. Zhang**, None; **F. Qin**, None; **B. Wu**, None; **Y. Jia**, None; **H. Xiao**, None; **F. Xiao**, None; **F. Zhang**, GlaxoSmithKline, 9.

Abstract Number: 1114

Survival and Cost of Biologic DMARDs in a Military Medical Center: A Quality Improvement Initiative

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SESSION INFORMATION
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Session Title: Health Services Research Poster II – ACR/ARP
Session Type: Poster Session (Monday)
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Background/Purpose: High drug costs and lack of transparency of these costs is a major concern in the United States. Biologic therapy for rheumatoid arthritis (RA) is expensive, ranging from $7,000 to $203,000 per patient annually. At our institution, the Department of Defense (DoD) negotiated cost for biologic therapies is not readily available to prescribing physicians. Additionally, there is little guidance on the next best therapy in RA treatment if oral DMARD therapy and an initial TNF inhibitor fails. As a Quality Improvement initiative, we investigated the DoD costs of available biologic treatments for RA. We hypothesized that there would be a change in prescribing patterns and substantial cost reductions if rheumatologists had readily available information on biologic medication prices.

Methods: During phase I of this QI project, we conducted a chart review of RA patients on biologics between January 2015 and December 2016. We documented which biologics were used, assigned a monetary cost for each patient, and assessed the overall impact on cost for each biologic therapy switch. Phase II of the project started with a 'cost awareness curriculum.' We acquired and distributed the biologic price-list to Rheumatology clinic personnel. We reviewed the prices and phase I results on a quarterly basis. Fifteen months after implementing the curriculum, we performed a second chart review to document which biologic treatments were utilized.

Results: The Phase I data analysis identified a lower overall use of non-anti-TNF biologic therapies. Among these other biologic therapies, there was an increased use of rituximab ($21,887/4 doses) and abatacept ($29,785/year) over the less costly tofacitinib ($14,633/year). Fifteen months after instituting the 'cost awareness curriculum' we again analyzed the use of biologics. We found that there was increased used of tofacitinib and decreased use of both abatacept and rituximab. This change in practice habits represented a cost savings of $10,232/month or $122,794 over 15 months.

Conclusion: Biologic drugs are now commonly used in Rheumatology, Gastroenterology, Oncology, and many other specialties. In the United States, there is little competition for biologics, but some are less expensive, especially when comparing oral medications to those that require infusions or injections. Drug costs are not transparent and co-pays vary between insurance companies. Physicians often prescribe the drug that is deemed 'first-line' or 'on formulary' by insurance companies. However, as demonstrated here, once empowered with knowledge of drug costs, physicians are able to save the patient and institution money by practicing cost-conscious medical care and choosing the less costly medication. In our clinic, rheumatologists selected the lower cost medication more often following education on the costs of available biologics, saving $122,794 over the 15 month analysis period.

Disclosure: S. Smilow, None; **C. Anderson**, None; **V. Sullivan**, None; **R. Stitt**, None; **P. Mastin**, None; **A. Collamer**, None; **J. Edison**, None.

Abstract Number: 1115

Switching Patterns Among Patients with Chronic Inflammatory Diseases Switching to an Infliximab Biosimilar or Remaining on Originator Infliximab (REMICADE)

Bruno Emond,[1] Kay Sadik,[2] Marie-Hélène Lafeuille,[1] Willy Wynant,[1] Aurélie Côté-Sergent,[1] Patrick Lefebvre,[1] Kimberly Woodruff,[2] and **Timothy Fitzgerald** [3], [1]Analysis Group, Inc, Montreal, QC, Canada, [2]Janssen Scientific Affairs, LLC, Titusville, NJ, [3]Janssen Scientific Affairs, LLC, Horsham, PA

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Background/Purpose: Chronic inflammatory diseases (CIDs) such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), plaque psoriasis (PsO), ankylosing spondylitis (AS), Crohn's disease (CD), and ulcerative colitis (UC) can be managed effectively with biologic agents such as originator infliximab (IFX). Although IFX biosimilars have been approved in the US since April 2016 for the treatment of CIDs, *they* have yet to be designated as *interchangeable.* The impact of switching patients stable on originator IFX to a biosimilar in the US is not well documented. This study compares switching patterns of patients stable on originator IFX switching to an IFX biosimilar (switchers) versus those remaining on originator IFX (continuers).

Methods: Symphony Health Solutions' Patient Transactional Datasets, which includes comprehensive longitudinal US claims data, was used (10/2012–11/2018) to identify adults with ≥2 claims for either RA, PsA, PsO, AS, CD, or UC, and ≥1 claim for originator or biosimilar IFX (Figure 1). The index date (on or after 4/5/2016) was the first IFX biosimilar claim for switchers or a random originator IFX claim for continuers. Pre-index, patients had to be stable on originator IFX (i.e., ≥5 originator IFX claims in the 12 months pre-index). Switchers were matched 1:3 to continuers using propensity score matching adjusted for covariates such as age, gender, and type of CID (full list in Table 1). Post-index switching patterns were compared between switchers and continuers using hazard ratios (HRs), Kaplan Meier (KM) curves, and log-rank tests. Of note, the database didn't include reasons for switching/discontinuation or prescriptions/services received outside of the network.

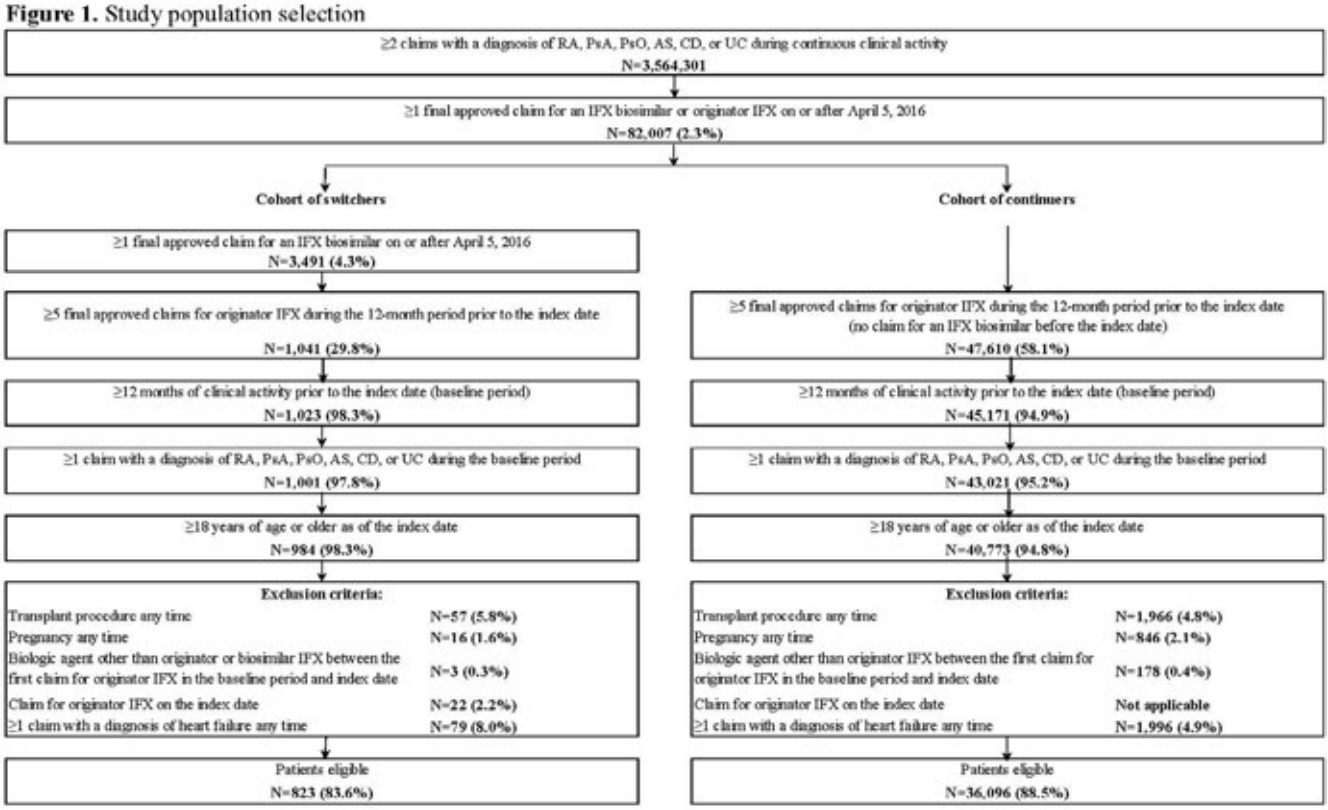
Table 1. Demographic characteristics measured at the index date

	Unmatched sample			Matched sample[1]		
	Patients switching to an IFX biosimilar	Patients remaining on originator IFX	Standardized difference	Patients switching to an IFX biosimilar	Patients remaining on originator IFX	Standardized difference
	N=823	N=36,096		N=823	N=2,469	
Age in years, mean ± SD [median]	57.9 ± 16.2 [61.0]	51.0 ± 16.9 [53.0]	41.7%	57.9 ± 16.2 [61.0]	57.1 ± 16.3 [60.0]	4.9%
Age categories, n (%)						
<35	89 (10.8%)	7,410 (20.5%)	27.0%	89 (10.8%)	260 (10.5%)	0.9%
35-44	100 (12.2%)	5,228 (14.5%)	6.9%	100 (12.2%)	299 (12.1%)	0.1%
45-54	130 (15.8%)	6,780 (18.8%)	7.9%	130 (15.8%)	378 (15.3%)	1.3%
>55	504 (61.2%)	16,678 (46.2%)	30.5%	504 (61.2%)	1,532 (62.0%)	1.7%
Female, n (%)	546 (66.3%)	21,962 (60.8%)	11.5%	546 (66.3%)	1,637 (66.3%)	0.1%
Year of index date, n (%)						
2016	8 (1.0%)	12,816 (35.5%)	100.0%	8 (1.0%)	23 (0.9%)	0.4%
2017	411 (49.9%)	11,612 (32.2%)	36.7%	411 (49.9%)	1,232 (49.9%)	0.1%
2018	404 (49.1%)	11,668 (32.3%)	34.6%	404 (49.1%)	1,214 (49.2%)	0.2%
US Region, n (%)						
South	260 (31.6%)	11,854 (32.8%)	2.7%	260 (31.6%)	781 (31.6%)	0.1%
Midwest	270 (32.8%)	10,286 (28.5%)	9.4%	270 (32.8%)	805 (32.6%)	0.4%
Northeast	76 (9.2%)	8,558 (23.7%)	39.8%	76 (9.2%)	258 (10.4%)	4.1%
West	210 (25.5%)	5,340 (14.8%)	27.0%	210 (25.5%)	606 (24.5%)	2.2%
Unknown	7 (0.9%)	58 (0.2%)	9.7%	7 (0.9%)	19 (0.8%)	0.9%
Type of insurance plan, n (%)						
Commercial	338 (41.1%)	23,889 (66.2%)	52.0%	338 (41.1%)	1,002 (40.6%)	1.0%
Medicare	355 (43.1%)	8,281 (22.9%)	44.0%	355 (43.1%)	1,063 (43.1%)	0.2%
Medicaid	107 (13.0%)	3,161 (8.8%)	13.7%	107 (13.0%)	324 (13.1%)	0.4%
Other	23 (2.8%)	765 (2.1%)	4.4%	23 (2.8%)	80 (3.2%)	2.6%

Notes:

1. Switchers were matched 1:3 to eligible continuers based on the propensity score of switching to an IFX biosimilar. The propensity score was estimated using a multivariable logistic regression, and baseline covariates included age, gender, year of index date, region, type of insurance plan, presence of RA (as an exact match factor), PsA, PsO, AS, CD, UC, inflammatory bowel disease (as an exact match factor), Quan-Charlson comorbidity index, pharmacy and medical costs per month, number of outpatient visits per month, place of service for index claim, and specialty of physician prescribing IFX at index date.

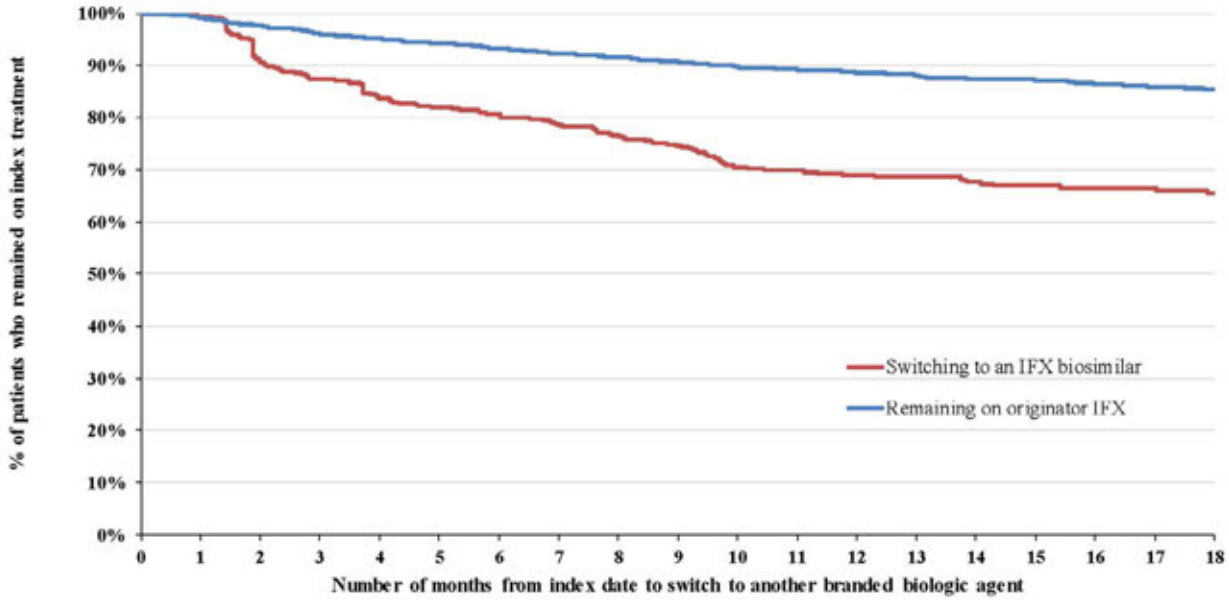
Figure 1. Study population selection



Results: After matching, 823 switchers and 2,469 continuers were included. Among switchers, 44.3%, 33.9%, and 17.4% had RA, CD, and UC, respectively, versus 44.3%, 32.8%, and 18.3% for continuers. Mean age was 57.9 (standard deviation [SD]=16.2) and 57.1 (SD=16.3) years among switchers and continuers, respectively; 66.3% were female in both cohorts (Table 1). Over a mean post-index period length of 350 (SD=197) and 321 (SD=214) days for switchers and continuers, respectively, 211 (25.6%) switchers and 225 (9.1%) continuers switched to another branded biologic agent (HR=2.92; P< 0.001). Of 211 switchers, 82.5% switched back to originator IFX and 17.5% switched to another branded biologic agent. The mean time to switch to another branded biologic agent was 142 (SD=110) days for switchers and 174 (SD=142) days for continuers. The KM rates of switchers and continuers remaining on index treatment were 87.3% and 96.2% at 3 months post-index, 80.8% and 93.4% at 6 months, and 68.9% and 88.7% at 12 months, respectively (all log-rank P< 0.001; Figure 2).

Conclusion: Patients with CIDs switching from originator to biosimilar IFX were almost 3 times more likely to switch to another branded biologic agent compared to patients remaining on originator IFX. Among those who switched to an IFX biosimilar and then to another branded biologic agent, >80% returned to originator IFX, on average within 5 months. Switching to IFX biosimilars should be carefully considered in light of the resulting risk of treatment instability and potential impact on clinical outcomes.

Figure 2. KM curve of time to switch to another biologic agent



KM rates (95% confidence interval)	3 months	6 months	9 months	12 months	18 months
Switching to an IFX biosimilar	87.3% (84.8, 89.5)	80.8% (77.7, 83.4)	74.9% (71.5, 78.1)	68.9% (65.0, 72.5)	66.1% (61.9, 70.0)
Remaining on originator IFX	96.2% (95.3, 96.9)	93.4% (92.2, 94.4)	90.8% (89.3, 92.0)	88.7% (87.1, 90.2)	85.7% (83.6, 87.6)
P-value of log rank test	<0.001	<0.001	<0.001	<0.001	<0.001

Disclosure: B. Emond, Analysis Group, Inc, 3, Janssen Scientific Affairs, LLC, 5; **K. Sadik**, Janssen Scientific Affairs, LLC, 3, Johnson & Johnson, 4; **M. Lafeuille**, Analysis Group, Inc, 3, Janssen Scientific Affairs, LLC, 5; **W. Wynant**, Analysis Group, Inc, 3, Janssen Scientific Affairs, LLC, 5; **A. Côté-Sergent**, Analysis Group, Inc, 3, Janssen Scientific Affairs, LLC, 5; **P. Lefebvre**, Analysis Group, Inc, 3, Janssen Scientific Affairs, LLC, 5; **K. Woodruff**, Janssen Scientific Affairs, LLC, 3, Johnson & Johnson, 4; **T. Fitzgerald**, Janssen Research & Development, LLC, 3, Janssen Scientific Affairs, LLC, 3, Johnson & Johnson, 1, 3, 4.

Abstract Number: 1116

Non-medical Switching from Reference to Biosimilar Etanercept - No Evidence for Nocebo Effect – a Retrospective Analysis of Real-life Data

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Background/Purpose: Real-world data about switching patients from originator product to a biosimilars are important to assess and to document the outcome of switches in clinical practice in order to confirm the low risk of major problems. It has been hypothesized that lack of efficacy and adverse drug events (ADEs) upon switching from reference biologics to biosimilar products are related to the nocebo effect [1]. To evaluate the effectiveness and safety of systematic non-medical switching from innovator etanercept (Enbrel®) to biosimilar etanercept (SB4 (Benepali®)) in adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) in a real-life setting based on different information strategies before switching.

Methods: Data of all adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) who had received innovator etanercept and were switched in our specialized center from innovator to biosimilar etanercept for economic reasons were retrospectively analysed. Whether or not patients were informed about the switch was left to the discretion of the treating physician. Disease activity and function were regularly assessed,

Table 1. Patient characteristics.

	Assessment	Baseline (n=84)	Follow-up 12 weeks (n=81)	Follow-up 24 weeks (n=74)
RA	DAS28	3,1 (1,4)	2,8 (1,0)	3,1 (1,3)
	HAQ	1,2 (0,7)	1,3 (0,7)	1,3 (0,7)
	CRP (mg/dl)	0,5 (0,6)	0,6 (0,8)	0,7 (0,9)
PsA	DAS28	2,9 (1,4)	1,9 (1,4)	2,8 (1,5)
	HAQ	0,8 (0,5))	0,9 (0,9)	0,9 (0,9)
	CRP (mg/dl)	0,4 (0,5)	0,6 (0,6)	0,6 (0,5)
axSpA	BASDAI	4,8 (2,5)	5,0 (2,5)	4,7 (2,4)
	ASDAS	2,6 (1,3)	2,7 (0,9)	2,7 (0,8)
	BASFI	5,3 (2,7)	5,5 (2,7)	4,9 (2,8

*Values are mean ± standard deviation

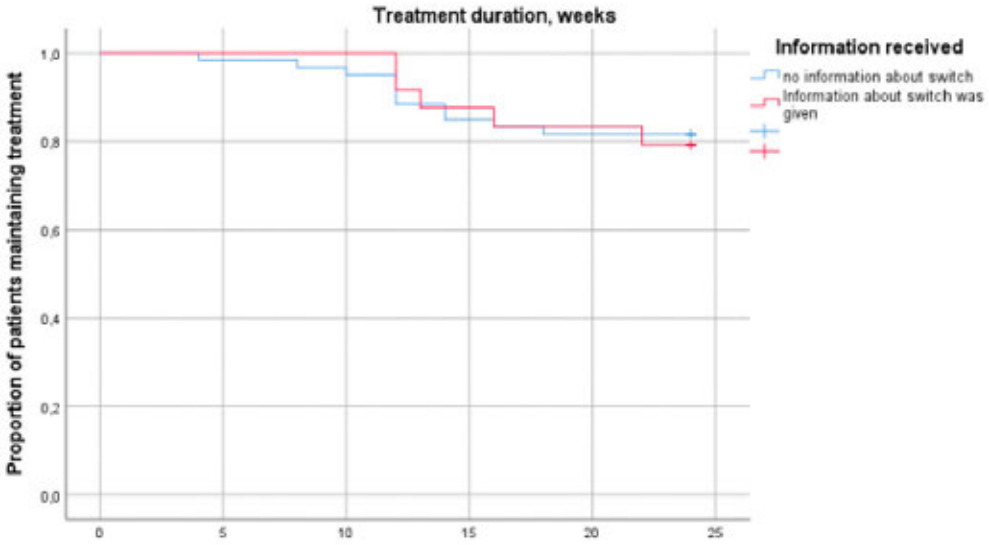

Figure 1. Retention of biosimilar stratified for patients with and without information.

and any changes were recorded in two consecutive visits at week 12 and 24. The scores documented at week 12 week after switching were taken as primary outcome. AEs were documented.

Results: A total of 84 patients were included (44 RA, 25 axSpA and 15 PsA patients), 24 of which had received information about switching (28.5%). The scores at week 12 of both, disease activity and function, remained rather unchanged (Table 1). Whether patients had been informed about switching or not did not influence outcomes or AE. The retention rate of the biosimilar was 96.4% (n=81) at week 12 and 87.6% (n=71) at week 24 (Figure 1). While 7 patients were lost to follow-up, 6 patients discontinued due to inefficacy or AE, including one malignant melanoma. Overall, 18 AEs were reported in 10 patients (12%). In 3 patients (3.6%) who had 5 AEs in the first 12 weeks the innovator was successfully re-administered.

Conclusion: Systematic switch from innovator to biosimilar etanercept was not associated with changes in disease activity or function in all three indications within 12 weeks. This was independent of information on the switch transmitted to the patients.

Disclosure: U. Kiltz, AbbVie, 2, 5, 8, ABBVIE, NOVARTIS, CHUGAI, JANSEN, MSD, UCB, 8, ABBVIE, NOVARTIS, LILLY,BIOCAD, GRUNENTHAL,UCB, 5, ABBVIE, NOVARTIS, PFIZER,BIOGEN, 2, Biocad, 2, 5, Biogen, 2, 5, Chugai, 2, 5, 8, Eli Lilly, 2, 5, Eli Lilly and Company, 5, Grünenthal, 2, 5, 8, Janssen, 8, Jasnssen, 2, 5, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8; **S. Tsiami**, None; **X. Baraliakos**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, BMS, 2, 5, 8, 9, Bristol-Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, 9, Chugai, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Lilly, 2, 8, 9, Merck, 2, 5, 8, MSD, 2, 5, 8, 9, Novartis, 2, 5, 8, 9, Novatis, 2, 5, 8, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9, UCB Pharma, 2, 5, 8, Werfen, 2, 5, 8; **J. Braun**, Abbott, 2, 5, AbbVie, 2, 5, 6, 8, Amgen, 2, 5, 8, Baxter, 2, 5, 8, Biogen, 2, 8, 9, BMS, 2, 5, 8, Boehringer, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Celgene, 2, 3, 5, 8, Celltrion, 2, 5, 8, Centocor, 2, 5, 8, Chugai, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Hexal, 2, 5, 8, Janssen, 2, 5, 8, Johnson & Johnson, 2, 5, Medac, 2, 5, 8, MSD, 2, 5, MSD (Schering-Plough), 2, 5, 8, Mundipharma, 2, 5, 8, Mylan, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, Pfizer (Wyeth, Hospira), 2, 5, 8, Roche, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, UCB Pharma, 2, 5, 8.

Abstract Number: 1117

Government Subsidization of Biologic Therapy for Inflammatory Arthritis in a Co-Funded Healthcare Model: A Singapore Experience

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Table 1

Consensus statement on initiation and continuation of a biologic or targeted synthetic disease modifying anti-rheumatic drug for rheumatoid arthritis requiring government subsidization		
	Median agreement score on a 5 point Likert scale† (% with agreement)	Voting round‡
1. A uniform disease activity measure, the DAS28-ESR should be used as the disease activity measure to assess RA activity.	5 (100%)	1
2. The patient must have at least moderate disease activity, defined as DAS28-ESR ≥ 3.2.	5 (100%)	1
3. The patient must have failed 2 csDMARD strategies (including MTX unless contraindicated) at optimal dose; at least one strategy must be a combination.	5 (100%)	2
4. An optimal duration of a strategy should be a minimum of three months.	5 (100%)	2
5. An optimal trial of therapy should include MTX at target dose of 15-20mg/week, unless contraindicated.	5 (90.9%)	1
6. For the first line biologic, approved TNFi, non-TNFi (abatacept, tocilizumab, rituximab) or tsDMARD (JAKi) may be considered, in no particular order of preference.	5 (100%)	2
7. If first line TNFi fails, second line treatment may be another TNFi, non-TNFi or tsDMARD, in no particular order of preference.	5 (100%	2
8. If a first line non-TNFi or tsDMARD fails, second line treatment may be a TNFi or another non-TNFi or tsDMARD.	5 (100%)	2
9. Co-morbidities, pregnancy/lactation and drug safety should be considered when determining treatment strategies and selecting bDMARD/tsDMARDs.	5 (100%)	1
10. A biosimilar may be substituted for the originator drug for better cost-effectiveness.	4 (90.91%)	1
11. All patients on bDMARD/tsDMARDs must have DAS28-ESR documented every three months; bDMARD/tsDMARD therapy may be continued if the patient has at least a EULAR moderate response by six months from commencement.	5 (100%)	1

DAS28-ESR: disease activity score 28-erythrocyte sedimentation rate, csDMARD: conventional synthetic disease modifying anti-rheumatic drug, MTX: methotrexate, TNFi: tumor necrosis factor inhibitor, tsDMARD: targeted synthetic DMARD, JAKi: Janus Kinase inhibitor, bDMARD: biologic DMARD, EULAR: European League Against Rheumatism

† Likert scale of 5 unless otherwise stated, where 1 = strongly disagree, 5 = strongly agree.
‡ Due to the drop out of one respondent, there were 11 respondents in the first voting round and 10 in the second.

SESSION INFORMATION
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Session Title: Health Services Research Poster II – ACR/ARP
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Background/Purpose: Real world utilization of biologic therapy for inflammatory arthritis often falls short of international best practice and is heavily influenced by affordability and national healthcare financing models. Healthcare in Singapore is delivered through a complex mix of regulated compulsory personal savings, limited hospitalization-focused personal and government aided medical insurance, and means-tested government subsidies for selected

Table 2

Consensus statement on initiation and continuation of a biologic disease modifying anti-rheumatic drug for psoriatic arthritis with peripheral joint involvement requiring government subsidization[§]		
	Median agreement score on a 5 point Likert scale[†] (% with agreement)	Voting round[‡]
1. Swollen and tender joint count should be used as the disease activity measure to assess PsA.	5 (100%)	1
2. Patient should have a minimum of three swollen AND tender joints/digits/entheses to be considered for biologic therapy.	N.A (73%)	1
3. Unless contraindicated, patient should have failed two csDMARD strategies at optimal doses for a minimum of three months each to be considered for biologic therapy.	5 (100%)	2
4. For dactylitis/enthesitis, failure of NSAIDs and/or local injection should be documented, if appropriate.	4 (91%)	1
5. For choice of first biologic, TNFi, IL17i, IL12/13i, tsDMARD (JAKi) may be considered.	5 for TNFi, IL17i, tsDMARD (100%) 4 for IL12/23i (100%)	2
6. If first line treatment with TNFi fails, second line may be another TNFi, IL17i, IL12/23i or tsDMARD.	5 (100% for TNFi, IL17i, tsDMARDs; 90% for IL12/23i)	2
7. If a first line treatment with a non-TNFi (IL17i, IL12/23i, tsDMARD) fails, second line treatment may be a TNFi or another non-TNFi.	5 (100%)	2
8. All patients on bDMARD/t1sDMARDs must have response to therapy measured and documented every three months.	5 (73%)	1
9. For continuation of therapy with bDMARD/1tsDMARDs, patient must achieve an adequate response by six months.[¶]	5 (100%)	1
10. Infliximab should be used in combination with methotrexate unless contraindicated.	5 (90%)	1
11. A biosimilar may be substituted for the originator drug for better cost-effectiveness.	4 (91%)	1

N.A: Not applicable, NSAID: nonsteroidal anti-inflammatory drug, IL12/23i: interleukin-12/23 inhibitor, IL17i: interleukin-17 inhibitor

§ For predominantly axial involvement, please refer to the AS/SpA recommendations. These recommendations are not intended to refer to children with PsA or patients with skin psoriasis alone.
¶ As there was no consensus on choice of response criteria (PsARC vs. 20% SJC & TJC improvement vs. either), recommendations from the previous chapter guidelines[1] to use PsARC as the response measure will be retained

Reference: [1]Lahiri M, Teng GG, Cheung PP, et al. (2015) Singapore Chapter of Rheumatologists consensus statement on the eligibility for government subsidy of biologic disease modifying anti-rheumatic agents for the treatment of psoriatic arthritis. Int J Rheum Dis.20:1527-40.

Table 3

Consensus statement on initiation and continuation of a biologic disease modifying anti-rheumatic drug for axial spondyloarthritis requiring government subsidization		
	Median agreement score on a 5 point Likert scale† (% with agreement)	Voting round‡
1. Patients should fulfil either ASAS criteria for spondyloarthritis or modified New York criteria for ankylosing spondylitis.	5 (91%)	1
2. Patients with active disease may be defined by either BASDI ≥4 or ASDAS ≥2.1.	4 (82%)	1
3. Patients should have failed two sequential NSAIDs at maximum tolerated doses for a total duration of at least four weeks and should be participants in an appropriate physiotherapy and exercise program.	5 (82%)	1
4. For patients with peripheral arthritis, sulfasalazine at optimal dose should have been used for at least 12 weeks unless contraindicated.	5 (91%)	1
5. Symptomatic enthesitis should have failed appropriate local treatment.	4 (73%)	1
6. If bDMARD is considered, either TNFi or IL17i may be considered as first line therapy.	5 (100% for TNFi; 70% for IL17i)	2
7. If first line bDMARD fails, switch to either another TNFi or IL17i.	5 (80% for TNFi; 100% for IL17i)	2 for TNFi, 1 for IL17i
8. The choice of bDMARD therapy should take into consideration patients' unique characteristics and the extra-articular manifestations of SpA such as uveitis and inflammatory bowel disease.	5 (82%)	1
9. All patients on bDMARD therapy should have response to therapy measured and documented every three months. For continuation of therapy with bDMARD, patients should achieve an adequate response at six months.	5 (100%)	1
10. Response should be monitored by the disease activity measure used to initiate biologic therapy, and is defined by ASDAS improvement ≥1.1 or BASDI improvement ≥2.0.	5 (100%)	1
11. A biosimilar may be substituted for the originator drug for better cost-effectiveness.	4 (91%)	1
ASAS: Assessment of SpondyloArthritis, BASDI: Bath Ankylosing Spondylitis Disease Activity Index, ASDAS: Ankylosing Spondylitis Disease Activity Score		

clinical indications. We describe our experience in translating current evidence into an applicable framework to guide government funding decisions to facilitate equitable access to biologic therapy.

Methods: A core working group (CWG) searched recently published guidelines of biologic agents in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (AxSpA) developed for best practice use (9 RA, 5 PsA and 4 AxSpA) or reimbursement (2 RA, 4 PsA and 2 AxSpA). Where appropriate, recent primary literature was reviewed and the evidence synthesized in the form of tables. A modified Delphi approach was used and statements were drafted for rating by an expert task force panel (TFP) comprising rheumatologists practicing in the public and

private sectors across Singapore. The TFP independently rated 3 separate sets of draft statements for RA, PsA and AxSpA after consideration of the synthesized evidence. Consensus was reached if there was at least 70% agreement (score of 4 or 5 on a five-point Likert scale). Statements not reaching consensus were discussed in a face to face meeting, and second round of independent voting was done, after rewording and/or editing statements if necessary. Next, government agencies were engaged to adopt the final statements to guide government funding. The guidelines will be disseminated to the relevant pharmaceutical companies to allow them to make informed decisions on drug pricing to be considered favourably in the government tender.

Results: Three sets of consensus statements were derived, pertaining to initiation, choice and continuation of biologic therapy for active RA, PsA or AxSpA (tables 1, 2, 3 respectively). These form an easily applicable framework to be used by practicing physicians and funding authorities.

Conclusion: We describe our experience in formulating evidence-based guidelines within the real-world practice which is heavily influenced by treatment affordability. Lessons learnt in engaging all relevant stakeholders may be applicable to guide nascent subsidization programs in healthcare economies worldwide.

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Abstract Number: 1118

US Community Rheumatologists' Knowledge and Perceptions of Biosimilar Expanded Indication Approval by Extrapolation

Ting-Chun Yeh,[1] Yolaine Jeune-Smith,[1] Eli Phillips,[1] Ajeet Gajra,[1] and Bruce Feinberg[1], [1]Cardinal Health Specialty Solutions, Dublin, OH

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Health Services Research Poster II – ACR/ARP
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To expand treatment options, increase access to life-saving medications, and lower healthcare costs through competition, the US Congress created an abbreviated licensure pathway for biosimilars.[1] Based upon scientific justification including: PK, PD, efficacy, safety, and immunogenicity data, two tumor necrosis factor inhibitor (TNFi) biosimilars were approved for all reference biologic indications (e.g., ankylosing spondylitis, psoriatic arthritis) despite clinical efficacy studies in just one indication (rheumatoid arthritis)[a]—a process known as extrapolation. Non-inferiority trial design for one approved indication and extrapolation based labeling for other indications represent potential barriers to physician adoption of biosimilars. This study aimed to assess community rheumatologists' perceptions and utilization patterns of the two TNFi biosimilars approved and commercialized in the US.

Methods: A live meeting in November 2018 surveyed US-based community rheumatologists regarding their perceptions and utilization patterns of biosimilars. Participants completed a web-based premeeting survey and live queries captured via an audience response system. Physician characteristics and responses were summarized using descriptive statistics.

Figure 1: Rheumatologists' Perceptions on Biosimilar Extrapolation

Would you prescribe a biosimilar in all indications that have been granted approval based on extrapolation?

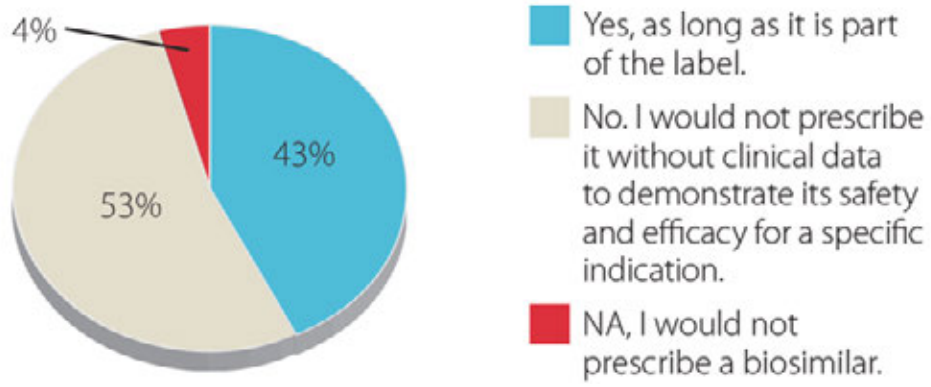
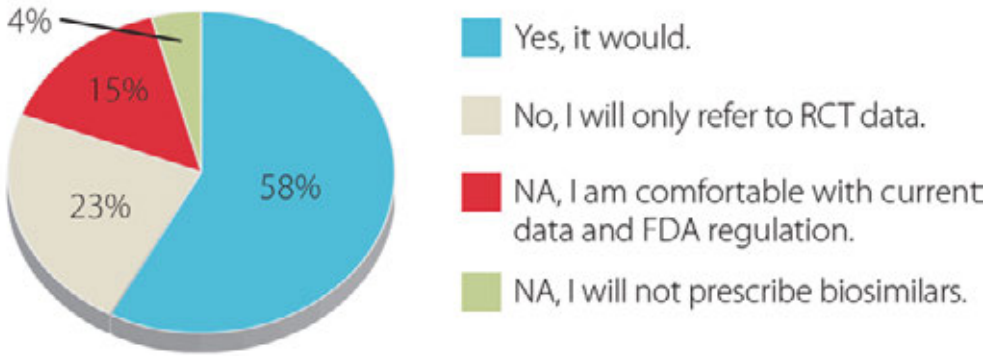


Figure 2: Real-Word Evidence (RWE) and Biosimilar Extrapolation

Would RWE data be sufficient for you to prescribe a biosimilar for an indication approved based on extrapolation?



Results: 54 rheumatologists participated describing their practices as: urban 48%, suburban 45%, and rural 7%. Median years in practice were 19 years (range 3-40). 67% have prescribed biosimilars since being commercially available in late 2016. Regarding their familiarity with biosimilars and the FDA approval process: 34% very familiar, 56% somewhat familiar, and 10% not. A minority of the rheumatologists (15%) expressed comfort with current biosimilar safety/efficacy data and FDA regulation. Regarding extrapolation-based labeling: 53% said they would not prescribe without data for a specific indication (Figure 1). Regarding additional data: 58% indicated that real-world evidence would suffice for an extrapolated indication, while 23% would only accept randomized controlled trials (Figure 2). Participants stated they are most likely to prescribe a biosimilar when it provides cost-savings to the patient or their practice with 48% requiring a 31-50% discount from the reference product for them to consider a biosimilar over the reference biologic. Various concerns remain regarding prescribing a biosimilar, including FDA evaluation process and payer coverage and/or reimbursement for a biosimilar.

Conclusion: The majority of the participating rheumatologists appear to be familiar with biosimilars and its FDA approval process, and they are open to prescribing them, especially when there are cost-savings. Further safety/efficacy data is needed for rheumatologists to willingly expand their use of biosimilars to the indications that were approved based on extrapolation.

[1]FDA.gov

[a]One of the TNFi biosimilars had an additional clinical study in Crohn's disease.

Disclosure: T. Yeh, Cardinal Health, 3; **Y. Jeune-Smith**, Cardinal Health, 3; **E. Phillips**, Cardinal Health, 3; **A. Gajra**, Cardinal Health, 3, ICON plc, 3; **B. Feinberg**, Cardinal Health, 3, 4.

Abstract Number: 1119

Patterns of Medication Use for Patients with Sarcoidosis: Data from the ACR's RISE Registry

Gabriela Schmajuk,[1] Julia Kay,[2] Jing Li,[2] Sonam Choden,[1] Esi Morgan,[3] Jinoos Yazdany,[2] and Andreas Reimold[4], [1]UCSF, SFVAMC Division of Rheumatology, San Francisco, CA, [2]UCSF Division of Rheumatology, San Francisco, CA, [3]Cincinnati Children's Hospital, University of Cincinnati, Cinncinati, OH, [4]Dallas VA and Univ of Texas Southwestern Medical Centers, Dallas, TX

SESSION INFORMATION
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Session Title: Health Services Research Poster II – ACR/ARP
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Background/Purpose: Sarcoidosis results in significant morbidity and mortality but is a generally understudied disease. There are currently no FDA approved drugs for the treatment of extra-pulmonary sarcoidosis, but rheumatologists use a variety of treatment strategies in this patient population. We used the ACR's RISE registry to analyze the spectrum of drugs used to treat sarcoidosis in real-world practice.

Methods: RISE is a national, EHR-enabled registry that passively collects data on all patients seen by participating practices, reducing the selection bias present in single-insurer claims databases. As of December 2017, RISE held validated data from 1,257 providers in 236 practices, representing ~36% of the U.S. clinical rheumatology workforce. Patients included in this study were ≥18 years old, had medication data available, and had ≥ 1 code for sarcoidosis between January 1 2017 and December 31 2017. We identified sarcoid-related disease manifestations during the calendar year including eye, lung, and joint involvement according to validated ICD code definitions. We assessed medication use, including conventional synthetic DMARDs, biologic DMARDs, new synthetic DMARDs, and glucocorticoids during 2017; patients were considered treated if they received ≥ 1 prescription for a drug from a given category.

Results: We found 3791 unique patients with ≥ 1 diagnosis of sarcoidosis from 188 practices. 77% were female; 50% white, 29% black; with mean age 58.2 ± 12.4. Specific manifestations included eye disease (3.6%), lung disease (24.7%), and joint disease (29.9%). Overall, 2094 (55.2%) were treated with at least one DMARD of any type. 13.5% received a biologic or new synthetic DMARD, the most common of which were TNF inhibitors (76.4% of this category; top drugs infliximab and adalimumab), followed by rituximab (5.2%), tofacitinib (5.0%), and abatacept (4.6%). Biologics and new synthetic DMARDs were most often prescribed for patients with joint involvement (see Figure). However, overall, 579 patients (15.3%) were prescribed glucocorticoid monotherapy; 597 (15.7%) were prescribed prolonged glucocorticoid therapy (prednisone 10 mg or equivalent for longer than 90 days). No significant variation was identified according to race, insurance status or geographic region after controlling for specific disease manifestations.

Conclusion: To our knowledge this is the first study to assess patterns of medication use for patients with sarcoidosis seen in U.S. rheumatology practices. Given that there are no approved drugs for extra-pulmonary sarcoidosis, the

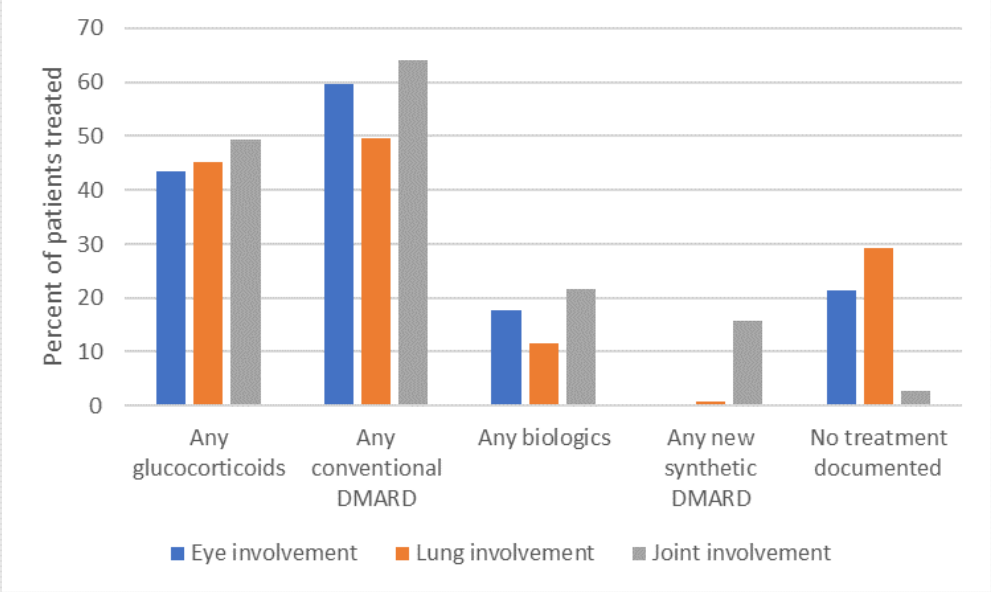

Figure. Percent of patients treated with each drug class, by sarcoid-related disease manifestation.

meaningful use of TNFi suggests that they have become standard of care, especially for the joint manifestations of this disease. Our finding that 15% of patients have prolonged use of moderate or high dose glucocorticoids suggests that there may be a significant need for new drug research and development in this area.

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

Disclosure: G. Schmajuk, None; **J. Kay**, None; **J. Li**, None; **S. Choden**, None; **E. Morgan**, None; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2; **A. Reimold**, Abbvie, 2, Pfizer, 2, Eli Lilly, 5.

Abstract Number: 1120

Prevalence of Burnout in Rheumatology Professionals

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SESSION INFORMATION

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Session Type: Poster Session (Monday)
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Background/Purpose: Burnout among physicians has major implications for health care. We measured prevalence of burnout in a large group of Rheumatology professionals attending a national Rheumatology meeting, using the Maslach Burnout Inventory (MBI)™, and assessed the association of burnout with various professional and personal factors.

Methods: The MBI™, a 22-item questionnaire that includes three domains, emotional exhaustion (EE), depersonalization (DP) and reduced personal accomplishment (PA), was administered to attendees at the Rheumatology Winter

Table: Frequency and percentage of MBI domains demonstrating burnout.

Domains	Freq.	Percent	Cum.
0	63	49.22	49.22
1	26	20.31	69.53
2	29	22.66	92.19
3	10	7.81	100.00
Total	128	100.00	100.00

Clinical Symposium, in February 2019. 128 attendees completed the MBI™ and a demographics questionnaire. Burnout for each domain was defined as EE≥27, DP≥10 and PA≤33**.** IRB waiver obtained from Mercy Hospital IRB. Statistical analysis was performed using Stata V 14 (Plano, TX).

Results: Of the 128 respondents, 51% demonstrated burnout in at least one MBI™ domain. 37.5% of all respondents reported EE burnout, 30.5% DP burnout and 21% PA burnout. 20% had burnout in 1 domain only, 22.7% had burnout in any 2 domains, and 7.8% had burnout in all 3 domains (Table). 34.6% of respondents reported not being happy with their EMR. Practitioners unhappy with their EMR were 2.86 times more likely to burnout (OR=2.86 p=0.015, 95% CI: 1.23-6.65). Compared to people who exercise at least once a week, lack of exercise was associated with a 5-fold increase in burnout. (OR=5.00 p= 0.016, 95% CI: 1.3 - 18.5). Work hours more than 60 hours per week was found to be positively associated with burnout (OR=2.6 p= 0.019, 95% CI: 1.16 -5.6) compared to work hours < 60 per week. Compared to other practice types, practitioners in group practice were 57% less likely to burnout (OR=0.43 p=0.029 95% CI: 0.20-0.92). Practitioners who spend > 20% of their time in work performing activities they find personally satisfying are 68% less likely to report burnout than people who spend less time (OR=0.32 p=0.005 95% CI: 0.15-0.71). Of note, sex, marital status, degree, income and years in clinical practice did not seem to have significant association with burnout in these respondents. There were too few smokers to have any effect. A trend was noted in taking more vacation time (< 3wks), but p-value was not significant (p=0.055). A similar trend toward less burnout in moderate drinkers vs. light drinkers was also noted (p=0.074)

Conclusion: This study confirms the reported high prevalence of physician burnout. The results are in line with the overall reported rate of 54.4% among US physicians showing the deeply pervasive nature of burnout syndrome, even in Rheumatology, which is traditionally considered a “low stress field”.

Reference:

1. Shanafelt TD, Hasan O, Dyrbye LN et al. Changes in burnout and satisfaction with work-life balance in physicians and the general US working population between 2011 and 2014. Mayo Clinic Proceedings. 2015;90(12):1600-1613

Disclosure: V. Tiwari, None; **A. Kavanaugh**, Abbott, 2, Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, 2, Amgen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 2, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, Pfizer Inc, 2, Roche, 2, UCB Pharma, 2; **G. Martin**, None; **M. Bergman**, Abbvie, 5, 8, AbbVie, 5, 8, AbbVie, BMS, Celgene Corporation, Genentech, Janssen, Merck, Novartis, Pfizer, Sanofi, 5, AbbVie, Celgene Corporation, Novartis, Pfizer, Sanofi, 8, Amgen, 5, 8, BMS, 5, 8, Celgene, 5, 8, Genentech, 5, Genentech/Roche, 5, 8, Genentech-Roche, 5, Gilead, 5, GlaxoSmithKline, 8, GSK, 8, Horizon, 5, Janssen, 5, 8, JNJ (parent of Janssen), 1, JNJ stock, 1, Johnson & Johnson, 1, 4, Johnson and Johnson, 1, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sandoz, 5, Sanofi, 5, 8, Sanofi/Regeneron, 5, 8, Sanofi-Regeneron, 5, 8.

Abstract Number: 1121

The Association Between Physician Sex and Faculty Rank Among Academic Rheumatologists in the United States

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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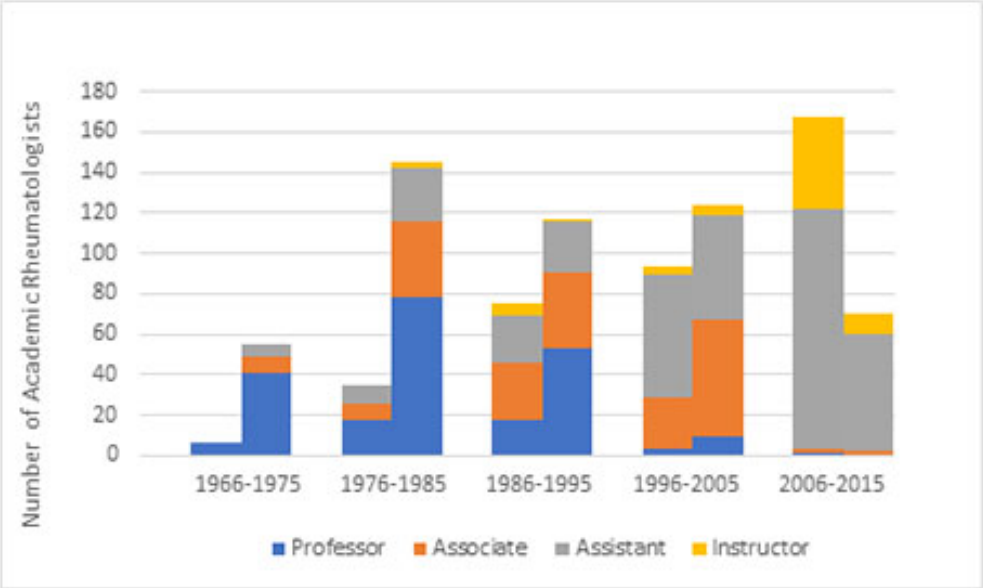
Background/Purpose: In contrast to historical trends, women now comprise more than half of rheumatology fellowship graduates in the United States (US). Differences in academic rank according to sex have been found in some medical specialties. Our objective was to determine the association between sex and academic rankings among US rheumatologists.

Methods: We identified all practicing US rheumatologists in 2015 using a comprehensive database of all licensed US physicians maintained by Doximity, an online physician networking service. This database contains several demographic and professional characteristics of U.S. physicians. Among academic rheumatologists, we determined the

Characteristics of Academic Rheumatologists in the United States

	Overall (N = 941)	Men (N = 551)	Women (N = 390)	P-value
Age (Mean, SD)	52.3 (12.3)	56.8 (11.9)	46.0 (9.7)	< 0.001
Faculty at Top 20 Med School (N, %)	320 (38.1)	184 (35.9)	136 (41.6)	0.096
Age groups, y (N, %)				< 0.001
Age <40	165 (18.4)	41 (7.8)	124 (33.5)	
Age 40-44	132 (14.7)	64 (12.1)	68 (18.4)	
Age 45-49	96 (10.7)	52 (9.9)	44 (11.9)	
Age 50-54	106 (11.8)	54 (10.2)	52 (14.1)	
Age 55-59	121 (13.5)	79 (15.0)	42 (11.4)	
Age 60-64	127 (14.1)	99 (18.8)	28 (7.6)	
Age 65+	151 (16.8)	139 (26.3)	12 (3.2)	
Year Since Residency (Mean, SD)	22.0 (12.9)	26.6 (13.0)	15.7 (9.8)	< 0.001
Faculty Rank (N, %)				< 0.001
Professor	249 (26.7)	200 (36.8)	49 (12.6)	
Associate	220 (23.6)	152 (28.0)	68 (17.5)	
Assistant	387 (41.5)	171 (31.5)	216 (55.5)	
Instructor	76 (8.2)	20 (3.7)	56 (14.4)	
FACR (N, %)	507 (53.9)	300 (54.5)	207 (53.1)	0.678
Publications				
Publication Count (Mean, SD)	20.6 (33.7)	26.4 (39.4)	12.4 (20.8)	< 0.001
Total First or Last Author (Mean, SD)	14.0 (28.9)	18.4 (33.9)	7.8 (17.9)	< 0.001
Any Publication (N, %)	739 (78.5)	449 (81.5)	290 (74.4)	0.009
National Institutes of Health grants				
NIH Grant Count (Mean, SD)	1.3 (3.9)	1.7 (4.4)	0.8 (3.0)	< 0.001
Any NIH Grant (N, %)	164 (17.4)	117 (21.2)	47 (12.1)	< 0.001
Clinical trials*				
Total Clinical Trials (Mean, SD)	0.2 (0.8)	0.2 (0.8)	0.2 (0.8)	0.676
Any Clinical Trial (N, %)	76 (8.1)	50 (9.1)	26 (6.7)	0.182
Total Medicare Volume ($, Mean, SD)	1,879.5 (2,637.4)	2,193.2 (2,961.9)	1,432.3 (2,011.3)	< 0.001

FACR, Fellow of the American College of Rheumatology
*Listed as principal investigator for registered studies on clinicaltrials.gov.



Academic Rank by Residency Graduation Period Among Women and Men

proportions of Professors, Associate Professors, Assistant Professors and Instructors among men and women. We compared sex differences in physician age, years since residency graduation, number of publications (from PubMed), number of National Institutes of Health (NIH) grants, registered clinical trials (from ClinicalTrials.gov), appointment at a top 20 medical school (as ranked by *U.S. News and World Report*), and total Medicare volume (obtained from Centers for Medicare and Medicaid Services). The primary outcome was the odds of being a Full Professor or Associate Professor, and the exposure of interest was sex. We used logistic regression to estimate the odds ratio (OR, 95% Confidence Interval) of Full or Associate professorship (vs Assistant Professor) by sex after adjusting for the above covariates. We also examined faculty rankings by 10-year period of residency graduation among men and women.

Results: Among 6,125 total practicing rheumatologists, 941 (15% overall) had academic faculty appointments in 2015, and 390 were women (41%). Women academic rheumatologists were younger (mean age 46.0 versus 56.8 years, $p< 0.001$) and completed residency more recently (mean 15.7 versus 26.6 years ago, $p< 0.001$) than men. Women had fewer total publications, first or last author publications, and NIH grants (Table 1; all $p< 0.001$). In unadjusted analyses, women academic rheumatologists were less likely to be Professor or Associate Professor than men (OR 0.52 [95% CI: 0.45-0.60]). These differences persisted within 10-year periods of residency graduation ($p=0.015$ for 1986-1995 and $p< 0.001$ for 1996-2005) (Figure 1). In fully-adjusted analyses, women were less likely to be Full or Associate Professors (vs. Assistant Professors) than men (aOR 0.76 [95% CI 0.59-0.99]. However, the adjusted odds of being a Full Professor (vs. Associate Professor or Assistant Professor) were similar among men and women (aOR 1.07 [95% CI 0.78-1.49].

Conclusion: Among academic rheumatologists, women are less likely than men to be Full or Associate Professors. While differences in workforce age explain some of these observations, they persisted within 10-year periods of training completion. To address these disparities, barriers to the advancement of women in academic rheumatology should be addressed, such as differences in research productivity, and how contributions to innovation, research, and education are assessed in academic promotion. As the workforce gender balance shifts in coming years, academic advancement of women in rheumatology should be fostered.

Disclosure: A. Jorge, None; **X. Fu**, None; **D. Blumenthal**, None; **N. Gross**, Doximity, 3; **M. Bolster**, Abbvie, 2, Corbus, 9, Cumberland, 9, Gilead, 5, Johnson & Johnson, 4, Johnson and Johnson, 4, Pfizer, 2; **Z. Wallace**, National Institute of Arthritis, Musculoskeletal, and Skin Diseases, 2, Rheumatology Research Foundation, 2.

Abstract Number: 1122

Factors Impacting Referral of Juvenile Idiopathic Arthritis Patients to a Tertiary Level Pediatric Rheumatology Center in North India

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SESSION INFORMATION

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Background/Purpose: JIA studies demonstrate that there is a "window of opportunity" early in the disease course during which appropriate management improves outcomes: prompt referral to pediatric rheumatology (PR) center is crucial for best results. There are no publications about patient's pathway until first PR visit from India. In this country, the number of JIA is huge: the estimated prevalence ranges from 350 000 to 1.3 million. Health-care costs are paid out of pocket by patients and there is a significant shortage of pediatric rheumatologists (PRsts) with approximately 15 PRst concentrated in urban centres. These parameters are likely to impact referral pathways. This study aimed to describe time from onset of symptoms to first PR visit of JIA patients to a tertiary center in India and to analyze predictive factors for time to referral.

Methods: This retrospective study is from data collected on JIA patients in the PR center, Institute of Child health, Sir Ganga Ram Hospital (SGRH) in New Delhi where both paid (private) and free (poor) patients are seen. JIA patients fulfilling ILAR 2004 criteria and seen at least twice from 01/10/2013 to 30/09/2018 were included. Data collected were: demographic details, history of the disease, referral practitioner, clinical and laboratory features, treatment. Patients

Table 1: Patient's characteristics at first presentation to PR center

	All JIA n=520 (100)	ERA n=247 (47.5)	sJIA n=124 (23.8)	pJIA n=69 (13.3)	oJIA n=68 (13.1)	und.JIA n=10 (1.9)	pso.JIA n=2 (0.4)
Age at first PR visit	10.0 [5.5, 13.2]	12.4 [10.1, 14.7]	6.2 [3.9, 9.9]	8.3 [4.2, 11.8]	5.1 [2.6, 8.6]	7.2 [5.2, 16.0]	6.5 [1.3, 11.6]
Sex female (%)	235 (45.2)	62 (25.1)	59 (47.6)	52 (75.4)	53 (77.9)	7 (70)	2 (100)
Time from symptoms onset to first assessment in PR (months)							
Whole cohort	4.1 [1.8, 15.6]	4.1 [1.5, 17.5]	3.8 [1.5, 11.0]	6.2 [2.8, 18.4]	4.6 [2.5, 14.9]	8.3 [2.2, 21.4]	1.2 [0.6, 1.7]
Patients diagnosed as JIA at first assessment in PR center (group A)	3.3 [1.4, 10.2]	3.1 [1.2, 12.4]	2.4 [1.3, 6.4]	3.5 [1.9, 10.4]	3.9 [2.1, 9.5]	8.3 [2.2, 21.4]	1.2 [0.6, 1.7]
Patients diagnosed as JIA before first assessment in PR center (group B)	13.8 [3.8, 34.5]	11.5 [3.4, 30.8]	13.1 [3.7, 50.0]	18.4 [7.5, 44.8]	19.0 [4.2, 33.8]	0	0
Time from symptoms onset to diagnosis (months)							
Whole cohort	3.3 [1.5, 11.2]	3.1 [1.3, 13.7]	2.4 [1.2, 6.5]	4.1 [2.3, 12.3]	3.9 [2.0, 10.7]	8.3 [2.2, 21.4]	1.2 [0.6, 1.7]
Patients diagnosed as JIA at first assessment in PR center (group A)	3.3 [1.4, 10.2]	3.1 [1.2, 12.5]	2.4 [1.3, 6.1]	3.5 [1.9, 10.4]	3.9 [2.1, 9.5]	8.3 [2.2, 21.4]	1.2 [0.6, 1.7]
Patients diagnosed as JIA before first assessment in PR center (group B)	4.3 [1.5, 15.8]	3.1 [1.4, 17.5]	2.7 [1.0, 9.5]	7.1 [3.8, 17.0]	4.6 [1.2, 15.2]	0	0
Time from symptoms onset to first PR visit <10 weeks (BSPAR guidelines)							
Whole cohort	160 (30.8)	78 (31.6)	47 (37.9)	14 (20.3)	16 (23.5)	3 (30)	2 (100)
Patients diagnosed as JIA at first assessment in PR center (group A)	145 (36.6)	71 (37.4)	41 (45.6)	13 (27.1)	15 (26.8)	3 (30)	2 (100)
Patients diagnosed as JIA before first assessment in PR center (group B)	15 (12.1)	7 (12.3)	6 (17.6)	1 (4.8)	1 (8.3)	0 (0)	0 (0)

Data are presented as frequencies (associated percentages) or as median [interquartile range]

JIA: juvenile idiopathic arthritis; oJIA: oligoarticular JIA; pJIA: polyarticular JIA; sJIA: systemic JIA; ERA: enthesitis related arthritis; psoJIA: psoriatic JIA; UndJIA: undifferentiated JIA; PR: pediatric rheumatology; BSPAR: british society for paediatric and adolescent rheumatology standards of care

Table 2: Comparison between patient's characteristics at first presentation to PR center

	Patients diagnosed as JIA at first assessment in PR center (group A, n=396)	Patients diagnosed as JIA before first assessment in PR center (group B, n=124)	p value
Age at onset (years)	8.7 [4.2, 11.8]	9.3 [5.4, 12.1]	NS
Age at diagnosis (years)	9.7 [4.9, 12.8]	10.0 [6.1, 12.7]	NS
Median time from onset of symptoms to first assessment in PR center (months)	3.3 [1.4, 10.2]	13.8 [3.8, 34.5]	<0.001
Median time from onset of symptoms to diagnosis (months)	3.2 [1.4, 10.2]	4.3 [1.5, 15.8]	NS
Median time from diagnosis to first assessment in PR center (months)	0	3.6 [1.2, 19.3]	<0.001
Musculoskeletal features:			
AJC	3 [1, 6]	4 [2, 8]	<0.01
Hip arthritis	94 (23.7)	28 (22.6)	NS
Cervical involvement	21 (5.3)	13 (10.5)	<0.05
ESR (mm/h)	51.0 [26.0, 82.0]	42.5 [21.3, 63.8]	<0.05
Ongoing treatment			
NSAIDS	125 (31.6)	60 (48.4)	<0.001
Corticosteroids (oral, IV, IM)	44 (11.1)	75 (60.5)	<0.001
Intra articular steroids	1 (0.25)	15 (12.1)	<0.001
DMARDS	0 (0.0)	102 (82.3)	<0.001
Biologics	0 (0.0)	9 (7.3)	<0.001
Alternative medicine	11 (2.8)	2 (1.6)	NS
Non attending to appropriate age school	36 (9.1)	20 (16.1)	<0.05
Referral (group A) or followed (group B)			
Pediatrician	198 (50)	24 (19.4)	<0.001
Adult rheumatologist	75 (18.9)	82 (66.1)	<0.001
General practitioner	8 (2)	0 (0)	NS
Orthopedist	75 (18.9)	18 (14.5)	NS
Self, relative or internet	32 (8.1)	0 (0)	<0.001
Other	8 (2)	0 (0)	NS
Median distance from the PR center (km)	79.6 [19.8, 422.3]	205.0 [39.0, 688.5]	<0.001

Data are presented as frequencies (associated percentages) or as median [interquartile range]
PR: pediatric rheumatology, JIA: juvenile idiopathic arthritis, AJC: active joint count, ESR: erythrocyte sedimentation rate, NSAIDS: nonsteroidal anti-inflammatory drugs, IV: intravenous, IM: intramuscular, DMARDS: disease-modifying anti-rheumatic drugs

Table 3: Association between patients characteristics and symptoms duration at first PR assessment

	Symptoms < 3 months	Symptoms >or= 3 months	p value
Sex female	89 (47.3)	88 (42.3)	NS
Age at first PR visit	9.4 [4.4, 12.4]	10 [5.2, 13.1]	NS
Private OPD	177 (94.1)	183 (88.0)	<0.05
Clinical examination			
AJC	2.5 [1, 5]	3 [1, 7]	NS
LROM	73 (38.8)	97 (46.6)	NS
History of:			
Familial history of inflammatory disease	38 (20.2)	22 (10.6)	<0.05
Joint pain	174 (93.5)	202 (96.2)	NS
Swelling	153 (82.3)	187 (89)	NS
Fever	95 (50.5)	81 (38.9)	<0.05
Rash	34 (18.1)	25 (12)	NS
MAS	5 (2.7)	4 (1.9)	NS
Heel or tibial tuberosity pain	13 (6.9)	16 (7.7)	NS
Inflammatory Back pain	47 (25.3)	53 (25.2)	NS
Morning stiffness	62 (33)	74 (35.7)	NS
Acute uveitis (red eye)	14 (7.4)	6 (2.9)	<0.05
Chronic uveitis (white eye)	25 (13.3)	38 (18.3)	NS
Median distance with the PR center	36.6 [17.6, 263.3]	167.5 [25.6, 529.5]	<0.001
Median ESR (mm/h)	64 [34, 90]	40 [22.5, 71]	<0.001

Data are presented as frequencies (associated percentages) or as median [interquartile range]
PR: pediatric rheumatology, OPD: out patient department, AJC: active joint count, LROM: limitation of range of motion, MAS: macrophage activation syndrome, ESR: erythrocyte sedimentation rate

previously assessed by PRst or with missing data were excluded. Mann-Whitney U-test, Chi square and logistic regression (univariate and multivariate) were used as appropriate to study factors that determined time to first PR visit.

Results: In all 520 patients were included (45% girls, median age 10 years, 71% were systemic JIA patients and enthesitis related arthritis patients (table 1)): 396 children were diagnosed at our PR center (group A), 124 were previously diagnosed as JIA and managed by non PRst before first PR visit (group B). Median time of symptom onset to first assessment in PR was 4.1 months and median distance travelled 119.5 km. Despite ongoing treatment at first PR visit, group B patients had more aggressive disease (active joint count 4 versus 3, $p< 0.01$; cervical involvement 10.5% versus 5.3 %, $p< 0.05$; children non attending to school 16.1% versus 9.1%, $p< 0.05$) and resided further away (205 km versus 79.6 km, $p< 0.001$). For group B patients, predominant referral doctor was adult rheumatologist (66%), for group A- pediatrician (50%) (table 2). On univariate analysis, factors that predicted PRst visit within 3 months were private patients, short distance to travel, family history of inflammatory disease, history of fever, history of acute uveitis or high ESR. On multivariate analysis all factors remained except high ESR.

Conclusion: Time to first PR assessment at this center is comparable to western countries(1). Cost of care and long distance to travel were factors that delayed consultation ; acuity of complaints, short distance to travel, adequate financial resources and a family member with rheumatologic condition hastened referral.

Possible factors to improve referral to PR centres would be to increase the number of PRst and to provide free medical insurance countrywide. Indeed many families can ill afford the travel and cost of care for a child with JIA.

Reference:

1. McErlane F et al. Rheumatology (Oxford). 2016 Jul

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Abstract Number: 1123

Healthcare Factors More Predictive of Smoking Cessation in Patients with Rheumatoid Arthritis Than Patient Characteristics

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Smoking doubles the risk of developing RA, and continuing to smoke after RA diagnosis is associated with worse disease control, treatment failure, and premature mortality. Further, smoking independently contributes to the top three causes of mortality in RA: cardiovascular disease, pulmonary disease, and cancer. Thus, smoking cessation is important for patients with RA. Many sociodemographic and socioeconomic factors are associ-

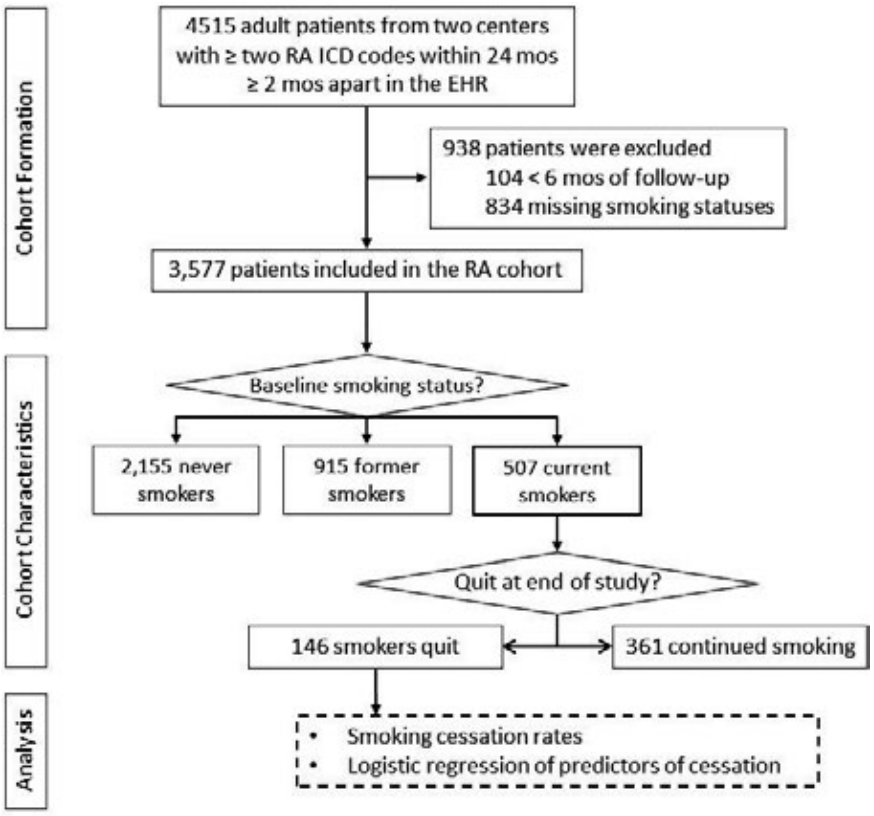

Figure 1. Rheumatoid Arthritis and Current Smokers Cohort Formation and Description.

ated with smoking, but factors that predict cessation, especially in patients with RA or chronic disease, are less clear. Identifying factors that predict likelihood of cessation, and populations that are less likely to quit, can help guide interventions. This study evaluated patient and healthcare factors as predictors of smoking cessation in patients with RA.

Methods: Electronic health record (EHR) data were abstracted for patients with at least one rheumatology and one primary care visit and at least two ICD diagnosis codes for RA at least two months apart from two Midwestern health systems (one rural community, one academic) in 2003-2016. Patients without baseline and end of cohort smoking statuses or without six months of follow-up were excluded. Logistic regression was used to determine predictors of smoking cessation.

Results: Overall, 3,577 patients with RA were included, with 14% (n=507) being current smokers at baseline (Figure 1). Among baseline smokers, 71% were seropositive (Table 1). Males and patients ages 40 to 59 were more likely to be current smokers. Current smokers were more likely to have a pulmonary comorbidity and to see primary care than never smokers (25% vs. 16% and 83% vs. 69% respectively; $p< 0.01$). Black patients were 2.77 times more likely to be current smokers (OR 2.77, CI 1.59, 4.82. $p< 0.01$) and patients who received Medicaid were over 4 times more likely to be smokers (OR 4.17, CI 3.37, 5.15, $p< 0.01$).

In this RA cohort, the overall smoking cessation rate was 5.7% per person year. Patients who were new to rheumatology care had 60% higher odds of quitting than patients already in rheumatology care (Adj. OR 1.60 CI 1.02, 2.50, $p=0.04$; Table 2). Patients in the rural community system were 1.66 times more likely to quit smoking (Adj. OR 1.66, CI 1.03, 2.69, $p = 0.04$). Odds of quitting increased 15% each year of follow-up (Adj. OR 1.15, CI 1.06, 1.25, $p< 0.01$).

Table 1. Patient characteristics by baseline smoking status

		Total Cohort (n=3577) n (%)	Never Smokers (n=2155) n (%)	Former Smokers (n=915) n (%)	Current Smokers (n=507) n (%)	p
Age at Observation	18-39	535 (15.0)	390 (18.1)	62 (6.8)	83 (16.4)	**<0.001**
	40-59	1511 (42.2)	888 (41.2)	330 (36.1)	293 (57.8)	
	60-79	1304 (36.5)	735 (34.1)	443 (48.4)	126 (24.9)	
	80+	227 (6.4)	142 (6.6)	80 (8.7)	5 (1.0)	
Male		941 (26.3)	419 (19.4)	350 (38.3)	172 (33.9)	**<0.001**
Race	White	3361 (94.0)	2020 (93.7)	876 (95.7)	465 (91.7)	**<0.001**
	Black	67 (1.9)	33 (1.5)	13 (1.4)	21 (4.1)	
	Other	149 (4.2)	102 (4.7)	26 (2.8)	21 (4.1)	
Ethnicity (Hispanic)*		49 (1.4)	33 (1.5)	9 (1.0)	7 (1.4)	0.494
Medicaid (ever)		698 (19.5)	328 (15.2)	153 (16.7)	217 (42.8)	**<0.001**
Anti-RF antibodies†		1398 (64.0)	752 (61.5)	378 (65.0)	268 (70.5)	**0.005**
Anti-CCP antibodies†		1317 (50.9)	695 (47.6)	371 (52.7)	251 (59.6)	**<0.001**
Seropositive (either RF or CCP)†		1766 (62.0)	958 (58.7)	489 (64.0)	319 (70.7)	**<0.001**
Cardiac Comorbidity		546 (15.3)	259 (12.0)	224 (24.5)	63 (12.4)	**<0.001**
Pulmonary Comorbidity		729 (20.4)	339 (15.7)	261 (28.5)	129 (25.4)	**<0.001**
Baseline Primary Care		2665 (74.5)	1478 (68.6)	763 (83.4)	424 (83.6)	**<0.001**
Baseline Rheumatology Care		1826 (51.1)	1086 (50.4)	483 (52.8)	257 (50.7)	0.472
System 1: Suburban academic health system		1891 (52.9)	1225 (64.8)	468 (24.8)	198 (10.5)	**<0.001**
System 2: Rural community health system		1686 (47.1)	930 (55.2)	447(26.5)	309 (18.3)	
Follow-up (yrs) (mean±sd)		6.0±3.5	6.7±3.7	4.9±2.7	5.0±2.8	**<0.001**

Due to missing values ^Age at RA diagnosis n=3230, *Ethnicity n=3549, †RF antibody n=2191, CCP antibody n=2594, any antibody n=2856.

Table 2. Models predicting smoking cessation at last follow-up in patients with RA

Explanatory Variable		Unadjusted Odds Ratio (CI)	Adjusted Odds Ratio (CI) (n=442)	p
Age at Observation	18-39	ref	ref	-
	40-59	0.68 (0.40, 1.14)	0.75 (0.42, 1.35)	0.336
	60-79	0.80 (0.45, 1.45)	0.88 (0.45, 1.72)	0.700
	80+	0.47 (0.05, 4.66)	0.44 (0.04, 4.44)	0.488
Male		0.98 (0.65, 1.47)	1.08 (0.68, 1.72)	0.735
Race	White	ref	ref	-
	Black	1.20 (0.47, 3.03)	1.50 (0.54, 4.20)	0.440
	Other	0.25 (0.06, 1.10)	0.17 (0.02, 1.36)	0.095
Ethnicity (Hispanic)		0.98 (0.19, 5.12)	2.47 (0.38, 16.07)	0.344
Medicaid (ever)		0.98 (0.67, 1.45)		
Seropositive (either RF or CCP)		0.58 (0.37, 0.89)	0.57 (0.35, 0.91)	**0.018**
Baseline Primary Care		0.86 (0.52, 1.44)		
New to Rheumatology (no baseline visits)		1.17 (0.79, 1.71)	1.60 (1.02, 2.50)	**0.041**
Cardiopulmonary Comorbidity		0.84 (0.55, 1.26)		
Rural Community Health System		1.33 (0.89, 2.00)	1.66 (1.03, 2.69)	**0.039**
Length of Study Follow-up (years)		1.13 (1.05, 1.21)	1.15 (1.06, 1.25)	**<0.001**

Conversely, seropositive patients were significantly less likely to quit (Adj. OR 0.57, CI 0.35, 0.91; p=0.02). Age, sex, race, ethnicity, and ever receiving Medicaid were not significant predictors of smoking cessation.

Conclusion: Healthcare factors, including health system and being new to rheumatology care, were more predictive of smoking cessation in patients with RA than patient factors, illustrating the importance of healthcare system support in cessation. While all RA patients should receive cessation support, seropositive patients, who are at higher risk for RA progression and mortality, were less likely to quit and may benefit from targeted cessation efforts. Emphasizing smoking cessation after a new RA diagnosis and leveraging system cessation interventions, as done subsequently in the academic system, could improve smoking cessation and outcomes in patients with RA.

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Abstract Number: 1124

The Direct and Indirect Costs of Illness Associated with Systemic Lupus Erythematosus in the USA, UK, France, and Germany: A Structured Review

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Type: Poster Session (Monday)
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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease. SLE tends to peak during prime working years, resulting in a high economic burden due to treatment costs and productivity losses. With the emergence of biologics in the treatment landscape of SLE, there is a renewed interest in understanding the economic burden of SLE. Therefore, the objectives of this study were to: (1) review current evidence on the direct and indirect costs associated with SLE in the USA, UK, France, and Germany; (2) examine the relationship between costs and disease and flare severity; (3) identify gaps in the evidence to inform future research.

Methods: MEDLINE was searched using a combination of cost and SLE-related keywords on November 16, 2018. The search yielded 232 titles and abstracts for screening. The results of the search were cross-checked against an existing systematic review for validation purposes.[1] Only English-language studies published after 2008 with populations from the USA, UK, France, and Germany were included.

Results: Mean annual direct costs in Europe ranged from €3,067 to €4,003 (2011 Euro) compared to $15,000 (2008 USD) to $30,000 (2010 USD) in the USA. Mean annual indirect costs of absenteeism and short-term disability in the USA were reported to be $6,195 and $6,620 (2010 USD), respectively. In the USA studies, medical costs consistently accounted for a greater proportion of the cost burden compared with medication costs, ranging from 65% to 85% depending on disease severity. Within medical costs, inpatient hospitalizations tended to be the primary cost driver. This differed from the European findings where medication costs comprised the largest proportion of total annual costs (UK: 40%, France: 62%, Germany 68%). This difference may be a consequence of when the studies were conducted, as it is unclear whether the use of biologics was captured in the USA studies.

In the USA, higher Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI) scores were associated with increased costs. Direct medical costs were 2.2, 1.3, and 3.4 times higher in severe patients than non-severe patients in UK, France, and Germany, respectively. Each new severe flare increased the total annual direct costs (UK: €650, France: €1,330 [2011 Euro]).

Conclusion: At the time this study was undertaken, there was a limited number of studies examining indirect costs in European countries. Indirect cost data were only available from the USA and most research focused on income loss and work productivity impairment. Little research was found on daily activity loss and caregiver costs. Additional studies aimed at quantifying total costs in SLE are warranted.

Reference:

1. Meacock R, Dale N, Harrison MJ (2013) The humanistic and economic burden of systemic lupus erythematosus. *Pharmacoeconomics* 31 (1): 49-61.

Disclosure: J. Lofland, Janssen Scientific Affairs, LLC, 3; **P. Berry**, Janssen Scientific Affairs, LLC, 3; **F. Pan**, Janssen Scientific Affairs, LLC, 3; **C. Karyekar**, Abbott, 3, BMS, 3, Janssen, 1, 3, Janssen Scientific Affairs, LLC, 3, Novartis, 3; **H. Guiang**, Janssen Scientific Affairs, LLC, 5; **R. McTavish**, Janssen Scientific Affairs, LLC, 5; **M. Thompson**, Janssen Scientific Affairs, LLC, 5.

Abstract Number: 1125

Health Care Resource Utilization and Costs in Patients with Juvenile Idiopathic Arthritis Treated with Abatacept and Other Targeted Disease Modifying Anti-rheumatic Drugs

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SESSION INFORMATION
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Session Title: Health Services Research Poster II – ACR/ARP
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is a common, chronic rheumatic disease of childhood that carries substantial economic impact on patients (pts) and families[1]. The objective of this study was to evaluate the healthcare resource utilization and costs of JIA pts treated with abatacept (ABA) vs. other biologics and targeted disease modifying anti-rheumatic drugs (tDMARDs).

Table1: Baseline Demographic and Clinical Patient Characteristics

	Abatacept Pts (n=26)	Other tDMARDs Pts (n=1,678)	p-value
Age (years) on index date, mean (SD)	13.46 (4.42)	12.09 (4.66)	0.3145
Female, n (%)	23 (88.46%)	1,160 (69.13%)	0.0337
Disease duration (days), mean (SD)	552.26 (576.71)	334.67 (526.23)	0.0108
Comorbidities, n (%)			
Asthma	4 (15.38%)	108 (6.44%)	0.0863
COPD	1 (3.85%)	15 (0.89%)	0.2189
Diabetes	1 (3.85%)	22 (1.31%)	0.2995
Lymphoma	0 (0.00%)	4 (0.24%)	1
Malignancy	0 (0.00%)	7 (0.42%)	1
Uveitis	3 (11.54%)	167 (9.95%)	-
Iridocyclitis *	2 (7.69%)	105 (6.26%)	0.7391
Prior medications, n (%)			
Biologic DMARDs	7 (26.92%)	228 (13.59%)	0.0765
Conventional DMARDs	21 (80.77%)	1,127 (67.16%)	0.142
Corticosteroids	14 (53.85%)	848 (50.54%)	0.7376
NSAIDs	17 (65.38%)	1,048 (62.46%)	0.7595

Table2: Change in HealthCare Resource Utilization Associated with the Initiation of Abatacept vs. Other-tDMARDs

	Abatacept pts (n=26)		Other tDMARDs Pts (n=1,678)		
	BL/FU Pts (N)	Change in number of healthcare service use* per patient, mean (SD)	BL/FU Pts (N)	Change in number of healthcare service use* per patient, mean (SD)	p-value
Inpatient admissions	0/1	0.04 (0.20)	84/54	-0.02 (0.38)	0.2915
Length of stay, days	0/1	0.08 (0.39)	84/54	-0.10 (2.43)	0.2939
Outpatient visits	26/25	-0.12 (7.13)	1,669/ 1,640	-1.60 (7.97)	0.1533
Emergency visits	8/6	-0.08 (1.67)	284/ 222	-0.05 (0.75)	0.1920
Urgent care visits	1/0	-0.04 (0.20)	65/57	0.00 (0.44)	0.5189
Pharmacy visits	25/25	-2.12 (9.48)	1,621/ 1,650	3.16 (5.98)	0.0018
All Cause Healthcare visits	26/26	-2.31 (14.29)	1,676/ 1,671	1.49 (11.19)	0.2426

*Change=(use in post-index period – use in pre-index period), positive difference means an increase in resource use in the follow-up period
BL/FU pts depicts the number of pts having visits in pre-index and post-index period respectively
Other DMARD (TNF and non-TNF) includes adalimumab, golimumab, infliximab, etanercept, certolizumab pegol, tocilizumab, rituximab and tofacitinib

Methods: Pts (age < 18 years) from Truven's MarketScan US Commercial Claims and Encounters claims database with ≥ 2 diagnoses of JIA (ICD-9: 714.3x or ICD-10: M08.xxx) separated by at least one day between 1 July 2006 till 31 March 2018 were split into 2 mutually exclusive cohorts of pts taking ABA vs. other tDMARDs as initial treatment on or after first JIA diagnosis. Index date was defined as the first prescription date for the drugs of interest. Healthcare resource use including inpatient, outpatient, emergency, urgent care visit and pharmacy visits and costs were calculated for the 6 months' pre-index period and post-index period (index date till date of treatment switching, discontinuation, enrollment end or 183 days, whichever is earliest). The other tDMARDs pts were also stratified by TNF vs. non TNF pts. Statistical differences were assessed using chi-square and Kruskal-Wallis tests with significance level of 0.05.

Results: A total of 1,704 pts (26 ABA and 1,678 biologics and other tDMARD pts) were included in the analysis. ABA pts are more likely to be female, have a longer disease duration and had more prior biologic use (Table 1). The num-

Table3: Change in medical costs among patients treated with abatacept and other tDMARDs

	Abatacept pts (n=26)	Non- TNF pts (n=45)	p-value*	TNF pts (n=1,633)	p-value*	All other tDMARDs (non-TNF and TNF) pts (n=1,678)	p-value*
Change in medical cost from pre-index period to post-index period, per patient**							
Inpatient costs	$669.28 ($3,412.68)	-$5,941.52 ($18,118.95)	0.0858	-$362.13 ($11,551.95)	0.3015	-$511.76 ($11,802.25)	0.2937
Outpatient costs	$1,950.85 ($20,277.18)	$21,243.07 ($29,877.39)	0.0099	-$574.82 ($11,469.87)	0.0325	$10.28 ($12,801.55)	0.0461
Emergency costs	-$121.99 ($1,833.94)	-$325.04 ($1,336.97)	0.9559	-$36.65 ($1,002.66)	0.213	-$44.39 ($1,013.62)	0.2264
Urgent care costs	-$5.29 ($26.98)	-$8.14 ($31.19)	0.6542	-$0.35 ($112.80)	0.4933	-$0.56 ($111.41)	0.5139
Pharmacy costs	$2,836.41 ($5,628.26)	-$2,943.06 ($26,178.76)	0.0209	$11,935.02 ($10,079.60)	<.0001	$11,536.02 ($11,074.01)	<0.0001
All Cause costs	$5,329.25 ($21,047.22)	$12,025.31 ($43,753.22)	0.3836	$10,961.05 ($19,271.05)	0.2057	$10,989.59 ($20,289.53)	0.2072

* compared with abatacept patients.
**Change=(costs in post-index period –costs in pre-index period), positive difference means an increase in resource use in the follow-up period
Other DMARDs includes adalimumab, golimumab, infliximab, etanercept, certolizumab pegol, tocilizumab, rituximab and tofacitinib

ber of total healthcare visit decreased by 2.31 per pt in ABA pts but increased by 1.49 per pt in other tDMARD pts. (Table 2) The difference was primarily driven by the change of pharmacy visits (-2.12 per ABA pt vs. +3.16 per other tDMARDs pt) As a result, the increase in the pharmacy related costs for other tDMARDs pts was $5,660.3 more than that in ABA pts (Table 3). The increase of total cost over time was numerically greater in other tDMARD pts, TNF pts and non-TNF pts although the differences were not statistically significant.

Conclusion: Despite a longer disease duration, pts initiated with ABA had a greater decrease in pharmacy visit and related cost in comparison with other tDMARDs pts. Further analysis is warranted to understand the cause of the differences and its implications.

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Abstract Number: 1126

A Medical Assistant Driven Quality Improvement Intervention Increases Rates of DEXA Screening Among RA Patients

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SESSION INFORMATION
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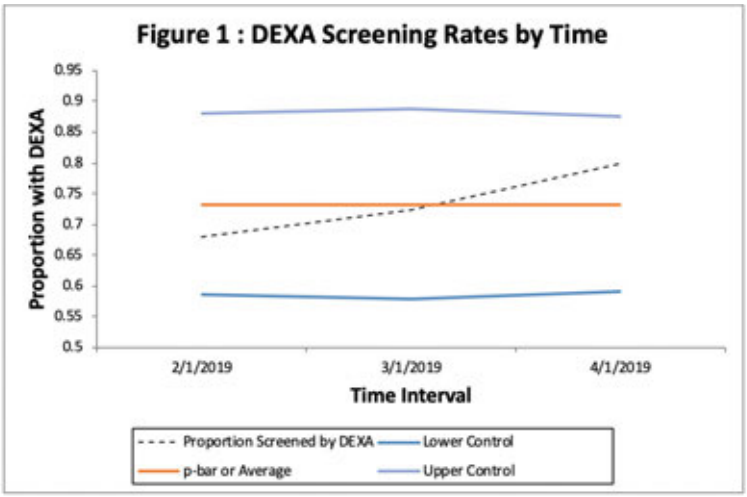
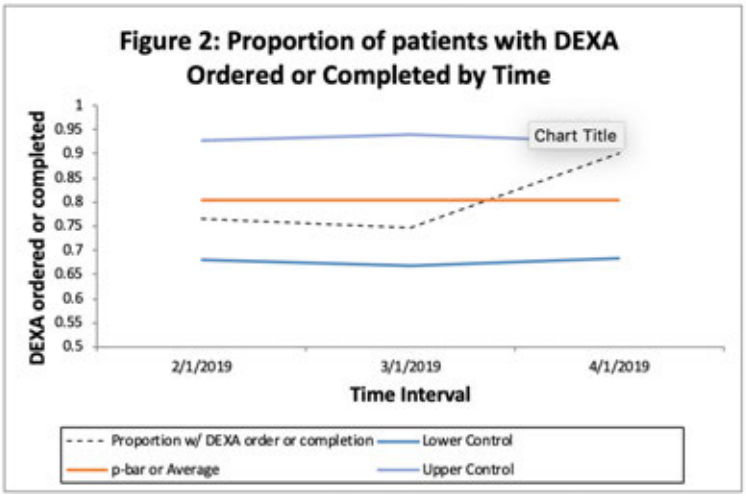
Background/Purpose: Rheumatoid arthritis (RA) patients are at increased risk for developing osteoporosis as compared to the general population, even after controlling for glucocorticoid use[1]. Identification and treatment of osteoporosis are important quality measures for prevention of fragility fractures. The National Osteoporosis Foundation recommends bone mineral density (BMD) testing with dual-energy x-ray absorptiometry (DEXA) starting at age 50 in





patients with significant osteoporosis risk factors, including a history of RA[2]. We used the Institute for Healthcare Improvement (IHI) Model for Improvement to implement and assess osteoporosis screening among rheumatoid arthritis patients seen in our academic rheumatology clinic.

Methods: Performance on DEXA screening was calculated as the proportion of RA patients ≥ 50 years old who had ever received a DEXA since 2012. The proportion of patients with an active DEXA order or completion was also measured. Our multidisciplinary quality improvement team utilized a medical assistant led intervention of pending orders for DEXA in patients meeting the following qualification criteria: age ≥ 50 years, RA diagnosis, no prior DEXA or existing order for DEXA, and at least 2 visits in the rheumatology clinic including one within 6 months. We generated two automated electronic health record reports, one to identify BMD screening candidates and one to measure uptake of orders and DEXA completion. Control charts were used to examine performance of these measures over time.

Results: Our clinic provides care for over 500 patients with RA who are ≥ 50 years old. Prior to the intervention, our baseline osteoporosis screening rate was 70% and the proportion of patients with an active DEXA order and/or completion was 76.5%. After our first Plan-Do-Study-Act (PDSA) cycle intervention, our DEXA screening rate increased to 77.3% and the rate of DEXA ordered and/or completed increased to 90% (Figure 1).

Conclusion: Using an interprofessional quality improvement team we were able to improve performance on DEXA ordering and screening, an important measure of health care quality for patients with RA. We plan to pursue future PDSA cycles in order to achieve a target DEXA screening rate of ≥ 85%.

Disclosure: S. French, None; **J. Ng**, None; **D. Young**, None; **M. Evans**, None; **T. Schmelzinger**, None; **G. Schmajuk**, None; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2; **A. Gross**, None.

Abstract Number: 1127

Interventions to Improve Time to Appointment and Outcome Variables in the Pediatric to Adult Transition of Care in Rheumatology

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SESSION INFORMATION

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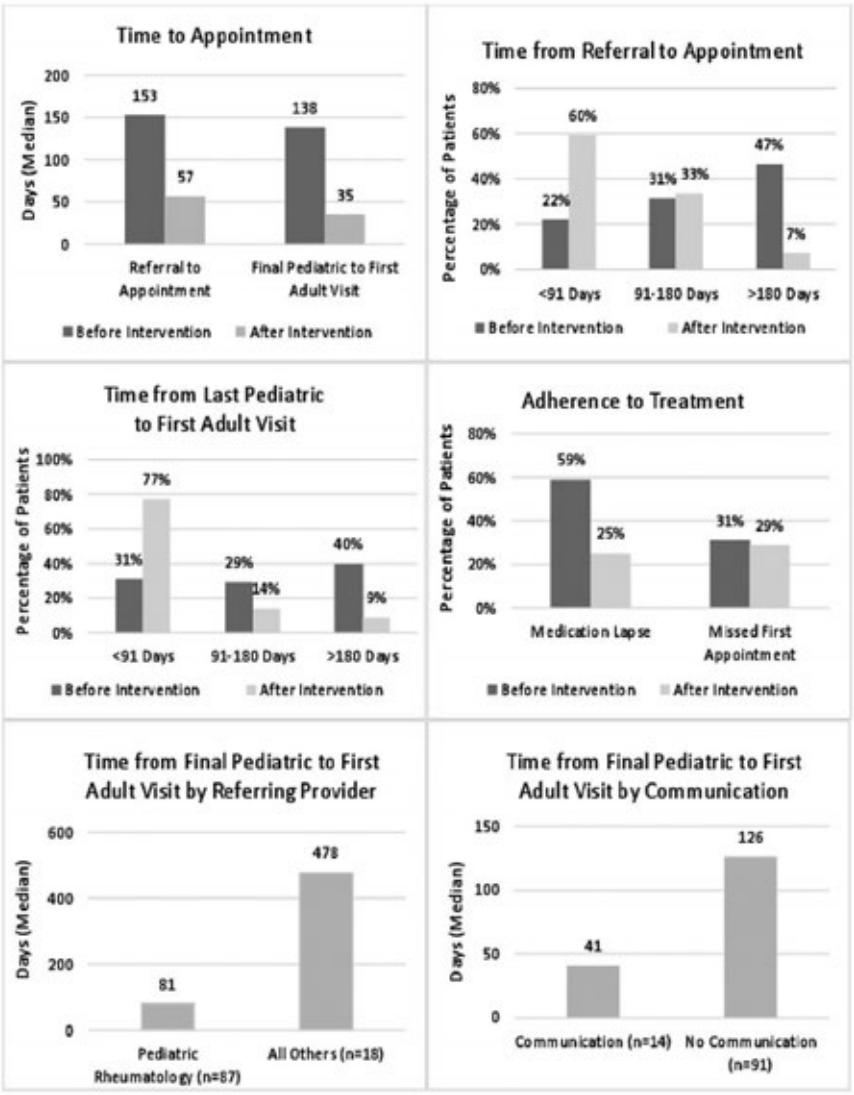
Background/Purpose: The transition from pediatric to adult care is a vulnerable period, in which poor health outcomes are reported amongst youth transferring to adult care. We sought to improve the efficiency of the referral process and established dedicated appointment slots for patients transferring from pediatric to adult care in our large safety-net hospital system.

Methods: A chart review was conducted from eight-six pediatric patients between ages 17 and 21 transitioning to a safety-net adult rheumatology clinic between March 2014 and February 2018 (pre-intervention) and 42 patients from March 2018 to April 2019 (post-intervention). Independent variables included demographic information, diagnoses, referring physician type (pediatric rheumatologist or other), communication between pediatric and adult physicians, and lapse in medical coverage of greater than 30 days between final pediatric and first adult visit. The relationship between these variables and outcomes of interest was analyzed including time between referral and first appointment, time between final pediatric and first adult visit, healthcare utilization between referral and first adult visit including hospitalizations and ED visits, and self-reported medication non-adherence at first visit. Comparisons were made using Chi-square and Mann-Whitney U tests.

Table 1. Demographics of Pediatric Patients Transitioning to Adult Rheumatology Clinic (n=128)

	Before Intervention Number (%)	After Intervention Number (%)	Comparison of Before vs After
Sex			
Female	62 (72)	35 (83)	p=0.16
Male	24 (28)	7 (17)	
Race/Ethnicity			
Hispanic	60 (70)	24 (57)	p=0.27
African-American/Black	14 (16)	11 (26)	
Caucasian	10 (12)	4 (10)	
Asian	2 (2)	3 (7)	
Diagnosis			
Connective Tissue Diseases	47 (55)	22 (52)	p=0.10
Juvenile Idiopathic Arthritis	34 (40)	12 (28)	
Other Rheumatic Diseases	5 (6)	7 (16)	
RDCI Comorbidity Index (Average)	0.95	1.1	p=0.31
Mean Age at Referral			
Referral by Pediatric Rheumatology	18.4 years	18.0 years	p<0.001
Referral by All Others	19.9 years	20.2 years	p=0.37
Referring Provider			
Pediatric Rheumatologist	63 (73)	34 (81)	p=0.34
All Other Providers	23 (27)	8 (19)	
Primary Coverage at Referral			
Coverage:	64 (74)	26 (62)	
Medicaid	11 (13)	1 (2)	p=0.21 (all types of insurance vs no insurance)
Title V Funding (CSHCN)	4 (5)	1 (2)	
Affordable Care Act Plan	2 (2)	7 (17)	
CHIP	1 (1)	3 (7)	
County Funding	4 (5)	4 (10)	
No Coverage			

CHIP: Children's Health Insurance Program; CSHCN: Children with Special Health Care Needs; RDCI (Rheumatic Disease Comorbidity Index)



Results: Pre-intervention, the interval between referral and appointment with adult rheumatology was a median of 158 days, which declined to a median of 35 days post intervention (average 80 days). Interval between final pediatric to first adult visit also declined from a median of 153 days to 57 days post-intervention ($p< 0.01$). As the intervention was based on identifying referrals from the main pediatric rheumatology clinics in the area, those who were not referred to adult care by pediatric rheumatologists continued to have prolonged time to first visit. Hospitalizations and emergency department visits during the interim period between pediatric and adult visits declined significantly, as did self-reported medication non-adherence at first adult visit (from 59% to 25%). Initial missed appointment with adult rheumatology remained unchanged by the intervention.

Conclusion: Youth transitioning into adult rheumatology experience significant delays to first adult rheumatology visit, but dedicated appointment slots and improving the referral process were effective in reducing time to first adult appointment, decreasing health care utilization during the transfer period, and decreasing self-reported medication non-adherence at first visit. It remains important that pediatric rheumatologists ensure they refer all appropriately-aged patients to adult care.

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Abstract Number: 1128

Physician-Patient Interaction and Medication Adherence in Lupus Nephritis

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Background/Purpose: The quality of physician-patient interaction can have a significant impact on medication adherence. Little is known about this relationship in patients with lupus nephritis (LN).

Methods: Cross-sectional, quantitative study. Data collected included demographics, current medication, SLEDAI, medication adherence, beliefs about medicines, shared decision-making (SDM), patient-doctor depth of relationship (PDDR); patient-doctor quality of relationship (PRDQ9), interpersonal trust in a physician (ITP), and illness perceptions.

Results: 98 patients satisfying the American College of Rheumatology (ACR) classification criteria for LN completed the questionnaires. Binary logistic regression indicated that medication adherence was significantly predicted by: (a) ITP (B= 0.85; Wald= 3.94; 95%CI: 1.01, 5.44; p=0.05); (b) timeline cyclical (B= -0.89; Wald= 4.95; 95%CI: 0.19, 0.90 p< 0.05) and beliefs about necessity of medicines (B= 0.75; Wald= 4.14; 95%CI: 1.03, 4.38; p< 0.05). Mediation analysis showed that BMQ_N significantly mediated the relationship between trust and medication adherence when adjusted for age (B= 0.48, CI95%= 0.06, 1.08 p< 0.01). A further mediation analysis showed that PDDR (B= 0.05, CI95%= 0.01, 0.09 p< 0.001), SDM (B= 0.07, CI95%= 0.01, 0.13 p< 0.001) and PDRQ9 (B= 0.08, CI95%= 0.01, 0.16 p< 0.001) significantly mediated the relationship between illness coherence and ITP.

Conclusion: Findings highlighted two key elements: (a) the importance of patient trust in their physician in relation to medication adherence and (b) patients' good understanding of their illness is linked to a better relationship with their doctor and greater participation in shared-decision making which is associated with increased trust. Tailored psycho-educational interventions could contribute to improving the quality of patient-doctor relationship, increase trust and SDM which, in turn, might improve medication adherence in patients with LN.

Disclosure: S. Georgopoulou, None; **L. Nel**, None; **S. Sangle**, None; **D. D'Cruz**, AstraZeneca, Bristol-Myers Squibb, 2, 5, Eli Lilly, Eli Lily, 2, 5, GlaxoSmithKline, 2, 5, Human Genome Sciences, 5, Idorsia, Merck Serono, 2, 5, Pfizer, Roche, 5, TEVA, 2, 5.

Abstract Number: 1129

Direct Medical and Societal Cost of Opioid Use in Symptomatic Knee Osteoarthritis Patients in the United States

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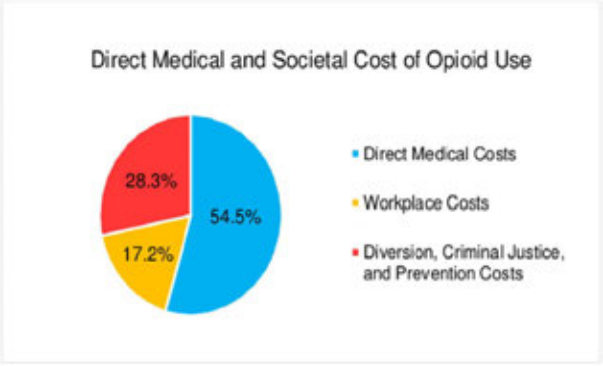
Background/Purpose: Symptomatic knee OA affects 14 million adults in the US. Recent estimates suggest that about 40% of people with knee OA are taking prescription opioids. Opioid use carries substantial societal costs associated with diverted opioid prescriptions and opioid use disorder (OUD), defined by the Diagnostic and Statistical Manual of Mental Disorders IV criteria for abuse and dependence. We sought to estimate the direct medical and societal cost associated with opioid consumption among patients with symptomatic knee osteoarthritis in the US.

Methods: We used a validated, widely published computer simulation model of knee OA (OAPol Model) to estimate lifetime direct medical costs associated with opioid use and the societal costs associated with opioid diversion and OUD in the US knee OA population. The direct medical costs of opioid use included the cost of medication, outpatient visits, and treatment complications including addiction and overdose. Medication, outpatient visit, and non-OUD related complication costs were derived from the 2017 Red Book, Healthcare Cost and Utilization Project, Medicare Physician Fee Schedule, and literature sources. The direct medical cost of opioid addiction and overdose was derived from published literature (Birnbaum 2011) at a per person annual cost of $16,600. Societal costs included diversion and OUD related impacts. The cost of diversion ($200/prescription) and OUD were derived from published literature (Birnbaum 2011). For those experiencing OUD, the per person cost was $17,200 for lost workplace productivity and $3,500 for criminal justice and prevention. Using data from Medicare Current Beneficiary Survey, we estimated the prevalence of opioid addiction, excluding those who overdose, among those with knee OA who had been prescribed opioids to be 0.93%. Using World Health Organization data, we estimated the prevalence of overdose to be 0.77%, resulting in a total estimated prevalence of addiction of 1.7% among knee OA opioid users. We discounted costs at 3% annually.

Results: We estimated 9 million persons have moderate or severe pain due to knee OA; the total lifetime direct medical and societal cost associated with opioid use was $14.8 billion. Direct medical costs of opioids were estimated at $897 per knee OA patient with moderate or severe pain. Societal costs per knee OA patient with moderate or severe pain were estimated at $283 for lost workplace productivity and $465 for diversion/criminal justice/prevention costs. Direct medical costs make up 55% ($8.1 billion) of the total direct medical and societal cost of opioid use in this population (Figure). The societal costs of opioid use due to lost workplace productivity costs make up 17 % ($2.6 billion) of the total cost of opioid use in this population, and diversion/criminal justice/prevention costs 28% ($4.2 billion).



Total cost of opioid use: $14.8 billion

Conclusion: The total direct medical and societal cost of strong opioid use in the US knee OA population is substantial. This could be due in part to the high prevalence of symptomatic knee OA in the US. Close to 50% of the total costs attributed to opioid use in this population is spent on diversion, criminal justice, prevention and work-related expenditures.

Disclosure: J. Huizinga, None; **E. Stanley**, None; **S. Song**, None; **J. Sullivan**, None; **J. Katz**, Flexion, 2, Flexion Therapeutics, 2, Samumed, 2; **E. Losina**, Flexion, 2, Flexion Therapeutics, 2, Pfizer, 2, Pfizer Inc, 2, Regeneron, 5, Regeneron Pharmaceuticals, 5, Roche/Genentech, 2, Samumed, 2, TissueGene, 2, Velocity, 5, Velocity Pharaceutical Development, 5, Velocity Pharmaceutical Development, 5.

Abstract Number: 1130

The Risk of Toxic Retinopathy Among Patients on Hydroxychloroquine

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Background/Purpose: Hydroxychloroquine (HCQ) is widely used in treatment of autoimmune rhuematological diseases. In particular, systemic lupus erythermatosus where it proved to prevent disease flare, reduce organ damage and decrease mortality. Although the drug has a favourable *safety profile however, it has been* associated with increased *risk of* severe retinal toxicity. Recent data has demonstrated that hydroxychloroquine retinopathy might be more common than previously recognized with an overall prevalence of 7.5%.

Table 1

Clinical characteristics of patients with HCQ Retinopathy

	Gender	Age, y	Diagnosis	Dose, mg	Duration, y	eGFR, ml/min	Steroid	Immunosuppression
1	F	51	SLE	400	7	75		
2	F	64	RA	400	8	87		SSZ + MTX
3	F	49	Overlap CTD	400	14	63		
4	F	64	SLE	400	32	65		
5	F	44	SLE	200	12	88	+	AZA
6	F	71	SLE	400	20	74	+	
7	F	59	RA	200	8	102	+	MTX
8	F	35	SLE	400	8	94	+	MTX
9	F	70	RA	200	19	105		MTX
10	F	51	SLE	200	24	75	+	

Note: SLE: Systemic Lupus Erythematosus, RA: Rheumatoid Arthritis, CTD: Connective Tissue Diseases, eGFR: estimated Glomerular Filtration Rate, SSZ: Sulfasalazine, MTX: Methotrexate, AZA: Azathioprine

Aim: To reassess and redetermine the overall prevelance of hydroxychloroquine induced retinopathy.

Methods: We retrospectively reviewed the records of 729 patients who were referred to hydroxychloroquine retinopathy screening clinic in the medical eye unit at St Thomas Hospital, London, UK. The following data were collected: age, gender, body weight, indication to use hydroxychloroquine, dosage, duration of treatment, use of steroids or other immunosuppressive therapy, previous kidney disease, estimated glomerular filtration rate (eGFR) and concurrent use of tamoxifen. The analytic statistics was carried out.

Results: A total of 729 patients (88.6% female and 11.4% male) were seen in HCQ retinopathy screening clinic. All patients were on HCQ with mean duration of 7.6 years. The mean age was 48 ±13.9 years (range 13-89). The main indications for HCQ use were systemic lupus erythermatosus (SLE) 50% and rheumatoid arthritis (RA) 17%. Approximately 34% of the patients were on oral corticosteroids and 46% were on conventional and/or biological disease-modifying antirheumatic drugs (DMARDs). Eight patients were on Tamoxifen. The mean HCQ dose was 260 mg (3.9 mg/kg) and the mean eGFR was 83 ml/min. History of renal diseases (lupus nephritis or chronic kidney disease) were reported in 19%, half of them with eGFR less than 60 ml/min. The average daily consumption of HCQ in patients with eGFR less than 30 ml/min was 1.9 mg/kg. Ten patients found to have definitive HCQ retinopathy with overall prevalence 1.4%. The prevalence increased to 2.8% and 5.4% in patients using HCQ for more than 5 years and 20 years or more, respectively. All were female with mean age of 55.8 years (range 35-76). The average daily dosage for patients with retinopathy was 5.17 mg/kg which was higher than patients with normal retinal exam 3.88 mg/kg (P value = 0.1). The mean duration for HCQ use in patients with toxicity was 15.8 years (range 7-32). Renal impairment or tamoxifen use were not observed in our cohort of patients with retinopathy. We found retinopathy is associated with prolonged duration of HCQ use (P< 0.05). The mean duration of HCQ use was 15.2 years in patients with retinopathy compared to 7.5 years for patients with normal retinal exam. In our study, there were no significant correlation between daily HCQ dosage and retinopathy (P=0.903). This might be attributed to the relatively lower daily HCQ dose used in our patient, especially in patients with low eGFR.

Conclusion: In our study, the overall prevalence of HCQ retinopathy was 1.4%, increased to 5.4% in patients using HCQ for 20 years or more. The risk of retinopathy was linked to the prolonged use of HCQ. Lower dosage (2 mg/kg) was found to be safe in patients with low eGFR.

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Abstract Number: 1131

Loss to Follow-up in Registries of Rheumatic Patients Treated with Biologics: A Potentially Valuable Hidden Real-world Data That Is Being Overlooked?

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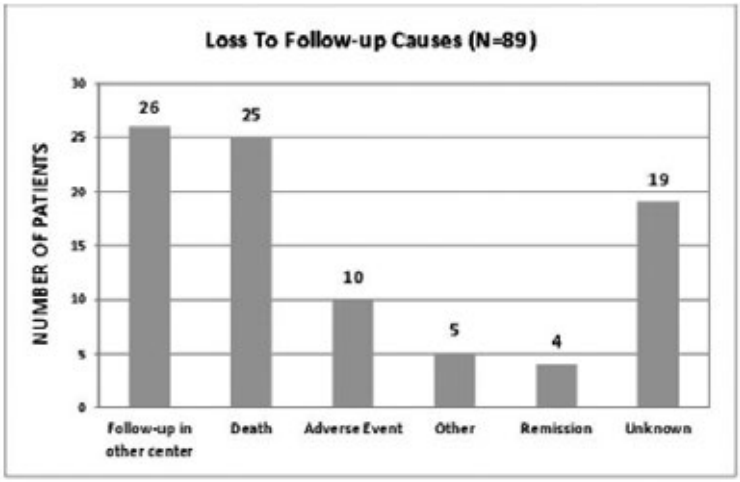
Background/Purpose: The information associated with loss to follow-up (LFU) patients may affect real-world data evaluation of the use of biologics that is not being adequately captured in registries.

Methods: We identified all patients (Pts) treated with biologics in our center who had no registered visits for more than 6 months, in the Rheumatic Diseases Portuguese Register, Reuma.pt.,. We retrieved baseline information from Reuma.pt and from the hospital electronic clinical record. We then performed a telephonic interview to characterize the reasons for LFU at our day care unit. For Pts unable to be contacted by telephone a letter of invitation to an appointment at the hospital was sent.

Results: From a total of 794 Pts registered in Reuma.pt at our center with active biologic therapy 227 did not have any information registered in the last 6 months. Of this, 36 Pts were on biologic therapy prescribed by other Departments (gastroenterology and dermatology) and maintained follow-up in these departments. 102 Pts had suspended biologic administration by medical indication and this information was registered in the hospital electronic clinical records but not updated in Reuma.pt. For 89 Pts no information could be retrieved from either the hospital electronic clinical record or Reuma.pt and we classified these Pts as true LFU.

Tabel 1. Demographic characteristics, diagnosis and biologic therapy of true loss to follow up patient.

POPULATION		TOTAL	FOLLOWED IN OTHER CENTRES	DIED	ADVERSE EFFECTS
		N = 89	N = 28	N = 26	N = 11
DEMOGRAPHIC CHARACTERISTICS	Male gender (%)	29 (32.6%)	11 (39.3%)	7 (28.0%)	2 (20%)
	Age (Y), mean ± SD	51.3 ± 20.0	49.1 ± 15.6	66.2 ± 14.7	51.3 ± 14.8
	Disease duration (Y), mean ± SD	15.7 ± 10.3	8.6 ± 6.7	14.3 ± 10.5	15.42 ± 12.1
	Biologic therapy duration (Y), mean ± SD	5.5 ± 3.5	4.8 ± 3.4	5.9 ± 3.5	6.98 ±2.8
	Previous biologic therapy (N), mean (max-min)	0.59 (0-4)	0.56 (0-2)	0.72 (0-6)	0.56 (0-3)
DIAGNOSIS, N (%)	Rheumatoid arthritis	43 (48.3%)	12 (43.8%)	21 (80.8%)	5 (45.5%)
	Spondyloarthritis	20 (22.5%)	5 (17.8%)	2 (7.6%)	4 (36.4%)
	Juvenile idiopathic arthritis	10 (11.2%)	4 (14.3%)	1 (3.9%)	-
	Psoriatic arthritis	8 (9.0%)	5 (17.8%)	1 (3.9%)	2 (27.3%)
	Autoinflammatory Syndrome	3 (3.4%)	1 (3.6%)	-	-
	Systemic lupus erythematous	2 (2.2%)	-	-	-
	Osteoporosis	2 (2.2%)	-	1 (3.9%)	-
	Vasculitis	1 (1.1%)	1 (3.6%)	-	-
LAST BIOLOGIC, N (%)	Etanercept	21 (24.7%)	9 (32.1%)	7 (26.9%)	2 (18.2%)
	Infliximab	19 (21.4%)	6 (21.4%)	2 (7.7%)	4 (36.4%)
	Adalimumab	14 (15.7%)	3 (10.7%)	6 (23.1%)	1 (9.1%)
	Rituximab	14 (15.7%)	2 (7.1%)	4 (15.4%)	2 (18.2%)
	Tocilizumab	9 (10.11%)	5 (17.9%)	3 (11.5%)	1 (9.1%)
	Golimumab	5 (5.6%)	2 (7.1%)	2 (7.7%)	1 (9.1%)
	Anacinra	3 (3.4%)	1 (3.57%)	-	-
	Abatacept	2 (2.3%)	-	1 (4.0%)	-
	Canakinumab	1 (1.12%)	-	-	-
	Denosumab	1 (1.12%)	-	1 (4.0%)	-



Graphic 1. Identified Causes of loss to follow up.

28 of these LFU Pts were being followed up in another Rheumatology center. The most frequent reasons for this change were: transfer of the follow-up to a newly created and closer Rheumatology Department (15); relocation to another city (6); administrative problems issues related to our Department/Hospital (5) and socio-economic reasons that were interfering with travelling to our department (2).

26 of the LFU Pts died, at a mean age of 66.3 years. The mean disease duration was 14.3 years and 20 Pts had RA. The mean duration of biologics was 5.9 years and 53.8% were under anti-TNF therapy, 16% under Anti-CD20 therapy and 12% under interleukin-6R inhibitors. Cause of death was identified in only 3 Pts: 1 had a myocardial infarction, 2 had complications of surgeries.

11 Pts who were LFU had stopped biologic therapy and abandoned follow-up by their own decision after suffering adverse effects attributed by the Pts to the use of biologics. 6 Pts had infections: cutaneous (n=3) or urinary tract related (n=3; with need for hospital admission in 2 of the cases). The remaining Pts stopped the drug because of cutaneous reactions (n=5).

4 Pts of the LFU were in remission and decided to stop the drug and the medical follow up. All of them believed that the disease was inactive without the need of medical drugs.

We were not able to contact 15 of the LFU pts.

Conclusion: Identifying LFU Pts and clarifying the reason for the loss of data in a register contributes to a better knowledge on strategies to discontinue biologics in stable pts, to a better pharmacovigilance of adverse effects and to more efficiency in data capture by registries. Due to data protection reasons It was impossible to have access to the Pts's death certificates.

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Abstract Number: 1132

Facility-Level Variation in Biologic Disease Modifying Agents for Medicare Enrollees with Rheumatoid Arthritis

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Session Time: 9:00AM–11:00AM

Background/Purpose: Biologic disease modifying agents (DMARDs) are an integral part of rheumatoid arthritis (RA) treatment, but the adoption of infusion-based products has not been reported. We examined Medicare claims to determine the relative market shares for biologic agents in beneficiaries with RA.

Methods: We identified Medicare enrollees with a least one diagnosis code from an inpatient or outpatient claim for RA between 2012-2016. We pulled their Medicare Part B claims (20% Part B sample) for biologic infusions using J-codes. We aggregated procedure claims to the facility level for facilities with at least 50 claims and characterized the distribution of individual biologic agents annually. We report trends in the adoption and reductions in use of agents overall and according to facility size.

Results: There were 27,143 Medicare enrollees with RA: mean age, 68.8 years ± 10.1; white, 86.6%, and black, 7.4%; female, 76.8%. Part B claims for biologics increased 31.3%: Infliximab was most common, though its use dropped from 51.8% to 33.4%; abatacept dropped from 30.6% to 26.0% (Table 1). Tocilizumab, certolizumab and golimumab increased use over time, and rituximab remained consistent (6.8%-7.4%). Biologic use varied significantly by facility size for all agents except infliximab (Table 2). Smaller facilities used more certolizumab (11.2%) and rituximab (11.9%).

Table 1. Annual distribution of claims for Part B biologic agents in Medicare beneficiaries with RA

Biologic agent	2012	2013	2014	2015	2016
Abatacept	30.6%	30.0%	25.5%	25.8%	26.0%
Certolizumab	N/A	N/A	8.7%	11.0%	12.6%
Golimumab	N/A	N/A	3.1%	5.6%	7.3%
Infliximab	51.8%	49.6%	42.2%	37.7%	33.4%
Rituximab	7.3%	7.4%	6.8%	6.8%	6.8%
Tocilizumab	10.2%	13.0%	13.7%	13.2%	14.0%
Number of claims	84,064	87,291	98,047	108,256	110,403

Table 2. Proportion of claims for each biologic by facility claim experience for Medicare beneficiaries with RA (2012-2016)

Biologic claims counts	Small <200	Small-Moderate >= 200 to 500	Moderate >= 500 to 1,000	Large >= 1,000
Abatacept*	24.5% (24.8)	30.6% (20.0)	28.7% (14.6)	26.9% (21.6)
Certolizumab*	11.2% (24.8)	7.3% (13.5)	7.0% (11.1)	5.9% (5.9)
Golimumab*	2.8% (6.7)	3.8% (5.3)	3.6% (4.9)	3.6% (4.3)
Infliximab	40.4% (30.6)	42.1% (21.8)	41.9% (16.4)	43.2% (14.3)
Rituximab*	11.9% (23.5)	4.8% (8.9)	5.3% (6.5)	4.9% (4.6)
Tocilizumab*	9.3% (16.3)	11.4% (13.2)	13.5% (10.9)	15.6% (10.3)
$p < 0.05$ from ANOVA testing means across facility size for each drug				

Conclusion: Office administration of biologic agents for RA has expanded by nearly one-third in 5 years. Infliximab and abatacept lost market share as newer agents were introduced; total share anti-TNF agent remained constant. Further research is needed to determine how facilities select between agents and the impact on patient outcomes.

Disclosure: D. Dalal, None; **T. Zhang**, None; **H. Verma**, None; **T. Shireman**, None.

Abstract Number: 1133

Medicare Spending (2012-2017) on Disease Modifying Agents Commonly Used in Rheumatoid Arthritis

Deepan Dalal,[1] Tingting Zhang,[2] and Theresa Shireman[2], [1]Brown University, Riverside, RI, [2]Brown University, Providence, RI

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Health Services Research Poster II – ACR/ARP
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Biologic disease modifying agents (DMARDs) have become an integral part of rheumatoid arthritis (RA) treatment guidelines, but they are associated with a substantial increase in direct medical care costs. Given Medicare's role in providing health care coverage to older adults, we assessed the impact biologic and conventional DMARDs have had on its drug expenditures.

Methods: We compiled six years (2012-17) of publicly available Medicare spending reports capturing DMARDs expenditures aggregated from Part B (infusions) and Part D (oral) claims. Data included: total expenditures (before rebates), beneficiary counts, and unit drug costs. We distinguished trends at the product level and subclasses, conventional and biologics DMARDs.

Results: Total spending for conventional DMARDs increased from $98 million to $579 million. Expenditures for methotrexate were surpassed by hydroxychloroquine expenditures in 2014-15 (Fig 1). The 6-fold increase in total spending was driven by increase in unit cost of drugs rather than increases in beneficiaries (738,000 to 1.13 million).

Total spending on biologic DMARDs rose from $4.3 billion to $10.0 billion with a more modest increase in the number of beneficiaries (252,225 to 353,960). Adalimumab expenditures rose from $674.8 million (2012) to $2.64 billion (2017): expenditures for etanercept ($1.76 billion) and rituximab ($1.75 billion) were the next highest (Fig 2).

Conclusion: Medicare expenditure for conventional agents increased dramatically but remained a fraction of the total spending (5.7%) on DMARDs when biologic agents were included. Rise in unit drug costs rather than increase in beneficiaries were often responsible for increased total spending. It is important to acknowledge that these products are also used for non-RA indications, and we were unable to account for manufacturers'

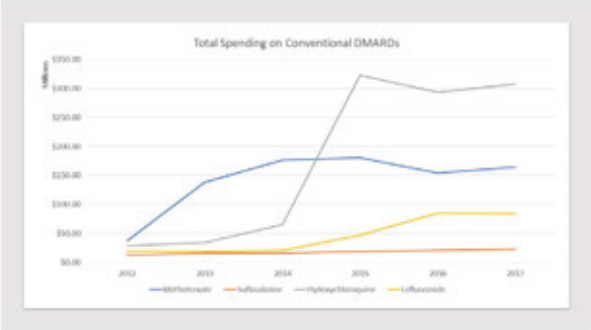

Figure 1. Trends in Medicare spending for conventional DMARDs.

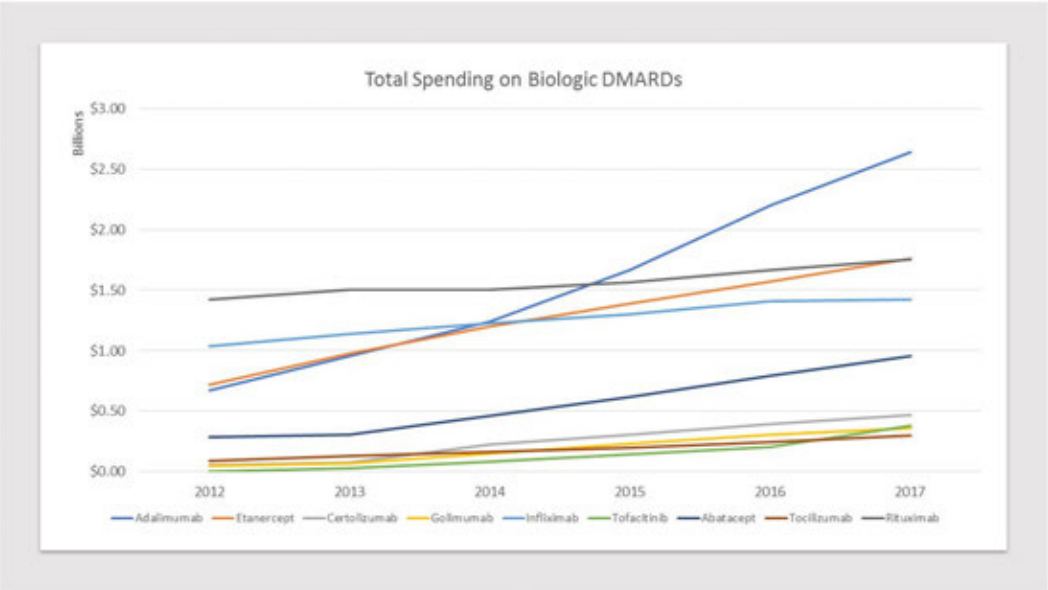

Figure 2. Trends in Medicare spending on biologic DMARDs.

rebates. Further work is needed to determine if increases in DMARD are offset by cost reductions and lead to better patient outcomes.

Disclosure: D. Dalal, None; **T. Zhang**, None; **T. Shireman**, None.

Abstract Number: 1134

Medicaid Spending (2013-2017) on Disease Modifying Agents Commonly Used in Rheumatoid Arthritis

Deepan Dalal,[1] Tingting Zhang,[2] and Theresa Shireman[2], [1]Brown University, Riverside, RI, [2]Brown University, Providence, RI

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Health Services Research Poster II – ACR/ARP
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The management of rheumatoid arthritis (RA) and other conditions have improved tremendously since the introduction of biologic disease modifying agents (DMARDs). However, these agents command a substantial price, adding more $20,000 to direct medical care costs in people with RA. We examined recent trends in Medicaid (public health insurance for low income US citizens) spending on DMARDs in this era of biologics.

Methods: We compiled data from 5 years (2013-17) of publicly available Medicaid spending reports: total expenditures (before rebates), unit costs, and doses dispensed at the product level. Expenditures were summed and compared between conventional and biologics DMARDs.

Results: Spending on conventional DMARDs increased from $24.2 million to $92.3 million (Fig 1): two-thirds was attributable to hydroxychloroquine which experienced a substantial increase in the price/unit ($0.22 to $1.31). Le-

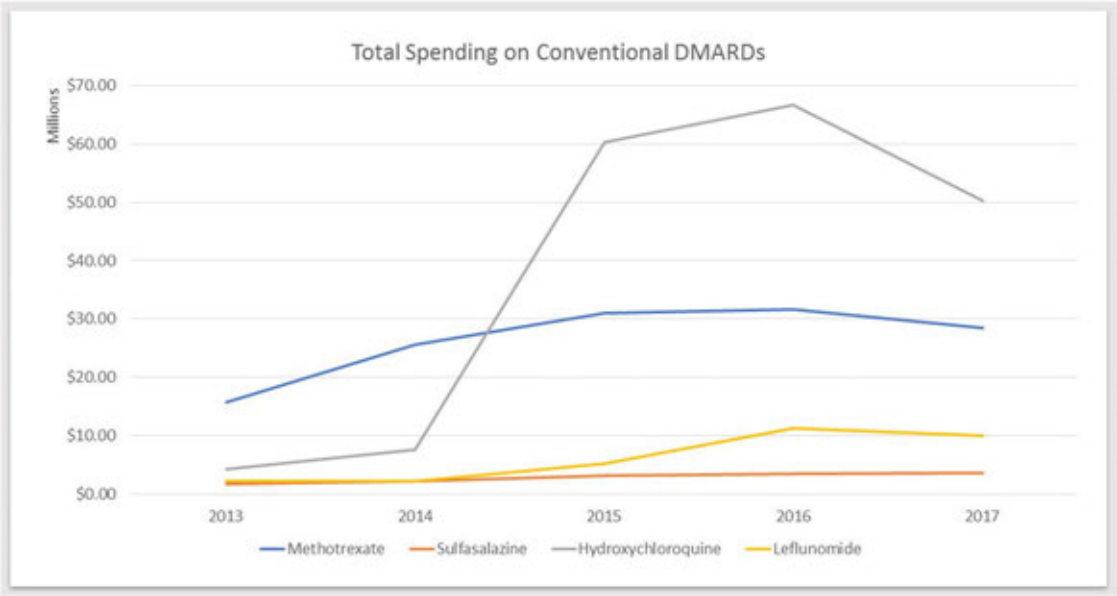

Figure 1. Trends in Medicaid Spending for conventional DMARDs.

flunomide unit costs also more than doubled and spending increased 4.4-fold. Methotrexate and sulfasalazine unit costs were stable.

Spending on biologics increased from $894 million to $3.1 billion: driven by a 5-fold increase in total spending on adalimumab whose cost/unit doubled (Fig 2). Spending on etanercept and infliximab increased more than doubled, unit cost increased by 82% and 45% respectively. Total spending on abatacept increased 5-folds ($19 million to $102 million).

Conclusion: Biologic agents has pushed Medicaid's expenditures for DMARDs from $918.2 million to more than $3 billion in just 5 years. Two conventional DMARDs had substantial unit cost increases, but their expenditure level

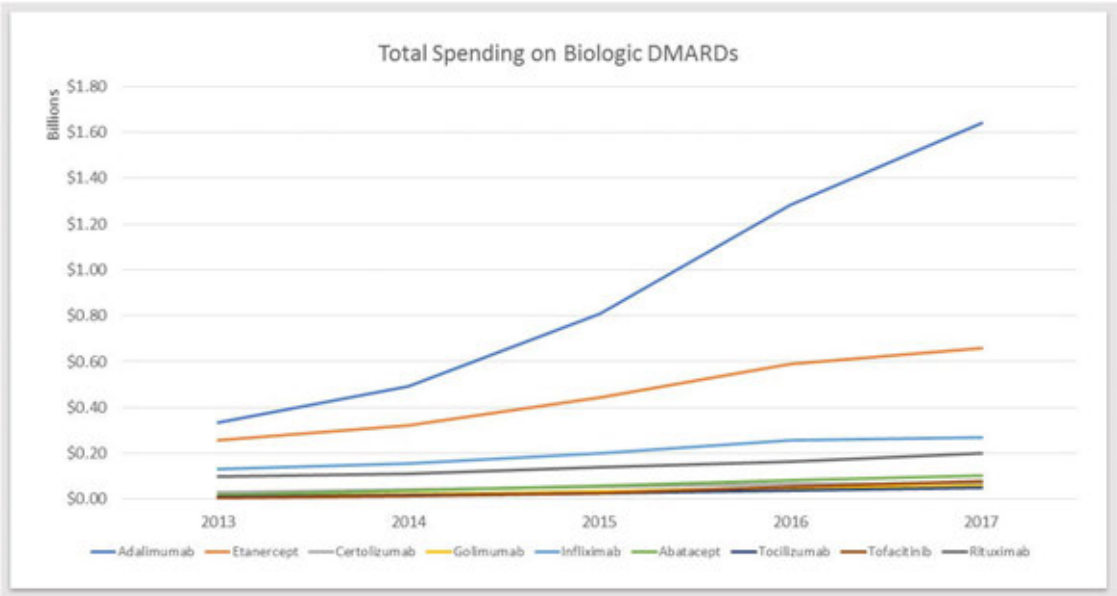

Figure 2. Trends in Medicaid Spending for biologic DMARDs.

remained a fraction (3%) of total DMARD spending. While not all of the biologics were used for RA, these increases should be carefully considered relative to their clinical benefit.

Disclosure: D. Dalal, None; **T. Zhang**, None; **T. Shireman**, None.

Abstract Number: 1135

Optimizing the Management of Flares in Patients with Rheumatoid Arthritis with the Help of Non-Physician Providers: Results of a Randomized Controlled Trial

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Health Services Research Poster II – ACR/ARP
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Background/Purpose: Flares in rheumatoid arthritis (RA) are common. The shortage of readily available specialized care may hinder early detection and timely management of RA flares. Engaging non-physician rheumatology providers in care of RA flares may be beneficial. We aimed to evaluate the effect of a flare management intervention guided by non-physician providers versus usual care between rheumatology visits on flare occurrence and RA disease activity.

Methods: Patients with established RA (2010 ACR/EULAR criteria) were randomized to the intervention arm versus usual care. The Flare Assessment in Rheumatoid Arthritis (FLARE-RA) questionnaire was administered monthly during the 24-month follow-up to all patients in the intervention arm to assess flare status [1]. Telephone nurse-led counseling or an expedited visit with a rheumatology provider was offered to patients in the intervention arm who indicated they were in flare. Patients in the usual care arm were followed by their rheumatology providers according to standards of care. OMERACT9 definition of flare was used to compare flare occurrence between the study arms [2]. All patients completed satisfaction surveys at baseline and at the end of the follow-up.

Results: 150 patients with RA were randomized to intervention (n=75) versus usual care (n=75). At baseline, the majority of patients in the intervention arm (51%) and in the usual care arm (60%, p=0.32) expressed interest in expedited appointments with their rheumatology provider if in RA flare. Patients in the intervention arm completed a median of 8.5 (range 1-24) questionnaires. RA flare was reported on 122 (19%) of these questionnaires; average FLARE-RA score: 2.57 on 0 (no flare) to 10 (maximum flare) scale. Patients agreed to have an expedited clinic visit with a rheumatology provider during 39 (32%) of flares. The majority of patients preferred to self-manage their flare (76, 62%) or receive nursing advice on flare management over the phone 7 (6%). There were no differences in DAS28-CRP, CDAI, SDAI, probability of anti-rheumatic treatment change by rheumatology provider, RA flare by OMERACT9 definition, or remission by CDAI between the study arms over 24-months of follow-up. At the end of the study, a higher proportion of patients in the intervention arm (44%) versus the usual care arm (21%, p=0.04) reported positive effect of participation in the study on the management of RA flares.

Conclusion: The flare management intervention guided by non-physician providers did not have any major effect on RA disease activity metrics over the 24-month follow-up. However, patients in the intervention arm reported a

positive effect of the intervention. More studies are needed to further understand patient preferences for optimal RA flare management and to design interventions to meaningfully address these preferences.

References:

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2. Bingham CO, et al. Developing a standardized definition for disease "flare" in rheumatoid arthritis (OMERACT 9 Special Interest Group). *J Rheumatol* 2009, 36:2335-2341.

Disclosure: E. Myasoedova, Pfizer, 2; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **R. Giblon**, Pfizer, 2; **K. McCarthy-Fruin**, None; **D. Schaffer**, Pfizer, 2; **K. Wright**, Pfizer, 2; **E. Matteson**, Boehringer Ingelheim, 5, Pfizer, 2, Sun Pharmaceuticals, 2; **J. Davis**, Abbvie, 5, Pfizer, 2, 5, Sanofi Genzyme, 5.

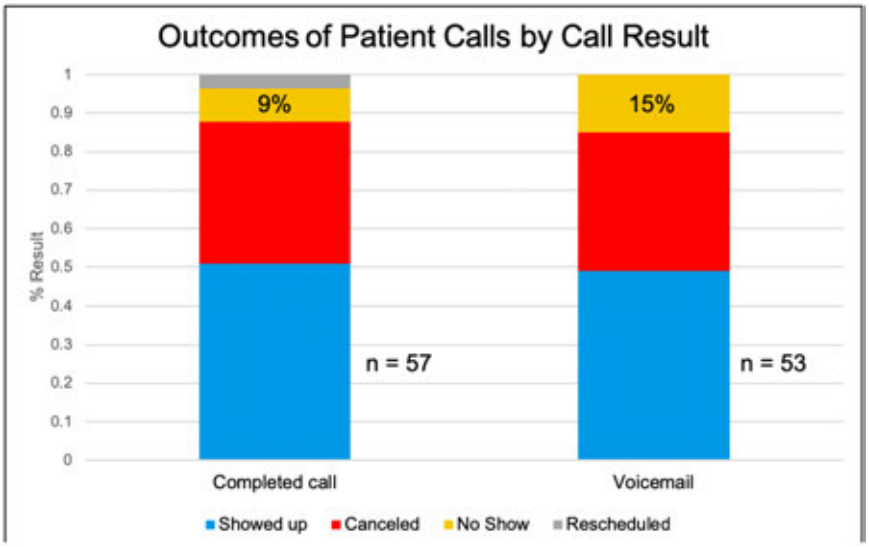
Abstract Number: 1136

Improving Access in an Academic Rheumatology Department by Reducing the No Show Rate

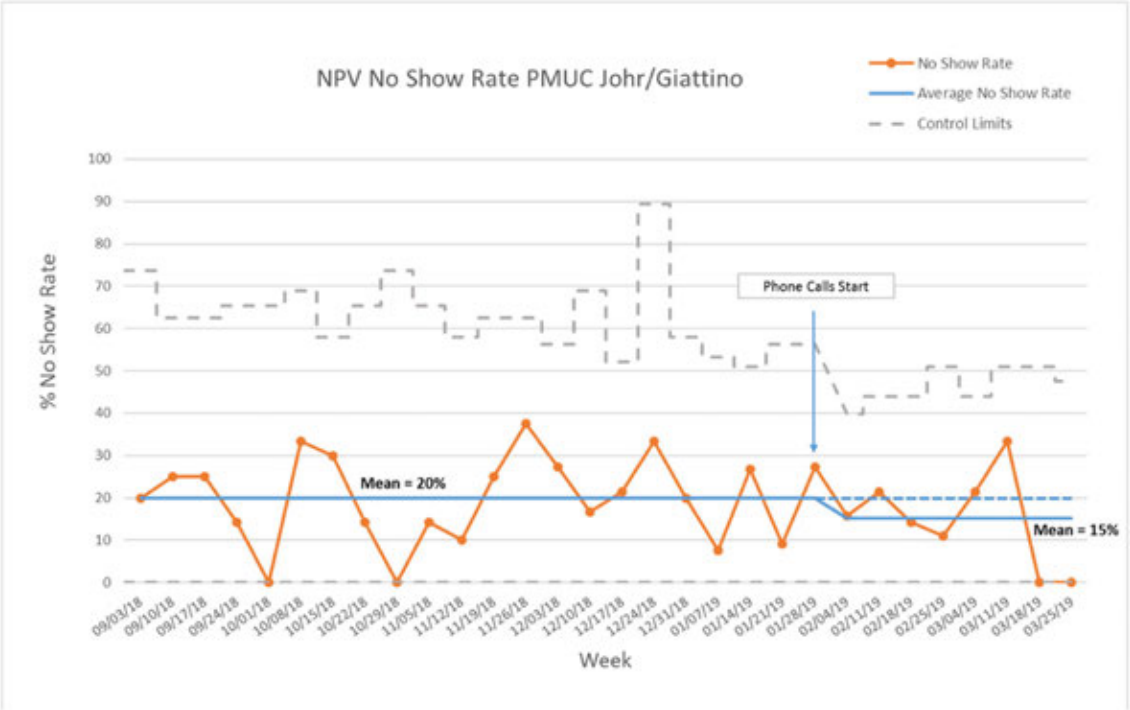
Richard Zamore [1], [1]Hospital of the University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Health Services Research Poster II – ACR/ARP
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: No shows are a widespread problem across medical practices, and lead to negative consequences for patients and providers (Mendel 2017). The rheumatology division at our institution has an access problem, with wait time up to five months for new patient visits (NPVs). NPV no shows lead to wasted resources that negatively impact patient access. A root cause analysis suggested that the most common reason for patients



Results of phone calls, divided by outcome of call.



Statistical process control chart. No show rate for NPVs by week for providers in pilot from September 2018 through March 2019. Dotted line represents continuation of mean and solid line represents non-statistically significant change in mean after intervention.

no showing for NPVs was because they forgot about the appointment. In addition, most patients (54%) reported not receiving a reminder, despite the fact that our institution sends out automated robocalls 48 hours prior to all appointments.

Methods: We used the A3 model to conduct a quality improvement project to decrease the no show rates for NPVs. Baseline no show rates for our four clinical practice sites were determined, and the site with the highest baseline rate (PMUC) was selected for the intervention. We then conducted a pilot of manual phone call reminders two weeks prior to NPVs for two providers at the PMUC practice site. Data was obtained using EMR reports and analyzed using statistical process control charts.

Results: Over the two month trial period, 110 patients were given manual phone call reminders. 57 patients had completed phone calls and 53 patients were left voicemails [Figure 1]. The no show rate for patients who had completed calls was lower than for those who were left voicemails (9% vs 15%) [Figure 1]. The no show rate for NPVs did not significantly decrease during the intervention period [Figure 2]. However, there was a nonsignificant decrease in the NPV no show rate from 20% to 15%. Secondary metrics to evaluate access were then assessed. The number of short term visits, defined as patients who had appointments made within one week of the visit date (typically patients off the waitlist), more the doubled during the intervention period [Table 1]. The total rate of NPVs seen by the two pilot providers increased by 38% [Table 1]. During the intervention period, an extra 0.57 NPVs were seen per provider per full clinic day, correlating with a revenue generation of about $100 per full provider clinical day.

Conclusion: We conducted a QI project that used manual phone call reminders to reduce the no show rate for NPVs at one of our clinical practice sites. While there was no significant decrease in the no show rate, the mean did decrease by 5% during the intervention period. Notably, there were more short term visits and an increase

Giattino-Johr Combined			
Result	Nov-Jan (before)	Feb-Mar (intervention)	Difference
# short term/clinic day*	0.63	1.32	2.11
# NPVs/clinic day	2.98	4.12	1.38
# RPV&REA/clinic day	15.8	16.56	1.05
# Additional NPVs/clinic day per provider:			0.57

*Short term: Appointments made within one week of appointment date; Giattino-Johr: Providers included in pilot; NPV: New patient visit; RPV: Return patient visit; REA: Reassign visit

in the total NPV rate seen during the intervention period, suggesting improved access. The likely reason for the larger increase in access metrics compared to the no show rate is that the intervention resulted in earlier cancellations leading to an increased opportunity to schedule patients in those open appointment slots. Due to institutional policy, we were not able to adapt automated robocalls, and it is not clear if earlier robocalls would similarly lead to an increase in short term visits and improved access. Our QI project suggests that manually calling patients two weeks prior to their NPV appointments may help decrease the no show rate and likely results in improved access. The revenue generated by the increased productivity suggests this a cost-effective and sustainable change.

Disclosure: R. Zamore, None.

Abstract Number: 1137

Predictors of Health-Related Quality of Life in Patients with Musculoskeletal Diseases: A Longitudinal Analysis from an Electronic Health Record Database

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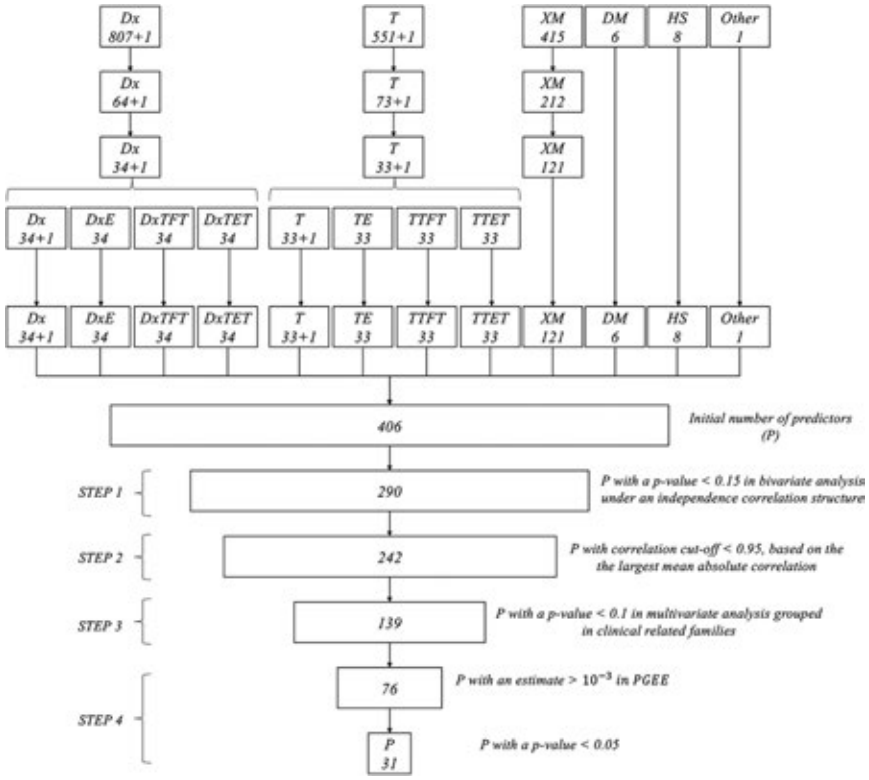
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Health Services Research Poster II – ACR/ARP
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Musculoskeletal diseases (MSKs) are the major cause of disability, affecting the patient's daily activities as well as their Quality of Life (QoL). Our objective is to analyze in a cohort of patients with MSKs the influence of demographic and clinical predictors in repeated measures of Health-Related QoL (HRQoL) obtained from a departamental electronic health record (EHR)

Methods: Patients attending the Hospital Clínico San Carlos rheumatology outpatient clinic (HCSC-MSK cohort) from April 1st, 2007 to November 30th, 2017 who were seen at least twice were included in this study. Our primary outcome was HRQoL collected in each patient's visit using the Rosser Classification Index (it ranges between 0 and



Predictor selection. Dx: Diagnoses. DxE: Diagnoses Episode. DxTFT: Diagnoses Total Follow-up Time. DxTET: Diagnoses Total Episode Follow-up Time T: Treatment. DxE: Treatment Episode. DxTFT: Treatment Total Follow-up Time. DxTET: Treatment Total Episode Follow-up Time. XM: Comorbidities and Concomitant Treatments. DM: Demographics. HS: Health Status.

1, the higher value, the higher HRQoL. It is calculated as the combination of two subscales: disability and distress). Demographic and clinical variables, such as diagnoses, treatments, and comorbidities were included as predictors. Variable selection was carried out in 4 steps. First, we developed a bivariate Generalized Estimating Equations model, selecting those variables with a p-value < 0.15. Second, those with a pair-wise absolute correlation < 0.95 were carried to the next step. Third, multivariate GEE analyses were performed including clinical related variables, and those independently associated with our primary outcome were selected with a p-value < 0.10. Finally, a Penalized GEE was implemented including all selected variables and using an independence correlation structure. Those with an estimate greater than 10^-3 and a p-value lower than 0.05 were considered to be independently associated with the HRQoL.

Results: A total of 19,299 patients with 101,649 outpatient visits were included in this study. From the initial 406 predictors, 290, 242, 139 were selected in the first, second and third steps (Figure 1). After multivariate PGEE analysis, 31 predictors independently associated with HRQoL were identified (Table 1). The predictors with a greater negative impact in HRQoL were the use of 3rd level analgesics and azathioprine, a pressence of kidney failure, fibromyalgia, and ischemic heart disease. Conversely, use of symptomatic slow action drugs for osteoarthritis, statins, lowering uric acid drugs, a diagnoses of mixed connective tissue disease, and better HRQoL in the past six months were independently associated with a positive impact in the HRQoL

Conclusion: We have identified several diagnoses, treatments and comorbidites independently associated with HRQoL in a cohort of patients followed up in a rheumatology outpatient clinic. This represent a first step in the implementation of value-based care for MSK patients, as we can now review the procedures associated with a worse HRQoL in an attempt to improve them.

Table 1 Multivariate penalized generalized estimating equations model analysing the influence of demographic and clinical related variables in the Health-Related Quality of Life of patients with musculoskeletal diseases.

Predictor	Category	Estimate	Robust S.E.	p-value
Analgesic 3rd level	TE	-0,8352256	0,22734746	0,00023898
Kidney failure	XM	-0,7217408	0,35727034	0,04336752
Fibromialgia	Dx	-0,5678731	0,13659076	3,22E-05
DMARDs Azathioprine	TE	-0,4272942	0,19239187	0,02635381
Ischemic heart disease	XM	-0,3444126	0,15864955	0,02993857
Ferrum	TE	-0,3169949	0,15012142	0,03472159
Neurologic disease	XM	-0,3140225	0,15508287	0,0428808
Biphosponates	TE	-0,188373	0,09209149	0,04080572
Analgesic 2nd level	TE	-0,1819801	0,05599111	0,0011534
Osteoarthritis of Knee	DxE	-0,1085494	0,04866939	0,02572469
Ostheoarthritis	DxE	-0,1083128	0,05091817	0,03340399
Occupation	Other	-0,0598987	0,01871537	0,00137184
NSAIDs	TE	0,08362664	0,03408404	0,01414568
Muscle Disorders	DxE	0,09420696	0,03874832	0,01504672
Raynaud Syndrome	DxE	0,10488766	0,05099522	0,03970419
Analgesic 1st level	TE	0,11145647	0,04728277	0,01841173
Hypothyroidism	XM	0,11388635	0,04550861	0,01233115
median547s	DM	0,11491715	0,04067689	0,00472627
Other uterus diseases	XM	0,12221725	0,04664215	0,00878479
Sjögren Syndrome	Dx	0,1237696	0,05981117	0,03851427
Calcium and Vitamin D	T	0,13404955	0,05848901	0,0219128
Oral antidiabetics	XM	0,14670243	0,05837214	0,01196323
Benign prostatic hyperplasia medication	XM	0,16115221	0,07403785	0,02950899
Helicobacter pylori infection	XM	0,1711002	0,05864266	0,00352652
Bio Adalimumab	T	0,17431108	0,07249084	0,01619041
ORL surgeries	XM	0,17868436	0,03921244	5,19E-06
Osteoporosis	Dx	0,18931408	0,07143628	0,00804653
DMARDs Oral Methotrexate	T	0,20543692	0,06650961	0,00200946
SYSADOA	T	0,23475572	0,05240493	7,48E-06
Statins	T	0,24331028	0,0871769	0,00525463
Mixed Connective Tissue Disease	DxE	0,25029787	0,08075475	0,00193859
Lowering uric acid drugs	T	0,48587037	0,12324188	8,07E-05
median182s	DM	0,65651738	0,04062363	9,51E-59
(Intercept)		23,0919422	0,02058523	0

Disclosure: L. Rodríguez-Rodríguez, None; **A. Madrid García**, None; **J. Font Urgelles**, None; **L. León**, None; **D. Freites Nuñez**, None; **C. Lajas**, None; **E. Pato Cour**, None; **J. Jover Jover**, None; **B. Fernández Gutiérrez**, None; **I. Abasolo Alcazar**, None.

Abstract Number: 1138

Outpatient Costs and Evaluation and Management (E&M) Expenditure Trends in Rheumatoid Arthritis (RA) Patients Treated with Biologic Therapies in US Community Practices

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Health Services Research Poster II – ACR/ARP

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: RA is an autoimmune disease affecting over 1.5 million Americans. Biologic disease-modifying antirheumatic drugs (bDMARDs) expanded treatment choices for RA patients (pts) in the last two decades with a significant impact on cost of care. As RA treatment evolves, there is a need for analysis of treatment costs in the modern era, particularly to inform new payment methodologies. As the majority of RA care in the US occurs in the community setting, we evaluated RA-related treatment costs in a community practice cohort.

Methods: Using electronic medical records from 8 large mid-Atlantic rheumatology practices, adult pts with RA diagnosis (International Classification of Diseases 9th revision (ICD- 9) 714, ICD-10 M05, M06) who initiated or switched to a new bDMARD during April 2016-March 2018 were selected. We accounted for cost of care provided by the rheumatology practices including E&M, DMARDs, bDMARDs, steroids, other services including drug administration and labs. Pts were followed for 12 months from initiation of biologic or switch. Annual costs were standardized to 2019 USD using Centers for Medicare & Medicaid Services Average Sales Price, Part D Medication Price, Physician, and Clinical Laboratory Fee Schedules. Comorbidities (comorbids) were assigned based on pt reported medications. Differences between pts with comorbids vs. without were assessed using t-test for continuous variables and chi-square

Table. Patient Characteristics and Costs

	All Pts N=2140	Without comorbidities n=396	With comorbidities n=1744	P-value[1]	PSM[2] without comorbidities n=350	PSM[2] with comorbidities n=350	P-value[1]
Age, mean (SD)	58.7 (13.8)	50.7 (14.4)	60.5 (13)	**<0.001**	51.9 (14.2)	52.5 (13.9)	0.575
Female, n (%)	1686 (79)	291 (73)	1395 (80)	**0.004**	266 (76)	266 (76)	1.000
Race, n (%)				**<0.001**			1.000
White	1531 (72)	265 (67)	1266 (73)		253 (72)	253 (72)	
Black	225 (11)	40 (10)	185 (11)		31 (9)	31 (9)	
Other	71 (3)	35 (9)	36 (2)		14 (4)	14 (4)	
Unknown	313 (15)	56 (14)	257 (15)		52 (15)	52 (15)	
Payer type, n (%)				**<0.001**			0.215
Commercial	861 (40)	214 (54)	647 (37)		197 (56)	197 (56)	
Medicaid	33 (2)	12 (3)	21 (1)		6 (2)	6 (2)	
Medicare	895 (42)	99 (25)	796 (46)		89 (25)	89 (25)	
Self-pay or Copay Assist	210 (10)	47 (12)	163 (9)		38 (11)	37 (11)	
Other	88 (4)	6 (2)	82 (5)		6 (2)	15 (4)	
Unknown	53 (2)	18 (5)	35 (2)		14 (4)	6 (2)	
New on biologic, n (%)	1985 (93)	374 (94)	1611 (92)	0.151	336 (96)	336 (96)	1.000
Received biosimilars, n (%)	22 (1)	3 (1)	19 (1)	0.554	3 (1)	1 (1)	0.316
Top 5 comorbidities, n (%)							
Hypertension	1191 (56)	0 (0)	1191 (68)	**<0.001**	0 (0)	214 (61)	**<0.001**
Psychiatric	872 (41)	0 (0)	872 (50)	**<0.001**	0 (0)	175 (50)	**<0.001**
Infection	446 (21)	0 (0)	446 (26)	**<0.001**	0 (0)	83 (24)	**<0.001**
Asthma/COPD	441 (21)	0 (0)	441 (25)	**<0.001**	0 (0)	82 (23)	**<0.001**
Diabetes	369 (17)	0 (0)	369 (21)	**<0.001**	0 (0)	56 (16)	**<0.001**
Cost PPPM, mean (SD)							
Total cost	55089.7 (62606.2)	49297.5 (52907.0)	56404.8 (64547.1)	**0.021**	47611.7 (49175.2)	47697 (55878.9)	0.983
Labs and other services	1097.2 (1546.2)	887.3 (1380.4)	1142.5 (1576.4)	**0.002**	884 (1373.4)	970.2 (1323.6)	0.430
bDMARDs	52041.6 (59254.7)	46845.9 (50637.5)	53221.4 (60993.5)	**0.030**	45165.5 (46666.5)	44969 (53756.9)	0.959
Other medications	1677.8 (5303.7)	1324.2 (4100.7)	1756.7 (5534.6)	0.100	1337.1 (4279.9)	1490.3 (2721.6)	0.599
E&M	575.3 (653.3)	531.2 (559.6)	585.3 (672.5)	0.097	526.5 (558.5)	564.3 (520.5)	0.355

1 Differences for continuous variables were assessed using t-test, differences for categorical variables were assessed using chi-square test. P-value <0.05 was considered significant.
2 PSM=propensity score matched.

test for categorical variables; costs were also assessed using propensity score matching (PSM) and generalized linear models (GLM) with gamma distribution and log link function to account for differences in pt characteristics.

Results: Of 2140 pts, 1744 (82%) had at least 1 comorbid. Compared to pts without comorbids, pts with comorbids were older, more likely to be white, female, and Medicare-insured (Table). Before accounting for differences in demographics, pts with comorbids had significantly higher costs of bDMARDs, labs/other services, and total costs. After accounting for differences in demographics using GLM, pts with comorbids had higher E&M costs ($569 (CI: 524-618) vs. $519 (CI: 471-573), p=0.027) but no difference in costs of bDMARDs, labs, other medications, and total costs. After PSM there were no differences in age, race, insurance, and gender between cohorts and 350 pts per group matched without replacement, representing 20% of pts with comorbids and 88% of pts without comorbids. Among PSM pts, there were no differences in annual costs between cohorts. Prescription of the commercially available biosimilars was found low (1%) during the study period, thus their impact on costs was not evaluated.

Conclusion: Among RA pts treated with bDMARDs in the community from 2016 to 2018, the majority of the pts had comorbids. Pts with comorbids had significant differences in their characteristics compared to those without comorbids and incurred higher RA-related annual costs, however when accounting for differences in pt characteristics, annual costs of RA-related care were not different between the groups. This initial analysis suggests that comorbids may not be driving costs of RA-related care as it has been presumed. Further research is warranted to evaluate the impact of individual comorbids.

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Abstract Number: 1139

Lifetime Direct Medical and Indirect Cost of Knee Osteoarthritis: Impact of Pain and Structural Severity

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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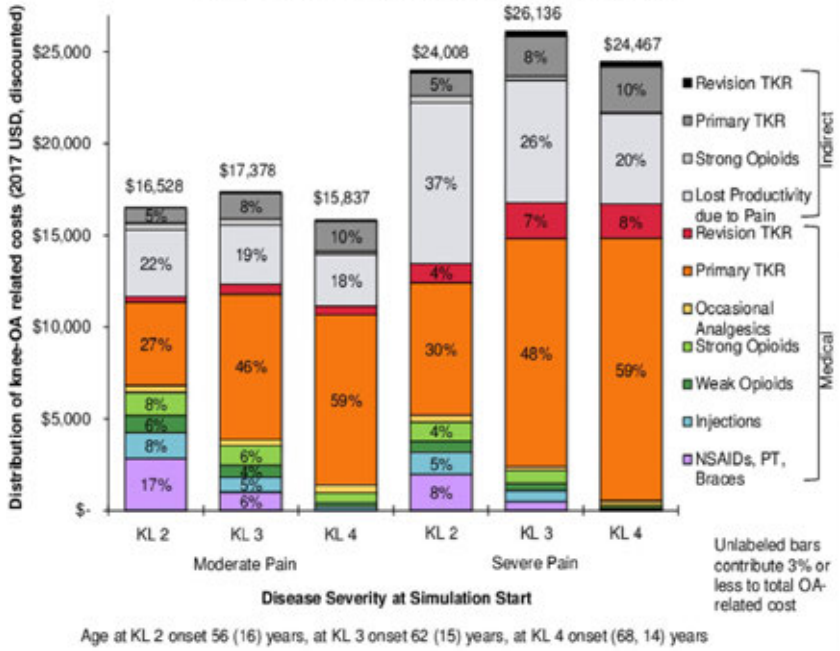
Session Time: 9:00AM–11:00AM

Background/Purpose: Symptomatic knee OA is a debilitating condition that affects 14 million adults in the US. We estimated the variability of lifetime OA-related direct and productivity costs as a function of pain and structural severity at presentation to care.

Methods: We used the Osteoarthritis Policy Model, a validated computer microsimulation of knee OA, to evaluate utilization of alternative treatment modalities and lifetime medical and productivity cost for individuals diagnosed with symptomatic and radiographic OA of Kellgren-Lawrence (KL) grade 2, 3, or 4 in moderate (mean 25) or severe (mean 55) pain on the Western Ontario and McMaster Universities Osteoarthritis Index pain scale (0-100, 100 is worst) at the time of presentation for OA care. The combinations of three radiographic grades and two pain categories yielded 6 cohorts. To determine the age of presentation to care for each cohort we used additional model runs, coupled

Figure: Average Lifetime Cost of OA Per-Person



Age at KL 2 onset 56 (16) years, at KL 3 onset 62 (15) years, at KL 4 onset (68, 14) years

with the national data on incidence and structural progression of knee OA. Treatments under consideration included NSAIDs, physical therapy, braces, corticosteroid injections, tramadol, strong opioids (e.g. oxycodone, hydromorphone, hydrocodone, morphine), and total knee replacement. We followed subjects from presentation to OA care until death. Direct medical costs of knee OA treatments were derived from Redbook Online and Medicare reimbursement data. The economic burden of OA was portrayed as the time cost of lost productivity and the societal costs associated with opioid use. Treatment efficacy and opioid-related costs were derived from published literature. Costs were discounted at 3% annually.

Results: Pain severity was the key driver of lifetime time OA-attributable costs, with severe pain adding about $8,000, increasing the discounted direct medical costs by 35% compared to moderate pain across all KL levels considered (Figure). Across all six cohorts, TKR was the largest contributor to the direct medical OA-related cost. The largest contributor to indirect cost was lost work productivity due to OA. The indirect costs comprised between 30%-45% of total (direct plus indirect) OA-attributable costs, ranging from $4,000-$5,000 for those in moderate pain to $8,000-$10,000 among those in severe pain. The percent of patients using strong opioids ranged from 10% (KL 4, severe pain) to 76% (KL 2, severe pain), and the average duration of opioids use ranged from 1.9 (KL 4, severe pain) to 2.7 years (KL 2, moderate pain). The percent of patients receiving TKR ranged from 40% among those followed from diagnosis with KL 2, moderate pain to 82% among those followed from the time they had been diagnosed with KL 4, severe pain. The average age of surgery ranged from 65 to 69 years depending on symptoms and structural severity.

Conclusion: Pain severity at presentation had much greater impact on medical and societal costs than structural severity at presentation. Indirect medical costs comprised between 29% and 44% of total medical OA-attributable costs. These data could be used by policy makers and payers to direct resources toward pain management and optimizing productivity among knee OA patients in the workforce.

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5, Roche/Genentech, 2, Samumed, 2, TissueGene, 2, Velocity, 5, Velocity Pharaceutical Development, 5, Velocity Pharmaceutical Development, 5.

Abstract Number: 1140

The Socioeconomic, Gender, Urban-rural, and Regional Disparities in the Risk of Acute Myocardial Infarction Among RA Patients

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: To assess socioeconomic (SES), gender, urban-rural, and regional disparities in the risk of acute myocardial infarction (MI) among rheumatoid arthritis patients.

Methods: We conducted a population-based cohort study using administrative health data on all individuals with RA across an entire Canadian province. RA incident cases were defined as first meeting previously published RA criteria between 1997 and 2009, using a 7 year wash-out period. Individuals with prior MI were excluded. The outcome was the first ever ICD code (ICD9 410 or ICD10 I21) for MI recorded in Hospital Discharge Data (in any position) or as the primary cause of death in Vital Statistics Data. Follow-up was from incident RA date to the date of first MI event, death, leaving the province, or March 31, 2015, whichever occurred first. We obtained patients' residency information, such as postal code and health regional authority (HA) from patient registry database, where a zero '0' in the second position of the postal code indicates a rural area. We defined low-income if an individual received a family-income-based MSP premium subsidy.

We compared disparities in incident rates (IR) of MI by SES, gender, rural/urban area and HA. We further estimated their hazard ratios (HR) using Cox proportional hazard model to evaluate the SES, gender, rural residency, and HA disparities in MI, adjusting for potential confounders.

Results: A total of 37,547 incident RA patients were identified, including 12,546 (33.4%) male, 6,527 (17.4%) rural, and 12,838 (34.2%) low income patients. Overall, 2,076 patients developed MI during 378,586 follow-up years with an incident rate of 5.5 per 1,000 person-years (PYs). The MI IRs varied with SES (low vs. med-high: 6.6 vs 4.9 per 1000 PYs), gender (male vs female:.8.1 vs 4.2), rural residency (rural vs urban: 6.4 vs 5.3), and HA (Interior 7.0, Fraser 5.0, Vancouver Coastal 4.7, Vancouver Island 5.1, Northern 6.1).

Adjusting for age, number of GP visits, prior hospital admission, comorbidities and medication use, low socioeconomic status (HR= 1.14, 95%CI=1.04~1.26, p=0.005), and male gender (HR=1.95, 95%CI=1.78~2.14, p< 0.001), rural residency (HR=1.13, 95%CI=1.01~1.27, p=0.038) were associated with an increased risk of MI. Compared with Vancouver Coastal HA, residency in Interior (HR=1.3, 95%CI=1.13~1.49, p< 0.001), and Northern HA (HR=1.62,

Table 1 Selected Baseline Characteristics.

Table 1 Selected Baseline Characteristics

Variables	N/Mean (%/SD)
N	37547
Demographics	
Low Income (N (%))	12838 (34.2)
Male (N (%))	12546 (33.4)
Rural (N (%))	6527 (17.4)
Health Authority (N (%))	
1. Interior	8109 (21.6)
2. Fraser	11537 (30.7)
3. Vancouver Coastal	7814 (20.8)
4. Vancouver Island	7280 (19.4)
5. Northern	2807 (7.5)
Age (Mean(SD))	57.34 (16.86)
Neighborhood Income Quintile (N (%))	
1 (Lowest)	8077 (21.5)
2	7560 (20.1)
3	7227 (19.2)
4	7002 (18.6)
5 (Highest)	6651 (17.7)
unknown	1030 (2.7)
Health Care Resource Utilization, previous 365 days	
Number of Physician Billing (Mean(SD))	25.81 (27.14)
Average Hospitalization Days (Mean(SD))	9.40 (43.25)
Hospitalization (N (%))	8126 (21.6)
Comorbidities, previous 365 days	
Charlson index (Mean(SD))	0.45 (0.95)
Hypotension (N (%))	9214 (24.5)
COPD (N (%))	1152 (3.1)
Angina (N (%))	1288 (3.4)
Prescription	
Anticoagolation (N (%))	1086 (2.9)
CVD drug (N (%))	11640 (31.0)
Diabetes (N (%))	2157 (5.7)
Statin (N (%))	4102 (10.9)
Traditional NSAID (N (%))	16582 (44.2)
COX2 (N (%))	5160 (13.7)
Contraceptives (N (%))	1101 (2.9)
Gluecorticosteroids (N (%))	5715 (15.2)

Table 2 MI Incidence, Incident Rate by Gender, SES, Rural-urban, and HA.

Table 2 MI Incidence, Incident Rate by Gender, SES, Rural-urban, and Health Regional Authority

Covariate	Group	MI	Person Years	Rate (95%CI) per 1,000 person-years
Gender	Male	985	121,806	8.1 (7.6, 8.6)
	Female	1,091	256,780	4.2 (4, 4.5)
Rural	Rural	433	67,587	6.4 (5.8, 7)
	Urban	1,643	310,999	5.3 (5, 5.5)
Income	Low	821	124,019	6.6 (6.2, 7.1)
	Med_high	1,255	254,567	4.9 (4.7, 5.2)
Health Authority	Interior	572	81,350	7 (6.5, 7.6)
	Fraser	583	116,401	5 (4.6, 5.4)
	Vancouver Coastal	362	76,789	4.7 (4.2, 5.2)
	Vancouver Island	382	74,829	5.1 (4.6, 5.6)
	Northern	177	29,218	6.1 (5.2, 7)

Table 3 Gender, SES, Rural-urban, Regional Disparity: Hazard Ratios from Univariate and Multivariable Cox Proportional Model.

Table 3 Gender, SES, Rural-urban, Regional Disparity: Hazard Ratios from Univariate and Multivariable Cox Proportional Model

	Univariate		Multivariable	
	HR (95%CI)	p	HR (95%CI)	p
Low vs Med_high Income	1.36 (1.24 ,1.48)	<.0001	1.14 (1.04 ,1.26)	0.0047
Male vs Female	1.92 (1.77 ,2.1)	0.0003	1.95 (1.78 ,2.14)	<.0001
Rural vs Urban	1.21 (1.09 ,1.35)	<.0001	1.13 (1.01 ,1.27)	0.0381
HA (vs. Vancouver Coastal)				
Interior	1.46 (1.28 ,1.67)	<.0001	1.3 (1.13 ,1.49)	0.0002
Fraser	1.05 (0.92 ,1.19)	0.495	1.05 (0.92 ,1.2)	0.4565
Vancouver Island	1.07 (0.92 ,1.23)	0.3935	0.99 (0.85 ,1.14)	0.8508
Northern	1.27 (1.06 ,1.52)	0.0086	1.62 (1.348 ,1.94)	<.0001

95%CI=1.35~1.94, p< 0.001) was associated with a higher risk of MI, but not Fraser (HR=1.05, 95%CI=0.92 ~1.20, p=0.46) or Vancouver Island HA (HR=0.99, 95%CI=0.85~1.14, p=0.85).

Conclusion: RA patients with a lower SES and male gender, and living in rural areas were more likely to develop a MI. Living in remote communities, such as Interior and Northern HA, were also associated with a higher risk of MI. These findings have important implications for patients, health care providers and health policy makers; and point to the need for further investigations to understand the underlying reasons for the differences identified, so that targeted interventions can be designed to address health inequities.

Disclosure: Y. Zheng, None; **H. Xie**, None; **J. Avina-Zubieta**, None; **K. Yazdani**, None; **J. Esdaile**, None; **D. Lacaille**, None.

Abstract Number: 1141

Racial Disparities in Lupus Medication Adherence

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Healthcare Disparities In Rheumatology Poster
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Background/Purpose: Medication non-adherence is common among SLE patients and is disproportionately more frequent in underrepresented racial minorities. We examined adherence gaps between minority and Caucasian SLE patients and explored factors associated with non-adherence that may present avenues for intervention.

Methods: Cross-sectional data were obtained via survey and chart review from consecutive SLE patients with ≥1 prescribed lupus medication. The Medication Adherence Self-Report Inventory (MASRI) was used to estimate adherence in the preceding month from 0-100%. High Self-reported Adherence was defined as MASRI ≥90%. Pharmacy refill data in the preceding 3 months were obtained by phone calls. High Refills was defined as a medication possession ratio of ≥80% for all prescribed SLE medications. High Composite Adherence was defined as having both High Self-reported Adherence and High Refills. Patient-provider interaction was measured using the Interpersonal Processes of Care survey, which has 7 domains on a 5-point Likert scale. Additional covariates included: self-

Table 1. Comparing those with high vs. low composite adherence.

	High adherence (n=47)	Low adherence (n=78)	P-value
Age, years, median [IQR]	48[38-56]	41[31-50]	0.01
Live with parents	6%	19%	0.04
Underrepresented racial minorities	51%	72%	0.02
Patient assessment of Provider Communication, median [IQR]			
Hurried Communication* (1=best)	1[1-1.5]	1.25[1-1.8]	0.03
Compassionate Respectful * (5=best)	5[4.8-5]	5[4.2-5]	0.06
Self-efficacy in taking meds^, median [IQR]	51[46-61]	47[41-55]	0.06
Anxiety^, median [IQR]	50[44-51]	53[40-60]	0.04
Pain intensity[ǂ], mean (SD)	3.5 (2.8)	4.2 (2.5)	0.08
Prescribed >2 SLE medications	53%	82%	0.001
SLE med regimen complexity*, median [IQR]	5[3-8]	8[5-10]	0.02
SLICC damage score, median [IQR]	1[0-2]	2[1-4]	0.03
SLAQ, median [IQR]	6[4-12]	9[7-15]	0.009
≥1 ER visit/hospitalization	45%	67%	0.02

*IPC-29 survey, score ranges 1-5, other domains (Elicited concerns, Explained results, Patient-centered decision making, Discrimination, and Disrespectful office staff) were non-significant
^PROMIS measures, general population mean score is 50, clinically significant difference is 5
[ǂ]Part of PROMIS-29, score ranges 0-10

efficacy, patient-reported health status, rheumatic medication regimen complexity, SLEDAI, Systemic Lupus Activity Questionnaire (SLAQ), and SLICC damage scores. Adherence measures were compared by race, and adherence groups were compared.

Results: 125 enrolled (36% Caucasians, 61% African American, 3% other). Median age was 43 (range 22-72), 95% were female, 51% had ≥ college education, and 49% had private insurance. 83 (66%) had High Self-reported Adherence, 59 (47%) had High Refills, and only 48 (38%) had High Composite Adherence. Minorities compared to Caucasians had lower rates of Self-Reported Adherence (58% vs 82%, p=0.005), Refills (40% vs. 60%, p=0.03), and Composite Adherence (30% vs. 61%, p=0.02). Among 75 taking disease modifying agents including MTX, LEF, AZA, and MMF, High Refill rate was 37% vs. 64% (p=0.03) for minorities compared to Caucasians. The racial gap in High Refill rate is largest for those on MMF (39% vs. 88%, p=0.01). Compared to the High Composite Adherence group, those with Low Composite Adherence were younger, more likely to live with parents, rated more Hurried communication with providers, had more anxiety, took a more complex SLE regimen, had higher SLICC Damage score, SLAQ, and more ER visits/hospitalizations. They also had a trend for less compassionate and respectful interaction with providers and lower self-efficacy in managing medications and treatments (table 1).

Conclusion: Significant racial disparities exist in SLE medication adherence, and the gap is most substantial for patients taking MMF, a crucial treatment for moderate to severe SLE. This gap likely contributes to known racial disparities in SLE outcomes. Improving communication, self-efficacy, mental health, and reducing medication burden may be avenues for intervention for a subset of non-adherent patients. Qualitative studies are needed to better understand barriers to adherence and to develop interventions that address this pressing racial disparity.

Disclosure: K. Sun, None; **A. Eudy**, GSK, 2; **J. Rogers**, None; **L. Criscione-Schreiber**, None; **J. Doss**, None; **R. Sadun**, None; **M. Clowse**, GSK, 2, UCB, 5.

Abstract Number: 1142

Barriers and Facilitators of Medication Adherence Among Minority SLE Patients: A Qualitative Study

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SESSION INFORMATION
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Background/Purpose: SLE disproportionately affects underrepresented racial minorities, groups that often have lower rates of medication adherence. This study aimed to explore barriers and facilitators of adherence to SLE medications among minority patients.

Methods: We conducted a qualitative descriptive study using semi-structured interviews. Twelve minority SLE patients who have been prescribed DMARDs and 12 lupus clinic personnel (including 6 doctors, 2 nurse practitioners, 1 pharmacist, and 3 nursing staff) were recruited through purposive sampling. We interviewed 8 patients who had not refilled DMARDs regularly and 4 who did. Interviews were audio-recorded, transcribed, and analyzed using applied thematic analysis. An interdisciplinary stakeholder group consisting of patients, providers, and staff then matched facilitators to barriers to identify potential interventions.

Results: Patient characteristics are summarized in table 1. We identified 4 major themes to barriers of medication adherence. These are:

1. External factors, including medication costs, difficulties with insurance, logistical issues with pharmacy, misinformation, and lapses in communication with providers;
2. Intrinsic factors including forgetfulness in taking medications, denial of having a chronic illness and need to take medications, under-treated depression, concerns about side effects, lack of knowledge of benefits of taking medications and consequences of nonadherence, lack of trust in the provider and health system, low health literacy, and beliefs in religion and alternative medicine;
3. Medication features, including high number of pills, large pill size, and side effects;
4. Physical limitations, including fatigue, mobility issues, and lack of medication taking skills.

The most frequently mentioned barriers were cost, lack of knowledge, and side effects.

We also identified 6 major themes that facilitate adherence. These are:

1. Organizational strategies, including using reminders and pill organizers;
2. Social support, including support from family, friends, and providers/staff at the lupus clinic;
3. Internal motivation, including knowledge of consequences of not taking medications and benefits of taking them, accountability to the provider, and staying healthy to care for others;
4. External factors, including being able to pay for medications, easy access to doctors and/or pharmacist;
5. Medication features, including the small pill size and simplified regimens.
6. Provider communication, including clear, frequent, and motivating communication.

The most frequently mentioned facilitators are using reminders and pill organizers, support from family and friends, and knowledge of consequences.

Table 1. Patient characteristics of interview participants (n=12)

Age, median [IQR]	36 [30-48]
Female	10 (83%)
SLE disease duration, median [IQR]	12 [8-17]
Race	
African American	11 (92%)
Native American	1 (8%)
Insurance status	
Private	6 (50%)
Medicaid	3 (25%)
Medicare	2 (17%)
None	1 (8%)
Marital status	
Single	8 (67%)
Married	3 (25%)
Separated	1 (8%)
Education	
Some high school	1 (8%)
High school degree	4 (33%)
Some college	3 (25%)
College degree	1 (8%)
Graduate degree	3 (25%)
Employment status	
Full time	5 (42%)
Part time	1 (8%)
Home maker	2 (17%)
Retired	1 (8%)
Unable to work	3 (25%)
DMARDs	
Mycophenolate	7 (58%)
Azathioprine	3 (25%)
Methotrexate	2 (17%)

Table 2. Matching facilitators to barriers identified.

Barriers	Matching Facilitators
External factors	• Social worker/pharmacist to help with cost and pharmacy issues • Provider communication
Intrinsic factors	• Organizational strategies such as use of pill boxes, mobile reminder apps • Internal motivation • Provider communication
Medication features	• Simplifying regimen • Remedies for side effects
Physical limitations	• Social support

Table 2 shows matching of facilitators to barriers.

Conclusion: We have identified a number of distinct barriers and facilitators to adherence among minority SLE patients. Although the most frequently cited barriers were cost, knowledge, and side effects, each patient faced a

distinct set of several predominant barriers, and each identified different sets of facilitators. These findings suggest a need for individualized intervention to improve adherence.

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Abstract Number: 1143

Racial Disparities in Factors Associated with SLICC Damage Score Among Patients with SLE

Kai Sun,[1] Amanda Eudy,[1] Jennifer Rogers,[1] Lisa Criscione-Schreiber,[1] Jayanth Doss,[1] Rebecca Sadun,[1] and Megan Clowse[1], [1]Duke University, Durham

Table 1. Patient demographics by race.

	Total (n=125)	Caucasian (n= 45)	Minority (n=80)	p-value
Age, years, median [IQR]	43 [33-52]	**46 [38-60]**	**41 [32-50]**	**0.002**
≥College education	51%	**71%**	**40%**	**0.001**
Disability	40%	**27**	**47**	**0.03**
Marital status				
Single	31%	**16%**	**41%**	**<0.001**
Married	44%	**62%**	**34%**	
Divorced	21%	**13%**	**25%**	
Widowed	3%	**9%**	**0%**	
Live with partner/spouse	51%	**67%**	**43%**	**0.009**
Medicaid	18%	**7%**	**23%**	**0.02**
IQR = interquartile range				

Table 2. Comparing patient characteristics between Caucasians and minorities.

	Caucasian (n= 45)	Non-Caucasians (n=80)	p-value
Interpersonal Process of Care			
Hurried communication*, median [IQR]	**1 [1-1.5]**	**1.3 [1-1.8]**	**0.01**
Elicit concerns†, median [IQR]	**4.8 [4-5]**	**5 [4.5-5]**	**0.5**
Explained results†, median [IQR]	**4.5 [3.5-5]**	**4.8 [4-5]**	**0.3**
Patient-centered decision making†, median [IQR]	**4.3 [3.5-5]**	**4.5 [3.8-5]**	**0.8**
Compassionate & respectful†, median [IQR]	**5 [4.2-5]**	**5 [4.4-5]**	**0.4**
Discrimination*, median [IQR]	**1 [1-1]**	**1 [1-1]**	**0.2**
Disrespectful office staff*, median [IQR]	**1 [1-1]**	**1 [1-1]**	**0.8**
Patient-reported Outcomes			
General Self-efficacy‡, median [IQR]	**52 [44-65]**	**52 [44-65]**	**0.7**
Self-efficacy in taking medications‡, median [IQR]	**52 [43-61]**	**48 [42-54]**	**0.2**
Fatigue‡, mean (SD)	**59(10)**	**54(11)**	**0.005**
Social health‡, mean (SD)	**44[38-52]**	**52[44-64]**	**0.003**
Clinical factors			
Years of diagnosis, median [IQR]	**14[8-18]**	**15[9 - 22]**	**0.3**
Rheumatic medication regimen complexity score, median [IQR]	**5[3 - 8]**	**8 [5 - 10]**	**0.005**
Prescribed Mycophenolate	**18%**	**45%**	**0.002**
Prescribed Prednisone	**27%**	**53%**	**0.005**
SLICC damage score, median [IQR]	**1[0 - 2]**	**2[1 - 4]**	**0.07**
SLEDAI, median [IQR]	**0.5[0 - 4]**	**2[0 - 6]**	**0.049**
SLAQ, median [IQR]	**10[5 - 14]**	**8[5 - 13]**	**0.3**
Fibromyalgia symptom severity score, median [IQR]	**4.3(2.3)**	**3.2(2.5)**	**0.02**

IQR = interquartile range; SD = standard deviation; SLAQ = systemic lupus activity questionnaire; SLEDAI = systemic lupus erythematosus disease activity index; SLICC = systemic lupus international collaborating clinics

*Scores range from 1-5, with lower being better; †Scores range from 1-5, with higher being better

‡A score of 50 represents the US population mean, a difference in 5 is clinically significant. Higher scores are better for self-efficacy and social health, but lower scores are better for fatigue.

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Healthcare Disparities In Rheumatology Poster

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Significant racial disparities exist in SLE outcomes. Few studies have examined modifiable factors intrinsic to physician/patient encounters that may contribute to such disparities. We aimed to explore potential areas for intervention to reduce racial disparities with a focus on patient self-efficacy and the quality of patient-provider interactions.

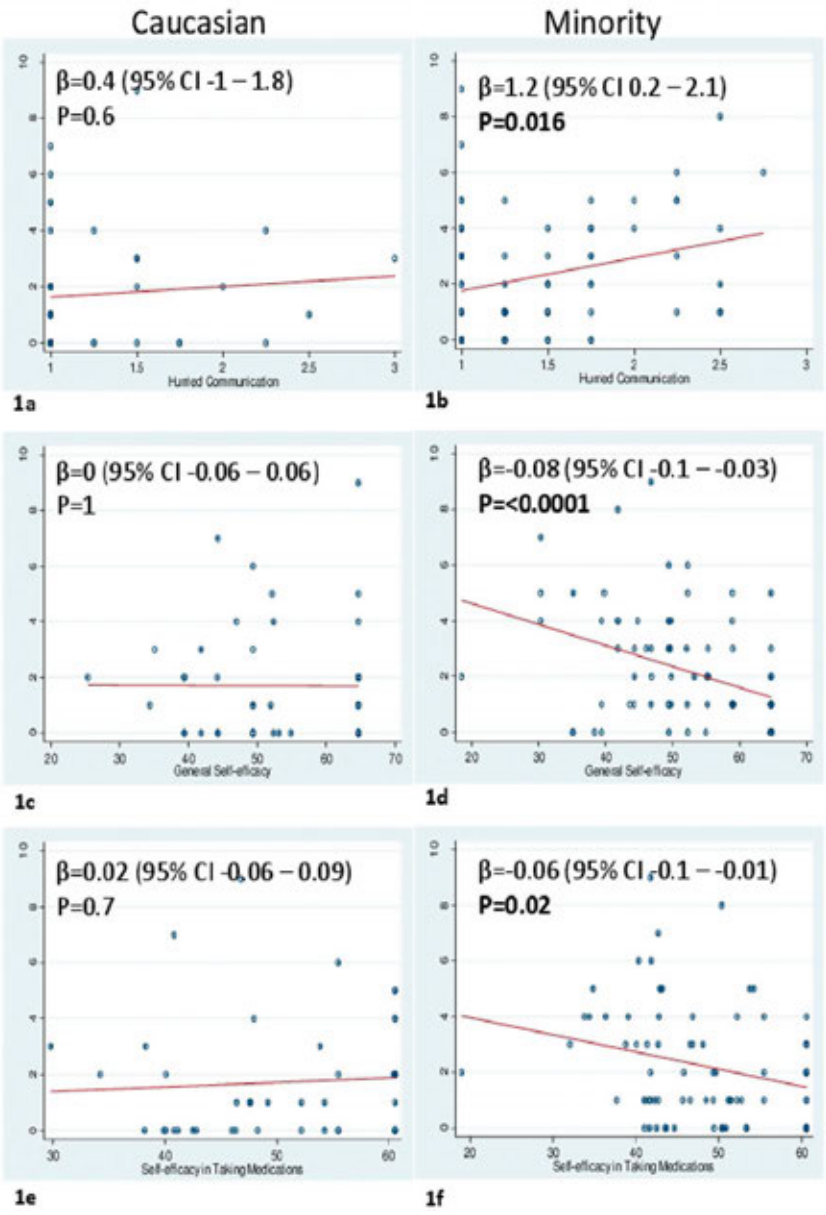

Figure 1 a-f showing correlation between damage scores and hurried communication (a, b), general self-efficacy (c, d), and self-efficacy in taking medications (e, f), stratified by race.

Methods: Cross-sectional data were collected from consecutive patients meeting ACR or SLICC criteria for SLE and actively being treated at a tertiary lupus clinic. Patient-provider interaction was measured using the Interpersonal Processes of Care survey (IPC-29), which has 7 domains on a 5-point Likert scale. General self-efficacy, self-efficacy for managing medications and treatments, and patient-reported health status were measured using Patient-Reported Outcomes Measurement Information System (PROMIS) short forms. Additional demographic and clinical information were gathered by survey and chart review. Bivariate analyses compared characteristics of Caucasian vs. minority patients. Linear regression analysis was performed to assess race-stratified association of SLICC damage scores with age, education, IPC-29 and patient self-efficacy scores.

Results: 125 patients were enrolled (36% Caucasian, 61% African American, 3% other). Minorities compared to Caucasians were younger, less likely to be college educated, married, live with partner or spouse, and more likely to be on Medicaid (table 1). Minorities reported less fatigue and better social health, took more complex rheumatic medication regimens, had higher SLEDAI, lower fibromyalgia symptom severity, and a trend for higher damage scores (table 2). Minorities rated more hurried communication with their providers, and there were no racial differences in self-efficacy scores. Among minorities, more hurried communication, lower general self-efficacy, and lower self-efficacy in managing medications and treatments were each associated with higher SLICC damage scores, but among Caucasians only older age (β=0.09 95% CI 0.06-0.14, $p< 0.001$) and ≤ college education (β= -2.6, 95% CI -3.8- -1.4, $p< 0.001$) were associated with higher damage scores (figure 1).

Conclusion: Minorities were from more disadvantaged sociodemographic backgrounds and had more active SLE. Overall, scores for patient-rated interactions with physicians in this selective sample were very good. However, minorities reported more hurried communication with their providers.

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Abstract Number: 1144

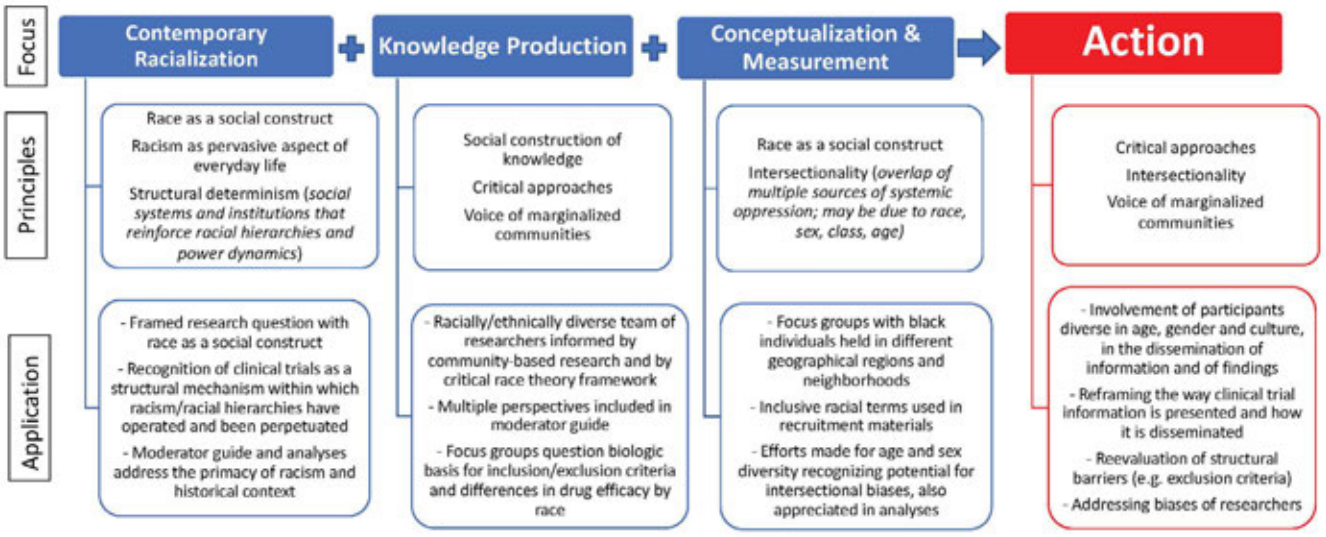
Understanding Clinical Trials Participation Among Individuals of African Descent with Lupus Through the Lens of Critical Race Theory: A Qualitative Analysis

Candace Feldman,[1] Jessica Williams,[1] Courtnie Phillip,[1] Corine Sinnette,[1] Karen Mancera-Cuevas,[2] Patricia Canessa,[3] Gina Curry,[4] Maryann Mason,[2] and Rosalind Ramsey-Goldman[2], [1]Brigham and Women's Hospital, Boston, MA, [2]Northwestern University, Chicago, IL, [3]IPHA, Chicago, IL, [4]University of Chicago, Chicago, IL

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Healthcare Disparities In Rheumatology Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite a disproportionate burden of lupus and poorer outcomes among individuals of African descent (hereafter "black") compared to white individuals, black individuals are underrepresented in lupus clinical trials. We aimed to explore the reasons behind this from the patient perspective using Critical Race

Figure 1. Application of the Public Health Critical Race Praxis (PHCRP) theoretical framework to begin to understand clinical trials participation among individuals of African descent with lupus



Ford CL, Airhihenbuwa CO. *Ethn Dis.* 2018; 28 (Suppl 1): 223-230
Ford CL, Airhihenbuwa CO. *Am J Public Health.* 2010;100 Suppl 1(Suppl 1):S30–S35.

Theory, applied to health equity research with the Public Health Critical Race Praxis (PHCRP). We hypothesized that ongoing racism and historical injustices contribute to the perpetuation of mistrust and to structural barriers within clinical trial design, which result in obstacles and fears that prevent some black individuals from participating in research.

Methods: We recruited black individuals with lupus, age ≥18 years old, and their caretakers (members of their support network who participate in their medical decision-making) to participate in focus groups. Participants were identified through community-based networks and organizations, lupus associations, and academic hospital networks in predominately black Boston and Chicago areas. A racially diverse, multidisciplinary study team developed our moderator guide incorporating PHCRP principles (**Figure 1**), and we used this framework to guide our analyses. Focus groups were transcribed verbatim. Three researchers read the transcripts and coded terms and from this, derived overarching themes, subthemes and proposed actions.

Results: We held 2 focus groups in Chicago (N=16) and two in Boston (N=15). The mean age was 54, 90% were female, and all participants identified as black. Twenty (65%) were diagnosed with SLE and 11 were caretakers. Thematic analysis of transcripts resulted in six key themes: skepticism of clinical trials/research (subthemes of trust, racism and historical context, and placebo arms), the greater good, SLE-specific factors, physician/institutional influences, social support influences, and trial/research-specific factors (subthemes of exclusion criteria, incentives and information presentation/ marketing of studies) (**Table**). Aspects of mistrust stemming from historical context and internalized and structural racism traversed themes. Analyses also revealed recurrent fears (e.g. being a "guinea pig") and structural barriers (e.g. exclusion criteria), as well as mediating factors (e.g. relationships with physicians and social networks), and motivating factors (e.g. contribution to a greater good) (**Figure 2**). Following the PHCRP framework, actions proposed by participants included reframing the way trial information is presented and disseminated, and reevaluation of structural barriers (e.g. exclusion criteria) (**Figure 1**).

Table 1. Selected quotes by focus group participants by theme and subtheme

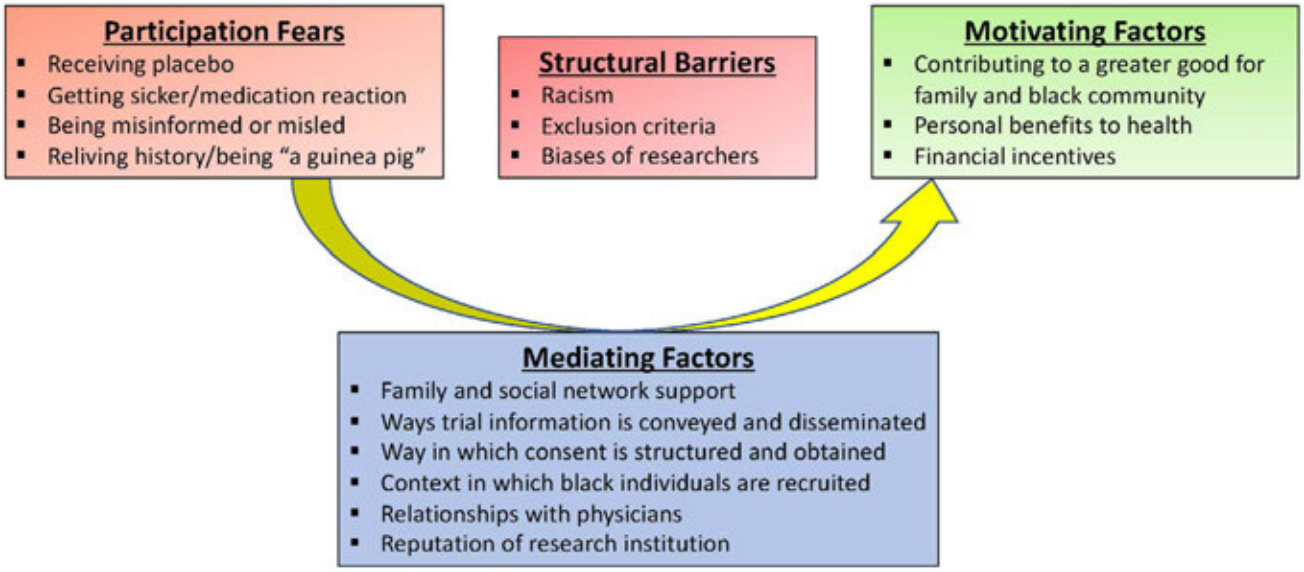
Themes	Selected Participant Quotes
Skepticism of Clinical Trials/ Research	
*Trust, racism and historical context**	"There is a deep mistrust within the African American community. First thing a lot of us think of is the Tuskegee Experiment…so there's a deep distrust between the medical community and the African American community and that's definitely a barrier, even if you are trusting and see the benefits. It still lingers in your thought process." **(C1)** "A lot of minorities, especially black families, 'cause we don't go to the hospital, we wait until the very last minute, so when we do go to the hospital, we die. Then you'll have people say, "Don't go to the hospital. They kill you..." **(B1)**
Placebo Arms	"If you're in the part of the group that gets the placebo…that borderlines on the ethical part and brings up the ethical questions…" **(C1)** "I would be a little disheartened or disillusioned if I was in this particular thing, this trial, for maybe six months and I was all this time, I was getting the placebo…I might have been in that group that was getting the placebo when they was getting the real deal over here…" **(B1)**
The Greater Good	"…if something's not going to help me immediately, I want to make it better for the future. It may help my daughters, it may help my grandkids. Who knows? Who knows what's in this gene pool?" **(C2)** "It's needed. It's needed. It's needed. Because every time you look around, they're always doing cancer research. Lupus is just as prevalent out there as cancer. It's mainly in our community…the black community." **(B1)**
SLE-specific Factors	"If I'm stable, why would I want to do a trial? Why would I want to rock the boat?" **(C2)** "I'm always afraid to participate because the drug interactions…it may interact negatively with some of the medicines, because I take a lot of medications." **(B1)**
Physician and Institutional Influences	"Another consideration would probably be who is doing this research…Patients may feel more comfortable with a reputable name like that versus some research facility that they haven't heard of, they know nothing about, have no connections." **(C2)**
(continued)	"For me that [the race of the researcher] doesn't matter. I just want to know that the person is truthful…if the person seems truthful and open and whatever, that's fine." **(B2)**
Social Support Influences	"I can't say yes or no [to participation] at this time." It's a topic with my family and myself and quite a few things. I would like to be part of clinical trials but the family is pretty adamant to say no...because they don't trust the process."* **(C1)** "My friends always say "Don't do it. Don't forget your history...It haunts a lot of us…Any person of color."* **(B1)**
Trial/Research-specific Factors	
Exclusion criteria	"A lot of the clinical trials, we would like to do them, but a lot of times, we don't qualify… most of the time, with African American women, we don't qualify for a lot of the studies unless you lie."* **(B1)**
Incentives	"It depends sometimes on the clinical trial, if it pays to participate. If it's a lot going on…I'll be like, are they paying for my parking? Are they compensating me?" **(B1)** "Yeah, I do a lot of research, so money's always good. But if it can help find a cure for certain things...It's for the money too, but it's to help also with research." **(B2)**
Information presentation and "marketing" of studies	"The patients don't feel the personal benefit to them and therefore it's difficult to say, "I'm gonna be part of it." I think part of the reason also is that these things are not well-explained. You see, they don't have people that actually sit down to walk people through what this really is. What are the pros? What are the cons? And how to overcome the things that you've been told to believe."* **(B2)** "To me, the communication on research also would make people at ease too, because the human mind can visualize …or see someone saying, it worked for me. So like a YouTube…if I can look it up and see that this person talked to me visually, saying, yeah, I went through it, this is what happened, and if it's out there you guys can take it." **(C2)**

*The subtheme of trust, racism and historical context was interwoven throughout the discussions and was relevant to multiple themes.

B1=Boston focus group 1, **B2**=Boston focus group 2, **C1**=Chicago focus group 1, **C2**=Chicago focus group 2

Conclusion: Issues of trust, racism and historical context permeated all four focus group discussions regardless of participant age. There were certain mediating factors, notably relationships between patients and their physicians, that increased the likelihood of participation in research. Our efforts to promote more inclusive, representative clinical trials should acknowledge the perpetuation of racism and the intersection of biases that occur with race, age and sex particularly in the context of lupus.

Figure 2. Schema of fears, structural barriers, motivating and mediating factors regarding research participation derived from focus groups with individuals of African descent ("Black") with lupus and their caregivers



Disclosure: C. Feldman, None; **J. Williams**, None; **C. Phillip**, None; **C. Sinnette**, None; **K. Mancera-Cuevas**, None; **P. Canessa**, None; **G. Curry**, None; **M. Mason**, None; **R. Ramsey-Goldman**, Exagen, 2.

Abstract Number: 1145

The Representation of Skin Tones in Images of Patients with Lupus Erythematosus

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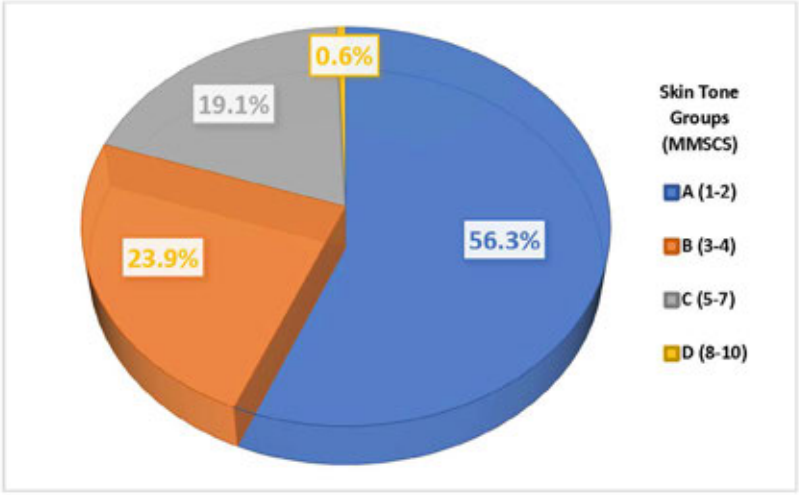
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Healthcare Disparities In Rheumatology Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Racial disparities exist in healthcare. Research shows that the disproportionate representation of race in educational materials contributes to this disparity. Race is a known risk factor for many diseases, including lupus erythematosus (LE), which predilects for women of color. Given the impact of LE in patients of color, healthcare professionals must learn to recognize the systemic and cutaneous manifestations in this population. We explore whether the skin tones in published images represent the populations that LE affects.

Methods: We conducted a descriptive study, reviewing images from internal medicine, dermatology, and rheumatology textbooks, online image libraries, UpToDate and a comprehensive search of Google Images. We selected textbooks published in the last five years that were available through our university's online medical library. We identified images by searching for "lupus" and "lupus rash." We excluded the images if they were in black-and-white, the skin was not clearly visible, or if they were duplicate images. We used the Massey-Martin

Figure 1. Skin Tone Representation in Published Images of Lupus by Groupings of Massey-Martin Skin Color Scale (MMSCS) Scores



Skin Color Scale (MMSCS) to grade skin tones from 1 (very light) to 10 (very dark). We sorted the images into four groups: A (MMSCS 1-2), B (MMSCS 3-4), C (MMSCS 5-7), and D (MMSCS 8-10). Each image was scored twice, once by AR, AW or LZ and once by HJ or MM. In cases of discrepancy, HJ or MM broke the tie. Descriptive statistics were used to analyze the data.

Results: In addition to UpToDate and Google Images, we found 70 dermatology textbooks, 37 rheumatology textbooks, 10 internal medicine textbooks, two minority skin atlases, and two image libraries that met criteria. After exclusions, 1316 images were assessed. The majority (56.3%) of all images represented the skin tones

Table 1. Skin Tone Representation by Resource Type by Groupings of Massey-Martin Skin Color Scale (MMSCS) Scores

Resource Type	A (1-2 MMSCS)	B (3-4 MMSCS)	C (5-7 MMSCS)	D (8-10 MMSCS)	Total
Textbooks	**234 (60.3%)**	**80 (20.6%)**	**73 (18.8%)**	**1 (0.003%)**	**388**
Dermatology	139 (54.7%)	58 (22.8%)	57 (22.4%)	0 (0.0%)	254
Rheumatology	95 (70.9%)	22 (16.4%)	16 (11.9%)	1 (0.01%)	134
Internal Medicine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0
Minority Atlases	**0 (0.0%)**	**8 (33.3%)**	**15 (62.5%)**	**1 (4.2%)**	**24**
Image Libraries	**331 (49.7%)**	**185 (27.8%)**	**144 (21.6%)**	**6 (0.01%)**	**666**
Visual Dx	300 (49.3%)	172 (28.2%)	131 (21.5%)	6 (0.01%)	609
ACR Image Library	31 (54.4%)	13 (22.8%)	13 (22.8%)	0 (0.0%)	57
Google Images	**158 (75.2%)**	**36 (17.1%)**	**16 (7.6%)**	**0 (0.0%)**	**210**
UpToDate	**18 (64.3%)**	**6 (21.4%)**	**4 (14.3%)**	**0 (0.0%)**	**28**
Total	**741**	**315**	**252**	**8**	**1316**

Table 2. Skin Tone Representation by Specialty Type by Groupings of Massey-Martin Skin Color Scale (MMSCS) Scores

Specialty Type	A (1-2 MMSCS)	B (3-4 MMSCS)	C (5-7 MMSCS)	D (8-10 MMSCS)	Total
Dermatology	438 (49.4%)	238 (26.9%)	203 (22.9%)	7 (0.01%)	886
Internal Medicine	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0
Rheumatology	126 (66.0%)	35 (18.3%)	29 (15.1%)	1 (0.01%)	191
Total	**564**	**273**	**232**	**8**	**1077**

of Group A (Figure 1). By resource type, minority atlases were the most inclusive of skin of color with 66.7% of images categorized in Groups C and D (Table 1). Image libraries provided the next best distribution of skin tones, while Google Images heavily published lighter skin tones (75.2%, Group A). By specialty, dermatology included the greatest variety of skin tones, followed by rheumatology (Table 2). No images in internal medicine texts met inclusion criteria.

Conclusion: We show that lighter skin tones are predominantly represented in a sampling of published images of LE. Ironically, this does not match the clinical demographic of LE. The lack of diversity in medical and online resources has been investigated as a potential causative factor in healthcare disparities. Our study adds to the current data highlighting the paucity of darker skin tones in medical resources. Further research is needed to determine if this affects the confidence and ability of healthcare providers to recognize LE in patients of color.

Disclosure: A. Rana, None; **A. Witt**, None; **H. Jones**, None; **M. Mwanthi**, None; **L. Zickuhr**, None.

Abstract Number: 1146

Therapy of Lupus Nephritis with Mycophenolate Mofetil in Routine Clinical Practice: Response Rates and Role of Ethnicity

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Randomized clinical trials have reported that 56-68% of patients with lupus nephritis treated with mycophenolate mofetil (MMF) respond to therapy, and a randomized clinical trial has suggested that African-American patients respond better to MMF than Caucasians. However, data on rates and the role of ethnicity on MMF response in routine clinical practice are limited. As part of initial efforts to improve prediction models and personalized medicine in patients with systemic lupus erythematosus (SLE), we calculated the response rate and defined the role of ethnicity on response to MMF in patients with lupus nephritis at a tertiary center.

Table 1: Comparison of Clinical Variables by Race

	African-American n=31 (33%)	Other Races n=62 (67%)	p-value
Female sex	31 (100%)	48 (77%)	0.004
Age at start of treatment (Median (IQR))	21 (18 – 37)	29 (19 – 42)	0.21
Serum creatinine at baseline (mg/dl); (Median, IQR)	0.81 (0.70 – 1.60)	0.91 (0.70 – 1.28)	0.63
Urine protein/creatinine ratio or 24hr proteinuria at baseline [g/dl] (Median, IQR)	1.9 (0.59 – 3.42)	1.8 (0.56 – 4.45)	0.99
IV methylprednisolone (concurrent use)	2 (6.5%)	4 (6.5%)	1.00
Hydroxychloroquine (concurrent use)	25 (81%)	51 (82%)	1.00
Prednisone (concurrent use)	31 (100%)	60 (97%)	0.55
Previous cycles of treatment on other immunosuppressants	15 (48%)	34 (55%)	0.66
Year of treatment initiation			0.56
Prior to 2008	9 (29%)	13 (21%)	
2008-2010	7 (23%)	11 (18%)	
2011-2012	7 (23%)	13 (21%)	
2013 to present	8 (26%)	25 (40%)	
MMF drug dosage at 6 months [mg/day] (Median, IQR)	2000 (1000 – 2000)	2000 (1000 – 2000)	0.91

Methods: This is a retrospective study using a de-identified version of patients' electronic health records (EHR) at a University-based Medical Center. We completed EHR review and identified a cohort of patients who met the following inclusion criteria: (1) diagnosed with lupus nephritis; (2) received treatment with MMF for lupus nephritis; (3) were new users of MMF; and (4) had laboratory data available at baseline. All patients had confirmed diagnoses of SLE by clinical record review; they also presented with proteinuria (urine protein-to-creatinine ratio or 24-hour proteinuria >0.5 g/g or g/d, respectively) or a renal biopsy indicating lupus nephritis. Response was defined as: (1) a decrease in urine protein/creatinine ratio (uPCR) to < 3.0 g/g in patients with baseline nephrotic range uPCR (≥3.0 g/g), or by ≥50% in patients with sub-nephrotic baseline uPCR (< 3.0 g/g); and (2) stabilization (±25%) or improvement in serum

Table 2: Multivariate Analysis

	African-American n=31 (33%)	Others n=62 (67%)	p-value
Responders	8	24	0.253
Response rate (%)	25.8	38.7	
Unadjusted odds ratio	0.55 (95% CI, 0.21 – 1.43)		0.220
Adjusted odds ratio – sex and propensity score (PS)*	0.34 (95% CI, 0.11 – 1.00)		0.049

* PS included age at first dose, uPCR at baseline, creatinine at baseline, mycophenolate (MMF) dose at 6 months, previous cycles of treatment with other immunosuppressants, year of treatment initiation, and concurrent use of solumedrol, plaquenil, and/or prednisone.

creatinine at six month. For patients who were lost to follow up prior to six months, we used the last observation carried forward as a method of imputing missing data. Univariate analysis was calculated using Fisher's exact text. To adjust for multiple potential confounders, we used propensity scores including age, baseline creatinine, calendar year, baseline proteinuria, use of hydroxychloroquine, use of methylprednisolone, use of prednisone, and history of prior immunosuppressant use.

Results: 93 patients met inclusion criteria; 31 (33%) were African-American, and 62 (67%) reported a different race or did not report race. Patient characteristics are presented in Table 1. A total of 32 (34.4%) patients were classified as MMF responders and 61(65.6%) as non-responders. Among African-American patients, the response rate was 25.8%; among other patients, it was 38.7% (p=0.25). After adjusting for the propensity score and sex, African-American patients had lower odds of responding to MMF than patients from other races [OR: 0.34, 95% CI (0.11 – 0.99) p=0.049].

Conclusion: A total of 34% patients with lupus nephritis responded to MMF at six months of treatment in routine clinical practice at a tertiary center. Our results suggest that—in contrast to what has been reported in a previous randomized control clinical trial—African-American patients with lupus nephritis had lower odds of responding to MMF than patients who reported other races.

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Abstract Number: 1147

Poverty and Systemic Lupus International Collaborating Clinics Damage Index (SDI) Are Significant Risk Factors for Hospitalization in SLE Patients

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Systemic Lupus Erythematosus (SLE) is associated with a high rate of hospitalizations and is the sixth highest reason for 30-day readmissions among all medical conditions in the USA. In SLE patients, lower socioeconomic status correlates with poorer disease outcomes and a higher mortality rate but whether poverty is a risk factor for hospitalization is not clearly understood.

To identify the impact of poverty as a risk factor for hospitalizations in SLE patients.

Methods: We designed a single center, retrospective study of SLE patients hospitalized to Strong Memorial Hospital in Rochester, New York. Billing data was analyzed to identify all hospitalizations that included an ICD-10 code for SLE as primary or secondary diagnosis for the period between July 1, 2013 and June 30, 2017. A diagnosis of SLE was confirmed by evaluating for the presence of American College Rheumatology Criteria or was assigned by a rheumatologist. The outcomes were high-risk patients (defined as those with 3 or more admissions per year) and we collected data on length of stay (LOS) and cost of admissions. The key independent variable was poverty based on the patient resident zip code. Areas of poverty were as defined by the Finger Lakes Health Systems Agency. Bivariate analysis followed by multivariable regression models that controlled for important patient-level confounders such as age, gender, race/ ethnicity, body mass index, disease activity measures (complements, dsDNA, Systemic Lupus International Collaborating Clinics Damage Index (SDI) and comorbidity index (CMI) were applied to assess the data.

Results: A total of 202 patients with SLE were admitted over the 4 year study period and 68 of these subjects were from zip codes associated with poverty. On bivariate analysis we found that patients living in the poverty associated zip codes were significantly more likely to be categorized as high risk patients (p=0.01) and were of African American origin (p=0.001). We also noted significantly higher median dsDNA levels among subjects from the areas associated with poverty (11.2) compared to patients from other zip codes (4.6) (p=0.01). No significant differences were noted for age, SDI, complement levels, total and average LOS as well as total and average cost of admissions between the two groups. We then created multivariable regression models to assess impact of poverty on the above mentioned outcomes of interest. Patients residing in areas with poverty associated zip codes were significantly more likely to be classified as high risk patients (OR 2.96; CI 1.09, 9.00; p=0.03) with higher SDI scores (OR 1.39; CI 1.07, 1.81; p=0.01). SDI was associated with significant risk for admissions (OR 1.26; P< 0.01), average cost above the median (OR 1.65; p< 0.01) and average LOS above the median (OR 1.37; p=0.01). Analysis focused on the African American population revealed that living in poverty areas remained a significant risk factor for hospitalization (p=0.04).

Conclusion: Socioeconomic factors and damage index are significant risk factors for hospitalizations in SLE patients. Early initiation of therapy, addressing the challenges of poverty and overcoming healthcare disparities are important goals to improve the health of lupus patients.

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Abstract Number: 1148

Examining Five Year Lupus Retention in Care in an Academic Cohort

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Healthcare Disparities In Rheumatology Poster
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Background/Purpose: SLE often causes silent damage, making routine clinic and lab monitoring critical for detecting new manifestations or flares. The 2012 ACR nephritis guidelines recommended lab testing, including complement tests at least every three months, for those with history of nephritis and at least every six months for those without. Using these definitions, we previously characterized lab-defined SLE retention in care as having at least one com-

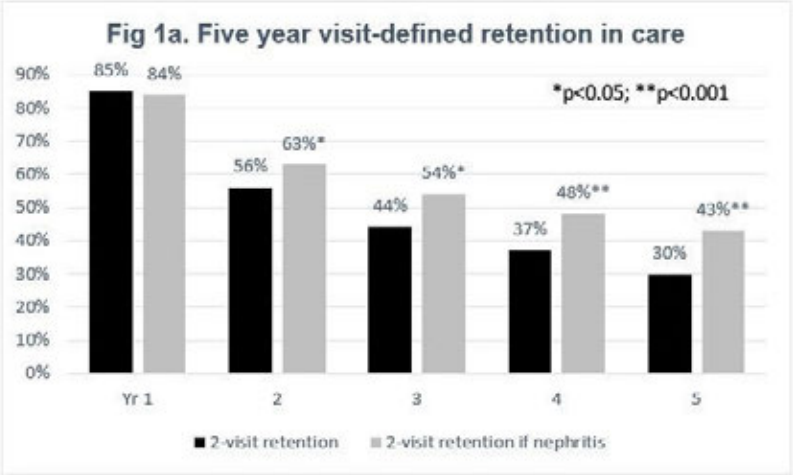
plement lab test every six months and visit-defined retention by at least two annual visits, similar to definitions used by the WHO and CDC in HIV metrics. Previously, we reported 60% visit-based and just 23% lab-based retention at 1 yr. The strongest predictor of retention gaps was living in the most disadvantaged neighborhood quartile, which predicted 59% lower visit retention. In this study, we sought to examine rates and predictors of longitudinal retention in an academic SLE cohort.

Methods: Potential SLE cases were identified using electronic health record searches for adults with at least one SLE code and at least one rheumatology and one primary care visit in 2003-2016. Cases were then manually validated using the 1987 ACR and 2012 SLICC SLE criteria to include definite lupus cases. Baseline sociodemographics, SES, and neighborhood disadvantage were included as potential predictors. For this study, annual rheumatology clinic visits and complement lab tests were counted in each six-month period. Lab-defined retention for patients with nephritis was two labs per six mos, while for patients without current or former nephritis it was one per six mos. Cases were followed up to five years and were censored for death, migration, or loss to follow-up. We used proportions and multivariable logistic regression to report rates and predictors of lab- and visit-defined retention in care using odds ratios and 95% confidence intervals.

Results: Overall, 630 cases met ACR or SLICC criteria for definite SLE and were included in the study, 88% met ACR criteria, and 157 had nephritis history. Overall, 90% were female, 82% white and mean age was 42.4 years old

Table 1. Prevalent lupus cohort description (n=630)

		Overall n (%)
Age at SLE observation		42.35 ± 14.65
Early onset SLE (<18)		31 (4.9%)
Adult onset SLE(18-49)		407 (64.6%)
Late onset SLE(≥50)		192 (30.5%)
Female		571 (90.6%)
Race	White	516 (81.9%)
	Black	77 (12.2%)
	Other	37 (5.9%)
Ethnicity	Hispanic	25 (4.0%)
RUCA	Urban	456 (72.4%)
	Suburban	110 (17.5%)
	Large town	54 (8.6%)
	Small town	10 (1.6%)
Medicaid Ever		140 (22.2%)
Smoking (ever)		252 (40.0%)
Neighborhood Disadvantage (Area Deprivation Index)		
1st (least disadvantage)		146 (23.4%)
2nd		147 (23.6%)
3rd		144 (23.1%)
4th (most disadvantage)		140 (22.4%)
Antiphospholipid Syndrome		83 (13.3%)
ACR Nephritis		157 (24.9%)
ACR Criteria		546 (87.5%)
SLICC Criteria		618 (98.0%)



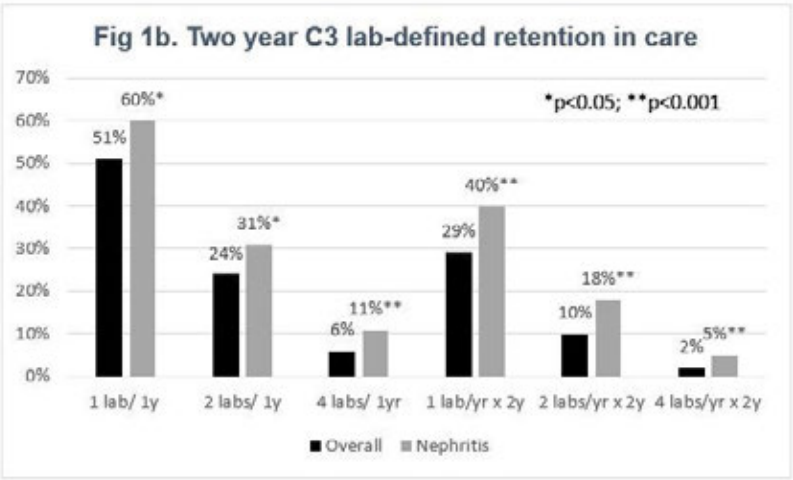


Table 2. Predictors of 2-year SLE retention in care in an academic cohort (n=630)

		Visit-Defined Adjusted OR (95% CI)	Lab-Defined Adjusted OR (95% CI)
Age at observation		1.00 (0.99,1.02)	0.99 (0.98, 1.02)
Female		0.85 (0.46, 1.56)	2.45 (0.71, 8.45)
Race	White	Ref	Ref
	Black	0.74 (0.43, 1.29)	0.54 (0.19, 1.51)
	Other	0.81 (0.39, 1.69)	1.11 (0.39, 3.18)
Ethnicity	Hispanic	0.93 (0.37, 2.36)	0.78 (0.17, 3.69)
RUCA	Urban	Ref	Ref
	Suburban	**1.86 (1.13, 3.07)**	0.52 (0.22, 1.33)
	Large town	1.48 (0.77, 2.85)	0.79 (0.25, 2.44)
	Small town	1.60 (0.37, 6.85)	--
Ever Smoking		0.79 (0.55, 1.15)	0.66 (0.35, 1.24)
Neighborhood Disadvantage by ADI			
1st (least disadvantaged)		Ref	Ref
	2nd Quartile	1.12 (0.69, 1.83)	0.68 (0.31, 1.48)
	3rd Quartile	0.69 (0.41, 1.14)	1.16 (0.55, 2.46)
4th (most disadvantaged)		0.82 (0.49, 1.37)	0.53 (0.22, 1.33)
Medicaid		1.10 (0.70, 1.75)	1.14 (0.54, 2.39)
Lupus Nephritis		**1.73 (1.14, 2.62)**	**2.73 (1.51, 4.91)**

(Table 1). Most patients (72%) were urban, 17.5% suburban, 10% from large or small towns, and 22% ever received Medicare. Two-visit-defined retention in care started at 85% and declined to 30% year five, compared to 84% year one and to 43% year five for patients with nephritis (Fig 1a). Complement defined retention was just 24% by two labs in year one and declined to 10% at year two (Fig 1b). This remained higher in nephritis patients 31% and 18% by two labs, but just 11 and 5% when requiring four labs per guidelines. Multivariable predictors of greater visit-defined retention included suburban residence and nephritis (Table 2).

Conclusion: Retention in lupus care began higher in our academic than our prior urban cohort but declined over time. Nephritis predicted more rheumatology visits, but lab-defined retention still fell far short of ACR guidelines showing opportunities for improvement. Suburban residence, likely representing higher education and resources, predicted better retention, showing the flipside of our prior findings of low retention with disadvantage, supporting a role for neighborhood context as a determinant of lupus care quality.

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Abstract Number: 1149

Are There Country Differences in Disease Activity and Life Impact of Psoriatic Arthritis? An Analysis of 436 Patients from 14 Countries

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Background/Purpose: In psoriatic arthritis (PsA), there is a substantial life impact perceived by patients, although many treatments are now available at least in countries with access to more costly drugs (ref 1,2). Country of patient care, and in particular Gross Domestic Product (GDP) may be linked to PsA outcomes. The lack of large international registries has not up to now allowed any comparison of outcomes according to the country.

Table. Disease activity of PsA patients in different tertiles of country GDP/capita

	Patients in lowest country GDP/capita tertile (N=113)	Patients in middle country GDP/capita tertile (N=179)	Patients in highest country GDP/capita tertile (N=144)	P value between the tertiles
Swollen joint count (0-66), mean (SD)	3.8 (11.1)	1.2 (5.4)	2.3 (3.8)	<0.001
Tender joint count (0-68), mean (SD)	5.6 (10.3)	3.3 (7.9)	5.7 (10.7)	0.003
Tender entheseal points, mean (SD)	0.6 (1.4)	0.5 (1.2)	0.7 (1.6)	0.252
Body surface area of psoriasis ≥5%, n (%)	20 (18.2)	13 (7.7)	7 (5.0)	0.001
Elevated acute phase reactants (CRP >5mg/L), n (%)	62 (54.9)	65 (36.3)	49 (34.0)	0.001
Physician's global assessment of PsA, mean (SD)	4.0 (2.4)	2.6 (2.5)	3.0 (2.4)	<0.001
Patient's global assessment of PsA (0-10), mean (SD)	5.0 (2.5)	3.6 (2.7)	4.2 (2.8)	<0.001
HAQ (0-3), mean (SD)	0.89 (0.72)	0.50 (0.59)	0.70 (0.67)	<0.001
PsAID12, mean (SD)	4.3 (2.4)	2.9 (2.3)	3.3 (2.5)	<0.001
Minimal disease activity state attained, n (%)	21 (18.6)	87 (48.6)	58 (40.3)	<0.001
DAPSA remission or low disease, n (%)	52 (46.0)	114 (63.7)	80 (55.6)	0.012

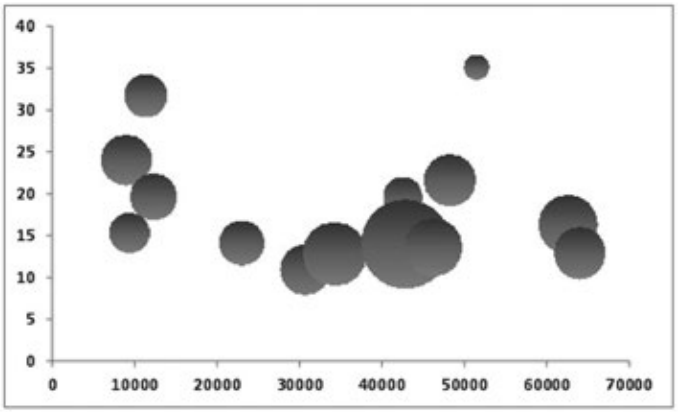
The objective was to explore potential differences in disease activity, disease impact and treatments across countries in PsA.

Methods: This was a cross-sectional analysis of an observational study (ReFlap, NCT03119805, ref3), which included adult patients with PsA with ≥ 2 years disease duration from 14 countries. Countries of inclusion were analysed separately, and classified into tertiles by GDP/capita (lowest tertile, Brazil, Turkey, Russia, Romania, Estonia; middle tertile: Spain, Italy, UK, France; highest tertile, Canada, Germany, Austria, USA and Singapore). Patient demographics, treatments prescribed (conventional synthetic DMARDs, biological DMARDs, glucocorticoids), disease impact (though patient global assessment, PGA, HAQ and the Psoriatic Arthritis Impact of Disease questionnaire, PSAID-12) and PsA disease activity (assessed through swollen and tender joint counts (of 66/68), CRP, entheseal points, psoriasis body surface area and the composite scores DAPSA and MDA) were analysed per coutrny and compared between the 3 tertiles of GDP/capita by non-parametric tests.

Results: Of the 466 patients, 436 had complete data available and were analysed: mean age 52.3 (SD 12.5) years, mean disease duration 10.1 (8.1) years, 218 (50.8%) male.

In countries with a lower GDP/capita, patients were slightly older, with a longer disease duration. There was a similar use of biologics (overall mean 60.5%) and of oral glucocorticoids (18.6%) but use of methotrexate was different (67.0% in the lowest GDP/capita tertile, versus 47.3% in the second and 53.4% in the highest tertile, p=0.007). Disease activity and impact were overall higher in the lowest GDP/capita countries (Table and Figure). The middle and highest GDP/capita tertiles had similar outcomes.

Figure. Mean DAPSA mapped against country GDP/capita for PsA patients from 14 countries



The x-axis represents the GDP/capita in US dollars of each country and the y-axis represents mean DAPSA in patients from each country. The size of the bubble represents the number of patients per country (range, 7 to 89).

Conclusion: In this exploratory comparison of disease patterns and treatments choices in 14 countries, we relied on a relatively small and selected population from tertiary centers which is a limitation. We observed a similar use of biologics but more use of methotrexate in countries with a lower GDP/capita, though glucocorticoid use was similar. Both disease activity and disease impact appeared more important in the lower GDP/capita countries. This raises questions on the link between disease activity, disease impact, treatment choices and other (external) society and culture related elements such as lifestyle/diet or health care systems.

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Abstract Number: 1150

Factors Associated with Participation in Rheumatic Disease-Related Research Among Underrepresented Populations: A Systematic Review

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Background/Purpose: Non-white racial/ethnic groups remain underrepresented in rheumatic disease-related research despite being disproportionately affected by these disorders. We aimed to systematically review the literature

Table 1: Summary of study design for studies included for analysis

First Author, Year	Disease of Interest	Number of Participants	Methods/Study Design
Dunbar-Jacob, 2004	RA	N=961	*Prospective cohort study:* Analyzed attrition rates measured at 4 distinct screening points for an RA trial: initial eligibility review, initial contact, adherence screen, and informed consent
Faith, 2018	SLE	N=33	*Prospective intervention study with qualitative analysis*: Patients assigned mentor for weekly meetings over 12 weeks. Post intervention focus groups held to discuss participants' experience in study
Lee, 2005	RA	N=191	*Cross sectional study utilizing clinical surveys:* Identified factors associated with willingness to participate in clinical trials
Lim, 2017	SLE	N=18	*Prospective randomized intervention study with qualitative analysis*: Simulation Phase II and Phase III anifrolumab studies for SLE with post-intervention interviews regarding participants' experience
Uribe, 2005	SLE	N=344	*Prospective Cohort Study:* Identified factors associated with poor compliance with study visits
Vina, 2012	SLE	N=182	*Cross sectional study utilizing telephone surveys:* Assessed predictors of participation in clinical trials
Vina, 2014	SLE	N=343	*Cross sectional study utilizing telephone surveys:* Assessed predictors of participation in clinical trials

Abbreviations: RA= rheumatoid arthritis, SLE = systemic lupus erythematosus

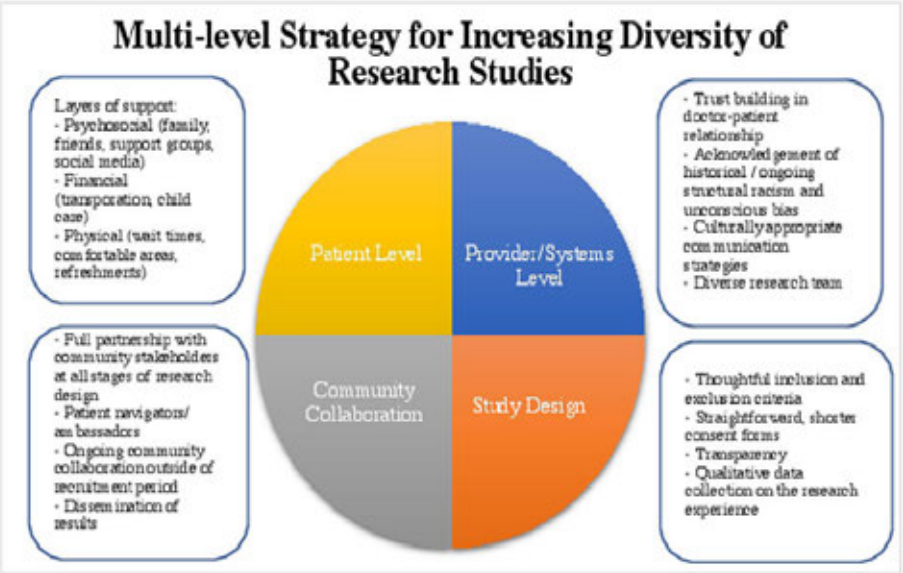

Figure 1. Multi-level Strategy for Increasing Diversity of Clinical Research.

regarding underrepresented patients' perceptions of participation in rheumatic disease research and to develop strategies to improve diversity.

Methods: A systematic search of Embase, Pubmed-MEDLINE, PsycINFO, and Cochrane was performed through November 2018. We identified 642 unique studies; seven met inclusion criteria (peer-reviewed articles, published in English in last 20 years, adult population, focus on underrepresented patients' participation in rheumatic research) by two independent reviewers. Data abstraction was performed and common themes and key differences were determined and adjudicated.

Results: The seven articles included (n=1,892 patients, range n=20 to n=961) evaluated factors associated with research participation of underrepresented populations. Five related to lupus, two to rheumatoid arthritis and five focused on African American patients, one on Hispanic. Five of the studies provided quantitative data through surveys (n=3) and chart review (n=2), while two utilized qualitative analyses. The key themes regarding underrepresented patients' perceptions of participating in research included: 1) importance of trust in the patient-physician relationship, 2) key motivators and barriers affecting willingness to participate, 3) the implications of strict inclusion criteria on study participant diversity and 4) the need for authentic academic-community partnerships with an understanding of heterogeneity within ethnic groups.

Conclusion: Overall, limited evidence exists regarding underrepresented patients' attitudes towards research participation in rheumatology, and further investigation is warranted. The themes identified provide a starting point for future interventions that promote increased diversity in rheumatic disease-related research studies.

Abbreviations: RA= rheumatoid arthritis, SLE = systemic lupus erythematosus

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Disclosure: K. Lima, None; **C. Phillip**, None; **J. Williams**, None; **J. Peterson**, None; **C. Feldman**, None; **R. Ramsey-Goldman**, Exagen, 2.

Abstract Number: 1151

The Impact of Gender on Time to Rheumatoid Arthritis Classification

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Background/Purpose: Rheumatoid arthritis differs between genders with regard to comorbidities, extra-articular manifestations, core measures of disease activity, and treatment response. Gender has not previously been associated with diagnostic delay in early RA, and the impact of gender on time to meeting ACR/EULAR classification criteria for RA is unknown. This study aimed to compare the time to fulfillment of 1987 and 2010 ACR/EULAR classification criteria between female and male patients with rheumatoid arthritis (RA), and to assess the potential impact of gender on the time to DMARD therapy.

Methods: Time from first provider-documented joint swelling to fulfillment of 1987 and 2010 ACR/EULAR criteria was measured in a population-based cohort of adults with incident RA in 2009-2014, who were stratified by male or female gender. Disease characteristics, time to start of DMARD therapy, and choice of initial DMARD therapy were compared between groups using Chi-square and rank sum tests.

Results: This study included 214 patients with RA (148 females and 66 males). Median times from first joint swelling to fulfillment of 1987 (6.5 vs 2.5 days, p=0.48) and 2010 (1 vs 0 days, p=0.34) classification criteria were not different between female and male patients. There was no difference in time from first joint swelling to first DMARD therapy in female vs male patients (15.5 vs 16 days, p=0.90), and methotrexate was used most frequently as first DMARD in both genders (61% female vs 64% male, p=0.76). Inflammatory markers were more commonly abnormal in male vs female patients at time of meeting 2010 criteria (83% vs 66%, p=0.010).

Table 1. Baseline characteristics of 214 patients at time of meeting 2010 ACR/EULAR classification criteria for RA.

Baseline characteristic	Female, N=148	Male, N=66	p-value
Age, mean (±SD), years	53.6 (±15.2)	59.1 (±12.5)	0.007
RF/ACPA positive	97 (67%)	46 (70%)	0.68
Current smoker	23 (16%)	15 (23%)	0.010
Former smoker	36 (24%)	26 (39%)	
Never smoker	89 (60%)	25 (38%)	
Obese (BMI ≥30kg/m^2)	60 (41%)	25 (38%)	0.71
≥10 joints involved	104 (70%)	46 (70%)	0.95
ESR and/or CRP elevated[1]	98 (66%)	55 (83%)	0.010
Presence of erosions	28 (19%)	19 (29%)	0.11

RF: rheumatoid factor; ACPA: anti-citrullinated peptide antibody; BMI: body mass index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.
[1] Elevated ESR and/or CRP were defined as higher than the upper limit of normal as defined by local laboratory standards.

Table 2. Comparison of time in days from first joint swelling to fulfillment of the 1987 or 2010 ACR/EULAR criteria and to first treatments between male and female patients with incident RA between 2009-2014.

Group		Female N=148	Male N=66	p-value
Overall	Median time to 1987 ACR/EULAR criteria, days (IQR)	6.5 (0, 122)	2.5 (0, 57)	0.48
	Median time to 2010 ACR/EULAR criteria, days (IQR)	1 (0, 94)	0 (0, 29)	0.34
	Median time to first DMARD, days (IQR)	15.5 (0, 100)	16 (4, 83)	0.90
	Median time to first glucocorticoid, days (IQR)	5 (0, 97)	9.5 (0, 81)	0.70
RF/ACPA-positive		Female N=99	Male N=46	
	Median time to 1987 ACR/EULAR criteria, days (IQR)	0 (0, 49)	25 (0, 44)	0.59
	Median time to 2010 ACR/EULAR criteria, days (IQR)	0 (0, 23)	0.5 (0, 32)	0.47
	Median time to first DMARD, days (IQR)	11 (0, 73)	16 (4, 83)	0.36
	Median time to first glucocorticoid, days (IQR)	7 (0, 97)	20 (0, 90)	0.32
RF/ACPA-negative		Female N=49	Male N=20	
	Median time to 1987 ACR/EULAR criteria, days (IQR)	65 (0, 398)	11 (0, 153)	0.063
	Median time to 2010 ACR/EULAR criteria, days (IQR)	165 (0, 254)	0 (0, 13)	0.035
	Median time to first DMARD, days (IQR)	60 (5, 210)	15 (1, 155)	0.25
	Median time to first glucocorticoid, days (IQR)	4 (0, 102)	0 (0, 12)	0.035

IQR: inter-quartile range

Among the 49 female and 20 male RF/ACPA-negative patients, females experienced a higher median time from first joint swelling to fulfillment of the 1987 (65 vs 11 days, p=0.063) and 2010 (65 vs 0 days, p=0.035) classification criteria. Similar proportions of females and males had >10 joints involved at the time they met 2010 criteria (82% vs 85%, p=0.74), but the time from first joint swelling to >10 joints involved was significantly longer for females than males (median 65 vs 0, p=0.038). Seronegative females were also more likely to be anti-nuclear antibody (ANA) positive than their male counterparts (30% vs 11%), but this difference did not reach statistical significance (p=0.11).

Conclusion: Overall there was no delay in meeting 1987 and 2010 ACR/EULAR classification criteria between female and male RA patients. However, among seronegative patients, females experienced a significant delay to meeting 2010 criteria from first clinically detected synovitis. This delay may be related to difficulty distinguishing RA from other diseases among seronegative females, or a delay in seeking healthcare among seronegative males.

Disclosure: C. Coffey, None; **J. Davis**, Abbvie, 5, Pfizer, 2, 5, Sanofi Genzyme, 5; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2.

Abstract Number: 1152

Low Rates of Bone Mineral Density Testing by Rheumatologists in Patients with Systemic Lupus Erythematosus and Glucocorticoid Therapy

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SESSION INFORMATION

Session Date: Monday, November 11, 2019
Session Title: Healthcare Disparities In Rheumatology Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) are at an increased risk of developing osteoporosis and clinical fractures compared to healthy controls. Bone loss in SLE is multifactorial from the negative effects of systemic inflammation and use of glucocorticoids (GCs). The American College of Rheumatology recommends bone mineral density (BMD) testing within 6 months of starting chronic GC therapy for autoimmune conditions, including SLE. Prior studies have not investigated the frequency of BMD testing in the setting of chronic GC therapy and SLE using an electronic health record (EHR) cohort. Using a real-world, EHR cohort, we assessed the frequency of BMD testing in patients with SLE and GC therapy. We evaluated patient and provider factors impacting BMD testing.

Methods: We identified SLE cases from a de-identified EHR with over 2.9 million subjects with decades of follow-up using a previously validated and published algorithm. We chart reviewed to collect demographic, medication, and BMD data. We assessed for ever use of oral or intravenous GCs from inpatient and outpatient electronic prescribing systems, provider notes, and phone messages. Long term GC use was defined as ≥ 90 days of continuous use. Patients prescribed GCs for non-rheumatologic issues were excluded from review. The provider ordering BMD testing was recorded. Lowest T-scores were recorded from the femoral neck and lumbar spine. When multiple BMD tests were performed, the lowest T-score was recorded. Our primary outcome was frequency of BMD testing in SLE patients with long term GC therapy. We also evaluated for differences in SLE cases who had BMD testing vs. not using the Mann-Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables.

Results: We conducted chart review on 729 SLE cases. Of these cases, 539 had available medication duration data with 475 (88%) with long term GC use. SLE cases with long term GC use had a current mean age of 54 ± 17 years and were predominantly female (89%) with 72% Caucasian, 22% African American, 4% Hispanic and 2% Asian. The median age at first BMD testing was 51 years. BMD testing was ordered in 40% of cases with long term GC use. Rheumatologists accounted for ordering 75% of the BMD tests. The median time from start of GCs to first BMD testing was 2.5 years. The mean T-score of cases with long term GC use was -1.4 ± 0.9. There were no differences

Table 1. Characteristics of SLE cases with long term glucocorticoid exposure with and without bone mineral density testing performed.

SLE case characteristics with long term GC use (n = 475)	BMD Testing Performed (n = 189)	BMD Testing Not Performed (n = 286)	p value*
Current Age, mean ± SD	60 ± 16	50 ± 16	<0.001
Age at first SLE billing code, mean ± SD	45 ± 15	37 ± 16	<0.001
Sex, n (%)			
Female	173 (41%)	250 (59%)	0.11
Male	15 (29%)	36 (71%)	
Race/Ethnicity, n (%)			
Caucasian	141 (43%)	184 (57%)	0.02
Black	28 (29%)	70 (71%)	
Hispanic	9 (50%)	9 (50%)	
Asian	1 (12%)	7 (88%)	

*Mann-Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables.

in sex between cases with or without BMD testing (Table 1). SLE cases with long term GC use and BMD testing were older compared to cases with long term GC use without BMD testing (60 ± 16 v. 50 ± 16, $p < 0.001$). Caucasians and Hispanics were more likely to have BMD testing than African Americans and Asians ($p = 0.02$).

Conclusion: Using a large EHR cohort, only 40% of SLE cases with long term GC use had BMD testing. SLE patients that were younger, African American, or Asian were all less likely to have BMD testing performed. These groups with the lowest rates of BMD testing are the same groups that are at highest risk of requiring a significant amount of GCs during their disease course and developing GC-related bone loss. Screening strategies for BMD testing should be implemented that target these high-risk groups.

Disclosure: J. Boone, None; **S. Tanner**, Amgen, 5, AstraZeneca, 5, UCB, 5, Regeneron, 8, Sanofi, 8, AstraZeneca, 8, Pfizer, 8; **A. Barnado**, NIH/NIAMS 5K08AR072757-02, 2.

Abstract Number: 1153

Double Trouble: Utility of Serial TB Screening in a Rheumatology Clinic Serving a Foreign-Born Population

Alice Fike,[1] Yanira Ruiz-Perdomo,[1] and James Katz[1], [1]NIAMS, BETHESDA, MD

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Healthcare Disparities In Rheumatology Poster
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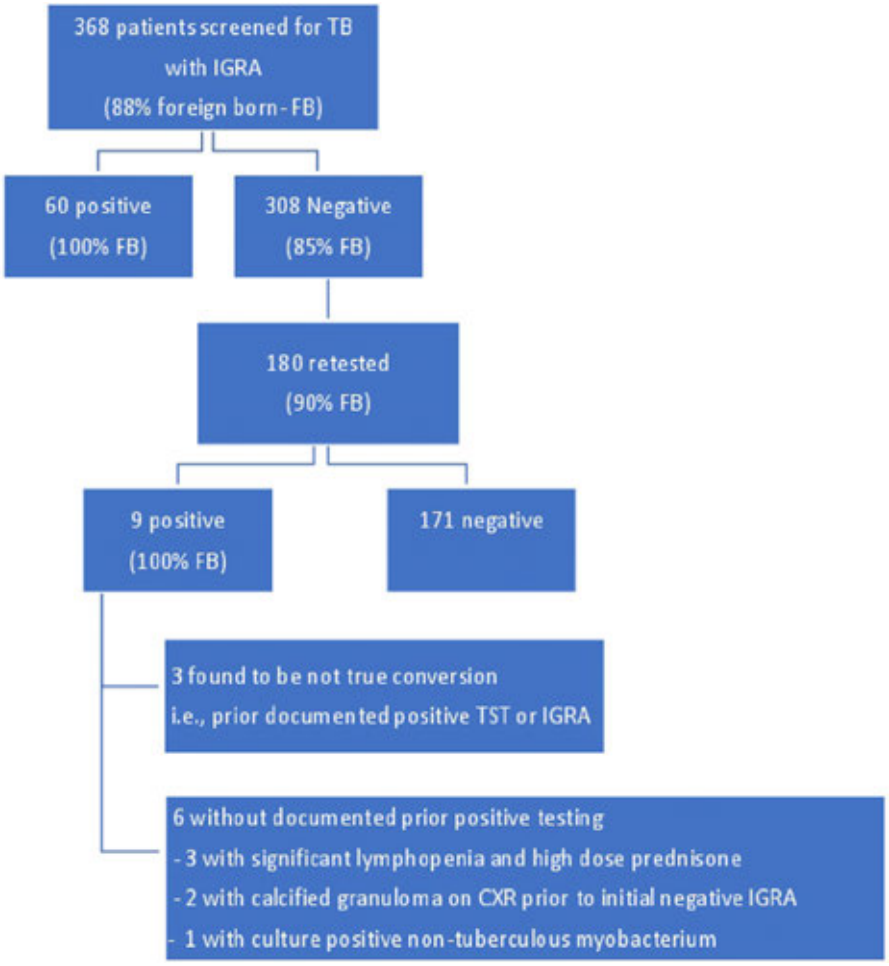
Session Time: 9:00AM–11:00AM

Background/Purpose: The potential for reactivation of tuberculosis (TB) in patients treated with anti-TNF or other immunosuppressive agents has been well described. Interferon-gamma release assays (IGRA) have improved latent TB infection (LTBI) detection. Evidence is accumulating that shows a negligible yield for periodic testing in U.S. born rheumatology patients. Does this evidence apply to patients born in TB endemic countries now living in the U.S.? Incident active TB disease in the United States disproportionately affects people born in countries with endemic TB.

Purpose: To determine the yield of serial TB screening using an IGRA (Quantiferon Gold-QFT) in a United States rheumatology clinic with a majority (80%) foreign born population.

Methods: We sought to determine the utility of serial TB screening in this population using retrospective cross- sectional study design. Between January 2013 and December 2018, a total of 368 patients received TB screening using IGRA. Positive results were classified as initial positive or as a conversion if there was evidence of prior negative test. Records showing conversion were reviewed further for evidence of prior positive result outside of our institution and reclassified as not true conversions accordingly.

Results: During the study period, 368 subjects received TB screening using an IGRA. Of those, 60 initially screened positive (16%). The initially positive patients were 100% foreign born and twice as likely than the general clinic population to have been born in a country WHO designated as high burden for TB. 308 patients were initially screened negative. Of those, 180 received serial testing with subsequent testing at least 6 months after the initial test. Nine of those patients later tested positive (5%); all were foreign born. Of these nine, further review revealed three were not true conversions. Of the six who appeared to have a true conversion, three were noted to have had significant lymphopenia (180-660 absolute) and were receiving high doses of prednisone (25-60 mg/day) at the time of their initial negative IGRA. Two other patients were noted to have had calcified granuloma on chest x-ray at the initial negative



Flowsheet of IGRA Screening and Outcomes, 2013-2019

Table 1. Demographics of Screened Patients by IGRA Results.

	ALL	Initial positive IGRA	Initial negative IGRA	Serial IGRA	Subsequent positive IGRA
	N = 368	n = 60	n = 308	n = 180	n = 9
Male	68 (18.5%)	12 (20%)	56 (18.2%)	31 (17.1%)	3 (33.3%)
Hispanic	250 (67.9%)	37 (61.7%)	213 (69.2%)	133 (73.9%)	9 (100%)
Birth Country, High Burden TB	36 (9.8%)	14 (23 .3%)	22 (7.1%)	14 (7.8%)	–
Foreign Born	323 (87.8%)	60 (100%)	263 (85.4%)	163 (90%)	9 (100%)

IGRA. The sixth patient was found to have non-tuberculous mycobacterium and was treated. There were no cases of active TB during the study period. No patients born in the United States tested positive at initial or subsequent testing.

Conclusion: Our study demonstrates utility in serial TB screening with an IGRA in a patient population with birth in TB endemic countries, as well as periodic travel to such regions. In our patient population the yield was greatest in patients from countries with a high burden of TB. History is vital when ordering an IGRA, particularly at the initial testing. Prior positive TB skin test, prior evaluation at the local health department, prior exposure to individuals with TB, or prior TB infection, exposure, and/or treatment should be a regular component of history-taking in clinics responsible for managing immunosuppressive agents. It is important to keep in mind the risk of occult LTBI in patients who are immunosuppressed and born in TB endemic countries despite a negative IGRA result.

Disclosure: A. Fike, None; **Y. Ruiz-Perdomo**, None; **J. Katz**, None.

Abstract Number: 1154

Hispanic Patients with Rheumatoid Arthritis Have Greater Discordance Between Patient and Physician Global Estimates Than Other Ethnic Groups, Explained Largely by Fibromyalgia (FM) According to a FM Assessment Screening Tool 3 (FAST3)

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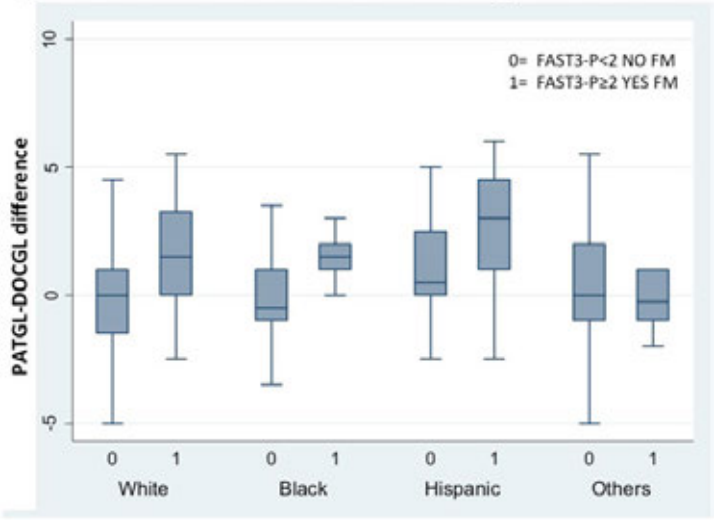
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Healthcare Disparities In Rheumatology Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Discordance between patient and physician global estimates has been described in many rheumatic diseases, including rheumatoid arthritis (RA)[1], and has been associated with decreased work productivity[2], greater radiological joint destruction and functional impairment[3], and a lower likelihood to be in remission[4]. The objective of this study was to compare the level of discordance according to self-reported race/ethnicity, and to estimate

Table: Characteristics of patients according to self-reported race/ethnicity and percentage of concordance/discordance in the four groups. **H** denotes the group with highest value.

	Whites N=100 (38%)	Blacks N=64 (25%)	Hispanics N= 60 (23%)	Others N= 36 (14%)	p
Age (yrs), mean (SD)	58.5 (15.2)	61.5 (13.4)	58.2 (15.0)	58.2 (11.7)	0.51
Women, %	70%	84%	80%	81%	0.15
Education (yrs), mean (SD)	13.2 (4.8)	12.6 (4.5)	11.2 (3.2)	14.4 (5.7) **H**	<0.001
Pain VAS (0-10)	4.5 (3.1)	5.4 (2.9)	5.9 (2.9) **H**	4.6 (2.6)	0.01
Physical Function (0-10)	2.4 (1.9)	2.3 (1.9)	3.4 (2.0) **H**	0.5 (1.2)	<0.001
Fatigue VAS (0-10)	2.7 (2.9)	3.4 (3.2)	4.1 (3.6) **H**	1.1 (2.0)	<0.001
Symptom checklist (0-60)	10.2 (8.5)	14.2 (9.5) **H**	10.5 (7.7)	11.7 (7.8)	0.061
Self-report RADAI (0-48)	10.6 (8.5)	11.3 (9.4)	12.9 (11.1) **H**	8.0 (6.3)	0.002
FAST3-P positive for FM, %	27%	37% **H**	37% **H**	23%	0.29
Global Estimates					
PATGL (0-10)	4.1 (3.0)	4.9 (2.6)	5.5 (2.9) **H**	3.9 (2.5)	0.005
DOCGL (0-10)	3.7 (2.7)	4.4 (2.2) **H**	3.8 (2.1)	3.8 (2.1)	0.10
➢ DOCINF (0-10)	1.7 (1.5)	2.5 (2.1) **H**	1.9 (2.1)	2.5 (2.3) H	0.06
➢ DOCDAM (0-10)	3.2 (2.6)	3.2 (2.2)	4.1 (2.6) **H**	3.4 (2.6)	0.10
➢ DOCSTR (0-10)	1.8 (2.8)	2.0 (2.5) **H**	1.9 (2.6)	1.3 (1.9)	0.68
Concordant/Discordance groups:					
➢ Negative discordance DOCGL-PATGL≥2/10	11 (11%)	8 (12%)	3 (5%)	5 (14%)	
➢ Concordant DOCGL=PATGL	75 (75%) H	44 (69%)	33 (55%)	27 (75%)	0.003
➢ Positive discordance PATGL-DOCGL≥2/10	14 (14%)	12 (19%)	24 (40%) **H**	4 (11%)	

Figure: PATGL-DOCGL difference according to FM status



the level of discordance in patients who met and did not meet criteria for concomitant fibromyalgia (FM) by a FM Assessment Screening Tool (FAST3-P).

Methods: At one site, patients complete a multidimensional health assessment questionnaire/routine assessment of patient index data (MDHAQ/RAPID3) (0-30) as part of routine care, which includes 0-10 scores for physical function, and 0-10 visual analogue scales (VAS) for pain, patient global estimate (PATGL), and fatigue, as well as a 0-60 symptom checklist, and a 0-48 RADAI self-report painful joint count. FAST3-P is a cumulative index based on a 0–3 sum of 1 point each for pain VAS≥6, RADAI self-report joint count≥16, and symptom checklist≥16 (positive screen for FM≥2). The treating rheumatologist completes a RheuMetric checklist including a physician global (DOCGL) and 3 VAS for inflammation (DOCINF), damage (DOCDAM) and distress (DOCSTR). Patients with primary diagnoses of RA (ICD codes) were classified into one of 3 groups based on the difference between DOCGL and PATGL: concordant group (PATGL-DOCGL within ±2/10), negative discordance (DOCGL-PATGL≥2/10), and positive discordance (PATGL-DOCGL≥2/10). Values are reported as medians (standard deviation) and percentages. Comparisons according to self-reported ethnicity groups were performed using ANOVA or Chi^2.

Results: The study included 260 RA patients: 38% Whites, 25% Black, 23% Hispanics, and 14% others. Age and sex were similar in the 4 groups. Education level was highest in “others,” (primarily Asian), followed by White, Black and Hispanic patients. Hispanic patients had poorer scores for pain, physical function, fatigue, and RADAI self-reported compared with other groups ($p< 0.001$) (Table). A higher percentage of Black and Hispanic patients screened positive for FM according to FAST3-P. Higher scores for PATGL with similar scores for DOCGL lead to higher rate of positive PATGL >DOCGL discordance in Hispanic patients versus others. The difference between PATGL-DOCGL was higher in patients with concomitant FM for each group except for “others” (Figure).

Conclusion: Hispanic patients with RA have poor scores on most MDHAQ self-reported measures compared with non-Hispanic Whites or Black despite similar physician assessments, leading to higher positive discordance rates. Concomitant FM in all RA patients may be an important contributor to discordance between DOCGL and PATGL, recognition of which could help improve the quality of care.

Reference:

1. Arthritis Care Res (Hoboken). 2014;66(6):934-42. 2. *Arthritis Res Ther* 2016, **18**(1):114. 3. *J Rheumatol* 2014, **41**(6):1061-1066. 4. Ann Rheum Dis. 2016;76(4):708-11.

Disclosure: I. Castrejon, None; **M. Riad**, None; **J. Block**, Abbvie, 2, ACR, 6, Agios, 7, Daiichi-Sankyo, 7, GlaxoSmithKline Consumer Healthcare, 5, Jannsen, 2, Medivir, 5, Novartis, 2, OARSI, Omeros, 7, Pfizer, 2, TissueGene, 2, Zynerba Pharma, 5; **T. Pincus**, Helath Services, 7, Medical History Services LLC, 6, 7, 9, Medical history services LLC, 6, 7.

Abstract Number: 1155

The Status of Latin-American Women in Rheumatology

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SESSION INFORMATION
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Session Type: Poster Session (Monday)
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Background/Purpose: Currently, Latin America does not have detailed information of women in rheumatologists based on education, working conditions, productivity, distribution of time between work activities and job satisfaction. The purpose of this survey was to provide more information of the rheumatology women in Latin America.

Methods: A digital survey was created using the Google Forms platform, it was approved and endorsed by the scientific committee of PANLAR and later sent to the different rheumatology associations of the region. The data was analyzed in the statistical program SPSS v.23.

Results: There were 318 women with an average age of 44 ± 10.7 [25-71], mostly mestizo ethnicity 60%, white 38%, indigenous 1%, African American 1% and Asian 1%. 58% are married, 28% are single, 8% are divorced, 5% are in free-union and 2% are widows. The mean number of children was 1.21 ± 1.11 [0-5]. The country with the largest number of rheumatologists was Argentina 32%, Brazil 16% and Mexico 11%. 37% of rheumatologists had at least one comorbidity, 17% thyroid disease, 7% osteoarthritis, 6% hypertension, 4% diabetes, 4% depression, 4% autoimmune diseases, 1% artery disease and 1% gout. 35% work in private hospitals, 27% private practice, 21% in government hospitals, 16% university hospitals and 1% in non-profit organizations. 86% is dedicated to adult rheumatology, 20% internal medicine, 15% pediatric rheumatology and 2% to immunology. The average of weekly work hours was 39.4 ± 18.3 [4-120], male rheumatologist weekly hours mean was 38.3 ± 17.1 [0-120]. 29% have training in musculoskeletal ultrasound, 75% training in densitometry reading and 50% training in musculoskeletal MRI. 72% have access to early arthritis clinic. 39% have an annual income below 19K, 19% between 20-29K, 11% between 30-39K, 14% between 50-99K, 9% between 40-49K and only 8% earn above 100K per year compared to male rheumatologist which 27% have an annual income below 19K, 12% between 20-29K, 12% between 30-39K, 19% between 50-99K, 10% between 40-49K and 20% earn above 100K per year. Regarding the satisfaction of the general practice, the average was 5.2 ± 1.25 [0-7], career options / professional growth 4.16 ± 2.01[0-7], geographic location 4.57 ± 2.11[0-7], income salary 3.2 ± 1.78 [0-7], job security 3.40 ± 1.87[0-7], colleagues and coworkers 4.42 ± 2.07[0-7]. 59% have a malpractice insurance. 88% have medical insurance and 70% retirement plan.

Conclusion: There are more women rheumatologist in the region compare to male rheumatologist. Women rheumatologist feel satisfied with their clinical practice, however, compared to male rheumatologist women have a lower annual income. This is the first study of its kind in Latin America.

Disclosure: G. Maldonado, None; **M. Intriago**, None; **E. Soriano**, Abbvie, 2, 5, 8, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, Amber, 8, Amgen, 5, 8, AMGEN, 5, 8, BMS, 8, BRISTOL, 8, Bristol MS, 8, BRISTOL MYERS SQUIBB, 8, Bristol-Myers Squibb, 8, eli lilly, 5, 8, Genzyme, 8, GENZYME, 8, GLAXO, 2, Glaxo, 2, glaxosmithkline, 2, GlaxoSmithKline, 2, GSK, 2, Janssen, 8, Lilly, 5, 8, LILLY, 5, 8, Novartis, 2, 5, 8, NOVARTIS, 2, 5, 8, PFIZER, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, 8, Roche, 2, 8, ROCHE, 2, 8, Sandoz, 5, SANDOZ, 5, Sanofi, 5, SANOFI, 5, SANOPHY, 5, UCB, 8; **C. Rios**, None.

Abstract Number: 1156

Differences in Clinical Outcomes According to the Healthcare Regime in Colombian Patients with Rheumatoid Arthritis

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Table 1. Demographic and clinical variables assessed for overall, subsidized, Contributory and Excellence Clinical Care Center healthcare regime in Colombian patients with RA.

Variable	Overall	Subsidized	Contributory	Excellence Clinical Care Center	p-value
n (%)	240(100)	80(33,3)	80(33,3)	80(33,3)	-
Men n (%)	52(21.6)	21(26.2)	12(15)	19(23,7)	-
Mean age (IC 95%)	53.7 (52-56)	50.6 (47-53)	58.6 (56-62)	51.9 (50-54)	0,0008
Early RA n (%)	49 (20.4)	13 (16.2)	17 (21.2)	19 (23.7)	-
Established RA n (%)	191(79.6)	67(83.7)	63(78.7)	61(77)	-
Patients with initial high disease activity n (%)	175(72.9)	48(60)	73(91.2)	55(68.7)	-
Patients with high disease activity at the end of follow-up n (%)	114(47.5)	52(65)	41(51.2)	21(26.2)	-
Mean number of days between scheduled follow-up appointments (CI 95%)	58.2 (55.2-61.2)	48.9 (44.1-53.8)	82.7 (79.6-85.7)	43 (40.5-45.5)	< 0.0001*
Mean number of days between real follow-up appointments (CI 95%)	86 (78.3-93.7)	120.8 (102.3-139.2)	92.9 (85.7-100.2)	44.4 (40.9-47.8)	<0.0005*
Mean percentage of appointments accomplished on time (CI 95%)	50.1 (33.3 - 66.7)	17.08 (0 - 33.3)	62.08 (33.3 – 66.7)	71.25 (66.7 - 100)	<0.0001*
Mean percentage of treatment adherence (CI 95%)	61.9 (66.7-75)	52 (50-67)	57.19 (50-75)	76.7 (66.7-100)	<0.0001*
Mean percentage of time with high disease activity during follow-up (CI 95%)	60.4 (53.7-68.1)	67.26 (53.8-100)	69.1 (60.6-100)	44.9 (28.6-56.8)	<0.0001*

* Statistically significant after applying Bonferroni Test
- High disease activity: patients with moderate (DAS28: 3.2-51) or severe disease activity (DAS28: >5.1) based on DAS28-ESR.
- CI 95%: Confidence interval 95%
- n: number of patients
- %: percentage

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Healthcare Disparities In Rheumatology Poster

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) generates high impact on patients and healthcare systems. Adequate control of disease activity depends to a large extent on the access to a Rheumatologist. The type of healthcare system adopted by the governments constitutes a major determinant for the access of patients to an adequate standard of care. Colombia has a contributory and public-subsidized health insurance system, which ensures a universal coverage of the population; however, differences in care access opportunities persist, especially for appointments with sub-specialties. The aim of this study was to compare the disease outcomes of Colombian patients with RA, based on their type of health regime.

Methods: A retrospective observational study of Colombian patients with RA (Meeting 2010 ACR/EULAR classification criteria), with at least 3 assessments by a rheumatologist, in three outpatient services of different regimes: Contributory (C), Subsidized (S), and an excellence clinical care center (C3). Data collected from clinical records during a follow-up period of 2 years include: age, RA classification, percentage of patients with initial and final high disease activity based on DAS-28 ESR, number of appointments, days between appointments (ordered and real), number of appointments accomplished on time, adherence to treatment, and percentage of time in high disease activity. Mean and 95% confidence intervals were calculated. Statistical differences were calculated using X2 or Kruskal-Wallis test and adjusted for multiple comparisons using the Bonferroni test, with a significance level of p< 0,005. Survival analysis for the achievement of remission/low disease activity during follow-up was developed. Mantel-Cox test was calculated to compare the survival curves for every regime.

Results: A total of 240 patients were included (80 patients per regime). Results are summarized in Table 1. Mean initial age was 53.7 years; 21.6% of patients were men; 79.6% of patients had established RA; 72.9% of patients had initial high disease activity; Mean percentage of time in high disease activity during follow-up was lower in C3 (44.9%), and higher in C (69.1%). At the end of the follow-up, S group had the highest proportion of patients remaining with high disease activity, and C3 the lowest. Survival curve analysis based on Mantel-Cox shows no significant difference between S and C groups (p=0.2903), but were significantly different compared to C3 group (p< 0.0001). Median survival in high disease activity was greater in the S group (293 days), followed by C (254 days), and finally by C3 (64 days).

Conclusion: Patients treated in the clinical care center had better outcomes based on higher adherence and lower disease activity scores, compared to the other regimes, especially those on Subsidized regime. The type of health-

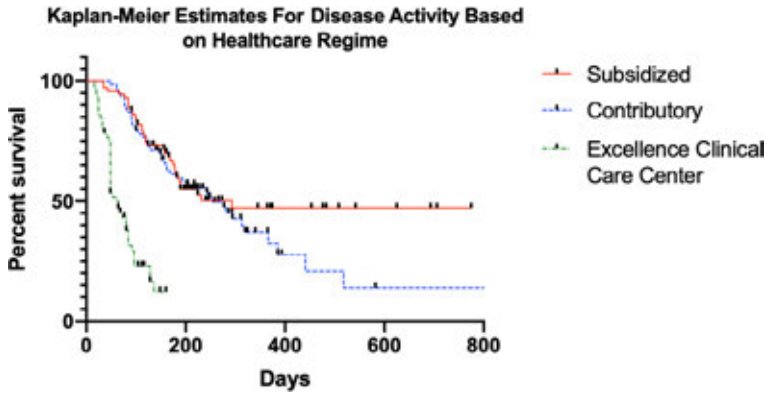


Figure 1. Kaplan-Meier curves for achievement of low disease activity during 2 years of follow-up.

care regime a patient has access to, is a major determinant of the disease outcomes, specially for chronic diseases in which the success of the treatment depends on a strict follow-up by a specialist. This differences in the access and outcomes are reflected in higher expenses for healthcare system, derived from complications and disabilities that patients could suffer, secondary to inadequate control of the disease.

Disclosure: J. Barahona-Correa, None; **J. Florez**, None; **M. Rodriguez**, None; **K. Ramirez**, None; **P. Mendez-Patarroyo**, None; **P. Coral-Alvarado**, None; **G. Quintana-López**, None.

Abstract Number: 1157

#WomeninRheumatology: Is There a Speaker Gender Gap at ACR Meetings?

Kanika Monga,[1] and Jean Liew[2], [1]University of Texas Health Science Center, Houston, TX, [2]University of Washington, Seattle, WA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Healthcare Disparities In Rheumatology Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: There is a gender gap – that is, proportionately more male than female physicians – across most medical specialties in Canada and the U.S. despite the current gender parity in medical school. Limited numbers of role models, sponsors, and mentors may contribute. A lack of women leaders and representation in certain specialties may perpetuate the gap further. A goal of attaining equal (or as close to equal as possible) representation at national conferences is essential.

Recent studies have quantified the gender gap among speakers at academic conferences. The largest study of 181 medical conferences held in North America over one decade found an increase in the proportion of female speakers from 25 to 34% over time, and that the underrepresentation of women was more marked at surgical compared to

Table. Proportion of moderator/speaker slots filled by women, by year.

	2017	2018
overall	42.8%	47.0%
Speakers	41.1%	46.9%
Moderators	46.5%	47.6%
Basic science	39.5%	41.4%
Clinical	43.5%	48.1%
By presentation type		
Pre-meeting	37.1%	43.9%
ACR general	35.2%	42.5%
AHRP general	56.8%	73.7%
Abstract	47.5%	50.1%
Workshop	24.6%	32.8%
Study group	43.3%	56.9%
Meet the Professor	36.3%	32.5%

medical conferences [Ruzycki, et al 2019]. The purpose of our study was to describe the proportion of female representation among speakers and moderators at the ACR meeting over the past two years.

Methods: Using the ACR Session Tracker from 2017 and 2018, we determined the proportions of women for each speaker or moderator slot. Individual speakers could be counted multiple times. We further categorized by basic versus clinical science presentation, and by type of session (pre-meeting, ACR general session, AHRP general session, abstracts, workshop, study group, or Meet the Professor).

Results: Overall, the proportion of combined female speakers and moderators was 42.8% in 2017 and 47.0% in 2018. The representation of female speakers increased from 2017 to 2018 by 4.2%, which in a conference of approximately 1100 presenters (total presenters at the 2018 conference) amounts to 46.2 persons. There were a greater proportion of female speakers in the clinical than in the basic science presentations (average 45.8% versus 40.5%). By session type, the AHRP sessions had the highest proportion of female representation (average 65.3%) while Meet the Professor and workshops had the lowest (34.4% and 28.7%, respectively).

Conclusion: The overall mean proportion of female speakers and moderators at ACR in the past two years was 44.9%. Compared to a prior study, the ACR had female representation slightly above the mean compared to major North American medical conferences held in 2017. This proportion is also comparable to the estimated U.S. adult rheumatology workforce data from 2015. Although the gender gap at recent ACR meetings was narrower as compared to other conferences, we must remain cognizant of its presence and continue to work towards equal representation.

Disclosure: K. Monga, None; **J. Liew**, None.

Abstract Number: 1158

Investigating Health Literacy and Numeracy in an Academic Center Lupus Cohort

Mithu Maheswaranathan,[1] Raeann Whitney,[2] Megan Clowse,[2] Amanda Eudy,[2] and Jennifer Rogers[2], [1]Duke University Medical Center, Durham, NC, [2]Duke University, Durham

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Healthcare Disparities In Rheumatology Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Up to 50% of American adults have basic or below basic health literacy and numeracy. Low health literacy is associated with increased health care costs and hospitalization rates as well as poor disease knowledge and self-management. Health numeracy is a form of quantitative health literacy with important implications on health. While studies have demonstrated the impact of low health literacy on patient outcomes in many diseases including rheumatoid arthritis, there is no recently published data investigating literacy and numeracy in SLE. The objectives of this study were to (1) assess baseline health literacy and numeracy of our SLE cohort and (2) evaluate clinical associations.

Methods: SLE patients in a university clinic meeting SLICC criteria from March through May 2019 were recruited. Health literacy was assessed using the Basic Health Literacy Screen (BHLS), Rapid Estimate of Adult Literacy in Med-

Table 1: Association Between Numeracy Scores and Patient Characteristics / Clinical Measures

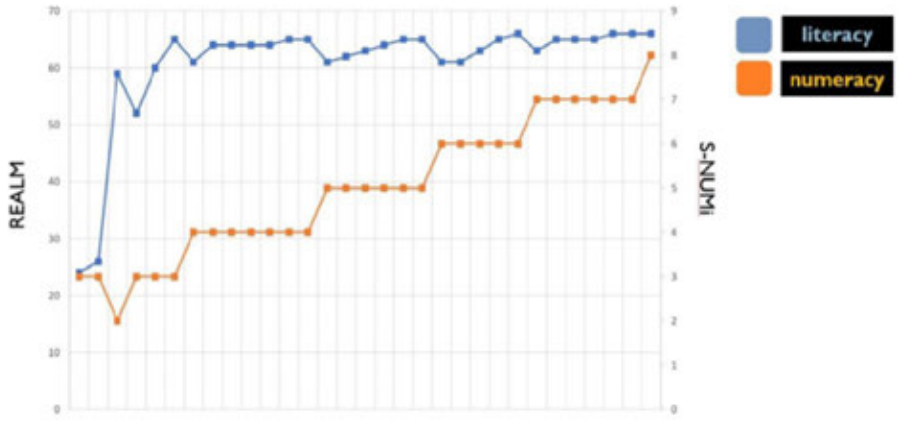
	High Numeracy s-NUMI 7 or 8 (n=8)	Low to Average Numeracy s-NUMI <7 (n=27)	p value
	% of Patients	% of Patients	
Gender			
Men (%)	0%	7%	1.0
Female (%)	100%	93%	
Race			
White (%)	63%	19%	0.03
Non-White (%)	38%	81%	
Age in Years (Range)	42 (34-60)	39 (22-63)	0.4
History of **Lupus Nephritis**	50%	48%	1.0
Cognitive Dysfunction	25%	33%	1.0
Medication Adherence	75% ± 37	82% ± 19	0.6
College Graduate	63%	44%	0.4
Medicaid	12.5%	59%	0.04
Disability	12.5%	41%	0.2
Income <$50,000 annually	38%	78%	0.08
	Score	Score	
Clinical SLEDAI	1.4 ± 2.5	2.4 ± 2.6	0.4
FSS [Fibromyalgia]	8.1±5.6	9.3±7.2	0.7
PHQ9 [Depression]	5.1 ± 4.1	7.0 ± 6.3	0.4

icine (REALM) and the Arthritis-Adapted REALM (A-REALM). Health numeracy was evaluated using the Shortened Subjective Numeracy Scale (SNS-3) and the Numeracy Understanding in Medicine Instrument Shortened Version (S-NUMi). Fisher's exact test was applied to categorical variables using STATA Version 15. The associations between health literacy and numeracy with clinical variables were analyzed using univariate and multivariate models.

Results: The study included 35 patients with SLE with an average age of 39 years, 94% were high school graduates and 49% college graduates, 69% had annual income < $50,000, and 71% were non-white. SLE disease duration averaged 14 years and current average clinical SLEDAI was 2.1. The majority of patients scored in the high school range for literacy (86% with REALM ≥ 61) and self-reported good reading skills (BHLS mean 13.2 [SD 2.5] out of 15). On the other hand, only 23% of patients scored in the high range for numeracy, and patients reported lower subjective math self-evaluation scores (SNS-3 12.5 [SD 4.3] out of 18).

Compared to patients with high numeracy, patients with a s-NUMI score consistent with average or low numeracy were more likely to be black, have significantly lower income or have Medicaid insurance (Table 1). There was not an association between numeracy and prior lupus nephritis, current lupus activity, self-reported medication adherence, or current pain, fatigue or depression; however, the study was under-powered to identify these differences. Interestingly, self-reported cognitive dysfunction was not different between groups.

Figure 1: Distribution of the Objective Literacy (REALM) and Numeracy (S-NUMi) Scores



Conclusion: In our study, the majority of SLE patients scored at the high school range for health literacy (86%) compared to only 23% demonstrating high numeracy scores. Our clinical experience suggests that patient understanding of lupus manifestations and treatment is not reflected in the high literacy scores found in this study. We hypothesize that a patient's ability to read words, as is tested in the REALM and A-REALM, is not sufficient to assess understanding of the complexity of SLE. Further studies are needed to investigate the impact of literacy and numeracy on disease understanding and medication adherence.

Disclosure: M. Maheswaranathan, None; **R. Whitney**, None; **M. Clowse**, GSK, 2, UCB, 5; **A. Eudy**, GSK, 2; **J. Rogers**, None.

Abstract Number: 1159

Deep Learning Social Media Analysis Demonstrated Gender-Specific Disparity in Side Effects from Rheumatoid Medications

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Healthcare Disparities In Rheumatology Poster
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Multiple studies revealed adverse side effects caused by different rheumatoid arthritis (RA) medications. However, little is known about gender differences in RA treatment and medications. Increasingly patients are sharing and searching for RA information on health-related social media. This study developed deep learning (DL) text analytical tools on top of health-related social media to identify gender-specific disparities in side effects reported by people taking 2 common medications for RA: Methotrexate/Trexall and Leflunomide/Arava.

Methods: Data from three well-known health-related social media, *WebMD* (https://www.webmd.com/drugs), Daily Strength (https://www.dailystrength.org) and and *Drugs.com* (https://www.drugs.com), were extracted from June

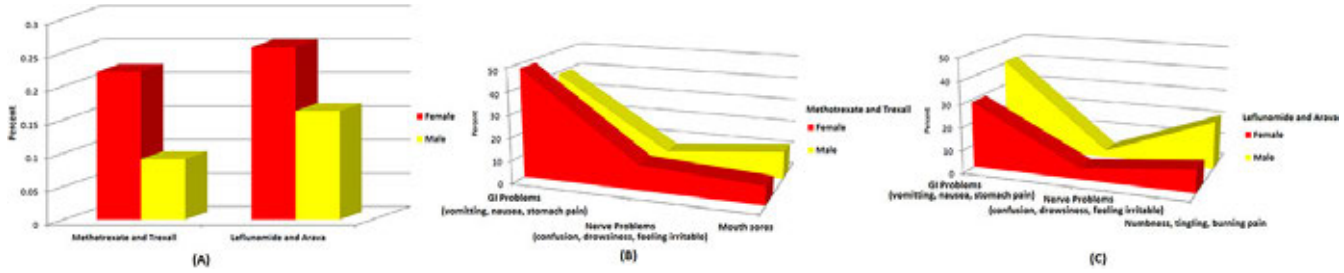


Figure 1. (A) Female and male's percentage who shared side effects experiences associated with Methotrexate (Methotrexate and Trexall) and Leflunomide (Leflunomide and Arava). One can see the number of adverse side effects posts generated by women was greater than those generated by men. Among 1,389 Methotrexate and Trexall associated posts shared by women (including side effects, indication, and/or other topics), over 307 posts were discussing side effects associated with this medication. For Leflunomide and Arava, this was 285 out of 1,105 messages posted by women. For men, it was 102 out of 1,119 posts and 137 out of 841 posts, respectively. (B and C) Gender-specific comparative visualizations across different side effects of Methotrexate-Trexall (B) as well as Leflunomide-Arava (C).

2013 to May 2019, including gender information and the text of posts. Since *Drugs.com* does not provide gender of the users, a top 3 name-to-gender inference service, namely NameAPI (https://www.nameapi.org) has been used to identify gender of the users based on their names. We segmented each post into a set of sentences as the units for DL, which used word2vec feature representation. An ensemble of deep neural networks was developed to identify sentences relating to drug adverse side effects. The training data consisted of a random subset of sentences annotated by three domain experts, where each sentence was classified as either describing a side effect (SE) or no side effect (No-SE). A total of 12,702 sentences (6,453 SE and 6,249 No-SE) were annotated, with high inter-annotator agreement of kappa=0.81. A baseline classifier for comparison was trained using Naïve Bayes with bag-of-word features.

Results: On 4-fold cross-validation, the DL classifier achieved an AUC of 0.897. The accuracy of the ensemble DL classifier outperformed the Naïve Bayes classifier significantly (p=0.04). With the best-tuned configuration, the DL classifier was then applied on 39,191 unseen new sentences for large-scale trend analysis, in which the overall disparity and disparity in five common SEs are shown in Figure 1. To focus on only RA-related sentences, we constrained messages to those that explicitly included at least one of: "RA", "R.A", "R.A.", "bone", and "joint". Figure 1 shows the visualization results.

Conclusion: The study demonstrated feasibility of developing highly accurate DL classifiers for identifying RA medication side effects in social media, providing gender disparity information using this wealth of data. Although social media may reflect biased prevalence of conditions due to subjective user behaviors, we were able to faithfully describe the data. In addition to improving our methods, future work will emphasize verifying/comparing such disparity by applying similar analysis on EHRs along with generic social media (e.g., Twitter, Google+, and reddit). The present work elucidates construction of a holistic patient-centered decision support framework that can be merged with a diverse range of clinical data, such as EHRs and clinical notes to help clinicians and patients assess benefits and risks of RA treatments, conducting the development of personalized medicine within the RA context.

Disclosure: A. P. Tafti, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **K. O'Neill**, None; **E. Myasoedova**, Pfizer, 2; **H. Liu**, None; **P. Sinicrope**, None; **J. Davis**, Abbvie, 5, Pfizer, 2, 5, Sanofi Genzyme, 5.

Abstract Number: 1160

Clinical Trials in Rheumatoid Arthritis Have Inadequate Racial/Ethnic, Gender and Age Diversity: A Systematic Review

Adrienne Strait,[1] Francine Castillo,[2] Sonam Choden,[3] Jing Li,[4] Evans Whitaker,[5] Titilola Falasinnu,[6] Gabriela Schmajuk,[3] and Jinoos Yazdany[4], [1]UCSF School of Medicine, San Francisco, CA, [2]University of California, San Francisco, San Francisco, CA, [3]UCSF, SFVAMC Division of Rheumatology, San Francisco, CA, [4]UCSF Division of Rheumatology, San Francisco, CA, [5]UCSF Medical Library, San Francisco, CA, [6]Department of Health Research and Policy, Stanford School of Medicine, Palo Alto, CA

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Healthcare Disparities In Rheumatology Poster

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Racial/ethnic minorities, women, and the elderly experience a disproportionate burden of disease in Rheumatoid Arthritis (RA), making it particularly important to examine drug therapies in these populations. Clinical evidence demonstrates that treatment responses to new RA biologic drugs differ significantly by race/ethnicity. Despite a national health agenda to improve the representation of diverse populations in clinical trials, there have been few large-scale analyses examining the diversity of clinical trial participants within rheumatology, and none focusing on RA. Our objective was to perform a comprehensive systematic review of RA randomized controlled trials (RCTs) published within the last 10 years in order to characterize the representation of racial/ethnic minorities, women, and the elderly.

Table 1: Characteristics of the 240 Rheumatoid Arthritis randomized controlled trials included in this review.

	Total no. of RCTs (%)	No. of RCTs with ≥1 U.S.-based site (%)
Overall	240 (100.0)	126 (52.5)
Gender inclusion		
Both males and females	231 (96.3)	124 (98.4)
Females only	3 (1.3)	0 (0.0)
Not reported	6 (2.5)	2 (1.6)
Age inclusion		
Trials that had exclusion criteria for any upper age limit	99 (41.3)	38 (30.2)
Exclusion by upper age limit		
Excluded >100 yo or >99 yo	3 (1.3)	3 (2.4)
Excluded >85 yo or >80 yo	21 (8.8)	11 (8.7)
Excluded >75 yo or >74 yo	43 (17.9)	16 (12.7)
Excluded >70 yo or >69 yo	14 (5.8)	4 (3.2)
Excluded >65 yo or >64 yo or >60 yo	18 (17.5)	4 (3.2)
Age reporting		
Trials reporting avg age and SD	193 (80.4)	96 (76.2)
Race/ethnicity reporting		
Race reported AND Hispanic ethnicity not mentioned	86 (35.8)	57 (45.2)
Race reported AND Hispanic reported as separate race	5 (2.1)	5 (4.0)
Race and ethnicity reported	12 (5.0)	11 (8.7)
Ethnicity only reported	27 (11.3)	8 (6.3)
Neither race nor ethnicity reported	110 (45.8)	45 (35.7)
Funding source		
Industry	205 (85.4)	119 (94.4)
Non-industry	19 (0.0)	5 (4.0)
Jointly funded	7 (2.9)	2 (1.6)
Not stated	9 (3.8)	0 (0.0)
Total enrollment		
≤ 50	32 (13.3)	7 (5.6)
51 to 100	28 (11.7)	8 (6.3)
101 to 200	37 (15.4)	12 (9.5)
≥ 200	143 (59.6)	99 (78.6)
Drug class under study		
Biologic or new synthetic DMARD	214 (89.2)	119 (94.4)
Conventional DMARD	15 (6.3)	4 (3.2)
Glucocorticoid	6 (2.5)	2 (1.6)
Other	5 (2.1)	1 (0.8)

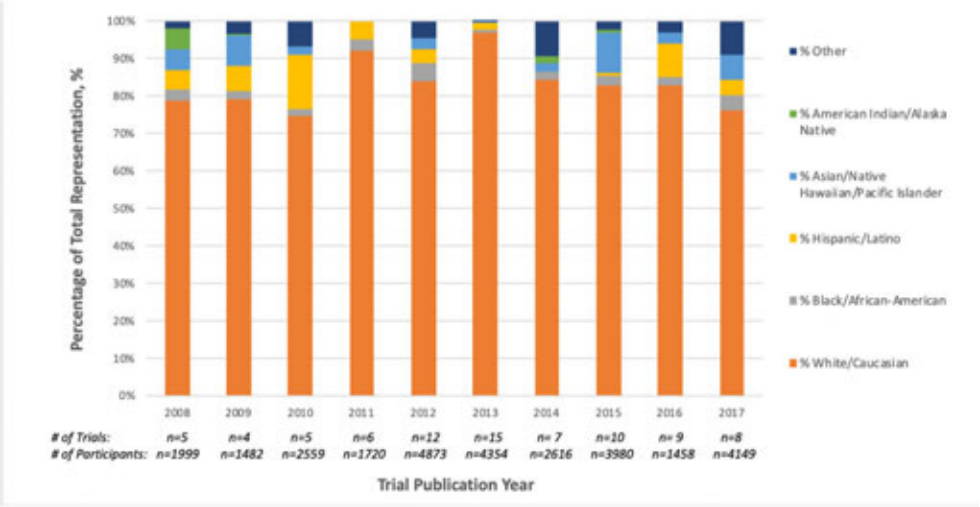


Figure 1: Trends in racial/ethnic representation in Rheumatoid Arthritis randomized controlled trials with at least one U.S.-based site between 2008 and 2017 (N=29,190 participants)

Methods: We identified RA RCTs that were published in PubMed (1/1/2008 to 1/1/2018), searching MEDLINE using "Rheumatoid Arthritis" and "humans" as MeSH terms and "randomized controlled trial" as a publication type. The titles and abstracts for all 1195 identified records were independently screened by two reviewers using a web-based application called Rayyan QCRI (https://rayyan.qcri.org). Full texts of remaining records (n=922) were screened using a process adapted from a previously published systematic review. Logistic regression models were used to assess changes in the proportion of subjects in each racial/ethnic and gender category over time. Chi-squared tests were used to 1) compare the proportion of trial enrollees across racial/ethnic groups to the overall demographics of the U.S. and 2) to compare the proportion of female and male enrollees to the overall age-adjusted gender prevalence of RA.

Results: A total of 240 RA RCTs were included in the review (Table 1). The enrollment of minority racial/ethnic groups in U.S.-based RA RCTs was significantly lower than the representation of these groups in the U.S. census population ($p < 0.001$). While racial and ethnic minorities comprise about 40% of the U.S. population, they only represented 16% of the RCT population for RA. The enrollment of males in RA RCTs with at least one U.S.-based site was significantly lower than the burden of male RA cases nationally (20.4% vs. 28.6%) ($p < 0.001$). There were no significant changes in the representation of racial/ethnic groups or gender over the observed period (p-trend >0.05) (Figure 1). Reporting of an upper age limit as exclusion criterion was observed in 41.3% (n=99) of the RA RCTs (Table 1).

Conclusion: Despite national efforts to increase clinical trial diversity, there was no trend to improved representation of minority racial/ethnic groups in U.S.-based RA RCTs over the period 2008-2017, with significant underrepresentation of these groups throughout. The results also suggest that men are underrepresented in RA RCTs and that the elderly are often excluded from RA RCTs.

Disclosure: A. Strait, None; **F. Castillo**, None; **S. Choden**, None; **J. Li**, None; **E. Whitaker**, None; **T. Falasinnu**, None; **G. Schmajuk**, None; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2.

Abstract Number: 1161

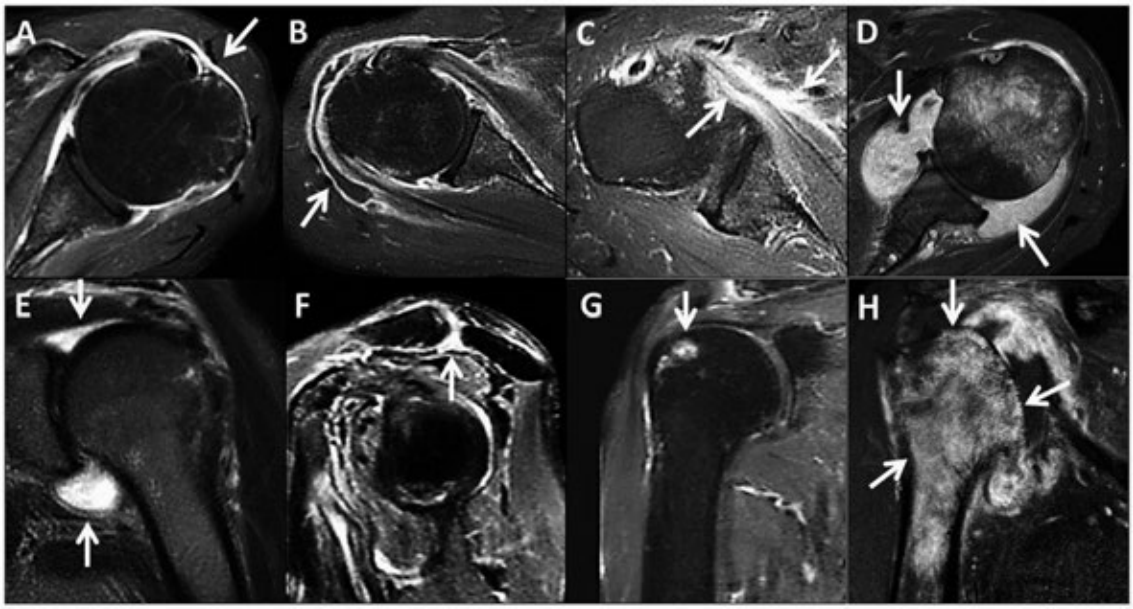
Gadolinium-Enhanced Magnetic Resonance Imaging in Shoulders Contributes Accurate Diagnosis and Predicting Recurrence to Patients with Polymyalgia Rheumatica

Kazuro Kamada,[1] Hiroyuki Nakamura,[1] Masato Tarumi,[1] Shun Tanimura,[1] and Tetsuya Horita[1], [1]Tomakomai City Hospital, Tomakomai, Japan

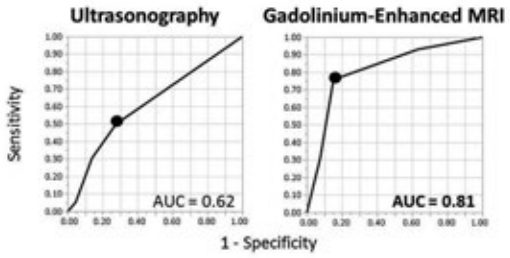
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Polymyalgia rheumatica (PMR) is a glucocorticoid-responsive muscle pain and stiffness, especially in the shoulders and hips. PMR is clinically diagnosed based on the symptoms, although accurate diagnosis is difficult because the symptoms can occur in many other rheumatologic and inflammatory conditions. Recently, it was reported that ultrasonography (US) in shoulders could detect the specific findings to PMR, such as biceps tenosynovitis and subdeltoid bursitis. Magnetic resonance imaging (MRI) also has an advantage of visualizing bone and muscle lesions; however, the application to PMR diagnosis has not been established yet. In this study, we evaluated gadlinium-enhanced MRI findings of the shoulder in patients with PMR. The purpose of this study is to assess whether gadlinium-enhanced MRI could improve diagnostic accuracy and prognosis prediction in patients with PMR.

Methods: This study included the consecutive patients who had bilateral shoulders pain and fulfilled the Bird classification criteria for PMR between June 2012 and June 2018 in Tomakomai City Hospital. Gadlinium-enhanced MRI and US in shoulders were performed in the all patients. We excluded patients declining participation in the study or having contraindications of gadlinium-enhanced MRI. PMR was diagnosed by at least two rheumatologists. MRI and US findings were evaluated by independent radiologists. 20 mg/day of prednisolone was initially administered to patients with PMR, and was tapered after remission. They were followed-up until June 2019 about recurrences.



	PMR (n = 58)	Non-PMR (n = 79)	p value
Ultrasonography in shoulders			
Biceps tenosynovitis, %	43	23	0.02
Subdeltoid bursitis, %	32	12	< 0.01
Glenohumeral synovitis, %	11	11	0.99
Gadolinium-Enhanced Magnetic Resonance Imaging in shoulders			
Enhancement of joint capsule, %	**69**	35	**< 0.01**
Enhancement of rotator cuff tendon, %	**72**	32	**< 0.01**
Enhancement of biceps tendon, %	12	6	0.24
Synovial hypertrophy, %	12	15	0.60
Shoulder joint effusion, %	64	44	0.02
Enhancement of glenohumeral joint, %	5	10	0.29
Focal bone edema in humerus head, %	59	19	**< 0.01**
Diffuse bone edema in humerus head, %	2	9	0.08



Recurrence	No (n = 30)	Yes (n = 24)	p value
Age, years	**76 (71-82)**	72 (66-77)	**0.04**
Sex (female), %	53	75	0.10
ESR, mm/h	87 (80-113)	99 (71-126)	0.68
MMP-3, ng/mL	238 (132-333)	196 (113-403)	0.69
Positive ultrasonography, %	52	52	0.97
Gadolinium-Enhanced Magnetic Resonance Imaging in shoulders			
Enhancement of joint capsule, %	77	67	0.41
Enhancement of rotator cuff tendon, %	**87**	58	**0.02**
Enhancement of biceps tendon, %	10	12	0.77
Synovial hypertrophy, %	3	**21**	**0.04**
Shoulder Joint effusion, %	60	67	0.61
Focal bone edema in humerus head, %	53	63	0.50

Results: 269 patients visited our hospital complaining of bilateral shoulders pain, and 175 of them fulfilled the Bird classification criteria for PMR. 137 patients received gadlinium-enhanced MRI and US examinations, and PMR was diagnosed in 58 patients. Enhancement of joint capsule (Fig. 1A), rotator cuff tendon (B) or biceps tendon (C), synovial hypertrophy (D), shoulder joint effusion (E), enhancement of glenohumeral joint (F) and/or focal (G) or diffuse (H) bone edema in humerus heads were found in the patients. Of these MRI findings, enhancement of joint capsule or

rotator cuff tendon and focal bone edema in humerus heads were significantly frequent in the PMR patients. If the three findings on MRI were used in combination to diagnose PMR, the sensitivity and specificity were 76% and 85%, respectively, higher than 50% and 72% of US findings (Fig. 2). In the follow-up study, PMR recurred in 24 patients (44%). Patients with recurrent PMR had younger ages, less enhancement of rotator cuff tendon and more synovial hypertrophy findings on MRI (Fig. 3).

Conclusion: Gadolinium-enhanced MRI displayed capsulitis, rotator cuff tendonitis and focal osteitis in shoulders, relatively specific to patients with PMR. Besides, rotator cuff tendonitis and synovial hypertrophy on MRI were associated with recurrences of PMR. Our study suggested that gadolinium-enhanced MRI in shoulders could contribute accurate diagnosis and predicting recurrence to patients with PMR.

Disclosure: K. Kamada, None; **H. Nakamura**, None; **M. Tarumi**, None; **S. Tanimura**, None; **T. Horita**, None.

Abstract Number: 1162

Changes in Novel Composite Scores of Disease Activity and Cumulative Damage Are Prognostic of Accelerated Knee Osteoarthritis: Data from the Osteoarthritis Initiative

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SESSION INFORMATION
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Background/Purpose: Composite imaging scores that reflect cartilage damage, bone marrow lesions (BMLs), and effusion-synovitis may enable us to conceptualize knee osteoarthritis (KOA) disease progression as two constructs: 1) disease activity = whole-joint dynamic disease processes that fluctuate over time and relates to knee pain, 2) cumulative damage = joint damage that has accrued over time and relates to radiographic disease severity. We aimed to determine if recently validated composite magnetic resonance (MR) metrics of KOA disease activity and cumulative damage can predict the development of accelerated KOA (AKOA).

Table 1. Baseline Group Characteristics. KOA: knee osteoarthritis; KL: Kellgren-Lawrence; SD: standard deviation; n: sample size.

Variables [(means (SD); except where noted)	AKOA (n=125)	Typical KOA (n=125)	No KOA (n=125)
Females, n(%)	79(63%)	79(63%)	79 (63%)
Age (years)	62.5(8.5)	58.4(8.4)	57.3(8.2)
Body mass index (kg/m²)	29.7(4.6)	28.1(4.4)	26.9(4.4)
Index knee KL Grade=0, n(%)	42(34%)	71(57%)	92 (74%)
WOMAC pain (0-20; score=pain)	2.6(3.3)	1.6(2.1)	1.4(2.0)
Use of Pain Medication, n(%)	72(58%)	61(49%)	47(38%)

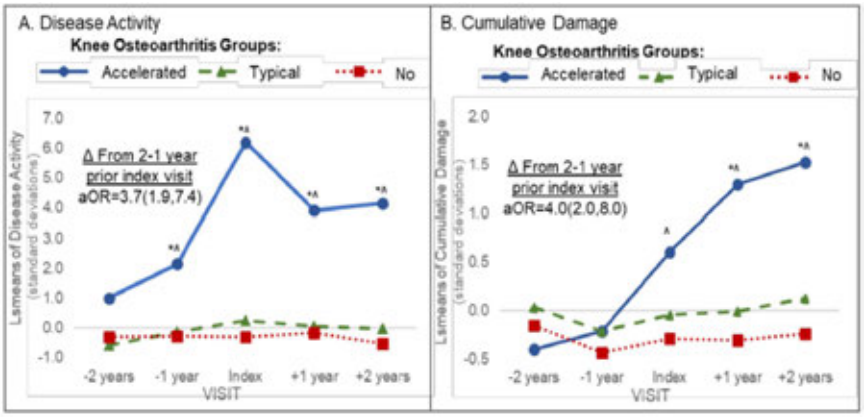

Figure 1. Differences in Disease Activity (Figure 1A) and Cumulative Damage (Figure 1B) in Individuals with Accelerated Compared to Typical and No Knee Osteoarthritis. Greater values for disease activity and cumulative damage are considered disease progression. The standardization of components allows the composite metrics to be interpreted as the amount of standard deviations away from the group overall group mean at the 2 year prior to index visit. LSmeans are statistically different in accelerated compared to typical(*) or no (^) knee osteoarthritis. Generalized linear mixed models were adjusted for sex and factors related to missing magnetic resonance data at the next visit (i.e., age, body mass index, injury, frequent knee pain, days with limited activity in prior month, overall global rating, and WOMAC pain). aOR = adjusted odds ratio (95% confiedence intervals). Logistic regression models were adjusted for sex, race, and baseline age, body mass index, KL grade, WOMAC pain, and use of pain medication.

Methods: We identified adults from the Osteoarthritis Initiative without radiographic KOA (i.e., Kellgren-Lawrence grade [KL] 0/1) at baseline. Three groups were identified based on annual radiographic disease progression over the first 48-months: 1) *AKOA*: progressed to KL 3/4; 2) *typical KOA*: any other increase in KL; 3) *no KOA*: no change in KL. The visit an adult met the AKOA or typical KOA criteria was defined as the index visit. We assessed cartilage damage in four tibiofemoral regions, BML volume in four tibiofemoral regions, and a whole knee effusion-synovitis volume on 3T MR images with semi-automated programs. We used annual images from two years before to two years after the index visit. Each MR metric was normalized to participant size and standardized from the earliest visit. We calculated disease activity as the sum of the standardized score from all four BML regions and effusion-synovitis. We calculated cumulative damage as the sum of the the standardized score from all four cartilage regions. To determine group differences across time in disease activity and cumulative damage, we used generalized linear mixed models with group (3 levels) and time (up to 5 levels) as independent variables. Additionally, change in the composite metrics from two to one year prior to the index visit was converted to a dichotomous variable to compare the worst tertile (greatest progression) to the other two tertiles. To establish the prognostic capability of disease activity and cumulative damage change, we used separate logistic regression models to determine if change in each composite metric prior to disease development was associated with future AKOA status (AKOA vs no AKOA).

Results: Table 1 provides the baseline characteristics for each group. Starting at one year prior to the index visit, the AKOA group had greater disease activity compared to the typical or no KOA groups (Figure 1A). Starting at the index visit, the AKOA group had worse cumulative damage compared to the typical or no KOA groups (Figure 1B). There were no differences at any time for either composite metrics between the typical and no KOA groups (Figure 1A and 1B). However, adults with the greatest increase in disease activity or cumulative damage from two to one year prior to the index visit were 3.7 and 4.0 times more likely to develop AKOA, respectively (Figure 1A and 1B).

Conclusion: Prior to AKOA development, disease activity and cumulative damage change are prognostic of AKOA development and progression.

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Abstract Number: 1163

Erosions Are the Most Often Reported Structural Lesion on MRI of the Sacroiliac Joints in axSpA Patients with IBP

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Background/Purpose: HLA-B27 and sacroiliitis on MRI form the basis of the Assessment of SpondyloArthritis international Society (ASAS) axial spondyloarthritis (axSpA) classification criteria. In addition, while not an entry criterion of the classification criteria, inflammatory back pain (IBP) is fundamental in the axSpA diagnostic process and it is endorsed as referral parameter in primary care. Besides inflammation on MRI, which is the hallmark of axSpA, there is still debate on the value of structural MRI lesions in these patients. The objective of this study was to report on MRI of the sacroiliac joints (MRI-SIJ) findings in newly diagnosed axSpA patients stratified for the presence of IBP and HLA-B27 positivity.

Methods: Newly diagnosed and anti-TNF naive axSpA patients of an ongoing Belgian (Be-Giant) cohort were included in this study. MRI-SIJ assessment was performed independently by 3 calibrated readers according to an adapted method of the Spondyloarthritis Research Consortium of Canada score, evaluating erosions, fatty lesions, sclerosis and ankylosis (T1-weighted and STIR images viewed simultaneously). Also, the ASAS definition of a positive MRI-SIJ was evaluated. MRI sum scores were calculated as 2 out of 3 (median) reader scores.

Results: In 138 axSpA patients MRI-SIJ data was available; 68 (49.3%) patients were male, 104 (75.4%) HLA-B27 positive and 131 (94.9%) patients fulfilled the IBP criteria according to ASAS. In the IBP+ patient groups, a large amount of structural MRI lesions were seen. In these groups, erosions are most frequently reported, with an average extent of 5 erosions. IBP- patients were rarely seen in this cohort and erosions and fatty lesions were the only structural lesions observed in these patients, with a much lower extent compared to the IBP+ patients (see table 1). There were no axSpA patients with negative MRI-SIJ, negative HLA-B27 and without IBP.

Table 1: Structural lesions seen on MRI in axSpA patients stratified for IBP, HLA-B27 and a positive MRI-SIJ.

Structural MRI lesions	IBP+ HLAB27+ MRI-SI+ n=77	IBP+ HLAB27+ MRI-SI- n=22	IBP+ HLAB27- MRI-SI+ n=27	IBP+ HLAB27- MRI-SI- n=5	IBP- HLAB27+ MRI-SI+ n=3	IBP- HLAB27+ MRI-SI- n=2	IBP- HLAB27- MRI-SI+ n=2	IBP- HLAB27 - MRI-SI- n=0
Gender, n(%) male	41 (53.2%)	13 (59.1%)	9 (33.3%)	2 (40.0%)	1 (33.3%)	1 (50.0%)	1 (50.0%)	-
Erosions*	61 (79.2%); 5.3±4.9	8 (36.4%); 4.9±6.6	20 (74.1%); 5.2±4.4	2 (40.0%); 5.0±5.7	1 (33.3%); 1.0±NA	1 (50%); 2.0±NA	1 (50%); 1.0±NA	0
Fatty lesions*	23 (29.9%); 8.6±7.0	5 (22.7%); 12.0±7.7	4 (14.8%); 13.0±5.3	3 (60.0%); 2.3±0.6	1 (50%); 2.0±NA	1 (50%); 2.0±NA	1 (50%); 3.0±NA	0
Sclerosis*	13 (16.9%); 4.4 ±3.1;	0	5 (18.5%); 3.0±1.6	2 (40.0%); 11.5±5.0	0	0	0	0
Ankylosis*	10 (13.0%); 11.2±8.6	2 (9.1%); 32.0±11.3	2 (7.4%); 8.0±5.7	0	0	0	0	0

*numbers reported are: number of patients with 1 or more of the given structural lesion (% from group total); mean±standard deviation of patients with 1 or more of the given structural lesion.

Conclusion: In this cohort of newly diagnosed anti-TNF naïve axSpA patients, structural lesions are frequently and with a high extent seen in IBP+ patients. Only in the IBP+ axSpA patients the previously reported threshold for axSpA patients of ≥3 erosions and ≥3 fatty lesions is maintained, as IBP- axSpA patients have far fewer lesions. IBP seems to be an indicator for the presence of structural MRI-SI lesions in newly diagnosed axSpA patients.

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Abstract Number: 1164

Novel Computer Assisted Methodology for Quantitative Assessment of MRI Treatment Responses to Apremilast in Patients with Psoriatic Arthritis

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Background/Purpose: Response to treatment in Psoriatic Arthritis (PsA) can be captured using the OMERACT PsA Magnetic Resonance Imaging Score (PsAMRIS). While reliable and valid, PsAMRIS interpretation requires a trained reader to assess inflammatory lesions on a discrete scale ranging from 0 to 3 and gives decrease values of changes which might not capture subtle changes in inflammation in small cohorts. In this study, we propose a novel computer-assisted imaging quantitative methodology to assess early response to treatment on a continuous scale and validate it by comparing its results with PsAMRIS synovitis scores.

Methods: 114 patients were treated with Apremilast 30mg BID, after a 5-day titration period. Patients had MRI scans at baseline, month 3 and 6. Given the need to rapidly assess the impact of new therapies on imaging structures, PsAMRIS responses were compared to those of a new novel computer-assisted quantitative method at 3 months.

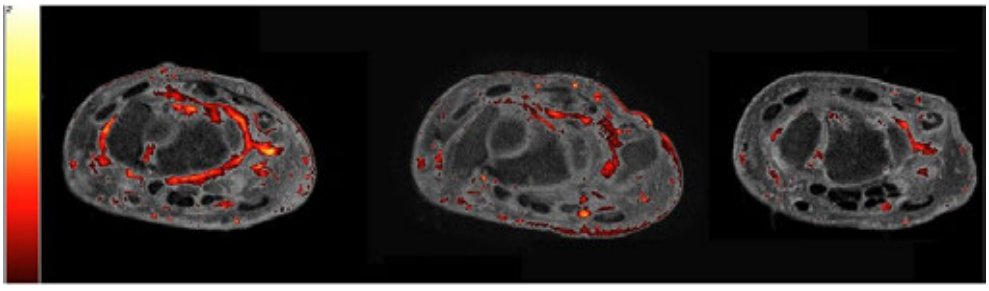

Figure 1. MRI scans and Norml maps superimposed on MRIs for a PsA patient imaged at baseline, Month 3 and 6.

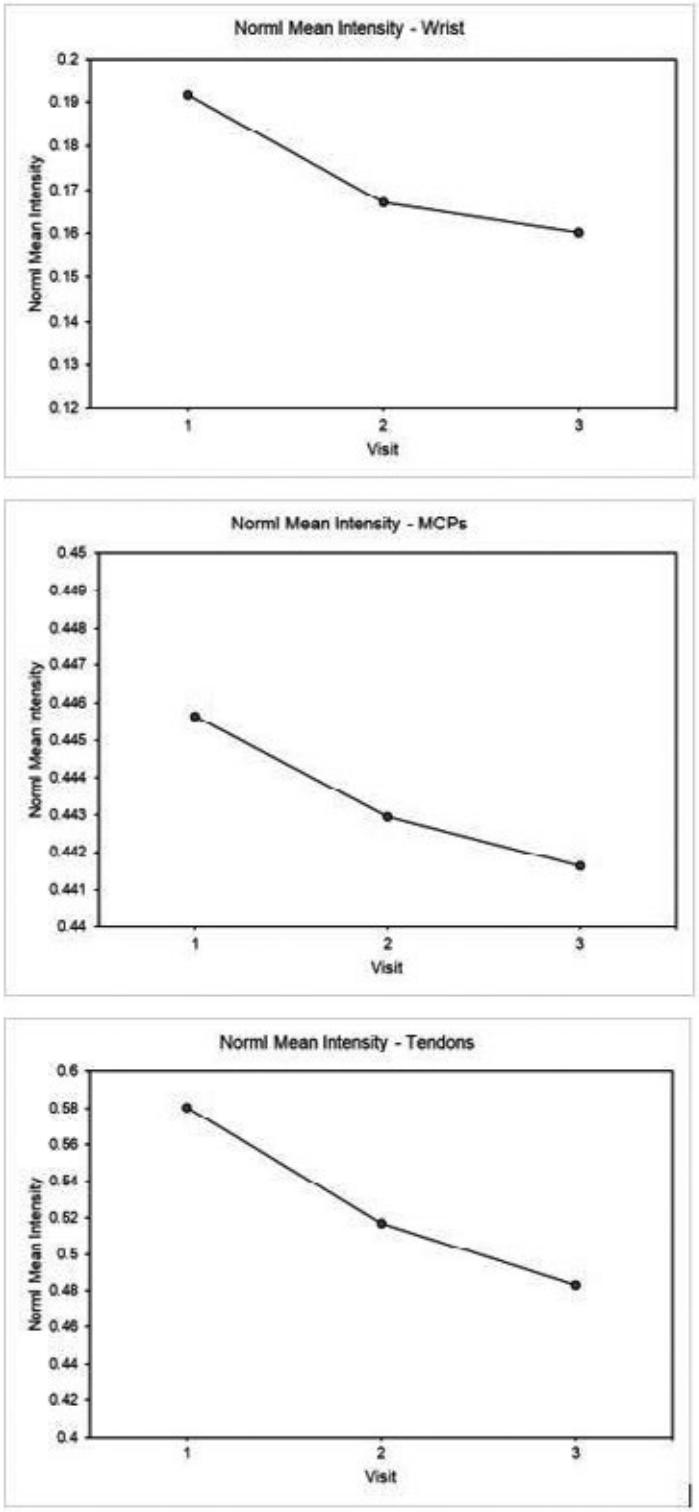

Figure 2. From the top: the mean values of Norml for the wrist, MCP and tendon at baseline, 3 and 6 months, showing reduction in inflammatory activity.

Images at baseline and 3 months were scored for synovitis using the PSAMRIS interpreted by an experienced reader and were read in blinded sequences. Images at baseline, 3 and 6 months were further processed using a novel computer-assisted quantitative method. At a pixel level, each pixel's intensity in the joint was normalized to the in-

tensity of a reference region (muscle). A heat map of normalized intensities was produced, highlighting areas of perfusion higher than that of healthy muscle (NormI), as shown in Figure 1. An experienced reader pre-defined regions of interest (ROIs) around the wrist and the metacarpophalangeal joint (MCP) joints. From these ROIs, the volume of inflammation was calculated in each joint and tendon. This was done by counting pixels that were enhanced above the intensity level of the normal muscle. Each enhanced pixel was given a weight corresponding to the degree of enhancement, allowing to differentiate areas of residual inflammation and high perfusion. This method has been validated, tested and implemented in the CE/FDA510 cleared software package Dynamika (IAG, Image Analysis Group). Patients with non-missing data were included in the final statistical analysis.

Results: IIn all cases a downward trend was observed at 3 months, indicating a reduction in inflammatory activity under treatment with Apremilast. At 3 months the NormI wrist score showed a reduction of 12% compared with the PsAMRIS synovitis score that reduced by 2%. Similar NormI results were observed for the MCPs and tendons (Figure 2). Results suggested continuous improvements over time, with reductions of 16.5% in the wrist, 0.9% in the MCPs and 16.7% in the tendons.

Conclusion: Computer assisted methodology has been developed to assess inflammation in patients with PsA and shown to be more responsive to changes in synovitis than the PsAMRIS at 3 months. Both methods demonstrated reduction of inflammation. This novel method could be used to provide early indications of treatment response. Further validation with larger datasets is planned.

Disclosure: P. Bird, Pfizer, 5, AbbVie, 5, Novartis, 5, Janssen, 5, Celgene, 5, Eli Lilly, 5; **M. Boesen**, Image Analysis LTD, 1, UCB, 5, Abbvie, 5, Eli Lilly, 5, Novartis, 5, Glenmark, 5, Pfizer, 5, Astra Zeneca, 5, Esaote, 9; **M. Hinton**, Image Analysis Limited, 3; **E. Sanverdi**, Image Analysis Limited, 3; **R. Hagoug**, Image Analysis Limited, 3; **C. Sabin**, Image Analysis Limited, 3; **P. Nakasato**, Celgene Corporation, 3; **B. Guerette**, Celgene Corporation, 3; **O. Kubassova**, Image Analysis Group, 1, 3, 4.

Abstract Number: 1165

Utility of Coronary Calcium Scoring (CCS) in the Spectrum of Connective Tissue Disorders (CTDs) for the Evaluation of Subclinical Coronary Atherosclerosis – a Systematic Review

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Background/Purpose: Recent literature shows that connective tissue disorders (CTDs) are positively associated with subclinical atherosclerosis via chronic activation of inflammatory pathways, or direct endothelial injury. Multidetector computed tomography (MDCT) is non-invasive and has emerged as a modality of estimating coronary calcium score (CCS) and prevalence of coronary arterial calcium (CAC) as a potential marker of risk for cardiac events, such as myocardial infarction. The objective of our study is to assess the utility of CCS, based on the current published data in CTDs as it relates to the presence of coronary atherosclerosis in CTDs.

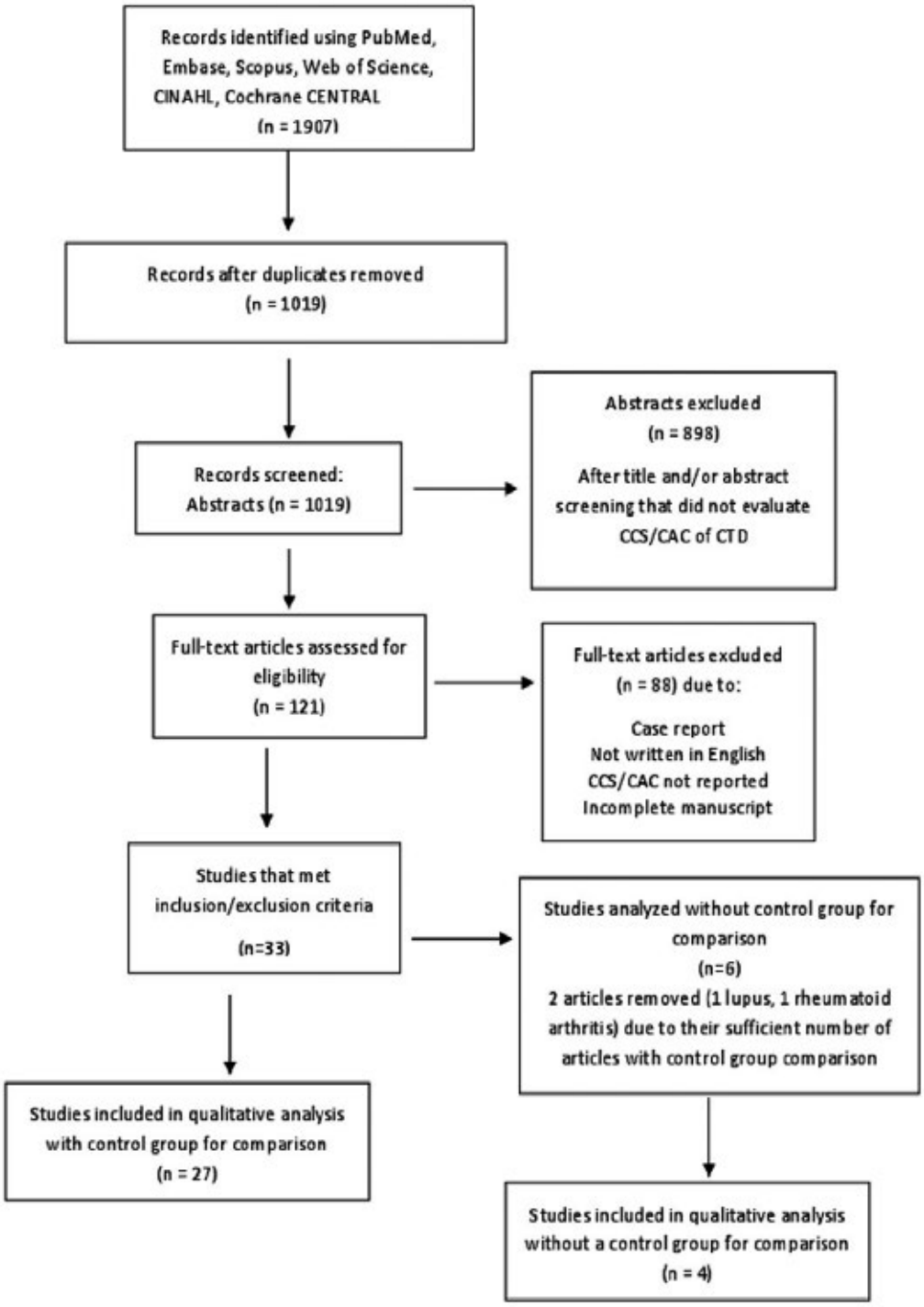

Figure 1. Flow Diagram - Search design

Methods: Following the PRIMSA guidelines, a literature search was done in PubMed, Embase, Scopus, Web of Science Core Collection, CINAHL, and Cochrane Database of Systematic Review. Inclusion criteria consisted of studies that investigated CCS in adults across the spectrum of CTDs, such as: rheumatoid arthritis (RA), seronegative spondyloarthropathies, systemic lupus erythematous (SLE), systemic sclerosis (SSc), idiopathic inflammatory myopathies (IIM) and vasculitides. Studies were excluded if a complete manuscript was not written in English, or if

Author, year	CTD / Sample size	Mean, median, or incidence/prevalence of CAC or CCS results (Agatston units)	Statistical significance
Abdel-Khalek et al. (2011)	RA - 60 Control - 20	RA Mean CCS: 126 ± 115.23 Control Mean CCS: 4.7 ± 4.03	p < 0.001
Asanuma et al. (2007)	Early RA - 90 Established RA - 67 Control - 87	Early RA (< 6 years) Median CCS: 0 (0-47) Established RA (> 10 years) Median CCS: 63 (0-368) Control Median CCS: 0 (0-18)	p < 0.001
Avalos et al. (2007)	Early RA - 57 Late RA - 60 Control - 65	Early RA (< 6 years) – Median CCS 0 (0–33.8) Late RA (> 10 years) – Median CCS 65.5 (0–400.5) Controls – Median CCS 0 (0–16.4)	p < 0.001
Chung et al. (2013)	RA - 155 Control – 835*	Median CCS RA - 3.1 (0-135.1) Median CCS control - 6.4 (0-119.6)	NS
Chung et al. (2005)	Early RA - 70 Established RA - 71 Control - 86	Early RA (< 5 years) - median CCS 0 (0-42.6), CAC in 42.9% Established RA (> 10 years) - median CCS 40.2 (0-358), CAC in 60.6% Control - median CCS 0 (0-19.2), CAC in 38.4%	p = 0.001
Giles et al. (2009)	RA - 195 Control - 1,073*	RA mean CCS: 175 ± 31 Control mean CCS: 122 ± 13	p = 0.002
Kakuta et al. (2016)	RA - 37 SSc - 24 SLE - 33 Control - 74	Median CCS RA – 0 (0-136) Median CCS SSc – 0 (0-111) Median CCS SLE – 0 (0-138) Median CCS Control – 30 (0-225)	NS
Kao et al. (2008)	SLE - 105 RA – 105 Control – 105	Prevalence of CAC: SLE - 47.6%, RA - 47.6%, Control - 35.2%	p = 0.02
Paccou et al. (2014)	RA - 75 Control - 75	RA CAC prevalence - 65.3% Control CAC prevalence - 49.3%	p = 0.04
Wang et al. (2009)	RA - 85 Control - 85	RA Mean CCS - 62.8 ± 197.0 Control Mean CCS - 11.3 ± 38.5	p = 0.002
Yiu et al. (2012)	RA - 85 SLE - 69 Control - 106	RA and SLE Mean CCS - 42.2 ± 154.3 Control Mean CCS - 1.4 ± 13.0	p < 0.01
Asanuma et al. (2003)	SLE - 65 Control - 69	SLE Mean CCS: 68.9 ± 244.2 Control Mean CCS: 8.8 ± 41.8	p = 0.002
Chung et al. (2006)	SLE - 93 Control – 65	SLE CAC incidence and Mean CCS - 19.4% and 39 ± 200 Control CAC incidence and Mean CCS - 6.2% and 4 ± 30	p = 0.02
Chung et al. (2008)	SLE - 113 Control - 80	SLE Mean CCS - 43.4 ± 189.8 Control Mean CCS - 3.8 ± 27.9	p = 0.002
Heshmat et al. (2015)	SLE - 30 Control - 30	SLE Mean CCS: 42 ± 111.09 Control Mean CCS: 0, no CAC was detected	p = 0.04
Kiani et al. (2015)	SLE - 80 Control – 241*	Age 45-54 CAC prevalence: SLE - 58%. Control - 22/125 (36%) Age 55-64 CAC prevalence: SLE - 57%. Control - 42/116 (36%)	Age 45-54: p < 0.001 Age 55-64: NS
Lertratanakul et al. (2014)	SLE - 149 Control - 124	CAC was more prevalent in SLE patients and had significantly higher progression	NS
Othman et al. (2013)	SLE - 60 Control - 60	SLE Mean CCS - 59.2 ± 20.3 Control Mean CCS - 2.6 ± 1.85	p < 0.001
Romero-Diaz et al. (2016)	SLE - 95 Control - 100	SLE - CAC incidence 18% Control - CAC incidence 7%	p = 0.03
Romero-Diaz et al. (2012)	SLE - 139 Control - 100	SLE - CAC incidence 7.2% Control - CAC incidence 1%	p = 0.02
Seyahi et al. (2013)	Takayasu - 47 SLE - 43 Control - 70	Takayasu CAC incidence: 11% SLE CAC incidence: 21% Control CAC incidence: 3%	Takayasu: NS SLE: p = 0.010
Yiu et al. (2009)	SLE - 50 Control - 50	SLE CAC prevalence - 42% Control CAC prevalence - 8%	p < 0.01
Khurma et al. (2008)	SSc - 17 Control - 17	SSc Mean CCS - 126.6 ± 251.0 Control Mean CCS - 14.7 ± 52.2	p = 0.003
Mok et al. (2011)	SSc - 53 Control - 106	SSc - 56.5% had CCS > 101 Control - 29.4% had CCS > 101	p = 0.01
Seung-Geun et al. (2013)	SSc - 41 Control – 123	SSc median CAC – 0 (0-133.5) Control median CAC – 0 (0-454.1)	NS
Diederichsen et al. (2015)	IIM - 76 Control – 48	IIM: Median CCS 18 (0 - >400) Control: Median CCS 5 (0 - >400)	NS
Seremet et al. (2014)	Psoriasis - 40 Control - 42	Psoriasis Mean CCS - 9.9 ± 35.2 Control Mean CCS - 2.8 ± 12.0	NS

Table 1. Descriptive summary of CCS/CAC of CTDs with control group for comparison. CTD = connective tissue disorder; CAC = coronary arterial calcium; CCS = coronary calcium score; RA = rheumatoid arthritis; SLE = systemic lupus erythematosus; SSc = systemic sclerosis; IIM = idiopathic inflammatory myopathy; NS = not significant; * = sample patients from Multi-Ethnic Study of Atherosclerosis [MESA] Study

it was a single case report. The quality of articles included were assessed using the Newcastle-Ottawa Scale (NOS) assessment scale for cohort studies and the Agency for Healthcare Research and Quality (AHRQ) criteria for cross-sectional studies.

Results: The initial search revealed 1907 citations, but after we eliminated duplicates, studies that did not reference CCS/CAC, and abstracts only, we reviewed 121 full text publications (Figure 1). 31 studies were included in this review (27 with healthy age/gender matched control group and 4 without). The CTDs analyzed in articles with a control group for comparison (Table 1) were: 11 RA, 14 SLE, 4 SSc, 1 IIM, 1 Takayasu arteritis, and 1 psoriasis. 9 out of 11 RA studies, 12 out of 14 SLE studies, and 2 out of 4 SSc studies showed statistically significant increased CCS or CAC prevalence/incidence when compared to control group. The CTDs analyzed without a control group for comparison

Author, year	CTD / Sample Size	Mean, median, or incidence/prevalence of CAC or CCS results (Agatston units)	Statistical significance
Kahn et al. (2012)	Kawasaki – 70 No control group	No coronary dilation (44/70) - none had CAC Transient dilation (12/70) - 1/11 patients had CAC With coronary aneurysm (14/70) – all patients had CAC and the highest CAC burden	NS
Kahn et al. (2017)	Kawasaki – 116 No control group	No coronary dilation (100/160) - 0 CAC Transient/persistent dilation (33/160) – 1 out of 33 patients had CAC Aneurysm (5/33) – all had CAC and the highest CAC burden	NS
Majka et al. (2013)	APS – 2,203* No control group	APS: CAC was prevalent in 9.5% of young adults (age 18-30) with APS antibodies.	NS
Aulie et al. (2014)	JIA – 84 No control group	22 of 84 JIA patients (26%) had a CCS above 0 16 patients had CCS 1-10 6 patients had CCS > 10	NS

Table 2. Descriptive summary of CCS/CAC of CTDs without control group for comparison. CTD = connective tissue disorder; CAC = coronary arterial calcium; CCS = coronary calcium score; APS = antiphospholipid syndrome; JIA = juvenile idiopathic arthritis; NS = not significant; * = sample patients from Coronary Artery Risk Development in Young Adults (CARDIA) study

(Table 2) were: 2 Kawasaki disease, 1 juvenile idiopathic arthritis (JIA), and 1 antiphospholipid syndrome (APS). These studies demonstrated increased CAC burden, however without statistically significant data.

Conclusion: This systematic review demonstrates that some CTDs (RA and SLE) have higher CCS and/or CAC incidence/prevalence compared to normal controls, while the SSc data is still ambiguous. This study also identified that aside from Takayasu arteritis and Kawasaki disease, there is currently no published data in the spectrum of vasculitides, which are associated with high inflammatory burden. Based on the current published data, it is unclear if MDCT-measured CCS is a reliable and generalizable tool to assess subclinical atherosclerosis across the spectrum of CTDs, however we ascertain that it can be useful for cardiovascular risk assessment in patients with SLE and RA.

Disclosure: S. Farshad, None; **A. Halalau**, None; **W. Townsend**, None; **E. Schiopu**, None.

Abstract Number: 1166

A New Risk Factor for Predicting the Long-term Outcome of Pulmonary Arterial Hypertension Associated with Connective Tissue Disease: Pulmonary Artery Size Measured by Chest Computed Tomography

Xiaodi Li,[1] xiaoxuan sun,[1] yinsu zhu,[1] Qiang wang,[1] and miaojia zhang[2], [1]A new risk factor for predicting the long-term outcome of pulmonary arterial hypertension associated with connective tissue disease: pulmonary artery size measured by chest computed tomography, Nanjing, China (People's Republic), [2]c, Nanjing, China (People's Republic)

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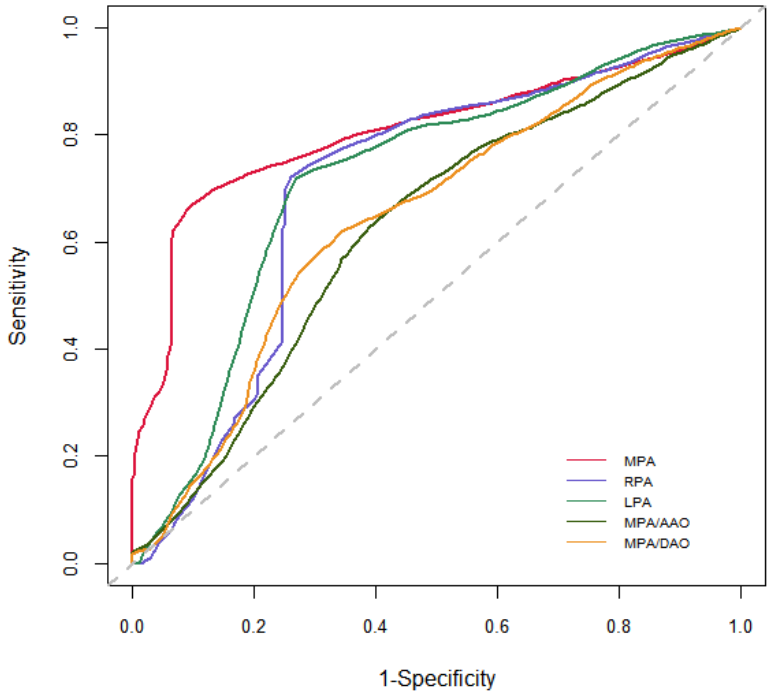
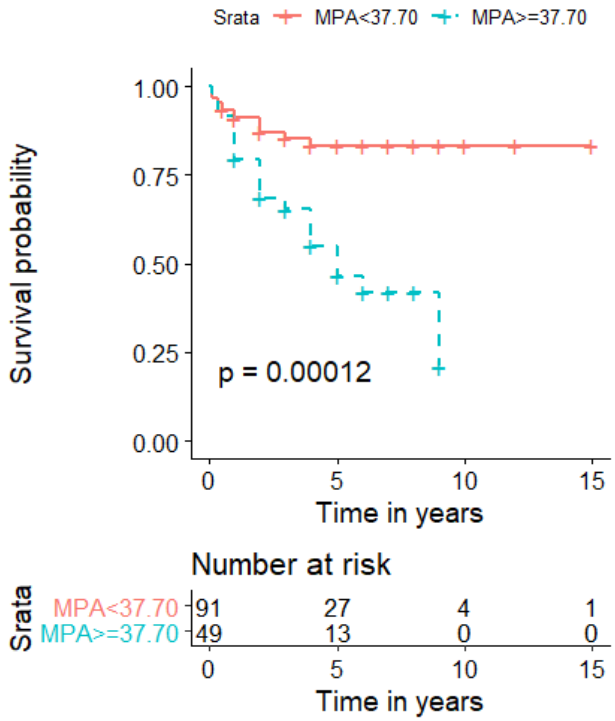
Background/Purpose: Most of the prognostic indicators are derived from right cardiac catheterization or biomarkers in patients with CTD-PAH. It is not clear whether the non-invasive parameters measured by chest CT are related to the clinical outcome of patients with CTD-PAH. Therefore, we want to explore whether the size of pulmonary artery measured on chest CT is related to the long-term prognosis of patients with CTD-PAH in Chinese population.

Methods: We retrospectively investigated 140 CTD-PAH patients diagnosed by echocardiography during Jan 2009 and May 2018 at the first affiliated hospital of Nanjing Medical University. The size of pulmonary trunk and its branches was maesured. by two professional radiologists. The primary endpoint was all-cause death. The ability of chest multi-slice CT parameters to predict all cause mortality was tested by time-dependent receiver operating characteristic (ROC) curve and the corresponding cut-off value were defined by difference maximization method.

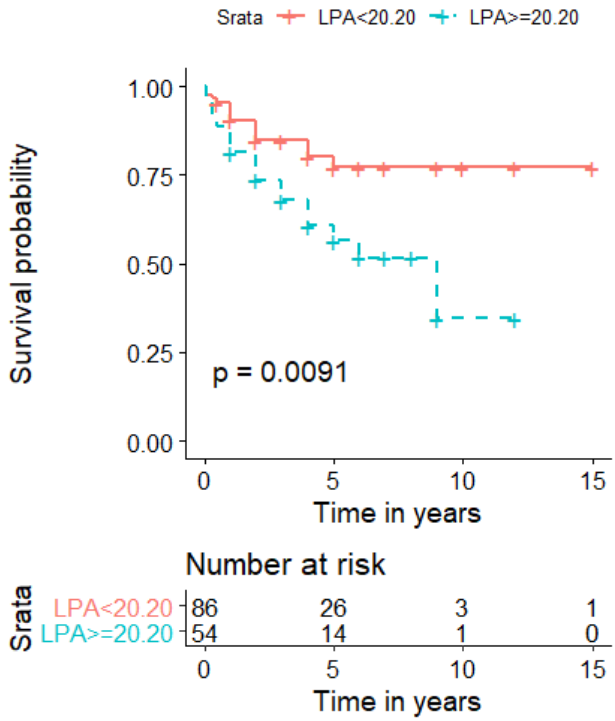
Results: During the observational period of 3.44 ± 0.23 years, 36 patients were died and the longest survival time was 15 years. The time dependent ROC curve suggested that Main pulmonary artery diameter (MPAd), right pulmonary artery diamete (PRAd) and Left pulmonary artery diameter (LPAd) may have the ability to predict mortality in patients with CTD-PAH , the corresponding cut-off values were 37.70 mm for MPAd, 20.46 mm for RPAd and 20.20 mm for LPAd. Patients with MPAd ≥ 37.70 mm (p=0.00012) and LPAd ≥ 20.20 mm (p=0.0091) exhibited poorer long-



Time-dependent ROC curve showing the prognostic value of MSCT parameters



Kaplan-Meier analysis showed significant differences in the prognosis between the patients with MPA diameter <37.70 mm and those with MPA diameter ≥37.70mm



Kaplan-Meier analysis showed significant differences in the prognosis between the patients with LPA diameter <20.20mm and those with LPA diameter ≥ 20.20 mm

term outcome. MPAd ≥ 37.70 mm (HR: 2.74; 95% CI: 1.37-5.48 p=0.004) and WHO functional class III-IV (HR: 3.32; 95% CI: 1.42-7.75 p=0.006) was the independent risk factor of poor outcome for patients with CTD-PAH.

Conclusion: Main pulmonary arterial ≥ 37.70 mm measured by chest multi-slice CT was an independent risk factor of the poor long-term prognosis in Chinese CTD-PAH patients.

Disclosure: x. li, None; **x. sun**, None; **y. zhu**, None; **Q. wang**, None; **m. zhang**, None.

Abstract Number: 1167

To Evaluate Spine Ankylosis, Vertebral Fractures and Bone Fragility on a Single Imaging Exam in Patients with Ankylosing Spondylitis: Myth or Reality?

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Imaging Of Rheumatic Diseases Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Spine ankylosis is a risk factor of osteoporosis and mortality in ankylosing spondylitis (AS). Recently, thoracic-abdomino-pelvic CT (TAP-CT) has demonstrated its ability to screen bone fragility through the scanographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1). CT-scans is a remarkable imaging technic to assess structural spine ankylosis and vertebral fractures (VF). Our objectives are to assess the association between the SBAC-L1 and spine structural lesions on CT and to determine both VF prevalence and percentage of AS patients under the fracture threshold (SBAC-L1 ≤ 145 HU).

Methods: On 1503 consecutive SpA patients followed from 2009 to 2017 at Nancy University hospital, only patients responding to New York criteria for AS and explored by a TAP-CT scan and X-rays (XR, spine, pelvis) within 2 years were included. Demographic and clinical characteristics were collected. CT spine structural lesions were assessed by two readers on erosions, syndesmophytes and ankylosis for the anterior part and on ankylosis for the posterior part (facet joints) from C7 to S1 vertebrae. mSASSS and anterior, posterior and total (anterior +posterior) ankylosing CT spine scores ranged from 0-72, 0-108, 0-108, and 0-216 respectively. The SBAC-L1 value under ≤ 145 HU defined the fracture threshold.

Results: 67 AS patients were included (median age: 61.2 years, 89% men, 59.7% HLAB27 +, NSAIDs 67.2% and TNF-i 58.2%). All patients presented sacroiliitis on XR and the mean mSASSS was 14.7±17.5. The mean anterior, posterior and total ankylosing CT spine scores were 32.4±39.9, 27±40.9 and 63.7±82, respectively. Ankylosing CT spine scores were highly reproducible (ICC >0.97; Kappa: 0.60-1). No CT structural lesion was observed in 27 patients (45%). Spine Ankylosis was depicted in 38 patients (56.7%). Exclusive anterior or posterior vertebral ankylosis was observed in 8 (11.9%) and 5 (7.4%) patients respectively and both parts in 25 patients (37.3%). The total ankylosing CT spine scores presented good correlations with the mSASSS (r=0.76 (0.60-0.87)). On CT, VFs (n=9) were detected in 5 patients (7.5%). The mean SBAC-L1 was 135.7 HU (±49.2) and 40 patients (59.7%) were under the fracture threshold. For the 5 patients with VFs, 4 patients had a SBAC-L1 ≤ 145UH and 3 of them presented spine ankylosis. We showed an inverse correlation between SBAC-L1 and anterior ankylosing CT spine score (r=-0,40; p≤0,01), with similar level of correlation for the two other scores. AS patients with spine ankylosis (anterior, posterior or both) presented more frequently a SBAC-L1 ≤145UH (p≤0.012).

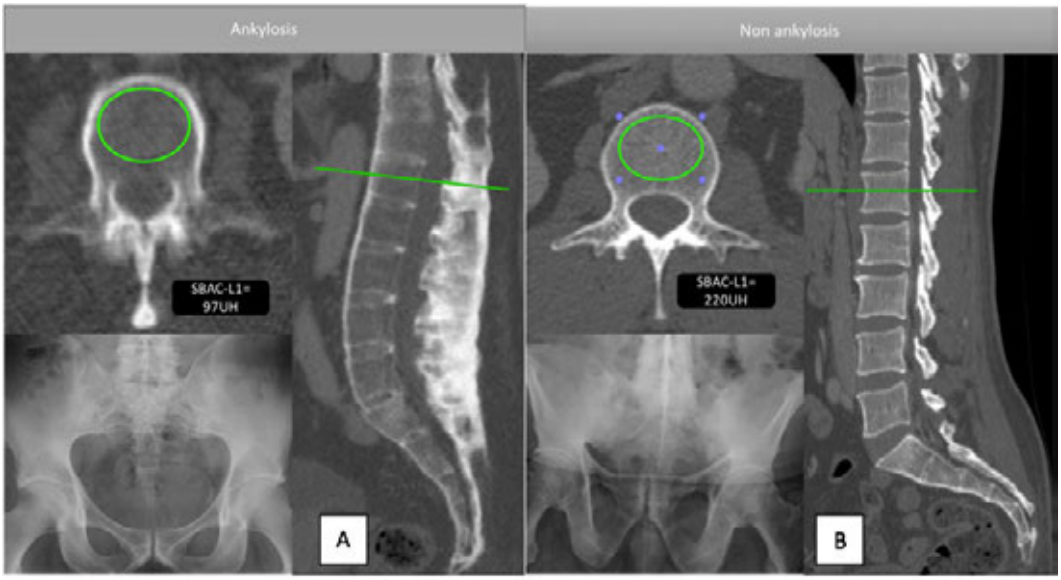

Figure 1: AS patients with sacroiliac joint ankylosis on radiography (A and B). Ankylosed spine in its anterior and posterior parts (A) and normal pattern (B) on sagittal slices. The SABC-L1 was calculated on axial slice of the first lumbar vertebra at 97UH in ankylosed versus 220UH in the non ankylosed spine.

Conclusion: we showed an inverse correlation between SBAC-L1 and total ankylosing CT spine score (r=-0,401; p≤0,01). AS patients with anterior and/or posterior vertebral ankylosis on CT-scans are more frequently under the fracture threshold for the SABC-L1. Four out of five AS patients with VF (prevalence: 7.4%) were under a SABC-L1≤145UH.

Disclosure: c. Morizot, None; **M. Fauny**, None; **E. Allado**, None; **F. Verhoeven**, None; **E. Albuisson**, None; **A. Pinzano-Watrin**, None; **I. Chary-Valckenaere**, None; **D. Loeuille**, None.

Abstract Number: 1168

Frequently Encountered Artifacts in Novel Application of Dual-Energy CT to Vascular Imaging: A Pilot Study

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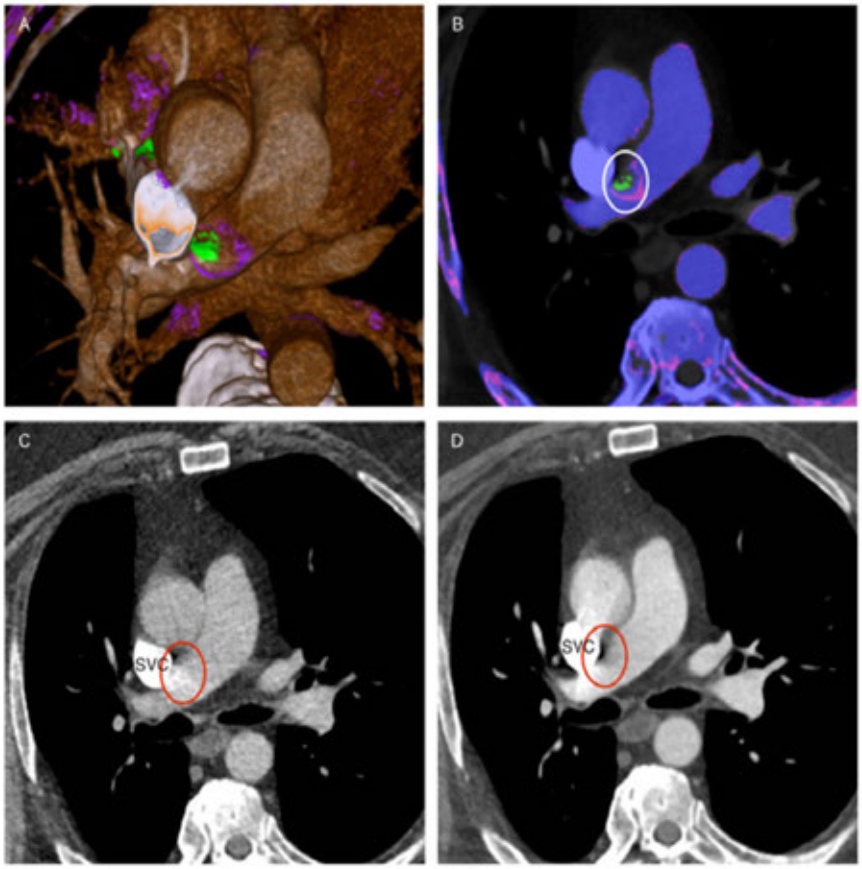
Image 1: Streak (Beam Hardening) Artifact



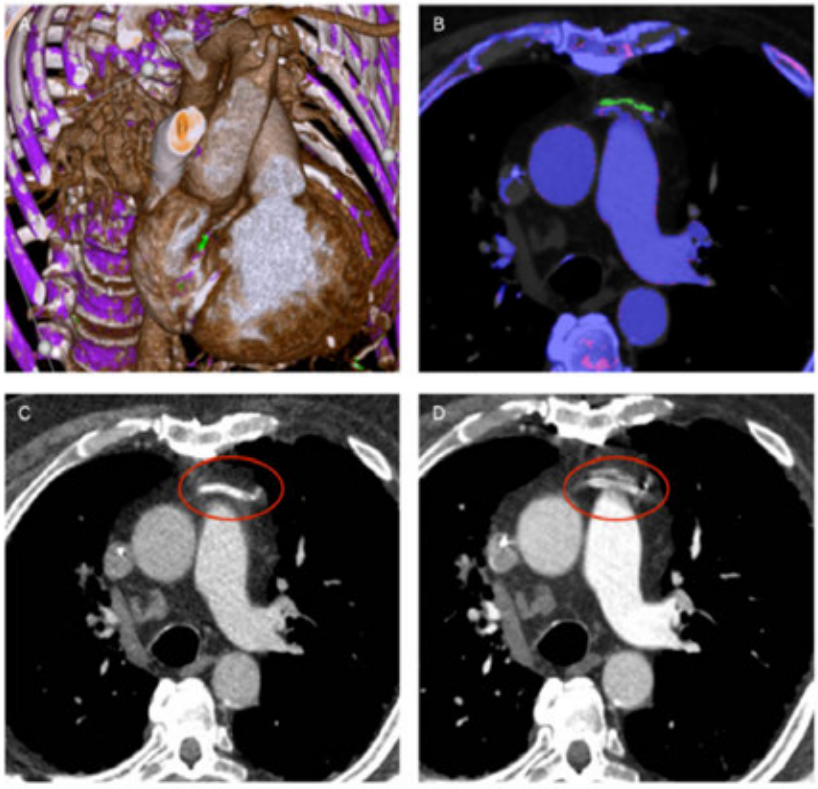
3D [A] and 2D [B] color-coded images that show green material posterolateral to the superior vena cava (SVC) which is filled with dense intravenous contrast. It has the appearance of the green material being in the pulmonary artery. High-energy [C] and low-energy [D] images at the same level which show heterogeneous areas of attenuation (circled in red) posterolateral to the superior vena cava due to beam hardening as the energy beam hits the dense contrast in the SVC.

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: One hypothesized link between cardiovascular disease and gout is the direct deposition of monosodium urate (MSU) crystals in atherosclerotic plaque. A 2018 ACR abstract used non-ECG-gated CT scans of the chest and neck in dual-energy mode to evaluate vascular MSU crystal deposition and reported that > 80% of patients with gout had vascular MSU deposition as well as some in healthy control patients, with no significant difference in the volume of MSU crystal deposition among gout and control patients. We reviewed 96 non-ECG gated DECT pulmonary angiograms (similar to the ACR abstract) to identify commonly encountered artifacts which could be misconstrued as true MSU deposition findings.

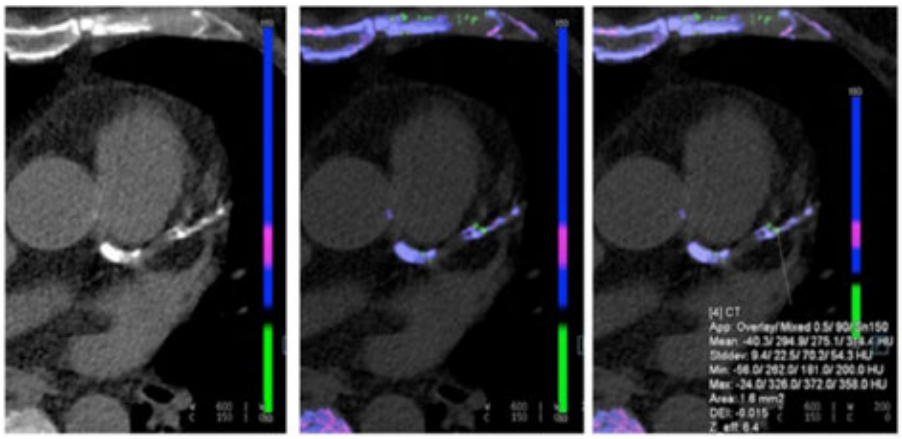
Methods: Consecutive patients with gout (ICD-10 code for gout and serum urate >6 mg/dL) who underwent non-ECG gated DECT pulmonary angiograms between 1/1/15 and 11/29/18 were identified using a clinical data repository. Age- and sex-matched controls were randomly chosen from a list of consecutive patients without gout who underwent the same imaging study. All images were acquired using dual-source, dual-energy CT scanners (Siemens Flash or Force DECT) and loaded into the postprocessing software (Syngo.via, Siemens, Germany) to apply an image-based two material decomposition algorithm to highlight MSU crystals in green. The images were reviewed by two radiologists ex-

Image 2: Misregistration due to Motion



3D [A] and 2D [B] color-coded images that show linear green material corresponding to a CABG vessel. High-energy [C] and low-energy [D] images at the same level. In C, there is one linear white band corresponding to the CABG vessel, while in D, it appears that there are two linear bands. This discrepancy is caused by motion when the low-energy image was acquired.

Image 3:



ECG-gated coronary dual-energy CT scan of a 68-year-old man with gout with subcutaneous tophi reveals evidence of MSU crystal deposition in the coronary artery.

perienced in interpreting DECT for MSU crystals. Presence of any green material in the vasculature was noted with its location for each patient, then further assessed with comparison to the grey-scale source images to determine if it was a true finding or artifact. Artifacts were classified into one of five categories: streak, misregistration due to motion, contrast mixing, foreign body, and noise. Three radiologists also reviewed two cases of ECG-gated coronary DECT scans.

Results: We identified 48 gout patients and 48 age- and sex-matched controls who had undergone 51 non ECG gated PE scans. The patients were mostly men (70.8%) with mean age 67 years. The majority of DECT scans, both of cases and controls, had green material in the vasculature (85% and 84%, respectively). The most common location of green material was in the superior vena cava or right atrium (81% in cases vs. 91% in controls), followed by the aorta (27% vs 47%, respectively) and coronary arteries (40% vs 21%, respectively). However, all green material in the vasculature were ultimately attributed to artifact with the most common types of artifacts being streak (**Image 1**) and misregistration due to motion (**Image 2**). However, images from the two gout patients using ECG-gated DECT scan showed coronary MSU deposits in both the grey-scale source images as well as dual energy impages, not meeting any of artifact criteria (**Image 3**).

Conclusion: Non-ECG gated Vascular DECT images are susceptible to various artifacts. Further investigation of this technology using ECG-gated CTs are warranted.

Disclosure: C. Yokose, None; **S. Eide**, None; **F. Simeone**, None; **K. Shojania**, None; **S. Nicolaou**, None; **F. Becce**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5.

Abstract Number: 1169

Influence of Steroid Treatment on ^{18}F-FDG PET/CT Accuracy to Detect Vascular and Musculoeskeletal Involvement in Patients with Polymyalgia Reumatica

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fluorine-18-fluorodeoxyglucose (^{18}F-FDG) PET/CT has been proposed as a promising tool for assessing both musculoskeletal and vascular involvement in patients with polymyalgia rheumatica (PMR). Glucocorticoids (GC) may decrease the intensity of ^{18}F-FDG uptake. Therefore, performance of PET/CT before steroid therapy is recommended. However, in many patients with PMR, large vessel vasculitis (LVV) is precisely suspected because of steroid resistance after a long-term treatment with GC. Our aim was to assess the influence of long-term medium-dose treatment on ^{18}F-FDG vascular and musculoskeletal uptake to discern if ^{18}F FDG PET/CT could be useful to evaluate patients with polymyalgia rheumatica under treatment with GC.

Methods: Single-center study of 75 patients with PMR diagnosis based on 2012 EULAR/ACR criteria. All patients underwent a PET/CT scan due to LVV suspicion based on the presence of atypical symptoms and/or persistent symptoms despite steroid therapy. We considered two groups: a) Steroid-naïve PMR patients. b) Steroid-resistant PMR patients. Both musculoskeletal and vascular ^{18}F-FDG uptake was assessed. The statistical analysis was performed with SPSS. Distributions of categorical variables were compared by Pearson Chi2 or Fisher exact test as appropriate.

Results: We evaluated 75 patients, 27 men and 48 women (mean age ± SD: 68.2 ± 10.7 years). PET/CT was performed in 14 steroid-naïve PMR patients (18.7%) and 61 steroid-resistant PMR patients (81.3%). Patients under steroid treatment had received a median dose of Prednisone of 10.0 [5.0-15.0] mg/day during 9.0 [2.0-22.0] months. Vascular ^{18}F-FDG uptake was more frequently detected in steroid-naïve patients. In regard with musculoskeletal ^{18}F-FDG uptake, no statistically significant differences were seen between both groups (**TABLE**).

Conclusion: Vascular ^{18}F-FDG uptake detection was higher in PMR patients with LVV suspicion who had never received GC. However, PET/CT was also useful to detect vascular involvement in most of the patients under a long-term medium-dose steroid treatment.

TABLE

	PMR patients (N=75)	**Steroid-naive patients (n=14)**	**Steroid-resistant patients (n=61)**	**P#**
Sex (women), n (%)	48 (64.0)	7 (50.0)	41 (67.2)	0.23
Age (years), mean ± SD	68.2 ± 10.7	65.5 ± 11.4	69.9 ± 10.5	0.29
ESR (mm/1sth), median [IQR]	41.0 [24.0-68.0]	43.5 [23.3-68.5]	41.0 [24.0-66.5]	0.92
CRP (mg/dL), median [IQR]	1.3[0.7-3.6]	1.6 [0.6-7.8]	1.3 [0.8-3.5]	0.77
F-FDG uptake				
Shoulders	45 (60.0)	9 (64.3)	36 (59.0)	0.72
Sternoclavicular joints	33 (44.0)	7 (50.0)	26 (42.6)	0.62
Hips	32 (42.7)	8 (57.1)	24 (39.3)	0.23
Cervical interspinous bursae	9 (12.0)	2 (14.3)	7 (11.5)	0.77
Lumbar interspinous bursae	29 (38.7)	4 (28.6)	25 (41.0)	0.40
Pubic symphysis	4 (5.3)	2 (14.3)	2 (3.3)	0.16
Subtrochanteric bursae	20 (26.7)	3 (21.4)	17 (27.9)	0.62
Ischial tuberosities	19 (25.3)	2 (14.3)	17 (27.9)	0.30
Knees	33 (44.0)	7 (50.0)	26 (42.6)	0.62
LVV	51 (68.0)	13 (92.9)	38 (62.3)	**0.027**

Comparisons between steroid-naïve patients and patients receiving corticosteroids

Disclosure: D. Prieto- Pena, None; **M. Calderón-Goercke**, None; **I. Martínez Rodríguez**, None; **I. Banzo**, None; **L. Sanchez-Bilbao**, None; **I. Gonzalez-Mazon**, None; **B. Atienza-Mateo**, None; **M. González-Gay**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 2, 5, EliLilly, 2, 5, Jansen, 2, Janssen, 2, MSD, 2, 5, 8, Novartis, 2, 5, Pfizer, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, Sobi, 5, 8; **R. Blanco**, None.

Abstract Number: 1170

Cortical Bone Erosion in the 2nd Metacarpal Bone Head: Association with Its Bone Mineral Density by HR-pQCT in Rheumatoid Arthritis Patients

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Imaging Of Rheumatic Diseases Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Periarticular trabecular bone loss and local cortical bone erosions are typical features of bone disease in rheumatoid arthritis (RA)[1] . Little, however, is known about the interactions between periarticular bone

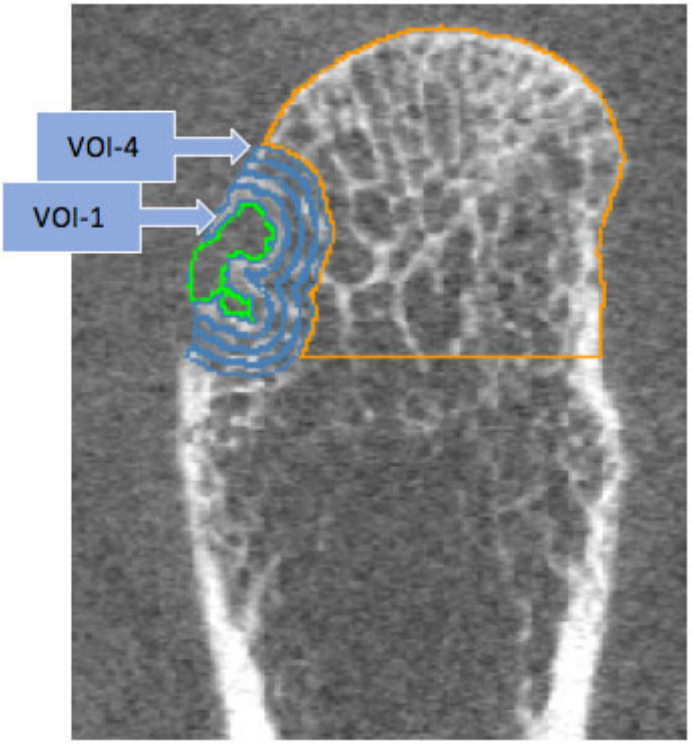

Figure 1. HR-pQCT imaging of 2nd MCP head from a RA patient (coronal plane). Demonstration of bone segmentation by MIAF, showing BMD of MCP head analyzed (orange line), erosion segmentation placed on radial quadrant (green line) and VOIs (1 to 4) (blue lines around erosion).

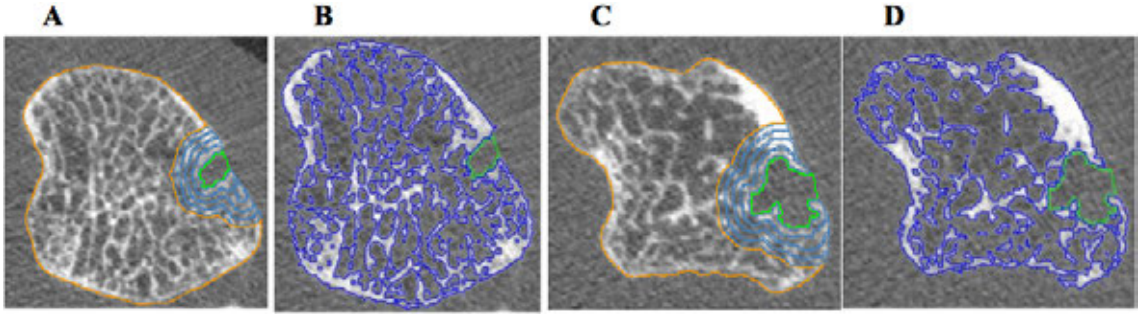

Figure 2. Axial plane of 2nd MCP head using HR-pQCT scan comparing two RA patients with erosion on radial quadrant. First patient: (A) erosion volume=6.75mm3 with 4 VOIs segmentation (blue lines) and (B) BMD segmentation (purple contouring=314.94mg/cm3). Second patient: (C) an important erosion volume= 19.33mm3 with 4 VOIs segmentation (blue lines) and (D) BMD segmentation (purple contouring=284.63mg/cm3).

loss and local bone erosions. The purpose of this study was test whether bone mineral density (BMD) in metacarpophalangeal (MCP) head, radius or tibia are associated with cortical bone erosions in RA patients.

Methods: Forty-seven RA female patients underwent high-resolution quantitative computed tomography (HR-pQCT) of 2 nd MCP joints of the dominant hand, and non-dominant distal radius and tibia in a cross-sectional study. Erosion volumewas assessed by the semi-automated Medical Image Analysis Framework (MIAF) software [2] . Clinical and laboratory variables were assessed, as well as Health Assessment Questionnaire (HAQ) and Hand Grip test. Trabecular bone mineral density (BMD) was measured in 4 particular volumes of interest (VOI-1-4= 1 the nearest to erosion) around the bone erosions (Figure 1). Further, total BMD of metacarpal head was also analyzed. Univariate and multivariate analysis were done to find out a relationship between erosion volume and BMD of metacarpal head, radius and tibia.

Results: The mean age was 40.2±5.9yrs, mean of disease duration 10.9±4.8yrs, median of disease activity score-28 (DAS-28) 2.66(1.97, 3.00), mean of HAQ 0.88±0.70 and mean of hand grip was 18.1±7.1N. Current treatment: glucocorticoids: 61.7%(n=29), conventional DMARDs (Disease Modifying Anti-Rheumatic Drugs): 80.9%(n=38) and biological DMARDs: 48.9%(n=23). There were found 43 erosions (0.9±1.2/patient) and 14 osteophytes (0.3±0.7/patient) in the 2ndMCP head. The joint gap mean was 80.6±34.9mm3, and erosion volume median was 0.26(0, 16.16) mm3. Volume of cortical bone erosions was negatively correlated with BMD in 2ndMCP head (r= -0.53, p< 0.001), VOI-4 (r= -0.48, p=0.017) and joint gap (r= -0.40, p=0.005); and it was positively correlated with number of erosions (r= 0.82, p< 0.001) and number of osteophytes (r= 0.32, p= 0.026). Furthermore, after the sample was categorized by absence or presence of erosion in 2ndMCP head it was found a significant difference between number of osteophyte (0.10±0.41vs.0.50±0.88, p=0.028), BMD of MCP head (321.53±37.12 vs.281.38±67.69mg/cm3, p=0.043) (Figure 2) and joint gap (93.59±36.94 vs.68.20±28.31, p=0.025), respectively. The multiple linear regression showed that BMD of 2ndMCP head was negatively associated with its volume of erosion (B= - 0.813, p=0.003, adjusted R2= 0.32), adjusted by number of erosions, number of osteophytes, joint gap, VOI-4 and volumetric trabecular BMD of radius.

Conclusion: Cortical bone erosions volume were associated with low BMD in the 2 nd MCP head, suggesting that this variable should also be included as an outcome parameter in the follow-up of RA patients.

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References:

1. Tam LS. J Rheumatol 2016;43(10):1911-3.
2. Figueiredo CP, et al. Semin Arthritis Rheum 2017;47(7):611-8.

Disclosure: C. Figueiredo, None; **M. Perez**, None; **A. Ribeiro**, None; **V. Caparbo**, None; **R. Pereira**, None.

Abstract Number: 1171

Evidence of Subclinical Joint Inflammation of Hands by Magnetic Resonance Imaging in Patients with Psoriatic Arthritis in Minimal Disease Activity – Interim Analysis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Subclinical inflammatory lesions detected by MRI are prevalent in hand joints of patients with *cutaneous psoriasis* (1). Yet, it is unknown whether these inflammatory changes persist in patients with *psoriatic arthritis (PsA) in low disease activity/clinical remission*. Minimal disease activity (MDA) is a validated composite index used for clinical evaluation in PsA(2). The purpose of this study is to estimate the prevalence of hand inflammatory changes in PsA patients with MDA versus non-MDA (active disease) using MRI.

Methods: Sixty consecutive prospectively recruited patients with peripheral PsA (CASPAR criteria) underwent clinical evaluation, questionnaires, and MRI of a predominantly involved hand within 72 hours of the clinical examination. MRI scans were scored for synovitis, tenosynovitis, periarticular inflammation, bone edema, bone erosion, and bone proliferation according to the OMERACT PsA MRI scoring system (PsAMRIS) method(3), performed by an expert musculoskeletal radiologist, blinded for clinical data.

Results: Clinical characteristics of the PsA cohort and prevalence of hand MRI lesions are presented in Table 1. The mean total PsAMRIS of the cohort was low (5.5 units [SD 9.1]), with synovitis of MCP joints being the most common finding (n=27 patients, [45%]). PsA duration was moderately correlated with the total PsAMRIS (Spearman's rank correlation rho 0.358, p=0.005).

MDA (n=19) and non-MDA (n=41) groups were comparable in age, BMI, psoriasis/PsA duration, skin disease severity, and treatment modalities. (Table 2) Total PsAMRIS units (mean [SD]) was similar in MDA and non-MDA groups: 6.1 [11.14] vs 6.1 [7.4], respectively (p=0.985). Remarkably, both groups had a similar prevalence of hand synovitis with predominant involvement of MCP joints: MDA vs non-MDA, n=8 [42.1%] vs 19 [46.3%], p=0.978. The prevalence of bone marrow edema, periarticular inflammation, and bone erosions was higher in the non-MDA group but did not reach statistical significance: MDA vs non-MDA, n=3 [15.8%] vs 10 [24.4%], p=0.678; n=1 [5.3%] vs 7 [17.1%], p=0.399; n=2 [10.5%] vs 6 [14.6%], p=0.978, respectively. Flexor tenosynovitis was detected only in the non-MDA group (n=10.0, [24%], p=0.047), whereas bone proliferation was detected only in the MDA group (n=3 [15.8%], p=0.048). Comparison of the prevalence of inflammatory MRI findings by grouping the extent of synovitis, bone marrow edema, and periarticular inflammation by severity did *not* change the results.

Table 1. Clinical characteristics and MRI findings in the PsA cohort (n=60).

Demographic characteristics	
Gender: male/female, n	24/36
Age, mean [SD]	53.3 [12.9]
BMI, mean [SD]	27.7 [4.4]
Disease characteristics	
Psoriasis duration, years, mean [SD]	21.7 [16.5]
Psoriasis severity scores: BSA, mean [SD] PASI, mean [SD]	 1.1 [2.4] 1.5 [3.3]
PsA duration, years, mean [SD]	11 [12.9]
Swollen joint count (SJC66), mean [SD]	1 [1.9]
Tender joint count (TJC68), mean [SD]	9.6 [10.7]
Dactylitis, n, [%]	7 [11.7]
C-reactive protein (CRP; mg/dL), mean [SD]	0.9 [0.9]
Patient pain, VAS, mean [SD]	5.0 [3.2]
Patient global assessment, VAS, mean [SD]	5.2 [3.1]
HAQ, mean [SD]	1.0 [0.8]
Physician global assessment, VAS, mean [SD]	2.4 [2.3]
Psoriatic arthritis disease activity score DAPSA, mean [SD]	22.3 [15.9]
Treatment modalities	
Current sDMARD, n, [%]	31 [51.7%]
Current methotrexate, n, [%]	26 [43.3%]
Current biologic treatment, n, [%] TNF inhibitors, n, [%] IL17 inhibitors, n, [%] IL12/IL23 inhibitor, n, [%]	33 [55.0%] 26 [43.3%] 7 [11.7%] 1 [1.7%]
Hand MRI findings	
PsAMRIS, units, mean [SD]	5.5 [9.1]
Synovitis (MCP, PIP, DIP joints), n, [%]	27 [45.0%]
Flexor tenosynovitis, n, [%]	10 [16.7%]
Periarticular inflammation, n, [%]	8 [13.3%]
Bone marrow edema, n, [%]	13 [21.7%]
Erosions, n, [%]	8 [13.3%]
Bone proliferation, n, [%]	8 [5.0%]

Legend:

BMI – body mass index, BSA – body surface area; PASI - psoriasis area severity index; DAPSA - Disease Activity Index for Psoriatic Arthritis (DAPSA); HAQ, health assessment questionnaire; IL – interleukin; IQR – interquartile range (IQR); MCP – metacarpophalangeal, PIP – proximal interphalangeal, DIP – distal interphalangeal, PsA – psoriatic arthritis; sDMARD – synthetic disease modifying anti-rheumatic drug; TNF – anti-tumor necrosis factor; VAS – visual analogue scale

Conclusion: This preliminary study results corroborate a high proportion of subclinical inflammation detected by MRI in joints of hand in PsA patients in MDA, whereas overall PsAMRIS scores were low in both MDA and non-MDA groups. These results need to be reproduced in a larger cohort.

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Table 2. Clinical characteristics and prevalence of MRI lesions of hands in patients with psoriatic arthritis stratified by minimal disease activity (MDA).

	MDA N=19	non-MDA N=41	p-value
Demographic characteristics			
Gender, Female, n, [%]	13 [68.4%]	23 [56.1%]	0.533
Age, mean [SD]	53.7 [12.5]	53.1 [14.2]	0.860
BMI, mean [SD]	27.0 [3.7]	28.0 [4.8]	0.457
Clinical Characteristics			
Psoriasis duration, years, mean [SD]	24.5 [18.9]	20.4 [15.3]	0.377
Psoriasis severity scores: BSA, mean [SD] PASI, mean [SD]	 1.7 [2.9] 1.7 [2.7]	 0.8 [2.2] 1.5 [3.5]	 0.217 0.833
PsA duration, years, mean [SD]	11.9 [16.0]	10.5 [11.3]	0.707
Swollen joint count (SJC66), mean [SD]	0.2 [0.5]	1.3 [2.2]	0.043
Tender joint count (TJC68), mean [SD]	2.1 [3.8]	13.1 [11.1]	<0.001
Dactylitis, n, [%]	2 [10.5]	5 [12.2]	1.000
C-reactive protein (CRP; mg/dL), mean [SD]	0.55 [0.7]	0.99 [0.99]	0.089
Psoriatic arthritis disease activity score DAPSA, mean [SD]	5.8 [7.1]	28.6 [13.4]	<0.001
Treatment modalities			
Current sDMARD, n, [%]	9 [47.4%]	22.0 [53.7]	0.860
Current methotrexate, n, [%]	7 [36.8%]	19.0 [46.3]	0.681
Current biologic treatment, n, [%] TNF inhibitors, n, [%] IL17 inhibitors, n, [%] IL12/IL23 inhibitor, n, [%]	13 [68.4%] 11 [57.9%] 2.0 [10.5%] 0.0 [0.0%]	20.0 [48.8%] 15.0 [36.6%] 5.0 [12.2%] 1.0 [2.4%]	0.253 0.204 1.000 1.000
Hand MRI findings			
PsAMRIS, units, mean [SD]	6.1 [11.14]	6.1 [7.4]	0.985
Synovitis, N, [%]	8 [42.1%]	19 [46.3%]	0.978
Flexor tenosynovitis, N, [%]	0 [0.0%]	10 [24.4%]	**0.047**
Periarticular inflammation, N, [%]	1 [5.3%]	7 [17.1%]	0.399
Bone edema, N, [%]	3 [15.8%]	10 [24.4%]	0.678
Bone erosion, N, [%]	2 [10.5%]	6 [14.6%]	0.978
Bone proliferation, N, [%]	3 [15.8%]	0 [0.0%]	**0.048**

Legend: BMI – body mass index, BSA – body surface area; PASI - psoriasis area severity index; DAPSA - Disease Activity Index for Psoriatic Arthritis (DAPSA); IL – interleukin; IQR – interquartile range (IQR); MCP – metacarpophalangeal, PIP – proximal interphalangeal, DIP – distal interphalangeal, PsA – psoriatic arthritis; sDMARD – synthetic disease modifying anti-rheumatic drug; TNF – anti-tumor necrosis factor; VAS – visual analogue scale

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Abstract Number: 1172

The Relationship Between Subclinical Inflammation and Bone Damage in Patients with Rheumatoid Arthritis Using Multimodality Imaging

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Many RA patients in clinical remission have evidence of bone marrow edema (BME) on magnetic resonance imaging (MRI), with radiographic bone damage progression appearing in a subset of patients.[1] While MRI provides excellent visualization of subclinical inflammation, bone resolution is relatively poor, limiting the correlation of inflammatory imaging findings to erosive change that may develop. High resolution peripheral quantitative computed tomography (HR-pQCT) provides superior detailed bone resolution, with improved erosion detection and quantification. The purpose of this study was to determine whether subclinical inflammation observed on MRI could be co-localized with erosive change visualized by HR-pQCT, thereby predicting bone damage progression over a 6-month follow-up period for RA participants in clinical remission.

Methods: Nine participants meeting the ACR/EULAR criteria for RA and in clinical remission were recruited to undergo contrast-enhanced MRI and HR-pQCT scans of the hand at two timepoints, six months apart. Disease activity between these timepoints was assessed monthly by questionnaire, examination, and inflammatory biomarkers. A multimodal image registration technique was developed to co-localize imaging findings on HR-pQCT and MRI. Synovitis and BME were assessed semi-quantitatively with MRI using the RAMRIS scoring system.[2] Bone erosion volume quantification was completed using a 3D segmentation technique using MIAF-Finger[3], with joint space width (JSW) assessed using a volumetric approach from HR-pQCT images.[4] Individual changes in HR-pQCT outcomes were compared against the least significant change (LSC) measured from scan-rescan reproducibility.

Results: The mean DAS28 for the 9 participants was 2.16 (SD 0.64) at the initial scan and 1.72 (SD 0.76) at follow-up. All participants had evidence of synovitis on MRI. Eight joints had evidence of BME at baseline. Twelve 2nd and

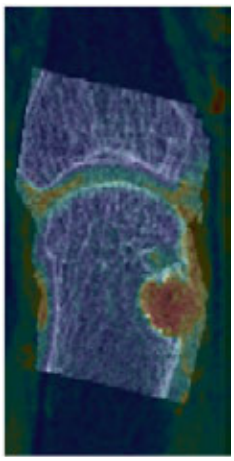

Figure 1. An HR-pQCT image overlaid with a transformed MRI image to localize inflammation (red) with bone damage.

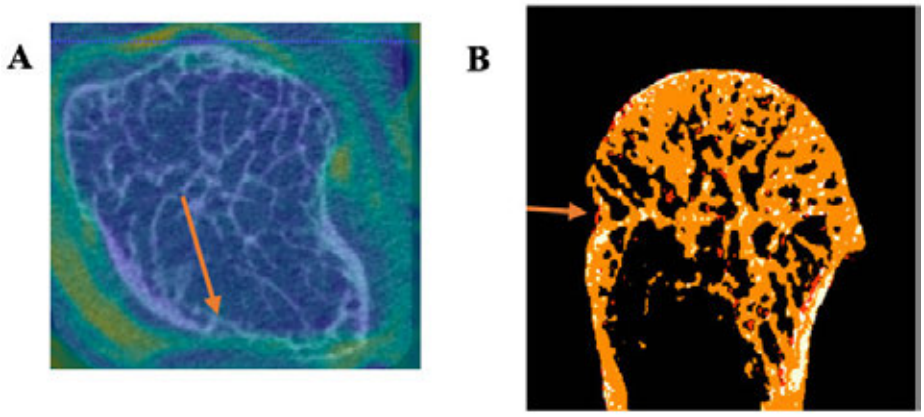

Figure 2. (A) An erosion in HR-pQCT (bone = white) overlaid with MR image indicating no evidence of inflammation at the site of the erosion at baseline. (B) When baseline and follow-up HR-pQCT images are registered and aligned to visualize bone loss and gain, there is evidence of bone formation (red) at the erosion. This erosion showed a decrease in volume over 6 months. Orange indicates stable bone while white indicates resorbed bone.

Table 1. Associations between MRI RAMRIS scores for synovitis and bone marrow edema (BME) at initial scan and 6-month changes in HR-pQCT erosion volume and minimum joint space width (JSW). Decrease, Stable, and Increase characterization determined with respect to the Least Significant Change. (N = 12 joints from 7 participants).

	MRI					
	Initial Synovitis Score			Initial BME Score		
HR-pQCT	0	1	2	0	1	2
Erosion Volume						
Decrease	0	1	0	1	0	0
Stable	0	4	7	7	4	0
Increase	0	0	0	0	0	0
Minimum JSW						
Decrease	0	0	1			
Stable	0	6	5			
Increase	0	0	0			

3rd MCP joints seen on HR-pQCT were co-localized with MRI using image registration (Figure 1). The presence of BME did not predict significant change in erosion volume (Table 1). In contrast, absence of BME and synovitis at the location of the erosion was associated with a decrease in erosion volume in one participant (Figure 2). The JSW outcomes remained stable in all joints, with the exception of one joint that showed a decrease in minimum JSW and another that had a decrease in the maximum JSW.

Conclusion: Even with highly sensitive imaging we did not detect erosive progression over the course of 6 months in patients with subclinical inflammation. However, the absence of localized subclinical inflammation was suggested to predict erosion healing. Findings will be confirmed in a larger cohort. This novel image registration technique for RA was able to co-localize areas of subclinical inflammation on MRI with joint damage on HR-pQCT, which could provide insights on the mechanisms of damage in RA that is not possible with either imaging approach alone.

Reference:

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Abstract Number: 1173

Magnetic Resonance Imaging in Patients in Clinical Remission: Tenosynovitis and Osteitis Are Independent Predictors of Radiographic and MRI Damage Progression

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SESSION INFORMATION

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Background/Purpose: Progression of structural joint damage develops in 20-30 % of patients with rheumatoid arthritis (RA) in clinical remission[1]. Known predictors of structural damage progression in both active RA and in remission are magnetic resonance imaging (MRI)-detected synovitis and in particular osteitis/bone marrow edema (BME), but the predictive value of adding MRI tenosynovitis assessment as potential predictor in patients in clinical remission has not been investigated. The purpose was to investigate the predictive value of baseline MRI inflammatory and damage parameters on 2 year MRI and radiographic damage progression in an RA cohort in clinical remission, following MRI and conventional treat-to-target (T2T) strategies.

Methods: Two hundred RA patients in clinical remission, defined as DAS28-CRP< 3.2 and no swollen joints, on conventional DMARDs, were included in the IMAGINE-RA trial[2]. In this study patients were randomized to a conventional DAS28 + MRI-guided T2T strategy targeting absence of BME vs a conventional DAS28 guided T2T strategy. Patients had baseline and 2 years contrast-enhanced MRIs of the dominant wrist and 2nd-5th MCP joints and radiographs

		Dependent variables, progression ≥1 from baseline to month 24[a]					
		MRI			X-ray		
		Erosion	JSN	Combined damage score	Erosion	JSN	TSS
Explanatory variables	MRI BME	1.13 (1.06-1.21) p<0.001	1.18 (1.08-1.29) p<0.001	1.22 (1.12-1.33) p<0.001			
	MRI Tenosynovitis	1.13 (1.03-1.25) p=0.01	1.21 (1.04-1.40) p=0.01	1.13 (1.02-1.26) p=0.02		1.10 (1.00-1.21) p=0.04	
	Age				0.96 (0.93-0.99) p=0.007		
[a]: Odds Ratio (95% confidence interval; CI) p-value; MRI combined damage score: sum score of MRI erosion and JSN scores.							

of hands and feet. Two experienced readers evaluated the MRIs and radiographs with known chronology according to the OMERACT RAMRIS scoring system and Sharp/van der Heijde method, respectively. The following potentially predictive baseline variables: MRI BME, synovitis, tenosynovitis, MRI and X-ray erosion and joint space narrowing (JSN) score, CRP, DAS28, smoking status, gender, age and patient group were tested in univariate logistic regression analyses with 2-year progression in MRI combined damage score, Total Sharp Score (TSS), and MRI and X-ray JSN and erosion scores as dependent variables. Variables with p< 0.1, age, gender and patient group were included in multivariable logistic regression analyses with backward selection.

Results: Based on univariate analyses MRI BME, synovitis, tenosynovitis, x-ray erosion and JSN, gender and age were included in subsequent multivariable analyses. Independent MRI predictors of structural progression were BME (MRI progression) and tenosynovitis (MRI and radiographic progression), see table.

Conclusion: This trial is the first to report that MRI tenosynovitis independently predicts both radiographic and MRI damage progression in RA patients in clinical remission. Further studies are needed to confirm MRI-determined tenosynovitis as predictor of progressive joint destruction in RA clinical remission.

References:

1. Lillegraven et al. Ann Rheum Dis 2012
2. Møller-Bisgaard et al. JAMA, 2019

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Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8.

Abstract Number: 1174

Prevalence of Subclinical Sacroiliitis in Young Patients with Inflammatory Bowel Disease Revealed by Entero-MRI

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sacroiliitis is one of the extraintestinal manifestations associated with inflammatory bowel disease (IBD), and may be underdiagnosed especially in the pediatric age. MR-enterography (Entero-MRI) is currently the imaging gold standard to assess intestinal disease activity and to detect complications in patients with IBD. Only few studies have been conducted on adult patients with IBD in order to define the role of this technique in assessing sacroiliitis, while no data are available on pediatric patients.

To study the prevalence of inflammatory sacroiliitis on MRI performed for intestinal investigation in an IBD pediatric population.

Methods: This is a retrospective study conducted on patients suffering from IBD followed in our gastroenterology department between 2010 and 2018 whose entero-RM (1.5 or 3 Tesla, Philips depending from year of scanning) were blindly and independently scored by two readers experienced in pediatric musculoskeletal imaging. Each sacroiliac joint was divided into 4 quadrants. Signs of sacroiliitis were identified according to the ASAS criteria, with a particular attention to the presence of bone marrow edema (using T2 weighted sequences with fat suppression), diffusion restriction in DWI sequences (Diffusion Weighted Imaging) or DWIBS (Diffusion Weighted Imaging with Background Suppression) and post-contrastographic uptake in dynamic acquisitions. Demographics, IBD characteristics, clinical, radiological, and laboratory data were recorded and a dedicated Excel database was constructed. Results were elaborated using descriptive statistics.

Results: 34 patients (10 F, 24 M, age at scanning range 5-20 yrs, median 15) were included in the study, for a total of 59 entero-MRI evaluated (some patients were subjected to more than one scan). Two out of 34 patients were affected by Ulcerative Colitis, 32 by Crohn disease. Joint examination resulted negative in all patients, and none complained of articular symptoms including back pain.

In 5 IBD patients (4 CD, 1 UC) a monolateral slight degree of sacroiliitis (grade 1) was radiologically identified. They were all males, without clinical-laboratory-radiologic inflammatory signs of intestinal activity, with the exception of a patient who presented signs of intestinal and sacroiliac inflammation at his first entero-MRI, while 18 months later, at his MRI control under pharmacological treatment, signs of sacroiliitis were still present in the absence of intestinal signs of inflammation.

Conclusion: Asymptomatic sacroiliitis was observed in about 15% of our IBD patients. Sacroiliac involvement therefore can be underdiagnosed in these patients. Entero-MRI with specific sequences could be a good tool to detect early signs of sacroiliac inflammation.

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Disclosure: T. Giani, None; **M. Di Maurizio**, None; **P. Lionetti**, None; **A. Bernardini**, None; **G. Ferrara**, None; **V. Filistrucchi**, None; **R. Cimaz**, None.

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Periarticular Inflammation and Bone Marrow Oedema Are Important in the Evaluation of Enthesitis on MRI in Patients with Peripheral and Axial SpA

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SESSION INFORMATION

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Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesitis is a hallmark feature of Spondyloarthritis (SpA), and frequently localizes at the Achilles tendon[1]. Enthesitis is predominantly measured with clinical scores like Leeds Enthesitis Index (LEI), however, magnetic resonance imaging (MRI) might represent a more sensitive tool to recognize enthesitis in both, bone and soft tissues[2], providing insight about the potential disconnect between pain at entheseal sites and objective inflammation. ACHILLES is the largest double blind, placebo-controlled, multicenter Phase 3 trial to date, designed to investigate enthesitis by clinical and imaging assessments in patients (pts) with active SpA. Here, we present the MRI parameters of the heel (evaluated by central readers) in pts who were not included in ACHILLES based on a negative MRI evaluation of the (local) investigator.

Methods: Pts (≥18 years) with active SpA (peripheral or axial) had to present in ACHILLES with clinical (LEI) and MRI-positive heel enthesitis (interpreted by either the local radiologist or rheumatologist), defined as enthesitis with/without bursitis and/or bone marrow edema with/without concomitant erosions in the area of the Achilles' tendon insertion and/or the plantar aponeurosis. The present analysis included heel MRI characteristics of pts who failed to meet the MRI study inclusion criteria based on local MRI evaluation. The MRIs of screen-failed pts were evaluated by

Table: MRI Parameters

		MRI positive n/N (%)	Not MRI positive n/N (%)
Enthesitis - Achilles tendon	Yes	6/12 (50.0)	0/34 (0)
	No	6/12 (50.0)	34/34 (100)
Bursitis - Achilles tendon	Yes	6/12 (50.0)	14/34 (41.2)
	No	6/12 (50.0)	20/34 (58.8)
Bone marrow oedema - Achilles tendon	Yes	3/12 (25.0)	0/34 (0)
	No	9/12 (75.0)	34/34 (100)
Enthesitis - Plantar aponeurosis	Yes	5/12 (41.7)	0/ (0)
	No	7/12 (58.3)	34/34 (100)
Bursitis - Plantar aponeurosis	Yes	4/12 (33.3)	2/34 (5.9)
	No	8/12 (66.7)	32/34 (94.1)
Bone marrow oedema - Plantar aponeurosis	Yes	6/12 (50.0)	0/34 (0)
	No	6/12 (50.0)	34/34 (100)
Active inflammation (Global)	Yes	12/12 (100)	17/34 (50.0)
	No	0/12 (0)	17/34 (50.0)
Periarticular inflammation	Present	8/12 (66.7)	6/34 (17.6)
	Absent	4/12 (33.3)	28/34 (82.4)
Quantification of bone oedema (PsAMRIS)	No oedema	6/12 (50.0)	34/34 (0)
	1-33% of bone edematous	6/12 (50.0)	
	1-33% of bone edematous; oedema length ≤ 0.5 cm	5/12 (41.7)	
	1-33% of bone edematous; oedema length > 0.5 cm	1/12 (8.3)	
Quantification of bone erosion (PsAMRIS)	No erosion	10/12 (83.3)	28/34 (82.4)
	1-10% of bone eroded	1/12 (8.3)	4/34 (11.8)
	11-20% of bone eroded	1/12 (8.3)	1/34 (2.9)
	Not applicable	0/12 (0)	1/34 (2.9)
Location of bone erosion	All patients with Location of bone erosion at Achilles tendon area	1/2 (50.0)	1/5 (20.0)
	Achilles tendon area insertion, other	1/2 (50.0)	1/5 (20.0)
	All patients with Location of bone erosion at Plantar aponeurosis area	1/2 (50.0)	2/5 (40.0)
	Plantar aponeurosis area, other	1/2 (50.0)	2/5 (40.0)
	All patients with Location of bone erosion at 'Other'	2/2 (100)	2/5 (40.0)
	Achilles tendon area, other	1/2 (50.0)	
	Plantar aponeurosis area, other	1/2 (50.0)	
	Other		2/5 (40.0)

N, total number of patients in a group
Active Inflammation (Global) is "Yes" in case at least one of the following direct parameters is "yes":
Achilles' enthesitis; Bursitis (Achilles' tendon); Bone oedema (Achilles' tendon insertion); Fascitis plantar aponeurosis; Bursitis (Plantar aponeurosis); Bone oedema (Plantar aponeurosis); Periarticular inflammation (PsAMRIS); Quantification of bone oedema (PsAMRIS)

two independent central readers, blinded to any screen failure reason, in a consensus read fashion. Centralized reading of the heel MRIs was performed according to the Psoriatic arthritis magnetic resonance imaging scoring system (PsAMRIS)[3]. Since PsAMRIS was developed initially for the hands, additional parameters were introduced to allow for more accurate representation of the heel: a) bone oedema (with 1-33% of bone oedematous) were further specified by oedema length ≤/ >0.5 cm and b) bone erosions were further specified by assessing the localization.

Results: Overall, 204 (128 PsA and 76 axSpA) pts were randomized and 94 pts failed screening. Of the 94 screen-failed pts, 46 pts failed due to MRI negative heel enthesitis as assessed by investigators. Upon assessment by central readers, 12/46 (26.1%) were found to be MRI positive and 34/46 (73.9%) MRI negative for heel enthesitis; MRI parameters of both groups are shown in the **Table**. Overall, 8/12 (67%) MRIs evaluated for positive enthesitis presented with periarticular inflammation and 6/12 (50%) with bone oedema. PsAMRIS based quantification of bone oedema revealed 1-33% of bone edematous for 6 cases, with only 1/6 having an oedema length of >0.5 cm. Enthesitis was centrally read in 6/12 (50%) MRIs at the Achilles tendon insertion and in 5/12 (42%) at the Plantar aponeurosis calcaneal insertion.

Conclusion: In central reading, concomitant periarticular inflammation and bone marrow oedema at the tendon insertion were found to be critical for the confirmation of enthesitis on MRI in patients suffering from SpA.

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Disclosure: X. Baraliakos, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, BMS, 2, 5, 8, 9, Bristol-Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, 9, Chugai, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Lilly, 2, 8, 9, Merck, 2, 5, 8, MSD, 2, 5, 8, 9, Novartis, 2, 5, 8, 9, Novatis, 2, 5, 8, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9, UCB Pharma, 2, 5, 8, Werfen, 2, 5, 8; **P. Sewerin**, AbbVie, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Celgene, 2, 5, 8, Chugai, 2, 5, 8, Hexal, 5, 8, Janssen-Cilag, 2, 5, 8, Lilly, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, Sanofi-Genzyme, 5, 8, Swedish Orphan Biovitrum, 5, 8, UCB, 2, 5, 8; **E. de Miguel**, AbbVie, 2, 5, 8, BMS, 8, BMS, MSD, UCB, Roche, 8, MSD, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 8, UCB, 8; **C. Kleinmond**, Novartis, 5; **A. Shekhawat**, Novartis, 3; **A. Wiedon**, Novartis, 3; **F. Behrens**, Abbvie, 2, 5, 8, Biotest, 5, 8, BMS, 5, 8, Boehringer, 5, 8, Celgene, 5, 8, Chugai, 2, 5, 8, Galapagos, 5, 8, Genzyme, 5, 8, Janssen, 2, 4, 5, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 5, 8, Sanofi-Genzyme, 5, 8, UCB, 5, 8.

Abstract Number: 1176

Development and Validation of a Preliminary MRI Sacroiliac Joint Composite Structural Damage Score in a 5-year Longitudinal Study of Patients with Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with axial spondyloarthritis (axSpA), MRI reliably detects structural lesions in the sacroiliac joints (SIJs). The SPARCC Sacroiliac joint (SIJ) Structural Score (SSS)(1) is a reliable and validated method to assess the individual structural lesions of the SIJs, i.e. fat lesion, erosion, backfill (fat metaplasia in an erosion cavity) and ankylosis. Several MRI studies have indicated that bone destruction, i.e. erosion, is often followed by formation of new bone in the erosion cavity (backfill), ultimately leading to ankylosis(2). The aim was to combine these lesions into a composite score for SIJ structural damage and to test it in a 5-year follow up study with patients with axSpA.

Methods: Thirty-three patients fulfilling ASAS criteria for axSpA were followed for 5 years after initiation of TNF inhibitor in the BIOSPA study(2). T1-weighted (T1w) and STIR MRI sequences of the SIJs acquired at weeks 0 and 46 and

Table 1. Baseline characteristics and correlation between clinical/MRI variables and The Composite AxSpA MRI Structural Damage Score for all patients, patients with no/minimal ankylosis (CSDS<108) and patients with almost complete ankylosis (CSDS≥108).

				Correlation				
Variables	Baseline			Baseline			Change 0-5 yrs	
	All	CSDS<108	CSDS≥108	All	CSDS<108	CSDS≥108	All	CSDS<108
Gender (male)	26 (78.8)	17 (73%)	9 (90%)	-	-	-	-	-
Age (years)	40.3 (10.9)	35 (21;62)	**46 (30;62)***	0.28	-0.99	-0.18	-	-
Symptom duration (years)	13.8 (12.1)	5.5 (1;33)	**20 (12;45)***	**0.58***	-0.10	-0.40	-	-
HLA-B27 (n (%))	26 (78.8)	17 (81%)	9 (90%)	-	-	-	-	-
ASDAS	3.83 (1.05)	3.9 (2.1;6))	3.5 (2.0;4.8)	-0.21	-0.17	0.06	-0.16	-0.04
BASDAI (0-10)	5.5 (1.8)	5.4 (3.2;9.8)	4.8 (3;8.1)	**-0.37***	**-0.49***	-0.06	0.14	-0.05
BASFI (0-10)	5.0 (21.3)	4.5 (1;8.3)	5 (1.5;9.9)	-0.10	-0.36	-0.29	-0.15	0.01
BASMI (0-10)	3.2 (1.7)	3 (0;6)	**4 (3;6)***	**0.37****	0.07	-0.24	0.11	0.15
CRP (mg/L)	31.7 (36.8)	18 (1.6;149)	18.5 (1.7;107)	-0.12	-0.04	-0.17	-0.29	-0.29
SPARCC SIJ Inflammation (0-72)	5.4 (8.9)	4 (0;37)	**0 (0;4)***	**-0.46****	-0.01	**-1.00****	**-0.54****	**-0.52***
SPARCC SSS Fat (0-40)	21.0 (15.6)	12 (0;40)	**39.5 (0;40)***	**0.57****	**0.56****	-0.31	**0.55****	**0.55****
SPARCC SSS Erosion (0-40)	5.4 (7.0)	6 (0;22)	**0 (0;0)*****	-0.28	**0.62****	-	0.05	0.15
SPARCC SSS Backfill (0-20)	3.1 (5.2)	2 (0;19)	**0 (0;0)****	-0.07	**0.83****	-	0.17	0.13
SPARCC SSS Ankylosis (0-20)	6.7 (8.9)	0 (0;7)	**20 (18;20)***	**0.82****	0.40	**1.00****	**0.64****	**0.70****
Composite Structural Damage Score	58.3 (46.9)	24 (0-93)	**120 (108-120)***	-	-	-	-	-
mSASSS (0-72)	10.5 (12.5)	4 (0-29)	17 (0-46)	0.27	0.09	0.18	-0.14	-0.15

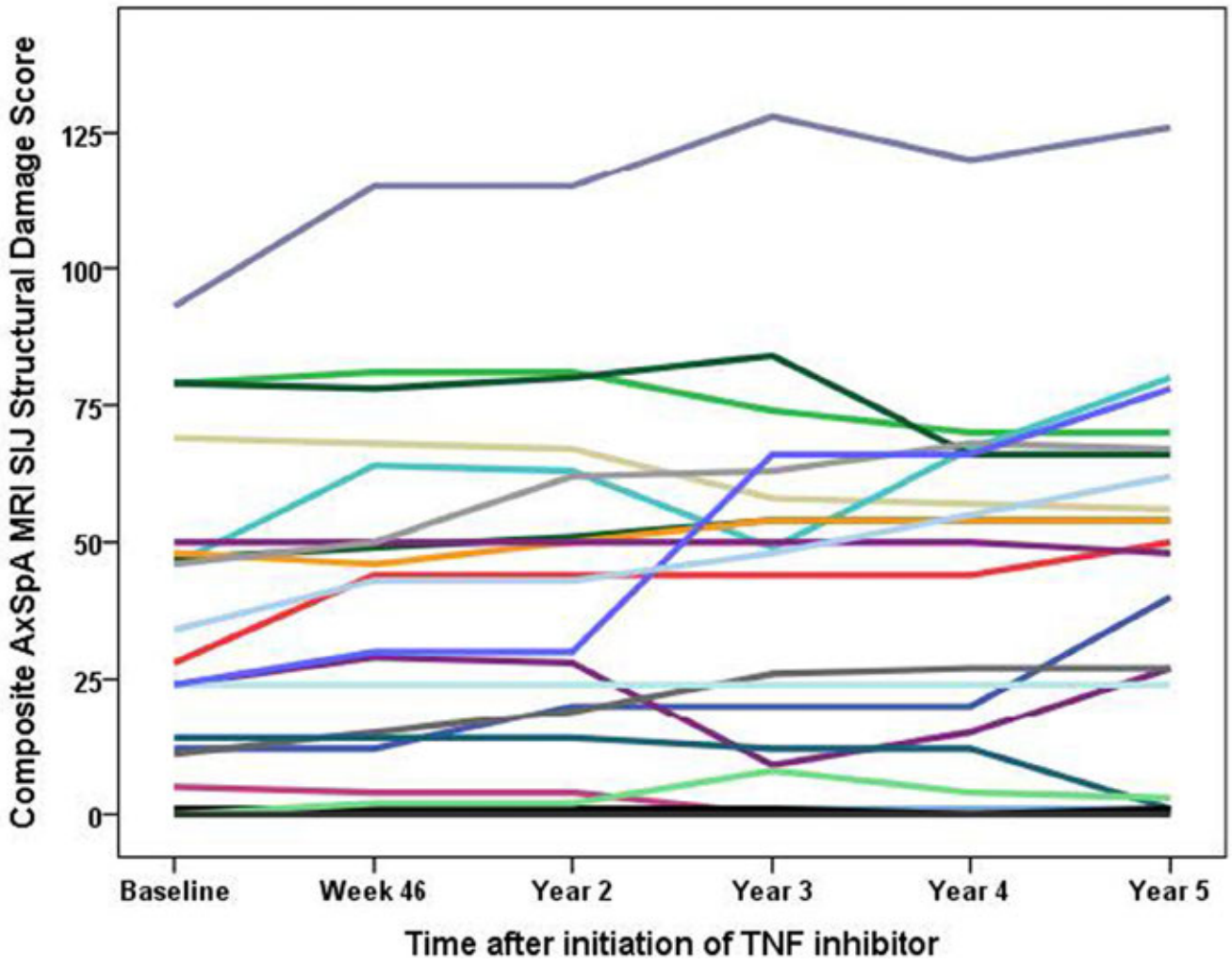
Data are shown as n (%), mean (SD) or median (min;max).
*p<0.05, **p<0.01, ***p<001, all 2-tailed. Tests are Chi-square test, Fisher's exact test, Mann-Whitney U-test or Spearman Rank Correlation analysis.

Table 2. Annual change in Composite AxSpA MRI SIJ Structural Damage Score (CSDS) for the sacroiliac joints

	0-46weeks	46weeks-2y	2-3y	3-4y	4-5y
CSDS, adjusted annual change	2.9 (6.3)	0.5 (1.9)	0.6 (8.7)	-0.2 (5.9)	1.8 (7.3)
CSDS<108, adjusted annual change	4.2 (7.3)	0.8 (2.3)	0.9 (10.7)	0.3 (7.1)	2.6 (8.8)
CSDS≥108, adjusted annual change	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Data are shown as mean (SD). The progression in CDDS (i.e. annual change) was calculated as the change between MRI scans divided by the exact time interval (yrs) between MRI assessments.

Figure 1



year 2, 3, 4, 5 were evaluated with SPARCC SIJ SSS. In each of 5 slices of each SIJ, erosion is scored 0-1 per joint quadrant (i.e. max score 2 per joint half, 4 per SIJ), backfill scored 0-1 per joint half (i.e. max 2 per SIJ) and ankylosis scored 0-1 per joint half (i.e. max 2 per SIJ). Based on this, a preliminary composite axSpA MRI SIJ Structural Damage Score (CSDS) was calculated: (Erosion score x1) + (backfill score x4) + (ankylosis score x6).

Results: Patients were divided into two groups: patients with almost complete bilateral ankylosis (CSDS≥108, n=10) and patients with no/minimal ankylosis (CSDS< 108, n=23). At baseline patients with CSDS< 108 were younger, had shorter symptom duration, lower BASMI, higher SPARCC Inflammation, lower SSS Fat, Erosion, Backfill and Ankylosis scores, as compared to patients with CSDS≥108. At baseline, CSDS correlated positively with symptom duration, BASMI and SSS Fat and Ankylosis, and negatively with BASDAI and SPARCC inflammation. Change in CSDS over 5 years correlated negatively with change in SPARCC Inflammation and positively with change in SSS Fat and Ankylosis. Change in CSDS over 5 years in patients with no/minimal ankylosis correlated negatively with change in SPARCC Inflammation and positively with change in SSS Fat and Ankylosis. There was no change in the group with almost complete ankylosis at baseline. (Table 1) Table 2 show the annual change CSDS over 5 years. It is noted in Figure 1, that many patients progressed the first 46 weeks, thereafter the progression decreases. However, the mean progression increases in the last year, based on a few patients with markedly increasing scores.

Conclusion: A preliminary Composite Structural Damage Score for MRI assessment of the sacroiliac joints in patients with axial spondyloarthritis, which allows scoring of MRI progression of erosion through backfill to ankylosis, is described for the first time. Progression was most pronounced in the first year after TNF-inhibitor initiation. Further validation is needed. This novel approach may be useful for monitoring structural progression in axSpA patients receiving different therapies.

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Disclosure: M. Wetterslev, None; **M. Østergaard**, AbbVie, 2, 8, 9, Abbvie, 2, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, UCB, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, 5, 8, Abbvie, Celgene, Centocor, Merck, and Novartis, 2, Abbvie, Celgene, Centocor, Merck, Novartis, 2, BMS, 2, 5, 8, 9, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8; **I. Juul Sørensen**, None; **U. Weber**, None; **A. Loft**, None; **G. Kollerup**, None; **L. Juul**, None; **G. Thamsborg**, None; **O. Rintek Madsen**, None; **J. Møller**, None; **S. Juhl Pedersen**, None.

Abstract Number: 1177

Near Infrared Indocyanine Green Imaging Reveals Altered Anatomy and Diminished Function in Lymphatic Vessels in the Hands of Rheumatoid Arthritis Patients During Flare

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Near infrared (NIR) imaging of indocyanine green (ICG) in rheumatoid arthritis (RA) models identified abnormal lymphatic vessel (LV) function, which can be quantified as ICG clearance from the injection site via longitudinal (days) NIR imaging. As the role of LV function in RA is unknown, we hypothesized that ICG clearance from hand web spaces and efferent LV contraction frequency of RA patients experiencing flare is significantly decreased compared to normal healthy volunteers. We also assessed the characteristics of filled LVs to examine if structural differences are present in RA lymphatics and healthy controls.

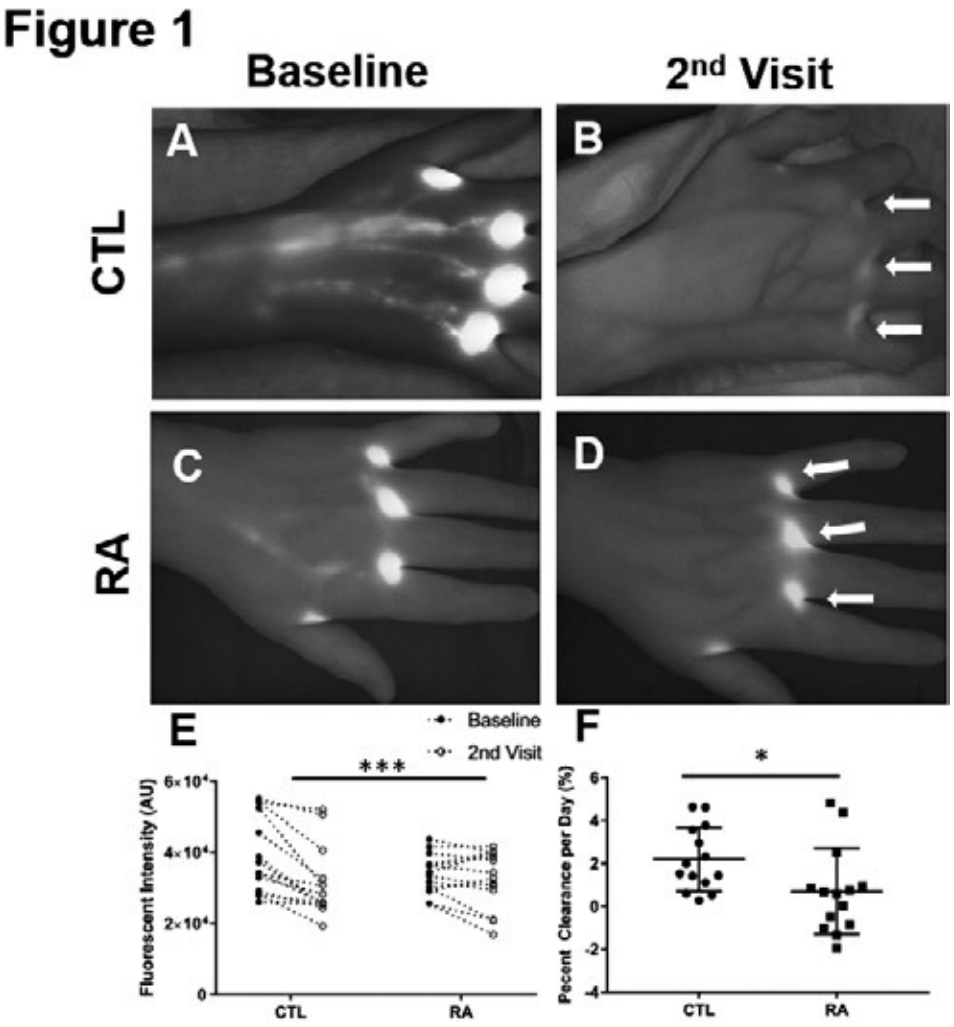

Figure 1. Impaired Lymphatic Clearance of ICG from the Hand in RA Subjects. ICG intensity was measured in left and right hands of 7 healthy control (CTL, n=14) and 5 RA subjects (n=14) after injection at the initial visit (Baseline) and at the second visit 7-15 days later (2nd Visit). Representative NIR images of a control subject at baseline (A) and at the second visit (B) show considerable clearance of the ICG at the injection sites (White Arrows), while in RA subjects (C, D) did not clear the ICG. When this was quantified, RA subjects had significantly less clearance (E, paired t-test,**p<0.001). Due to the variable time period between baseline and subjects second visit, the percent clearance per day is plotted for each interval (F, t-test, *p<0.05).

Methods: The web spaces of both hands of 12 healthy controls (CTL) and 7 subjects with RA flare (ACR 2010 RA criteria) were injected with 0.1ml of 100μM ICG on 2-4 separate occasions, and the hands underwent NIR imaging. To measure clearance of ICG from the web spaces, 7 CTL and 7 RA subjects were reimaged 7-9 or 13-15 days after the first injections, and the remaining NIR fluorescence was measured via region of interest (ROI) analysis (Paired t-test). Controlling for the number of days between subjects, the change in intensity between the initial and second visit was divided by the number of days between visits (t-test). Lymphatic contractions for LVs were determined from graphs of ROI intensity across time to calculate contractions per minute, and assessed via Wilcoxon Rank Test. To assess the branching structure of the vessels, manual segmentation of the lymphatic network and subsequent spatial mapping was performed (t-test). Then two independent graders quantified the total number of bifurcations of the LVs. Median values for each hand across all visits and graders were used to test for differences (Wilcoxon Rank-Sum Test).

Results: Representative NIR images of CTL and RA hands at baseline, and at the second visit, demonstrate the dramatic retention of ICG at the injections sites (White Arrows) in RA subjects (Fig 1 A-D). Statistical analysis revealed a decrease in ICG clearance in the RA subjects vs. CTLs (Fig 1 E, ***p< 0.001). When controlling for days between

Figure 2

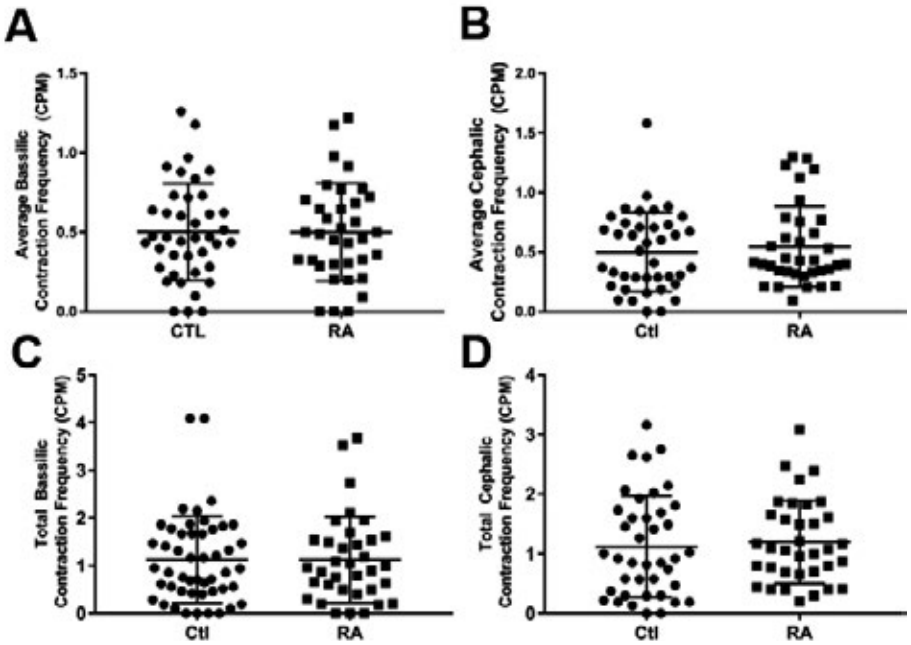

Figure 2. Lymphatic contraction frequency is not different between healthy controls and RA subjects. Lymphatic contraction frequency was calculated via ROI analysis of 10 minutes observing the dorsal aspect of the hand. An ROI was placed over the basilic and cephalic associated vessels at the wrist. These data for each vessel were either averaged or summed to generate average basilic (A) and cephalic (B) contraction frequency; or total basilic (C) and cephalic (D) contraction frequency. There were no statistical difference between the groups for any of these outcomes.

Figure 3

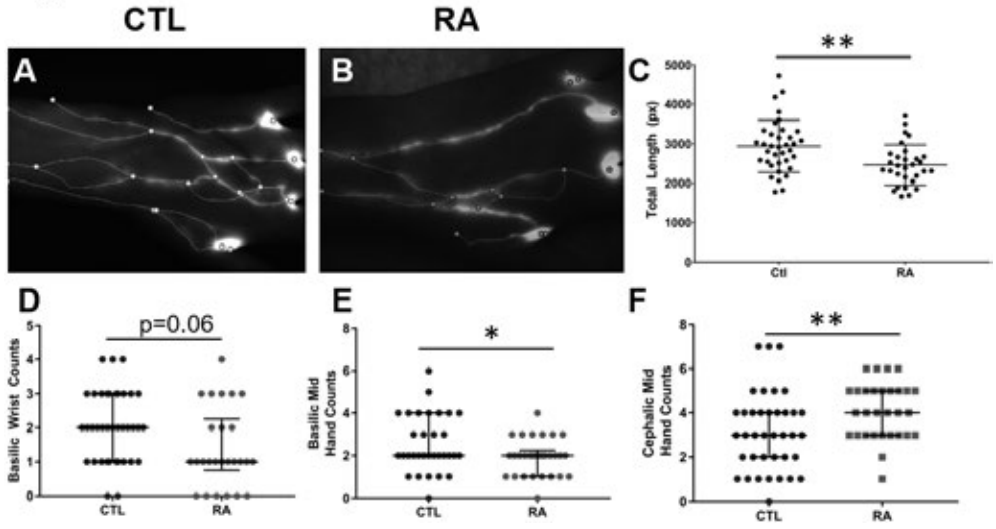

Figure 3. RA subjects have significantly less lymphatic vessels in their hands compared to healthy controls. Videos and still images were used to manually segment the lymphatic vessel network in the dorsal aspects of the hands. Spatial graphs were then generated to map to the lymphatic network. Representative stills of CTL (A) and RA (B) hands with overlaid spatial graphs show significant variation between the two. Accordingly, RA subjects have significantly less total graph length is calculated (C, t-test, M± SD, **p<0.01). To investigate where anatomically these lymphatic network differences, we manually scored how many vessels were present at the wrist, mid hand and near the injection sites. Interestingly, we found significantly fewer vessels on the lateral side of the hand (basilic associated vessels, D and E) while there was an increase in cephalic sided vessels (F, Wilcoxon Sum Rank Test, Median and IQR, *p<0.05, **0.001).

the initial visit and second visit the relationship persisted (Fig 1F, *p< 0.05). Interestingly, no difference in contraction frequency was observed between CTLs and RA subjects (Fig 2A-D). However, there was significantly decreased total length in the spatial structure of the lymphatic network (Fig 3A-C, *p< 0.05). This decreased length was primarily attributed to a lack of basilic associated ICG filled vessels in RA subjects (Fig 3D-F, *p< 0.05).

Conclusion: Imaging outcomes of LV function in mice have demonstrated diminished clearance of lymph from inflamed joints during arthritic progression. Herein, we show a significant reduction in ICG clearance and altered anatomic structure in RA subjects' hands during flare. The accumulation and retention of inflammatory cells and molecules in RA joints as a result of diminished lymphatic clearance may be a critical factor in the initiation and persistence of synovitis. This clinical pilot demonstrates the feasibility of quantifying LV function, and warrants formal investigation in clinical trials.

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Abstract Number: 1178

Clinical Utility of DECT in the Diagnosis of Gout at Mayo Clinic in Florida

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is the most common inflammatory arthritis in the United States and worldwide. Precipitation of monosodium urate crystals in joints and soft tissues leads to inflammation and the clinical signs and symptoms of gout. Identification of urate crystals on synovial fluid analysis remains the gold standard for diagnosis. However, arthrocentesis is not always a viable option, particularly if the patient presents without active inflammation or effusion on exam. Dual energy computed tomography (DECT) is another tool for noninvasive diagnosis of gout and

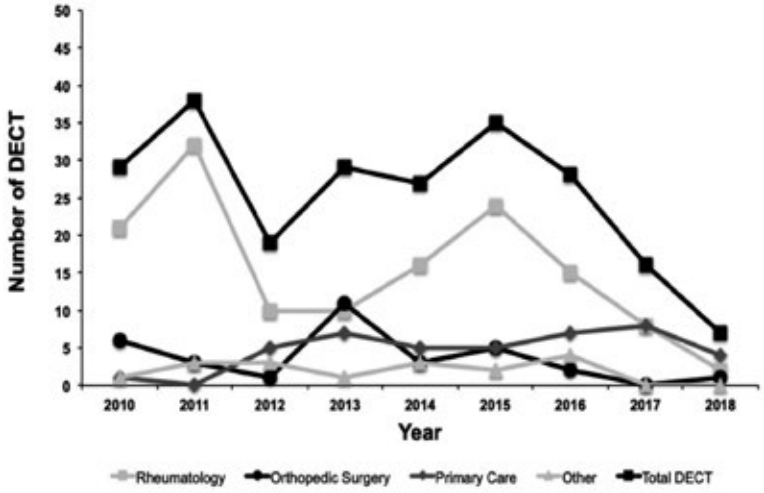

Figure 1. Number of DECT ordered per year by specialty.

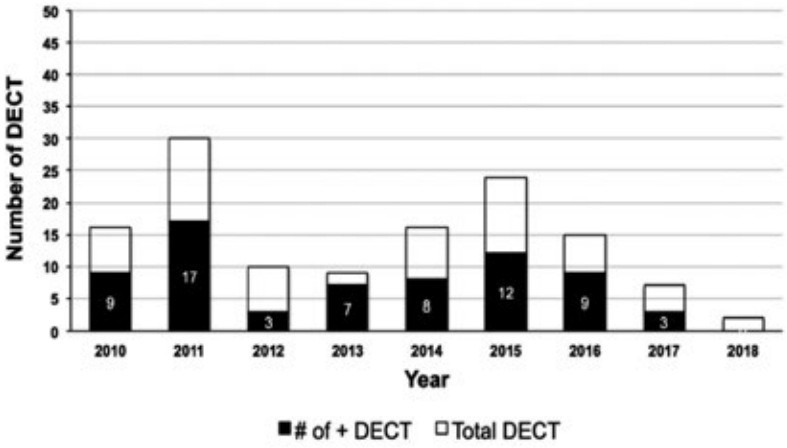

Figure 2. Total number of DECT ordered per year for initial diagnosis of gout by the rheumatology department at Mayo Clinic in Florida. Number of positive of DECT are shown in black. Year 2018 represents January through April.

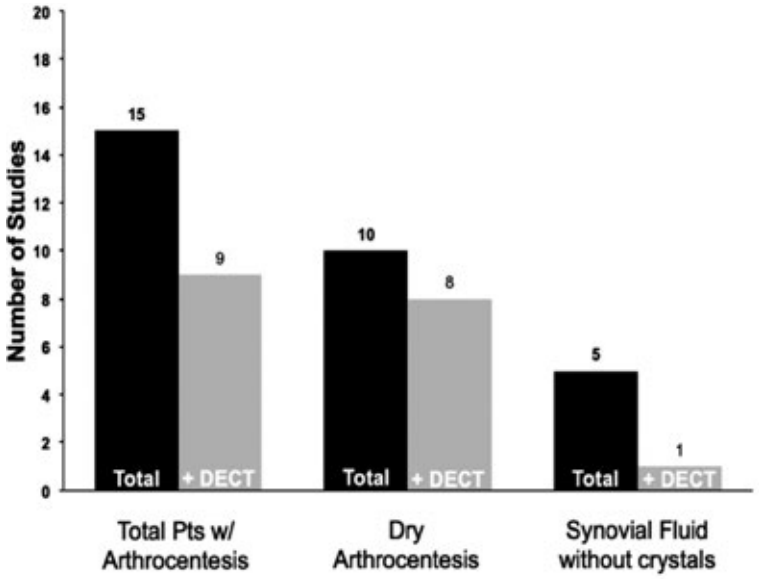

Figure 3. Did DECT aid in gout diagnosis in patients with negative arthrocentesis? 15 total patients underwent arthrocentesis in the rheumatology department. No fluid was obtained on 10 patients. Synovial fluid was examined for 5 patients.

can be utilized in the acute or chronic stages. The 2015 American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) classification criteria for gout recognize a role for DECT in diagnosis. In our retrospective study, we analyzed how DECT is utilized in a cohort of patients at Mayo Clinic in Jacksonville, Florida. We sought to determine better clinical parameters for ordering DECT in our rheumatology department.

Methods: Our retrospective study was approved by the institutional review board. Informed consent was waived due to the retrospective nature of the study. DECT scans performed from January 2010 to April 2018 were identified using radiology software by a board certified, fellowship trained radiologist with expertise in musculoskeletal imaging. Lower extremity, upper extremity, and spine DECT were included.

Results: 228 DECT were ordered over the observation period. Rheumatology accounted for the highest percentage (60%) of tests ordered, followed by primary care physicians (18%). 211 studies were requested to aid in the initial diagnosis of the patient's concern with 129 ordered by rheumatology. Whereas the number of scans ordered by other departments changed little over the eight year observation period, DECT studies, ordered by rheumatology, decreased from 2015 onward. DECT was positive for urate 53% of the time (68 of 129) when ordered for initial diagnosis by rheumatology. Arthrocentesis was attempted on 15 patients to establish a diagnosis of gout. No synovial fluid was obtained from 10 of 15 patients. 80% of these patients had DECT performed which positively identified urate crystals. The other 5 patients, who underwent arthrocentesis, had synovial fluid examined by microscopy with 4 of 5 identifying no crystals. One patient with negative fluid analysis underwent repeat arthrocentesis showing positively birefringent rhomboid crystals. One patient with no crystals on microscopy had a positive DECT scan. Ultrasound (US) was performed on 6 patients in the clinic by the rheumatologist prior to DECT imaging. Double contour sign was identified on each patient. DECT confirmed the diagnosis of gout in these six patients.

Conclusion: The utilization of DECT in gout diagnosis is likely to continue to increase given that it is noninvasive, an accepted criterion in the ACR/EULAR 2015 guidelines, and more readily available. Our study highlights that DECT can be a useful tool in gout diagnosis when there is diagnostic uncertainty, no active inflammation or effusion on exam, and arthrocentesis cannot be obtained. Though the cohort was small, US can be a viable option as a noninvasive tool in gout diagnosis.

Disclosure: E. Gilbert, None; **H. Garner**, None; **A. Abril**, None.

Abstract Number: 1179

Resting-State Functional Connectivity of Pain Processing Brain Region Associated with Therapeutic Response to Biologics in Rheumatoid Arthritis and Spondyloarthritis

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SESSION INFORMATION
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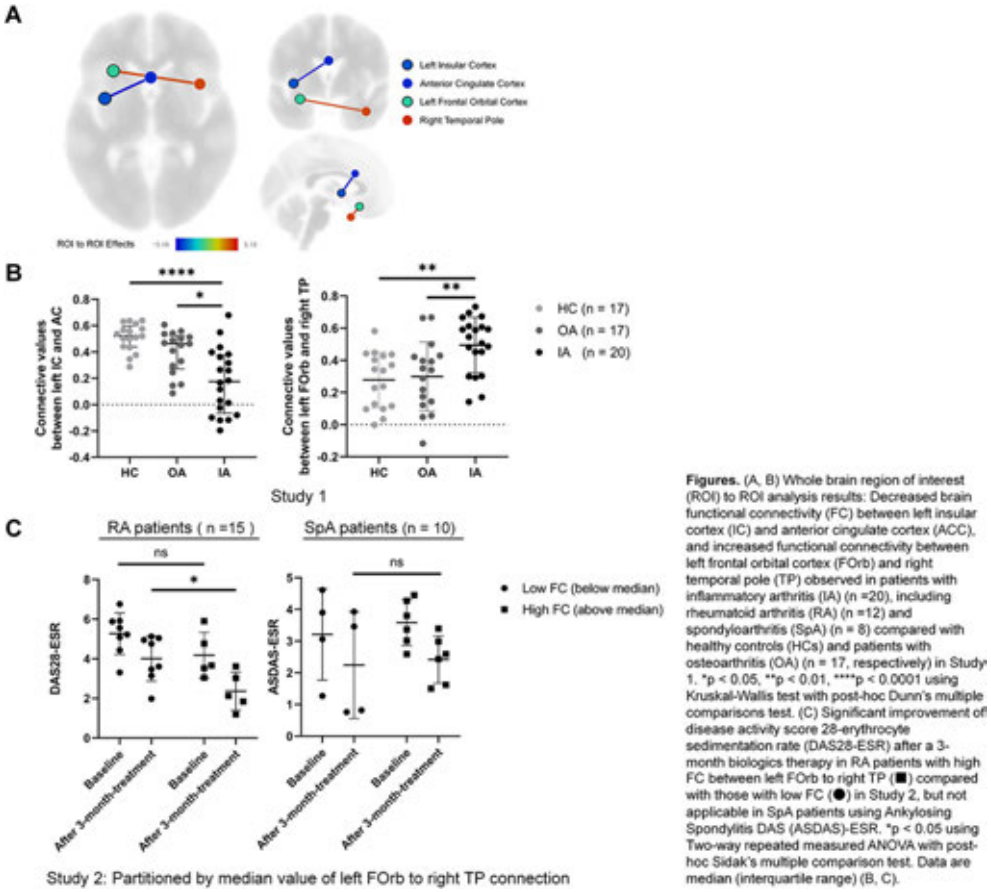
Background/Purpose: Discriminating inflammatory pain from non-inflammatory pain is critical to determine therapeutic strategy in inflammatory arthritis (IA) such as rheumatoid arthritis (RA) and spondyloarthritis (SpA). Previous studies showed that resting-state functional MRI (rs-fMRI) could detect abnormal functional connectivity (FC) of brain areas related to chronic pain and could predict disease course as in chronic lumbar pain. However, the difference of FC between inflammatory and non-inflammatory pain is still unknown. This study aimed to clarify the abnormal FC related to inflammatory pain and whether it could predict the response of treatment in IA.



Figures. (A, B) Whole brain region of interest (ROI) to ROI analysis results: Decreased brain functional connectivity (FC) between left insular cortex (IC) and anterior cingulate cortex (ACC), and increased functional connectivity between left frontal orbital cortex (FOrb) and right temporal pole (TP) observed in patients with inflammatory arthritis (IA) (n =20), including rheumatoid arthritis (RA) (n =12) and spondyloarthritis (SpA) (n = 8) compared with healthy controls (HCs) and patients with osteoarthritis (OA) (n = 17, respectively) in Study 1. *p < 0.05, **p < 0.01, ****p < 0.0001 using Kruskal-Wallis test with post-hoc Dunn's multiple comparisons test. (C) Significant improvement of disease activity score 28-erythrocyte sedimentation rate (DAS28-ESR) after a 3-month biologics therapy in RA patients with high FC between left FOrb to right TP (■) compared with those with low FC (●) in Study 2, but not applicable in SpA patients using Ankylosing Spondylitis DAS (ASDAS)-ESR. *p < 0.05 using Two-way repeated measured ANOVA with post-hoc Sidak's multiple comparison test. Data are median (interquartile range) (B, C).

Methods: IA patients requiring biologics (n = 46; RA 28, SpA 18) and healthy controls (HCs, n = 17) underwent rs-fMRI in Hokkaido University Hospital. For controls of non-inflammatory pain, rs-fMRI dataset of patients with osteoarthritis (OA) (n = 17) was obtained from OpenNEURO (https://doi.org/10.18112/openneuro.ds000208.v1.0.0). IA patients were split into two groups (Study 1 or Study 2), depending on whether or not the patients had clinical follow-up data after biologics therapy. In Study 1, to identify the abnormal FC related to inflammatory pain, rs-fMRI-derived FC values to whole brain connectivity were retrospectively analyzed in IA patients (n = 20; RA 12, SpA 8) by comparing with OA patients and HCs (n = 17, respectively). In Study 2, IA patients treated with biologics were prospectively evaluated with disease activity score 28-erythrocyte sedimentation rate (DAS28-ESR) and Ankylosing Spondylitis DAS-ESR (ASDAS-ESR) in RA patients (n = 15) and SpA patients (n = 10), respectively before treatment and after a-3-month therapy. We then analyzed the association between the detected FC and disease activity.

Results: From the whole brain analyses in Study 1, significant connective values between left insula cortex (IC) and anterior cingulate cortex (ACC), and left frontal orbital cortex (FOrb) and right temporal pole (TP) were found in IA patients compared with OA patients and HCs (Figure. 1A, B). In Study 2, the connectivity values of left FOrb and right TP partitioned by median value of IA patients could discriminate significant improvement of DAS28-ESR after treatment in RA patients, although there was no association with the improvement of ASDAS-ESR in SpA patients (Figure. 1C).

Conclusion: RA and SpA patients shared neurobiologic features of the abnormal functional connections between left IC and ACC, and left FOrb and right TP, which are brain regions involving pain processing and decision making. High FC value between left FOrb and right TP would predict the superior therapeutic outcomes regarding disease activity in patients with RA, suggesting that this abnormal FC would be associated with inflammatory pain.

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Abstract Number: 1180

Confirmation of Manual Cartilage Segmentation Findings by Automated Segmentation: Retrospective Analysis of MRI Images from a Sprifermin Phase II Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
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Background/Purpose: Sprifermin is under investigation as a potential disease-modifying osteoarthritis drug (DMOAD). 2-yr results from the FORWARD study showed significant dose-dependent modification of cartilage thickness in the total femorotibial joint (TFTJ), medial and lateral femorotibial joints (MFTC, LFTC), and central medial and lateral TFTJ subregions, by quantitative (q)MRI (Hochberg et al. ACR 2017).

This post hoc analysis aimed to determine whether qMRI findings from FORWARD (manual segmentation) could be reproduced in the same cartilage regions using an independent method (automated segmentation), on the same dataset/time period.

Methods: Pts were randomized 1:1:1:1:1 to: sprifermin 100 µg q6mo; 100 µg q12mo; 30 µg q6mo; 30 µg q12mo; and placebo (n=110/110/111/110/108). Cartilage thickness was assessed at baseline and 6, 12, 18, and 24 months using 1.5- or 3-Tesla MRI images, analysed manually. The same images were analysed by automated cartilage segmentation using active appearance models, a supervised machine learning method, to produce maps of cartilage thickness for weight-bearing femoral and tibial cartilage surfaces, subdivided into anatomical masks. Results were blinded for treatment and timepoint for both methods. No statistical comparisons between methods were conducted.

Endpoints were change from baseline in: 1) cartilage thickness in the TFTJ, MFTC and LFTC, using regions duplicated based on published data; 2) cartilage thickness in the central subregion of the medial and lateral tibia and femur (cMT, cMF, cLT, cLF [conventions used by the automated analysis investigators]). As in previous analyses, treatment effect was assessed by observed changes and adjusted using repeated ANCOVA on change from baseline, including

Table 1. Change in cartilage thickness with sprifermin 100 µg q6mo vs placebo using automated segmentation.

	Mean (SD) change from baseline at Yr 2, mm		
Region	Sprifermin 100 µg q6mo	Placebo	P value
TFTJ	0.05 (0.11)	-0.04 (0.08)	P<0.001
MFTC	0.03 (0.15)	-0.04 (0.14)	P=0.011
LFTC	0.07 (0.12)	-0.04 (0.10)	P<0.001
cMT	0.02 (0.18)	-0.07 (0.17)	P=0.008
cLT	0.09 (0.20)	-0.05 (0.18)	P<0.001
cLF	0.09 (0.11)	0.00 (0.08)	P<0.001
cMF	0.02 (0.17)	-0.04 (0.16)	P=0.061

treatment group, timepoint, and country as fixed factors, baseline value as covariate and treatment by timepoint as interaction.

Results: Based on automated segmentation, statistically significant, dose-dependent structural modification of cartilage thickness was observed over 2 yrs with sprifermin vs placebo for the TFTJ (overall treatment effect and dose response across all doses, both P< 0.001), MFTC (P=0.004 and P=0.044), and LFTC (both P< 0.001). Table 1 shows changes from baseline for sprifermin 100 µg q6mo and placebo. Statistically significant dose-dependent structural modification of cartilage over 2 yrs was observed for sprifermin vs placebo in the cMT (100 µg q6mo), cLT (100 µg q6mo, q12mo) and cLF (100 µg q6mo, q12mo). In the cMF, there was no treatment effect, but there was a linear trend for dose responsiveness. The results showed a consistent pattern to those obtained using manual segmentation.

Conclusion: Cartilage thickness assessed by automated segmentation provided a consistent pattern of structural modification in FORWARD compared with manual segmentation. This is the first time that two independent methods of image analysis have reached the same conclusions in an interventional DMOAD trial. The findings strengthen the conclusions that sprifermin modifies cartilage loss/structural progression in knee OA.

Disclosure: A. Brett, Imorphics, Manchester, UK, 3; **M. Bowes**, Imorphics, Manchester, UK, 3; **P. Conaghan**, Abbvie, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, 8, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Eli Lilly, 8, EMD, 5, EMD Serono, 5, EMD Serono Research and Development Institute, Inc., 5, 8, Flexion, 5, 8, Flexion Therapeutics, 5, 8, Galapagos, 5, 8, Glaxo Smith Kline, 5, GlaxoSmithKline, 5, 8, Lilly, 8, Medivir, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Samumed, 5, 8, Serono, 5, Stryker, 5, 8; **C. Ladel**, Merck KGaA, Darmstadt, Germany, 3; **J. Kraines**, EMD Serono Research and Development Institute, Inc., 3, EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), 3; **H. Guehring**, Merck KGaA, Darmstadt, Germany, 3; **F. Moreau**, EMD Serono Research and Development Institute, Inc., 3, EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), 3; **F. Eckstein**, Chrondrometrics GmbH, 1, 3, Merck KGaA, Darmstadt, Germany, 5, Samumed LLC, 5, Galapagos, 5, Abbvie, 5, Bioclinica, 5, Kolon TissueGene, 5, Novartis, 5, Servier, 5, Roche, 5.

Abstract Number: 1181

Tocilizumab in Aortitis: A Multicenter Study of 79 Patients

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Llanio,[27] Antonio García,[28] Carmen Larena,[29] Lara Sanchez-Bilbao,[1] Iñigo Gonzalez-Mazon,[3] Natalia Palmou-Fontana,[3] Vanesa Calvo-Río,[1] Carmen González-Vela,[1] Alfonso Corrales,[30] María Varela-García,[4] Elena Aurrecoechea,[6] Raquel Dos Santos,[31] Sabela Fernández,[20] Jose Luis Hernández,[1] Miguel Angel González-Gay,[32] and Ricardo Blanco[33], [1]Hospital Marqués de Valdecilla, Santander, Cantabria, Spain, [2]Rheumatology Department. Hospital Marqués de Valdecilla, Santander, Cantabria, Spain, [3]Rheumatology, Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain, [4]Complejo Hospitalario de Navarra, Navarra, Navarra, Spain, [5]Rheumatology Department, Hospital Universitario de la Princesa, IIS-Princesa, Madrid, Spain, Madrid, Spain, [6]Hospital de Sierrallana, Torrelavega, Cantabria, Spain, [7]Hospital de La Princesa, Madrid, Madrid, Spain, [8]Complejo Asistencial Universitario de León, León, Castilla y Leon, Spain, [9]Complejo Hospitalario Universitario Pontevedra, Pontevedra, Galicia, Spain, [10]Rheumatology Department, Hospital Universitario de Bellvitge, Barcelona, Spain, Barcelona, Catalonia, Spain, [11]Hospital Alto Deba, Mondragon, Pais Vasco, Spain, [12]Division of Rheumatology, Instituto de Investigación Sanitaria-Hospital Clinico Universitario de Santiago, Santiago de Compostela, Spain, Santiago de Compostela, Spain, [13]Complexo Hospitalario Universitario de Vigo, Vigo, Galicia, Spain, [14]Hospital Ramón y Cajal, Madrid, Madrid, Spain, [15]Hospital Universitario Lucus Augusti, Lugo, Galicia, Spain, [16]Hospital General Universitario de Elda, Elda, Spain, [17]Hospital Río Carrión, Palencia, Castilla y Leon, Spain, [18]Hospital La Mancha Centro, Alcázar de San Juan, Castilla-La Mancha, Spain, [19]Hospital de Basurto, Bilbao, Pais Vasco, Spain, [20]Hospital Universitario San Agustín, Avilés, Asturias, Spain, [21]Department of Internal Medicine, Hospital Vall d'Hebron, Barcelona, Spain., Barcelona, Catalonia, Spain, [22]Hospital Miguel Servet, Zaragoza, Aragon, Spain, [23]Hospital Mateu Orfila, Menorca, Islas Baleares, Spain, [24]Complejo Hospitalario Universitario de Ourense, Ourense, Galicia, Spain, [25]Hospital Universitario Nuestra Señora de la Candelaria, Tenerife, Canarias, Spain, [26]Hospital Universitario Virgen Macarena, Sevilla, Andalucia, Spain, [27]Hospital Arnau de Vilanova, Lérida, Catalonia, Spain, [28]Hospital Virgen de las Nieves, Granada, Andalucia, Spain, [29]Hospital Universitario Ramón y Cajal, Madrid, Madrid, Spain, [30]Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, IDIVAL, Santander, Spain, Santander, Spain, [31]Complejo Hospitalario Universitario de Santiago, Santiago de Compostela, Galicia, Spain, [32]Universidad de Cantabria and IDIVAL, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [33]Rheumatology, Hospital Universitario Marques de Valdecilla, Santander, Spain

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Imaging Of Rheumatic Diseases Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Aortitis can be idiopathic or associated with other conditions. It is frequently refractory to conventional immunosuppressive therapy. Tocilizumab (TCZ), an anti-IL-6 receptor antibody seems to be effective and safe.

Our aim was to assess the efficacy and safety of TCZ at short and long follow-up in a series of patients with Aortitis.

Methods: Retrospective, multicenter study of 79 patients diagnosed of inflammatory aortitis based on imaging techniques (PET/CT, CT angiography and/or MR angiography).

Results: We study 79 patients (61 w/ 18 m). 59 (74.7%) cases were Aortitis secondary to Giant Cell Arteritis (GCA), while 20 (25.3%) were idiopathic. The mean age was 71±8.5 years vs 64.2±7.1 years, respectively (p=0.001). At time of disease diagnosis more than a half of patients (59.5%) presented as main symptom polymyalgia rheumatica

TABLE

	Idiopathic aortitis (n=20)	Aortitis secondary to GCA (n=59)	p
EFFICACY OF TCZ			
Prolonged remission, n (%)			
Month 6	5 (41.7)	23 (45.1)	0.830
Month 12	5 (45.5)	14 (41.2)	0.803
Month 24	3 (75)	18 (85.7)	0.527
Relapses, n (%)			
Month 1	2 (15.4)	1 (3.3)	0.213
Month 3	2 (16.7)	5 (10.4)	0.546
Month 6	1 (9.1)	8 (16.3)	0.544
Month 12	1 (9.1)	4 (11.8)	1.000
Month 24	0	1 (4.8)	1.000

(PMR). Aortitis was diagnosed with PET/CT (71 patients), angioRMN (12 patients) and angioCT (8 patients). Prior to TCZ treatment, 61 (77.2%) patients had received conventional immunosuppressive drugs, 59 (74.7%) of them received MTX. After 24 months of treatment with TCZ, more than 75% of patients reached a prolonged remission in both groups (p=0.527), with only 4% of relapses after the same follow-up period (p=1.000). 40 (50.6%) patients had a control image technique (PET/CT) throughout follow up. 4 (3 secondary to GCA and 1 idiopathic) patients reached a complete improvement in uptake after one year of treatment.

Conclusion: Our results show that idiopathic aortitis occurs in younger patients compared with aortitis secondary to GCA. TCZ proved to be effective in both pathologies, allowing clinical and analytical improvement, as well as a reduction of corticoid dose, without increasing the risk of relapse. However, the improvement in imaging techniques seems to be slower.

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Abstract Number: 1182

Fluorescence Optical Imaging in the Diagnosis of Individuals Suspected of Arthritis Development – a Probabilistic Approach

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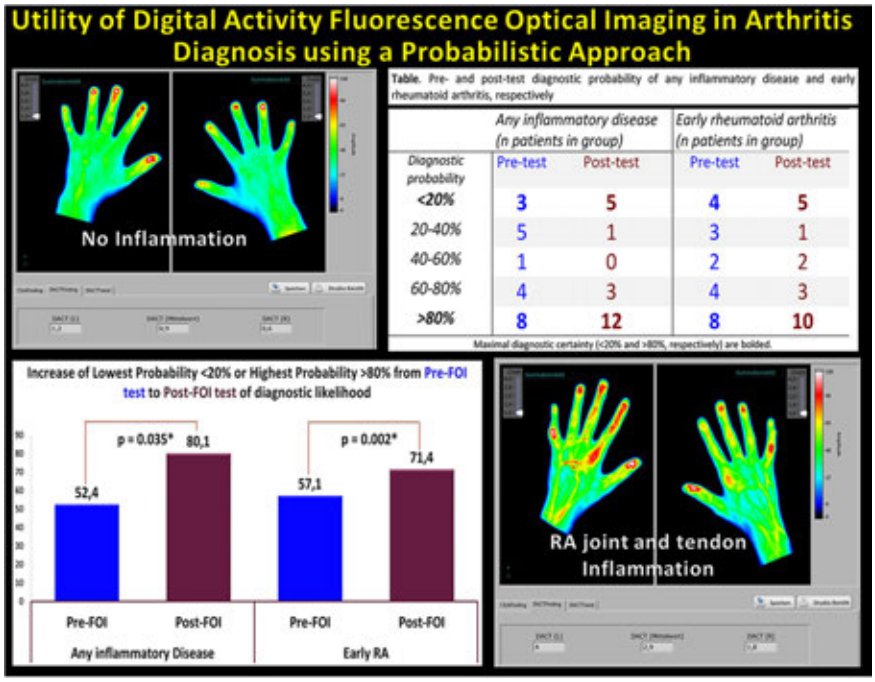
Background/Purpose: Among the arsenal of available techniques for arthritis prediction and diagnosis, fluorescence optical imaging (FOI) has shown to be useful in detecting clinically manifest and silent synovitis of the hands of patients with various rheumatic diseases. Using a probabilistic approach, we now assess the diagnostic utility of FOI in individuals that are at increased risk of inflammatory arthritis (RA in particular).

Methods: Those suspected of inflammatory arthritis were referred to the rheumatology unit and clinic of the Karolinska University Hospital. On acquiring informed consent and medical history, the standard clinical examination coupled with ultrasound findings of the hands and feet were assessed. Laboratory results included ESR, CRP, RF



Fluorescence optical Images of normal and inflamed hand joints together with results of probability changes from minimal to maximal certainty of arthritis diagnosis, before and after FOI examination

and ACPA tests. Using the above information, a diagnostic probability assessment was completed by the responsible rheumatologist, where the probability of a) any inflammatory joint disease and b) Rheumatoid/RA was given on a 5 point scale - ranging from unlikely (0-20%) to very likely (80-100%) probability. Subsequently, an FOI examination was performed. After reviewing the image reports in consensus, post-FOI diagnostic probabilities were again scored using the same scale. If no score change in the probability resulted, then the rheumatologist was asked to mark whether FOI was still helpful in the diagnostic decision making. Proportions of individuals with maximal and minimal diagnostic certainty pre-and post-test were compared using Fisher exact tests, and one-sample binomial tests for assessing the helpfulness of FOI in the absence of pre-and post-test probability score changes.

Results: Of 24 individuals screened, 21 without prior rheumatic diagnosis were included (67% female, 11 RF (+), 10 ACPA (+), with age average and symptom duration (SD) of 56 (±18) years and 14 (±15) months respectively). The final diagnosis were: early RA (n=17), other inflammatory joint disease (n=3), and non-inflammatory joint disease (n=1). Regarding diagnosis of any inflammatory arthritis, where the proportion of patients for whom the diagnostic certainty was maximal - namely, combining < 20% (lowest probability) or >80% (highest probability) of diagnostic likelihood - there was an increase from 52% (n=11/21) maximal certainty before FOI to 80% (n=17/21) maximal certainty after FOI (p=0.035). Regarding early RA, the maximal diagnostic certainty increased from 57% (n=12/21) to 71% (n=15/21) (p=0.002), respectively. The availability of ultrasound findings confirm the FOI effect. Therefore, in the event that the FOI diagnostic certainty scores did not change, pre- vs. post-test (15/21 cases, any inflammatory joint disease; 13/21 cases, early RA), the diagnosing rheumatologist indicated that FOI was still helpful in setting a final diagnosis for most cases (87% (13/15) p=0.007; 85% (11/13). p=0.022, respectively).

Conclusion: Fluorescence optical imaging significantly increased the diagnostic certainty and confidence of rheumatologists in establishing the presence and absence of inflammation in individuals suspected of inflammatory arthritis. The changes from pre-to post-test quantify the diagnostic utility of fluorescence optical imaging in probabilistic terms.

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Abstract Number: 1183

Gout and Serum Urate Levels Are Associated with Lumbar Spine Monosodium Urate Deposition and Chronic Low Back Pain: A Dual-Energy CT Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Imaging Of Rheumatic Diseases Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: More than 130 cases of gout of the spine have been reported, with presenting symptoms including acute back pain, neuropathy, and spinal compression; diagnosis is usually based on imaging identification of a mass, followed by tissue confirmation of monosodium urate (MSU) deposition.(Toprover et al. Curr Rheum Rep. 2015.) It is likely that many more cases of gout involve the spine in an asymptomatic manner, or with non-specific back symptoms that are never formally diagnosed.

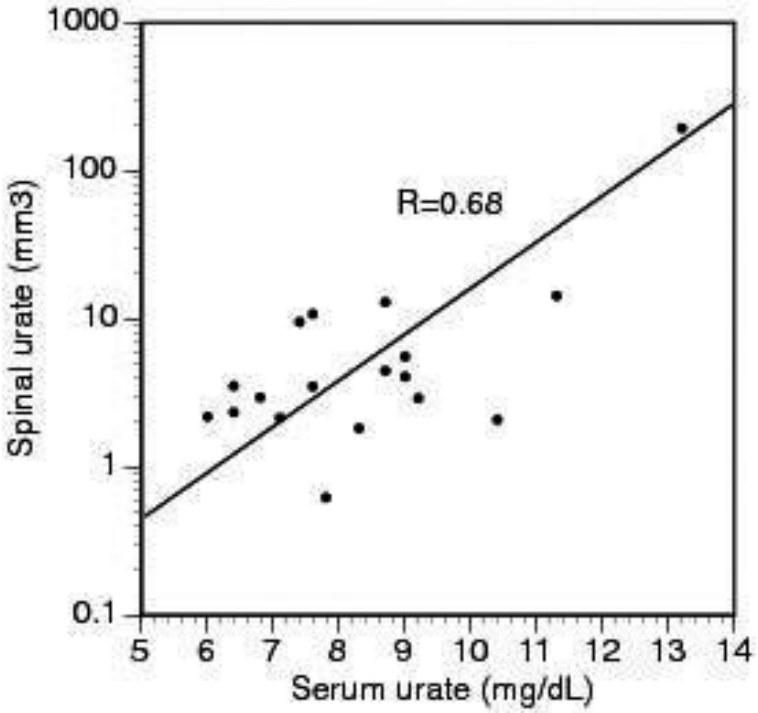

Figure 1. Correlation between serum urate level and spinal urate deposition in subjects with gout

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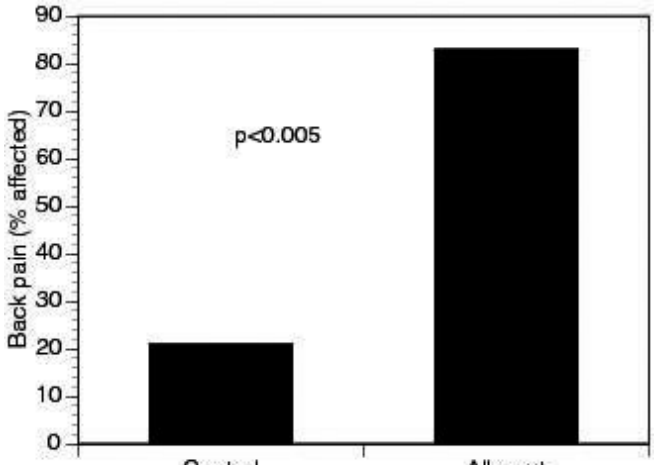

Figure 2. Back pain in controls vs gout subjects.

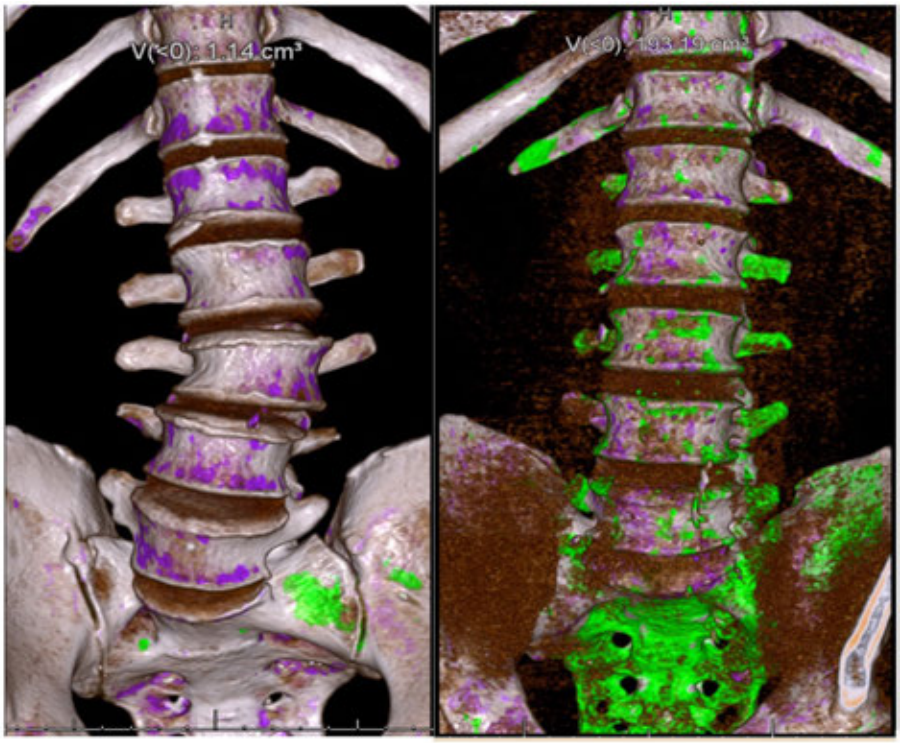

Figure 3. Comparison of DECT scan of control (left) vs gout patient (right)

Methods: Using dual-energy CT (DECT), our study aims to determine the prevalence and extent of urate deposition in the lumbosacral spines of patients with clinical tophaceous gout, vs non-tophaceous gout vs control subjects without gout. We are recruiting 25 controls, 25 non-tophaceous and 25 tophaceous gout patients, 50-80 years old. Exclusion criteria include known pseudogout, RA, spondyloarthropathy or active spinal malignancy. All gout subjects meet current ACR/EULAR classification criteria, and have an entry serum urate (sU) of >6.8 mg/dL, or sU >6.0 mg/dL on ULT for < 6 months. Demographics, gout history, back pain data (including Aberdeen back pain scale), sU, ESR, and CRP are collected. Subjects undergo DECT of the lumbosacral spine to assess for MSU deposition.

Results: To date, 32 subjects have completed the study: 14 controls, 14 non-tophaceous and 4 tophaceous gout subjects. For these preliminary evaluations, all gout subjects (n=18) are pooled together. To date, all recruited subjects are male. All control subjects identify as white; gout subjects identify as white (61.1%), Black (33.3%) or Hispanic (5.5%). Control and gout subjects have similar mean age in years (controls, 61±1.0 vs gout, 63.3±1.5), but differ in serum creatinine (controls, 1.0±0.1 mg/dL vs gout, 1.5±-0.2 mg/dL, p=0.02). Mean sU is higher in the gout group (controls, 5.3±0.2 mg/dL vs gout, 8.4±0.4 mg/dL, p< 0.05). Gout patients have higher CRP (controls, 1.8±0.5 mg/L vs gout, 9.6±3.3 mg/L, p=0.05), ESR (controls, 11.5± 2.6 mm/h, vs gout, 22.3±4.3mm/h, p=0.06), and MSU deposition in the spine (controls, 2.3 ± 0.2 cm3 vs gout, 15.5±10.5 cm3, p=0.28). When a single outlier gout subject with very high sU and extensive spinal MSU was excluded, spinal MSU deposition between controls and gout patients became significant (controls, 2.3±0.8 cm3 vs gout, 5.0±1.0 cm3, p=0.02). Gout patients reported more back pain (controls, 21% vs gout, 83%, p< 0.005) and greater back pain scores (controls, 4.1±1.6, vs. gout, 10.5±3.4, p=0.12). When plotted against sU, spinal MSU volumes were proportional to sU for controls (R=0.32) and more strongly for gout subjects (R=0.68), suggesting the possibility of spinal MSU deposition even in non-gout individuals.

Conclusion: In these preliminary analyses, gout patients had higher inflammatory markers, greater spinal MSU deposition, and increased rates and severity of back pain compared with non-gout controls. In all patients, spinal MSU deposition was proportional to sU. These data suggest that MSU deposition in the spine is common among gout patients, is associated with sU level, and may be associated with low back pain.

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Abstract Number: 1184

Rheumatoid Arthritis Activity Assessment with Cellphone Thermal Camera Imaging Compared to Clinical and Ultrasound Assessments

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The assessment of active joints is a core component of widely used outcome measures in rheumatoid arthritis (RA). However, variability exists within and across examiners in clinical assessment of active joint counts.

Our objective was to explore the ability of noncontact digital thermographic imaging to assess inflammatory arthritis activity, compared to clinical and ultrasound (US) evaluation.

Methods: Cross-sectional pilot study of 20 RA patients (ACR criteria). Each patient had 3 independent (blinded) assessments of their hand joints activity with: 1) clinical with swollen and tender joints counts (SJC, TJC) and DAS28 score; 2) US with mode B and doppler (DP) according to EULAR/OMERACT" guidleines (MyLab60®, Esaote Biomedica, Genoa, Italy, 4–13 MHz broadband linear array transducer), and 3) thermographic assessment. Thermal images were obtained with an infrared thermal cellphone camera FLIR One® and analyzed either with a software detecting

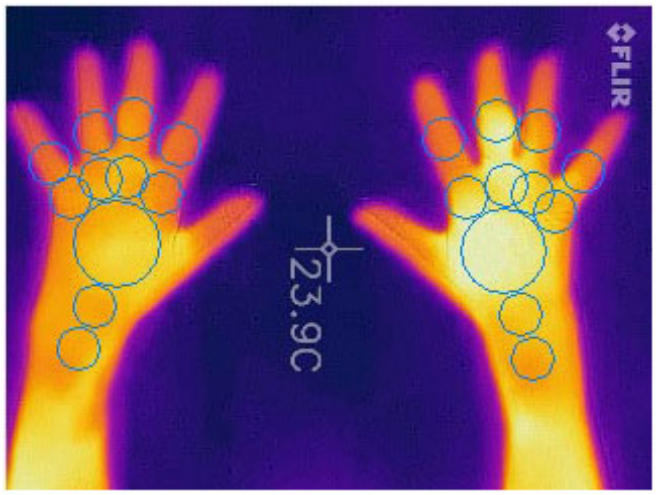

Figure. Automatic detection of 22 ROI (arthritis on the right carp, MCP 3 and IPP 3)

22 predetermined regions of interest (ROI) and either with a simple colour reading (arthritis yes/no) (Figure). For each ROI, we measured the difference between the ROI temperature and the homolateral forearm considered as reference area (ΔT°). Statistical analysis: Description with mean ± standard deviation (SD), and specificity (Sp) and sensitivity (Se) analysis.

Results: The main characteristics of the 20 RA patients were the following (mean±SD): age: 59.5 years, disease duration: 17.5 years, ACPA+: 85%, TJC: 5.1±5.6, SJC : 3.5±3.2, DAS28: 3.8±1,3. The mean ROI temperature of the 351 analyzed joints was 36.3 °C and the forearm temperature was 36.6°C. Clinical vs thermographic assessment: Mean ΔT° of swollen and tender joints was – 0.42 °C ± 0.74 and –0.15°C± 0.88, respectively versus– 0.36 °C ± 0.85 and– 0.46 °C ± 0.62. Mean ΔT° was – 0.08°C ± 0,4 in DAS28 < 2.6 group , – 0.39°C ± 0.91 in DAS 28 ≥ 2.6 - ≤5.1 [TP1] group and – 0.10 ± 0.64 in DAS 28 > 5.1 group. US vs thermographic assessment: The mean ΔT° of the 22 joints with synovitis DP2 and of the 17 joints with DP3 was – 0.48 °C ± 0.99 and – 0.02 °C ± 0.60, respectively. The simple colour reading was able to detect DP2 synovitis with Sp = 0.92 and Se = 0,24 and DP3 synovitis with Sp = 0.94 and Se = 0,19.

Conclusion: Thermographic assessment with a thermal smartphone camera of RA activity is a promising technology, that still needs further refinement before considering its daily use.

Disclosure: C. Paris, None; **P. Lafforgue**, Chugai, 8, Amgen, 8, BMS, 8, Lilly, 8, Abbvie, 8, Pfizer, 8, Biogaran, 8; **V. Pradel**, None; **C. Richez**, astrazeneca, 5, 8, BMS, 5, 8, Glenmark, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8; **T. Pham**, Abbvie, 8, Amgen, 8, Biogen, 8, BMS, 8, Celgene, 8, Fresenius-Kabi, 8, Janssen, 8, Lilly, 8, Medac, 8, MSD, 8, Nordic, 8, Novartis, 8, Pfizer, 8, Roche-Chugai, 8, Sandoz, 8, Sanofi, 8, UCB, 8.

Abstract Number: 1185

New Imaging Modality to Evaluate Arthritis in Lupus Based on Frequency-domain Optical Transmission

Anca Askanase,[1] Fiamma Van Biema,[2] Alessandro Marone,[2] Youngwan Kim,[2] Tommy Chen,[2] Teja Kapoor,[2] Laura Geraldino,[2] Yevgeniya Gartshteyn,[3] and Andreas Hielscher[2], [1]Columbia University Medical Center, New York, NY, [2]Columbia University School of Medicine, New York, NY, [3]Columbia University School of Medicine, Glen Rock, NJ

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Imaging Of Rheumatic Diseases Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: 95% of the people with SLE experience joint pain, stiffness and swelling at some time during their illness. It is currently difficult to both diagnose and estimate the severity of lupus arthritis.This studyexplores the clinical utility of frequency-domain optical transmission (FDOT) measurements to distinguish affected finger joints from healthy ones.

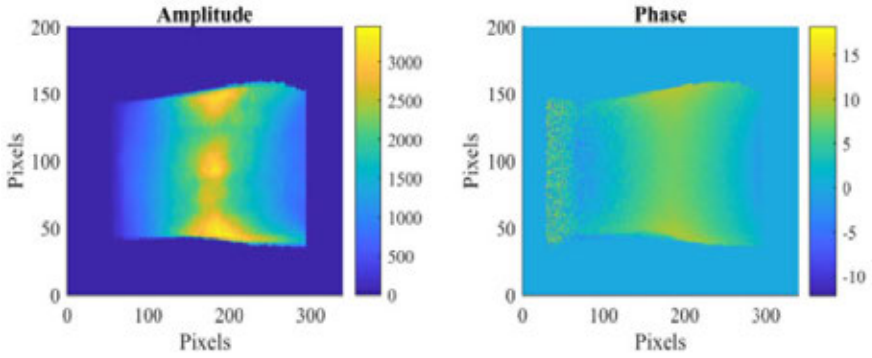

Figure 1. Example of the mean images for amplitude (on the left) and phase (on the right) obtained for the same PIP of a healthy subject.

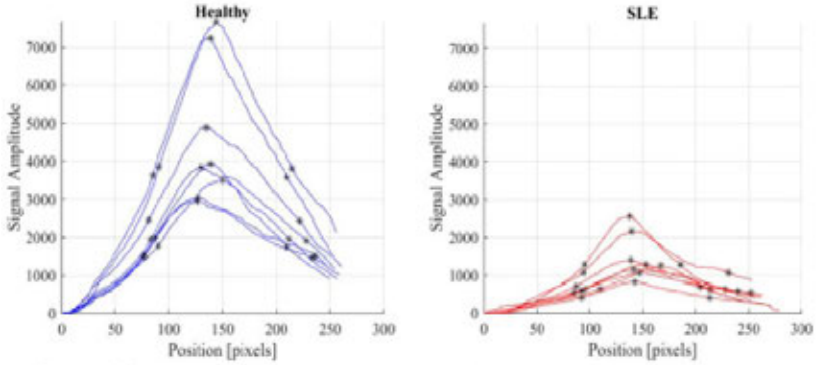

Figure 2. Mean amplitudes of the output signals considering only the finger area in the pictures along the length of the fingers. In blue on the left is a healthy subject, in red on the right a SLE patient. In each graph, there are 8 curves, one for each PIP considered. The black dots mark the peak positions and the positions were the signal is 40% of the peak value.

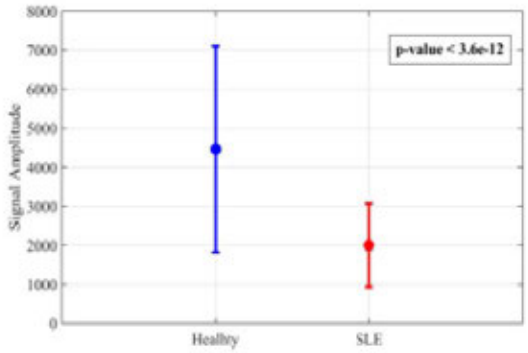

Figure 3. Mean and Standard Deviations of the maximum values of the signal amplitudes estimated in Healthy (blue) and SLE (red) patients. The mean values and standard deviations are respectively 4462 ± 263in Healthy and 2003 ± 1069 in SLE patients.

Methods: The FDOT system is operated at a frequency of 600MHz. The laser diode produces a 1-mm diameter beam at 670nm light with a power of 8mW. Transmitted light intensity is measured using an ICCD camera operated in homodyne mode.

For data acquisition, the laser beam is guided to 11 positions, separated by 2 mm from each other, on the top of the finger, scanning along a sagittal plane in the forward direction with a modulation frequency of 600 MHz. PIP II -V of both hands were scanned. The time required to set-up the system and scan a single finger was about 2 min. 10 patients with SLE with active arthritis were evaluated (9 women, mean age 42 ± 9.1 years). All patients had arthritis by physical exam: swelling, tenderness and pain in each finger joint. 4 healthy controls were also examined (3 women, mean age 28.7 ± 4.4 years). A total of 80 fingers from SLE patients and 32 fingers from healthy volunteers were analyzed.

Results: The raw data obtained consisted in 16 pictures for each of the 11 source positions for a total of 176 images per finger. The data was processed using a fast Fourier transformation, obtaining values for the amplitude, phase and the DC components for all source positions. An example of the 2D distribution of the mean values for amplitude and phase for a healthy PIP subject can be seen in Figure 1. From the 2D images, a linear mean value of the amplitudes and phases along the length of the finger was calculated. An example of the amplitude behaviors from healthy joints and SLE joints are shown in Figure 2.

The maximum values of the signal amplitudes in healthy volunteers is considerably higher (4462 ± 2638) than in SLE patients (2003 ± 1069). An ANOVA analysis (using MATLAB embedded function anova1) shows that these differences are statistically significant between healthy and SLE patients (p value < 3.6e-11), as shown in Figure 3.

From the ROC curve analysis, the best cut-off plane holds a sensitivity of 100% and a specificity of 80% to distinguish between joints of Healthy volunteers and SLE patients, with an area under the curve (AUC) of 0.9.

Conclusion: FDOT can differentiate healthy joints from those of SLE patients. We foundstatistically significant differences between the max signal amplitudes of the two groups. The ROC analysis showed high sensitivity and specificity. Further development of this technology is likely to improve the evaluation of SLE arthritis in clinical trials and practice.

Disclosure: A. Askanase, None; **F. Van Biema**, None; **A. Marone**, None; **Y. Kim**, None; **T. Chen**, None; **T. Kapoor**, None; **L. Geraldino**, None; **Y. Gartshteyn**, None; **A. Hielscher**, None.

Abstract Number: 1186

How Accurate Is Physical Joint Inflammation of the MTP-joints and What Can We Learn from Additional MRI on Forefoot Involvement in Early Arthritis?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Magnetic resonance imaging (MRI) is more sensitive than physical examination in detecting inflammation. This has predominantly been studied in metacarpophalangeal-(MCP) and wrist-joints. Data on the

concordance and discordance of physical examination (PE) and MRI-detected inflammation of metatarsophalangeal-(MTP)joints is scarce, which is surprising as physical examination of these joints is challenging.We aimed to study the concordance and discordance of arthritis upon PE with MRI-detected inflammation of MTP-joints. Analyses on MCP-joints were included for comparison.

Methods: 1764 MTP(2-5)-joints and 1764 MCP(2-5)-joints of 441 consecutive patients presenting with early inflammatory arthritis (36% RA, 64% other inflammatory arthritides) underwent PE of joint swelling by two independent readers, and 1.5T contrast-enhanced MRI of unilateral MTP- and MCP-joints. MRI-detected synovitis and bone marrow oedema were scored according to the RA MRI score (RAMRIS), and tenosynovitis according to Haavardsholm by two experienced readers. For a joint to be classified as PE+ swelling had to be observed by both assessors. MRI-positivity required the presence of the same MRI-inflammatory feature on joint level that was scored by both readers≥1. MRIs were further studied by two other, independent observers among whom an experienced musculoskeletal radiologist by consensus reading, to investigate the presence of contrast-enhancement of the soft tissues that was not scored according to RAMRIS guidelines. Analyses were done on joint level, joints were grouped as PE+MRI+, PE–MRI–, PE+MRI– and PE–MRI+.

Results: Physical examination of joints and MRI were concordant in 79% of MTP-joints (4% PE+MRI+, 74% PE–MRI–). For the MCP-joints this was 71% (15% and 53% respectively). Next discordance was studied. Subclinical joint inflammation (PE–MRI+) was present in 17% of MTP-joints. This was less frequent than in MCP-joints, where subclinical inflammation was present in 29% joints. Discordance in the opposite direction (PE+MRI–) was present in 5% of all MTP-joints (this was 55% of all PE+ MTPs). PE+MRI- occured less frequent at MCP-joints (3% of all MCPs were PE+MRI, which is 15% of the PE+ MCPs). Subsequently, MRI-detected contrast-enhancement of the soft tissues were studied to see if they could form an explanation for the felt arthritis. Of the PE+MRI- MTP-joints, 43% showed contrast-enhancement of the soft tissues, while in PE-MRI- joints this was 22%. Finally, to better understand this contrast-enhancement, its' frequency was compared between RA and other inflammatory arthritides, And was 53% vs. 22% respectively (OR 4.1, 95% CI 3.3-5.0).

Conclusion: Joint examination and MRI were mostly concordant in MTP- and MCP-joints. In MTP-joints MRI-detected subclinical joint inflammation occured in 14% of joints, which was less frequent than the MCP-joints where this was 27%. Clinical joint swelling without MRI-detected joint inflammation according to RAMRIS occured more in the MTPs and was in part caused by contrast-enhancement of soft tissues; this was more frequent in RA suggesting it to be inflammatory in nature. Further detailed imaging studies are needed to further characterize its' nature

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Abstract Number: 1187

Delayed Gadolinium-enhanced MR Imaging of Cartilage - A Pilot Study to Measure the Effect of Adalimumab Plus MTX versus Placebo Plus MTX on Cartilage in Early RA Patients (CAR-ERA-Study)

Philipp Sewerin,[1] Miriam Frenken,[2] Ralph Brinks,[3] Christoph Schleich,[2] Daniel Benjamin Abrar,[2] Stefan Vordenbaeumen,[4] Ruben Sengewein,[5] Jutta Richter,[6] Matthias Schneider,[7] and Benedikt Ostendorf[4], [1]Department of Rheumatology & Hiller Research Unit, University Hospital Düsseldorf,, Duesseldorf, Germany, [2]Institute for Diagnostic and Interventional Radiology, UKD, Heinrich Heine University, Duesseldorf, Germany, [3]Policlinic for Rheumatology & Hiller Research Centre for Rheumatology, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany, [4]Policlinic and Hiller Research Unit of Rheumatology, UKD, Heinrich Heine University, Duesseldorf, Germany, [5]Policlinic and Hiller Research Unit of Rheumatology,, Duesseldorf, Germany, [6]Department and Hiller Research Unit of Rheumatology, Heinrich-Heine University Duesseldorf, Duesseldorf, Nordrhein-Westfalen, Germany, [7]Policlinic for Rheumatology & Hiller Research Centre for Rheumatology, Heinrich-Heine-University Duesseldorf, Düsseldorf, Germany

SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: The purpose of this longitudinal study is to compare the effect of Adalimumab plus Methotrexate (MTX) versus MTX monotherapy on glycosaminoglycan content (GAG) in cartilage in patients with early rheumatoid arthritis (eRA) who have not received a disease-modifying antirheumatic drug (DMARD) or biological treatment using biochemical gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC).

Methods: Cartilage integrity of finger joints and the wrist of the clinically dominant hand of 14 patients with eRA who met the ACR/EULAR classification criteria were evaluated at baseline prior to any DMARD or biological therapy and 12 and 24 weeks after Adalimumab plus MTX therapy (10 patients, 6 females, mean age 44.9 years, range: 19-65 years) or placebo plus MTX therapy (4 patients, 2 female, mean age 46.7 years, range: 24-64 years). In this prospective double-blind study, patients were randomly assigned to both groups. dGEMRIC of MCP joints of the index and middle as well as OMERACT RAMRI scores, including synovitis, edema, and erosion subscores were registered at all timepoints.

Results: The Adalimumab + MTX therapy group showed a trend to higher dGEMRIC indices of the second and third MCP joints compared to the placebo + MTX therapy group between baseline and 24-week follow-up (ADA+MTX: dGEMRIC mean change 85.8, range -156.2 – 346.5; Placebo+MTX: dGEMRIC mean change -30.75, range -273.0 – 131.0; p = 0.37). Furthermore, there has been an improvement between baseline and 24-week follow-up in RAMRI score for the total RAMRI score (ADA+MTX: mean change -5.6, range -17 – 4; Placebo+MTX: mean change -1.25, range -6 – 6). RAMRI score for synovitis improved for most patients under therapy (ADA+MTX: 70%; Placebo+MTX: 75%). RAMRI score for edema improved for some patients (ADA+MTX: 50%; Placebo+MTX: 25%). RAMRI score for erosion has remained almost unchanged (improvement ADA+MTX: 0%; Placebo+MTX: 25%).

Conclusion: In patients with eRA, Adalimumab therapy showed a trend towards biochemical cartilage improvement after 24 weeks therapy. One possible explanation is a reduction of inflammation at the level of the MCP joint by Adalimumab. These results support the concept of early treatment for RA to stop and even reverse cartilage damage in inflamed joints. Furthermore, dGEMRIC appears to be an important tool for the early detection of molecular cartilage damage in RA.

Disclosure: P. Sewerin, AbbVie, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Celgene, 2, 5, 8, Chugai, 2, 5, 8, Hexal, 5, 8, Janssen-Cilag, 2, 5, 8, Lilly, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, Sanofi-Genzyme, 5, 8, Swedish Orphan Biovitrum, 5, 8, UCB, 2, 5, 8; **M. Frenken**, None; **R. Brinks**, None; **C. Schleich**, None; **D. Abrar**, None; **S. Vordenbaeumen**, None; **R. Sengewein**, None; **J. Richter**, None; **M. Schneider**, None; **B. Ostendorf**, None.

Abstract Number: 1188

Novel PET-Coronary Flow Reserve Imaging to Assess for Coronary Microvascular Dysfunction in Systemic Lupus Erythematosus Compared to Subjects with Diabetes Mellitus and Controls

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging Of Rheumatic Diseases Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: High risk of premature cardiovascular disease (CVD) among SLE patients is well documented, but the best means to detect the earliest stages of CVD in SLE are not known. Coronary microvascular dysfunction is thought to be one of the earliest detectable abnormalities and can be detected by measuring coronary flow reserve (CFR) with positron emission tomography (PET) scanning. PET-CFR is an emerging prognostic imaging technique used to detect increased CVD risk including death in non-SLE populations, even among those without overt obstructive coronary artery disease. We aimed to measure coronary microvascular function by CFR in active SLE patients and to compare findings to those of patients with diabetes mellitus (DM) and non-SLE, non-DM controls.

Methods: We identified SLE patients with active disease (SLE disease activity index > 6), internal organ involvement and no history of known coronary artery disease, followed at the Brigham and Women's Hospital Lupus Center. Premenopausal women and similar aged female controls without SLE or DM were enrolled as comparisons. Demographic and clinical data were collected. All subjects underwent rest and then stress myocardial perfusion PET scans, from which we measured regional and global left ventricular myocardial blood flow (in mL/min/g of tissue) and calculated the CFR as the ratio of myocardial blood flow during stress to that at rest. We used t-tests and Chi-squared tests to compare subject demographic characteristics, and ANOVA tests to compare mean global myocardial blood flow and CFR values between SLE, DM and control subjects.

Results: We studied 8 SLE, 12 DM and 6 control female subjects, all with normal PET scans indicating no evidence of obstructive CAD. Demographics are shown in Table 1. All SLE subjects were anti-dsDNA positive, 5/8 had lupus nephritis, and their mean SLEDAI score was 10 (SD 4.5) (Table 1). Rest myocardial blood flow was comparable across the three groups. Adenosine-stimulated myocardial blood flow was similar in SLE and pre-menopausal diabetic women (2.64 ± 0.52), but 21% lower in SLE patients than in controls (2.44 ± 0.28 vs. 3.09 ± 0.32 mL/min/g, $p < 0.05$) (Table 2). Although SLE patients were younger than the pre-menopausal DM women, they showed similar reduction in global CFR (Figure 1). Compared to controls, subjects with active SLE had a 22% reduction in global CFR (2.84 ± 0.41 vs 3.63 ± 0.96, $p < 0.05$).

Conclusion: Subjects with active SLE had a significant reduction in coronary microvascular function compared to non-diabetes, non-SLE controls. This reduction was similar to that observed in slightly older premenopausal women

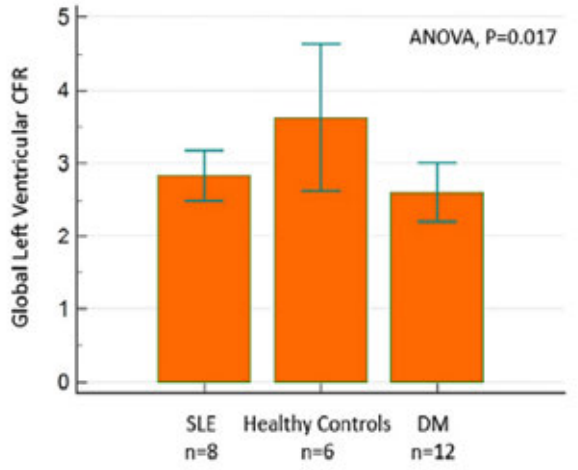
Table 1. Subject Characteristics: SLE, Diabetes Mellitus (DM), and Non-SLE, Non-DM Controls undergoing PET-Coronary Flow Reserve (CFR) Imaging

	SLE n=8	Diabetes Mellitus (DM) n=12	p*	Controls n=6	p**
Baseline age, years, mean (SD)	29 (4.6)	41 (10.7)	0.01	33 (6.4)	0.02
Female, n (%)	8 (100)	12 (100)		6 (100)	
White, n (%)	2 (25)	12 (100)		6 (100)	
Non-white, n (%)	6 (75)	-		-	
ACR criteria for SLE, mean (SD)	5.3 (1.7)	-		-	
SLEDAI score, mean (SD)	10 (4.5)	-		-	
SLE Duration, years, median (IQR)	1.5 (0.3, 4.6)	-		-	
Anti-dsDNA positive, n (%)	8 (100)	-		-	
Lupus Nephritis, n (%)	5 (62.5)	-		-	
Receiving immunosuppressant, n (%)	7 (87.5)	-		-	
Receiving anti-hypertensive, n (%)	5 (62.5)	-		-	
Receiving prednisone, n (%)	4 (50)	-		-	
Prednisone dose, mg/d, mean (SD)***	26.5 (10.8)	-		-	

* comparing SLE and DM, ** comparing SLE and Controls, ***among the 4 subjects receiving prednisone

Table 2. Coronary Flow Reserve (CFR) Measures of the SLE, Diabetes mellitus (DM) and Non-SLE, Non-DM Control Subjects by PET-CFR				
	SLE n=8	Diabetes Mellitus (DM) n= 12	Controls n=6	p*
Rest MBF LV, mean (SD)	0.87 (0.13)	1.01 (0.13)	0.89 (0.17)	0.06
Stress MBF LV, mean (SD)	2.44 (0.28)	2.64 (0.52)	3.09 (0.32)	0.03
CFR LV, mean (SD)	2.84 (0.41)	2.60 (0.62)	3.63 (0.96)	0.02
* ANOVA test of the differences in the means				

Figure 1. Mean Coronary Flow Reserve (CFR) in SLE compared to subjects with Diabetes mellitus and Non-SLE, Non-DM Controls



with diabetes mellitus. These preliminary findings suggest that coronary microvascular dysfunction, likely driven by inflammation in active SLE, may be an early marker of CVD risk among SLE patients, as it is in DM patients. Although studies are needed, PET-CFR may prove to be a useful tool for stratifying SLE patients in terms of their risks of CVD events and death.

We thank the John J. Holland and Virginia M. Bruen Fund for Systemic Lupus Erythematosus Research for supporting this study.

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Abstract Number: 1189

Baylor Rheumatology Initiative: Developing and Guiding Engagement (BRIDGE) Transition Pathway Creation and Implementation

Priyanka Moolchandani,[1] Cristina Saez,[1] Marietta DeGuzman,[1] Eyal Muscal,[1] Andrea Ramirez,[1] Anna Carmela Sagcal-Gironella,[1] Saimun Singla,[1] Amanda Brown,[1] Monica Marcus,[1] Martha Curry,[1] Maria Pereira,[1] M. Brad Nelson,[1] Pooja Patel,[1] W. Blaine Lapin,[1] Jennifer Rammel,[1] LeeGee Huang,[2] Blanca Sanchez-Fournier,[2] JaLeen Rogers,[2] Ariel Washington,[2] Anne Dykes,[2] Miriah Gillispie-Taylor,[1] and Tiphanie Vogel[1], [1]Baylor College of Medicine, Houston, TX, [2]Texas Children's Hospital, Houston, TX

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Measures Of Healthcare Quality Poster II: Improving Care
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Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with pediatric rheumatologic diseases live well into adulthood, necessitating transition from pediatric to adult medical providers. GotTransition.org details 6 core elements clinicians can implement to create effective transition: policy, registry, readiness, planning, transfer and completion.

Methods: The core elements were used to design a transition pathway. A transition policy was created, and a patient registry constructed. Provider-led education on readiness and planning were structured during clinic visits using an electronic medical record-based tool. Patient self-reported transition readiness was assessed with a patient-administered survey, the ADAPT (Adolescent Assessment of Preparation for Transition). All rheumatology providers gave input through monthly transition meetings. Provider participation was encouraged through Maintenance of Certification points.

Results: The transition policy was acknowledged and signed by 33 patients during a pilot release. 481 return patients age 14-19 years were identified by review of clinic schedules and added to the transition registry. ADAPT surveys were completed by 101 patients. Most respondents were 15-18 years of age (79%), female (70%), and Caucasian (77%); 41% were Hispanic. 28% had juvenile arthritis and 18% had lupus. Most patients had private insurance (59%) or Medicaid/Children's Health Insurance Program (36%). Not unexpectedly, ADAPT scores increased with age, and older adolescents (18-19 years) achieved the highest averages: counseling in transition self-management (58/100) and prescription medications (93/100), and in transfer planning (33/100). All patients had scores >50/100 for medications. There was no significant difference in survey results with respect to diagnosis or age at diagnosis. Since the project began, 25 high-risk patients, average age 19.4 years, have transferred into an on-site transition clinic. Transitioned patients attended their first adult appointment an average of 3.2 months from their last pediatric appointment, and only 11% required hospitalization within the first year after transition.

Conclusion: Effective healthcare transitions are critical to the wellbeing of patients with childhood-onset rheumatologic conditions. The creation of a transition pathway in rheumatology clinic has been well received by patients and providers. We have demonstrated good scores for counseling in medications and identified a need to improve self-management and planning counseling. Future directions will include 1) formalizing the final 2 elements of the pathway for all transitioning patients, including standardizing a transition letter to the adult rheumatology provider, and 2) further assessing outcomes. Our ultimate goal is to create a sustainable and successful BRIDGE between pediatric and adult rheumatology care.

Disclosure: P. Moolchandani, None; **C. Saez**, None; **M. DeGuzman**, None; **E. Muscal**, None; **A. Ramirez**, None; **A. Sagcal-Gironella**, None; **S. Singla**, None; **A. Brown**, None; **M. Marcus**, None; **M. Curry**, None; **M. Pereira**, None; **M. Nelson**, None; **P. Patel**, None; **W. Lapin**, None; **J. Rammel**, None; **L. Huang**, None; **B. Sanchez-Fournier**, None; **J. Rogers**, None; **A. Washington**, None; **A. Dykes**, None; **M. Gillispie-Taylor**, None; **T. Vogel**, None.

Abstract Number: 1190

A Quality Improvement Project to Increase Documentation Efficiency in an Academic Rheumatology Practice

David Leverenz,[1] Jon Golenbiewski,[1] Brian Andonian,[1] Katherine Kaufman,[1] Philip Chu,[1] Mithunan Maheswaranathan,[1] Andrew Johannemann,[1] Jayanth Doss,[2] and Lisa Criscione-Schreiber[2], [1]Duke University, Durham, NC, [2]Duke University, Durham

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Background/Purpose: All providers, including rheumatologists, spend approximately half of their day documenting in an electronic health record (EHR). Excessive documentation is a key contributor to burnout, which is associated with reduced quality of care and poor patient satisfaction. We performed a quality improvement project to increase documentation efficiency in an academic rheumatology practice.

Methods: We used Signal, an Epic analytic data tool, to obtain documentation performance metrics. Our primary aim was to reduce average "time in notes per appointment" from over 10 min to 8 min (Epic's nationwide rheumatology average). Secondary measures included average time in the EHR from 7pm-7am and note composition metrics. To assess need and impact, we distributed a pre and post-survey to providers in our practice regarding their documentation practices, satisfaction with documentation time, and engagement with interventions. Using Plan-Do-Study-Act (PDSA) methodology, we conducted these cycles: (1) dictation training, (2) a presentation on recommendations to increase efficiency, and (3) optional individual training sessions with EHR experts. Signal data was recorded weekly except for 7pm-7am time, which was recorded monthly. Data is analyzed using descriptive statistics.

Results: Average "time in notes per appointment" was 11.4 min at baseline, 12 min after PDSA1, 11 min after PDSA2, and 11 min after PDSA3 (Figure 1). Average time in the EHR from 7pm-7am was 33.3 min at baseline vs. 29

Figure 1: Time in Notes per Appointment

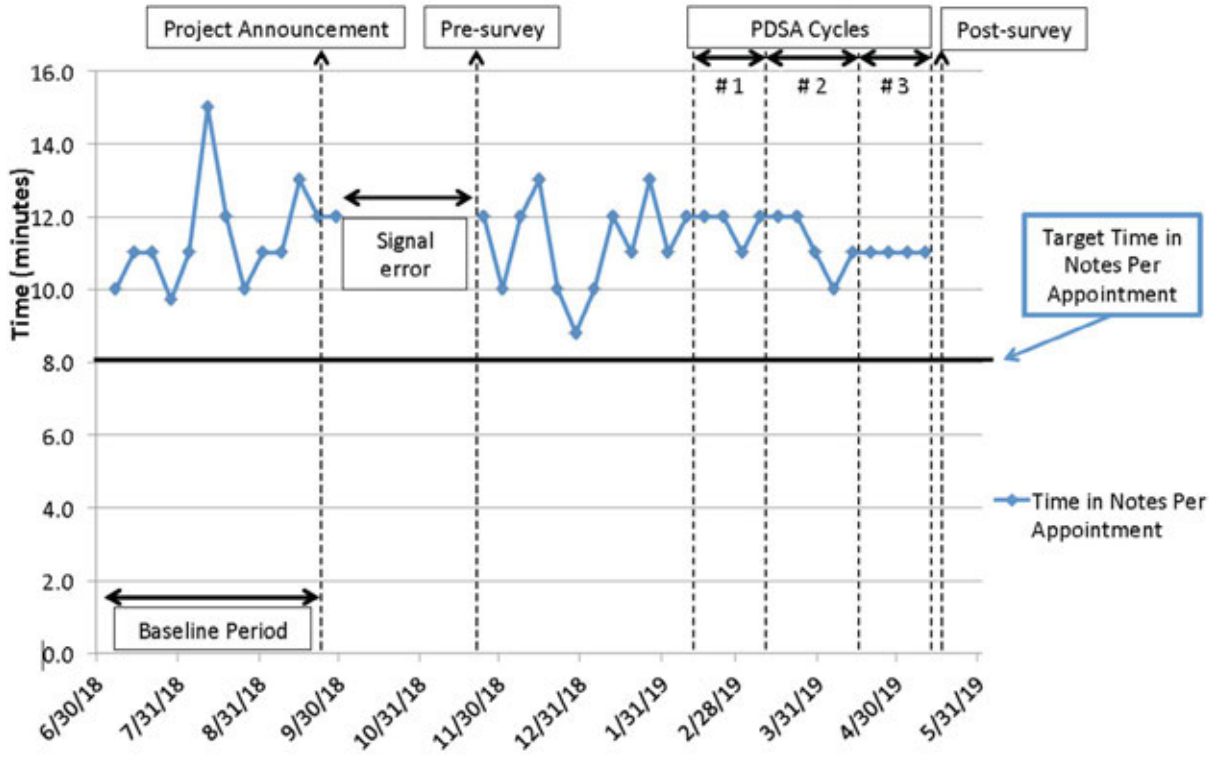
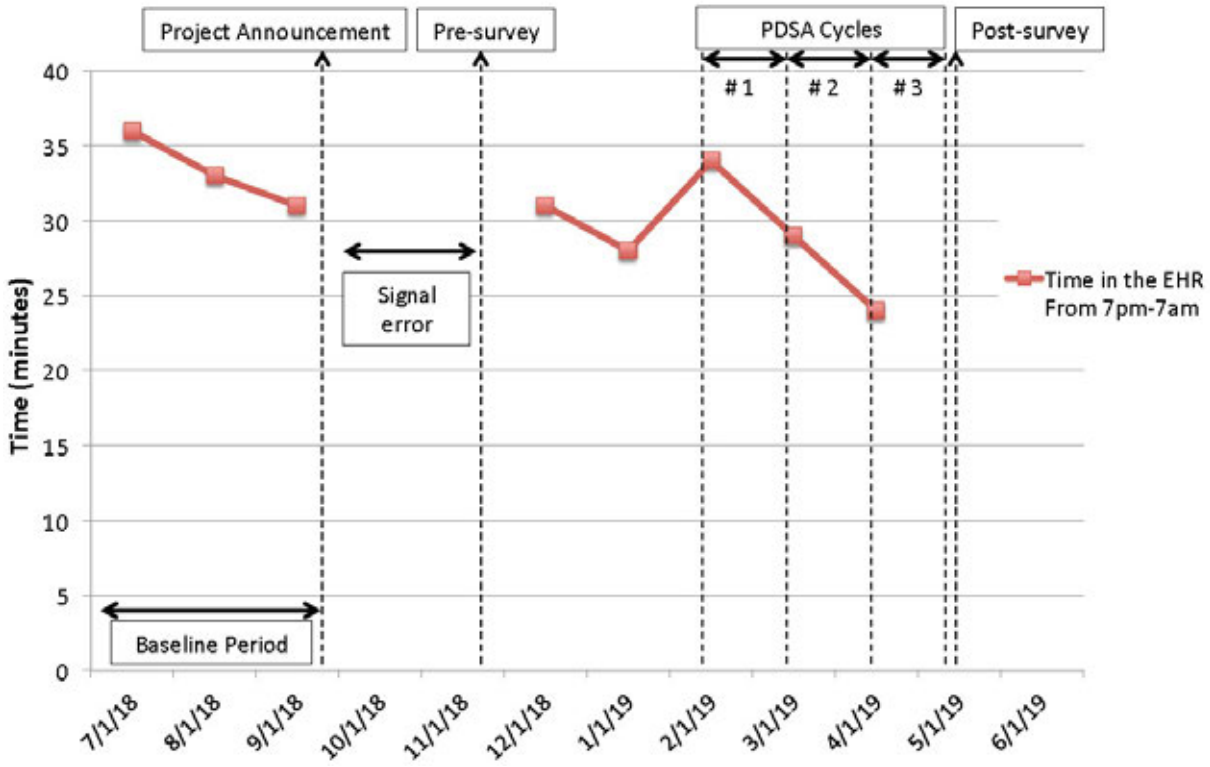
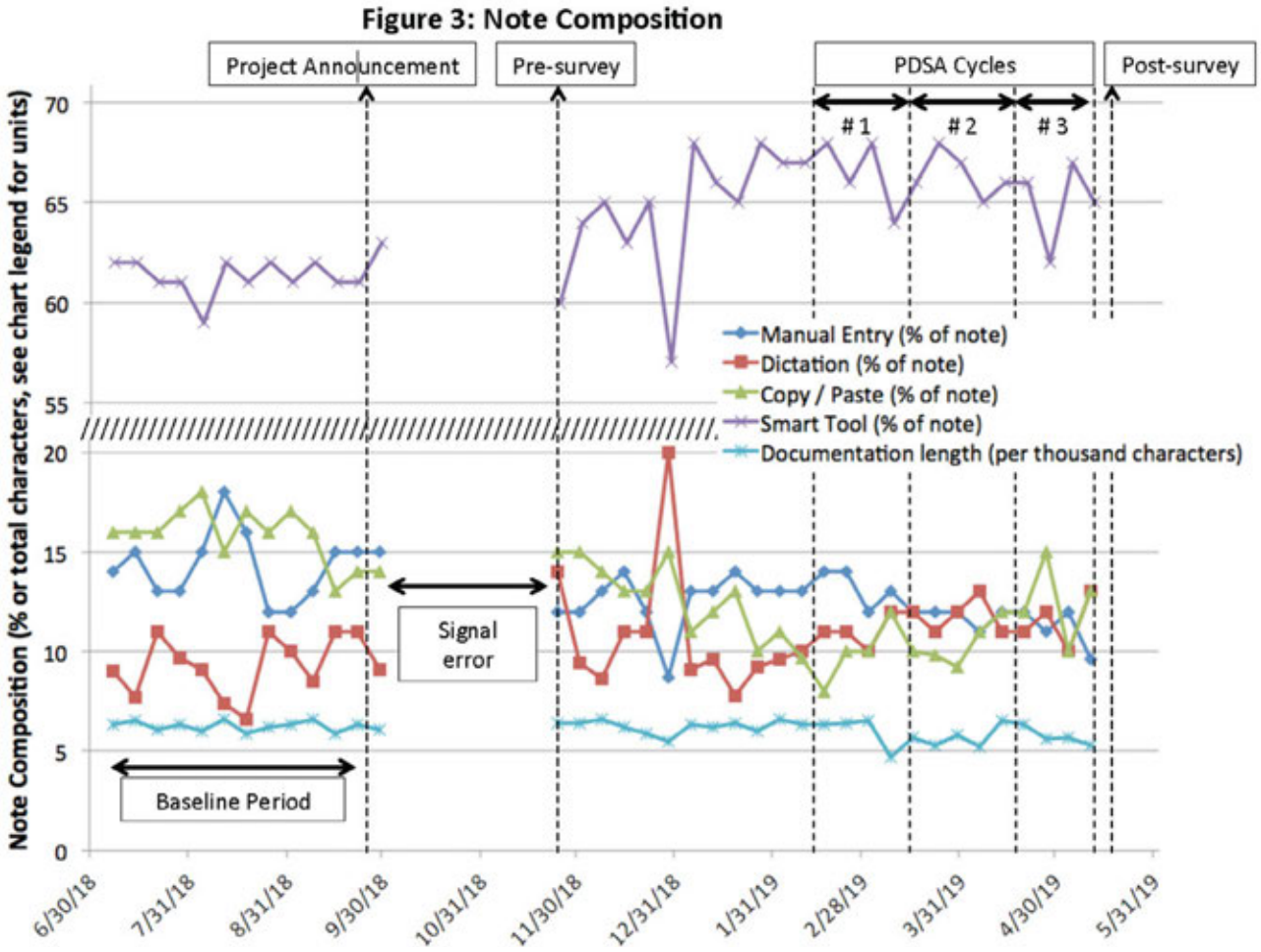


Figure 2: Time in the EHR From 7pm to 7am



min after PDSA1 and 24 min after PDSA2, data pending from PDSA3 (Figure 2). Average note composition percentages at baseline vs. after PDSA1, 2, and 3 were: manual entry 14.3 vs. 12, 12, and 9.6%; dictation 9.3 vs. 12, 11, and 13%; copy/paste 15.9 vs. 10, 12, and 13%; smart tool 61.3 vs. 66, 66, and 65%. Average documentation length was 6.25K characters at baseline vs. 5.7K, 6.5K and 5.3K (Figure 3). Twenty-five of 27 (93%) providers responded to both the pre and post-surveys. Satisfaction with documentation time on the pre- vs. post-survey was: "completely" or "very dissatisfied" 44% vs. 32%; "dissatisfied" 40% vs. 40%; and "satisfied" 16% vs. 28%. Respondents wrote notes from home "often" or "almost always" in 60% vs. 37.5%. Missing out on activities outside of work in order to finish notes occurred "often" or "almost always" for 24% vs. 12.5%. Regarding engagement with interventions, 32% of post-survey respondents reported newly using dictation software, 36% increased their use of dictation, and 52% modified note templates.

Conclusion: Though we did not meet our aim of reducing average time in notes per appointment, interventions led to providers using more dictation and smart tools with a corresponding reduction in manual data entry. Perhaps most importantly, both Signal and survey data suggested that providers spent less time in the EHR at home after our interventions; the percentage reporting missing out on activities outside work to document dropped by half. Practice-wide focus on improving documentation efficiency led to improved satisfaction with the documentation process and enabled providers to enjoy more activities outside of work. Future measurement targets may include care quality and burnout metrics.



Disclosure: D. Leverenz, None; **J. Golenbiewski**, None; **B. Andonian**, None; **K. Kaufman**, None; **P. Chu**, None; **M. Maheswaranathan**, None; **A. Johannemann**, None; **J. Doss**, None; **L. Criscione-Schreiber**, None.

Abstract Number: 1191

Application of the Systemic Lupus Erythematosus (SLE) Quality Indicators in Patients Attending a Young Adult Transition Program

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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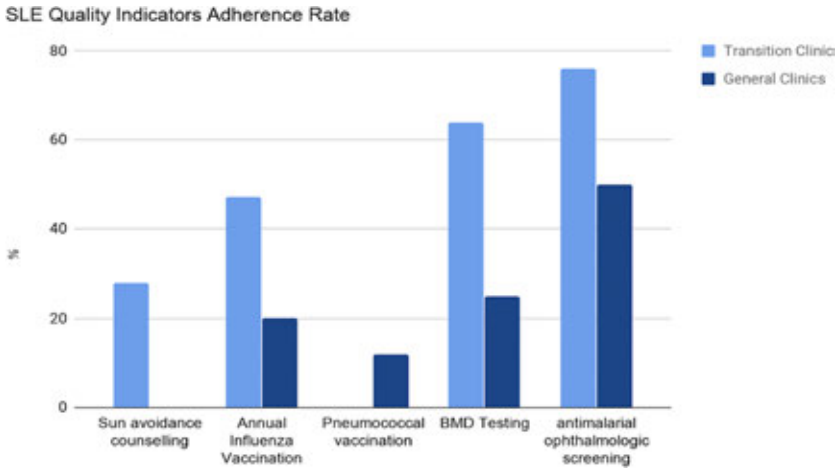

Background/Purpose: Systemic lupus erythematosus is a multisystemic rheumatic disease affecting 1 in 1000 individuals with a 10:1 female predominance. Childhood-onset SLE (CSLE) constitutes approximately 15% of all SLE diagnoses and, when compared to adult-onset disease, CSLE is typically more severe with increased disease and treatment-associated morbidity and mortality. While long term survival of patients with SLE has improved significantly in recent decades morbidity from the disease, itself and its treatment remains an ongoing challenge. Quality indicators (QIs) for SLE have been proposed for adult-onset disease, focused on health maintenance and management of disease- and treatment-related morbidity. These, in turn, may serve as proximate surrogates for longer-term SLE-associated outcomes. The literature reveals that these are performed suboptimally in virtually every clinical setting studied, citing time constraints, forgetfulness, and more pressing issues to address. In efforts to ascertain whether the optimal quality of care is being delivered to these at-risk cSLE patients, and with a view to tailoring Quality Improvement interventions that would be most impactful, we measured the consistency with which five SLE Qis were applied in a young adult transition cohort compared to routine care.

Methods: A comprehensive chart review of all patients attending a young adult SLE transition clinic at a single, tertiary care site was conducted. The three most recent visits were reviewed. Binary data were abstracted from each chart to determine whether there was documentation of sun avoidance counseling, annual influenza vaccine counseling, bone health screening, and anti-malarial-associated ophthalmologic screening, over the visits abstracted. The data were then compared with patients attending the clinics of the two physicians who see the majority of lupus patients at the same institution. Suboptimal adherence was defined as less than 80% in any of the five quality indicators and a difference of < 35% was treated as comparable between the two groups.

Results: A total of 16/57 (28%) patients were counseled regarding sun avoidance. Out of 32 patients on immunosuppressive therapy; 15 (47%) had annual influenza vaccine counseling and none (0/32) received pneumococcal vaccination. Of patients at risk of osteoporosis; 64% underwent BMD testing. Among patients receiving antimalarials; 43/56 (76%) had their eye exam up to date. The comparator group had a comparable rate in sun avoidance counseling (0%), pneumococcal vaccine (12%) and HCQ-associated eye screening (50%) and worse in annual influenza vaccine (20%) and osteoporosis screening (25%).

Conclusion: The Young Adult Transition Program is adhering suboptimally to the five reviewed QIs, as has been demonstrated in studies at other institutions. Efforts to improve uptake of these QIs will be undertaken, with Quality Improvement interventions driven by the results of a root cause analysis for each QI.

Disclosure: A. Aboabat, None; **E. Silverman**, None; **A. Steiman**, None.

Abstract Number: 1192

Effect of a Clinical Decision Support System on a Quality Indicator of Glucocorticoid-induced Osteoporosis and Trends of Drug Treatment in a Japanese Hospital

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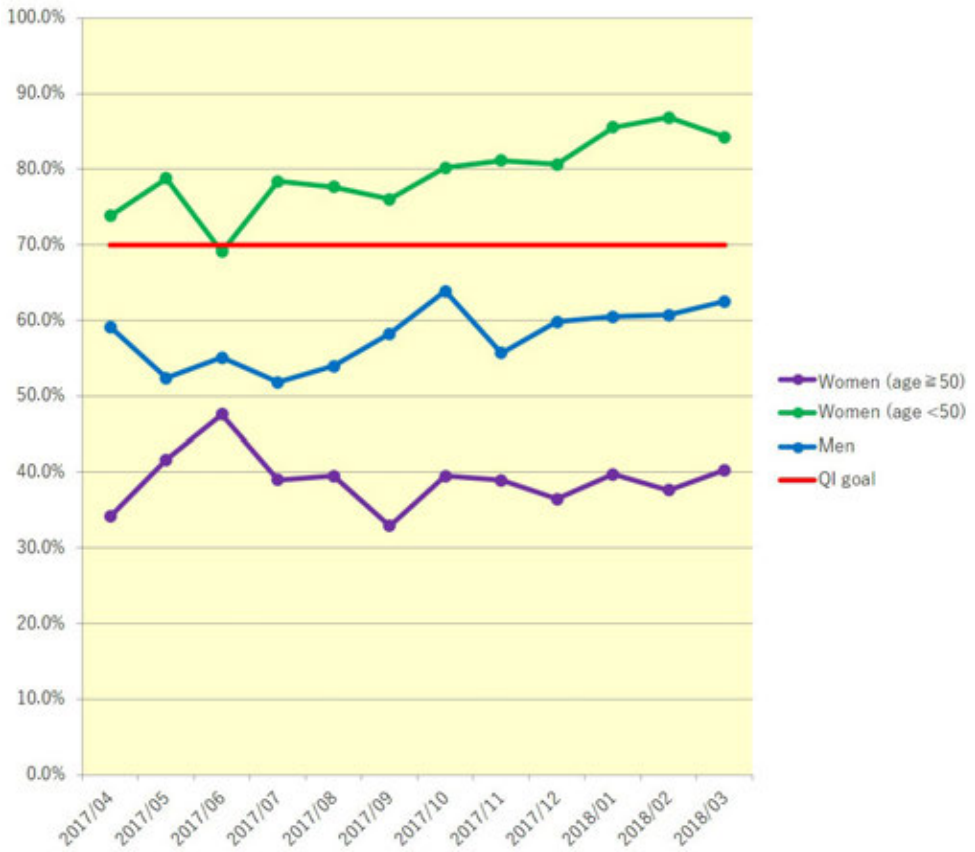

Figure 1. QI trends in each group

Background/Purpose: Glucocorticoid-induced osteoporosis (GIOP) is a common, preventable and treatable complication of glucocorticoid therapy. We defined quality indicator (QI) for GIOP and took a hospital-wide systematic approach with QI monitoring to improve real-world GIOP care. However, there was still room for improvement. Then, we introduced a clinical decision support system (CDSS) in our electronic health record (EHR) to increase the prescription rate of anti-osteoporotic drugs.

Methods: We defined a QI for GIOP care for the prescription rate of anti-osteoporotic drugs according to 2010 American College of Rheumatology GIOP management recommendations, with the target being patients prescribed ≥7.5 mg prednisolone daily or its equivalent for ≥3 months. We monitored the glucocorticoid and anti-osteoporotic medication dose for all patients who visited our hospital, since May 2011. In October 2017, we introduced CDSS to EHR in Immuno-Rheumatology Center (IRC) in our hospital. CDSS were developed as a guide for clinicians to prescribe anti-osteoporotic drugs appropriately. CDSS were designed to appear as a box in a display on the date of target patients' visit, if they have not been prescribed anti-osteoporotic drugs. Clinicians can choose to prescribe the drugs or not. If they didn't prescribe the drugs, they were urged to choose the reasons and such cases were excluded from QI monitoring. We retrospectively analyzed QI trends for 6 months before and after the induction of the CDSS in 2017-2018.

Results: The total number of participants was 3072, 1573 in 6 months before and 1499 after the induction of the CDSS, with pooled QI rates of 57.9% and 61.6%. The number of participants from IRC was 1815(59.0%). Changes in QI improvements between the periods are statistically significant. In subanalysis, the prescription rate for women who were younger than 50 years old and men showed an increasing trend(Fig 1).

Conclusion: CDSS that guide clinicians to prescribe anti-osteoporotic drugs improved QI of GIOP. In addition, changes of rheumatologists' prescription contributed to the improvement of QI in the whole of our hospital.

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Abstract Number: 1193

EMR-integrated Disease Activity Calculators Improve Treatment to Target in Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Undertreatment of RA can lead to cumulative joint damage as well as negatively impact emotional health. Recent evidence favors a treat-to-target strategy to achieve remission or low disease activity (DA) using objective scores such as the clinical disease activity index (CDAI) or the DAS28. We hypothesized that integration of CDAI and DAS28 calculators into electronic medical records (EMR) would improve treatment to target.

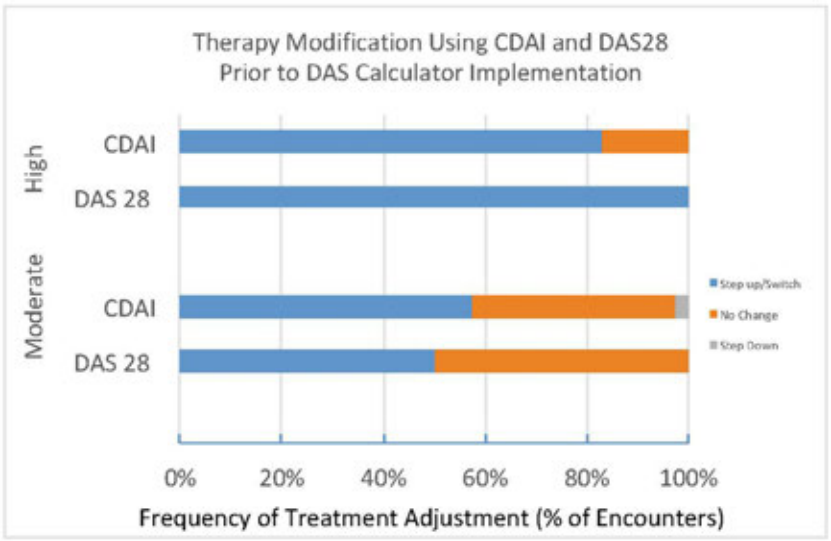

Figure 1. modification of RA treatment to target prior to implementation of EMR DAS calculators.

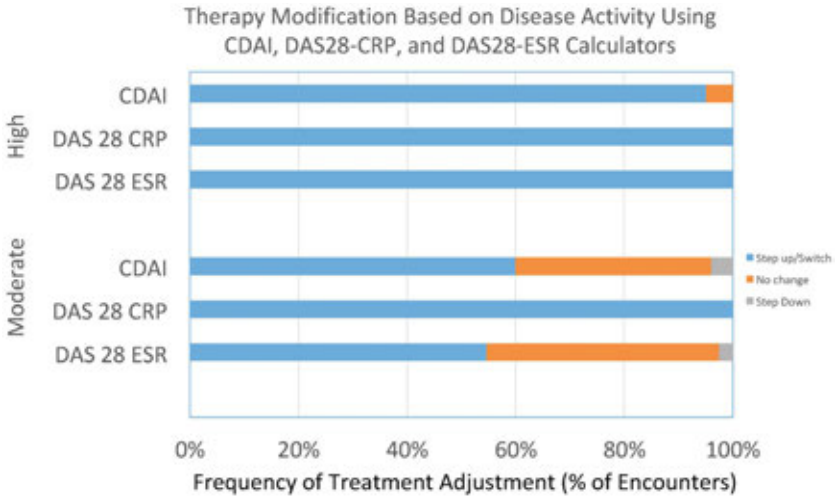

Figure 2. modification of RA treatment to target after implementation of EMR-based CDAI and DAS28 calculators.

Methods: We performed a retrospective chart review of all RA patients in our academic rheumatology clinic who had a documented DA score, comparing treatment practices for 18 months before and after calculator implementation (March 2015). We identified patients using ICD-9 and ICD-10 codes for RA. Before implementation, we used natural language processing to search note text for CDAI, DAS, DAS28, DAS 28, and "disease activity score." After implementation, we searched for results of DAS28-ESR, DAS28-CRP, and CDAI calculators in patient charts. We analyzed charts for a step-up/switch (addition or increase in dose of steroid or addition, dose increase, or change of synthetic or biologic DMARD), no change, or step down in therapy in response to the first moderate or high score for each patient.

Results: Prior to incorporation of DA calculators in the EMR, out of 732 patients, 14% had at least one recorded CDAI and 4% had at least one DAS28, respectively. After implementation, out of 895 patients, 23% , 2.6%, and

17% had at least one recorded CDAI, DAS28-CRP, and DAS28-ESR, respectively. Both before and after calculator implementation, therapy was intensified the majority of the time in patients with moderate (50-60%) or high activity (80-100%) (see figures 1 and 2).

Conclusion: As expected, implementation of EMR-integrated DA calculators greatly improved DA score documentation. However, even after calculator integration in our EMR, scores were recorded < 25% of the time, with CDAI being the most commonly used measure. For patients in whom DA calculators are used, providers in our clinic adjusted therapy in response to DA level about 50-60% of the time after a moderate DAS and about 90% of the time after a high DA score, suggesting that they are following the treat-to-target recommendations. Targeted education to increase provider use of existing DA calculators may thus lead to improved patient outcomes. We plan to systematically examine charts to understand why there was no change or a step down in therapy in patients with moderate or high DA. Future studies include examining the time to initiation of biologic therapy in newly diagnosed RA patients before and after implementation of EMR DA calculators to assess impact on prescribing practices.

Disclosure: G. Barbera, None; **J. Kahlon**, None; **M. Patel**, None; **S. Pompa**, None; **A. Jayatilleke**, None.

Abstract Number: 1194

Can an MDHAQ (Multidimensional Health Assessment Questionnaire) 60-Symptom Checklist to Monitor Early Medication Outcomes (MDHAQ/MEMO60) Detect Adverse Events of High-Risk Medications?

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Background/Purpose: Adverse events of medications have been reported to account for 5% of hospital admissions in the US, and as many as 10% in the elderly. Strategies for vigilance for adverse events are actively promoted by physicians, pharmacies, pharmacists, and pharmaceutical companies. Some adverse events are relatively obvious, such as a severe rash or severely abnormal laboratory test. However, many adverse events are common symptoms, such as fatigue, headache, anxiety, which might not be recognized as adverse events until present over long periods, particularly in elderly individuals who have one or more chronic conditions. An MDHAQ (multidimensional health assessment questionnaire) has been found to be useful in all rheumatic diseases studied[1]. The MDHAQ includes a 60-symptom checklist that can be used to monitor adverse events. We analyzed a hypothesis that a 60-symptom checklist to monitor early medication outcomes (MDHAQ/MEMO60) could be useful to recognize adverse events in patients who are treated with RA medications.

Methods: At one academic rheumatology site, all patients complete an MDHAQ at all visits prior to seeing the rheumatologist to add to quality of care. The 2-page MDHAQ includes 0-10 scales for physical function + pain + patient global VAS, compiled into a continuous 0-30 RAPID3 (routine assessment of patient index data), to depict

Symptom listed on MDHAQ/MEMO60	RA patients N=711 (100%)	Methotrexate	Leflunomide	HCQ	Etanercept	Infliximab	Adalimumab	Anakinra	Abatacept	Rituximab
Headache	251 (35%)	X		X		X	X	X	X	
Unusual fatigue	237(33%)	X		X		X				X
Anxiety-feeling nervous	179 (25%)			X						
Cough	132 (19%)		X				X		X	
Dizziness	127 (18%)	X		X					X	
Loss of hair	116 (16%)	X	X	X						
Nausea	95 (13 %)	X	X	X		X		X	X	X
Skin rash or hives	92 (13%)	X	X			X	X	X		X
Stomach pain/cramps	92 13%)	X	X	X		X		X	X	
Eye problems	92 (13%)	X		X						
Anorexia/weight loss	90 (13%)	X		X						
Diarrhea	63 (9%)	X	X	X	X			X		
Fever	55 (8%)	X			X	X				
Mouth sores	45 (6%)	X								X

Table. Number and percent of 711 patients with RA who self-reported specific symptoms on the MDHAQ/MEMO checklist at the first visit recorded in the electronic medical record.

clinical status. The MDHAQ also includes a 60-symptom checklist to recognize comorbidities, review of systems, and potential adverse events associated with medications. Completed paper versions of MDHAQ from routine care are scanned into an Epic electronic medical record (EMR) and copied into a data repository for retrospective analyses. A list of common adverse events of many specific DMARDs (disease-modifying antirheumatic drugs) and biological agents used to treat rheumatoid arthritis (RA) was compiled from websites of the FDA, pharmaceutical companies, and Up-to-date.® A retrospective review of scanned MDHAQs at the first visit were included in a database of ICD-code-identified RA patients. This database was analyzed to recognize symptoms self-reported on MDHAQ/MEMO60 which were listed as common adverse events for RA medications , using simple descriptive statistics.

Results: Among 711 RA patients identified at their first visit, 84% were females, mean age was 58.5 (15.2) years, 40% were White, 30% Black, 23% Latino, 7% "other." Among commonly-listed specific adverse events associated with RA medications, more than 30% of 711 patients reported headache and/or unusual fatigue (Table); 20-30% anxiety-feeling nervous; 10-20% cough, dizziness, hair loss, nausea, skin rash or hives, stomach pain or cramps, eye problems, and/or weight loss; and 5-10% diarrhea, fever, and/or mouth sores (Table).

Conclusion: MHDAQ/MEMO60 may prove valuable to detect adverse events of high-risk medications. A program involving completion of a weekly remote electronic MDHAQ at home for 12 weeks after initiation of a new medication may be a cost-effective approach for early recognition of efficacy and detection of adverse events.

Reference:

1. Castrejon I. Bull Hosp Jt Dis (2013). 2017;75(2):93-100.

Disclosure: S. Abu Mehsen, None; **I. Castrejon**, None; **T. Pincus**, Helath Services, 7, Medical History Services LLC, 6, 7, 9, Medical history services LLC, 6, 7.

Abstract Number: 1195

Quantitative Physician Global Assessment of Damage And/or Distress, in Addition to Inflammation, at Routine Rheumatology Care: Documenting the Complexity of Rheumatology Patient Encounters as a Rationale for Possible Higher Reimbursement?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Measures Of Healthcare Quality Poster II: Improving Care
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Background/Purpose: Quantitative clinical measures and indices such as DAS28, CDAI, SLEDAI, BASDAI, are designed to assess inflammation, reflecting a goal to prevent long-term damage, and are effective in patients selected for high activity in clinical trials. However, in rheumatology routine care, many patients have clinically important damage of joints and other organs and/or distress, as fibromyalgia, manifested by similar signs and symptoms to those seen in inflammation, i.e., functional disability, pain, fatigue, high patient global assessment and tender joint counts, but damage and distress are not recorded quantitatively. Patients with many non-rheumatic diseases, e.g., diabetes, also may have clinically important damage and/or distress, which is usually ignored unless presenting an acute problem, as signs and symptoms differ from the "gold-standard" biomarker (hemoglobin A1c) that is predominant in clinical decisions[1]. By contrast, rheumatology signs and symptoms of damage and/or distress may be similar to those of inflammation. The expertise of the rheumatologists may be viewed to recognize whether findings are primarily a result of inflammation, damage, and/or distress, and possibly 2 or 3 of these variables. This process involves greater complexity in the examination room than application of a gold-standard biomarker acquired (and reimbursed) elsewhere, and may provide a rationale for higher reimbursement, but is not recorded quantitatively. We examined a hypothesis that many routine care patients have findings of 2 or 3 components of inflammation, damage and/or distress to explain a physician global assessment (DOCGL).

Table. Physician ratings of VAS for inflammation, damage and distress in and % of DOCGL 567 patients and (% of total) seen in routine clinical care

INFLAMMATION %	INF 0-20%	INF 21-40%	INF 41-100%	%INF Total
VAS INF 0-2.0	309 (54%)	35 (6%)	48 (8%)	392 (69%)
VAS INF 2.1-4.0	10 (2%)	28 (5%)	73(13%)	111 (20%)
VAS INF 4.1-10.0	6 (1%)	9 (2%)	49 (9%)	64 (11%)
Total	325 (57%)	72 (13%)	170 (30%)	567
DAMAGE %	DAM 0-20%	DAM 21-40%	DAM 41-100%	% DAM Total
VAS DAM 0-2.0	164 (29%)	24 (4%)	44 (8%)	232 (41%)
VAS DAM 2.1-4.0	20 (4%)	39 (7%)	129 (23%)	188 (33%)
VAS DAM 4.1-10.0	10 (2%)	13 (3%)	124 (22%)	147 (26%)
Total	194 (34%)	76 (13%)	297 (52%)	567
DISTRESS %	STR 0-20%	STR 21-40%	STR 41-100%	% STR Total
VAS STR 0-2.0	126 (22%)	14 (2.4%)	92 (16%)	232 (41%)
VAS STR 2.1-4.0	142 (25%)	10 (2%)	36 (6%)	188 (33%)
VAS STR 4.1-10.0	125 (21%)	9 (1%)	13 (2%)	147 (26%)
Total	393 (69%)	33 (6%)	141 (25%)	567

Methods: Rheumatologists at one academic site complete a RheuMetric checklist which includes a physician global assessment (DOCGL) scores on a 0-10 visual analogue scale (VAS), and 3 additional 0-10 VAS subscales for inflammation (DOCINF), damage (DOCDAM), and distress (DOCSTR), as well as the % of DOCGL attributed to each of the 3 variables (Total=100%) to explain the basis for DOCGL. VAS scores classified as 0-2, 2.1-4, 4.1-10, and % of DOCGL classified as 0-20, 21-40, 41-100% were compared using descriptive statistics and cross-tabulations.

Results: In 567 unselected patients, DOCINF was >4/10 in 11%, vs 26% each for DOCDAM and DOCSTR (Table), indicating that 37% (=100-11-26-26) had at least 2 clinically important (VAS >2) variables, and 9% all 3 (data not shown). The proportion of patients in whom DOCGL was regarded as explained >40% by inflammation was 30%, vs damage in 52% and distress in 25% (Table). Therefore, a single basis for signs and symptoms was most prominent only in a minority of patients.

Conclusion: Quantitative rheumatologist VAS indicate that organ damage and patient distress often are as prominent as inflammation, and patients may have 2 or 3 bases for signs and symptoms. If confirmed at other sites, the results suggest a rationale to record a VAS for inflammation, damage, and distress, to document greater complexity of rheumatology encounters vs those based on a "gold standard" biomarkers, and possible adjustments in reimbursement for quantitative data to document the expertise of rheumatologists.

Reference:

1. Castrejon et al. Arthritis Care Res. 2012;64(8):1250-5.

Disclosure: T. Pincus, Helath Services, 7, Medical History Services LLC, 6, 7, 9, Medical history services LLC, 6, 7; **I. Castrejon**, None; **J. Block**, Abbvie, 2, ACR, 6, Agios, 7, Daiichi-Sankyo, 7, GlaxoSmithKline Consumer Healthcare, 5, Jannsen, 2, Medivir, 5, Novartis, 2, OARSI, Omeros, 7, Pfizer, 2, TissueGene, 2, Zynerba Pharma, 5.

Abstract Number: 1196

Patient Preference for an Electronic MDHAQ/RAPID3 (Multidimensional Health Assessment Questionnaire/ Routine Assessment of Patient Index Data), Which Gives Similar Results Compared to a Paper Version

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Measures Of Healthcare Quality Poster II: Improving Care
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Background/Purpose: A self-report multi-dimensional health assessment questionnaire (MDHAQ) includes RAPID3 (routine assessment of patient index data), which is informative in all rheumatic diseases in which it has been studied. An electronic version of the MDHAQ (eMDHAQ) could offer several advantages, including completion at home rather than in the waiting area, as well as completion from any site between visits to report possible change in status and/or adverse events of a medication. Furthermore, the eMDHAQ includes 3 additional features beyond RAPID3 requiring computer software: a. MDHAQ/FAST3 (fibromyalgia assessment screening tool) - a 0–3 clue to fibromyalgia (FM) with 80% agreement with formal FM criteria; b. MDHAQ/MEMO60 (monitoring early medication outcomes) - using weekly

MDHAQ Variable:	Paper	I-Pad	Diff. (95%CI)	ICC (95%CI)
Physical Function (0-10)	2.0 (1.7)	2.0 (1.7)	0.04 (-0.6, 0.6)	0.96 (0.94, 0.98)
Pain (0-10)	5.3 (3.2)	5.1 (3.1)	0.3 (-0.8, 1.4)	0.87 (0.80, 0.92)
Patient global (0-10)	4.8 (2.8)	4.5 (2.8)	0.3 (-0.7, 1.3)	0.94 (0.90, 0.96)
RAPID3 (0-30)	12.1 (7.1)	11.4 (7.2)	0.7 (-1.7, 3.2)	0.93 (0.88, 0.95)
Symptom checklist (0-60)	9.9 (8.5)	10.8 (9.5)	-0.9 (-4.1, 2.2)	0.75 (0.62, 0.84)
RADAI-48 (0-48)	9.9 (8.9)	11.4 (10.7)	-1.4 (-7.9, 1.9)	0.81 (0.71, 0.88)

Table. Mean (SD) values and ICC for paper MDHAQ versus I-pad e MDHAQ in 65 unselected with various rheumatic diseases patients.

remote electronic monitoring for 12 weeks after a new medication to analyze efficacy and adverse events; c.MDHAQ/LUCID (lifetime updatable clinical informatics database) - to provide medical history information in medical record format for physicians and to allow patients to save and update their medical history at a secure, HIPAA-compliant website for use with any doctor. We compared scores on an eMDHAQ vs paper version of MDHAQ at the same encounter, as well as patient preferences for the electronic vs paper MDHAQ.

Methods: All patients with all diagnoses complete a paper MDHAQ at all visits in the waiting area as part of routine clinical care. The MDHAQ includes 0-10 scores for physical function, pain and patient global visual analog scales (VAS), compiled into 0-30 RAPID3, as well as a 0–48 self-report painful joint count, and 0–60 symptom checklist. For this study, at the conclusion of the visit, the rheumatologist asked a patient if she/he would volunteer to complete an eMDHAQ on an iPad, indicating no problem if a patient declined. Patients who volunteered then completed an iPad eMDHAQ, with identical content to the paper MDHAQ. The patient also completed a 3-query questionnaire of 2 VAS concerning the value of the MDHAQ to the patient or the doctor (0= no value, 10= great value), and a query concerning preference for eMDHAQ vs paper MDHAQ or no preference. Test-retest reliability was examined by intraclass correlation coefficients (ICC).

Results: In 65 study patients, ICCs for physical function, patient global VAS, and RAPID3 were >0.9 indicating excellent reliability between the paper and Ipad eMDHAQ, and for pain, self-report painful joint count, and symptom checklist ≥0.75, indicating good reliability. The mean ratings for the value of MDHAQ were 8.85/10 to the patient and 8.88/10 to the doctor. Among the 65 patients, 43 (66%) preferred the eMDHAQ, 7 (11%) the paper MDHAQ, and 15 (23%) indicated no preference.

Conclusion: An eMDHAQ provides similar results to a paper MDHAQ. Most patients preferred the eMDHAQ to paper, although about 20% of patients likely will require a paper MDHAQ. An eMDHAQ offers remote completion before and/or between visits, and to report problems and/or adverse events, as well as unique electronic features. eMDHAQ is designed to interface with any electronic medical record (EMR), although that requires interaction with the EMR vendor, which may be difficult. The eMDHAQ appears useful independent of the EMR.

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Abstract Number: 1197

Factors Associated with Clinical Disease Activity Index Adoption at an Academic Rheumatology Practice

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Background/Purpose: The 2015 American College of Rheumatology (ACR) guidelines for the treatment of rheumatoid arthritis (RA) strongly recommend using a treat-to-target (T2T) strategy that has demonstrated improved outcomes compared to a non-targeted approach. The crux of any T2T treatment pathway is accurate and consistent disease activity measurement using an ACR endorsed tool like the clinical disease activity index (CDAI). The aim of our study was to measure trends and predictors of CDAI adoption at our tertiary academic rheumatology practice comprised of community-based and teaching sites.

Methods: Consecutive adult RA patients at our tertiary care rheumatology practice beginning 10/1/18 were prospectively identified using a previously validated codified algorithm. As part of the T2T approach implementation, CDAI questionnaire completion rates by 21 providers were measured longitudinally. The formula utilized for CDAI calculation was 'number of times CDAI score was completed' divided by 'total number of RA outpatient opportunities to complete CDAI'. Performance data was tracked longitudinally over 7 months and shared transparently at monthly intervals as aggregate and individual performance reports with all providers. We also segregated performance data by teaching faculty, trainees, non-physician providers, and disease activity level to help predict performance.

Results: A total of 3838 RA office visits with 21 providers were utilized for calculating aggregate CDAI performance metrics from 10/1/18 through 4/30/19 (Figure 1). Aggregate performance steadily improved from 10% to 26% over the 7 month period. Fellow trainees (NDV, AA) were found to have 90-100% CDAI utilization. Performance was noted to be skewed to a mean of 70% CDAI use by 6 teaching faculty compared to lower or no CDAI use at community-based sites. Sharing performance reports monthly by provider and aggregate via email was correlated with perfor-

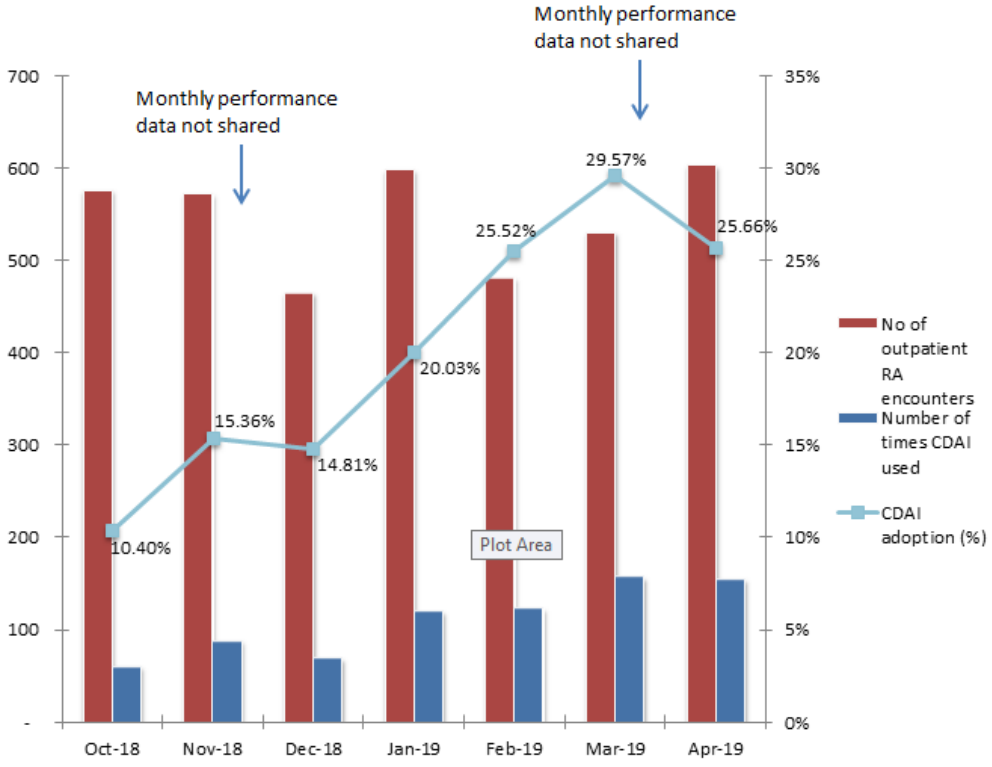

Figure 1. Clinical Disease Activity Index (CDAI) performance trend over 7 months

mance improvement in the month following the report, whereas a decline was noted in months of 12/18 and 4/19 where the previous month's reports were not shared.

Conclusion: Longitudinally tracking performance metrics and sharing data transparently could be vital to implementing a disease activity measurement. Providers at teaching sites and trainees may be early adopters and are more likely to demonstrate steady performance improvement. We believe that this deeper understanding of variation would be helpful in building the foundation of future T2T based treatment pathways.

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Abstract Number: 1198

Practice Based Education Program to Increase Vaccination Rate in Patients on Immunotherapeutic Agents

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Background/Purpose: Immunosuppressive agents have changed the course of debilitating autoimmune conditions. Despite their advantages, these agents come with risk of vaccine preventable infections.[1]Multiple organizations recommend scheduled influenza and pneumococcal vaccinations in all patients on chronic immunosuppression.[2,3]

Clarity regarding indication and timing of vaccinations has been problematic as new biologic therapies enter clinical practice. A 1996 Medicare survey of 16,000 patients on biologics showed a common reason for low adherence is not knowing the indications or vaccine schedules.[5]While physician specialists often initiate biologic therapy, primary care physicians typically have more access to vaccines. As a result, according to the Center for Disease Control (CDC) in 2014, vaccination adherence remains low amongst high-risk persons aged 19-64 years.[4]

In an outpatient primary care setting, we implemented a protocolized vaccination program for patients on immunosuppressive medications to increase influenza and pneumococcal vaccination adherence by at least 15% for each vaccine.

Methods: A retrospective, chart analysis identified 756 patients on biologic agents in Internal Medicine and Rheumatology practices. From this population, each patient was evaluated for compliance with CDC guidelines for immunocompromised patients for Influenza, Pneumococcal 13-Valent Conjugate and Pneumococcal Polyvalent vaccines. After data was collected, each practice received educational outreach and resources to serve as reminders to improve vaccination adherence. After the completion of the subsequent influenza season, the same patients were reviewed to obtain adherence data after the intervention.

Results: Of the patients studied, a majority of patients 65.2% (n=493) had rheumatoid arthritis, 19.6% had psoriatic arthritis, 7.0% had ankylosing spondylitis, and 8.1% had other conditions. The most common medications used were etanercept (35.5%, n=268) and adalimumab (35.1%, n=265). Prior to the educational program, 62.0% (n=469)

received influenza vaccinations, 34.0% (n=257) received pneumococcal 13-valent conjugate and 51.9% (n=392) received pneumococcal 23 vaccination. After the program, 65.1% (n=487) received influenza, 49.9% received pneumococcal 13-valent conjugate and 59.8% (n=447) received pneumococcal 23 vaccine. Overall, adherence to vaccination schedule increased from 18.9% (n=143) to 29.9% (n=224).

Conclusion: Patients on biologic therapies remain vulnerable to vaccine preventable illnesses such as Pneumococcal Pneumonia and Influenza. Based on our quality improvement initiative, there was an increase in overall vaccination adherence by 11% (n=81) in an at risk patient population. Despite this, inadequate resources and communication issues still remained an obstacle for primary care providers and specialists. In response to feedback from clinicians, a vaccination clinic is being developed in order to improve access to patients requiring vaccinations. Additionally, we have been working to optimize our best practice alert advisory through EMR, to improve communication between providers for our at risk population.

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Abstract Number: 1199

Improving Rates of Cervical Cancer Screening and HPV Vaccination in Patients with Lupus

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Background/Purpose: Patients with lupus have higher rates of cervical dysplasia and pre-malignant cervical lesions. At our institution, an urban referral center for patients with lupus, rates of HPV vaccination and cervical cancer screening were unknown. The aim of our quality improvement project was to determine the rate of HPV vaccination completion and cervical cancer screening compliance among the lupus patients seen in our institution as well as to implement a process to increase patient education and improve both rates within the outpatient rheumatology, nephrology and dermatology clinics over three months.

Methods: Using administrative records, all patients with a diagnosis of lupus seen in the clinics over a 3-year period were identified, of whom 11.4% were male and 88.6% female. A chart review of 332 patients was performed by a single physician to determine the rate of HPV vaccination completion and the rate of compliance with cervical cancer screening. We implemented a system to flag providers through the electronic health record regarding streamlined access to vaccination and facilitating referral for screening exams. Patients were also provided educational brochures about their increased risk of developing cervical lesions, recommended screening and HPV vaccination guidelines. Three months after implementing these processes, we re-evaluated the rates of HPV vaccination and cervical cancer screening.

Results: Prior to the intervention, 41.6% of lupus patients had received HPV vaccination, which was 24.4% lower than the national average for the general population. Cervical cancer screening was 43.8% pre-intervention, which was 32.2% lower than the national average. After implementing the system to flag providers and increase

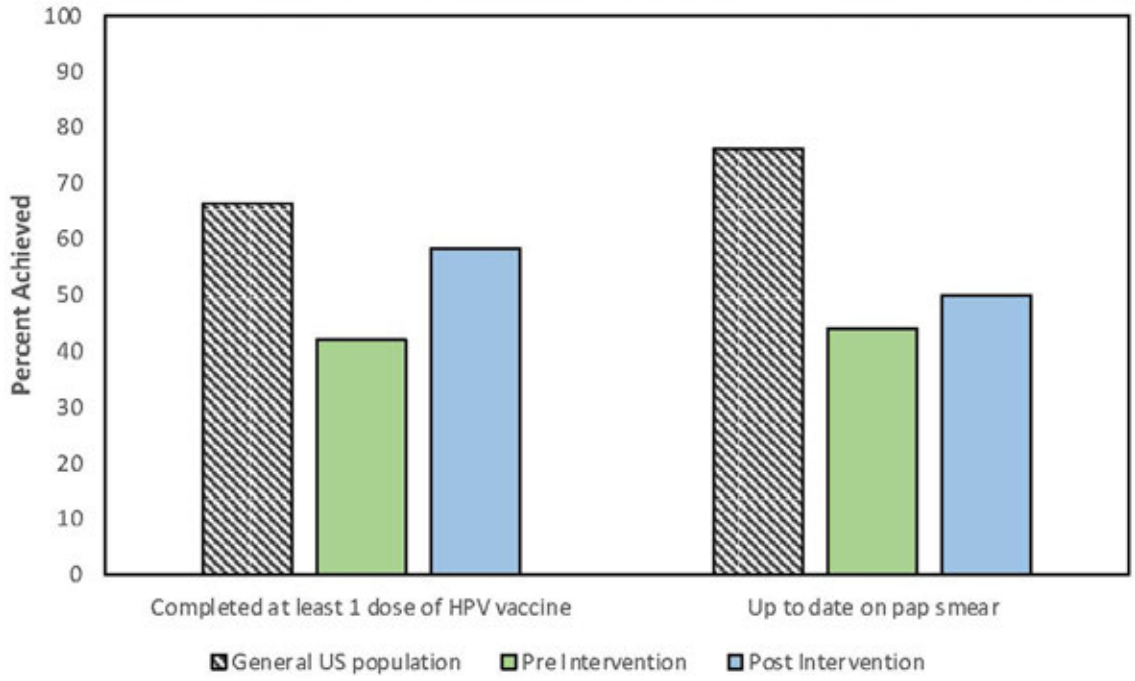

Figure 1. Rates of HPV vaccination and pap smears among lupus patients at our institution and in the general US population.

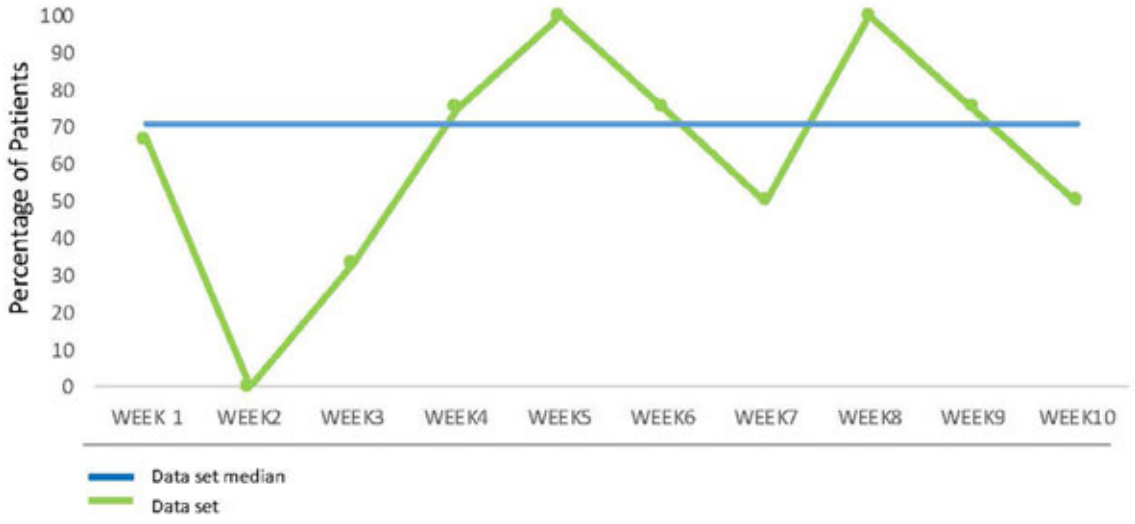

Figure 2. A run chart representing percent of lupus patients seen in outpatient rheumatology, nephrology, and dermatology clinics that were provided educational materials on cervical cancer screening and HPV vaccination.

patient education, we were able to improve these rates. Over three months, 71.8% of all patients seen in the clinics were provided education and 38.5% of eligible patients were appropriately referred to either their PCP or to Gynecology to complete cervical cancer screening. Post-intervention, the HPV vaccination rate increased from 41.6% to 58.3% and cervical cancer screening increased from 43.8% to 50%, both of which remained below the national average.

Conclusion: By raising awareness amongst providers in rheumatology, nephrology and dermatology and by implementing processes to facilitate HPV vaccination and cervical cancer screening, rates for both increased. However, rates are still below the national averages for the general population. Further work is needed to improve rates of cervical cancer screening and HPV vaccination in lupus, given the increased risk of cervical dysplasia.

Disclosure: N. Desai, None; **H. Menn-Josephy**, Advance Medical Ltd., 5, Aurinia pharmaceuticals, 6, Mallinckrodt pharmaceuticals, 6; **R. Bonegio**, None; **C. Lam**, Biogen, 2; **A. Kancharla**, None; **M. York**, None.

Abstract Number: 1200

Influenza Vaccination Rates Among Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis on Immunosuppressive Therapy: Findings from a Large Public Hospital

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Background/Purpose: Influenza infection constitutes a significant cause of morbidity and mortality in patients living with Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA). The risk of influenza-related morbidity and mortality is higher in these subsets of patients owing to impaired immune responses and the use of immunosuppressive therapy. Therefore, the Advisory committee on vaccination practices highly recommend yearly influenza vaccination to improve clinical outcomes in these patients. There is limited data on Influenza vaccination rate in patients with SLE and RA on immunosuppressive therapy.

Methods: Data was obtained from the electronic medical record (EMR) system of one of the ambulatory arms of Grady Memorial Hospital. Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis who visited the clinic during the influenza season from October 1, 2018 to May 31, 2019 were included. Patients were asked to complete a questionnaire on demographics, influenza vaccination status, use of immunosuppressive therapy, method of influenza awareness and smoking status. Data was confirmed with the EMR. MS excel and SAS 9.4 software were used for data management and analysis.

Results: A total of 83 patients were included in the study. 62.6% of the population had Rheumatoid arthritis while 37.4% had SLE. All patients were on immunosuppressive medications which included methotrexate, leflunomide, cyclosporine, mycophenolate mofetil and azathioprine. Based on demographics, 78.3% were female and 21.7% were male. Mean population age was 53.5. Our patient population was predominantly African American (91.6%) and the educational level of majority of the participants was high school (41%). The most common setting for vaccination was during a primary care doctor's visit (66.1%; n=37/56) compared to 32.1% (n=18/56) who received vaccination at their Rheumatology clinic visit. 77% of the total population were non-smokers.

The overall flu vaccination coverage was 67.5% which is higher than the CDC reported 2018-2019 national coverage rate of 46.3% in patients with high risk conditions. 67.3% of the RA population (n=35/52) received the influenza vaccine while 67.7% of the SLE population (n=21/31) received the influenza vaccine. The 2019 flu vaccination coverage amongst SLE patients in this ambulatory arm increased by 37.7% compared to the 2017-2018 coverage rates. For the 32.5% of the total population that declined the flu shot, perceived lack of efficacy of the influenza vaccine was the most cited reason (37%), followed by aversion to all vaccines (25.9%).

Conclusion: Our data demonstrates an overall improvement in coverage rates compared to reports from our local 2017-2018 survey and the recent CDC national coverage rate generally. Given the lower rate of awareness provided by Rheumatologists about the flu shot in comparison to primary providers, we propose more patient education on the part of Rheumatologists on the need for influenza vaccination and on the perceived lack of inefficacy of the influenza vaccine. More studies should evaluate factors that contribute to the relatively high coverage rate seen in RA and SLE patients.

Disclosure: J. Aniekwena, None; **T. Olanipekun**, None; **V. Effoe**, None.

Abstract Number: 1201

Are We Meeting Benchmarks for Wait Times to Pediatric Rheumatology Care for Juvenile Idiopathic Arthritis (JIA)?

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Background/Purpose: Wait time to pediatric rheumatology care for patients with Juvenile Idiopathic Arthritis (JIA) is a nationally endorsed quality measure in Canada. Target wait times for systemic JIA are 7 days from referral to pediatric rheumatology care, and 4 weeks for other JIA categories. The purpose of this study was to measure this quality indicator and evaluate factors associated with JIA wait times at a single academic pediatric rheumatology center.

Methods: This was a retrospective cohort study of patients with a diagnosis of JIA participating in a pharmacogenetics study who had demographic and disease-related data collected prospectively between 2002-2018. The time between referral date and first pediatric rheumatology visit was extracted from clinic charts and clinical variables from a pharmacogenetics study database. Factors evaluated included JIA category, age, sex, distance from the clinic, baseline number of active joints, pain and C-reactive protein (CRP) at the first clinic visit. Distance from clinic was calculated by geocoding the latitude and longitude of the patient's postal code using the Postal Code Conversion File, with distance calculations made using ArcGIS by calculating the shortest distance to the clinic using roadways. Urban versus rural classification of patient residence was according to Statistics Canada definitions. Descriptive characteristics and wait time measures are reported using medians (interquartile range, IQR) given the non-normal distributions. Non-parametric Kruskal-Wallis rank test was used to examine whether there was any difference in wait times among patients with different categories of JIA. Cox proportional hazard modelling was used to evaluate potential factors associated with wait time.

Results: 164 patients with JIA were eligible for inclusion, of which 116 were female (71%). The median age at diagnosis was 8.0 (IQR 3.5, 12.0) years. The majority of patients had oligoarticular JIA (n=75, 46%) or rheumatoid factor-negative polyarticular JIA (n=48, 29%) and 6 patients had systemic JIA (4%). The majority of patients (n=102, 62%) were from Calgary. The median network distance for patients between their residence and the clinic was 22.8 kilometers (IQR 13.5, 127.8). There was a median of 22 days between referral and pediatric rheumatologist visit (IQR 9, 45), and there was no significant difference between the wait times among JIA categories (p=0.055). Overall, 62% of JIA cases met the established wait time benchmarks. Using Cox-proportional hazard modeling, higher age was associated with longer wait times (HR 0.94, 95% CI 0.89, 0.98, p=0.005).

Conclusion: The median wait time from referral to pediatric rheumatologist visit for patients with JIA in this study met the national benchmark, although some patients experienced long wait times for appointments. Wait times did not significantly differ by JIA category but older patients waited longer. This work highlights the importance of monitoring of wait times as a quality indicator.

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Abstract Number: 1202

Testing Rheumatoid Arthritis Performance Measures to Optimize Treat to Target Strategies

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: The purpose of this study was to operationalize and report on 3 Rheumatoid Arthritis (RA) performance measures previously identified in the Patient-Centered Framework for Measuring, Monitoring and Optimizing RA care in Canada: 1) the number of visits where a patient was in moderate or high disease activity where a follow-up visit was booked within ≤ 3 months; 2) the number of visits with moderate or high disease activity where the disease activity was subsequently documented as low or in remission within 6 months; 3) the percentage of patients in remission at any point during the measurement period.

Methods: The performance measures were tested in an RA cohort over the period between 08/2016 to 05/2019 using a web-based tool (Rheum4U). Rheum4U is designed as a pragmatic quality improvement and research tool and collects baseline characteristics, sociodemographic factors, patient reported outcomes, and disease activity using composite scores (DAS28) calculated at the point of care. The study was conducted at 2 outpatient University-affiliated rheumatology clinics staffed by 15 participating rheumatologists and 1 nurse practitioner. Consecutive patients were recruited and consented for inclusion at any point during their disease course and data entered into the Rheum4U platform at each clinical encounter, with the timing of encounters and treatment changes being at the

discretion of the attending rheumatologist and patient. Standard DAS28 cutoffs for disease activity were used in the study.

Results: 500 patients with RA (with n=1627 visits) were included in the analysis, 75% were female with a mean (SD) age of 55 (14) years. The mean length of follow-up was 413 (238) days and the mean number of visits was 4 (2) for patients with > 1 visit. There was a disease activity score (DAS28) calculated at 1202 of the 1627 visits (74%). 503 visits (42% of visits with a DAS28 score) were in patients with moderate or high disease activity with at least 1 follow-up. Amongst all visits (n=503) for patients with a documented moderate or high disease activity score, 147 follow-up visits (30%) occurred within ≤ 3 months and low disease activity or remission was achieved at 100 visits (20%) within ≤ 6 months. The percentage of visits where the patient was documented to be in remission at any point over follow-up was 35% (n=425/1202 with a DAS28 score) and an additional 6% were in low disease activity (n=67).

Conclusion: While just over 40% of patients reached a state of remission or low disease activity over the follow-up period, we have identified critical areas for process and outcome improvements. Specifically, only 30% of visits where a moderate or high disease activity was documented had a follow-up visit within 3 months, and only 20% of follow-up visits documented low disease activity or remission within 6 months. This work highlights the importance of quality measures as a tool to help guide adherence to treat-to-target strategies.

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Abstract Number: 1203

Psychometric Properities of the Patient Related Outcome Measure FACIT-Fatigue in Rheumatic Arthritis and Psoriatic Arthritis: A Literature Review

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

Background/Purpose: Fatigue is an important patient reported outcome in rheumatoid arthritis (RA) and psoriatic arthritis (PsA) research. FACIT-Fatigue is a 13-item patient reported outcome (PRO) instrument designed to assess fatigue and its impact on daily activities and function over the past seven days. In this study we reviewed published evidence on the psychometric properties of FACIT-Fatigue in patients with rheumatoid arthritis (RA) or psoriatic arthritis (PsA) including content validity, reliability, , and ability to detect change.

Methods: For content validity, a search of PubMed and Ovid databases used the following terms: (“conceptual” OR ”content validity” OR “qualitative” OR “debrief*”) AND (“rheumatoid arthritis”/”psoriatic arthritis” OR “RA”/”PsA”)

Table 1. Content Validity of the Patient Reported Outcome Measure FACIT-Fatigue in Rheumatoid Arthritis and Psoriatic Arthritis

Disease	Results	Reference
RA	Majority of patients (14/17) indicated that FACIT-Fatigue captured their fatigue experience.	Kaiser, 2016, in press
RA	From these 13 studies, 58 patient descriptors were provided. 39 (67%) were mapped to the FACIT-Fatigue items.	Carr, 2003 Connolly, 2015 Feldthusen, 2013 Hewlett, 2005 Kaiser, 2016, in press Mortada, 2015 Nicklin, 2010 Nikolaus, 2010 Repping-Wuts, 2008
PsA		Gossec, 2014 Moverley, 2015 Stamm, 2007 Tillett, 2015

Table 2. Published Analyses of Psychometric Properties and Ability to Detect Change in the Patient Reported Outcome (PRO) FACIT-Fatigue in Rheumatoid Arthritis and Psoriatic Arthritis

Psychometric Property:	Disease	Study Design	Results		Reference
Reliability					
Internal Consistency Reliability	RA	RCT	Good to excellent internal consistency reliability (Cronbach's Alpha ≥0.80)		Cella, 2005
Test-Rest Reliability	PsA	Obs	Excellent test-retest reliability (Intra-class Correlation Coefficient>0.9)		Chandran, 2007
Construct Validity			**Comparator to FACIT-Fatigue**	**Correlation Coefficient**	
Convergent Validity	RA	RCT	Multidimensional Assessment of Fatigue SF-36	-0.84 to -0.88 0.72 to 0.84	Cella, 2005
	RA	Obs	HAQ-DI DAS28	-0.42 -0.44	Mittendorf, 2007
	RA	Obs	DAS28 CDAI Tender joint count	-0.80 -0.83 -0.73	Singh, 2014
	RA	Obs	HAQ-DI PaGA Pain Intensity PhGA DAS28	-0.68 -0.64 -0.62 -0.47 -0.48	Campbell, 2012
	PsA	Obs Obs	Fatigue Severity Score PASI Psoriasis Disability Index	- 0.79 (95% CI: -0.85 to -0.72) -0.35 (p<0.01) -0.30 (p<0.01)	Chandran, 2007 Carneiro, 2010
	PsA	Obs	Actively Inflamed Joint Count	0.43 (p<0.01)	Chandran, 2007
	PsA	RCT	DAS 28	-0.42 (p<0.001)	Ritchlin, 2014
Known Groups Validity			**FACIT-Fatigue Scores Differed Among Patients Distinguished by:**		
	RA	Obs	DAS-28 levels of disease activity		Campbell, 2012
	PsA	RCT	PsA vs General Population		Ritchlin, 2014
	PsA	Obs	PsA vs General Population		Chandran, 2007
	PsA	Obs	DAS-28 levels of disease activity		Arancibia, 2014 Aranc
	PsA	RCT	Degree of skin involvement		Mease, 2015
Ability to Detect Change			**Changes in FACIT-Fatigue scores were related to measures of improvement in disease activity:**		
	RA RA	RCT RCT	ACR signs and symptoms (ACR20, ACR50, ACR70, and ACR-N)		Cella, 2005 Strand, 2014
	RA	RCT	SDAI		Strand, 2014
	RA	RCT RCT	DAS-28-CRP		Emery, 2015 Bergman 2012
	RA	RCT	HAQ-DI, Total Sharp Score		Emery, 2015
	PsA	RCT	DAS28		Ritchlin, 2014
	PsA	RCT	PASI		Mease, 2015
	PsA	Retro	PhGA		Touma, 2013
	PsA	RCT	Minimal Disease Activity		Mease, 2015

ACR=American College of Rheumatology; CDAI=Clinical Disease Activity Index; CI=confidence interval; DAS-28-CRP=Disease Activity Score 28-C-Reactive Protein ; HAQ-DI=Health Assessment Questionnaire-Disability Index ; Obs=observational study; PASI=Psoriasis Area and Severity Index; PhGA=Physician Global Assessment of Disease Activity; PsA=psoriatic arthritis; PtGA=Patient Global Assessment of Disease Activity; RA=rheumatoid arthritis; RCT=randomized controlled trial; Retro=retrospective study; SDAI=Simplified Disease Activity Index

AND "fatigue". For the psychometric measures, the search used the following terms: ("FACIT-F" OR "FACIT-Fatigue" OR "FACIT Fatigue") AND ("rheumatoid arthritis"/"psoriatic arthritis" OR "RA"/PsA") AND "fatigue." Search filters were used to exclude: 1) articles that are not available in the English language; and 2) articles not published within

the last 15 years (2001 – 2016). Abstracts and full-publications involving observational cohorts and clinical trials were reviewed for reports of FACIT-Fatigue psychometric properties in RA and PsA patient studies.

Results: A total of 81 papers were included in this study. The content of the FACIT-Fatigue items maps well to descriptors used by patients to express their experience of RA-related fatigue, and almost all of the items (except the item "too tired to eat") were found to be acceptable by patients, supporting its content validity. The instrument also possesses good to excellent reliability, including Cronbach's alpha (≥ 0.80), test-retest reliability, and intra-class correlation. Moderate to high correlations were also found between the FACIT-Fatigue and other measures of fatigue, as well as measures of disability and disease activity, such as HAQ-DI, DAS28, Psoriasis Area and Severity Index and, Psoriasis Disability Index. The known-groups validity of the instrument was also demonstrated in studies of RA and PsA patients based on disease status and scores relative to the general population. Studies also showed that changes in FACIT-Fatigue scores were associated with changes in multiple clinical outcome measures, such as ACR improvement criteria, changes in DAS28, and physician global assessment, suggesting the ability of the FACIT-Fatigue to detect changes in RA and PsA disease activity. Table 1 summarizes the content validity evidence and Table 2 provides summaries of the psychometric properties of FACIT-Fatigue.

Conclusion: This review demonstrated evidence of content validity and strong psychometric properties of FACIT-fatigue in patients with RA and PsA, supporting its use in RA and PsA studies.

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Abstract Number: 1204

Improvements in Health-Related Quality of Life in Psoriatic Arthritis Patients Treated with Intravenous Golimumab, an Anti-TNFα Monoclonal Antibody: 1-Year Results of a Phase III Trial

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SESSION INFORMATION

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Session Title: Measures Of Healthcare Quality Poster II: Improving Care

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Session Time: 9:00AM–11:00AM

Background/Purpose: In the randomized, phase 3, GO-VIBRANT study, more patients with psoriatic arthritis (PsA) achieved ACR 20/50/70 after 24 weeks IV treatment with the anti-TNFa monoclonal antibody golimumab (GLM-IV) than placebo (PBO) ($p< 0.001$). After cross-over from PBO to GLM-IV at week 24, 52-week achievement of ACR responses was similar between the two treatment groups.[1] Here we examine effects on measures of health-related quality of life (HRQoL) for up to 52 weeks of treatment.

Methods: Adult patients with active PsA who met CASPAR criteria (N=480) were randomized (1:1) to GLM-IV 2 mg/kg at weeks 0, 4, then every 8 weeks or matching PBO through week 20 then cross-over to GLM-IV at weeks 24, 28, then every 8 weeks. Physical function was assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI). Measures of HRQoL included Short-Form-36 Physical and Mental Component Summaries (SF-36 PCS/MCS), Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue, EuroQol-5D visual analog scale (EQ-VAS), and Dermatology Life Quality Index (DLQI), assessed at weeks 0, 8, 14, 24, 36, and 52.

Results: GLM- IV and PBO groups had comparable HRQoL characteristics at baseline (Table 1). At 24 weeks, changes from baseline were greater for GLM-IV vs PBO, respectively (HAQ-DI, -0.63 vs -0.14; SF-36 PCS, 9.4 vs 2.4; SF-36 MCS, 5.3 vs 0.8; FACIT-Fatigue, 9.2 vs 2.3; EQ-VAS, 20.2 vs 5.5; and DLQI, -8.1 vs -1.9). At week 24 more

Table 1. Changes from Baseline in HR-QoL Measures from Week 24 to Week 52 in the Placebo-Controlled, Randomized, Phase 3 Study GO-VIBRANT of Patients with Active Psoriatic Arthritis

	GLM-IV 2 mg/kg			PBO → Week 24 crossover to GLM-IV 2 mg/kg		
	n	Baseline Score (mean ± SD)	Change from Baseline (mean ± SD)	n	Baseline Score (mean ± SD)	Change from Baseline (mean ± SD))
HAQ-DI						
Baseline	237	1.3 ± 0.6		236	1.3 ± 0.6	
Week 24	237		-0.63± 0.5*	236		-0.14 ± 0.5
Week 36	237		-0.64 ± 0.6	236		-0.50 ± 0.5
Week 52	237		-0.66 ± 0.6	236		-0.56 ± 0.5
SF-36 PCS						
Baseline	237	33.1 ± 6.9		236	34.0 ± 7.2	
Week 24	237		9.4 ± 8.1*	236		2.4 ± 6.1
Week 36	237		9.8 ± 8.2	236		8.1 ± 7.5
Week 52	237		10.6 ± 8.9	236		9.0 ± 8.2
SF-36 MCS						
Baseline	237	43.5 ± 11.4		236	42.5 ± 10.2	
Week 24	237		5.3 ± 10.2*	236		0.8 ± 7.4
Week 36	237		5.3 ± 10.7	236		4.4 ± 8.8
Week 52	237		5.4 ± 10.8	236		3.8 ± 9.5
FACIT-Fatigue						
Baseline	237	27.9 ± 9.6		236	27.7 ± 9.7	
Week 24	237		9.2 ± 9.8*	236		2.3 ± 7.8
Week 36	218		9.6 ± 9.6	215		8.1 ± 8.7
Week 52	218		9.9 ± 10.6	215		8.2 ± 9.3
EQ VAS						
Baseline	237	46.9 ± 20.1		236	46.2 ± 20.3	
Week 24	237		20.2 ± 24.2*	236		5.5 ± 23.1
Week 36	218		21.0 ± 25.3	215		17.7 ± 25.7
Week 52	218		21.6 ± 27.6	215		20.8 ± 25.7
DLQI						
Baseline	194	12.0 ± 7.5		195	10.0 ± 6.8	
Week 24	194		-8.1 ± 7.7*	195		-1.9 ± 5.9
Week 36	194		-7.6 ± 7.6	195		-5.8 ± 6.8
Week 52	194		-7.8 ± 7.2	195		-5.8 ± 7.4

*P vs PBO <0.0001, P values are nominal, not adjusted for multiplicity.
SF-36 results were calculated using a Mixed-effect Repeated Measures statistical model. EQ VAS, HAQ-DI, FACIT-fatigue, and DLQI results were calculated using Analysis of Covariance.
DLQI=Dermatology Life Quality Index; EQ VAS= EuroQol-5D questionnaire, visual analog scale; FACIT-Fatigue= Functional Assessment of Chronic Illness Therapy; GLM-IV=intravenous golimumab; HAQ-DI= Health Assessment Questionnaire-Disability Index; HR-QoL=Heath-related Quality of Life; PBO=placebo; SF-36 PCS/MCS=Short-Form-36 Physical / Mental Component Summaries

Table 2. Achievement of Minimal Clinically Important Difference (MCID) from Baseline† from Week 24 to Week 52 in the Placebo-Controlled, Randomized, Phase 3 Study GO-VIBRANT of Patients with Active Psoriatic Arthritis				
	GLM-IV 2 mg/kg		PBO → Week 24 crossover to GLM-IV 2 mg/kg	
	n	Patients with ≥MCID from baseline, %	n	Patients with ≥MCID from baseline, %
HAQ-DI				
Week 24	241	69.3*	239	32.6
Week 36	241	68.9	239	56.5
Week 52	241	71	239	62.8
SF-36 PCS				
Week 24	241	69.7*	239	29.3
Week 36	241	69.3	239	63.2
Week 52	241	73.4	239	66.9
SF-36 MCS				
Week 24	241	46.9*	239	29.3
Week 36	241	47.7	239	46.0
Week 52	241	50.6	239	42.3
FACIT-Fatigue				
Week 24	231	70.1*	221	43.0
Week 36	218	72.5	215	69.3
Week 52	218	69.3	215	69.8
†Minimal clinically important differences from baseline are HAQ-DI=0.35[2], SF-36=5[3], FACIT-Fatigue=4[4]. * P vs PBO <0.0001, P values are nominal, not adjusted for multiplicity. FACIT= Functional Assessment of Chronic Illness Therapy; GLM-IV=intravenous golimumab HAQ-DI= Health Assessment Questionnaire-Disability Index; MCID=minimal clinically important difference; PBO=placebo; SF-36 PCS/MCS=Short-Form-36 Physical / Mental Component Summaries				

patients receiving GLM-IV than PBO achieved minimal clinically important improvements from baseline in HAQ (≥0.35 points),[2] SF-36 (≥5points),[3] and FACIT-fatigue (≥4 points).[4] Among patients randomized to GLM-IV, changes in HRQoL measures were maintained from week 24 to week 52. Among patients randomized to PBO, after switching to GLM-IV at week 24, improvements in HRQoL measures from week 36 to week 52 were comparable to those of patients originally randomized to GLM-IV (Tables 1 and 2).

Conclusion: Improvements in HRQoL among patients with PsA after 24 weeks' GLM-IV treatment were greater than PBO and were maintained through week 52 of treatment. Patients switching from PBO to GLM-IV at week 24 experienced improvements in HRQoL by week 36, which were maintained through week 52 and were similar to those achieved by patients originally randomized to GLM-IV.

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Eli Lilly, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 2, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, Pfizer Inc, 2, Roche, 2, UCB Pharma, 2.

Abstract Number: 1205

Real-World Remission Outcomes in the First Year Following RA Diagnosis Vary Considerably with the Disease Activity Index Used and a Sizable Proportion Have Persistent Active Disease Across All Measures: Results from the Canadian Early Arthritis Cohort (CATCH)

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SESSION INFORMATION

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Background/Purpose: Early RA diagnosis and initiation of DMARDs following a treat-to -target approach is recommended to optimize remission outcomes. Several RA disease activity indices are commonly used in research and practice. The choice of index however, may impact treatment decisions and quality improvement (QI) program eval-

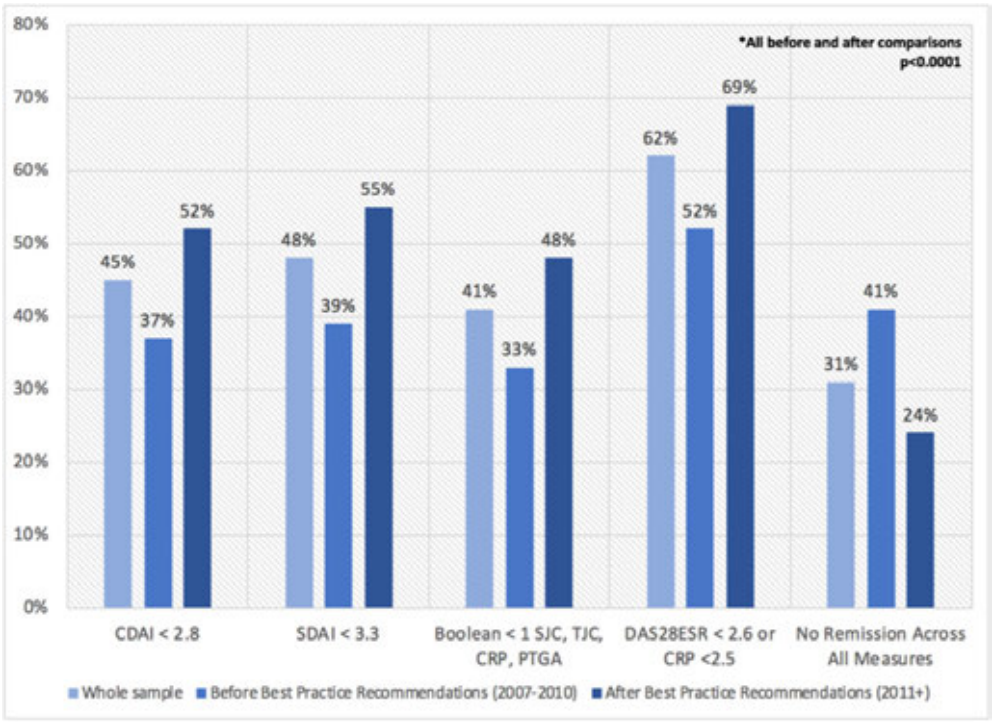

Figure 1 Prevalence and Improvement in Remission Outcomes by 12-Months Across 4 Commonly used Clinical Remission Indices.

Table 1 Multivariable Logistic Regression Predicting Persistent Disease Activity Across All Clinical Disease Activity Indices in the first year of Follow up			
	Whole sample OR (95% CI)	Women	Men
Age	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)	1.03 (1.00, 1.05)
Sex	1.85 (1.30, 2.64)	NA	NA
Education (higher than high school)	0.57 (0.42, 0.76)	0.57 (0.40, 0.80)	0.59 (0.31, 1.11)
Symptom duration, months	1.07 (1.02, 1.12)	1.07 (1.01, 1.13)	1.06 (0.95, 1.18)
RF or ACPA +[◆]	1.38 (0.96, 2.01)	1.15 (0.75, 1.77)	2.32 (1.02, 5.29)
Smoking			
Never or past	Ref	Ref	Ref
Current	1.04 (0.72, 1.50)	0.86 (0.56, 1.34)	2.03 (0.96, 4.30)
Obesity[◆]	1.78 (1.23, 2.57)	2.19 (1.43, 3.34)	0.95 (0.43, 2.10)
Rheumatic Disease Comorbidity Index (0-9)	1.07 (0.95, 1.20)	1.04 (0.91, 1.19)	1.21 (0.94, 1.55)
TJC28	1.05 (1.02, 1.08)	1.07 (1.03, 1.11)	0.99 (0.93, 1.05)
SJC28	0.99 (0.96, 1.03)	0.98 (0.94, 1.02)	1.04 (0.97, 1.10)
Pain	1.13 (1.07, 1.19)	1.12 (1.05, 1.19)	1.15 (1.02, 1.30)

uations. Study objectives were to: 1) compare remission outcomes in the first year across 4 commonly used clinical disease activity indices; 2) estimate changes in remission over time across indices coinciding with release of RA best practice recommendations, and 3) identify predictors of persistent active disease across all measures.

Methods: Data were from patients with early RA (symptoms < 1 year, 100% Met ACR/EULAR RA criteria) enrolled in a prospective national ERA cohort study between Jan- 2007 and Mar-2018. Study participants had active disease at enrollment, were treated with DMARDs, and completed clinical evaluations, laboratory assessments and patient-reported outcomes every 3-months for the first 12-months of follow up. T-tests and chi-squared tests were used to compare patient characteristics, early treatment strategies, and remission outcomes using 4 commonly used clinical indices (DAS28< 2.6 OR DAS28CRP < 2.5, CDAI ≤ 2.8, SDAI≤ 3.3, and ACR/EULAR Boolean remission - SJC28, TJC28, CRP, PGA all ≦ 1). Logistic regression was used to identify predictors of persistent active disease across all measures by 12-months among baseline sociodemographic, RA clinical characteristics and patient-reported outcomes.

Results: Among 1202 adults eligible for this analysis, 877 (73%) were women, mean (sd) age was 55 (14), average disease activity was high across measures (DAS28 5.1 (1.4); CDAI 27 (14); SDAI 29 (15)) and majority (98%) were treated with csDMARDs +/- MTX. Remission by 12-months varied considerably across indices ranging from 33% to 62%, though improvement in remission before and after implementation of best practice recommendations was similar across all indices (~+15%) (Figure 1). 378 (31%) did not achieve remission across all indices. In adjusted logistic regression models, persistent active disease across indices was associated with baseline older age, female sex, longer symptom duration, positive serology, obesity, tender joints and higher pain (Table 1). In stratified analyses by sex, persistent active disease was more strongly associated with obesity and more tender joints in women, and positive serology and smoking in men.

Conclusion: The choice of index had a sizable impact on remission classification with important implications for decision-making surrounding treatment intensification in clinical practice. However all indices showed similar levels of improvement in remission before and after implementation of best practice recommendations suggesting that choice of index may be less important when evaluating QI programs. In the interim, in the absence of a single "best measure" that also takes in to account the patient's perspective, study results looking across measures point to unmet needs for achieving remission in approximately 1 in 3 ERA patients.

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Abstract Number: 1206

Performance of the Patient-Reported Outcomes Measurement Information System 29 (PROMIS-29) Item Profile in a Cohort of Australians with RA, OA and Other Inflammatory Arthritic Conditions

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Background/Purpose: Guarded support for PROMIS-29 assessment in musculoskeletal disease has been reported in RA, OA, FM and SLE patients[1]. The performance of PROMIS-29 compared to legacy measures in Australian patients with RA, OA and other inflammatory arthritic conditions (IA) has not been examined. The aim of this study was to determine similarities and differences to performance of the multidimensional health assessment questionnaire (MDHAQ).

Methods: All consented patients complete a MDHAQ and the static 29 item PROMIS profile (PROMIS-29) questionnaire prior to seeing their rheumatologist. A cross sectional sample of 113 RA, 25 OA and 58 patients with IA (ankylosing spondylitis, psoriatic arthritis and inflammatory arthritis) was analysed. PROMIS-29 assesses 7 domains: physical function, anxiety, depression, fatigue, sleep disturbance, satisfaction with participation in social roles, pain interference and a 0-10 pain intensity scale. Scores are standardised against US normative population data producing T

MDHAQ scores	RA (n=113)	OA (n=25)	IA (n=56)	P value
Physical Function	2.8 (2.2)	3.5 (2.3)	2.6 (2.1)	NS
PTGL	4.6 (3.1)*	6.4 (2.4)*	4.8 (2.7)	*0.02
Fatigue	4.1 (3.3)*	6.1 (2.2)*	4.4 (3.0)	*0.01
Pain	4.8 (3.0)*	6.6 (2.4)*^	4.8 (2.8)^	*0.01 ^0.03
Sleep	1.2 (1.0)	1.5 (1.0)	1.2 (1.1)	NS
Anxiety	0.8 (0.8)	0.8 (0.9)	0.8 (0.9)	NS
Depression	0.8 (0.9)	1.0 (0.9)	0.7 (0.8)	NS
Symptom review	10.7 (9.0)	14.9 (8.5)	10.6 (8.5)	NS
RADAI	15.6 (13.7)	19.8 (12.3)^	12.2 (9.1)^	^0.04
PROMIS-29 T scores				
Physical function	39.9 (8.9)	36.0 (6.8)^	42.5 (9.5)^	^0.007
Satisfaction with social role	46.4 (10.8)*	40.9 (8.9)*^	49.0 (11.2)^	*0.06 ^0.006
Fatigue	52.4 (11.5)	56.3 (10.0)	52.9 (11.7)	NS
Pain interference	59.6 (9.0)*	65.39 (7.1)*^	57.4 (9.8)^	*0.005 ^0.0004
Sleep	54.0 (8.5)	55.6 (9.0)	52.4 (9.9)	NS
Anxiety	52.5 (11.1)	55.2 (11.5)	50.7 (10.3)	NS
Depression	51.7 (10.7)	53.5 (11.5)	49.6 (10.6)	NS
Pain VAS	4.8 (2.8)*	6.7 (2.2) *^	4.5 (2.7)^	*0.006 ^0.003

Values are means and standard deviations
*OA vs RA
^OA vs IA

Table 1 Participating subject MDHAQ and PROMIS-29 characteristics by condition.

scores with a mean of 50 and a standard deviation of 10. The MDHAQ assesses physical function (0-10), sleep disturbance, anxiety and depression (0-3.3), pain (0-10 VAS), patient global assessment (PTGL) (0-10 VAS), self-report joint count (RADAI) (0-48), 60 question symptom review and fatigue (0-10 VAS). Means and standard deviations (SD) of PROMIS T scores and MDHAQ variables and percentage of patients achieving minimum and maximum values for each variable were calculated. ANOVA compared PROMIS-29 T scores and MDHAQ means across disease groups. Floor effect is defined as the 'best' possible score and ceiling as the 'worst' possible score, irrespective of the direction of the scale. A substantial floor or ceiling effect is defined as ≥15% with either score.

Results: Patients were predominantly female with a mean age of 57.4 +/-14.4 years and mean disease duration >14 years. OA and RA patients were significantly older than IA patients ($p< 0.04$). MDHAQ scores for PTGL, fatigue and pain were significantly higher in OA than RA ($p\leq0.04$) (Table 1). Pain and RADAI were also higher in OA than in IA ($p\leq0.04$). The PROMIS-29 mean T scores for physical function, satisfaction with social role, pain interference and mean Pain VAS were significantly worse in the OA patients than the IA patients ($p\leq0.007$). Satisfaction with social role and pain interference were also significantly worse in the OA than the RA group ($p\leq0.06$). No significant differences between RA and IA were seen by any MDHAQ or PROMIS-29 measure. Significant floor effects were found for MDHAQ and PROMIS-29 depression and anxiety in all groups. MDHAQ sleep disturbance, also demonstrated significant floor effects across all groups. A ceiling effect was only seen in OA pain interference.

Conclusion: PROMIS-29 and MDAHQ scores performed similarly across a range of comparable domains but differed for physical function and fatigue assessment. Significant floor effects were found for both instruments. Each provides data for constructs not available in the other, which should be considered when choosing a tool to inform clinical care.

Reference:

1. Katz P et al. (2017) Arthritis Care & Research 69(9):1312-1321

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Abstract Number: 1207

A Quality Improvement Intervention to Reduce 30-Day Hospital Readmission Rates Among Patients with Systemic Lupus Erythematosus

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic immune-mediated disease with significant morbidity and mortality that often requires inpatient hospitalization. SLE has one of the highest 30-day hospital readmission rates among chronic diseases in the United States with 30-day readmission rates reported in the literature of 16.5-36%. Prior studies have focused on identifying risk factors associated with readmission. The aim of our study was to reduce 30-day readmission rates among SLE patients at the University of Colorado Hospital by implementing a multidisciplinary post-discharge intervention.

Methods: Using our inpatient consult log, we collected baseline data on the 30-day readmission rate of SLE patients from 7/2016 through 10/2016. We excluded patients who do not get their rheumatology care at our clinic as they would not be impacted by our intervention. We designed a post-discharge intervention that engages the rheumatology fellows, attendings and clinic nurses. We created a message template in the electronic medical record (EMR) that is sent by the rheumatology consult fellow to the clinic nurses when the patient is discharged from the hospital. This includes information about medication changes, future infusions, future labs and follow-up appointments. The nurses contact the patient by telephone within 48 hours of discharge to review the information and answer any questions. We collected post-intervention data from 12/2018 through 2/2019.

Results: Prior to intervention, 87 patient charts were manually reviewed for inclusion and 18 patients met criteria of having SLE and being followed by our clinic. The 30-day readmission rate among these patients was 44%. The patients who were readmitted within 30 days were 100% female, average age 36 years old, 75% non-Caucasian (Hispanic or African American) and 50% had a public payor form of insurance (Medicare or Medicaid). The reasons for readmission were as follows: 37% SLE flare, 37% infection, 25% other medical issue. Following our intervention, the 30-day readmission rate among our patients with SLE was 28%, which is a 16% decrease compared to pre-intervention. Implementation of the intervention was assessed by documentation of the post-discharge message sent by the fellow to the nursing staff in the EMR. This was found in 28% of hospitalized SLE patients. Of those patients who had the message and intervention performed, only 1 was readmitted within 30 days.

Conclusion: A quality improvement intervention involving a post-discharge telephone call decreased the 30-day readmission rate among patients with SLE followed at the University of Colorado rheumatology clinic from 44% to 28%. There was overall low implementation of the intervention by the rheumatology fellows, however, this is likely because the intervention was preferentially performed for only the highest risk patients, which was effective in pre-

venting readmission amongst these patients. In the future, we will be working towards more uniform implementation of our intervention. This is one of the first studies to describe a possible intervention to improve the unacceptably high hospital readmission rates among SLE patients.

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Abstract Number: 1208

Outpatient Readmission in Rheumatology: A Machine Learning Predictive Model of Patient's Return to the Clinic

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Background/Purpose: Readmissions can be defined as the return of a patient to a healthcare setting after a discharge. Attention has been mainly focused on readmissions following inpatient hospitalizations. In the outpatient setting, readmissions have been far less studied. As the first step in preventing outpatient readmission, the assessment of the individual patient's risk could be useful to help identify those subjects at greatest risk, so, in a further step we could focus the delivery of an intervention in those patients to reduce their risk. Therefore, our objective was to develop and validate a machine learning predictive model based on Random Forest, to estimate the risk of readmission in an outpatient rheumatology clinic after discharge (outpatient readmission).

Methods: Patients stored in a departmental electronic health record from April 1st, 2007 to November 30th, 2016, and followed-up until November 30th, 2017, were included in this study. Only readmissions taking place between 2 and 12 months after discharge were analyzed. Discharge episodes were split into training, validation and test datasets. Clinical and demographic variables, including diagnoses, treatments, quality of life, and comorbidities, were used as predictors. Models were developed using Random Forest in the training dataset, though the combination of several tuning parameters. Models that maximized the area under the receiver operating characteristic curve (ROC-AUC) in the validation set were assessed in the test set. The model with the highest AUC-ROC in the test dataset was considered as the best final model

Results: 17,772 patients (18,648 discharges episodes) were analyzed and 2,513 (13.5%) discharges episodes were classified as outpatient readmissions. 39,120 possible model combinations were finally tested. The best final model showed an AUC-ROC of 0.677 a sensitivity of 0.479 and a specificity of 0.757. The most important variables were related to follow-up duration, number of previous discharges, corticosteroid and Disease-Modifying Antirheumatic Drugs use, polyarthritis diagnoses, and quality of life

Conclusion: We have developed a predictive model for outpatient readmission in a rheumatology setting. Identification of patients with higher risk could optimize the allocation of healthcare resources

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Patient-reported Outcome Measures in Systemic Lupus Erythematosus: Use in Clinical Practice - Preliminary Results from the Integrate Project

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Table 1: Characteristics of the participating experts (n=167)

		n	%
Gender			
	Male	74	44.3
	Female	93	55.7
Age (years)			
	<=30	11	6.6
	31-40	67	40.1
	41-50	46	27.5
	51-60	31	18.6
	61-70	12	7.2
Years licensed as a physician (years)			
	0-5	15	9.0
	6-10	34	20.4
	11-15	44	26.4
	16-25	38	22.8
	>25	36	21.6
Years licensed as a rheumatologist (years)			
	0-5	62	37.1
	6-10	27	16.2
	11-15	33	19.8
	16-25	31	18.6
	>25	14	8.4
Years treating SLE patients (years)			
	0-5	39	23.4
	6-10	45	27.0
	11-15	28	16.8
	16-25	35	21.0
	>25	20	12.0
SLE patients treated each year			
	0-30	45	27.0
	31-60	34	20.4
	61-90	26	15.6
	>90	62	37.1

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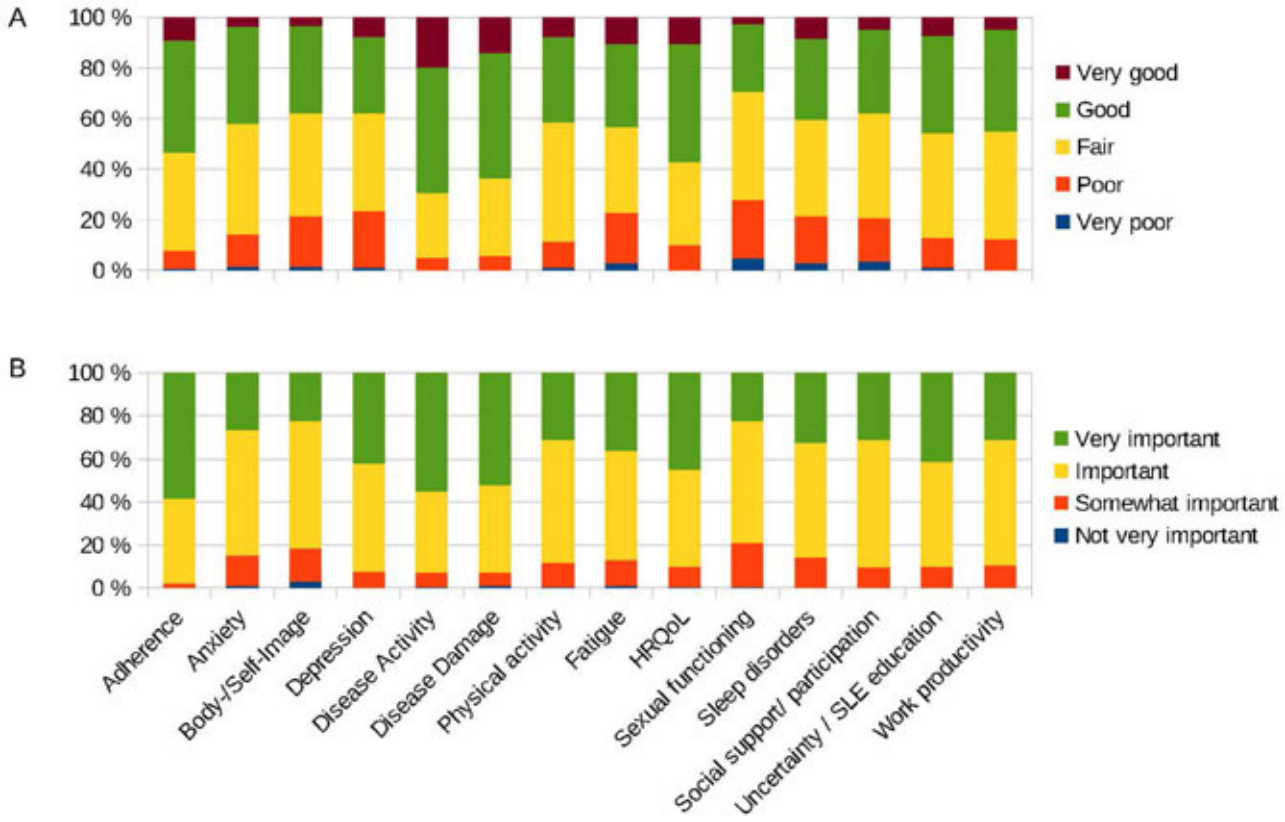
Background/Purpose: Due to improved mortality and morbidity in systemic lupus erythematosus (SLE), non-clinical indicators and outcomes, especially patient-reported ones, have become increasingly important in disease management in the past decades. The objective of our study was to identify dedicated standardized instruments (Patient-reported outcome measures; PROMS) for non-clinical indicators currently in use, and to demonstrate their relevance via their utilization by Lupus experts.

Methods: To identify relevant non-clinical indicators, a systematic literature search was performed using the PubMed database in January 2018. In addition, guidelines, recommendations, consensus reports on the management and monitoring of SLE-patients as well as selected review articles on quality of life, disease burden, and patient-reported outcome were screened. Subsequently, a literature search was conducted for each of the non-clinical indicators to identify all dedicated patient-reported questionnaires in use. A questionnaire for SLE experts was compiled on the basis of the results obtained, covering the utilization of non-clinical indicators, their specific questionnaires and possible obstacles. The questionnaire was distributed to members of the European Lupus Society (SLEuro), as well as other Lupologists.

Figure 1: Self-reported overall experience (A) and the perceived importance (B) of the 14 identified patient-reported outcome domains



Results: A total of 21 non-clinical indicators were identified, 7 of which did not have a standardized questionnaire. For the remaining 14 non-clinical indicators, 50 different questionnaires were found. 167 lupus experts from 43 countries participated in our study, of whom 57% stated to be members of a regional or national reference center for SLE. 73% claimed to treat more than 30 and 37% more than 90 SLE-patients per year (see table 1). Self-reported overall experience and the perceived importance of the 14 identified patient-reported outcome domains by the lupus experts are shown in figure 1. 31% reported to use PROMS to monitor disease outcome in their lupus patients, e.g. for assessing (health-related) quality of life (22.9%) or fatigue (15.7%). The top 5 reasons for not using PROMS were 'Lack of time' 87%, 'Lack of linguistically validated questionnaires' 32%, 'Lack of validated questionnaires' 28%, 'Discordance with my assessment/impression' 15%, and 'Poor credibility of the results' 12%.

Conclusion: Despite the increasing importance of PROMS received for regulatory studies in recent years, their use has not yet become established in routine use among lupus experts. Although numerous PROMS on different endpoints are available, they are relatively rarely used in everyday clinical practice nor for clinical decision-making. Better availability of validated multilingual instruments and better incentives (proven benefit for care, additional remuneration) could contribute to improved utilization.

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Abstract Number: 1210

Utilization of a Multispecialty Team for the Diagnosis of Giant Cell Arteritis Reduces Patient Morbidity

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Background/Purpose: Giant Cell Arteritis (GCA) is an autoimmune vasculitis, most common in older adults with a peak incidence in the seventh decade. The diagnosis is often considered in any patient over age 50 years with new-onset headache, acute visual disturbances, jaw claudication, or elevated inflammatory markers. Because the manifestations of GCA can vary considerably, accurate diagnosis can be challenging. Even in the setting of a negative temporal artery (TA) biopsy, many patients are treated empirically based on the perceived probability of disease. This approach can lead to significant morbidity from prolonged medication exposure and unnecessary procedures. The aim for this project was to look at the impact of a collaborative effort amongst three specialties, rheumatology, neurology, and ophthalmology, a consultation based "GCA team"; the goal of which was to improve how GCA is diagnosed and subsequently managed.

Methods: We conducted a retrospective study of all patients suspected to have GCA at our institution over the last 2.5 years either been seen by the GCA team or not. The GCA team met either in person or had a conference call to discuss each case to make a joint decision regarding the diagnosis and treatment. Data extracted included patient demographics, symptoms on presentation, labs, biopsy results and accumulative prednisone dose.

Results: A total of 36 patients (23 female, 13 male) were evaluated; 26 were seen by the GCA team and 10 were not. The mean ages of patients between the GCA team and No GCA team were similar [71.2 (SD 11.0) vs 70.4 (SD 13.0)], as well as the mean ESR (52.0 vs 54.4), and presenting clinical symptoms: visual complaints (76.9% vs 80.0%) and headache/ jaw claudication/ TA tenderness (46.2% vs 40.0%).

All patients not seen by the GCA team underwent bilateral TA biopsy; however, none were positive on histology. Regardless, all were continued on high dose prednisone with a 6-month cumulative mean dose of 5,350 mg.

Of the 26 patients seen by the GCA team, 10 were determined to be low probability (LP) for GCA and thus were spared TA biopsy. These patients were recommended a rapid steroid taper and the cumulative mean dose of prednisone was only 491 mg. Over 6 months of follow-up, none of these patients had a subsequent diagnosis of GCA.

Compared to patients deemed high probability (HP) by the GCA team, LP patients were younger in age (71.0 vs 74.0), more often female (80% vs 55%), had lower ESR (44.6 vs 72.8), and presented with more visual complaints (70% vs 54.5%).

In the 13 HP GCA patients, 12 underwent TA biopsy (one refused) with 6 biopsies read as positive for GCA. Over 6 months of follow up, none of these patients had flares after they were started on treatment.

Conclusion: While the accuracy of a GCA diagnosis cannot be determined in our cohort of patients not seen by the GCA team, it is likely that evaluation by a multispecialty team would have found several to be low probability for GCA, especially as none of the patients had a positive TA biopsy. By adopting a collaborative approach to diagnosing GCA, unnecessary biopsies and unnecessary corticosteroid exposure can be avoided. More prospective data are needed to provide an accurate assessment of this team approach for GCA which can serve as a model for other healthcare facilities.

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Improving Exercise Counselling of Patients with Inflammatory Arthritis: A Quality Improvement Project

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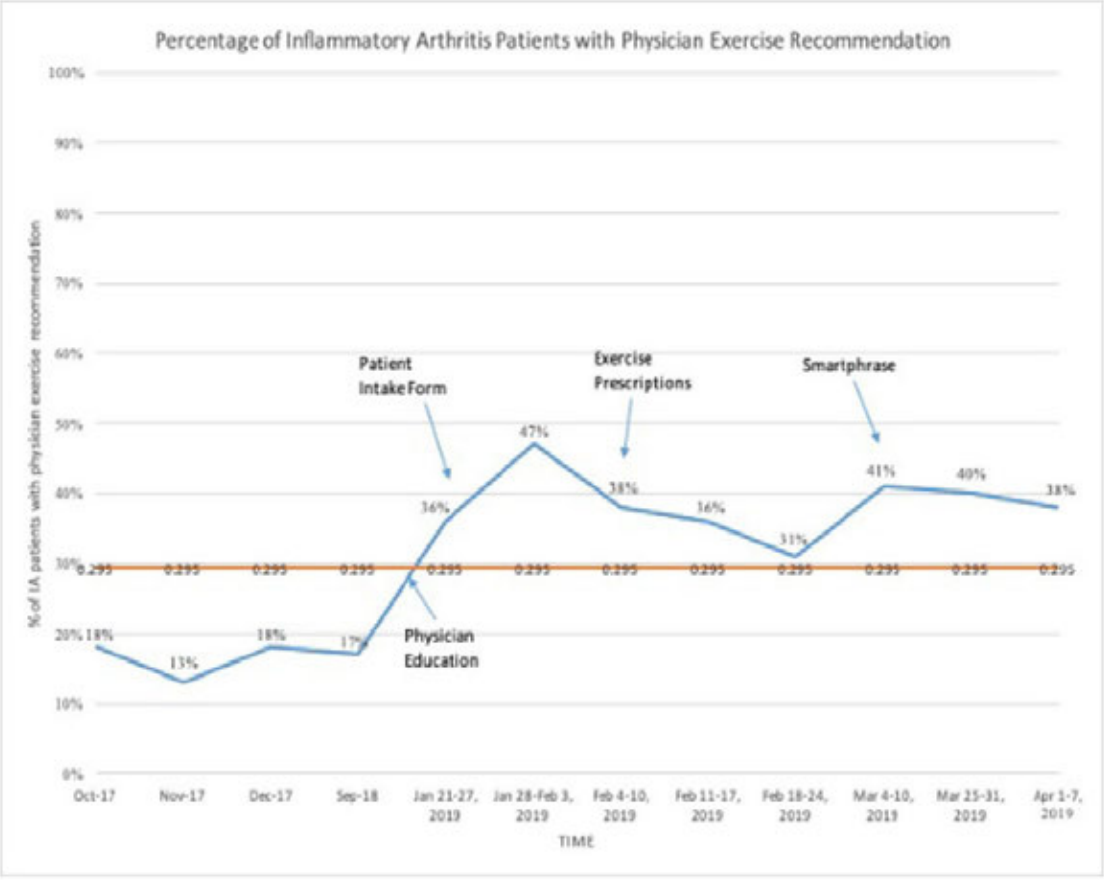
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Regular aerobic exercise has been shown to improve inflammatory arthritis (IA) symptoms and may reduce the risk of cardiovascular events observed in these patients. Practice guidelines recommend regular exercise in the management of patients with IA. Despite this, exercise is infrequently assessed and recommended in routine rheumatology care, and few patients with IA achieve the level of exercise recommended in the Canadian physical activity guidelines. The aim was to increase documentation of physician exercise counselling in patients with IA by 50% by April 30, 2019.

Methods: Baseline data on documented exercise recommendation to patients with IA (defined as a physician diagnosis of rheumatoid arthritis or psoriatic arthritis) were collected at a single academic rheumatology clinic in Toronto, Canada, over four weeks in September 2018. Rheumatologists and patients were interviewed to determine barriers to exercise counselling and uptake. Four Plan-Do-Study-Act (PDSA) cycles were completed between January and April, 2019. Interventions included assessing level of exercise participation on patient intake forms, rheumatologist education, providing a standardized exercise prescription pad in all clinic rooms, creation of a smartphrase to assist electronic record documentation, and poster reminders about exercise counselling in the clinical setting. The primary outcome was the percentage of patients who had documentation of exercise recommendation by their rheumatologist from clinic charts. The weekly percentage of patients with IA, for whom a physician recommendation to exercise was documented, was calculated from a sample (approximately 50%) of weekly follow-up patients.



Run chart demonstrating proportion of patients with inflammatory arthritis who received a physician recommendation to exercise.

Results: Baseline physician exercise recommendation was 15%. Over eight weeks of study, this increased to a mean of 38% (range 31-47%) and showed special cause variation based on eight consecutive points above the mean (Figure). There were no reports of patient adverse events or negative impact on clinical efficiency.

Conclusion: In this quality improvement study, physician education regarding exercise counselling, provision of written exercise prescriptions, education and reminders increased the documentation of physician recommended exercise in patients with IA. Future research is required to determine if increasing exercise counselling translates into increased levels of exercise among IA patients and if this is effective and feasible at other centres.

Disclosure: A. Albasri, None; **T. Al-Araimi**, None; **S. Gottheil**, None; **L. King**, None; **S. Koppikar**, None; **J. Shamis**, None; **S. Lake**, None; **G. Natasha**, None.

Abstract Number: 1212

Psychological Profile in Patients with Rheumatic Diseases in China: A Study of HADS Self-assessment with Smart System of Disease Management (SSDM)

Yongfu Wang,[1] Jianhong Wu,[2] Yasong Li,[3] Henglian Wu,[4] Yang li,[5] Hua Wei,[6] Xiaoqi Chen,[7] Bin Wu,[8] Zhenbin li,[9] Jinli Ru,[10] Wenqiang Fan,[11] Shengguang Li,[12] Fang He,[13] Yi Zhao,[14] Fen Li,[15] Bin Wu,[16] Feng Wang,[17] Miaojia Zhang,[18] Lirong Kang,[19] Hui Xiao,[20] Yuhua Jia,[21] Bing Wu,[22] Fei Xiao,[23] and Hui Song[24], [1]The First Affiliated Hospital of BaoTou Medical College, Baotou, Nei Mongol, China (People's Republic), [2]Dazhou Central Hospital, Dazhou, Sichuan, China (People's Republic), [3]Zhejiang provincial people's hospital, Hangzhou, Zhejiang, China (People's Republic), [4]Dongguan donghua hospital, Dongguan, Guangdong, China (People's Republic), [5]The Second Affiliated Hospital of Harbin Medical University, Haerbin, China (People's Republic), [6]Northern Jiangsu People's Hospital, Yangzhou, China (People's Republic), [7]Zhongnan Hospital of Wuhan University, wuhan, China (People's Republic), [8]The First People's Hospital of Jingzhou, jingzhou, China (People's Republic), [9]The 980th Hospital of the PLA Joint Logistic Support Force, shijiazhuang, China (People's Republic), [10]The Second Hospital of Shanxi Medical University, Shanxi, Shanxi, China (People's Republic), [11]Central Hospital of XinXiang, Xinxiang, Hainan, China (People's Republic), [12]Peking University International Hospital, beijing, China (People's Republic), [13]Suining Central Hospital, suining, China (People's Republic), [14]Xuanwu Hospital, Capital Medical University, Beijing, China, beijing, China (People's Republic), [15]The Second Xiangya Hospital of Central South University, changsha, China (People's Republic), [16]Chongqing Hospital of Traditional Chinese Medicine, Chongqing, Chongqing, China (People's Republic), [17]Central Hospital of Xiangyang, xiangyang, China (People's Republic), [18]Jiangsu Province Hospital, The first affiliated hospital of Nanjing medical university, nanjing, China (People's Republic), [19]The First Affiliated Hospital of BaoTou Medical College, baotou, China (People's Republic), [20]Shanghai Gothic Internet Technology Co., Ltd, shanghai, Shanghai, China (People's Republic), [21]Shanghai Gothic Internet Technology Co., Ltd., Shanghai, Shanghai, China (People's Republic), [22]Shanghai Gothic Internet Technology Co., Ltd, Shanghai, China (People's Republic), [23]Shanghai Gothic Internet Technology Co., Ltd., shanghai, China (People's Republic), [24]Beijing Jishuitan Hospital, Beijing, Beijing, China (People's Republic)

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Measures Of Healthcare Quality Poster II: Improving Care
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The patients with chronic diseases such as rheumatic diseases suffer from physical pain and/or disability. In addition, psychological morbidities have also been found in patients with rheumatic diseases. Hospital Anxiety and Depression Scale (HADS) is commonly applied to assess the mental health of patients with rheumatic diseases.

Smart System of Disease Management (SSDM) is a mobile application which has two application systems for both patients and doctors for rheumatic diseases management. The patient application system provides functions includ-

Table 1. Prevalence of anxiety and depression in patients with rheumatic diseases

Disease	Frequency no. (%)	Female (%)	Age (years)		Anxiety (%)	Depression (%)
			Mean	SD		
RA	12203 (37%)	85%	49.98	17.1	10%	18%
SLE	6327 (19%)	94%	36.03	12.94	12%	21%
SS	2423 (7%)	94%	46.77	14.36	14%	21%
AS	1918 (6%)	42%	32.34	12.11	14%	21%
Gout	1104 (3%)	33%	43.80	15.8	11%	18%
OA	1057 (3%)	80%	49.50	15.8	13%	20%
MCTD	963 (3%)	94%	42.94	14.47	12%	21%
UCTD	935 (3%)	93%	37.59	12.32	13%	19%
PM/DM	863 (3%)	75%	44.86	15.14	10%	17%
APS	442 (1%)	96%	33.36	7.49	9%	14%
Scleroderma	330 (1%)	86%	44.91	13.59	11%	21%
Vasculitis	294 (1%)	68%	47.84	17.74	14%	21%
BD	230 (1%)	72%	39.04	12.73	16%	18%
PsA	263 (1%)	65%	40.65	12.87	10%	15%
Others	3941 (12%)	79%	42.18	15.35	11%	19%
Total	33293 (100%)	81%	41.34	16.55	12%	19%

ing self-assessment, medication management, adverse events management and laboratory records. After input by patients, all the data will be synchronized to the mobile terminal of authorized rheumatologists. Based on these data, rheumatologists can evaluate and follow up with their patients and provide consultation service through SSDM via text or voice message. The rheumatologists can also adjust therapeutic regimens based on patients' profiles.

The purpose of this study is to explore the profile of psychological morbidities in patients with rheumatic diseases.

Methods: The patients were educated and trained to perform HADS assessments using SSDM by the rheumatologists. The HADS self-assessments data could be extracted from the mobile terminal for further analysis. The HADS scale consists of two subscales for anxiety (HADS-A) and depression (HADS-D) which have 7 items, respectively. Both subscales range from 0 to 21, with higher scores indicating greater anxiety and depression. A score between 11 and 21 indicates a probable case of anxiety or depression.

Results: From June 2016 to May 2019, 33,293 adult patients (82% females; 18% males) with a mean age of 41.34 ± 16.55 years from 380 hospitals performed self-evaluation of HADS using SSDM. 34 rheumatic diseases were assessed, including RA (12,203; 37%), SLE (6,327; 19%), SS (2,423, 7%), AS (1,918; 6%), gout (1,104; 3%), OA (1,057; 3%), MCTD (963; 3%), UCTD (935; 3%), PM/DM (864; 3%), etc.

Table 1 presents the number and percentage of patients with rheumatic diseases accompanied by anxiety or depression. The ratio of probable anxiety was 10% in RA, 12% in SLE, 14% in SS, 14% in AS, 11% in Gout, 13% in OA, 12% in MCTD, 13% in UCTD and 10% in PM/DM. The prevalence of probable depression was 18% in RA, 21% in SLE, 21% in SS, 21% in AS, 18% in Gout, 20% in OA, 21% in MCTD, 19% in UCTD and 17% in PM/DM.

Conclusion: SSDM can be used for HADS self-assessments by patients with rheumatic diseases. RA was recorded as the most prevalent condition, followed by SLE. 10% to 21% patients could be classified as probable case of anx-

iety or depression according to HADS scores. The prevalence of anxiety was usually lower than that of depression in patients with rheumatic diseases in this study.

Disclosure: Y. Wang, None; **J. Wu**, None; **Y. Li**, None; **H. Wu**, None; **Y. li**, None; **H. Wei**, None; **X. Chen**, None; **B. Wu**, None; **Z. li**, None; **J. Ru**, None; **W. Fan**, None; **S. Li**, None; **F. He**, None; **Y. Zhao**, None; **F. Li**, None; **B. Wu**, None; **F. Wang**, None; **M. Zhang**, None; **L. Kang**, None; **H. Xiao**, None; **Y. Jia**, None; **B. Wu**, None; **F. Xiao**, None; **H. Song**, None.

Abstract Number: 1213

A Retrospective Review and Prospective Intervention for Outpatient Follow-Up of Hospitalized Patients in Rheumatology

Shakaib Hayat,[1] and Stanley Ballou[2], [1]Case Western Reserve University (MetroHealth), Cleveland, OH, [2]Metrohealth medical center, Cleveland, OH

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Measures Of Healthcare Quality Poster II: Improving Care
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: There is lack of appropriate outpatient follow-up (F/U) for hospitalized rheumatology patients, which can result in disease recurrence and recurrent inpatient admissions[1]. This is a financial burden on the

Table 1a	Comparison of follow-up patients			
	Total	Followed Up		
	no.	no. (%)		
Pre-intervention	24	8 (33.33)		
Post-intervention	17	10 (58.82)		
Table 1b	**Comparison of follow-up patients by repeat admission: no. (%)**			
	No repeat admission	Repeat admission		
Pre-intervention	6 (40)	2 (22.22)		
Post-intervention	10 (66.66)	0 (0)		
Table 1c	**Comparison of follow-up patients by method of appointment: no. (%)**			
	Phone (post hosp.)	Prior to/at discharge	Letter	None
Pre-intervention	4 (50)	2 (25)	1 (100)	1 (14.29)
Total	8 (33.33)	9 (33.33)	1 (4.17)	7 (29.17)
Post-intervention	0 (0)	10 (62.5)	0 (0)	0 (0)
Total	0 (0)	16 (94.12)	0 (0)	1 (5.88)
Table 1d	**Comparison of follow-up patients that are established rheumatology patients vs new: no. (%)**			
	Established	New		
Pre-intervention	6 (46.15)	2 (18.18)		
Post-intervention	6 (66.66)	4 (50)		
Table 1e	**Comparison of follow-up patients by disposition: no. (%)**			
	Home	Nursing Home	LTAC	Transferred to another facility
Pre-intervention	7 (46.66)	1 (11.11)	0 (0)	0 (0)
Post-intervention	5 (55.55)	4 (66.66)	0 (0)	1 (100)

Table 2	Comparison of follow-up patients by addition of new high risk medication changes: no. (%)						
	High dose steroids	Lower dose steroids	Colchicine	DMARD	NSAID	Allopurinol	None
Pre-intervention	3 (50)	1 (25)	1 (25)	2 (100)	0 (0)	0 (0)	1 (14.28)
Total	6 (25)	4 (16.67)	4 (16.67)	2 (8.33)	1 (4.17)	0 (0)	7 (29.17)
Post intervention	4 (66.66)	3 (60)	0 (0)	3 (100)	0 (0)	1 (100)	2 (50
Total	6 (35.29)	5 (29.41)	1 (5.88)	3 (17.65)	0 (0)	1 (5.88)	4 (23.53)

Table 3a	Comparison of follow-up patients by race: no. (%)			
	Black	White	Hispanic/ Puerto	
Pre-intervention	4 (33.33)	3 (30)	1 (0.5)	
Post-intervention	6 (66.66)	3 (42.8)	1 (100)	
Table 3b	**Comparison of follow-up patients with PCP vs without PCP: no. (%)**			
	PCP	No PCP		
Pre-intervention	8 (40)	0 (0)		
Post-intervention	9 (69.2)	1 (25)		
Table 3c	**Comparison of follow-up patients by diagnosis and reason for consult: no. (%)**			
	Crystal arthritis	CTD	Vasculitis	Other
Pre-intervention	1 (20)	6 (40)	1 (33.33)	0 (0)
Post-intervention	2 (50)	4 (57.14)	3 (60)	1 (100)
Table 3d	**Comparison of follow-up patients by insurance type: no. (%)**			
	Medicaid/Medicare	Private	None and/or financial assistance	
Pre-intervention	6 (31.58)	2 (40)	0 (0)	
Post-intervention	6 (50)	3 (100)	1 (50)	

healthcare system due to unnecessary hospital admissions and emergency room visits[2]. Inpatients are often started on high risk medications. Due to lack of F/U in management, they may be at risk of developing adverse events.

Methods: We initiated an IRB-approved retrospective analysis on all hospitalized patients at an urban academic medical center who underwent a rheumatology consultation from 7/17/2017 – 8/31/2017, and whom were expected to follow up in clinic. Tabulated data for each patient included whether the patient followed up within 2 weeks of their expected appointment along with several variables. We subsequently conducted a prospective intervention study for all consulted inpatients during 2/1/2019 – 3/15/2019, which involved: 1) Each patient was explained the importance of F/U (particularly skilled nursing facility (SNF) patients). 2) A business card was provided with appointment date and time. 3) The consult team assured that administrative staff contacted each patient for a convenient appointment if unable to be made during hospitalization before discharge. 4) Disease-specific handouts were given to each patient, particularly gout patients. 5) Financial barriers were addressed by an inpatient social worker, and the option to follow up at satellite campuses was offered. Retrospective analysis was then repeated on data from this intervention group.

Results: The pre-intervention group had an overall low percentage of F/U (33%). Important contributors to low follow up included: patients without an established rheumatologist (18%), patients with no appointment made for F/U (29%), and patients discharged to a SNF (11%).

The post-intervention group (versus the pre-intervention group) had a higher percentage of post-discharge F/U for all patients (58% vs 33%). The post-intervention group F/U rate was also higher for the following: patients without repeat admission (66% vs 40%), scheduling of F/U appointment before discharge (62% vs 25%), patients without established rheumatologist (50% vs 18%), and patients discharged to SNF (66% vs 11%). Interestingly, among specific diseases analyzed (CTD, vasculitis, other), patients admitted for crystal-induced arthritis had the greatest improvement in F/U rate (50% vs 20%). All other categories examined showed improvement in the post-intervention group F/U rate as well.

Conclusion: A systems-based intervention is effective in improving outpatient follow up for hospitalized rheumatology patients. Particular focus should be on patient education, addressing financial and transportation barriers, and arranging follow up before discharge, all in a protocolized manner.

References:

1. Jackson C, et al. Timeliness of Outpatient Follow-up: An Evidence-Based Approach for Planning After Hospital Discharge. Ann Fam Med Mar 2015 vol. 13 no. 2 115-122.
2. Thomas EJ, et al. Patient noncompliance with medical advice after the emergency department visit. Ann Emerg Med. 1996 Jan;27(1):49-55.

Disclosure: S. Hayat, None; **S. Ballou**, None.

Abstract Number: 1214

The Effects of Pegloticase on Mean Arterial Blood Pressure: An Age Modulated Relationship?

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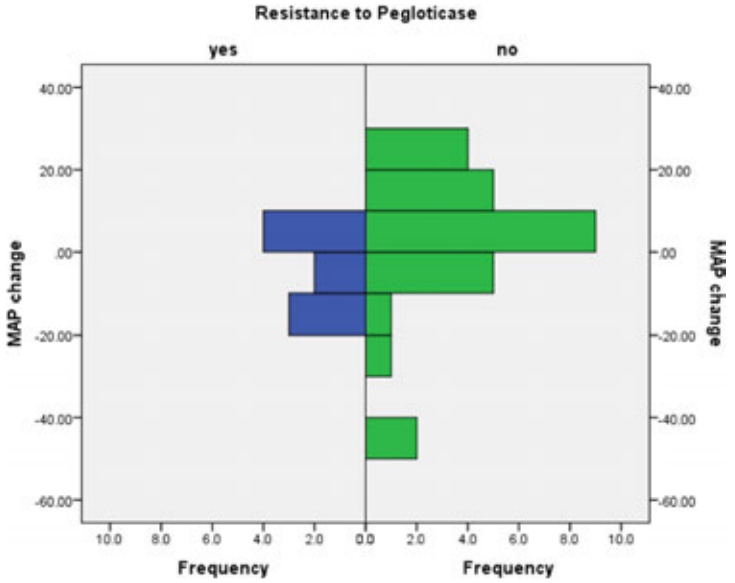
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Multiple studies indicate hyperuricemia as an independent risk factor for hypertension. However, the association is found to be age-dependent and weakens as the patient age. We determined the effect of Pegloticase (a plasma uric acid lowering agent) induced low serum uric acid level on mean arterial blood pressure (MAP). We also studied the following possible confounders to the MAP lowering effects of Pegloticase as mentioned above: Body Mass Index (BMI) estimated Glomerular Filtration Rate (eGFR) and Random Blood Sugar (RBS).

Methods: This retrospective study was conducted at the outpatient clinical department of Buffalo Rheumatology and Medicine. Catholic Health Institutional Review Board ethically approved the study. We recruited 36 patients of age 40 years o above receiving Pegloticase 8mg every two weeks. Patients were divided into two groups: responder and non-responder to Pegloticase, based upon individual serum uric acid levels (< 2mg/dl serum uric acid level was considered to be a response to Pegloticase). The difference in Mean Arterial Pressure (MAP) was noted when treatment was begun until when treatment was completed. A similar trend of difference in following confounders was observed at initiation and completion of therapy: BMI, eGFR and RBS. The data were analysed separately for the Pegloticase resistant and non-resistant group through SPSS 16.0.



Population pyramid showing Mean Arterial Pressure change in the Pegloticase resistant and non-resistant group.

	MAP mmHg	MAP mmHg	Systolic BP mmHg	Systolic BP mmHg	Diastolic BP mmHg	Diastolic BP mmHg
	Pre-Drug	Post-Drug	Pre-Drug	Post-Drug	Pre-Drug	Post-Drug
MEAN	100.26	99.86	141.31	141.64	79.75	78.97
STANDARD DEVIATION	12.008	18.10	17.67	26.43	14	16.65
MINIMUM	77	67.33	107	108	53	42
MAXIMUM	122.67	154.67	179	222	110	136
MEDIAN	101.16	97.83	140	131.5	77.5	77.5

The pre- and post- Pegloticase descriptive statistics for blood pressure

Results: Our study sample included 28 males (77.8 %) and 8 females (22.2 %). The mean age of patients was 67.89 years ± 12.97 SD. Patients' baseline characteristics are summarised in table 1. Each patient received 8 mg of a sustained dose of Pegloticase for a mean of 7.56 months. No statistically significant change in MAP was noted in either responder (t=-1.19, p=0.266) or non-responder group (t=0.534, p=0.598) from the time when therapy was initiated to when therapy was completed. Mean arterial pressure difference remains statistically non- significant and same across different durations of Pegloticase use (p =0.154). Furthermore, no statistically significant change

was noted in following confounders for recruited patients: the eGFR (Z=-1.44, p=0.150), RBS (Z=-0.729, p= 0.46) and BMI (Z=-1.538,p=0.124).

Conclusion: Our study doesn't show any significant change in the mean arterial pressure irrespective of the effect of Pegloticase on serum uric acid levels. This could be because most of our recruited patients were elderly with a mean age of 67.89 years ± 12.97 SD. Thus one can conclude that the relationship of uric acid with hypertension appears to be dampened with age. Although our results could be consistent with a differential role for uric acid in age-related hypertension, other possibilities remain. For example, uric acid may be associated with only certain forms of hypertension (e.g. one accompanying metabolic syndrome) as opposed to the isolated systolic hypertension related to arterial stiffening. More large-scale clinical studies are needed in this regard to dissect the role of uric acid in hypertensive individuals. We also did not find any significant changes in the considered confounding variables from the beginning towards the end of the study, indicating age as a significant determinant for Pegloticase induced lowering of MAP.

Disclosure: S. Waheed, None; **H. Zubair**, None; **a. ubaid**, None; **f. waheed**, None; **L. Burns**, None.

Abstract Number: 1215

A Multicenter, Randomized, Double-blind, Placebo-controlled, Dose-Ranging Study to Evaluate Efficacy and Tolerability of SHR4640 in Patients with Hyperuricemia

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hyperuricemia, a common metabolic disorder, predisposes patients to develop gout due to the deposition of insoluble urate in joints. Safety concerns are frequently raised with commonly prescribed uricosurics. The purpose of present trial is to assess the efficacy and safety of SHR4640 - a highly selective URAT1 inhibitor in hyperuricemic subjects in China.

Methods: Subjects with gout and serum uric acid (sUA) ≥480 μmol/L, or subjects without gout but with (sUA ≥480 μmol/L) or without (sUA ≥540 μmol/L) cardiovascular dysfunction were enrolled. All eligible subjects were randomly assigned (1:1:1:1:1) to monotherapy of SHR4640 2.5, 5, 10 mg, benzbromarone 50 mg and placebo, respectively. The primary endpoint was the proportion of subjects achieving sUA target of ≤360 μmol/L after 5-week treatment. This trial was registered with ClinicalTrials.gov, NCT03185793.

Results: A total of 197 subjects received assigned treatments. Subjects were predominantly male (99.5%) and associated with gout (95.9%), with a median age of 41.0 years (range, 18.0 to 69.0). The sUA targets were achieved in 32.5%, 72.5% and 61.5% of subjects receiving SHR4640 5 mg, 10 mg and benzbromarone 50 mg, respectively, which were significantly higher than that of placebo (0%, $P < 0.05$, Figure 1). The sUA was 596.2 ± 87.5 μmol/L at the baseline, and was reduced by 18.0%, 32.2%, 47.0% and 41.4% after 5-week treatment with SHR4640 2.5 mg, 5

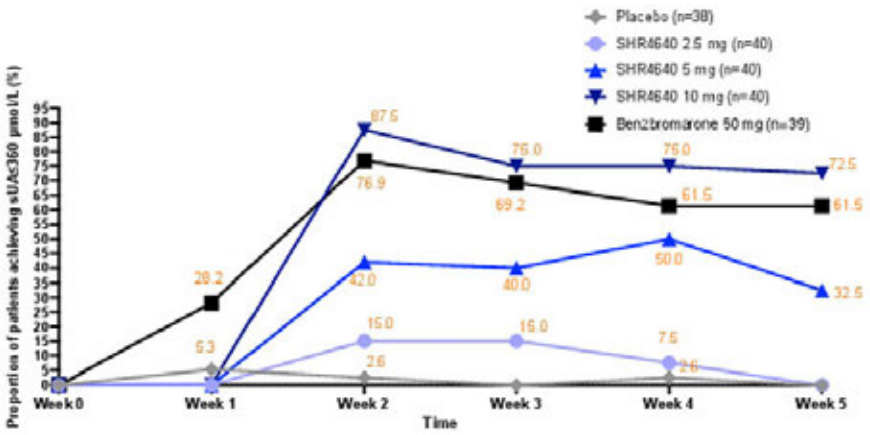

Figure 1. Proportion of patients achieving serum urate (sUA) target levels of ≤360μmol/l by week 1-5. The starting dose of SHR4640 and benzbromarone were 1 and 25 mg once daily at week 1, respectively, and then increased to the fixed dose at weeks 2-5.

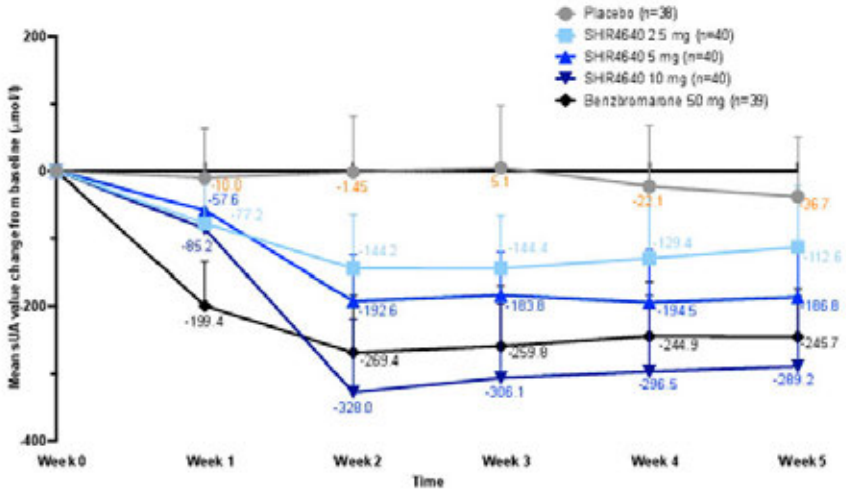

Figure 2. Serum urate (sUA) value change from baseline at each study visit. Values are the mean±SD. The starting dose of SHR4640 and benzbromarone were 1 and 25 mg once daily at week 1, respectively, and then increased to the fixed dose at weeks 2-5.

mg, 10 mg and benzbromarone 50 mg, respectively, which were significantly greater than that of placebo (5.8%, $P < 0.05$, Figure 2). The incidence of gout flare requiring intervention was similar across all groups. SHR4640 was well-tolerated. Occurrences of AEs were comparable across all treatment groups, although the incidence of transient elevated serum creatinine was slightly higher in SHR4640 10 mg as comparing with others (serum creatinine elevations between 1.5-fold and 2-fold over baseline occurred in 5.0% [n=2] of patients on SHR4640 10 mg, 0% in other groups, Table 1). Serious AE including death was not reported.

Table 1. Adverse events.

Adverse event	Placebo (N=38)	SHR4640 2.5 mg (N=40)	SHR4640 5 mg (N=40)	SHR4640 10 mg (N=40)	Benzbromarone 50 mg (N=39)	SHR4640 total (N=120)
Gout flares	14 (36.8)	17 (42.5)	19 (47.5)	17 (42.5)	18 (46.2)	53 (44.2)
Upper respiratory infection	3 (7.9)	8 (20.0)	5 (12.5)	8 (20.0)	10 (25.6)	21 (17.5)
Diarrhea	1 (2.6)	3 (7.5)	5 (12.5)	2 (5.0)	1 (2.6)	10 (8.3)
Hyperlipidemia	2 (5.3)	4 (10.0)	3 (7.5)	2 (5.0)	1 (2.6)	9 (7.5)
Arthralgia	1 (2.6)	1 (2.5)	4 (10.0)	4 (10.0)	2 (5.1)	9 (7.5)
Elevated serum creatinine	3 (7.9)	0	3 (7.5)	5 (12.5)	0	8 (6.7)
Alanine aminotransferase increased	1 (2.6)	2 (5.0)	4 (10.0)	1 (2.5)	2 (5.1)	7 (5.8)
Hypertriglyceridemia	2 (5.3)	0	2 (5.0)	4 (10.0)	3 (7.7)	6 (5.0)
Leukocytosis	1 (2.6)	1 (2.5)	1 (2.5)	2 (5.0)	1 (2.6)	4 (3.3)
Neutrophil count increased	0	1 (2.5)	1 (2.5)	2 (5.0)	0	4 (3.3)
Back pain	2 (5.3)	2 (5.0)	1 (2.5)	1 (2.5)	1 (2.6)	4 (3.3)

Conclusion: The present trial demonstrated greater sUA-lowering effect of SHR4640 5 mg and 10 mg versus placebo, with a generally tolerable safety profile. SHR4640 represents a new treatment option for subjects with hyperuricemia in China.

Disclosure: Y. Lin, None; **X. Chen**, None; **P. Ye**, None; **W. Geng**, None; **R. Ning**, Jiangsu Hengrui Medicine Co., Ltd, 3; **Y. Tai**, Jiangsu Hengrui Medicine Co., Ltd, 3; **C. Bao**, None.

Abstract Number: 1216

Pilot, Randomized, Double-Blinded, Placebo Controlled Efficacy AndSafety Study of a Transdermal Alkalinizing and Pain Relieving Treatment ForAcute Gout Flare

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is characterized by a build-up of uric acid crystals in and around the joints. Uric acid crystal formation and dissolution is affected by pH. There are reports in the literature of the use of alkalization agents, such as sodium bicarbonate, to treat gout. Theoretically, an alkalinizing agent such as sodium bicarbonate (baking soda) may increase the systemic and/or local pH and may allow pH sensitive uric acid crystals to dissolve

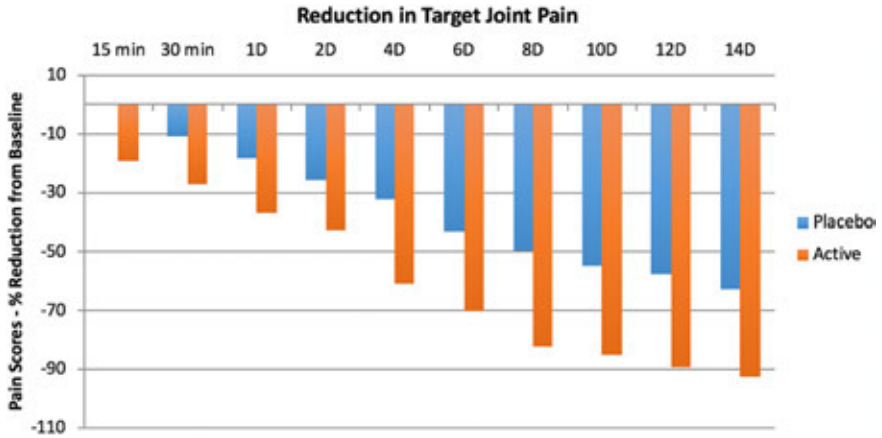


Figure 1. The active treatment subjects (N=12) had pain scores that averaged about 1.3 points lower than the placebo patients (N=12) (p=0.0041). The figure shows the % reduction in pain scores over time in the target joint.

resulting in temporary relief of pain and shortening duration of a gout flare, however oral sodium bicarbonate use causes intolerable gastrointestinal side-effects. Purpose of study was to determine if sodium bicarbonate in a patented transdermal drug delivery system can effectively and safely reduce pain and shorten duration of an acute gout flare. This delivery system has been shown to effectively deliver sodium bicarbonate transdermally in prior animal and human studies.

Methods: This pilot study is prospective, double-blinded, randomized, and placebo-controlled in design. Twenty-four subjects, female and male, aged 18+, with clinical diagnosis of gout, history of uric acid >6.8mg/dl, on stable medication regimen, presenting in clinic within 36 hours of initiation of acute gout attack and prescribed 0.6 mg/ daily colchicine were included. Exclusion criteria included >stage 3 kidney disease, tophaceous gout, and recent/ concurrent initiation of other pain medications (e.g. NSAID, corticosterioids). Subjects were randomized to receive placebo lotion or sodium bicarbonate transdermal lotion (33% sodium bicarbonate and 0.5% menthol) and instructed to apply to the entire limb of up to three affected joints (target joint and up to two other joints). Outcome measures included pain (numeric rating scale, 0-10), time to resolution (50% reduction in pain), range of motion and subject satisfaction. Time-points were baseline,15 & 30 min, and 1,2,4,6,8,10,12, and 14 days. Adverse events were collected. Statistical analysis was repeated measures ANOVA with $p< 0.05$ as significant.

Results: The active treatment subjects (N=12) had pain scores that averaged about 1.3 points lower than the placebo patients (N=12) (p=0.004). The figure shows the % reduction in pain scores over time in the target joint. The secondary joint (N=9 for both groups) also had a significant (p=0.04) reduction in pain with average pain of 1.2 points lower than control. The mean time to resolution for the target joint was 4.1 days in placebo group and 2.2 days in the active group. The mean time to resolution for the secondary joint was 2.8 days in the control group and 1.6 days in the active group. Among those who attained improved ROM, average time was 2.5 days in placebo group and 1.7 days in active group. No treatment related adverse events reported.

Conclusion: Topical transdermal sodium bicarbonate lotion use resulted in a highly significant (p=0.004) reduction in pain, as early as 15 min, and may speed resolution of acute gout attacks and improvement of range of motion.

Disclosure: S. Reddy, None; **R. Mabaquiao**, None; **L. Misell**, Dyve Biosciences, 3, 4.

Abstract Number: 1217

Phase 2 Dose-ranging Study of SEL-212 in Symptomatic Gout Patients: Selection of Doses for Further Clinical Development

Rehan Azeem,[1] Alan Kivitz,[2] Horacio Plotkin,[1] Lloyd Johnston,[1] Takashi K. Kishimoto,[1] Justin Park,[1] Stephen Smolinski,[1] and Wesley DeHaan[1], [1]Selecta Biosciences, Watertown, MA, [2]Altoona Center for Clinical Research, Duncansville, PA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is caused by the deposition of monosodium urate (MSU) crystals in joints due to chronic hyperuricemia. Long-term treatment focuses on reducing serum uric acid (sUA) levels, thus allowing MSU crystals to dissolve. Administration of uricase, a non-human enzyme that catalyzes the conversion of uric acid into the water-soluble allantoin, has emerged as a therapy for the treatment of patients with gout that is refractory to conventional treatments. Currently approved uricase products are immunogenic, which results in decreased efficacy as anti-drug antibodies (ADAs) develop as well as increased safety concerns. SEL-212 is a novel combination product consisting of pegadricase co-administered with proprietary ImmTOR tolerogenic nanoparticles. ImmTOR has been designed to mitigate the formation of ADAs to pegadricase by inducing tolerogenic dendritic cells and antigen-specific regulatory T cells. Mitigating the formation of ADAs is vital in maintaining a sustained control of sUA levels in patients. Here we describe the results of a Phase 2 clinical trial (NCT02959918) designed to identify the appropriate doses of the 2 components for further development of SEL-212.

Methods: In this open-label dose-ranging study, patients with symptomatic gout (≥1 tophus, gout flare within previous 6 mo, and/or gouty arthropathy) and hyperuricemia (sUA ≥6 mg/dL) were enrolled and treated with pegadricase at 0.2 or 0.4 mg/kg alone, or combined with 0.05 to 0.15 mg/kg ImmTOR. Treatments were administered intravenously monthly for 3 cycles of SEL-212, followed by 2 additional cycles with pegadricase alone or SEL-212 (see **Table**). Dosing was stopped in patients demonstrating sUA ≥1.0 mg/dL on Day 21 after the previous dose. Safety, tolerability, sUA, ADAs, and clinical outcomes were monitored throughout the study.

Results: A total of 152 patients enrolled in the study. The average age was 54.8 (range 23-75) years, most were male (90.8%), and the mean duration of symptomatic gout was 8.0 years. When administered alone at either dose, pegadricase resulted in a rapid reduction in sUA, which was not sustained due to ADA formation in 5 of 6 patients. The addition of ImmTOR at ≥0.1 mg/kg reduced ADA formation, allowing sustained reduction in sUA, but these responses were attenuated when ImmTOR was removed during cycles 4 and 5. The combination of pegadricase (0.2 mg/kg) and ImmTOR (0.1 or 0.15 mg/kg) was given during all 5 cycles in 3 additional cohorts. In these cohorts, 66% of evaluable patients (21/32) maintained sUA levels below 6 mg/dL at Week 20 after 5 monthly doses of SEL-212, and 100% of patients who had sUA < 6 mg/dL at 12 weeks maintained control through 20 weeks. Sustained reduction of sUA levels correlated with low or no ADAs. The percentage of patients experiencing flares in these 3 cohorts declined from 35% during month 1 to 9%-10% during months 3, 4, and 5.

Conclusion: Based on these results, the combination of pegadricase (0.2 mg/kg) and ImmTOR (0.15 mg/kg) were selected for use in a head-to-head comparison study of SEL-212 to pegloticase, a pegylated uricase currently FDA approved for use in patients with treatment-refractory gout (NCT03905512).

Pegadricase dose mg/kg	ImmTOR dose mg/kg	Evaluable patients, n
0.02	0.08[a]	6
0.04	0.08[a]	8
0.02	0.1[a]	10
0.04	0.1[a]	10
0.04	0.125[a]	8
0.02	0.15[a]	9
0.04	0.15[a]	11
0.02	0.15[b]	18
0.02	0.15/0.1[b,c]	6
0.02	0.1[b]	8

[a]ImmTOR was given with the first 3 of 5 monthly treatments.
[b]ImmTOR was given with all 5 monthly treatments.
[c]ImmTOR was dosed at 0.15 mg/kg in the first treatment and at 0.1 mg/kg at the subsequent treatments.

Cohort layout for ImmTOR dose of 0.08 mg/kg and above

Disclosure: R. Azeem, Selecta Biosciences, 1, 3; **A. Kivitz**, AbbVie, 5, Amgen, 1, 4, 5, Boehringer Ingeleheim, 5, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 5, 8, Flexion Therapeutics, 8, Genzyme, 5, 8, Gilead, 1, 4, 5, Gilead Sciences, Inc., 4, Horizon, 8, Janssen, 5, Janssen Research & Development, LLC, 2, Merck, 8, Novartis, 1, 4, 8, Pfizer, 1, 4, 5, 8, Regeneron, 1, 5, 8, Sanofi, 1, 4, 5, 8, Sun Pharma, 5, SUN Pharma Advanced Research, 5, UCB, 5; **H. Plotkin**, Selecta Biosciences, 1, 3; **L. Johnston**, Selecta Biosciences, 1, 3; **T. Kishimoto**, Selecta Biosciences, 1, 3; **J. Park**, Selecta Biosciences, 1, 3; **S. Smolinski**, Selecta Biosciences, 1, 3; **W. DeHaan**, Selecta Biosciences, 1, 3.

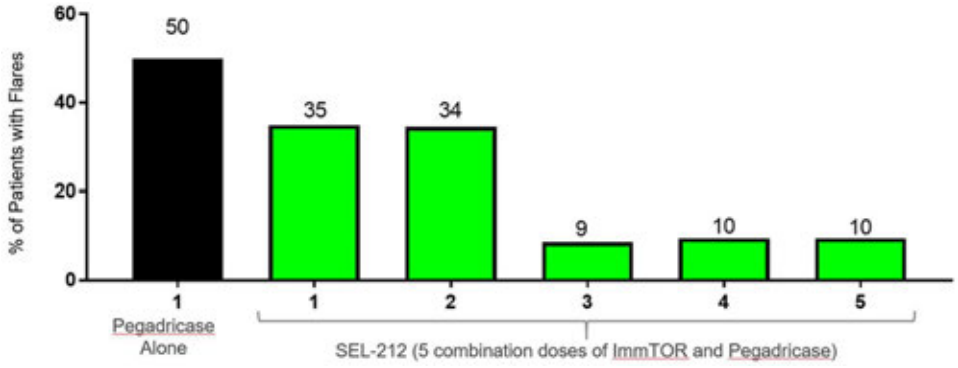
Abstract Number: 1218

Monthly Dosing of ImmTOR Tolerogenic Nanoparticles Combined with Pegylated Uricase (Pegadricase) Enables Sustained Reduction of Acute Gout Flares in Symptomatic Gout Patients

Rehan Azeem,[1] Justin Park,[1] Horacio Plotkin,[1] Alan Kivitz,[2] Lloyd Johnston,[1] Takashi K. Kishimoto,[1] Stephen Smolinski,[1] and Wesley DeHaan[1], [1]Selecta Biosciences, Watertown, MA, [2]Altoona Center for Clinical Research, Duncansville, PA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Long term gout treatment focuses on reducing sUA levels, thus allowing MSU crystals to dissolve. Rapid dissolution of MSU crystals during initial phase of urate lowering therapy (ULT) is associated with an increased incidence (75%) and frequency (2.1 flares/patient/month)* of acute gout flares contributing to poor treatment compliance. During ULT initiation, colchicine, NSAIDs or corticosteroids are used for gout flare prophylaxis. Pegylated uricases are therapies for the treatment of chronic gout. However, their efficacy and safety are limited by induction of anti-drug antibodies (ADA). SEL-212 is a novel combination product consisting of pegadricase co-



% of Patients with Flare by Treatment Month

administered with proprietary ImmTOR tolerogenic nanoparticles. We report here data on gout flares from a Phase 2 study in symptomatic gout patients.

Methods: Patients with symptomatic gout (≥1 tophus, gout flare within 6 months or gouty arthropathy) and elevated serum uric acid (sUA) ≥6 mg/dL were randomized to receive doses of pegadricase (0.2 mg/kg or 0.4 mg/kg) alone or in combination with ImmTOR (0.05 to 0.15 mg/kg). Treatments were administered intravenously monthly for 3 cycles of SEL-212, followed by 2 additional cycles with pegadricase alone or SEL-212. Safety, tolerability, sUA, and ADAs were monitored. Here we report on the patients that received 5 combination doses of ImmTOR and pegadricase.

94% (49/52) of all randomized patients received premedication for gout flare prevention as per standard of care in the form of colchicine (1.2 mg as loading dose, 0.6 mg QD for the remainder of their participation), ibuprofen, or equivalent dose of NSAID.

Results: Demographics of 46 patients treated with 28-day cycles x5 combination doses of ImmTOR and pegadricase as compared to 6 patients treated with pegadricase alone were 23-70 years old vs. 41-64 years old (mean 53.6 vs. 51.8 years), male 97.8% vs. 100%, and white 73.9%. vs. 33.3%. The mean BMI at baseline was 34.5 vs. 38.9 kg/m^2. 71.7% vs. 100% of patients were obese with mean duration of established or symptomatic gout was 12.5 vs. 12.8 years. 43 patients were evaluable for gout flare analysis.

In the first month 50% of patients who received pegadricase alone had flares compared to 35% receiving SEL-212. There were no patients with initial flares after second month of treatment.

Data analyzed as combined months in patients receiving SEL-212, showed flare incidence of 37.0% (months 1-3) and 13.6% (months 4-5), flare frequency was 0.83 flares/patient (months 1-3) and 0.27 flares/patient (months 4-5). Mean duration of the gout flares was 6.1 days, with majority of the gout flares (97.7%) being categorized as mild/moderate, with 2.3% (n=1) noted as severe in intensity. Adjustments to gout flare prevention medication were not required for 69.6% of the patients. No gout flares resulted in patient discontinuation or were reported as a study drug related serious adverse event.

Conclusion: Monthly dosing of ImmTOR combined with pegadricase has been well-tolerated and has a lower incidence of flares at the initiation of therapy relative to pegylated uricases alone and the reported ULT flare incidence, and the effect persists over the duration of therapy.

*JAMA. 2011;306(7):711-720

Disclosure: R. Azeem, Selecta Biosciences, 1, 3; **J. Park**, Selecta Biosciences, 1, 3; **H. Plotkin**, Selecta Biosciences, 1, 3; **A. Kivitz**, AbbVie, 5, Amgen, 1, 4, 5, Boehringer Ingeleheim, 5, Boehringer Ingelheim, 5, Celgene, 8, Flexion,

5, 8, Flexion Therapeutics, 8, Genzyme, 5, 8, Gilead, 1, 4, 5, Gilead Sciences, Inc., 4, Horizon, 8, Janssen, 5, Janssen Research & Development, LLC, 2, Merck, 8, Novartis, 1, 4, 8, Pfizer, 1, 4, 5, 8, Regeneron, 1, 5, 8, Sanofi, 1, 4, 5, 8, Sun Pharma, 5, SUN Pharma Advanced Research, 5, UCB, 5; **L. Johnston**, Selecta Biosciences, 1, 3; **T. Kishimoto**, Selecta Biosciences, 1, 3; **S. Smolinski**, Selecta Biosciences, 1, 3; **W. DeHaan**, Selecta Biosciences, 1, 3.

Abstract Number: 1219

Uric Acid Level as a Predictor of Long Term Mortality in Advanced Age Population

Gabriel Breuer,[1] Marwan Abu Sneineh,[1] and Gideon Nesher[1], [1]Shaare Zedek Medical Center, Jerusalem, Yerushalayim, Israel

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hyperuricemia is associated with the development, progression and outcome of several diseases. The purpose of this study is to evaluate the serum uric acid (UA) levels as predictor of long-term mortality in elderly population aged 60 years and above. In a previous study we showed that short term mortality is inversely related to uric acid levels (Table 1).

Methods: Patients older than 60 years who were hospitalized in the departments of geriatrics and internal medicine in one medical center during a period of 4 months (March-June 2014) were included in this observational study. Data on clinical parameters and UA levels were collected during the first 48 hours of their hospitalization. The short-term mortality of this cohort was reported in a previous study, and we have continued to follow this cohort for 3.5 more years. Mortality data had been collected from databases of the Ministry of Internal Affairs, and the major medical centers in Jerusalem. Excluded were patients for whom mortality data were missing (unknown status or date of mortality). Demographic and clinical data were collected on admission including UA serum levels within 48 hours from admission Effect of UA serum levels and all relevant confounding parameters on all-cause mortality was assessed using regression analyses.

Results: 624 patients were included in our study. Mean age was 77.2 ± 14.6 years. Overall, 381 patients died during the follow up period (61.1%). Mortality rate in the hyperuricemic group (UA > 7 mg/dl) was higher (69.1%) than in normo-uricemic patients (58.4%, p= 0.004). The median survival for hyperuricemic patients was significantly shorter compared to normo-uricemic patients (606 and 1018 days, respectively, (p< .0001). (Figure 1)

Conclusion: Elevated levels of UA in an acute setting is a predictor of both short and long-term mortality.

Table 1 Short term mortality- Published data (Eur J Intern Med. 2017;44:74-76)

Uric Acid Level, mg/dl	Mortality, n (%)
0-3.4	12/119 (10)
3.5-7.5	51/478 (11)
7.6-9.4	29/136 (21)
9.5 and above	34/96(35)

p<0.001 for difference between serum UA above or below 7.5 mg/dl
p =0.008 for difference between serum UA 7.6 -9.4mg/dl and 9.5 and above

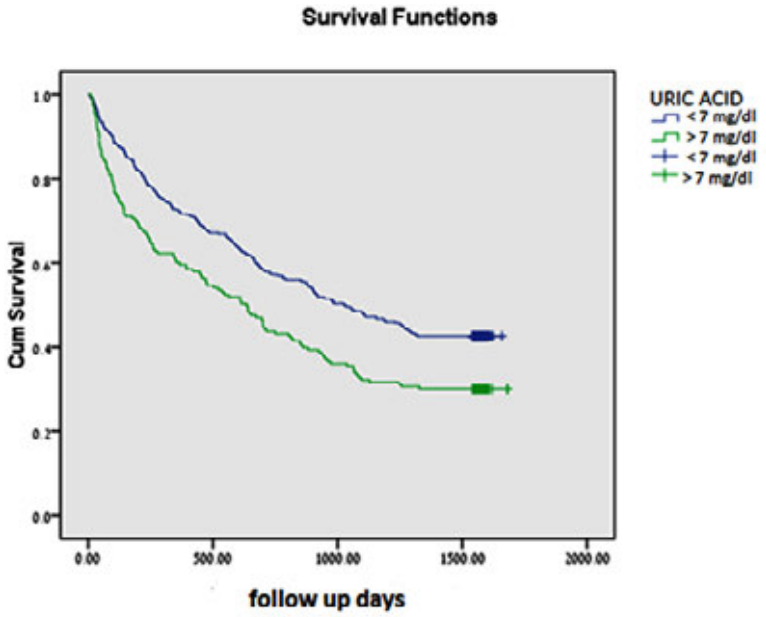


Figure 2: Kaplan-Meier mortality curves during the follow-up period.

Figure 1. Long-term survival of patients with hyperuricemia and normo-uricemia following admission in an acute-care setting.

Disclosure: ????. Breuer????, None; **M. Abu Sneineh????????**, None; **G. Nesher**, None.

Abstract Number: 1220

How Are Flares Reported in Long-term Gout Clinical Trials? A Content Analysis of Randomized Controlled Trials

Sarah Stewart,[1] Amy Tallon,[2] William Taylor,[3] Angelo Gaffo,[4] and Nicola Dalbeth[2], [1]University of Auckland, Auckland, Auckland, New Zealand, [2]University of Auckland, Auckland, New Zealand, [3]University of Otago, Otago, New Zealand, [4]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Prevention of gout flares is a central concern to patients with gout. There are many potential ways that gout flares could be reported in long-term clinical trials. The aim of this study was to analyse methods used to measure and report gout flare outcomes in long-term randomized controlled trials (RCTs).

Methods: A systematic search of electronic databases, supplemented with hand-searching of relevant references lists, was conducted. Articles were included if they were RCTs or articles reporting on analyses of RCT data (i.e. open label extension studies) and reported the impact of an intervention on the prevention of flares in people with gout. The modified Jadad scale was used to assess quality. Gout flare data relating to protocols, outcomes and reporting methods were extracted and synthesised separately for studies of anti-inflammatory prophylaxis and urate lowering/ other long term therapy.

Results: A total of 38 articles were included, with 10 reporting outcomes for anti-inflammatory prophylaxis and 28 for urate lowering/other long term therapy. The overall quality score of all articles was good. However, there was marked heterogeneity across trials in gout flare-related entry criteria, flare definitions, data capture methods, reporting methods and time periods used to report gout flares. Anti-inflammatory prophylaxis studies used multiple methods to report gout flare outcomes (mean (SD) 4.3 (2.5) methods/article), while the majority of urate lowering/other long term therapy studies used a single method to report gout flare outcomes. The most common reporting method was the proportion of patients with at least one gout flare (n = 29 articles), followed by the mean number of gout flares per patient (n = 18 articles) (**Table**). Only studies of anti-inflammatory prophylaxis therapy reported flare duration or pain (**Table**).

Conclusion: There is wide variation in methods used to measure and report gout flare outcomes in long-term RCTs. Studies of anti-inflammatory prophylaxis interventions generally report a range of flare characteristics, including incidence, number of flares, flare duration, and pain intensity. In contrast, studies of urate lowering/other long term therapy report limited data, mostly the proportion of participants experiencing flare. These findings support the development of standardized methods to measure and report gout flare outcomes that reflect the burden of flares for studies in which gout flare prevention is an outcome of interest.

Disclosure: S. Stewart, None; **A. Tallon**, None; **W. Taylor**, None; **A. Gaffo**, Amgen, 2; **N. Dalbeth**, Abbvie, 5, 8, 9, Amgen, 2, AMGEN, 2, AstraZeneca, 2, 5, 8, 9, Dyve, 5, 8, 9, Dyve BioSciences, 5, Hengrui, 5, 8, 9, Horiaon, 5, 8, Horizon, 5, 8, 9, Janssen, 5, 8, 9, Kowa, 5, 8, 9, Pfizer, 5, 8, 9.

Table. Number of studies using each gout flare reporting method

	Method	Studies of anti-inflammatory prophylaxis therapy (n = 10)	Studies of urate lowering/other long term therapy (n = 28)
Proportion of patients with gout flares	Proportion of patients with ≥ 1 gout flare	7	22
	Proportion of patients with ≥ 2 gout flares	4	1
	Proportion of patients with ≥ 3 gout flares	1	0
	Proportion of patients with ≥ 4 gout flares	0	1
	Proportion of patients with 1 gout flare	2	0
	Proportion of patients with no gout flares	1	0
	Proportion of patients who withdrew from the study due to a gout flare	0	1
	Proportion of patients requiring hospital admission for a flare	0	1

Abstract Number: 1221

Impact of Psoriasis Disease Activity and Other Risk Factors on Serum-urate Levels in Patients with Psoriasis and Psoriatic Arthritis - A Post-hoc Analysis of Pooled Data from Three Phase 3-trials with Secukinumab

Mats Dehlin,[1] Andreas Fasth,[2] Maximilian Reinhardt,[3] and Lennart Jacobsson[4], [1]Dept of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden, Gothenburg, Sweden, [2]Medical Affairs, Novartis Sverige AB, Kista, Sweden, Stockholm, Sweden, [3]Medical Affairs, Novartis Pharma GmbH, Nürnberg, Germany, Nürnberg, Germany, [4]Dept of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden, Gothenburg, Sweden

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Increased serum uric acid (sUA), hyperuricemia, has been reported to be associated with psoriasis (1). Increased cell turnover in psoriatic skin lesions has been proposed as a potential mechanism, but results are conflicting (1). In this study we assessed levels of sUA to degree and severity of skin involvement measured by Psoriasis Area Severity Index (PASI) at baseline and after treatment with the IL-17A inhibitor, secukinumab. The objectives were to adress the following questions: 1) are PASI and sUA levels correlated; and 2) are changes in PASI associated with changes in sUA during treatment of psoriasis.

Methods: Subjects with psoriasis/psoriatic arthritis (N=1042/204 (19.6%)) with concomitant psoriatic arthritis in three RCTs (ERASURE, FIXTURE and SCULPTURE) treated with secukinumab (dose 300 mg, n=628) or placebo (n=414) were pooled and included. At baseline values for sUA and PASI and the following co-variates were assessed; age, sex, BMI, renal function defined as eGFR, medication with diuretics (%), these are all variables known to affect sUA levels. To assess change in PASI (ΔPASI) and sUA (ΔsUA) the differences (week 12 minus baseline) in subjects receiving active drug were used. Multivariable linear regression, adjusting for identified co-variates, was used to assess the association between PASI and sUA at baseline with all subjects pooled and to assess the association between ΔsUA and ΔPASI over 12 weeks intervention in only those treated with secukinumab. All continuous variables

Table 1 Multivariate linear regression at baseline in all subjects (n=1042) with sUA as dependent variable adjusting for all covariates in the table. Increase in continuous variable parameter estimates represent the change in sUA per 1 standard deviation (at baseline) difference in PASI and co-variates.

	Parameter estimate	95% C.L.	p-value	$R^2 = 0.33$
PASI at baseline	11.2 (2.4)	6.5, 15.9	<0.0001	
Age	-20.4 (3.1)	-26.6, -14.3	<0.0001	
Sex (ref: man)	-82.6 (5.2)	-92.9, -72.4	<0.0001	
eGFR	-30.3 (3.1)	-36.5, -24.2	<0.0001	
Diuretic user (ref: no)	33.6 (10.1)	13.7, 53.4	0.001	
BMI	25.5 (2.4)	20.8, 30.3	<0.0001	

Table 2 Multivariate linear regression with ΔsUA (week 12 - baseline) as dependent variable in subjects treated with secukinumab (n=628), adjusting for age, sex, eGFR, Diuretic use and BMI at baseline. Increase in continuous variable parameter estimates represent the change in ΔsUA per 1 standard deviation (at baseline) difference in PASI and co-variates.

	Parameter estimate	95% C.L.	p-value	$R^2 = 0.06$
ΔPASI (SD) (week 12 - baseline)	16.0 (2.9)	10.3, 21.7	<0.0001	

were standardized with the exception of the dependent variable sUA, hence an increase in parameter estimates represent the change in sUA per 1 standard deviation (at baseline) difference in PASI and other continuous co-variates.

Results: Baseline characteristics; 70% were male, 6% were on diuretics and mean (SD) age, BMI and e GFR were 45 (13) yrs, 29.2 (6.8) kg/m2 and 96 (17) mL/min/1.73m2, respectively. From baseline to week 12, in patients treated with secukinumab, mean (SD) PASI decreased from 23.7 (SD: 10) to 2.9 (SD: 5) and sUA from 366 (SD: 96) to 359 (SD: 94) μmol/L. At baseline, covariates explained 33% of the variance in sUA with a significant contribution of PASI. A higher PASI value of 1 SD (10 units) was associated with 11.2 (p >0.0001) μmol/L higher value of sUA in the fully adjusted model. Other co-variates had larger effects (table 1). During 12 week follow-up, co-variates explained little of the variation in ΔsUA (R2=0.06), but there was a significant association with ΔPASI (Table 2) in fully adjusted model.

Conclusion: Both the degree and change in skin involvement in psoriasis were modestly associated with sUA, supporting a potential pathophysiological relationship. Known risk factors for sUA had however a larger impact cross-sectionally. Furthermore, sUA decreased modestly with 12 week treatment with secukinumab.

Reference:

1. Li X, Miao X, Wang H, Wang Y, Li F, Yang Q, et al. Association of serum uric acid levels in psoriasis: A systematic review and meta-analysis. Medicine (Baltimore) 2016;95:e3676.

Disclosure: M. Dehlin, None; **A. Fasth**, None; **M. Reinhardt**, Novartis Pharma GmbH, 3; **L. Jacobsson**, None.

Abstract Number: 1222

Relationships Between Allopurinol Dose, Oxypurinol Levels and Serum Urate – in Search of an Oxypurinol Therapeutic Concentration

Lisa Stamp,[1] Peter Chapman,[2] Murray Barclay,[3] Anne Horne,[4] Christopher Frampton,[3] Tony Merriman,[5] Daniel Wright,[6] Jill Drake,[3] and Nicola Dalbeth[4], [1]University of Otago, Christchurch, Christchurch, Canterbury, New Zealand, [2]Christchurch Hospital, Christchurch, New Zealand, [3]University of Otago, Christchurch, Christchurch, New Zealand, [4]University of Auckland, Auckland, New Zealand, [5]University of Otago, Birmingham, AL, [6]University of Otago, Dunedin, New Zealand

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Lack of a standardised allopurinol dose, with marked inter-individual variation in the dose required to achieve target urate contribute to failure to reach target serum urate levels. Given this variability in allop-

Table. Sensitivity and specificity of minimum oxypurinol concentration to achieve target urate (<0.36mmol/L).

CrCL	ROC AUC (SE)	Oxypurinol minimum concentration (µmol/l)	Sensitivity	Specificity	NPV	PPV
Entire group (n=2219)	0.65 (0.01)	103.6	59.5%	64.2%	59.3%	63.4%
<30ml/min (n=284)	0.69 (0.03)	181.8	62.4%	76.6%	74.4%	65.2%
30-<60ml/min (n=844)	0.67 (0.02)	172.8	51.5%	75.5%	60.3%	68.3%
>60ml/min (n=1091)	0.73 (0.02)	82.9	59.5%	75.7%	60.7%	74.8%

urinol responses, the ability of plasma oxypurinol levels to guide allopurinol dosing would be an advantage. Previous studies examining the relationship between oxypurinol and serum urate have been conflicting, with some showing no relationship and some an inverse relationship. Defining a therapeutic range has been challenging. The aim of this study was to determine the factors that influence the serum urate lowering response to allopurinol dose escalation and the conversion of allopurinol to oxypurinol, and to determine if there is a minimum therapeutic oxypurinol level.

Methods: Data from 129 participants in a 24-month open, randomized, controlled, parallel-group, comparative clinical trial were analysed. Allopurinol dose, serum urate and plasma oxypurinol concentrations were available at multiple time points. A slope for the association between allopurinol dose and serum urate was calculated for each individual as a measure of sensitivity to allopurinol. A slope for the association between allopurinol dose and plasma oxypurinol was calculated for each individual as a measure of allopurinol metabolism. Receiver operator characteristic (ROC) curves were used to identify oxypurinol concentration predictive of achieving serum urate < 6mg/dl.

Results: There were a wide range of serum urate concentrations for each allopurinol dose. Although there was a significant association between sensitivity to allopurinol (change in urate) and allopurinol metabolism (change in oxypurinol) for each 100mg increment in allopurinol dose (r=-0.60; p< 0.001), there was substantial variation between individuals (Figure 1 b and c).Body mass index (p=0.023), CrCL (p=0.037), ABCG2 Q141K (p=0.019), and baseline urate (p=0.004) were all associated with sensitivity to allopurinol, independent of other measured confounding variables. The oxypurinol ROC curve AUC to achieve serum urate < 6mg/dl was 0.65, with similar AUC values across all three CrCL groups (Table). The optimal minimum oxypurinol level for achieving target was strongly associated with CrCL (Table).

Conclusion: Although there is a relationship between change in oxypurinol and change in serum urate concentration, a minimum therapeutic oxypurinol is dependent on CrCL and cannot reliably predict serum urate target. Other variables, including ABCG2 Q141K genotype, impact on sensitivity to allopurinol.

Disclosure: L. Stamp, None; **P. Chapman**, None; **M. Barclay**, None; **A. Horne**, None; **C. Frampton**, None; **T. Merriman**, Ardea Biosciences, 2, 5, AstraZeneca, 2, 5, Ironwood Pharmaceuticals, 2; **D. Wright**, None; **J. Drake**, None; **N. Dalbeth**, Abbvie, 5, 8, 9, Amgen, 2, AMGEN, 2, AstraZeneca, 2, 5, 8, 9, Dyve, 5, 8, 9, Dyve BioSciences, 5, Hengrui, 5, 8, 9, Horiaon, 5, 8, Horizon, 5, 8, 9, Janssen, 5, 8, 9, Kowa, 5, 8, 9, Pfizer, 5, 8, 9.

Abstract Number: 1223

Enteral Administration of ALLN-346, a Recombinant Urate-degrading Enzyme, Decreases Serum Urate in a Pig Model of Hyperuricemia

Danica Grujic,[1] Kateryna Pirzynowska,[2] Paulina Szczurek,[3] Stefan Pierzynowski,[2] Aditi Desphande,[4] Olha Drahanchuck,[5] Nadia Mosiichuk,[6] and Jarek Wolinski[7], [1]Allena Pharmaceuticals, Boston, [2]Lund University, Anara AB,/SGPlus, Lund, Sweden, [3]National Research Institute of Animal Production, Vitanano Sp. z o.o./PROF, Balice, Poland, [4]Allena Pharmaceuticals, Newton, MA, [5]Polish Academy of Sciences, Vitanano Sp. z o.o./PROF, Jablonna, Poland, [6]Lund University, Lund, Sweden, [7]Polish Academy of Sciences, Vitanano Sp. z o.o./PROF, Jablonna, Poland

SESSION INFORMATION

Session Date: Monday, November 11, 2019

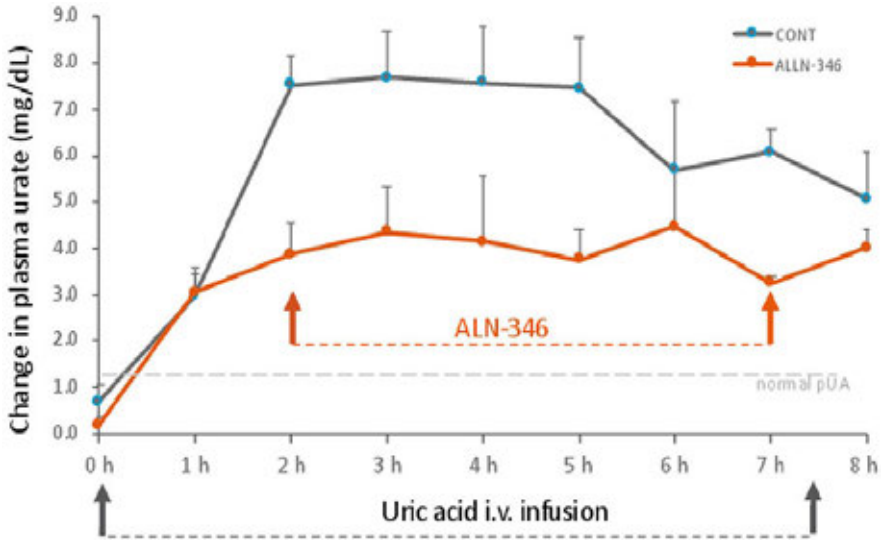
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Uric acid homeostasis is determined as a balance between production, intestinal secretion and renal excretion. Around 2/3 of uric acid is excreted by the kidneys, while the remaining 1/3 is excreted by intestine. In people with impaired renal function and hyperuricemia extra-renal elimination ranges between ~50-70% and plays important role in urate homeostasis.[1] Existing urate-lowering therapies including oral xanthine oxidase inhibitors, uricosurics, and intravenous uricase agents have limitations either in efficacy or tolerance which contribute to refractoriness. ALLN-346 is an orally administered, non-absorbed, recombinant urate degrading enzyme designed to degrade urate secreted in the intestinal tract and thereby reduce hyperuricemia. Previously, we demonstrated in a urate oxidase KO mouse that 7d of ALLN-346 oral therapy reduces hyperuricemia to the similar extent as allopurinol.[2] Here, we tested whether enteral administration of ALLN-346 to pigs with acute hyperuricemia[3] could reduce plasma urate (pUA) and urine urate excretion.

Methods: 7 juvenile pigs (mean bw 17.3kg) with normal kidney function, and with jugular vein catheters for uric acid infusion and blood collection, were administered with ALLN-346 via a duodenal port following induction of hyperuricemia with uric acid infusion. Study was done in pigs that were fed 3x/d (1.0% bw/meal) and watered *ad lib.* A control run of hyperuricemia was performed by chronic i.v. infusion of uric acid via jugular catheter (10 mg/kg from 40 mg/mL uric acid in 40% glucose) for 7.5h. After 36h wash out, a treatment with ALLN-346 was performed 2h after



start of uric acid infusion, when hyperuricemia was induced. ALLN-346 was given hourly to duodenum as a bolus suspension in saline (6 x 10,560u). To estimate changes in pUA, blood was collected at baseline and hourly during the 8h experiment, and $AUC_{0\text{-}8h}$ was calculated. Urine was collected for uric acid analysis. Intestinal samples were analyzed for expression of ABCG2 urate transporter, that regulates serum UA, by Western Blot (WB) with pig anti-BCRP/ABCG2 antibody (Abcam).

Results: pUA at baseline was < 1 mg/dL. Uric acid infusion resulted in an immediate increase in pUA, with mean Cmax of 7.7 mg/dL at 3h, and calculated AUC0-8h of 44.3 mg*h/dL. Administration of ALLN-346 attenuated the rise in pUA with Cmax reduced to 4.5 mg/dL and AUC0-8h of 27.5mg*h/dL. The difference between the treatment and control run in pUA was 38% (p=0.0009). The urine uric acid excretion was reduced 16% with ALLN-346 compared to control run. WB confirmed expression of ABCG2 in small intestine, being the highest in the jejunum and ileum.

Conclusion: The results of this pilot experiment in pigs with acute hyperuricemia confirm that intestine plays an active role in urate elimination in conditions of severe hyperuricemia and suggests the potential for ALLN-346 acting in the intestinal tract to reduce pUA levels and overall urate burden in people with hyperuricemia and gout. Further studies are planned to confirm these findings.

References:

1. Sorensen LB. Role of Intestinal tract in the elimination of uric acid. Arthr. (1965)
2. Grujic D et al, ACR 2018
3. Szczurek P et al. Oral uricase eliminates blood uric acid in the hyperuricemic pig model PLoS One. (2017)

Disclosure: D. Grujic, None; **K. Pirzynowska**, None; **P. Szczurek**, None; **S. Pierzynowski**, None; **A. Desphande**, None; **O. Drahanchuck**, None; **N. Mosiichuk**, None; **J. Wolinski**, None.

Abstract Number: 1224

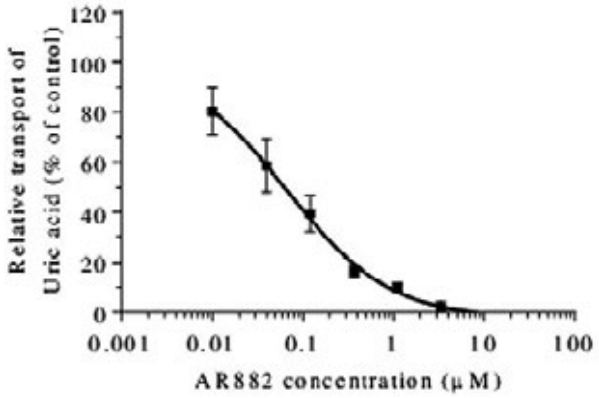
AR882, a Potent and Selective URAT1 Inhibitor with a Favorable Pharmacological, Pharmacokinetic and Toxicity Profile

Rongzi Yan,[1] Nanqun Zhu,[2] zancong shen,[3] Shunqi Yan,[4] and Litain Yeh[1], [1]Arthrosi Therapeutics, Laguna Hills, [2]Consultant, Laguna Hills, CA, [3]Arthrosi Therapeutics, San Diego, CA, [4]Arthrosi Therapeutics. Inc, Laguna Hills, CA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: AR882 is a potent and selective inhibitor of uric acid transporter 1 (URAT1), which is responsible for a majority of reabsorption of filtered uric acid from the renal tubular lumen. By inhibiting URAT1, AR882 increases uric acid urinary excretion and thereby lowers serum uric acid (sUA). Preclinically, AR882 has demonstrated inhibitory effect on uric acid uptake and good tolerability in pharmacology, pharmacokinetic and toxicology studies.

Methods: The inhibition of AR882 on human URAT1-mediated uptake of [^{14}C]uric acid was studied in Madin-Darby Canine Kidney (MDCKII) cells expressing human URAT1. Inhibitory potential to human organic anion transporter (OAT) 4, a transporter reported involving uric acid uptake, was also tested in human embryonic kidney (HEK) 293



Inhibition of URAT1-mediated Uric Acid Uptake by AR882

cells expressing human OAT4. Absorption, distribution, excretion of AR882 were evaluated following single oral or intravenous administration in multiple species. Metabolic stability of AR882 was evaluated in microsomes and hepatocytes *in vitro* across species including human and *in vivo* in rats, dogs and monkeys. Drug-drug interaction (DDI) evaluations with major renal transporters were conducted in HEK293 cells expressing P-glycoprotein, OAT1, OAT3, OAT4, and organic cation transporter 2 (OCT2) transporters. Toxicity and toxicokinetics of AR882 were assessed following oral repeat-dose administration to Sprague-Dawley rats and cynomolgus monkeys for durations up to 4 weeks.

Results: AR882 exhibited high potency against URAT1 with an IC_{50} of 67 nM, compared to lesinurad (IC_{50} = 7.3 μM, Zurampic® Package Insert) or benzbromarone (IC_{50} = 196 nM). An IC_{50} of 2.89 μM against OAT4 indicated that AR882 is highly selective for URAT1. AR882 was well absorbed in rats, dogs, and monkeys, with a mean T_{max} of 1-2 hours. Bioavailability ranged between 76% and 88% across the tested species. *In vitro* metabolic profiling and *in vivo* clearance suggesting AR882 is extremely stable. In animals, unchanged parent compound was recovered in the urine at concentrations sufficient for complete inhibition of URAT1. Transporter evaluations with major efflux and uptake transporter in kidney revealed no DDI potential and no active-transportation involvement. Using allometric scaling, a low therapeutic dose of AR882 is anticipated in human. Rats and monkeys were selected as the species for toxicology evaluation based on metabolic profiling. In 4-week oral repeat-dose toxicology and toxicokinetic studies, AR882 was well tolerated at doses up to 50 mg/kg/day and 150 mg/kg/day in rats and monkeys, respectively. The exposures achieved in animals were substantially higher than the observed human exposure at the anticipated therapeutic doses of 25 mg – 100 mg in clinical study

Conclusion: AR882, a selective URAT1 inhibitor with superb potency for URAT1-mediated uric acid reabsorption has been discovered and developed for the treatment of gout at a low anticipated daily dose. AR882 exhibited favorable pharmacokinetic and DDI properties, as well as an excellent safety profile in preclinical studies.

Disclosure: R. Yan, None; **N. Zhu**, None; **z. shen**, arthrosi, 3, arthrosi therapeutics, 3; **S. Yan**, None; **L. Yeh**, None.

Abstract Number: 1225

Limits of Detection of Monosodium Urate Crystals in Synovial Fluid by Ultrasound

John FitzGerald,[1] Andrea Ramirez Cazares,[2] and Veena Ranganath[2], [1]UCLA, Los Angeles, CA, [2]University of California Los Angeles, Los Angeles, CA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate limits of detection of ultrasound to detect monosodium urate crystals suspended in synovial fluid.

Methods: Serial dilutions were made mixing liquid tophus aspirated from an olecranon bursa with crystal free synovial fluid aspirated from a patient with knee osteoarthritis. For each dilution, beginning with the undiluted liquid tophus aspirate, crystal free synovial fluid was mixed with each subsequent dilution in a 1:1 ratio creating dilutions from 1:1 to 1:1024. At each dilution, the MSU suspensions in eppendorf tubes were scanned with GE Logic linear probe settings ranging from low to high frequency as needed for optimal imaging and penetration. Compensated polarized light microscopy images at 10x and 40x were obtained for each dilution.

Results: Ultrasound evidence of MSU crystals (snowstorm appearance) were still evident in serial dilutions up until 1:128. Corresponding histology imaged by compensated light microscopy revealed that large crystal aggregates were rare but there were still a high number of crystals (~100) per low power field. Further dilutions resulted in ultrasound images that were indistinguishable from crystal free aspirates of synovial fluid despite persistence of lower frequency MSU crystals.

Conclusion: Ultrasound is sensitive for detecting modest frequency of MSU crystals suspended in synovial fluid. Never-the-less, MSU crystals are still present in synovial fluid beyond ultrasound detection.

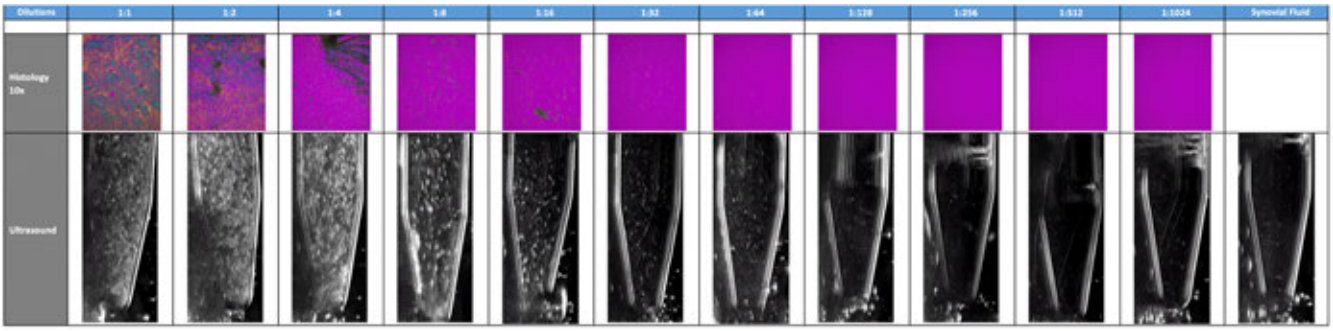


Figure 1: Serial dilutions of liquid tophus.

Disclosure: J. FitzGerald, None; **A. Ramirez Cazares**, None; **V. Ranganath**, genentech, 2, bristol meyer squibb, 2, 5, pfizer, 2, mallinckrodt, 2.

Abstract Number: 1226

Neutrophil Activation Identifies Patients with Active Polyarticular Gout – a Role for Neutrophil Biomarkers in Monitoring Gout Disease Activity and Severity

Daisy Vedder,[1] Martijn Gerritsen,[1] Mike Nurmohamed,[2] Ronald van Vollenhoven,[3] and **Christian Lood** [4],
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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

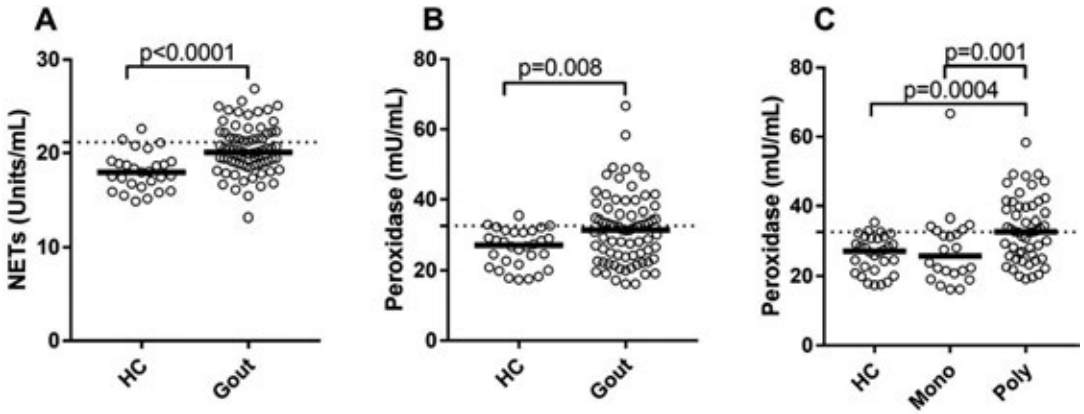
Background/Purpose: Neutrophils are key immune cells participating in host defense through several mechanisms, including the formation of neutrophil extracellular traps (NETs). Excessive neutrophil activation has been linked to inflammation and autoimmunity, including gout. In gout models, uric acid crystals induce NETosis. NETs are known to induce inflammation and partake in induction of tissue damage. The role of NETs, however, in human gout has not been extensively investigated.

Our objective is to investigate the clinical utility of neutrophil-derived biomarkers in gout. We hypothesize that uric acid crystals activate neutrophils to form NETs contributing to immune cell activation, with subsequent arthritis and joint damage.

Methods: Plasma samples from 75 gout patients participating in the 'Reade gout cohort Amsterdam' were compared with 30 healthy controls (HC). Levels of NETs, and NET-derived markers (cell-free DNA and peroxidase activity) were analyzed using a MPO-DNA ELISA, as well as fluorimetry. Levels of calprotectin were analyzed by ELISA. Mitochondrial as well as genomic DNA levels were analyzed by qPCR. All markers were compared with HC and related to markers of inflammation and disease activity.

Results: Levels of NETs, as well as other neutrophil biomarkers, were increased in gout patients as compared to HC ($p< 0.01$, Figures 1A-B). No associations were found between markers of cell death (cfDNA and NETs) and disease activity. Genomic DNA, but not mitochondrial DNA, was elevated among gout patients ($p< 0.05$), and related to number of gout attacks ($r=0.44$, $p=0.002$). Peroxidase activity correlated with disease activity (RAPID score: $r=0.43$, $p=0.01$, RAPID function: $r=0.54$, $p=0.001$) and inflammation markers (CRP: $r=0.40$, $p< 0.001$, and ESR: $r=0.43$, $p< 0.001$). Involvement of ankle and wrist resulted in significant higher peroxidase levels compared to mono-articular disease ($p=0.01$, and $p=0.03$, respectively), indicating peroxidase activity being a marker of polyarticular gout (Figure 1C). Calprotectin (S100A8/A9) correlated with the inflammation markers CRP and ESR ($r=0.30$, $p=0.01$, and $r=0.30$, $p=0.001$, respectively) and morning stiffness, especially in patients with chronic polyarticular gout ($r=0.61$, $p=0.001$).

Conclusion: To our knowledge, this is the first report demonstrating presence of NETs in the peripheral blood of gout patients. Although markedly elevated, levels of NETs did not associate with markers of disease activity or inflammation, possibly due to the lack of inflammatory mitochondrial DNA within the NETs. Even so, our data demonstrate an important role of neutrophils in gout pathogenesis, with neutrophil activation markers associating with characteristics of active, and more pronounced polyarticular disease.



Disclosure: D. Vedder, None; **M. Gerritsen**, None; **M. Nurmohamed**, AbbVie, 2, 8, BMS, 2, 8, Celgene, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Merck, 2, 8, Pfizer, 2, 8, Roche, 2, 8, UCB, 2, 8; **R. van Vollenhoven**, AbbVie, 2, 9, Arthrogen, 2, AstraZeneca, 9, Biotest, 9, BMS, 2, 9, Celgene, 9, GSK, 2, 9, Janssen, 9, Lilly, 2, 9, medac, 9, Merck, 9, Novartis, 9, Pfizer, 2, 9, Roche, 9, UCB, 2, 9; **C. Lood**, None.

Abstract Number: 1227

A Neutrophil Signature Is Strongly Associated with Cardiovascular Risk in Gout

Daisy Vedder,[1] Martijn Gerritsen,[1] Mike Nurmohamed,[2] Ronald van Vollenhoven,[3] and **Christian Lood** [4],
[1]Amsterdam Rheumatology & immunology Center / Reade, Amsterdam, Netherlands, [2]Amsterdam Rheumatology and immunology Center location Reade and Amsterdam UMC location VU medical center, Amsterdam, Netherlands, [3]Amsterdam Rheumatology and Immunology Center ARC, Amsterdam, the Netherlands, Amsterdam, Netherlands, [4]University of Washington, Seattle, WA

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Session Date: Monday, November 11, 2019
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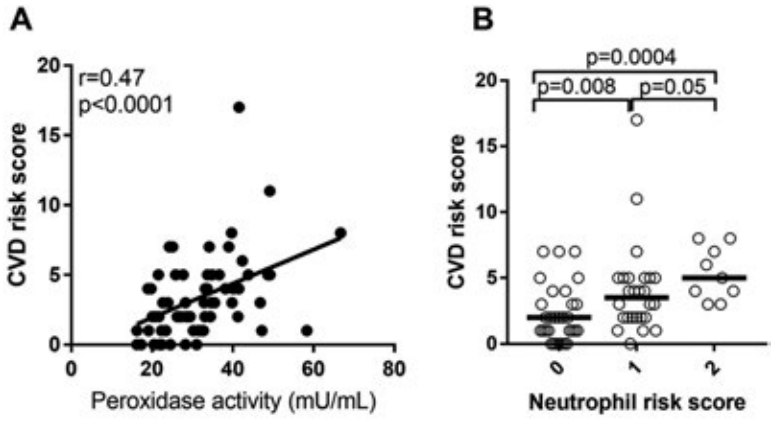
Background/Purpose: Patients with gout have an increased cardiovascular morbidity and mortality, not fully explained by traditional cardiovascular risk factors. Xanthine oxidase-induced oxidative stress, increased lipid oxidization and chronic low-grade inflammation have been suggested as important contributors. Neutrophils, through formation of neutrophil extracellular traps (NETs), partake in pro-thrombotic and atherogenic processes contributing to cardiovascular disease. However, the role of NETs in cardiovascular disease in human gout is not known.

Our objective is to investigate the association between neutrophil activation and cardiovascular risk in gout patients. We hypothesize that neutrophil activation mediates inflammation, as well as activation of and damage to endothelial cells, thus partaking in atherosclerosis development.

Methods: Plasma samples from 75 gout patients participating in the 'Reade gout cohort Amsterdam' were analyzed. Patient data was collected on disease activity, demographics, comorbidities, medication and cardiovascular risk assessments. Measurements included anthropometry, vital parameters (RR, HF) and lab variables. Levels of NETs, and NET-derived markers (cell-free DNA and peroxidase activity) were analyzed using an MPO-DNA ELISA, and fluorimetry. Levels of calprotectin were analyzed by ELISA. Markers of NETosis were related to traditional cardiovascular risk factors and 10 year risk of cardiovascular mortality (SCORE EU).

Results: No associations were found between markers of cell death (cfDNA and NETs) and cardiovascular risk. However, markers of neutrophil activation, including peroxidase activity correlated with BMI ($r=0.31$, $p=0.008$), waist-hip ratio ($r=0.52$, $p< 0.001$), cholesterol ratio ($r=0.51$, $p< 0.001$), and triglycerides ($r=0.42$, $p< 0.001$). These associations were even stronger in patients with chronic, polyarticular gout. Peroxidase activity was strongly associated with the 10 year risk of cardiovascular comorbidity ($r=0.47$, $p< 0.001$, Figure 1A). Calprotectin levels were elevated in gout patients with hypertension ($p=0.005$) and diabetes ($p=0.02$), with calprotectin levels associating with diabetes independently of BMI (OR=6.2, $p=0.04$). Finally, we constructed a neutrophil risk score ranging from 0-2 based on positivity for peroxidase and/or calprotectin to identify patients with a 'neutrophil activation signature'. The neutrophil risk score strongly associated with CVD risk (Figure 1B). Patients with neutrophil activation signature (risk score 1-2) had markedly elevated cardiovascular risk score ($p=0.001$), with 67.7% of the patients having high cardiovascular risk, versus 32.3% of the patients without a neutrophil activation signature (OR=2.9, $p=0.03$).



Conclusion: We have demonstrated that neutrophil activation markers are associated with a 10-year risk of cardiovascular comorbidity in gout patients. These results highlight an important, an unappreciated, role of neutrophils in development of fatal comorbidities in gout. Further studies are warranted to determine the prognostic value of a neutrophil activation signature in development of cardiovascular disease.

Disclosure: D. Vedder, None; **M. Gerritsen**, None; **M. Nurmohamed**, AbbVie, 2, 8, BMS, 2, 8, Celgene, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Merck, 2, 8, Pfizer, 2, 8, Roche, 2, 8, UCB, 2, 8; **R. van Vollenhoven**, AbbVie, 2, 9, Arthrogen, 2, AstraZeneca, 9, Biotest, 9, BMS, 2, 9, Celgene, 9, GSK, 2, 9, Janssen, 9, Lilly, 2, 9, medac, 9, Merck, 9, Novartis, 9, Pfizer, 2, 9, Roche, 9, UCB, 2, 9; **C. Lood**, None.

Abstract Number: 1228

Soluble Triggering Receptor Expressed on Myeloid cells-1 (sTREM-1) Ameliorates Monosodium Urate Crystals (MSUC)-induced Inflammation in a Mouse Air-pouch Model of Gout

Vitaly Kliminski,[1] and **Yair Molad** [2], [1]Laboratory of Inflammation Research, Felsenstein Medical Research Center, Tel Aviv University, Petach Tikva, Israel, [2]Rabin Medical Center, Beilinson Hospital, and Tel Aviv University, Petach Tikva, HaMerkaz, Israel

SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Myeloid cells membrane-bound TREM-1 (mTREM-1) amplifies toll like receptor (TLR)-4-mediated myeloid cells activation, accompanied by release of soluble TREM-1 (sTREM-1) that acts as a decoy receptor. Previous studies suggest an upregulation of mTREM-1 in gout. TGFβ was previously shown to play an anti-inflammatory role in the spontaneous resolution of gout attack**.** In this study, we aimed to determine the effect of sTREM-1 in gout.

Methods: We've used a synthetic peptide inhibitor of TREM-1 (LP17) that is a conserved domain (LQVTDSGLYRCVIYHPP) of the extracellular portion of TREM-1 in an air-pouch mouse model of gout to determine the role of sTREM-1 in MSU crystal (MSUC)-induced inflammation.

Results: MSU crystals injected into the air-pouch induced an increase of mTREM-1 surface expression on CD11b-positive leukocytes by magnitude of 1.77 of (assessed by FACS) (p=0.013, n=3), as well as an increase of exudate sTREM-1 level (assessed by ELISA) by 397.4% (2082.02±630.21 vs. 418.6±323.7pg/ml, n=4, p=0.017). The synthetic peptide inhibitor of TREM-1 (LP17) injected into the air-pouch together with MSU crystals attenuated the inflammatory response by significant reduction of leukocyte count (MSUC+LP17: 0.83x106±6.8 vs. MSUC: 1.92x106±15.9, n = 5, p=0.041) , exudate level of TNFα (MSUC+LP17: 14.5±2.1 vs. MSUC: 27.9±3 pg/ml, n=3, p=0.036) and the chemokine CCL3/MIP1α level (MSUC+LP17: 11.8±8.2 vs. MSUC: 23.7±11.8 pg/ml, p=0.049). In contrast, the exudate level of the anti-inflammatory cytokine TGFβ was not affected by LP17 (PBS: 23.4±31.46pg/ml, MSUC: 123.57±51.96pg/ml, p< 0.0001; MSUC+LP17: 156.72±154.75pg/ml, n=10, p=NS).

Conclusion: Soluble TREM-1 (LP17) ameliorates MSU crystal-induced inflammation through several modes of action, as is demonstrated by significant decrease of exudate leukocyte count, as well as TNFα and CCL3 levels. Moreover, LP17 didn't change TGFβ level, suggesting synergistic anti-inflammatory effects of sTREM-1 and TGFβ that leads to the resolution of gout attack.

Disclosure: V. Kliminski, None; **Y. Molad**, None.

Abstract Number: 1229

AR882, a Potent and Selective Uric Acid Lowering Agent Acting Through Inhibition of Uric Acid Reuptake, Shows Excellent Pharmacokinetics and Pharmacodynamics in a Phase 1 Clinical Trial

zancong shen,[1] Elizabeth Polvent,[2] Vijay Hingorani,[3] Shunqi Yan,[4] Rongzi Yan,[4] and **Litain Yeh** [4], [1]Arthrosi Therapeutics, San Diego, CA, [2]Arthrosi Therapeutics, Laguna Hills, CA, [3]Arthrosi Therapeutics, San Diego, [4]Arthrosi Therapeutics, Laguna Hills

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: AR882 is a potent and selective uric acid transporter 1 (URAT1) inhibitor under development for the treatment of hyperuricemia or gout. A Phase 1 single ascending dose clinical study in healthy adult male subjects was conducted to evaluate pharmacokinetics and dose-dependent serum uric acid (sUA) lowering effect.

Methods: Analysis of sUA reduction was conducted in a randomized, double-blind, placebo-controlled single dose study with 31 healthy male volunteers. Eight subjects per group (6 active and 2 placebo) were planned to be dosed AR882 under fasted conditions at 15, 50, or 100 mg with an immediate release formulation, or at 50 mg following a high-fat, high- calorie meal. Correlation of increased uric acid excretion in urine with sUA lowering was assessed to further evaluate the effect of URAT1 inhibition in the tubule. Laboratory safety tests, vital signs, and electrocardiograms were collected throughout the study

Results: Following administration of AR882, exposure of AR882 exhibited dose proportional increase and was significantly lower than the no-observed-adverse-effect level (NOAEL) in rats and monkeys. The rate of absorption was moderate (Tmax 3-5 hours) with a half-life of AR882 of approximately 10-13 hours. When administrated with a high-fat, high-calorie meal, AR882 absorption was slower (Tmax 8 hours), with Cmax lowered by approximately 33% but AUC was similar to that in the fasting conditions. The mean changes in sUA at the 24 hours postdose from baseline

were 2.0% in the pooled placebo group, -5.8%, -42.4% and -58.4% in the 15 mg, 50 mg (P< 0.001 vs placebo) and 100 mg (P< 0.001 vs placebo) fasted groups, respectively. Time to reach highest sUA reduction range between 12 – 36 hr post-dose with median TEmax at 24 hr post-dose. sUA returned to baseline after 4 to 5 days post-dose following 50 mg and 100 mg dosing. Food did not alter sUA lowering effect of AR882. sUA lowering effect was similar among subjects irrespective of differing sUA baseline values which ranged between 3 to 9 mg/dL. Urinary excretion of AR882 and uric acid were evaluated on Day 1 at 6 to 12 hours intervals. Significantly higher amounts of uric acid were eliminated through urine on Day 1 at all collection intervals, indicating sustained inhibition of URAT1 over 24 hours following dosing. AR882 was well tolerated at all doses tested. All adverse events (AEs) were mild in severity and no serious adverse events (SAEs) were reported. There were no clinically significant laboratory or ECG abnormalities noted.

Conclusion: AR882 exhibited outstanding ability to reduce sUA level at ≥ 50 mg (> 40% reduction following a single dose). It is anticipated the sUA lowering will accumulate following multiple doses.

Disclosure: z. shen, arthrosi, 3, arthrosi therapeutics, 3; **E. Polvent**, Arthrosi Therapeutics, Inc., 3, 4; **V. Hingorani**, arthrosi therapeutics, 5, arthrosi therapeutics, 5; **S. Yan**, Arthrosi Therapeutics, Inc., 1, 3, 4, 6; **R. Yan**, None; **L. Yeh**, None.

Abstract Number: 1230

Do Serum Urate-Associated Genetic Variants Influence Gout Risk in People on Diuretics? Analysis of the UK Biobank

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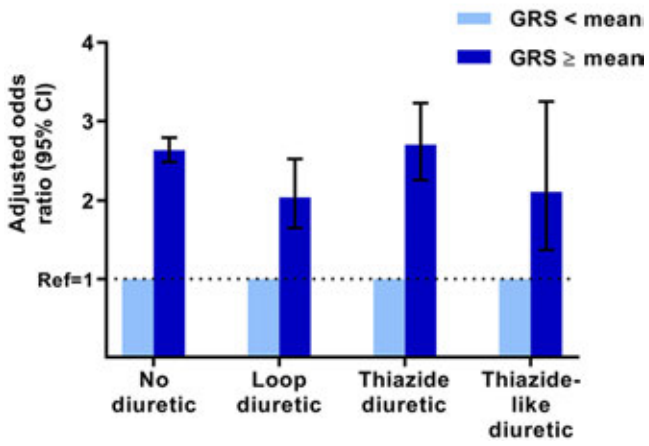
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Genome-wide association studies have identified single nucleotide polymorphisms (SNPs) associated with serum urate and gout. An association between diuretic use and gout has also been reported by many investigators. The aim of this study was to examine whether serum urate-associated genetic variants differ in their influence on gout risk in people taking a diuretic compared to those not taking a diuretic, and to test for interactions between these genetic variants and diuretic use for gout association.

Methods: This research was conducted using the UK Biobank Resource. Participants of European ethnicity, aged 40-69 years, and with genome-wide genotypes were included. Gout was defined using a validated definition (self-report of gout or urate-lowering therapy use). Medication use (including diuretics) and co-morbidity data were collected via self-report. The 10 serum urate-associated SNPs with the strongest association for gout as reported by Cadzow et al (Arthritis Res Ther 2017) were tested for their association with gout according to diuretic use. Gene-diuretic interactions for gout association were tested using a genetic risk score (GRS) and individual SNPs by logistic regression adjusting for age, sex, body mass index, kidney failure, heart failure and hypertension.

Figure: Association between genetic risk score (GRS) and gout according to diuretic use. Data were adjusted by age, sex, body mass index, hypertension, renal failure and heart failure.



Results: Data were available for 359,876 participants, including 7,342 gout cases (2.0%). Gout was present in 1,197 (4.0%) diuretic users and 6,145 (1.9%) non-diuretic users; OR [95% CI] 2.21 [2.08-2.36] for diuretic users compared to non-diuretic users. After adjustment, use of a loop diuretic was positively associated with prevalent gout (OR 2.34 [2.08-2.63]), but thiazide diuretics were inversely associated with prevalent gout (OR 0.60 [0.55-0.66]). Compared with a lower GRS (below the mean), a higher GRS (mean or higher) was positively associated with gout in those not on diuretics (OR 2.63 [2.49-2.79]), in those on loop diuretics (OR 2.04 [1.65-2.53]), in those on thiazide diuretics (OR 2.70 [2.26-3.23]), and in those on thiazide-like diuretics (OR 2.11 [1.37-3.25]) with similar ORs and overlapping confidence intervals (Figure). The use of a loop diuretic with the presence of a higher GRS exerted the highest ORs for gout association; compared to non-diuretic users with a lower GRS, the OR for gout was 6.04 [5.18-7.04] in loop diuretic users with a higher GRS.

Conclusion: In people on diuretics, serum urate-associated genetic variants contribute strongly to gout risk, with a similar effect to that observed in those not taking a diuretic. These findings suggest that the contribution of genetic variants is not restricted to people with 'primary' gout and genetic variants play an important role in gout susceptibility in the presence of other risk factors.

Disclosure: R. Narang, None; **G. Gamble**, None; **A. Phipps-Green**, None; **R. Topless**, None; **M. Cadzow**, None; **L. Stamp**, None; **T. Merriman**, Ardea Biosciences, 2, 5, AstraZeneca, 2, 5, Ironwood Pharmaceuticals, 2; **N. Dalbeth**, Abbvie, 5, 8, 9, Amgen, 2, AMGEN, 2, AstraZeneca, 2, 5, 8, 9, Dyve, 5, 8, 9, Dyve BioSciences, 5, Hengrui, 5, 8, 9, Horiaon, 5, 8, Horizon, 5, 8, 9, Janssen, 5, 8, 9, Kowa, 5, 8, 9, Pfizer, 5, 8, 9.

Abstract Number: 1231

Improvement in Hepatic Fibrosis Estimated by Fibrosis-4 (FIB-4) Index in Subjects with Chronic Refractory Gout Treated with Pegloticase

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Hyperuricemia is associated with non-alcoholic fatty liver disease (NAFLD) (Yang C et al. *PlosOne*2017; 12:e0177249; Jaruvongvanich V et al. *Eur J Gastroenterol Hepatol* 2017; 29:1031), but the relationship to fibrosis remains uncertain (Jaruvongvanich V et al. Eur *J Gastroenterol Hepatol* 2017; 29:694). Moreover, it is not known whether lowering serum urate will affect the course of NAFLD. The availability of data from two randomized trials of pegloticase, a pegylated recombinant mammalian uricase that profoundly decreases serum urate, afforded the opportunity to test the hypothesis that lowering urate might improve NAFLD.

Methods: Databases from patients with chronic refractory gout who participated in two randomized 6-month clinical trials (RCTs) of pegloticase were analyzed (Sundy JS et al. JAMA. 2011; 306 (7):711-20). Sub-sets who had persistent urate lowering to levels < 1 mg/dL in response to biweekly pegloticase (responders, n=36) were compared to those who received placebo (n=43). Since liver biopsy information was not available on these subjects, we relied on the Fibrosis-4 Index (Fib-4), a validated non-invasive estimate of liver fibrosis in a variety of liver diseases (Sterling RK et al. Hepatol 2006; 43:1317; Shah AG et al. Clin Gastroenterol Hepatol 2009;7:1104) calculated from measurements of AST, ALT, platelet count and age (Age x AST/platelets x$\sqrt{}$ALT). A Fib-4 value of 1.3 is an indication that further evaluation of NAFLD is warranted.

Results: At baseline, the mean Fib-4 values were 1.40 ± 0.86 in pegloticase responders and 1.04 ± 0.53 in subjects receiving placebo. Subjects receiving placebo exhibited a change of 0.26 ± 0.41 in the Fib-4 score over the six months of the RCTs compared with 0.13 ± 0.62 in the pegloticase responders (p=0.048; by linear regression). When only the subjects with a Fib-4 value > 1.3 were considered (n=27), a significant difference in the change in the Fib-4 values over the 6 months of the trial between pegloticase responders and those receiving placebo was also observed (-0.15 ± 0.67 vs 0.37 ± 0.42, p=0.04, 2-sample Wilcoxon test). The correlation between serum urate area under the curve (AUC) over the 6 months of the trial and the change in Fib-4 value was r_s=0.33, p=0.0004 (Spearman rank-order correlation coefficient). Finally, multivariate analysis indicated serum urate AUC (as a surrogate measure for group) is the main contributor to the change in Fib-4 values (p=0.018 by linear regression).

Conclusion: The data are consistent with the conclusion that persistent lowering of serum urate had a significant impact on Fib-4 levels, implying a possible effect on the course of NAFLD. These results support consideration of a more complete analysis, involving liver biopsy examinations, of the impact of profound urate-lowering on liver inflammation and fibrosis.

Disclosure: N. Schlesinger, amgen, 2, Astra Zeneca, 2, Horizon, 5, horizon, 5, IFM Therapeutics, 5, Mallinckrodt Pharmaceuticals, 5, Novartis, 5, olatec, 5, pfizer, 2, selecta, 5; **A. Yeo**, Horizon, 3; **P. Lipsky**, Horizon, 5, Janssen Research & Development, LLC, 2.

Abstract Number: 1232

Whole Blood RNA Sequencing Study of Gout Cases and Controls Demonstrates Transcriptomic Differences with Relevance to Inflammatory Cell Activation

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: The transcriptomic changes accompanying the transition from asymptomatic hyperuricemia to gout are currently unknown but may be important for identifying and understanding important molecular triggers of gout. We tested the hypothesis that gene expression differences would be seen between whole blood from individuals with gout versus normouricemic and hyperuricemic (non-gout) controls.

Methods: Peripheral blood samples were collected (directly into PAXgene RNA tubes) from 13 gout patients, 3 normuricemic and 3 hyperuricemic controls from the gout Rheumatology Database and Repository (RADAR) at the University of Alabama at Birmingham. Whole blood mRNA was isolated using poly A selection and the transcriptome was sequenced. Sequences were quality controlled and then aligned to the genome using the Spliced Transcripts Alignment to a Reference (STAR) software package. We tested for fold change differences in mRNA content between controls and gout cases using the R statistical computing package DESeq2.

Results: RNA sequencing yielded an average of 25 M reads per sample with an average read length of 125 bases. Forty eight gene transcripts were significantly differentially expressed (P value < 0.05), after correction for multiple testing, between gout cases and controls (normouricemic plus hyperuricemic). Of these differentially expressed gene transcripts, six that were overexpressed in gout compared to controls (Transcobalamin 1-*TCN1*, Amine oxidase-*AOC1*, Matrix metallopeptidase 8-*MMP8*, Cysteine rich secretory protein 3-*CRISP3*, Secretory leukocyte peptidase inhibitor-*SLPI* and Olfactomedin 4-*OLFM4*) are known to be involved in neutrophil degranulation. Another notable transcript significantly upregulated in gout cases was the S100 calcium binding protein A8-*S100A8*, which is associated with the production of reactive oxygen species (ROS). Transmembrane protein 176B-*TMEM176B*, was significantly downregulated in gout cases compared to controls.

Conclusion: The upregulation of genes that implicate pathways representing neutrophil biology (degranulation and ROS production) is consistent with the known role of neutrophils in gout pathogenesis. It is possible that this reflects true differences in the neutrophil gene expression program of gout-affected individuals compared to hyperuricemic and/or normouricemic controls. Reduced expression of *TMEM176B* has been shown to associate with activation of the NLRP3 inflammasome. Our whole transcriptomic study in gout patients and controls highlights the central role of inflammatory cell activation in the pathogenesis of gout.

Disclosure: R. Reynolds, None; **T. Merriman**, Ardea Biosciences, 2, 5, AstraZeneca, 2, 5, Ironwood Pharmaceuticals, 2; **A. Szalai**, None; **N. Sumpter**, None; **S. Bridges**, None; **J. Edberg**, None.

Abstract Number: 1233

Identification and Characterization of a Novel Dysfunction Variant p.I242T in ABCG2 Transporter in a Family with Early-onset Hyperuricamia and Gout

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SESSION INFORMATION
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Background/Purpose: *ABCG2* is a high-capacity urate transporter gene. Common dysfunctional variants of *ABCG2* that result in decreased urate excretion in humans are major causes of hyperuricemia and gout – especially in pediatric-onset patients [1]. In the present study, we identified and functionally characterized a novel *ABCG2* variant in a family with early-onset hyperuricemia and gout.

Methods: Fifty-three years old woman was examined for intermittent pain of distal interphalangeal joints and plants of non-inflammatory character. At age of 9, she was found to have hyperuricemia and then she started a strict low-purine diet. Nor medical reports either the levels of uric acid from that period are unfortunately available. At clinical examination, Heberden´s nodes and palpable resistance on plants were observed. In laboratory findings, there was a slightly elevated level of uric acid (371 μmol/L) and low level of vitamin D in her serum. Her son, a 33-year-old man, has the first gout attack at the age of 30 in the first metatarsal joint and since then the gout attack repeats twice a year. In biochemical characterization, hyperuricemia (569 μmol/L of uric acid), hyperglycaemia (5.9 mmol/L of glucose) and low level of vitamin D were found.

To explore the cause of this familial hyperuricemia and gout, we performed a metabolic investigation. The results of purine metabolism suggested that their hyperuricemia were mainly due to a defect in the urate excretion system and did not result from an excess production of urate. Based on two separate measurements of the patients' fractional excretion of urate and urinary urate excretion, their hyperuricaemia could be classified as renal underexcretion type. Since this type of hyperuricemia is reportedly related to ABCG2 dysfunction, we analyzed *ABCG2* coding regions of our patients using their genomic DNA, as described previously [2]. Prediction of the possible impact of allelic variant on protein function was determined using PolyPhen, Provean, Mutation Taster, and SIFT predictive software. Functional validation of an ABCG2 variant we found was performed using ABCG2-expressing plasma membrane vesicles as we report previously [3].

Results: We identified a novel heterozygous variant c.725T >C (p.I242T) in *ABCG2* gene in the proband and her son. In silico predictions of the possible impact of this variant on protein function were consistent as strong deleterious. Cell-based functional assays showed that this novel variant has little effect on the expression and subcellular localization of ABCG2 protein, whereas I242T variant had no urate transport activity.

Conclusion: In conclusion, our findings suggest a causal relationship between the hitherto undescribed variant of *ABCG2* and very early familiar onset of hyperuricemia/gout. Our identification of novel dysfunctional ABCG2 variant confirmed a key role of ABCG2 transporter as a a key genetic determinant in the onset of hyperuricemia/gout.

References:

1. Stiburkova B, et al. *Arthritis Res Ther*. 2019 Mar 20;21(1):77.
2. Stiburkova B, et al. *Rheumatology (Oxford)*. 2017 Nov 1;56(11):1982-1992.
3. Toyoda Y, et al. *Cells*. 2019 Apr 18;8(4). pii: E363.

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Disclosure: B. Stiburkova, None; **Y. Toyoda**, None; **K. Pavelcova**, None; **M. Klein**, None; **T. Takada**, None; **H. Suzuki**, None.

Abstract Number: 1234

Inconsistency in Uric Acid Reference Ranges Among 20 Top United States Hospitals: What Is "Normal"?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Elevated serum uric acid (UA) concentration is associated with the urate crystal deposition disorders gout and nephrolithiasis, as well as hypertension, the metabolic syndrome, chronic kidney disease, and cardiovascular disease. Hyperuricemia is often defined as a serum urate level greater than 6.8 – 7.0 mg/dL, a physicochemical cutoff above which monosodium urate crystals precipitate in body fluids. Here, we determined whether leading United States (U.S.) hospitals used this physicochemical cutoff in their definition of the reference ranges for serum UA, and if the reference ranges were consistent across institutions.

Methods: The top 20 hospitals listed in the U.S. News & World Report Best Hospitals 2018-2019 rankings were queried. Data were obtained in May 2019 using either online publicly available information, or by telephone contact with the laboratory. Information about the type of assay used to measure serum uric acid was obtained. Reference ranges reported by each laboratory for adult males and females were obtained. If a given laboratory reported age-dependent reference ranges for a given sex, the median UA thresholds for that sex were used.

Results: All surveyed laboratories reported utilizing enzymatic (uricase) methods, which were obtained from a variety of instrument manufacturers. The median reported upper limit of the reference range (ULRR) for UA in males was 8.0 mg/dL (range 7.0 – 9.0 mg/dL). The median reported ULRR for females was 6.6 mg/dL (range 5.7 – 8.0 mg/dL). Among the 20 laboratories, 12 different upper limits were used for males, and 11 different upper limits were used for females. For adult males, 15% of hospitals reported an ULRR of 6.8 – 7.0, while 85% used an ULRR greater than 7.0, and 0% used an ULRR less than 6.8. For adult females, 15% of hospitals used an ULRR of 6.8 – 7.0, 30% used an ULRR greater than 7.0, and 55% used an ULRR less than 6.8. Only one laboratory used an age-adjusted reference range.

Conclusion: The upper limits of the reference ranges for serum UA reported by leading U.S. hospitals do not consistently align with the physicochemical definition of hyperuricemia. Additionally, there is considerable variability in the ULRR among surveyed hospitals. This likely reflects use of population-based distributions rather than physicochemical criteria to define hyperuricemia. Most surveyed hospitals used an ULRR for adult females which was lower than 6.8. Most hospitals surveyed used an ULRR for adult males which was higher than 7.0. This practice may result in under-recognition of clinically significant hyperuricemia and under-dosing of uric acid lowering agents in the treatment of gout in male patients.

Disclosure: B. Frankel, None; **G. Hughes**, None; **M. Wener**, None.

Abstract Number: 1235

Monthly Dosing of ImmTOR Tolerogenic Nanoparticles Combined with Pegylated Uricase (Pegadricase) Mitigates Formation of Anti-Drug Antibodies Resulting in Sustained Uricase Activity in Symptomatic Gout Patients

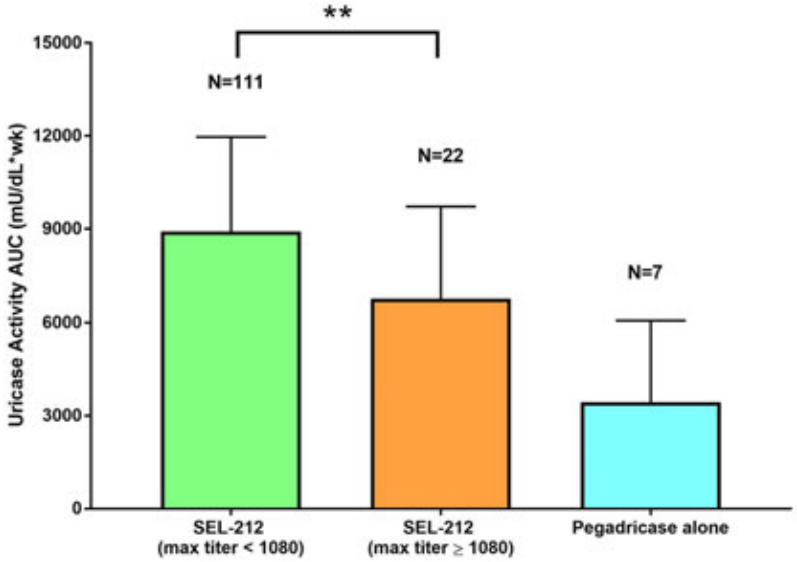
Wesley DeHaan,[1] Alan Kivitz,[2] Rehan Azeem,[1] Horacio Plotkin,[1] Lloyd Johnston,[1] Takashi K. Kishimoto,[1] Justin Park,[1] Stephen Smolinski,[1] and Sheldon Leung[1], [1]Selecta Biosciences, Watertown, MA, [2]Altoona Center for Clinical Research, Duncansville, PA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is caused by the deposition of monosodium urate (MSU) crystals in joints due to chronic hyperuricemia. Long term treatment focuses on reducing sUA levels, thus allowing MSU crystals to dissolve.

Pegylated uricases are therapies for treatment of severe chronic gout. However, uricases are limited by induction of anti-drug antibodies (ADA) that can compromise efficacy and safety. SEL-212 is a novel combination product consisting of pegadricase co-administered with proprietary ImmTOR tolerogenic nanoparticles. ImmTOR has been designed to mitigate the formation of ADAs by inducing tolerogenic dendritic cells and antigen-specific regulatory T cells. Prolonged therapeutic activity of uricase (pegadricase) is vital in maintaining a sustained control of serum uric acid (SUA) levels in patients. We report data on ADA [anti-uricase] and uricase activity from an open label study of monthly SEL-212 treatment in symptomatic gout patients.

Methods: Patients with symptomatic gout (≥1 tophus, gout flare within 6 months or gouty arthropathy) and elevated SUA ≥6 mg/dL were treated with fixed doses of pegadricase (0.2 mg/kg) in combination with ImmTOR (0.1 and 0.15 mg/kg), or pegadricase (0.2 or 0.4 mg/kg) alone as a control. Patients were infused in 28-day cycles up to 5 times. Safety, tolerability, sUA, ADAs, and uricase activity were monitored.



Effect of Treatment and Antibody Titer on Uricase Activity

Results: Demographics of 46 patients treated with 28-day cycles x5 combination doses of ImmTOR and pegadricase as compared to 6 patients treated with pegadricase alone was 23-70 years old vs. 41-64 years old (mean 53.6 vs. 51.8 years), male 97.8% vs. 100%, and white 73.9%. vs. 33.3%. The mean BMI at baseline was 34.5 vs. 38.9 kg/m2. 71.7% vs. 100% of patients were obese with mean duration of established or symptomatic gout as 12.5 vs. 12.8 years. 43 SEL-212 patients were evaluable for this analysis. The majority of treatment periods with SEL-212 had maximum antibody titers < 1080 (83.4%, 111/133) while 14.3% (1/7) treatment periods of pegadricase alone had maximum antibody titers < 1080. AUC of uricase activity was significantly higher in treatment periods where maximum ADA titers were below 1080 (p=0.0029). For all treatment periods for patients receiving SEL-212 in which their maximum anti-uricase titer was < 1080 (n=111), the mean uricase activity AUC was 8924 ± 3044 (mean ± SD) while in treatment periods where the maximum anti-uricase titer was ≥1080 (n=22), the mean uricase activity AUC was 6776 ± 2949. In treatment periods where control cohort patients received pegadricase alone (n=7), uricase activity had a mean AUC of 3437 ± 2635 which was lower than both SEL-212 treated groups. Six of the 7 treatment periods had maximum antibody titers ≥1080. For SEL-212 patients that had titers < 1080, the uricase activity AUCs were sustained over the 5 treatment periods and corresponding serum uric acid levels remained low.

Conclusion: By mitigating the formation of ADAs, monthly dosing of ImmTOR combined with pegadricase increases uricase activity in symptomatic gout patients relative to pegadricase alone. When anti-uricase titers are < 1080, patients show sustained uricase activity, enabling 28 day treatment intervals.

Disclosure: W. DeHaan, Selecta Biosciences, 1, 3; **A. Kivitz**, AbbVie, 5, Amgen, 1, 4, 5, Boehringer Ingeleheim, 5, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 5, 8, Flexion Therapeutics, 8, Genzyme, 5, 8, Gilead, 1, 4, 5, Gilead Sciences, Inc., 4, Horizon, 8, Janssen, 5, Janssen Research & Development, LLC, 2, Merck, 8, Novartis, 1, 4, 8, Pfizer, 1, 4, 5, 8, Regeneron, 1, 5, 8, Sanofi, 1, 4, 5, 8, Sun Pharma, 5, SUN Pharma Advanced Research, 5, UCB, 5; **R. Azeem**, Selecta Biosciences, 1, 3; **H. Plotkin**, Selecta Biosciences, 1, 3; **L. Johnston**, Selecta Biosciences, 1, 3; **T. Kishimoto**, Selecta Biosciences, 1, 3; **J. Park**, Selecta Biosciences, 1, 3; **S. Smolinski**, Selecta Biosciences, 1, 3; **S. Leung**, Selecta Biosciences, 1, 3.

Abstract Number: 1236

Subcutaneous or Oral Methotrexate Exposure and Response to Pegloticase in Uncontrolled Gout Patients in a Community Rheumatology Practice

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Pegloticase is an infused biologic for uncontrolled gout patients that is highly effective but can cause anti-drug antibodies that lead to a lack of therapeutic response. Based on data from randomized clinical trials, 42% of uncontrolled gout patients treated with pegloticase remain responders at 6 months of therapy. Low to moderate levels of immunomodulation treatment with medications such as methotrexate have been shown to attenuate the formation of anti-drug antibodies to biologic medicines in patients with rheumatoid arthritis. There are published cases in gout patients suggesting that low to moderate doses of methotrexate or azathioprine attenuate the development of anti-drug antibodies to pegloticase, allowing uncontrolled gout patients in need of pegloticase

therapy to remain on the medicine and achieve a more complete therapeutic outcome. The objective of the present case series was to determine whether exposure to oral or subcutaneous (subQ) methotrexate improved gout patients' response to pegloticase in a single community rheumatology practice.

Methods: A retrospective chart review was conducted in a rheumatology practice where uncontrolled gout patients starting pegloticase therapy are typically co-treated with methotrexate. All patients receiving any form or schedule of methotrexate before or while on pegloticase were included, and data extracted on their response including duration of pegloticase therapy, gout flares, infusion reactions, methotrexate dosing details, and lab values including uric acid levels, liver function tests, renal function, hemoglobin and white blood cell count. Complete blood count (CBC) and comprehensive metabolic panel (CMP) parameters were monitored closely in all patients treated with methotrexate.

Results: Ten uncontrolled gout patients fit the inclusion criteria. Nine patients were male, the average age was 52.3 years, and all had visible tophi. Methotrexate exposure varied, with 1 patient receiving oral and 9 receiving subQ administration; all but 1 patient started on methotrexate prior to pegloticase, and most patients received 25 mg of methotrexate subQ weekly. Of the 10 patients, at the time of data cutoff, 5 were complete responders, having received an average of 16.4 doses or ~32 weeks of therapy. Three were responding and still actively on pegloticase at the time of data extraction, having received 10, 5 and 2 doses respectively. Two patients had ceased therapy, 1 for loss of response and a mild infusion reaction and 1 due to methotrexate injection related issues. One patient had a gout flare requiring prednisone treatment. LFTs and CBC parameters remained stable during therapy with both methotrexate and pegloticase except for 1 patient who had a mild, transient alcohol-related LFT elevation and pancytopenia that improved with transfusion and cessation of methotrexate. This patient remained on pegloticase and continued as a responder.

Conclusion: When used concurrently with pegloticase, methotrexate appears to attenuate the formation of clinically significant anti-drug antibodies allowing uncontrolled gout patients to receive a more complete duration of pegloticase therapy. No new safety concerns were noted during this project.

Disclosure: J. Albert, Horizon, 8; **T. Hosey**, Horizon, 3, 4; **B. LaMoreaux**, Horizon, 3, 4.

Abstract Number: 1237

Treatment with OLT1177™, an Oral NLRP3 Inflammasome Inhibitor, Reduces Systemic Inflammation During Gout Flares in Humans

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SESSION INFORMATION

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Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Gout flares are characteristically mediated by the pro-inflammatory cytokine interleukin (IL)-1β. Uptake of monosodium urate (MSU) crystals by macrophages activates the nucleotide-binding domain and leucine-rich repeat containing family, pyrin domain containing 3 (NLRP3) inflammasome, which converts intracellular

pro-interleukin-1β (pro-IL-1β) to mature bioactive IL-1β by proteolytic cleavage. In the presence of concomitant pro-inflammatory stimuli, i.e., Toll-Like Receptor (TLR) agonists, transcription of IL-1β gene is induced and pro-IL-1β is rapidly converted into its active form. IL-1β binds to its receptor (IL-1R1) and induces a cascade of secondary inflammatory mediators including prostaglandins, cytokines and chemokines, resulting in a fulminant joint inflammation. Recently, OLT1177™, a β-sulfonyl nitrile compound, safe in humans, was shown to inhibit the NLRP3 inflammasome and inhibit joint inflammation in murine models of acute arthritis. This study explores the mechanisms by which oral OLT1177™ inhibits joint inflammation in humans with gout flares.

Methods: 29 patients with a gout flare were treated according to protocol with four different doses of OLT1177™ for 8 days (EudraCT: 2016-000943-14). Blood was drawn at baseline, days 3, 7 and 14 (7 days after finishing treatment). Haematology was evaluated as a marker of systemic inflammation. Plasma was collected for assessment of circulating cytokines. Peripheral blood mononuclear cells (PBMCs) were isolated and cultured under unstimulated or stimulated conditions with a TLR ligand in combination with MSU crystals after which intra- and extracellular cytokine production were assessed.

Results: Treatment of acute gout flares in humans with oral OLT1177™ demonstrates a reduction in white blood cell counts, mainly neutrophils, in all cohorts. In cohorts receiving 2000mg, 1000mg or 300mg, both circulating IL-1β and IL-6 and *ex vivo* IL-1β and IL-6 production by stimulated PBMCs were reduced during treatment with the strongest effect in the cohort with the highest dose OLT1177™. In unstimulated PBMCs on day 3, ratio of intracellular pro-IL-1β and IL-1β revealed inhibition of the NLRP3 inflammasome by oral OLT1177™ treatment. All these markers of inflammation are relevant parameters that correlate with target joint pain.

Conclusion: Oral OLT1177™, safe in humans, is a potential drug for the treatment of gout flares and other NLRP3 mediated diseases.

Disclosure: V. Kluck, None; **T. Jansen**, AbbVie, Celgene Corporation, 5, Grunenthal, Sobi, 8, Olatec, Grunenthal, 2; **M. Janssen**, None; **I. Tengensdal**, None; **K. Schraa**, None; **M. Cleophas**, None; **D. Skouras**, Olatec Therapeutics LLC; **C. Marchetti**, None; **C. Dinarello**, Olatec Therapeutics LLC; **L. Joosten**, Olatec Therapeutics LLC.

Abstract Number: 1238

Monosodium Urate and Calcium Pyrophosphatecrystal-induced Interleukin 1 Production Depends on Glucose Uptake Through Glut1 Transporter

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Monosodium urate (MSU) andmonoclinic calcium pyrophosphate dihydrated(mCPPD)crystals are responsible for relapsing acute arthritis which is driven by interleukin 1β (IL-1β).IL-1βproductionrelies on-

NLRP3 inflammasome activationleading to ASC and caspase-1 recruitment. In tumor cells and in LPS-stimulated macrophages a switch of cell metabolisms toward glycolysis favors IL-1β production.

The aims of this study were to assess 1/ whethercrystal-induced NLRP3 activation and IL-1βproduction involved glucose metabolism and 2/ how MSU and mCPPD crystals induced glucose uptake focusing on the role of glucose transporter Glut1.

Methods: Synthetic and pyrogen-free MSU andmCPPDcrystalswere used to stimulate THP-1 cells and mouse bone marrow-derived macrophages (BMDM). Cells were stimulated in presence or absence of glucose (2g/L) and pyruvate (10mM).Glycolysis was inhibited by 2-deoxy-glucose (2DG) and the role of glucose transporter 1 (Glut1)was assessed by pharmacological inhibitor (STF-31) and siRNA. IL-1β production was quantified by ELISA.Metabolomicanalysis was performed by mass spectrometry.Glucose uptake was determined using ^{18}F-DG (Fluor18 labeled-2DG) and positron emission tomography (PET). Glut1 membrane localization was assessed by flux cytometry and confocal microscopy, ASC speck formation by confocal microscopy. *In vivo*, we used murine air pouch model to assess the effects of 2DG and Glut1 inhibition in crystal-mediated inflammation.Glut1 membrane localization ofcirculating neutrophils was compared to synovial fluid neutrophils harvested during gout flare.

Results: *In vitro*, both MSU and mCPPDcrystal-induced IL-1β secretion and ASC speck formationwere inhibitedwhen cells were cultured in glucose-free medium or in presence of 2DG.Similarly,MSU and mCPPD crystal-induced inflammation was abrogated in mice treated with 2DG.In THP-1 cells stimulated by MSU and mCPPD crystals, metabolomicanalysis displayedalteration of glycolysis pathway and Krebs'cycle and decrease of intracellular ATP production. Interestingly, MSU and mCPPD crystals increased glucoseuptake*in vitro, ex vivo and in vivo*.Crystal-induced glucose uptake was inhibited by STF-31 and decreased in THP-1 cells transfected with Glut1 siRNA.Next, we observed that MSU and mCPPD crystals increased membrane localization of Glut1 in THP-1, BMDM and neutrophils infiltrated in air pouch lavages and membranes. Glut1 membrane localization was positively correlated with IL-1β production. Moreover, during gout flare, the proportion of Glut1 positive neutrophils was higher in synovial fluid neutrophils than in circulating neutrophils. Finally, STF-31 treatment decreased,*in vitro,*glucose uptake and IL-1 β production induced by MSU and mCPPD crystals, and *in vivo*MSU and mCPPD crystal-induced inflammation.

Conclusion: Glucose uptake through Glut1 transporter enhanced IL-1β production induced by MSU and mCPPD-crystals. Studies to decipher how these crystals induced Glut1 membrane localization are ongoing. Similarly, we investigate how glycolysis regulates NLRP3 and ASC activation. Decreasing Glut1 membrane localization might be a potential target to dampen crystal-induced inflammation.

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Abstract Number: 1239

The Association Between Urate and CSF Markers of Alzheimer's Disease in a Population-Based Sample of 70-Year-Olds

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Urate is a powerful antioxidant that accounts for approximately 60% of free-radical scavenging capacity in the human body. The diagnosis of Alzheimer's dementia (AD) is preceded by years of progressive cognitive impairment. Mild cognitive impairment (MCI) or predementia in AD is characterized by a certain pattern of cerebrospinal fluid (CSF) biomarkers beginning with a decrease of amyloid-β_{42} (Aβ) in CSF and followed by its aggregation in brain and hyperphosphorylation of the tau protein. The worldwide prevalence of dementia ranges between 5 to 7% with higher incidence of predementia reported in men before the age of 70-75 years. Urate has been suggested to exert potentially neuroprotective effects and might therefore alter the risk of dementia by virtue of its antioxidant abilities. A long-term follow-up study in Swedish women cohort has recently indicated a protective role of serum urate (SU) in the development of dementia. However, the relationship between urate and predementia remains elusive. The study was aimed to investigate the association between SU and predementia using the baseline data from a general population sample of 70-year-olds in Sweden.

Methods: The baseline sample was derived from the population-based H70 Gothenburg Birth Cohort that includes the data of every 70-year-old in Gothenburg, Sweden, born during 1944 (on prespecified birthdates). Overall, this cohort represents the data for 1,203 individuals (46.5% male) collected between 2014 and 2016. For this

Table 1. Demographic characteristics of the individuals included in the analysis, * Six out of 317 individuals (one male and five females) were missing the information for ApoE allele, ΔValues presented as mean ± standard deviation, β; Beta, ApoE+; Individuals carrying ApoE risk allele, ApoE-; Individuals carrying other/normal allele.

	All	Males	Females
Total number, n (%)*	317	165 (52.05)	152 (47.94)
Serum urate μmol/L)Δ	322.96 ± 76.38	355.84 ± 69.39	286.78 ± 66.94
Amyloid-β (pg/mL)Δ	718.94 ± 224.58	701.81 ± 231.58	737.53 ± 214.85
Total tau (pg/mL)Δ	331.09 ± 134.58	335.41 ± 135.93	326.39 ± 133.39
Phospho tau (pg/mL)Δ	49.36 ± 17.18	49.69 ± 17.30	49.01 ± 17.11
ApoE+	114	69	45
ApoE-	197	95	102

Table 2. Association of serum urate with markers of predementia, CSF; Cerebrospinal fluid, β (95% CI); Beta estimate (95% confidence interval), p; p-value, ApoE+; Individuals carrying ApoE risk allele, ApoE-; Individuals carrying other/normal allele.

CSF marker (pg/mL)	All		Males		Females	
	β (95% CI)	p	β (95% CI)	p	β (95% CI)	p
			Amyloid-β			
All	0.136 (-0.19 ; 0.46)	0.41	0.485 (-0.02 ; 0.99)	0.06	0.112 (-0.41 ; 0.63)	0.67
ApoE+	0.441 (-0.13 ; 1.02)	0.13	0.861 (-0.12 ; 1.83)	0.08	0.208 (-0.53 ; 0.95)	0.57
ApoE-	0.020 (-0.33 ; 0.37)	0.91	0.102 (-0.41 ; 0.61)	0.69	0.177 (-0.47 ; 0.82)	0.59
			Total tau			
All	-0.004 (-0.20 ; 0.19)	0.96	-0.156 (-0.46 ; 0.14)	0.31	0.075 (-0.24 ; 0.39)	0.64
ApoE+	-0.002 (-0.43 ; 0.42)	0.99	-0.028 (-0.68 ; 0.62)	0.93	-0.012 (-0.68 ; 0.66)	0.96
ApoE-	-0.208 (-0.21 ; 0.17)	0.84	-0.152 (-0.43 ; 0.13)	0.28	0.131 (-0.22 ; 0.47)	0.45
			Phospho tau			
All	-0.005 (-0.03 ; 0.02)	0.96	-0.025 (-0.06 ; 0.02)	0.19	0.021 (-0.02 ; 0.06)	0.32
ApoE+	-0.004 (-0.057 ; 0.05)	0.86	-0.015 (-0.09 ; 0.06)	0.71	-0.001 (-0.08 ; 0.07)	0.97
ApoE-	-0.0004 (-0.026 ; 0.02)	0.96	-0.021 (-0.05 ; 0.01)	0.23	0.035 (-0.01 ; 0.08)	0.14

study, measurements for SU and three CSF markers, $A\beta_{42}$, total tau and phospho tau, were analyzed from a subset (n=322) of the H70 cohort. The information for the presence of *APOE* risk allele (for single nucleotide polymorphism/ SNPs *rs7412* and *rs42935*) for each individual in this subset was also analyzed. Data for individuals with baseline prevalent dementia (n=5) was excluded from the analysis. Linear regression was performed to assess the association between SU and each CSF marker in overall and gender stratified groups. The groups were further stratified for the presence of *APOE* risk (ApoE+) or otherwise normal (ApoE-) allele. A $p > 0.05$ was designated to indicate a significant association. All analyses were performed using statistical software R (v3.5.2).

Results: Overall, 52% of the participants in the analysis were males. Individuals had a mean SU value of 322.9 (males; 355.8 and females; 286.7). A total of 114 individuals were carrying risk allele for *APOE*, with a higher percentage of males (~60%) being the carriers (Table 1). Regression analysis indicated only a trend of positive association between SU and Aβ in male subset (β = 0.48 pg/mL, $p = 0.06$), which persisted when assessed in ApoE+ group (β = 0.86 pg/mL, $p = 0.08$). The positive estimate was also observed in female subset (β = 0.11 pg/mL, $p = 0.67$), albeit not significant. No association for SU was observed for both total tau (β = -0.004 pg/mL, $p = 0.96$) and phospho tau (β = -0.005 pg/mL, $p = 0.96$) (Table 2).

Conclusion: In seventy-year old males we identify a possible protective effect of urate on predementia, defined as decreased CSF levels of amyloid-β and reflecting amyloid build-up in the brain. This effect seems to be further strengthened in the presence of APOE-ε4.

Disclosure: T. Fatima, None; **L. Jacobsson**, None; **L. Johansson**, None; **M. Dehlin**, None; **I. Skoog**, None.

Abstract Number: 1240

A Randomized, Phase 2 Study Evaluating the Efficacy and Safety of Anakinra in Difficult-To-Treat Acute Gouty Arthritis: The anaGO Study

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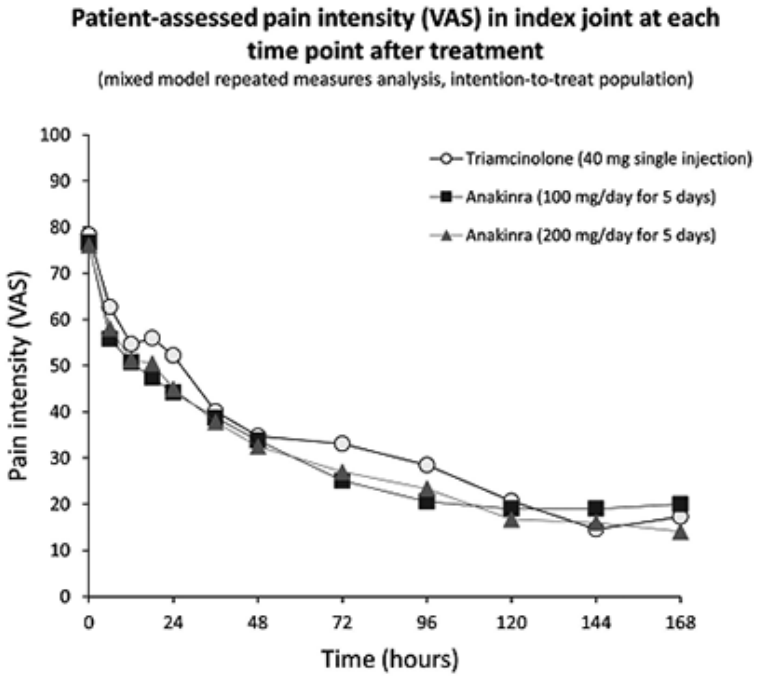
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Metabolic & Crystal Arthropathies Poster II: Clinical Trials & Basic Science
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In gout, urate crystals deposited in and around joints trigger episodes of acute arthritis, mediated by the proinflammatory cytokine IL-1β. In uncontrolled studies, the IL-1 receptor antagonist anakinra appears effective in reducing pain and signs of acute flares in patients with difficult-to-treat gout. However, confirmatory, adequately-powered, prospective trials are lacking. The 'anaGO-study' (anakinra in gout) was a multi-center, randomized, double-blind, double-dummy, phase 2 study investigating the efficacy and safety of anakinra in acute gout (NCT03002974).

Methods: Patients were recruited who had acute gout based on ACR/EULAR 2015 gout classification criteria, and were unsuitable for anti-inflammatory therapy with NSAIDs and colchicine due to contraindication, intolerance or inefficacy. The primary objective was to evaluate the efficacy of two regimens of anakinra (100 or 200 mg daily s.c.



injections for 5 days) compared to triamcinolone (single i.m. injection 40 mg) with respect to patient-assessed pain intensity. Patients were randomized to each group in a 1:1:1 ratio and stratified by urate-lowering therapy use (yes/no) and BMI (< 30.0 or ≥30.0 kg/m2). The primary endpoint was change in pain intensity from baseline to 24-72 hours (average of 24, 48 and 72 hours) in the most affected joint measured on a visual analogue scale (0-100 VAS). Secondary outcomes included: time to onset of effect, time to response, time to pain resolution, time to rescue medication use, patient's and physician's assessments of global response, clinical signs, inflammatory biomarkers, and safety.

Results: 165 patients were randomized; 110 to anakinra (56 to 100 mg/day, 54 to 200 mg/day) and 55 to triamcinolone; 108 and 53 were included in the primary analysis, respectively. The median (range) age was 55 (25-83) years, 87% were male, mean disease duration was 8.7 years and mean number of self-reported flares during the past year was 4.5. The pain intensity, from baseline to 24-72 hours, decreased in both treatment groups; mean (95% CI) change was -39.4 (-46.8, -32.0) for triamcinolone and -41.2 (-46.3, -36.2) for anakinra. The 100 mg and 200 mg doses of anakinra were comparably effective in decreasing pain (100 mg/day: -41.8 [-48.9, -34.8] and 200 mg/day: -40.7 [-47.9, -33.4]). Mean (95% CI) difference in pain reduction between anakinra and triamcinolone treatment groups was -1.8 (-10.8, 7.1) (p-value = 0.688 for primary endpoint). The majority of secondary efficacy endpoints were numerically in favor of anakinra, and in most instances also statistically significant, in comparison to triamcinolone, e.g. physician's assessment of clinical signs at 72 hours and patient's and physician's assessment of global response at Day 8. No unexpected safety findings were identified in any of the treatment groups.

Conclusion: Anakinra and triamcinolone reduced patient-assessed gout flare pain to similar degrees in patients for whom conventional therapy was ineffective or contraindicated. Both doses of anakinra showed comparable efficacy in pain reduction. The majority of secondary efficacy endpoints favored anakinra. Anakinra was shown to be an additional option for use during acute gout flares.

Disclosure: K. Saag, Abbvie, 5, AbbVie, 5, Amgen, 2, 5, Ampel, 2, Bayer, 5, Gilead, 5, Horizon, 2, 5, Ironwood/AstraZeneca, 2, 5, Kowa, 5, kowa, 5, Mereo, 2, Radius, 5, Radius Health, 2, 5, Roche/Genentech, 5, SOBI, 2, 5, Sobi, 2, 5, Takeda, 2, 5, Teijin, 5, Tejin, 5; **A. So**, Sobi, 5, Grunenthal, 5; **P. Khanna**, Horizon, 5, Sobi, 5; **R. Keenan**, Sobi,

5, Selecta, 5, Horizon, 5; **S. Ohlman**, Sobi, 1, 3; **T. Kullenberg**, Sobi, 1, 3; **L. Osterling Koskinen**, Sobi, 1, 3; **M. Pillinger**, Sobi, 5, Horizon, 5; **R. Terkeltaub**, Astra-Zeneca, 2, 5, Horizon, 5, Selecta, 5, SOBI, 5, Sobi, 5.

Abstract Number: 1241

Further Characterizing Morphea Subsets Using a Multi-center, Prospective, Cross-sectional Analysis of Morphea in Adults and Children

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Table 1: Demographic and clinical characteristics of morphea by age at onset

Characteristic	All patients (n=944)	Pediatric Onset (N=497)*	Adult Onset (N=443)	P Value
Age (y), median (IQR)	16 (8-44)	9 (5-12)	45 (31-58)	<0.001[a]
Sex, n (%)				<0.001[b]
Male	203 (22%)	131 (26%)	71 (16%)	0.001[b]
Female	741 (78%)	366 (74%)	372 (84%)	
Race, n (%)				0.001[b]
Caucasian	722 (76%)	394 (79%)	325 (73%)	
Non Caucasian	212 (24%)	96 (19%)	116 (26%)	
Subtypes, n (%)				<0.001[b]
Linear	582 (62%)	454 (90%)	128 (29%)	
ECDS	*78 (13%)*	*45 (10%)*	*33 (26%)*	
PRS	*77 (13%)*	*48 (11%)*	*29 (23%)*	
Generalized	225 (24%)	26 (5%)	199 (46%)	
Plaque	90 (10%)	8 (2%)	82 (18%)	
Mixed	44 (5%)	14 (4%)	29 (7%)	
LoSCAT component score, median (IQR)				
mLoSSI	4 (0-10)	3 (0-7)	6 (0-17)	<0.001[a]
LoSDI	9 (5-19)	8 (5-16)	11 (6-22)	0.002[a]
PGA-A	20 (0-40)	20 (0-41)	20 (0-40)	0.420[a]
PGA-D	30 (15-41)	34 (21-49)	20 (10-30)	<0.001[a]
Clinical features and disease modifiers, n (%)				
Deep Involvement	409 (43%)	97 (20%)	312 (72%)	<0.001[b]
Dermal Involvement	245 (32%)	85 (17%)	160 (37%)	<0.001[b]
Hair Loss in Lesion	122 (16%)	60 (12%)	62 (14%)	0.369[b]
Limited Range of Motion	201 (21%)	123 (25%)	78 (18%)	0.008[b]
Joint Deformity	56 (6%)	52 (10%)	4 (1%)	<0.001[b]
Erythema	122 (13%)	117 (24%)	5 (1%)	<0.001[b]
Functional Abnormality – by location, n (%)				
Face/Head/Neck	19 (2%)	10 (2%)	9 (2%)	0.231[b]
Trunk	29 (3%)	18 (4%)	10 (2%)	0.022[b]
Lower Extremity	147 (16%)	87 (18%)	59 (14%)	0.003[b]
Upper Extremity	92 (10%)	50 (10%)	41 (9%)	0.462[b]

IQR, Interquartile range; *ECDS,* en Coup de Sabre; *PRS,* Parry-Romberg Syndrome; *LoSCAT,* Localized Scleroderma Cutaneous Assessment Tool; *mLoSSI,* modified Localized Scleroderma Skin Severity Index; *LoSDI,* Localized Scleroderma Skin Damage Index; *PGA-A,* Physician Global Assessment of Disease Activity; *PGA-D,* Physician Global Assessment of Disease Damage.

* Pediatric onset was defined as onset of disease <18 years

[a] Values computed with Mann-Whitney U Test

[b] Values computed with chi-square test

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: There have been few large, prospective cohort studies performed on morphea, or localized scleroderma. Most that exist focus exclusively on either pediatric or adult populations, or are retrospective. The objective of this study was to examine two combined prospective databases (Morphea in Adults and Children and National Registry for Childhood-Onset Scleroderma) in order to further characterize these patients and determine subtle features of disease.

Methods: We conducted a cross-sectional analysis using both traditional univariate statistics as well as a multivariate approach – a principal component analysis (PCA). All patients were scored using the Localized Scleroderma Cutaneous Assessment Tool, a validated outcome measure that includes disease activity (modified Localized Scleroderma Skin Severity Index (mLoSSI)) and damage (Localized Scleroderma Skin Damage Index (LoSDI)) components.

Table 2 Rotated Component Matrix[a] of clinical features in 719 morphea patients

Clinical Features	Components				
	1	2	3	4	5
FunAb in lower extremities (toes, ankles, knee, hips)	**0.774**	0.085	0.010	0.149	0.019
FunAb in upper extremities (finger, wrist, elbow)	**0.771**	0.040	-0.016	0.155	0.032
Limited range of motion	**0.770**	0.045	-0.002	-0.039	0.194
PGA-D	**0.668**	0.017	-0.194	-0.025	-0.235
LoSDI	**0.636**	0.071	0.068	0.359	-0.262
FunAb in face and/or neck	0.462	0.027	0.185	0.070	0.056
Patient reported fatigue	0.075	**0.730**	0.184	-0.029	-0.018
Patient reported headaches	-0.044	**0.657**	-0.012	-0.107	0.001
Patient reported joint pain	0.283	**0.626**	0.036	0.104	0.036
Patient reported muscle pain	0.193	**0.619**	0.215	0.089	0.191
Patient reported vision changes	-0.055	**0.511**	-0.193	-0.084	-0.013
Depression	-0.082	0.457	0.056	0.032	-0.137
Dermal involvement	-0.071	0.045	**0.706**	0.007	0.067
Deep involvement	0.210	0.051	**0.680**	-0.138	-0.037
Erythema	0.055	-0.037	**-0.597**	0.112	0.380
Deformity	0.277	-0.064	-0.343	-0.299	0.107
Patient reported hair loss	0.227	0.280	-0.308	-0.159	-0.234
mLoSSI	0.292	-0.023	0.013	**0.861**	-0.045
PGA-A	0.157	-0.083	-0.255	**0.785**	0.198
Swelling	0.056	0.016	0.134	0.003	**0.653**
Hair Loss	0.229	0.044	0.264	-0.170	-0.483
FunAb in trunk (back, shoulders)	0.454	-0.042	0.100	-0.176	0.461

FunAb, functional abnormality; *mLoSSI*, modified Localized Scleroderma Skin Severity Index; *LoSDI*, Localized Scleroderma Skin Damage Index; *PGA-A*, Physician Global Assessment of Disease Activity; *PGA-D*, Physician Global Assessment of Disease Damage.

[a] Rotation converged in 10 iterations. Extraction method was a principal components analysis with varimax rotation and Kariser normalization.

Marked numbers indicate factor loadings > |0.5|

Table 3: Rotated Component Matrix* of SKINDEX 29+3 Questions in 300 adult morphea patients

SKINDEX 29+3 Questions	Components			
	1	2	3	4
Makes showing affection difficult	**0.803**	0.172	0.048	0.226
Affects desire to be with others	**0.779**	0.320	0.234	0.181
Affects interactions with others	**0.760**	0.306	0.268	0.239
Affects how close I can be with those I love	**0.744**	0.269	0.205	0.280
Do things by myself due to my skin	**0.746**	0.313	0.278	0.125
Skin is a problem for the people I love	**0.657**	0.043	0.136	0.255
Interferes with my sex life	**0.644**	0.194	0.112	0.276
Affects my social life	**0.643**	0.370	0.448	0.133
Humiliated by my skin	**0.623**	0.609	-0.023	0.015
Tend to stay at home due to my skin	**0.605**	0.186	0.453	0.273
I feel lonely due to my skin	0.482	0.476	0.385	-0.038
Annoyed by my skin	0.186	**0.754**	0.164	.160
Frustrated with my skin	0.301	**0.753**	0.182	0.178
I worry my skin condition is getting worse	0.084	**0.750**	0.207	0.157
Embarrassed of my skin	**0.526**	**0.705**	-0.016	0.009
Angry about my skin	0.315	**0.682**	0.204	0.057
Ashamed of my skin	**0.578**	**0.649**	0.029	0.023
I worry about getting scars from my skin	0.155	**0.666**	-0.040	0.283
I worry my condition is serious	0.092	**0.621**	0.405	0.232
My skin makes me feel depressed	**0.505**	**0.590**	0.287	0.127
Skin causes tightness, joint pain that limits activities	0.135	0.193	**0.758**	0.273
My skin makes it hard to work or do hobbies	0.389	0.109	**0.712**	0.286
Skin makes me tired	0.309	0.204	**0.624**	0.250
My skin affects my ability to sleep	0.273	0.021	**0.630**	0.443
Worry that my skin may affect internal organs	0.054	0.425	**0.552**	0.150
Skin Burns or Stings	0.222	0.144	0.370	**0.697**
Skin itches	0.107	0.317	0.122	**0.712**
Skin is irritated	0.122	0.326	0.306	**0.697**
Skin hurts	0.110	0.134	0.523	**0.608**
Skin is sensitive	0.192	0.301	0.352	**0.603**
Water bothers my skin	0.328	-0.042	0.054	**0.654**
My skin bleeds	0.210	0.065	0.113	0.330
Worry about the side-effects from treatment	0.123	0.470	0.197	0.269

* Rotation converged in 10 iterations. Extraction method was a principal components analysis with varimax rotation and Kariser normalization.

Marked numbers indicate factor loadings > |0.5|

Results: Of the 944 participants, 497 (53%) had pediatric onset morphea, and 433 (47%) had adult onset morphea. **[Table 1]** Caucasian (76%), female (78%) and linear morphea (62%) patients compromised the majority of the cohort. Adult onset patients had significantly higher mLoSSI and LoSDI scores than pediatric onset disease ($p < 0.001$ and $p = 0.002$, respectively), but pediatric onset patients had a significantly higher PGA-D score ($p < 0.001$). Adult-onset patients were significantly more likely to have deep (72%, 312/443) and dermal (37%, 160/443) involvement ($p < 0.001$ for both), but children were significantly more likely to have erythema of lesions crossing the joint (24%, 117/497, $p < 0.001$), limited range of motion (LROM) (25%, 123/497, $p = 0.$) and joint deformity (10%, 52/497, $p < 0.001$). Children were also significantly more likely to have functional abnormalities in the trunk (4%, 18/497, $p = 0.022$) and lower extremity (18%, 87/497, $p = 0.003$).

Further analysis of the clinical and patient-reported symptoms by PCA determined 4 relevant latent phenotypes (F1-F3). **[Table 2]** F1 described patients who had LROM in their extremities with high damage scores, while F2 depicted patients with patient reported complaints related to fatigue, pain and depression. F3 described patients with deep dermal and underlying tissue involvement. F4 captures patients with highly active disease.

A PCA of the SKINDEX 30+3 quality of life questionnaire in adults revealed 4 significant factors (F1-F4). **[Table 3]** F1 represented questions regarding social isolation and overall self-consciousness, while F2 represented patients who exhibited pre-occupation with their skin condition and a higher proportion of emotions questions. F3 characterized patients who had functional impairment and F4 patients with mostly skin related symptoms.

Conclusion: In summary, our large, prospective cross-sectional study demonstrated several novel observations in addition to previously reported findings in morphea. These findings change practice by describing new subsets of morphea patients, including a group with characteristics of chronic pain syndrome and various cohorts with psycho-social impact. These results should be further explored to allow providers to provide more targeted management of these cohorts of morphea patients.

Disclosure: S. Prasad, None; **K. Schollaert**, None; **R. Haley**, None; **K. Torok**, None; **H. Jacobe**, None.

Abstract Number: 1242

Impact of Smoking Status on Remission in Hidradenitis Suppurativa

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hidradenitis Suppurativa (HS) is an inflammatory disease of the apocrine sweat glands characterized by recurrent abscessing inflammation. The molecular drivers of HS are poorly understood, but smoking

Table 1. Baseline demographics by smoking status in the current, never and past smoker groups.

	Current smoker (n=28)	Never smoker (n=80)	Past smoker (n=24)	p-value
Age at Baseline, years (Mean ±SD)	44 ± 11	35 ± 13	30 ± 13	0.002
Sex, % female	64%	78%	75%	0.39
Race				
African American	68%	53%	54%	0.77
Caucasian	32%	41%	42%	
Asian	0%	5%	4%	
Other	0%	1%	0%	
Pain score	2.35 ± 3.59	2.15 ± 3.02	4.17 ± 3.50	0.01
Baseline BMI (kg/m^2)	34.12 ± 8.16	32.09 ± 7.19	33.87 ± 7.22	0.36
Baseline HSS	53 ± 52	49 ± 55	49 ± 45	0.62
Hurley Stage	2.0 ± 1.1	1.9 ± 1.1	2.1 ± 0.9	0.76
Active Nodule Count	3.3 ± 2.2	2.9 ± 2.5	3.3 ± 2.0	0.76

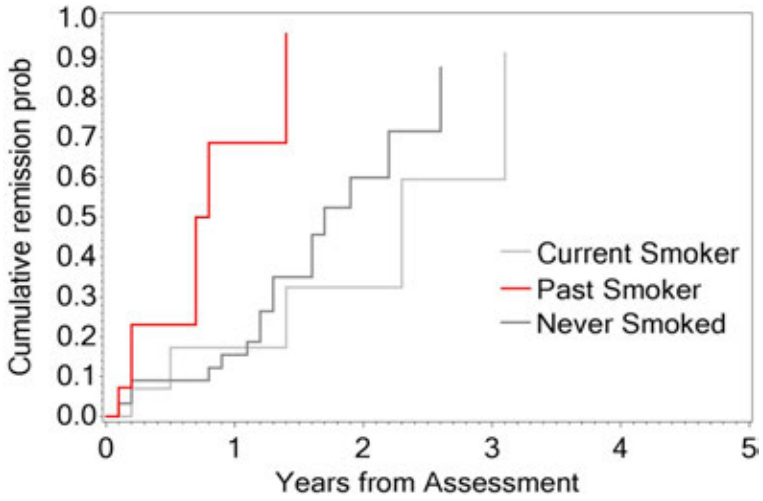

Figure 1. Kaplan Meier analysis of the three cohorts demonstrating cumulative probability of remission based on achieving HiSCR over time (years since enrollment). Patients who continued to smoke had the lowest rates of achieving remission compared to the past and never smokers (p=0.046)

is strongly associated with disease activity. The US Food and Drug Administration (FDA) recently approved tumor necrosis factor-alpha inhibitors (TNF-i) for HS. However, little is known about the relationship between smoking and remission rates in patients receiving TNF-i therapy for HS. The purpose of this study was to investigate the relationship between smoking and HS remission rates in a longitudinal cohort of patients receiving ongoing therapy for HS.

Methods: This study was conducted through the Wound Etiology and Healing Study (WE-HEAL Study), an IRB approved biospecimen and data repository for tracking outcomes in HS. All subjects gave written informed consent for longitudinal collection of their data while they received treatment according to standard of care. Demographic data, baseline medical comorbidities, smoking and disease activity scores were collected. Patients were categorized by smoking status at last follow up (current, never, past). Disease activity was assessed using Hurley Stage, Hidradenitis Sartorius Score (HSS), and Active Nodule (AN) Count. Remission was a binary outcome based on achieving the Hidradenitis Suppurativa Clinical Response (HiSCR). Statistical analysis was conducted using SAS version 9.4. Multivariable Cox proportional hazard model was used for analysis.

Results: At the time of data lock, there were 132 patients in the WE-HEAL HS cohort: current smokers (21%), past smokers (18%), never smokers (61%). There was no statistically significant difference between the groups in regards sex, race or baseline body mass index (BMI). The past smoker group had a higher baseline pain score (p=0.01) and current smokers tended to be slightly older (p=0.002). There was no significant difference between the three groups in baseline disease activity scores (Table 1).

Time to remission did not differ significantly between smoking categories in univarible KM analysis (log-rank p = .18). However, after adjusting for age, ever receiving MTX, TNFi, or opioids, and ever having HS surgery, the HR for current smoker vs past smoker reaching remission is 0.31 (0.10-0.98) (p=.046). This indicates that past smokers reach remission more quickly than current smokers (**Figure 1**). Never-smoked differed from past-smoker only at a trend level of significance (aHR 0.43 [0.18-1.04], p=.06). The only other covariate associated with remission was ever receiving opioids. Those who did receive opioids had reduced likelihood of reaching remission (aHR 0.24 [0.08-0.72], p=.01).

Conclusion: The current analysis shows that patients who continue to smoke demonstrate lower and slower rates of achieving remission than those who stop smoking or never smoked. This data not only supports the strong benefit of smoking cessation in HS management, but also suggests that smoking may impact the immune drivers of HS.

Disclosure: A. Agarwal, None; **M. Mangini**, None; **D. Jones**, None; **C. Hood**, None; **R. Amdur**, None; **V. Shanmugam**, AbbVie, 2.

Abstract Number: 1243

Anakinra Treatment in Recurrent Pericarditis: Single Center Experience

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Recurrent pericarditis (RP), however the etiology is unknown in the majority, may be observed in autoinflammatory diseases such as familial Mediterranean fever (FMF) and tumor necrosis factor receptor-1 associated periodic syndrome (TRAPS). Colchicine has long been used to treat pericarditis related to FMF as well as patients with idiopathic recurrent pericarditis (IRP) (1). Alternative treatments have been reported for cases with colchicine resistant RP.

The aim is to present our data regarding anakinra treatment in recurrent pericarditis either related to FMF or idiopathic, who are resistant to colchicine.

Methods: Patients who had recieved anakinra with a diagnosis of recurrent pericarditis either idiopathic or secondary to FMF followed in our autoinflammatory disease center between 2014-2018 are evaluated retrospectively. From patients' files, demographic and clinical features, response to other treatment approaches such as NSAID, corticosteroid, colchicine, were evaluated. All patients have been genetically screened for monogenic autoinflammatory diseases (MEFV, TRAPS, MVK, NLRP3, NOD2). Patients who had at least 3 attacks were administered anakinra 100 mg/day. Therapeutic efficacy, as well as side effect profile of anakinra is also assessed.

Table 1. Demographic features and treatment response during anakinra therapy

Patient ID #	Age	Sex	Diagnosis	Duration of pericarditis follow-up (mo)	Prior medications	Number of recurrences before anakinra	Anakinra treatment duration (mo)	Time to corticosteroid discontinuation (mo)	Number of recurrences after daily dose of anakinra
1*	23	M	IRP	129	Colchicine, NSAIDs, CS, HCQ	6	52	9	No
2	32	F	IRP	128	Colchicine, NSAIDs	7	4	NA	No
3*	40	F	IRP	21	Colchicine, CS	6	8	1	No
4	20	M	IRP	11	Colchicine, CS	3	8	2	No
5	25	M	FMF	30	Colchicine, CS	5	15	1	No

F: Female, M: Male, CS: Corticosteroid, HCQ: Hydroxychloroquine, NA: Not applicable
*Dose tapering was unsuccessful in these patients

Results: There were 5 patients (3 male and 2 female) with the diagnosis of RP, 1 was related to FMF and 4 were idiopathic. The mean age of the group was 28±8 (range 20-40). All patients diagnosed with IRP were negative for autoinflammatory genetic screening, while a MEFV variant (K695R het.) was detected in the FMF patient. Median duration of follow-up was 30 months (range 11-129). In table 1, demographic and clinical features are given. The median number of recurrence was 6 before anakinra treatment. No episode of pericarditis was observed in any of the patients after the initiation of anakinra. The response to anakinra persisted even after the dose was reduced to 100 mg/alternate day in 3 patients, however in 2, recurrence of pericarditis was observed and anakinra was escalated to initial dose. It was possible to discontinue corticosteroid treatment in all patients. Currently all patients continue anakinra treatment. No side effect including injection site reaction, has been observed by now.

Conclusion: Anakinra seems to be a safe and effective treatment approach for colchicine resistant recurrent pericarditis. However recurrence may occur during dose tapering.

Disclosure: Z. Toker Dincer, None; **O. Corbali**, None; **S. Ugurlu**, None; **H. Ozdogan**, None.

Abstract Number: 1244

Tocilizumab - An Effective Rescue Therapy for Refractory Unclassified Autoinflammatory Diseases in Children

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
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Background/Purpose: Evidence based treatment options for children and adults with unclassified autoinflammatory diseases (AID) are limited. Frequently, IL-1-inhibition is primarily tried to control the severe autoinflammatory symptoms. Tocilizumab (TMB) is approved for treatment of systemic juvenile idiopathic arthritis[1]. The aim of this study was to evaluate efficacy and safety of Tocilizumab (TMB) in patients with unclassified AID, who did not achieve remission by IL-1-blockade therapy.

Methods: A single-center retrospective cohort study included consecutive children with typical clinical AID features of chronic recurrent fevers and increased inflammatory markers. All children did not meet any of the new classification criteria[2] for either familial Mediterranean fever (FMF); tumor necrosis factor receptor-associated periodic syndrome (TRAPS); mevalonate kinase deficiency (MKD); cryopyrin-associated periodic syndrome (CAPS) or periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA). All patients were non-responders to IL-1-inhibitors (canakinumab or anakinra) and subsequently received TMB (8-12mg/kg i.v. every 2 weeks). Data collection included demographics, clinical phenotype, inflammatory markers, duration and dose of IL-1-inhibition, disease activity (physician and patient global assessment). Outcome: remission was defined as VAS of the physician global assessment ≤ 2 and inflammatory markers in the normal reference range (CRP ≤ 0.5mg/dl and/or SAA ≤ 10mg/l).

Results: Seven patients met the inclusion criteria, five males (71%) and two females (29%); median age at start of TMB therapy was 9 years (range 2-17). First follow-up was after 3 months (range 3-6) and second follow-up was after 12 months (range 10-14) of TMB therapy. At baseline, median disease activity (VAS physician) was 4 (range 2-6) and decreased to 1 (range 0-5) at first follow-up and again 1 (range 0-3) at second follow-up. Median CRP decreased from

1.23 mg/dl at baseline to 0.01 mg/dl at first follow-up. At baseline, median SAA levels were 20 mg/l (range 1-1010) and decreased to 1 mg/l (range 1-1.9) at first follow-up. At first follow-up, 4/7 patients (57%) achieved remission and at second follow-up, 4/5 patients met remission criteria (80%). One patient, who did not achieve remission at first follow-up, fulfilled the remission criteria at second follow-up. Over the entire observation period, a total of 5 patients (71%) achieved remission. Adverse events (neutropenia) were observed in 2 patients (29%).

Conclusion: TMB appears to be an effective treatment option for patients with unclassified AIDs, who do not respond favorably to IL-1-blockade. No unexpected adverse events occured. Clinical features and inflammatory markers rapidly improved; the response was sustained at the 12 months follow-up. Translational studies are urgently required to define the optimal treatment target in unclassified AIDs early on.

References:

1. de Benedetti F, et al. N Engl J Med 2012; 367:2385-2395
2. Gattorno M, Hofer M, Federici S, et al. Ann Rheum Dis 2019; April 24

Disclosure: J. Kuemmerle-Deschner, Novartis, 2, 5, 8, SOBI, 2, 5, 8; **D. Sturm**, None; **S. Benseler**, Novartis, 8, SOBI, 8.

Abstract Number: 1245

Efficacy of Canakinumab Treatment in Adult-onset Still's Disease

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Adult-onset Still's disease (AOSD) is a rare auto-inflammatory condition characterized by fever, arthritis, skin rash, and multi-organ inflammation. The pathogenesis of AOSD is centrally mediated by the pro-inflammatory cytokine interleukin (IL)-1β; anakinra, a recombinant inhibitor of the IL-1β receptor, has long represented the cornerstone of biologic therapy for AOSD. More recently, a new agent blocking IL-1β has also entered the clinical arena, that is, the monoclonal antibody canakinumab. Here, we describe the use of canakinumab both as first-line and rescue IL-1 blocker in 10 patients with AOSD, and report the highly promising results of this treatment approach.

Methods: Detailed clinical information were retrospectively retrieved for AOSD patients followed up in our Rheumatology Unit and treated with canakinumab. Information pertained to: disease duration; clinical features; AOSD course; previous and concomitant treatment with conventional synthetic DMARD or biologic agents; levels of inflammatory markers (ESR, CRP, and ferritin); dose of corticosteroid therapy before and after canakinumab initiation. Changes in these parameters upon canakinumab treatment were recorded, and statistical significance of differences evaluated with non-parametric tests. A p-value < 0.05 was considered significant.

Sex, Age (years)	Disease duration (months)	Disease manifesations	AOSD course	Therapy before CAN (mg)	bDMARD before CAN	Follow-up (months)	Therapy after CAN (mg)	Response to CAN	Side effects
M, 21	17	A-R-F-S	SD	PDN (15) MTX (20)	None	18	MTX (20)	Complete	None
M, 41	25	A-R-F-L-HSM	SD	PDN (25) MTX (20)	None	9	PDN (5) MTX (15)	Complete	None
F, 62	60	A-F-L-S	SD	PDN (10) MTX (10)	None	12	MTX (10)	Complete	None
M, 37	11	A-F-P-R	SD	PDN (25) MTX (20)	None	9	PDN (2.5) MTX (20)	Complete	None
F, 62	7	A-F-L-P-R	SD	PDN (35) MTX (15)	None	3	PDN (15) MTX (10)	Partial	None
F, 44	230	A-F-L-P-R	CAD	PDN (7.5) MTX (15)	ETN ADA TCZ ANK	4	PDN (2,5) MTX (20)	Partial	None
M, 31	48	A-F-HSM-R	SD	PDN (25)	ANK	2	PDN (12.5)	Partial	None
M, 69	21	A-F-R-L-P	SD	PDN (25)	ANK TCZ	6	PDN (10)	Complete	Leukopenia
F, 74	204	A-F	CAD	MTX (20) PDN (15)	ANK, ETN	4	PDN (5) MTX (20)	Partial	None
F, 51	72	A-F-P-R	CAD	PDN (10) MTX (20)	ANK	6	MTX (20)	Partial	Zoster

	Pre-CAN	Post-CAN	P value
CRP (mg/dL)	24.12 ± 14.13	5.56 ± 3.19	0.005
ESR (mm/1h)	47.20 ± 26.95	20.60 ± 18.60	0.005
Ferritin (ng/mL)	889.70 ± 397.27	184 ± 144.64	0.007
Steroid dose (mg/day)	19.25 ± 8.98	5.25 ± 5.46	0.005

Table 1. Disease duration refers to the duration of disease before initiation of canakinumab (CAN). Disease manifestations: A, arthritis; F, fever; R, rash; P, pharyngitis; S, serositis; L, lymphadenopathies; HSM, hepatosplenomegaly. Therapy before biologics indicates the treatment regimen that was being administered at the time of biologic initiation; therapy after biologics indicates the maintenance therapy that was being administered together with biologics at the last follow-up visit. PDN, prednisone; MTX, methotrexate,; ANK, anakinra; ETN, etanercept; ADA, adalimumab; TCZ, tocilizumab. SD, systemic disease.

Results: Ten patients with severe AOSD received canakinumab 300 mg 4 weekly following failure of conventional treatment with corticosteroids, DMARDs, or anakinra. Detailed clinical features and responses to therapy are reported in **Table 1.** Median AOSD duration at the time of canakinumab initiation was 36.5 months (range 18-65); median follow-up after canakinumab initiation was 9 months (4-18). Five patients received canakinumab as first-line biologic agent, whereas five patients received it following failure of anakinra. Regardless of previous treatment status, canakinumab treatment led to rapid clinical responses; in 6 out of 10 patient this clinical response was complete. Resolution of fever and skin rash was followed by progressive improvement in arthritis. Inflammatory organ involvement (i.e. pericardial inflammation) also resolved. Efficacy on clinical manifestations was mirrored by significant reductions in serum pro-inflammatory markers CRP, ESR, and ferritin. Sustained efficacy allowed for discontinuation or tapering of corticosteroid or DMARD therapy.

Conclusion: Biologic therapy of AOSD with canakinumab was associated with rapid and marked clinical responses, leading to substantial clinical amelioration in all patients and allowing for robust steroid-sparing effects. Earlier use

was associated with optimal responses, but treatment with canakinumab was also effective in difficult-to-treat patients following failure of IL-1 receptor blockade with anakinra.

Disclosure: C. Campochiaro, GSK, 8, GSK, SOBI, Pfizer, 5, 8, Pfizer, 8, SOBI, 5; **A. Tomelleri**, None; **D. Giacomo**, GSK, 8, Pfitzer, 8, SOBI, 5, SOBI, Novartis, SOBI, Pfizer, 5, 8; **N. Farina**, None; **E. Baldissera**, Sobi, 8, Sanofi, 5, Roche, 8, Pfizer, 8, Novartis, 8, Abbvie, 8, Alfa-sigma, 8; **G. Cavalli**, SOBI, Novartis, Pfizer, 5, 8; **L. Dagna**, Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI., 5, 8.

Abstract Number: 1246

Using PROMIS Data to Assess Activity of Inflammatory Eye Disease

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SESSION INFORMATION
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Background/Purpose: Diagnosing and managing patients with inflammatory eye disease (IED) requires close interdisciplinary care with rheumatologists adjusting systemic, potentially toxic, therapies based on exam findings visualized by ophthalmologists. Surveys of patient reported outcomes have been used to influence medical decision making in other chronic medical conditions (including rheumatologic disease), but utility has not been assessed in patients with IED. We evaluated use of PROMIS (Patient-Reported Outcomes Measurement Information System) data in tracking ocular disease activity and response to therapy in these patients.

Methods: We identified patient charts containing an ICD code diagnosis for uveitis or scleritis, who were seen two or more times by specialists in IED through Cleveland Clinic's rheumatology and ophthalmology departments between July 2016 and December 2018. These charts were individually reviewed to ensure there were at least two data points available for study inclusion where PROMIS data was collected within two weeks of a documented ophthalmic exam. Demographics and disease characteristics were noted. PROMIS data and ophthalmic exam findings were documented for each patient's initial and each subsequent encounter meeting inclusion criteria.

Table 1. Repeated measures correlation between eye exam findings and PROMIS measures.

	PROMIS domain	Correlation coefficient	95% CI	p-value*
Conjunctival injection	Physical	-0.064	(-0.19, 0.068)	0.34
	Mental	-0.11	(-0.24, -0.020)	0.094
	Function	0.026	(-0.11, 0.16)	0.70
Anterior chamber inflammation	Physical	-0.21	(-0.34, 0.085)	**0.0012**
	Mental	-0.18	(-0.31, -0.053)	0.0060
	Function	-0.16	(-0.29, -0.034)	0.013
Vitreous inflammation	Physical	-0.004	(-0.14, 0.13)	0.96
	Mental	-0.003	(-0.14, 0.13)	0.97
	Function	0.10	(-0.031, 0.23)	0.13

*p-value less than 0.0025 is considered significant.

Results: 87 patients were included in final analysis (74 uveitis patients and 13 scleritis patients). We found no significant differences in PROMIS or PHQ scores when comparing uveitis to scleritis patients. In regards to correlation of specific exam findings to different PROMIS measures, there was found to be a significant negative correlation ($r = -0.21$, $p = 0.0012$) between extent of anterior chamber inflammation and reported physical health PROMIS scores. Presence of vascular leakage on fluorescein angiography was found to be associated with worse physical health PROMIS scores at 1 year follow-up ($p = 0.007$), though this was not seen at other time points. No association between PROMIS scores and OCT findings was discovered. In comparing groups of patients on different therapies, there were no significant differences found in PROMIS scores reported in patients on biologic vs nonbiologic therapies.

Conclusion: Anterior chamber inflammation correlated with worse reported physical function which is likely a consequence of anterior chamber inflammation more frequently causing symptoms apparent to the patient thereby affecting their perceived health. Presence of vascular leakage on fluoroscein angiography was found to be associated with worse physical health PROMIS scores at 1 year follow-up. Our findings warrant further investigation into how patient reported outcomes can assist in monitoring ocular disease activity outside of an ophthalmology exam room.

Disclosure: J. Hedrick, None; **R. Hajj-ali**, None; **Y. Jin**, None; **S. Srivastava**, Bausch and Lomb, 2, 5, Allergan, 2, 5, Clearside, 2, 5, Regeneron, 5, Santen, 2, 5, Sanofi, 2, 5, Zeiss, 2, 5, Optos, 5, Novartis, 2, Bioptigen, 7, Synergetics, 7, Ohio Department of Development TECH-13-059, 2.

Abstract Number: 1247

Adult-Onset Still's Disease and Spondyloarthritis: Overlapping Syndrome or Incidental Association? A Series of 5 Cases

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SESSION INFORMATION

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Background/Purpose: Some forms of spondyloarthritis (SpA) such as SAPHO syndrome are classified as autoinflammatory disorders. Association with adult onset Still's disease (AoSD) has never been reported. We reported a case-series of 5 patients who presented features of both diseases.

Methods: Out of our cohort of 57 AoSD patients followed in our reference center, we identified 4 cases combining diagnosis of AOSD, on the basis of Yamaguchi's and/or Fautrel's classification criteria fulfilment, and SpA according to at least one classification criteria fulfilment: ASAS criteria for axial or peripheral spondylarthri-

Table. patients' characteristics. –*The patient presented 2 out of the 3 criteria needed (arthritis + enthesitis). AOSD, Adult-Onset Still's Disease - DIP, distal interphalangeal joint – MRI, magnetic resonance imaging –MTP, metatarsophalangeal joint - PIP, proximal interphalangeal joint - SpA, spondylarthropathy.

	Case 1	Case 2	Case 3	Case 4	Case 5
General Data					
Sex (Female/Male)	M	F	M	F	M
Age (years)	56	45	46	53	17
Age at onset of AOSD symptoms (years)	48	39	28	46	16
Age at onset of SpA symptoms (years)	37	42	40	51	17
Ethnicity	Caucasian	Caucasian	Caucasian	Caucasian	African
AOSD criteria fulfillment					
Yamaguchi's	Yes	Yes	Yes	Yes	Yes
Fautrel's	Yes	Yes	Yes	Yes	Yes
SpA criteria fulfillment					
ASAS criteria – axial Spondyloarthritis	No	No	No	Yes	Yes
ASAS criteria – peripheral Spondyloarthritis	No*	No	No	Yes	No
Amor's criteria for Spondyloarthritis	Yes	No	No	Yes	No
CASPAR for Psoriatic Arthritis	No	Yes	Yes	No	No
Spondyloarthritis data at onset					
Family background with psoriasis	Yes	No	No	No	No
Personal medical history of skin psoriasis	No	Yes	Yes	Yes	No
Swollen joints	Yes	Yes	Yes	Yes	Yes
Enthesitis	Yes	No	Yes	No	Yes
Acne	No	No	No	Yes	No
Skin psoriasis	No	Yes	Yes	No	No
Inflammatory back pain	No	No	No	Yes	Yes
HLA B27 status	Negative	Negative	Negative	Unknown	Negative
Radiological signs (through disease evolution)	Carpal ankylosis, DIP narrowing, bilateral calcaneal enthesophyte	Carpal ankylosis, DIP ankylosis, MTP ankylosis	Bilateral carpal ankylosis; erosion, ankylosis and reconstruction signs	Left sacroiliitis, multifocal osteitis (vertebrae, iliac bone), osteolytic bone	Bilateral sacroiliitis on MRI, bilateral coxitis

tis, Amor's criteria for spondyloarthritis or CASPAR criteria for Psoriatic Arthritis (PsA). A fifth patient, followed in another university center and combining both diseases according to the same criteria, was subsequently included. Medical past history, family background, AOSD and SpA onset and evolution, clinical, biological and radiological features, and treatment response were extracted retrospectively from medical chart through a pre-defined form.

Results: The 5 patients (3M, 2W) displayed the following characteristics **(Table):** mean age 43.4 ± 15.4 years, mean age at AoSD and SpA onset 35.4 ± 13.3 and 37.4 ± 12.5 years respectively, mean follow-up duration 8.0 ± 6.2 years (range 1-18 years). Four patients were Caucasian, one African, with no consanguinity. SpA manifestations occurred after AoSD onset in 4 patients (mean delay 5.2 ± 4.7 years); AoSD was diagnosed 11 years after SpA diagnosis in the 5th patient. At AoSD onset, the 4 cardinal symptoms were present: mean fever 39.2 ± 0.8°C, arthralgia and arthritis and skin rash in all patients, mean white blood count was 16,091 ± 4302/mm3 (89.2% of polymorphonuclears), mean ESR 74 ± 33 mm, mean CRP 156.5 ± 74.5 mg/L, mean ferritin was 658.6 ± 340.9 µg/L.

SpA-related symptoms are indicated in the **Table**. Two patients fulfilled the criteria for axial spondyloarthritis, two for peripheral spondyloarthritis, three for PsA and one for SAPHO syndrome. Three patients had personal and one had familial medical history of skin psoriasis. HLA B27 was negative in 4 patients (status unavailable in one patient). Besides the classical AOSD carpal ankylosis and narrowing of proximal and distal interphalangeal (PIP, PID) joints found in 3 patients, radiological features of SpA were observed: bilateral calcaneal enthesophytes; uni- or bilateral sacroiliitis suggestive of spondyloarthritis **(Figure 1)**; erosion, ankylosis and reconstruction "PsA-like" signs on PIP

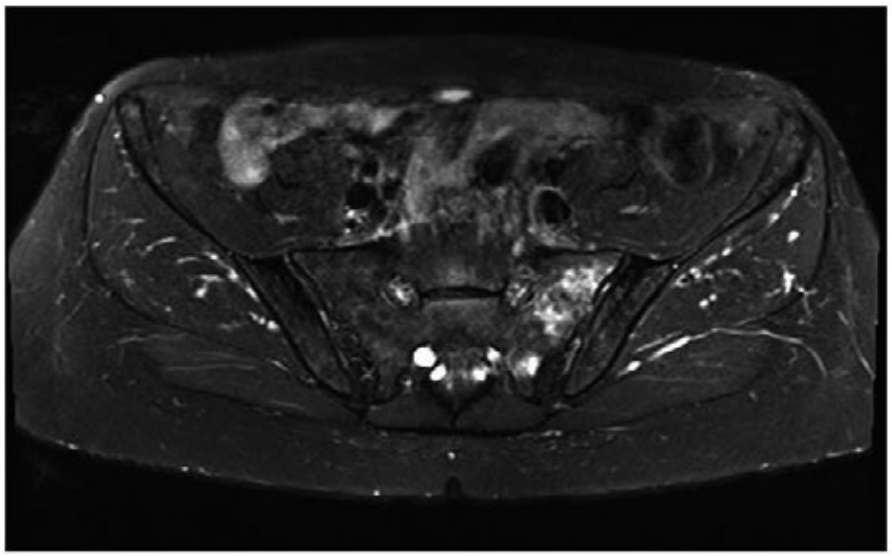

Figure 1. Inflammatory sacroiliitis suggestive of spondylarthritis on MRI.

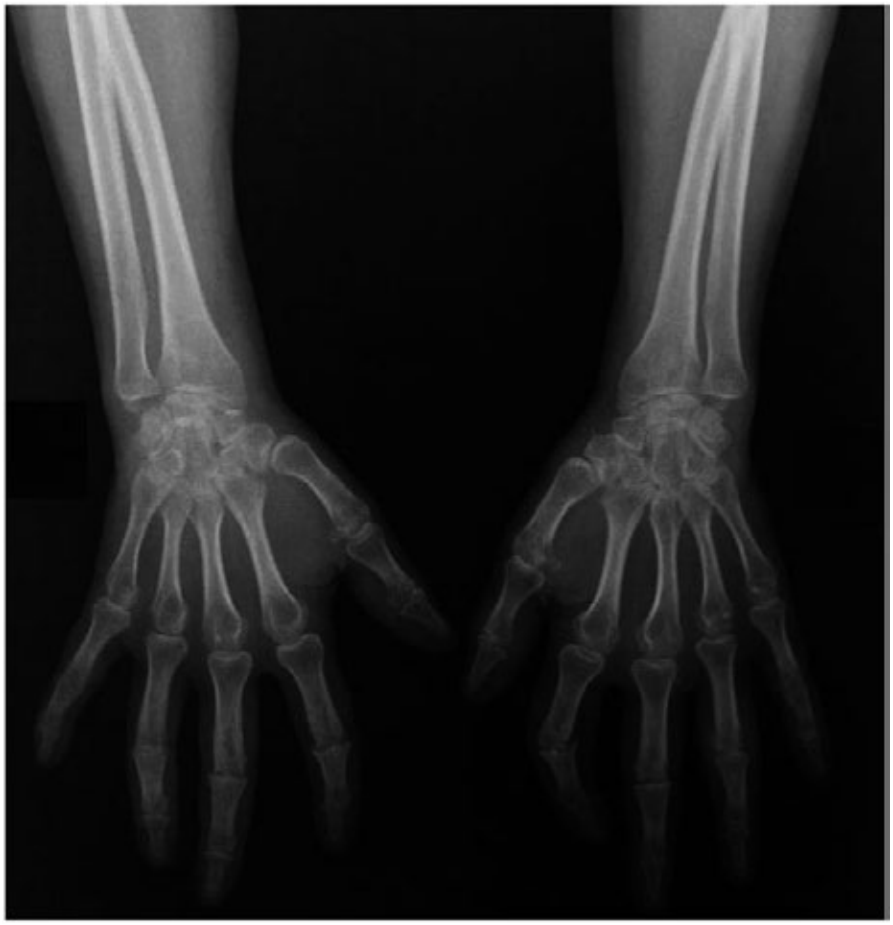

Figure 2. Besides the classical bilateral carpal ankylosis, please note erosion, ankylosis and reconstruction “Psoriatic Arthritis-like” signs on proximal and distal interphalangeal joints.

and DIP **(Figure 2)**; multifocal osteitis and osteolytic bone lesion suggestive of SAPHO. Articular symptoms responded well to biotherapies prescribed for AOSD (anakinra, tocilizumab or TNF inhibitors) in 4 patients; in the 5th patient, prednisone and methotrexate were sufficient to control symptoms.

Conclusion: The prevalence of SpA in our AOSD cohort was around 7.0%, thus greater than the prevalence of 0.3% in the French general population (Saraux et al. Ann Rheum Dis. 2005 Oct;64(10):1431-5). The association of both diseases suggests a possible pathophysiological link between these 2 entities.

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Abstract Number: 1248

Clinical Manifestations and Management of US Patients with SAPHO (Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis) Syndrome, a Retrospective Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The SAPHO syndrome is a rare inflammatory disorder of bones, joints and skin first coined by Chamot in 1987 characterized by synovitis, acne, pustulosis, hyperostosis and osteitis[1]. No validated diagnostic criteria exist; diagnostic delay is not uncommon and observational data from the Western Hemisphere is sparse

Methods: Adult patients with a diagnosis of SAPHO seen between 2001 and 2018 at a single tertiary referral center were retrospectively identified. Cases were reviewed by a physician abstractor to determine whether they fulfilled either of the following 2 proposed criteria for SAPHO: Benhamou[1,2] or modified Kahn (2003)[3]. Sociodemographics, clinical characteristics, laboratory parameters, radiology, histopathology, management and outcomes were abstracted from direct medical record review. Patients with non-inflammatory bony lesions, infectious osteitis and CRMO were excluded.

Results: Twenty-one patients with complete clinical and treatment data were identified (71% female, 76% Caucasian). The average age at the time of diagnosis was 36.9 ± 13.4 years and the mean time from symptom onset to diagnosis was 3.4 years. 20/21 had cutaneous involvement: 10 with palmoplantar pustulosis or psoriasis vulgaris and 10 with severe acne. Osteoarticular manifestations included anterior chest wall/clavicle 15 (71%), peripheral arthritis 9 (43%), inflammatory back pain 8 (38%) and 2 (10%) with mandibular osteitis. Uveitis and mucositis were uncommon (2 out of 21 cases). 52% had elevated inflammatory markers at diagnosis while HLA-B27 positivity was uncommon (1/11). 13 of 13 radionuclide bone scans performed were positive while 8 of 9 MRI's were diagnostic.

18 patients (86%) were treated with NSAIDs; addition of immunosuppressive therapy with oral DMARDs (n=14, 66%) and TNF inhibitor (n=12, 57%) was quite common. 9 of 12 patients treated with TNFi experienced loss of efficacy requiring an alternate TNF inhibitor or switch to IL 17 or 23 blockade. 6/21 received oral antibiotics (doxycycline or penicillin); 50% of whom responded well. 7/21 proved refractory requiring bisphosphonate therapy; 5/7 responded at time of last follow up. Outcomes were favorable overall with 15 (71%) being in/near remission at the end of the follow up period (mean of 3 years). 2 patients required reconstructive surgery; and they both had active disease at last visit.

Conclusion: This large case series presents a heterogenous group of SAPHO patients with a long period of follow up. A significant delay was noted between symptom onset and diagnosis. Concomitant cutaneous and osteoarticular manifestations were seen in the majority (20) of patients. HLA B27 was frequently negative in our group; advanced imaging with bone scan or MRI helped to confirm the diagnosis. Though NSAID and DMARD use were quite common, biologic and/or bisphosphonate therapy was frequently required. Female predominance and chest wall involvement in this series may explain the lack of response to NSAIDs[4].Further studies are needed to guide diagnostic strategies and management. Greater awareness and multi-disciplinary collaboration are imperative in the provision of care to these patients.

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Disclosure: D. Bekele, None; **P. Karmacharya**, None; **K. Wright**, Pfizer, 2; **C. Michet**, None.

Abstract Number: 1249

Pelvic Congestion Syndrome, an Uncommon Cause of Osteoarticular Pain

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

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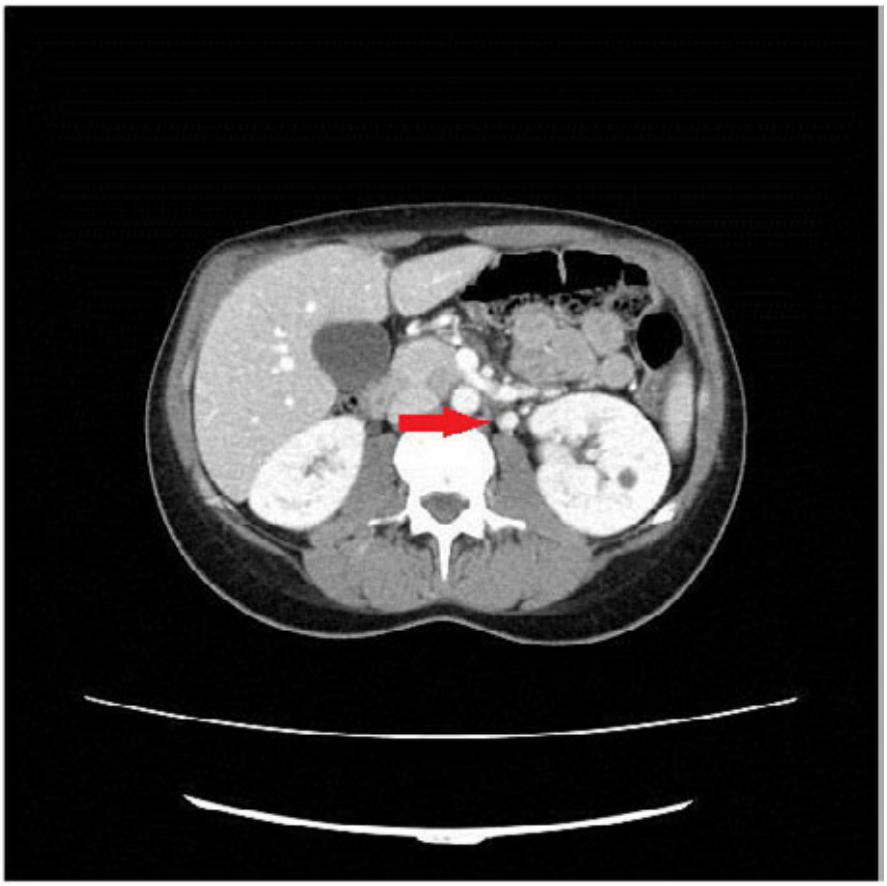
Session Time: 9:00AM–11:00AM

Background/Purpose: Background: The pelvic congestion syndrome (PCS) is an under and often misdiagnosed entity that appears more frequently in premenopausal age and multiparous women. The pathophysiology consists of a sum of phenomena including venous stasis and inversion of the pelvic venous flow that cause varicose veins and congestion. The left ovarian vein is usually the most affected. Typically it presents as a dull, chronic abdominal-pelvic (AP) pain, which worsens with menstruation and prolonged standing, and lasts longer than six months. Pain is associated with dyspareunia and varicosities in lower limbs (LL) and genitals. It is challenging and important to consider



ANGIO CT: left ovarian vein (red arrow) with contrast reflux due to venous insufficiency. It is accompanied by prominence and dilation of the bilateral periuterine venous plexuses with predominance of the left side.

atypical clinical presentations that simulate osteoarticular (OA) pathologies. It is usually diagnosed by Angio-CT, and a safe, definitive and successful treatment is the embolization of the affected vein.

Purpose: to evaluate the characteristics of those patients diagnosed with PCS in our University hospital from January 2014 to May 2018, paying close attention to the atypical forms of presentation that simulate OA pathology.

Methods: We included all patients from our center who were operated by embolization due to a PCS from January 2014 to May 2018. Socio-demographic variables, forms of presentation, pain characteristics, associated symptoms, patient management and outcome data were collected.

Results: Sixty women were included with a mean age of 43 years at diagnosis, 87% (n=52) were multiparous, with a mean of 2 previous pregnancies. In 95% (57) of all cases the duration of symptoms until the diagnosis exceeded 6 months. Patients were classified according to presence and location of pain in 4 groups: 1. Women with AP pain, 23% (14); 2. Women with OA pain 5% (3); 3. Women with mixed AP and OA pain, 59% (35); and 4. Women with other symptoms 13% (8). Regarding patients from groups 2 and 3 (only OA pain or mixed pain) (38), 90% (34) of them presented low back pain, 53% (20) hip pain and 40% (15) sciatic pain. Only 5% (3) of all patients were evaluated by a rheumatologist.

As for the pain characteristics from groups 1, 2 and 3 (52), in 72% (37) of patients it was diurnal, in 48% (25) it worsened with menstruation, in 62% (32) it worsened with prolonged standing and in 35% (18) it worsened at rest. Among

the associated manifestations, stand out the presence of LL varicose veins in 74% (38) of patients, genital varicosities in 58% (30), dyspareunia in 42% (22), dysmenorrhea in 40% (21), hemorrhoids in 37% (19) and dysuria in 18% (9). All patients underwent embolization of the affected vein, with an initial Visual Analogue Scale (VAS) mean of 7.38 over 10, and final VAS mean of 2.63. The mean recovery time was 36 days. The evolution was good or very good in 84% (32) of patients with mixed (AP and OA) pain and in 57% (8) of those who only had AP pain. Less than 2% (1) had a recurrence without the need for reoperation.

Conclusion: PCS is a rare entity, typically associated with long lasting AP pain, but, in more than half the cases, is accompanied with OA symptoms, mainly low back pain. It is important and challenging for the rheumatologist to identify these patients, since treatment is usually safe and effective, and diagnostic delay worsens their quality of life.

Disclosure: M. Castillo-Vilella, None; **J. Tandaipan**, None; **L. Berbel**, None; **L. Moga**, None; **G. Salvador**, None; **S. Martínez-Pardo**, None; **N. Giménez**, None.

Abstract Number: 1250

Can Patient-Reported Outcomes and Disease Activity Scores Predict Patient Acceptable Symptom State in Adult-Onset Still's Disease?

Emre Bilgin,[1] Timuçin Kaşifoğlu,[2] Ahmet Omma,[3] Cemal Bes,[4] Muhammet Çınar,[5] Hakan Emmungil,[6] Orhan Küçükşahin,[7] Servet Akar,[8] Kenan Aksu,[9] Fatih Yıldız,[10] Nilüfer Kanıtez,[11] Abdulsamet Erden,[12] Sezin Turan,[13] Ediz Dalkılıç,[14] Selime Ermurat,[15] Mutlu Hayran,[16] and **Umut Kalyoncu** [17], [1]Hacettepe University Vasculitis Centre, Ankara, Turkey, Ankara, Turkey, [2]Eskişehir Osmangazi University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Eskişehir, Turkey, [3]Ankara Numune Education and Research Hospital, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey, [4]University of Medical Sciences, İstanbul, Turkey, [5]University of Medical Sciences, Ankara, Turkey, [6]Trakya University, Edirne, Turkey, [7]Liv Hospital, Ankara, Turkey, [8]Izmir Katip Celebi University, Faculty of Medicine, Division of Rheumatology, İzmir, Turkey, [9]Ege University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, İzmir, Turkey, [10]Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Kahramanmaraş, Turkey, [11]Koç University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, İstanbul, Turkey, [12]Ministry of Health Ankara City Hospital, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey, [13]Trakya University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Edirne, Turkey, [14]Uludağ University, Bursa, Turkey, [15]Uludağ University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Bursa, Turkey, [16]Hacettepe University, Faculty of Medicine, Department of Preventive Oncology, Ankara, Turkey, [17]Hacettepe University Department of Rheumatology, Ankara, Turkey

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Adult-onset Still's disease (AOSD) is a rare, chronic and auto-inflammatory disorder with multisystemic involvement. Patient Acceptable Symptom State (PASS) is the highest level of disease activity that patients feel quite well. Till now, there is no valid information for the possible cut-off values of patient-reported outcomes (PRO) or activity scores for AOSD patients to predict PASS. To determine cut-off values of PROs and activity scores to predict PASS in AOSD patients, we conducted this study.

Methods: We conducted a cross-sectional, multicenter study. All AOSD patients were fulfilled the Yamaguchi criteria. Still activity score (SAS) [1 point for neutrophilia ≥65%, 1 point for ferritin≥350 ng/ml, 2 point for fever and 2 point for arthralgia-additional 1 point if swollen joint number is equal or grater than 2], Pouchet's systemic score (SS) [1

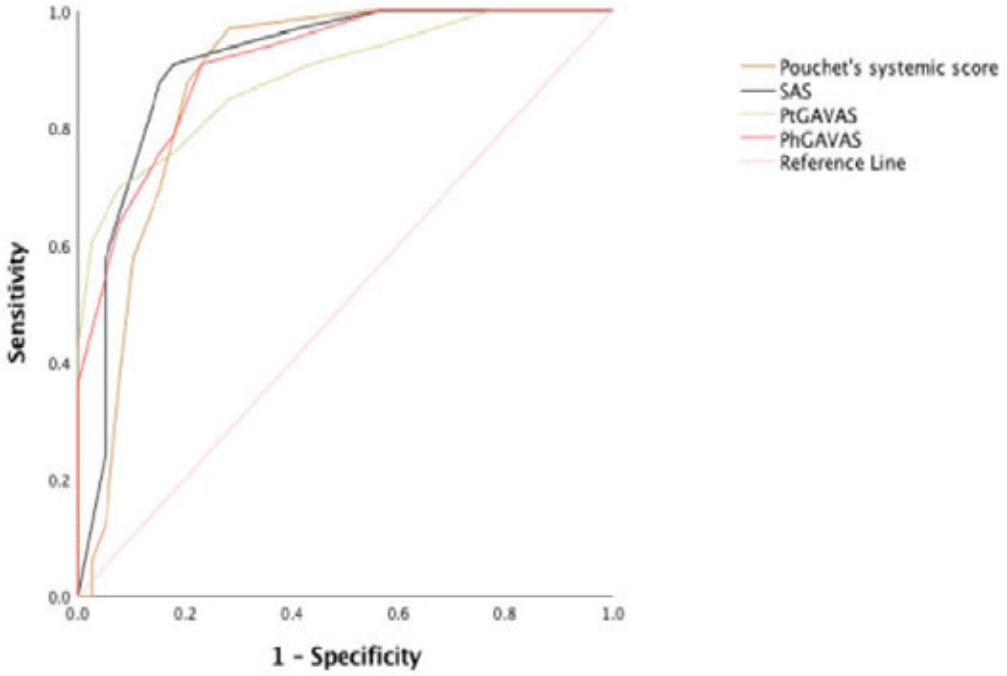


Figure 1. ROC analysis for PROs and disease activity scores.

point for each of the following manifestation: fever, typical rash, pleuritis, pneumonia, pericarditis, hepatomegaly, or abnormal liver function tests, splenomegaly, lymphadenopathy, leukocytosis >15,000/mm2, sore throat, myalgia, and abdominal pain], visual analog scale (VAS) (0–10 cm) for physician's (PhGA) and patient's (PtGA) global assessment

Parameter	Sensitivity (%)	Specificity (%)	Area Under Curve (AUC)	Confidence Interval	P
Pouchet's systemic score (SS)					
-SS ≤ 2	79	87.9			
-SS ≤ 3	82	79	0.87	0.79-0.96	<0.001
-SS ≤4	84	70			
Still Activity Score (SAS)					
-SAS ≤ 3	82.1	91			
-SAS ≤ 4	84.6	87.9	0.91	0.84-0.98	<0.001
-SAS ≤ 5	95	58			
Physician's Global VAS					
- PhVAS≤2	77	91			
- PhVAS≤3	82.1	78.8	0.91	0.84-0,97	<0.001
- PhVAS≤4	84.6	75.8			
Patient's Global VAS					
- PtVAS≤3	72	85			
- PtVAS≤4	82.1	75.7	0.88	0.81-0.96	<0.001
- PtVAS≤5	92.3	69.7			

were used to determination of the disease activity. To assess PASS, we asked patients whether they would be okay or not, if the disease activity will be the same as now during the next month. Receiver operator curve (ROC) analysis was done to find cut-off values.

Results: Total of 72 (71% female) AOSD patients were enrolled. Mean age was 41 (13) years and median disease duration was 2 (0–30) years. Median SS and SAS were 3 (0-10) and 4 (0-7), respectively. Mean PtGA and PhGA were 4.29 (3.15) and 3.54 (3.07), respectively. Cross-sectional frequency of AOSD findings were as follow; fever 34 (47%), rash 27 (37.5%), arthritis 25 (34.7%), arthralgia 52 (72.2%), sore throat 30 (41.7), myalgia 38 (52.8), lymphadenopathy 13 (18.1%), splenomegaly 20 (27.8%), hepatomegaly 16 (22.2%), pleuritic pain 5 (6.9%), pericarditis 4 (5.6%), hemophagocytic syndrome 2 (2.8%). Mean (SD) ESR (mm/h), CRP (mg/dl), ferritin level and leukocyte count were 36.8 (34), 5.4 (7.3), 1758 (4070) and 9960 (4178), respectively. ROC analysis, area under curve, confidence intervals, sensitivity and specificity for different cut-off values were given in **Table 1 and Figure 1**.

Conclusion: In this study, all PROs and activity scores performed well to predict PASS. Still activity score seems to perform better over SS. To the best of our knowledge, this is the best study reporting cut-off values for PROs and activity scores to predict PASS.

Disclosure: E. Bilgin, None; **T. Kaşifoğlu**, None; **A. Omma**, None; **C. Bes**, None; **M. Çınar**, None; **H. Emmungil**, None; **O. Küçükşahin**, None; **S. Akar**, Abbvie, 2, 5, Amgen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5; **K. Aksu**, None; **F. Yıldız**, None; **N. Kanıtez**, None; **A. Erden**, None; **S. Turan**, None; **E. Dalkılıç**, None; **S. Ermurat**, None; **M. Hayran**, None; **U. Kalyoncu**, UCB, 5.

Abstract Number: 1251

The Impact of Aging on Familial Mediterranean Fever Patients

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Familial Mediterranean Fever (FMF) is a monogenic autoinflammatory disorder with innate immune activation with an onset before age 20 in approximately 90% of the patients. There is scarce data on the effect of aging on FMF patients over 40 years of age. This study aims to collect data on FMF patients who have survived over 40 years of age. Here we report our preliminary data on disease course and treatment status and comorbidities of our patients with FMF.

Methods: Among the FMF patients who have been followed in our FMF outpatient clinic with a pool of approximately 5000 patients, those who have aged 40 and over are being included to the study. As by today 180 patients are considered for evaluation. The files of patients were reviewed and a standard questionnaire was used to interview the patients. Here we report the results of 100 of these patients (56%) who were contacted for this purpose. These patients were questioned on their demographic characteristics, comorbid conditions, colchicine treatment details, and attack information. In order to see the trend of the change in the parameters assessed, the patients were divided into two groups based on their present age (Group 1: 40-50 years, Group 2: ≥50 years).

Results: A total of 100 (78 F, 22M) patients were evaluated. There were 61(46F, 15M) patients aged between 40-50 years and 39 (32F, 7M) over 50. The demographic characteristics and clinical features of these patients are given in Table 1. Besides 3, all patients were still on colchicine regularly. Ninety-six percent of the patients declared overall benefit from colchicine therapy; however 38% experienced a side effect related to this treatment. Over 88% of the patients reported decrease in severity and frequency of FMF attacks. The mean daily colchicine dose was lower in the age 50 and over group (1.7±0,77 mg versus 1,35 ±0,38 mg). There were no patients with AA amyloidosis in neither age group. The mean duration from the last attack increased from 15.3 ±19.7 months to 35.6± 52 months in the older patients. One or more additional disease was present in 75% of this patient group.

Conclusion: According to our preliminary data the majority of the patients continue to take colchicine after age of 40. However, the frequency of FMF attacks as well as daily colchicine dose decrease as the patients get older. With well-designed trials stopping colchicine treatment may be considered in a subgroup of patients after 50 years of age. Approximately ¾ of the FMF population over 40 years of age has a comorbidity that necessitates additional medications which underlines the need for special attention.

Table 1: Clinical course and co-morbidities in two age groups over 40 years

n	Group 1* (n=61)	Group 2** (n=39)	p
Sex (F:M); current age (mean±SD) (yr)	(46 :15) ;45.5 ± 2.29	(32:7); 57.05 ± 6.81	0,43;<0.001
Mean duration since the last episode, (mean±SD, mo)	**15.3 ± 19.7 (1-60)**	**35.67 ± 52.05 (1-276)**	**0,012**
Number of patients on colchicine therapy, n (%)	59 (96.7)	38 (97.4)	NS
Mean colchicine dose, mg/day (current)	**1.7±0.76**	**1.41±0.45**	**0.03**
Number of patients with decrease in attack severity, n (%)	54(88,5)	35 (89,7)	NS
Number of patients with decrease in attack frequency, n (%)	57(93,4)	37 (94,8)	NS
Co-morbidities, n (%)			
Hypertension, n (%)	12(19.6)	13 (33.33)	NS
Hypothyroidism, n (%)	12(19,6)	4(10,2)	NS
Type 2 Diabetes Mellitus, n (%)	5(8.2)	5(12.82)	NS
Rheumatological diseases, n (%)	5(8,2)	3(7,7)	NS
Cardiac disease, n (%)	3(4,9)	2(5,1)	NS
Malignancies, n (%)	2(3,2)	2(5.13)	NS
Additional medications (number of patients, %)	36 (61)	29 (74.3)	NS

Disclosure: S. Ugurlu, None; **O. Aydin**, None; **B. Egeli**, None; **A. Soykut**, None; **D. Demir**, None; **H. Ozdogan**, None.

Abstract Number: 1252

Pattern of Arthropathy in Patients with Cystic Fibrosis

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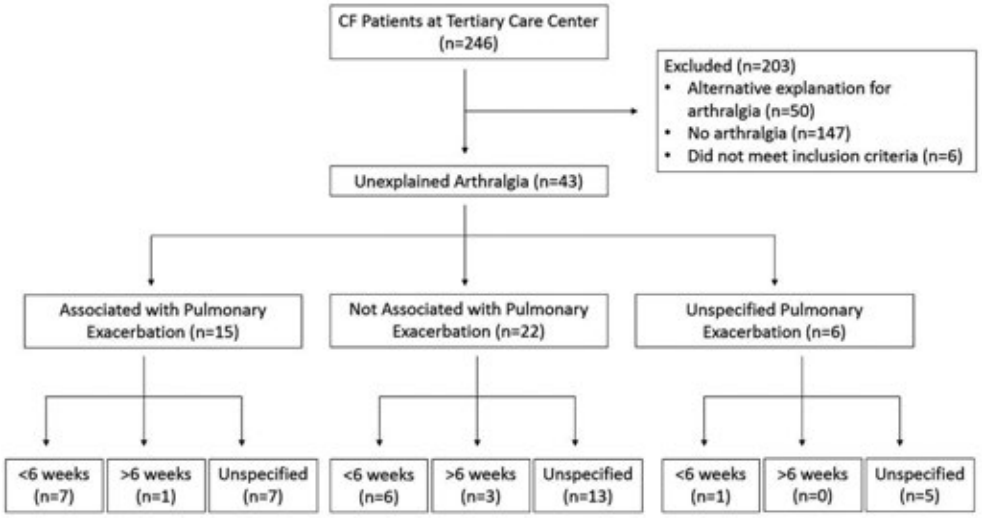
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Arthropathy is a rare but debilitating manifestation of cystic fibrosis (CF) that has no formal definition. This study attempts to characterize the spectrum of arthropathy in CF patients.

Methods: A retrospective chart review was conducted on 246 adult CF patients within the Pulmonary CF Clinic who were seen at a single tertiary care center between January 1, 2008 and December 31, 2017. Charts were individually reviewed for description of joint symptoms. Patients were excluded if they had an alternative explanation for joint symptoms. Association of joint symptoms with pulmonary exacerbation were abstracted and defined based on clinical diagnosis of the treating physician. Pattern of joint involvement, duration of symptoms (acute as defined by < 6 weeks and chronic >6 weeks), and therapies utilized for joint pain were also abstracted.

Results: In the overall cohort of 246 adult CF patients, 43 (17%) had unexplained joint symptoms; 128 (52%) were female and 42 (97%) self-reported as Caucasian. In those with unexplained arthralgia, 28 of 43 (65%) were female. The joint symptoms were not associated with pulmonary exacerbations in 22 patients (51%). In 15 (35%) patients, there was association between joint symptoms and pulmonary exacerbations while in 6 (14%) it was not specified. In 18 patients, the duration of symptoms was described and 14/18 had symptoms lasting less than 6 weeks. Knee (23), ankles (13), hips (10), and wrists (10) were the most affected joints. However, both small and large joints were affected. Both symmetric and asymmetric presentations were noted. No individuals had findings of sacroiliac joint involvement. No patients had evidence of erosions. The most commonly used medications were NSAIDs. In the overall cohort of CF patients who had unexplained joint symptoms, therapies utilized were NSAIDs (25, 58%), aceta-



Summary of Patient Cohort

minophen (10, 23%), and prednisone (9, 21%). Hydroxychloroquine was the most frequently used DMARD (7, 16%) followed by sulfasalazine (1, 2.3%). No biologics were used in this cohort. There were no individuals with hypertrophic osteoarthopathy in this cohort. There were no reports of fluoroquinolone associated tendinopathy or voriconazole induced periostitis.

Conclusion: This study characterizes the variety of joint symptoms in CF patients and expands on current knowledge. Females were most likely to experience arthralgia and the knee was the most commonly affected joint. Arthralgia was associated with pulmonary exacerbations in only 35% of patients. Understanding the diverse spectrum of arthropathy will result in greater recognition and improvement in quality of life for CF patients.

Disclosure: D. Pham, None; **M. Maz**, None; **M. Crosser**, None; **M. Krause**, None.

Abstract Number: 1253

Novel Nonsense Variant and Entire Deletion of *TNFAIP3* Cause Haploinsufficiency of A20 Clinically Distinct from Behçet's Disease

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
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Session Time: 9:00AM–11:00AM

Background/Purpose: Haploinsufficiency of A20 (HA20) is caused by loss-of-function *TNFAIP3* variants. Phenotypic and genetic features of HA20 remain uncertain; therefore, clinical distinction between HA20 and Behçet's disease (BD) requires clarification.

Table 1. Clinical features of haploinsufficiency of A20 (HA20) and Behçet's disease (BD)

Characteristics	HA20 (n=54)	(%)	BD (n=520)	(%)	p	Odds ratio	95%CI	
Age at onset (years) (mean ± SD)	6.0 ± 6.5		36.4 ± 12.3		< 0.001			
Childhood onset (< 16 years old)	49 /53	92.5	10 /520	1.9	< 0.001	624.75	188.92	2065.98
Familial	15 /25	60.0	19 /332	5.7	< 0.001	24.71	9.80	62.29
Recurrent fever	37 /51	72.5	39 /364	10.7	< 0.001	22.02	10.99	44.30
Oral ulcer	46 /52	88.5	518 /520	99.6	< 0.001	0.03	0.01	0.15
Genital ulcer	34 /52	65.4	372 /520	71.5	0.35	0.75	0.41	1.37
Eye involvement	5 /52	9.6	330 /520	63.5	< 0.001	0.06	0.02	0.16
Skin involvement	28 /52	53.8	461 /520	88.7	< 0.001	0.15	0.08	0.27
Arthritis	21 /54	38.9	245 /520	47.1	0.25	0.71	0.40	1.27
Gastrointestinal involvement	22 /53	41.5	78 /520	15.0	< 0.001	4.02	2.21	7.31
Vascular involvement	7 /53	13.2	41 /520	7.9	0.18	1.78	0.76	4.19
CNS involvement	5 /53	9.4	57 /520	11.0	0.73	0.85	0.33	2.21
Fulfilling ISG criteria for BD	23 /54	42.6	468 /520	90.0	< 0.001	0.08	0.05	0.15

Methods: We have collected twelve Japanese BD-like families. Probands of these families were analyzed by whole exome sequencing (WES) and subsequent Sanger sequencing or quantitative PCR. Copy number variants (CNVs) were examined using WES data with two algorithms: the eXome-Hidden Markov Model (XHMM) and a program based on the relative depth of coverage ratios developed by Nord et al. To observe mutational effects of the nonsense variant, RT-PCR was performed. Clinical features were compared between 54 HA20 patients (including previously reported and new cases) and BD cohorts (520 Japanese BD patients accumulated at our facility and pediatric BD from the Pediatric Behçet's disease (PEDBD) study by Kone-Paut et al.) Statistical analysis was performed with SPSS version 22 (IBM Japan, Tokyo, Japan). Categorical variables were analyzed using the chi-square test. Continuous variables were examined using Student's t-test. A *p* value less than 0.05 was considered statistically significant.

Results: Among Twenty-five patients from twelve families, two novel *TNFAIP3* pathogenic changes were found in two families (16.7%, 2 of 12): nonsense variant in one family and a 236 kb deletion at 6q23.3 containing *TNFAIP3* in another family. The nonsense variant may be subjected to nonsense-mediated mRNA decay (NMD). Four HA20 patients in the two families presented with childhood-onset recurrent oral and genital ulcers and were initially diagnosed and treated as BD. Consistent with the clinical features of HA20, recurrent, refractory fever attacks (3/4), and digestive ulcers (2/4) were observed. A comparison of clinical features between HA20 patients and cohorts of BD patients revealed that some features are shared between HA20 and BD as previously reported: recurrent oral and genital ulcers, and skin, eye, musculoskeletal and gastrointestinal involvement. While several critical features were more specific to HA20: early-onset, familial occurrence, recurrent fever attacks, gastrointestinal involvement, and infrequent ocular involvement (Table 1).

Conclusion: We identified a novel nonsense variant and deletion of the entire *TNFAIP3* gene in two unrelated Japanese HA20 families. Genetic screening of *TNFAIP3* should be considered for familial BD-like patients with early-onset recurrent fevers.

Disclosure: N. Tsuchida, None; **Y. Kirino**, None; **Y. Soejima**, None; **H. Nakajima**, None; **S. Miyatake**, None; **N. Matsumoto**, None.

Abstract Number: 1254

A Retrospective Medical Chart Review of Patients with Periodic Fever Syndromes Initiating Canakinumab in the United States

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Periodic fever syndromes (PFS) is a group of rare autoinflammatory diseases that includes cryopyrin-associated periodic syndromes (CAPS), hyperimmunoglobulin D syndrome/mevalonate kinase deficiency (HIDS/MKD), TNF receptor-associated periodic syndrome (TRAPS), and familial Mediterranean fever (FMF). Although canakinumab (CAN) has been approved in the United States (US) for patients (pts) with the aforementioned PFS, there have been limited studies on prescribing patterns among physicians who have initiated CAN in real world

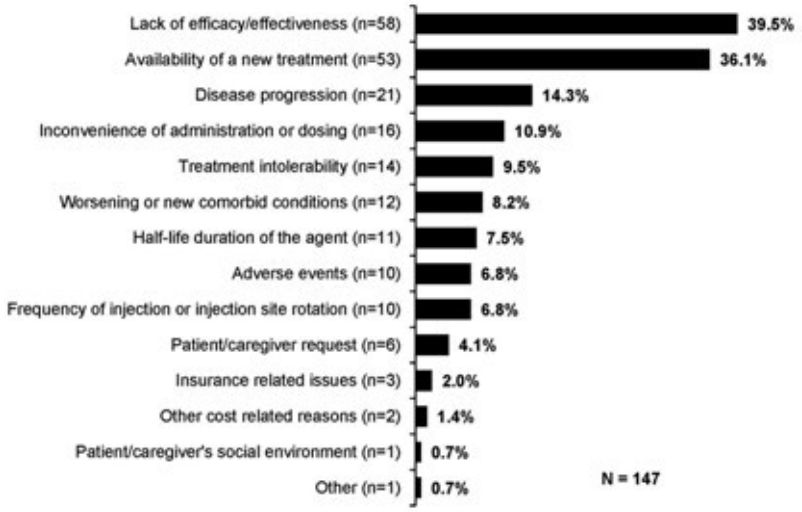

Figure 1. Reasons by PFS patients for discontinuation of treatments prior to canakinumab initiation

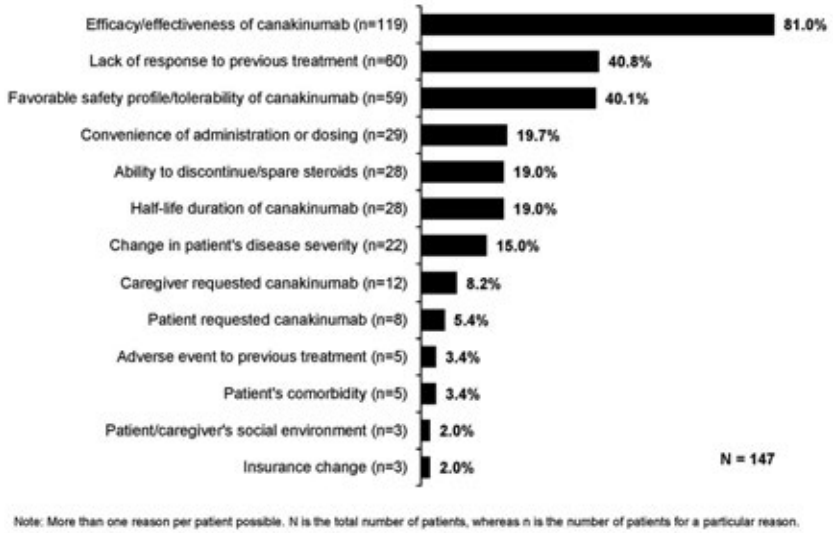

Figure 2. Reasons by PFS patients for the initiation of canakinumab treatment

settings. We assessed the clinical and treatment profiles of PFS pts who were prescribed CAN and the physician reason(s) for initiating CAN in US clinical practice.

Methods: Online medical charts were reviewed retrospectively to collect data from US rheumatologists/ dermatologists/ allergists / immunologists on pts (pediatrics [Ped; < 18 yrs] and adults [Adt; ≥18 yrs]) diagnosed with PFS who were initiated on CAN therapy by the responding physician between 2016 and 2018. Online case report forms were used to collect information on pt demographics, disease characteristics at CAN initiation, pre-CAN treatment history, and CAN prescribing patterns. Reasons for discontinuation of previous treatment and initiation of CAN were also collected.

Results: Medical charts were reviewed by 58 physicians who had specialty in rheumatology (26; Adt 88%, Ped 12%), dermatology (15; Adt 73%, Ped 27%), allergy (9; Adt 44%, Ped 56%), and immunology (8; Adt 38%, Ped 62%). Of the 147 pts, 57% were male and 46% were Ped. The mean age at CAN initiation was 21.7 yrs (Adt, 31.9 yrs; Ped, 9.9 yrs). Among PFS subtypes, 37% pts had CAPS, 27% TRAPS, 27% FMF, 7% HIDS/MKD and 3% mixed PFS subtypes. Median age at PFS diagnosis was 13 yrs (IQR: 6-20 yrs). The key methods of diagnosis were assessment of clinical symptoms and complications (87%), age of onset (63%), and family history/ancestry (57%). The main diagnoses which were ruled out included fever of unknown origin (70%), urticaria or rash/allergy (54%), and recurrent infection (51%). The severity of PFS was mild (22%), moderate (69%), or severe (8%) at CAN initiation. The most common symptoms at CAN initiation were fever (79%), fatigue/malaise (57%), skin rashes (44%), erythema (29%), arthralgia (26%), and myalgia (25%). Most pts (91%) received other long-term treatments in the last line of therapy prior to CAN including NSAIDs (28%), anakinra (24%), and colchicine (22%). The main reasons for discontinuation of treatment prior to CAN were lack of efficacy/effectiveness (40%) and availability of a new treatment (36%; Fig. 1). Decision to start CAN was made by both physician and pt/caregiver (61%), by physician only (35%), and by pt/caregiver only (4%). The prime reasons for CAN initiation included efficacy/effectiveness (81%), lack of response to previous treatment (41%) and favorable safety/tolerability profile (40%; Fig. 2).

Conclusion: Results from this study provide insight into the reasons for CAN initiation in PFS pts, with efficacy/effectiveness, lack of response to previous treatment and favorable safety/tolerability profile being the most common reasons.

Disclosure: P. Hur, Novartis, 3, Novartis Pharmaceuticals Corporation, 3, Novartis Pharmaceuticals Corporations, 3; **K. Lomax**, Novartis Pharmaceuticals Corporation, 3, Novartis Pharmaceuticals Corporations, 3; **R. Ionescu-Ittu**, Analysis Group, Inc., 3, Novartis Pharmaceuticals Corporation, 5, Novartis Pharmaceuticals Corporations, 5; **A. Manceur**, Analysis Group, Inc., 3, Novartis Pharmaceuticals Corporation, 5, Novartis Pharmaceuticals Corporations, 5; **J. Xie**, Analysis Group, Inc., 3, Novartis Pharmaceuticals Corporation, 5, Novartis Pharmaceuticals Corporations, 5; **J. Cammarota**, Analysis Group, Inc., 3, Novartis Pharmaceuticals Corporation, 5, Novartis Pharmaceuticals Corporations, 5; **N. Sanghera**, Novartis Pharmaceuticals Corporation, 3, Novartis Pharmaceuticals Corporations, 3; **A. Grom**, AB2 Bio Ltd, 2, 5, AB2Bio, 2, 5, Children's Hospital Medical Center, 3, Novartis, 2, 5, Novartis Pharmaceuticals Corporation, 2, 5, Novartis Pharmaceuticals Corporations, 5, NovImmune, 2, 5, Novimmune, 2, 5.

Abstract Number: 1255

Is Exon 2 Associated with FMF or a New Disease?

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

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Session Time: 9:00AM–11:00AM

Background/Purpose: In Familial Mediterranean Fever (FMF), patients having exon 10 mutations, specifically M694V, M680I, and V726A are more common and their disease profiles tend to complicate more. Hence, among the 10 exons of the MEFV gene, the association between FMF and these mutations are well known. Other mutations, especially the ones in exon 2, can be defined as benign polymorphisms due to being rare. The objective of this study was to understand the clinical nature of patients having mutations of E148Q and R202Q in exon 2 as well as how these mutations affect their complaints and treatment response.

Methods: In this study, we reported patients with FMF diagnosis according to Tel Hashomer criteria, who had mutations of E148Q, R202Q or both. These patients were a randomized subset of the ones followed in our outpatient rheumatology clinic. Clinical features of these patients were collected from their files. In terms of symptoms abdominal pain, chest pain, fever, arthritis, arthralgia, myalgia, erysipelas-like rash were noted. In terms of complications, renal FMF-related systemic AA Amyloidosis was noted. Also, we checked the family history of FMF. These patients were compared with the control group of patients having M694V mutation. M694V was selected as the control group because this mutation is well known scientifically and is the most frequent among FMF patients.

Results: The clinical symptoms of the patients are summarized in Table 1. One of the primary outcomes of this study was the treatment response. 98% of the patients were treated with colchicine when they were diagnosed with FMF. Fifty-two patients (91%) responded to colchicine in the control group whereas 33 (78%) responded to colchicine in Exon 2 group. To further digest the exon 2 patients, all of the patients in the R202Q group, 68% of the E148Q group, and 80% of the mixed exon 2 group responded to colchicine. Family history was positive in 9 patients (36%) of E148Q group, in 1 patient (8%) of R202Q group, in 1 patient (20%) in mixed exon 2 group which equals a total of 11 patients (26%). In the control group, 39 patients (68%) had an FMF diagnosis in their family. Amyloidosis was reported in one patient with E148Q mutation, one patient with R202Q mutation, two patients with M694V mutation.

Conclusion: In conclusion, in comparison with M694V patients, patients with exon 2 mutations, tend to have more atypical symptoms of FMF such as chest pain, arthralgia, and myalgia. The presentation of these symptoms is milder than the typical symptoms of FMF. The fact of low colchicine response in exon 2 patients cannot be overlooked as

Table 1. Clinical symptoms of patients with different exon mutations

	E148Q (3H+22h)*(n=25)	R202Q (0H+12h)(n=12)	Mixed E148Q +R202Q (n=5) (0H+5h)	Total of Exon 2 patients (3H+39h) (n=42)	Control M694V (n=57) (20H+37h)
Abdominal Pain	15 (%60)	10 (%83)	3 (%60)	28 (%66)	51 (%89)
Fever	12 (%48)	8 (%66)	3 (%60)	23 (%54)	44 (%77)
Chest Pain	10 (%40)	2 (%16)	2 (%40)	14 (%33)	13 (%22)
Arthritis	8 (%32)	0	1 (%20)	9 (%21)	20 (%35)
Arthralgia	21 (%84)	6 (%50)	4 (%80)	31 (%73)	25 (%43)
Myalgia	10 (%40)	0	0	10 (%23)	3 (%5)
Erysipelas-like rash	3 (%12)	1 (%8)	0	4 (%9)	3 (%5)

*H: homozygous h: heterozygous

well. Therefore, exon 2 mutations can be evaluated as a separate clinical entity; in fact, these cases should also be further searched for a potential autoinflammatory disorder.

Disclosure: B. Kulaksiz, None; **B. Egeli**, None; **O. Aydin**, None; **S. Ugurlu**, None.

Abstract Number: 1256

Comparison of FMF Patients with Age of Onset Before 20 versus 40 Years and Over

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
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Session Time: 9:00AM–11:00AM

Background/Purpose: Familial Mediterranean fever (FMF) is a disease with an onset before 20 years of age in 90% of the patients. However late onset FMF defined as age of onset over 40 years is being recognized more frequently. To better define patients with FMF who had their first attack before age 40 and compare them with early onset patient group in Turkish population

Methods: The files of 2180 FMF patients followed in a single center between 2008-2017 who have fulfilled Tel-Hashomer criteria, were reviewed regarding the age of onset 40 years and over (index patients, Group 1). For control purposes files before and after the index patients were browsed and first patients with an onset before age 20 years (Group 2) were included. The demographic, clinical and genetic characteristics are compared between these 2 sub-groups.

Results: Patients with an onset after 40 years consisted 2.7% of our FMF population. 50 of the 59 patients with an onset 40 years or over were re-evaluated and compared with early onset group consisting of 100 patients (Table 1). The delay in diagnosis, and disease duration were significantly longer and number of patients with M694V homozy-

Table 1. Demographic, clinical and genetic features of the study groups

	≥40 years n=50	**≤20 years n= 100**	**p**
Sex (F:M); present age (mean±SD) (yr)	32:18; **57.2±7.9**	62:38; **31.8±9.1**	NS; **<0.001**
Mean age at onset, (mean±sd) (yr)	**45.6±5.2**	**8.7±4.8**	**<0.001**
Mean age at diagnosis (mean ±sd) (yr)	**50.4±7.3**	**19.1±11.2**	**<0.001**
Delay in diagnosis (mean ±sd) (yr)	**4.8±5.5**	**10.4±11.8**	**<0.001**
Mean disease duration (mean ±sd) (yr)	**11.5±6.4**	**23.1±10.8**	**<0.001**
Abdominal pain, n (%)	44(88)	89(89.0)	NS
Chest pain, n (%)	7(14.0)	27 (27.0)	NS
Fever, n (%)	**30(60.0)**	**81(81.0)**	**0.005**
Arthritis, n (%)	12(24.0)	33(33.0)	0.25
Myalgia, n (%)	**1(2.0)**	**12(12.0)**	**0.04**
Amyloidosis, n (%)	1(2.0)	3(3.0)	NS
Positive family history, n (%)	33(68.7)	62 (65.2)	NS
Response to colchicine, n (%)	**37(82.2)**	**93 (94.8)**	**0.014**
M694VHomozygous, n (%)	**2(4.5)**	**23(25.8)**	**0.003**
N of M694Vallelles	**24(48)**	**82 (82)**	**0.014**
No mutation, n (%)	3(6.8)	2(2.2)	NS

gosity and M694V allele frequency were significantly more frequent among group 2. In general, phenotypes of both onset groups were similar, the only significant differences being the frequency of fever and myositis which were less common among group 1. Also, response to colchicine was more pronounced in group 1. One other interesting observation was the low incidence of amyloidosis in a group with such a significant delay in diagnosis and thus treatment.

Conclusion: FMF should be included among the differential diagnosis of patients over 40 years of age with recurrent autoinflammatory manifestations. Less than 3% of FMF patients experience their first attacks after 40 years of age. The frequency of M694V is significantly less in the late onset group, pointing out a milder disease.

Disclosure: S. Ugurlu, None; **O. Aydin**, None; **H. Ozdogan**, None.

Abstract Number: 1257

Recommendation on Colchicine Dosing and Definition of Colchicine Resistance/Intolerance in the Management of Familial Mediterranean Fever

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disease and colchicine is the drug of choice for its treatment. However, about 5-10% of FMF patients do not respond to colchicine, even when they are fully compliant. Anti-interleukin(IL)-1 treatments are used for the patients who are resistant to colchicine. Treatment with IL-1 inhibitors have been shown to be effective in clinical trials and in several case series. The objective of this report is to produce evidence-based recommendations to define "colchicine resistance", as well as compliance and intolerance, to guide rheumatologists and other health professionals in the treatment and follow-up of patients with colchicine-resistant FMF.

Methods: A consensus meeting with 12 experts followed a systemic literature review and Delphi questionnaire. The expert committee consisted of pediatric rheumatologists with expertise in FMF. Parameters for colchicine resistance/intolerance/compliance derived from the literature were evaluated by a pre-meeting online questionnaire. All parameters were discussed with a nominal group technique during the meeting. Recommendations were accepted if more than 80% agreement was reached. If agreement was below 80% a second round of discussion was held.

Results: The systematic literature review yielded 264 articles. Of these, 38 were selected for expert review. After the literature review, Delphi survey, and round table discussion, recommendations that reached consensus levels were:

1. Colchicine is the drug of choice for the treatment of FMF and compliance is a critical issue. For the following statements, it is assumed that the patient is compliant with colchicine.
2. When utilizing colchicine to treat FMF, it is recommended to adjust the dose based on disease activity, with the maximal dose in children depending on age (and weight).
3. The maximum recommended colchicine dose for the treatment of FMF is between 1-3 mg per day, depending on age, limited by signs of toxicity and tolerability.
4. For a patient receiving the maximum tolerated dose of colchicine, resistance to colchicine is defined as ongoing disease activity (as reflected by either recurrent clinical attacks [average one or more attacks per month over a three-month period], or persistently elevated C-reactive protein or serum amyloid A in between attacks [depending on which is available locally)), in the absence of any other plausible explanation.
5. Amyloid A amyloidosis develops as a consequence of persistent inflammation, which may be a manifestation of colchicine resistance.
6. Colchicine intolerance, which generally manifests as gastrointestinal symptoms (such as diarrhea and nausea), is common and can limit the ability to achieve or maintain the effective dose. Dose-limiting toxicity is rare and may include elevated liver function tests, leukopenia, azoospermia etc.
7. Active disease and intolerance to colchicine affect quality of life.
8. Various patient reported outcomes to be used to guide FMF disease management were outlined.

Conclusion: The suggested recommendations are intended to improve patient care in FMF, to make a personalized treatment plan.

Disclosure: S. Ozen, Enzyvant, 8; **E. Sag**, AbbVie, 2; **E. Ben-Chetrit**, None; **M. Gattorno**, Novartis, 2, 5, 8, SOBI, 2, 5, 8, Eurofever Registry, 2; **A. Gul**, TR-Pharm, 5, Novartis, 5; **P. Hashkes**, Novartis, 5, Novartis, 8; **I. Kone-Paut**, None; **H. Lachmann**, Novartis, SOBI, 5; **E. Tsitsami**, None; **M. Twilt**, None; **F. De Benedetti**, AbbVie, 2, BMS, 2, Novartis, 2, Novartis, Novimmune, Hoffmann- La Roche, SOBI, AbbVie, Pfizer, 2, Novimmune, 2, Pfizer, 2, Roche, 2, Sanofi, 2, Sobi, 2, Swedish Orphan Biovitrum, 2, UCB, 2; **J. Kuemmerle-Deschner**, Novartis, 2, 5, 8, SOBI, 2, 5, 8.

Abstract Number: 1258

Effects of Intravenous Golimumab, an Anti-TNFα Monoclonal Antibody, on Health-Related Quality of Life in Patients with Ankylosing Spondylitis: 1-Year Results of a Phase III Trial

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SESSION INFORMATION

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Background/Purpose: In patients with ankylosing spondylitis (AS), IV administration of the anti-TNFa antibody golimumab (GLM-IV) resulted in improvements in composite measures of various aspects of the disease (eg, ASAS percent response, BASDAI, and BASFI) that were greater than placebo (PBO) at week 16 or earlier in the GO-ALIVE

study.[1] The improvements were maintained for up to 1 year of treatment.[2] Here we examine treatment effects on health-related quality of life (HRQoL).

Methods: Adult patients with definite AS (per modified NY criteria), BASDAI ≥4, total back pain VAS ≥4, CRP ≥0.3 mg/dL, and inadequate response to NSAIDs were randomized to GLM-IV 2mg/kg at weeks 0 and 4 then every 8 weeks, or to PBO at weeks 0 and 4 and GLM-IV at weeks 16 and 20, then every 8 weeks. Stable doses of methotrexate (≤ 25 mg/week), sulfasalazine, hydroxychloroquine, NSAIDs, other analgesics, and low dose oral corticosteroids were permitted for patients who were receiving these medications at baseline. Measures of HRQoL included the Ankylosing Spondylitis Quality of Life questionnaire (ASQoL), Short Form-36 physical and mental component summary scores (SF-36 PCS/MCS), Medical Outcomes Study Sleep Scale (MOS-SS), and EuroQoL visual analog scale (EQ VAS), each measured at weeks 16, 28, and 52. P values provided are nominal, not adjusted for multiplicity.

Results: At week 16, patients with AS receiving GLM-IV had greater improvements from baseline in HRQoL than those receiving PBO in each measure, respectively (ASQoL, -5.4 vs -1.8; SF-36 PCS, 8.5 vs 2.9; SF-36 MCS, 6.5 vs 0.78; MOS-SS, 6.6 vs 2.5; and EQ VAS, 20.3 vs 4.8; all p< 0.001), see Table. Changes from baseline were maintained through week 52 in patients randomized to GLM-IV. Patients switched from PBO to GLM IV at week 16 demonstrated improvement from baseline by week 28, which was maintained through week 52 and was similar to that of patients who received GLM IV at baseline (Table).

Table. Changes from Baseline in HR-QoL Measures from Week 16 to Week 52 in the Placebo-Controlled, Randomized, Phase 3 Study GO-ALIVE of Patients with Ankylosing Spondylitis

	GOL 2 mg/kg			PRO → Week 24 crossover to GOL 2 mg/kg		
	n	Baseline Score	Change from Baseline (mean ± SD)	n	Baseline Score	Change from Baseline (mean ± SD)
AS QoL						
Baseline	104	12.8 ± 4.04		102	12.4 ± 4.1	
Week 16	104		-5.4 ± 5.0*	102		-1.8 ± 4.6
Week 28	104		-5.3 ± 5.2	102		-5.3 ± 4.8
Week 52	104		-5.5 ± 5.3	102		-5.4 ± 5.3
SF-36 PCS						
Baseline	104	32.4 ± 5.6		102	32.1 ± 5.9	
Week 16	104		8.5 ± 7.5*	102		2.9 ± 6.2
Week 28			9.1 ± 8.0	102		9.3 ± 7.1
Week 52	104		9.5 ± 8.8	102		9.7 ± 8.1
SF-36 MCS						
Baseline	104	40.0 ± 10.4		102	41.9 ± 10.2	
Week 16	104		6.5 ± 9.1*	102		0.78 ± 10.0
Week 28	104		6.2 ± 10.9	102		5.6 ± 9.7
Week 52	104		7.3 ±10.6	102		5.1 ± 11.9
MOS-SS						
Baseline	104	40.2 (7.8)		102	39.5 (8.3)	
Week 16	104		6.6 ± 7.2*	102		2.5 ± 8.2
Week 28	104		6.6 ± 8.1	102		5.9 ± 8.3
Week 52	104		6.9 ± 8.6	102		6.8 ± 9.2
EQ VAS						
Baseline	104	41.6 ± 22.7		102	41.3 ± 18.1	
Week 16	104		20.3 ± 24.6*	98		4.8 ± 23.5
Week 28	102		20.5 ± 27.9	97		22.5 ± 23.1
Week 52	101		21.9 ± 26.8	95		24.3 ± 23.7

*P vs placebo<0.001. P values are nominal, not adjusted for multiplicity.
ASQoL and and SF-36 results were calculated using a Mixed-effect Repeated Measures statistical model. MOSS-SS and EQ VAS results were calculated using an Analysis of Covariance model.
ASQoL=Ankylosing Spondylitis Quality of Life EQ VAS= EuroQol-5D questionnaire, visual analog scale; HRQoL=Heath-related Quality of Life; SF-36 PCS/MCS=Short-Form-36 Physical / Mental Component Summaries

Conclusion: Improvements in HRQoL among patients with active AS treated with GLM-IV were greater than PBO at week 16 and were maintained through week 52. Patients switching from PBO to GLM-IV at week 16 experienced improvements in HRQoL by week 28 and maintained the improvement through week 52 at levels similar to those of the patients originally randomized to GLM-IV.

References:

1. Deodhar et al. *J Rheum*. 2018;45:341
2. Reveille et al. *J Rheum*. 2019. https://doi.org/10.3899/jrheum.180718.

Disclosure: J. Reveille, Abbvie, 2, CB, 5, Eli Lilly, 2, 5, 8, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 5, Pfizer, 2, 5, UCB, 5; **A. Deodhar**, AbbVie, 2, 5, 9, Abbvie, 5, 8, Abbvie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, and UCB Pharma, 5, 8, AbbVie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GSK, Galapagos, Janssen, Novartis, Pfizer and UCB, 5, AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Glaxo Smith and Klein, Janssen, Novartis, Pfizer, UCB, 5, Amgen, 5, 8, 9, BMS, 2, 5, 8, BMS, Eli Lilly, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, 2, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, UCB Pharma, 2, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, 8, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, 9, Eli Lilly and Company, 2, 5, Eli Lilly,, 5, Eli Lilly, GSK, Novartis, Pfizer and UCB, 2, Galagagos, 5, Galapagos, 5, 8, 9, Glaxo Smith & Klein, 2, Glaxo Smith & Kline, 2, 5, 8, Glaxo Smith Klein, 5, Glaxo SmithKlein, 2, 5, GlaxoSmithKlein, 2, 5, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, Janssen, 2, 5, 8, 9, Janssen Pharmaceutica, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9; **D. Harrison**, Janssen Research & Development, LLC, 3; **E. Hsia**, Janssen Research & Development, LLC, 3; **E. Chan**, Janssen Research & Development, LLC, 3; **S. Kafka**, Janssen Research & Development, LLC, 3, Janssen Scientific Affairs, LLC, 1, 3; **K. Lo**, Janssen Research & Development, LLC, 3; **L. Kim**, 3anssen Research & Development, LLC, 3, Janssen Research & Development, LLC 3; **C. Han**, Janssen Research & Development, LLC, 3, Janssen Research & Development, LLC, 3.

Abstract Number: 1259

Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis (SAPHO): A Case Series

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: SAPHO is a chronic multisystemic illness with predominantly skin and joint manifestations. Disease presentation is heterogenous; proposed diagnostic criteria include chronic multifocal aseptic osteomyelitis and osteitis of the long bones1,2. Due to SAPHO's rarity, treatment is based on observational studies and case reports. Anti-TNF therapy is increasingly used in refractory SAPHO cases. We present a series of 10 patients diagnosed with SAPHO and their response to various anti-TNF agents.

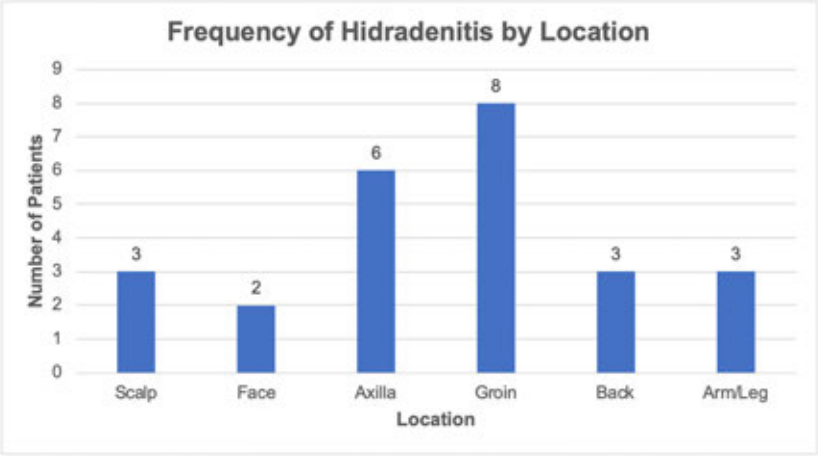
Methods: We performed a retrospective single-center study of SAPHO patients on anti-TNF therapy followed by rheumatology and dermatology from 2014 to 2017. Patients 18 or older were screened for SAPHO using ICD-10 codes for hidradenitis suppurativa, acne vulgaris, pustulosis, palmar pustulosis, palmoplantar pustulosis, AS, inflammatory spondylopathy, seronegative SpA, and inflammatory arthritis in combination. Patients were excluded if an

Patient Age (years), Sex	Treatments Tried					Response		Follow-up Duration (Weeks)
	Methotrexate	Infliximab	Adalimumab	Etanercept	Golimumab	Articular	Dermatologic	
52, Female		Yes					Discontinued due to brittle hair, alopecia	234
	Yes					Persistent synovitis and hand swelling		
32, Male					Yes	Significant improvement in joint pain		9
60, Female				Yes		Joint pain and hidradenitis initially resolved after first dose followed by relapse		395
		Yes				Joint pain resolved	Hidradenitis improved	
24, Male		Yes				Joint pain resolved	Clearing hidradenitis, residual groin drainage; acne resolved. Hidradenitis recurred with treatment lapse	383
			Yes			No joint pain, active hidradenitis or acne. Maintained remission		
40, Female	Yes	Yes					Worsening hidradenitis. New involvement in hands, gluteal folds	160
24, Female		Yes				Second infusion improved joint pain	First infusion improved hidradenitis, facial acne. Occasional flare	14
36, Male *	Yes				Yes	Synovitis and hidradenitis controlled on golimumab		49
61, Female			Yes			Improved hidradenitis and joint pain initially, worsened after four years		532
	Yes	Yes				No acne, hidradenitis or synovitis. Sustained remission.		
46, Male	Yes	Yes					Acne and pustules resolved after infliximab	129
45, Female				Yes		Arthritis improved	No change in acne and hidradenitis	284
	Yes	Yes				Resolution of joint pain with infliximab. Fluctuating joint symptoms closer to infusion due date	Initial clearing of hidradenitis with infliximab	

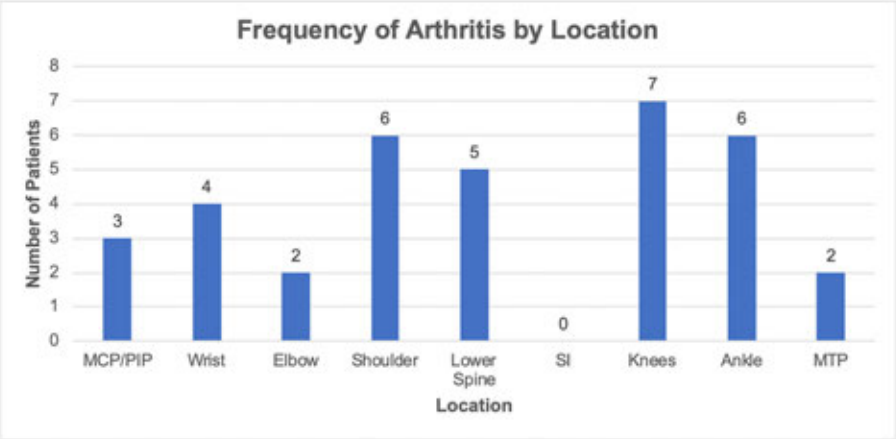
Summary of dermatologic and articular response to various disease modifying treatments.

alternate diagnosis was made, lost to follow-up, or did not start anti-TNF therapy. We identified 10 SAPHO patients treated with TNF inhibitors and characterized their articular and dermatologic responses.

Results: 10 patients (6 female, 4 male) with a mean age of 38 years (range 19-52) were followed for an average period of 50 months (range 2–122). 6 of the 10 patients (60%) had prior MTX or bisphosphonate use. Infliximab was used in 8 patients of whom 6 had significant improvement in pustulosis and joint pain while 2 patients experienced



Hidradenitis predominantly involved the groin and axilla, with less involvement of peripheral limbs, scalp and face.



Location of arthritis varied between axial and peripheral involvement. Predominant joints included shoulders, knees and lower spine.

worsening symptoms. 4 patients (40%) required two or more anti-TNF agents. The average ESR and CRP were 32 mm/hr and 5.8 mg/L at the outset and 26 mm/hr and 2.52 mg/L at the end of therapy, respectively.

Conclusion: Anti-TNF therapy is effective in treating cutaneous and articular manifestations of refractory SAPHO. Infliximab was most widely used in our study and associated with marked improvement in acne, pustulosis and arthritis. Etanercept was less effective in treating skin than articular disease. Golimumab and adalimumab showed similar clinical response. At present, a lack of validated response criteria specific for SAPHO limits objective assessment of therapeutic response. Further research is needed to better gauge response to therapy.

Disclosure: D. Verma, None; **S. Shah**, None; **A. Jayatilleke**, None.

Abstract Number: 1260

The Study of Peripheral Blood Lymphocyte Subsets and CD4+T Subsets in Recurrent Polychondritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Relapsing polychondritis (RP) is an uncommon systemic connective tissue disorder characterized by recurrent and episodic inflammation of cartilaginous tissues, such as ear, nose, joint, and respiratory tract. Recently, some researches suggest that immune disorders lead to autoimmune diseases. But little research has been done on the status of immune function in RP patients. Therefore, we analyzed the lymphocyte subsets in peripheral blood of RP patients to explore their immune function. Therefore we analyzed absolute counts and percentages of lymphocyte subsets and CD4+T subsets in peripheral blood of RP patients to explore their immune function and laid a foundation for further treatment.

Table I. Absolute counts and percentage of PB lymphocytes in the study participants (n=17).

Variable	RP patients (n=17)	Healthy donors (n=17)	p-value
PB lymphocyte(cells/μl)	median (quartile range)	median (quartile range)	
T	1092.00(900.23-1036.77)	1573.00(1401.71-1825.50)	0.002
B	170.22(118.70-292.74)	246.00(164.50-318.61)	0.213
CD4+T	620.09(502.39-883.28)	913.00(815.84-1073.00)	0.003
CD8+T	391.00(322.72-638.98)	432.11(414.00-718.00)	0.274
NK	203.00(92.45-273.79)	341.00(209.47-429.00)	0.020
CD4+T/CD8+T,ratio	1.46(1.33-1.85)	2.26(1.42-2.48)	0.122
PB lymphocyte %			
T%	72.57(67.77-78.82)	73.00(66.99-75.50)	0.892
B%	12.29(9.01-15.17)	11.00(7.32-14.00)	0.586
CD4+T%	41.20(36.53-46.01)	43.00(39.00-49.00)	0.496
CD8+T%	27.58(22.70-32.00)	21.00(18.91-27.50)	0.079
NK%	12.00(6.00-18.31)	15.21(8.50-17.79)	0.518

Table II. Absolute counts and percentage of cd4+T cells in the study participants (n=17).

Variable	RP patients (n=17)	Healthy donors (n=17)	p-value
CD4+T subsets (cells/μl)	median (quartile range)	median (quartile range)	
Th1	89.43(58.51-175.34)	87.74(68.41-164.13)	0.812
Th2	7.44(4.77-9.53)	10.22(8.00-14.70)	0.031
Th17	6.07(3.53-12.13)	5.59(4.09-9.45)	0.838
Treg	24.28(16.24-34.17)	46.33(42.69-58.04)	P<0.001
Th1/Th2	13.00(7.56-22.19)	10.21(5.45-17.32)	0.245
Th1/Treg	3.33(2.11-6.84)	1.95(1.54-3.65)	0.018
Th2/Treg	0.27(0.21-0.35)	0.21(0.16-0.30)	0.114
Th17/Treg	0.25(0.17-0.37)	0.13(0.08-0.17)	0.001
CD4+T subsets%			
Th1%	13.00(8.40-19.08)	10.76(8.01-20.01)	0.518
Th2%	1.00(0.66-1.67)	1.02(0.90-1.65)	0.586
Th17%	0.88(0.69-1.27)	0.68(0.45-0.92)	0.112
Treg%	3.80(2.37-4.65)	5.21(4.56-5.89)	0.001

Methods: Absolute counts and percentages of peripheral blood lymphocyte subsets and CD4+T subsets, which were from 17 patients (8 women and 9 men) diagnosed as RP and 17 healthy controls, were assessed by flow cytometry and compared. All statistical analyses were performed with SPSS v. 22.0. Continuous variables were reported as median. For all study variables, comparison among controls and RP subjects was based on the non-parametric Wilcoxon Mann-Whitney exact test. For all analyses, we used two-sided tests, with p-values < 0.05 denoting statistical significance.

Results: Our study recruited 17 patients who met the inclusion criteria. The average age of patients was 45.23 year. As shown, when compared with healthy controls, RP patients had lower absolute counts of T cells (1573.00/μl vs. 1092.00/μl, p=0.002), CD4+ T cells (913.00/μl vs. 620.09/μl, p=0.003), and NK cells (341.00/μl vs. 203.00/μl, p=0.02). No difference was reported when comparing the percentage and absolute number of B cell, the percentage of CD8+T cells and the ratio of CD4+/CD8+ T cells between RP patients and healthy group. In CD4+ T cells, the proportion and absolute counts of Treg cells were significantly reduced in RP patients in comparison with controls (proportion,

3.80% vs. 5.21%, p< 0.001; absolute counts, 24.28/μl vs. 46.33/μl,p=0.001). The absolute counts of Th2 cells was reduced in RP patients in comparison with controls (7.44/μl vs. 10.22/μl, p=0.031). But there were no significant difference between the percentage and absolute counts of Th17 or Th1 cells in patients with RP and healthy controls. But RP patients had higher ratio of Th17/Treg (0.25 vs. 0.13, p=0.001), Th1/Treg(3.33 vs. 1.95, p=0.018).

Conclusion: Our data suggested that the immune-inflammation in RP patients may be related to the depletion of NK cells and Treg cells. The relative decrease of Treg cells may lead to the relative increase of helper T cells, which leads to uncontrollable inflammatory response.

Disclosure: F. Hu, None; **N. Yan**, None; **J. Liang**, None; **X. li**, None; **C. Wang**, None.

Abstract Number: 1261

The Time Lag – the Race in Diagnosis and Management of Hemophagocytic Lymphohistiocytosis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

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Session Time: 9:00AM–11:00AM

Background/Purpose: Hemophagocytic lymphohistiocytosis (HLH) is an aggressive and life-threatening syndrome of disordered immune activation marked by excessive inflammation. Immunosuppression remains the mainstay of therapy after targeting the underlying trigger. Both the diagnosis and management of HLH remain challenging, as the disease can mimic a wide spectrum of clinical disorders and immunosuppression can become delayed. A multidisciplinary approach is crucial for the early diagnosis and treatment of this disorder to help improve outcomes. The aim of our study is to explore the relation between time to sub-specialty consultation, HLH consideration and immunosuppression initiation with 30-day mortality.

Methods: We performed a retrospective chart review of HLH patients' age >18 years identified in the electronic medical records by ICD 9/10 coding for HLH and confirmed by chart review. Patients were characterized as having definitive HLH (defined as meeting 5/8 parameters according to the 2004 HLH diagnosis criteria) and probable HLH (defined as meeting 4/8 parameters on the HLH criteria or if they had hemophagocytosis on biopsy). Patients with incomplete clinical data and those not meeting criteria for definitive or probable HLH were excluded. Clinical demographics, underlying etiology, HLH parameters, hospital day of HLH as a diagnostic consideration, time to sub-specialty consultation (rheumatology, allergy/immunology, hematology/oncology, infectious disease, and critical care), hospital day of immunosuppression initiation and 30-day mortality were identified. Student's t-test was used for comparison of continuous variables.

Results: During the study period, we identified 90 patients with HLH based on ICD coding. After excluding 64 patients based on insufficient clinical data for diagnosis of HLH, 20 patients were identified as having definitive HLH and 6 patients were identified as having probable HLH (Figure 1). Majority of patients 15/26 (58%) were males with a mean (SD) age of 42 (18). Infection (46%) was the most common secondary cause for HLH with 6/11 (54%) as viral etiolo-

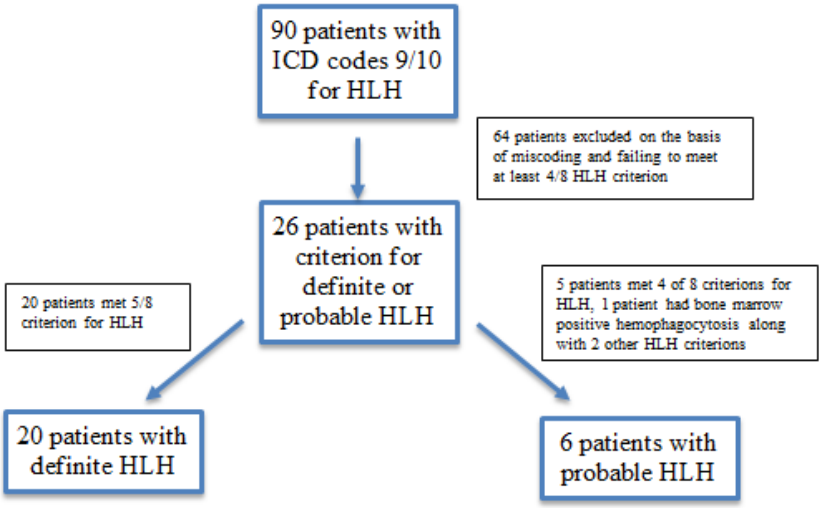

Figure 1. Flowchart of Inclusion/Exclusion Criterion

gies. Corticosteroids were the preferred first line immunosuppressive therapy in all patients. The 30-day mortality in our cohort was 7/26 (27%). The mean (SD) time to any sub-specialty consultation was 1.8 days (1.2) in patients who survived and 3 days (2.3) in patients who died (p=0.23). The mean (SD) time lag from admission to HLH consideration was 6.7 (5.3) vs. 4.6 (3.6) (p=0.26), while the mean (SD) time lag from consideration of HLH to immunosuppression was 2 days (2.7) vs. 8.4 days (8.8) SD (p=0.10) in patients who survived and died respectively.

Conclusion: Among adult patients with definitive or probable HLH seen at a single center, we did not find a statistical significant association between time to sub-speciality consultation, time lag to immunosuppression, and mortality. Our study was not adequately powered to detect small differences and future larger studies are warranted, so appropriate interventions can be developed.

Disclosure: S. Patel, None; **B. Ayesha**, None; **A. Broder**, None; **I. Gendlina**, None; **I. Murakhovskaya**, None; **M. Ramesh**, None; **Y. Balagula**, None; **A. Kumthekar**, None.

Abstract Number: 1262

Clinical Features of Elderly-onset Adult Still's Disease

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The peak age at the onset of adult Still's disease (ASD) has been between 20 and 35 years old. However, the proportion of elderly-onset ASD (EOASD) is increasing in Japan, a country of super-aged society. Therefore, we investigated the clinical features of EOASD in comparison with non-elderly-onset ASD.

Methods: A total of 20 patients with the diagnosis of ASD according to the classification criteria by Yamaguchi et al. between May 2013 and October 2018 in our department were enrolled in this study. Their medical records were intensively reviewed for demographics, clinical manifestations, laboratory data, treatments received and outcome.

Results: Six patients with the age of onset ≥ 65 years (median 71 years old, 5 women) and 14 patients < 65 years (median 38 years old, 12 women). There were no between-group differences in the frequency of fever, sore throat, arthralgia, leukocytosis, liver function abnormality, seronegativity and serum ferritin levels. However, typical rash (50% versus 92%) and lymphadenopathy (50% versus 92%) tended to be less frequently observed in EOASD as compared with non-elderly-onset ASD, and as a result, the number of fulfilled items of Yamaguchi criteria was significantly smaller in EOASD than non-elderly-onset ASD (the median value of 5.5 and 7.5, respectively, p=0.0036). With regard to the treatment, glucocorticoids were administered in 19 patients (initial daily dose of prednisolone 50 mg/day for both groups), and tocilizumab was added in 20% and 35% of EOASD and non-elderly-onset ASD patients respectively. The prognosis was fair except for one patient with non-elderly-onset ASD developing fatal sepsis.

Conclusion: EOASD was not rare (30% of ASD) and showed comparable clinical features and outcomes with non-elderly-onset ASD.

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Abstract Number: 1263

The Prevalence and Patterns of Celiac Disease Associated Arthropathy and Coexistence of Celiac Disease with Rheumatic Disorders in a Single Tertiary Medical Center

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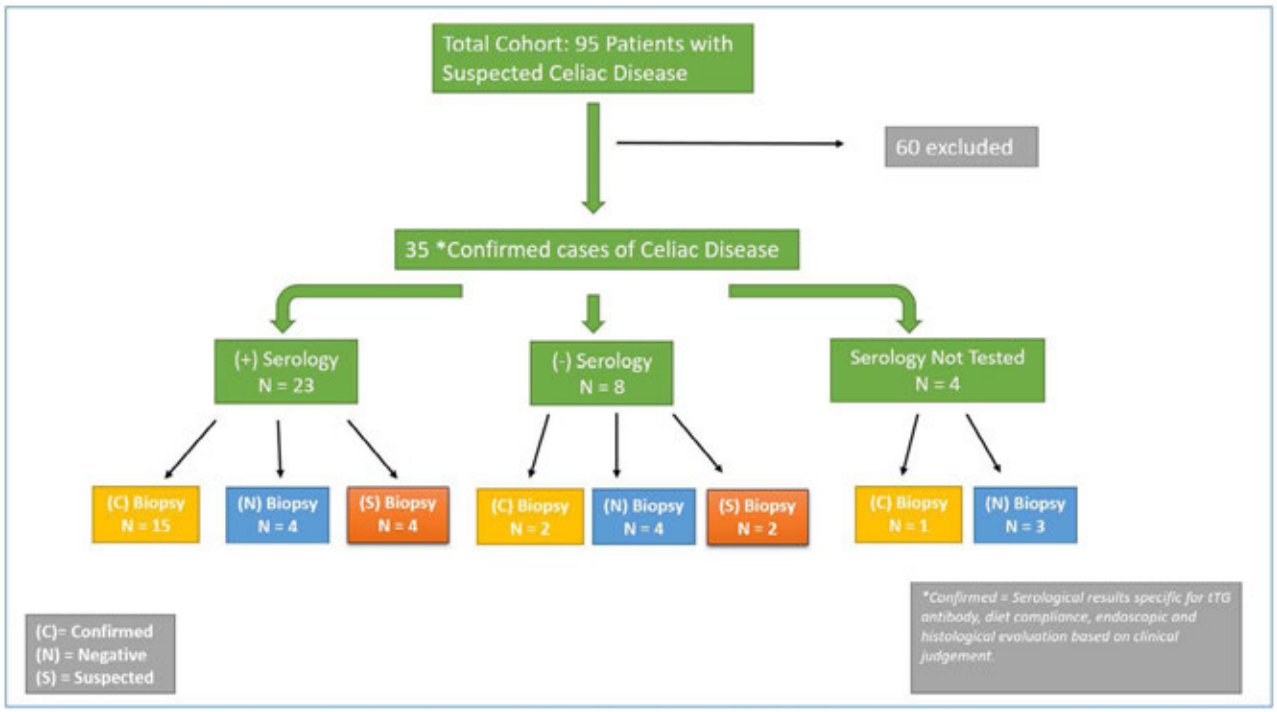
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Celiac disease (CD) is a gluten-sensitive enteropathy that develops in genetically predisposed individuals. Arthropathy has been reported as an extra-intestinal manifestation of CD. The pathogenesis of arthropathy is unclear; however, the immunologically mediated mucosal injury may lead to absorption of immune complexes or gut-derived antigens which may provoke antibody mediated autoimmune diseases including rheumatic diseases and arthropathy. We report a retrospective chart review of 35 confirmed cases of CD associated arthropathy and coexisting rheumatic or inflammatory disorders.

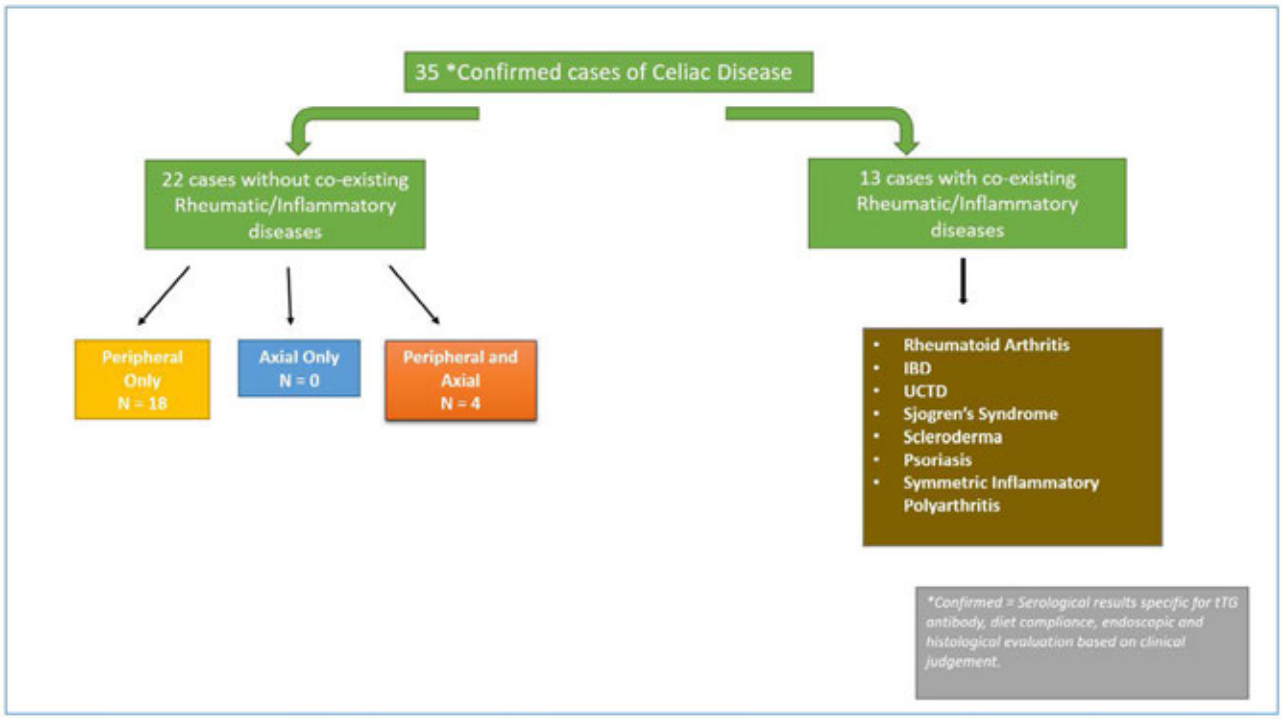
Methods: Heron database was used to search for patients seen by Gastroenterology and/or Rheumatology between January 2008 to January 2018 with suspected CD based on ICD-9 code for CD. These charts were retrospectively reviewed to determine who had confirmed CD, joint pain and pattern of involvement, dietary compliance, and other inflammatory or rheumatic disorders. The diagnosis of CD was based on serology specific for tissue transglutaminase (tTG) antibody, endoscopic and histological results, compliance with gluten free diet, and clinical judgement.



Celiac Abstract Image 1Total Cohort with Suspected Celiac Disease

Results: A total of 95 patients with suspected CD were identified. 35/95 had confirmed CD. Of the 35 patients, 29 were female and 34 self-identified as Caucasian. The average age of patients was 49 years. Of the 35 patients, 22 patients did not have a co-existing rheumatic or inflammatory disorder. This cohort of 22 patients endorsed symptoms in the following distribution: 82% (18/22) had peripheral only, 0% (0/22) had axial only, and 18% (4/22) had peripheral and axial involvement. Of the 22 patients, 54% (14/22) endorsed arthropathy in small joints, 91% (20/22) in medium joints, and 82% (18/22) in large joints. Improvement in arthralgia after transitioning to a gluten-free diet was reported in 4/22 patients. A total of 13/35 with confirmed CD diagnosis had a rheumatic and/or inflammatory disorder. Rheumatoid Arthritis had the highest prevalence at 11% (4/35) followed by IBD (3), UCTD (2), Sjorgen's Syndrome (1), Scleroderma (1), Symmetric Inflammatory Polyarthritis (1), and Psoriasis (1). Fibromyalgia, a non-inflammatory condition, was reported in 6% (2/35) of patients. 3 patients were not seen by rheumatology.

Conclusion: CD associated arthropathy and coexistence of CD with rheumatic and/or inflammatory disorders are under-recognized. Our data demonstrates that 63% of patients had CD associated arthropathy who appear to be a unique subset separate from those with coexisting CD and rheumatic/inflammatory disorders. Identifying the association and pattern of arthropathy in CD will aid in management of patients who either present to a gastroenterologist with extra-intestinal manifestations or to a rheumatologist with gastrointestinal manifestations. The awareness that CD can coexist in rheumatic diseases will aid rheumatologists in more effective recognition and management of patients with such presentations.



Celiac Abstract Image 2 Confirmed Cases of Celiac Disease

Disclosure: A. Moudgal, None; **P. Bhadbhade**, None; **A. Haikal**, None; **M. Maz**, None.

Abstract Number: 1264

Quality of Life in Patients with SAPHO Syndrome: A Single-center Survey of 588 Patients

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare autoimmune disease with heterogeneous presentation and severe disease burden. Factors influencing the quality of life (QoL) in patients with SAPHO syndrome remained under-recognized. We aim to assess the impact of various current symptoms (osteoarticular, dermatological and nail) on QoL in SAPHO patients.

Methods: A cross-sectional survey was conducted based on a previously established single-center dynamic cohort of SAPHO syndrome.[1, 2] Electronic questionnaires were distributed to patients recruited from January 2004 and December 2018 via a patient committee. Patients with active disease were asked to report their current clinical presentation (osteoarticular, dermatological and nail) and fill out the EuroQol five dimensions questionnaire (EQ-5D). Health related quality of life results measured by the EQ-5D were converted to a utility score using the Chinese time trade-off value set.[3] In addition, for those with osteoarticular manifestations, disease activity was measured using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). The Dermatology Quality of Life Index (DLQI) was obtained from the patients with dermatological manifestations.

Results: A total of 588 questionnaires were issued and 521 were retrieved. 60 were in remission at the time of examination. For the EQ-5D dimensions, patients reported the most problems (of any level) with pain or discomfort (52.6% [95% CI 48•0–57.2]) and fewest problems with self-care (10.1% [7.6–13•2]). Patients with current osteoarticular symptoms had a significant lower EQ-5D score than those without, which remained significant after adjustment for covariates (age, gender, smoking, and BMI). Meanwhile, such a relationship was not shown for dermatological and nail manifestations. For patients with skin lesions, DLQI was significantly lower at the presence of osteoarticular symptoms or nail lesions, even after adjusting for covariates.

Table 1 Basic characteristics of patients included in the study

Characteristics	n=521*
Gender, male, n (%)	164 (31.5)
Age, years, mean (SD)	43.3 (12.9)
Current smoker, n (%)	155 (29.6)
BMI (kg/m^2), mean (SD)	23.7 (3.4)
Current osteoarticular symptoms, n (%)	335 (64.3)
Current dermatological manifestations, n (%)	350 (67.2)
Current nail manifestations, n (%)	190 (36.5)
EQ-5D utility index (n=461), median (IQR)	0.847 (0.748-0.939)
EQ-5D mobility, n (%)**	118 (25.9)
EQ-5D self-care, n (%)**	46 (10.1)
EQ-5D usual activities, n (%)**	82 (17.9)
EQ-5D pain or discomfort, n (%)**	240 (52.6)
EQ-5D anxiety or depression, n (%)**	159 (34.9)
BASDAI (n=335), mean (SD)	3.0 (1.8)
DLQI (n=350), median (IQR)	6 (2-10)

*If not indicated otherwise.

**Adjusted percentage reporting any level of problem.

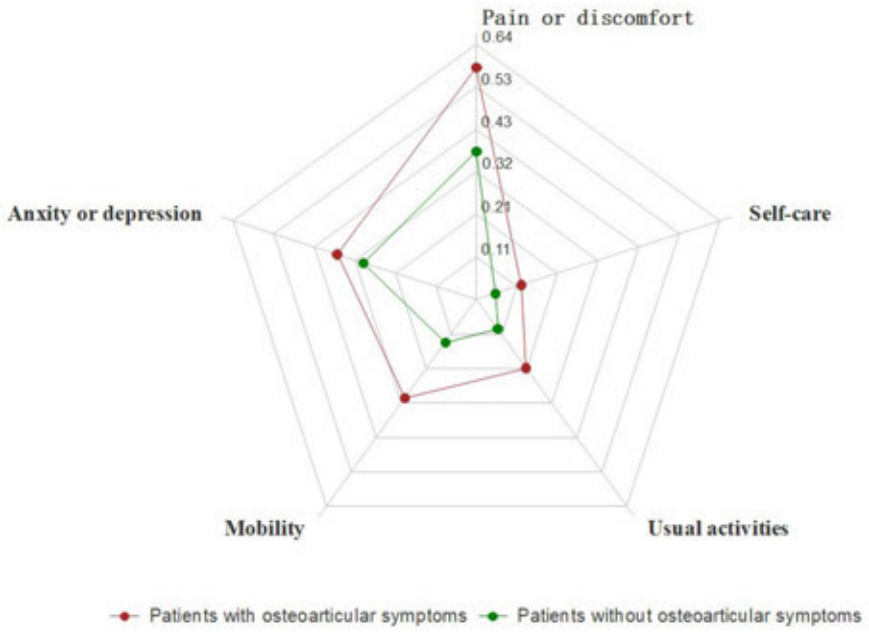

Figure 1. EQ-5D for patients with and without osteoarticular symptoms

Table 2 Correlations between the quality of life and variables

Variables	Outcome	Correlation (95% CI)	P-value
	EQ-5D utility index (n=461)		
Age		**-0.0017 (-0.0028, -0.0006)**	**0.003**
Current osteoarticular manifestations		**-0.065 (-0.096, -0.034)**	**<0.001***
Current dermatological manifestations		**-0.003 (-0.036, 0.030)**	**0.860**
Current nail manifestations		**-0.005 (-0.033, 0.023)**	**0.729**
BMI in Kg/m²		**-0.002 (-0.006, 0.002)**	**0.307**
BASDAI (n=335)		**-0.061 (-0.068, -0.054)**	**<0.001***
	DLQI (n=350)		
Age		**-0.054 (-0.108, 0.001)**	**0.052**
Current osteoarticular manifestations		**2.05 (0.62, 3.47)**	**0.005***
Current nail manifestations		**1.79 (0.45, 3.12)**	**0.009***
BMI in Kg/m²		**0.19 (-0.01, 0.38)**	**0.057**
BASDAI (n=237)		**0.54 (0.34, 0.74)**	**<0.001***

Correlation between different variables was analyzed by univariate regression.

*** Still significant after adjusting for covariates**

Conclusion: Our findings suggested a negative correlation between osteoarticular symptoms and QoL in SAPHO syndrome. Effectively controlling osteoarticular symptoms may be pivotal in improving patient QoL. Nail involvement, which is under-recognized previously, also had a negative influence on QoL in SAPHO patients.

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Disclosure: Z. Li, None; **C. Li**, None; **Y. Cao**, None; **Y. Xiang**, None; **Y. Li**, None; **W. Zhang**, None.

Abstract Number: 1265

Mandibular Involvement in SAPHO Syndrome: A Single-center Retrospective Study of 26 Patients

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Table 1 Demographic characteristics of the SAPHO patients with an affected mandible (n=26)

Variables	
Age (years), median (IQR)	28 (21-40)
Sex (Males/Females), n(%)	10/16 (38.5/61.5)
Disease duration (years old) at baseline, median (IQR)	2 (1-8)
Age at onset of symptoms (years), median (IQR)	22 (14-27)
Age at onset of oral symptoms (years), median (IQR)	25 (15-28)
Duration of diagnosis (years), median (IQR)	2 (0.8-3.0)
BMI (kg/m^2), median (IQR)	23 (18.9-26.0)
Smoking habit, n (%)	3 (11.5)
Positive family history, n (%)†	7 (26.9)
Oral invasive operation in one month before the onset, n (%)	10 (38.5)

†Positive family history: family history of SAPHO syndrome, palmoplantar pustulosis, psoriasis,and autoimmune inflammatory arthritis.

BMI: body mass index; IQR: interquartile ranges.

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a heterogeneous chronic inflammatory disease of unknown etiology. Mandibular involvement appeared in approximately 10% of the SAPHO patients,(1) and the treatment for mandible lesions, including surgery and conservative treatment, has not reached consensus. However, these patients were rarely discussed, mainly in case reports. Here we first reported the patients with mandible involvement from the largest cohort of SAPHO syndrome(2) and explored their demographic, clinical, and scintigraphic characteristics and treatment.

Methods: From January 2004 to June 2019, 618 patients were recruited at Peking Union Medical College Hospital (PUMCH) in a previously established single-center dynamic cohort of SAPHO syndrome.(2) The demographic, clinical, scintigraphic, and laboratory data were collected at baseline. The mandibular involvement was confirmed by

Table 2 Baseline clinical, scintigraphic, and laboratory characteristics of the SAPHO patients with an affected mandible (n=26)

Variables	
Affected part of the mandible, n(%)	
Left side, n(%)	7 (26.9)
Right side, n(%)	10 (38.5)
Bilateral, n(%)	9 (34.6)
Oral symptoms, n(%)	
Jaw Pain, n(%)	24 (92.3)
Swelling of the ipsilateral face, n(%)	22 (84.6)
limitation of mouth opening, n(%)	20 (76.9)
Skin manifestations, n(%)	15 (57.7)
PPP, n(%)	8 (30.1)
SA, n(%)	7 (26.9)
VAS, median (IQR)	5 (3-6)
BASDI, median (IQR)	1.5 (1-3.2)
BASFI, median (IQR)	1.2 (0-2.3)
hs-CRP (mg/ml), median (IQR)	6.41 (2.39-21.59)
HLA-B27 positive, n (%)	0 (0)
Lesion sites on bone scintigraphy, n (%)	12 (65.4)
Anterior chest wall, n(%)	10 (38.5)
Axial, n(%)	4 (15.4)
Vertebrae, n(%)	4 (15.4)
Sacroiliac joints, n(%)	2 (7.7)
Peripheral, n(%)	12 (46.2)
Shoulder, n(%)	4 (15.4)
Hip, n(%)	3 (11.5)
Knee, n(%)	2 (7.7)
Ankle, n(%)	1 (3.8)
Long bones of the limbs, n(%)	1 (3.8)

SA: severe acne; PPP: palmoplantar pustulosis; IQR: interquartile ranges; VAS: Visual Analogue Scale; BASDI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; hs-CRP: high-sensitivity C-reactive protein.

Table 3 Treatment and follow-up of the SAPHO patients with an affected mandible (n=26)

Variables	
Surgery intervention before baseline, n(%)	14 (53.8)
Curettage, n(%)	12 (46.1)
Resection of unilateral mandible	2 (7.7)
Surgical treatment before baseline (%)	100
Medical treatment history at baseline, n(%)	21 (80.8)
NSAIDs, n(%)	16 (61.5)
Glucocorticoids, n(%)	8 (30.1)
Antibiotics, n(%)	14 (53.8)
TNF-α inhibitors, n(%)	5 (19.2)
Biphosphonates, n(%)	1 (3.8)
Medical treatment in PUMCH, n(%)	26 (100)
NSAIDs, n(%)	16 (61.5)
Minocycline, n(%)	10 (38.5)
Glucocorticoids, n(%)	9 (34.6)
DMARDs, n(%)	6 (23.1)
Tripterygium wilfordii Hook F(TII) , n(%)	8 (30.8)
TNF-α inhibitors, n(%)	5 (19.2)
JAK inhibitors, n(%)	2 (7.7)
IL-6 inhibitors, n(%)	1 (3.8
Biphosphonates, n(%)	14 (22.7)
Effect of the treatment in PUMCH§	
Improvement in oral symptoms, n(%)	24 (92.3)
Patients with pain now, n(%)	8 (30.8)
VAS now, median (IQR)	1.5 (1, 2.25)
Patients with face swelling now, n(%)	1 (3.8)
Patients with limitation of mouth opening now, n(%)	2 (7.7)
Improvement in other osteoarticular symptoms, n(%)	2 (13.3) †
Improvement in dermatological symptoms, n(%)	4 (26.7) *

† Of the patients with other osteoarticular involvement, 13.3% had an improvement in those osteoarticular symptoms.

* Of the patients with skin lesions, 26.7% had an improvement in dermatological symptoms.

§ SAPHO patients with mandibular involvement only received conservative treatment in PUMCH.

PUMCH: Peking Union Medical College Hospital; IQR: interquartile ranges; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs; DMARDs: disease-modifying antirheumatic drugs; TNF-α inhibitors: Tumor necrosis factor alpha inhibitors; JAK inhibitors: Janus kinase inhibitors; IL-6 inhibitors: Interleukin 6 inhibitors; VAS: Visual Analogue Scale.

X-ray, scintigraphy, or biopsy. In May 2019, the prescription data was collected from the hospital information system, and the electronic questionnaire was distributed to all patients with mandibular involvement to ensure their medical compliance and to obtain their improvement in symptoms.

Results: A total of 26 SAPHO patients with mandibular involvement were identified, and all of them responded (38.5% male, median age 28 years old,and follow-up duration 2.1 years). Their median age at onset of symptoms was 22 years old (IQR 21-40 years old), younger than the median age of oral symptoms (25 years old, IQR 15-28 years old). Seven (26.9%) patients had a positive family history, and ten (38.5%) had received oral invasive operation in one month before the onset. Unilateral mandibular involvement was more common (65.4%). Skin lesions appeared in 15

(57.7%) patients, among which seven (26.9%) were affected by severe acne. The whole body bone scintigraphy revealed more peripheral osteoarticular involvement (46.2%) than anterior chest wall involvement (38.5%) or axial skeleton involvement (14.2%). All of the 14 (53.8%) patients undergoing surgery intervention relapsed, while conservative treatment led to an improvement of oral symptoms in most patients (24, 92.3%). Less improvement was observed in dermatological (13.3%) and other osteoarticular symptoms (26.7%).

Conclusion: Mandibular involvement in SAPHO syndrome is predominant in young-aged women. Familial inheritance factors and oral invasive operation may be possibly correlated with its onset. Conservative treatment instead of surgery might be recommended, although their efficacy on non-oral involvement remains challenging.

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Disclosure: Y. Li, None; **C. Li**, None; **M. Wang**, None; **Y. Cao**, None; **Y. Xiang**, None; **Z. Li**, None; **W. Zhang**, None; **J. zhao**, None.

Abstract Number: 1266

AGBL3 as a Novel Gene Associated with Hereditary Hypocomplementemic Urticarial Vasculitis and Favorable Response to Rituximab

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Urticarial skin lesions are well-known features of autoinflammatory disorders associated with NLRP3 and NLRP12 variants. However hereditary forms of hypocomplementemic urticarial vasculitis (HUV) with or without lupus features have been associated with DNASE1L3 variants in limited number of Turkish, Arabic and Italian families. We herein aimed to define the clinical phenotype and treatment responses of a patient with HUV due to a homozygous deleterious variant of a novel gene, AGBL3 (ATP/GTP binding protein-like 3).

Methods: Last year we described a novel gene variant in a patient with autoinflammatory features and HUV, who was negative for DNASE1L3 variants. Whole exome sequencing of the genomic DNA revealed a deleterious homozygous c.769C >T mutation in AGBL3 gene, which results in early termination of the protein (p.Gln257Ter) and deletion of the functional carboxypeptidase domain. The AGBL3 is suggested to catalyze the deglutamylation of polyglutamate side chains, especially in proteins such as tubulins. This variant was not found before in all reported databases including 1000 Genomes Project data. We herein describe the clinical features and treatment responses of the index case.

Results: The index case was 23-year-old male patient of Assyrian origin, who had consanguineous parents. He was evaluated in our clinic because of recurrent attacks of fever, urticarial rash on the extremities and trunk, conjunctival injections and arthralgia, without a trigger or more frequently following an infection. His 2-3 days lasting attacks started when he was 13 and recurred more frequently at warm conditions or following hot baths. He had highly elevated CRP and ESR during attacks, but his acute phase response did not return to normal values in between the flares. Low C3 and C4 values were also observed during asymptomatic periods. His ANA test became positive during the course of his disease with an increase in titers during the last years. The biopsy of skin lesions revealed findings compatible with urticarial vasculitis. He responded only partially to corticosteroids, but no obvious clinical and laboratory response could be seen with canakinumab and anakinra treatments. Following serologic evolution of the disease, his treatment was switched to rituximab. A favorable response both in clinical and laboratory findings was observed following two cycles of 1g infusions at 2-week intervals. He developed less frequent and milder attacks, which occurred only after infections; and acute phase response was reduced to near normal values in between attacks.

Conclusion: This case reveals AGBL3 metallocarboxypeptidase gene as a novel autoinflammatory gene associated with hypocomplementemic urticarial vasculitis. Potential pathogenic mechanisms and clinical picture are considered to be different from DNASE1L3 variants, which are also associated with monogenic lupus and defects in DNA clearance. Long term follow-up and search for other patients associated with AGBL3 variants among DNASE1L3-variant-negative hypocomplementemic urticarial vasculitis patients are required for better clarification of the AGBL3-associated clinical phenotype.

Disclosure: A. Gul, None; **N. Abaci**, None; **S. Sirma-Ekmekci**, None.

Abstract Number: 1267

Epidemology, Clinical Features and Relationship to Biological Therapy of Uveitis in Axial Spondyloarthritis: Single Center University Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Uveitis is one of the most frequent extra articular manifestation of spondyloarthritis (SpA). Biological therapy, especially monoclonal TNF inhibitors, are useful to prevent and to treat refractory non-infectious uveitis. However, other biologics had been related to paradoxical uveitis. Our aim was to assess a) the epidemiological and clinical features of uveitis associated to SpA and b) its relationship with biological treatment used in SpA.

Methods: We set up an observational study of patients who developed uveitis form a cohort of 255 consecutive unselected patients with axial SpA (axSpA) classified according to the ASAS criteria. They were divided into: a) ankylosing spondylitis (AS) according to New York modified criteria (n= 193) b) non-radiographic axSpA (nr-axSpA) (n= 62). All these patients were followed in a single reference University Hospital.

Results: We studied 255 patients with axSpA axSpA (151 men / 104 women); mean age 37.8 ± 10.6 years. In 36 (14.2%) patients at least one episode of uveitis was observed after a follow-up 12.4 ± 4.5 years. The underlying ax-SpA diseases were AS (n=31) and nr-axSpA (n= 5). The mean age at onset of uveitis was 45.7±14.2 years. Uveitis was diagnosed in 5 patients before SpA diagnosis. In the remaining patients (n=31) it was detected after a median of 6 [2-15] years of follow-up after SpA diagnosis. Pattern of uveitis was anterior and acute in all cases, and unilateral in 83%. None of them presented intermediate or posterior uveitis. Median of anterior chamber cells was 1 [1-2] cells. Comparison of baseline characteristics and clinical features between patients who developed uveitis and those who did not is shown in **Table 1**. Almost all patients who developed uveitis were HLAB27 positive. In these patients a lower frequency of enthesitis and inflammatory bowel disease was observed.

Table 1.

	Uveitis N= 36	Non uveitis N= 219
Baseline general features		
Age, years (mean±SD)	45.7 ± 14.2	44.7 ± 12.1
Sex, n (m/w) (%)	21/15 (58.3/41.7)	130/89 (59.4/40.6)
HLAB27, positive n (%)	35 (97.2)	130 (59.4)
Disease Characteristics		
Follow-up of AxSpa, year (mean±SD)	13.64 ± 7.6	12.16 ± 9.73
AS, n (%)	31 (86.1)	162 (74.0)
nr-AxSp, n (%)	5 (13.9)	57 (26.0)
Peripheral arthritis, n (%)	9 (25.0)	67 (30.6)
Hip affection, n (%)	3 (8.3)	15 (6.8)
Enthesitis, n (%)	9 (25.0)	81 (37.0)
Dactylitis, n (%)	2 (5.5)	14 (6.4)
Psoriasis, n (%)	4 (11.1)	24 (11.0)
Inflammatory bowel disease, n (%)	1 (2.8)	15 (6.8)
Family history, n (%)	12 (33.3)	58 (26.5)

Table 2.

	Patients (n)	Years after onset of treatment (mean ± SD)	Episodes of uveitis after the onset of treatment (n)
Adalimumab:	3	4.1 ± 3.5	6
Secukinumab:	3	4.2 ± 1.9	1
Certolizumab:	1	3.50 ± 0	0
Golimumab:	1	6.0 ± 0	0
Infliximab:	1	11.8 ± 0	1
Anti TNF	6	5.6 ± 4.0	7
Anti IL-17	3	4.2 ± 1.9	1

Cumulative incidence of uveitis episodes related to each biological agent is shown in **Table 2**. Patients treated with secukinumab developed 2.72 episodes of uveitis/100 patients/year, meanwhile those who received monoclonal anti TNF presented 2.53 episodes/100 patients / year.

Conclusion: The most frequent clinical pattern of uveitis in patients with SpA was acute unilateral anterior uveitis which appeared in most patients after 6 years of follow-up. Almost all of them were HLA B27 positive. No differences were found in cumulative incidence between secukinumab and monoclonal anti-TNF.

Disclosure: I. Gonzalez-Mazon, None; **L. Sanchez-Bilbao**, None; **J. Rueda-Gotor**, None; **D. Martinez-Lopez**, None; **D. Prieto- Pena**, None; **M. Calderón-Goercke**, None; **J. Martín-Varillas**, None; **B. Atienza-Mateo**, None; **M. Gonzalez-Gay**, Abbvie, 2, 5, 8, Celgene, 5, 8, Janssen, 2, MSD, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, Sanofi, 5, 8, Sobi, 5, 8; **R. Blanco**, None.

Abstract Number: 1268

Different Colchicine Preparations for Familial Mediterranean Fever: Are They the Same?

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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Colchicine is the mainstay of treatment for prevention of attacks and associated amyloidosis in Familial Mediterranean Fever (FMF). Two approved colchicine preparations are currently available in Turkish market. In case of resistance or adverse effects, it is a common practice for Turkish rheumatologists to change the colchicine preparation with an imported one. The aim of this study was to assess the benefit of the imported colchicine in Turkish adult patients with FMF resistant or intolerant to domestic colchicine preparations.

Methods: Adult patients followed up with a clinical diagnosis of FMF, meeting Tel Hashomer criteria, resistant or intolerant to domestic colchicine preparations, and under treatment with a particular brand of imported colchicine were identified retrospectively and included in the study. Patients using anti-interleukin-1 or other biological agents were excluded. Disease characterisitcs, *ME*diterranean *FeV*er gene (*MEFV*) mutations, attack frequencies before and after the imported colchicine were specified for each patient from their medical records. Resistance to colchicine was defined as suggested by the EULAR. Frequency of attacks and colchicine doses before and after the imported colchicine were compared. Mann-Whitney U or Kruskal-Wallis tests were used for comparison of distributions of unrelated samples and Wilcoxon signed rank test for repeated measurements. $p< 0.05$ was considered statistically significant.

Results: A total of 59 patients were included in the study. Thirty-six (61%) patients were female and median age was 29 (interquartile range: 22-38) years. Median duration of disease was 6 (interquartile range: 2-14) years. There were 46 (78%) patients carrying exon 10 mutations in homozygous or compound heterozygous forms. Eight (14%) patients had isolated exon 10 mutations in heterozygous form and three (5.1%) had an exon 10 and the E148Q mutations together. No patient had isolated E148Q mutation in homo- or heterozygous forms. Mutant allele frequencies and characteristics of the attacks were given in Figure 1.

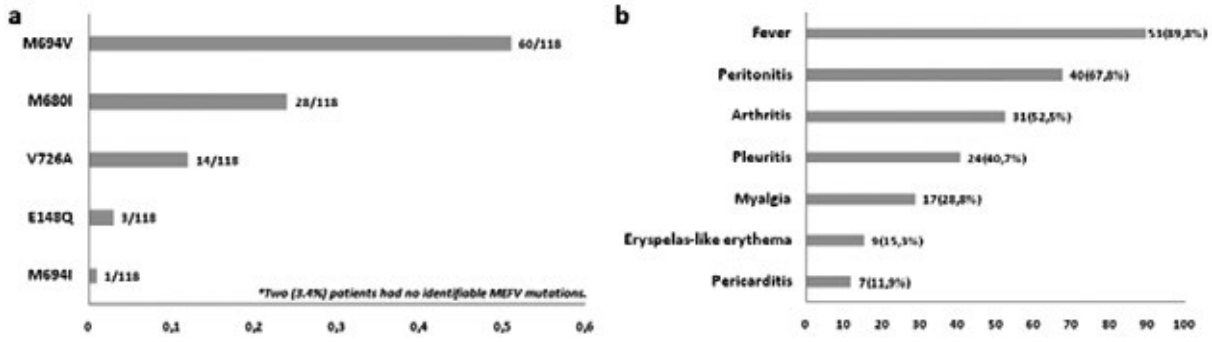
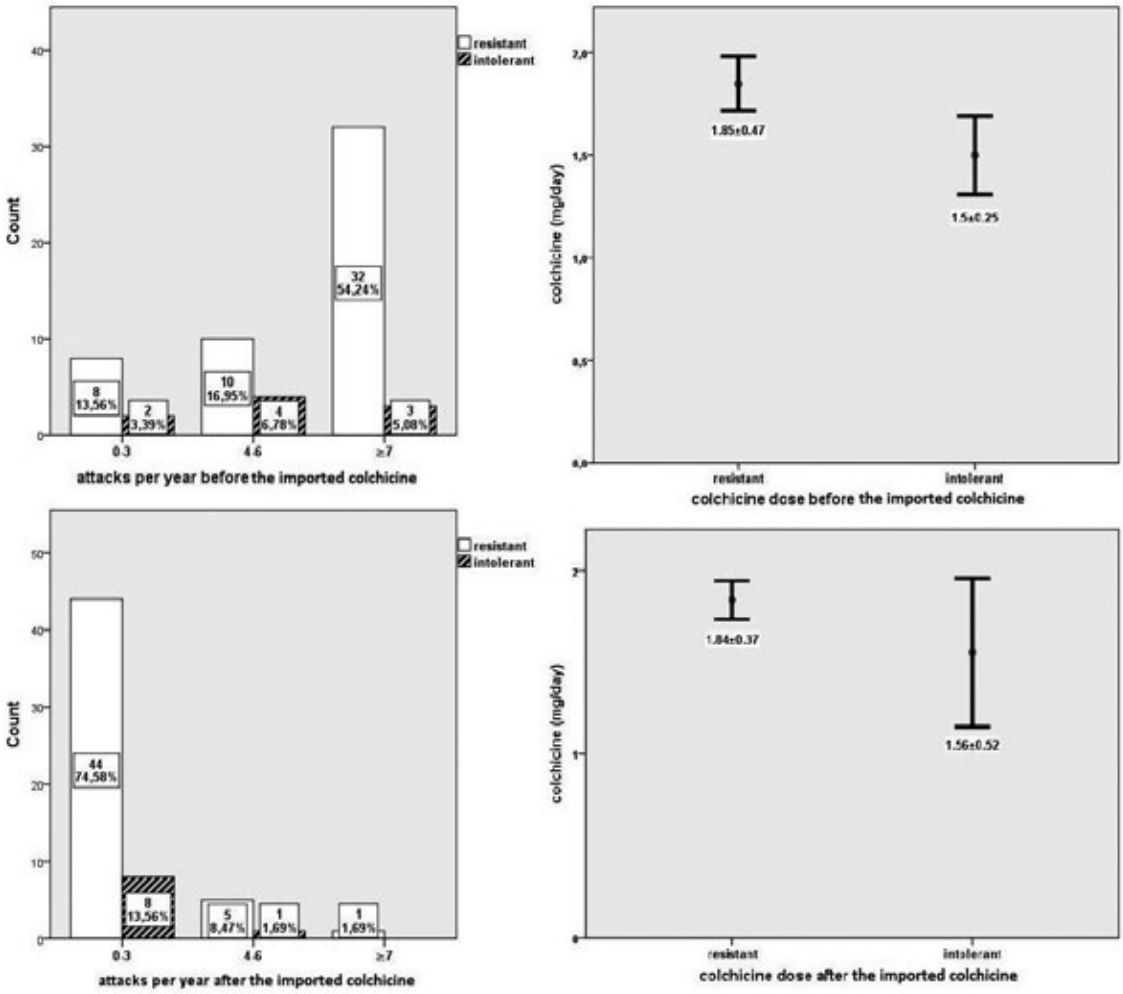


Figure 1. a. Allelic frequencies of the MEFV gene mutations. b. Characteristics of the attacks.



p<10⁻⁶ for difference of distributions of attacks in resistant cases; p=0.014 for difference of distributions of attacks in intolerant cases; p=0.9 for difference of daily colchicine doses in resistant cases; p=0.71 for difference of daily colchicine doses in intolerant cases before and after the imported colchicine.

Figure 2. Distributions of attacks and daily colchicine doses before and after the imported colchicine.

Fifty (84.8%) and 9 (15.2%) patients had resistance and intolerance to domestic colchicine preparations, respectively. Median number of attacks in the last three months before the imported colchicine was three (range 0-6). Although daily colchicine doses did not differ before and after the imported colchicine, number of attacks per year significantly

Study	Method	Dose	Form	C_{max} (ng/mL)	T_{max} (h)	$AUC_{0\text{-}last}$ (ng·h/mL)	Last Measurement (h)	Brand (Country)
Achtert G, 1989	RIA	0.76 mg	coated tablet	4.15 ± 2.35	1.15 ± 0.38	23.95 ± 12.1	72	Brand A (Germany)
		1 mg	oral solution	4.88 ± 3.9	1.13 ± 0.42	28.01 ± 14.74		
Girre C, 1989	RIA	1 mg	tablet	3.9*	1*	26.3 ± 3.52	48	Brand B (France)
Rochdi M, 1994	RIA	1 mg	tablet	5.5 ± 1.4	1.03 ± 0.5	N/P	48	Brand B (France)
Ferron GM, 1996	RIA	1 mg	tablet	5.64 ± 1.37	1.01 ± 0.56	47.9 ± 12.2	48	Brand B (France)
		1 mg	oral solution	6.5 ± 1.03	1.07 ± 0.55	62.3 ± 15.5		
Amanova A, 2014	HPLC	1 mg	coated tablet	0.13 ± 0.02	3.3 ± 1	2.12 ± 0.64	24	Brand C (Turkey)

*RIA = Radioimmunoassay; HPLC = High Performance Liquid Chromatography; C_{max} = peak plasma concentration; T_{max} = time to reach C_{max}; $AUC_{0\text{-}last}$ = area under plasma colchicine concentration - time curve from time zero to the last colchicine measurement; N/P = not provided. *Standard deviations were not reported.*

Table 1. Pharmacokinetic properties of different colchicine preparations after single oral doses in subjects with normal renal and hepatic functions.

reduced both in resistant and intolerant cases (Figure 2) after a median follow up of 19 (range 8-60) months under the imported colchicine. The decrease in number of attacks were more prominent in resistant cases (Figure 2).

Pharmacokinetic studies performed with different brands of colchicine after single oral doses in healthy subjects or FMF patients with normal renal and hepatic functions were summarized in Table 1.

Conclusion: Turkish FMF patients with ongoing attacks under domestic colchicine preparations may benefit from imported colchicine. This seems to be explainable by difference in pharmacokinetic properties of different colchicine preparations.

Disclosure: H. Emmungil, None; **U. İlgen**, None; **S. Turan**, None; **S. Yaman**, None; **O. Küçükşahin**, None.

Abstract Number: 1269

Effective Treatment of TNFα Inhibitors in Chinese Patients with Blau Syndrome

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Blau syndrome (BS) is a rare dominantly inherited autoinflammatory disorder associated with mutations in the *NOD2* gene. BS is mainly seen in Caucasian patients. Biologic therapy of BS yielded diversity results. We aimed to evaluate clinical features and outcomes of Chinese patients with BS who were treated with TNFα inhibitors.

Methods: A total of four patients with BS were diagnosed and treated with infliximab (IFX) at Peking Union Medical College Hospital during 2015 to 2018, and were followed up for 18 months. All patients were systematically studied for treatment outcomes including the clinical manifestations and inflammatory markers. We also conducted a comprehensive literature review about TNFα inhibitors therapy in BS.

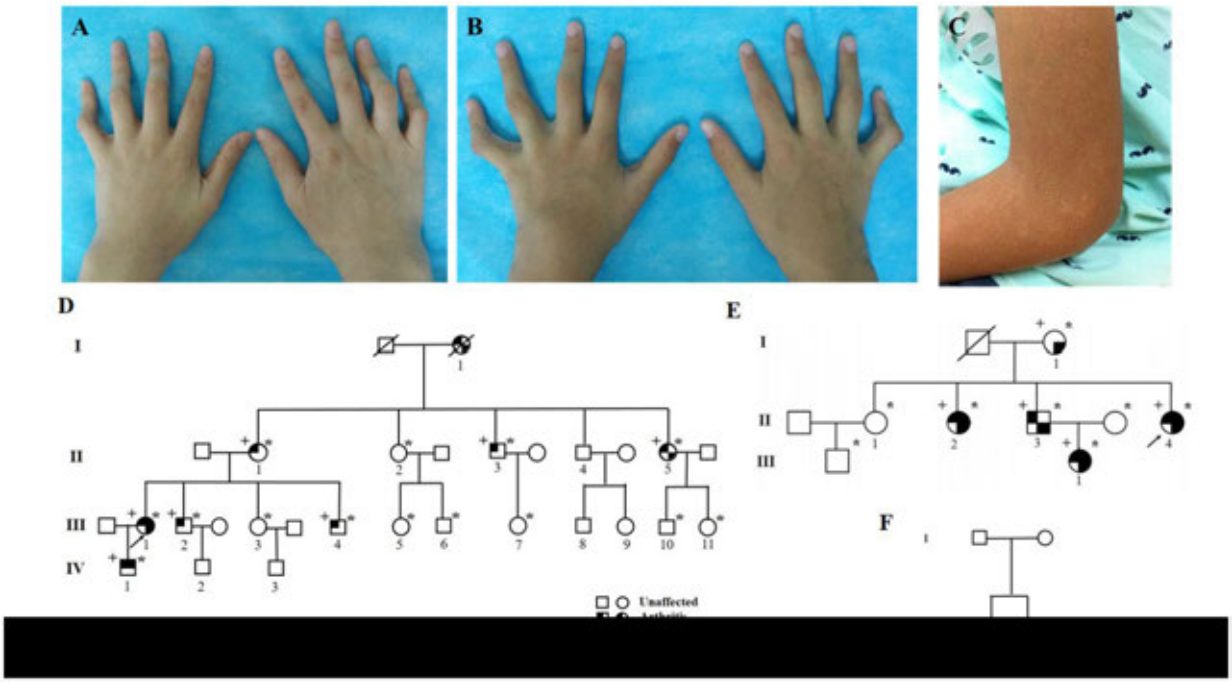

Figure 1. Pedigrees and phenotypes of Chinese patients with BS. Camptodactyly of patients 1 (A) and 2 (B); Papules on the upper limbs of patient 2 (C); Pedigrees of patients 1 and 2 (D), 3 (E) and 4 (F).

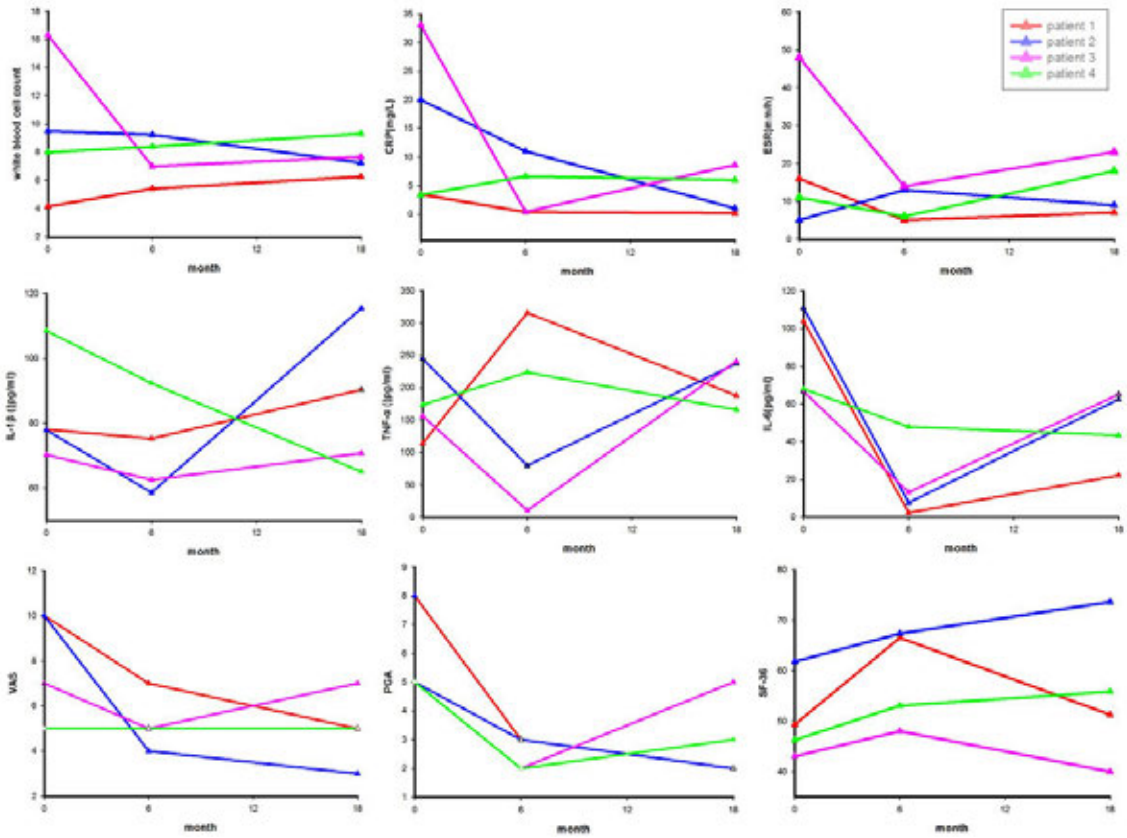

Figure 2. Changes in disease activity and inflammatory markers of patients. Overall, WBC, CRP, ESR, IL-1β, IL-6, VAS and PGA decreased, and SF-36 increased at the first follow-up of 6-month. TNFα decreased at the first follow-up for patients 2 and 3, but increased for patients 1 and 4. At the last visit of 18-month, WBC, ESR and CRP remained normal in all except patient 3, whose ESR and CRP increased to above normal range. Among all the patients, serum levels of IL-1β, TNFα and IL-6 were higher than those at the first follow-up, except patient 4. For patients 1 and 2, VAS and PGA reduced further at the last follow-up, while for patients 3 and 4, they slightly increased. CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; VAS: visual analogue scale; PGA: physician global assessment; SF-36: Short Form-36.

Table 1 Demographic and clinical features of four Chinese patients with BS

Patients	1	2	3	4
Gender	female	male	female	female
Age at diagnosis (years)	32	8	36	25
Age at onset (years)	6	0.5	7	6
Ethnicity	Han	Han	Han	Han
Family history	+	+	+	-
Clinical features				
Joint	+	+	+	+
Skin	+	+	+	-
Eye	+	-	+	+
Fever	+	-	-	-
NOD2 variants	R334W	R334W	R334W	R334Q
Laboratory findings				
WBC ($\times 10^9$/L)	4.15	9.5	16.3	7.99
CRP (mg/L)	3.48	20.0	33.01	3.4
ESR (mm/h)	16	5	48	11
IL-1β (pg/ml)	78.0	77.8	70.2	108.5
TNFα (pg/ml)	114.0	245.0	156.2	174.0
IL-6 (pg/ml)	104.0	111.0	66.7	68.0
VAS	10	10	7	5
PGA	8	5	5	5
SF-36	49.31	61.81	43	46.25
Treatments				
IFX	5 mg/kg every 6-8 weeks for 6months/5 mg/kg every 12 weeks	5 mg/kg every 8 weeks	5 mg/kg every 6-8 weeks for 6months/5 mg/kg every 12 weeks	3 mg/kg every 8 weeks for 6 months/3 mg/kg every 12-16 weeks
MTX	15 mg weekly for 6 months/12.5 mg weekly	10 mg weekly	15 mg weekly for 6 months/Discontinuation due to side effects	10 mg weekly for 6 months/Discontinuation due to side effects
Prednisone	Not used	Not used	Not used	15mg/day tapered to 5mg/day

WBC: white blood cells; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; VAS: visual analogue scale; PGA: physician global assessment; SF-36: Short Form-36; IFX: infliximab; MTX: methotrexate

Results: These four BS patients were all Chinese Han, and three of them were women. The mean age of disease onset was 4±3.5 years, and the mean time of diagnosis delay was 19±11 years. All of the 4 patients received IFX plus methotrexate, and had achieved clinical remission of skin lesions and polyarthritis rapidly, and normalization of ESR and CRP, improvements in inflammatory cytokines, patient visual analogue scale, physician global assessment and SF-36 as well, at the first follow-up of 6 months. The disease relapsed in two patients after they lengthened the interval of IFX due to the financial limitation and discontinued methotrexate because of the side effects. According to the 38 English-language publications, 62 patients with BS were presented who underwent TNFα inhibitors therapy, including IFX used in 31, adalimumab in 24 and etanercept in 7. IFX was well tolerated in 27 patients, while 2 still had uveitis, and the other 2 experienced an adverse drug reaction to IFX infusion. Adalimumab was useful in 21 BS

patients, although the other 3 didn't get well controlled. Five BS patients who were given etanercept yielded good responses, but 2 discontinued because of etanercept-induced myelopathy or an exacerbation of arthritis.

Conclusion: Early recognition and effective treatment of BS is very important to avoid the irreversible organ damage such as loss of vision, joint deformities. TNFα inhibitors including IFX may be a promising approach for BS patients who have unsatisfactory response to corticosteroids and traditional DMARDs. Due to the sample limitation of our study, more clinical trials are required.

Disclosure: J. Chen, None; **Y. Luo**, None; **M. Zhao**, None; **D. Wu**, None; **Y. Yang**, None; **W. Zhang**, None; **M. Shen**, None.

Abstract Number: 1270

Effectiveness and Safety of Off-label Use of Tocilizumab in Refractory Autoimmune Diseases: A Multicenter Study

Martin Michaud,[1] Thomas Sene,[2] Pascal Chazerain,[2] Geoffrey Urbanski,[3] Frederique Retornaz,[4] Boris Bienvenu,[5] Laurent Chiche,[4] Florian Catros,[6] Laurent Sailler,[7] Laurent Alric,[8] Jean Thomas Giraud,[9] Léo Caudrelier,[10] Slim Lassoued,[10] Sophie Ancellin,[6] Olivier Lidove,[2] and Francis Gaches[6], [1]Joseph Ducuing Hospital, Toulouse, France, [2]Hôpital Croix Saint Simon, Paris, France, [3]CHU Angers, Angers, France, [4]Hôpital Européen, Marseille, France, [5]Hôpital Saint Joseph, Marseille, France, [6]Hôpital Joseph Ducuing, Toulouse, France, [7]University Hospital of Toulouse, Toulouse, France, [8]CHU Toulouse, Toulouse, France, [9]Hôpital de Tarbes, Tarbes, France, [10]Hôpital de Cahors, Cahors, France

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: There is increasing evidence of Tocilizumab (TCZ) efficacy in refractory auto-immune diseases. The present study aimed at evaluating the real-world experience of using TCZ in patients with refractory autoimmune diseases.

Methods: This is a retrospective, descriptive and multicenter study from 9 departments of Internal Medicine. Demographic, clinical and therapeutic data were collected. Glucocorticoid sparing effect was evaluated with Fisher's exact test, with statistical significance set at 0.05.

Results: Fifty five patients were included (20 men, 35 women). Mean age was 56 ± 16.7 years (range 23 - 80).

TCZ was used in:

- 15 connective tissue diseases (27%): relapsing polychondritis (n=6), systemic sclerosis (n=5), anti-synthetase syndrome (n=1), and unclassified connective tissue disease (n=3).
- 10 vasculitis (18%): Takayasu arteritis (n=7), Cogan disease (n=1), panarteritis nodosa (n=1), unclassified vasculitis (n=1).
- 12 ophthalmologic conditions (21.8%): non infectious posterior uveitis (n=10), sympathetic ophtalmia (n=1), Basedow orbitopathy (n=1).
- 8 adult-onset Still's diseases (AOSD) (14.5%).
- 7 cases of polymyalgia rheumatica (12.7%)
- 3 miscellaneous diseases (5.5%): idiopathic AA amyloidosis, multicentric non HHV8 Castelmann disease, Erdheim

Chester disease (1 case each).

Mean disease duration of the disease at TCZ initiation was 7 ± 6.3 years. In 48 cases (87%) TCZ was administered for refractory diseases to corticosteroids and/or immunosuppressive drugs. Previous therapies included corticosteroids (83%), methotrexate (66%), TNF inhibitor drug (44%), azathioprine (20.8%), mycophenolate (12%), cyclophosphamide (8%), rituximab (10%), hydroxychloroquine (6%), anakinra in 2 patients and interferon, dapsone, etoposide, leflunomide, abatacept, salazopyrin or intra-venous immunoglobulin in 1 patient each.

TCZ was associated with methotrexate in 3 cases (5.4%) and route of TCZ administration was mainly intravenous (96%).

At the end of the follow up, 43 patients (78%) were still using TCZ, with a mean follow up period of 21.7 ± 22.6 months (range 1-90). Daily corticosteroid use significantly decrease from 15.3 ± 15.5 mg to 4.47 ± 4.9 mg ($p< 0.005$).

A complete response was observed in 5 patients (71%) with polymyalgia rheumatica, in 6 patients (75%) with AOSD, in 4 patients (66%) with relapsing polychondritis, in 7 patients (70%) with uveitis, in six patients (85%) with Takayasu arteritis, in 3 patients (75%) with unclassified connective tissue disease and in 3 patients (60%) with systemic sclerosis.

TCZ was withdrawn in 12 patients (2%), because of treatment failure in 3 patients, loss of efficacy in 2 patients or side effect in 7 patients. Side effects occured in 15 patients. They were infection (2 pneumonias, zona, sinus infection), pruritus (n=2), urticaria (n=1), dyslipidemia (n=1), high blood pressure (n=2), infusion-related reaction (n=1), bullous dermatitis (n=1), acute renal failure (n=1), angioedema (n=1), mouth ulcers (n=1).

Conclusion: In conclusion, TCZ is used off-label in daily practice to treat various refractory autoimmune diseases with a good short-term efficacy and tolerance.

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Abstract Number: 1271

Adult-Onset Still's Disease Prognosis Score: Clinical Patterns, Complications and Biologic Treatment

Ivette Casafont-Solé,[1] Susana Holgado,[1] Javier Narváez,[2] Maribel Mora,[3] Josep Roca,[4] Anahy Brandy-Garcia,[1] Lourdes Mateo,[1] Melania Martínez-Morillo,[1] Laia Gifre,[1] Maria Aparicio-Espinar,[1] Águeda Prior-Español,[1] Anne Riveros-Frutos,[1] Clara Sangüesa,[1] Jordi Camins-Fàbregas,[1] Annika Nack,[1] Joan Miquel Nolla,[3] and Alejandro Olivé-Marqués[4], [1]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [2]Rheumatology Department, Hospital Universitario de Bellvitge, Barcelona, Spain, Barcelona, Catalonia, Spain, [3]Hospital Universitari de Bellvitge, Hospitalet de Llobregat, Spain, [4]Hospital Universitari Germans Trias i Pujol, Badalona, Catalonia, Spain

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

BASAL CHARACTERISTICS (n=64)			
	n (%)		n (%)
Sex (women)	36 (59,4)	Myalgia	22 (34,3)
Fever	62 (96,8)	Abdominal pain	9 (14,1)
Arthralgia	61 (95,3)	Hepatomegaly	12 (18,7)
Arthritis	50 (78,1)	Pericarditis	8 (12,5)
Odynophagia	51 (82,3)	Pleuritis	11 (17,2)
Rash	55 (85,9)	Lung involvement	2 (3,1)
Lymphadenopathies	32 (50,0)	ANA positive	3 (4,7)
Weight lose	16 (25,0)	FR positive	3 (4,7)
Splenomegaly	17 (26,6)	Biologic treatment	24 (37,5)
Clinical course		Systemic score	
Monocyclic	27 (42,2)	<7	50 (78,1)
Polycyclic	18 (28,1)	≥7	14 (21,9)
Chronic	19 (29,7)		

COMPLICATIONS	TOTAL (%) N=64	SS < 7 N=50	SS ≥ 7 N=14	p-Value
Macrophage activation syndrome	5 (7,8)	2	3	<0.05
Myocarditis	1 (1,6)	0	1	0.500
Secondary amyloidosis	2 (3,1)	0	2	0.060
Renal involvement	3 (4,7)	0	3	<0.05
All-cause mortality	5 (7,8)	3	2	0.970

BIOLOGIC TREATMENT	TOTAL (%) N=64	SS<7 N=50	SS ≥ 7 N=14	p-Value	
Si	24 (37,5)	14	10	<0.05	OR 6.4 CI 95% (1.8-26.7) p=0.005
No	40 (62,5)	36	4		

Background/Purpose: Adult-onset Still's disease (AOSD) is a low prevalent disease with an unpredictable clinical course and variable prognosis. Sometimes, it requires biologic treatment in early phases of the pathology. A prognosis score has been described, which has never been applied in a Spanish case series.

Methods: Retrospective analysis realized in two University Hospitals. Clinical, laboratory, AOSD-related complications data, administered biologic treatments and number of deaths (AOSD related or not) were recorded. SS

was applied at the onset of the disease development, assigning a point to each of the following 12 variables: fever, exanthema, pleuritis, pneumonitis, pericarditis, alteration of liver tests or hepatomegaly, splenomegaly, lymphadenopathy, odynophagia, leukocytosis > 15,000/mm^3, myalgia and abdominal pain. A ≥ 7 score has been validated on other populations as the one which identifies the patients with high risk of complication. The relationship between prognosis score value and the next parameters was determined: clinical course, complications, biologic treatments administered and AOSD-related mortality. Sensitivity and Specificity of the SS value as a predictor of biologic treatment necessity was determined.

Results: Data from 64 patients was analyzed. Each patient was characterized for the presence of AOSD-related complications such as macrophage activation syndrome (MAS), myocarditis, renal involvement (tubulointerstitial nephritis, acute renal failure), secondary amyloidosis and AOSD-related death and all-causes death. After applying the SS, values of < 7 were obtained in 50 patients (78,13%) and of ≥7 in 14 patients (21,87%). MAS and renal involvement were significantly related with a score of ≥7 (Table 1). Myocarditis and secondary amyloidosis were not significantly associated with a high SS value. Even so, analyzing each case individually, it was found that they presented a score of ≥7, except for lung involvement. Biologic treatment requirement along the disease course was related to a score of ≥7 (OR: 6.4, IC95% [1.8%-26.7%]). Instead, it was not related to the different clinical patterns or the all-cause deaths. Related to sensitivity and specificity of the SS as a predictor of biologic treatment requirement, we observed that a value of ≥7 was the one which the highest area under the curve in the ROC curve (AUC = 0,629) in our population, with a sensitivity of 41,7% and specificity of 90%.

Conclusion: The prognosis score described by *Pouchot et al* could be useful to identify those patients with high risk of developing clinical complications and those who will need biologic treatment along the course of their disease. If a patient has a >7 score, the development of a macrophage activation syndrome or renal complications may be considered. Furthermore, the necessity of biologic treatment should be considered (Sensitivity: 41,7%, Specificity: 90%). It is necessary a higher number of patients to determine if the score could be useful to estimate the death risk related to AOSD complications.

Disclosure: I. Casafont-Solé, None; **S. Holgado**, None; **J. Narváez**, None; **M. Mora**, None; **J. Roca**, None; **A. Brandy-Garcia**, None; **L. Mateo**, None; **M. Martínez-Morillo**, None; **L. Gifre**, None; **M. Aparicio-Espinar**, None; **????. Prior-Español**, None; **A. Riveros-Frutos**, None; **C. Sangüesa**, None; **J. Camins-Fàbregas**, None; **A. Nack**, None; **J. Nolla**, None; **A. Olivé-Marqués**, None.

Abstract Number: 1272

Biological Therapy in Non Ischaemic Optic Neuritis Associated to Immune-mediated Inflammatory Diseases: Multicenter Study

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Case	Sex/Age (years)	Underlying disease	Laterality	Immunosuppressive drugs before biological therapy	Biological therapy
1	Man/29	Idiopathic	Right	AZA	TCZ
2	Man/26	Idiopathic	Bilateral	AZA	TCZ
3	Man/21	Idiopathic	Bilateral	MTX, AZA	ADA
4	Woman/25	Behçet´s disease	Right	MTX, CyA	ADA
5	Woman/39	Behçet´s disease	Right	MTX, MMF	IFX
6	Woman/14	Neuroretinitis	Bilateral	MTX	ADA
7	Man/56	SLE	-	Hydroxychloroquine, MMF, CFM	RTX
8	Woman/43	Neuromyelitis optica	Bilateral	AZA	RTX
9	Man/43	Relapsing polychondritis	Bilateral	MTX, CFM	IFX, TCZ
10	Woman/24	Pars planitis	Bilateral	MTX, AZA	ADA
11	Woman/13	Idiopathic	Bilateral	MTX	ADA
12	Woman/25	Idiopathic	Bilateral	MTX	IFX, TCZ

ADA: adalimumab, AZA: azathioprine, CFM: cyclophosphamide, CyA: cyclosporine A, HCQ: hydroxychloroquine, IFX: infliximab, MMF: mycophenolate, MTX: methotrexate, RTX: rituximab, SLE: systemic lupus erythematosus, TCZ: tocilizumab

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies
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Background/Purpose: Non ischaemic optic neuritis (NION) is a severe inflammation of the optic nerve that may lead to blindness. It can be primary or associated to immune mediated inflammatory diseases (IMIDs). The treatment of the NION is based on systemic corticosteroids and conventional immunosuppressive drugs. Our aim was to assess the efficacy of the biological treatment in refractory NION to conventional treatment.

Methods: Multicenter study of 12 patients diagnosed with NION refractory to systemic corticosteroids and at least one conventional immunosuppressive drug. The main outcomes were visual acuity (VA) and optical coherence tomography (OCT) of the optic nerve and the ganglionar cells. Comparisons were made between baseline and the 1st week, 1st and 6th month and 1st year. (STATISTICA, StatSoft Inc. Tulsa, Oklahoma, USA).

Results: We studied 12 patients (19 affected eyes) (5 men/ 7 women); mean age of 29.8 ±12.9 years. The underlying diseases were systemic lupus erythematosus (n=1), neuromyelitis optica (n=1), neuroretinitis (n=1), relapsing polychondritis (n=1), pars planitis (n=1), Behçet´s disease (n=2) and idiopathic (n=5). Before biological treatment and besides oral corticosteroids, patients had received intravenous (IV) methylprednisolone boluses (n=9), cyclosporine A (n=1), cyclophosphamide (n=2), mycophenolate (n=2), hydroxychloroquine (n=1), methotrexate (n=8) and azathioprine (n=5). Biological treatment was bases on rituximab (n=2) (2 IV, doses of 1 g/every 2 weeks and every 6 moths), adalimumab (n=5) (40 mg/1-2 week), tocilizumab (n=4) (8 mg/kg/2-4 weeks) and infliximab (n=3) (5 mg /kg at 0, 2 and 6 week and then every 8 weeks). The characteristics of the 12 patients are shown in the TABLE.

After biological treatment we observed an improvement in the ocular parameters: VA [0.66±0.32 to 0.84±0.29; p= 0.03], OCT of the optic nerve [123.20±58.28 to 190.54±175.38; p= 0.11], and OCT of the ganglionar cells [369.55±137.37 to 270.67±23.21; p= 0.03] at one year. After a mean follow-up of 29.09 ±19.23 months, there were no severe adverse effects.

Conclusion: Biologic therapy in NION idiopathic or associated to IMIDs, refractory to conventional treatment, seems to be effective.

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Abstract Number: 1273

Certolizumab Therapy in Patients with Uveitis During Pregnancy: Multicenter Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease Poster II: Autoinflammation Related Diseases & Therapies

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Uveitis often occur in women who are in their reproductive years. The management of uveitis during pregnancy is a challenge, making the physician to re-evaluate the patient's current therapy and offer alternative options with the lowest risk to the patient and fetus. Certolizumab pegol (CZP) is a PEGylated Fc-free anti-TNF therapy that differs from others anti-TNF because it does no bind the neonatal Fc receptor (FcRn). Thus,

TABLE 1

Case	Age (years)	Underlying disease	Uveitis pattern	Laterality	Immunosuppressive drugs before CZP	Combined treatment during pregnancy
1	34	SpA	Anterior	Unilateral	MTX, AZA, ADA	Yes (AZA)
2	37	SpA	Anterior	Bilateral	MTX, AZA, IFX, ADA, GOLI	No
3	40	SpA	Anterior	Bilateral	AZA, ADA	Yes (AZA)
4	38	SpA	Anterior	Unilateral	CyA, ETN, ADA, IFX, GOLI	No
5	23	Vogt-Koyanagi-Harada	Panuveitis	Bilateral	AZA	Yes (AZA)
6	33	Idiopathic	Anterior	Unilateral	MTX, AZA, ADA, ETN	No
7	35	Rheumatoid Arthritis	Anterior	Unilateral	MTX	Yes (AZA)
8	35	SpA	Anterior	Unilateral	SSZ, ADA	Yes (SSZ)

ADA: adalimumab, AZA: azathioprine, CyA: cyclosporine A, ETN: etanercept, GOLI: golimumab, IFX: infliximab, MTX: methotrexate, SpA: spondyloarthritis, SSZ: sulfasalazine.

TABLE 2

	Gestational age	Multiple gestation	Preconception CZP exposure	Trimester(s) of CZP exposure	Labor complications	Maternal infections	Neonatal infections (< 6 months after birth)	Congenital malformations	Lactation
1	Full term	no	yes	1,2,3	no	No	No	no	no
2	Full term	no	no	2,3	no	No	No	no	no
3	Full term	yes (dichorionic)	no	2,3	no	No	No	no	no
4	Full term	yes (dichorionic)	no	2,3	no	No	No	no	no
5	Full term	no	yes	1,2,3	no	No	No	no	no
6	Full term	no	no	2,3	no	No	No	no	yes
7	Full term	no	no	2,3	no	yes (urinary tract)	No	no	yes
8	Full term	no	yes	1,2,3	no	No	No	no	yes
9	Full term	no	yes	1,2,3	no	No	No	no	no

CZP does not undergo across the placenta conferring a more secure profile. However, clinical data about the use of CZP in patients with uveitis during pregnancy are absence. Our aims were: a) to assess the evolution of uveitis in pregnant patients under treatment with CZP and b) to provide information on the pregnancy outcomes of women and neonates exposed to CZP.

Methods: National Multicenter study of 8 women with uveitis who received CZP during pregnancy and their 9 neonates who were exposed to CZP. The main visual outcomes were visual acuity (VA) and anterior chamber (AC) cells. We also assessed the presence of complications during pregnancy and labor, maternal and neonatal infections and malformations. Comparisons were made between baseline and the 1st week, 1st and 6th month and 1st year. (STATISTICA, StatSoft Inc. Tulsa, Oklahoma, USA).

Results: We studied 8 women (11 affected eyes); mean age of 34.3 ± 5.1 years. The underlying diseases were spondyloarthritis (n=5), Vogt-Koyanagi-Harada (n=1), rheumatoid arthritis (n=1) and idiopathic (n=1). Before CZP treatment and besides oral corticosteroids, patients had received methotrexate (n=4), azathioprine (n=5), adalimumab (n=5), infliximab (n=2), golimumab (n=2), etanercept (n=2), sulfasalazine (n=1) and cyclosporine A (n=1). The characteristics of the 8 patients are shown in **TABLE 1**. Seven out of 8 patients had anterior uveitis while the remaining patient had panuveitis diagnosis. During CZP treatment we observed an improvement in the mean of VA [0.6±0.27 to 0.72±0.29; p= 0.14] and the mean of AC cells [2.25±1.28 to 0.33±0.08; p= 0.03] after 6 months of treatment. Pregnancy and neonatal outcomes are shown in **TABLE 2**. In half of the patients CZP was initiated before pregnancy. In the remaining patients CZP was initiated during the first trimester. No pregnancy nor labor complications were reported (preeclampsia, premature rupture of membranes, miscarriages or pre-term births). There was one case of multiple gestation (dichorionic). Cesarean delivery was reported in two patients. All neonates were healthy newborns with a mean birth weight of 3080±560 grams and a mean birth length of 50.9±2.8 cm. Fetal pH and APGAR score was normal in all of them. Three neonates received maternal lactation. In regard with infections, only one woman presented a mild urinary tract infection during pregnancy. No infections nor malformations were found in neonates after a follow-up of 6 months.

Conclusion: CZP seems to be effective and safe in patients with uveitis during pregnancy.

Disclosure: D. Prieto- Pena, None; **V. Calvo Río**, None; **M. Calderón-Goercke**, None; **O. Maíz Alonso**, None; **J. Jimenez-Aberasturi**, None; **R. Veroz**, None; **M. Blanco**, None; **J. Santos**, None; **F. Navarro**, None; **A. Gallego**, None; **R. Demetrio**, None; **V. Martínez Taboada**, None; **M. González-Gay**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 2, 5, EliLilly, 2, 5, Jansen, 2, Janssen, 2, MSD, 2, 5, 8, Novartis, 2, 5, Pfizer, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, Sobi, 5, 8; **R. Blanco**, None.

Abstract Number: 1274

New Aspects of Clinical and Immunological Characteristics in Patients with Anti-KS Antibody

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Muscle Biology, Myositis & Myopathies Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-KS antibody, an anti-aminoacyl tRNA synthetase (ARS) antibody, is found mainly in patients with interstitial lung disease (ILD) accompanied by polymyositis/dermatomyositis (PM/DM). Although anti-KS antibody has a stronger association with ILD compared with PM/DM, the clinical characteristics of anti-KS antibody have not been examined in detail. The aim of this study was to clarify the clinical and immunological features of patients with anti-KS antibody.

Methods: PM/DM or ILD patients who visited Tokai University Hospital between 2010 and 2018 were screened. Autoantibodies were identified by immunoprecipitation assays and all clinical and immunological data were collected retrospectively. ILD was diagnosed based on the findings of computed tomography. The clinical and immunological features of anti-KS positive patients were assessed. Comparisons between anti-KS positive patients and other anti-ARS positive patients were examined. Statistical analyses were performed using the Fisher's exact test.

Results: Fifteen anti-KS positive patients were identified. Ten were female and 5 were male, with an average age of 62.5 years (range, 40-80 years). Final diagnoses were 6 patients with ILD alone, 4 with clinically amyopathic DM (CADM) and ILD, 3 with Sjögren's Syndrome (SjS) and ILD, one each with rheumatoid arthritis (RA) and ILD, or CADM/SjS overlap and ILD. Although various diagnoses were determined for these patients, all patients had ILD with chronic onset and a chronic clinical course. Five patients (33%) presented with dyspnea as an initial symptom. On high-resolution computed tomography analysis, 10 (67%) of 15 patients revealed radiographic features of non-specific interstitial pneumonia (NSIP) and 4 (27%) had a usual interstitial pneumonia (UIP) pattern and one (7%) had an organizing pneumonia (OP) pattern. As for skin manifestations, 9 (60%) had mechanic's hands, 4 (27%) had Gottron's sign and one (7%) each had the heliotrope rash or palmar papules. Interestingly, all anti-KS positive showed no clinical muscle weakness or serum creatine kinase elevation. Moreover, seven of 15 patients (47%) had sicca syndrome and were positive for anti-SSA and/or anti-SSB antibodies. There was a significantly high frequency of sicca syndrome in anti-KS positive patients compared with anti-Jo-1 positive patients (47% vs. 12%, P=0.02).

Conclusion: These results suggest that anti-KS antibody positive patients might form a distinguishable subset that is closely associated with sicca syndrome and CADM as well as chronic type ILD.

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Abstract Number: 1275

Spectrum of Organ Involvement in Idiopathic Inflammatory Myopathies, Frequency of Comorbidities, and Relationship to Anti-SSA/SSB Positivity

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SESSION INFORMATION
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Session Title: Muscle Biology, Myositis & Myopathies Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are chronic autoimmune diseases with systemic features and multiple comorbidities. Of the myositis associated antibodies seen in this population, anti-SSA/SSB are most frequently reported. However, limited literature has been published on their utility in clinical risk assessment.

Aim: To describe the spectrum of organ involvement and frequency of comorbidities in IIM patients and relation to anti-SSA/SSB positivity.

Table 1: Comparison of demographics in anti-SSA/SSB positive and negative groups

	SSA/SSB positive (n=34)	SSA/SSB negative (n=65)
Age (yrs)	55	53.5
Sex	79% female 21% male	75% female 25% male
Race	32% Caucasian 32% African-American 18% Asian or Pacific Islander 3% American Indian or Alaskan Native 15% Unknown	48% Caucasian 32% African-American 6% Asian or Pacific Islander 0% American Indian or Alaskan Native 14% Unknown
Myositis subset	69% DM 20% PM 3% DM and IMNM 8% PM and IMNM	53% DM 35% PM 3% DM and IMNM 6% PM and IMNM 3% PM and UCTD
Antibody Subtypes	26% Anti-Jo-1 Ab 0% Anti-PL-7 Ab 3% Anti-PL-12 Ab 0% Anti-EJ Ab 0% Anti-OJ Ab 9% Anti-MDA5 Ab 3% Anti-PM/Scl-100 Ab 15% Anti-RNP Ab	8% Anti-Jo-1 Ab 2% Anti-PL-7 Ab 0% Anti-PL-12 Ab 3% Anti-EJ Ab 0% Anti-OJ Ab 3% Anti-MDA5 Ab 2% Anti-PM/Scl-100 Ab 9% Anti-RNP Ab

DM = dermatomyositis, PM = polymyositis IMNM= immune-mediated necrotizing myopathy , UCTD= undifferentiated connective tissue disease

Methods: We queried the Northwell Myositis Center database for patients with IIM between 1/1/2007 to 4/6/2018. Patients were selected if they met 2017 European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) classification criteria for IIM and had anti-SSA/SSB data available. Anti-SSA/SSB was measured using a commercially available fluorescent bead-based immunoassay. Anti-SSA and SSB were combined and analyzed as a single group because anti-SSB was only found in association with anti-SSA in this cohort. The frequency of myositis specific antibodies, organ involvement and comorbidities was collected. Statistical analyses included Chi-square, Fisher's Exact test, and Wilcoxon Rank Sum test to determine statistical differences in group distributions and McNemar's test was performed to compare groups.

Results: Ninety-nine (99) patients were included in this analysis. The SSA/SSB positive (n=34) and negative (n=65) groups had similar distributions for age, gender, and race (Table 1). Despite the presence of muscle weakness during their clinical course, the majority (82/99) did not show evidence of muscle atrophy on magnetic resonance imaging (MRI). There was no difference in the prevalence of calcinosis, cardiac, or gastrointestinal involvement between groups. As anticipated, the frequency of ILD was significantly higher in the anti-SSA/SSB positive cohort (56% of SSA/SSB positive in comparison to 25% of SSA/SSB negative, p-value= 0.0084). The overall frequency of diabetes in our cohort was 42%, four times higher than reported for general population. The frequency of hypertension in our cohort was also as high (40%). There was no significant difference in the rate of diabetes, hypertension, or cardiovascular events between SSA/SSB positive and negative groups. There was 4% (4/99) myocardial infarctions and no cerebrovascular accidents. Venous thromboembolic events (VTE) were observed in 10% of patients with the majority (83%) occurring within three years of diagnosis. Presence of anti-SSA/SSB did not confer additional risk for VTE. Finally, SSA/SSB positivity was not associated with malignancies in our cohort. Neoplasms occurred in 14 anti-SSA/SSB negative patients (compared with 2 anti-SSA/SSB positive), though more than 18 years prior IIM diagnosis and not likely associated with the autoimmune disease.

Conclusion: Patients with IIM had high frequencies of diabetes, hypertension and VTE which was independent of anti-SSA/SSB status. We observed a statistically significant increase in prevalence of ILD in the anti-SSA/SSB positive IIM cohort patients suggesting that the presence anti-SSA/SSB antibodies is a harbinger of pulmonary manifestations in IIM.

Disclosure: A. Valle, None; **G. Marder**, GSK, 2; **M. Barilla-Labarca**, None; **S. Narain**, Exagen, 2.

Abstract Number: 1276

Myositis Specific Antibodies and Clinical Features in Patients from Argentina

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SESSION INFORMATION
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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To know the frequency of myositis specific antibodies (MSAs) and myositis associated antibodies(MAAs) and their relation with clinical features in patients with idiopathic inflammatory myopathy(IIM) from a Registry of Argentina.

Methods: Adults with IIM were enrolled in a retrospective way.Demographics,clinical and laboratory features were registered.Diagnosis of interstitial lung disease (ILD) was based on physician review of chest-x-ray, CT and/or pulmonary function tests.ANA were done in 291 patients, anti-Ro in 283, anti-Pm-Scl in 205,anti-Jo-1 in 263. MSAs against PL-12, PL-7, SRP and Mi-2 were done in 190 and anti: EJ, OJ, TIF1ϒ, MDA5, SAE, NXP2,Ku and Ro 52 were studied in 83 patients. These antibodies were detected by Immunoblot and ANA by IFI. Statistics: descriptive and Chi-squared.Stata v.11

Results: Were included 304 patients, 217(71%) women, mean age at diagnosis 46±15 years. Caucasian 42%, mestizos 37% and amerindios 8%. DM was described in 43%, PM 31,5%,IBM 1,6%, antisynthetase syndrome(ASS) in 18%, CADM 3,6%,IMNM 1,6% and overlap myositis in 21,7%. Arthritis was present in 32%, RP 34% and ILD in 26,6%.

MAAs(±): ANA 62,5%, Ro 19% and Pm-Scl: 4,8%.

MSAs (±): Jo-1 16%, Mi-2 11%, SRP and Pl-7 2,6% each and Pl-12:1,5%. Other MSAs were studied in 83 patients: anti-MDA5 13,2%, TIF1ϒ 8,4%, NXP2 3,6%,anti-SAE1,2%.Two patients had OJ and EJ.

Anti-Jo-1(+) was found in 37/41(90%) PM patients (p< 0,000), arthritis in 56% vs 31% in Jo-1(-) (p=0,005), ILD in 73% vs 15% Jo-1(-) (p< 0,000).

Anti-Mi-2 was found in 20/21 DM patients, 12 caucasians and 6 mestizos, none had ILD or anti Ro+ when were compared con Mi-2(-) 0% vs 27,3%(p=0,002) and 0% vs 26% (p=0,008),respectively, all Mi-2+ had increase CK value (100%) vs 78% Mi-2(-) p < 0,000.

The presence of MDA5 was associated with arthritis 72% vs 29%(p=0,01), ILD 63,6% vs 19,4% (p=0,005) and normal CK values 91% vs 16,6%(p< 0,000) when it was compared with patients without the antiboby. Anti Tif1 was present in 7/83 patients (8.4%),5 had DM and 2 had CADM, 1 patient had cancer.

Conclusion: Anti-Jo-1,anti-MDA5 and anti- Mi-2 were the most frequent MSAs found in our population, followed by anti- TIF1γ.

Anti-Mi-2 was present in DM while anti-Jo-1 was frequent in antisynthetasa syndrome with ILD and mainly in PM patients.

Anti-MDA5 was seen in DM with normal CK and also related to ILD and arthritis.

All patients anti-Tif1γ positive had DM and only one had cancer.

There are differences in the frequency of MSAs probably related with ethnic background or geography but the clinical phenotypes remains similar.

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Abstract Number: 1277

Damage and Comorbidities in a Cohort of Patients with Idiopathic Inflammatory Myopathy

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SESSION INFORMATION
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Session Title: Muscle Biology, Myositis & Myopathies Poster II
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Background/Purpose: Idiopathic Inflammatory Myopathies (IIM) remain a major clinical challenge worldwide. The precise aetiopathogenesis of this chronic and disabling disorder remains elusive which precludes the development of novel and effective therapeutic strategies. The most visible consequence of this lack of effective therapies is the damage caused to these patients with the consequent decrease in quality of life, high morbidity and mortality. The complexity of managing these diseases is even higher because of the vast comorbidities affecting these patients.

Methods: Retrospective review of the cohort of patients followed in a dedicated unit of a tertiary hospital, with special incidence in damage and comorbidities, between January 2008 and December 2018. Damage was assessed by Myositis Damage Index (MDI) score. Comorbidities were scored according to Charlson Comorbidity Index in the last year of the study (2018).

Results: Ninety four patients were included, 79 women and 15 men, with a medium age at diagnosis of 46 years-old and a medium follow-up of 12 years. Paraneoplastic myopathies accounted for 20.2% of the cases and overlap myopathies were present in 19.1%. A definitive diagnosis was obtained in 37.2% of patients, according to Bohan and Peter criteria and 42.6% according to ACR/EULAR classification criteria. Only 8.5% of patients were documented in sustained remission without drugs. Damage scores were calculated as a whole and individually for the 11 dimensions of MDI score. Only 13.8% of the patients presented with MDI score of zero, meaning that more than 86% presented with some kind of damage. The majority of this was cardiovascular damage, along with its end-organ consequenc-

es, and psichiatric. Mortality occurred in 17% of patients with a medium age of 65 years-old and the most common cause was malignancy. Average MDI extent was 5.56 (range: 0-38) but average MDI severity was 87.6 (range: 0-110). Comorbidities were present in 90.5% of patients and essentially overlap with damage as they are mainly its consequence and so the most common are also cardiovascular risk and secondary organic diseases. Average Charlson Comorbidity Index was 4.6 predicting an average survival at 10 years of 52%. Of note, almost 10% of patients present with immunodeficiency unrelated to immunosuppressive therapy, mainly humoral.

Conclusion: Damage is high in IIM patients and is mainly cardiovascular, as opposed to muscle/ cutaneous damage. This appears essentially the result of the therapy used to control the disease, particularly prolonged systemic steroids, and persistent inflammation in refractory patients. A better knowledge of the disease physiopathology is essential for an improvement of its therapeutic strategies, particularly aiming steroid-free regimens.

Disclosure: A. Campar, None; **C. Vasconcelos**, None.

Abstract Number: 1278

Inpatient Epidemiology of Dermatomyositis and Polymyositis in the United States

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Session Title: Muscle Biology, Myositis & Myopathies Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Dermatomyositis (DM) and polymyositis (PM), collectively known as idiopathic inflammatory myositis (IIM), are autoimmune disorders characterized by inflammation of skeletal muscle, especially in the proximal group. Data on inpatient epidemiology, resource utilization, and healthcare expenditures of IIM are not well described. The aim of this study was to explore those characteristics using a large national inpatient database.

Methods: This retrospective cohort study used the data from the National Inpatient Sample (NIS), the largest public inpatient database in the US, in the year 2005-2014. Data for more than seven million individual hospitalization across all-payers from over 4,000 non-federal acute care hospitals across 40 states are recorded annually in the NIS database. All patients with ICD9-CM diagnostic codes for DM or PM were included. Patients with inclusion body myositis were excluded. The primary outcome was determining the inpatient prevalence of IIM. Secondary outcomes included determining inpatient mortality, morbidity, most common discharge diagnoses, resource utilization, hospital length of stay (LOS), and inflation-adjusted total hospital costs and charges. Multivariate regression analyses were used to adjust for age, gender, Charlson Comorbidity Index, income in patient zip code, hospital region, location, size, and teaching status.

Results: A total of 160,528 admissions of patients with a diagnosis of DM/PM occurred in the study period. The mean age was 58.0 years and 68.7% were female. For the primary outcome, the inpatient prevalence of DM/PM was 41.9 cases per 100,000 discharges. The most common reasons for hospitalization were DM/PM itself, pneumonia, sepsis, AKI, and urinary tract infection. Patients with DM/PM displayed significantly increased odds of inpatient all-cause mortality compared to patients admitted for all other causes. Patients with DM/PM displayed significantly high-

Table 1 – Adjusted odds ratios, means and additional adjusted means in patients with IIM compared to patients admitted with other medical conditions

Variable	Odds Ratio	95% Confidence Interval	p-value
Mortality	2.22	2.10-2.35	<0.01
Shock	2.33	2.18-2.50	<0.01
ICU	1.94	1.84-2.05	<0.01
AKI	1.12	1.08-1.17	<0.01
Multi-organ failure	1.83	1.77-1.90	<0.01
Arteriography	1.15	1.06-1.25	<0.01
CT Scan	1.90	1.50-2.41	<0.01
MRI	1.68	1.35-2.09	<0.01
Mean Costs/Charges/LOS			
Costs ($USD)	$16,817		
Charges ($USD)	$55,774		
Length of Stay (days)	7.0		
Variable			
Additional Adjusted Costs	$4,217	3869-4563	<0.01
Additional Adjusted Charges	$13,531	12184-14879	<0.01
Additional Adjusted LOS (days)	1.7	1.6-1.8	<0.01

er morbidity odds of shock, ICU stay, AKI, and multiorgan failure when compared to patients admitted for all other reasons. Patients with DM/PM were also found to have increased odds of utilizing special investigations, including CT, MRI, and arteriography. Patients with associated diagnosis of DM/PM displayed higher hospital costs, charges and LOS compared to patients with no DM/PM (Table 1).

Conclusion: The inpatient prevalence of DM/PM was higher than what would be expected from the overall incidence. Hospitalizations of these patients were associated with a significantly higher morbidity and mortality. The mean total hospital costs, charges, and LOS for patients admitted with DM/PM were higher than patients without DM/PM.

Disclosure: P. Ungprasert, None; **W. Cheungpasitporn**, None; **C. Thongprayoon**, None; **K. Wijarnpreecha**, None; **P. Kroner**, None.

Abstract Number: 1279

Response Rate and Sustained Remission in Idiopathic Inflammatory Myopathies Receiving Conventional Immunosuppressive Stepwise Management

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Muscle Biology, Myositis & Myopathies Poster II
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Background/Purpose: Information regarding response rate and sustained remission in patients with idiopathic inflammatory myopathies (IIM), polymyositis (PM), dermatomyositis (DM), in Hispanics with non-biological treatment is scarce. We performed a study to estimate the response rates and sustained remission during the disease course of patients with IIM treated with conventional immunosuppressive agents.

Methods: A retrospective longitudinal study from medical records of patients with MII at a single rheumatology reference center in Mexico was performed. Medical records were reviewed to determine clinical presentation, serum creatine kinase (CK) levels, initial treatment and outcome measures such as the muscle strength assessed by the manual muscle testing of 8 muscle groups (MMT8), Health Assessment Questionnaire Disability index (HAQ-Di) during follow-up. The primary outcome was time to achieve sustained remission, defined as no evidence of active myositis for ≥ 6 months while not receiving glucocorticoids and the presence of all of the following: 1) improvement of muscle strength; 2) normal muscle enzyme levels; 3) tapering immunosuppressive agents or withdrawal. Interval between first remission and first relapse was recorded. Additionally, status of remission was reported at the end of follow up for each patient.

Results: Data from 76 patients, which 81.4% had DM and 14.6% had PM; female 8.26%, mean age of 39 (SD ± 12.6) years; Interval between symptom onset and first assessment showed a median of 185 (RIQ 64 - 518) days; All patients received a standardized stepwise treatment with glucocorticoids and either a single or combined therapy with methotrexate (MTX) or azathioprine (AZA) until remission was achieved; Remission was observed in 68.42%, with a median time required for achieving remission of 22.2 (RIQ 11 - 46) months. From the sub group of patients achieving remission 78.85% had sustained remission and 41.18% showed relapses with a median of relapse-free survival time of 15.16 (RIQ 6 - 32) months during follow up. The median follow-up period for the entire cohort was 38 (RIQ 21 - 108) months; During final visit, the proportion of subjects in remission were 55.3%, normal muscle strength 58.9%, chronic

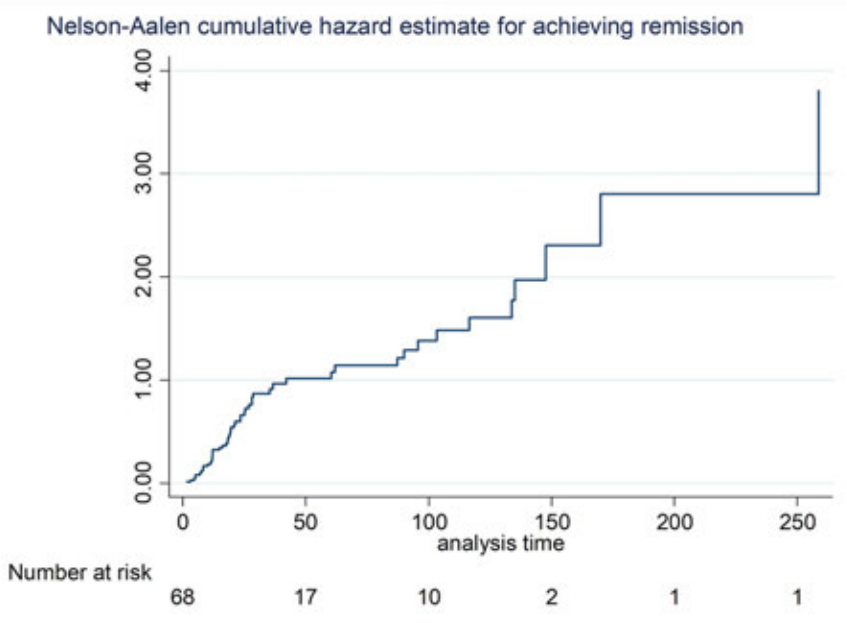

Figure 1. Cumulative hazard estimate for achieving remission.

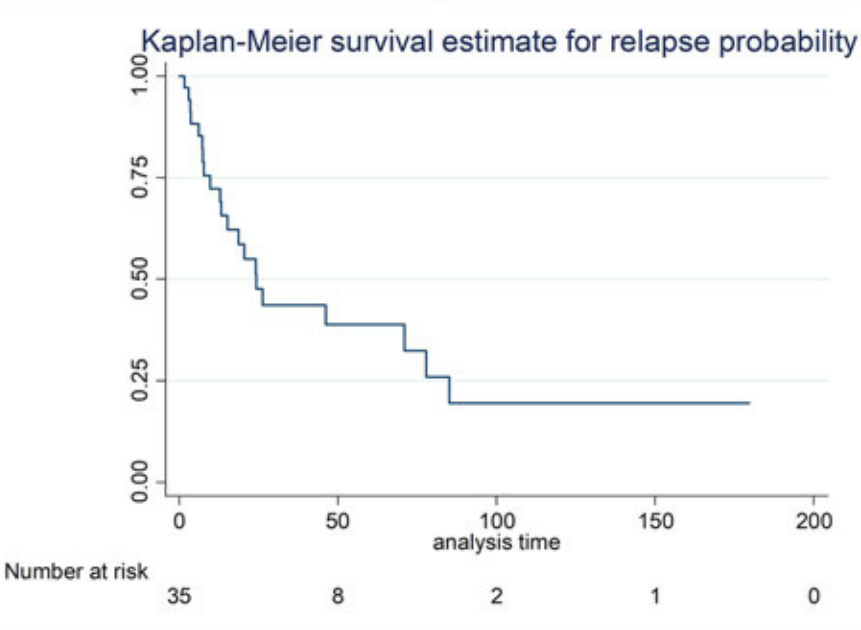

Figure 2. Kaplan Meier estimate for relapse-free survival.

muscular damage in 16.1%, normal CPK and muscle enzymes in 75%; Treatment with glucocorticoids in 46.4% and any immunosuppressive agent in 82.1% With median of HAQ-Di score of 0 (RIQ 0 - 0.35).

Conclusion: Treatment of IIM with conventional immunosuppressive agents results in a high rate of subjects achieving remission, however, most subjects required prolonged time with continued immunosuppressive therapy and relapses are frequent, which may account in significative muscle damage burden during follow up.

Disclosure: A. Sánchez-Rodríguez, None; **C. Gómez-Ruiz**, None; **A. Montes-Yanes**, None; **G. Medrano-Ramírez**, None.

Abstract Number: 1280

JAK Inhibitors: A Promising Molecular-targeted Therapy in Dermatomyositis

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Background/Purpose: We previously observed *in vitro* that IFN-I reproduces dermatomyositis (DM) pathological findings, that pathogenic effects may be prevented *in vitro* by JAK inhibitor (JAKinh) therapy and an improvement was observed clinically using JAKinh in four refractory DM patients. Our objective was to expand this observation clinically and to describe the evolution of refractory DM patients treated with JAKinh.

Methods: DM patients were considered refractory if the disease remained active after at least two different lines of immunosuppressive therapy combined with corticosteroids (CS) +/- intravenous immunoglobulins (IVIg). Disease activity was assessed using the Medical Research Council scale (MRC-5) and the Cutaneous DM Disease Area and Severity Index (CDASI) every 3 months. Health Assessment Questionnaire (HAQ) and modified Rankin Scale (mRS) were performed to assess patients reported quality-of-life and disability, respectively. Tolerability and adverse events were also monitored.

Results: Twelve refractory DM patients treated with JAKinh were identified. All patients were females, mean age at diagnosis was 49.4±23.2 years and most patients (n=9/12) presented a myositis-specific autoantibody (TIF1gamma n=6; SAE n=2; MDA5 n=1). One patient presented an ovarian cancer at initial diagnosis, 7 years prior to JAKinh therapy. On average, these patients previously received 3±2 lines of immunosuppressive therapy and all of them IVIg. At JAKinh initiation (ruxolitinib n=6; baricitinib n=6), mean disease duration was 8.3±10.4 years, CS dose was 7±7 mg/day, all other immunosuppressive agents were discontinued and 3 patients were treated with IVIg concomitantly. At baseline, mean CDASI-activity score was 31±13, deltoid MRC-5 was 4.3±0.7, psoas MRC-5 was 4.2±0.8, CK level was 333±783, HAQ was 1.5±0.8 and mRS was 1.4±1.0. At 3-months follow-up, a significant improvement of CDASI-activity score (>5 points) was observed in all patients, except one, and mean CDASI-activity score was 16±10 (p=0.0036). At last-follow up, mean treatment duration with JAKinh was 11.6±6.8 months and all patients were still receiving JAKinh therapy. Mean CDASI-activity score was 8±1 (absolute delta % change -74%, p< 0.0001), deltoid MRC-5 was 4.4±0.9 (-2%, NS), psoas MRC-5 was 4.4±0.8 (+5%, NS), CK level was 127±79 (-62%, NS), HAQ was 0.8±0.6 (-46%, NS) and mRSwas 1.3±0.9 (-13%, NS). Mean CS dose was 4±4 mg/day (-42%, NS) and no patients had IVIg. Over this period, 1 patient presented a herpes zoster infection and another a bronchitis. One patient was briefly hospitalized for a non-severe pneumonia and a superficial thrombophlebitis, and presented one year later a deep vein thrombosis and pulmonary embolism requiring hospitalization.

Conclusion: Altogether this case series support the use of JAKinh in the management of refractory cutaneous DM patients demonstrating a sustained remission at one year.

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Abstract Number: 1281

Maintenance Therapy for anti-MDA5-Positive Dermatomyositis Patients with Interstitial Lung Disease: Can They Achieve Drug-Free Remission?

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Background/Purpose: Interstitial lung disease (ILD) accompanied by anti-melanoma differentiation associated gene 5 (MDA5)-positive dermatomyositis (DM) is often rapidly progressive and associated with poor life prognosis in Japanese patients. Recently, combined immunosuppressive therapy such as high-dose glucocorticoid (GC), cal-

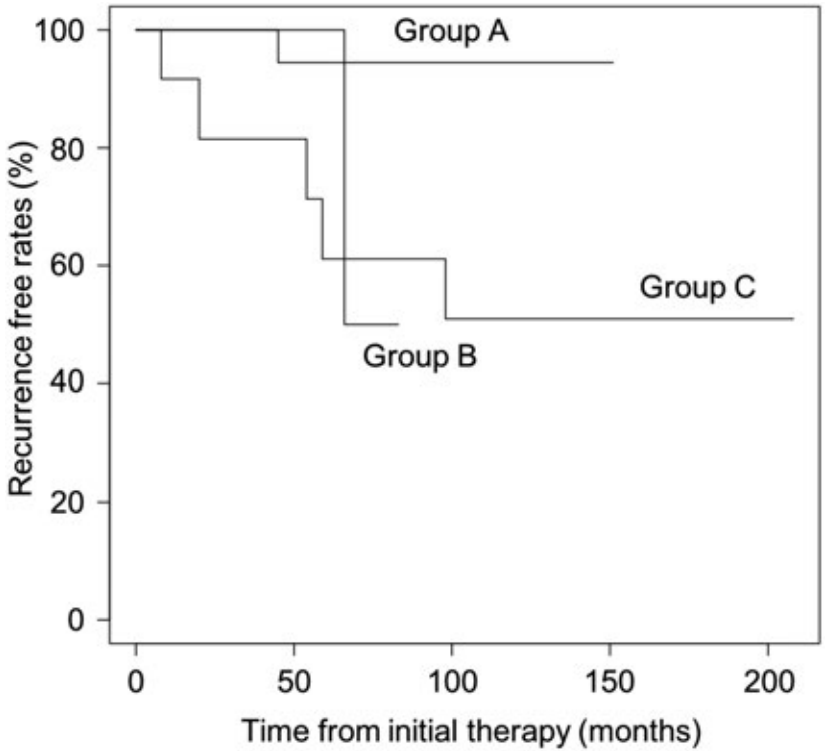

Figure 1. Relapse-free survival rates (Kaplan-Meier)

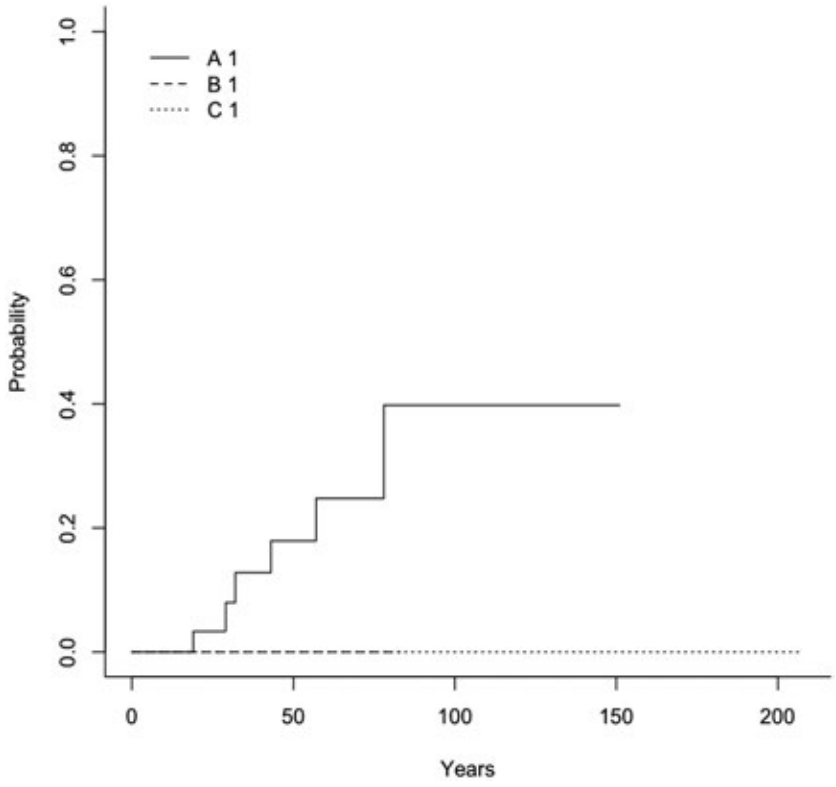

Figure 2. Drug free rates from Glucocorticoid

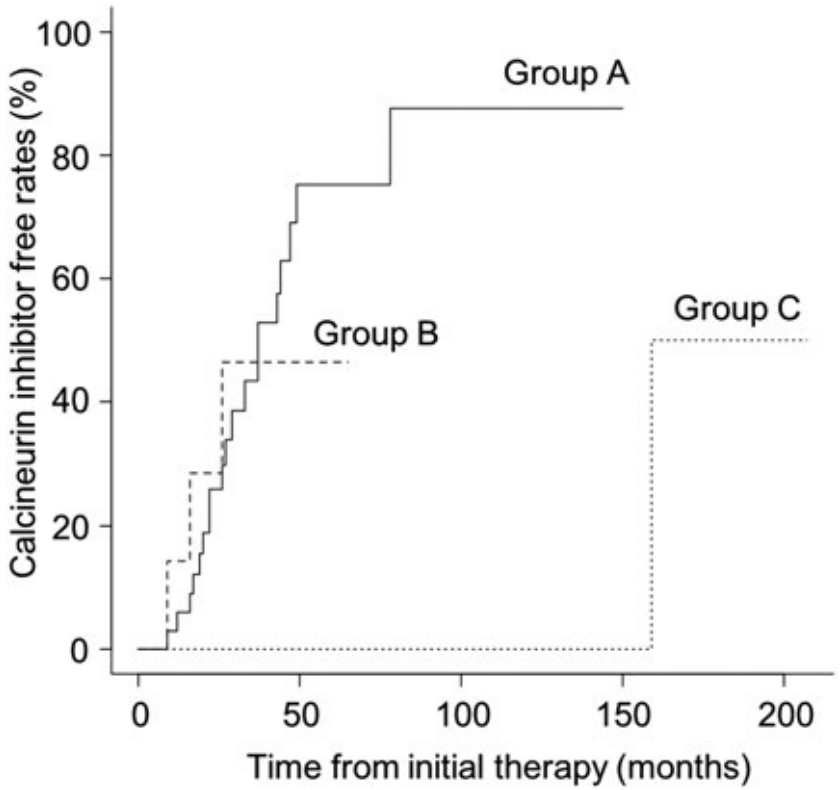

Figure 3. Drug free rates from Calcineurin inhibitor

cineurin inhibitor (CNI), and intravenous cyclophosphamide (IVCY) has been suggested to be so effective that the prognosis has been improved. However, after achieving remission, appropriate maintenance therapy is still unclear. In this study, we evaluated the effect of induction therapy on maintenance therapy and looked into the possibility of drug-free remission.

Methods: We retrospectively examined the medical records of 86 anti-MDA5-positive adult DM-ILD patients in Kyoto university hospital. There were 57 patients who had achieved remission and survived more than 6 months. According to the induction treatment, we classified into 3 groups, Group A (n=37); simultaneous triple combination therapy (GC, CNI and IVCY with all drugs started within a week), Group B (n=8); step-up triple combination therapy (initiation of IVCY delayed up to 3 month)) and Group C (n=12); mono/dual-therapy (GC with or without CNI). We compared the recurrence rates by using log-rank test. We also compared the maintenance dose of GC at 36 months since initial treatment and the rates of drug free patients.

Results: The recurrence rates of Group A, B and C were not significantly different (p=0.07, log-rank test). The recurrence rates at 36 months since initial treatment were 0%, 0%, 19%, respectively (Figure 1). The dose of GC in Group A, B and C were 3.4±2.2 vs 4.0±1.2 vs 6.3±2.2 mg/day, respectively (p< 0.05, Kruskal-Wallis test). Although the drug free rates from GC were not significantly different (13% vs 0% vs 0%, p=0.07, Figure 2), the CNI free rates of Group A were significantly higher than that of Group C (43% vs 0%, p< 0.01 with Bonferroni correction, Figure 3).

Conclusion: Triple combined immunosuppressants for induction therapy could reduce the maintenance dose of immunosuppressants and the risk of recurrence in anti-MDA5-positive DM-ILD. Moreover, initial combination therapy might lead some patients to achieve drug-free remission.

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Co. Ltd, 8, Mitsubishi Tanabe Pharma Corporation, 8, Pfizer Inc, 8, UCB Japan Co. Ltd, 8; **M. Hashimoto**, Astellas, 8, Ayum, 9, Brystol-Meyers, 8, Chugai, 9, Tanabe-Mitsubishi, 8, 9, UCB Japan, 9; **H. Yoshifuji**, Astellas Pharma, 2, Chugai Pharmaceutical, 8; **M. Tanaka**, None; **K. Ohmura**, None.

Abstract Number: 1282

Female Sex Is a Risk Factor for Failure to Achieve Remission in Polymyositis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Adults with polymyositis demonstrate wide variability in responses to treatment, and the risk factors for failure to achieve remission in polymyositis are largely unknown. The aim of our study was to identify risk factors for failure to achieve remission in adult polymyositis.

Methods: In this retrospective chart review, we collected data on patients with a diagnosis of polymyositis who were seen in the rheumatology clinic at John H. Stroger Hospital of Cook County (Illinois, USA) between 2006 and 2011. Patients were included if they had “definite” or “probable” polymyositis based on the 1975 Bohan and Peter criteria. Remission was defined as normal muscle strength and creatinine kinase (CK) level < 200 mg/dL. Baseline characteristics were compared between those who achieved remission at any point during follow-up and those who did not. Chi square tests or Fisher’s exact test were used to compare categorical variables and two-tailed Student’s t-tests were used to compare continuous variables. Univariate logistic regression analysis was used to calculate unadjusted odds ratios (ORs) for the outcome of failure to achieve remission. A multivariable logistic regression was conducted using age, female sex, race, follow-up time, and clinical variables with a univariate screen p-value < 0.2 as predictors. A p-value of 0.05 was set at the threshold for statistical significance.

Results: 40 patients, 95% of whom had biopsy-proven polymyositis, were included in this study. The mean age of the study population was 43.7 years, and 65% of the patients were women. African Americans and Hispanics constituted 80% and 18% of our study population, respectively. Mean duration of follow-up (in months) was 71.6 and 81.8 in those who failed to achieve remission and those who achieved remission respectively. 78.3% of those who failed to achieve remission were women, versus 47.1% of those who achieved remission (p=0.041). Women were less likely to achieve remission compared to men (OR 5.39 [95% CI 1.18-24.57]; p=0.019), even after adjusting for age, race and months of follow-up. Treatments were similar between those who achieved remission and those who did not.

Conclusion: In this small retrospective cohort of African American and Hispanic patients with polymyositis, female sex was a risk factor for failure to achieve remission. Because treatments were similar between groups, we hypothesize that less aggressive treatment of polymyositis disease activity in women may be the cause of this sex disparity.

Table 1. Characteristics of patients with polymyositis who failed to achieve remission versus those who achieved remission

Values listed as mean (95% CI) or % (N/Total)	No remission (N=23)	Remission (N=17)	P-value
Age at first visit in years	42.3 (37.0-47.6)	45.4 (39.9-51.2)	0.395
Female sex	78.3 (18/23)	47.1 (8/17)	0.041
Race			0.295
African American	87.0 (20/23)	70.6 (12/17)	
Hispanic	13.0 (3/23)	23.5 (4/17)	
Polymyositis features			
Biopsy-proven	95.7 (22/23)	94.1 (16/17)	1.000
Months of follow-up	71.6 (27.2-116.0)	81.8 (37.5-126.0)	0.743
Initial muscle strength 4 or greater	42.9 (6/14)	60.0 (9/15)	0.356
Initial prednisone dose, mg	49.4 (37.1-61.7)	58.1 (52.5-63.7)	0.189
Initial creatine kinase	6606.1 (2294.7-10917.5)	5100.4 (2848.8-7352.0)	0.533
Dysphagia	42.9 (6/14)	30.0 (3/10)	0.678
Fever	5.6 (1/18)	6.7 (1/15)	1.000
Myalgias	61.5 (8/13)	50.0 (5/10)	0.580
Arthritis	35.7 (5/14)	27.3 (3/11)	1.000
ILD	31.8 (7/22)	23.5 (4/17)	0.725
Raynaud's	18.2 (4/22)	5.9 (1/17)	0.363
Anti-Jo1 antibodies	30.8 (4/13)	37.5 (3/8)	1.000
ANA positive	66.7 (14/21)	75.0 (12/16)	0.583
Anti-dsDNA antibodies	10.5 (2/19)	13.3 (2/15)	1.000
Anti-RNP antibodies	33.3 (4/18)	15.4 (2/13)	1.000
Treatments			
Prednisone	100 (23/23)	100 (17/17)	1.000
Methotrexate	60.9 (14/23)	47.1 (8/17)	0.385
Azathioprine	52.2 (12/23)	58.8 (10/17)	0.676
Cyclophosphamide	8.7 (2/23)	11.8 (2/17)	1.000
IVIG	13.0 (3/23)	11.8 (2/17)	1.000
Rituximab	4.4 (1/23)	5.9 (1/17)	0.826

ANA=antinuclear antibody, RNP=ribonuclear protein, ILD=interstitial lung disease, IVIG=intravenous immunoglobulin

Table 2. Multivariable logistic regression model of risk factors for failure to achieve remission in polymyositis

	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age, per year increase	0.97 (0.92-1.03)	0.386	0.97 (0.91-1.04)	0.370
Female sex	4.05 (1.02-16.01)	0.046	5.39 (1.18-24.57)	0.029
African American race	2.78 (0.56-13.76)	0.211	3.06 (0.52-17.94)	0.215
Months of follow-up	1.00 (0.99-1.01)	0.735	1.00 (0.99-1.00)	0.308

OR=odds ratio

Disclosure: P. Lingamaneni, None; **C. Richardson**, RUSH University Medical Center, 3; **S. Kambhatla**, None; **A. Manadan**, RUSH University Medical Center, 3.

Abstract Number: 1283

Risk Factors of Cancer-Associated Inflammatory Myopathies: A Multicenter Study

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SESSION INFORMATION
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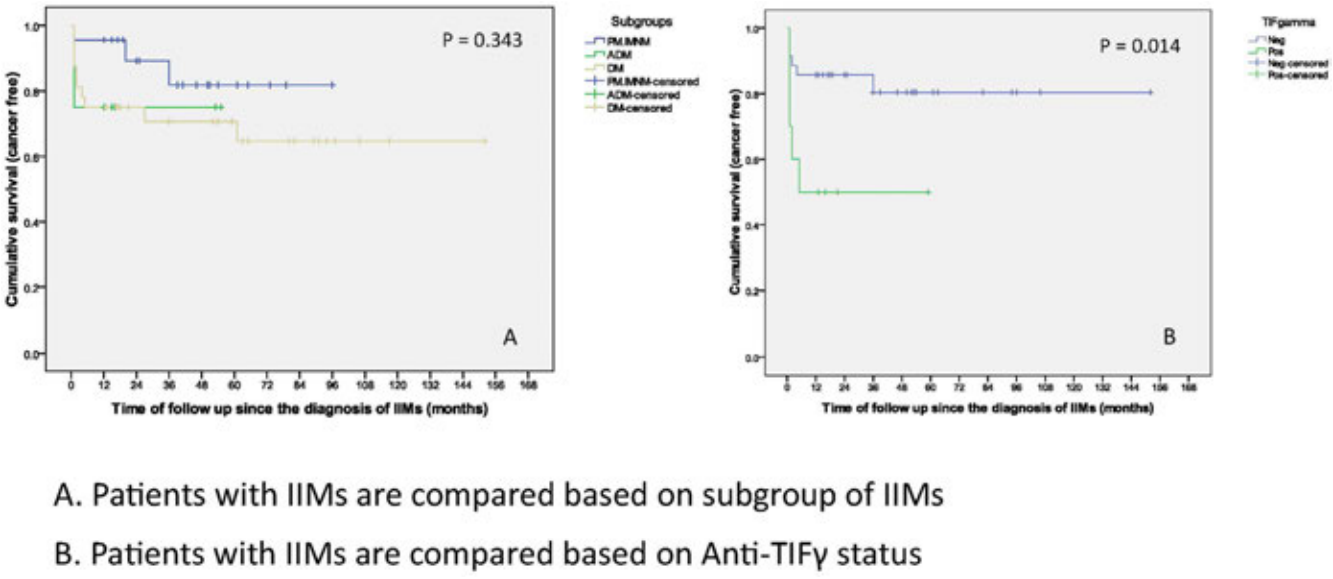
Background/Purpose: The association between idiopathic inflammatory myopathies (IIMs) and malignancies in Thai population has been rarely reported. The objective of our study was to determine the risk factors of cancer in IIMs patients and to describe cancer screening methods, natural history and response to treatment in Thailand.

Methods: We retrospectively studied 74 IIMs patients according to 2017 EULAR/ACR classification criteria from 2 tertiary hospitals (Ramathibodi Hospital and Siriraj Hospital, Bangkok, Thailand). Clinical, and laboratory data, cancer screening methods, natural history, and treatment outcome were recorded. After enrollment and informed consent, blood collection for myositis-specific autoantibodies (MSAs) was done in some feasible patients to complete the laboratory data. We performed a univariate analysis using logistic regression analysis to identify clinical and laboratory predictors for cancer.



A. Patients with IIMs are compared based on subgroup of IIMs

B. Patients with IIMs are compared based on Anti-TIFγ status

Figure 1. Kaplan-Meier method with log-rank test for comparison of survival curves of cancer free status

Results: Form 74 IIMs patients, we classified 25 patients in polymyositis/immune-mediated necrotizing myopathy (PM/IMNM) subgroup, 40 patients in dermatomyositis (DM) subgroup, and 9 patients in amyopathic dermatomyositis (ADM) subgroup. The mean age at diagnosis IIMs was 54.7 ± 14.7 years. Fourteen patients (18.9%) were male. Cancer was identified in 26 out of 74 IIMs patients (35.1%). Blood collection for myositis profile after enrollment was done in 17 patients. Factors that were associated with an increased risk of malignancy included DM subgroup (OR 3.27, 95%CI 1.02-10.45, P=0.045) and positive anti-TIFγ (OR 8.80, 95%CI 2.37-32.64, P=0.001). Malignancy risk also increased in IIMs patients with a positive antinuclear antibody (ANA), at titer ≥ 1:80 (OR 4.24, 95%CI 1.71-10.49, P=0.002). However, the difference was not statistically significant with the higher titer (≥1:320) of ANA (OR 1.88, 95%CI 0.63-5.59, P=0.258). While interstitial lung disease (ILD) was associated with below-than-average risk of malignancy (OR 0.11, 95%CI 0.01-0.88, P=0.040). Eighteen cases of cancer (69.2%) were diagnosed within one year before or after the diagnosis of IIMs. Median cancer diagnosis time was 1.0 month, range -57 to 61 months after IIMs diagnosis. Breast cancer was the most common cancer (31%), followed by ovarian cancer (15%). In 5 patients, cancer was detected by more extensive screening beyond age-appropriate cancer screening. IIMs patients with cancer tended to use less immunosuppressive agents compared with IIMs without cancer. However, they had a worse prognosis, with more proportion of expired patients compared to IIMs patients without cancer (OR 30.5, 95% CI = 3.45-270.83, P= 0.002). The causes of death in IIMs were cancer in 6 patients and infection in 3 patients.

Conclusion: DM subgroup and the presence of anti-TIFγ significantly increased the risk for malignancy, while ILD decreased the risk. Most cancer cases were diagnosed within one year before or after the diagnosis of IIMs, and some of them were detected by more extensive cancer screening. IIMs patients with cancer used less immunosuppressive agents, but they had a worse prognosis.

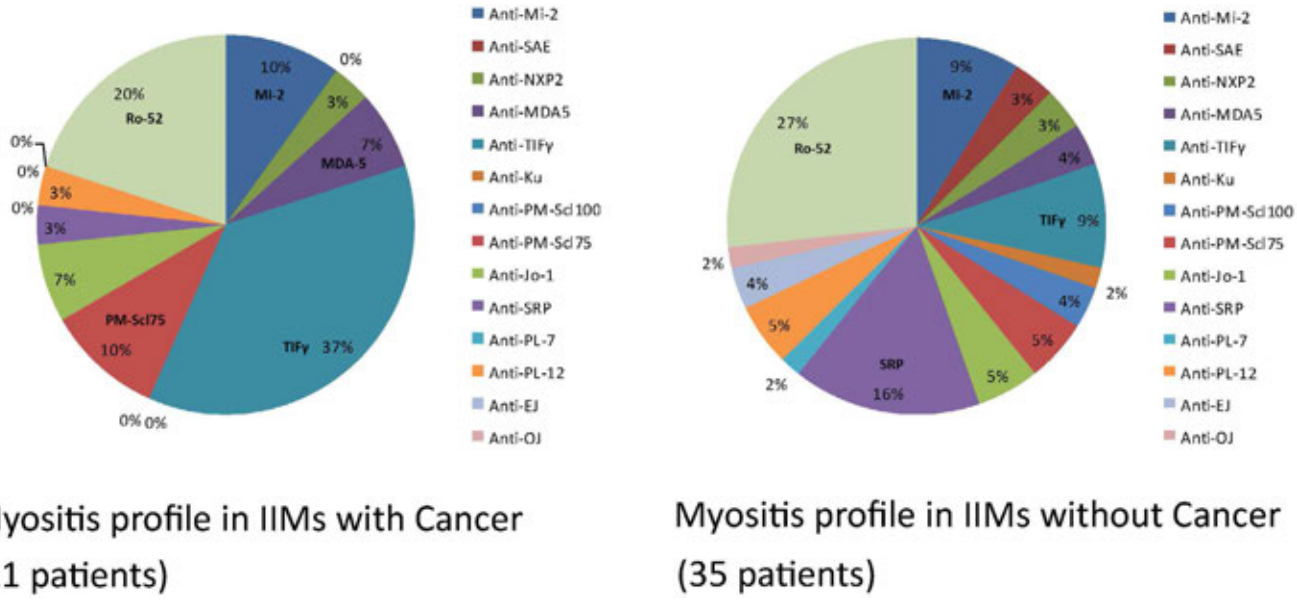


Figure 2. Myositis profile in idiopathic inflammatory myopathies with cancer and without cancer

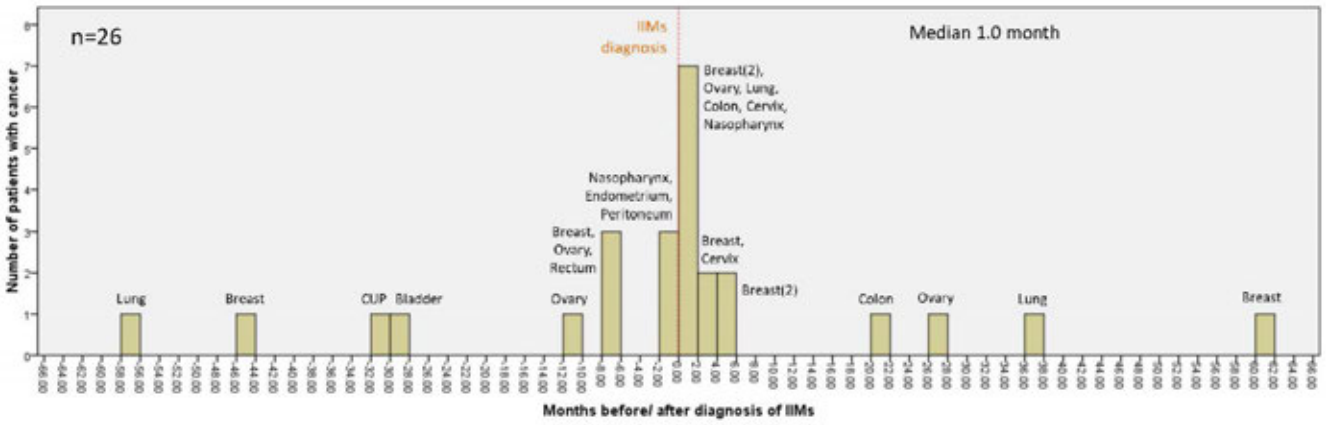


Figure 3. Relationship between time of cancer diagnosis and idiopathic inflammatory myopathies diagnosis

Disclosure: N. Pongtarakulpanit, None; **K. Yongchairat**, None; **W. Kachamart**, None; **C. Dejthevaporn**, None; **N. Rajatanavin**, None; **P. Chevaisrakul**, None.

Abstract Number: 1284

Idiopathic Inflammatory Myopathies: Are Muscle Biopsies Still Needed?

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SESSION INFORMATION
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Background/Purpose: Inflammatory myopathies (IM) are a heterogeneous group of diseases characterized by muscle inflammation. In Argentina, there are few pathologists specialized in muscle biopsies and for this reason, there are limitations to perform good quality biopsies.

The objectives of this study are to estimate the frequency of muscle biopsy in patients with IM belonging to Argentinean Society of Rheumatology database, identify the variables associated with its performance and to apply the new EULAR-ACR criteria to the subgroup of patients with biopsy.

Methods: 179 patients with IM were included. Demographic, clinical, laboratory, images and treatment characteristics were collected from medical records.

The muscle biopsy information was obtained from the pathology report of each participating hospital. Therefore, there was no standardization in the report.

To analyze differences between the groups, Chi square was performed for categorical variables and T test or Mann Whitney for continuous variables according to their distribution. Logistic regression analysis was performed for the analysis of variables associated with performing a muscle biopsy.

Results: Table 1 describes clinical characteristics of the cohort. The frequency of muscle biopsies in the cohort was 58 (32%). Table 2 shows variables associated to not having muscle biopsy performed.

In the logistic regression analysis, the presence of positive antibodies OR 0.21 (CI 95% 0.05- 0.99) and heliotrope rash 0.11 (CI 95% 0.02 to 0.75) were independently associated with NOT performing biopsy.

The complete biopsy report was available in 37 of 52 patients who undergone biopsy. In those patients we applied the EULAR-ACR criteria for inflammatory myopathies with and without biopsy(1).

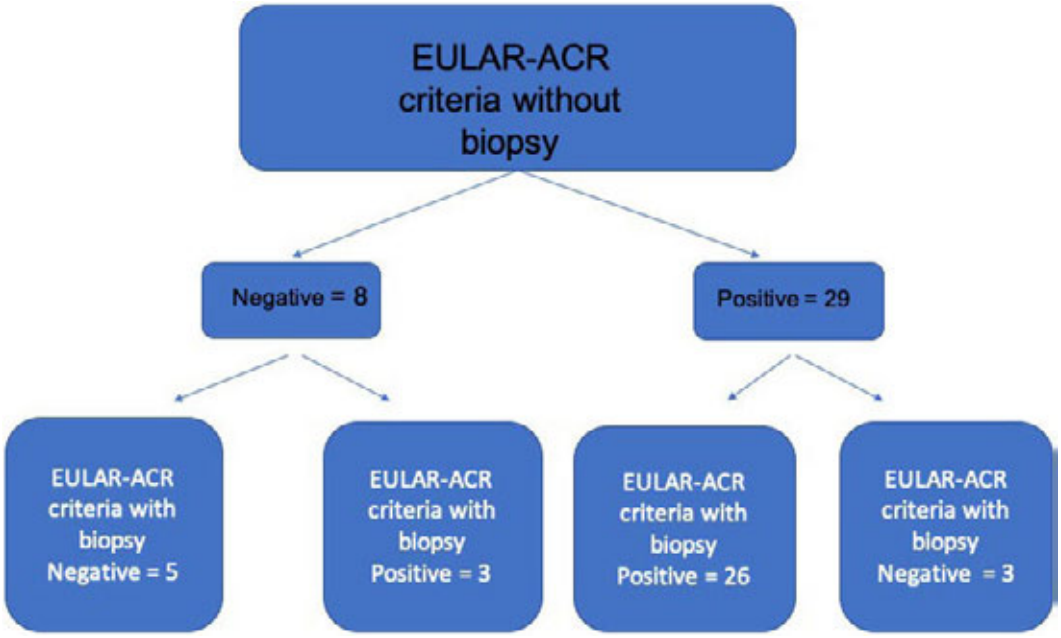
Conclusion: Muscle biopsy was performed in only one third of patients with IM from our cohort. Patients with myositis-specific antibodies and heliotrope rash were biopsied less frequently. If criteria without biopsy are applied to

Table 1. Clinical characteristics of the cohort.

	n =179
Age, mean (SD)	52 (16.2)
Disease Duration, mean (DS) years	5.3 (5.7)
Sex	
Female, n (%)	132 (73)
Male, n (%)	47 (26)
Ethnia	
Caucasian, n (%)	52 (30)
Mestizo, n (%)	75 (43)
Others, n (%)	48 (27)
Subclassification, n (%)	
Dermatomyositis (DM)	82 (46)
Amyopathic DM	28 (16)
Polymyositis	46 (26)
Inclusion body myositis	1 (0.6)
Necrotizing myopathy	1 (0.6)
Anti-synthetase syndrome	20 (11)
No data	1 (0.6)
Arthritis, n (%)	68 (38)
Raynaud phenomenon, n (%)	63 (35)
Interstitial lung disease, n (%)	58 (35)
Cardiac involvement, n (%)	7 (4)
DM rash, n (%)	91 (50)
Malignancy, n (%)	18 (10)

Table 2. Variables associated to not having muscle biopsy performed.

	NO Biopsy (%)	Biopsy (%)	p
Dermatomyositis	62.4	60.4	0.94
Arthritis	**44**	**28**	**0.05**
Mechanic hands	12.4	3.5	0.10
Heliotrope rash	**45**	**28**	**0.05**
Gottron papules	**44**	**23**	**0.01**
Raynaud phenomenon	**41**	**23**	**0.02**
Cardiac involvement	6.1	0	0.15
Interstitial lung disease	**40**	**21**	**0.03**
Myositis specific antibodies	**85**	**59**	**0.03**
Elevated CK	**69**	**89**	**0.007**
Myopathic EMG	84.8	94.3	0.32
Abnormal MRI	25.3	40.4	0.09



patients with biopsy most of them will fulfill criteria. Given the difficulties to obtain a good quality muscle biopsy, we propose to only perform muscle biopsy to those patients who do not fulfill non biopsy EULAR-ACR criteria.

Reference:

1. Lundberg IE, Tjärnlund A, Bottai M, Werth VP, Pilkington C, Visser M De, et al. 2017 European League Against Rheumatism / American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. Ann Rheum Dis. 2017;69(12):2271–82.

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Abstract Number: 1285

Changes in Nail-fold Capillary Abnormalities, and Serum FGF and VEGF Levels in Dermatomyositis Patients with anti-MDA5 Antibody During the Clinical Course

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Capillary abnormalities in the nail-fold are a characteristic finding of microangiopathy in autoimmune connective tissue diseases, including dermatomyositis and systemic sclerosis. A previous study reported an association between nail-fold capillary findings and disease activity in patients with dermatomyositis. To examine the changes in nail-fold capillary abnormalities, and serum fibroblast growth factor (FGF) and vascular endothelial growth factor (VEGF) levels in dermatomyositis patients with anti-melanoma differentiation-associated gene 5 (MDA5) antibody (Ab) during the clinical course.

Methods: Capillary abnormalities were evaluated by capillaroscopy in 11 patients with anti-MDA5 Ab at baseline and after treatment. Capillary abnormalities included

irregularly enlarged capillaries, reduced capillaries, hemorrhage, capillary ramifications, disorganization of the vascular array, loss of capillaries, and giant capillaries. Serum levels of FGF and VEGF were measured by ELISA.

Results: At baseline, i rregularly enlarged capillaries were observed in 10 of 11 cases, but after treatment, they were significantly reduced in only 3 cases (91% vs 27%, $p < 0.001$). Hemorrhage was observed in all cases at baseline, but disappeared in all cases after treatment (100% vs 0%, $p < 0.001$). Although the difference was not significant, reduced capillaries slightly improved (58% vs 33%, $p = 0.219$). Serum FGF levels significantly increased between baseline and after treatment (0.5 ± 0.8 pmol/L vs 1.0 ± 0.6 pmol/L, $p < 0.005$), but serum VEGF levels were comparable between baseline and after treatment (382 ± 330 pg/ml vs 302 ± 200 pg/ml, $p = 0.11$).

Conclusion: These data suggest that capillary abnormalities are reversible and improved by treatment. In addition, F

GF may function in the pathophysiology of microvascular abnormalities in dermatomyositis patients with anti-MDA5 Ab.

Table 1. Nail-fold capillary findings between baseline and after treatment

	At baseline (n = 11)	After treatment (n = 11)	P
Irregularly enlarged capillaries	10 (91%)	3 (27%)	<0.001
Reduced capillaries	7 (64%)	4 (36%)	0.219
Hemorrhage	11 (100%)	0 (0%)	<0.0001
Capillary ramifications	0 (0%)	1 (9%)	0.307
Disorganization of the vascular array	0 (0%)	1 (9%)	0.307
Loss of capillaries	0 (0%)	0 (0%)	-
Giant capillaries	0 (0%)	0 (0%)	-

Disclosure: Y. Hamaguchi, None; T. Matsushita, None; N. Mugii, None; K. Takehara, None.

Disclosure: Y. Hamaguchi, None; **T. Matsushita**, None; **N. Mugii**, None; **K. Takehara**, None.

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Patients with Anti-tRNA Synthetase Syndrome Are More Likely to Present to Pulmonary Clinic and Have a Higher Prevalence and Severity of Lung Disease Than Patients with Other Types of Myositis or Systemic Sclerosis

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Background/Purpose: Interstitial lung disease (ILD) is a significant cause of morbidity and mortality in idiopathic inflammatory myopathies (IIM) as well as systemic sclerosis (SSc). The purpose of this study is to compare the prevalence, physiology, and radiographic findings in IIM as well as to analyze the utilization of screening/monitoring plans in different clinical and antibody defined patient subsets.

Methods: Patients diagnosed with polymyositis (PM), dermatomyositis (DM), anti-aminoacyl tRNA synthetase syndrome (ARS), limited cutaneous systemic sclerosis (lcSS), or diffuse cutaneous systemic sclerosis (dcSS) were identified from the MYSTIC cohort (VUMC IRB 141415) and using subject locator (VUMC IRB 180672). The presence of ILD was identified from chart abstraction. Radiographic patterns of ILD were ascertained from the initial CT scan. American Thoracic Society (ATS) criteria were used to grade severity of lung disease by forced vital capacity (FVC) and diffusion lung capacity for carbon monoxide (DLCO) percentages. If multiple pulmonary function tests (PFTs) were available, the most severe value was used. Symptom onset was defined as the start of any clinical manifestation of IIM or SSc.

Results: Patient characteristics are shown in Table 1. Sixty-nine of 131 patients had ILD with the highest prevalence in ARS (81.5%) and dcSS (71.4%). Overall, most patients had CT morphology other than usual interstitial pneumonia (UIP) (Table 2). Non-Jo1 (45.5%) ARS were most frequently classified as UIP. Severe restriction was present in 36.4%

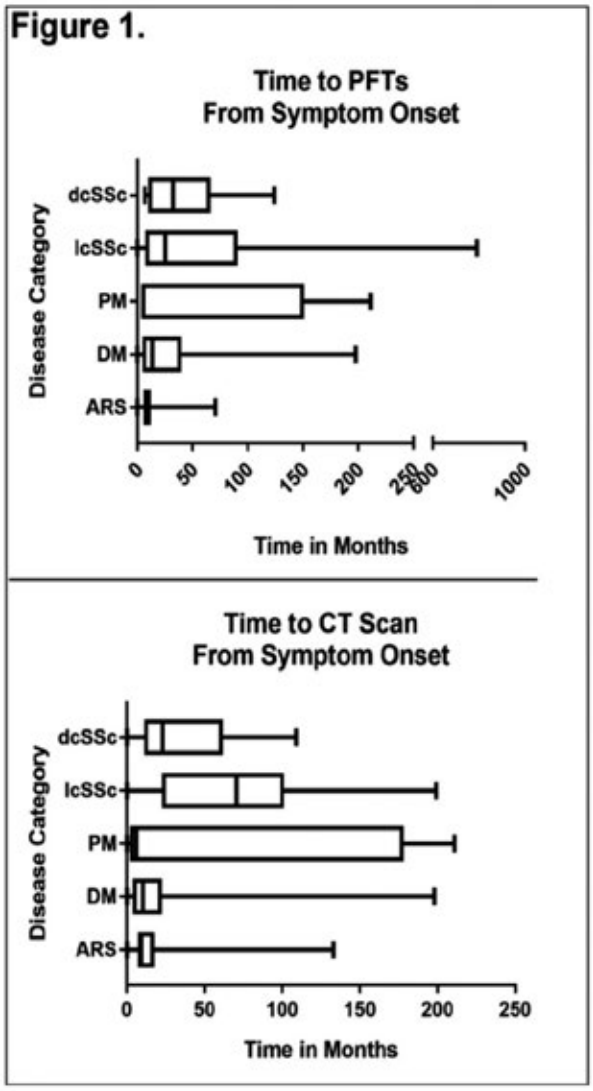
of Jo-1+ and 63.6% of non-Jo-1 ARS patients, compared with 33.3% of dcSS patients. Similarly, 72.7% of ARS patients (54.5% Jo-1+ and 90.9% non-Jo-1) and 55.6% of dcSS had severe gas exchange deficits. Supplemental oxygen use was 25.9% in ARS and 14.3% in dcSS. Despite the prevalence of ILD at 45% and 43.9% in lcSS and DM, respectively, physiologic severity was less than for ARS or dcSS. FVC was severely restricted in only 12.5% of lcSS cases and 5.6% of DM cases. Over 62% of lcSS patients had severe reduction in DLCO, but this is likely due to concomitant pulmonary hypertension. The time from symptom onset to first PFT or HRCT was the shortest with

Table 1: Patient Characteristics

	DM N = 41 (%)	PM N = 14 (%)	Jo-1 ARS N = 15 (%)	Non Jo-1 ARS N = 12 (%)	lcSS N = 35 (%)	dcSS N = 14 (%)	Total N = 131 (%)
Age Range (Mean)	26-78 (59.8)	44-82 (58.8)	46-71 (55.5)	36-71 (47.8)	21-86 (59.1)	19-80 (58.3)	19-86 (58.2)
Female	30 (73.2%)	11 (78.6%)	11 (73.3%)	9 (75%)	30 (85.7%)	9 (64.3%)	100 (76.3%)
Caucasian	39 (95.1%)	11 (78.6%)	10 (66.7%)	5 (41.7%)	30 (85.7%)	10 (71.4%)	105 (80.2%)
African American	2 (4.9%)	3 (21.4%)	3 (20%)	6 (50%)	5 (14.3%)	1 (7.1%)	20 (15.3%)
Other	0	0	2 (1.3%)	1 (8.3%)	0	3 (21.4%)	3 (2.3%)
ILD Present	18 (43.9%)	3 (21.4%)	11 (73.3%)	11 (91.7%)	16 (45.7%)	10 (71.4%)	69 (52.7%)
Pulmonary Hypertension	3 (7.3%)	1 (7.1%)	4 (26.7%)	4 (33.3%)	12 (34.3%)	5 (35.7%)	29 (22.1%)
Supplemental Oxygen	3 (7.3%)	0	3 (20%)	4 (33.3%)	8 (22.9%)	2 (14.3%)	20 (15.3%)

Table 2: Pulmonary Phenotypes

Radiographic Patterns							
		DM N = 15 (%)	PM N = 2 (%)	Jo-1 ARS N = 11	Non-Jo-1 ARS N = 11 (%)	lcSS N = 17 (%)	dcSS N = 6 (%)
	NSIP	3 (20%)	1 (50%)	5 (45.5%)	3 (27.3%)	4 (23.5%)	5 (83.3%)
	Atypical for UIP	2 (13.3%)	0	0	2 (18.2%)	0	0
	Consistent with UIP	2 (13.3%)	0	3 (27.3%)	5 (45.5%)	3 (17.6%)	1 (16%)
	Other	8 (53.3%)	1 (50%)	3 (27.3%)	1 (9.1%)	10 (58.8%)	0
Physiologic Severity							
		DM N = 18 (%)	PM N = 3 (%)	Jo-1 ARS N = 11 (%)	Non-Jo-1 ARS N = 11 (%)	lcSS N = 16 (%)	dcSS N = 9 (%)
Restriction							
	No Restriction	3 (16.7%)	0	3 (27.3%)	0	3 (18.8%)	1 (11.1%)
	Mild - FVC 65-79%	7 (38.9%)	2 (66.7%)	2 (18.2%)	1 (9.1%)	6 (37.5%)	2 (22.2%)
	Moderate - FVC 50-64%	7 (38.9%)	0	2 (18.2%)	3 (27.3%)	5 (31.3%)	3 (33.3%)
	Severe - FVC <50%	1 (5.6%)	1 (33.3%)	4 (36.4%)	7 (63.6%)	2 (12.5%)	3 (33.3%)
Gas Exchange							
	DLCO - 65-79%	2 (11.1%)	1 (33.3%)	4 (36.4%)	0	2 (12.5%)	0
	DLCO - 50-64%	6 (33.3%)	2 (66.7%)	1 (9.1%)	1 (9.1%)	3 (18.8%)	2 (22.2%)
	DLCO - <50%	10 (55.6%)	0	6 (54.5%)	10 (90.9%)	10 (62.5%)	5 (55.6%)



the ARS group (Figure 1). ARS patients (72.7%), particularly the non-Jo-1 ARS (100%), were more likely than other groups (34%) to be seen first in pulmonary clinic.

Conclusion: In our cohort, ARS had the highest prevalence and severity of ILD. ARS patients, especially non-Jo-1 ARS patients, were more likely to be seen initially in pulmonary clinic and receive earlier screening for ILD. However, these patients may also have delayed diagnosis due to lack of extra-pulmonary symptoms thus presenting with more severe disease. Implementing routine screening for ARS in pulmonary clinics may identify patients earlier and change management.

Disclosure: B. Sohn, None; **E. Wilfong**, None; **L. Crofford**, None.

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Anti-mitochondrial Autoantibodies in Idiopathic Inflammatory Myopathies

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SESSION INFORMATION

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Background/Purpose: Autoantibodies found in adult and juvenile myositis patients are often associated with specific clinical features. Prior reports have suggested that the myositis-associated autoantibody, anti-mitochondrial autoantibodies (AMA), may be associated with cardiac involvement in adults with myositis. No studies have examined the prevalence or significance of AMA in children with myositis. The purpose of this study was to define the prevalence of AMA in juvenile myositis and to investigate phenotypic differences between myositis patients with and without AMA.

Methods: We screened sera from 302 patients with juvenile dermatomyositis, 25 patients with juvenile polymyositis, and 44 patients with juvenile connective tissue disease-myositis overlap from a national myositis registry study and 92 juvenile healthy controls for AMA by ELISA, [M2 EP (MIT3) ELISA, Quanta Lite, INOVA Diagnostics, San Diego, CA]. Clinical characteristics were compared between myositis patients with and without AMA.

Results: AMA were found in 4/371 (1%) of juvenile myositis patients and 1/92 (1%) of juvenile healthy controls. Of the juvenile myositis patients, 3/4 had dermatomyositis and 1/3 had polymyositis. Onset of myositis was between 3.6 and 12.4 years of age. Two patients were positive for anti-p155/140 autoantibodies, one was positive for anti-MJ autoantibodies and one was myositis-specific autoantibody negative. All patients had muscle weakness and 3/4 patients had either Gottron's papules or heliotrope rash. Three patients had dysphagia, 2/4 patients had calcinosis, and 2/4 patients had atypical cutaneous findings including orbital swelling and panniculitis. Overall, no distinguishing clinical features were present in the AMA positive children, and none of the AMA positive children had cardiac involvement.

Conclusion: AMA are rare in juvenile myositis and the prevalence of AMA is equivalent to that observed in healthy controls. AMA are not associated with a specific clinical phenotype in juvenile myositis.

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Abstract Number: 1288

Line Blot Immunoassay in Inflammatory Myopathies: Diagnostic Accuracy and Factors Predicting Positive Results in Routine Clinical Practice

Fergus To,[1] Clara Ventín Rodríguez,[2] Shuayb Elkhalifa,[3] James Lilleker,[4] and Hector Chinoy[4], [1]University of British Columbia, Vancouver, Canada, [2]Complejo Hospitalario Universitario de A Coruña, A Coruña, Spain, [3]Department of Immunology, Salford Royal NHS Foundation, Salford, United Kingdom, [4]University of Manchester, Manchester, United Kingdom

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Background/Purpose: To evaluate the real-world accuracy of a line blot immunoassay (LIA) for myositis-specific (MSA) and myositis-associated (MSA) autoantibody testing in patients at a tertiary rheumatology and neurology centre.

Methods: Adults tested with the EUROLINE Inflammatory Myopathies 16 Ag LIA at Salford Royal NHS Foundation Trust between January 1, 2016-July 30, 2018 were identified. Cases were reviewed to determine if LIA results were true or false positives. Accuracy was calculated for the autoantibodies (Abs), stratified into strong and weak positivity. Factors associated with true positive results were evaluated.

Results: In total, 342 patients were analysed. 67/342 (19.6%) had a final diagnosis of IIM, 120/342 (35.1%) with connective tissue disease (CTD) without IIM, and 121/342 (35.4%) without IIM or CTD. In IIM patients, 50/71 (70.4%) Abs detected were strongly positive and 48/50 (96.0%; 19 MSAs, 29 MAAs) of these were true positives. 21/71 (29.6%; 7 MSAs, 14 MAAs) were weakly positive. Only 15/21 (71.4%; 3 MSAs, 12 MAAs) of these were true positives. In CTD without IIM patients, 31/61 (51.0%; 5 MSAs, 26 MAAs) Abs detected were strong positives. Only 24/31 (77.4%; 0 MSAs, 24 MAAs) were true positives. 30/61 (49.2%; 13 MSAs, 17 MAAs) were weakly positive and 16/30 (53.3%; 0 MSAs, 16 MAAs) of these were true positives. In patients without CTD or IIM, 46 Abs (24 MSAs, 22 MAAs) were detected. All were false positives, 17/46 (37.0%; 7 MSAs 10 MAAs) of which were strong positives. Individual Abs specificities were 98.2-100% for weakly positive Abs and 97.5-100% for strongly positive Abs. The odds ratio (OR) of a true positive result was significantly associated with a pre-test working diagnosis of IIM (OR 50.8, 95%CI 13.66-189.22, $p< 0.001$) and strongly positive antibody results (OR 4.38, 95%CI 2.32-8.26, $p< 0.001$).

Conclusion: We demonstrated a high diagnostic specificity for IIM in a real-world setting using a commercially available LIA. However, a significant burden of false positive results was evident in those with low pre-test likelihood of IIM and for weak positive Ab results.

Disclosure: F. To, None; **C. Ventín Rodríguez**, None; **S. Elkhalifa**, None; **J. Lilleker**, None; **H. Chinoy**, None.

Abstract Number: 1289

Antigen Bead Array versus ELISA to Detect anti-cN1A Antibodies in Patients with Sporadic Inclusion Body Myositis and Correlation with Clinical, Serological and Histological Features

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Background/Purpose: Antibodies to cytosolic 5'-Nucleotidase 1A (anti-cN1A or NT5C1A) are considered the only currently known serum biomarker for sporadic Inclusion Body Myositis (sIBM). They are reported in 33-76% of sIBM patients but little is known on their possible correlation with clinical, serological and histological features. Few studies have shown that anti-cN1A positive patients with sIBM present with a more severe phenotype and increased mortality risk.

Aims: To analyze the prevalence of anti-cN1A autoantibodies in a Swedish cohort of patients with sIBM by applying suspension antigen bead array and a commercially available ELISA assay. To explore whether the anti-cN1A autoantibodies could identify a distinct subgroup of sIBM with specific clinical or laboratory characteristics.

Methods: Reactivity to one N-terminal and one C-terminal protein fragment of the NT5C1A antigen was investigated by using a suspension bead array platform in serum samples from 46 patients with sIBM, 30 with Polymyositis (PM) and 30 with Dermatomyositis (DM), HLA matched. The ELISA kit was then used for 31/46 sIBM samples as well as in 33 DM and 43 PM samples. Plasma samples from 17 patients with Systemic Lupus Erythematosus (SLE) and 9 SLE-controls were also screened by ELISA. Clinical, serological and histological data of the sIBM cohort were collected at time of diagnosis and accumulated data during the disease course. The 46 sIBM patients were defined as having anti-cN1A antibodies if they tested positive by at least one of the two assays.

Results: The antigen bead array showed a sensitivity of 34.8% of identifying sIBM and a specificity of 83.3% when performed with the N-terminal fragment. The sensitivity decreased to 6,5% and the specificity increased to 93,5% when the test was run with the C-terminal fragment. The sensitivity and specificity for the ELISA assay were 41,9% and 74,5%, respectively. A statistically significant correlation was found between the ELISA and the antigen bead array results (N-terminal fragment) (Spearman's rho 0.74, p value < 0.001). In the sIBM cohort, 19 seropositive and 27 seronegative to anti-cN1A antibodies were identified. No statistically significant differences in any of the analyzed variables were found between the 2 groups, but some interesting trends were observed. At time of diagnosis, seropositive patients had more frequently finger flexor weakness and reported higher score on patient visual analogue scale (VAS) for disease activity than the seronegative group. At first biopsy, increased amount of connective and/or fat tissue was found more commonly in anti-cN1A positive patients. More anti-cN1A positive than negative patients had positive history of falls and did not reach stabilization nor remission after the first year from diagnosis, independently of the use of immunosuppressive treatment.

Conclusion: Positivity to anti-cN1A antibodies is highly specific for sIBM diagnosis, as previously reported. The results from the antigen bead array suggest that the main epitope may be localized at the N-terminal region of the NT5C1A protein. In our cohort, anti-cN1A antibodies were not associated to any specific features but the seropositive group seemed to present with a more aggressive disease course.

Disclosure: A. Notarnicola, None; **F. Bonomi**, None; **C. Hellstrom**, None; **E. Pin**, None; **H. Idborg**, None; **P. Nilsson**, None; **I. Lundberg**, Astra Zeneca, 2, Corbus, 5, Bristol Myers Squibb, 2, Roche, 4, Novartis, 4.

Abstract Number: 1290

Identification of Distinctive Interferon Gene Signatures in Different Types of Inflammatory Myopathy

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Muscle Biology, Myositis & Myopathies Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Activation of the type 1 interferon (IFN1) pathway is a prominent feature of dermatomyositis (DM) muscle and may play a role in the pathogenesis of this disease. However, the relevance of the IFN1 pathway in patients with other types of myositis, such as the antisynthetase syndrome (AS), immune-mediated necrotizing myopathy (IMNM), and inclusion body myositis (IBM), is largely unknown. Moreover, the activation of the type 2 interferon (IFN2) pathway has not been comprehensively explored in myositis. In this cross-sectional study, our objective was to analyze both IFN1 and IFN2 pathway activation in myositis by performing RNAseq on muscle biopsy samples from 119 patients with DM, IMNM, AS, or IBM as well as on 20 normal muscle biopsies.

Methods: The expression of IFN1- and IFN2-inducible genes was compared between the different groups.

Results: The expression of IFN1-inducible genes was high in DM, moderate in AS, and low in IMNM and IBM. In contrast, the expression of IFN2-inducible genes was high in DM, IBM, and AS but low in IMNM. The expression of IFN-inducible genes correlated with the expression of genes associated with inflammation and muscle regeneration. Of note, ISG15 expression levels alone performed as well as composite scores relying on multiple genes to monitor activation of the IFN1 pathway in myositis muscle biopsies.

Conclusion: IFN1 and IFN2 pathways are differentially activated in different forms of myositis. This observation may have therapeutic implications since immunosuppressive medications may preferentially target each of these pathways.

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Abstract Number: 1291

Semi-Quantitative and Quantitative Evaluation of Magnetic Resonance Imaging in Patients with Idiopathic Inflammatory Myopathies – a Subanalysis of the Prometheus Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Muscle Biology, Myositis & Myopathies Poster II
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Background/Purpose: Prometheus study was a prospective, randomized, assessor-blind multicenter trial, comparing the efficacy and safety of the glucocorticoid (GC) monotherapy versus combination therapy with methotrexate (MTX) and GC in patients with polymyositis (PM) and dermatomyositis (DM). Muscle MRI has been used to assess disease activity and response to treatment. To assess MRI findings two different methods were used: semi-quantitative scoring system and quantitative assessment using manual measuring tool and picture analysis provided by TomoCon® Workstation.

Methods: For semi-quantitative assessment of edema, we used scoring 0, 1, 2, and 3 according to intensity of signal in each of the 16 thigh muscles. Muscle damage was evaluated in three basic thigh muscle compartments and pelvic muscles using Goutallier grading (0 – 5) based on extent of fatty replacement. Both sides were assessed by two evaluators, an average was made for each muscle, and values were summed up in the total score (MRI Semi-Quantitative total edema score = MRI S-Q TES). TomoCon® software provides pixel analysis in manually selected regions of interest. Manual muscle test (MMT8) and CK were measured and patient's global assessment (PGA), physician's GA (PhGA) and muscle disease activity (MDA) were recorded on visual analogue scales.

Results: Seventeen patients had MR images taken before the baseline visit, 8 had also the second MRI after 3 months of therapy. There was a significant reduction of MRI S-Q TES after 3 months in patients with PM and DM (from the mean 17.4 points, SD 13.7 to 8.0 points, SD 12.3; p=0.025). No significant progression of fatty atrophy was observed (from 16.0 points, SD 8.8, to 19.4, SD 4.6; p=0.3). At baseline, a significant correlation between MRI S-Q TES and PGA was noted (p=0.027). There was also a borderline negative association of MRI S-Q TES with muscle strength evaluated by MMT 8 (p=0.053). We noted a significant association between MRI S-Q TES and MRI Quantitative total edema score (MRI Q TES) (p=0.04) as well as between semi-quantitative and quantitative edema scores comparing individual muscles (p=0.0004). There was also a borderline association of MRI S-Q TES with MRI atrophy score (p=0.061). In a subset of 8 patients with longitudinally performed two MRI evaluations we found a good correlation between initial MRI S-Q TES and the level of serum CK (p=0.028). However, no correlation was seen between the level of improvement in MRI S-Q TES and drop in CK or with any other clinical parameters after 3 months of treatment.

Conclusion: Compared to the results of established semi-quantitative scoring method we demonstrated a good reliability of newly proposed quantitative evaluation system of muscle edema. This system was applied to record degree of muscle edema in a subpopulation of patients with PM and DM, treated in the clinical study. A significant association between MRI S-Q TES and MRI Q TES was found. Correlations of MRI scores with clinical and laboratory parameters were demonstrated.

Acknowledgements: Supported by the project (Ministry of Health, Czech Republic) for conceptual development of research organization 00023728 (Institute of Rheumatology).

Disclosure: K. Kubinova, Ministry of Health, Czech Republic, project 00023728, 2; **J. Vencovský**, projeMinistry of Health, Czech Republic, project 00023728, 2.

Abstract Number: 1292

Abnormal High Density Lipoprotein Particle Size and Number in Idiopathic Inflammatory Myopathies

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Muscle Biology, Myositis & Myopathies Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Vascular inflammation and damage are implicated in the pathogenesis of idiopathic inflammatory myopathies (IIM), particularly dermatomyositis (DM). High and low density lipoprotein (HDL, LDL) particles strongly influence the vascular endothelium, but little data has characterized these particles in IIM patients. The current work evaluates standard cholesterol levels as well as the particle number and size of HDL, LDL and very low density lipoproteins (VLDL) in IIM patients compared to healthy controls.

Methods: In a cross sectional analysis of 87 patients with IIM and 47 healthy controls (HC), we measured the quantitative lipoprotein profile by nuclear magnetic resonance spectroscopy (NMR). Cardiovascular risk factors and medications were obtained by questionnaire/chart review, and inflammatory markers and autoantibodies (ab) were measured by standard methods. Myositis disease activity was assessed using physician global 100 mm visual analogue scales (VAS) and CPK levels.

Results: The majority of patients in the IIM group had DM with a mean disease duration of 5 years and moderate disease activity (Table 1). Traditional fasting cholesterol levels were generally similar between patients with IIM and HC with mildly elevated triglycerides in the IIM group. Multiple differences in particular size and number including higher LDL particle number (LDL-P), larger HDL and VLDL size, and lower HDL particle number (HDL-P) were noted between IIM patients and HC. Multivariate (MV) models adjusted for demographics, factors known to affect lipid particle size/number (hypertension, diabetes, body mass index, statin use) and variables different in univariate comparison (ESR), were constructed for each significant lipid variable in table 1. Larger HDL size was strongly associated with IIM diagnosis, and smaller HDL-P was associated with disease activity in MV models. Triglycerides, LDL-P number and VLDL size were no longer associated with IIM diagnosis or disease activity in MV analysis. Patients with p155/140 ab had significantly larger HDL size, and patients with MDA5 ab had significantly lower HDL-P compared to patients without ab.

Mean(SD) unless specified, T test or Wilcoxon rank sum test for continuous variables, chi-square test or Fisher's exact test for categorical variables, *ab data available in 61 IIM patients

N=78 IIM patients with physician global disease activity VAS availableFigure 2_revised

Table 3. Multiple Linear Regression Models for Lipid Outcomes

Variables	HDL-P model				HDL size model			
	Total group (N=134)		IIM group (N=87)		Total group (N=134)		IIM group (N=87)	
	β	p	β	p	β	p	β	p
IIM vs controls	-1.4	0.40	-		0.4	**0.001**	-	
Physician global disease activity VAS (0-10cm)	-		-1.3	**0.01**	-		0.003	0.94
Age, every 10yrs	0.6	0.19	0.5	0.41	0.01	0.81	-0.001	0.98
Gender, Female (vs Male)	0.5	0.76	2.0	0.31	0.4	**0.001**	0.4	**0.01**
Race, White (vs non-white)	2.6	0.07	3.6	**0.04**	-0.1	0.45	-0.2	0.24
Hypertension, yes	-0.9	0.69	-0.2	0.94	0.3	0.07	-0.4	0.05
Diabetes, yes	4.1	0.20	8.7	**0.03**	0.3	0.21	0.3	0.29
Body mass index, kg/m^2	0.004	0.96	-0.2	0.17	-0.01	0.38	-0.01	**0.60**
Statin use, yes	0.2	0.94	-6.2	0.11	-0.13	0.49	-0.1	0.79
ESR every 10mm/hr	-1.0	**0.003**	-0.9	**0.01**	-0.01	0.66	-0.02	0.35
Prednisone, mg/day	-		0.03	0.41	-		0.004	0.30

Conclusion: In a cross sectional analysis of IIM patients and healthy controls, larger HDL size was strongly associated with IIM diagnosis, and lower HDL-P was associated with higher physician global disease activity by VAS. Altered HDL size and particle number have previously been associated with vascular risk, and further work is needed to evaluate their role in vascular damage in patients with IIM.

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Abstract Number: 1293

Multiple Subpopulations of Lymphocytes Were Absolutely Decreased in Dermatomyositis/polymyositis Patients and Restored by Low-dose IL-2

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

Background/Purpose: Dermatomyositis (DM) and polymyositis (PM) are rare chronicinflammatory disorders with significant associated morbidityand mortality despite treatment, characterized by subacute onset of proximal muscle weakness, elevated muscle enzymes, and inflammatory infiltrates on muscle biopsy. Although several hypotheses

have been proposed for triggers of inflammation in the diseases, growing evidences have focused on the immune disorders. However, the quantitative changes of lymphocyte subsets in DM/PM are unclear and whether low-dose IL-2 could rebalance the lymphocyte subsets and further benefit to remission disease activity of DM/PM patients is unknown. This study aimed to investigate the quantitative status of peripheral blood lymphocyte subsets in the patients for the exploration of pathogenesis and evaluate the safety and efficacy of low-dose IL-2 therapy in patients with DM/PM.

Methods: From February 2016 to October 2018, total 147 patients with PM/DM and 128 gender and age matched healthy individuals were enrolled in this study. The absolute numbers of T, B, NK, CD4+T, CD8+T, Th1, Th2, Th17 and Treg cells in peripheral blood of these individuals were detected by flow cytometry combined with standard absolute counting beads. Patients in IL-2 group (n=31) were not only given traditional treatments, but injected subcutaneously human IL-2 (aldesleukin) at 50 WIU per day for a 5-day course. The demographic features, clinical manifestations and laboratory indicators were compared before and after the treatment.

Results: Patients with PM/DM had lower levels of Treg cells as well as T, CD4+T, CD8+T, Th1, Th2, and Th17 compared with those of the healthy controls ($P < 0.05$), which was correlated with disease activity($P < 0.05$).

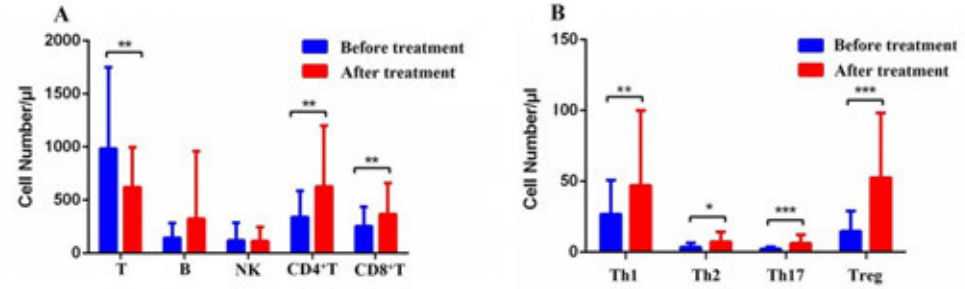

Figure 2: Changes of peripheral lymphocyte subsets after different treatments (n=31). Absolute numbers of T, CD4+T, CD8+T, Th1, Th2, Th17 and Treg cells in patients were significantly increased after treatment. *P<0.05, **P <0.01, ***P <0.001.

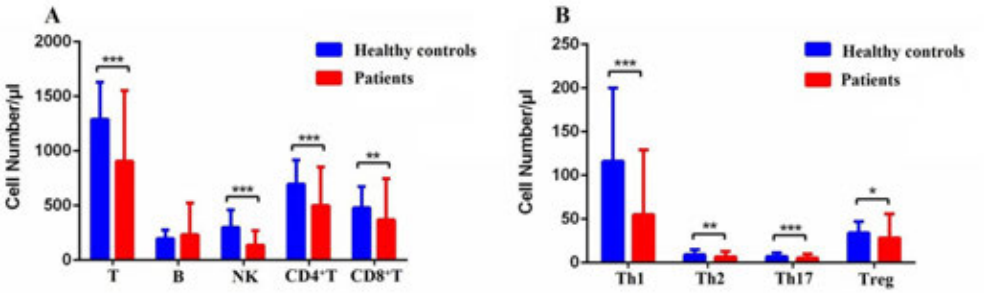

Figure 1: Comparison of absolute numbers of peripheral lymphocyte subsets between patients with PM/DM (n=147) and health controls (n=128). All the lymphocytes subpopulations were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired *t*-test. Patients had lower levels of T, NK,CD4+T, CD8+T, Th1, Th2, Th17 and Treg cells in PB compared with those of healthy controls. *P < 0.05, **P <0.01, ***P <0.001.

After IL-2 administration, the absolute numbers of peripheral lymphocyte subsets in patients were significantly increased ($P < 0.05$), leading to a better remission compared with the patients received conventional therapy ($P < 0.05$).

Conclusion: The difference status of peripheral lymphocyte subsets, especially Tregs, between PM/DM patients and healthy individuals suggests that lymphocyte subsets may be involved in and play an important role in the pathogenesis of patients. Low-dose IL-2 can effectively increase the level of Treg cells as well as other lymphocytes to some degree and maintain the immunologic balance, which may help for PM/DM patients' symptoms remission without over-treatment and evaluated side effect. But long-term benefits of IL-2 therapy are required to further study.

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Abstract Number: 1294

Alterations in Activin A-Myostatin-Follistatin System Associate with Disease Activity in Inflammatory Myopathies

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Muscle Biology, Myositis & Myopathies Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study was to investigate myokines involved in muscle atrophy such as myostatin, follistatin and activin A, in idiopathic inflammatory myopathies (IIM). Recent findings show that rather than myostatin alone, the activin A-myostatin-follistatin system is believed to play an important role in musculoskeletal growth, development and aging. The myostatin biology known by now encourages considering its blocking therapy in IIM as the muscle weakness and atrophy persist in patients even after the suppression of inflammation.

Methods: A total of 94 patients with IIM and 155 healthy controls (HC) were enrolled in the study. Apart from serum samples taken during regular patients' visits, 20 IIM patients and 21 HC underwent a muscle biopsy. Circulating concentrations of myostatin, follistatin, activin A and TGF-β1 were assessed by ELISA. The expression of myokines and associated genes involved in myostatin signalling pathway in muscle tissue was determined by real-time PCR using TaqMan® Gene Expression Assays.

Results: We report decreased levels of circulating myostatin (2024±1111 vs. 2647±792 pg/ml; p=0.0003) and increased follistatin (1542±564 vs. 1332±670 pg/ml; p=0.008) in IIMs compared to HC. Activin A levels were higher in IIM (394±142 vs. 334±132 pg/ml; p=0.013) compared to controls while no significant difference was observed for serum TGF-β1. Myostatin was significantly correlated to disease activity measures such as muscle disease activity (muscle DA) (r=-0.289, p=0.015) and manual muscle testing of 8 muscles (MMT8) (r=0.366, p=0.002). On the other hand, follistatin correlated positively with muscle DA (r=0.235, p=0.047). Gene expression analysis showed higher follistatin (p=0.040) and myostatin inhibitor FSTL3 (p=0.008) levels and lower expression of activin receptor type 1B (ALK4) (p=0.034), signal transducer SMAD3 (p=0.023) and atrophy-related E3 ligase atrogin-1 (p=0.0009) in IIM muscle tissue compared to controls.

Conclusion: The findings of this study contradict the expected pattern of activin A-myostatin-follistatin system in muscle wasting diseases by showing lower myostatin and higher follistatin in circulation and attenuated expression of ALK4, SMAD3 and atrogin-1 in skeletal muscle of patients with inflammatory myopathies, suggesting the existence of an internal mechanism aimed at reducing further loss of muscle proteins during myositis. Furthermore, we show that the activin A-myostatin-follistatin system disturbance is more profound in patients with more active disease.

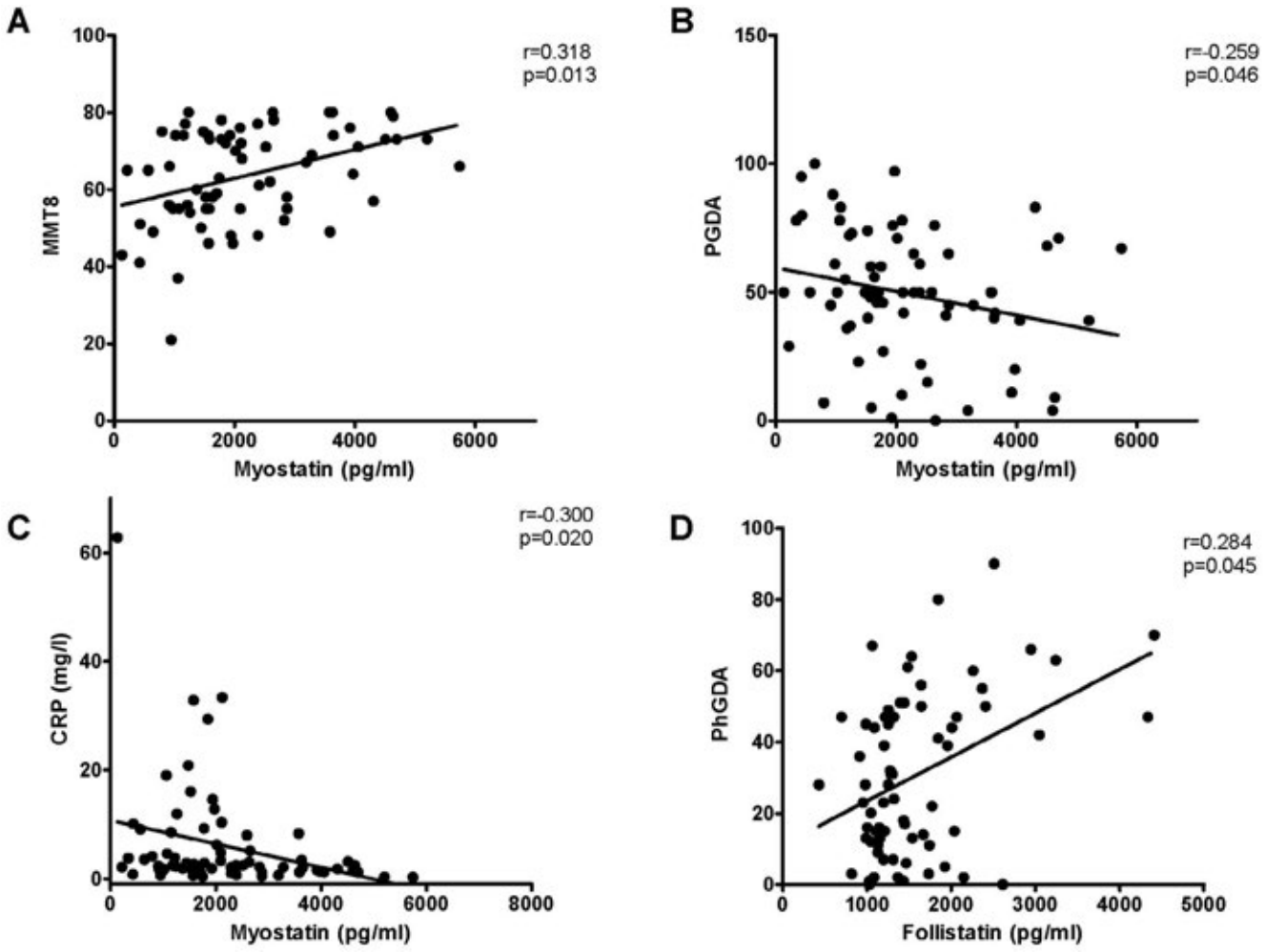

Figure 2_revised

The associations of serum myostatin (A, B, C) and follistatin (D) levels with clinical parameters in IIM patients. Correlation coefficients and significance levels displayed in scatterplots were calculated by partial correlation analysis with correction for age, BMI and glucocorticoid dose. MMT8 - Manual muscle testing of 8 muscles; PGDA - Patient's global assessment of disease activity; CRP - C-reakctive protein; PhGDA - Physician's global assessment of disease activity.

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Abstract Number: 1295

Otoferlin Is Increased in Muscle and PBMCs from Untreated Children with Juvenile Dermatomyositis: Possible Association with Decreased Circulating Natural Killer Cells

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Background/Purpose: Juvenile Dermatomyositis (JDM) is a rare inflammatory myopathy in which the immunoregulatory control is not well understood. Collaboration with A.R. French, MD/PhD, documented the hypophosphorylation of phophplipaseCγ2 in Natural Killer (NK-CD3-CD16/56+) cells from untreated JDM (JCI Insight 123236, 2018). This investigation evaluates JDM skin, muscle and blood for the presence of Otoferlin. Otoferlin is a member of the dysferlin family, and has strong Ca^{+2} binding ability in its C2 domain. Among other potential targets, NK cells utilize calcium flux to discharge their granules which create pores and inflict cellular damage. The goal of this study was to validate the increased Otoferlin levels in JDM tissues and determine the possible association between levels of Otoferlin and NK cells in blood drawn from untreated JDM.

Methods: After obtaining age-appropriate informed consent (IRB# 2008-13457), the JDM child's clinical variables, including age, gender, duration of untreated disease (DUD) and Disease Activity Scores (DAS skin, muscle total), were entered into REDCap. The study had 2 phases: 1) *discovery* by RNASeq of increased tissue based Otoferlin in untreated JDM skin, muscle and blood compared to healthy controls. The RNASeq study also compared healthy children's peripheral blood mononuclear cells (PBMCs) with those from active, untreated JDM (n=11) and 7 samples when the same child was clinically quiescent. Otoferlin levels were determined at both time points by qRT-PCR; 2) *validation,* by qRT-PCR of the increased Otoferlin in a larger cohort of 23 untreated JDM PBMCs (2 had no NK values); definite/probable JDM, mean age7.33 (±4.16), 90.5% female, 90.5% white compared with sera from 15 age-gender -matched healthy controls. The data were analyzed by Pearson correlation and student's T test.

Results: These studies confirmed that the 21 untreated active JDM had decreased circulating NKs in 71.4%. NK cell # was inversely associated with increased serum concentrations of Otoferin, p=0.008; Pearson's correlation coefficient=-0.556. The serum levels of Otoferlin were not associated with the age, gender or DUD of the children with JDM, but were highly associated with the DAS-muscle, p=0.0036, but not skin (p=0.94); or total (p=0.10). Otoferlin was increased in PBMCs from untreated active, but not treated inactive JDM, p=0.00056.

Conclusion: Conclusion: We have documented a new component in the pathophysiology of untreated JDM—Otoferlin–which is increased in JDM muscle > PBMCs > controls, and appears to be associated with decreased NKs. Speculation: Otoferlin, perhaps by virtue of its Ca+2 binding capacity and interaction with lipid membranes, may contribute to both NK dysfunction and distribution in untreated children with active JDM.

Disclosure: L. Pachman, Reveragen, 2, SBIR grant Eric P. Hofffman, PhD RevaraGen, unrelated.,, 9; **W. Marin**, None; **G. Morgan**, None; **M. Curran**, None; **K. Ardalan**, None; **C. Huang**, None; **E. Roberson**, None.

Abstract Number: 1296

Increased MxA Protein Expression and Dendritic Cells in Spongiotic Dermatitis Differentiates Dermatomyositis from Eczema

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Dermatomyositis (DM) is conventionally characterized by interface dermatitis (ID) on skin histopathology. A subset of patients with clinically diagnosed DM have skin biopsies showing spongiotic dermatitis (SD), a histopathology more commonly seen in eczema. Diagnosis of DM is challenging, with significant delays following initial presentation. Our goals were as follows: 1) to identify the percentage of clinically diagnosed DM patients with skin biopsies showing SD, 2) to identify cytokine and cell markers that can determine if a skin biopsy showing SD is consistent with DM in a patient with clinical DM.

Methods: Biopsies from 10 DM patients with SD histopathology (DM-SD) were compared to biopsies from 10 healthy controls, 10 patients with eczema, and 12 DM patients with ID histopathology (DM-ID). Skin biopsies were stained by H&E and by immunohistochemistry for MxA, IFN-β, CD11c (mDC), and BDCA2 (pDC). Mucin expression was assessed using Hale's iron colloidal stain. Cytokines and mucin were quantified as area percent and mean intensity. Cells were quantified as mean number of cells per high power field. Fisher's exact test was used to compare baseline patient characteristics. One-way ANOVA with Bonferroni's multiple comparison test was used to compare protein expression between groups.

Results: 11 of 164 (6.7%) patients with a clinical diagnosis of DM at our tertiary care center were identified as having SD. MxA, IFN-β, CD11c (mDC), and BDCA2 (pDC) protein expression was significantly higher in DM-SD compared to eczema ($p < 0.01$) and healthy controls ($p < 0.0001$) (Fig. 1, 2). Expression of MxA, IFN-β, and BDCA2 were not significantly different between DM-SD and DM-ID (Fig. 1, 2). Eosinophils identified on H&E were not significantly dif-

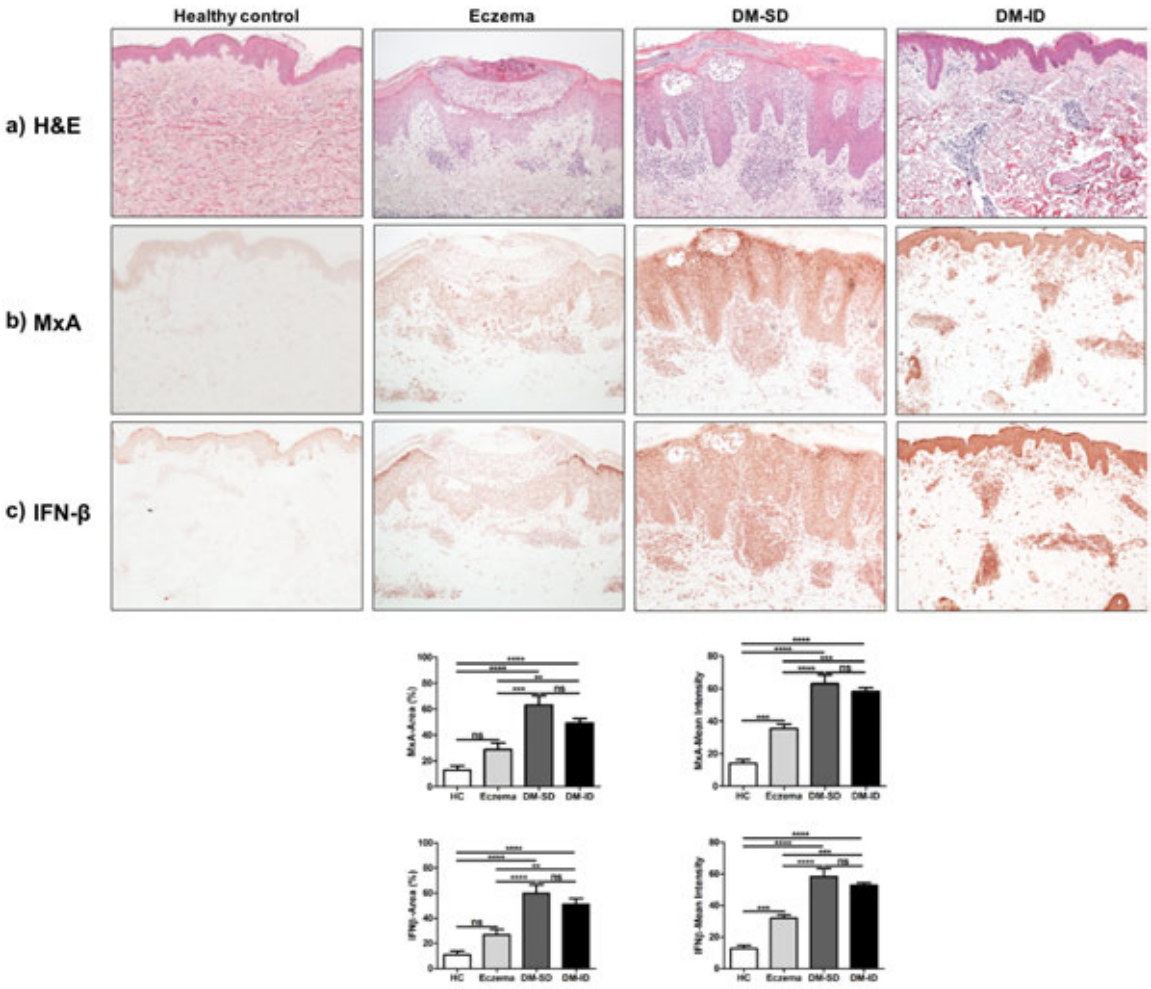

Figure 1. Comparison of skin biopsies from healthy controls, and patients with eczema, DM-SD, and DM-ID. a) H&E stain; b) MxA immunohistochemical protein expression; and c) IFN-b–β immunohistochemical protein expression. Note: All images at 10x objective magnification. Area and intensity values represent both epidermis and dermis. Data are displayed as group mean ± SEM.

ferent between DM-SD and eczema patients, although both were significantly higher compared to healthy controls and DM-ID ($p < 0.01$) (Fig. 2). Mucin was not significantly different between eczema, DM-SD, and DM-ID, although all were significantly elevated compared to healthy controls ($p < 0.0001$).

Conclusion: MxA, IFN-β, CD11c (mDC), and BDCA2 (pDC) protein expression were significantly higher in DM-SD compared to eczema skin lesions. These markers can therefore be helpful to distinguish between DM-SD versus eczema.

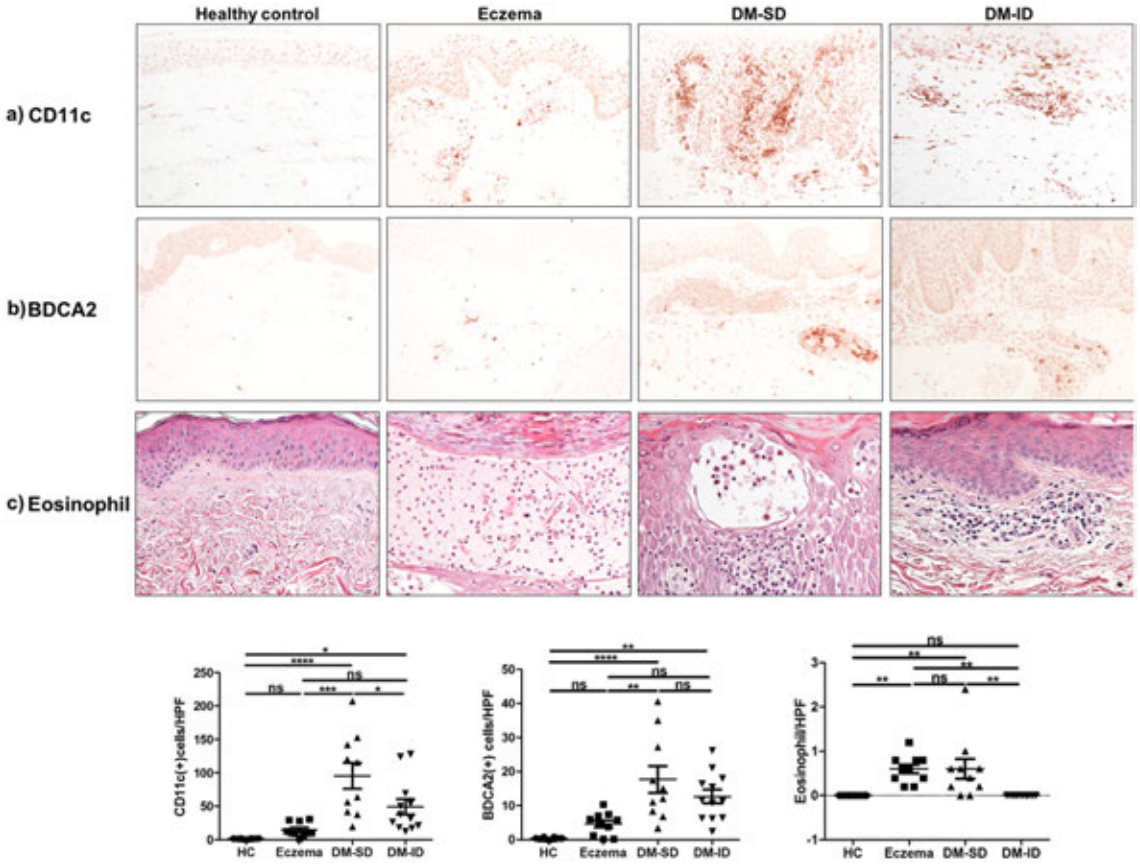

Figure 2. Comparison of cell types in skin biopsies from healthy controls, and patients with eczema, DM-SD, and DM-ID. a) CD11c immunohistochemical protein expression; b) BDCA2 immunohistochemical protein expression; c) Eosinophils on H&E 40x stain. Note: All other images at 10x objective magnification. CD11c is a marker for myeloid dendritic cells and BDCA2 is a marker for plasmacytoid dendritic cells. Data are displayed as group mean ± SEM.

Disclosure: M. Zeidi, None; **K. Chen**, None; **B. Patel**, None; **R. Lim**, None; **V. Werth**, Biogen, 2, 5, Corbus Pharmaceuticals, 2, 9, University of Pennsylvania, 9.

Abstract Number: 1297

Increased Hsp90 in Plasma and Muscle Tissue Associates with Disease Activity and Skeletal Muscle Involvement in Idiopathic Inflammatory Myopathies

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SESSION INFORMATION

Session Date: Monday, November 11, 2019
Session Title: Muscle Biology, Myositis & Myopathies Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Heat shock proteins (Hsps) are chaperones playing important roles in skeletal muscle physiology, adaptation to exercise or stress, and activation of inflammatory cells.

The aim of our study was to assess Hsp90 expression in muscle biopsies and plasma of patients with idiopathic inflammatory myopathies (IIM) and to characterize its association with IIM-related features.

Methods: Total of 277 patients with IIM (198 females; mean age 54.8; disease duration 4.1 years; dermatomyositis (DM, 104)/polymyositis (PM, 108)/cancer associated myositis (CAM, 31)/ necrotizing myopathy (IMNM, 25) and 157 healthy individuals (92 females; mean age 47.0) were included in plasma analysis. Muscle biopsy samples (PM, DM, IMNM, myodystrophy, myasthenia gravis) were stained for Hsp90α (Thermo Fisher Scientific, USA) and Hsp90β (Abcam, UK). Plasma Hsp90 was measured by ELISA kit (eBioscience, Vienna, Austria). The cytokines were performed using Bio-Plex Pro™ human Cytokine 27-plex Assay (BIO-RAD, California, USA .Data are presented as median.

Results: In muscle biopsies, Hsp90 expression of both subunits was higher in IIM than in controls. Increased Hsp90 was detected in perifascicular degenerating and regenerating fibers, inflammatory cells (DM, PM), and necrotic and regenerating fibers (IMNM). Plasma Hsp90 levels were increased in IIM patients compared to healthy controls ($p< 0.0001$), and in individual subgroups of IIM vs. healthy controls ($p< 0.0001$ for all) (Tab1). When adjusted for age and sex, these differences remained still significant ($p< 0.0001$). Hsp90 was higher in males compared to females ($p=0.040$) and in patients with ILD ($p=0.003$), with cardiac involvement ($p=0.004$), with dysphagia ($p=0.018$) and with presence of anti-Ro52 autoantibodies ($p=0.036$) (Tab2). Hsp90 levels in all patients positively correlated with muscle enzymes (Tab.3). Increased Hsp90 was associated with disease activity and skeletal muscle involvement (Tab.3). Interestingly, out of all clinical parameters listed in above-mentioned univariate analysis, in multiple regression analysis Hsp90 levels in IIM patients were significantly affected by muscle enzymes only ($p< 0.0001$, $\beta=0.345$). Furthermore, Hsp90 positively correlated with some crucial cytokines involved in pathogenesis of myositis (Tab.3).

Conclusion: We demonstrate increased Hsp90 expression in IIM muscle biopsy samples, specifically in inflammatory cells, degenerating, regenerating and/or necrotic fibers. Increased Hsp90 plasma levels in IIM patients are associated with disease activity and damage, and with the involvement of proximal skeletal muscles, heart and lungs.

Tab.1

Characteristics	Median (IQR)
ZK	9.76 (7.5 – 13.8)
IZM	55.9 (46.9 – 62.5)
DM	22.0 (14.1 – 41.2)
PM	19.7 (14.3 – 42.2)
CAM	18.9 (11.7 – 29.7)
IMNM	19.6 (16.3 – 45.5)

Tab.2

Clinical parameters	(+) median (IQR)	(-) median (IQR)
Gender (+ female/ - male)	19.6 (13.4 – 35.6)	25.3 (15.6 – 50.0)
+ ILD / -ILD	25.4 (15.5 – 50.7)	18.9 (12.8 – 30.3)
+ CI / - CI	27.5 (18.1 – 51.5)	19.3 (13.3 – 39.3)
+ dysphagia / - dysphagia	25.0 (15.9 – 50.0)	18.2 (13.4 – 34.3)
+ Ro52 / - Ro52	29.5 (55.4 – 15.5)	19.2 (13.9 – 31.5)

Tab.3

Clinical parameters	Spearman's r	p – value
LDH	0.554	< 0.0001
AST	0.383	< 0.0001
ALT	0.181	0.003
PtDGA – Patient's disease activity	0.223	< 0.001
PhDGA – Physician's disease activity	0.217	< 0.001
MITAX – Myositis intention to treat activity index	0.175	0.004
MYOACT – Myositis disease activity assessment visual analogue scales	0.159	0.012
Pulmonary disease activity	0.201	0.001
Muscle disease activity	0.146	0.018
MMT8 (manual muscle test 8), total score	-0.126	0.042
- m. biceps brachii	-0.125	0.043
- m. gluteus maximus	-0.159	0.011
- m. iliopsoas	-0.143	0.023
MDI – Myositis damage index – extent	0.215	0.003
MDI – Myositis damage index – severity	0.150	0.041
MDI – Myositis damage index – extension	0.187	0.011
Current Prednisone equivalent dose	0.183	0.006
Cytokines		
IL-1b	0.188	0.002
IL-2	0.269	< 0.0001
IL-4	0.190	0.002
IL-6	0.182	0.003
IFN-γ	0.229	< 0.0001

Acknowledgement: Supported by AZV-16-33542A, MHCR 023728 and SVV – 260373.

Disclosure: H. Storkanova, None; **S. Oreska**, None; **M. Spiritovic**, None; **B. Hermankova**, None; **O. Kryštůfková**, None; **H. Mann**, None; **M. Komarc**, None; **J. Zamecnik**, None; **K. Pavelka**, AbbVie, 8, Abbvie, 5, 8, Amgen, 5, 8, BMS, 8, Egis, 5, 8, Lilly, 5, 8, MSD, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 8; **J. Vencovsky**, None; **L. Senolt**, None; **M. Tomcik**, None.

Abstract Number: 1298

A Randomised Clinical Trial of *Curcuma Longa* Extract for Treating Symptoms and Effusion-Synovitis of Knee Osteoarthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Osteoarthritis – Clinical Poster I

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

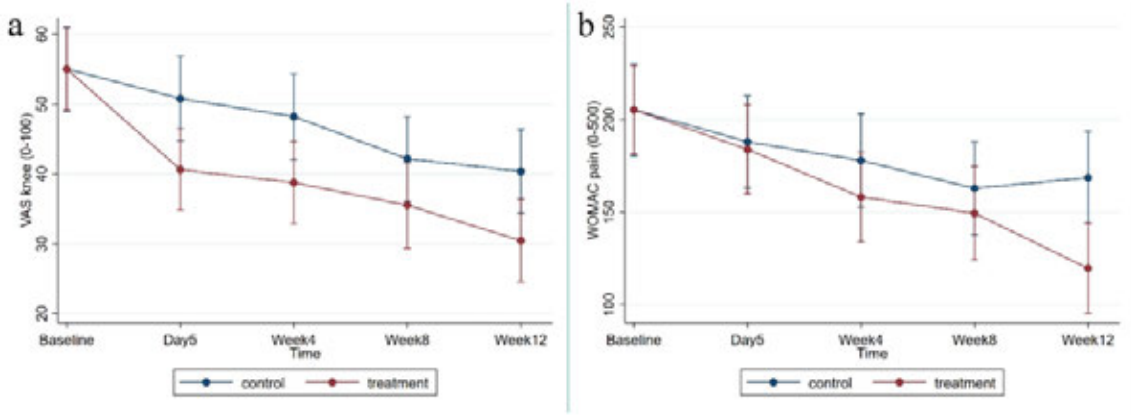

Figure 1. Change in knee pain over 12 weeks in the treatment and placebo groups a) VAS Pain; b) WOMAC pain

Background/Purpose: Pharmacological therapies are limited, associated with off-target effects, are frequently contraindicated, and only modestly effective for pain in osteoarthritis (OA). Effusion and synovitis are common in OA and are associated with symptomatic and structural progression of OA. *Curcuma longa* (Turmeric) extract has anti-inflammatory effects and is gaining popularity in the treatment of OA despite the lack of high-quality evidence. The CurKOA trial aimed to compare the efficacy of *Curcuma longa* extract versus identical placebo for treating knee pain and effusion-synovitis in an inflammatory phenotype of OA identified using ultrasound scan.

Methods: In this double-blind trial, we randomised 70 participants with significant knee pain (≥40 mm knee pain on visual analogue score [VAS] scale), knee OA (ACR clinical criteria) and presence of a moderate amount of ultrasound-defined effusion/synovitis (≥4 mm thickness in the suprapatellar region) to receive *Curcuma longa* extract (80% Turmerosaccharides and 20% Curcumin extract, 2x500 mg capsules/day) (n=36) or identical placebo (n=34) for 12 weeks. The primary outcome measures were change in knee pain (assessed by VAS) and MRI-defined effusion-synovitis volume over 12 weeks. Secondary outcomes included changes in knee pain and function (WOMAC), OARSI-OMERACT treatment responders and change in T2 relaxation time (milliseconds, ms) of the cartilage. Linear mixed-effects models were used, with adjustment for baseline values of the outcome measure.

Results: Of the 112 participants screened, a total of 70 participants (age 61.8±8.6 years, 56% female) were randomised, and 68 (97%) completed the 12 week assessments.

Primary outcomes: There was a reduction in VAS knee pain in the treatment (-23.75 [-29.78 to -17.73]) and placebo (-14.64 [-20.80 to -8.47]) group, with a significant between-group difference of -9.11mm [-17.79 to -0.44] (Figure 1a) equivalent to a standard effect size of 0.49. There was a reduction in the MRI assessed effusion-synovitis volume in the treatment (-2.38 mL [-4.09 to -0.68]) and placebo (-3.63 mL [-5.39 to -1.88]) group, with no significant between-group difference (1.25 mL [-1.21 to 3.72]).

Secondary outcomes: Significant changes favouring the treatment group were seen in WOMAC knee pain (between-group difference: -47.22 [-81.22 to -13.22]) (Figure 1b), WOMAC function (between-group difference: -112.26 [-222.79 to -1.74]) and OARSI-OMERACT treatment responders (63% in the treatment group and 38% in the placebo group [Risk Ratio, RR=1.64 (1.00 to 2.70)]. No significant change in T2 relaxation time of the femoral cartilage (average values of T2 relaxation time between group difference -0.38 ms [-1.10 to 0.34]) was seen. The number of adverse

events was similar in the treatment (n=18) and placebo (n=29) groups, and there were no adverse events related to the treatment.

Conclusion: *Curcuma longa* extract significantly improved knee pain in an inflammatory phenotype of knee OA patients over 12 weeks. There was a moderate standard effect size of the treatment which appears greater than other conventional pharmacological therapies. In this short term study, *Curcuma longa* extract had no effect on knee structural measures assessed using MRI.

Disclosure: Z. Wang, None; **G. Jones**, None; **T. Winzenberg**, None; **G. Cai**, None; **L. Laslett**, None; **D. Aitken**, None; **I. Hopper**, None; **R. Jones**, None; **C. Ding**, None; **J. Fripp**, None; **B. Antony**, None.

Abstract Number: 1299

Clinical Significance of Magnetic Resonance Imaging Derived Femur Bone Shape in Young Adults

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The femur bone shape derived from magnetic resonance imaging (MRI) of the knee is associated with the incidence and progression of knee osteoarthritis (OA), and predicts total knee replacement in older adults. However, the clinical significance of the femur bone shape has not been studied in a population-based young adult sample. This study aims to describe whether three-dimensional (3D) femur bone shape derived from knee MRI is associated with knee symptoms in young adults.

Methods: Participants (n = 180, age 31 to 41 years) were selected from the Childhood Determinants of Adult Health (CDAH) Knee Cartilage Study, which was a follow-up of the CDAH study. Participants' knee symptoms were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaires, and participants underwent a 1.5T MRI scan of their knee. T1-weighted, fat suppressed, 3D SPGR MRI sequences were segmented with an active appearance model (AAM) previously constructed and validated in an Osteoarthritis Initiative study. The femur bone shape found by AAM is projected orthogonally onto a femur shape vector to obtain a vector score. The femur shape vector defined 0 as the average healthy femur shape and higher values in the positive direction portray more likeness to OA with each unit representing one standard deviation. Logistic regressions were used to describe the associations between the highest quartile of femur shape vectors (OA-like shape) with demographic factors and WOMAC knee symptoms.

Results: Participants had a mean age of 35.5±2.8 years, mean BMI of 25.1±4.1 kg/m^2, were 51% male and largely asymptomatic (34% with any knee pain). The highest quartile of femur vector scores–the group considered to have

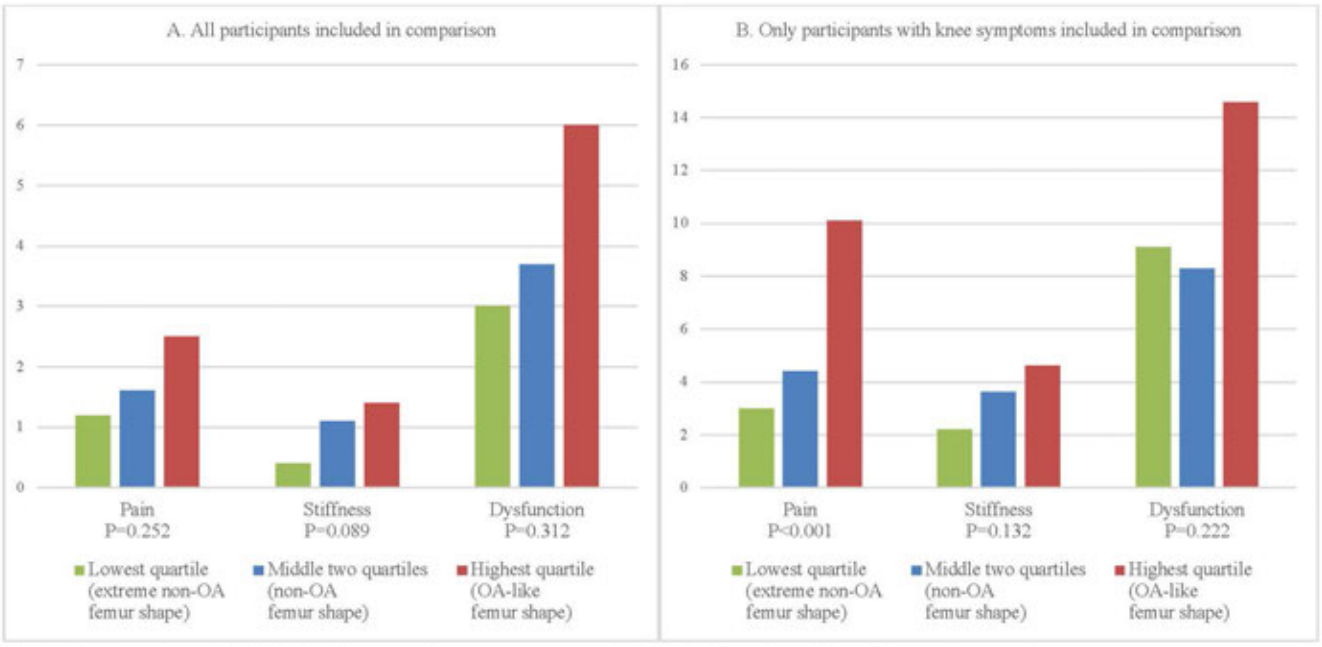

Figure 1. Comparisons of WOMAC knee symptoms among young adults in different quartiles of femur shape vector scores

*** bar graphs show the average total WOMAC pain, stiffness and dysfunction scores for each group**

an OA-like femur shape–had vector scores higher than +0.40. OA-like femur shape was not associated with age (OR 0.96, 95% CI 0.85 to 1.09), gender (OR 1.93, 95% CI 0.95 to 3.93), or body-mass index (OR 1.05, 95% CI 0.97 to 1.14). There was no association between OA-like femur shape and total WOMAC pain (OR 1.06, 95% CI 0.97 to 1.15), total WOMAC stiffness (OR 1.08, 95% CI 0.93 to 1.25) and total WOMAC dysfunction (OR 1.02, 95% CI 0.98 to 1.06) (Figure 1A). However, in symptomatic young adults, OA-like femur shape was associated with higher knee pain scores (OR 1.33, 95% CI 1.07 to 1.66) (Figure 1B).

Conclusion: OA-like femur bone shape is not associated with knee symptoms in population-based young adults. However, OA-like femur bone shape is associated with higher pain scores in young adults experiencing any knee pain.

Disclosure: M. Vo, None; **M. Bowes**, Imorphics (Stryker), 3, OrthoTrophix, 9; **A. Venn**, None; **F. Cicuttini**, None; **L. March**, BMS, 8, Janssen, 8; **T. Dwyer**, None; **T. Meng**, None; **M. Cross**, None; **G. Jones**, None; **S. Balogun**, None; **C. Ding**, None; **B. Antony**, None.

Abstract Number: 1300

Predictor of Placebo Response in Hand Osteoarthritis: A Post Hoc Analysis of Two Randomized Controlled Trials

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) in hands is common in middle-aged and elderly population. The mainstay treatment of hand OA is to control the symptoms with a combination of non-pharmacological and pharmacological interventions. Prior randomized clinical placebo-controlled trials (RCT) involving patients with hand OA showed that placebo itself significantly improved pain in those patients. The objective of this post hoc analysis was to identify the factors associated with good placebo response in patients with hand OA.

Methods: This post hoc analysis of two double-blind, placebo-controlled, randomized trials investigating efficacy of GCSB-5 or diacerein in hand OA analyzed the efficacy of the placebo in patients with hand OA. The efficacy endpoints included the changes at baseline and 4 weeks for the following variables: AUSCAN (Australian/Canadian

Osteoarthritis Hand Index) pain score (0–100), AUSCAN stiffness score (0–100), AUSCAN function score (0–100), patient global assessment (0–100), physician global assessment (0–100). A clinically meaningful improvement in pain was defined as an improvement in AUCAN pain of 10 (0-100) or more.

Results: In RCT 1, the mean improvement in AUSCAN pain was -6.0 ± 19.7. However, the placebo-response varied markedly between the OA patients (range -76.4 to 33.2) from baseline. Clinically meaningful improvement in pain was observed in 37 (36.3%) patients. Patients with worse AUSCAN pain (44.9 ± 19.8 vs. 53.1 ± 19.0, p=0.044) and physician global assessment (38.9 ± 11.4 vs. 44.6 ± 14.8, p=0.031) at baseline was associated with clinical meaningful improvement. Structural joint changes such as tender, swollen, enlarged or deformed joint counts did not differ between placebo responders and non-responders. Pain improvement correlated with the respective pain level at baseline (r=0.155, p< 0.001). In a validation study with RCT 2, patients showed a similar placebo response. Improvement in pain, stiffness and function correlated with their respective baseline value in RCT 2 as well.

Conclusion: This post hoc analysis of two prospective, double-blind, randomized, placebo-controlled studies showed that clinically meaningful response to placebo was observed in up to one third of patients with hand OA. This positive placebo response was associated with high pain level at baseline. Further researches are needed to optimize and utilize the benefit of placebo response in OA.

Figure 1

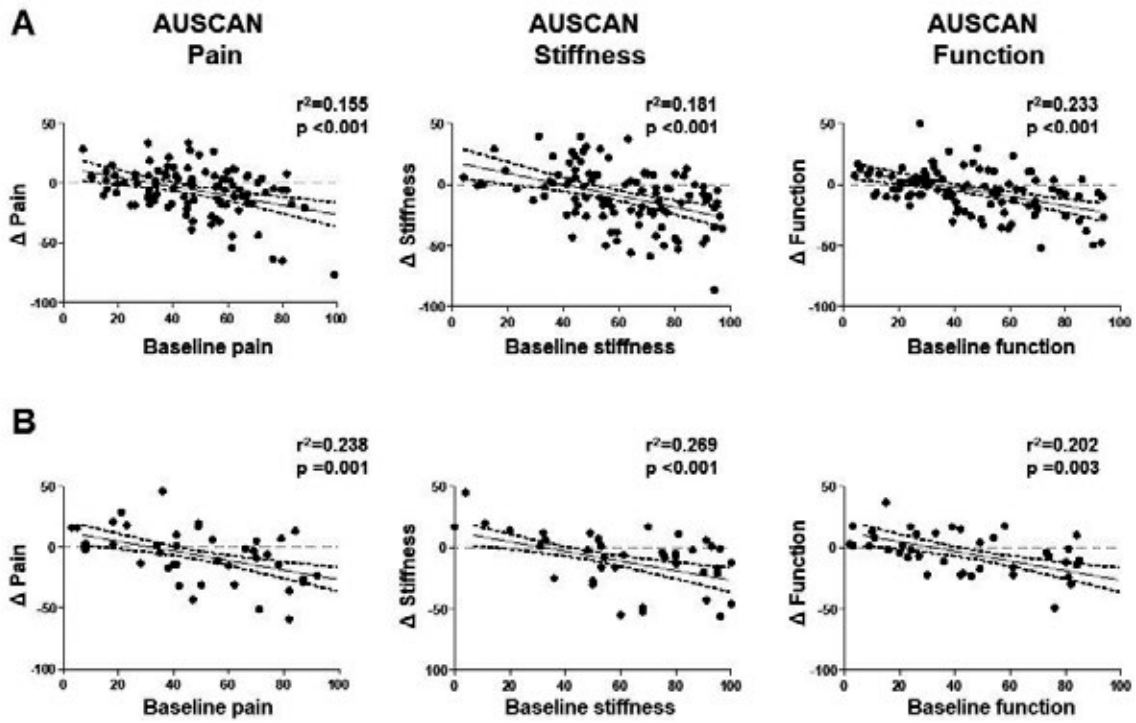

Figure 1. Correlation between pain, stiffness and function at baseline and placebo response in patients with hand osteoarthritis in RTC 1 (A) and RTC 2 (B). Correlation was examined using Pearson correlation.

Disclosure: S. Ahn, None; **J. Park**, None; **K. Shin**, None; **Y. Lee**, Seoul National University Bundang Hospital, 3; **Y. Song**, Astellas Pharma, Inc., 9; **Y. Choi**, None; **E. Lee**, Seoul National University Hospital, 3.

Abstract Number: 1301

Rates of Incident Radiographic Knee Osteoarthritis and Knee Replacement by Sex and Race, Across Three Large, Diverse Cohorts

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies have suggested differences in the development of incident radiographic knee osteoarthritis (RKOA) and the receipt of knee replacement (KR) by sex and race. We now have the opportunity to compare outcomes from three of the largest and most diverse osteoarthritis cohorts, that is, the Osteoarthritis Initiative (OAI), the Multicenter Osteoarthritis Study (MOST) and the Johnston County Osteoarthritis Project (JoCo OA). Our objective was to describe sex- and race-specific rates of incident RKOA and KR in OAI, MOST and JoCo OA.

Methods: Participants from OAI, MOST and JoCo OA with knees at risk of developing incident ROA (i.e., Kellgren-Lawrence Grade [KLG] 0 or 1 at baseline) or knees at risk for KR (KL 0 to 4 at baseline) were eligible for inclusion. Participants in all three cohorts underwent bilateral posteroanterior fixed-flexion weight-bearing knee radiographs with similar acquisition protocols. RKOA was defined as KLG ≥ 2. KR (i.e., total or partial) was verified by operative

Table 1. Baseline Characteristics, Rates of Incident RKOA and KR

	OAI (n=4796)	MOST (n=3026)	JoCo OA (n=3288)
Mean age (SD, range), years	61.2 (9.2) 45-79	62.5 (8.11) 50–79	62.1(9.0) 45-89
Women, n (%)	2804 (58.5%)	1820 (60.2%)	2216 (67.4%)
White, n (%)	3790 (79.1%)	2519 (83.2%)	2262 (68.8%)
African American (AA), n (%)	874 (18.2%)	464 (15.3%)	1026 (31.2%)
Other, n (%)	127 (2.7%)	43 (1.4%)	N/A
Mean BMI (SD), kg/m^2	28.6 (4.8)	30.7 (5.97)	30.8 (6.6)
KLG, knees			
0, n (%)	3471 (38.5%)	2521 (41.6%)	1312 (39.9%)
1, n (%)	1576 (17.5%)	1028 (17.0%)	1119 (34.0%)
2, n (%)	2376 (26.4%)	936 (15.5%)	359 (10.9%)
3, n (%)	1234 (13.7%)	1001 (16.5%)	268 (8.2%)
4, n (%)	295 (3.3%)	460 (7.6%)	144 (4.4%)
Knee replacement (KR), n (%)	58 (0.6%)	78 (2.6%)	86 (2.6%)
Not read/missing (n)	582	28	
Crude Risk of Incident Radiographic OA (RKOA)*			
	4920 knees	**3235 knees**	**2431 knees**
White women	324/2366 = 13.7%	382/1644 = 23.2%	217/1150 = 18.9%
AA women	77/438 = 17.6%	66/234 = 28.2%	97/476=20.4%
White men	190/1874 = 10.1%	214/1180 = 18.1%	112/606 = 18.5%
AA men	24/242 = 9.9%	34/177 = 19.2%	38/199 =19.1%
Crude Incident RKOA Rate per 1000 knee-years (95% CI)			
White women	29 (26 - 33)	36 (33 – 40)	32 (28 – 37)
AA women	41 (32 - 52)	46 (36 – 59)	35 (29 – 43)
White men	21 (18 - 24)	28 (25 – 32)	31 (26 – 38)
AA men	22 (15 - 34)	30 (21 – 43)	34 (25 – 46)
Adjusted Incident ROA Rate of per 1000 knee-years (95% CI)**			
White women	29 (26 - 32)	36 (32 – 40)	31 (27 – 36)
AA women	33 (26 - 43)	38 (29 – 48)	33 (27 – 41)
White men	19 (16 - 22)	26 (23 – 30)	32 (27 – 39)
AA men	19 (13 - 30)	29 (20 – 42)	30 (21 – 42)
Crude Risk of Knee Replacement (KR)			
	8723 knees	5889 knees	3202 knees
White women	266/3987=6.7%	401/2954 = 13.6%	42/1449=2.9%
AA women	45/1070=4.2%	60/588 = 10.2%	29/705=4.1%
White men	185/3177=5.8%	195/2017 = 9.7%	12/780=1.5%
AA men	16/489=3.3%	6/324 = 1.8%	2/268=0.7%
Crude Rate of KR per 1000 knee-years (95% CI)			
White women	12 (10 - 13)	16 (14 – 18)	5 (3 – 7)
AA women	8 (5 - 11)	9 (6 – 14)	7 (5 – 11)
White men	10 (9 - 12)	11 (9 – 13)	3 (1 – 5)
AA men	6 (4 - 11)	2 (0.8 – 4.9)	1 (0 – 5)

reports or on a subsequent knee x-ray. We used Poisson regression with ln(time) offset and robust standard errors to estimate rates of incident RKOA and rates of KR, adjusted for age and BMI.

Results: Baseline characteristics and results are summarized in Table 1. The baseline characteristics were similar between OAI (n=4796) and MOST (n=3026). JoCo OA (n=3288) had a larger proportion of women, African Americans (AA), and milder disease (i.e., proportionately more KLG 1 at baseline) due to its population-based nature. The sex- and race-specific rates of incident RKOA were comparable in JoCo OA, whereas rates of incident RKOA were notably higher among women, and particularly AA women, compared to men in OAI and MOST. KR rates were higher for white men and women in OAI and MOST; overall rates of KR were lower in JoCo OA, but AA women had the highest rates in that cohort.

Conclusion: These preliminary results represent the first step in harmonizing data across three large, diverse, longitudinal OA cohort studies and will allow direct comparison across these cohorts in the future. These data point to potential regional differences in incident RKOA and KR by sex and race, or to potential differences in enrollment criteria across the three cohorts. Future work will include pooling data from these cohorts, taking advantage of the substantial number of AAs, to allow for direct comparisons and the investigation of underlying risk factors that may explain differences in the rates of incident RKOA and KR, as well as other outcomes.

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Abstract Number: 1302

Subcutaneous Tanezumab vs NSAID for the Treatment of Osteoarthritis: Efficacy and General Safety Results from a Randomized, Double-Blind, Active-Controlled, 80-Week, Phase-3 Study

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SESSION INFORMATION
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Background/Purpose: Tanezumab is a monoclonal antibody that inhibits nerve growth factor and is under investigation for chronic pain treatment. Tanezumab administered intravenously was effective and generally well tolerated in prior osteoarthritis (OA) studies. In patients (pts) with OA and moderate-severe pain taking oral nonsteroidal anti-inflammatory drugs (NSAID), we assessed the efficacy and general safety/tolerability of switching to subcutaneous (SC) tanezumab vs further treatment with oral NSAID. (Adjudicated joint safety events are reported in a separate abstract.)

Methods: Eligible pts had hip or knee OA based on ACR criteria with x-ray confirmation; baseline (BL) WOMAC Pain and Physical Function subscale scores of ≥5 (11-pt numerical rating scale); BL Patient's Global Assessment of OA

(PGA-OA) of "fair," "poor," or "very poor"; history of inadequate pain relief with acetaminophen; inadequate pain relief with/intolerance to tramadol or an opioid; or unwillingness to take an opioid. Pts were on a stable dose of oral NSAID before study entry and during the 1-mo screening period. Pts were randomized to receive tanezumab (2.5 mg or 5 mg SC every 8 wk) or NSAID (naproxen 500 mg, celecoxib 100 mg, or diclofenac ER 75 mg orally bid) over the 56-wk treatment period. Co-primary efficacy endpoints were change from BL to wk 16 in WOMAC Pain, WOMAC Physical Function, and PGA-OA scores. The key secondary efficacy endpoint was the proportion of pts with ≥50% reduction in WOMAC Pain score at wk 16. Efficacy endpoints were also assessed at wk 56. Safety monitoring included treatment-emergent adverse events (TEAEs) during the 56-wk treatment period and 24-wk safety period.

Results: Of 3,021 randomized pts, 2,996 were included in both the efficacy and safety analyses. A total of 1,312 completed the treatment period (NSAID, n=446 [45%]; tanezumab 2.5 mg, n=447 [45%]; and tanezumab 5 mg, n=419 [42%]) and 2,227 completed the safety period (n=757 [76%]; n=741 [74%]; and n=729 [73%], respectively). At BL, mean age was 60.3-61.2 y; OA duration, 8.5-9.1 y; 64-66% were female; and for 85-86%, the knee was the OA index joint. At wk 16, pts receiving tanezumab 5 mg had statistically significant improvement in WOMAC Pain and WOMAC Physical Function compared with pts receiving NSAID, but not in PGA-OA (Table 1). Improvement in co-primary endpoints with tanezumab 2.5 mg was not significantly different than that with NSAID at wk 16. At wk 56, neither tanezumab dose was significantly different than NSAID. The incidence of TEAEs overall and serious TEAEs was greatest with tanezumab 5 mg and similar between tanezumab 2.5 mg and NSAID (Table 2). Eight deaths occurred in tanezumab-treated pts and none in NSAID-treated pts; the investigators did not consider any deaths to be treatment-related.

Conclusion: In pts with hip or knee OA and moderate-severe pain despite NSAID therapy, pts who switched from NSAID to tanezumab 5 mg SC had greater improvement in OA pain and physical function, but not PGA-OA, at wk 16 than pts who continued NSAID therapy. Differences in efficacy endpoints between tanezumab 2.5 mg SC and NSAID

Co-primary Efficacy Endpoint*	NSAID (n=996)	Tanezumab 2.5 mg (n=1,002)	Tanezumab 5 mg (n=998)
WOMAC Pain†			
Mean (range) BL score	6.96 (2.6, 10.0)	7.01 (3.6, 10.0)	7.02 (1.6, 10.0)
LS mean (SE) change from BL at wk 16	-3.07 (0.11)	-3.22 (0.11)	-3.33 (0.11)
Difference of LS means (SE)		-0.15 (0.11)	-0.26 (0.11)
p-value		0.160	0.015
LS mean (SE) change from BL at wk 56	-2.42 (0.14)	-2.44 (0.13)	-2.37 (0.13)
Difference of LS means (SE)		-0.02 (0.14)	0.05 (0.14)
p-value		0.878	0.708
WOMAC Physical Function‡			
Mean (range) BL score	6.99 (2.4, 10.0)	7.09 (1.5, 10.0)	7.08 (1.1, 10.0)
LS mean (SE) change from BL at wk 16	-3.08 (0.11)	-3.27 (0.11)	-3.39 (0.11)
Difference of LS means (SE)		-0.19 (0.11)	-0.31 (0.10)
p-value		0.069	0.003
LS mean (SE) change from BL at wk 56	-2.41 (0.14)	-2.45 (0.14)	-2.36 (0.13)
Difference of LS means (SE)		-0.05 (0.14)	0.05 (0.14)
p-value		0.731	0.733
PGA-OA§			
Mean (range) BL score	3.44 (1.0, 5.0)	3.49 (1.0, 5.0)	3.46 (2.0, 5.0)
LS mean (SE) change from BL at wk 16	-0.94 (0.04)	-0.96 (0.04)	-0.97 (0.04)
Difference of LS means (SE)		-0.02 (0.04)	-0.04 (0.04)
p-value		0.633	0.343
LS mean (SE) change from BL at wk 56	-0.66 (0.05)	-0.65 (0.05)	-0.60 (0.05)
Difference of LS means (SE)		0.01 (0.05)	0.06 (0.05)
p-value		0.886	0.281
Key Secondary Efficacy Endpoint*: 50% Responders – WOMAC Pain			
Pts with ≥50% reduction from BL to wk 16, no. (%)	512 (51.5)	549 (54.9)	562 (56.5)
Odds ratio vs NSAID [95% CI]		1.15 [0.96, 1.37]	1.22 [1.02, 1.46]
p-value		0.132	0.026

Intent-to-treat population (ie, all randomized pts who received ≥1 dose of SC study medication); co-primary endpoints: multiple imputation for missing data, ANCOVA; 50% responders: mixed BL/last observation carried forward, logistic regression. BL, baseline; LS, least square; PGA-OA, Patient's Global Assessment of osteoarthritis; pts, patients; SC, subcutaneous; SE, standard error

*Co-primary efficacy endpoints were change from BL to wk 16 in WOMAC Pain, WOMAC Physical Function, and PGA-OA scores. A graphical multiple comparisons procedure was used for efficacy analyses to control the family-wise type I error rate. A tanezumab dose would have potentially been considered superior to NSAID for the secondary efficacy endpoint only if the between-treatment difference had been significant over all three co-primary endpoints. †WOMAC Pain subscale (11-point numerical rating scale): higher score denotes higher pain levels. ‡WOMAC Physical Function subscale (11-point numerical rating scale): higher score denotes worse function. §PGA-OA scores range from 1 = "very good" to 5 = "very poor."

Table 1. Summary of efficacy of tanezumab SC compared with NSAID in pts with OA at wk 16 (primary endpoint) and wk 56 (end of treatment period).

	Number of Pts (%)					
	NSAID (n=996)		Tanezumab 2.5 mg (n=1,002)		Tanezumab 5 mg (n=998)	
Safety/Tolerability Outcome	**Wk 56**	**Wk 80**	**Wk 56**	**Wk 80**	**Wk 56**	**Wk 80**
TEAEs	601 (60.3)	666 (66.9)	629 (62.8)	681 (68.0)	670 (67.1)	744 (74.5)
Serious TEAEs	46 (4.6)	66 (6.6)	51 (5.1)	78 (7.8)	80 (8.0)	110 (11.0)
Deaths*	0	0	2 (0.2)	4 (0.4)	3 (0.3)	4 (0.4)
Treatment discontinuation due to TEAE†	52 (5.2)	52 (5.2)	53 (5.3)	53 (5.3)	88 (8.8)	88 (8.8)
Study withdrawal due to TEAE	7 (0.7)	8 (0.8)	23 (2.3)	23 (2.3)	20 (2.0)	22 (2.2)
Most frequent TEAEs‡						
Arthralgia	117 (11.7)	155 (15.6)	133 (13.3)	174 (17.4)	165 (16.5)	215 (21.5)
Nasopharyngitis	40 (4.0)	56 (5.6)	57 (5.7)	67 (6.7)	67 (6.7)	75 (7.5)
Back pain	35 (3.5)	46 (4.6)	34 (3.4)	42 (4.2)	55 (5.5)	69 (6.9)
OA	23 (2.3)	33 (3.3)	39 (3.9)	57 (5.7)	54 (5.4)	99 (9.9)
Joint swelling	10 (1.0)	15 (1.5)	43 (4.3)	45 (4.5)	48 (4.8)	53 (5.3)
Peripheral edema	17 (1.7)	19 (1.9)	19 (1.9)	21 (2.1)	43 (4.3)	45 (4.5)
Pain in extremity	28 (2.8)	39 (3.9)	31 (3.1)	37 (3.7)	37 (3.7)	48 (4.8)
Paresthesia	13 (1.3)	14 (1.4)	18 (1.8)	18 (1.8)	30 (3.0)	32 (3.2)
Fall	46 (4.6)	64 (6.4)	65 (6.5)	84 (8.4)	53 (5.3)	75 (7.5)
Headache	25 (2.5)	31 (3.1)	56 (5.6)	58 (5.8)	45 (4.5)	51 (5.1)
Musculoskeletal pain	37 (3.7)	46 (4.6)	43 (4.3)	58 (5.8)	41 (4.1)	63 (6.3)
Upper respiratory tract infection	59 (5.9)	70 (7.0)	57 (5.7)	64 (6.4)	45 (4.5)	51 (5.1)

OA, osteoarthritis; pts, patients; SC, subcutaneous; TEAE, treatment-emergent adverse events

*None of the 5 deaths occurring in the treatment period were considered by investigators to be treatment related: 4 of the 5 deaths were due to cardiovascular causes (ie, myocardial infarction or cardiac arrest); 1 death was due to pulmonary embolism. All 5 patients had relevant medical history of hypertension and/or coronary artery disease. None of the 3 deaths occurring in the safety period were considered by investigators to be treatment related: 2 of the 3 deaths were due to respiratory failure in patients with chronic lung disease and extensive histories of tobacco use; 1 of the 3 deaths was due to mixed morphine/codeine toxicity. Two additional deaths (1 in the tanezumab 5-mg group and 1 in the NSAID group) occurred after pts' final study visit and are not included in this table. †Discontinued study drug but continued in the study. ‡Occurring in ≥3% of pts in the treatment period (excluding joint safety events [reported in separate abstract]).

Table 2. Summary of the general safety/tolerability of tanezumab SC compared with NSAID in pts with OA at wk 56 (end of treatment period) and wk 80 (end of study).

did not reach statistical significance. The general safety/tolerability profile of tanezumab was consistent with that seen in prior tanezumab OA studies.

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Abstract Number: 1303

Intra-Articular TPX-100 Significantly Delays Pathological Bone Shape Change at 6 and 12 Months in Moderate to Severe Tibiofemoral OA

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Background/Purpose: Pathological bone shape changes in the femur precede cartilage changes in knee OA and predict disease onset and progression to joint failure (Neogi 2013; Barr 2016). As reported previously, TPX-100-1, a randomized, double-blind, placebo-controlled, 12-month trial of IA TPX-100 in subjects with bilateral, mild-moderate (ICRS grades 2-3) patellofemoral OA, demonstrated statistically significant and clinically meaningful improvements in knee physical function (KOOS/WOMAC scales) in TPX-100-treated knees compared to placebo-exposed knees at 6 and 12 months (McGuire 2017). On quantitative MRI, only 14% of knees had measurable patella cartilage thickness changes, with no treatment differences demonstrated in this primary structural outcome measure. Post-hoc analyses

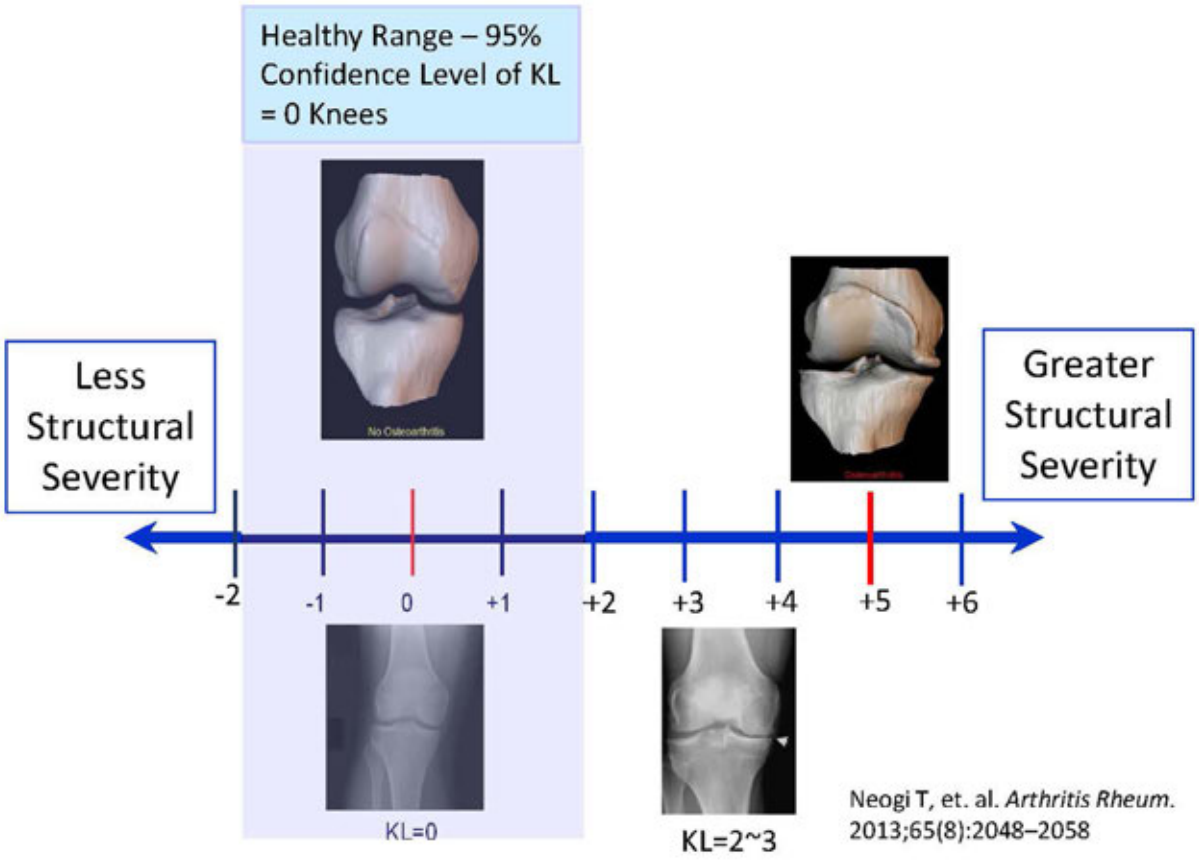

Figure 1. Three Dimensional Bone Shape: B Score

McGuire_Femur Bone Shape_ Figure 1

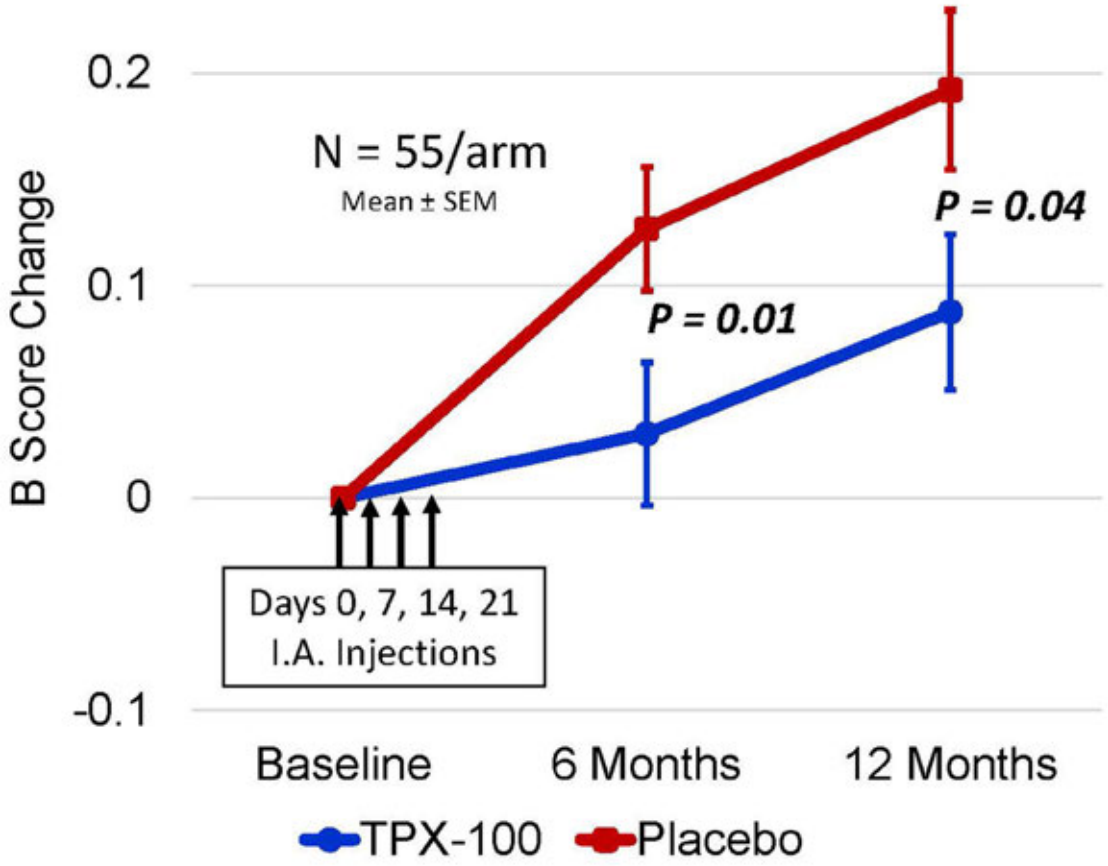

Figure 2. TPX-100 Significantly Delayed Pathological Bone Shape Change in Femur

McGuire_Femur Bone Shape_ Figure 2

revealed that 68 (73%) of these subjects also had moderate to severe (ICRS 2-4) bilateral tibiofemoral OA (TFOA), in whom similar significant clinical benefits in favor of TPX-100 were demonstrated (McGuire 2018). Study TPX-100-5 was designed to investigate MRI-based femoral bone shape changes in TPX-100-treated knees compared with placebo knees in subjects with bilateral moderate-severe TFOA at baseline.

Methods: Bone shape changes from baseline to 6 and 12 months were analyzed by an automated method (Imorphics, Inc.) blind to treatment assignment, clinical and cartilage imaging results. Sufficient MRI image quality allowed analysis of bone shape changes in 55 of 68 subjects (81%) using active appearance model (AAM), a form of statistical shape analysis that can be used to discriminate OA versus non-OA shapes. Computed “B-Scores” range from -2 (‘non-OA’) to +6 (‘severe OA’) (Fig 1).

Results: MRIs of 110 knees from 55 subjects were analyzed. Of these, ≥91% had moderately-severe or severe (ICRS Grade 3 or 4) TFOA at baseline, equally distributed between TPX-100-treated and placebo-exposed knees. TPX-100-treated knees had significantly less bone shape change at 6 and 12 months (p=0.01 and P=0.04, respectively; Fig 2). Compared with historical controls from the OAI, the trajectory of bone-shape change in TPX-100-treated knees was

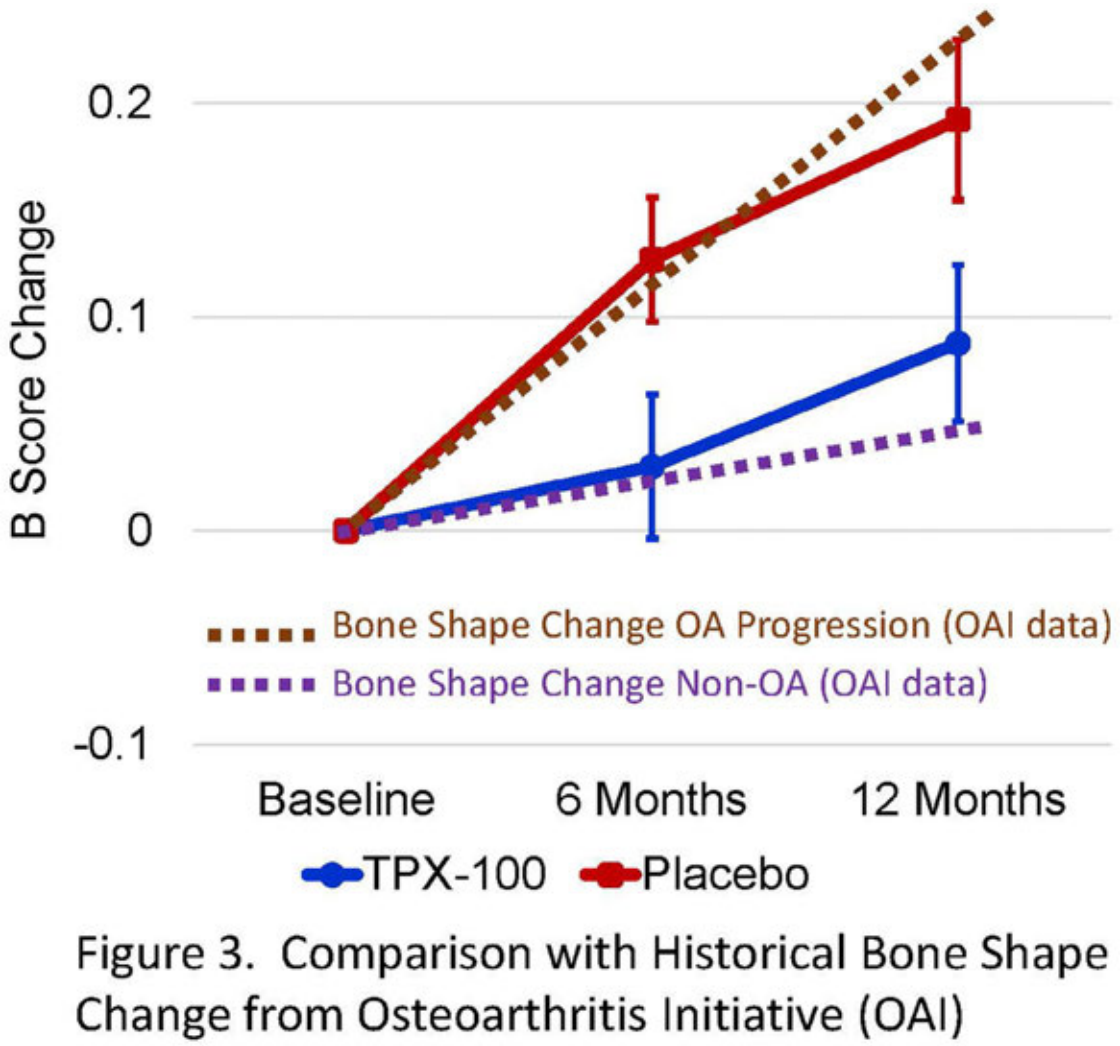

Figure 3. Comparison with Historical Bone Shape Change from Osteoarthritis Initiative (OAI)

McGuire_Femur Bone Shape_Figure 3

similar to that observed in “non-OA” knees at 6 months, while that of placebo-exposed knees was similar to that of OA progressors (Fig 3).

Conclusion: Femoral bone shape change is progressive in normal aging and is accelerated in knee OA. Increasing change predicts worsening of symptomatic and radiographic knee OA and joint failure. After a single, 4-injection series (200 mg/injection), TPX-100 treatment in subjects with moderate to severe TFOA was associated with significantly slowed pathological femoral bone-shape change at 6 and 12 months compared with placebo. Delay or stabilization of structural pathology combined with robust and sustained improvement in physical knee function strongly supports further development of IA TPX-100 as a candidate DMOAD.

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Abstract Number: 1304

Efficacy and Safety of Hylan G-F 20 versus Intra-Articular Corticosteroids in Patients with Knee Osteoarthritis: A Systematic Literature Review, Meta-Analysis, and Network Meta-analysis

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SESSION INFORMATION

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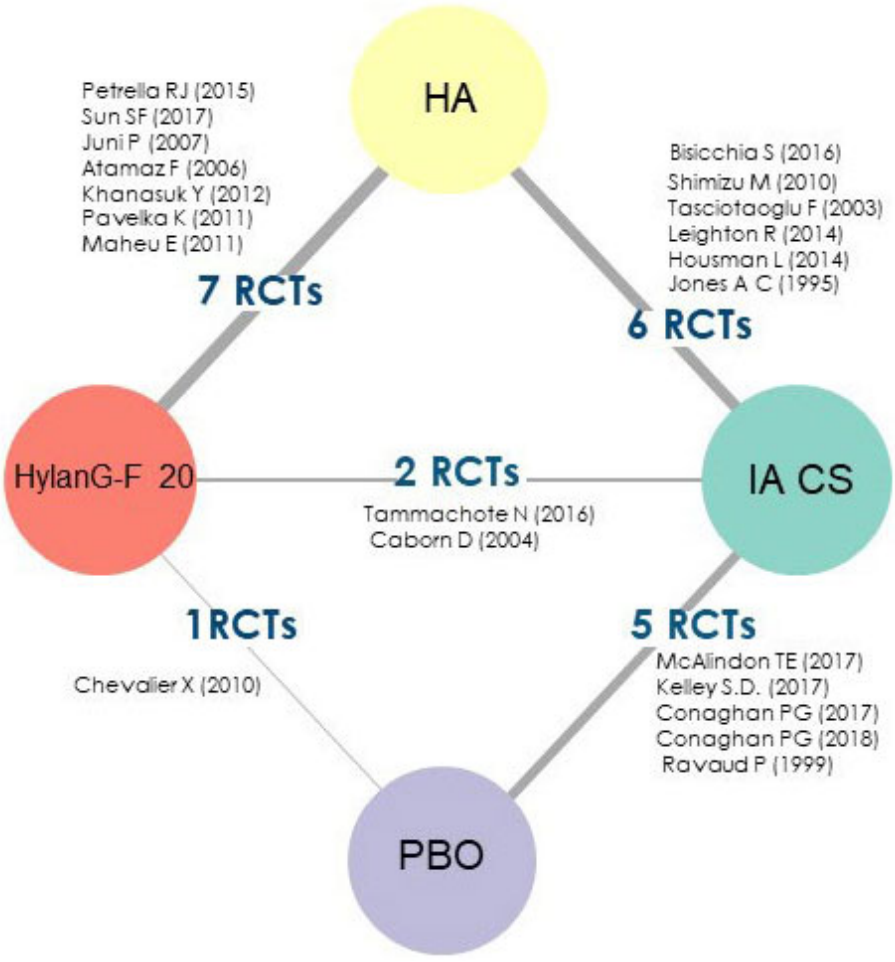

Figure 1. Network diagram for analysis of WOMAC/VAS pain at 6 months

Background/Purpose: Knee OA is a progressive joint disease which affects more than 250 million people worldwide. Meta-analysis (MA) has demonstrated that IA CS were more effective for pain relief than IA HA in the short term (up to 6 weeks) for knee OA. Hylan G-F 20 (Synvisc/Synvisc-One) is a high molecular weight HA indicated for the treatment of knee OA. However, the relative efficacy and safety of Hylan G-F 20 versus IA CS is not well understood due to the lack of head-to-head randomized controlled trials (RCTs). The objective of this research was to better evaluate the clinical efficacy and safety of Hylan G-F 20 versus IA CS in knee OA using both direct (pairwise) MA and network meta-analysis (NMA).

Methods: We systematically searched MEDLINE, Embase, and CENTRAL to identify RCTs on Hylan G-F 20 and IA CS compared to any treatment of knee OA. Two independent reviewers performed the literature review. Relevant study and patient characteristics (including whether ACR criteria were used for the diagnosis of knee OA) and outcome data were extracted. In a direct meta-analysis, we compared Hylan G-F 20 and IA CS using a random-effects model to estimate the pooled standardized mean difference (SMD) or mean difference (MD). In a Bayesian NMA framework, we used a random-effects or fixed-effect model based on the best fit. Efficacy was evaluated at 1, 3, and 6 (+/- 0.5) months (mo); and at the final follow-up for safety outcomes. A pain hierarchy was used to select one outcome from each study: (1) WOMAC pain (2) VAS pain (3) WOMAC, Walking Pain (4) VAS, Pain on Nominated Activity (5) VAS, Walking Pain (6) VAS, Weight-bearing Pain.

Results: Forty-five RCTs (8,047 patients) met the inclusion criteria. Of these, 26 (5,858 patients) used ACR diagnostic criteria, and 2 directly compared Hylan G-F 20 with IA CS. The NMA network consisted of 4 nodes (Hylan G-F 20, other IA HA, IA CS, and IA placebo) (see Figure 1 for an example of the network). In the direct meta-analysis, Hylan G-F 20 was superior to IA CS by 6 months based on the WOMAC index (overall score), SMD (95% Confidence Interval [CrI]): -6.08 (-10.00, -2.17). In the NMA, the analysis of change in WOMAC/VAS pain showed that Hylan G-F 20 may be equivalent to IACS in the short-term, but superior by 6 months, SMD (95% Credible Interval [CrI]): -0.13 (-0.25, -0.01) (See Table 1). In terms of the WOMAC overall score, WOMAC physical function and Lequesne Index, the results were not statistically significant at any timepoint. With regard to safety relative to IA CS, patients treated with Hylan G-F 20 had a estimated higher odds of treatment-related adverse events (AEs) (OR 2.72 [95% CrI]: 0.83, 9.75), but a lower odds of serious AEs (OR 0.53 [95% CrI]: 0.05, 2.53) and injection-site reactions (OR 0.71 [95% CrI]: 0.12, 4.45), even though the differences between the two groups were not statistical significant.

Effect Estimate	WOMAC Overall, 1 mo	WOMAC Overall, 3 mo	WOMAC Overall, 6 mo	WOMAC/VAS Pain, 1 mo	WOMAC/VAS Pain, 3 mo	WOMAC/VAS Pain, 6 mo
SMD (95% CrI)	-0.12 (-0.57, 0.38)	-0.32 (-0.68, 0.043)	-0.48 (-1.07, 0.16)	0.183 (-0.08, 0.43)	-0.126 (-0.41, 0.16)	-0.13 (-0.26, -0.01)*
Comparison	WOMAC Physical Function, 1 mo	WOMAC Physical Function, 3 mo	WOMAC Physical Function, 6 mo	Lequesne Index, 1 mo	Lequesne Index, 3 mo	Lequesne Index, 6 mo
SMD (95% CrI)	-0.45 (-1.3, 0.19)	-0.38 (-0.95, 0.091)	-0.28 (-1, 0.46)	-0.7 (-2.3, 1.0)	-0.15 (-0.2, 0.96)	-0.39 (-1.8, 1.0)
Comparison	Adverse Events	Serious Adverse Events	Treatment-Related Adverse Events	Injection Site Reaction	Study Withdrawal Due to Adverse Events	Study Withdrawal Due to Lack of Efficacy
OR (95% CrI)	1.32 (0.94, 1.93)	0.53 (0.05, 2.53)	2.72 (0.83, 9.75)	0.71 (0.12, 4.45)	0.96 (0.32, 2.82)	0.96 (0.41, 2.12)

Table 1. Summary of the network meta-analysis results (Hylan G-F 20 versus IA CS). Note. Negative SMD values indicate an effect favoring Hylan G-F 20. An OR above 1 favors IA CS. *Statistically significant ($p < 0.05$).

Conclusion: Overall, the results of this analysis suggest that in patients with knee OA, Hylan G-F 20 may be similar to IA CS in improving symptoms in the short term, but superior to IA CS by 6 mo. Both agents were relatively well tolerated, with no clear differences in safety while SAE seem to be more frequent with CS injections.

Disclosure: X. Chevalier, Sanofi, 8, Ibsa, 8, Pfizer, 5, Labpharm, 5; **B. Sheehan**, Sanofi-Aventis, 5, 8; **C. Whittington**, Doctor Evidence, 3; **C. Ho**, Doctor Evidence, 3; **W. Ngai**, Sanofi, 1, 3, Sanofi US, 1, 3; **G. Campos**, Sanofi-Aventis, 5, 8.

Abstract Number: 1305

Quality Improvement in Diagnostic and Therapeutic Arthrocentesis in the Flexed Knee Using Pneumatic Compression of the Suprapatellar Bursa

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SESSION INFORMATION
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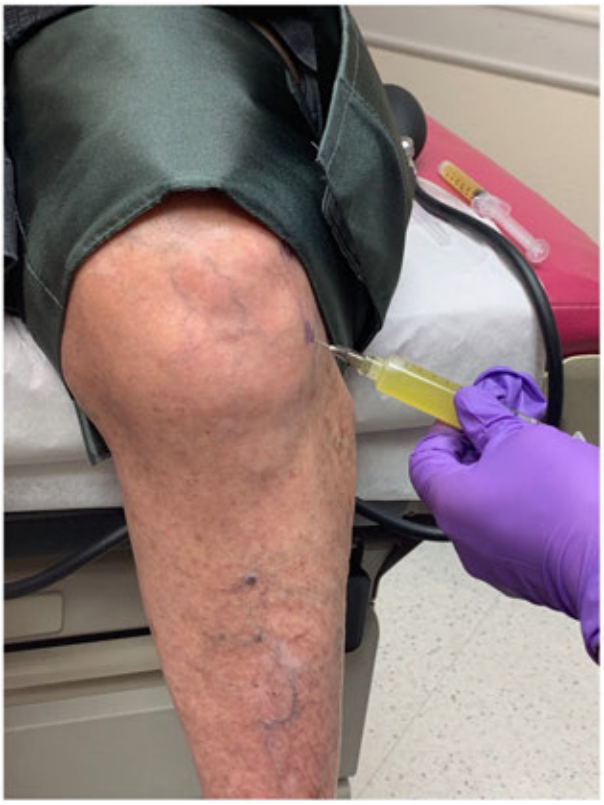
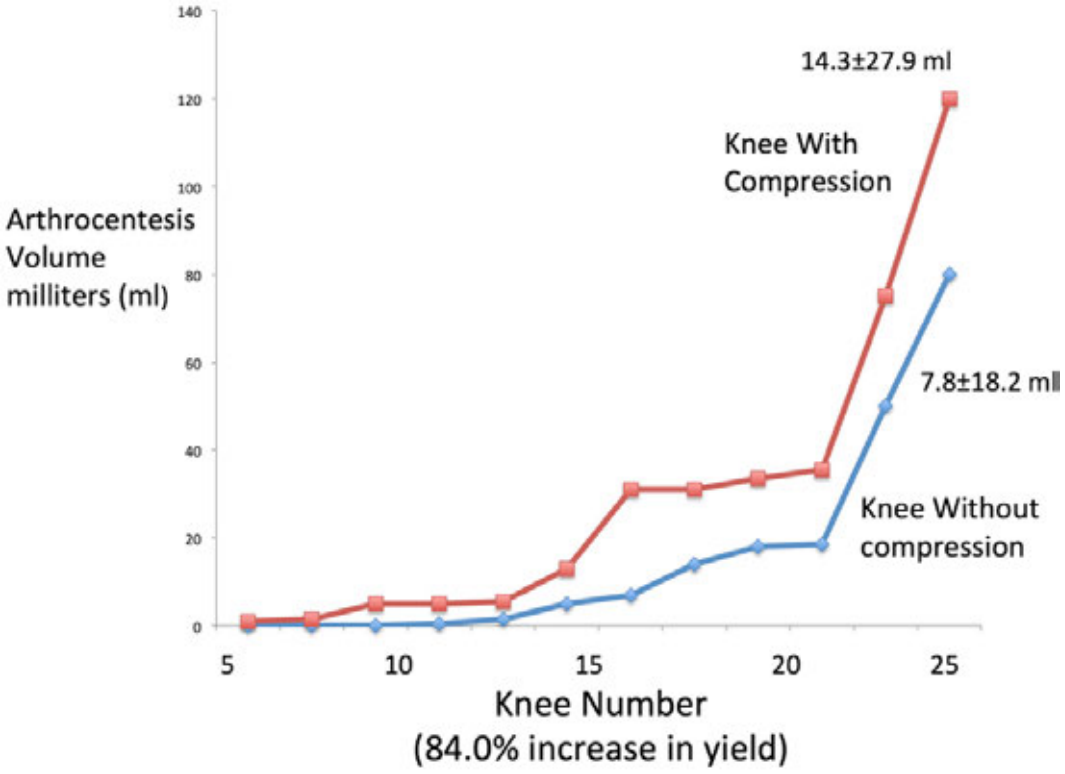
Background/Purpose: Arthrocentesis is an essential procedure in diagnosing inflammatory and septic arthritis and is a basic procedure for intra-articular therapy, including therapeutic arthrocentesis and intra-articular injection. Complete arthrocentesis before injection of corticosteroid or hyaluronan confirms the diagnosis, reduces the possibility of superimposed infection, reduces patient pain, and improves response to the injected drug. Meehan et al and others have demonstrated that constant external compression of the knee improves arthrocentesis yield and outcomes. As a quality improvement process, we used a pneumatic compression cuff to apply constant compression to the flexed knee to remove the operator`s hands from potential needlestick, mobilize synovial fluid, and permit more complete arthrocentesis.

Methods: 25 consecutive painful knees (11 OA, 9 OA/RA, 4 RA, 1 RA/septic joint) underwent arthrocentesis performed conventionally and with pneumatic compression. The mean age of the population was 61.3±14.3 years with male:female of 1: 2.1. Pre-procedural pain according to the 10 cm Visual Analogue Pain Scale (VAS) was 8.0±1.2 cm.The quality intervention was designed as a paired study in the same knee: that is, first conventional arthrocentesis in the flexed knee position using the inferolateral approach was performed and quality and outcome measures were obtained. After fluid return ceased, a pneumatic leg cuff, which was placed over the suprapatellar bursa prior to starting the procedure, was inflated to 60 millimeters Hg. Arthrocentesis was then re-attempted, and quality measures were obtained once again.



Arthrocentesis in flexed knee position, using a pneumatic leg cuff



Arthrocentesis yield from the knee with and without pneumatic compression

Results: Procedural pain according to the 10 cm VAS was 3.9±2.8cm and post-procedural pain was 1.0±1.3 cm. In 25 painful knees, conventional arthrocentesis yield was 7.8±18.2 ml and using pneumatic compression was 14.3±27.9 ml, an 84.1% increase (Figure 2). When the 13 effusive knees were analyzed separately, conventional arthrocentesis yield was 18.2±22.7 ml and using pneumatic compression was 27.9±28.6 ml, a 53.3% increase. The mean enhanced arthrocentesis yield reported here with the pneumatic compression in the flexed knee is similar to improved fluid yield that we have reported previously of 16.7±11.3 ml with elastomeric compression of the flexed knee ($p = 0.69$) and both are similar to the 16.9±15.7 ml arthrocentesis yield that was reported in conventional extended knee arthrocentesis ($p = 0.69$) (Yaqub et al 2018).

Conclusion: The technique of constant compression using a pneumatic cuff mobilizes residual synovial fluid and improves arthrocentesis success. The use of a pneumatic leg cuff in the flexed knee is a low-cost quality improvement technique that can readily be incorporated into clinical musculoskeletal practice and is particularly useful for performing arthrocentesis in patients in the sitting position, confined to wheelchairs, or with flexion contractures of the knee. Further, since the pneumatic cuff is spatially superior to the inferolateral portal at the puncture site, errant synovial fluid flows down the leg away from the cuff and does not contaminate the device unlike compression devices used in the extended knee positioning.

Disclosure: F. Jafari Farshami, None; **J. Trost**, None; **W. Sibbitt**, None; **M. Muruganandam**, None; **P. Band**, None; **M. Fangtham**, None; **N. Emil**, None; **W. Hayward**, None; **L. Haseler**, None; **A. Bankhurst**, None.

Abstract Number: 1306

Risk Factors for Pain After Total Joint Replacement in Osteoarthritis: Different Pain Measures, Distinct Predictors?

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SESSION INFORMATION
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Background/Purpose: Prognostic factors for pain persistence after total joint replacement (TJR) in osteoarthritis (OA) have been repeatedly proposed. These factors are commonly considered to act independently, unrelated to each other, even with regard to the various pain intensity measures used. Here, we purpose that pain outcomes post-TJR relate to different aspects of the pain experience and explore how predictive modeling may lead to different results regarding pain persistence risk factors.

Methods: We conducted a prospective longitudinal study of knee and hip OA patients, assessing multiple measures by questionnaires of quality, mood, affect, health and quality of life, together with radiographic evaluation and performance-based tasks before and 6 months after TJR. These factors were firstly used in a principal component analysis (PCA), thus applying a data reduction technique, and then used to build multivariate regression models (stepwise hierarchical regression: α-to-enter 0.05 and α-to-remove 0.10) for four distinct pain intensity outcomes (NRS, BPI Pain, KOOS pain and SF-36 pain). All pain outcomes were modeled at baseline and post-surgery, both as absolute value and also as score change (% residual pain) for the latest.

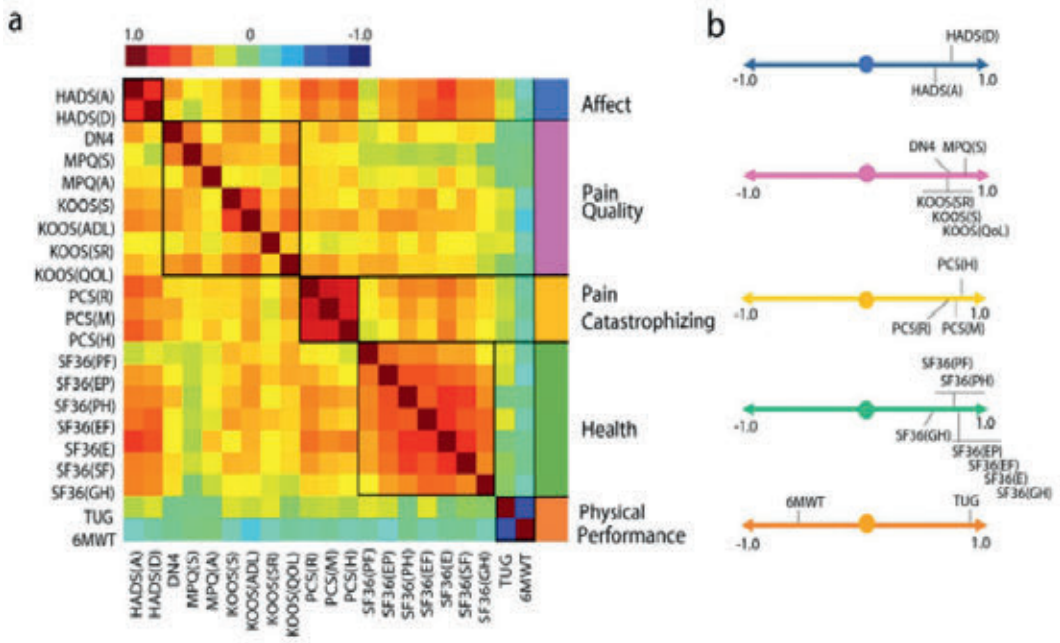

Figure 1. Principal component analysis identified five factors characterizing baseline KOA. a. Correlation matrix ordered based on principal component analysis results (Pearson's r represented by color bar). The five identified components were labeled according to membership properties. b. Factor loadings are shown for the five components. 6MWT, six minute walking test; DN4, The Neuropathic Pain 4 questions; HADS(A), The Hospital Anxiety and Depression Scale, Anxiety; HADS(D), The Hospital Anxiety and Depression Scale, Depression; KOOS, Knee Injury and Osteoarthritis Outcome Score, (ADL – Function in daily living), (S -Knee Symptoms), (SR – Function in sport and recreation), (QOL – knee related quality of life); MPQ, McGill Pain Questionnaire, (A – Affective score) (S – Sensory score); PCS, Pain Catastrophizing Scale, (R – Rumination subscale), (M – Magnification subscale), (H – Helplessness subscale); SF36, Short-form (36) Health Survey, (PF – Physical Functioning), (PH – physical role functioning), (EP – emotional role functioning), (EF – energy/fatigue), (E – emotional well-being), (SF – social functioning), (GH – general health); TUG, Timed -up and go test.

Table 1. Multiple regression models for KOA pain intensity at baseline for four different pain intensity measures. Displayed statistics are from the final step of each model. b, unstandardized regression coefficient; SE, standard error; β, standardized regression coefficient; F, obtained F-value; t, obtained t-value; R2, proportion of variance explained. * $p \leq 0.05$, ** $p \leq 0.01$. Displayed statistics are from the final step for each dependent variable. BPI Severity, Brief Pain Inventory Pain: severity subscale; HOOS Pain, Hip Injury and Osteoarthritis Outcome Score: pain subscale; NRS, Numeric Rating Scale; SF36 Pain, Short-form (36) Health Survey: pain subscale.

Model	b	SE	β	t	p	Adjusted R^2
BPI Pain Severity						
Pain Quality	2.526	.670	.385	3.770	.000	
Pain Catastrophizing	1.430	.639	.229	2.239	.028	
						.275**
						F(2,92)=18.816
NRS						
Pain Quality	0.851	0.162	0.479	5.258	.000	
						.229**
						F(1,93)=27.652
KOOS Pain						
Pain Quality	11.499	1.126	.713	10.216	.000	
Physical Performance	2.426	1.123	.151	2.160	.033	
						.573**
						F(1,92)=63.379
SF36 Pain						
Health	10.553	1.514	.602	6.970	.000	
Pain Quality	3.438	1.573	.189	2.186	.031	
						.513**
						F(2,92)=50.504

Results: A total of 84 knee OA and 24 hip OA patients completed the study. For the four pain scales, pair-wise comparisons revealed that pain intensity estimates were significantly lower only for BPI pain severity at baseline (mean differences [SD]: NRS: -1.72 [-2.44, -0.99], KOOS/HOOS: -1.436 [-2.158, -0.71], SF36: -2.06 [-2.78, -1.4], p< 0.001) and higher 6 months post-surgery with SF-36 pain (NRS: 1.038 [0.23,1,81], BPI: 1.354 [0.57,2.14], p< 0.003). The PCA for questionnaire variables identified 5 distinct components, accounting for 70% of the variability of the data. These were labeled accordingly to its factor loadings as pain quality, affect, catastrophizing, health and physical performance (Figure 1). Hierarchical models showed pain quality as the common dominant factor accounting for higher pain intensity throughout all scales pre-surgery, with additional

Table 2. Multiple regression models for post-surgical KOA pain intensity, and for percentage residual pain at 6-months post-surgery, for four different pain intensity measures. b, unstandardized regression coefficient; SE, standard error; β, standardized regression coefficient; F, obtain F-value; t, obtained t-value; R2, proportion variance explained. Gender: male coded as 0, female coded as 1. * $p \leq 0.05$, ** $p \leq 0.01$. Displayed statistics are from the final step for each dependent variable. BPI Severity, Brief Pain Inventory Pain: severity subscale; HOOS Pain, Hip Injury and Osteoarthritis Outcome Score: pain subscale; NRS, Numeric Rating Scale; SF36 Pain, Short-form (36) Health Survey: pain subscale.

Post-surgical Pain Intensity						
Model	**b**	**SE**	**β**	**t**	**p**	**Adjusted R^2**
BPI Pain Severity						
Affect	2.845	.670	.408	4.246	.000	
Pain Duration	.277	.096	.278	2.893	.005	
						.238** F(2,82)=13.952
NRS						
No predictive model – no variables entered in the equation.						
KOOS Pain						
Affect	5.688	2.229	.284	2.522	.013	
Gender	9.756	4.320	.221	2.259	.027	
Health	4.246	2.026	.231	2.060	.043	
						.234** F(3,81)=9.338
SF36 Pain						
Health	7.032	2.292	.310	3.068	.003	
Gender	15.176	5.520	.278	2.749	.007	
						.196* F(2,82)=9.730
% Residual Pain						
Model	**b**	**SE**	**β**	**t**	**p**	**Adjusted R^2**
BPI Pain Severity						
Pain Duration	1.413	.536	.274	2.635	.01	
Health	7.681	3.451	.232	2.226	0.029	
						.114** F(2,82)=6.267
NRS						
No predictive model – no variables entered in the equation.						
KOOS Pain						
Physical Performance	9.276	3.036	.321	3.055	.003	
						.092** F(1,83)=9.335
SF36 Pain						
Gender	24.210	8.088	.316	2.993	.004	
						.088** F(1,83)=8.959

influences for each outcome (Table 1). Different models were elicited for absolute versus relative pain intensity (change in pain vs pre-TJR) after surgery, with the variance explained by each model being overall lower for change in pain. Again, explanatory variables were also distinct considering the four different pain outcome measures (Table 2).

Conclusion: These results demonstrate that different pain scales relate to distinct facts of the pain experience, resulting in defining distinct prognostic factors for persistence of pain post-TJR. These models allow for distinction between post-TJR absolute pain levels vs degree of improvement from the pre-op state. Structured and comprehensive methodological approaches regarding pain metrics are necessary in order to better understand and derive clinical prognostic factors in post-TJR pain.

Disclosure: J. Barroso, None; **K. Wakaizumi**, None; **T. Schnitzer**, AbbVie, 2, Aptinyx, Astellas, Calibr, Eli Lilly and Company, 2, 5, Flexion, 2, Galapagos, 2, GlaxoSmithKline, Grunenthal, 2, Kolon TissueGene, 2, Pfizer, 2, 5, Regeneron, 2, Sanofi, Vertex; **V. Galhardo**, None; **A. Apkarian**, None.

Abstract Number: 1307

A Prospective, Multi-center, Randomized, Clinical Trial Comparing the Effectiveness and Safety of Cooled Radiofrequency Ablation versus a Single Injection of Hyaluronic Acid in the Management of OA Knee Pain

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Session Time: 9:00AM–11:00AM

Background/Purpose: This prospective, randomized, multi-center study was conducted to compare pain relief, functional improvement, and the safety of cooled radiofrequency ablation (CRFA) to hyaluronic acid (HA) to treat OA knee pain.

Methods: 177 patients underwent diagnostic block injections and those who had a minimum of 50% pain relief were randomized to receive either CRFA on 4 genicular nerves or a single intraarticular HA injection. 175 patients were treated (n=88 CRFA and 89 HA) and subsequently evaluated for pain (numerical rating system=NRS), function (WOMAC), Global Perceived Effect (GPE), and safety at 1, 3, and 6 months.

Results: The two treatment groups had statistically similar demographics and pain at baseline. One hundred and fifty-eight patients completed 6-months post treatment (n=76 CRFA and 82 HA). In the CRFA group, 71.1%

Table 1. Numeric Rating Scale Through 6 Months- Usual Level of Pain (Index Knee)

	Baseline		1 Month		3 Month		6 Month	
	CRFA	HA	CRFA	HA	CRFA	HA	CRFA	HA
WOMAC Total Score								
N	88	88	87	84	84	85	76	82
Mean	66.1	67.7	36.6	44.4	32.2	47.2	33.6	53.6
SD	13.2	13.3	23.1	21.4	23.1	22.1	22.9	22.9
Median	65.6	66.7	31.3	44.8	29.2	49.0	31.8	56.3
Minimum	28.1	38.5	0.0	7.3	0.0	0.0	0.0	2.1
Maximum	92.7	97.9	100.0	92.7	79.2	92.7	89.6	96.9
Difference between means (CRFA-HA) and 95% CI	-1.7 (-5.6, 2.3)		-7.8 (-14.5, -1.0)		-15.0 (-21.9, -8.1)		-19.9 (-27.1, -12.7)	
P-value (difference between groups)	0.4051*		0.0239*		<0.0001*		<0.0001*	
Percent Improvement from Baseline in WOMAC Total Score								
N	--	--	86	84	83	85	75	82
Mean	--	--	44.7	34.3	49.9	30.2	48.2	22.6
SD	--	--	33.2	29.9	36.3	32.0	32.3	29.9
Median	--	--	49.3	33.1	56.3	27.9	45.2	15.9
Minimum	--	--	-77.8	-48.8	-40.7	-34.7	-13.7	-40.0
Maximum	--	--	100.0	88.5	100.0	100.0	100.0	95.0
Difference between means (CRFA-HA) and 95% CI	--	--	10.3 (0.7, 19.9)		19.7 (9.3, 30.1)		25.5 (15.7, 35.3)	
P-value (difference between groups)	--	--	0.0348*		0.0003*		<0.0001*	

**T-test for two independent means, **Wilcoxon rank sum test for two independent samples, [§]paired t-test, [†]Fisher exact test for two categorical variables, [††]Chi-square test for two categorical variables*

Table 2 WOMAC Total Normalized Score Through 6 Months

	Baseline		1 Month		3 Month		6 Month	
	CRFA	HA	CRFA	HA	CRFA	HA	CRFA	HA
USUAL Level of Pain								
N	89	88	86	84	84	85	76	82
Mean	6.9	7.0	3.0	4.0	2.3	3.9	2.7	4.5
SD	0.8	1.0	2.4	2.5	2.1	2.5	2.3	2.7
Median	7.0	7.0	3.0	4.0	2.0	4.0	2.0	5.0
Minimum	6.0	6.0	0.0	0.0	0.0	0.0	0.0	0.0
Maximum	9.0	10.0	10.0	10.0	9.0	10.0	10.0	10.0
(95% CI)	(6.7, 7.1)	(6.8, 7.2)	(2.5, 3.5)	(3.4, 4.5)	(1.8, 2.7)	(3.4, 4.5)	(2.2, 3.2)	(3.9, 5.1)
Difference between means (CRFA-HA) and 95% CI	-0.1 (-0.4, 0.1)		-1.0 (-1.7, -0.3)		-1.7 (-2.4, -1.0)		-1.8 (-2.6, -1.0)	
P-value (difference between groups)	0.3407*		0.0085*		<0.0001*		<0.0001*	
Subjects with ≥50% Improvement from Baseline (n/N (%))								
Yes	--	--	56/86 (65.1)	36/84 (42.9)	64/84 (76.2)	41/85 (48.2)	54/76 (71.1)	31/82 (37.8)
No	--	--	30/86 (34.9)	48/84 (57.1)	20/84 (23.8)	44/85 (51.8)	22/76 (28.9)	51/82 (62.2)
P-value (difference between groups)	--		0.0036[††]		0.0002[††]		<0.0001[††]	

**T-test for two independent means, **Wilcoxon rank sum test for two independent samples, [§]paired t-test, [†]Fisher exact test for two categorical variables, [††]Chi-square test for two categorical variables*

Table 3. Global Perceived Effect After 6 Months

	1 Month		3 Month		6 Month	
n/N (%)	**CRFA**	**HA**	**CRFA**	**HA**	**CRFA**	**HA**
Global Perceived Effect Score						
1-Worst ever	0/87 (0.0)	0/84 (0.0)	1/84 (1.2)	0/85 (0.0)	1/76 (1.3)	1/82 (1.2)
2-Much worse	1/87 (1.1)	2/84 (2.4)	0/84 (0.0)	2/85 (2.4)	0/76 (0.0)	2/82 (2.4)
3-Worse	5/87 (5.7)	4/84 (4.8)	4/84 (4.8)	16/85 (18.8)	2/76 (2.6)	24/82 (29.3)
4-Not improved but not worse	12/87 (13.8)	26/84 (31.0)	13/84 (15.5)	24/85 (28.2)	18/76 (23.7)	22/82 (26.8)
5-Improved	27/87 (31.0)	30/84 (35.7)	21/84 (25.0)	22/85 (25.9)	24/76 (31.6)	16/82 (19.5)
6-Much Improved	34/87 (39.1)	22/84 (26.2)	37/84 (44.0)	19/85 (22.4)	25/76 (32.9)	14/82 (17.1)
7-Best Ever	8/87 (9.2)	0/84 (0.0)	8/84 (9.5)	2/85 (2.4)	6/76 (7.9)	3/82 (3.7)
P-value (difference between groups)	0.0010**		<0.0001**		<0.0001**	
Distribution of Global Perceived Effect Score						
Not Improved/Worse	18/87 (20.7)	32/84 (38.1)	18/84 (21.4)	42/85 (49.4)	21/76 (27.6)	49/82 (59.8)
Improved	69/87 (79.3)	52/84 (61.9)	66/84 (78.6)	43/85 (50.6)	55/76 (72.4)	33/82 (40.2)
P-value (difference between groups)	0.0124††		0.0001††		<0.0001††	

***Wilcoxon-Mann-Whitney test for location, †Fisher exact test for two categorical variables, ††Chi-square test for two categorical variables*

of patients (95%CI 60.9-81.2) had ≥50% reduction in NRS pain score compared to 37.8% (95%CI 27.3-48.3) in the HA group (p< 0.0001, primary endpoint) (Table 1). The mean NRS was 2.7 ± 2.3 for the CRFA group and 4.5 ± 2.7 for the HA group (p< 0.0001). The mean WOMAC score improvement from baseline was 48.2% in the CRFA group and 22.6% in the HA group (p< 0.0001) (Table 2). At 6 months, 72.4% (55/76) of subjects in the CRFA group reported improvement in Global Perceived Effect compared to 40.2% (33/82) in the HA group (p< 0.0001) (Table 3). No serious adverse events related to either procedure were noted, and overall adverse event profiles were similar.

Conclusion: In this study, CRFA treated patients demonstrated a significant improvement in pain relief and overall function compared to patients treated with HA. Further follow-up from this study will evaluate the long-term durability of cooled RFA in this patient population.

Disclosure: A. Chen, Avanos Medical, 2, 5, 8; **F. Khalouf**, Avanos Medical, 2, 5, 8; **M. DePalma**, Avanos Medical, 2, 5, 8; **K. Zora**, Avanos Medical, 2, 5, 8; **L. Kohan**, Avanos Medical, 2, 5, 8; **M. Guirguis**, Avanos Medical, 2, 5, 8; **D. Beall**, Avanos Medical, 2, 5, 8; **E. Loudermilk**, Avanos Medical, 2, 5, 8; **M. Pingree**, Avanos Medical, 2, 5, 8; **I. Badiola**, Avanos Medical, 2, 5, 8; **J. Lyman**, Avanos Medical, 2, 5, 8.

Abstract Number: 1308

Subject Enrichment Criteria for Phase 3 Studies of Lorecivivint (SM04690), a Potential Disease-Modifying Knee Osteoarthritis Drug: A Post Hoc Study on the Effects of Baseline Comorbid Pain and Joint Space Width on Patient-Reported Outcomes

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SESSION INFORMATION
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Background/Purpose: Patient-reported outcomes (PROs) in knee osteoarthritis (OA) trials have been difficult to accurately measure due to heterogenous sources of pain (e.g., from comorbid conditions or joint structure damage) which confound subjects' symptom discrimination. To improve the measurement accuracy of changes in PROs due to knee OA treatments, trial inclusion criteria must be optimized. Lorecivivint (LOR) is a CLK/DYRK1A inhibitor that modulates the Wnt pathway and is a potential disease-modifying knee OA drug. A post hoc analysis from a 24-week Phase 2b trial assessed the effects of LOR on PROs in subjects without comorbid pain and with baseline medial joint space width (mJSW) 2-4 mm, limiting JSW heterogeneity. Results from the selected Phase 3 dose of 0.07 mg LOR are reported here.

Methods: Knee OA subjects with KL grades 2-3 and Pain Numeric Rating Scale (NRS, [0-10]) ≥4 and ≤8 in the target knee and < 4 in the contralateral knee received a single, 2mL, IA injection of 0.03 mg, 0.07 mg, 0.15 mg, or 0.23 mg LOR or vehicle placebo (PBO) in the target knee at baseline. Positioned, fixed-flexion radiographs were captured at

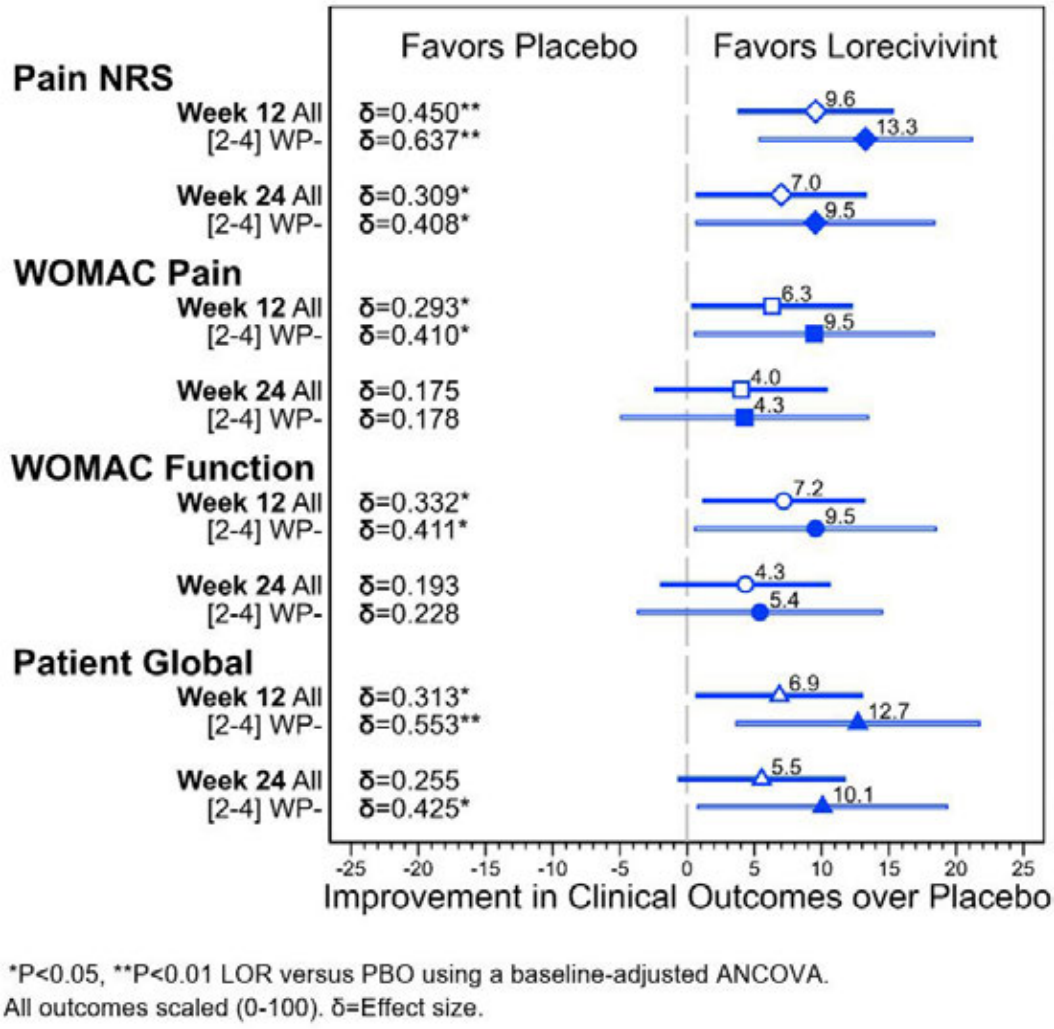

Figure 1. Treatment estimates (95% CI) and effect sizes of clinical outcomes of lorecivivint 0.07 mg compared to placebo using All Subjects and subjects with baseline mJSW [2-4mm] without widespread pain (WP-).

baseline with fixed-location mJSW measured by a central, treatment-blind reader. WPI was collected at screening with pre-specified enrollment of 80% of (WP-, Widespread Pain Index [WPI] ≤ 4, and Symptom Severity Score Question 2 ≤ 2) subjects. PRO endpoints included change from baseline in weekly average of daily OA target knee pain by NRS, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain [0-100], WOMAC Physical Function [0-100], and Patient Global Assessment (PtGA) (VAS [0-100]). Point estimates and effect sizes of the Full Analysis Set (FAS, all dosed subjects) compared to a post hoc completer analysis of subjects with baseline mJSW 2-4 mm who were WP- are reported.

Results: 635 subjects (91.4%) completed the study (mean age 59.0 [±8.5] years, BMI 29.0 [±4.0] kg/m2, female 58.4%, KL3 57.3%). In both FAS and mJSW 2-4 mm who were WP- subjects, significant improvements compared to PBO (P< 0.05) were seen in Pain NRS, WOMAC Pain, WOMAC Function, and PtGA for the 0.07 mg LOR dose group at Week 12 (Figure 1).The effect sizes were improved in the mJSW 2-4 mm who were WP- group in comparison to the FAS for the 0.07 mg LOR dose at Weeks 12 and 24.

Conclusion: In this post hoc analysis of LOR-treated knee OA subjects, those with baseline mJSW 2-4 mm without widespread pain showed improved PRO effect sizes compared to those in the Full Analysis Set beyond the initial significant improvements seen in the Full Analysis Set. These increased point estimates and confidence intervals may help to improve power calculations and create more homogenous populations to test new therapies.

Disclosure: S. Kennedy, Samumed, LLC, 1, 3; **C. Swearingen**, Samumed, LLC, 1, 3; **J. Tambiah**, Samumed, LLC, 1, 3; **D. Clauw**, Aptinyx, 2, 5, Daiichi Sankyo, 5, Daiichi Snakyo, 5, Eli Lilly, 5, Intec Pharma, 5, Nix Paterson LLP, 8, Nix Patterson LLP, 8, Pfizer, 2, 5, Pfizer Inc, 2, 5, 8, Samumed, 5, Theravance, 5, Tonix, 5, Williams & Connolly LLP, 8, Williams and Connolly LLP, 8, Zynerba, 5; **P. Conaghan**, Abbvie, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, 8, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Eli Lilly, 8, EMD, 5, EMD Serono, 5, EMD Serono Research and Development Institute, Inc., 5, 8, Flexion, 5, 8, Flexion Therapeutics, 5, 8, Galapagos, 5, 8, Glaxo Smith Kline, 5, GlaxoSmithKline, 5, 8, Lilly, 8, Medivir, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Samumed, 5, 8, Serono, 5, Stryker, 5, 8.

Abstract Number: 1309

Concordance of Baseline Pain Measures (Across Two Reporting Instruments) Influences Treatment Effect: Post Hoc Analysis of a Phase 3 Randomized Controlled Trial of Triamcinolone Acetonide Extended-Release in Patients with Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In a Phase 3 randomized controlled study, differing efficacy results were observed when triamcinolone acetonide extended-release (TA-ER) was compared to conventional TA crystalline suspension (TAcs) with two different pain measures, average daily pain (ADP) using a 0-10 numeric rating scale (NRS) and Western Ontario

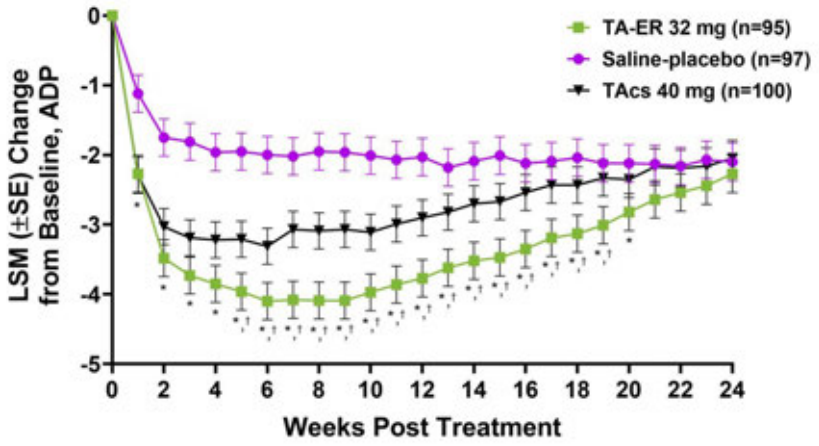
and McMaster Universities Osteoarthritis Index (WOMAC-A subscale). Trial enrollment criteria may have contributed to this discrepancy, as a moderate-to-severe ADP score of ≥5 to ≤9 was required at baseline whereas no limitations were placed on baseline WOMAC-A score (0-4 Likert). This allowed for randomization of patients who reported their knee pain as mild via WOMAC-A criteria. This post hoc analysis assessed treatment effects in those patients who reported moderate-to-severe OA pain prior to treatment on both ADP and WOMAC-A scales.

Methods: This post hoc analysis included adults (≥40 years) with knee OA (Kellgren-Lawrence Grade 2-3) who reported moderate-to-severe knee OA pain at baseline using both instruments (ADP ≥5 to ≤9 and WOMAC-A ≥2) from a Phase 3 randomized controlled study (concordant pain reporters; n=292). Patients received a single intra-articular injection of TA-ER 32 mg (n=95), TAcs 40 mg (n=100), or Saline-placebo (n=97). Patient-reported ADP-intensity (including area under the effect [AUE] curves), WOMAC-A (pain), WOMAC-B (stiffness), WOMAC-C (function), Knee In-

	TA-ER 32 mg *n* = 95	Saline-placebo *n* = 97	TAcs 40 mg *n* = 100
Sex, n (%)			
Male	33 (34.7)	37 (38.1)	40 (40.0)
Female	62 (65.3)	60 (61.9)	60 (60.0)
Age, years, mean (SD)	61.1 (9.15)	61.3 (8.91)	61.0 (10.10)
Race, n (%)			
American Indian or Alaska Native	0	0	0
Asian	9 (9.5)	9 (9.3)	10 (10.0)
Black or African American	9 (9.5)	3 (3.1)	9 (9.0)
Native Hawaiian or Another Pacific Islander	3 (3.2)	1 (1.0)	2 (2.0)
White	74 (77.9)	84 (86.6)	79 (79.0)
Other	0	0	0
BMI (kg/m^2), mean (SD)	30.33 (5.042)	30.41 (4.847)	30.94 (4.748)
BMI category, n (%)			
Normal (18.0-24.9 kg/m^2)	14 (14.7)	13 (13.4)	12 (12.0)
Overweight (25.0-29.9 kg/m^2)	34 (35.8)	30 (30.9)	30 (30.0)
Class I obesity (30.0-34.9 kg/m^2)	26 (27.4)	37 (38.1)	40 (40.0)
Class II obesity (35.0-39.9 kg/m^2)	21 (22.1)	17 (17.5)	18 (18.0)
Morbid obesity (≥40.0 kg/m^2)	0	0	0
Years since primary diagnosis, mean (SD)	8.3 (7.40)	6.3 (5.79)	7.6 (6.98)
Kellgren-Lawrence grade, n (%)			
2	49 (51.6)	44 (45.4)	43 (43.0)
3	46 (48.4)	53 (54.6)	56 (56.0)
4	0	0	1 (1.0)
Weekly ADP intensity score at baseline, n (%)			
5-5.9	34 (35.8)	28 (28.9)	34 (34.0)
6-6.9	32 (33.7)	35 (36.1)	28 (28.0)
≥7	29 (30.5)	34 (35.1)	38 (38.0)
Weekly ADP intensity score at baseline, mean (SD)	6.42 (0.944)	6.54 (1.005)	6.49 (0.947)
WOMAC-A pain score, mean (SD)	2.37 (0.339)	2.36 (0.348)	2.37 (0.316)

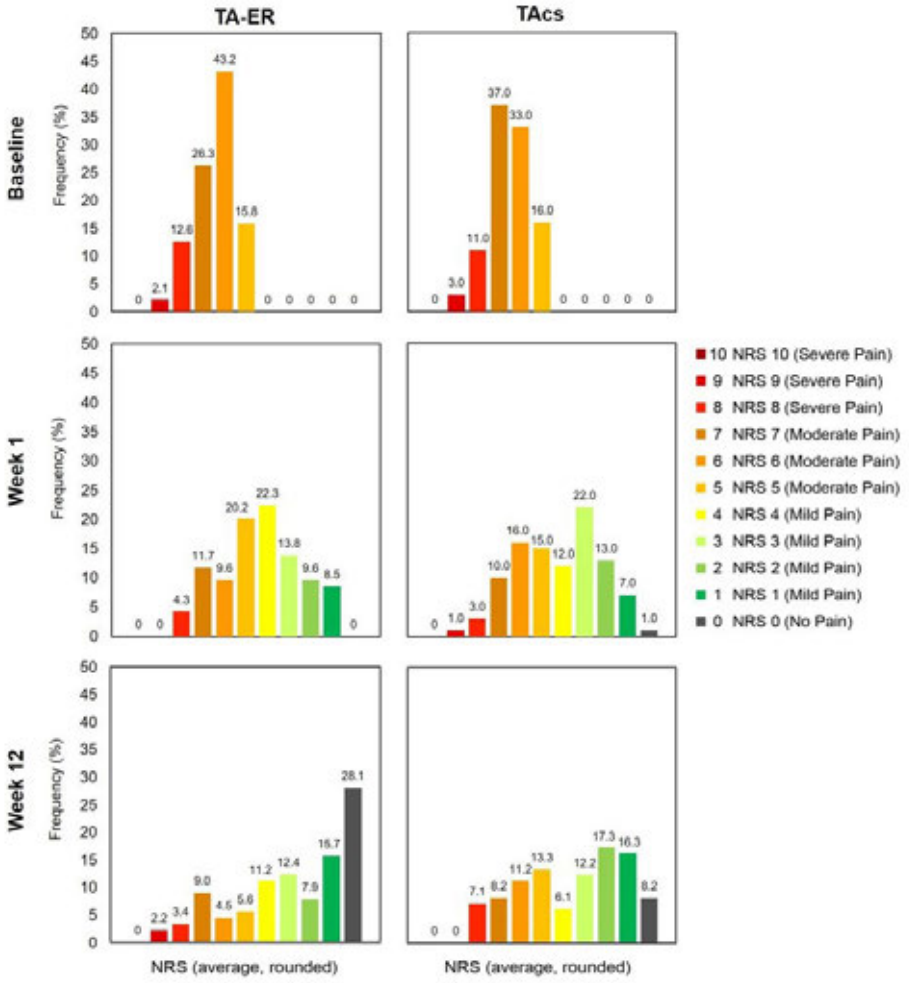
ADP, average daily pain; BMI, body mass index; SD, standard deviation; TAcs, triamcinolone acetonide crystalline suspension; TA-ER, triamcinolone acetonide extended-release; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 1. Demographic and Baseline Characteristics of Concordant Pain Reporters



*$P < 0.05$ vs Saline-placebo; †$P < 0.05$ vs TAcs.
ADP, average daily pain; LSM, least-squares mean; TAcs, triamcinolone acetonide crystalline suspension; TA-ER, triamcinolone acetonide extended-release.

Figure 1. Mean Changes from Baseline in ADP Scores Over Time in Concordant Pain Reporters



ADP-intensity scores rated on a 0–10 NRS, with 0 indicating "no pain" and 10 indicating "pain as bad as you can imagine."
ADP, average daily pain; NRS, numeric rating scale; TAcs, triamcinolone acetonide crystalline suspension; TA-ER, triamcinolone acetonide extended-release.

Figure 2. Frequency Distribution of ADP Scores at Baseline, Week 1, and Week 12

jury and Osteoarthritis Outcome Score Quality of Life (KOOS-QoL), rescue medication use, Patient Global Impression of Change (PGIC), and adverse events (AEs) were assessed throughout the study.

Results: Baseline characteristics (**Table 1**) and AE profiles were consistent with the full analysis population. TA-ER significantly ($P < 0.05$) improved ADP scores compared with TAcs (Weeks 5-19) and Saline-placebo (Weeks 1-20) (**Figure 1**). $AUE_{Weeks1–12}$ and $AUE_{Weeks1–24}$ were statistically significantly greater for TA-ER compared with TAcs (-47.7 [-94.4, -1.0] and -98.4 [-194.5, -2.3], respectively; $P < 0.05$ for both) and Saline-placebo (-136.1 [-184.2, -88.0] and -212.1 [-311.1, -113.1], respectively; $P < 0.0001$ for both). At Week 12, the proportion of patients who reported they had no knee pain (ADP score=0) was greater with TA-ER (~28%) compared with TAcs (~8%) (**Figure 2**); ~20% of patients who received TA-ER still reported no knee pain at Week 16. TA-ER significantly ($P < 0.05$) improved WOMAC-A, -B, -C, KOOS-QoL, rescue medication use, and PGIC compared with TAcs and Saline-placebo through at least Weeks 4-12.

Conclusion: In patients with knee OA who reported concordant moderate-to-severe pain at baseline across two different reporting instruments, TA-ER provided statistically significant and clinically meaningful pain relief for ≥16 weeks compared with conventional TAcs and Saline-placebo, and also improved stiffness, function, and QoL. Concordant pain reporters were better able to discern treatment effect; results of this post hoc analysis have implications for study design and patient recruitment of future trials evaluating efficacy of analgesics.

Disclosure: P. Conaghan, Abbvie, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, 8, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Eli Lilly, 8, EMD, 5, EMD Serono, 5, EMD Serono Research and Development Institute, Inc., 5, 8, Flexion, 5, 8, Flexion Therapeutics, 5, 8, Galapagos, 5, 8, Glaxo Smith Kline, 5, GlaxoSmithKline, 5, 8, Lilly, 8, Medivir, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Samumed, 5, 8, Serono, 5, Stryker, 5, 8; **E. Ross**, None; **A. Kivitz**, AbbVie, 5, Amgen, 1, 4, 5, Boehringer Ingeleheim, 5, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 5, 8, Flexion Therapeutics, 8, Genzyme, 5, 8, Gilead, 1, 4, 5, Gilead Sciences, Inc., 4, Horizon, 8, Janssen, 5, Janssen Research & Development, LLC, 2, Merck, 8, Novartis, 1, 4, 8, Pfizer, 1, 4, 5, 8, Regeneron, 1, 5, 8, Sanofi, 1, 4, 5, 8, Sun Pharma, 5, SUN Pharma Advanced Research, 5, UCB, 5; **D. Turk**, AcelRx, 5, Eli Lilly, 5, GlaxoSmithKline/Novartis, 5, Pfizer, 5; **A. Spitzer**, DuPuy, 2, 5, Johnson & Johnson, 5, Fidia, 2, 5, Flexion Therapeutics, 2, 5, 8, Medtronic, 5, Sanofi-Aventis, 5, 8, Zimmer, 5, 8; **D. Jones**, None; **R. Lanier**, None; **A. Cinar**, Flexion Therapeutics, 1, 3, Alexion Pharmaceuticals, Inc, 1; **J. Lufkin**, Flexion Therapeutics, 1, 3; **S. Kelley**, Flexion Therapeutics, 1, 3.

Abstract Number: 1310

Osteoarthritis: What's in a Name?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
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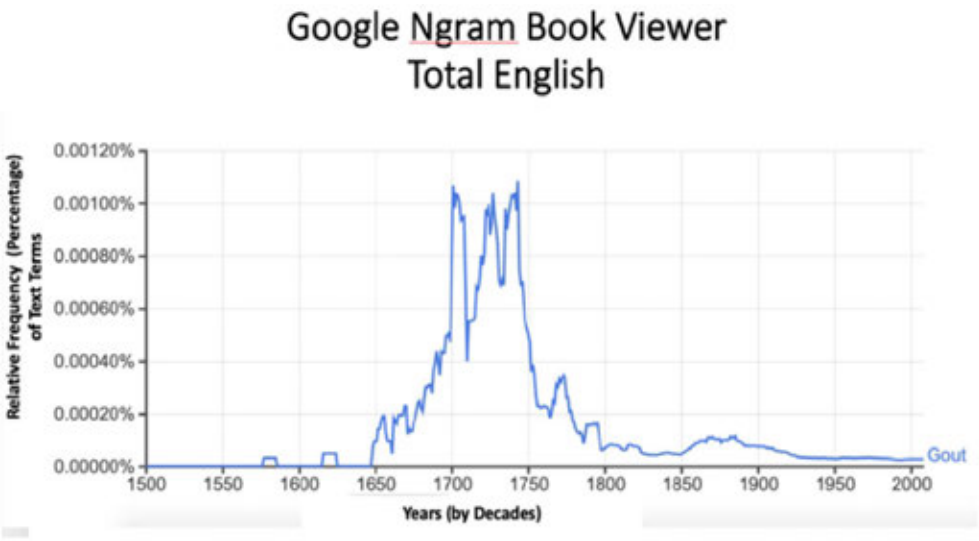
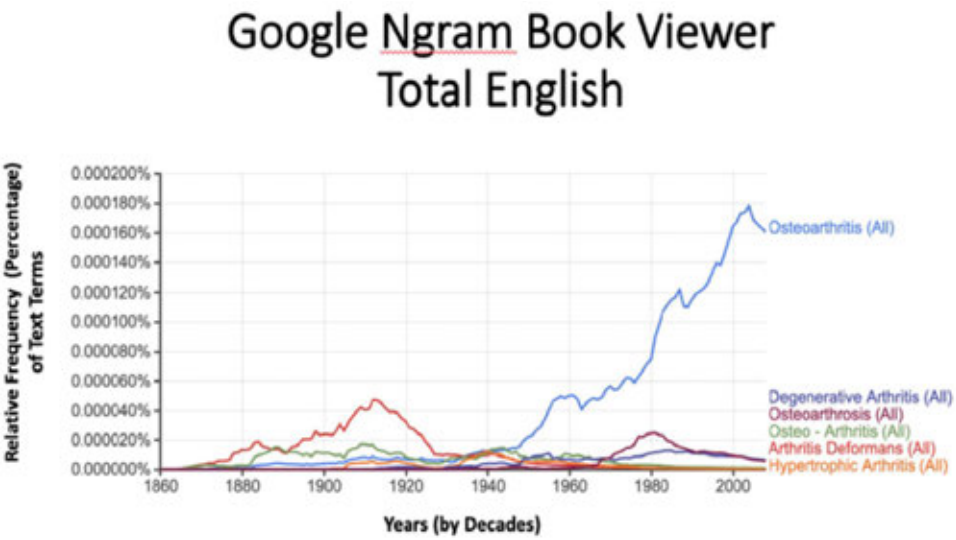
Session Time: 9:00AM–11:00AM

Background/Purpose: The nomenclature of "osteoarthritis" (OA) has been a source of confusion and likely misdiagnosis for centuries. Prior to 1759, most patients with joint diseases were labeled as having gout. It was then that the physician-anatomist, John Hunter, first documented the gross pathology of cartilage deterioration that would eventually be called OA. Other pundits variously referred to it by many different names. The goal of this research was to analyze the chronology and rationale for naming the conventional predecessors of OA.



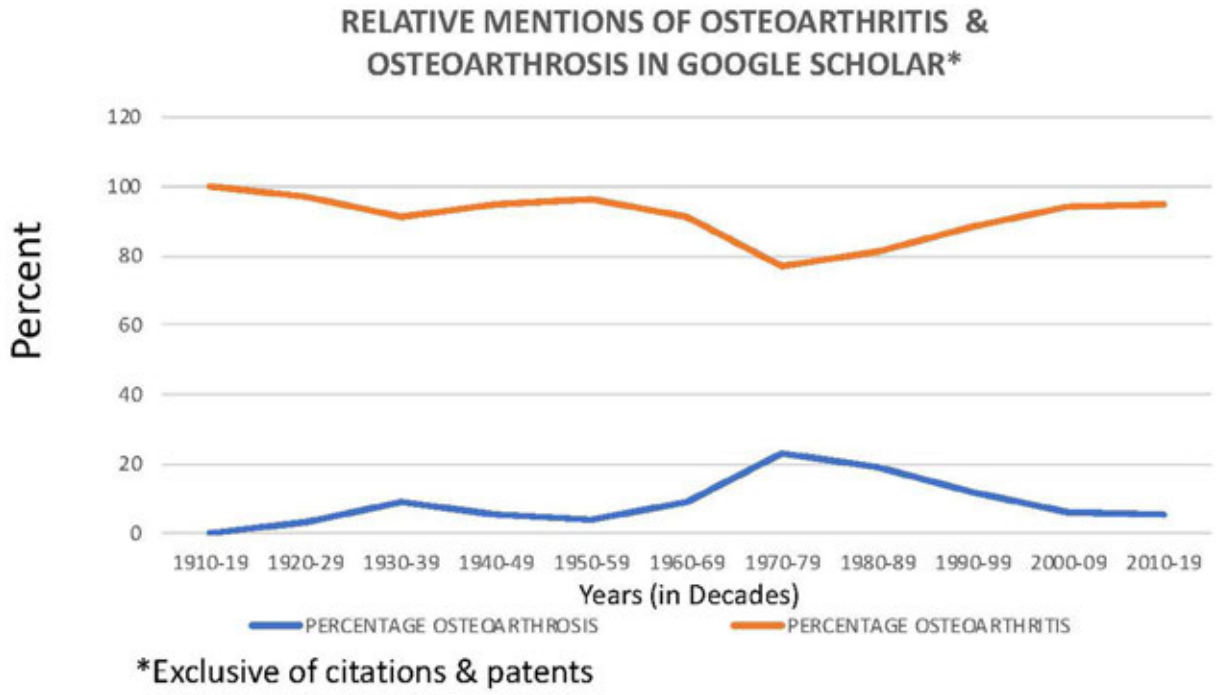
Google Ngram Viewer Gout 5-31-19 Google Ngram Viewer - Gout



Abstract Google N-Gram.docx. 5-31-19 Google Ngram Viewer - OA, O-A, Arthritis Deformans, DJD, Hypertrophic Arthritis

Methods: Google Scholar (GS), a search engine that indexes the text of academic literature, measured the usage of the terms: OA, osteo-arthritis (O-A), arthritis deformans (AD), hypertrophic arthritis (HA), degenerative joint disease (DJD) and osteoarthrosis. The terminology prevalence was plotted on a graph for each decade after 1800 to create a timeline. The Google Ngram Viewer (GNV), an online search engine that charts printed word citations, enabled a comparative graphic display between the years 1500 and 2008. A comprehensive literature search of significant discoveries and insights during this period was performed to determine if there was associated joint inflammation.

Results: The peak use of “gout” between ~1760 and 1840 may have reflected an age of scientific enlightenment rather than true prevalence. A century after Hunter’s discovery, Rudolf Virchow’s introduction of AD in 1863 applied to a mix of now-recognized OA and RA. This confounding designation persisted in the literature, eventually being adopted by his student, Sir William Osler, in 1892 and Ralph Pemberton as late as 1929. Richard von Volkmann is often credited for first using hyphenated O-A for the degenerative process, but a computerized search of his 1865 writings failed to reveal any mention of the term. In 1869, O-A originally appeared in The Nomenclature of Diseases published



OA vs Osteoarthrosis Mentions 5-31-19
Google Scholar Percentage of Literature Mentions for Osteoarthrosis & Osteoarthritis

by the Royal College of Physicians of London. The report, though it conflated O-A with RA, gained some traction with increased usage of O-A by the mid-1860s. In 1890, the influential physician Archibald Garrod still listed both O-A and AD as clinical varieties of RA. In 1910, he completely reversed his position by announcing: "I am convinced that the malady called 'osteo-arthritis'… is wholly distinct from those already referred to…," thus using O-A as a recognizable separate entity for the first time in the medical literature. In that same year, Joel Goldthwait and his group introduced with regularity the unhyphenated form of OA. Despite these clarifications, AD, DJD and HA continued to prevail. "Osteoarthrosis" was prevalent, mainly in the British literature, from ~1960 to 2000 because of the inference that OA was noninflammatory. By 1950, the term OA gained rising popularity and now reflects an inherent scientifically proven inflammatory component.

Conclusion: In the history of humanity, OA has been appropriately titled for only ~100 years. Reviewers of pre-20th century literature cannot be confident that O-A, as described then, was the actual disease known today. Optimistically, the validity of "itis" as a suffix in OA indicating inflammation will translate to improved management.

Disclosure: W. Katz, None.

Abstract Number: 1311

Prevalence of Symptomatic Axial Osteoarthritis and Poliarticular Phenotypes in Spain: EPISER 2016 Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a heterogeneous group of diseases with common clinical and radiographic manifestations involving the peripheral and axial skeletal. OA is the most prevalent rheumatic disease. There are very few publications focused in axial OA. In 2016, the Spanish Society of Rheumatology (SER) started a population descriptive study (EPISER 2016) to analyze the prevalence of 13 rheumatic diseases in Spain, including peripheral (hip, knee and hand) and axial (cervical and lumbar spine) OA.

Objectives: To estimate in adult population the prevalence in Spain of symptomatic OA of hand, knee, hip, cervical and lumbar spine and associated factors.

Methods: EPISER 2016 study is a cross-sectional, population-based descriptive study. To estimate the symptomatic OA prevalence, adult population aged 40 or older was selected. The initial recruitment was made through by a call center. In a second phase rheumatologists confirmed the diagnosis. Diagnostic criteria to confirm new diagnosis of peripheral OA were ACR criteria of hand, knee and hip. The axial OA diagnostic criteria to confirm new diagnosis were both clinical and radiographic. Clinical criteria: mechanical pain longer than 3 months of evolution and stiffness of less than 30 minutes or absence of it; and radiographic criteria: vertebral osteophytes or reduction of intervertebral space with sclerosis of vertebral plate and sclerosis in interapofisary joints. To confirm the diagnosis, it was necessary that both clinical criteria and at least one radiographic criterion were met.

Results: The sample of the EPISER study was 3,336 subjects ≥ 40, of whom 978 had peripheral or axial OA. The mean age was 64.72 years, 730 were women, 62.6% had basic education, 64,8% were overweight or obese and 83,9% were ex-smokers or non-smokers . The prevalence of global OA (peripherical+axial) was 29.35%. Prevalence of peripheral and axial OA was 19,62% and 19,17% respectively. According the prevalence of polyarticular phenotypes, the phenotype combining axial and peripheral OA was 9,66% and the phenotype combining OA in 2 or more peripherical joints (hand, knee o hip) was 5,64%.

The characteristics of patients with peripheral and axial OA follow similar patterns (Table 1).

Table 1: Sample of OA patients of the EPISER study

	GLOBAL	PERIPHERAL	AXIAL
40-49	125 (12,8)	53 (8,2)	91 (13,7)
50-59	242 (24,7)	131 (20,2)	167 (25,2)
60-69	257 (26,3)	181 (27,9)	189 (28,5)
70-79	201 (20,6)	158 (24,3)	127 (19,1)
≥ 80	153 (15,6)	126 (19,4)	90 (13,6)
Northern	259 (26,5)	172 (26,5)	177 (26,7)
Mediterranean	378 (38,7)	268 (41,3)	247 (37,2)
Centre	341 (34,9)	209 (32,2)	240 (36,1)
Rural	212 (21,7)	145 (22,3)	135 (20,3)
Urban	766 (78,3)	504 (77,7)	529 (79,7)
Basic studies	611 (62,6)	431 (66,4)	425 (64)
Medium	207 (21,2)	122 (18,8)	138 (20,8)
Higher	158 (16,2)	94 (14,5)	101 (15,2)
Normal weight	266 (27,2)	149 (23)	192 (28,9)
Under weight	4 (0,4)	2 (0,3)	2 (0,3)
Overweight	405 (41,4)	260 (40,1)	267 (40,2)
Obesity	229 (23,4)	175 (27)	157 (23,6)
Non smoker	561 (57,4)	387 (59,6)	383 (57,7)
Former smoker	259 (26,5)	177 (27,3)	165 (24,8)
Smoker	158 (16,2)	85 (13,1)	116 (17,5)

Table 2: multivariate analysis of axial OA

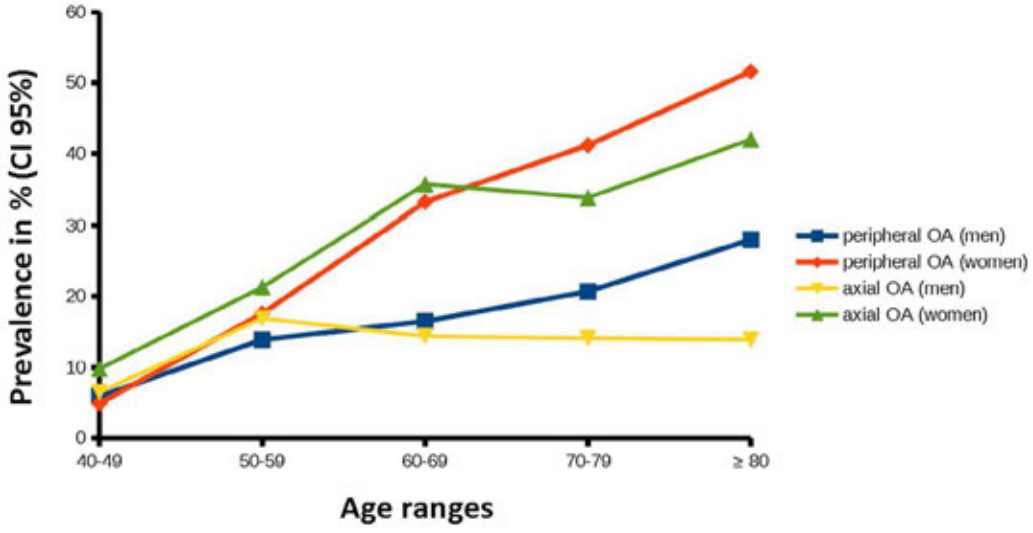
		CERVICAL OA		LUMBAR OA
	p value	OR (TI 95%)	p value	OR (TI 95%)
40-49				
50-59	<0,001	2,047 (1,387- 3,022)	<0,001	2,000 (1,438-2,781)
60-69	<0,001	3,347 (2,270-4,934)	<0,001	3,228 (2,319-4,494)
70-79	<0,001	2,337 (1,495-3,654)	<0,001	3,200 (2,223-4,607)
≥ 80	<0,001	2,916 (1,751-4,854)	<0,001	4,049 (2,667-6,148)
Women	<0,001	2,241 (1,660-3,025)	<0,001	2,324 (1,816-2,973)
Northern				
Mediterranean	0,013	1,486 (1,089-2,029)	0,161	0,832 (0,643-1,076)
Centre	0,007	1,565 (1,132-2,163)	0,036	1,322 (1,019-1,716)
Basic studies				
Medium	0,009	0,659 (0,481-0,902)	0,071	0,788 (0,609-1,020)
Higher	<0,001	0,431 (0,304-0,613)	<0,001	0,433 (0,322-0,583)
Normal weight				
Under weight	0,840	0,857 (0,192-3,821)	0,998	<0,001
Overweight	0,208	1,197 (0,905-1,584)	0,001	1,528 (1,201-1,945)
Obesity	0,002	1,679 (1,209-2,332)	<0,001	2,490 (1,881-3,295)

Prevalence of cervical OA was 10.10%. In the multivariate analysis, it was observed that cervical OA is more frequent in women and older subjects, with the prevalence peak between 60-69 years. It is also more frequent in subjects with obesity and in subjects with a basic education level (Table 2 and Figure 1).

Prevalence of lumbar OA was 15.52%. Multivariate analysis also showed that lumbar OA is more frequent in women and it increases with age (prevalence peak in ≥80 years). Greater association was observed with obesity or overweight and with basic study levels. Lumbar OA prevalence was higher in population from centre of Spain compared with other areas.

Conclusion: EPISER2016 study shows similar prevalence of peripheral and axial OA. Lumbar OA is more prevalent than cervical OA. Axial OA in Spain is more frequent in women, increases with age with a peak between 60-69 years

Figure 1: Prevalence of peripheral and axial OA by gender



for cervical OA and ≥ 80 years for lumbar OA. Both cervical and lumbar OA are more frequent in patients with obesity or overweight and with basic studies.

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Abstract Number: 1312

Knee Morphology Associates with Tibio-Femoral and Patello-Femoral Osteoarthritis: A Case-Control Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
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Session Time: 9:00AM–11:00AM

Background/Purpose: Although several morphological features of the hip joint predispose to hip osteoarthritis (OA), only a few are known to associate with knee OA. The aim of this study was to identify novel morphological features associated with knee OA in addition to those already known.

Table 1 Association of morphological features and Knee OA, PFJOA and TFJOA

Morphological features	Knee OA aOR (95%CI)	PFJOA aOR (95%CI)	TFJOA aOR (95%CI)
PFJ			
Sulcus angle*	0.83(0.80,0.87)*	0.85(0.80,0 .90)*	0.88(0.84,0.92)*
Condylar angle*	0.52(0.48,57)*	0.48(0.41,0.56)*	0.60(0.55,0.66)*
Patellar angle	0.99(0.96,1.02)	0.96(0.91,1.01)	0.98(0.95,1.02)
Patellar thickness*	0.93(0.86,1.01)	0.74(0.61,0.89)*	0.96(0.87,1.05)
Patellar width	0.97(0.94,1.04)	0.96(0.91,1.00)	0.98(0.95,1.02)
Condylar width	1.02(0.99,1.05)	1.00(0.93,1.08)	0.99(0.96,1.01)
Intercondylar width*	0.92(0.88,0.96)*	0.91(0.83,1.02)	0.97(0.93,1.01)
Medial condylar height	0.95 (0.81,1.1)	0.93(0.80,1.10)	0.86(0.75,1.98)
Lateral condylar height	0.79(0.71,1.8)	1.18(0.02,1.36)	1.23(0.01,1.35)
TFJ			
Condylar plateau angle	0.96(0.80,1.2)	1.07(0.70,1.62)	1.02(0.83,1.25)
Distal femoral tilt*	1.13(1.01,1.07)*	1.25(0.99,1.58)	1.37(1.20,1.57)*
Proximal tibial tilt*	1.19(1.00,1.43)*	1.15(0.87,1.50)	1.38(1.15,1.64)*

**-Significant association at p<0.004(Bonferroni corrected); aOR- odd ratio adjusted for age, gender, height and weight; PFJ- Patello -femoral joint; TFJ- Tibio-femoral joint.*

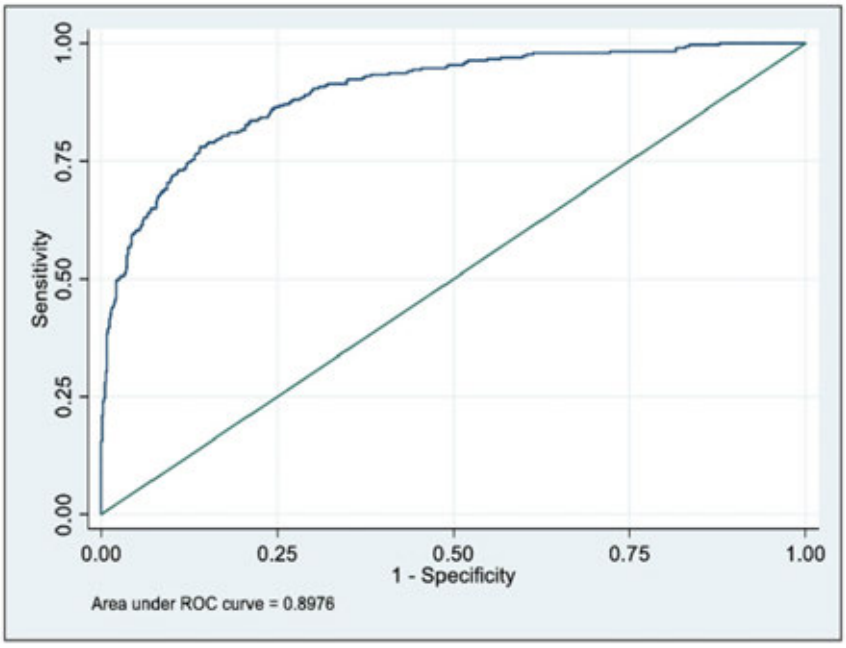

Figure 1 ROC curve for PFJOA (with sulcus angle, condylar angle, patellar thickness and distal femoral tilt, age, gender, height, weight)

Methods: This was a case control study using data from the Genetics of Osteoarthritis and Lifestyle (GOAL) study. It included: (1) 315 unilateral knee OA cases, defined as no knee pain and no radiographic OA (defined as osteophyte score ≤1 and joint space narrowing score 0 according to Nottingham line drawing atlas) in one knee but pain and

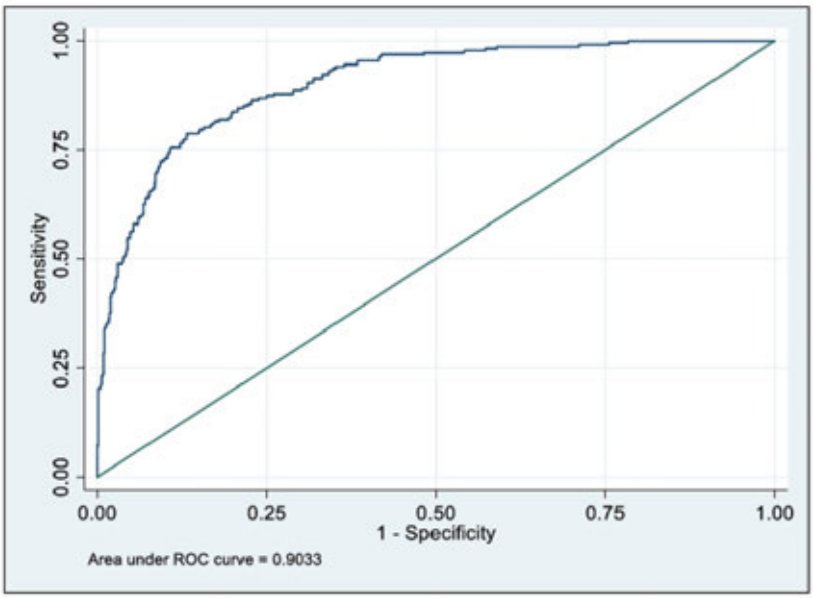

Figure 2 ROC curve for TFJOA (with sulcus angle, condylar angle, distal femoral tilt, age, gender, weight, height)

radiographic OA in the contralateral knee which also fulfilled ACR criteria for knee OA; (2) 816 controls, defined as participants without knee pain and radiographic OA in both knees.

The morphology of unaffected knees of people with unilateral knee OA were compared to the morphological features of the same side of normal controls under the assumption that the unaffected knees in cases would have the same morphologic feature as the affected knee before it developed OA.

Patello-femoral joint (PFJ) and tibio–femoral joint (TFJ) radiographic measurements were undertaken by a single observer (Table 1). Symmetry of measurements between right and left knees were examined in controls using minimal detectable change (MDC). Association of individual morphological measure and unilateral knee OA (defined as OA in PFJ or TFJ), PFJ OA or TFJ OA was determined using logistic regression adjusted for age, gender, height and weight. Diagnostic ability of the significant morphological features, together with age, gender, height and weight for each OA outcome was determined using receiver operating characteristic (ROC) curves.

Results: The mean (SD) for age, height and weight of cases and controls were 64(8.6) and 62(8.5) years, 166.7(14.2) and 167.5(11.1) cm, and 78.3(14.4) and 77.1(15.7) kg respectively. Mean difference between left and right sides in controls was less than the MDC for all measurements suggesting right-left symmetry. Narrow sulcus and condylar angles, increasing patellar thickness and intercondylar width associated with knee OA (Table 1). Increasing distal femoral and proximal tibial tilt associated with knee OA. ROC curves including all significant morphological features and age, gender, height and weight predicted knee, PFJ, and TFJ OA with area under the curve (AUC) of 0.91, 0.89, and 0.90 respectively (Fig.1, 2). As distal femoral and proximal tibial tilt were correlated (r=0.54), only distal femoral tilt was included in the model. Sensitivity analysis replacing distal femoral tilt with proximal tibial tilt did not change the results

Conclusion: We have identified six morphological features associated with knee OA. These features together with age, gender, height and weight predicted OA status accurately. There were some variations between morphological features associated with TFJ OA, and PFJ OA. However, sulcus angle and condylar angle associated with both PFJ and TFJ OA suggesting potential shared mechanisms for these variants in predisposing to both PFJ and TFJ OA.

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Abstract Number: 1313

Readmissions After Staged vs Simultaneous Bilateral Total Knee Replacements (TKR)

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Table 1. Demographics and baseline scores, overall and by cohort

	Cohort 1 Staged BTKR* (N=371) <1 year	Cohort 2 Primary TKR 1 Admission (N=3256)	Cohort 3 Primary TKR 2 Admissions (N=445) >1 year	Cohort 4 Simultan. BTKR (N=568)	p-value
Age, years, mean ± SD	68 [62, 76]	69 [61, 76]	69 [62, 75]	65 [59, 70]	<.0001
Sex, n (%)					0.008
Female	264 (71.16%)	2092 (64.25%)	312 (70.11%)	373 (65.67%)	
Male	107 (28.84%)	1164 (35.75%)	133 (29.89%)	195 (34.33%)	
Race					
Black	41 (11.08%)	235 (7.23%)	44 (9.89%)	25 (4.4%)	0.0003
Hispanic	18 (4.86%)	142 (4.37%)	23 (5.17%)	18 (3.17%)	0.415
Other	20 (5.40%)	177 (5.44%)	28 (6.29%)	53 (9.33%)	0.004
White	291 (78.65%)	2697 (82.96%)	350 (78.65%)	472 (83.1%)	0.036
ASA Status					
1	—	107 (3.29%)	—	15 (2.64%)	0.404
2	229 (61.73%)	2396 (73.63%)	339 (76.18%)	514 (90.49%)	<.0001
3	134 (36.12%)	751 (23.08%)	96 (21.57%)	39 (6.87%)	<.0001
Type of anesthesia, n (%)					
Combination	315 (84.91%)	2814 (86.43%)	380 (85.39%)	539 (94.89%)	<.0001
Epidural	15 (4.04%)	109 (3.35%)	13 (2.92%)	11 (1.94%)	0.248
Femoral nerve block	12 (3.23%)	99 (3.04%)	21 (4.72%)	11 (1.94%)	0.088
General	—	45 (1.38%)	—	—	0.097
Other	0 (0%)	11 (0.33%)	0 (0%)	0 (0%)	—
Spinal	23 (6.2%)	178 (5.47%)	26 (5.84%)	—	<.0001
ICD-9 comorbidities	786 (83.71%)	2650 (81.39%)	384 (86.29%)	451 (79.4%)	<.0001
Baseline KOOS					
KOOS Pain	41.7 [27.8, 52.8]	47.1 [36.1, 58.3]	44.4 [33.3, 55.6]	44.4 [33.3, 55.6]	<.0001
KOOS Symptoms	46.4 [32.1, 57.1]	50 [35.7, 60.7]	50 [35.7, 60.7]	46.4 [35.7, 60.7]	0.100
KOOS Activities of Daily Living ADL	44.6 [30.9, 57.4]	50 [41.2, 64.7]	48.5 [36.8, 60.3]	48.5 [39.7, 61.8]	<.0001
KOOS Quality of Life (QOL)	17.7 [0, 31.3]	25 [12.5, 37.5]	18.8 [6.3, 37.5]	18.8 [6.3, 31.3]	<.0001
Physical Component Score (PCS) (SF12)	29.4 [25.2, 34.8]	33.3 [28.1, 39.3]	32.6 [26.9, 37.6]	33.2 [28.7, 39.6]	<.0001
Mental Component Scores (MCS) (SF12)	49.2 [40, 58.3]	52.1 [41.6, 60]	50.3 [40.5, 60.3]	52.8 [42.8, 61.5]	0.040

*Indicates staged BTKR < 1 year; BTKR same admission staged excluded (N=37). Note: cells containing less than 11 observations have been omitted to comply with SPARCS data reporting rules. TKR- Total knee replacement; KOOS-Knee Injury and Osteoarthritis Outcome Scores; SF-12 Short Form1; ASA- American Association of Anesthesiologists

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The safety of bilateral total knee replacements (BTKR) under the same anesthesia as compared to staging within 12 months is debated. The advantage is one anesthesia, one postoperative rehabilitation and a shorter recuperation., but may . incur greater risk of complications and readmissions, Our aim is to compare the rate of readmissions for patients undergoing 1) simultaneous BTKR 2) unilateral TKR, 3) staged BTKR >12 months or 4) staged B TKRs < 12 months.

Methods: All New York State (NYS) residents enrolled in the Hospital for Special Surgery Knee Replacement Registry >18 years old with a first primary TKR between 1/1/2008 and 12/31/2010 were eligible. We excluded prior revision TKR, inflammatory arthritis, 2 non-TKA surgical procedures. Demographics and PROs(HOOS/KOOS and SF12) were collected at the time of surgery. We used the NY Statewide Planning and Research Cooperative System (SPARCS) to identify readmissions via links to claims from all non-federal NYS hospitals. The cohorts were 1) simultaneous BTKR 2) unilateral TKR, 3) staged BTKR >12 months or 4) staged B TKRs < 12 months. Included readmission diagnoses were the Center for Medicare and Medicaid (CMS) Complications (TKR specific) and cerebral vascular accident ,acute renal failure, GI bleed, and mortality within 90 days. The distribution of continuous variables was assessed using the Shapiro-Wilk test. Non-normally distributed variables are summarized as median [IQR] and compared using the Kruskal-Wallis test. Categorical variables are summarized as frequency (percent) and compared using the Chi-Squared test.

Results: We included 4,640 patients linked to SPARCs with 95 unplanned readmissions (Table 1). Simultaneous BTKR patients were younger, more often male, had fewer co-morbidities, and had higher rates of American Society of Anesthesiology Score of 2. Health related QOL at baseline was better for simultaneous BTKR than staged < 1 year on the SF-12 PCS and SF-12 MCS . More staged < 1 year were readmitted, however there was no significant difference in readmission across the four cohorts compared (p=.961). At >90 days, there was a trend towards significance in readmissions for transfusions (p=.090) across the four cohorts. Readmissions for sepsis differed across the four cohorts (p=.019), with higher rates in the simultaneous BTKR group. No differences in VTE or MI were observed. Readmission for mechanical complications at >90 days differed across the cohorts (p=.0006) with a slightly increased rate of readmission in those staged < 1 year.

Conclusion: Further study is required to address whether simultaneous BTKR increases risk for readmission, compared to BTKR staged < 1 year. BTKR patients in our institution were younger and had less comorbidities,, which may reflect careful screening for simultaneous BTKR candidates, and the comparatively lower rates of early readmission for simultaneous BTKR patients (with the exception of readmission for sepsis). While we observed potentially meaningful differences in rates of readmission for transfusions, sepsis, and mechanical complications, across four cohorts of TKR replacement patients, these unadjusted comparisons require additional research.

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Abstract Number: 1314

Patient-Specific Reference Values for Objective Physical Function Tests: Cross-Sectional Analysis Using Data from the Osteoarthritis Initiative

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SESSION INFORMATION

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Background/Purpose: Despite an inter-play between objective physical function measures and various patient characteristics, no large-scale investigations in knee osteoarthritis (KOA) have explored complex interactions or established patient-specific reference values for these tests across sex, age, radiographic severity, and body mass index (BMI). The purpose of this study was to: 1) determine the extent to which interactions among patient characteristics were associated with objective physical function, and 2) use a large community-based cohort of adults with or at risk for KOA to establish patient-specific reference values of objective physical function tests.

Methods: We included participants from the Osteoarthritis Initiative (OAI) with data on objective physical function tests and patient characteristics (i.e., age, BMI, and radiographic KOA severity: Kellgren-Lawrence Grade [KL]) at the baseline visit. We included three objective physical function tests: 20-meter walk test (20m), chair stand test (CS), and 400-meter test (400m). For the 20m, participants completed two trials at their habitual walking speed. For the CS, participants completed two trials in which they completed sit-to-stands as quickly as possible. For the 400m, participants completed one trial of walking ten 40-meter laps at their habitual walking speed. To determine how each

Degree of Interaction	Variables Included in Model	Objective Physical Function Test		
		20-meter walk Interaction p-value	Chair stand test Interaction p-value	400-meter walk Interaction p-value
2-way	sex*age	0.09	0.23	**<0.01***
	sex*KL	**<0.01***	**0.01***	**0.02***
	sex*BMI	**0.03***	0.64	**<.0001**
	age*KL	0.33	0.34	0.93
	age*BMI	0.79	0.10	0.14
	KL*BMI	0.44	0.88	0.29
3-way	sex*age*KL	0.17	0.15	0.39
	sex*age*BMI	0.16	0.06	0.93
	sex*KL*BMI	0.13	0.31	**0.05***
	age*KL*BMI	0.64	0.57	0.54
4-way	sex*age*KL *BMI	0.48	0.51	0.32

Table 1. Regression Analysis Results Highlighting the Interaction Between Patient Characteristics that Relate with Objective Physical Function Tests. BMI = body mass index, KL = Kellgren-Lawrence Grade, p = regression analysis interaction p-value, *: p<0.05

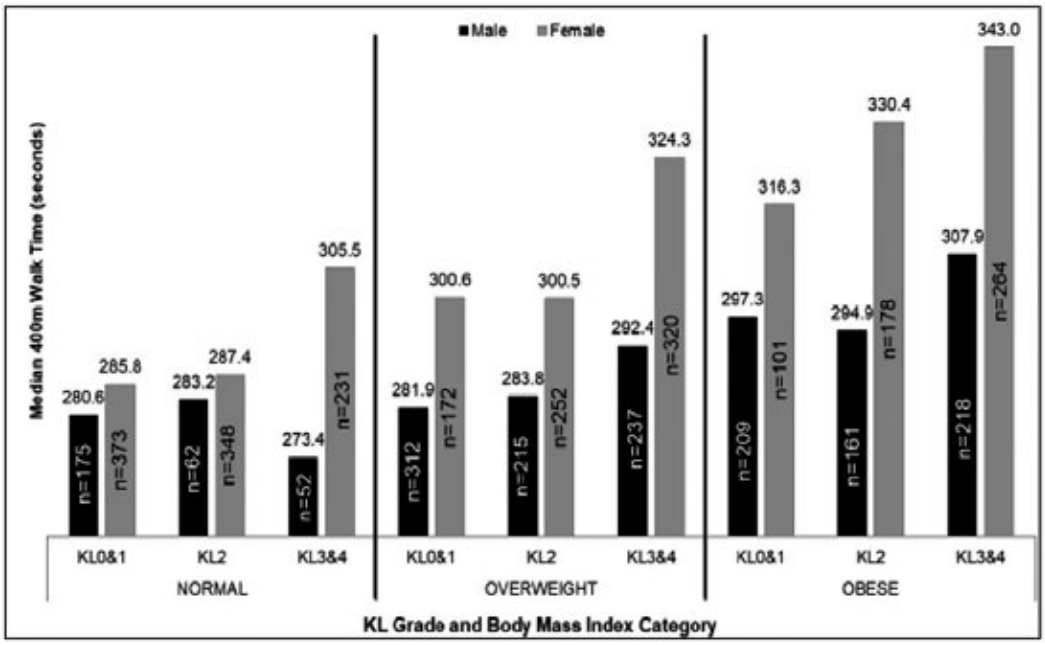

Figure 1. 400-Meter Walk Performance by Sex, KL Grade, and BMI Category. Greater median 400-meter walk time indicates worse objective physical function; KL = Kellgren-Lawrence Grade

objective physical function is influenced by any combination of these patient characteristics, we used a single linear regression model to evaluate all two-, three-, and four-way interactions. To establish patient-specific reference values for each objective physical function test, we created percentile scores from minimum to maximum in 10% increments for all combinations of the patient characteristics for each test. Subsets for two-way reference values were separated by: sex (male, female); age (five-year increments from 45-80 years); KL (KL0 - KL4); and BMI (18.5-25 kg/m^2, 25-30 kg/m^2, 30-35 kg/m^2, >35 kg/m^2). Due to smaller subset sample sizes, three- and four-way references were separated by: age (45-60, 60-70, and 70-80 years); KL (KL0/1, KL2, KL3/4); and BMI (18.5-25 kg/m^2, 25-30 kg/m^2, >30 kg/m^2).

Results: We included 3,880 individuals who were on average 61$\pm$9 years old with a BMI of 29$\pm$5 kg/m^2. For all physical function tests, there was no statistically significant four-way interaction between sex, age, KL, and BMI (Table 1). However, all physical function tests had at least one significant three-way or two-way interaction. Figure 1 highlights the interaction between sex, KL, and BMI for the 400m. We created reference value tables for each physical function test across all combinations of patient characteristics for two-, three-, and four-way interactions. Table 2 provides an example of two- and three-way interaction tables for the 400m.

Conclusion: Rather than rely on a single cut-off for all adults with or at risk for KOA, our analysis highlights the need for reference values within clinically relevant subsets that indicate a patient's relative level of physical function. Further work is needed convert these extensive reference value tables to a format that can be easily translated into clinical practice.

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Abstract Number: 1315

Relation of MRI-detected Structural Damage in the Patellofemoral Joint to Pain and Performance Based Function: The MOST Study

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SESSION INFORMATION

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Session Title: Osteoarthritis – Clinical Poster I

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Session Time: 9:00AM–11:00AM

	Sex	KL Grade	BMI Status (kg/m²)	n	Percentiles (seconds)										
					Min	10%	20%	30%	40%	50%	60%	70%	80%	90%	Max
Two-Way sex*BMI	Male		<25	289	900.0	334.7	312.0	296.0	288.2	278.6	266.5	259.8	248.9	235.5	174.3
			25-30	764	900.0	344.7	323.0	307.6	295.6	285.1	276.0	265.6	258.0	243.3	176.9
			30-35	465	900.0	366.8	339.8	320.2	307.9	298.8	288.5	278.9	263.8	247.0	194.3
			>35	123	900.0	392.8	350.4	332.9	322.9	304.9	295.4	287.0	273.1	253.9	227.7
	Female		<25	646	900.0	355.0	326.4	311.7	299.4	288.6	278.8	270.5	260.4	250.1	189.4
			25-30	778	900.0	375.2	347.6	327.6	315.4	305.1	295.3	283.6	273.7	259.9	187.7
			30-35	559	900.0	402.3	361.1	346.8	335.2	324.2	312.1	300.3	291.5	274.4	186.1
			>35	256	900.0	465.6	403.0	376.0	359.2	345.6	329.6	318.4	304.6	288.7	225.0
Three-Way sex*KL*BMI	Male	KL0&1	<25	175	481.9	327.2	308.7	295.3	287.2	280.6	265.5	258.3	246.0	234.2	174.3
		KL2	<25	62	900.0	357.4	318.0	300.9	294.3	283.2	273.8	260.1	251.0	244.3	213.1
		KL3&4	<25	52	437.8	349.3	316.8	294.9	286.2	273.4	266.0	261.9	253.0	233.4	174.3
		KL0&1	25-30	312	900.0	340.3	315.3	303.5	290.5	281.9	274.9	265.8	259.2	245.0	176.9
		KL2	25-30	215	900.0	344.7	320.8	305.3	292.4	283.8	274.5	264.3	257.1	241.9	192.9
		KL3&4	25-30	237	900.0	346.1	329.1	315.9	303.5	292.4	281.4	267.5	257.2	244.1	190.4
		KL0&1	>30	209	900.0	358.5	334.2	318.1	305.6	297.3	290.3	279.6	262.8	243.9	194.3
		KL2	>30	161	571.0	376.5	337.2	319.5	304.9	294.9	286.2	276.8	262.3	247.3	200.7
		KL3&4	>30	218	900.0	381.9	349.8	332.2	320.0	307.9	296.0	284.6	271.6	256.1	224.4
	Female	KL0&1	<25	373	900.0	347.3	322.0	308.0	295.8	285.8	277.4	270.0	258.3	245.0	189.4
		KL2	<25	348	486.3	355.0	323.9	310.5	295.3	287.4	277.7	270.2	262.8	251.5	206.3
		KL3&4	<25	231	685.9	374.7	342.8	327.5	316.8	305.5	288.7	277.7	267.2	258.4	241.6
		KL0&1	25-30	172	900.0	363.6	338.7	320.8	310.6	300.6	289.4	281.7	271.1	257.5	218.3
		KL2	25-30	252	900.0	370.0	343.1	325.1	310.5	300.5	288.4	281.3	271.3	259.9	207.0
		KL3&4	25-30	320	900.0	398.5	363.8	348.6	333.9	324.3	314.1	302.1	286.1	268.6	187.7
		KL0&1	>30	101	900.0	372.7	348.7	337.0	326.2	316.3	304.6	294.4	286.3	273.0	220.7
		KL2	>30	178	900.0	424.1	374.5	358.9	343.6	330.4	315.4	306.7	296.0	281.5	186.1
		KL3&4	>30	264	900.0	462.4	395.7	371.0	353.2	343.0	331.7	317.7	307.2	285.5	235.4

Table 2. Reference Values for 400-meter Walk Time Across a Two-Way and Three-Way Combination of Patient Characteristics. KL = Kellgren-Lawrence, BMI = body mass index, n = sample size. 50% = median. All values in meter per second.

Table 1. Adjusted means for MRI features among number of subregions affected			
Outcome: Mean VAS Pain (0 to 100 mm)			
# of subregions affected	Full-thickness cartilage damage	BMLs	Definite osteophytes
0	14.1 (12.6, 15.6)	11.8 (10.1, 13.4)	11.0 (9.5, 12.6)
1 or 2	14.7 (12.8, 16.6)	15.6 (14.1, 17.1)*	11.1 (9.3, 12.8)
3 or 4	21.6 (17.1, 26.0)**	16.9 (14.0, 19.7)*	16.6 (14.0, 19.2)**
Outcome: Chair Stands (time to complete 5, seconds)			
# of subregions affected	Full-thickness cartilage damage	BMLs	Definite osteophytes
0	11.5 (11.2, 11.8)	11.2 (10.9, 11.5)	10.8 (10.5, 11.1)
1 or 2	11.1 (10.7, 11.5)	11.3 (11.0, 11.6)	11.6 (11.2, 11.9)*
3 or 4	12.3 (11.4, 13.2)***	11.5 (10.9, 12.1)	11.9 (11.4, 12.4)*
*significant difference from 0 **3 or 4 group different from others *** 3 or 4 group different from 1 or 2 group			

Maxwell et al PF OA MRI table
Clinical outcomes for number of PFJ Subregions with MRI-detected structural damage

Table 2. Adjusted odds for MRI features among number of subregions affected						
Outcome: At least mild pain on stairs						
	Full-thickness cartilage damage		BMLs		Definite osteophyte	
# of subregions affected	n/N (%)	Adjusted OR (95% CI)	n/N (%)	Adjusted OR (95% CI)	n/N (%)	Adjusted OR (95% CI)
0	344/695 (49.5)	1.0 (REF)	184/433 (42.5)	1.0 (REF)	224/509 (44.0)	1.0 (REF)
1 or 2	212/342 (62.0)	1.6 (1.2, 2.1)	319/525 (60.8)	2.1 (1.6, 2.7)	225/371 (60.7)	1.4 (1.1, 1.9)
3 or 4	43/55 (78.2)	3.3 (1.7, 6.5)	96/134 (71.6)	3.3 (2.2, 5.2)	150/212 (70.8)	1.6 (1.0, 2.4)
Outcome: Walking less than 6,000 steps/day						
	Full-thickness cartilage damage		BMLs		Definite osteophyte	
# of subregions affected	n/N (%)	Adjusted OR (95% CI)	n/N (%)	Adjusted OR (95% CI)	n/N (%)	Adjusted OR (95% CI)
0	395/582 (67.9)	1.0 (REF)	250/374 (66.8)	1.0 (REF)	302/420 (71.9)	1.0 (REF)
1 or 2	186/287 (64.8)	1.0 (0.7, 1.4)	276/431 (64.0)	0.97 (0.7, 1.3)	200/319 (62.7)	1.6 (1.1, 2.4)
3 or 4	18/45 (40.0)	2.3 (1.1, 4.4)	73/109 (67.0)	0.77 (0.5, 1.3)	97/175 (55.4)	2.1 (1.3, 3.4)

Background/Purpose: Osteoarthritis (OA) of the knee is one of the most common causes of disability in the U.S. Often overlooked, OA specific to the patellofemoral joint of the knee (PFJ OA) is highly prevalent, and often occurs

in isolation from tibiofemoral (TFJ) OA. While MRI-detected structural damage in the PFJ are related to the development of TFJ lesions, little is known about the clinical significance of these lesions, or the impact of cumulative tissue damage across the four subregions of the PFJ (medial/lateral patella and trochlea). The purpose of this study is to determine the cross-sectional relationship of the number of PFJ subregions with structural MRI-defined tissue damage with knee pain, performance-based function, and physical activity in people with or at high risk of knee OA.

Methods: We performed a cross-sectional analysis using 60-month data from the NIH-funded Multicenter Osteoarthritis Study. OA features in the four PFJ subregions were scored semi-quantitatively using the WORMS method by two musculoskeletal radiologists. We created a 3 level exposure variable for the number of PFJ subregions with structural damage: (0, 1 or 2, 3 or 4). Three different MRI features were assessed separately: full-thickness cartilage damage (WORMS 2.5, 5-6), bone marrow lesions (BMLs) (≥1), and definite osteophytes (≥2) in the PFJ. Relation of number of PFJ subregions to knee pain severity (VAS pain) and repeated chair stand time was assessed using ANCOVA. Relation of the odds of at least mild pain with stairs (WOMAC pain scale) and walking < 6,000 steps/day (a level of physical activity associated with risk of incident functional limitation) was assessed using logistic regression. Separate models were created for each PFJ MRI feature. Each analysis was adjusted for age, sex, BMI, previous knee injury/surgery, and coincident TFJ MRI feature.

Results: 1099 knees had complete MRI WORMS readings and performance based function assessed at the 60-month visit. The mean (SD), age and BMI of this sample was 66.8 (7.5) and 29.6 (4.8), respectively; 65% were female. In general, a higher number of PFJ subregions with any MRI-defined structural damage were associated with higher pain levels and longer time to complete 5 chair stands than those with fewer subregions affected (Table 1). Participants with full-thickness cartilage damage or BMLs in 3 or 4 compartments had three times the odds of pain on climbing stairs (Table 2). Participants with full-thickness cartilage damage in at least three compartments or osteophytes in at least one compartment have 2.3 and 2.1 times the odds of walking < 6,000 steps/day (Table 2).

Conclusion: Having damage in multiple subregions of the PFJ is associated with increased pain, decreased function, and greater odds of walking < 6,000 steps/day. The specific outcomes affected depended on the type of tissue damage, with full-thickness cartilage damage appearing to have the most impact across all outcomes. In addition to cartilage damage, osteophytes are associated with walking less steps/day, and BMLs with pain on stair climbing.

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Abstract Number: 1316

Frail Patients Have Less Pain After Total Hip Replacement

Lisa Mandl,[1] Charles Cornell,[1] Michael Cross,[1] Alejandro Gonzalez Della Valle,[1] Mark Figgie,[1] Seth Jerabek,[1] Marianna Frey,[2] John Roberts IV,[3] Justin Do,[3] Mayu Sasaki,[3] Nathaniel Hupert,[4] Jackie Finik,[3] and Steven Magid[1], [1]Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, New York, NY, [2]Hospital for Special Surgery, New York, NY, New York, [3]Hospital for Special Surgery, New York, NY, New York, NY, [4]Weill Cornell Medicine, New York, NY, New York, NY

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
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Pre-Operative Characteristics

Hip patients	Non-frail (n=302)	Frail (n=30)	p-value
Age (years)	71 [67, 76]	77.5 [70, 83]	**0.001**
Previous TKR/TKR	96 (31.89%)	15 (51.72%)	**0.04**
Depression (CESD)	55 (18.21%)	12 (40%)	**0.008**
Back pain	106 (35.22%)	18 (62.07%)	**0.008**
Race: white	287 (95.67%)	28 (93.33%)	0.64
Ethnicity: Hispanic	11 (3.69%)	0 (0%)	0.61
Sex: Male	108 (35.76%)	9 (30%)	0.69
PROMIS physical function	38.1 [34.5, 43.1]	34.5 [30, 36.4]	**<0.001**
PROMIS anxiety	48.1 [40.3, 56]	51.8 [44.1, 55.7]	0.18
PROMIS depression	41 [41, 49.1]	48.9 [41, 54.9]	**0.022**
PROMIS fatigue	48.6 [43.2, 55]	55.2 [53.1, 62.7]	**<0.001**
PROMIS sleep disturbance	51.1 [44.2, 55.1]	53.1 [49.2, 60.9]	**0.04**
PROMIS ability to participate	46.9 [42.4, 53.6]	43.3 [39, 48]	**0.007**
PROMIS pain interference	61 [55.7, 65.5]	64.2 [59.9, 66.7]	**0.006**
PROMIS pain intensity score	6 [4, 7]	7 [6, 8]	**0.003**
HOOS symptoms	50 [35, 60]	36.3 [22.5, 60]	**0.035**
HOOS pain	47.5 [37.5, 57.5]	40 [26.3, 47.4]	**0.003**
HOOS daily living	48.5 [39.7, 61.8]	41.2 [25.7, 54.4]	**0.026**
HOOS sport and rec	25 [12.5, 43.8]	9.4 [0, 28.1]	**0.003**
HOOS quality of life	25 [12.5, 37.5]	18.8 [6.3, 31.3]	**0.025**

BOLD=p-value < 0.05
HOOS Scores represent patient-reported outcome measures scored along a normal distribution with a mean of 50. A score of 100 indicate no problems and 0 indicates extreme problems.

PROMIS T-scores are reported as standardized T-scores, with 50 representing the population mean. A T-Score of 5 is considered a clinically meaningful difference.

AAOS.2020.Hips.Frailty.Table

Background/Purpose: To determine whether frailty is associated with patient outcomes 1 year after total hip replacement (THR).

Methods: Patients ≥65yo scheduled for elective primary THR for osteoarthritis were recruited from a musculoskeletal specialty hospital. All were approved for surgery by an internist. Frailty was defined using composite criteria designed for surgical candidates, evaluated at point of care. Hip Injury and Osteoarthritis Outcome Score (HOOS) and PROMIS29 were administered pre-operatively and at 1-year. Depression was measured using the Center for

Epidemiologic Studies Depression Scale (CES-D 10). A subset of patients had frailty assessed by their surgeon pre-operatively using the brief, self-report Clinical Frailty Scale for Physicians. Wilcoxon rank-sum and Fisher's exact tests were used to compare continuous variables and categorical variables, respectively, across frailty status. Multivariable linear and logistic regressions were modeled for each patient-related outcome, adjusting for confounders identified *a priori* using a directed acyclic graph approach. Spearman correlation coefficients were calculated to evaluate the correlation between frail scales.

Results: 332 hip replacement subjects enrolled, 9% of whom were frail. Frail THR subjects were older, more likely to be depressed, have concurrent back pain, and were also more likely to have had a previous hip or knee replacement. 91.4% provided 1-year follow-up. In a multivariable linear regression controlling for age, gender, race, back pain, education, Charlson comorbidity index, and PROMIS29 anxiety and depression, frailty predicted a clinically meaningful improvement in HOOS pain (β=10.4), which was statistically significant (p=0.01). Frailty also predicted a significant decrease in PROMIS pain interference T-score at 1-year, (β=3.9; p-value 0.023), controlling for the same potential confounders. Frailty did not predict other HOOS subscales or PROMIS29 domains at 1-year. Frailty did not predict cumulative severe adverse events through 1 year or OMERACT-OARSI responder status at 1-year. There was a strong correlation between our frailty definition and the Fried frailty phenotype, (r=0.79; p< 0.001), but a poor correlation with the orthopedic surgeon's frailty assessment (r=0.16; p=0.78).

Conclusion: Frailty was a strong predictor of less hip-related pain and less overall pain interference 1 year after THR in older adults undergoing elective primary THR. Frailty was not associated with odds of adverse events or OMERACT-OARSI responder status. Surgeon assessment of frailty is not an accurate proxy for the frailty phenotype. Appropriately screened frail patients should not be discouraged from having THR for pain relief, particularly given the known risks of long term NSAIDS and narcotics. These data can aid in surgical decision making for frail patients contemplating THR.

Disclosure: **L. Mandl**, Annals of Internal Medicine, 3, Annals of Internal Medicine- Associate Editor, 3, UpToDate, 7, Wolters Kluwer - Author at UptoDate, 7, Wolters Kluwer - Author at UpToDate, 7, Wolters Kluwer- Author at UpToDate, 7; **C. Cornell**, None; **M. Cross**, Acelity, 2, 5, 8, Bone and Joint Journal 360, 6, Depuy, 5, Exactech, Inc., 2, 5, Flexion Therapeutics, 5, 8, Imagen, 4, Insight Medical, 4, Intellijoint, 2, 4, 5, Journal of Orthopaedics and Traumatology, 6, Parvizi Surgical Innovation, 4, Smith + Nephew, 5, Techniques in Orthopaedics, 6, Zimmer, 5; **A. Gonzalez Della Valle**, Intellijoint Surgical, 2, 5, Link Orthopaedics, 5, OrthoDevelopment, 5, 7, Orthosensor, 5, 7; **M. Figgie**, Insight, 4, Lima, 7, Mekanika, 4, Wishbone, 4, 5, 7; **S. Jerabek**, Imagen, LLC, 4, Stryker Orthopaedics, 5, 7; **M. Frey**, None; **J. Roberts IV**, None; **J. Do**, None; **M. Sasaki**, None; **N. Hupert**, None; **J. Finik**, None; **S. Magid**, None.

Abstract Number: 1317

Frail Patients Have Worse Function After Total Knee Replacement

Lisa Mandl,[1] Charles Cornell,[1] Michael Cross,[1] Alejandro Gonzalez Della Valle,[1] Mark Figgie,[1] Seth Jerabek,[1] Marianna Frey,[2] John Roberts IV,[3] Justin Do,[3] Mayu Sasaki,[3] Nathaniel Hupert,[4] Jackie Finik,[3] and Steven Magid[1], [1]Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, New York, NY, [2]Hospital for Special Surgery, New York, NY, New York, [3]Hospital for Special Surgery, New York, NY, New York, NY, [4]Weill Cornell Medicine, New York, NY, New York, NY

SESSION INFORMATION
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Pre-Operative Characteristics

Knee Replacement Patients	Non-frail (n=458)	Frail (n=29)	p-value
Age (years)	72 [68, 77]	75 [70, 78]	0.096
Previous TKR/TKR	170 (37.2%)	13 (45.0%)	1.00
Depression (CESD)	50 (10.9%)	18 (51.4%)	**<0.001**
Back pain	127 (28.0%)	18 (51.4%)	**0.006**
Race: white	433 (94.8%)	33 (94.3%)	0.71
Ethnicity: Hispanic	14 (3.1%)	1 (2.9%)	1.00
Sex: Male	168 (36.7%)	8 (22.9%)	0.14
PROMIS physical function	39.3 [35.5, 43.4]	34.2 [27.9, 38.3]	**<0.001**
PROMIS anxiety	48.1 [40.3, 54.1]	54.1 [47.9, 62.9]	**<0.001**
PROMIS depression	41 [41.0, 48.9]	53.3 [41.0, 56.1]	**<0.001**
PROMIS fatigue	46.1 [39.8, 51.0]	57.1 [51.0, 60.8]	**<0.001**
PROMIS sleep disturbance	49.6 [44.2, 53.0]	51.1 [44.2, 55.8]	0.183
PROMIS ability to participate	51.7 [44.2, 58.1]	42.3 [37.2, 44.9]	**<0.001**
PROMIS pain interference	58.9 [54.2, 62.7]	66.7 [58.7, 67.9]	**<0.001**
PROMIS pain intensity score	5 [3, 7]	7 [4, 8]	**0.005**
KOOS symptoms	57.1 [39.3, 67.9]	50.0 [32.1, 58.3]	**0.015**
KOOS pain	52.8 [41.7, 63.9]	41.7 [36.1, 55.6]	**0.008**
KOOS daily living	57.4 [45.6, 67.6]	44.1 [36.8, 60.3]	**0.001**
KOOS sport and rec	20 [5, 35]	20 [0, 30]	0.375
KOOS quality of life	25 [18.8, 43.8]	18.8 [12.5, 37.5]	0.250

BOLD=p-value < 0.05
KOOS Scores represent patient-reported outcome measures scored along a normal distribution with a mean of 50. A score of 100 indicate no problems and 0 indicates extreme problems.

PROMIS T-scores are reported as standardized T-scores, with 50 representing the population mean. A T-Score of 5 is considered a clinically meaningful difference.

Pre-Op Table (TKR)

Background/Purpose: To determine whether frailty is associated with patient outcomes 1 year after total knee replacement (TKR).

Methods: Patients ≥65yo scheduled for elective primary TKR for osteoarthritis were recruited from a musculoskeletal specialty hospital. All were approved for surgery by an internist. Frailty was defined using composite criteria designed for surgical candidates, evaluated at point of care. Knee Injury and Osteoarthritis Outcome Score (KOOS) and PROMIS29 were administered pre-operatively and at 1-year. Depression was measured using the Center for Epidemiologic Studies Depression Scale (CES-D 10). A subset of patients had frailty assessed by their surgeon pre-

operatively using the brief, self-report Clinical Frailty Scale for Physicians. Wilcoxon rank-sum and Fisher's exact tests were used to compare continuous variables and categorical variables, respectively, across frailty status. Multivariable linear and logistic regressions were modeled for each patient-related outcome, adjusting for confounders identified *a priori* using a directed acyclic graph approach. Spearman correlation coefficients were calculated to evaluate the correlation between frail scales.

Results: 487 knee replacement subjects enrolled, 6% of whom were frail. Frail TKR subjects were more likely to be depressed and have concurrent back pain. 89.9% provided 1-year follow-up. In a multivariable linear regression controlling for age, gender, race, back pain, education, Charlson comorbidity index, and PROMIS29 anxiety and depression, frailty predicted a statistically significant decrease in KOOS Function in Daily Living score at 1-year (β=7.0; p=0.04). Frailty also predicted a significant decrease in PROMIS29 physical function, (β=4.7; p-value 0.002), and a small increase in PROMIS29 Pain Intensity, (β=0.69; p-value 0.047), at 1-year. Frailty did not predict other KOOS subscales or PROMIS29 domains at 1-year. Frailty did not predict cumulative severe adverse events through 1-year or OMERACT-OARSI responder status at 1-year. There was a strong correlation between our frailty definition and the Fried frailty phenotype, (r=0.79; p< 0.001), but a poor correlation with the orthopedic surgeon's frailty assessment (r=0.18; p=0.6).

Conclusion: Frailty was a strong independent predictor of worse KOOS knee-specific function and PROMIS29 global physical function 1 year after TKR in older adults undergoing elective primary TKR. Frailty was not associated with odds of adverse events or OMERACT-OARSI responder status. Surgeon assessment of frailty is not an accurate proxy for the frailty phenotype. These data can help manage expectations of frail patients contemplating TKR. Future studies should assess if targeted interventions to improve frailty can lead to better post-operative function.

Disclosure: **L. Mandl**, Annals of Internal Medicine, 3, Annals of Internal Medicine- Associate Editor, 3, UpToDate, 7, Wolters Kluwer - Author at UptoDate, 7, Wolters Kluwer - Author at UpToDate, 7, Wolters Kluwer- Author at UpToDate, 7; **C. Cornell**, None; **M. Cross**, Acelity, 2, 5, 8, Bone and Joint Journal 360, 6, Depuy, 5, Exactech, Inc., 2, 5, Flexion Therapeutics, 5, 8, Imagen, 4, Insight Medical, 4, Intellijoint, 2, 4, 5, Journal of Orthopaedics and Traumatology, 6, Parvizi Surgical Innovation, 4, Smith + Nephew, 5, Techniques in Orthopaedics, 6, Zimmer, 5; **A. Gonzalez Della Valle**, Intellijoint Surgical, 2, 5, Link Orthopaedics, 5, OrthoDevelopment, 5, 7, Orthosensor, 5, 7; **M. Figgie**, Insight, 4, Lima, 7, Mekanika, 4, Wishbone, 4, 5, 7; **S. Jerabek**, Imagen, LLC, 4, Stryker Orthopaedics, 5, 7; **M. Frey**, None; **J. Roberts IV**, None; **J. Do**, None; **M. Sasaki**, None; **N. Hupert**, None; **J. Finik**, None; **S. Magid**, None.

Abstract Number: 1318

In an International, Multicentre, Double-blind, Randomised Study in Knee Osteoarthritis Patients, Diacerein Was Found as Effective as Celecoxib in Reducing Pain and Disease Symptoms

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: There was a need to ascertain in a clinical trial the comparative efficacy of diacerein, an IL-1 inhibitor, vis-à-vis celecoxib, a COX-2 inhibitor, in relieving knee osteoarthritis (OA) symptoms. The primary outcome of this study was to show that diacerein is non-inferior to celecoxib in terms of pain reduction (WOMAC A pain subscale) after 6 months of treatment in moderate-to-severe symptomatic knee OA patients.

Methods: A randomised double-blind multicentre trial was conducted in four European countries (Spain, Belgium, Austria, Czech Republic) and in Canada evaluating treatment with diacerein versus celecoxib in patients with OA diagnosed according to ACR criteria, with KL grade 2-3 knee OA and moderate-to-severe pain (VAS pain score [0-100 mm] while walking on a flat surface ≥ 40 mm). Eligible patients were randomised to treatment for 6 months with either diacerein 50 mg once daily for the first month and twice daily thereafter, or celecoxib 200 mg once daily. The primary outcome was the change from baseline in WOMAC pain subscale (0-50 scale) after 6 months of treatment. Secondary outcomes included WOMAC function and stiffness, VAS pain, presence of joint swelling/effusion, rescue medication consumption, percentage of OMERACT-OARSI responders, and SF-36. A total of 380 patients were randomised in the study. The primary outcome assessment on the per protocol set (PPS) (n=288) was followed by sensitivity analysis on the ITT population (n=370). Exploratory statistical analysis on other efficacy criteria and safety were performed.

Results: The analysis of the PPS population showed that the adjusted mean change in WOMAC pain was -11.14 (SEM, 0.91) with diacerein (n=140) and -11.82 (0.89) with celecoxib (n=148). Diacerein met the non-inferiority criterion, as the upper bound of the 95% CI is inferior to the pre-specified non-inferiority margin of 5 (inter-group difference 0.67; 95% CI -1.83 to 3.18; p=0.597). The sensitivity analysis using the ITT population was supportive of those results. All other exploratory outcomes demonstrated no difference between the two treatment groups. The OMERACT-OARSI responder rate (PPS) at 6 months was similar in the diacerein (62.1%) and celecoxib (60.1%) groups. The incidence of adverse events related to drug treatment was in general low and balanced between groups. The only exception was a greater incidence of gastrointestinal side effects (diarrhoea) in the diacerein vs. the celecoxib group (10.2% vs. 3.7%, respectively), but accounted for 4.8% of permanent discontinuation in the diacerein group compared to 1.6% in the celecoxib group. In all but one patient, this diarrhoea was considered to be of a mild-to-moderate grade with complete resolution in all cases.

Conclusion: This clinical trial showed that in patients with moderate-to-severe knee OA pain, diacerein has comparable efficacy to celecoxib with respect to reducing pain and stiffness and improving function after 6 months in a clinically relevant manner. The drug also demonstrated a good safety profile with positive benefit to risk ratio.

Disclosure: **J. Pelletier**, ArthroLab Inc., 1, TRB Chemedica, 5; **J. Raynauld**, ArthroLab Inc., 5; **P. Paiement**, ArthroLab Inc., 3; **M. Dorais**, ArthroLab Inc., 5; **J. Martel-Pelletier**, ArthroLab Inc., 1, TRB Chemedica, 5.

Abstract Number: 1319

Impact of ACL Injury Management on the Development of Knee Osteoarthritis: A Meta-analysis

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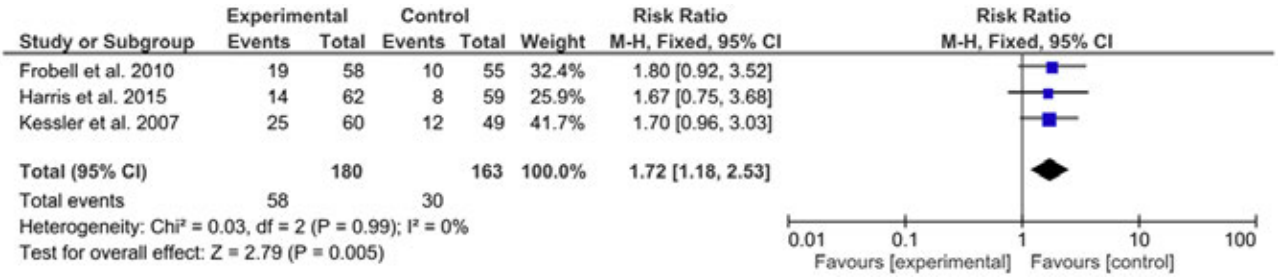
SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Osteoarthritis – Clinical Poster I



Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Background: The development of knee's osteoarthritis after anterior cruciate ligament ACL injury is now widely recognized. The impact of surgical or rehabilitative management on the development of post-traumatic osteoarthritis is still debated.

We present here a meta-analysis about the evolution and progression of knee's osteoarthritis after ACL surgery or conservative management

Methods: A systematic litterature's review was conducted using PubMed, EMBASE, Medline, and Cochrane library data. Only RCTs with a conservative group and a surgical group after anterior cruciate ligament (ACL) injury were included, and if they reported radiographic results of injured knees using the Kellgren and Laurence (KL) classification score. Heterogeneity was evaluated by Cochrane's Q and *I2* statistics.

Results: Six studies were included after litterature's review (February 8, 2019 at May 15, 2019). Three studies met the inclusion criteria and were retained for the meta-analysis. Of the 343 injured knees, 180 underwent ACL reconstruction and 163 received conservative treatment. The relative risk of knee's osteoarthritis was higher after surgery than after conservative treatment (RR 1.72[1.18-2.53], I^2=0%.

Conclusion: The results of this meta analyse show that ACL reconstruction surgery predisposes to knee's osteoarthritis compared to conservative management. This suggests that a review of practices could be considered by promoting non-surgical management in the young subject.

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Abstract Number: 1320

Individual Socio-economic Status and Symptomatic Hip and Knee Osteoarthritis: A Longitudinal Study, Results from the KHOALA Cohort

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SESSION INFORMATION
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Background/Purpose: We analyzed the association between individual socio-economic status (SES) variables and clinical symptoms (function, pain and quality of life) in patients with symptomatic knee and/or hip osteoarthritis.

Methods: The prospective study used data from baseline to the 7-year follow-up visit of the Knee and Hip OsteoArthritis Long-term assessment (KHOALA) cohort. Function and pain were measured by Western Ontario and McMaster Universities Index of Osteoarthritis (WOMAC), and the quality of life by Medical Outcomes Study Short Form 36 (SF-36). Individual SES variables included educational level (5 categories), occupational status (7 categories), the monthly income per household (5 categories) and precarious status (EPICES score ≥30.17). We used a mixed model for repeated measures to analyze our outcomes measured annually at baseline to year 7 of follow-up.

Results: Eight hundred and seventy-eight patients were included. In univariate analyses, SES characteristics were significantly associated with WOMAC function, pain scores and SF-36 score ($p< 0.0001$ for educational level, occupational status, monthly income and precarious status), with a gradient against the less educated, the least qualified professional categories, the lowest monthly income and against precarious patients. In multivariate analyses adjusted on confounding factors (body mass index (BMI), axe, sex, year, education, occupational status, monthly income, precarious status, Kellgren-Lawrence score, groll score, metabolic equivalent of task (MET), evolutive time….), the WOMAC function score was associated with occupational status ($p=0.0393$) and precarious status (ß=1.81, 95% CI=0.72 to 2.90, $p=0.00011$). The WOMAC pain score was associated with occupational status ($p=0.0128$) and with educational level ($p=0.0232$). We didn't observe a significant interaction between the time and the SES variables. Mental SF-36 score was associated with monthly income per household ($p< 0.0001$) and the precarious status (ß=-2.41, 95% CI=-3.83 to -0.99, $p=0.0016$). The physical SF-36 score was associated with educational level ($p=0.0059$) and precarious status (ß=-1.52, 95% CI=-2.15 to -0.88, $p< 0.0001$).

Conclusion: Our results suggest that individual SES characteristics have a significant impact on function and pain in hip and knee OA even taking into account various risk factors.

Disclosure: **P. Baudart**, None; **A. Rat**, Pfizer, lilly, 5; **C. Marcelli**, None; **J. Bryère**, None.

Abstract Number: 1321

What Is the Relationship Between the 3 Knee Bones in Osteoarthritis? Baseline and Longitudinal Associations Using a Latent Growth Modelling Approach on 37,583 MR Images from the Osteoarthritis Initiative

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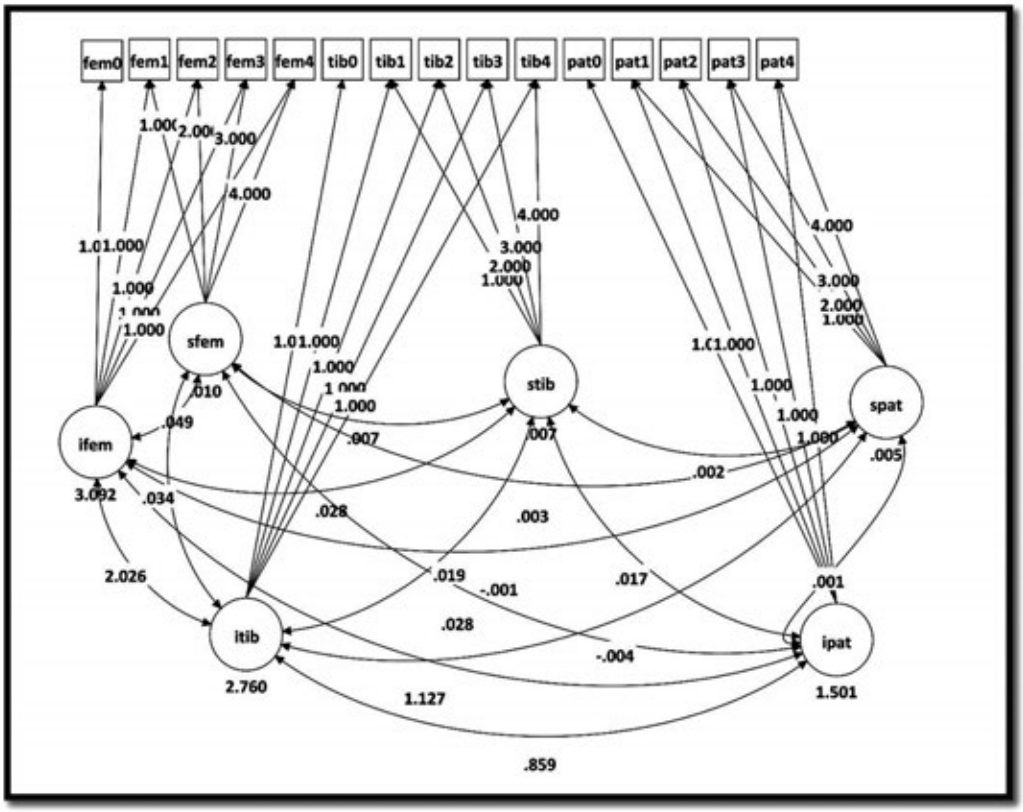
Background/Purpose: 3D femur bone shape measured by statistical shape modelling (SSM) provides a responsive biomarker of knee OA. However it is unclear how the 3 knee bones (femur, tibia and patella) relate to each other and whether responsiveness is only femur-specific. We assessed baseline and longitudinal relationships between the 3 knee bones and examined factors influencing these.

Methods: We included 4796 Osteoarthritis Initiative participants with 4 year follow up (37,583 MRIs, 5031 knees without OA at baseline). 3D bone data was computed by Imorphics (Manchester, UK) from MRIs using SSMs. Briefly, an OA vector is constructed for each bone, defined as a line passing through mean shapes of bone with

Fig. 1 Parallel process growth curve model of change in all 3 bones



* fem0-fem4 = femur baseline to year 4; tib0-tib4 = tibia baseline to year 4 & pat0-pat4 = patella baseline to year 4
*ifem= femur intercept, sfem= femur slope
*itib= tibia intercept, stib=tibia slope
*ipat=patella intercept, spat=patella slope
* Values at the bottom of each growth factor ("6 o`clock posit ion") represent variances of that growth factor

Table 1 Parameter estimates from Latent Growth Curve model

Model	Intercept (95% CI)	Slope (95% CI)	Intercept/slope covariance (95%CI)	RMSEA (<0.08)	CFI (>0.95)	SRMR (<0.08)
Overall (one group model)						
Femur	1.03 (0.99,1.07)	0.100 (0.09,0.10)	0.06 (0.06,0.07)	0.057	0.997	0.004
Tibia	0.87 (0.83,0.91)	0.05 (0.05,0.06)	0.03 (0.02,0.03)	0.047	0.997	0.006
Patella	0.69 (0.66,0.72)	0.05 (0.05,0.06)	0.01 (0.00,0.01)	0.043	0.996	0.007
Multi group models						
Femur				0.067	0.995	0.004
Male model	0.93 (0.87,1.00)	0.07 (0.07,0.08)	0.05 (0.04,0.06)			
Female model	1.10 (1.04,1.16)	0.12 (0.12,0.13)	0.07 (0.06,0.08)			
Tibia				0.059	0.996	0.006
Male model	0.82 (0.76,0.88)	0.04 (0.03,0.04)	0.02 (0.01,0.03)			
Female model	0.91 (0.86,0.96)	0.07 (0.06,0.07)	0.03 (0.02,0.04)			
Patella				0.064	0.993	0.010
Male model	0.56 (0.52,0.61)	0.04 (0.03,0.04)	0.00 (-0.01,0.01)			
Female model	0.77 (0.73,0.82)	0.07 (0.06,0.07)	0.01 (0.00,0.02)			
Parallel process model for femur				0.046	0.993	0.005

Covariances between latent variables in males	Estimate	Standard Error	p-value
Femur intercept with femur slope	0.050	0.005	<0.001
Femur intercept with tibia intercept	2.026	0.081	<0.001
Femur intercept with patella intercept	1.127	0.056	<0.001
Femur intercept with tibia slope	0.028	0.005	<0.001
Femur intercept with patella slope	-0.001	0.005	0.814
Femur slope with tibia slope	0.007	0.000	<0.001
Femur slope with patella slope	0.003	0.000	<0.001
Tibia intercept with tibia slope	0.019	0.004	<0.001
Tibia intercept with patella intercept	0.859	0.051	<0.001
Tibia intercept with patella slope	-0.004	0.005	0.480
Tibia slope with patella slope	0.002	0.000	<0.001
Patella intercept with patella slope	0.001	0.004	0.811

Values in brackets are cut-offs for good fit; RMSEA= Root Mean Square Error of Approximation; CFI=Comparative Fit Index
SRMR= Standardized Root Mean Square Residual.

and without OA, parameterised as shape components. Individual bone shapes are projected orthogonally onto this vector. Zero is defined as the mean position along the vector in those with a KL score of 0 for 4 consecutive years (Non-OA group); +1 unit is 1SD of the Non-OA group. Analyses were stratified by gender, independently for each bone. Correlation analysis was performed between bones. Next, bones classed as “OA” (bones falling above the 95th percentile of the Non-OA group) were described for all possible combinations using proportions. Latent Growth Curve Modelling (Mplus) identified growth patterns for each bone. After establishing the best-fitting models we tested the effect of covariates (age, weight, ethnicity, pain and history of knee surgery) on intercept and slope. Lastly parallel process growth models were fitted by modelling growth in all bones using one model, allowing each bone to co-vary.

Results: Positive correlation was seen between bones (femur vs tibia, *r*=0.68; femur vs patella, r=0.55& tibia vs patella, *r* =0.45). In the 3775 OA knees, 25% had all 3 bones classed as OA, 19% exclusively femur, 15% tibia, 11% patella and 20% had femur+tibia. Linear growth models showed excellent fit to the data (Table 1).Greatest rate of change, representing worsening was seen in femur (slope ~ 0.10). Increase in femur was 0.06 units/unit of baseline femur (Table 1). Rate of change in females was twice that of males. Age had no effect, but ethnicity particularly in females influenced all bones (lower intercepts in Caucasians). Ethnicity was also associated with slopes in both femur and tibia in females (Table 2). Only weight in females was associated with patella slope. Knee pain and body weight explained most intercept and slope variance (Table 2), prior knee surgery influenced baseline scores but explained

Table 2 Effect of covariates on growth curves

	Male models				Female models			
Covariate	Estimate Intercept (95% CI)	Estimate slope (95% CI)	*Intercept variance explained (%)	*Slope variance explained (%)	Estimate Intercept (95% CI)	Estimate slope (95% CI)	*Intercept variance explained (%)	*Slope variance explained (%)
Femur univariable								
Age	0.015 (0.007, 0.024)	0.000 (0.000, 0.001)	0.7	-	0.019 (0.011, 0.027)	-0.001 (-0.001, 0.000)	0.9	-
Weight	0.023 (0.018, 0.029	0.001(0.001, 0.001)	3.7	10.0	0.035 (0.030, 0.039	0.002 (0.002, 0.003)	8.1	5.0
Ethnicity	-0.403(-0.613, -0.194)	0.001 (-0.001, 0.016)	0.7	-	-0.675 (-0.830, -0.520)	-0.018 (-0.033, -0.004)	2.6	-
Pain	0.154 (0.125, 0.183)	0.008 (0.006, 0.010)	5.5	10.0	0.148 (0.128, 0.168)	0.011 (0.009, 0.013)	7.3	5.0
Surgery	0.746 (0.582, 0.910)	0.019 (0.007, 0.030)	3.9	-	0.881 (0.696, 1.066)	0.052 (0.034, 0.069)	3.1	-
All covariates (multivariable)	-	-	**13.9**	-	-	-	**21.4**	**10.0**
Tibia univariable								
Age	0.019 (0.011, 0.027)	0.000 (-0.001, 0.000)	-	-	0.020 (0.011, 0.027)	0.000 (-0.001, 0.000)	1.4	-
Weight	0.023 (0.017, 0.001)	0.001(0.000, 0.001)	3.8	14.3	0.024 (0.020, 0.028)	0.002 (0.001, 0.002)	5.2	10.0
Ethnicity	-0.020 (-0.219, 0.179)	-0.003 (-0.017, 0.011)	-	-	-0.291 (-0.422, -0.161)	-0.020 (-0.032, -0.009)	0.7	-
Pain	0.114 (0.086, 0.142)	0.006 (0.004, 0.008)	3.3	14.3	0.103 (0.086, 0.142)	0.008 (0.086, 0.121)	5.1	10.0
Surgery	0.579 (0.423, 0.736)	0.011(0.000, 0.022)	2.6	-	0.714 (0.423, 0.736)	0.027 (0.000, 0.022)	3.0	-
All covariates (multivariable)	-	-	**11.2**	**14.3**	-	-	**13.4**	**10.0**
Patella univariable								
Age	0.022 (0.016, 0.028)	0.000 (-0.001, 0.001)	3.0	-	0.020 (0.014, 0.025)	0.000 (-0.001, 0.001)	1.7	-
Weight	0.015 (0.011, 0.019)	0.000 (0.000, 0.000)	3.3	-	0.028 (0.024, 0.031)	0.001 (0.000, 0.001)	10.0	-
Ethnicity	-0.326 (-0.475, -0.178)	0.006 (-0.001, 0.023)	1.0	-	-0.528 (-0.639, -0.416)	0.007 (-0.006, 0.019)	3.1	-
Pain	0.091 (0.070, 0.111)	0.001 (-0.001, 0.004)	3.9	-	0.080 (0.070, 0.111)	0.004 (-0.001, 0.004)	4.2	-
Surgery	0.259 (0.141, 0.377)	-0.008 (-0.021, 0.005)	1.0	-	0.321 (0.186, 0.456)	0.015 (0.000, 0.029)	1.4	-
All covariates (multivariable)	-	-	**12.6**	-	-	-	**17.4**	**20.0**

* As covariates were added to the unconditional model, the significance of the variance accounted for by the covariates was tested by fitting a reduced model in which the covariates' effect on the growth parameters were constrained to be zero and conducting the appropriate chi square test between the 2 models.
Ethnicity reference = non-white group, Pain = WOMAC Knee pain, Surgery = history of knee surgery (includes meniscectomy, arthroscopy and ligament repair)

little variance. Interrelationships between all 3 bones in their disease starting points and rates of change were statistically significant (Table 1, Figure 1).

Conclusion: There was positive correlation between the 3 bones, stronger between femur and tibia. All bones changed linearly; rate of change of femur twice that of tibia and patella and the rate in females twice that of males. Level of baseline disease, body weight and pain were important determinants of change, with similar effects on femur and tibia. Effects on patella were small, possibly due to difficulty in measuring this small bone. It therefore seems likely that the femur, tibia and patella bones are part of a single disease process, with the femur providing the greatest change.

Disclosure: **B. Dube**, None; **M. Bowes**, Imorphics (Stryker), 3, OrthoTrophix, 9; **E. Hensor**, None; **S. Kingsbury**, None; **P. Conaghan**, Abbvie, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, 8, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Eli Lilly, 8, EMD, 5, EMD Serono, 5, EMD Serono Research and Development Institute, Inc., 5, 8, Flexion, 5, 8, Flexion Therapeutics, 5, 8, Galapagos, 5, 8, Glaxo Smith Kline, 5, GlaxoSmithKline, 5, 8, Lilly, 8, Medivir, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Samumed, 5, 8, Serono, 5, Stryker, 5, 8.

Abstract Number: 1322

Evaluation of Intra-articular CNTX-4975 in Subjects with Painful Bilateral Knee Osteoarthritis: Effects on Pain with Walking and Patient Impression of Change in Pain

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A double-blind, randomized, placebo-controlled trial (TRIUMPH; NCT02558439) with a single 1 mg intra-articular (IA) injection of CNTX-4975 (highly purified *trans*-capsaicin) into one knee for management of moderate to severe pain associated with knee osteoarthritis (OA) revealed a statistically significant and clinically meaningful decrease in pain with walking vs placebo through 24 weeks post-dose. The present open-label study (NCT03472677) evaluated the efficacy and safety of a prefilled syringe with an aqueous formulation of CNTX-4975. Presented here are the 6-week outcomes after bilateral CNTX-4975 injections.

Methods: Subjects (aged 45-75 y) with bilateral moderate to severe painful knee OA (numeric pain rating scale [NPRS, 0–10]) score of 4–9 inclusive required for enrollment) for ≥3 months before study entry received a single IA injection of CNTX-4975 1 mg into each knee, with 7 days (±2 days) between injections. ACR criteria were met by 67% of subjects for knee OA as assessed by knee pain, radiographic findings, and age >50 y; the other 33% had pain and radiographic findings, but were aged 47–49 y. IA lidocaine 2% (without epinephrine, 15 mL) was given 3–30 minutes before injection of CNTX-4975. Skin around the knee was cooled before lidocaine injection and throughout the procedure using different methods, and temperature changes in the knee joint were documented with an IA temperature probe. Pain with walking over the previous 24 hours was rated by the NPRS at baseline and at 6 weeks (trial end). Subjects also rated the change in pain in each knee using the Patient Global Impression of Change (PGIC) scale (7-point categorical scale from very much worse to very much improved). Knees were examined to determine the presence of injection site reactions, and adverse events were recorded.

Results: Fifteen subjects (30 knees) with bilateral knee OA (12 male, 3 female; mean age, 57 y) were enrolled and completed the study. Baseline and day 42 NPRS scores were averaged across both knees. At 6 weeks, pain rating by NPRS was reported as 0 in 13 of 30 assessments (15 subjects, both knees), and pain score was reported as ≤3 of 10 for 26 of 30 knees. A similar pattern of improvement was evident with the PGIC (**Table**): in 26 of 30 recordings, subjects described pain at trial end as much or very much improved. No subject reported pain as being unchanged or worse in either knee. Treatment-emergent adverse events (TEAEs) reported on the day of injection were nausea (n=3), headache (n=2), vasovagal attack, dizziness, elevated blood pressure, and tachycardia (n=1 each); all were reported as mild with 2 (vasovagal attack and 1 report of nausea) deemed possibly related to treatment. TEAEs reported after the day of injection were insect bite (n=2) and hay fever, vasovagal attack, back pain, acid reflux (esophageal), allergic conjunctivitis, and bruise (n=1 each); all were mild and deemed unlikely or not related to study treatment.

Table: PGIC* in Subjects With Bilateral Painful Knee Osteoarthritis		
	Day 42	
Subject	Left	Right
1006	1	1
1007	1	1
1008	1	1
1009	2	3
1010	2	2
1011	2	2
1012	2	3
1013	1	1
1014	1	1
1015	1	1
1016	1	1
1017	1	1
1018	2	1
1019	1	1
1020	3	3

PGIC, Patient Global Impression of Change.
*7-point categorical scale; 1=very much improved, 2=much improved, 3=minimally improved, 4=no change, 5=minimally worse, 6=much worse, 7=very much worse.

Conclusion: Pain in bilateral osteoarthritic knees was rated much or very much improved in 87% of assessments, and >40% of knees were reported pain free at 5–6 weeks post CNTX-4975 injection.

Disclosure: **R. Stevens**, Centrexion Therapeutics Corp, 3, 4; **K. Guedes**, Centrexion Therapeutics Corp, 3; **N. Mistry**, Centrexion Therapeutics Corp, 3; **P. Tiseo**, Centrexion Therapeutics Corp, 3; **D. Lascelles**, Centrexion Therapeutics Corp, 9; **M. Mendoza**, Centrexion Therapeutics Corp, 3; **D. Ball**, None.

Abstract Number: 1323

Autologous Conditioned Serum and Plasma Rich in Growth Factors Show Stronger Evidence of Efficacy Than Other Kinds of Platelet-Rich Plasma

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Osteoarthritis – Clinical Poster I

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: While there is growing evidences for the efficacy of platelet-rich plasma (PRP), there is still no standardized composition. There are 3 major types of PRP: Leukocytes Rich (LR), Leukocytes Poor (LP), and Autologous Conditioned Serum (ACS) or Plasma Rich in Growth Factor (PRGF) which are without any cells. Since 2014 no meta-analysis tried to compare separately the different type of PRP. The purpose of this meta-analysis was to compare separately each kind of PRP versus hyaluronic acid (HA) for osteoarthritis (OA) to find if one of them stands out.

Methods: Randomized Controlled Trials (RCTs) at least single blinded, comparing the use of PRP an HA for OA were retrieved from PubMed, Cochrane, Embase until May 2019 and from abstracts of EULAR and ACR congrersses for the last 3 years. We chose the most used follow-up time, which was 6 months. Two readers extracted the Western Ontario and McMaster University Arthritis Index (WOMAC) and any other pain scale, and adverse events. The pooled data where analyzed with Review Manager 5.3.5.

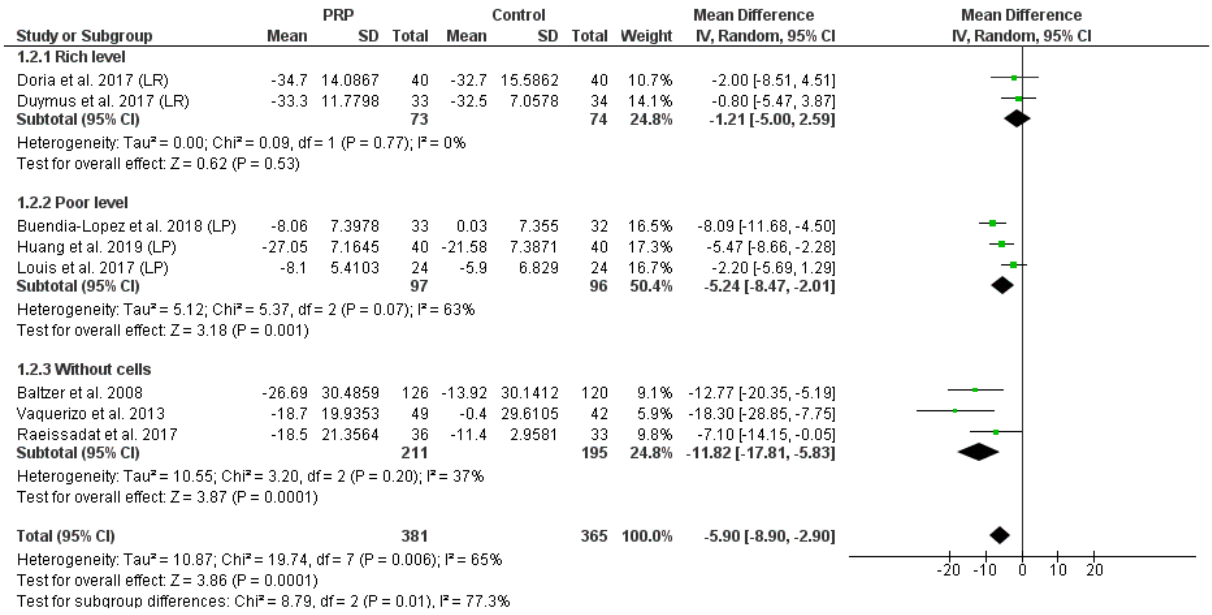

Figure 1. WOMAC changes at 6 months in different subgroups of PRP versus HA

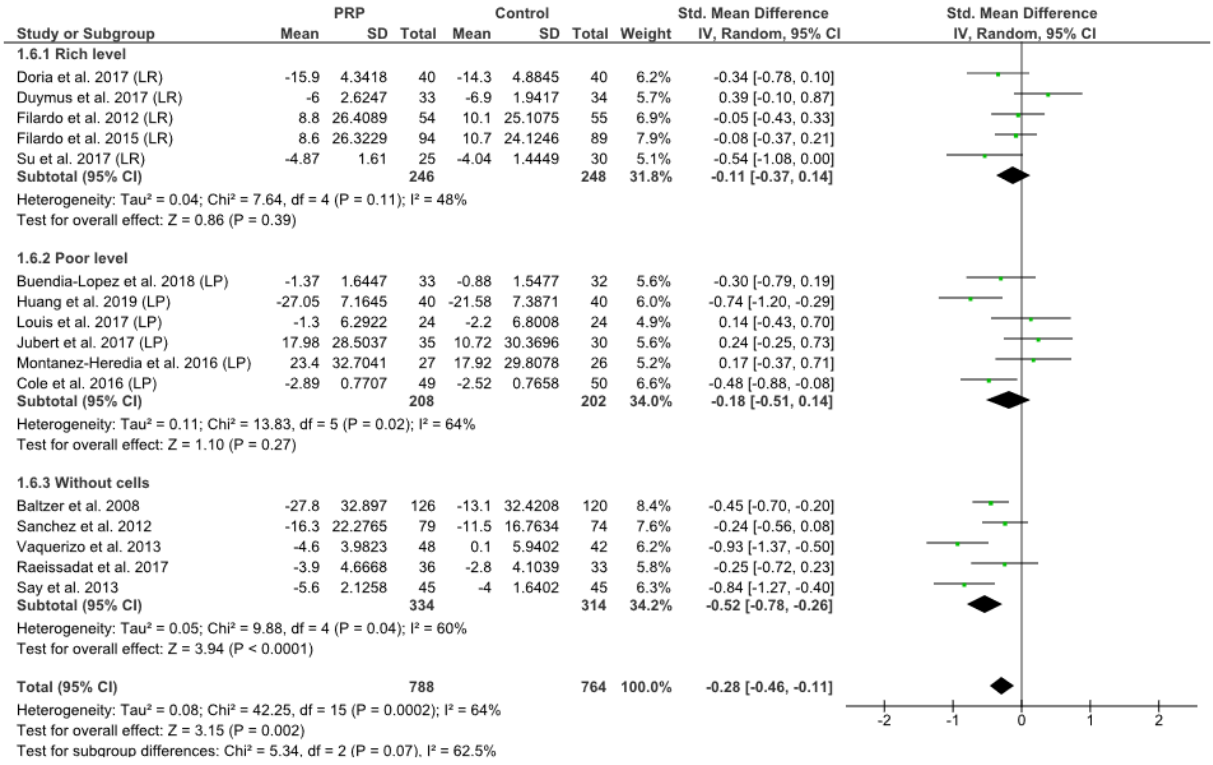

Figure 2. Standardize mean difference of pain scales at 6 months in different subgroups of PRP versus HA

Results: 1139 results were screened, 24 RCTs met the inclusion criteria, and only 16 where enough detailed to be meta-analyzed. The present meta-analysis indicated that only PRGF/ACS and LP PRP reduced significantly the WOMAC score compared with HA. The WOMAC was reduced by 5.24 points with LP-PRP and 11.82 points with ACS/PRGF (Fig.1). Concerning the pain scales only the ACS/PRGF group shown a significant difference versus HA (Fig.2). We found no link between injected platelet quantity and WOMAC index.

Conclusion: ACS/PRGF have stronger evidence of efficacy than LP or LR PRP. These results are consistent with the theorical models explaining the ways of action of PRP. Numbers of authors theorizes that anti-inflammatory cytokines contained in the platelets (like IL-1ra, TGF-β, IL-10) are responsible for the effect of PRP, while leukocyte (containing pro-inflammatory cytokines and metalloproteases) are harmful for the cartilage. The principal limit of this meta-analysis is the heterogenicity of the studies probably due to the absence of standardization of PRP, indeed inside this 3 subgroups, the preparations can still differs by the platelet concentration, the activation of platelet -chemical, physical or unactivated- or the injection scheme . No conclusion can be drawn about the superiority of one kind of PRP since we lack face to face studies.

Disclosure: **L. SOLE**, None; **A. Beck**, None; **T. Barnetche**, None; **P. Vergne-Salle**, None.

Abstract Number: 1324

Visceral Fat Deposition Associated with Pain in Osteoarthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Animal model studies have demonstrated the significant role of inflammation in the pathogenesis of osteoarthritis (OA) and of pain. Visceral fat, rather than subcutaneous fat, is a major source of proinflammatory cytokines and adipokines. In this study, we examined whether amount of visceral fat was associated with the risk of knee OA or musculoskeletal pain.

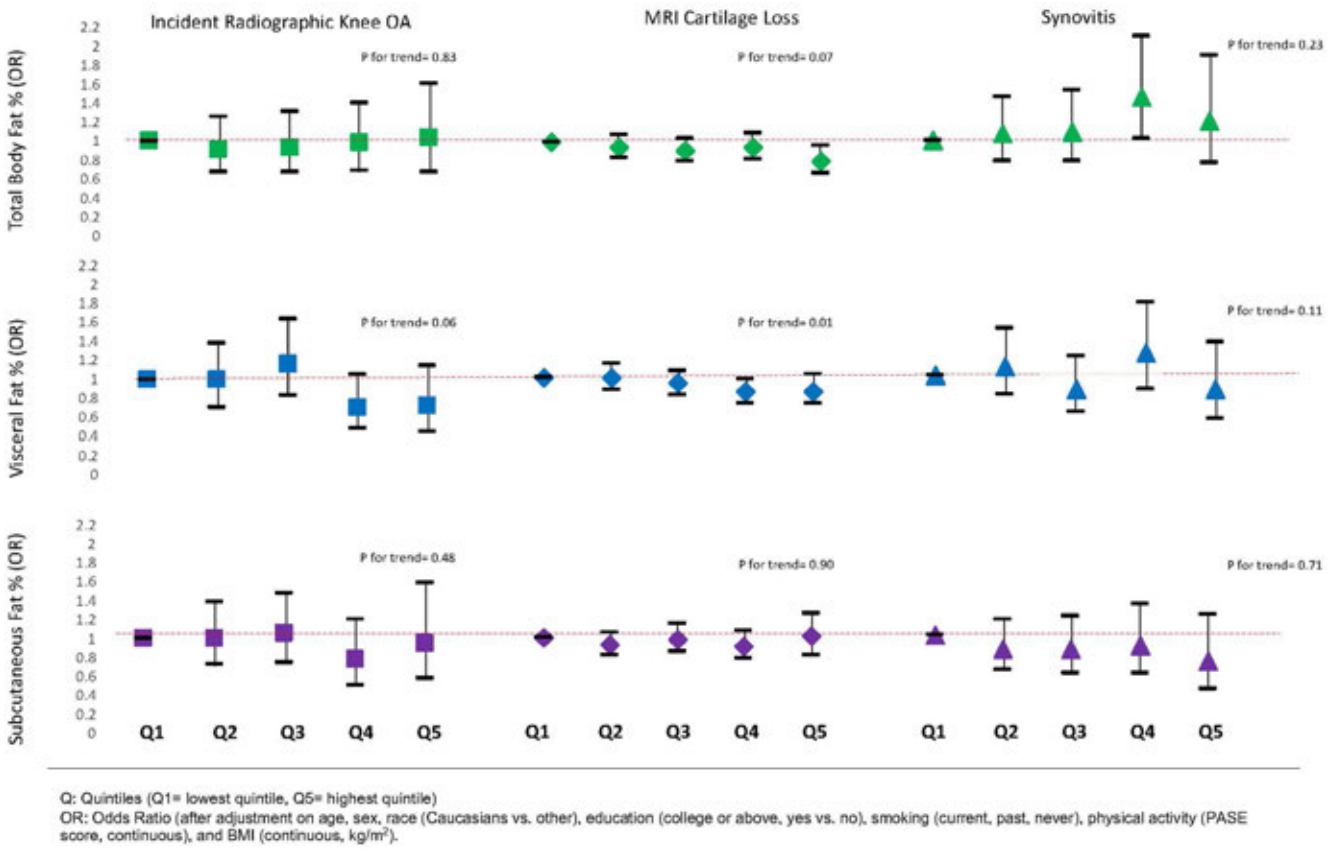

Figure 1. Association Between Fat Depots and Structural Outcomes

Methods: Participants in the Multicenter Osteoarthritis Study (MOST), a NIH funded longitudinal cohort study of persons at risk of or with knee OA underwent whole body dual energy x-ray absorptiometry (DEXA) scans at baseline that were assessed for total body fat as well as visceral fat and subcutaneous fat in the torso. In addition, participants had knee x-rays, rated severity of their knee pain and identified sites of joint pain on a body homunculus at the baseline, 30 month, and 60 month study visits. The association between the size of the fat depots with structural outcomes from baseline through 60 months (incident x-ray OA, MRI cartilage loss and worsening synovitis scores) and with pain outcomes over the same period (worsening pain; widespread pain and the number of painful joint sites) was assessed. We tested the association of sex specific quintiles of fat depot size with OA and pain outcomes performing regression analysis adjusted for age, sex, race, education, smoking, physical activity and BMI. For pain outcomes, we also adjusted for depressive symptoms and for all outcomes, adjusted for baseline status of the outcome (e.g. for WOMAC pain change, we adjusted for WOMAC pain at baseline).

Results: We studied 2,961 participants, of whom, 60.7% were women, mean age was 62.5 years and BMI 30.5 kg/m^2. After adjustment for covariates including BMI, we found no association of any fat depot size with incident

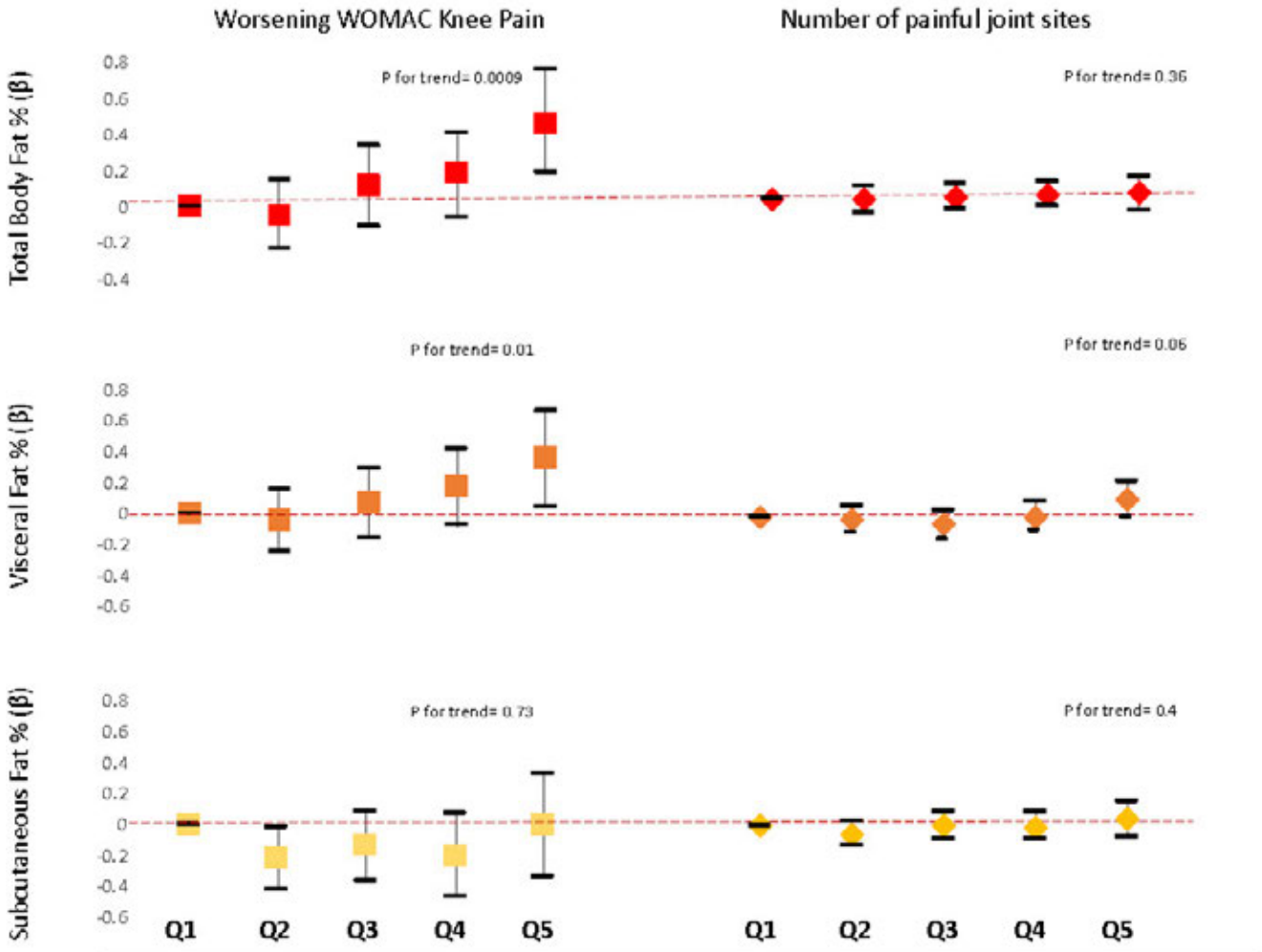

Figure 2. Association Between Fat Depots and Pain Outcomes

x-ray OA, cartilage loss or worsening synovitis on MRI (see figures below). On the other hand, total body fat and visceral fat deposit size were associated with worsening knee pain. Visceral fat in addition was associated with the number of painful joints and similar results were seen in the analyses of incident widespread pain. Subcutaneous fat was not associated with any of these pain measures. In these analyses, fat depots were associated with OA outcomes before analytic adjustment for BMI but positive results for only pain outcomes persisted after BMI adjustment.

Conclusion: Visceral fat and total body fat are associated with increased musculoskeletal pain. We found no relationship between body fat and structural changes in OA. Further investigation into identification of specific inflammatory markers produced by body visceral fat may provide further insight into these findings.

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Abstract Number: 1325

Safety, Tolerability, Pharmacokinetics and Pharmacodynamics in Healthy Male Japanese Subjects of the ADAMTS-5 Inhibitor S201086/ GLPG1972, a Potential New Treatment in OA

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The disintegrin and metalloproteinase with thrombospondin motifs-5 (ADAMTS-5) is a key enzyme in OA (Verma P, *et al.* J Cell Biochem 2011;112:3507-14). In preclinical models of OA, S201086, a potent and selective inhibitor of ADAMTS-5, protects from cartilage degradation (Clement-Lacroix, *et al.* Osteoarthritis Cartilage 2017;25:S58). Therefore, S201086 is co-developed by Servier and Galapagos (GLPG1972) as a potential new treatment in OA.

The objective of this phase I study was to assess and compare the safety, tolerability, pharmacokinetics and pharmacodynamics of S201086 in healthy male Japanese and Caucasian subjects.

Methods: Six ascending single doses of S201086 (50 mg to 1500 mg) were administered orally as tablets in fasting conditions in 6 groups of 8 Japanese subjects (aged 20-45 years) and 3 ascending multiple doses (300, 600 or 1050 mg/day for 14 days) were administered orally as tablets in fed conditions in 3 groups of 8 Japanese subjects. Additionally, 2 cohorts of 8 Caucasian subjects received either a single oral dose of 300 mg or repeated oral dose of

Table - Comparison of ARGS concentration relative change from baseline to last day of treatment according to dose in Japanese participants

		S 201086 300 mg (N = 6)	S 201086 600 mg (N = 6)	S 201086 1050 mg (N = 6)	Placebo (N = 6)
Descriptive Statistics					
(D14 pre-dose – Baseline) / Baseline	n	6	6	4	6
	Mean ±SD	-42.67 ± 8.81	-53.70 ± 6.50	-54.11 ± 5.20	13.35 ± 16.53
	Median	-46.80	-53.64	-55.78	10.75
	Q1 ; Q3	-47.50 ; -35.86	-59.33 ; -48.15	-57.88 ; -50.33	-1.44 ; 24.48
	Min ; Max	-51.02 ; -28.02	-62.14 ; -45.27	-58.01 ; -46.86	-3.45 ; 38.98
Statistical analysis					
	E (SE)	56.01 (6.156)	67.04 (6.156)	67.45 (6.883)	
	95% CI	43.08 ; 68.95	54.11 ; 79.97	52.99 ; 81.91	
	p-value	< 0.0001	< 0.0001	< 0.0001	

LEGEND:
Analysis of variance model on factor dose
(1) Estimate (Standard Error) of the difference between dose means: Placebo minus 300 mg Japanese, 600 mg or 1050 mg
(2) Two-sided 95% Confidence Interval of the estimate
(3) Two-sided p-value of the dose effect

300 mg once daily for 14 days. In each group, 6 subjects received S201086 and 2 placebo. Plasma was collected at several time points for the quantification of S201086 by LC-MS/MS. Plasma pharmacokinetic parameters were calculated via non-compartmental analysis using Phoenix® WinNonlin® software. Pharmacodynamics was assessed by measurement of the aggrecan ARGS neoepitope levels in serum by ELISA.

Results: No serious adverse drug reactions were observed after administration of single and multiple ascending doses of S201086 in either Japanese or Caucasian subjects. Most adverse events were of mild to moderate intensity and were resolved by the end of the study. Following single administration to Japanese subjects, C_{max} and AUC increased proportionally with doses from 50 to 600 mg and slightly less than dose-proportionally from 600 to 1500 mg, consistent with what was previously observed in the first in-human study in healthy Caucasian subjects (van der Aar E, *et al.* Osteoarthritis Cartilage 2018;26:S310). In Japanese subjects, after 14-days administration, a limited 1.2- to 1.4-fold accumulation was observed on both C_{max} and AUC at Day 14 as compared to Day 1, and the steady-state exposure increased dose-proportionally within the 300-1050 mg dose range. Taking the inter-subject variability into account, no difference was observed in C_{max} and AUC between Caucasian and Japanese subjects after single administrations of 300 mg and repeated administrations of 300 mg once daily for 14 days. The serum ARGS neoepitope levels decreased between baseline and last day of treatment for S201086-treated subjects but not for subjects receiving placebo. This decrease was similar for the 3 tested doses in Japanese subjects and was significant as compared to the placebo-treated subjects (see Table).

Conclusion: S201086 was shown to be safe and well-tolerated in Japanese and Caucasian healthy male subjects with a suitable PK profile and a significant decrease of the ARGS neoepitope, indicating target engagement. A global Phase 2 study to evaluate the efficacy of S201086 in patients with knee OA is ongoing (NCT03595618).

Disclosure: **A. Lalande**, Institut de Recherches Internationales Servier, 3; **N. Kuzniatsova-Mouchette**, Institut de Recherches Internationales Servier, 3; **F. Chassereau**, Institut de Recherches Internationales Servier, 3; **J. Geronimi**, Institut de Recherches Internationales Servier, 3; **S. Larsson**, None; **A. Struglics**, None; **S. Lohmander**, Pfizer, 8,

Roche, 5, GSK, 5, Johnson & Johnson, 5, Galapagos, 5, Regeneron, 5; **M. Pueyo**, Institut de Recherches Internationales Servier, 3.

Abstract Number: 1326

Safety Profile to Date of the Novel, Intra-articular Agent Lorecivivint (LOR; SM04690), a CLK/DYRK1A Inhibitor That Modulates the Wnt Pathway, in Subjects with Knee Osteoarthritis

Ismail Simsek,[1] Chris Swearingen,[1] Sarah Kennedy,[1] Jeyanesh Tambiah,[1] **Yusuf Yazici**,[2] Nancy Lane,[3] and Marc C. Hochberg[4], [1]Samumed, LLC, San Diego, [2]Samumed, LLC, San Diego, CA, [3]University of California at Davis Medical Center, Sacramento, CA, [4]University of Maryland School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent concerns over osteoarthritis (OA) pharmacotherapy safety have led to revision of treatment guidelines and highlight the need for therapies with good safety profiles. Lorecivivint (LOR; SM04690) is a small-molecule, intra-articular (IA) CLK/DYRK1A inhibitor which modulates the Wnt pathway and is in development as a potential disease-modifying treatment for knee OA. A pooled analysis of safety data from three completed placebo-controlled studies of this new agent is reported here.

Methods: Safety data were pooled from three randomized controlled trials evaluating four concentrations (0.03 mg, 0.07 mg, 0.15 mg, and 0.23 mg) of a single IA LOR injection in subjects with moderate-to-severe symptomatic knee OA. Two trials (NCT02095548; NCT03122860) evaluated subjects for 24 weeks and one trial (NCT02536833) for 52 weeks. Two subject groups were compared: a LOR-exposed group (subjects who received any dose of LOR) and a control group (non-LOR treated subjects). Adverse events (AEs) and serious AEs (SAEs) were collected and categorized using the Medical Dictionary for Regulatory Activities (MeDRA) classification. Bone health AEs were also categorized upon medical review. Proportions of subjects with treatment-emergent AEs and SAEs were calculated for control and LOR-exposed groups. Incidence rates of bone health AEs were estimated per 100 person-years [PY] exposure for LOR and control groups.

Results: The overall incidence of AEs and SAEs were infrequent in both treated (total 350/848 [41.3%], SAE 20/848 [2.4%], 559 PY exposure) and control subjects (total 138/360 [38.3%], SAE 4/360 [1.1%], 219 PY exposure). The most common AE reported in the treated subjects was arthralgia (treated 7.6%, control 7.2%) and it was the only AE reported at >5% in either subject group (Fig. 1). Of joint-specific AEs categorized by the affected joint (Fig. 2), target-knee arthralgia was most common (treated 6.5%, control 5.3%). No AEs in other joints exceeded an incidence of 2% in either group. In all categories, individual AEs were reported at comparable rates between groups and no SAEs were deemed related to LOR by investigators.

There were 16 bone-health-related AEs in 12/1208 (1.0%) subjects; the rate of bone health AEs per 100 PY exposure was 1.61 for LOR and 1.37 for control. Of the bone health AEs, 2 were osteopenia/osteoporosis in 2 LOR-treated postmenopausal women and 14 were fractures in 10 subjects (7 LOR 1.25/100 PY, 3 control 1.37/100 PY). All frac-

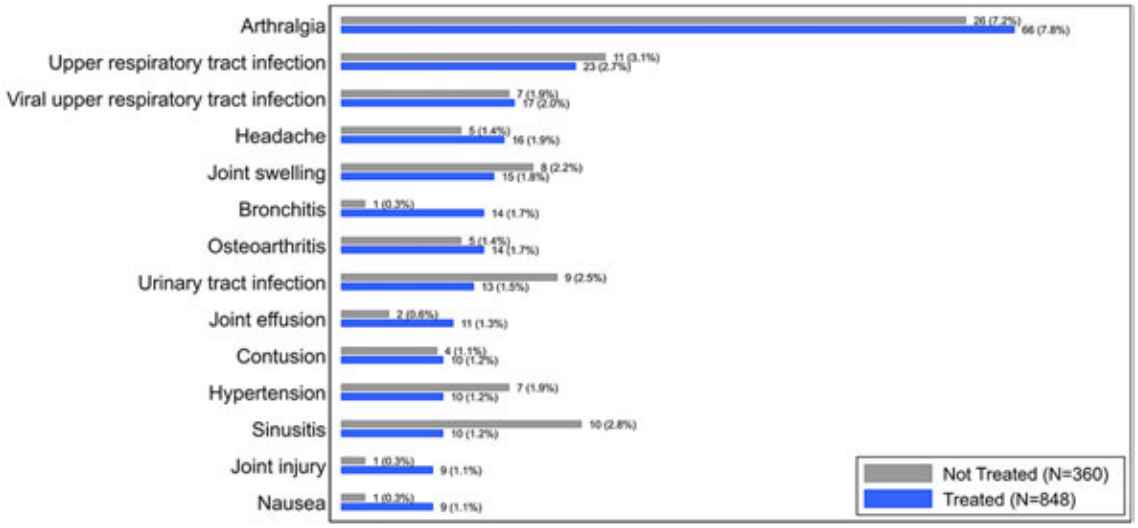

Figure 1. Adverse event summary of the total clinical trial population (N=1208) for events occurring in at least 1% of the treated population.

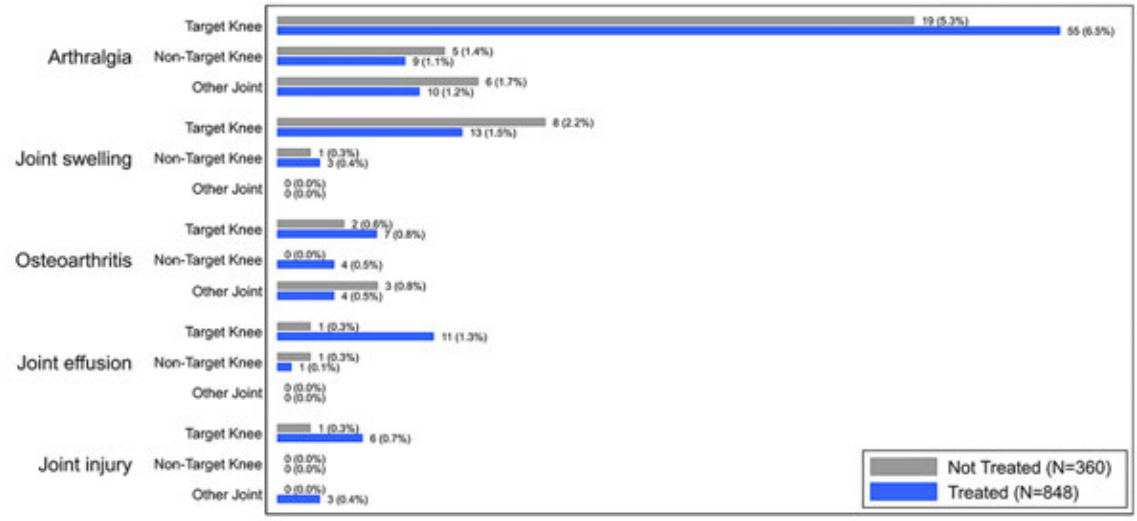

Figure 2. Joint-specific adverse event summary of the total clinical population (N=1208) for events occurring in at least 1% of the treated population and subcategorized by affected joint.

tures were adjudicated and determined to be caused by trauma and all healed uneventfully within the expected timeframe. Bone health AE incidence rates between LOR and control were similar.

Conclusion: In total exposure to date (559 PY), IA LOR for the treatment of knee OA appeared to be safe and well tolerated. These data support the continued evaluation of LOR as a treatment for OA.

Disclosure: I. Simsek, Samumed, LLC, 1, 3; **C. Swearingen**, Samumed, LLC, 1, 3; **S. Kennedy**, Samumed, LLC, 1, 3; **J. Tambiah**, Samumed, LLC, 1, 3; **Y. Yazici**, Samumed, LLC, 1, 3, 4, 6; **N. Lane**, Amgen Inc., 5, 8, GSK, 5, Radius Health, Inc., 8; **M. Hochberg**, Bioiberica SA, 5, Bone Therapeutics, 5, BriOri Biotech, 4, Bristol Myers Squibb, 5, Eli Lilly, 5, Elsevier, 7, EMD Serono, 5, EMD Serono Research and Development Institute, Inc., 5, Galapagos, 5, Galapagos, IQVIA and Hoffman LaRoche, 9, IBSA Biotechniq SA, 5, Novartis Pharma AG, 5, Pfizer, 5, Pfizer Inc, 5, Plexxikon,

5, Regenosine, Samumed LLC, Symic Bio Inc., Theralogix LLC, TissueGene Inc., TLC Biopharmaceuticals, Inc., and Zynerba, 5, Rheumcon, Inc, 3, Samumed LLC, 5, Theralogix LLC, 4, 5, TissueGene Inc, 5, UpToDateTM, 7.

Abstract Number: 1327

The Novel, Intra-articular CLK/DYRK1A Inhibitor Lorecivivint (LOR; SM04690), Which Modulates the Wnt Pathway, Improved Responder Outcomes in Subjects with Knee Osteoarthritis: A Post Hoc Analysis from a Phase 2b Trial

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Lorecivivint (LOR, SM04690) is a small-molecule, intra-articular (IA) CLK/DYRK1A inhibitor which modulates the Wnt pathway and has demonstrated beneficial effects on patient-reported outcomes (PROs) in two Phase 2 trials in subjects with knee OA relative to placebo (PBO). Representing PROs as discrete threshold responses instead of as changes in mean point estimates may better evaluate clinically meaningful benefits experienced by trial subjects. This post hoc analysis was conducted to measure the proportion of subjects treated with LOR in a 24-week Phase 2b study who achieved 30%, 50%, or 70% improvement over baseline by Pain Numeric Rating Scale (NRS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC Function, and Patient Global Assessment (PtGA). Results from the Phase 3 selected dose of 0.07 mg LOR are presented here.

Methods: Subjects had ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2-3, and Pain NRS scores ≥4 and ≤8 in the target knee and < 4 in the contralateral knee. A single, 2mL, IA injection of 0.03 mg, 0.07 mg, 0.15 mg, or 0.23 mg LOR or vehicle PBO was given in the target knee at baseline. The proportion of subjects meeting thresholds of 30%, 50%, and 70% improvements over baseline in the PROs of weekly average of daily Pain NRS [0-10], WOMAC Pain [0-100], WOMAC Function [0-100], and PtGA [0-100] at Week 12 was determined. The odds ratios (OR) of achieving each threshold improvement level were calculated.

Results: 635 subjects (91.4%) completed the study (mean age 59.0±8.5 years, BMI 29.0±4.0 kg/m2, female 58.4%, KL3 57.3%). Treatment with 0.07 mg LOR versus PBO at Week 12 led to 1) significantly ($P< 0.05$) increased odds of having a 30% response in Pain NRS (OR 2.47 [1.45, 4.19]) and WOMAC Function (OR 1.86 [1.10, 3.12]), 2) significantly increased odds of achieving a 50% response for WOMAC Pain (OR 1.79 [1.06, 3.03]) and PtGA (OR 2.28 [1.25, 4.16]), and 3) numerically, but not significantly, more subjects achieved a 70% response in all PROs. Improvements were maintained through Week 24.

Conclusion: LOR, in development as a potential disease-modifying knee OA drug, demonstrated significantly higher odds ratios of achieving and maintaining clinically relevant improvements in PROs compared to placebo from Week 12 through Week 24. Phase 3 studies are ongoing.

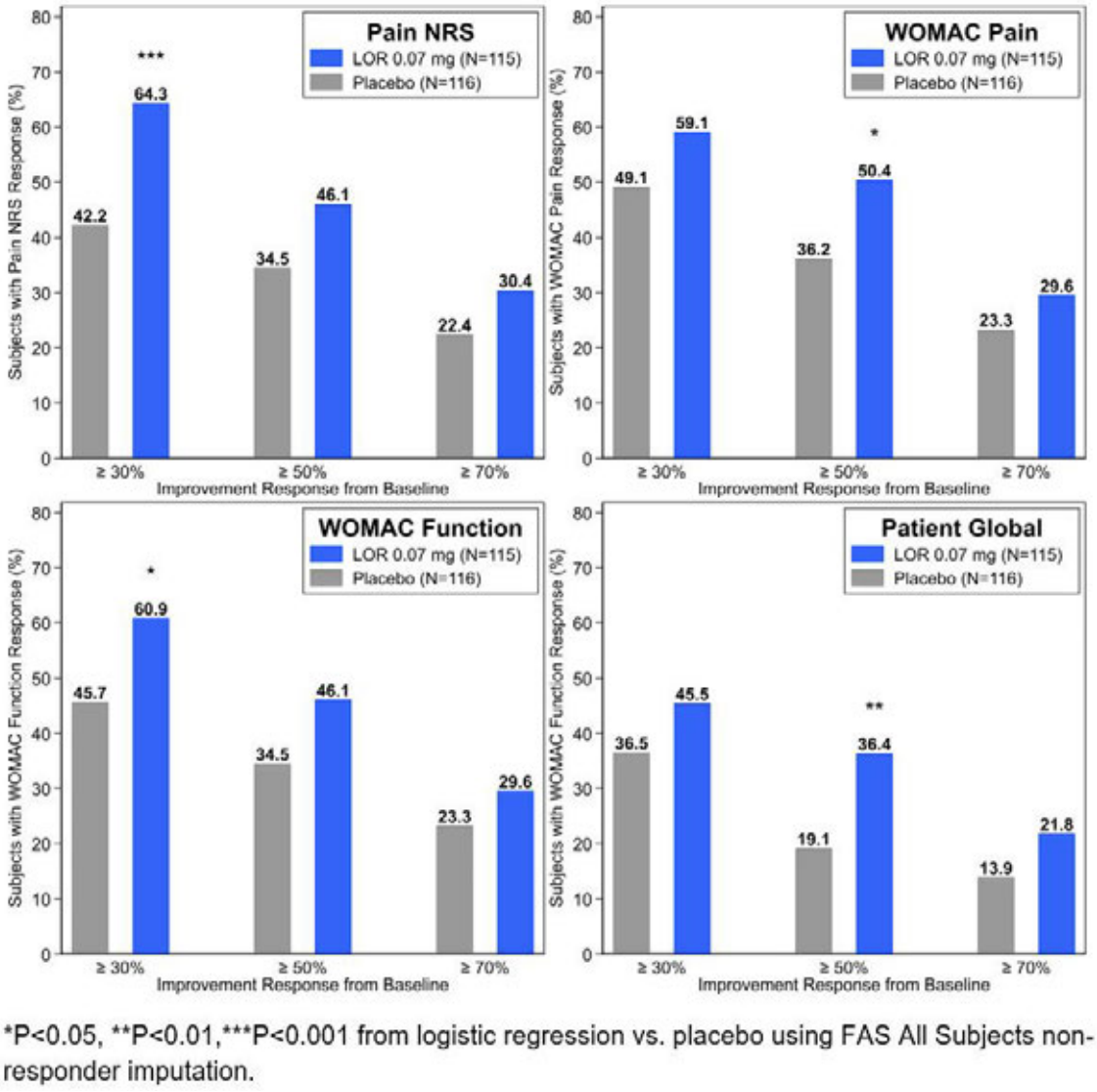

Figure Responder outcomes at Week 12 from a Phase 2b LOR trial for Pain NRS, WOMAC Pain, WOMAC Function, and Patient Global Assessment

Disclosure: **Y. Yazici**, Samumed, LLC, 1, 3, 4, 6; **S. Kennedy**, Samumed, LLC, 1, 3; **C. Swearingen**, Samumed, LLC, 1, 3; **J. Tambiah**, Samumed, LLC, 1, 3.

Abstract Number: 1328

The Patient's Perspective on a Disease Flare During Tapering of DMARDs in Rheumatoid Arthritis

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SESSION INFORMATION

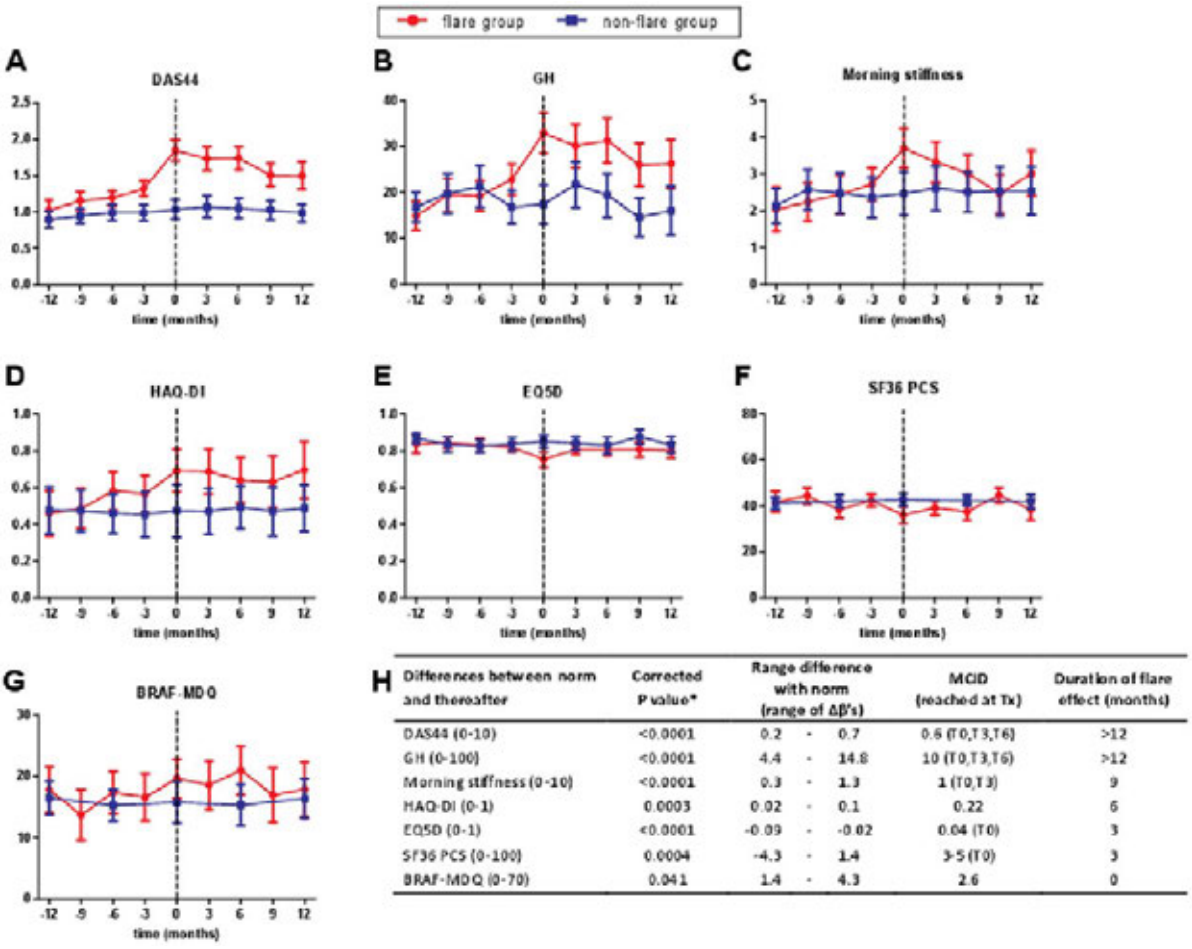
Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies have shown that it is possible to taper DMARDs in RA patients with an inactive disease, but this is accompanied with a higher chance of disease flares. Current recommendations advise to taper DMARDs from a clinical viewpoint. However, data on the feasibility of tapering DMARDs from a patient's perspective are sparse. Therefore, the objective of this study is to determine the impact and length of a disease flare, on patient reported outcome (PROs) in rheumatoid arthritis (RA) patients, who are tapering treatment.

Methods: Data were used from the TARA trial; A multicenter, randomised controlled trial with well-controlled RA patients, DAS≤2.4 & SJC≤1, gradually tapering treatment. PROs of patients with a flare, DAS >2.4 or SJC >1, were compared at the moment of flare, 3 months prior to flare and every 3 months thereafter with their own norm. The norm was set at the average of DAS and PROs 12, 9 and 6 months prior to flare, which in our opinion was the best reference for well-controlled disease (figure 1A-G). Linear Mixed Models were used to determine within flaring patients if a flare altered DAS, VAS general health (GH), morning stiffness, functional ability (HAQ-DI), fatigue (BRAF-MDQ), quality of life (EQ-5D, SF36), anxiety and depression (HADS), and worker productivity over time, and if so, the duration was determined. For sick leave and unemployment we used descriptive statistics.



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Differences between norm and thereafter	Corrected P value*	Range difference with norm (range of Δβ's)	MCID (reached at Tx)	Duration of flare effect (months)
DAS44 (0-10)	<0.0001	0.2 - 0.7	0.6 (T0,T3,T6)	>12
GH (0-100)	<0.0001	4.4 - 14.8	10 (T0,T3,T6)	>12
Morning stiffness (0-10)	<0.0001	0.3 - 1.3	1 (T0,T3)	9
HAQ-DI (0-1)	0.0003	0.02 - 0.1	0.22	6
EQ5D (0-1)	<0.0001	-0.09 - -0.02	0.04 (T0)	3
SF36 PCS (0-100)	0.0004	-4.3 - 1.4	3-5 (T0)	3
BRAF-MDQ (0-70)	0.041	1.4 - 4.3	2.6	0

Figure 1 (A-G) Patient reported outcomes that show an effect of flare. For all outcomes the mean is shown, error bars indicate 95% confidence intervals. T0 indicates the moment of flare for the flare group, for the non-flare group this is the original T12. (H) Summary of the comparison of the overal differences with the norm, which is the mean of -T12, -T9, and -T6. *Bonferoni corrected, n=11. Abbreviations: BRAF-MDQ; Bristol Rheumatoid Arthritis Fatigue - Multidimensional Questionnaire, DAS; disease activity score, EQ5D; European Quality of Life questionnaire with 5 dimensions, GH; visual analogue scale (VAS) for General Health, HAQ-DI; health assessment questionnaire, MCID; minimal clinically important difference, SF36 PCS; Short form 36 physical component score.

Results: In total, 113 patients experienced a flare. Patients who had a flare had a less stable course of the outcomes over time, compared with patients without a flare (Figure 1A-G). When comparing all time points to the norm, statistical significant differences were found for DAS ($p< 0.0001$), GH ($p< 0.0001$), morning stiffness ($p< 0.0001$), HAQ-DI ($p=0.0003$), EQ-5D ($p< 0.0001$), SF36 physical component scale (SF36-PCS) ($p=0.0004$), and the BRAF-MDQ ($p=0.04$) (Figure 1A-H). The DAS and GH significantly worsened at the moment of flare and this effect lasted >12 months. Morning stiffness and HAQ-DI worsened at the moment of flare and these PROs returned to their norm values 6 months thereafter (Figure 1H). The EQ5D and the SF36-PCS only worsened at the moment of flare. The BRAF-MDQ was not significantly different from the norm when comparing separate time points. For DAS, GH, morning stiffness, EQ-5D, SF36-PCS, and BRAF-MDQ the effect sizes were above the minimal clinically important difference (MCID) for >3 months (figure1H). Although the amount of sick leave increased from 1 to 1.3 days per month in the 6 months after flare and the worker productivity declined with 10% in the 3 months after a flare, these differences were not significant.

Conclusion: A disease flare influenced patients' lives, which was mainly physical, and lasted at least 6 months. Although on a group level the effect size for each PRO is not always greater than the specific MCID, a disease flare can still be of great importance for the individual patient**.**

Disclosure: E. van Mulligen, None; **A. Weel**, None; **M. Kuijper**, None; **M. Hazes***, None; **A. van der Helm-van Mil**, None; **P. de Jong**, None.

Abstract Number: 1329

Pooled Safety Analyses from Phase 3 Studies of Filgotinib in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL) is an orally administered, selective inhibitor of Janus Kinase 1 (JAK1) that is under development for the treatment of RA and other inflammatory diseases. The safety and efficacy of FIL has been investigated in the FINCH clinical program that includes three Phase 3, randomized, multicenter studies in patients (pts) with moderate to severely active RA, who had an inadequate response to MTX (FINCH 1; NCT02889796); who were receiving conventional DMARDs and had an inadequate response to biological therapies (FINCH 2; NCT02873936); or who were MTX naïve and initiating MTX alone or in conjunction with FIL or receiving FIL monotherapy (FINCH 3; NCT02886728). Here we present pooled safety data from the double-blind, active and placebo controlled periods of FINCH 1–3 up to 24 weeks.

Table 1. Frequency of treatment-emergent AEs and all deaths across FINCH 1–3 Phase 3 studies (weeks 0–24)

n (%)	Placebo + MTX/csDMARD N = 1,039	ADA 40mg + MTX N = 325	FIL 100 mg + MTX/csDMARD N = 840	FIL 200 mg + MTX/csDMARD N = 1,038	FIL 200 mg N = 210	FIL Total N = 2,088
Treatment-emergent AE	614 (59.1)	185 (56.9)	527 (62.7)	663 (63.9)	113 (53.8)	1303 (62.4)
Treatment-emergent serious AE	37 (3.6)	14 (4.3)	37 (4.4)	44 (4.2)	10 (4.8)	91 (4.4)
Treatment-emergent AE of Interest	253 (24.4)	91 (28.0)	232 (27.6)	289 (27.8)	54 (25.7)	575 (27.5)
Infectious AE	244 (23.5)	88 (27.1)	229 (27.3)	283 (27.3)	53 (25.2)	565 (27.1)
Serious Infectious AE	10 (1.0)	8 (2.5)	13 (1.5)	13 (1.3)	3 (1.4)	29 (1.4)
Herpes Zoster	4 (0.4)	2 (0.6)	5 (0.6)	6 (0.6)	1 (0.5)	12 (0.6)
Hepatitis B or C	1 (0.1)	1 (0.3)	0 (0)	2 (0.2)	0 (0)	2 (0.1)
Opportunistic Infections	0 (0)	1 (0.3)	0 (0)	1 (0.1)	0 (0)	1 (0)
Active TB	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
MACE	5 (0.5)	1 (0.3)	2 (0.2)	2 (0.2)	1 (0.5)	5 (0.2)
DVT/PE	3 (0.3)	0 (0)	0 (0)	1 (0.1)#	0 (0)	1 (<0.1)#
Malignancy Excluding NMSC	4 (0.4)	1 (0.3)	1 (0.1)	0 (0)	0 (0)	1 (<0.1)
NMSC	0 (0)	0 (0)	0 (0)	1 (0.1)	0 (0)	1 (<0.1)
Gastrointestinal Perforations	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Death	2 (0.2)	0 (0)	1 (0.1)	3 (0.3)	0 (0)	4 (0.2)

ADA, adalimumab; csDMARD, conventional synthetic DMARD; DVT, deep vein thrombosis; FIL, filgotinib; MACE, major adverse cardiac event; NMSC, Nonmelanoma Skin Cancer; PBO, placebo; PE, pulmonary embolism; TB, tuberculosis. # excludes one event of retinal vein occlusion.

Methods: The FINCH studies enrolled pts who had a diagnosis of RA (2010 ACR/EULAR criteria) and had ≥ 6 swollen joints and ≥ 6 tender joints at both screening and Day 1. Safety analyses included pts who had received at least one dose of study drug. Pts in FINCH 1 and 2 who did not experience at least a 20% improvement in both swollen joint count and tender joint count by Week 14 discontinued study drug and switched to standard of care. Week 24 safety data from the FINCH 1, 2, and 3 were aggregated and summarized by the number and percentage of pts with events or abnormalities for categorical values. The key safety endpoints reported are treatment-emergent adverse events (AE), treatment-emergent serious AEs, treatment-emergent AEs of interest, all death and treatment-emergent laboratory abnormalities.

Results: This pooled safety analyses assessed 3,452 pts across FINCH 1–3, including 2,088 pts who received FIL. At Week 24, the frequency of treatment-emergent AEs were similar between pts who received FIL and those in the control arms of the FINCH studies (Table 1). Furthermore, the proportions of pts with treatment-emergent AEs of interest were also similar across groups. The most common treatment-emergent AEs were infections, notably upper respiratory tract and nasopharyngitis. Laboratory abnormalities occurred at similar rates with FIL and placebo or active control and were mostly mild to moderate (Grade 1 & 2). Overall, the frequency of major adverse cardiac events (MACE), herpes zoster virus, deep vein thrombosis (DVT) and pulmonary embolism (PE) was low, and similar across groups. The incidences of MACE were 0.2% for FIL, 0.3% for adalimumab (ADA), and 0.5% for placebo/csDMARD. Additionally, the incidences of DVT/PE were < 0.1% for FIL, 0% for ADA, and 0.3% for placebo/csDMARD.

Conclusion: Although gathered over a short duration (24 weeks), pooled data from this large safety database describing a broad population of pts with RA highlights the favorable safety and tolerability profile of FIL in pts with RA both as a monotherapy and in conjunction with MTX/csDMARD.

Disclosure: K. Winthrop, AbbVie, 5, Abbvie, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, Gilead Sciences, Inc., 5, GSK, 5, Lilly, 5, Pfizer, 2, 5, Roche, 5, UCB, 5, UCB Pharma, 5, UCB Pharma, Pfizer, Bristol-Myers Squibb, Eli Lilly, AbbVie, and Roche., 2, 5; **M. Genovese**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 9, Astellas, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck Serono, 2, 5, Galapagos, 2, 5, Galapagos NV, 2, 5, 9, Genentech/Roche, 2, 5, Gilead, 2, 5, Gilead Science, 9, Gilead Sciences, Inc., 2, 5, 9, GSK, 5, Lilly, 2, 5, 9, Novartis, 2, 5, Pfizer, 2, 5, 9, Pfizer Inc, 2, 5, Pfizer, Inc., 9, Pzier, 9, RPharm, 5, Sanofi Genzyme, 2, 5, Vertex, 2, 5; **B.**

Combe, AbbVie, 5, BMS, 5, 8, Chugai, 5, 8, Eli Lilly, 5, Eli Lilly and Company, 5, 8, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, UCB, 5, USD, 5; **Y. Tanaka**, Abbvie, 8, AbbVie, 5, 8, Asahi-kasei, 2, Asahi-Kasei, 2, Asahi-kasei, BMS, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Ono, Pfizer, Sanofi, Takeda, UCB, 2, Astellas, 8, Astellas Pharma, 9, Astellas Pharma, Inc., 2, 3, 5, 8, 9, Astellas, BMS, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi-Tanabe, Pfizer, Sanofic, UCB, YL Biologics, 8, BMS, 2, 5, 8, Bristol-Myers, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Daiichi-Sankyo, 2, 8, Daiichi-Sankyo, Astellas, Eli Lilly, Chugai, Sanofi, Abbvie, Pfizer, YL Biologics, Bristol-Myers, 8, Eisai, 2, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 8, Genzyme, 5, Glaxo-Smithkline, UCB, Mitsubishi-Tanabe, Novartis, Eisai, Takeda, Janssen, Asahi-kasei, 8, Janssen, 8, Mitsubishi-Tanabe, 2, 8, Mitsubishi-Tanabe, Bristol-Myers, Eisai, Chugai, Takeda, Abbvie, Astellas, Daiichi-Sankyo, Ono, MSD, Taisho-Toyama., 2, Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, 2, Novartis, 8, Ono, 2, Pfizer, 5, 8, Pfizer Inc, 8, Roche, 5, Sanofi, 2, Takeda, 2, 8, Teijin, 8, UCB, 2, YL Biologics, 8; **A. Kivitz**, AbbVie, 5, Amgen, 1, 4, 5, Boehringer Ingeleheim, 5, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 5, 8, Flexion Therapeutics, 8, Genzyme, 5, 8, Gilead, 1, 4, 5, Gilead Sciences, Inc., 4, Horizon, 8, Janssen, 5, Janssen Research & Development, LLC, 2, Merck, 8, Novartis, 1, 4, 8, Pfizer, 1, 4, 5, 8, Regeneron, 1, 5, 8, Sanofi, 1, 4, 5, 8, Sun Pharma, 5, SUN Pharma Advanced Research, 5, UCB, 5; **F. Matzkies**, Gilead Sciences, Inc., 1, 3, 4; **B. Bartok**, Gilead Sciences, Inc., 3, 4; **L. Ye**, Gilead Sciences, Inc., 3, 4; **Y. Guo**, Gilead Sciences, Inc., 3, 4; **C. Tasset**, Galapagos, 1, 3, Galapagos NV, 3, 4; **J. Sundy**, Gilead Sciences, Inc., 3, 4; **E. Keystone**, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Gilead Sciences, Inc., 2, 5, Lilly Pharmaceuticals, 2, 5, Merck, 2, 5, 8, Pfizer Pharmaceuticals, 2, 5, 8, PuraPharm, 2, Sanofi, 2, AstraZeneca, 5, Bristol-Myers Squibb, 5, 8, Celltrion, 5, Crescendo Bioscience, 5, F. Hoffman-La Roche Inc, 5, 8, Genentech Inc, 5, Janssen, 5, 8, Sandoz, 5, Sanofi-Genzyme, 5, 8, Samsung Bioepsis, 5, UCB, 8; **R. Westhovens**, Celltrion, 5, 8, 9, Celltrion, Inc., 2, 5, Galapagos, 5, 8, Galapagos NV, 5, 9, Galapagos/Gilead, 2, 5, Gilead Sciences, Inc., 5, 8, 9; **W. Rigby**, Abbvie, 5, AbbVie, 5, BMS, 5, Bristol-Myers Squibb, 5, Gilead Sciences, Inc., 5, Pfizer, 5, Roche, 5; **G. Burmester**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma., 5, 8, AbbVie Inc., 5, 8, BMS, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Merck Shar & Dohme, 5, 8, MSD, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche, Sanofi-Genzyme, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Union Chimique Belge, 2, 5, 8.

Abstract Number: 1330

No Difference in Treatment Continuation of Different Biologics in Elderly Patients > 70 Years Compared to Younger Patients ≤ 65 Years

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Due to demographic changes an increasing number of persons reach an age above 70 years. Therefore, the adequate therapy of elderly patients with rheumatoid arthritis (RA) is an increasingly important topic. The aim of this study was to compare treatment continuation of several biologic (b)DMARDs in patients ≤ 65

with elderly patients > 70 years, stratified by onset of disease (young onset (< 65 years) and late onset (≥ 65 years)) and by seropositivity.

Methods: The German register RABBIT is a prospective longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one conventional synthetic (cs)DMARD failure. For the current analysis patients who were enrolled with a bDMARD between 01/2007 and 04/2018 were included. Kaplan Meier methods were applied to analyse treatment continuation.

Results: Among the 9,819 RA patients included in the analysis, 7,972 were ≤ 65 years old and 1,847 were older than 70 years (among them 180 patients above 80 years). Among the patients ≤ 65 years, 28% received a csDMARDs and 72% a bDMARD, while among the patients above 70 years, 35% received a csDMARDs and 65% a biological. Elderly patients with a young disease onset (YORA) were more frequently women and more frequently seropositive, on average had a higher number of prior csDMARD treatment failures, a worse physical function and were more likely to have joint erosions than elderly patients with late disease onset (LORA) (Table 1). On all bDMARD treatments investigated, elderly RA patients showed the same treatment continuation as seen in younger patients. While neither the age of the patients nor the age at disease onset changed the continuation of biologicals, patients being seronegative had a significantly lower continuation with rituximab and abatacept treatment, irrespective of age (Figure 1).

Conclusion: These results suggest that bDMARD treatment may be used for elderly patients with the same effectiveness as in younger patients.

Table 1. Baseline characteristics of patients, stratified by age and disease onset. Where not otherwise indicated numbers are mean (SD)

Parameter	*≤ 65 years*	*> 70 years, LORA*	*> 70 years, YORA*
N	7,972	1,009	838
Age in years	51.6 (9.5)	76.4 (3.9)	74.3 (2.9)
Female patients	74.7%	72.7%	79.4%
Disease duration in years	8.6 (7.8)	4.4 (3.4)	20.4 (10.4)
Number of prior csDMARDs	2.1 (1.1)	1.7 (0.9)	2.5 (1.2)
ESR	27.2 (21.3)	34.6 (24.5)	33.9 (23.6)
CRP	13.4 (20)	15.3 (20.5)	16.4 (23.4)
DAS28	4.8 (1.3)	5.0 (1.3)	5.2 (1.3)
Number of comorbidities	1.8 (1.9)	3.4 (2.6)	3.7 (2.5)
Patients with >3 comorbidities	26.9%	55.5%	62.4%
Patients with no comorbidities	28.1%	4.6%	4.2%
Seropositive patients (RF/ACPA)	72.4%	69.1%	81.3%
% of full physical function	67.5 (22.4)	60.3 (24.4)	55.4 (23.4)
Glucocorticoid dose in mg/d	6.0 (6.2)	6.1 (4.5)	5.6 (4.4)
Patients with joint erosions	47.9%	46.2%	76.0%

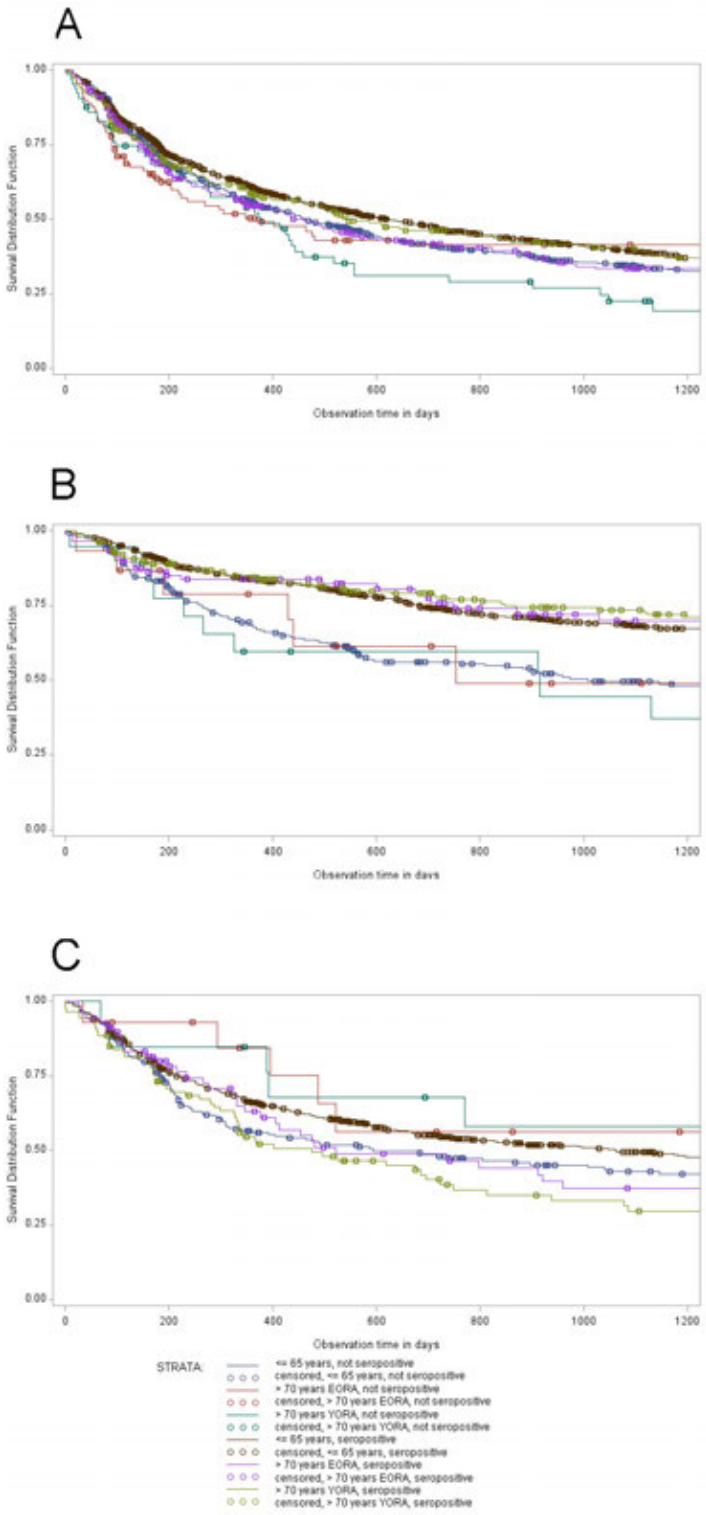

Figure 1. Treatment continuity in (A) TNF inhibitors, (B) abatacept and rituximab, (C) tocilizumab

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Disclosure: **A. Strangfeld**, AbbVie, BMS, MSD, Pfizer, Roche, Takeda and UCB, 8; **K. Krüger**, Abbvie, BMS, Merck, Pfizer, Roche, UCB, 8; **B. Manger**, None; **C. Kneitz**, None; **A. Zink**, Astra Zeneca, BMS, Lilly, Pfizer, Roche und UCB, 5, 8; **M. Schaefer**, None.

Abstract Number: 1331

No Confirmation of Increased Risk of Idiopathic Facial Nerve Palsy Under Tocilizumab

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Spontaneous reports of nine facial paralyses and five facial pareses made by healthcare professionals from Europe have recently prompted EMA's Pharmacovigilance Risk Assessment Committee (PRAC) to consider a potentially increased risk of idiopathic facial nerve palsy for patients receiving tocilizumab. The objective was to assess whether this signal can be confirmed with data of a large data set with known denominators for various treatments, comparing the risk in patients with rheumatoid arthritis (RA) receiving tocilizumab with the risk in patients receiving other DMARDs.

Methods: The German register RABBIT is a prospective longitudinally followed cohort of RA patients with a new start of a DMARD after at least one conventional synthetic (cs)DMARD failure. For this analysis, patients were included who were enrolled with a biologic (b)DMARD start between 01/2007 and 04/2018. DMARD specific, unadjusted incidence ratios were calculated.

Results: Between 2007 and 2018, a total of 20 facial nerve palsies were observed in 11,963 RABBIT patients, of those, three were excluded due to obvious reasons (e.g. stroke) leaving 17 idiopathic facial nerve palsies. Three of them were observed in tocilizumab patients, leading to an incidence rate of 0.47 per 1,000 PY (95% CI: 0.10, 1.14), which is higher than the incidence rate observed in patients receiving conventional synthetic (cs)DMARDs (0.21, 95% CI: 0.04; 0.51) but does not stand out among the incidence rates observed for other biologicals (see figure). The overall incidence of an idiopathic facial nerve palsy among patients receiving (synthetic or biological) DMARDs was 0.37 (95% CI: 0.22, 0.57) which is higher than the incidence of idiopathic facial nerve palsies in the general population (with 20-25 cases per 100,000 [1]). Age and gender were roughly equally distributed among patients with and without idiopathic facial nerve palsies. Patients with idiopathic facial nerve palsies had longer disease duration, more frequently presented with joint erosions and with prior treatment with biologics (see table). They also had more comorbidities. In one patient with idiopathic facial nerve palsy receiving treatment with rituximab (original biologic) a Sjoegrens' syndrome was reported as comorbidity, which is associated with an increased risk of neuropathies.

Conclusion: The overall incidence of idiopathic facial nerve palsies among RA patients receiving DMARDs was higher than the incidence in the general population. However, an increased risk for patients receiving tocilizumab compared to patients treated with other biologicals cannot be confirmed. The incidence of idiopathic facial nerve palsies is higher for patients receiving biologicals compared to patients receiving csDMARDs. This might be due to the higher disease activity. However, the small number of cases with an idiopathic facial nerve palsy is a limiting factor in analysing and interpreting these results.

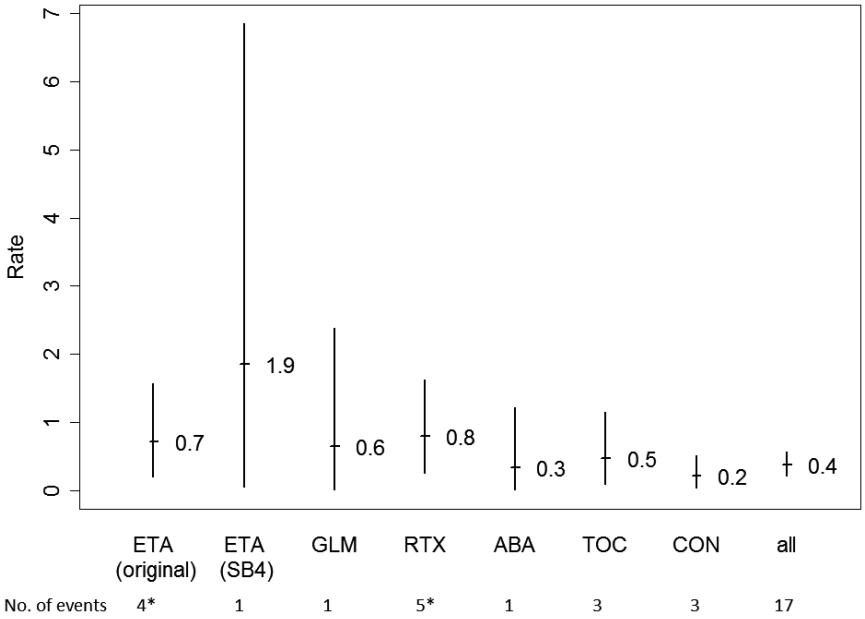

Figure. Unadjusted incidence rates for idiopathic facial nerve palsies per 1,000 patient years under treatment and 95% confidence interval. *One patient was exposed to both Etanercept (original) and Rituximab at the time of event.

Parameter	FNP	No FNP
N	17	11,946
Age	60.6 (12.6)	57.5 (12.7)
Women	12 (70.6%)	8,922 (74.7%)
Disease duration	14.7 (10.7)	9.4 (8.9)
Prior biologic therapies	1.4 (1.3)	0.5 (1)
RF or ACPA positive	14 (82.4%)	8,701 (73.4%)
Joint erosions	10 (71.4%)	5,753 (50.9%)
DAS28-ESR	4.8 (1.2)	4.9 (1.3)
ESR	29.1 (17.5)	28.9 (22.4)
CRP	15.8 (15.3)	14.4 (20.7)
% of physical function	55.3 (28.7)	65.4 (23.3)
Actual glucocorticoid therapy	14 (82.4%)	9,280 (77.8%)
Actual glucocorticoid dose (mg/d)	9.8 (9.7)	8.9 (9)
Ever smoked	8 (47.1%)	6,432 (56.9%)
Sjoegrens' syndrome	1 (5.9%)	152 (1.3%)
Number of comorbidities	3.9 (3.3)	2.2 (2.2)

Table. Baseline characteristics of patients with idiopathic facial nerve palsy (FNP) compared to all patients without the event. For continuous variables, mean and standard deviation are reported, while for categorical variables absolute numbers and percentages are reported.

Reference:

1. Finsterer, J.: Management of peripheral facial nerve palsy. Eur Arch Otorhinolaryngol. 2008 265:743-752.

Disclosure: **A. Strangfeld**, AbbVie, BMS, MSD, Pfizer, Roche, Takeda and UCB, 8; **Y. Meissner**, Pfizer, 8; **M. Schaefer**, None; **L. Baganz**, None; **M. Schneider**, None; **E. Wilden**, None; **S. Zinke**, None; **A. Zink**, Astra Zeneca, BMS, Lilly, Pfizer, Roche und UCB, 5, 8.

Abstract Number: 1332

United States Rheumatology Practice-Based Real-World Evidence of Infusion Reactions in Rheumatoid Arthritis Patients Treated with Intravenous Golimumab or Infliximab: Impact of Prior Biologic Exposure and Methotrexate Utilization

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: AWARE (Comparative and Pragmatic Study of Golimumab IV Versus Infliximab in Rheumatoid Arthritis) is an ongoing Phase 4 comparator study designed to provide a real-world assessment of intravenous golimumab (GLM) and intravenous infliximab (IFX) in patients with rheumatoid arthritis (RA). The study recently reached its Primary Endpoint (comparison of the overall incidence of infusion reactions in GLM- vs IFX-treated patients after 52 weeks) with the last patient reaching 52 weeks of treatment or discontinuation from the study. AWARE also records prior use of biologic medications and concomitant use of methotrexate (MTX). Here we report the incidence of infusion reactions among GLM and IFX patients, examining the influence of prior biologic exposure or concurrent use of MTX, reported at baseline.

Methods: AWARE is a prospective, noninterventional, observational, multicenter, 3-year study conducted in the US. RA patients (1,270 adults) were enrolled at the time of initiating treatment with GLM or IFX. All treatment decisions were made at the discretion of the treating rheumatologist. An infusion reaction was any adverse event that occurred during an infusion or within 1 hour after the infusion of either GLM or IFX. Imputations were not performed on these AWARE data. Data shown are mean ± standard deviation.

Results: Demographics are shown in Table 1 and the incidence of infusion reactions in the different AWARE cohorts is shown in Table 2. Demographically, GLM and IFX patients were, sex and utilization of MTX at baseline. Both age and disease duration of GLM patients was greater than IFX patients by approximately 2 years. There was a higher proportion of bionaïve patients in the IFX-treated group compared with the GLM-treated group. Overall, infusion reactions occurred more frequently among IFX-treated patients compared with GLM-treated patients. The difference in infusion reaction rates between the IFX- and GLM-treated patients was also evident among subgroups of both

Table 1. Baseline Characteristics in the AWARE Study		
	GLM (n=685)	IFX (n=585)
Age (years)	60.9 ± 13.43	58.0 ± 12.85
Sex (% female)	85.0 %	79.5 %
Disease Duration (years)	9.16 ± 9.975	7.20 ± 9.716
Bionaïve (%)	33.0%	48.6%
MTX plus (%)	75.4%	75.1%
MTX=methotrexate		

Table. Baseline characteristics of patients with idiopathic facial nerve palsy (FNP) compared to all patients without the event. For continuous variables, mean and standard deviation are reported, while for categorical variables absolute numbers and percentages are reported.

Table 2. Infusion Reactions in AWARE in Subsets of Patients ± Prior Biologic Use or ± Concurrent MTX								
	GLM (n=685)		IFX (n=585)		GLM (n=685)		IFX (n=585)	
	Bionaïve	Non-Bionaïve	Bionaïve	Non-Bionaïve	No MTX Use	MTX Use	No MTX Use	MTX Use
Infusion Reactions	6/242 (2.5%)	21/443 (4.7%)	36/251 (14.3%)	47/334 (14.1%)	15/265 (5.7%)	12/420 (2.9%)	44/229 (19.2%)	39/356 (11.0%)
Medication for Infusion Reactions	33.3%	59.1%	78.9%	73.6%	50.%	58.3%	73.6%	77.6%
MTX=methotrexate								

bionaïve vs non-bionaïve patients, and among both MTX non-users vs MTX users (characteristics reported at baseline). GLM patients did not report any serious or severe infusion reactions. These were reported rarely (3 of 585 pts) in IFX-treated patients. Among GLM and IFX pts with an infusion reaction, 55.6% of GLM and 77.1% of IFX pts had at least one medication for infusion reaction. Infusion reactions accounted for 9.7% and 35.1% of discontinuations due to adverse events in GLM and IFX pts, respectively.

Conclusion: Whether bionaïve, non-bionaïve, MTX non-user or MTX user at baseline, the incidence of infusion reactions was notably lower among GLM- vs IFX-treated pts. Serious and/or severe infusion reactions did not occur among GLM patients and were rare among IFX patients. IFX patients were more commonly administered mediation for an infusion reaction compared to GLM patients. Infusion reactions accounted for almost four times the number of discontinuations related to adverse events in IFX patients compared to GLM patients.

Disclosure: **S. Schwartzman**, AbbVie, 5, 8, Amgen, 4, Boston Scientific, 4, Crescendo Bioscience, 5, Dermtech, 5, Eli Lilly and Company, 5, 8, Genentech, 8, Gilead Sciences, 4, 5, Janssen Pharmaceutica, 5, 8, Janssen Research & Development, LLC, 2, Medtronic, 4, Myriad Genetics, 5, 9, National Psoriasis Foundation, 6, Novartis, 5, 8, Pfizer, 4, 8, Regeneron, 5, 8, Samsung, 5, Sanofi, 5, 8, UCB, 5, 8; **A. Broadwell**, AbbVie, 5, 8, Amgen, 5, 8, AstraZeneca, 5, Celgene, 5, 8, Eli Lilly, 2, 5, GSK, 8, Horizon, 8, Janssen, 2, 5, 8, Janssen Research & Development, LLC., 2, Mallinckrodt, 8, Novartis, 5, 8, Pfizer, 5, 8, Radius, 8, Sandoz, 5, Sanofi-Regeneron, 8, UCB, 8; **A. Kivitz**, AbbVie, 5, Amgen, 1, 4, 5, Boehringer Ingeleheim, 5, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 5, 8, Flexion Therapeutics, 8, Genzyme, 5, 8, Gilead, 1, 4, 5, Gilead Sciences, Inc., 4, Horizon, 8, Janssen, 5, Janssen Research & Development, LLC, 2, Merck, 8, Novartis, 1, 4, 8, Pfizer, 1, 4, 5, 8, Regeneron, 1, 5, 8, Sanofi, 1, 4, 5, 8, Sun Pharma, 5, SUN Pharma Advanced Research, 5, UCB, 5; **S. Black**, Janssen Research & Development, LLC, 3, Janssen Scientific Affairs, LLC, 3, Janssen Scientific Affairs, LLC,, 3; **S. Xu**, Janssen Research & Development, LLC, 3; **S. Kafka**, Janssen Research & Development, LLC, 3, Janssen Scientific Affairs, LLC, 1, 3.

Abstract Number: 1333

The Comparative Risk of Osteoporotic Fractures Among Patients with Rheumatoid Arthritis Receiving TNF Inhibitors versus Other Biologics: A Nation-wide Cohort Study in Korea

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with an increased risk of osteoporosis and osteoporotic fracture, but little is known about comparative risk of osteoporotic fractures between different biologic agents. We therefore aimed to investigate the comparative risk of osteoporotic fractures among RA patients who initiated TNF inhibitors (TNFi), abatacept, and tocilizumab.

Table 1. Risk of osteoporotic fractures in TNF inhibitor initiators vs. abatacept initiators and tocilizumab initiators

	TNF inhibitor (n=2,307)			Abatacept (n=588)			HR (95% CI)
	Events	PYs	IR per 100 PY	Events	PYs	IR per 100 PY	
Primary outcome							
Osteoporotic fracture	47	2,898	1.62	12	715	1.68	0.98 (0.48-2.03)
Secondary outcomes							
Vertebral fracture	25	2,916	0.86	8	719	1.11	0.87 (0.36-2.09)
Non-vertebral fracture	22	2,925	0.75	4	725	0.55	1.23 (0.33-4.61)
	TNF inhibitor (n=2,462)			Tocilizumab (n=640)			HR (95% CI)
	Events	PYs	IR per 100 PY	Events	PYs	IR per 100 PY	
Primary outcome							
Osteoporotic fracture	54	3,153	1.71	16	771	2.08	0.90 (0.48-1.70)
Secondary outcomes							
Vertebral fracture	30	3,175	0.95	10	778	1.29	0.90 (0.41-1.99)
Non-vertebral fracture	24	3,185	0.75	6	782	0.77	0.91 (0.32-2.58)

IR is per 100 person-years. IR=incidence rate, HR=hazard ratio, CI=confidence interval, PY=person-years

Methods: We identified patients aged ≥ 40 years with at least two ICD-10 diagnosis codes for RA who initiated TNFi, abatacept, or tocilizumab from the 2002-2015 Korean National Health Insurance Service datasets. The primary outcome was a composite osteoporotic fracture endpoint of spine, hip, forearm or humerus requiring hospitalization. Secondary outcomes were vertebral and non-vertebral fractures. Follow-up period started from the day after the first dispensing date of the study drug to the earliest date among the following events: discontinuation of the study drugs, outcome occurrence, disenrollment, end of study dataset, or death. Propensity score (PS) matching with a variable ratio up to 10:1 was conducted for TNFi versus abatacept initiators and for TNFi versus tocilizumab initiators to adjust for baseline confounding. We estimated hazard ratios (HRs) and 95% confidence interval (CI) of osteoporotic fracture risks comparing TNFi to abatacept or tocilizumab by Cox proportional hazard models stratified by a matching ratio.

Results: We included 2,307 TNFi initiators and 588 abatacept initiators, and 2,462 TNFi initiators and 640 tocilizumab initiators in each PS-matched cohort. The incidence of the primary outcome per 100 person-years was 1.62 and 1.68 for initiators of TNFi and abatacept, and 1.71 and 2.08 for initiators of TNFi and tocilizumab, respectively. The HRs for the primary outcome were 0.98 (95% CI 0.48-2.03) comparing TNFi versus abatacept initiators and 0.90 (95% CI 0.48-1.70) comparing TNFi versus tocilizumab initiators. The adjusted risks of secondary outcomes were also comparable between RA patients initiating TNFi versus abatacept, or versus tocilizumab (Table 1).

Conclusion: We did not find a significant difference in the risk of osteoporotic fractures between TNFi and abatacept initiators, or between TNF inhibitor and tocilizumab initiators in this Korean population-based cohort study.

Disclosure: E. Park, None; **A. Shin**, None; **Y. Dong**, None; **Y. Ha**, Seoul National University Bundang Hospital, 3; **Y. Lee**, None; **E. Lee**, Seoul National University Hospital, 3; **Y. Song**, Astellas Pharma, Inc., 9; **E. Kang**, Seoul National University Bundang Hospital, 3.

Abstract Number: 1334

Patterns of Fatigue in Rheumatoid Arthritis Patients Who Received Biological and Targeted Synthetic Disease-Modifying Antirheumatic Drugs

Dalifer Freites Nuñez,[1] Leticia León,[2] Marta Redondo,[3] Cristina Vadillo Font,[4] Pia Lois,[5] Arkaitz Mucientes Ruiz,[4] Luis Rodríguez-Rodríguez,[6] Benjamín Fernández Gutiérrez,[7] Juan Angel Jover Jover,[4] and lydia Abasolo Alcazar[4], [1]Hospital Clínico San Carlos, MADRID, Spain, [2]Fundación para la Investigación Biomedica, Madrid, Madrid, Spain, [3]Universidad Camilo José Ceja, Madrid, Madrid, Spain, [4]HOSPITAL CLINICO SAN CARLOS, MADRID, Spain, [5]Hospital Clínico San Carlos, Madrid, Madrid, Spain, [6]Fundación para la Investigación Biomedica, Madrid, Spain, [7]Hospital Clínico San Carlos, Madrid

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Fatigue is one of the most frequent symptoms in patients with rheumatoid arthritis (RA), affecting more than 80% of them. The experience of fatigue is multidimensional. **Purpose:** to identify the factors associated with fatigue on its different subscales (Physical, Living, Cognitive and Emotional).

Methods: Cross-sectional study. 79 patients were included, patients were being followed up in the rheumatology outpatient clinic of Hospital Clínico San Carlos, Madrid, Spain. Data were collected between July 2018 and May

2019. All patients met the ACR/EULAR 2010 criteria and they were in treatment with Biological agent (anti-TNF and Non anti-TNF) or Targeted Synthetic DMARD (jakinibs). Main variable: Fatigue was assessed by the multidimensional fatigue scales, the Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAF-MDQ). Covariables: Sociodemographic, Disease-related variables, clinical and treatment. Statistical analysis. A descriptive analysis was carried out for the different variables. To identify factors independently associated to BRAF-MDQ and its subscales, multivariable linear regression was applied. Results were expressed as coef with their corresponding 95% CI. A value of $p < 0.05$ was accepted as statistically significant.

Results: A total of 79 patients were evaluated, 66 were females (83%), the mean age (SD) was 56.64(11.63) years old and mean disease duration (SD) was 14.81 (7.60) years. RF was positive in 54% of patients. 67% of the patients were in active on work status and 22% were retired. Regarding comorbidities, 42% had dyslipidemia, 43% hypertension, 14% hypothyroidism and 15% depression. DAS28-ESR and SDAI mean scores of the patients were 2.63 (0.94), 8.54 (6.30) respectively. HAQ mean (SD) was 0.88 (0.64) and the rest of the clinical, treatment characteristics, and the scores of the fatigue instruments are shown in *Table 1*. The factors affecting the BRAF-MDQ and its different subscales was evaluated in multivariate analyze *Table 2*. Our results shows a correlation between disability and the different dimensions of the BRAF-MDQ ($p < 0.001$). Patients who reported good sleep quality had less physical and living fatigue. Age and male sex was negatively associated with physical fatigue, besides a positive RF was associated with less physical and living fatigue. In addition, an association between depression and cognitive fatigue was observed. Different disease activity index and treatments did not result statistical significance in the final multivariate model.

Conclusion: It is important to evaluate fatigue in a multidimensional perspective, each of the different subscales could be modulated by different factors. The results of our study indicated that disability predicts in all subscales of fatigue, however, other factors can configure different patterns of fatigue in RA patients, and identify them is key to the approach of this complex symptom.

Variable	Descriptive statistics
Glucocorticoids mg/day, mean (SD)	4.72(1.52)
Treatment, n (%)	
Conventional DMARDs	63 (79.75)
Anti TNF	40 (65.57)
Non-Anti TNF	17 (27.87)
Synthetic target DMARDs (Jakinibs)	4 (6.59)
HAQ (0-3) mean (SD)	0.88 (0.64)
VAS pain mean (SD)	40.25 (25.00)
Sleep quality self-report, n (%)	
Good	29 (38.67)
Poor	46 (61.33)
BRAF-MDQ (0-70), mean (SD)	22.45 (14.80)
Physical (0-22)	10.81 (5.54)
Living (0-21)	5.31 (4.94)
Cognitive (0-15)	3.30 (3.29)
Emotional (0-12)	3.02 (2.85)
BRAF-NRS, mean ± SD	
Fatigue severity (0-10)	4.89 (2.35)
Effect of fatigue (0-10)	4.74 (2.41)
Coping with fatigue (0-10)	3.82 (2.50)

Table 1. Characteristics of the study group.

	Physical Coef. (SE)	Living Coef. (SE)	Cognitive Coef. (SE)	Emotional Coef. (SE)
Age	-0.084 (0.0356)**	0.005 (0.033)	-0.042 (0.027)	-0.005 (0.024)
Sex	-2.632 (1.255)**	-2.212 (1.162)	-0.931 (0.845)	-0.389 (0.741)
RF positive	-2.494 (0.871)**	-2.561 (0.807)**	---	---
HAQ≥1.1	3.296 (0.744)*	3.990 (0.655)*	2.366 (0.547)*	2.594 (0.447)*
Depression	---	---	2.354 (0.906)**	---
Good Sleep quality	-2.953 (0.866)**	-2.151 (0.768)**	---	---

BRAF-MDQ Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire, *p < 0.001, **p < 0.05. Cells represent beta coefficients with standard error

Table 2. Multivariate analyses of BRAF-MDQ and its subscales.

Disclosure: **D. Freites Nuñez**, None; **L. León**, None; **M. Redondo**, None; **C. Vadillo Font**, None; **P. Lois**, None; **A. Mucientes Ruiz**, None; **L. Rodríguez-Rodríguez**, None; **B. Fernández Gutiérrez**, None; **J. Jover Jover**, None; **I. Abasolo Alcazar**, None.

Abstract Number: 1335

Tumor Necrosis Factor Alpha Inhibitor (TNF-α Inhibitor) Exposure and Risk of Hip Fracture in Veterans with Rheumatoid Arthritis: A Nested Case Control Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) have a much greater risk of sustaining a hip fracture than those without RA. Hip fractures cause significant morbidity and mortality. Some studies have reported beneficial effects of tumor necrosis alpha-inhibitors (TNFα-I) on markers of bone health. However, whether use of TNFα-I decreases the risk of hip fractures in patients with RA remains unclear.

Methods: Using national VA data from 2000-2011, a retrospective cohort of adult veterans with RA was identified using an algorithm that combined coded diagnoses with use of specific antirheumatic medications. This algorithm had a positive predictive value of 81% for identification of patients with RA compared with manual chart review. Two years of continuous baseline enrollment was required prior to cohort entry. Veterans with prior hip fracture, cancer, and serious renal, liver, or lung disease identified during the baseline period were excluded. From this RA cohort, cases of incident hip fracture that required hospitalization were identified using a validated algorithm. Incidence density sampling was used to select up to 20 at-risk controls per case. Controls were matched to cases on age, VA integrated service network and time since cohort entry. Pharmacy data were used to assess disease modifying anti-rheumatic drug (DMARD) exposure in the 12 months preceding the index date of hip fracture. To be considered a user of a given medication, a minimum of 180 days of use was required. Cases and controls were classified into one of four mutually exclusive exposure categories: non-biologic DMARD users (reference), TNFα-I biologic DMARD users, non-TNFα-I biologic DMARD users, and other users. Multivariable conditional logistic regression was used to assess the association between medication exposure and the risk of hip fracture by computing odds ratios adjusted for demographics, glucocorticoid use, BMI and other risk factors for hip fractures.

Results: During follow-up, 462 hip fracture cases and 8226 matched controls were identified from the underlying cohort of veterans with RA. The mean age of cases and controls was 75 years. In multivariable analyses that accounted for relevant covariates, hip fracture cases had similar odds of exposure to TNFα-I compared with controls (adjusted odds ratio [aOR]: 0.97 [95% confidence interval, 0.60 – 1.60]).

Conclusion: In this preliminary assessment, use of TNFα-I was not associated with a decreased risk of hip fractures compared with use of non-biologic DMARDs among veterans with RA. The cohort is currently being updated to include data through 2017.

Disclosure: **S. Homann**, None; **C. Grijalva**, None; **S. Tanner**, Amgen, 5, AstraZeneca, 5, UCB, 5, Regeneron, 8, Sanofi, 8, AstraZeneca, 8, Pfizer, 8; **J. Morrow**, None.

Abstract Number: 1336

Systematic Literature Review and Meta-Analysis of DAS28 Clinical Response Rates Among Advanced Therapies in Biologic-Naïve Patients with Rheumatoid Arthritis

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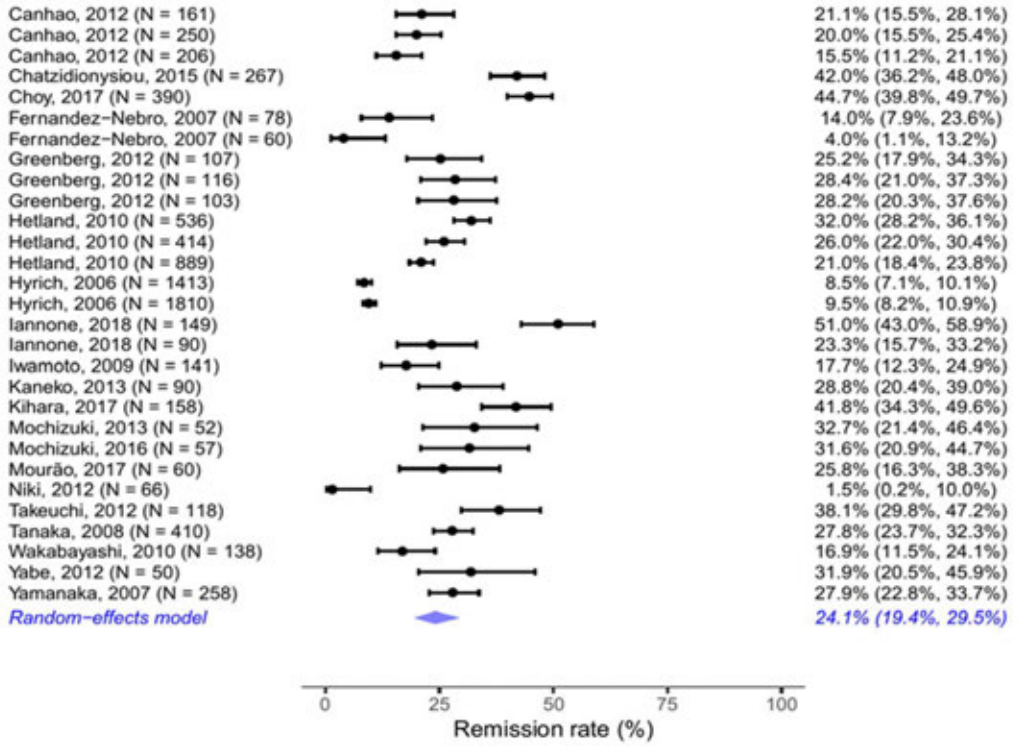
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Biologic (b) and targeted synthetic (ts) DMARDs have demonstrated efficacy for the treatment of rheumatoid arthritis (RA) in clinical trials; however, real-world evidence on the effectiveness of bDMARDs/tsDMARDs has demonstrated a high unmet need reaching remission or LDA, even for the non-stringent DAS28 definitions. This systematic literature review (SLR) and meta-analysis was conducted to quantify real-world DAS28 clinical response rates, due to its high frequency of DAS28 reporting in the past literature, among patients with moderate to severe RA after 6 months of their first bDMARD/tsDMARD treatment.

Methods: An SLR was conducted using the MEDLINE and EMBASE databases and ACR (2015–2017) and EULAR (2015–2018) congress databases. The SLR included single- and multi-arm real-world observational studies that reported DAS28 remission outcomes (DAS28 < 2.6) at 6 months after bDMARD/tsDMARD treatment initiation in biologic-naïve adults with RA (N ≥50 per treatment arm). A traditional random-effects meta-analysis was conducted to estimate the DAS28 remission rates overall. Heterogeneity of studies for each treatment was assessed using the Cochran's Q statistic and I^2 statistic. In addition to DAS28 remission, DAS28 LDA rates, SDAI and CDAI remission rates were summarized descriptively.

Results: A total of 20 studies reported 6-month DAS28 remission data and were included in the analysis; only studies using bDMARDs met the inclusion criteria. Based on the meta-analysis (8,637 patients from studies conducted in 11 countries), the overall DAS28 remission rate was 24.1% (95% credible interval [CrI]: 19.4%, 29.5%; Figure). Remission rates by DAS28 measurement type were similar: DAS28–CRP, 24.5% [CrI 20.2%, 29.4%]; DAS28–ESR, 29.8% [CrI 24.8%, 35.4%]. Among the 20 included studies, a total of 9 reported the percentage of patients with LDA

Figure. Remission Rates Among All Studies



Heterogeneity	
	DAS28
I^2	95.7%
Q	652.0
Q p-value	<0.001

Note:
Multiple rows per study are shown when the study included multiple treatments

at 6 months, with some studies defining LDA as DAS28 ≥2.6 to < 3.2 while others as DAS28 ≥2.3 to < 2.7. The LDA rates ranged between 15% and 60% for DAS28 ≥2.6 to < 3.2 and between 11% and 56% for DAS28 ≥2.3 to < 2.7.

Conclusion: Despite treatment with bDMARDs, a large proportion of patients with RA do not achieve remission, even by the least stringent definition of remission, as by the DAS28 criteria (the rates of which are often higher than ACR70 response rates). Results from stringent remission criteria, e.g. the ACR/EULAR remission, have been reported too infrequently, but would show even much lower numbers indicative of a high unmet need in the RA treatment landscape and call for better treatment strategies.

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Disclosure: D. Aletaha, AbbVie, 2, 5, 8, AbbVie, Janssen, Lilly, Novartis, Pfizer, and Roche, 5, AbbVie, Merck Sharp and Dohme, and Roche., 2, Amgen, 5, 8, Bristol-Myers Squibb, 8, Bristol-Myers Squibb, Celgene, Merck Sharp and Dohme, and UCB, 8, Celgene, 5, 8, Janssen, 5, Lilly, 5, 8, Medac, 5, 8, Merck, 5, 8, Merck Sharp and Dohme, 2, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, Sandoz, 5, 8, Sanofi/Genzyme, 5, 8, UCB, 8; **R. Sawant**, AbbVie, 1, 3; **P. Zueger**, AbbVie, 1, 3; **E. Cook**, Analysis Group, Inc., 3, 9; **F. Mu**, Analysis Group, Inc., 3, 9; **V. Garg**, AbbVie, 1, 3; **K. Betts**, Analysis Group, Inc., 3, 9.

Abstract Number: 1337

Fatigue Levels Are Not Associated with Inflammatory Activity, but with Subjective Outcomes: Results from a Longitudinal Study of Patients with Rheumatoid Arthritis Initiating bDMARD Therapy

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Fatigue is a sensation of weakness and lack of energy which is common in patients with rheumatoid arthritis (RA), contributing to reduced quality of life. Fatigue may be associated with inflammatory activity as well as with bio-psycho-social factors. However, these associations may be changed during effective treatment. The present study explores this issue by assessing the cross-sectional and longitudinal associations between fatigue and inflammatory markers (ultrasound, clinical and C-reactive protein (CRP) assessments) as well as bio-psycho-social factors.

Methods: A total of 208 patients with established RA (mean (SD) age 53 (13) years, disease duration 10 (9) years, 81% women, 79% anti-CCP positive) were examined when initiating biologic DMARDs at baseline as well as after 1, 2, 3, 6 and 12 months, including fatigue (0-10, as part of the RAID score), patient-reported outcome measures

Table 1.
Cross-sectional correlations between fatigue and several variables (Spearman's rho) at all visits *p<0.05, **p<0.001

	Baseline n=208	1 month n=208	2 months n=204	3 months n=197	6 months n=183	12 months n=152
Patient's global VAS	0.72**	0.73**	0.69**	0.70**	0.74**	0.67**
Joint pain VAS	0.64**	0.69**	0.63**	0.62**	0.67**	0.49**
MHAQ	0.63**	0.59**	0.53**	0.51**	0.57**	0.47**
SF36 Mental Health scale score	-0.57**	-0.66**	-0.54**	-0.56**	-0.55**	-0.52**
Pain catastrophizing	0.58**	0.61**	0.53**	0.49**	0.46**	0.45**
28 tender joint count	0.47**	0.50**	0.40**	0.46**	0.47**	0.32**
Examiner's global VAS	0.31**	0.29**	0.26**	0.29**	0.32**	0.21*
CRP	0.14*	0.11	0.11	0.10	0.18*	0.08
28 swollen joint count	0.20*	0.12	0.12	0.05	0.11	0.01
Sum score GS	0.00	0.01	0.00	0.01	0.04	0.04
Sum score PD	0.02	0.02	0.01	0.01	0.04	0.04

Table 2.
The predictive value of baseline fatigue on PROMs, clinical, laboratory and ultrasound scores (GS and PD) at follow-up, adjusted for age, sex and disease duration, and presented as the standardized regression coefficient (β) and adjusted R square (R).

	1 month β, R	2 months β, R	3 months β, R	6 months β, R	12 months β, R
Patient's global VAS	0.60, 0.35**	0.55, 0.30**	0.47, 0.22**	0.52, 0.26**	0.48, 0.21**
Joint pain VAS	0.56, 0.31**	0.49, 0.23**	0.44, 0.19**	0.49, 0.23**	0.44, 0.17**
MHAQ	0.54, 0.28**	0.16, 0.03*	0.43, 0.17**	0.49, 0.22**	0.51, 0.23**
SF36 Mental Health scale score	-0.54, 0.30**	-0.44, 0.19**	-0.44, 0.20**	-0.51, 0.26**	-0.46, 0.21**
Pain catastrophizing	0.55, 0.30**	0.51, 0.27**	0.49, R.24**	0.38, 0.15**	0.40, 0.14**
28 tender joint count	0.44, 0.19**	0.37, 0.13**	0.41, 0.16**	0.38, 0.14**	0.29, 0.07**
Examinator's global VAS	0.21, 0.04*	0.15, 0.02*	0.23, 0.05*	0.28, 0.07**	0.19, 0.02*
CRP	NS	NS	NS	0.16, 0.03*	NS
28 swollen joint count	NS	NS	NS	NS	NS
Sum score GS	NS	NS	NS	NS	NS
Sum score PD	NS	NS	NS	NS	NS

(PROMs) (joint pain VAS, patient's global disease activity VAS (PGA), MHAQ, pain catastrophizing , SF-36 Mental Health scale score), clinical examinations (performed by a study nurse including examiner's global disease activity VAS (EGA), 28 tender and swollen joint counts (28TJC, 28SJC)) and CRP. Ultrasound examinations (semi-quantitative scoring (0-3)) of grey scale (GS) and power Doppler (PD)) were performed of 36 joints and 4 tendons by one rheumatologist (HBH; Siemens Acuson Antares, excellence version, 5-13 MHz probe). Correlations were assessed by Spearman's rho. The predictive value of baseline fatigue on ultrasound, clinical and laboratory assessments as well as PROMs were explored for all follow-up visits by use of multiple linear regression analysis with adjustment for demographic values (age, sex and disease duration).

Results: Fatigue levels diminished during follow-up (baseline median (IQR) 5 (3-7), 12 months 2 (1-5)). Table 1 shows the strong cross-sectional correlations between fatigue and scores of PROMs, low correlations with EGA/SJC/CRP and lack of correlations with ultrasound scores. Baseline fatigue levels predicted scores of PROMs at all examinations (table 2). No/low associations were found between baseline fatigue and 28SJC/EGA/sum score GS and PD at follow-up.

Conclusion: Fatigue was strongly correlated with all PROMs but had low/no associations with objective measures of inflammation. Baseline fatigue predicted all the subjective outcomes at follow-up, but not CRP, SJC or ultrasound. Thus, fatigue was presently not associated with inflammatory activity, but with subjective outcomes.

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Abstract Number: 1338

Joint-specific Responses to Tofacitinib and Methotrexate in Rheumatoid Arthritis: A Post Hoc Analysis of Data from ORAL Start

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

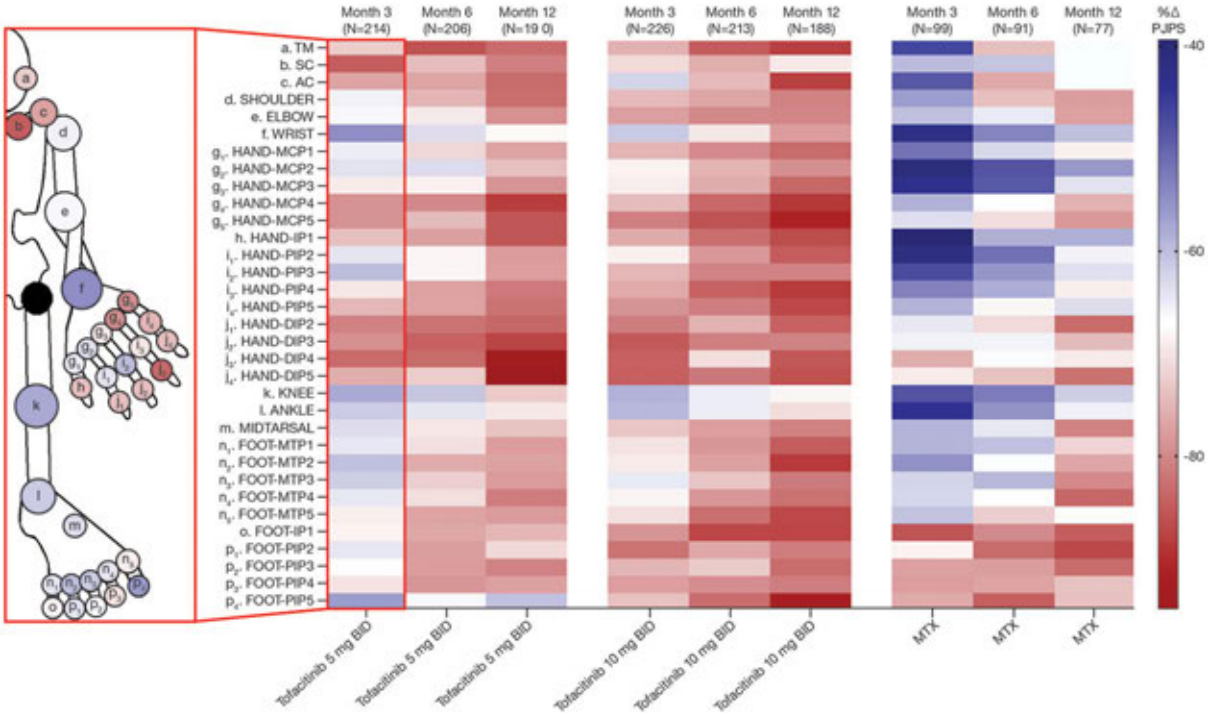
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

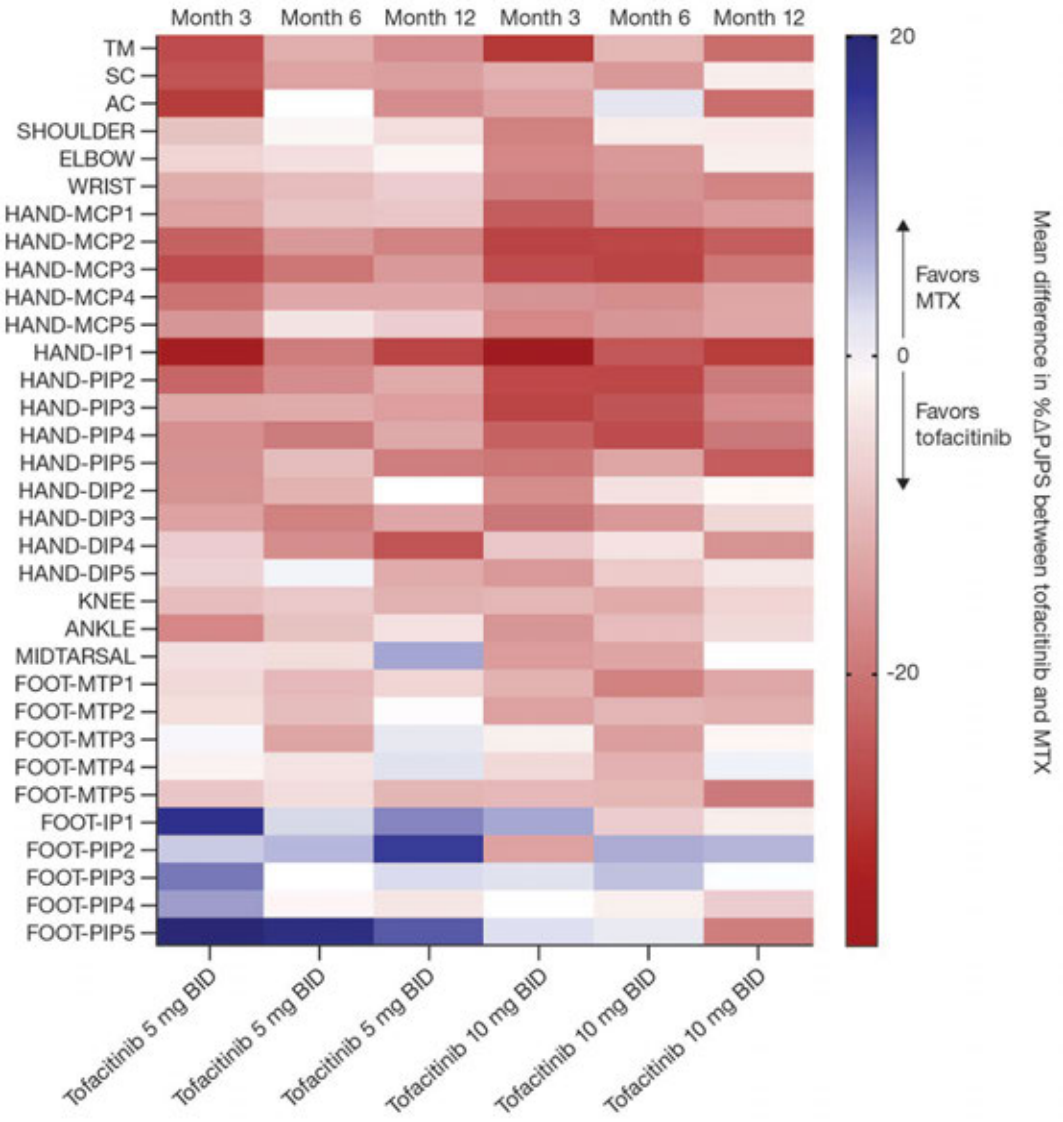
Background/Purpose: Despite systemic inflammatory cues, RA affects synovial joints variably. Tofacitinib is an oral JAK inhibitor for the treatment of RA. Previous post hoc analyses of data from ORAL Standard and ORAL Strategy showed differences in the degree/rate at which joints respond to tofacitinib ± MTX and adalimumab + MTX.[1] However, clear patterns relating to specific agents were generally not seen, possibly as most patients (pts) received combination therapy with MTX. Here, we further characterize joint-specific responses to tofacitinib monotherapy and MTX using data from the Phase 3 study ORAL Start (NCT01039688).

Figure 1. Heat map of %ΔPJPS for each joint across treatment groups at Months 3, 6, and 12, and homunculus illustrating the joint-specific %ΔPJPS for tofacitinib 5 mg BID at Month 3



Pts were enrolled from ORAL Start (NCT01039688). This analysis was based on pts who had baseline PJPS >0
N for each joint may vary; the maximum value of N is listed for each time point
Lower %ΔPJPS represents better efficacy
%Δ, percentage change from baseline; AC, acromioclavicular; BID, twice daily; DIP, distal interphalangeal; IP, interphalangeal; MCP, metacarpophalangeal; MTP, metatarsophalangeal; MTX, methotrexate; PIP, proximal interphalangeal; PJPS, paired joint pathology score; SC, sternoclavicular; TM, temporomandibular

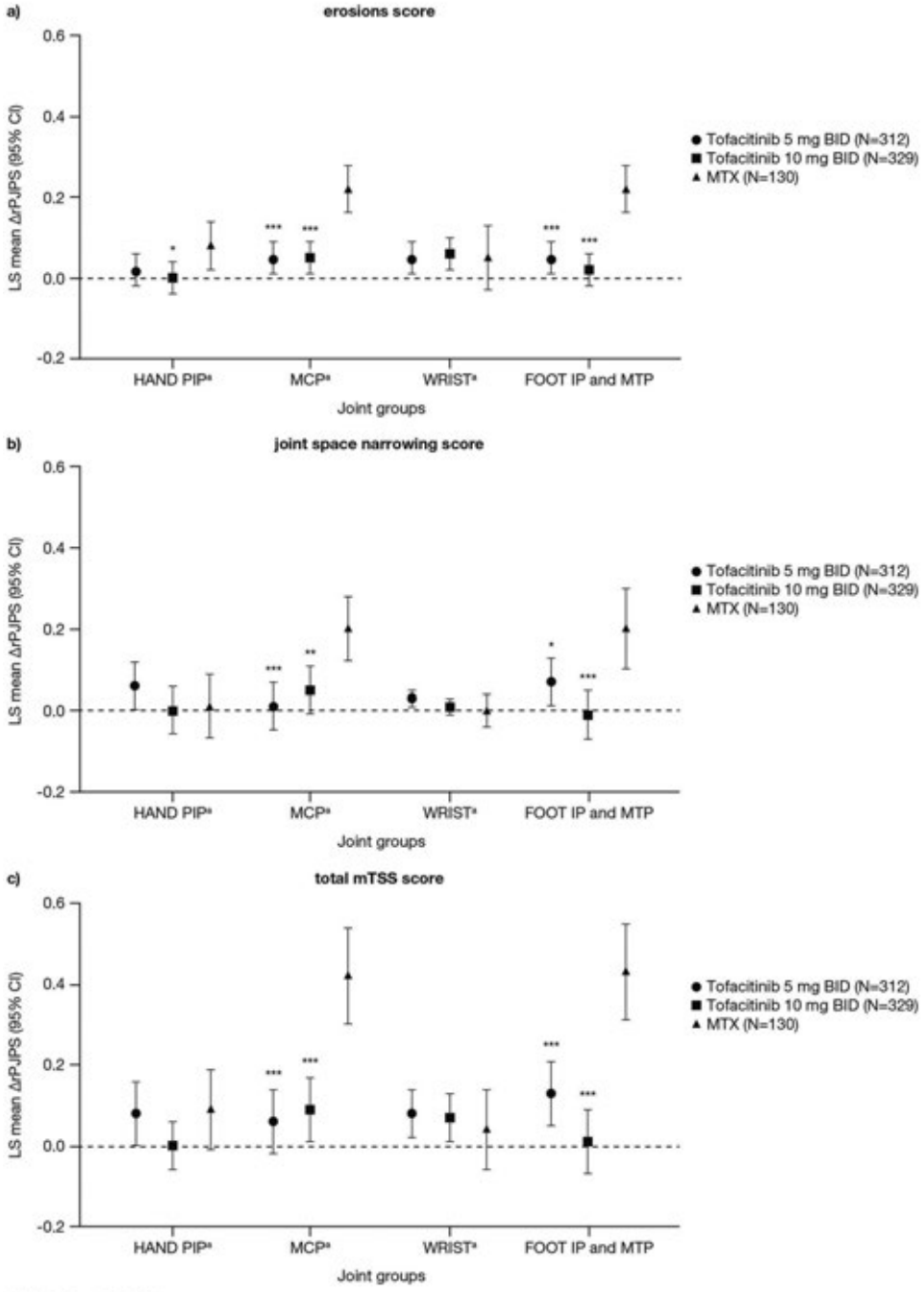
Figure 2. Heat map of the mean difference in %ΔPJPS between tofacitinib doses and MTX



Refer to Figure 1 for N numbers
%Δ, percentage change from baseline; AC, acromioclavicular; BID, twice daily; DIP, distal interphalangeal; IP, interphalangeal; MCP, metacarpophalangeal; MTP, metatarsophalangeal; MTX, methotrexate; PIP, proximal interphalangeal; PJPS, paired joint pathology score; SC, sternoclavicular; TM, temporomandibular

Methods: This was a post hoc analysis of Month (M)3, 6, and 12 data from ORAL Start in which pts with newly diagnosed, active RA received tofacitinib 5 or 10 mg twice daily (BID), or MTX (starting dose 10 mg/week and titrated up to 20 mg/week). A paired joint pathology score (PJPS), a combination of bilateral tender/swollen joint counts ranging from 0 (neither) to 4 (both sides tender/swollen), was calculated. Percentage changes from baseline in PJPS (%ΔPJPS) for each joint were presented in a heat map. To show treatment-specific effects at each joint, differences in %ΔPJPS for each tofacitinib dose, minus the MTX group, were calculated and presented in a further heat map. Joint damage in the hand PIP joints, MCP joints, wrist, and foot IP and MTP joints was assessed using the modified Total Sharp Score (mTSS). For each component of the mTSS composite score (erosion, joint space narrowing) and total score, a radiographic PJPS (rPJPS; combination of bilateral mTSS subscores in each joint group) was calculated

Figure 3. LS mean change from baseline (95% CI) in radiographic PJPS for a) erosions score, b) joint space narrowing score, and c) total mTSS score in 4 joint groups at Month 12



[a]Tofacitinib 5 mg BID, N=311
Data are based on a mixed model for repeated measures adjusted for age, geographic region, RA disease duration, disease activity (measured by DAS28-4[ESR]), and baseline value of the endpoint
Tofacitinib 5 or 10 mg BID vs MTX: *p<0.05; **p<0.01; ***p<0.001; No multiplicity adjustments were made for statistical comparisons as they were for exploratory use only
Δ, change from baseline; BID, twice daily; CI, confidence interval; IP, interphalangeal; LS, least squares; MCP, metacarpophalangeal; MTP, metatarsophalangeal; mTSS, modified Total Sharp Score; MTX, methotrexate; PIP, proximal interphalangeal; rPJPS, radiographic paired joint pathology score

and mean ΔrPJPS at M12 for each joint group presented. Statistical comparisons between tofacitinib vs MTX were performed using a repeated measures mixed model.

Results: Across treatment arms, all joints showed a treatment response (%ΔPJPS ranged from -95% to -39%), with responses generally improving over time (Figure 1). As previously reported,[1] irrespective of treatment, the wrist,

knee, and ankle responded less well than other joints. Differences in %ΔPJPS showed better responses for tofacitinib vs MTX in most joint locations, excepting some foot joints (Figure 2). Radiographic progression was minimal in all 4 joint groups (hand PIP joints, MCP joints, wrist, and foot IP and MTP joints) with both tofacitinib doses (Figure 3). The greater %ΔPJPS seen in the foot for MTX vs tofacitinib did not translate into improved radiographic outcomes at M12: ΔrPJPS in the foot were significantly worse for MTX vs tofacitinib across each endpoint (Figure 3), as were ΔrPJPS in the MCP joints.

Conclusion: Wide variation in RA joint-specific responses to tofacitinib 5 and 10 mg BID, and MTX, was seen in this post hoc analysis. Tofacitinib was generally more effective than MTX in all joints, except some foot joints. Enhanced efficacy in the distal lower limb has not been described with MTX before. Radiographic progression was minimal in the tofacitinib arms, while in the MTX arm, significantly more radiographic progression was observed in the MCP joints and foot.

Reference:

1. Ciurea A et al. Ann Rheum Dis 2019; In Press.

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Abstract Number: 1339

Risk of Immunotherapy Related Toxicity in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) have changed the therapeutic landscape in oncology leading to cures in some cancer types. However, patients with pre-existing autoimmune diseases (AIDs) were largely excluded from ICI trials due to concern for increased toxicity. In clinical practice some patients with rheumatoid arthritis (RA) have been treated with ICIs, but the risks of toxicity and/or disease flare have not been clearly outlined. Here we present data on the safety and efficacy of ICI therapy in patients with RA.

Methods: We conducted a single institution retrospective analysis to evaluate the safety and efficacy of ICI therapy (anti-CTLA-4 and anti-PD-1) among patients with pre-existing AIDs treated from 2011 to 2018. Primary endpoints were incidence of immune-related adverse events (irAEs) and AID flares. The secondary endpoint was overall survival (OS). Subgroup analysis for patients with RA was performed with percentages and medians reported.

Results: Of 84 patients with pre-existing autoimmunity who developed malignancy and were treated with ICIs, we identified 22 patients with RA. Sixteen (73%) were female and 6 (27%) male (median age 67). Most patients had no evidence of active disease 20 (91%) as indicated by their treating physician. Sixteen (73%) patients were receiving RA immunomodulatory therapy at start of ICI, with 8 (36%) patients receiving systemic corticosteroids and 7 (32%) patients on methotrexate.

Malignant conditions included 7 (32%) with melanoma, 7 (32%) with non-small cell lung cancer (NSCLC) as well as others. Thirteen patients (59%) were treated with pembrolizumab, 9 (41%) with nivolumab and 4 (18%) received ipilimumab.

IrAEs occurred in 7 (32%) patients with only 2 (9%) developing severe, grade 3 irAEs, a total of 41% developing toxicity of any grade. The most common toxicities were dermatitis 4 (18%) and colitis 3 (14%). ICI was temporarily discontinued due to irAEs in 5 (23%) patients. Only 1 patient required permanent ICI discontinuation. RA flares occurred in 12 (55%) patients. Most patients 9 (75%) received treatment with oral corticosteroids for RA flare. ICI was permanently discontinued due to flare in only one patient. Overall either flare, irAE or both occurred in 16 (73%) patients. Median OS for patients with RA after start of ICI was 10.5 months.

Conclusion: In our cohort, approximately half of the RA patients experienced flare and fewer had an irAE after initiation of ICI compared to a rate of 5-60% for any grade irAEs and 7-30% in severe irAEs in patients without autoimmune diseases depending on agent used. Most symptoms were manageable and a minority of patients required discontinuation of cancer-directed therapy. While this is a small cohort, the results of this analysis suggest that patients with RA experience severe irAEs at a rate similar to the population without autoimmune diseases. Further study is warranted to determine if ICIs may be offered to patients with RA as first line agents when used for an FDA approved indication. The choice of ICI and its effect on OS in this population also requires further prospective investigation.

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Abstract Number: 1340

Patterns of Sustained Remission and Subsequent DMARD Tapering in Early Rheumatoid Arthritis: Data from the Canadian Early Arthritis Cohort

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) treatment emphasizes aggressive titration of disease-modifying antirheumatic drugs (DMARDs) with the goal of achieving disease remission. This often includes the use of multiple DMARDs in combination, which can have a significant impact on patients' lives and add costs to the healthcare system. The primary objective of our study was to describe the patterns of sustained remission and subsequent treatment reduction in the usual clinical practice for patients with early RA. Furthermore, we wished to assess for an effect of tapering medications on the risk of disease flare.

Methods: Patients (age >18) enrolled in the Canadian early ArThritis CoHort (CATCH) between January 2007 to March 2017 were analyzed. CATCH is a prospective, observational study of patients with early inflammatory arthritis (symptoms < 1 year) treated in rheumatology clinics across Canada. The analysis cohort included patients with a diagnosis of RA according to the 1987 or 2010 ACR/EULAR classification criteria, active disease at enrolment (DAS28 >2.6) and those treated with at least one DMARD or biologic agent within the first three months of study enrolment. We defined sustained remission as achieving a DAS28 < 2.6 at two consecutive follow-up visits at least six months apart. Reduction of therapy was defined as a minimum of a 25% dose reduction of conventional synthetic, targeted, or biologic DMARDs. Descriptive statistics were used to summarize the time to remission and reductions in DMARD therapy. Logistic regression analysis was used to assess predictors of sustained remission.

Results: Eight hundred and thirty-seven (40%) of the 2,097 eligible patients achieved sustained remission during the study period. Of these, 60% did so within the first 18 months and 92% within the first four years (Figure 1). The mean (SD) baseline DAS28 was 5.1 (1.3), and HAQ-DI was 1.0 (0.7). At the time of remission, 80% were prescribed methotrexate (55% subcutaneously), 71% were prescribed combination therapy with other conventional synthetic DMARDs, and 13% were prescribed a biologic agent. In the year after attaining sustained remission, 327 (39%) patients reduced treatment in the following pattern (patients may have had more than one change): 250 patients reduced or stopped methotrexate, 196 patients reduced or stopped non-methotrexate DMARDs, and 34 patients reduced or stopped biologic agents. For those that reduced or stopped a biologic, only one patient did so due to side effects. Of the 250 patients who reduced or stopped methotrexate, 25 were for a side effect. Of the 636 patients with outcome data available, 54% remained in sustained remission 12-18 months after first achieving it. This was not associated with tapering DMARDs [odds ratio (95% confidence interval) tapering versus not tapering: 0.96 (0.66 – 1.41)].

Conclusion: Achieving sustained remission occurred in 40% of early RA patients in usual clinical practice. Treatment reductions following sustained remission occurred in over a third of patients over the next 12 months and consisted mainly of adjustment in non-biologic DMARDs. Further study is required to determine whether or not medications can be tapered safely without disease flare.

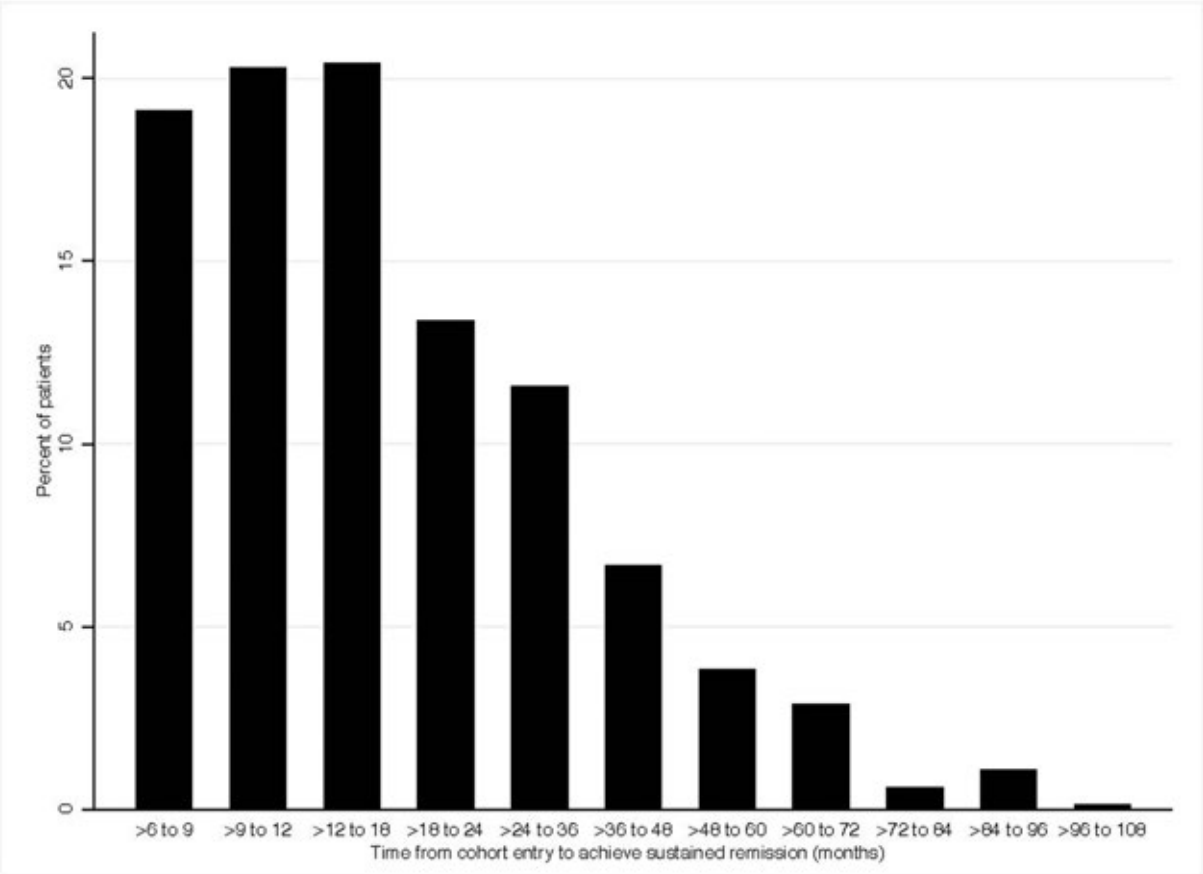

Figure 1. Bar graph demonstrating distribution of time (in months) to achieve first sustained disease remission

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UCB, 2, 5, 8; **C. Thorne**, Abbvie, 2, 5, Amgen, 2, 5, CaREBiodam, 2, Celgene, 2, 5, Centocor, 5, Janssen, 5, Lilly, 5, Medexus/Medac, 5, 8, Merck, 5, Novartis, 2, 5, Pfizer, 2, 5, Sandoz, 5, Sanofi, 5; **D. Tin**, None; **G. Hazlewood**, None.

Abstract Number: 1341

Impact of Tocilizumab on Anxiety and Depression in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Mood disorders, such as anxiety and depression are extremely prevalent amongst patients with rheumatoid arthritis (RA). In this study we sought to assess the impact of treatment with tocilizumab (TCZ), an IL-6 antagonist, upon anxiety and depressive symptoms in a cohort of RA patients.

Methods: This study was part of a larger, multi-center study performed at 13 medical centers in Israel between January 2014 and July 2015. Study participants were adults diagnosed with RA who received a weekly subcutaneous injection of tocilizumab for 24 weeks. We used the Hamilton Depression (HDRS) and Anxiety (HAMA) scores in order to assess the severity of depression and anxiety respectively. RA disease activity indices and depression and anxiety levels were assessed at baseline, 4 weeks and study completion. Patients whose anxiety and/or depression levels decreased significantly, e.g., a decrease ≥ 25% in anxiety and/or depression levels between baseline and study end, were compared with patients for whom they did not. Logistic regression identified factors associated with significant decrease, in addition we assessed correlations between levels of depression and anxiety with scores reflecting the disease activity of the rheumatoid disease.

Results: Ultimately, 91 patients were included in the study. The mean age was 54 years and the majority were female (79%). The mean score in all disease activity indices as well as depression and anxiety levels decreased dramatically from baseline to study completion. Sixty patients (66%) demonstrated a significant decrease in anxiety and/or depression levels. When logistic regression was performed, an HDRS score indicative of depression at study baseline demonstrated an independent association with a significant psychiatric response whilst older age and increased weight were negatively associated. Older age and increased weight were negatively associated with a significant decrease. The following correlations were observed with the HAMA and HDRA scores respectively; HAQ-DI ($r=0.4$, 0.42), DAS28 ($r=0.29$, 0.32) and CDAI (0.28 and 0.33), all of them were statistically significant ($p< 0.01$).

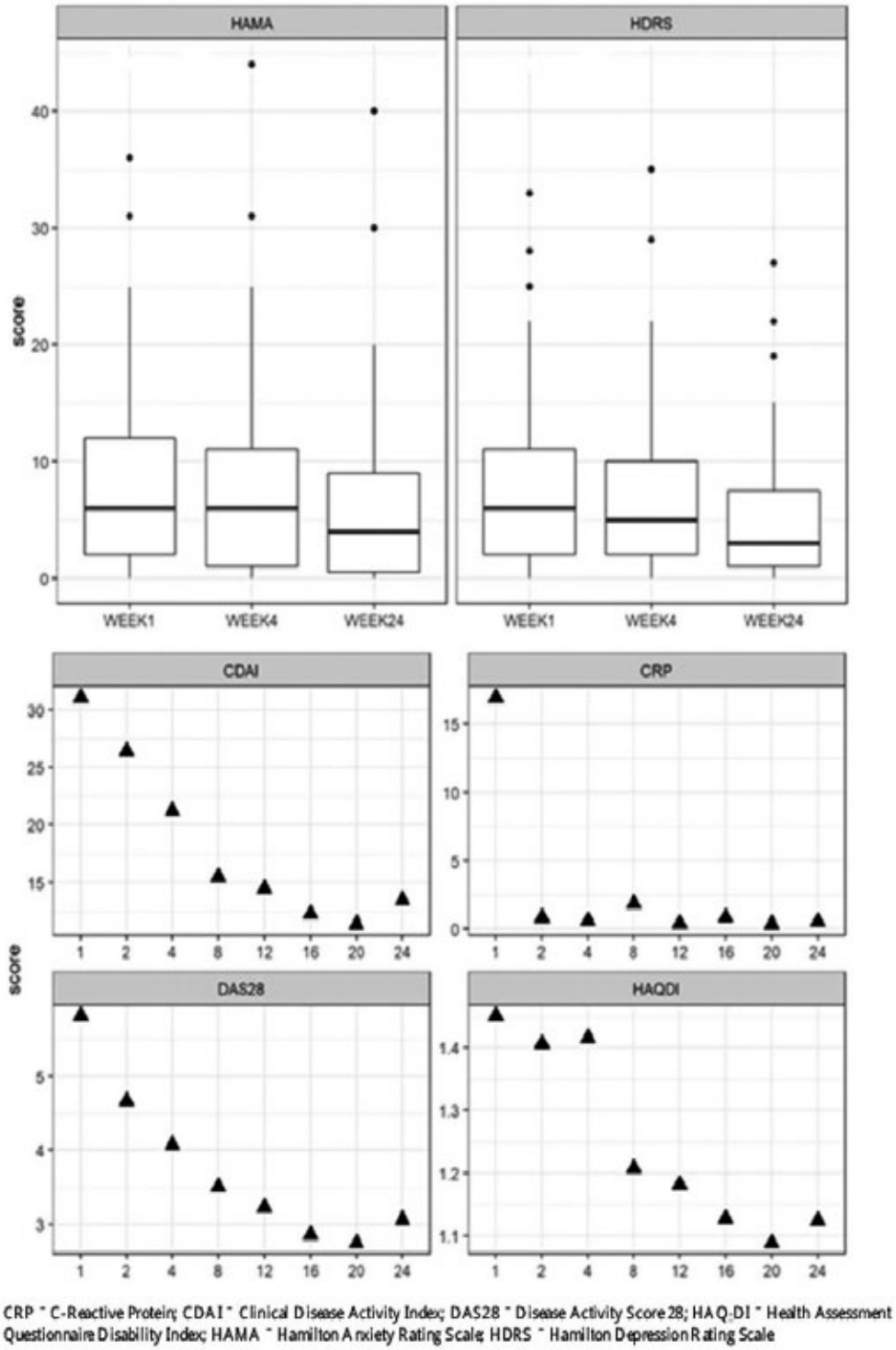

Fig.1
Comparison of variation in disease activity indices throughout the study

Conclusion: This study has demonstrated a favorable impact of TCZ therapy on parameters reflecting depression and anxiety severity in patients with RA.

	Odds Ratio	CI 95%	P-value
Pre-anxiety**	0.28	0.07 ¯ 1.01	0.058
Pre-depression***	9.70	1.93 ¯ 65.38	0.010
Male sex	1.39	0.67 ¯ 2.98	0.380
Age (Per 1 year increment)	0.97	0.95 ¯ 1.00	0.042
Weight (Per 1 kg increment)	0.96	0.94 ¯ 0.98	<0.001
RA duration (Per 1 year increment)	1.03	1.00 ¯ 1.08	0.081
RF positive	0.59	0.29 ¯ 1.17	0.136
Anti-CCP positive	1.57	0.76 ¯ 3.29	0.224
Joint damage	1.02	0.53 ¯ 2.01	0.949
CDAI (Per 1-unit increment)	0.98	0.97 ¯ 1.00	0.095

CI ¯ confidence interval; RA ¯ rheumatoid arthritis; RF ¯ rheumatoid factor; Anti-CCP ¯ anti-cyclic-citrullinated peptides; CDAI ¯ clinical disease activity index

* Significant response ¯ e.g., a decrease in over 25% in HAMA or HDRS levels from baseline to study completion.

** Patients with a HAMA score of 18 or above at study initiation.

*** Patients with a HDRS score of 18 or above at study initiation.

TABLE
Factors associated with significant decrease* in anxiety and/or depression levels on logistic regression

Disclosure: **S. Tiosano**, None; **Y. Yavne**, None; **A. Watad**, None; **P. Langevitz**, None; **M. Lidar**, None; **J. Feld**, None; **M. Tishler**, None; **S. Aamar**, None; **O. Elkayam**, None; **A. Balbir-Gurman**, Pfizer, 5, 8; **Y. Molad**, None; **S. Ehrlich**, None; **D. Amital**, None; **H. AMITAL**, None.

Abstract Number: 1342

Identification of Heterogenous Treatment Response Trajectories to anti-IL6 Receptor Treatment in Rheumatoid Arthritis

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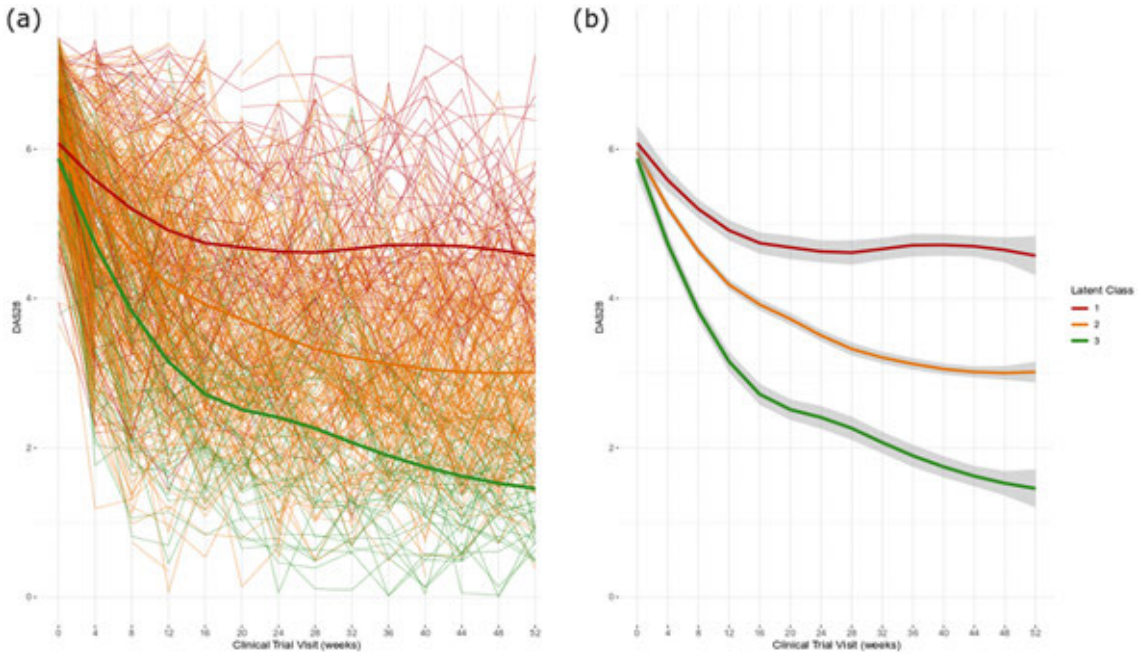
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a complex autoimmune disease with a fluctuating course of disease activity and progression. Although treatments have improved substantially in recent years thanks to the development of novel drugs, response is not guaranteed. Also, response is often monitored in a binary, and not a dynamic way, resulting in loss of information about the level of response. The aim of this study was to identify heterogeneity



All patient trajectories of DAS28 in response to Tocilizumab anti-IL6 treatment, with three identified latent trajectories of DAS28 in response to Tocilizumab over a 52-week clinical trial

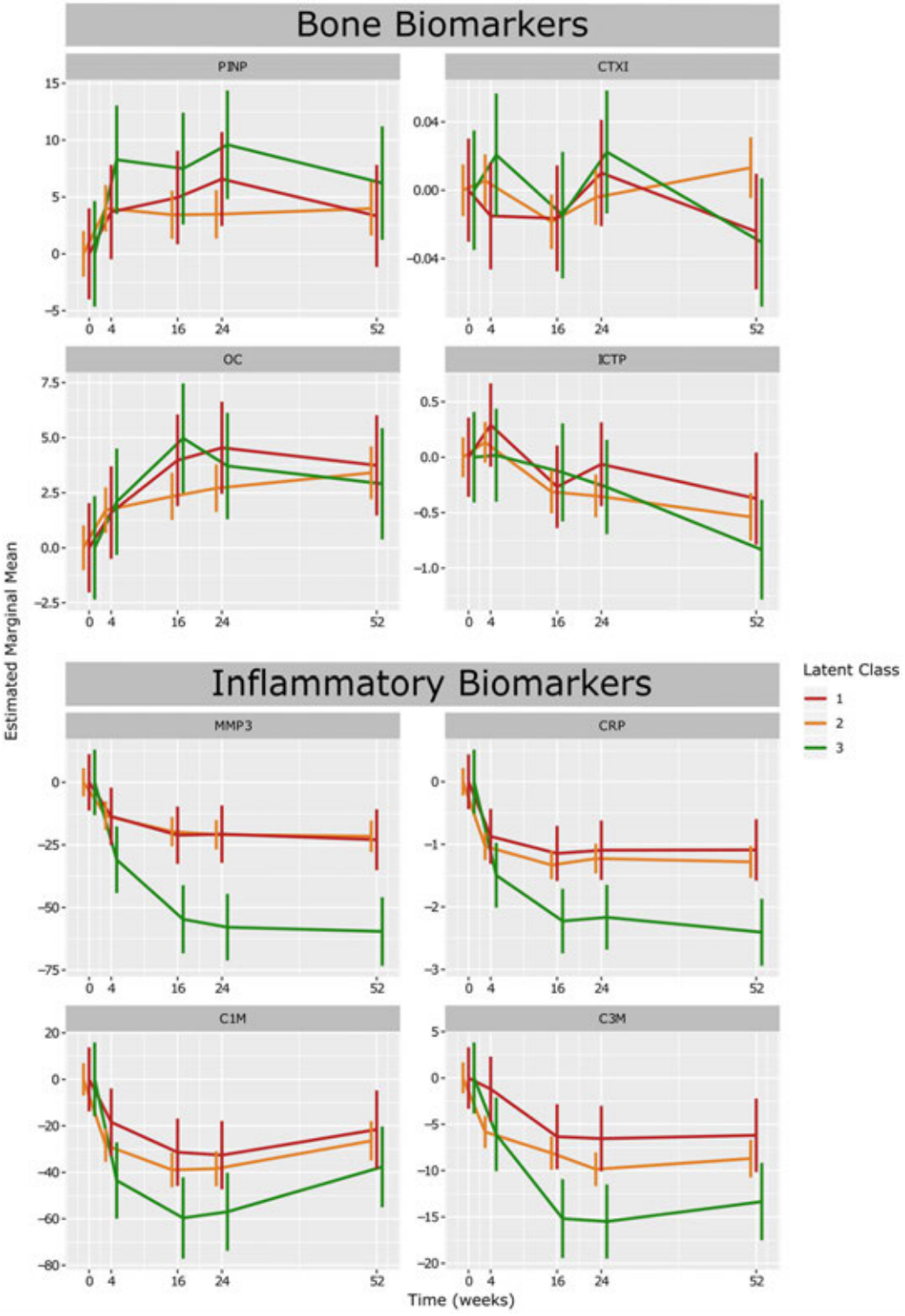
in Disease Activity Score 28 (DAS28) in response to tocilizumab in RA patients and investigate molecular and clinical factors which may cause this.

Methods: Longitudinal clinical and biochemical data, as well as baseline demographics for 485 RA patients receiving 4 or 8 mg/kg tocilizumab in combination with MTX, were extracted from the LITHE phase III clinical study (NCT00106535), and post-hoc and exploratory analysis was conducted. Latent class mixed models were used in order to identify distinct trajectories of patients' disease activity using DAS28 after the initiation of treatment. The optimal number of classes was selected using Bayesian Information Criteria (BIC) and Akaike Information Criteria (AIC). Longitudinal and cross-sectional measurements were then analysed using linear mixed effects models in order to characterise patients by serological biomarker levels, and other clinical factors, and identify correlations between drug response and patient characteristics.

Results: Trajectory analysis identified three distinct response subgroups of patients: class 1 (n = 85, 25.9%), class 2 (n=338, 63.9%) and class 3 (n=62, 10.4%). All groups started with a high DAS28 on average (DAS28 > 5.1). Class 1 showed the least reduction in DAS28, with a significantly higher proportion of patients seeking escape therapy ($p < 0.001$). Class 3 showed significantly higher rates of improvement in DAS28 achieving remission status, as well as having the highest rates of patients achieving ACR response levels ($p < 0.001$). Biomarkers associated with inflammation, MMP-3, CRP, C1M, and C3M, were markedly decreased from baseline levels in class 3 in response to treatment compared to the other classes.

Conclusion: Identification of more distinct patient populations of drug response may allow for more targeted therapeutic treatment regimens. Treatment strategies should consider the initial state of disease severity as well as clinical and biochemical disease parameters to achieve optimal response rates.

Estimated marginal means for absolute change in the level of bone and inflammatory biomarkers after initiation of tocilizumab for each latent class



Estimated marginal means for absolute change in the level of bone and inflammatory biomarkers after initiation of tocilizumab for each latent class

Disclosure: **J. Blair**, None; **C. Bager**, Nordic Biosceince Proscion, 3; **M. Tang**, Nordic Biosceince Proscion, 3; **M. Karsdal**, Nordic Biosceince, 1, 3, Nordic Bioscience, 1, 2, 3, 4, 5; **A. Bay-Jensen**, Nordic Bioscience, 1, 2, 3; **S. Brunak**, Nordic Biosceince Proscion, 6, Intomics, 6.

Abstract Number: 1343

Pop a Pill or Give Myself a Shot? Patient Perspectives of Disease-modifying Anti-rheumatic Drug (DMARD) Choice for Rheumatoid Arthritis (RA)

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

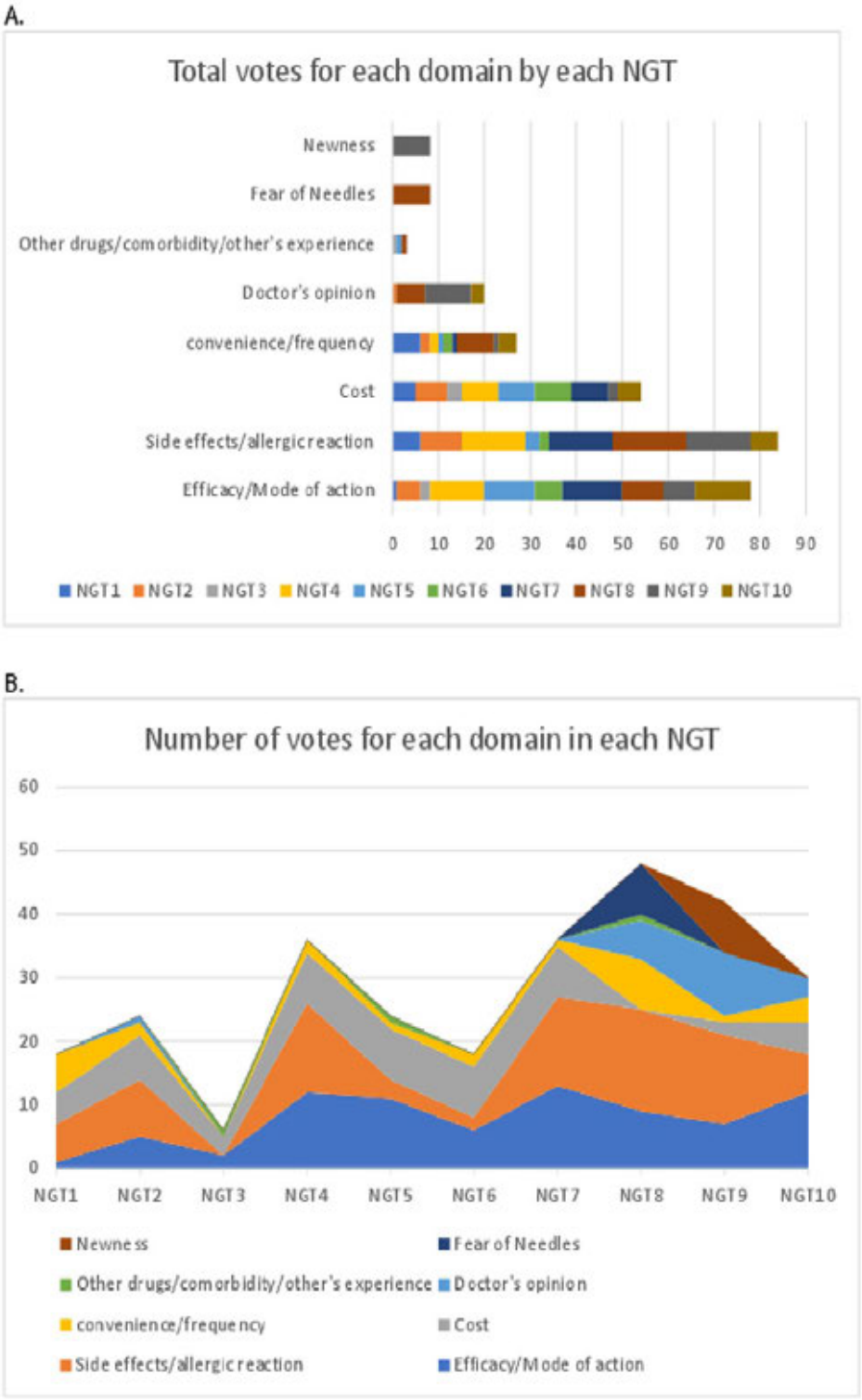
Background/Purpose: Little is known about the patient perspective related to DMARD choice in RA. Our objective was to assess how patients decide whether to add traditional oral DMARDs or injectable biologic DMARDs to methotrexate for the treatment of active RA.

Methods: We conducted 10 nominal groups in patients with RA from rheumatology clinics at two tertiary care centers at Birmingham (n=6; 21 patients) and New York City (n=4; 26 patients). Patients provided responses to the question "What sort of things are important to you when you make a decision between adding pills versus injectable medications to treat rheumatoid arthritis when methotrexate fails to control RA disease activity?" Patients nominated, discussed and voted for the responses.

Results: Forty-seven patients participated in 10 nominal groups, who were predominantly female (85%), 70% white, with a mean (standard deviation) age of 64.5 years and 58% with >10 year RA duration. Present/past DMARDs included methotrexate in 91% and biologics and/or Jak-inhibitors in 68% of participants. The mean MD-HAQ score was 2 on a 0-10 scale and the mean RAPID-3 score on a 0-30 scale was 9.1. The main responses ranked by patients were as follows.

Efficacy/mode of action was among the voted domains in 10/10 nominal groups and got 28% of the votes (78/282 votes; Figure 1). *Side effects/fear of side effects* was among the voted domains in 9/10 nominal groups and got 30% of the votes (84/282 votes). *Cost* was among the voted domains in 9/10 nominal groups and got 19% of the votes (54/282 votes). Out of pocket costs, including co-payments and patient responsibility for the drug cost was the most important aspect of the medication cost that impacted the choice. *Convenience/frequency of use* was among the voted domains in 9/10 nominal groups and got 10% of the votes (27/282 votes). *Doctor's opinion* was among the voted domains in 4/10 nominal groups and got 7% of the votes (20/282 votes). Patients greatly valued their rheumatologist's opinion, which was either a strong factor or a deciding factor for them. *Other drugs/comorbidity/other patient's experience/effects on other people* was among the voted domains in 3/10 nominal groups and got 1% of the votes (3/282 votes). Many patients worried about drug-drug interactions and contra-indications in the presence of other systemic conditions. *Fear of Needles* was among the voted domains in 1/10 nominal groups and got 3% of the votes (8/282 votes). People expressed "Fear of injections" "Anxiety about self-injecting", and "Nauseating concept if you are not a medical person". *The newness of the medication* was among the voted domains in 1/10 nominal groups and got 3% of the votes (8/282 votes).

Conclusion: Our qualitative study identified the patient perspective of DMARD choice between oral versus injectable drugs once methotrexate fails to control disease activity. This knowledge can help in informative shared decision-making in regular clinical care.



Figures_RA_meds_NGT_abstract

Figure 1. Domains associated with choice of oral triple therapy vs. adding injectable biologics (n=47), shown as total votes by each NGT (A) and the number of votes in each NGT (B) Figure legend: We show each domain in the figure panels and either the total votes across all NGTs showing the split by each NGT (A), with x-axis showing the total number of votes or the number of votes within each NGT (B), with y-axis showing the number of votes within each NGT

Disclosure: **J. Singh**, Amarin pharmaceuticals, 1, 4, Clearview healthcae partners, 5, Clearview healthcare partners, 5, Clinical Care options, 5, Horizon, 5, Medisys, 5, OMERACT, 6, Putnam associates, 5, Spherix, 5, the Amer-

ican College of Rheumatology, 5, The American College of Rheumatology, 5, The National Institues of Health, 5, the National Institutes of Health, 5, Viking therapeutics, 1, 4, WebMD, 5; **H. Tornberg**, None; **S. Goodman**, BMC Rheumatology, 5, 6, Calgene, 5, Celgene, 5, Current Rheumatology reports, 5, Current Rheumatology Reports, 6, Horizon, 2, 5, horizon, 2, Novartis, 2, 5, NYU College of Medicine, 3, NYU Langone College of Medicine, 3, Pfizer, 2, 5, Regenosine, 4, 9, Roche, 2, UCB, 5.

Abstract Number: 1344

Increased High Molecular Weight Adiponectin and Lean Mass During Tocilizumab Treatment in Patients with Rheumatoid Arthritis: A 12 Month Multicenter Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular (CV) diseases. Dyslipidemia is a known adverse reaction to tocilizumab (TCZ). TNFa blockade in RA patients has been associated with weight gain, increase in fat mass and variations in serum adipokines. Adiponectin (Adp) plays a role in the metabolism of glucose and lipids. Numerous studies have confirmed the beneficial role of Adp in insulin sensitivity and CV disease prevention, especially its high molecular weight (HMW) isoform. Increased Adp levels are associated with a reduced risk for coronary heart disease.

Objectives: To analyse the changes in serum adipokines and especially Adp (total and HMW) and body composition during TCZ therapy in RA.

Methods: multicenter open-label study (NCT02843789). All patients enrolled had active RA (DAS28≥ 3.2) with previous inadequate response to a csDMARDs and/or bDMARDs. They all were TCZ naïve and received TCZ IV according to the patient/physician shared decision. Patients were evaluated at baseline, 1, 3, 6, and 12 months. Clinical assessment included body mass index, waist circumference, DAS28 and HAQ scores. Laboratory parameters of inflammation (ESR, CRP, IL-6), lipid parameters (total cholesterol, LDL and HDL cholesterol, triglycerides), metabolic parameters (glycemia, insulin), serum Adp (total and HMW), leptin, resistin, and ghrelin were measured at each time point. Body composition (lean mass, fat mass, % of fat, fat in the android and gynoid regions) was evaluated at baseline, 6, and 12 months (DEXA, Lunar GE). Our primary criteria was the changes in Adp (total and HMW) at 6 months.

Results: 107 patients (78 F; mean age ± SD: 56.6 yr ± 13.5; disease duration: 9.9 yr ± 8.1; previous biological treatment: 64.5%; corticosteroids: 69%; concomitant csDMARD: 72.8% including MTX: 61.6%) were included. 97 were

still on treatment at month 6 and 77 completed the study at 12 months. Most of the patients (95%) received TCZ IV 8 mg/kg. Patients were responding to TCZ with a significant DAS28 decrease between baseline and months 6 and 12. HAQ, ESR, and CRP levels significantly decreased along the study (Table 1). Both total and HMW Adp increased from baseline to month 6 and month 12 (total Adp: baseline vs month 6: p=0.055; HMW Adp: baseline vs month 6: p=0.02, baseline vs month 12: p=0.057).BMI and waist circumference significantly increased at month 6 and 12, as well as lean mass (p=0.0097 at month 6 and p=0.021 at month 12). Fat mas, % of fat and android/abdominal fat did

	Baseline (n=107)	**M6** (n=97)	**M12** (n=77)
DAS28	4.93 ± 1.3	2.5 ± 1.2 ***	2.3 ± 1.3 ***
HAQ	1.4 ± 0.6	0.97 ± 0.6 ***	0.98 ± 0.6 ***
ESR (mm/h)	27.8 ± 22.8	6.1 ± 7.1 ***	5.8 ± 1.8 ***
CRP (mg/L)	17.7 ± 26.7	2.4 ± 4.4 ***	2.3 ± 4.5 ***
Body mass index (Kg/m2)	26.4 ± 5.5	26.7 ± 5.5 *	27.2 ± 5.8 ***
Waist circumference (cm)	90.3 ± 13.2	93.2 ± 14.7 ***	93.9 ± 15.3 ***
Lean mass (g)	40.762 ± 8.39	41.79 ± 8.81 **	42.11 ± 8.98 *
Fat mass (g)	27.67 ± 12.05	27.45 ± 10.74	28.15 ± 11.39
Total chol (mmol/L)	5.2 ± 1.2	5.7 ± 1.2 ***	5.6 ± 1.2
LDL chol (mmol/L)	2.9 ± 1	3.4 ± 0.9 ***	3.4 ± 0.9 ***
HDL chol (mmol/L)	1.6 ± 0.5	1.7 ± 0.6	1.6 ± 0.4
Total/HDL Chol	**3.58 ± 1.30**	**3.59 ± 0.95**	**3.8± 1.2**
Total adiponectin (µg/mL)	14.54 ± 8.1	14.6 ± 7.5	14.2 ± 7.6
HMW adiponectin (µg/mL)	7.3 ± 5.4	7.5 ± 5.4 *	6.8 ± 4.6
Leptin (ng/mL)	32.64 ± 26.9	32.6 ± 27.3	32.8 ± 27.5
Resistin (ng/mL)	10.5 ± 4.9	10.8 ± 4.9	10.9 ± 5.3
Ghrelin (pg/mL)	2121.9 ± 1309.4	2074.8 ± 1278.4	2035 ± 1304.3

Table 1. clinical, laboratory parameters, serum adipokines and body composition measurements during 12 months of tocilizumab treatment (* p <0.05; ** p <0.01; ***p <0.005).

not change over the study. Lipid parameters (total cholesterol and LDL cholesterol) increased while glycaemia and insulin remained stable. Serum leptin, resistin and ghrelin did not change during the follow-up.

Conclusion: TCZ treatment in RA patients was associated with a significant increase in HMW Adp, increase in total Adp and also a significant gain of lean mass, while fat mass (total fat or abdominal fat) did not change. These variations in Adp during TCZ treatment may have a positive impact on the CV risk of RA patients and may contribute to the protective role of TCZ against the CV burden in RA. In addition, TCZ may have an anabolic impact on lean mass and thus on skeletal muscle.

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Abstract Number: 1345

Are There Differences in Efficacy and Safety of Biological Disease-modifying Antirheumatic Drugs Between Elderly-onset and Young-onset Rheumatoid Arthritis?

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To compare efficacy and safety of biological disease-modifying antirheumatic drugs (bDMARDs) between elderly-onset rheumatoid arthritis (EORA) and young-onset rheumatoid arthritis (YORA) patients.

Methods: Patients with rheumatoid arthritis (RA) aged ≧18 years enrolled in a Japanese multicenter observational registry between Sep 2009 and December 2017 who had ≧3.2 disease activity score in 28 joints-erythrocyte sedimentation rate (DAS28-ESR) when initiating bDMARDs were included. EORA was defined as RA with onset at 60 or over. Considering selection bias in the estimation of effects of time-varying treatments and clustering effects by individual, a generalized estimating equation model with an inverse probability of treatment weighting was used to assess the relationship between age onset and clinical effectiveness at 48 weeks. Primary outcome was Clinical Disease Activity Index (CDAI) score at 48 weeks. Secondary outcomes included biologic retention at 48 weeks, achievement of CDAI remission, and low disease activity (LDA)/remission. Biologic retention rate was compared using a cox proportional hazards model.

Results: Among a total of 7183 patients in the registry, proportion of patients on bDMARDs was lower in the EORA as compared to the YORA (18.3 % vs 28.0 %, p < 0.001). Of the 989 bDMARDs initiators, 364 (36.8%) were identified as EORA. After adjusting for differences in baseline characteristics between the two age groups, there was no significant difference in CDAI score at 48 weeks (1.01, 95% CI=-0.62-2.64, p=0.22). There was a trend of lower remission in the EORA (OR=0.52, 95%CI=0.24-1.14, p=0.10), but LDA/remission rate was similar (OR=0.86, 95%CI=0.29-2.52,

TABLE 1.

Clinical characteristics of elderly-onset RA and young-onset RA patients at initiation of bDMARDs

Characteristic	EORA (*n* = 364)	YORA (*n* = 624)	P-value
Age, years	72.8 ±7.0	54.5±14.0	<0.001
Female sex, n (%)	267 (73.4)	536 (85.9)	<0.001
Disease duration (years)	4.3±4.6	11.2±10.9	<0.001
RF-positive, n (%)	241 (73.7)	460 (82.1)	0.004
ACPA-positive, n (%)	250 (84.2)	448 (84.9)	0.84
TJC	5.3±5.6	5.0±4.8	<0.001
SJC	4.4±4.1	4.0±3.6	0.005
PtGA VAS, 0-100mm	59.2±25.0	56.2±24.9	0.06
PGA VAS, 0-100mm	41.4 ± 21.9	42.4±23.4	0.50
DAS28-ESR	5.1±1.1	4.9±1.0	0.13
SDAI	22.6±12.1	20.9±10.5	0.03
CDAI	19.8±10.8	18.9±9.6	0.20
mHAQ	1.02±0.68	0.82±0.70	<0.001
MTX use, n (%)	210 (57.7)	401 (64.3)	0.04
MTX dosage, mg/week	8.7±3.0	9.2±3.3	0.06
Glucocorticoid use, n (%)	140 (38.5)	239 (38.3)	1.00
Glucocorticoid dosage (mg/day)	5.9±3.5	6.1±4.5	0.70
Sulfasalazine use, n (%)	54 (14.8)	51 (8.2)	<0.001
Other DMARDs use, n (%)	46 (12.6)	99 (15.9)	0.19
1ST bio (%)	231 (63.5)	309 (49.5)	<0.001

p=0.77). Drug maintenance rates (HR=0.95, 95%CI=0.55-1.35, p=0.78) and adverse events discontinuation rates (HR=0.78, 95%CI=0.38-1.18, p=0.22) were similar between the two age groups adjusting other confounders.

Conclusion: In RA patients initiating bDMARDs, improvements in clinical disease at 48 weeks were comparable between EORA and YORA. Drug maintenance and adverse events discontinuation rates were similar between the two age groups.

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Abstract Number: 1346

Post-Traumatic Stress Disorder, Depression, Anxiety and Persistence of Methotrexate and TNF Inhibitors in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Post-traumatic stress disorder (PTSD) is associated with worse outcomes among U.S. Veterans with rheumatoid arthritis (RA) in addition to reduced medication adherence in other chronic disorders. This study examined the association between PTSD and DMARD discontinuation, accounting for comorbidity and other potential confounders that may impact this relationship.

Methods: VA administrative data were used to define unique dispensing episodes of methotrexate (MTX), self-injectable TNF inhibitors (TNFi), other DMARDs, and prednisone for Veterans with a prior diagnostic code for RA. Discontinuation was defined as a lapse in drug refill >90 days. Patient characteristics and diagnosis codes were linked to treatment courses. Patient characteristics were analyzed based on the first dispensing episode of each unique DMARD. Some patients switched TNFi's over time and thus accounted for multiple dispensing episodes. Diagnosis codes (using a "lifetime" lookback) were used to delineate RA patients into 3 mutually exclusive groups: PTSD (with or without depression/anxiety), depression and/or anxiety without PTSD, and none of the aforementioned diagnoses. Multivariate Cox proportional hazards models were used to evaluate associations between psychiatric diagnoses and time to DMARD discontinuation. Covariates included age, sex, race (Black vs. White), calendar year (2005-2009 vs.

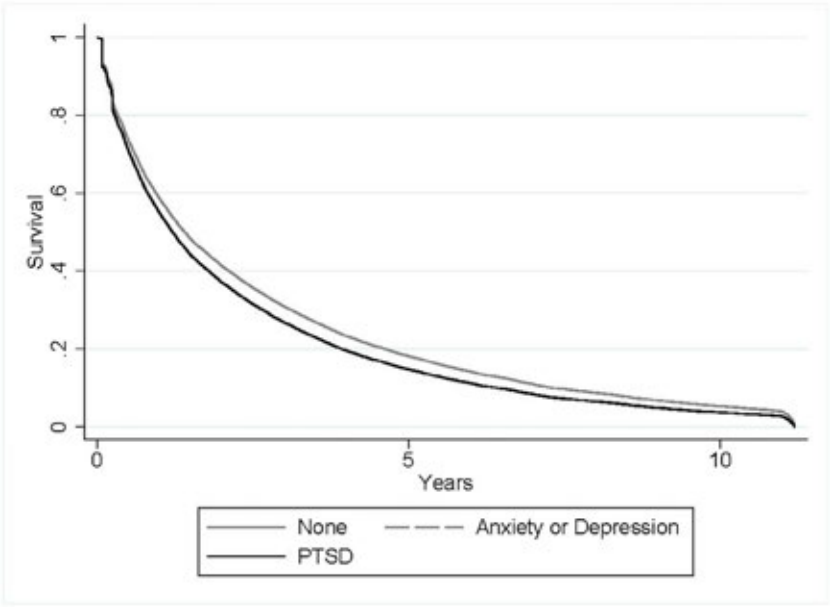

Figure 1. Methotrexate drug survival (Note that PTSD and Anxiety/Depression groups have significant overlap in this figure)

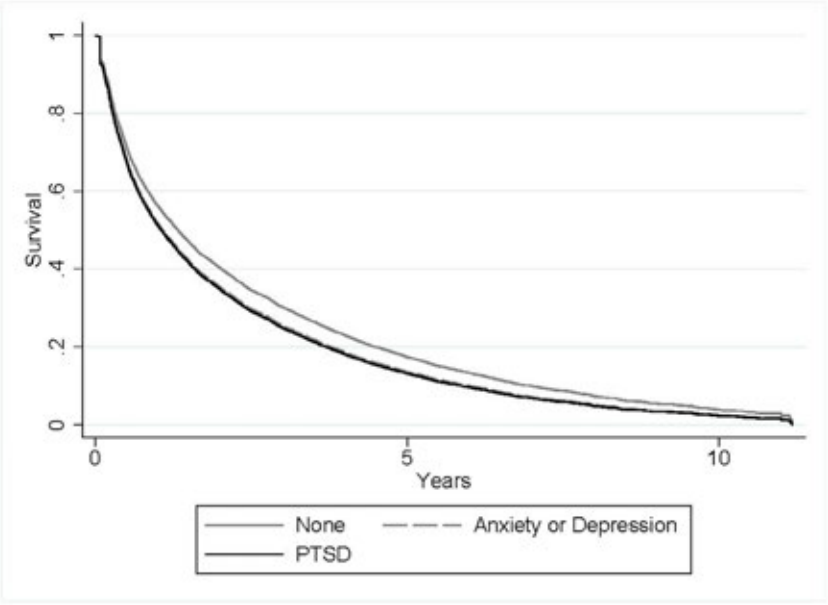

Figure 2. TNF inhibitor drug survival (Note that PTSD and Anxiety/Depression groups have significant overlap in this figure)

2010-2014), BMI, other DMARDs, Rheumatic Disease Comorbidity Index (RDCI), CRP, anti-CCP status, RA duration >5 years, diabetes, hypertension, CHF, history of malignancy, and current smoking status.

Results: There were 15,082 dispensing episodes of MTX in 15,082 unique patients and 8,412 dispensing episodes for TNFi in 7,092 unique RA patients. Patients were predominantly Caucasian (74% MTX, 77% TNFi) and male (88% MTX, 87% TNFi). Median drug survival was 1.30 years (95% CI 1.27-1.35) for MTX and 1.18 years (95% CI 1.13-1.24) for TNFi. Comorbid PTSD was seen in 20% of those initiating MTX and 22% of those initiating TNFi. Depression and/

or anxiety (without PTSD) was seen in 23% of those initiating MTX and 27% of those initiating TNFi. After adjusting for covariates, PTSD was associated with a greater likelihood of discontinuing both MTX [HR 1.12 (1.07,1.18) p< 0.001; Figure 1] and TNFi [HR 1.16 (1.09,1.23) p< 0.001; Figure 2]. Risk of discontinuation in depression/anxiety without PTSD was comparable to that seen in PTSD for both MTX [HR 1.12 (1.07,1.17) p< 0.001] and TNFi [HR 1.14 (1.08,1.21) p< 0.001].

Conclusion: Veterans with RA and a diagnosis of PTSD, depression, or anxiety discontinued DMARDs sooner than those without these diagnoses, even after accounting for a number of other factors. Rates of discontinuation were similar for those with PTSD compared to those with depression and/or anxiety alone and were similar between MTX and TNFi. PTSD, anxiety, and depression may contribute to lower persistence of RA therapy due to non-adherence, apparent lack of response, or a greater incidence of adverse events.

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Abstract Number: 1347

Achievement of Remission in Two Early Rheumatoid Arthritis Cohorts Implementing Different Treat-To-Target Strategies

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SESSION INFORMATION
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Background/Purpose: A treat-to-target (TTT) approach results in superior outcomes compared to conventional care in patients with rheumatoid arthritis (RA). However, TTT strategies are still not widely adopted in clinical practice and many patients never reach the target of remission. We compared achievement of remission in two early RA cohorts, examining whether a TTT strategy implemented in a randomized controlled trial (RCT) led to superior outcomes compared to a TTT approach implemented in an observational study.

Methods: Data were provided by two Norwegian multicenter studies, the ARCTIC trial and the NOR-VEAC observational study. Both studies included DMARD-naïve RA-patients in the period 2010-2016 and implemented a TTT strategy. All patients fulfilled the 2010 ACR/EULAR classification criteria for RA. The target in the ARCTIC trial was stringent remission defined as a Disease Activity Score (DAS44) < 1.6 plus no swollen joints, while the target in the NOR-VEAC study was the less stringent DAS28 remission (DAS28< 2.6). In the current study we assessed: 1)

Table 1 Baseline characteristics in the ARCTIC trial and the NOR-VEAC observational study after propensity score weighting

Baseline characteristics*	ARCTIC (n=183)	NOR-VEAC (n=277)	SMD
Age	52.5	53.1	-0.047
Female, %	64.7	63.3	0.030
ACPA positive,%	79.3	78.9	0.010
RF positive,%	67.3	67.5	-0.004
CDAI	22.8	22.9	-0.009
DAS28	4.8	4.8	-0.007
Symptom duration, months	4.7	4.8	-0.015

*Mean if not otherwise indicated

SMD, standardized mean difference; ACPA, anti-citrullinated protein antibodies; RF, rheumatoid factor; CDAI, Clinical Disease Activity Index; DAS28, Disease Activity Score 28 joint count

achievement of the study specific treatment targets and 2) achievement of a stringent remission defined by the ACR/

Table 2 Achievement of study specific treatment targets during follow-up in the ARCTIC trial and the NOR-VEAC observational study

	ARCTIC (n=183)	NOR-VEAC (n=277)
Study specific targets:	**DAS<1.6 + no swollen joints**	**DAS28<2.6**
3 months, %	37.2	47.4
6 months, %	53.4	56.3
12 months, %	69.4	67.0
24 months, %	66.5	66.1

DAS, Disease Activity Score (44 joint count); DAS28, Disease Activity Score 28 joint count

EULAR Boolean criteria during follow-up over 24 months. We assessed achievement of the study specific targets using descriptive analyses and compared achievement of ACR/EULAR Boolean remission using logistic regression with inverse probability of censoring weights to account for missing data. For the comparative analyses we balanced the two cohorts on baseline covariates using propensity score weights.

Results: We included 183 patients from the ARCTIC trial and 277 patients from the NOR-VEAC study. After baseline balancing with propensity score weights, patients in the two cohorts were similar with regard to age, sex, ACPA positivity and disease activity (**Table 1**). Patients in both cohorts started with methotrexate (MTX) monotherapy. At 12 months, more patients in the NOR-VEAC study than in the ARCTIC trial were still treated with MTX monotherapy (79% vs. 67%), while more patients in ARCTIC had switched to another synthetic DMARD regimen or started a biologic DMARD. At 24 months, 25% of patients in both cohorts had switched to a biologic DMARD, while 17% of patients in the ARCTIC trial and 9% of patients in the NOR-VEAC study had switched to another synthetic DMARD regimen. More than half of patients in each cohort had reached the study specific targets at 6 months, and this increased to more than 2/3 in both cohorts at 12 and 24 months (**Table 2**). The odds of reaching ACR/EULAR Boolean remission during follow-up were higher in the ARCTIC trial compared to the NOR-VEAC study, with statistically significant differences at 3 months (OR 1.73; 95% CI 1.03-2.89), 12 months (OR 1.97, 95% CI 1.21-3.20) and 24 months (OR 1.82; 95% CI 1.05 – 3.16; **Table 3**).

Table 3 Odds of achieving ACR/EULAR Boolean remission in the ARCTIC trial versus the NOR-VEAC observational study during follow-up*

Study visit	OR	95% CI	*p*-value**
3 months	1.73	(1.03 – 2.89)	0.04
6 months	1.44	(0.88 – 2.38)	0.15
12 months	1.97	(1.21 – 3.20)	0.01
24 months	1.82	(1.05 – 3.16)	0.03

*Cohorts were balanced on baseline covariates using inverse probability of treatment weights using the propensity score. Multiple imputation by chained equations was used to impute missing variables at existing visits in the NOR-VEAC study.
**Estimates were obtained using logistic regression with inverse probability of censoring weights.
ACR/EULAR Boolean remission, C-reactive protein ≤1, swollen joint count 28 ≤1, tender joint count 28 ≤1 and patient´s global assessment ≤1; OR, odds ratio; CI, confidence interval

Conclusion: Our results suggest that TTT is feasible and successful in clinical practice, similar to clinical trials. The odds of reaching the stringent ACR/EULAR Boolean remission during follow-up was higher in the ARCTIC trial than in the NOR-VEAC observational study, suggesting that targeting a more stringent remission improves the outcome of a TTT strategy.

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Abstract Number: 1348

Impact of Tofacitinib on the Individual Components of the ACR Composite Score in Patients with Rheumatoid Arthritis: A Post Hoc Analysis of Phase 3 Trials

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Table 1. Percentage of patients treated with tofacitinib 5 mg BID + csDMARDs or PBO + csDMARDs who reported an a) ACR20 response and ≥20% improvement from BL in each component of the ACR20 score, b) ACR50 response and ≥50% improvement from BL in each component of the ACR50 score, and c) ACR70 response and ≥70% improvement from BL in each component of the ACR70 score up to Month 6

	Week 2		Month 1		Month 3		Month 6	
	Tofacitinib 5 mg BID (N=294)	PBO[a] (N=151)	Tofacitinib 5 mg BID (N=769)	PBO[a] (N=390)	Tofacitinib 5 mg BID (N=737)	PBO[a] (N=378)	Tofacitinib 5 mg BID (N=705)	PBO[a] (N=170)
a) ACR20 response and ≥20% improvement from BL in each component of the ACR20 score								
ACR20 response, n (%)	79 (26.9)	17 (11.3)	320 (41.6)	75 (19.2)	453 (61.5)	111 (29.4)	490 (69.5)	116 (68.2)
ACR score component (≥20% improvement from BL), n (%)								
TJC	148 (50.3)	65 (43.1)	492 (64.0)	189 (48.5)	581 (78.8)	216 (57.1)	612 (86.8)	153 (90.0)
SJC	157 (53.4)	79 (52.3)	559 (72.7)	218 (55.9)	613 (83.2)	234 (61.9)	622 (88.2)	154 (90.6)
CGA	141 (48.0)	60 (39.7)	526 (68.4)	188 (48.2)	586 (79.5)	217 (57.4)	612 (86.8)	138 (81.2)
PtGA	138 (46.9)	51 (33.8)	453 (58.9)	158 (40.5)	501 (68.0)	153 (40.5)	491 (69.7)	106 (62.4)
Pain	129 (43.9)	53 (35.1)	448 (58.3)	150 (38.5)	516 (70.0)	160 (42.3)	515 (73.1)	113 (66.5)
HAQ-DI	118 (40.1)	38 (25.2)	357 (46.4)	124 (31.8)	446 (60.5)	145 (38.4)	466 (66.1)	87 (51.2)
CRP	232 (78.9)	46 (30.5)	613 (79.7)	142 (36.4)	566 (76.8)	155 (41.0)	553 (78.4)	82 (48.2)
CRP	232 (78.9)	46 (30.5)	613 (79.7)	142 (36.4)	566 (76.8)	155 (41.0)	553 (78.4)	82 (48.2)
b) ACR50 response and ≥50% improvement from BL in each component of the ACR50 score								
ACR50 response, n (%)	18 (6.1)	2 (1.3)	111 (14.4)	9 (2.3)	233 (31.6)	33 (8.7)	295 (41.8)	44 (25.9)
ACR score component (≥50% improvement from BL), n (%)								
TJC	70 (23.8)	26 (17.2)	276 (35.9)	76 (19.5)	422 (57.3)	115 (30.4)	483 (68.5)	122 (71.8)
SJC	96 (32.7)	29 (19.2)	372 (48.4)	116 (29.7)	487 (66.1)	152 (40.2)	541 (76.7)	132 (77.7)
CGA	48 (16.3)	17 (11.3)	256 (33.3)	68 (17.4)	381 (51.7)	101 (26.7)	455 (64.5)	103 (60.6)
PtGA	57 (19.4)	18 (11.9)	229 (29.8)	67 (17.2)	317 (43.0)	75 (19.8)	330 (46.8)	55 (32.4)
Pain	49 (16.7)	16 (10.6)	225 (29.3)	64 (16.4)	328 (44.5)	73 (19.3)	360 (51.1)	62 (36.5)
HAQ-DI	43 (14.6)	11 (7.3)	158 (20.6)	44 (11.3)	267 (36.2)	64 (16.9)	272 (38.6)	45 (26.5)
CRP	169 (57.5)	14 (9.3)	510 (66.3)	57 (14.6)	470 (63.8)	84 (22.2)	464 (65.8)	42 (24.7)
c) ACR70 response and ≥70% improvement from BL in each component of the ACR70 score								
ACR70 response, n (%)	1 (0.3)	0 (0.0)	25 (3.3)	1 (0.3)	80 (10.9)	8 (2.1)	133 (18.9)	9 (5.3)
ACR score component (≥70% improvement from BL), n (%)								
TJC	31 (10.5)	10 (6.6)	141 (18.3)	36 (9.2)	270 (36.6)	63 (16.7)	324 (46.0)	74 (43.5)
SJC	51 (17.4)	12 (8.0)	190 (24.7)	49 (12.6)	342 (46.4)	93 (24.6)	404 (57.3)	89 (52.4)
CGA	16 (5.4)	5 (3.3)	93 (12.1)	23 (5.9)	207 (28.1)	48 (12.7)	276 (39.2)	51 (30.0)
PtGA	20 (6.8)	8 (5.3)	110 (14.3)	27 (6.9)	171 (23.2)	35 (9.3)	204 (28.9)	22 (12.9)
Pain	18 (6.1)	5 (3.3)	109 (14.2)	24 (6.2)	184 (25.0)	39 (10.3)	202 (28.7)	32 (18.8)
HAQ-DI	18 (6.1)	5 (3.3)	76 (9.9)	19 (4.9)	128 (17.4)	30 (7.9)	160 (22.7)	22 (12.9)
CRP	115 (39.1)	8 (5.3)	379 (49.3)	28 (7.2)	364 (49.4)	49 (13.0)	363 (51.5)	25 (14.7)

Data were pooled from three Phase 3 studies: ORAL Scan (NCT00847613); ORAL Sync (NCT00856544); ORAL Standard (NCT00853385). All patients received background csDMARDs

Analysis is based on observed case data (without imputation) of patients with all 7 components assessed

[a]PBO patients received PBO from Study Day 1 up to either M3 (for non-responders) or M6 (for responders). At M3, PBO non-responders were advanced to tofacitinib 5 or 10 mg BID; therefore, all patients reported under PBO at M6, would have been PBO responders at M3. Patients were considered non-responders if there was <20% improvement in both tender/painful and swollen joint counts at M3

ACR20/50/70, improvement in American College of Rheumatology criteria of 20/50/70%; BID, twice daily; BL, baseline; CGA, Clinician Global Assessment; CRP, C-reactive protein; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; HAQ-DI, Health Assessment Questionnaire-Disability Index; M, month; PBO, placebo; PtGA, Patient Global Assessment; SJC, swollen joint count; TJC, tender joint count

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Tofacitinib is an oral JAK inhibitor for the treatment of RA. In clinical trials, standard criteria for measuring treatment efficacy in patients (pts) with RA include ACR response rates, composite scores that represent ≥ 20/50/70% improvement in seven components of disease activity. This post hoc analysis evaluated the impact of tofacitinib 5 mg BID + csDMARDs, and placebo (PBO) on each ACR score component.

Methods: Efficacy data for tofacitinib 5 mg BID and PBO were pooled from three Phase (P)3 PBO-controlled trials (ORAL Scan, NCT00847613; ORAL Sync, NCT00856544; ORAL Standard, NCT00853385) of tofacitinib + csDMARDs (mostly MTX) in RA pts with inadequate response to ≥ 1 csDMARD. Endpoints summarized descriptively included proportions of pts achieving: ACR20/50/70 responses, and ≥ 20/50/70% improvements from baseline (BL) in individual ACR components (TJC, SJC, CGA, PtGA, Pain, HAQ-DI, and CRP) from Week (W)2 through Month (M)6, and mean percent improvement from BL in all components for ACR20 responders at M3.

Results: Compared with csDMARD-IR pts receiving PBO, greater proportions of csDMARD-IR pts receiving tofacitinib + csDMARDs achieved ≥ 20% improvement from BL in all ACR components by W2, with proportions generally increasing at all subsequent time points to M6 (Table 1a); typically, higher proportions of pts achieved ≥ 20% improvement from BL in individual components vs overall ACR score. Overall, through M6, a higher proportion of pts achieved ≥ 20% improvement for primary components (TJC and SJC) vs the secondary components CGA, PtGA,

Table 2. Mean percent improvement from baseline in ACR score components in patients treated with tofacitinib 5 mg BID + csDMARDs who achieved an ACR20 response at Month 3

ACR score component (N=453)	Mean percent improvement from baseline (SD)
TJC	70.1 (22.8)
SJC	74.3 (22.4)
CGA	58.9 (28.3)
PtGA	49.4 (46.5)
Pain	52.1 (46.3)
HAQ-DI	42.6 (55.6)
CRP[a]	18.6 (314.5)

Data were pooled from three Phase 3 studies: ORAL Scan (NCT00847613); ORAL Sync (NCT00856544); ORAL Standard (NCT00853385). All patients received background csDMARDs

Analysis is based on observed case data (without imputation) of patients with all of 7 components assessed

[a]Median percent improvement for CRP was 76.7%

ACR20, improvement in American College of Rheumatology criteria of 20%; BID, twice daily; CGA, Clinician Global Assessment; CRP, C-reactive protein; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; HAQ-DI, Health Assessment Questionnaire-Disability Index; PtGA, Patient Global Assessment; SJC, swollen joint count; TJC, tender joint count

Pain, and HAQ-DI; among secondary components, ≥ 20% improvement rates were numerically highest for CGA (excepting CRP at W2 and M1 in pts receiving tofacitinib). In contrast, ≥ 50% and ≥ 70% improvement rates with tofacitinib were numerically higher for PtGA and Pain vs CGA at W2 (Table 1b-c). Among pts achieving an ACR20 response at M3, mean percent improvement from BL was > 70% for primary components, and ranged from 18.6% to 58.9% for secondary components (Table 2).

Conclusion: In this post hoc analysis of pooled P3 data, tofacitinib treatment was associated with rapid and sustained improvements in all ACR components. In tofacitinib- and PBO-treated pts, physician-reported measures (TJC, SJC, and CGA) were found to contribute somewhat more to the achievement of overall ACR20 response, compared with pt-reported outcomes (PROs; PtGA, Pain, and HAQ-DI). This numerical trend may be reflective of the subjective nature of PROs and overall wellbeing of the pt, and thus, their reduced sensitivity to anti-inflammatory treatment. Intriguingly, with more stringent endpoint criteria at earlier time points, some PROs had a somewhat greater contribution to overall ACR response, which may be attributable to rapid symptomatic improvement in these pts. While ACR scores are not generally used in the clinic, individual components may be measured; thus, these data may help guide clinical expectations with new therapies.

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Abstract Number: 1349

Earlier Biologic Initiation over Two Decades of Real World Observational Data from the RAPPORT Biologics Registry of Northern Alberta, Canada

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
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Background/Purpose: Rheumatoid (RA) and psoriatic arthritis (PsA) are inflammatory arthritides associated with significant potential functional disability if not well controlled. We reviewed the baseline demographic and disease characteristics over nineteen years in the RAPPORT registry to understand changes in prescribing patterns of biologic disease modifying anti-rheumatic drugs (bDMARDs) over time.

Methods: The **R**heumatoid **A**rthritis **P**harmacovigilance **P**rogram and **O**utcomes **R**esearch in **T**herapeutics (RAPPORT) registry is a large prospective inception cohort for Northern Albertan inflammatory arthritis (IA) patients about to start advanced therapy with at least 4 months of exposure to conventional synthetic DMARDs (csDMARD) including parenteral weekly methotrexate, methotrexate plus a DMARD in combination, and leflunomide. We compared baseline demographic and disease characteristics in two cohorts according to registration year: 2000-2010 (n=1071) and 2011-2019 (n=1632). Specifically, we compared patient demographics including age, sex, education, comorbidities and smoking status; disease characteristics including tender and swollen joint count, HAQ, patient global, CRP, and DAS28, symptom duration; and first bDMARD therapy. Descriptive statistics were use to asses baseline demographics along with univariate analysis for comparison of variables between cohorts.

Results: Of the 2703 RAPPORT patients, IA patients in the later cohort (2011 onwards) were started on biologic therapy an average of 2.61 years earlier from symptom duration ($p< 0.001$) (Table 1). There were differences in the pattern of bDMARD prescriptions within and between classes between the two cohorts; however, there were no significant differences in age, sex or number of comorbidities (Table 1). The prevalence of self-reported depression and osteoarthritis were higher in the later cohort but there was no difference in heart disease or associated cardiovascular risk factors (hypertension, diabetes). Statistically significant but clinically unimportant differences in markers of disease activity including HAQ, swollen joint count, and CRP were found between cohorts (Table 2). Biologic DMARD prescriptions in the latter cohort showed increased TNF inhibitor use and increased use of other classes (Table 3).

Conclusion: Prescribing patterns of bMDARDs changed between the first and second decade of RAPPORT with earlier introduction of bDMARDS in IA patients from time of diagnosis. Possible reasons include the rapid increase in availability of bDMARDs between and across classes and increased uptake and confidence in bDMARD use by prescribing rheumatologists over time. Further work to evaluate the impact of bDMARD prescription patterns on patients and society is planned.

Table 1. **Baseline characteristics of all RAPPORT patients starting first biologic DMARD**				
Date of enrollment		**2000-2010**	**2011-2019**	**P-value**
		(n = 853)	(n = 1521)	
Diagnosis	RA	711 (83.35)	1209 (79.49)	0.02
	PsA	142 (16.65)	312 (20.51)	
Age (years)	Mean (SD);Median (IQR)	52.98 (13.04) 53.39 (44.61 - 61.69)	52.13 (14.52) 53.68 (42.0 - 61.88)	0.16
Sex	Male	256 (30.01)	460 (30.24)	0.91
	Female	597 (69.99)	1061 (69.76)	
		(n = 824)	(n = 1413)	
Education	Grade School	97 (11.77)	101 (7.15)	<0.01
	High School	378 (45.87)	576 (40.76)	
	College/University	349 (42.35)	736 (52.09)	
Duration of Symptoms (years)	Mean (SD); Median (IQR)	13.37 (11.01) (n = 837) 10.39 (4.57 - 19.89)	10.76 (10.41) (n = 1425) 7.29 (2.94 - 15.13)	<0.01
Duration of Diagnosis (years)	Mean (SD); Median (IQR)	11.49 (10.45) (n = 838) 8.9 (3.40 - 16.95)	8.26 (9.37) (n = 1431) 4.53 (1.45 - 11.74)	<0.01
		(n = 833)	(n = 1374)	
Smoking status (N (%))	Current smoker	209 (25.09)	355 (25.84)	0.01
	Ex-smoker	332 (39.86)	459 (33.41)	
	Never smoker	292 (35.05)	560 (40.26)	
Comorbidities (N (%))	Heart disease	54 (6.85) (n=788)	77 (5.73) (n=1344)	0.23
	Hypertension	226 (28.18) (n=802)	373 (27.49) (n = 1357)	0.73
	Lung disease	57 (7.21) (n = 791)	115 (8.53) (n = 1348)	0.28
	Diabetes	60 (7.58) (n = 792)	118 (8.73) (n = 1351)	0.35
	Cancer	28 (3.55) (n = 789)	33 (2.44) (n = 1353)	0.14
	Depression	159 (20.33) (n = 782)	331 (24.68) (n = 1341)	0.02
	Osteoarthritis	347 (44.89) (n = 773)	510 (39.35) (n = 1296)	0.01

Table 2. Markers of disease activity (mean (SD); Median (IQR))			
Date of enrollment	**2000-2010**	**2011-2019**	**P-value**
CRP (mg/L)	836 (98.12) (n = 852)	1449 (94.89) (n = 1527)	<0.01
	39.63 (136.66) 9.40 (4.0 - 24.50)	67.68 (217.64) 9.10 (2.90 - 25.45)	<0.01
Patient Pain	6.84 (2.24) (n = 836) 7.0 (5.0 - 8.0)	6.45 (2.29) (n = 1473) 7.0 (5.0 - 8.0)	<0.01
Patient Global	6.43 (2.30) (n = 839) 7.0 (5.0 - 8.0)	6.29 (2.24) (n = 1471) 6.0 (5.0 - 8.0)	0.13
Health Assessment Questionnaire (HAQ)	1.58 (0.69) (n = 842) 1.63 (1.13 - 2.13)	1.42 (0.62) (n = 1337) 1.38 (1.0 - 1.88)	<0.01
Tender joint count	14.39 (8.55) (n = 853) 14.0 (7.0 - 22.0)	14.50 (8.61) (n = 1521) 14.0 (8.0 - 22.0)	0.76
Swollen joint count	8.10 (5.63) (n = 853) 7.0 (4.0 - 11.0)	7.10 (5.29) (n = 1521) 6.0 (3.0 - 10.0)	<0.01
DAS28 CRP	4.63 (1.12) 4.73 (3.97 - 5.38)	4.53 (1.14) 4.65 (3.88 - 5.33)	0.02

Table 3: Biologic agents and classes of bDMARDs prescribed over time			
	2000-2011	**2011-2019**	**P-value**
Specific bDMARDs			
Etanercept (Enbrel)	144 (17.14) (n = 840)	79 (6.40) (n = 1234)	<0.01
Adalimumab (Humira)	72 (8.57) (n = 840)	42 (3.41) (n = 1232)	<0.01
Anakinra (Kineret)	11 (1.31) (n = 840)	4 (0.32) (n = 1232)	0.01
Infliximab (Remicade)	84 (10.0) (n = 840)	33 (2.68) (n = 1232)	<0.01
Abatacept (Orencia)	8 (0.96) (n = 836)	16 (1.30) (n = 1231)	0.48
Rituximab (Rituxan)	11 (1.32) (n = 835)	6 90.49) (n = 1231)	0.04
Tocilizumab (Actemra)	1 (6.67) (n = 15)	7 (1.21) (n = 580)	0.19
Certolizumab (Cimzia)	0 (0.0) (n = 15)	6 (1.03) (n = 581)	>0.99
Golimumab (Simponi)	1 (6.67) (n = 15)	6 (1.03) (n = 583)	0.16
Ustekinumab (Stelara)	0 (0.0) (n = 15)	2 (0.34) (n = 581)	>0.99
bDMARD Classes			
cs-DMARD	212 (19.79)	1 (0.06)	<0.01
TNF Inhibitor	817 (76.28)	1330 (81.50)	
IL-17 Blocker	0 (0.0)	18 (1.10)	
IL-1 Anatagonist	3 (0.28)	1 (0.06)	
ts-DMARD	0 (0.0)	77 (4.72)	
T-cell Costimulation Inhibitor	12 (1.12)	124 (7.60)	
B-cell Depletor	26 (2.43)	24 (1.47)	
IL-6 Blocker	1 (0.09)	57 (3.49)	
IL-12/23 Blocker	0 (0.0)	0 (0.0)	

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Abstract Number: 1350

Patient Disease Trajectories in Baricitinib-2 Mg-Treated Patients with Rheumatoid Arthritis and Inadequate Response to Biologic DMARDs

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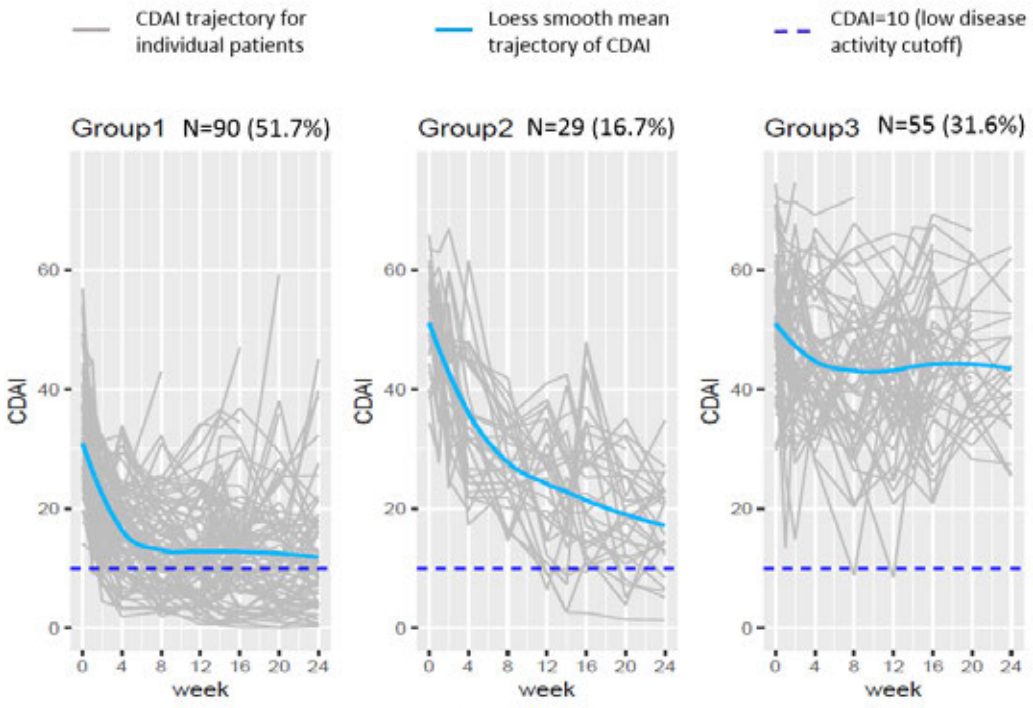
Figure. Response patterns of baricitinib 2-mg-treated patients in the RA-BEACON trial based on CDAI trajectory over time (0-24 weeks)



	Group 1	Group 2	Group 3
Baseline CDAI, Mean (SD)	33.9 (9.0)	51.3 (8.1)	52.2 (11.0)
CDAI at Wk 4, Mean (SD)	16.1 (7.5)	35.0 (11.3)	45.2 (10.5)
Change at Wk 4, ΔCDAI (%)	-17.8 (52.6)	-16.3 (31.7)	-7.0 (13.4)
CDAI at Wk 12 , Mean (SD)	12.0 (7.7)	24.6 (9.9)	43.4 (12.2)
Change at Wk 12, ΔCDAI (%)	-21.8 (64.4)	-26.7 (52.0)	-8.8 (17.0)
CDAI at Wk 24, Mean (SD)	11.8 (9.4)	17.3 (8.0)	42.6 (10.6)
Change at Wk24, ΔCDAI (%)	-22.1 (65.3)	-34.0 (66.3)	-9.6 (18.3)

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Baricitinib (BARI), a selective Janus kinase 1 and 2 inhibitor, is approved for the treatment of moderately-to-severely active RA in over 60 countries. In the RA-BEACON[1] phase 3 trial, BARI 2-mg demonstrated clinical efficacy in patients (pts) with RA and an inadequate response to biologic DMARDs. The objectives of this analysis were to assess the response patterns to BARI 2-mg in the RA-BEACON trial and to describe the demographic and clinical characteristics for pts within each response pattern.

Methods: Observed data from all BARI 2-mg treated pts in the RA-BEACON trial (N=174) up to 24 weeks, protocol mandated rescue, treatment discontinuation, or loss to follow-up were included in the analysis. A Growth Mixture Model was used to classify the longitudinal disease patterns based on the time course of Clinical Disease Activity Index (CDAI) improvement from week 0 to week 24. Baseline characteristics and disease measures were described between groups. The trajectories of HAQ-Disability Index (DI), pain, tender joint count (TJC), and swollen joint count (SJC) within each response pattern were also examined.

Results: BARI 2-mg treated pts were classified into 3 groups based on their CDAI trajectory patterns (Figure). Group 1 (n=90, 52%) had lower baseline CDAI (mean=34), achieved 53% improvement in group mean of CDAI at week 4 (change from baseline, ΔCDAI -18), 64% improvement at week 12 (ΔCDAI -22), and maintained similar improvement through 24 weeks. Group 2 (n=29, 17%) had higher baseline CDAI (mean=51), achieved 32% improvement in mean CDAI at week 4 (ΔCDAI -16) with greater improvement at week 12 (52%, ΔCDAI -27) and week 24 (66%, ΔCDAI -34). Group 3 (n=55, 32%) had a baseline CDAI (mean=52) similar to group 2, but had smaller improvement, achieving 18% improvement in CDAI (ΔCDAI -10) at week 24. The distributions of HAQ-DI, pain, TJC, and SJC within each response pattern showed a trajectory similar to the corresponding group CDAI trajectory. Baseline characteristics for these 3

Table. Selected Patient Characteristics at Baseline*

	Group 1 (N=90)	Group 2 (N=29)	Group 3 (N=55)
Age (years)	54.1 (11.6)	59.9 (11.1)	54.2 (9.6)
Male, n (%)	19 (21.1)	6 (20.7)	12 (21.8)
Body Mass Index (kg/m^2)	31.0 (7.6)	31.4 (7.9)	30.2 (8.4)
Rheumatoid Factor positive, n (%)	69 (76.7)	22 (75.9)	37 (67.3)
ACPA positive, n (%)	66 (73.3)	23 (79.3)	35 (63.6)
High-sensitivity C-Reactive Protein (hsCRP) (mg/L)	18.7 (22.3)	18.8 (18.6)	22.3 (24.7)
Erythrocyte Sedimentation Rate (mm/hr)	40.8 (23.2)	43.8 (18.0)	51.4 (25.3)
Duration of RA (years)	13.4 (7.5)	15.8 (8.5)	13.1 (8.6)
≥3 bDMARD use, n (%)	23 (25.6)	7 (24.1)	20 (36.4)
Tender Joint Count 28	12.4 (5.2)	20.8 (3.8)	21.7 (5.5)
Swollen Joint Count 28	8.9 (3.9)	16.3 (4.8)	16.0 (6.2)
Physician's Global Assessment of Disease Severity	62.0 (17.6)	69.9 (13.9)	73.4 (14.9)
Patient's Global Assessment of Disease Severity	62.5 (20.5)	71.8 (14.1)	73.2 (17.7)
Patient's Assessment of Pain	57.2 (22.9)	64.9 (20.5)	69.5 (17.3)
HAQ-DI	1.5 (0.5)	1.7 (0.6)	2.0 (0.5)
DAS28-hsCRP	5.5 (0.7)	6.6 (0.6)	6.6 (0.8)

*Data reported as mean (SD) unless otherwise indicated

groups are presented in Table 1. Compared to groups 1 and 2, group 3 had more pain, worse physical function (HAQ-DI), and a larger proportion of pts who used ≥3 bDMARDs at baseline.

Conclusion: There are three response patterns to BARI 2-mg treatment in the RA-BEACON trial. The majority of BARI 2-mg treated pts achieved good response (groups 1 and 2, 68%) with at least 50% improvement in CDAI by week 12. Response was observed as early as week 4 and was maintained or continued to improve in these groups through week 24. Pts with less response (group 3) tended to be more treatment experienced with more pain and worse physical function at baseline.

Reference:

1. Genovese MC et al. *N Engl J Med* 2016,374(13):1243-52; NCT01721044

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Abstract Number: 1351

Mortality of Rheumatoid Arthritis Patients, Treated to Target at Low Disease Activity: 17-years Follow-up of the BeSt Cohort

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis is known to be associated with increased mortality over the years when compared to the general population. In the BeSt study, 508 patients were treated to target (Disease Activity Score ≤2.4) for 10 years between April 2000 and August 2012. At the end of the initial study follow-up observed mortality in

Table 1. BeSt study cohort mortality - stratified for initial treatment strategy

	Sequential monotherapy n=126	Step-up combination therapy n=121	Initial combination therapy with prednisone n=133	Initial combination therapy with infliximab n=128
N (%) †	38 (30)	31 (26)	41 (31)	33 (26)
SMR (95% CI)	1.41 (1.03–1.94)	1.20 (0.84-1.70)	1.53 (1.13-2.09)	1.31 (0.93-1.85)

SMR: standardized mortality ratio (number observed deaths/number expected deaths); CI: confidence interval.

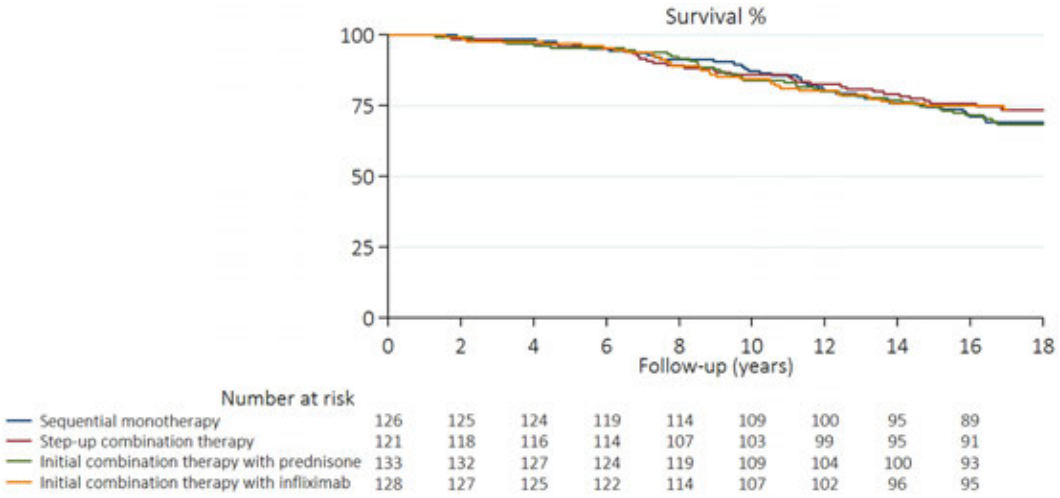

Figure 1. Survival curves per initial treatment strategy

the BeSt cohort was similar to mortality in the general population. In the current study we evaluated the mortality in the BeSt cohort after 17 years follow-up and compared it to the general Dutch population.

Methods: In the BeSt study 508 patients diagnosed with early RA were randomized to four initial treatment strategies: 1. Sequential monotherapy; 2. Step-up combination therapy; 3. Initial combination therapy with prednisone; or 4. Initial combination therapy with infliximab. During the 10-year follow-up period treatment was aimed at low disease activity (DAS ≤2.4) and adjusted every three months if necessary. After 10-years patients were treated and followed-up according to regular care. We explored mortality through the Dutch state registry for mortality (Centrum voor Familiegeschiedenis) and treating rheumatologist. Mortality in the BeSt cohort was compared to the general Dutch population (Statistics Netherlands) matched by gender, age, and calendar year using the standardized mortality ratio (SMR). Kaplan-Meier curves and the log-rank test were used to compare survival among the initial treatment strategies.

Results: The mean duration of follow-up in alive patients was 17 years (range 16-18). In total, 143 patients died (28%) compared to a total of 105 (21%) expected deaths in the reference population. The overall SMR after 17 years was 1.37 (95% CI: 1.16-1.61). Within the study population, no statistically significant difference in survival-curves was observed between the four initial treatment strategies (log-rank p=0.76) (table 1, and figure 1).

Conclusion: After (mean) 17 years of follow-up there was increased mortality in the BeSt study cohort compared to the general Dutch population. We observed no difference in survival among the four treatment strategies.

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Abstract Number: 1352

Effects of Upadacitinib on Patient-Reported Outcomes After 24 Weeks in Patients with Active Rheumatoid Arthritis and an Inadequate Response to Conventional Synthetic or Biologic Disease-Modifying Anti-Rheumatic Drugs: Results from SELECT-NEXT and SELECT-BEYOND Phase 3 Studies

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment with upadacitinib (UPA), a selective Janus kinase-1 (JAK-1) inhibitor, resulted in significant and clinically meaningful improvements in patient-reported outcomes (PROs) at Week 12 in patients with RA with inadequate responses to csDMARDs (csDMARD-IR) or bDMARDs (bDMARD-IR).[1,2] The current analysis evaluated the potential long-term benefits of UPA on PROs in these patients.

Methods: SELECT-NEXT (NCT02675426) and SELECT-BEYOND (NCT02706847) are ongoing Phase 3, randomized controlled trials (RCTs) which randomized patients with active RA on a stable dose of csDMARDs to receive UPA 15 mg or 30 mg once daily (QD) for 24 weeks or placebo for 12 weeks then UPA 15 mg or 30 mg. In this analysis, we report on PROs in patients treated with UPA from the start of study for 24 weeks, including: Patient Global Assessment of Disease Activity (PtGA), pain by visual analog scale (VAS), Health Assessment Questionnaire-Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F; SELECT-NEXT only), and duration and severity of morning (AM) stiffness. Mean changes from baseline and 95% confidence intervals (CIs) were calculated for each PRO at Week 24. The percentages of patients who continued to report improvements ≥ minimum clinically important differences (MCIDs) at Week 24 were calculated among patients who reported clinically meaningful responses for a given PRO at Week 12.

Results: Overall, 622 and 434 patients completed the double-blind phase of SELECT-NEXT and SELECT-BEYOND, respectively. At Week 24, patients reported improvements from baseline across all PROs: PtGA, pain VAS, HAQ-DI, FACIT-F, duration and severity of AM stiffness in SELECT-NEXT (Table 1) and SELECT-BEYOND (Table 2). In SELECT-NEXT, 85% to 93% of patients treated with UPA 15 mg and 77% to 90% with UPA 30 mg maintained responses ≥ MCIDs from Week 12 to Week 24. Similarly, in SELECT-BEYOND, 66% to 88% of patients treated with UPA 15 mg and 70% to 86% with UPA 30 mg maintained clinically meaningful responses from Week 12 to Week 24.

Conclusion: Substantial and clinically meaningful improvements in disease activity, physical function, pain, fatigue, and AM stiffness were consistently reported over 24 weeks in csDMARD-IR and difficult-to-treat bDMARD-IR patients with active RA who continued to receive UPA 15 mg or 30 mg QD.

Table 1. Mean change in PRO scores and maintenance of MCID responses at Week 24 (SELECT-NEXT)						
PRO	UPA 15 mg QD			UPA 30 mg QD		
	n	Mean Change from BL (95% CI)	Responders, n/N[a,b] (%)	n	Mean Change from BL (95% CI)	Responders, n/N[a,b] (%)
PtGA	200	−37.4 (−41.6, −33.3)	136/153 (88.9)	188	−37.2 (−41.2, −33.3)	135/158 (85.4)
Pain VAS	200	−37.7 (−41.6, −33.7)	140/158 (88.6)	188	−39.8 (−43.5, −36.2)	141/160 (88.1)
HAQ-DI	199	−0.73 (−0.81, −0.64)	139/156 (89.1)	188	−0.67 (−0.75, −0.59)	125/148 (84.5)
FACIT-F	195	10.4 (8.9, 11.9)	117/138 (84.8)	184	9.2 (7.7, 10.7)	95/123 (77.2)
Severity AM stiffness[c]	200	−3.4 (−3.8, −3.0)	146/165 (88.5)	184	−4.0 (−4.4, −3.7)	155/172 (90.1)
Duration AM stiffness[d]	200	−101.7 (−129.7, −73.6)	53/57 (93.0)	185	−92.7 (−115.5, −69.9)	51/57 (89.5)
[a]Patients who discontinued treatment and missing observations were imputed using non-response imputation. [b] n/N = number of patients with MCID response at Week 24 / number of patients reporting improvements ≥ MCID at Week 12. [c] Assessed on a numeric scale of 1–10, with 10 being the worst level. [d] Duration in minutes. BL, baseline.						

Table 2. Mean change in PRO scores and maintenance of MCID responses at Week 24 (SELECT-BEYOND)						
PRO	UPA 15 mg QD			UPA 30 mg QD		
	n	Mean Change from BL (95% CI)	Responders, n/N[a,b] (%)	n	Mean Change from BL (95% CI)	Responders, n/N[a,b] (%)
PtGA	153	−29.5 (−33.7, −25.3)	105/119 (88.2)	134	−33.0 (−38.3, −27.7)	86/101 (85.1)
Pain VAS	153	−29.3 (−33.5, −25.1)	98/120 (81.7)	133	−33.0 (−38.3, −27.7)	89/103 (86.4)
HAQ-DI	153	−0.46 (−0.55, −0.36)	85/102 (83.3)	133	−0.56 (−0.67, −0.44)	74/89 (83.1)
Severity AM stiffness[c]	154	−3.3 (−3.8, −2.9)	111/131 (84.7)	135	−3.6 (−4.1, −3.1)	100/119 (84.0)
Duration AM stiffness[d]	130	−70.9 (−99.9, −42.0)	19/29 (65.5)	112	−129.8 (−186.1, −73.4)	21/30 (70.0)
[a]Patients who discontinued treatment and missing observations were imputed using non-response imputation. [b] n/N = number of patients with MCID response at Week 24 / number of patients reporting improvements ≥ MCID at Week 12. [c] Assessed on a numeric scale of 1–10, with 10 being the worst level. [d] Duration in minutes. BL, baseline.						

Reference:

1. Strand V, et al. *Ann Rheum Dis.* 2018;77(Suppl 2):A989; 2. Strand V et al. *Ann Rheum Dis.* 2018;77(Suppl 2):A990.

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Abstract Number: 1353

Impact of Smartphone Application Based Management in Rheumatoid Arthritis: SMART- RA Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) treatment has improved considerably over the years. However, patient compliance remains critical to treatment outcomes. Patient compliance still poses challenges in day-to-day care of RA patients and treatment outcomes. In a technology driven era, with more people having access to smart phones, unique opportunities exist for use of phone based technologies to improve patient care in chronic diseases. This study aims to investigate the impact of smart phone application (HealthCius) on inflammatory disease activity and quality of life in RA patients receiving standard treatment.

Methods: 75 consecutive patients fulfilling the 2010 Rheumatoid Arthritis Classification Criteria for RA were recruited in this observational study. Subjects were randomized into 2 groups. First, having access to a smart phone were assigned to the intervention group using the Healthcius application (n=45) and second, the control group not using

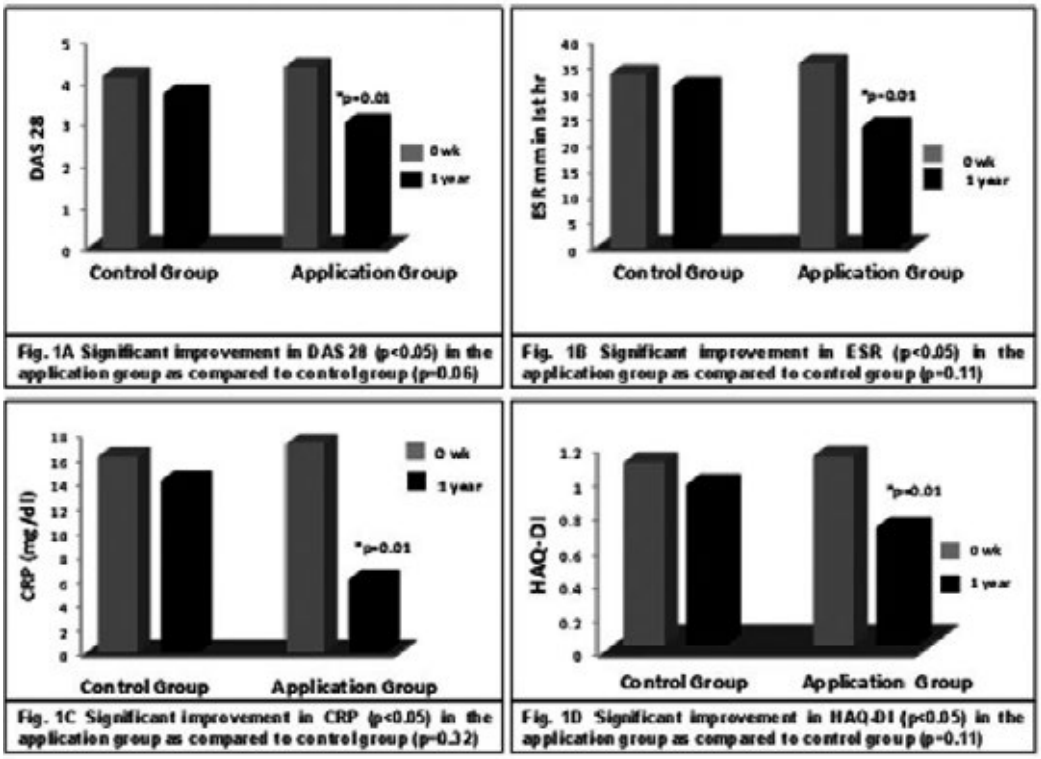

Fig. 1A Significant improvement in DAS 28 ($p<0.05$) in the application group as compared to control group ($p=0.06$)

Fig. 1B Significant improvement in ESR ($p<0.05$) in the application group as compared to control group ($p=0.11$)

Fig. 1C Significant improvement in CRP ($p<0.05$) in the application group as compared to control group ($p=0.32$)

Fig. 1D Significant improvement in HAQ-DI ($p<0.05$) in the application group as compared to control group ($p=0.11$)

Comparison between application group and control group

the application (n=30). The patients in two groups received standard treatment for RA. The application was designed after obtaining feedback from health care providers, patient counselors and RA patients using a questionnaire. To the patients, the app was their individual treatment plan. It helped them comply with the plan by providing an easy to refer checklist, reminders, alerts and a visual dashboard of their progress through the day. The app served as the doctor's virtual assistant inside the patient's smart phone. For the doctor, it was a live dashboard of all patients and their real time compliance levels. The data reported by the patients was available to the doctor in the form of time sliced charts and trend lines. Therefore, this app is designed to leverage technology to shift the patients' focus every day on to their treatment plan thereby driving up compliance and better health outcomes. Outcome measures included erythrocyte sedimentation rate (ESR), C-Reactive protein (CRP), disease activity score (DAS28) and health assessment questionnaire (HAQ-DI) at baseline and after 1 year.

Results: The two groups did not differ significantly for baseline characteristics. There was a significant difference between the control and intervention group for DAS28 ($p < 0.05$), ESR ($p \leq 0.05$), CRP ($p \leq 0.05$) and HAQ-DI ($p \leq 0.5$) after 1 year in favor of smart phone application. Analysis within the groups revealed significant improvement in DAS28 ($p < 0.05$) (Fig.1A), ESR ($p=0.01$) (Fig.1B), CRP ($p=0.001$) (Fig.1C) and HAQ-DI ($p=0.01$) (Fig.1D) in the application group as compared to control group. Impact of DMARDs usage was also evaluated at the end of the study and it was found that the average drug usage of DMARDs was more in control group than the intervention group.

Conclusion: The study suggested that there was greater improvement in inflammatory disease activity and quality of life in smart phone application assisted RA patients suggesting that smart phone technology can be used to leverage health benefits in RA.

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Abstract Number: 1354

A Comparison of Convergent Validity and Sensitivity to Change of the Conventional Scoring Method to Alternative Scoring Methods of the Health Assessment Questionnaire in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The HAQ disability index (HAQ-DI) is the most widely used disease-specific measure of physical disability in RA. This study explores the sensitivity to change of 3 scoring methods of the HAQ-DI in relation to disease activity in active RA patients.

Methods: Patient data was extracted from an international RA database, the Measurement of Efficacy of Treatment in the Era of Outcome in Rheumatology (METEOR) database. All adult patients fulfilling the 2010 ACR/EULAR RA classification criteria with complete data with respect to the 20 questions of the HAQ-DI and components of the DAS28 (4 variable) using the ESR (DAS28-ESR(4)) for 2 visits at least 6 – 12 months apart with high disease activity at visit 1, (DAS28-ESR(4) > 5.1) were included in the study. Three scoring methods of the HAQ-DI: 1) the conventional method (HAQ-8), 2) the Tomlin method (HAQ-T) and 3) the 20-item method (HAQ-20) were analysed against the EULAR response criteria dichotomized for good/moderate response group versus the no response group. The proportion of patients achieving the minimally clinical important difference (MCID) of the HAQ-DI was compared in the EULAR responder and non-responder groups. Logistic regression analysis was used to determine independent predictors of achieving a minimally clinical important improvement (MCII) (improvement in HAQ-DI ≥ 0.22) of the HAQ-DI.

Results: Of the 5 539 patients in the METEOR database at the time of data extraction, 421 patients met the inclusion criteria. The mean age (SD) and disease duration (SD) of this cohort of patients were 55.0 (13) years and 10.5 (9.5) years respectively at visit 1. The median DAS28-ESR(4) (IQR) declined from 5.9 (5.4-6.6) to 5.2 (3.7-6.0) over a mean period (SD) of 8.7 (1.9) months and 47 % of patients had a good/moderate EULAR response. Median HAQ-8 (IQR) improved from 1.6 (1.1-2.1) to 1.4 (0.9-1.9); median HAQ-T (IQR) improved from 1.2(0.7-1.6) to 0.7 (0.4-1.4) and median HAQ-20 improved from 1.2 (0.8-1.6) to 0.9 (0.5-1.4) with similar effect sizes. All three scoring methods showed good agreement. The proportion of patients who achieved the MCII of the HAQ-DI was significantly higher in the EULAR good/moderate response group (64%) compared to the EULAR no response group (11%). The strongest independent predictor of achieving a MCII of the HAQ-DI is EULAR response. The odds of achieving a MCII of the HAQ-8 is 7.11 higher if a good/moderate EULAR response is achieved compared to having no response.

Conclusion: The 3 methods performed similarly in assessing sensitivity to change with no particular advantage using alternative methods of scoring compared to the conventional method of scoring the HAQ-DI. By achieving a good or moderate EULAR response over 60% of RA patients with long-standing disease can attain a clinically significant improvement in their physical function.

Disclosure: L. Winchow, None; **N. Govind**, None; **E. Musenge**, None; **A. Chopra**, None; **T. Huizinga**, Abblynx, 2, 5, 8, Abbott, 2, 5, 8, Biotest AG, 2, 5, 8, Boehringer Ingelheim, 2, 5, 8, Boeringher Ingelheim, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Crescendo Bioscience, 2, 5, 8, Eli Lilly, 2, 5, 8, Epirus, 2, 5, 8, Galapagos, 2, 5, 8, Janssen, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Nycomed, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, Sanofi-Aventis, 2, 5, 8, Takeda, 2, 5, 8, UCB, 2, 5, 8, Zydus, 2, 5, 8; **M. Tikly**, None.

Abstract Number: 1355

A Comparison of Clinical Improvement Following a Major Therapeutic Change Utilizing Updated Treatment Thresholds Defined by Three Different Disease Activity Measures

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

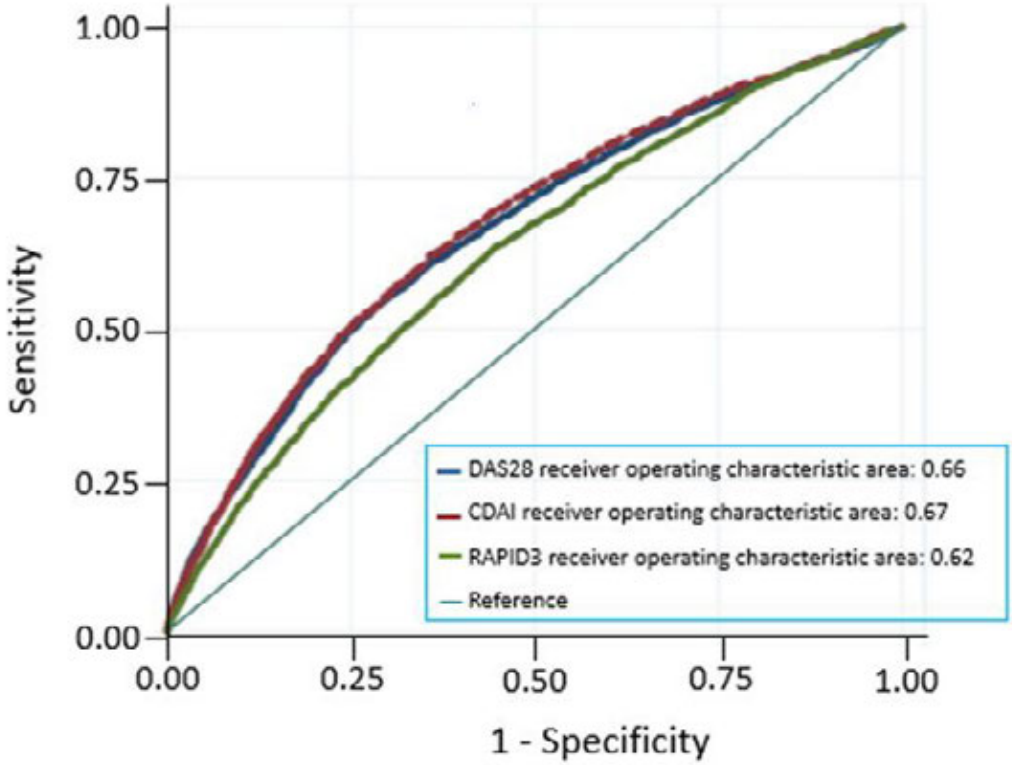
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite ACR recommendations to initiate a major therapeutic change (MTC) in rheumatoid arthritis (RA) patients with moderate/severe disease activity, our recent work has shown that MTC is only implemented in about 50% of these patients and that the decision to initiate MTC occurs most often at higher levels than recommended by ACR guidelines – a Youden-MTC threshold (Figure 1). This analysis evaluated the potential for ACR20 response following MTC above and below the Youden-MTC threshold for MTC and compared ACR response potential across different levels of disease activity as reported by three different Disease Activity Measures (DAMs) - DAS28, CDAI, and RAPID3 – Youden-MTC threshold and DAMs defined in Figure 1.

Methods: The clinic visit was the unit of observation for US Veterans enrolled in the VA Rheumatoid Arthritis (VARA) registry between 1/1/2006 and 9/30/2017. Eligible visits had: 1) DAS28, CDAI, and RAPID3 recorded; 2) all DAMs at two visits 18 months prior to and one visit between 60 and 180 days after the eligible visit; 3) 18 months baseline data. MTC definition (measured from 7 days before to 30 days after visit) included: 1) initiation of new biologic or

Figure 1. Empirical Cut for Maximum Risk of Major Therapeutic Change (MTC) Based on Maximum Youden Index for - Disease Activity Score for 28 joint count (DAS28), Clinical Disease Activity Index (CDAI), and Routine Assessment of Patient Index Data 3 (RAPID3).

	Empirical Optimal Cut point (95%CI)	Youden Index	Sensitivity Cut point	Specificity Cut point	AUROC Cut point	AUROC Total
DAS28	4.02 (3.7 - 4.36)	0.252	0.55	0.70	0.63	0.66
CDAI	12.9 (10.6 - 15.1)	0.263	0.62	0.64	0.63	0.67
RAPID3	3.81 (3.31 - 4.3)	0.189	0.64	0.55	0.59	0.62



Sauer BC, et al. Thresholds for Disease Activity Measures - DAS28, CDAI, and RAPID3. Do Not Align with Clinical Practice Patterns of Rheumatoid Arthritis (RA) Disease Management Decisions [abstract]. Arthritis Rheumatol. 2018; 70 (suppl 10). #2870

non-biologic disease-modifying antirheumatic drug (DMARD) or prednisone; 2) escalation of DMARD dose by ≥25%; or 3) increase in monthly average prednisone dose by 25%; and/or 4) injection of 2 or more joints with corticosteroids. ACR20 response after each eligible visit was determined at the next follow-up visit between 60 and 180 days after the eligible visit date and stratified by disease activity by the different DAMs and the Youden-MTC threshold. The G-computation with Generalized Estimating Equations (GEE) model was fitted using the exchangeable working covariance structure to account for clustering of visits within patients.

Results: In 1,208 VARA patients, there were 6,138 eligible visits – 1,773 (28.9%) with MTC and 4,365 (71.1%) without MTC. Demographic, clinical, disease stability, and DMARD use are reported in Table 1. Eligible visits with MTC had a higher rate of ACR20 response in comparison to visits without MTC at all levels of disease activity with the percent of patients with ACR response after MTC increasing with higher disease activity level particularly above the Youden threshold (Table 2). While MTC was not common below Youden-MTC threshold, ACR 20 response was still significantly greater for both DAS28 and RAPID3 in the Low Moderate group. ACR20 responses were more common in patients with disease activity above Youden-MTC with DAS28 and CDAI than RAPID3.

Conclusion: Following MTC, the ACR20 response was most likely in patients with disease activity above the Youden-MTC threshold even though the risk ratios were similar across all categories classified as active disease by ACR criteria, including the Low Moderate group. RAPID3 classified more patients at higher disease activity levels which resulted in larger effect estimates (on risk ratio scale) even though the prevalence of ACR20 response was lower. Therefore, DAS28 and CDAI may be preferred DAMs for directing MTC decisions as patients with high disease activity by these DAMs were associated with higher ACR20 response than patients with high disease activity by RAPID3.

Table 1. Demographic and Clinical Characteristics in 1,208 Patients Providing 6,138 Eligible Visits. The median number of visits per patient is 3 and interquartile range is 1-6.

	Visits with MTC (n=1,773)	Visits without MTC (n=4,365)
Age, mean years (SD) [95% CI]	63.3 (10.9) [62.8-63.8]	65.9 (11.0) [65.6-66.2]
Male sex, n (%) [95% CI]	1625 (91.7%) [90.3%-92.9%]	3974 (91.0%) [90.2%-91.9%]
Caucasian race, n (%) [95% CI]	1409 (79.5%) [77.5%-81.3%]	3568 (81.7%) [80.6%-82.9%]
RA duration, mean years (SD) [95% CI]	14.2 (11.9) [13.6-14.7]	15.6 (12.3) [15.2-16.0]
RDCI* score mean (SD) [95% CI%]	2.2 (1.5) [2.2-2.3]	2.3 (1.5) [2.2-2.3]
Rheumatoid Factor status, n (%) [95% CI]		
Positive	1589 (89.6%) [88.1%-91.0%]	3928 (90.0%) [89.1%-90.9%]
Negative	183 (10.3%) [8.9%-11.8%]	433 (9.9%) [9%-10.8%]
Missing	1 (0.1%) [0%-0.3%]	4 (0.1%) [0%-0.2%]
anti-CCP** status, n (%) [95% CI]		
Positive	1484 (83.7%) [81.9%-85.4%]	3622 (83.0%) [81.8%-84.1%]
Negative	288 (16.2%) [14.6%-18%]	739 (16.9%) [15.8%-18.1%]
Missing	1 (0.1%) [0%-0.3%]	4 (0.1%) [0%-0.2%]
DAM stability***, n (%) [95% CI]		
Better	512 (28.9%) [26.8%-31.0%]	709 (16.2%) [15.2%-17.4%]
No change	749 (42.2%) [39.9%-44.6%]	2306 (52.8%) [51.3%-54.3%]
Worse	512 (28.9%) [26.8%-31.0%]	1350 (30.9%) [29.6%-32.3 %]
bDMARD**** prescribed within last month[a] n (%) [95% CI]	194 (10.9%) [9.5%-12.5%]	664 (15.2%) [14.2%-16.3%]
bDMARD prescribed within last year[b] n (%) [95% CI]	671 (37.8%) [35.6%-40.1%]	1953 (44.7%) [43.3%-46.2%]
csDMARD***** prescribed within last month,[a] n (%) [95% CI]	387 (21.8%) [19.9%-23.8%]	1382 (31.7%) [30.3%-33.1%]
csDMARD prescribed within last year,[b] n (%) [95% CI]	1505 (84.9%) [83.1%-86.5%]	4031 (92.3%) [91.5%-93.1%]
Prednisone prescribed within last month,[a] n (%) [95% CI]	180 (10.2%) [8.8%-11.7%]	396 (9.1%) [8.2%-10.0%]
Prednisone prescribed within last year,[b] n (%) [95% CI]	954 (53.8%) [51.5%-56.1%]	1926 (44.1%) [42.6%-45.6%]
MTC 8 - 90 days before the index date, n (%) [95% CI]	201 (11.3%) [9.9%-12.9%]	701 (16.1%) [15.0%-17.2%]

* RDCI, Rheumatic Disease Co-morbidity Index;
** anti-CCP, anti- cyclic citrullinated peptide antibody
*** Disease activity measure (DAM) stability was defined by the comparison of baseline DAMs during the 18 months prior to the eligible visit in comparison to the DAM on the eligible visit. Better = improvement/decrease of DAS28 ≥ 0.6 from baseline to eligible visit, Worse = deterioration/increase of DAS28 ≥0.6 form baseline to eligible visit, and No change = DAS28 did not change by greater than 0.6.
**** bDMARD = biologic DMARD
***** csDMARD = conventional synthetic DMARD
a = prescribed within last month = prescription dispensed between 8 to 30 days of eligible visit
b = prescribed within last year = prescription dispensed between 8 to 365 days of eligible visit

	Risk ACR20 Response (%) Model 3 GEE		
DAS28	Visits with MTC	Visits without MTC	Risk Ratio
Overall effect	15% (13%, 16%)	9% (8%, 10%)	1.69 (1.46, 1.95)
Remission and Low (<3.2)	1.7% (0.6%, 3.1%)	1.4% (0.9%, 2.1%)	1.21 (0.41, 2.47)
Low Moderate (3.2 - 4.02)	10% (7%, 14%)	5% (4%, 7%)	1.98 (1.21, 2.86)
High Moderate* (4.03- 5.1)	19% (16%, 23%)	13% (11%, 16%)	1.51 (1.12, 1.93)
High (>5.1)	35% (32%, 40%)	20% (16%, 23%)	1.81 (1.51, 2.19)
CDAI			
Overall effect	15% (13%, 16%)	9% (8%, 10%)	1.66 (1.43, 1.91)
Remission and Low (<10.0)	1.3% (0.4%, 2.5%)	1.1% (0.7%, 1.7%)	1.14 (0.34, 2.54)
Low Moderate (10.0 - 12.9)	8% (4%, 12%)	6% (4%, 9%)	1.24 (0.54, 2.26)
High Moderate* (13.0- 22.0)	21% (17%, 25%)	11% (9%, 13%)	1.95 (1.51, 2.50)
High (>22.0)	31% (27%, 35%)	19% (16%, 22%)	1.60 (1.35, 1.92)
RAPID3			
Overall effect	17% (15%, 19%)	7.5% (6.7%, 8.4%)	2.23 (1.91, 2.60)
Remission and Low (≤2.0)	6% (3%, 9%)	3% (2%, 4%)	1.92 (0.91, 3.46)
Low Moderate (>2.0 to 3.81)	14% (11%, 18%)	6% (5%, 8%)	2.20 (1.59, 3.03)
High Moderate* (3.82 - 4.0)	11% (5%, 20%)	4% (1%, 8%)	2.89 (0.94,10.0)
High (>4.0)	23% (21%, 26%)	10% (9%, 12%)	2.26 (1.91, 2.69)

*High Moderate disease defined by disease activity above the Youdin index for each DAM. Youdin values represent the inflection point in the received operator characteristic (ROC) curve at which the DAM score for each DAM was associated with the greatest ability to predict MTC. The Youdin index for each DAM was:

DAS 28 = 4.02
CDAI = 12.9
RAPID3 = 3.81

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Abstract Number: 1356

DAS28-CRP Cut-offs for High Disease Activity Assessment Is Lower Than DAS28-ESR in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) disease activity and treatment response are usually assessed by using Disease Activity Score 28-joint count (DAS28), which can be calculated using erythrocyte sedimentation rate (ESR) or C reactive protein (CRP). It has been shown that DAS28-CRP values are lower than corresponding DAS28-ESR values, especially when assessing high disease activity. However, existing guidelines do not specify how cut-offs for high disease activity differ between these two calculations. Most existing studies that compare DAS28-CRP and DAS28-ESR are drawn largely on data from clinical trials or registries. Due to potential variation between laboratories and clinical assessment at separate institutions, existing data must be validated by and compared to data from single institutions. The relationship between high disease activity cut-offs for DAS28-ESR and DAS28-CRP must be carefully characterized in order to adequately assess clinical trial data. The purpose of our study was to compare the DAS28-ESR and DAS28-CRP values from a single institution.

Methods: We conducted a chart review for new diagnoses of RA (ICD-9 714) from January 1, 2005 to September 1, 2018 at Trinity Health in Minot, ND. Patients were excluded if they (i) had received previous treatment with a DMARD,

(ii) were currently receiving treatment with steroids upon referral, or (iii) did not contain the data necessary to calculate both ESR and CRP disease activity scores. Disease severity was calculated using the Disease Activity Scores DAS28-ESR and DAS28-CRP; these values were compared with t-test. P-values were two-sided, and p-value < 0.05 was considered significant. The number of patients with high disease activity (> 5.1) was compared using ESR and CRP data to calculate the proportion of discordance. A receiver Operator Curve and Youden's Index was used to calculate the DAS28-CRP high disease activity cut off estimation that corresponds to DAS28-ESR of > 5.1.

Results: A total of 171 newly diagnosed RA patients met inclusion criteria. The mean DAS28-ESR of patients on presentation was 5.061 (SD = 1.15). The mean DAS-28 CRP was 4.134 (SD = .99). The difference between mean DAS28-ESR and DAS28-CRP was statistically significant (p < .001). The prevalence of patients who met high disease activity criteria (> 5.1) for DAS28-ESR was 48.5% and for DAS28-CRP was 14.6%. Discordance between these two parameters was 33.9%. Kappa coefficient was .307, which corresponds to a minimal level of agreement. Receiver Operator Curve and Youden's index analysis suggested that the cut off point for high disease activity of DAS28-CRP > 4.06, which corresponds to DAS28-ESR > 5.1.

Conclusion: There is a significant difference between DAS28-ESR and DAS28-CRP, especially when assessing high disease activity of RA, even if they are performed and calculated at a single institution.

Disclosure: J. Greenmyer, None; **J. Stacy**, None; **J. Beal**, None; **E. Diri**, None.

Abstract Number: 1357

Leptin-adjustment of the Multi-biomarker Disease Activity (MBDA) Score Reduces the Influence of Adiposity

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Obesity and excess adiposity influence inflammatory markers and bias assessments of disease activity, most notably among women. A leptin-adjusted multi-biomarker disease activity (MBDA-LA) score has been developed to account for the effects of age, sex and adiposity and improves prediction of radiographic damage progression. We aimed 1) to determine if the adjusted measure demonstrates a reduced association with adiposity, 2) to assess the impact of the leptin-adjustment on the score over the range of adiposity, and 3) to assess relationships between MBDA scores and clinical disease activity.

Methods: Patients with RA, ages 18-75 years, were recruited from clinical practices and completed whole-body DXA to quantify fat mass indices (FMI, kg/m^2). Age-, sex-, and race-specific Z-Scores were calculated based on the distributions in a healthy reference population. Clinical disease activity was assessed with the CDAI and swollen joint count. van der Heijde-Sharpe (vdHS) scores were determined at baseline by a trained radiologist. MBDA assays were performed on stored serum samples. Descriptive statistics described relationships between the FMI Z-Score and the MBDA and the MBDA-LA. Clinical disease activity, swollen joint count (SJC), and radiographic damage were also compared across categories of MBDA scores.

Table 1: Baseline patient characteristics.		
	Men	Women
N	52	52
Age (yrs)	59.1 (11.5)	53.0 (12.8)
Black, N (%)	13 (25%)	19 (36%)
BMI	27.3 (5.4)	30.3 (8.0)
FMI Z-Score	-0.28 (1.3)	0.05 (1.1)
DAS28(CRP)	3.09 (1.13)	3.21 (1.24)
Disease Duration	11.4 (10.9)	11.6 (11.9)
CRP, mg/dL	0.8 (0.5, 1.2)	0.8 (0.5, 1.4)
CCP Positive, N (%)	45 (87%)	40 (78%)
vdHS (N=93)	13 (4, 73)	10.5 (2, 47)
HAQ	0.71 (0.59)	0.83 (0.67)
MBDA	40.0 (13.8)	42.1 (16.6)
$MBDA_{LA}$	43.6 (13.4)	42.1 (15.3)
Leptin, ng/mL	15.1 (21.5)	48.9 (41.5)

Table 1. Baseline patient characteristics.

Results: There were 104 participants (50% female) with mean (SD) age of 56.1 (12.5) and mean BMI of 28.8 (6.9) (Table 1). The unadjusted MBDA score was strongly associated with BMI among women (Women: Rho=0.46 [p< 0.001]; Men: Rho=-0.12), while the MBDA-LA was not associated with BMI in women, and was inversely correlated in men (Women: Rho=0.17; Men: Rho=-0.32 [p=0.02]). The unadjusted MBDA score was also strongly associated with FMI Z-Score among women (Figure) (Women: Rho=0.42 [p=0.002]; Men: Rho=-0.10; p for interaction=0.01). The MBDA-LA was not significantly associated with FMI Z-Score in women or men (Female: Rho= 0.17; Male: Rho=-0.26). Leptin-adjustment reduced the MBDA score in the highest quartile of FMI in women but not men, and increased the MBDA score in the lowest FMI quartiles in both women and men (Figure); these patients in the lowest FMI quartile had the highest median swollen joint counts (p=0.05 for men, p=0.78 for women) (Figure). The MBDA-LA reclassified 4 women (8%) and 9 men (17%) into higher disease activity categories, and reclassified 2 women (4%) and 2 men (4%) into lower categories. CDAI, SJC, and radiographic scores were similar across activity categories for the unadjusted MBDA score and MBDA-LA (Table 2).

Conclusion: Leptin-adjustment of the MBDA score reduces bias related to excess adiposity in women with RA. The adjustment results in lower MBDA scores in women with greater adiposity, and higher MBDA scores in women and men with lesser adiposity. The use of the MBDA-LA may reduce misclassification due to excess adiposity and

Table: Clinical assessments across categories of the unadjusted and leptin-adjusted MBDA Scores.						
	CDAI		Swollen Joint Count		vdHS	
	MBDA	$MBDA_{LA}$	MBDA	$MBDA_{LA}$	MBDA	$MBDA_{LA}$
MBDA Category						
Low	14.6 (10.9)	13.9 (9.9)	2 (1, 5)	2 (1, 5)	9 (1, 33.5)	9 (3, 32)
Moderate	13.2 (10.0)	14.4 (11.4)	2 (0, 5)	3 (0, 6)	10 (4, 49)	10 (2, 53)
High	18.4 (12.3)	17.7 (11.8)	4 (1, 8)	5 (2, 7)	20.5 (5, 70.5)	18 (4, 73)

Table 2. Clinical assessments across categories of the unadjusted and leptin-adjusted MBDA Scores.

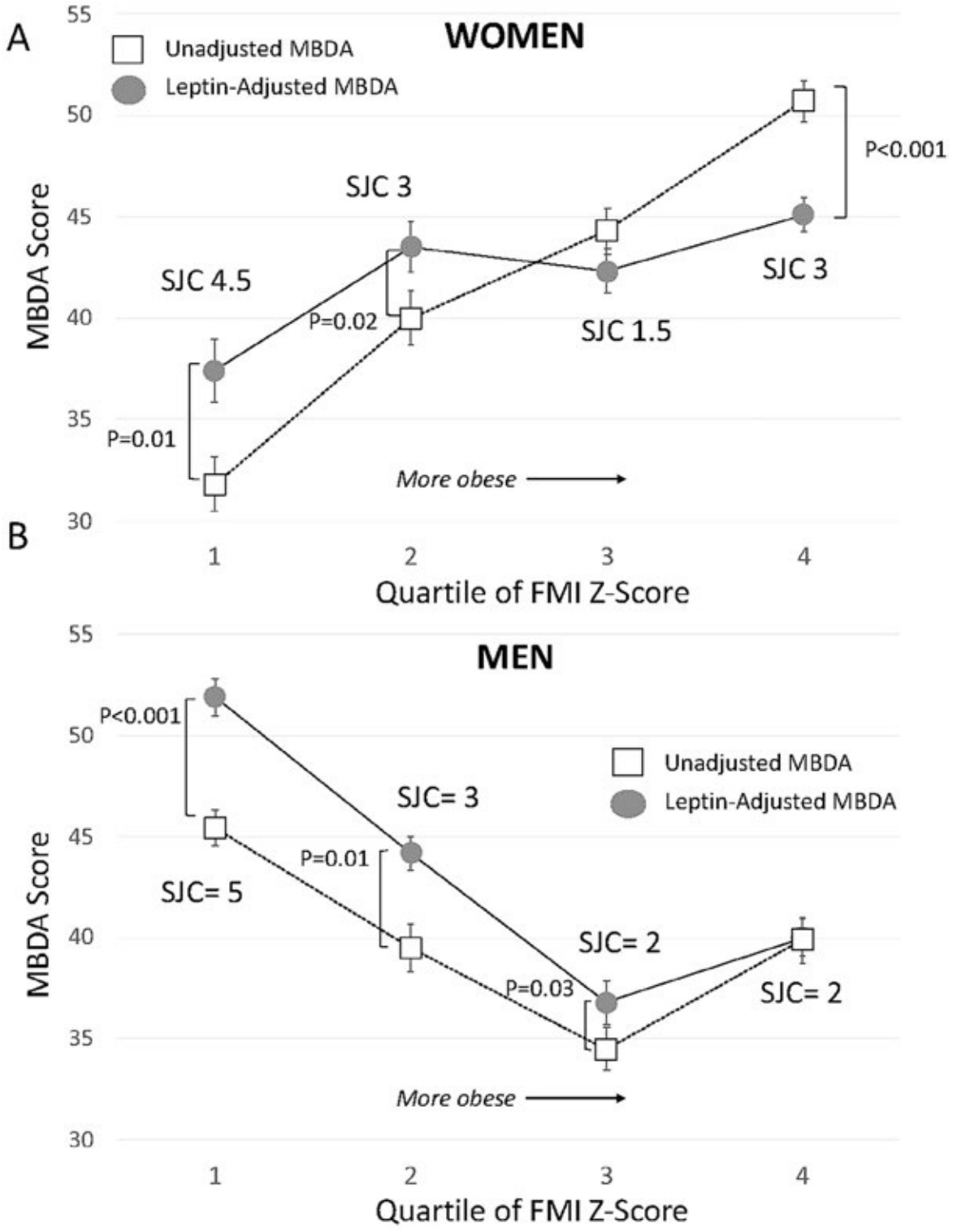

Figure: Associations between FMI Z-Score and unadjusted and leptin-adjusted MBDA Scores in Women and Men with RA

improve identification of active disease among patients with lower adiposity. High MBDA-LA scores among men with low adiposity may reflect severe disease or excess comorbidity in this group.

Disclosure: J. Baker, Bristol-Myers Squib, 5, Burns-White LLC, 5, Myriad RBM, 2; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2,

5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **D. Chernoff**, Myriad RBM, 3; **M. George**, AbbVie, 5, Bristol Myers Squibb, 2, Bristol-Myers Squibb, 2.

Abstract Number: 1358

Defining Minimal Clinically Important Changes for the Patient Activity Scale-II

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The Patient Activity Scale (PAS)-II is an accepted disease activity measure used in the care of patients with rheumatoid arthritis (RA). A clinically important change in this score has not been defined for patients with RA. We aimed to define the Minimal Clinically Important Improvement (MCII) and Worsening (MCIW) for the PAS-II using anchor- and distribution-based methods.

Methods: Data from *Forward,* The National Databank for Rheumatic Diseases was utilized. Data are collected at 6-month intervals by questionnaires. Data shown in these analyses spans four 6-month data collection periods: (A) January 2017 (n = 3680, (B) July 2017 (n = 3504), (C) January 2018 (n = 3737), and (D) July 2018 (n = 3102). Both anchor-based and distribution-based methods were used to estimate MCII and MCIW. For the anchor-based analyses, the primary anchors used were comparisons of pain and general health to six months ago (e.g., "Compared to 6 months ago, would you say your pain is: much better now, somewhat better now, about the same, somewhat worse, or much worse?"). Mean changes in PAS-II scores and effect sizes were summarized and averaged over the 4 change periods. For the distribution-based calculations, we used 0.5 and 0.35 standard deviations. We further stratified analyses based on PAS-II score (above/below 3.7), hypothesizing that the MCII and MCIW would be dependent on the baseline PAS-II score.

Results: The population (baseline from Period A, n=3680) average age was 64.9 (12.0) years with an average disease duration of 20.8 (12.7) years and an average PAS-II of 3.3 (2.2). The population was 83.1% female, 91.3% white and 43% ever-smokers. For pain and health-related anchor questions, the MCIW was defined as approximately 0.50 to 0.55, respectively (Table 1), representing a small effect size (d=0.23-0.25). The MCII was defined as 0.39 to 0.45 (d=0.18, 0.21), respectively. Stratifying by the PAS-II score affected the results obtained by anchor-based methods. The MCIW for anchor-based methods among participants in low disease activity (< 3.7) was approximately 1.1 [1.09/1.11 (pain/general health)], while the MCII for those in moderate to high disease activity (>3.7) was 1.09 (1.15/1.02) (Table 2). These changes represented a large effect size. Distribution-based methods for 0.5 SD and 0.35 SD were 1.08 and 0.76, respectively. Results were similar in each 6-month data collection periods.

Conclusion: We defined minimal clinically important change for the PAS-II as a change in the score of 0.5 units. Among participants with moderate to high PAS-II, the MCII was estimated to be 1.1 and among participants with in

Table 1. Minimum important change defined by anchor-based methods.

	Somewhat worse		Somewhat better	
Comparison	Δ PAS-II score	Effect size	Δ PAS-II score	Effect size
Pain A-B	0.53	0.25	-0.47	-0.22
Pain B-C	0.53	0.25	-0.47	-0.22
Pain C-D	0.56	0.26	-0.43	-0.20
Mean	**0.55**	**0.25**	**-0.45**	**-0.21**
Health A-B	0.54	0.25	-0.40	-0.19
Health B-C	0.53	0.25	-0.47	-0.22
Health C-D	0.44	0.21	-0.31	-0.14
Mean	**0.50**	**0.23**	**-0.39**	**-0.18**

Table 2. Minimum important change over three six-month periods in individuals with RA: anchor-based analyses by baseline PAS-2 score

	PAS-II <3.7				PAS-II ≥3.7			
	Somewhat worse		Somewhat better		Somewhat worse		Somewhat better	
Comparison	Δ PAS-II score	Effect size	Δ PAS-II score	Effect size	Δ PAS-II score	Effect size	Δ PAS-II score	Effect size
Pain								
A-B	1.03	0.96	-0.10	-0.09	0.13	0.10	-1.08	-0.86
B-C	1.17	1.10	-0.02	-0.02	0	0	-1.19	-0.95
C-D	1.06	1.00	-0.01	-0.01	0.16	0.13	-1.18	-0.93
Mean	**1.09**	**1.02**	**-0.04**	**-0.04**	**0.10**	**0.08**	**-1.15**	**-0.92**
General health								
A-B	1.10	1.03	-0.05	-0.05	0.10	0.08	-0.92	-0.74
B-C	1.17	1.10	0.02	0.02	0.09	0.07	-1.28	-1.02
C-D	1.05	0.99	0.02	0.02	0.07	0.06	-0.85	-0.67
Mean	**1.11**	**1.04**	**0.00**	**0.00**	**0.09**	**0.07**	**-1.02**	**-0.81**

low disease activity, the MCIW was 1.1. These data suggest that only a more substantial worsening is likely be important to patients that report low activity. Similarly, only a substantial improvement will be important to patients who report high activity. The characterization of clinically meaningful changes in disease activity is important for clinical research studies and clinical settings where this disease assessment is used.

Disclosure: J. Baker, Bristol-Myers Squib, 5, Burns-White LLC, 5, Myriad RBM, 2; **P. Katz**, None; **K. Michaud**, FORWARD, The National Databank for Rheumatic Diseases, 3, Pfizer, 2, Pfizer & Rheumatology Research Foundation, 2, Rheumatology Research Foundation, 2, University of Nebraska Medical Center, 3.

Abstract Number: 1359

Correlation of Ultrasound Guided Synovial Biopsies and Surgical Synovial Biopsies in Patients with Inflammatory Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

	Patient 1	Patient 2	Patient 3
Age	65	81	32
Sex	Female	Male	Female
Ethnicity	Caucasian	Caucasian	Asian
Involved joints	Left 4th PIP	Right knee	Left wrist
ESR (mm/hr)	35	88	44
C-RP (mg/L)	1.72	136	2.7
Rheumatoid factor	Negative	Negative	Positive
Anti CCP	Negative	Negative	Positive
X ray findings	Severe joint space narrowing at left 4th PIP joint	Soft tissue swelling with moderate joint effusion	Progressive severe left radio carpal joint space narrowing and mild mid carpal joint space narrowing
MRI findings	Moderate synovitis of 4th PIP joint with adjacent bone marrow edema without obvious erosions	Extensive hypertrophic synovial thickening with a moderate to large joint effusion and medial and lateral meniscus tear	Marked progressive inflammatory arthritic changes of carpal and carpometacarpal joints
Ultrasound findings	Grade 3 synovitis with grade 1 Doppler signal in the left 4th PIP joint with large osteophytes and hyper echoic signal	Grade 3 synovitis with grade 2 power Doppler, and a double contour sign	Grade 3 synovitis with grade 2 doppler signal
Ultrasound guided synovial biopsy findings	Benign dense fibrous tissue, compatible with synovium	Acute on chronic synovitis with hyperplastic synovial lining. The synovium had a dense inflammatory infiltrate of neutrophils, lymphocytes and plasma cells	Benign synovial tissue, with synovial lining cells, and marked chronic lymphoplasmacytic inflammatory changes with scattered acute inflammatory cells compatible with active rheumatoid arthritis
Surgical synovial biopsy findings	Benign fibro connective tissue	Hyperplastic synovium with acute and chronic inflammation	Lymphoplasmacytic synovitis

Table 1 Comparison of Demographic and Clinical Characteristics of Patients who Underwent USGSB and Surgical Biopsies in the Same Joint

Background/Purpose: Synovial biopsy is often performed when other methods of evaluation prove non-diagnostic in the assessment of persistent joint synovitis, whether in the setting of undifferentiated inflammatory arthritis (UIA) or rheumatoid arthritis (RA). The utility of synovial biopsy is well established. Several methods are used to perform synovial biopsies, such as arthroscopic surgery, fluoroscopic-guided and blind needle synovial biopsies. In recent years, ultrasound (US) technology has progressed significantly with improved image resolution and increased feasibility of US-guided synovial needle biopsies (USGSB). In this study, we compare histopathological findings of USGSB to surgical synovial biopsies of the same joint in patients with persistent synovitis.

Methods: Between 2016-2019, 25 patients were referred to a single rheumatology practice at an academic medical center for persistent joint synovitis and underwent USGSB. Chart review was performed to identify those patients who had surgical biopsies performed on the same joint. For each patient, tissue samples were sent to pathology in formalin for standard histologic evaluation, methanol for anhydrous histologic evaluation (to allow crystal visualization), and a sterile container for cultures.

Results: Of 25 patients who underwent USGSB, 3 patients also underwent surgical biopsies in the same joint within 12 months of the original biopsy. The age of the patients ranged from 32-81 years old. The main demographic and clinical characteristics of the patients and biopsy sites are presented in Table 1.

In patient (pt) 1, USGSB of the left 4th proximal interphalangeal (PIP) joint showed benign dense fibrous tissue, compatible with synovium, with similar findings found on a subsequent surgical arthroscopic biopsy, performed for persistent synovitis. Pt 2 was referred for chronic right knee monoarthritis 1 year after surgical arthroscopic synovial biopsy and meniscectomy, which showed hyperplastic synovium with acute and chronic inflammation; USGSB

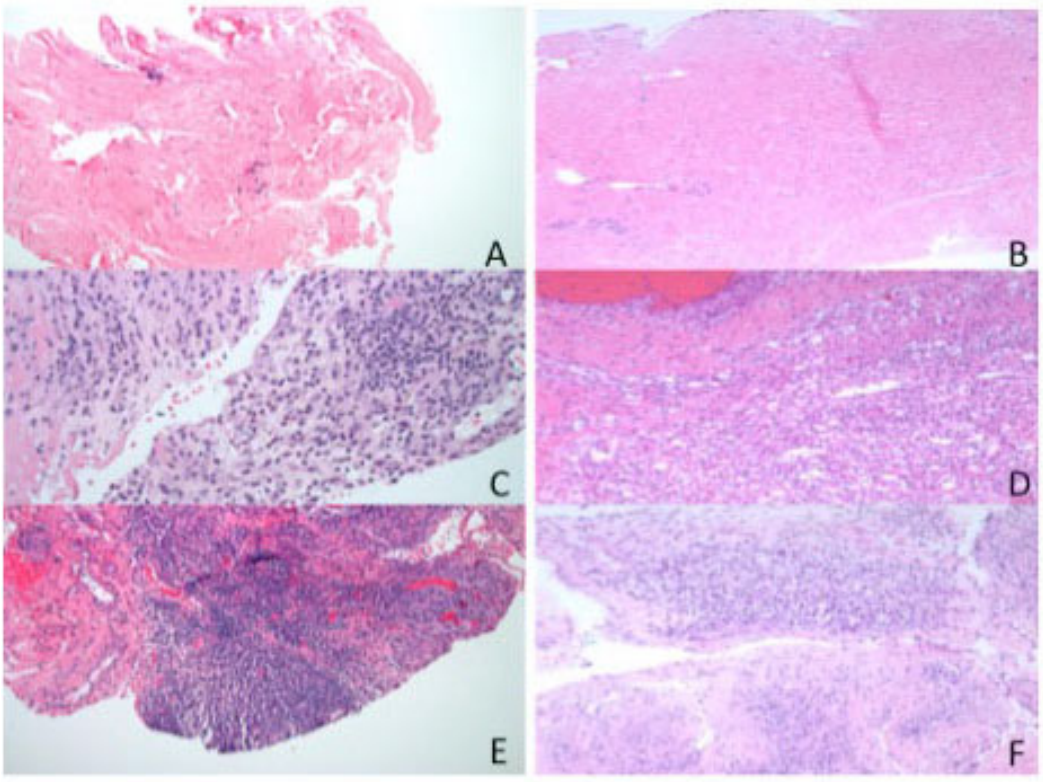

Figure 1. Histologic analysis of synovial sample of A. Left 4th PIP USGSB showing benign dense fibrous tissue B. Arthroscopic synovial biopsy of left 4th PIP joint showing benign dense fibrous tissue C. Right knee USGSB showing acute on chronic synovitis with predominant inflammatory infiltrate of neutrophils D. Right knee surgical synovial biopsy showing acute on chronic inflammation E. Left wrist USGSB showing marked chronic lymphoplasmacytic inflammatory changes F. Surgical biopsy of left wrist synovium showing lymphoplasmacytic synovitis

showed similar findings. Pt 3 had RF +, CCP + rheumatoid arthritis, previously failing multiple biologic and non-biologic DMARDs, and then developed persistent left wrist monoarthritis, suspicious for infection. USGSB showed benign synovial tissue and marked chronic lymphoplasmacytic inflammatory changes with scattered acute inflammatory cells compatible with active rheumatoid arthritis. Subsequent therapeutic left wrist surgical synovectomy identified the same pathology as was found with USGSB.

Conclusion: This study demonstrated that USGSB led to similar pathological results as those obtained by more traditional surgical methods. The three patients underwent synovial biopsies of different joint locations including small, medium and large joints. The surgical biopsies did not produce new or additional information beyond that obtained from the USGSB. All patients tolerated the USGSB well without any complications.

When compared to surgical or fluoroscopic guided biopsies, the USGSB technique has advantages including lower cost, no radiation exposure, and local anesthesia. In addition, we found that USGSB had concordant pathologic findings with surgical biopsies.

Disclosure: K. Lim, None; **A. Ben-artzi**, None; **L. Forbess**, None; **S. Faber**, None; **M. Ishimori**, None.

Abstract Number: 1360

Ultrasound Guided Synovial Biopsies Safely Aid in the Assessment of Inflammatory Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
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Background/Purpose: Synovial biopsies have an important role in the diagnostic evaluation of patients with undifferentiated inflammatory arthritis (UIA) whose clinical examination and blood and synovial fluid testing do not yield a diagnosis. Several methods are used to perform synovial biopsies, including arthroscopic surgery, fluoroscopic guided and blind needle synovial biopsies. In recent years, ultrasound (US) technology has progressed significantly with improved image resolution, musculoskeletal US expertise, and feasibility of US-guided synovial needle biopsies (USGSB). We studied the safety, tolerability, and utility of USGSB in patients with UIA and rheumatoid arthritis (RA).

Methods: Between 2016-2019, we identified all patients referred for USGSB to a single academic medical center. 2 groups of patients underwent this procedure, patients with UIA and those with RA with significant synovitis despite therapy. Chart review was performed to identify clinical characteristics of these patients. For each patient, tissue samples were sent to pathology in formalin for standard histologic evaluation, methanol for anhydrous histologic evaluation, and sterile containers for typical and atypical cultures.

Results: A total of 25 patients were referred for USGSB. There were 18 patients (72%) with UIA and 7 (28%) with RA. All patients presented with inflammatory arthritis > 6 weeks duration. 8 patients had monoarthritis, 4 with oligoarthritis and 13 with polyarthritis. Of the 13 patients with polyarthritis, 7 were previously diagnosed with RA. Demographic and clinical characteristics of patients are shown in Table 1. The results of the biopsies are detailed in Table 2.

Of the 25 USGSB performed, 20 biopsies (80%) retrieved synovial lining cells and thus passed quality control. 5 had no synovial lining cells and therefore were deemed inadequate. Overall, 7 of 25 biopsies showed normal synovium (including 4 RA) and 6 demonstrated chronic lymphocytic inflammation. Among the 6 biopsies with chronic lymphocytic inflammation, 2 were already diagnosed with RA and had been treated with biologic therapy. Among the 4 RA patients with normal synovium on USGSB, one was treated with chronic low dose prednisone and all were on biologic therapy.

The use of USGSB resulted in a definitive diagnosis in 13 out of 14 patients with UIA, while 1 patient remained with the diagnosis of UIA. Among the 13 patients with a definitive diagnosis, 11 of the synovial biopsies helped to achieve a final diagnosis. 2 patients had acute neutrophilic predominant inflammation on USGSB and were treated with empiric antibiotics for presumed infectious arthritis, although cultures were subsequently negative. One patient had septic arthritis. Three patients had CPPD crystals consistent with pseudo gout. One patient had PVNS. The detail of final diagnoses can be seen in Table 3.

All patients tolerated the USGSB procedure well without any complications such as bleeding or infection. Three reported increased stiffness in the biopsied joint, which was resolved over several days.

Conclusion: USGSB is a well-tolerated procedure. Given the minimally invasive nature of the technique, it can be a useful tool to aid in the diagnosis of challenging cases of inflammatory arthritis.

	Undifferentiated arthritis (18)	Rheumatoid arthritis (7)
Mean age (years)	58	56
Gender (female)	12 (67%)	4 (57%)
Clinical presentation		
Monoarthritis	8	-
Oligoarthritis	4	-
Polyarthritis	6	7
Mean inflammatory markers		
ESR (mm/hr)	30	41
C-RP (mg/l)	19	5
Serologies		
Rheumatoid factor	0/18 (0%)	1/7 (14%)
Anti-CCP	0/18 (0%)	4/7 (57%)
HLA-B27	2/13 (15%)	0/4 (0%)
Location of the joints biopsied		
Large joint	8	4
Knee		
Medium joint	4	1
Wrist		
Small joint	1	-
MCP	2	1
PIP	1	-
MTP	1	-
Sternoclavicular joint	1	1
Tenosynovial sheath (wrist and ankle)		

Table 1. Demographic and clinical characteristics of patients who underwent USGSB

	Undifferentiated arthritis (Number of biopsies)	Rheumatoid arthritis (Number of biopsies)
Normal synovium	3	4
Chronic lymphocytic inflammation	4	2
Unspecified neutrophilic inflammation	2	-
Infectious arthritis	1	-
Crystal arthritis	3	-
PVNS	1	-
Inadequate sample	4	1

Table.2 Histological findings from USGSB

Final diagnosis	Values
Rheumatoid arthritis	2
Reactive arthritis	3
Undifferentiated arthritis	1
Pseudo gout	3
Presumed infectious arthritis	2
Osteoarthritis	1
PVNS	1
Septic arthritis	1
Total	14

Table 3. Final diagnoses of patients with UIA after USGSB

Disclosure: K. Lim, None; **A. Ben-artzi**, None; **L. Forbess**, None; **S. Venuturupalli**, None; **J. Jalas**, None; **M. Ishimori**, None.

Abstract Number: 1361

Utility of Rheumatoid Arthritis Impact of Disease (RAID) in Routine Care; Identification of Patients Achieving DAS28 Remission or Low Disease Activity, and Burden of Unmet Patient Reported Outcomes

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SESSION INFORMATION
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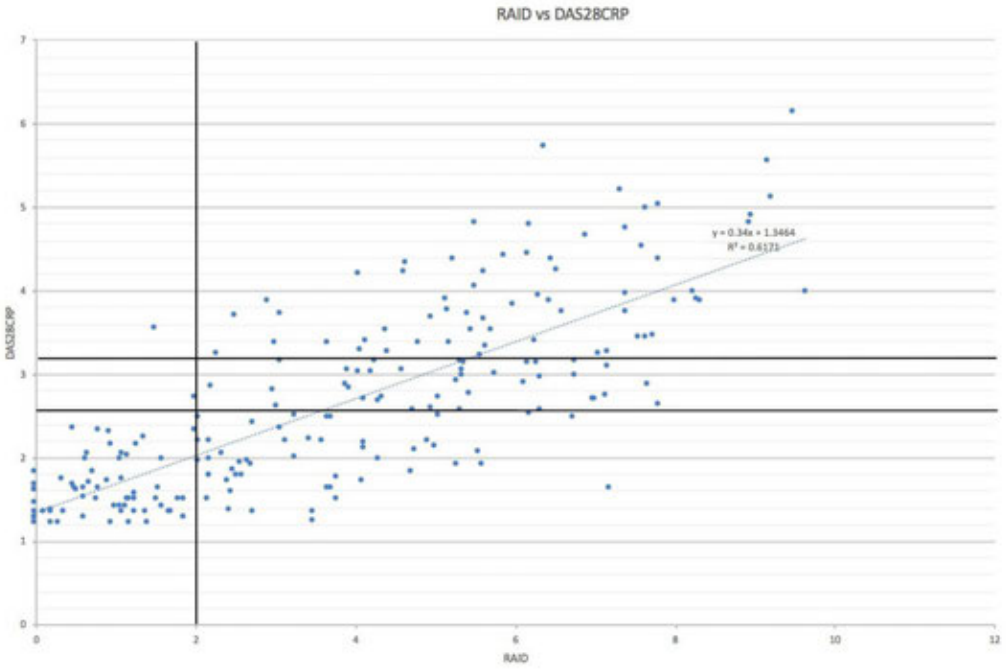
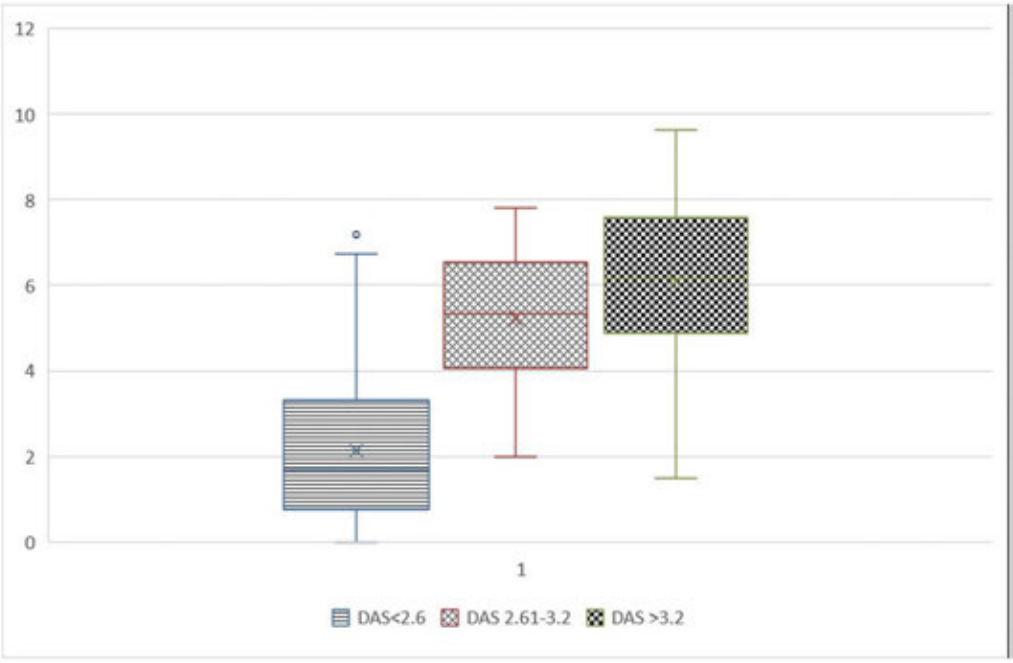
Background/Purpose: ACR/EULAR guidelines recommend remission or low DAS28 as the treat to target goal for patients with rheumatoid arthritis (RA). Alternative patient reported outcomes include the rheumatoid arthritis impact of disease (RAID), a self-reported index which assesses seven domains by visual analogue scale: pain, disability, fatigue, sleep, coping, physical and emotional well-being. Responses are weighted differently, producing a final score from 0-10. A score less than 2 is considered a patient-acceptable status. We have assessed the relation of RAID to (i)

DAS28 categories in routine care, (ii) it's utility to identify patients in DAS28 remission (RDAS) or low disease activity (LDAS) and (iii) the burden of unmet patient needs in those achieving RDAS/LDAS.

Methods: RA patients attending for routine review in the outpatient clinic at St George's Hospital were assessed. DAS28 CRP and ESR scores were recorded and RAID questionnaires completed by patients and calculated using the on-line EULAR tool. Summary statistics and Spearman correlation coefficient were analysed on Excel and Mann-Whitney U tests using socscistatistics.com.





Results: 219 patients with established RA were assessed, 81.3% female, mean age 58.8 years, 72.1% RF positive and 79.5% ACPA positive. The number of patients per DAS28 CRP category was RDAS (< 2.6) n=119 (54.6%), LDAS (2.6-3.2) n=34 (15.6%), moderate (MDAS 3.21-5.1) n= 60 (27.5%), high (HDAS >5.1) n= 5 (2.3%). RAID scores correlated strongly with patient global (r=0.69), DAS28 CRP (r=0.62) and DAS28 ESR (r=0.55) but poorly with tender joint count (r=0.30), swollen joint count (r=0.14), ESR (r=0.15) and CRP (r=0.09). The mean RAID score per DAS28 CRP category was RDAS 2.14, LDAS 5.23, M+HDAS 6.09. RAID scores were significantly different (Mann-Witney U) between RDAS versus LDAS (p< 0.00001), RDAS versus M+HDAS (p< 0.00001), LDAS versus M+HDAS (p=0.02). Similar significant differences in RAID scores were found between DAS28 ESR categories. Of 66 patients with RAID < 2, DAS28 CRP was < 2.6 in 64 (97%) and < 3.2 in 65 (98.5%). Of 151 patients with DAS28 CRP < 3.2, RAID was >2 in 86 (57%) with fatigue followed by sleep being the worst scoring domains.

Conclusion: In patients with established RA in routine care, RAID strongly correlates with patient global and DAS28, and scores are significantly lower in patients achieving RDAS versus LDAS and either RDAS or LDAS versus M+HDAS. Virtually all patients with a RAID score < 2 are in DAS28 remission or low disease activity defined by DAS28, and this could be used to minimise unnecessary consultations. However, over half of all patients with DAS28 < 3.2 have unacceptable RAID, and fatigue dominates the unmet needs driving this unacceptable state.

Disclosure: J. Mistry, None; **M. Sibley**, None; **C. Smith**, None; **M. Sumbwanyambe**, None; **P. Kiely**, None.

Abstract Number: 1362

Relationship Between Waking Functions and Disease Activity in Rheumatoid Arthritis Patients Analyzed by Wearable Device

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: We reported that the prevalence of sarcopenia was 28% and locomotive syndrome was 52% in patients with rheumatoid arthritis (RA)[1]. It is unknown that waking relates with disease activity and body composition in RA patients. Recently, we can quantify number of steps, walking strength, and consumption energy by wearable device. We investigated the relative factors with waking of RA patients, and relationship with disease activity by using wearable device.

Methods: We used the date from prospective observational study (CHIKARA study, UMIN000023744) started form 2016. 85 from 100 RA patients entered and attached with wearable activity meter (HJA-750C; OMRON, Japan) during 7 consecutive days. We calculated the average daily number of steps, walking exercise (EX) (Mets x Time), and calorie consumption. The relationship of disease activity, body composition, muscle function, sarcopenia, locomotive syndrome, and frailty was analyzed by uni- and multivariate analysis. We investigated the correlation of number of steps and locomotive syndrome by ROC curve analysis.

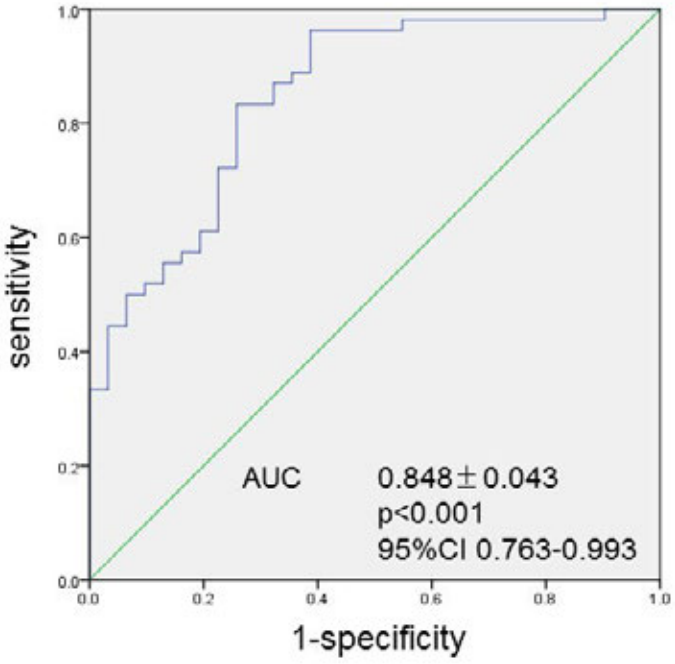
Results: Mean age was 65.2 years (women n=67, men n=18), disease duration was 7.7 years, DAS28-ESR was 3.12, and HAQ was 0.6. Number of steps and walking EX were negatively correlated with matrix metalloproteinase-3, DAS28-ESR, HAQ, locomotive syndrome, and frailty, and positively correlated with leg muscle score, muscle power,

	Univariate		Multivariate	
	R	P	β	P
MMP3	-0.294	0.006		
DAS28ESR	-0.300	0.005		
HAQ	-0.431	<0.001		
Locomotive syndrome	-0.581	<0.001	-0.276	0.017
Frailty	-0.565	<0.001		
Leg muscle score	0.342	0.001		
Muscle power	0.622	<0.001	0.414	<0.001
Muscle speed	0.583	<0.001		
Grip strength	0.287	0.008		
Walking speed	0.537	<0.001		

Table 1. Relative factors of number of steps in patients with RA

muscle speed, grip strength, and walking speed by univariate analysis (Table 1). Calorie consumption positively correlated with muscle mass and bone mass in addition to those factors. Locomotive syndrome and muscle power were detected as independently associated with number of steps and walking EX on multivariate analysis (Table 1). About calorie consumption, only muscle power was detected as an independent relative factor. When number of steps were

Figure 1



under 3333 by ROC curve analysis (Figure 1), the odds ratio of locomotive syndrome increased 14.4-hold (95%CI: 5.0-41.6) compared with over 3333 ($p < 0.001$).

Conclusion: Locomotive syndrome and muscle power were independent relative factor of number of steps and walking EX. Over 3333 steps per day was recommended to prevent locomotive syndrome in RA patients.

Disclosure: M. Tada, None; **Y. Yamada**, None; **K. Mandai**, None; **N. Hidaka**, None.

Abstract Number: 1363

Longitudinal Work Transitions in Early Inflammatory Arthritis Patients: Are There Targets for Intervention to Improve Employment?

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Background/Purpose: Historically, increasing proportions of patients with rheumatoid arthritis stop working on long-term follow-up, often due to arthritis. The trajectory of work transitions in early arthritis in the era of targeted treatment is unknown. Since decreasing employment may lead to loss of employment or work disability, we aimed to delineate the longitudinal transition trajectory of early arthritis patients and to identify predictors of decreasing employment.

Methods: This is a single center retrospective inception longitudinal cohort study of early inflammatory arthritis (EIA) patients whose symptom-onset£1 year at diagnosis. Patients were treated to target remission. Disease activity score 28 (DAS28– 3 variables), and patient reported outcomes were collected at each visit. Work status has been recorded annually. The primary outcome was employment states: full-time (FT), part-time (PT), unemployed, homemaker/ student, work disability (WD), retired (RE). We used the Markov multistate model, adjusted for interval censoring, to model the longitudinal transition trajectory of employment. The states in the model are: FT, PT, no income (NI: unemployed, homemaker & students), WD (self-reported) and RE (the only absorbing state). Probabilities of employment were calculated. Candidate predictors, both time-invariant and time-varying, including: sociodemographics, EIA activity, patterns of joint involvement (large upper or lower extremity joints, small upper or lower extremity joints), functional capacity (health assessment questionnaire, HAQ), quality of life (Short Form 36, SF36) and self-reported comorbidities (other chronic diseases, mental illnesses) were tested for association with employment transitions.

Results: 312 patients (76.5% females) diagnosed from 2000-2017, who were not retired at the baseline visit, had a median age at diagnosis was 45.3 years (33.3– 52.7, 25th-75th percentiles P), median duration of follow-up was 4.3 years (1.1– 9.8, 25th-75th P), median baseline DAS28 of 4 (2.9– 5.1, 25th-75th P) and 48% were rheumatoid factor positive. At baseline, 51% were working FT, 14% PT, 7% were students, 13% were homemakers, 8% WD. Baseline median completed school years was 12 yrs (12-15, 25th-75th P). Patients were most likely to stay in the same state of employment they were in at baseline, at 1, 5, 10 yrs (Table 1). Probabilities of transitioning to a FT/PT state from baseline NI increased to 0.33 (5 yrs) and 0.45 (10 yrs) and from baseline WD increased from 0.22 (5yrs) to 0.31 (10 yrs).

Table 1: Transition probabilities of employment states at 1, 5 and 10 years after baseline

State	Full Time	Part Time	No Income	Work Disabled	Retired
			1-year transition probabilities		
Full Time	0.94	0.01	0.01	0.02	0.02
Part Time	0.03	0.90	0.03	0.02	0.01
No Income	0.06	0.03	0.88	0.02	0.02
Work Disabled	0.04	0.02	0.03	0.87	0.04
			5-year transition probabilities		
Full Time	0.76	0.04	0.04	0.06	0.10
Part Time	0.15	0.61	0.11	0.07	0.06
No Income	0.22	0.11	0.53	0.06	0.08
Work Disabled	0.15	0.07	0.09	0.50	0.18
			10-year transition probabilities		
Full Time	0.60	0.07	0.06	0.08	0.19
Part Time	0.24	0.40	0.14	0.10	0.13
No Income	0.31	0.14	0.31	0.08	0.16
Work Disabled	0.22	0.09	0.11	0.27	0.30

Older age was protective of transitioning from PT to NI (hazard ratio, HR 0.87; 95% CI 0.82-0.93). Increased fatigue was associated with increased transitions from PT to NI (HR 1.02, 95%CI 1.00-1.04). Better SF36 was protective of transition from FT to WD (0.92, 95% CI 0.86-0.98). Sex, education, arthritis features, comorbidities & mental health were not associated with employment transitions.

Conclusion: Employment states in EIA patients changed dynamically over time. Even individuals who had NI or were WD at diagnosis had increased probabilities of moving into a working state over time. This work identified potential targets for intervention strategies to help EIA patients gain or regain employment.

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Abstract Number: 1364

Affect of Obesity on Multi-Biomarker Disease Activity (MBDA) Measurements in Rheumatoid Arthritis (RA) Patients

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

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Session Time: 9:00AM–11:00AM

	n	%
Total	244	
Age		
(Median Age ± SD)	59 ± 13.9	
18-40	30	12.3
41-64	128	52.5
≥65	86	35.3
Sex		
Female	199	81.6
Male	45	18.4
BMI		
≤25.9 (normal)	70	28.7
26-29.9 (overweight)	49	20.1
≥30 (obese)	125	51.2
Seropositive		
Y	175	71.7
N	65	26.6
Unknown	4	1.6

Table 1. Patient demographics

Test	Agree	Over-Diagnose	Under-Diagnose	Kappa
Unadjusted	78 (32.0%)	149 (61.1%)	17 (7.0%)	0.060 (– 0.010, 0.131)
Total Adjusted	84 (34.4%)	141 (57.8%)	19 (7.8%)	0.069 (– 0.006, 0.144)
Leptin Adjusted	54 (22.1%)	183 (75.0%)	7 (2.9%)	0.030 (– 0.018, 0.078)
BMI Adjusted	88 (36.1%)	125 (51.2%)	31 (12.7%)	0.078 (– 0.001, 0.156)

Table 2. Degree of agreement between DAS-28 and MBDA (Vectra) disease activity scores

Test	Sample Mean Difference	Test Statistic Value	Degrees of Freedom	P-Value
DAS28	1.19	5.69	74.5	< 0.0001
Unadjusted	5.62	3.27	100.0	0.001
Total Adjusted	2.76	2.04	115.3	0.022
Leptin Adjusted	8.25	5.01	101.7	< 0.001
BMI Adjusted	4.55	3.22	112.9	0.001

Table 3. Welch-approximated two-sample t-test (testing the nullhypothesis that the mean disease activity score in the fibromyalgia group is less than or equal to the mean disease activity scores in the non-fibromyalgia group)

Background/Purpose: The goal for treatment of RA is to obtain low disease activity for better outcomes. In order to achieve low disease activity, it is important to have an accurate way to measure disease activity. Historically, RA disease activity has been measured by scoring systems. The disease activity score in 28 joints (or DAS-28) is one of the most popular measurement tools for disease activity in RA. DAS-28 includes subjective measures of disease activity. Some patients, especially those with co-morbidities such as fibromyalgia, might have higher subjective disease activity than others. Recently, more objective measurements of RA disease activity have been popularized. MBDA (or Vectra DA) is one of these objective measures of disease activity. It uses 12 biomarkers to calculate a disease activity score. Some of the biomarkers included in the MBDA (leptin, CRP and IL-6) can be higher in obese patients. The aim of this study is to study the effects of obesity on MBDA.

Methods: Charts of 244 patients with RA seen by WellStar Medical Group (WMG) rheumatology between January 1, 2014 and April 1, 2019 who had MBDA testing were retrospectively reviewed for this study. MBDA score was compared to DAS-28 score (based on physician notes from the same visit as when Vectra DA lab was drawn) in patients with normal, overweight and obese BMIs.

Results: Adjusted MBDA scores agreed more closely with disease severity (low, moderate or high) by DAS-28 scoring than unadjusted MBDA scores. Still, only 84 of 244 total adjusted MBDA scores agreed with DAS-28 disease activity scores. BMI-adjusted MBDA scores are most closely correlated with DAS-28 scores and this correlation is most apparent in overweight patients (κ = 0.207, 95% CI [0.019,0.394]). However, using a regression equation (DAS28= 1.261 + 0.043 x Leptin-adjusted score - 0.011 x BMI-adjusted score) DAS-28 scores seem to correlate more closely with MBDA scores. MBDA scores tended to show higher levels of disease activity overall than DAS-28 scores (see Table 2). In Fibromyalgia patients, mean disease activity scores were higher than in patients without Fibromyalgia in both DAS-28 and MBDA scoring systems (see Table 3).

Conclusion: MBDA scores may be adversely affected by obesity. A prospective randomized controlled study in a bigger cohort of patients is needed to further investigate this correlation.

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Abstract Number: 1365

Construct Validation of PROMIS Short Form and Profile-29 T-Scores with SF-36 in Rheumatoid Arthritis Patients Treated for 1 Year: Results from a Real World Evidence-Based Study in the United States

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SESSION INFORMATION
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Background/Purpose: Use of PROs to assess health-related quality of life in clinical practice, research studies, and clinical trials in Rheumatoid Arthritis (RA) remains an ongoing area of research. SF36 is commonly used in RA trials but is not feasible for routine use in clinical practice settings. The PROMIS (Patient Reported Outcomes Measurement Information System) may address this gap but has not been widely assessed in RA patients starting therapy in a real-world comparative effectiveness study, nor examined in that setting in relation to the SF36 and Clinical Disease Activity Index (CDAI). These were evaluated in AWARE (Comparative and Pragmatic Study of Golimumab IV Versus Infliximab in Rheumatoid Arthritis), an ongoing Phase 4 study providing real-world assessment of IV Tumor Necrosis Factor inhibitor (TNFi) medications in RA pts.

Methods: AWARE is a prospective, noninterventional, 3-year study at 88 US sites. RA pts were enrolled when initiating TNFi treatment. Treatment decisions were made by treating rheumatologists. We report baseline PROMIS-29 (7 domains and pain intensity), PROMIS Pain Interference (PI) Short Form (SF) 6b (PI6b) and PROMIS Fatigue (F) Short Form 7a (F7a), domain T-Scores, and SF36 subdomain and Component Scores (CS) in AWARE patients. Here we report baseline data obtained from the final 1-year AWARE dataset. Correlations between PROMIS measures and comparable SF36 component scores were calculated using Pearson Correlations. Data is shown as mean ± standard deviation (SD).

Results: At baseline, mean CDAI of all pts (n=1262) was 32.3±15.6, with 70.4% in High Disease Activity (HDA, CDAI >22), 22.8% in Moderate DA (>10 and ≤22), 6.1% in Low DA (>2.8 and ≤10) and 0.7% in Remission (≤2.8). Mean PROMIS scores were >0.5 SD worse than population means for Physical Function (PF, 38.1±6.84), PI (63.4±7.68), F (58.8±9.95), Sleep Disturbance (55.1±8.68); and Ability to Participate in Social Roles/Activities (PSRA, 43.4±8.58). Baseline Depression and Anxiety were within 0.5 SDs of population T-scores. PI6b, F7a, and P29 domain T-scores correlated with the comparable SF36 subdomain and component scores (r's >0.58), excepting sleep for which no comparable SF36 element was applicable. Examples include: P6b (r=-0.80) and P29-PI (0.81) with SF-36 Bodily Pain; F7a (-0.77) and P29-F (-0.77) with SF36 Vitality; P29-PF with SF36 PF (0.77), Role-Physical (0.69), and Physical CS (0.73); P29 Anxiety with SF36 Mental Health (-0.72), Role- Emotional (-0.56), Mental CS (-0.70); and P29-PRSA with SF36-Social Functioning (0.71). Mean PROMIS-29 T-scores (except Anxiety and Sleep Disturbance) among patients with HDA were significantly different from patients with MDA, LDA or remission ($p < 0.001$ for all). Further, mean PROMIS T-scores of PF, F, PSRA, PI, Pain Intensity, PI6b and P7a among patients with MDA were significantly different from patients with more or less active RA (by CDAI category).

Conclusion: Analysis of baseline results from a large cohort of RA patients indicates high correlations between individual P29 domain T-scores and SF36 component scores, as well as categorical CDAI, providing strong evidence of PROMIS construct validity in a real-world population of RA patients.

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Abstract Number: 1366

Self-joint Counts by People with Rheumatoid Arthritis: Does a Video Increase Accuracy and Does It Matter?

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SESSION INFORMATION
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Background/Purpose: As a tool for self-monitoring and reporting RA disease activity, a smartphone app was developed to enable people with rheumatoid arthritis (RA) to record their disease activity, including self-reported 28 tender (28TJC) and swollen joint counts (28SJC). Studies suggest self-joint counts by people with RA are relatively similar to those by rheumatologists (28TJC more similar than 28SJC) but little is known about the effects of training on self-joint count accuracy. In collaboration with people with RA we refined techniques for joint self-examination and produced an instructional video. The aims of this study were to determine how patient self-joint counts, and derived disease activity scores, compared to rheumatologist joint counts and whether this was affected by a self-training video.

Methods: Patients (n=100) meeting EULAR/ACR 2010 criteria for RA attending clinics in 3 centres self-reported RA disease activity measures using the app, including a self-examination joint count. Patients were then randomised to either complete the self-report joint count a second time (Pt 2) with no further instruction (n=49) or to complete the self-report after watching the video (n=51). Blinded to patient data, a rheumatologist completed a 28-joint count, which was taken as the “gold standard”.

Results: Most participants were female (77%), had mean age 60.2 years (range 33-83 years), duration of RA 17.0 years (range 0.25-55 years) and 45% were using a biologic DMARD. Video and no-video group participants did not differ on demographic or disease characteristics but the video group had lower smartphone ownership (68% versus 85%, p=0.042). First and second patient-reported joint counts showed high correlation and did not change after watching the video, suggesting that watching the video had no training effect (Pearson R for 28TJC Rheum vs Pt 2 No video 0.568, Video 0.508; 28SJC Rheum vs Pt 2 No video 0.281, Video 0.386). Compared to rheumatologist assessment, people with RA consistently reported higher 28TJC and 28 SJC (28TJC Pt 2 vs rheum mean diff 3.01 (SD 5.76), 28SJC Pt 2 vs rheum mean diff 1.49 (SD 5.49)) but these differences were not statistically significant. Patient-derived DAS28 was never more than one disease activity category higher than rheumatologist-derived DAS28.

Conclusion: People with RA are consistent in reporting of self-joint counts and a training video did not change reporting. Although patients scored their joint counts higher than rheumatologists, the difference was small and not significant and would not invalidate the use of patient-reported scores for clinical purposes.

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An Engineered Glove for the Computerised Quantification of Hand Disability in Rheumatoid Arthritis

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SESSION INFORMATION

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Background: Rheumatoid arthritis (RA) is a long-term, progressive, and disabling autoimmune disease. The disease activity can be quantified by the Disease Activity Score 28-joint count C reactive protein (DAS28-CRP) but the evaluation of disability function (DF) is actually mainly performed only by subjective Patient Reported Outcomes (PROs) like Health Assessment Questionnaire (HAQ). Hence there are no objective and affordable tests to quantify the DF. The Hand Test System (HTS, ETT) is an engineered glove that can evaluate hands motility[1], nowadays applied for neuroscience studies.

Purpose: To quantify by HTS the DF of RA patients (RApts) by the analysis of speed and right execution of fingers opposition movement in both hands, evaluated. To verify the correspondence with the HAQ and DAS28(CRP).

Methods: In this pilot study 14 consecutives RApts (3 males, 11 females, age 61±11,5 years, mean duration of disease 11,21±5,07 years), classified according to 2010 ACR/EULAR criteria[6], and 13 healthy controls (HC – 7 males, 6 females, age 50±15 years) were enrolled. After consent, all participants undergone HTS test; a multiple finger evaluation (MFE) and a single finger evaluation (SFE) were performed analyzing the touches between the finger tips during the opposition movements of the hands in standard sequences of movements. A dedicated software provided the physician these quantitative parameters: Touch Duration (TD), Inter Tapping Interval (ITI) and Movement Rate (MR). RApts compiled the HAQ and a DAS28-CRP was performed. Continue variables were summarized as mean and standard deviation or median and interquartile range, discrete variables were summarized with count and percentage. Variables with skewed distribution was converted to natural logarithm. T-test was used to compare log glove parameters between groups. Pearson's r and p value were used to report the correlation between log-converted glove parameters and HAQ score.

Results: In MFE, glove parameters TD and ITI were found significantly higher in RApts (TD 257.34 ± 123.93 ms, ITI 377.8 ± 211.35 ms) than HC (TD 172.25 ± 59.36 ms, ITI 177.98 ± 78.53 ms) ($p = 0.004$ and $p < 0.001$) and MR was significantly lower in RApts (1.51 ± 0.47 Hz) compared to HC (2.87 ± 0.9 Hz) ($p < 0.001$). There was a trend of increased TD at the increasing of DAS28-CRP (P=0.178). TD of RApts had a significant correlation with the total score of the HAQ (Pearson $r = 0.79$, $p = 0.001$). In SFE not swollen and not tender fingers of RApts performed slightly better than a clinically active finger (AF) but significantly worse than average HC finger (ANOVA, $p < 0.001$).

Conclusion: HTS is a totally safe and promising tool to quantify in an objective manner the DF of the hands in RApts. The significant correlation found with HAQ highlights the loss of motility of the hands as one of the main determinant of DF. The non-significative result with DAS28-CRP is likely due to the low number of subjects enrolled. Further studies are ongoing with larger number of RApts to validate its application to monitor the improving or the worsening of RA in order to optimize pharmacological treatments. The study is now extended to the hands in other Rheumatic and Musculoskeletal Diseases.

Reference:

1. Signori et al PLoS One 2017.18;12:e0186524

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Abstract Number: 1368

One Size Fits All : Replacing ESR by γGT in DAS28 Calculation Permits a Dual Evaluation of Joint Activity Together with Cardiovascular Risk

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Background/Purpose: Patients with rheumatoid arthritis (RA) experience premature mortality that is largely due to cardiovascular disease (CVD). Ample evidence suggests that elevated γGT activity is associated with increased risk of CVD. Our aim was to assess the determinants of increased γGT activity in patients with RA, focusing on markers of disease activity and cardiovascular risk factors.

Methods: Cross-sectional study including successive RA patients hospitalized in the Rheumatology department of Cochin Hospital for a 12-month period. Data on liver function, disease activity, hepatotoxic and cardiovascular risk factors were systematically collected and all patients were assessed by Power Doppler Ultrasound (PDUS) performed on 32 joints. DAS28-γGT was calculated by replacing ESR by γGT in the following formula: $0.56^{*}\sqrt{TJ\text{-}28}+0.28^{*}\sqrt{SJ\text{-}28}+2^{*}ln(\gamma GT)+0.014^{*}GH$

Results: We included 124 patients: 85% were women and mean age was 58 years. Thirty-one patients (25%) had isolated γGT increase. γGT correlated with CRP (r=0.30, p=0.002) (Figure 1A). No correlation was observed between γGT and ESR, DAS28 or DAS28-CRP. γGT were significantly increased in patients with alcohol consumption (median (range): 35 (20-144) UI/L *vs*. 22 (7-219) UI/L, p=0.012), type 2 diabetes mellitus (35 (8-215) UI/L *vs*. 21 (7-219) UI/L, p=0.024), blood hypertension (35 (8-215) UI/L *vs*. 21 (7-219) UI/L, p=0.024), dyslipidemia (28 (7-219) UI/L *vs*. 19 (8-215) UI/L, p=0.004) and metabolic syndrome (48 (14-219) UI/L *vs*. 21 (7-144) UI/L). γGT levels gradually increased with the number of cardiovascular risk factors (p< 0.001) (Figure 1B). In multivariate analysis, γGT levels > 35 UI/L was associated with CRP > 10 mg/L (OR : 4,88, 95% CI 1,59-15,03) and the presence of dyslipidemia (OR: 3.13, 5% CI 1.09-8.97). Given that γGT reflected both systemic inflammation and metabolic condition, we constructed a composite index called DAS28- γGT to test the merit of this marker for the global evaluation of RA. DAS28- γGT remains a reliable marker of RA disease activity which correlated with DAS28 (r=0.50, p< 0.001), DAS28-CRP (r=0.70, p< 0.001), ESR (r=0.30, p< 0.001), CRP (r=0.50, p< 0.001), global OMERACT-EULAR synovitis Score on PDUS (r=0.22, p=0.024) and HAQ (r=0.35, p< 0.001). Patients with blood hypertension (median (range) 8.16 (5.41-12.14) *vs* 7.26 (4.80-11.47) p=0.012), dyslipidemia (8.24 (4.80-12.14) *vs*. 7.08 (5.04-11.81), p=0.011) and metabolic syndrome (8.47 (6.23-12.03) *vs.* 6.40 (4.80-12.14)) were more likely to have increased DAS28-γGT. Conversely to the DAS28 and DAS28-CRP, DAS28-γGT steadily increased according to the number of cardiovascular risk factors (Figure 1C), and had a diagnostic value for the presence of at least 2 cardiovascular risk factors characterized by an AUC of 0.70 (p< 0.001) compared to 0.51 for DAS28 and DAS28-CRP (Figure 1D)

Conclusion: Our results support that γGT levels may be considered as markers of systemic inflammation, metabolic syndrome and cardiovascular risk in patients with RA. We propose an original index, the DAS28-γGT, able to evaluate both disease activity and cardiovascular risk. This index would deserve further validation in prospective cohorts.

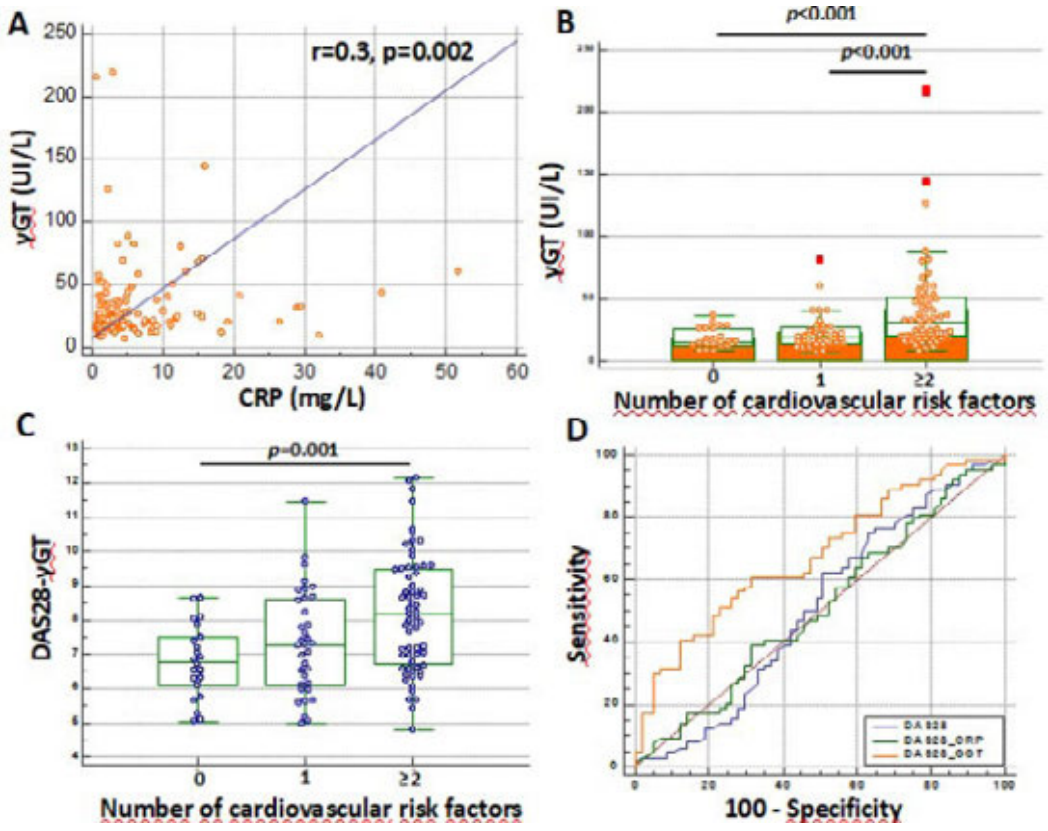

Figure 1. A. Rank correlation between γGT (UI/L) and CRP (mg/L) ; B. γGT level (UI/L) according to the number of cardiovascular risk factors (0 , 1 or ≥ 2 risk factors) ; C. DAS28-γGT value according to the number of cardiovascular risk factors (0 , 1 or ≥ 2 risk factors) ; D. ROC curve of DAS28, DAS28-CRP and DAS28-γGT

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Abstract Number: 1369

Angiogenic Factors for Assessing Rheumatoid Arthritis in the Era of Sonographic Diagnosis and Biologic Therapy

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SESSION INFORMATION
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Background/Purpose: Previously, we demonstrated the direct pro-inflammatory role of the vascular endothelial growth factor (VEGF) and the placenta growth factor (PlGF), and angiogenic factors in rheumatoid arthritis (RA) pathogenesis (Arthritis Rheum 2009, Nat Immunol 2019). Here, we investigated whether these factors can reflect ultrasound (US)-defined synovitis, disease activity, and treatment response in RA patients.

Methods: US was performed to determine synovial hypertrophy (GSUS) and vascularity (PDUS) scores in RA patients (n=54) who underwent arthrocentesis; GSUS ≥2 or PDUS ≥1 was defined as severe synovitis. Serum samples were obtained from 157 RA patients, and among them, RA patients with disease activity score 28 (DAS28) > 3.2 underwent serial serum sampling 6 months after treatment with conventional DMARD (cDMARD, n=53) or biologic DMARD (bDMARD, n=49). Angiogenic proteins primarily produced by synoviocytes, including VEGF, PlGF, soluble flt-1 (sflt-1), and IL6, were measured in the synovial fluid (SF) and sera using an enzyme-linked immunosorbent assay.

Results: SF and serum VEGF, PlGF, sflt-1, and IL6 concentrations were significantly elevated in RA patients compared with osteoarthritis controls. For SF, RA patients with severe synovitis on US examination showed higher concentrations of PlGF, but not VEGF, than those without. In contrast, serum VEGF, but not PlGF, reflected well synovitis severity in the joints, correlating with acute phase reactants and DAS28. In cDMARD users, the serial follow-up of serum VEGF, IL6, ESR, and CRP could all predict the treatment response. However, in biologic drug users (n=49), serial monitoring of VEGF only, but neither IL6 nor CRP, significantly predicted treatment response. Using a multiple logistic regression model, older age, low baseline sharp score, and high VEGF difference were associated with good and moderate treatment response; area under the ROC curve from this model was 0.872.

Conclusion: Angiogenic factors PlGF and VEGF represent well the joint pathology of RA assessed by US. Serum VEGF shows a better value to predict a therapeutic response to anti-rheumatic drugs than CRP and IL6, particularly in patients treated with biologic agents.

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Abstract Number: 1370

Not All Joints Are Equal: Challenge DAS28 System and Identify Factors Leading to a Mismatch Between T2T and HAQ Among RA Patients Through Data Mining from Smart System of Disease Management (SSDM)

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Treat to target (T2T), achieving a DAS28 score lower than 3.2, is the strategy recommended by ACR and EULAR. Health assessment questionnaire (HAQ) is the most widely used in assessment of physical function in RA. However, the T2T may not be always associated with low HAQ score. The purpose of this study is to quantify phenomena of mismatch between T2T and HAQ in RA patients and identify influential factors from real-world data mining in SSDM.

Methods: SSDM are mobile APPs of disease management. The patients were trained by physician to conduct their DAS28 and HAQ self-assessments with SSDM. The data were synchronized with physicians' and uploaded onto cloud for analysis.

Two phases studies were designed. Phase I: from June of 2015 to May of 2018, to identify impact factor for mismatch; phase II: from June 2018 to May 2019, validation.

Results: From June 2015 to May 2019, 54,149 RA patients from 587 hospitals in China used SSDM, of which 41,234 patients made 84,538 times of DAS28 & HAQ self-assessments. Phase I: Total 48,751 assessment from 25,151 pa-

Table 1. The mean scores for each functioning category in HAQ and the top 3 target joints.

	Mean score	Knee	Wrist	Shoulder	Middle finger	Elbow	Index finger	Other fingers
1 Dress yourself including shoelaces and buttons	0.43		0.43	0.34	0.22			0.12
2 Get in and out of bed	0.3	0.3	0.24	0.15				
3 Lift a full glass to your mouth	0.32		0.32	0.26	0.16			
4 Walk outdoors on flat ground	0.38	0.38	0.3	0.19				
5 Wash and dry your body	0.48		0.48	0.38		0.24		
6 Bend down to pick up clothing from the floor *	0.81*	0.81	0.65	0.42				
7 Turn faucets (or corks) on and off	0.47		0.47		0.38		0.24	
8 Get in and out of a car	0.48	0.48	0.38	0.24				
Total scores	3.67	1.97	3.27	1.98	0.76	0.24	0.24	0.12
Mean score	0.46	0.49	0.41	0.28	0.25	0.24	0.24	0.12
impact factors		4	3.4	2.3	2.1	2	2	1

* $P < 0.001$

Table 1. The mean scores for each functioning category in HAQ and the top 3 target joints.

tients included. Among them, 25,738 assessments from 13,110 patients reached T2T. The mean numbers of tender and swollen joints were 1.53 and 1.32, respectively. However, 8,762 assessments (34.04%) of 5,905 patients had abnormal physical function (HAQ > 0), which score for 8 functional tests was 3.67. The "Bend down to pick up cloth from the floor" was the commonest, with a mean score of 0.81, significantly higher than other functional test score, $P< 0.001$. The analysis of correlation between physical dysfunction and the affected joints showed the knees were the major contributor to the mismatch, following by wrists and shoulders. Table 1 showed the mean scores for each functioning category in HAQ and the top target joints. According to the cluster weights for the impacts of affected joints on physical function, the weighted coefficient of impacting factors (IF) on physical function was obtained: knee=4, followed by wrist=3.4, shoulder=2.3, middle finger=2.1, elbow=2, index finger=2, other finger=1. Phase II: total 35,787 assessments from19,941 patients were included. Among them, 18,618 assessments from 10,776 patients achieved T2T, but 5,500 assessments from 3,979 patients (29.54%) had abnormal physical function (HAQ > 0, mean 3.49). After excluding 1,621 assessments without joint involvements, 3,879 left for validation. With standard DAS28 calculator, IFs of knee*4, wrist*3.4, shoulder*2.3, middle finger*2, orther finger*1 were applied for calculation, and 3,373 (86.96%) assessments turn out to be DAS28 >3.2(Mean: 4.19±0.01, Median: 4.08), major mismatches were overcome.

Conclusion: Over 1/4 RA patients suffer from physical dysfunctions though T2T are achieved. Diseased knees, wrists and shoulders are the major contributors to physical dysfunction and to the mismatch between T2T and HAQ. While elbow and finger joints influence on HAQ less. Therefore, not all joints are equal and T2T guided by current DAS28 may mislead. Joints of knees, wrists and middle fingers deserve higher IF (2.1-4) in DAS28. A modified DAS28 should be considered and a special attention should also be paid on these top three joints for rehabilitations.

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Abstract Number: 1371

Create an Algorithm of Outcome Forecasting and Decision Making for RA Treatment: Data Mining and Machine Learning via the Smart System of Disease Management (SSDM)

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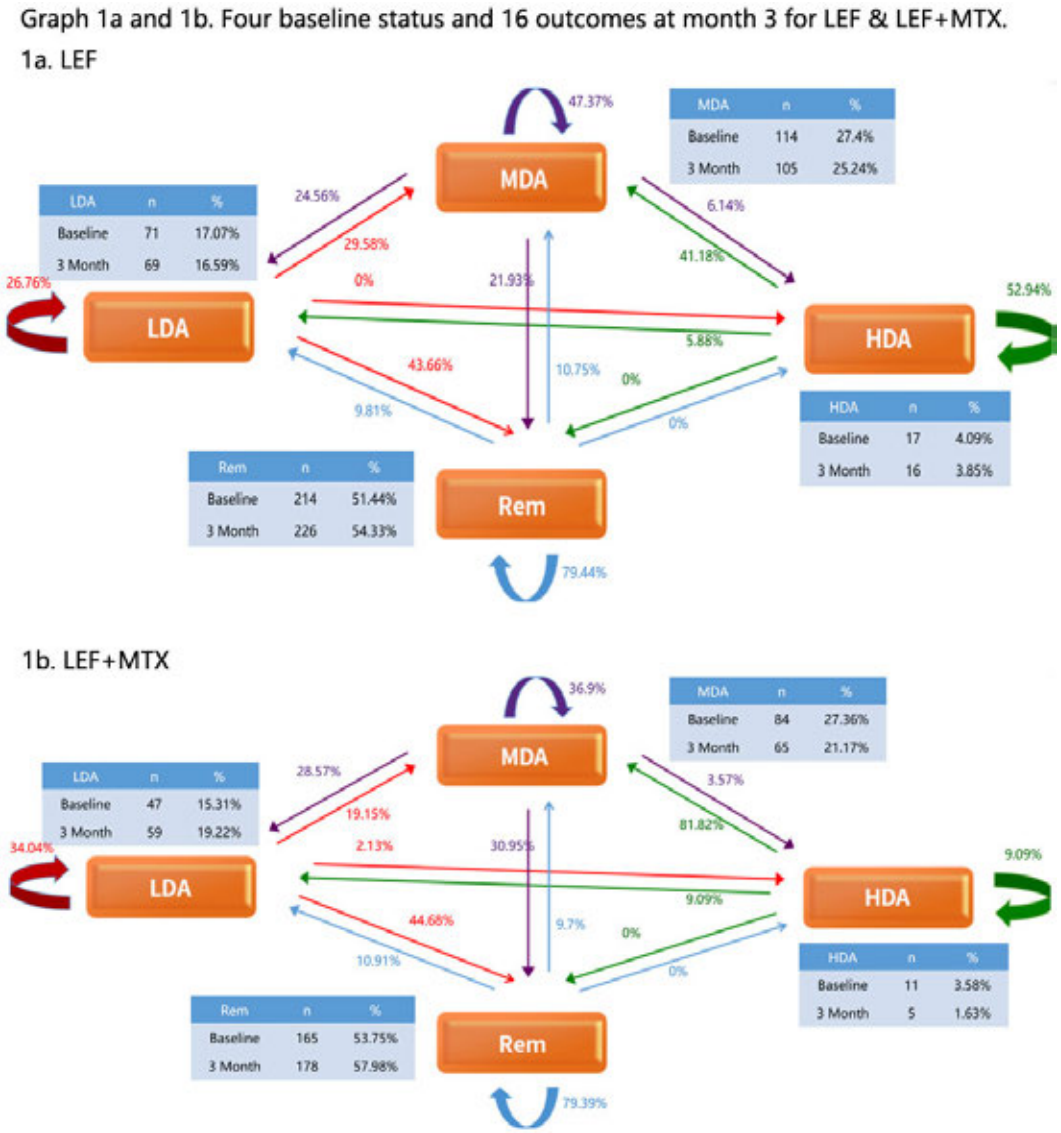

Figure 1. A. Rank correlation between γGT (UI/L) and CRP (mg/L) ; B. γGT level (UI/L) according to the number of cardiovascular risk factors (0 , 1 or ≥ 2 risk factors) ; C. DAS28-γGT value according to the number of cardiovascular risk factors (0 , 1 or ≥ 2 risk factors) ; D. ROC curve of DAS28, DAS28-CRP and DAS28-γGT

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

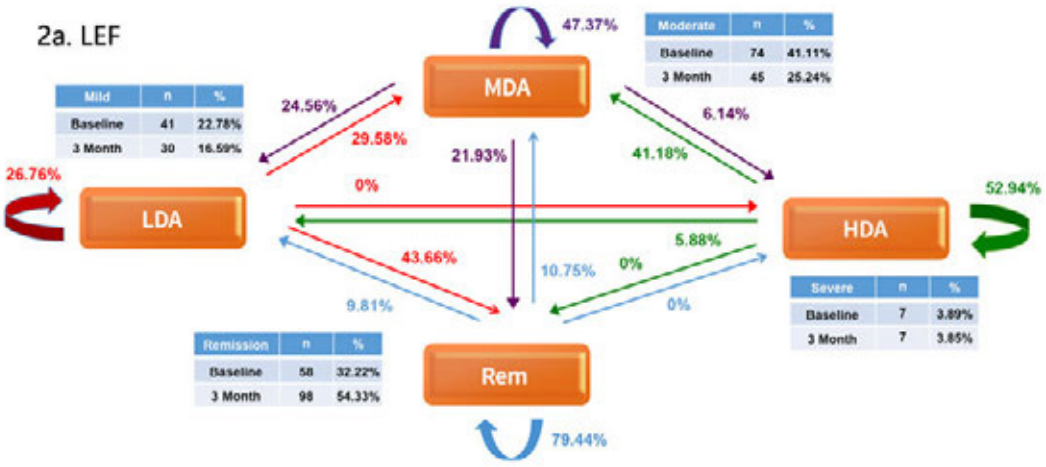
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

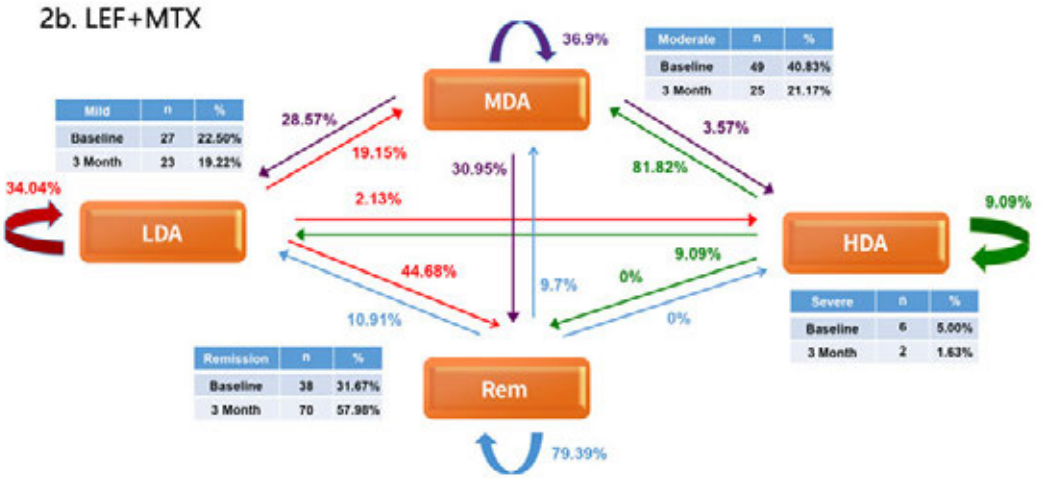
Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

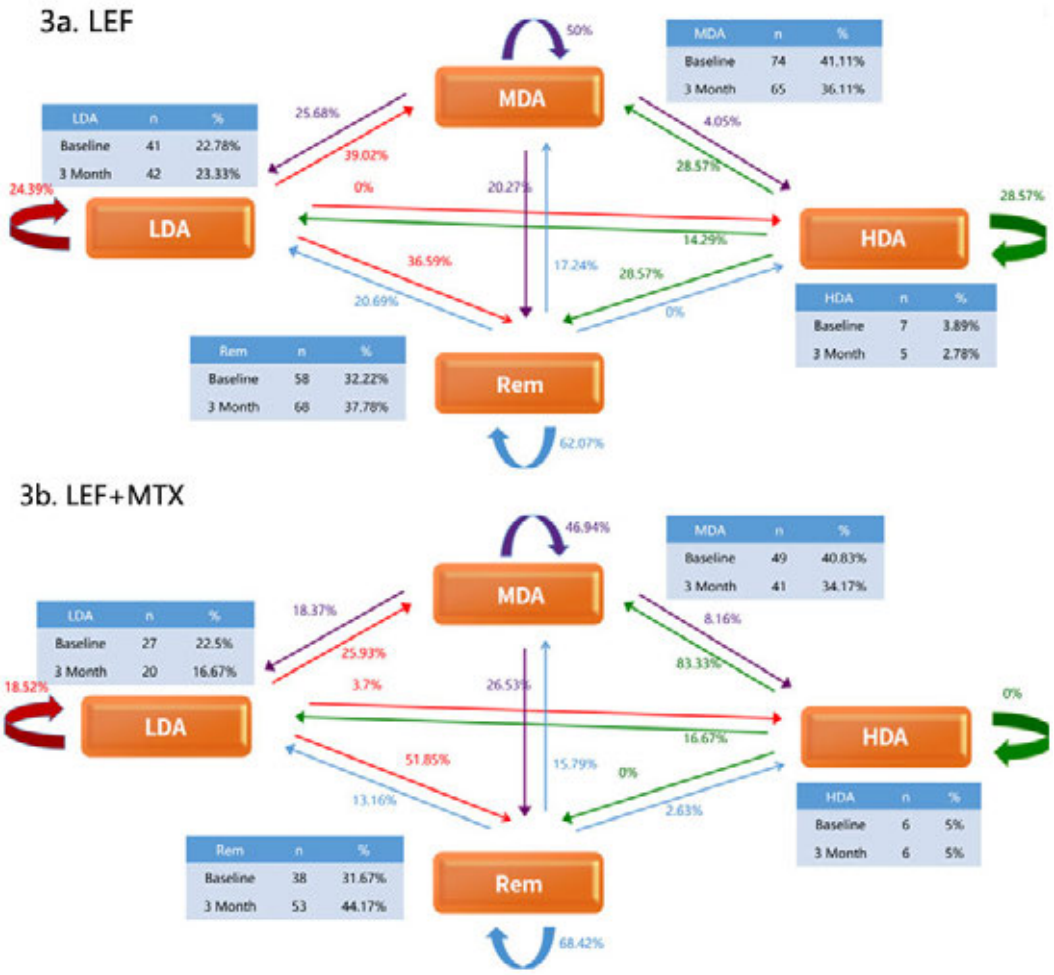
Background/Purpose: Daily health care deals with a wide spectrum of RA patients from statuses of remission (R) to disease activities at low (L), moderate (M) and high (S) based on DAS28. Each patient has 4 potential outcomes of

Graph 2a & 2b. The probability of outcome prediction (P(B)) for patients





Graph 3a and 3b. The true outcomes of DAS28 at month 3 served as evidence



either R, or L, or M, or S at certain time layer. But predicting efficacy and selecting regimens are in trial-and-error style. The objective of this study is to develop an algorithm for efficacy prediction and regimen selection in RA via SSDM.

Methods: SSDM includes 2 APPs for both physicians and patients. The patients input medication and laboratory test results, and perform self-evaluation (DAS28) after training. The data synchronizes to the physician's APP and the advices could be delivered.

In order to develop a prediction model, top 2 regimens, Leflunomide (LEF, 5-10 mg/d) and LEF+MTX (7.5-10mg/w) were selected as samples from SSDM database. Repeat evaluation of DAS28 scores were extracted at 3 months interval.

The study was divided into 2 phases: phase 1. To develop Markov model and generate the probability (P) of prior believe, P(B|A), based on Bayes Theorem, and phase 2. Calculate P of posterior believe, P(A|B), and validate the reliability comparing with true evidence of outcome via Intra-group correlation coefficient (ICC).

Results: From June 2014 to May 2019, 54,149 RA patients from 587 centers registered in SSDM. Among those with 3 months data available, 416 patients with LEF and 307 with LEF+MTX who registered before June 1 of 2018 were enrolled in phase 1, and 180 patients with LEF and 120 with LEF+MTX after June 1 of 2018 were included as phase II. There were no significant difference considering gender, age, race, disease history and DAS28 distribution between

2 phases. Phase I: Four baseline status (P(A)) and 16 outcomes at month 3 (P(B)) for LEF or LEF+MTX are presented in graph 1a and 1b, respectively, based on Markov Chain. The algorithm of probabilistic inference for next month 3 outcome was created as Σ p{Xt+1|Xt (Rt, Lt, Mt, Ht)}=1 0< t< ∞. The beta distribution and P(B|A) were generated. Phase II: The probability of outcome prediction (P(B)) for patients was calculated using the DAS 28 at baseline via the Bayes algorithm: P(A|B)=P(B|A)*P(A)/P(B) and were shown in graph 2a & 2b. The true outcomes of DAS 28 were obtained through repeat self-valuation at month 3 served as evidence (graph 3a & 3b). Comparing the distribution of evidence with those in P(A|B), ICC for LEF was 0.90, and ICC for LEF+MTX was 0.96, which indicated high inter-observer reliability. Based on the algorithm, the inferences of efficacy for both LEF and LEF+MTX were obtained. The advices were that LEF at low dose was good for RA with R and L, but for RA with H, adding MTX was preferred. Both were good for M.

Conclusion: Through patterns extraction, data mining and modeling, a master algorithm of efficacy prediction and decision making for RA were developed. Following data inputting and machine leaning, an artificial intelligent system in assisting clinical practice may be achieved with SSDM.

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Abstract Number: 1372

Adherence to Treatment with Intravenous Biological Agents in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures – ARP
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The adherence to the therapeutic regimen in patients with Rheumatoid Arthritis (RA) varies between 30 and 80%. Classically, it is mentioned that the adherence to intravenous medication (IV) may be better than oral or subcutaneous, however there are few studies that analyzed it. **Objective**: To evaluate the adherence to biological (-b)DMARDs IV in patients with RA in clinical practice and to determine the factors that could have an impact on the adherence.

Methods: Observational study. Patients ≥18 years of age, with a diagnosis of RA according to ACR/EULAR 2010 criteria, who received at least 3 infusions of the b-DMARD IV abatacept (ABA) and/or tocilizumab (TCZ), during the course of their illness. Medical records, were reviewed to collect: sociodemographic data, clinical characteristics of the disease, comorbidities, disease activity, functional capacity by HAQ. Information was obtained on previous and concomitant treatments for b-DMARD, including steroids and conventional (-c) DMARDs, number of infusions of b-DMARD received, date of their initiation and discontinuation and causes of suspension. Adherence was calculated as the number of infusions received during the treatment period, considering a 28 days interval between infusions as

optimal. *Statistical analysis*: descriptive statistics, Chi2 test or Fisher's exact test, Student's T test and Mann Whitney test. Multiple logistic regression model to evaluate predictors of good adherence (≥80%).

Results: 67 patients were included, 94% were women, with a median disease duration of 13.8 years (IQR 8-18,2). 82.1% (55 patients) had medical coverage, 60% corresponded to social work. The median distance to the infusion center was 15 km (IQR 6.5-27). As a concomitant treatment, 72.4% received c-DMARD (without significant differences between ABA and TCZ), 52.7% prednisone and 64.3% NSAIDs. After 3 months of treatment, the baseline DAS28 decreased from 5.46 (IQR 4.77- 5.99) to 3.87 (IQR 2.79-4.68), $p < 0.001$, and the baseline HAQ-A from 2 (IQR 1.5-2) to 1 (IQR 1-2), $p< 0.001$. After a median follow-up time of 2.42 years (IQR 1.2-4.7), 38 patients (56.5%) discontinued definitively the b-DMARD IV. The most frequent causes of suspension were inefficiency in 62.9%, AE in 20% and lack of provision in 14.3%. The median survival was 4 years, without significant differences between ABA and TCZ. The median number of infusions per year was 10.17 (IQR 8.3-10.9), equivalent to an adherence of 78.2%, considering as an optimum of 13 infusions/year. Excluding suspension of b-DMARD IV by AE and/or surgeries, the median number of infusions per year was 10.8 (IQR 9.3-11.6), equivalent to an adherence of 83.1%. The median infusions/year correlated negatively with the distance to the infusion center (Rho: - 0.27, $p = 0.003$) and was significantly lower in patients without health coverage (8.5 ±2.5 vs 10.7 ±1.5, $p < 0.001$). In the multivariate analysis, having health coverage was the only variable that remained associated with better adherence ≥80% (OR: 6.27, 95% CI 1.1- 37.9, $p = 0.04$).

Conclusion: Adherence to treatment with b-DMARD IV was acceptable, however our patients lose, on average of 3 infusions per year. The only independent predictor associated with good adherence was having health coverage.

Disclosure: G. Luna, None; **f. dal Pra**, None; **E. Schneeberger**, None; **L. Macias Oviedo**, None; **G. Citera**, AbbVie, 5, 8, Abbvie, 2, 5, 8, BMS, 5, BRISTOL MYERS SQUIBB ARGENTINA, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, Gema Biotech, 2, 5, 8, Genzyme, 5, Janssen, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi Genzyme, 5, 8.

Abstract Number: 1373

Performance of CQR5 vs CQR19 in the Evaluation of Adherence to Tofacitinib in Daily Clinical Practice

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures – ARP
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the adherence to treatment with Tofacitinib in patients with Rheumatoid Arthritis (RA) using both versions of the self-questionnaire Compliance Questionnaire Rheumatology: CQR19 and CQR5. Secondary objectives were to determine the variables associated with adherence to Tofacitinib and to compare the performance of both questionnaires.

Methods: A cross-sectional study was carried out. We included patients ≥18 years old, with a diagnosis of RA according to ACR-EULAR 2010 criteria under treatment with Tofacitinib. Sociodemographic data and clinical disease

characteristics, such as disease duration, Rheumatoid Factor and anti-CCP status, ESR (mm/h), CRP (mg/l) pain and global disease assessment by Numerical Visual Scale (NVA), joint count (28), DAS28, presence and duration of morning stiffness were recorded. Previous treatments (b-DMARD and c-DMARD), concomitant treatments,date of beginning and dose of Tofacitinib (5 mg BID or 11 mg XR), date of discontinuation and its reasons (adverse events (AE) or lack of provision) were consigned. All patients completed self-questionnaires CQR19 and CQR5, CQR19 includes 19 items evaluated by Likert scale of 4 points with a final value of 0 (no adherence) to 100 (perfect compliance). CQR5 is a simplified version, which includes 5 items of the original CQR19, and was previously validated. *Statistical analysis:* Descriptive statistics. T-test or Mann Whitney to compare the continuous variables, Chi^2 test or Fisher's exact test to compare the categorical ones. Kappa concordance index. Multiple logistic regression in order to determine variables associated with adherence.

Results: We included 52 patients, 82.7% women, with a median age *(m*) of 57.7 years, disease duration *m* 16 years. 63.5% had comorbiditiesand 27% were smokers. DAS28 *m* 2.25. 65.4% had received b-DMARD prior to Tofacitinib. 86.5% of the patients treated with Tofacitinib used 5 mg BID and 48% received Tofacitinib as monotherapy. In 52% the concomitant treatment was: Methotrexate 63% and Leflunomide 33.3%. The median time of Tofacitnib treatment was 13 months. 40,4% patients temporarily suspended treatment and in 50% of the cases, it was due to infections: 4 cases of Herpes Zoster, 4 lower urinary tract infections and 2 pneumonias acquired from the community and the rest of the cases for other reasons, such as scheduled surgeries and/or lack of provision. All the events were solved without complications. Only one patient permanently stopped treatment due to lack of provision. Median CQR19 was 89.5. The 84.6% had an adherence ≥ 80%. The variables significantly associated with adherence ≥ 80% were the presence of comorbidities [70.5% vs 29.5% (p = 0.014)] and older age (60 ± 9 years old vs. 45 ± 6 years old, p = 0.033). Using the CQR5, a similar percentage of patients (82.7%) were adherent, however, the concordance with CQR19 was low (ƙ: 0.227).In the multivariate analysis, older age was the only variable independently associated with greater treatment adherence [OR: 1.09 (95% CI 1.06-1.18), p = 0.037].

Conclusion: The treatment adherence of Tofacitinib was very good for both presentations. Older age was associated with higher adherence. The agreement between the questionnaires CQR19 and CQR5 was low.

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Abstract Number: 1374

Real-World Evidence: Infections Among RA Patients Switching from First Biologic DMARD to Another Treatment in the US

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Infections are common safety events monitored in RA patients.[1] ACR guidelines limit the use of live vaccines in patients who are on biologic (b)DMARDs or Janus kinase inhibitor (JAKi).[2] The presence of comorbidities and treatment-related serious infections may lead to treatment discontinuation. This study aimed to update

Table 1. Prevalence of Infection During 12-Month Pre-Index Date by Index Treatment

	Serious infections	Opportunistic infection	Herpes zoster
All patients (n=4656)	13.7%	6.4%	1.9%
Index monotherapy (n=2149)	15.1%	7.3%	2.1%
TNFi (n=1305)	14.3%	7.4%	1.9%
Non-TNFi (n=521)	16.7%	6.9%	2.3%
JAKi (n=323)	15.8%	7.4%	2.8%
Index combination therapy (n=2507)	12.5%	5.7%	1.7%
csDMARD + TNFi (n=1740)	12.3%	5.8%	1.6%
csDMARD + Non-TNFi (n=569)	11.8%	5.1%	1.6%
csDMARD + JAKi (n=198)	16.2%	7.1%	3.0%

csDMARD, conventional synthetic DMARD; JAKi, Janus kinase inhibitor; TNFi, TNF-α inhibitor.

estimates of the prevalence and incidence of various infections among patients switching from a first bDMARD to another treatment and estimate healthcare costs associated with them.

Methods: In a US health plan claims database, we selected adult RA (≥2 RA diagnoses) patients who newly initiated a bDMARD (1/1/2012–3/31/2017) and switched to another bDMARD or JAKi (index date; ID). All patients had continuous enrollment 12-months pre- and ≥12-months post-ID. Prevalence (12-month pre-ID) and while-on-treatment incidence per 100 patient-years (P100PY) of serious infections, opportunistic infections, and herpes zoster were evaluated overall and by index treatment. For incidence rates, patients with no prior events were followed from ID until the first event or the end of index treatment. Unadjusted mean annualized all-cause healthcare costs (total, medical, and pharmacy) were assessed during index treatment and compared between patients with and without infections of interest.

Table 2. Duration of Index Treatment and Incidence Rate per 100 Patient-years while on Treatment, by Index Treatment

	Mean treatment duration (months)	Serious infection		Opportunistic infection		Herpes zoster	
		IR	PY	IR	PY	IR	PY
All patients	13.2	12.1	3978	5.4	4526	2.2	4864
Index monotherapy	9.9	11.7	1366	5.6	1559	2.5	1675
TNFi	9.3	10.7	803	5.8	897	2.2	972
Non-TNFi	10.7	13.3	345	3.7	410	1.4	439
JAKi	10.8	12.9	217	8.0	251	5.3*	264
Index combination therapy	16.1	12.3	2612	5.2	2967	2.1	3189
csDMARD + TNFi	15.5	12.8	1739	4.7	1985	1.9	2134
csDMARD + Non-TNFi	17.7	12.6	657	6.0	747	1.9	802
csDMARD + JAKi	16.7	7.0†	215	7.3	235	4.3††	254

csDMARD, conventional synthetic DMARD; IR, incidence rate; JAKi, Janus kinase inhibitor; TNFi, TNF-α inhibitor; PY, patient-years.

† P-value = 0.023 (JAKi vs. bDMARD within combination therapy).

* P-value = 0.002 (JAKi vs. bDMARD within monotherapy).

†† P-value = 0.011 (JAKi vs. bDMARD within combination therapy).

Table 3. Per-patient-per-year (PPPY) Healthcare costs over the Duration of Index Treatment in Patients with and without infection, USD

	With comorbidity		Without comorbidity		p-value
	Mean	SD	Mean	SD	
Serious infection					
Total cost (medical + pharmacy)	$66,588	$53,696	$53,263	$31,103	<0.0001
Total medical cost	$32,671	$49,220	$18,656	$31,533	<0.0001
Total pharmacy cost	$33,917	$27,128	$34,607	$22,421	0.5324
Opportunistic infection					
Total cost (medical + pharmacy)	$59,525	$40,741	$54,369	$33,963	0.0230
Total medical cost	$25,141	$32,467	$19,824	$34,114	0.0180
Total pharmacy cost	$34,384	$33,603	$34,545	$22,223	0.9155
Herpes zoster					
Total cost (medical + pharmacy)	$55,291	$36,686	$54,622	$34,310	0.8421
Total medical cost	$24,523	$37,722	$19,997	$33,954	0.1741
Total pharmacy cost	$30,769	$19,234	$34,625	$23,023	0.0858

Results: 4,656 patients switched from a first bDMARD to another treatment: median age 54 years, 78% female, mean duration of RA 1.8 years. After initial bDMARD, 46% of patients used monotherapy (61% TNF-α inhibitor (TNFi), 24% non-TNFi, 15% JAKi), and 54% used another bDMARD or JAKi in combination with csDMARD (69% TNFi + csDMARD, 23% non-TNFi + csDMARD, 8% JAKi + csDMARD). Pre-index prevalence rates ranged 12–17% for serious infections, 5–7% for opportunistic infections, and 2–3% for herpes zoster and were comparable among treatments (Table 1). While on index treatment, incidence rates ranged 7–13 P100PY for serious infections, 4–8 P100PY for opportunistic infections, and 1–5 P100PY for herpes zoster. Incidence rates varied among different treatments (Table 2). Total unadjusted healthcare costs were significantly higher in patients with serious infections ($66,588 vs $53,263; $p< 0.0001$) or opportunistic infections ($59,525 vs $54,369; $p=0.023$) than without these infections. Cost differences were primarily associated with medical costs (Table 3).

Conclusion: Serious infections, opportunistic infections, and herpes zoster affected RA patients switching from their first bDMARD to another treatment. While on index treatment, incident infections were associated with increased unadjusted costs, posing additional economic burden. Adjusted analyses are needed to estimate the economic burden of these infections accounting for difference in patient cohorts. Clinicians should factor the burden of infections into their clinical decisions.

References:

1. Ramiro S, et al. Ann Rheum Dis. 2017; 76: 1101-1136.
2. Singh JA, et al. Arthritis & Rheumatology. 2016; 68:1-26.

Disclosure: R. Dore, AbbVie, 2, 5, 8, AbbVie, Inc., 5, 8, 9, Abbvie, Inc., 2, 5, 8, Amgen, 2, 5, 8, 9, Biogen, 2, 9, Gilead Science, 2, 5, Gilead Sciences, Inc., 2, 5, 9, Lilly, 2, 5, 8, 9, Novartis, 2, 5, 9, Pfizer, 2, 8, 9, Radius, 8, Regeneron, 8, Sanofi, 8, UCB, 2, 8, 9, VCB, 8; **J. Antonova**, Gilead Science, 1, 3, Gilead Sciences, Inc., 1, 3; **H. Huang**, IQVIA, 9; **L. Chang**, Gilead Science, 9, Gilead Sciences, Inc., 1, 3, Lilly, 9; **X. Wang**, IQVIA, 9; **M. Genovese**, AbbVie, 2, 5, Abbvie, 2,

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Abstract Number: 1375

Patient-Reported Outcomes of Upadacitinib versus Adalimumab Use in Patients with Moderately to Severely Active Rheumatoid Arthritis and an Inadequate Response to Methotrexate: 26-Week Analysis of a Phase 3 Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with active rheumatoid arthritis (RA), 12-week treatment with upadacitinib (UPA) while on background MTX therapy resulted in significant and clinically meaningful improvements in patient-reported outcomes (PROs) compared with placebo (PBO); these improvements with UPA treatment also met or were superior to adalimumab (ADA) treatment.[1] The current analysis evaluated the potential long-term benefits of UPA versus ADA with background MTX on PROs in patients with active RA.

Methods: SELECT-COMPARE (NCT02629159) is an ongoing Phase 3, randomized, double-blind study where patients with moderately to severely active RA and inadequate responses to MTX received UPA 15 mg once daily (QD), ADA 40 mg every other week (EOW), or PBO while on background MTX therapy. PROs included: Patient Global Assessment of Disease Activity (PtGA), pain by visual analog scale (VAS), HAQ-DI, Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), and duration and severity of morning (AM) stiffness. The data cutoff for this analysis was July 6, 2018. Mean changes from baseline and 95% confidence intervals (CIs) were calculated for each PRO at Week 26. The percentages of patients who continued to report improvements ≥ minimum clinically important differences (MCID) in PRO scores at Week 26 were calculated based on those with MCID improvements at Week 12.

Results: Patients treated with UPA or ADA reported clinically meaningful changes from baseline in all PtGA, pain VAS, HAQ, FACIT-F, and duration and severity of AM stiffness at Week 26 (Table). Higher proportions of patients receiving UPA (74% to 84% of patients) continued to have clinically meaningful responses from Weeks 12 to 26 than with ADA (66% to 70% of patients; all P values < 0.05 except FACIT-F).

Conclusion: Clinically meaningful improvements in physical function, pain, fatigue, and AM stiffness were reported by patients with inadequate response to methotrexate with active RA at Week 12 which continued over 26 weeks with UPA 15 mg QD or ADA 40 mg EOW, with higher proportions maintaining these responses with UPA 15mg QD than ADA 40 mg EOW.

Table. Mean change in PRO scores and maintenance of MCID[a] responses at Week 26 (SELECT-COMPARE)					
PRO	Mean change from baseline (95% CI)		Patients maintained response from Week 12 to Week 26, n (%)		
	UPA 15 mg QD	ADA 40 mg EOW	UPA 15 mg QD	ADA 40 mg EOW	*P* Value
PtGA	−37.0 (−39.3, −34.7)	−35.0 (−38.3, −31.6)	379 (80.0)	150 (68.5)	0.001
Pain VAS	−38.0 (−40.2, −35.9)	−36.0 (−39.1, −32.8)	383 (79.3)	157 (69.2)	0.003
HAQ	−0.76 (−0.82, −0.71)	−0.69 (−0.75, −0.62)	363 (78.1)	158 (68.4)	0.006
FACIT-F	10.2 (9.4, 11.0)	9.9 (8.7, 11.2)	306 (74.1)	136 (67.3)	0.080
Severity AM stiffness[b]	−4.1 (−4.3, −3.9)	−3.8 (−4.1, −3.6)	421 (80.0)	182 (70.0)	0.002
Duration AM stiffness[c]	−101.4 (−117.7, −85.0)	−106.8 (−127.8, −85.8)	162 (83.5)	61 (65.6)	0.001

[a]MCID was defined as reduction of ≥10 mm for PtGA and for pain VAS, reduction of ≥0.22 units for HAQ-DI, increase of ≥4.0 points for FACIT-F, reduction of ≥10 mm for severity of AM stiffness and reduction proxied at 1/2 standard deviation of mean baseline value for duration of AM stiffness. [b]Assessed on a numeric scale of 1–10, with 10 being the worst level. [c] Duration in minutes. [d]*P* values comparing the proportion of responders between the UPA 15 mg arm and the ADA 40 mg arm were calculated using a Chi-square test.

Reference:

1. Strand V, et al. Poster FRI0137 presented at EULAR 2019; Madrid, Spain.

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Abstract Number: 1376

Impact of 24- or 26-Week Upadacitinib Monotherapy on Patient-Reported Outcomes in Patients with Moderately to Severely Active Rheumatoid Arthritis and No Prior Use of or an Inadequate Response to Methotrexate: Results from Two Phase 3 Trials

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Treatments, Outcomes, & Measures

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment with upadacitinib (UPA) monotherapy, a selective Janus kinase-1 (JAK-1) inhibitor, resulted in significant and clinically meaningful improvements in patient-reported outcomes (PROs) at Week 12 or 14 in patients with RA with no prior use of MTX (MTX-naïve) and an inadequate response to MTX (MTX-IR).[1,2] The current analysis evaluated the potential long-term benefits of UPA monotherapy on PROs in these patients.

Methods: SELECT-EARLY (NCT02706873) and SELECT-MONOTHERAPY (NCT02706951) are ongoing Phase 3, randomized controlled trials where MTX-naïve or MTX-IR patients (respectively) with active RA received UPA monotherapy (15 mg or 30 mg once daily [QD]) or weekly MTX. Here we report on PROs in SELECT-EARLY and SELECT-MONOTHERAPY patients who continued UPA for 24 or 26 weeks, respectively. PROs included: Patient Global Assessment of Disease Activity (PtGA), pain by visual analog scale (VAS), Health Assessment Questionnaire-Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F; SELECT-EARLY only), and duration and severity of morning (AM) stiffness. Mean changes from baseline and 95% confidence intervals (CIs) were calculated for each PRO at Week 24/26. The percentages of patients who continued to report improvements ≥minimum clinically important differences (MCIDs) at Week 24/26 were calculated among those who reported clinically meaningful changes in a given PRO at Week 12/14 (SELECT-EARLY and SELECT-MONOTHERAPY, respectively).

Results: MTX-naïve patients reported improvements from baseline in all PROs at Week 24 (Table 1). Of MTX-naïve patients reporting improvements ≥MCIDs at Week 12, 83% to 90% treated with UPA 15 mg and 84% to 90% with UPA 30 mg maintained clinically meaningful responses ≥MCIDs at Week 24. MTX-IR patients also reported improvements from baseline across all PROs at Week 26 (Table 2). Of MTX-IR patients reporting improvements ≥MCIDs at Week 14, 84% to 90% treated with UPA 15 mg and 85% to 94% with UPA 30 mg maintained clinically meaningful responses ≥MCIDs at Week 26.

Conclusion: A substantial proportion of MTX-naïve and MTX-IR patients with active RA treated with UPA 15 mg or 30 mg QD monotherapy continued to report clinically meaningful improvements in disease activity, physical function, pain, fatigue, and AM stiffness through Week 24/26.

Reference:

1. Strand V, et al. Poster THU0192 presented at EULAR 2019; Madrid, Spain; 2. Strand V, et al. *Arthritis Rheumatol.* 2018;70(Suppl 10):abstract 2547.

Table 1. Mean changes in PRO scores and maintenance of MCID responses at Week 24 (SELECT-EARLY)

PRO	UPA 15 mg QD			UPA 30 mg QD		
	n	Mean Change from BL (95% CI)	Responders, n/N[a,b] (%)	n	Mean Change from BL (95% CI)	Responders, n/N[a,b] (%)
PtGA	291	−39.7 (−43.1, −36.2)	209/248 (84.3)	280	−42.0 (−45.5, −38.4)	202/230 (87.8)
Pain VAS	291	−41.7 (−45.0, −38.3)	210/249 (84.3)	280	−42.7 (−46.1, 39.2)	214/241 (88.8)
HAQ-DI	291	−0.92 (−1.00, −0.83)	222/248 (89.5)	280	−0.90 (−0.99, −0.82)	217/247 (87.9)
FACIT-F	293	11.5 (10.1, 12.9)	172/207 (83.1)	289	10.2 (8.8, 11.6)	170/203 (83.7)
Severity AM stiffness[c]	290	−4.6 (−4.9, −4.3)	230/262 (87.8)	282	−4.5 (−4.8, −4.1)	236/262 (90.1)
Duration AM stiffness[d]	290	−137.9 (−162.6, −113.1)	100/120 (83.3)	282	−107.7 (−126.1, −89.3)	101/115 (87.8)

[a] Patients who discontinued treatment and missing observations were imputed using non-response imputation. [b] n/N = number of patients reporting improvements ≥MCID at Week 24 / number of patients with MCID response at Week 12. [c] Assessed on a numeric scale of 1–10, with 10 being the worst level. [d] Duration in minutes. BL, baseline.

Table 2. Mean change in PRO scores and maintenance of MCID responses at Week 26 (SELECT-MONOTHERAPY)						
PRO	UPA 15 mg QD			UPA 30 mg QD		
	n	Mean Change from BL (95% CI)	Responders, n/N[a,b] (%)	n	Mean Change from BL (95% CI)	Responders, n/N[a,b] (%)
PtGA	193	−29.9 (−34.1, −25.7)	112/132 (84.8)	197	−34.9 (−38.5, −31.3)	140/158 (88.6)
Pain VAS	193	−30.9 (−35.1, −26.7)	116/139 (83.5)	197	−36.7 (−40.3, −33.1)	138/162 (85.2)
HAQ-DI	193	−0.66 (−0.76, −0.56)	124/140 (88.6)	197	−0.77 (−0.86, −0.68)	136/148 (91.9)
Severity AM stiffness[c]	194	−3.3 (−3.7, −2.9)	144/160 (90.0)	196	−3.9 (−4.2, −3.5)	167/178 (93.8)
Duration AM stiffness[d]	194	−92.9 (−123.5, −62.2)	50/58 (86.2)	196	−95.5 (−120.3, −70.7)	54/60 (90.0)
[a] Patients who discontinued treatment and missing observations were imputed using non-response imputation. [b] n/N = number of patients reporting improvements ≥MCID at Week 26 / number of patients with MCID response at Week 14. [c] Assessed on a numeric scale of 1–10, with 10 being the worst level. [d] Duration in minutes. BL, baseline.						

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Abstract Number: 1377

MTX Withdrawal in Patients with RA Who Achieve Low Disease Activity with Tofacitinib Modified-Release 11 Mg Once Daily + MTX: An Assessment of the Impact on the Short Form-36 Patient-Reported Outcome

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Tofacitinib +/- background MTX has been shown to be an effective treatment for reducing RA disease activity by many validated patient-reported outcomes (PROs),[1,2] including the Short Form-36 Health Survey (SF-36). However, the impact of MTX with-

Table 1. Mean SF-36 component and domain scores, and changes in scores, during the open-label phase of patients who received treatment during the double-blind phase of ORAL Shift

	Tofacitinib MR 11 mg QD monotherapy (N=264)[a]				Tofacitinib MR 11 mg QD + MTX (N=266)[a]			
	Baseline, mean (SD)	Week 12, mean (SD)	Week 24, mean (SD)	Change from baseline to Week 24, mean (SD)	Baseline, mean (SD)	Week 12, mean (SD)	Week 24, mean (SD)	Change from baseline to Week 24, mean (SD)
SF-36 components								
Physical Component Summary	33.75 (8.01)	41.31 (8.81)	43.01 (8.79)	9.26 (8.84)	33.06 (7.59)	40.40 (8.62)	43.49 (8.79)	10.42 (8.73)
Mental Component Summary	43.30 (11.24)	48.41 (9.82)	49.81 (9.31)	6.51 (10.66)	43.38 (11.38)	48.25 (10.14)	49.90 (10.07)	6.51 (9.60)
SF-36 domains								
Physical Functioning	34.34 (9.99)	40.58 (10.12)	42.26 (10.18)	7.92 (10.37)	33.29 (9.80)	39.97 (10.20)	43.07 (10.01)	9.78 (9.67)
Role Physical	35.24 (9.30)	42.55 (9.13)	44.55 (9.13)	9.20 (10.02)	34.46 (8.90)	41.41 (9.51)	43.77 (9.81)	9.31 (9.56)
Bodily Pain	34.09 (7.19)	44.02 (9.30)	46.14 (9.07)	12.05 (9.50)	33.74 (6.68)	42.88 (8.41)	46.36 (8.73)	12.61 (9.80)
General Health Perception	36.82 (8.42)	41.81 (9.00)	43.02 (9.64)	6.20 (8.45)	37.03 (8.32)	42.16 (8.24)	44.58 (8.72)	7.55 (8.54)
Vitality	42.68 (9.15)	49.75 (8.87)	51.34 (9.31)	8.64 (10.67)	42.42 (9.49)	49.05 (9.27)	50.94 (9.52)	8.52 (9.85)
Social Functioning	38.40 (10.93)	45.55 (9.94)	46.87 (9.46)	8.47 (11.40)	38.39 (10.84)	44.44 (9.78)	47.39 (9.18)	9.00 (10.56)
Role Emotional	37.81 (12.77)	43.14 (11.40)	45.45 (10.63)	7.64 (12.08)	36.50 (12.65)	43.04 (10.98)	45.03 (10.86)	8.53 (11.79)
Mental Health	42.30 (10.92)	47.63 (9.72)	48.74 (9.38)	6.43 (10.66)	43.00 (10.78)	47.55 (10.24)	49.45 (10.25)	6.45 (9.57)

[a]PRO data are from all patients who received at least one dose of tofacitinib monotherapy or tofacitinib + MTX during the double-blind phase. The number of patients who completed each outcome measure (n) may be less than the overall N

Value at baseline is defined as the last non-missing measurement on or prior to the first dosing date in the open-label phase

MR, modified-release; MTX, methotrexate; PRO, patient-reported outcome; QD, once daily; SD, standard deviation; SF-36, Short Form-36 Health Survey

Table 2. Changes in SF-36 component and domain scores during the double-blind phase of patients who received treatment during the double-blind phase of ORAL Shift

	Tofacitinib MR 11 mg QD monotherapy N=264[a]		Tofacitinib MR 11 mg QD + MTX N=266[a]		Difference between change from Week 24 to Week 36, tofacitinib monotherapy vs tofacitinib + MTX, LSM (95% CI)	Difference between change from Week 24 to Week 48, tofacitinib monotherapy vs tofacitinib + MTX, LSM (95% CI)
	Change from Week 24 to Week 36, LSM (95% CI)	Change from Week 24 to Week 48, LSM (95% CI)	Change from Week 24 to Week 36, LSM (95% CI)	Change from Week 24 to Week 48, LSM (95% CI)		
SF-36 components						
Physical Component Summary	-1.42 (-2.27, -0.56)	-0.83 (-1.69, 0.03)	-0.60 (-1.44, 0.25)	-0.92 (-1.77, -0.07)	-0.82 (-2.01, 0.37)	0.09 (-1.11, 1.29)
Mental Component Summary	-1.25 (-2.19, -0.30)	-0.65 (-1.65, 0.34)	-0.43 (-1.36, 0.50)	0.03 (-0.95, 1.01)	-0.82 (-2.13, 0.49)	-0.68 (-2.06, 0.70)
SF-36 domains						
Physical Functioning	-1.32 (-2.30, -0.35)	-0.46 (-1.42, 0.51)	-0.88 (-1.85, 0.08)	-0.97 (-1.92, -0.02)	-0.44 (-1.79, 0.92)	0.52 (-0.82, 1.85)
Role Physical	-1.69 (-2.63, -0.76)	-0.88 (-1.89, 0.12)	-0.02 (-0.95, 0.90)	-0.15 (-1.14, 0.84)	-1.67 (-2.97, -0.37)	-0.73 (-2.13, 0.66)
Bodily Pain	-2.03 (-3.07, -0.99)	-1.46 (-2.53, -0.39)	-0.58 (-1.61, 0.45)	-0.71 (-1.76, 0.35)	-1.45 (-2.90, -0.01)	-0.75 (-2.23, 0.73)
General Health Perception	-0.98 (-1.84, -0.12)	-0.43 (-1.30, 0.44)	-0.87 (-1.72, -0.02)	-1.05 (-1.91, -0.18)	-0.11 (-1.30, 1.08)	0.62 (-0.60, 1.83)
Vitality	-1.30 (-2.29, -0.31)	-0.77 (-1.80, 0.26)	-0.15 (-1.13, 0.83)	-0.25 (-1.27, 0.76)	-1.15 (-2.52, 0.22)	-0.52 (-1.94, 0.91)
Social Functioning	-0.98 (-1.95, -0.01)	-1.06 (-2.10, -0.02)	-0.84 (-1.80, 0.12)	-0.55 (-1.58, 0.47)	-0.14 (-1.50, 1.21)	-0.51 (-1.95, 0.93)
Role Emotional	-1.80 (-2.90, -0.69)	-0.83 (-1.89, 0.24)	-0.69 (-1.78, 0.40)	-0.36 (-1.41, 0.69)	-1.11 (-2.64, 0.43)	-0.47 (-1.95, 1.01)
Mental Health	-1.22 (-2.22, -0.22)	-0.34 (-1.40, 0.73)	-0.32 (-1.31, 0.67)	0.12 (-0.93, 1.17)	-0.90 (-2.29, 0.49)	-0.46 (-1.94, 1.02)

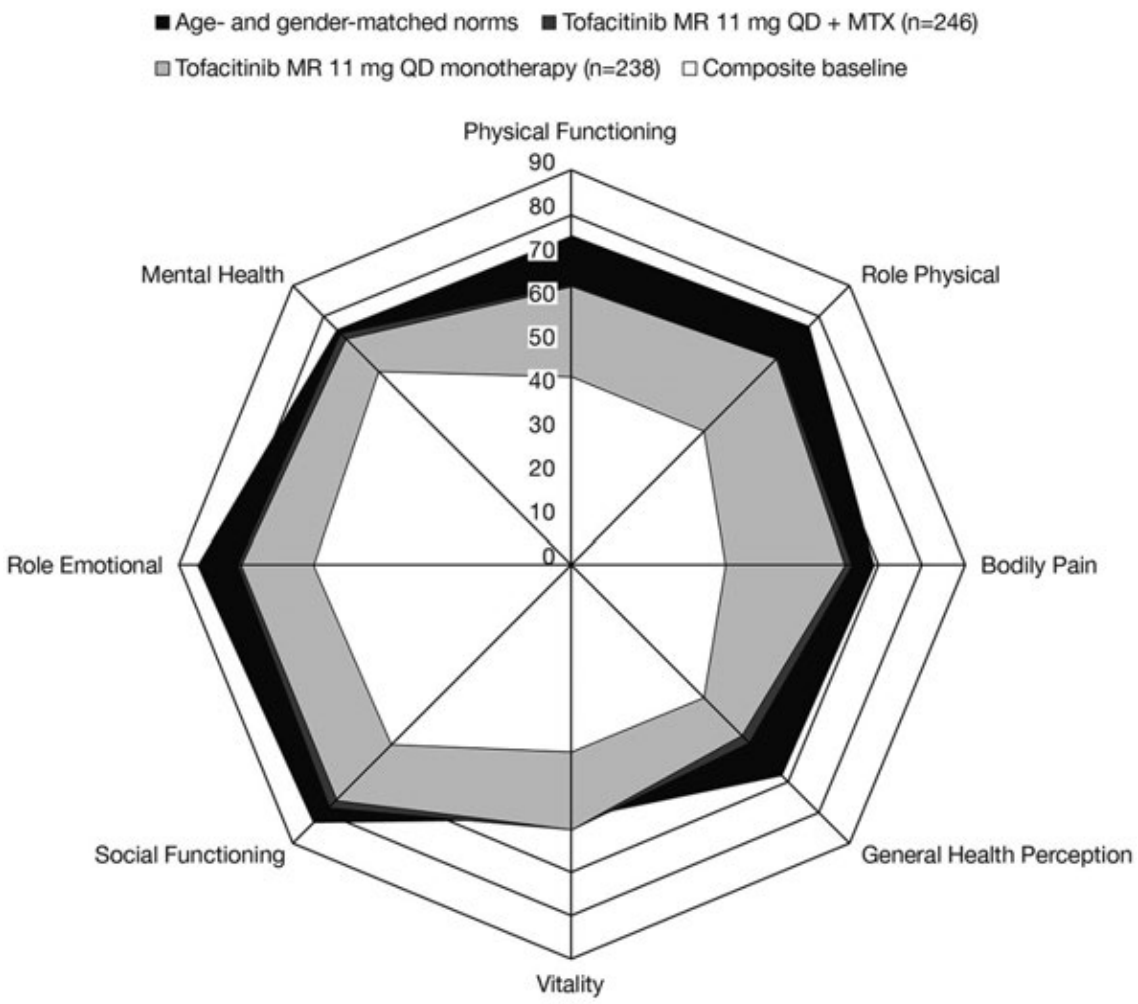
[a]PRO data are from all patients who received at least one dose of tofacitinib monotherapy or tofacitinib + MTX during the double-blind phase. The number of patients who completed each outcome measure (n) may be less than the overall N

Value at randomization is defined at the last non-missing measurement on or prior to the first dosing date in the double-blind phase

Outcomes were analyzed using linear MMRM: change = treatment + visit + treatment x visit + baseline SF-36 + prior use of bDMARD; unstructured covariance model; denominator degrees of freedom estimated using Kenward-Roger method

bDMARD, biologic disease-modifying antirheumatic drug; CI, confidence interval; LSM, least squares mean; MMRM, mixed model repeat measure; MR, modified-release; MTX, methotrexate; PRO, patient-reported outcome; QD, once daily; SF-36, Short Form-36 Health Survey

Figure 1. Mean SF-36 domains expressed on a 0–100 scale at Week 48 in patients who received treatment in the double-blind phase of ORAL Shift



Age- and gender-matched norms are weighted by the age-gender distribution of patients at the screening visit, for the subset of randomized patients.

MR, modified-release; MTX, methotrexate; QD, once daily; SF-36, Short Form-36 Health Survey

drawal in patients (pts) with RA who achieve low disease activity (LDA) or remission with tofacitinib in combination with MTX is unclear.

Methods: ORAL Shift (NCT02831855) was a global Phase 3b/4 study in pts aged ≥ 18 years with moderate to severe RA and an inadequate response to MTX. Pts received open-label (OL) tofacitinib modified-release (MR) 11 mg once daily (QD) + MTX (tofacitinib + MTX) for 24 weeks. Pts achieving LDA (Clinical Disease Activity Index ≤ 10) at Week (W)24 entered the 24-week double-blind (DB) MTX withdrawal phase and were randomized 1:1 to receive tofacitinib MR 11 mg QD + placebo (tofacitinib monotherapy; ie blinded MTX withdrawal) or continue tofacitinib + MTX. The SF-36 includes Physical and Mental Component Summary (PCS and MCS, respectively) and 8 individual domain scores, and was administered to pts during the OL and DB phases. We report the following SF-36 data (norm-based scores) in pts who achieved LDA and were treated in the DB phase: mean scores at baseline (BL), W12 and W24 (OL phase; post hoc); mean changes from BL to W24 (OL phase; post hoc); least squares mean (LSM) changes from W24 to W36 and W48 (DB phase; pre-defined secondary endpoint); and mean scores at W48 (DB phase; post hoc). SF-36 mean scores at W48 were re-expressed on the 0–100 scale, along with BL values combined in a single group, for comparison with SF-36 values of a 1998 US age and gender matched normative population (A/G norms).

Results: In all, 694 pts received tofacitinib + MTX in the OL phase; 530 achieved LDA at W24 and were treated in the DB phase (tofacitinib monotherapy: n=264; tofacitinib + MTX: n=266). Demographics and pt characteristics at OL phase BL were similar between treatment arms. Mean changes from BL to W24 showed improvements in SF-36 PCS, MCS, and all domain scores (Table 1). LSM changes from W24 to W36 and W48 in SF-36 PCS, MCS, and all domain scores (except Role Physical and Bodily Pain at W36) were similar in both treatment arms (Table 2). By W48, Vitality scores exceeded and Mental Health scores were comparable with A/G norms in both treatment arms (Figure 1).

Conclusion: In the OL phase, pts receiving tofacitinib MR 11 mg QD + MTX reported improvements in health-related quality of life by SF-36 PCS, MCS, and domains. In pts who achieved LDA, MTX withdrawal during the DB phase resulted in similar SF-36 scores, compared with patients continuing combination therapy. These findings are consistent with those from ORAL Shift disease activity measures and PROs (primary and secondary efficacy endpoints; reported elsewhere),[3] and reinforce that pts receiving tofacitinib MR 11 mg QD + MTX who achieve LDA, may withdraw MTX up to W48 without significant worsening of PROs.

References:

1. Strand et al. Rheum 2016; 55: 1031-41.
2. Strand et al. Arth Res Ther 2015; 17: 307.
3. Cohen et al. Ann Rheum Dis 2019; 78: A260.

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Abstract Number: 1378

High Baseline Serum IL-6 Predicts Increased Sarilumab Treatment Response for Patient Reported Symptoms and Health-Related Quality of Life Among Rheumatoid Arthritis Patients with Inadequate Response to Methotrexate

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: IL-6 is a key cytokine in the pathogenesis of rheumatoid arthritis (RA) and is elevated in serum and synovial fluid of RA patients. However, the impact of baseline IL-6 levels on patient-reported RA symptoms and health-related quality of life (HRQoL) has not been explored in clinical trials evaluating IL-6 blockade. Sarilumab, a human monoclonal antibody targeting IL-6 receptor alpha, plus methotrexate (MTX) significantly improved clinical and patient reported outcomes vs MTX alone among inadequate responders (IR) to MTX in the MOBILITY randomized controlled trial (NCT01061736). This *post-hoc* analysis evaluated if baseline IL-6 levels can predict greater improvements in symptoms and HRQoL with sarilumab + MTX vs MTX.

Methods: 1193 of 1197 patients in the intent-to-treat population with moderate-to-severely active RA receiving MTX or sarilumab (150 mg or 200 mg subcutaneous every 2 weeks) + MTX, with baseline IL-6 values were included. Serum IL-6 was measured by immunoassay (Quantikine IL-6). Patients were grouped into tertiles according to baseline IL-6 levels (high, medium and low, see Table). Patient-reported RA symptoms and HRQoL were measured at baseline and post-treatment (Weeks [W] 24 and 52): pain visual analog scale (VAS), SF-36 physical (PCS) and mental component scores (MCS), FACIT-Fatigue (FACIT-F) and sleep VAS. Linear regression on changes from baseline in symptoms and HRQoL were performed with IL-6 tertile, treatment, prior biologic use, and region as stratification factors, and baseline IL-6 tertile-by-treatment interactions (with placebo and low IL-6 tertile as references) as fixed effects, to assess the predictivity of IL-6 levels. *P*-values of the interaction for each sarilumab group were provided using placebo and low tertile as references. Pairwise comparisons of symptoms and HRQoL improvements between treatment groups were also performed in each tertile; differences in least squares mean vs placebo, and 95% CIs were calculated.

Results: At baseline, patients in the high IL-6 tertile had greater disease activity, more radiographic structural damage, elevated levels of CRP levels, and poorer symptoms and HRQoL (pain VAS, SF36-PCS, and sleep VAS; data not shown) vs those in lower IL-6 levels ($P < 0.05$) and generally reported greater RA symptoms and HRQoL improvements with sarilumab vs placebo (Table). Significant differences (interaction *P*-value < 0.005) between high and low tertiles were evident in pain VAS (W52) and SF-36 PCS (W24 and W52) with 200 mg; SF-36 MCS with both 150 mg and 200 mg (W52) and FACIT-F scores with both 150 mg and 200 mg (W24 and W52). The incidence of treatment emergent adverse events was similar across IL-6 groups.

Conclusion: Among MTX-IR RA patients, high baseline IL-6 levels may predict better improvements in patient-reported RA symptoms and HRQoL with sarilumab treatment vs placebo than those with low levels. This findings support previous analyses, which showed that across clinical and radiographic endpoints, patients with elevated

Table. Impact of IL-6 at baseline on differences in mean patient-reported RA symptoms and HRQoL improvement for sarilumab versus placebo in MTX-IR patients with RA

Estimated difference (95% CI) in least squares mean change from baseline vs placebo		Sarilumab 150 mg			Sarilumab 200 mg		
		Low IL-6 (n = 126)	Medium IL-6 (n = 129)	High IL-6 (n = 146)	Low IL-6 (n = 128)	Medium IL-6 (n = 147)	High IL-6 (n = 121)
Pain VAS:	Week 24	-5.5 (-11.6, 0.6)	-15.1 (-22.6, -7.5)*	-9.5 (-16.3 , -2.8)	-9.1 (-15.2, -3.1)	-13.4 (-20.8, -6.1)	-15.7 (-22.7, -8.7)
	Week 52	-3.9 (-10.7, 2.8)	-12.5 (-20.5, -4.5)	-12.3 (-19.9, -4.7)	-4.4 (-11.1, 2.3)	-11.7 (-19.7, -3.8)	-15.7 (-23.6, -7.9)*
SF-36 PCS:	Week 24	1.8 (-0.1, 3.6)	2.5 (0.2, 4.8)	4.7 (2.4, 6.9)	1.9 (0.1, 3.7)	3.1 (0.8, 5.4)	5.1 (2.7, 7.4)*
	Week 52	2.3 (0.0, 4.6)	1.8 (-0.8, 4.4)	5.4 (2.9, 8.0)	1.3 (-1.0, 3.5)	2.3 (-0.3, 4.9)	6.7 (4.2, 9.3)**
SF-36 MCS:	Week 24	2.1 (-0.6, 4.7)	1.7 (-1.1, 4.5)	1.2 (-1.4, 3.8)	3.9 (1.4, 6.5)	3.5 (0.8, 6.3)	5.1 (2.4, 7.7)
	Week 52	-1.0 (-4.1, 2.0)	0.5 (-2.4, 3.4)	5.3 (2.1 8.5)**	1.5 (-1.5, 4.4)	1.2 (-1.7, 4.2)	7.1 (3.9, 10.4)*
FACIT-Fatigue:	Week 24	0.6 (-1.4 , 2.7)	3.1 (0.7, 5.5)	4.3 (2.0 , 6.6)*	1.7 (-0.4 , 3.7)	3.3 (0.9 , 5.6)	5.2 (2.8 , 7.5)*
	Week 52	0.2 (-2.4, 2.8)	2.0 (-0.6, 4.6)	5.2 (2.7, 7.8)**	-0.3 (-2.9, 2.3)	2.2 (-0.4, 4.8)	7.3 (4.8, 9.9)**
Sleep VAS:	Week 24	-4.2 (-10.6, 2.2)	-8.1 (-13.7, 1.5)	-8.6 (-15.8, -1.4)	-3.3 (-9.6, 3.1)	-3.3 (-10.7, 4.1)	-12.0 (-19.4, -4.5)
	Week 52	0.5 (-7.0, 7.9)	-5.9 (-14.0, 2.2)	-9.3 (-16.9, -1.6)	-2.1 (-9.5, 5.3)	-3.4 (-11.5, 4.7)	-9.7 (-17.7, -1.8)

Note: Categorization of baseline IL-6 level was based on its tertile distribution (Low: 1.6-9.6 pg/mL ; medium: 9.8-30.7 pg/mL; high (31.2-648.7 pg.mL). * and ** denote significant difference (interaction *P* value < 0.05 and *P* < 0.01, using placebo & low IL6 as references) between high or medium IL6 group and low IL6 group in PRO improvement difference between treatment arm and placebo arm. LS-means differences and 95% confidence intervals are calculated within each IL-6 group.

baseline IL-6 levels had greater responses to sarilumab compared with MTX or adalimumab than those without IL-6 elevations. Prospective validation is warranted to confirm these data.

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Abstract Number: 1379

Glucocorticoid Dose Is Progressively Reduced in Patients with RA Receiving Sarilumab: Results from the Open-Label EXTEND Study

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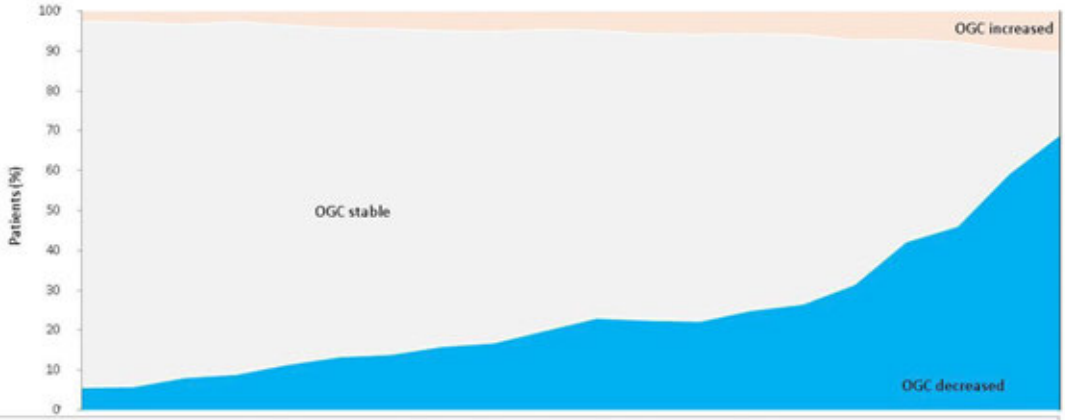
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: EXTEND (NCT01146652) is a long-term, open-label extension (OLE) study of sarilumab for the treatment of RA. This post hoc analysis assessed changes in oral glucocorticoid (OGC) use over time in patients receiving sarilumab 200 mg every 2 weeks (dose reduction to 150 mg every 2 weeks was permitted to manage laboratory abnormalities or per investigator's discretion) in combination with conventional synthetic DMARD (csDMARD) in EXTEND.

Methods: The analysis included patients who had either completed the placebo-controlled Phase 3 studies of sarilumab + csDMARD (NCT01061736 and NCT01709578) or met protocol-defined lack of efficacy after 12 weeks (NCT010709578) and were subsequently treated with sarilumab in the OLE study. Reported total daily oral doses were subsequently converted to prednisone equivalent daily doses (PED) using published conversion tables.[1,2] Patients were categorized into groups by PED dose at enrollment into the OLE: 0–< 5 mg/d, 5–< 10 mg/d and ≥10 mg/d. Patients with a baseline or post-baseline PED < 1 mg/d were imputed to 0 mg/d. PED doses were analyzed over 12-week intervals up to Week 216. Change from baseline for average PED was tested for nominal significance using a Wilcoxon-Pratt-Lehman test for non-parametric data.

Results: In the analysis population, 891/1353 patients (65.9%) had ≥1 record of OGC use. Of the patients with use of OGC, 137 (15.4%) received baseline daily PED of 0–< 5 mg, 515 (57.8%) 5–< 10 mg, and 239 (26.8%) received ≥10 mg. The mean (±SD) PED was 6.3 (±3.1) mg/d at baseline and decreased over the study period (21.3% mean reduction at 4 years; nominal $P < 0.0001$). During the Week 49–60 interval, 660/776 patients (85.1%) had stable PED, 90/776 patients (11.6%) had decreased PED, and 26/776 (3.4%) had increased PED (Figure). This difference increased throughout follow-

Figure. Proportion of patients who had stable OGC dose or whose dose increased or decreased over time



Treatment intervals (weeks)

	1–12	13–24	25–36	37–48	49–60	61–72	73–84	85–96	97–108	109–120	121–132	133–144	145–156	157–168	169–180	181–192	193–204	205–216	217–228	229–240
Patients, N	870	843	820	793	776	762	745	726	702	680	612	556	513	478	446	421	357	236	128	39
Proportion of patients with dose increase	2.4	2.6	3.2	2.5	3.4	4.1	4.3	4.8	5	4.4	4.7	5.6	5.7	5.6	5.8	7.1	7	7.6	9.4	10.3
Proportion of patients with stable dose	91.8	91.3	88.5	88.4	85.1	82.4	81.6	79.1	78.1	75.4	72.1	71.8	71.9	69.2	67.5	61.3	50.7	46.2	31.3	20.5
Proportion of patients with dose decrease	5.8	6	8.3	9.1	11.6	13.5	14.1	16.1	17	20.1	23.2	22.7	22.4	25.1	26.7	31.6	42.3	46.2	59.4	69.2

up, such that 109/236 patients (46.2%) had decreased PED and 18/236 (7.6%) had increased PED by Week 205–216. When grouped by baseline PED, patients with PED ≥5 mg were more likely than patients with PED < 5 mg to decrease their dose. Baseline characteristics and efficacy by PED reduction will be presented.

Conclusion: Long-term treatment of RA with sarilumab was associated with a substantial frequency of decreased OGC dose and the proportion of patients who reduced their OGC dose increased with time. Reductions were more common among patients with baseline prednisone equivalent doses ≥5 mg/d.

Disclosure: R. Fleischmann, AbbVie, 2, 5, Acea, 2, 5, Akros, 5, Amgen, 2, 5, AstraZeneca, 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, 5, Celltrion, 5, Celtrion, 2, 5, Centrexion, 2, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck-Serono, 2, 5, EMD Serono, 2, EMD-Serano, 2, EMD-Serono, 2, Genentech, 2, 5, Genetech, 2, GlaxoSmithKline, 2, 5, GSK, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Merck, 2, Nektar, 2, Novartis, 2, 5, Pfizer, 2, 5, Pfizer Inc, 2, 5, Regeneron, 2, Resolve, 2, Roche, 2, Samsung, 5, Sandoz, 5, Sanofi Genzyme, 2, Sanofi-Aventis, 2, 5, Sanofi-Aventis, 2, 5, Sanofi-Genzyme, 2, Selecta, 2, Tahio, 5, Taiho, 5, UCB, 2, 5; **C. Selmi**, AbbVie, 2, 5, 8, 9, Alfa-Sigma, 5, 8, 9, Biogen, 5, 8, 9, Bristol-Myers Squibb, 5, 8, 9, Celgene, 5, 8, 9, Eli-Lilly, 5, 8, 9, GlaxoSmithKline, 5, 8, 9, Janssen, 2, 5, 8, 9, Merck Sharp and Dohme, 2, 5, 8, MSD, 2, 5, 8, 9, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, Roche, 5, 8, 9, Sanofi-Genzyme, 5, 8, 9, UCB, 5, 8, 9; **M. González-Gay**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 2, 5, EliLilly, 2, 5, Jansen, 2, Janssen, 2, MSD, 2, 5, 8, Novartis, 2, 5, Pfizer, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, Sobi, 5, 8; **H. van Hoogstraten**, Novartis, 1, Regeneron, 1, Sanofi, 1, 3, Zambon (Dr Falk for PhD research), 2; **O. Hagino**, Sanofi, 1, 3, 4; **T. Rajput**, Cytel, 3; **G. St John**, Regeneron, 1, 3, 4, Regeneron Pharmaceuticals, Inc, 1, 3; **F. Buttgereit**, Medac, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, Roche/Chugai, 2, 5, 8, Roche-Chugai, 2, 5, 8, Sanofi-Genzyme, 2, 5, 8; **M. Genovese**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 9, Astellas, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck Serono, 2, 5, Galapagos, 2, 5, Galapagos NV, 2, 5, 9, Genentech/Roche, 2, 5, Gilead, 2, 5, Gilead Science, 9, Gilead Sciences, Inc., 2, 5, 9, GSK, 5, Lilly, 2, 5, 9, Novartis, 2, 5, Pfizer, 2, 5, 9, Pfizer Inc, 2, 5, Pfizer, Inc., 9, Pzier, 9, RPharm, 5, Sanofi Genzyme, 2, 5, Vertex, 2, 5.

Abstract Number: 1380

Patient Characteristics, Treatment Patterns, and Treatment Persistency in Biologic DMARD-Experienced Rheumatoid Arthritis Patients in a US RA Registry

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Multiple treatment options are available for patients with RA. ACR guidelines recommend initiating treatment with a conventional synthetic DMARD (csDMARD). If a patient fails to achieve the treat-to-target goal, ACR guidelines recommend adjusting therapy by adding another csDMARD or switching to another mechanism

		Monotherapy (n=2689)					Combination therapy (n=5917)					
	All initiations	All monotherapy	csDMARDs	TNFi	non-TNFi or JAKi	p-value[1]	All combination therapy	csDMARDs	TNFi	non-TNFi or JAKi	p-value[2]	p-value[3]
	n=8606	*n=2689*	*n=384*	*n=821*	*n=1484*		*n=5917*	*n=1595*	*n=1863*	*n=2459*		
Gender – Female	81%	80%	78%	82%	80%	0.25	81%	79%	82%	83%	0.002	0.28
Age group, n	*n=8589*	*n=2680*	*n=383*	*n=817*	*n=1480*	*0.007*	*n=5909*	*n=1593*	*n=1861*	*n=2455*	*0.21*	*0.69*
18–34	4%	4%	5%	5%	3%		3%	4%	3%	3%		
35–44	9%	10%	6%	11%	10%		9%	8%	10%	9%		
45–54	20%	19%	16%	20%	19%		20%	20%	21%	20%		
55–64	31%	30%	30%	31%	30%		31%	32%	30%	31%		
65–74	26%	26%	26%	24%	27%		27%	26%	27%	27%		
75+	10%	11%	16%	9%	11%		9%	9%	8%	10%		
Race/Ethnicity, n	*n=8540*	*n=2667*	*n=381*	*n=814*	*n=1472*	*0.04*	*n=5873*	*n=1584*	*n=1853*	*n=2436*	*0.45*	*0.25*
White	85%	85%	83%	84%	87%		85%	85%	84%	84%		
Hispanic	7%	7%	7%	8%	7%		7%	7%	7%	7%		
Black	5%	5%	7%	5%	4%		6%	5%	5%	6%		
Asian	1%	1%	1%	1%	1%		1%	1%	1%	2%		
Other	2%	1%	3%	2%	1%		2%	2%	2%	2%		
Education, n	*n=8458*	*n=2641*	*n=371*	*n=808*	*n=1462*	*0.12*	*n=5817*	*n=1565*	*n=1834*	*n=2418*	*0.05*	*0.92*
Primary	2%	2%	3%	1%	2%		2%	3%	2%	2%		
High school	39%	39%	42%	40%	37%		39%	41%	37%	38%		
College/university	59%	59%	54%	59%	60%		59%	57%	61%	60%		
Work Status, n	*n=8405*	*n=2632*	*n=376*	*n=805*	*n=1451*	*<0.001*	*n=5773*	*n=1559*	*n=1816*	*n=2398*	*0.008*	*0.001*
Full time	32%	30%	20%	36%	29%		34%	33%	36%	32%		
Part time	8%	7%	7%	8%	7%		8%	9%	9%	8%		
Disabled	20%	22%	26%	21%	21%		20%	21%	17%	21%		
Retired	30%	31%	36%	27%	32%		29%	29%	29%	30%		
Other	10%	10%	10%	9%	10%		9%	8%	10%	10%		

Table 1. Baseline Demographic Characteristics of Patients by the Type of Treatment Initiated csDMARD, conventional synthetic DMARD; JAKi, Janus kinase inhibitors, TNFi, tumor necrosis factor inhibitors.

of action. The aim of this study was to evaluate patient characteristics and treatment patterns and persistency in RA patients who have previously been treated with a biologic DMARD (bDMARD).

Methods: In the Corrona US RA Registry, we identified instances when adult bDMARD-experienced patients initiated another treatment regimen (index date, between 01/2013–11/2018) and had a 6-month follow-up visit. New regimens were categorized as csDMARDs, tumor necrosis factor inhibitors (TNFi), and non-TNFi bDMARDs or Janus kinase inhibitors (JAKi). Fisher's exact test was used for categorical variables and Kruskal-Wallis or Wilcoxon rank-sum tests were used for continuous variables.

Results: Within 5616 bDMARD-experienced patients, 8606 DMARD initiations met study criteria. Most patients were female (81%) and younger than 65 years of age (**Table 1**).

The index treatment regimens were combination therapy (68.8%) or monotherapy (31.2%). Among monotherapies, csDMARDs comprised 14% and TNFi 31%; among combination therapies, csDMARD comprised 27% and TNFi 31%. In monotherapy, the mean RA disease duration was shortest in csDMARD (11.9 years) and longest in non-TNFi or JAKi (13.6 years); similar trends emerged among combination therapies—11.9 years (csDMARD) and 13.0 years (non-TNFi or JAKi; **Table 2**).

The overall 6-month treatment persistency was 74%, similar in both monotherapy and combination therapy. At 12 months, 52% of patients on monotherapy and 54% of those on combination therapy persisted on their index treatment (**Table 3**). Based on unadjusted analyses, persistency varied based on drug class among monotherapies at both 6 months (non-TNFi or JAKi 79%, csDMARDs 70%, TNFi 68%) and 12 months (non-TNFi or JAKi 55%, csDMARD

		Monotherapy (n=2689)					Combination therapy (n=5917)					
	All initiations	All monotherapy	csDMARDs	TNFi	non-TNFi or JAKi	p-value[1]	All combination therapy	csDMARDs	TNFi	non-TNFi or JAKi	p-value[2]	p-value[3]
	n=8606	*n=2689*	*n=384*	*n=821*	*n=1484*		*n=5917*	*n=1595*	*n=1863*	*n=2459*		
Lifestyle characteristics												
Smoking history, n	*n=8539*	*n=2662*	*n=380*	*n=815*	*n=1467*	*0.73*	*n=5877*	*n=1584*	*n=1849*	*n=2444*	*0.51*	*0.10*
Never smoked	49%	51%	50%	50%	51%		49%	47%	49%	49%		
Former smoker	32%	31%	28%	32%	32%		32%	32%	32%	32%		
Current smoker	19%	18%	23%	18%	17%		19%	21%	19%	19%		
Disease characteristics												
Duration of RA (years)	*n=7221*	*n=2251*	*n=326*	*n=709*	*n=1216*	*<0.001*	*n=4970*	*n=1399*	*n=1590*	*n=1981*	*<0.001*	*0.003*
Mean (SD)	12.5 (10.2)	13.0 (10.7)	11.9 (10.1)	12.6 (10.9)	13.6 (10.6)		12.2 (9.9)	11.9 (10.0)	11.4 (9.5)	13.0 (10.2)		
CCP status	*n=3717*	*n=1080*	*n=149*	*n=349*	*n=582*	*0.46*	*n=2637*	*n=740*	*n=838*	*n=1059*	*0.36*	*0.004*
Never positive	47%	51%	52%	53%	49%		45%	45%	47%	44%		
Positive at least once	53%	49%	48%	47%	51%		55%	55%	53%	56%		
RF status	*n=4413*	*n=1310*	*n=182*	*n=419*	*n=709*	*0.02*	*n=3103*	*n=863*	*n=992*	*n=1248*	*0.55*	*0.24*
Never positive	34%	35%	38%	40%	32%		33%	32%	35%	33%		
Positive at least once	66%	65%	62%	60%	68%		67%	68%	65%	67%		
Erosive disease status	*n=6927*	*n=2163*	*n=315*	*n=687*	*n=1161*	*0.002*	*n=4764*	*n=1345*	*n=1515*	*n=1904*	*<0.001*	*0.01*
Never present	68%	70%	77%	73%	67%		67%	70%	70%	64%		
Ever present	32%	30%	23%	27%	33%		33%	30%	30%	36%		
Rheumatoid nodules status	*n=7270*	*n=2262*	*n=329*	*n=713*	*n=1220*	*0.13*	*n=5008*	*n=1405*	*n=1605*	*n=1998*	*0.51*	*0.82*
Never present	100%	100%	100%	100%	100%		100%	100%	100%	100%		
Positive at least once	0%	0%	0%	0%	0%		0%	0%	0%	0%		
Number of prior DMARDs	*n=8606*	*n=2689*	*n=384*	*n=821*	*n=1484*	*<0.001*	*n=5917*	*n=1595*	*n=1863*	*n=2459*	*<0.001*	*0.64*
Mean (SD)	4.2 (2.0)	4.2 (2.1)	3.3 (1.7)	3.9 (2.1)	4.6 (2.1)		4.2 (2.0)	3.7 (1.8)	4.0 (1.9)	4.6 (2.0)		

Table 2. Baseline Lifestyle and Clinical Characteristics of Patients by the Type of Treatment Initiated csDMARD, conventional synthetic DMARD; JAKi, Janus kinase inhibitors, SD, standard deviation; TNFi, tumor necrosis factor inhibitors.

	All initiations (n=8606)	Monotherapy (n=2689)					Combination therapy (n=5917)					
		All monotherapy	csDMARDs	TNFi	non-TNFi or JAKi	p-value[1]	All combination therapy	csDMARDs	TNFi	non-TNFi or JAKi	p-value[2]	p-value[3]
Persistency of initiation therapy through 6-month visit[4]	*n=8606*	*n=2689*	*n=384*	*n=821*	*n=1484*	*<0.001*	*n=5917*	*n=1595*	*n=1863*	*n=2459*	*<0.001*	*0.44*
Discontinued before 6-month visit	26%	26%	30%	32%	21%		26%	31%	26%	24%		
Persistency through 6-month visit	74%	74%	70%	68%	79%		74%	69%	74%	76%		
Persistency of initiation therapy through 12-month visit[4]	*n=4999*	*n=1540*	*n=205*	*n=501*	*n=834*	*0.02*	*n=3459*	*n=887*	*n=1135*	*n=1437*	*0.44*	*0.12*
Discontinued before 12-month visit	47%	48%	52%	52%	45%		46%	46%	47%	45%		
Persistency through 12-month visit	53%	52%	48%	48%	55%		54%	54%	53%	55%		

Table 3. Treatment Persistency by the Type of Treatment Initiated bDMARD, biologic DMARD; csDMARD, conventional synthetic DMARD; JAK, Janus kinase; JAKi, JAK inhibitors, SD, standard deviation; TNFi, tumor necrosis factor inhibitor. 1) P-value compares the difference among the 3 monotherapies. 2) P-value compares the difference among the 3 combination therapies. 3) P-value compares the difference between all monotherapies and combination therapies. 4) The 6-month visit is defined as a follow up visit occurring ≥3- and ≤9-months following initiation, and the 12-month visit is defined as a follow up visit occurring >9 and ≤15 months following initiation. Based on the cohort inclusion criteria, all patients have a 6-month visit but not all patients have a 12-month visit, which is reflected in the lower sample size for persistency through the 12-month visit. Note 1: p-values were calculated based on Fisher's exact tests for categorical variables; the Kruskal-Wallis tests (3 group comparisons) or Wilcoxon rank sum tests (2 group comparisons) for continuous variables. For ease of interpretation, some tests for categorical variables were calculated based on collapsed groups (eg, Age <55 vs Age ≥55, White vs non-White for race, college/university vs others for education, full-time vs others for work status, and current vs other for smoking). P-values are presented to aid with establishing patterns; care must be taken since we have not formally accounted for the multiple comparisons. Note 2: Note that discontinuation is defined as discontinuation of the index DMARD, no matter whether the patient added another DMARD following initiation of the index DMARD. This is particularly relevant for index csDMARD initiations, because patients may add a bDMARD/JAK while continuing to receive the index csDMARD. In contrast, for index bDMARD initiations, patients will generally need to discontinue the index bDMARD in order to switch to a different bDMARD.

48%, TNFi 48%). Similar results were seen among combination therapies at 6 months (non-TNFi or JAKi 76%, csDMARDs 69%, TNFi 74%) and 12 months (non-TNFi or JAKi 55%, csDMARD 54%, TNFi 53%; **Table 3**).

Conclusion: In bDMARD-experienced patients, demographic and clinical characteristics varied depending on the type of next treatment, most of which were combination therapy. csDMARD patients demonstrated low (48%–54%) 12-month persistence, suggesting a substantial unmet need in this patient population. Persistency differed among the different drug groups both for monotherapy and combination therapy. Clinicians need to closely monitor patients and revise therapy as needed in this patient population.

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Abstract Number: 1381

High Serum IgA and High Proportion of Activated Th17 and Activated Treg Cells Are Predictive Biomarkers for Remission Achievement with Abatacept in Patients with Early, Seropositive Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Abatacept (ABT) is a soluble fusion protein, which links cytotoxic T-lymphocyte-associated protein 4 to the modified Fc portion of IgG1. Seropositivity and a shorter disease duration are well known to be associated with response to ABT in patients with rheumatoid arthritis (RA), however, discrimination of seropositive patients who will respond to ABT is still challenging. The aim of this study is to identify predictive biomarkers for remission achievement with ABT in patients with seropositive RA.

Methods: We enrolled patients with seropositive RA (rheumatoid factor and/or anti-cyclic citrullinated peptide antibody [anti-CCP] positive) who had started ABT from 2010 through 2018 in Keio University Hospital. Early RA was defined as ABT initiation within two years from diagnosis with erosion score less than three in hand X-rays. Laboratory tests and immunophenotyping were conducted before ABT initiation and at 6 months, and compared between patients in remission and non-remission group according to clinical disease activity index (CDAI) at 6 months.

Results: One hundred and three seropositive RA patients who were treated with ABT were enrolled. Among them, 24 and 79 patients were classified into early and established RA, respectively. While in early RA, patients in remission showed higher serum IgA levels, anti-CCP titre and neutrophil count than patients in non-remission (351 mg/dL vs 289 mg/dL, p=0.12; 304 IU/mL vs 156 IU/mL p=0.06 and 6437/uL vs 4751/uL, p=0.10, respectively), no specific laboratory finding was identified in established patients. Receiver operating analysis demonstrated an optimal cut-off value of baseline serum IgA levels, anti-CCP titre, and neutrophil count to predict CDAI remission achievement in early RA as 342 mg/dL with sensitivity of 66.7%, specificity of 86.7%, and area under the curve (AUC) of 0.659, 330 IU/mL with sensitivity of 44.4%, specificity of 86.7%, and AUC of 0.741, 6200/uL with sensitivity of 55.6%, specificity of 86.7% and AUC of 0.704, respectively. In immunophenotyping analysis of peripheral blood of 33 patients (10 early and 23 established patients), primary component analysis demonstrated that the early patients and the established patients in remission made different clusters (Figure 1A-C). The proportion of activated Th17 (aTh17) cells and activated Treg (aTreg) cells were significantly higher in the early patients in remission compared to those in non-remission (aTh17/Th17, 2.86 % vs 1.0 %, p=0.01; aTreg/Treg, 34.3% vs 16.6%, p=0.02), while this difference was not seen in established RA (Figure 1D). Serum IgA at baseline and change in the proportion of effector memory CD4 T cells, and the count of neutrophil at baseline and change in the proportion of effector CD4 T cells were significantly correlated in early RA (Figure 2). Furthermore, the changes were also significantly correlated with changes in CDAI.

Conclusion: We identified serum IgA titer and the count of neutrophil were predictive biomarkers for response to ABT in patients with seropositive and early RA. Immunophenotyping analysis suggested they might reflect upregulation of effector helper T cell subsets, which could be inhibited by ABT.

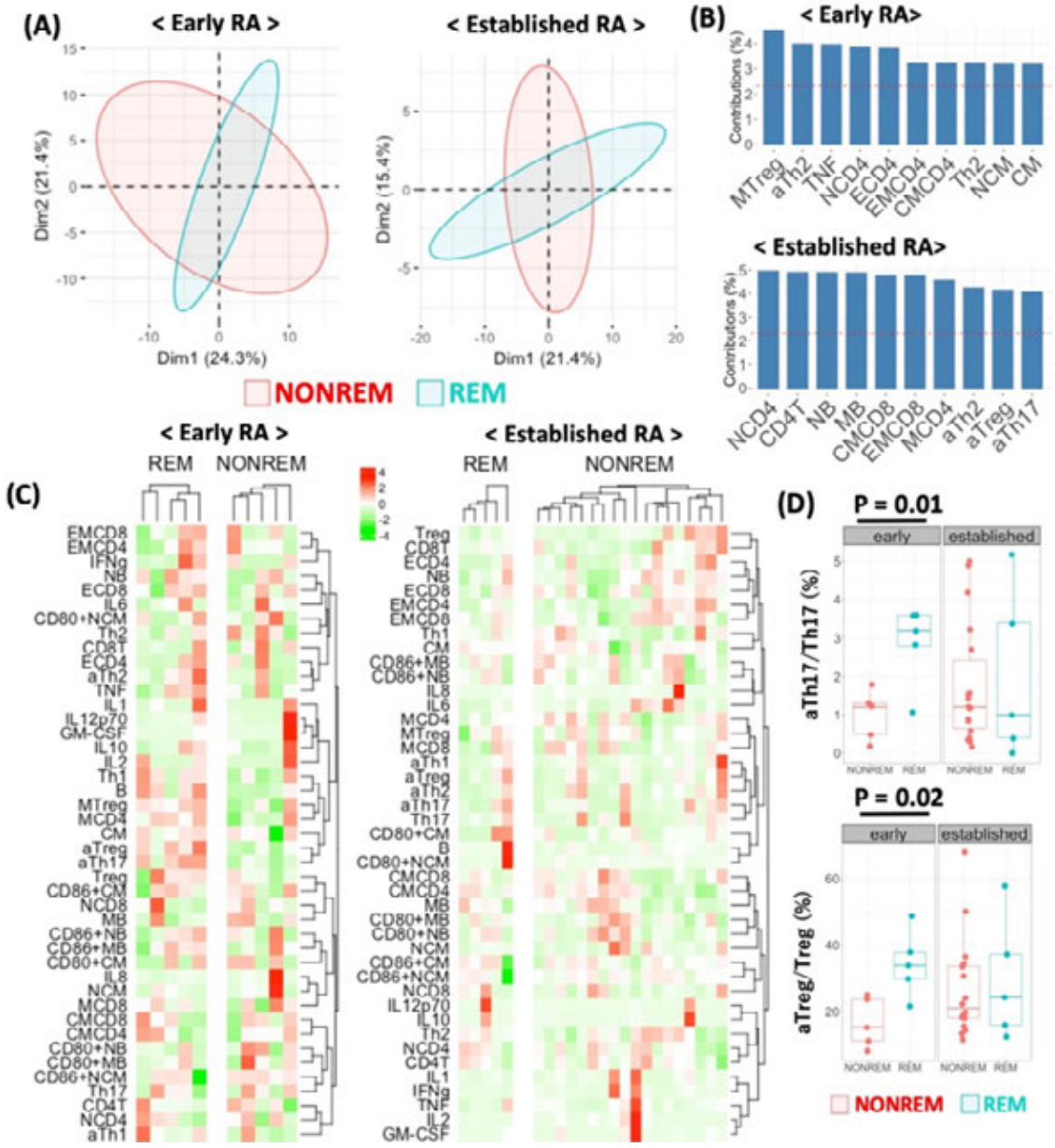

Figure 1. Immunophenotyping analysis before ABT initiation. A, Primary component analysis using immunophenotyping data. B, Top 10 of variables which contributed to make clusters in figure 2A. C, Hierarchical clustering analysis with heatmap using cell subpopulations. D, Comparison of the proportion of activated Th17 (above) and activated Treg (below) between remission and nor-remission group in patients with early RA and established RA. aTh1, activated Th1; aTh2, activated Th2; aTh17, activated Th17; aTreg, activated regulatory T cell; B, B cell; CM, classical monocyte; CMCD4, central memory CD4 T cell; CMCD8, central memory CD8 T cell; ECD4, effector CD4 T cell; ECD8, effector CD8 T cell; EMCD4, effector memory CD4 T cell; EMCD8, effector memory CD8 T cell; GM-CSF, granulocyte macrophage colony-stimulating factor; IL, interleukin; MB; memory B cell; MTreg, memory regulatory T cell; NB, naive B cell; NCD4, naive CD4 T cell; NCD8, naive CD8 T cell; NCM, non-classical monocyte; NONREM, non-remission; REM, remission; Treg, regulatory T cell.

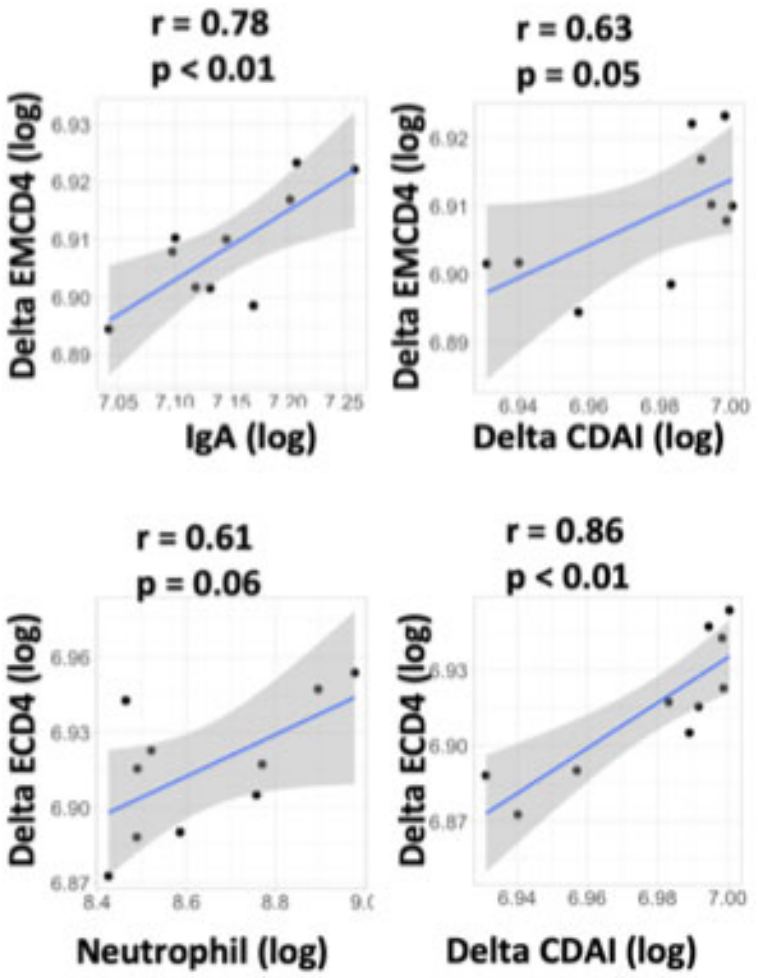

Figure 2. Association between immunophenotyping data, IgA and neutrophil. Scatter plot of IgA and change of the proportion of effector memory CD4 T cells (top left), change of CDAI and the proportion of effector memory CD4 T cells (top right), neutrophil count and change of the proportion of effector CD4 T cells (bottom left) and change of CDAI and the proportion of effector CD4 T cells (bottom right). CDAI, clinical disease activity index; ECD4, effector CD4 T cell; EMCD4, effector memory CD4 T cell.

Disclosure: J. Inamo, None; **Y. Kaneko**, AbbVie, 2, Astellas, 2, Ayumi, 2, Bristol-Myers, 2, Chugai, 2, Eisai, 2, Eli Lilly, 2, Hisamitsu, 2, Jansen, 2, Kissei, 2, Mitsubishi Tanabe, 2, Pfizer, 2, Sanofi, 2, Takeda, 2, UCB, 2; **J. Kikuchi**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **T. Takeuchi**, AbbVie, 2, 5, 8, AbbVie GK, 2, 9, Asahi Kasei, 2, Asahikasei, 2, Asahikasei Pharma Corp., 2, Astellas, 2, 8, 9, Astellas Pharma Inc, 2, Astellas Pharma, Inc., 2, 5, 8, 9, Astra Zeneca, 2, AstraZeneca, 8, AYUMI, 2, 9, AYUMI Pharmaceutical Corporation, 2, BMS, 2, 8, Boehringer-ingelheim, 9, Bristol–Myers K.K., 9, Bristol-Myers, 2, Bristol-Myers Squibb, 8, Chugai, 2, 8, 9, Chugai Pharmaceutical Co, Ltd., 2, Daiichi Sankyo, 2, 8, 9, Daiichi Sankyo Co., Ltd., 2, Eisai, 2, 5, 8, 9, Eisai Co., Ltd., 2, Eli Lilly, 2, 8, Eli Lilly Japan, 9, Gilead Sciences, Inc., 9, GlaxoSmithKline K.K, 9, GSK, 8, Janssen, 2, 8, Janssen Pharmaceutical K.K, 9, Mitsubishi Tanabe, 2, 9, Mitsubishi Tanabe Pharma Co., 2, Mitsubishi-Tanabe Pharma Corp, 2, 8, 9, Nippon Kayaku, 2, Nipponkayaku, 2, 9, Nipponkayaku Co.Ltd., 2, Novartis, 2, 8, Novartis Pharma K.K, 2, 9, Novartis Pharma K.K., 2, Pfizer, 2, 8, Pfizer Japan, 2, 9, Pfizer Japan Inc., 2, Sanofi, 8, Sanofi K.K, 9, Shionogi & Co., 2, Shionogi & Co., LTD., 2, Taiho, 2, 8, 9, Taisho, 9, Taisho Toyama, 2, 8, Takahashi Industrial and Economic Research Foundation, 2, Takeda, 2, 8, Takeda Pharmaceutical Co., Ltd., 2, Teijin, 2, 8, UCB, 8, 9, UCB Japan, 9.

Abstract Number: 1382

The Efficacy of Low Dose Prednisone for Remission Induction in Newly Diagnosed Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoids (GCs) are commonly used in RA patients as remission induction monotherapy or as bridging therapy when starting DMARD/biologic therapy. Despite the ubiquity of GC use in RA treatment, agreed upon standard dosages, particularly for remission induction in newly diagnosed patients, remain elusive. Past studies indicated that the well-known long term adverse effects of GCs are directly related to cumulative dose. Therefore, identification of the lowest GC dose that reproducibly induces remission is imperative. The purpose of our study was to assess the response of newly diagnosed RA patients to low dose prednisone monotherapy (defined as less than or equal to 10 mg/day).

Methods: We conducted a chart review for new diagnoses of RA (ICD-9 714) from January 1, 2005 to September 1, 2018 at Trinity Health Group in Minot, ND. Patients treated with $\leq$ 10 mg prednisone daily for at least six weeks were included. Those previously treated with a DMARD or already started on a GC upon referral were excluded. Disease severity was calculated using the Disease Activity Score (DAS28-ESR). Response to treatment was determined based on the change in the DAS28-ESR score before and after treatment. The European League Against Rheumatism (EULAR) response criteria was used to categorize response to therapy as good, moderate, or no response.

Results: A total of 1386 patients were screened and 201 of them met inclusion and exclusion criteria. The average dose of prednisone was 8 mg daily, ranging between 5 and 10 mg, for an average of 42.2 days. Average age at presentation was 55.1. Majority of them were female (65.7%) and white (91.5%). The average DAS28-ESR score among our entire cohort dropped from 5.1 ± 1.1 at presentation to 2.7 ± 1.3 after 6 weeks of treatment with low dose prednisone ($p < 0.001$). The average DAS28-ESR of our seropositive patients (n=134) dropped from 5.2 ± 1.1 to 2.7 ± 1.3 ($p< 0.001$), and that of our seronegative patients (n=67) dropped from 4.9 ± 1.2 to 2.6 ± 1.1 ($p< 0.001$). As defined by the EULAR response criteria, 69.7% of patients showed a good response to treatment, 20.4% showed a moderate response, and only 10% showed no response. At presentation, 50.2% of the total cohort qualified as having either severe disease according to DAS28-ESR score. After treatment, only 5% qualified for severe disease, and 54.2% had reached remission.

Conclusion: Low dose prednisone monotherapy leads to statistically significant improvement in clinical severity of RA in newly diagnosed patients.

Disclosure: J. Greenmyer, None; **J. Stacy**, None; **J. Beal**, None; **A. Sahmoun**, None; **E. Diri**, None.

Abstract Number: 1383

Glucocorticoid Tapering in Monthly 1-mg Decrements Does Not Result in Clinically Manifest Adrenal Insufficiency in Patients with Rheumatoid Arthritis: Learnings from a Phase 3/4 Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
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Background/Purpose: Systemic glucocorticoids (GCs) are used to treat serious inflammatory diseases but are associated with adverse events. Guidelines recommend tapering GCs to the lowest possible dose and discontinuing them as soon as possible. Physicians have concerns that reductions, even from low doses, may increase disease symptoms or cause adrenal insufficiency, especially in patients receiving GCs long term. The expectation of adrenal insufficiency risk may be inflated by false positives in cortisol testing of patients without relevant symptoms and by a lack of robustly designed GC taper trials. The international, multicenter SEMIRA trial evaluated a taper scheme in rheumatoid arthritis (RA) patients receiving tocilizumab (TCZ) ± conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).[1] The objective of this analysis was to determine whether GC tapering in the SEMIRA trial resulted in any cases of adrenal insufficiency.

Methods: Eligible patients, diagnosed per revised 1987 ACR criteria, had low disease activity or remission for ≥4 weeks and were receiving a stable prednisone regimen (5 mg/day) + TCZ ± csDMARDs for ≥4 weeks. Patients had to have received ≥6 months' total TCZ + GCs (prednisone equivalent 5-15 mg/day). Patients were randomly assigned (1:1) to double-blind continued prednisone 5 mg/day (n = 128) or prednisone taper (n = 131). TCZ ± csDMARDs remained stable during the 24-week study. The prednisone taper consisted of 1-mg decrements every 4 weeks starting at randomization and ending at GC discontinuation (week 16). RA flares were treated with prednisone 5 mg/day for 2 weeks. The primary assessment was maintenance of disease control with GC discontinuation. The protocol provided evidence-based guidance for diagnosis and management of adrenal insufficiency. Confirmatory testing was recommended for patients with suspected adrenal insufficiency, but routine precautionary ACTH stimulation testing was not mandated.

Results: In the taper arm, 65% of patients achieved "treatment success" by meeting all key secondary end point components (maintained low disease activity, experienced no flares, and had no confirmed adrenal insufficiency necessitating replacement therapy) at week 24 versus 77% of continued patients (risk ratio for treatment success, 0.833 [95% CI, 0.714-0.972]; $p = 0.021$). None of the taper patients required ACTH stimulation testing, and no cases of adrenal insufficiency were reported.

Conclusion: SEMIRA demonstrated the usefulness of a new standardized GC dose taper scheme. Two-thirds of patients receiving TCZ underwent successful tapering and could stop GCs entirely, which is higher than the spontaneous 35% discontinuation rate observed in real-world RA patients[2] and underscores the potential to further reduce glucocorticoid burden. Clinical adrenal insufficiency was not observed; thus, routine laboratory testing may be unnecessary in real-world applications of this taper scheme.

Reference:

1. Burmester GR et al. *Arthritis Rheumatol* 2018;70(suppl 10):L18. 2. Yagız B et al. *Arthritis Rheumatol* 2018;70(suppl 10):627.

Disclosure: F. Buttgereit, Medac, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, Roche/Chugai, 2, 5, 8, Roche-Chugai, 2, 5, 8, Sanofi-Genzyme, 2, 5, 8; **J. Nebesky**, F. Hoffmann La-Roche, Inc., 3, 4; **G. Burmester**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma., 5, 8, AbbVie Inc., 5, 8, BMS, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Merck Shar & Dohme, 5, 8, MSD, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche, Sanofi-Genzyme, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Union Chimique Belge, 2, 5, 8; **C. Bernasconi**, Roche, 5; **M. John**, Roche, 3, 4; **M. Donath**, Roche, 5, Roche, MSD, NovoNordisk, Lilly, Boehringer Ingelheim, AstraZeneca, 5.

Abstract Number: 1384

Duration of Oral Corticosteroid Therapy Does Not Change with the Addition of a Parenteral Injection: Results from a Real-World Canadian Early RA Cohort

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SESSION INFORMATION
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Session Title: RA – Treatments Poster II: Established Treatments
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Session Time: 9:00AM–11:00AM

Background/Purpose: Synthetic glucocorticoids (steroids) are recommended for and commonly used in rheumatoid arthritis (RA) as initial "bridge therapy", acting to rapidly reduce the inflammatory response and associated symptoms. Current treatment guidelines in several countries recommend short-term use at a low dose, and tapered quickly due to side effect profile. Steroids are given as oral alone and often combined with parenteral (intramuscular and intra-articular) formulations; patients may receive both to control RA inflammation, perhaps with the intent of being able to shorten the duration of exposure to steroids. The objective of this study was to compare duration of oral steroid exposure among those who receive oral monotherapy to those who receive both oral and parenteral formulations.

Methods: Data were from patients with classifiable early RA enrolled in a nationwide real-world early rheumatoid arthritis cohort, with at least 24 months of follow-up. Patients were stratified based on steroid use (oral only vs combination parenteral and oral, regardless of DMARD exposure) within the first 3 months, to account for a potential lag time for the treating rheumatologist to decide steroid initiation was necessary. Persons who already received steroids before study entry were excluded, to avoid prevalent user bias. Parenteral use without an oral steroid was not con-

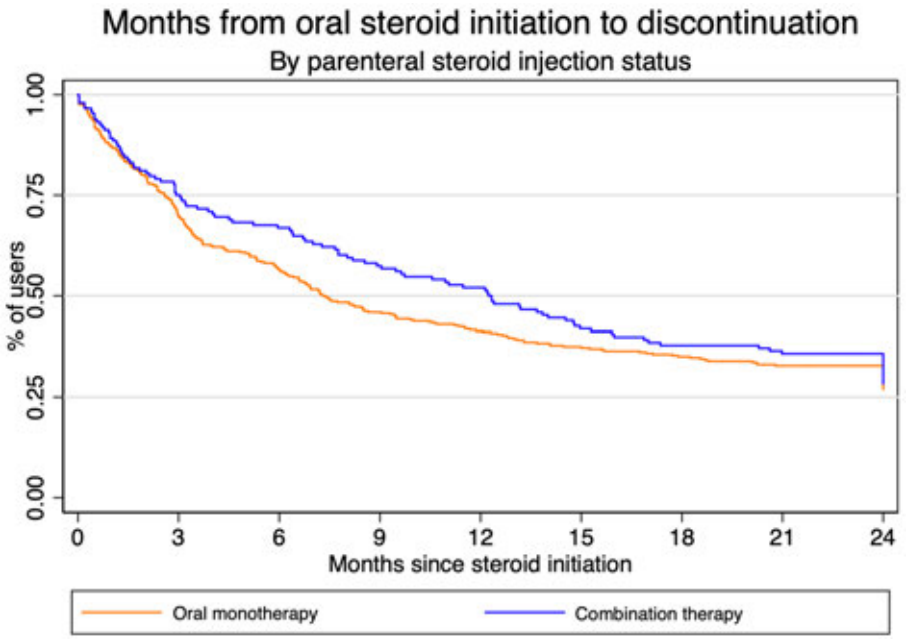

Figure 1. Immunophenotyping analysis before ABT initiation. A, Primary component analysis using immunophenotyping data. B, Top 10 of variables which contributed to make clusters in figure 2A. C, Hierarchical clustering analysis with heatmap using cell subpopulations. D, Comparison of the proportion of activated Th17 (above) and activated Treg (below) between remission and nor-remission group in patients with early RA and established RA. aTh1, activated Th1; aTh2, activated Th2; aTh17, activated Th17; aTreg, activated regulatory T cell; B, B cell; CM, classical monocyte; CMCD4, central memory CD4 T cell; CMCD8, central memory CD8 T cell; ECD4, effector CD4 T cell; ECD8, effector CD8 T cell; EMCD4, effector memory CD4 T cell; EMCD8, effector memory CD8 T cell; GM-CSF, granulocyte macrophage colony-stimulating factor; IL, interleukin; MB; memory B cell; MTreg, memory regulatory T cell; NB, naive B cell; NCD4, naive CD4 T cell; NCD8, naive CD8 T cell; NCM, non-classical monocyte; NONREM, non-remission; REM, remission; Treg, regulatory T cell.

sidered in this analysis, due to an inability to reliably ascertain duration of exposure from an injection. Kaplan-Meier survival curves were constructed to compare steroid persistence time between oral and combination routes of administration, and differences between curves were tested using the log-rank test.

Results: Of 1,573 participants recruited to the overall study between 2007-2017 with at least 24 months of follow-up, 533 (35%) received either oral or combination steroids. Combination steroid users were less likely to be female, to have a higher education and to be currently employed **(Table).** Disease activity at 3 months was highest in the combination steroid groups, as were the physician and patient global assessments of disease. The median duration of oral steroid use did not differ significantly between those receiving oral or combination steroids when parenteral steroid injections were given within the first 3 months of follow-up (7 months oral monotherapy versus 11 months combination, Mann-Whitney U test p-value = 0.20). Throughout follow-up, the discontinuation patterns were similar (**Figure),** and there was no difference in Kaplan-Meier survival curves (p-value = 0.29).

Conclusion: Combination steroids were used in people with more active disease, but combining oral and parenteral steroids did not reduce the duration of oral steroid treatment in this prospective observational cohort compared with those receiving oral steroids alone nor did they reduce disease activity more so than oral steroids. The subset of patients receiving combination steroids may have more persistent disease, and may benefit from closer monitoring and use of more intensive DMARD or other advanced therapeutic strategies.

Table: Characteristics of participants, by steroid route, in first three months of CATCH study follow-up

	Oral Only (n=386)	Combination (n=157)
Age in years	57 (15)	55 (14)
Female	267 (69%)	101 (65%)
Education > high school	220 (57%)	76 (48%)
Currently employed	192 (50%)	71 (45%)
Body mass index, kg/m^2	28.1 (6.0)	29.4 (5.3)
Underweight (<18.5)	3 (1%)	2 (1%)
Normal (18.5-24.9)	76 (20%)	28 (18%)
Overweight (25.0-29.9)	73 (19%)	33 (21%)
Obese (>=30.0)	64 (16%)	42 (27%)
Missing	*170 (44%)*	*52 (33%)*
Current or past smoker	226 (59%)	101 (64%)
Number of comorbidities other than RA		
0	79 (21%)	34 (22%)
1	90 (24%)	32 (21%)
2	86 (22%)	25 (16%)
3 or more	128 (33%)	65 (42%)
Symptom duration at study entry, months	5.4 (3.0)	5.2 (2.8)
Morning stiffness ≥1 hour	242 (63%)	103 (66%)
Seropositive	240 (62%)	109 (69%)
DAS28-ESR score at 3 months, (0-9.4)	3.5 (1.5)	4.1 (1.6)
Remission (< 2.6)	73 (19%)	25 (16%)
Low (2.6 – 3.2)	41 (11%)	12 (8%)
Moderate (> 3.2 – 5.1)	87 (22%)	48 (30%)
High (> 5.1)	185 (48%)	72 (46%)
Physician global assessment, 0-10	3 (2)	3 (3)
Patient global assessment, 0-10	4 (3)	5 (3)
Methotrexate use	337 (87%)	137 (87%)
Among users, dose >=20 mg/week	242 (72%)	

Continuous variables are presented as mean (standard deviation), and categorical variables as number (%).

Figure 2. Association between immunophenotyping data, IgA and neutrophil. Scatter plot of IgA and change of the proportion of effector memory CD4 T cells (top left), change of CDAI and the proportion of effector memory CD4 T cells (top right), neutrophil count and change of the proportion of effector CD4 T cells (bottom left) and change of CDAI and the proportion of effector CD4 T cells (bottom right). CDAI, clinical disease activity index; ECD4, effector CD4 T cell; EMCD4, effector memory CD4 T cell.

Disclosure: K. Andersen, National Heart, Lung and Blood Institute (NHLBI) Pharmacoepidemiology T32 Training Program (T32HL139426-01)., 2, National Heart, Lung and Blood Institute Pharmacoepidemiology T32 Training Program (T32HL139426-01)., 2; **O. Schieir**, None; **M. Valois**, None; **S. Bartlett**, Abbie, 2, Abbvie, 2, 5, Bayer, 5, International Society of QOL Research, 6, Janssen, 5, 8, Lilly, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, Pfizer Inc, 8, PROMIS International, 6, UCB, 5, 8; **L. Bessette**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, Amgen, BMS, Janssen, Roche, UCB Pharma, AbbVie Inc, Pfizer, Merck, Celgene, Sanofi, Eli Lilly, and Novartis., 2, 5, 8, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Bristol-Myers-Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5; **G. Boire**, Abbvie, 2, Amgen, 2, 5, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, Eli Lilly, 2, 5, Lilly, 2, 5, Merck, 2, 8, Novartis, 2, Pfizer, 2, 5, 8; **G. Hazlewood**, None; **C. Hitchon**, Pfizer, 2, UCB, 2, UCB Canada, 2; **E. Keystone**, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 5, Astra-Zeneca, 5, Biotest, 5, BMS, 2, 5, 8, Celltrion, 5, Crescendo, 5, Crescendo Bioscience, 5, F. Hoffmann-La Roche Inc, 2, 5, 8, Genentech, 5, Genentech Inc., 5, Genzyme, 5, Gilead, 2, 5, Gilead Sciences, Inc., 5,

Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 5, 8, Pfizer, 2, 5, 8, Pfizer Pharmaceuticals, 2, 5, 8, Roche, 2, 5, 8, Sandoz, 5, Sanofi, 2, 5, 8, Sanofi-Aventis, 2, 8, UCB, 5, 8; **J. Pope**, AbbVie, 5, Abbvie, 5, Actelion, 5, Actellion, 5, Amgen, 2, 5, AstraZeneca, 2, Astra-Zeneca, 2, Bayer, 2, 5, BMS, 2, 5, Eicos Sciences, 5, Eli Lilly & Company, 5, Eli Lilly and Company, 5, EMERALD, 5, Emerald, 5, Genzyme, 5, Janssen, 5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8; **D. Tin**, None; **C. Thorne**, Abbvie, 2, 5, Amgen, 2, 5, CaREBiodam, 2, Celgene, 2, 5, Centocor, 5, Janssen, 5, Lilly, 5, Medexus/Medac, 5, 8, Merck, 5, Novartis, 2, 5, Pfizer, 2, 5, Sandoz, 5, Sanofi, 5; **V. Bykerk**, AbbVie, 5, Amgen, 1, 2, 3, 5, 8, Brainstorm Therapeutics, 1, 2, 3, 5, 8, Bristol-Myers Squibb, 5, Genentech, 5, Gilead, 5, NIH, 2, Pfizer, 1, 2, 3, 5, 8, Regeneron, 5, Regeneron Pharmaceuticals, Inc, 5, Sanofi, 5, Sanofi/Genzyme-Regeneron, 5, Sanofi-Genzyme/Regeneron, 1, 2, 3, 5, 8, Scipher, 1, 2, 3, 5, 8, The Cedar Hill Foundation, 9, UCB, 1, 2, 3, 5, 8, UCB Pharma, 5; **C. (CATCH) Investigators**, Amgen, 2, Pfizer Canada, 2, AbbVie Corporation, 2, Medexus Inc., 2, Eli Lilly Canada, 2, Merck Canada, 2, Sandoz Canada Biopharmaceuticals, 2.

Abstract Number: 1385

Discontinuation of Oral Glucocorticoid After Initiation of Biological DMARDs Due to a Higher Dose of Methotrexate; A Retrospective Observational Study Based on Data from a Japanese Multicenter Registry Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In the treatment of rheumatoid arthritis (RA), glucocorticoid that provide anti-inflammatory effects is an important drug. We recommend discontinuing of glucocorticoid as soon as possible, but many patients have taken oral glucocorticoid for the long term in daily clinical practice. On the other hand, there are several reports on discontinuation of glucocorticoid due to the initiation of biological disease-modifying antirheumatic drugs (bDMARD). The aim of this study is to examine association of methotrexate (MTX) dose with discontinuation of glucocorticoid after 52 weeks since initiation of 1st bDMARDs.

Methods: This study was based on data from a Japanese multicenter registry, Tsurumai Biologics Communication Registry (TBCR), and enrolled 3119 patients who used bDMARDs from 2008 Oct to 2015 Oct. We examined the status of oral glucocorticoid use after 52 weeks since initiation of bDMARDs as 1st bDMARDs. In predictive analyses, discontinuation of glucocorticoid after 52 weeks since initiation of bDMARDs was used as outcome variable. Factor associated with baseline characteristics at the time of initiation of bDMARDs was assessed with univariate and stepwise forward multivariate logistic regression. Propensity score matching (PS) matching was used to align the patients background with selection bias in observational studies. The adjustment variables were age, disease duration, sex, disease activity, seropositivity, and glucocorticoid dose.

Results: 564 patients who used glucocorticoid and MTX when bDMARDs was initiated as 1st bDMARDs were included (Table 1). 164 cases (29.1%) were discontinued glucocorticoid up to 52 weeks after initiation of bDMARDs. In the multivariate analysis, age (odds ratio (OR) 0.98), MTX dose (OR1.11) and glucocorticoid dose (OR0.87) were

Table 1 Baseline characteristics at the time of initiation of bDMARDs

	n=564
Age, years	57.2±13.5
Disease duration, years	8.8±9.2
Female, %	80.5
DAS28-CRP	4.70±1.16
Seropositivity, %	88.8
MTX dose, mg/week	8.0±2.7
MTX ≤ 8mg, %	75.9
MTX > 8mg, %	24.1
Glucocorticoid dose, mg/day	4.8±2.1
Glucocorticoid dose ≤ 5mg, %	85.5
Glucocorticoid dose > 5mg, %	14.5
TNF inhibitor use, %	87.8
Infliximab, %	35.5
Etanercept, %	30.3
Adalimumab, %	14.7
Golimumab, %	5.3
Certolizumab pegol, %	2.0
Tocilizumab, %	4.4
Abatacept, %	7.8

Table 2 Factor associated with baseline characteristics at the time of initiation of bDMARDs

	Continuation (n=400)	Discontinuation (n=164)	Univariate Odds ratio (95% CI)	Multivariate Odds ratio (95% CI)
Age, years	58.4 ± 12.9	54.3 ± 14.3	0.98 (0.97-0.99)*	0.98 (0.97-0.99)*
Disease duration, years	9.4 ± 9.4	7.5 ± 8.5	0.98 (0.95-0.99)*	–
Female, %	80.3%	81.1%	1.06 (0.67-1.68)	–
DAS28-CRP	4.78 ± 1.15	4.50 ± 1.16	0.81 (0.69-0.96)*	–
Seropositivity, %	90.0%	86.1%	0.69 (0.38-1.25)	–
MTX dose, mg/week	7.7 ± 2.5	8.8 ± 3.0	1.16 (1.09-1.24)*	1.11 (1.03-1.21)*
Glucocorticoid dose, mg/day	4.9 ± 2.1	4.3 ± 2.1	0.86 (0.78-0.95)*	0.87 (0.78-0.97)*
TNF inhibitor use, %	88.8%	85.4%	0.74 (0.43-1.26)	–

Data are presented as mean±standard deviation. 95% CI, 95% confidence interval; bDMARDs, biological disease-modifying antirheumatic drugs; DAS28, disease activity score in 28 joints; CRP, serum c-reactive protein; MTX, methotrexate; TNF, tumor necrosis factor. *P < 0.05

independently predictive factors of discontinuation of glucocorticoid at the time of initiation of bDMARDs (Table 2). When we adjusted factors of baseline characteristic by using propensity score matching of the patients group taking MTX≤8mg and MTX >8mg, 105 pairs were extracted (Table 3). In the patients group taking MTX >8 mg, discontinuous

Table 3 Baseline characteristic of the patients at the time of initiation of bDMARDs before and after propensity score matching

	before propensity score matching			after propensity score matching		
	MTX≤8mg (n=428)	MTX>8mg (n=136)	p-value	MTX≤8mg (n=105)	MTX>8mg (n=105)	p-value
Age, year*	58.2 ± 13.1	54.2 ± 14.2	0.002	54.7 ± 15.6	54.6 ± 14.4	n.s.
Disease duration, year*	9.6 ± 9.0	6.1 ± 9.3	<0.001	6.0 ± 6.0	5.7 ± 7.5	n.s.
Female, %**	82.9%	72.8%	0.013	78.1%	73.3%	n.s.
DAS28-CRP*	4.76 ± 1.12	4.52 ± 1.24	0.038	4.53 ± 1.26	4.51 ± 1.26	n.s.
Scropositivity, %**	91.0%	82.4%	0.017	85.7%	84.8%	n.s.
Glucocorticoid dose, mg/day*	4.7 ± 1.9	5.0 ± 2.7	n.s.	5.3 ± 2.2	4.9 ± 2.8	n.s.

Data are presented as mean±standard deviation. bDMARDs, biological disease-modifying antirheumatic drugs; MTX, methotrexate; DAS28, disease activity score in 28 joints; CRP, serum c-reactive protein. *Student's t test, **chi-squared test.

rate of glucocorticoid (41.0%) was significantly higher. Regarding the clinical course, DAS28-CRP at baseline was 4.53 in the group of patients taking MTX >8 mg, and 4.51 in the group of patients taking MTX≤8 mg, and there was no obvious significant difference. At 52 weeks, 2.87 in the group of patients taking MTX >8 mg, and 2.59 in the group of patients taking MTX≤8 mg, and there was also no obvious significant difference. Further, there was no obvious significant difference in the rate of change in disease activity.

Conclusion: This cohort study investigated the association with discontinuation of oral glucocorticoid and MTX dose in the patients treated with bDMARDs. In the clinical practice, MTX dose at the time of initiation of bDMARDs was predictive factor of discontinuation of glucocorticoid. A higher dose of MTX associated with discontinuation of glucocorticoid in the patients treated with bDMARDs. Glucocorticoid use suggested that it could be decreased or discontinued in the patients treated with bDMARDs.

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Abstract Number: 1386

Association Between Baseline Anti-citrullinated Protein Antibody Status and Response to Abatacept or Non-TNF Inhibitor Therapy in Patients with RA: Results from a US National Observational Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In a US national observational study conducted in a clinical practice setting, patients who were positive (+) for anti-cyclic citrullinated peptide (CCP) antibodies at baseline showed a greater clinical response to treatment with abatacept (ABA), but not an anti-TNF inhibitor (TNFi), compared with those who were anti-CCP negative (–).[1] This study assessed whether baseline anti-CCP status was associated with response to ABA or non-TNFi in patients with RA.

Table 1. Adjusted mean improvement from baseline in disease and disability outcomes at 6 months, by anti-CCP status, for abatacept or non-TNFi initiators (by time period of drug initiation)

	Abatacept (2/1/2006)			Rituximab (2/1/2006)		
Adjusted outcome*	**Anti-CCP–**	**Anti-CCP+**	**p value**	**Anti-CCP–**	**Anti-CCP+**	**p value**
n	383	599		73	171	
Primary outcome: Δ CDAI	4.12 (0.14)	7.82 (0.12)	0.001	0.87 (0.42)	7.51 (0.26)	0.002
Δ mHAQ	0.00 (0.01)	0.09 (0.00)	<0.001	0.07 (0.02)	0.16 (0.01)	0.076
Δ patient global assessment	2.84 (0.27)	10.03 (0.22)	<0.001	0.63 (1.01)	11.84 (0.51)	0.006
	Abatacept (2/1/2010)			**Tocilizumab (2/1/2010)**		
	Anti-CCP–	**Anti-CCP+**	**p value**	**Anti-CCP–**	**Anti-CCP+**	**p value**
n	331	467		192	207	
Primary outcome: Δ CDAI	3.99 (0.21)	7.85 (0.19)	0.001	5.81 (0.36)	6.26 (0.32)	0.705
Δ mHAQ	0.00 (0.01)	0.09 (0.01)	<0.001	0.05 (0.01)	0.07 (0.01)	0.969
Δ patient global assessment	2.50 (0.34)	9.94 (0.29)	<0.001	8.14 (0.66)	5.68 (0.64)	0.109
	Abatacept (12/1/2012)			**Tofacitinib (12/1/2012)**		
	Anti-CCP–	**Anti-CCP+**	**p value**	**Anti-CCP–**	**Anti-CCP+**	**p value**
n	223	262		202	218	
Primary outcome: Δ CDAI	3.46 (0.16)	5.98 (0.15)	0.103	3.96 (0.15)	4.85 (0.17)	0.912
Δ mHAQ	0.01 (0.01)	0.06 (0.01)	0.245	0.02 (0.01)	0.06 (0.01)	0.348
Δ patient global assessment	0.94 (0.33)	6.74 (0.26)	0.012	5.64 (0.45)	8.70 (0.47)	0.560

Data are presented as mean (standard error). For continuous variables, significance tests used a mixed model linear regression analysis with site as the random effect (to adjust for potential site differences in treatment patterns)

*Adjusted for baseline covariates that differed by CCP status ($p<0.1$)

Δ=change; ABA=abatacept; anti-CCP+=anti-CCP positive, ≥20 U/mL; anti-CCP–=anti-CCP negative, <20 U/mL; CCP=cyclic citrullinated peptide; mHAQ=modified HAQ; mHAQ=modified HAQ; TNFi=TNF inhibitor

Methods: Patients with RA from the Corrona registry, aged ≥18 years, who initiated ABA, rituximab (RTX), tocilizumab (TCZ) or tofacitinib (TOF) from 12/1/2005–2/28/2019 were included. Eligible patients had to have anti-CCP measures at/prior to index date (ABA or non-TNFi initiation date), must never have used ABA prior to index date and had to have 6 months' follow-up after index date. Patient characteristics at index were compared by anti-CCP status (+, ≥20 U/mL; –, < 20 U/mL). Outcomes included changes in CDAI (primary), modified HAQ and patient global assessment (PGA) from baseline to 6 months, and proportion of patients achieving LDA or remission, minimal clinically important difference in CDAI and modified ACR response at 6 months. Predicted mean differences were estimated using mixed-effects linear regression models adjusting for baseline covariates (if $p < 0.1$) with site as a random effect; odds ratios were estimated using a mixed logistic regression model with the anti-CCP– group as a reference and site as a random effect. Responses for ABA, RTX, TCZ and TOF were estimated separately; comparison of responses to ABA and specific non-TNFi were estimated within a similar time period of initiation (2006, 2010 or 2012).

Table 2. Adjusted odds ratios (with confidence intervals) for the association between anti-CCP status and achieving a clinical response to treatment with abatacept or a non-TNFi at 6 months*

	Abatacept	**Rituximab**
Achievement of LDA†	1.71 (1.17, 2.50)	3.41 (1.06, 11.01)
Achievement of remission†	2.46 (1.35, 4.49)	2.88 (0.55, 15.23)
MCID CDAI§	1.67 (1.22, 2.27)	1.08 (0.54, 2.18)
mACR20¶	1.89 (1.32, 2.71)	2.38 (0.95, 5.95)
mACR50¶	3.13 (1.90, 5.14)	3.39 (0.86, 13.42)
mACR70¶	2.90 (1.49, 5.63)	6.97 (0.79, 61.24)
	Abatacept	**Tocilizumab**
Achievement of LDA†	1.82 (1.19, 2.78)	1.30 (0.69, 2.44)
Achievement of remission‡	2.71 (1.38, 5.33)	0.87 (0.39, 1.94)
MCID CDAI§	1.65 (1.17, 2.33)	0.78 (0.48, 1.26)
mACR20¶	1.88 (1.26, 2.80)	0.92 (0.53, 1.59)
mACR50¶	3.45 (1.95, 6.11)	0.89 (0.44, 1.82)
mACR70¶	3.52 (1.65, 7.52)	0.84 (0.34, 2.06)
	Abatacept	**Tofacitinib**
Achievement of LDA†	1.26 (0.72, 2.19)	1.10 (0.64, 1.88)
Achievement of remission‡	2.16 (0.96, 4.86)	0.95 (0.42, 2.13)
MCID CDAI§	1.40 (0.92, 2.11)	0.98 (0.64, 1.51)
mACR20¶	1.72 (1.03, 2.88)	0.99 (0.61, 1.62)
mACR50¶	2.56 (1.20, 5.43)	1.07 (0.56, 2.04)
mACR70¶	3.62 (1.20, 10.91)	1.22 (0.46, 3.28)

For binary outcomes, odds ratios were estimated using a mixed model logistic regression analysis with site as the random effect (to adjust for potential site differences in treatment patterns)

*Adjusted for baseline covariates that differed by baseline CCP status ($p<0.1$)

†CDAI ≤10 (among those with moderate or higher disease activity)

‡CDAI ≤2.8 (among those with LDA or higher)

§Drop of 2 if LDA, drop of 6 if moderate disease activity, drop of 11 if high disease activity

¶mACR based on 2 out of 4 measures (not using ESR or CRP)

CCP=cyclic citrullinated peptide; mACR20/50/70=20/50/70% improvement in modified ACR criteria; MCID=minimal clinically important difference; TNFi=TNF inhibitor

Results: Overall, 982 ABA, 399 TCZ, 244 RTX and 420 TOF initiators were identified. Across treatments, anti-CCP+ (vs anti-CCP–) patients had longer disease duration and were more likely to have erosive changes on X-ray; additionally, a higher percentage were RF+ and more were in ACR functional class III–IV at index. Association of response at 6 months by anti-CCP status is shown in Tables 1 and 2. During most time periods, adjusted mean changes in CDAI, modified HAQ and PGA were significantly higher for anti-CCP+ vs anti-CCP– patients for ABA (Table 1). For ABA-treated patients, the odds of achieving most secondary outcomes were significantly higher for anti-CCP+ vs anti-CCP– groups (Table 2). Adjusted mean change in CDAI and PGA (Table 1) and odds of achieving LDA were significantly higher (Table 2) in anti-CCP+ vs anti-CCP– groups for RTX-treated patients; differences in other secondary outcomes were observed but were not statistically significant (Tables 1 and 2). No significant differences were seen by anti-CCP status for TCZ- and TOF-treated patients. Limitations included sample size and relatively short length of treatment time.

Conclusion: In patients treated with abatacept and RTX, but not TCZ or TOF, those who were anti-CCP+ had a greater clinical response than anti-CCP– patients at 6 months' follow-up post index.

Reference:

1. Harrold LR, et al. *J Rheumatol* 2018;**45**:32–9.

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Abstract Number: 1387

Low Probability of Clinical Worsening Following Switching Biologic DMARD in Patients with RA and Partial Response to Adalimumab

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Guidelines recommend adjusting therapy in patients with RA who fail to reach low disease activity or remission. Partial responders to a TNF inhibitor may decline treatment changes for fear of clinical worsening and losing the response they had so far achieved. Little is known about the likelihood of worsening after switching therapy to a drug with a different mechanism of action, and this limits patients' ability to make informed decisions. We performed a post hoc analysis to assess the effect of switching from adalimumab to sarilumab in patients with RA who partially responded to adalimumab in MONARCH (NCT02332590), a head-to-head study of sarilumab versus

adalimumab monotherapy. At the end of the trial, patients on adalimumab were switched to sarilumab 200 mg q2w for the open-label extension (OLE).

Methods: Thresholds of change in Clinical Disease Activity Index (CDAI) of ±6 and ±12 units were used to define meaningful improvement/worsening, anchored at the OLE baseline (BL). Partial responders to adalimumab or sarilumab were characterized at OLE BL and defined as having had a clinically meaningful change in CDAI (≤–12 if MONARCH BL CDAI >22 or ≤–6 if MONARCH BL CDAI >10 to ≤22) during MONARCH while still having moderate-to-high disease activity (CDAI >10) at OLE BL. Response was assessed by change in CDAI from OLE BL at Week 24. The proportions of partial responders achieving meaningful improvement or worsening were calculated.

Results: There were 369 patients enrolled in MONARCH, of whom 320 (87%) entered OLE—155 switching from adalimumab to sarilumab, 165 continuing sarilumab. Of the patients in OLE, 52% were partial responders at OLE BL: switch, n=91/155 (59%); continuation, n=74/165 (45%). Mean (SE) CDAI at OLE BL was 19.56 (0.86) in switch partial responders and 18.99 (1.02) in continuation partial responders, with mean (SE) change in CDAI from OLE BL at Week 24 of –7.37 (1.10) and –5.52 (0.94), respectively (Table). Based on a CDAI threshold of ±6, improvement in disease activity was observed in 57% (switch) and 43% (continuation), while worsening was observed in 6% and 4% of patients. No change (–6 to +6) was evident in 37% (switch) and 53% (continuation). Based on a CDAI threshold of ±12, improvement in disease activity was observed in 27% (switch) and 17% (continuation), while worsening was observed in 2% and 1%, and no change (–12 to +12) was evident in 71% and 81%, respectively. Other efficacy

Table. Summary of efficacy endpoints among CDAI partial responders*

	Adalimumab→sarilumab*	Sarilumab→sarilumab*
N at OLE baseline	91	74
Week 24 observed cases	83	70
CDAI		
At OLE baseline, mean (SE)	19.56 (0.86)	18.99 (1.02)
Change from OLE baseline to Week 24, mean (SE)	–7.37 (1.10)	–5.52 (0.94)
Improvement in CDAI, n/N (%) of patients		
Change from OLE baseline of –6	47/83 (57)	30/70 (43)
Change from OLE baseline of –12	22/83 (27)	12/70 (17)
Worsening in CDAI, n/N (%) of patients		
Change from OLE baseline of +6	5/83 (6)	3/70 (4)
Change from OLE baseline of +12	2/83 (2)	1/70 (1)
No change in CDAI, n/N (%) of patients		
Change from OLE baseline –6 to +6	31/83 (37)	37/70 (53)
Change from OLE baseline –12 to +12	59/83 (71)	57/70 (81)
Physician Global Assessment		
Change from OLE baseline to Week 24, mean (SE)	–11.28 (1.78)	–5.61 (1.75)
Patient Global Assessment		
Change from OLE baseline to Week 24, mean (SE)	–15.73 (2.28)	–7.47 (1.80)
Swollen joint count (SJC28)		
SJC at OLE baseline, mean (SE)	4.08 (0.34)	4.61 (0.40)
Change from OLE baseline to Week 24, mean (SE)	–1.32 (0.51)	–1.89 (0.33)
Tender joint count (TJC28)		
TJC at OLE baseline, mean (SE)	7.53 (0.56)	7.64 (0.63)
Change from OLE baseline to Week 24, mean (SE)	–3.35 (0.57)	–2.33 (0.67)
DAS28-ESR		
Change from OLE baseline to Week 24, mean (SE)	–1.62 (0.15)†	–0.75 (0.12)

*Partial responders, defined as change in CDAI of −12 (if MONARCH baseline CDAI >22) or −6 (if MONARCH baseline CDAI >10 to ≤22) and CDAI >10 at OLE baseline; †n=84.

measures demonstrated improvements from baseline (Table). No new safety signals emerged during OLE, and the adverse event profile among switch patients was similar to that of continuation patients.

Conclusion: Among adalimumab partial responders who switched to sarilumab, there was a low (6%) likelihood of clinical worsening, and almost all patients (94%) experienced clinical improvement or had no change. These findings can help inform patients' and clinicians' shared decision making when considering changes in RA therapy.

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Abstract Number: 1388

The Association Between Treatment of Abatacept or Other Target Disease-Modifying Anti-rheumatic Drugs and Type 2 Diabetes Mellitus (T2DM)-Related Healthcare Resource Utilization and Costs in Commercially Insured Rheumatoid Arthritis Patients with T2DM

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Type 2 diabetes mellitus (T2DM)-related complications are costly, and there is lack of information regarding the comparative impact of target disease-modifying anti-rheumatic drugs (tDMARDs) on commercially insured rheumatoid arthritis (RA) patients with T2DM. The objective of this study was to compare T2DM-related healthcare resource utilization (HCRU) and associated costs in TNF-a inhibitors (TNFi)-experienced patients with RA and T2DM receiving abatacept, other non-TNFi, or TNFi.

Methods: A retrospective, observational study was conducted with Truven MarketScan (January 1, 2008- March 31, 2018). The study population included TNFi-experienced adult patients with RA and T2DM initiating abatacept, TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab) or other non-TNFi (tocilizumab, anakinra, sarilumab, rituximab, tofacitinib) in the study period. The date of the tDMARD initiation was assigned as the index date. Patients were eligible in the analysis if they had 2+ diagnosis of RA separately at least 7 days, 1+ diagnoses of T2DM or were treated with anti-diabetes medications, and had at least 12 months of continuous enrollment prior to the index date. Patients with T1DM or malignancy were excluded. The follow-up period ended at earliest of (1) end of patient insurance enrollment; (2) end of overall study period; (3) end of index treatment date due to discontinuation or switching. Patients demographics and key clinical characteristics were measured in the baseline period. T2DM-related HCRU and associated costs including inpatient stay, outpatient visits, ER visits, and pharmacy costs were measured on a per-patient-per-month (PPPM) basis (2018 USD). Patients treated with abatacept were matched to TNFi and non-TNFi cohorts separately by propensity score (PS) adjusted with confounders such as comorbidities, HCRU and costs.

Results: A total of 4,322 patients initiating abatacept, non-TNFi or TNFi were identified. Overall, most patients were female (75.6%) with an average age of 58 years (Table 1). Unadjusted results showed abatacept is associated with the lowest T2DM-related hospitalization rates per 1,000 patients per month compared to non-TNFi and TNFi (12.2 vs 15.9 vs 12.8). Moreover, T2DM-related complication costs (PPPM) in abatacept group was the lowest than non-TNFi and TNFi ($798 vs $1,130 vs $823) (Table 2). After propensity score matching, a total of 971 pairs of abatecept vs non-TNFi patients, and 1,065 pairs of abatecept vs TNFi paitents were included in the adjusted results. Patients initiating abatacept had $267 lower adjusted T2DM-related complication costs as compared to non-TNFi and $92 lower costs than TNFi cohorts (Table 3).

Conclusion: TNFi-experienced RA patients with T2DM who initiated abatacept had lower rates of T2DM-related hospitalization and lower costs compared to patients who initiated a TNFi or other non-TNFi, which were shown in both unadjusted and adjusted results. The findings suggest that abatacept may be able to reduce the complications of T2DM and hereby lower the T2DM-related costs in RA patients.

Disclosure: Q. Xia, Bristol-Myers Squibb Company, 3, 4; **X. Han**, Bristol-Myers Squibb, 3, Bristol-Myers Squibb Company, 3; **Y. Bao**, BMS, 1, 3, Bristol-Myers Squibb Company, 3, 4; **V. Patel**, Bristol-Myers Squibb, 3; **V. Rajagopalan**, Bristol-Myers Squibb Company, 5; **F. Lobo**, Bristol-Myers Squibb, 1, 3, Bristol-Myers Squibb Company, 1, 3.

Abstract Number: 1389

Treatment Response to Biologic DMARDs in Patients with RA: A Retrospective Analysis of the RISE Registry

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: ACR guidelines recommend treatment for patients with RA based on baseline (BL) disease activity. In patients with an inadequate response to conventional synthetic DMARDs, escalation to biologic DMARDs is recommended, although specific algorithms are not specified. The aim of this study was to compare treatment

Table 1. Baseline Characteristics

	Overall (N=4322)	Abatacept (n=503)	TNFi (n=2894)	Other tDMARDs (n=925)	p value*
Mean (SD) age, years	59.6 (13.9)	63.6 (12.7)	58.5 (14.1)	61.0 (13.2)	<0.001
Female	3417 (79.1)	407 (80.9)	2252 (77.8)	758 (81.9)	0.015
Race					0.097
White	2795 (64.7)	334 (66.4)	1862 (64.3)	599 (64.8)	
Black	419 (9.7)	50 (9.9)	284 (9.8)	85 (9.2)	
Asian	77 (1.8)	7 (1.4)	56 (1.9)	14 (1.5)	
Other	334 (7.7)	41 (8.2)	219 (7.6)	74 (8.0)	
Missing	697 (16.1)	71 (14.1)	473 (16.3)	153 (16.5)	
Ethnicity					0.055
Hispanic or Latino	290 (6.7)	35 (7.0)	194 (6.7)	61 (6.6)	
Not Hispanic or Latino	3798 (87.9)	455 (90.5)	2529 (87.4)	814 (88.0)	
Missing	234 (5.4)	13 (2.6)	171 (5.9)	50 (5.4)	
Mean (SD) BMI, kg/m^2	30.9 (7.4)	30.6 (7.4)	30.4 (7.3)	30.4 (7.6)	0.867
Prior MTX use documented in RISE	2706 (62.6)	275 (54.7)	1934 (66.8)	497 (53.7)	<0.001
Prior biologic use documented in RISE	241 (5.6)	37 (7.4)	129 (4.5)	75 (8.1)	<0.001
CCI score, mean (SD)	1.5 (1.1)	1.5 (1.0)	1.5 (1.2)	1.4 (1.0)	0.971
Serologic status					0.337
RF+/anti-CCP+	1122 (26.0)	128 (25.4)	734 (25.4)	260 (28.1)	
RF−/anti-CCP+ or RF+/anti-CCP−	952 (22.0)	119 (23.7)	627 (21.7)	206 (22.3)	
RF−/anti-CCP−	2248 (52.0)	256 (50.9)	1533 (53.0)	459 (49.6)	
Disease activity instrument documented					N/A
CDAI	1152 (26.7)	134 (26.6)	786 (27.2)	232 (25.1)	
RAPID3	3166 (73.3)	368 (73.2)	2106 (72.8)	692 (74.8)	
Other	4 (0.1)	1 (0.2)	2 (0.1)	1 (0.1)	
Mean (SD) time between baseline and follow-up disease activity, months	10.1 (3.4)	9.9 (2.7)	10.2 (3.6)	10.0 (3.2)	0.080

Data are n (%), unless otherwise stated

*For comparison between treatment groups

CCI=Charlson Comorbidity Index; RAPID3=Routine Assessment of Patient Index Data 3; RISE=Rheumatology Informatics System for Effectiveness, TNFi=TNF inhibitor, tDMARD=targeted DMARD

response, using disease activity scores, to abatacept (ABA), TNF inhibitors (TNFi) or other non-TNFi targeted (t) DMARDs in patients with RA.

Methods: This was a retrospective, observational cohort study using data from the US-based Rheumatology Informatics System for Effectiveness (RISE) registry. The study period included all observations from inception (June 2014) through December 2017. The index date was the date of first prescription of a new tDMARD. Adult patients (≥18 years) with ≥1 International Classification of Diseases code for RA, a prescription for a new tDMARD, documented results for RF and CCP antibody tests and at least one disease activity score < 6 months before and ≥6 months after index date were included. Covariates were assessed during a 6-month BL period preceding the index date. BL disease activity and changes in disease activity (measured by RAPID3 or CDAI scores) ≥6 months after index date were compared across ABA, TNFi (adalimumab, certolizumab, etanercept, golimumab or infliximab) and other non-TNFi

Table 2. Disease Activity at Baseline and Change From Baseline at ≥6 Months

	Abatacept (n=503)	TNFi (n=2894)	Other tDMARDs (n=925)	p value*
Baseline disease activity				
RAPID3 score†	4.2	4.5	4.9	NA
CDAI score‡	17.8	15.5	15.6	NA
Mean (SD) change from baseline at ≥6 months post index date				
RAPID3†	−0.4 (3.7)	−0.1 (3.7)	−0.1 (4.4)	0.02
CDAI‡	−5.2 (13.9)	−3.1 (11.7)	−3.6 (11.8)	0.11

RAPID3 [0–10]: remission, 0–1; low, >1–2; moderate, >2–4; high, >4–10; RAPID3 [0–30]: remission, 0–3; low, >3–6; moderate, >6–12; high, >12–30. CDAI [0–76]: remission, ≤2.8; low, >2.8–10; moderate, >10–22; high, >22

*For comparison between treatment groups

†Abatacept, n=362; TNFi, n=2078; other tDMARD, n=685

‡Abatacept, n=134; TNFi, n=780; other tDMARD, n=232

NA=not available; RAPID3=Routine Assessment of Patient Index Data 3; tDMARD=targeted DMARD; TNFi=TNF inhibitor

tDMARD (baricitinib, sarilumab, tofacitinib, tocilizumab or rituximab) treatment groups. Disease activity at ≥6 months was compared by treatment and by BL disease activity using validated cut-points (see definitions in footnote below). A one-way ANOVA was used to test patient demographics and the change in RAPID3 and CDAI scores from BL to ≥6 months across treatments.

Results: Of the 4322 patients included, 503, 2894 and 925 patients received ABA, TNFi and other tDMARDs, respectively. The mean (SD) age was 59.6 (13.9) years and the majority were female (Table 1). Mean BL RAPID3 scores were similar between groups and mean BL CDAI scores were highest in the ABA group (Table 2). The improvement in RAPID3 score from BL to ≥6 months was greater with ABA than with TNFi or other tDMARDs (p=0.02). Although not statistically significant, a similar trend was seen for change in CDAI score. After 6 months, the proportion of patients with high disease activity was lower in the ABA vs TNFi or other tDMARD groups, across all BL disease activities: 33% of patients in the ABA group improved improved to lower levels of disease activity at ≥6 months after the index date vs patients in the TNFi (17%) or other tDMARD (24%) groups.

Conclusion: In this retrospective study, abatacept-treated patients were older and had higher BL CDAI scores than comparator groups. Nevertheless, after ≥6 months, abatacept was associated with a trend toward greater improvements in disease activity compared with other treatments, regardless of BL disease activity. More work is needed to understand whether these differences are clinically meaningful.

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Disclosure: X. Han, Bristol-Myers Squibb, 3; **J. Bryson**, Bristol-Myers Squibb, 1, 3, 4; **D. Crosby**, Bristol-Myers Squibb, 1, 3; **M. Evans**, None; **G. Schmajuk**, None.

Abstract Number: 1390

Prediction of Clinical Response to Abatacept in Rheumatoid Arthritis Patients Through the Determination of Anti-Carbamylated Proteins Antibodies Levels

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Carbamylation is a non-enzymatic irreversible post-translational modification of proteins. The presence of anti-carbamylated protein antibodies (anti-CarP) has been observed in rheumatoid arthritis (RA). In particular, it was recently demonstrated that the 16% of anti-citrullinated proteins antibodies (ACPA) negative RA patients had a positivity for anti-CarP, showing a more severe disease course than that of seronegative RA. This study was focused to verify whether anti-CarP antibodies can be used as a predictive factor of clinical response to abatacept (ABA, CTLA4-Ig).

Methods: Sixty rheumatoid arthritis patients (F/M=49/11; media (±standard deviation) of age= 57 (±12.1) years; CRP (C Reactive Protein)-DAS28= 4.59 (±0.99); ACPA positive (n (%))=51 (85); RF positive=35 (58)), treated with ABA were enrolled. A home-made ELISA for anti-CarP immunoglobulin G (IgG) and a commercial anti-CCP3.1 kit (Inova Diagnostic) for ACPA IgG were applied to determine serum levels every six months of therapy. Rheumatoid Factor (RF) IgG (Siemens) was also tested.

Results: At baseline, we found that 30% of our patients were positive for anti-CarP antibodies. Anti-CarP positive patients (n=18) were younger (p=0.01) with a longer disease duration(p=0.05) and with higher levels of CRP ($p< 0.05$), when compared to anti-CarP negative patients (n=42). Considering the entire cohort, a significant reduction of anti-CarP titre after twelve-months of treatment was shown ($p< 0.01$). A significant reduction of CRP-DAS28 in the first six months of therapy was found in the subgroup of anti-CarP positive patients in comparison with the negative ones (p=0.03). No significant results were found by dividing the cohort using the positivity to ACPA and/or RF.

Conclusion: The precocious onset and a longer disease duration in anti-CarP positive patients might suggest them as a specific risk factors for RA in this subgroup of patients. The link between the anti-CarP positivity at baseline and the reduction of disease activity during the first six months of treatment let us to hypothesize that anti-CarP antibodies, but not ACPA and/or RF, could be a predictive factor of a good clinical response to ABA.

Shi J, PNAS USA 2011; Shi J, ARD 2014; Trouw LA, Autoimmun Rev 2012.

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Abstract Number: 1391

Connective Tissue Remodeling Is Differently Modulated by Tocilizumab versus Methotrexate Monotherapy in Patients with Early RA: The AMBITION Study

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SESSION INFORMATION

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Background/Purpose: Response to treatments in Rheumatoid Arthritis (RA) is assessed by symptomatic changes, such as ACR-response and DAS28. However, such assessments do not provide information about the effect of the treatment at tissue level. Chronic inflammation is a harmful mechanism, which manifests in upregulated tissue remodeling and release of extracellular matrix (ECM) metabolites into circulation. Released ECM metabolites are biomarkers of tissue remodeling and give insight to treatment effect at tissue level. The purpose of this study was to investigate if tissue remodeling is modulated by tocilizumab (TCZ) and methotrexate (MTX) in the AMBITION study.

Table 1. ANCOVA comparison between treatment groups and measured biomarkers change to week 8.

Treatment group	Mean change at week 8 (%)	Lower 95%-CI	Upper 95%-CI	Treatment comparison	Difference (%)	p<0.05
Inflammation-driven connective tissue metabolite (C1M)						
Placebo	101	85	116	TCZ vs Placebo	-25	0.0319
MTX	100	90	109	MTX vs Placebo	-1	ns
TCZ	76	66	87	TCZ vs MTX	-24	0.004
Inflammation-driven connective tissue metabolite (C3M)						
Placebo	106	97	79	TCZ vs Placebo	-32	<0.0001
MTX	90	84	95	MTX vs Placebo	-16	0.0072
TCZ	74	69	116	TCZ vs MTX	-16	0.0001
Cartilage degradation metabolite (C2M)						
Placebo	104	92	115	TCZ vs Placebo	-6	ns
MTX	104	98	110	MTX vs Placebo	0	ns
TCZ	98	92	105	TCZ vs MTX	-6	ns
Basement membrane remodeling metabolite (C4M)						
Placebo	104	95	113	TCZ vs Placebo	-37	<0.0001
MTX	89	83	94	MTX vs Placebo	-15	0.0161
TCZ	67	61	72	TCZ vs MTX	-22	<0.0001
C-reactive protein metabolite (CRPM)						
Placebo	109	88	130	TCZ vs Placebo	-36	0.011
MTX	100	88	112	MTX vs Placebo	-9	ns
TCZ	73	61	85	TCZ vs MTX	-27	0.0078
C-reactive protein (CRP)						
Placebo	128	9	54	TCZ vs Placebo	-97	0.0001
MTX	101	79	123	MTX vs Placebo	-27	ns
TCZ	31	90	166	TCZ vs MTX	-70	<0.0001

Methods: The AMBITION study is a phase III RCT in which TCZ monotherapy (8 mg/kg every 4 weeks) was compared to MTX monotherapy (starting at 7.5 mg/kg and titrated to 20 mg/kg) over 24 weeks in patients with early RA. Tissue metabolites were measured in baseline and 8-weeks sera from 387 patients by validated ELISA assays. Connective tissue remodeling was measured by C1M and C3M (type I and III collagen degradation), cartilage degradation by C2M (type II collagen degradation), basement membrane remodeling by C4M (type IV collagen degradation), systemic inflammation by C-reactive protein (CRP) and tissue specific inflammation by CRPM (an MMP-derived CRP metabolite). Comparison between treatment and response groups were done by ANCOVA, Spearman's correlation and Logistic regression adjusted for age, gender, BMI and disease duration.

Results: Connective tissue remodeling biomarkers, C1M and C3M, were significantly ($P< 0.05$) inhibited by TCZ and C3M by MTX ($P=0.0072$) compared to placebo (see table 1). The inhibition of C1M and C3M with TCZ was respectively 24% and 16% greater than that of MTX ($P=0.004$ and $P=0.0001$). C4M was likewise inhibited by both TCZ and MTX, but the effect of TCZ was 22% greater than MTX ($P< 0.0001$). In contrast, TCZ and MTX had minimal effect on C2M when compared to placebo or baseline. MTX had no effect on CRP and CRPM compared to placebo or baseline, whereas TCZ reduced the level of CRP and CRPM to 31% and 73% of baseline. In the patients treated with TCZ none of the tested biomarkers correlated to 8 and 16-week changes in DAS28. In the MTX group changes in C4M and CRPM were correlated to 8-week changes in DAS28 (rho=0.21 and 0.19, $P< 0.05$), whereas only C4M correlated to 16-week changes in DAS28 (rho=0.19, $P< 0.05$). Patients with ACR70 response at week 8 had the highest difference between treatments in the inhibition of C1M; 36% for TCZ and 14% for MTX.

Conclusion: This study shows that tissue remodeling in the RA patients can be differently modulated by Tocilizumab and Methotrexate. Both treatments downregulate tissue remodeling and slower the disease progression. Tocilizumab showed a more tissue-protective effect and greater improvement of the disease symptoms than that of Methotrexate.

Disclosure: P. Drobinski, None; **A. Bay-Jensen**, Nordic Bioscience, 1, 2, 3; **M. Karsdal**, Nordic Biosceince, 1, 3, Nordic Bioscience, 1, 2, 3, 4, 5; **A. Siebuhr**, Nordic Bioscience, 3.

Abstract Number: 1392

The Relationship Between Abatacept Exposure and CD86 Receptor Occupancy in Rheumatoid Arthritis Patients Following Subcutaneous Administration and Its Association to Patient Outcomes

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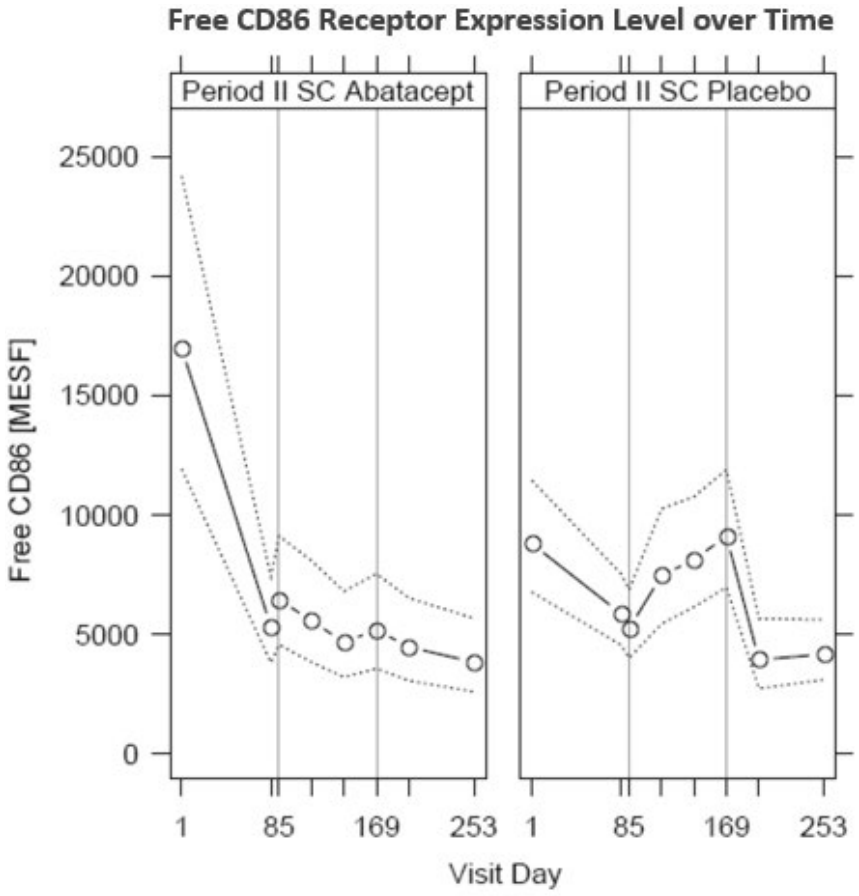
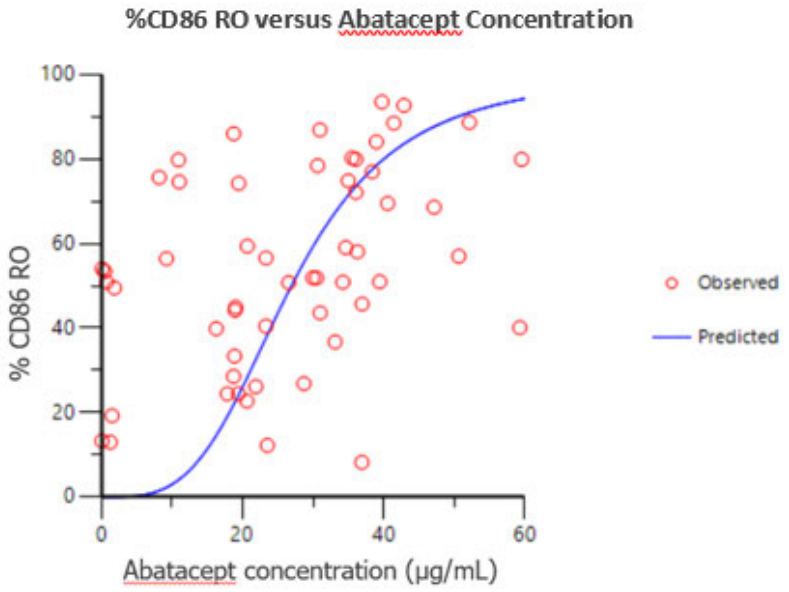
Background/Purpose: The purpose of this investigation was to characterize the relationship between systemic exposure of abatacept and measures of target engagement to further support dosing recommendations for abatacept.

Methods: The ALLOW study was a multinational, multicenter, randomized, double-blind, withdrawal study in patients with mild to moderate RA on a stable background of methotrexate to evaluate the immunogenicity and safety of subcutaneous (SC) abatacept. A key exploratory objective in this study was assessing the extent of CD86 receptor saturation in RA subjects following 125 mg weekly SC abatacept during lead-in, withdrawal, and re-introduction pe-





riods. The time course of abatacept concentrations as well as total and free CD86 expression levels on the surface of peripheral blood monocytes were measured upon initiation of abatacept as well as during the withdrawal and re-introduction phases using validated assays and was described by an extended linear model. Percentage of CD86 Receptor Occupancy (RO) was derived from the free CD86 expression levels at baseline and post-treatment. The relationship between abatacept concentrations and percentage of CD86 RO was characterized by a Sigmoidal Emax Model.

Results: Steady-state abatacept trough concentrations were achieved by Day 57 and were consistent from Days 57 to the end of the lead-in period/beginning of the withdrawal period (Day 85). On Day 85, mean free CD86 expression levels were comparable between the patients randomized to the SC abatacept and SC placebo groups for the withdrawal period. Upon withdrawal of abatacept therapy on Day 85, mean abatacept trough concentrations declined and mean free CD86 expression levels increased over time to baseline levels by the end of the withdrawal period on Day 169 (Figure 1, right panel). For patients who continued to receive SC abatacept, mean steady-state trough abatacept concentrations remained consistent while mean free CD86 expression levels incrementally decreased over time (Figure 1, left panel). Binding of abatacept to the CD86 receptor appears to be concentration dependent and was well described by a Sigmoidal Emax model with an EC_{50} (CV%) of 26.9 µg/mL (21.1%) (Figure 2). Administration of the approved SC dosing regimen results in steady state trough concentrations of approximately 25-34 µg/mL[1-4]. Overall, the CD86 binding characteristics are in good agreement with previous exposure-response analyses, where near maximal efficacy (i.e. DAS28 score and ACR20/50/70) is driven by steady state trough concentrations of 10 µg/mL or higher, which is achievable for the approved SC dosing abatacept regimen[5].

Conclusion: Establishing PK/RO relationships associated with patient outcomes enables guidance of dose administration for SC abatacept in RA.

Disclosure: G. Abelian, Bristol-Myers Squibb, 3; **S. Gao**, Bristol-Myers Squibb, 1, 3, 4; **Y. Gandhi**, Bristol-Myers Squibb, 1, 3, 4, CSL Behring, 3, 4; **B. Vakkalagadda**, Allergan, 3, 4, Bristol-Myers Squibb, 3, 4; **V. Perera**, Bristol-Myers Squibb, 1, 3; **B. Murthy**, Bristol-Myers Squibb, 1, 3.

Abstract Number: 1393

Impact of Sarilumab on Unacceptable Pain and Inflammation Control in Moderately-to-Severely Active Rheumatoid Arthritis (RA) Patients in 3 Phase 3 Studies

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Background/Purpose: Pain, a core-set domain and a troubling symptom to patients with RA, may be directly related to inflammation. Unacceptable pain (UP) levels may persist despite treatment-induced inflammation control, i.e. refractory pain (RP). Sarilumab is a subcutaneously-administered interleukin-6 receptor antagonist for treatment of adults with moderately to severely active RA with an inadequate response or intolerance to 1 or more disease-modifying antirheumatic drugs (DMARD-IR). In 3 randomized controlled trials (RCTs) of sarilumab 150 mg or 200 mg every 2 weeks (q2w) vs comparators, we previously observed meaningful improvements in pain. This study assessed UP and RP for sarilumab vs comparators in these trials.

Methods: Data were from RCTs of sarilumab 150 mg and 200 mg q2w vs placebo (+conventional DMARDs for all): MOBILITY [NCT01061736] (24/52 weeks) and TARGET [NCT01709578] (24-weeks); and MONARCH [NCT02332590] sarilumab 200 mg q2w vs adalimumab 40 mg q2w monotherapies. Post-hoc analyses were conducted on the odds ratios (ORs) of pain outcomes: UP (based on patient acceptable symptom state [PASS] on a threshold of visual

Table. Demographics and clinical characteristics of trial populations

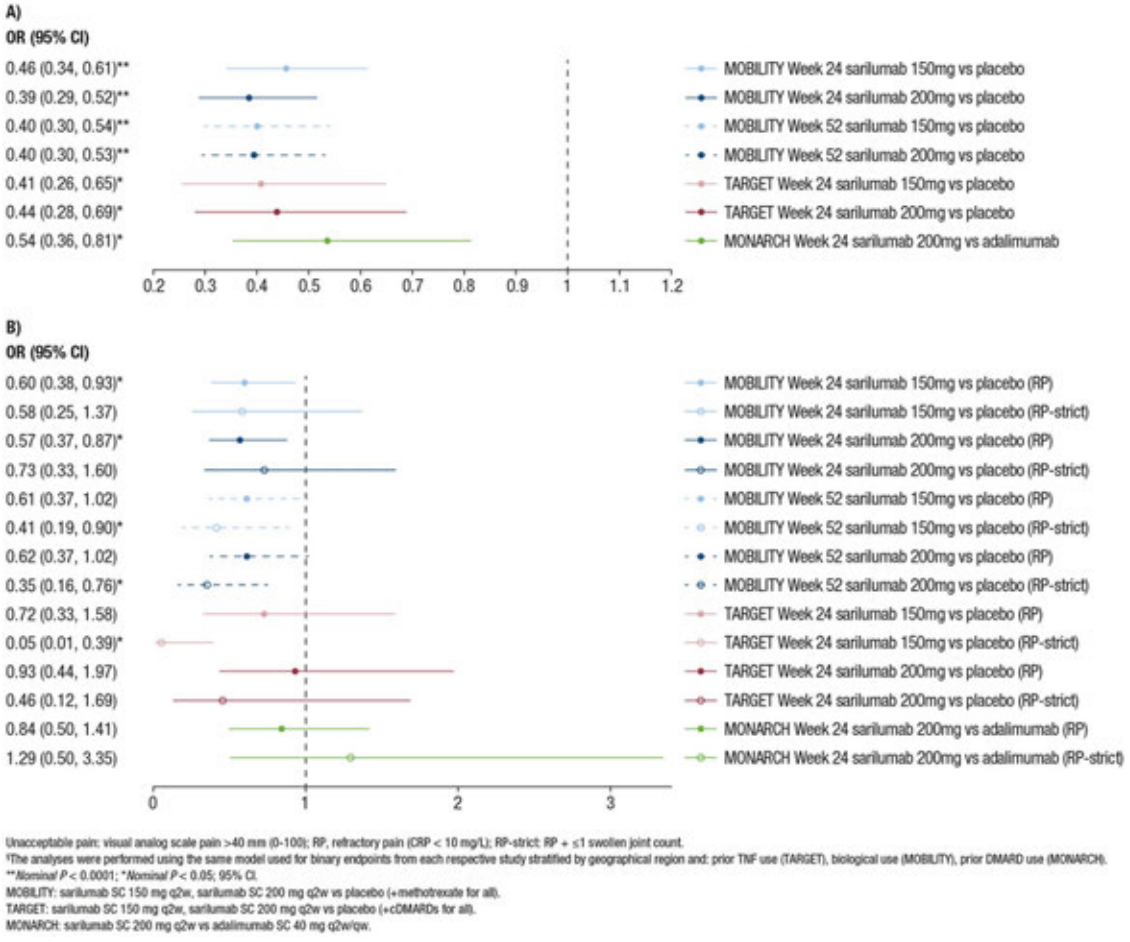
Demographic/clinical characteristic:			
	MOBILITY		
	Placebo + methotrexate (n = 398)	**150 mg q2w + methotrexate (n = 400)**	**200 mg q2w + methotrexate (n = 399)**
Age, years, mean ± SD	50.9 ± 11.2	50.1 ± 11.9	50.8 ± 11.8
Female, n (%)	321 (80.7)	319 (79.8)	337 (84.9)
Race, White–Caucasian, n (%)	343 (86.2)	345 (86.3)	343 (86.0)
Duration of RA, years, mean ± SD	9.1 ± 8.1	9.5 ± 8.5	8.6 ± 7.0
SJC (66 assessed), mean ± SD	16.7 ± 9.3	16.6 ± 9.0	16.8 ± 9.7
	TARGET		
	Placebo + csDMARD(s) (n = 181)	**150 mg q2w + csDMARD(s) (n = 181)**	**200 mg q2w + csDMARD(s) (n = 184)**
Age, years, mean ± SD	51.9 ± 12.4	54.0 ± 11.7	52.9 ± 12.9
Female, n (%)	154 (85.1)	142 (78.5)	151 (82.1)
Race, White–Caucasian, n (%)	124 (68.5)	134 (74.0)	130 (70.7)
Duration of RA, years, mean ± SD	12.0 ± 10.0	11.6 ± 8.6	12.7 ± 9.6
SJC (66 assessed), mean ± SD	20.2 ± 11.3	19.6 ± 11.2	20.0 ± 11.9
	MONARCH		
	Adalimumab SC 40 mg q2w/qw (n = 185)		**Sarilumab SC 200 mg q2w (n = 184)**
Age, years, mean ± SD	53.6±11.9		50.9±12.6
Female, n (%)	150 (81.1)		157 (85.3)
Race, White–Caucasian, n (%)	164 (88.6)		171 (92.9)
Duration of RA, years, mean ± SD	6.6 ± 7.8		8.1 ± 8.1
SJC (66 assessed), mean ± SD	17.5 ± 10.3		18.6 ± 10.7

analog scale pain >40 mm [0–100]), RP (UP+C reactive protein < 10 mg/L), and RP-strict (RP+ ≤1 swollen joint count [SJC]), and associations between pain and fatigue (FACIT-Fatigue) and disease activity (Health Assessment Questionnaire [HAQ], SJC and tender joint count [TJC]).

Results: Across all 3 trials (with similar patient baseline characteristics per arm in each trial; **Table**) sarilumab 150 mg and 200 mg had lower odds of UP vs comparators (nominal $P < 0.05$; **Figure**). MOBILITY: both sarilumab doses had lower odds (nominal $P < 0.05$) of RP vs placebo at Week 24 (sarilumab 150 mg: 0.60 [0.38, 0.93]; sarilumab 200 mg: 0.57 [0.37, 0.87]) and Week 52 (sarilumab 150 mg: 0.64 [0.37, 1.02]; sarilumab 200 mg: 0.62 [0.37, 1.02]), and RP-strict at Week 52 (sarilumab 150 mg: 0.41 [0.19, 0.90]; sarilumab 200 mg: 0.35 [0.16, 0.76]); TARGET: sarilumab 150mg had lower odds (nominal $P < 0.05$) of RP-strict at Week 24 (0.05 [0.01; 0.39]) (**Figure**). Higher pain level was associated with worse levels of FACIT-fatigue, HAQ, SJC and TJC (all $P < 0.001$), and UP had mostly moderate agreements with the likelihood of achieving response (minimal clinically important differences) on all these outcomes (*Kappa* coefficient values 0.41–0.60).

Conclusion: In this post hoc analysis of 3 RCTs in DMARD-IR patients, sarilumab was associated with lower odds of unacceptable pain or refractory pain vs comparators. Further research is needed regarding the sources of persistant pain and the potential role of inflammation control in patients with RA.

Figure. ORs[§] for outcomes: A) unacceptable pain, B) refractory pain (RP) or RP-strict



Unacceptable pain: visual analog scale pain >40 mm (0-100); RP, refractory pain (CRP < 10 mg/L); RP-strict: RP + ≤1 swollen joint count.
[§]The analyses were performed using the same model used for binary endpoints from each respective study stratified by geographical region and: prior TNF use (TARGET), biological use (MOBILITY), prior DMARD use (MONARCH).
**Nominal $P < 0.0001$; *Nominal $P < 0.05$; 95% CI.
MOBILITY: sarilumab SC 150 mg q2w, sarilumab SC 200 mg q2w vs placebo (+methotrexate for all).
TARGET: sarilumab SC 150 mg q2w, sarilumab SC 200 mg q2w vs placebo (+cDMARDs for all).
MONARCH: sarilumab SC 200 mg q2w vs adalimumab SC 40 mg q2w/qw.

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Abstract Number: 1394

Association Between Baseline Anti-CCP2 Antibody Concentration and Clinical Response After 6 Months of Treatment with Abatacept or a TNF Inhibitor in Biologic-Experienced Patients with RA: Results from a US National Observational Study

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Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In the AMPLE trial, patients (pts) with RA with higher baseline anti-CCP2 antibody concentrations showed a better response to treatment with abatacept (ABA) than those with lower concentrations.[1] This association was not observed with adalimumab treatment.[1] The present study assessed the association between

Table 1. Differences in Baseline Disease Characteristics and Treatment Response at 6 Months Among Patients Initiating Abatacept by Anti-CCP2 Quartile at Baseline

	Anti-CCP2+				
	Quartile 1 (n=30)	Quartile 2 (n=37)	Quartile 3 (n=36)	Quartile 4 (n=35)	p value
Baseline disease characteristics					
CDAI	24.2 (9.8)	28.0 (12.2)	29.2 (11.9)	32.3 (12.5)	0.041
SJC28	5.3 (4.3)	7.9 (4.6)	9.5 (5.9)	9.1 (5.4)	0.005
CRP	2.1 (1.8)	9.5 (14.7)	11.1 (13.1)	19.3 (19.2)	<0.0001
DAS28 (CRP)	4.3 (0.8)	4.8 (1.1)	4.8 (1.0)	5.3 (1.1)	0.004
RF	110.8 (140.8)	136.4 (163.6)	362.8 (672.9)	320.7 (380.2)	<0.0001
mHAQ	0.6 (0.5)	0.4 (0.4)	0.6 (0.6)	0.7 (0.6)	0.049
PtGA (VAS 0–100)	54.3 (28.1)	53.0 (23.4)	51.3 (29.5)	58.8 (29.6)	0.720
Physician global assessment (VAS 0–100)	40.5 (18.6)	47.0 (20.4)	51.2 (18.3)	54.5 (20.9)	0.031
Patient-reported pain (VAS 0–100)	53.9 (27.8)	51.4 (25.4)	52.8 (28.0)	65.7 (28.9)	0.067
Patient–reported fatigue (VAS 0–100)	59.0 (28.1)	55.7 (24.1)	54.0 (32.1)	58.2 (29.0)	0.844
Treatment response at 6 months					
ΔCDAI	–9.8 (13.9)	–14.4 (13.3)	–16.3 (13.8)	–19.6 (14.1)	0.037
Adjusted β (95% CI)*	Reference	–1.7 (–6.8, 3.4)	–2.7 (–7.8, 2.5)	–3.2 (–8.6, 2.1)	0.208
ΔmHAQ	–0.1 (0.4)	0.0 (0.2)	–0.2 (0.3)	–0.3 (0.4)	0.012
Adjusted β (95% CI)*	Reference	0.02 (–0.13, 0.16)	–0.06 (–0.21, 0.08)	–0.18 (–0.33, –0.02)	0.012
ΔPatient-reported pain	–7.5 (25.6)	–12.8 (24.4)	–15.8 (23.1)	–32.8 (35.2)	0.010
Adjusted β (95% CI)*	Reference	–7.5 (–18.9, 3.8)	–9.6 (–21.0, 1.9)	–19.4 (–31.1, –7.6)	0.002
ΔPatient-reported fatigue	–4.5 (26.4)	–6.7 (26.0)	–10.1 (29.3)	–19.2 (32.0)	0.220
Adjusted β (95% CI)*	Reference	–3.8 (–15.9, 8.2)	–8.3 (–20.5, 3.8)	–14.3 (–26.7, –2.0)	0.015
ΔPtGA	–8.1 (26.7)	–16.9 (24.7)	–17.2 (25.9)	–24.6 (34.1)	0.140
Adjusted β (95% CI)*	Reference	–10.3 (–21.2, 0.6)	–11.1 (–22.1, –0.2)	–13.7 (–24.9, –2.6)	0.022

Data are mean (SD), unless otherwise stated

Differences between baseline measures of disease activity across CCP2+ quartiles were assessed using one-way ANOVA for DAS28 (CRP) and physician global assessment and the Kruskal–Wallis test for nonparametric measures (CDAI, SJC, CRP, RF, mHAQ and PtGA)

Anti-CCP2 quartiles: quartile 1, 10–94 U/mL; quartile 2, 94–296 U/mL; quartile 3, 296–876 U/mL; quartile 4, >876 U/mL

*β is the beta coefficient from the linear regression model, adjusted for age, sex, baseline CDAI or PROs, co-morbidity index and current MTX use

ANOVA=analysis of variance; mHAQ=modified HAQ; PRO=patient-reported outcome; PtGA=patient global assessment; VAS=visual analog scale

Table 2. Differences in Baseline Disease Characteristics and Treatment Response at 6 Months Among Patients Initiating Any TNFi by Anti-CCP2 Quartile at Baseline

	Anti-CCP2+				
	Quartile 1 (n=36)	Quartile 2 (n=34)	Quartile 3 (n=32)	Quartile 4 (n=35)	p value
Baseline disease characteristics					
CDAI	29.1 (10.8)	32.3 (12.5)	26.2 (11.2)	29.8 (13.7)	0.255
SJC28	7.6 (4.6)	9.4 (5.9)	7.4 (4.2)	7.6 (6.0)	0.427
CRP	15.5 (30.8)	17.1 (24.3)	12.2 (14.2)	13.3 (27.0)	0.966
DAS28 (CRP)	4.9 (1.1)	5.1 (1.0)	4.6 (1.0)	4.9 (1.2)	0.315
RF*	111.0 (173.2)	182.9 (353.3)	342.0 (559.1)	617.8 (1042.6)	<0.0001
mHAQ	0.5 (0.4)	0.6 (0.6)	0.3 (0.3)	0.8 (0.6)	0.003
PtGA (VAS 0–100)	50.4 (23.3)	57.1 (22.5)	40.5 (27.2)	59.4 (24.8)	0.012
Physician global assessment (VAS 0–100)	52.1 (14.5)	52.9 (17.4)	51.3 (19.8)	51.9 (19.2)	0.987
Patient-reported pain (VAS 0–100)	54.8 (28.3)	56.8 (26.4)	45.4 (26.3)	60.8 (26.4)	0.136
Patient-reported fatigue (VAS 0–100)	51.6 (29.4)	51.7 (29.7)	47.4 (29.8)	58.2 (28.7)	0.463
Treatment response at 6 months					
ΔCDAI	−12.2 (13.6)	−15.3 (11.5)	−14.3 (11.2)	−9.9 (15.7)	0.707
Adjusted β (95% CI)†	Reference	−1.2 (−6.8, 4.4)	−3.6 (−9.3, 2.1)	3.0 (−2.5, 8.5)	0.441
ΔmHAQ	0.0 (0.4)	−0.1 (0.5)	0.0 (0.4)	−0.1 (0.4)	0.522
Adjusted β (95% CI)†	Reference	−0.14 (−0.31, 0.03)	−0.12 (−0.29, 0.05)	−0.01 (−0.18, 0.16)	0.944
ΔPatient-reported pain	−12.6 (26.4)	−15.0 (27.5)	−10.8 (34.7)	−13.5 (30.0)	0.964
Adjusted β (95% CI)†	Reference	−0.2 (−12.5, 12.1)	−4.3 (−16.9, 8.4)	2.6 (−9.5, 14.8)	0.830
ΔPatient-reported fatigue	−8.9 (29.2)	−8.9 (32.2)	−11.6 (33.5)	−5.9 (23.2)	0.890
Adjusted β (95% CI)†	Reference	−0.1 (−11.8, 11.7)	−5.5 (−17.4, 6.5)	6.9 (−4.8, 18.5)	0.405
ΔPtGA	−10.3 (23.4)	−17.4 (24.5)	−13.7 (30.6)	−12.2 (27.1)	0.724
Adjusted β (95% CI)†	Reference	−3.2 (−14.2, 7.7)	−7.8 (−19.0, 3.4)	2.9 (−7.9, 13.7)	0.810

Data are mean (SD), unless otherwise stated

Differences between baseline measures of disease activity across CCP2+ quartiles were assessed using one-way ANOVA for DAS28 (CRP) and physician global assessment and the Kruskal–Wallis test for nonparametric measures (CDAI, SJC, CRP, RF, mHAQ and PtGA)

Anti-CCP2 quartiles: quartile 1, 10–94 U/mL; quartile 2, 94–296 U/mL; quartile 3, 296–876 U/mL; quartile 4, >876 U/mL

*n=35, 32, 31 and 34 for quartiles 1 to 4, respectively

†β is the beta coefficient from the linear regression model, adjusted for age, sex, baseline CDAI or PROs, co-morbidity index and current MTX use

ANOVA=analysis of variance; mHAQ=modified HAQ; PRO=patient-reported outcome; PtGA=patient global assessment; TNFi=TNF inhibitor; VAS=visual analog scale

baseline (BL) anti-CCP2 concentration and 6-month treatment responses to ABA or any TNF inhibitor (TNFi) in a real-world setting.

Methods: CERTAIN (Comparative Effectiveness Registry to study Therapies for Arthritis and Inflammatory CoNditions) is a prospective cohort study of adult pts with RA,[2] recruited from the Corrona network, who had at least moderate disease activity (CDAI >10) and either started therapy with or switched to a TNFi or non-TNF biologic. Pts were followed for 12 months (mths) or until they switched/discontinued biologic therapy. This analysis included pts from CERTAIN who initiated ABA or any TNFi, were CCP3+ (>20 U/mL), had CDAI >10 at BL and had serum samples at BL and at 6 mths. Eligible pts also had known BL anti-CCP2 concentration and serostatus (–, ≤10 U/mL; +, >10 U/

mL) and prior biologic exposure. TNFi initiators were matched to ABA initiators based on CDAI by line of therapy. BL demographics, pt and disease characteristics were compared within treatment groups using descriptive statistics. Treatment response by BL anti-CCP2 quartile in anti-CCP2+ pts, assessed by change from BL at 6 mths in CDAI and patient-reported outcomes (PROs: modified [m]HAQ, pain, fatigue and patient global assessment [PtGA]), was evaluated separately in the ABA and TNFi groups using a linear regression model adjusted for age, sex, CDAI or PROs at initiation, co-morbidity index and current MTX use.

Results: In total, 151 matched biologic-experienced ABA and TNFi initiators were included (13 and 14 were anti-CCP2– and 138 and 137 were anti CCP2+, respectively). At BL, median age was 57–60 years (yrs), 74–75% were female, median duration of RA was 10–12 yrs and mean BMI was 29.2–29.8. There were significant differences between anti-CCP2 quartiles at BL in mean CDAI, SJC28, CRP, DAS28 (CRP), RF, mHAQ and physician global assessment, and in mean RF, mHAQ and PtGA among TNFi initiators. Among ABA initiators (Table 1), but not TNFi initiators (Table 2), a greater improvement at 6 mths in CDAI and all PROs was observed with increasing CCP2 quartile. In the adjusted analysis, among ABA initiators, there was a numerically greater improvement in CDAI ($p=0.208$) and statistically significantly greater improvements in all PROs ($p< 0.05$) with increasing anti-CCP2 quartile.

Conclusion: In a relatively small sample of abatacept-treated pts, higher anti-CCP2 concentrations at BL were associated with significantly greater improvement in PROs in the adjusted and unadjusted models, a numerically greater improvement in CDAI score in the adjusted model and a significantly greater improvement in CDAI score in the unadjusted model after 6 mths. This association was not observed in a small sample size of TNFi-treated pts.

References:

1. Sokolove J, et al. *Ann Rheum Dis* 2016;**75**:709–14.
2. Pappas DA, et al. *BMC Musculoskelet Disord* 2014;**15**:113.

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Disclosure: L. Harrold, AbbVie, 5, Bristol-Myers Squibb, 5, Corrona, 1, Genentech, 5, Pfizer, 2, 3; **J. Bryson**, Bristol-Myers Squibb, 1, 3, 4; **T. Lehman**, Bristol-Myers Squibb, 3; **J. Zhuo**, Bristol-Myers Squibb, 1, 3; **S. Gao**, Bristol-Myers Squibb, 1, 3, 4; **X. Han**, Bristol-Myers Squibb, 3, Bristol-Myers Squibb Company, 3; **A. Schrader**, None; **S. Rebello**, Corrona, LLC, 3; **J. Kremer**, AbbVie, 2, 5, Amgen, 5, Bristol-Myers Squibb, 2, 5, Corrona, 1, Genentech, 2, 5, Gilead, 5, Lilly, 2, 5, Novartis, 2, Pfizer, 2, 5, Regeneron, 5, Sanofi, 5.

Abstract Number: 1395

Risk of Immunization to Rituximab in Systemic Autoimmune Diseases and Rheumatoid Arthritis: Frequency and Risk Factors. Analysis of the Efficacy of an Alternative Treatment by Ofatumumab

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The most widely used B cell targeted therapies in auto-immune diseases (AID) is Rituximab (RTX), a murine chimeric monoclonal antibody. Among RTX's side effects, immunization and anti-drug antibodies to RTX (RTX-ADA) production have been reportedbut their consequences are poorly described. The immunization rate against RTX in rheumatoid arthritis (RA) is 2.7-9.2% and data is lacking in sAID.

We aimed to evaluate the frequency, consequences and predictive factors of RTX-ADA in RA and sAID, as well as the use of an alternative B-cell targeted therapy, ofatumumab (OFA).

Methods: All patients with RA or sAID treated with RTX from 2012 to 2017 in our tertiary reference centre for RA and sAIDwere retrospectively studied. All patients who were tested for RTX-ADA were identified. Clinical and biological characteristics of RTX immunized patients were compared to those of non-immunized patients. For patients treated with OFA, clinical and biological efficacy was obtained before and after treatment.

Results: 199 patients were treated with RTX (RA: 124, sAID: 75 including 38 primary Sjögren's Syndrome (pSS), 15 systemic lupus erythematous, 7 myositis, 6 overlap syndrome, 5 ANCA-associated vasculitides and 4 other sAID). 62/199 (31.1%) patients were tested for RTX-ADA because of a loss of clinical efficacy or absence of B-cell depletion (43.4%), a long delay between cycles (13.2%), a reaction during the first infusion (7.5%) or at subsequent infusions (35.8%). 14 were positive: 3/35 RA (8.6%) and 11/27 (40.7%) other sAID, (p=0.0025). None of the patients who experienced a reaction to the first RTX infusion were positive for RTX-ADA. Among the whole RTX-treated patients, the frequency of RTX-ADA was 2.4% and 14.7% in RA and in other sAID, respectively (p=0.003). Most of the immunized patients experienced delayed infusion reactions (11/14 [78.5%]). Delayed reactions were observed within the first 15 days after the infusion, and after a median 2 cycles [range; 1-2]. They were mainly rash (72.7%), fever (54.5%) and/or abdominal pain (36.3%). Predictive factors of immunization were a sAID compared to RA (40.7% vs 8.6%, p=0.0025) and African origin (57.1% vs 4.2%, p< 0.001). Neither hypergammaglobulinemia, rheumatoid factor, disease activity, nor associated immunosuppressive therapy were associated with RTX-ADA. Among 23 tested patients with SLE or pSS, anti-SSA antibodies were positive in 9/10 (90%) immunized patients versus in only 8/13 (61.5%) non immunized patients (p=0.18). Three pSS patients immunized against RTX were treated with OFA because of associated cryoglobulinemic vasculitis or MALT lymphoma. All 3 experienced complete remission of their disease without any recurrence of infusions reactions. No other adverse event was reported.

Conclusion: Immunization against RTX is an event leading to loss of efficacy, absence of B-cell depletion and infusion reactions at the 2nd or subsequent infusions. Testing for RTX-ADA must be realized in patients presenting one of these three features, especially if they are of African origin and treated for a sAID. Our results suggest that immunized patients can be treated safely with OFA although OFA should be further evaluated in sAID.

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Abstract Number: 1396

Persistence of Tocilizumab Therapy Among Patients with Rheumatoid Arthritis: Data from the US-Based Corrona Rheumatoid Arthritis Registry

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

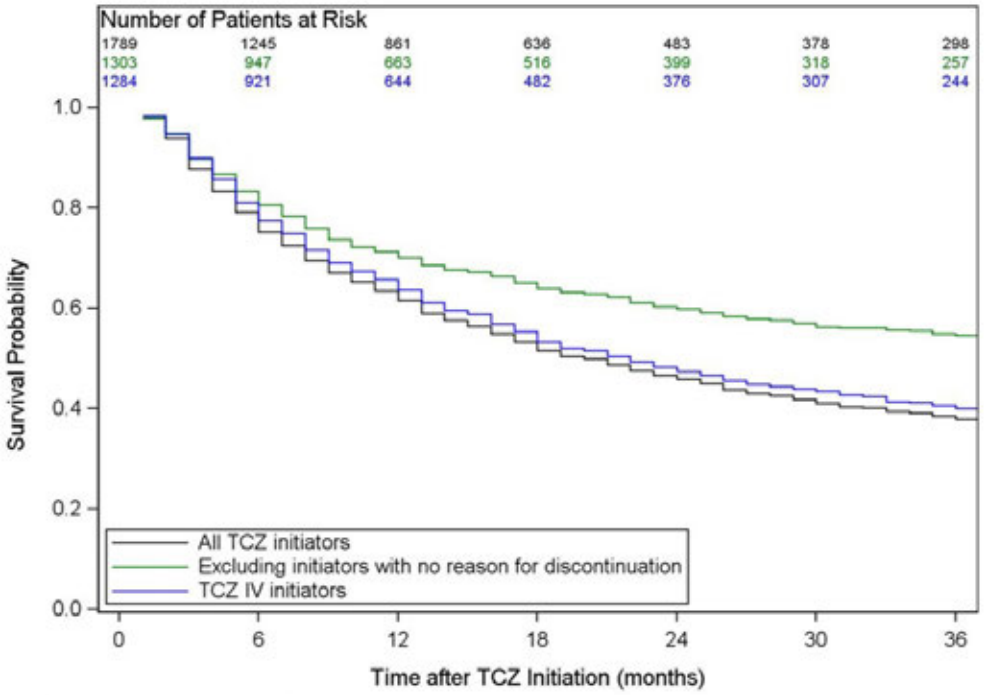
Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Understanding persistence of biologic therapies and factors associated with discontinuation can help inform treatment decisions for patients with rheumatoid arthritis (RA). We sought to evaluate the persistence of tocilizumab (TCZ) therapy and identify factors associated with its discontinuation among US patients with RA in routine clinical practice.

Methods: Eligible participants were TCZ-naïve patients enrolled in the Corrona RA registry who initiated TCZ after January 1, 2010 and had ≥ 1 follow-up visit. Persistence of therapy was defined as maintaining continuous TCZ treatment with no interruptions; patients were considered no longer persistent upon the first discontinuation of TCZ.

Figure 1. Kaplan-Meier Plots of Persistence of TCZ Therapy



IV, intravenous; TCZ, tocilizumab.

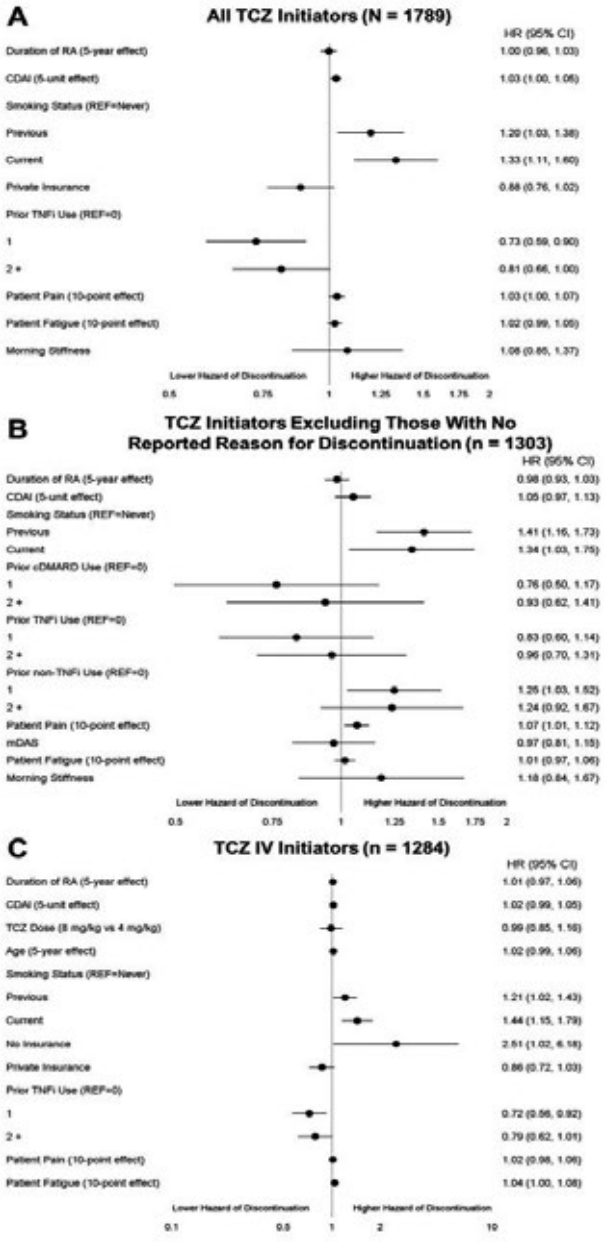
Table 1. Baseline Characteristics of TCZ Initiators With ≥ 1 Follow-Up Visit

Characteristic	TCZ Initiators (N = 1789)
Female, n (%)	1449 (81.0)
Age, mean (SD), years	58.5 (12.6)
Duration of RA, mean (SD), years	12.0 (9.6)
White, n (%)	1512 (85.0)
Previous or current smoker, n (%)	873 (49.1)
BMI category, n (%)	
Underweight/normal weight	439 (24.6)
Overweight	542 (29.3)
Obese	825 (46.1)
Work Status, n (%)	
Full or part time	902 (50.8)
Student	42 (2.4)
Disabled	346 (19.5)
Retired	488 (27.4)
Insurance, n (%)	
None	11 (0.6)
Private	1322 (73.9)
Medicaid	92 (5.1)
Medicare	681 (38.1)
History of comorbid conditions, n (%)	
Hypertension	596 (33.3)
Diabetes	185 (10.3)
Malignancy	110 (6.1)
Cardiovascular disease	736 (41.1)
Prior medication use, n (%)	
cDMARDs	1702 (95.1)
Any biologic	1671 (93.4)
0	118 (6.6)
1	466 (26.0)
≥ 2	1205 (67.4)
TNFi	1580 (88.3)
0	209 (11.7)
1	673 (37.6)
≥ 2	907 (50.7)
Non-TNFi biologic	922 (51.5)
0	867 (48.5)
1	712 (39.8)
≥ 2	210 (11.7)
Concomitant medication, n (%)	
Monotherapy	515 (28.8)
Combination therapy	1274 (71.2)
Prednisone use, n (%)	608 (34.0)
CDAI (0-76), mean (SD)	23.2 (14.2)
mDAS (1.69-8.75), mean (SD)	4.7 (1.4)
Patient pain (0-100), mean (SD)	53.6 (26.7)
Patient fatigue (0-100), mean (SD)	54.8 (28.3)
mHAQ (0-3), mean (SD)	0.6 (0.5)
Morning stiffness, n (%)	1586 (89.3)

BMI, body mass index; CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; mDAS, modified Disease Activity Score; mHAQ, modified Health Assessment Questionnaire; RA, rheumatoid arthritis; TCZ, tocilizumab; TNFi, tumor necrosis factor inhibitor.

Persistence was calculated using Kaplan-Meier survival analysis for the overall population; secondary analyses evaluated persistence excluding patients who stopped TCZ with no reported reason for discontinuation (patients with non-medical reasons for discontinuation [eg, insurance] were censored) and in only those patients who initiated intravenous (IV) TCZ. Cox proportional hazards modeling was used to identify factors associated with persistence.

Figure 2. Estimated Effects of Covariates on Duration of TCZ Persistence Among (A) All TCZ Initiators, (B) TCZ Initiators Excluding Those With No Reported Reason for Discontinuation and (C) TCZ IV Initiators



CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IV, intravenous; mDAS, modified Disease Activity Score; RA, rheumatoid arthritis; REF, reference; TCZ, tocilizumab; TNFi, tumor necrosis factor inhibitor.

Results: A total of 1789 TCZ initiators were included. Patient characteristics at the time of TCZ initiation are summarized in **Table 1**. Most patients (93.4%) had prior biologic use and 67.4% had received ≥ 2 prior biologics (**Table 1**). Overall, 28.8% initiated TCZ as monotherapy (**Table 1**). Among all TCZ initiators, the median (95% CI) duration of persistence was 20 (18 to 22) months (**Figure 1**). Factors associated with an increased hazard of TCZ discontinuation included smoking and higher baseline CDAI, whereas prior tumor necrosis factor inhibitor (TNFi) use was associated with a reduced hazard (**Figure 2A**). After excluding patients with no reported reason for discontinuation (remaining

n = 1303), the median (95% CI) duration of persistence was 46 (38 to 55) months (**Figure 1**); smoking, use of 1 prior non-TNFi and higher baseline patient pain score were associated with an increased hazard of discontinuation (**Figure 2B**). Among the 1284 patients who initiated TCZ IV, median (95% CI) duration of persistence was 22 (19 to 25) months (**Figure 1**); smoking, lack of insurance and higher baseline patient fatigue score were associated with a increased hazard of discontinuation, whereas use of 1 prior TNFi was associated with a decreased hazard (**Figure 2C**).

Conclusion: In this real-world population of US patients with RA, TCZ was most frequently initiated after an inadequate response to ≥ 2 biologics. Overall median duration of persistence was approximately 20 months and was higher (46 months) when patients with no reported reason for TCZ discontinuation were excluded. As expected, factors indicative of higher baseline disease activity were associated with shorter persistence.

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Abstract Number: 1397

Comparative Effectiveness of Tocilizumab in Combination with Methotrexate versus Tumor Necrosis Factor Inhibitors (TNFis) in Combination with Methotrexate in Patients with Rheumatoid Arthritis with Prior Exposure to TNFis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical studies have demonstrated the efficacy of tocilizumab (TCZ) administered with methotrexate (MTX) in improving rheumatoid arthritis (RA) disease activity in patients who have had an inadequate response to tumor necrosis factor inhibitors (TNFis). The objective of this study was to compare the effectiveness of TCZ + MTX with that of TNFis + MTX in patients with RA who had prior exposure to TNFis in routine clinical practice.

Methods: Eligible participants were TCZ-naïve patients from the Corrona RA registry who initiated TCZ + MTX or a TNFi + MTX after January 1, 2010 and had a 6-month follow-up visit. Patients in both groups must have used ≥ 1 TNFi, had a Clinical Disease Activity Index (CDAI) score available at initiation (baseline) and 6 months and had a CDAI score > 10 at baseline. The primary outcome was mean change in CDAI from baseline to 6 months. Secondary outcomes included achievement of low disease activity (LDA; CDAI ≤ 10) and mean change in modified Health Assessment Questionnaire (mHAQ) at 6 months. Patients were grouped by baseline MTX dose (≤ 10 mg; > 10 to ≤ 15 mg; >

Table. Outcomes at 6 months in patients who initiated TCZ + MTX compared with those who initiated TNFi + MTX in the trimmed population.

	Change in CDAI		Achievement of LDA		Change in mHAQ	
	Unadjusted Mean (SD)	Adjusted β (95% CI)*	Unadjusted Response Rate, n (%)	Adjusted OR (95% CI)*	Unadjusted Mean (SD)	Adjusted β (95% CI)*
Overall						
TCZ (n = 402)	−9.0 (14.2)	—	110 (27.4)	—	−0.06 (0.43)	—
TNFi (n = 703)	−8.1 (13.2)	0.02 (−1.52 to 1.55)	220 (31.3)	0.81 (0.59 to 1.10)	−0.09 (0.40)	−0.05 (−0.10 to 0.00)
≤ 10 mg MTX						
TCZ (n = 47)	−8.1 (13.2)	—	12 (25.5)	—	−0.06 (0.54)	—
TNFi (n = 90)	−7.0 (13.6)	−2.86 (−7.17 to 1.44)	24 (26.7)	1.59 (0.56 to 4.50)	−0.13 (0.45)	−0.10 (−0.26 to 0.06)
> 10 to ≤ 15 mg MTX						
TCZ (n = 80)	−10.5 (15.4)	—	28 (35.0)	—	−0.04 (0.55)	—
TNFi (n = 165)	−8.9 (14.3)	−0.32 (−3.82 to 3.19)	54 (32.7)	0.55 (0.28 to 1.09)	−0.08 (0.41)	−0.06 (−0.18 to 0.06)
> 15 to ≤ 20 mg MTX						
TCZ (n = 153)	−8.3 (13.2)	—	44 (28.8)	—	−0.08 (0.36)	—
TNFi (n = 274)	−8.1 (12.9)	0.58 (−1.80 to 2.95)	84 (30.7)	0.85 (0.51 to 1.41)	−0.08 (0.39)	0.01 (−0.07 to 0.08)
> 20 mg MTX						
TCZ (n = 58)	−11.6 (13.8)	—	19 (32.8)	—	−0.07 (0.43)	—
TNFi (n = 72)	−10.7 (13.6)	−0.14 (−4.57 to 4.29)	25 (34.7)	0.95 (0.39 to 2.36)	−0.14 (0.35)	−0.11 (−0.23 to 0.01)

CDAI, Clinical Disease Activity Index; LDA, low disease activity; mHAQ, modified Health Assessment Questionnaire; MTX, methotrexate; OR, odds ratio; TCZ, tocilizumab; TNFi, tumor necrosis factor inhibitor.
*TCZ + MTX (reference group) compared with TNFi + MTX. Adjusted for potential confounding variables.

15 to ≤ 20 mg; > 20 mg); outcomes were compared between patients initiating TCZ and those initiating a TNFi overall and within each MTX dose group using propensity score (PS)-trimmed populations. As a sensitivity analysis, TCZ and TNFi initiators in each group were PS-matched 1:1 and outcomes were assessed in the matched populations. Linear and logistic regression models were estimated in the trimmed and matched populations, adjusting for covariates not balanced after PS trimming or matching, respectively.

Results: A total of 415 TCZ + MTX initiators and 725 TNFi + MTX initiators met the inclusion criteria prior to PS trimming or matching. The overall trimmed population included 402 TCZ + MTX initiators and 703 TNFi + MTX initiators. In the trimmed population, patient demographics were generally comparable between TCZ + MTX and TNFi + MTX initiators; the mean age was 57.1 years in the TCZ + MTX group and 57.7 years in the TNFi + MTX group, the majority of patients in both groups were female (> 79%) and white (> 82%) and the mean duration of RA was 11.8 and 10.5 years in the TCZ + MTX and TNFi + MTX groups, respectively. Higher proportions of patients initiating TCZ had received ≥ 2 prior biologics (66.0% to 76.3%) compared with those initiating a TNFi (33.2% to 42.2%) across all MTX dose groups. Patients initiating TCZ had higher mean baseline CDAI scores (26.5 to 29.3) than those initiating a TNFi (24.7 to 27.5). Patients in both cohorts had improvement in CDAI scores at 6 months regardless of baseline MTX dose. Improvement in CDAI and mHAQ and the odds of achieving LDA were comparable between TCZ and TNFi initiators across all MTX groups in the trimmed population after adjustment for potential confounding variables (Table). Similar results were observed in the PS-matched cohorts.

Conclusion: In this real-world population of US patients with RA who had prior TNFi exposure, there was no statistically significant or clinically meaningful difference in the effectiveness of therapy in patients who initiated TCZ + MTX compared with TNFi + MTX.

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Abstract Number: 1398

Sarilumab and Tocilizumab Receptor Occupancy (RO), and Effects on C-Reactive Protein (CRP) Levels, in Patients with Rheumatoid Arthritis (RA)

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SESSION INFORMATION
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Background/Purpose: The in vitro binding affinity of sarilumab (K_D 61.9 pM) for the human interleukin-6 receptor (IL-6R) is 15–22-fold higher than that of tocilizumab. This study evaluated the relationship between IL-6R receptor occupancy (RO), pharmacodynamic (PD) variables (eg CRP), and the potential clinical relevance of the differences between sarilumab and tocilizumab.

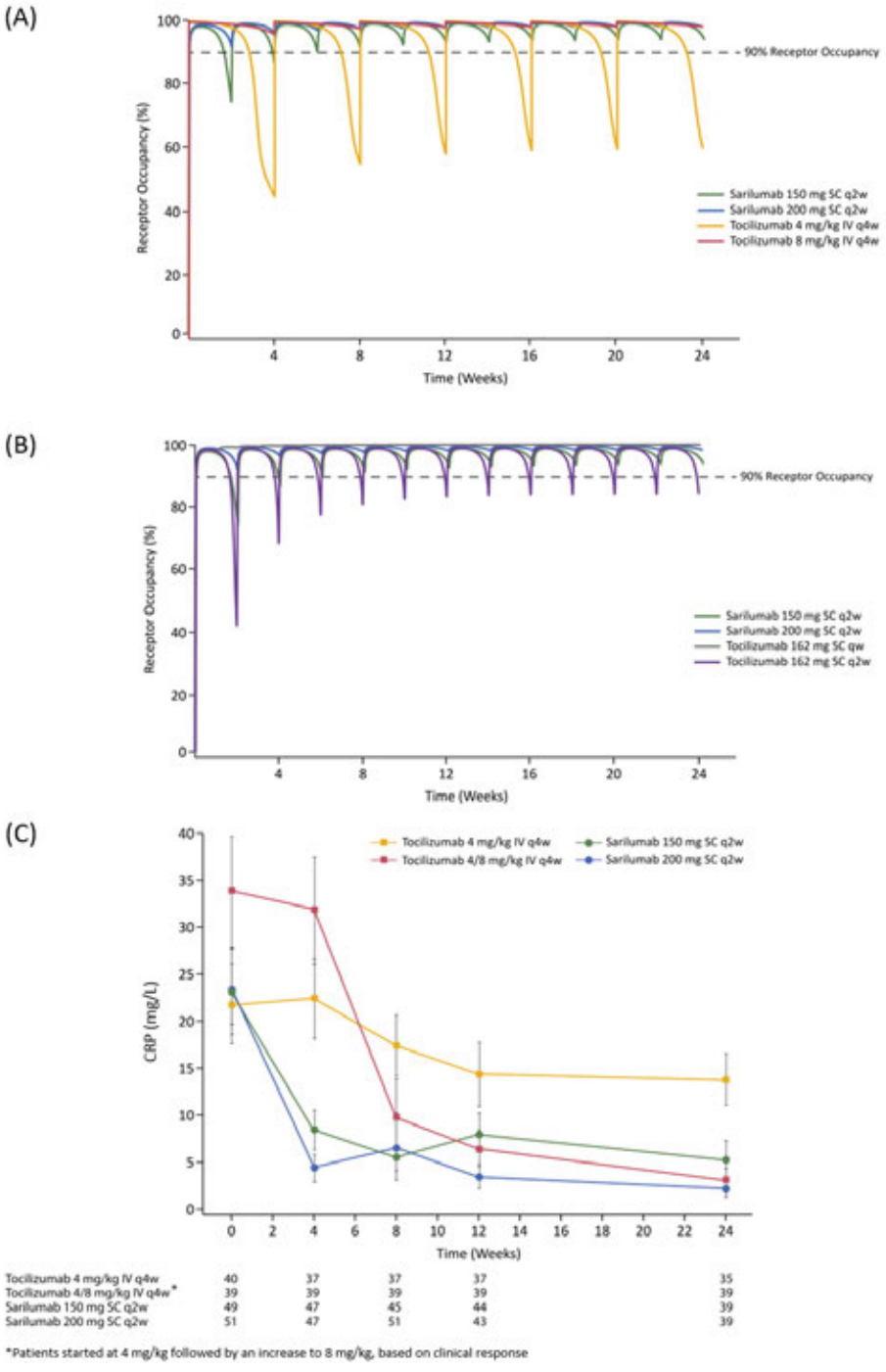
Methods: Binding to soluble IL-6R (sIL-6R) in vivo translates into the quasi-steady-state target-mediated drug disposition pharmacokinetics (PK) and indirect-response PD model with inhibition of elimination of sIL-6R and unbound sIL-6R concentration for both sarilumab and tocilizumab. PK/PD models simulated sIL-6R RO over time for: sarilumab 200 and 150 mg subcutaneously (SC) once every 2 weeks (q2w); tocilizumab 162 mg SC q2w and once every week (qw); and tocilizumab 4 and 8 mg/kg intravenously (IV) once every 4 weeks (q4w). RO profiles were compared with changes in CRP levels following administration of sarilumab SC and tocilizumab IV in patients with RA (ASCERTAIN; NCT01768572); during the study period, 60.8% of patients receiving tocilizumab required a dose increase from 4 to 8 mg/kg IV q4w, based on clinical response.

Results: Sarilumab 200 mg SC q2w achieved >90% RO after the first dose, which was maintained over the dosing interval throughout the 24-week treatment period; at 150 mg SC q2w, RO was >90% from the second dose onwards. Tocilizumab 162 mg SC q2w achieved RO >90% after the first dose but this decreased to < 50% before the second dose. The RO for tocilizumab 4 mg/kg IV q4w was >99% after the first dose at Week 1 but decreased over the dosing interval to < 50% before the second dose. At trough steady state (Week 24), RO was greater with sarilumab 200 mg SC q2w (98%) and 150 mg SC q2w (94%) versus tocilizumab 162 mg SC q2w (84%) and 4 mg/kg IV q4w (60%). At the higher dose (8 mg/kg IV q4w) or dosing frequency (162 mg SC qw), tocilizumab maintained RO ≥99% at steady state, similar to sarilumab 200 mg SC q2w. CRP levels were inversely associated with RO at trough in patients with

RA; the greatest suppression in CRP levels occurred with sarilumab SC (either dose) or with the tocilizumab 8 mg/kg IV q4w (Figure). Proportionally smaller CRP reductions were observed with tocilizumab 4 mg/kg IV q4w, consistent with the lower RO of tocilizumab at this dose.

Conclusion: The higher IL-6R binding affinity of sarilumab translated into higher RO and greater reduction in CRP levels when compared with tocilizumab. Sarilumab 200 mg SC q2w led to a rapid and sustained suppression of CRP over the 24-week treatment course; the higher dose (IV) or increased dosing frequency (SC) of tocilizumab was

Figure. sIL6-R RO for (A) sarilumab SC vs tocilizumab IV and (B) sarilumab SC vs tocilizumab SC, and (C) CRP levels after sarilumab SC and tocilizumab IV



*Patients started at 4 mg/kg followed by an increase to 8 mg/kg, based on clinical response

required to maintain the same degree of RO and CRP suppression. CRP may be a useful tool in clinical practice for patients treated with an IL-6R blocker.

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Abstract Number: 1399

Evaluation of Effectiveness and Usage Patterns of Tofacitinib in Treatment of Rheumatoid Arthritis in Australia: An Analysis from the OPAL-QUMI Real World Dataset

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SESSION INFORMATION

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Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Limited data from large real-world patient populations exist to describe treatment outcomes of patients who receive tofacitinib for the management of RA in Australia. The objective of this study was to evaluate effectiveness and treatment patterns of tofacitinib in a large real-world cohort of Australian adult patients with RA.

Methods: Routinely collected, de-identified clinical data were sourced from the Optimising Patient outcomes in Australian rheumatology – Quality Use of Medicines Initiative (OPAL-QUMI) dataset. Data from adult patients with a diagnosis of RA, who initiated treatment with tofacitinib or a biologic disease-modifying antirheumatic drug(bDMARD) and had at least 12 months of follow-up between March 2015 and September 2018, were included.Descriptive analyses were performed on overall and propensity score matched populations. Treatment effectiveness was evaluated from baseline to month 18 by DAS28-ESR, simple disease activity index (SDAI) and clinical disease activity index (CDAI) measures. Treatment persistence, in part a surrogate for efficacy, was estimated by Kaplan-Meier methods.

Treatment pattern evaluation included percentage of patients receiving monotherapy or combination therapy at treatment initiation.

Results: 1950 patients were included in the matched population (1300 bDMARD initiators; 650 tofacitinib initiators). Patients were predominantly aged 55 to 74 years (57.8%), and female (81.2%). At baseline, median disease duration was 107 and 120 months, with 16.1% and 17.3% of patients in DAS28-ESR defined disease remission for the bDMARD and tofacitinib groups respectively. After three months of treatment, 49.1% and 49.7% had achieved DAS remission and after 18 months of treatment, 52.4% and 57.8% of patients had achieved DAS remission in the bDMARD and tofacitinib groups respectively. At 18 months the percentage of patients achieving CDAI/SDAI remission was similar with 29.2%/29.0% bDMARD patients and 30.9%/30.5% tofacitinib patients reporting CDAI/SDAI remission respectively. The median persistence of treatment was similar for bDMARD and tofacitinib groups: 33.8 (95% confidence interval (CI) 28.8 to 40.4) and 34.2 (95% CI 32.2 to not reached) months, respectively. In the overall population, more patients were prescribed tofacitinib as monotherapy (43.4%) compared to bDMARD monotherapy (33.4%).

Conclusion: In this analysis of a large real world dataset, tofacitinib demonstrated treatment effectiveness and persistence that was similar to bDMARDs. Overall, there was a trend for more use of tofacitinib as monotherapy than bDMARDs.

Disclosure: P. Bird, Pfizer, 5, AbbVie, 5, Novartis, 5, Janssen, 5, Celgene, 5, Eli Lilly, 5; **G. Littlejohn**, Janssen, 5, AbbVie, 5, 8, Merck Sharp & Dohme, 8; **B. Butcher**, All, 9; **T. Smith**, None; **C. da Fonseca Pereira**, Pfizer, 1, 3; **D. Witcombe**, Pfizer, 1, 3; **H. Griffiths**, Pfizer, 5, Novartis, 5, Janssen, 5, 8, AbbVie, 5, Roche, 5, BMS, 9.

Abstract Number: 1400

Real Life Retention of Tofacitinib in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Tofacitinib (Xeljanz) is an approved treatment for Rheumatoid Arthritis (RA) but data on its use in "real life" are limited. We sought to analyze Tofacitinib drug retention in the Israeli registry and compare it to other mechanism of action agents (Etanercept, Golimumab, Tocilizumab, and Abatacept). Our hypothesis is that Tofacitinib drug retention is mainly influenced by the number of prior therapeutic lines and is similar to other biologic agents.

Methods: This prospective cohort study was based on data from the Israeli registry of RA, status February 2019. We included patients with RA according to the EULAR/ACR criteria. The primary end point was "drug retention". *Episode* was defined 'time on drug' as the period between treatment initiation and treatment discontinuation. We compared drug retention using Kaplan-Meier and Cox models over time with mixed-effects models for longitudinal data.

Results: A total of 864 eligible treatment courses (episodes) were retrieved from January 2010 until February 2019, including 111 Tofacitinib, 242 Etanercept , 99 Golimumab, 297 tocilizumab and 115 Abatacept. In the complete

cohort, the median age at diagnosis and at the time of episode was 47 (range: 0.5-87) and 59 (17-88) years, respectively; median disease duration was 10 (0.5-40) years. [for Tofacitinib only: the median age at the time of episode was 66 (21-88) years; median disease duration was 14 (0.5-50) years.] Tofacitinib was mostly prescribed as third or late line of therapy (64%), similar to Abatacept (63%), (p=0.892). Tofacitinib [HR 1.92, 95% CI:1.33-2.76] as well as all drugs considered had reduced drug survival (Etanercept [HR 1.65, 95% CI:1.26-2.18], Abatacept [HR 1.89, 95% CI:1.35-2.64], Golimumab [HR 1.56, 95% CI:1.08-2.24], Tofacitinib [HR 1.92, 95% CI:1.33-2.76]), in comparison with Tocilizumab which significantly had the best retention rate, at all lines of treatment. Interestingly, Tofacitinib median drug survival (15.8 [95% CI: 8.6-23.1] months) was non-inferior to Etanercept (26.4 [95%CI: 5.9-46.9]; p=0.426), Abatacept (20.3 [95%CI: 9.8-30.9; p=0.157), and Golimumab (15.1 [95%CI: 5.9-24.3]; p=0.698) at first and second line of biologics treatment. In a multivariate analysis, an advanced treatment line was associated with reduced Tofacitinib drug survival (p< 0.05). Age at episode, the duration of disease, body mass index, concomitant use of Methotrexate with Tofacitinib (HR 1.34, 95% CI [0.62-2.90]) and smoking were not found as parameters that influence drug survival.

Conclusion: The line of treatment with Tofacitinib may have influence on its survival. Moreover, there is no statistical difference in drug retention between Tofacitinib and the other compared bDMARDs except for Tocilizumab with demonstrated a longer survival.

Disclosure: A. Croiteru, None; **M. Lidar**, Pfizer, 5, 8; **T. Reitblat**, None; **D. Zisman**, Pfizer, 5, 8; **A. Balbir-Gurman**, Pfizer, 5, 8; **T. Meshiach**, None; **R. Almog**, None; **O. Elkayam**, Pfizer, 2, 5, 8.

Abstract Number: 1401

Australian Rheumatoid Arthritis (RA) Biologic Treatment Pathways: An Australian Rheumatology Association Database (ARAD) Analysis

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SESSION INFORMATION
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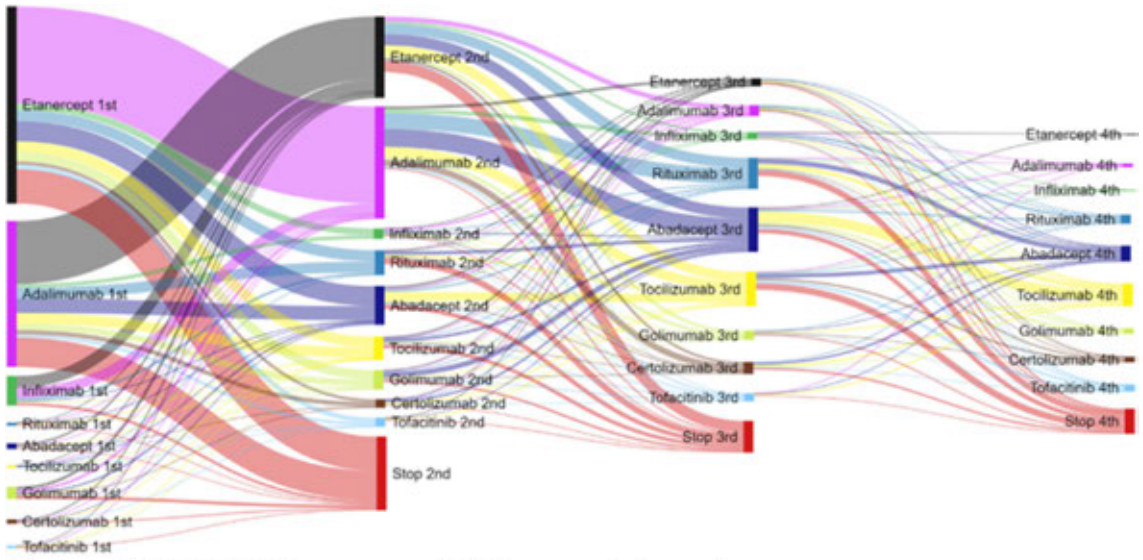
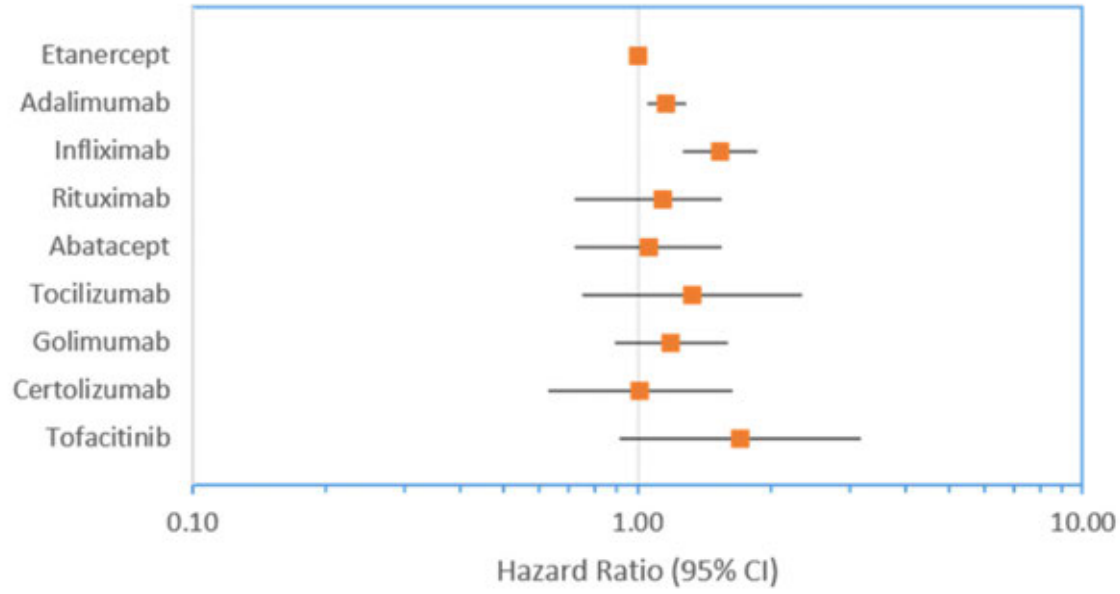
Background/Purpose: To describe current biologic disease-modifying antirheumatic drug (bDMARD) treatment patterns for Australian Rheumatology Association Database (ARAD) participants with Rheumatoid Arthritis (RA) including switching and reasons for switching.

Methods: ARAD, a voluntary longitudinal observational database established in 2001, collects long-term outcome data for people with inflammatory arthritis in Australia. Participants complete semi-annual, then annual questionnaires. Reasons for stopping bDMARD therapy, such as inefficacy or side-effects, were extracted from Sept. 2001 to May 2018 for all RA participants. Logistic regression was used to evaluate the characteristics of participants who switched compared to those who did not at first switch point. Switching patterns determined for each bDMARD and time on first, second and third-line bDMARDs were analysed using Cox regression survival analysis methods.

Results: 3,470 RA participants were included in the analysis. First-line bDMARDS were etanercept (ETA, n=1,414), adalimumab (ADA, n=1,024), infliximab (INX, n=155), golimumab (n=98), abatacept (ABA, n=66), certolizumab (n=38), tocilizumab (TOC, n=21), rituximab (n=24) and tofacitinib (TOF, n=23). 47.7% starting first-line bDMARD therapy switched to another bDMARD, 50.5% switched from second-line therapies and 42.3% switched from third-line therapies. Inefficacy (52.8%) or side effects (20.6%) were the most commonly cited reasons for stopping therapy, irrespective of line of treatment. Factors associated with switching compared to those continuing first-line use were female gender, tertiary education, more recent questionnaire year, higher HAQ score, current prednisolone and current opioid use as shown in the table. Switching due to side effects were more strongly associated with a higher HAQ score and longer duration of disease than with inefficacy.



Flow of bDMARD use - switching and stopping



Cox proportional hazard for stopping first-line bDMARD therapy

	Univariate			Multivariable		
Factor	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Age						
<50	1.00			1.00		
50-69	0.99	(0.83-1.18)	0.91	1.09	0.89-1.32	0.76
70+	0.71	(0.55-0.93)	0.01	0.86	0.65-1.15	0.06
Patient Gender						
Male	1.00		<0.01	1.00		
Female	1.37	(1.15-1.63)		1.32	(1.09-1.59)	0.01
Education Level						
Tertiary	1.00			1.00		
Secondary	0.85	(0.71-1.03)	0.09	0.82	(0.67-1.00)	0.05
Not completed secondary	0.73	(0.60-0.89)	<0.01	0.69	(0.56-0.86)	<0.01
Questionnaire year	0.96	(0.94-0.98)	<0.01	0.94	(0.92-0.96)	<0.01
HAQ Score	1.22	(1.09-1.36)	<0.01	1.18	(1.05-1.34)	0.01
Current Prednisolone						
No	1.00		<0.01	1.00		
Yes	1.32	(1.10-1.58)		1.36	(1.12-1.67)	<0.01
Current opioid						
No	1.00			1.00		
Low potency	1.37	(1.14-1.64)		1.23	(1.01-1.49)	0.03
High potency	1.70	(1.25-2.31)		1.71	(1.23-2.37)	<0.01

Table - Univariate and multivariable - significant factors associated with switching bDMARD compared to continuing use

Figure 1 shows the complex pattern of use of specific bDMARDs. The bars on the left represent the first-line bDMARD, subsequent use is represented as progressing from left to right. The thickness and colour of the lines indicate the number switching to the next line of bDMARD or stopping use.

The median time on first-line bDMARD varied from 258 days for ABA to 98 days for TOF. Compared with first-line ETA, participants were more likely to stop first-line ADA (HR 1.16; 95%CI: 1.04-1.29) and INX (HR 1.52; 95%CI: 1.26-1.85), whereas no differences were seen for other first-line bDMARDs (figure 2). For second-line therapies, compared to ETA, the risk of stopping was higher for INX and lower for TOC and TOF. For third-line, the risk of stopping was lower for all bDMARDs except INX.

Conclusion: Based on ARAD data, the treatment algorithm for bDMARD use in Australia is complex. Overall, around 50% of ARAD participants switch to another bDMARD therapy irrespective of the first, second or third-line bDMARD used. 50% of stoppages were due to inefficacy and 20% were due to side effects.

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Abstract Number: 1402

Efficacy, Safety and Continuation Rate of Abatacept and Tocilizumab in Patients with Rheumatoid Arthritis : The Comparative Observational Study

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Background/Purpose: Biologic agents used in patients with rheumatoid arthritis (RA) have increased in recent years. Abatacept (ABT) has been described as relatively safe for elderly patients because of lower risk of infectious events than other biologic agents. Tocilizumab (TCZ) was approved for marketing for use in patients with RA in Japan ahead of other countries in 2008. Randomized controlled trials have been shown the efficacy and safety of ABT and TCZ in RA patients. It is required to compare biologic agents in real clinical practice. Therefore, we investigated the efficacy, safety, and continuation rate of ABT and TCZ in patients with RA.

Methods: One hundred eighty three patients with RA treated with ABT or TCZ retrospectively observed for 12 months in Saitama Medical University Hospital since 2010 to 2018. We compared the baseline characteristics, disease activity, physical disability, drug continuation rate, and adverse events between the patients treated with ABT and TCZ.

Results: In ABT group (n=85) compared with TCZ group (n=98), we found older age at initiation of biologics (ABT vs. TCZ: 64 vs. 58 years, p=0.011), higher HAQ-DI score (1.5 vs. 1.0, p=0.003), higher titer of rheumatoid factor (318.2 vs. 126.5 IU/mL, p=0.001), and fewer MTX-users (44.7 vs. 62.2%, p=0.025). Disease duration, rate of female, naïve rate of biologics, body weight, DAS28-ESR4, CDAI, MMP-3, the positive rate of rheumatoid factor and anti-CCP antibody, dose of MTX and PSL at baseline were similar between the groups. CDAI and HAQ-DI significantly decreased at one year after initiation compared to baseline in both groups. The patients who achieved remission or low disease activity in CDAI at one year after initiation tended to be lower in ABT group than TCZ group (67.3 vs. 82.4%, p=0.061). There was no significant difference in the drug continuation rate (81.2 vs. 80.6%). In the patients who discontinued ABT or TCZ during one year of observational period, the rate of adverse events (10.6 vs.12.2%) and inefficacy rate (7.1 vs. 5.1%) as reasons for discontinuation were not significantly different between the groups. Infection occurred most commonly as adverse events in both groups (4.7 vs. 7.1%). In ABT group, the rate of PSL-users and daily dose of PSL significantly decreased in one year after initiation compared to those at baseline (69% vs. 60%, P=0.031, 6.4 vs. 6.0mg/day, p=0.002). In TCZ group, the rate of PSL-users and daily dose of PSL significantly decreased one year after initiation (60 vs. 35%, p< 0.001, 5.1 vs. 3.6 mg/day, p=0.003).

Conclusion: ABT was tended to be selected for patients, who had disadvantageous conditions such as older age, higher HAQ-DI, fewer MTX users at baseline, and ABT-treated patients achieved lower rates of remission or low disease activity one year after initiation compared to TCZ-treated patients. In spite of these different backgrounds of patients, rate of discontinuation for inefficacy, adherence, and safety were equivalent between the two groups.

Disclosure: M. Matsuda, None; **Y. Funakubo Asanuma**, None; **T. Wada**, None; **N. Kouzu**, None; **K. Sato**, None; **T. Mimura**, None.

Abstract Number: 1403

CDAI Analysis of Dose Escalation in a Trial of Infliximab for Rheumatoid Arthritis

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SESSION INFORMATION
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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In the START (Safety Trial for Rheumatoid Arthritis with Remicade Therapy) trial, patients (pts) with active rheumatoid arthritis (RA) received placebo (PBO), or infliximab (IFX) 3 mg/kg or 10 mg/kg, with a primary endpoint of safety at week 22. Pts receiving IFX 3 mg/kg had dose escalation if they met prespecified criteria for lack of response at week 22, which was assessed by combined swollen and tender joint count, S/TJC, (primary nonresponders). They also received dose escalation if they experienced a flare after week 22 (secondary nonresponders, not analyzed here) (1,2). In a post hoc analysis, we examine the effects of IFX dose escalation in the primary nonresponders, using the more relevant tool Clinical Disease Activity Index (CDAI), which includes the 28 S/TJC as well as pt and physician global assessments.

Figure 1. Percentage of Patients by CDAI Category among Primary Nonresponders to Infliximab 3 mg/kg Who Received Dose Escalation

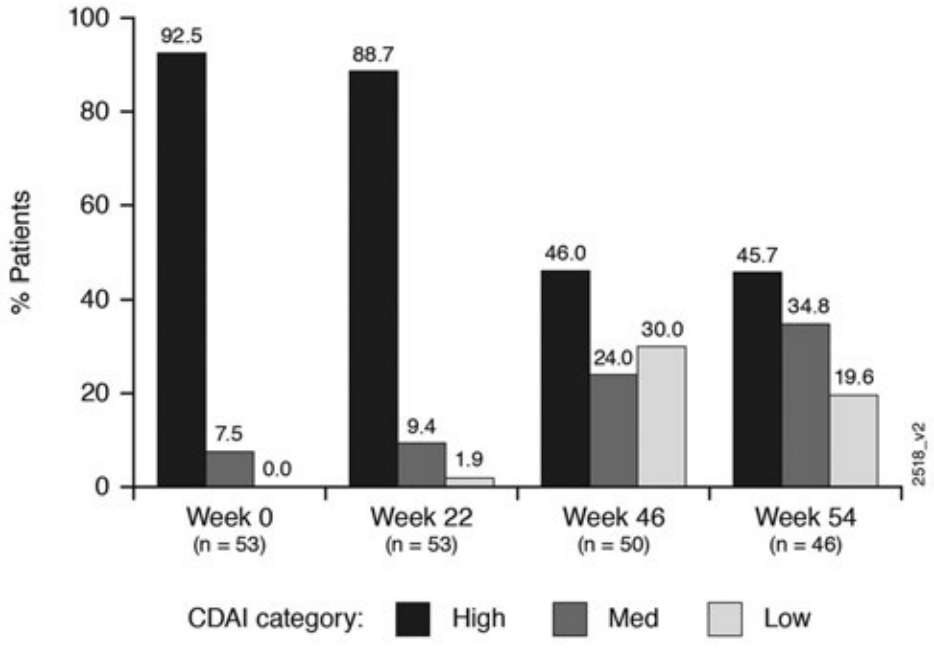
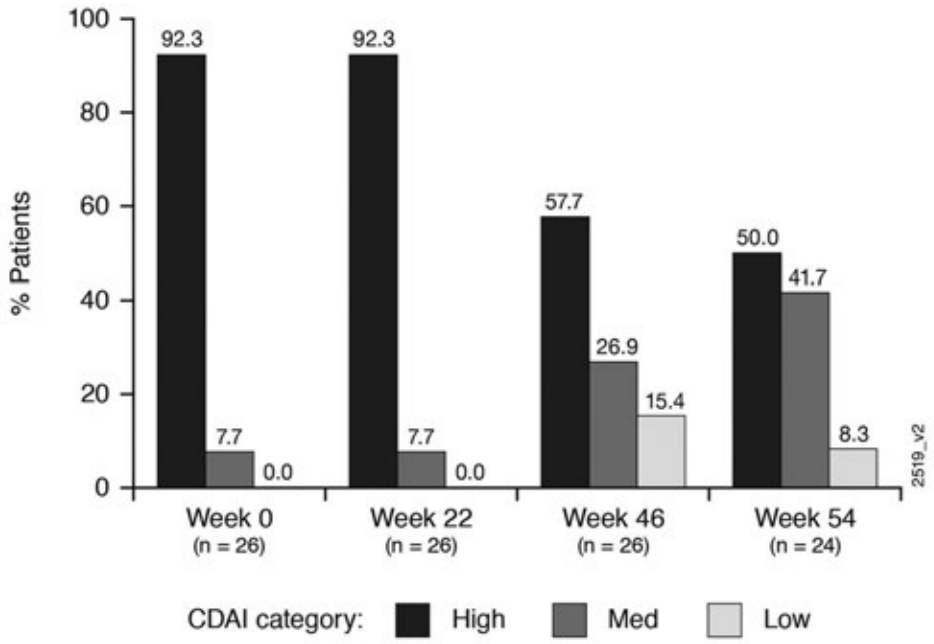


Figure 2. Percentage of Patients by CDAI Category among Primary Nonresponders Receiving Infliximab Doses ≥ 6 mg/kg



Methods: Adult START pts (N=1082) with 6 swollen and 6 tender joints, despite treatment with methotrexate (MTX), were randomized: PBO (n=363), IFX 3 mg/kg (n=360), or IFX 10 mg/kg (n=361) at weeks 0, 2, 6, and 14. At week 22, PBO pts switched to IFX 3 mg/kg for the remainder of the study, and pts randomized to IFX 3 mg/kg continued dosing every 8 weeks or received dose escalation (in increments of 1.5 mg/kg) every 8 weeks if there was lack of response (< 20% improvement from baseline in S/TJC). The study was terminated after 54 weeks (2).

Results: Among the 360 pts randomized to 3 mg/kg, 220 did not receive dose escalation during the study, 109 pts received dose escalation, and 31 discontinued or were from an excluded site. 53 of those receiving dose escalation were primary non-responders with lack of response at week 22 (2). Baseline characteristics were generally similar among these subgroups (80% female, mean 53 years old, SJC=15, TJC=22, and MTX 15 mg/week). Of the primary non-responders (n=53), IFX doses escalated to an average of 6.3 mg/kg (range 4.5 – 10 mg/kg). CDAI scoring (high, moderate, and low) improved from 89%, 9%, and 2% at week 22 to 46%, 24%, and 30% at week 46, and did not substantially improve further at week 54 (Figure 1). Among the subset of these pts who received doses ≥6 mg/kg (n=26), the average IFX dose was 7.7 mg/kg (range 6 – 10 mg/kg), and the CDAI scores (high, moderate, and low) of 92%, 8%, and 0% at week 22 improved to 58%, 27% and 15% at week 46, and also did not substantially improve further at week 54 (Figure 2).

Conclusion: In this analysis of CDAI in pts who initiated IFX 3 mg/kg and were dose escalated starting at week 22 (average dose 6.3 mg/kg), dose escalation generally improved pts' CDAI category (Figure 1). In a subset of pts who were escalated to doses ≥ 6 mg/kg (average dose 7.65 mg/kg), no further improvements in categorical CDAI were noted (Figure 2). Although START showed no increased risk of serious infections among pts receiving approved doses of INF vs PBO, pts who were treated with 10 mg/kg loading doses and maintenance therapy had more serious infections (relative risk=3.1) (1). These findings may be of clinical significance when considering dose escalation to higher doses of IFX.

References:

1. Westhovens et al. Arthritis Rheum. 2006;54:1075.
2. Rahman et al. Ann Rheum Dis. 2007;66:1233.

Disclosure: J. Tesser, Janssen Research & Development, LLC, 2; **S. Black**, Janssen Research & Development, LLC, 3, Janssen Scientific Affairs, LLC, 3, Janssen Scientific Affairs, LLC,, 3; **R. Lin**, Janssen Research & Development, LLC, 3, Janssen Research & Development, LLC,, 3; **W. Langholff**, Janssen Research & Development, LLC, 3; **J. Uy**, Janssen Research & Development, LLC, 3; **S. Kafka**, Janssen Research & Development, LLC, 3, Janssen Scientific Affairs, LLC, 1, 3.

Abstract Number: 1404

Treatments Patterns Among Patients with Rheumatoid Arthritis Treated with a Biologic Disease-modifying Anti-rheumatic Drug: A Nation-wide Study in Korea

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SESSION INFORMATION
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Background/Purpose: Limited data are available on whether patients with rheumatoid arthritis (RA) are treated with conventional disease-modifying anti-rheumatic drugs (cDMARDs) according to the current recommendations before they initiate biologic DMARDs (bDMARDs) or JAK inhibitors (JAKis). We examined the treatment patterns among Korean RA patients who received bDMARDs or JAKis in a real world setting, using the 2002-2016 Korean National Health Insurance Service database that covers the entire Korean population.

Methods: We identified RA patients who initiated bDMARDs (TNF inhibitor, abatacept, rituximab and tocilizumab) or JAKis (tofacitinib). Their treatment patterns during 1 year after RA diagnosis (defined as free of any RA diagnosis or any DMARD use for one year before the diagnosis) and prior to the initiation of index drugs (bDMARDs or JAKis) were examined regarding: initial cDMARD used, dose and parenteral use of methotrexate (MTX), use and time to combination therapy of cDMARDs, and steroid use.

Results: 10,145 RA patients were identified who used index drugs from the database (mean age 57 years, 82% female). Among them, 6,986 patients had identifiable dates for RA diagnosis (mean age 57 years, 79% female). The mean (SD) duration from RA diagnosis to index drug initiation was 1,425 (1,162) days with 1,509 (22%) patients having a duration ≤1 year. At diagnosis, the most common 1st cDMARD used was hydroxychloroquine (63%), followed by MTX (55%) and sulfasalazine (29%) with steroids used in 75%. During the 1 year from the diagnosis, 85% of patients eventually used MTX, 42% ever used MTX ≥ 15mg/week, only 3% used parenteral MTX, and 85% patients used combined cDMARDs with a mean 188 days from the RA diagnosis to combination therapy. Patients whose maximal

Table 2. Treatment patterns before bDMARD initiation

	At RA dx N =6,986	During 1-year post-RA dx N =6,986	During 1-year period prior to bDMARD initiation N =10,145
Dose regimen of MTX			
Mean maximal dose, mg/week	-	14.1 ± 13.1	14.6 ± 15.4
Maximal MTX dose ever used, %			
< 10 mg/week	-	11.1 (13.0)†	8.3 (9.4)‡
10 - <15 mg/week	-	32.5 (38.2)†	34.3 (38.5)‡
15 - <20 mg/week	-	33.7 (39.6)†	37.8 (42.4)‡
≥ 20 mg/week	-	7.9 (9.3)†	8.7 (9.7)‡
Subcutaneous MTX users, %	0.4	2.8	3.9
Any csDMARD combination, %	47.2	85.7	98.9
MTX based csDMARD combination, %	39.2	79.1	82.0
Steroid users, %	75.2	61.9	97.5
Cumulative dose of steroid, mg (prednisolone equivalent dose)	-	2023 ± 1528	1899 ± 1329

† % among 5,953 MTX users
‡ % among 9,028 MTX users

MTX dose reached 20mg/week were rare (9%) and 62% were still on steroid after 1 year. During the 1 year prior to the index drug use (n = 10,145), the most common cDMARD was MTX used in 89% patients with 46% who ever used ≥ 15mg/week and 4% of parenteral users, followed by hydroxychloroquine (55%), leflunomide (52%), sulfasalazine (38%), and tacrolimus (20%). All patients used combination therapy and 98% steroids.

Conclusion: These data indicate that a substantial proportion of RA patient did not try maximal dose or parenteral use of MTX during the 1 year post-diagnosis as recommended by the current treatment guideline. Instead, they often used cDMARDs combination therapy. During the 1 year before initiating bDMARDs or JAKis, they were treated with intensive cDMARD combination therapy rather than escalating their MTX dose

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Disclosure: M. Kim, None; **A. Shin**, None; **S. Shin**, None; **Y. Ha**, Seoul National University Bundang Hospital, 3; **Y. Lee**, Seoul National University Bundang Hospital, 3; **E. Lee**, Seoul National University Hospital, 3; **Y. Song**, Astellas Pharma, Inc., 9; **E. Kang**, Seoul National University Bundang Hospital, 3.

Abstract Number: 1405

Expression of Uncoupling Protein-1 in Subcutaneous Fat Is Increased by Tocilizumab

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Adipose tissue is an important player in cardiovascular (CV) morbidity. Thermogenic brown adipocytes, rich with uncoupling protein 1 (UCP1), increase metabolic and CV health.

The aim of this study was to study the impact of anti-rheumatic treatment on production of UCP1 in subcutaneous fat of RA patients.

Methods: Samples of subcutaneous fat were collected from 125 female RA patients by aspiration from periumbilical region. Expression of UCP1 and a reverse cholesterol transport protein ABCA1 were measured by qPCR and analysied with respect to anti-rheumatic treatment and clinical disease activity. Bt treatment, the patient comprised 4 major groups including tocilizumab (Toci, n=14), anti-TNF (n=29), methotrexate monotherapy (n=47) and methotrexate-sulfasalazine-hyroxychloroquine (tripple therapy, n=15). CV risk was estimated with the Framingham risk algorithm.

Results: Measurable expression of UCP1 was found in 54.6% of the studied fat tissue samples. Patients on Toci had measurable expression of UCP1 in 79%, which was significantly more often than among TNFi-treated (45%, p=0.04) and MTX-treated patients (42%, p=0.02). Patients on triple therapy had also often measurable UCP1 levels compared to other groups (69% vs 43%, p=0.035). Toci patients have more lean body mass than patients treated with TNFi. This was based on lower BMI in Toci and TNFi treated patients compared to triple therapy (24.1 vs 27.1, p=0.041; 23.6 vs 27.1, p=0.017; respectively). Additionally, the estimated mucle mass by creatinin/height ratio was significantly lower in TNFi than in triple therapy (p=0.034) and Toci (p=0.008).Clinically, the treatment groups were similar in age, disease activity DAS28 and disease duration with the except for Toci. Toci patients were older (65 vs 57, p=0.04) and had numerically longer disease duration (17y vs 7y) and lower DAS28 (1.98 vs 3.11).

Notably, Toci patients had significantly higher TC compared to TNFi (p=0.027), and triple therapy (p=0.041). Triple therapy had the lowest TC levels (p=0.017). The differences were due to LDL, here patients on Toci had higher LDL than TNFi (p=0.09) and triple therapy (p=0.015). Serum HDL was similar. These differences in serum lipids were not related to expression of ABCA1 or UCP1. Despite the difference in the serum lipid profile, the estimated CV risk was significantly lower in Toci compared to MTX patients (4.1[0.87-5.75] vs 6.6[3.9-9], p=0.041).

Conclusion: In this study is Toci treatment is associated with persistent UCP1 production by adipose tissue. This was followed by lower estimated CV risk and favourable body composition in female RA patients.

Disclosure: L. Lyngfelt, None; **M. Erlandsson**, None; **K. Andersson**, None; **S. Silfverswärd**, None; **M. Bokarewa**, None.

Abstract Number: 1406

Impact on Costs and Quality of Life over 5 Years of Treat-to-target Treatment Strategies Initiating Tocilizumab, Methotrexate or Their Combination in Early Rheumatoid Arthritis: Economic Evaluation of the U-Act-Early Trial

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Table Mean difference in costs (x € 1.000) and QALYs with 95% confidence interval (discounted values).

	TCZ+MTX vs. MTX	TCZ vs. MTX
Over 2 years		
Medication costs	14.8 (11.9 to 17.6)	15.9 (13.2 to 18.5)
Direct healthcare costs	10.1 (5.2 to 15.2)	-1.4 (-5.1 to 2.2)
Indirect non healthcare costs	-0.8 (-1.4 to -0.2)	0 (-0.8 to 1.0)
Productivity loss costs*	0.6 (-6.1 to 7.3)	-5.0 (-11.8 to 1.5)
Productivity loss costs§	0.5 (-1.1 to 2.0)	-0.3 (-1.9 to 1.2)
Total costs and effect		
Healthcare perspective	24.9 (18.8 to 31.1)	14.5 (9.4 to 19.5)
Societal perspective*	24.7 (16.6 to 33.1)	9.5 (1.2 to 17.5)
Societal perspective§	24.5 (18.6 to 30.7)	14.2 (9.1 to 19.3)
QALYs	0.04 (-0.04 to 0.11)	0.01 (-0.08 to 0.09)
Over 5 years		
Medication costs	14.5 (9.0 to 19.9)	16.9 (11.5 to 22.3)
Direct healthcare costs	18.7 (9.0 to 28.3)	-0.5 (-7.4 to 6.2)
Indirect non healthcare costs	-5.4 (-6.9 to -4.0)	-4.0 (-5.7 to -2.4)
Productivity loss costs*	0.9 (-12.6 to 14.3)	-10.6 (-24.0 to 2.8)
Productivity loss costs§	1.0 (-2.1 to 3.9)	-0.2 (-3.2 to 2.8)
Total costs and effect		
Healthcare perspective	33.2 (21.3 to 45.2)	16.4 (6.5 to 26.0)
Societal perspective*	28.8 (12.7 to 45.5)	1.7 (-14.3 to 17.6)
Societal perspective§	28.9 (17.3 to 40.4)	12.1 (2.4 to 21.7)
QALYs	0.12 (-0.03 to 0.27)	0.01 (-0.15 to 0.18)

TCZ+MTX= initiation of tocilizumab + methotrexate strategy group, TCZ= initiation of tocilizumab + placebo-methotrexate strategy group, MTX= initiation of methotrexate + placebo-tocilizumab strategy group, Medication costs= all RA medication costs, Direct healthcare costs= all costs related to healthcare, also for other diseases (RA medication costs excluded), Indirect non healthcare costs= patient and family costs (e.g. travel costs, buying stair lift, etc.), Productivity loss costs= costs related to work loss or being less productive, *=using human capital approach, §=using friction costs approach, only counting costs for a period of absence up to 85 days, Healthcare perspective= direct healthcare costs + medication costs, Societal perspective= direct healthcare costs + indirect not healthcare costs + productivity loss costs + medication costs, QALY= quality-adjusted life years

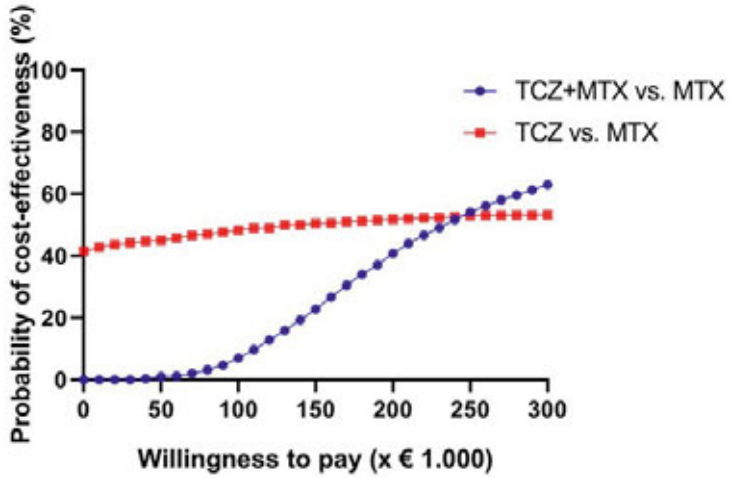

Figure Cost-effectiveness acceptability curve for the TCZ based initiation treatment strategy groups versus the MTX initiation strategy group over 5 years, using the societal perspective (human capital approach).

TCZ+MTX= initiation of tocilizumab + methotrexate strategy group, TCZ= initiation of tocilizumab + placebo-methotrexate strategy group, MTX= initiation of methotrexate + placebo-tocilizumab strategy group

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: U-Act-Early was a 2-year multicentre, double-blind, randomized, placebo-controlled trial in early (DMARD-naïve) RA patients treated to the target of remission. Patients were assigned to step-up treatment strategies starting with tocilizumab (TCZ), methotrexate (MTX) or their combination (TCZ+MTX).[1] If the treatment target was not achieved, MTX and/or TCZ was added. When patients achieved and remained in remission for ≥ 24 weeks, medication was tapered and finally stopped.[1] Patients were followed for 3 years after the trial, during which treatment was at the discretion of the rheumatologist. The current study compares quality-adjusted life years (QALYs) and direct and indirect costs over 5 years between TCZ, MTX or TCZ+MTX initial strategy.

Methods: Costs were based on reported resource use and reference prices.[2] QALYs were calculated based on the EQ5D using Dutch tariff.[2] The economic evaluation considered all 317 randomized patients according to their allocated strategy group, using imputation with chained equations nested in bootstraps (5000 samples) to account for missing data and uncertainty.[3]

Total costs were calculated from the healthcare as well as the societal perspective. Values were discounted using a discount rate of 4% per year for costs, and 1.5% for QALYs according to Dutch guidelines for economic evaluations in healthcare.[2]

Differences in costs and QALYs were calculated for TCZ+MTX vs. MTX and TCZ vs. MTX over a 2 year and 5 year time horizon. Cost-effectiveness acceptability curves were constructed to illustrate the probability of TCZ(+MTX) being cost-effective at different willingness to pay (WTP) thresholds.

Results: Approximately 80% of all patients were employed at baseline, and worked on average 24 hours weekly without differences between strategy groups.

Differences in costs per category (i.e. costs for medication, direct healthcare, indirect non healthcare, and productivity loss) and QALYs are shown in the Table. Differences in QALYs increased between 2 and 5 years, without becoming statistically significant. In most cost categories, no differences were observed either over 2 or 5 years. Medication costs were, as expected, higher in the treatment strategies initiating TCZ. Savings were made in indirect non healthcare costs for TCZ+MTX and TCZ respectively, and productivity loss costs were numerically lower for TCZ. The probability of TCZ(+MTX) being a cost-effective intervention over 5 years, using different WTP thresholds for a QALY, was in general low, and somewhat higher for TCZ compared to TCZ+MTX, see Figure.

Conclusion: Based on current analyses, early initiation of TCZ, with or without MTX, is not cost-effective compared to MTX initiation in a step-up treat-to-target treatment strategy over 2 or 5 years in early RA patients. However, these outcomes are based on limited data.

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Disclosure: M. Verhoeven, None; **J. Tekstra**, None; **A. Pethö-Schramm**, F. Hoffmann-La Roche, CH, 3; **M. Borm**, Roche Nederland B.V., 3; **J. van Laar**, Roche, 2, 8, Arthrogen, 5, Thermofisher, 2, BMS, 8, MSD, 2, Eli Lilly, 8, Gesynta, 5, Leadiant, 5, Arxx Tx, 5, Astra Zeneca, 2, Sanofi, 8; **F. Lafeber**, None; **J. Bijlsma**, Lilly, 8, Roche, 2, 8; **J. Jacobs**, Roche, 2; **P. Welsing**, None.

Abstract Number: 1407

Baricitinib Provides Better Pain Relief Across All Disease Activity Levels Compared with Placebo and Adalimumab in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In Phase 3 trial, RA-BEAM, baricitinib (BARI), a JAK1/JAK2 inhibitor, was associated with significant clinical improvements vs. placebo (PBO) and adalimumab (ADA) in RA patients.[1] Although BARI and ADA had similar improvement in swollen joint count, BARI demonstrated statistically significantly greater pain improvement. While pain is a generic feature of inflammation, not all pain in RA is due to inflammation, and the contribution of different pathways to pain is unclear. In this post hoc analysis, we assessed the relationship between pain improvement and disease activity and evaluated whether BARI provided additional pain improvement vs. PBO and ADA across levels of disease activity.

Methods: 1,305 patients on stable background MTX were randomized 3:2:3 to and treated with PBO, 40 mg subcutaneous ADA every other week, or daily, oral 4 mg BARI. Pain was assessed with a 0-100 mm visual analog scale (VAS); pain improvement from baseline to Week 12 was grouped by ≤30%, >30% to ≤50%, >50% to ≤70%,

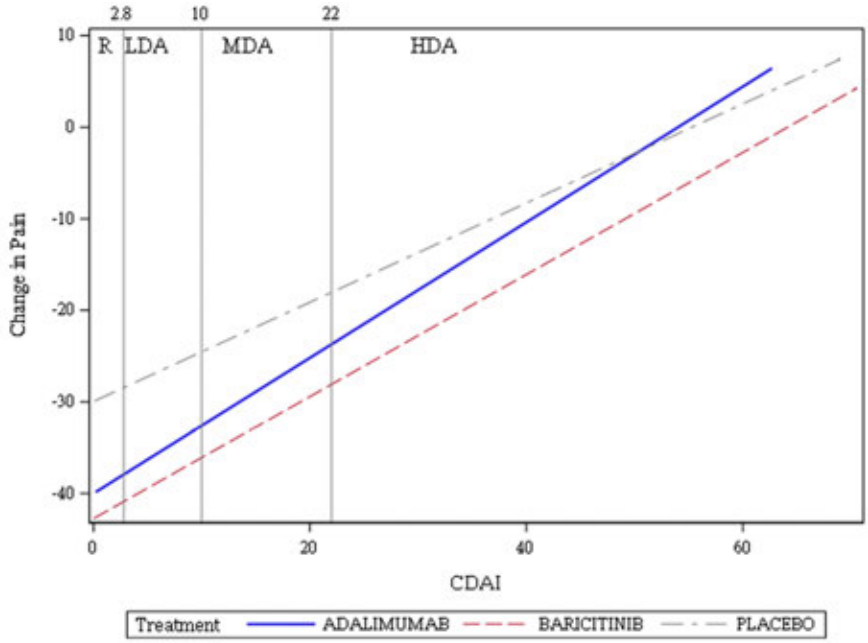
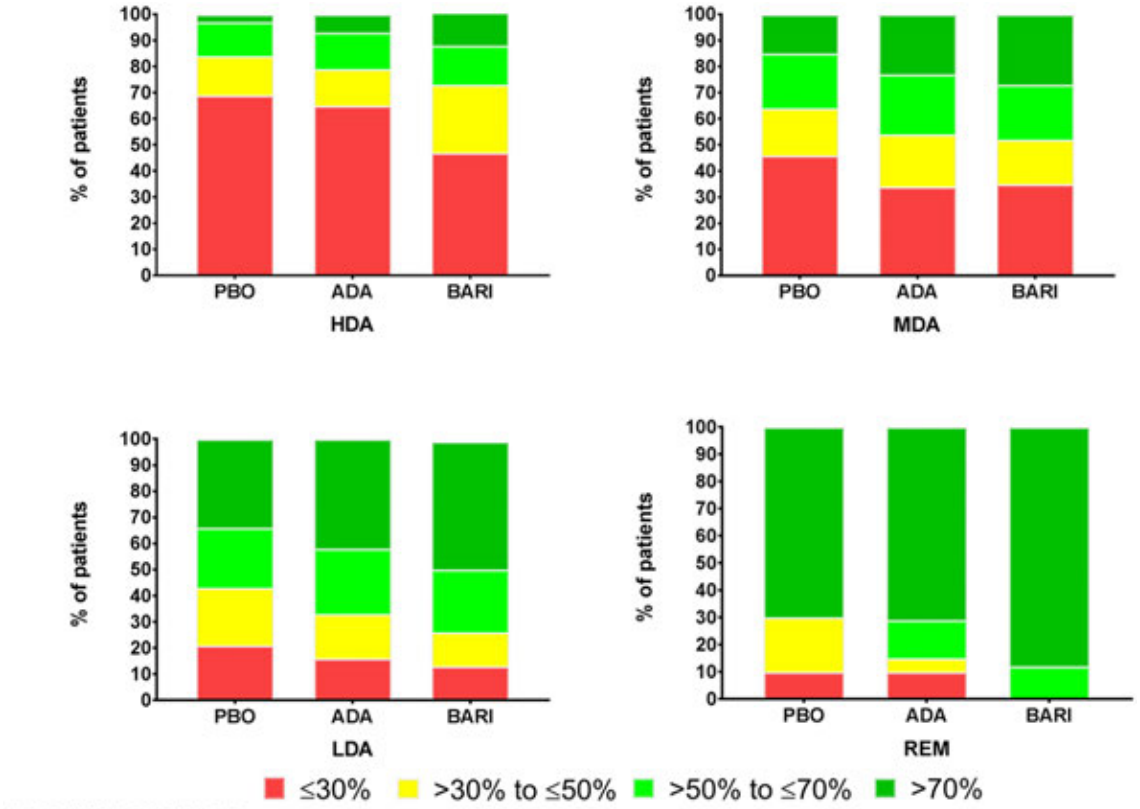


Figure 1. Estimated change in pain VAS by CDAI values at Week 12



N: PBO, 478; ADA, 323; BARI, 477

Abbreviations: ADA: adalimumab, BARI: baricitinib; HDA: high disease activity; LDA: low disease activity; MDA: moderate disease activity; PBO: placebo; REM: remission

Figure 2. Distribution in percentage improvement from baseline pain VAS to Week 12 by treatment and disease activity (CDAI)

	Estimated change in pain from baseline at the given disease activity threshold values								
Disease Activity Measure	**REM**			**LDA**			**MDA**		
CDAI	**CDAI = 2.8**			**CDAI = 10**			**CDAI =22**		
	PBO	ADA	BARI	PBO	ADA	BARI	PBO	ADA	BARI
	-28.4	-37.9	-40.9	-24.5	-32.6	-36.1	-18.0	-23.7	-28.1
SDAI	**SDAI = 3.3**			**SDAI = 11**			**SDAI =22**		
	PBO	ADA	BARI	PBO	ADA	BARI	PBO	ADA	BARI
	-28.9	-37.7	-40.9	-24.8	-32.3	-35.8	-19.0	-24.5	-28.6
DAS28-CRP	**DAS28-CRP = 2.6**			**DAS28-CRP = 3.2**			**DAS28-CRP = 5.1**		
	PBO	ADA	BARI	PBO	ADA	BARI	PBO	ADA	BARI
	-30.6	-35.1	-39.2	-26.6	-30.8	-34.6	-13.9	-17.4	-20.1
DAS28-ESR	**DAS28-ESR = 2.6**			**DAS28- ESR = 3.2**			**DAS28- ESR = 5.1**		
	PBO	ADA	BARI	PBO	ADA	BARI	PBO	ADA	BARI
	-32.3	-37.8	-42.9	-28.9	-34.1	-39.1	-18.0	-22.5	-26.9

HDA values are those in excess of the threshold value for MDA and are not presented

Abbreviations: ADA: adalimumab, BARI: baricitinib, CDAI: Clinical Disease Activity Index; CRP: C-reactive protein; DAS28: Disease Activity Score for 28 joints; ESR: erythrocyte sedimentation rate; LDA: low disease activity; MDA: moderate disease activity; PBO: placebo; SDAI: Simplified Disease Activity Index

and >70%[2]. Disease activity was measured with the Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), Disease Activity Score for 28 joints (DAS28) with C-reactive protein (CRP), and DAS28 with erythrocyte sedimentation rate (ESR). To evaluate change in pain with disease activity, regression was used with continuous change in pain VAS score from baseline to Week 12 as the outcome and continuous CDAI/SDAI/DAS28-CRP/DAS28-ESR values, treatment, and the interaction term between treatment and disease activity as explanatory variables. Last observation carried forward was used to impute missing values. Pain VAS change at Week 12 was estimated from regression for all treatments if patients achieved remission (REM)/low disease activity (LDA)/moderate disease activity (MDA) as defined by the corresponding clinical measure. Analyses were not adjusted for multiplicity. Data visualization with the percentage of pain VAS improvement vs. disease activity was created to examine pain improvement with treatment over time.

Results: With CDAI, 91% of patients had high disease activity and 9% had MDA across all treatments at baseline. At Week 12, the percentage of patients who achieved REM with PBO, ADA, and BARI, respectively, were 2%, 7%, 8%; for LDA: 15%, 27%, 33%; for MDA: 33%, 40%, 38%.[3] At all CDAI values, the estimated change in pain VAS for BARI was greater vs. PBO and ADA (Figure 1); the BARI line is below lines for PBO and ADA across the CDAI range. Similar trends were observed with other disease activity measures (Table). Figure 2 shows the percentage of patients with ≤30%, >30% to ≤50%, >50% to ≤70%, and >70% pain improvement from baseline at Week 12 by disease activity. BARI demonstrated greater pain improvement vs. ADA and PBO in all disease activity categories. With CDAI/SDAI, greater differentiation between BARI and ADA was observed as CDAI/SDAI values increased.

Conclusion: BARI provided additional pain improvement vs. PBO and ADA when disease activity was controlled and across all levels of disease activity, as measured by CDAI, SDAI, DAS28-CRP, or DAS28-ESR at Week 12.

Reference:

1. Taylor, NEJM, 2017; 2. http://www.immpact.org/; 3. Nash ACR abstract 2017

Disclosure: P. Taylor, AbbVie, 5, Abbvie, 5, Biogen, 5, Celgene, 2, 5, Eli Lilly and Company, 2, 5, Fresenius, 5, Fresenius SE & Co, 5, Fresnius, 5, Galapagos, 2, 5, Gilead, 5, GlaxoSmithKline, 5, Janssen, 2, 5, Lilly, 2, 5, Nordic Pharma, 5, NORDIC Pharma, 5, Pfizer, 5, Pfizer Inc, 5, Roche, 5, Sanofi, 5, UCB, 5; **J. Pope**, AbbVie, 5, Abbvie, 5, Actelion, 5, Actellion, 5, Amgen, 2, 5, AstraZeneca, 2, Astra-Zeneca, 2, Bayer, 2, 5, BMS, 2, 5, Eicos Sciences, 5, Eli Lilly & Company, 5, Eli Lilly and Company, 5, EMERALD, 5, Emerald, 5, Genzyme, 5, Janssen, 5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8; **K. Ikeda**, Abbvie Japan, 8, AbbVie Japan, 8, Bristol-Myers Squibb Japan, 8, Mitsubishi Tanabe Pharma, 2, Novartis Japan, 8; **X. Zhang**, Eli Lilly and Company, 1, 3; **B. Jia**, Eli Lilly and Company, 1, 3; **H. Zhang**, Eli Lilly and Company, 2; **A. Quebe**, Eli Lilly & Company, 3, 4, Eli Lilly and Company, 1, 3; **Y. Chen**, Eli Lilly and Company, 1, 3; **C. Gaich**, Eli Lilly & Company, 3, 4, Eli Lilly and Company, 1, 3, 4; **T. Holzkaemper**, Eli Lilly and Company, 1, 3; **A. Cardoso**, Eli Lilly and Company, 1, 3; **A. Sebba**, Eli Lilly and Company, 8, Genentech, 8, Sanofi, 8, Regeneron, 8, Gilead, 8.

Abstract Number: 1408

Efficacy of Pharmacological Treatment in Rheumatoid Arthritis: A Systematic Literature Review Informing the 2019 Update of the EULAR Recommendations for Management of Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Via a systematic literature review of contemporary efficacy data of pharmacological therapies in RA we sought to inform the 2019 update of the EULAR recommendations for the management of RA.

Methods: A systematic literature review to investigate the efficacy of any DMARD (conventional synthetic (cs) DMARD, bDMARD, tsDMARD) or glucocorticoid (GC) therapy in patients with RA. MEDLINE, Embase and the Cochrane Library were searched for articles published between 2016 and March 8th 2019. Open-label studies were acceptable for strategy trials or trials investigating treatment changes

Results: Of 7876 unique abstracts 234 were selected for detailed review with 136 finally included. Twenty-one studies investigated the efficacy of bDMARDs vs. placebo, with 14 studies meeting their primary efficacy endpoint (PEP). Seven head-to-head (H2H) trials comparing bDMARDs and three H2H trials comparing tsDMARD to bDMARDs were included (Table 1). Twenty placebo-controlled trials demonstrated efficacy of JAK inhibitors across different patient populations. Two studies investigated switching of bDMARD therapy in TNFi primary non-responding patients: one trial evaluated the superiority of switching to non-TNFi bDMARDs and met its PEP, while the second evaluated superiority of switching from adalimumab to certolizumab-pegol (CZP) but did not meet its PEP. Stopping or tapering of bDMARDs and/or csDMARDs/GCs was investigated in 22 studies. Using concomitant csDMARDs when tapering bDMARDs lowered the risk of flaring, while tapering csDMARDs in patients with ongoing bDMARD therapy increased the risk of flaring in most studies. All studies investigating biosimilars (n=17) showed non-inferiority compared to their reference products. Further, switching between bDMARD originators and their respective biosimilars showed non-inferiority across all studies (n=11). An open-label strategy trial compared an MRI-guided treat-to-target (T2T) strategy to a conventional T2T strategy (using DAS28-CRP) and failed to show any benefit regarding clinical outcome or radiographic progression. Another open-label strategy RCT stratified patients naïve to csDMARDs according to poor prognostic factors into different csDMARD/GC combination regimes and reported comparable clinical and radiographic results across groups.

Conclusion: The efficacy of many different bDMARDs as well as tsDMARDs was shown in studies included in this SLR. Switching to TNFi or non-TNFi bDMARDs after TNFi treatment failure seems to be feasible. Tapering of bD-

Table 1. Head-to-head studies investigating biological DMARDs or tsDMARDs versus other biological DMARDs.

Population	Study	Agent	Control	Type	RoB	PEP
Biological DMARDs						
MTX-IR	Burmester 2017 (MONARCH)	Sarilumab mono (Anti-IL6)	Adalimumab mono	S	low	met
	Smolen 2016 (EXXELERATE)	Certolizumab-pegol (anti-TNF)	Adalimumab	S	low	not met
	Genovese 2018	ABT-122 (anti-TNF/IL17A)	Adalimumab	S	low	not met
	Taylor 2018 (SIRROUND-H)	Sirukumab mono (anti-IL6)	Adalimumab mono	S	low	met
csDMARD-IR	Porter 2016 (ORBIT)	Rituximab (anti-CD20)	anti-TNF	NI	high	met
TNFi-IR	Blanco 2017 (NURTURE 1)	Secukinumab (anti-IL17)	Abatacept	S	low	not met*
mixed cs/bDMARD-IR	Weinblatt 2018 (EARTH EXPLORER 2)	Mavrilimumab (anti-GM-CSF)	Golimumab	S	low	not met
Targeted synthetic DMARDs						
MTX-IR	Taylor 2017 (RA-BEAM)	Baricitinib+MTX	Adalimumab + MTX	S	low	Met
	Fleischmann ACR 2018 (SELECT-COMPARE)	Upadacitinib+MTX	Adalimumab + MTX	S	abstract	Met
	Fleischmann 2017 (ORAL-Strategy)	Tofacitinib mono Tofacitinib + MTX	Adalimumab + MTX	NI	low	Not Met Met

RoB: Risk of Bias

PEP: Primary efficacy endpoint

Type: Superiority (S), Non-inferiority (NI)

* superior to placebo, not superior to active comparator

MARDs as well as csDMARDs is possible in patients achieving long-standing clinical remission but may increase the risk of disease flare. Biosimilars were non-inferior to their reference products.

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Lilly, 2, 5, 8, Janssen, 2, 5, 8, Leo, 5, Lilly, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8; **J. Bijlsma**, Lilly, 8, Roche, 2, 8; **G. Burmester**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma., 5, 8, AbbVie Inc., 5, 8, BMS, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Merck Shar & Dohme, 5, 8, MSD, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche, Sanofi-Genzyme, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Union Chimique Belge, 2, 5, 8; **M. de Wit**, Abbvie, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen-Cilag, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8; **L. Falzon**, None; **R. Landewé**, Abbott, 2, 5, 8, Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8.

Abstract Number: 1409

Comparison of Healthcare Resource Utilization and Costs of Type 2 Diabetes Mellitus (T2DM)-Related Complications in Medicare Beneficiaries with Rheumatoid Arthritis (RA) and T2DM Who Initiated Treatment with Abatacept versus Other Targeted Disease-Modifying Anti-Rheumatic Drugs

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Use of abatacept, a targeted DMARD (tDMARD), in patients with RA has shown to improve whole-body insulin sensitivity and reduce HbA1c levels.[1] Comparative evidence on type 2 diabetes mellitus (T2DM) related outcomes against other tDMARDs is lacking. We measured the healthcare resource utilization (HCRU) and costs associated with T2DM in tDMARD-naïve Medicare beneficiaries with RA and T2DM who initiated treatment with abatacept, tumor necrosis factor inhibitors (TNFi), or other non-TNFi.

Methods: Patients initiating abatacept, a TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab), or other non-TNFi (anakinra, rituximab, sarilumab, tocilizumab, tofacitinib) from 2010 through 2017 were identified in a retrospective cohort using 100% Medicare fee-for-service (FFS) claims (Parts A/B/D). Elderly patients (≥65 years of age) were included if they had ≥2 diagnoses of RA, ≥1 diagnosis of T2DM or treated with T2DM medications, no recent history of cancer, and were continuously enrolled for 12 months pre-index date or the date of tDMARD initiation. Post-index follow-up was until discontinuation of the index treatment, disenrollment, death, or end of study period, whichever occurred first. Patients who initiated abatacept were propensity score (PS) matched to initiators of TNFi and non-TNFi separately on baseline demographics, comorbidities, medications, T2DM-related healthcare re-

Table. Rates and costs of T2DM-related complications after initiating tDMARDs

Measures	PS-matched cohort 1		PS-matched cohort 2	
	Abatacept (N = 2,664)	TNFi (N = 2,664)	Abatacept (N = 1,507)	Other Non-TNFi (N = 1,507)
Mean Age	73.7	73.9	73.5	73.2
Mean CCI Score	4.8	4.8	4.8	4.8
Mean Duration of Follow-up (days)	394.8	301.8	346.1	282.2
T2DM-related HCRU by setting of care during follow-up, Per 1000 Patients Per Month				
Hospitalizations	23.0*	26.0	25.5*	32.7
Cardiovascular	18.5*	20.4	19.4*	25.9
Cerebrovascular	1.8	1.7	1.4*	2.6
Metabolic	0.5	0.4	0.6	1.2
Nephropathy	8.6	10.0	8.7	11.7
Neuropathy	3.5	3.6	4.3	6.2
Peripheral Vascular Disease	2.7*	3.4	2.8	4.0
Retinopathy	0.5	0.7	0.6	0.8
ER Visits	14.4	15.0	16.6	16.9
Hospital Outpatient Visits	118.5	106.2	132.7*	150.4
Physician Office Visits	601.3*	651.6	645.3	656.3
T2DM-related complication costs, PPPM				
Total Medical	$589	$647	$653*	$812
Inpatient	$313	$335	$359	$460
ER	$16	$15	$16	$15
Hospital Outpatient	$80	$75	$82	$95
Physician Office	$97	$95	$102	$97
Other Medical (includes costs related to skilled nursing facility, home health and DME, and hospice utilization)	$82*	$127	$95*	$145
Follow-up T2DM Medication Costs, PPPM	$45*	$69	$55	$63

*P<0.05

T2DM = Type 2 diabetes mellitus, DME = durable medical equipment, PPPM = per-patient per month

source use and costs. T2DM-related complications include neuropathy, nephropathy, cerebrovascular, cardiovascular, retinopathy, peripheral vascular disease and metabolic from the validated Diabetes Severity Complication Index (DCSI).[2] The HCRU of T2DM-related complications was measured using the counts of inpatient stay, ER visits and outpatient visits per 1,000 patients per month whereas costs (2019 USD) were measured as per-patient per month (PPPM).

Results: A total of 2,664 PS-matched pairs of abatacept and TNFi's users, and 1,507 PS-matched pairs of abatacept and other non-TNFi's users were identified. During follow-up, the rate of hospitalizations associated with T2DM-

related complications per 1,000 patients per month was the lowest in abatacept group compared to both TNFi (23.0 vs. 26.0) and other non-TNFi groups (25.5 vs. 32.7). Similar trends were observed for ER visits and outpatient care. The major driver of T2DM-related healthcare costs for each group was hospitalizations. PPPM T2DM-related complication costs decreased following tDMARD initiation in abatacept (˃20%) and TNFi (17%) users and increased in non-TNFi users (1.5%). During follow-up, PPPM T2DM-related costs were $58 and $159 lower for abatacept versus TNFi and non-TNFi initiators, respectively.

Conclusion: In Medicare FFS beneficiaries with RA and T2DM, abatacept initiators had lower T2DM-related HCRU and costs compared to initiators of TNFis and non-TNFis. These findings suggest that use of abatacept as a first line tDMARD could help reduce the clinical and economic burden associated with T2DM in patients with RA.

References:

1. Ursini F, et al. *Medicine* (Baltimore). 2015;94(21):e888.
2. Glasheen WP, et al. *J Diabetes Complications.* 2017;31(6):1007-1013.

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Abstract Number: 1410

Cycling of Tumor Necrosis Factor-α (TNF-α) Inhibitors versus Switching to Different Mechanism of Action in Rheumatoid Arthritis Patients with Inadequate Response to TNF-α Inhibitor: A Bayesian Network Meta-analysis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: TNF inhibitors are a common treatment for rheumatoid arthritis (RA), but there is no best practice for when a specific TNF inhibitor stops working[1]. The main options are to 'cycle' patients onto a different TNF inhibitor, or to 'switch' patients onto a drug with a different mechanism of action. Building on a previous developed systematic review of existing RCTs and observational studies, this network meta-analysis (NMA) assess the clinical comparative efficacy of 'cycling' versus 'switching'.

Methods: We conducted a literature search in MEDLINE, Embase and Cochrane Library in June 2018. RCTs and observational studies investigating second-line treatments for rheumatoid arthritis, respectively for TNF inhibitor (adalimumab, infliximab, etanercept, certolizumab, golimumab) and drugs with different mechanism of action (Moa) were considered.

The outcomes included the mean reduction in HAQ score; proportion of patients with a clinically meaningful HAQ reduction (defined as a reduction of at least 0.22); proportion of patients with a 20% (ACR20), 50% (ACR50) or 70% (ACR70) response on the ACR score; proportion of patients achieving a DAS28 score below 2.6 (classified as remission) or between 2.6 and 3.2 (classified as low disease activity); mean change in DAS28 score; rate of serious adverse events (SAEs); and number of withdrawals for any reason or due to adverse events or lack of treatment efficacy.

Risk of bias was assessed both RCTs and observational studies through Cochrane Risk of Bias Tool and Newcastle-Ottawa Scale respectively. We classed interventions as 'cycle', 'switch' or placebo and performed three models of NMA: a fixed effect model, a random-effect model and hierarchical Bayesian network meta-analysis[2,3] for each outcome with appropriate data**.**

Results: We identified 9 RCTs (4 for 'cycling' and 5 for 'switching') and 16 observational studies (8 for 'cycling' and 8 for 'switching') meeting our inclusion criteria, with patient numbers ranging from small studies of 15 patients up to 1683 patients. The proportion of females in the studies were at least 71.1% and the mean age of participants ranged from 45.1 to 59.0 years.

ACR20 – main results – all studies

Statistic	Fixed	LB	UB	Random	LB	UB	Hierarchical	LB	UB
DIC	100			101			111		
OR cycle vs PBO	2.81	2.12	3.89	2.88	1.76	6.07	3.31	1.69	10.46
OR switch vs PBO	3.86	3.11	4.87	3.80	2.50	5.67	3.77	2.12	7.26
OR switch vs cycle	1.38	1.06	1.78	1.33	0.63	2.08	1.14	0.32	2.39

ACR50 – main results – all studies

Statistic	Fixed	LB	UB	Random	LB	UB	Hierarchical	LB	UB
DIC	76			77			98		
OR cycle vs PBO	3.86	2.53	6.20	3.82	1.99	6.55	3.84	1.87	7.39
OR switch vs PBO	5.15	3.68	7.52	5.27	3.31	8.29	5.33	3.26	8.82
OR switch vs cycle	1.35	0.96	1.81	1.38	0.88	2.41	1.39	0.69	2.69

Withdrawals due to lack of efficacy – main results – all studies

Statistic	Fixed	LB	UB	Random	LB	UB	Hierarchical	LB	UB
DIC	94			69			111		
OR cycle vs PBO	0.23	0.1	0.5	0.32	0.02	7.01	0.31	0.02	6.75
OR switch vs PBO	0.08	0.05	0.13	0.1	0.01	0.67	0.09	0.01	0.69
OR switch vs cycle	0.35	0.19	0.62	0.3	0.02	4.17	0.29	0.02	3.78

DIC: Deviance Information Criterion; OR: Odds Ratio; PBO: Placebo; LB: Lower Bound; UP: Upper Bound; Fixed: Fixed Effect Estimate; Random: Random Effect Estimate; Hierarchical: Hierarchical Estimate.

The fixed effects NMA suggested a 0.99 probability that 'switch' was the better strategy for increasinng the odds of a clinically meaningful improvement in ACR20 (OR: 1.38 [95% CI: 1.06-1.78]). 'Switch' was also associated with fewer rates of withdrawals due of lack of efficacy (OR: 0.35 [95% CI: 0.19-0.62]) and withdrawals for any reasons.

Random effects and hierarchical Bayesian models reflected additional uncertainty but gave similar results. (Figure 1)

Conclusion: Results suggest that "switching" to a drug with a different mechanism of action is more effective and with lower rates of withdrawals than "cycling" to a different TNF inhibitor after first-line TNF inhibitor failure. Further trials to directly compare 'cycling' with 'switching' is warranted to better assess the comparative efficacy.

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Abstract Number: 1411

Positivity of Anti-Ro/SSA Antibody Confer Poor Response and Persistence with Abatacept Therapy

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Rheumatoid arthritis (RA) occasionally overlaps Sjogren's syndrome (SS), and RA patients with secondary SS have a higher disease activity of RA and worse joint damage compared with RA patients without SS.

A previous report indicated that the positivity of anti-Ro/SSA antibody (Ab), which is diagnostic maker for SS, was an independent factor associated with poor response to tumor necrosis factor inhibitors in RA patients. While, abatacept have showed the efficacy of both synovitis and glandular symptoms in RA patients with secondary SS. However, few reports show comparable efficacy of abatacept therapy between anti-Ro/SSA Ab-negative and -positive patients with RA.

To clarify whether the positivity of baseline anti-Ro/SSA Ab influence response to abatacept therapy, we compared clinical profiles between anti-Ro/SSA Ab-negative and -positive patients with RA using a multicenter RA ultrasonography prospective cohort.

Table 1. Baseline participant characteristic by positivity or negativity of anti-Ro/SSA antibody (univariate analysis)

Variables	All patients (n = 51)	Anti-Ro/SSA Ab-negative group (n = 35)	Anti-Ro/SSA Ab-positive group (n = 16)	p-value
Patient characteristics at baseline				
Age (years)	70.0 (66.0 – 77.0, n = 51)	73.0 (67.0 – 79.0, n = 35)	66.5 (57.5 – 72.3, n = 16)	0.04
Disease duration (month)	32.0 (12.0 – 132.0, n = 51)	31.0 (12.0 – 120.0, n = 35)	56.0 (9.8 – 249.0, n = 16)	0.92
Male gender (%)	12/51 (23.5%)	10/35 (28.6%)	2/16 (12.5%)	0.30
Smoking history (%)	9/51 (17.6%)	7/35 (20.0%)	2/16 (12.5%)	0.70
Comorbidity at baseline				
Interstitial pneumonia (%)	13/51 (25.5%)	10/35 (28.6%)	3/16 (18.8%)	0.73
Definite diagnosis of SS (%)	8/51 (15.7%)	1/35 (2.9%)	7/16 (43.8%)	< 0.001
Medication at baseline				
Concomitant prednisolone use (%)	29/51 (56.9%)	22/35 (62.9%)	7/16 (43.8%)	0.24
Doses of concomitant prednisolone (mg/day)	2.0 (0.0 – 5.0, n = 51)	4.0 (0.0 – 5.0, n = 35)	0.0 (0.0 – 6.4, n = 16)	0.36
Concomitant DMARDs use (%)	43/51 (84.3%)	31/35 (88.6%)	12/16 (75.0%)	0.24
Concomitant methotrexate use (%)	25/51 (49.0%)	17/35 (48.6%)	8/16 (50.0%)	1.00
Clinical disease activity at baseline				
Baseline DAS28-ESR	5.2 (4.3 – 5.9, n = 51)	5.3 (3.9 – 5.9, n = 35)	5.0 (4.6 – 6.0, n = 16)	0.90
Baseline DAS28-CRP	4.2 (3.5 – 5.1, n = 51)	4.4 (3.4 – 5.1, n = 35)	4.1 (3.8 – 5.2, n = 16)	0.79
Baseline SDAI	20.5 (14.4 – 30.7, n = 51)	20.5 (14.1 – 30.7, n = 35)	20.4 (17.2 – 30.4, n = 16)	0.75
Baseline CDAI	19.0 (14.0 – 27.0, n = 51)	18.0 (14.0 – 26.5, n = 35)	20.3 (16.9 – 28.5, n = 16)	0.33

Table 1. Baseline participant characteristic by positivity or negativity of anti-Ro/SSA antibody (univariate analysis)

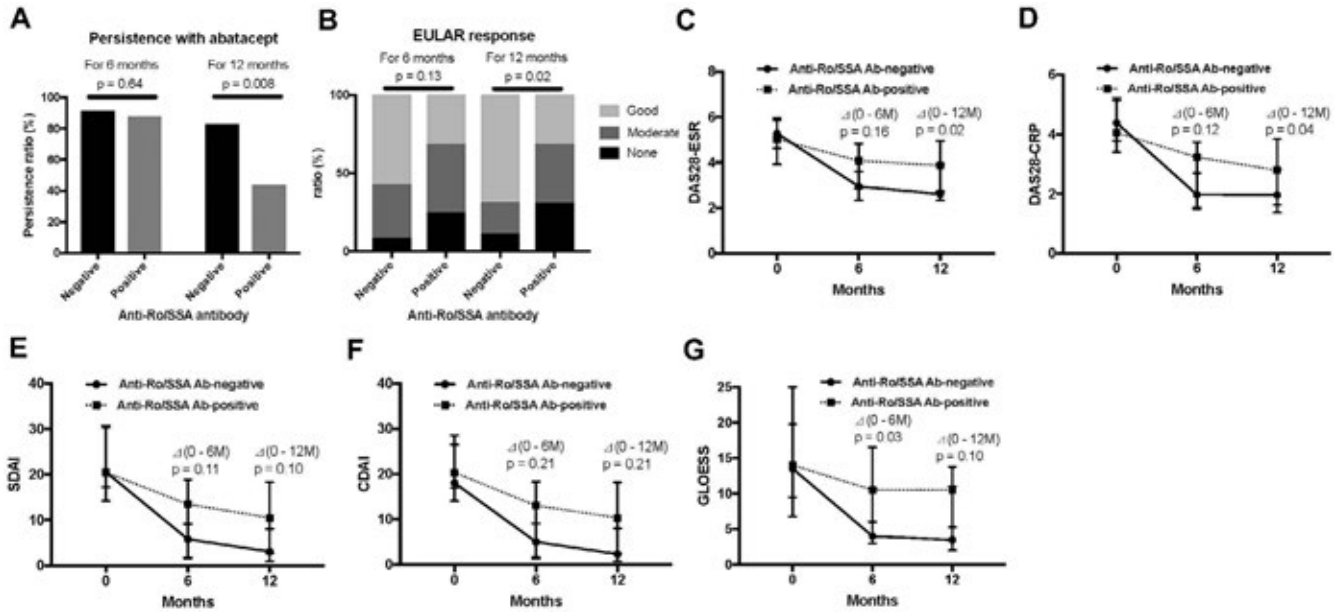

Figure 1. Persistence, response, and each disease activity indicator at 6 or 12 months by positivity or negativity of anti-Ro/SSA antibody

Methods: We initially reviewed Japanese RA patients who newly started abatacept therapy as a first biological DMARDs between June 2013 and April 2018. Subsequently, we excluded patients whose baseline anti-Ro/SSA Ab status were uncleared and patients with baseline low disease activity at the initiation of abatacept therapy. Overall, enrolled total 51 patients were divided into anti-Ro/SSA Ab-negative and -positive groups of 35 and 16, respectively, according to the result of anti-Ro/SSA Ab assay. The Global OMERACT-EULAR Synovitis Score (GLOESS), which is composite PDUS scores of the greyscale (GS) and power Doppler (PD), was calculated at above examined 22 joints as an indicator of comprehensive ultrasonography activity.

Results: The median age at baseline was significantly higher in anti-Ro/SSA Ab-negative group ($p = 0.04$). Anti-Ro/SSA Ab-positive group had significantly higher frequencies of definite SS diagnosis and baseline antinuclear antibody $\geq$ 80 times ($p < 0.001$, $p = 0.02$, respectively). The persistence ratio and the percentage of EULAR good responders at 12 months were significantly higher in anti-Ro/SSA Ab-negative group ($p = 0.008$, $p = 0.02$, respectively). Although there was no significant difference in changes in both SDAI and CDAI scores between anti-Ro/SSA Ab-negative and -positive groups, both DAS28-ESR and DAS28-CRP scores decreased significantly at 12 months in anti-Ro/SSA Ab-negative group ($p = 0.02$, $p = 0.04$, respectively). In addition, GLOESS scores also decreased significantly at 6 months in anti-Ro/SSA Ab-negative group ($p = 0.03$). Univariate and multivariate analyses showed that negativity of anti-Ro/SSA Ab was an independent factor associated with good responders to abatacept therapy.

Conclusion: Our results indicate that the positivity of anti-Ro/SSA Ab confer poor response and persistence to abatacept therapy by comprehensive assessments.

Table 2. Comparison of selected variables associated with good responders to abatacept treatment in multiple logistic regression analysis (continuous variables)

	Variables		p-value	OR (95% CI)
Model 1	Disease duration (month)	1 increase	0.27	1.003 (0.998–1.009)
	Male gender (%)	Presence	0.23	2.980 (0.505–17.564)
	Definite diagnosis of SS (%)	Presence	0.08	0.158 (0.020–1.231)
	Doses of concomitant prednisolone (mg/day)	1 increase	0.10	0.893 (0.780–1.023)
	Baseline antinuclear antibody ≥ 80 times (%)	Presence	0.72	0.788 (0.215–2.891)
Model 2	Disease duration (month)	1 increase	0.40	1.002 (0.997–1.008)
	Male gender (%)	Presence	0.18	3.656 (0.552–24.233)
	Baseline anti-Ro/SSA Ab positive (%)	Presence	0.03	0.198 (0.046–0.854)

Table 2. Comparison of selected variables associated with good responders to abatacept treatment in multiple logistic regression analysis (continuous variables)

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Efficacy and Safety of Tofacitinib Modified-Release 11 Mg Once Daily + MTX in RA Patients with an Inadequate Response to MTX: Open-Label Phase Results from a Global Phase 3b/4 MTX Withdrawal Study

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Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. The tofacitinib modified-release (MR) 11 mg once daily (QD) formulation was first approved in the US in 2016 for the treatment of patients (pts) with moderate to severe RA and an inadequate response or intolerance to MTX. ORAL Shift is the first global study of tofacitinib MR 11 mg QD + MTX. Efficacy and pt-reported outcomes (PROs), and safety, from the open-label (OL) phase of ORAL Shift are reported here.

Methods: ORAL Shift (NCT02831855) was a global Phase 3b/4 study in pts aged ≥ 18 years with moderate to severe RA and an inadequate response to MTX. Pts received OL tofacitinib MR 11 mg QD + MTX (tofacitinib + MTX) for 24 weeks; those achieving low disease activity (LDA; Clinical Disease Activity Index [CDAI] ≤ 10) at Week (W)24 entered the 24-week double-blind (DB) MTX withdrawal phase, where the primary endpoint was assessed (data reported elsewhere).[1] Outcomes from the OL phase, reported descriptively here, include: mean change from baseline (BL) to W12 and W24 in disease activity measures, and PROs; rates of ACR and HAQ-Disability Index (DI) response, and LDA and remission, at W12 and W24 (see Table 1); and safety (see Table 2).

Results: In the OL phase, 694 pts received tofacitinib + MTX. Most pts were female (76.7%), white (85.6%), with a mean age of 56.8 years and mean RA duration of 8.8 years. At W24 (end of the OL phase), 526 (75.8%) pts achieved CDAI-defined LDA (Table 1). In the OL phase, Disease Activity Score in 28 joints, ESR (DAS28-4[ESR]) improved with

Table 1. Efficacy and patient-reported outcomes during the open-label phase

	Tofacitinib MR 11 mg QD + MTX N=694[a]	
Change from baseline[b], mean (SD)	W12	W24
DAS28-4(ESR)	-1.96 (1.19)	-2.67 (1.25)
DAS28-4(CRP)	-1.89 (1.18)	-2.62 (1.19)
SDAI	-20.26 (12.47)	-27.01 (13.07)
CDAI	-19.63 (12.10)	-26.24 (12.61)
HAQ-DI	-0.48 (0.52)	-0.62 (0.58)
FACIT-F	6.91 (9.34)	9.25 (10.06)
Pain VAS	-26.53 (26.04)	-36.10 (27.03)
PtGA	-26.80 (27.49)	-37.52 (27.11)
Response, n (%)		
ACR20[c,d]	424 (61.1)	502 (72.3)
ACR50[c,d]	230 (33.1)	417 (60.1)
ACR70[c,d]	119 (17.2)	244 (35.2)
HAQ-DI[d,e]	431 (62.1)	412 (59.4)
LDA, n (%)		
DAS28-4(ESR) ≤3.2[d]	166 (23.9)	272 (39.2)
CDAI ≤10[d]	268 (38.6)	526 (75.8)
Remission, n (%)		
DAS28-4(ESR) <2.6[d]	91 (13.1)	156 (22.5)
CDAI ≤2.8[d]	76 (11.0)	146 (21.0)
ACR-EULAR Boolean[d,3]	53 (7.6)	122 (17.6)

[a]Efficacy data are from the full analysis set (all patients who received at least one dose of tofacitinib + MTX during the open-label phase). The number of patients assessed for each efficacy outcome measure may be less than the overall N; [b]Value at baseline is defined as the last non-missing measurement on or prior to the first dosing date in open-label phase; [c]20/50/70% improvement in tender and swollen joint counts and 20/50/70% improvement in three of the five other criteria (PtGA, PGA, HAQ-DI, Pain [VAS], and CRP), relative to open-label phase baseline; [d]Non-responder imputation; [e]HAQ-DI decrease of ≥0.22, relative to baseline.
ACR, American College of Rheumatology; CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; DAS28-4(CRP), Disease Activity Score in 28 joints, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; EULAR, European League Against Rheumatism; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDA, low disease activity; MR, modified-release; MTX, methotrexate; PGA, Physician Global Assessment of Arthritis; PtGA, Patient Global Assessment of Arthritis; QD, once daily; SDAI, Simplified Disease Activity Index; VAS, visual analog scale; W, Week

Table 2. Safety outcomes during the open-label phase

	Tofacitinib MR 11 mg QD + MTX N=694[a]
AEs, n (%)	362 (52.2)
SAEs, n (%)	20 (2.9)
Discontinuations due to AEs, n (%)	41 (5.9)
Deaths, n (%)	0
Most common (≥2%) AEs by MedDRA PT, n (%)	
Nasopharyngitis	35 (5.0)
Upper respiratory tract infection	33 (4.8)
Nausea	20 (2.9)
Urinary tract infection	19 (2.7)
Headache	17 (2.4)
Hypertension	17 (2.4)
Diarrhea	16 (2.3)
ALT increased	16 (2.3)
Dizziness	15 (2.2)
AEs of special interest, n (%)	
Serious infections	5 (0.7)
Herpes zoster[b]	4 (0.6)
Malignancies excluding NMSC[c]	2 (0.3)
NMSC[c]	1 (0.1)
MACE[c]	0
Opportunistic infections[c]	0
GI perforation[c]	0
PE	0

[a]Safety data are from the safety analysis set (all patients who received at least one dose of tofacitinib + MTX during the open-label phase). Events are counted up to 28 days beyond the last dose. [b]All herpes zoster events reported involved one or two adjacent dermatomes and were non-serious; [c]Reviewed by an independent adjudication committee
AE, adverse event; ALT, alanine aminotransferase; GI, gastrointestinal; MACE, major adverse cardiovascular event; MedDRA, Medical Dictionary for Regulatory Activities; MR, modified-release; MTX, methotrexate; n, number of patients with an event; NMSC, non-melanoma skin cancer; PE, pulmonary embolism; PT, preferred term; QD, once daily; SAE, serious adverse event

mean (standard deviation) changes from BL of -1.96 (1.19) and -2.67 (1.25) at W12 and W24, respectively (Table 1). Mean changes from BL at W12 and W24 showed improvements in all other efficacy outcomes and PROs (Table 1). ACR20/50/70 and HAQ-DI response rates, and LDA and remission rates, improved from W12 to W24 (Table 1). Adverse events (AEs), serious AEs, and discontinuations due to AEs were reported by 52.2%, 2.9%, and 5.9% of pts, respectively; no deaths were reported (Table 2). The most common AEs were nasopharyngitis and upper respiratory tract infections. AEs of special interest each occurred in ≤ 1% of pts (Table 2).

Conclusion: Tofacitinib MR 11 mg QD + MTX improved disease activity and PROs in pts with moderate to severe RA and an inadequate response to MTX. No new safety risks were observed. Efficacy and safety in this OL phase appeared consistent with that of tofacitinib immediate-release 5 mg twice daily[2], with the DB phase of ORAL Shift.[1]

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Abstract Number: 1413

Efficacy of Tofacitinib Monotherapy, Tofacitinib with Methotrexate and Adalimumab with Methotrexate in Patients with Early (≤ 2 Years) vs Established (> 2 Years) Rheumatoid Arthritis: A Post Hoc Analysis of Data from ORAL Strategy

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SESSION INFORMATION
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Background/Purpose: Tofacitinib is an oral JAK inhibitor for the treatment of RA. Greater improvements in efficacy outcomes have been reported with tofacitinib 5 mg BID ± conventional synthetic DMARDs in patients (pts) with early vs established RA.[1,2] This post hoc analysis of ORAL Strategy data evaluated the efficacy and safety of tofacitinib monotherapy, tofacitinib + methotrexate (MTX), and adalimumab (ADA) + MTX, stratified by baseline (BL) RA duration.

Methods: ORAL Strategy (NCT02187055) was a P3b/4, 1-yr, double-blind, triple-dummy, active comparator-controlled study. MTX inadequate-responders were randomized 1:1:1 to receive tofacitinib 5 mg BID (tofa mono), tofacitinib 5 mg BID + MTX (tofa+MTX), or ADA SC 40 mg Q2W + MTX (ADA+MTX); MTX was dosed at 15–25 mg/wk except in cases of intolerance/toxicity. In this analysis, pts were stratified by BL RA duration as having early (≤ 2 yrs) or established (> 2 yrs) RA. Efficacy outcomes (Months [M]3, 6 and 12): ACR20/50/70; change from BL (Δ) in DAS28-4(ESR), Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI); and rates of DAS28-4(ESR)-, SDAI- and CDAI-defined low disease activity (≤ 3.2, ≤ 11, and ≤ 10, respectively) and remission (< 2.6, ≤ 3.3, and ≤ 2.8, respectively). Nominal p values for treatment comparisons were calculated without multiplicity

Table 1. Demographics and disease characteristics at baseline, and safety up to Month 12

	Early RA (≤2 years) N=241			Established RA (>2 years) N=905		
	Tofacitinib monotherapy N=80	Tofacitinib + MTX N=83	Adalimumab + MTX N=78	Tofacitinib monotherapy N=304	Tofacitinib + MTX N=293	Adalimumab + MTX N=308
Baseline demographics and disease characteristics[a]						
Age (years), mean (SD)	47.1 (12.9)	46.2 (13.8)	49.2 (13.5)	50.4 (12.0)	51.0 (13.1)	51.0 (13.3)
Female, n (%)	66 (82.5)	69 (83.1)	60 (76.9)	253 (83.2)	242 (82.6)	260 (84.4)
RA duration (years), mean (SD)	1.0 (0.5)	1.1 (0.5)	1.0 (0.5)	10.4 (7.7)	9.4 (6.9)	10.0 (7.1)
DAS28-4(ESR), mean (SD)	6.6 (0.8)	6.4 (0.8)	6.4 (1.0)	6.5 (0.9)	6.6 (0.9)	6.5 (1.0)
SDAI, mean (SD)	41.9 (12.6)	38.9 (11.1)	39.9 (12.9)	39.8 (13.1)	42.4 (13.6)	39.8 (13.5)
CDAI, mean (SD)	40.0 (12.2)	37.2 (10.9)	38.2 (12.4)	38.2 (12.6)	40.5 (13.1)	38.2 (13.0)
HAQ-DI, mean (SD)	1.6 (0.6)	1.4 (0.7)	1.5 (0.6)	1.6 (0.6)	1.6 (0.6)	1.6 (0.6)
RF+, n (%)	45 (56.3)	42 (50.6)	47 (60.3)	214 (70.4)	203 (69.5)	212 (69.3)
Anti-CCP+, n (%)	59 (73.8)	56 (67.5)	52 (66.7)	232 (76.3)	223 (76.1)	246 (79.9)
Prior medications						
TNFi, n (%)	2 (2.5)	1 (1.2)	0	26 (8.6)	15 (5.1)	19 (6.2)
Non-TNFi, n (%)	1 (1.3)	1 (1.2)	0	18 (5.9)	13 (4.4)	20 (6.5)
MTX dose[b] (mg/wk)	16.4 (3.2)	17.1 (3.1)	16.9 (3.7)	16.6 (3.5)	16.5 (3.9)	16.3 (3.7)
GC use, n (%)	50 (62.5)	47 (56.6)	39 (50.0)	178 (58.6)	168 (57.3)	184 (59.7)
GC dose[b] (mg/day), mean (SD)	7.0 (3.1)	6.6 (2.4)	6.5 (3.5)	7.7 (15.5)	6.4 (2.6)	6.4 (2.4)
Safety, n (%)						
AEs	52 (65.0)	47 (56.6)	53 (67.9)	174 (57.2)	184 (62.8)	200 (64.9)
SAEs	10 (12.5)	2 (2.4)	8 (10.3)	25 (8.2)	24 (8.2)	16 (5.2)

[a]N for each assessment may differ from N for each treatment group; [b]Average dose immediately prior to randomization
AE, adverse event; Anti-CCP, anti-cyclic citrullinated peptide antibody; CDAI, Clinical Disease Activity Index; DAS28-4(ESR), Disease Activity Score in 28 joints based on erythrocyte sedimentation rate; GC, glucocorticoid; HAQ-DI, Health Assessment Questionnaire-Disability Index; MTX, methotrexate; RA, rheumatoid arthritis; RF, rheumatoid factor; SAE, serious adverse event; SDAI, Simplified Disease Activity Index; SD, standard deviation; TNFi, tumor necrosis factor inhibitor; wk, week

adjustment; $p < 0.05$ was considered significant. Treatment-emergent AEs and serious AEs (SAEs) were assessed throughout the study.

Results: In total, 241 pts had early RA (tofa mono: N=80; tofa+MTX: N=83; ADA+MTX: N=78; mean RA duration: 1.0–1.1 yrs); 905 pts had established RA (tofa mono: N=304; tofa+MTX: N=293; ADA+MTX: N=308; mean RA duration: 9.4–10.4 yrs). BL demographics and disease characteristics were generally comparable for early vs established RA pts, with some expected differences (the latter were slightly older, and a greater proportion had received prior biologic DMARDs); RF+ and anti-CCP+ rates were higher for established RA pts (Table 1). ACR50 and ΔDAS28-4(ESR) were generally similar for tofa mono and tofa+MTX up to M12 in early RA but significantly greater with tofa+MTX in established RA ($p < 0.05$); generally, ADA+MTX was not statistically different vs tofa+MTX in early RA (Figure 1). Trends were similar for all outcomes. AE rates were generally similar in early vs established RA. Trends for SAEs were less clear; rates were lowest for tofa+MTX in early RA and higher for both tofacitinib arms vs ADA+MTX in established RA (Table 1).

Conclusion: Efficacy was similar for tofa mono and tofa+MTX in early RA, and significantly higher with tofa+MTX in established RA. ADA+MTX was numerically but not always significantly more effective than tofacitinib in early RA. AE rates were generally similar regardless of BL RA duration. These findings, especially in established RA, are consistent with the conclusion of the primary analysis.[3] Limitations to this post hoc analysis include low numbers of early RA pts.

References:

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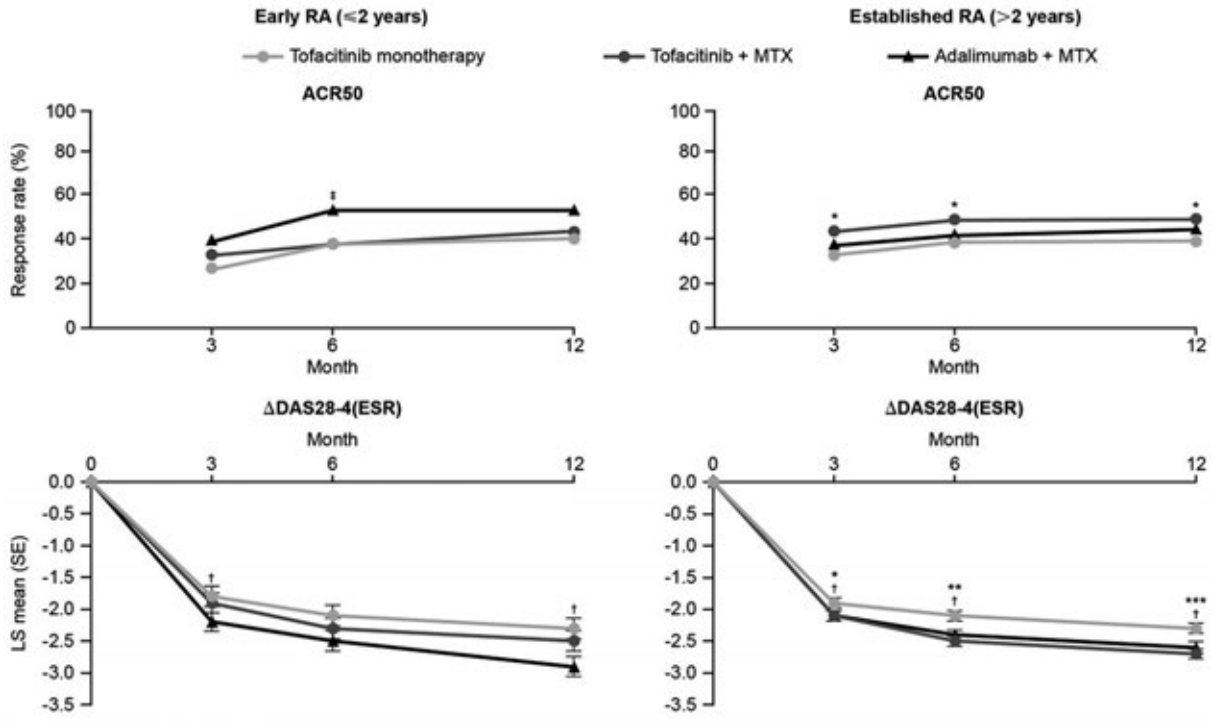
Figure 1. ACR50[a] response rates and ΔDAS28-4(ESR) up to Month 12 (FAS)



[a]Using non-responder imputation
*p<0.05, **p<0.001, ***p<0.0001 tofacitinib monotherapy vs tofacitinib + MTX; †p<0.05 tofacitinib monotherapy vs adalimumab + MTX; ‡p<0.05 tofacitinib + MTX vs adalimumab + MTX
Δ, change from baseline; ACR, American College of Rheumatology; DAS28-4(ESR), Disease Activity Score in 28 joints based on erythrocyte sedimentation rate; FAS, full analysis set; LS, least squares; MTX, methotrexate; RA, rheumatoid arthritis; SE, standard error

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Janssen, 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Medimmune, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, Novartis- Sandoz, 5, Novartis-Sandoz, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 5, Roche, 2, 5, Roche;, 2, 5, 8, Samsung, 5, 8, Sanofi, 5, 8, Sanofi-Aventis, 5, UCB, 5, 8; **R. Fleischmann**, AbbVie, 2, 5, Acea, 2, 5, Akros, 5, Amgen, 2, 5, AstraZeneca, 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, 5, Celltrion, 5, Celtrion, 2, 5, Centrexion, 2, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck-Serono, 2, 5, EMD Serono, 2, EMD-Serano, 2, EMD-Serono, 2, Genentech, 2, 5, Genetech, 2, GlaxoSmithKline, 2, 5, GSK, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Merck, 2, Nektar, 2, Novartis, 2, 5, Pfizer, 2, 5, Pfizer Inc, 2, 5, Regeneron, 2, Resolve, 2, Roche, 2, Samsung, 5, Sandoz, 5, Sanofi Genzyme, 2, Sanofi-Aventis, 2, 5, Sanofi-Aventis, 2, 5, Sanofi-Genzyme, 2, Selecta, 2, Tahio, 5, Taiho, 5, UCB, 2, 5.

Abstract Number: 1414

Improvement of Mental Health and Quality of Life During Therapy with Tocilizumab

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In rheumatoid arthritis (RA), the proinflammatory cytokine IL-6 is associated with mental disorders such as depression and anxiety.[1] Furthermore, depression and anxiety are comorbidities associated with a lower response to RA therapy.[2]

In this interim analysis (data cut-off 1 Feb 2019) of the non-interventional study ARATA, we analyzed the possible influence of depressiveness and anxiety on the effectiveness of tocilizumab (RoActemra®) therapy for the first time

Methods: The ARATA study (NCT02251860) examined the effectiveness and tolerability of subcutaneous tocilizumab therapy in patients with RA in routine practice for up to 104 weeks. Patients were divided into subgroups according to Beck Depression Inventory (BDI)-II or State-Trait Inventory (STAI-X2) category at baseline.

Results: The safety and effectiveness sets were comprised of 627 and 574 patients, respectively. Patients in all depressive symptom and anxiety categories benefitted from tocilizumab therapy (tables 1 and 2), regardless of baseline characteristics. Patients had an overall reduction in depressiveness, and a slight reduction of fear and anxiety in all depressiveness categories. During tocilizumab treatment, patients with positive answers to the question about su-

icidal ideation benefitted the most in regards to disease activity outcomes (DAS28-ESR, CDAI), while patients with severe depressive symptoms benefitted the least. The more severe anxiety categories had greater proportions of patients with a HAQ-DI improvement of at least 0.5 at week 104.

Results in patients-reported outcomes mirrored the results in effectiveness outcomes. Patients without, with mild or with moderate depressive symptoms and patients with positive answers to the question about suicidal ideation had

			Depressive symptoms (BDI-II)				
Parameter		Total N= 1292/1198¥	None N= 265/249¥	Mild N= 96/88¥	Moderate N= 91/85¥	Severe N= 59/55¥	Suicidal ideation N=74/68¥
Median CRP, mg/dl (range)	Week 104	0.40 (0.0-14.9)	0.30 (0.0-14.9)	0.55 (0.0-4.2)	0.30 (0.0-1.8)	0.57 (0.0-3.7)	0.34 (0.0-3.7)
Median ESR, mm/1h (range)	Week 104	6.0 (0.0-112.0)	5.0 (1.0-112.0)	8.0 (0.0-80.0)	8.0 (2.0-44.0)	8.5 (2.0-92.0)	4.0 (2.0-56.0)
BDI-II [SD]	Week 104	10.2 [10.6]	6.0 [5.9]	12.0 [9.4]	13.7 [11.2]	23.8 [15.0]	22.6 [16.5]
	Change from BL	-3.7 [9.2]	-0.3 [5.8]	-4.2 [9.3]	-10.0 [11.9]	-12.2 [9.8]	-8.0 [12.0]
STAI-X1** [SD]	Week 104	38.9 [12.1]	35.1 [10.0]	39.8 [11.3]	42.2 [10.0]	51.6 [12.1]	48.7 [12.9]
	Change from BL	-4.2 [11.1]	-2.8 [8.8]	-4.5 [11.5]	-6.2 [14.1]	-4.0 [10.1]	-4.1 [13.9]
STAI-X2 [SD]	Week 104	38.5 [11.4]	34.4 [9.7]	38.6 [9.6]	42.5 [10.1]	51.4 [11.0]	48.9 [11.3]
	Change from BL	-3.2 [8.7]	-1.7 [8.0]	-4.5 [9.5]	-5.4 [11.8]	-6.1 [8.3]	-6.8 [10.4]
DAS28-ESR [SD]	Week 104	2.4 [1.4]	2.3 [1.3]	2.7 [1.5]	2.5 [1.4]	2.8 [1.3]	2.0 [0.9]
	Change from BL	-2.5 [1.7]	-2.5 [1.8]	-2.3 [1.5]	-2.5 [1.9]	-2.4 [1.9]	-2.9 [1.5]
< 2.6; % (n/N)*	Week 104	60.2 (274/455)	69.4 (77/111)	52.5 (21/40)	60.0 (24/40)	56.3 (9/16)	80.0 (20/25)
CDAI [SD]	Week 104	8.4 [9.0]	6.5 [7.1]	8.7 [10.4]	6.6 [6.7]	11.6 [7.2]	6.3 [6.1]
	Change from BL	-16.6 [13.4]	-17.2 [12.2]	-16.7 [11.7]	-17.7 [13.1]	-12.7 [11.7]	-20.2 [12.3]
≤ 2.8; % (n/N)*	Week 104	32.5 (173/532)	39.1 (54/138)	31.1 (14/45)	40.8 (20/49)	14.3 (3/21)	44.1 (15/34)
HAQ-DI [SD]	Week 104	0.9 [0.7]	0.7 [0.6]	1.0 [0.8]	0.9 [0.6]	1.5 [0.7]	1.1 [0.8]
	Change from BL	-0.3 [0.6]	-0.2 [0.6]	-0.3 [0.7]	-0.5 [0.7]	-0.3 [0.4]	-0.3 [0.7]
HAQ-DI improvement % (n/N)	Change from BL ≥ 0.5	19.9 (118/592)	20.8 (30/144)	26.5 (13/49)	32.0 (16/50)	19.0 (4/21)	30.6 (11/36)
Median fatigue VAS. mm (range)	Week 104	38.0 (0.0-98.0)	29.0 (0.0-97.0)	41.0 (1.0-88.0)	36.0 (0.0-84.0)	66.0 (18.0-87.0)	68.0 (0.0-98.0)
	Change from BL	-11.0 (-97.0-79.0)	-8.5 (-97.0-64.0)	-29.0 (-94.0-70.0)	-19.0 (-77.0-30.0)	+3.0 (-78.0-29.0)	-2.0 (-77.0-37.0)
Median insomnia VAS. mm (range)	Week 104	27.0 (0.0-100.0)	16.5 (0.0-93.0)	32.0 (0.0-97.0)	26.0 (0.0-100.0)	62.0 (18.0-94.0)	45.0 (0.0-95.0)
	Change from BL	-8.5 (-90.0-83.0)	-0.5 (-89.0-83.0)	-18.0 (-77.0-43.0)	-23.5 (-80.0-24.0)	-14.0 (-67.0-24.0)	-15.5 (-88.0-50.0)
Median pain VAS, mm (range)	Week 104	30.0 (0.0-98.0)	24.5 (0.0-97.0)	32.0 (0.0-90.0)	28.0 (0.0-80.0)	40.0 (16.0-92.0)	40.0 (0.0-98.0)
	Change from BL	-22.0 (-98.0-74.0)	-6.5 (-98.0-46.0)	-15.0 (-88.0-29.0)	-31.5 (-82.0-17.0)	+2.0 (-80.0-17.0)	-18.5 (-82.0-74.0)

Data are expressed as mean unless otherwise stated.
¥Safety/effectiveness set
CRP and ESR were analyzed in the safety set.
BDI-II, STAI-X1 and STAI-X2, DAS 28-ESR, CDAI, HAQ-DI, fatigue, insomnia and pain were analyzed in the effectiveness set. At week 104, 184/1198 patients had completed the BDI-II, 250/1198 patients had completed the STAI-X1 and 248/1198 patients had completed the STAI-X2. Baseline data was not available for all patients.
*Patients with data at the visit
Abbreviations: BL=baseline, CRP=C-reactive protein, ESR=erythrocyte sedimentation rate, BDI-II=Beck Depression Inventory (no depressive symptoms: BDI-II score 0-13; mild depressive symptoms: BDI-II score 14-19; moderate depressive symptoms: BDI-II Score 20-28; severe depressive symptoms: BDI-II Score 29-63; Suicidal ideation= answer on BDI-II question "9. Suicidal ideation" ≥ 1), SD=standard deviation, STAI=State-Trait Anxiety Inventory (mild fear or anxiety: X1 or X2 score 20-≤30; moderate fear or anxiety: X1 or X2 score 31-≤50; severe fear or anxiety: X1 or X2 score > 50), DAS-28=Disease Activity Score, CDAI=Clinical Disease Activity Index, HAQ-DI=Health Assessment Questionnaire-Disability Index, VAS=Visual Analog Scale

reductions in fatigue, insomnia and pain. In contrast to insomnia, patients with severe depressive symptoms had slight increases in fatigue and pain.

Fatigue, insomnia, and pain were reduced in all three anxiety categories – the more severe the anxiety category, the greater the reductions were in insomnia and pain.

			Anxiety measured by STAI-G (form X2)		
Parameter		**Total N=1292/1198¥**	**Mild N=108/103¥**	**Moderate N=414/387¥**	**Severe N=143/134¥**
Median CRP*, mg/dl (range)	Week 104	0.40 (0.0-14.9)	0.20 (0.0-2.3)	0.31 (0.0-14.9)	0.33 (0.0-3.7)
Median ESR*, mm/1h (range)	**Week 104**	**6.0 (0.0-112.0)**	**6.0 (1.0-39.0)**	**6.0 (0.0-112.0)**	**7.5 (2.0-80.0)**
BDI-II** [SD]	Week 104	10.2 [10.6]	4.2 [5.0]	8.8 [8.0]	21.0 [14.6]
	Change from BL	-3.7 [9.2]	-1.6 [7.2]	-3.7 [8.5]	-5.6 [13.1]
STAI-X1 [SD]**	**Week 104**	**38.9 [12.1]**	**30.0 [8.1]**	**38.1 [10.5]**	**49.5 [12.2]**
	Change from BL	**-4.2 [11.1]**	**-0.5 [8.4]**	**-3.9 [9.8]**	**-8.8 [14.6]**
STAI-X2** [SD]	Week 104	38.5 [11.4]	28.6 [7.7]	38.1 [9.5]	49.9 [10.0]
	Change from BL	-3.2 [8.7]	+2.1 [7.7]	-3.2 [7.6]	-8.2 [9.7]
DAS28-ESR [SD]**	**Week 104**	**2.4 [1.4]**	**2.2 [1.1]**	**2.4 [1.4]**	**2.6 [1.3]**
	Change from BL	**-2.5 [1.7]**	**-2.6 [1.7]**	**-2.5 [1.7]**	**-2.6 [1.6]**
< 2.6 ; % (n/N)***	Week 104	60.2 (274/455)	65.3 (32/49)	63.7 (114/179)	59.6 (34/57)
CDAI [SD]**	**Week 104**	**8.4 [9.0]**	**6.3 [6.1]**	**7.7 [8.6]**	**8.0 [7.6]**
	Change from BL	**-16.6 [13.4]**	**-17.3 [11.4]**	**-17.1 [12.5]**	**-18.0 [12.1]**
≤ 2.8; % (n/N)***	Week 104	32.5 (173/532)	34.4 (22/64)	38.5 (80/208)	31.0 (22/71)
HAQ-DI score [SD]**	**Week 104**	**0.9 [0.7]**	**0.6 [0.7]**	**0.8 [0.7]**	**1.2 [0.7]**
	Change from BL	**-0.3 [0.6]**	**-0.2 [0.6]**	**-0.3 [0.6]**	**-0.3 [0.6]**
HAQ-DI improvement % (n/N)	Change from BL ≥0.5	19.9 (118/592)	17.2 (11/64)	24.2 (53/219)	29.7 (22/74)
Median fatigue VAS [mm] (range)**	**Week 104**	**38.0 (0.0-98.0)**	**17.0 (0.0-88.0)**	**35.5 (0.0-97.0)**	**49.0 (0.0-98.0)**
	Change from BL	**-11.0 (-97.0-79.0)**	**-6.5 (-94.0-64.0)**	**-10.5 (-97.0-70.0)**	**-9.5 (-94.0-39.0)**
Median insomnia** VAS [mm] (range)	Week 104	27.0 (0.0-100.0)	8.0 (0.0-93.0)	24.0 (0.0-100.0)	33.0 (0.0-97.0)
	Change from BL	-8.5 (-90.0-83.0)	-1.0 (-82.0-83.0)	-7.0 (-85.0-66.0)	-19.0 (-90.0-50.0)
Median pain** VAS [mm] (range)	Week 104	30.0 (0.0-98.0)	16.5 (0.0-83.0)	27.0 (0.0-98.0)	40.0 (0.0-92.0)
	Change from BL	-22.0 (-98.0-74.0)	-16.0 (-82-44.0)	-21.0 (-98.0-74.0)	-26.0 (-88.0-24.0)

Data are expressed as mean unless otherwise stated
¥Safety/effectiveness set
*CRP and ESR were analyzed in the safety set
** BDI-II, STAI-X1 and STAI-X2. DAS 28-ESR, CDAI, HAQ-DI, fatigue, insomnia and pain were analyzed in the effectiveness set
***Patients with data at the visit
Abbreviations: see Table. 1

Adverse events were documented more often for patients with depressive symptoms and anxiety. However, there was no difference in serious adverse events. Discontinuation due to adverse events increased with more severe depressive symptoms and anxiety.

Conclusion: For the first time, the influence of depressiveness and anxiety on TCZ effectiveness was investigated in a German collective of RA patients in routine practice. The interim analysis of the non-interventional ARATA study underlines not only the clinical effectiveness and safety, but also a positive influence of the therapy on depressiveness, anxiety, fear, fatigue, insomnia and pain. Patients with severe depression did not benefit from fatigue and pain despite improved disease activity.

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Abstract Number: 1415

Effect of Tofacitinib on the Qualitative Profile of High Density Lipoproteins Molecules in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

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Background/Purpose: Patients with rheumatoid arthritis (RA) have an increased risk for cardiovascular diseases. Recent studies found that RA patients present dysfunctional high density lipoproteins (HDL) with low activity of paraoxonase 1 (PON1), which might contribute to the increased cardiovascular risk. Tofacitinib has been associated with an increase in total cholesterol (TC) and low density lipoproteins (LDL-c). The objective of this study was to compare functional markers of HDL at baseline and 3 months after tofacitinib in patients with RA.

Methods: Patients diagnosed with RA (ACR / EULAR 2010 criteria) who started tofacitinib were included from January 2016. Patients with personal history of cardiovascular disease, renal, hepatic or thyroid alterations were excluded.

Table 1. Baseline characteristics of patients with Rheumatoid Arthritis.

	Biologic DMARD naive (n =16)	With previous biologic DMARD (n= 18)	P value	Total (n =34)
Age at diagnosed, years, mean (SD)	54.3 (15.9)	42.4 (18.6)	0.06	47.7 (17.9)
Female, n (%, CI 95%)	13 (81.2, 53.0-94.3)	18 (100)	**0.05**	31 (91.17)
Duration of disease, months, median (IQR)	102 (53-132)	150 (108-192)	**0.04**	120 (78-180)
Positive FR, n (%, CI 95%)	11 (68.7, 41.5-87.2)	13 (72.2, 46.3-88.7)	0.82	24 (70.6,52.4-83.9)
Anti CCP, n (%, CI 95%)	12 (75.0, 47.1-90.9)	16 (88.9, 62.5-97.5)	0.29	28 (82.3, 64.8-92.2)
Baseline DAS 28, mean (SD)	4.9 (1.19)	5.2 (0.96)	0.40	5.1 (1.1)
Baseline HAQ, mean (SD)	1.25 (0.69)	1.24 (0.62)	0.99	1.25 (0.64)
Use of statins, n (%, CI 95%)	3 (18.7, 5.7-46.9)	0	**0.05**	3 (8.8, 2.7-25.2)
Current use of corticosteroids, n (%, CI 95%)	9 (56.3, 30.8-78.7)	14 (77.8, 51.6-91.9)	0.18	23 (67.6, 49.5-81.7)
Baseline total cholesterol(mg/dl), mean (SD)	205 (34)	187 (35.6)	0.1425	196 (35.5)
Baseline HDL (mg/dl), mean (SD)	55 (12.6)	57 (13.4)	0.7211	55.8 (13)
Baseline LDL (mg/dl), mean (SD)	124 (33)	105 (34)	0.1021	114 (34)
Baseline Triglycerides (mg/dl), mean (SD)	137 (43)	109 (31)	**0.0341**	122 (39)
Baseline PON (nmol/ml.min), mean (SD)	130 (47)	166 (78)	0.1129	149 (67)
Baseline ARE (umol/ml.min), mean (SD)	103 (32)	114 (24)	0.2870	109 (29)
Baseline CETP (%/ml.h), mean (SD)	149 (29)	144 (36)	0.6931	146 (32)

Table 2. Baseline and at 3 months values of functional parameters of HDL.

	Biologic DMARD naive (n =16)	P valor	With previous biologic DMARD (n= 18)	P valor	Total group	p
Baseline PON, mean (SD)	130 (47)	0.0299	166.6 (78)	0.3328	149 (67)	Mean difference 4.4 P 0.32
PON 3 months, mean (SD)	145.6 (66)		161 (74)		153.9 (69.5)	
Baseline ARE, mean (SD)	103.6 (32.5)	**0.0164**	114 (24)	0.3225	109 (29)	Mean difference 3.1 P 0.29
ARE 3 months, mean (SD)	114 (29)		111 (25)		112.3 (26.4)	
Baseline CETP, mean (SD)	149 (29)	0.084	144 (36)	0.8804	146.3 (32.2)	Mean difference 5.4 P 0.36
CETP 3 months, mean (SD)	161 (40)		143 (24)		151.6 (33.6)	

DAS-28, lipid profile and ultrasensitive C-reactive protein (usPCR) values were analyzed by standardized methods at baseline and 3 months after tofacitinib. The activity of PON1 was evaluated on two substrates, paraoxon (PON activity) and phenylacetate (ARE activity). Differences in quantitative variables were analyzed through paired Wilcoxon test and McNemar test was used for qualitative variables. Correlations were analyzed with Spearman test.

Results: Patients baseline characteristics are shown in Table 1. Patients were positive for rheumatoid factor in 70.6% (95% CI 52.4-83.9) and anti-CCP in 82.3% (95% CI 64.8-92.2). Eighteen patients (52.95%) were biologic DMARDs failures and the remaining ones received tofacitinib after conventional DMARDs failure. At three months of follow up, DAS28 decreased significantly (-24%, $p < 0.001$), and TC, C-LDL, HDL-C and C-non-HDL levels increased significantly (TC: + 8%, $p = 0.046$, LDL-C: 8%, $p = 0.046$; HDL-C: + 8%, $p = 0.027$ and C-non-HDL: + 13%, $p = 0.031$). No changes were observed in PON or ARE activity associated with tofacitinib use in the whole cohort. Sub analysis on patients not previously treated with biologic DMARDs showed a significant increase in the activity of ARE and PON (Table 2). None of the groups showed significant changes in the cholesteryl ester transfer protein (CETP).

Conclusion: On biologic DMARD naïve patients, treatment with tofacitinib improved the antioxidant activity of HDL (paroxonase activity), in spite of an increase in the overall lipoprotein levels. This might provide additional protection to the accelerated atherosclerotic process.

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Abstract Number: 1416

B Cell Profile for Early Identification of Optimal Responders to TNF-inhibitors in Rheumatoid Arthritis

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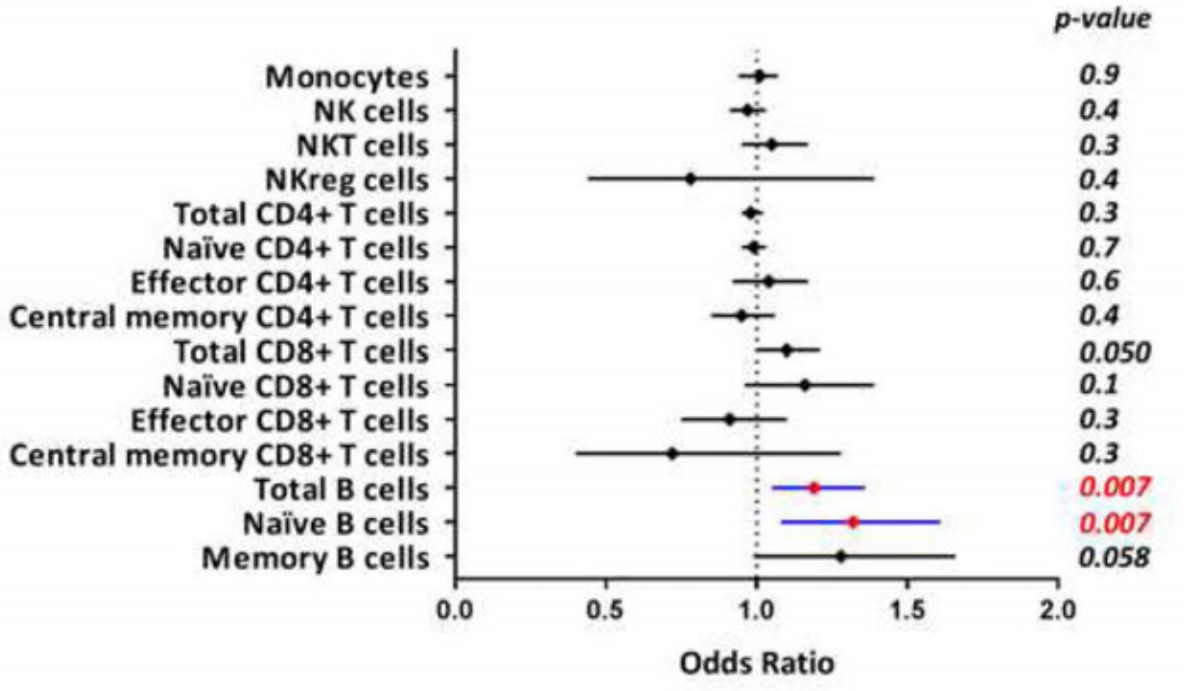
Background/Purpose: Rheumatoid arthritis (RA) is a chronic, inflammatory and heterogeneous autoimmune disorder of unknown etiology characterized by progressive joint damage. Although TNF inhibitors (TNFi) have contributed to change the natural history of RA, approximately 30-50% of patients do not respond to this therapy and only a maximum of 47% achieved clinical remission. The aim of this study was to investigate whether the blood immunological profile at baseline of patients with RA could contribute to predict clinical remission to TNFi.

Methods: This is a prospective bi-center pilot study including 98 patients with RA that initiated a TNFi therapy. Clinical activity was assessed at baseline and after 6 months of treatment by disease activity score 28 (DAS28), considering optimal response if patients reached remission (DAS28≤2,6). We obtained PBMC before treatment and different leukocyte subsets were evaluated by flow cytometry in a FACSCantoII instrument. Baseline characteristics of the patients included in the study were collected. All the analyses were adjusted by sex, anti-citrullinated peptide antibodies (ACPA), rheumatoid factor (RF), baseline-c reactive protein (CRP) and baseline-DAS28 through univariable and multivariate logistic regression models (odds ratio; 95% CI; p value).

Results: At 6 months of follow-up, 39% of patients reached remission by DAS28 (REM patients). Univariable analyses were performed to investigate the association between clinical remission and baseline variables: a significant association was found for positivity of RF, presence of ACPA, lower CRP and lower baseline DAS28. In the multivariate analysis, only lower baseline DAS28 (OR: 0.32; 95% CI: 0.18-0.56; p< 0.0001) remained independently associated with REM after 6m of treatment. Basal leukocyte profile clearly differentiated between REM versus no-REM patients. REM patients showed higher percentage of B cells (OR=1.19; 95%; CI:1.05-1.35; p=0.007) and naive B cells (Bn; OR=1,32; 95%; CI:1.08-1.61; p=0.007) than no-REM patients at baseline (Figure 1). The other PBMC subsets (monocytes, NK cells, CD4+ and CD8+ T cells subtypes) did not show statistical differences.

Conclusion: Our results suggest that B cell profile would be the group of determinant cells to organize the response to TNFi in patients with RA. Further studies are necessary for a better understanding of the biological meaning of the increase in the naive B cells in REM patients.



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Long-Term Effectiveness and Safety of Infliximab, Golimumab and Golimumab-IV in Rheumatoid Arthritis Patients from a Prospective Observational Registry

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Background/Purpose: Long-term registries are essential to evaluate new therapies in a patient population that differs from clinical trials and usually varies over time. The purpose was to describe the profile of rheumatoid arthritis (RA) patients treated with infliximab (IFX), golimumab subcutaneous (GLM) or intravenous (GLM-IV) in Canadian routine care, along with its effectiveness and safety.

Methods: A total of 1577 RA patients treated with IFX, GLM or GLM-IV were enrolled into the Biologic Treatment Registry Across Canada (BioTRAC) between 2006-2015, 2010-2017 and 2014-2017, respectively. Study visits occurred at baseline and every 6 months thereafter. Effectiveness was assessed with changes in TJC28, SJC28, MDGA, PtGA, pain, HAQ, and acute phase reactants. Safety was evaluated with the incidence of adverse events (AEs) and drug survival.

Results: Of the 890 IFX-, 530 GLM- and 157 GLM-IV-treated patients, the proportion of females were 75.7%- 77.1%, the mean age were 55.8-57.7 and the mean disease duration were 6.5-8.6 years. Most patients were bio-naive (> 80%).

A significant decrease in disease duration and disease activity scores (DAS, TJC, SJC, HAQ, AM stiffness, MDGA, PtGA, CRP, ESR) were observed in the IFX cohort over time ($p< 0.001$). Interestingly, baseline disease duration and disease activity scores for the GLM cohort (DAS, TJC, SJC, PtGA, Pain, CRP, ESR) were higher than in the IFX cohort from 2010-2012 when GLM was first introduced while the mean MDGA remained the same between the two groups.

Treatment with IFX, GLM and GLM-IV significantly improved all disease parameters over time ($P< 0.001$) from baseline to 6 months and up to 120, 78 and 42 months, respectively. The proportion of patients in SDAI remission at 12, 24 and 36 months reached 16.2%, 20.8% and 22.8% in IFX-patients; 34.7%, 47.5% and 52.7% in GLM-patients and 33.8%, 47.5% and 61.9% in GLM-IV-patients ($p=0.1978$ and $p=0.0081$ vs IFX).

AEs were reported for 61.5%, 67.4% and 59.2% (105, 113 and 82.6 events/100 PYs) and SAEs for 21.2%, 15.5% and 3.8% (11.7, 11.2 and 4.68 events/100 PYs) covering 2714, 1077 and 257 years of exposure for IFX, GLM and GLM-IV-treated patients, respectively. The most frequently occurring AEs were arthralgia and upper respiratory tract infection (>5%). Eighteen, 7 and 1 deaths occurred among IFX-, GLM- and GLM-IV-treated patients, respectively. The proportion of patients who discontinued treatment were 74.0% over a mean 3.0 years of exposure to IFX-, 52.8% over 2.0 years of exposure to GLM and 45.2% over 1.6 year of exposure to GLM-IV.

Conclusion: In this real-world study of Canadian patients with RA, differences in baseline characteristics between patients treated with an anti-TNF over time and between agents shows potential selection biases when selecting a given therapy and may impact the proportion of patients achieving a target-specific outcome. Treatment significantly reduced disease activity and improved functionality in a similar fashion and were also safe and well tolerated.

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Predictors of Response, Adverse Events and Treatment Retention in RA Patients Treated with Either Subcutaneous- or Intravenous-Golimumab in a Prospective, Observational Registry

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Background/Purpose: The Biologic Treatment Registry Across Canada (BioTRAC) was a prospective, observational registry that enrolled rheumatoid arthritis (RA) patients treated with either subcutaneous golimumab (GLM-SC) or intravenous golimumab (GLM-IV) between 2010 and 2017. The registry was closed in June 2018.

Methods: Patient visits occurred at baseline and every 6 months thereafter. Multivariate logistic regression was used to identify independent predictors of achieving specific efficacy and safety endpoints and included the following covariates: age, gender, disease duration, enrolment period, concomitant medication, smoking and employment.

Results: A total of 687 Golimumab treated patients (530 GLM-SC and 157 GLM-IV) were enrolled and followed for a mean of 2.0 and 1.6 years, respectively. Most patients were bio-naive (> 80%).

DAS28-CRP low disease activity was more likely to be achieved with lower baseline DAS28-CRP [OR (95% CI): 0.73 (0.57–0.92); p=0.009], among those with concomitant DMARD use [2.86 (1.35–6.08); p=0.006], and in patients who were employed [2.26 (1.18–4.33); p=0.014]. However, it was less likely among those with baseline concomitant corticosteroid (CS) use [0.55 (0.30–0.99); p=0.047]. DAS28-CRP remission was more likely to be achieved in males [OR (95% CI): 2.06 (1.10–3.86); p=0.023], later enrolment [2013–2015 vs. 2010–2012: 1.91 (1.02–3.59); p=0.045], and among those with concomitant DMARD use [3.15 (1.53–6.51); p=0.002] and less likely in patients with baseline concomitant CS use [0.37 (0.22–0.62); p< 0.001]. A HAQ-DI < 0.5 was more likely to be achieved with lower age [OR (95% CI): 0.98 (0.96–1.00); p=0.023), in males [2.00 (1.10–3.67); p=0.024], lower baseline HAQ-DI scores [0.13 (0.08–0.20); p< 0.001], higher baseline CRP levels [1.01 (1.00–1.02); p=0.009], in patients who were employed [2.0 (1.09–3.53); p=0.026], and among those with GLM-SC vs. GLM-IV treatment [2.19 (1.12–4.31); p=0.023].

AEs were more likely to occur with lower baseline CDAI [OR (95% CI): 0.98 (0.97–1.00); p=0.023], and in patients with baseline concomitant CS [1.62 (1.04–2.52); p=0.032] or NSAID use [1.79 (1.19–2.70); p=0.005], whereas SAEs were less likely to occur in patients enrolled later [2013–2015 vs. 2010–2012: 0.42 (0.23–0.79); p=0.007 and 2016–2017 vs. 2010–2012: 0.18 (0.08–0.44); p< 0.001], and in those with baseline DMARD use [0.37 (0.18–0.79); p=0.009].

Early treatment period (2013–2015 vs. 2016–2017: 0.58 [0.39–0.87], p=0.008) and concomitant DMARD use [0.58 (0.37–0.90); p=0.016] increased the likelihood of treatment continuation.

Conclusion: In this real-world, long-term prospective cohort of RA patients treated with golimumab, concomitant DMARD use at baseline appears to be a positive predictor of achieving treatment targets, avoiding SAEs and treatment retention. Patients with concomitant CS at baseline, however, were less likely to meet efficacy endpoints and at higher risk of AEs. Finally, patients enrolled later had a lower likelihood of experiencing an SAE but a higher likelihood of discontinuation, possibly driven by the larger availability of treatment options and/or more rigorous adherence to treat to target guidelines.

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Cost-per-Responder Analysis of Sarilumab for the Treatment of Moderately-to-Severely Active Rheumatoid Arthritis (RA)

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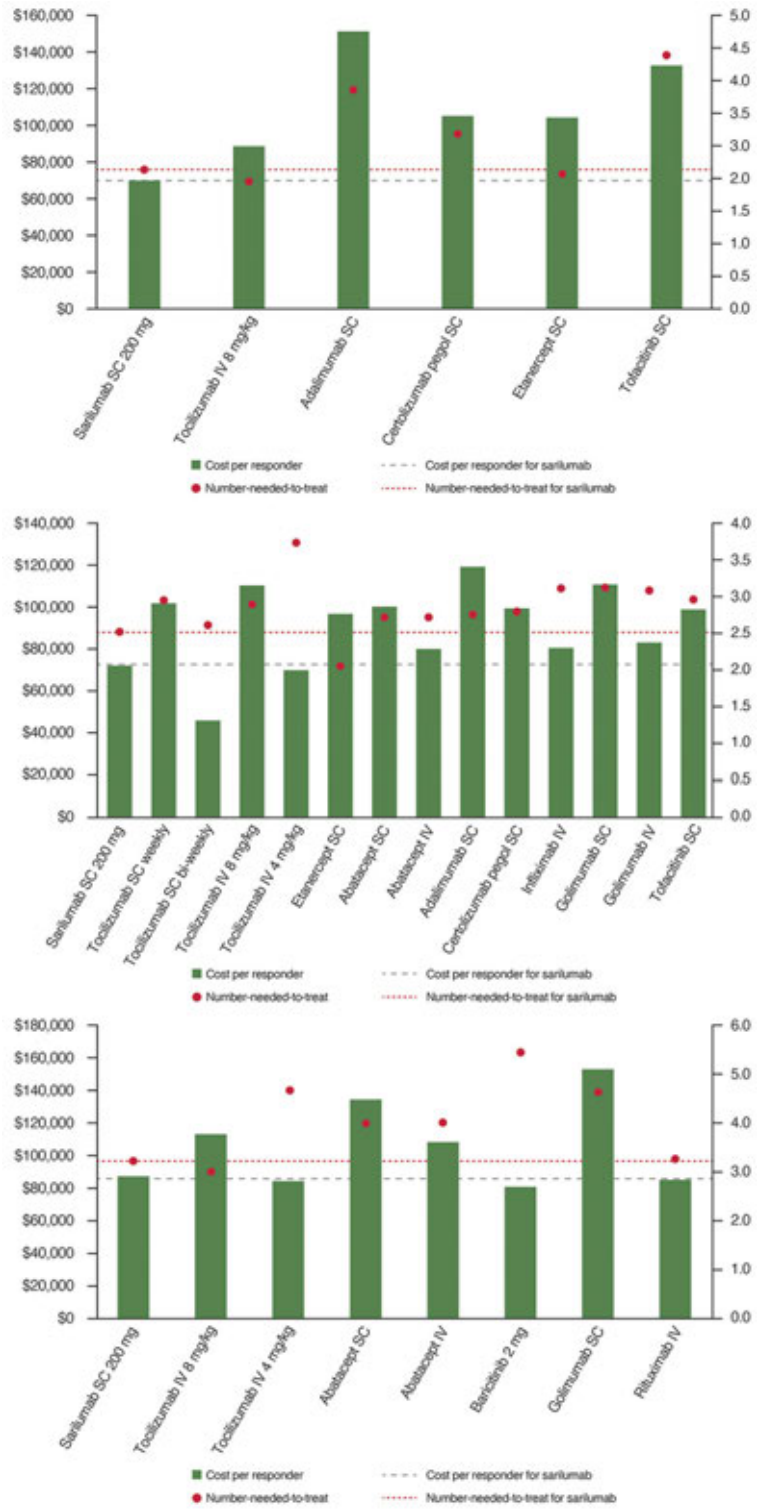
Background/Purpose: Network meta-analyses (NMA) have been conducted to compare the efficacy and safety of sarilumab, a fully human monoclonal antibody against the interleukin 6 receptor α, vs other monotherapies for patients with RA who were inadequate responders to, inappropriate candidates for, or intolerant of conventional synthetic disease-modifying antirheumatic drugs (csDMARD-IR)[1] and vs other combination treatments with methotrexate in patients with inadequate response to csDMARDs[1] or anti-tumor necrosis factor therapy[2] (csDMARD-IR and TNF-IR, respectively). Using this comparative efficacy data, the present study evaluated 1-year costs associated with obtaining treatment response with sarilumab 200 mg subcutaneous (SC) vs other currently used therapies in these patient populations.

Methods: Cost-per-responder (CPR) analyses were conducted on 2018 US wholesale acquisition costs of drugs and administration. The number-needed-to-treat (NNT) to obtain one responder per American College of Rheumatology (ACR)50 was derived from the NMAs of sarilumab.[1,2] Responders were assumed to receive treatment for 12 months; non-responders were assumed to stop treatment after 6 months without subsequent treatments. Scenario analyses were conducted on ACR20 and ACR70 criteria.

Results: For monotherapies in csDMARD-IR (**Figure A**), the NNT for sarilumab (2.4) was lower vs all comparators except etanercept (2.3) and tocilizumab intravenous (IV) 8 mg/kg (2.2). Sarilumab had the lowest CPR ($69,440) vs all treatments (ranging from $150,348 for adalimumab SC to $88,291 for tocilizumab IV 8 mg/kg). For combinations in csDMARD-IR (**Figure B**), the NNT for sarilumab (2.5) was lower vs all comparators except etanercept (2.1). Sarilumab CPR ($72,438) was lower vs all comparators ($119,559 for adalimumab SC to $80,409 for abatacept IV) except lower

dose intensities of tocilizumab (IV and SC). In TNF-IR (**Figure C**), the NNT for sarilumab (3.2) was lower vs all combinations except vs tocilizumab IV 8 mg/kg (3.0). Sarilumab CPR ($87,047) was lower vs all comparators ($152,551 for golimumab SC to $107,761 for abatacept IV) except tocilizumab IV 4 mg/kg, baricitinib 2 mg and rituximab IV. Scenario analysis results were similar except per ACR70 lower CPRs for certolizumab and etanercept monotherapies, and a higher CPR for tocilizumab IV 4 mg/kg in combination (csDMARD-IR and TNF-IR populations).



Conclusion: Due to the lower NNT for sarilumab vs most comparators and reasonable cost, sarilumab achieved better CPR outcomes vs all monotherapies, vs all combinations except lower dose intensities of tocilizumab in csDMARD-IR and except baricitinib and rituximab in the TNF-IR population.

References:

1. Choy E et al. RMD Open. 2019;5:e000798.
2. Choy E et al. Adv Ther. 2019;36:817–827.

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Abstract Number: 1420

Heterogeneity in the Pattern of Use of JAK-inhibitors Between Countries Participating in an International Collaboration of Registers of Rheumatoid Arthritis Patients (the JAK-pot Study)

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Table 1 : Baseline characteristics of patients treated with JAK-inhibitors (baricitinib and tofacitinib) by country or register																	
	AT	CA	CH	CZ	DE	ES	FI	GB	IL	IT	MET*	NO	PT	RO	RU	SI	TR
n	62	128	758	160	327	153	137	435	136	152	36	72	26	252	531	114	324
Tofacitinib[1] (%):	38.7	100	82.5	78.1	42	51.0	53.3	15	100	30.3	33.3	94.4	65.4	35.3	100	49.1	100
Age (mean, SD)	61.2 (11.7)	58.2 (11.4)	59.3 (12.9)	57.5 (10.4)	59.5 (12.1)	59.5 (12.1)	54.4 (12.6)	60 (12.4)	63.0 (12.6)	57.5 (12.7)	54.8 (12.5)	57.5 (13.5)	53.7 (14.0)	57.7 (11.7)	50.6 (13.3)	59.9 (10.3)	50.7 (12.2)
Women (%)	80.6	83.6	80.9	84.4	73.7	73.7	76.6	75	86.0	77.6	82.9	83.3	84.6	89.3	82.5	83.3	84.6
Disease duration, years (mean, SD)	13.5 (10.3)	11.9 (11.2)	13.5 (10.1)	14.9 (9.2)	11.5 (9.4)	11.9 (8.8)	13.2 (11.2)	14 (10.3)	15.0 (11.3)	13.4 (10.6	14.9 (10.2)	12.7 (8.8)	18.3 (8.9)	11.9 (8.7)	10.5 (8.5)	11.8 (8.2)	16.3 (21.4)
Seropositive (%)	64.3	78.4	71.2	87.5	77.5	49.7	80.2	70	57.4	70.0	86.7	67.5	91.7	92.5	84.7	86.8	68.9
Number of previous bDMARDs(%)																	
0	19.4	34.4	17.3	61.3	45.3	17.7	61.3	26	47.1	48.7	19.4	16.7	19.2	71.8	58.2	6.1	60.2
1	21.0	14.1	22.2	6.9	22.3	11.8	20.4	14	30.1	28.3	21.0	15.3	38.5	18.3	23.5	38.6	18.5
2	25.8	18.0	23.2	11.2	11.9	15.03	13.1	13	14.0	14.5	25.8	15.3	15.4	8.3	11.7	20.2	10.2
≥3	33.9	33.6	37.3	20.6	20.5	55.5	5.1	31	18.8	8.6	33.9	52.8	26.9	1.6	6.6	35.1	11.1
Concomitant treatment (%)																	
None	51.6	15.6	47.0	36.9	0.9	4.6	30.7	34	22.1	40.1	47.2	52.8	30.8	11.5	19.4	47.4	60.2
MTX	37.1	27.3	26.1	53.8	59.4	38.6	16.1	25	12.5	43.4	11.1	44.4	34.6	31.7	59.3	31.6	16.4
MTX and other	0.0	35.9	2.4	2.5	36.3	41.2	24.1	15	60.3	3.9	11.1	1.4	7.7	20.6	7.5	2.6	4.9
Other csDMARDs	11.3	21.1	24.5	6.9	3.4	15.7	29.2	18	5.1	12.5	30.6	1.4	26.9	36.1	13.7	18.4	18.5
Concomitant glucocorticoids (%)	67.7	55.5	33.0	51.9	70.3	99.1	59.9	32	75.3	76.3	50.0	45.8	88.5	32.9	38.2	30.7	14.2
DAS28 (mean, SD)	4.2 (1.0)	4.6 (1.2)	4.1 (1.4)	5.2 (1.8)	4.8 (1.3)	4.9 (1.5)	3.6 (1.4)	5.6 (1.2)	4.3 (1.2)	4.2 (1.3)	4.0 (1.2)	4.4 (1.7)	5.1 (1.7)	6.1 (1.1)	5.3 (1.4)	5.1 (1.5)	4.3 (1.2)
CDAI (mean, SD)	19.1 (7.3)	24.9 (11.7)	19.7 (13.0)	28.4 (18.4)	25.5 (12.5)	NA	14.0 (9.2)	NA	15.4 (6.8)	18.4 (11.2)	14.4 (10.8)	19.4 (13.5)	27.5 (16.5)	32.4 (12.8)	26.7 (13.1)	24.8 (13.9)	16.1 (11.4)
ESR (mean, SD)	NA	26.6 (19.5)	19.9 (18.2)	31.1 (25.1)	24.7 (21.0)	30.5 (28.3)	20.0 (21.3)	31.7 (25.2)	27.2 (20.4)	25.1 (20.3)	25.8 (26.2)	25.2 (20.4)	28.1 (22.9)	46.6(24 .5)	34.1 (21.1)	34.2 (25.4)	35.5 (22.7)
CRP (mean, SD)	10.7 (9.8)	15.4 (25.0)	9.1 (14.6)	18.8 (31.4)	11.7 (15.2)	7.51 (12.9)	11.2 (17.5)	22.8 (29.9)	21.2 (17.2)	8.3 (11.9)	3.7 (3.8)	11.9 (20.6)	15.9 (24.4)	28.8 (33.8)	26.5 (36.4)	16.9 (22.1)	19.8 (28.6)
HAQ-DI (mean, SD)	1.1 (0.8)	1.5 (0.7)	0.9 (0.7)	1.5 (0.7)	1.4 (0.7)	NA	1.1 (0.8)	1.7 (0.7)	NA	1.00 (0.8)	1.02(0. 8)	0.8 (0.6)	1.53 (0.58)	1.81 (0.46)	1.45 (0.70)	1.22 (0.76)	1.00 (0.61)
Range of available year of treatment initiation	2016-now	2013-now	2016-now	2017-now	2017-now	2016-now	2016-now	2014-now	2012-now	2014-now	2012-now	2016-now	2016-now	2016-now	2012-now	2016-now	2014-now

AT : Austria, CA : Canada, CH : Switzerland, CZ : Czech Republic, DE: Germany, ES: Spain, FI: Finland, GB: United Kingdom, IL: Israel, IT: Italy, NO: Norway, PT: Portugal, RO: Romania, RU: Russia, SI: Slovenia, TR: Turkey

*MET: The METEOR registry is an international registry comprising several countries such as the Netherlands and Portugal.

[1]Tofacitinib vs baracitinib treatment

Table 1 Baseline characteristics of patients treated with JAK-inhibitors (baricitinib and tofacitinib) by country or register

Table 2: Information on market introduction, reimbursement and national recommendation about JAKi																	
	AT	CA	CH	CZ	DE	ES	FI	GB	IL	IT	NL	NO	PT	RO	RU	SI	TR
BARICITINIB																	
Introduction in the market	2017	2018	2017	2019	2017	2017	2017	2017	2019	2018	2017	2017	2017	2018	2019	2017	No
Reimbursement	2017	2018	2017	2019	2017	2018	2017	2017	2019*	2018	2017	2017	-[3]	2018	Pending	2017	-
Reimbursed for bionaive patients	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	-	Yes	-	Yes	-
National guidelines:	No	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	-	Yes	No	No	-
- Recommend use in non-bionaive rather than any patients	-	No	-	No	No	No	-	No	-	-	No	No	-	No	-	-	-
- Recommend concomitant csDMARDs	-	Yes	-	Yes	Yes	Yes	-[1]	Yes	-	-	Yes	No	-	Yes	-	-	-
- Recommendations depends on seropositive status	-	No	-	No	No	No	-	No	-	-	No	No	-	No	-	-	-
TOFACITINIB																	
Introduction in the market	2017	2014	2013	2018	2017	2017	2018	2017	2014	2018	2017	2017	2017	2017	2013	2018	2014
Reimbursement	2017	2015	2013	2018	2017	2018	2018	2017	2014	2018	2017	2017	2019[3]	Pending	2017	2018	2015
Reimbursed for bionaive patients	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes[2]	Yes	Yes	Yes	Yes	-	Yes	Yes	Yes
National guidelines:	No	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	No	Yes	No	Yes
- Recommend use in non-bionaive rather than any patients	-	No	-	No	No	No	-	No	-	-	Yes	No	-	-	No	-	No
- Recommend concomitant csDMARDs	-	No	-	Yes	Yes	Yes	-[1]	Yes	-	-	Yes	No	-	-	Yes	-	Yes
- Recommendations depends on seropositive status	-	No	-	No	No	No	-	No	-	-	No	No	-	-	No	-	No
Glucocorticoid national recommendations	No	No	No	Yes	Yes	Yes	Yes	No	No	No	Yes	No	No	No	Yes	No	Yes
- Use at baseline	-	-	-	Yes	Yes	Yes	Yes	-	-	-	Yes	-	-	-	Yes	-	Yes
- Rapid tapering	-	-	-	Yes	Yes	Yes	Yes	-	-	-	Yes	-	-	-	Yes	-	Yes

AT : Austria, CA : Canada, CH : Switzerland, CZ : Czech Republic, DE: Germany, ES: Spain, FI: Finland, GB: United Kingdom, IL: Israel, IT: Italy, NL: Netherlands, NO: Norway, PT: Portugal, RO: Romania, RU: Russia, SI: Slovenia, TR: Turkey

*Reimbursement starting in June 2019

1: There are no national recommendation but in the label it is recommended together with methotrexate if possible

2: Reimbursement since 2014 in non-bionaive patients and since 2016 in bionaïve patients

3: The decision to reimburse by the National Health System may take a long time. Patients with other health systems (e.g. private insurance) can have access to the medication as soon as EMA approves it.

Table 2 Information on market introduction, reimbursement and national recommendation about JAKi

Background/Purpose: In many countries, JAK-inhibitors (JAKi) have been recently accepted for the treatment of patients with rheumatoid arthritis (RA). However, prescription patterns may differ notably between countries, which may influence effectiveness and safety analyses. The purpose of this study was to evaluate how and to whom JAKi are prescribed as a first investigation of an international collaboration of registers aiming at analysing the effectiveness and safety of JAKi.

Methods: Patients with diagnosis of RA, treated with either tofacitinib or baricitinib, and included in one of the registers participating in the JAK-pot collaboration registers (17 registers) were investigated. We used standard descriptive statistics to evaluate patient-, disease-, and treatment characteristics, as well as year of treatment initiation. Information on marketing and reimbursement date and national recommendations/guidelines were also retrieved using a questionnaire sent to a register representative in each country of the collaboration.

Results: A total of 3,804 patients initiating JAKi were included, with 4 countries having access only to tofacitinib (Table 1). Patients were on average >50 years old, with disease duration >10 years and mostly female. Patients generally had moderate to high disease activity (DAS28 > 3.2) at JAKi initiation, high levels of inflammatory markers and mild to moderate disability (Table 1). Seropositivity status (ACPA or RF) varied from 49.7 to 92.5% as could be expected since none of the countries had recommendations related to antibodies (Table 2). Treatment characteristics varied widely between countries: between 6.1 and 61.3% of patients had not received a previous bDMARDs (but only in one country JAKi was recommended only after failure of bDMARDs, Table 2); between 0.9 to 60.2% patients were prescribed JAKi as monotherapy; between 14.2 to 99.1% received concomitant glucocorticoids. Indeed, national recommendations on the use of concomitant csDMARD treatment varied by country (Table 2) but in every country, JAKi was prescribed after at least one csDMARDS failure. The first years of JAKi initiation in the registers ranged from 2012 to 2016 depending on the availability of this class of treatment (Tables 1 and 2). In some countries, compassionate use was possible before market availability.

Conclusion: JAKi were prescribed to a population that was similar in terms of age, gender, disease duration, disease activity and functional disability between countries, but differed greatly in terms of seropositivity, number of previous bDMARDs and use of csDMARD co-medication, which was not attributable to differences in national treatment recommendations. These differences must be taken into account when analyzing the real-life effectiveness and safety of JAKi across different countries and in collaborative studies.

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Abstract Number: 1421

Effect of Tocilizumab on HDL and LDL Characteristics in Patients with Rheumatoid Arthritis: Preliminary Results

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	Total (n =34)
Age at diagnosed, years, mean (SD)	46.9 (16.5)
Age at inclusion in study, years, mean (DS)	63.2 (13.4)
Female, n (%, CI 95%)	31 (91,2, 76.3-98.1)
Disease duration, months, median (IQR)	155 (98-276)
Positive FR, n (%, CI 95%)	25 (73.5, 55.6-87.1)
Anti CCP, n (%, CI 95%)	16/22 (73, 49.8-89.3)
Baseline DAS (ESR) 28, mean (SD)	5.3 (1)
Baseline DAS (cpr) 28, mean (SD)	4.5 (0.98)
Baseline HAQ, mean (SD)	1.36 (0.6)
Statins, n (%, CI 95%)	6 (17.7, 6.7-34.5)
Previous biologics, n (%, CI 95%)	25 (74, 55.6-87.1)
Previous TNFi, median (IQR)	1 (0-1)
Current corticosteroid use, n (%, CI 95%)	14 (41.2, 24.6-59.3)
Baseline total cholesterol (mg/dl), mean (SD)	195 (44)
Baseline HDL (mg/dl), mean (SD)	56.1 (15.3)
Baseline LDL (mg/dl), mean (SD)	114.2 (40.1)
Baseline tryglicerides (mg/dl), mean (SD)	128.4 (46.2)
Baseline C-VLDL (mg/dl), mean (SD)	24.7 (8.4)
Baseline C-no HDL (mg/dl), mean (SD)	138.9 (41.2)
Baseline VLDL/TG (mg/dl), mean (SD)	0.2 (0.054)
Baseline TG/HDL (mg/dl), mean (SD)	2.5 (1.3)
Baseline LDLox (pg/ml), mean (SD)	174 (23)
Baseline ARE (umol/ml.min), mean (SD)	73.86 (22.1)
Cholesterol efflux (%), mean (SD)	5.97 (1.7)
ARE/HDL (umol/ml.min), mean (SD)	1.38 (0.55)

Table 1. Baseline characteristics of patients with Rheumatoid Arthritis.

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

	Total n=34	P value
Baseline usCRP (mg/l), mean (SD)	14.5 (26.3)	**0.005**
usCRP 3 months (mg/l), mean (SD)	0.9 (1.4)	
Baseline ESR (mm/h), mean (SD)	37.8 (23.1)	**< 0.0001**
ESR 3 months (mm/h), mean (SD)	9.8 (11)	
Baseline DAS 28 (CPR), mean (SD)	4.5 (0.98)	**< 0.0001**
DAS 28 (CPR) 3 months	2.4 (1.2)	
Baseline DAS 28 (ESR), mean (SD)	5.3 (1)	**< 0.0001**
DAS 28 (ESR) 3 months, mean (SD)	2.6 (1.4)	
Baseline HAQ, mean (SD)	1.4 (0.6)	**0.0045**
HAQ 3 months, mean (SD)	1.07 (0.6)	
Baseline total cholesterol (mg/dl), mean (SD)	195 (43.9)	**0.03**
Total cholesterol (mg/dl) at 3 months, mean (SD)	213 (49.8)	
Baseline HDL (mg/dl), mean (SD)	56.1 (15.3)	0.125
HDL (mg/dl) 3 months, mean (SD)	58.9 (18.7)	
Baseline LDL (mg/dl), mean (SD)	114.2 (40.1)	**0.0072**
LDL (mg/dl) 3 months, mean (SD)	127.1 (44.2)	
Baseline TG (mg/dl), mean (SD)	128.4 (46.4)	0.2002
TG (mg/dl) 3 months, mean (SD)	139.4 (54)	
Baseline LDLox (pg/ml), mean (SD)	174.1 (23)	**0.0156**
LDLox 3 months (pg/ml), mean (SD)	163.2 (26.9)	
Baseline ARE (umol/ml.min), mean (SD)	73.8 (22)	

Table 2. Baseline and 3 months after the start of treatment values of characteristics of HDL and LDL.

Background/Purpose: In patients with Rheumatoid Arthritis (RA), qualitative alterations of low and high density lipoproteins (LDL and HDL, respectively) might partially explain their increased cardiovascular risk. Tocilizumab has been associated with increase in lipids, including triglycerides (TG) and cholesterol levels, in all its lipoprotein fractions. The aim of this study was to compare, in patients with RA, the effect of tocilizumab on HDL and LDL characteristics at baseline and 3 months after the start of treatment.

Methods: patients diagnosed with RA (ACR/EULAR 2010 criteria) who received tocilizumab were included from November 2016. Patients with personal history of cardiovascular disease, renal, hepatic or thyroid alterations were excluded. Clinical assessment (Health assessment questionnaire -HAQ-, DAS28) lipid profile, and ultrasensitive C reactive protein (usCRP) by standardized methods were collected in all patients at baseline and after three months of follow up. Lipoproteins characteristics were measured with the activity of paraoxonase (PON1) evaluated through the activity of arylesterase (ARE), and by the ability to promote the efflux of cholesterol from foam cells generated in vitro, and by levels of oxidized LDL (LDLox). Changes were evaluated by paired means difference tests and correlations between lipoproteins characteristics and acute phase reactants were analyzed by Spearman tests.

Results: baseline characteristics of the 34 patients included are shown in Table 1. Most of the patients were seropositive (table 1). Twenty-five patients (74%) had been previously treated with other biologics disease-modifying antirheumatic drugs (DMARDs) while 9 (26%) received tocilizumab after conventional DMARDs failure. 59% of patients used monotherapy tocilizumab and 41% used concomitant conventional DMARD (methotrexate: 71.4%). At three months, DAS28 (-51%, $p < 0.001$), HAQ (-23.57%, $p = 0.0045$) and usCRP decreased significantly. Total cholesterol and LDL-C levels increased significantly after 3 months of treatment (CT: 9.2%, $p = 0.03$ and LDL-C: 11.29%, $p = 0.0072$). A decrease in LDLox was observed after 3 months of treatment (11.29%, $p = 0.0156$). No changes were observed in arylesterase activity or HDL capacity to promote cholesterol efflux ($p > 0.05$) in the whole group (Table 2). Changes in HDL efflux correlated positively with ARE activity ($r = 0.58$, $p = 0.03$), and with CRP levels reduction ($r = -0.77$, $p = 0.021$).

Conclusion: treatment with tocilizumab decreased LDLox levels, (a classic risk factor for cardiovascular disease) in spite an increase in total cholesterol and LDL-C levels. Decreases in usCRP levels significantly correlated with an improvement of HDL anti atherogenic capacities.

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Abstract Number: 1422

Reduction in CD4 TEMRA Cells and Its Association with DAS28 (CRP) < 2.6 Treatment Response with Abatacept in Patients with Early, ACPA+, DMARD-Naïve RA

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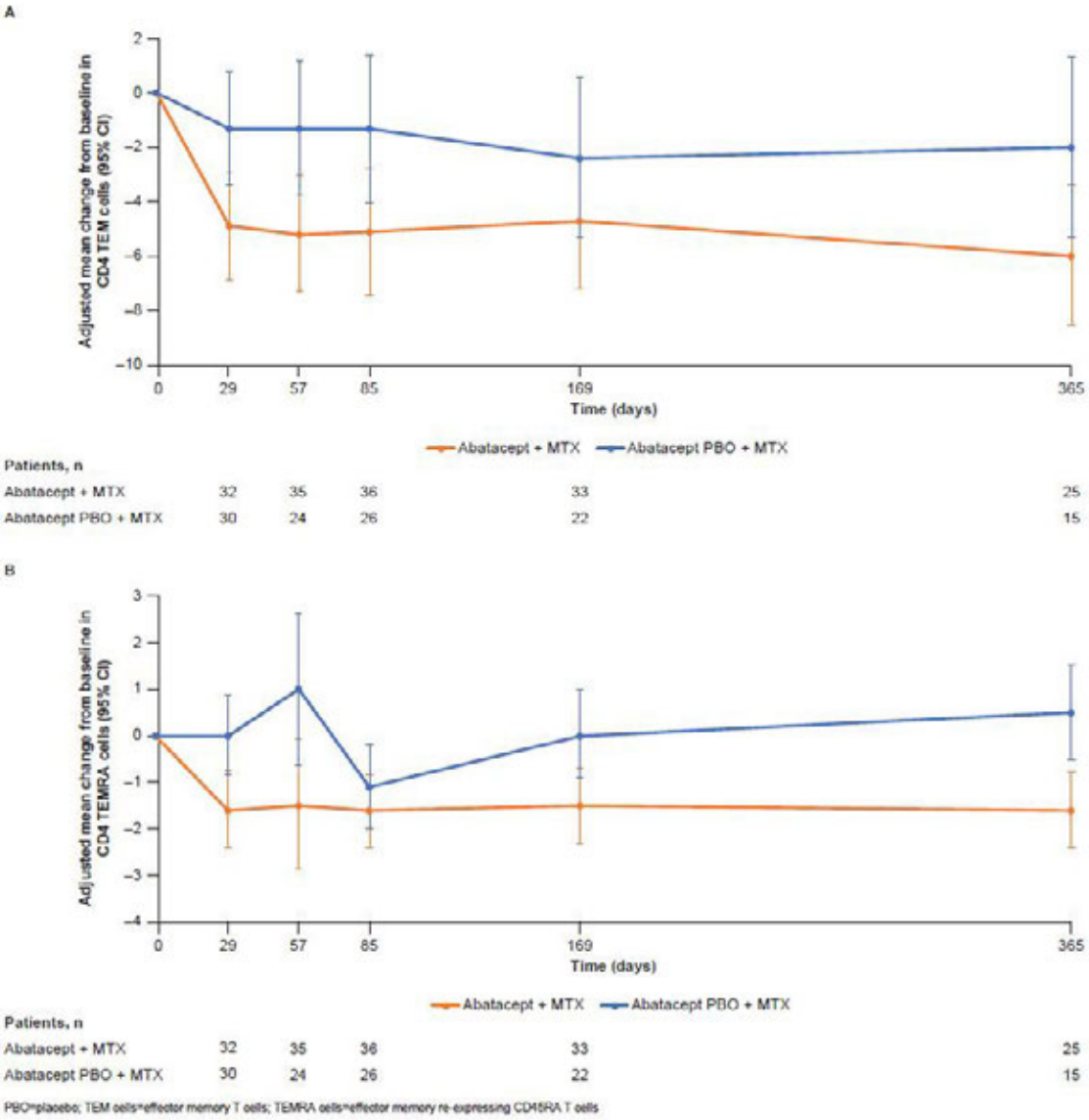
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: T-cell profiles are heterogeneous between individuals and consist of naïve T cells, memory T cells (including effector memory T cells [TEM] and central memory T cells [TCM]) and short-lived or terminally differentiated effector cells (effector memory re-expressing CD45RA [TEMRA] cells).[1] CD4 TEMRA cells (CD4+CD8–CD45RA+CD197–) vary in frequency and function, including distinct cytotoxic properties, between healthy individuals.[2] However, their role in RA is unknown. The ongoing Phase IIIb Assessing Very Early Rheumatoid arthritis Treatment (AVERT)-2 trial (NCT02504268) aims to assess the efficacy and safety of abatacept (ABA) + MTX, vs ABA placebo (PBO) + MTX, in achieving clinical remission in DMARD-naïve adults with early RA, using stringent SDAI ≤3.3 criteria.[3] We assessed the pharmacodynamic modulation of CD4 T-cell phenotypes and its association with ABA treatment (tx) response in AVERT-2.

Methods: AVERT-2 is a 132-week (wk), randomized, double-blinded study of ACPA+ and DMARD-naïve adults with RA diagnosis ≤6 months (ACR/EULAR 2010 criteria). Patients (pts) were randomized (3:2) to wkly SC ABA 125 mg + MTX vs ABA PBO + MTX for 56 wks (induction period [IP]) and then entered a 48-wk de-escalation period. Immune cell phenotyping via flow cytometry was performed on samples from a subset of pts in cohort 1 (all pts randomized who received ≥1 dose in the IP) through Wk 52. Data were analyzed using FlowJo® software. Estimates of adjusted mean change from baseline (BL) over time in CD4 T cells were from a repeated measures mixed model that included BL CD4 cell count, tx group, time and time-by-BL and time-by-tx group interaction. Changes over time were analyzed by whether pts achieved DAS28 (CRP) < 2.6 at Wk 52.

Results: Overall 58 pts who received ABA + MTX and 43 pts who received ABA PBO + MTX were included. BL demographics and disease characteristics at BL and Wk 52, between immune-cell–phenotyped and non-immune-cell–phenotyped cohorts, were comparable. BL DAS28 (CRP) scores were similar across these two cohorts for the ABA + MTX (5.80 vs 5.53, respectively) and ABA PBO + MTX (5.84 vs 5.58, respectively) tx arms. At the earliest time sampled (Month 1), a reduction in CD4 TEM and CD4 TEMRA cells was seen with ABA + MTX (Figure), which was sustained through Wk 52. Adjusted mean changes (95% CI) at Wk 52 with ABA + MTX vs ABA PBO + MTX were –6.0 (–8.6, –3.4) vs –2.0 (–5.3, 1.3) for TEM, and –1.6 (–2.4, –0.8) vs 0.5 (–0.5, 1.5) for TEMRA cells. Responders with DAS28 (CRP) < 2.6 at Wk 52 had greater reduction in these cell types with ABA + MTX vs ABA PBO + MTX (CD4 TEM: –6.5 [–10.2, –2.9] vs 4.2 [–2.8, 11.2]; CD4 TEMRA: (–2.9 [–4.0, –1.9] vs 1.2 [–0.4, 2.7]). This difference was not seen in non-responders. No association was observed with CD4 TCM cells between responders and non-responders.

Figure. Adjusted Mean Change From Baseline in (A) CD4 TEM Cells and (B) CD4 TEMRA Cells



PBO=placebo; TEM cells=effector memory T cells; TEMRA cells=effector memory re-expressing CD45RA T cells

Conclusion: Changes in CD4 TEM and CD4 TEMRA cells, probably suggestive of reduced proinflammatory immune response, were associated with abatacept response of DAS28 (CRP) < 2.6 in pts with seropositive RA.

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Abstract Number: 1423

Patient-Reported Outcomes of Abatacept in Combination with MTX in Early, MTX-Naïve, ACPA Positive Patients with RA: 1-Year Results from a Phase IIIb Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Early biologic use can improve long-term control of RA, and early use of abatacept (ABA) + MTX has demonstrated sustained improvements in selected patient-reported outcomes (PROs).[1,2] AVERT-2 (NCT02504268) is an ongoing, large, Phase IIIb, randomized, double-blinded study evaluating efficacy and safety of SC ABA + MTX vs ABA placebo (PBO) + MTX in ACPA positive (+) patients (pts) with early RA (disease duration ≤6 months) for 56 weeks, followed by a 48-week de-escalation.[3] Results of a *post hoc* analysis of PROs at 24 and 52 weeks in the AVERT-2 study are presented.

Methods: For the induction period, pts were randomized to SC ABA (125 mg weekly) + MTX or ABA PBO + MTX for 56 weeks. Key inclusion criteria: age ≥18 years; RA diagnosis ≤6 months (ACR/EULAR 2010 criteria); ACPA+; CRP >3 mg/L (upper limit of normal/ESR ≥28 mm/h); TJC ≥3 and SJC ≥3; DMARD naïve. PROs included pain (visual analog scale [VAS], 0–10 cm), pt assessment of disease activity (PtDA; VAS, 0–10 cm), physical function (HAQ-DI; 0–3), fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue), Work Productivity and Activity Impairment (WPAI) questionnaire and pt overall quality of life (Short-Form 36 [SF-36] physical component summary [PCS]/mental component summary version 2.0). Adjusted mean change from baseline (adMCFB) and the proportion of pts attaining a minimal clinically important difference (MCID; values defined in Table 2)[4] at 24 and 52 weeks were calculated

Table 1. AdMCFB in PROs at Weeks 24 and 52; ITT Analysis

	Baseline*	Week 24				Week 52			
	Mean (SD)	n	Mean (SD)	adMCFB	Adjusted mean difference in CFB between treatments (p value)	n	Mean (SD)	adMCFB	Adjusted mean difference in CFB between treatments (p value)
Pain VAS									
ABA + MTX	66.33 (22.60)	427	24.72 (20.72)	−41.07	−8.66 (<0.0001)	396	22.43 (21.66)	−42.69	−7.14 (0.0001)
ABA PBO + MTX	65.60 (22.28)	274	33.15 (24.86)	−32.41		239	28.05 (23.38)	−35.55	
Patient global disease activity VAS									
ABA + MTX	65.53 (22.85)	427	26.02 (21.18)	−38.22	−7.47 (<0.0001)	396	22.08 (20.23)	−41.51	−7.09 (<0.0001)
ABA PBO + MTX	62.92 (23.64)	274	32.98 (22.52)	−30.76		239	27.49 (21.36)	−34.42	
HAQ-DI									
ABA + MTX	1.57 (0.70)	436	0.68(0.61)	−0.89	−0.17 (0.0001)	401	0.60 (0.59)	−0.96	−0.17 (0.0001)
ABA PBO + MTX	1.61 (0.70)	283	0.87 (0.69)	−0.72		246	0.76 (0.65)	−0.79	
SF-36 PCS									
ABA + MTX	34.51 (8.05)	436	45.61 (8.56)	11.09	2.30 (0.0001)	402	47.33 (8.34)	12.53	2.49 (0.0001)
ABA PBO + MTX	34.32 (7.95)	283	43.22 (8.72)	8.79		247	45.20 (8.56)	10.04	
SF-36 MCS									
ABA + MTX	43.96 (11.41)	436	48.45 (10.40)	4.79	−0.16 (0.8232)	402	48.74 (10.47)	4.91	−0.87 (0.2300)
ABA PBO + MTX	42.84 (11.61)	283	48.14 (10.88)	4.95		247	49.57 (10.47)	5.78	
FACIT-Fatigue									
ABA + MTX	23.87 (11.49)	436	14.35 (9.98)	−9.82	−0.87 (0.2146)	401	13.19 (9.48)	−10.67	−1.16 (0.1048)
ABA PBO + MTX	25.35 (12.05)	283	15.76 (10.51)	−8.95		246	14.22 (9.83)	−9.51	
WPAI presenteeism									
ABA + MTX	51.21 (27.42)	182	25.22 (25.05)	−25.57	0.70 (0.7970)	172	18.66 (21.60)	−31.21	−4.64 (0.0699)
ABA PBO + MTX	49.66 (28.10)	119	24.29 (23.53)	−26.27		110	22.55 (22.15)	−26.57	
WPAI absenteeism									
ABA + MTX	16.74 (27.88)	196	6.68 (19.63)	−9.60	1.27 (0.5032)	185	5.46 (16.77)	−10.98	3.11 (0.0505)
ABA PBO + MTX	16.19 (26.24)	126	5.52 (16.14)	−10.87		115	2.22 (6.49)	−14.09	

Estimates of adjusted mean change are from a repeated measures mixed model that includes baseline value, treatment group, time, time-by-baseline and time-by-treatment group interaction

Decreases in score indicate an improvement for all PROs, except SF-36 PCS and MCS, where increases in score indicate an improvement

*n numbers at baseline for each outcome match those presented for Week 24

ABA=abatacept; adMCFB=adjusted mean change from baseline; CFB=change from baseline; FACIT=Functional Assessment of Chronic Illness Therapy; ITT=intent-to-treat; MCS=mental component summary; PBO=placebo; PCS=physical component summary; PRO=patient-reported outcome; SF-36=Short Form-36; VAS=visual analog scale; WPAI=work productivity and activity impairment

for each PRO in the intention-to-treat population. AdMCFB was estimated using a mixed effect model with repeated measures.

Results: Of the 752 randomized pts, 451 were treated with ABA + MTX and 301 with ABA PBO + MTX. Baseline characteristics were similar across treatment arms.3 The adMCFB showed improvements in all PROs at both time-points for both treatment arms (Table 1), with ABA + MTX vs ABA PBO + MTX showing greater magnitude of improvement in pain PtDA, HAQ-DI and SF-36 PCS at both Weeks 24 and 52 ($p \leq 0.0001$). For all PROs except WPAI, more than half of pts achieved the MCID (Table 2). Compared with ABA PBO + MTX, a significantly greater proportion of ABA + MTX–treated pts attained the MCID in pain, PtDA and HAQ-DI at Weeks 24 and 52 ($p < 0.05$). Although there was no difference at Week 24, by Week 52 a greater proportion of pts attained the MCID in SF-36 PCS with ABA + MTX than with PBO + MTX.

Table 2. Percentage of Patients Attaining MCID in PROs at Weeks 24 and 52; ITT Analysis

	Week 24			Week 52		
	ABA + MTX (n=451)	ABA PBO + MTX (n=301)	p value	ABA + MTX (n=451)	ABA PBO + MTX (n=301)	p value
Pain VAS	80.9	69.4	0.0003	75.4	65.1	0.0023
Patient global disease activity VAS	77.8	67.4	0.0015	75.4	63.1	0.0003
HAQ-DI	82.5	75.7	0.0242	77.2	69.4	0.0178
SF-36 PCS	80.0	75.4	0.1320	78.9	66.1	0.0001
SF-36 MCS	51.2	52.2	0.8005	51.4	51.2	0.9403
FACIT-Fatigue	64.3	65.1	0.8189	63.4	58.5	0.1724
WPAI presenteeism	29.0	29.2	0.9554	30.6	27.2	0.3216
WPAI absenteeism	14.0	15.9	0.4537	14.4	14.3	0.9613

MCID: patient global assessment of pain and patient global assessment of disease activity (decrease >10 mm), HAQ-DI (decrease ≥0.22 units), SF-36 PCS and MCS (increase ≥2.5), FACIT-Fatigue (decrease ≥4.0), WPAI presenteeism and absenteeism (decrease ≥7)[4]

Missing values at Week 24 and Week 52 are imputed as not attaining MCID

p values are assessed by chi-square test if n≥5 and Fisher's exact test otherwise

ABA=abatacept; FACIT=Functional Assessment of Chronic Illness Therapy; ITT=intent-to-treat; MCID=minimal clinically important difference; MCS=mental component summary; PBO=placebo; PCS=physical component summary; PRO=patient-reported outcome; SF-36=Short Form-36; VAS=visual analog scale; WPAI=work productivity and activity impairment

Conclusion: In pts with early RA, treatment with abatacept + MTX and abatacept PBO + MTX were both associated with substantial improvements in PROs and quality of life by 24 weeks that were sustained over 1 year. Compared with abatacept PBO + MTX, a significantly greater proportion of abatacept + MTX–treated pts reported clinically meaningful improvements in pain, PtDA and function (HAQ-DI) by 24 weeks; this difference was sustained at 52 weeks. Further long-term follow-up analysis including impact of de-escalation of therapy is warranted.

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Abstract Number: 1424

The Effect of HLA-DRB1 Risk Alleles (Shared Epitope) on Changes in Immune Cell Subsets and Disease Activity Following Treatment with Abatacept versus Adalimumab in Seropositive Biologic-Naïve Patients with Early, Moderate-to-Severe RA: Data from a Head-to-Head Single-Blinded Trial

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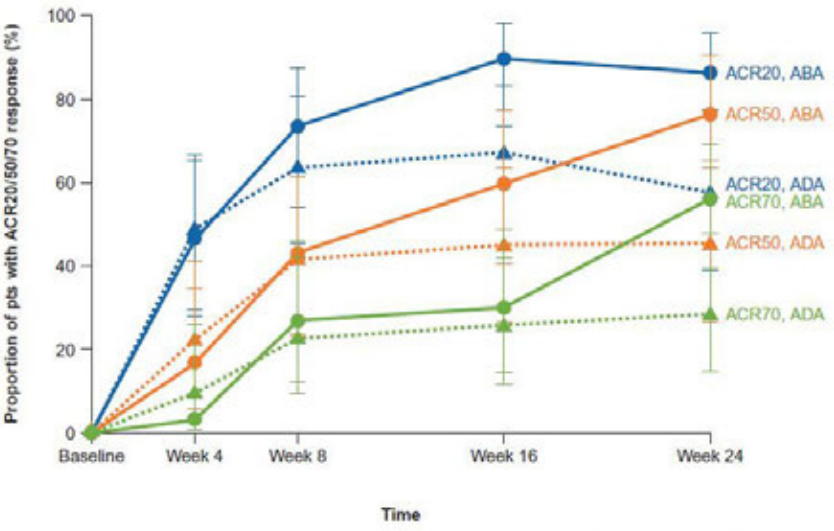
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Mechanistic differences between biologic DMARDs are poorly understood. Exploring these mechanisms includes assessing the role of *HLA-DRB1* alleles containing the shared epitope (SE), which are present in 85% of anti-CCP2+ patients (pts) with RA,[1] and changes in immune cell subsets relevant in RA. In a head-to-head (H2H) study, abatacept (ABA) markedly altered immune cell subsets in pts with RA.[2] In the present study, numerically higher efficacy responses with ABA versus adalimumab (ADA) were reported after 24 weeks (wks) in the overall population, specifically in SE+ pts.[3] In the analysis reported here, we explored the relationship between *HLA-DRB1* SE genotype and the effects of ABA or ADA on immune cell subsets and disease activity.

Methods: This H2H, single-blinded trial (NCT02557100) in biologic-naïve pts with active RA enrolled anti-CCP+ (>3x upper limit of normal), RF+ adults with early (≤12 months of symptoms), moderate-to-severe RA (ACR/EULAR 2010 criteria). Pts were randomized 1:1 to SC ABA 125 mg wkly or SC ADA 40 mg every 2 wks (both with stable MTX) for 24 wks. Pts were grouped by *HLA-DRB1* SE genotype (–, no SE allele; +, ≥1 SE allele). Efficacy was assessed to Wk 24 by proportions of ACR20/50/70 responders in ABA versus ADA arms by SE status. Changes in immune cell subsets with ABA versus ADA were measured by flow cytometry to Wk 24 in the overall population and by SE status. Benjamini–Hochberg procedure with a 10% false positive discovery rate was used to select significant immune cell subsets in the overall population.

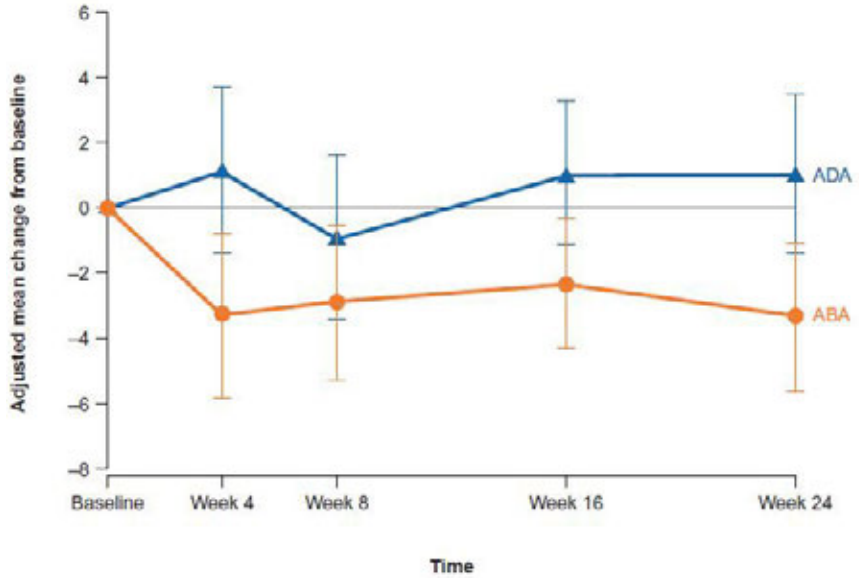
Results: 80 pts were treated: 40 ABA (9 SE–, 30 SE+, 1 SE unknown) and 40 ADA (9 SE–, 31 SE+). Baseline characteristics were similar between treatment (tx) arms. Mean (SD) age, disease duration and DAS28 (CRP) were 46.0 (14.4) years, 5.5 (2.6) months and 5.2 (1.1), respectively; 75% were female. SE+ pts versus SE– pts had greater (mean [SD]) CRP (16.1 [27.8] vs 4.8 [3.5] mg/L), anti-CCP2 (1216.6 [1525.1] vs 368.1 [433.6] U/mL) and RF levels (148.5 [130.1] vs 78.2 [44.2] kU/L); other characteristics were similar. SE+ pts had similar or numerically higher ACR20/50/70 responses with ABA versus ADA as early as Wk 8 and sustained to Wk 24 (Figure 1). At Wk 24, ABA significantly changed the proportions of key immune cell subsets versus ADA (tx difference [95% CI]): naïve CD4+ T cells (8.7 [5.6, 11.7]; p< 0.0001), naïve CD8+ T cells (6.3 [1.9, 10.7]; p=0.0059), CD8+ CD28– T cell (–4.3 [–7.7, –0.9]; p=0.0136; Figure 2), CD4+ effector memory T cells (–4.4 [–7.6, –1.2]; p=0.0086) and regulatory T cells (–1.6 [–2.2, –0.9]; p< 0.0001) in the overall population. The differential reduction in CD8+ CD28– T cells by tx group in the overall population was driven by the SE+ pts (Figure 3).

Figure 1. Proportion of SE+ Patients With ACR Responses Over Time



Error bars show 95% CIs. At all time points: ABA n=30, ADA n=31. Missing values are imputed as non-responders. Estimates of difference (95% CI) for ABA vs ADA at Week 24 were 28.6 (4.6, 51.7), 31.5 (6.8, 54.5), 27.6 (1.4, 50.5), for ACR20/50/70, respectively
ABA=abatacept; ACR20/50/70=20/50/70% improvement in ACR criteria; ADA=adalimumab; pts=patients; SE=shared epitope

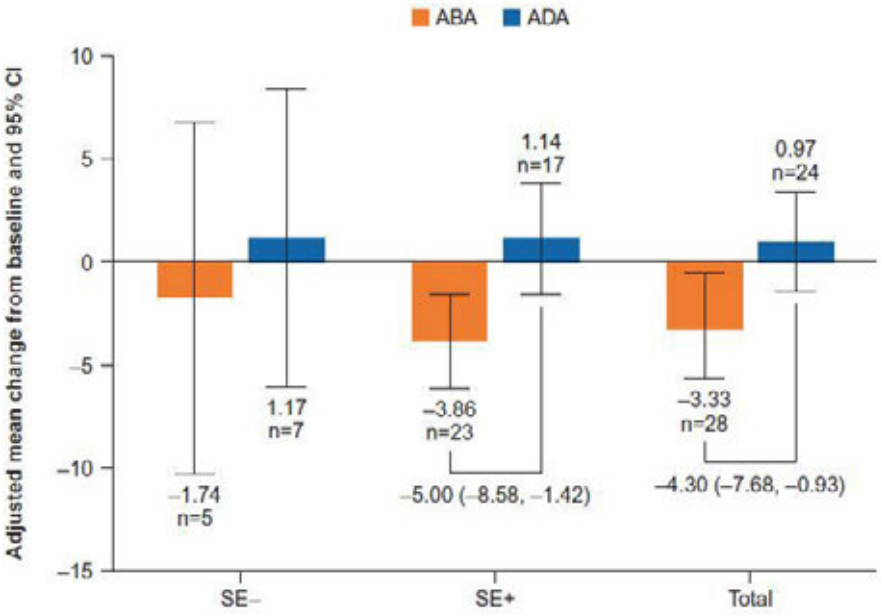
Figure 2. Adjusted Mean Change From Baseline in CD8+ CD28− T cells Over Time During the Single-Blind Treatment Period



ABA, n	34	31	34	33	28
ADA, n	31	30	30	27	24

Error bars represent 95% CI
ABA=abatacept; ADA=adalimumab

Figure 3. Adjusted Mean Change From Baseline in Percentage of CD8+ CD28− T Cells at Week 24 by Shared Epitope Status



Error bars represent 95% CI
ABA=abatacept; ADA=adalimumab; SE=shared epitope

Conclusion: In this anti-CCP2+ early RA population, abatacept was effective in SE+ pts and had a significant effect on key immune cell subsets involved in adaptive immune response, relevant in RA, versus adalimumab.

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Abstract Number: 1425

Effect of ACPA IgM Serostatus on Efficacy Outcomes Following Treatment with Abatacept or Adalimumab: A *Post Hoc* Analysis of a Phase III Head-to-Head Trial

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

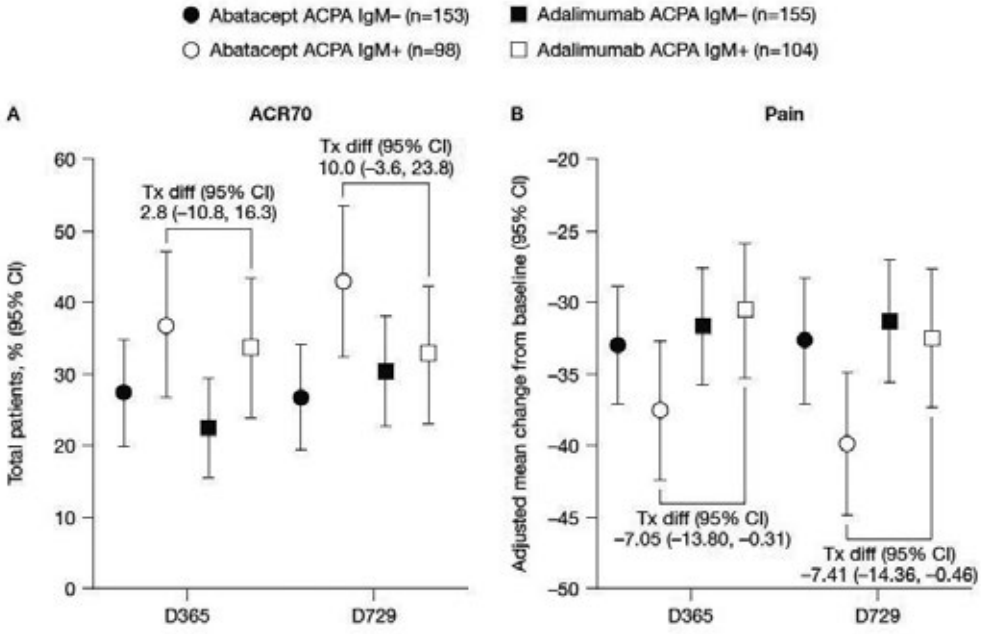
Background/Purpose: Anti-citrullinated protein antibody (ACPA) is a marker for early, erosive RA.[1] In the Abatacept (ABA) versus adaliMumab (ADA) comParison in bioLogic-naïvE RA subjects with background MTX (AMPLE; NCT00929864) trial, higher versus lower baseline (BL) ACPA IgG levels were associated with improved clinical outcomes, and in patients (pts) with high ACPA IgG levels, ABA was associated with improved outcomes compared with ADA.[2] The persistent presence of IgM is more indicative of continuous immune activation than IgG.[1] In the Assessing Very Early Rheumatoid arthritis Treatment (AVERT) trial, ABA + MTX had greater clinical efficacy in pts who were ACPA IgM positive (+) compared with ACPA IgM negative (–) at BL, and in seroconverters versus non-seroconverters.[3] This *post hoc* analysis of the AMPLE trial compared the treatment differences between ABA and ADA over 2 years, in pts who were ACPA IgM+ at BL by Day (D) 365 seroconversion status.

Table 1. Proportion of Patients With Seroconversion to from ACPA IgM+ to ACPA IgM– Status by Treatment Over Time

ACPA IgM seroconversion, n/N (%)	Converter	
	Abatacept	Adalimumab
Day 85	16/84 (19)	9/88 (10)
Day 365	22/87 (25)	20/81 (25)
Day 729	13/52 (25)	16/59 (27)

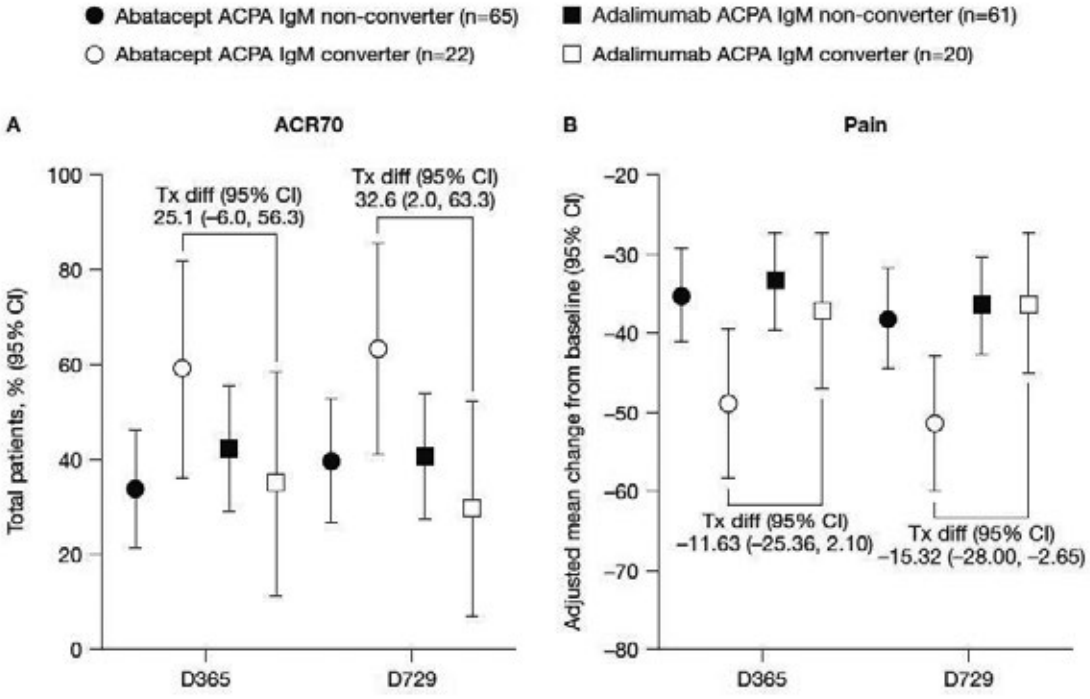
Subgroup analysis based on seroconversion status was done for Day 365 only, where there were n≥20 per subgroup
n=number of patients who seroconverted; N=total number of patients with baseline ACPA IgM+ status
ACPA=anti-citrullinated protein antibody

Figure 1. Clinical Outcomes by Baseline ACPA IgM Seroreactivity: (A) Proportion of Patients With ACR70 Response and (B) Adjusted Mean Change From Baseline in Pain



ACPA=anti-citrullinated protein antibody; D=Day; Tx diff=treatment difference

Figure 2. Clinical Outcomes by ACPA IgM Seroconversion: (A) Proportion of Patients With ACR70 Response and (B) Adjusted Mean Change From Baseline in Pain



ACPA=anti-citrullinated protein antibody; D=Day; Tx diff=treatment difference

Methods: The AMPLE trial (NCT00929864) has been published.[4] Samples, including those from ACPA+ pts were analyzed by ELISA to determine ACPA IgM serostatus. Outcomes over 2 years of treatment were analyzed by treatment group, based on BL ACPA IgM serostatus, and seroconversion to ACPA IgM– status, at D365. Analysis of covariance models were used to assess the adjusted mean changes, with treatment as factor and BL values and screening DAS28 (CRP) randomization stratification as covariates.

Results: Of 646 pts with RA (1987 ACR criteria[5]) in the AMPLE study, BL ACPA IgM status was available for 510 pts: 308 ACPA IgM– and 202 ACPA IgM+. BL characteristics were comparable between ACPA IgM+ and ACPA IgM– groups, and among all ACPA IgM+ pts across treatment arms between seroconverters at D365 versus non-converters. In pts who were ACPA IgM+ at BL, ABA was associated with a numerically higher ACR70 response rate (Figure 1A) and greater reduction in pain (Figure 1B) than ADA at D365 and D729. The trend in treatment difference for ACR70 and pain was consistent over time (data not shown). By D365, a similar proportion of pts from each treatment group seroconverted from ACPA IgM+ to ACPA IgM– status (Table 1). In pts who seroconverted from ACPA IgM+ at BL to ACPA IgM– at D365, ABA was associated with a greater numerical improvement in ACR70 response (Figure 2A) and reduction in pain (Figure 2B) than ADA at D365 and D729.

Conclusion: ACPA IgM seropositive status at BL predicted numerically better clinical outcomes after 365 and 729 days of treatment in abatacept-treated pts compared with ADA-treated pts. Among the subset of pts who seroconverted to ACPA IgM– status, abatacept treatment was associated with numerically better clinical responses. ACPA IgM+ status may help identify a subset of pts with active RA who respond better to abatacept treatment.

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Abstract Number: 1426

Impact of TNF Inhibitor Cycling with Adalimumab and Etanercept vs Switching to Tofacitinib

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Tofacitinib is an oral JAK inhibitor for the treatment of RA. It was approved for RA by the US FDA in Nov 2012. TNFi cycling in non-responder patients (pts) with RA may be reinforced by payers limiting access to similarly indicated advanced therapies with different mechanisms of action, such as tofacitinib. In a retrospective analysis, adalimumab (ADA) and etanercept (ETN) were the most common prior bDMARDs for pts with RA initiating ETN and ADA, respectively, with no other advanced therapy history.[1] We assessed the impact of TNFi cycling with ADA and ETN vs switching to tofacitinib.

Methods: This retrospective cohort study used the US-based IBM® MarketScan® Commercial and Medicare Supplemental insurance claims databases to identify pts with RA who newly started index medication with tofacitinib or select TNFi (ADA or ETN) between Jan 2014 and Sep 2016. Eligible pts had continuous enrolment for ≥ 12 months pre-/post-index and their only pre-index advanced therapy (bDMARD or JAK inhibitor) claim was for non-index ADA or ETN. Pts were analyzed by treatment switch: ADA to tofacitinib; ADA to ETN; ETN to tofacitinib; ETN to ADA. Outcomes assessed over 12 months post-index were: persistence without a ≥ 60-day gap in index therapy or switch;

Table. Demographics, baseline clinical characteristics, adherence, persistence, effectiveness (proxy), and costs in patients with RA switching from ADA to tofacitinib or ETN, and ETN to tofacitinib or ADA: data from the US-based IBM® MarketScan® Commercial and Medicare Supplemental insurance claims databases[a]

	ADA to tofacitinib (N=287)	ADA to ETN (N=79)	P value	ETN to tofacitinib (N=262)	ETN to ADA (N=112)	P value
Female, n (%)	243 (84.7)	62 (78.5)	0.1913	219 (83.6)	85 (75.9)	0.0806
Age, mean (SD)	55.2 (11.1)	50.5 (11.6)	0.0013	54.5 (12.3)	53.4 (12.1)	0.4068
Medicare Supplemental, n (%)	54 (18.8)	5 (6.3)	0.0075	46 (17.6)	13 (11.6)	0.1482
Quan-Charlson Comorbidity Index Score, mean (SD)	1.8 (1.2)	1.7 (1.3)	0.7460	1.9 (1.4)	1.6 (1.2)	0.1039
Baseline RA-related costs, mean $ (SD)	27,391 (20,611)	16,359 (15,754)	<0.0001	22,780 (16,635)	18,432 (15,755)	0.0192
Persistence[b,c], n (%)	145 (50.5)	29 (36.7)	0.0295	120 (45.8)	43 (38.4)	0.1857
Duration of therapy (days)[b,c], mean (SD)	239.0 (134.5)	203.7 (133.2)	0.0387	234.3 (131.1)	219.8 (126.1)	0.3194
Effectiveness proxy (patients meeting criteria)[b], n (%)						
Met all criteria below	85 (29.6)	11 (13.9)	0.0050	59 (22.5)	17 (15.2)	0.1061
Adherence (PDC ≥0.8)	129 (45.0)	24 (30.4)	0.0201	102 (38.9)	37 (33.0)	0.2799
No dose escalation	272 (94.8)	77 (97.5)	0.3135	251 (95.8)	91 (81.3)	<0.0001
No new csDMARD	221 (77.0)	52 (65.8)	0.0432	184 (70.2)	72 (64.3)	0.2573
No advanced therapy switch	221 (77.0)	51 (64.6)	0.0249	208 (79.4)	75 (67.0)	0.0103
No new[d]/increased[e] oral glucocorticoid	244 (85.0)	66 (83.5)	0.7474	213 (81.3)	97 (86.6)	0.2118
<2 days intra-articular injections	237 (82.6)	59 (74.7)	0.1141	200 (76.3)	93 (83.0)	0.1497
Change in RA-related costs, mean $ (SD)						
Total	10,048 (27,257)	17,681 (21,412)	0.0220	14,188 (19,538)	21,595 (20,979)	0.0011
Prescription	9,260 (19,001)	15,566 (17,959)	0.0086	12,140 (14,603)	19,712 (15,916)	<0.0001

[a]Categorical variables were compared using chi-square tests and continuous variables were compared using t-tests. There was no correction for multiple comparisons
[b]12-month follow-up
[c]<60-day gap and no advanced therapy switches
[d]≤30 days of oral glucocorticoid between Months 3-12 post-index in patients with no glucocorticoid prescriptions for 6 months pre-index
[e]No increase in oral glucocorticoid dose ≥20% during Months 6-12 post-index (for those with 6 months of pre-index glucocorticoid use)
ADA, adalimumab; csDMARD, conventional synthetic disease-modifying antirheumatic drug; ETN, etanercept; PDC, proportion of days covered; RA, rheumatoid arthritis; SD, standard deviation

duration of therapy; effectiveness, estimated based on a validated claims-based algorithm. Changes in 12-month post-index RA-related (medical and pharmacy) costs were assessed.

Results: Of 740 pts: 549 switched from ADA or ETN to tofacitinib; 191 cycled between ADA and ETN (Table). Pts switching to tofacitinib had significantly ($p < 0.05$) higher baseline (BL) RA-related costs vs pts who cycled between ADA and ETN. Pts who switched from ADA to tofacitinib were older and a greater % were Medicare Supplemental beneficiaries, vs pts who cycled from ADA to ETN. In pts who switched from ADA to tofacitinib vs those who cycled from ADA to ETN: persistence and duration of therapy were significantly higher and longer, respectively; and the % effectively treated was significantly higher, driven by better adherence, and no new csDMARDs or advanced therapy switch. A significantly lower % of pts who switched from ETN to tofacitinib had an advanced therapy switch or dose escalation thereafter vs pts who cycled from ETN to ADA. A numerically, but not significantly, higher % of pts switching from ETN to tofacitinib were persistent and effectively treated vs pts cycling from ETN to ADA. RA-related cost increases were significantly lower in pts who switched to tofacitinib vs pts who cycled between ADA and ETN, driven by significantly smaller increases in prescription costs.

Conclusion: Pts who switched from ADA or ETN to tofacitinib had higher persistence, effectiveness, and significantly lower change in RA-related costs vs pts cycling between ADA and ETN. Further adjusted analyses are planned to understand potential delays in tofacitinib use due to access barriers promoting 1st-line TNFi use. Larger sample sizes may be needed to further evaluate statistical differences for pts switching from ETN to tofacitinib vs ADA.

Reference:

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Abstract Number: 1427

Comparison of Real-World Persistence of Subcutaneously Administered Biologic Disease-Modifying Antirheumatic Drug Therapies Among Patients with Rheumatoid Arthritis Switching from Another Biologic

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The EULAR and ACR clinical guidelines recommend switching to a different disease-modifying antirheumatic drug (DMARD) when biologic-treated patients experience treatment failure or toxicity. Lack of efficacy and adverse events are among the most commonly reported reasons for switching biologic therapies. Limited information is available regarding biologic therapy persistence across subcutaneously administered (SC) biologic

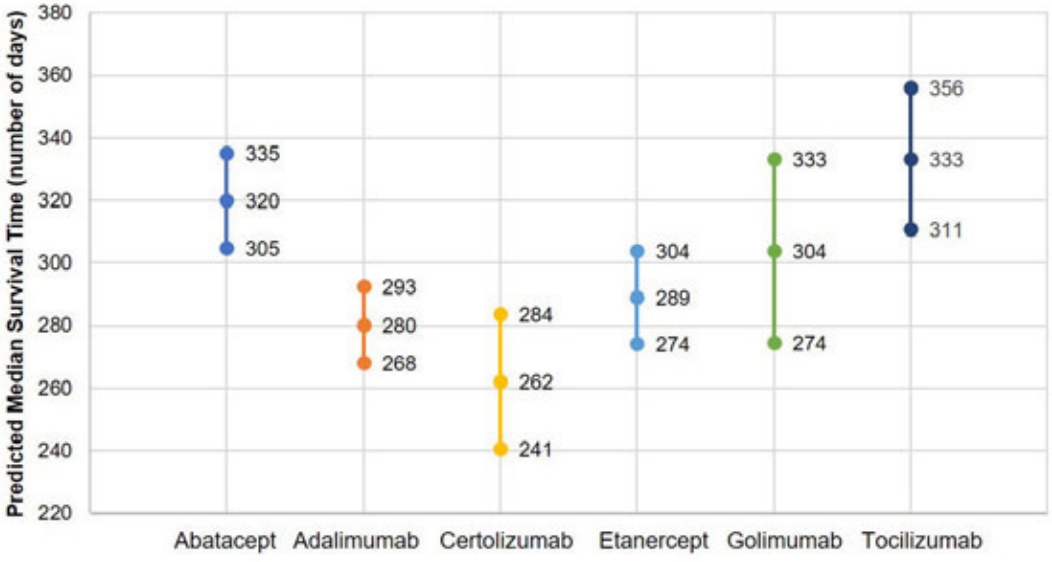
agents in the real-world setting, as well as comparative information on biologic persistence for SC biologics among patients with rheumatoid arthritis (RA) who are not naïve to biologic treatment. This study compared the persistence of SC biologic DMARDs (bDMARDs) in patients with RA as subsequent-line therapy following a failure of first-line bDMARDs.

Methods: US administrative claims data were used to create a longitudinal cohort of adult patients with RA initiating SC biologic between 1/1/2012 and 6/30/2017 (initiation date = index). Patients were required to have failed 1st bDMARD to enter study (but could later switch therapy) and to have 6 and at least 3 months of continuous enrollment pre- and post-index (date of prescription for bDMARD). Those with other autoimmune conditions were excluded from the study. Outcomes were biologic persistence, defined as number of days between initiation date and last supplied day of last fill. Parametric survival models with exponential distribution with robust variance estimator were used to compare outcomes for tocilizumab versus other biologics, adjusting for differences in baseline characteristics, accounting for correlation among different bDMARD episodes.

Results: There were 10,301 patients with 12,704 bDMARD episodes: abatacept (n = 2,988), adalimumab (n = 3,599), certolizumab (n = 982), etanercept (n = 2,760), golimumab (n = 745), or tocilizumab (n = 1,630). Mean age ranged from 51.0 to 53.3 years. Mean [SD] Elixhauser comorbidity scores were significantly higher ($P < 0.001$) for tocilizumab (2.8 [2.3]) compared with abatacept (2.5 [2.2]), adalimumab (2.5 [2.1]), certolizumab (2.4 [2.0]), etanercept (2.4 [2.0]) or golimumab (2.4 [2.2]). Adjusted median days (95% CI) of persistence were: abatacept 320 (305, 335); adalimumab 280 (268, 293); certolizumab 262 (241, 284); etanercept 289 (274, 304); golimumab 304 (274, 333); and tocilizumab 333 (311, 356). Tocilizumab had significantly ($P < 0.05$) higher persistence compared with adalimumab, certolizumab and etanercept (**Figure 1**). Of patients who were observed for 12 months, 45% of patients initiated tocilizumab biweekly and 55% initiated weekly. Of the 347 patients initiating biweekly tocilizumab, 33% switched to weekly over 12-month follow up; the mean time to switch was 177 days. After 12 months of follow-up, approximately 68% of patients finished on weekly dosing and 32% on biweekly dosing.

Conclusion: Among patients with RA who previously used ≥ 1 other biologic, tocilizumab-treated patients had similar or statistically significantly better biologic persistence compared with other biologics.

Figure 1. Adjusted Persistence (with 95% CI) of Biologic DMARDs Among Patients with RA



DMARD, disease-modifying antirheumatic drug.

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Disclosure: J. Best, Genentech, 1, 3, Genentech, Inc., 1, 3; **L. Tominna**, Genentech, Inc., 3; **I. Abbass**, Genentech, Inc., 3.

Abstract Number: 1428

Time to Discontinuation of Tofacitinib in Rheumatoid Arthritis Patients with and Without Methotrexate: Results from a Rheumatoid Arthritis Cohort

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SESSION INFORMATION
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Background/Purpose: Tofacitinib (TOFA) is an oral, small molecule drug which can be used as an alternative to biologic disease modifying antirheumatic drugs (bDMARDs) for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX). We aimed to evaluate the discontinuation rate of this drug, with and without concurrent MTX, and with and without prior biologic use, in patients with RA in the Ontario Best Practices Research Initiative (OBRI).

Methods: RA patients enrolled in the OBRI initiating their TOFA within 30 days prior to or any time after enrolment between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2017 were included. Patients were excluded if they had ≤ 2 visits and ≤ 6 months' follow-up. Time to discontinuation due to (1) any reason, (2) lack/loss of response, and 3) adverse events (AEs) were assessed using Kaplan-Meier survival to compare patients 1) with and without MTX use; 2) with or without prior biologic use at initiation of TOFA was assessed using Kaplan-Meier survival analysis. Cox proportional hazards regression model was also used to assess TOFA discontinuation adjusting for propensity score to balance the two treatment groups.

Results: Among the 131 patients, 70 (53.4%) received TOFA without MTX and 61 (46.6%) TOFA with MTX. Mean (SD) age and disease duration were 60.2 (9.8) years and 13.7 (9.3) years, respectively. The majority were females (89.3%) and most had prior biologic use history (74.0%). Discontinuation was reported in 44 (33.6%) of all TOFA patients with a median survival of 31.3 months. Overall retention of TOFA at 6, 12 and 24 months was 80.5%, 63.1% and 53.5% respectively. These findings are very similar to the results reported from the RHUMADATA registry at ACR 2018.[1] Fifteen (34.0%) patients stopped their TOFA due to non-response/loss of response, 22 (50.0%) due to adverse events, and 7 (16%) due to other reasons. Discontinuation due to any reason was borderline significantly lower in the "TOFA with MTX" group compared with "TOFA without MTX" group. There was no significant difference in TOFA discontinuation between the two groups of patients with and without prior biologic use (Logrank p=0.77).

Conclusion: We found that half of the RA patients remained on TOFA 31 months after initiation. TOFA retention is similar between patients with and without MTX group specifically for lack/loss of response or adverse events reasons. However, the interpretation of results is limited because of small sample size. Merging data with other RA registries in Canada is proposed to increase study power and to provide more robust results.

Reference:

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Abstract Number: 1429

Results at 6 Months of Abatacept vs TNF-α Blockers in Patients with Severe, Long-standing, DMARDs Resistant Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Since January 2016, Chilean patients with rheumatoid arthritis (RA), with severe activity despite the use of 3 DMARDs for at least 6 months, have guaranteed access to biologics. In the first year the only first-line option was abatacept, in the second year etanercept and adalimumab were added. Our objetive was to evaluate the efficacy at 6 months of abatacept vs TNF-α blockers as first-line biologic.

Methods: Real life, prospective-cohort, single-center study. Only RA patients with a DAS28 ESR greater than 5.1 or with ≥ 6 painful joints, ≥3 swollen joints, ESR ≥30 mm/h, and morning stiffness ≥45 minutes on 2 evaluations, separated between 30-120 days, were allowed to postulate for biologic treatment. Included patients during 2016 received abatacept as first-line biologic, and since 2017 the first-line biologic was selected by randomizing patients in order of attention to abatacept, etanercept or adalimumab, unless there was a particular condition that made it preferable one over another (latent tuberculosis, intersticial lung disease). Tapering of other DMARDs and prednisone was done depending on the clinician's judgment. The patients were followed for 6 months, DAS28 ESR change was evaluated and the EULAR response criteria was calculated. HAQ, other medications use changes, and adverse events were evaluated. Comparisons were made between abatacept and TNF-α blockers (etanercept/adalimumab). Multivariate analysis was performed taking into account age, sex, years with symptoms, comorbidities, smoking, BMI, CCP status, DMARDs, corticoids, NSAIDs and tramadol use, and baseline DAS28.

Results: 123 patients were enrolled (table 1 for baseline characteristics). Users of TNF-α blockers had a significantly greater decrease in DAS28 ESR, higher rate of remission, higher rate of good EULAR response, and a lower rate of failure according to the physician (Table 2). These differences maintained statistical significance ($p < 0.05$) after multivariate analysis. A higher BMI was significantly related, after multivariate analysis, to a lower reduction of DAS28 ESR and lower rate of remission after 6 months. For HAQ there was no difference in the reduction and the result after 6 months of biologic treatment (from 1.9 to 1.5). The median number of DMARDs and the median prednisone dose was reduced without differences between groups. The rate of tramadol use saw a 10.9% reduction in the abatacept group and 2.5% in the TNF-α blocker group (table 3). After multivariate analysis more years with symptoms was related to higher rate of tramadol use after 6 months of biologics. The rate of adverse events (AE) was higher in the TNF-α blocker group (39.1 vs 27.7%) but the rate of serious events was higher in the abatacept group (30.4 vs 22.2% of all AE), although no significant differences were found.

Conclusion: At 6 months, in this real life study, more than 80% of the patients with severe, long standing, DMARDs resistant, RA had at least a moderate response to biologic treatment. This improvement was significantly higher in the

Table 1. Baseline Characteristics of the Participants

	Total	Abatacept	TNF inhibitor	P
No. patients	123	83	40	NA
Age, mean (SD), y	55.1 (10.8)	55.8 (10.4)	53.7 (11.5)	NS
Women, n (%)	112 (91.2)	75 (90.4)	37 (92.5)	NS
Years with symptoms, median (IQR)	10 (6-15.5)	10 (6-15)	10.5 (8-15-5)	NS
Anti-CCP positive, n (%)	106 (86.2)	71 (85.5)	35 (87.5)	NS
BMI, median (IQR)	28.7 (25.8-31.8)	28.7 (25.9-32.8)	28 (25.7-31.1)	NS
ILD, n (%)	5 (4.1)	5 (6)	0	NA
Comorbidity, n (%)				
Diabetes Mellitus 2	32 (26)	24 (28.9)	8 (20)	NS
Hypertension	62 (50.4)	48 (57.8)	14 (35)	0.018
Tobacco use	26 (21.1)	17 (20.5)	9 (22.5)	NS
Latent tuberculosis	14 (11.4)	13 (15.7)	1 (2.5)	0.35
Drugs,n (%)				
Methotrexate	85 (69.1)	59 (71.1)	26 (65)	NS
Sulfasalazine	75 (61)	47 (56.6)	28 (70)	NS
Hydroxychloroquine	81 (65.9)	52 (62.7)	29 (72.5)	NS
Leflunomide	69 (56.1)	46 (55.4)	23 (57.5)	NS
Prednisone	117 (95.1)	80 (96.4)	37 (92.5)	NS
Celecoxib	106 (86.2)	74 (89.2)	32 (80)	NS
Tramadol	47 (38.2)	39 (47)	8 (20)	0.004
Work situation, n (%)				
Unemployed	1 (0.8)	0	1 (2.5)	NS
Working with contract	20 (16.3)	11 (13.3)	9 (22.5)	NS
Working without contract	9 (7.3)	6 (7.2)	3 (7.5)	NS
Housewife	31 (25.2)	23 (27.7)	8 (20)	NS
Retire	16 (13)	10 (12)	6 (15)	NS
Disability pension	46 (37.4)	33 (39.8)	13 (32.5)	NS

Table 2. Response to Treatment Measured by DAS28 ESR				
	Total	Abatacept	TNF inhibitor	P
No. patients	123	83	40	
DAS28 ESR at baseline, median (IQR)	6.1 (5.7-6.6)	6.1 (5.7-6.5)	6.1 (5.7-6.7)	NS
DAS28 ESR at 6 months, median (IQR)	3.7 (3.1-4.7)	4.1 (3.3-5.2)	3.3 (2.7-4)	<0.001
Reduction of DAS28 ESR, mean (SD)	2.2 (1.2)	1.9 (1.2)	2.9 (1.1)	<0.001
Disease activity according to DAS28 ESR at the end of follow-up, n (%)				
Remission (DAS28 ESR <2.6)	14 (11.4)	6 (7.2)	8 (20)	0.037
Low (DAS28 ESR ≤3.2)	22 (17.9)	12 (14.5)	10 (25)	NS
Moderate (DAS28 ESR >3.2 and ≤5.1)	63 (51.2)	43 (51.8)	20 (50)	NS
High (DAS28 ESR >5.1)	24 (19.5)	22 (26.5)	2 (5)	0.004
Response according to EULAR criteria, n (%)				
None	18 (14.6)	17 (20.5)	1 (2.5)	0.006
Moderate	69 (56.1)	48 (57.8)	21 (52.5)	NS
Good	36 (29.3)	18 (21.7)	18 (45)	0.008
Response according to law 20.850 criteria, n (%)				
None	13 (10.6)	12 (14.5)	1 (2,5)	NS
Moderate	9 (7.3)	8 (9.6)	1 (2.5)	NS
Significant	101 (82.1)	63 (75.9)	38 (95)	0.011
Failure according to physician, n (%)	21 (16.8)	19 (22.9)	2 (5)	0,019
Inefficacy,n	11	10	1	NA
Adverse event, n	10	9	1	NA

TNF-α blocker group. Although the abatacept group had more comorbidities the difference with the TNF-α blocker group remained significant after multivariate analysis.

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Abstract Number: 1430

Predictors of Response to Etanercept-Methotrexate Treatment: Post-hoc Analysis of a Randomized, Open-label Study in Latin American Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Etanercept (ETN) plus methotrexate (MTX) was shown to be superior to MTX plus another conventional disease-modifying anti-rheumatic drug (DMARD) in an open-label, randomized study of Latin American patients with rheumatoid arthritis (RA). Determining possible predictors of response would allow a more personalized approach to the treatment of RA in this heterogeneous population. The aim of this post hoc analysis was to identify potential predictors of response to 24- and 128-week treatment ETN+MTX in Latin American patients with RA.

Table 1: Baseline demographic and disease characteristics of responders and non-responders (observed cases)

	Week 24			Week 128		
Baseline Characteristic*	Responders (n=70)	Non-Responders (n=199)	P-value	Responders (n=19)	Non-Responders (n=35)	P-value
Age, years	**45.4 ± 12.1**	**49.4 ± 11.7**	**0.015**	48.0 ± 10.9	48.7 ± 12.1	0.845
Women, n (%)	**56 (80.0)**	**180 (90.5)**	**0.022**	**15 (79.0)**	**34 (97.1)**	**0.028**
Race, n (%)						
White	37 (52.9)	90 (45.2)	0.640	7 (36.8)	7 (20.0)	0.188
Mestizos	15 (21.4)	42 (21.1)		7 (36.8)	8 (22.9)	
African-Latin American	8 (11.4)	29 (14.6)		1 (5.3)	3 (8.6)	
Other	10 (14.3)	38 (19.1)		4 (21.1)	17 (48.6)	
BMI, kg/m²	26.6 ± 5.3 (n=68)	26.4 ± 5.1 (n=196)	0.849	26.4 ± 3.4	24.6 ± 3.8	0.088
Disease duration, years	8.3 ± 7.1	7.6 ± 6.9	0.465	7.0 ± 5.7	9.1 ± 7.7	0.320
CRP, mg/L	19.9 ± 27.0	21.4 ± 25.5	0.684	23.9 ± 33.6	27.6 ± 33.1	0.702
ESR, mm/h	**37.9 ± 11.9** (n=69)	**44.5 ± 17.4** (n=197)	**0.004**	**39.6 ± 15.9**	**52.3 ± 20.1**	**0.022**
Physician Global Assessment	**6.2 ± 1.6** (n=68)	**6.9 ± 1.6** (n=195)	**0.002**	**5.9 ± 1.9** (n=16)	**7.0 ± 1.5** (n=32)	**0.029**
Total HAQ score	**1.4 ± 0.7**	**1.7 ± 0.7**	**<0.001**	1.5 ± 0.7	1.7 ± 0.7	0.348
mTSS	39.3 ± 53.5 (n=64)	40.0 ± 46.7 (n=192)	0.918	34.0 ± 33.3	44.4 ± 34.3 (n=33)	0.290
VAS PAIN	**59.7 ± 23.5** (n=68)	**67.3 ± 20.1** (n=196)	**0.010**	63.1 ± 30.0 (n=16)	68.3 ± 13.3 (n=33)	0.405

* Data are mean ± SD unless stated otherwise.

BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HAQ, health assessment questionnaire; mTSS, modified total Sharp score; SD, standard deviation; VAS, visual analog scale.

Table 2: Odds ratios for predictors of response at Week 24 and Week 128

Baseline Characteristic	OR (95% CI)	P-value
	Week 24	
Age (≤49 years vs >49 years)	3.33 (1.61, 6.90)	0.001
BMI (>28.5 kg/m^2 vs ≤28.5 kg/m^2)	3.40 (1.57, 7.36)	0.002
Disease duration (>4.1 years vs ≤4.1 years)	2.69 (1.30, 5.53)	0.007
ESR (≤42 mm/h vs >42 mm/h)	2.67 (1.20, 5.95)	0.016
Physician Global Assessment score (≤6.0 vs >6.0)	2.87 (1.43, 5.75)	0.003
Total HAQ score (≤1.63 vs >1.63)	4.22 (1.99, 9.01)	<0.001
	Week 128	
ESR (≤35 mm/h vs >35 mm/h)	14.29 (3.13, 66.67)	0.001

BMI, body mass index; ESR, erythrocyte sedimentation rate; HAQ, health assessment questionnaire.

Methods: During Phase 1 (24 weeks) of this study (NCT00848354), patients from Latin America with MTX-resistant, moderate to severe RA were randomized 2:1 to receive open-label ETN 50 mg/week plus MTX (ETN+MTX, n=281) or an additional conventional DMARD (hydroxychloroquine or sulfasalazine) plus MTX (DMARD+MTX; n=142). Phase 2 (104 weeks) was an optional extension period allowing the continuation with Phase 1 treatment or the addition, discontinuation or titration of the other DMARD therapy. In this analysis, response was defined as Disease Activity Score-28 for Rheumatoid Arthritis with erythrocyte sedimentation rate (DAS28-ESR) score < 2.6 (DAS28-ESR remission). Baseline variables between responders and non-responders were compared using chi-square test (discrete) or one-way ANOVA (continuous). Odds of attaining response in the ETN+MTX group at Weeks 24 and 128 (observed cases) were estimated using a stepwise logistic regression model.

Results: At 24 and 128 weeks, 26% (70/269) and 35% (n=19/54) of patients in the ETN+MTX group achieved DAS28-ESR remission, respectively. On average, Week 24 and Week 128 responders had lower baseline scores of ESR and PGA, and were more likely to be men than non-responders (Table 1). In addition, Week 24 responders were on average younger and had lower baseline total HAQ and VAS pain scores, compared to non-responders. Significantly higher odds of attaining remission at Week 24 were associated with baseline age ≤49 years, BMI >28.5 kg/m^2, disease duration >4.1 years, ESR ≤42 mm/h, PGA ≤6, and Total HAQ score ≤1.63; ESR ≤35 mm/h was a predictor of response at Week 128 (Table 2). Fewer predictors of response at Week 128 compared to Week 24 may be due to lower predictability of long-term events or due to a loss of statistical power, based on the smaller sample size for Week 128.

Conclusion: Factors that predicted response to therapy were younger age, higher body mass index, longer disease duration, and an overall lower disease activity. Limitations of this post hoc analysis include the small sample size for Week 128. Further studies are needed to confirm these predictors of response.

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Abstract Number: 1431

Real-Life Golimumab Persistence in Patients with Chronic Inflammatory Rheumatic Disease: Results of the GO PRACTICE Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

Session Type: Poster Session (Monday)

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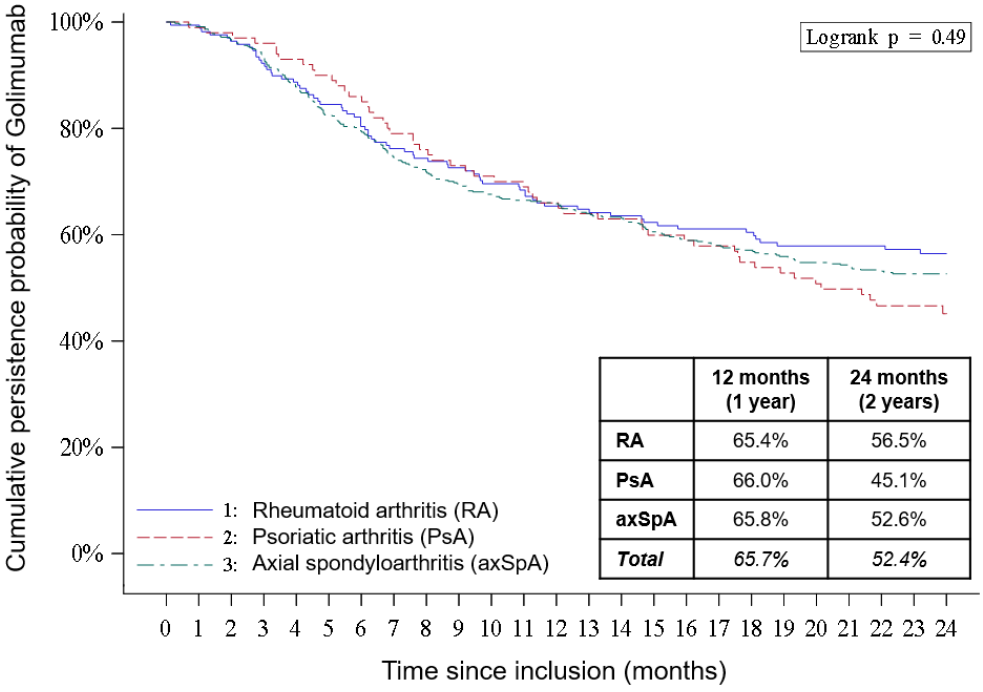
Background/Purpose: The GO PRACTICE study was initiated following a demand by the French Health Authorities for long-term data on the real-life use of golimumab (**GLM**) in patients with rheumatoid arthritis (**RA**), psoriatic arthritis (**PsA**) or axial spondyloarthritis (**axSpA**). The primary objective was to assess the persistence of GLM over 2 years after initiation. Secondary objectives included evaluations of 1) clinical disease activity from baseline to 2 years, 2) changes in patient-reported disease activity, functional abilityand quality of life (**QoL**), and 3) GLM clinical safety.

Methods: Observational, prospective, multicenter French study. Patients ≥18 years with RA, PsA and axSpA were included consecutively following GLM initiation, and followed-up for 2 years. Data were collected at baseline, year 1 and



	12 months (1 year)	24 months (2 years)
RA	65.4%	56.5%
PsA	66.0%	45.1%
axSpA	65.8%	52.6%
Total	*65.7%*	*52.4%*

Kaplan-Meier curves showing the cumulative persistence probability of GLM over 24 months for RA, PsA and axSpA patients

year 2. GLM persistence was estimated with the Kaplan-Meier method. Clinical disease activity was measured using the Disease Activity Score 28 (**DAS28**) for RA and PsA, and the Ankylosing Spondylitis Disease Activity Score (**ASDAS**) for axSpA. Patient-reported disease activity was measured with the Routine Assessment of Patient Index Data 3 (**RAPID3**) for RA and PsA, and the Bath Ankylosing Spondylitis Disease Activity Index (**BASDAI**) for axSpA. Functional ability was assessed with the Health Assessement Questionnaire (**HAQ**) and QoL was assessed with the EQ-5D and SF-12 surveys.

Results: From January 2015 to March 2016, 770 patients were selected at 134 sites, of which 754 were included in the analysis. Mean age was 46 years and 61% were female. Most had axSpA (63%), then RA (23%) and PsA (14%). Mean duration of rheumatic disease was 7.6 years; 37% had previously received biologics; the proportion of patients who received 1, 2, 3 and ≥4 biologics were 18%, 11%, 6% and 2%, respectively. Most patients were prescribed 50 mg GLM monthly (97%). Concomitant treatments included DMARDs (38%), corticosteroids (19%) and NSAIDs/analgesics (71%). GLM persistence at 2 years was 52.4% (56.5%, 45.1% and 52.6% in RA, PsA and axSpA, respectively). Disease activity showed clinically significant improvements from baseline to 2 years in patients persisting on GLM: for RA, mean DAS28-CRP from 4.3±1.1 to 2.3±0.8 ($p < .0001$), mean RAPID3 from 4.5±1.8 to 1.8±1.7 ($p < .0001$); for PsA, mean DAS28-CRP from 3.9±1.0 to 2.0±0.8 ($p < .0001$), mean RAPID3 from 5.3±1.4 to 2.8±2.2 ($p < .0001$); for axSpA, mean ASDAS-CRP from 3.2±0.8 to 1.7±1.0 ($p < .0001$), mean BASDAI from 5.5±1.6 to 2.8±1.9, ($p < .0001$). HAQ, EQ-5D and SF-12 scores also improved significantly over 2 years. GLM was discontinued by 67 (8.9%) patients due to intolerance or adverse event (**AE**); reported AEs were consistent with GLM's known safety profile. Post-hoc multivariate analyses with patients' sociodemographic and medical history variables showed that for GLM discontinuation over the 2 years, gastrointestinal disease was a risk factor in RA [HR 3.9, CI95% (2.0-7.6)] and being female was a risk factor in axSpA [HR 1.9, CI95% (1.4-2.6)]. GLM was re-prescribed to 338 (93.4%) of 362 patients who persisted on GLM at 2 years.

Conclusion: Real-life GLM persistence is satisfactory at 2 years and is accompanied by clinical improvements in RA, PsA and axSpA patients.

Disclosure: R. Flipo, MSD, 5, Sanofi, 5; **F. Tubach**, MSD, 5; **J. Ouaniche**, MSD, 5; **P. Goupille**, AbbVie, 5, Amgen, 5, Biogaran, 5, BMS, 5, Celgene, 5, Eli Lilly, 5, Hospira, 5, Janssen-Cilag, 5, MSD, 5, Pfizer, 5, Sanofi-Genzyme, 5, UCB, 5; **E. Lespessailles**, MSD, 5; **N. Gouyette**, MSD, 3; **N. Harid**, MSD, 3; **S. Sequiera**, MSD, 9; **P. Bertin**, MSD, 5; **B. Fautrel**, AbbVie, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Boehringer Ingelheim, 8, Celgene, 5, 8, Eli Lilly and Company, 2, 5, Janssen, 5, 8, Lilly, 8, Medac, 5, 8, MSD, 2, 5, 8, NORDIC Pharma, 5, 8, Novartis, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, Sanofi-Aventis, 5, SOBI, 5, 8, UCB, 5, 8.

Abstract Number: 1432

Tapering and Discontinuing Prednisolone Without Deteriorated Disease Control by Optimizing Methotrexate in Patients with Rheumatoid Arthritis Under Stable Treatment – 2-year Results in the Real-world Clinical Practice –

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SESSION INFORMATION

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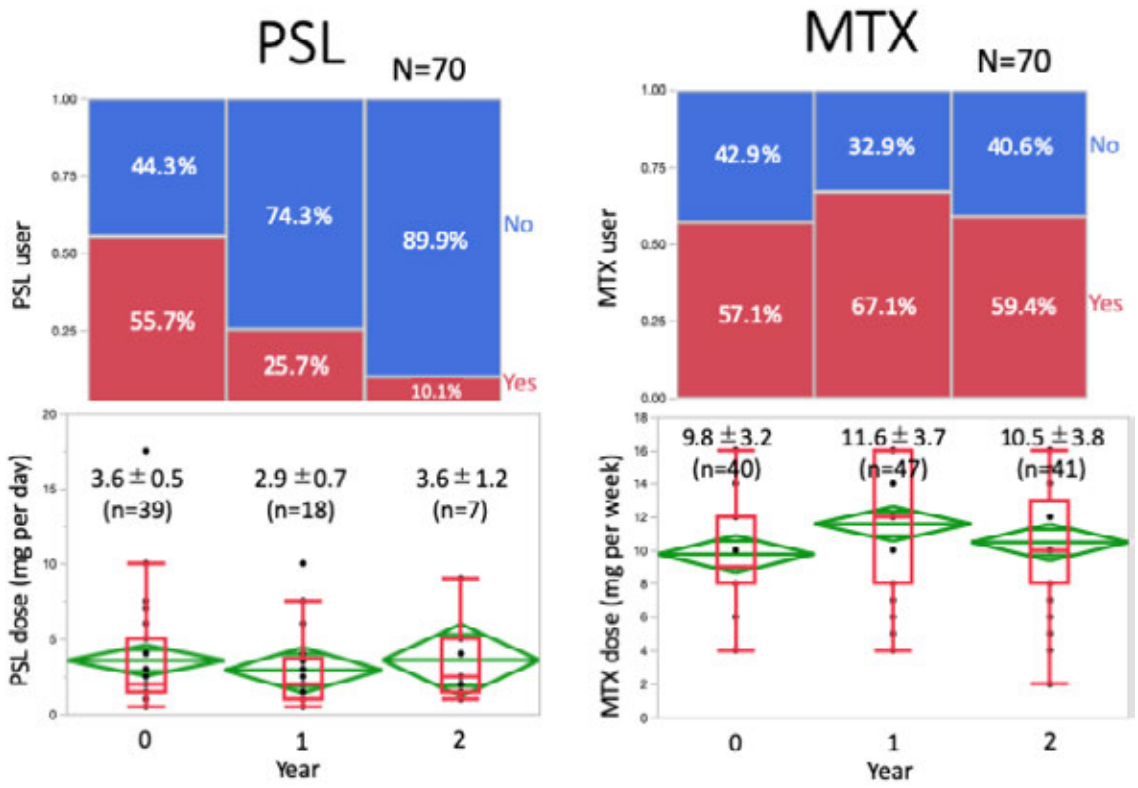


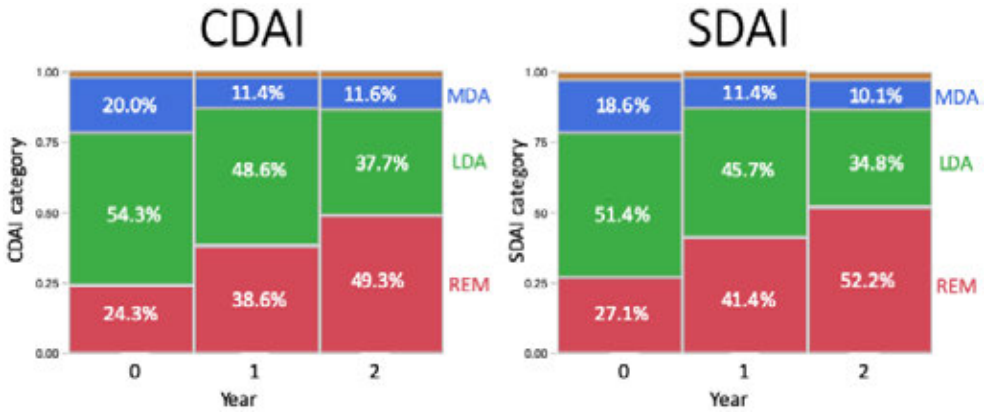
Proportion and dosage of PSL and MTX at BL, year-1, and year-2.

Background/Purpose: To determine whether prednisolone (PSL) could be tapered or discontinued without deterioration of disease control through optimizing methotrexate (MTX) for 2-yrs in patients with rheumatoid arthritis (RA) under stable treatment.

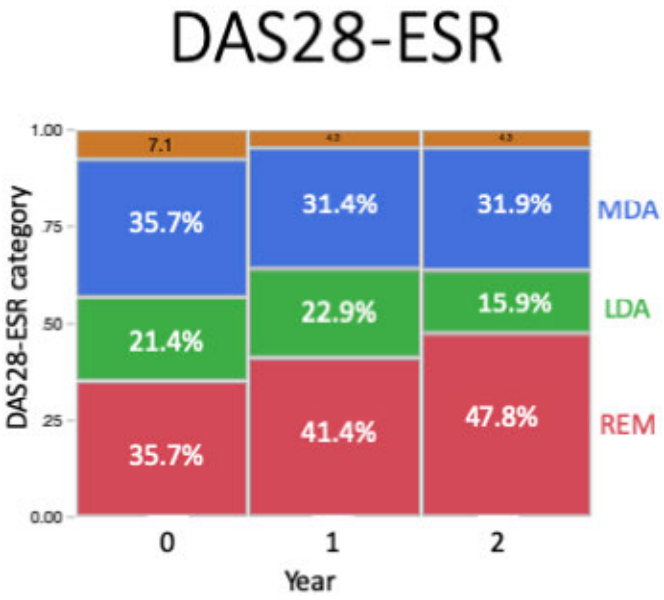
Methods: Patients with RA who fulfilled ARA 1987 criteria and/or ACR/EULAR 2010 criteria and had regularly visited our clinic for ≥1year under stable treatment were consecutively registered during Sep-Oct 2016. Clinical demographics as well as disease status and medication at baseline (BL), year-1- and -2 were collected. The basic therapeutic strategy was to increase MTX while reducing PSL as much as possible, based on patient's consent agreement. Initiation of biological DMARDs (bDMARDs) or JAK inhibitors (JAKi) was allowed if required.

Results: 70 patients were enrolled to the study. Age (median [IQR]) 62 [51, 68] years; female 69%; disease duration 6.8 [3.4, 13.7] years. Proportion of the patients using MTX at BL, 1 and 2 years were 57, 67 and 59%, respectively, while doses (mean ± SD) of MTX were 9.8 ± 3.2, 11.6 ± 3.7 and 10.5 ± 3.8 mg per week, respectively. Percentage of the patients using PSL were 56, 26 and 10%, respectively, while doses of PSL were 3.6 ± 3.4, 2.9 ± 2.6 and 3.6 ± 2.8mg per day, respectively. bDMARDs/JAKi users were 16, 18 and 26, newly initiated in 2 and 8 during BL-1-2years. CDAI / SDAI / DAS28(ESR) -remission ratio at BL, 1-year and 2-years were; 24/ 39/ 49%, 27/ 41/ 52%, and 35/ 41/ 48%, respectively. These results were consistent in patients without bDMARDs/JAKi. Severe adverse events were found in two patients (peritoneal cancer in one, myelodysplastic syndromes in one).

Conclusion: PSL was successfully discontinued in 90% of the patients by optimizing MTX with or without bDMARDs/JAKi with improved disease control in patients with RA under stable treatment. However, tapering PSL to withdrawal required more than 6 months in the majority of the patients that might delay clinical decision-making of starting bDMARDs or JAKi.



Proportion of disease activity categories in CDAI and SDAI at BL, year-1, and year-2.



Proportion of disease activity categories in DAS28-ESR at BL, year-1, and year-2.

Disclosure: S. Hirata, AbbVie, 2, 8, Astellas, 8, Ayumi, 8, Bristol-Myers Squibb, 5, 8, Chugai, 8, Eisai, 8, Eli Lilly, 2, 8, Jansen, 8, Kissei, 8, Pfizer, 8, Sanofi, 8, Takeda, 8, Tanabe-Mitsubishi, 8, UCB, 2, 5, 8; **T. Omoto**, None; **H. Kohno**, None; **H. Watanabe**, None; **K. Yukawa**, None; **T. Tokunaga**, None; **T. Kuranobu**, None; **K. Oi**, None; **Y. Yoshida**, None; **T. Sugimoto**, None; **S. Mokuda**, None; **K. Oda**, None; **T. Nojima**, None; **E. Sugiyama**, AbbVie, 2, 8, Astellas, 2, 8, Ayumi, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Eisai, 2, 8, Eli Lilly, 2, 8, Kissei, 2, 8, Pfizer, 2, 8, Sanofi,, 2, 8, Takeda, 2, Tanabe-Mitsubishi, 2, 8, Actelion, 8.

Abstract Number: 1433

Association Between Seropositivity and Discontinuation of Tumor Necrosis Factor Inhibitors Due to Insufficient Response in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
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Background/Purpose: Discontinuation of biologic therapy in rheumatoid arthritis is attributable to various reasons, with the most important cause being insufficient response. In this study, we investigated the association between rheumatoid factor (RF) and anti–citrullinated protein autoantibody (ACPA) status and the discontinuation of tumor necrosis factor inhibitors (TNFi) therapy due to ineffectiveness in bio-naïve rheumatoid arthritis (RA) patients.

Methods: This study included patients enrolled in the Tsurumai Biologic Communication Registry in Japan. The crude comparison of TNFi discontinuation due to insufficient response between seropositive and seronegative patients was analyzed using the cumulative incidence function of competing events and Gray test. We assessed the associations between baseline characteristics and discontinuation of TNFi treatment due to insufficient response using Fine-Gray proportional hazard regression. Fine-Gray proportional hazard analysis considered competing events of interest, including insufficient response, adverse event, palliation, and personal reasons.

Results: Of 1237 patients evaluated, 79.3% were positive for RF and 85.4% for ACPA; 72.6% were double positive and 11.1% were double negative. TNFi therapy had been discontinued because of insufficient response at 200 weeks in 19.8% RF-positive, 16.7% RF-negative, 23.0% ACPA-positive, and 13.8% ACPA-negative patients. There was a significantly higher discontinuation rate due to insufficient response in ACPA positive patients than in ACPA negative patients using Gray test, with a similar trend as that for RF status. RF positivity was significantly predictive of the discontinuation of TNFi treatment due to insufficient response using Fine-Gray proportional hazard regression analysis after adjusting for baseline characteristics, including age, sex, stage, class, disease activity at baseline, methotrexate use, and prednisolone use (hazard ratio 1.73 [95% confidence interval 1.07–2.80]).

Conclusion: Using Fine-Gray proportional hazard regression, we demonstrated that RF positivity was related to a higher discontinuation rate of TNFi treatment due to insufficient response in bio-naïve RA patients.

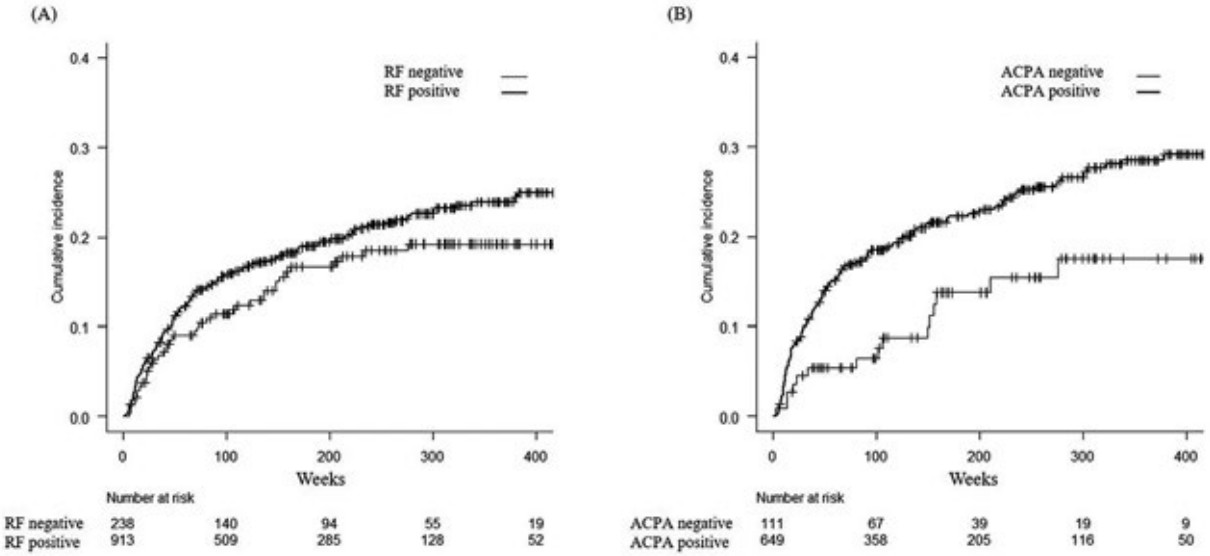

Table 1 Characteristics of RA patients at baseline by RF and ACPA status

	RF (n = 1151; 3407 patient-years)		
	RF positive (n = 913)	RF negative (n = 238)	*P*†
Age, years (SD)	56.6 (13.5)	53.1 (14.7)	<0.001
Female, no. (%)	737 (80.8)	195 (82.3)	0.64
DAS28ESR (SD)	5.28 (1.33)	4.87 (1.38)	<0.001
Stage I+II/III+IV, no. (%)	312/569 (35.4/64.6)	103/120 (46.2/53.8)	0.0032
Class I+II/III+IV, no. (%)	543/338 (61.6/38.4)	174/49 (78/22)	<0.001
Current MTX treatment, no. (%)	584 (82.7)	191 (90.1)	0.009
MTX dose, mg/week (SD) ‡	8.15 (2.60)	8.56 (2.75)	0.062
Current PSL treatment, no. (%)	383 (58.1)	98 (51.0)	0.083
PSL dose, mg/day (SD) ‡	5.22 (2.71)	4.96 (1.75)	0.37
BMI, kg/m^2 (SD)	22.0 (3.56)	21.7 (3.79)	0.32
ADA/CZP/ETN/GLM/IFX, no. (%)	133/24/467/40/244 (14.6/2.6/51.4/4.4/26.9)	37/7/95/22/77 (15.5/2.9/39.9/9.2/32.4)	0.003

Data are presented as mean, unless otherwise stated. SD: standard deviation; RA: rheumatoid arth
BMI: body mass index; ADA: adalimumab; CZP: certolizumab pegol; ETN: etanercept; GLM: g

ACPA: anti-citrullinated protein antibody; DAS28ESR: Disease Activity Score in 28 joints calcu

† Chi-square test for categorical variables and t-test for continuous variables.

‡ MTX dose and PSL dose were mean value in patients with concomitant MTX and PSL treatme

Table 2 Fine-Gray proportional hazard regression for discontinuation of

Model including RF status (n = 643)		
Variable	HR (95% CI)	*P*
RF positive	1.73 (1.07-2.80)	0.023
Age at baseline	0.98 (0.97-0.99)	0.035
Sex (referent: male)	0.89 (0.58-1.38)	0.63
Methotrexate use	1.68 (0.96-2.96)	0.069
Prednisolone use	1.20 (0.83-1.75)	0.31
Stage III + IV (referent: I + II)	0.99 (0.98-1.01)	0.97
Class III + IV (referent: I + II)	1.00 (0.98-1.02)	0.67
DAS28ESR at baseline	1.31 (1.14-1.51)	<0.001

HR: hazard ratio; 95% CI: 95% confidence interval; RF: rheumatoid fact
Disease Activity Score in 28 joints calculated with erythrocyte sedimenta

Disclosure: Y. Ogawa, None; **N. Takahashi**, Abbvie, 8, Astellas Pharma, 8, Bristol-Myers Squibb, 8, Chugai Pahrmaceutical, 8, Eisai, 8, Janssen Pharmaceutical, 8, Pfizer, 8, Takeda Pharma, 8, Tanabe Mitsubishi Pharma, 8, UCB, 8; **T. Kojima**, AbbVie, 2, 8, Abbvie, 8, Astellas, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Chugai Pahrmaceutical, 2, 8, Chugai Pharmaceutical CO., LTD., 2, 8, Daiichi-Sankyo, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Janssen Pharmaceutical, 8, Lilly, 2, 8, Mitsubishi Tanabe, 2, 8, Novartis, 2, 8, Pfizer, 2, 8, Takeda, 2, 8, Tanabe Mitsubishi Pharma, 8; **N. Ishiguro**, AbbVie, 2, 8, Abbvie, 2, 8, Asahi Kasei, 2, 8, Astellas, 2, 8, Astellas Pharma, 2, 8, Bristol-Myers Squibb, 2,

8, Chugai, 2, 8, Chugai Pahrmaceutical, 2, 8, Chugai Pharmaceutical CO.,LTD., 2, 8, Daiichi-Sankyo, 2, 8, Eisai, 2, 8, Eli Lilly, 2, 8, Janssen Pharmaceutical, 8, Kaken, 2, 8, Lilly, 8, Medical Corporation Sanjinkai, 2, 5, 8, Medical Corporation Toukoukai, 2, 5, 8, Mitsubishi Tanabe, 2, 8, Ono, 2, 8, Otsuka, 2, 8, Pfizer, 2, 8, Taisho Toyama, 2, 8, Takeda, 2, 8, Tanabe Mitsubishi Pharma, 2, 8, UCB, 8, Zimmer Biomet, 2, 8.

Abstract Number: 1434

Improvement in Matrix metalloproteinase-3 Levels at 12 Weeks Independently Predicts Achievement of Low Disease Activity at 52 Weeks in Bio-switch Patients with Rheumatoid Arthritis Treated with Abatacept

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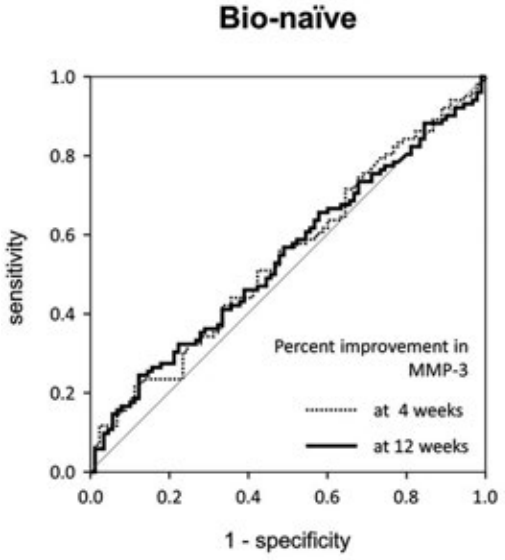
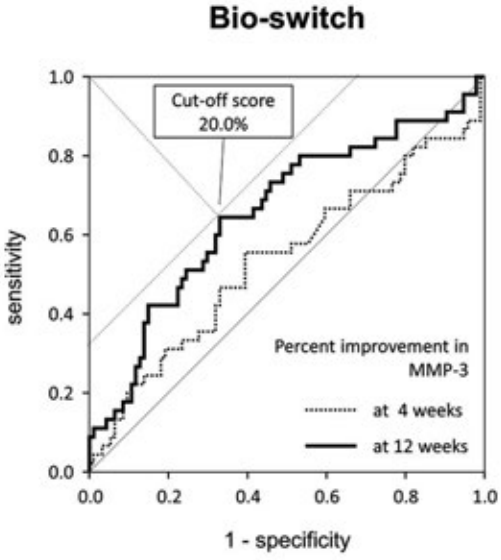
Background/Purpose: Japanese post-marketing surveillance (PMS) data demonstrated that effectiveness of abatacept in rheumatoid arthritis (RA) patients with previous biologics treatment (bio-switch) was significantly lower than that in bio-naïve patients. Useful predictive factors for good clinical response of abatacept is necessary especially in the bio-switch patients. Serum matrix metalloproteinase-3 (MMP-3) is an enzyme produced by synoviocytes which can be used to predict clinical effectiveness and joint destruction in RA patients. However, little is known about the relationship between MMP-3 and effectiveness of abatacept. This study aimed to study whether serum MMP-3 levels can predict good clinical effectiveness of abatacept in the bio-switch RA patients using data from a multicenter cohort.

Methods: Participants were consecutive 423 RA patients treated with abatacept, observed for longer than 52 weeks, and registered in the TBCR, a Japanese multicenter registry system for RA patients treated with biologics. Multivariate logistic regression analysis was used to study predictive factors for achievement of low disease activity at 52 weeks separately in bio-naïve and bio-switch group.

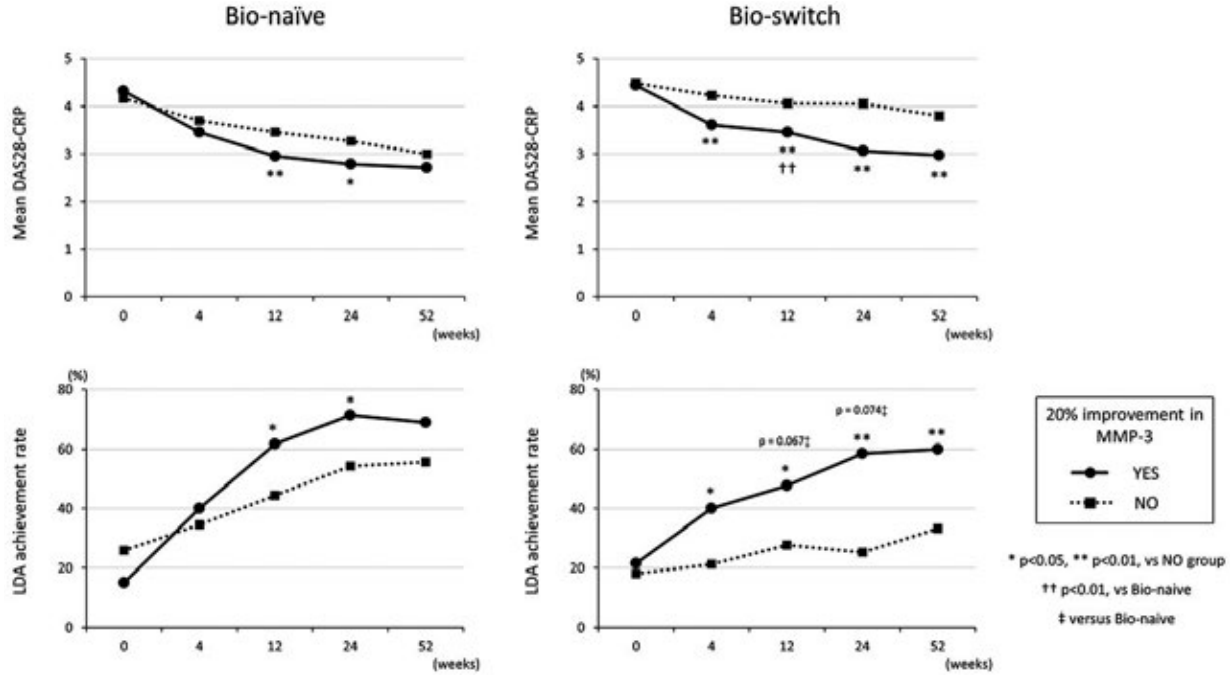
Results: A total of 189 bio-switch and 234 bio-naïve patients were included in this study. ROC analysis revealed that MMP-3 improvement rate at 12 weeks, compared to 4 and 24 weeks, had highest AUC and the best cut-off value was 20.0% at 12 weeks for predicting achievement of low disease activity (LDA) at 52 weeks in the bio-switch group (Figure 1, right panel). We performed multivariate logistic regression analysis to study independent predictive factors for LDA at 52 weeks using patients‘ background factors as well as 20% improvement of MMP-3 at 12 weeks. In the bio-naïve group, DAS28-CRP score at baseline was the only predictive factor, while the achievement of 20% improvement of MMP-3 at 12 weeks was an independent predictive factor (adjusted OR: 3.550, p=0.005) in addition to DAS28-CRP in the bio-switch group (Table). In the bio-switch group, patients that achieved 20% improvement of MMP-3 at 12 weeks demonstrated significantly higher achievement rate of LDA at 52 weeks compared to those that did not achieved 20% improvement (60.0 vs 33.3%, p=0.001) (Figure 2).





	AUC	std. Err.	95% CI
at 4 weeks	0.595	0.043	0.512-0.679
at 12 weeks	0.586	0.042	0.504-0.669

	AUC	std. Err.	95% CI
at 4 weeks	0.538	0.050	0.439-0.636
at 12 weeks	0.644	0.048	0.550-0.737



	Bio-naive		Bio-switch	
variables	adjusted OR (95% CI)	p-value	adjusted OR (95% CI)	p-value
Age	0.998 (0.962-1.035)	0.926	0.990 (0.951-1.030)	0.627
Male (vs female)	0.672 (0.289-1.566)	0.357	0.954 (0.266-3.418)	0.943
RF positive	2.117 (0.912-4.913)	0.081	0.427 (0.127-1.430)	0.167
with concomitant MTX	1.628 (0.764-3.468)	0.207	1.310 (0.522-3.289)	0.565
with concomitant PSL	0.680 (0.320-1.442)	0.314	0.580 (0.230-1.465)	0.249
DAS28-CRP @baseline	0.590 (0.413-0.844)	***0.004***	0.646 (0.449-0.930)	***0.019***
mHAQ score @baseline	0.672 (0.363-1.246)	0.207	0.588 (0.267-1.291)	0.186
20% improvement of MMP-3	1.884 (0.885-4.010)	0.100	4.277 (1.658-11.028)	***0.003***

Conclusion: In the bio-switch patients, we sometimes have difficulty to obtain good clinical response of abatacept and it would be even more important to judge whether to continue abatacept or whether to add other anti-rheumatic drugs as early as possible.

Our results suggest that improvement in MMP-3 levels at 12 weeks is key to predicting the clinical efficacy of abatacept at 1 year. It will be important to pay closer attention not only to major clinical indices such as DAS28, but also to changes in MMP-3 levels, in order to optimize clinical outcomes when treating Bio-switch patients with abatacept.

Disclosure: N. Takahashi, Abbvie, 8, Astellas Pharma, 8, Bristol-Myers Squibb, 8, Chugai Pahrmaceutical, 8, Eisai, 8, Janssen Pharmaceutical, 8, Pfizer, 8, Takeda Pharma, 8, Tanabe Mitsubishi Pharma, 8, UCB, 8; **T. Kojima**, AbbVie, 2, 8, Abbvie, 8, Astellas, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Chugai Pahrmaceutical, 2, 8, Chugai Pharmaceutical CO., LTD., 2, 8, Daiichi-Sankyo, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Janssen Pharmaceutical, 8, Lilly, 2, 8, Mitsubishi Tanabe, 2, 8, Novartis, 2, 8, Pfizer, 2, 8, Takeda, 2, 8, Tanabe Mitsubishi Pharma, 8; **K. Terabe**, None; **S. Asai**, AbbVie, 8, Abbvie, 8, Astellas, 8, Bristol-Myers Squibb, 8, Chugai, 8, Chugai Pahrmaceutical, 8, Chugai Pharmaceutical CO.,LTD., 8, Daiichi-Sankyo, 8, Eisai, 8, Janssen, 8, Janssen Pharmaceutical, 8, Pfizer, 8, Takeda, 8, Tanabe Mitsubishi Pharma, 8, UCB Japan, 8; **N. Ishiguro**, AbbVie, 2, 8, Abbvie, 2, 8, Asahi Kasei, 2, 8, Astellas, 2, 8, Astellas Pharma, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Chugai Pahrmaceutical, 2, 8, Chugai Pharmaceutical CO.,LTD., 2, 8, Daiichi-Sankyo, 2, 8, Eisai, 2, 8, Eli Lilly, 2, 8, Janssen Pharmaceutical, 8, Kaken, 2, 8, Lilly, 8, Medical Corporation Sanjinkai, 2, 5, 8, Medical Corporation Toukoukai, 2, 5, 8, Mitsubishi Tanabe, 2, 8, Ono, 2, 8, Otsuka, 2, 8, Pfizer, 2, 8, Taisho Toyama, 2, 8, Takeda, 2, 8, Tanabe Mitsubishi Pharma, 2, 8, UCB, 8, Zimmer Biomet, 2, 8.

Abstract Number: 1435

Acute Effects of IL-6 Blockade, TNFα Inhibitor or Glucocorticoids on Bone Turnover Markers and Wnt Inhibitors in Early Rheumatoid Arthritis

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SESSION INFORMATION
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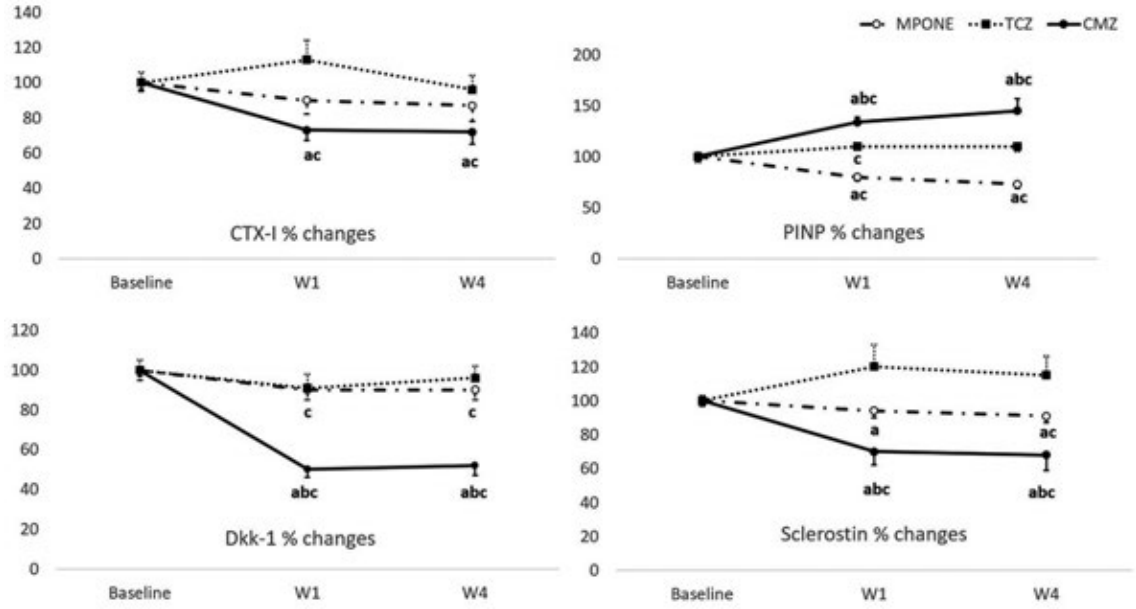

Figure 1. Bone turnover markers and Wnt inhibitors changes after 1 and 4 weeks of treatment with methyl-prednisolone (MPONE), tocilizumab (TCZ) and certolizumab pegol (CMZ)

Background/Purpose: Wnt signaling is an important regulator of bone remodeling and it is involved in the pathogenesis of focal and systemic bone loss in Rheumatoid Arthritis (RA) patients. The aim of the present study is to investigate the short-term effects of three different anti-inflammatory therapies on Wnt inhibitors and bone turnover markers (BTMs) in patients with early RA.

Methods: We performed a retrospective analysis of prospectively collected data. We enrolled women affected by early RA (< 12 months) according to 2010 ACR/EULAR criteria who started treatment with certolizumab pegol (200 mg SC weekly), tocilizumab (162 mg SC weekly) or methyl-predinsolone (8 mg daily). Women enrolled in the study were required to have positive RF and/or positive ACPA and active disease (DAS28 ≥2.6) despite stable treatment with subcutaneous methotrexate (10-15 mg/week) for at least 6 months. Clinical parameters and blood samples were collected at baseline, week 1 and week 4.

Results: Data were obtained for 14 patients treated with certolizumab pegol, 14 patients treated with tocilizumab and 20 patients treated with methyl-prednisolone. Mean DAS28 at baseline was 4.0 ± 0.7 No difference in any of the tested parameters was found at baseline. The percent changes of the serum levels of bone turnover markers, Dkk-1 and sclerostin are reported in **Figure 1**. CTX-I, Dkk-1 and sclerostin decreased abruptly after 1 week of treatment with certolizumab pegol (-27% ± 21.5%, -50% ± 13.2% and -30% ± 30.4% respectively), and similar results were found after 4 weeks. Methyl-prednisolone induced comparable changes, albeit less evident, on CTX-I and Wnt inhibitors. We found an increase in PINP serum levels after treatment with anti-TNFα, while we observed a decrease with methyl-prednisolone. Tocilizumab did not significantly affect BTMs or Wnt inhibitors.

Conclusion: TNFα inhibition seems to have a strong and quick effect on BTMs and Wnt inhibitors, which was not observed with IL-6 blockade, at least in the short-term. Glucocorticoid treatment exerts similar, though less prominent, changes, potentially linked to the suppression of inflammation, nonetheless it still show some undesired effects on bone metabolism (ie, suppression of bone formation).

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Abstract Number: 1436

Analysis of Adverse Events of Methotrexate (MTX), bDMARDs and Tofacitinib (TOFA) Reported to Pharmaceuticals and Medical Devices Agency (PMDA), Japan

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Background/Purpose: Among DMARDs (disease modifying anti-rheumatic drugs), methotrexate (MTX), bDMARDs (biologic DMARDs) and JAK (Janus kinase) inhibitors are the major. Many adverse events of these are reported to Pharmaceuticals and Medical Devices Agency (PMDA) from all over Japan and listed in the Japanese Adverse Event Report database (JADER). There have been few studies adopting on that database concerning DMARDs.

Methods: The total numbers and numbers of each adverse event related to MTX, bDMARDs, and TOFA were searched in JADER of PMDA homepage, year by year. Biologic DMARDs included those covered by Japanese Health Insurance System for Rheumatoid Arthritis: Infliximab (IFX), Etanercept (ETN), Tocilizumab (TCZ), Adalimumab (ADA), Abatacept (ABT), Golimumab (GOL), Certolizumab pegol (CZP). Conventional synthetic DMARDs other than MTX were out of search this time.

Categories of adverse events were only partially reclassified to suit the clinical entities. Adverse events searched included infectious diseases, cytopenia, pulmonary diseases, lymphoproliferative diseases, and other tumors. The

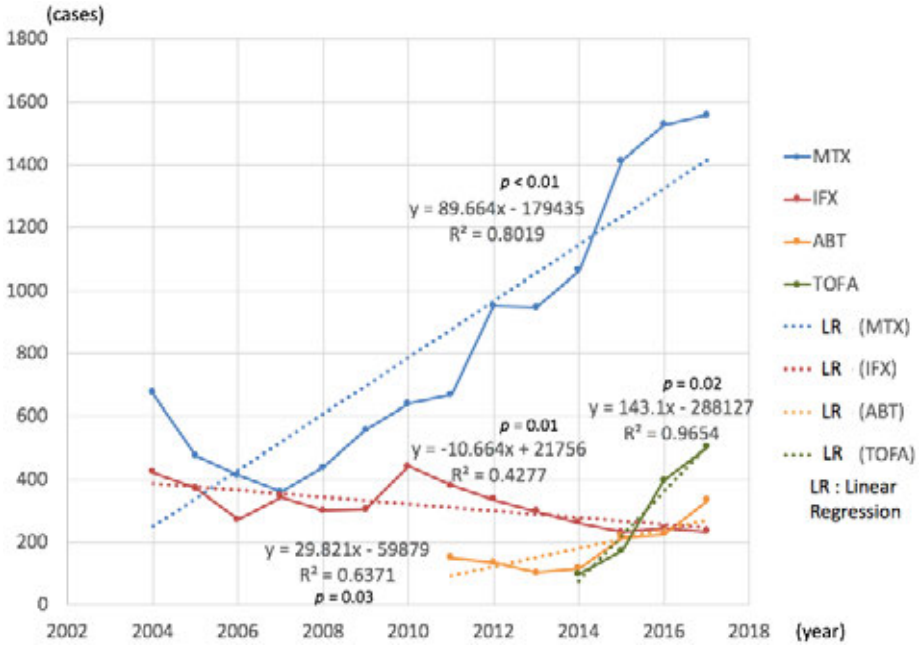

Figure 1. Total number of adverse events of DMARDs - with significant change -

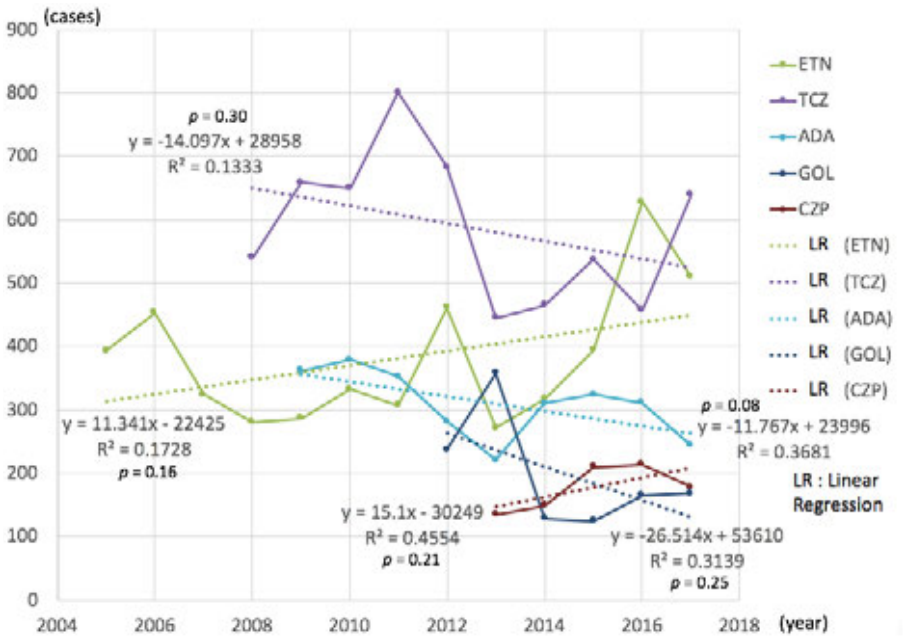

Figure 2. Total number of adverse events of bDMARDs - with no significant change -

data of the first year of introduction of the drugs were not included because of that total prescription number might have differed from that in the years afterward. Linear regression analysis was adopted, and the statistical significance was by $p < 0.05$.

Results: The total number of adverse events related to MTX has increased significantly year by year (average 90 cases per year, correlation coefficient (CC) = 0.80, $p < 0.01$) (Figure 1). As for either ABT (average 30 / year, CC = 0.64, $p = 0.03$) or TOFA (average 143 / year, CC = 0.97, $p = 0.02$), the numbers were also increased. But the numbers decreased as for IFX (average -11 / year, CC = 0.43, $p = 0.01$) by each year, whereas other DMARDs showed no significant increase or decrease (Figure 2).

For MTX, LPD (lymphoproliferative disorders) contributed most to the increase among the detailed adverse events (average 41/ year, CC = 0.85). Secondary, infections other than those specified (average 8.0 / year, CC = 0.66) and solid tumor (average 6.6 / year, CC = 0.88) contributed (Table 1).

As for ABT, solid tumor (average 4.7 / year, CC = 0.59), pneumonia (average 4.0 / year, CC = 0.59) and other infections (average 3.6 / year, CC = 0.50) were top 3. As for TOFA, other infections (average 19 / year, CC = 0.99), pneumonia (average 16 / year, CC = 0.91) and herpes zoster (average 16 / year, CC = 0.91) contributed.

IFX related adverse events were decreased, including other infections (average -4.0 / year, CC = 0.62), pneumonia (average -3.8 / year, CC = 0.81) and gastrointestinal disorder (average -2.0 / year, CC = 0.46).

Conclusion: The adverse events related to MTX, ABT, TOFA have been increasingly reported to PMDA. Among them, LPD under MTX has more and more.

	slope (cases per year)	R-squared	*p* value
Cytopenia	5.0	0.38	0.02
Gastrointestinal disorders	4.6	**0.74**	< 0.01
Pneumonia (bacterial)	2.2	0.20	0.11
Pneumocystis pneumonia	0.7	0.05	0.42
Tuberculosis	0.3	0.08	0.32
Herpes zoster	0.4	0.14	0.18
Infections other than the listed	8.0	0.66	< 0.01
Lymphoproliferative disorders	41.0	**0.85**	< 0.01
Solid tumor	6.6	**0.88**	< 0.01
Renal and urinary disorders	2.6	**0.90**	< 0.01
Interstitial pneumonitis	- 2.3	0.21	0.10
Skin and subcutaneous tissue disorders	1.3	0.43	0.01
Nervous system disorders	1.9	**0.70**	< 0.01
Injury, poisoning and procedural complications	2.7	0.68	< 0.01
Total	89.7	**0.80**	< 0.01

Table 1. Yearly increase of adverse events related to MTX - linear regression analysis -

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Comparison of the Efficacy and Safety of Abatacept in Rheumatoid Arthritis Patients with and Without Interstitial Lung Disease

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Background/Purpose: Interstitial lung disease (ILD) is one of complication in patients with rheumatoid arthritis (RA) and its presence often has an effect on the management of RA. As the presence of ILD is thought to be one of risk factors of pulmonary infection, careful attention should be needed when biological products are used for the treatment of RA with ILD. Although the usefulness of biologics in RA patients without ILD has been already shown, the utility of biologics in patients with RA complicated with ILD remains unclear. Therefore, the aim of this study is to examine differences in the efficacy and safety of biologics for RA with ILD and without ILD.

Methods: Patients with RA who fulfilled the ACR 1987 or 2010 ACR/EULAR classcication criteria and were treated with Abatacept (ABT) at Tokai University Hospital between 2009 and 2018 were enrolled. We retrospectively collected clinical information from medical records and stored computerized database. We compared the efficacy and safety between RA patients with ILD and without ILD. Both disease activities and safety were evaluated using DAS28-CRP, CDAI, SDAI, occurrence of adverse events and continuation rate of ABT at 52 weeks. Statistical analyses were performed using paired T-test, Man-Whitney test, and the log-rank test.

Results: Twenty-eight patients with RA were enrolled. Among these patients, 2 patients were excluded because of lack of data. Of these 26 patients, 15 (58%) were complicated with ILD. There were no significant differences in age, gender, disease duration, positivity of rheumatoid factor or anti-citrullinated peptide antibodies, DAS28-CRP, CDAI and SDAI score at baseline of each group. However, RA with ILD group had significantly higher rate of combination use and the dosage of PSL than RA without ILD group at baseline. DAS28-CRP, CDAI and SDAI were significantly improved after treatment at 52 weeks in both group (RA with ILD group: 3.8 vs. 2.6, $P< 0.05$; 16.4 vs. 4.4, $P< 0.001$; 15.7 vs. 4.2, $P< 0.001$, RA without ILD group: 3.6 vs. 2.1, $P=0.004$; 18.1 vs. 6.5, $P< 0.05$; 16.6 vs. 6.2, $P< 0.05$, respectively). There were no significant differences in mean % change of DAS28-CRP, CDAI and SDAI at 52 weeks between both groups (-1.5 vs. -1.9, $P=0.8$, -12.0 vs. -11.6, $P=0.8$, -11.5 vs. -10.3, $P=0.7$, respectively). There was no significant difference in the continuation rate of ABT between two groups (93.3% vs. 100%, $P=0.4$).

Conclusion: These results suggested that ABT demonstrated the same efficacy and safety in patients with RA complicated with ILD as well as RA without ILD.

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Discontinuation of Concomitant Methotrexate in Japanese Patients with Rheumatoid Arthritis Treated with Tocilizumab: An Interventional Study

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Background/Purpose: Biological DMARD (bDMARD) concomitant with methotrexate (MTX) has made great progress in the treatment of rheumatoid arthritis (RA) in these decades. There are various issues relating to safety, efficacy and economics in clinical practice during long-term therapy. Some patients discontinue MTX due to toxicity including gastrointestinal (GI) disorders. Thus, de-escalation of MTX during treatment with bDMARD while maintaining a favourable disease activity state may be beneficial treatment option from the perspective of reducing adverse events. The efficacy of tocilizumab (TCZ) has been demonstrated in monotherapy as well as with concomitant MTX, opening up the possibility of MTX discontinuation in these patients if disease control can be maintained.

This study aimed to evaluate the efficacy and safety of MTX discontinuation in RA patients with sustained low disease activity undergoing combination therapy with TCZ plus MTX.

Methods: This multicentre, open-label, uncontrolled, prospective 64-week study included RA patients maintaining low disease activity (Clinical Disease Activity Index [CDAI] ≤10) for ≥12 weeks with TCZ plus MTX. MTX was discontinued following 12 weeks of biweekly administration while continuing TCZ therapy. The rescue treatments were performed if the CDAI score was >10 and at the discretion of the investigator and/or upon patient request. The primary endpoint was the proportion of patients maintaining low disease activity with no flare at week 36 (24 weeks after MTX discontinuation). Disease flare was defined as a CDAI score >10 or intervention with the rescue treatments for any reasons. Assuming that 80% of patients would maintain low disease activity at week 36, 43 patients were calculated as necessary to prove the clinical feasibility of discontinuing MTX at a power of ≥80% with a threshold response rate of 60%. Secondary endpoints were GI symptoms (Frequency Scale for Symptoms of Gastro-oesophageal reflux disease score), physical function (HAQ-DI), and quality of life(EQ-5D).

Results: A total of 49 patients completed 36 weeks of therapy. Table 1 shows the baseline (week 0) characteristics of patients included in the efficacy analyses. The proportions (95% CI) of patients who maintained low disease activity without a flare at weeks 12, 24, and 36 were 87.8% (75.2 – 95.4%), 81.6% (68.0 – 91.2%), and 75.5% (61.1 – 86.7%), respectively (Fig. 1). The lower limit of the 95% CI at week 36 exceeded the assumed threshold response rate of 60%, demonstrating the clinical feasibility of MTX discontinuation. The prevalence of gastro-oesophageal reflux disease, defined as a Frequency Scale for Symptoms of Gastro-oesophageal reflux disease score ≥8, significantly decreased from week 0 to 12 (27.1% to 18.4%; $P = 0.025$) (Fig. 2). No significant impairment were observed in the HAQ-DI and EQ-5D from week 0 to 36 (Fig. 3).

Patient characteristics at baseline

	Total, n = 49		
Age, years	62	±	10
Female, %	84		
Weight, kg	55	±	11
Disease duration, years	11	±	8
Route of TCZ, intravenous/subcutaneous, %	65/35		
Rheumatoid factor positive, %	79		
Anticyclic citrullinated peptide positive, %	90		
MTX dose, mg/week	8.2	±	2.3
Use of glucocorticoids, %	29		
CDAI	2.7	±	2.5
CDAI ≤2.8, %	67		
CRP, mg/dl	0.04	±	0.06
HAQ-DI	0.472	±	0.613
EQ-5D	0.822	±	0.17

Data are shown as mean ± SD or percentage.

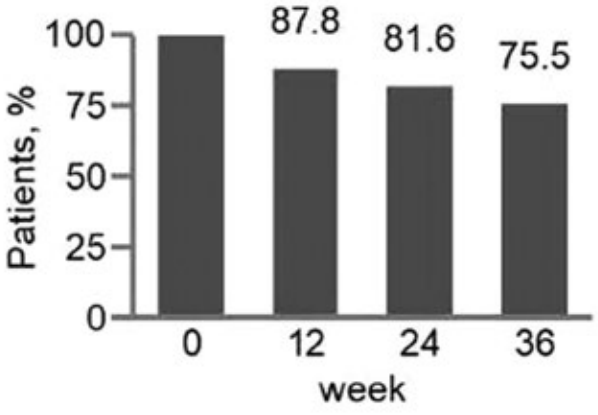

Figure 1. Proportion of patients maintaining low disease activity without a flare.

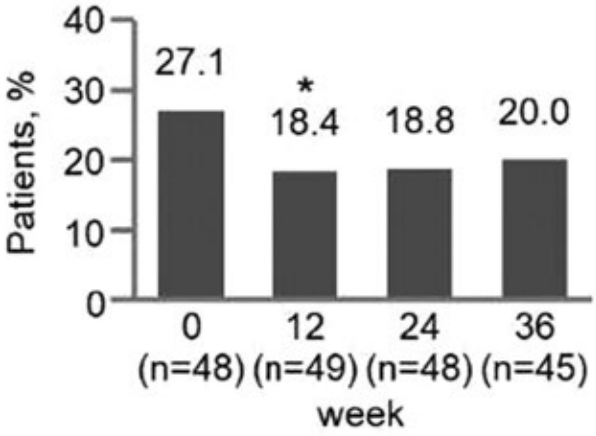

Figure 2. Prevalence of gastro-oesophageal reflux disease defined as a FSSG score ≥8. *$P < 0.05$ vs. week 0 by McNemar's test.

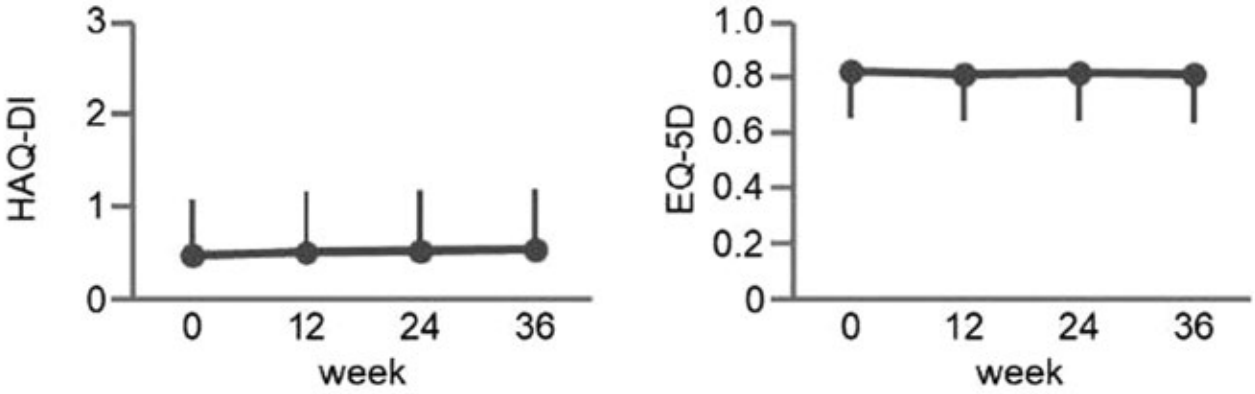

Figure 3. Changes in Health Assessment Questionnaire Disability Index (HAQ-DI) and EuroQol-5 dimension (EQ-5D) from week 0 to 36. Values represent mean (standard deviation).

Conclusion: Discontinuation of concomitant MTX is clinically feasible for maintaining low disease activity without impairment of physical function and QOL, and may be beneficial from the perspective of reducing GI symptoms in RA patients treated with TCZ.

Conflict of interest: This study was supported by grant from Chugai Pharmaceutical CO.,LTD.

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Pharma, 8; **S. Asai**, AbbVie, 8, Abbvie, 8, Astellas, 8, Bristol-Myers Squibb, 8, Chugai, 8, Chugai Pahrmaceutical, 8, Chugai Pharmaceutical CO.,LTD., 8, Daiichi-Sankyo, 8, Eisai, 8, Janssen, 8, Janssen Pharmaceutical, 8, Pfizer, 8, Takeda, 8, Tanabe Mitsubishi Pharma, 8, UCB Japan, 8; **M. Hanabayashi**, None; **M. Hayashi**, None; **N. Takahashi**, AbbVie, 8, Asahi Kasei, 8, Astellas, 8, Bristol-Myers Squibb, 8, Chugai, 8, Chugai Pharmaceutical CO.,LTD., 8, Daiichi-Sankyo, 8, Eisai, 8, Eli Lilly, 8, Janssen, 8, Mitsubishi Tanabe, 8, Ono, 8, Pfizer, 8, Takeda, 8, UCB Japan, 8; **Y. Kuwatsuka**, None; **M. Ando**, None; **N. Ishiguro**, AbbVie, 2, 8, Abbvie, 2, 8, Asahi Kasei, 2, 8, Astellas, 2, 8, Astellas Pharma, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Chugai Pahrmaceutical, 2, 8, Chugai Pharmaceutical CO.,LTD., 2, 8, Daiichi-Sankyo, 2, 8, Eisai, 2, 8, Eli Lilly, 2, 8, Janssen Pharmaceutical, 8, Kaken, 2, 8, Lilly, 8, Medical Corporation Sanjinkai, 2, 5, 8, Medical Corporation Toukoukai, 2, 5, 8, Mitsubishi Tanabe, 2, 8, Ono, 2, 8, Otsuka, 2, 8, Pfizer, 2, 8, Taisho Toyama, 2, 8, Takeda, 2, 8, Tanabe Mitsubishi Pharma, 2, 8, UCB, 8, Zimmer Biomet, 2, 8.

Abstract Number: 1439

Effect of Baricitinib on Functional Impairment in RA Patients with Moderate Disease Activity and an Inadequate Response to Conventional DMARDs

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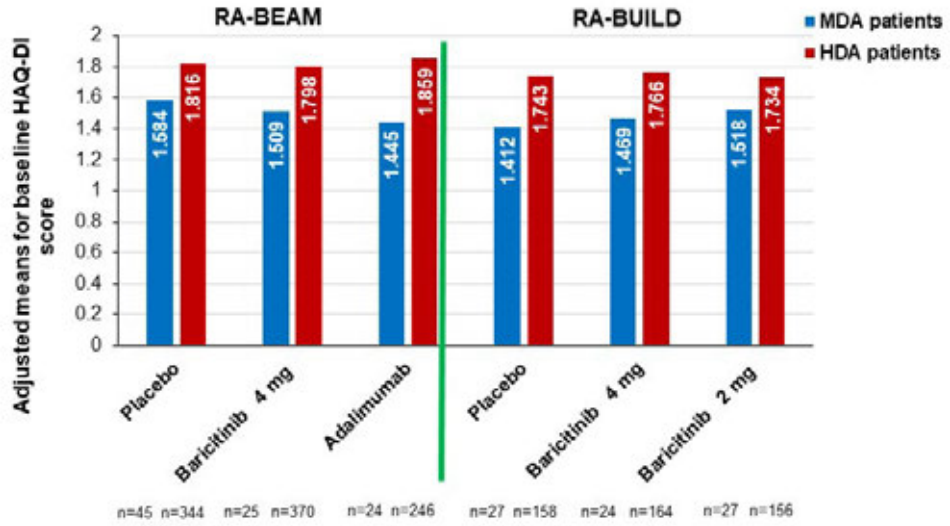
Background/Purpose: In RA, disease activity correlates with physical function[1] and there is a link between joint damage and functional disability[2]. In many countries, RA patients (pts) with inadequate response (IR) to MTX or other conventional DMARDs (cDMARDs) are not eligible for potentially more effective treatments, such as biologic or targeted synthetic DMARDs (tsDMARDs), unless they have high disease activity (HDA). Thus, managing RA pts with persistent moderate disease activity (MDA) despite cDMARD treatment poses a problem. Baricitinib (BARI) is a tsDMARD approved for the treatment of moderate to severe RA in adults. This post-hoc analysis assessed if RA pts with MDA benefit from improved physical function with BARI treatment to the same extent as pts with HDA

Methods: Pts analysed were from the modified intention-to-treat populations in the two BARI phase 3 studies RA-BEAM[3] (MTX-IR) and RA-BUILD[4] (cDMARD-IR) with moderate to severe disability (HAQ-Disability Index [HAQ-DI] score ≥1), MDA (Simplified Disease Activity Index [SDAI] score 11.1–26.0) or HDA (SDAI score >26.0) and non-missing SDAI data at baseline. All pts fulfilled ACR criteria for RA. Pts from RA-BEAM received BARI 4 mg + MTX once daily (n=396), adalimumab 40 mg every 2 weeks + MTX (n=270) or placebo (PBO) + MTX (n=390); pts from RA-BUILD received BARI 4 mg (n=189) or 2 mg (n=186) or PBO (n=185). Multivariable linear regression (MLR) models were used to estimate mean HAQ-DI scores at baseline and week (wk) 24 for the treatment arms stratified by baseline disease activity (MDA or HDA SDAI). Age, RA duration, BMI, high sensitivity CRP, baseline SDAI disease activity (MDA or HDA), treatment and treatment-by-baseline SDAI interaction were included as covariates. The MLR model for HAQ-DI at wk 24 was further adjusted by baseline HAQ-DI

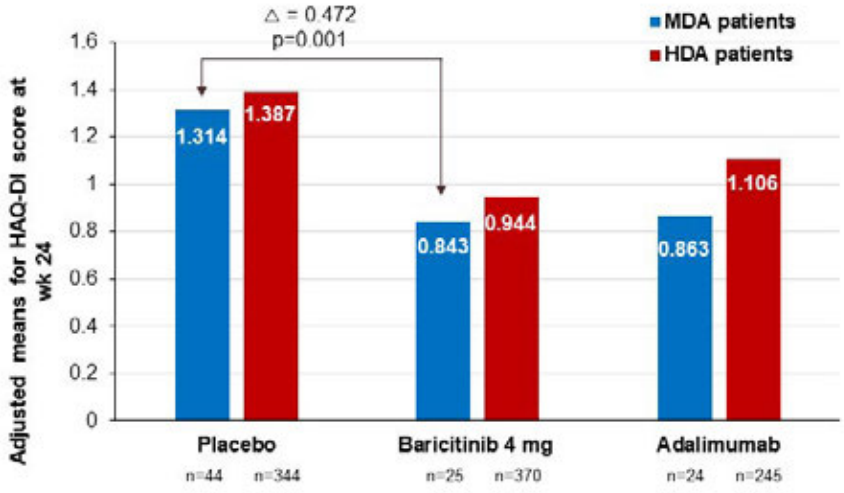
Results: Mean adjusted HAQ-DI scores at baseline were greater in pts with HDA than in those with MDA (Fig. 1). In pts from RA-BEAM with MDA at baseline, the mean adjusted HAQ-DI score at wk 24 was 0.472 points greater in PBO

Figure 1. Baseline mean adjusted HAQ-DI scores in pts from RA-BEAM and RA-BUILD with MDA or HDA



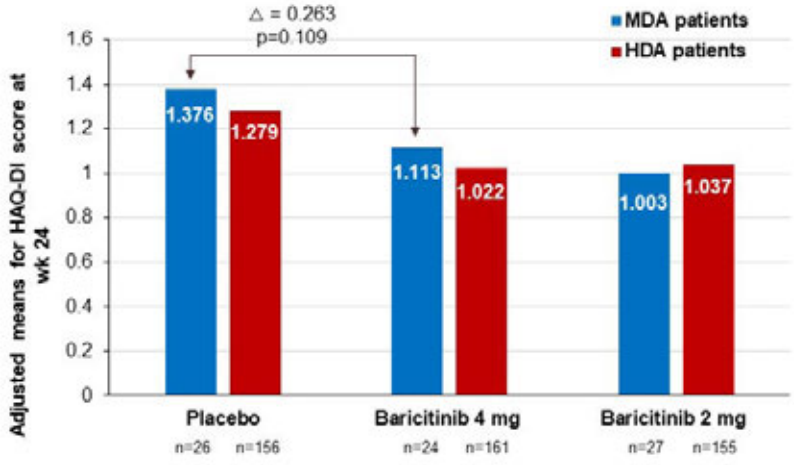
Data presented for patients with HAQ-DI ≥1 and non-missing data after MLR. Patient numbers do not match those presented in the text due to some missing data for the baseline covariates used in the MLR.
HAQ-DI, Health Assessment Questionnaire-Disability Index; HDA, high disease activity; MDA, moderate disease activity; MLR, multivariable linear regression; pts, patients.

Figure 2. Mean adjusted HAQ-DI scores at wk 24 in pts from RA-BEAM with MDA or HDA at baseline



Data presented for patients with HAQ-DI ≥1 and non-missing data after MLR. Patient numbers do not match those presented in the text due to some missing data for the baseline covariates used in the MLR.
HAQ-DI, Health Assessment Questionnaire-Disability Index; HDA, high disease activity; MDA, moderate disease activity; MLR, multivariable linear regression; pts, patients; wk, week; △, difference in HAQ-DI score.

Figure 3. Mean adjusted HAQ-DI scores at wk 24 in pts from RA-BUILD with MDA or HDA at baseline



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than in BARI 4 mg pts (Fig. 2; p=0.001). A similar pattern of improved physical function with BARI was seen in RA-BUILD, but the adjusted mean difference in HAQ-DI score between PBO and BARI 4 mg (0.263) was not statistically significant (Fig. 3; p=0.109). In pts with HDA at baseline, the mean adjusted HAQ-DI score at wk 24 was 0.443 points greater (p< 0.001) with PBO than with BARI 4 mg in RA-BEAM, and 0.257 points greater (p< 0.001) in RA-BUILD

Conclusion: MTX-IR and/or cDMARD-IR RA pts with MDA and moderate to severe disability at baseline treated with BARI show a similar pattern of improvement in physical function vs. PBO-treated pts to that seen in pts with HDA, supporting early use of BARI in MDA pts. As for those with HDA, pts with persistent MDA despite MTX and/or other cDMARD treatment could benefit from access to biologic and tsDMARDs to prevent disability progression.

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Abstract Number: 1440

Relationship Between Adalimumab Concentrations, Plasma Cytokines, Anti-drug Antibodies and Disease Activity in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Therapeutic drug monitoring (TDM) would be important if there was evidence to support the utility of measured drug concentrations in making changes to dose in order to improve drug efficacy and/or reduce toxicity. To determine the influence from variables, including patient characteristics and disease activity, on adalimumab concentrations and to assess the relationships between adalimumab concentrations, the presence of anti-drug antibodies (ADAs) and disease activity in RA.

Methods: 156 people with RA, receiving adalimumab for at least 4 months were recruited. Disease activity assessed by DAS28 with responders defined as DAS28≤3.2. Serum and plasma obtained for measurement of adalimumab concentrations and ADAs, and a panel of cytokines in a sub-group.

Results: Univariate analysis revealed a negative correlation between weight, DAS28, SJC28, TJC28, CRP, pain VAS, fatigue VAS, physicians global, duration of morning stiffness, and adalimumab concentrations. NZ Europeans, those on methotrexate, those without ADAs, and those with DAS28≤3.2 had higher adalimumab concentrations. Multivariate analysis, which included the presence of ADAs, revealed CRP ($p< 0.001$), weight ($p< 0.004$) and ethnicity ($p< 0.001$) were all independently negatively associated with adalimumab concentrations. There was a negative correlation between IL-6 and adalimumab concentrations ($r=-0.038$; $p< 0.01$). There was a negative correlation between adalimumab concentration and DAS28 ($r=-0.37$; $p< 0.0001$). Adalimumab concentrations were higher in those with DAS28 ≤3.2 compared to those with DAS28 >3.2 (median (IQR) 10.8 (6.4-20.8) mg/l vs.7.1 (1.5-12.6) mg/l; $p < 0.001$). Anti-drug antibodies were measured in the 45 participants with an adalimumab concentration < 5mg/l. 23/45 (51%) had HMSA titer >2 indicating the presence of anti-drug antibodies and of these 8/23 (34.8%) had an anti-drug antibody/adalimumab ratio ≥8AU, consistent with these being neutralizing antibodies. Adalimumab concentrations were lower in those with anti-drug antibody ratios ≥8AU compared to those with anti-drug antibody ratios < 8AU (mean (95%CI) 0.43 (0.00-1.06) vs. 1.84 (1.39-2.37) p=0.001). Adalimumab concentrations were lower in those 23 with HMSA titer >2 compared to those without ADA (mean (95%CI) 1.01 (0.00-1.56) vs. 2.47 (1.75-3.38) p=0.002).

Conclusion: Adalimumab concentration correlates negatively with markers of inflammatory disease activity in RA. Adalimumab concentration in the range 5 to 7 mg/l detected in serum are associated with better inflammatory disease control. Very low drug concentrations (< 5mg/l) are associated with the detection of anti-drug antibodies. These associations are consistent with the hypothesis that achieving an adequate serum adalimumab concentration is important for disease control and that the presence of ADA may be one mechanisms important in drug resistance.

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Abstract Number: 1441

Is Background Methotrexate Still Advantageous in Extending TNF Drug Survival in the Elderly: An Analysis of the British Society for Rheumatology Biologics Register – Rheumatoid Arthritis

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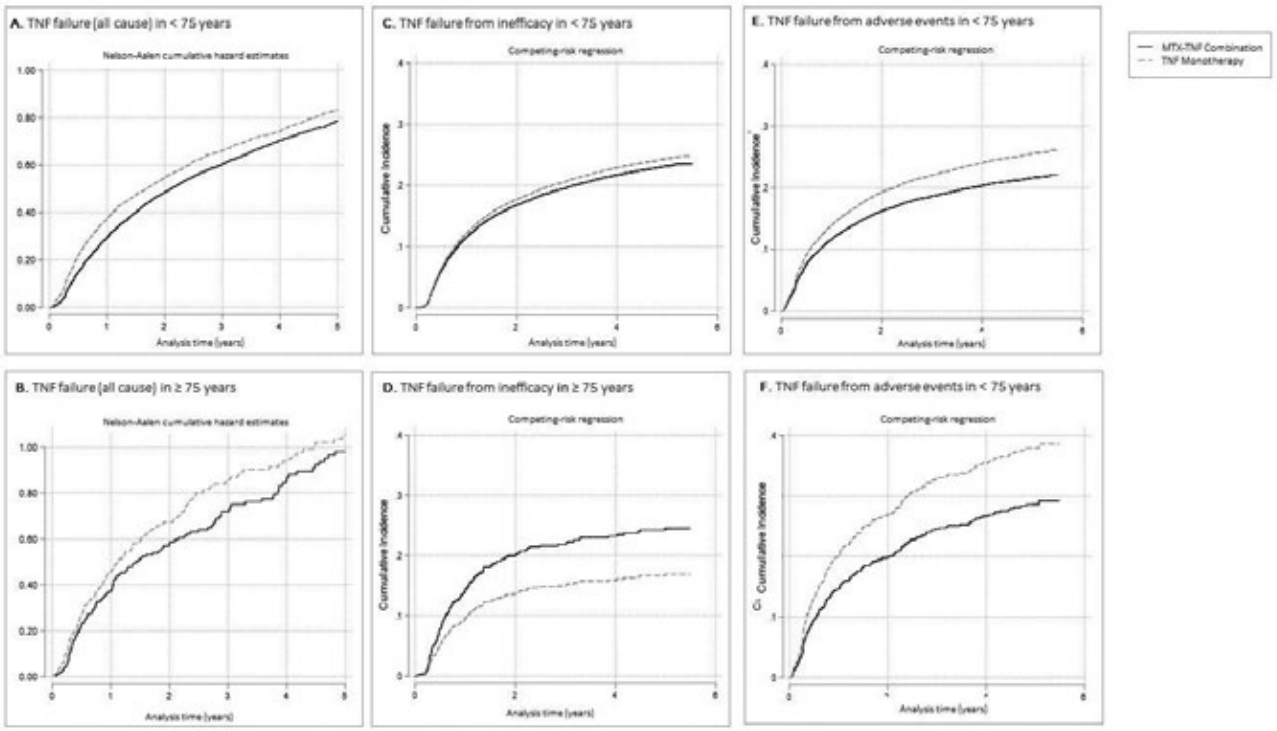
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Long-term observational data from national registries in rheumatoid arthritis allow the examination of TNF drug survival rates. Despite a good initial response to a TNF inhibitor, efficacy can wane over time. Secondary failure may result from the formation of antidrug antibodies (ADA). Concomitant immunosuppression with methotrexate increases TNF inhibitor concentrations via the suppression of ADAs, prolonging TNF drug survival [1]. It is plausible that the production of ADA is less robust in elderly adults, as the aging immune system undergoes a gradual process of decline, termed immunosenescence. This may eliminate the need for concomitant immunosuppression with methotrexate. The objective of this study was to evaluate drug survival with TNF monotherapy compared to combination therapy with methotrexate in rheumatoid arthritis older adults (≥75 years).

Methods: Patients from the British Society for Rheumatology Biologics Register (BSRBR-RA), a prospective observational cohort study, who were biologic naïve and commencing their first TNF inhibitors were included in the analysis. The cohort was stratified according to age at registration: < 75 and ≥75 years. Cox proportional hazards were generated to compare the risk of TNF discontinuation between patients prescribed TNF monotherapy compared to TNF-methotrexate combination. Three models were developed evaluating treatment discontinuation; 1) any cause 2) inefficacy and 3) adverse events. Propensity score models were used to address confounding by indication.

Results: The analysis included 15,700 patients, of which 14, 932 (95%) were < 75 years old. Comorbidity burden and RA disease activity were higher in the ≥75 cohort. Fifty two percent of patients discontinued TNF therapy during the follow up period. Persistence with therapy was higher in the < 75 cohort. Patients receiving TNF monotherapy were more likely to discontinue compared to patients receiving concomitant methotrexate [hazard rate (HR) 1.12 (1.06-1.18) p=< 0.001]. This finding only held true in patients in the < 75 cohort. Examining TNF discontinuation by cause revealed patients ≥75 receiving TNF monotherapy were less likely to discontinue TNF due to inefficacy [HR 0.66 (0.43-0.99) p=0.04] and more likely to discontinue therapy from adverse events [HR 1.21 (1.11-1.32) p< 0.001] (figure 1). These results were supported by the propensity score analyses.

Conclusion: TNF monotherapy is associated with an increase in treatment failure. In the older adults the disadvantage of TNF monotherapy on drug survival is no longer seen. Patients over 75 have fewer discontinuations due to inefficacy compared to younger patients. We speculate that this may reflect a decline in immunogenicity associated with immunosenescence.



Reference:

1. Kalden JR, Schulze-Koops H. Immunogenicity and loss of response to TNF inhibitors: implications for rheumatoid arthritis treatment. Nature reviews Rheumatology. 2017;13(12):707-718.

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Abstract Number: 1442

Comparison of Sustained Clinical Remission And/or Low Disease Activity Rate Between Rapidly and Gradually De-escalation of Abatacept in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: However biological DMARDs (bDMARDs) and treatment strategies have improved the outcomes of rheumatoid arthritis (RA), it is unknown who can taper or stop bDMARDs and strategies for de-escalation.

We analyze predictors of tapering of withdrawal failure in rheumatoid arthritis (RA) patients treated with abatacept. This study will assess and compare (1) characteristic of patients who achieve remission (REM) or low disease activity

(LDA) as who can taper abatacept and (2) two de-escalation methods, rapidly and gradually de-escalation in patients who respond first-line therapy.

Methods: Cases were recruited to SHin-yokohama Arthritis REgister (SHARE) between 2015 and 2019 (n=3,674). Patients were diagnosed according to ACR/EULAR 2010 classification criteria, and treated with DMARDs which included abatacept (n=248). In 248 (Male24, Female224 cases, RA duration 11.3+/-8.0 years, CDAI 24.5+/-14.7) cases, Clinical Disease Activity Index (CDAI) , Health Assessment Questionnarie-Disability Index (HAQ-DI), anti-CCP2 and patients clinical parameters were analyzed. Two de-escalation methods were compared in this study. In rapidly de-escalation methods, abatacept were decreased to half dose in patients with stable REM/LDA over 12 weeks. In gradually de-escalation methods, abatacept were decreased to 75%, 50%, 33%, 25%, 20%, 17%, 14%, 12.5% in order with stable REM/LDA over 12 weeks.

Results: Of 248 patients, 161 patients (73.2%) were achieved to REM and/or LDA within 6 months after using abatacept.

(1) Multivariate logistic regression examined the predictors to detect who can taper abatacept. Higher anti-CCP2 titer patients were correlate with patients who achieve remission (REM) or low disease activity (LDA) in patients treated with abatacept (OR 0.99, 95%CI 0.994-0.999, p=0.0016). ROC analysis of anti-CCP2 showed cut-off value of 84.5 U/ml with the area under the curve was 0.7633. (2) Comparison of sustained REM and/or LDA rate between rapidly and gradually de-escalation methods of abatacept in rheumatoid arthritis. 11 cases were tapered abatacept with rapidly de-escalation method and 88 patients were with gradually de-escalation method. Gradually de-escalation method showed less relapse rate tapered abatacept after 6 months (6.8% vs. 63.6%, p< 0.0001) and showed less swollen joints (0.1+/10.6 joints vs. 0.4+/-0.7 joints, p=0.004) compared with rapidly de-escalation method. (3) Sustained REM and/or LDA rate after tapered abatacept using gradually de-escalation method were 63.4% in 12 months and 82.7% in 24 months.

Conclusion: A combination of high anti-CCP2 titer and tapering abatacept using gradually de-escalation method may help to predict successful abatacept deduction in RA patients with sustained clinical REM and/or LDA.

Disclosure: M. Yamasaki, None.

Abstract Number: 1443

Real World Switching Patterns of Etanercept Original and Biosilmilar in Germany

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: We have previously evaluated switching dynamics between etanercept biologic original (EtnBO) and etanercept biosimilars (EtnBS) over approximately 18 months following the first EtnBS launch in Germany (February 2016). As new data has become available, analysis was repeated over longer time-periods.

Methods: Patients receiving their first EtnBS prescription in February 2016-October 2018 were retrospectively identified in the German Longitudinal Prescriptions database (IQVIA® LRx, January 2008-October 2018). The proportion, mean age and gender of patients previously treated with EtnBO was determined using a 12-month lookback period. For these patients, the proportions of those switching to other biologics and of those switching back to EtnBO were evaluated, along with mean age, gender and median time to switch-back. The analysis was performed separately for patients initiating EtnBS in three consecutive 11-month time-periods from EtnBS launch: February 2016-December 2016 (period 1), January 2017-November 2017 (period 2), and December 2017-October 2018 (period 3).

Results: Of 16,543 identified patients (56 years, 34% males) initiating EtnBS, 4,471 (27%) had prior EtnBO (56 year, 38% males): 1,311 in period 1, 1,683 in period 2 and 1,653 in period 3. After initiation, the proportion of patients who switched from EtnBS to other biologics in period 1, 2 and 3 respectively was 186 (14%), 187 (11%) and 71 (4%) and of those who switched back to EtnBO was 278 (21%), 381 (23%) and 278 (17%). The median time to switch-back was similar across the 3 periods (3-4 months), as was the age and gender distribution across the different patient groups.

Conclusion: This study confirms previous findings on switching dynamics between EtnBO and its biosimilars and shows that approximately a fifth of patients in the entire study period switch back to EtnBO after 3-4 months from EtnBS initiation. Future research should explore factors influencing switching dynamics.

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Abstract Number: 1444

Tofacitinib in Patients with Rheumatoid Arthritis and Indicative of Depression And/or Anxiety: A Post Hoc Analysis of Phase 3 and Phase 3b/4 Clinical Trials

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Depression and anxiety are common in patients (pts) with RA[1] and can lead to reduced quality of life, functional capacity, and RA treatment response.[2-4] Elevated IL-6 levels have been associated with depressive symptoms in pts with RA.[5] The 36-Item Short Form Health Survey (SF-36) Mental Component Summary score (MCS) ≤ 38 has been used as an identifier of probable major depressive disorder (pMDD) and/or probable generalized anxiety disorder (pGAD) in pts with RA.[6] Tofacitinib is an oral JAK inhibitor for the treatment of RA. We assessed the prevalence of pMDD and/or pGAD by SF-36 MCS ≤ 38 status in tofacitinib clinical trials for RA, and tofacitinib efficacy by baseline (BL) pMDD and/or pGAD status.

Methods: In this post hoc analysis, data were pooled from 5 Phase (P)3 trials and 1 P3b/4 trial. Pts receiving tofacitinib 5 or 10 mg BID, adalimumab 40 mg every other week (ADA), or placebo (PBO), with a non-missing BL SF-36 MCS, were included. Demographics and BL disease characteristics were reported by BL pMDD and/or pGAD status (SF-36 MCS ≤ 38 [presence] or > 38 [absence]). At Months (M)3/6/9/12: SF-36 MCS change from BL (Δ) was estimated by modeling of pooled data, and the % of pts with pMDD and/or pGAD was reported. Efficacy endpoints were estimated at M3/6/12 by linear models, comparing tofacitinib-treated pts by BL pMDD and/or pGAD status.

Results: BL pMDD and/or pGAD were reported in 44.5%, 39.8%, 45.4%, and 39.1% of pts receiving tofacitinib 5 mg BID, tofacitinib 10 mg BID, ADA, and PBO, respectively. At BL, higher CRP levels and worse disability, fatigue, pain, and sleep were reported in pts with pMDD and/or pGAD vs those without (Table 1). A numerically, and sometimes significantly ($p < 0.05$), greater increase in SF-36 MCS was reported in pts receiving tofacitinib vs PBO or ADA (Figure 1a). The % of pts with BL pMDD and/or pGAD who continued to have pMDD and/or pGAD reduced over time,

Table 1. Demographics and baseline disease characteristics, stratified by treatment group and baseline pMDD and/or pGAD status (SF-36 MCS ≤38 or >38)

	SF-36 MCS ≤38 (baseline pMDD and/or pGAD)				SF-36 MCS >38 (no baseline pMDD and/or pGAD)				Overall			
	Tofacitinib 5 mg BID (N=870)	Tofacitinib 10 mg BID (N=477)	Adalimumab 40 mg Q2W (N=264)	Placebo (N=263)	Tofacitinib 5 mg BID (N=1083)	Tofacitinib 10 mg BID (N=721)	Adalimumab 40 mg Q2W (N=317)	Placebo (N=409)	Tofacitinib 5 mg BID (N=1953)	Tofacitinib 10 mg BID (N=1198)	Adalimumab 40 mg Q2W (N=581)	Placebo (N=672)
Age, mean (SD)	51.5 (12.0)	51.4 (11.5)	50.3 (12.8)	52.9 (11.5)	52.2 (12.4)	53.3 (11.7)	52.2 (12.8)	52.2 (12.3)	51.9 (12.2)	52.5 (11.6)	51.3 (12.8)	52.5 (12.0)
Female, n (%)	756 (86.9)	422 (88.5)	224 (84.8)	220 (83.7)	880 (81.3)	592 (82.1)	249 (78.5)	325 (79.5)	1636 (83.8)	1014 (84.6)	473 (81.4)	545 (81.1)
Anti-anxiety or anti-depressant medication use on Day 1, n (%)	64 (7.4)	37 (7.8)	11 (4.2)	25 (9.5)	53 (4.9)	44 (6.1)	16 (5.1)	19 (4.7)	117 (6.0)	81 (6.8)	27 (4.7)	44 (6.6)
HAQ-DI, mean (SD)	1.7 (0.6)	1.7 (0.6)	1.7 (0.6)	1.7 (0.6)	1.3 (0.7)	1.3 (0.7)	1.4 (0.6)	1.3 (0.7)	1.5 (0.7)	1.5 (0.7)	1.5 (0.6)	1.4 (0.7)
CRP (mg/L), mean (SD)	19.2 (24.3)	19.4 (27.2)	19.1 (25.1)	17.5 (18.7)	16.6 (19.6)	16.2 (18.7)	15.1 (18.4)	15.1 (19.1)	17.7 (21.8)	17.5 (22.5)	16.9 (21.8)	16.0 (19.0)
FACIT-F, mean (SD)	21.4 (8.8)	22.1 (8.9)	21.4 (8.6)	22.9 (9.3)	32.8 (9.0)	33.2 (9.2)	32.3 (8.7)	33.2 (9.5)	27.7 (10.6)	28.8 (10.6)	27.4 (10.2)	29.1 (10.6)
Pain (VAS), mean (SD)	66.9 (21.3)	66.2 (20.5)	64.4 (21.8)	66.1 (21.6)	54.6 (22.1)	54.6 (23.6)	54.8 (22.0)	52.6 (22.0)	60.1 (22.6)	59.2 (23.1)	59.1 (22.4)	57.8 (22.9)
MOS sleep score, mean (SD)	51.6 (18.7)	50.8 (18.1)	53.8 (15.9)	51.4 (19.2)	34.7 (17.8)	35.1 (17.4)	34.5 (17.9)	36.0 (17.9)	41.7 (20.0)	41.3 (19.2)	43.2 (19.5)	42.0 (19.9)
SF-36 PCS, mean (SD)	31.6 (6.8)	31.9 (6.1)	31.5 (6.9)	31.6 (6.7)	32.7 (8.4)	32.8 (8.5)	32.6 (7.5)	33.2 (8.6)	32.2 (7.8)	32.5 (7.6)	32.1 (7.2)	32.6 (7.9)
SF-36 MCS, mean (SD)	29.8 (6.4)	30.3 (6.1)	30.1 (6.1)	30.1 (6.3)	48.7 (7.6)	49.4 (7.6)	48.4 (7.6)	49.5 (7.7)	40.3 (11.8)	41.8 (11.7)	40.1 (11.5)	41.9 (11.9)

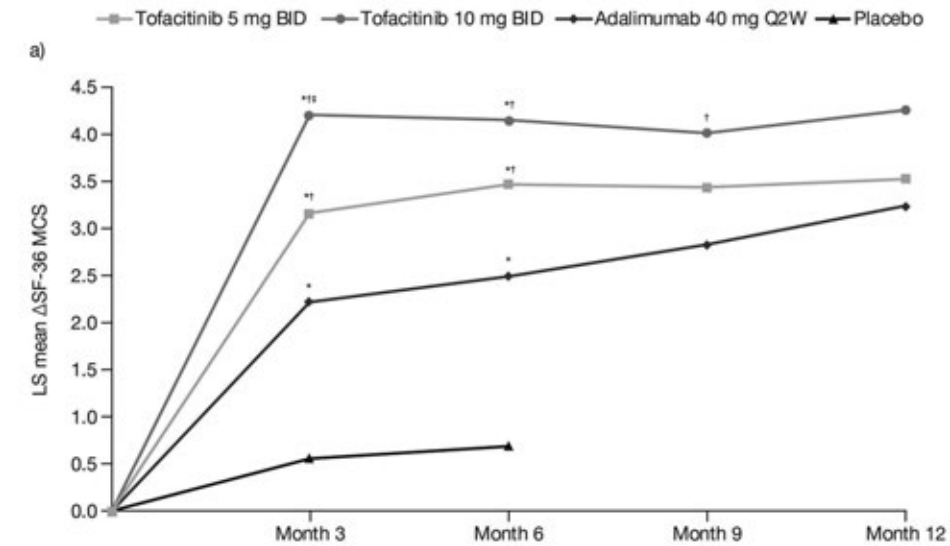
Data were pooled from 5 Phase 3 trials and 1 Phase 3b/4 trial of tofacitinib in RA

Results are presented descriptively; no modeling was performed

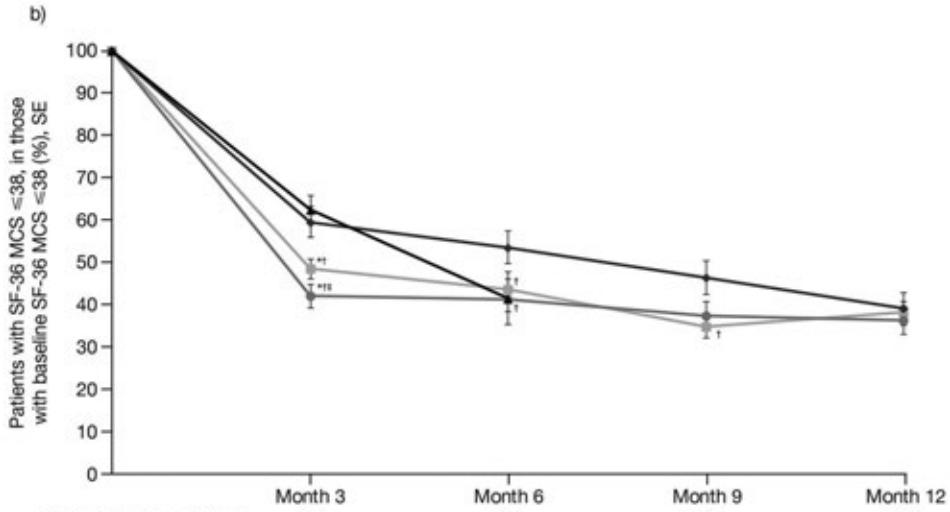
N for each assessment may differ from N for each treatment group

BID, twice daily; CRP, C-reactive protein; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCS, Mental Component Summary score; MOS, Medical Outcomes Study; PCS, Physical Component Summary score; pGAD, probable generalized anxiety disorder; pMDD, probable major depressive disorder; Q2W, every other week; RA, rheumatoid arthritis; SD, standard deviation; SF-36, Short Form-36 health survey; VAS, visual analog scale

Figure 1. a) ΔSF-36 MCS at Month 3, 6, 9, and 12; b) percentage of patients with pMDD and/or pGAD (SF-36 MCS ≤38) over time, in those with baseline pMDD and/or pGAD (SF-36 MCS ≤38)



	Month 3	Month 6	Month 9	Month 12
Tofacitinib 5 mg BID, N	1847	1762	1075	1284
Tofacitinib 10 mg BID, N	1122	1056	443	663
Adalimumab 40 mg Q2W, N	557	526	499	469
Placebo, N	611	175		



	Month 3	Month 6	Month 9	Month 12
Tofacitinib 5 mg BID, N	870	870	723	723
Tofacitinib 10 mg BID, N	477	477	341	341
Adalimumab 40 mg Q2W, N	264	264	264	264
Placebo, N	263	76		

*p<0.05 vs placebo; †p<0.05 vs adalimumab; ‡p<0.05 vs tofacitinib 5 mg BID in a) difference in LS mean and b) OR (not shown)
Data were pooled from 5 Phase 3 trials and 1 Phase 3b/4 trial of tofacitinib in RA
Δ, change from baseline; BID, twice daily; LS, least squares; MCS, Mental Component Summary score; N, number of evaluable patients; OR, odds ratio; pGAD, probable generalized anxiety disorder; pMDD, probable major depressive disorder; Q2W, every other week; RA, rheumatoid arthritis; SE, standard error; SF-36, Short Form-36 health survey

and was generally lower in pts receiving tofacitinib vs PBO or ADA (Figure 1b). In tofacitinib-treated pts, efficacy was generally similar regardless of BL pMDD and/or pGAD status (Table 2).

Conclusion: In this post hoc analysis, around 40% of pts with RA had BL pMDD and/or pGAD identified by SF-36 MCS ≤ 38. Improvement in SF-36 MCS was greater in pts receiving tofacitinib vs ADA or PBO. In tofacitinib-treated

Table 2. Comparison of efficacy endpoints at Month 3, 6, and 12, between tofacitinib-treated patients by baseline pMDD and/or pGAD status (SF-36 MCS ≤38 vs >38[a])

	Tofacitinib 5 mg BID				Tofacitinib 10 mg BID			
	SF-36 MCS ≤38	SF-36 MCS >38	OR (95% CI)	P value	SF-36 MCS ≤38	SF-36 MCS >38	OR (95% CI)	P value
ACR20 response rate (%)[b]								
Month 3	55.1	57.9	0.89 (0.74, 1.08)	0.2330	62.7	64.5	0.93 (0.73, 1.18)	0.5427
Month 6	61.7	62.8	0.96 (0.79, 1.16)	0.6511	67.5	67.4	1.00 (0.78, 1.28)	0.9929
Month 12	58.4	58.6	0.99 (0.80, 1.22)	0.9279	62.2	59.0	1.15 (0.86, 1.54)	0.3580
ACR50 response rate (%)[b]								
Month 3	25.9	29.2	0.85 (0.70, 1.03)	0.1022	30.0	33.9	0.83 (0.65, 1.07)	0.1561
Month 6	36.0	38.0	0.92 (0.76, 1.11)	0.3724	42.9	41.7	1.05 (0.83, 1.33)	0.6868
Month 12	33.8	34.3	0.98 (0.80, 1.20)	0.8366	37.3	39.8	0.90 (0.68, 1.20)	0.4735
ACR70 response rate (%)[b]								
Month 3	10.1	11.0	0.91 (0.69, 1.18)	0.4704	14.6	14.9	0.98 (0.71, 1.35)	0.8931
Month 6	16.5	16.5	1.00 (0.79, 1.26)	0.9901	22.4	21.6	1.05 (0.79, 1.39)	0.7476
Month 12	18.3	17.5	1.06 (0.83, 1.34)	0.6560	21.5	23.8	0.87 (0.64, 1.20)	0.4128
DAS28-4(ESR) remission (<2.6) rate (%)[b]								
Month 3	5.38	7.35	0.72 (0.49, 1.05)	0.0872	10.1	9.84	1.02 (0.68, 1.55)	0.9084
Month 6	5.90	8.46	0.68 (0.49, 0.94)	0.0199*	11.8	13.6	0.85 (0.60, 1.21)	0.3573
Month 12	7.99	11.9	0.64 (0.47, 0.89)	0.0073**	9.42	14.4	0.62 (0.40, 0.95)	0.0268*
ΔHAQ-DI, LS mean[c]	**SF-36 MCS ≤38**	**SF-36 MCS >38**	**Difference (95% CI)**	**P value**	**SF-36 MCS ≤38**	**SF-36 MCS >38**	**Difference (95% CI)**	**P value**
Month 3	-0.41	-0.43	0.01 (-0.04, 0.06)	0.6008	-0.48	-0.52	0.04 (-0.03, 0.10)	0.2576
Month 6	-0.49	-0.48	-0.01 (-0.06, 0.04)	0.6617	-0.57	-0.58	0.01 (-0.06, 0.07)	0.7793
Month 12	-0.52	-0.52	-0.01 (-0.06, 0.05)	0.8475	-0.60	-0.61	0.01 (-0.07, 0.08)	0.8842

*p<0.05; **p<0.01

Data were pooled from 5 Phase 3 trials and 1 Phase 3b/4 trial of tofacitinib in RA

[a]Baseline pMDD and/or pGAD was defined by SF-36 MCS ≤38

[b]Logistic regression models were fit by month. The models included fixed effects of treatment (including placebo and adalimumab), baseline 'pMDD and/or pGAD' status (MCS ≤ or >38), treatment-by-baseline-status interaction, study (ORAL Scan, Solo, Sync, Standard, Step, Strategy), geographic region (US, EU/Canada, Latin America, other), and anti-depressant/anti-anxiety medication use on Day 1 (yes or no). Missing responses were imputed as failures. For patients randomized to a placebo sequence in a study where they may have advanced to tofacitinib post Month 3, only placebo observations were included in the model

[c]A mixed-effects linear model was fit applying the same effects as in the logistic regression models, except: the model was longitudinal and included the effect of month (3, 6, 9, and 12) as a main effect, and two- and three-way interactions involving month, treatment, and baseline status, along with baseline value of the dependent variable. Patients were included as a random effect and compound symmetry was used to model covariance. Missing data due to 'missing at random' were implicitly imputed by this modeling approach

Δ, change from baseline; ACR, American College of Rheumatology; BID, twice daily; CI, confidence intervals; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; LS, least squares; MCS, Mental Component Summary score; OR, odds ratio; pGAD, probable generalized anxiety disorder; pMDD, probable major depressive disorder; Q2W, every other week; RA, rheumatoid arthritis; SF-36, Short Form-36 health survey

pts, the % with SF-36 MCS ≤ 38 (ie identified as having pMDD and/or pGAD) reduced by around 60% at M12. Tofacitinib efficacy was similar in those with and without BL pMDD and/or pGAD (identified using SF-36 MCS). Limitations include using SF-36 MCS to identify probable rather than confirmed MDD or GAD. Future research is required to replicate the findings of this study using a gold-standard psychiatric interview against which to validate the use of SF-36 MCS ≤ 38.

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Abstract Number: 1445

Pre-Biologic Use of Janus Kinase Inhibitors for the Treatment of Rheumatoid Arthritis in the United States

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Tofacitinib was the first Janus kinase (JAK) inhibitor FDA approved for the treatment of RA in November 2012, five- and one-half years later, baricitinib, also received approval. The oral delivery of JAKs make them particularly appealing treatment options for patients with moderate to severe disease, however, many patients still receive a TNF-α-inhibitor in the first-line biologic/JAK treatment setting. With two JAKs available and several JAK entities in clinical development, it is important to understand how US rheumatologists are prescribing these agents in relation to biologics, why patients typically discontinue first-line JAK treatment, and how likely rheumatologists are to prescribe consecutive JAK inhibitors to their RA patients.

Methods: An independent market analytics firm collaborated with US rheumatologists (n=101) to conduct analysis of the RA Market. Data were collected via an online survey fielded in May 2019 and included physician demographics and attitudinal survey responses.

Results: US Rheumatologists estimate that half of their biologic/JAK-treated RA patients are on a first-line agent. Despite increased advanced treatment options available, TNF-α-inhibitors continue to dominate first-line advanced systemic therapy, with rheumatologists reporting 79% are prescribed a TNF-α-inhibitor prior to JAKs or other biologics. Just 8% are treated with a JAK-inhibitor prior to biologic therapy, though use does significantly increase with each consecutive line of therapy, and 18% and 26% of all second- and third-line biologic/JAK-treated RA patients, respectively, are prescribed either tofacitinib or baricitinib. The most common reasons for pre-biologic JAK discontinuation include primary efficacy failure/lack of initial response (41%) and secondary efficacy failure/waning efficacy over time (29%). Aspects such as tolerability, safety concerns, and patient adherence also play a role, albeit to a much lesser degree than those related to efficacy. When first-line JAK patients discontinue due to primary efficacy

failure they are the most likely to be prescribed a TNF-α-inhibitor in the second-line setting. Of note, one-quarter of first-line JAK patients who have discontinued due to primary efficacy failure will bypass TNF inhibitor treatment and move from a JAK to the IL-6 inhibitor, tocilizumab. Only 6% report that when a lack of initial response is at play, they will prescribe a consecutive JAK-inhibitor; however, if a patient discontinues due to waning response, respondents are more likely to cycle JAKs, with 11% of all secondary JAK failures prescribed another JAK. When JAK cycling occurs, it is most often attributed to patient preference for oral treatments.

Conclusion: With two JAK inhibitors currently available in the US RA armamentarium, and several late stage JAKs in development, the relationship and typical treatment protocol for JAK use is important to understand. Current pre-biologic use of JAKs is limited at just 8% of all first-line patients, though use of the class does increase in later lines of therapy. Currently, rheumatologists' propensity to cycle consecutive JAK therapies for the treatment of RA is minimal, and when it does occur, is most commonly patient-driven.

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Abstract Number: 1446

Golimumab as First, Second or at Least Third Biologic Agent in Patients with Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Ankylosing Spondylitis (AS) – Post Hoc Analysis of a Non-Interventional Study in Germany

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments Poster II: Established Treatments
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Table: Effectiveness parameters at BL vs month 24 with GLM use as 1st, 2nd, at least 3rd line

	1st line (bDMARD-, naïve)	2nd line bDMARD	3rd line (at least)
RA DAS28-ESR			
visit 1, month 0, BL	n=303	n=104	n=64
DAS28 [SD]	5.0 ± 1.3	4.9 ± 1.3	5.1 ± 1.5
visit 9, month 24:	n=128	n=32	n=24
DAS28 [SD]	2.9 ±1.3*	2.9 ± 1.*	3.4 ± 1.5*
PsA PsARC			
visit 1 month 0, BL	n=286	n=136	n=79
visit 9, month 24:	n=113	n=25	n=12
PsARC. response n (%)	76.4%	51.0%	50.0%
AS BASDAI			
visit 1, month 0, BL	n=290	n=130	n=58
BASDAI [SD]	5.0 ± 2.0	4.9 ± 2.0	5.7 ± 2.0
visit 9, month 24:	n=157	n=64	n=24
BASDAI [SD]	2.1 ±1.8*	2.9 ± 2.4*	2.9 ± 2.0*

*p<.0001 vs BL

Background/Purpose: The aim of this post hoc analysis is to assess effectiveness of GLM used as first, second, or at least third biologic agent in RA, PsA and AS in a real-life setting.

Methods: Post hoc analysis of the non-interventional, GO-NICE study with RA, PsA and AS patients starting GLM 50mg SC in a real practice setting in Germany, details were shown earlier (1,2). Endpoint measures DAS28, PsARC, and BASDAI are shown as observed.

Results: In 1458 patients with RA, PsA or AS, GLM was administered as first (n=305, 286, 292, respectively), second (n=104, 136, 130), or at least third biologic agent (n=64, 79, 58). In total, 43.0, 30.8, 39.1% of patients with RA, 53.1, 38.2, 34.2% with PsA, and 53.8, 49.2, 41.4% with AS completed the study until month 24. **RA pts.** (n=473): Baseline DAS28 scores were 5.0, 4.9, 5.1 in 1st, 2nd, and at least 3rd line use of GLM, respectively, and dropped significantly over time in all groups. Remission rates increased to 27.5%, 19.5%, and 14.5% (month 3) to 45.3%, 50.0% and 33.3% after 24 months of treatment, respectively. **PsA pts**. (n=501): PsARC response was achieved in 76.4%, 51.0% and 50.0% respectively in patients with GLM use as 1st, 2nd, at least 3rd line at 24 months. **AS pts.** (n=483): Patients with at least 2 previous bDMARDs had higher BASDAI at BL than patients with GLM use in first or second line: 5.7 vs. 5.0, and 4.9. After 24 months of treatment, the mean BASDAI scores decreased significantly ($p< 0.001$ vs. BL) to 2.1, 2.9, 2.9 in 1st, 2nd, and at least 3rd line use of GLM, respectively.

Conclusion: In this post-hoc analysis of the non-interventional study, Golimumab as first, second or at least third biologic agent were an effective treatment and showed remarkable improvements in clinical parameters DAS28, PsARC, and BASDAI in patients with RA, PsA, and AS.

Significant improvements of DAS28 and BADSAI was arrived after 3 months vs. BL and maintained over 24 months.

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Abstract Number: 1447

Comparison of Ultra High-resolution Ultrasound (UHFUS) of Labial Salivary Glands and Conventional Salivary Gland Ultrasonography in Primary Sjögren's Syndrome Assessment

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Labial salivary gland (LSG) biopsy remains a key tool for the diagnosis of primary Sjögren's syndrome (pSS). Nowadays, however, interest is growing in non-invasive methods able to supplement more invasive diagnostic procedures. Last-generation ultra high-resolution ultrasound (UHFUS) transducers, which can produce frequencies up to 70 MHz and achieve tissue resolution up to 30 μm, have recently opened up new possibilities for the study of a variety of superficial targets. In this work, we investigated the diagnostic accuracy of UHFUS in detecting LSGs involvement in patients with suspected SS and compared UHFUS findings with both LSG histopathology and conventional SGUS.

Methods: We enrolled consecutive patients undergoing a complete diagnostic work-up for suspected pSS, including conventional SGUS and LSG biopsy. The same expert pathologist assessed LSG focus score (FS) also reporting number of foci, presence of ectopic germinal centers (GCs) and percentage of total area infiltrated. UHFUS of LSG was performed by specialized radiologists scanning first the central compartment of the inferior lip, and then both peripheral compartments. The following parameters were evaluated: distribution of the glands, parenchymal inhomogeneity (score 0-3, from normal to evident), fibrosis and eco color-Doppler vascular pattern and grade of vascular intensity.

Results: We included 75 patients with suspected pSS. At the end of the work-up, pSS diagnosis was confirmed in 42/75 (56%) cases. With respect to no-SS sicca controls, pSS patients presented higher UHFUS inhomogeneity scores in both central (p=0.001) and peripheral labial compartments (p=0.001) as well as higher degree of central (p=0.003) and peripheral fibrosis (p=0.002). Considering a score ≥2 in parenchymal inhomogeneity as suggestive for pSS, UHFUS appeared less specific than conventional SGUS (UHFUS Sp=72% vs SGUS Sp=93%) but more sensitive (UHFUS Se=79% vs SGUS Se = 53%). Moreover, in comparison with conventional SGUS, the correlation coefficients between UHFUS inhomogeneity and LSG FS (UHFUS r=0.503** *vs* SGUS r=0.290*), number of foci (UHFUS r=0.493** *vs* SGUS r=0.307*), number of ectopic GCs (UHFUS r=0.315** *vs* SGUS r=0.173), and percentage of total area infiltrated (UHFUS r=0.506** *vs* SGUS r=0.332) were significantly higher.

Conclusion: The use of UHFUS of LSG in pSS appeared feasible and sensitive potentially offering unique advantages over the conventional imaging modalities in pSS assessment.

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Abstract Number: 1448

Ultrasonography of Major Salivary Glands in Primary Sjögren's Syndrome: Identification of Distinct Evolving Patterns in the Long-Term Follow-up

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: to evaluate the longitudinal changes of major salivary glands ultrasonography (SGUS) in primary Sjögren's Syndrome (pSS) and to investigate its relationship with patients' imaging pattern of presentation.

Methods: Patients with pSS underwent a complete SGUS examination at baseline and subsequently during follow-up. The echostructure of each gland on B-mode images was graded on a 5-point scale (0–4), and a SGUS score ≥2 was defined as pathological. Hypo-anechoic areas in the glands were defined as isolated (< 25% of the surface), localized (25-50%) and diffuse-scattered (>50%). Number of intra-parotid lymph nodes, presence of hyperechoic bands in more than 50% of the parenchyma and gland size were also recorded.

Results: We included 133 pSS patients (2M:131F, mean age 51±14 yrs) followed for a median follow-up of 24 months (IQR, 12-36 months). At baseline, 48/133 (36.1%) patients had a normal SGUS pattern, 14/133 (10.5%) presented a SGUS pattern characterized by mild inhomogeneity in the glands with no hypo-anechoic areas and 71/133 (53.4%) had a SGUS score ≥2 with a number of hypo-anechoic areas varying greatly among subjects. Patients with a normal SGUS pattern presented less frequently hypergammaglobulinemia, Rheumatoid Factor, anti-Ro/SSA and anti-LA-SSB positivity, whereas patients with a SGUS score ≥2 were significantly younger, had more frequently a history of chronic recurrent parotitis and presented a higher focus score in their labial glands, and a lower unstimulated salivary flow (p< 0.01). At the end of the follow-up, we did not observe any significant change in the number of hypo-anechoic areas; by contrast, 36/133 (27%) patients presented a variation in the number of intra-parotid lymph nodes and 50/133 (37.6%) presented an increase in salivary gland fibrosis and/or a decrease in glandular size. Considering patients' imaging pattern of presentation, pSS subjects with normal SGUS pattern at the baseline had significantly lower rates of new damage (p=0.001) when compared with the other two imaging patterns.

Conclusion: SGUS pattern of presentation may predict damage accrual in pSS, allowing to personalized medical treatments in clinical practice.

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Abstract Number: 1449

Clinical Phenotyping of Patients with Primary Sjögren's Syndrome Using Salivary Gland Ultrasonograhpy

Esther Mossel,[1] Jolien van Nimwegen,[1] Robin Wijnsma,[1] Alja Stel,[1] Konstantina Delli,[1] Greetje van Zuiden,[1] Lisette Olie,[1] Leonie Los,[1] Arjan Vissink,[1] Frans Kroese,[1] Suzanne Arends,[2] and Hendrika Bootsma[3], [1]University Medical Center Groningen, University of Groningen, Groningen, Netherlands, [2]Dept. of Rheumatology and Clinical Immunology - University Medical Center Groningen (UMCG), University of Groningen, Groningen, Netherlands, [3]University of Groningen, Groningen, Netherlands

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Salivary gland ultrasonography (SGUS) is a promising tool in primary Sjögren's syndrome (pSS). The objective of this study was to investigate SGUS abnormalities in relation to patient characteristics, disease activity and disease damage in patients with pSS in daily clinical practice.

Methods: The REgistry of Sjögren Syndrome LongiTudinal (RESULT) cohort is an ongoing observational prospective cohort study at the University Medical Center Groningen. For the present analysis, we used data from the baseline visit of patients with pSS, fulfilling the ACR-EULAR criteria, who were included between January 2016 and December 2018 (n=186). At baseline, clinical, patient-reported, functional, imaging, histopathological and serological parameters were obtained according to a fixed protocol. Patients underwent ultrasonographic examination according to the Hocevar scoring system (range 0-48)[1]. SGUS score was considered positive if the Hocevar score was ≥15[2]. Patient characteristics, disease activity and disease damage were compared between SGUS positive and SGUS negative pSS patients.

Results: In total, 172 out of 186 patients were included, with a mean age of 53 years (SD 13.9) and median disease duration of 8 years (IQR 4.0-13.0). 136 patients (79%) were SGUS positive. SGUS positive patients had significant longer disease duration (8.5 vs. 5.0 years; p=0.003), higher EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) (4.0 vs. 2.0; p=0.028) and higher Sjögren's Syndrome Disease Damage Index (SSDDI) (2.0 vs. 1.5; p=0.018) compared to SGUS negative patients. Furthermore, SGUS positive patients more often had a positive parotid gland biopsy (i.e. focus score≥1) (90.1% vs. 50.0%; p< 0.001), unstimulated whole saliva flow rate (UWS) ≤0.1ml/min (74.8% vs. 45.7%; p=0.001) and ocular staining score (OSS) ≥5 (41.0% vs. 8.3%; p< 0.001). With respect to serological parameters, SGUS positive patients more frequently had anti-SSA/SSB antibodies (94.1% vs. 75.0% and 61.5% vs. 25.0%), higher levels of IgG (16.9 vs. 11.2; p< 0.001) and rheumatoid factor (21.0 vs. 2.1; p< 0.001), and showed lower levels of leucocytes (5.2 vs. 6.3; p=0.002) and complement C3 and C4 (1.10 vs. 1.20; p=0.012 and 0.18 vs. 0.20; p=0.015). Regarding patient-reported outcome measurements, SGUS positive patients experienced significantly less fatigue (7.0 vs. 8.0; p=0.024) and pain (4.5 vs. 7.0; p< 0.001), as measured by EULAR Sjögren Syndrome Patient Reported Index (ESSPRI), and more often rated their symptoms as acceptable (75.6% vs. 58.3%; p=0.042). SGUS total score showed highest correlation with OSS (ρ=0.532) and UWS (ρ=-0.551).

Conclusion: SGUS positive patients had longer disease duration, higher disease activity and more disease damage compared to SGUS negative patients, whereas SGUS negative patients experienced more fatigue and pain. Therefore, SGUS could assist in the stratification of pSS patients and herewith provide another step towards personalized medicine.

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1 Hocevar A, *et al. Rheumatology (Oxford)* 2005;44:768–72.
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Abstract Number: 1450

Salivary Gland Hypofunction in a Mouse Model for Sjögren's Syndrome Is Strongly Associated with Hyperglycemia

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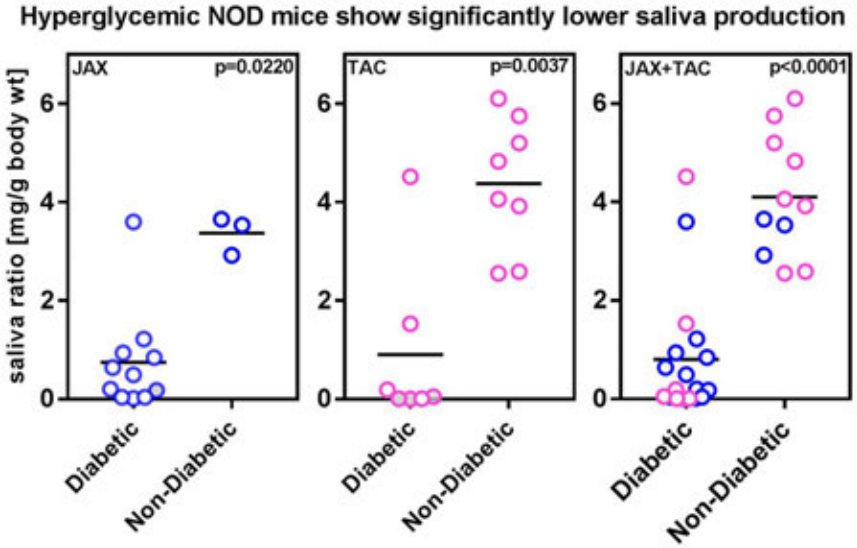
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: It has been demonstrated that the non-obese diabetes (NOD) mice from the Jackson Laboratory (JAX) have a distinct gut microbiome and higher incidence of type I diabetes than NOD mice from the Taconic Biosciences. Since the female NOD mice recapitulate several features of Sjögren's syndrome, this study was undertaken to test the hypothesis that the incidence and severity of Sjögren's syndrome-like disease will be distinct in NOD mice from JAX and Taconic.

Methods: Seven week old female NOD mice were purchased from JAX (n=15) and Taconic (n=15). Mice were monitored at different time points for hyperglycemia (non-fasting blood sugar >250mg/dL), pilocarpine-induced salivation, serum IgG levels, ANA, and circulating cytokines. Mice were euthanized at 22wk of age, and submandibular glands were evaluated for the presence of inflammatory foci and antibody deposition.

Results: At 20 wks of age, 80% of JAX mice were hyperglycemic, in comparison with only 46% from Taconic. The JAX mice had significantly higher total serum IgG (p=0.0007), IL-2 (p=0.0009), IL-6 (p=0.0287), TNFα (p=0.0447) and IP-10 (p=0.013) levels than the Taconic mice. The incidence of ANA was similar between the two groups. Although the severity of sialoadenitis was significantly higher in Taconic mice (p=0.0289), the loss of saliva production was more prominent in JAX mice. Surprisingly, a trend of higher saliva production was seen in mice with higher salivary



Hyperglycemia is associated with salivary gland hypofunction. Pilocarpine induced saliva was measured in female NOD mice at 20wks of age. A blood sugar of >250mg/dl was considered diabetic. Statistical analysis done by using the Mann-Whitney test and a $p<0.05$ considered significant.

gland inflammation. In both groups, the hyperglycemic mice had significantly lower ($p< 0.0001$) pilocarpine-induced salivation than mice with normal blood sugar levels. Furthermore, hyperglycemia was significantly associated with higher circulating IL-1β ($p=0.0174$), IL-16 ($p=0.007$) and lower IL-10 ($p=0.0227$) levels.

Conclusion: Our data demonstrate that in the NOD mouse model for Sjögren's syndrome, salivary gland dysfunction is strongly associated with hyperglycemia, rather than the ANA response and the level of salivary gland inflammation. Our data suggest that metabolic syndrome should be evaluated in SS patients and efforts made to reduce hyperglycemia.

Disclosure: B. Allushi, None; **J. Papinska**, None; **H. Bagavant**, None; **U. Deshmukh**, None.

Abstract Number: 1451

Histological Characteristics in SICCA Syndrome - Clinical and Serological Association

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SESSION INFORMATION
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Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session (Monday)
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Background/Purpose: The xerostomia and/or xerophtalmia (SICCA syndrome: items I and II of 2002 AECG criteria) are conspicuous characteristics of primary Sjögren´s syndrome (pSS). pSS diagnostic criteria include anti-SSA and anti-SSB antibodies, keratoconjunctivitis SICCA and characteristic findings in minor salivary gland biopsy (MSGB). Up to 40% of the cases with negative autoantibodies have been cataloged as pSS based on MSGB results.

Objective: The aim of this study was to compare the clinical and serological characteristics associated with inflammatory or non-inflammatory findings in the MSGB.

Methods: It is a cohort study of cases of SICCA syndrome attending the Rheumatology Department. At the time of patient inclusion an interview was conducted and clinical charts reviewed, obtaining the follow information; sex, age, evolution time of symptoms, history of mumps, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), antinuclear antibodies (ANA), Schirmer´s test and histopathological (Chilshom and Mason) study of MSGB.

Results: One hundred fifty-one females and one male patients were included. Mean age was 51.9±9.2 years. Patients were classified into inflammatory subgroup (n=110) when they presented MSGB focus score ≥1, or non-inflammatory subgroup (n=42) when displayed a MSGB focus score < 1. According with AECG 2002 inside of the inflammatory subgroup 57 patients (52%) fulfilled criteria for pSS and only 5 (12%) in the non-inflammatory subgroup ($p=0.0001$), additionally it was found that 11 patients (10%) had parotitis in the inflammatory subgroup while no patients in the non-inflammatory subgroup ($p=0.03$).

No differences were found in both groups for the following variables: age (years) 52±9.7 vs 51.6±8.1 (p=0.8), time of evolution (months) 71.6±55.4 vs 70.3±8.6 (p=0.99), arthralgia 98 patients (89%) vs 36 (86%) (p=0.58), Schirmer´s positive test 66 (70%) vs 32 (91%) (p=0.01), ESR > 20 in 67 (63%) vs 25 (59%) (p=0.85); positive CRP 30 (29%) vs 15 (36%) (p=0.43), positive RF 33 (31%) vs 20 (48%) (p=0.058), positive ANA in 41 (42%) vs 21 (49%) (p=0.46), fibrosis in MSGB 13 patients (12%) vs 6 (14%) (p=0.78).

Conclusion: In patients with SICCA, MSGB is essential to confirm the diagnosis, majorly in those who lack evidence for systemic autoimmunity, such as the relevant autoantibodies or concomitant autoimmune diseases. It should also be performed for this purpose when the sole evidence for systemic autommunity by the performance of anti-La/SSB or anti-Ro/SSA antibodies is not available. In these clinical settings, the test has particular utility if the results would influence the choice of therapies for non SICCA manifestations, such as fatigue, arthritis, or another systemic symptom.

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Abstract Number: 1452

Comparison of Clinical Phenotype, Serological Characteristics and Histologic Features Between Males and Females Patients with Primary Sjögren's Syndrome (pSS)

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Background/Purpose: Primary Sjögren's syndrome (pSS) is a female predominant autoimmune disease and very few studies have been conducted to investigate the phenotypic differences of the disease between the two genders. The purpose of this study is to investigate whether gender in pSS interferes with clinical manifestations, serology, disease course and lymphoma development, in a multi-center analysis from three centers specializing in Sjögren's Syndrome [Udine, Piza, Athens-(UPA)].

Methods: The combined cohorts of the 3 Mediterranean centers were harmonized and 82 male pSS patients, who fulfill the 2016 ACR/EULAR criteria for Sjögren's, were recruited from a pool of 1605pSS patients (n=254from Udine, n=753from Piza, n=598fromAthens). Each male was matched to a female patient in a 1:2 ratio, according to age and

disease duration from SS onset. Glandular (dry mouth, dry eyes, parotid gland enlargement) and extra-glandular manifestations (Raynaud's phenomenon, lymphadenopathy, arthralgias/arthritis, palpable purpura, liver involvement, kidney involvement, lymphoma) as well as serology (anti Ro/SSA, anti La/SSB, rheumatoid factor, cryoglobulinemia, low C4 complement levels) and histologic features (focus score, presence of germinal centers) were recorded and compared. Statistical analysis for categorical data was performed by Fisher exact test or χ^2square test accordingly and numerical data with Man-Whitney test.

Results: The median age of disease onset was 50 years (range: 15-77 years) for the male group and 50 years (range: 15-78 years) for the females. The median disease duration was 7,73 years (range: 0-26 years) and 8,38 years (range: 0-26 years) for males and females respectively. The male to female ratio in the total harmonized population was approximately 1:20. Interestingly, males with pSS had statistically significant higher frequency of lymphoma compared to females [15/82 (18.2%) vs 9/163 (5.5%) respectively, p=0.003]. Anti-La/SSB antibodies were more frequently detected in males compared to females [41/81 (50,6%) vs 54/162 (33.3%), respectively, p=0.015]. Finally, the prevalence of sicca manifestations including both dry mouth and dry eyes was higher among females compared to males [97,5% vs 91,2%, p=0.046, for dry mouth and 96,3% vs 87,8% for dry eyes, p=0.022, respectively].

Conclusion: To our knowledge this is the largest study comparing males with females pSS patients after applying the 2016 ACR/EULAR classification criteria. The higher frequency of lymphoma among males without classical risk factors may suggest distinct lymphomagenesis mechanisms between the two genders, implying that gender could be an independent risk factor for lymphoma development among pSS patients. Furthermore, the difference in the prevalence of anti-La/SSB antibodies and sicca symptoms indicates a potential role of gender and hormones in the production of autoantibodies and the clinical phenotype of pSS.

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Baseline EULAR Sjögren's Syndrome Patient-Reported Index Has a Significant Impact on the Longitudinal Course of Sjögren's Syndrome

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Background/Purpose: The EULAR Sjögren's syndrome (SS) disease activity index (ESSDAI) and EULAR SS Patient-Reported Index (ESSPRI) have been validated as disease activity and outcome measures for primary SS. However, there has been few studies on longitudinal ESSPRI and ESSDAI changes. We therefore aimed to prospectively investigate their temporal changes and to analyze the clinical features associated with a favorable course of ESSPRI in pSS patients.

Methods: A total of 115 pSS patients were evaluated using the ESSPRI, ESSDAI, EQ5-D, Fatigue Severity Score (FSS), Beck Depression Inventory (BDI), EULAR Sicca Score (ESS), Xerostomia Inventory (XI), patient's global assessment (PGA) for pSS, and visual analog scale (VAS) scores for symptoms. After a median 3 (range 3.0-3.2) years, 100 patients repeatedly completed the questionnaires. The favorable course was defined as an improvement in ESSPRI (from baseline ESSPRI≥5 to follow-up ESSPRI< 5) or maintenance of ESSPRI< 5, and the unfavorable course as worsening of ESSPRI (from baseline ESSPRI< 5 to follow-up ESSPRI≥5) or maintenance of an unsatisfactory symptom status (ESSPRI≥5). The minimal clinically important improvement (MCII) was defined as decreased at least one point or 15% of ESSPRI in patients with ESSPRI≥5.

Results: The ESSPRI remained stable over 3 years although VAS scores for arthralgia, myalgia, anxiety, and PGA were significantly reduced (all P< 0.001). Serum IgG levels (P< 0.01) and ESSDAI scores (P< 0.05) were significantly reduced but clinical ESSDAI scores were unchanged during the follow-up. Fourteen (28.0%) showed the worsening of ESSPRI among patients with baseline ESSPRI< 5 (n=50) and 16 (36.0%) showed the improvement of ESSPRI among those with baseline ESSPRI≥5 (n=50). Only 8 (16.0%) achieved MCII in ESSPRI in patients with unsatisfactory symptom status at the baseline and 52 (52.0%) had a favorable course in total patients. Patients with MCII had higher total and clinical ESSDAI scores (all P< 0.001) and more lacrimal flow (P< 0.05) at the diagnosis than those without MCII. Patients with favorable course had lower scores of ESS, FSS, BDI, and XI and VAS levels for oral or eye dryness, myalgia, anxiety, and PGA. On the contrary, they showed higher ESSDAI scores than those with unfavorable course. Unexpectedly, the use of bupropion increased in patients with favorable course (19.2% vs 8.3%) and in patients with an improvement of unsatisfactory ESSPRI (50.0% vs 11.8%, p=0.01), when compared to those without, respectively. Multivariate analysis revealed that the favorable course was significantly associated with low levels of anxiety (OR 5.6), low ESS scores (OR 8.0), moderate-to-high ESSDAI (OR 7.1), bupropion use (OR 7.9), and baseline ESSPR< 5 (OR 5.8).

Table 1. Multivariate analysis by logistic regression of factors associated with favorable ESSPRI outcome

Parameters	Beta	SE	P-value	OR	(95% CI)
Favorable ESSPRI outcome as a dependent variable (1st model)[a]					
Baseline ESSPRI	-0.644	0.143	<0.001	0.525	(0.397-0.695)
Bupropion usage	2.038	0.759	0.007	7.678	(1.733-34.008)
Favorable ESSPRI outcome as a dependent variable (2nd model)[b]					
Baseline ESSPRI<5	1.755	0.626	0.005	5.787	(1.696-19.734)
Lowest quartile of ESS	2.077	0.748	0.005	7.984	(1.842-34.607)
Lowest quartile of Anxiety VAS	1.715	0.616	0.005	5.559	(1.662-18.586)
Moderate to high disease activity (ESSDAI≥5)	1.963	0.760	0.010	7.119	(1.604-31.594)
Bupropion usage	2.069	0.826	0.012	7.921	(1.569-39.976)

[a]The first model included age, bupropion usage, EQ-5D VAS, ESS, ESSPRI, FSS, BDI-II, XI, overall oral dryness VAS, nocturnal oral dryness VAS, overall eye dryness VAS, eyeball pain VAS, OSDI score, Myalgia VAS, Anxiety VAS, PGA VAS, and ESSDAI.

[b]For the second model, we converted some of continuous variables into categorical variables, including EQ-5D index scores or VAS levels in the highest quartile; XI scores, OSDI scores, myalgia VAS levels, anxiety VAS levels, or PGA VAS levels in the lowest quartile; FSS≥4; BDI-II≥14; ESSDAI≥5; ESSPRI<5.

Conclusion: This study suggests that baseline ESSPRI provides a prognostic value for its longitudinal change, and the presence of extra-glandular features and more residual exocrine function could be associated with a favorable outcome in pSS. Additionally, bupropion may have beneficial effect on temporal changes in ESSPRI.

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Abstract Number: 1454

Sjögren's Syndrome Foundation National Survey: The Impact and Burden of Oral Symptoms

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SESSION INFORMATION
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Background/Purpose: Sjögren's syndrome (SS) is the second most common systemic autoimmune disease, typically characterized by ocular and oral sicca. SS is associated with reduced quality of life and increased costs, but the contribution of oral symptoms to morbidity is unclear. The Sjögren's Syndrome Foundation conducted a national survey of 2,962 adults with SS. We hypothesized that oral symptoms of SS predict reduced quality of life and financial burden in SS.

Methods: This survey included adults with self-reported SS. Oral symptoms/signs were assessed by frequency (never to daily) of eight categories: parotid swelling, dry mouth, oral ulcers, oral candidiasis, dysphasia ("trouble speaking"), dysphagia, sialolithiasis/gland infection, and caries. We calculated the prevalence of oral symptoms/signs (classified as present if symptoms occurred ≥ monthly) and current/ever use of oral treatments. We performed multivariable logistic regression to evaluate the association between oral symptoms (predictor) and quality of life and financial burden (outcome variables), adjusted for age, sex, race, and employment. Binary (present = "a lot of negative impact" or "a great deal of negative impact"; absent = no or "some negative impact") quality of life/financial burden outcomes included: 1) challenge of living with SS, 2) financial burden, 3) activities of daily living (ADLs), and 4) ability to work.

Table 1. Medication Use Among Adult Patients with SS (n=2962)

	Ever Use	Prevalence	Current Use	Prevalence
Saliva Substitutes	1812	0.61	1033	0.89
Oral Comfort Agents	2475	0.84	1876	0.63
Fluoride	1996	0.67	1462	0.49
Chorhexadine Rinse/Non-Fluoride Remineralizing	1173	0.40	556	0.19
Secretagogues	1785	0.60	1059	0.36

Table 2. Impact of Oral Symptoms on Quality of Life and Financial Burdens (n=2962)

Quality Outcome Measure	Oral Symptoms	Frequency of Symptoms	OR	95%CI
Daily Challenge Living With SS				
	Oral Ulcers	Never (ref)		
	n=1150 (40%)	Once/Few Times Yearly	1.88	1.42-2.48
		Monthly/Almost Monthly	3.12	2.18-4.46
		Weekly/Almost Weekly	6.44	3.44-12.06
		Daily/Almost Daily	4.70	2.26-9.78
	Dysphasia	Never (ref)		
	n=1354 (47%)	Once/Few Times Yearly	1.51	1.09-2.08
		Monthly/Almost Monthly	2.11	1.41-3.15
		Weekly/Almost Weekly	2.78	1.92-4.05
		Daily/Almost Daily	7.05	3.96-12.56
	Dysphagia	Never (ref)		
	n=1646 (56%)	Once/Few Times Yearly	1.43	1.05-1.94
		Monthly/Almost Monthly	1.62	1.16-2.27
		Weekly/Almost Weekly	3.10	2.14-4.49
		Daily/Almost Daily	5.08	3.14-8.19
Activities of Daily Life				
	Dysphasia	Never (ref)		
	n=1354 (47%)	Once/Few Times Yearly	1.48	1.14-1.92
		Monthly/Almost Monthly	1.87	1.42-2.47
		Weekly/Almost Weekly	2.57	2.02-3.27
		Daily/Almost Daily	2.77	2.15-3.57
	Dysphagia	Never (ref)		
	n=1646 (56%)	Once/Few Times Yearly	1.18	0.89-1.56
		Monthly/Almost Monthly	1.87	1.42-2.46
		Weekly/Almost Weekly	2.69	2.08-3.47
		Daily/Almost Daily	3.03	2.32-3.96
Ability to Work				
	Oral Ulcers	Never (ref)		
	n=1150 (40%)	Once/Few Times Yearly	1.18	0.95-1.48
		Monthly/Almost Monthly	1.67	1.3-2.14
		Weekly/Almost Weekly	1.72	1.26-2.35
		Daily/Almost Daily	2.47	1.6-3.82
	Dysphasia	Never (ref)		
	n=1354 (47%)	Once/Few Times Yearly	1.21	0.94-1.57
		Monthly/Almost Monthly	1.64	1.22-2.21
		Weekly/Almost Weekly	1.79	1.38-2.31
		Daily/Almost Daily	2.02	1.53-2.67

Results: The 2,962 survey participants were 92.6% white, 95.6% female, and averaged 65.1 years of age. Most respondents had dry mouth (96.5%) followed by dysphagia (57.5%), dysphasia (47.0%), oral ulcers (40.0%), caries (22.4%), parotid swelling (17.7%), oral candidiasis (8.8%), and sialolithiasis/gland infection (3.8%). Eighty-four percent of respondents used oral comfort agents, 67% used fluoride, and 60% used secretagogues previously, but less than half currently use fluoride and secretagogue treatment (Table 1). Significant dose dependent relationships between frequency of oral symptoms quality of life/financial burden measures were observed. Dysphasia impacted all four quality/financial measures including daily living challenges (OR 7.05 [95% CI 3.96-12.56), ADLs (OR 2.77 [95%CI 2.15-3.57), work ability (OR 2.02 [95% CI 1.53-2.67]), and financial burden (OR 3.08 [95% CI 2.34-4.06]) (Table 2). Oral ulcers and dysphagia impacted three of four quality/financial measures (Table 2).

Conclusion: Oral symptoms occurred in the majority of SS respondents, yet less than half of respondents remain on secretagogue or fluoride therapies. This lack of persistence might reflect reduced perceived symptomatic benefits or cost burdens of SS. Dysphasia impacted all four outcome categories in a dose dependent manner by symptom frequency with up to a seven fold odds increase in the challenges with daily living. Dysphasia, oral ulcers, and dysphagia most strongly impacted multiple quality of life measures compared to other oral aspects, potentially identifying dysphasia, oral ulcers, and dysphagia as important but underutilized patient reported outcome measures. Furthermore, these findings highlight the potential importance of targeted treatment toward dysphasia and dysphagia.

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Abstract Number: 1455

B and T Cell Immunologic Features Associated with Higher Disease Activity Score and Focus Score in Primary Sjögren Syndrome

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SESSION INFORMATION
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Background/Purpose: Primary Sjögren syndrome (pSS) is a systemic autoimmune disease with an incompletely understood pathogenesis and heterogenous disease manifestations. Identifying cellular immune changes that may predict disease severity could lead to identification of biomarkers and potential targets for therapy. We examined a cohort of pSS patients to identify the cellular immunologic features significantly associated with disease activity, as measured by the EULAR Sjögren's syndrome disease activity index (ESSDAI) and the focus score on minor salivary gland (MSG) biopsy.

Methods: 35 participants who met the ACR 2016 classification criteria for pSS were recruited. Peripheral blood cellular immunological changes were assessed by flow cytometry and transcript levels of BAFF, interferon (IFN)-induced and plasma cell-expressed genes were quantified by NanoString. Normalized Log_2 transformed expression levels of 5 IFN-induced genes were summed to generate the IFN5 score. Associations between the ESSDAI, focus score, and cellular immunological changes were evaluated using Spearman's correlation coefficient.

Results: The ESSDAI was significantly correlated with the focus score ($r=0.64$, $p< 0.01$). The majority of T and B cell populations, including the proportions of naïve, class-switched memory, un-switched memory, and $CD27^-$ memory B cells and their activation, as well as IFN-γ-, IL-17-, or IL-21-producing T cells, did not correlate with either measure of disease activity. However, the proportion of transitional B cells ($CD27^-IgD^+CD24^{hi}CD38^{hi}$; $r=0.40$, $p=0.03$) and proportion of activated memory T follicular helper cells ($CXCR5^+PD1^{hi}$) in the $CD4^+$ T cell compartment ($r=0.39$, $p=0.05$) and $CD3^+$ T cell compartment ($r=0.42$, $p=0.04$) were significantly associated with the focus score. In addition, the frequency of T regulatory cells ($CD4^+FOXP3^+HELIOS^+$) was positively correlated with the ESSDAI ($r=0.61$, $p=0.04$). Type

I IFN-induced gene expression, as measured by the IFN5 score, was significantly associated with both focus score (r=0.37, p=0.05) and ESSDAI (r=0.37, p=0.04).

Conclusion: The findings suggest that elevated levels of IFN-induced gene expression and increased proportions of T follicular helper cells are potential biomarkers of increased disease activity and may constitute good targets for disease treatment.

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Abstract Number: 1456

The Increased Ratio of Blood CD56^{bright} to CD56^{dim} NK Cells Is a Distinguishing Feature of Primary Sjögren's Syndrome

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Background/Purpose: To investigate the characteristic and clinical significance of peripheral blood CD56 NK cell subsets in patients with primary Sjögren's syndrome (pSS).

Methods: From November 2017 to November 2018, 52 patients fulfilled the 2002 AECG criteria or 2012 ACR criteria of pSS and 20 healthy volunteers were enrolled in this study. The proportion and absolute number of NK cells and CD56 NK cell subsets in peripheral blood samples were detected by flow cytometry. Disease activity was determined by score of EULAR Sjogren's syndrome disease activity index (ESSDAI). Other laboratory parameters such as anti-nuclear antibody (ANA), anti-SSA/SSB, C-reactive protein (CRP) and the treatment regimen were extracted from the clinical system. The ROC curve was used to assess the diagnostic value of the ratio of CD56bright NK to CD56dim NK.

Results: The proportion and absolute number of peripheral blood NK cells were reduced in pSS patients compared to healthy controls. The proportion of CD56^{bright} NK cell subset was increased and its absolute number was decreased. The proportion and absolute number of CD56^{dim} NK cell subset were decreased. Moreover, the ratio of CD56^{bright}NK to CD56^{dim}NK was significantly elevated in pSS patients than that in healthy controls. ROC curve analysis indicated that the area under the curve (AUC) of the peripheral blood CD56^{bright}NK/CD56^{dim}NK was 0.838, and the best diagnostic cut-off point was 0.0487 for pSS patients. Furthermore, the decreased blood CD56^{dim}NK cell count was increased again after treatment in pSS patients consistent with the decreased ESSDAI and serum IgG level.

Conclusion: The ratio of blood CD56^{bright}NK to CD56^{dim}NK may be a valuable biomarker for the diagnosis of pSS. The absolute counts of CD56^{dim} NK cell subsets is sensitive to the treatment response in pSS patients.

Disclosure: B. Ming, None; **T. Wu**, None; **L. Dong**, None.

Abstract Number: 1457

Neurological Involvement in a Cohort of Primary Sjogren's Syndrome Patients: Results of a Multicenter Italian Study

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SESSION INFORMATION

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Background/Purpose: The course of primary Sjögren's syndrome (pSS) may be characterized by extra-glandular and potentially life-threatening manifestations. Among these, neurological involvement represents a clinical challenge due to its heterogeneous clinical presentation and diagnostic complexity. Indeed, reported prevalence of central (C) and peripheral (P) nervous system (NS) involvement is high variable due to lack of unified definition and diagnostic tools. Moreover, the association between disease clinical and serological manifestations and SN involvement remains unclear. Aim of this study was to evaluate the prevalence of neurological involvement in a pSS cohort and to investigate factors associated with this risk.

Methods: Data of a cohort of pSS patients fulfilling the 2002 AEGC criteria and enrolled in an Italian multicenter database (the Italian Group of SS Study-GRISS) were retrospectively analyzed. Disease clinical and serologic data were sistematically collected with specific analysis of CNS and PNS involvement. Clinical and serologic features associated with SN involvement were investigated. The Shapiro–Wilk test was used to assess the normal distribution of variables. The chi-squared test and the Mann–Whitney *U*-test were used for comparisons of categorical variables and non-normally distributed continuous variables, respectively. Separate multivariate logistic regression analysis was performed.

Results: The cohort comprised 1.707 patients (1.629 F, 78 M). Mean age at diagnosis was 52±14 and mean disease duration 6±7 years. Prevalence of NS involvement was 4.5% (78/1.707). PNS manifestations were recorded in 61 (3,6%), including 29 sensorimotor neuropathy, 17 pure sensory neuropathy, 8 sensory or sensorimotor polyneuropathy, 6 small-fiber neuropathy and 1 mononeuritis multiplex. CNS manifestations were recorded in 13 (0,8%), including 4 cerebral vasculitis, 3 trasverse myelitis, 2 otpic neuritis, 2 cranial nerve involvement and 1 multiple sclerosis-like syndrome. No diagnosis was available in 4 patients. Male sex was associated with higher risk of NS involvement (10% M vs 4% F, p= 0.025). Patients with NS involvement showed significant higher frequency of articular involvement (76% vs 62%), purpura (24% vs 7%), other organ involvement (96% vs 38%) lymphoma (9% vs 4%), low complement (42% vs 19%), leukopenia (39% vs 24%) and cryoglobulins (20% vs 4%). Median salivary gland focus score was higher in patients without NS involvement (p=0.001). At multivariate analysis, male sex (OR=2,7; 95% CI 1,1, 6), other organ involvement (OR=15; 4,5, 50,6), low complement (OR=2; 1,2, 3,5) and cryoglobulins (OR=3; 1,4,

6,3) were independently associated with NS involvement risk. Higher focus score was associated with lower risk (OR=0.7; 0,5, 0,9).

Conclusion: Results of this multicenter study highlight that, although not frequent, NS involvement in pSS is protean and mainly characterizing male sex. The association with specific clinical and serologic disease features suggests that vasculitis may exert a prominent role in its pathogenesis. Awareness of these factors may help in predict neurological complications in different subgroups of patients and provide insight into better therapeutic approach.

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Abstract Number: 1458

Dual Analysis with Nerve Ultrasound and Skin Biopsy in Painful Neuropathy Associated with Sjögren's Syndrome

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: 6% of primary Sjögren's syndrome (pSS) patients manifests as various forms of neuropathies including painful sensory neuropathy (PSN), which can be treatable with immunomodulatory drugs such as steroid and immunoglobulin. Our objective is to evaluate usefulness of ultrasound (US) in detecting abnormality of peripheral nerves, and to elucidate the relationship between US findings, histopathological findings and treatment response to immunomodulatory drugs. Recently, nerve US and skin biopsy with analysis of intraepidermal nerve fiber density (IENFD) have increasingly been used for the assessment of various forms of neuropathies. In PSN, skin biopsy is reported to be the most sensitive test for the diagnosis. There is an emerging evidence to suggest association of peripheral nerve swelling on US in patients with PSN. However, there has been no reports assessing the efficacy of peripheral nerve US in pSS associated neuropathy.

Methods: We conducted retrospective chart review from 2017 to 2019. Included patients were pSS fulfilling 2016 ACR-EULAR criteria, and were diagnosed as having neuropathic pain by Neurology specialist. We obtained clinical, serological, and electrophysiological features. On US analysis, we used LOGIQ S8 and LOGIQ ePremium devices. In each of patients, we obtained axial images to measure cross sectional area (CSA) of right median, ulnar, tibial, and sural nerve. Measurement of CSA was preformed by manually tracing the area along the nerve's hyperechoic rim. Additionally, intraneural vascular flow was assessed by using power doppler technique. Skin biopsy was performed on right lateral thigh and lower leg. IENFD was measured by counting number of nerve fibers entering epidermis. Information about pharmacological treatment was also obtained, and treatment response to immunomodulatory drugs were assessed.

Results: We included 12 patients who underwent US and skin biopsy, and seven of them already completed measurement of IENFD. Majority of these patients were advanced age, and female gender dominated. Duration of neuro-

pathic pain was chronic, ranging from one to five years except one patient with very chronic course over 18 years. Pain was described as burning or tingling sensation, distributed on bilateral arms and legs, although two patients showed truncal involvement. Three patients also showed various degree of sensory ataxia. Only two patients showed decreased pain sensation on neurological exam. Five patients were anti-SSA antibody positive. On nerve US, increased CSA of sural nerve was observed in four patients. And three of them also showed decreased IENFD. Majority of patients showed decreased IENFD of lower leg. Only one patient showed increased intraneural vascular flow.

Case	Age	Gender	Duration	Neuropathic pain	Sensory ataxia	Sensory loss	DTRs	Diagnostic tests for SS	Extraglandular Sx	ESSDAI
1	69	F	4 Y	Bil hands and fingers Bil lower legs NRS 7	(+)	(-)	UE 1+ LE -	Anti-SS-A Shirmer's test Ocular stain Scintigraphy	None	16
2	77	M	3 Y	Left palm Bil feet NRS 6	(+)	(+)	UE 1+ LE ±	Anti-SS-A Scintigraphy	Hypergammaglobulinemic purpura MDS	23
3	71	F	1.5 Y	Bil hands and legs NRS 7	(-)	(-)	1+	Shirmer's test Ocular stain Salivary gland biopsy	None	15
4	76	F	6 Y	Bil feet NRS 8	(-)	(-)	1+	Anti-SS-A Salivary flow rate	Fever, myalgia, hypergammaglobulinemic purpura	20
5	54	M	3 Y	Bil legs, followed by trunk and bil arms	(-)	(-)	UE 1+ LE -	Anti-SS-A Salivary flow rate	Thrombocytopenia	13
6	77	F	18 Y	Bilateral arms and legs Truncal band-like sensation	(+)	(-)	UE 2+ PTR 2+ ATR -	Shirmer's test Salivary flow rate Scintigraphy Salivary gland biopsy	Arthralgia	19
7	63	F	2 Y	Bil arms and legs	(-)	(+)	UE 2+ PTR 2+ ATR1+	Anti-SS-A Ocular stain	Arthritis	10

Abbreviations. ATR: achilles tendon reflex, Bil: bilateral, DTRs: deep tendon reflexes, F: female, LE: lower extremity, M: male, MDS: myelodysplastic syndrome, PTR: patellar tendon reflex, Sx: symptom, UE: upper extremity, Y: year(s)

Clinical features of patients.

Case	Peripheral nerve ultrasound				Intraneural vascular flow	NCS	Skin biopsy/IENFD (n/mm)	
	Median N	Ulnar N	Sural N	Tibial N				
1	Wrist 9.5 Elbow 8.9	Wrist 5.4 Elbow 6.6	**4.6**	6.8	None (After Tx)	**SNAP Amp ↓**	Thigh Lower leg	43.2 17.1
2	Wrist 6.6 Elbow 8.4	Wrist 4.4 Elbow 5.5	**3.0**	9.2		**SNAP Amp ↓**	Thigh Lower leg	**7.7** **3.9**
3	Wrist 12.3 Elbow 5.1	Wrist 3.8 Elbow 9.2	2.9	8.6	None (After Tx)	Normal	Thigh Lower leg	37.1 17.7
4	Wrist 7.6 Elbow 9.4	Wrist 3.7 Elbow 4	2.9	12.9	None (After Tx)	Normal	Thigh Lower leg	27.3 **6.2**
5	Wrist 9.2 Elbow 13	Wrist 6.1 Elbow 7.4	**3.3**	11.2		**SNAP Amp ↓**	Thigh Lower leg	**3.6** **3.3**
6	Wrist 4.4 Elbow 7.4	Wrist 2.5 Elbow 9.5	0.9	14.4	None (After Tx)	**SNAP ND or Amp ↓**	Thigh Lower leg	**0.4** **0**
7			**3.7**	21.8	**Increased**	Normal	Thigh Lower leg	**7.3** **8.7**

Abbreviation. Amp: amplitude, N: nerve, ND: not detected, SNAP: sensory nerve action potential, Tx: treatment.

Ultrasonographic, electrophysiological, and histopathological Findings.

Case	Non-immunomodulatory drugs		Immunomodulatory drugs	
1	Gabapentin Enacarbil	Not effective	Predonisolone 30mg/day	Not effective
2	Pregabalin	Effective	Predonisolone 20mg/day	Not effective
3	Tramadol/acetaminophen, duloxetine	Not effective	Predonisolone 30mg/day	**Effective**
4	Tramadol/acetaminophen	Effective	Predonisolone 30mg/day	**Effective**
5	Pregabalin	Effective	None	
6	Pregabalin	Effective	mPSL 500mg x3 days and PSL 15mg/day	**Effective**
7	None		None	

Choice of treatment and the response.

Five patients were treated with moderate dose of predonisolone. Three of them showed significant improvement, as judged from description of treating physician.

Conclusion: Our patients with pSS-associated PSN showed heterogenous clinical, US, and histological findings. Nerve swelling and decreased IENFD were observed in many of them. Steroid therapy was effective in three out of five patients. These changes might reflect inflammatory environment within nerve fibers and resultant axonal loss.

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Systemic Manifestations of Primary Sjögren Syndrome out of the ESSDAI Classification: Prevalence and Clinical Relevance in a Large International, Multi-ethnic Cohort of Patients

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SESSION INFORMATION

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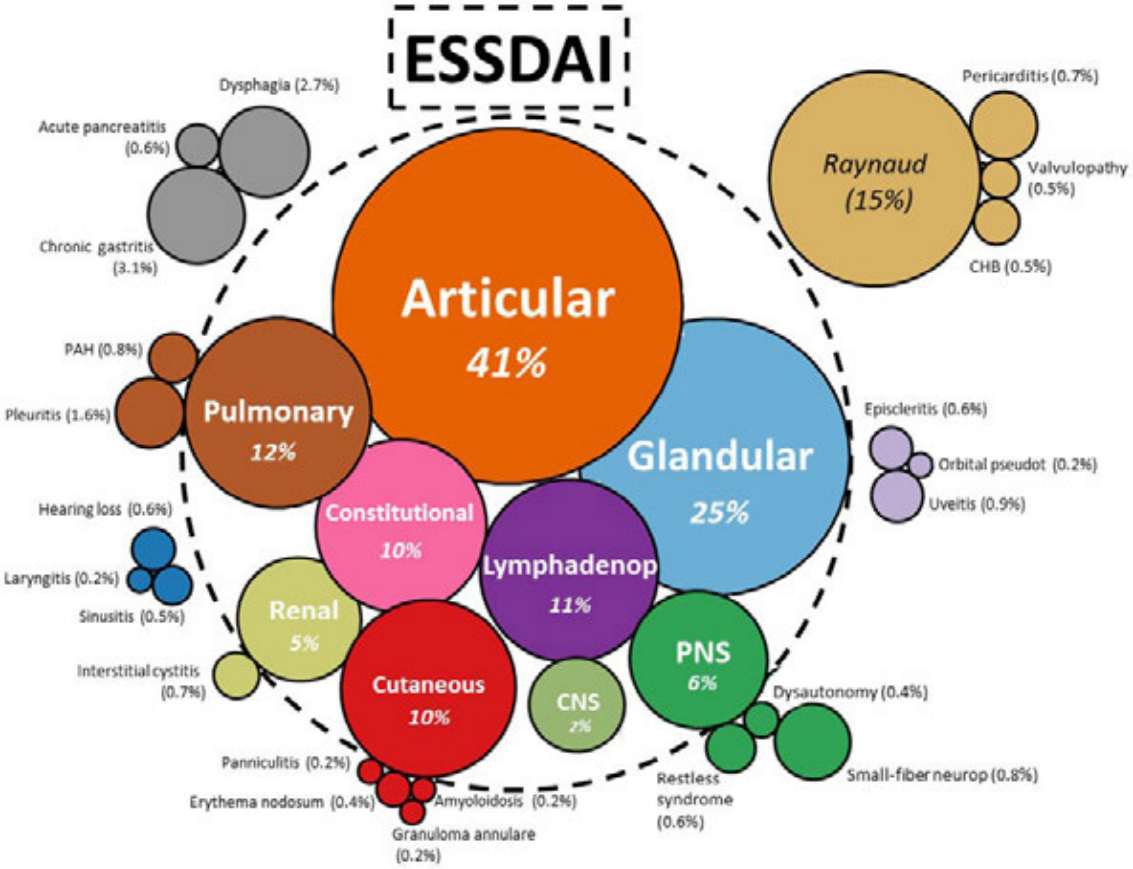
Background/Purpose: To analyse the frequency and characterize the systemic presentation of primary Sjögren syndrome (SjS) out of the ESSDAI classification in a large international, multi-ethnic cohort of patients.

Methods: The Big Data Sjögren Project Consortium is an international, multicentre registry based on worldwide data-sharing and cooperative merging of pre-existing clinical SjS databases from leading centres in clinical research in SjS from the five continents. A list of 26 organ-by-organ systemic features not currently included in the ESSDAI classification was defined according to previous studies; these features were retrospectively recorded.

Results: Information about non-ESSDAI features was available in 6331 patients (5,917 female, mean age at diagnosis 52 years, mainly White (86.3%). A total of 1641 (26%) of 6331 patients presented at least one of the out of ESSDAI systemic features listed in Annex 1; among them, there were 359 (22%) patients who presented two or more of these features. The most frequent organs involved included cardiovascular in 1079 (17%) patients, digestive in 390 (6.2%), pulmonary in 145 (2.3%), neurological in 110 (1.7%), ocular in 97 (1.5%), ENT in 80 (1.3%), cutaneous in 55 (0.9%) and urological features in 43 (0.7%) patients (Figure). Cardiovascular manifestations were the most frequent organ-specific group of non-ESSDAI features reported in our patients (17% of the total cohort), with Raynaud phenomenon being reported in 15%. Patients with systemic disease due to non-ESSDAI features had a lower frequency of dry mouth (90.7% vs 94.1%, $p< 0.001$) and positive minor salivary gland biopsy (86.7% vs 89%, $p=0.033$), a higher



frequency of anti-Ro/SSA (74.7% vs 68.7%, p< 0.001), anti-La/SSB antibodies (44.5% vs 40.4%, p=0.004), ANA (82.7% vs 79.5%, p=0.006), low C3 levels (17.4% vs 9.7%, p< 0.001), low C4 levels (14.4% vs 9.6%, p< 0.001), and positive serum cryoglobulins (8.6% vs 5.5%, p=0.001). Systemic activity measured by the ESSDAI, clinESSDAI and DAS was higher in patients with systemic disease out of the ESSDAI in comparison with those without these features (p< 0.001 for all comparisons).

Conclusion: More than a quarter of patients with primary SjS may have systemic manifestations not currently included in the ESSDAI classification, with a wide variety of cardiovascular, digestive, pulmonary, neurological, ocular, ENT, cutaneous and urological features that increase the scope of the systemic phenotype of the disease. However, the individual frequency of each of these non-ESSDAI features was very low, except for Raynaud phenomenon. The results of this study, together with the already-published evidence supporting a pivotal role of systemic disease in primary SjS, are pointing out the need of a future re-evaluation about how we are defining, classifying and diagnosing primary SjS.

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Abstract Number: 1460

Minor Salivary Gland Biopsy and Dry Ocular Tests to Detect Occult Sjögren Syndrome in Patients with Interstitial Pneumonia with Autoimmune Features

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Background/Purpose: Interstitial lung disease (ILD) are a heterogeneous group of diseases that could be either idiopathic or secondary to environmental exposure, drugs or connective tissue disease (CTD). ILD related to CTD has different treatment options and different survival depending on the underlying CTD disease. Interstitial pneumonia with autoimmune features (IPAF) is the term used to describe patients with interstitial lung disease that have clinical or serological markers that suggest an underlying autoimmune process, but do not meet stablished criteria of a CTD. This diagnosis is made based on three domains: clinical, serologic and intrathoracic morphologic features. It is not known if Sjögren's Syndrome (SS) is underdiagnosed among patients with IPAF. The aim of the study is to define the utility of performing a Minor Salivary Gland Biopsy (MSGB) and dry eye tests (DET) in patients with IPAF to detect occult SS.

Methods: Prospective study. Interstitial Lung Disease patients without defined Connective Tissue Disease and at least one criteria of one or more IPAF classification domains were included. A MSGB, Schirmer's test (ST) and Ocular Staining Score (OSS) were performed in a blinded manner by experienced specialists. MSGB was considered positive when at least 1 focus of lymphocytes was detected, while DET were positive if OSS $\geq$ 5 and/or ST $\leq$5 secs. SS diagnosis was according to the 2016 ACR EULAR criteria.

Results: 534 patients on first consult were screened. 67 patients had at least one IPAF criteria, of which 53 (79.1%) were female with a mean age (SD) of 64.18 years (10.81). Positive ST in 36 (53.73%), positive OSS in 29 (43.28%) and positive MSGB in 36 (53.73%) were found. 27 (40.29%) met SS diagnostic criteria. Of these, 2 (7.41%) and 8 (29.6%) did not report dry eyes or dry mouth respectively, 16 (59.25%) had negative anti RO, 22 (81.48%) negative anti LA, 7 (25.92%) negative ANA, and 10 of 17 (58.8%) negative RF. Comparing patients with and without SS we found a significant higher proportion of patients with ANA (+), positive DET and positive MSGB in the SS population.

Conclusion: We found a significant proportion of patients with occult SS in our study population. Most of these patients with IPAF met Sjogren criteria despite having negative anti Ro, anti LA or RF. In addition to physical examination and immunological profile, the MSGB and dry eye tests should be considered in the evaluation of patients with IPAF.

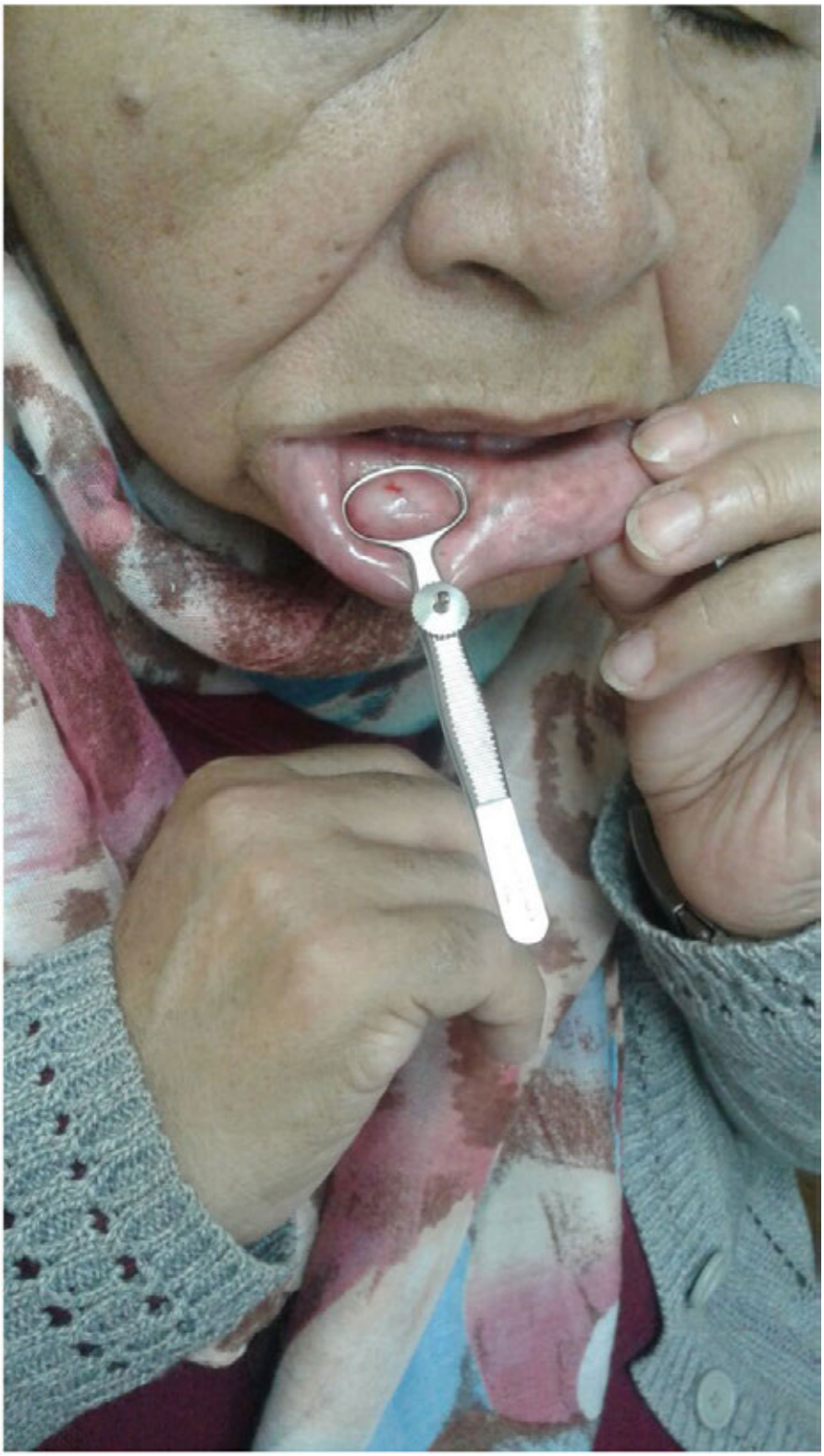

Image 1. Minor Salivary Gland Biopsy

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Abstract Number: 1461

Pulmonary Cysts: Very Common Finding on Computed Tomography of the Chest of Asymptomatic Patients with Primary Sjögren's Syndrome

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Background/Purpose: The presence of pulmonary cysts is a relatively unusual radiological finding, but frequently described in patients with primary Sjögren's syndrome (pSS). Its true meaning, however, remains unclear, and may be associated with other forms of interstitial lung disease, lymphoma, or even a benign finding. Previous data on the subject are retrospective and also involve secondary forms of the disease, besides contemplating mainly symptomatic patients. Our main objective is to evaluate the prevalence of pulmonary cysts in asymptomatic respiratory patients with pSS, as well as possible clinical-laboratory association factors.

Methods: From September 2017 to April 2019, patients with pSS and without any form of respiratory symptomatology were selected for high-resolution computed tomography (HRCT). Patients older than 18 years and classified as having Sjögren's syndrome (SS) were included according to the American-European Consensus of 2002 (68.5% of the individuals met the 2016 ACR criteria). Only patients with the primary form of the disease were recruited. A single, experienced radiologist evaluated the images. A cyst was defined by the presence of a clearly demarcated airspace surrounded by thin (< 2 mm) walls. Numbers, size, and lung distribution of cysts were analyzed. Epidemiological, clinical, and laboratory data were extracted from medical records. Data from pSS patients with and without pulmonary cysts were compared, and Fisher's exact test was used to evaluate statistical association.

Results: Thirty-five pSS patients (median age 52.3±17; 100% female) and respiratory asymptomatic patients underwent CT of the thorax. Of these, 11 (31%) presented evidence of pulmonary cysts, mainly in the lower lobe (75%) and with a size varying from 0.3 to 6.6 cm. No extraglandular (renal, neurological, cutaneous, articular or hematologic), autoantibody (anti-Ro, anti-La, RF, ANA) or laboratorial manifestations (complement dosage, cryoglobulins, protein electrophoresis) were statistically associated with pulmonary cysts found on chest CT.

Conclusion: The high prevalence of pulmonary cysts in asymptomatic respiratory patients with pSS reinforces their probable benign nature, as well as the important association of this unusual pulmonary finding with this form of connective tissue disease. No clinical-laboratory element related to pSS was associated with this pulmonary manifestation. Prospective evaluation of this and other studies is necessary for a better understanding of the evolutionary nature of pulmonary cysts.

Disclosure: A. Pugliesi, None; **P. Bellini**, None; **R. Zerbini Mariano**, None; **M. Bertolo**, None; **Z. Sachetto**, None.

Abstract Number: 1462

Pathogenesis of Vaginal Dryness in Primary Sjögren's Syndrome: A Histopathological Case-control Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Women with primary Sjögren's syndrome (pSS) often experience vaginal dryness, but the pathogenesis of this symptom is unknown. Previously, we reported impaired vaginal health and presence of a subepithelial infiltrate in the vagina of women with pSS[1]. In the current analysis, we quantitatively studied changes in lymphocyte subsets, endothelial cells and soluble immune markers in the vagina and endocervix of women with pSS, compared to age-matched controls, which may explain vaginal dryness.

Methods: Gynaecological examinations were performed in 10 premenopausal women with pSS, fulfilling the ACR-EULAR criteria, with symptoms of vaginal dryness, and 10 premenopausal non-pSS controls scheduled for laparoscopic procedures. Participants with inflammatory or infectious gynaecological morbidity were excluded. Endocervical swab and cervicovaginal lavage samples were collected, in which levels of pro-inflammatory chemokines and cytokines were analyzed using a multiplex bead based immunoassay. Mid-vaginal biopsies and endocervical biopsies were collected and stained for leucocyte markers, caldesmon for smooth muscle cells, ERG for endothelial cells and anti-podoplanin (clone D2-40) for lymphatic endothelium. The number of positive pixels/μm^2 was calculated digitally using Aperio ImageScope v 12.1.

Results: One pSS patient was excluded due to chlamydia, and 2 controls due to discovery of endometriosis during their laparoscopy. In the remaining 9 patients and 8 controls, median age was 36 years (IQR 33-46) and 41 years (36-44), respectively (p=0.61). A higher level of CXCL10 was measured in endocervical swabs of pSS patients (median 37.1 pg/ml, IQR 19.4-66.1) compared to controls (median 12.6 pg/ml, IQR 5.9-31.1, p= 0.046). No differences were found in levels of APRIL, BAFF, RANKL, TNF-α, CCL2, CXCL11, CXCL13, IL6, IL7 or IL8. One vaginal biopsy from a control was excluded from analysis as it was too superficial, consisting for 98% of epithelium. Three pSS and two control cervix biopsies which did not show representative endocervical tissue were excluded from analysis. The number of CD45+ and CD3+ cells (expressed as number of positive pixels/μm^2) in vaginal biopsies was significantly higher in pSS patients (p=0.012 for CD45, p=0.008 for CD3). Lymphocytic infiltration was mainly located in the subepithelial layer, with aggregates in dermal papillae. Endocervical CD45+ leucocytic infiltrates were seen in patients as well as controls, but CD20+ positive pixels/μm2 were significantly higher in pSS patients (p=0.041). Importantly, there was a significantly lower number of vascular smooth muscle cells (caldesmon+ pixels/μm2) in the vagina of pSS (p=0.031). In the endocervix, no significant differences were seen in endothelial or smooth muscle cells.

Conclusion: Our findings indicate that in addition to chronic inflammation, vascular disturbances in the vaginal mucosa are likely to contribute to vaginal dryness in women with pSS.

Reference: [1]JF Van Nimwegen et al. Arthritis Rheumatol. 2017; 69 (suppl 10). https://acrabstracts.org/abstract/subepithelial-infiltrate-of-the-vagina-in-primary-sjogrens-syndrome-the-cause-of-vaginal-dryness/.

Disclosure: J. van Nimwegen, Bristol-Myers Squibb, 5, 8; **K. van der Tuuk**, None; **S. Liefers**, None; **G. Verstappen**, None; **R. Wijnsma**, None; **H. Hollema**, None; **M. Mourits**, None; **H. Bootsma**, Bristol-Myers Squibb, 2, 5, 8, GlaxoSmithKline, 2, 5, HarmonicSS, 2, MedImmune, 2, 5, Medimmune, 5, Novartis, 5, 8, Roche, 2, 5, UCB, 2, 5, Union Chimique Belge, 5; **F. Kroese**, Bristol-Myers Squibb, 2, 5, 8, Janssen-Cilag, 8, Roche, 8.

Abstract Number: 1463

Positive Rate of Small Intestinal Bacterial Overgrowth Test (SIBO) Was Significant Correlations to Disease Activity of Primary Sjogren's Syndrome (pSS)

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SESSION INFORMATION
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Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

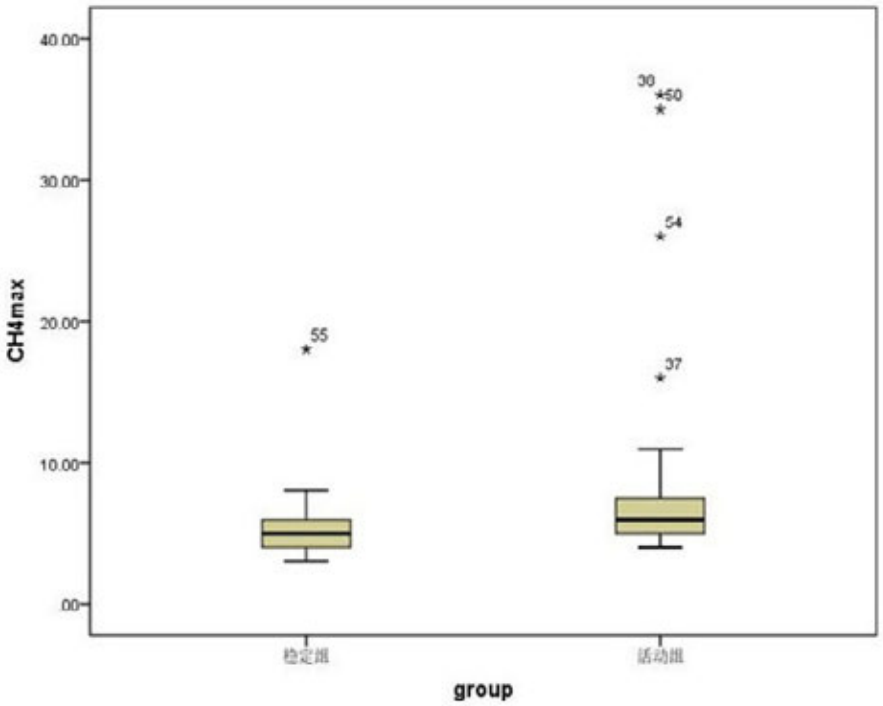
Background/Purpose: Primary Sjogren's syndrome (pSS) is a chronic inflammatory autoimmune disease that primarily affects the exocrine glands, which is involved in gastrointestinal unavoidably. Once intestinal flora imbalance, it will have a major impact on health. The Small intestinal bacterial overgrowth test (SIBO) is an important method for detecting bacterial growth in the small intestine.

To investigate the difference in the positive rate of SIBO between disease active and stable patients with pSS, and to retrospectively analyze the correlation between disease activity and SIBO.

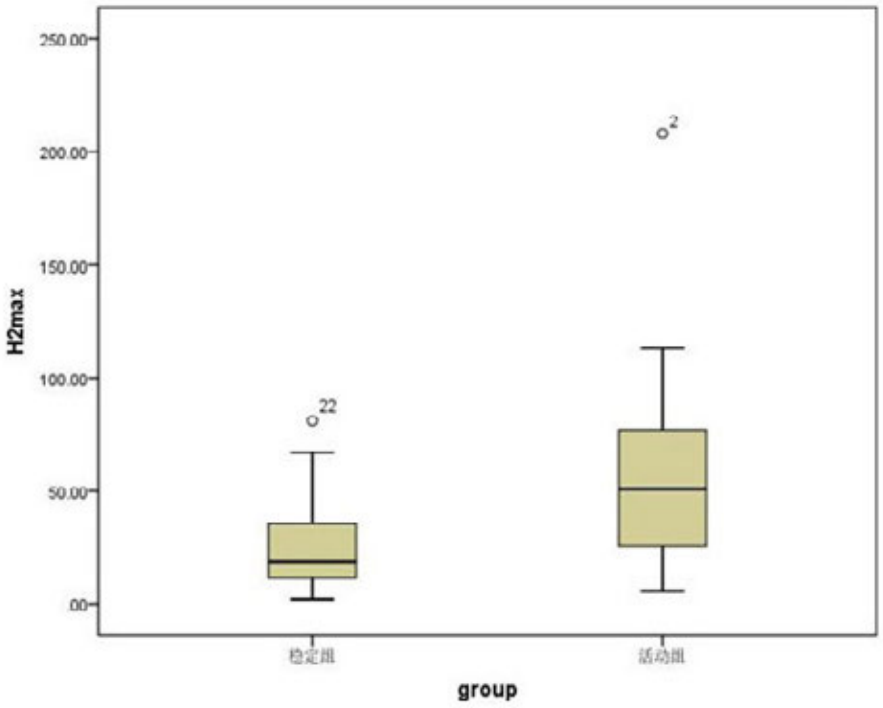
Methods: Total 60 patients with pSS diagnosed and treated in our hospital were selected as subjects of this study from October 2018 to March 2019, according to the PSS Disease Activity Rating System (SSDAI) scores. They were divided into Group A: active period (point≥5 points), 30 cases and group B: stable period (point< 5 points), 30cases. Two sets of clinical data were collected, including SSDAI scores and SIBO. The difference between the percentage of active and stable SIBO positive patients was compared. The maximum sum of hydrogen and methane in the two groups was tested by rank sum test, and the correlation between pSS disease activity and SIBO positive rate was analyzed.

Table 1 Comparison of SIBO positive rate between active period and stable period [n (%)]

	SIBO positive	SIBO negative	total
active period	28 (93.33%)	2 (6.67%)	30 (100%)
stable period	17 (56.67%)	13 (43.33%)	30 (100%)
Total	45 (75.00%)	15 (25.00%)	60 (100%)



Mann-Whitney U test of two sets of CH4MaX independent samples



Mann-Whitney U test of two sets of H2MaX independent samples

Results: The positive rate of SIBO in patients with active pSS was significantly higher than that in stable phase, and the difference was statistically significant (P< 0.05), as shown in Table 1. The two groups were compared with H2MaX or CH4MaX, and the Mann-Whitney U test results were statistically significant (P=0.001, P=0.003), as shown in image1 and image2.

Conclusion: SIBO positive rate was significant correlations to pSS disease activity. So, correcting intestinal flora imbalance combined with conventional treatment may bring greater benefits to patients with Sjogren's syndrome.

Disclosure: x. li, None; **X. li**, None; **s. dong**, None; **S. Zhang**, None; **J. Chen**, China; **g. liu**, None.

Abstract Number: 1464

The Oral Microbiome as a Risk Factor for Benign or Pathologic Autoimmunity Associated with Anti-SSA/Ro Positivity and Mimicry for Von Willebrand Factor Type a Domain Protein (vWFA) of *L. Mirabilis*

Robert Clancy,[1] Miranda Marion,[2] Peter Izmirly,[1] Hannah Ainsworth,[3] Timothy Howard,[3] Mala Masson,[1] Jill Buyon,[1] and Carl Langefeld[3], [1]NYU School of Medicine, New York, [2]Wake Forest School of Medicine, Winston-Salem, NC, [3]Wake Forest School of Medicine, Winston-Salem

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoantibody production precedes SLE or SS by years, including anti-Ro. Anti-Ro$^+$ mothers of children with congenital heart block (CHB) are a unique population at risk for pathologic autoimmunity, as many are asymptomatic (Asym/UAS) and become aware of autoantibodies due to fetal disease and yet have a 10-year progression rate to SS/SLE of 20%-30%. We hypothesized that variation in the oral microbiome correlates with transition to SLE or SS and pathogenicity involves sequence homology between Ro60 and bacterial von Willebrand factor type A domain protein (vWFA).

Methods: The oral microbiome of 25 anti-Ro$^+$ mothers of CHB children (Asym/UAS, N=9; SS/SLE, N=16) and 7 healthy controls (HC) were processed using 16S ribosomal RNA sequencing. Analysis of variance methods compared the centered log ratio transformed relative abundances for 1) HC vs. anti-Ro$^+$ mothers, and 2) assuming an ordering of severity from HC < Asym/UAS < SS/SLE. To adjust for multiple comparisons, a taxonomic stepdown method coupled with false discovery rate (FDR) was used. The Basic Local Alignment Search Tool evaluated homology of Ro60 at aa 371-381 and peptides of vWFA.

Results: Sequencing 16S rRNA identified microorganisms from 2 kingdoms, 16 phyla, 25 classes, 41 orders, 70 families, 164 genera, and 166 species. The Shannon Index (H) revealed that for each taxonomic level except species, there were significant reductions in diversity in the anti-Ro$^+$ mothers relative to HC ($P \leq 0.05$). There were global differences in the microbiota of these mothers relative to HC (perMANOVA P=0.00049). The phylum *Actinobacteria* was more abundant in the anti-Ro$^+$ mothers vs HC (P_{FDR}=0.0231). Within *Actinobacteria*, the class *Coriobacteriia* and subsequent lower taxonomic levels down to *Atopobium parvulum*, all exhibited increases in relative abundance in the anti-Ro$^+$ mothers compared to HC. There was a significant reduction in the relative abundance as clinical severity increased within one of the most frequent phyla, *Proteobacteria* (P_{FDR}=0.030; mean±SD; HC 0.24±0.07; Asym/UAS 0.19±0.12; SS/SLE 0.11±0.08). The difference in the relative abundances between Asym/UAS and SS/SLE within *Proteobacteria* was significant (P=0.042). Within *Proteobacteria*, the common class *Betaproteobacteria* also showed reduced relative abundance with increasing clinical severity (P_{FDR}=0.0037; HC 0.11±0.04; Asym/UAS 0.072±0.07; SS/SLE 0.031±0.04). These ordered differences were maintained down the taxonomic hierarchy to the genus (*Lautropia*, P_{FDR}=0.0072) and species within this genus (*L. mirabilis*, P_{FDR}=0.012). Next, sequences of vWFA secreted by these taxa were evaluated. For a comparison of Ro60 T cell epitope, FLLAVDVSASMNQ, the vWFA, VLVVFDNSSSMTA

AA Sequence	Protein
FLLAVDVSASMNQ	Ro60
LLLLLDVSGSMAG (WP_005674879.1)	vWFA *Lautropia mirabilis*
VLVVFDNSSSMTA (WP_012809344.1)	vWFA *Atopobium parvulum*

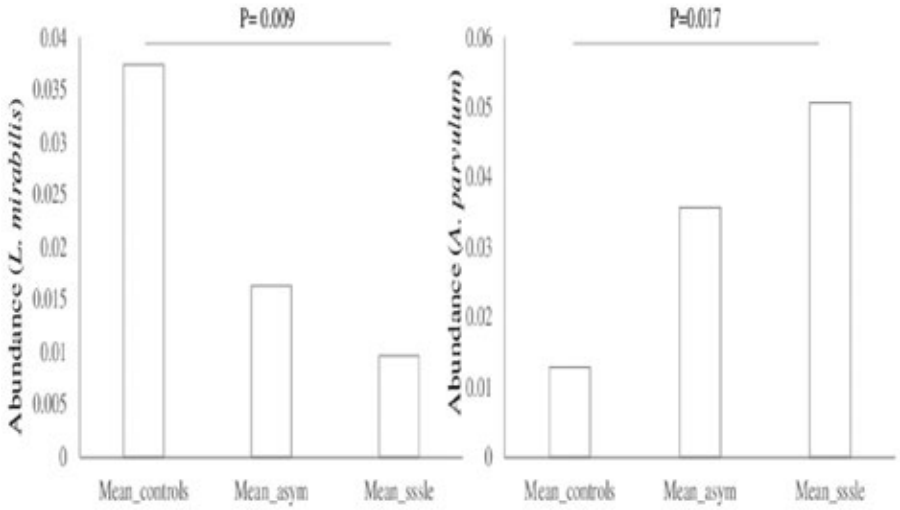


Figure 1. Sequence homology of human Ro60 and peptides found in bacterial vWFA (upper panel) and associations of targeted taxa and anti-Ro+ mothers vs controls (lower panel). For the former, note that Ro60 shares seven of its first 11 aa with L. mirabilis vWFA, while it shares only five with A. parvulum vWFA (sharing denoted by yellow and disharmony by red). For the latter, note the depletion of L mirabilis, possibly occurring secondary to a pathologic role of anti-Ro along with an expansion of A. parvulum, an opportunistic taxon.

vWFA of *A. parvulum* was not a fit due to the aromatic and polar aa at positions 5 and 9, respectively. In contrast, the vWFA of *L. mirabilis*, LLLLLDVSGSMAG, was identical at 7 of the first 11 aa.

Conclusion: These data provide evidence that the microbiome differs along a clinical spectrum of autoimmunity. In part, the data reflect a path involving depletion of *L. mirabilis*, which is secondary to a pathologic role of anti-Ro along with an expansion of *A. parvulum*, an opportunistic taxon.

Disclosure: R. Clancy, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **M. Marion**, None; **P. Izmirly**, GlaxoSmith-Kline, 5; **H. Ainsworth**, None; **T. Howard**, None; **M. Masson**, None; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **C. Langefeld**, None.

Abstract Number: 1465

Diversity Analysis of Intestinal Flora in Patients with Sjogren's Syndrome

Xiao-juan Mao,[1] **Sheng-xiao Zhang**,[2] Xu-fang Yin,[2] Ming-xing Zhang,[1] Jia Wang,[1] Min-jing Chang,[2] Meng-ting Qiu,[1] Jia-qian Zhang,[1] Chong Gao,[3] and Xiao-feng Li[1], [1]The Second Hospital of Shanxi Medical University, Taiyuan, China (People's Republic), [2]The Second Hospital of Shanxi Medical University, Taiyuan, Shanxi, China (People's Republic), [3]Brigham and Women's Hospital, Harvard Medical School, Boston

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Sjogren's syndrome (SS) is characterized by lymphocyte infiltration of exocrine gland, resulting in decreased exocrine function and dry symptoms, affecting the quality of life of patients. Studies have found that intestinal microbial imbalance is associated with sjogren's syndrome. This study aims to detecte the differences

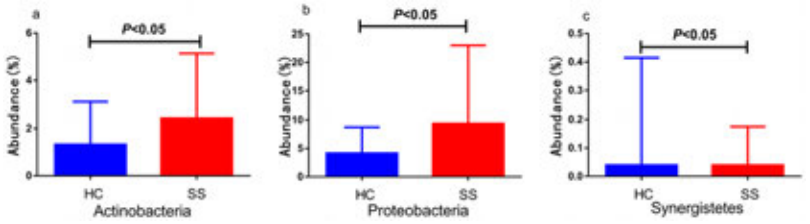


Figure1 The phylum level profile for SS patients and healthy control.

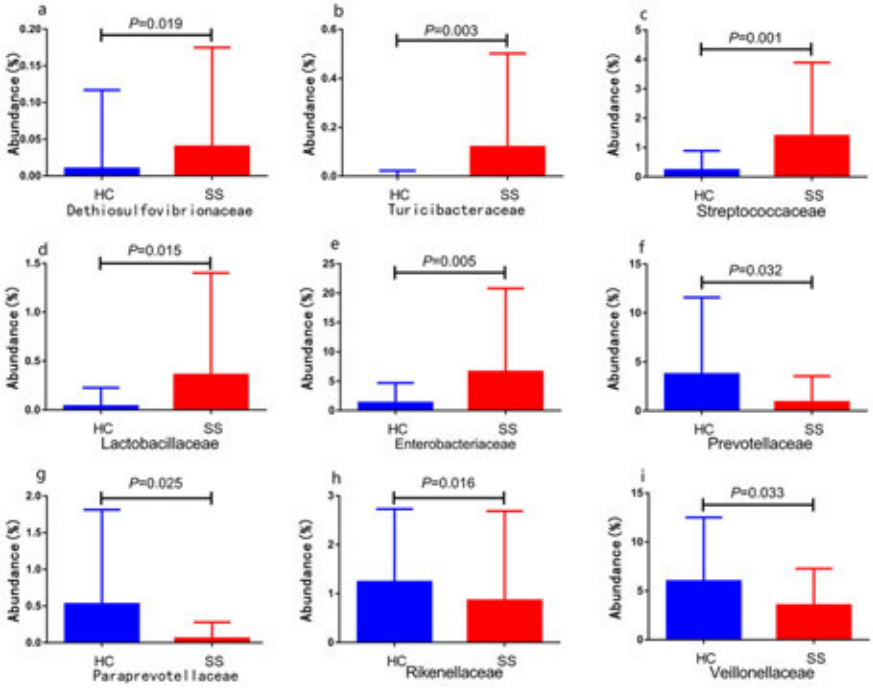


Figure2 The division level profile for SS patients and healthy control

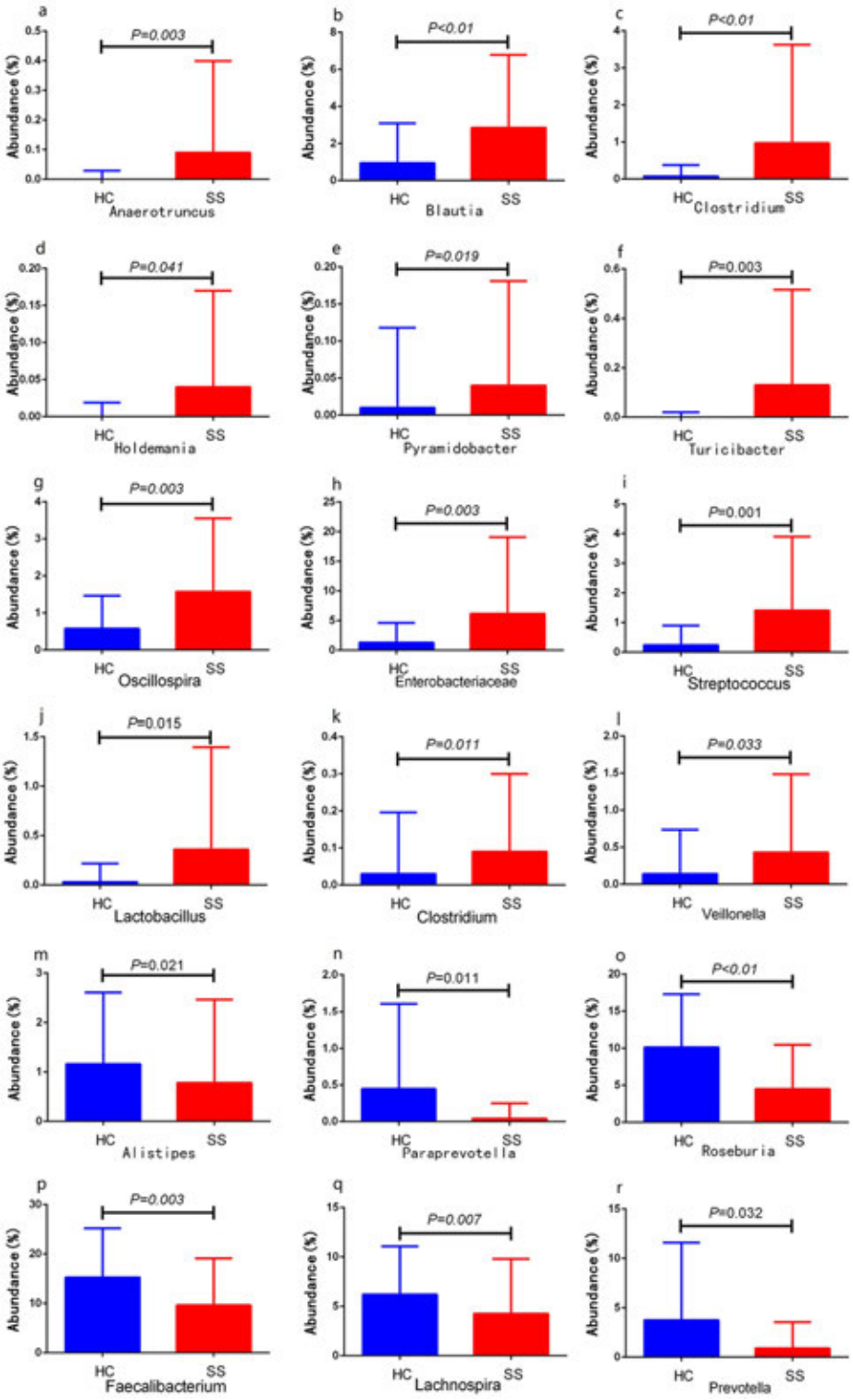


Figure3 The genus level profile for SS patients and healthy control

of microbial population distribution in stool samples of healthy individuals and patients with sjogren's syndrome (SS), and explore the changes of intestinal flora in SS patients.

Methods: The 16s rRNA V3 region in the stool samples of 29 SS patients was qualitatively analyzed by using 16s high-through put sequencing platform, and compared with that of 126 healthy controls (HC).

Results: Patients with SS had an increased feces bacterial flora of bacteria species OTU information (P< 0.01) and the diversity index (Shannon) increased (P< 0.05), though only a slightly difference of Evenness index compared with that of HC (P >0.05). As for intestinal flora abundance patients had more Actinobacteria, Proteobacteria, Synergistetes at phylum level (P< 0.05) and also had a large amounts of Dethiosulfovibrionaceae, Turicibacteraceae, Streptococcaceae, Lactobacillaceae, Enterobacteriaceae at division level (P< 0.05) but a lower proportion of Prevotellaceae, Paraprevotellaceae, Rikenellaceae, Veillonellaceae (P< 0.05). When considered genus level, there were also more percentages in Anaerotruncus, Blautia, Clostridium, Holdemania, Pyramidobacter, Turicibacter, Oscillospira, Enterobacteriaceae, Streptococcus, Lactobacillus, Clostridium, Veillonella (P< 0.05), but smaller proportion of Alistipes, Paraprevotella, Roseburia, Faecalibacterium, Lachnospira, Prevotella (P< 0.05) in SS patients when compared with those of HC.

Conclusion: The diversity and equilibrium of bacterial community in intestinal microecology of SS patients were significantly different from that of normal population.

Disclosure: X. Mao, None; **S. Zhang**, None; **X. Yin**, None; **M. Zhang**, None; **J. Wang**, None; **M. Chang**, None; **M. Qiu**, None; **J. Zhang**, None; **C. Gao**, None; **X. Li**, None.

Abstract Number: 1466

Evaluation of Changes in Oral Health-Related Quality of Life over Time in Patients with Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II

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Background/Purpose: In addition to xerostomia symptoms, patients with Sjögren's syndrome (SS) experience pain and discomfort in the oral cavity, and difficulties in speaking and eating, due to refractory stomatitis, oral ulcer, glossitis, atrophy in the oral mucosa and tongue, and increased carious teeth. These dry mouth symptoms cause not only intraoral problems but also psychological and social problems; therefore, oral health-related quality of life (OHRQoL) is broadly deteriorated in SS patients. However, no previous reports have documented changes in OHRQoL evaluated over time in SS patients. In this study, we evaluated OHRQoL in SS patients and identified their specific troubles. Furthermore, we monitored OHRQoL over time in the same SS patients, and revealed changes in the troubles and the relationship with their clinical conditions.

Methods: Thirty-five SS patients (22 with primary SS and 13 with secondary SS; 32 women and 3 men; mean age, 56.2 ± 13.2 years; mean disease duration, 5.8 ± 3.7 years) and 23 non-SS (control) individuals (18 women and 5 men; mean age, 56.1 ± 17.4 years) participated in this study. All SS patients met the 2012 American College of Rheumatology classification criteria for SS. Individuals with factors affecting intraoral lesion formation, saliva secretion, or OHRQoL were excluded. OHRQoL was quantitatively evaluated with the Japanese version of shortened Oral Health Impact Profile (OHIP-14), which is a self-administered questionnaire (maximum possible score, 56 points). Saliva

secretion was measured by the chewing gum test method. Twenty-two SS patients and 14 non-SS individuals completed 3-year follow-up, and underwent the OHIP-14 survey and saliva secretion measurement again three years after the first evaluation.

Results: The SS group had a significantly higher OHIP-14 score (i.e., lower OHRQoL) than the non-SS group (11.3 ± 9.4 vs 7.1 ± 7.6; p=0.027). The high-score SS group was significantly more advanced in age (61.5 ± 10.4 vs 52.7 ± 14.0; p=0.026) and had a significantly smaller amount of saliva secretion (6.9 ± 4.2 vs 9.3 ± 4.4 ml/ 10min; p=0.047) compared to the low-score SS group. Among individual items in OHIP-14, scores for "Trouble pronouncing words," "Uncomfortable to eat," "Self-conscious," and "Diet unsatisfactory" were significantly higher in the SS group than in the non-SS group. In the SS group, the OHIP-14 score significantly increased over 3 years (10.2 ± 8.8 vs 12.6 ± 9.2; p=0.040), while the score remained unchanged in the non-SS group. A negative correlation was found between the change rate of saliva secretion amount and the OHIP-14 score change over 3 years in the SS group (r_s=–0.418, p=0.027). Among individual OHIP-14 items, scores for "Irritable with others," "Difficulty doing jobs," "Life unsatisfying," and "Unable to function" significantly increased in 3 years, and scores for other items remained comparable with baseline scores.

Conclusion: In SS patients, a decrease in OHRQoL occurred over 3 years and was associated with a decrease in saliva secretion. Moreover, SS patients' troubles in social life and mental aspect were found to intensify over time.

Disclosure: N. Azuma, None; **Y. Katada**, None; **A. Nishioka**, None; **M. Sekiguchi**, None; **M. Kitano**, None; **S. Kitano**, None; **H. Sano**, None; **K. Matsui**, Bristol-Myers Squibb, 5, 8.

Abstract Number: 1467

Clinical Characteristics of Primary Sjögren's Syndrome in Adult Patients Diagnosed at Age Less Than or Equal to 35 Years versus Those over 35 Years of Age

Noel Agustin Callahuara Goiburu,[1] Patricia Sasaki,[1] Anastasia Secco,[2] Catalan Pellet,[3] Nadia Riscanevo,[4] Janet Flores,[5] Francisco Caeiro,[5] cristina Amitrano,[6] Cecilia Asnal,[7] Alejandro Nitsche,[8] Carolina Segura Escobar,[9] Julia Demarchi,[10] Damian Duartes,[10] Lida santiago,[11] Laura Raiti,[12] Vanesa Cruzat,[13] Carla Gobbi,[14] Paula Alba,[15] Silvia Papasidero,[16] Sofia Velez,[17] Vicente Juarez,[18] and Gabriela Salvatierra[19], [1]Rivadavia, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [2]Hospital Rivadavia, Caba, Buenos Aires, Argentina, [3]Rivadavia, CABA, Argentina, [4]Hospital Privado de Córdoba, Cordoba, Cordoba, Argentina, [5]Hospital Privado de Córdoba, Cordoba, Argentina, [6]Hospital Aleman, CABA, Argentina, [7]Instituto Centenario, Buenos Aires, Buenos Aires, Argentina, [8]Hospital Aleman, Ciudad Autonoma de Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina, [9]Hospital Británico, Buenos Aires, Buenos Aires, Argentina, [10]Hospital Británico, Ciudad Autonoma de Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina, [11]OMI, Ciudad Autonoma de Buenos Aires, Argentina, [12]Clinica Bessone, Buenos Aires, Buenos Aires, Argentina, [13]Clinica Bessone, Buenos Aires, Argentina, [14]CÁTEDRA DE CLÍNICA MÉDICA I, HOSPITAL CÓRDOBA, FACULTAD DE CIENCIAS MÉDICAS, UNIVERSIDAD NACIONAL DE CÓRDOBA, ARGENTINA, Cordoba, Cordoba, Argentina, [15]UNIDAD DE REUMATOLOGÍA, CÁTEDRA DE SEMIOLOGÍA, HOSPITAL CÓRDOBA, FACULTAD DE CIENCIAS MÉDICAS, UNIVERSIDAD NACIONAL DE CÓRDOBA, ARGENTINA, Cordoba, Cordoba, Argentina, [16]Hospital General de Agudos Dr. E. Tornú, Ciudad Autónoma de Buenos Aires, Buenos Aires, Argentina, [17]Consultorio Privado S.V, Buenos Aires, Buenos Aires, Argentina, [18]Hospital Milagros de Salta, Salta, Salta, Argentina, [19]IPRI, Santiago del estero, Santiago del Estero, Argentina

SESSION INFORMATION

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Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Table 1 General Characteristics

	Diagnosis ≤ 35 years n: 100	Diagnosis > 35 years n: 565	P value
Female sex (%)	92.11	95.69	0.18
Hypothyroidism ((%)	15	21.95	0.115
Diabetes (%)	1	2.48	0.359
Follow-up time (years) (mean, RIQ)	4 (1-8)	3 (1-6)	0.15
Corticosteroids (%)	32.88	34.26	0.819
Hydroxychloroquine (%)	85.92	78.39	0.148
Inmunosuppresants (%)	15	17.20	0.588
Symptomatic Treatm(%)	90.22	93.03	0.565
Pilocarpine (%)	27.14	29.87	0.646

Table 2. **Results**

Glandular Manifestations	Diagnosis ≤ 35 years n: 100 (%)	Diagnosis > 35 years n: 565 (%)	P value
Xerophthalmia	**90.72**	**95.64**	**0.043**
Xerostomia	87.37	90.33	0.377
Xeroderma	**42.35**	**55.36**	**0.026**
Xerovagina	30.86	39.18	0.153

Systemic Manifestations (ESSDAI)	Diagnosis ≤ 35 years n: 100 (%)	Diagnosis > 35 years n: 565 (%)	P value
Articular	66.00	68.32	0.647
Cutaneous	11.00	9.38	0.613
Pulmonary (Persistent dry cough)	**6.00 (4.04)**	**15.40 (11.47)**	**0.012 (0.03)**
Renal	**6.00**	**1.59**	**0.016**
PNS	**4.04**	**11.31**	**0.015**
CNS	1.00	2.65	0.279
Haematological	23.00	21.42	0.723
Biological	54.05	56.26	0.724
Parotid swellig	31.63	27.39	0.388
Muscular	2.02	1.62	0.513

Background/Purpose: Although there is little information, the debut of primary Sjögren's syndrome in adult patients aged less than or equal to 35 years, would be expressed with less pronounced Sicca manifestations and with a high degree of systemic commitment. For this reason, we decided to compare the behavior of the disease in the Argentine population with a diagnosis of primary Sjögren's syndrome at age less than or equal to 35 years versus those older than 35 years.

Methods: Cross-sectional observational analytical study. We analyzed the data of patients older than 18 years, with diagnosis of primary Sjögren's syndrome (American-European criteria 2002 / ACR EULAR 2016), included in the GESSAR database (Sjögren Syndrome Study Group of the Argentine Society of Rheumatology), with minus one control in the last 12 months. The presence of systemic manifestations assessed from the domains of the ESSDAI and the glandular manifestations, and as possible confounders were considered: sex, diabetes, hypothyroidism, treatments and time of follow-up in years of each group. The continuous variables were described as mean and standard deviation or median and interquartile range (RIQ), according to distribution and sample size. The categorical variables were expressed in percentages. For the bivariate analysis, for the continuous variables, the Student or Mann Whitney test was used according to distribution and sample size. The categorical variables were analyzed using Chi square or Fisher's exact test, according to the expected frequency distribution table. A $p < 0.05$ was considered statistically significant.

Results: 665 patients were included. One hundred of them with an age at diagnosis ≤ 35 years and with a mean age at diagnosis of 29 ± 4 years, 92% of them women. The average age at diagnosis of the group > 35 years was 54 ± 11 years. Within the glandular manifestations, statistically significant differences were found between ≤ 35 years vs >35 years, in xerophthalmia (90.72% vs 95.64%, *p*: 0.04) and xeroderma (42.35% vs 57.36%, *p*: 0.03). No significant differences were found in xerostomia (87.37% vs 90.33%, *p*: 0.38), nor xerovagina (30.86% vs 39.18%, *p*: 0.15). Statistically significant differences were found between ≤35 years vs >35 years in the following domains of ESSDAI: peripheral nervous system (4.05 vs 11.32, *p*: 0.03), respiratory (6% vs 15.40%, *p*: 0.01) and renal (6% vs. 1.59%, *p*: 0.02). In a subanalysis of ESSDAI domains, significant differences were found in arthritis (37.37% vs 27.16%, *p*: 0.04) and persistent dry cough (4.04% vs 11.47%, *p*: 0.03).

Conclusion: A significantly lower frequency of xerophthalmia and xeroderma was observed in the group ≤35 years old compared to those >35 years old. Regarding systemic activity, less involvement of the peripheral nervous system and pulmonary domain and higher in the renal domain, with statistically significant differences. These results suggest a lower glandular compromise in patients diagnosed at a younger age, without a characteristic differential pattern in terms of systemic involvement.

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Effects of Resistive Exercise on Fatigue and Disease Activity in Women with Primary Sjogren's Syndrome

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SESSION INFORMATION
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Background/Purpose: Fatigue is a frequent symptom of pSS, considered debilitating and the most important cause of dysfunction in these patients. The present study aimed to assess the effectiveness of resistive exercise as a non-pharmacological intervention for reducing fatigue in primary Sjögren's Syndrome patients (pSS).

Methods: This is a single-blinded randomized clinical trial performed at the Ophthalmology outpatient clinic and at the Center for Psychobiology Studies at the Federal University of São Paulo, Brazil. Participants were randomized into a resistive exercise program and a control group and evaluated by a blinded evaluator. We used ESSDAI to evaluate disease activity; ESSPRI to evaluate fatigue, pain and dryness; PROFAD, VAS–fatigue and FACIT-fatigue for fatigue; and VAS-pain for pain. (Table 1) Participants from the exercise group performed a resistive program of 16 weeks with a one-hour duration, 2 times a week.

Results: We evaluated 73 female patients diagnosed with pSS according to the European-American Consensus Group Criteria and with complaints of fatigue. A total of 59 participants were included and randomized for exercise group (n=29) and control group (n=30). Participants in the exercise group had mean age of 62.1 years (SD=12.9) and a mean time of disease symptoms of 19 years (SD=10.4). The mean age in the control group was 58.1 years old (SD=10.2) and mean symptom time was 13.8 years (SD=9.3), with no difference between groups ($p< 0.001$). According to ESSDAI, there was no significant difference in disease activity between the two groups over the study time. All scales related to fatigue and pain presented better scores in the exercise group when comparing to control group. (See Table 2 for detailed results) ESSPRI- fatigue exercise group had a mean score of 6.5 before and of 2.23 after intervention and control group a mean score of 5.52 versus 6.03; ESSPRI- pain exercise group mean score of

Table 1 - Questionnaires

Questionnaire	Definition
ESSDAI	EULAR Sjögren's Syndrome Disease Activity Index: to evaluate disease activity;
ESSPRI	EULAR Sjögren's Syndrome Patient Reported Index: to evaluate fatigue, pain and dryness;
PROFAD	Profile of Fatigue and Discomfort: to evaluate fatigue in different domains (somatic, mental, arthralgia, vascular)
VAS-fatigue	Visual Analog Scale: to evaluate fatigue
FACIT-fatigue	Functional Assessment of Chronic Illness Therapy – fatigue: to evaluate fatigue
VAS-pain	Visual Analog Scale: to evaluate pain

Table 2 - Questionnaires scores before and after intervention

	Control				Exercise				p-intergroup
	INITIAL		FINAL		INITIAL		FINAL		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	FINAL
VAS PAIN	5.8	2.7	6	2.8	6	2.9	3.1	2.5	< 0.01
VAS FATIGUE	6.1	3	6.4	2.6	6.7	2.2	2.4	1.9	< 0.001
ESSDAI	3.3	3.4	3.1	3.2	2.5	3.5	1.9	3.2	0.223
PROFAD									
Somatic	3.52	2.03	3.14	1.96	2.98	1.72	1.14	1.21	< 0.001
Mental	3.6	2.21	3.98	2.23	3.57	2.03	3.03	2.03	0.322
Arthralgia	3.38	2.04	3.26	1.68	2.55	1.82	1.45	1.55	< 0.001
Vascular	1.31	2.39	1.07	1.93	1.38	2.24	1.28	1.94	0.776
FACIT	30.5	12.8	30.4	12	34	10.1	42.4	10.3	< 0.001
ESSPRI									
Dryness	6.07	2.78	6.86	2.39	7.73	1.76	7.73	8.44	0.17
Fatigue	5.52	3.05	6.03	2.87	6.5	2.37	2.23	2.13	< 0.001
Pain	5.55	2.97	5.28	2.85	5.57	3.13	2.8	2.82	< 0.001

5.57 before and of 2.8 after intervention and control group mean score of 5.55 before versus 5.28 after intervention. The exercise group had an initial mean in VAS-fatigue of 6.7 dropping significantly to 2.4 at the end of the training while the control group had no difference from the beginning to the final time. Also, VAS-pain in exercise group was 6 and dropped to 3.1 while in the control group had no difference. In the PROFAD questionnaire, the mean physical fatigue score in the exercise group was initially 2.98 dropping to 1.14 at the end and in the control group, the results did not present significant variation; in PROFAD- arthralgia, initial and final means scores in exercise group were 2.55 and 1.45 respectively, while in the control group there was no significant variation between the initial and final scores. Regarding FACIT, there was a significant improvement in the score for fatigue in the exercise group at the end of the exercise program (initial mean of 34 and final mean score of 42.4) while in the control group there was no significant difference.

Conclusion: The present study states that after a resistive 16-week exercise program, patients with primary Sjogren's Syndrome improved the parameters related to fatigue and pain with no effect in reducing or increasing disease activity.

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New 2019 SLE EULAR/ACR Classification Criteria for SLE Are Valuable for Distinguishing Patients with SLE from Patients with pSS in Daily Practice

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Background/Purpose: The new 2019 SLE EULAR/ACR Classification Criteria for Systemic lupus erythematosus (SLE) have been developed to find a better equilibrium between specificity and sensitivity compared to SLE ACR-1997 and SLE SLICC. Given the biological and clinical similarities and the frequent overlap between SLE and primary Sjögren's Syndrome (pSS), these criteria could be useful in clinical practice for differentiating SLE from pSS.

The aim of this study was to explore the utility of the 2019 SLE EULAR/ACR criteria compared to SLE ACR-1997 and SLE SLICC criteria for differentiating in clinical practice SLE from pSS and overlap between both.

Methods: This retrospective study included 3 different groups of patients followed in Department of Rheumatology, Hopitaux Universitaires Paris Sud: (i) 49 SLE patients (diagnosis made by the clinician with exclusion of patients with another connective tissue disease associated). (ii) 49 pSS patients randomly chosen from the Paris Sud database, fulfilling the pSS ACR/EULAR 2016 criteria, with exclusion of patients with association of another connective tissue disease (iii) 26 SLE/Sjögren's Syndrome (SS) overlap patients based on clinical diagnosis, made of 13 patients diagnosed as SLE and presenting objective signs of associated SS (minor salivary glands biopsy Focus Score ≥ 1, and/or objective sicca syndrome) and 13 patients diagnosed as SS with anti-DNA antibodies.

The biological, immunological, and clinical data were collected at diagnosis, or at the first visit at the centre. SLE ACR-1997, SLE SLICC and 2019 SLE EULAR/ACR criteria were tested in each group. Categorical variables were compared using a Chi^2 or Fischer's exact test as appropriate. Quantitative variables were compared with Kruskal-Wallis test.

Results: As shown in Table, the 2019 SLE EULAR/ACR criteria were met in 97.9% of the SLE patients vs 4.2% of the pSS patients ($p< 0.001$). Interestingly, patients from the overlap group fulfilled both criteria for SLE and SS confirming the capacity of the criteria to detect the overlap. Lymphopenia and biological inflammation were significantly associated with SLE (respectively 33% vs 14%, $p=0.004$ and 28% vs 14%, $p< 0.001$), whereas initial rheumatoid factor detection was significantly associated with pSS (3.5% vs 35%, $p=0.001$). Systematic assessment of sicca syndrome could help to differentiate SLE from pSS. Overlap syndrome patients had a more systemic disease than pSS patients as assessed by the EULAR Sjögren's syndrome Disease Activity Index (ESSDAI): respectively 5.6 vs 9.7 ($p=0.001$).

Conclusion: In conclusion this study shows that the new 2019 SLE EULAR/ACR criteria for SLE can be useful in clinical practice helping to differentiate between SLE and pSS and detecting overlap presentations.

Characteristics		SLE pants	pSS patients	Overlap patients	p-value
General features	Mean age at diagnosis, years (SD)	33 (11.88)	54 (13.96)	41 (16.43)	p = 3.67E-9
	Female, n (%)	40 (81.6)	49 (100)	26 (100)	p = 0.001
	Mean SLEDAI, mean (SD)	11.32 (7.20)	x	6.5 (5.34)	p = 0.002
	Mean ESSDAI, mean (SD)	x	5.55 (3.28)	9.65 (5.43)	p = 0.001
	Mean disease duration, years (SD)	14.2 (8.8)	14.4 (6.5)	14 (5)	p = 0.748
Clinical features	Fever, n (%)	9 (18.37)	1 (2.04)	3 (11.53)	p = 0.003
	Photosensitivity, n (%)	9 (18.37)	2 (4.08)	4 (15.38)	p = 0.082
	Acute/subacute lupus, n (%)	22 (44.90)	0 (0)	4 (15.38)	p = 2.48E-7
	Chronic lupus, n (%)	8 (16.32)	0 (0)	0 (0)	p = 0.001
	Oral ulcerations, n (%)	6 (12.24)	2 (4.08)	0 (0)	p = 0.083
	Non-scarring alopecia, n (%)	7 (14.29)	0 (0)	2 (7.69)	p = 0.024
	Pleurisy, n (%)	7 (14.29)	0 (0)	0 (0)	p = 0.003
	Pericarditis, n (%)	4 (8.16)	0 (0)	1 (3.84)	p = 0.121
	Adenomegalies, n (%)	10 (20.40)	3 (6.12)	5 (19.23)	p = 0.099
	Myalgias, n (%)	4 (8.16)	14 (28.57)	5 (19.23)	p = 0.034
	Arthralgias, n (%)	45 (91.84)	41 (83.67)	19 (73.08)	p = 0.097
	Synovitis, n (%)	26 (53.06)	3 (6.12)	8 (30.77)	p = 2.50E-6
	Cough, n (%)	0 (0)	12 (24.49)	9 (34.61)	p = 0.0001
Biological features	Leukopenia*, n (%)	9 (18.36)	3 (6.12)	4 (23.07)	p = 0.178
	Lymphopenia**, n (%)	16 (32.65)	7 (14.29)	13 (50)	p = 0.004
	Mean CRP, mg/L (SD)	13.68 (28.13)	9.32 (13.98)	7.66 (15.22)	p = 0.0004
Immunological features	ANA >1/80 IIF, n (%)	48 (97.96)	36 (73.47)	25 (96.15)	p = 0.003
	Anti-DNA, n (%)	44 (89.80)	0 (0)	26 (100)	p = 1E-23
	Anti-Sm, n (%)	19 (38.77)	0 (0)	7 (26.92)	p = 1E-5
	RF positivity, n (%)	1 (2.04)	17 (34.69)	11 (42.30)	p = 0.001
	APL, n (%)	20 (40.82)	7 (14.28)	7 (26.92)	p = 0.013
	Hypocomplementemia C3 ↓, n (%)	13 (26.53)	0 (0)	3 (11.54)	p = 5.83E-5
	Hypocomplementemia C4↓, n (%)	24 (48.98)	9 (18.36)	9 (34.6)	p = 0.006
	Hypergammaglobulinemia ***, n (%)	18 (58.06)	21 (43.75)	22 (88.46)	p = 0.0002
	Mean serum gammaglobulin level, g/L (SD)	15.4 (5.44)	14.3 (6.44)	19.1 (6.58)	p = 0.002
Renal features	Significant glomerular proteinuria, n (%)	17 (34.69)	0 (0)	1 (3.85)	p = 1.53E-6
Sets of criteria	SLE ACR-1997, n (%)	38 (77.6)	1 (2.1)	10 (38.5)	p = 2.02E-13
	SLE SLICC, n (%)	48 (97.9)	4 (8.3)	20 (76.9)	p = 2.18E-19
	2019 SLE EULAR/ACR, n (%)	48 (97.9)	2 (4.2)	22 (84.6)	p = 3.02E-21
	pSS ACR/EULAR 2016, n (%)	0 (0)	49 (100)	26 (100)	p= 1.000

Table: Patients characteristics

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Health-Related Quality of Life in Primary Sjogren's Syndrome: Insights from Using PROMIS and Comparison to ESSPRI

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SESSION INFORMATION

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Table 1. Baseline demographic and clinical characteristics of patients who met 2016 ACR/EULAR Classification Criteria for Sjogren's Syndrome.

Demographic/Clinical Characteristic	Primary Sjogren's Syndrome (n=99)
Age, median (IQR)	57 (43, 66)
Gender, (n, % female)	89 (90%)
Race (n, % white)	80 (81%)
ESSPRI, median (IQR)	
Total	5.3 (3.7, 6.8)
Pain (0-10)	4.5 (2, 7)
Dryness (0-10)	6 (5, 8)
Fatigue (0-10)	6 (4, 7)
Hydroxychloroquine (n, %)	63 (64%)
Rituximab (n, %)	7 (7%)
Methotrexate (n, %)	11 (11%)
Leflunomide (n, %)	3 (3%)
Azathioprine (n, %)	3 (3%)
PROMIS Global Profile Mean T-Score (SD)	
Pain Interference	56.6 (11.5)
Physical Function	44.5 (10.0)
Fatigue	56.9 (11.0)
Social Participation	48.0 (11.1)
Sleep Disturbance	52.9 (8.7)
Anxiety	55.2 (9.6)
Depression	50.8 (8.9)

ESSPRI= EULAR's Sjogren's Syndrome Patient Reported Index.

Background/Purpose: Sjogren's Syndrome (SS) is a chronic, autoimmune disease affecting the exocrine glands that may negatively affect health-related quality of life (HRQL). The importance of measuring symptoms and impacts has increasingly been recognized in patient care and clinical trials. Patient Reported Outcome Measurement Information System (PROMIS) provides universal HRQL instruments, but has not been previously implemented in SS. Currently, EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI) is widely utilized in SS but is limited in measuring HRQL domains. We sought to evaluate how selected PROMIS domains in SS would compare to US normative values and how scores may correlate with the ESSPRI.

Methods: This was a cross-sectional evaluation of adult patients with SS who completed PROMIS short-forms (SF) (depression 4a, anxiety 4a, fatigue 8a, physical function 10a, pain interference 8a, sleep disturbance 4a, participation in social roles and activities 8a) and had a clinical assessment between May 2018-March 2019. PROMIS T-scores are normalized to a score of 50 with a standard deviation of 10 in the US population; higher scores indicate more of the concept being measured; and a clinically meaningful difference is generally considered ½ SD, or 5 T-score units for some domains. Descriptive statistics, including means and proportions, were calculated for disease-related and sociodemographic variables. Pearson correlation was used to evaluate the relationship between subdomains of the ESSPRI and PROMIS.

Results: Ninety-nine individuals met the 2016 ACR criteria for SS and completed PROMIS SF and clinical measures. Individuals with SS had a median age (IQR) of 57 (43, 66) and were mostly female (90%) and white (81%) (Table 1). Median (IQR) ESSPRI scores were 5.33 (3.66, 7), indicating moderate patient-reported disease activity; median (IQR) ESSRPI subdomain scores were 5 (2, 7) for pain, 6 (5, 8) for dryness, and 6 (4, 7) for fatigue. PROMIS scores for pain interference, fatigue, physical function, and anxiety were at least ½ SD worse than US population normative values. PROMIS pain interference (r=0.78) and fatigue (r=0.79) highly correlated with ESSPRI pain and fatigue sub-domains, respectively. PROMIS fatigue was highly correlated with pain interference (r=0.78) and negatively correlated with social participation (r=-0.71); pain interference was negatively correlated with social participation (r=-0.78) and physical

Table 2. Correlation between ESSPRI domains and PROMIS domains in patients with primary Sjogren's Syndrome.

	ESSPRI Pain (n=96)	ESSPRI Fatigue (n=96)	ESSPRI Dryness (n=96)	PROMIS Pain Interference (n=99)	PROMIS Physical Function (n=98)	PROMIS Fatigue (n=98)	PROMIS Social Participation (n=99)	PROMIS Sleep Disturbance (n=97)	PROMIS Anxiety (n=96)	PROMIS Depression (n=97)
ESSPRI Pain	1.00									
ESSPRI Fatigue	0.67	1.00								
ESSPRI Dryness	0.40	0.33	1.00							
PROMIS Pain Interference	0.78	0.60	0.30	1.00						
PROMIS Physical Function	-0.68	-0.60	-0.45	-0.73	1.00					
PROMIS Fatigue	0.52	0.79	0.20	0.71	-0.66	1.00				
PROMIS Social Participation	-0.61	-0.71	-0.31	-0.78	0.81	-0.84	1.00			
PROMIS Sleep Disturbance	0.50	0.53	0.23	0.55	-0.53	0.62	-0.55	1.00		
PROMIS Anxiety	0.24	0.33	0.07	0.48	-0.35	0.52	-0.49	0.49	1.00	
PROMIS Depression	0.30	0.33	0.05	0.47	-0.33	0.49	-0.47	0.52	0.80	1.00

function (r=-0.73) (Table 2). PROMIS anxiety and depression were highly correlated (r=0.80) with each other but not with other ESSPRI or PROMIS domains.

Conclusion: In our SS cohort, PROMIS pain interference and fatigue scores highly correlated with respective ESSPRI domains. Levels of PROMIS pain interference, fatigue, physical function, and anxiety were at least ½ SD worse than US population normative values. Pain interference and fatigue were not highly correlated with anxiety or depression. PROMIS instruments should be considered for use in SS research and clinical care. Future work will require validation in a larger cohort of SS patients and across broader demographics.

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Polyautoimmunity and Major Organ Involvement Prevalence in Sjögren´s Syndrome: Thyroid, Liver, Lung and Kidney as Targets. a Single Center Cross Sectional Study

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Background/Purpose: Polyautoimmunity has been described to be associated with primary Sjögren´s syndrome (SjS) and the most frequent observed associated autoimmune diseases (AID) are autoimmune thyroid disease, autoimmune hepatitis and primary biliary cirrhosis, which are common organ-specific AID. In the same track, renal and lung involvement has increasingly been documented in SjS further highlighting its systemic nature. Objective: To describe and classify prevalence of polyautoimmunity and major organ involvement in a primary SjS-cohort.

Methods: This cross-sectional study included 179 patients [160 (89%) females and 19 (11%) males] diagnosed with primary SjS and fulfilling the ACR classification criteria that had been admitted to our outpatient clinic between December 2008 and December 2018. Demographic and disease-specific characteristics were recorded in all patients.

Results: In our cohort the median age at diagnosis was 57 years (range: 20-85). Thyroid AID was found in 55/179 (30%) patients, with the following distribution: Hashimoto thyroiditis without (n=21) and with hypothyroidism (n=22), Graves's disease without (n=4) and with thyroidectomy (n=8). Liver AID was detected in 8/179 patients (4%), 3 patients with autoimmune hepatitis and 5 patients with primary biliary cirrhosis. Regarding major organ involvement, 20/179 (11%) patients had renal manifestations: renal insufficiency (n=12), glomerulonephritis (n= 3), interstitial ne-

phritis (n=2) and IgA nephritis (n=3). Eight/179 (4%) patients had lung manifestations: interstitial fibrosis (n=6), emphysema (n=1) and chronic obstructive pulmonary disease (n=1).

Conclusion: Our results add evidence for the presence of polyautoimmnunity and major organ involvement in SjS. We found a slightly lower prevalence of polyautoimmunity and major organ involvement compared to recently reported data. Nonetheless, extra-glandular organ involvement should be assessed in order to elucidate cumulative damage and how it might impact outcome, prognosis and therapeutic approaches in SjS.

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Abstract Number: 1472

Primary Sjögren's Syndrome and Development of Another Connective Tissue Disease During Follow-up

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's Syndrome (pSS) is a chronic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands. Is the connective tissue disease that is most frequently associated with other autoimmune disorders and approximately 30% of these patients have another associated autoimmune condition. To date, no studies have evaluated the frequency of another autoimmune connective tissue disease development in patients with initial diagnosis of pSS.

OBJECTIVES: To determine the frequency of patients who, following the diagnosis of pSS, developed another autoimmune rheumatic disease during their follow-up using the GESSAR database (Sjögren Syndrome Study Group of the Argentine Society of Rheumatology). To detail the connective tissue diseases that occurred most frequently in these patients. To describe the clinical, serological and salivary gland histology characteristics of these patients.

Methods: Descriptive, observational, cross-sectional study. We analyzed the data of patients diagnosed with pSS (American-European criteria 2002 / ACR-EULAR 2016), included in the GESSAR database. It was considered the

development of another connective tissue autoimmune disease in those cases in which the diagnosis was added during follow-up.

Results: 681 patients were included, mean of following in years was 4.7 años (SD 4.94), 94.8% were women, mean age of 54 (+/- 14) and mean age at diagnosis of 50 (+/- 13) years. Of the total of patients, 30 (4.41%) developed another autoimmune rheumatic disease, according to the classification criteria for each disease, in its evolution. The median time to development was 4 (ICR 2-9). They were: Rheumatoid Arthritis (RA) 14 patients, scleroderma 9 patients, lupus (SLE) 5 patients, dermatomyositis 1 patient and RA plus SLE 1 patient. The mean age of this subgroup was 53 (+/- 14), with a mean age at diagnosis of pSS 48 (+/- 13), 91 % were women. Regarding the SICCA symptoms: 96% reported xerophthalmia, and 86.2% xerostomia to the diagnosis of pSS. With respect to the objective tests: 92% had positive Schirmer test, 88.24% Bengal Rose test or Lisamine Green or positive staining score, 81.2% positive sialometry, Ro + 82.1% and La + 33.33% of patients. Of the 30 patients, 14 had a minor salivary gland biopsy, 12 of them with positive results. Prior to the diagnosis of RA, 78% of the patients presented with arthralgia and arthritis, 12 had RF + and in 2 of the 14 patients the dose of ACPA was recorded and the result was positive. Prior to the diagnosis of scleroderma, 44% of the patients who developed this disease had raynaud's phenomenon and 22.22% ANA with centromeric pattern, 1 patient with PHT and 3 patients with esophagitis due to reflux. 20% of patients who added SLE also presented raynaud's phenomenon. 1 patient had anticardiolipin +, 100% reported arthralgia and 80% had arthritis.

Conclusion: Of all the patients analyzed, 4.4% developed another connective tissue disease during their follow-up. We consider the importance of recognizing this possibility in order to arrive at an early diagnosis. The presence of certain clinical and serological manifestations could be considered as suggestive of the subsequent development of another autoimmune rheumatic disease.

Disclosure: M. Rodriguez, None; **A. Secco**, None; **C. Pellet**, None; **n. herscovich**, None; **c. Amitrano**, None; **C. Asnal**, None; **A. Nitsche**, None; **J. Demarchi**, None; **d. duartes**, None; **F. Caeiro**, None; **V. Saurit**, None; **N. Riscanevo**, None; **S. Papasidero**, None; **C. Gobbi**, None; **I. raiti**, None; **v. cruzat**, None; **L. santiago**, None; **S. Velez**, None; **G. Salvatierra**, None; **V. Juarez**, None.

Abstract Number: 1473

Syndecan-1 Is a Potential Biomarker for Salivary Glandular Function and Disease Activity in Patients with Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II

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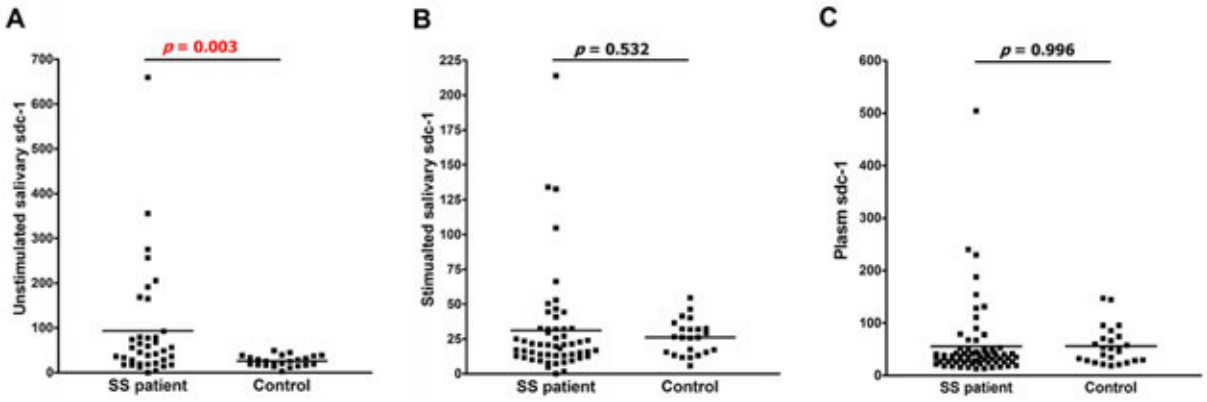

Figure. The levels of syndecan-1 in plasma and unstimulated and stimulated saliva from patients with Sjogren's syndrome and normal controls.

Background/Purpose: Sjögren's syndrome (SS) is known as autoimmune epithelitis, because epithelial cells in the glands are the primary target of disease and play a major role in pathogenesis of SS by mediating the development, maintenance and progression of the local autoimmune inflammatory response. Syndecan-1 (sdc-1), a transmembrane heparin sulfate proteoglycan, is predominantly expressed on epithelial cells and functions as coreceptors through binding to variant ligands. Furthermore, sdc-1 functions as soluble HSPG that can function as paracrine or autocrine effectors, or competitive inhibitors by ectodomain shedding. However, the expression and clinical significance of sdc-1 in patients with SS remain unclear. In this study, we investigated the expression of sdc-1 in minor salivary glands and association of syndecan-1 levels in plasma and saliva with disease activity and glandular functional parameters in SS patients.

Methods: We measured the levels of sdc-1 in plasma and unstimulated and stimulated saliva by ELISA and assessed the salivary flow rates in 70 SS patients and 26 normal controls. We also performed disease activity indexes, salivary gland scan, serologic markers and minor salivary gland biopsies in SS patients.

Results: Salivary gland tissue sections obtained from patients and normal controls were stained with monoclonal anit-sdc-1 antibody. Sdc-1 was up-regulated in ductal epithelial cells from patients and showed a more intense staining in severe inflamed glandular tissue. In specimen from patients, sdc-1 stain was also detected in infiltrating plasma cells as well as glandular epithelial cells. The mean unstimulated and stimulated salivary flow rates were significantly lower in patients than controls ($p< 0.001$). The levels of unstimulated salivary sdc-1 from patients were significantly higher than those from controls ($p=0.003$) and reversely correlated with unstimulated salivary flow rates ($r=-0.358$, $p=0.032$) and ejection fraction of parotid ($r=-0.363$, $p=0.027$) and submandibular glands ($r=-0.485$, $p=0.002$) on salivary gland scan. The levels of plasma sdc-1 were not different between patients with controls but showed a significant correlation with EULAR's Sjögren's Syndrome Disease Activity Index ($r=0.507$, $p< 0.001$) and EULAR's Sjögren's Syndrome Patient Reported Index ($r=0.267$, $p=0.033$). Minor salivary gland specimens included 68.3% with focus scores of ≥1 per 4mm2. Focus scores of ≥ 2 were significantly associated with higher levels of unstimulated salivary sdc-1, serum anti-Ro positivity and ocular stained scores and lower parotid gland functions on salivary gland scan. Those with higher levels of unstimulated salivary sdc-1 were 12.5 times (95% CI 1.76–88.74) more likely to have a focus score ≥2.

Conclusion: The levels of unstimulated salivary sdc-1 reflected the glandular function and degree of minor salivary gland inflammation. The levels of plasma sdc-1 showed a significant correlation with disease activity indexes in SS patients. These results suggested that the levels of unstimulated salivary and plasma sdc-1 are potential biomarkers for salivary glandular function and disease activity, respectively, in SS patients.

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Abstract Number: 1474

Factors Influencing the ESSPRI Index in Primary Sjögren's Syndrome

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The ESSPRI is a validated index for measuring symptoms (pain, fatigue and dryness) in primary Sjögren's syndrome (pSS). Herein we evaluated its association with disease and non-disease related variables, and its variation though the follow-up.

Methods: We included consecutive patients with pSS according to the ACR/EULAR classification criteria who attended a referral tertiary center during 2016-2018. We excluded patients with another connective disease. A single rheumatologist interviewed the patients and registered the following variables: demographics, scholarship, smoking, menopause, body mass index, disease duration, comorbidities such as diabetes mellitus, hypothyroidism, depression, and fibromyalgia as well as the Charlson comorbidity index. We also asked about the current use of hormonal replacement, diuretics, anticholinergics antihistamines, prednisone and immunosuppressors. We evaluated the non-stimulated whole salivary flow (NSWSF), Schirmer-I test, and scored the ESSDAI and the ESSPRI. In addition, in a subset of patients, we scored a second ESSPRI during a follow-up time within 6-36 months. We used descriptive statistics, X2 test, T student test, Mann–Whitney U test and Wilcoxon signed-rank test as appropriated. We used logistic regression analysis reporting OR and 95% CI. A two-tailed $P< 0.05$ was considered statistically significant. All analyses were performed using the SPSS.

Results: We included 130 patients, most of them were women (98.4%), mean age 57 years±13.4 and median disease duration of 9.3 years. Ocular and oral symptoms were present in 93.8% and 88.4%, respectively. The median ESSPRI score was 6, being the median score 6 for fatigue, 4 for pain and 8 for dryness. Eighty patients (61.5%) had an ESSPRI score >5 points. When we compared this group vs. the group with an ESSPRI ≤5 (n=50), the first group had a higher frequency of fibromyalgia (12.5% vs. 2%, p=0.05) and depression (30% vs. 10%, p=0.008) as well as a lower NSWSF (0.2 ml/15 min vs. 1.1 ml/15 min, p=0.05). We did not observe differences among the rest of the variables. At the logistic regression analysis, the variables that remained associated were depression (OR 3.7, 95% CI 1.23-11.3, p=0.02) and NSWSF (OR 0.59, 95% CI 0.36-0.97, p=0.03).

In 62 patients, we performed a second ESSPRI assessment after a median time of 25 months (6-41). Now, the median ESSPRI score was 5.1, being the median score 5 for fatigue, 4 for pain and 6 for dryness. When we compared the basal and the follow up ESSPRI results, we found a statistically difference between the overall ESSPRI score (p=0.01), the fatigue (p=0.02) and dryness (p=0.004) domains, but not for pain. Among the patients with a second ESSPRI score, 44 (70%) patients increased their ESSPRI in ≥1 points. None of the studied variables were associated with this change in the ESSPRI.

Conclusion: We observed that the ESSPRI was associated with low NSWSF, but also with non-disease related variables such as depression. Most of the patients experienced a variation of this score though the follow- up, nevertheless the variables that might influence its change remains to be elucidated.

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Comparison of Different Remission Indices in Patients with Psoriatic Arthritis: A Post Hoc Analysis of Data from Phase 3 Tofacitinib Studies

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

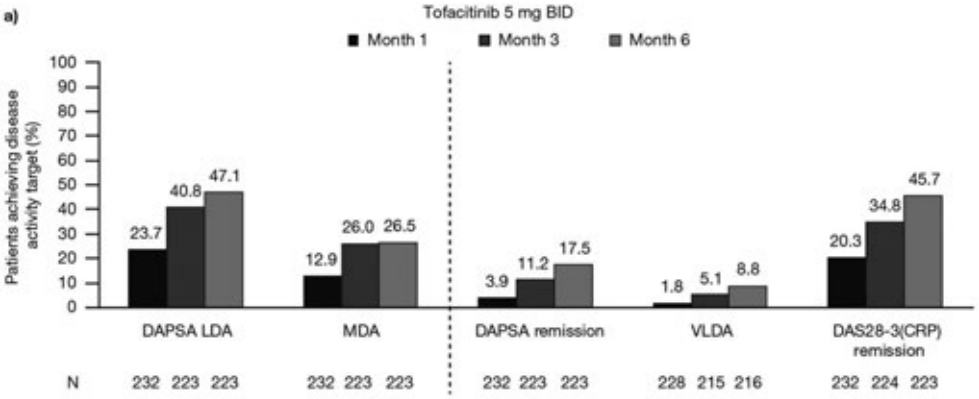
Session Time: 9:00AM–11:00AM

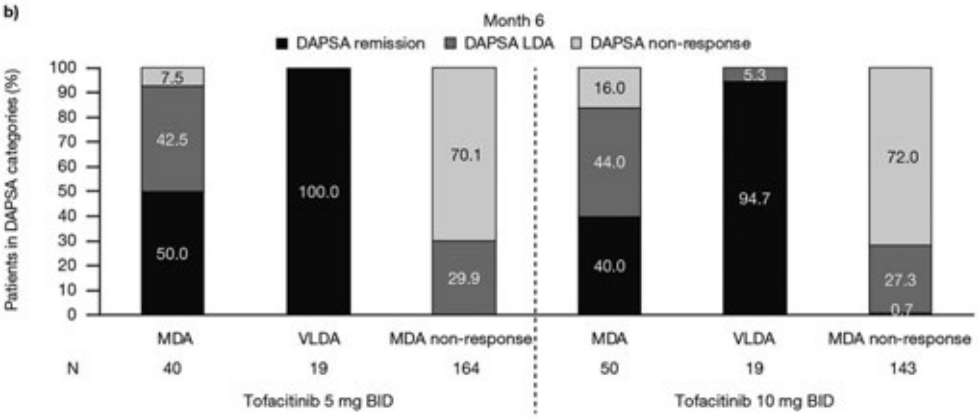
Background/Purpose: An international task force has agreed that remission or low disease activity (LDA) are key treatment targets for patients (pts) with PsA, and recommends the Disease Activity Index in Psoriatic Arthritis (DAPSA) or minimal disease activity (MDA) to assess respective disease activity states.[1] Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. In this post hoc analysis, we compared DAPSA LDA with MDA, and DAPSA remission with very low disease activity (VLDA) and DAS28-3(CRP) remission, in pts with PsA receiving tofacitinib.

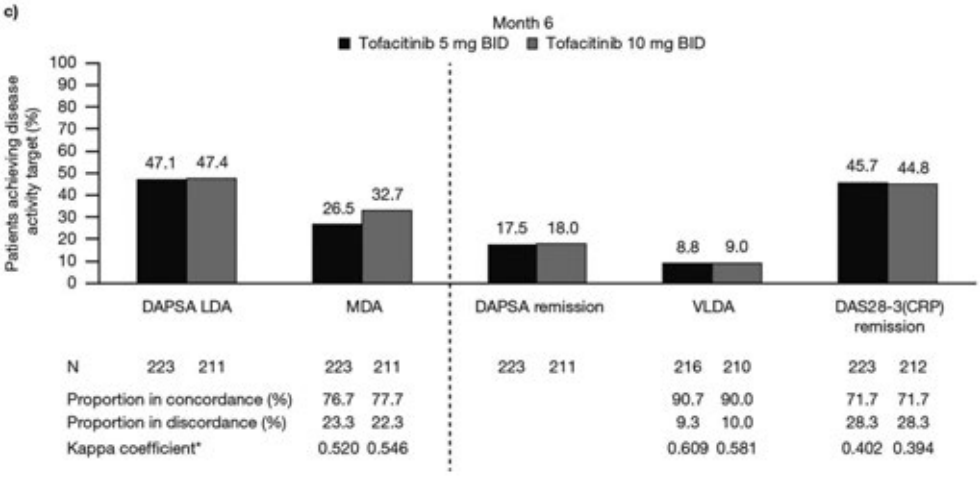
Methods: Data were pooled from 2 Phase 3 studies (OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439]) for pts receiving tofacitinib 5 or 10 mg twice daily (BID) or placebo (PBO). DAPSA was determined by summing: swollen joint count (SJC66); tender joint count (TJC68); Patient's Global Assessment of Arthritis (PtGA; visual analog scale [VAS]); pain (VAS); and CRP. Pts were classified as achieving MDA or VLDA when meeting ≥ 5 (MDA) or 7 (VLDA) of the following criteria: TJC68 ≤ 1; SJC66 ≤ 1; Psoriasis Activity and Severity Index ≤ 1 or body surface area ≤ 3%; pain (VAS) ≤ 15; PtGA (VAS) ≤ 20; HAQ-DI ≤ 0.5; tender entheseal points (using Leeds Enthesitis Index) ≤ 1. A logistic regression model was used to assess demographic and baseline characteristics as predictors of a trend in DAPSA scores at Month (M)3. DAPSA LDA (≤ 14), MDA, DAPSA remission (DAPSA ≤ 4), VLDA, and DAS28-3(CRP) remission (DAS28-3[CRP] < 2.6) rates were compared at M1, M3, and M6 for pts receiving tofacitinib 5 mg BID, and at M6 for pts receiving tofacitinib 5 or 10 mg BID. Agreement between disease activity indices at M6 was evaluated using a kappa test. The percentage of tofacitinib-treated pts who achieved MDA, VLDA, and non-response was reported at M6 stratified by achievement of DAPSA LDA, remission, or non-response.

Results: This analysis included 709 pts: tofacitinib 5 mg BID, n=237; tofacitinib 10 mg BID, n=236; PBO, n=236. Older pts treated with tofacitinib, and pts with higher baseline PsA activity and HAQ-DI treated with tofacitinib or PBO were significantly ($p < 0.05$) more likely to have a worse DAPSA response at M3; Hispanic/Latino pts treated with tofacitinib or PBO were significantly more likely to have a better DAPSA response at M3 than pts of other ethnicities (Table 1). DAPSA LDA, MDA, remission (DAPSA and DAS28-3[CRP]), and VLDA rates generally increased from M1

Figure 1. Percentage of patients receiving a) tofacitinib 5 mg BID achieving DAPSA LDA, MDA, DAPSA remission, VLDA, or DAS28-3(CRP) remission at Month 1, 3, or 6; b) tofacitinib 5 or 10 mg BID achieving MDA or VLDA, by DAPSA categories at Month 6; c) tofacitinib 5 or 10 mg BID achieving DAPSA LDA, MDA, DAPSA remission, VLDA, or DAS28-3(CRP) remission at Month 6







*Kappa test of agreement between: DAPSA LDA and MDA; DAPSA remission and VLDA or DAS28-3(CRP) remission
BID, twice daily; DAPSA; Disease Activity Index for Psoriatic Arthritis; DAS28-3(CRP), Disease Activity Score in 28 joints, CRP; LDA, low disease activity; MDA, minimal disease activity; N, number of evaluable patients; VLDA, very low disease activity

Table 1. Demographics and baseline disease characteristics as predictors of a trend in DAPSA scores at Month 3, in patients treated with tofacitinib or PBO

		Remission (DAPSA ≤4)	Low disease activity (4< DAPSA ≤14)	Moderate disease activity (14< DAPSA ≤28)	High disease activity (DAPSA >28)	p value[a]
N	All tofacitinib	53	131	114	146	
	Placebo	16	40	58	104	
Age (years), mean (SD)	All tofacitinib	48.7 (13.6)	47.9 (11.9)	48.3 (12.8)	51.9 (10.8)	0.0268
	PBO	49.2 (15.8)	45.9 (11.5)	48.7 (12.8)	49.2 (12.4)	0.5422
Ethnicity, n (%)						
Hispanic/Latino	All tofacitinib	14 (26.4)	20 (15.3)	10 (8.8)	5 (3.4)	0.0002
Not Hispanic/Latino		39 (73.6)	111 (84.7)	104 (91.2)	141 (96.6)	
Hispanic/Latino	PBO	6 (37.5)	11 (27.5)	5 (8.6)	2 (1.9)	0.0001
Not Hispanic/Latino		10 (62.5)	29 (72.5)	53 (91.4)	102 (98.1)	
BMI (kg/m^2), mean (SD)	All tofacitinib	29.1 (5.4)	29.8 (6.0)	29.7 (5.9)	31.2 (7.0)	0.0996
	PBO	27.8 (5.7)	28.7 (4.9)	29.0 (5.4)	29.6 (6.1)	0.5956
DAPSA, mean (SD)	All tofacitinib	33.6 (18.5)	35.9 (16.3)	45.3 (19.6)	63.3 (24.6)	<0.0001
	PBO	26.3 (10.1)	28.8 (13.9)	34.5 (15.8)	54.6 (22.4)	<0.0001
SJC66, mean (SD)	All tofacitinib	8.1 (6.2)	9.8 (6.7)	11.8 (8.4)	17.5 (13.0)	<0.0001
	PBO	7.6 (5.3)	7.1 (5.0)	8.6 (5.7)	13.8 (10.4)	0.0001
TJC68, mean (SD)	All tofacitinib	14.4 (11.9)	14.4 (8.8)	21.3 (12.5)	31.9 (14.8)	<0.0001
	PBO	9.8 (4.2)	12.9 (8.5)	14.7 (10.1)	27.2 (15.6)	<0.0001
PtGA (VAS), mean (SD)	All tofacitinib	51.6 (26.0)	52.0 (23.1)	55.5 (21.5)	62.6 (20.8)	0.0006
	PBO	42.8 (25.9)	42.1 (21.2)	50.7 (21.5)	62.1 (21.5)	<0.0001
HAQ-DI, mean (SD)	All tofacitinib	1.0 (0.7)	1.1 (0.6)	1.3 (0.6)	1.4 (0.6)	<0.0001
	PBO	1.0 (0.9)	0.9 (0.6)	1.1 (0.7)	1.3 (0.6)	0.0084
LEI, mean (SD)	All tofacitinib	1.1 (1.3)	1.2 (1.4)	2.1 (1.9)	3.0 (2.1)	<0.0001
	PBO	1.0 (1.6)	1.1 (1.6)	1.4 (1.4)	2.5 (1.8)	<0.0001
Pain (VAS), mean (SD)	All tofacitinib	52.5 (24.5)	51.9 (24.0)	56.4 (22.5)	63.1 (20.5)	0.0004
	PBO	40.1 (24.9)	41.5 (23.6)	52.8 (23.7)	60.4 (22.6)	0.0001

[a]p value for trend in baseline parameter across Month 3 DAPSA categories, from an ordered logistic regression model of Month 3 DAPSA categories with baseline parameter as predictor
BMI, body mass index; DAPSA, Disease Activity Index for Psoriatic Arthritis; HAQ-DI, HAQ-Disability Index; LEI, Leeds Enthesitis Index; N, number of patients in DAPSA category; n, number of patients; PBO, placebo; PtGA, Patient's Global Assessment of Arthritis; SD, standard deviation; SJC, swollen joint count; TJC, tender joint count; VAS, visual analog scale

to M6 (Figure 1a). At M6, most tofacitinib-treated pts who achieved MDA, and all who achieved VLDA, were also in DAPSA remission or LDA (Figure 1b). Moderate agreement (defined by kappa values 0.41–0.60) was observed between DAPSA LDA and MDA, and between DAPSA remission and VLDA (Figure 1c).

Conclusion: Remission and LDA rates generally increased over time in pts with PsA receiving tofacitinib. DAPSA LDA showed moderate agreement with MDA, and DAPSA remission showed moderate agreement with VLDA, confirming that DAPSA is a useful measurement tool to assess disease activity in pts with PsA treated with tofacitinib.

Reference:

1. Smolen JS et al. Ann Rheum Dis 2018;77:3-17.

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Abstract Number: 1476

Impact of Alternate Mechanism of Action Biologics and Tofacitinib on TNF-α Inhibitor Prescribing in Psoriatic Arthritis: Results from Annual National Patient Chart Audits

Lynn Price,[1] Phil Pouliot,[1] and Lauren Schmitt[1], [1]Spherix Global Insights, Exton, PA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: TNF-α inhibitor therapy has long been the standard of care for adult patients diagnosed with moderate to severe psoriatic arthritis (PsA), though several new biologics and small molecules have recently received FDA approval for the treatment of PsA. This research sought to understand the extent to which biologics and small molecules with a different mechanism of action (MOA) have been adopted for the treatment of PsA and their impact on the use of well-established TNFs.

Methods: An independent market analytics firm collaborated with US rheumatologists (n=192) to conduct a retrospective chart review of patients diagnosed with psoriatic arthritis (PsA) (n=994), who had switched from one biologic therapy or apremilast to another in the prior twelve weeks. Rheumatologists were able to submit up to seven PsA patient charts. Data were collected in March 2019 and included clinical and non-clinical patient demographics, as well as physician demographics and attitudinal survey responses. This study was a non-longitudinal trending analysis to 2016, 2017, and 2018 audits following the same methodology.

Results: 83% of rheumatologists reported recent changes to the management of their PsA patients and the two most commonly recalled treatment shifts were: more aggressive/earlier use of biologics in general and increased use of non-TNF agents for the treatment of PsA. Despite increased PsA treatment options, annual reported rates of PsA patient switching have remained stable since 2016, with rheumatologists reporting approximately one-quarter of biologic/apremilast-treated patients switch brands within a given year. Audited switches between TNF agents have significantly and consecutively decreased year-over-year: in 2016, consecutive TNF cycling accounted for 52% of audited patients, a figure that has declined with each audit and is presently just 35%. Conversely, switches from a TNF to an alternative MOA agent have significantly increased during the same period from 13% to 30%, respectively. The growth in the switching share of alternative MOAs is driven primarily by increased use of the IL-17 inhibitors, secukinumab and ixekizumab, as well as the oral JAK inhibitor, tofacitinib.

Conclusion: Increased biologic and small molecule options for the treatment of PsA has resulted in US rheumatologists switching fewer patients to a TNF in second- or later-lines of therapy, and a notable and significant decline in the practice of TNF cycling. Though TNF inhibitors remain the predominant MOA for the treatment of PsA, the introduction of secukinumab, ixekizumab, and tofacitinib have had a direct impact on the PsA switching environment, and in particular, use of the TNF class.

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Golimumab Improves Direct Costs of Healthcare Utilization and Indirect Costs Within Patients with RA, PsA, and as - Analysis of a Non-Interventional Study in Germany

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Background/Purpose: Rheumatic diseases are associated with pain, loss of functionality, fatigue, hospitalization, sick leave, and work disability. This results in high economic burden for patients and society.Golimumab (GLM) is an effective but costly treatment option for patients with moderate to severe, active rheumatic diseases.

The aim of this analysis of the GO-NICE study was to investigate the direct and indirect costs of healthcare utilization and sick leave after starting a treatment with GLM.

Methods: Data from outpatients collected in the non-observational study GO-NICE in 1,483 patients with RA (n = 474), PsA (n=501), and AS (n=483) in 158 sites (2010-2015) in Germany were analysed. Details on the study design, patient characteristics, clinical and patient-reported outcomes, and safety data have been reported earlier [1,2].

Table: Costs per patient and year (Subgroup patients with RA)

	RA biologic-naïve (n=265)			RA with biologics as pre-treatment (n=208)		
	Baseline	Month 24	Changes	Baseline	Month 24	Changes
Consultation fees / €	354	168	- 186	369	178	- 191
Physiotherapy, massages etc. / €	162	59	- 103	144	91	- 53
Hospitalisation / €	939	99	- 840	1,163	423	- 740
Rehabilitation measures / € (in- and outpatients)	163	55	- 109	148	0	- 148
Direct med. costs / € (excl. medication)	1,618	381	- 1,237	1,823	692	- 1,131
Comedication / €	498	417	- 81	417	414	- 3
Biologicals / €	0	19,082	+ 19,082	21,673	19,082	- 2,591
Medication / €	498	19,498	+ 19,000	22,091	19,496	- 2,595
Absenteeism / €	2,991	892	- 2,099	3,028	464	- 2,564
Total / €	5,107	20,771	+ 15,664	26,942	20,653	- 6,289

Direct medical and indirect costs per patient and year were calculated for consultations, physiotherapy, massages, hospitalisations and inpatient rehabilitation, medication (DMARDs, Glucocorticoids, NSAIDs, and biologics) as well as sick leave days. Findings were shown for RA-, PsA- and AS-patients and categorised by biologic-naïve patients and patients previously treated with a biologic argent. The 6-month periods prior baseline (BL) / start of a GLM therapy vs. month 24 (M24) were compared.

For this calculation standardized evaluation rates were used (Bock et al. (2015), AG MEG of the DGSMP (2005). Costs for prescribed and documented medication were calculated by the mean cost per defined daily dose (based 2010-2015). Indirect costs were estimated through the human capital approach (HCA).

Results: Data from 758 biologic-naïve patients (n = 265 RA, 247 PsA and 246 AS) and 694 patients with biologics as pre-therapy (n = 208 RA, 252 PsA and 234 AS) were included in the analysis.

Direct medical costs (excluding medication) decreased in all 6 groups, min. 765€ (PsA pre-treatment group) and max. 2,426€ (AS pre-treatment) as well as the costs due to work disability / absenteeism, min. 855€ (PsA pre-treatment) and max. 2.564€ (RA pre-treatment, table).

Total costs in biological-naïve patients increased due to the additional expense of the biologic agent.

Absolute changes in costs totalled 15,665€ (RA-, table), 15,799€ (PsA-) and 14,764€ (AS-patients) per patient and year when comparing the BL vs. M24 periods.

Total savings of 6,289€ (RA-, table), 2,617€ (PsA-), and 5,555€ (AS-patients) per patient and year were observed in the group of biologic-pre-treated patients.

Conclusion: Costs of healthcare utilization, as well as work disability, decreased after starting GLM within an observation period of 24 months, for patients with RA, PsA, and AS.

Due to the high costs of TNFi therapy, drug costs in the group of biologic-naive patients rose markedly. Savings were observed in the group of patients previously treated with a biologic argent.

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Abstract Number: 1478

Systematic Literature Review and Network Meta-Analysis Comparing Incidence of Uveitis and IBD in Axial Spondyloarthritis Patients Treated with Anti-TNF versus Anti-IL17A in Placebo Controlled Randomized Trials

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

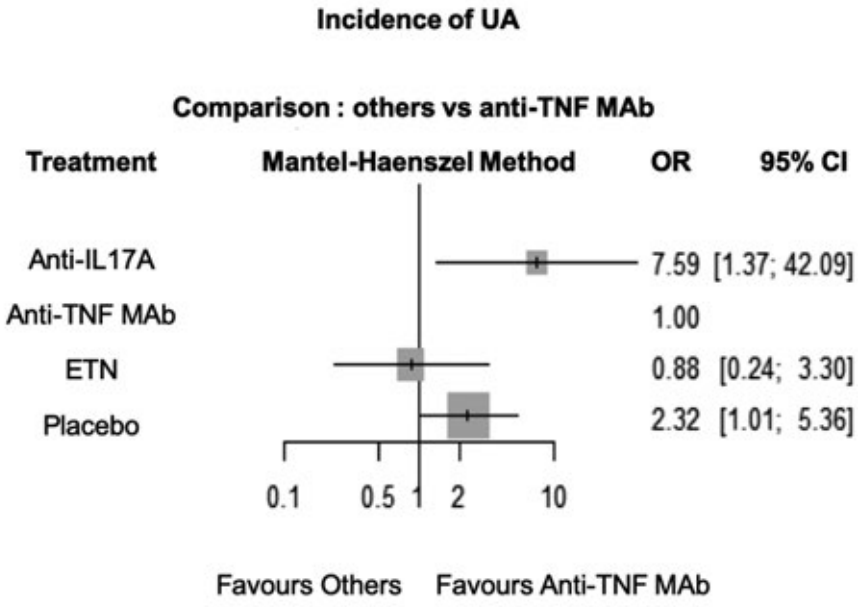
Background/Purpose: Inflammatory bowel diseases (IBD) and anterior uveitis (AU) are frequent extra-articular features of axial spondyloarthritis (axSpA). Although effect of anti-TNF on IBD and AU are well known, data are lacking for anti-IL17A. Our objective was to assess and compare the incidence of IBD and AU in axSpA patients treated with anti-TNF and anti-IL17A.

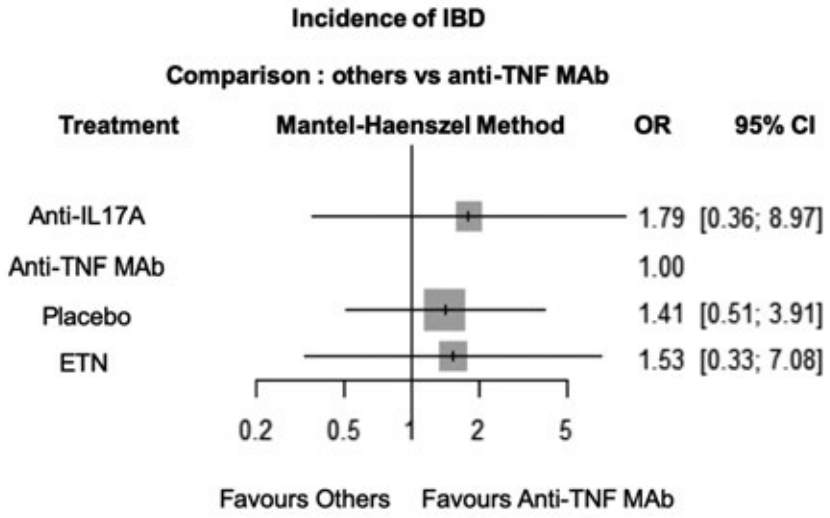
Methods: A systematic literature review was performed by 2 independent reviewers in 3 databases (PubMed, EMBase and Cochrane) until 2019/04/04 and completed with 2016-18 ACR and EULAR abstracts. We included randomized controlled trials (RCT) assessing anti-TNF (monoclonal antibodies (Mab): adalimumab, certolizumab, golimumab, infliximab, and soluble receptor fusion protein: etanercept (ETN)) or anti-IL17A (ixekizumab, secukinumab) versus placebo or another biologic in axSpA according to ASAS criteria and reporting safety data on IBD or UA. History of IBD or AU was not an exclusion criterion in these RCTs, although recent onset or active IBD/AU was. The risk of bias in included RCTs was evaluated according to the Cochrane risk of bias tool. Data from these studies was used to perform a network meta-analysis to assess incidence of IBD and UA under each treatment, using the Mantel-Haenszel method relevant for rare events (netmeta R Package).

Results: Out of initially 725 studies, 31 were included for analysis, provided a total of 3888 treated patients (anti-TNF MAb: 2011, ETN: 699, anti-IL17A: 1178) and 2207 placebo-receiving axSpA patients. The mean study duration was 20.8 weeks ± 17.4 (SD), median: 16 weeks. Incidence of AU was 1.09%, 2.14%, 3.53%, 3.26% per year in anti-TNF MAb, ETN, anti-IL17A and placebo groups, respectively. Incidence of IBD was 0.22%, 1.28%, 2.17%, 0.48% per year in anti-TNF MAb, ETN, anti-IL17A and placebo groups, respectively.

Incidence of UA was reduced with anti-TNF MAb compared to anti-IL17A (OR = 7.59; IC95% 1.37-42.09) and placebo (OR = 2.32; IC95% 1.01-5.36) (Figure 1). There was no statistical difference between anti-TNF MAb and ETN. There was no statistical difference in IBD incidence between anti-TNF MAb, ETN, anti-IL17A and placebo (Figure 2). No evidence of inconsistency was found in this network model.

Conclusion: In RCT assessing anti-TNF and anti-IL17A in axSpA, incident AU or IBD are rare events. However, this network meta-analysis demonstrate that anti-IL17A are associated with a higher incidence of AU compared to placebo and anti-TNF, while there was no statistical difference between treatments concerning IBD incidence.





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Abstract Number: 1479

Multi-Symptom Impact on the EQ5D Index in Bio-naïve Active Psoriatic Arthritis Patients: An Analysis Through Week 24 of the GO-VIBRANT Study

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SESSION INFORMATION

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Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized by peripheral arthritis, axial inflammation, dactylitis, enthesitis and skin and nail psoriasis. The impact of skin and joint components of the disease on patient health-related quality of life (HRQoL) has been described in previous research but the impact of other major clinical manifestations has not been similarly characterized. This analysis quantified the impact of the major clinical manifestations of PsA on patient reported HRQoL, as estimated by disease state preference (utility) derived from the EQ-5D index in a randomized clinical trial.

Methods: This analysis used data from a multicenter, randomized, double-blind, placebo-controlled trial of intravenous (IV) Golimumab in biologic naïve patients with active PsA (GO-VIBRANT study). Patient baseline characteristics of the GO-VIBRANT study population have been previously described (1). Core outcome measures recommended by OMERACT (Outcome Measures in Rheumatology Clinical Trials) and guideline on utility mapping by ISPOR (International Society for Pharmacoeconomics and Outcome Research) were used to guide initial attribute selection. Utility was derived from patient responses to the EQ-5D index, which assesses mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, and was completed at weeks 0, 8, 14, and 24 in the trial (placebo-controlled period). EQ5D index is used as a measure of overall health and is an outcome commonly used in health economic analyses. Multivariate analysis was performed using a Mixed-Effect Repeated Measures model based on observed data until week 24 in pooled patient population.

Results: Based on univariate analyses and evaluation of collinearity between variables, the following attributes were included in the multivariate models: age, gender, region, PsA disease duration, PASI score, enthesitis, dactylitis, tender joint count (TJC), swollen joint count (SJC), C-reactive protein (CRP mg/L) and Health Assessment Questionnaire-Disability Index (HAQ-DI). In the final model, PASI score (β=-0.00126, p=0.0006), enthesitis (β=-0.01237, p=0.03), TJC (β=-0.00112, p< 0.0001), CRP (β=-0.00079, p< 0.0001) and HAQ-DI (β=-0.1664, p< 0.0001) were all statistically significantly associated with the EQ-5D index. A sensitivity analysis among a subgroup of patients who had spondylitis with peripheral joint arthritis as their primary arthritic presentation of PsA showed that spinal pain (β=0.0101, p< 0.0001), as measured by question #2 of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), was also statistically significantly associated with the EQ-5D index in the multivariate model.

Conclusion: Multiple PsA clinical manifestations including psoriasis, enthesitis, TJC, spinal pain, CRP, and physical function were statistically significantly associated with utility among PsA patients as derived from the EQ-5D index. These findings indicate that consideration of multiple clinical manifestations of PsA is warranted when evaluating the impact of PsA on patients.

Reference:

1. Kavanaugh A, et al. Arthritis Rheumatol. 2017 Nov;69(11):2151-2161.

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Abstract Number: 1480

Clinical Characteristics and Treatment Profiles of Patients with Ankylosing Spondylitis Who Initiated Secukinumab and Other Biologics: Results from the Corrona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Secukinumab is the only non–tumor necrosis factor inhibitor biologic therapy approved for the treatment of ankylosing spondylitis (AS) in the United States. Patients with AS in clinical trials who receive biologics, including secukinumab, may not be representative of those treated in real-world clinical practice due to differences in patient characteristics, practice patterns, physician experience, and insurance coverage (ie, access). Few real-world studies have characterized patients with AS who initiate secukinumab. The Corrona PsA/SpA Registry collects data on a robust list of outcome measures, many of which overlap with those used in clinical trials. We aim to describe the characteristics of patients who initiated secukinumab and other biologics for the treatment of AS in the Corrona PsA/SpA Registry.

Methods: This study included patients aged ≥ 18 years with AS (and without concurrent PsA diagnosis) enrolled in the Corrona PsA/SpA Registry who initiated secukinumab or other biologics (adalimumab, etanercept, certolizumab pegol, infliximab, and golimumab) between April 2017 and December 2018. Patient demographics, clinical characteristics, treatment profiles, disease activity, quality of life, and work productivity were assessed at the time of biologic initiation (baseline) and compared between patients who initiated secukinumab and other biologics using *t* tests or Wilcoxon rank-sum tests for continuous variables and χ^2 or Fisher exact tests for categorical variables.

Results: Of the 106 patients with AS who initiated a biologic, 26 (24.5%) initiated secukinumab and 80 (75.5%) initiated other biologics. Secukinumab initiators were similar to patients who initiated other biologics in terms of demographics and clinical characteristics except that a higher proportion of secukinumab initiators had a history of prior biologic use

Table 1. Demographic and Clinical Characteristics and Treatment Profiles Among Patients With AS Who Initiated Secukinumab or Other Biologics*

Characteristic9	Secukinumab Initiators (n = 26)	Other Biologic Initiators (n = 80)	*P* Value
Age, mean (SD), years	47.7 (12.5)	47.3 (14.7)	0.88
Female, n (%)	14 (53.8)	40 (50.0)	0.73
White, n (%)	26 (100)	72 (90.0)	0.37
Work status, n (%)			
Full time	18 (69.2)	36 (45.0)	0.26
Part time	0	6 (7.5)	
Disabled	3 (11.5)	14 (17.5)	
Retired	2 (7.7)	14 (17.5)	
Other	3 (11.5)	10 (12.5)	
BMI, mean (SD), kg/m^2	28.7 (7.9)	31.3 (7.7)	0.06
Symptom duration, mean (SD), years	14.8 (8.9)	13.9 (12.1)	0.35
Disease duration, mean (SD), years	6.8 (6.5)	5.5 (8.8)	0.06
HLA-B27 positive test result, n (%)	16 (61.5)	43 (53.8)	0.49
Comorbidities, n (%)			
Hypertension	10 (38.5)	28 (35.0)	0.75
Depression	3 (11.5)	18 (22.5)	0.22
Hyperlipidemia	4 (15.4)	13 (16.3)	1.00
Anxiety	1 (3.8)	15 (18.8)	0.11
Cardiovascular disease	3 (11.5)	11 (13.8)	1.00
Serious infections	5 (19.2)	6 (7.5)	0.13
Uveitis	1 (3.8)	9 (11.3)	0.45
Diabetes mellitus	2 (7.7)	6 (7.5)	1.00
Fibromyalgia	2 (7.7)	5 (6.3)	1.00
Metabolic syndrome	2 (7.7)	5 (6.3)	1.00
Psoriasis	2 (7.7)	4 (5.0)	0.63
Nail psoriasis	1 (3.8)	2 (2.5)	1.00
Crohn disease	0	3 (3.8)	1.00
Ulcerative colitis	1 (3.8)	1 (1.3)	0.43
Any cancer (excluding NMSC)	1 (3.8)	1 (1.3)	0.43
Prior csDMARD use, n (%)	7 (26.9)	16 (20.0)	0.46
Prior biologic use, n (%)	18 (69.2)	36 (45.0)	0.03
Number of prior biologics, n (%)			< 0.01
0	8 (30.8)	44 (55.0)	
1	6 (23.1)	25 (31.3)	
≥ 2	12 (46.2)	11 (13.8)	
Current csDMARD use, n (%)	2 (7.7)	11 (13.8)	0.51

BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HLA-B27, human leukocyte antigen B27; NMSC, nonmelanoma skin cancer.
* Other biologics included adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab.

(69.2% vs 45.0%; $P = 0.03$) and were more likely to have used a higher number of prior biologics compared with other biologic initiators ($P < 0.01$; **Table 1**). No significant differences were observed between patients who initiated secukinumab and other biologics in terms of measures of disease activity, quality of life, and work productivity (**Table 2**).

Conclusion: In this real-world study of US patients with AS, secukinumab initiators had similar demographics, clinical outcomes, disease burden and patient reported outcomes compared with other biologic initiators, with the exception of higher prior biologic use.

Table 2. Disease Activity, Quality of Life, and Work Productivity Among Patients With AS Who Initiated Secukinumab or Other Biologics*

Characteristic	Secukinumab Initiators (n = 26)	Other Biologic Initiators (n = 80)	*P* Value
ASDAS, mean (SD)	3.1 (0.9)	3.2 (0.9)	0.84
BASDAI (0-10), mean (SD)	5.7 (1.7)	5.4 (2.1)	0.52
BASFI (0-10), mean (SD)	4.7 (2.5)	4.2 (2.4)	0.30
Lateral lumbar flexion (average of left and right), mean (SD), cm	30.2 (20.1)	28.4 (21.3)	0.69
Enthesitis, n/m (%)	12/26 (46.2)	31/80 (38.8)	0.50
SPARCC Enthesitis Index (1-16), mean (SD)	5.6 (3.1)	4.6 (2.9)	0.24
Dactylitis, n/m (%)	2/26 (7.7)	2/80 (2.5)	0.25
Dactylitis count (1-20), mean (SD)	1.5 (0.7)	1.5 (0.7)	1.00
Tender joint count (0-68), mean (SD)	3.3 (5.0)	3.7 (7.0)	0.39
Swollen joint count (0-66), mean (SD)	0.4 (1.0)	0.9 (2.0)	0.61
Physician global assessment (VAS 0-100), mean (SD)	40.7 (20.3)	41.2 (20.9)	0.92
Physician global assessment of psoriasis (VAS 0-100), mean (SD)	36.2 (19.3)	29.1 (22.6)	0.61
Patient pain (VAS 0-100), mean (SD)	66.6 (22.5)	58.9 (25.5)	0.21
Patient fatigue (VAS 0-100), mean (SD)	54.3 (26.3)	53.1 (25.9)	0.81
Morning stiffness, n/m (%)			0.77
< 30 minutes	5/26 (19.2)	13/80 (16.3)	
≥ 30 minutes	21/26 (80.8)	67/80 (83.8)	
HAQ-S (0-3), mean (SD)	0.78 (0.63)	0.99 (0.73)	0.61
EQ VAS (0-100), mean (SD)	55.8 (21.3)	55.2 (21.6)	0.82
WPAI domains, mean (SD)			
Current employment, n/m (%)	19/26 (73.1)	42/80 (52.5)	0.07
% Work time missed	10.7 (14.3)	11.9 (25.3)	0.32
% Impairment while working	43.3 (24.4)	36.1 (23.8)	0.28
% Overall work impairment	46.9 (26.4)	41.7 (28.8)	0.52
% Activity impairment	51.0 (28.7)	48.5 (28.1)	0.69

ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; EQ, Euroqol questionnaire; HAQ-S, Health Assessment Questionnaire for the Spondyloarthropathies; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment Questionnaire.

* All values were calculated based on available data. All variables had < 20% missing data. Other biologics included adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab.

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and UCB, 2, Abbvie, Amgen, Brsitol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Brsitol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Brsitol Myers Squibb,Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, Amgen, 2, 5, 6, 8, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, and UCB, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 2, 5, Boerhinger Ingelheim, 5, Bristol Myers Squibb, 2, 5, 8, Bristol Myers Squibb Co., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8, Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8.

Abstract Number: 1481

Real-World Use of Apremilast in Combination with Biologic Therapy in Patients with Psoriatic Arthritis: Findings from the Corrona Psoriatic Arthritis/Spondyloarthritis Registry

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Apremilast (APR), an oral phosphodiesterase 4 inhibitor, demonstrated efficacy in adult patients with active PsA despite prior use of csDMARDs and/or biologics in phase III studies of PsA (Kavanaugh. *Ann Rheum Dis*. 2014; Cutolo. *J Rheumatol*. 2016; Edwards. *Ann Rheum Dis*. 2016). Although APR has been studied in combination with csDMARDs, APR in combination with biologic therapies has not been studied. The objective of this analysis was to understand the characteristics at treatment initiation of US patients with PsA in the real-world setting who are prescribed APR + biologic therapy and to compare them with patients treated with biologic monotherapy and patients treated with biologic therapy + csDMARDs.

Methods: Adult patients diagnosed with PsA and enrolled in the Corrona PsA/Spondyloarthritis Registry who received APR + biologic therapy, biologic monotherapy, or biologic therapy + csDMARDs for PsA from March 2013 to March 2019 were included. For biologic monotherapy, the index date was defined as the date of the treatment initiation visit. For combination therapy, the index date was defined as the date of the treatment initiation visit for the second/add-on drug. Patient demographics, clinical/treatment characteristics, disease activity, and physician- and patient-reported outcomes at the index date were summarized using descriptive statistics for continuous (mean [SD], median [interquartile range]) and categorical (n [%]) variables.

Results: In all, 961 patients were included in the analysis (APR + biologic: n=93; biologic monotherapy: n=405; biologic therapy + csDMARDs: n=463). Mean age was generally comparable across groups (**Table 1**). A greater proportion of females were treated with APR + biologic vs biologic monotherapy and biologic + csDMARDs (**Table 1**). Comorbidity history was generally similar among the groups, but the proportion of patients with depression and diabetes was numer-

Table 1. Patient Demographics and Comorbidity Profile at the Index Date

Characteristic	APR + Biologic Therapy Total n=93	Biologic Monotherapy Total n=405	Biologic Therapy + csDMARD Total n=463
Age, mean (SD), years	51.0 (11.6)	52.4 (13.0)	53.8 (12.6)
Female, n (%)	57 (61.3)	219 (54.2)	245 (53.1)
Race, n (%)			
White	85 (94.4)	382 (95.5)	414 (91.8)
African American	2 (2.2)	0 (0.0)	5 (1.1)
Asian	0 (0.0)	11 (2.8)	9 (2.0)
Other	3 (3.3)	7 (1.8)	23 (5.1)
Body mass index, mean (SD), kg/m^2	33.6 (8.1)	32.2 (7.1)	32.2 (7.6)
History of comorbidities, n (%)			
Psoriasis	54 (58.1)	264 (65.2)	278 (60.0)
Nail psoriasis	36 (38.7)	185 (45.7)	197 (42.5)
Hypertension	33 (35.5)	150 (37.0)	194 (41.9)
Diabetes mellitus	24 (25.8)	52 (12.8)	70 (15.1)
Depression	22 (23.7)	71 (17.5)	77 (16.6)
Hyperlipidemia	21 (22.6)	95 (23.5)	116 (25.1)
Metabolic syndrome	6 (6.5)	28 (6.9)	26 (5.6)
Serious infection*	5 (5.4)	12 (3.0)	20 (4.3)
Cardiovascular disease§	3 (3.2)	20 (4.9)	17 (3.7)
Anxiety	1 (1.1)	16 (4.0)	14 (3.0)
Cancer‡	1 (1.1)	14 (3.5)	19 (4.1)
Fibromyalgia	1 (1.1)	17 (4.2)	13 (2.8)
Uveitis	1 (1.1)	4 (1.0)	3 (0.6)

The n represents the total sample; number of patients with data available may vary. For biologic monotherapy, the index date was defined as the date of the treatment initiation visit. For combination therapy, the index date was defined as the date of the treatment initiation visit for the second/add-on drug.

*Includes infections that led to hospitalization or intravenous antibiotics: joint/bursa, sinusitis, diverticulitis, sepsis, pneumonia, bronchitis, gastroenteritis, meningitis, urinary tract infection, upper respiratory tract infection, mycobacterium tuberculosis, or infection of other specified site. §Combined histories of myocardial infarction, acute coronary syndrome, coronary artery disease, congestive heart failure, peripheral arterial thromboembolic event, peripheral artery disease, cardiac revascularization procedure, ventricular arrhythmia, cardiac arrest, unstable angina, stroke, transient ischemic attack, peripheral ischemia or gangrene (necrosis), pulmonary embolism, carotid artery disease, or other cardiovascular event. ‡Excludes non-melanoma of the skin.

Table 2. Disease Characteristics and Treatment Profile at the Index Date

Characteristic	APR + Biologic Therapy Total n=93	Biologic Monotherapy Total n=405	Biologic Therapy + csDMARD Total n=463
PsA duration, mean (SD), years	11.2 (8.1)	11.5 (10.2)	11.2 (10.5)
Years since PsA diagnosis, mean (SD)	7.6 (5.8)	8.4 (8.3)	8.4 (9.1)
Prior medication use, n (%)			
Biologic	84 (90.3)	311 (76.8)	283 (61.1)
nbDMARD	74 (79.6)	291 (71.9)	423 (91.4)
Targeted synthetic	43 (46.2)	62 (15.3)	23 (5.0)
Prednisone	17 (18.3)	74 (18.3)	107 (23.1)
Current prednisone use, n (%)	8 (8.6)	21 (5.2)	54 (11.7)
MDA, n (%)	17 (19.5)	110 (29.4)	112 (27.1)
DAS28 remission, n (%)	20 (32.8)	88 (36.8)	94 (34.7)
SJC (0-66), mean (SD)	1.5 (2.2)	2.4 (4.0)	2.8 (4.7)
TJC (0-68), mean (SD)	7.7 (11.7)	5.9 (9.4)	6.2 (9.5)
Presence of enthesitis, n (%)	27 (29.0)	108 (26.7)	125 (27.0)
SPARCC enthesitis score, mean (SD)	3.3 (2.6)	3.6 (3.1)	3.9 (3.0)
Presence of dactylitis, n (%)	13 (14.0)	58 (14.3)	52 (11.2)
Dactylitis count (1-20), mean (SD)	2.8 (3.0)	2.6 (2.2)	2.8 (3.4)
Physician's Global Assessment of Arthritis (0-100 mm VAS), mean (SD)	22.6 (19.2)	24.6 (21.6)	25.1 (22.7)
Patient's Global Assessment of Arthritis (0-100 mm VAS), mean (SD)	46.4 (24.6)	41.9 (26.9)	44.1 (27.0)
HAQ-DI, mean (SD)	1.0 (0.7)	0.8 (0.6)	0.8 (0.7)
Patient-reported overall pain (0-100 mm VAS), mean (SD)	52.5 (27.0)	46.9 (29.8)	46.4 (28.8)
Body surface area >3%, n (%)	29 (31.2)	149 (37.9)	138 (30.9)
cDAPSA, mean (SD)	19.6 (14.9)	17.4 (14.6)	18.2 (14.9)
cDAPSA group, n (%)			
Remission	9 (10.3)	60 (15.7)	59 (13.8)
Low	26 (29.9)	120 (31.3)	135 (31.5)
Moderate	34 (39.1)	128 (33.4)	151 (35.3)
High	18 (20.7)	75 (19.6)	83 (19.4)

The n represents the total sample; number of patients with data available may vary.

cDAPSA=Clinical Disease Activity in Psoriatic Arthritis; DAS28=28-item Disease Activity Score; HAQ-DI=Health Assessment Questionnaire-Disability Index; MDA=minimal disease activity; SJC=swollen joint count; SPARCC=Spondyloarthritis Research Consortium Canada; TJC=tender joint count; VAS=visual analog scale.

ically greater in the APR + biologic group and the proportion of patients with hypertension was numerically greater in the biologic + csDMARD group vs the other groups. The proportion of patients with comorbid psoriasis and nail psoriasis was highest in the biologic monotherapy group (**Table 1**). Mean duration of PsA was comparable across groups (**Table 2**). The majority (90.3%) of the APR + biologic group had received prior biologic therapy (**Table 2**). Disease activity was generally similar among groups based on mean cDAPSA score, proportion of patients in DAS28 remission, mean SJC (0-66) and TJC (0-68), presence of enthesitis and dactylitis, SPARCC enthesitis score, and mean dactylitis count, although fewer patients in the APR + biologic group had minimal disease activity (MDA) vs the other groups (**Table 2**). Mean PhGA and PtGA, as well as HAQ-DI, and pain VAS scores were similar among groups.

Conclusion: The majority of US patients who received APR + biologic were previously exposed to biologics. Patients initiating APR + biologic had similar characteristics vs those initiating biologic monotherapy and biologic + csDMARDs; however, fewer were in MDA at the time of initiation of the second/add-on drug. This suggests a greater use of APR + biologic combination in patients who previously were unable to achieve MDA.

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Abstract Number: 1482

Secukinumab Provides Sustained Improvement of Enthesitis in Ankylosing Spondylitis Patients: A Pooled Analysis of Four Pivotal Phase 3 Trials

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesitis can be a debilitating spondyloarthritis (SpA) manifestation and the cause of pain, reduced quality of life and impaired physical function.[1,2] Herein, we evaluated the effect of secukinumab on axial and peripheral enthesitis in ankylosing spondylitis (AS) patients with baseline enthesitis (BLE) across all Maastricht AS EnthesiS (MASES) sites (N=13), axial sites [N=11; 13 MASES minus Achilles tendons (AT); AxS] and peripheral sites (N=6; AT + lateral condyles of humerus/femur; PS) and the AT (N=2) at Weeks 16 and 52.

Methods: This post hoc analysis pooled data across 4 secukinumab studies in AS (MEASURE 1-4) from patients originally randomized to secukinumab 150mg (approved dose in AS), 300mg (MEASURE 3 only), or placebo (PBO) with BLE (MASES >0). Study designs have been reported previously.[3-5] Evaluations include mean change from BL in MASES, complete resolution (CR; MASES=0) and improvement from BL in MASES score of ≥5 counts. Mixed-effect model repeat measurement (MMRM) analysis was done on change from BL in MASES score and non-responder imputation for resolution of enthesitis at Week 16; data are reported as observed at Week 52.

Table. Summary of results

	Secukinumab 150mg N=355		Secukinumab 300mg N=58		PBO N=280
	Week 16	Week 52[o]	Week 16	Week 52[o]	Week 16
LS mean change from BL in MASES score*					
Overall MASES[a]	-2.4‡	-3.5	-2.9§	-3.9	-1.9
AxS[b]	-2.3‡	-3.2	-2.9§	-3.6	-1.8
PS[c]	-1.3	-1.9	-1.6	-2.1	-1.2
AT[d]	-1.0	-1.2	-1.0	-1.3	-0.8
Complete resolution of enthesitis (MASES=0)#, %					
Overall MASES[a]	40.8§	56.4	36.2	52.9	28.9
AxS[b]	42.7§	58.6	42.1	60.0	30.1
PS[c]	46.3	65.5	52.5	69.7	38.3
AT[d]	57.0	78.4	55.0	77.8	48.0
Improvement from BL in MASES score (≥5 counts)#, %					
Overall MASES[a]	23.7	34.1	27.6	43.1	16.1
AxS[b]	20.1	28.0	22.8	32.0	15.4

§P <0.01; ‡P <0.05 vs PBO. *P-values from repeated MMRM until Week 16. #P-values from logistic regression model. Secukinumab 150mg (n=[a]355, [b]344, [c]229, [d]128); 300mg (n=[a]58, [b]57, [c]40, [d]20) and PBO (n=[a]280, [b]272, [c]188, [d]98). [o]Observed data. N, number of patients analysed; n, number of patients with measurement; AT, Achilles tendon site; AxS, axial entheseal site; BL, baseline; LS, least squares; MASES, Maastricht Ankylosing Spondylitis Enthesis; PS, peripheral site; PBO, placebo

Results: A total of 355 (70.4%), 58 (76.3%), and 280 (72%) patients had BLE in 150mg, 300mg and PBO groups, respectively. BL characteristics were generally comparable across groups. At Week 16, mean change from BL for overall MASES and AxS was greater for secukinumab 150mg (-2.4 and -2.3; both $p< 0.05$) and 300mg (-2.9 and -2.9; both $p< 0.01$) vs PBO (-1.9 and -1.8). At Week 16, patients treated with secukinumab 150mg (40.8% and 42.7%) and 300mg (36.2% and 42.1%) vs PBO (28.9% and 30.1%) achieved CR of enthesitis based on overall MASES and at AxS, respectively. A higher proportion of patients treated with secukinumab 150/300mg vs PBO achieved a higher threshold of improvement (≥5 counts) in overall MASES at Week 16. Further improvements were observed for all endpoints at Week 52 (Table).

Conclusion: Secukinumab 150mg and 300mg were associated with higher mean change in MASES and complete resolution of enthesitis at overall MASES and axial sites compared to placebo in AS patients at Week 16, which further increased through Week 52.

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Abstract Number: 1483

Effect of Phosphodiesterase 4 Inhibition with Apremilast on Cardiometabolic Outcomes in Psoriatic Arthritis – Initial Results from the Immune Metabolic Associations in Psoriatic Arthritis (IMAPA) Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is associated with obesity and increased cardiometabolic risk. Weight loss has been noted in association with the phosphodiesterase 4 (PDE4) inhibitor apremilast. Studies also suggest a potential role for PDE4 in glucose metabolism. We aimed to investigate the effects of PDE4 inhibition with apremilast on metabolic and vascular status in PsA.

Methods: The Immune Metabolic Associations in Psoriatic Arthritis (IMAPA) study was a prospective, open label study of adults receiving apremilast as part of routine care for PsA and/or psoriasis. Cardiometabolic, anthropometric, and disease activity assessments were performed at baseline, months 1, 3, and 6 of apremilast treatment in 60 patients. A subgroup underwent endothelial function assessment by Endo-PAT (n=38) and MRI of abdominal fat distribution (n=25) at baseline and 3 months of apremilast treatment. The primary endpoints were change in body weight and glucose homeostasis parameters after 3 months of PDE4 inhibition with apremilast. Secondary outcomes included change in lipid profile, blood pressure, endothelial function, visceral, subcutaneous, and liver fat percentage on MRI. Repeated measures mixed models were used to compare mean changes in outcomes.

Results: 60 participants were recruited; median age (IQR) 55 (43, 62) years, 63% female, median disease duration (IQR) 8.0 (2.0, 12.2) years. To date, outcome data available for n=59 at baseline, n=54 month 1, n=49 month 3, and n=43 month 6. Results are summarised in table 1. Mean weight loss after 3 and 6 months apremilast treatment was -1.4kg (95% CI -2.1, -0.6, p=0.001) and -2.2kg (95% CI -3.1, -1.4, p< 0.001), respectively. >5% weight loss was achieved in 6.1% (3/49) and 21.4% (9/42) after 3 and 6 months treatment, respectively. There was no statistically significant change in HbA1c, fasting, 1 hour and 2 hour glucose and insulin concentrations, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), and area under the OGTT curve for glucose or insulin after 3 months treatment. Small reductions in total cholesterol, HDL-C, and LDL-C were seen at 3 months. Mean systolic BP decreased by 4.7mmHg after 6 months, however this was no longer statistically significant after excluding antihypertensive use. There was no statistically significant change in Reactive Hyperemia Index (RHI). Median liver fat fraction was 8.12% (IQR 4.00-13.89) at baseline. There was a modest reduction in abdominal subcutaneous adipose tissue (ASAT), with no change in visceral adipose tissue or liver fat fraction after 3 months treatment. Statistically significant improvements in 66/68 joint count, DAS28-ESR, PtGA, PGA, pain-VAS, LEI, and PASI were seen at month 6. These were independent of weight changes.

Conclusion: Apremilast was associated with modest weight loss and reduced disease activity over 6 months. There was no statistically significant change in glucose parameters or endothelial function, although there was minimal gly-

caemic and vascular dysfunction at baseline. Apremilast was associated with reduced total cholesterol, LDL-C, and HDL-C and modest reductions in ASAT at 3 months. Improvements in disease activity with apremilast appear largely independent of weight change in this cohort.

Variable	Baseline N=59	Change at Month 1 N=54	P value	Change at Month 3 N=49	P value	Change at Month 6 N=43	P value
Weight (kg)	93.0 (75.8, 107.2)	-1.2 (-2.0, -0.5)	**0.001**	-1.4 (-2.1, -0.6)	**0.001**	-2.2 (-3.1, -1.4)	**<0.001**
BMI (kg/m^2)	32.9 (26.8, 40.0)	-0.5 (-0.8, -0.1)	**0.006**	-0.4 (-0.8, -0.1)	**0.009**	-0.8 (-1.1, -0.4)	**<0.001**
HbA1c (mmol/mol) *	37.2 (4.8)	-0.5 (-1.6, 0.6)	0.377	0.6 (-0.5, 1.7)	0.305	-0.6 (-1.8, 0.6)	0.304
Fasting glucose (mmol/L) *	5.2 (4.9, 5.8)	0.1 (-0.2, 0.4)	0.616	0.2 (-0.1, 0.5)	0.241	0.2 (-0.1, 0.5)	0.210
1 hour glucose (mmol/L) *	8.7 (6.3, 10.9)	-	-	0.3 (-0.4, 1.0)	0.371	0.1 (-0.7, 0.9)	0.860
2 hour glucose (mmol/L) *	6.7 (5.5, 7.8)	-	-	-0.3 (-1.0, 0.4)	0.370	-0.6 (-1.3, 0.2)	0.158
Fasting insulin (µU/ml) *	12.4 (8.6, 20.1)	4.2 (0.05, 8.4)	**0.048**	3.2 (-1.0, 7.4)	0.136	4.6 (0.02, 9.2)	**0.049**
1 hour insulin (µU/ml) *	98.3 (60.5, 146.9)	-	-	12.4 (-9.7, 34.5)	0.270	-0.5 (-25.7, 24.7)	0.970
2 hour insulin (µU/ml) *	61.0 (38.8, 109.9)	-	-	-9.1 (-26.9, 8.8)	0.320	-17.7 (-38.1, 2.6)	0.088
OGTT Glucose AUC (mmol/min/L) *	946 (824, 1126)	-	-	17 (-42, 75)	0.572	-9 (-76, 58)	0.791
OGTT Insulin AUC (µU/min/mL) *	9794 (6549, 13480)	-	-	576 (-1025, 2177)	0.481	5 (-1825, 1835)	0.996
HOMA-IR *	1.64 (1.12, 2.61)	0.50 (0.04, 0.97)	**0.032**	0.38 (-0.08, 0.84)	0.109	0.50 (-0.00, 1.01)	0.052
Total cholesterol (mmol/L) *	4.7 (1.1)	-0.2 (-0.4, 0.0)	0.096	-0.2 (-0.5, -0.01)	**0.042**	-0.1 (-0.3, 0.2)	0.473
HDL-C (mmol/L) *	1.3 (1.1, 1.6)	-0.1 (-0.1, 0.0)	0.088	-0.1 (-0.2, -0.005)	**0.037**	-0.02 (-0.1, 0.1)	0.575
LDL-C (mmol/L) *	2.6 (2.0, 3.1)	-0.1 (-0.3, 0.03)	0.104	-0.2 (-0.4, -0.04)	**0.016**	-0.1 (-0.3, 0.1)	0.403
Triglycerides (mmol/L) *	1.3 (0.8, 1.7)	0.03 (-0.1, 0.2)	0.722	0.1 (-0.04, 0.3)	0.136	0.02 (-0.2, 0.2)	0.834
Systolic BP (mmHg)	132 (120, 146)	-1.1 (-4.9, 2.8)	0.590	-1.4 (-5.4, 2.6)	0.500	-4.7 (-8.9, -0.5)	**0.028**
Diastolic BP (mmHg)	78 (70, 84)	2.5 (0.02, 5.0)	0.049	1.2 (-1.4, 3.8)	0.349	-0.7 (-3.4, 2.0)	0.620
RHI †	2.21 (1.82, 2.7)	-	-	-0.13 (-0.33, 0.07)	0.196	-	-
VAT (L) ‡	5.76 (4.51-6.58)	-	-	-0.13 (-0.33, 0.08)	0.227	-	-
ASAT (L) ‡	8.70 (6.13-12.93)	-	-	-0.24 (-0.47, -0.01)	**0.039**	-	-
Total abdominal fat (L) ‡	13.55 (12.64-19.10)	-	-	-0.36 (-0.75, 0.02)	0.066	-	-
Liver fat fraction (%) ‡	8.12 (4.00-13.89)	-	-	0.002 (-0.02, 0.02)	0.792	-	-
66 Swollen Joint Count	7 (3, 14)	-2.8 (-4.6, -1.1)	**0.002**	-2.4 (-4.2, -0.6)	**0.008**	-3.3 (-5.1, -1.4)	**0.001**
68 Tender Joint Count	11 (5, 17)	-2.5 (-4.6, -0.4)	**0.018**	-1.6 (-3.7, 0.5)	0.140	-4.4 (-6.7, -2.2)	**<0.001**
DAS28-ESR	4.4 (3.6, 5.4)	-0.3 (-0.6, -0.03)	**0.031**	-0.3 (-0.6, -0.05)	**0.022**	-0.5 (-0.8, -0.2)	**0.001**
PASI	3.8 (1.2, 9.2)	-2.2 (-3.6, -0.9)	**0.001**	-2.4 (-3.7, -1.0)	**0.001**	-1.6 (-3.0, -0.1)	**0.037**

*Blood results available for: n=45 at baseline, n=42 at month 1, n=42 at month 3, and n=32 at month 6. †RHI: reactive hyperaemia index, normal >1.67. n=38 at baseline, n=31 at month 3. ‡Body fat composition parameters n=25 at baseline, n=21 at month 3. ASAT, abdominal subcutaneous adipose tissue; AUC, area under curve; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; OGTT, oral glucose tolerance test; VAT, visceral adipose tissue.

Table 1. Baseline metabolic, vascular, and disease activity markers and change after 1, 3, and 6 months of apremilast. Baseline values are mean (SD) for normally distributed variables or median (IQR) for non-normally distributed variables. Mean change (95% CI) compared to baseline.

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Abstract Number: 1484

The Impact of Time Since First Diagnosis on the Efficacy and Safety of Tofacitinib in Patients with Active Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

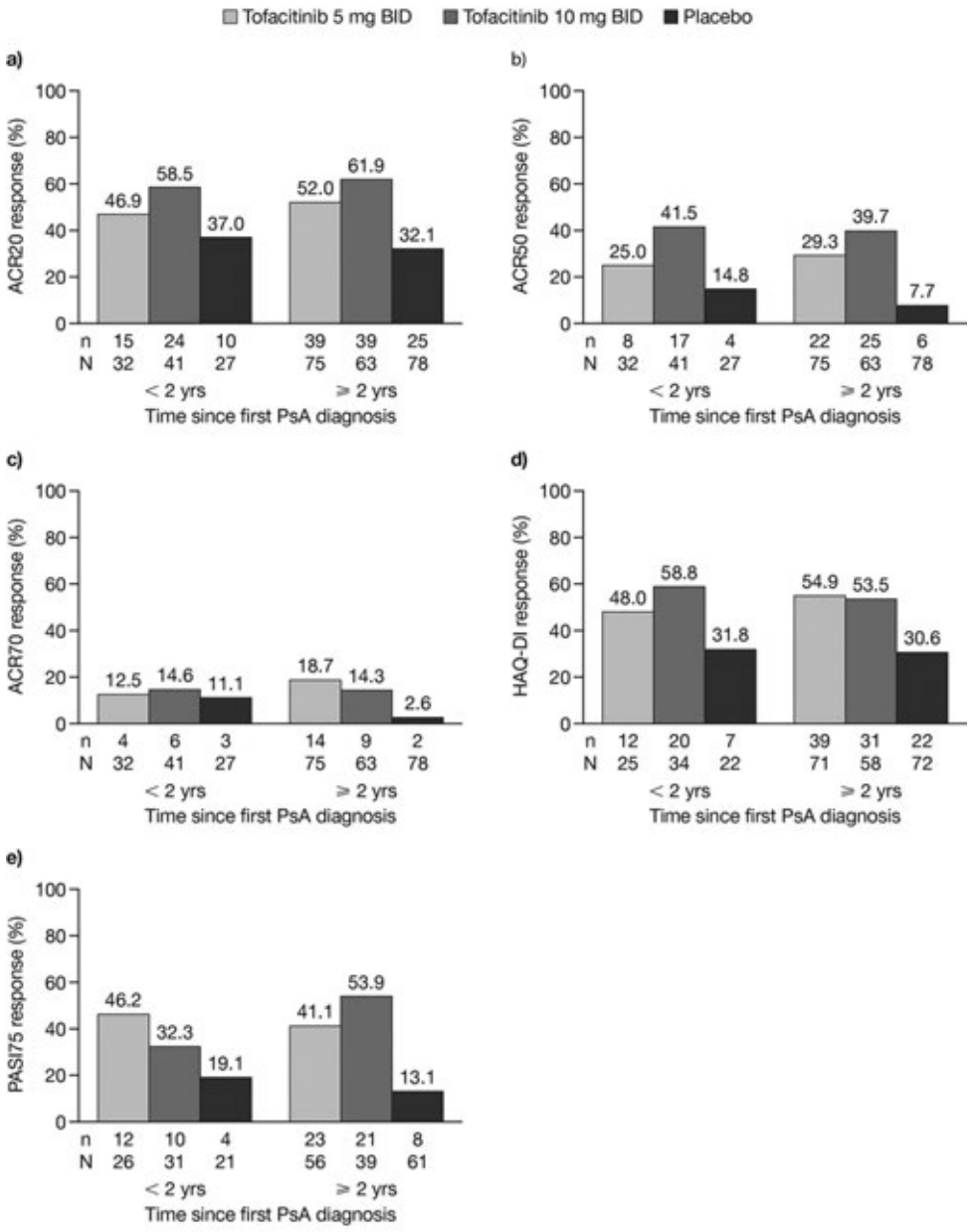
Background/Purpose: Early identification, diagnosis, and treatment of psoriatic arthritis (PsA) is important in preventing long-term joint damage and disability, and the associated socioeconomic consequences.[1] Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. Here, we assessed the efficacy and safety of tofacitinib in patients (pts) with PsA, stratified by time since first PsA diagnosis.

Methods: In this 12-month, randomized, placebo (PBO)-controlled, Phase 3 study (OPAL Broaden [NCT01877668]),[2] pts received tofacitinib 5 or 10 mg twice daily or PBO. Pts had active PsA and an inadequate response to ≥ 1 conventional synthetic DMARD. Pts were stratified by time since first PsA diagnosis: < 2 yrs and ≥ 2 yrs. Efficacy outcomes included response rates at Month (M)3 for ACR20/50/70, HAQ-DI, and Psoriasis Area and Severity Index (PASI)75. Safety outcomes up to M3 were also assessed.

Results: This analysis included 316 pts; 100 pts in the < 2 yrs group, and 216 in the ≥ 2 yrs group. Baseline demographics and characteristics were generally similar between treatment groups and across stratification groups; however, pts in the ≥ 2 yrs group were older (mean age: 49.6 yrs vs 44.6 yrs in the < 2 yrs group). Mean disease duration was 1.0 yrs (min–max: 0.3–1.8 yrs) for the < 2 yrs group, and 8.8 yrs (min–max: 2.0–39.0 yrs) for the ≥ 2 yrs group. At M3, the response rates for ACR20/50/70, HAQ-DI, and PASI75 were greater in tofacitinib-treated pts, compared with PBO-treated pts for both the < 2 yrs and the ≥ 2 yrs group (Figure 1). Across the efficacy outcomes, the response rates for tofacitinib-treated pts in the < 2 yrs group were similar to the ≥ 2 yrs group; however, for pts treated with tofacitinib 10 mg, PASI75 response was lower in the < 2 yrs group. Response rates were higher with PBO in the < 2 yrs group vs the ≥ 2 yrs group. The difference in ACR20 response rates for tofacitinib 5 mg and 10 mg vs PBO was 9.8% and 21.5%, respectively, in the < 2 yrs group; and 20.0% and 29.9%, respectively, in the ≥ 2 yrs group. Adverse events (AEs), serious AEs, discontinuations due to AEs, deaths, and most common AEs are reported in Table 1. There was one case of herpes zoster (tofacitinib 5 mg, < 2 yrs group).

Conclusion: For pts with active PsA, the efficacy of tofacitinib was greater than PBO, irrespective of disease duration; however, PBO response was generally greater in the < 2 yrs group vs ≥ 2 yrs group. Due to the low numbers in the < 2 yrs group and the post hoc nature of this analysis, these results should be interpreted with caution. Safety outcomes were consistent with those previously reported for tofacitinib in pts with PsA.[3]

Figure 1. Percentage of patients with a) ACR20, b) ACR50, c) ACR70, d) HAQ-DI, and e) PASI75 response at Month 3, stratified by time since first PsA diagnosis (< 2 yrs and ⩾ 2 yrs)



ACR20/50/70 are calculated as a ⩾ 20/50/70% improvement from baseline in tender and swollen joint counts, and a ⩾ 20/50/70% improvement from baseline in 3 of the 5 remaining ACR core measures

HAQ-DI response was defined as the number of patients achieving a reduction from baseline ⩾ 0.35 in HAQ-DI in patients with a baseline HAQ-DI ⩾ 0.35

PASI was only performed if ⩾ 3% of subject's BSA is affected at baseline. PASI75 response was defined as a ⩾ 75% reduction from baseline in PASI

ACR, American College of Rheumatology; BID, twice daily; HAQ-DI, Health Assessment Questionnaire-Disability Index; N, number of patients with a non-missing disease duration; n, number of patients in each category; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis

Table 1. Summary of AEs up to Month 3, stratified by time since first PsA diagnosis (< 2 yrs and ≥ 2 yrs)

	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo
< 2 yrs since first PsA diagnosis			
	N=32	N=41	N=27
AEs, n (%)	9 (28.1)[a]	21 (51.2)	9 (33.3)
Serious AEs, n (%)	3 (9.4)	1 (2.4)	0
Discontinuations due to AEs, n (%)	3 (9.4)	0	0
Deaths, n (%)	0	0	0
AEs occurring in > 5% of any treatment group, n (%)			
Headache	2 (6.3)	5 (12.2)	1 (3.7)
Upper respiratory tract infection	0	4 (9.8)	1 (3.7)
Nasopharyngitis	0	3 (7.3)	0
≥ 2 yrs since first PsA diagnosis			
	N=75	N=63	N=78
AEs, n (%)	33 (44.0)	26 (41.3)	28 (35.9)
Serious AEs, n (%)	0	0	1 (1.3)
Discontinuations due to AEs, n (%)	0	0	1 (1.3)
Deaths, n (%)	0	0	0
AEs occurring in > 5% of any treatment group, n (%)			
Headache	2 (2.7)	5 (7.9)	3 (3.8)
Upper respiratory tract infection	2 (2.7)	1 (1.6)	4 (5.1)
Nasopharyngitis	4 (5.3)	3 (4.8)	3 (3.8)

[a]Herpes zoster (n=1)

AEs, adverse events; BID, twice daily; N, number of patients with a non-missing disease duration; n, number of patients in each category; PsA, psoriatic arthritis

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Abstract Number: 1485

Secukinumab Provides Improvement in Nail Psoriasis and Inhibition of Radiographic Progression in Psoriatic Arthritis Patients with Nail Phenotype: 52-Week Results from a Phase III Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

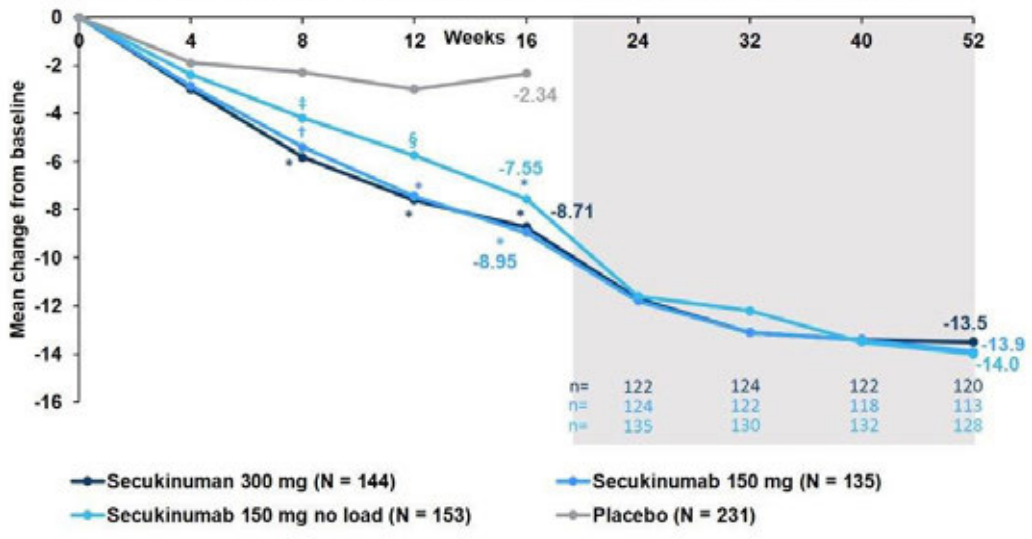
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Nail psoriasis (PsO) is present in up to 80% in psoriatic arthritis (PsA) patients (pts) and associated with significant pain, psychosocial disability, decreased physical function and quality of life (QoL).[1] Nail PsO is considered as one of the six core PsA domains by GRAPPA[2] and is a predictor of severe disease with joint involvement and structural damage. Secukinumab (SEC) has demonstrated efficacy for pts with nail PsO in the TRANSFIGURE study[3] and improvement in signs and symptoms and low radiographic progression in pts with PsA

Figure 1: mNAPSI Score through Week 52 in PsA Patients with Nail Psoriasis



*$P < 0.0001$; †$P < 0.001$; §$P < 0.01$; ‡$P < 0.05$ versus placebo.
MMRM data through Week 16 and observed data presented from Week 20-52 (shaded area).
N, total number of patients with nail psoriasis in each group; n, number of evaluable patients

Table: Summary of results

Variable	Wk	SEC 300 mg N=144	SEC 150 mg N=135	SEC 150 mg no LD N=153	PBO N=231
mTSS score[1]	24	-0.04 (128)	0.3 (102)	-0.03 (124)	0.4 (146)
	52	-0.2 (134)	0.2 (119)	0.2 (136)	-
ACR20[2]	16	66.7*	60.0*	61.4*	29.0
	52	81.2 (133)	73.7 (118)	77.9 (136)	-
ACR50[2]	16	43.1*	40.7*	32.0*	9.1
	52	54.1 (133)	45.8 (118)	50.7 (136)	-
PASI 90[1,2,3]	16	52.0*	36.8*	31.0*	7.6
	52	62.3 (69)	50.7 (75)	49.3 (75)	-
HAQ-DI[1]	16	-0.6*	-0.5*	-0.5*	-0.2
	52	-0.6 (132)	-0.6 (117)	-0.6 (136)	-
SF-36 PCS[1]	16	7.82*	6.90*	6.00*	2.29
	52	8.0 (134)	6.71 (123)	7.93 (137)	-
PsAQoL[1]	16	-3.6*	-3.6*	-3.0†	-1.1
	52	-3.9 (134)	-4.2 (122)	-3.8 (137)	-
Resolution of enthesitis, %[4]	16	58.2†	56.8†	47.2‡	34.3
	52	81.5 (92)	68.7 (80)	70.7 (82)	-
Resolution of dactylitis, %[4]	16	63.8†	52.6‡	59.2†	32.4
	52	78.8 (52)	79.6 (49)	80.3 (66)	-

*P<0.0001; †P<0.001; §P<0.01; ‡P<0.05 vs. PBO. NRI data for binary and MMRM data for continuous variables presented at Wk 16. Observed data presented at Wk 52.

[1]Mean change from baseline;

[2]% responders (n); [3]Data from pts with BL psoriasis ≥3% BSA: N=75 [300 mg]; 87 [150 mg], 84 [150 mg no LD] and 118 [PBO]; [4]Data from pts with enthesitis/dactylitis at BL: N=98/58 [300 mg]; 88/57 [150 mg], 89/76 [150 mg no LD] and 140/102 [PBO]

ACR 20/50, American College of Rheumatology (ACR) criteria scores of 20 and 50; BL, baseline; LD, load; HAQ-DI, Health assessment questionnaire disability index; mTSS, modified total sharp score; N, number of pts with nail PsO in each group; n, number of evaluable pts; PASI, psoriasis area and severity index; PCS, Physical Component Score; PsAQoL, Psoriatic Arthritis Quality of Life; pts, patients; SF-36, Short Form Health Survey,

in FUTURE 5 (NCT02404350) study[4].Here, we report the efficacy of SEC on nail PsO, and other facets of disease, including radiographic progression, in the nail subset through 52 weeks (wks) from the FUTURE 5 study.

Methods: Pts (N=996) with active PsA, were randomized to subcutaneous SEC 300 mg loading dosage (LD; 300 mg), 150 mg LD (150 mg), 150 mg no LD or placebo (PBO). All groups received SEC or PBO at baseline (BL), Wks 1, 2, 3, and 4, and then every 4 wks. Efficacy assessments through Wk 52 included mNAPSI, radiographic progression (mTSS), ACR, PASI, HAQ-DI, SF-36 PCS, PsAQoL and resolution of dactylitis and enthesitis. Analyses through Wk 16 used non-

responder imputation (NRI) for binary and mixed-effect model repeated measure (MMRM) for continuous variables. Observed data are presented for radiographic progression at Wks 24 and 52, and for all efficacy endpoints at Wk 52.

Results: A total of 663/996 (66.6%) PsA pts had concomitant nail PsO at BL. Demographics and BL disease characteristics were balanced between treatment groups in the nail subset, which were comparable with overall population. The total mean Nail Psoriasis Severity Index (mNAPSI) score at BL was 16.4. SEC 300 and 150 mg doses improved nail PsO vs. placebo (PBO) at Wk 8, 12 and 16 ($P < 0.0001$), with further improvements through Wk 52 (Figure). Mean change from baseline in mTSS score at Wks 24 and 52 are shown in the Table. Proportions of pts with no radiographic progression (change from BL in mTSS ≤0.5) with SEC at 52 Wks were 94.0% (300 mg LD), 83.5% (150 mg LD), and 88.4% (150 mg No LD). ACR20/50 and PASI 90 responses, resolution of dactylitis and enthesitis, physical function and QoL were also improved with SEC vs. PBO at Wk 16 with sustained improvements through 52 wks (Table).

Conclusion: Secukinumab provided sustained improvements in nail disease, signs and symptoms of PsA, physical function and QoL along with low radiographic progression through 52 wks in PsA pts with moderate to severe nail PsO.

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4. *Mease PJ et al., Arthritis Rheumatol.* 2018; 70 (suppl 10).

Disclosure: P. Nash, AbbVie, 2, 5, 8, Abbvie, 2, 8, Amgen, 2, 5, 8, BMS, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8; **P. Mease**, Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, Roche, UCB, 2, 5, Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB, 8, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Abbvie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer and UCB., 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB, 2, Abbvie, Amgen, Brsitol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Brsitol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Brsitol Myers Squibb,Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, Amgen, 2, 5, 6, 8, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, and UCB, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 2, 5, Boerhinger Ingelheim, 5, Bristol Myers Squibb, 2, 5, 8, Bristol Myers Squibb Co., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8, Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8; **B. Kirkham**, AbbVie, 2, 5, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Novartis, 2, 5, 8; **A. Balsa**, BMS, 2, Roche Pharma, 2; **A. Singhal**, AbbVie, 2, 8, Amgen, 2, AstraZeneca, 2, Bristol-Myers Squibb, 2, Fujifilm, 2, Gilead, 2, Janssen, 2, Lilly, 2, Mallinckrodt, 2, MedImmune, 2, Nichi-Iko, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, UCB, 2; **E. Quebe-Fehling**, Novartis, 3; **L. Pricop**, Noavrtis, 1, 3, Novartis, 1, 3, 4; **C. Gaillez**, Novartis, 3.

Abstract Number: 1486

Infliximab Serum Trough Levels Predict Non-clinical Response in Patients with Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Infliximab (Ifx) has proven to be efficacious for improving symptoms in patients with axial SpA(axSpA). Several factors may influence the pharmacokinetic-pharmacodynamic of Ifx and its relation with clinical response such as: disease activity, anti-drug antibodies and the use of concomitant conventional synthetic DMARDs. The prediction of early response through Ifx concentrations could be a feasible tool to optimize the early detection of non-responders to Ifx therapy.

The main objective is to identify if serum Ifx trough levels at early stages of treatment could predict the non-response in patients with axSpA. The secondary objective was to analyze if early drug levels could also predict the development of secondary inefficacy.

Methods: Observational study including 75 patients with axSpA recruited from the axSpA-Paz cohort treated with Ifx and monitored during 52 weeks (W).. Serum Ifx levels and ADA were measured by capture and bridging ELISA respectively at baseline, W2, W6, W12 and W24. Disease activity was assessed at baseline, W24 and W52 by the Ankylosing Spondylitis Disease Activity Score (ASDAS) and clinical response was defined by ΔASDAS≥1.1. The association between serum Ifx trough levels at early stages and clinical response at W52 was evaluated. After that, receiver operating characteristic (ROC) curves for the outcome of clinical response after 52W of treatment were employed to determine the best cut-off values for serum Ifx trough levels. The association between the best cut-off Ifx levels at early stages and clinical outcomes was evaluated by a logistic regression analysis. Ifx survival was evaluated through Kaplan-Meier curves.

Results: Out of the 75 patients studied, 37(49%) were non-responders and 38 (51%) were responders. During the treatment with Ifx, 35(47%) patients discontinued Ifx, most of them due to secondary inefficacy 27/35(77%). Patients with good response after 52W tended to have higher Ifx concentrations compared with non- responder patients at W12: 6.9(4.7-10.7) vs 3.1(0.7-8.5); p=0.006. In addition, patients with concomitant MTX had higher serum Ifx trough levels (median and IQR) than patients without MTX at different time points: at W6: 25.9(16-40) vs 16(11.3-26.6); p=0.008; at W12: 8.6(5.2-12) vs 3.8(1.7-7.7); p=0.005 and at W22: 4.7(2.1-8.3) vs 3.1(0.6-5.1); p=0.007; respectively). ROC curve for serum Ifx concentrations at W12 showed an area under the curve of 0.687 (95% confidence interval (CI): 0.558-0.815), p< 0.01). A cut-off of 6.7 µg/mL showed a sensitivity of 52% and specificity of 71%.Values < 6.7 µg/mL were found to be associated with lower ΔASDAS at W52 (OR: 2.7; 95%CI: 1.0-7.1). The regression analysis

showed that Ifx concentrations < 6.7 µg/mL at W12 also predict the dropout due to secondary inefficacy (OR: 3.5; 95%CI: 1.2-10.2). The mean survival time was significantly shorter in patients with Ifx levels at W12 < 6.7 µg/mL compared with patients with levels above this cut-off: 5.3 years (95% CI: 4.1-6.5) vs 8 years (95% CI: 6.4-9.7);p=0.03.

Conclusion: Serum Ifx trough levels at W12< 6.7 µg/mL are associated with non-clinical response during the first year of Ifx therapy, more risk to develop secondary inefficacy and a shorter drug survival in patients with axSpA.

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Abstract Number: 1487

Impact of TNF-α Inhibitor on Lipid Profile and Atherogenic Index of Plasma in Axial Spondyloarthritis: Two-year Follow-up Data from the Catholic Axial Spondyloarthritis COhort (CASCO)

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the influence of TNF-α inhibitor on lipid profile and atherogenic index of plasma (AIP) in axial spondyloarthritis (axSpA) patients with long term use of stable dose TNF-α inhibitor.

Methods: axSpA patients were enrolled in the Catholic Axial Spondyloarthritis COhort (CASCO). We collected their data annually and analyzed their lipid profile and AIP [logarithm of ratio of triglyceride (TG) to high density lipoprotein cholesterol (HDL-C)]. Comparison was conducted between TNF-α inhibitor user group and non-user group. Additionally, lipid profile and AIP of TNF-α inhibitor user group were compared over 2 years.

Results: A total of 238 axSpA patients were enrolled for the present study, including 132 TNF-α inhibitor users and 106 non-users. Changes of total cholesterol (TC), TG, low density lipoprotein cholesterol (LDL-C), and HDL-C over 2 years did not show significant difference between TNF-α inhibitor user group and non-user group. When baseline data and two-year follow-up data were compared within the TNF-α inhibitor user group, there was no significant increase in TG, LDL-C, HDL-C, or AIP. Only TC level was slightly increased in the two-year follow data for the TNF-α inhibitor user group (177.86 ± 28.73 vs. 183.08 ± 29.82, P = 0.019).

Conclusion: Long term use of stable dose TNF-α inhibitor didn't increase atherogenic lipid profile or AIP compared to the control group. Furthermore, atherogenic lipid profile or AIP was not increased significantly in the TNF-α inhibitor user group over two-year follow up. Therefore, using TNF-α inhibitor for a long-term might not affect atherosclerosis of axSpA.

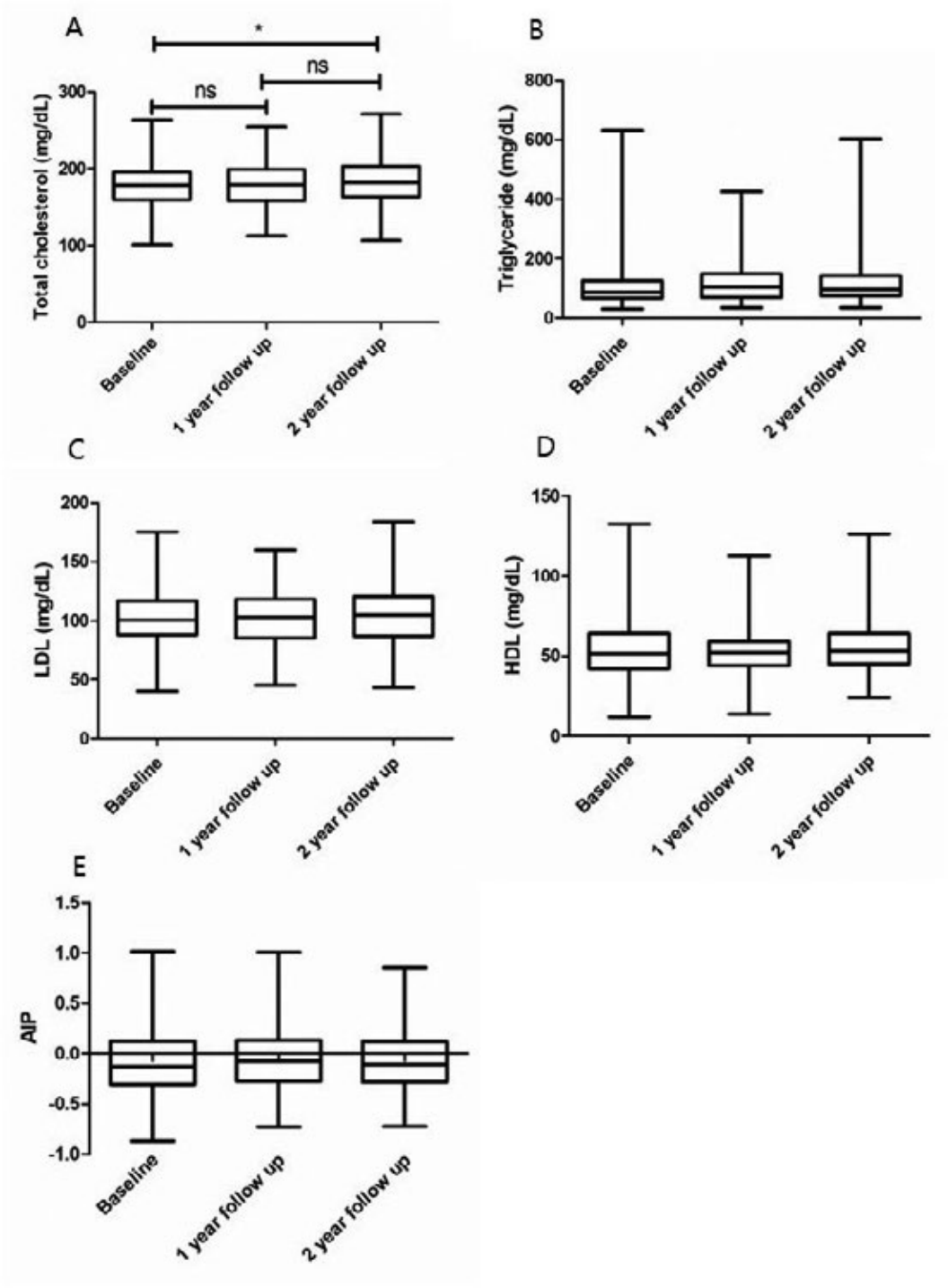
A
*
ns
ns
Total cholesterol (mg/dL)
300
200
100
0
Baseline
1 year follow up
2 year follow up
B
Triglyceride (mg/dL)
800
600
400
200
0
Baseline
1 year follow up
2 year follow up
C
LDL (mg/dL)
200
150
100
50
0
Baseline
1 year follow up
2 year follow up
D
HDL (mg/dL)
150
100
50
0
Baseline
1 year follow up
2 year follow up
E
AIP
1.5
1.0
0.5
0.0
-0.5
-1.0
Baseline
1 year follow up
2 year follow up

Table 1. Comparison of baseline characteristics between TNF-α inhibitor user and non-user

	TNF-α inhibitor non user (N=106)	TNF-α inhibitor user (N=132)	*P*
Age (year)	36.8 ± 11.4	38.9 ± 11.9	0.172
Follow up duration (year)	6.5 ± 6.3	8.7 ± 6.6	**0.009**
Male gender (%)	69 (65.1%)	106 (80.3%)	**0.013**
BMI (kg/m^2)	23.2 ± 3.1	23.7 ± 3.0	0.280
Current smoker (%)	23 (22.1%)	30 (23.6%)	0.909
Current drinker (%)	73 (70.2%)	81 (63.3%)	0.333
Alcohol consumption (unit/week)	7.1 ± 12.5	9.0 ± 13.3	0.288
Uveitis Hx. (%)	56 (53.8%)	58 (45.7%)	0.269
IBD (%)	1 (1.0%)	4 (3.1%)	0.502
Dactylitis Hx. (%)	6 (5.8%)	14 (11.0%)	0.239
Psoriasis (%)	5 (4.8%)	7 (5.5%)	1.000
BASDAI (0-10)	3.3 ± 1.6	2.6 ± 2.0	**0.005**
ASDAS-CRP (0-10)	2.0 ± 0.9	1.7 ± 0.9	**0.012**
ASDAS-ESR (0-10)	2.1 ± 0.8	1.8 ± 1.0	**0.008**
BASFI (0-10)	0.8 ± 1.3	1.1 ± 1.5	0.071
Co-morbidity			
HTN (%)	6 (5.7%)	23 (17.4%)	**0.011**
CAD Hx. (%)	0 (0.0%)	1 (0.8%)	1.000
DM (%)	3 (2.8%)	5 (3.8%)	0.964
Osteoporosis (%)	11 (10.4%)	10 (7.6%)	0.598
Medication			
ASAS NSAID index (0-100)	50.0 ± 34.8	30.8 ± 36.7	**< 0.001**
Sulfasalazine (%)	65 (61.3%)	13 (9.8%)	**< 0.001**
Methotrexate (%)	1 (0.9%)	2 (1.5%)	1.000
Oral steroid (%)	1 (0.9%)	3 (2.3%)	0.775
Bisphosphonate (%)	12 (11.3%)	15 (11.4%)	1.000
Vitamin D (%)	41 (38.7%)	54 (40.9%)	0.829
Laboratory finding			
ESR (mm/hr)	16.6 ± 13.5	13.2 ± 15.5	0.080
CRP (mg/dL)	0.6 ± 1.6	0.3 ± 0.9	0.103
HLA-B27 positive (%)	98 (94.2%)	111 (94.1%)	1.000
TC (mg/dL)	171.4 ± 27.6	177.6 ± 28.7	0.094
TG (mg/dL)	101.4 ± 63.1	111.8 ± 82.9	0.274
LDL-C (mg/dL)	99.1 ± 24.2	102.0 ± 24.5	0.356
HDL-C (mg/dL)	51.9 ± 16.0	53.7 ± 19.3	0.431
AIP	-0.119 ± 0.343	-0.085 ± 0.378	0.473

Table 2. Comparison of 2-year follow up lipid profile between TNF-α inhibitor user and non-user

	TNF-α inhibitor non user (N=106)	TNF-α inhibitor user (N=132)	*P*
Change of TC (mg/dL)	7.63 ± 25.28	5.64 ± 25.47	0.549
Change of TG (mg/dL)	10.54 ± 62.93	4.68 ± 78.17	0.532
Change of LDL-C (mg/dL)	3.64 ± 19.98	2.61 ± 20.79	0.702
Change of HDL-C (mg/dL)	1.97 ± 13.07	1.44 ± 12.99	0.753
Change of AIP	0.026 ± 0.293	0.002 ± 0.275	0.519
AIP class (2 year f/u)			0.761*
Low risk (AIP<0.11)	75 (70.8%)	99 (75.0%)	
Intermediate risk (0.11≤AIP≤0.21)	10 (9.4%)	11 (8.3%)	
High risk (AIP>0.21)	21 (19.8%)	22 (16.7%)	

* The Mantel–Haenszel $\chi 2$ test was used.

Disclosure: H. Min, None; **S. Kwok**, None; **S. Lee**, None.

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Ixekizumab Demonstrates Improvement Comparable to Adalimumab Across ACR Components in Biologic-Naïve Patients with Psoriatic Arthritis

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Background/Purpose: In patients (pts) with active psoriatic arthritis (PsA) and inadequate response or intolerance to conventional synthetic DMARD (csDMARD), use of a biologic DMARD (bDMARD) is often recommended.[1] Multiple bDMARD treatments are available, and head-to-head trials comparing their safety and efficacy provide valuable information to physicians in choosing the best bDMARD for each pt. SPIRIT-H2H is the first completed large head-to-head (H2H) superiority study in active PsA.[2] The study demonstrated superiority at Week 24 of ixekizumab (IXE), an IL-17A antagonist, over adalimumab (ADA), a TNF inhibitor, on a combined endpoint. Improvement in individual American College of Rheumatology (ACR) components is presented.

Methods: Data from the SPIRIT-H2H (NCT03151551) (Phase 3b/4, 52-week, multicenter study) were evaluated. All pts met Classification for Psoriatic Arthritis criteria and are bDMARD-naïve with inadequate response to csDMARD, active PsA (≥3 tender joints [TJ] and ≥3 swollen joints [SJ]), and plaque psoriasis (PsO; body surface area [BSA] ≥3%). Pts were randomized (1:1, stratified by baseline concomitant csDMARD and moderate-to-severe plaque psoriasis) to IXE or ADA on-label PsA or PsO dosing based on the absence/presence of moderate-to-severe plaque psoriasis (de-

fined: BSA ≥10% + Psoriasis Area Severity Index [PASI] ≥12 + static Physician Global Assessment ≥3). All pts could remain on stable dose of csDMARD. A blinded assessor counted TJ (68) and SJ (66). Other ACR components analyzed included C-reactive protein (CRP) and those completed by the unblinded pt and investigator: HAQ-Disability Index (HAQ-DI), joint pain by visual analog scale (VAS), Physician's and Pt's Global Assessments. The primary outcome was the percentage of pts meeting ≥50% or ≥70% improvement in each ACR component at Week 24 and is summarized by treatment groups. Logistic regression analysis was used to detect any treatment group differences at Week 24 on intent-to-treat population. Missing data were imputed using the nonresponder imputation method.

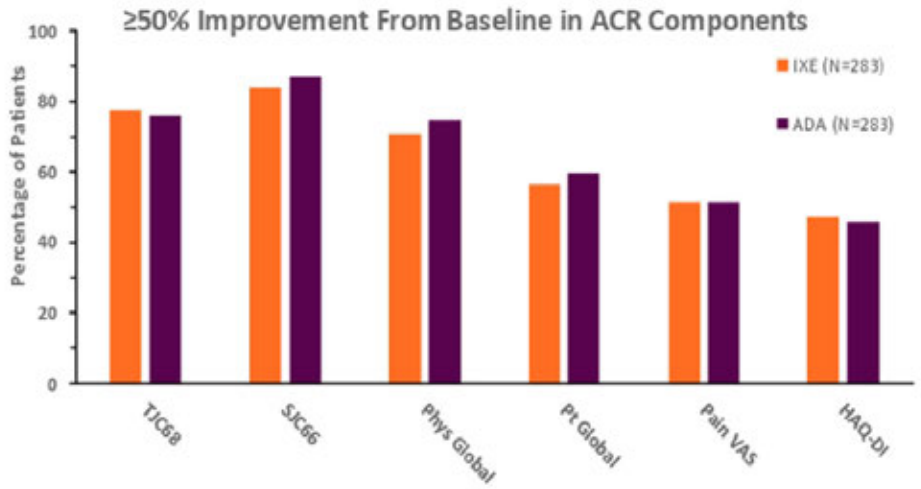
Results: 566 pts were randomized (283 in each arm) with baseline demographics and disease characteristics generally well balanced between groups. IXE and ADA provided comparable efficacy as measured by the percentage of pts achieving ≥50% improvement from baseline at Week 24 for ACR components (Figure 1) other than CRP, where significantly more pts treated with ADA had ≥50% improvement compared with IXE ($p < .05$). No significant differences in the percentage of pts achieving ≥70% improvement from baseline in all ACR components, including CRP, were observed between IXE and ADA groups (Figures 2-3), for both open-label and blinded outcome measures.

Conclusion: In biologic-naïve PsA pts, IXE has comparable efficacy to ADA at Week 24 as determined by the percentage of pts achieving ≥50% or ≥70% improvement in clinical components and in pt-reported outcomes of ACR.

References:

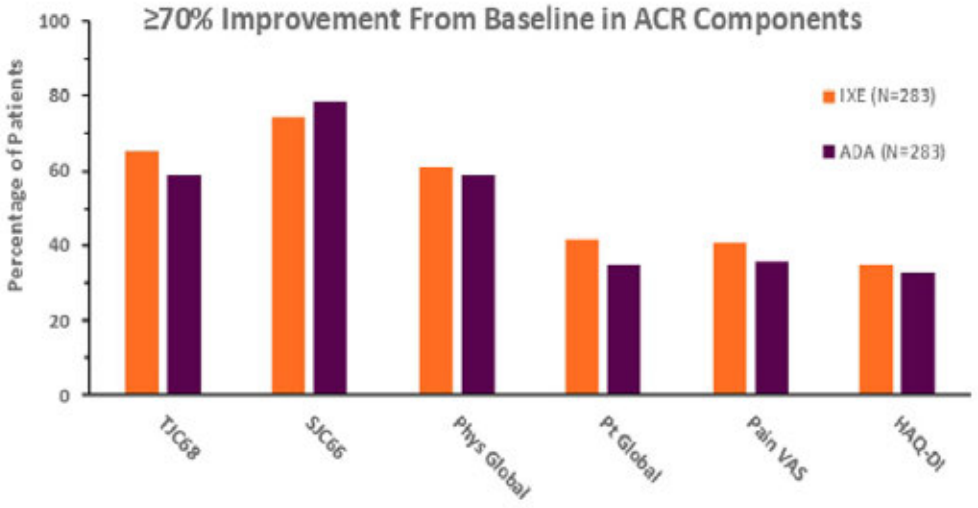
1. Singh JA, et al. Arth Rheum 2019; 71:5-32
2. Available at https://clinicaltrials.gov/ct2/show/results/NCT03151551?term=spirit-h2h{00AMP00}rank=1

Figure 1. Percentage of Pts Showing ≥50% Improvement in Open-label (Physician's and Pt's Global Assessments, Joint Pain VAS, HAQ-DI) and Blinded (TJC68, SJC66) ACR Components at Week 24: IXE vs ADA



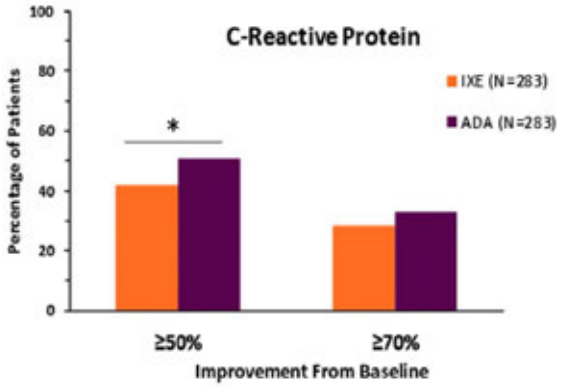
Abbreviations: ADA, adalimumab; HAQ-DI, Health Assessment Questionnaire-Disability Index; IXE, ixekizumab; Phys Global, Physician's Global Assessment; Pt Global, Patient's Global Assessment; SJC66, swollen joint count 66; TJC68, tender joint count 68; VAS, visual analog scale.

Figure 2. Percentage of Pts Showing ≥70% Improvement in Open-label (Physician's and Pt's Global Assessments, Joint Pain VAS, HAQ-DI) and Blinded (TJC68, SJC66) ACR Components at Week 24: IXE vs ADA



Abbreviations: ADA, adalimumab; HAQ-DI, Health Assessment Questionnaire-Disability Index; IXE, ixekizumab; Phys Global, Physician's Global Assessment; Pt Global, Patient's Global Assessment; SJC66, swollen joint count 66; TJC68, tender joint count 68; VAS, visual analog scale.

Figure 3. Percentage of Pts Showing Improvement From Baseline in CRP at Week 24: IXE vs ADA



*p<0.05, IXE vs ADA; as calculated using logistic regression analysis with treatment, concomitant csDMARD use at baseline, and moderate-to-severe plaque psoriasis involvement as factors.

Abbreviations: ADA, adalimumab; CRP, C-reactive protein; IXE, ixekizumab.

Disclosure: M. Husni, Abbvie, 5, AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, Regeneron, Sanofi-Genzyme, UCB, 5, Abbvie, Amgen, Janssen, Novartis, Lilly, Regeneron, Pfizer and UCB, 5, Bristol-Myers Squibb, 5, Eli Lilly, 5, Genentech, 5, Janssen, 5, Janssen Research & Development, LLC, 2, 3, Novartis, 5, PASE questionnaires, 7, Pfizer,

5, Sanofi-Genzyme, 5, UCB, 5; **K. Gowin**, Lilly, 9, Pfizer, 8, Celgene, 8, Sanofi-Genzyme, 8, Abbvie, 8; **A. Gellett**, Eli Lilly and Company, 1, 3; **A. Trevelin Sprabery**, Eli Lilly and Company, 1, 3; **C. Helt**, Eli Lilly, 1, 3, Eli Lilly and Company, 1, 3; **V. Geneus**, Eli Lilly, 1, 3; **M. Rossini**, Abiogen, 5, Biogen, 5, Eli Lilly, 5, 8, Novartis, 5, UCB, 5.

Abstract Number: 1489

Impact of Apremilast on PsA Impact of Disease Core Components in Patients with a Limited Number of Active Joints: Results from a Real-World Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

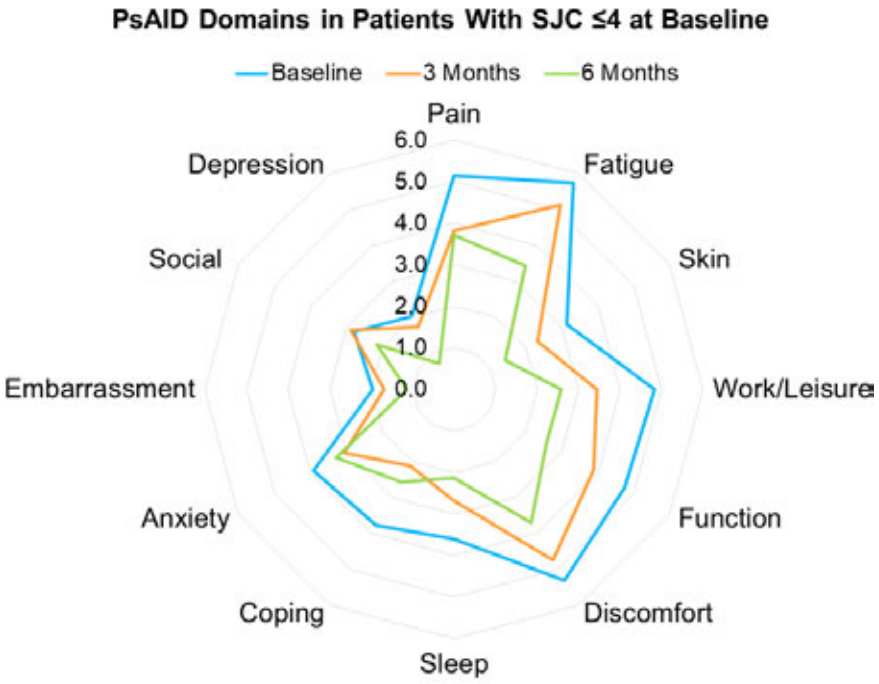
Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Recent data suggest that patients with moderately active psoriatic arthritis (PsA) and a limited number of active joints have a high likelihood of achieving treatment goals with apremilast treatment (McInnes I, et al. *Ann Rheum Dis.* 2018;77(Suppl 2). Abstract 0927. Coates LC, et al. *Arthritis Rheumatol.* 2018;70(Suppl 10). Abstract 1607). Real-world evidence on the effect of apremilast on patients' perception of the impact of their disease is limited. Here, we describe the effects of apremilast on the impact of disease in the real-world as measured by the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire in PsA patients with a swollen joint count (SJC) ≤4 at baseline.

Methods: The prospective, multicenter, observational REWARD study (NCT02875184; The Netherlands) is investigating apremilast treatment in real-world patients with PsA. Descriptive statistics were assessed for disease measures, including SJC (0-66) and tender joint count (TJC; 0-68), PsAID (0-10), and Patient's Perception of Pain based on the visual analog scale (VAS; 0-100 mm) among patients with a limited number of swollen joints (SJC ≤4) at baseline. We report the effects of apremilast on these disease measures at treatment initiation and at the first 6 months of treatment with a data cutoff of December 2018.

Results: A total of 48 patients from 9 clinics who were receiving apremilast were included in this interim analysis. Among these patients, 31 (65%) had SJC ≤4 and 17 (35%) had SJC >4 at baseline. Of the patients with SJC ≤4 at baseline, 18 and 8 had at least 3 and 6 months of follow-up, respectively, at the time of data cutoff. Results are reported for patients with available data at each time point. Baseline characteristics for patients with SJC ≤4 included a mean age of 54 years, mean body mass index of 29.1 kg/m^2, and mean years since PsA diagnosis of 7.0 years; 58% of patients were female, 90% had prior cDMARD use, and 29% had prior biologic use. For patients with SJC ≤4, disease measures were reported as follows: The mean SJC at baseline, 3, and 6 months were 1.1, 0.6, and 0.1 and the mean TJC at baseline, 3, and 6 months were 4.5, 3.6, and 1.5, respectively. The mean PsAID scores at baseline, 3, and 6 months were 4.2, 3.4, and 2.6, respectively. Individual PsAID domain scores by time points are shown (Figure). Patients with a limited number of swollen joints showed gradual improvements in all domains of the PsAID. Mean Pain VAS scores at baseline, 2 weeks, 6 weeks, 3 months, and 6 months were 47, 48, 39, 29, and 26, respectively, in these patients.



Data as observed. Of the patients with SJC ≤4 at baseline, 16 and 7 had at least 3 and 6 months of follow-up, respectively, at the time of data cutoff with PsAID values available at each visit.

Conclusion: Results from the real-world, prospective, multicenter, observational REWARD study suggest that PsA patients with a limited number of active swollen joints may benefit from apremilast treatment. Apremilast was associated with improvements in the perceived impact of disease, as observed by reductions in the PsAID and its core components.

Disclosure: T. Jansen, AbbVie, Celgene Corporation, 5, Grunenthal, Sobi, 8, Olatec, Grunenthal, 2; **E. Kroot**, None; **A. van Vliet**, Celgene Corporation, 3; **J. Pander**, Celgene Corporation, 3; **M. Vis**, AbbVie, Celgene Corporation, Eli Lilly, Novartis, Pfizer, 5, AbbVie, Celgene Corporation, Novartis, Pfizer, 5, Novartis, Pfizer, 2.

Abstract Number: 1490

Blockage of TNFα and IL-12/23 Improves Depressive Symptoms in Patients with Psoriatic Arthritis – Analysis of Clinical Trial Data

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

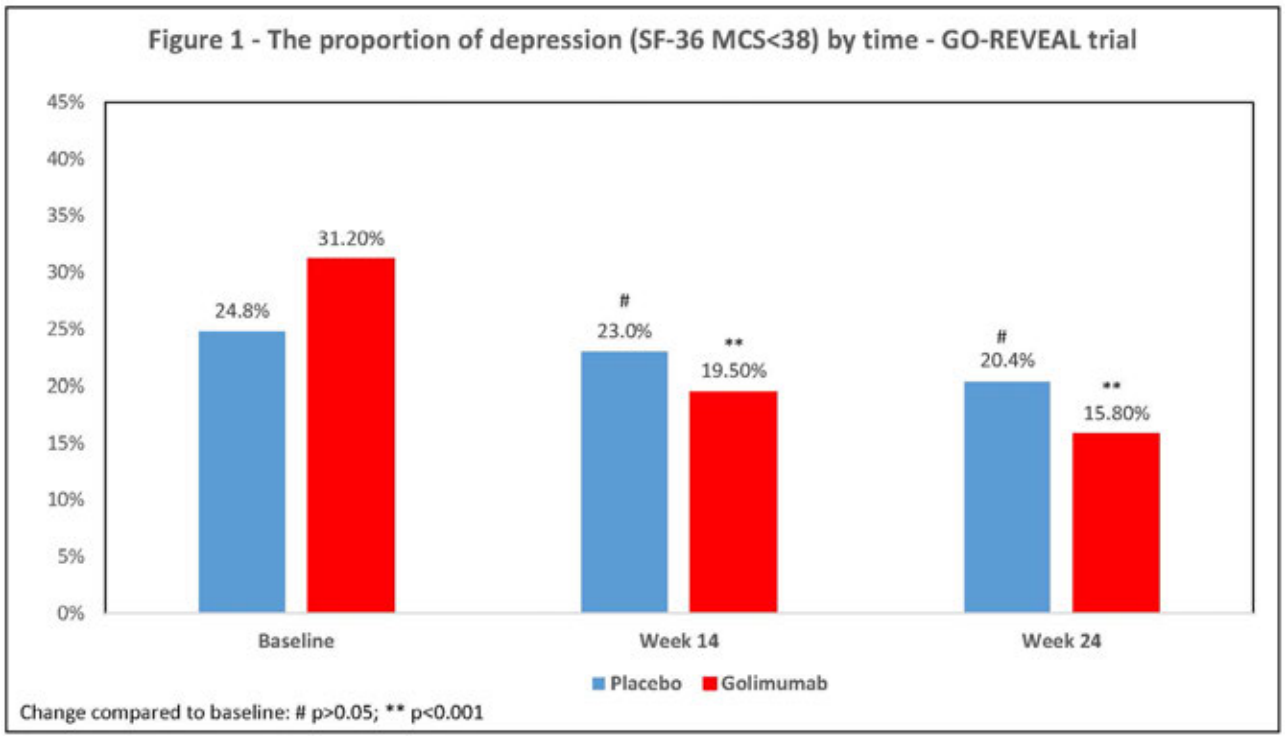
Session Type: Poster Session (Monday)

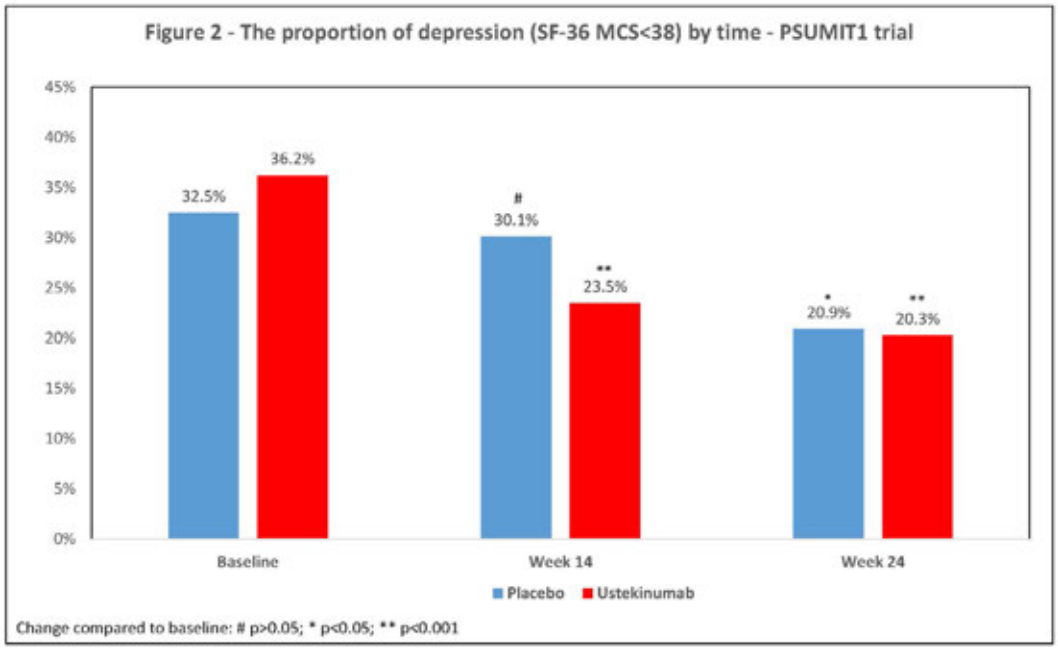
Session Time: 9:00AM–11:00AM

Background/Purpose: The prevalence of depression is increased in patients with psoriatic arthritis (PsA). Little is known about the impact of effective control of inflammation on depressive mood in patients with PsA and the direct impact of therapies for PsA on depression. The aim of the study was to assess the effect of golimumab (TNFα blocker) and ustekinumab (IL-12/23blocker) on improving depressive symptoms in patients with PsA participating in clinical trials.

Methods: Data from three phase 3, randomized, double blinded placebo-control clinical trials assessing the efficacy of golimumab (GO-REVEAL) and ustekinumab (PSUMIT1 and 2) were analyzed. For each trial the analysis included all patients who were randomized to receive the study drug or placebo. The analysis included information collected during the double-blind portion of the trial (baseline, 14-16 and 24 weeks). The Short-Form Health Survey (SF-36) mental component summary (MCS) score was used to assess the change in depressive symptoms over time in each treatment arm. A threshold of SF-36-MCS < 38 was used to define a state of depression (sensitivity of 87%, sensitivity of 80% and accuracy of 83%)1. The change in proportion of patients classified as being depressed was compared with baseline for each treatment arm using chi square test (Odds Ratio (OR)).

Results: A total of 1,332 patients were enrolled in the three trials (GO-REVEAL 405, PSUMIT1 615, PSUMIT2 312). The mean age was 47 years and the proportion of females ranged from 39.8% and 52.6%. The proportions of patients classified as being in depression at baseline were: 29.4% (GO-REVEAL), 34.9% (PSUMIT-1) and 38.8% (PSUMIT2). Overall, a significant decrease in the proportion of patients with depression was found in the treatment arms of all three studies. In the GO-REVEAL trial the proportion of depression reduced from 31.2% (baseline) to 19.5% (W14: OR 0.54; p=0.001) and 15.8% (W24: OR 0.41;p< 0.001, Figure 1) in the golimumab arm. In the PSUMIT1 trial the proportion of depression decreased from 36.2% (baseline) to 23.5% (W16: OR 0.54;p< 0.001) and 20.3% (W24: 0.45;p< 0.001, Figure 2) in the ustekinumab arm. In the PSUMIT2 trial the proportion of depression decreased from 37.5% (baseline) to 25.5% (W14: OR 0.57;p=0.009) and 21.2% (W24:

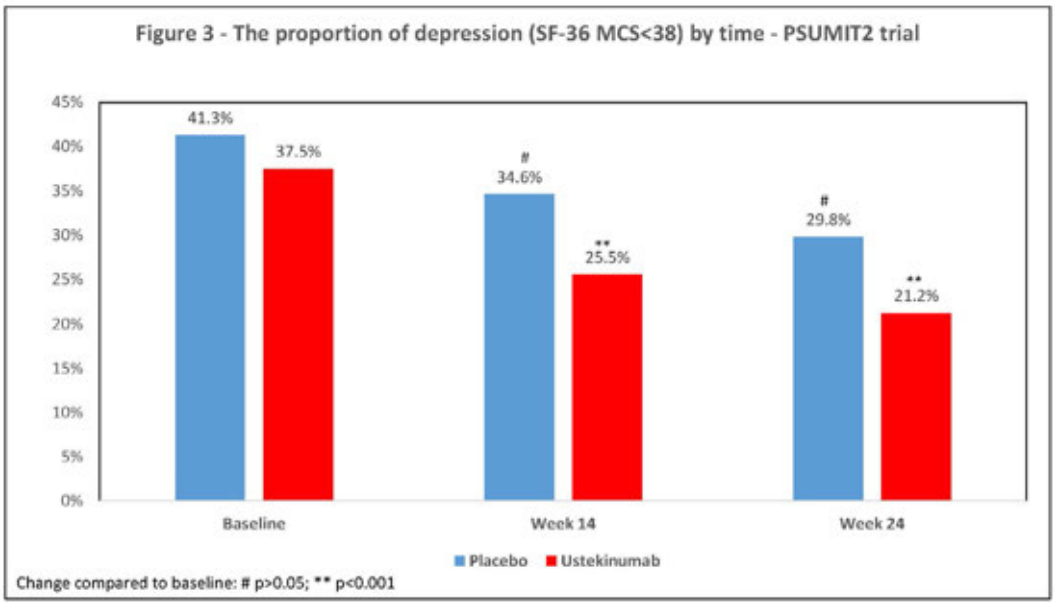




OR 0.45;p< 0.001, Figure 3) in the ustekinumab. In general, minimal changes were seen in the proportion of depression in the placebo arm of all three studies.

Reference: Matcham F et al. Usefulness of the SF-36 Health Survey in screening for depressive and anxiety disorders in rheumatoid arthritis. BMC musculoskeletal disorders. 2016;17:224

Conclusion: Blockage of TNFα and IL-12/23 was associated with a significant improvement in depressive symptoms in patients with PsA participating in clinical trials.



Disclosure: L. Eder, Abbvie, 2, 5, 8, Celgene, 5, Janssen, 5, Lily, 2, 5, Novartis, 2, 5, Pfizer, 2, 8, UCB, 2; **A. Ogdie**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Takeda, 5, Amgen, 2, 4, 5, 8, Amgen to Forward National Databank, 2, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 4, 5, 8, Corrona, 5, CORRONA, 5, From Noavrtis to husband, 7, Lilly, 5, Lily, 5, Novartis, 2, 5, 7, Novartis to UPenn, 2, Novartis, Pfizer, 2, Pfizer, 2, 5, Pfizer Inc, 2, 5, Pfizer to UPenn, 2; **Y. Zhong**, None.

Abstract Number: 1491

Long-term Clinical Outcome of Anti-TNF Treatment in Patients with Early Axial Spondyloarthritis: 10-year Data of the Etanercept vs. Sulfasalazin in Early Axial Spondyloarthritis Trial

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Long-term data on anti-TNF treatment in patients with early axial spondyloarthritis (SpA) is scarce. The objective of this analysis was to assess the long-term clinical efficacy (up to 10 years of treatment) of a tumor necrosis

factor (TNF) inhibitor etanercept (ETN) in patients with early axial spondyloarthritis, who participated in the long-term (until year 10) extension of the ESTHER (Etanercept vs. Sulfasalazine in Early Axial Spondyloarthritis Trial) trial (1).

Methods: In the previously reported ESTHER trial, patients with early active axial SpA [including both non-radiographic axial SpA (nr-axSpA) and radiographic axial SpA (r-axSpA)/ankylosing spondylitis (AS)] with a symptom duration of < 5 years and a positive MRI of the sacroiliac joints (SIJs) and/or the spine at baseline) were treated with ETN (n= 40) or sulfasalazine (SSZ) (n= 36) during the first year (1). At year 1, all patients who were not in remission continued with - or switched (in case of SSZ therapy) to – ETN for up to 10 years in total (1). Patients in remission discontinued their therapy and were followed-up until end of year 2; in case of remission loss, ETN was (re)-introduced and continued till the end of year 10.

Results: Out of 76 initial patients, 25% (n=19, 12 with r-axSpA and 7 with nr-axSpA) completed year 10 of the study. At baseline, completers were significantly more often male and showed lower values of patient (PGA) and physician global assessments of disease activity (PhGA), ASDAS (Ankylosing Spondylitis Disease Activity Score), BASMI (Bath Ankylosing Spondylitis Metrology Index), and AS-QoL (Ankylosing Spondylitis Quality of Life Questionnaire) as compared to non-completers (Table 1). When analyzing clinical data of the completers, mean BASDAI, BASFI and ASDAS values were constantly < 2 during the follow up with no statistically significant differences between the r-axSpA and nr-axSpA sub-groups (Table 2, Figure 1B). In the entire group, a sustained clinical response was observed over 10 years of follow up (Figure 1A). A total of 39 serious adverse events were documented over the 10 years of the study,

Figure 1: Observed response rates to etanercept (A) and the course of disease related parameters in study completers (n=19) (B).

Table 1: Baseline characteristics of patients with axial spondyloarthritis who completed the study as compared to patients who dropped out.

	Completer (n=19)	Non-Completer (n=57)	p value
Age, years	32.5 (7.4)	32.8 (8.9)	0.91
Male patients, n (%)	15 (78.9)	29 (50.9)	***0.034***
Symptomduration, years	1.1 (1.2)	1 (1.7)	0.81
HLA-B27 positivity, n (%)	18 (94.7)	44 (77.2)	0.091
CRP, mg/l	7.5 (10.5)	12 (15.1)	0.062
Elevated CRP (CRP>5mg/l), n (%)	7 (38.9)	33 (62.3)	0.088
ESR, mm/h	16.8 (15.7)	23.3 (19.5)	0.21
Clinical Arthritis, n (%)	4 (21.1)	15 (26.3)	0.65
Swollen-joint count (0-64)	1.9 (4.4)	1.8 (4.4)	0.92
Clinical Enthesitis, n (%)	9 (47.4)	35 (61.4)	0.40
Enthesitis (0-17)	2.8 (2.9)	4.3 (4.4)	0.20
Fulfilled New York criteria, n (%)	12 (63.2)	27 (47.4)	0.24
Patient global (0-10)	6.1 (1.9)	7.2 (1.7)	***0.025***
Physician global (0-10)	5.5 (1.5)	6.5 (1.2)	***0.007***
ASDAS	3 (0.7)	3.5 (0.8)	***0.042***
BASDAI (0-10)	5.4 (1.1)	5.8 (1.3)	0.27
BASFI (0-10)	4 (2.1)	4.4 (2)	0.41
BASMI (0-10)	1.2 (1.3)	2 (1.6)	***0.039***
AS-QoL (0-18)	7.6 (3.9)	10.1 (3.9)	***0.019***
EQ-5D (0-1)	0.7 (0.3)	0.6 (0.3)	0.13
Treatment with ETN during 1st year, n (%)	12 (63.2)	28 (49.1)	0.30

while six of them were seen as possibly associated with ETN treatment, which lead in five patients (one lymphoma, one sarcoidosis, one demyelinating neurological disease, one elevated liver enzymes and one recurrent minor infections) to an ETN discontinuation.

Conclusion: A sustained clinical response was shown over the 10 years of the study for the completers with comparable rates between r-axSpA and nr-axSpA. ETN was well tolerated across the entire treatment period and showed a good safety profile with no new safety signals.

Acknowledgements: The ESTHER study was supported by an unrestricted research grant from Pfizer. Murat Torgutalp's (MT) work at Charité - Universitätsmedizin was supported by an award from the Scientific and Technological Research Council of Turkey (TUBITAK).

Reference:

1. Song IH, Hermann K, Haibel H, Althoff CE, Listing J, Burmester G, et al. Effects of etanercept versus sulfasalazine in early axial spondyloarthritis on active inflammatory lesions as detected by whole-body MRI (ESTHER): a 48-week randomised controlled trial. Ann Rheum Dis. 2011;70(4):590-6.

Table 2. Long-term efficacy of etanercept in patients with AS (n=12) and nr-axSpA (n=7), who completed 10 years of the ESTHER trial.

		Baseline	Week 24	Year 1	Year 2	Year 3	Year 4	Year 6	Year 8	Year 10
BASDAI	AS	5 (0.7)	2.4 (1.6)	2.3 (2.1)	1.9 (1.8)	1.6 (1.6)	1.8 (1.7)	1.5 (1.1)	1.6 (1.7)	1.9 (1.9)
	nr-axSpA	6.2 (1.4)	3.2 (2.4)	2.3 (1.8)	1.7 (1.8)	1.2 (1.0)	1 (0.8)	1.2 (0.8)	1.3 (0.8)	1.4 (1.1)
BASFI	AS	3.5 (1.8)	1.4 (1.2)	1.8 (1.5)	1.5 (1.8)	1.4 (1.5)	1.4 (1.6)	1.4 (1.4)	1.6 (1.9)	1.6 (1.9)
	nr-axSpA	4.7 (2.6)	2.2 (2.0)	1.6 (1.5)	0.9 (0.8)	0.6 (0.6)	0.6 (0.5)	0.7 (0.5)	0.9 (0.7)	0.9 (0.9)
BASMI	AS	2.3 (1.0)	2.5 (1.3)	2.5 (1.2)	2.2 (1.3)	2.3 (0.9)	2.6 (1.1)	2.1 (1)	2.3 (1.2)	2.2 (1.3)
	nr-axSpA	2.5 (0.8)	2.7 (1.0)	2.4 (0.9)	1.7 (0.5)	1.8 (0.8)	1.6 (0.7)	1.7 (0.7)	2 (1.1)	2.1 (0.9)
ASDAS	AS	2.9 (0.6)	1.5 (0.6)	1.3 (0.7)	1.2 (0.6)	1.1 (0.7)	1 (0.6)	1.1 (0.7)	1.1 (0.8)	1.2 (0.9)
	nr-axSpA	3.3 (0.7)	1.7 (0.7)	1.2 (0.5)	1.2 (0.9)	0.7 (0.5)	0.8 (0.5)	0.6 (0.3)	0.8 (0.5)	0.9 (0.3)
CRP (mg/L)	AS	9.1 (12.9)	1.6 (0.5)	1.5 (0)	2.2 (3.5)	1.6 (2.4)	1.2 (1.2)	2.1 (2.7)	2.9 (4.7)	2.1 (2.4)
	nr-axSpA	5 (4.6)	2.8 (3.4)	2.5 (2.45)	2.2 (2.6)	2.7 (5.8)	2.4 (5.1)	0.4 (0.2)	1.8 (2.7)	1.7 (1.8)
ASAS 20	AS	-	75%	75%	83.3%	66.7%	83.3%	90%	83.3%	83.3%
	nr-axSpA	-	85.7%	100%	100%	85.7%	100%	100%	100%	100%
ASAS 40	AS	-	58.3%	66.7%	66.7%	66.7%	83.3%	70%	83.3%	66.7%
	nr-axSpA	-	57.1%	71.4%	85.7%	85.7%	85.7%	100%	85.7%	100%
ASAS 5/6	AS	-	41.7%	33.3%	58.3%	75%%	83.3%	70%	83.3%	66.7%
	nr-axSpA	-	42.9%	57.1%	71.4%	85.7%	85.7%	71.4%	85.7%	71.4%
ASAS PR	AS	-	41.7%	50%	58.3%	54.5%	66.7%	50%	66.7%	66.7%
	nr-axSpA	-	57.1%	71.4%	71.4%	71.4%	57.1%	85.7%	71.4%	57.1%
BASDAI 50	AS	-	58.3%	58.3%	66.7%	72.7%	83.3%	80%	75%	66.7%
	nr-axSpA	-	42.9%	85.7%	85.7%	100%	100%	100%	100%	100%

Disclosure: F. Proft, Abbvie, 5, 8, BMS, 8, MSD, 8, Novartis, 5, 8, Novartis Pharma, 2, Pfizer, 5, 8, Roche, 8, UCB, 5, 8; **M. Torgutalp**, Scientific and Technological Research Council of Turkey (TUBITAK), 9; **A. Weiß**, None; **M. Protopopov**, MSD, 8, Novartis, 5, 8, Pfizer, 8; **V. Rios Rodriguez**, AbbVie, 5, 8, MSD, 5, 8, Novartis, 5, 8; **H. Haibel**, AbbVie, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8; **O. Behmer**, Pfizer Inc., 3; **J. Sieper**, AbbVie, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Novartis, 5, 8; **D. Poddubnyy**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 2, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8.

Abstract Number: 1492

Exposure-Response Analyses for Upadacitinib Efficacy and Safety in Ankylosing Spondylitis – Analyses of the SELECT-AXIS I Study

Mohamed Ismail,[1] Ahmed Nader,[1] Insa Winzenborg,[2] In-Ho Song,[3] and Ahmed Othman[1], [1]AbbVie Inc., North Chicago, IL, [2]AbbVie Deutschland GmbH & Co. KG, Ludwigshafen am Rhein, Germany, [3]AbbVie Inc., North Chicago, IL, USA, North Chicago, IL

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib, a selective inhibitor of Janus kinase 1 (JAK1), is currently being evaluated for the treatment of several autoimmune disorders, including axial spondyloarthritis (axial SpA). In the SELECT-AXIS I study (NCT03178487), upadacitinib 15 mg once-daily (QD) demonstrated favorable efficacy in ankylosing spondylitis (AS) patients who had an inadequate response to non-steroidal anti-inflammatory drugs and who were naïve to biological disease modifying antirheumatic drugs. The purpose of this analysis was to a) explore the relationship between upadacitinib exposures and several AS efficacy endpoints and safety parameters to support dose selection for future studies and b) compare upadacitinib plasma exposures in subjects with AS to subjects with rheumatoid arthritis to assess disease-related differences in upadacitinib pharmacokinetics (PK).

Methods: The analyses included data from 187 subjects in the SELECT-AXIS I study. Subjects were randomized to receive upadacitinib 15 mg QD (n=93) or matching placebo (n=94). PK samples were taken at pre-defined visits and modeled using a population approach. Within the evaluated dose, exposure-response quartile plots were created to assess the relationship between upadacitinib average plasma concentrations and the probability of achieving Week 14 efficacy endpoints (ASAS 40, ASAS 20, ASAS partial remission [PR]) or experiencing adverse events/relevant changes in laboratory variables (lymphopenia [Grade 3 per CTCAE or higher], infection, decreases in hemoglobin).

Results: Upadacitinib plasma concentrations (Table 1) and PK parameters (drug clearance and volume of distribution) in subjects with AS were similar to those previously observed in subjects with RA in the SELECT-BEYOND and SELECT-NEXT studies.

Subjects in the active treatment arm had statistically significant higher response rates for ASAS 40, ASAS 20, and ASAS PR compared to those in the placebo arm. However, within the single active treatment arm there were no clear exposure-response relationships between increasing upadacitinib average concentrations and the probability of achieving the evaluated efficacy outcomes, suggesting achieving the plateau of response. With increasing upadacitinib exposure, there was an increase in the percentage of subjects experiencing decreases of hemoglobin of ≥ 1 g/dL from baseline; with no subjects having ≥ 2 g/dL decreases of hemoglobin from baseline. There were no upadacitinib exposure-dependent increases in percentage of subjects experiencing lymphopenia or infection. There was a single observed case of Grade 2 neutropenia in a subject receiving active treatment and no observed cases of serious infections.

Conclusion: Upadacitinib pharmacokinetics are similar in subjects with AS and RA. Upadacitinib 15 mg QD dose is predicted to maximize efficacy in subjects with AS. Overall, the results of this analysis support selection of the upadacitinib 15 mg QD dose for further evaluation in future studies in AS/axial SpA.

Indication	Median C_{avg}	5th Percentile	95th Percentile
Ankylosing Spondylitis	15.0 ng/mL	9.60 ng/mL	30.0 ng/mL
Rheumatoid Arthritis (SELECT-BEYOND and SELECT-NEXT)	14.5 ng/mL	9.80 ng/mL	29.2 ng/mL

Table 1. Predicted median average upadacitinib plasma concentrations within a dosing interval (Cavg) in AS and RA subjects receiving upadacitinib 15 mg QD.

Disclosure: M. Ismail, AbbVie Inc., 3; **A. Nader**, AbbVie Inc., 1, 3; **I. Winzenborg**, AbbVie Inc., 1, 3; **I. Song**, AbbVie, 3, 4; **A. Othman**, AbbVie Inc., 1, 3.

Abstract Number: 1493

Improvement in the Signs and Symptoms of Psoriatic Arthritis with Ixekizumab Compared to Adalimumab in Patient Subgroups Defined by Baseline Disease Characteristics

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Multiple biologic DMARD (bDMARD) treatments are available for PsA, but there is limited research that compares the safety and efficacy of these treatments. Head-to-head (H2H) studies may improve the strength of PsA treatment guidelines and provide valuable guidance to physicians in selecting optimal treatment.[1] SPIRIT-H2H, the first completed H2H superiority study in active PsA, showed superiority of ixekizumab (IXE), an IL-17A antagonist, over adalimumab (ADA), a TNF inhibitor, on a combined endpoint at Week 24.[2] Here we report the Week 24 efficacy of IXE and ADA in subgroups defined by baseline disease characteristics.

Methods: SPIRIT-H2H (NCT03151551) is a 52-week, multicenter, open-label, blinded assessor study in bDMARD-naïve patients who were inadequate responders to conventional synthetic DMARD (csDMARD) with active PsA (≥3 tender joint count [TJC] and ≥3 swollen joint count [SJC]) and plaque psoriasis (body surface area [BSA] ≥3%). All patients met Classification Criteria for PsA. Patients were randomized 1:1 to IXE or ADA on-label dosing based on presence/absence of moderate-to-severe psoriasis (BSA ≥10% + Psoriasis Area and Severity Index [PASI] ≥12 + static Physician Global Assessment [sPGA] ≥3). A blinded assessor measured TJC, SJC, enthesitis, dactylitis, PASI, sPGA, BSA, and fingernail psoriasis. This post hoc subgroup analysis assessed efficacy in patients with baseline enthesitis (presence/absence), dactylitis (presence/absence), fingernail psoriasis (presence/absence), BSA (10% cutoff), and CRP (6 mg/L cutoff). Week 24 outcomes were compared between IXE and ADA at ACR20/50/70 responses and minimal disease activity (MDA). Missing data were imputed by nonresponder imputation. While the post hoc analysis was not controlled for multiplicity, all comparisons were analyzed by Fisher's exact test.

Results: The Table summarizes Week 24 efficacy outcomes by subgroup. There were no statistical differences between IXE and ADA at ACR20 and ACR50 response rates across all of the examined subgroups. ACR70 responses were comparable across subgroups, except significantly more IXE-treated patients with baseline fingernail psoriasis achieved ACR70 than ADA-treated patients (p=.02). Significantly more IXE- than ADA-treated patients achieved MDA-6 in subgroups with baseline enthesitis (p=.002), without dactylitis (p=.015), with fingernail psoriasis (p< .001), CRP≤6 mg/L (p=.046), and BSA ≥10% (p=.01). All other subgroups analyzed demonstrated comparable efficacy on IXE and ADA.

A limitation of this analysis is that it was completed post hoc, not controlled for multiplicity, and patients were not stratified by these baseline disease characteristics.

Table: Efficacy Outcomes at Week 24 in patient subgroups defined by baseline disease characteristics (NRI)

Baseline Disease Characteristic	Week 24 Outcome	Treatment Group	ACR20	ACR50	ACR70	MDA-6[a]
Baseline Enthesitis	LEI>0 OR SPARCC>0	ADA (Nx=172)	114 (66.3%)	73 (42.4%)	36 (20.9%)	50 (29.1%)
		IXE (Nx=193)	130 (67.4%)	90 (46.6%)	57 (29.5%)	87 (45.1%)**
	LEI=0 OR SPARCC=0	ADA (Nx=111)	90 (81.1%)	59 (53.2%)	37 (33.3%)	54 (48.6%)
		IXE (Nx=89)	65 (73.0%)	53 (59.6%)	33 (37.1%)	52 (58.4%)
Baseline Dactylitis	LDI-B>0	ADA (Nx=58)	45 (77.6%)	31 (53.4%)	14 (24.1%)	19 (32.8%)
		IXE (Nx=42)	28 (66.7%)	23 (54.8%)	13 (31.0%)	21 (50.0%)
	LDI-B=0	ADA (Nx=225)	159 (70.7%)	101 (44.9%)	59 (26.2%)	85 (37.8%)
		IXE (Nx=240)	167 (69.6%)	120 (50.0%)	77 (32.1%)	118 (49.2%)*
Baseline Fingernail Psoriasis	NAPSI>0	ADA (Nx=177)	129 (72.9%)	82 (46.3%)	39 (22.0%)	57 (32.2%)
		IXE (Nx=191)	136 (71.2%)	101 (52.9%)	63 (33.0%)*	95 (49.7%)***
	NAPSI=0	ADA (Nx=105)	75 (71.4%)	50 (47.6%)	34 (32.4%)	47 (44.8%)
		IXE (Nx=92)	59 (64.1%)	42 (45.7%)	27 (29.3%)	44 (47.8%)
Baseline CRP	CRP ≤6 mg/L	ADA (Nx=167)	124 (74.3%)	74 (44.3%)	41 (24.6%)	61 (36.5%)
		IXE (Nx=167)	110 (65.9%)	81 (48.5%)	48 (28.7%)	80 (47.9%)*
	CRP >6 mg/L	ADA (Nx=109)	76 (69.7%)	55 (50.5%)	30 (27.5%)	42 (38.5%)
		IXE (Nx=109)	82 (75.2%)	60 (55.0%)	40 (36.7%)	55 (50.5%)
Baseline BSA	BSA <10%	ADA (Nx=179)	128 (71.5%)	80 (44.7%)	43 (24.0%)	65 (36.3%)
		IXE	109 (64.1%)	79 (46.5%)	49 (28.8%)	76 (44.7%)

Conclusion: IXE and ADA are associated with comparable efficacy in the signs and symptoms of PsA in patient subgroups defined by baseline enthesitis, dactylitis, fingernail psoriasis, BSA, and CRP.

References:

1. Singh JA, *et al*. Arthritis Rheumatol. 2019 Jan;71(1):5-32.
2. Available at: https://clinicaltrials.gov/ct2/show/results/NCT03151551?term=spirit-h2h{00AMP00}rank=1

Disclosure: J. Merola, AbbVie, 2, 5, 8, Aclaris, 2, 5, Almirall, 2, 5, Amgen, 5, Biogen, 2, 5, Biogen Idec, 2, 5, Biogen IDEC, 5, Brigham and Women's Hospital, Harvard, 3, Burrage Capital Management Boston Advisory Board, 6, Celgene, 2, 5, Dermavant, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 5, GlaxoSmithKline, 5, GSK, 2, 5, Incyte, 2, 5, Janssen, 2, 5, Leo Pharma, 2, 5, Lilly, 5, Merck, 5, Merck Research Laboratories, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Regeneron, 5, Samumed, 2, 5, Sanofi, 5, Sanofi Regeneron, 2, 5, Science 37, 5, Sun Pharma, 2, 5, UCB, 2, 5; **A. Trevelin Sprabery**, Eli Lilly and Company, 1, 3; **A. Gellett**, Eli Lilly and Company, 1, 3; **C. Lin**, Eli Lilly and Company, 1, 3; **D. McGonagle**, AbbVie, 9, Abbvie, 2, 8, BMS, 9, Celgene, 2, 8, 9, Janssen, 2, 8, Johnson & Johnson, 9, Lilly, 2, 8, MSD, 9, Novartis, 2, 8, 9, Pfizer, 2, 8, 9, UCB, 8, 9.

Abstract Number: 1494

Guselkumab Was More Effective Than Secukinumab in Patients with Plaque Psoriasis and the Subset of Patients with Self-Reported Psoriatic Arthritis in a Randomized, Double-blind, Head-to-head Comparison Study over 1 Year

Joseph Merola,[1] Shu Li,[2] Ming-Chun Hsu,[2] Chetan Karyekar,[3] Susan Flavin,[2] Bruce Randazzo,[4] and Laura Coates[5], [1]Brigham and Women's Hospital, Harvard Med School, Boston, MA, [2]Janssen Research & Development, LLC, Spring House, PA, [3]Janssen Global Services, LLC, Horsham, PA, [4]Janssen Research & Development, LLC/University of Pennsylvania, Spring House/Philadelphia, PA, [5]University of Oxford, Oxford, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

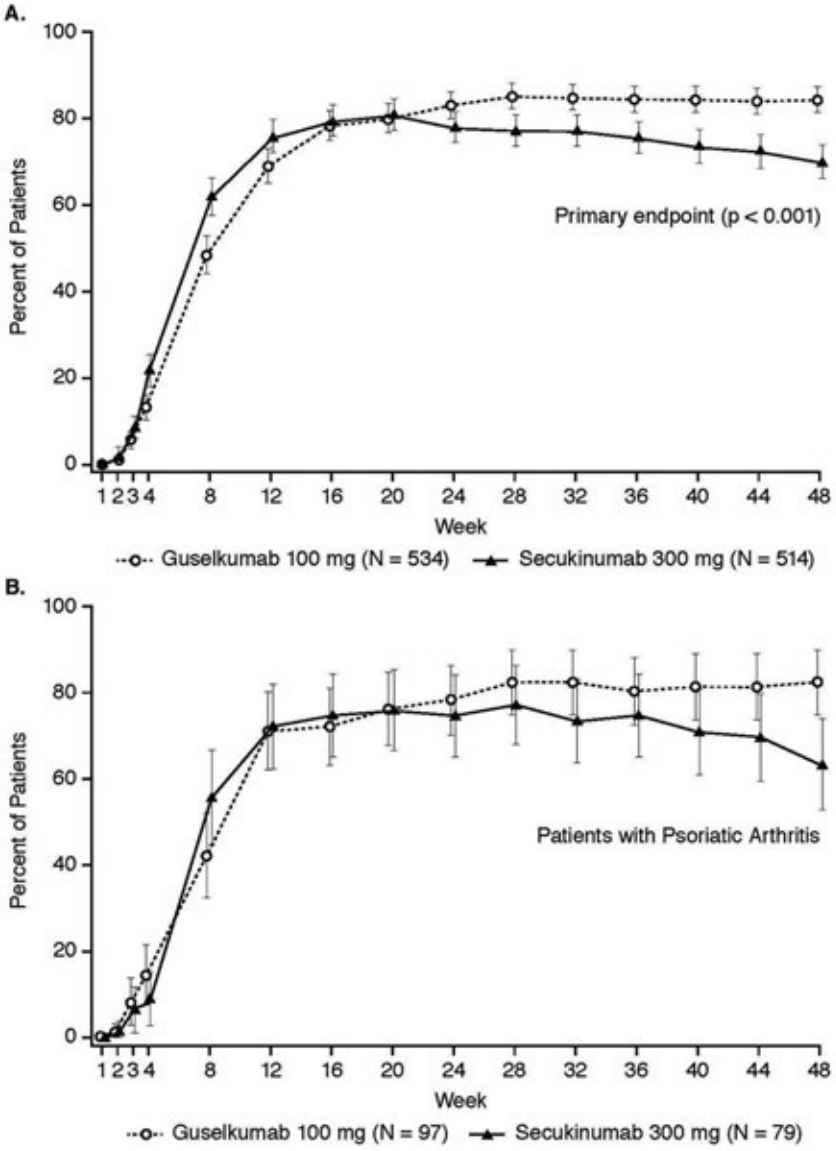
Background/Purpose: Guselkumab (GUS, an antibody against IL-23) and secukinumab (SEC, an antibody against IL-17A) are both approved for the treatment of psoriasis (PsO). Up to 30% of patients with PsO may have psoriatic arthritis (PsA).

The ECLIPSE study compared efficacy and safety of GUS vs SEC in patients with plaque PsO. Post hoc analyses examined outcomes in the subgroup of patients with self-reported psoriatic arthritis (PsA).

Methods: ECLIPSE was a randomized, double-blind trial of adults with moderate-to-severe plaque PsO who received GUS 100 mg at Weeks 0, 4, then every 8 weeks, or SEC 300 mg at Weeks 0, 1, 2, 3, and 4, then every 4 weeks (both being administered according to their labeling), both through Week 44. The primary endpoint was the proportion of patients achieving ≥90% improvement compared to baseline in the Psoriasis Area and Severity Index (PASI) score at Week 48. Cochran-Mantel Haenszel chi-square testing stratified by investigator was used to compare treatment-group responses.

Results: Overall, treatment groups [GUS (n=534), SEC (n=514)] were comparable at baseline: weight 89kg, 24% body surface area PsO, and Investigator Global Assessment (IGA) moderate (76%) or severe (24%). These characteristics were similar to those of subgroups with self-reported PsA [GUS (n=97), SEC (n=79)]. In the overall population, the primary endpoint of PASI 90 response at Week 48 was achieved by 84.5% of GUS vs 70.0% of SEC patients (treatment difference 14.2 [95% CI=9.2%,19.2%], P< 0.001). Among patients with PsA, the primary endpoint of PASI 90 response at Week 48 was achieved by 82.5% of GUS vs 63.3% of SEC patients (treatment difference 19.2% [95% CI=5.0%, 33.4%]). Beyond week 20, in both the overall study population and the PsA subpopulation, GUS-treated patients maintained the PASI 90 response while SEC-treated patients had a reduction in response through week 48 (Figure). In the overall population, results of the first major secondary endpoint (proportion of patients with a PASI 75 response at both Week 12 and 48) showed non-inferiority of GUS vs SEC (GUS-84.6% vs SEC-80.2% of patients, p< 0.001), but superiority was not demonstrated (p=0.062). Adverse events observed in the overall population and PsA subgroup were generally consistent with the established safety profiles for GUS and SEC.

Figure. Proportion of Patients Achieving PASI 90 Response (95% CI)



A. Total ECLIPSE population of patients with moderate to severe plaque psoriasis.
B. Subgroup of patients with Psoriatic Arthritis.
Non-responder imputation was used for missing data.
CI=Confidence interval, PASI 90=90% improvement in the Psoriasis Area and Severity Index (PASI).

Conclusion: In the subset of patients with self-reported PsA in the ECLIPSE study, GUS demonstrated better maintenance of response and higher efficacy at approximately one year compared with SEC in the treatment of moderate to severe plaque PsO. These findings were consistent with those for the overall study population of patients with plaque PsO. AEs observed were generally consistent with the established safety profiles for GUS and SEC.

Disclosure: J. Merola, Janssen Research & Development, LLC, 2; **S. Li**, Janssen Research & Development, LLC, 3; **M. Hsu**, Janssen Research & Development, LLC, 3; **C. Karyekar**, Abbott, 3, BMS, 3, Janssen, 1, 3, Janssen Scientific Affairs, LLC, 3, Novartis, 3; **S. Flavin**, Janssen Research & Development, LLC, 3; **B. Randazzo**, Janssen Research & Development, LLC, 3; **L. Coates**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, AbbVie, Amgen, BMS, Celgene Corpo-

ration, Eli Lilly, Galapagos, Janssen, MSD, Novartis, Pfizer, Prothena, Sun Pharma, UCB, 5, Abbvie, Amgen, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB, 5, Abbvie, Amgen, Lilly, Novartis, Pfizer, UCB, 8, AbbVie, Celgene Corporation, Eli Lilly, Janssen, Novartis, UCB, 8, AbbVie, Celgene Corporation, Eli Lilly, Novartis, Pfizer, 2, AbbVie, Celgene Corporation, Novartis, Pfizer, 2, Abbvie, Celgene, Novartis, Pfizer, Lilly, 2, Amgen, 5, 8, Biogen, 8, Bristol-Myers Squibb, 5, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, Gilead, 5, Janssen, 2, 5, 8, Janssen Research & Development, LLC, Lilly, 2, 5, 8, MSD, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 8, Prothena, 5, Sun Pharma, 5, UCB, 5, 8, UCB Pharma, 5.

Abstract Number: 1495

Real Life 12 Year Retention Rate of Subcutaneous Anti-TNF in Spondyloarthritis. Results from a Multicenter Cohort of 1170 Patients

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

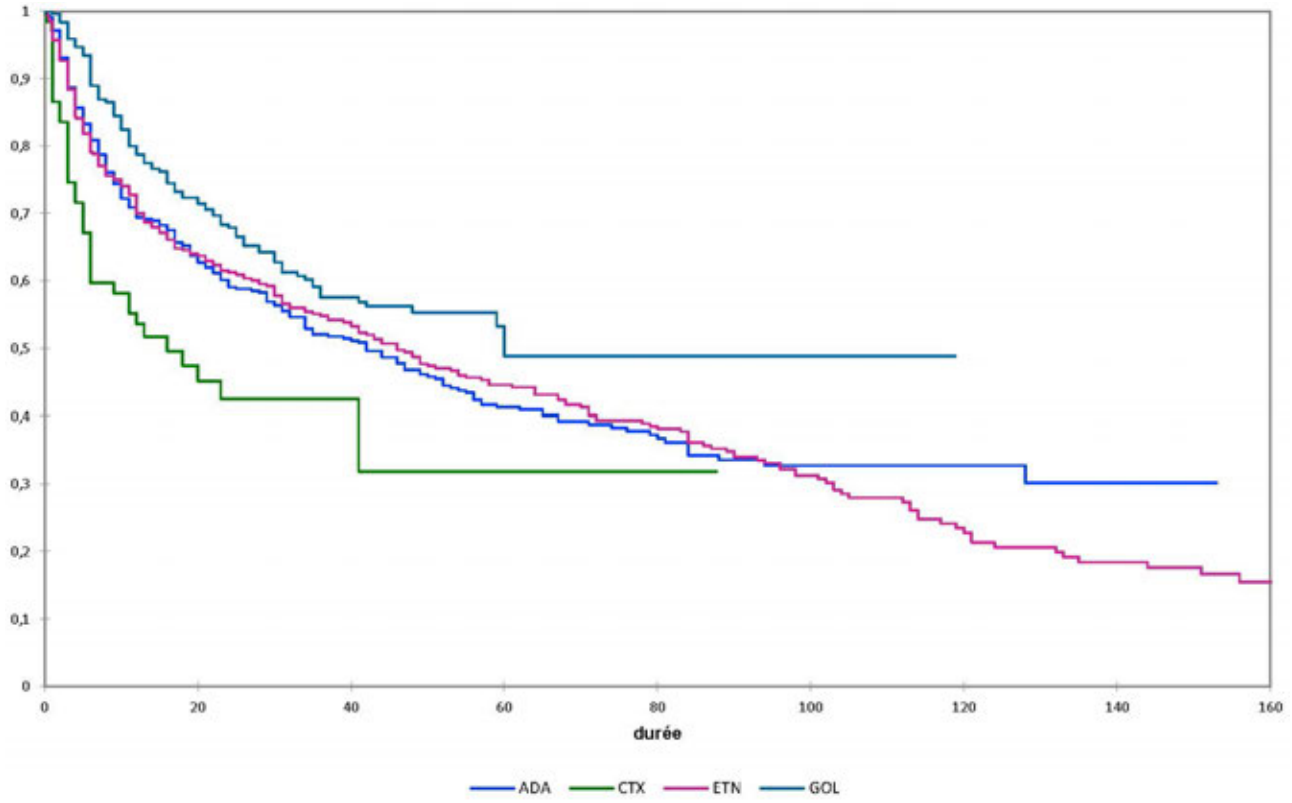
Background/Purpose: Drug survival is used as a tool for treatment effectiveness and safety especially in real-world data. The objective of the study was to evaluate long term survival of subcutaneous TNF inhibitors (TNFi) in spondyloarthritis (SA) patients and to compared drug survival between the different lines.

Methods: Multicentric, retrospective, longitudinal and observational study included all patients with SA under TNFi since 2004, with a record in RIC France. The first part of the study analysed the survival of the fourth anti-TNF : etanercept (ETN), adalimumab (ADA), golimumab (GOL) and certolizumab (CTZ) since their first prescription. The second part of the study included the patients from January 2013 to March 2018, as CTZ has been available in January 2013. Drug survival has been analysed at 6 months, 1, 2, 3 et 5 years for the 1st, 2nd et 3rd course with Kaplan-Meier test compared with log-rank test.

Results: On the total population (n=1170), ADA and ETN has a comparable mean drug survival (MDS) of 42 and 46 months respectively. CTZ has a MDS of 16 weeks and GOL of 60 weeks.

When we analysed the records of the 425 patients treated since January 2013 (836 TNFi treatment) the characteristics were at TNFi initiation : a mean-age of 43.3 years, 45.6% female, mean SA duration of 8.6 years (+/- 12) and the mean BASDAI was 5.43. 824 TNFi have been analysed and 439 were on course

418 first course TNFi with a drug survival at one year at 70 % for adalimumab (ADA), at 58 % for etanercept (ETA), at 85 % for certolizumab (CTZ) and at 83% pour le golimumab (GOL).



In second course of TNFi (n=230), drug survival was at one year of 58 % for ADA, at 62 % ETA, at 57 % for CTZ. and 66 % for GOL.

In third course or more (n=176) drug survival was at one year of 67% for ADA, 76% for ETA, 51% for CTZ and 86% for GOL.

Data for predicting factors of survival are on analysed.

Conclusion: In this retrospective study of real world, golimumab has the best drug survival, in the long-term evaluation as well as the 5 years evaluation and also whatever the line of treatment. Predicting factors of survival might explain this result.

Disclosure: G. Baudens, None; **P. Coquerelle**, None; **M. Guyot**, None; **S. Loiseau-Pères**, None; **L. Marguerie**, None; **F. Maury**, None; **V. Eric**, None; **J. Letarouilly**, None; **J. Salmon**, Janssen, 8; **R. Flipo**, MSD, 5, Sanofi, 5; **E. Gervais**, None.

Abstract Number: 1496

Comparative Effectiveness of Ustekinumab and TNF Inhibitors in Patients with Psoriatic Arthritis in a Real-world, Multicenter Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Among the treatment options for PsA, IL-12/23 inhibition with ustekinumab (UST) was the first new biologic mode of action after TNF inhibitors (TNFi). Few data are available from real-world settings comparing the effectiveness of UST to standard TNFi. The objective of this study was to investigate 6-mo treatment responses to UST or TNFi in the 8-country, real-world PsABio study, especially achievement of LDA and remission.

Methods: The PsABio study (NCT02627768) evaluates effectiveness, tolerability and persistence of 1st, 2nd or 3rd-line UST or TNFi in PsA. Proportions of patients (pts) reaching MDA/VLDA and cDAPSA were evaluated. Baseline (BL) and 6-mo data were compared among pts receiving UST or TNFi for full 6 mo (completers), and ITT analysis including pts switching/stopping original treatment during 6-mo observation period, imputed as non-responders. Propensity score (PS) was used to adjust for BL covariates in country, age, gender, BMI, smoking (yes/no), co-morbidities (cardiovascular/metabolic syndrome), PsA type (axial, polyarticular, oligoarticular), psoriasis BSA, disease duration, cDAPSA, PsAID-12, dactylitis, enthesitis, FiRST score, line of biologic (b)DMARD, synthetic DMARD use, and steroid or NSAID use. Factors potentially modifying PS-adjusted treatment effect were investigated.

Results: For N=930 pts, 796 (93.0% and 93.6% of UST- and TNFi-treated, respectively) had evaluable data at BL and 6 mo (Table 1). ITT analysis (n=868) included pts who had stopped/switched before 6 mo (UST: n=28/426 [6.6%], TNFi: n=44/442 [10.0%]). For MDA assessment, 761 (ITT) and 701 (completers) had data for both visits. Both UST and TNFi led to achievement of MDA (up to 35%), VLDA (up to 11%), cDAPSA LDA (up to 57%) and cDAPSA remission (up to 22%) (Table 2). At BL, significant differences between UST and TNFi groups existed in age (higher on UST), line of treatment (UST more frequently 3rd-line), NSAID use (lower in UST), methotrexate use (less concomitant treatment in UST), FiRST score (more chronic widespread pain in UST), and skin involvement (higher in UST). After PS adjustment for BL differences, odds ratios (OR) for reaching MDA, VLDA, cDAPSA LDA or remission at 6 mo, were not statistically different between UST and TNFi (Table 2). In the ITT set, pts with low-grade skin disease (BSA< 3%)

and those with oligoarticular disease had a lower chance of achieving MDA when given UST (OR: 0.45 [0.29, 0.85] and 0.62 [0.39, 0.97] respectively) compared with TNFi, but responses to UST tended to be better in pts with higher grade skin disease (>10% of BSA) and with polyarticular disease at BL (OR: 2.08 [0.88, 4.95] and 1.57 [0.88, 2.82] respectively). Similar results were seen in the analysis obtained with cDAPSA LDA or remission as treatment target.

Table 1: Observed baseline characteristics of the 868 ITT patients and 796 completer patients

	UST ITT	TNFi ITT	UST Completers	TNFi Completers
N	426	442	398	398
Age, years	51.2 (12.5)	48.5 (12.6)	51.1 (12.6)	48.6 (12.7)
Gender (male), %	43.0	45.7	43.2	47.5
Time since initial diagnosis, years	7.54 (8.13)	6.21 (6.63)	7.39 (8.06)	6.12 (6.48)
Cardiovascular/ metabolic syndrome comorbidity, %	41.3	35.5	40.2	35.2
Dactylitis at baseline, %	18.8	20.8	18.1	21.9
Enthesitis at baseline, %	48.9	51.9	49.3	53.3
PsA characteristics: %				
Axial involvement	35.4	37.2	34.9	36.5
Oligoarticular	22.4	28.9	23.0	30.8
Polyarticular	66.7	64.7	65.6	62.5
sDMARD exposure, %				
Previous exposure	88.3	93.0	87.9	93.7
Ongoing exposure at baseline	39.7	55.2	39.9	55.8
Other treatments exposure, %				
NSAIDs	54.5	69.5	54.5	69.8
Steroids	32.4	34.4	31.7	33.7
BMI, kg/m^2	28.6 (6.3)	27.7 (5.0)	28.6 (6.4)	27.7 (5.00)
Psoriasis BSA, %				
<3%	38.4	50.1	37.5	47.4
3–10%	34.9	35.7	34.7	37.9
>10%	26.7	14.1	27.8	14.7
cDAPSA	31.0 (20.3)	29.8 (18.6)	30.8 (20.3)	29.5 (18.4)
Swollen joint count (66)	6.0 (8.12)	5.8 (7.38)	6.0 (8.21)	5.9 (7.51)
Tender joint count (68)	12.5 (12.5)	11.3 (10.8)	12.4 (12.5)	11.0 (10.4)
CRP (mg/dL)	1.33 (2.95)	1.55 (2.86)	1.34 (3.03)	1.49 (2.78)
FiRST total score	3.50 (2.01)	3.12 (1.95)	na	na
FiRST score ≥ 5	39.3%	29.0	na	na
Total PsAID (over past week)	5.71 (2.17)	5.52 (2.08)	5.70 (2.18)	5.48 (2.08)
RF/CCP positive (%)	2.0/3.0	5.6/2.8	na	na

cDAPSA, clinical Disease Activity in Psoriatic Arthritis; FiRST, Fibromyalgia Rapid Screening Tool; ITT, intention to treat; na, not available; PsAID, Psoriatic Arthritis Impact of Disease; sDMARD, synthetic disease-modifying antirheumatic drug.

Table 2: Observed disease outcomes (MDA, VLDA, LDA and remission) at Month 6

Variable	All patients (ITT population)		Completers	
	UST	TNFi	UST	TNFi
MDA, % achieved (observed)	26.4	30.8	28.5	34.8
PS adjusted OR (95% CI), UST compared to TNFi	0.87 (0.61, 1.25)		0.81 (0.56, 1.17)	
VLDA, % achieved(observed)	8.3	9.6	8.9	10.8
PS adjusted OR (95% CI), UST compared to TNFi	0.74 (0.42, 1.30)		0.69 (0.39, 1.22)	
cDAPSA LDA/remission, % achieved (observed)	45.7	50.7	49.4	57.3
PS adjusted OR (95% CI), UST compared to TNFi	0.74 (0.53, 1.04)		0.65 (0.46, 0.93)	
cDAPSA remission, % achieved (observed)	14.9	19.2	16.2	21.7
PS adjusted OR (95% CI), UST compared to TNFi;	0.73 (0.46, 1.15)		0.65 (0.41, 1.04)	

cDAPSA, clinical Disease Activity index for PSoriatic Arthritis; CI, confidence interval; ITT, intention to treat; LDA, low disease activity; MDA, minimal disease activity; OR, odds ratio; PS, propensity score; VLDA, very low disease activity.

Conclusion: UST and TNFi, when used as 1st-, 2nd- or 3rd-line bDMARD in a routine care setting, provide clinically relevant regression of disease signs and symptoms and allow achievement of MDA, LDA or remission in many PsA pts after 6 mo of treatment. After PS adjustment for BL imbalances, clinical results achieved were comparable between UST and TNFi.

Disclosure: J. Smolen, AbbVie, 2, 5, 8, Abbvie, 2, 5, Amgen, 5, 8, AstraZeneca, 2, 5, 8, Astra-Zeneca, 5, Astro, 5, 8, BMS, 5, Celgene, 5, 8, Celltrion, 5, Celtrion, 5, 8, Chugai, 5, Eli Lilly and Company, 2, 5, Gilead, 5, GlaxoSmithKline, 5, 8, ILTOO, 5, 8, ILTOO Janssen, 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Medimmune, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, Novartis- Sandoz, 5, Novartis-Sandoz, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 5, Roche, 2, 5, Roche;, 2, 5, 8, Samsung, 5, 8, Sanofi, 5, 8, Sanofi-Aventis, 5, UCB, 5, 8; **P. Athanassiou**, None; **P. Bergmans**, Janssen, 3, Johnson & Johnson, 1, 4; **I. Bondareva**, Pfizer, 2, Janssen, 2, Biocad, 2; **K. De Vlam**, Johnson & Johnson, 5; **E. Gremese**, AbbVie, 5, 8, BMS, 5, 8, Celgene, 5, 8, Janssen, 5, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **B. Joven-Ibáñez**, Celgene, 8, Novartis, 8, MSD, 8, Pfizer, 8, AbbVie, 8, Janssen, 8; **T. Korotaeva**, Pfizer, 5, 8, MSD, 5, 8, Novartis, 5, 8, AbbVie, 5, 8, Celgene, 5, 8, Biocad, 5, 8, Janssen, 5, 8, UCB, 5, 8, Lilly, 5, 8, Novartis-Sandoz, 5, 8; **W. Noël**, Janssen, 3; **M. Nurmohamed**, Pfizer, 2, 5, 8, AbbVie, 2, 5, 8, Roche, 2, 5, 8, BMS, 2, 5, 8, MSD, 2, 5, 8, Mundipharma, 2, 5, 8, UCB, 2, 5, 8, Janssen, 2, 5, 8, Menarini, 2, 5, 8, Lilly, 2, 5, 8, Sanofi, 2, 5, 8, Celgene, 2, 5, 8; **P. Sfikakis**, None; **S. Siebert**, Abbvie, 2, 5, 8, AbbVie, 2, 5, BMS, 2, Boehringer Ingelheim, 2, 5, 8, Celgene, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8; **P. Smirnov**, Janssen, 3; **E. Theander**, Janssen, 3; **L. Gossec**, Abbvie, 5, AbbVie, 5, Abbvie, Biogen, BMS, Celgene, Lilly, Novartis, Pfizer, SAnofi-Aventis, UCB, 5, Amgen, 5, Biogen, 5, BMS, 2, 5, Celgene, 5, Celgene Corporation, 2, Janssen, 5, Lilly, 2, 5, MSD, 5, Nordic Pharma, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 5, Sanofi-Aventis, 5, UCB, 5.

Abstract Number: 1497

Efficacy of Secukinumab in a US Patient Population with Psoriatic Arthritis: A Subgroup Analysis of the Phase 3 FUTURE Studies

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Secukinumab (SEC), a selective inhibitor of interleukin 17A, demonstrated rapid, significant, and sustained improvement in the signs and symptoms of PsA, with a favorable safety profile, in the phase 3 FUTURE studies (FUTURE 1–5).[1-5] These studies were conducted in several countries worldwide, including the United States. We evaluated SEC treatment in the US patient (pt) subpopulation in these studies and report pooled efficacy findings for SEC vs placebo (PBO).

Methods: Data from US pts enrolled in FUTURE 2 (NCT01752634), 3 (NCT01989468), 4 (NCT02294227), and 5 (NCT02404350) were pooled and included in this hypothesis-generating analysis. These studies used approved SEC doses, with pts receiving SEC 300 or 150 mg with subcutaneous loading dose (LD), 150 mg without LD, or PBO. FUTURE 1 (NCT01392326) was excluded because pts received an intravenous LD, which is not approved for treating PsA. Assessments included ACR20/50/70 and additional disease activity and quality of life (QOL) outcome measures at week 16. Responses were calculated using nonresponder imputation. No adjustment was made for multiple comparisons.

Results: Of 279 pts included in this pooled analysis, 72 were randomized to SEC 300 mg with LD, 83 to SEC 150 mg with LD, 34 to SEC 150 mg without LD, and 90 to PBO. Baseline characteristics were similar across treatment groups (**Table 1**). Most pts had a BMI of ≥ 30 kg/m^2 and had been previously treated with tumor necrosis factor inhibitors (TNFis). At week 16, ACR20/50/70 response rates were numerically higher with all doses of SEC than with PBO; responses were seen as early as week 4 (**Figure 1**). SEC also improved other disease manifestations, including joint, skin, and nail disease, and various QOL measures; resolution of enthesitis and dactylitis was observed in approximately 50% of pts (**Table 2**). Overall, SEC 300 mg led to higher response rates than SEC 150-mg doses. SEC 150 mg with LD was associated with better response rates than that without LD.

Conclusion: SEC was efficacious in US pts with PsA, leading to rapid improvements in clinical endpoints and QOL. In general, US pts treated with SEC 300 mg achieved the highest response rates, including ACR50/70 response. SEC 150 mg also led to clinical benefits, with an LD regimen associated with higher response rates. Although US pts had high BMIs and a large proportion had been treated with ≥ 2 TNFis, response rates in these pts were similar to those seen in the overall pooled pt population.[6,7] Our findings are consistent with those from previous studies and show that SEC is an effective treatment for pts with PsA.

Table 1. Patient Characteristics at Baseline

Characteristic	SEC 300 mg (n = 72)	SEC 150 mg (n = 83)	SEC 150 mg, no LD (n = 34)	PBO (n = 90)
Age, mean (SD), years	51.2 (14.5)	50.5 (12.2)	53.5 (10.6)	52.1 (12.0)
Sex, n (%)				
Male	27 (37.5)	42 (50.6)	16 (47.1)	39 (43.3)
Female	45 (62.5)	41 (49.4)	18 (52.9)	51 (56.7)
Race, n (%)				
White	64 (88.9)	76 (91.6)	33 (97.1)	83 (92.2)
Asian	2 (2.8)	1 (1.2)	0	0
Black or African American	1 (1.4)	0	0	4 (4.4)
American Indian or Alaska Native	0	2 (2.4)	0	0
Other	5 (6.9)	4 (4.8)	1 (2.9)	2 (2.2)
Unknown	0	0	0	1 (1.1)
Weight, mean (SD), kg	87.2 (20.2)	95.8 (20.4)	96.5 (26.3)	90.6 (20.1)
BMI, mean (SD), kg/m^2	31.1 (6.4)	33.1 (6.7)	33.7 (6.8)	32.1 (7.6)
Time since PsA diagnosis, mean (SD), years	7.7 (8.9)	6.6 (8.8)	5.0 (4.7)	7.6 (8.3)
Prior TNFi therapies, n (%)				
0	30 (41.7)	36 (43.4)	16 (47.1)	43 (47.8)
1	22 (30.6)	30 (36.1)	12 (35.3)	24 (26.7)
≥ 2	20 (27.8)	17 (20.5)	6 (17.6)	23 (25.6)
Methotrexate use at randomization, n (%)	22 (30.6)	23 (27.7)	12 (35.3)	26 (28.9)
Patients with specific disease characteristics, n (%)				
Psoriasis affecting ≥ 3% of BSA	34 (47.2)	36 (43.4)	11 (32.4)	38 (42.2)
Presence of enthesitis	45 (62.5)	66 (79.5)	23 (67.6)	61 (67.8)
Presence of dactylitis	30 (41.7)	35 (42.2)	12 (35.3)	31 (34.4)
Disease and QOL scores, mean (SD)				
Tender joint count (78 joints)	25.71 (18.39)	26.37 (18.22)	23.56 (18.60)	24.36 (16.84)
Swollen joint count (76 joints)	12.22 (10.94)	14.10 (9.90)	14.32 (13.03)	14.43 (13.39)
DAS28-CRP score	4.83 (1.03)	5.09 (1.03)	5.00 (1.17)	4.77 (1.19)
HAQ DI score	1.07 (0.55)	1.21 (0.59)	1.17 (0.68)	1.20 (0.64)
PsA pain, VAS 0-100 mm	50.96 (23.84)	55.72 (22.26)	52.61 (24.58)	53.88 (23.78)
Patient global assessment, VAS 0-100 mm	54.88 (23.51)	56.60 (21.77)	55.42 (24.74)	54.98 (22.84)
Physician global assessment, VAS 0-100 mm	53.96 (16.39)	53.60 (17.54)	54.91 (19.50)	51.40 (19.03)

BSA, body surface area; HAQ-DI, Health Assessment Questionnaire-Disability Index; PBO, placebo; SEC, secukinumab; VAS, visual analog scale.

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3. Nash P, et al. *Arthritis Res Ther*. 2018;20:47.
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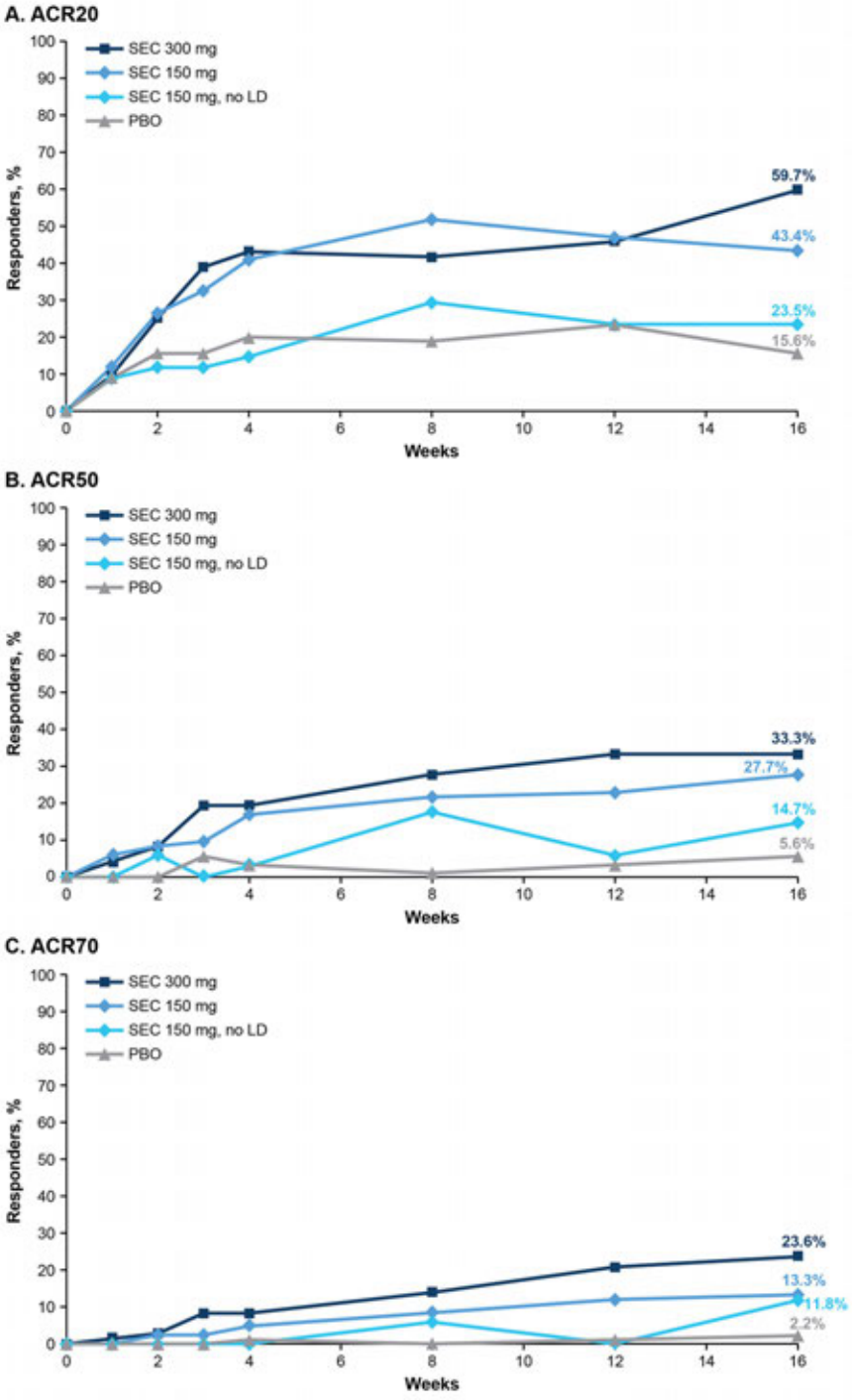
Figure 1. ACR20 (A), ACR50 (B), and ACR70 (C) Response Rates From Baseline to Week 16



PBO, placebo; SEC, secukinumab.

Table 2. Response in Additional Outcomes at Week 16

Responders, n/n (%)	SEC 300 mg (n = 72)	SEC 150 mg (n = 83)	SEC 150 mg, no LD (n = 34)	PBO (n = 90)
TJC78, ≥ 50% reduction	43/72 (59.7)	51/83 (61.4)	13/34 (38.2)	25/90 (27.8)
SJC76, ≥ 50% reduction	44/72 (61.1)	47/83 (56.6)	12/34 (35.3)	31/90 (34.4)
Leeds enthesitis index, ≥ 50% improvement	30/45 (66.7)	41/66 (62.1)	13/23 (56.5)	22/61 (36.1)
Leeds enthesitis index, complete resolution	21/45 (46.7)	35/66 (53.0)	8/23 (34.8)	16/61 (26.2)
Leeds dactylitis index, ≥ 50% improvement	17/30 (56.7)	20/35 (57.1)	6/12 (50.0)	15/31 (48.4)
Leeds dactylitis index, complete resolution	16/30 (53.3)	17/35 (48.6)	4/12 (33.3)	8/31 (25.8)
PASI75	27/34 (79.4)	14/36 (38.9)	6/11 (54.5)	2/38 (5.3)
PASI100	8/34 (23.5)	4/36 (11.1)	1/11 (9.1)	1/38 (2.6)
mIGA 2011 0/1	21/34 (61.8)	10/36 (27.8)	1/11 (9.1)	2/38 (5.3)
mNAPSI75	16/44 (36.4)	15/61 (24.6)	3/20 (15.0)	5/55 (9.1)
PsA pain, VAS 0-100 mm, ≥ 3-point improvement	47/72 (65.3)	62/83 (74.7)	21/34 (61.8)	42/90 (46.7)
HAQ DI, MCID 0.35	44/72 (61.1)	42/83 (50.6)	14/34 (41.2)	22/90 (24.4)
SF-36 PCS, MCID ≥ 2.5	44/72 (61.1)	46/83 (55.4)	19/34 (55.9)	31/90 (34.4)
SF-36 MCS, MCID ≥ 2.5	38/72 (52.8)	45/83 (54.2)	11/34 (32.4)	39/90 (43.3)

mIGA, modified Investigator Global Assessment 2011; MCID, minimum clinically important difference; mNAPSI75, 75% improvement in the modified Nail Psoriasis Severity Index; PASI75, 75% reduction in the Psoriasis Area and Severity Index; PASI100, 100% reduction in the Psoriasis Area and Severity Index, PBO, placebo, PCS, physical component summary, SEC, secukinumab, SF-36, 36-Item Short Form Health Survey; SJC, swollen joint count; TJC, tender joint count.

Disclosure: A. Kivitz, AbbVie, 5, Amgen, 1, 4, 5, Boehringer Ingeleheim, 5, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 5, 8, Flexion Therapeutics, 8, Genzyme, 5, 8, Gilead, 1, 4, 5, Gilead Sciences, Inc., 4, Horizon, 8, Janssen, 5, Janssen Research & Development, LLC, 2, Merck, 8, Novartis, 1, 4, 8, Pfizer, 1, 4, 5, 8, Regeneron, 1, 5, 8, Sanofi, 1, 4, 5, 8, Sun Pharma, 5, SUN Pharma Advanced Research, 5, UCB, 5; **J. Kremer**, AbbVie, 2, 5, Amgen, 5, Bristol-Myers Squibb, 2, 5, Corrona, 1, Genentech, 2, 5, Gilead, 5, Lilly, 2, 5, Novartis, 2, Pfizer, 2, 5, Regeneron, 5, Sanofi, 5; **C. Legerton**, AbbVie, 2, Amgen, 2, Bristol-Myers Squibb, 2, Novartis, 2, Pfizer, 2, Lilly, 2, UCB, 2, GSK, 2, GSK/HGS, 2, Gilead, 2, R-Pharm, 2, INFLARx, 2, Regeneron, 2, Corrona, 2; **J. Palmer**, Novartis, 3, 4; **X. Meng**, Novartis, 3, 4; **L. Pricop**, Noavrtis, 1, 3, Novartis, 1, 3, 4; **A. Singhal**, AbbVie, 2, 8, Amgen, 2, AstraZeneca, 2, Bristol-Myers Squibb, 2, Fujifilm, 2, Gilead, 2, Janssen, 2, Lilly, 2, Mallinckrodt, 2, MedImmune, 2, Nichi-Iko, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, UCB, 2.

Abstract Number: 1498

A Randomized, Placebo-Controlled Study Evaluating the Safety and Efficacy of Secukinumab in US Biologic-Naive Patients with Active Psoriatic Arthritis and Psoriatic Skin Lesions

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

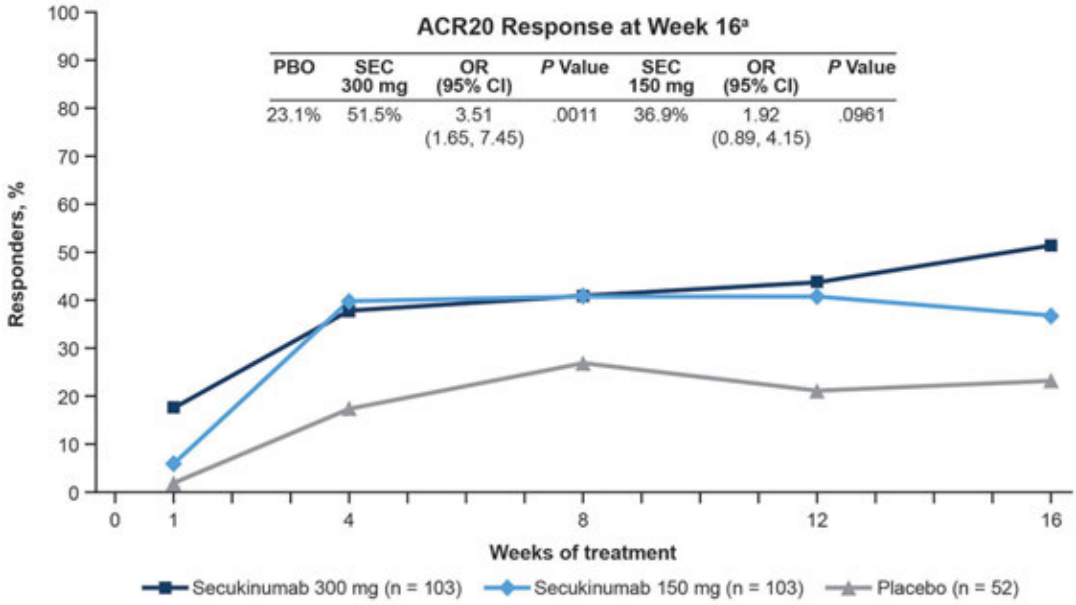
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis that often develops in patients (pts) with psoriasis. Secukinumab (SEC) inhibits IL-17A, a key inflammatory cytokine in the pathogenesis of PsA. SEC is approved for treatment of PsA based on the phase 3 FUTURE studies, where SEC proved superior to placebo (PBO) in improving signs and symptoms of PsA. Although pts from several countries were included, US pts were under-represented. We report findings from CHOICE (NCT02798211), a phase 4 study which evaluated SEC vs PBO in US biologic-naive pts with PsA with psoriatic skin lesions.

Methods: CHOICE was a randomized, double-blind, controlled trial conducted in the United States. Biologic-naive pts with active PsA by CASPAR criteria and psoriatic skin lesions (PASI ≥ 1) were enrolled. Pts were randomized 2:2:1 to receive SEC 300 mg, SEC 150 mg, or PBO, respectively, with a weekly loading dose up to Week 4, and every 4 weeks thereafter for 16 weeks. After Week 16, all pts randomized to PBO, and nonresponders from the SEC 150-mg group received SEC 300 mg up to Week 52. The primary objective was to show superiority of SEC 300 mg vs PBO in ACR20 response at Week 16. Secondary and exploratory objectives included the effect of SEC on dactylitis, enthesitis, psoriasis, remission status, RAPID3 score, and safety. Long-term (up to Week 52) efficacy and safety were also assessed.

Results: In total, 258 pts were randomized to SEC 300 mg (n = 103), SEC 150 mg (n = 103), or PBO (n = 52). Pts in all treatment groups had comparable baseline characteristics. In general, pts in CHOICE were older, had a higher mean weight, and higher baseline joint involvement than pts in the FUTURE studies. The study met its primary objective with a greater percentage of pts treated with SEC 300 mg achieving ACR20 response at Week 16 compared with PBO (51.5% vs 23.1%; odds ratio [OR], 3.51 [95% CI: 1.65, 7.45]; *P* = .0011, using logistic regression) (**Figure 1**). ACR20 responses were numerically higher with SEC 150 mg than PBO (36.9%; OR, 1.92 [95% CI: 0.89, 4.15]; *P* = .0961). SEC also led to higher ACR50/70 response rates, higher rates of minimal disease activity, lower RAPID3 scores, and improvements in other variables compared with PBO (**Table 1**). Response rates were generally sustained over time with SEC, with the percentage of responders increasing after uptitration of SEC dose. The most commonly reported adverse events (AEs) with SEC at Week 16 were diarrhea and upper respiratory tract infections (**Table 2**). No inflam-

Figure 1. ACR20 Response Over Time up to Week 16[a]



[a] ORs, 95% CIs, and *P* values are based on logistic regression.

Table 1. Summary of Select Secondary and Exploratory Efficacy Results at Week 16[a]

Outcome	PBO	SEC 300 mg	Odds Ratio (95% CI)	*P* Value	SEC 150 mg	Odds Ratio (95%CI)	*P* Value
ACR50	5.8%	28.2%	6.30 (1.81, 21.88)	.0038	24.3%	4.77 (1.36, 16.77)	.0149
ACR70	1.9%	17.5%	10.50 (1.36, 81.30)	.0243	10.7%	5.42 (0.67, 43.64)	.1120
Resolution of Enthesitis (LEI + SPARCC)[b]	17.9%	37.8%	2.85 (1.08, 7.50)	.0341	39.5%	2.65 (1.01, 6.93)	.0489
Resolution of Dactylitis	17.4%	40.8%	3.27 (0.96, 11.20)	.0587	38.5%	3.40 (0.98, 11.76)	.0529
MDA	3.8%	26.2%	8.75 (1.99, 38.45)	.0041	26.2%	8.34 (1.89, 36.85)	.0051
RAPID3 score[c]							
Mean (SD)	14.59 (6.1)	10.17 (7.1)	–	–	10.17 (6.4)	–	–
Change from baseline, mean (SD)	−1.19 (4.8)	−4.72 (5.7)	–	–	−3.70 (6.1)	–	–
LSM of treatment	−0.78	-4.57	−3.80[d] (−5.65, −1.94)	<.0001	−3.67	−2.89[d] (−4.78, −1.00)	.0028
PASI75	16.3%	64.6%	9.49 (3.73, 24.16)	<.0001	54.2%	6.38 (2.51, 16.24)	.0001
PASI90	9.3%	49.4%	9.86 (3.19, 30.45)	<.0001	36.1%	5.21 (1.68, 16.21)	.0043
PASI100	2.3%	25.3%	14.38 (1.86, 111.53)	.0107	18.1%	9.82 (1.24, 77.90)	.0307

ACR50/70, 50% or 70% improvement in American College of Rheumatology response; LEI, Leeds Enthesitis Index; LSM, least squares mean; MDA, minimal disease activity; PASI75/90/100, 75%, 90%, or 100% improvement in the Psoriasis Area and Severity Index; PBO, placebo; SEC, secukinumab; SPARCC, Spondyloarthritis Research Consortium of Canada Enthesitis Index.
[a] ORs, 95% CIs, and *P* values are based on logistic regression; [b] Results are from the combined LEI and SPARCC. Enthesitis was determined in patients who had an enthesitis score ≥ 1 when sites from LEI and SPARCC were assessed together at baseline; [c] LSM, LSM of treatment differences, 95% CI, and *P* values are based on an analysis of covariance (ANCOVA) model. [d] LSM of the treatment difference.

matory bowel disease was reported; 3 pts (SEC 300 mg, n = 1; SEC 150 mg, n = 2) had *Candida* infections at Week 16. Only 1 pt in each SEC group discontinued treatment by Week 16 due to AEs. One death occurred during the study (cardiac arrest, PBO group).

Table 2. Common AEs Regardless of Study Drug Relationship up to Week 16 (in ≥ 3% of patients)

Preferred Term	SEC 300 mg n (%)	SEC 150 mg n (%)	PBO n (%)
All AEs	59 (57.3)	61 (59.2)	27 (51.9)
Diarrhea	6 (5.8)	6 (5.8)	1 (1.9)
Upper respiratory tract infection	6 (5.8)	2 (1.9)	0
Hypertension	5 (4.9)	4 (3.9)	0
Sinus congestion	4 (3.9)	0	0
Nasopharyngitis	3 (2.9)	4 (3.9)	1 (1.9)
Fatigue	3 (2.9)	5 (4.9)	0
Headache	3 (2.9)	4 (3.9)	2 (3.8)
Abdominal pain	2 (1.9)	2 (1.9)	2 (3.8)
Sinusitis	2 (1.9)	1 (1.0)	2 (3.8)
Musculoskeletal pain	2 (1.9)	1 (1.0)	3 (5.8)
Arthralgia	1 (1.0)	2 (1.9)	4 (7.7)
Pain in extremity	1 (1.0)	3 (2.9)	3 (5.8)
Psoriatic arthropathy	1 (1.0)	4 (3.9)	0
Back pain	1 (1.0)	4 (3.9)	0
Peripheral edema	1 (1.0)	0	2 (3.8)
Psoriasis	1 (1.0)	4 (3.9)	0
Respiratory tract congestion	0	0	2 (3.8)

Conclusion: SEC 300 mg was superior to PBO in leading to rapid and significant improvements in symptoms of PsA in US biologic-naive patients. Benefits were observed with both SEC doses; however, responses were generally higher with SEC 300 mg. Overall, findings in CHOICE were consistent with previous studies and suggest that SEC 300 mg is safe and efficacious as a first-line biologic treatment for pts with PsA.

Disclosure: T. Nguyen, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Allmiral, 8, Bristol-Myers Squibb, 2, 5, Biogen Idec, 2, Celgene, 5, 8, Lilly, 2, 5, 8, Corrona, 5, GSK, 2, Janssen, 5, Merck, 2, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi Regeneron, 2, 5, 8, Sun Pharma, 8, UCB, 5; **M. Churchill**, Novartis, 2; **R. Levin**, AbbVie, 2, 8, Amgen, 2, Bristol-Myers Squibb, 8, Gilead, 5, Lilly, 2, Myriad Genetics, 5, Pfizer, 2, Sanofi, 2, 8, UCB, 2; **G. Valenzuela**, AbbVie, 5, Bristol-Myers Squibb, 2, Celgene, 5, GSK, 5, Janssen, 5, Lilly, 2, 5, Merck, 2, 5, MLKCDT, 2, Novartis, 2, 5, Pfizer, 2, 5, Sanofi Regeneron, 2, 5, UCB, 5; **J. Merola**, AbbVie, 2, 5, 8, Aclaris, 2, 5, Almirall, 2, 5, Amgen, 5, Biogen, 2, 5, Biogen Idec, 2, 5, Biogen IDEC, 5, Brigham and Women's Hospital, Harvard, 3, Burrage Capital Management Boston Advisory Board, 6, Celgene, 2, 5, Dermavant, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 5, GlaxoSmithKline, 5, GSK, 2, 5, Incyte, 2, 5, Janssen, 2, 5, Leo Pharma, 2, 5, Lilly, 5, Merck, 5, Merck Research Laboratories, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Regeneron, 5, Samumed, 2, 5, Sanofi, 5, Sanofi Regeneron, 2, 5, Science 37, 5, Sun Pharma, 2, 5, UCB, 2, 5; **A. Ogdie**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Takeda, 5, Amgen, 2, 4, 5, 8, Amgen to Forward National Databank, 2, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 4, 5, 8, Corrona, 5, CORRONA, 5, From Noavrtis to husband, 7, Lilly, 5, Lily, 5, Novartis, 2, 5, 7, Novartis to UPenn, 2, Novartis, Pfizer, 2, Pfizer, 2, 5, Pfizer Inc, 2, 5, Pfizer to UPenn, 2; **A. Orbai**, AbbVie, 2, Celgene, 2, Eli Lilly, 2, 5, Horizon, 2, Janssen, 2, 5, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 5, UCB, 5; **J. Scher**, Amgen, 5, Bristol-Myers Squibb, 5, Janssen, 5, Novartis, 2, 5, Pfizer, 2, UCB, 5; **A. Kavanaugh**, Abbott, 2, Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, 2, Amgen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 2, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, Pfizer Inc, 2, Roche, 2, UCB Pharma, 2; **S. Agawane**, Novartis, 3, Novartis Healthcare Pvt Ltd, 3; **F. Kianifard**, Novartis, 3, 4; **C. Rollins**, Novartis, 3, 4; **O. Chambenoit**, Novartis, 3, 4.

Abstract Number: 1499

Golimumab Persistence in Biologic Naive and Non-Naive Patients with Axial Spondyloarthritis: Results of the GO PRACTICE Study

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The pivotal GO AFTER study **[1]** and the ongoing observational GO BEYOND study investigate GLM efficacy in rheumatoid arthritis (**RA**) patients who previously received biologics. However, clinical studies of GLM in axial spondyloarthritis (**axSpA**) are lacking. Using data from the GO PRACTICE study, we examined GLM persistence in patients with axSpA.

The primary objective of the study was to estimate GLM persistence at 2 years from initial prescription, as a first line of treatment (in biologic naïve patients: BN) and as a second or further line of treatment (in biologic pretreated patients: **BP**). Secondary outcomes included evaluations of changes over 2 years in 1) clinical disease activity, and 2) patient-reported disease activity, pain, functional ability and quality of life (**QoL**).

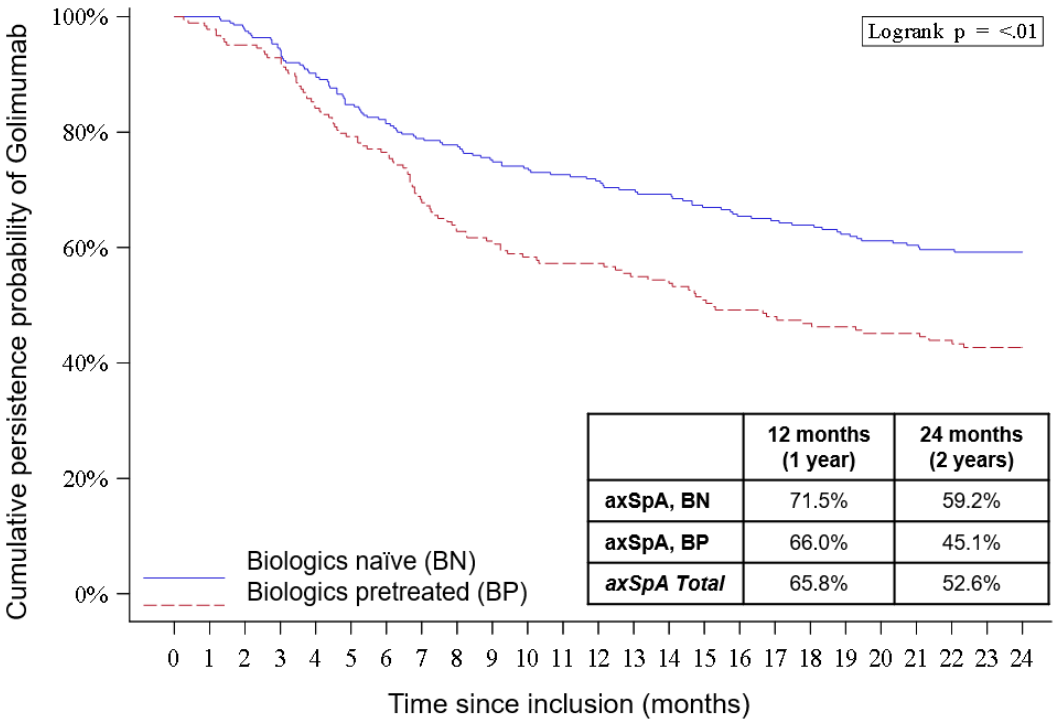
Methods: This was an observational, prospective, multicenter French study, that recruited adult patients with RA, psoriatic arthritis or axSpA, who were newly prescribed GLM. Patients were followed-up over 2 years; data were collected at baseline, 1 year and 2 years. This abstract presents findings originating from the axSpA cohort of the GO PRACTICE study. GLM persistence was estimated with the Kaplan-Meier method. Clinical disease activity was assessed with the Ankylosing Spondylitis Disease Activity Score (**ASDAS**) and patient-reported disease activity was evaluated with the Bath Ankylosing Spondylitis Disease Activity Index (**BASDAI**). Pain was evaluated using a visual analogue scale (**VAS**), functional ability with the Health Assessment Questionnaire (**HAQ**) and QoL with the EQ-5D and SF-12 questionnaires.

Results: From January 2015 to March 2016, 478 axSpA patients (constituting 63% of the total cohort) from 134 sites were included in the study. Mean age was 43 years and 55% were female; 61% were BN (n=291) and 39% were

	BN patients		BP patients		
	Baseline	2 years	Baseline	2 years	*p**
ASDAS-CRP, Mean score (SD)	3.2 (0.8)	1.5 (0.9)	3.1 (0.8)	2.0 (1.0)	*p* =.0051
BASDAI, Mean Score (SD)	5.3 (1.7)	2.6 (1.9)	5.7 (1.6)	3.1 (2.0)	*p* <.0001

**p* is from a 2-factor repeated-measures model testing the significance of the effect of prior biologic treatment on score evolution, adjusted to time

Disease activity scores at baseline and 2 years for biologics naïve (BN) and biologics pretreated (BP) axial spondyloarthritis (axSpA) patients who were persisting on golimumab.



	12 months (1 year)	24 months (2 years)
axSpA, BN	71.5%	59.2%
axSpA, BP	66.0%	45.1%
axSpA Total	65.8%	52.6%

BP (n=187). Mean duration of axSpA illness was 5.5 and 10.7 years in BN and BP patients, respectively ($p < .001$). At baseline, most were prescribed 50 mg GLM monthly (97%); DMARDs, corticosteroids and NSAIDs or analgesics were co-prescribed to 34%,17% and 90% of axSpA patients, respectively. GLM persistence over 2 years was significantly higher in BN than BP patients (59.2% vs 45.1%, logrank $p < .01$). For BN and BP patients persisting on GLM at 2 years, disease activity (Table 1) and patient-reported outcomes showed significant improvements, with improvements being more important in BN patients. GLM was well tolerated in axSpA patients (n=478), with 46 (9.6%) discontinuing due to intolerance. In the BN group, 18 patients (6.2%) discontinued GLM due to primary treatment failure, compared to 28 BP patients (15%). GLM was re-prescribed to 213 (88%) of the 241 patients persisting on GLM at 2-years. Post-hoc multivariate analysis showed that being female was a risk factor for GLM discontinuation in axSpA (HR1.9, IC95% 1.4-2.6).

Conclusion: Golimumab is associated with clinical improvements and good persistence in patients with axial spondyloarthritis, especially those who are biologic naïve

Reference:

1. Smolen JS, *et al*; *Arthritis research & therapy* 2015,**17**:14Kaplan-Meier plots showing the cumulative persistence probability of golimumab over 24 months in axial spondyloarthritis (axSpA) patients who were biologics naïve (BN) and biologics pretreated (BP).

Disclosure: R. Flipo, MSD, 5, Sanofi, 5; **F. Tubach**, MSD, 5; **J. Ouaniche**, MSD, 5; **P. Goupille**, AbbVie, 5, Amgen, 5, Biogaran, 5, BMS, 5, Celgene, 5, Eli Lilly, 5, Hospira, 5, Janssen-Cilag, 5, MSD, 5, Pfizer, 5, Sanofi-Genzyme, 5, UCB, 5; **E. Lespessailles**, MSD, 5; **N. Gouyette**, MSD, 3; **N. Harid**, MSD, 3; **J. Fayette**, MSD, 9; **P. Bertin**, MSD, 5; **B. Fautrel**, AbbVie, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Boehringer Ingelheim, 8, Celgene, 5, 8, Eli Lilly and Company, 2, 5, Janssen, 5, 8, Lilly, 8, Medac, 5, 8, MSD, 2, 5, 8, NORDIC Pharma, 5, 8, Novartis, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, Sanofi-Aventis, 5, SOBI, 5, 8, UCB, 5, 8.

Abstract Number: 1500

Effectiveness of Switching Between TNF Inhibitors in Patients with Axial Spondyloarthritis: Is the Reason to Switch Relevant?

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Over the last years, and mostly due to lack of alternatives, it has been common practice to start a second TNF inhibitor (TNFi) in patients with axial spondyloarthritis (axSpA) who discontinue their first TNFi. Evidence informing on the effectiveness of this strategy in clinical practice is limited. Importantly it remains unclear whether the reason for discontinuation of the first TNFi influences the response to the second. We aimed to assess whether the reason of discontinuation of the first TNFi influences the response to the second TNFi.

Methods: Patients with axSpA from the ReumaPt national registry, who discontinued their first TNFi and started a second TNFi were included in this analysis. In addition, patients were required to have complete data on Ankylosing Spondylitis Disease Activity Score (ASDAS) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at baseline, 3 and 6 months after starting the first TNFi. Afterwards, patients were followed every 6 months up to 12 years. The main outcome was the ASDAS clinically important improvement (ASDAS CII). Secondary outcomes were ASDAS major important improvement (ASDAS MI); ASDAS low disease activity (ASDAS LDA); ASDAS inactive disease (ASDAS ID) and BASDAI 50. The reason for discontinuation of the first TNFi was defined as: i) Primary failure, if

Table - Association between the reason for discontinuation of the first TNFi and response to the second TNFi

Reason to discontinue first TNFi*	Outcome for the second TNFi OR (95% CI)				
	ASDAS-MII (N=125)	ASDAS-CII (N=125)	ASDAS-ID (N=155)	ASDAS-LDA (N=155)	BASDAI50 (N=141)
(ref Primary failure)					
-Secondary failure	**5.3 (1.4;19.5)**	2.3 (0.9;6.0)	**5.3 (1.4;21.4)**	1.1 (0.5;2.3)	1.4 (0.6;3.1)
-Adverse events	3.4 (0.9;12.4)	1.8 (0.7;4.5)	**8.7 (2.4;31.5)**	1.0 (0.5;1.9)	1.1 (0.5;2.4)
-Other	1.5 (0.1;15.6)	1.2 (0.3;4.7)	**7.2 (1.5;34.2)**	1.1 (0.4;2.6)	0.4 (0.1;1.7)

*GEE models with the reason of discontinuation of the first TNFi as predictor (reference category: primary failure); all models adjusted for age and gender. OR in bold are statistically significant (p<0.05).

ASDAS CII was not achieved at 3 or 6 months; ii) Secondary failure if ASDAS CII was achieved at 3 or 6 months but lost in ≥1 visit during follow-up; iii) Adverse events; iv) Other (e.g. pregnancy, surgery). The response to the first TNFi at 3 and 6 months was compared to the response to the second TNFi at the same visits, adjusting for age and gender. The association between the reason of discontinuation of the first TNFi (predictor) and response the second TNFi over time was tested in generalized estimating equations (GEE) models, adjusted for age and gender.

Results: In total, 155 patients (58% male, mean age 41 (SD:11) years) were included, with a median follow-up time on the second TNFi of 1.5 years. Patients had a lower response to the second TNFi compared to the first TNFi according to the main outcome (ASDAS CII) at 3 months (41% vs 51%) and 6 months (35% vs 56%). There was no association between the reason to discontinue the first TNFi and response to the second TNFi as defined by ASDAS CII (Table). This association was present for the most stringent outcomes, namely ASDAS MI and ASDAS ID. Compared to patients who discontinued their first TNFi due to primary failure, patients were more likely to achieve ASDAS ID with the second TNFi when they discontinued their first TNFi due to secondary failure (OR: 5.3 [(95%CI: 1.4; 21.4]), adverse events (OR: 8.7 [2.4; 31.5]), or other reasons (OR: 7.2 [1.5; 34.2]).

Conclusion: In patients with axSpA, response to the second TNFi is worse compared to the first TNFi. The reason to discontinue the first TNFi seems to influence the response to the second TNFi. Patients with a secondary failure to the first TNFi have a better response to the second TNFi compared to those discontinuing the first TNFi due to a primary failure, particularly when response is defined by the most stringent outcomes.

Disclosure: S. Rodrigues-Manica, None; **A. Sepriano**, None; **F. Pimentel-Santos**, None; **N. Gouveia**, None; **A. Barcelos**, Bene, 8, MSD, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Eli-Lilly, 5; **J. Branco**, None; **M. Bernardes**, Janssen-Cilag, 5, 8, Novartis, 5, AbbVie, 5, Amgen, 5, Pfizer, 5, Eli-Lilly, 5, Biogen, 5, Glaxo-Smith-Kline, 5; **R. Miriam-Ferreira**, None; **E. Vieira-Sousa**, None; **S. Barreira**, None; **F. Vinagre**, None; **R. Roque**, None; **H. Santos**, AbbVie, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Janssen-Cilag, 5, 8, Eli-Lilly, 5; **N. Madeira**, None; **J. Rovisco**, None; **A. Daniel**, None; **S. Ramiro**, AbbVie, 5, 8, Eli Lilly, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8.

Abstract Number: 1501

Ixekizumab: 52-Week Efficacy and Safety in Radiographic Axial Spondyloarthritis Patients with Prior Inadequate Response/Intolerance to Tumor Necrosis Factor Inhibitors

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SESSION INFORMATION

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Background/Purpose: Week 16 results from COAST-W (NCT02696798) showed that ixekizumab (IXE) was superior to placebo (PBO) in improving the signs and symptoms of active radiographic axial spondyloarthritis (r-axSpA) in patients with prior inadequate response (IR) or intolerance to tumor necrosis factor inhibitors (TNFi).[1] Long-term efficacy and safety of IXE in this population have not been reported. The objective of the study was to assess the efficacy and safety of IXE through 52 weeks of continuous treatment in TNF-IR patients.

Methods: Adults with active r-axSpA (Assessment of SpondyloArthritis international Society [ASAS] criteria) and prior IR/intolerance to 1-2 TNFi were randomized 1:1:1 to PBO or 80 mg IXE every 2 (IXEQ2W) or 4 weeks (IXEQ4W). At Week 16, patients assigned to IXE continued with IXE, and patients assigned to PBO were randomized at 1:1 to IXEQ2W or IXEQ4W through Week 52.

Results: Of 212 patients initially randomized to IXE, 169 (80%) completed Week 52. Both IXE regimens led to sustained improvements in disease activity through 52 weeks (Table). Previously reported[1] improvements in function, objective inflammation, quality of life, health status, and overall function were sustained/further improved through 52 weeks. Patients initially randomized to PBO who switched to IXE rapidly achieved similar levels of improvement in signs and symptoms as patients initially randomized to IXE (Table). The frequency of treatment-emergent adverse events (AEs) through 52 weeks was similar between IXE regimens. In patients who received ≥1 IXE dose (N=305), 16 (5%) reported serious AEs and 23 (7.5%) discontinued due to AEs. Safety through 52 weeks of IXE was consistent with safety through 16 weeks.[1]

Conclusion: These are the first long-term data on the efficacy and safety of IXE in r-axSpA patients with prior IR/intolerance to TNFi. Both IXE regimens provided similar and sustained improvement in signs and symptoms through 52 weeks, with no unexpected safety signals. Patients who switched to IXE after initial PBO treatment rapidly achieved similar levels of improvement in signs and symptoms of r-axSpA as patients originally randomized to IXE. These findings indicate that in r-axSpA patients with prior IR/intolerance to TNFi, treatment with an alternative mode of action can be successful.

Table: Clinical improvement in signs and symptoms at Weeks 16 and 52 in patients treated with IXE for up to 52 weeks and in patients initially treated with PBO and then IXE from Week 16 onwards

Response, n (%) Nonresponder Imputation (Extended Treatment Period Population[a])	PBO/ All IXE (N=93)	IXEQ4W/ IXEQ4W (N=98)	IXEQ2W/ IXEQ2W (N=90)
ASAS20			
Week 16	31 (33.3)	54 (55.1)	46 (51.1)
Week 52	50 (53.8)	60 (61.2)	47 (52.2)
ASAS40			
Week 16	13 (14.0)	28 (28.6)	30 (33.3)
Week 52	36 (38.7)	39 (39.8)	30 (33.3)
ASDAS <2.1[b]			
Week 16	5 (5.4)	20 (20.4)	16 (17.8)
Week 52	27 (29.0)	27 (27.6)	24 (26.7)

[a]Patients who received ≥1 IXE dose during Weeks 16-52.
[b]Indicates low disease activity.
ASDAS=Ankylosing Spondylitis Disease Activity Scale.

Reference

1. Deodhar et al. Arthritis Rheumatol, 2018

Disclosure: M. Dougados, Pfizer, 2, 5, 8, Abbvie, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, UCB, 2, 5, 8, Novartis, 2, 5, 8; **J. Sieper**, AbbVie, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Novartis, 5, 8; **X. Baraliakos**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, BMS, 2, 5, 8, 9, Bristol-Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, 9, Chugai, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Lilly, 2, 8, 9, Merck, 2, 5, 8, MSD, 2, 5, 8, 9, Novartis, 2, 5, 8, 9, Novatis, 2, 5, 8, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9, UCB Pharma, 2, 5, 8, Werfen, 2, 5, 8; **F. Van den Bosch**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, Bristol-Myers Squibb, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sanofi and UCB, 5, 8, ABBVIE, CELGENE, ELI LILLY, GALAPAGOS, MERCK, NOVARTIS, PFIZER, VCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **W. Maksymowych**, Eli Lilly and Company, 2, 5, 8, AbbVie, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8, Celgene, 5, Boehringer Ingelheim, 5, Galapagos, 5, CaRE Arthritis, 6; **J. Ermann**, Boehringer Ingelheim, 2, Eli Lilly, 5, Novartis, 5, Pfizer, 2, UCB, 5; **X. Li**, Eli Lilly and Company, 1, 3; **G. Gallo**, Eli Lilly, 1, 3, 4, Eli Lilly and Company, 1, 3, 4; **H. Carlier**, Eli Lilly and Company, 1, 3, 4; **L. Gensler**, AbbVie, 2, 5, Abbvie, 2, 9, Amgen, 2, Amgen, AbbVie and Novartis, 2, Center for Disease Control, 8, Division of Vaccine Injury Compensation, 8, Eli Lilly, 5, 9, Eli Lilly and Company, 9, Galapagos, 5, 9, Galapagos, Janssen, Eli Lilly, Novartis, Pfizer, and UCB, 5, Janssen, 5, 9, Novartis, 2, 5, 9, Pfizer, 2, 9, Spondylitis Association of America, 6, Spondyloarthritis Research and Treatment Network (SPARTAN), 6, UCB, 2, 5, 9, UCB Pharma, 2, 9.

Abstract Number: 1502

The Effect of Tofacitinib on Residual Pain in Patients with Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Current treatments for PsA have proven effective in reducing patient (pt)-reported pain;[1,2] however, residual pain often remains. Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. This descriptive analysis evaluated the effect of tofacitinib, adalimumab and placebo on residual pain in pts with PsA whose inflammation was attenuated after 3 months of therapy.

Methods: Data were included from OPAL Broaden (NCT01877668), a randomized, double-blind, placebo-controlled Phase 3 trial of 12 months' duration in pts with PsA.[3] Pts were randomized to receive tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, adalimumab 40 mg subcutaneous injection every 2 weeks (Q2W), or placebo. This analysis assessed pts with 'residual pain' at Month (M)3. Residual pain was considered as pain in pts with complete attenuation of inflammation at M3, defined by a swollen joint count (SJC) of 0 and CRP levels < 6 mg/L. Pain was measured by a visual analog scale (VAS; 0 ["no pain"] – 100 mm ["most severe pain"]). Changes in pain from baseline to M3 and residual pain (VAS pain reported at M3) were assessed.

Results: Demographics and baseline disease characteristics have previously been reported in the primary study, and were generally similar between treatment groups.[3] At M3, 99/422 (23.5%) pts with PsA had achieved SJC of 0 and CRP < 6 mg/L. At M3, more tofacitinib-treated (tofacitinib 5 mg BID, n=23/107 [21.5%]; tofacitinib 10 mg BID, n=33/104 [31.7%]) and adalimumab-treated pts (n=30/106 [28.3%]) achieved SJC of 0 and CRP < 6 mg/L vs placebo (n=13/105 [12.4%]). Baseline pain appeared numerically higher in the tofacitinib treatment group (tofacitinib 5 mg BID = 54.7 mm; tofacitinib 10 mg BID = 58.4 mm) vs adalimumab (47.7 mm) and placebo (50.4 mm). In pts who achieved SJC of 0 and CRP < 6 mg/L at M3, improvements in pain from baseline to M3 appeared numerically greater in pts receiving tofacitinib vs those receiving placebo (Figure 1a). When considering absolute (residual) pain at M3, mean residual pain was similar across treatment groups (ranging from 22.7–29.2 mm; Figure 1b), despite a higher baseline pain in tofacitinib treatment groups.

Conclusion: Changes from baseline in pain and absolute pain at M3 suggest that in pts with PsA whose inflammation has been completely attenuated, tofacitinib might have an effect on residual pain not obviously attributable to inflammation. However, the sample population was small, and there were large standard deviations. To confirm these results and to understand the mechanisms by which tofacitinib may improve residual pain, a meta-analysis will be performed, using individual participant data from pts with rheumatic disease who have participated in tofacitinib randomized controlled trials.

References

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3. Mease P et al. N Engl J Med 2017; 377: 1537-1550.

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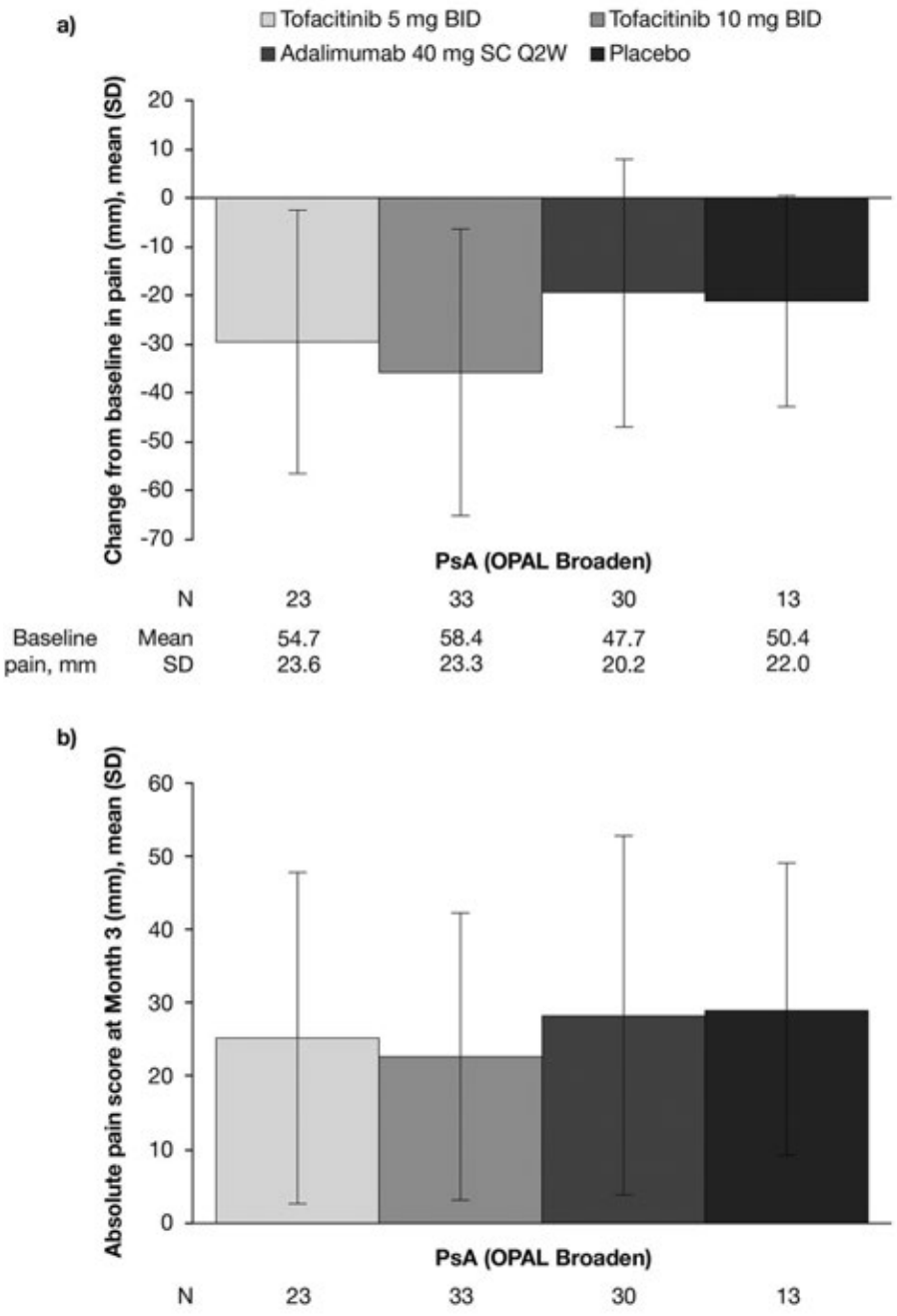
Figure 1. Change from baseline in a) pain to Month 3 and b) absolute pain at Month 3 in patients with PsA and SJC=0 and CRP <6 mg/L by treatment group



Only patients who reported SJC of 0 and CRP <6 mg/L at Month 3 were included in this analysis. Mean pain is measured by a visual analog scale from 0–100 mm where 0 = "no pain" and 100 = "most severe pain"
BID, twice daily; CRP, C-reactive protein; PsA, psoriatic arthritis; Q2W, once every 2 weeks;
SC, subcutaneous injection; SD, standard deviation; SJC, swollen joint count

BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **C. Bingham**, Abbvie, 5, AbbVie, 5, BMS, 2, 5, Bristol Meyer Squibb, 2, 5, Bristol Myers-Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Eli/Lilly, 5, Genentech/Roche, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Pfizer Inc, 5, Regeneron/Sanofi, 5, Sanofi/Regeneron, 5; **P. Taylor**, AbbVie, 5, Abbvie, 5, Biogen, 5, Celgene, 2, 5, Eli Lilly and Company, 2, 5, Fresenius, 5, Fresenius SE & Co, 5, Fresnius, 5,

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Abstract Number: 1503

Safety Profile of Ixekizumab Treatment in Patients with Moderate-to-Severe Plaque Psoriasis and Psoriatic Arthritis: Integrated Analysis of 18 Clinical Trials

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Background/Purpose: Ixekizumab (IXE) is a high-affinity monoclonal antibody that specifically targets IL-17A. Pooled safety data from IXE studies in moderate-to-severe plaque psoriasis (PsO) and psoriatic arthritis (PsA) have been reported previously.[1, 2] The purpose of this analysis is to report integrated safety results of IXE collected as of March 21, 2019.

Methods: All safety data from controlled and uncontrolled trials were integrated from 14 PsO and 4 PsA studies. The longer-term follow-up was 5 years for PsO trials and 3 years for PsA trials. Safety data were integrated from an all IXE exposure-safety population (defined as all patients receiving ≥1 dose of IXE) by indication. We report exposure-adjusted incidence rates (IRs) per 100 patient-years (PY) at 1-year intervals (over the entirety of exposure) for up to 5 years for adverse events (AEs). Major adverse cerebro-cardiovascular events (MACE) and inflammatory bowel disease (IBD) were adjudicated by an external adjudication committee.

Results: A total of 6091 (17499.3 PY) patients from PsO trials and 1401 (2228.6 PY) patients from PsA trials were analyzed. The Table summarizes safety results for both treatment populations over 1-year intervals. Overall, the IRs for treatment-emergent AEs (TEAEs), serious AEs, and serious infections remained stable with continued IXE exposure, whereas the IRs of patients reporting infections or injection site reactions decreased over time. The most common TEAEs in PsO and PsA were nasopharyngitis, upper respiratory tract infection, and injection-site reaction; most were reported as mild or moderate in severity Opportunistic infections were limited to oral and esophageal candidiasis and localized herpes zoster. Over the entirety of exposure in PsO and PsA studies, respectively, IRs for AEs leading to study drug discontinuation (2.8 and 5.1), serious SAE (5.4 and 6.0) and death (0.2 and 0.3) were reported. The rate of suicide ideation or behavior was 0.1in PsO studies and less than 0.1 in PsA studies. There were no completed suicides in both PsO and PsA studies. In both PsO and PsA studies, IRs for safety topics of special interest in PsO and PsA included, IBD (adjudicated; 0.2 and 0.1), depression (1.2 and 1.7), non-melanoma skin cancer (0.3 and 0.4), other malignancies (0.5 and 0.3) and MACE (0.5 and 0.5), respectively.

Conclusion: The results support a favorable and consistent long-term safety profile of IXE treatment in patients with moderate-to-severe PsO (17499.3 PY) or active PsA (2228.6 PY).

Table: Exposure-adjusted incidence rate of TEAEs over time by 1-year interval of exposure to ixekizumab

	Psoriasis					Psoriatic Arthritis		
	Year [0,1) 5583.0 PY	Year [1,2) 3403.7 PY	Year [2,3) 3106.0 PY	Year [3,4) 2881.9 PY	Year [4,5) 2371.1 PY	Year [0,1) 1189.8 PY	Year [1,2) 689.0 PY	Year [2,3) 347.1 PY
TEAEs ≥1	86.0 (83.6, 88.5)	70.6 (67.8, 73.5)	65.9 (63.1, 68.8)	61.9 (59.1, 64.8)	63.0 (59.9, 66.3)	88.1 (82.9, 93.6)	71.3 (65.2, 77.9)	67.1 (59.0, 76.3)
SAEs	6.6 (5.9, 7.3)	6.8 (6.0, 7.8)	6.6 (5.7, 7.5)	6.9 (6.0, 8.0)	5.8 (4.9, 6.8)	6.0 (4.7, 7.5)	7.7 (5.9, 10.1)	5.5 (3.5, 8.6)
Serious infections	1.3 (1.1, 1.7)	1.4 (1.0, 1.8)	1.7 (1.3, 2.2)	1.4 (1.0, 1.9)	1.4 (1.0, 2.0)	1.5 (1.0, 2.4)	1.3 (0.7, 2.5)	0.9 (0.3, 2.7)
Infections	57.0 (55.1, 59.0)	41.7 (39.5, 43.9)	38.1 (36.0, 40.3)	35.8 (33.7, 38.1)	35.5 (33.2, 37.9)	53.0 (49.1, 57.3)	42.5 (37.9, 47.7)	38.9 (32.9, 46.0)
Injection site reactions	15.7 (14.7, 16.8)	4.3 (3.6, 5.0)	2.2 (1.7, 2.8)	2.3 (1.8, 2.9)	1.7 (1.3, 2.3)	21.5 (19.0, 24.3)	3.5 (2.3, 5.2)	2.3 (1.2, 4.6)
Malignancies	0.9 (0.7, 1.2)	0.8 (0.5, 1.2)	0.9 (0.6, 1.3)	0.8 (0.6, 1.2)	0.8 (0.5, 1.2)	0.3 (0.1, 0.9)	1.2 (0.6, 2.3)	1.2 (0.4, 3.1)
NMSC	0.5 (0.3, 0.7)	0.2 (0.1, 0.4)	0.4 (0.2, 0.7)	0.2 (0.1, 0.5)	0.2 (0.1, 0.5)	0.3 (0.1, 0.8)	0.6 (0.2, 1.5)	0.6 (0.1, 2.3)
Malignancies excluding NMSC	0.4 (0.3, 0.6)	0.6 (0.4, 0.9)	0.5 (0.3, 0.8)	0.6 (0.4, 1.0)	0.5 (0.3, 0.9)	0.1 (0.0, 0.6)	0.6 (0.2, 1.5)	0.6 (0.1, 2.3)
MACE	0.5 (0.4, 0.7)	0.6 (0.4, 0.9)	0.3 (0.2, 0.6)	0.7 (0.4, 1.0)	0.4 (0.2, 0.7)	0.3 (0.1, 0.8)	1.2 (0.6, 2.3)	0.3 (0.0, 2.0)

IRs=exposure-adjusted incidence rates per 100 patient-years; MACE=major adverse cardiovascular event; N=total number of patients analyzed at each time point; NMSC=non-melanoma skin cancer; PY=patient-years; SAEs=serious adverse events; TEAEs=treatment-emergent adverse events.
All data are IRs (95% confidence intervals).

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Abstract Number: 1504

Subcutaneous Secukinumab 150 Mg Provides Rapid and Sustained Relief in Total and Nocturnal Back Pains, Morning Stiffness, and Fatigue in Patients with Active Ankylosing Spondylitis over 4 Years

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Background/Purpose: Ankylosing spondylitis (AS) is a chronic inflammatory condition. Pain, stiffness, and fatigue are reported as the most troubling symptoms by 70–80%, 20–40%, and 50–60% of patients (pts) with AS, respectively.[1-5] Early and sustained relief of these symptoms are essential for effective AS management.[4,6] Secukinumab (SEC) provided sustained relief in pain and fatigue in AS pts over 2 years in the MEASURE 2 study.[7] Here we report the effect of subcutaneous (s.c.) SEC 150mg on key clinical symptoms (pain, morning stiffness, and fatigue) in pts with AS over 208 weeks (wks) in the MEASURE 2 study.

Methods: The MEASURE 2 study design has been reported previously. This post hoc analysis assessed the mean change from baseline at Week (Wk) 208 in total and nocturnal back pain scores (by visual analog scale [0–100]; ASAS outcome component), overall level of spinal pain (neck, back, or hip) from BASDAI score, and morning stiffness (overall level; mean of question 5 and 6 of BASDAI score). Additionally, the SF-36 physical component summary (PCS) score, overall level of fatigue (BASDAI question 1), FACIT-Fatigue score, and pts meeting minimal clinically important difference (MCID) criteria across multiple clinical domains were also assessed. Data are shown for pts originally randomized to SEC 150mg and placebo. Data are reported as observed for overall population and by prior anti-TNF therapy status (naïve vs inadequate response/intolerance [IR]).

Results: Baseline clinical characteristics were generally comparable across the treatment groups SEC 150mg (N=72) and placebo (N=74); total mean back pain score was 67.7±17.79, nocturnal back pain score (0–100 mm scale) was 64.9±19.58, and morning stiffness was 6.5±2.11. SEC 150mg-treated pts reported rapid and early reductions in pain scores by Wk 4, which were sustained through Wk 208 (Table). Improvements with SEC 150mg were also reported in nocturnal back pain, morning stiffness, physical function (SF-36 PCS) and fatigue (overall level of fatigue and FACIT-Fatigue) as early as Wk 4, which were sustained at Wk 208 (Table). A higher proportion of SEC 150mg-treated pts met MCID criteria at Wk 16 vs placebo across multiple clinical domains, which was sustained or further improved through Wk 208. Improvements were observed in both anti-TNF-naïve and -IR pts, with a greater magnitude of improvement in anti-TNF-naïve pts.

Conclusion: SEC 150mg was associated with rapid and clinically meaningful improvement in total back pain and nocturnal back pain, morning stiffness, and fatigue, with improvements sustained over 4 years of treatment.

Table: Summary of results					
Endpoints, mean change ± SD	Treatment group	Wk 4	Wk 16	Wk 104	Wk 208
Pain					
Total back pain	SEC 150 mg	–25.86 ± 26.19	–29.0 ± 25.08	–36.37 ± 28.08	–32.81 ± 29.17
	Placebo	–10.47 ± 22.04	–12.22 ± 25.79	N/A	N/A
Nocturnal back pain	SEC 150 mg	–28.99 ± 26.35	–32.57 ± 27.51	–38.59 ± 28.51	–35.90 ± 28.05
	Placebo	–5.70 ± 26.20	–9.70 ± 26.85	N/A	N/A
Overall level of spinal pain	SEC 150 mg	–2.32 ± 2.39	–2.54 ± 2.55	–3.55 ± 2.43	–3.07 ± 2.52
	Placebo	–1.05 ± 1.89	–1.28 ± 2.36	N/A	N/A
Morning stiffness					
Overall level	SEC 150 mg	–2.24 ± 2.62	–2.46 ± 2.91	–3.57 ± 2.76	–3.32 ± 2.88
	Placebo	–0.96 ± 2.31	–0.86 ± 2.28	N/A	N/A
Physical function					
SF-36 PCS	SEC 150 mg	5.30 ± 6.86	6.93 ± 7.10	8.89 ± 8.0	8.15 ± 8.48
	Placebo	2.56 ± 4.98	2.02 ± 6.04	N/A	N/A
Fatigue					
Overall level	SEC 150 mg	–1.77 ± 2.43	–2.12 ± 2.38	–3.42 ± 2.44	–3.08 ± 2.38
	Placebo	–0.99 ± 1.92	–1.12 ± 2.05	N/A	N/A
FACIT-Fatigue	SEC 150 mg	6.39 ± 8.93	9.35 ± 9.56	11.18 ± 9.96	11.09 ± 10.42
	Placebo	2.02 ± 7.06	3.65 ± 8.30	N/A	N/A

Observed data are presented through Wk 208; SEC 150 mg, N = 72 and placebo, N = 74
n = 71, 67, 59, and 57 pts with a value at both baseline and Wks 4, 16, 104, and 208, respectively, in the SEC 150 mg group; n = 70 and 64 pts with a value at both baseline and Wks 4 and 16, respectively, in the placebo group; N/A, not applicable; N, number of randomized pts; n, number of evaluable pts; SD, standard deviation; SEC, secukinumab; Wk, week

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Abstract Number: 1505

Persistence with Etanercept in Patients with Ankylosing Spondylitis or Psoriatic Arthritis in Germany: A Real-World Analysis

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Background/Purpose: Ankylosing spondylitis (AS) and psoriatic arthritis (PsA) treatment includes biologics, prescribed on a long-term basis. As persistence data from real-world practice are limited, the current study analyzes persistence with etanercept treatment for up to 5 years in AS or PsA patients in Germany.

Methods: Patients diagnosed with AS or PsA with a first etanercept bio-original (ETNBo) prescription recorded between 1 January 2008 and 31 December 2012 were retrospectively identified in German Statutory health insurance claims data (ICD-10 code M45 and L40.5, respectively) and followed until 31 December 2015 or until the end of their record. The index date was defined as the first ETNBo prescription after an etanercept-free period of ≥12 months.

Treatment persistence was estimated as days between index date and discontinuation, defined as a gap of ≥90 days after last etanercept prescription. Analyses were also stratified by whether or not the patients were bio-naive, i.e. having no record of initiating a biologic in the 12 months before index. Persistence was evaluated using Kaplan-Meier analysis. Differences between strata were compared using a log-rank test.

Results: We identified 340 patients diagnosed with AS (mean age at index: 44 years [SD 12], 64% male) and 415 with PsA (49 years [SD 12], 51% male). Most patients were considered bio-naïve (AS: 72%; PsA: 73%).

The median etanercept persistence for AS was 14 months (95%CI: 10–17; IQR: 5–40) and for PsA 13 months (95%CI: 11–17; IQR: 4–43). Persistence for AS ranged from 52% (95%CI: 47%–57%) at 1 year to 16% (95%CI: 12%–20%) at 5 years, and for PsA from 51% (95%CI: 46%–55%) at 1 year to 18% (95%CI: 14%–22%) at 5 years.

For AS, the median etanercept persistence was similar between bio-naïve patients (14 months [95%CI: 10–19) and those with biologic use in the 12 months prior to etanercept (13 months [95%CI: 8–18]) (log-rank test, p-value=0.528). For PsA, median persistence in bio-naïve patients was 15 months (95%CI: 11–19) versus those receiving a biologic in the 12 months pre-index (9 months [95%CI: 5–13]) (log-rank test, p-value=0.065).

Conclusion: This is one of the longest analyses on the real-world persistence of a biologic in AS and PsA. Among new etanercept users in AS and PsA, a quarter of patients were persistent with etanercept for more than 40 months. These results are similar to recent reports from analysis of US claims data[1,2]; however future research should explore clinical factors influencing persistence over such long time periods.

Disease cohort	Stratification	Estimates	1-year	2-year	3-year	4-year	5-year	Median
AS	-	**Persistence**	**0.52**	**0.34**	**0.27**	**0.19**	**0.16**	**14.0**
		95% CI	0.47-0.57	0.29-0.39	0.22-0.32	0.15-0.24	0.12-0.20	10.0-17.0
AS	Prior biologic*	**Persistence**	**0.52**	**0.32**	**0.25**	**0.17**	**0.15**	**13.0**
		95% CI	0.41-0.61	0.23-0.41	0.17-0.34	0.10-0.25	0.08-0.24	8.0-18.0
AS	No prior biologic*	**Persistence**	**0.52**	**0.35**	**0.27**	**0.20**	**0.16**	**14.0**
		95% CI	0.46-0.58	0.29-0.42	0.22-0.33	0.15-0.26	0.11-0.22	10.0-19.0
PSA	-	**Persistence**	**0.51**	**0.37**	**0.30**	**0.22**	**0.18**	**13.0**
		95% CI	0.46-0.55	0.32-0.42	0.25-0.34	0.18-0.26	0.14-0.22	11.0-17.0
PSA	Prior biologic*	**Persistence**	**0.42**	**0.31**	**0.25**	**0.17**	**0.16**	**9.0**
		95% CI	0.33-0.51	0.23-0.40	0.18-0.34	0.10-0.25	0.09-0.24	5.0-13.0
PSA	No prior biologic*	**Persistence**	**0.54**	**0.39**	**0.31**	**0.23**	**0.19**	**15.0**
		95% CI	0.48-0.59	0.34-0.45	0.26-0.37	0.19-0.28	0.15-0.24	11.0-19.0

* In the 12-month period pre-index

Table 1: Yearly Proportion of Etanercept Persistence and Median Persistence (Months)

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Abstract Number: 1506

Long-Term Certolizumab Pegol Treatment of Axial Spondyloarthritis Is Associated with Rapid and Sustained Reduction of Active Inflammation and Minimal Structural Changes in the Spine: 4-Year MRI Results

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammation of the spine is believed to trigger a repair mechanism that results in syndesmophyte formation in axial spondyloarthritis (axSpA) patients (pts).[1] Bone marrow fatty lesions (FLs) and axial skel-

Table: A) Counts of inflammatory lesions, fatty lesions, sclerosis and erosions at the patient-level [a] through 204 wks' CZP treatment (MMRM estimates)

Least Squares Mean (SE)	Week				
	0	12	48	96	204
Inflammatory lesion count	**4.9 (0.5)**	**2.8 (0.4)**	**2.5 (0.3)**	**2.7 (0.3)**	**2.8 (0.4)**
Patients observed, n	89	88	68	70	55
Fatty lesion count	**6.9 (0.7)**	**7.3 (0.7)**	**7.3 (0.8)**	**7.5 (0.8)**	**7.4 (0.8)**
Patients observed, n	89	88	69	69	55
Sclerosis count	**0.1 (0.1)**	**0.1 (0.1)**	**0.1 (0.1)**	**0.1 (0.1)**	**0.1 (0.1)**
Patients observed, n	89	88	69	69	55
Erosion count	**0.0 (0.0)**	**0.0 (0.0)**	**0.0 (0.0)**	**0.0 (0.0)**	**0.0 (0.0)**
Patients observed, n	89	88	69	69	55

B) Presence/absence of fatty lesions in vertebral edges [b] through 204 wks' CZP treatment by baseline MRI lesion type (observed cases)

% of VEs observed [c]		Week							
		12		48		96		204	
		FL+	FL−	FL+	FL−	FL+	FL−	FL+	FL−
FL−INFL+ at baseline n=346	VEs observed, n	338		243		278		205	
	INFL+	**8.9**	**39.3**	**9.1**	**26.3**	**9.4**	**18.3**	**11.2**	**20.5**
	INFL−	**13.0**	**38.8**	**14.0**	**50.6**	**22.3**	**50.0**	**22.4**	**45.9**
	New FLs, n [d]	74	–	56	–	88	–	69	–
FL−INFL− at baseline n=1866	VEs observed, n	1797		1429		1418		1018	
	INFL+	**0.2**	**4.2**	**0.5**	**5.3**	**0.5**	**4.2**	**0.4**	**5.2**
	INFL−	**4.7**	**90.9**	**6.3**	**87.9**	**7.1**	**88.2**	**6.9**	**87.5**
	New FLs, n [d]	89	–	97	–	107	–	74	–
FL+INFL+ at baseline n=329	VEs observed, n	326		220		293		220	
	INFL+	**42.9**	**4.9**	**34.5**	**4.5**	**31.1**	**1.4**	**30.9**	**1.8**
	INFL−	**46.9**	**5.2**	**57.3**	**3.6**	**61.4**	**6.1**	**60.5**	**6.8**
FL+INFL− at baseline n=586	VEs observed, n	575		424		494		337	
	INFL+	**10.6**	**0.9**	**6.1**	**1.2**	**7.3**	**1.4**	**7.4**	**1.2**
	INFL−	**76.7**	**11.8**	**78.8**	**13.9**	**78.1**	**13.2**	**75.1**	**16.3**

MRI Set. [a] Wk 0 CZP patients only. [b] All CZP-treated patients, including those switching from PBO to CZP treatment at Wks 16/24. [c] Unless stated otherwise. [d] The number of observed VEs FL− at BL recorded as FL+. BL: Baseline; CZP: certolizumab pegol; INFL: inflammatory lesion; MMRM: mixed model repeated measures; PBO: placebo; SE: standard error; VE: vertebral edge; wk: week.

eton erosions, visible on MRI T1 sequences, are post-inflammatory changes that contribute significantly to models predicting new bone formation.[2] It has previously been assumed that resolution of inflammatory lesions (INFLs) in anti-TNF treated axSpA pts may be associated with an increase in FLs.[3,4] RAPID-axSpA was a long-term study in pts with radiographic (r)-axSpA / ankylosing spondylitis or non-radiographic (nr)-axSpA treated with certolizumab pegol (CZP), which rapidly suppressed active inflammation of the spine, with pts showing limited spinal radiographic progression over 4 years.[5] Here, the incidence and association of active inflammation and chronic lesions (FLs, sclerosis, and erosions) in the spine of CZP treated axSpA pts over 4 years is reported.

Methods: RAPID-axSpA (NCT01087762) was double-blind and placebo (PBO)-controlled to Week (Wk) 24, dose-blind to Wk 48, and open-label to Wk 204. Baseline (BL) CZP-randomized pts (200 mg every 2 weeks [Q2W] or 400 mg Q4W) continued their assigned dose throughout; BL PBO-randomized pts received CZP from Wk 16 (non-responders) or Wk 24. Blinded spinal MRI scans at BL, Wk 12, 48, 96, and 204 were assessed by 2 central readers to evaluate the presence/absence of active INFLs (Short Tau Inversion Recovery [STIR] sequence), FLs, sclerosis and erosions (T1 sequence) in vertebral edges (VEs) (present if recorded so by both readers). AxSpA pts with a valid BL and ≥1 post-BL assessment were included. Mean pt level lesion counts were estimated from mixed models with repeated measures (MMRM) fitted on observed data from CZP or PBO pts. Associations between INFLs and FLs at the VE level for all pts were described using cross-tabulations.

Results: Of 325 randomized pts, 136 were eligible for these analyses. In BL CZP pts (n=89), active INFLs were reduced, and FL counts only slightly increased by Wk 12; both were sustained at a low level to Wk 204 (**Table A**). Very few VEs with erosions and sclerosis were observed at BL, and no changes in their frequency were observed to Wk 204 (**Table A**). Over 204 wks, the risk of developing new FLs was greater in VEs with vs without INFLs at BL, regardless of changes to INFLs in these VEs post-BL (**Table B**). At BL the prevalence of FLs was greater in pts with >3 vs ≤3 years' disease duration and more new FLs developed in pts with >3 years disease duration (data not shown).

Conclusion: Long-term CZP treatment in axSpA pts was associated with rapid and sustained reduction in active inflammation, no increase in sclerosis and erosions, and a negligible increase in FLs in VEs over 4 years. More FLs developed in VEs in pts with >3 years disease duration and with INFLs at BL than without, which was not affected by resolution of INFLs, providing evidence of the importance of early treatment in pts with active axSpA.

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Abstract Number: 1507

Certolizumab Pegol Improves Work and Household Productivity and Social Participation over 1 Year of Treatment in Patients with Non-Radiographic Axial Spondyloarthritis

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Table: Workplace and household productivity over 52 wks in patients with nr-axSpA from the C-axSpAnd trial (Full Analysis Set)

WPS responses:	Baseline		Wk 12		Wk 52 [a]			
Mean, median	PBO + NBBM	CZP + NBBM	PBO + NBBM	CZP + NBBM	PBO + NBBM		CZP + NBBM	
Imputation	LOCF	LOCF	LOCF	LOCF	LOCF	OC	LOCF	OC
Productivity in the workplace (employed patients) [b]								
N	123	124	122	129	124	46	132	100
Work days missed due to arthritis in the previous month	**3.5**, 0.0	**3.7**, 0.0	**2.1**, 0.0	**0.9**, 0.0	**2.0**, 0.0	**0.7**, 0.0	**0.3**, 0.0	**0.1**, 0.0
Days with work productivity reduced by ≥50% due to arthritis in the previous month [c]	**6.0**, 3.0	**6.5**, 3.0	**5.5**, 2.0	**1.9**, 0.0	**5.5**, 2.0	**3.0**, 0.0	**0.9**, 0.0	**0.6**, 0.0
Level of arthritis interference with work productivity [d]	**4.9**, 5.0	**4.6**, 5.0	**4.2**, 4.0	**2.4**, 2.0	**4.1**, 4.0	**2.4**, 1.0	**1.5**, 0.0	**0.9**, 0.0
Household productivity and social participation (all patients)								
N	157	159	158	159	158	52	159	120
Household work days missed due to arthritis in the previous month	**5.6**, 3.0	**6.2**, 3.0	**4.5**, 2.0	**2.6**, 0.0	**4.3**, 1.0	**1.9**, 0.0	**2.0**, 0.0	**1.0**, 0.0
Household work days with productivity reduced by ≥50% due to arthritis in the previous month [c]	**8.0**, 5.0	**8.0**, 5.0	**6.9**, 4.0	**3.6**, 0.0	**6.9**, 4.0	**3.1**, 0.0	**3.0**, 0.0	**1.4**, 0.0
Level of arthritis interference with household productivity [d]	**5.0**, 5.0	**4.9**, 5.0	**4.0**, 4.0	**2.5**, 2.0	**3.9**, 4.0	**2.5**, 2.0	**1.9**, 0.0	**1.1**, 0.0
Days missed family/social/leisure activities due to arthritis per month	**3.9**,1.0	**4.2**, 1.0	**2.7**, 0.0	**1.6**, 0.0	**2.5**, 0.0	**0.6**, 0.0	**1.4**, 0.0	**0.5**, 0.0

[a] Due to the large proportion (66%) of PBO pts switching to open-label CZP treatment, both LOCF and OC data are presented for Wk 52; [b] Based only on employed patients at each visit; [c] Does not include work days missed counted in previous question; [d] 0-10 scale, 0=no interference, 10=complete interference. CZP: certolizumab pegol 200 mg Q2W; LOCF: last observed carried forward; OC: observed case; NBBM: non-biologic background medication; PBO: placebo; wk: week; WPS: Work Productivity Survey

Background/Purpose: Patients (pts) with non-radiographic axial spondyloarthritis (nr-axSpA) report substantial impairment of productivity and daily activities due to the burden of their disease, similar to pts with ankylosing spondylitis.[1,2] Certolizumab pegol (CZP) treatment has been shown to significantly improve work and household productivity and social participation compared to placebo (PBO) in active nr-axSpA pts up to 24 weeks (wks).[1] Improvements were maintained over 4 years of CZP treatment in RAPID-axSpA.[3] The C-axSpAnd study demonstrated the impact of CZP in combination with non-biologic background medication (NBBM) on signs and symptoms of nr-axSpA compared to PBO + NBBM.[4] Here, we report work and household productivity and social participation from C-axSpAnd.

Methods: C-axSpAnd (NCT02552212) is a 3-year, phase 3, multicenter study including a 52 wk double-blind, PBO-controlled period (completed). Pts had active nr-axSpA, objective signs of inflammation (elevated CRP and/or positive MRI of the sacroiliac joint), and previous inadequate response to ≥2 NSAIDs and were randomized 1:1 to CZP (400 mg at Wks 0, 2, and 4, then 200 mg every 2 wks) + NBBM or PBO + NBBM. The validated arthritis-specific Work Productivity Survey (WPS) assessed the impact of nr-axSpA on work and household productivity and social participation.[5] Missing data were imputed using last observation carried forward (LOCF) post hoc in the Full Analysis Set (FAS, all randomized pts who received ≥1 dose of study medication).

Results: 317 pts were randomized (CZP + NBBM: 159; PBO + NBBM: 158). Mean age at baseline (BL) was 37.3 years and 51.4% of pts were female. At BL, the majority of pts (CZP + NBBM: 124 [77.8%]; PBO + NBBM: 123 [78.0%] pts)

were employed and reported a mean 3.7 (CZP + NBBM) and 3.5 (PBO + NBBM) work days missed per month due to their disease (**Table**). By Wk 12, work absenteeism substantially improved in the CZP + NBBM group compared with the PBO + NBBM group (0.9 vs 2.1 days missed per month, LOCF), with further improvements at Wk 52 (0.3 vs 2.0 days missed per month, LOCF). Between Wk 12 and Wk 52, a majority of PBO pts (104 [65.8%]) switched to open-label CZP, impacting imputed outcomes at Wk 52. Despite this, similar patterns of improvement following CZP + NBBM treatment were seen for absenteeism, work days with impaired productivity, household days with missed/reduced productivity and social participation between imputed and observed case data (**Table**). Improvements were similar between male and female pts (data not shown).

Conclusion: CZP treatment resulted in improvements in work and household productivity and social participation for nr-axSpA pts as early as Wk 12 compared to background medication only, with benefits maintained to Wk 52.

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Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8; **M. Rudwaleit**, Abbott, 5, AbbVie, 5, 8, BMS, 5, 8, Bristol Myers-Squibb, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Eli Lilly, 5, 8, Eli Lily, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB Pharma, 5, 8; **S. Hall**, AbbVie, 2, 5, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, UCB Pharma, 2, 5; **L. Bauer**, UCB Pharma, 3; **B. Hoepken**, UCB Pharma, 3; **N. de Peyrecave**, UCB Pharma, 3; **T. Kumke**, UCB Pharma, 3; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5.

Abstract Number: 1508

Certolizumab Pegol-Treated Patients with Non-Radiographic Axial Spondyloarthritis Demonstrate Improvements in Sleep Quality and Other Patient Reported Outcomes

Lianne Gensler,[1] Jonathan Kay,[2] Walter P. Maksymowych,[3] Nigil Haroon,[4] Lars Bauer,[5] Bengt Hoepken,[5] Natasha de Peyrecave,[6] Thomas Kumke,[7] and **Atul Deodhar**[8], [1]University San Francisco California, San Francisco, CA, [2]UMass Memorial Medical Center and University of Massachusetts Medical School, Worcester, MA, [3]University of Alberta/ CARE ARTHRITIS, Edmonton, AB, Canada, [4]Toronto Western Hospital, Krembil Research Institute, University of Toronto, Toronto, ON, Canada, [5]UCB Pharma, Monheim am Rhein, Germany, [6]UCB Pharma, Slough, United Kingdom, [7]UCB Pharma, Monheim, Germany, [8]Oregon Health & Science University, Portland, OR

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Pain, fatigue, morning stiffness and impaired sleep are some of the main symptoms contributing to reduced quality of life (QoL) in patients (pts) with non-radiographic axial spondyloarthritis (nr-axSpA).[1] Additionally, pts who are poor sleepers have been shown to have higher disease activity, fatigue scores and nocturnal back pain.[2] Certolizumab pegol (CZP) treatment has demonstrated improvements in multiple manifestations of nr-axSpA disease, including pt-reported outcomes (PROs) and QoL.[3,4] We report PROs for nr-axSpA pts treated with CZP or placebo (PBO) from the C-axSpAnd study – the first 52-week (Wk) PBO-controlled study to investigate the efficacy of an anti-TNF agent in a population with active nr-axSpA and objective signs of inflammation (elevated CRP and/or MRI positive).

Table: Clinical PROs in nr-axSpA patients treated with PBO or CZP

Mean (SD)	Baseline		Wk 12		Wk 48			
	PBO	CZP	PBO LOCF	CZP LOCF	PBO LOCF	CZP LOCF	PBO OC	CZP OC
	(n=158)	(n=159)	(n=158)	(n=159)	(n=158)	(n=159)	(n=52)	(n=124)
MOS Sleep Scale: Sleep Problems Index I [a]	39.5 (8.5)	41.3 (9.7)	42.2 (9.2)	46.0* (9.1)	41.3 (8.5)	47.1** (9.3)	46.0 (8.3)	48.8 (8.2)
MOS Sleep Scale: Sleep Problems Index II [a]	39.2 (8.6)	41.4 (9.6)	42.0 (9.1)	46.2** (9.1)	41.1 (8.5)	47.5** (9.3)	45.8 (8.1)	49.2* (8.3)
	Baseline		**Wk 12**		**Wk 52**			
	PBO	CZP	PBO LOCF	CZP LOCF	PBO LOCF	CZP LOCF	PBO OC	CZP OC
	(n=158)	(n=159)	(n=158)	(n=159)	(n=158)	(n=159)	(n=51)	(n=121)
Nocturnal spinal pain NRS	6.6 (2.1)	6.6 (2.3)	5.6 (2.6)	3.4** (2.7)	5.4 (2.8)	2.7** (2.7)	3.5 (2.4)	2.0** (2.1)
BASDAI: Fatigue [b]	7.2 (1.4)	7.1 (1.6)	6.1 (2.2)	4.4** (2.4)	5.9 (2.3)	3.7** (2.7)	4.0 (2.0)	3.1* (2.3)
BASDAI: Morning stiffness [c]	6.7 (1.8)	6.9 (1.8)	5.5 (2.4)	3.6** (2.4)	5.2 (2.6)	2.9** (2.4)	3.2 (1.9)	2.3* (2.1)

[a] Final assessments for Sleep Problems Index I and II were conducted at Wk 48 - a higher score indicates improved sleep; [b] BASDAI Q1; [c] Average of BASDAI Q5+Q6. For LOCF, if there were missing data at the time point of interest, the last available double-blind post baseline measurement was carried forward to that time point. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CZP: certolizumab pegol; LOCF: last observation carried forward; nr-axSpA: non-radiographic axial spondyloarthritis; NRS: numerical rating scale; MOS: Medical Outcomes Study; OC: observed case; PBO: placebo; PRO: patient-reported outcome; SD: standard deviation; Wk: week. P-values (for CZP vs PBO mean change from baseline at Wk 12 and Wk 52) of <0.05 or <0.001 are denoted by * and **, respectively, and were derived from an ANCOVA model where response (dependent variable) is the change from baseline, with baseline score as a fixed-effect covariate and treatment group, region, and MRI/CRP classification as fixed effect categorical factors (independent variables).

Methods: C-axSpAnd (NCT02552212) is a 3-year, phase 3, multicenter study including a 52-Wk double-blind (DB), PBO-controlled period (completed); patients who had an inadequate response to ≥2 non-steroidal anti-inflammatory drugs were randomized 1:1 to PBO or CZP (400 mg at Wks 0/2/4, then 200 mg every 2 wks).[3] Clinical PROs collected included: Sleep Problems Index scores I (6 items) and II (9 items) from the Medical Outcomes Study Sleep Scale (which assesses sleep disturbance, adequacy, somnolence, quantity, snoring, and awakening short of breath or with a headache),[5] nocturnal spinal pain (numerical rating scale [NRS]), fatigue (BASDAI Q1), and morning stiffness (average of BASDAI Q5 and Q6). Post-hoc analyses of minimal clinically important differences (MCID [≥1-point improvement]) for fatigue and nocturnal spinal pain were conducted.[6] Variables were analyzed using an ANCOVA model including baseline score as a covariate and fixed effects for treatment group, region and MRI/CRP classification. All p-values were nominal. Missing values or data at time points following the discontinuation of the DB study treatment were imputed using last observation carried forward.

Results: 317 pts with nr-axSpA were randomized to CZP (n=159) or PBO (n=158); 54 (34%) and 125 (79%) patients treated with PBO or CZP, respectively, completed Wk 52. Pts treated with CZP showed greater improvements (indicated by higher scores) in Sleep Problems Index II scores vs PBO-treated pts at Wk 12 (mean change from baseline: 4.8 [CZP] vs 2.2 [PBO]; p< 0.001). Improvements were also seen in other clinical PROs (**Table**). By Wk 12, greater proportions of pts treated with CZP vs PBO experienced at least a MCID response in fatigue (85.4% vs 57.6%, respectively) and nocturnal spinal pain (82.8% vs 58.9%, respectively); results were sustained through Wk 52.

Conclusion: Nr-axSpA patients treated with CZP showed substantial improvements in sleep quality and other clinical outcomes important to patients; future analyses of these data will explore associations between sleep quality and other clinical PROs.

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Impact of Age and Disease Duration on the Response to IL-17A Inhibitor (Secukinumab) Treatment in Ankylosing Spondylitis: Pooled Results from the Phase 3 MEASURE Studies

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SESSION INFORMATION

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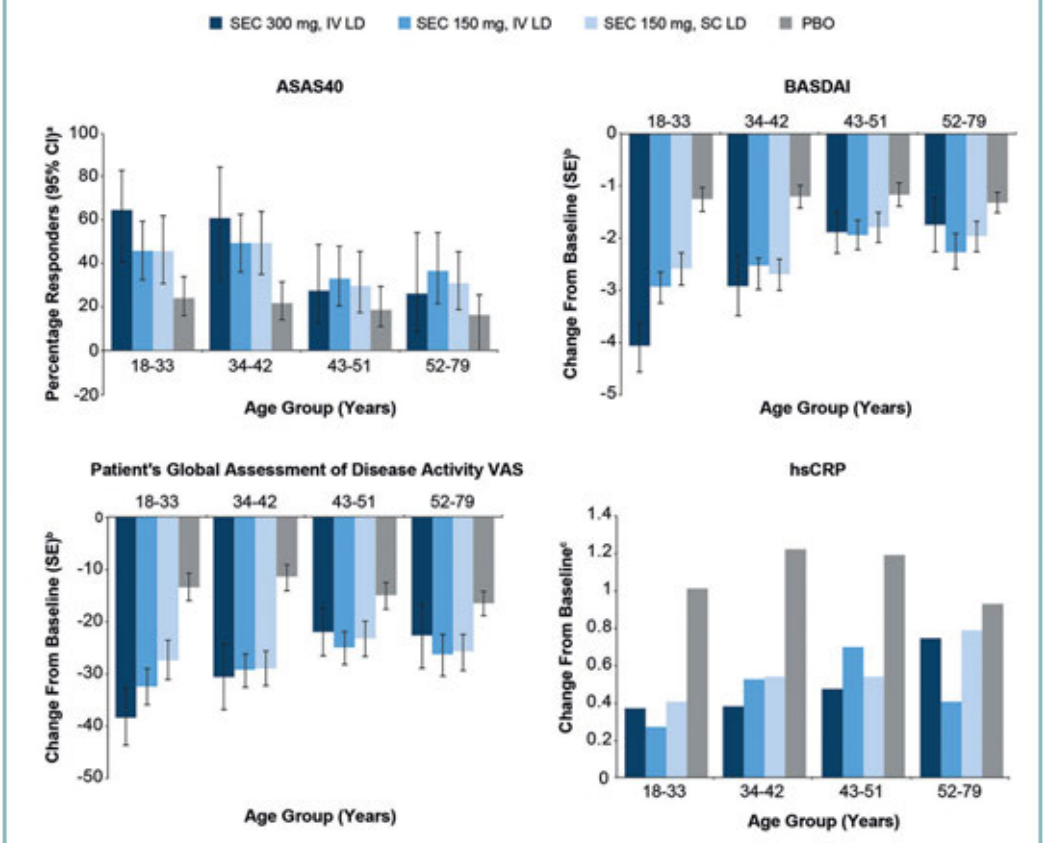
Background/Purpose: Ankylosing spondylitis (AS), a chronic inflammatory disease involving the sacroiliac joints and spine, is associated with pain, stiffness, disability, and reduced quality of life.[1,2] Therefore, prompt diagnosis and treatment of patients (pts) is critical. In this post hoc analysis, we assessed the impact of age and disease duration (DD; defined as time since diagnosis) on responses in pts with AS treated with secukinumab (SEC) or placebo (PBO) in the phase 3 MEASURE trials.

Table 1. Baseline Characteristics by Age Group of Patients Included From the Phase 3 MEASURE Studies

	Secukinumab 300 mg, IV LD (n = 76)	Secukinumab 150 mg, IV LD (n = 199)	Secukinumab 150 mg, SC LD (n = 188)	Placebo (n = 389)
Study				
MEASURE 1		125		122
MEASURE 2			72	74
MEASURE 3	76	74		76
MEASURE 4			116	117
Total	76	199	188	389
Age range, years				
Age, mean (SD), years				
18-33	27.0 (3.6)	27.4 (4.0)	28.5 (3.8)	28.1 (3.8)
34-42	38.6 (2.6)	37.9 (2.7)	38.1 (2.5)	38.1 (2.5)
43-51	46.7 (2.9)	46.6 (2.5)	47.5 (2.5)	47.1 (2.5)
52-79	58.2 (6.2)	58.7 (5.0)	59.0 (5.6)	59.1 (5.9)
Time since first diagnosis of AS, mean (SD)				
18-33	2.2 (2.9)	3.9 (3.4)	2.6 (2.9)	3.3 (3.5)
34-42	2.9 (3.6)	4.4 (4.8)	6.2 (7.2)	5.5 (5.7)
43-51	6.4 (8.1)	8.3 (7.6)	10.3 (10.3)	8.3 (8.3)
52-79	10.2 (10.1)	10.1 (10.2)	12.6 (13.0)	11.2 (12.0)
No prior anti-TNF therapies, n (%)				
18-33	17 (81.0)	44 (81.5)	31 (68.9)	71 (71.7)
34-42	11 (78.6)	40 (69.0)	34 (69.4)	81 (81.8)
43-51	22 (84.6)	39 (78.0)	27 (60.0)	60 (69.8)
52-79	7 (46.7)	26 (70.3)	37 (75.5)	64 (61.0)
Methotrexate use at randomization, n (%)				
18-33	1 (4.8)	6 (11.1)	6 (13.3)	11 (11.1)
34-42	2 (14.3)	7 (12.1)	2 (4.1)	8 (8.1)
43-51	4 (15.4)	6 (12.0)	4 (8.9)	9 (10.5)
52-79	6 (40.0)	8 (21.6)	6 (12.2)	13 (12.4)
Disease scores, mean (SD)				
Patient's global assessment of disease activity (0-100 mm)				
18-33	66.9 (18.4)	64.6 (19.3)	67.4 (17.6)	70.1 (16.7)
34-42	71.6 (17.9)	65.1 (19.8)	72.9 (15.3)	69.8 (16.0)
43-51	74.2 (12.8)	68.0 (18.4)	74.4 (15.9)	70.5 (16.4)
52-79	80.8 (16.3)	72.4 (14.5)	69.9 (14.7)	71.4 (17.4)
hsCRP, mg/L				
18-33	12.0 (17.0)	16.8 (21.1)	21.7 (34.9)	16.0 (19.4)
34-42	13.4 (15.9)	16.9 (23.4)	16.5 (33.8)	15.2 (23.6)
43-51	8.4 (6.5)	11.6 (13.6)	18.3 (46.4)	15.1 (19.5)
52-79	12.2 (14.8)	22.4 (27.7)	12.6 (20.3)	12.0 (15.4)
BASDAI				
18-33	6.9 (1.2)	6.4 (1.7)	6.6 (1.5)	6.8 (1.4)
34-42	7.1 (1.3)	6.5 (1.5)	7.0 (1.4)	6.9 (1.4)
43-51	6.9 (1.4)	6.6 (1.4)	7.1 (1.3)	6.6 (1.3)
52-79	7.1 (1.7)	6.9 (1.5)	6.7 (1.2)	6.9 (1.3)

AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; hsCRP, high-sensitivity C-reactive protein; IV, intravenous; LD, loading dose; SC, subcutaneous; SD, standard deviation; TNF, tumor necrosis factor.

Figure 1. Response Between Different Age Groups in ASAS40, BASDAI, Patient's Global Assessment of Disease Activity VAS, and hsCRP at Wk 16

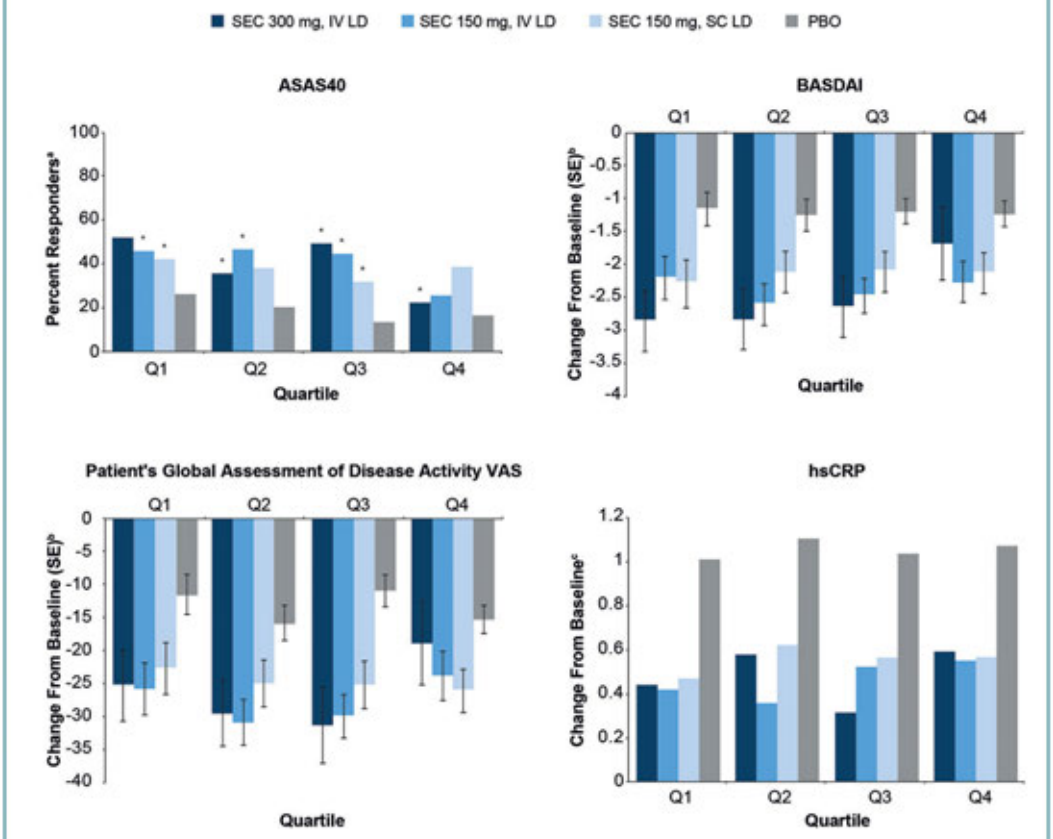


ASAS, Assessment in Ankylosing Spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CI, confidence interval; hsCRP, high-sensitivity C-reactive protein; IV, intravenous; LD, loading dose; LSM, least squares mean; MMRM, mixed-model repeated-measures; PBO, placebo; SC, subcutaneous; SE, standard error; SEC, secukinumab; VAS, visual analogue scale.
[a] Observed data. Full analysis set. [b] MMRM analysis. Within group differences. Full anaysis set. [c] MMRM analysis. Within group differences. Full analysis set. Exponentially transformed LSM, geometric mean ratio of post-baseline/baseline. A value <1 indicates a reduced CRP.

Methods: Pts with active AS from MEASURE 1 (M1; NCT01358175), 2 (M2; NCT01649375), 3 (M3; NCT02008916), and 4 (M4; NCT02159053) randomized controlled trials (RCTs) were included.[3-8] Pts received subcutaneous (SC) SEC 300 or 150 mg with an intravenous (IV) loading dose (M1, M3), SEC 150 mg with an SC loading dose (M2, M4), or PBO (M1-4). Pooled data from different RCTs (IV or SC loading) may be considered heterogeneous and are generalizable to a wider patient population. Data were pooled from M1-4 at the end of the 16-wk treatment period, and responses were analyzed according to 4 age groups: 18-33, 34-42, 43-51, and 52-79 y. Responses were assessed using outcome measures such as ASAS20/40, BASDAI, BASMI, hsCRP, SF-36 (PCS/MCS), and disease activity/back pain instruments. Similar analyses assessed treatment responses by quartiles of time since diagnosis (0-0.97 y [Q1], 0.98-3.47 y [Q2], 3.49-9.79 y [Q3], and 9.88-50.19 y [Q4]). Time since diagnosis was used as a surrogate marker of DD as symptom duration was not collected. No adjustment was made for multiple comparisons.

Results: 852 pts were included in this analysis (SEC, n = 463; PBO, n = 389) (Table 1); 95.5% completed 16 wk of treatment. Baseline demographics were similar across trials (Table 1). Mean time since AS diagnosis differed across age groups: 3.2 y in the 18-33 group and 11.3 y in the 52-79 group. The proportion of TNF inhibitor–naive pts was higher in the 18-33 group vs the 52-79 group (74.4% vs 65.0%). At Wk 16, greater improvements in ASAS20/40, BASDAI, SF-36, hsCRP, and VAS disease activity/back pain scores were reported in younger (18-33 and 34-42) vs older age groups (43-51 and 52-79) treated with SEC (Fig. 1). When stratified by DD, there was a higher proportion of TNF inhibitor–naive pts in Q1 vs Q4 (92.0% vs 61.8%), and pts with a shorter DD (Q1-Q2) had greater improvements in ASAS40; reductions in hsCRP levels were greatest in Q1 pts (Fig. 2).

Figure 2. Differences in Response Between Disease Duration Groups in ASAS40, BASDAI, Patient's Global Assessment of Disease Activity VAS, and hsCRP Scores at Wk 16



ASAS, Assessment in Ankylosing Spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CI, confidence interval; hsCRP, high-sensitivity C-reactive protein; IV, intravenous; LD, loading dose; LSM, least squares mean; MMRM, mixed-model repeated-measures; PBO, placebo; SC, subcutaneous; SE, standard error; SEC, secukinumab; VAS, visual analogue scale.
[a] Nonresponder imputations. Full analysis set. * $P < .05$. [b] MMRM analysis. Within group differences. Full analysis set. [c] MMRM analysis. Within group differences. Full analysis set. Exponentially transformed LSM, geometric mean ration of post-baseline/baseline. A value < 1 indicates a reduced CRP.

Conclusion: SEC treatment led to rapid and sustained improvements in all outcome measures at Wk 16, regardless of age or DD. Older pts reported greater burden of disease. A trend toward higher responses was evident in those with shorter DD. Younger pts had better responses, likely due to shorter DD and a higher proportion being biologic naive. These results emphasize the importance of early AS treatment to delay disease progression and improve pt outcomes.

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Lilly, GSK, Galapagos, Janssen, Novartis, Pfizer and UCB, 5, AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Glaxo Smith and Klein, Janssen, Novartis, Pfizer, UCB, 5, Amgen, 5, 8, 9, BMS, 2, 5, 8, BMS, Eli Lilly, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, 2, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, UCB Pharma, 2, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, 8, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, 9, Eli Lilly and Company, 2, 5, Eli Lilly,, 5, Eli Lilly, GSK, Novartis, Pfizer and UCB, 2, Galagagos, 5, Galapagos, 5, 8, 9, Glaxo Smith & Klein, 2, Glaxo Smith & Kline, 2, 5, 8, Glaxo Smith Klein, 5, Glaxo SmithKlein, 2, 5, GlaxoSmithKlein, 2, 5, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, Janssen, 2, 5, 8, 9, Janssen Pharmaceutica, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9; **P. Mease**, Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, Roche, UCB, 2, 5, Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB, 8, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Abbvie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer and UCB., 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB, 2, Abbvie, Amgen, Brsitol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Brsitol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Brsitol Myers Squibb,Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, Amgen, 2, 5, 6, 8, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, and UCB, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 2, 5, Boerhinger Ingelheim, 5, Bristol Myers Squibb, 2, 5, 8, Bristol Myers Squibb Co., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8, Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8; **P. Machado**, Novartis, 1, 3, 4; **X. Meng**, Novartis, 3, 4; **V. Strand**, Abbvie, 5, AbbVie, 5, Amgen, 5, Amgen, Abbvie, Bayer, BMS, Boehringer Ingelheim, Celltrion, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, UCB, 5, AstraZeneca, 5, AURA, 8, Bayer, 5, BMS, 5, Boehringer Ingelheim, 5, Celgene, 5, Celltrion, 5, Cleveland Clinic, 8, CORRONA, 5, Crescendo, 5, Crescendo Bioscience, 5, Eli Lilly, 5, EMD Serono, 5, Genentech, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Inmedix, 5, Janssen, 5, Kezar, 5, Lilly, 5, Merck, 5, NACCME, 8, Novartis, 5, Pfizer, 5, Purdue, 8, RA Forum, 8, RAN, 8, Regeneron, 5, Roche, 5, Samsung, 5, Sandoz, 5, Sanofi, 5, Servier, 5, Setpoint, 5, SLRA, 8, UCB, 5, Up to Date, 7, Washington University, 8, WIR, 8, WRA, 8; **M. Magrey**, AbbVie, 2, Abbvie, 2, Abbvie, UCB and Amgen, 2, Amgen, 2, 5, Eli Lilly, 5, Eli Lilly and Company, 5, Eli Lily, Novartis, 5, Novartis, 5, 9, UCB, 2, UCB Pharma, 2.

Abstract Number: 1510

Ixekizumab Improves Fatigue, Pain, and Sleep up to 52 Weeks in Patients with Radiographic Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (axSpA) is an inflammatory condition affecting sacroiliac joints and axial skeleton, characterized by fatigue, spinal pain, and sleep disturbances that negatively affect patient health-related quality of life.[1] Ixekizumab (IXE) has demonstrated efficacy in treatment of radiographic axial spondyloarthritis (r-axSpA) in both biologic disease-modifying antirheumatic drug (bDMARD) naïve and tumor necrosis factor inhibitor (TNFi) experienced patients.[2,3] The purpose of this analysis was to evaluate the impact of IXE on fatigue, spinal pain and sleep pattern in patients with r-axSpA over 52 weeks.

Methods: COAST-V and COAST-W were Phase 3 randomized controlled trials (RCTs) conducted to evaluate the efficacy and safety of IXE in bDMARD-naïve and TNFi-experienced patients with r-axSpA, respectively. In both RCTs, patients were randomized to receive IXE 80mg once every two weeks (IXEQ2W), IXE 80 mg once every 4 weeks (IXEQ4W), active reference arm (adalimumab 40 mg [ADAQ2W]) in COAST-V or placebo (PBO) up to Week 16. Patients initially randomized to IXE continued on the same regimen up to Week 52. Patients on PBO were re-randomized to either IXEQ2W or IXEQ4W at Week 16. After a washout period of 6 weeks, patients on ADA were switched to either IXEQ2W or IXEQ4W regimens and received their first IXE dose at Week 20. Fatigue Numeric Rating Scale (NRS) and Jenkins Sleep Evaluation Questionnaire (JSEQ) data were collected at baseline, Weeks 8, 16, 36 and 52. Patient global assessments of disease activity, spinal pain and spinal pain at night were collected at baseline and each post-baseline visit to Week 52. Mean changes from baseline up to Week 16 were analyzed using mixed effects model of repeated measures (MMRM). After Week 16, changes from baseline during extended treatment period were summarized as raw means after imputing the missing data using modified Baseline Observation Carried Forward (mBOCF).

Results: At Week 52, IXEQ2W and IXEQ4W treatments continued to improve fatigue, patient global assessment of disease activity, spinal pain and sleep in bDMARD-naive and TNFi-experienced patients (Table 1). Significant reductions in fatigue and spinal pain at night were reported as early as Week 8 and Week 1 respectively, in patients treated with IXE compared with PBO. Improvements in these parameters at Week 16 with both IXE arms were maintained up to Week 52 (Figure 1).

Conclusion: Fatigue, spinal pain, and sleep improved with IXE treatment over 52 weeks in both biologic-naïve and TNFi-experienced patients with r-axSpA.

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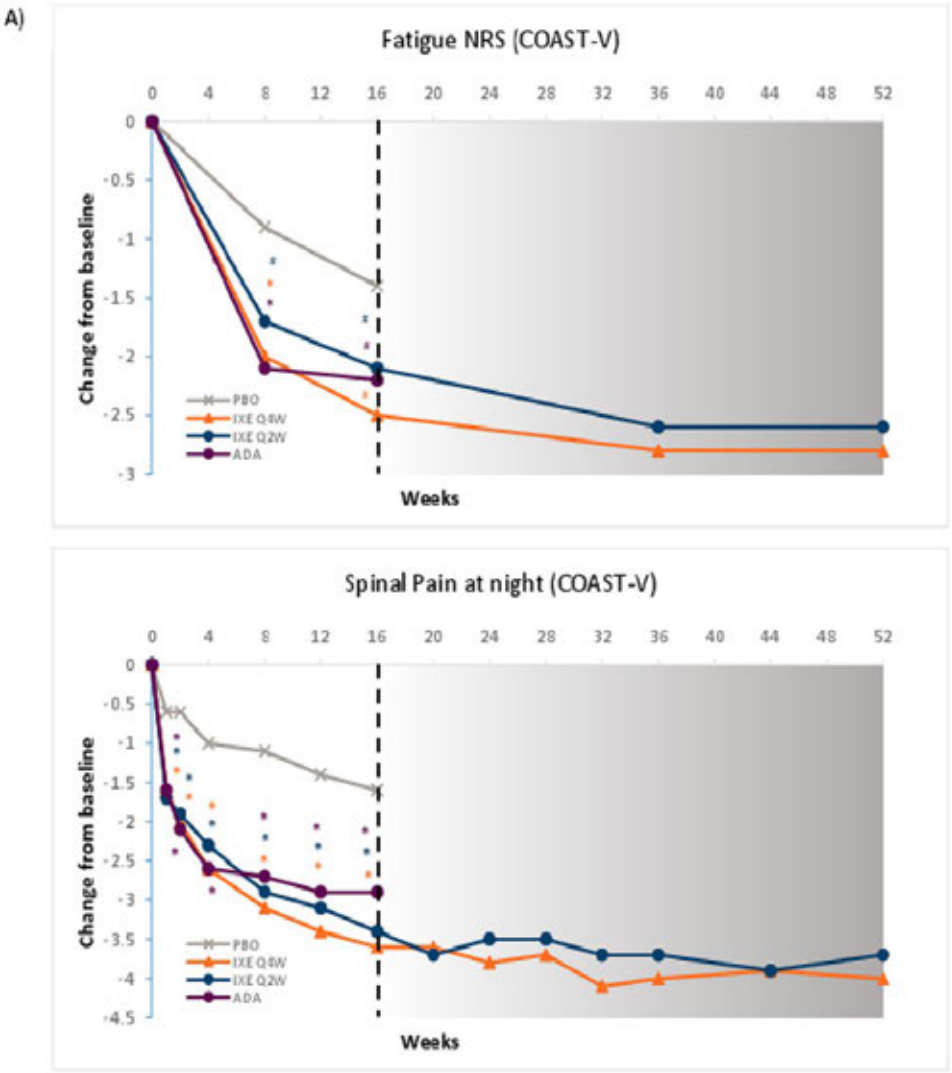
			Mean (Standard Deviation)			
Parameter	Study	Timepoint	IXEQ2W/ IXEQ2W	IXEQ4W/ IXEQ4W	ADA/IXE	PBO/IXE
Fatigue NRS 0 (no fatigue) to 10 (as bad as you can imagine)	COAST-V	Baseline	6.7 (1.7)	6.7 (1.7)	6.7 (1.7)	6.9 (1.7)
		Week 52	-2.6 (2.6)	-2.8 (2.7)	-2.7 (2.7)	-2.7 (2.4)
	COAST-W	Baseline	7.2 (2.0)	7.5 (1.7)	-	7.2 (1.6)
		Week 52	-2.0 (2.7)	-2.8 (2.5)	-	-2.3 (2.6)
Patient Global Assessment of Disease Activity; 0 (not active) to 10 (very active)	COAST-V	Baseline	7.1 (1.6)	6.9 (1.5)	7.1 (1.7)	7.1 (1.7)
		Week 52	-3.4 (2.5)	-3.2 (2.8)	-3.1 (2.7)	-3.1 (2.8)
	COAST-W	Baseline	7.8 (1.7)	7.9 (1.7)	-	7.9 (1.5)
		Week 52	-2.6 (2.8)	-3.0 (2.8)	-	-3.0 (3.0)
Spinal pain 0 (no pain) to 10 (most severe pain)	COAST-V	Baseline	7.2 (1.5)	7.2 (1.3)	7.0 (1.6)	7.4 (1.4)
		Week 52	-3.7 (2.5)	-3.8 (2.7)	-3.3 (2.5)	-3.2 (2.6)
	COAST-W	Baseline	7.8 (1.6)	7.9 (1.5)	-	7.8 (1.3)
		Week 52	-2.8 (2.7)	-3.1 (2.7)	-	-3.0 (2.9)
JSEQ 0 to 20 with higher scores indicating greater sleep disturbance	COAST-V	Baseline	8.7 (5.1)	7.1 (5.3)	8.5 (5.4)	8.4 (4.9)
		Week 52	-3.7 (4.6)	-2.2 (4.3)	-2.6 (5.3)	-2.7 (4.9)
	COAST-W	Baseline	10.4 (5.4)	9.9 (5.8)	-	10.3 (5.5)
		Week 52	-2.7 (5.5)	-3.8 (5.9)	-	-3.9 (5.8)

Values at Week 52 are changes from baseline in respective domain (mBOCF)

ADA, adalimumab; IXE, ixekizumab; JSEQ, Jenkins Sleep Evaluation Questionnaire; NRS, Numeric Rating Scale; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks.

Table. Change from baseline in fatigue, patient global assessment of disease activity, spinal pain and sleep in biologic-naive (COAST-V) and TNFi-experienced (COAST-W) patients with r-axSpA (extended treatment population)

tica, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9; **P. Mease**, Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, Roche, UCB, 2, 5, Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB, 8, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Abbvie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer and UCB., 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB, 2, Abbvie, Amgen, Brsitol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Brsitol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Brsitol Myers Squibb,Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, Amgen, 2, 5, 6, 8, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, and UCB, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 2, 5, Boerhinger Ingelheim, 5, Bristol Myers Squibb, 2, 5, 8, Bristol Myers Squibb Co., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8, Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8; **P. Rahman**, AbbVie, 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, and Novartis, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, and UCB, 5, AbbVie, Eli Lilly, Pfizer, Novartis , UCB, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 2, 5, 8, Janssen Inc., 2, 5, 8, Janssen, Novartis, 2, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **V.**



*p≤.001; *p<.05 versus placebo; Changes from baseline (least square mean) up to Week 16 were analyzed using MMRM model; after Week 16 changes were summarized for patients initially randomized to IXE Q4W and IXE Q2W and who entered extension period, using mean (gray shaded area) and missing data were imputed using mBOCF

ADA, adalimumab; IXE, ixekizumab; MMRM, mixed-effects model of repeated measures; mBOCF, modified baseline observation carried forward; NRS, Numeric Rating Scale; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks

Figure. Change from baseline in fatigue, spinal pain at night over 52 weeks in A) Biologic-naive patients (Coast-V) and B) TNFi-experienced patients (COAST-W)

Navarro-Compán, AbbVie, 5, 8, Bristol, 8, Bristol, Roche, 8, Eli Lilly and Company, 5, 8, Eli Lilly, Novartis, Abbvie, UCB, MSD, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, Roche, 8, UCB, 5, 8; **V. Strand**, Abbvie, 5, AbbVie, 5, Amgen, 5, Amgen, Abbvie, Bayer, BMS, Boehringer Ingelheim, Celltrion, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, UCB, 5, AstraZeneca, 5, AURA, 8, Bayer, 5, BMS, 5, Boehringer Ingelheim, 5, Celgene, 5, Celltrion, 5, Cleveland Clinic, 8, CORRONA, 5, Crescendo, 5, Crescendo Bioscience, 5, Eli Lilly, 5, EMD Serono, 5, Genentech, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Inmedix, 5, Janssen, 5, Kezar, 5, Lilly, 5, Merck, 5, NACCME, 8, Novartis, 5, Pfizer, 5, Purdue, 8, RA Forum, 8, RAN, 8, Regeneron, 5, Roche, 5, Samsung, 5, Sandoz, 5, Sanofi, 5, Servier, 5, Setpoint, 5, SLRA, 8, UCB, 5, Up to Date, 7, Washington University, 8, WIR, 8, WRA, 8; **T. Hunter**, Eli Lilly, 1, 3, Eli Lilly and Company, 1, 3; **D. Sandoval**, Eli Lilly, 1, 3, Eli Lilly and Company, 1, 3; **J. Lisse**, Eli Lilly, 1, 3, Eli Lilly

and Company, 1, 3; **F. Zhao**, Eli Lilly, 1, 3, 4, Eli Lilly and Company, 1, 3, 4; **H. Marzo-Ortega**, AbbVie, 5, 8, AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, 5, Abbvie, Celgene, Janssen, Lilly, Novartis, Pfizer, Ucb, 5, 8, AbbVie, Celgene, Janssen, Lilly, Novartis,Pfizer and UCB, 8, Celgene, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 2, 5, 8, Janssen and Novartis, 2, Janssen, Novartis, 2, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8.

Abstract Number: 1511

Drug Survival of Ustekinumab in Psoriatic Arthritis: A Real-World Multicentric Cohort of 252 Patients

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Ustekinumab (UST) is a new biological Disease-modifying AntiRheumatic Drug (bDMARD) available in psoriatic arthritis (PsA), targeting respectively IL12-23. Real-world data are missing for this drug on the contrary to TNF inhibitors. Median drug survival of TNF inhibitors is between 10 and 12 months according to the most recent studies (1).There are only few studies with a low number of patients in UST. Studying drug survival in PsA is important, since new therapies have been launched such IL-17 inhibitors or apremilast.

Methods: This is a retrospective, national, multicentric, non-sponsored by any pharmaceutical company study from patients suffering from PsA (CASPAR criteria or diagnosis confirmed by the rheumatologist) from July 2011 to March 2019. UST has been launched in October 2014. Drug survival was defined as the time from initiation to discontinuation (stop/switch) of bDMARDs. Kaplan-Meier survival curves and Cox-regression analyses [hazard ratios (HR) and 95% confidence intervals (CIs)] were used adjusting for patient demographics, disease characteristics, corticosteroid therapy, co-therapy with methotrexate, previous line of bDMARDs posology of UST and switch to 90 mg every 3 months when patients were at 45 mg every 3 months. Reasons of discontinuation were collected and pooled as primary failure, secondary failure and adverse events. Primary inefficacy was defined as an insufficient response to

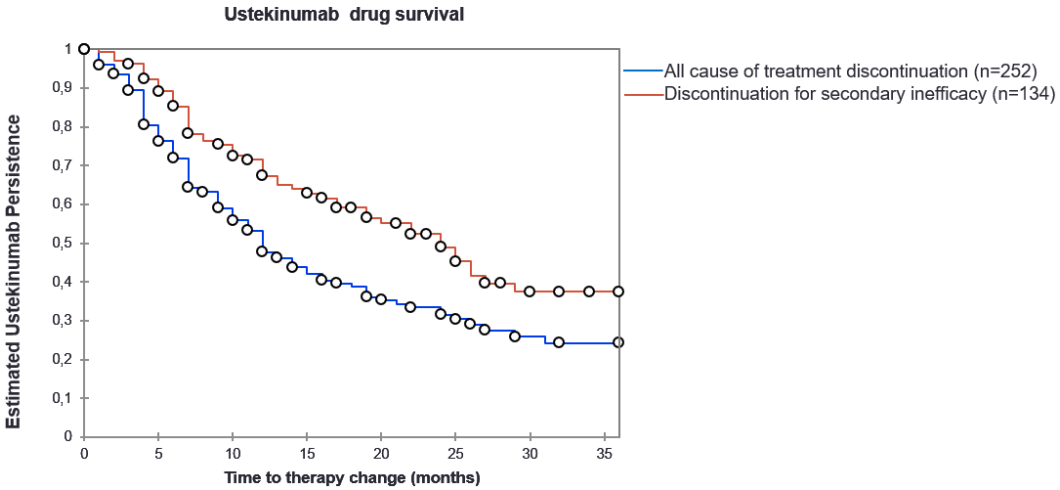

Figure. Drug survival of ustekinumab in psoriatic arthritis

treatment during the six months after the initiation. Secondary inefficacy was defined as a loss of response to treatment after an initial six-month response.

Results: 252 patients were included with a mean follow-up ≥ 6 months: 183 patients satisfy CASPAR. At baseline, the mean age was 49.2 (11.2) years old. 58% of patients were women. 49% of patients were non-smoker. The body mass index was 28.8 (6.3) kg/m². The disease duration was 10.2 (8.9) years. 44% of patients presented axial and peripheral form. 97% of patients presented psoriasis. The mean Charlson Index was 1.3 (1.5). Patients were bDMARDs-naïve in 22%, had a previous bDMARDs in 16% and more than two bDMARDs in 54% and had co-therapy with methotrexate in 39% and 27% of patients received corticosteroid therapy . Patients had a switch to 90 mg every 3 months in 10%. The mean DAS28-CRP was 3.88 (1.3) and the mean CRP was 27.5 (42.7) mg/L. The median drug survival for UST was 12 months (95%CI: 10-15) (Fig1). Baseline high CRP levels and satisfying CASPAR criteria were associated with a favorable drug survival for UST, respectively (HR=1.007, 95%CI 1.002–1.012 and HR=5.56, 95%CI 2.79-11.13), whereas disease duration and nail psoriasis were associated with an unfavorable one, respectively (HR=0.965, 95%CI 0.00–0.99 and HR=0.52, 95%CI 0.00-0.84). 14 patients under UST stopped their treatment due to side effects.

Conclusion: This real-world study for drug survival on PsA is among the studies with the largest number of patients for UST. Drug survival of UST seems similar to the survival of TNF inhibitors (1).

Reference

1 Walsh JA et al. Care Spec Pharm. 2018;24:623-631.

Disclosure: J. Letarouilly, None; **B. Flachaire**, UCB pharma, BMS, Novartis, 9; **C. Labadie**, None; **J. Sellam**, Janssen, 8; **P. Richette**, Janssen, 8; **P. Dieudé**, None; **P. Claudepierre**, Janssen, 8; **B. Fautrel**, AbbVie, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Boehringer Ingelheim, 8, Celgene, 5, 8, Eli Lilly and Company, 2, 5, Janssen, 5, 8, Lilly, 8, Medac, 5, 8, MSD, 2, 5, 8, NORDIC Pharma, 5, 8, Novartis, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, Sanofi-Aventis, 5, SOBI, 5, 8, UCB, 5, 8; **E. Houvenagel**, Janssen, 8, Novartis, 8; **C. Nguyen**, None; **M. Guyot**, None; **N. Segaud**, None; **F. Maury**, None; **L. Marguerie**, None; **X. Deprez**, Janssen, 8; **J. Salmon**, Janssen, 8; **G. Baudens**, None; **E. Gervais**, None; **I. Chary-Valckenaere**, None; **P. Lafforgue**, Chugai, 8, Amgen, 8, BMS, 8, Lilly, 8, Abbvie, 8, Pfizer, 8, Biogaran, 8; **D. Loeuille**, None; **C. Richez**, astrazeneca, 5, 8, BMS, 5, 8, Glenmark, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8; **T. Pham**, Abbvie, 8, Amgen, 8, Biogen, 8, BMS, 8, Celgene, 8, Fresenius-Kabi, 8, Janssen, 8, Lilly, 8, Medac, 8, MSD, 8, Nordic, 8, Novartis, 8, Pfizer, 8, Roche-Chugai, 8, Sandoz, 8, Sanofi, 8, UCB, 8; **R. Flipo**, Janssen, 8, Novartis, 8.

Abstract Number: 1512

Retention Rates and Response of Anti-TNF Treatments in the Enteropathic Spondylitis: HUR-BIO Real Life Results

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Enteropathic spondylitis (eSpA) is younger brother of spondyloarthritis, and the retention rate of biological DMARD in eSpA was not yet clear. The objective of this study was to assess anti-TNF response and retention rate in enteropathic spondylitis patients.

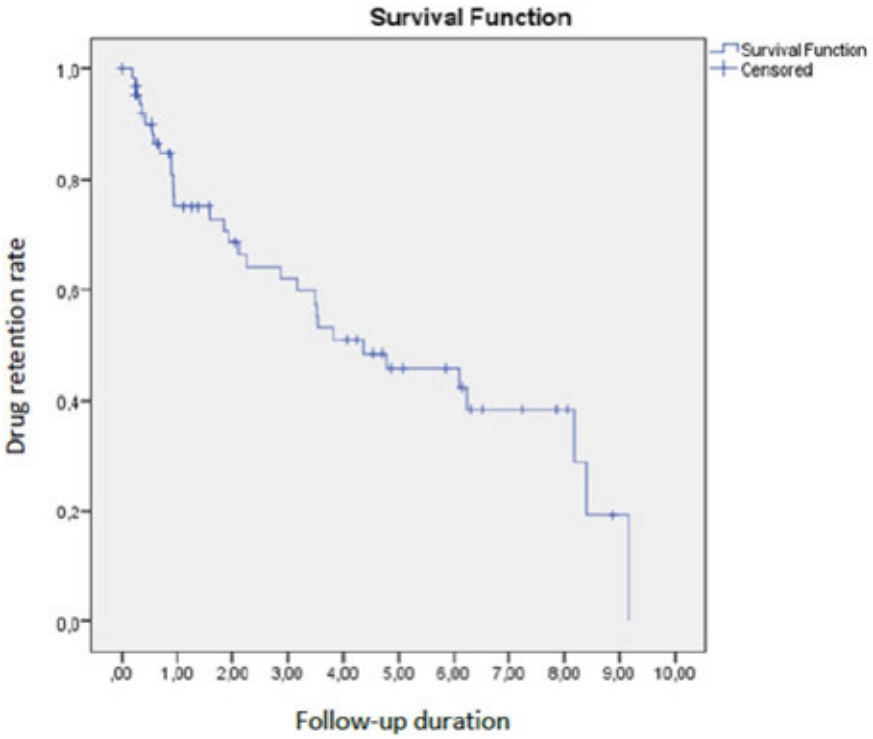
Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a prospective, single center database of biological treatments since 2005. Sacroiliitis was defined as modified New York criteria or based on magnetic resonance imaging. Enteropathic spondylitis was defined as inflammatory bowel disease (IBD) and radiological sacroilitis with inflammatory back pain/spine symptoms. Demographic, clinical, laboratory, therapeutic data and imaging features were collected from this database: age, gender, age at disease onset, disease duration, type of IBD. Baseline disease activity before the first biologic DMARD initiation was assessed with BASDAI, BASFI, VAS-patient global assessment, ESR and CRP. Retention rates for first biologic DMARDs were assessed by Kaplan-Meier survival analysis. Anti-TNF response was defined as BASDAI50% improvement, ASAS partial remission, and ASAS 20% improvement.

Results: HUR-BIO SpA registry included 2576 SpA patients, and 90 (3.5%) patients had enteropathic arthritis (EA). Sixty four (71.1%, 47% female) of 90 patients had sacroiliitis and those patients enrolled into analysis. Mean age was 45.0 ± 12.0 years, mean disease duration was 9.2 ± 6.9 years. Of the 64 eSpA, IBD type was ulcerative colitis (UC) in 34 (53%) patients, Crohn's disease (CD) in 30 (47%) patients. Initial bDMARDs were infliximab 26 (40.6%), adalimumab 24 (37.5%), etanercept 9 (14.1%), golimumab 4 (6.3%) and certolizumab 1 (1.6%). Forty one (64.0%) out of 64

Table 1: Anti-TNF response in enteropathic spondylitis

	First Control Visit	Last Control Visit
BASDAI50% response n (%)	23 (48)	20 (40)
ASAS partial remission	18 (38)	18 (36)
ASAS 20% improvement	12 (25.5)	16 (32)
First control visit performed 4.9 ± 3.9 months later, available for 47 patients. Control visit performed 54 ± 39 months later and available for 50 patients.		

Figure 1: Retention rate for first biological DMARD



eSpA patients used concomitant cDMARDs. Baseline disease activity parameters were as follows; BASDAI 5.7 ± 2.1, BASFI 4.3 ± 2.7, patient global assessment-VAS 6 .0 ± 1.9, ESR 38 ± 27 mm/hour, and CRP 3.2 ± 3.6 mg/dl. Patients were followed mean 54 ± 39 months. First control visits were performed 4.9 ± 3.9 months later. Anti-TNF response rate were shown in table 1. The cumulative retention rate of the TNF inhibitors at 12-, 24-, 36-, 48-, and 60-months of follow-up visits were 75.1, 68.6, 62.0, 50.9, and 45.8%, respectively (Figure 1). No differences were identified according to the use of concomitant DMARDs (p = 0.393) or IBD type (p=0.144).

Conclusion: Retention rate for first TNF inhibitor was not different from other SpA subtypes in HUR-BIO registry (1). IBD subtype or concomitant synthetic DMARDs did not have effect on the retention rate of anti-TNF treatments. ASAS partial remission was achieved only one third of eSpA patients during follow-up.

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Abstract Number: 1513

Impact of Baseline Body Mass Index on the Efficacy and Safety of Tofacitinib in Patients with Psoriatic Arthritis

Christopher Ritchlin,[1] Alexis Ogdie,[2] Jon Giles,[3] Juan Gomez-Reino,[4] Philip Helliwell,[5] Lori Stockert,[6] Pamela Young,[6] Wael Joseph,[6] Rajiv Mundayat,[7] Daniela Graham,[8] John Woolcott,[6] and Ana Romero[9], [1]Division of Allergy, Immunology and Rheumatology, Center for Musculoskeletal Research, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA, Rochester, NY, [2]Department of Medicine and Rheumatology and Department of Epidemiology and Biostatistics, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, [3]Division of Rheumatology, Columbia University, New York, NY, [4]Hospital Clínico Universitario, Santiago de Compostela, Spain, [5]University of Leeds, Leeds, United Kingdom, [6]Pfizer Inc, Collegeville, PA, [7]Pfizer Inc, New York, NY, [8]Pfizer Inc, Groton, CT, [9]Pfizer Inc, Barcelona, Spain

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

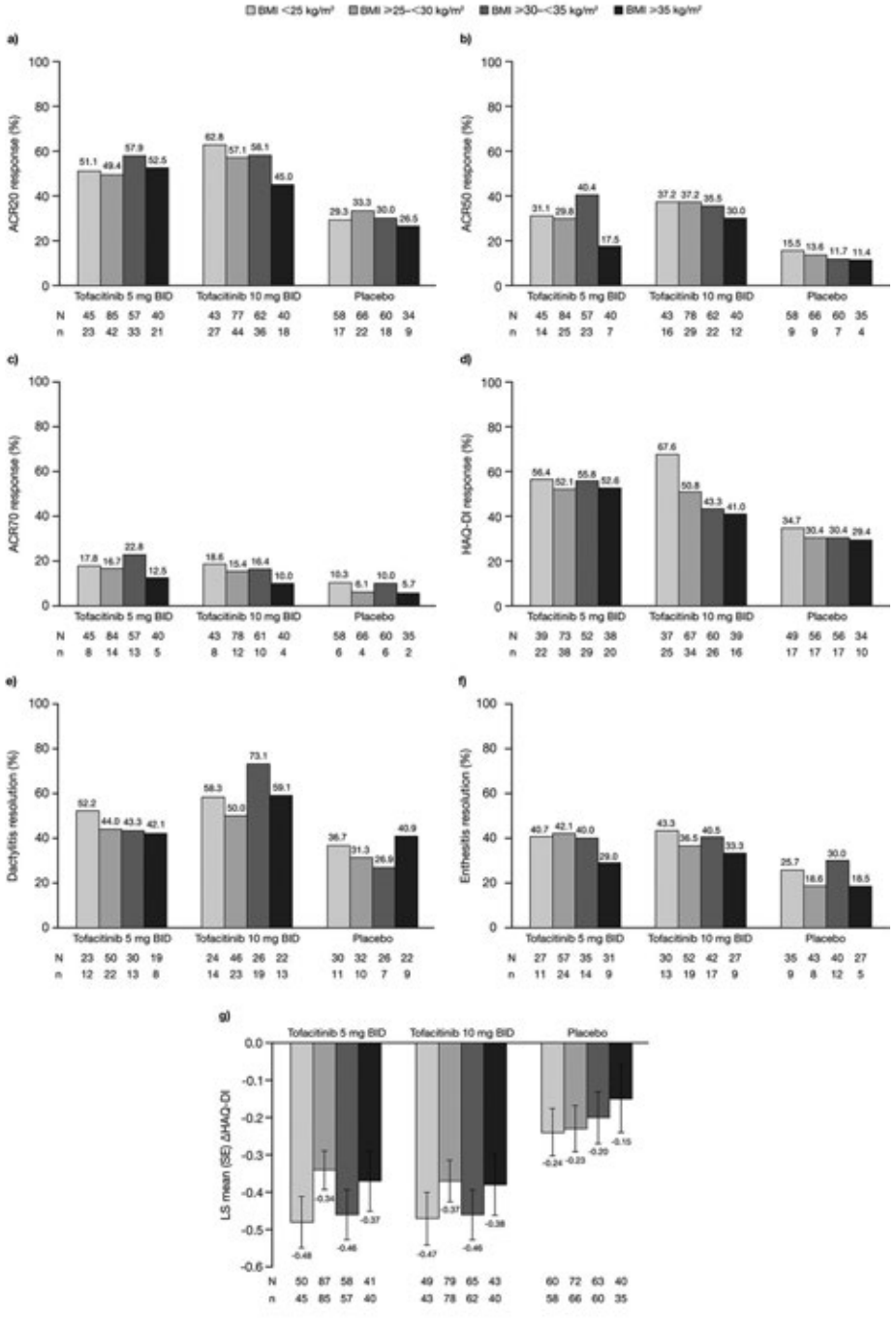
Session Time: 9:00AM–11:00AM

Background/Purpose: Obesity is highly prevalent in PsA (~45%),[1] and has previously been associated with a reduced response to TNF inhibitors.[2] Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. This post hoc analysis assessed tofacitinib efficacy and safety in pts with PsA, by baseline (BL) BMI category.

Methods: Data were pooled from two placebo (PBO)-controlled, double-blind, Phase 3 studies in pts with active PsA and an inadequate response to ≥ 1 conventional synthetic DMARD (OPAL Broaden [12 months; NCT1877668]) or to ≥ 1 TNF inhibitor (OPAL Beyond [6 months; NCT01882439]).[3,4] This analysis included pts randomized to tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, or PBO, stratified by BL BMI: < 25 kg/m^2, ≥ 25 – < 30 kg/m^2, ≥ 30 – < 35 kg/m^2, or ≥ 35 kg/m^2. Efficacy and safety were reported to Month M3. Efficacy outcomes included ACR20/50/70, HAQ-DI, and Psoriasis Area and Severity Index (PASI)75 responses, dactylitis and enthesitis absence rates, and changes from BL in Short Form-36 Version 2 (SF-36v2) Physical (PCS) and Mental Component Summary (MCS) scores, and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scores at M3. Safety outcomes included adverse events (AEs), such as cardiovascular (CV) events, and changes in liver function tests (LFTs) and lipid levels.

Results: This analysis included 710 pts; 43.8% were obese (BMI ≥ 30). At BL, 161 pts had a BMI < 25, 238 had a BMI ≥ 25 – < 30, 186 had a BMI ≥ 30 – < 35 and 125 had a BMI ≥ 35. Most pts were white (92.5–96.8%), middle-aged (44.5–51.2 yrs) and female (49.5–65.6%). Compared with the rest of the world, there were greater proportions of obese pts in Russia/Eastern Europe (35.1%) and US/Canada (31.8%). Higher BL BMI appeared correlated with increased prevalence of metabolic syndrome (4.3% in BMI < 25 to 76.0% in BMI ≥ 35) and CRP levels > 2.87 mg/L (49.1% in BMI < 25 to 84.0% in BMI ≥ 35). Higher proportions of pts (42.5–47.9%) in BL BMI categories < 35 reported no prior biologic DMARD use, vs pts with a BL BMI ≥ 35 (33.6%). At M3, efficacy improvements were generally greater in tofacitinib-treated pts, vs PBO-treated pts (Figure 1). In pts with a BL BMI ≥ 35, there was a trend towards fewer pts responding (Figure 1), and mean changes from baseline in SF-36v2 PCS, MCS and FACIT-F appeared lower (Table 1), vs pts in lower BL BMI categories. Up to M3, the proportions of pts with AEs, lipid levels, and percentage change from BL in LFTs, were generally similar across all BL BMI categories. There were three CV events: non-fatal cerebrovascular accident, transient ischemic attack (both tofacitinib 5 mg BID, BMI ≥ 30 – < 35), and artery revascularization (PBO; BMI ≥ 35).

Figure 1. a) ACR20,[a] b) ACR50,[a] c) ACR70,[a] and d) HAQ-DI[b] responses, e) dactylitis resolution rates,[c] f) enthesitis resolution rates,[c] and g) LS mean change from baseline in HAQ-DI at Month 3 by baseline BMI and treatment group (pooled data from OPAL Broaden and OPAL Beyond)



[a]ACR20/50/70 are calculated as a ≥20/50/70% improvement from baseline in tender and swollen joint counts and ≥20/50/70% improvement from baseline in 3 of the 5 remaining ACR core measures
[b]HAQ-DI response was defined as the number of patients achieving a reduction from baseline ≥0.35 in HAQ DI, considered the minimal clinically important difference
[c]Dactylitis resolution rates, defined as the absence of dactylitis in all of the 20 assessed digits, and enthesitis resolution rates, defined as the absence of enthesitis in all of the 6 assessed sites, were only assessed in patients who reported a baseline value of DSS or LEI >0, respectively
Δ, change from baseline; ACR, American College of Rheumatology; BID, twice daily; BMI, Body Mass Index; HAQ-DI, Health Assessment Questionnaire-Disability Index; LS mean, least squares mean; N, number of patients with a non-missing BMI evaluable at Month 3; n, number of patients in each category; SE, standard error

Conclusion: Regardless of BL BMI, tofacitinib demonstrated greater efficacy than PBO in pts with PsA. Similar to other advanced therapies,[2] reduced efficacy was generally observed in tofacitinib and PBO pts with a BL BMI ≥ 35. Tofacitinib safety appeared consistent across all BL BMI categories.

References

1. Labitigan M et al. Arthritis Care Res (Hoboken) 2014;66:600-7.
2. Singh S et al. PloS one 2018;13:e0195123-e0195123.

Table 1. LS mean (95% CI) changes from baseline in patient-reported outcomes at Month 3 by baseline BMI and treatment groups (pooled data from OPAL Broaden and OPAL Beyond)

	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo
N			
<25 kg/m^2	51	49	61
≥25–<30 kg/m^2	87	79	72
≥30–<35 kg/m^2	58	65	63
≥35 kg/m^2	42	43	40
LS mean ΔSF-36v2 PCS (95% CI)			
<25 kg/m^2	7.1 (5.0, 9.1)	6.7 (4.6, 8.8)	3.0 (1.1, 4.9)
≥25–<30 kg/m^2	5.3 (3.7, 6.8)	5.4 (3.9, 7.0)	2.4 (0.6, 4.1)
≥30–<35 kg/m^2	6.2 (4.1, 8.3)	6.7 (4.6, 8.8)	2.4 (0.3, 4.4)
≥35 kg/m^2	2.9 (0.6, 5.2)	4.3 (2.0, 6.5)	4.1 (1.6, 6.5)
LS mean ΔSF-36v2 MCS (95% CI)			
<25 kg/m^2	6.8 (4.2, 9.4)	6.1 (3.4, 8.7)	5.9 (3.5, 8.4)
≥25–<30 kg/m^2	4.4 (2.5, 6.3)	3.1 (1.1, 5.0)	1.6 (-0.5, 3.8)
≥30–<35 kg/m^2	6.2 (3.6, 8.7)	5.7 (3.1, 8.2)	4.4 (1.9, 7.0)
≥35 kg/m^2	4.1 (0.5, 7.6)	5.8 (2.2, 9.3)	4.0 (0.2, 7.7)
LS mean ΔFACIT-F (95% CI)			
<25 kg/m^2	9.3 (6.9, 11.7)	8.1 (5.7, 10.5)	4.9 (2.7, 7.1)
≥25–<30 kg/m^2	6.6 (4.7, 8.5)	6.1 (4.2, 8.0)	3.7 (1.5, 5.9)
≥30–<35 kg/m^2	7.5 (5.2, 9.8)	7.2 (4.9, 9.5)	3.6 (1.3, 5.9)
≥35 kg/m^2	5.9 (2.7, 9.1)	4.8 (1.7, 7.9)	5.1 (1.7, 8.5)

N is the number of pts in each treatment group, stratified by BL BMI; the number of pts assessed for each endpoint may be fewer than N

Δ, change from baseline; BID, twice daily; BMI, Body Mass Index; CI, confidence interval; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; LS, least squares; N, number of patients randomized and treated; SF-36v2, Short-Form 36 Version 2; MCS, Mental Component Summary; PCS, Short-Form Physical Component Summary

3. Mease P et al. N Engl J Med 2017;377:1537-50.
4. Gladman D et al. N Engl J Med 2017;377:1525-36.

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Abstract Number: 1514

Inadequate Response Within a Year of Biologic and Oral Synthetic DMARD Treatment Initiation Among Psoriatic Arthritis Patients in the USA Real-World Setting

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Real-world biologic persistence in PsA patients is lower compared to persistence in clinical trials. A comprehensive description of patterns of inadequate response (IR) to treatment is lacking. Frequency and timing of IR to biologics in the 1st year of treatment among PsA patients is described in this study.

Methods: This retrospective observational study analyzed USA commercial claims data (IBM® MarketScan®) from 2012–2017. Eligible PsA patients were biologic naïve (no claims for ≥1 year), ≥18 years old, with continuous enroll-

Table: The index biologic (n, %) in the cohort of 7,236 biologic-naïve PsA patients

Index treatment	Number of patients	% of total cohort
Adalimumab	3,015	42
Etanercept	2,100	29
Apremilast	1,165	16
Infliximab	347	5
Ustekinumab	294	4
Golimumab	128	2
Certolizumab pegol	122	2
Secukinumab	62	1
Ixekizumab	3	0

ment in the database in the 12-month baseline and follow-up periods. Diagnoses were based on International Classification of Diseases (ICD) 9/10 codes. Index date was the 1st claim for a biologic or apremilast (small molecule; **Table**). Persistence was defined as treatment with the index biologic with gaps of ≤90 days over 12 months. IR was defined as follows: 110% of the label-recommended dose for ≥30 days (above-label dosing), new biologic initiation within 90 days of discontinuing index biologic (switch), addition of a corticosteroid/immunosuppressant/biologic with ≥30 days of overlap (add-on treatment), and index biologic cessation (>90 days with no treatment) (non-switch discontinuation). Patients were classified according to the first IR event experienced.

Results: A total of 7,236 patients met the inclusion criteria. Persistence at 12 months was 48%, and was higher in males (53%) vs females (44%). Seventy-one percent of patients experienced an IR event in follow-up; the most frequent events were non-switch discontinuation (30%), followed by above-label dosing (16%), biologic switch (14%) and add-on treatment (11%). Median time from treatment initiation to IR event was 4.0 months, and was shortest for add-on treatment (3.1 months) and longest for biologic switch (4.6 months). Among the 1,716 patients with ≥12 months of follow-up after non-switch discontinuation, 53% had no subsequent biologic in the following 12 months, 31% restarted the index biologic, and 16% started a new biologic. IR distribution was similar irrespective of comorbid psoriasis and most recent provider (rheumatologist/dermatologist/other). Females (n=4,036) were more likely to experience an IR event than males (n=3,200) (74% vs 66%). Median time to IR event in females was 3.9 months vs 4.4 months in males.

Conclusion: IR to first biologic treatment, comprised primarily of adalimumab and etanercept, is common in PsA. Female patients are more likely to experience an IR event and to experience an event sooner vs males. Index biologic discontinuation (for >90 days) is common, with half of discontinuers remaining without a biologic exposure for ≥1 year, while the remaining discontinuers appeared to be taking a biologic drug holiday before restarting or initiating a new biologic. These variable treatment patterns suggest a variety of factors (including IR and others) are driving biologic discontinuation. Analysis of patient-level factors, such as clinical response and treatment access, is necessary to better understand the drivers of IR and to improve real-world treatment persistence.

Disclosure: S. Grabich, UCB Pharma, 1, 3; **A. Sheahan**, UCB Pharma, 1, 3; **O. Davies**, UCB Pharma, 1, 3; **R. Suruki**, UCB Pharma, 1, 3.

Abstract Number: 1515

Infections in Patients with Active Radiographic Axial Spondyloarthritis Treated with Ixekizumab in 2 Phase 3 Clinical Trials

Marina Magrey,[1] Victoria Navarro-Compán,[2] Sandra Garces,[3] Xenofon Baraliakos,[4] David Sandoval,[3] Jeffrey Lisse,[3] Silvia Santisteban,[3] David Adams,[3] Fangyi Zhao,[3] and Robert Inman[5], [1]Division of Rheumatology, The MetroHealth System and School of Medicine, Case Western Reserve University, Cleveland, OH, [2]University Hospital La Paz, IdiPaz, Madrid, Spain, [3]Eli Lilly and Company, Indianapolis, IN, [4]Rheumazentrum Ruhrgebiet-Ruhr-University Bochum, Herne, Germany, Herne, Germany, [5]University of Toronto, University Health Network, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Ixekizumab (IXE) is a high-affinity monoclonal antibody that selectively targets IL-17A. IL-17 inhibitors have shown efficacy for radiographic axial spondyloarthritis (r-axSpA), with IXE currently under study. As

Table 1. Summary of Infections from the COAST-V Study

	DB Treatment Period (Wk 0-16) Safety Population[a]			Combined DB and Extended Treatment Periods (Wk 0-52) Safety Population[a,b]		Extended Treatment Period (Wk 16-52) Extended Treatment Period Population[c]		
	PBO (N=86)	ADA Q2W (N=90)	IXE Q4W (N=81)	IXE Q2W (N=83)	IXE Q4W (N=81)	IXE Q2W (N=83)	PBO/IXE (N=86)	ADA/IXE (N=86)	IXE/IXE (N=157)
Infection Category	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
At least 1 infection	13 (15.1)	19 (21.1)	16 (19.8)	17 (20.5)	30 (37.0)	36 (43.4)	34 (39.5)	19 (22.1)	50 (31.8)
Mild	10 (11.6)	16 (17.8)	13 (16.0)	15 (18.1)	22 (27.2)	27 (32.5)	20 (23.3)	15 (17.4)	38 (24.2)
Moderate	3 (3.5)	2 (2.2)	3 (3.7)	1 (1.2)	7 (8.6)	6 (7.2)	14 (16.3)	4 (4.7)	9 (5.7)
Severe	0	1 (1.1)	0	1 (1.2)	1 (1.2)	3 (3.6)	0	0	3 (1.9)
Serious infections	0	1 (1.1)	1 (1.2)	1 (1.2)	1 (1.2)	2 (2.4)	1 (1.2)	1 (1.2)	1 (0.6)
Most common infections									
Nasopharyngitis	6 (7.0)	6 (6.7)	6 (7.4)	5 (6.0)	11 (13.6)	10 (12.0)	17 (19.8)	7 (8.1)	15 (9.6)
Upper respiratory tract infection	4 (4.7)	2 (2.2)	7 (8.6)	4 (4.8)	8 (9.9)	10 (12.0)	4 (4.7)	4 (4.7)	12 (7.6)
Discontinuations due to infections	0	0	0	1 (1.2)	0	2 (2.4)	1 (1.2)	0	1 (0.6)
Opportunistic infections[d,e]									
Esophageal candidiasis	0	0	0	0	0	0	1 (1.2)	0	0
Fungal esophagitis	0	0	0	0	0	0	1 (1.2)	0	0
Herpes simplex	0	0	0	0	0	0	1 (1.2)	0	0
Herpes zoster (any form)	0	0	0	0	0	0	2 (2.3)	1 (1.2)	0

ADA = adalimumab 40 mg; DB = double-blind; IXE = ixekizumab 80 mg; N = number of patients in the analysis population; n = number of patients in the specified category; PBO = placebo; Q4W = every 4 weeks; Q2W = every 2 weeks; Wk = week

[a]The Safety Population was defined as all randomized patients who received at least 1 dose of study treatment.

[b]The analysis population for the combined DB and Extended Treatment Periods included only patients in the Safety Population who were initially randomized to IXE Q4W or Q2W.

[c]The Extended Treatment Period Population was defined as all patients who received at least 1 dose of IXE treatment during the Extended Treatment Period.

[d]Opportunistic infections were identified by review of a pre-identified list of potential opportunistic infections using Medical Dictionary for Regulatory Activities preferred terms.

[e]Includes both opportunistic infections and potential opportunistic infections.

Table 2. Summary of Infections from the COAST-W Study

	DB Treatment Period (Wk 0-16) Safety Population[a]			Combined DB and Extended Treatment Periods (Wk 0-52) Safety Population[a,b]		Extended Treatment Period (Wk 16-52) Extended Treatment Period Population[c]	
	PBO (N=104)	IXE Q4W (N=114)	IXE Q2W (N=98)	IXE Q4W (N=114)	IXE Q2W (N=98)	PBO/IXE (N=93)	IXE/IXE (N=188)
Infection Category	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
At least 1 infection	10 (9.6)	34 (29.8)	23 (23.5)	58 (50.9)	43 (43.9)	32 (34.4)	62 (33.0)
Mild	5 (4.8)	20 (17.5)	14 (14.3)	34 (29.8)	22 (22.4)	14 (15.1)	32 (17.0)
Moderate	5 (4.8)	13 (11.4)	9 (9.2)	23 (20.2)	20 (20.4)	17 (18.3)	29 (15.4)
Severe	0	1 (0.9)	0	1 (0.9)	1 (1.0)	1 (1.1)	1 (0.5)
Serious infections	0	2 (1.8)	0	2 (1.8)	1 (1.0)	2 (2.2)	1 (0.5)
Most common infections							
Nasopharyngitis	2 (1.9)	5 (4.4)	4 (4.1)	8 (7.0)	6 (6.1)	3 (3.2)	7 (3.7)
Upper respiratory tract infection	3 (2.9)	9 (7.9)	4 (4.1)	13 (11.4)	11 (11.2)	5 (5.4)	12 (6.4)
Discontinuations due to infections	0	2 (1.8)	0	3 (2.6)	0	0	1 (0.5)
Opportunistic infections[d,e]							
Esophageal candidiasis	0	0	1 (1.0)	1 (0.9)	1 (1.0)	0	1 (0.5)
Oral candidiasis	0	0	0	1 (0.9)	0	0	1 (0.5)
Herpes zoster (any form)	0	1 (0.9)	0	1 (0.9)	0	1 (1.1)	0

DB = double-blind; IXE = ixekizumab 80 mg; N = number of patients in the analysis population; n = number of patients in the specified category; PBO = placebo; Q4W = every 4 weeks; Q2W = every 2 weeks; Wk = week

[a]The Safety Population was defined as all randomized patients who received at least 1 dose of study treatment.

[b]Analysis for the combined DB and Extended Treatment Periods included only patients in the Safety Population who were initially randomized to IXE Q4W or Q2W.

[c]The Extended Treatment Period Population was defined as all patients who received at least 1 dose of IXE treatment during the Extended Treatment Period.

[d]Opportunistic infections were identified by review of a pre-identified list of potential opportunistic infections using Medical Dictionary for Regulatory Activities preferred terms.

[e]Includes both opportunistic infections and potential opportunistic infections.

biologics may be associated with increased infections, we report on infections in patients with active r-axSpA treated with IXE.

Methods: Eligible patients met ASAS axSpA criteria, had radiographic sacroiliitis according to mNY criteria, and were either biologic-naïve (COAST-V: NCT02696785) or biologic-experienced (COAST-W: NCT02696798). Patients randomized to receive 16 weeks of double-blinded (DB) subcutaneous (SC) IXE 80 mg (once every 4 weeks [Q4W] or 2 weeks [Q2W]), placebo (PBO), or adalimumab (ADA, active reference) 40 mg Q2W (COAST-V only). All patients initially randomized to PBO or ADA (COAST-V) rerandomized to IXE at Weeks 16 through 52. The number and percentage of patients with infections are summarized for DB (Weeks 0 to 16), extended (Weeks 16 to 52), and combined treatment periods (Weeks 0 to 52).

Results: Total patients randomized were 341 in COAST-V (Table 1) and 316 in COAST-W (Table 2).

In COAST-V through Week 16, infections occurred in 19.8% (16/81), 20.5% (17/83), and 15.1% (13/86) of IXE Q4W, IXE Q2W, and PBO patients, respectively, and through Week 52 in 37.0% (30/81) and 43.4% (36/83) of patients initially randomized to IXE Q4W and Q2W, respectively. In COAST-W through Week 16, infections occurred in 29.8% (34/114), 23.5% (23/98), and 9.6% (10/104) of IXE Q4W, IXE Q2W, and PBO patients, respectively, and through Week 52 in 50.9% (58/114) and 43.9% (43/98) of patients initially randomized to IXE Q4W and Q2W, respectively.

In both studies, serious infections were reported in < 2% of IXE patients through Week 16 and in < 3% of patients during extended treatment. Most infections were mild or moderate in severity, and the most common infections were upper respiratory tract infection and nasopharyngitis. Overall, < 3% of patients discontinued due to infection, and no deaths due to infections occurred in either study.

In COAST-V, no IXE patients reported opportunistic infections through Week 16, and < 3% of patients reported opportunistic infections during extended treatment (esophageal candidiasis, fungal esophagitis, herpes simplex, herpes zoster [unidermatomal]). In COAST-W, ≤1% of IXE patients reported opportunistic infections through Week 16 (esophageal and oral candidiasis, herpes zoster), and < 2% of patients reported opportunistic infections during extended treatment (esophageal and oral candidiasis, herpes zoster). Opportunistic infections were mild or moderate in severity and none were serious. No tuberculosis cases were reported in either study and most candida and herpes infections resolved without recurrence.

Conclusion: Infection frequencies in COAST-V and COAST-W over 52 weeks are consistent with those in previous IXE PsA and PsO trials. Infection frequencies were similar between the IXE doses and study periods, with minimal difference between studies; thus, previous exposure to biologics did not affect the incidence of infections. Incidences of serious infections, opportunistic infections, and discontinuations due to infections were low in both studies.

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Abstract Number: 1516

Achievement of RAPID3 and cDAPSA Treatment Targets Is Associated with Control of Articular and Extra-Articular Manifestations of Active Psoriatic Arthritis in Subjects Treated with Apremilast

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SESSION INFORMATION

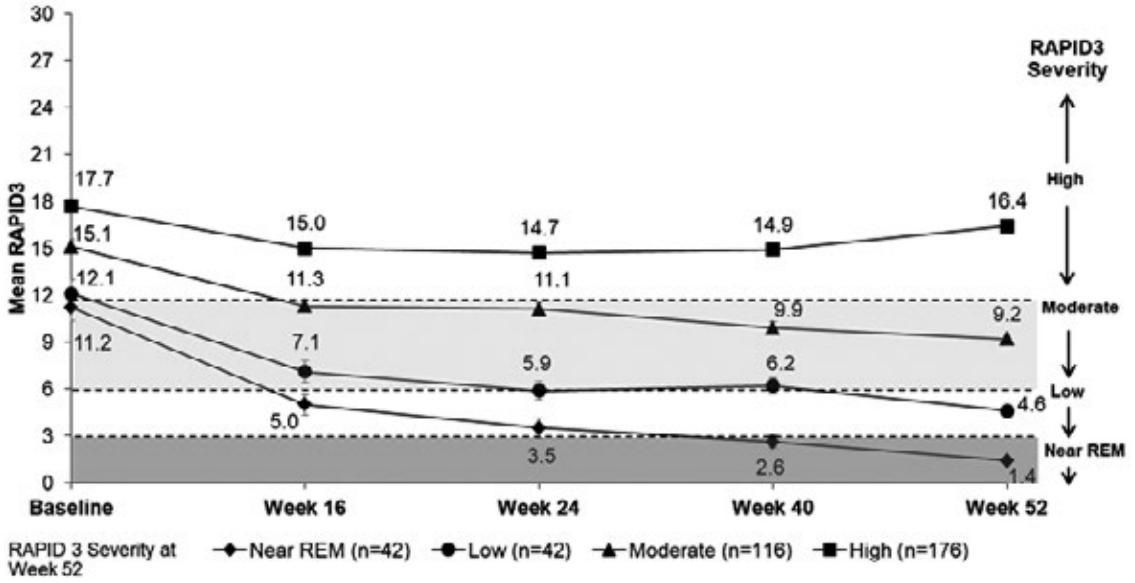
Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

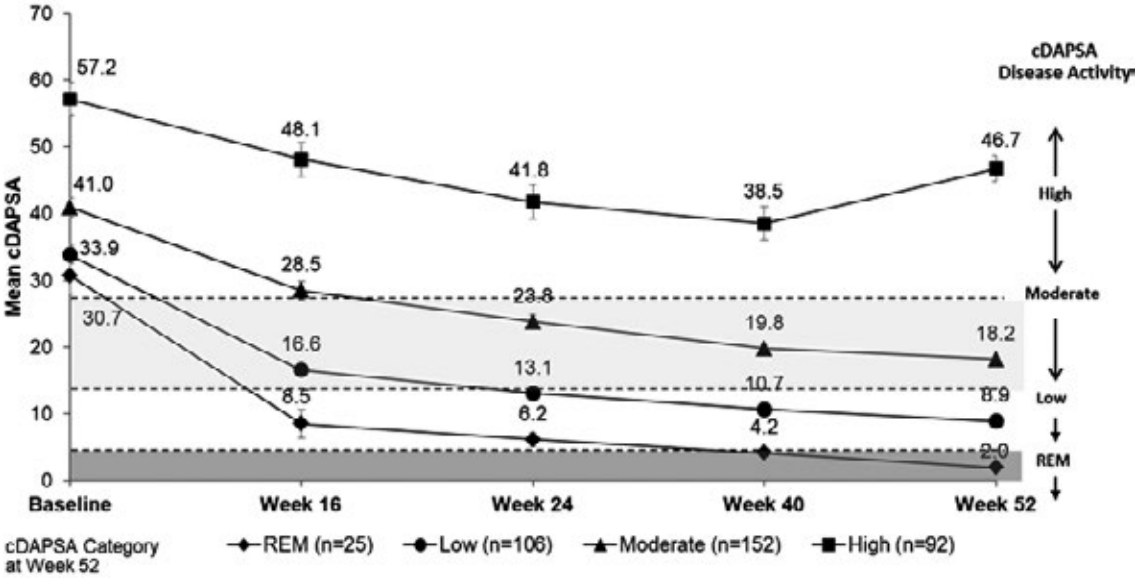
Session Time: 9:00AM–11:00AM

Figure 1. RAPID3 (0-30) Through Week 52 (N=376) by RAPID3 Category at Week 52: Subjects Receiving APR 30 mg BID From Baseline



Includes subjects randomized at baseline who had RAPID3 components available at Week 52; data are as observed. RAPID3 Near remission: ≤3; low severity: >3 to ≤6; moderate severity: >6 to ≤12; and high severity: >12 to 30. REM=remission. Error bars represent standard error of the mean

Figure 2. Disease Activity (cDAPSA [0–154]) Through Week 52 (N=375) by cDAPSA Category at Week 52 in Subjects Receiving APR 30 mg BID From Baseline



Includes subjects assigned to receive APR 30 mg twice daily at baseline who had cDAPSA components available at Week 52. Data are as observed. High disease activity, cDAPSA >27; moderate disease activity, cDAPSA >13 to ≤27; low disease activity, cDAPSA >4 to ≤13; remission (REM), cDAPSA ≤4. Error bars represent standard error of the mean.

Articular and Extra-articular Disease Activity in Subjects Achieving RAPID3 and cDAPSA Treatment Targets at Week 52

	RAPID3 ANALYSIS				cDAPSA ANALYSIS			
	Subjects With Near REM at Week 52		Subjects With Low Severity at Week 52		Subjects With REM at Week 52		Subjects With LDA at Week 52	
Mean	BL	Week 52	BL	Week 52	BL	Week 52	BL	Week 52
SJC (0-66)	10.2	1.6	8.4	2.1	9.1	0.1	8.8	1.1
TJC (0-68)	14.6	2.5	14.8	6.3	12.2	0.4	14.8	2.5
PAP (VAS 0-100 mm)	45.8	5.7	45.4	19.4	50.6	7.2	51.2	25.1
PtGA (VAS 0-100 mm)	44.1	7.2	44.9	15.4	44.5	7.7	51.5	28.0
PhGA (VAS 0-100 mm)	48.5	12.8	50.8	15.4	48.8	8.4	50.7	13.7
PASI* (0-72)	9.4	5.2	6.9	2.4	9.5	2.7	8.2	4.0
MASES[§] (0-13)	2.7	0.9	3.6	2.0	1.9	0.4	3.3	1.2
Dactylitis count (0-20)[¶]	3.1	0.6	2.6	0.6	2.3	0.0	2.8	0.5
HAQ-DI (0-3)	0.7	0.0	0.9	0.3	0.9	0.1	1.0	0.6

Data are as observed and n values vary by time point based on number of subjects with available data at a given point. *Assessed in subjects with ≥3% psoriasis-involved body surface area at BL. §Assessed in subjects with enthesitis at BL. ¶Assessed in subjects with dactylitis at BL. PhGA=Physician Global Assessment of Disease Activity; PASI=Psoriasis Area and Severity Index; MASES=Maastricht Ankylosing Spondylitis Enthesitis Score.

Background/Purpose: The Routine Assessment of Patient Index Data 3 (RAPID3) is an outcome measure of disease activity entirely derived from patient self-reported measures (Health Assessment Questionnaire-Disability Index [HAQ-DI] or multidimensional HAQ [MDHAQ], Pain visual analog scale [VAS], and Patient's Assessment of Disease Activity [PtGA] VAS). The Clinical Disease Activity in Psoriatic Arthritis (cDAPSA; 0-154) includes objective and subjective physician assessments (i.e., a composite of swollen and tender joints counts [SJC and TJC]), along with Patient's Assessment of Pain (PAP) and PtGA. In subjects receiving apremilast (APR), we examined trajectories for improvement in RAPID3 scores among subjects achieving RAPID3 near remission (REM) or low severity, cDAPSA among subjects achieving cDAPSA REM or low disease activity (LDA), and psoriatic arthritis (PsA) manifestations not measured by either outcome measure by Week 52.

Methods: Pooled analyses of the phase III PALACE 1, 2, and 3 studies were performed for subjects assigned to receive APR 30 mg BID at baseline (BL). Subjects with available scores on RAPID3 and cDAPSA components at Week 52 were included and grouped according to RAPID3 categories at Week 52 (near REM: ≤3; low severity: >3 to ≤6; moderate severity: >6 to ≤12; and high severity: >12 to 30) and cDAPSA categories at Week 52 (REM: ≤4; LDA: >4 to ≤13; moderate disease activity: >13 to ≤27; high disease activity: >27). Mean RAPID3 and cDAPSA scores were assessed from BL through Week 52. Other measures of PsA disease activity were reported longitudinally by RAPID3 and cDAPSA categories at Week 52.

Results: The RAPID3 and cDAPSA analysis included 376 and 375 APR subjects, respectively. Achievement of near REM or low severity (RAPID3) or REM or LDA (cDAPSA) by Week 52 with APR were associated with improvements over time in mean RAPID3 (**Figure 1**) and cDAPSA (**Figure 2**) trajectories. Subjects who achieved cDAPSA treatment targets were associated with no or mild articular and extra-articular manifestations at Week 52. Achieving RAPID3 treatment targets at Week 52 was associated with improvements in articular and extra-articular disease activity, although not all manifestations were controlled at Week 52 (**Table**). In both RAPID3 and cDAPSA analyses, similar improvements in SJC and TJC were observed for patients with REM or low severity (RAPID3) or REM or LDA (cDAPSA) at Week 52. In the RAPID3 analysis, mean TJC was higher than expected at Week 52, and achieving near REM RAPID3 scores was not associated with lower mean Psoriasis Area and Severity Index scores.

Conclusion: Subjects who achieved RAPID3 and cDAPSA targets showed early improvements in disease activity by Week 16 and sustained improvements to Week 52 with continued treatment. Achievement of treatment targets was also associated with improvements in other domains not captured directly by RAPID3 or cDAPSA. Given that some patients may exhibit different disease outcomes from the population, a more comprehensive assessment may help better evaluate treatment targets.

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Abstract Number: 1517

Effect of Long-Term Treatment with Secukinumab on Cardio-Metabolic Profile in Patients with Active Ankylosing Spondylitis and Psoriatic Arthritis: Pooled 3 Year Analysis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic inflammation may influence cardio-metabolic profiles and increases the risk of CV disorders in ankylosing spondylitis (AS) and psoriatic arthritis (PsA) patients (pts)[1]. Treatment with tumor necrosis factor (TNF) and Janus Kinase inhibitors have reported increased total cholesterol (TC) and triglycerides (TG) despite reduction in inflammation[2,3]. Here, we present the long-term effect of secukinumab (SEC), a fully human monoclonal

Key Cardio-metabolic parameters in AS and PsA pts through Wk 156 (Overall population)						
Parameters	Time points	AS		PsA		
		SEC 150 mg (N=504)	PBO (N=388)	SEC 300 mg (N=461)	SEC 150 mg (N=907)	PBO (N=681)
TG fasting, mmol/L	BL	1.3	1.3	1.5	1.5	1.6
	Wk 16	1.4	1.3	1.6	1.6	1.5
	Wk 104	1.4	–	1.6	1.6	–
	Wk 156	1.4	–	1.6	1.6	–
TC/HDL-C	BL	3.7	3.7	3.7	3.8	3.8
	Wk 16	3.7	3.6	3.8	3.9	3.8
	Wk 104	3.6	–	3.8	3.8	–
	Wk 156	3.8	–	3.8	4.1	–
Serum glucose, fasting, mmol/L (mg/dL)	BL	5.2 (93.6)	5.1 (91.8)	5.5 (99.0)	5.5 (99.0)	5.4 (97.2)
	Wk 16	5.3 (95.4)	5.1 (91.8)	5.6 (100.8)	5.6 (100.8)	5.6 (100.8)
	Wk 104	5.3 (95.4)	–	5.7 (102.6)	5.6 (100.8)	–
	Wk 156	5.3 (95.4)	–	6.0 (108.0)	5.7 (102.6)	–
Systolic/ diastolic BP, mmHg	BL	125/78	125/78	128/80	128/80	127/80
	Wk 16	125/78	125/78	126/79	129/80	127/80
	Wk 104	123/77	–	128/80	126/79	–
	Wk 156	122/75	–	126/79	126/79	–
BMI, kg/m^2	BL	27.1	27.0	29.8	30.1	29.3
	Wk 16	27.5	27.4	–	29.9	29.2
	Wk 104	26.8	–	30.0	30.4	–
	Wk 156	26.7	–	30.0	30.5	–
CRP, mg/L	BL	16.2	14.6	10.1	11.5	11.1
	Wk 16	6.9	14.8	4.3	4.9	10.4
	Wk 104	6.0	–	4.9	5.7	–
	Wk 156	6.5	–	5.1	5.5	–
AS; ankylosing spondylitis; BMI, body mass index; BP, blood pressure; CRP, C-reactive protein; HDL-C, high density lipoprotein cholesterol; N, total number of pts at baseline; PBO, placebo; PsA, psoriatic arthritis; SEC, secukinumab; TG; triglycerides; TC, total cholesterol; Wk, week						

Table: Key Cardio-metabolic parameters in AS and PsA pts through Wk 156 (Overall population)

antibody that directly inhibits interleukin (IL) -17A, on key cardio-metabolic parameters in AS and PsA pts from a pooled analysis of phase 3 clinical trials, through 156 weeks (wks).

Methods: This *post hoc* analysis pooled data from MEASURE 1–4 studies in AS (N=892) and FUTURE 2–5 studies in PsA (N=2049), and included pts treated with SEC 150 mg and SEC 300/150 mg, respectively, or placebo (PBO; Wk 16 data). Serum glucose, body mass index (BMI), TG, TC/high-density lipoprotein cholesterol (TC/HDL-C), systolic/ diastolic blood pressure (BP), C-reactive protein (CRP) levels were assessed at baseline (BL), Wks 16, 104 and 156 in overall population and in sub-groups by prior anti-TNF therapy and concomitant methotrexate (MTX) usage.

Results: BL characteristics were generally comparable across SEC and PBO groups in both disease cohorts. Serum glucose, systolic/diastolic BP, BMI, and lipid (TG, TC/HDL) levels were minimally altered in SEC treated pts with AS and PsA through Wk 156 (**Table**); mean change from BL in AS: TG (mmol/L) = 0.1–0.2, TC/HDL-C = ±0.2, glucose (mmol/L) = 0.08–0.2, BMI (kg/m^2) = 0.08–0.9, BP (mmHg) = ±0.2/±0.9 (systolic/diastolic) and mean change from BL in PsA: TG (mmol/L) = 0.003–0.2, TC/HDL-C = ±0.2, glucose (mmol/L) = ±0.3, BMI (kg/m^2) = 0.1–1.7, BP (mmHg) = ±4.0/±1.0 (systolic/diastolic). CRP reductions were observed through Wk 156 (**Table**). Results were broadly similar in sub-groups by prior anti-TNF therapy and concomitant MTX use through Wk 156.

Conclusion: Secukinumab was associated with minimal changes in cardio-metabolic parameters over 3 years in patients with ankylosing spondylitis and psoriatic arthritis. These findings suggest that anti-IL-17 therapy may be an option in patients with cardio-metabolic risk factors, however, further research is needed.

References

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Abstract Number: 1518

Tumour Necrosis Factor Inhibitor Monotherapy versus Combination Therapy with Conventional Synthetic Disease-modifying Anti-rheumatic Drugs for the Treatment of Psoriatic Arthritis: A Combined Analysis of European Biologics Databases

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	ATTRA- Czech Republic		Bari - Italy		Bath - UK		HeBRT - Greece		SCQM - Switzerland	
	n	Median survival time (years) (CI_{95})	n	Median survival time (years) (CI_{95})	n	Median survival time (years) (CI_{95})	n	Median survival time (years) (CI_{95})	n	Median survival time (years) (CI_{95})
All	**658**	**5.9 (4.7, 7.6)**	**300**	**4.9 (4.1, 6.6)**	**199**	**4.8 (3.6, 6.6)**	**314**	**6.9 (4.9, NA)**	**824**	**2.8 (2.5, 3.7)**
Treatment regimen at baseline (combination therapy with any csDMARD including MTX)										
Monotherapy	141	4.8 (3.8, NA)	110	6.9 (4.7, NA)	86	3.2 (1.3, 6.5)	77	4.3 (2.9, 8.3)	363	2.6 (1.7, 3.3)
Combination therapy	517	5.9 (4.7, 7.3)	190	4.3 (3.2, 6.2)	113	6.1 (4.5, NA)	237	7.2 (5.3, NA)	461	3.1 (2.6, 4.7)
p-value*		0.6054		**0.0303**		**0.0105**		0.0609		**0.0288**
Treatment regimen at baseline (combination therapy with MTX)										
Monotherapy	141	4.8 (3.5, NA)	110	6.9 (4.7, NA)	86	3.2 (1.3, 6.5)	77	4.3 (2.9, 8.3)	363	2.6 (1.7, 3.3)
Combination therapy	363	6.3 (4.5, 8.0)	146	4.9 (3.9, 6.6)	75	6.1 (4.5, NA)	204	NA (5.4, NA)	320	4.3 (3.0, 6.3)
p-value*		0.5550		0.0737		**0.0135**		**0.0208**		**0.0020**
Age										
18-49 years	370	6.6 (4.3, 8.9)	157	6.0 (4.1, 8.2)	99	5.1 (3.6, NA)	157	7.2 (4.9, NA)	447	3.8 (2.8, 4.6)
50 years and over	288	5.4 (4.4, 7.6)	143	4.5 (3.4, 6.2)	100	4.8 (3.2, NA)	157	6.9 (4.3, NA)	377	2.2 (1.6, 2.9)
p-value*		0.9958		0.3319		0.7923		0.9289		**0.0089**
Sex										
Female	320	5.7 (4.2, 8.2)	160	3.8 (2.7, 4.9)	99	2.4 (1.6, 6.1)	142	4.3 (2.8, 7.8)	417	2.0 (1.5, 2.7)
Male	338	5.9 (4.6, 8.9)	140	7.0 (5.5, 10.7)	100	6.6 (4.8, NA)	172	NA (5.9, NA)	407	4.2 (3.2, 5.6)
p-value*		0.6075		**0.0036**		**0.0100**		**0.0035**		**<0.0001**

*p-value from Log Rank test to compare the equality of the survival; NA – did not reach 50% drop-out

Table 1. Median survival times from TNFi initiation to discontinuation of first TNFi stratified by baseline treatment regimen and database.

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: A large proportion of psoriatic arthritis (PsA) patients are prescribed a tumour necrosis factor inhibitor (TNFi) in combination with methotrexate (MTX), however the value of combination therapy in PsA remains unresolved. This study aimed to investigate whether TNFi combination therapy with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) is more effective or improves TNFi drug survival compared to TNFi monotherapy.

Methods: Five PsA biologics cohorts were investigated between 2000 and 2015; the ATTRA registry (Czech Republic), the Swiss Clinical Quality Management PsA registry, the Hellenic Registry of Biologics Therapies (Greece), the University of Bari PsA biologics database (Italy) and the Bath PsA cohort (UK). Adults (≥18 years) with a clinical diagnosis of PsA who were new (first line) users of TNFi during the study period and registered in their respective database from TNFi initiation were eligible for inclusion. Exposure treatment groups at baseline included TNFi monotherapy, TNFi combination therapy with any csDMARD and a subgroup of TNFi combination therapy with MTX. Drug persistence was analysed using Kaplan-Meier and equality of survival using Log-Rank tests. Comparative effectiveness was investigated using logistic regression with propensity scores. Separate analyses were performed on: (a) the combined Italian and Swiss cohorts for change in rate of DAS-28; and (b) the combined Italian, Swiss and Bath cohorts for change in rate of HAQ.

Results: There were 2294 eligible patients identified from the contributing databases, of which 34% started TNFi in monotherapy and 66% in combination therapy. Patient characteristics and baseline disease activity and severity were generally similar across treatment groups within the databases. The majority of patients (82% monotherapy and 66% combination therapy) did not have changes to their baseline treatment regimen before discontinuing their first TNFi. In the Swiss (p=0.002), Greek (p=0.021) and Bath (p=0.014) databases, patients starting treatment on TNFi in combination with MTX had longer drug survival compared to monotherapy, whilst

in Italy patients starting on monotherapy persisted longer (p=0.030) (Table 1). In all but the Czech database, men persisted significantly longer on their first TNFi than women (Table 1). In the combined Italian/Swiss dataset (n=1066) there was no significant difference in the rate of change of DAS28 between those on TNFi monotherapy versus TNFi combination with any csDMARD (combined Relative Risk (RR_{adj}) 0.98 CI_{95} 0.95-1.03) or when compared to those on TNFi+MTX (RR_{adj} 0.98 CI_{95} 0.95-1.02). Similarly, when also including the Bath cohort (n=1205), there was a comparable rate of change of HAQ in patients on TNFi monotherapy compared with combination with any csDMARD (RR_{adj} 1.01 CI_{95} 0.99-1.04) and when compared to those on TNFi+MTX combination (RR_{adj} 1.02 CI_{95} 0.99-1.05).

Conclusion: Combination therapy of a TNFi with a csDMARD does not appear to affect improvement of disease activity or HAQ. Combination therapy may, however, improve TNFi drug survival. Gender appears to be a major risk factor in determining TNFi survival, with males persisting on treatment for longer.

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Abstract Number: 1519

Predicting Response to Biologic Therapy in Patients with Axial Spondyloarthritis (axSpA)

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In axial spondyloarthritis (axSpA), the clinical benefits of TNF inhibition (TNFi) are well documented although, by design, most studies report average benefits in groups of patients. Inevitably, a subset of patients will not respond to therapy. Identifying characteristics of these patients is important as it may inform the use of TNFi in clinical practice. The aim of the current study was to identify factors that predict satisfactory treatment response, in a nationwide register of patients commencing TNFi.

Methods: The British Society for Rheumatology Biologics Register for Ankylosing Spondylitis (BSRBR-AS) recruited biologics-naïve patients with axSpA from 83 secondary care rheumatology centres across Great Britain between 2012 and 2017. Clinical data was collected from patients' medical records, and additional data was collected via postal questionnaires. Treatment response was determined at the first eligible follow-up and was defined as moving from high/very high Ankylosing Spondylitis Disease Activity Scale score (ASDAS≥2.1) to

Baseline predictor[1]		Odds ratio (95%CI) Univariate association	Odds ratio (95%CI) Independent predictors
Clinical factors			
Disease activity	BASDAI	0.71 (0.60-0.85)	
	ASDAS	0.74 (0.55-0.99)	
Bath indices	Function (BASFI)	0.70 (0.61-0.81)	
	Metrology (BASMI)	0.83 (0.70-0.99)	
	Global health (BASG)	0.68 (0.57-0.81)	
Presence of extra-spinal manifestation [Reference = Absence of symptom]	Heel enthesitis	1.18 (0.51-2.73)	
	Uveitis	1.15 (0.62-2.12)	
	Dactylitis	1.63 (0.53-5.01)	
	Psoriasis	0.80 (0.33-1.93)	
	Inflammatory bowel disease	0.76 (0.32-1.81)	
	Peripheral joint disease	0.87 (0.46-1.67)	
Classification criteria [Reference = modified New York]	ASAS imaging	0.89 (0.50-1.56)	
	ASAS clinical	1.84 (0.51-6.62)	
Pain	Spinal VAS	0.84 (0.74-0.96)	
CRP (mg/dL)		0.99 (0.97-1.01)	
Comorbidity count		0.51 (0.35-0.75)	0.60 (0.38-0.95)
BMI (kg/m^2)		0.94 (0.89-1.001)	
Socioeconomic factors			
Highest education level [Reference = Secondary school]	Apprenticeship	1.97 (0.80-4.86)	1.43 (0.50-4.08)
	College	1.17 (0.57-2.42)	1.01 (0.43-2.36)
	University	2.64 (1.26-5.53)	1.72 (0.72-4.10)
	Further degree	3.51 (1.29-9.54)	2.62 (0.82-27.5)
Deprivation (quintiles) [Reference = 1, Least deprived]	2	0.59 (0.29-1.23)	
	3	0.39 (0.17-0.85)	
	4	0.43 (0.19-0.99)	
	5, Most deprived	0.36 (0.14-0.93)	
Employment [Reference = Full-time work]	Part-time	0.23 (0.09-0.57)	0.28 (0.11-0.74)
	Unpaid/seeking	0.21 (0.04-1.04)	0.24 (0.05-1.28)
	Retired	0.68 (0.30-1.55)	0.90 (0.33-2.47)
	Retired/unemployed due to ill-health	0.04 (0.01-0.18)	0.04 (0.005-0.34)
	Student	2.90 (0.29-28.7)	2.67 (0.26-27.5)
Patient-reported outcomes			
Quality of life	ASQoL (range: 0-18[2])	0.82 (0.76-0.88)	
Physical health	SF12 Physical summary (range 0-100[3])	1.07 (1.03-1.10)	
Mental health	SF12 Mental summary (range 0-100[3])	1.06 (1.04-1.09)	1.05 (1.01-1.08)
	HADS anxiety (range 0-21[2])	0.87 (0.81-0.93)	
	HADS depression (range 0-21[2])	0.86 (0.80-0.93)	
Fatigue/Sleep**	Chalder Fatigue Scale (range 0-11[2])	0.87 (0.80-0.93)	
	Jenkins Sleep Scale (range 0-20[2])	0.94 (0.89-0.98)	
Smoking [Reference = Never]	Ex	0.66 (0.36-1.21)	
	Current – light	0.30 (0.10-0.97)	
	Current – heavy	0.72 (0.32-1.59)	
Alcohol drinking [Reference = ≤14 units/week]	Never	0.20 (0.04-0.92)	
	Ex	0.45 (0.21-0.96)	
	Current >14 units/week	1.30 (0.42-4.05)	

1 For non-categorical variables, results are given per 1 unit increase
2 High score = worse
3 High score = better

Table. Factors associated with response to TNFi, among patients with axSpA

moderate/inactive disease activity (ASDAS< 2.1). Factors associated with treatment response were assessed using logistic regression. Thereafter, a forward stepwise logistic regression model was used to identify which group of factors best predicted treatment response. Analysis was conducted on the June 2017 BSRBR-AS dataset.

Results: 249 participants were eligible for the current analysis; 69% were male, with median age 47yrs (inter-quartile range: 36-56). 96% met the ASAS imaging criteria, of which 67% had ankylosing spondylitis.

Median follow-up was 14wks, at which point 35% were classified as treatment responders. For every 1 unit increase in disease activity (BASDAI) there was a 29% decrease in the odds of response (odds ratio 0.71; 95%CI 0.60-0.85). A similar effect was seen with increasingly poor function (BASFI: 0.70; 0.61-0.81). Other factors associated with response on univariable analysis were wide-ranging, including clinical, socioeconomic and patient-reported factors, see Table 1.

Only four independent predictors of response were identified. Patients in full-time employment and with high education were more likely to respond, as were those with better mental health scores. Increasing comorbidities was associated with poor response. The final model demonstrated a good level of fit with positive (PPV) and negative predictive values (NPV) of 63% and 77% respectively.

Conclusion: Four variables, none of them disease specific, identified axSpA patients commenced on biologic therapy, who were unlikely to have responded, four months later. Other patients may need additional therapeutic approaches and additional support (e.g. support so that they do not lose their job) to achieve optimal outcomes.

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Abstract Number: 1520

Long-Term Treatment Patterns of Biologics and Apremilast Among Patients with Moderate-to-Severe Plaque Psoriasis by Psoriatic Arthritis Status

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Long-term real-world treatment patterns of psoriasis patients are not well characterized, especially those with comorbid psoriatic arthritis (PsA). This study examined the treatment patterns among psoriasis patients who newly initiated a biologic or apremilast (APR) by PsA status.

Methods: Using a large US claims database, adult patients with psoriasis were classified into 5 mutually exclusive cohorts based on their initial index medication between 01/01/2015 and 08/31/2018: secukinumab (SEC), adalimumab (ADA), ustekinumab (UST), etanercept (ETA), or APR. Eligible patients had no index medication use in the 12-month pre-index period, and had continuous medical and pharmacy benefits in the 12-month pre-index and 24-month post-index periods. Subgroups were created by the presence of a PsA diagnosis over the 12-month pre-index period.

Rates of discontinuation, adherence (proportion of days covered [PDC], adherent if PDC ≥0.8), non-persistence, and switching were compared between patients with and without PsA within each cohort. Treatment gaps were defined as 4 weeks for ETA and APR, 8 weeks for ADA, 10 weeks for SEC, and 18 weeks for UST.

Results: A total of 7,773 psoriasis patients were included: 275, 2,684, 910, 1,063, and 2,841 patients for SEC, ADA, UST, ETA, and APR, respectively, and the proportions of patients with PsA were 35.3%, 35.1%, 22.0%, 45.7%, and 24.8%, respectively. Over the 24-month post-index period, discontinuation rates for patients with and without PsA were: SEC: 54.6% vs. 43.8%; ADA: 48.3% vs. 53.0%; UST: 52.5% vs. 34.4%; ETA: 38.1% vs. 45.4%; and APR: 47.7% vs. 43.4% (all $p< 0.05$ except SEC). Adherence rates were: SEC: 30.9% vs. 34.8%; ADA*: 30% vs. 25.5%; UST: 17.5% vs. 23.9%; ETA*: 26.5% vs. 16.8%; and APR: 22.4% vs. 22.9% (*$p< 0.05$). Non-persistence rates were: SEC: 69.1% vs. 65.7%; ADA: 71% vs. 74.4%; UST*: 68.5% vs. 55.5%; ETA*: 82.1% vs. 90.3%; and APR: 86.6% vs. 84.8% (*$p< 0.05$). Overall switching rates were high for all groups (24.8%–55.1%, all $p< 0.05$ except ETA).

Conclusion: About 22%–46% moderate-to-severe psoriasis patients who initiated biologics or APR had comorbid PsA. Over 24-month post-index period, overall adherence was poor and discontinuation, non-persistence, and switching were high for all groups. Maintaining long-term therapy is still a challenge for psoriasis patients. Treatments that overcome the hurdle of poor adherence to self-administration may be helpful.

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Abstract Number: 1521

Ixekizumab Is Effective in the Treatment of Radiographic Axial Spondyloarthritis Regardless of the Level of C-Reactive Protein or Magnetic Resonance Imaging Scores

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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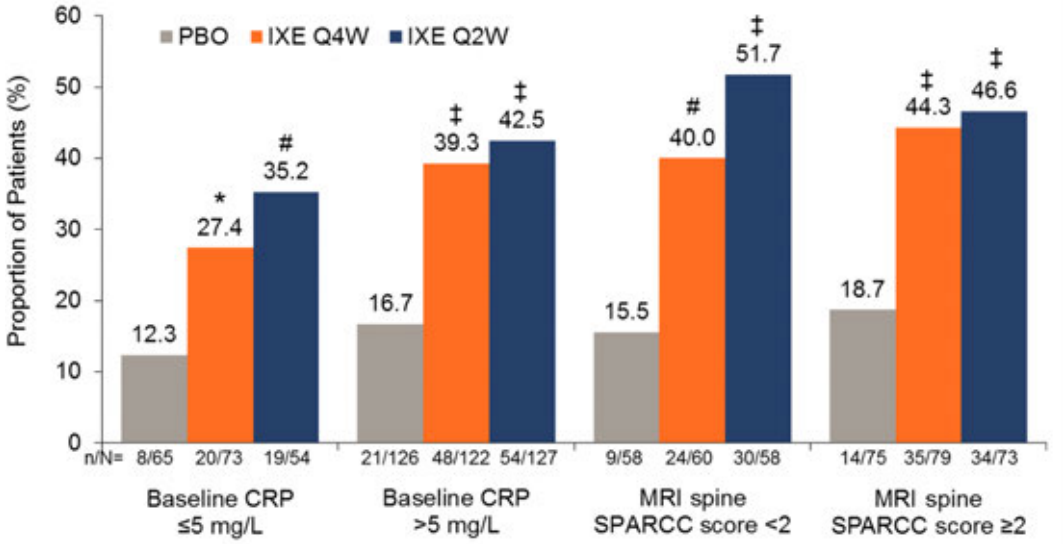
Session Time: 9:00AM–11:00AM

Background/Purpose: IL-17 plays an important role in the pathogenesis of radiographic axial spondyloarthritis (r-axSpA). Elevated CRP levels in serum predict response to TNF inhibitors (TNFi).[1-4] The role of baseline spine MRI as a predictor of response has not been investigated for IL-17 inhibitors. This study evaluates response rates at week (wk) 16 with ixekizumab (IXE), an IL-17A antagonist, in patients with ankylosing spondylitis (AS)/r-axSpA and elevated or normal/low inflammation as measured by CRP or spinal MRI.

Figure 1 **COAST-V/W Integrated Dataset, ITT ASAS40 Response at Week 16, NRI**



*p<.05, #p<.01, ‡p<.001 versus placebo. ASAS40=Assessment in SpondyloArthritis international Society 40% response rate; CRP=C-reactive protein; ITT=intent-to-treat; IXE=ixekizumab; n=number of patients in the specified category; N=number of patients in the analysis population; NRI=nonresponder imputation; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SPARCC=Spondyloarthritis Research Consortium of Canada

Methods: Two Phase 3, randomized, double-blind, placebo (PBO)-controlled trials (COAST-V, NCT02696785; COAST-W, NCT02696798) enrolled biologic-naive or TNFi-experienced patients, respectively, with active disease (BASDI ≥4 and spinal pain ≥4 on a numeric rating scale) and an established diagnosis of r-axSpA and fulfilling Assessment of SpondyloArthritis international Society (ASAS) criteria (sacroiliitis on radiograph by modified New York [mNY] criteria and ≥1 spondyloarthritis feature). All patients fulfilling ASAS criteria also fulfilled mNY criteria for AS. Patients were treated with IXE (80 mg every 2 or 4 wks [Q2W, Q4W]) or PBO; adalimumab (40 mg Q2W) was an active reference arm in COAST-V. We examined ASAS 40% (ASAS40) response rates at wk 16 for the intent-to-treat population by baseline CRP (≤5 or >5 mg/L) and/or MRI spine inflammation (Spondyloarthritis Research Consortium of Canada [SPARCC] spine score < 2 or ≥2). Baseline spine MRI (scored by central readers) was available in 96% of patients in COAST-V and 51% in COAST-W. Higher scores reflect greater baseline disease activity. Missing data for ASAS40 were imputed by nonresponder imputation.

Results: In the COAST-V/W integrated dataset that combined biologic-naive and TNFi-experienced populations, significantly more patients treated with IXE achieved ASAS40 response at wk 16 than with PBO in the baseline CRP elevated (>5 mg/L) group (39.3%, 42.5%, and 16.7% for IXE Q4W, IXE Q2W, and PBO, respectively; p< .001 for IXE Q4W, IXE Q2W vs PBO) and in the baseline CRP normal (≤5 mg/L) group (27.4%, 35.2%, and 12.3% for IXE Q4W, IXE Q2W, and PBO, respectively; p< .05 for IXE Q4W, p< .01 for IXE Q2W vs PBO, Fig 1), and the magnitude of response with IXE between elevated vs normal CRP groups was not statistically significant. Notably, a significantly higher proportion of patients achieved ASAS40 at wk 16 with IXE than with PBO, regardless of whether MRI spine SPARCC scores were < 2 (40%, 51.7%, and 15.5% for IXE Q4W, IXE Q2W, and PBO, respectively; p< .01 for IXE Q4W, p< .001 for IXE Q2W vs PBO) or ≥2 (44.3%, 46.6%, and 18.7% for IXE Q4W, IXE Q2W, and PBO, respectively; p< .001 for IXE Q4W, IXE Q2W vs PBO, Fig 1). Among the patients (n=79) with MRI spine SPARCC score < 2 and CRP ≤5 mg/L, the ASAS40 responses at wk 16 were 13%, 29%, and 48% for PBO, IXE Q4W, and IXE Q2W, respectively, with statistically significantly greater improvement for IXE Q2W vs PBO (p< .05).

Conclusion: IXE demonstrated rapid efficacy in the treatment of AS/r-axSpA at wk 16 irrespective of baseline serum CRP levels or spinal MRI score.

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4. Vastesaeger et al. 2011

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Abstract Number: 1522

Inflammatory Bowel Disease and Anterior Uveitis in Patients Treated with Ixekizumab for Radiographic Axial Spondyloarthritis: Results from Two Phase 3 Studies Through 52 Weeks

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Radiographic axial spondyloarthritis (r-axSpA) is a chronic inflammatory disease involving the axial skeleton; inflammatory bowel disease (IBD) and acute anterior uveitis (AAU) are common extra-articular manifestations. IBD has been reported in 3–10% of ankylosing spondylitis (AS) patients (pts).[1] Exposure-adjusted incidence rates (EAIRs) of IBD in AS pts treated with TNF inhibitors (TNFi) have been reported as 0.2–2.3 per 100 person years (PY)[3]. The frequency of AAU in AS has been reported as 33%[2] and the EAIR of AAU has been reported as 2.6–3.5 per 100 PY.[4]

Ixekizumab (IXE) is a high-affinity mAb targeting IL-17A with established efficacy and safety in pts with r-axSpA.[5,6] We summarize IBD and AAU cases reported from 2 pivotal studies of IXE in r-axSpA.

Methods: COAST-V (NCT02696785) and COAST-W (NCT02696798) are phase 3, randomized, controlled studies in pts with r-axSpA naïve to biological DMARDs (bDMARDs) or pts who previously failed 1 or 2 TNFi (TNFi-experienced), respectively. Full study designs have been described previously[5,6]. Pts with a history of IBD or AAU were not excluded if these conditions were stable. At each study visit, pts were evaluated for any symptoms of AAU and IBD. AAU events were con-

Table 1. Incidence and exposure-adjusted incidence rates for inflammatory bowel disease and acute anterior uveitis in ixekizumab-treated patients across COAST-V and COAST-W.

	COAST-V and COAST-W
Number of patient who received at least 1 dose of ixekizumab	641
Exposure, total person years[a]	510.1
IBD[b]	
Patients entering study with history of IBD, n (%)[c]	14 (2.1%)
Patients with ≥1 reported event of IBD, n (%)[b]	8 (1.2%)
Patients with history (diagnosis) of IBD, n	3
Patients with no history of IBD, n	5
IBD EAIRs	
Patients with CD, n (%), [EAIR]	4 (0.6%), [0.8]
Patients with UC, n (%), [EAIR]	2 (0.3%), [0.4]
Patients with IBD NOS, n (%), [EAIR]	2 (0.3%), [0.4]
AAU[d]	
Patients entering study with history of AAU,n (%)[c]	145 (22.1%)
Patients with ≥1 reported event of AAU, n (%)[d]	20 (3.1%)
Patients with history (diagnosis) of AAU, n (%)	15
Patients with no history of AAU, n (%)	5
AAU EAIR	3.9

[a]Sum of exposure for any ixekizumab-treated pts in the blinded dosing treatment period and the extended treatment period in both studies. [b]IBD events were identified from the narrow terms and events (MedDRA Version 21.0) that can occur with IBD as specified in the program safety analysis plan and adjudicated following EPIMAD criteria. [c]Pts with previous history of IBD or AAU were calculated based on the total number of randomized patients across both trials (N = 656). [d]AAU was identified using the preferred term "iridocyclitis" (MedDRA Version 21.0); AAU cases were evaluated by ophthalmologists.

firmed by an ophthalmologist. IBD events were adjudicated following Registre Epidemiologique des Maladies de l'Appareil Digestif (EPIMAD) criteria. EAIRs were calculated by the number of patients experiencing these events per 100 PY.

Results: Across both studies, 2.1% of pts had a history of IBD, and there were 4 cases of Crohn's disease (CD), 2 cases of ulcerative colitis (UC), and 2 cases of IBD not otherwise specified (IBD NOS) among patients treated with IXE and 1 case of UC on placebo. Most patients who had events of IBD had a prior diagnosis of IBD or prior gastrointestinal history potentially indicative of IBD. EAIRs for CD, UC, and IBD NOS were 0.8, 0.4, and 0.4 per 100 PY, respectively (Table 1). Four patients permanently discontinued IXE treatment due to IBD.

Across both studies, 20.1% of pts had a history of AAU, and 20 pts reported events of AAU, 15 of those had a prior history of AAU. One case resulted in drug interruption, and 1 case resulted in permanent discontinuation of IXE treatment due to AAU. The EAIR for AAU was 3.9 per 100 PY (Table 1).

Conclusion: In IXE-treated r-axSpA pts, frequencies of IBD and AAU were in the range of those seen in AS pts.[1, 2] EAIRs of IBD were numerically similar to those seen in TNFi-treated AS pts for both studies. More and longer-term data are required to better understand the incidence rates of IBD and AAU in r-axSpA pts treated with IXE.

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AAU=acute anterior uveitis; CD=Crohn's disease; EAIR=exposure-adjusted incidence rate per 100 patient years; EPIMAD=Registre Epidemiologique des Maladies de l'Appareil Digestif; IBD=inflammatory bowel disease; n=number of patients in the specified category; NOS=not otherwise specified; UC=ulcerative colitis.

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Impact of Body Weight on Efficacy of Tildrakizumab in Moderate-to-Severe Plaque Psoriasis

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SESSION INFORMATION

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Background/Purpose: Tildrakizumab (TIL) is a high-affinity, anti–interleukin-23p19 monoclonal antibody approved for the treatment of moderate-to-severe chronic plaque psoriasis. An inverse efficacy–body weight relationship has been reported for multiple fixed-dose systemic agents in patients with psoriasis, who tend to be of greater weight than the general population. We conducted a post hoc analysis of pooled data from 2 randomized, placebo (PBO)-controlled, phase 3 trials (reSURFACE 1 [NCT01722331] and 2 [NCT01729754]) to evaluate the impact of body weight on TIL efficacy in psoriasis.

Methods: In reSURFACE 1 and 2, patients were randomized to PBO or TIL 100 or 200 mg in Part 1 (Week [W] 0–12) and rerandomized in Parts 2 (W12–28) and 3 (W28–64 [reSURFACE 1] or W28–52 [reSURFACE 2]). Treatment was administered at W0, W4, and every 12 weeks thereafter. The median percentage improvement in Psoriasis Area and Severity Index (PASI) is reported for patients randomized to TIL 100 mg at baseline up to W52, or PBO up to W12. Data were stratified by weight decile, calculated separately for Parts 1 and 2 combined, and Part 3. A nonresponder imputation analysis was used.

Results: For Parts 1 and 2 (n=616), median weight (range) for the TIL 100-mg group at baseline was 86.3 kg (40.9–194.7 kg); median PASI was 17.9. For patients who entered Part 3 (n=329), median weight at baseline was 86.0 kg (47.0–194.7 kg); median PASI was 18.0. At W12, a slightly greater median percentage improvement in PASI was observed in the lower weight deciles: 87.4%, 86.6%, 83.6%, 88.9%, 81.5%, 84.3%, 83.1%, 78.0%, 76.7%, and 77.5% (lowest to highest decile). By W28, the difference in improvement between lowest and highest decile had narrowed: 91.6%, 91.9%, 92.6%, 90.4%, 91.1%, 90.6%, 91.2%, 87.7%, 87.0%, and 86.0%. At W52, efficacy was well maintained across all weight deciles: 100%, 96.9%, 96.9%, 96.6%, 96.6%, 97.2%, 95.3%, 93.4%, 93.5%, and 90.8%. For PBO (n=309), median weight at baseline was 85.7 kg (44.0–180.2 kg), and median PASI was 17.7. At W12, there was little improvement, with no distinct pattern, in PASI vs baseline (range: 1.2%–25.3%).

Conclusion: A modest weight-efficacy relationship with TIL 100-mg treatment was observed through W12, with more rapid efficacy in the lower weight deciles. Efficacy improved across deciles through W28, with a decreased difference between the lightest and heaviest deciles due to more rapid improvement in the latter. Efficacy responses in W28 PASI 75 responders were well-maintained, with >90% median PASI improvement across deciles at W52.

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Abstract Number: 1524

Tildrakizumab Efficacy on Psoriasis in Patients with Psoriatic Arthritis—An Analysis from a Phase 2 Study

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	TIL 200 mg Q4W (n = 78)	TIL 200 mg Q12W (n = 79)	TIL 100 mg Q12W (n = 77)	TIL 20 mg Q12W (n = 78)	PBO Q4W (n = 79)
Age, years, mean ± SD	50.1 ± 13.3	49.3 ± 11.2	49.2 ± 11.9	47.2 ± 13.4	48.1 ± 13.3
Female, n (%)	46 (59.0)	37 (46.8)	47 (61.0)	41 (52.6)	44 (55.7)
Race					
White, n (%)	76 (97.4)	78 (98.7)	75 (97.4)	75 (96.2)	74 (93.7)
Black or African American	0	0	1 (1.3)	1 (1.3)	3 (3.8)
Other	2 (2.6)	1 (1.3)	1 (1.3)	2 (2.6)	2 (2.5)
Weight, kg, mean ± SD	85.1 ± 19.7	87.1 ± 19.5	83.6 ± 18.9	85.1 ± 18.1	85.3 ± 20.2
BMI, kg/m^2, mean ± SD	30.1 ± 6.5	30.2 ± 6.5	29.5 ± 6.8	29.4 ± 5.2	29.5 ± 6.0
Duration of PsA, years, mean ± SD	6.9 ± 7.3	6.8 ± 6.3	6.3 ± 7.2	6.6 ± 6.7	7.3 ± 8.0
Prior anti–TNF-α therapy, n (%)*	18 (22.8)	17 (21.8)	19 (23.8)	19 (24.4)	18 (23.7)
Swollen joint count, mean ± SD	10.4 ± 7.4	10.0 ± 8.0	11.0 ± 8.2	9.4 ± 6.4	11.8 ± 9.8
Tender joint count, mean ± SD	16.6 ± 11.9	19.5 ± 13.9	21.3 ± 14.8	19.0 ± 13.0	19.7 ± 14.7
C-reactive protein (mg/L), mean ± SD	7.8 ± 18.6	10.5 ± 14.4	10.6 ± 20.0	10.7 ± 14.0	13.0 ± 20.8
BSA (%), mean ± SD	11.9 ± 16.0	9.0 ± 12.4	12.8 ± 16.0	10.4 ± 14.1	8.2 ± 12.2
BSA ≥3%, n (%)	53 (67.9)	44 (55.7)	54 (70.1)	41 (52.6)	42 (53.2)
PASI, mean ± SD†	7.6 ± 9.8	6.2 ± 7.4	8.8 ± 9.5	6.6 ± 7.0	5.0 ± 6.5

Table 1. Patient demographics and baseline disease characteristics. *For prior anti-TNF-α therapy, total patients analyzed (N) = 79, 78, 80, 78, and 76 for TIL 200 mg Q4W, TIL 200 mg Q12W, TIL 100 mg, TIL 20 mg, and PBO. †For prior baseline PASI, total patients analyzed (N) = 75, 79, 76, 75, and 75 for TIL 200 mg Q4W, TIL 200 mg Q12W, TIL 100 mg, TIL 20 mg, and PBO. Shown for randomized patients who received ≥1 dose of study drug. BMI, body mass index; BSA, body surface area; PBO, placebo; PsA, psoriatic arthritis; Q4W, every 4 weeks; Q12W, every 12 weeks; SD, standard deviation; TIL, tildrakizumab.

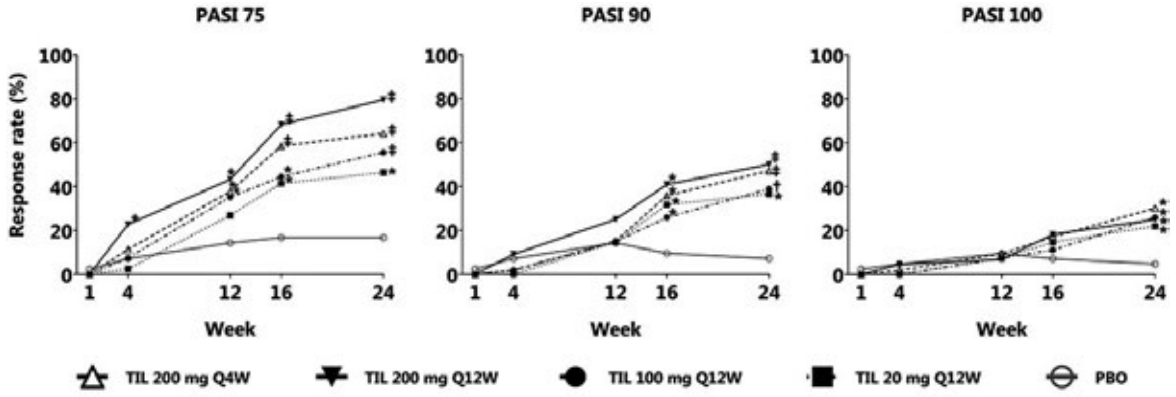

Figure 1. PASI 75/90/100 response rates§ §Response rates calculated in patients with BSA ≥3% at baseline, missing responses were imputed as nonresponses. *P <0.05; †P <0.001; ‡P <0.0001 vs PBO. BSA, body surface area; PASI, Psoriasis Area and Severity Index; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Tildrakizumab (TIL) is a high-affinity anti–interleukin-23p19 monoclonal antibody approved by the FDA to treat moderate-to-severe plaque psoriasis. A randomized, double-blind, multidose, placebo-controlled, phase 2b study (NCT02980692) is underway to evaluate the efficacy and safety of TIL for the treatment of PsA. In this interim analysis of the phase 2b study, the effect of TIL on Psoriasis Area and Severity Index (PASI) 75/90/100 response rates was evaluated in study patients with PsA and measurable psoriasis (≥3% of the body surface area [BSA] affected at baseline).

Methods: Patients ≥18 years of age with active PsA (Classification of Psoriatic Arthritis criteria)[1] were stratified by prior anti-TNF use (yes/no) and baseline body weight (≤90 kg and ≥90 kg), and randomized 1:1:1:1:1 to receive TIL (200 mg once every 4 weeks [Q4W], 200 mg every 12 weeks [Q12W], 100 mg Q12W, or 20 mg Q12W to week 24) or placebo (PBO Q4W to week 24). PASI75/90/100 were prespecified endpoints and assessments were conducted by an independent assessor. Efficacy was analyzed in the full analysis set, defined as all randomized subjects who received ≥1 dose of study drug. Safety assessments included treatment-emergent adverse event (TEAE) monitoring.

Results: Of 500 patients screened, 391 patients met inclusion criteria with 77–79 per treatment arm (TIL 200 mg Q4W, TIL 200 mg Q12W, TIL 100 mg Q12W, and TIL 20 mg Q12W vs PBO) of which, 234 patients had BSA ≥3% at baseline (41–54 per treatment arm, **Table 1**). Mean age (SD) was 48.8 (12.6), 96.7% white, average body mass index 29.7, and 23.3% were anti–TNF-experienced. At week 24, 61.5%/43.2%/26.0% in combined TIL arms vs 16.7%/7.1%/4.8% in the PBO arm achieved PASI 75/90/100 responses (**Figure 1**). The most frequent TEAEs included nasopharyngitis (pooled TIL arms 5.4% vs PBO 6.3%) and upper respiratory tract infection (pooled TIL arms 3.5% vs PBO 1.3%). No deaths were reported.

Conclusion: By week 24, TIL significantly improved PASI 75/90/100 in patients with PsA and psoriasis vs PBO. Numerically, 200-mg dosing led to higher PASI 75 and 90 responses by week 24 compared with 100-mg dosing in patients with mild to moderate psoriasis and PsA. Further studies that are powered to compare the 100-mg vs 200-mg dose are needed to confirm this observation. Improvements in skin responses were significant vs PBO as early

as week 4 for PASI 75 in the TIL 200 mg Q12W arm. These data provide evidence that TIL significantly improves psoriasis in patients with PsA and is well tolerated in a mixed population of anti–TNF-naïve and -experienced patients.

Editorial and writing support was provided by Marie-Louise Ricketts, PhD, of AlphaBioCom, LLC.

Reference

1. Taylor W, et al. *Arth Rheum*, 2006; 54: 2665-2673.

Disclosure: A. Gottlieb, AbbVie, 5, 6, Abbvie, 5, Allergan, 5, 6, Amgen, 8, Avotres Therapeutics, 5, 6, Beiersdorf, 5, 6, Boehringer Ingelheim, 2, 5, 6, Boerhinger Ingelheim, 2, 5, Bristol Myers Squibb Co., 5, Bristol-Myers Squibb, 5, 6, Celgene Corp, 5, Celgene Corp., 5, 6, Dermira, 5, 6, Eli Lilly, 5, 6, 8, 9, Foamix, Incyte, 2, 5, 6, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, Leo, 5, LEO, 5, 6, Lily, 5, Merck, Novartis, 2, 5, 6, 8, Ortho Dermatologics, 8, Reddy Labs, 5, 6, Sun Pharmaceutical Industries, 5, Sun Pharmaceutical Industries, Inc., 5, 6, 8, UCB, 2, 5, 6, Valeant, 5, 6, XBiotech, 2, 5, 6, Xbiotech, 2, 5; **A. Orbai**, AbbVie, 2, Celgene, 2, Eli Lilly, 2, 5, Horizon, 2, Janssen, 2, 5, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 5, UCB, 5; **R. Ballerini**, Sun Pharmaceutical Industries, Inc., 3; **R. Chou**, Sun Pharmaceutical Industries, Inc., 5; **S. Rozzo**, Sun Pharmaceutical Indsutries, Inc, 3, Sun Pharmaceutical Industries, Inc, 3, Sun Pharmaceutical Industries, Inc., 3; **A. Mendelsohn**, Johnson and Johnson, 1, 4, Sun Pharmaceutical Industries, Inc, 3, Sun Pharmaceutical Industries, Inc., 3; **L. Espinoza**, None.

Abstract Number: 1525

Safety of Tildrakizumab in Psoriatic Arthritis: An Interim Analysis from a Randomized, Double-blind, Placebo-controlled Phase 2b Trial

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Tildrakizumab (TIL) is an anti–interleukin-23p19 monoclonal antibody approved by the FDA for treatment of moderate-to-severe plaque psoriasis[1,2] and is under investigation for treatment of PsA. The objective of this analysis was to evaluate the safety of TIL in patients with active PsA at 24 weeks from the randomized, double-blind, placebo-controlled, multiple-dose, phase 2b TIL trial (NCT02980692).

Methods: Patients ≥18 years old with a diagnosis of PsA (by the Classification of Psoriatic Arthritis criteria[3]) and ≥3 tender and ≥3 swollen joints were randomized 1:1:1:1:1 to 5 treatment arms (administered by subcutaneous injection)—200 mg TIL every 4 weeks (Q4W), 200 mg TIL every 12 weeks (Q12W), 100 mg TIL Q12W, 20 mg TIL Q12W, or placebo to week 24. Treatment-emergent adverse events (TEAEs) were monitored throughout the study; and defined as events that occurred on/after the first dose of TIL but before week 24, or on/before the last dose if the subject discontinued treatment before week 24 (coded by Medical Dictionary of Regulatory Activities v20.1).

Results: In total, 391/500 patients screened met inclusion criteria. Patient demographics and baseline disease characteristics were consistent across the groups (**Table 1**). At 24 weeks, 61 (78.2%) TIL 200 mg Q4W, 64 (81.0%) TIL

Patient Demographics[1]	TIL 200 mg Q4W (N = 78)	TIL 200 mg Q12W (N = 79)	TIL 100 mg Q12W (N = 77)	TIL 20 mg Q12W (N = 78)	PBO (N = 79)
Age, years	50.1 ± 13.3	49.3 ± 11.2	49.2 ± 11.9	47.2 ± 13.4	48.1 ± 13.3
Female, n (%)	46 (59.0)	37 (46.8)	47 (61.0)	41 (52.6)	44 (55.7)
BMI, kg/m², mean ± SD	30.1 ± 6.5	30.2 ± 6.5	29.5 ± 6.8	29.4 ± 5.2	29.5 ± 6.0
Disease Characteristics[1]					
Duration of PsA, years	6.9 ± 7.3	6.8 ± 6.3	6.3 ± 7.2	6.6 ± 6.7	7.3 ± 8.0
Prior anti–TNF-α therapy, n (%)*	18 (22.8)	17 (21.8)	19 (23.8)	19 (24.4)	18 (23.7)
Patient GADA	57.8 ± 18.3	61.1 ± 20.7	60.3 ± 20.2	61.9 ± 17.4	65.2 ± 18.1
Physician GADA	54.0 ± 16.1	55.4 ± 16.2	57.3 ± 17.3	59.4 ± 14.4	59.5 ± 15.6
BSA, (%)	11.9 ± 16.0	9.0 ± 12.4	12.8 ± 16.0	10.4 ± 14.1	8.2 ± 12.2
BSA ≥3%, n (%)	53 (67.9)	44 (55.7)	54 (70.1)	41 (52.6)	42 (53.2)
HAQ score	1.0 ± 0.6	1.0 ± 0.6	1.0 ± 0.7	1.1 ± 0.6	1.2 ± 0.6
PASI, mean ± SD†	7.6 ± 9.8	6.2 ± 7.4	8.8 ± 9.5	6.6 ± 7.0	5.0 ± 6.5

Table 1. Baseline demographics and clinical disease characteristics in tildrakizumab and placebo treatment groups. Data presented as mean ± SD unless otherwise noted. 1Shown for randomized patients who received ≥1 dose of study drug. *For prior anti–TNF-α therapy, total patients analyzed (N) = 79, 78, 80, 78, and 76 for TIL 200 mg Q4W, TIL 200 mg Q12W, TIL 100 mg, TIL 20 mg, and PBO. †For prior baseline PASI, total patients analyzed (N) = 75, 79, 76, 75, and 75 for TIL 200 mg Q4W, TIL 200 mg Q12W, TIL 100 mg, TIL 20 mg, and PBO. BMI, body mass index; BSA, body surface area; GADA, global assessment of disease activity; HAQ, health assessment questionnaire disability index; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; SD, standard deviation; TIL, tildrakizumab.

200 mg Q12W, 60 (77.9%) TIL 100 mg Q12W, 71 (91.0%) TIL 20 mg Q12W, and 74 (93.7%) placebo patients completed treatment, respectively. Reasons for discontinuation included an adverse event in 1 (1.3%), 2 (2.5%), 1 (1.3%), 2 (2.6%), and 0 patients, respectively, and lack of efficacy in 9 (11.5%), 12 (15.2%), 13 (16.9%), 0, and 0 patients, respectively.

At week 24, 156 (50.0%) TIL-treated and 34 (43.0%) placebo-treated patients had any TEAE, 7 (2.2%) and 2 (2.5%) a serious TEAE, and 35 (11.2%) and 10 (12.7%) a treatment-related TEAE, respectively. The most commonly reported TEAEs were nasopharyngitis (17 [5.4%] TIL-treated vs 5 [6.3%] placebo-treated), headache (15 [4.8%] vs 2 [2.5%]), and hypertension (11 [3.5%] vs 4 [5.1%]), respectively (**Table 2**). The most commonly reported serious TEAE was hypertension (2 [0.6%] in TIL-treated patients, **Table 3**). One patient (0.3%) in the TIL group had a serious infection (chronic tonsillitis). At 24 weeks, there were no reports of candidiasis, inflammatory bowel disease, major adverse cardiac events, significantly increased liver enzymes, or malignancies. In addition, no deaths or discontinuations due to TEAEs were reported. There were no significant elevations in laboratory parameters that led to a serious TEAE designation.

Conclusion: These findings demonstrate that TIL is well tolerated with low rates of TEAEs and serious TEAEs reported during the first 24 weeks of the phase 2b trial.

Editorial support was provided by Puneet Dang, PhD, of AlphaBioCom, LLC.

References

1. Reich K, et al. *Lancet*. 2017; 390:276-288.
2. ILUMYA™ (tildrakizumab-asmn) injection, for subcutaneous use. [Full prescribing information]; August 2018.
3. Taylor W, et al. *Arthritis Rheum*.2006; 54(8):2665-2673.

System Organ Class	Any TIL arm (N = 312)	Placebo (N = 79)
Infections and infestations	69 (22.1)	15 (19.0)
Investigations	25 (8.0)	5 (6.3)
Nervous system disorders	24 (7.7)	3 (3.8)
Musculoskeletal and connective tissue disorders	24 (7.7)	3 (3.8)
Gastrointestinal disorders	19 (6.1)	4 (5.1)
Vascular disorders	13 (4.2)	5 (6.3)
Injury, poisoning, and procedural complications	9 (2.9)	5 (6.3)

Table 2. Number of treatment-emergent adverse events (≥5%) reported by system organ class at 24 weeks. Shown as n (%) for randomized patients who received ≥1 dose of study drug. TIL, tildrakizumab.

Serious Adverse Event	Any TIL arm (N = 312)	Placebo (N = 79)
Hypertension	2 (0.6)	0
Osteoarthritis	1 (0.3)	1 (1.3)
Parathyroid tumor benign	0	1 (1.3)
Hypokalemia	1 (0.3)	0
Ovarian cyst	1 (0.3)	0
Ovarian cyst ruptured	1 (0.3)	0
Syncope	1 (0.3)	0
Chronic tonsillitis	1 (0.3)	0

Table 3. Number of serious treatment-emergent adverse events reported by preferred term at 24 weeks. Shown as n (%) for randomized patients who received ≥1 dose of study drug. TIL, tildrakizumab.

Disclosure: C. Ritchlin, AbbVie, 2, 5, 9, Amgen, 2, 5, BMS, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Lilly, 5, Novartis, 5, Pfizer, 2, Pfizer Inc, 5, UCB, 2, 5; **V. Strand**, AbbVie, 5, Amgen, 5, AstraZeneca, 5, Bayer, 5, BMS, 5, Boehringer Ingelheim, 5, Celltrion, 5, CORRONA, 5, Crescendo, 5, Eli Lilly, 5, Genentech/Roche, 5, GSK, 5, Janssen, 5, Merck, 5, Novartis, 5, Pfizer, 5, Regeneron Pharmaceuticals Inc., 5, Samsung, 5, Sandoz, 5, Sanofi, 5, UCB, 5; **R. Ballerini**, Sun Pharmaceutical Industries, Inc., 3; **R. Chou**, Sun Pharmaceutical Industries, Inc., 5; **S. Rozzo**, Sun Pharmaceutical Indsutries, Inc, 3, Sun Pharmaceutical Industries, Inc, 3, Sun Pharmaceutical Industries, Inc., 3; **A. Mendelsohn**, Johnson and Johnson, 1, 4, Sun Pharmaceutical Industries, Inc, 3, Sun Pharmaceutical Industries, Inc., 3; **A. Kavanaugh**, Abbott, 2, Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, 2, Amgen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 2, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, Pfizer Inc, 2, Roche, 2, UCB Pharma, 2.

Abstract Number: 1526

Efficacy and Safety of Tildrakizumab 100 Mg for Plaque Psoriasis in Patients Randomized to Treatment Continuation vs Treatment Withdrawal with Retreatment upon Relapse in a Phase 3 Study

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SESSION INFORMATION
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Background/Purpose: We assessed residual plaque psoriasis in patients successfully treated with anti–interleukin-23p19 monoclonal antibody tildrakizumab (TIL) who interrupted treatment, relapsed, and were retreated vs continuously treated patients in a post hoc analysis of reSURFACE 1.

Methods: reSURFACE 1 was a 3-part, double-blind, randomized, controlled, 64-week phase 3 study of TIL 100 mg in adults with moderate-to-severe plaque psoriasis (NCT01722331).[1] Patients receiving TIL 100 mg at weeks 0, 4, and 16, and every 12 weeks thereafter who achieved ≥75% relative improvement in Psoriasis Area and Severity Index (PASI) score from baseline at week 28 were rerandomized to receive placebo (N = 113) or continue TIL 100 mg (N = 116). Residual disease (PASI score) and adverse events (AEs) were evaluated every 4 weeks through week 64. Relapse was defined as ≥50% loss of maximum PASI response; successful retreatment as regaining ≥50% of previous maximum PASI response. Patients rerandomized to placebo who relapsed were reassigned to TIL 100 mg; those retreated for ≥12 weeks were included in efficacy analyses. Missing data were imputed using last-observation-carried-forward.

Results: The 61/113 (54.0%) patients rerandomized to placebo who relapsed had median PASI scores at baseline, week 28, and time of relapse of 20.3, 0.8, and 11.0, respectively. Median (interquartile range [IQR]) time to relapse was 238 (167, 294) days. Among 51 patients retreated for ≥12 weeks, median (IQR) time to regain response was 28 (28, 48) days. Median PASI scores were 5.9, 3.2, and 2.7 after 4 (n = 51), 8 (n = 46), and 12 weeks (n = 33) of retreatment, respectively. At week 64 (n = 61), 72.1%/31.2%/13.1% of these patients achieved PASI 75/90/100 responses, respectively.

The 52/113 (46.0%) patients who did not relapse 36 weeks after rerandomization to placebo (week 64) had median PASI scores of 0.8, 2.6, and 4.0 at weeks 28, 52, and 64, respectively. Of patients who continued TIL, 8/116 (6.9%) relapsed after week 28—7 on only 1 visit—and 100% completed the study with median (IQR) PASI score 1.4 (0.0, 3.4). For 108/116 (93.1%) patients who maintained response on TIL 100 mg, median (IQR) PASI at weeks 28, 52, and 64 was 1.0 (0.0, 2.2), 1.0 (0.0, 2.4), and 1.2 (0.0, 3.0).

Two AEs of interest occurred in 2/113 (1.8%) responders rerandomized to placebo after week 28 (cerebellar infarction and basal cell carcinoma). In patients rerandomized to TIL after week 28 (including partial responders), 3/135 (2.2%) reported 4 AEs of interest (basal cell carcinoma, Bowen's disease, carcinoma in situ of the skin, and sinusitis).

Conclusion: In reSURFACE 1, 46.5% of patients treated with TIL 100 mg for 28 weeks and rerandomized to placebo for 36 weeks did not relapse 48 weeks after last TIL dose. In patients who relapsed, residual disease was successfully treated with TIL 100 mg within a median of 28 days. Continuation of TIL was associated with low residual disease; 93.1% of patients responded and all completed the study. Approximately 50% of patients who continued TIL 100 mg to week 52 had residual PASI scores ≤1.0.

Medical writing support was provided by Judy Phillips, DVM, PhD, of AlphaBioCom, LLC.

Reference

1. Reich K, et al. Lancet. 2017;390:276–288.

Disclosure: W. Cantrell, None; **P. Lee**, Merck, 9; **E. Tanghetti**, Galderma, 5, Allergan, 5, Hologic, 5, Novartis, 5, Ortho Derm, 5; **A. Mendelsohn**, Johnson and Johnson, 1, 4, Sun Pharmaceutical Industries, Inc, 3, Sun Pharmaceutical Industries, Inc., 3; **J. Parno**, Kyowa Kirin Pharmaceutical Development, Inc, 9, Kyowa Kirin Pharmaceutical Development, Inc., 9, Sun Pharmaceutical Industries, Inc, 3, 9; **S. Rozzo**, Sun Pharmaceutical Indsutries, Inc, 3, Sun Pharmaceutical Industries, Inc, 3, Sun Pharmaceutical Industries, Inc., 3; **W. Liao**, AbbVie, 2, Amgen, 2, Janssen, 2, Novartis, 2, Regeneron/Sanofi, 2, Pfizer, 2.

Abstract Number: 1527

Limited Changes in Hematological Parameters During Tildrakizumab Treatment: Post Hoc Analysis of Data from the Tildrakizumab Psoriasis Clinical Program

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Background/Purpose: Tildrakizumab (TIL) is a high-affinity, anti–interleukin-23p19 monoclonal antibody with demonstrated efficacy for the treatment of chronic plaque psoriasis in a phase 2b (P05495 [NCT01225731]) and 2 phase 3 clinical studies (reSURFACE 1 [NCT01722331] and 2 [NCT01729754]).[1,2] We evaluated hematological laboratory findings for evidence of drug-induced changes following TIL treatment using data from 3 randomized, placebo-controlled trials.

Methods: Data were pooled from the P05495 and reSURFACE 1 and 2 trials of patients with moderate to severe chronic plaque psoriasis. Here we report changes at week 52 vs baseline in hematological parameters for patients with continuous exposure to TIL 100 mg or 200 mg administered at week 0 and week 4, and every 12 weeks thereafter up to week 52 (P05495 and reSURFACE 2) or week 64 (reSURFACE 1). An analysis of changes in hematological parameters from baseline to worst values obtained relative to reference ranges is also reported.

Results: Among patients with continuous exposure to TIL 100 mg and 200 mg, limited changes in hematological parameters were observed. Mean (standard deviation) changes at week 52 vs baseline for TIL 100 mg (N = 249 patients with data) were 0.3% (2.4) for hematocrit, 0.1 g/dL (0.7) for hemoglobin, $-4.0 \times 10^3/\mu L$ (37.0×10^3) for platelets, $0.1 \times 10^3/\mu L$ (0.4×10^3) for lymphocytes, $0 \times 10^6/\mu L$ (0.3×10^6) for erythrocytes, and $-0.5 \times 10^3/\mu L$ (1.6×10^3) for neutrophils. Corresponding values for TIL 200 mg (N = 204 patients with data) were 0.3% (2.4) for hematocrit, 0.1 g/dL (0.8) for hemoglobin, $-6.8 \times 10^3/\mu L$ (36.9×10^3) for platelets, $0 \times 10^3/\mu L$ (0.5×10^3) for lymphocytes, $0 \times 10^6/\mu L$ (0.2×10^6) for erythrocytes, and $-0.4 \times 10^3/\mu L$ (1.9×10^3) for neutrophils. Similarly, limited changes were also seen for leukocytes, monocytes, eosinophils, lymphocytes/leukocytes, eosinophils/leukocytes, and basophils/leukocytes. The majority of patients (80.1%–100%) had hematological parameter values within normal ranges at baseline; worst values for most of these patients remained within normal ranges over 52 weeks. No changes correlated with adverse events such as infections or thrombocytopenia.

Conclusion: In this pooled analysis of phase 2b and phase 3 trials, only limited changes in hematological parameters—including white blood cells, erythrocytes, and platelets—were observed in patients treated with TIL over 52 weeks. Based on these data, patients receiving TIL are unlikely to require routine laboratory testing for hematological parameters.

Medical writing support was provided by Judy Phillips, DVM, PhD, of AlphaBioCom, LLC.

References

1. Papp K, et al. *Br J Dermatol*. 2015;173:930–939.
2. Reich K, et al. *Lancet*. 2017;390:276–288.

Disclosure: H. Glover, Pfizer, 5, 8, Galderma, 5, 8, Aqua, 5, 8, Ortho Dermatologics, 5, 8; **K. Kucera**, AbbVie, 5, 8, Novartis, 5, 8, Ortho Dermatologics, 5, 8, Pfizer, 5, 8, Encore, 5, 8, Sun Pharmaceutical Industries, Inc, 5, 8; **A. Mendelsohn**, Johnson and Johnson, 1, 4, Sun Pharmaceutical Industries, Inc, 3, Sun Pharmaceutical Industries, Inc., 3; **J. Parno**, Kyowa Kirin Pharmaceutical Development, Inc, 9, Kyowa Kirin Pharmaceutical Development, Inc., 9, Sun Pharmaceutical Industries, Inc, 3, 9; **S. Rozzo**, Sun Pharmaceutical Indsutries, Inc, 3, Sun Pharmaceutical Industries, Inc, 3, Sun Pharmaceutical Industries, Inc., 3; **F. Ferritto**, Promius, 5, 8, EPI, 5, 8, AbbVie, 5, 8, Encore, 5, 8; **R. Block**, Ortho Dermatologics, 8, Cutanea, 8, Medimetriks, 4.

Abstract Number: 1528

Resolution of Enthesitis and Dactylitis Is Maintained over Two Years of Ixekizumab Treatment in Patients with Psoriatic Arthritis

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Background/Purpose: Enthesitis and dactylitis are prominent peri-articular domains of involvement in PsA.[1] The activity of enthesitis and dactylitis can vary over time.[1] Some conventional and more biologic DMARDs have demonstrated improvements in enthesitis and dactylitis. Ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets IL-17A, has shown sustained improvement in signs and symptoms of active PsA, including enthesitis and dactylitis.[2] The purpose of this study is to examine patients who had resolution of enthesitis and dactylitis with treatment, to see if efficacy was maintained for up to 2 years of IXE treatment.

Methods: Data was integrated from two Phase 3, double-blind, randomized controlled trials in biologic DMARDs-naïve (SPIRIT-P1) and TNF inhibitor (TNFi; SPIRIT-P2) experienced patients who received subcutaneous: placebo, adalimumab (SPIRIT-P1 only; reference arm) 40 mg every 2 weeks, or IXE 80 mg every 2 weeks (Q2W) or every 4 weeks (Q4W) after a 160-mg starting dose. At Week 24, PBO patients were re-randomized to IXEQ2W or IXEQ4W. All

Table. Baseline demographics of the maintenance primary population

	LEI=0		LDI-B=0	
	IXE Q4W/Q4W (N=80)	IXE Q2W/Q2W (N=65)	IXE Q4W/Q4W (N=76)	IXE Q2W/Q2W (N=51)
Age (years)	48.2 (12.4)	48.7 (13.4)	47.3 (12.1)	47.2 (12.8)
Male, n (%)	39 (48.8%)	31 (47.7%)	41 (53.9%)	26 (51.0%)
Time since PsA onset (years)	10.6 (9.8)	10.9 (7.1)	10.0 (8.1)	9.5 (7.3)
TJC (68 joints)	19.5 (11.7)	20.8 (13.8)	21.6 (12.8)	22.6 (15.4)
SJC (66 joints)	12.6 (9.3)	11.8 (8.4)	14.5 (11.4)	15.2 (10.1)
CRP (mg/L)	17.7 (27.4)	12.5 (21.2)	16.4 (24.3)	19.0 (31.7)
LEI>0	2.5 (1.4)	2.5 (1.5)	2.9 (1.5)	3.1 (1.6)
LDI-B>0	67.3 (97.9)	54.7 (35.4)	59.4 (90.8)	52.2 (42.2)

Unless otherwise indicated, data presented here are mean (SD).

IXE=ixekizumab; IXE80Q2W=IXE 80 mg every 2 weeks; IXE80Q4W=IXE 80 mg every 4 weeks; LDI-B=Leeds dactylitis index-basic; LEI=Leeds enthesitis index; N=total number of analyzed patients in each subgroup; SD=standard deviation; SJC= swollen joint count; TJC=tender joint count.

patients met the Classification Criteria for PsA. Maintenance primary population included patients who were initially randomized to IXE, completed their Week 24 visit, and had resolution of baseline enthesitis or dactylitis at Week 24. Resolution was defined as Leeds enthesitis index (LEI=0) or Leeds dactylitis index-basic (LDI-B=0). Percentage of patients who maintained LEI and LDI-B resolution were presented up to Week 108 by using the observed method.

Results: In this analysis, we evaluated patients that had enthesitis (LEI >0; N=145) and/or dactylitis (LDI-B >0; N=127) present at baseline that had resolved at Week 24 of IXE treatment. Baseline LEI scores were 2.5 for patients who had resolved their enthesitis, and baseline LDI-B scores were 56.7 for patients who had resolved their dactylitis. Patient demographics and disease characteristics in both groups were similar (Table). Resolution of enthesitis and dactylitis was maintained up to 108 weeks of continuous IXE treatment by LEI=0 (>80%) and LDI-B=0 (100%) groups, respectively. Responses were similar for both IXE dosing regimens (Figure).

Conclusion: Resolution of enthesitis or dactylitis can be maintained over 2 years of treatment with IXE in patients with PsA.

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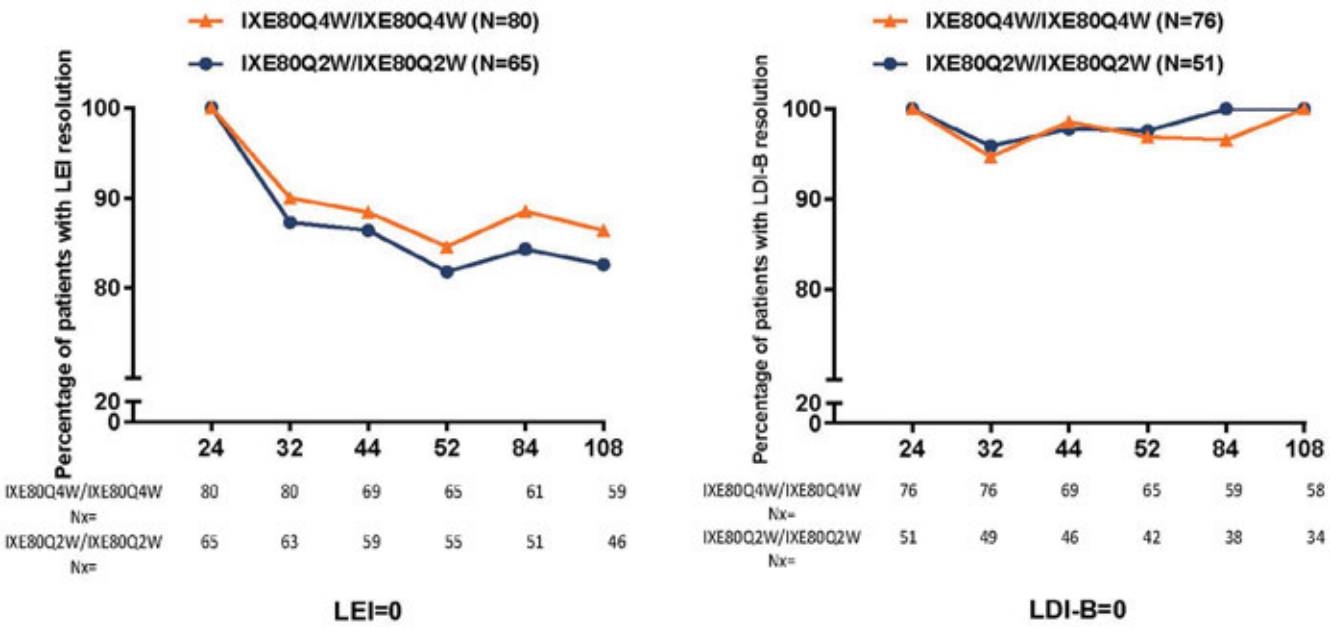

Figure.

Disclosure: A. Kavanaugh, Abbott, 2, Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, 2, Amgen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 2, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, Pfizer Inc, 2, Roche, 2, UCB Pharma, 2; **L. Eder**, Abbvie, 2, 5, 8, Celgene, 5, Janssen, 5, Lily, 2, 5, Novartis, 2, 5, Pfizer, 2, 8, UCB, 2; **J. Smolen**, AbbVie, 2, 5, 8, Abbvie, 2, 5, Amgen, 5, 8, AstraZeneca, 2, 5, 8, Astra-Zeneca, 5, Astro, 5, 8, BMS, 5, Celgene, 5, 8, Celltrion, 5, Celtrion, 5, 8, Chugai, 5, Eli Lilly and Company, 2, 5, Gilead, 5, GlaxoSmithKline, 5, 8, ILTOO, 5, 8, ILTOO Janssen, 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Medimmune, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, Novartis- Sandoz, 5, Novartis-Sandoz, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 5, Roche, 2, 5, Roche;, 2, 5, 8, Samsung, 5, 8, Sanofi, 5, 8, Sanofi-Aventis, 5, UCB, 5, 8; **M. Hufford**, Eli Lilly and Company, 1, 3; **C. Lin**, Eli Lilly and Company, 1, 3; **A. Trevelin Sprabery**, Eli Lilly and Company, 1, 3; **D. McGonagle**, AbbVie, 9, Abbvie, 2, 8, BMS, 9, Celgene, 2, 8, 9, Janssen, 2, 8, Johnson & Johnson, 9, Lilly, 2, 8, MSD, 9, Novartis, 2, 8, 9, Pfizer, 2, 8, 9, UCB, 8, 9.

Abstract Number: 1529

The Efficacy and Safety of Anti-TNFα Treatment in Ankylosing Spondylitis Patients with Late Onset Compared to Those with Adult Onset; The Data from TURKBIO Registry

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The first symptoms of ankylosing spondylitis (AS) patients usually begin prior to 45 years, but can occur later in life. The purpose of this study is to evaluate the efficacy and safety of anti-TNFα treatment in late-onset AS (LoAS) patients in comparison to those with adult onset AS (AoAS).

Methods: We studied AS patients in TURKBIO registry between the dates of January 2011 and November 2018. All the patients fulfilled the modified New York criteria for AS and were classified into 2 groups based on their age at symptom onset: AoAS (age >16 but ≤45 years); and LoAS (age >45 years). In both groups, the following data were evaluated and compared: (1) epidemiological variables (2) clinical manifestations, including signs and symptoms at diagnosis; (3) laboratory results (4) disease activity markers and follow-up parameters (BASDAI, ASDAS-CRP and HAQ); (5) previous and current treatments (6) adverse events.

Results: A total of 2551 AS patients (91,1% with AoAS and 8.9% with LoAS) were included in the study. LoAS group had more female patients, older age, shorter disease duration, shorter diagnostic delay, higher initial ESR and less HLA-B27 positivity compared to the AoAS (Table 1). Peripheral arthritis (not statistically significant) and dactylitis was seen more common in the LoAS. The frequency of other involvements was similar between the groups (Table1).The frequency of using drugs was similar between each groups although the use of glucocorticoids and sulphasalazine was more common in the LoAS. Switching from the first anti-TNFa treatment to the second one was more common in the AoAS. However, there was found no significant difference between the two groups in 2 or more switch ratios (Table 1). At the latest visit after the anti-TNFα therapy, the mean improvement in BASDAI was significantly higher in the AoAS (Table 2). A total of 10 (4.4%) serious adverse events were reported in LoAS and 39 (1.7%) in AoAS patients in the follow-up (HR: 2.62; 95% CI: 1.32–5.18). Severe infections were the most commonly seen serious adverse events (1.3% in LoAS and 0.8% in AoAS), followed by rash and allergic reactions (0.9% in LoAS and 0.3% in AoAS).

Table 1. Demographic and clinical characteristics of patients with AoAS and LoAS

	AoAS (≤45 yrs)	LoAS (>45 yrs)	p-value
N	2324	227	
Sex (male), n (%)	1411 (61)	109 (48)	**<0.001**
Age, yrs	43.07 ± 10.26	62.10 ± 8.59	**<0.001**
Duration of disease, yrs	14.50 ± 9.42	8.53 ± 6.27	**<0.001**
Delay of diagnosis, yrs	6.12 ± 6.61	3.59 ± 4.37	**<0.001**
HLA-B27 positivity, (%)	64	44	**<0.001**
Uveitis, n (%)	192 (8)	14 (6)	0.328
Peripheral arthritis, n (%)	389 (17)	50 (22)	0.055
Enthesitis, n (%)	339 (15)	31 (14)	0.779
Dactylitis, n (%)	77 (3)	15 (7)	**0.019**
Inflammatory bowel disease, n (%)	41 (2)	7 (3)	0.254
Psoriasis, n (%)	30 (1)	0 (0)	0.162
Treatment, n (%)			
NSAIDs	762 (33)	70 (31)	0.600
Sulphasalazine	176 (8)	35 (15)	**<0.001**
Methotrexate	111 (5)	16 (7)	0.179
Glucocorticoid	62 (3)	15 (7)	**0.002**
Anti-TNFα	1467 (63)	134 (59)	0.252
Secukinumab	31 (1)	2 (1)	0.788
Anti-TNFα switch, n (%)			
One switch	359 (15)	22 (10)	**0.026**
Two switch	113 (5)	7 (3)	0.297
Three switch	25 (1)	3 (1)	0.996
Four switch	8 (0.3)	0 (0)	0.792

AoAS: adult-onset ankylosing spondylitis, **LoAS:** late-onset ankylosing spondylitis

***Continuous variables were presented as mean ±SD for both table**

Tuberculosis was observed in 2 patients (0.9%) in LoAS and 9 (0.4%) in AoAS, malignancy in 3 patients (1.3%) in LoAS and 6 (0.3%) in AoAS.

Conclusion: Our data showed that almost 8.9% of the patients with AS had late-onset of symptoms. The results suggested that LoAS patients might have different demographic, clinical features, disease activity parameters at baseline. The frequency of anti-TNFα use and response rate to the treatment was also similar in LoAS to those in AoAS patients. The patients with LoAS seem to have more common severe adverse events compared to the AOAS patients possibly related to their older age.

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Table 2 Changes in follow-up parameters between the baseline and the latest visits in patients on biologicals

	AoAS (≤45 yrs) n. 1467			LoAS (>45 yrs) n. 134		
	Baseline (mean±SD)	**Latest follow up (mean±SD)**	**Change (mean±SD)**	**Baseline (mean±SD)**	**Latest follow up (mean±SD)**	**Change (mean±SD)**
BASDAI	38.9±22.6	23.7±21.6*	15.2±23.6	34.6±22.1	23.4±21.1*	11.2±20.8**
BASFI	29.3±22.7	20.9±19.9*	8.3±20.2	30.4±23.8	24.1±23.4*	6.3±20.3
ASDAS-CRP	2.70 ± 1.19	1.98 ± 1.08*	0.72 ± 1.23	2.69 ± 1.21	2.03 ±1.08*	0.65 ± 1.17
CRP (mg/L)	16.66+24.32	11.33+18.87*	5.33+24.60	19.20+26.37	13.71+18.27*	5.49+25.25
HAQ	0.78±0.60	0.59±0.47*	0.19±0.52	0.92±0.69	0.71±0.58*	0.21±0.55

*Baseline vs the latest visits, $p<0.05$
**Change between the baseline and the latest visits in AoAS vs LoAS groups, $p<0.05$

O. Gunduz, None; **A. Tufan**, None; **S. Akar**, Abbvie, 2, 5, Amgen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5; **M. Birlik**, None; **I. Sari**, None; **N. Akkoç**, None; **F. Onen**, Tofacitinib (Pfizer), 8.

Abstract Number: 1530

Real World Effectiveness of Secukinumab in Patients with Ankylosing Spondylitis: Findings from a Recent Cross Sectional Survey of Rheumatologists and Patients in Europe

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) can lead to reduced physical functioning and quality of life. Secukinumab has demonstrated clinical benefits in AS patients in clinical trials[1-2]. The purpose of this study was to assess effectiveness of secukinumab in AS in a real-world setting.

Methods: This was a cross-sectional survey of rheumatologists and patients in France, Germany, Italy, Spain, and UK. Data were collected online from June-December 2018 via physician-completed patient record forms. Patients receiving any treatment for AS were included in the survey (n=1392). Patients receiving secukinumab >4 months were included in this analysis. Physicians reported patient overall disease severity (mild/moderate/severe), pain (1-10 scale), global VAS score, and BASDAI score for 2 time points – the initiation of secukinumab, and at the time of data

Table 1: Patient outcomes at initiation of secukinumab and at their current consultation, mean (SD)

	At initiation of secukinumab (n=359)	At current consultation (n=359), length of time received secukinumab		
		4-<6 months (n=54)	6-<12 months (n=171)	12+ months (n=134)
Overall disease severity, n (%)				
Mild	7 (1.9)	32 (59.3)	116 (67.8)	91 (67.6)
Moderate	179 (49.8)	21 (38.9)	48 (28.1)	42 (31.3)
Severe	171 (47.6)	1 (1.9)	7 (4.1)	1 (0.7)
Don't know	2 (0.6)	-	-	-
BASDAI score[a]	6.2 (1.9)	3.1 (1.8)	2.9 (1.7)	2.9 (2.0)
BASDAI score < 4, n (%)[a]	17 (10)	11 (52.4)	56 (66.7)	52 (68.4)
Pain score (1-10)	7.1 (1.4)	3.4 (1.6)	3.3 (1.8)	2.8 (1.7)
Physician global VAS score (1-100)[a]	56.2 (24.2)	25.5 (25.8)	21.9 (19.5)	25.3 (21.1)
Patient global VAS score (1-100)[a]	63.4 (26.4)	22.9 (20.7)	26.2 (20.2)	27.5 (23.5)

[a]Calculated on available data.

collection (current consultation). Outcomes at the current consultation were grouped according to length of time receiving secukinumab (4 - < 6, 6 - < 12, 12+ months). Physicians also reported patient demographic and disease characteristics, current symptoms present, concomitant and previous treatments, time since diagnosis, and physician satisfaction with secukinumab, while patients reported their current satisfaction, quality of life, work, and functioning measures at their current consultation (EQ5D, WPAI, ASAS HI). Data were analysed descriptively.

Results: 359 AS patients were receiving secukinumab >4 months at their current consultation. Patient mean age was 45.4 years, with 25% female, 67% working full time, and a mean BMI of 25.7. On average, patients were diagnosed with AS for 7.1 years, had received secukinumab for 10.6 months, and for 53% of patient secukinumab was their 1st advanced therapy (specifically bDMARDs or tsDMARDs), 30% their 2nd and 17% their 3rd or more. 15% of patients were also receiving a csDMARD concurrently. 9% of patients had enthesitis, and 20% had spinal fusion. Patients reported a mean EQ5D utility score of 0.83, mean WPAI overall work impairment percentage of 27.4%, and mean ASAS HI score of 5.4 at their current consultation. 83% of patients and 92% of physicians reported being satisfied with secukinumab.

Between initiation of treatment and their current consultation, patients achieved a reduction in disease activity scores and disease severity. The proportion of patients achieving a BASDAI score < 4, increased from 10 to 68%. This pattern was seen regardless of length of time receiving secukinumab (Table 1).

Conclusion: Secukinumab provided overall effectiveness and satisfaction in both physicians and patients in a real-world, clinical setting. Significant improvements were seen across all outcomes, regardless of length of time receiving treatment, highlighting an early and sustained response to secukinumab.

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Novartis, 3; **P. Conaghan**, Abbvie, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, 8, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Eli Lilly, 8, EMD, 5, EMD Serono, 5, EMD Serono Research and Development Institute, Inc., 5, 8, Flexion, 5, 8, Flexion Therapeutics, 5, 8, Galapagos, 5, 8, Glaxo Smith Kline, 5, GlaxoSmithKline, 5, 8, Lilly, 8, Medivir, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Samumed, 5, 8, Serono, 5, Stryker, 5, 8.

Abstract Number: 1531

ALPN-101, a First-in-Class Dual ICOS/CD28 Antagonist, Suppresses Key Effector Mechanisms Underlying Rheumatoid and Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: ALPN-101 is an Fc fusion protein of a human inducible T cell costimulator ligand (ICOSL) variant immunoglobulin domain (vIgD™) designed to simultaneously inhibit the CD28 and ICOS costimulatory pathways. CD28 and ICOS each play a role in T cell activation and adaptive immunity which can contribute to autoimmune disease when dysregulated. ALPN-101 has previously been shown to have potent immunosuppressive activity in various *in vitro* and *in vivo* models of disease, including acute graft-versus host disease and multiple sclerosis. We report here *in vitro* analyses using PBMC from rheumatoid arthritis (RA) and psoriatic arthritis (PsA) patients and from healthy donors. ALPN-101 demonstrated superior suppression of human T cell activation and potent reduction of inflammatory mediators known to contribute to the pathogenesis of RA, PsA, and juvenile idiopathic arthritis (JIA). Additionally, the efficacy of ALPN-101 was confirmed *in vivo* in a mouse model of collagen-induced arthritis (CIA).

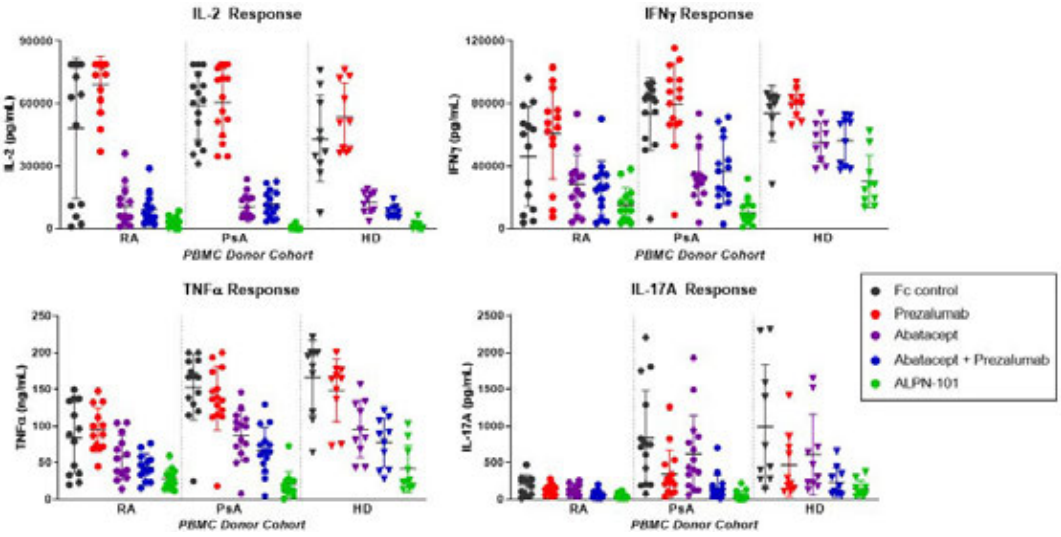

Figure 1: ALPN-101 Potently Inhibits T Cell Activation In Vitro in PBMC from Healthy Donors, Rheumatoid Arthritis, and Psoriatic Arthritis Patients. In vitro stimulation of healthy donor (HD), rheumatoid arthritis (RA), and psoriatic arthritis (PsA) patient PBMC with artificial APC [fixed K562 expressing cell surface OKT3 (anti-CD3)/CD80/CD86/ICOSL)] at a 20:1 ratio. Test articles were added at 100 nM and supernatants were collected and assayed for cytokine concentrations after a 48 hr incubation. ALPN-101 demonstrated statistically significant superiority to prezalumab, abatacept, or a combination of prezalumab+abatacept for the majority of donors and analytes tested.

Methods: Healthy donor, RA, and PsA patient PBMC or Th17-skewed T cell cultures were stimulated with K562 cells expressing CD80, CD86, ICOSL, and anti-CD3 (OKT3) to evaluate the potency of ALPN-101 to suppress pro-inflammatory cytokine production. The activity of dual pathway inhibition by ALPN-101 was compared to the CD28-only inhibitor abatacept (CTLA-4-Fc) and to the ICOS pathway inhibitor prezalumab (AMG-557; anti-ICOSL, Creative Biolabs). ALPN-101 was tested *in vivo* vs. abatacept in a CIA model in which male DBA/1 mice were immunized with bovine collagen in Freund's adjuvant on Days 0 and 18.

Results: Compared to abatacept, prezalumab, or combination abatacept + prezalumab, ALPN-101 demonstrated superior suppression of pro-inflammatory cytokine (i.e. TNF-α, IFN-γ, IL-1β, IL-2, IL-6, IL-17A, GM-CSF, RANKL, etc.) release from stimulated healthy and patient PBMCs (Fig. 1), and suppressed T cell proliferation in Th17-skewed cultures. The administration of ALPN-101 also consistently resulted in significant disease reduction in the mouse CIA model (including decreased paw inflammation, serum cytokines, and anti-collagen antibodies), matching or exceeding the activity of abatacept.

Conclusion: The immunosuppressive efficacy of dual CD28/ICOS antagonist ALPN-101 is superior to CD28 or ICOS costimulatory pathway inhibitors, administered individually or in combination, in human *in vitro* and/or mouse *in vivo* translational studies. The data suggest that ALPN-101 may significantly improve upon the clinical efficacy of currently approved therapeutics like abatacept for treatment of inflammatory diseases, including rheumatoid, psoriatic, and juvenile idiopathic arthritis. A Phase 1 clinical trial with ALPN-101 in healthy volunteers is underway, and trials in inflammatory arthritis and other inflammatory diseases are targeted to begin soon.

Disclosure: L. Evans, Alpine Immune Sciences, 1, 3, 4; **S. Dillon**, Alpine Immune Sciences, 1, 3, 4; **K. Lewis**, Alpine Immune Sciences, 1, 3, 4; **S. Bort**, Alpine Immune Sciences, 1, 3, 4; **E. Rickel**, Alpine Immune Sciences, 1, 3, 4; **J. Yang**, Alpine Immune Sciences, 1, 3, 4; **M. Wolfson**, Alpine Immune Sciences, 1, 3, 4; **S. Mudri**, Alpine Immune Sciences, 1, 3, 4; **K. Susmilch**, Alpine Immune Sciences, 1, 3, 4; **S. Levin**, Alpine Immune Sciences, 1, 2, 3, 4; **S. MacNeil**, Alpine Immune Sciences, 1, 3, 4; **M. Rixon**, Alpine Immune Sciences, 1, 3, 4; **J. Hillson**, Alpine Immune Sciences, 1, 3, 4; **S. Peng**, Alpine Immune Sciences, 1, 3, 4, 6; **K. Swiderek**, Alpine Immune Sciences, 1, 3, 4.

Abstract Number: 1532

Withdrawal of Ixekizumab Results in Loss of Efficacy in Multiple Clinical Domains in Patients with Psoriatic Arthritis Who Had Achieved Minimal Disease Activity: Results from the SPIRIT-P3 Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Ixekizumab (IXE), a high affinity monoclonal antibody that selectively targets interleukin-17A, has been demonstrated to improve the signs and symptoms, disease activity, and quality of life of patients with

MDA Component	Treatment	N	Events		Median time to loss of response in weeks (95% CI)	p-value
			n	%		
TJC ≤1[a]	IXE	56	27	48	64.3 (24.14, NA))	0.002
	PBO	57	41	72	22.3 (12.29, 28.71)	
SJC ≤1[b]	IXE	72	11	15	NA (NA, NA)	<.001
	PBO	73	33	45	28.7 (20.14, NA)	
PASI Total Score ≤1[c]	IXE	73	9	12	NA (NA, NA)	<.001
	PBO	77	34	44	36.0 (24.14, 48.14)	
BSA ≤3%[d]	IXE	73	3	4	NA (NA, NA)	<.001
	PBO	78	19	24	NA (36.00, NA)	
Pain VAS Score ≤15[e]	IXE	72	30	42	NA (36.14, NA)	<.001
	PBO	68	61	90	16.1 (12.14, 22.71)	
Patient Global disease Activity VAS Score ≤20[f]	IXE	77	20	26	NA (NA, NA)	<.001
	PBO	74	56	76	20.57 (16.14, 28.14)	
HAQ-DI ≤0.5[g]	IXE	69	14	20	NA (NA, NA)	0.759
	PBO	68	15	22	NA (48.14, NA)	
Tender Entheseal Points ≤1[h]	IXE	73	15	21	NA (NA, NA)	0.427
	PBO	72	14	19	NA (60.29, NA)	

p-value is from adjusted log-rank test stratified by geographic region and cDMARD use

[a]RWITT population who had TJC ≤1 at randomization; [b]RWITT population who had SJC ≤1 at randomization; [c]RWITT population who had PASI ≤1 at randomization; [d]RWITT population who had BSA ≤3 at randomization; [e]RWITT population who had pain VAS ≤15 at randomization; [f]RWITT population who had Patient Global Disease Activity VAS ≤20 at randomization; [g]RWITT population who had HAQ-DI ≤0.5 at randomization; [h]RWITT population who had tender Entheseal Points ≤1 at randomization

Percentage was calculated as n/N X 100

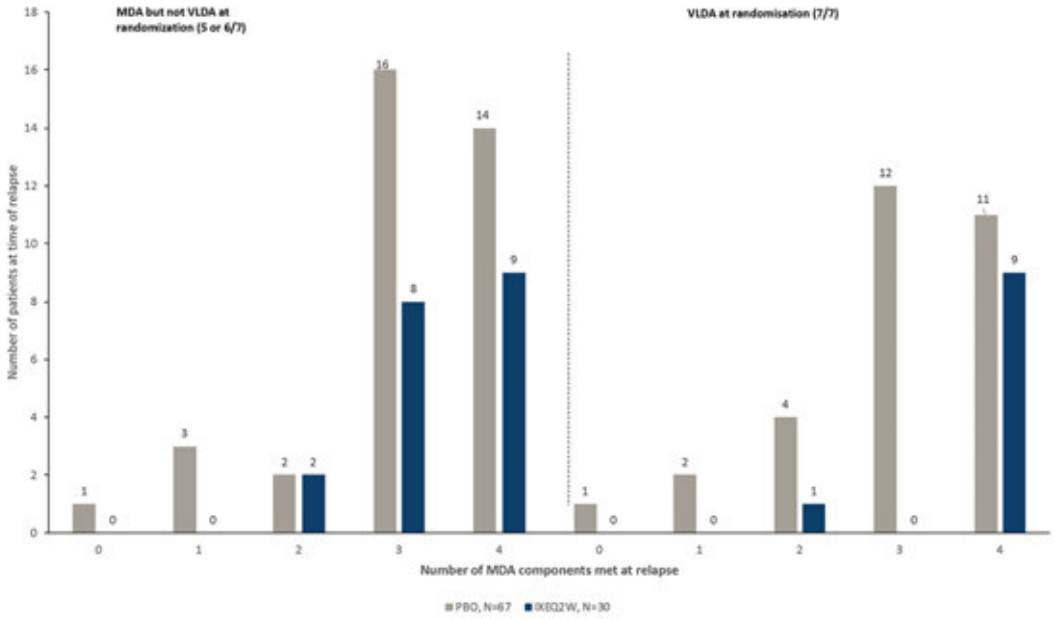
NA=cannot be estimated due to insufficient events in analysis duration

BSA=Body Surface Area; cDMARD=conventional synthetic DMARD; CI=confidence interval; HAQ-DI=Health Assessment Questionnaire Disability Index; IXE=ixekizumab; MDA=minimal disease activity; N=number of patients who met the individual MDA component at time of randomization in each category; n=number of patients with loss of response in each category; PASI=Psoriasis Area and Severity Index; PBO=placebo; RWITT=randomized withdrawal intent-to-treat; SJC=Swollen Joint Count; TJC=Tender Joint count; VAS=Visual Analog Scale

Table. Time to loss of response of individual components of MDA in RW intent-to-treat population

active PsA. SPIRIT-P3 was a randomized withdrawal (RW) phase 3b clinical trial that demonstrated that in patients who achieved sustained minimal disease activity (MDA) after open label (OL) IXE treatment, continued IXE treatment was superior to IXE withdrawal (placebo, PBO) in maintaining MDA. In this pre-specified and post-hoc analysis, we assessed the impact of IXE withdrawal on the individual components of MDA.

Methods: In SPIRIT-P3 (NCT02584855), patients with active PsA who were naïve to biologic DMARDs received OL treatment with IXE 80 mg every two weeks (Q2W) after a 160-mg starting dose for at least 36 weeks. Patients who achieved MDA (at least 5 out of 7 components [see table]) for three consecutive months between Weeks 36 and 64 were flexibly randomized 1:1 to IXE Q2W or placebo (PBO) and evaluated up to Week 104 in a double-blind manner. Patients were considered relapsed if they lost MDA at any point during the RW and received IXEQ2W thereafter. Kaplan-Meier product limit method was used to estimate time to loss of response of individual components in the RW intent-to-treat population. Treatment comparisons were done between groups using adjusted log-rank test stratified



IXE=ixekizumab; MDA=minimal disease activity; N=number of patients in each group; PBO=placebo; VLDA=very low disease activity.

Figure. Patients meeting number of components of MDA met at the time of relapse in PBO and IXE groups in relapse population

by geographic region and conventional synthetic DMARDs (cDMARD) use. A p-value < 0.05 was considered to be significant. Number of components of MDA met at randomization and at time of relapse in both PBO and IXE groups were assessed in the relapse population.

Results: A total of 394 patients entered into the OL treatment period; 158 (40%) of whom met three consecutive months of MDA and randomized to IXE (N=79) or PBO (N=79) in the RW period. At time of randomization, 77 patients (37 assigned to PBO; 40 assigned to IXEQ2W) had achieved very low disease activity (VLDA; i.e., meeting 7 out of 7 components). Overall, significantly more patients randomized to PBO than IXE relapsed during the RW period (data not shown). Among patients who had VLDA at randomization, 30 (81%) of PBO patients and 10 (25%) of IXE patients met relapse criteria. Time to relapse was significantly shorter in patients on PBO than IXE-treated patients for 5 out of 7 individual components (Tender joint count, Swollen joint count, PASI/BSA, patient pain VAS, Patient Global Disease Activity VAS) of MDA ($p < 0.01$, Table). Among patients who relapsed, 18 (60%) from IXEQ2W and 25 (37%) from PBO groups met 4 out of 7 components at time of relapse (figure).

Conclusion: In patients with sustained MDA, IXE withdrawal led to relapse in components of MDA, particularly tender and swollen joints, patient reported joint pain and disease activity, and psoriasis. IXE withdrawal, relative to continued treatment, was associated with relapse in multiple components of MDA within individual patients, even in patients who had achieved VLDA.

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Abstract Number: 1533

The Performance Characteristics of Composite Measures Used in a Randomized Trial Examining Etanercept and Methotrexate as Monotherapy or in Combination in Patients with Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Composite measures of disease activity are used in psoriatic arthritis (PsA), but their relative performance and contributions of individual components to overall scores are unclear. Primary results were reported* from a phase 3 trial that randomized methotrexate (MTX)- and biologic-naïve patients with active PsA to weekly: MTX 20 mg; etanercept (ETN) 50 mg; or ETN 50 mg + MTX 20 mg. At week 24, the ETN-containing arms were significant-

ly more effective than MTX monotherapy in achieving an American College of Rheumatology 20 response (primary endpoint) and Minimal Disease Activity response (key secondary endpoint). Compared with MTX monotherapy, the ETN-containing arms also had a composite score change from baseline at week 24 that was larger with Psoriatic Arthritis Disease Activity Score (PASDAS) and numerically higher with Activity Index for Psoriatic Arthritis (DAPSA).* Here we further examine the trial composite measures by analyzing contributions of individual components to the change in overall composite scores from baseline at week 24 for: PASDAS, DAPSA, Disease Activity Score (DAS28-CRP), Clinical Disease Activity Index (CDAI), and Simplified Disease Activity Index (SDAI).

Methods: Using the full analysis set of 851 patients, the median and mean (95% CI) contribution of each individual domain change to the composite measure change from baseline at week 24 was calculated. Analyses were repeated for PASDAS in patient subsets with enthesitis or dactylitis at baseline.

Results: The ETN-containing arms had a greater composite score change from baseline at week 24 compared with MTX monotherapy; PASDAS and DAS28-CRP had relatively greater changes compared with DAPSA, CDAI, and SDAI (Table 1). For DAPSA, DAS28-CRP, CDAI, and SDAI, the joint count changes contributed most to score changes, while the global assessment changes contributed less (Table 2). In contrast, the global assessment changes contributed the most to the PASDAS score changes, with less contribution from joint count changes (Table 3). Contribution of enthesitis change to the PASDAS score change in those with enthesitis at baseline was similar to that of the joint counts; in those with dactylitis at baseline, the contribution of dactylitis change was more than that of the joint counts. Except for DAS28-CRP, the composite score changes showed minimal contributions from changes in CRP. Overall, the contributions of changes in the individual components to the composite score changes were similar between treatment arms.

Conclusion: Results show that changes in "joint-focused" composite endpoints (DAPSA, DAS28-CRP, CDAI, and SDAI) are driven most by joint count changes and less by global assessment changes. Change in PASDAS, which captures a wider range of disease domains, was driven most by global assessment changes (and somewhat by physical function) and less by other domain changes depending on the patient population. Changes in CRP consistently contributed less than other components. Results were consistent across treatment arms.

*Mease et al. Arthritis Rheumatol. 2019 Feb 12. https://doi.org/10.1002/art.40851 [Epub ahead of print].

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Composite Measure: Mean (SE) change from baseline	Methotrexate Monotherapy N = 284	Etanercept Monotherapy[a] N = 284	Methotrexate plus Etanercept[a] N = 283
DAS28-CRP	-1.55 (0.08)	-1.97 (0.08) P<0.001	-1.86 (0.08) P=0.01
CDAI	-15.74 (0.85)	-17.12 (0.78) P=0.26	-16.43 (0.85) P=0.59
SDAI	-15.96 (0.86)	-17.75 (0.81) P=0.15	-17.01 (0.87) P=0.41
DAPSA	-22.59 (1.4)	-24.99 (1.3) P=0.24	-24.92 (1.4) P=0.23
PASDAS	-1.98 (0.10)	-2.64 (0.10) P<0.001	-2.63 (0.11) P<0.001

CDAI, Clinical Disease Activity Index; DAPSA, Disease Activity Index for Psoriatic Arthritis; DAS28-CRP, Disease Activity Score (28 joints) using C-reactive protein; PASDAS, Psoriatic Arthritis Disease Activity Score; SDAI, Simplified Disease Activity Index; SE, standard error.
[a]P-values are for comparisons with the methotrexate monotherapy arm and are unadjusted.

Table 1. Composite Measure Change from Baseline at Week 24

Median (mean: 95% CI) component contribution to the overall score[a]	DAPSA			DAS28-CRP			CDAI			SDAI		
	MTX N=284	ETN N=284	MTX+ETN N=283	MTX N=284	ETN N=284	MTX+ETN N=283	MTX N=284	ETN N=284	MTX+ETN N=283	MTX N=284	ETN N=284	MTX+ETN N=283
Tender Joint Count[b]	0.46 (0.61: 0.18, 1.03)	0.43 (0.69: 0.26, 1.11)	0.44 (0.4: 0.10, 0.69)	0.48 (0.49: 0.34, 0.61)	0.44 (0.68: 0.32, 1.04)	0.45 (0.55: 0.30, 0.80)	0.36 (0.38: 0.20, 0.56)	0.33 (0.33: 0.29, 0.38)	0.33 (-0.02: -0.46, 0.42)	0.36 (0.43: 0.24, 0.61)	0.32 (0.33: 0.29, 0.38)	0.32 (0.56: -0.13, 1.25)
Swollen Joint Count[c]	0.32 (0.28: 0.02, 0.55)	0.28 (0.20: 0.07, 0.33)	0.30 (0.52: -0.00, 1.03)	0.23 (0.22: 0.17, 0.27)	0.21 (0.30: 0.17, 0.43)	0.21 (0.42: 0.14, 0.69)	0.26 (0.33: 0.25, 0.40)	0.25 (0.23: 0.19, 0.27)	0.24 (0.31: 0.16, 0.47)	0.26 (0.33: 0.25, 0.41)	0.24 (0.23: 0.19, 0.27)	0.22 (0.34: 0.19, 0.49)
Physician Global Assessment	---	---	---	---	---	---	0.19 (0.27: 0.15, 0.39)	0.22 (0.28: 0.17, 0.40)	0.20 (0.45: 0.20, 0.70)	0.19 (0.42: -0.00, 0.84)	0.21 (0.11: -0.09, 0.32)	0.20 (-0.02: -0.63, 0.59)
Patient Global Assessment	0.09 (0.12: -0.02, 0.27)	0.11 (0.05: -0.15, 0.24)	0.11 (0.04: -0.08, 0.15)	0.19 (0.15: -0.00, 0.30)	0.21 (-0.04: -0.46, 0.37)	0.21 (-0.09: -0.65, 0.46)	0.14 (0.03: -0.19, 0.24)	0.17 (0.15: 0.03, 0.27)	0.16 (0.26: 0.11, 0.40)	0.13 (-0.17: -0.59, 0.26)	0.17 (0.29: 0.10, 0.48)	0.15 (0.07: -0.14, 0.29)
Patient Global Assessment Joint Pain	0.09 (0.09: -0.03, 0.21)	0.09 (0.11: 0.06, 0.16)	0.10 (0.06: -0.08, 0.17)	---	---	---	---	---	---	---	---	---
C-Reactive Protein	0.0 (-0.11: -0.37, 0.16)	0.01 (-0.04: -0.16, 0.09)	0.01 (0.00: -0.03, 0.04)	0.05 (0.16: 0.05, 0.26)	0.11 (0.07: -0.03, 0.16)	0.11 (0.13: 0.03, 0.23)	---	---	---	0.0 (-0.01: -0.05, 0.04)	0.01 0.03 (0.01, 0.06)	0.01 0.05 (0.02, 0.09)

CDAI, Clinical Disease Activity Index; CI, confidence interval; DAPSA, Disease Activity Index for Psoriatic Arthritis; DAS28-CRP, Disease Activity Score (28 joints) using C-reactive protein; ETN, etanercept; MTX, methotrexate; SDAI, Simplified Disease Activity Index.
[a]Contributions to the overall score are calculated by [change from baseline in each of the component scores / change from baseline in the overall score]. Positive values indicate changes in the same direction as the change in overall score. Negative values indicate changes in the opposite direction as the change in overall score.
[b]Represents a 28-joint count except for DAPSA, which had a 68-joint count.
[c]Represents a 28-joint count except for DAPSA, which had a 66-joint count.

Table 2. Contribution of Each Component Measure Change to the Change in the Composite Score From Baseline to Week 24 for DAPSA, DAS28-CRP, CDAI, and SDAI

Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, Roche, UCB, 2, 5, Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB, 8, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Abbvie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer and UCB., 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB, 2, Abbvie, Amgen, Brsitol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Brsitol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Brsitol Myers Squibb,Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, Amgen, 2, 5, 6, 8, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Leo, Eli Lilly, Merck, Novartis,

	PASDAS Full Analysis Set			PASDAS: Subgroup With Leeds Enthesitis Index of >0 at Baseline			PASDAS: Subgroup With Tender Dactylitis Count >0 at Baseline		
Median (mean; 95% CI) component contribution to the overall score[a]	MTX N=284	ETN N=284	MTX+ETN N=283	MTX N=191	ETN N=189	MTX+ETN N=196	MTX N=98	ETN N=96	MTX+ETN N=90
Physician Global Assessment	0.36 (-0.47; -1.93, 0.99)	0.35 (0.08; -0.48, 0.63)	0.36 (0.41; 0.21, 0.61)	0.31 (-0.90; -3.12, 1.33)	0.33 (-0.08; -0.91, 0.76)	0.34 (0.35; 0.09, 0.61)	0.31 (-1.85; -6.00, 2.29)	0.29 (0.21; 0.11, 0.31)	0.30 (0.29; 0.23, 0.35)
Patient Global Assessment	0.23 (0.41; -0.13, 0.94)	0.25 (0.31; 0.19, 0.43)	0.24 (0.47; -0.04, 0.99)	0.24 (0.55; -0.27, 1.36)	0.24 (0.28; 0.12, 0.45)	0.23 (0.58; -0.17, 1.32)	0.21 (1.00; -0.44, 2.44)	0.25 (0.26; 0.22, 0.31)	0.22 (0.27; 0.14, 0.39)
SF-36 PCS	0.10 (0.01; -0.26, 0.28)	0.09 (-0.43; -1.24, 0.37)	0.08 (0.15; 0.01, 0.29)	0.09 (-0.06; -0.45, 0.33)	0.09 (-0.69; -1.91, 0.52)	0.08 (0.21; 0.04, 0.39)	0.06 (0.15; 0.04, 0.25)	0.10 (0.10; 0.08, 0.12)	0.07 (0.15; -0.01, 0.31)
Swollen Joint Count (66)	0.09 (0.10; 0.05, 0.15)	0.08 (0.03; -0.07, 0.13)	0.08 (-0.06; -0.33, 0.21)	0.07 (0.07; -0.01, 0.14)	0.07 (-0.01; -0.16, 0.14)	0.08 (-0.11; -0.49, 0.28)	0.07 (0.13; 0.05, 0.20)	0.07 (0.06; 0.04, 0.08)	0.07 (0.12; 0.06, 0.18)
Tender Joint Count (68)	0.04 (0.02; -0.01, 0.05)	0.03 (0.05; -0.02, 0.12)	0.04 (-0.02; -0.18, 0.13)	0.03 (0.03; 0.01, 0.05)	0.03 (0.05; -0.05, 0.16)	0.03 (-0.07; -0.29, 0.15)	0.03 (0.02; -0.01, 0.05)	0.03 (0.02; 0.01, 0.04)	0.03 (0.01; -0.01, 0.04)
Leeds Enthesitis Index	0.0 (0.68; -0.22, 1.58)	0.0 (0.54; -0.48, 1.56)	0.0 (-0.07; -0.32, 0.18)	0.08 (1.04; -0.34, 2.41)	0.09 (0.83; -0.71, 2.37)	0.08 (-0.11; -0.46, 0.25)	0.0 (0.71; -0.68, 2.11)	0.05 (0.04; -0.01, 0.09)	0.05 (0.05; 0.04, 0.07)
Tender Dactylitis Count	0.0 (0.47; -0.13, 1.08)	0.0 (0.25; -0.00, 0.51)	0.0 (0.17; -0.09, 0.43)	0.0 (0.55; -0.32, 1.42)	0.0 (0.37; -0.02, 0.76)	0.0 (0.20; -0.17, 0.58)	0.21 (0.97; -0.65, 2.58)	0.16 (0.27; 0.11, 0.42)	0.17 (0.20; 0.14, 0.25)
C-Reactive Protein	0.01 (-0.23; -0.53, 0.08)	0.04 (0.17; -0.00, 0.35)	0.03 (-0.04; -0.15, 0.06)	0.02 (-0.28; -0.74, 0.17)	0.04 (0.24; -0.03, 0.50)	0.03 (-0.07; -0.22, 0.07)	0.02 (-0.13; -0.48, 0.21)	0.04 (0.04; 0.02, 0.05)	0.04 (-0.09; -0.36, 0.18)

CI, confidence interval; ETN, etanercept; MTX, methotrexate; PASDAS, Psoriatic Arthritis Disease Activity Score; PCS, physical component summary; SF-36, Short Form 36 (health survey).
[a]Contributions to the overall score are calculated by [change from baseline in each of the component scores / change from baseline in the overall score]. Positive values indicate changes in the same direction as the change in overall score. Negative values indicate changes in the opposite direction as the change in overall score.

Table 3. Contribution of Each Component Measure Change to the Change in the Composite Score From Baseline to Week 24 for PASDAS

Pfizer, Sun Pharmaceutical Industries, and UCB, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 2, 5, Boerhinger Ingelheim, 5, Bristol Myers Squibb, 2, 5, 8, Bristol Myers Squibb Co., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8, Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8; **A. Ogdie**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Takeda, 5, Amgen, 2, 4, 5, 8, Amgen to Forward National Databank, 2, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 4, 5, 8, Corrona, 5, CORRONA, 5, From Noavrtis to husband, 7, Lilly, 5, Lily, 5, Novartis, 2, 5, 7, Novartis to UPenn, 2, Novartis, Pfizer, 2, Pfizer, 2, 5, Pfizer Inc, 2, 5, Pfizer to UPenn, 2; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, GSI, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5; **V. Strand**, Abbvie, 5, AbbVie, 5, Amgen, 5, Amgen, Abbvie, Bayer, BMS, Boehringer Ingelheim, Celltrion, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, UCB, 5, AstraZeneca, 5, AURA, 8, Bayer, 5, BMS, 5, Boehringer Ingelheim, 5, Celgene, 5, Celltrion, 5, Cleveland Clinic, 8, CORRONA, 5, Crescendo, 5, Crescendo Bioscience, 5, Eli Lilly, 5, EMD Serono, 5, Genentech, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Inmedix, 5, Janssen, 5, Kezar, 5, Lilly, 5, Merck, 5, NACCME, 8, Novartis, 5, Pfizer, 5, Purdue, 8, RA Forum, 8, RAN, 8, Regeneron, 5, Roche, 5, Samsung, 5, Sandoz, 5, Sanofi, 5, Servier, 5, Setpoint, 5, SLRA, 8, UCB, 5, Up to Date, 7, Washington University, 8, WIR, 8, WRA, 8; **L. van Mens**, None; **L. Liu**, Amgen Inc., 1, 3, 4; **P. Yen**, Amgen Inc., 1, 3, 4; **D. Collier**, Amgen Inc., 1, 3, 4, Amgen, Inc, 1, 3; **G. Kricorian**, Amgen Inc., 1, 3, 4; **J. Chung**, Amgen Inc., 1, 3, 4; **P. Helliwell**, AbbVie, 2, 8, Amgen, 8, Celgen, 8, Celgene, 8, Galapagos, 8, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, Pfizer, 8, Pfizer Inc, 8, UCB, 8.

Abstract Number: 1534

Long-term Safety of Filgotinib in Patients with Psoriatic Arthritis, Week 52 Safety Data from a Phase 2 Open-Label Extension Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL) is an orally administered, selective Janus Kinase 1 (JAK1) inhibitor in development for psoriatic arthritis (PsA). Efficacy and safety of FIL in patients with active PsA were evaluated in a 16-week phase 2 study (EQUATOR)[1]. After 16 weeks, patients could roll-over to an Open Label Extension (OLE) Study (EQUATOR2) for the purpose of evaluating long-term safety and efficacy. The aim of this analysis was to assess safety and efficacy through 52 weeks of exposure to filgotinib.

Methods: Patients who completed the randomized, double-blind, placebo controlled study were eligible for participation in the OLE, during which all patients received once daily (qd) open-label FIL 200mg. In this interim analysis of OLE, for the safety analysis, all data were included from the screening in the core study up to the data cut of 18 April 2019 in the OLE. For the efficacy analysis, all data until OLE Week 52 visit (for each patient) were included (observed case analysis).

Results: Of the 131 pts randomized and dosed in EQUATOR, 124 (95%) completed the study and 122 (93%) enrolled in EQUATOR2; 50% were female and mean age was 50. At this interim analysis, 106/122 (87%) remained in the OLE (premature discontinuations during OLE due to: 4 for safety, 11 withdrew consent, and 1 for other reasons). Cumulative patient years of exposure (PYE) on FIL were 160, median time on FIL was 66 weeks. Key safety data are summarized in Table 1. Laboratory abnormalities are shown in Table 2. At week 52, 34% of the patients fulfilled criteria for minimal disease activity and 81%, 55%, and 33% of patients, respectively, achieved ACR20/50/70 responses.

Conclusion: FIL 200mg qd was generally well tolerated and the safety profile in PsA was comparable to that observed in the FIL rheumatoid arthritis studies. The data from this interim analysis suggest that further improvement of the patient condition can be expected beyond 16 weeks of treatment.

Disclosure: L. Coates, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, AbbVie, Amgen, BMS, Celgene Corporation, Eli Lilly, Galapagos, Janssen, MSD, Novartis, Pfizer, Prothena, Sun Pharma, UCB, 5, Abbvie, Amgen, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB, 5, Abbvie, Amgen, Lilly, Novartis, Pfizer, UCB, 8, AbbVie, Celgene Corporation, Eli Lilly, Janssen, Novartis, UCB, 8, AbbVie, Celgene Corporation, Eli Lilly, Novartis, Pfizer, 2, AbbVie, Celgene Corporation, Novartis, Pfizer, 2, Abbvie, Celgene, Novartis, Pfizer, Lilly, 2, Amgen, 5, 8, Biogen, 8, Bristol-Myers Squibb, 5, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, Gilead, 5, Janssen, 2, 5, 8, Janssen Research & Development,

Rate Per 100 PYE (number of events)	Filgotinib (200mg qd)	Placebo*
	PYE=160	PYE=20
Treatment-emergent AEs (TEAEs)	213.9 (342)	371.0 (74)
Serious TEAEs	5.6 (9)	5.0 (1)
TE Infections	62.5 (100)	100.3 (20)
Serious TE Infections	1.9 (3)	0
Malignancy	0.6 (1)	0
Herpes Zoster	0.6 (1)	0
Deep Vein Thrombosis/Pulmonary Embolism	0	0
Active Tuberculosis	0	0
Major Adverse Cardiac Events (adjudicated)	0.6 (1)	0
Death	0.6 (1)^	0

*Data during the core study, from patients assigned to placebo. ^1 patient died due to pneumonia on day 106 in the core study.

Table 1: Key safety events

	Filgotinib (200mg qd)	Placebo
≥ Grade 2	N=128†	N=66
Hemoglobin Decrease	0	0
Lymphocytes Decrease	11.1%	4.5%
Neutrophils Decrease	5.5%	0
Platelets Decrease	0	0
ALT Increase	1.6%	1.5%
Creatinine Increase	0.8%	0

†Total number of patients exposed to FIL in core or extension study, and to PBO in the core study

Table 2: Key treatment-emergent lab abnormalities

LLC, Lilly, 2, 5, 8, MSD, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 8, Prothena, 5, Sun Pharma, 5, UCB, 5, 8, UCB Pharma, 5; **P. Mease**, Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, Roche, UCB, 2, 5, Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB, 8, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Abbvie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer and UCB., 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB, 2, Abbvie, Amgen, Brsitol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Brsitol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Brsitol Myers Squibb,Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, Amgen, 2, 5, 6, 8, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, and UCB, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 2, 5, Boerhinger Ingelheim, 5, Bristol Myers Squibb, 2, 5, 8, Bristol Myers Squibb Co., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8,

Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, GSI, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5; **F. Van den Bosch**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie, Bristol-Myers Squibb, Celgene, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sanofi and UCB, 5, 8, ABBVIE, CELGENE, ELI LILLY, GALAPAGOS, MERCK, NOVARTIS, PFIZER, VCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **A. Rychlewska-Hanczewska**, None; **C. Tasset**, Galapagos, 1, 3, Galapagos NV, 3, 4; **L. Meuleners**, Galapagos NV, 3, 4; **M. Trivedi**, Gilead Sciences Inc, 1, 3; **J. Gao**, Gilead Sciences Inc, 1, 3; **R. Besuyen**, Galapagos NV, 3, 4; **P. Helliwell**, AbbVie, 2, 8, Amgen, 8, Celgen, 8, Celgene, 8, Galapagos, 8, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, Pfizer, 8, Pfizer Inc, 8, UCB, 8.

Abstract Number: 1535

Achievement of Very Low Disease Activity and Remission Treatment Targets Is Associated with Reduced Radiographic Progression in Patients with Psoriatic Arthritis Treated with Certolizumab Pegol

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

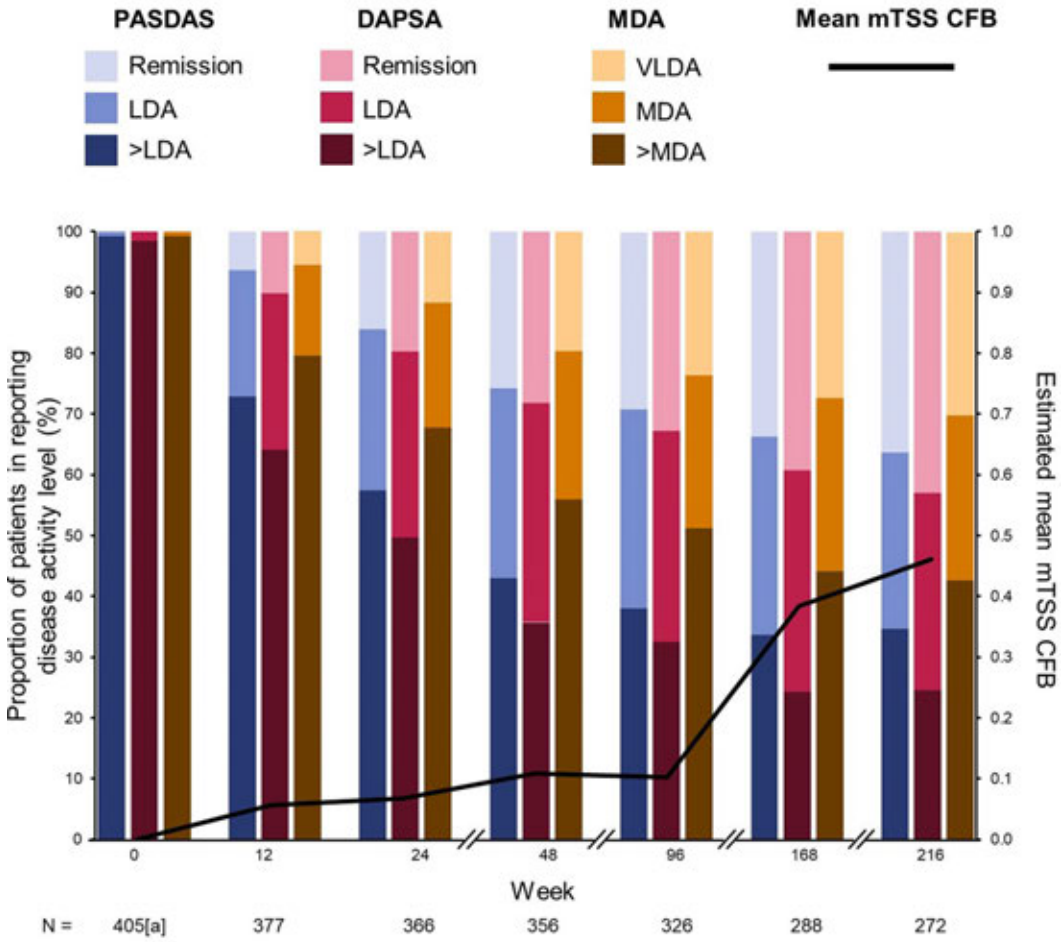
Session Time: 9:00AM–11:00AM

Background/Purpose: Several disease activity measures and thresholds have been recommended as psoriatic arthritis (PsA) treatment targets, although consensus on the most appropriate assessment tool is lacking.[1] Initial reports suggest low disease activity (LDA) and remission may be associated with minimal structural progression in PsA. Here we evaluate the relationship between PsA disease activity and structural progression over 216 weeks' (wks') treatment with certolizumab pegol (CZP), an Fc-free, PEGylated, anti-TNF that has shown long-term efficacy and safety in PsA.[2]

Methods: Patients (pts) enrolled in RAPID-PsA (NCT01087788) with active PsA (≥3 tender joints; ≥3 swollen joints; ESR≥28 mm/hour and/or CRP >upper limit of normal) who had failed treatment with ≥1 conventional synthetic DMARD were randomized 1:1:1 to CZP 200 mg every 2 wks (Q2W), CZP 400 mg every 4 wks (Q4W) (all CZP pts received CZP 400 mg at Wks 0/2/4) or placebo. CZP-randomized pts received the same dose to Wk 216; placebo-pts were re-randomized to CZP 200 mg Q2W or 400 mg Q4W at Wk 16 or 24.[2]

Pts were heterogenous for structural damage and disease duration at baseline. Disease activity was assessed using 3 disease activity measures: minimal disease activity (MDA) criteria (achievement of MDA=5–6/7 MDA criteria; achievement of very LDA [VLDA]=7/7 MDA criteria), Psoriatic Arthritis Disease Activity Score (PASDAS [LDA=score of >1.9–≤3.2; remission=≤1.9]), Disease Activity Index for Psoriatic Arthritis (DAPSA [LDA= >4–≤14; remission=≤4]).

Figure: Observed disease activity levels and estimated mean mTSS change from baseline (mixed effects model) through Wks 0–216 pooled for all randomized patients



[a]Baseline PASDAS data were only available for 398 patients. Data were pooled for all patients randomized to CZP and placebo. Radiographs were taken at Wks 0, 12, 24, 48, 96, 168 and 216. Mean CFB in mTSS was estimated using a hierarchical mixed effects model for repeated measures. The proportion of patients achieving each disease activity level is observed case. PASDAS LDA: >1.9−≤3.2; PASDAS remission: ≤1.9; DAPSA LDA: >4−≤14; DAPSA remission: ≤4; MDA: 5–6/7 MDA criteria; VLDA: 7/7 MDA criteria. CFB: change from baseline; CZP: certolizumab pegol; DAPSA: Disease Activity Index of Psoriatic Arthritis; LDA: low disease activity; MDA: minimal disease activity; mTSS: modified Total Sharp Score; PASDAS: Psoriatic Arthritis Disease Activity Score; VLDA: very low disease activity; wk: week.

Radiographs taken through Wks 0–216 were read in 4 reading campaigns using van der Heijde modified Total Sharp Score (mTSS) for PsA. A subgroup of pts considered at highest risk of structural progression (baseline mTSS >median for all pts) was also assessed. Mean change from baseline (CFB) in mTSS, and associations with disease activity states, were estimated using a hierarchical linear mixed effects model (fixed effects: reading campaign, interactions of concurrent disease activity levels with time; random effects: pt, and reading campaign nested within pt) which allowed the trajectory of mean mTSS, and impact of disease activity levels on this, to be different between each timepoint at which radiographs were taken.

Results: Of 409 randomized pts, 407 were assessed for mTSS at least once. At Wk 0, mean (standard deviation) DAPSA was 44.5 (22.7), PASDAS was 6.0 (1.1). 3/409 (0.7%) pts reported MDA. The proportion of pts achieving remission/VLDA states increased to Wk 216, as did estimated mean mTSS, although overall progression was low (Wk 216 estimated mean mTSS CFB: 0.46; standard error: 0.16) (**Figure**). For all disease activity measures, remission/

Table: Estimated mTSS progression at Wk 216 if a patient had a given disease activity level at all assessments over 216 wks of treatment by MDA, PASDAS and DAPSA categories pooled for all randomized patients (mixed effects model)

		mTSS estimated mean CFB (standard error)	
		All patients (N=407)	Baseline mTSS >median (N=202)
PASDAS	Remission	-0.20 (0.25)	-0.55 (0.49)
	LDA	0.01 (0.23)	-0.07 (0.47)
	>LDA	1.31 (0.22)	2.54 (0.43)
DAPSA	Remission	-0.34 (0.23)	-0.67 (0.46)
	LDA	0.40 (0.22)	0.81 (0.44)
	>LDA	1.37 (0.24)	2.46 (0.48)
MDA	VLDA	-0.40 (0.28)	-0.84 (0.55)
	MDA	0.39 (0.24)	0.55 (0.48)
	>MDA	0.89 (0.20)	1.73 (0.39)

mTSS estimated mean CFB: ≤0; ≤0.5; >0.5. Data were pooled for all patients randomized to CZP and placebo through Wks 0–216. Mean CFB in mTSS was estimated at Wk 216 using a hierarchical mixed effects model for repeated measures. PASDAS LDA: >1.9–≤3.2; PASDAS remission: ≤1.9; DAPSA LDA: >4–≤14; DAPSA remission: ≤4; MDA: 5–6/7 MDA criteria; VLDA: 7/7 MDA criteria. CFB: change from baseline; CZP: certolizumab pegol; DAPSA: Disease Activity Index of Psoriatic Arthritis; LDA: low disease activity; MDA: minimal disease activity; mTSS: modified Total Sharp Score; PASDAS: Psoriatic Arthritis Disease Activity Score; VLDA: very low disease activity; wk: week.

VLDA states were associated with mTSS estimated mean CFB ≤0 in both the overall group of pts and those considered at highest risk of structural progression at baseline (**Table**).

Conclusion: These data indicate that achievement of remission in PsA is important to prevent further structural damage, particularly when pts have pre-existing structural changes. This supports the rationale for strict disease activity targets.

References

1. Coates L. Arthritis Rheumatol 2018;70:345–55.
2. van der Heijde D. RMD Open 2018;4:e000582.

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Abstract Number: 1536

A Novel MK2 Inhibitor for the Treatment of Ankylosing Spondylitis and Other Inflammatory Diseases

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Post-transcriptional control of cytokine and chemokine gene expression is an important checkpoint during inflammation. The MAPKAPK2 (MK2) pathway in particular is critical in regulating the expression of TNF-α and other inflammatory factors by promoting the stability and translation of their transcripts (Kotlyarov 1999 *Nat Cell Biol*; Neininger 2002 *J Biol Chem*). Illustrating the centrality of this pathway, MK2 knockout mice are protected from inflammation in various inflammatory models (Kotlyarov 1999 *Nat Cell Biol*; Hegen 2006 *J Immunol*). We hypothesized that inhibition of MK2 would regulate the production of TNF-α and other inflammatory mediators and would therefore ameliorate diseases in which these cytokines and chemokines play a role, including ankylosing spondylitis (AS).

Methods: A novel inhibitor of MK2 was evaluated in vitro for inhibition of lipopolysaccharide (LPS)-induced inflammatory cytokines from peripheral blood mononuclear cells (PBMCs), and for inhibition of IL-17 production from Th17 polarized cells. In addition, the impact of MK2 inhibition on osteoclast function was assessed using a bone resorption assay. The in vivo effect of the MK2 inhibitor was evaluated in an animal model of joint inflammation. The safety, tolerability, and pharmacokinetics (PK) of single ascending doses of the MK2 inhibitor were evaluated in an ongoing first-in-human (FIH) study. Ex vivo stimulation of PBMCs from participants in the FIH study was conducted to assess the pharmacodynamic properties.

Results: The MK2 inhibitor reduced production of TNF-α and chemokines such as monocyte chemoattractant protein-1 (MCP-1) following in vitro LPS stimulation of PBMCs from healthy donors and patients with AS in a concentration-dependent manner. In addition, decreased IL-17 production was observed in polarized Th17 cells from healthy volunteers. The MK2 inhibitor modulated osteoclastogenesis and reduced osteoclast activity in vitro. In an animal model of spondyloarthropathy, dose-dependent reduction in peripheral joint disease severity was observed. In the FIH study, the MK2 inhibitor was safe and well tolerated when administered orally as single ascending doses to healthy participants. A favorable PK profile was observed across the single dose range tested. In an ex vivo LPS-stimulation assay, PBMCs from study participants secreted reduced levels of TNF-α following administration of the MK2 inhibitor.

Conclusion: We describe an inhibitor of MK2 that reduces expression of inflammatory mediators in vitro and inhibits joint inflammation in an animal model of spondyloarthropathy. Inhibition of TNF-α production was demonstrated in PBMCs from healthy volunteers. Further investigation of this MK2 inhibitor in diseases mediated by MK2-modulated inflammatory factors, such as TNF-α and IL-17, is warranted.

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Abstract Number: 1537

Concomitant Treatment with Methotrexate Does Not Increase the Efficacy of Ustekinumab or TNF Inhibitors in Psoriatic Arthritis: Results from a Real-world, Multicenter Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The additional benefit of methotrexate as a concomitant treatment in PsA has not been fully elucidated. Observational data exist for concomitant methotrexate (MTX) use with TNF inhibitors (TNFi) and suggest no additional benefit. No real-world data currently exist for ustekinumab (UST). The objective of this study was to investigate the additive effect of MTX on the ability to reach composite treatment targets beyond monotherapy with UST or TNFi, as well as the ability to improve patient-reported outcomes in a real-world clinical setting in 8 European countries.

Methods: The PsABio study (NCT02627768) evaluates effectiveness, tolerability and persistence of 1st, 2nd or 3rd-line UST or TNFi in patients with PsA. Proportions of patients reaching minimal disease activity (MDA)/very low disease activity (VLDA) and clinical Disease Activity in Psoriatic Arthritis (cDAPSA) low disease activity (LDA) or remission, as well as reaching the 12-item Psoriatic Arthritis Impact of Disease questionnaire (PsAID-12) patient acceptable symptom state (PASS). Baseline (BL) and 6-month data were compared in patients receiving UST or TNFi in an intention to treat (ITT) analysis, including patients who switched/stopped original treatment during the 6-month observation period, who were imputed as non-responders. Logistic regression was used to assess the effect of concomitant conventional synthetic (cs)DMARD use within UST and TNFi cohorts adjusted for baseline PSAID-12, gender, smoking, number of comorbidities, steroid use, NSAID use, dactylitis, biologic (b)DMARD treatment line, BSA, enthesitis, PsA category. Comparison of the UST and TNFi treatment effect and the interaction with csDMARD co-therapy was done using logistic regression analysis that included propensity score (PS) to adjust for BL covariates age, gender, smoking, comorbidities, psoriasis BSA, PsA type, disease duration, cDAPSA, PsAID-12, enthesitis, dactylitis, Fibromyalgia Rapid Screening Tool (FiRST) score, line of bDMARD, csDMARD use, and steroid or NSAID use.

Results: Of 930 patients, data was available for 868 ITT patients (Table 1), including patients who had switched/stopped before 6 months (UST: n=28/426 [6.6%], TNFi: n=44/442 [10.0%]). For MDA assessment, 761 patients had data for both visits. Co-therapy with MTX did not increase the likelihood of achieving any of the outcomes in either the UST or TNFi cohorts (Table 2). After PS adjustment, co-treatment with MTX did not influence treatment effects

Table 1: Baseline characteristics of the 868 ITT patients

	UST	TNFi
N	426	442
Age, years	51.2 (12.5)	48.5 (12.6)
Gender (male), %	43.0	45.7
Disease duration since initial diagnosis, years	7.54 (8.13)	6.21 (6.63)
BMI, kg/m²	28.6 (6.3)	27.7 (5.0)
Smoking status (current smoker)	24.5%	24.9%
PsA joint involvement, %		
Axial involvement	35.4	37.2
Oligoarthritis	22.4	28.9
Polyarthritis	66.7	64.7
Swollen joint count (66)	6.0 (8.12)	5.8 (7.38)
Tender joint count (68)	12.5 (12.5)	11.3 (10.8)
Enthesitis at baseline, %	48.9	51.9
Dactylitis at baseline, %	18.8	20.8
Psoriasis BSA, %		
<3%	38.4	50.1
3–10%	34.9	35.7
>10%	26.7	14.1
cDAPSA at baseline	31.0 (20.3)	29.8 (18.6)
CRP (mg/dL)	1.33 (2.95)	1.55 (2.86)
csDMARD exposure, %		
Ongoing exposure at baseline, any csDMARD	39.7	55.2
Ongoing exposure at baseline, MTX co-treatment	29.8	42.3
Other treatments exposure at baseline, %		
NSAIDs	54.5	69.5
Steroids	32.4	34.4
FiRST total score	3.50 (2.01)	3.12 (1.95)
FiRST ≥5 %	39.3	29.0
Total PsAID-12 (0–10)	5.71 (2.17)	5.52 (2.08)
Rheumatoid factor/cyclic citrullinated peptide positive, %	2.0/3.0	5.6/2.8

Values are mean (standard deviation) unless otherwise indicated.

differently when added to UST compared with TNFi. The concomitant use of any csDMARD or other csDMARDs apart from MTX yielded very similar results (data not shown).

Conclusion: In a real-world setting, concomitant treatment with MTX in addition to UST or TNFi was not associated with enhanced effects across a broad variety of disease outcomes, including disease activity, impact of the disease, and skin involvement within or between treatment cohorts, after PS adjustment for baseline confounders.

Table 2: Effect of MTX co-therapy versus UST- or TNFi_-monotherapy on disease outcomes at Month 6

Percentage achieving outcome	UST + MTX	UST-monotherapy	TNFi + MTX	TNFi-monotherapy
MDA	23.7	27.5	27.8	32.1
VLDA	5.7	9.8	5.4	12.0
cDAPSA LDA	36.7	48.6	48.8	53.7
cDAPSA remission	11.6	16.8	15.1	22.2
PsAID-12 PASS	47.9	56.7	54.4	58.1
BSA improvement (≥1 category)*	50.0	51.2	49.4	43.0
OR (95% CI) of achieving outcome	UST + MTX vs UST-monotherapy (UST cohort)†	TNFi + MTX vs TNFi-monotherapy (TNFi cohort)†	UST vs TNFi (MTX co-therapy group)‡	UST vs TNFi (monotherapy group)‡
MDA	0.82 (0.43, 1.56)	0.89 (0.50, 1.60)	0.83 (0.47, 1.48)	0.96 (0.58, 1.60)
VLDA	0.60 (0.21, 1.68)	0.41 (0.16, 1.00)	0.89 (0.30, 2.63)	0.73 (0.35, 1.53)
cDAPSA LDA	0.70 (0.40, 1.24)	0.91 (0.53, 1.56)	0.52 (0.30, 0.89)	0.83 (0.52, 1.35)
cDAPSA remission	0.63 (0.28, 1.44)	0.62 (0.31, 1.24)	0.74 (0.33, 1.62)	0.73 (0.39, 1.36)
PsAID-12 PASS	0.80 (0.44, 1.46)	0.77 (0.44, 1.35)	0.78 (0.46, 1.30)	0.85 (0.52, 1.39)
BSA improvement (≥1 category)*	0.96 (0.43, 2.12)	0.98 (0.55, 1.77)	0.97 (0.55, 1.69)	1.00 (0.60, 1.67)

*BSA categories: <3%, 3–10%, and >10%. †Within treatment cohort OR for MTX co-therapy vs UST- or TNFi-monotherapy. ‡OR for UST vs TNFi adjusted for propensity score.
CI, confidence interval; OR, odds ratio.

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Abstract Number: 1538

The Effects of Apremilast Therapy on Deployability in Active Duty U.S. Army Soldiers with Plaque Psoriasis and Psoriatic Arthritis

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SESSION INFORMATION

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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Apremilast is a novel oral phosphodiesterase 4 inhibitor that is used for plaque psoriasis (PsO) and psoriatic arthritis (PsA). This medicine is unique in that it is oral and does not require refrigeration or laboratory monitoring. It also does not increase infection risk and has a small side-effect profile in comparison to other agents. These characteristics make apremilast a potentially useful therapy for active duty (AD) military patients who may deploy to austere environments. This retrospective chart review examined the use of apremilast in the Army for PsO and PsA in an effort to describe the effects that it may have on troop deployability.

Methods: Study subjects included AD U.S. Army personnel who were started on apremilast for PsO or PsA between March 31, 2014, and January 1, 2018. A list of candidates was obtained via the defense pharmacy analytics section. In order to be considered for inclusion, prior dermatology or rheumatology documentation needed to be available in the military health record confirming diagnosis of PsO or PsA. Each patient's records were reviewed to assess the efficacy and tolerability of treatment by listing duration of treatment, any discontinuation of therapy, or documented adverse events. Military records were then examined to confirm current deployability. Primary endpoints consisted of deployments while on apremilast and current deployability. Resulting data points were subsequently organized and reported in a descriptive manner for the purpose of analyzing practice patterns in this patient population.

Results: 227 study subjects were included. The patient population was predominantly male (n=209, 92.1%) with an average age of 38. 165 (72.7%) had PsO, and 62 (27.3%) had PsA. As of the date of initial data extraction (April 3, 2019), 63 (27.8%) were still on apremilast, but the remainder had discontinued the medication. The average duration of treatment was 15.2 months for all patients. When available, the most common reason for discontinuation was lack of efficacy (n=58). The most common reported adverse effect was gastrointestinal upset (n=30). 85 patients with both PsO and PsA had deployments during the study timeframe until April 2019. Of the patients with deployments meeting the above criteria, 22 patients with PsO and 5 with PsA were able to deploy while on apremilast. Of the 129 patients who were still AD at initial data extraction, 119 (92.2%) were reported as "Deployable" on military records.

Conclusion: Further research is needed to determine the impact of apremilast on deployability in the U.S. Army. Despite the limitations arising from record heterogeneity and the descriptive nature of this study, this data does provide insight into caring for patients that cannot be given other agents due to career concerns. In our military experience, the medical separation process is almost invariably started when a patient is given an immunosuppressive medication. In examining this data, providers who take care of AD patients should consider apremilast as an alternative therapeutic option in PsO and PsA for maintaining both disease control and deployability while remaining mindful that a lack of efficacy could be a future concern.

Disclosure: A. Price, None; **V. Wagler**, None; **C. Donaldson**, None; **P. Mastin**, None.

Abstract Number: 1539

Ustekinumab and TNF Inhibitors Similarly Improve Patient-perceived Impact of Psoriatic Arthritis but Differentially Affect the Scale Subdomains: Results from a European Observational Cohort Study

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SESSION INFORMATION

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Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis strongly impacts patients' quality of life (QoL). Insights on the effects of biologic treatments on different domains of health-related QoL in a real-world setting are lacking. The objective of this study was to investigate the effect of 6 months of therapy with ustekinumab (UST) or TNF inhibitor (TNFi) on the Psoriatic Arthritis Impact of Disease questionnaire (PsAID-12) and its subdomains.

Methods: The PsABio study (NCT02627768) evaluates effectiveness, tolerability and persistence of 1st, 2nd or 3rd-line UST or TNFi in patients with PsA. Changes from baseline (BL) to 6 months were evaluated in total PsAID-12 and subdomains. Completer analyses were performed on patients staying on UST or TNFi for the full 6 months as well as intent-to-treat (ITT) analyses using non-responder imputation. PsAID-12 was also analyzed as change above the minimal clinical important difference (MCID) of -1.25 points (Holland R, et al. Ann Rheum Dis. 2018;77:343–347), and a patient-acceptable state of PsAID-12 score ≤4. UST and TNFi effectiveness were compared using propensity scores (PS) to adjust for BL confounders.

Results: Of 930 patients, 886 (426 on UST and 442 on TNFi) had evaluable data at BL and 6 months (ITT population, Table 1). This population analysis included patients who had stopped/switched UST (6.6%) or TNFi (10.0%) before 6 months. At BL, significant differences between UST and TNFi groups existed in terms of age (UST patients were older), line of treatment (UST more frequently 3rd-line), NSAID and methotrexate use (less in UST), FiRST score (more chronic widespread pain in UST), and skin involvement (higher in UST). In the ITT analysis, after 6 months, PsAID-12 total score improved by 27.6% for UST (95% confidence interval [CI] 21.6, 33.5) and 32.8% for TNFi (95% CI 28.4, 37.1). MCID improvement was reached by 53.9% (95% CI 48.8, 58.9) of UST and 57.7% (95% CI 52.4, 62.8) of TNFi-treated patients; and 53.1% (95% CI 48.1, 58.1) and 55.4% (95% CI 50.3, 60.4) respectively achieved the patient acceptable state of PsAID (PS-adjusted OR [95% CI] UST vs TNFi: 0.85 [0.61, 1.19]). All PsAID domains also demonstrated improvement (Table 2), with differences between UST and TNFi for the subdomains of impact of pain and skin problems (Table 2).

Table 1: Baseline characteristics of 868 PsA patients starting UST or TNFi

	UST	TNFi
N	426	442
Age, years	51.2 (12.5)	48.5 (12.6)
Gender (male), %	43.0	45.7
Disease duration, years	7.5 (8.1)	6.2 (6.6)
Dactylitis at baseline, %	18.8	20.8
Enthesitis at baseline, %	48.9	51.9
PsA characteristics: %		
Axial involvement	35.4	37.2
Oligoarticular disease	22.4	28.9
Polyarticular disease	66.7	64.7
csDMARD exposure, %		
Previous exposure	88.3	93.0
Ongoing exposure at baseline	39.7	55.2
Other BL treatments, %		
NSAIDs	54.5	69.5
Oral glucocorticoids	32.4	34.4
BMI, kg/m²	28.6 (6.3)	27.7 (5.0)
Swollen joint count (66)	6.0 (8.1)	5.8 (7.4)
Tender joint count (68)	12.5 (12.5)	11.3 (10.8)
BSA of psoriasis, %		
<3%	38.4	50.1
3–10%	34.9	35.7
>10%	26.7	14.1
cDAPSA	31.0 (20.3)	29.8 (18.6)
CRP (mg/dL)	1.3 (3.0)	1.6 (2.9)
Total PsAID-12 (0–10)	5.7 (2.2)	5.5 (2.1)
FiRST total score	3.5 (2.0)	3.1 (2.0)
FiRST score ≥5, %	39.3	29.0

Mean (standard deviation) or percentage is presented.
cDAPSA, clinical Disease Activity in Psoriatic Arthritis; csDMARD, conventional synthetic disease-modifying antirheumatic drug. FiRST, Fibromyalgia Rapid Screening Tool

Conclusion: Both UST and TNFi treatment for 6 months are efficacious in reducing impact of PsA and improving patients' QoL, measured by PsAID-12. After PS adjustment for BL imbalances, the improvements seen with UST and TNFi were not significantly different with regard to total PsAID score, though differences were noted for impact of pain (favoring TNFi) and skin problems (favoring UST). This is the first report on the effects of these drugs on QoL in a real-life setting.

Table 2: Change in PsAID-12 and subdomains at month 6 (ITT analyses)

PSAID-12 Total and domains	UST Mean (95% CI) change from baseline	TNFi Mean (95% CI) change from baseline	PS-adjusted UST vs TNFi regression coefficient (95% CI)
Total PsAID-12 (0–10)	-1.82 (-2.04, -1.59)	-1.91 (-2.13, -1.69)	0.15 (-0.19, 0.50) p=0.377
Pain	-1.73 (-1.99, -1.47)	-2.31 (-2.57, -2.04)	0.51 (0.10, 0.93) p=0.015*
Fatigue	-1.59 (-1.87, -1.31)	-1.82 (-2.09-1.54)	0.18 (-0.26, 0.61) p=0.428
Skin problems, including itching	-2.66 (-3.01, -2.31)	-1.52 (-1.83, -1.21)	-0.75 (-1.26, -0.24) p=0.004**
Difficulties to participate fully in work and/or leisure activities	-1.70 (-2.00, -1.40)	-2.08 (-2.38, -1.77)	0.43 (-0.03, 0.90) p=0.068
Difficulties in doing daily physical activities	-1.71 (-1.99, -1.43)	-2.14 (-2.43, -1.86)	0.42 (-0.02, 0.85) p=0.059
Discomfort	-1.97 (-2.27, -1.67)	-2.24 (-2.53, -1.96)	0.30 (-0.15, 0.75) p=0.189
Sleep difficulties	-1.74 (-2.05, -1.43)	-1.83 (-2.14, -1.52)	0.12 (-0.37, 0.60) p=0.637
Coping	-1.55 (-1.83, -1.27)	-1.85 (-2.13, -1.57)	0.26 (-0.17, 0.68) p=0.242
Anxiety, fear and uncertainty	-1.71 (-2.02, -1.40)	-1.65 (-1.95, -1.35)	-0.05 (-0.54, 0.43) p=0.830
Embarrassment and/or shame due to appearance	-1.86 (-2.20, -1.52)	-1.37 (-3.00, 0.00)	-0.09 (-0.57, 0.39) p=0.712
Difficulties to participate fully in social activities	-1.59 (-1.92, -1.25)	-1.68 (-2.00, -1.36)	0.22 (-0.28, 0.72) p=0.383
Depression	-1.49 (-1.78, -1.19)	-1.43 (-1.72, -1.13)	-0.04 (-0.49, 0.42) p=0.873

*Favors TNFi, ** Favors UST.

Disclosure: L. Gossec, Abbvie, 5, AbbVie, 5, Abbvie, Biogen, BMS, Celgene, Lilly, Novartis, Pfizer, SAnofi-Aventis, UCB, 5, Amgen, 5, Biogen, 5, BMS, 2, 5, Celgene, 5, Celgene Corporation, 2, Janssen, 5, Lilly, 2, 5, MSD, 5, Nordic Pharma, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 5, Sanofi-Aventis, 5, UCB, 5; **S. Siebert**, Abbvie, 2, 5, 8, AbbVie, 2, 5, BMS, 2, Boehringer Ingelheim, 2, 5, 8, Celgene, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8; **P. Bergmans**, Janssen, 3, Johnson & Johnson, 1, 4; **K. De Vlam**, Johnson & Johnson, 5; **E. Gremese**, AbbVie, 5, 8, BMS, 5, 8, Celgene, 5, 8, Janssen, 5, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **B. Joven-Ibáñez**, Celgene, 8, Novartis, 8, MSD, 8, Pfizer, 8, AbbVie, 8, Janssen, 8; **E. Korendowych**, AbbVie, 2, 5, Novartis, 5, Janssen, 5, UCB, 5, Pfizer, 2, 5; **T. Korotaeva**, Pfizer, 5, 8, MSD, 5, 8, Novartis, 5, 8, AbbVie, 5, 8, Celgene, 5, 8, Biocad, 5, 8, Janssen, 5, 8, UCB, 5, 8, Lilly, 5, 8, Novartis-Sandoz, 5, 8; **W. Noël**, Janssen, 3; **M. Nurmohamed**, Pfizer, 2, 5, 8, AbbVie, 2, 5, 8, Roche, 2, 5, 8, BMS, 2, 5, 8, MSD, 2, 5, 8, Mundipharma, 2, 5, 8, UCB, 2, 5, 8, Janssen, 2, 5, 8, Menarini, 2, 5, 8, Lilly, 2, 5, 8, Sanofi, 2, 5, 8, Celgene, 2, 5, 8; **C. Richez**, astrazeneca, 5, 8, BMS, 5, 8, Glenmark, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8; **P. Sfikakis**, None; **P. Smirnov**, Janssen, 3; **E. Theander**, Janssen, 3; **J. Smolen**, AbbVie, 2, 5, 8, Abbvie, 2, 5, Amgen, 5, 8, AstraZeneca, 2, 5, 8, Astra-Zeneca, 5, Astro, 5, 8, BMS, 5, Celgene, 5, 8, Celltrion, 5, Celtrion, 5, 8, Chugai, 5, Eli Lilly and Company, 2, 5, Gilead, 5, GlaxoSmithKline, 5, 8, ILTOO, 5, 8, ILTOO Janssen, 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Medimmune, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, Novartis- Sandoz, 5, Novartis-Sandoz, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 5, Roche, 2, 5, Roche;, 2, 5, 8, Samsung, 5, 8, Sanofi, 5, 8, Sanofi-Aventis, 5, UCB, 5, 8.

Abstract Number: 1540

Biologic Use and Reasons for Switching Biologic Therapy in Patients with Non-radiographic Axial Spondyloarthritis in the United States:Findings from a US Survey

Atul Deodhar,[1] **Theresa Hunter**,[2] Elizabeth Holdsworth,[3] Nicola Booth,[4] and David Sandoval[5], [1]Oregon Health & Science University, Portland, OR, [2]Eli Lilly and Company, Indianapolis, [3]Adelphi Real World, Manchester, England, United Kingdom, [4]Adelphi Real World, Bollington, United Kingdom, [5]Eli Lilly and Company, Indianapolis, IN

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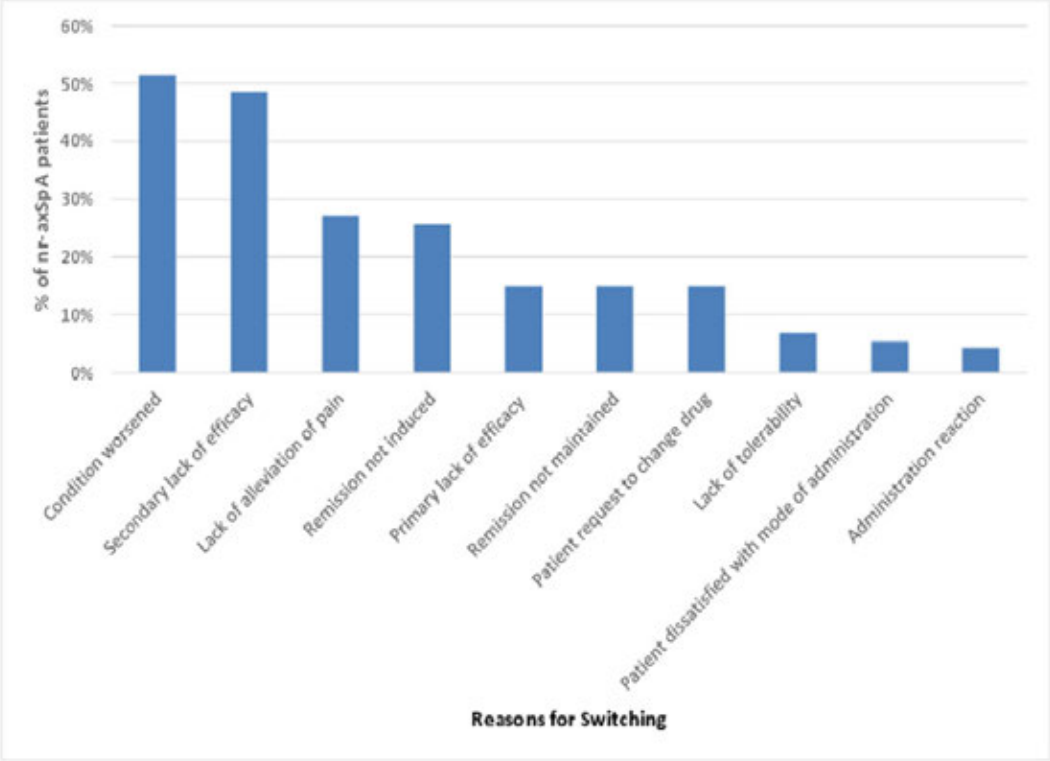
Figure 1. Top 10 reasons that US nr-axSpA patients switched to adifferent biologic



Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The FDA approved the first biologic for the treatment of nr-axSpA in the US in March 2019. The objective of our study was to describe biologic use and reasons for switching biologic therapy among patients with non-radiographic axial spondyloarthritis (nr-axSpA).

Methods: Data from a real world, cross-sectional survey of rheumatologists and their consulting nr-axSpA patients in the United States were analyzed descriptively. Data were collected from Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Patients who had physician confirmed diagnosis of nr-axSpA were eligible to participate. Rheumatologists completed record forms for their patients, containing information on current medication use and reasons for switching biologics.

Results: Data from 88 rheumatologists and 495 nr-axSpA patients were included in this analysis. The majority of nr-axSpA patients were male (53.3%), with a mean age of 44.2 years, and 69.8% of patients reported working full-time. Of the 495 nr-axSpA patients, 48.1% were receiving a biologic agent and no csDMARD, 18.4% csDMARD (no biologic), 18.2% NSAIDS/COX-2 (no biologic or csDMARD), 11.5% a biologic and a csDMARD, 2.0% were receiving no therapy, and 1.8% other therapy (no biologic, csDMARD or NSAID/COX-2). Of the 295 patients receiving a biologic, 78.0% were receiving their first, 13.9% their second and 8.1% their third or more biologic. Of the 74 nr-axSpA patients that switched from a previous biologic to their current biologic, physicians reported that 51.4% switched due to condition worsening, 48.6% had a loss of response over time, 27.0% switched due to a lack of pain alleviation, and 25.7% of patients switched because remission was not induced (Figure 1).

Conclusion: This survey suggests that around 60% of nr-axSpA patients were receiving biologic therapy. Switching of biologics is frequent in nr-axSpA patients and is usually due to lack of efficacy, loss or response, and effort to accomplish remission.

Disclosure: A. Deodhar, AbbVie, 2, 5, 9, Abbvie, 5, 8, Abbvie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, and UCB Pharma, 5, 8, AbbVie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GSK, Galapagos, Janssen, Novartis, Pfizer and UCB, 5, AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Glaxo Smith and Klein, Janssen, Novartis, Pfizer, UCB, 5, Amgen, 5, 8, 9, BMS, 2, 5, 8, BMS, Eli Lilly, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, 2, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, UCB Pharma, 2, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, 8, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, 9, Eli Lilly and Company, 2, 5, Eli Lilly,, 5, Eli Lilly, GSK, Novartis, Pfizer and UCB, 2, Galagagos, 5, Galapagos, 5, 8, 9, Glaxo Smith & Klein, 2, Glaxo Smith & Kline, 2, 5, 8, Glaxo Smith Klein, 5, Glaxo SmithKlein, 2, 5, GlaxoSmithKlein, 2, 5, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, Janssen, 2, 5, 8, 9, Janssen Pharmaceutica, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9; **T. Hunter**, Eli Lilly, 1, 3, Eli Lilly and Company, 1, 3; **E. Holdsworth**, None; **N. Booth**, Adelphi Real World, 3; **D. Sandoval**, Eli Lilly, 1, 3, Eli Lilly and Company, 1, 3.

Abstract Number: 1541

Early Treatment Failure with Apremilast Among Biologic-naïve Patients with Psoriatic Arthritis

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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical studies have shown that a large proportion of psoriatic arthritis (PsA) patients treated with apremilast failed to achieve improved physical function or experienced severe gastrointestinal (GI) symptoms. This study used administrative claims data to evaluate the proportion of biologic treatment-naïve patients experiencing early treatment failure with apremilast, identify characteristics associated with early treatment failure with apremilast, and assess subsequent treatment use after apremilast discontinuation in the real-world setting.

Methods: Adult biologic-naïve patients with PsA and apremilast use during Q1 2013 to Q3 2016 were selected from the IBM MarketScan Research Database (Copyright © 2017 Truven Health Analytics LLC, All Rights Reserved). The index date was defined as the first claim for apremilast after PsA diagnosis. Patients were required to have continuous enrollment during the 6 months before (baseline period) and the 6 months after the index date (study period). Early treatment failure was defined as the occurrence of treatment discontinuation, GI-related healthcare encounters, treatment switching/addition, or dose escalation/reduction within the 6-month study period. Time to treatment failure was described using the Kaplan-Meier method. A logistic regression model was used to assess characteristics associated with early treatment failure with apremilast. Subsequent treatment use was assessed through the end of continuous enrollment among patients who discontinued apremilast within 6 months.

Results: A total of 1,503 biologic-naïve patients with PsA who were treated with apremilast were included, 869 (57.8%) with and 634 (42.2%) without early treatment failure. Median time to apremilast failure was 3.9 months and

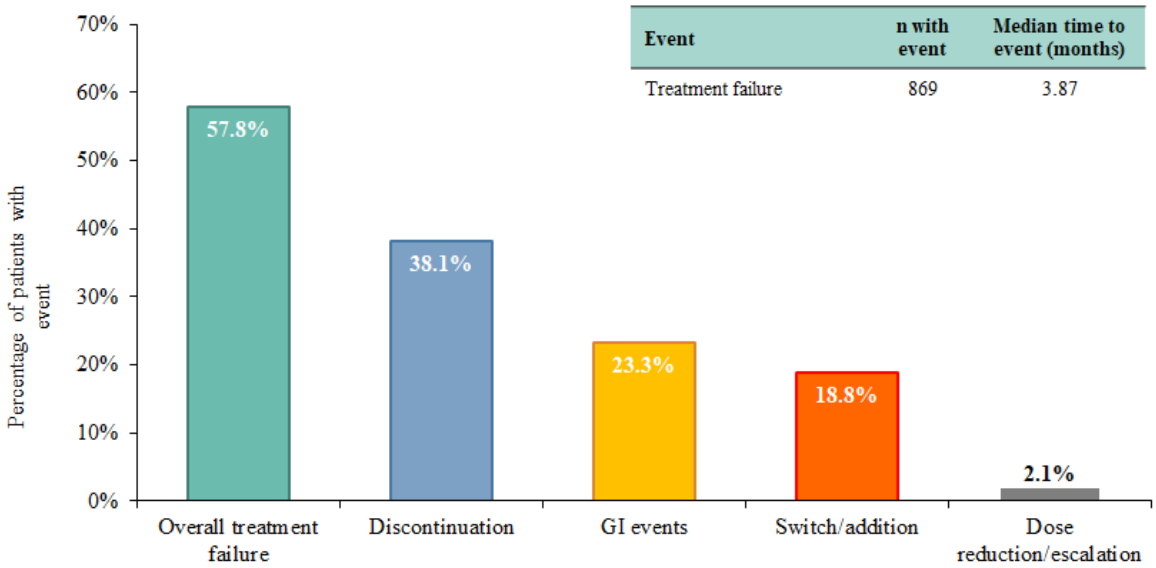

Figure 1. Early treatment failure rates with apremilast

Table 1. Characteristics associated with early treatment failure with apremilast

	Odds ratio [95% CI]	*P*-value	
Female	1.22 [0.99, 1.51]	0.068	
Comorbidities			
CCI ≥1	1.23 [0.99, 1.54]	0.064	
GI-related comorbidities	1.76 [1.32, 2.34]	<0.001	*
Treatment Use			
Orally administered corticosteroids	1.27 [1.01, 1.59]	0.041	*
Opioids	1.29 [1.04, 1.61]	0.022	*

** denotes p-value <0.05; CCI: Charlson Comorbidity Index; CI: confidence interval*

treatment discontinuation was the most common treatment failure event (**Figure 1**). Clinically relevant baseline characteristics that were significantly different between patients with and without early apremilast failure were included in the model (**Table 1**). Presence of GI-related comorbidities (odds ratio [OR]: 1.76, p< 0.001), orally administered corticosteroid use (OR: 1.27, p=0.04), and opioid use (OR: 1.29, p=0.02) were significantly associated with a higher risk of early treatment failure with apremilast. Among the 572 patients (38.1%) who discontinued apremilast within 6 months, 46.5% did not have subsequent treatment use; 20.3% subsequently initiated adalimumab, 15.7% subsequently initiated etanercept, 9.2% subsequently initiated secukinumab, and 9.2% subsequently initiated ustekinumab.

Conclusion: This retrospective claims study showed that approximately 60% of biologic-naïve PsA patients treated with apremilast experienced treatment failure within 6 months. Presence of GI-related comorbidities, use of orally administered corticosteroids, and use of opioids before apremilast initiation were associated with an increased risk of early treatment failure. In addition, approximately 54% of patients initiated a subsequent treatment following apremilast discontinuation. The results of this real-world study are consistent with findings from clinical trials.

Disclosure: K. Betts, AbbVie, 9; **P. Patel**, AbbVie, 3, 4; **J. Song**, AbbVie, 9; **J. Zhao**, AbbVie, 9; **Y. Wang**, Analysis Group, Inc., 9; **J. Griffith**, AbbVie, 3, 4; **E. Wu**, AbbVie, 9.

Abstract Number: 1542

Long-Term Effectiveness and Safety of Infliximab and Golimumab in Ankylosing Spondylitis Patients from a Prospective Observational Registry

Proton Rahman,[1] Derek Haaland,[2] Dalton Sholter,[3] Michael Starr,[4] Arthur Karasik,[5] Michelle Teo,[6] Sanjay Dixit,[7] Ariel Masetto,[8] Anna Jaroszynska,[9] Pauline Boulos,[7] Emmanouil Rampakakis,[10] Meagan Rachich,[11] Odalis Asin-Milan,[11] Allen Lehman,[11] and **Francois Nantel** [11], [1]Memorial University, Newfoundland, NL, Canada, [2]Waterside Clinic, Barrie, ON, Canada, [3]Rheumatology Associates, Edmonton, AB, Canada, [4]Montreal General Hospital, Montreal, QC, Canada, [5]Toronto, ON, Canada, [6]Balfour Medical Clinic, Penticton, BC, Canada, [7]McMaster University, Hamilton, ON, Canada, [8]Université de Sherbrooke, Sherbrooke, QC, Canada, [9]Oakville, ON, Canada, [10]JSS Medical Research, Montreal, Canada, [11]Janssen Inc., Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Long-term registries are essential to evaluate new therapies in a patient population that differs from clinical trial and usually varies over time. The purpose was to describe the profile of ankylosing spondylitis (AS) patients treated with infliximab (IFX) or golimumab (GLM) treatment in Canadian routine care along with its long-term effectiveness and safety.

Methods: 810 AS patients treated with IFX or GLM were enrolled into the Biologic Treatment Registry Across Canada (BioTRAC) registry between 2005-2015 and 2010-2017, respectively. Study visits occurred at baseline and every 6 months thereafter, as needed per routine care. Effectiveness was assessed with changes in ASDAS, BASDAI, BASFI, MDGA, HAQ-DI, PtGA, back pain and acute phase reactants. Safety was evaluated with the incidence of adverse events (AEs) and drug survival rates.

Results: Of the 389 IFX- and 421 GLM-treated patients, the proportion of males were 62.7% and 59.1%, the mean age were 45.6 and 45.7 years and the mean disease duration were 8.6 and 6.0 years, respectively. Most patients were bio-naive (>82.7%). Interestingly, we observed a significant decrease in disease duration in the IFX cohort from a median of 8.0 to 3.5 and 1.0 years in 2005-2008, 2009-2012 and 2013-2015, respectively ($p< 0.001$). A reduction in baseline BASFI score (6.3 vs. 5.9 vs 5.1; P=0.011) and in the proportion of patient in ASDAS very high disease activity (48.4%, 43.8%, 30.3%; p=0.004) were also observed. As for the GLM cohort, most disease parameters including median disease duration (1.6 years), mean baseline BASFI (5.3) and the proportion of patients in ASDAS very high disease activity (48%) remained similar from 2010-2017.

Treatment with both IFX and GLM significantly improved all disease parameters over time ($P< 0.001$) from baseline up to 120 and 84 months, respectively, with similar efficacy between agents. AEs were reported for 67.9% and 70.5% (136 and 131 events/100 PYs) and SAEs for 15.4% and 8.1% (10.5 and 8.45 events/100 PYs) covering 1251.3 and 674.8 years of exposure for IFX- and GLM-treated patients, respectively. The most frequently occurring AEs (>7% of patient in either group) were upper respiratory tract infection, arthralgia and back pain. Two deaths occurred in IFX-treated patients (myocardial infarct, drowning) and two among GLM-treated patients (oropharyngeal cancer; neutropenia, staphylococcal/pseudomonas infections, septic shock).

The proportion of patients who discontinued treatment were 65.8% over a mean 3.2 years of exposure in the IFX cohort and 56.8% over 1.6 years in the GLM cohort.

Conclusion: Both IFX and GLM treatment significantly reduced disease activity and improved functionality in a similar fashion and were well tolerated in patients with AS. Differences in baseline characteristics over time demonstrate improvement in early diagnosis of AS and earlier access to biologic therapies.

Disclosure: P. Rahman, AbbVie, 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, and Novartis, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, and UCB, 5, AbbVie, Eli Lilly, Pfizer, Novartis , UCB, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 2, 5, 8, Janssen Inc., 2, 5, 8, Janssen, Novartis, 2, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **D. Haaland**, Janssen Inc., 5; **D. Sholter**, Janssen Inc., 5, 8; **M. Starr**, Janssen Inc., 2; **A. Karasik**, Janssen Inc., 5; **M. Teo**, Janssen Inc., 8; **S. Dixit**, Janssen Inc., 5; **A. Masetto**, None; **A. Jaroszynska**, Janssen Inc.; **P. Boulos**, Janssen Inc., 2; **E. Rampakakis**, None; **M. Rachich**, Janssen Inc., 3; **O. Asin-Milan**, Janssen Inc., 3; **A. Lehman**, Janssen Inc., 1, 3; **F. Nantel**, Janssen Inc., 1, 3.

Abstract Number: 1543

Long-Term Effectiveness and Safety of Infliximab, Golimumab and Ustekinumab in Psoriatic Arthritis Patients from a Prospective Observational Registry

Proton Rahman,[1] Regan Arendse,[2] Isabelle Fortin,[3] Andrew Chow,[4] Majed Khraishi,[5] Suneil Kapur,[6] Michel Zummer,[7] Raheem Kherani,[8] Jonathan Chan,[9] Emmanouil Rampakakis,[10] Meagan Rachich,[11] Odalis Asin-Milan,[11] Allen Lehman,[11] and **Francois Nantel** [11], [1]Memorial University, Newfoundland, NL, Canada, [2]University of Saskatchewan, Saskatoon, SK, Canada, [3]Centre de Rhumatologie de l'Est du Quebec, Rimouski, QC, Canada, [4]Credit Valley Rheumatology, Mississauga, ON, Canada, [5]Nexus Clinical Research, Memorial University of Newfoundland, St. Johns, NL, Canada, [6]University of Ottawa, Ottawa, ON, Canada, [7]Ch Maisonneuve-Rosemont, Montreal, QC, Canada, [8]University of British Columbia, Richmond, BC, Canada, [9]Artus Health Clinic, Vancouver, BC, Canada, [10]JSS Medical Research, Montreal, Canada, [11]Janssen Inc., Toronto, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Long-term registries are essential to evaluate new therapies in a patient population that differs from clinical trials and usually varies over time. The purpose of this study was to describe the profile of psoriatic arthritis (PsA) patients selected for treatment with infliximab (IFX), golimumab (GLM) or ustekinumab (UST) treatment in Canadian routine care and to describe the long-term real-world effectiveness and safety of these agents.

Methods: 462 PsA patients treated with IFX, GLM or UST were enrolled into the Biologic Treatment Registry Across Canada (BioTRAC) registry between 2006-2015, 2010-2017 and 2014-2017, respectively. Study visits occurred at baseline and every 6 months thereafter. Effectiveness was assessed with changes in TJC28, SJC28, skin, enthesitis, dactylitis, pain, HAQ, acute phase reactants. Safety was evaluated with the incidence of adverse events (AEs) and drug survival rates.

Results: Of the 111 IFX-, 281 GLM- and 70 UST-treated patients, the proportion of males were 52.3%, 46.3% and 37.1%, the mean age was 48.4, 52.8 and 53.1 years and the mean disease duration was 5.8, 6.1 and 5.7 years, respectively. Most patients were bio-naive (85.6%, 77.9% and 55.7% for IFX, GLM and UST, respectively ($p< 0.001$). A

reduction in mean baseline duration of morning stiffness was observed in the IFX cohort (from 69.8 to 42.6 to 23 min in 2006-2008 to 2009-2012 to 2013-2015; p=0.003). Most other baseline disease parameters remained similar over time in all three cohorts. However, UST-treated patients had lower mean baseline DAS28 CRP (3.4 vs 3.9; p=0.0031), SJC (3.8 vs 5.3; p=0.0046) and higher PASI (4.8 vs 2.2; p=0.0061) compared to patients treated with GLM.

Treatment with IFX, GLM and UST was associated with significant improvements in all disease parameters over time (P< 0.001) from baseline up to 84, 84 and 40 months, respectively with similar efficacy between agents. The only exception was the proportion of patients in minimal disease activity at 12, 24 and 36 months which reached 40.7%, 50.0% and 55% in IFX-patients; 64.7%, 68.8% and 78.9% in GLM-patients and 58.8%, 60.0% and 83.3% in UST-patients (p=0.004 and p< 0.001 vs IFX).

AEs were reported for 74.8%, 69.8% and 52.9% (138, 114 and 115 events/100 PYs) and SAEs for 19.8%, 8.5% and 5.7% (8.8, 7.2 and 8.0 events/100 PYs) covering 325, 567 and 87 years of exposure for IFX-, GLM- and UST-treated patients, respectively. One, one and no death occurred IFX-, GLM- and UST-treated patients, respectively. The proportion of patients who discontinued treatment were 63.1%, 50.9% and 50.0% over a mean exposure of 2.9, 1.9 and 1.2 years to IFX, GLM and UST, respectively.

Conclusion: Differences in baseline characteristics between patients treated with an anti-TNF over an anti-IL12/23 agent suggest that the level of joint to skin involvement might be driving physician choice when the time comes to choose a biologic agent. IFX, GLM and UST treatment significantly reduced disease activity and improved functionality in a similar fashion and were well tolerated in patients with PsA.

Disclosure: P. Rahman, AbbVie, 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, and Novartis, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, and UCB, 5, AbbVie, Eli Lilly, Pfizer, Novartis , UCB, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 2, 5, 8, Janssen Inc., 2, 5, 8, Janssen, Novartis, 2, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **R. Arendse**, Janssen Inc., 5, 8; **I. Fortin**, Janssen Inc., 2; **A. Chow**, Janssen Inc., 2; **M. Khraishi**, Janssen Inc., 8; **S. Kapur**, Janssen Inc., 2; **M. Zummer**, Janssen Inc., 2; **R. Kherani**, Janssen Inc., 2; **J. Chan**, Janssen Inc., 8; **E. Rampakakis**, None; **M. Rachich**, Janssen Inc., 3; **O. Asin-Milan**, Janssen Inc., 3; **A. Lehman**, Janssen Inc., 1, 3; **F. Nantel**, Janssen Inc., 1, 3.

Abstract Number: 1544

Predictors of Response, Adverse Events and Treatment Retention in Ankylosing Spondylitis Patients Treated with Golimumab in a Prospective, Observational Registry

Proton Rahman,[1] Ariel Masetto,[2] Michelle Teo,[3] Pauline Boulos,[4] Dalton Sholter,[5] Suneil Kapur,[6] Emmanouil Rampakakis,[7] Meagan Rachich,[8] Odalis Asin-Milan,[8] Allen Lehman,[8] and **Francois Nantel** [8], [1]Memorial University, Newfoundland, NL, Canada, [2]Université de Sherbrooke, Sherbrooke, QC, Canada, [3]Balfour Medical Clinic, Penticton, BC, Canada, [4]McMaster University, Hamilton, ON, Canada, [5]Rheumatology Associates, Edmonton, AB, Canada, [6]University of Ottawa, Ottawa, ON, Canada, [7]JSS Medical Research, Montreal, Canada, [8]Janssen Inc., Toronto, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The Biologic Treatment Registry Across Canada (BioTRAC) was a prospective, observational registry that enrolled ankylosing spondylitis (AS) (radiographic axial SpA) patients treated with subcutaneous golimumab (GLM) between 2010 and 2017. The registry was closed in June 2018.

Methods: Patient visits occurred at baseline and every 6 months thereafter. Multivariate logistic regression was used to identify independent predictors of achieving specific efficacy and safety endpoints and included the following covariates: age, gender, disease duration, enrollment period, concomitant medication, smoking and employment.

Results: A total of 421 patients were enrolled and followed for a mean duration of 1.6 years. The proportion of male gender was 59.1% and the mean disease duration at baseline was 6.0 years (SD=10.1 years). Most patients were bio-naive (>82%).

ASDAS clinically important improvement was more likely to be achieved with higher baseline ASDAS-CRP score [OR (95%): 2.28 (1.51–3.45); p< 0.001], however less likely in patients with baseline concomitant DMARD use [0.31 (0.12–0.80); p=0.015]. ASDAS major improvement was more likely to be achieved with lower age [OR (95%): 0.94 (0.91–0.97); p< 0.001], higher baseline ASDAS-CRP score [OR (95%): 2.93 (1.80–4.75); p< 0.001], and higher baseline CRP levels [1.04 (1.00–1.07); p=0.025]. ASAS partial remission was more likely to be achieved with lower age [OR (95%): 0.97 (0.94–0.99); p=0.013], male vs. female gender [OR (95%): 2.22 (1.10–4.48); p=0.025], lower baseline ASDAS-CRP [0.67 (0.48–0.94); p=0.020], and higher baseline CRP levels [1.01 (1.00–1.02); p=0.048].

AEs were more likely to occur with older age [1.02 (1.00–1.05); p=0.024] and concomitant DMARD use [3.03 (1.17–7.85); p=0.022], yet less likely in patients who enrolled later [2016–2017 vs. 2010–2012: 0.36 (0.15–0.85); p=0.019]. SAEs were also less likely to occur in patients who enrolled later [2013–2015 vs. 2010–2012: 0.29 (0.10–0.84); p=0.023 and 2016–2017 vs. 2010–2012: 0.15 (0.03–0.64); p=0.010].

Increased treatment retention for AS patients treated with GLM were significantly associated with earlier enrollment period (2010-2012 vs. 2016-2017: HR [95% CI]: 0.51 [0.29–0.89], p=0.017; 2013-2015 vs. 2016-2017: 0.65 [0.44–0.95], p=0.027), and male gender [0.49 (0.35–0.68); p< 0.001].

Conclusion: In this real world, long-term prospective cohort of AS patients treated with GLM, male patients were more likely to achieve a positive treatment response and sustained treatment persistence. Baseline concomitant DMARDs was associated with a lower treatment response, possibly through its association with more complex non-axial disease. Later enrollment period was associated with a lower risk of experiencing an AE but with a higher risk of early treatment discontinuation, possibly driven by the greater availability of alternative therapies.

Disclosure: P. Rahman, AbbVie, 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, and Novartis, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, and UCB, 5, AbbVie, Eli Lilly, Pfizer, Novartis , UCB, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 2, 5, 8, Janssen Inc., 2, 5, 8, Janssen, Novartis, 2, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **A. Masetto**, None; **M. Teo**, Janssen Inc., 8; **P. Boulos**, Janssen Inc., 2; **D. Sholter**, Janssen Inc., 5, 8; **S. Kapur**, Janssen Inc., 2; **E. Rampakakis**, None; **M. Rachich**, Janssen Inc., 3; **O. Asin-Milan**, Janssen Inc., 3; **A. Lehman**, Janssen Inc., 1, 3; **F. Nantel**, Janssen Inc., 1, 3.

Abstract Number: 1545

Ixekizumab Significantly Improves Self-reported Overall Health as Measured by Short-Form-36 in Patients with Active Non-radiographic Axial Spondyloarthritis: 16- and 52-Week Results of a Phase 3 Randomized Trial (COAST-X)

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

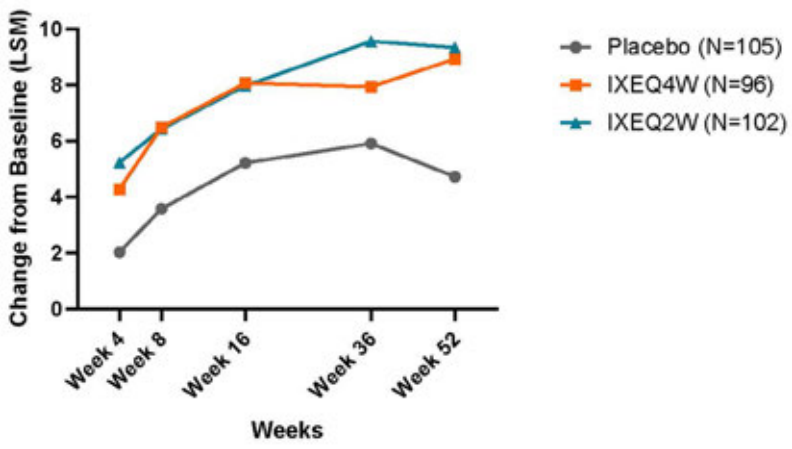
Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies have determined that axial spondyloarthritis (axSpA) significantly impairs patients' health-related quality of life (HRQoL).[1] The patients with nr-axSpA have the same disease burden as patients with r-axSpA.[2] We report the HRQoL results at Weeks 16 and 52 in patients with nonradiographic (nr)-axSpA treated with Ixekizumab (IXE).

Methods: COAST-X (NCT02757352) is a Phase 3, multicenter, randomized, double-blind, placebo (PBO)-controlled, parallel-group, clinical trial. Enrolled patients were adults with active nr-axSpA as per the Assessment of SpondyloArthritis international Society (ASAS) criteria, with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and total back pain ≥4, and with no prior treatment with biologic agents. Patients who fulfilled the definition of sacroiliitis

Figure: SF-36 physical component summary LSM changes from baseline



per modified New York (mNY) criteria were excluded. Patients were randomized in a 1:1:1 ratio to subcutaneous PBO, 80 mg IXE every 4 (Q4W) or 2 weeks (Q2W) up to Week 52. For patients who needed rescue and switched to IXE 80 mg Q2W, observations after rescue were considered as missing. Changes from baseline in SF-36 up to Week 52 were analyzed by mixed model for repeated measures without imputation for missing data.

Results: From baseline to Week 16, Physical Component Summary (PCS) significantly differed between PBO and IXE Q4W (p=0.013), and IXE Q2W (p=0.015) groups. Significant improvement over PBO was noted as early as Week 4 (IXE Q4W: p=0.015; IXE Q2W: p< 0.001) and it was maintained until Week 52 (IXE Q4W: p=0.012; IXEQ2W: p=0.006). Since the baseline MCS values were within the normal range across all treatment groups, no significant improve-

Table: SF-36 baseline scores and change from baseline (LSmean) at Week 16 and Week52

	Placebo (n=105)			IXE Q4W (n=96)			IXE Q2W (n=102)		
	Baseline	Change at Week 16	Change at Week 52	Baseline	Change at Week 16	Change at Week 52	Baseline	Change at Week 16	Change at Week 52
Physical Component Summary	32.6	5.2 (0.8)	4.7 (1.2)	33.5	8.1 (0.8)*	8.9 (1.1)*	31.9	8.0 (0.8)*	9.3 (1.1)*
Mental Component Summary	48.3	1.9 (0.8)	3.5 (1.2)	47.2	3.0 (0.8)	4.4 (1.0)	47.7	3.6 (0.8)	4.2 (1.0)
Domains:#									
Physical Function	34.0	5.2 (0.8)	4.3 (1.2)	35.7	7.7 (0.8)*	8.7 (1.1)*	34.3	8.0 (0.8)*	9.7 (1.1)**
Role-Physical	36.4	4.3 (0.8)	4.8 (1.2)	36.9	6.4 (0.8)	7.1 (1.0)	36.0	6.8 (0.8)*	7.7 (1.0)
Bodily Pain	33.4	5.4 (0.8)	6.1 (1.3)	33.4	8.2 (0.8)*	8.9 (1.1)	32.6	8.8 (0.8)*	10.3 (1.1)*
General Health	39.1	3.3 (0.7)	4.8 (1.1)	38.6	5.2 (0.7)	6.6 (0.9)	37.2	4.3 (0.7)	5.2 (1.0)
Vitality	43.3	3.9(0.8)	5.0 (1.3)	42.2	6.4 (0.8)*	8.0 (1.1)	41.8	6.6 (0.8)*	7.5 (1.1)
Social Functioning	41.7	3.2 (0.9)	4.5 (1.2)	41.2	6.0 (0.9)*	8.1 (1.0)*	41.2	6.3 (0.9)*	8.2 (1.0)*
Role-Emotional	43.9	2.3 (0.9)	3.5 (1.2)	43.7	3.9 (0.9)	4.7 (1.0)	43.6	4.6 (0.9)	5.1 (1.0)
Mental Health	45.1	3.0 (0.8)	4.1 (1.1)	44.7	3.5 (0.8)	4.8 (0.9)	45.1	4.1 (0.8)	5.0 (0.9)

*p<0.05 vs placebo; **p <0.001 vs placebo

#Only domain scores are t-score values

ments were observed from baseline in Mental Component Summary (MCS) at Week 16 or Week 52 compared with the placebo group.

Conclusion: Patients with nr-axSpA treated with IXE demonstrated an improvement over PBO in self-reported HRQoL at Week 16 and throughout Week 52 as measured by SF-36. The improvement was significant for PCS and some domains. Significant improvements were also observed as early as the first time the instrument was applied (Week 4).

Study Sponsor Statement: This study was supported by Eli Lilly and Company. Lilly participated in the study design, data collection, and the analysis and reporting of study results.

References

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2. Zhao SS, et al. *Rheumatology (Oxford)*. 2019. https://doi.org/10.1093/rheumatology/kez171.

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Abstract Number: 1546

Effectiveness and Retention Rate of Secukinumab for Psoriatic Arthritis and Axial Spondyloarthritis: Real-life Data from the Italian LORHEN Registry

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Observational data on the use of secukinumab for the treatment of spondyloarthritides are still lacking. The aim of this study is to evaluate the effectiveness and the 3-year retention rate of secukinumab in psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) patients in a real-life setting.

Methods: Data of all PsA and axSpA patients (diagnosed according to CASPAR and ASAS criteria, respectively) treated with secukinumab were prospectively collected in the Italian multicentric LORHEN registry. Effectiveness was measured as the mean change from baseline of Disease Activity in PSoriatic Arthritis score (DAPSA) in PsA and Ankylosing Spondylitis Disease Activity Score (ASDAS) in axSpA patients. Rates of DAPSA remission and ASDAS inactive disease were also computed. The 3-year retention rate was calculated by the Kaplan-Meier method and compared between PsA and axSpA by a log-rank test. A descriptive analysis of reasons for discontinuation was performed.

Results: The study population included 195 PsA (55.4% females, mean age 50.7 [±11.8] years, mean disease duration 10 [±7.8] years, mean baseline DAPSA 23.12 [±12.3]) and 94 axSpA (61.7% males, mean age 49.1 [±12.7] years, mean disease duration 10.4 [±9.4] years, mean baseline ASDAS 3.41 [±1.1]) patients who received secukinumab as first (26.5 and 33%, respectively) or subsequent biologic agent. Compared with baseline, the 3-, 6- and 12-month mean values of both DAPSA (12.6 [±9], 11.2 [±10.5] and 9.3 [±7.5], respectively) and ASDAS (2.23 [±0.9], 2.15 [±0.9], and 1.84 [±0.9], respectively) were significantly decreased ($p< 0.001$ for all the timepoints). The 3-, 6-, and 12-month rates of remission/inactive disease were 15.5, 25.4, and 30.5% in PsA and 18, 23.7, and 28.6% in axSpA group, respectively. One- and 3-year retention rate (figure 1) were respectively 79.4% and 66.6% in PsA and 72.3% and 70.1% in axSpA patients, with no significant difference between the two groups ($p=0.517$). The most frequent reason for withdrawal was inefficacy in both PsA (n=41) and axSpA (n=20), whereas only 8 PsA and 6 axSpA patients discontinued secukinumab because of adverse events.

Conclusion: Our real-life data confirmed the effectiveness and the favorable safety profile of secukinumab for both PsA and axSpA, resulting in a high 3-year retention rate.

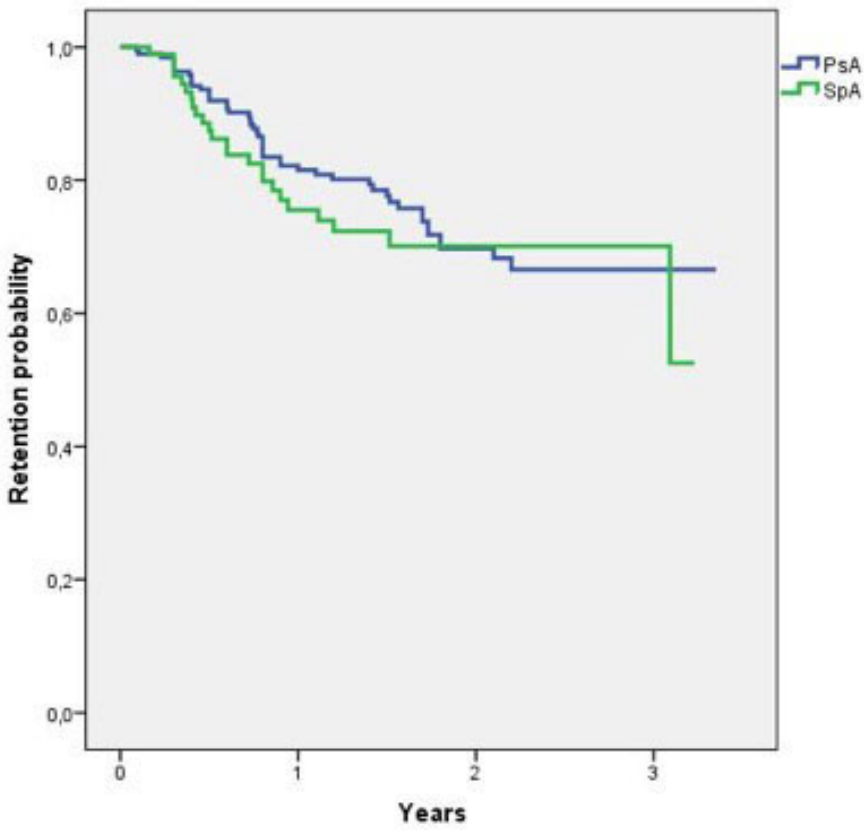


Figure 1: secukinumab retention rate in PsA and axSpA patients.

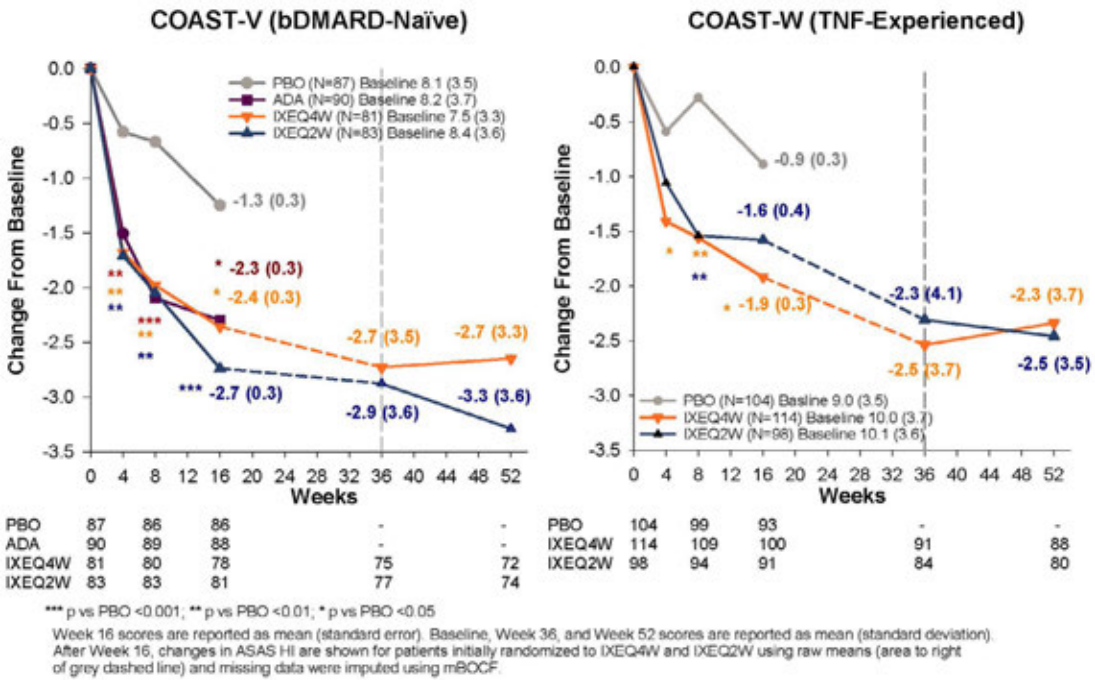
Disclosure: E. Favalli, None; **A. Marchesoni**, None; **S. Balduzzi**, None; **C. Montecucco**, None; **C. Lomater**, None; **G. Crepaldi**, None; **S. Tamanini**, None; **C. Bazzani**, None; **E. Fusaro**, None; **M. Priora**, None; **A. Ianniello**, None; **R. Caporali**, None.

Abstract Number: 1547

Ixekizumab Improves Self-reported Overall Functioning and Health as Measured by the Assessment of SpondyloArthritis International Society Health Index in Patients with Active Radiographic Axial Spondyloarthritis: 52-Week Results of Two Phase 3 Randomized Trials

Uta Kiltz,[1] Désirée van der Heijde,[2] Annelies Boonen,[3] Lianne Gensler,[4] Theresa Hunter,[5] Fangyi Zhao,[6] Baojin Zhu,[5] Rebecca Bolce,[5] Hilde Carlier,[5] and Jürgen Braun[7], [1]Rheumazentrum Ruhrgebiet/Ruhr University Bochum, Herne, Germany, Herne, Germany, [2]Leiden University Medical Center, Leiden, Netherlands, [3]Maastricht University Medical Center, Maastricht, Netherlands, [4]University San Francisco California, San Francisco, CA, [5]Eli Lilly and Company, Indianapolis, [6]Eli Lilly and Company, Indianapolis, IN, [7]Rheumazentrum Ruhrgebiet/Ruhr University, Herne, Germany

Figure 1. ASAS HI Change From Baseline



*** p vs PBO <0.001; ** p vs PBO <0.01; * p vs PBO <0.05

Week 16 scores are reported as mean (standard error). Baseline, Week 36, and Week 52 scores are reported as mean (standard deviation). After Week 16, changes in ASAS HI are shown for patients initially randomized to IXEQ4W and IXEQ2W using raw means (area to right of grey dashed line) and missing data were imputed using mBOCF.

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

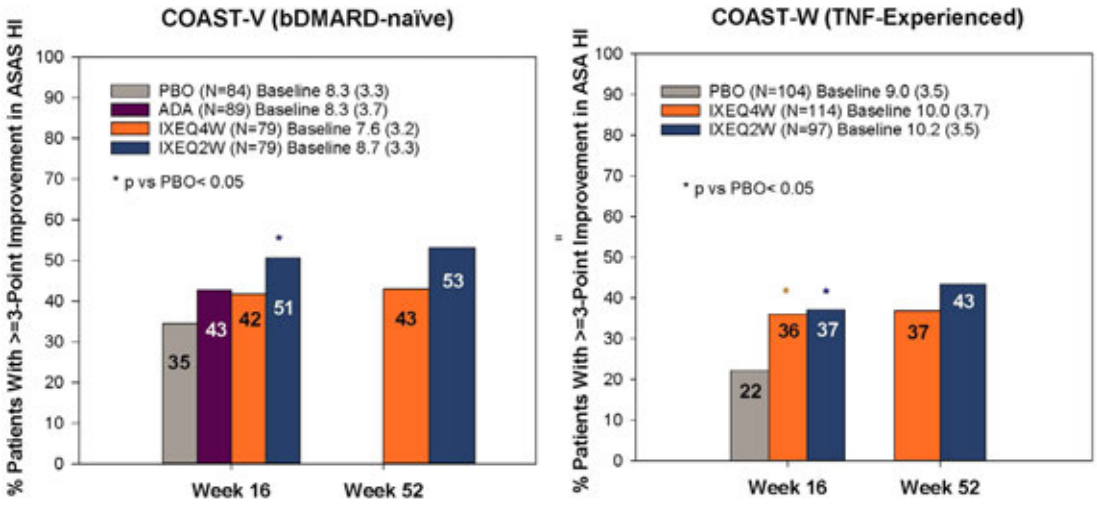
Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The Assessment of SpondyloArthritis international Society Health Index (ASAS HI) measures health, disability, and functioning in patients (pts) with spondyloarthritis (SpA)[1,2]. The purpose of this study was to assess the impact of 52 weeks of ixekizumab (IXE) treatment on overall functioning and health in 2 phase 3 trials of pts with ankylosing spondylitis (AS)/radiographic axial SpA (r-axSpA) who were either biologic (b)DMARD-naïve (COAST-V [NCT02696785]) or who previously failed or were intolerant to up to 2 TNF-inhibitors (TNF-experienced) (COAST-W [NCT02696798]).

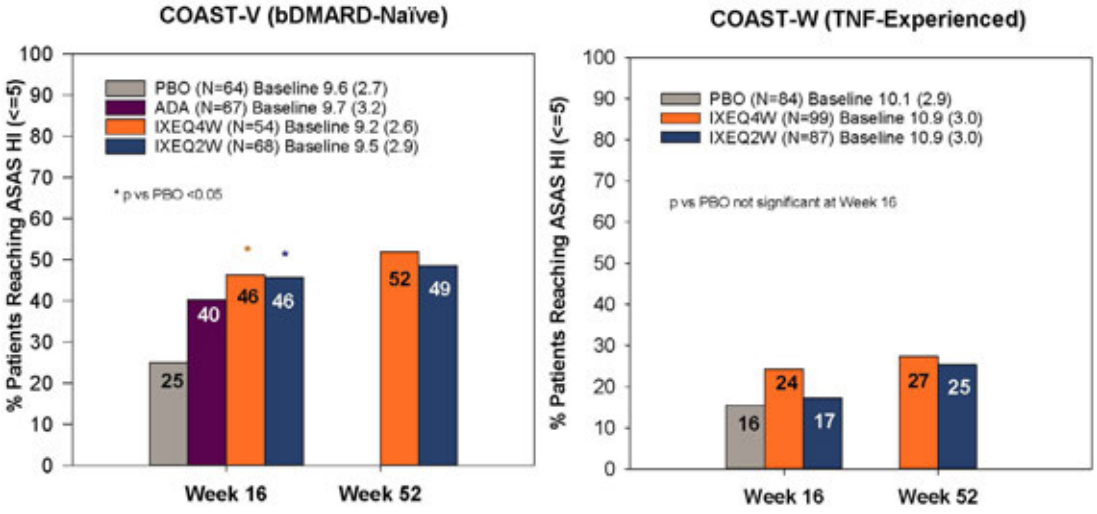
Methods: Pts were originally randomized equally to IXE 80mg every 2 weeks (Q2W), every 4 weeks (Q4W), placebo (PBO) or (in COAST-V only) to adalimumab (ADA) 40mg Q2W. At Week16, original PBO and ADA patients were rerandomized 1:1 to either IXE regimen. All pts were treated for up to 52 weeks. Change from baseline in ASAS HI (score 0-17 with higher score indicating worse health [1,2]) up to Week 16 was analyzed using a mixed-effects model of repeated measures. Changes beyond Week 16 through Week 52 (only for pts originally randomized to IXE) were

Figure 2. Percentages of Patients With >=3 (SDC) Improvement in ASAS HI Scores From Baseline



The analyses were based on patients with baseline ASAS HI score >= 3. Week 52 data are for patients initially randomized to IXEQ4W and IXEQ2W.
Baseline scores are reported as mean (standard deviation).

Figure 3: Percentages of Patients Achieving ASAS HI Good State (<=5)



The analyses were based on patients with baseline ASAS HI score > 5. Week 52 data are shown for patients initially randomized to IXEQ4W and IXEQ2W. Baseline scores are reported as mean (standard deviation).

summarized with missing data imputed using modified baseline observation carried forward (mBOCF) approach. Categorical data were summarized with nonresponder imputation for missing data. For the ASAS HI, the smallest detectable change [SDC] was reported as 3.0 and patients having an ASAS HI total score ≤ 5 were defined as being in a good health state [2].

Results: At baseline, mean (standard deviation) ASAS HI scores were 8.1 (3.6) and 9.7 (3.6) in COAST-V and COAST-W, respectively. At Week 16, IXEQ4W-treated pts had improved ASAS HI scores versus PBO in both trials [3, 4]. Improvement was sustained or further increased through Week 52 (Figure 1). The proportions of pts continuously treated with IXE and having reached SDC (Figure 2) and achieving ASAS HI good state (Figure 3) were maintained at Week 52. Among pts originally randomized to PBO but switched to IXE at Week16, the percentages of pts with improvement above SDC or achieving an ASAS HI good state through 52 weeks were 45% and 36% in bDMARD-naive, and 41% and 31% in TNF-experienced pts, respectively.

Conclusion: Continued treatment with IXE through 52 weeks led to sustained improvement in ASAS HI as measured by change from baseline, and proportions of pts achieving a change above SDC or good ASAS HI state in both in bDMARD-naïve and in TNF-experienced pts.

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1. Kiltz, et al. *Ann Rheum Dis*. 2015;74:830-835.
2. Kiltz , et al. *Ann Rheum Dis*. 2018;77:1311-1317.
3. van der Heijde, et al. *Lancet* 2018;392:2441-2451.
4. Deodhar, et al. *Arthritis Rheumatol*. 2019;71-599-611.

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5, 6, 8, Amgen, 2, 5, 8, Baxter, 2, 5, 8, Biogen, 2, 8, 9, BMS, 2, 5, 8, Boehringer, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Celgene, 2, 3, 5, 8, Celltrion, 2, 5, 8, Centocor, 2, 5, 8, Chugai, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Hexal, 2, 5, 8, Janssen, 2, 5, 8, Johnson & Johnson, 2, 5, Medac, 2, 5, 8, MSD, 2, 5, MSD (Schering-Plough), 2, 5, 8, Mundipharma, 2, 5, 8, Mylan, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, Pfizer (Wyeth, Hospira), 2, 5, 8, Roche, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, UCB Pharma, 2, 5, 8.

Abstract Number: 1548

Drug Survival of Secukinumab for Axial Spondyloarthritis in a Real-World Setting Possible Response Factors

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Secukinumab is a newly introduced biologic therapy against IL-17 which has been proved effective in patients with ankylosing spondylitis (AS) in clinical trials and it has been added to the most recent national and international treatment guidelines. However, real-world data of its use is still scarce. This study aims to analyze drug survival of secukinumab for axial spondyloarthritis (AxSpA) in a real world setting and identify response factors.

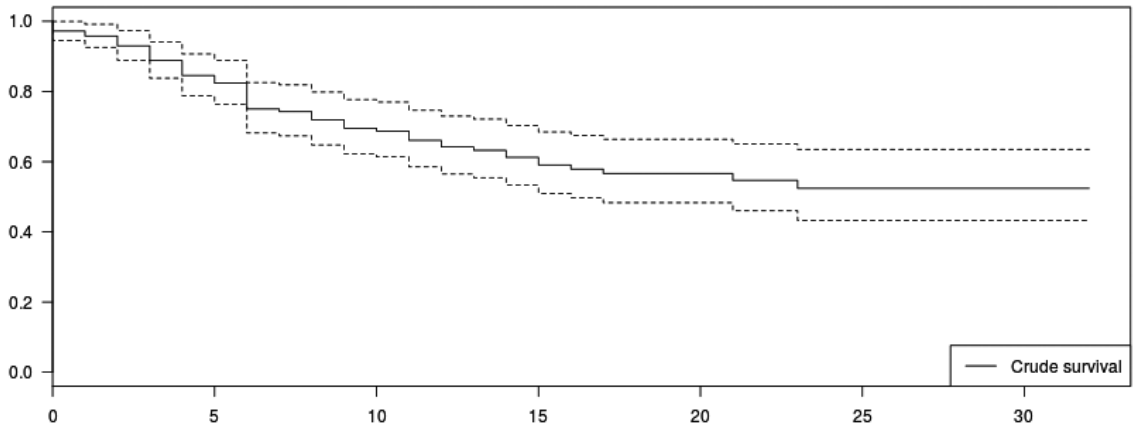

Figure. Time to withdrawal of secukinumab measured in months.

Methods: Multicentric observational, retrospective, longitudinal study conducted in 4 tertiary hospitals of the Madrid region. Patients over 18 y.o. with clinical diagnosis of AxSpa and having received at least one dose of secukinumab between January 2016 and October 2018 were included. Medical records were reviewed to collect demographic and clinical data related to AxSpA, its features and treatment. Statistical analysis was performed including bivariate analisys (considering withdrawal of drug during study period or not) and survival analysis with Kaplan-Meier and Cox regression. Reasons for discontinuating therapy were described. To detect inffluential variables, demographic characteristics, HLA-B27 positivity, radiographic features, previous biologic therapies, comorbidities and extra-articular involvement were analyzed.

Results: Out of 143 patients included, 89 (62%) mantained secukinumab therapy at the end of the observation period (Dec 31, 2018), with an average drug survival time of 17 ± 8,2 months. 54 patients (38%) withdrawn therapy, due to primary ineffectiveness (26) , secundary ineffectiveness (14), adverse events (7) and other reasons (7). Median time to withdrawal was 6 months (0-21). No significative differences were found between groups, but a tendency to higher number of female patients (55% vs 41%, p 0,07), non radiographic AxSpA (35% vs 27%, p 0,053) and lower HLA-B27 positivity (50% vs 65%, p 0,052) was noted in the group withdrawing therapy. Previous exposure to biologic therapy did not differ (75% vs 71%, p 0,37). Number of bDMARDs before Secukinumab therapy was also similar in both groups; the proportion of patients with previous exposure to 2 or more bDMARDs were 17% vs 22% (p 0.373). Neither differences were found in all other variables studied (demographic, hip arthropathy, syndesmophytes, extra-articular involvement -uveitis, psoriasis, inflammatory bowel disease- nor in comorbidities (tobacco exposure, hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, malignancy).

Conclusion: This study assesing drug survival of secukinumab in real-world setting showed a trend to lower drug survival in comparison to clinical trial data. No differences were found in the treatment withdrawal group. Population in which secukinumab is prescribed in real-world setting differs from clinical trials, with higher previous exposure to bDMARDs and higher comorbidity.

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Abstract Number: 1549

Primary 1-Year Data of Ixekizumab in Biologic Disease-Modifying Anti-rheumatic Drug-Naïve Patients with Radiographic Axial Spondyloarthritis Including Data in Patients Rerandomized from Adalimumab to Ixekizumab

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

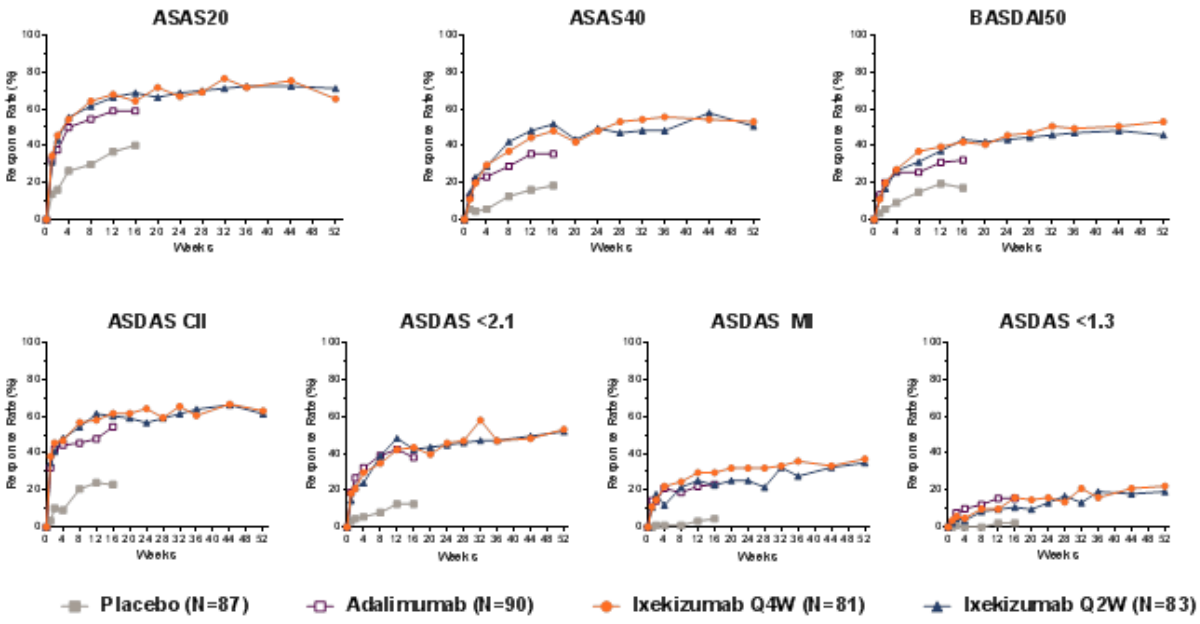
Background/Purpose: During 16 weeks of blinded treatment, ixekizumab (IXE) and an adalimumab (ADA) active reference arm were found superior to placebo (PBO) in improving signs and symptoms of radiographic axial spondyloarthritis (r-axSpA).[1] Here, we assess the safety and efficacy of continuous treatment with IXE through 52 weeks in patients with r-axSpA and describe clinical response at Week 52 for patients who switched to IXE following 16 weeks of treatment with either ADA or PBO.

Efficacy of IXE in bDMARD-naïve patients with active r-axSpA		
Mean (±SD) change from baseline at Week 52 mBOCF (intent-to-treat)	**IXE Q4W (N=81)**	**IXE Q2W (N=83)**
ASDAS-CRP	-1.7 (1.2)	-1.6 (1.0)
BASDAI[a]	-3.3 (2.5)	-3.1 (2.3)
C-Reactive Protein (mg/L)	-9.2 (12.4)	-9.6 (14.5)
BASFI	-2.8 (2.5)	-2.8 (2.4)
SF-36 PCS[b]	8.3 (9.5)	8.1 (7.5)
ASAS Health Index	-2.7 (3.3)	-3.3 (3.6)
SPARCC Spine Score (observed)[c]	-8.8 (17.3)	-8.5 (15.9)

Efficacy in patients rerandomized from adalimumab to ixekizumab			
Response (%) NRI, extended treatment period population[d]	**PBO/All IXE (N=86)**	**ADA/All IXE (N=86)**	**All IXE/All IXE (N=164)**
ASAS40			
Week 16	18.6	36.0	50.0
Week 52	46.5	51.2	51.8

[a]BASDAI items included 1) Fatigue, 2) Spinal pain, 3) Peripheral arthritis, 4) Enthesitis, 5) Intensity, and 6) Duration of morning stiffness. Items were scored on a 0-10 numeric rating scale.
[b]SF-36 analyses based on 2009 US norms
[c]SPARCC Spine: N=72 (IXE Q4W), N=68 (IXE Q2W)
[d]Includes all patients who received ≥1 dose of IXE during Weeks 16-52
ADA=adalimumab; BASFI=Bath Ankylosing Spondylitis Functional Index; IXE=ixekizumab; mBOCF=modified Baseline Observation Carried Forward; NRI=nonresponder imputation; PBO=Placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SF-36 PCS=Medical Outcomes Study 36-Item Short-Form Health Survey Physical Component Summary; SPARCC=Spondyloarthritis Research Consortium of Canada

Clinical improvements in r-axSpA disease activity in bDMARD-naïve patients with active r-axSpA through Week 52 of treatment with ixekizumab (NRI).



Analyses were conducted on the intent-to-treat population according to initially assigned treatments.
Adalimumab represents an active reference arm. The study was not powered to test equivalence or non-inferiority of the active treatment arms to each other, including ixekizumab versus adalimumab.
ASAS = Assessment of SpondyloArthritis International Society, ASDAS = Ankylosing Spondylitis Disease Activity Scale, BASDAI50 = ≥50% improvement from baseline in the Bath Ankylosing Spondylitis Disease Activity Index, CII = Clinically Important Improvement (ASDAS change from baseline ≥1.1), MI = Major Improvement (ASDAS change from baseline ≥2.0 or reached the minimum ASDAS score), Q2W= every 2 weeks, Q4W= every 4 weeks

Methods: Participants were biologic disease-modifying anti-rheumatic drug (bDMARD)-naïve adult patients with active r-axSpA per Assessment of Spondyloarthritis (SpA) international Society (ASAS) criteria (sacroiliitis centrally defined by modified New York criteria and ≥1 SpA feature) and inadequate response or intolerance to non-steroidal anti-inflammatory drugs. Patients were randomized 1:1:1:1 to receive 80 mg IXE every 2 (Q2W) or 4 weeks (Q4W), 40 mg adalimumab (ADA) Q2W (active reference arm), or PBO. At Week 16, patients assigned to IXE continued their assigned treatment and patients receiving PBO or ADA were re-randomized 1:1 to IXE Q2W or IXE Q4W through Week 52.

Results: Of 164 patients initially randomized to IXE, 146 (89%) completed Week 52. IXE Q4W and IXE Q2W led to persistent improvements in disease activity, function, objective inflammation (MRI and C-reactive protein), quality of life, health status, and overall functioning for up to 52 weeks (Figure and Table). For patients initially assigned to PBO or ADA, ASAS40 response showed a numerical increase upon switching to IXE (Table). Frequencies of treatment-emergent adverse events (AEs) were similar between IXE dosing regimens. Among patients with ≥1 dose of IXE (N=336), serious AEs occurred in 20 (6%) patients. There were no deaths and 11 (3%) patients discontinued due to AEs.

Conclusion: Persistent improvements in the signs and symptoms of r-axSpA were observed through Week 52 in patients who received continuous treatment with IXE. ASAS40 response rates at Week 52 were numerically similar between patients who received continuous treatment with IXE and patients who switched from ADA to IXE. No unexpected safety signals were observed through 52 weeks of treatment.

Reference

1. van der Heijde et al. Lancet, 2018.

Disclosure: C. Wei, AbbVie, 2, 5, BMS, 2, 5, Celgene, 2, 5, Chugai, 5, Eisai, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi-Aventis, 5, TSH Biopharm, 2, 5, UCB Pharma, 2, 5; **L. Gensler**, AbbVie, 2, 5, Abbvie, 2, 9, Amgen, 2, Amgen, AbbVie and Novartis, 2, Center for Disease Control, 8, Division of Vaccine Injury Compensation, 8, Eli Lilly, 5, 9, Eli Lilly and Company, 9, Galapagos, 5, 9, Galapagos, Janssen, Eli Lilly, Novartis, Pfizer, and UCB, 5, Janssen, 5, 9, Novartis, 2, 5, 9, Pfizer, 2, 9, Spondylitis Association of America, 6, Spondyloarthritis Research and Treatment Network (SPARTAN), 6, UCB, 2, 5, 9, UCB Pharma, 2, 9; **J. Walsh**, AbbVie, 2, 5, ABBVIE, NOVARTIS, LILLY, AMGEN, UCB, 5, Amgen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, PFIZER, ABBVIE, 2, UCB, 5; **R. Landewé**, Abbott, 2, 5, 8, Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8; **T. Tomita**, AbbVie, 5, 8, Astellas, 5, 8, BMS, 5, 8, Eisai, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Mitsubishi Tanabe, 5, 8, Novartis, 5, 8, Takeda, 5, 8, Pfizer, 5, 8; **F. Zhao**, Eli Lilly, 1, 3, 4, Eli Lilly and Company, 1, 3, 4; **G. Gallo**, Eli Lilly, 1, 3, 4, Eli Lilly and Company, 1, 3, 4; **H. Carlier**, Eli Lilly and Company, 1, 3, 4; **M. Dougados**, Pfizer, 2, 5, 8, Abbvie, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, UCB, 2, 5, 8, Novartis, 2, 5, 8.

Abstract Number: 1550

Ixekizumab Demonstrates Consistent Improvement up to Week 108 in Psoriatic Arthritis Across Individual ACR Components for Patients Naïve to Biologic DMARDs or with Previous Inadequate Response to TNF Inhibitors

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: While the composite ACR core data set is considered a standard for assessing disease severity and improvement in PsA, understanding the response rates of the individual ACR components may be more useful in guiding clinical decisions.[1] Here we present the efficacy response across all ACR components to Week 108 in PsA patients treated with ixekizumab (IXE), a high-affinity monoclonal antibody that specifically targets IL-17A, approved for the treatment of adults with active PsA and moderate-to-severe psoriasis.

Methods: In 2 Phase 3 randomized controlled trials, patients who met Classification Criteria for PsA and were biologic DMARD (bDMARD)-naïve (SPIRIT-P1) or had an inadequate response to 1 or 2 TNFi (SPIRIT-P2) received sub-

Table: Overview of ACR Components at Week 108 of the Intent-to-Treat Population who were randomized to IXE at Week 0 (observed data)

		SPIRIT-P1				SPIRIT-P2			
		Mean Baseline Score		Mean Change from Baseline at Week 108		Mean Baseline Score		Mean Change from Baseline at Week 108	
Parameters		IXE Q4W (N=107)	IXE Q2W (N=103)	IXE Q4W (N=107)	IXE Q2W (N=103)	IXE Q4W (N=122)	IXE Q2W (N=123)	IXE Q4W (N=122)	IXE Q2W (N=123)
TJC Score	Nx; Mean (SD)	107; 20.5 (13.7)	103; 21.5 (14.1)	73; -17.6 (12.5)	67; -19.2 (12.4)	121; 22.0 (14.1)	123; 25.0 (17.3)	79; -18.5 (13.9)	63; -18.8 (12.8)
SJC Score	Nx; Mean (SD)	107; 11.4 (8.2)	103; 12.0 (7.2)	73; -9.5 (7.6)	67; -11.6 (7.4)	121; 13.0 (11.1)	123; 13.5 (11.5)	79; -10.5 (9.3)	63; -11.8 (10.9)
PhyGA	Nx; Mean (SD)	96; 57.6 (18.7)	96; 58.5 (19.0)	66; -45.4 (22.5)	61; -49.0 (21.2)	105; 60.3 (20.9)	96; 64.6 (16.8)	68; -45.9 (23.3)	56; -50.5 (21.9)
Pain VAS	Nx; Mean (SD)	104; 60.1 (19.4)	99; 58.4 (21.7)	71; -34.4 (25.2)	65; -41.6 (26.2)	120; 63.9 (21.4)	120; 62.7 (20.9)	79; -33.4 (26.4)	62; -34.3 (25.8)
PatGA	Nx; Mean (SD)	104; 62.7 (19.1)	99; 62.5 (19.9)	71; -37.7 (26.0)	65; -47.2 (26.5)	120; 66.4 (20.5)	120; 66.0 (20.5)	79; -37.4 (27.8)	62; -39.1 (24.7)
HAQ-DI	Nx; Mean (SD)	103; 1.2 (0.5)	99; 1.2 (0.6)	70; -0.6 (0.5)	65; -0.6 (0.6)	120; 1.2 (0.6)	120; 1.2 (0.6)	79; -0.4 (0.6)	62; -0.5 (0.6)
CRP	Nx; Mean (SD)	107; 12.8 (16.4)	103; 15.1 (25.9)	73; -9.1 (16.4)	67; -13.0 (32.7)	119; 17.0 (27.5)	123; 13.5 (26.1)	63; -15.4 (30.1)	47; -5.4 (19.7)

IXE=ixekizumab; IXE Q4W=IXE 80 mg Q4W; IXE Q2W= IXE 80 mg Q2W; N=number of patients in the analysis population; Nx=number of patients with non-missing data; PatGA=Patient's Global Assessment of Disease Activity; PhyGA=Physician Global Assessment; SD=standard deviation; SJC= swollen joint count (66); TJC=tender joint count (68).

cutaneous IXE 80 mg every 2 weeks (Q2W) or every 4 weeks (Q4W), after a 160-mg starting dose. The change from baseline at Week 108 for all components of ACR was assessed: tender joint count (TJC), swollen joint count (SJC), physician global assessment (PhyGA), patient's assessment of pain visual analog scale (VAS), patient's global assessment of disease activity (PatGA), HAQ-Disability Index (HAQ-DI) and CRP. Observed results are reported for the intent-to-treat (ITT) population who were initially randomized to IXE at baseline (Week 0). At Week 16, inadequate responders (< 20% improvement in both TJC and SJC) received rescue therapy and were analyzed as non-responders at Weeks 20 and 24. From Week 32 and at each subsequent visit, patients were discontinued from the study if they failed to achieve ≥20% improvement in both TJC and SJC.

Results: When evaluating group-level changes to 2 years (Week 108), patients treated with the approved PsA dosing of IXE Q4W showed comparable mean change from baseline in clinical components of ACR (TJC, SJC, PhyGA, pain VAS, PatGA, and HAQ-DI) regardless of prior TNFi failure (Table). The median (maximum, minimum) change from baseline in laboratory measure of CRP was comparable between IXE Q4W-treated patients in both populations: SPIRIT-P1, -3.9 (-99.1, 9.2); SPIRIT-P2, -2.3 (-142.0, 8.2).

Conclusion: Irrespective of whether bDMARD-naïve or having prior inadequate response or intolerance to TNFi, IXE Q4W-treated patients with PsA achieved comparable efficacy across all clinical components of ACR as measured by mean change from baseline at Week 108.

Reference

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Disclosure: A. Turkiewicz, AbbVie, 2, 5, 8, GeneTech, 2, 5, 8, Janssen, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Regeneron, 2, 5, 8, Sanofi, 2, 5, 8; **A. Trevelin Sprabery**, Eli Lilly and Company, 1, 3; **A. Gellett**, Eli Lilly and Company, 1, 3; **S. Young Park**, Eli Lilly and Company, 1, 3; **A. Constantin**, AbbVie, 5, BMS, 5, Gilead, 5, Janssen, 5, Eli Lilly and Company, 5, Novartis, 5, Sanofi, 5, UCB, 5.

Abstract Number: 1551

Does Retention and Remission Rates to 2nd and 3rd TNF Inhibitors in Patients with Axial Spondyloarthritis Depend on the Reason from Withdrawal to the Previous Treatment? – Real World Data from 12 European Countries in the EuroSpA Research Collaboration

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Table: Baseline characteristics, retention and remission rates of axSpA patients initiating 2nd and 3rd TNFi overall and stratified by reason of withdrawal from the previous TNFi (AE or LOE)

	2nd TNFi (n=7953)*		3rd TNFi (n=2782)**	
	Baseline characteristics			
Age, years	43(35-52)		44(36-53)	
Male	55%		52%	
HLA-B27	66%		66%	
Concomitant csDMARD/prior csDMARD	28% / 68%		30% / 74%	
Disease duration, years	5(2-11)		6(3-12)	
First TNFi drug Infliximab/ Etanercept / Adalimumab / Certolizumab / Golimumab	14% / 34% / 32% / 5% / 16%		19% / 24% / 28% / 7% / 21%	
BASDAI	56(37-71)		59(40-74)	
BASFI	44(23-65)		47(27-70)	
BASMI	20(10-40)		30(10-50)	
	Retention rates			
6 / 12 / 24 months (95% CI)	81% (80-82%) / 72% (71-73%) / 64% (62-65%)		81% (80-83%) / 72% (70-73%) / 62% (60-64%)	
	Initiating 2nd TNFi because of AE on 1st TNFi	Initiating 2nd TNFi because of LOE on 1st TNFi	Initiating 3rd TNFi because of AE on 1st TNFi	Initiating 3rd TNFi because of LOE on 1st TNFi
6 months (95% CI)	77% (75-79%)	78% (77-80%)	77% (73-80%)	80% (78-82%)
12 months (95% CI)	68% (66-70%)	68% (66-69%)	68% (64-72%)	69% (67-72%)
24 months (95% CI)	61% (58-63%)	58% (56-60%)	61% (56-65%)	58% (56-61%)
	Response rates			
	LUNDEX adjusted ***		LUNDEX adjusted ***	
BASDAI<4 at 6 / 12 / 24 months	44% / 36% / 27%		37% / 30% / 21%	
ASDAS inactive disease at 6 / 12 / 24 months	18% / 15% / 11%		13% / 10% / 7%	
	Initiating 2nd TNFi because of AE on 1st TNFi	Initiating 2nd TNFi because of LOE on 1st TNFi	Initiating 3rd TNFi because of AE on 1st TNFi	Initiating 3rd TNFi because of LOE on 1st TNFi
	LUNDEX adjusted * **			
BASDAI<4 at 6 / 12 / 24 months	46% / 37% / 29%	39% / 32% / 23%	39% / 28% / 25%	35% / 28% / 19%
ASDAS inactive disease at 6 12 / 24 months	21% / 16% / 14%	13% / 11% / 8%	15% / 13% / 9%	11% / 8% / 6%

*Data are as observed, median (IQR) or percentage; csDMARD: conventional synthetic Disease Modifying Anti Rheumatic Drug; TNFi: tumor necrosis factor inhibitor; BASDI: Disease Activity Score 28 joint-count; DAPSA28: Disease Activity index for Psoriatic Arthritis 28 joint-count; *number of patients with available data varied from n 1480-7953; **number of patients with available data varied from n 519-2782; ***LUNDEX adjusted: crude value adjusted for drug retention*

SESSION INFORMATION

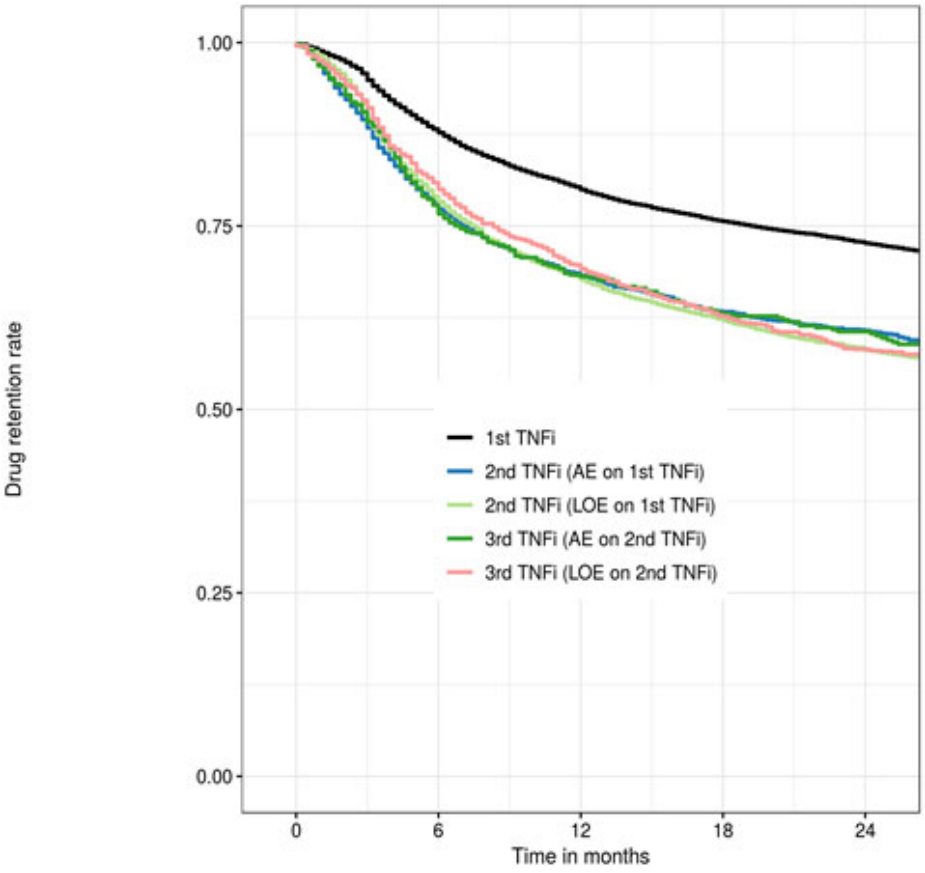
Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Tumour necrosis factor inhibitors (TNFi) are efficacious in patients with axial spondyloarthritis (axSpA), but still some patients switch to a different TNFi because of adverse effects (AE) or lack of effect (LOE). The EuroSpA Collaboration has previously demonstrated a 1-year retention rate of 79% and 6 months LUNDEX adjusted BASDAI< 4 of 59%[1] in patients initiating the first TNFi treatment. Little is known about the effectiveness of switching to a second and third TNFi in patients with axSpA.



Numbers at risk

	0	6	12	18	24
1st TNFi	23956	19550	16312	13799	11844
2nd TNFi (AE on 1st TNFi)	1829	1317	1050	880	763
2nd TNFi (LOE on 1st TNFi)	4057	2948	2282	1866	1560
3rd TNFi (AE on 2nd TNFi)	541	390	310	260	219
3rd TNFi (LOE on 2nd TNFi)	1521	1128	887	717	597

Time in months

Figure: Kaplan-Meier curves (top) showing drug retention rates up to 24 months for 1st TNFi*, for 2nd (AE or LOE on 1st TNFi) and 3rd TNFi (AE or LOE on 2nd TNFi). The table (bottom) shows the number of patients who were still being treated at the corresponding time points
*previously reported

We aim to investigate retention and response rates at 6, 12 and 24 months in patients with axSpA initiating the 2nd and 3rd TNFi in clinical practice across Europe. Secondly, to investigate whether the outcomes were associated with the reason for withdrawal (AE or LOE) from the previous treatment.

Methods: Prospectively collected data on axSpA patients in routine care from 12 European registries were pooled. Kaplan-Meier estimation was used to investigate TNFi retention rates. LUNDEX adjusted[2] response rates were calculated for BASDAI< 4 and ASDAS inactive disease (ASDAS< 1.3). Group comparisons were performed by Chi-square test.

Results: A total of 7953 patients initiating their 2nd TNFi and 2782 patients initiating 3rd TNFi were included. Baseline characteristics are shown in the Table.

The overall retention rates for both 2nd and 3rd TNFi at 12 months were 72 % (Figure). Corresponding retention rates for the individual registries ranged from 52-90% and 54-89%, respectively. In both patients who stopped 1st TNFi due to AE or LOE, 12-month retention rate for the 2nd TNFi treatment was 68 %. In patients who stopped the 2nd TNFi due to AE or LOE, 12-month retention rates for the 3rd TNFi treatment were 68 % and 69%, respectively.

For the 2nd and 3rd TNFi, 6 months LUNDEX adjusted BASDAI< 4 were 44% and 37% (p< 0.001), respectively, and for ASDAS inactive disease 18% and 13% (p=0.003) (Table).

Conclusion: Data from 12 European countries demonstrated decreasing response rates with increasing number of previous TNFi, although with only minor difference between 2nd and 3rd. Patients who had withdrawn from the previous TNFi due to LOE had retention rates and remission rates similar to those who had withdrawn due to AE.

Acknowledgement: Novartis Pharma AG and IQVIA for supporting the EuroSpA collaboration.

References

1. Brahe et al. ACR 2018
2. Arthritis Rheum, 2006, 54(2), p:600-6

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Abstract Number: 1552

Clinically Meaningful Improvement in Skin and Nail Psoriasis in Bio-naïve Active Psoriatic Arthritis Patients Treated with Intravenous Golimumab: Results Through Week 52 from a Phase-3 Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: GO-VIBRANT is a Phase 3 trial of intravenous (IV) golimumab (GLM) in adult patients (pts) with active psoriatic arthritis (PsA). Clinically meaningful improvements in skin and nail psoriasis (PsO) and in Dermatology Life Quality Index (DLQI) that were significantly greater than placebo (PBO) at weeks (wks) 14 & 24 were previously reported.[1]

To evaluate improvement in skin and nail PsO and DLQI with IV GLM through wk52.

Methods: Adult bio-naïve PsA pts with active disease (≥5 swollen & tender joints, CRP ≥0.6mg/dL, active plaque psoriasis or documented history), despite treatment w/csDMARDs &/or NSAIDs, were randomized to IV GLM 2mg/kg at wks 0/4 & every 8 wks thereafter or PBO at wks 0/4/12/20 with crossover to GLM at wk24. Pts with ≥3% body surface area (BSA) psoriasis at baseline (BL) were assessed using Psoriasis Area and Severity Index (PASI, 0-72) of 75/90/100% improvement scale, modified Nail Psoriasis Severity Index (mNAPSI, 0-130) in pts with mNAPSI >0 at BL, and DLQI (0-30) scale.

Results: 394 pts (PBO:n=198; GLM:n=196) had ≥3% BSA psoriasis at BL; 76.5% had mNAPSI >0 at BL (mean 18.6). Pts on IV GLM achieved a greater PASI 75 response rate (RR) vs PBO at wk24 (64.8% vs 13.1%, p< 0.001). At wk52, PASI 75 RR was maintained in pts who continued IV GLM treatment and increased numerically in those who crossed-over from PBO to IV GLM (PBO→IV GLM) at wk24 (71.9% and 60.6%, respectively). At wk24, pts on IV GLM achieved significantly greater PASI 90/100 RR vs PBO. At wk52, PASI 90/100 RR was maintained among those continually on IV GLM and increased numerically in PBO→IV GLM pts (Table). At wk24, significantly greater proportions of pts on IV GLM ± BL methotrexate (MTX) achieved PASI 90/100 vs PBO. By wk52, both ± BL MTX, PASI 90/100 responses were maintained in those continually on IV GLM and increased numerically in PBO→IV GLM pts (Table). The mean decrease (improvement) from BL in the mNAPSI score was also greater with IV GLM vs PBO at wk24, overall and in groups ± BL MTX. At wk52, mNAPSI RR was maintained with continual IV GLM and increased numerically in PBO→IV GLM pts (Table). At wk24, the mean decrease (improvement) from BL in DLQI was greater with IV GLM vs PBO (–8.1 vs –1.9, p< 0.001). At wk52, mean DLQI improvement was maintained in pts continually on IV GLM and increased numerically in PBO→IV GLM pts (-7.8 vs -5.8). Similar patterns were seen in subgroups ± BL MTX. In pts with DLQI improvement >1 at baseline, rate of simultaneous achievement of both PASI 50 response & improvement in DLQI ≥5 was greater at wk24 with IV GLM (59.2%) vs PBO (8.1%, p< 0.001). At wk52, both were achieved by 56.6% continually on IV GLM vs 41.4% of PBO→IV GLM pts. Similar patterns were seen for simultaneous achievement of both improvement in DLQI ≥5 & PASI 75/90/100 at wks 24 and 52.

Table. Change from Baseline in PASI 90/100 and mNAPSI through Week 52				
	Week 24[1]		Week 52	
	PBO	IV-GLM 2 mg/kg	PBO→ IV-GLM 2 mg/kg at Wk 24	IV-GLM 2 mg/kg
Pts evaluable for improvement from BL in PASI, n	198	196	198	196
PASI 90 (%) % Diff (95% CI)	7.6	42.9 35.3 (27.4, 43.1)*	41.9	56.1
PASI 100 (%) % Diff (95% CI)	5.6	25.5 20.0 (13.2, 26.9)*	18.7	28.6
+ BL MTX, n	142	131	142	131
PASI 90 (%) % Diff (95% CI)	9.2	45.8 36.6 (26.9, 46.4)*	40.8	58.0
PASI 100 (%) % Diff (95% CI)	7.0	30.5 23.5 (14.6, 32.4)*	18.3	32.8
- BL MTX, n	56	65	56	65
PASI 90 (%) % Diff (95% CI)	3.6	36.9 33.4 (20.7, 46.1)*	44.6	52.3
PASI 100 (%) % Diff (95% CI)	1.8	15.4 13.6 (4.2, 23.0)**	19.6	20.0
Pts (mNAPSI >0) evaluable for change from BL in mNAPSI, n	170	197	170	197
Mean mNAPSI (SD) LS Mean diff (95% CI)	-3.7 (14.5)	-11.4 (16.4) -8.4 (-10.8, -6.0)*	-12.9 (16.2)	-12.1 (16.7)
+ BL MTX, n	121	129	121	129
Mean mNAPSI (SD) LS Mean diff (95% CI)	-5.8 (14.9)	-10.0 (15.6) -7.3 (-10.2, -4.4)*	-14.4 (16.1)	-10.1 (15.4)
- BL MTX, n	49	68	49	68
Mean mNAPSI (SD) LS Mean diff (95% CI)	1.7 (11.7)	-14.1 (17.6) -12.2 (-16.6, -7.8)*	-9.3 (16.0)	-15.8 (18.5)
	[1] Husni, ME et al. ACR 2018 *p<0.001; **p=0.010 BL, baseline; CI, confidence interval; GLM, golimumab; MTX, methotrexate; PASI, Psoriasis Area and Severity Index; PBO, placebo; Pts, patients			

Conclusion: Clinically meaningful improvements in skin and nail psoriasis and psoriasis quality of life after IV GLM treatment of PsA pts were maintained from 24 to 52 weeks of treatment.

Reference

1. Mease P et al. *EULAR* June 2018, Amsterdam, NL.

Disclosure: P. Mease, Janssen Research & Development, LLC, 2; **M. Husni**, Abbvie, 5, AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, Regeneron, Sanofi-Genzyme, UCB, 5, Abbvie, Amgen, Janssen, Novartis, Lilly, Regeneron, Pfizer and UCB, 5, Bristol-Myers Squibb, 5, Eli Lilly, 5, Genentech, 5, Janssen, 5, Janssen Research & Development, LLC, 2, 3, Novartis, 5, PASE questionnaires, 7, Pfizer, 5, Sanofi-Genzyme, 5, UCB, 5; **S. Chakravarty**, Janssen Research & Development, LLC, 3, Janssen Scientific Affairs, LLC, 1, 3, Johnson & Johnson, 1, 3; **S. Kafka**, Janssen Research & Development, LLC, 3, Janssen Scientific Affairs, LLC, 1, 3; **D. Harrison**, Janssen Research & Development, LLC, 3; **D. Parenti**, Janssen Scientific Affairs, LLC, 3; **L. Kim**, 3anssen Research & Development, LLC, 3,

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Abstract Number: 1553

Impact of Peripheral Swollen and Tender Joints at Baseline on Response to Treatment with Secukinumab in Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: AS is a chronic, inflammatory disease of the axial skeleton associated with pain, stiffness, disability, and reduced quality of life (QOL).[1] AS is defined by inflammation in spinal joints and radiographic changes at the sacroiliac joints, but patients (pts) frequently also have peripheral involvement, including swollen and tender joints (STJ),[2] a feature associated with worse overall disease activity.[3] Secukinumab is an IL-17 inhibitor approved for AS based on findings from the phase 3 MEASURE studies, in which it showed superiority to placebo in improving symptoms of AS.[4-6] We explored whether peripheral STJ in pts with AS might be prognostic of outcomes following secukinumab treatment.

Methods: Data from MEASURE 1 (NCT01358175), 2 (NCT01649375), 3 (NCT02008916), and 4 (NCT02159053) were pooled from baseline to week 16 and included in this hypothesis-generating analysis. No adjustments for multiple comparisons were made. Pts with active AS received subcutaneous (SC) secukinumab every 4 weeks at doses of 300 mg with intravenous (IV) loading dose (LD), 150 mg with IV LD, 150 mg with SC LD, or placebo. Response to treatment was analyzed in pts with or without peripheral STJ at baseline. Peripheral joint involvement was assessed using a 44-joint STJ count. Response was assessed using multiple outcome measures, including Assessment in AS 20/40 (ASAS20/40), ASAS Partial Remission, BASDAI, BASFI, BASMI, disease activity and back pain assessments, and QOL questionnaires.

Results: Of 852 pts included in this pooled analysis, 814 completed 16 weeks of treatment with secukinumab (n = 450) or placebo (n = 364). On average, pts with no peripheral STJ were younger and more likely to be male; pts with STJ had higher CRP levels, had higher BASDAI and BASFI, had been diagnosed longer, and had more often received prior TNF inhibitors (TNFis) and DMARDs, suggesting more severe disease (**Table 1**). Overall, secukinumab led to significantly higher response rates than placebo in all outcome measures, regardless of the presence of STJ (**Figure 1, Table 2**). However, response rates tended to be numerically higher in pts with no STJ, with higher response rates seen for ASAS20/40 and ASAS partial remission (**Figure 1**). Overall, reductions in disease activity and back pain were also numerically greater in pts with no STJ (**Table 2**). QOL improvements were similar in pts with or without STJ.

Conclusion: Secukinumab led to significant improvements in efficacy outcomes, regardless of peripheral joint involvement. Pts with STJ were more difficult to treat, showing numerically lower responses to treatment.

Table 1. Demographics and Disease History

	No swollen and tender joints					≥ 1 swollen and tender joints				
	Secukinumab					Secukinumab				
Demographic Variable	300 mg, IV LD[a] n = 24	150 mg, IV LD[a] n = 64	150 mg, SC LD[b] n = 63	Placebo n = 133	Total N = 284	300 mg, IV LD[a] n = 52	150 mg, IV LD[a] n = 135	150 mg, SC LD[b] n = 125	Placebo n = 256	Total N = 568
Age, years										
Mean	**38.8**	**37.9**	**41.4**	**40.3**	**39.9**	**43.6**	**42.6**	**44.6**	**44.7**	**44.1**
SD	10.53	10.91	10.54	11.29	11.00	12.16	11.47	12.57	12.63	12.30
Age group, n (%)										
< 65 years	24 (100.0)	64 (100.0)	62 (98.4)	129 (97.0)	279 (98.2)	50 (96.2)	130 (96.3)	118 (94.4)	243 (94.9)	541 (95.2)
≥ 65 years	0	0	1 (1.6)	4 (3.0)	5 (1.8)	2 (3.8)	5 (3.7)	7 (5.6)	13 (5.1)	27 (4.8)
Sex, n (%)										
Male	17 (70.8)	51 (79.7)	44 (69.8)	108 (81.2)	220 (77.5)	33 (63.5)	79 (58.5)	83 (66.4)	149 (58.2)	344 (60.6)
Race, n (%)										
White	22 (91.7)	49 (76.6)	60 (95.2)	115 (86.5)	246 (86.6)	37 (71.2)	85 (63.0)	122 (97.6)	218 (85.2)	462 (81.3)
Asian	1 (4.2)	8 (12.5)	2 (3.2)	11 (8.3)	22 (7.7)	1 (1.9)	14 (10.4)	2 (1.6)	13 (5.1)	30 (5.3)
American Indian or Alaska Native	1 (4.2)	2 (3.1)	0	1 (0.8)	4 (1.4)	5 (9.6)	10 (7.4)	1 (0.8)	8 (3.1)	24 (4.2)
Black or African American	0	0	1 (1.6)	1 (0.8)	2 (0.7)	2 (3.8)	2 (1.5)	0	2 (0.8)	6 (1.1)
Other	0	5 (7.8)	0	5 (3.8)	10 (3.5)	6 (11.5)	24 (17.8)	0	15 (5.9)	45 (7.9)
Unknown	0	0	0	0	0	1 (1.9)	0	0	0	1 (0.2)
AS disease state, mean (SD)										
Time since first diagnosis, years	4.8 (7.4)	6.0 (6.4)	8.0 (9.2)	6.8 (7.8)	6.7 (7.8)	5.6 (7.3)	6.4 (7.3)	7.9 (10.2)	7.3 (9.0)	7.1 (8.8)
PGA of disease activity, VAS 0-100 mm	72.1 (18.3)	60.9 (18.2)	66.7 (14.8)	71.4 (17.5)	68.0 (17.6)	73.4 (15.8)	70.0 (18.1)	73.4 (16.1)	70.0 (16.2)	71.0 (16.6)
Total back pain, VAS 0-100 mm	73.9 (13.5)	62.9 (17.8)	70.3 (13.5)	71.6 (16.4)	69.5 (16.3)	74.1 (15.9)	70.7 (17.7)	72.2 (15.9)	71.1 (16.0)	71.5 (16.4)
Nocturnal back pain, VAS 0-100 mm	75.9 (18.2)	58.2 (19.7)	68.3 (15.3)	70.4 (18.1)	67.7 (18.6)	74.3 (17.1)	67.7 (21.2)	69.8 (18.1)	67.8 (18.6)	68.8 (19.1)
BASFI	6.1 (2.1)	5.0 (2.1)	5.6 (2.1)	5.9 (2.1)	5.6 (2.1)	6.6 (1.6)	6.5 (2.0)	6.6 (1.9)	6.3 (2.0)	6.4 (1.9)
BASDAI	6.9 (1.1)	5.8 (1.4)	6.3 (1.4)	6.7 (1.4)	6.4 (1.4)	7.0 (1.5)	6.9 (1.5)	7.1 (1.2)	6.9 (1.3)	7.0 (1.4)
BASMI (linear)	3.3 (1.7)	4.0 (1.7)	3.4 (1.7)	3.9 (1.6)	3.8 (1.7)	3.5 (1.4)	3.9 (1.7)	4.0 (1.9)	3.9 (1.5)	3.9 (1.6)
BASMI (lateral spinal flexion), cm	12.4 (5.4)	10.6 (6.8)	11.7 (5.3)	10.9 (6.4)	11.2 (6.2)	11.9 (4.8)	10.9 (5.2)	10.9 (5.3)	10.6 (4.9)	10.8 (5.1)
hsCRP, mg/L	9.1 (9.6)	18.3 (25.4)	8.9 (9.4)	13.3 (18.0)	13.1 (18.3)	12.0 (14.7)	15.7 (19.9)	21.3 (41.4)	15.2 (20.4)	16.4 (26.1)
No. of prior TNFis, n (%)										
0	20 (83.3)	54 (84.4)	44 (69.8)	100 (75.2)	218 (76.8)	37 (71.2)	95 (70.4)	85 (68.0)	176 (68.8)	393 (69.2)
≥ 1	4 (16.7)	10 (15.6)	19 (30.2)	33 (24.8)	66 (23.2)	15 (28.8)	40 (29.6)	40 (32.0)	80 (31.3)	175 (30.8)
Medication at randomization, n (%)										
Methotrexate	1 (4.2)	3 (4.7)	3 (4.8)	10 (7.5)	17 (6.0)	12 (23.1)	24 (17.8)	15 (12.0)	31 (12.1)	82 (14.4)
Sulfasalazine	4 (16.7)	14 (21.9)	4 (6.3)	25 (18.8)	47 (16.5)	16 (30.8)	42 (31.1)	22 (17.6)	72 (28.1)	152 (26.8)
Dose, mean (SD), g/day	1.8 (0.5)	1.8 (0.5)	2.1 (0.6)	1.8 (0.7)	1.8 (0.6)	2 (0.7)	1.8 (0.5)	1.9 (0.7)	1.9 (0.6)	1.9 (0.6)
Corticosteroid	0	7 (10.9)	2 (3.2)	11 (8.3)	20 (7.0)	7 (13.5)	20 (14.8)	13 (10.4)	39 (15.2)	79 (13.9)
Dose, mean (SD), g/day	0	6 (2.2)	5 (0)	7 (2.6)	6.5 (2.3)	8.7 (2.9)	7.8 (2.7)	4.7 (2.5)	7.3 (2.5)	7.1 (2.8)

hsCRP, high-sensitivity C-reactive protein; PGA, patient global assessment; VAS, visual analog scale.
[a] IV LD, intravenous loading dose of 10 g/kg at weeks 0, 2, and 4.
[b] SC LD, subcutaneous loading dose of 150 mg at weeks 0, 1, 2, 3, and 4.

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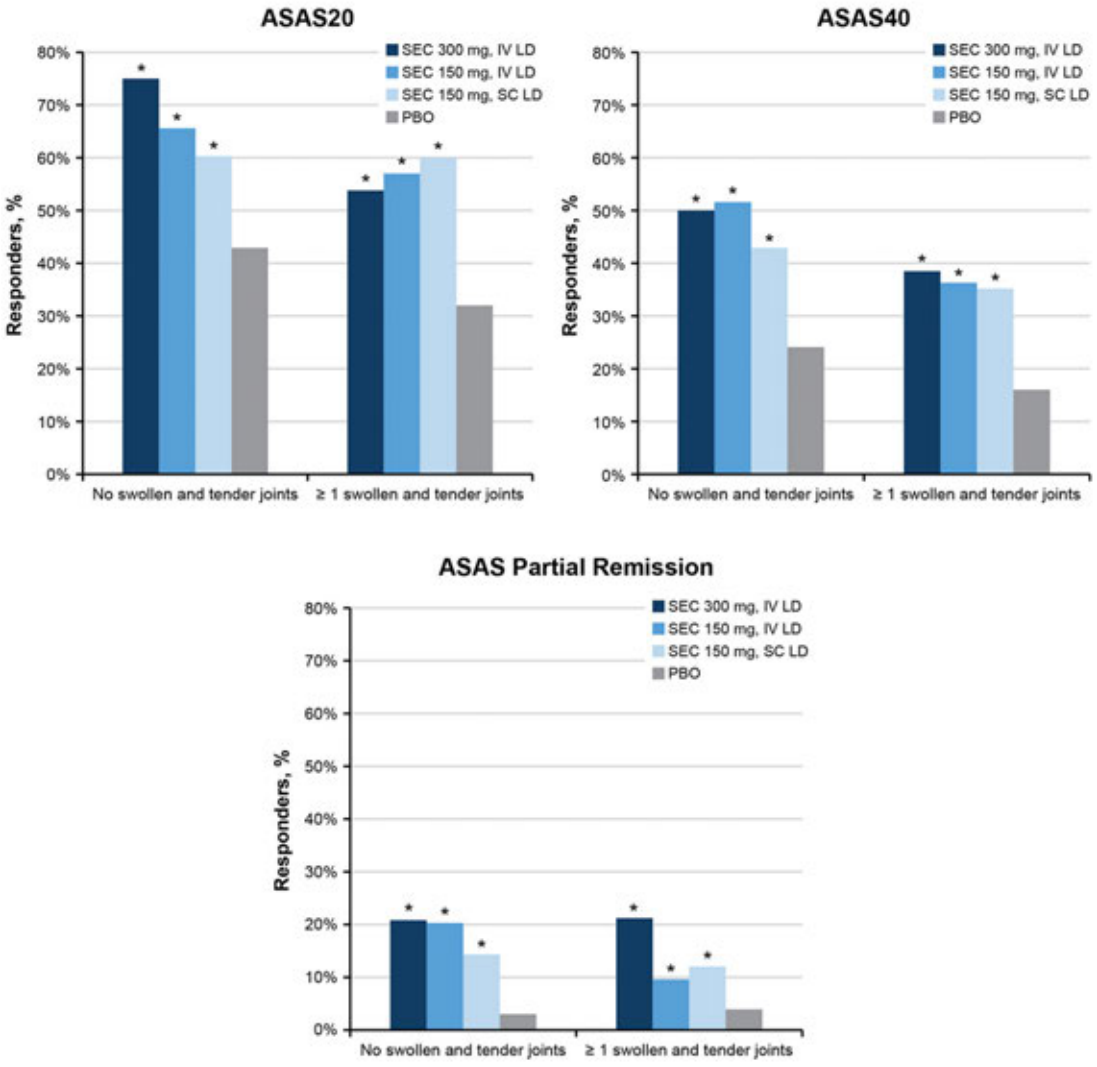
Figure 1. ASAS Response Rates at Week 16



PBO, placebo; SEC, secukinumab.
* $P < .05$ (nominal P value vs PBO).

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Table 2. Response in Other Measures at Week 16

	No swollen and tender joints				≥ 1 swollen and tender joints			
	Secukinumab				Secukinumab			
Change from BL, mean (SE)[a]	**300 mg, IV LD[b] n = 24**	**150 mg, IV LD[b] n = 64**	**150 mg, SC LD[c] n = 63**	**Placebo n = 133**	**300 mg, IV LD[b] n = 52**	**150 mg, IV LD[b] n = 135**	**150 mg, SC LD[c] n = 125**	**Placebo n = 256**
PGA of disease activity, VAS 0-100 mm	−30.2 (5.0)*	−34.8 (3.2)*	−24.4 (3.1)*	−13.0 (2.3)	−27.3 (3.3)*	−26.5 (2.0)*	−27.1 (2.1)*	−14.5 (1.5)
Total back pain, VAS 0-100 mm	−28.7 (5.1)*	−35.6 (3.3)*	−27.1 (3.2)*	−14.9 (2.3)	−27.4 (3.4)*	−27.0 (2.1)*	−25.8 (2.2)*	−14.9 (1.6)
Nocturnal back pain, VAS 0-100 mm	−32.2 (5.2)*	−37.1 (3.4)*	−29.8 (3.2)*	−15.1 (2.3)	−30.2 (3.5)*	−26.8 (2.2)*	−25.4 (2.2)*	−14.4 (1.6)
BASFI	−2.2 (0.4)*	−2.1 (0.3)*	−1.9 (0.3)*	−1.0 (0.2)	−2.5 (0.3)*	−1.9 (0.2)*	−2.0 (0.2)*	−0.9 (0.1)
BASDAI	−2.9 (0.4)*	−2.9 (0.3)*	−2.3 (0.3)*	−1.3 (0.2)	−2.6 (0.3)*	−2.3 (0.2)*	−2.2 (0.2)*	−1.2 (0.1)
BASMI (linear)	−0.5 (0.2)	−0.6 (0.1)*	−0.3 (0.1)	−0.2 (0.1)	−0.5 (0.1)	−0.4 (0.1)	−0.5 (0.1)*	−0.2 (0.1)
hsCRP, mg/L, $\log_e$(treatment/baseline)[d]	0.5 (1.2)*	0.4 (1.1)*	0.6 (1.1)*	1.1 (1.1)	0.4 (1.1)*	0.5 (1.1)*	0.5 (1.1)*	1.1 (1.1)
Change from BL in QOL measures,[e] mean (SE)[a]								
SF-36 mental component score	–	5.0 (1.3)	3.7 (1.1)	2.4 (0.9)	–	2.8 (1.0)	5.4 (0.8)*	2.6 (0.7)
SF-36 physical component score	–	6.2 (1.0)*	5.2 (0.9)*	1.8 (0.7)	–	6.4 (0.8)*	5.9 (0.6)*	3.1 (0.5)
ASQOL	–	−4.9 (0.7)*	−3.9 (0.6)*	−1.8 (0.4)	–	−3.2 (0.5)*	−3.8 (0.4)*	−1.8 (0.3)

ASQOL, Ankylosing Spondylitis Quality of Life; BL, baseline.
* $P < .05$ (nominal P value vs PBO).
[a] Least square means and SE are from mixed-effect model repeated measures with: treatment, visit, TNFi status as factors, baseline and weight as covariates; treatment by visit and baseline by visit as interaction terms.
[b] IV LD, intravenous loading dose of 10 g/kg at weeks 0, 2, and 4.
[c] SC LD, subcutaneous loading dose of 150 mg at weeks 0, 1, 2, 3, and 4.
[d] A value < 1 indicates a reduction in CRP.
[e] MEASURE 3 did not include QOL outcomes.

8, Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8; **A. Deodhar**, AbbVie, 2, 5, 9, Abbvie, 5, 8, Abbvie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, and UCB Pharma, 5, 8, AbbVie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GSK, Galapagos, Janssen, Novartis, Pfizer and UCB, 5, AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Glaxo Smith and Klein, Janssen, Novartis, Pfizer, UCB, 5, Amgen, 5, 8, 9, BMS, 2, 5, 8, BMS, Eli Lilly, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, 2, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, UCB Pharma, 2, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, 8, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, 9, Eli Lilly and Company, 2, 5, Eli Lilly,, 5, Eli Lilly, GSK, Novartis, Pfizer and UCB, 2, Galagagos, 5, Galapagos, 5, 8, 9, Glaxo Smith & Klein, 2, Glaxo Smith & Kline, 2, 5, 8, Glaxo Smith Klein, 5, Glaxo SmithKlein, 2, 5, GlaxoSmithKlein, 2, 5, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, Janssen, 2, 5, 8, 9, Janssen Pharmaceutica, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9; **R. Calheiros**, Novartis, 3, 4; **X. Meng**, Novartis, 3, 4; **T. Fox**, Novartis, 3, 4; **X. Baraliakos**, AbbVie, 2, 4, 5, 8, Biocad, 2, 5, Bristol-Myers Squibb, 2, 4, 5, 8, Celgene, 2, 5, 8, Chugai, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, MSD, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5, 8.

Abstract Number: 1554

Effect of Secukinumab on Radiographic Progression Through 2 Years in Patients with Active Psoriatic Arthritis: End-of-study Results from a Phase III Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Secukinumab (SEC) provided sustained efficacy, inhibition of radiographic progression, and stable safety profile over 52 Weeks (Wks) in patients (pts) with psoriatic arthritis (PsA) in the FUTURE 5 study.[1,2] Here we report the end-of-study (2-year) results of the effect on radiographic progression of SEC in pts with PsA in the FUTURE 5 study.

Methods: Adults (N = 996) with active PsA were randomized to subcutaneous SEC 300 mg load (300 mg), 150 mg load (150 mg), 150 mg no load, or placebo at baseline, Wks 1, 2, 3, and 4, and every 4 wks thereafter. Pts could have the SEC dose escalated from 150 mg to 300 mg starting from Wk 52, based on physicians' judgement. Radiographic progression (mean change in van der Heijde-modified total Sharp score [vdH-mTSS]) was based on hand/wrist/foot radiographs obtained at baseline, Wks 16 (non-responders), 24, 52, and 104, assessed by two blinded readers (plus an adjudicator if required). Radiographic data were analyzed using linear mixed-effects model (random intercept, random slopes) at Wks 24 and 52, and as observed at Wk 104. Data are shown for pts originally randomized to SEC (300 and 150 mg); the 150 mg groups also includes pts who had their dose escalated to 300 mg. Analyses by prior anti-TNF (naïve vs inadequate response/intolerance [IR]; stratification factor) use were also done.

Results: Overall, 85% (300 mg), 82% (150 mg), and 75% (150 mg no load) of pts completed 2 years of treatment. A total of 86 (39%) and 92 (41%) pts had their dose escalated to 300 mg in the 150 mg and 150 mg no load groups, respectively. In overall population, the proportions of pts with no radiographic progression (change from baseline in mTSS ≤0.5) with SEC were 89.5% (300 mg), 82.3% (150 mg), and 81.1% (150 mg no load) at 2 years; the corresponding proportions of pts for change from baseline in mTSS ≤0.0 were: 81.2%, 69.1% and 73.4%, respectively. Radiographic progression was low in SEC-treated pts in the overall population and by prior anti-TNF use over 2 years (Table). Clinical responses were also sustained through 2 years of SEC treatment.

Conclusion: Low radiographic progression was observed over 2 years of treatment with SEC 300 and 150 mg in pts with PsA.

Table. Summary of Radiographic Results through Wk 104 Mean change in vdH-mTSS				
	300 mg	150 mg[1]	150 mg no load[1]	Placebo
Overall population	**N = 222**	**N = 220**	**N = 222**	**N = 332**
Wk 24[a]	n = 217 0.03 (0.13)[$]	n = 213 0.14 (0.13)[‡]	n = 210 –0.10 (0.13)[†]	n = 296 0.51 (0.11)
Wk 52[a]	n = 217 –0.18 (0.17)	n = 215 0.11 (0.18)	n = 211 –0.20 (0.18)	-
Wk 104[b]	n = 191 0.37 (4.18)	n = 181 0.52 (2.66)	n = 169 0.41 (2.20)	-
Anti-TNF-naïve	**N = 154**	**N = 155**	**N = 158**	**N = 234**
Wk 24[a]	n = 152 –0.01 (0.17)[‡]	n = 149 0.11 (0.17)	n = 151 –0.24 (0.17)[$]	n = 214 0.50 (0.14)
Wk 52[a]	n = 152 –0.27 (0.23)	n = 151 0.08 (0.23)	n = 151 –0.38 (0.23)	-
Wk 104[b]	n = 139 –0.07 (1.52)	n = 137 0.37 (2.26)	n = 124 0.42 (2.33)	-
Anti-TNF-IR	**N = 68**	**N = 65**	**N = 64**	**N = 98**
Wk 24[a]	n = 65 0.14 (0.19)	n = 64 0.22 (0.20)	n = 59 0.28 (0.20)	n = 82 0.55 (0.18)
Wk 52[a]	n = 65 0.07 (0.22)	n = 64 0.19 (0.23)	n = 60 0.31 (0.23)	-
Wk 104[b]	n = 52 1.56 (7.54)	n = 44 0.97 (3.62)	n = 45 0.38 (1.84)	-

[†]$P < 0.001$; [$]$P < 0.01$; [‡]$P < 0.05$ versus placebo at Wk 24

[1]150 mg and 150 mg no load groups included 77 and 79 pts with radiographic results, respectively, who had dose escalation at Wk 52 or later

[a]Mean change (SE) from linear mixed-effects model (random intercept, random slopes) analysis; at Wk 24, included pts with baseline and at least 1 post-baseline radiographs at Wk 16/24 and at Wk 52, included pts with baseline and at least 1 post-baseline evaluable radiographs at Wk 16/24/52

[b]Mean change (SD) from observed analysis included pts with evaluable radiograph at both baseline and Wk 104

IR, inadequate response; N, total number of randomized pts; SD, standard deviation; SE, standard error; TNF, tumor necrosis factor; vdH-mTSS, van der Heijde-modified total Sharp score; Wk, week

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2. Mease PJ, et al. *Arthritis Rheumatol*. 2018;70(suppl 10).

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Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8; **P. Rahman**, AbbVie, 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, and Novartis, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, and UCB, 5, AbbVie, Eli Lilly, Pfizer, Novartis , UCB, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 2, 5, 8, Janssen Inc., 2, 5, 8, Janssen, Novartis, 2, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **H. Tahir**, AbbVie, Janssen, Eli Lilly, and Novartis, 8, Novartis, Eli-Lilly, 2; **A. Singhal**, AbbVie, 2, 8, Amgen, 2, AstraZeneca, 2, Bristol-Myers Squibb, 2, Fujifilm, 2, Gilead, 2, Janssen, 2, Lilly, 2, Mallinckrodt, 2, MedImmune, 2, Nichi-Iko, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, UCB, 2; **E. Böttcher**, Amgen, Roche, Eli Lilly, Pfizer, MSD, Novartis, 5, Amgen, Roche, Eli Lilly, Pfizer, MSD, Novartis, 8; **S. Navarra**, Abbott, 8, Abbott, Astellas, Johnson & Johnson, Novartis, Pfizer, 8, Astellas, 8, Johnson & Johnson, 8, Novartis, 8, Pfizer, 8; **A. Readie**, Novartis, 1, 3; **S. Mpofu**, Novartis, 1, 3; **E. Delicha**, Novartis, 5; **L. Pricop**, Noavrtis, 1, 3, Novartis, 1, 3, 4; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5.

Abstract Number: 1555

Drug Survival and Safety of Biosimilar CT-P13 versus Reference Infliximab in Patients with Ankylosing Spondylitis: Data from the Korean College of Rheumatology Biologics Registry

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SESSION INFORMATION

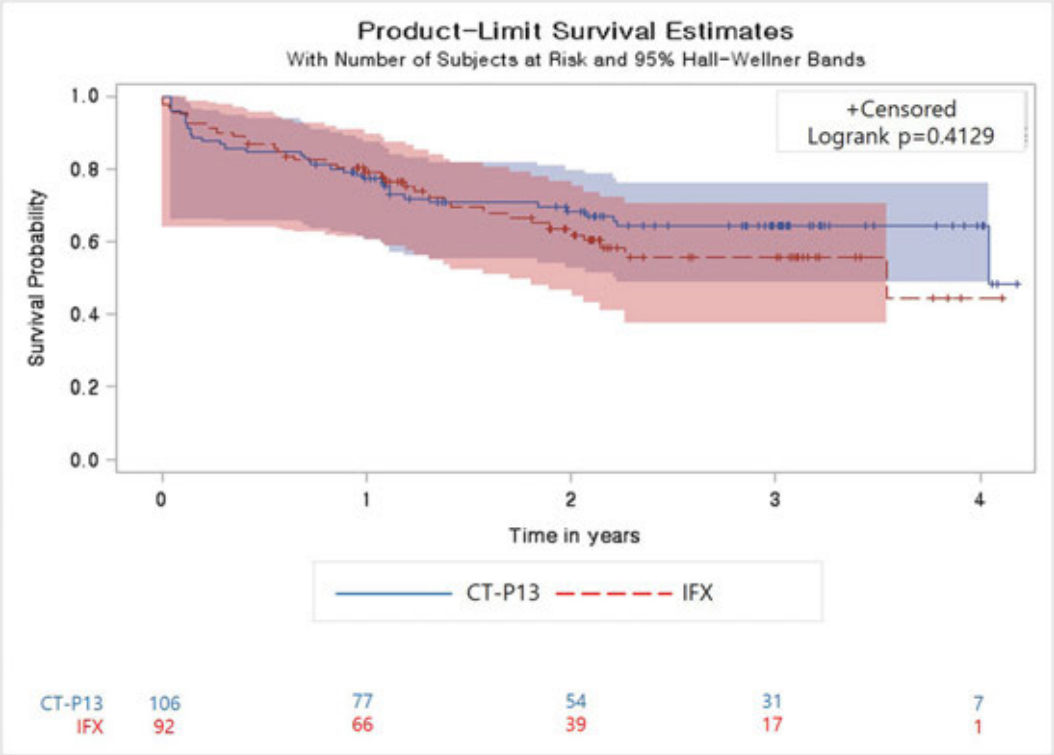
Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: CT-P13 is the first biosimilar of the reference infliximab (IFX) prescribed for rheumatoid arthritis, ankylosing spondylitis (AS), Crohn's disease, ulcerative colitis, psoriasis, and psoriatic arthritis. There are few studies showing long-term, real-world data of its drug survival or safety.



Figure

To evaluate drug retention, efficacy and safety of CT-P13 versus IFX in patients with AS enrolled in the Korean College of Rheumatology Biologics (KOBIO) registry.

Methods: Subjects were registered patients with AS who initiated CT-P13 or IFX between Dec 2012 and Dec 2017. Patients in the two groups were matched via propensity score based on age, gender, and baseline Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). In result, 124 patients were selected in each group. Drug retention, efficacy, and adverse events (AEs) in both groups were assessed over the 4-year follow-up period.

Results: The median treatment duration was 2.1 years in CT-P13, and 1.8 years in IFX treated patients (p = 0.1148). Overall, 79% of patients received each agent as first-line therapy. Drug retention of CT-P13 versus IFX was comparable in the total patient population (p = 0.4129, **Figure**), for first-line users (p = 0.1532) and second or more lines of users (p = 0.4452). Changing or discontinuing the agent occurred in 31.5% of patients in the CT-P13 group, and 33.1% in the IFX group. The most common reason for change or discontinuation was lack of efficacy (CT-P13 group: 38.5%; IFX group: 24.4%). CT-P13 and IFX users demonstrated comparable improvements in BASDAI, ASDAS-ESR, ASDAS-CRP and the ASDAS improvement criteria. In total, 13 AEs were reported in the CT-P13 group and 17 in the IFX group that led to treatment change or discontinuation.

Conclusion: In this real-world study, long-term data from Korean patients with AS show that CT-P13 has a drug retention rate comparable to IFX, and also similar efficacy along with an acceptable safety profile.

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Abstract Number: 1556

Exposure–Response Modeling of an Oral, Selective Tyrosine Kinase 2 (TYK2) Inhibitor, BMS-986165, for Pain Visual Analog Scale Score, in Patients with Psoriasis and Musculoskeletal Symptoms

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

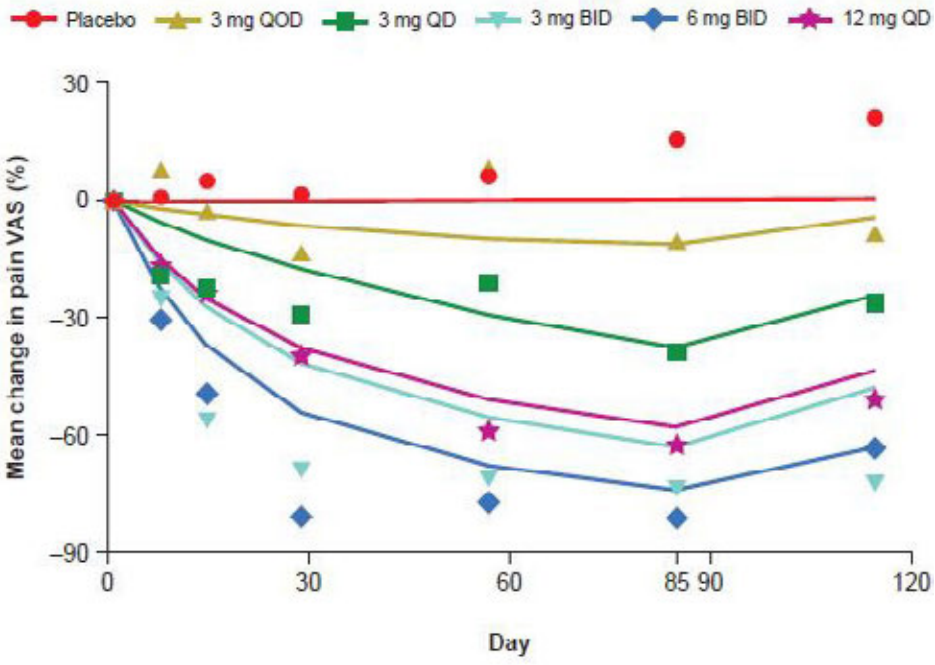
Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: BMS-986165 is an oral, selective inhibitor of TYK2, an enzyme that activates signal transducer and activator of transcription (STAT)-dependent cytokine signaling pathways, including the IL-12/IL-23 signaling pathway. IL-12/IL-23 signaling has a key role in the pathogenesis of skin disease in both psoriasis (PsO) and PsA. In a 12-week Phase 2 study in adults with PsO that included those with musculoskeletal symptoms, BMS-986165 demonstrated a dose-dependent Psoriasis Area and Severity Index (PASI) 75 response and a favorable safety profile.[1] Further analysis was conducted in this study to explore the impact of BMS-986165 on pain scores using exposure–response modeling in those with baseline musculoskeletal symptoms.

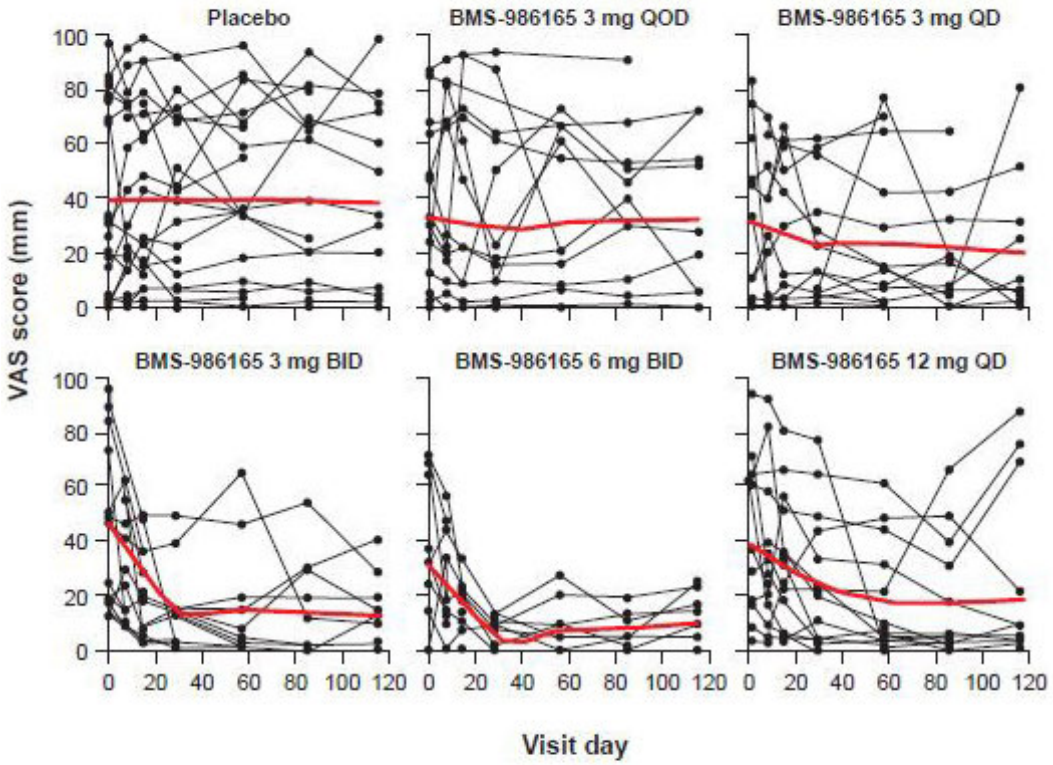
Methods: A longitudinal exposure–pain visual analog scale (VAS) score model was developed to describe the effect of BMS-986165 on pain VAS scores over time in patients with PsO and musculoskeletal symptoms at baseline

Figure 1: Observed and simulated mean percent change from baseline in pain VAS score



Symbols: observed data; lines: simulated data; treatment ended at Day 85.
BID=twice daily; QD=every day; QOD=every other day; VAS=visual analog scale.

Figure 2: Observed pain VAS score by visit



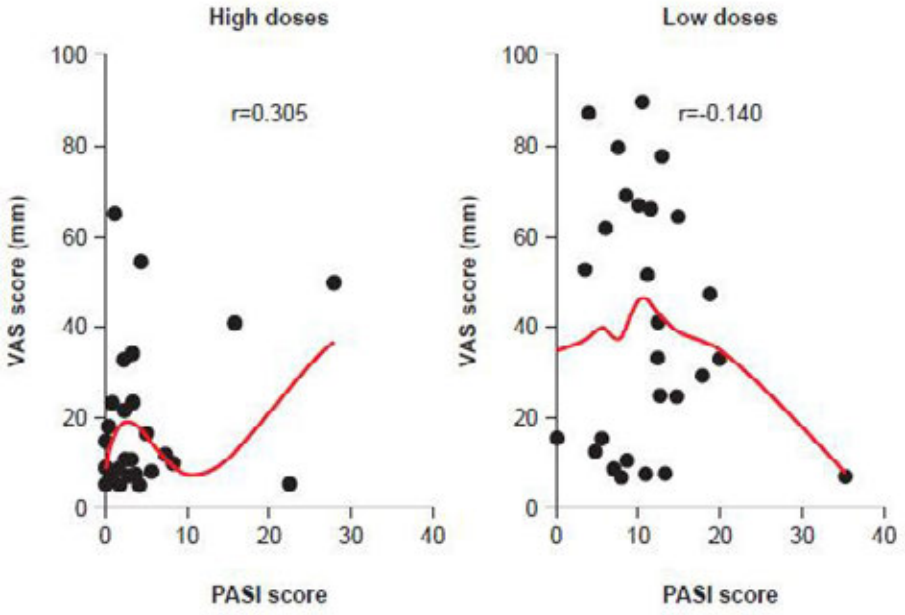
Filled circles: observed data; black solid lines: individual profiles; red lines: LOESS (locally weighted smoothing).
Treatment ended at Day 85.
BID=twice daily; QD=every day; QOD=every other day; VAS=visual analog scale.

in the Phase 2 study (NCT02931838).[1] The exposure data (steady-state minimum plasma drug concentration) were derived from a population pharmacokinetics model and the response data were the pain VAS scores measured on Days 1, 8, 15, 29, 57, 85 (on treatment), and 115 (off-treatment follow-up). The response data from 87 patients were modeled with exposure using a nonlinear mixed effects model. Simulations were performed to compare results for different dosing regimens. Additionally, correlation of median pain VAS and PASI scores were compared across the dose groups.

Results: Median model-simulated percent change from baseline pain VAS score ranged from -62% to -89% across BMS-986165 dosage regimens over 12 weeks; observed and simulated mean percent change are shown in Figure 1. Visual predictive checks of the exposure–response model demonstrated the model-predicted VAS score generally agreed overall with the observed data. BMS-986165 demonstrated a dose-related improvement in pain VAS score, with a sustained effect observed after treatment ended on Day 85 (Figures 1 and 2). A clear relationship between BMS-986165 exposure and pain VAS score reduction can be established. Correlation between median pain VAS and PASI scores was weak overall, suggesting that pain improvements could not be entirely explained by improvements in skin disease (Figure 3).

Conclusion: The relationship between BMS-986165 exposure and pain VAS score, in patients with PsO and baseline musculoskeletal symptoms, was captured using a nonlinear mixed effects exposure–response model. BMS-986165 demonstrated dose-dependent improvements in pain. Pain and PASI scores were weakly correlated. The decreased

Figure 3: Correlation of pain VAS and PASI scores at Day 85



A trend toward a stronger correlation at high versus low dosages of BMS-986165 was observed
High doses: 3 mg BID, 6 mg BID, and 12 mg QD; low doses: placebo and 3 mg QOD.
Red line: LOESS (locally weighted smoothing); treatment ended at Day 85.
BID=twice daily; PASI=Psoriasis Area and Severity Index; QD=every day; r=Pearson correlation coefficient; VAS=visual analog scale.

pain scores with BMS-986165 treatment, which were not well-correlated with improvements in PASI scores, were suggestive of improvements in joint inflammation.

Reference

1. Papp K, et al. *N Engl J Med.* 2018;379:1313-1321.

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Abstract Number: 1557

Secukinumab Effectiveness in 1134 Patients with Psoriatic Arthritis Treated in Routine Clinical Practice in 11 European Countries in the EuroSpA Research Collaboration Network

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster II: Treatment of Axial Spondyloarthritis & Psoriatic Arthritis

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Secukinumab represents a relatively new approach to treating patients with psoriatic arthritis (PsA) and has shown promising results in RCTs. However, there is a lack of real-life evidence on secukinumab effectiveness. Hence, the aim of this study was to determine the 6- and 12-month secukinumab retention rates as well as the crude and LUNDEX corrected proportions of patients in remission and low disease activity (LDA) at 6 and 12 months after treatment initiation based on observational registries in Europe. This was assessed overall as well as by prior biologic disease-modifying anti-rheumatic drug (bDMARD)/targeted synthetic (ts)DMARD use.

Methods: Data from PsA patients treated with secukinumab in routine care from 11 countries in the European Spondyloarthritis (EuroSpA) Research Collaboration Network were pooled. Time from treatment initiation to data cut was ≥ 12 months regardless of treatment duration and cover start date between May 2015 and April 2018. Crude and LUNDEX[1] adjusted Disease Activity Score with 28 joints and CRP (DAS28CRP) and Disease Activity index for

			All patients (n=1134)	b/tsDMARD naïve patients (n=242)	1 prior b/tsDMARD (n=232)	2 or more prior b/tsDMARDs (n=660)	p-value*
Age (years), mean (SD) n available			51.5 (11.4) n=1134	49.3 (12.0) n=242	50.8 (10.9) n=232	52.5 (11.2) n=660	0.001
Male, % n available			41.4% n=1134	50.4% n=242	46.6% n=232	36.4% n=660	<0.001
Years since diagnosis, mean (SD) n available			9.1 (8.1) n=797	7.0 (7.4) n=202	8.0 (7.5) n=178	10.7 (8.3) n=417	<0.001
Current smokers, % n available			18.5 % n=1068	20.8% n=231	21.9% n=215	16.6% n=622	0.14
Baseline CRP (mg/L), median (25-75th percentiles) n available			5 (2-13) n=908	7 (2-19) n=197	4 (2-8) n=166	5 (2-13) n=545	<0.001
Baseline ESR (mm/h), median (25-75th percentiles) n available			17 (8-33) n=647	20 (9-36) n=159	14 (7-32) n=122	16 (7-31) n=366	0.19
Baseline Pain (0-100), median (25-75th percentiles) n available			67 (47-80) n=797	66 (50-80) n=139	60 (39-79) n=143	69 (49-81) n=515	0.002
Baseline Fatigue (0-100), median (25-75th percentiles) n available			70 (52-85) n=655	65 (47-80) n=104	65 (45-78) n=109	74 (55-87) n=442	<0.001
Average (95%CI) drug retention time in weeks, censored by 26 weeks n available			24.4 (24.1-24.6) n=1134	25.2 (24.8-25.6) n=242	24.2 (23.5-24.8) n=232	24.2 (23.8-24.5) n=660	0.11
Average (95%CI) drug retention time in weeks, censored by 52 weeks n available			44.8 (44.0-45.6) n=1134	47.2 (45.8-48.7) n=242	44.2 (42.4-46.1) n=232	44.2 (43.1-45.3) n=660	0.02
Average (95%CI) time in weeks to secukinumab withdrawal in patients who withdrew due to loss of efficacy or adverse events before 12 months, n of *events*			23.6 (22.3-25.0) n=359	25.3 (22.1-28.5) n=60	22.4 (19.5-25.3) n=74	23.5 (21.8-25.3) n=225	0.44
Secukinumab retention rate, % (95%CI) *n at risk at 6/12 months*		**6 months**	84.5% (82.4-86.7%) n=936	88.7% (84.8-92.8%) n=214	83.7% (79.0-88.6%) n=190	83.3% (80.5-86.2%) n=532	0.11
		12 months	73.6% (71.1-76.3%) n=789	80.6% (75.7-85.8%) n=186	73.0% (67.5-79.0%) n=163	71.2% (67.8-74.9%) n=440	0.02
DAPSA28, median (25-75th percentiles) n available		**Baseline**	27.5 (18.5-38.5) n=676	30.4 (20.0-43.2) n=127	23.2 (14.4-33.1) n=110	27.6 (19.0-38.5) n=439	0.001
		6 months	15.2 (8.5-25.0) n=654	9.3 (3.8-16.8) n=124	15.5 (9.5-22.0) n=114	17.1 (10.3-27.1) n=416	<0.001
		12 months	10.2 (4.4-15.9) n=134	5.2 (3.0.-10.6) n=48	11.5 (6.5-17.1) n=25	13.2 (7.3-21.6) n=61	<0.001
DAS28CRP, median (25-75th percentiles)		**Baseline**	4.2 (3.5-5.0) n=745	4.4 (3.5-5.2) n=157	3.9 (2.7-4.6) n=129	4.3 (3.4-5.1) n=459	<0.001
		6 months	3.1 (2.2-4.1) n=675	2.5 (1.7-3.3) n=126	3.1 (2.2-3.8) n=123	3.3 (2.5-4.2) n=426	<0.001
		12 months	2.5 (1.5-3.3) n=175	2.1 (1.6-3.0) n=64	2.4 (2.0-3.3) n=39	2.8 (2.2-3.8) n=72	0.002
DAPSA28≤4, % n available	**6 months**	**Crude**	12.1% n=654	25.8% n=124	9.6% n=114	8.7% n=416	<0.001
		LUNDEX adjusted**	10.0% n=654	22.8% n=124	7.9% n=114	7.01% n=416	<0.001
	12 months	**Crude**	17.9% n=134	27.1% n=48	8% n=25	14.8% n=61	0.09
		LUNDEX adjusted**	12.5% n=134	20.8% n=48	5.6% n=25	9.9% n=61	0.08
DAS28CRP<2.6, % n available	**6 months**	**Crude**	33.2% n=675	52.4% n=126	34.1% n=123	27.2% n=426	<0.001
		LUNDEX adjusted**	27.4% n=675	46.3% n=126	27.9% n=123	21.9% n=426	<0.001
	12 months	**Crude**	55.4% n=175	65.6% n=64	56.4% n=39	45.8% n=72	0.07
		LUNDEX adjusted**	38.5% n=175	50.4% n=64	39.6% n=39	30.5% n=72	0.07
DAPSA28 >4 and ≤14, % n available	**6 months**	**Crude**	34.3% n=654	44.4% n=124	34.2% n=114	31.3% n=416	0.03
		LUNDEX adjusted**	28.3% n=654	39.3% n=124	28.0% n=114	25.2% n=416	0.008
	12 months	**Crude**	49.3% n=134	62.5% n=48	52.0% n=25	37.7% n=61	0.04
		LUNDEX adjusted**	34.3% n=134	48.0% n=48	36.5% n=25	25.1% n=61	0.04
DAS28CRP ≤3.2, % (95%CI), n available	**6 months**	**Crude**	52.3% n=675	70.6% n=126	55.3% n=123	46.0% n=426	<0.001
		LUNDEX adjusted**	43.2% n=675	62.4% n=126	45.3% n=123	37.1% n=426	<0.001
	12 months	**Crude**	72.6% n=175	81.3% n=64	71.8% n=39	65.3% n=72	0.11
		LUNDEX adjusted**	50.5% n=175	62.5% n=64	50.5% n=39	43.5% n=72	0.08

***Comparisons between b/tsDMARD naïve and non-naïve patients were performed with ANOVA for normally distributed data and with Kruskal-Wallis for skewed data. Drug retention is compared with Kaplan-Meier with log-rank test. **LUNDEX adjusted treatment outcome = (number of patients still treated at the respective timepoints / number of patients starting treatment x (% of patients achieving the respective treatment outcomes). CRP, C-reactive protein; DAPSA28, Disease Activity index for Psoriasis arthritis with 32 joint count; DAS28CRP, 28-joint disease activity score with CRP.**

Table

PSoriatic Arthritis with 28 joints (DAPSA28) [2] remission and LDA rates were calculated. Group comparisons between b/tsDMARD naïve, and 1 or 2 or more prior b/tsDMARD users were performed with ANOVA, Kruskal-Wallis or Chi-square test, or with Kaplan-Meier analyses with log rank test, as appropriate.

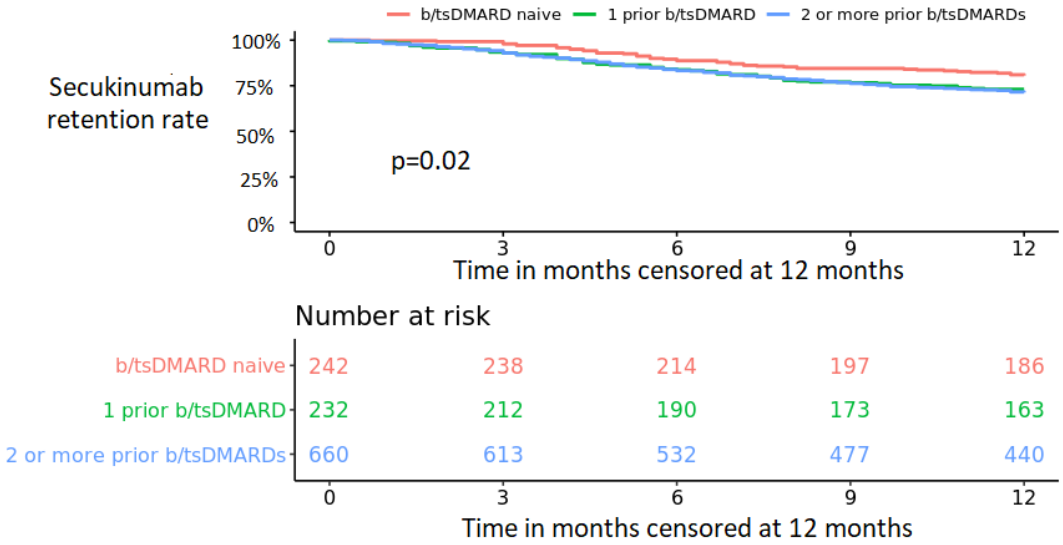

Figure. Pooled 12-month secukinumab retention rates for PsA patients in EuroSpA stratified by b/tsDMARD naive patients, patients treated with 1 prior b/tsDMARD or 2 or more prior b/tsDMARDs (log rank test; p<0.001).

Results: A total of 1134 PsA patients were included, thereof 21 patients who started treatment in year 2015, 375 in 2016, 623 in 2017 and 115 in 2018. Overall 6/12-month secukinumab retention rate was 85%/74% and significantly higher in b/tsDMARD naïve compared with non-naïve patients after 12, but not 6 months (table, figure). Overall 6- and 12-month DAS28< 2.6/DAPSA28≤4 was achieved by 33%/12% and 55%/18% of the patients, respectively and 6- and 12-month DAS28/DAPSA28 LDA by 52%/34% and 73%/49%, respectively. B/tsDMARD naïve patients compared with patients treated with 1 or 2 or more previous b/tsDMARDs had shorter time since diagnosis, higher baseline disease activity, a higher proportion were men and a higher proportion achieved LUNDEX adjusted 6-month remission.

Conclusion: This study of >1100 patients in 11 European countries provided real-world data on the effectiveness of secukinumab in patients with PsA, adding evidence to existing RCTs. A majority of the patients were treated with 2 or more previous b/tsDMARDs, were female and had long disease duration. Overall retention rate was 85%/74% at 6/12 months, respectively, with significantly higher retention rates for b/tsDMARD naïve compared with patients treated with 1 or 2 or more previous b/tsDMARDs after 12, but not 6 months. Overall, a higher proportion of bionaïve than previous b/tsDMARD users achieved remission, regardless of remission criteria.

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2. Michelsen et al. Ann Rheum Dis 2018;77:1736-1741.

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Abstract Number: 1558

Should Lupus Podocytopathy Be a Subclass in Class I and Class II Lupus Nephritis?

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SESSION INFORMATION
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Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
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Background/Purpose: Evidence of podocyte effacement on electron microscopy and significant proteinuria in a systemic lupus erythematosus (SLE) patient with biopsy proven minimal mesangial (MM), mesangial proliferation (MsP) and focal segmental glomerulosclerosis (FSGS) is the defining quality of lupus podocytopathy (LP). Our objective is to recognize the prevalence of LP and significant proteinuria in SLE patients with biopsy proven class I, class II and/or FSGS.

Methods: In this single center retrospective study, two independent reviewers evaluated records from 96 hospitalized patients admitted with ICD-10 codes corresponding to a diagnosis of glomerular disease and/or tubulointerstitial nephropathy in SLE from 2015 to 2018.

Results: The prevalence of LP in our cohort was 8.33% (Table 1). Seventy-five percent of our cohort were females and of African descent. Class II lupus nephritis (LN) was the most common pathological diagnosis (50% of patients); followed by class I LN (37.5%), and one case of FSGS (12.5%). Five patients presented with significant proteinuria (62.5%). Majority of the patients had active disease, presenting with low C3 levels (62.5%). Most patients received corticosteroids (CS), either pulse dose steroids or high dose prednisone being the most common mode (62.5%); four

Table 1. Characteristics of SLE patients with Lupus Podocytopathy in addition to Pre- and Post-treatment Values

Patient	Pathology report	Age	Gender	Ethnicity /race	Progression	PRE Prot/crea	POST prot/crea	BUN/crea	BUN/crea - after	ANA	Anti-dsDNA	C3/C4	Treatment
1	Class I LN; IF with rare mesangial - capillary deposits; EM- podocyte foot processes segmentally effaced.	41 YO	M	AA	CKD II	836	72	21/1.09	26/1.45	Positive	1. 640	33/<8	Prednisone 40mg + MMF
2	Class II LN; EM: less than 20% focal podocyte foot process fusion.	58 YO	F	NH	CKD I	2049	1190	20/1.04	13/1.05	Positive	Negative	173/26	leflunomide
3	Class I LN; additionally, glomeruli with segmental sclerosis and foot process effacement by EM.	30 YO	F	AA	Class III - Deceased (2017)	9899	2270	27/1.53	32/0.67	Positive 1.640	Negative	138/53	solumedrol 500mg IV + MMF
4	Class I LN; IF with minimal mesangial deposits. Podocyte foot process are segmentally irregular	29 YO	F	AA	Stable	574	275	21/1.45	19/1.2	Negative	Negative	153/23	None

patients received a combination of CS and Mycophenolate mofetil (MMF). All of the patients treated with CS and MMF demonstrated greater than 50% improvement in the urine protein/creatinine ratio with mean duration of 27.5 days and persisted in remission. The patient with the FSGS pattern despite having greater than 50% improvement in protein/creatinine ratio relapsed to LN class III within 2 years.

Conclusion: It is important to recognize a subset of patients presenting with clinical signs of nephrotic syndrome despite biopsy demonstrating class I or class II LN. The literature outlines LP as a spectrum, from MM to FSGS, with worse response to treatment in patients with FSGS. [1] As demonstrated in our cohort of predominantly ethnic minorities with Class I and class II LN with LP patterns, majority had a favorable response to CS in combination with MMF; the only patient with the FSGS pattern underwent relapse. A larger cohort with longer duration of study period is needed to suggest recommendations for LP. It may be beneficial to treat LP in Class I and II LN when associated with proteinuria.

Disclosure: W. Bembry, None; **D. Lopez**, None; **C. Mesa**, None; **N. Patel**, None; **M. Guevara**, None.

Abstract Number: 1559

Routine Clinical Pathology Measurements Are Predictive of the Risk of Organ Damage Accrual in SLE

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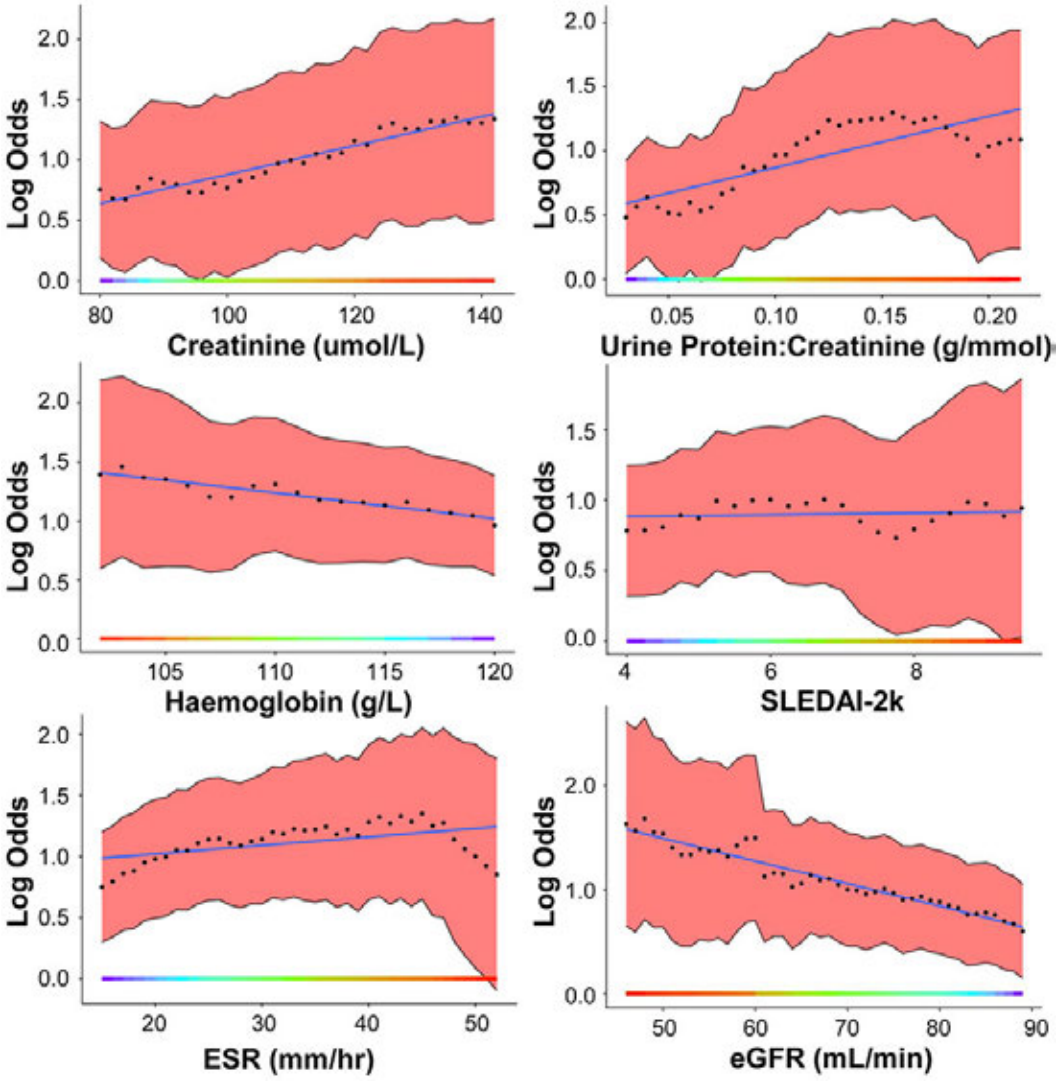

Figure. Ln (natural log) odds ratio for damage transition vs time-adjusted mean of laboratory variables. Red region (95%CI) lying above the y=0 line indicates the risk is statistically significant ($p<0.05$). Regression lines (blue) indicate the risk of damage increase is approximately proportional with the distance from normal pathology measure range.

Background/Purpose: Prevention of permanent organ damage, a major predictor of morbidity and mortality, is a key goal in the treatment of SLE. Physician-measured disease activity scores have only weak predictive value for damage accrual risk, and are in part subjective. Routine pathology laboratory measurements provide objective, continuous biological data, but their association with damage accrual risk in SLE has not been studied.

Methods: Longitudinal data were collected prospectively in a single centre SLE patient cohort between 2007-2017. Variables recorded at each visit included disease activity (SLEDAI-2k), drug treatment and routine pathology measurements. Organ damage (SLICC-SDI) was measured annually. Longitudinal patient data were split into annual periods, and each visit was assigned as being in a "damage transition" or "non-damage transition" period based on whether SDI increased at the subsequent annual measure. Time-adjusted means (TAMs) of laboratory variables were calculated for each period, and multivariable logistic regression analysis of the association with damage accrual (adjusting for age, gender, race, previous organ damage and prednisolone dose) was performed, with Holm-Bonferroni correction.

Results: 893 annual periods, comprising 5082 visits from 245 patients (85.6% female, 50.2% Caucasian), were analysed. Five of 16 routine laboratory variables were significantly associated with risk of damage accrual: estimated glomerular filtration rate (eGFR) ($p< 0.01$), creatinine ($p< 0.01$), urine protein:creatinine ratio ($p< 0.01$), ESR ($p< 0.001$), and haemoglobin ($p< 0.001$). Moreover, the odds of damage increase were proportional to the deviation of each of these variables from its respective normal range (Figure). SLEDAI-2k was also significantly associated with damage accrual ($p< 0.001$), but the association of SLEDAI-2k with damage did not exhibit this proportionality.

Conclusion: Routine pathology measures are proportionally associated with organ damage risk in SLE. These measures have potential as biomarkers for identifying patients at risk of organ damage from SLE.

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Abstract Number: 1560

Imbalance Between Th17 and Regulatory T Cells in Patients with Systemic Lupus Erythematosus Combined EBV/CMV Viremia

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
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Session Time: 9:00AM–11:00AM

Background/Purpose: Infection is common and is one of the leading causes of morbidity and mortality in Systemic Lupus Erythematosus (SLE) patients . Excessive using glucocorticoid and DMARDs lead to decrease immune function, which increasing opportunistic infection, such as EBV or CMV. Recent study show that the imbalance between T help cell 17 (Th17) and regulatory T cell (Treg cell) is a pivotal cause of autoimmune disease. However, the relationship between imbalance of Th17/ Treg and SLE combined EBV or CMV viremia is unknown. We will investigate the

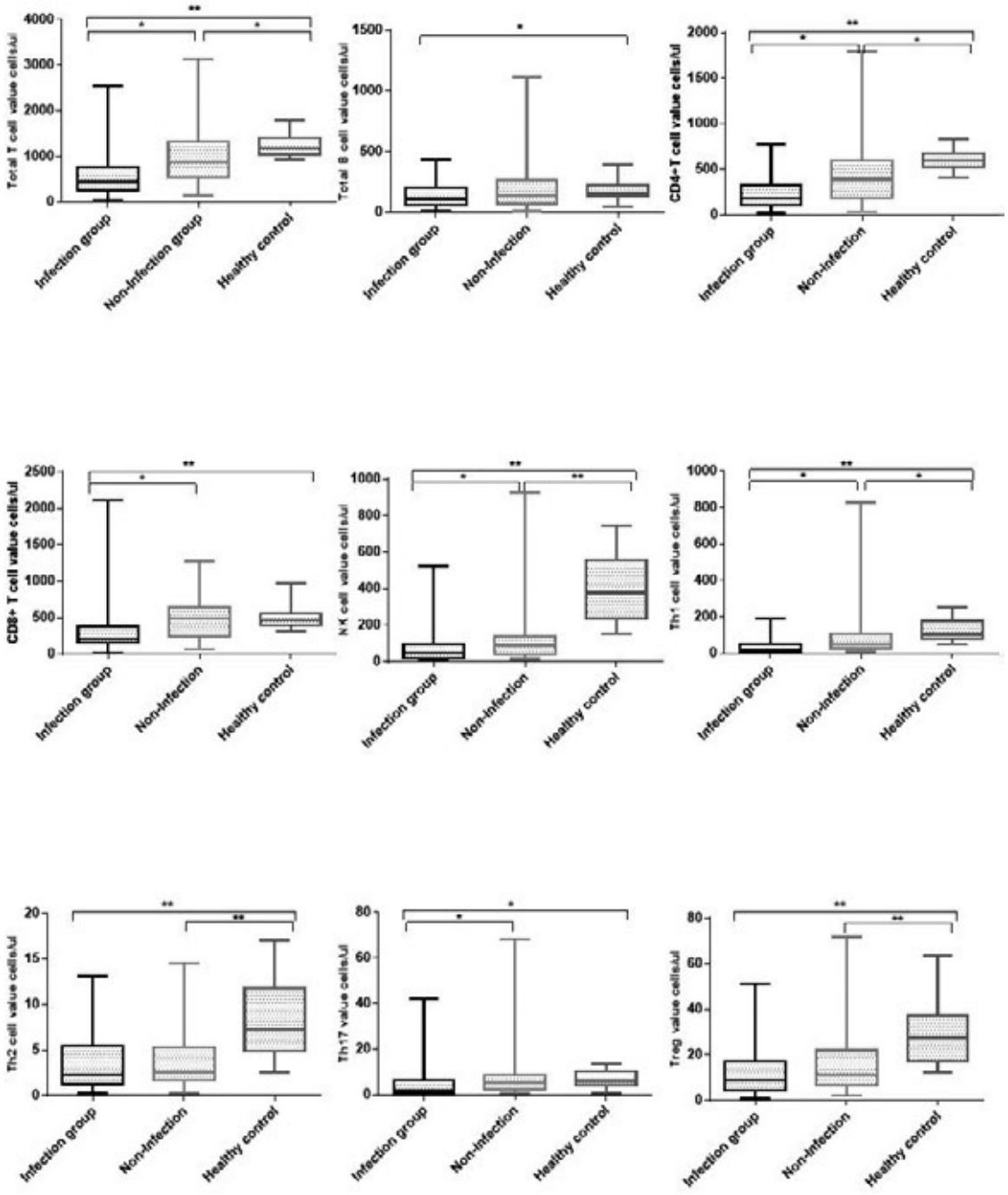

Figure. Comparsion of the absolute value of lymphcytes and CD4+ T cell subsets among SLE patients combined EBV / CMV viremia(n=36),SLE patients without any infection (n=30)and healthy control(n=20).(*P<0.05,**P<0.001).

characteriatic of lymphocytes cell subsets ,especially the CD4+ T subsets in patients with SLE combined EBV / CMV viremia.

Methods: Clinical records of SLE patients combined EBV and CMV viremia (Group infection), 36 SLE patients combines EBV or CMV *Viremia*, hospitalized in ShanXi medical university the second Hospital, were analyzed. As control, we selected 20 health persons (Group health) whose age matched with group infection, 30 SLE patients without any infection. The absolute numbers of Treg cell and effector lymphocytes cell subsets in peripheral blood were examined by flow cytometry.

Results: (1) Compared with SLE patients without infection,36 SLE patients combined EBV or CMV viremia, including 29 patients with EBV, 13 patients with CMV, 6 patients combined EBV and CMV, the absolute number of total T cell (P=0.001), NK cell (P=0.021), CD4+T cell (P=0.000), CD8+T cell (P=0.002), Th1 cell (P=0.002), Th17 (P=0.022) lower than it the non-infection group.The absolute number of and(CD4+CD25+FOXP3+)Treg (P=0.195), Th2 cell (P=0.290) has no obvious difference between them. **(2)** And the absolute value of total T lymph cell (P=0.000), total B lymph cell (P=0.015), NK cell (P=0.000), CD4+T cell (P=0.000), CD8+T cell (P=0.000), Th1 cell (P=0.000), Th2 cell (P=0.000), Th17(P=0.003) and Treg (P=0.000) in infection group significantly lower than healthy control. **(3)**Compared with the healthy control, the absolute number of Total T cell (P=0.011), NK cell (P=0.000), CD4+T cell (P=0.002), Th1 (P=0.005), Th2 cell (P=0.000) and Treg (P=0.000) in non-infection group evidently lower, but there is no siginificant difference in absolute number of Th17 (P=0.325), total B lymph cell (P=0.431), CD8+T cell (P=0.680).

Conclusion: Distortion of the Th17/Treg balance favoring the pro-inflammatory Th17 side is hence believed to contribute to exacerbation of autoimmune disorders.In our study, compared with non-infection group, the absolute count of pro-inflammatory Th17 cells in infection group obviously decreased, this suggests that Th17 might be leading factor of Th17/Treg imbalance in patients with combined SLE EBV or CMVviremia. Appropriate immunodulatory therapy for CD4+ T subsets on the basis of antiviral therapy for SLE patients with EBV or CMV may be beneficial .

Disclosure: R. Su, None; **Y. Liu**, None; **X. Zheng**, None; **X. Li**, None; **C. Wang**, None.

Abstract Number: 1561

Decreased Nocturnal Blood Pressure Dipping in Patients with Systemic Lupus Erythematosus: Association with Markers of Inflammation

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SESSION INFORMATION
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Background/Purpose: Blood pressure follows a circadian rhythm; usually systolic blood pressure (SBP) drops by more than 10% during the night. Absence of this phenomenon, known as “non-dipping” is a cardiovascular risk factor independent of hypertension. Patients with systemic lupus erythematosus (SLE) have a high prevalence of hypertension and cardiovascular event risks, but little is known about nocturnal blood pressure dipping in patients with SLE and its association with inflammatory markers.

Methods: Twenty-six patients with SLE and 26 control subjects frequency-matched for age, race and sex were included in this study. All subjects were 18 years of age or older. Patients with SLE met the American College of Rheumatology revised classification criteria for SLE. Control subjects did not have SLE or other autoimmune diseases. We calculated nocturnal blood pressure dipping using data from ambulatory 24-hour blood pressure measurements. Blood pressure measurements were divided into daytime and nighttime periods defined by the patients’ reported hours of sleep. The average systolic blood pressure (mm Hg) was obtained for each period, and the nighttime/daytime systolic blood pressure ratio was calculated. We measured plasma concentrations of 92 inflammation-related markers using a multiplex immunoassay (Inflammation panel; Olink Bioscience, Uppsala, Sweden). Wilcoxon-rank sum tests and Fisher exact test were used to compare blood pressure results between patients with SLE and control

	Rho-coefficient	p-value
CDCP1 (CUB domain-containing protein-1)	-0.61	0.002
CX3CL1 (Fractalkine)	-0.61	0.002
CSF-1 (Macrophage colony-stimulating factor-1)	-0.56	0.004
IL-18 (Interleukin-18)	-0.54	0.006
IL-15 RA (Interleukin-15 receptor subunit-α)	-0.53	0.008
IL-10 RB (Interleukin-10 receptor subunit-β)	-0.51	0.01
MCP3 (Monocyte chemotactic protein-3)	-0.50	0.01
IL-6 (Interleukin-6)	-0.49	0.01
IL 18 R1 (Interleukin-18 receptor-1)	-0.49	0.02
MMP-10 (Matrix metalloproteinase-10)	-0.47	0.02
SLAMF1 (Signaling lymphocytic activation molecule-1)	-0.47	0.02
CASP8 (Caspase-8)	-0.46	0.02
CCL23 (C-C motif chemokine-23)	-0.44	0.03
PDL1 (Programmed cell death1 ligand-1)	-0.42	0.04
B – NGF (β-nerve growth factor)	-0.43	0.04
CCL3 (C-C motif chemokine-3)	-0.42	0.04

Table. Correlation between Nocturnal Blood Pressure Drop and inflammatory biomarkers in SLE patients

subjects. Spearman correlations were used to assess the correlation between blood pressure night dipping (expressed in %) and the inflammatory biomarkers in patients with SLE.

Results: SLE patients have a decreased nocturnal dipping [7% (5 – 13%)], compared to controls [12% (8-20%)] p=0.01. In patients with SLE, lower blood pressure dipping was significantly associated with many inflammatory markers (Table) including CDCP1 (CUB domain-containing protein-1, involved in complement activation), IL15RA (Interleukin-15 receptor subunit-α, which enhances apoptosis), and SLAMF1 (Signaling lymphocytic activation molecule-1, which promotes immunoglobulin production).

Conclusion: Nocturnal blood pressure dipping was less pronounced in patients with SLE compared to control subjects. Lower nocturnal blood pressure dipping was associated with multiple markers of inflammation in patients with SLE.

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Abstract Number: 1562

The Association of Body Weight Fluctuation and All-Cause Mortality in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Variable	Low Body Weight Fluctuation (N = 345)^*	High Body Weight Fluctuation (N = 345)#	p-value
Age (years)	45 [33-55]	38 [28-48]	<0.001
Female (%)	317 (92)	301 (87)	0.06
Race			0.004
White (%)	267 (77)	241 (70)	
Black (%)	60 (17)	94 (27)	
Other (%)	18 (5)	10 (3)	
Weight			
Baseline (kg)	68 [57-81]	85 [70-100]	<0.001
Average successive variation (kg)	1.27 [0.95-1.5]	2.6 [2.17-3.47]	<0.001
Number of weight measurements	21 [9-41]	14 [7-29]	<0.001
Person years of observation time	7.2 [4.5-11.5]	8.6 [5.8-12.3]	0.002
Charlson Comorbidity Index (points)	0 [0-2]	0 [0-2]	0.09
Immunologic markers at time of SLE diagnosis			
C3 (mg/dl)	113 [90-133]	113 [86-135]	0.77
C4 (mg/dl)	22 [14-29]	21 [15-29]	0.92
CRP (mg/l)	2.9 [1.0-12.2]	4.0 [1.0-12.6]	0.66
Corticosteroids (%)	289 (84)	258 (75)	0.005

^Continuous values are presented as median [interquartile range] and categorical variables are presented as n (%).
*N = 345 except as noted for the following variables: Weight (N = 330), C3 (N = 318), C4 (N = 305), CRP (N = 255).
#N = 345 except as noted for the following variables: Weight (N = 330), C3 (N = 317), C4 (N = 297), CRP (N = 247).

Table 1: Baseline characteristics by weight fluctuation in patients with SLE.

Variable	IRR (95% CI)	p-value
Weight fluctuation (univariate)	1.497 (0.90-2.48)	0.116
Weight fluctuation (multivariate*)	2.009 (1.16-3.47)	0.012
Baseline weight (univariate)	0.997 (0.98-1.01)	0.587
Baseline weight (multivariate*)	0.989 (0.98-1.00)	0.142

*Multivariate analyses were adjusted for age, sex, race, and baseline Charlson comorbidity index.

Table 2: Association of weight fluctuation and baseline weight with all-cause mortality.

Background/Purpose: Recent studies have suggested that body weight fluctuation in the general population is an independent risk factor for overall mortality. These findings are of particular concern for patients with systemic lupus erythematosus (SLE), who have a significantly elevated risk of mortality compared to the general population. However, little is known about the nature of body weight fluctuation and its association with mortality in SLE patients. We hypothesized that patients with SLE who had greater body weight fluctuation would have increased mortality risk compared to patients with SLE who had lower body weight fluctuation.

Methods: We used a previously validated algorithm (positive predictive value of 94%) to assemble a cohort of SLE patients from a de-identified version of an academic medical center's electronic health record. We extracted outpatient weight measurements and reviewed cases with outlier values to confirm their accuracy. We excluded (1) patients with fewer than three visits or age less than 18 years at the time of the first relevant ICD9 code (710.0 for SLE), (2) weights from 90 days prior to and 270 days after an occurrence of pregnancy, and (3) weights measured during inpatient or emergency department visits. We then conducted a retrospective cohort study in which body weight fluctuation (measured as average successive variability) was analyzed to identify associations with demographic variables, clinical characteristics, and outcomes among SLE patients. We used a Poisson regression and adjusted for age, sex, race, and baseline Charlson comorbidity index in the multivariate analysis. The primary outcome was all-cause mortality.

Results: A total of 690 SLE patients met inclusion criteria. Patients with body weight fluctuation below the median were described as "low body weight fluctuation," while patients with body weight fluctuation above the median were termed "high body weight fluctuation." High body weight fluctuation correlated significantly with several baseline characteristics, including younger age, black race, and higher weight (Table 1). In the multivariate analysis, there was a significant association between body weight fluctuation and mortality (incidence rate ratio [IRR]: 2.009; 95% confidence interval [CI] 1.16-3.47; p = 0.012; Table 2).

Conclusion: In patients with SLE, high fluctuation in body weight, but not baseline BMI nor weight, was associated with increased mortality independent of age, race, sex, and baseline comorbidities. This association may indicate that early recognition by providers of weight fluctuation—even more than BMI or body weight—has the potential to decrease mortality in SLE patients.

Disclosure: S. Bayefsky, Rheumatology Research Foundation, 2; **A. Dickson**, None; **T. Reese**, Rheumatology Research Foundation, 2; **J. Gandelman**, Vanderbilt University School of Medicine Research Immersion Program, 2, Rheumatology Research Foundation, 2; **M. Shuey**, NIH DK108444-01A1, 2; **A. Barnado**, NIH/NIAMS 5K08AR072757-02, 2; **K. Barker**, None; **C. Stein**, None; **V. Kawai**, NIH K23GM117395, 2, NIH NIGMS K23GM117395, 2, NIH/NIGMS K23GM117395, 2, NIH, 2, NIH, 2; **C. Chung**, Lupus Research Alliance, 2, NCATS/NIH CTSA grant ULTR000445, 2, Rheumatology Research Foundation, 2, Veterans Health Administration CDA, 2.

Abstract Number: 1563

Interstitial Lung Disease in Patients with Systemic Lupus Erythematosus: Who Should We Screen?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a disease with a variety of clinical manifestations but interestingly interstitial lung disease (ILD) is rare. The literature to date has not identified consistent markers to help with clinical decision making regarding screening for SLE-ILD. Some of these features may depend on specific ethnic variation based on the population studied. We retrospectively identified patients with SLE and ILD at our institution over a twenty-year period to try to identify an SLE-ILD phenotype in our Northwest US SLE population to aid in decisions about screening.

Methods: We conducted a review of our electronic record database at University of Washington Medical center, looking for patients with the diagnosis of SLE who were seen between 1998-2018 in our Rheumatology outpatient clinics. We identified 1335 SLE patients by using the International Classification of Diseases (ICD) 9 and 10 codes. We also identified 29 patients with a diagnosis of SLE-ILD. Diagnosis was confirmed by individual medical record review by a rheumatologist based on history, exam, laboratory, and imaging findings. Clinical and serologic data for each patient was recorded and analyzed and compared to a control group of SLE patient without ILD.

Results: SLE-ILD was found in only 2% of our SLE population. SLE-ILD appears to be more common in Asians (31 vs 14% SLE-ILD vs control population). More than half of the patients who will develop SLE-ILD, will develop it in first

2 years after SLE diagnosis. NSIP is the most common type of SLE-ILD (72.2%) followed by UIP (24%). Common clinical features include the presence of Raynaud's phenomenon (RP) and gastrointestinal esophageal reflux disease (GERD) and both were present in greater than 70% of SLE-ILD patients. Of note, 34% of our SLE-ILD patients had co-existing pulmonary hypertension. Chest x-ray missed ILD changes in almost 30% and required CT scan to make the diagnosis. Common serologic findings included speckled ANA (66%), anti-SM, RNP or SM/RNP antibodies (59%). Seventy-four percent of patients responded (stable or improved) to therapy (most common therapy was MMF). Forced vital capacity measurement (FVC) changed at an average rate of only 1.65 %/year in this population. Those with a UIP pattern on CT tended to do worse (43% worse UIP vs 19% NSIP). Only one death occurred in this population over the study period of unknown cause.

Conclusion: Our retrospective study showed that ILD is a rare manifestation of SLE. Patients with the combination of RP, GERD, and either anti-SM, RNP, or SM/RNP antibodies should be considered high risk for developing SLE-ILD and intermittent screening with pulmonary function tests that include FVC and DLCO measurements. Given that 41% of our patients also had pulmonary hypertension ECHO should also be considered in patients with SLE-ILD especially those with relatively low DLCO. Screening should be considered early in the disease process in patients with this phenotype and Asian patients especially should be watched closely.

Disclosure: M. Al-ani, None; **B. Han**, None; **G. Gardner**, None.

Abstract Number: 1564

Renal Arteriosclerosis Predicts Cardiovascular Disease in Lupus Nephritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Patients with lupus nephritis (LN) have a 9-fold higher risk of cardiovascular disease (CVD), highlighting the urgent need to target CVD prevention. Studies in IgA nephropathy and transplant report that severe renal arteriosclerosis (ASCL) on biopsies is an early predictor of CVD. We previously reported a high burden of renal ASCL, accelerated by two decades in LN patients compared to healthy peers. We saw 80% positive predictive value of reported ASCL, but 50% of pathology reports overlooked renal ASCL in LN biopsies due to lack of standard systematic reporting of vascular lesions. Therefore, we aimed to examine whether overlooked renal ASCL was partially responsible for the prior negative studies on renal ASCL and CVD in LN. *We hypothesized that renal ASCL would be an early predictor of CVD in LN when over-read pathology and reports were incorporated.*

Methods: We identified all LN patients who underwent a kidney biopsy 1994-2017 at an academic center using a comprehensive native renal biopsy database. Data included socio-demographics and pathology reports from the first renal biopsy. SLE diagnosis was validated using ACR and SLICC 2012 criteria. CVD events were validated using American Heart Association guidelines. At the time of kidney biopsy, chronic kidney disease (CKD) stage and atherosclerotic cardiovascular disease (ASCVD) risk factors were recorded. Pathology reports were reviewed for reported renal ASCL, classified using Banff donor kidney biopsy ASCL grading: none, mild, moderate or severe. A blinded

Table 1. Demographics of LN patients *n=189*

Factor	Category	n, (%)
Age	Age, Median (Range)	25 (2-79) yrs
Gender	Female	148 (78%)
	Male	41 (23%)
Race	White	138 (73%)
	Non White	22 (17%)
ASCVD Risk Factors	>1 risk factors	64 (34%)
Chronic Kidney Disease	Stage ≥ 3	50 (27%)
SLE duration	<2 years	93 (49%)
Reported Renal Arteriosclerosis (ASCL)	Mild	43 (24%)
	Moderate	13 (6%)
	Severe	2 (1%)
Over-read or Reported Renal Arteriosclerosis (ASCL)	Mild	50 (27%)
	Moderate	17 (9%)
	Severe	5 (3%)
CVD events	Over 10 yr-follow-up	22 (12%)

pathologist over-read 25% of biopsies using Banff ASCL grading. When pathology reports lacked any comment on the presence or absence of renal ASCL, we supplemented the over-read renal ASCL grade. Multivariable logistic regression examined relationships with CVD events.

Results: Among 189 incident LN patients with kidney biopsies, 78% were female, 78% white and the median age was 25 (2-79), 27% had ≥ 3 CKD stage and 34% had >1 ASCVD risk factors. Overall, 32% had any and 7% had moderate-severe reported renal ASCL. The prevalence of any and moderate-severe by reported or over-read renal ASCL was 38% and 12% (Table 1). We found 22 CVD events from 1 year before LN through 10 years of follow-up, comparable to published rates in LN *(12% vs 11%, p 0.9)*.

In the group with reported renal ASCL, multivariable analyses showed that ≥ 3 CKD stage increased risk of CVD by 5-fold (*Adjusted OR 5.4, CI 1.8-18, p 0.004*; Table 2) but reported renal ASCL was not a predictor of CVD. However, examining reported or over-read renal ASCL, multivariable analysis showed that severe renal ASCL at LN diagnosis increased risk of CVD by 10-fold compared to those without ASCL (OR 9.6,CI 1.2-99, p 0.038). CKD stage ≥ 3 remained a predictor; >1 ASCVD risk factors and age were not predictors.

Conclusion: Systematic grading and reporting of renal ASCL in at first LN biopsy is critical, because severe renal ASCL can predict CVD in LN patients. In future studies, we recommend over-reading all biopsies to grade renal ASCL and examining CVD associations in diverse LN cohorts.

Table 2. Predictors of CVD in LN reported & over-read renal arteriosclerosis (ASCL)

	Reported Renal ASCL		Reported or Over-read Renal ASCL	
Predictor	Adjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
ASCL - None	ref	ref	ref	ref
ASCL - Mild	0.5 (0.1-2)	0.3	0.7 (0.2-2.3)	0.6
ASCL - Moderate	1.4 (0.2-8.2)	0.7	0.9 (0.1-4.4)	0.9
ASCL - Severe	$1.3 X10^8$ (NA)	0.9	**9.6 (1.2-99)**	**0.038**
Age <30 years	ref	ref	ref	ref
Age ≥30 years	1.4 (0.4-4.7)	0.6	1.8 (0.5-5.7)	0.3
≦ 1 ASCVD risk factor	ref	ref	ref	ref
>1 ASCVD risk factors	0.6 (0.2-1.8)	0.3	0.6 (0.2-1.8)	0.4
CKD stage <3	ref	ref	ref	ref
CKD stage ≥3	**5.4 (1.8-4.7)**	**0.004**	**4.2 (1.4-13)**	**0.01**

Disclosure: S. Garg, None; **S. Panzer**, None; **K. Hansen**, None; **C. Plafkin**, None; **M. Smith**, None; **C. Bartels**, Pfizer, 2, Pfizer Independent Grants for Learning and Change, 2.

Abstract Number: 1565

Assessment of the QRISK2, QRISK3, SLE Cardiovascular Risk Equation, Framingham and Modified Framingham Risk Calculators as Predictors of Cardiovascular Disease Events in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Tool	CVD Status	Low Risk (<10%) (%)	Median Risk (10 – 20%) (%)	High Risk (>20%) (%)
QRISK2	Cases	81	14	4
	Controls	93	5	2
FRS	Cases	78	16	6
	Controls	93	6	1
QRISK3	Cases	53	27	20
	Controls	78	13	9
mFRS	Cases	54	25	21
	Controls	83	10	7
SLECRE	Cases	39	29	32
	Controls	64	23	13

Table 1. Percentage of cases and controls classified as low (<10%), median (10-20%) and high risk of developing CVD according to each CVD risk assessment tool.

Background/Purpose: Systemic lupus erythematosus (SLE) is recognized as an independent risk factor for cardiovascular disease (CVD). This study aimed to determine which cardiovascular risk assessment tool amongst the QRISK2, QRISK3, Framingham (FRS), Modified FRS (mFRS) or SLE Cardiovascular Risk Equation (SLECRE) best predicts CVD in SLE. QRISK3, mFRS and SLECRE are CVD risk assessment tools that consider SLE in risk prognosticating patients.

Methods: Single-centre analyses on prospectively collected data of 1887 SLE patients were performed to compute 10-year CVD risk scores for each tool. Tools' scores were evaluated against CVD development at or within ten years for cases (CVD events) and controls (no CVD events). For cases, the index date for risk score calculation was chosen 10 years, or as close to 10 years as possible prior to the CVD event. Similarly, for controls, risk scores were calculated as close to 10 years as possible prior to the most recent clinic appointment. Proportions of patients classified as low risk (< 10%), median risk (10-20%) and high risk (>20%) of developing CVD according to each tool were determined. Sensitivity, specificity, positive/negative predictive values and c-statistics of these tools were analyzed.

Results: 232 total CVD events were seen in the cohort including myocardial infarction, stroke, transient ischemic attack, heart failure and CVD death. QRISK2 and FRS performances were similar, while the QRISK3 and mFRS performances were similar. The SLECRE classified the highest number of patients as median-high risk (Table 1). The sensitivities and specificities are as follows for each tool: QRISK2 (19%, 93%), FRS (22%, 93%), mFRS (46%, 83%), QRISK3 (47%, 78%), SLECRE (61%, 63%), respectively. The tools were similar in negative predictive value, ranging from 89% (QRISK2) to 92% (SLECRE). The FRS and mFRS had the greatest c-statistics, both equaling 0. 73, demonstrating the greatest predictive accuracy amongst the tools, while the QRISK3 and SLECRE had the lowest (0. 67).

Conclusion: While the mFRS performance was superior to the FRS, the QRISK3 did not outperform the mFRS. Although the SLECRE had the highest sensitivity, it had the lowest specificity, demonstrated by grouping the most

cases and controls in the median-high risk category. Several factors are important to consider when deciding which risk assessment tools to utilize clinically: ease of use, sensitivity/specificity, and laboratory data accessibility. Thus, the mFRS continues to be a practical tool with a simple, intuitive scoring system appropriate for the ambulatory clinic setting based on the initial weighting of the FRS while adjusting for SLE.

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Abstract Number: 1566

HER2 as a Biomarker of Proliferative Lupus Nephritis in Children

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SESSION INFORMATION
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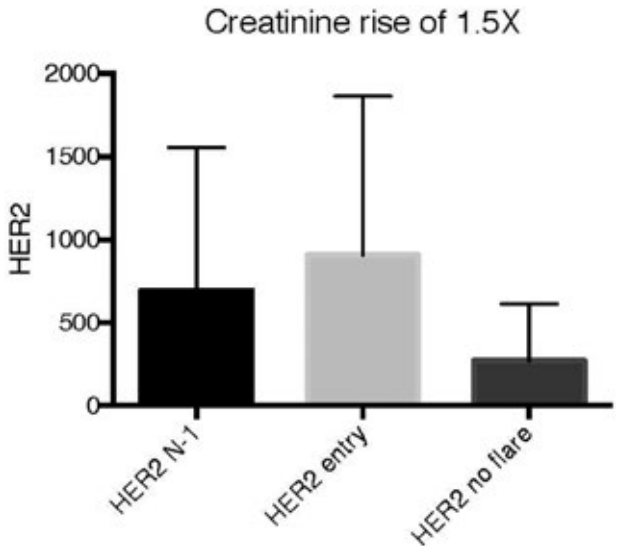
Background/Purpose: Lupus nephritis is a common feature of SLE and confers a poor prognosis. 20-50% of patients with lupus nephritis ultimately develop chronic kidney disease and renal failure in spite of efforts to induce remission of nephritis. Chronic kidney disease is epidemiologically associated with more frequent relapses and lack



9 patients with creatinine rise of 1

Figure 1. Urinary HER2 stratified by 1.5X rise in serum creatinine. HER2 N-1 represents the mean HER2 at the time point prior to the rise in serum creatinine. HER2 entry represents the mean of the HER2 at study entry for those who went on to have a rise of 1.5 over entry creatinine. HER2 no flare displays the HER2 levels in patients who never flared. HER2 N-1 and HER2 entry are significantly different than HER2 no flare.

of remission after treatment. Both relapse and lack of remission are difficult to detect on a background of pre-existing renal disease. Proteinuria can represent residual damage. There have been intense efforts in recent years to identify urinary biomarkers, often exploiting known inflammatory features. We identified a urine biomarker that tracks proliferative aspects of lupus nephritis, HER2. This study was designed to test the sensitivity and specificity of HER2 in urine as a biomarker for active lupus nephritis.

Methods: This study design prospectively collects urine every 3 months in 100 pediatric patients with known lupus nephritis. Mean follow up at the time of writing is 3 years. Control groups include RF+ JIA, amplified pain and healthy teen females. HER2, TWEAK and VCAM are measured by ELISA. Clinical data are collected on structured CRFs at each visit. Flares of lupus nephritis are defined by SLEDAI-R (renal SLEDAI) and increased serum creatinine.

Results: Elevated urinary HER2 was observed lupus patients compared to all the control cohorts. The specificity of HER2 in lupus nephritis compared to other kidney disorders was assessed and HER2 was elevated specifically with active lupus nephritis but not vasculitis, IgA nephropathy or acute kidney injury. There was a significant association of urinary HER2 levels with SLEDAI-R by ANOVA ($P < 0.0001$) with a peak association with SLEDAI-R=8. When individual components of SLEDAI-R were assessed, all were associated with an increase in HER2 over non-flare patients. We validated the association of HER2 with SLEDAI-R in a cross-sectional study of adults. In the longitudinal pediatric cohort, we analyzed the subset of patients with a 1.5 fold rise in serum creatinine. HER2 was significantly elevated at the time point preceding the rise in creatinine (HER2 N-1) and at study entry (HER2 entry) for these patients (Figure 1). HER2 outperforms TWEAK and VCAM in these analyses.

Conclusion: We conclude that urinary HER2 is significantly associated with active lupus nephritis and increased levels precede flares detectable by a rise in creatinine.

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Abstract Number: 1567

Cachexia in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
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Background/Purpose: Cachexia is a syndrome that may accompany a range of diseases, including cancer, chronic heart failure, chronic obstructive pulmonary disease, and rheumatoid arthritis. It is associated with central and systemic increases of pro-inflammatory factors, and with decreased quality of life, poor responses to pharmacological treatment and shortened survival. Despite an abundance of data from other inflammatory diseases, cachexia in systemic lupus erythematosus remains a largely undescribed syndrome. Using the Fearon criteria for defining cachexia

Table 1. Patient characteristics			
	All (n=2452[1])	**Cachexia (n=1067[2])**	**No cachexia (n=825[2])**
Age at cohort entry			
<30	798 (32.5%)	373 (35.0%)	272 (33.0%)
30-44	987 (40.3%)	409 (38.3%)	343 (41.6%)
45-59	528 (21.5%)	223 (20.9%)	162 (19.6%)
60+	139 (5.7%)	62 (5.8%)	48 (5.8%)
Age mean(SD)	37.6 (12.9)	37.3 (13.2)	37.3 (12.7)
Ethnicity			
Black	960 (39.2%)	450 (42.2%)	280 (33.9%)
White	183 (7.5%)	541 (50.7%)	471 (57.1%)
Other	1309 (53.4%)	76 (7.1%)	74 (9.0%)
Sex			
Female	2266 (92.4%)	988 (92.6%)	761 (92.2%)
Male	186 (7.6%)	79 (7.4%)	64 (7.8%)
Initial BMI			
<20	220 (9.7%)	47 (4.4%)	127 (15.4%)
20-25	782 (34.5%)	424 (39.7%)	310 (37.6%)
25-30	632 (27.9%)	374 (35.1%)	224 (27.2%)
30-35	635 (28.0%)	222 (20.8%)	164 (19.9%)

(5% stable weight loss in 6 months without starvation relative to the average weight in all prior cohort visits AND/OR weight loss >2% without starvation relative to the average weight in all prior cohort visits and a BMI < 20), we have previously shown that more than half of the Hopkins Lupus Cohort patients met cachexia criteria within the first five years of cohort entry. We decided to revisit this analysis using the Evans criteria for defining cachexia, criteria which are more specific, more extensive, and have been shown to have a better prediction of survival.

Methods: 2406 patients in a prospective SLE cohort had their weight assessed at each visit. Patients were categorized into five predetermined groups based on weight: low (BMI< 20 kg/m2), normal weight (reference, BMI 20-24.9 kg/m2), overweight (25-29.9 kg/m2), obese (BMI 30-34.9 kg/m2), and severely obese (BMI >35 kg/m2). Cachexia was defined based on modified Evans criteria as 5% stable weight loss in 12 months without starvation relative to

Table 2: Risk of cachexia within 5 years of cohort entry		
	Risk of Cachexia within 5 years of cohort entry (95% CI)[1]	P-value for difference by patient characteristics[2]
All	56% (53%, 59%)	
Age at cohort entry		0.7279
<30	58% (53%, 62%)	
30-44	56% (52%, 60%)	
45-59	53% (47%, 58%)	
60+	59% (48%, 69%)	
Ethnicity		0.0029
Black	59% (55%, 63%)	
White	54% (50%, 57%)	
Other	55% (45%, 65%)	
Sex		0.3484
Female	56% (54%, 59%)	
Male	53% (44%, 62%)	
Initial BMI		<0.0001
<20	16% (11%, 23%)	
20-25	59% (55%, 63%)	
25-30	64% (60%, 69%)	
30-35	58% (52%, 63%)	
[1] Based on Kaplan Meier estimates [2] Based on log tank test		

the average weight in all prior cohort visits AND/OR BMI< 20 and 3 out of the following criteria: ESR >20mm/h, hemoglobin < 12g/dL, albumin < 3.2g/dl, and anorexia. Risk of cachexia within 5 years of cohort entry was based on Kaplan Meier estimates.

Results: See Table 1 and Table 2

Conclusion: Within five years of cohort entry, more than half of the Hopkins Lupus cohort patients develop cachexia as defined by Evans criteria. This prevalence of cachexia is higher than the one reported in breast cancer (25%) or

hematological malignancies (40%), and similar to the rates reported for lung cancer (50%). The highest risk of cachexia was seen among African Americans, while those with a BMI< 20 had the lowest risk. Cachexia is an under recognized syndrome in patients with lupus affecting a large proportion of patients regardless of the criteria used for its definition. Further studies are needed to elucidate the implications of cachexia in the response to treatment, long term outcomes, quality of life, as well as its role as a potential cardiovascular risk factor in SLE.

Disclosure: G. Stojan, None; **J. Li**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 1568

High Risk Low Attenuation Non-Calcified Coronary Plaque in Lupus vs. Controls

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Background/Purpose: The presence of low attenuation noncalcified plaque (< 30 Haunsfield units) is one of the most characteristic vessel changes in unstable coronary plaques. Low-attenuation noncalcified plaques (< 30 Haunsfield Units) contain necrotic cores that are characterized by endothelial dysfunction, oxidative stress, and inflammation. They have been shown to be a better predictor of future cardiovascular events compared to traditional cardiovascular risk factors in the general population. Accelerated atherosclerosis leading to premature coronary artery disease remains the major cause of late death in SLE. We sought to characterize low attenuation noncalcified plaque in patients with systemic lupus erythematosus versus controls.

Methods: A total of 72 patients who met the ACR or SLICC classification criteria for SLE had CT angiogram studies, 30 of which had follow up CT angiograms. A total of 100 healthy controls who had two CT angiograms were included in the study. Coronary plaque area was measured by manual tracing for the difference between the area within the external elastic membrane and the area of the vessel lumen at the site of maximal luminal narrowing as observed on a cross-sectional coronary CT angiography image. A noncalcified plaque was defined as a low-density mass >1 mm2 in size, located within the vessel wall and clearly distinguishable from the contrast-enhanced coronary lumen and the surrounding pericardial tissue. Each noncalcified plaque detected within the vessel wall was evaluated with the minimum CT density. T-test was used to evaluate baseline characteristics between lupus patients and controls. Paired *t*-test or Wilcoxon signed ranks test were used to compare plaque volume between baseline and follow-up for each cohort. Fisher's exact test was used to evaluate the association between change in low attenuation NCP and demographic and clinical variables including sex, race, age at baseline, ever smoking (from history file), diabetes, hypertension, hyperlipidemia, obesity, lupus anticoagulant, anticardiolipin, anti-beta 2 glycoprotein, hydroxychloroquine and immunosuppressant use, anti- dsDNA, low C3, low C4, antihypertensive, and statin use.

Results: See Table 1 and Table 2

Conclusion: Women with lupus have a significantly higher burden of low attenuation NCP compared to healthy controls in all age subgroups except in those >60 years of age. A similar trend was seen in men but the number of patients was small. While the NCP and low attenuation NCP burden significantly regressed over time in controls, no

Table 1: Mean (SD) of Low Density Non-calcified Plaque at baseline

Sex	Age	Low Density Non-calcified Plaque				
		SLE		Controls		
		n	Mean (SD)	n	Mean (SD)	p
All	All	66	457.92 (207.53)	100	42.19 (52.30)	<0.0001
Female	<44	19	63.119.18)	0	- (-)	-
	45-59	33	450.52 (150.37)	3	53.37 (31.6)	<0.0001
	60+	5	695.2 (570.58)	21	21.58 (25.59)	0.0576
Male	<44	3	412.33 (216.58)	2	51.15 (72.34)	0.1176
	45-59	5	516.4 (76.83)	22	46.84 (57.8)	<0.0001
	60+	1	582 (-)	52	47.56 (57.54)	-

Table 2: Volume progression/regression (mm^3) within each cohort

	JHU Mean diff(SD)	p-value	UCLA Mean diff(SD)	p-value
Change in Total Plaque volume	12.25 (335.11)	0.7608	-7.97 (105.13)	0.0435
Change in Total CAC Plaque	5.97 (28.70)	0.4132	24.87 (72.28)	0.0002
Change in Total NCP plaque	6.27 (322.46)	0.8712	-32.84 (110.67)	<0.0001
Change in Low Attenuation NCP plaque	-13.56 (93.29)	0.4570	-6.90 (27.62)	0.0002
Change in Remodeling index	0.09 (0.87)	0.6013	-0.12 (0.88)	0.6219

significant changes were seen in the plaque burden of lupus patients. Statin use did not affect progression of NCP or low attenuation NCP plaque.

Disclosure: G. Stojan, None; **J. Li**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 1569

Poor Long-term Renal Outcome in Systemic Lupus Erythematosus Without Abnormal Urinalysis: A Possible Link with Silent Lupus Nephritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: It has been well investigated that patients with lupus nephritis (LN) have worse prognosis than those without. Recently reported, about 20% of SLE patients without abnormal urinalysis have histopathologically proven lupus nephritis, so-called silent LN. Here, we investigated long-term renal outcome in SLE patients without abnormal urinalysis and additionally determined whether their renal outcomes correlates with abnormal B lymphocyte activity in circulation.

Figure 1

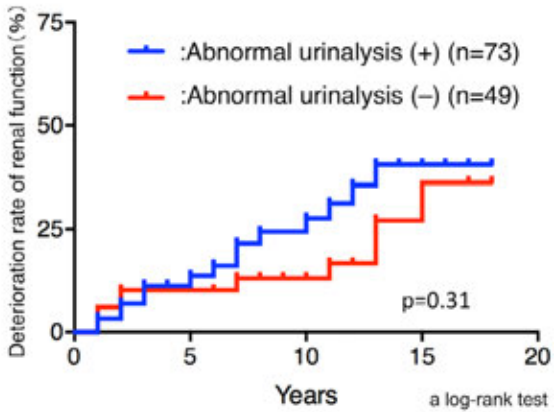

Figure 1. Deterioration rate of renal function. There was no significant difference between patients with and without abnormal urinalysis in SLE.

Figure 2

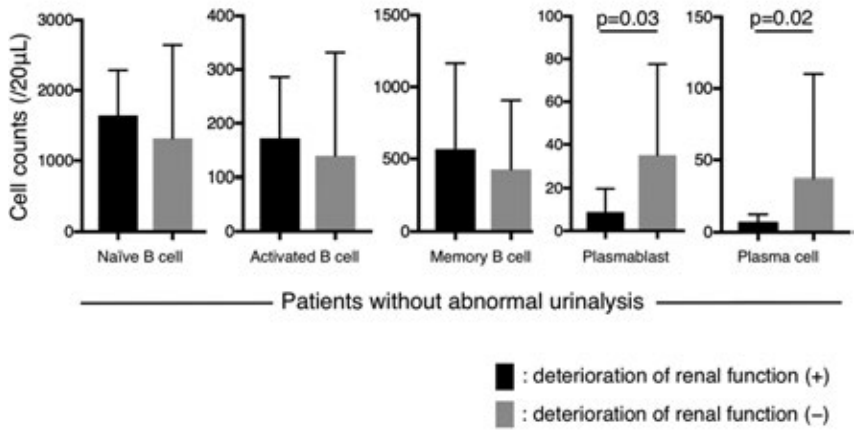

Figure 2. Fluorescence-activated cell sorting analysis of peripheral B cells. A significant lower number of plasmablast and plasma cell was observed in patients without abnormal urinalysis for deterioration of renal function.

Methods: We retrospectively evaluated newly diagnosed SLE patients from 2000 to 2018 in our hospital. All the patients were divided them into 2 groups according to the presence of abnormal urinalysis during the observation. Abnormal urinalysis was defined as a persistent proteinuria (more than 50 mg/dL or 0.5 g/gCr for more than 3 months). Deterioration of renal function (more than 40% eGFR decline from baseline) was compared between them. For the patients without abnormal urinalysis, the distribution of B cell subsets was compared by fluorescence-activated cell sorting analysis using anti-CD19, 20, 27, 38, 138, and IgD antibodies depending on the deterioration of renal function.

Results: Seventy-three patients with abnormal urinalysis and 62 without were evaluated. Among patients with abnormal urinalysis, 62 (84.9%) had biopsy-proven LN. Patients with abnormal urinalysis had a higher titer of anti-dsDNA antibodies ($p< 0.01$), SLEDAI score ($p< 0.01$), maximum dose of prednisolone ($p=0.04$), percentage of IVCY use ($p< 0.01$) and MMF use ($p< 0.01$) than those without. There was no significant difference in observational periods (10.1 vs 11.6 years, $p=0.43$) and cumulative deterioration rate of renal function (19.7 vs 16.1%, $p=0.31$) between them (Figure 1). For patients without abnormal urinalysis, a higher positivity of anti-Sm antibody (70.0% vs 5.0%, $p< 0.01$) and a lower count of plasmablast (CD19+/27+/IgD+/38+/138–) ($p=0.03$) and plasma cell (CD138+) ($p=0.02$) were observed in patients with deteriorated renal function than those without (Figure 2).

Conclusion: Long-term renal outcome was not significantly different between patients with and without abnormal urinalysis for about 10-years observation. Positivity of anti-Sm antibody and decreased number of peripheral plasmablast and plasma cell might be surrogate markers for deterioration of renal function in patients without abnormal urinalysis. Silent LN might contribute to our results and further analysis performing renal biopsy is needed.

Disclosure: H. Hanaoka, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **J. Kikuchi**, None; **S. Saito**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **H. Takei**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **K. Hiramoto**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **T. Oshige**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **N. Seki**, None; **H. Tsujimoto**, None; **Y. Kaneko**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **T. Takeuchi**, AbbVie, 2, 5, 8, AbbVie GK, 2, 9, Asahi Kasei, 2, Asahikasei, 2, Asahikasei Pharma Corp., 2, Astellas, 2, 8, 9, Astellas Pharma Inc, 2, Astellas Pharma, Inc., 2, 5, 8, 9, Astra Zeneca, 2, AstraZeneca, 8, AYUMI, 2, 9, AYUMI Pharmaceutical Corporation, 2, BMS, 2, 8, Boehringer-ingelheim, 9, Bristol–Myers K.K., 9, Bristol-Myers, 2, Bristol-Myers Squibb, 8, Chugai, 2, 8, 9, Chugai Pharmaceutical Co, Ltd., 2, Daiichi Sankyo, 2, 8, 9, Daiichi Sankyo Co., Ltd., 2, Eisai, 2, 5, 8, 9, Eisai Co., Ltd., 2, Eli Lilly, 2, 8, Eli Lilly Japan, 9, Gilead Sciences, Inc., 9, GlaxoSmithKline K.K, 9, GSK, 8, Janssen, 2, 8, Janssen Pharmaceutical K.K, 9, Mitsubishi Tanabe, 2, 9, Mitsubishi Tanabe Pharma Co., 2, Mitsubishi-Tanabe Pharma Corp, 2, 8, 9, Nippon Kayaku, 2, Nipponkayaku, 2, 9, Nipponkayaku Co.Ltd., 2, Novartis, 2, 8, Novartis Pharma K.K, 2, 9, Novartis Pharma K.K., 2, Pfizer, 2, 8, Pfizer Japan, 2, 9, Pfizer Japan Inc., 2, Sanofi, 8, Sanofi K.K, 9, Shionogi & Co., 2, Shionogi & Co., LTD., 2, Taiho, 2, 8, 9, Taisho, 9, Taisho Toyama, 2, 8, Takahashi Industrial and Economic Research Foundation, 2, Takeda, 2, 8, Takeda Pharmaceutical Co., Ltd., 2, Teijin, 2, 8, UCB, 8, 9, UCB Japan, 9.

Abstract Number: 1570

Can the Montreal Cognitive Assessment (MoCA) Improve the Automated Neuropsychological Assessment Metrics (ANAM) Performance in Screening for Cognitive Impairment in Lupus Patients?

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

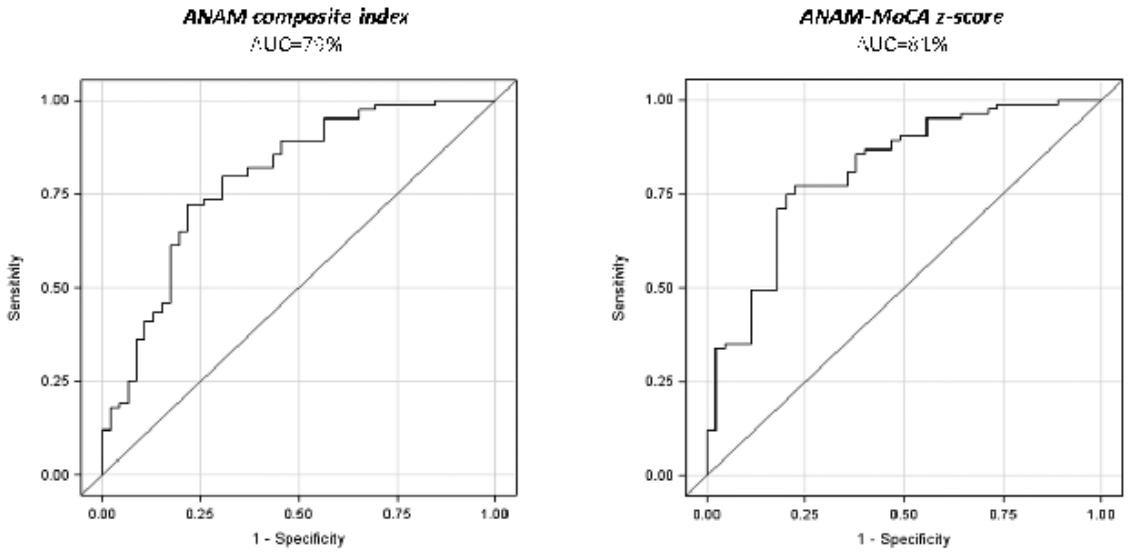
Session Title: SLE – Clinical Poster II: Comorbidities

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In a related study, we have shown evidence to support the validity of the Automated Neuropsychological Assessment Metrics (ANAM) for the screening of cognitive impairment (CI) in adult systemic lupus

Figure 1: Receiver operating characteristic (ROC) curves for identifying cognitive impairment based on the performances of *ANAM composite index* and of the *ANAM-MoCA z-score*



AUC: Area under the curve

***ANAM composite index* calculated by the following equation: ANAM-index=31.85-0.06*TP/CSL -0.06*PCT/CSD-0.02*TP/SRTR-0.14*PCT/GNG-9.93*CV/SP-0.0008*MS/TPZ+9.74*MR/TL-6.38*CV/TCRT**

[TP: throughput; CSL: code substitution learning; PCT: percentage of correct responses; CSD: code substitution delay; SRTR: simple reaction time repeated; GNG: go/no go; CV: coefficient of variation of reaction time; SP: spatial processing; MS: Mean-Score; TPZ: tower puzzle; MR: mean reaction time; TL: tapping left hand; TCRT: two choice reaction time]

ANAM-MoCA z-score is a combination of the *ANAM composite index* and the MoCA score both standardized to obtain z-score

erythematosus (SLE) using a novel **derived *ANAM composite index***. The Montreal Cognitive Assessment (MoCA) is a brief assessment tool commonly used for screening of CI in the general population and SLE. **The aim of this study was to assess whether the MoCA can improve the performance of the ANAM in screening for CI in SLE compared to the American College of Rheumatology (ACR) Neuropsychological Battery (NB).**

Methods: Between 2016 and 2019, consecutive adult SLE patients were administered the ACR NB, MoCA and ANAM on the same day. Using age- and gender-stratified normative data, patients were classified on the ACR NB as having CI if a z-score of ≤-1.5 was observed in ≥ 2 domains; or non-CI if no domain had a z-score of ≤-1.5 An ANAM composite index was calculated for each patient according to its equation (Figure 1) using selected ANAM subtests and scores and standardized to obtain a z-score. MoCA scores were multiplied by negative 1 to make them compatible with the ANAM composite index (where a higher score corresponds to a higher probability of CI) and standardized to obtain z-scores. The z-scores of the ANAM composite index and of the MoCA were summed to achieve a combined ANAM-*MoCA z-score* with a mean of 0 and standard deviation of 2 and with equal weights from both instruments. The performance of the *ANAM composite index* and the *ANAM-MoCA z-score* to screen for CI against NB were evaluated using Receiver operating characteristic **(**ROC) curve analysis. The Area Under the Curve (AUC) was calculated for both as well as the improvement in CI identification for the combined *ANAM-MoCA z-score* compared to the *ANAM compo*site *index* alone.

Results: 211 patients were enrolled. Mean age and SLE disease duration at study visit were 42 ± 12 years and 15 ± 10 years, respectively. CI was diagnosed by the ACR NB in 45.5% (n=96) of patients and no CI in 24.6% (n=52). The *ANAM composite index* showed good ability to identify CI operationalised on NB with AUC of 79% (95% confidence interval): 0.71, 0.88). Adding the MoCA score to create the *ANAM-MoCA z-score* demonstrated AUC of 81% (95% confidence interval: 0.73, 0.89), an improvement of 2.5% (**Figure 1**).

Conclusion: ANAM is a promising tool for screening of CI in SLE patients. The addition of the MoCA to the ANAM score, improves the performance of the ANAM only to a small extent but sufficient to move AUC from good to excellent category. Further research is required to enhance ANAM screening ability and usefulness.

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Abstract Number: 1571

Validity Evidence Supports the Use of Automated Neuropsychological Assessment Metrics (ANAM) as a Screening Tool for Cognitive Impairment in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Table 1: Best ANAM logistic regression model with the most discriminatory subtests and corresponding scores selected by manual step-down variable selection and its derived equation for calculating ANAM-index

ANAM Subtest	ANAM Score	Slope ± SE	p-value
1. Code substitution learning	TP	-0.0576 ± 0.034	0.09
2. Code substitution delay	PCT	-0.0587 ± 0.02	**0.01**
3. Simple reaction time- repeated	TP	-0.0195 ± 0.01	**0.03**
4. Go no go	PCT	-0.1401 ± 0.08	0.063
5. Spatial processing	CV	-9.9252 ± 3.22	**0.002**
6. Tower puzzle	MS	-0.0008 ± 0.0007	0.25
7. Tapping left hand	MR	9.7445 ± 7.10	0.17
8. Two choice reaction time	CV	-6.3786 ± 3.16	**0.044**
Intercept		31.8509 ± 9.08	<0.001

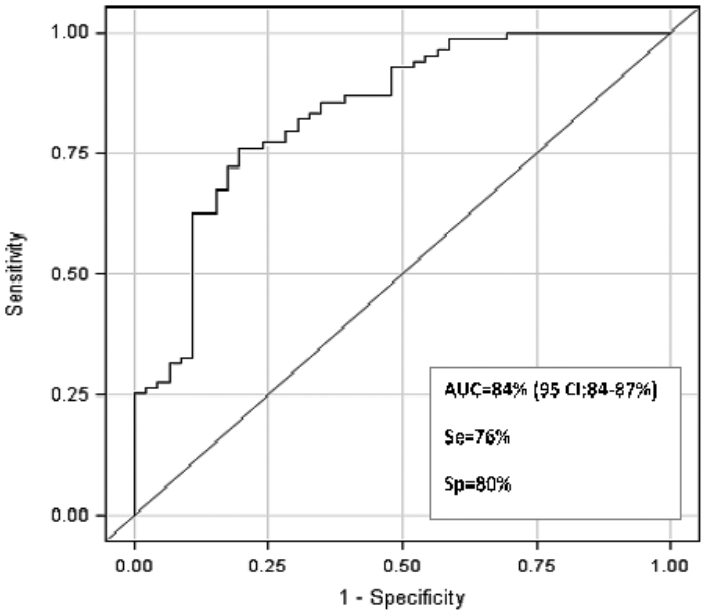
Formula of ANAM-index=31.85-0.06*TP/CSL -0.06*PCT/CSD-0.02*TP/SRTR-0.14 *PCT/GNG-9.93*CV/SP-0.0008*MS/TPZ+9.74*MR/TL-6.38*CV/TCRT

ANAM= Automated Neuropsychological Assessment Metrics; PCT=percentage of correct responses; CV=coefficient of variation of reaction time; MR=mean reaction time; TP=throughput; MS=Mean-Score; CSL=code substitution learning; CSD=code substitution delay; SRTR=simple reaction time repeated; GNG=go/no go; SP=spatial processing; TPZ=tower puzzle; TL=tapping left hand; TCRT=two choice reaction time

Background/Purpose: Cognitive impairment (CI) is highly prevalent in Systemic Lupus Erythematosus (SLE). Screening for CI in SLE may be delayed, if relying on the American College of Rheumatology (ACR) neuropsychological battery (NB), which is time- and resource- intensive. The **Automated Neuropsychological Assessment Metrics (**ANAM) is a quick and low-cost computer-based screening tool for CI**. The overarching aim of this study was to assess the performance of the ANAM as a screening tool for CI in SLE patients employing the ACR NB as the gold standard**. The specific objective were to: (a) determine the ability of the ANAM to differentiate between SLE patients with and without CI, (b) assess the ability of selected ANAM subtests to accurately identify CI, and (c) derive an ANAM composite index and cut-off to facilitate its use.

Methods: Between 2016 and 2019, 211 consecutive adult SLE patients were administered the ACR NB and the ANAM on the same day. Using age- and gender-stratified normative data, patients were classified on the ACR NB as having CI if a z-score of ≤-1.5 was observed in ≥ 2 domains; or non-CI if no domain had a z-score of ≤-1.5. **First**, ***discriminative validity*** of the ANAM was assessed by its ability to differentiate between CI and non-CI patients com-

Figure 1: Receiver operating characteristic (ROC) curve for identifying cognitive impairment based on the performance of ANAM best model using subtests selected by step-down multivariate analysis



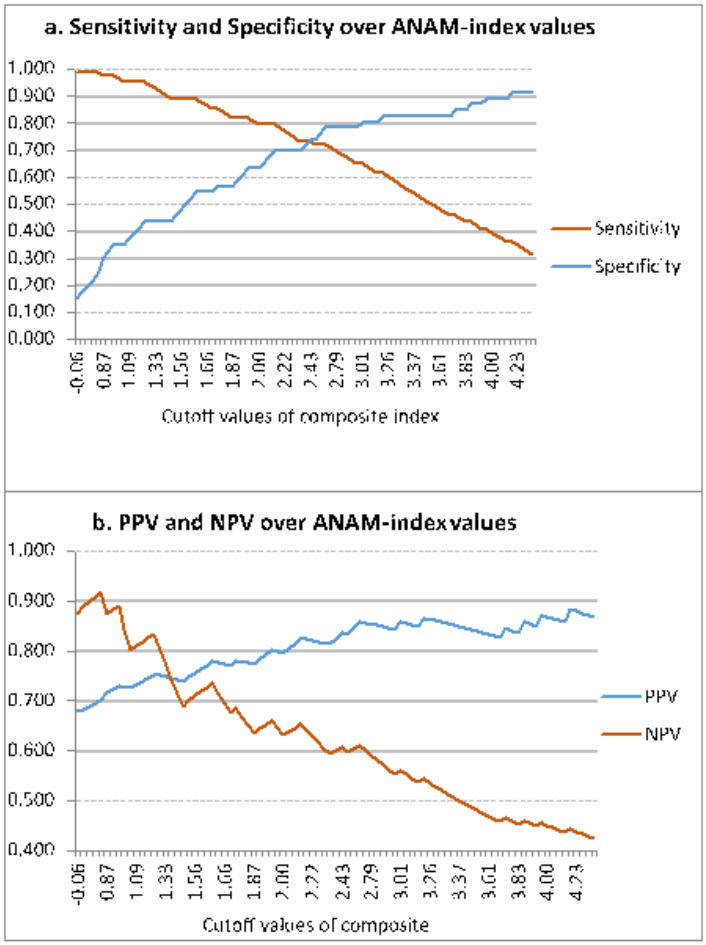
ANAM= Automated Neuropsychological Assessment Metrics; AUC: area under the curve; Se: sensitivity; Sp: specificity

pared to the ACR NB. All 15 ANAM subtests and their scores (percentage of correct responses [PCT], mean reaction time [MR], throughput [TP], and coefficient of variation [CV]) were studied. **Second,** we developed 6 ANAM models and the most discriminatory subtests and scores within each model were selected using logistic regression analyses. The area under the receiver operating characteristics curve (AUC) was calculated to establish ANAM models construct validity against the ACR NB. **Third**, an ***ANAM composite index and cut-off*** were derived for the best selected model using the sum of the subtests' scores multiplied by their parameter estimate from the logistic regression. The sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (PPV) of the ANAM *composite index* and cut-off, to differentiate CI from non-CI were evaluated.

Results: Patients with non-CI performed better on the majority of ANAM subtests in PCT, MR and TP scores compared to those with CI, providing support for ANAM ***discriminative validity***. CI was accurately identified by the best ANAM model (Table 1) with an excellent AUC of 84% [95% confidence interval: 0.84, 0.87] (Figure 1), providing support for the ***construct validity of the ANAM model*** using 8 selected ANAM subtests and corresponding scores. The derived ***composite index*** (equation provided in Table 1) demonstrated good performance with AUC of 79%. The proposed ***cut-off*** yielded Se, Sp, PPV and NPV of 80%, 70%, 83% and 65%, respectively. Figure 2 demonstrates the performance of the composite index over different cut-off values.

Conclusion: This study provides support for the validity of the ANAM along with 8 selected subtests for the screening of CI in adult SLE in the selected model. We derived an ***ANAM composite index*** and a ***cut-off*** to serve as a summary measure of cognitive performance of SLE patients. This will enhance the applicability and interpretation of the ANAM in clinical practice.

Figure 2: Performance of the candidate ANAM composite index for identifying cognitive impairment over different cut-off values



ANAM= Automated Neuropsychological Assessment Metrics; NPV: negative predictive value; PPV: positive predictive value

Cut-off 2.17 provides a Se of 80% and Sp of 70% with PPV 83% and NPV 65%

Cut-off 1.61 provides a Se of 88% and Sp of 54% with PPV 78% and NPV 74%

Disclosure: O. Tayer-Shifman, None; **R. Green**, None; **D. Beaton**, None; **L. Ruttan**, None; **J. Wither**, None; **M. Tartaglia**, None; **M. Kakvan**, None; **S. Lombardi**, None; **N. Anderson**, None; **J. Su**, None; **D. Bonilla**, None; **M. Zandy**, None; **M. Choi**, None; **M. Fritzler**, Alexion Canada, 7, BioRad, 5, Dr. Fooke Laboratorien GmbH, 5, Euroimmun GmbH, 5, 7, ImmunoConcepts, 7, Inova Diagnostics, 5, 7, 8, Inova Diagnostics Inc. San diego, CA, 5, Inova Dx, Mikrogen GmbH, 5, Werfen International, 5; **Z. Touma**, None.

Abstract Number: 1572

Persistent Cognitive Impairment in Lupus Patients over 1 Year and Associated Factors

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Table 1: Demographics of patients with persistent CI compared to stable non-CI patients

	Stable non-CI (N=49)	Persistent CI (N=16)	p value
Sex, N (%)			0.137
Female	44 (89.8%)	12 (75.0%)	
Male	5 (10.2%)	4 (25.0%)	
Age at enrolment, yrs, Mean ± SD	43.93 ± 12.28	43.45 ± 13.52	0.895
Age at enrollment, yrs			0.331
18-29	5 (10.2%)	4 (25.0%)	
30-39	17 (34.7%)	2 (12.5%)	
40-49	10 (20.4%)	3 (18.8%)	
50-59	10 (20.4%)	5 (31.3%)	
60-65	7 (14.3%)	2 (12.5%)	
Race			0.096
Caucasian	32 (65.3%)	10 (66.7%)	
Black	6 (12.2%)	5 (33.3%)	
Chinese	2 (4.1%)	0 (0.0%)	
Others	9 (18.4%)	0 (0.0%)	
Highest education level, N (%)			0.12
Grade 8 or High-school	11 (23.4%)	7 (43.8%)	
College or university	36 (76.6%)	9 (56.3%)	
Employment, N (%)			0.46
Employed	28 (57.1%)	9 (56.3%)	
Retired	2 (4.1%)	0 (0.0%)	
Homemaker	3 (6.1%)	0 (0.0%)	
Student	2 (4.1%)	1 (6.3%)	
Looking for work	0 (0.0%)	1 (6.3%)	
Disabled/sick leave	12 (24.5%)	5 (31.3%)	
Other	2 (4.1%)	0 (0.0%)	
Marital status, N (%)			0.065
Single	19 (38.8%)	7 (43.8%)	
Married/common law	27 (55.1%)	5 (31.3%)	
Widowed/divorced/separated	3 (6.1%)	4 (25.0%)	

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Table 2: Clinical characteristics of patients with persistent CI compared to stable non-CI patients

	Stable non-CI (N=49)	Persistent CI (N=16)	p value
Age at SLE diagnosis, yrs, Mean ± SD	28.14 ± 9.55	28.26 ± 12.54	0.969
SLE disease duration, yrs, Mean ± SD	15.78 ± 10.93	15.19 ± 9.94	0.847
Number of ACR criteria, Mean ± SD	6.47 ± 1.21	6.31 ± 1.49	0.672
SDI score, Mean ± SD	0.96 ± 1.41	0.94 ± 1.34	0.957
SLEDAI-2K, Mean ± SD	2.77 ± 2.43	2.69 ± 3.18	0.913
Adjusted Mean SLEDAI-2K, Mean ± SD	2.71 ± 2.44	3.31 ± 3.93	0.471
SLE cumulative manifestation[§], N (%)			
CNS	18 (36.7%)	6 (37.5%)	0.956
Vascular	12 (24.5%)	3 (18.8%)	0.636
Musculoskeletal	25 (51.0%)	10 (62.5%)	0.424
Renal	11 (22.4%)	5 (31.3%)	0.478
Skin	36 (73.5%)	8 (50.0%)	0.081
Serosal	9 (18.4%)	5 (31.3%)	0.276
Immunologic	40 (81.6%)	10 (62.5%)	0.115
Hematologic	16 (32.7%)	4 (25.0%)	0.565
COMORBIDITIES			
Depression (BDI-II), N (%)	14 (31.1%)	5 (35.7%)	0.748
Mean score ± SD	14.40 ± 11.87	18.14 ± 13.67	0.324
Anxiety (BAI), N (%)	7 (15.6%)	4 (28.6%)	0.275
Mean score ± SD	13.82 ± 9.99	20.14 ± 13.42	0.062
Fatigue severity score (FSS), Mean ± SD	4.07 ± 1.78	5.33 ± 1.36	**0.019**
Pain transformed score[¶], Mean ± SD	63.91 ± 26.18	48.71 ± 23.34	0.057
Fibromyalgia, N (%) ever diagnosed	19 (38.8%)	7 (43.8%)	0.724
Antiphospholipid syndrome, N (%)	16 (32.7%)	4 (25.0%)	0.565
CVE, N (%) ever	3 (6.1%)	4 (25.0%)	**0.034**
Diabetes, N (%)	0 (0%)	0 (0%)	
Hypertension, N (%) ever	23 (46.9%)	7 (43.8%)	0.824
Dyslipidemia, N (%) ever	30 (61.2%)	9 (56.3%)	0.724
Smoking, N (%) past 5 years	9 (18.4%)	4 (25.0%)	0.565
IMMUNOLOGY			
Positive anti dsDNA, N (%) ever	38 (77.6%)	10 (62.5%)	0.234
Low complements, N (%) ever	37 (75.5%)	9 (56.3%)	0.141
Positive ENA, N (%) ever			
Anti RNP	26 (54.2%)	8 (50.0%)	0.772
Anti Ro	22 (45.8%)	7 (43.8%)	0.885
Anti La	11 (22.9%)	3 (18.8%)	0.727
Anti Sm	18 (37.5%)	7 (43.8%)	0.657
aPL, N (%) ever	25 (52.1%)	6 (37.5%)	0.312
Abnormal brain imaging, N (%) ever	10 (20.4%)	5 (31.3%)	0.371
Head CT scan	2 (4.1%)	3 (18.8%)	0.056
Brain MRI	7 (14.3%)	3 (18.8%)	0.667
Brain scan or SPECT	5 (10.2%)	1 (6.3%)	0.635
Treatment			
Glucocorticosteroids, N (%)	19 (38.8%)	10 (62.5%)	0.097
dose, Mean ± SD	7.70 ± 8.33	3.85 ± 1.96	0.162
Antimalarials, N (%)	40 (81.6%)	11 (68.8%)	0.276
Immunosuppression, N (%)	29 (59.2%)	9 (56.3%)	0.836
ASA, N (%)	8 (16.3%)	3 (18.8%)	0.822
Anticoagulation, N (%)			
Warfarin	2 (4.1%)	2 (12.5%)	0.224
Other anticoagulants	2 (4.1%)	0 (0.0%)	0.412
Psychotropic medications, N (%)	19 (38.8%)	7 (43.8%)	0.724
Pain medications, N (%)	15 (31.3%)	6 (37.5%)	0.645

All variables measured at baseline unless stated otherwise

SLE: systemic lupus erythematosus; ACR: American College of Rheumatology; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index, excluding cognition component; SLEDAI-2K: SLE Disease Activity Index 2000; BDI-II: BECK Depression Inventory-II, cut-off score of ≥18 was used to define depression; BAI: BECK Anxiety Inventory, cut-off score of ≥ 22 was used to define anxiety; CVE: Cardiovascular event including stroke, transient ischemic attack, myocardial infarction or atherosclerotic congestive heart failure; aPL: antiphospholipid antibodies; ASA: acetylsalicylic acid.

Hypertension defined as blood pressure of >140/90 or antihypertensive treatment; Dyslipidemia defined as abnormal total cholesterol or on specific treatment

[§]According to SLEDAI-2K

[¶]Transformed score from bodily pain domain of 36-Item Short Form Survey (SF-36), low score corresponds to higher pain reported

Background/Purpose: Cognitive impairment (CI) is a common manifestation of systemic lupus erythematosus (SLE) and its course may change over time. The objective was to determine the prevalence of persistent CI in SLE patients over 1 year time and investigate the associated factors.

Methods: Consecutive SLE patients, aged 18-65 years, who attended a single centre (2016- 2019) were included. Patients were administered the Neuropsychological Battery (NB) at baseline (T0), 6 months (T1) and 12 months (T2). Patients' scores were compared to normative data to obtain z-scores. CI was operationalized on the NB as a z-score of ≤-1.5 on ≥2 domains. Three groups were identified: Persistent CI group - CI present in all 3 assessments; stable non-CI group - CI not present in all 3 assessments; or fluctuating CI group - CI was on 1-2 assessments. At each visit, data on sociodemographic, clinical and laboratory/medications were collected. Fatigue was measured by the Fatigue Severity Score (FSS), pain by the transformed scale of the Bodily Pain domain of SF-36 and anxiety by BECK Anxiety Inventory (BAI). Patients with persistent CI were compared to stable non-CI patients. Multivariable polynomial logistic regression was performed on all 3 groups to study the likelihood of a patient classified to adjunct worse group.

Results: The prevalence of CI was 40%, 26% and 38% at T0, T1 and T2 respectively among 111 patients who completed all 3 assessments. Sixteen patients (14%) experienced persistent CI, 46 (41%) fluctuating CI and 49 (44%) stable non-CI. Patients with persistent CI had higher proportion of **male**, **Black**, and **widowed/divorced/separated** patients compared to stable non-CI group (**Table 1**). A higher level of **fatigue**, **pain** and **anxiety** were identified in persistent CI group (**Table 2**). The persistent CI group showed higher proportions of **cardiovascular events (CVEs)** and abnormal brain imaging. Glucocorticoid use was higher while antimalarial use was lower in the persistent CI group with no difference in immunosuppressives, aspirin, pain or psychotropic medications. There were no differences in SLE manifestations, other comorbidities (e.g. fibromyalgia and antiphospholipid syndrome), SDI, SLEDAI-2K and immunological profile.

The Multivariate analysis on all 3 groups showed that **Black** [odds ratio (OR) of 2.9 (95% confidence interval: 1.1-7.7, p 0.03)] and **Fatigue** [OR 1.3 (1.04-1.7; p 0.02)] **were associated with a higher likelihood of being classified in the adjunct worse group.**

Conclusion: Persistent CI was found in 14% of the patients in all 3 assessments over 1 year. Higher proportion of male, Black, CVE, fatigue and anxiety were observed among patients with persistent CI. Black patients and fatigue were also associated with a higher likelihood of being classified in the adjunct worse group. Our results advocate for further research into the associated factors with CI persistence in SLE patients. This demonstrates the complexity of the underlying factors associated with persistence CI – genetic/epigenetic, disease severity, sociodemographic, comorbidities (fatigue, anxiety, etc.), which requires further research.

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Abstract Number: 1573

Incidence and Predictors of Atherosclerotic Vascular Events in a Multicentre Inception SLE Cohort

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The prevalence of atherosclerotic vascular events (AVE) in published literature of an inception cohort with SLE is 10%. We aimed to investigate the accrual and the associated factors of AVE in a multinational multiethnic inception cohort of patients with SLE.

Methods: A large 33-centre multinational inception cohort of SLE patients was followed yearly according to a standardized protocol between 1999-2017. Patients (≥4 ACR criteria) entered the cohort within 15 months of SLE diagnosis. Patients with at least one follow-up visit after enrolment were identified. AVEs were collected and attributed on a specialized form. Diagnosis of AVE was confirmed using standard clinical criteria, relevant laboratory data and imaging. Attribution to atherosclerosis (AS) was made on the basis of SLE being inactive at the time of the event, and/or the presence of typical AS changes on imaging or pathology and/or evidence of AS elsewhere. Analysis included descriptive statistics, prevalence, rate of AVE's per 1000 patient-years of follow-up and univariable / multivariable time-dependent survival regressions.

Table 1. The distribution of first AVE (N = 61) in 1710 patients	
Follow-up	**AVE**
Sudden Death	2 (3.28%)
Angina	20 (32.79 %)
Chronic Heart Failure	9 (14.75)
Insertion of Pacemaker	2 (3.28%)
Intermittent Claudication	6 (9.84%)
Myocardial Infarction	12 (19.67%)
Stroke	6 (9.84%)
Transient Ischemic Attack	4 (6.56%)

Results: Of the 1848 patients enrolled in the cohort, 1710 who had at least one follow up visit and comprised the study sample. 88.6% were female, 49.4% Caucasian, 16.4% Black, 15.0% Asian, 15.5% Hispanic and 3.7% other. At enrolment mean (SD) disease duration was 5.7 ± 4.2 months, age rolment was 35.2 ± 13.4 years and SLEDAI-2K was 5.4 ± 5.4. The prevalence of AVEs was 3.6% and the rate per 1000-patient years was 4.6. Sixty-one patients had atherosclerotic events after enrolment (Table 1). Univariate time-dependent Cox regression revealed the predictive factors for AVE were female sex, average steroid dose and antimalarial treatment. Multivariable analyses confirmed female gender had an independent protective effect [hazard ratio and 95% confidence interval [HR (95%CI)] [0.531 (0.288, 0.992)], as did antimalarial treatment [0.517 (0.306, 0.874)] (Table 2). Since only 1305 patients had been tested for antiphospholipid antibodies (APLA) this analysis was repeated in those patients with APLA results. In these patients in the multivariable analysis female sex and antimalarial therapy were protective and APLA, SLEDAI-2K and BMI were predictive (results not shown).

Conclusion: The prevalence of AVE in this study is much lower than previously published data. Female sex and antimalarials were protective for AVE. In patients with APLA similar factors were protective but the APLA, SLEDAI-2K and BMI were predictive for AVE. In clinical practice all classic risk factors should be monitored and treated as they are in the general population.

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Table 2. Univariate and multivariable analyses of predictors for first AVE in 1710 SLE patients				
	Univariate Analysis		Multivariable Analysis	
Predictors	Hazard Ratio (95% CI)	p value	Hazard Ratio (95% CI)	p value
Age at SLE DX	1.05(0.98,1.13)	0.204		
female	0.53(0.29,0.97)	0.040	0.53(0.29,0.99)	0.047
Caucasian	1.38(0.77,2.46)	0.279		
SLEDAI score *	1.04(0.98,1.11)	0.213		
Currently a smoker vs. non-smoker *	1.48(0.64,3.42)	0.357		
Ex-smoker vs. non-smoker *	1.53(0.87,2.70)	0.140		
glucose abnormal comparing to normal *	0.94(0.44,1.99)	0.873		
SBP>140 or DBP>90 regardless of treatment vs. normal BP *	0.96(0.50,1.81)	0.891		
Abnormal total cholesterol regardless of treatment vs. normal *	1.28(0.72,2.28)	0.397		
BMI *	1.03(0.99,1.07)	0.112	1.04(0.998,1.08)	0.065
family history of sudden death, MI, angina or stroke *	1.28(0.73,2.24)	0.395		
average oral steroid dose (mg/day) *	1.02(1.001,1.04)	0.041		
Antimalarials treated vs. not treated	0.52(0.31,0.88)	0.0141	0.52(0.31,0.87)	0.014
Immunosuppressive treated vs. not treated	1.08(0.64,1.81)	0.7798		
*time dependent variables				

5, Equillium, 5, Exagen Diagnostics, 5, Genentech, 5, Human Genome Sciences/GlaxoSmithKline, 2, Kyowa Hakko Kirin, 2, Pfizer, 2, Takeda, 2, UCB, 2; **M. Inanc**, None; **R. van Vollenhoven**, AbbVie, 2, 9, Arthrogen, 2, AstraZeneca, 9, Biotest, 9, BMS, 2, 9, Celgene, 9, GSK, 2, 9, Janssen, 9, Lilly, 2, 9, medac, 9, Merck, 9, Novartis, 9, Pfizer, 2, 9, Roche, 9, UCB, 2, 9; **M. Ramos**, None; **D. Kamen**, None; **S. Jacobsen**, None; **C. Peschken**, Astra Zeneca, 2, Celgene, 2, Janssen, 2; **A. Askanase**, None; **T. Stoll**, None.

Abstract Number: 1574

Causes of Death in SLE: Analysis of Inpatient Death from 2000-2018 in a Tertiary Care Hospital in India

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Parameter	Early death (n=35)	Control SLE patients (n=70)	p value
Age at onset	35.65±14.36	28.8 ±12.7	**0.01**
Gender(M:F)	7:39	7:85	ns
Duration of disease	15.9±24.8	17.7±24.7	ns
Hb(<8g/dl)	14(41.2%)	16(23.5%)	ns
Lymphocyte(<1500/ul)	15(48.4%)	33(54.1%)	ns
PLT(<1 lakh/cu mm)	19(55.9%)	10(14.7%)	**<0.001**
CRP(mg/dl)	7.08±7.36	2.6±3.94	**0.002**
S Creatinine (mg/dl)	1.6±0.86	1.1±0.94	**0.03**
S Albumin(G/dl)	2.3±0.7	3.3±0.8	**0.0001**
Low C3 (<60mg/dl)	9(64.3%)	32(47.8%)	ns
Low C4(<15mg/dl)	8(57.1%)	43(64.2%)	ns
High ds DNA (>30 IU)	12(85.7%)	48(71.6%)	ns
SLEDAI	15.1±6.7	11.7±6.6	**0.01**

Table1: Baseline Characteristics and Investigation in Early death group and SLE control patients

Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Mortality in Systemic lupus erythematosus (SLE) has reduced over the years but it is still two to three folds as compared to general population. The major causes of death in SLE are infections and cardiovascular disease. In India due to increased burden of infection and limited access to health care, the causes may be different thus, we studied the causes of death in SLE and its predictors at a tertiary care center in India.

Methods: All patients with SLE (fulfilling ACR 1997 criteria) admitted during 2000-2018 were screened. The records of patients who died in hospital were retrieved and data on disease variables and cause of death were collected. Active disease was defined as patients having SLEDAI2k ≥5. Infections were either bacteriologically proven or based on radiological or serological evidence. Predictor's for death during first admission at the time of diagnosis of SLE were analyzed by comparing them with two SLE controls (having registration number before and after the index case) who survived. Statistical analysis was done using SPSSv23.0

Results: Among 920 patients admitted during this period,74 died. The mean age at death was 39.2±16.5 years. Thirty-three patients died of infection, 17 of disease activity and 23 patients had features of both infection and flare. Lower respiratory tract was the most common site of infection followed by gastrointestinal and urinary tract. Nine patients died of tuberculosis (TB), of which one patient had multidrug resistance pulmonary TB and 5 had disseminated TB. Two patients died of drug toxicity (methotrexate induced cytopenia,anticoagulant induced intracranial bleed).

Among 35 patients who died when diagnosis of SLE was made,12 had active disease ,6 had infection and 18 had features of both. In contrast in patients on follow up (n=39) 27(69.2%) died of infection alone. Comparing these 35 patients who died during the first admission,to 70 control SLE patients, they had older age at onset, low platelet count and albumin, higher serum creatinine, CRP and SLEDAI .(Table1)

Conclusion: Infections are the most common cause of in-hospital mortality in our cohort of SLE patients. TB is still a major concern in India. High disease activity is associated with risk for early mortality.

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Abstract Number: 1575

Lymphocyturia Is a Good and Cheap Biomarker for Active Lupus Nephritis and Is Sensitive to Change

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Multiple urinary biomarkers have been described for lupus nephritis, however none has reached the clinic due to either complex methodology or low discriminatory power. Recently, urinary CD4 and CD8 T cells have shown high specificity for active lupus nephritis (LN). Thus we studied whether urinary lymphocyte count by simple staining of sediment or T cell count by flowcytometry can serve as a simple and cheap biomarker.

Methods: Patients with active LN (ALN) defined as renal SLEDAI (rSLEDAI) >4, active lupus without nephritis (ANR) defined as SLEDAI >4, inactive nephritis (IN) defined as rSLEDAI ≤4 and SLEDAI < 4, and age matched healthy controls(HC)were included. Renal biopsy was done if not contraindicated. Lymphocytes in the urine were stained using Kovak stain and reported as number of cells/high power field. CD3 T cells were counted by FACS using anti-CD3

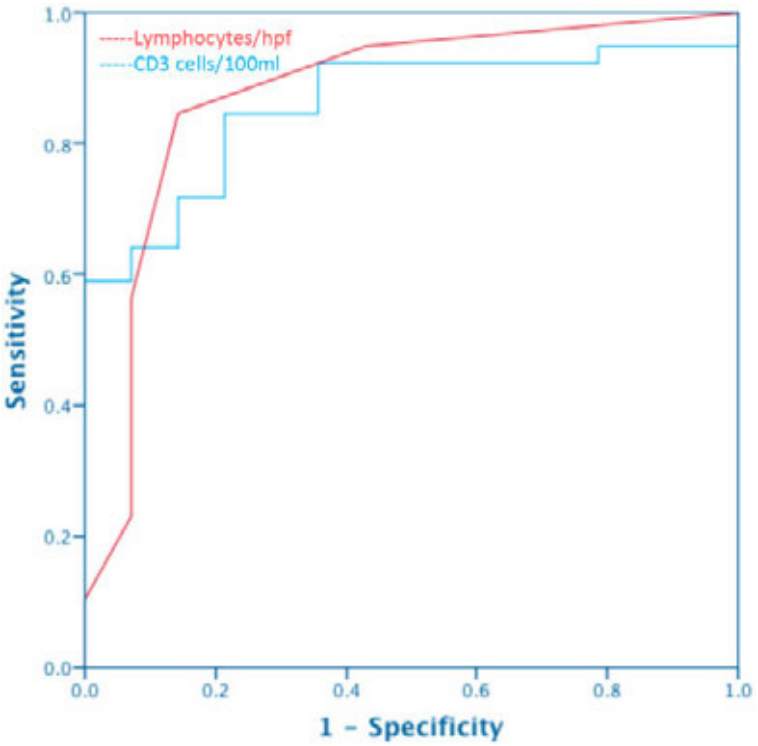

Figure 1: ROC curve of lymphocyturia and urinary CD3 cells to differentiate ALN from IN

antibody and DAPI for live gate. Immunohistochemistry was done on formalin fixed paraffin blocks of renal biopsy for CD3 and the distribution and number of cells was counted. Statistical analysis was done using SPSSv23.0

Results: Among 74 patients, 44 had ALN (40 females, mean age 30 years and mean SLEDAI:12.9±6.5), 10 had ANR disease (9 females, mean age: 27 years, mean SLEDAI:8.3±3.74)and 20 patients had IN (19 females, mean age: 33 years, mean SLEDAI:0.35±0.74). 10 healthy controls (all females, mean age:26 years) The median(IQR)Lymphocyte count in the urine was 4(7) in ALN as compared to ANR [2(3.5),p=0.1], IN (0, p< 0.001) and HC(0,p< 0.001). The median CD3 count by FACS was 2793(8982) in ALN as compared to ANR [209(539.2), p=0.001],IN [86(303),p< 0.001] and HC [115(195),p< 0.001).There was moderate correlation between lymphocyturia and urinary CD3 count (r=0.59, p< 0.001).

Lymphocyturia had moderate correlation with SLEDAI (r=0.59, p< 0.001), rSLEDAI(r=0.58, p< 0.001). Similarly, urinary CD3 cell count had moderate correlation with SLEDAI (r=0.47,p< 0.001), rSLEDAI (r=0.54, p< 0.001).The ROC curve for lymphocyturia to differentiate ALN from IN (AUC: 0.87) and for CD3 (AUC: 0.874)[Fig 1].

In 15 patients of ALN on follow up, there was a excellent correlation between change in SLEDAI and change in lymphocyte count (r=0.845,p< 0.001).In 31 patients with renal biopsy, there was a moderate correlation between the CD3 cells by IHC in tubulointerstitial compartment and urinary CD3 cells(r=0.55,p=0.001) however there was no relation with glomerular CD3 count

Conclusion: Lymphocyturia measured by simple staining of urinary sediment can be a cheap and effective marker of active LN and can be used to follow up patients with active nephritis in resource poor countries.

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Abstract Number: 1576

Prevalence and Outcome of Thrombocytopenia in Systemic Lupus Erythematosus – Single Centre Cohort Analysis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To characterize the frequency of thrombocytopenia in SLE and determine its time of onset during the course of the disease, severity and impact on mortality.

Methods: This was a single centre cohort analysis of 708 patients with SLE (fulfilling the revised ACR criteria) followed for a period of 5 to 40 years (January 1979 – December 2018). We reviewed the patients' clinical notes identifying the presence of thrombocytopenia, and ascertained other clinical and serological features of the disease. Thrombocytopenia was classified as mild (100-149x10^9/L), moderate (31-99x10^9/L) or severe (≤30x10^9/L platelets). It

was also classified as asymptomatic (no relation to any bleeding event), with minor bleeding or with major bleeding. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software.

Results: A total of 163 patients (23.0%) were identified as having developed thrombocytopenia sometime during the course of SLE. Mean age at diagnosis of SLE was 28.37 (SD=13.33 years), ranging from 7 to 77 years; 149 (91.4%) patients were female and 14 (8.6%) male. Twenty two patients (13.5%) had isolated ITP before the diagnosis of SLE. Median follow-up time was 19 years (IQR=13). The median time from diagnosis of SLE to development of thrombocytopenia was 8 years (IQR=14). Most patients (N=65, 39.9%) had mild thrombocytopenia, 38 (23.3%) moderate and 31 (19.9%) severe thrombocytopenia. More than half the patients (N=90, 55.2%) developed asymptomatic thrombocytopenia, while 27 (16.6%) presented with minor bleeding but only 5 patients (3.1%) had major bleeding events in the context of thrombocytopenia. The development of severe thrombocytopenia anytime during the course of SLE was associated with an increased risk of death (HR=3.57, p=.025). When considering the survival rates after the development of thrombocytopenia it was found that there is an increased risk of death for male patients (HR=3.41, p=.036) and for those who present with concomitant haemolytic anaemia (HR=3.07, p=.027). There was no statistical correlation found between the presence of bleeding events and mortality.

Conclusion: The presence of severe thrombocytopenia (platelets $\leq 30x10^9$) in patients with SLE is associated with an increased risk of death, regardless of bleeding events. Male patients with SLE and thrombocytopenia (any degree) have an increased mortality risk, as have those who develop concomitant thrombocytopenia and haemolytic anaemia.

Disclosure: T. Costa Pires, None; **R. Caparrós-Ruiz**, None; **D. Isenberg**, None.

Abstract Number: 1577

The Impact of the New American College of Cardiology/American Heart Association Definition of Hypertension on Cardiovascular Events in Systemic Lupus Erythematosus

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SESSION INFORMATION
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Session Title: SLE – Clinical Poster II: Comorbidities
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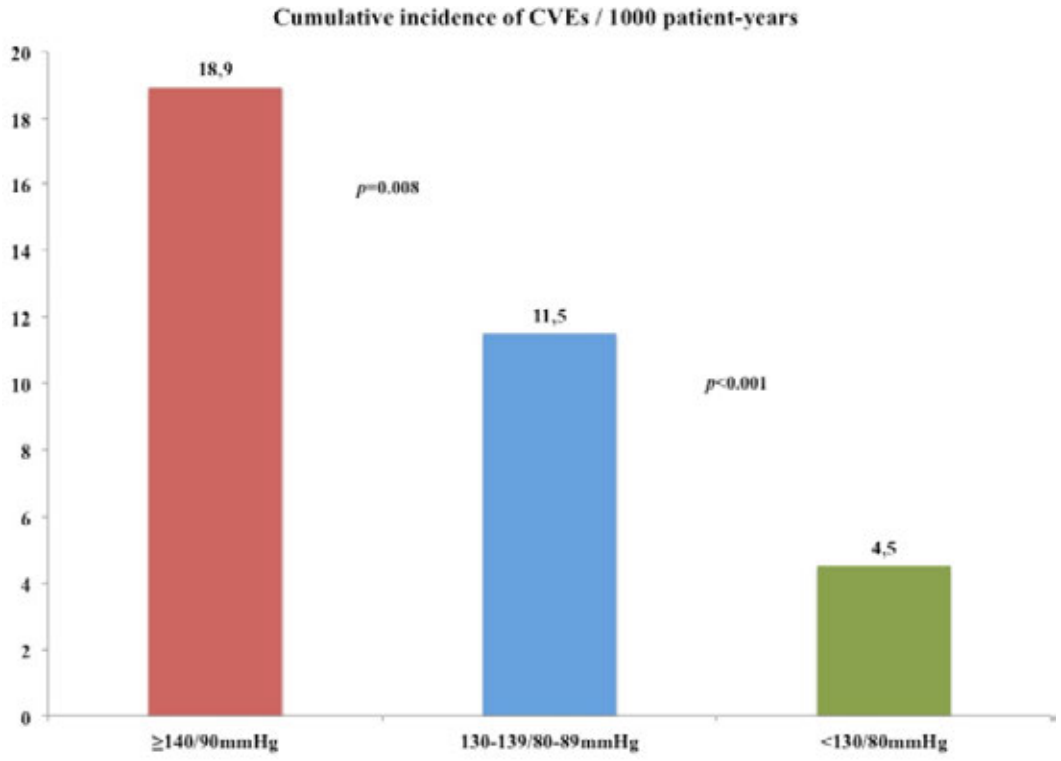
Session Time: 9:00AM–11:00AM

Background/Purpose: The 2017 guidelines by the American College of Cardiology/American Heart Association (ACC/AHA) define hypertension at a threshold of ≥130/80mmHg for the systolic and diastolic blood pressure (SBP, DBP) respectively instead of ≥140/90mmHg. Studies in patients with systemic autoimmune diseases, where BP is fluctuating over time due to various reasons, were not considered. The aim of the present study was to assess the impact of the new definitions on the prevalence and incidence of atherosclerotic cardiovascular events (CVEs) in systemic lupus erythematosus (SLE).

Methods: Patients from the Lupus Clinic with at least two years of follow-up and no previous atherosclerotic CVEs were included. Since the blood pressure (BP) in lupus patients varies particularly in the early phases, we calculated the adjusted mean BP over the first two years and divided the patients into three groups (≥140/90mmHg,



130-139/80-89mmHg and < 130/80mmHg). Patients were followed until the first occurrence of a CVE (new onset of: angina, myocardial infarction, congestive heart failure, coronary angioplasty or by-pass graft, transient ischemic attack, stroke and cardiovascular death) or the last visit. Prevalence and incidence rates of CVEs were calculated separately for each group. SAS 9.4 was used for statistics (time-to-event analysis); p< 0.05 was considered significant.

Results: 1532 patients satisfied the inclusion criteria (88.1% females, mean age at baseline 36.2±14.3 years, mean disease duration 6.1±6.3 years). The prevalence of hypertension by the previous definition was 10.1% (155/1532) and with the current definition 30.7% (471/1532); the rest 1061 (69.3%) were normotensives. After a mean follow-up of 10.8 years, there were 124 CVEs (104 non-fatal and 20 fatal) among all patients. The total prevalence of CVEs in the three groups was 32/155 (20.6%) in the ≥140/90mmHg, 41/316 (13%) in the 130-139/80-89mmHg and 51/1061 (4.8%) in the normotensive group, respectively. The cumulative incidence per 1000 patient-years is shown in Figure 1. Similar trends (gradually increasing incidence rates from the normotensives to the 130-139/80-89mmHg and the ≥140/90mmHg groups) were found individually for the coronary artery disease (CAD) events, cerebrovascular events and cardiovascular deaths.

Conclusion: SLE patients with an adjusted mean BP of 130-139/80-89mmHg over two years developed approximately 2.5fold more CVEs compared to normotensive patients. The new definition of hypertension highlights a group of patients with a high incidence of CVEs who should be targeted for more intensive therapy in order to improve cardiovascular outcomes.

Disclosure: K. Tselios, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, GSI, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5; **J. Su**, None; **M. Urowitz**, None.

Abstract Number: 1578

Factors Implicated in the Development of Early Osteonecrosis in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

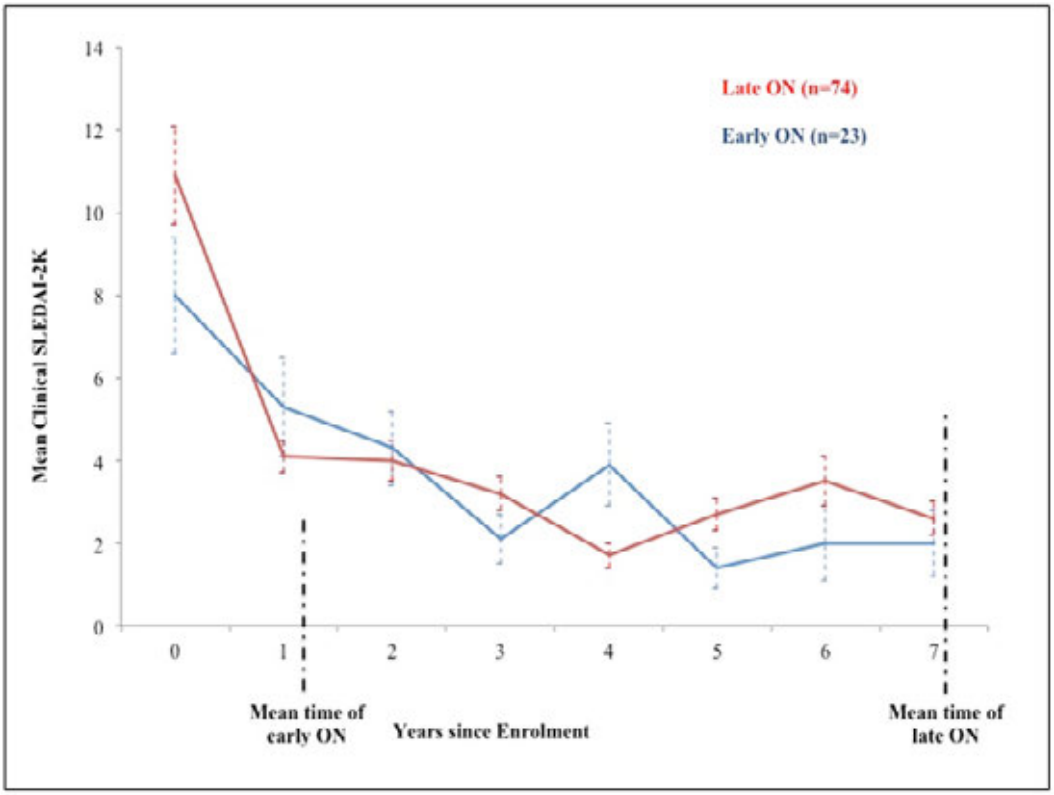
Background/Purpose: Osteonecrosis (ON) complicates approximately 15-20% of patients with systemic lupus erythematosus (SLE) on an average of six years after diagnosis. However, a small subgroup of patients will develop ON early, sometimes in a few weeks after treatment initiation. It is possible that these patients display an increased "end-organ sensitivity" and, in turn, an increased responsiveness to the administered treatment (particularly glucocorticosteroids). The aim of this study was to evaluate if patients who develop early ON will achieve better control of their disease over time compared to individuals with late ON.

Methods: Inception patients (enrolled in the Lupus Clinic within 18 months of diagnosis) who developed symptomatic ON were retrieved from the electronic database and divided into four quartiles based on the time to ON development. Patients in the first quartile were compared to individuals of the remaining three quartiles as per the demographic, clinical, immunological and therapeutic characteristics. Outcomes also included the adjusted mean SLE Disease Activity Index-2000 (SLEDAI-2K) from diagnosis until the development of ON and the severity of ON (affected joints/patient at ON diagnosis, at 12 months after ON and at the last visit). Descriptive statistics were used.

Results: Ninety-seven inception patients developed ON (time range 0.1-19.9 years from diagnosis). Twenty-three patients developed ON within 1.3 years after diagnosis (1st quartile, mean 1.2±0.6 years) whereas 74 developed ON later (2nd-4th quartiles, mean 7.4±5.2 years). There were no significant differences regarding age, sex distribution and race/ethnicity between the two groups. Initial SLEDAI-2K was higher in the patients with late ON (12.9±10.2 vs. 9.6±7, $p< 0.001$) as well as the initial prednisone dose (39.2±25.6 vs. 26.9±17.2, $p< 0.001$). For the first 12 months since diagnosis (approximately the time of early ON development), the average daily prednisone dose was similar between groups (21.6±12.1 vs. 21.3±10.7mg/day) as well as the cumulative prednisone dose (10.5±7.1 vs. 9.4±5.5grams). The evolution of the mean clinical SLEDAI-2K for seven years from diagnosis (approximately the time of late ON development) in the two groups is shown in the figure.

Concerning ON severity, this was comparable between groups both at ON diagnosis (1.46 vs. 1.43 affected joints/patient), at 12 months after ON (1.78 vs. 1.91 affected joints/patient) and at the last visit (3.3 vs. 2.87 affected joints/patient).

Conclusion: The early ON group had a lower disease activity score, lower initial steroid dose and a similar cumulative dose at one year, but developed ON within 1.3 years of diagnosis. Thus, other factors, such as genetic predisposition and organ responsiveness may be implicated in early development of ON.



Disclosure: K. Tselios, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, GSI, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5; **J. Su**, None; **M. Urowitz**, Janssen Research & Development, LLC, 2, UCB Pharma, 9.

Abstract Number: 1579

Presence of Antiphospholipid Antibodies in Patients with SLE and Venous Thromboembolic Events of African American and Caucasian Race

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SESSION INFORMATION

Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
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Background/Purpose: Risk of thrombosis is elevated in patients with systemic lupus erythematosus (SLE) compared to healthy individuals, especially during the first year after diagnosis. The increased risk for events may be related to co-occurrence of antiphospholipid syndrome (APS) but can also be seen in patients with SLE without APS. Higher SLE disease activity has been hypothesized to contribute to increased risk for thrombotic events. In this study we aim to explore differences in antiphospholipid antibody (aPL) positivity in patients with SLE and venous thrombo-

Table: Patient and Clinical Characteristics of Caucasian and African American patients with SLE and Venous Thromboembolic Events
SD: Standard Deviation, IR: Interquartile Range, SLE: Systemic Lupus Erythematosus, aPL: Antiphospholipid Antibody

	Total (n=97)	Caucasian (n=59)	African American (n=38)	p-value
Female sex	85 (88%)	48 (81%)	37 (97%)	*0.019*
Current age (mean, ±SD, in years)	48 (±14)	48 (±15)	50 (±14)	0.400
Age at SLE diagnosis (median, IR, in years)	28 (19-39)	29 (19-39)	28 (19-39)	0.981
Hispanic ethnicity	16 (16%)	16 (27%)	0	*<0.001*
BMI (median, IR, in years)	28 (24-32)	28 (24-33)	29 (23-32)	0.950
Smoking (former or current)	24 (25%)	20 (34%)	4 (11%)	*0.009*
Severe SLE	55 (57%)	31 (53%)	24 (63%)	0.303
Lupus Nephritis	36 (37%)	18 (31%)	18 (47%)	0.132
Significant aPL profile	35 (36%)	27 (46%)	8 (21%)	*0.013*

embolic (VTE) events between Caucasian and AA race. Based on our clinical experience we hypothesize that AA with SLE and VTE events are less likely to have a significant aPL profile compared to Caucasians.

Methods: Patients with diagnosis of SLE and VTE events of Caucasian and AA race were retrieved from the electronic medical record of a large Rheumatology practice based at an academic hospital. All patients had to fulfill ACR and/or SLICC criteria for SLE. Relevant clinical and laboratory characteristics were recorded. Significant aPL profile was defined as presence of moderate-to-high aPL titers (anti-cardiolipin IgG/IgM ≥40 units and/or anti-β_2 glycoprotein I IgG/IgM ≥40 units), and/or positive lupus anticoagulant >1.3. Definition of severe SLE included but was not limited to history of lupus nephritis, central nervous system lupus, severe cytopenias, vasculitis, pulmonary hemorrhage, myocarditis, lupus pneumonitis, severe myositis and lupus enteritis. T-test, Wilcoxon rank-sum test, chi-square and Fisher's exact test were used to compare patient characteristics. Logistic regression was used to explore predictors of a significant aPL profile.

Results: Ninety-seven patients were identified that fulfilled ACR and/or SLICC criteria for SLE, had history of VTE and available aPL tests (Table). Of those, 59 were Caucasian and 38 AA. Twenty-seven (46%) out of 59 Caucasians had a significant aPL profile compared to 8 out of 38 (21%) AA (p=0.013). Recorded VTE events included deep venous thrombosis of extremities, pulmonary embolism, thrombosis of renal, portal, retinal, splenic, mesenteric and sinus vein, and microthrombotic events. Using logistic regression, AA with SLE and VTE events were 66% less likely (95% CI 0.12-0.96, p=0.041) to have a significant aPL profile compared to Caucasians after controlling for age, gender, Hispanic ethnicity, smoking status and SLE severity.

Conclusion: From this study of 97 patients of AA and Caucasian race with history of SLE and VTE events, AA were less likely to have a significant aPL profile compared to Caucasians. These results suggest that a negative aPL profile in AA patients with SLE does not confer a decreased risk for thrombotic events. Further analysis will explore differences in disease activity at time of VTE events between AA and Caucasians.

Disclosure: E. Gkrouzman, None; **J. Davis-Porada**, None; **M. Peng**, None; **K. Kirou**, None.

Abstract Number: 1580

Development of Comorbidity in Danish Nationwide Cohort of Newly Diagnosed Patients with *Systemic Lupus Erythematosus*

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
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Session Time: 9:00AM–11:00AM

Background/Purpose: Development of comorbidity over time in patients with systemic lupus erythematosus (SLE) is not well characterized. To provide a detailed and comprehensive picture hereof, we estimated the incidence of frequent Charlson, Elixhauser and SLICC-ACR damage index (SDI) comorbidities following diagnosis in a large inception cohort of patients with SLE compared with matched population controls.

Methods: All patients aged 18 + years at first time registration with SLE International Classification of Diseases (ICD) codes in the Danish National Patient Register (DNPR) from January 1, 1996 to July 31, 2018 and no SLE ICD codes prior to 1996 were included (incident cases, n=3178). The date of first SLE registration was set as index date and baseline for follow-up. For each SLE case, 19 general population comparators were matched by gender and age at index date using the Danish Civil Registration System (n=60090). ICD-coded diagnoses during outpatient and inpatient care were retrieved from the DNPR and DNPR-Psychiatry (for psychosis and depression). For osteoporosis, hypertension and diabetes, we used first date of ICD codes in the DNPR or date of first filled prescription of medication for these conditions (National Register of Medicinal Product Statistics).

We identified prevalent comorbidities at baseline and excluded these individuals from analyses of incident events. For comorbidities and mortality, incidence rates (IRs) per 1000 person-years and adjusted incidence rate ratios (IRRs) with corresponding 95% confidence intervals (95% CI) were estimated during time intervals (0-1, 1-2, 2-5, 5-10 years) after index date. Poisson regression estimated IRR adjusted for age at index date and gender.

Results: 84% of patients with SLE and general population comparators were female; mean age at baseline was 47 years. Most comorbidities studied occurred more frequently during follow up in SLE patients compared with general population controls (Figure); nearly every 95% CI for these IRRs excluded the null. For most comorbidities and mortality, adjusted IRRs were highest in the first year of follow-up and decreased over time. The highest first-year IRRs (range: 15-56) were seen for typical features of SLE, including coagulopathy, renal disease, polyneuropathy and pulmonary circulation disease. Osteoporosis also occurred frequently during the first years of SLE. The IRRs for depression were consistently increased to about 2.0 during the whole follow-up. The highest IRRs during 5-10 years of follow-up were seen for renal disease, coagulopathy and osteoporosis.

Conclusion: This study provides a unique and comprehensive overview of the occurrence and timing of comorbidity in a nationwide, incident cohort of adult Danish SLE patients. We saw the highest comorbidity rates during the first year of follow-up, which may be due to features of SLE disease presentation as well as increased surveillance. However, compared to the general population the patients also demonstrated consistently increased rates of a broad

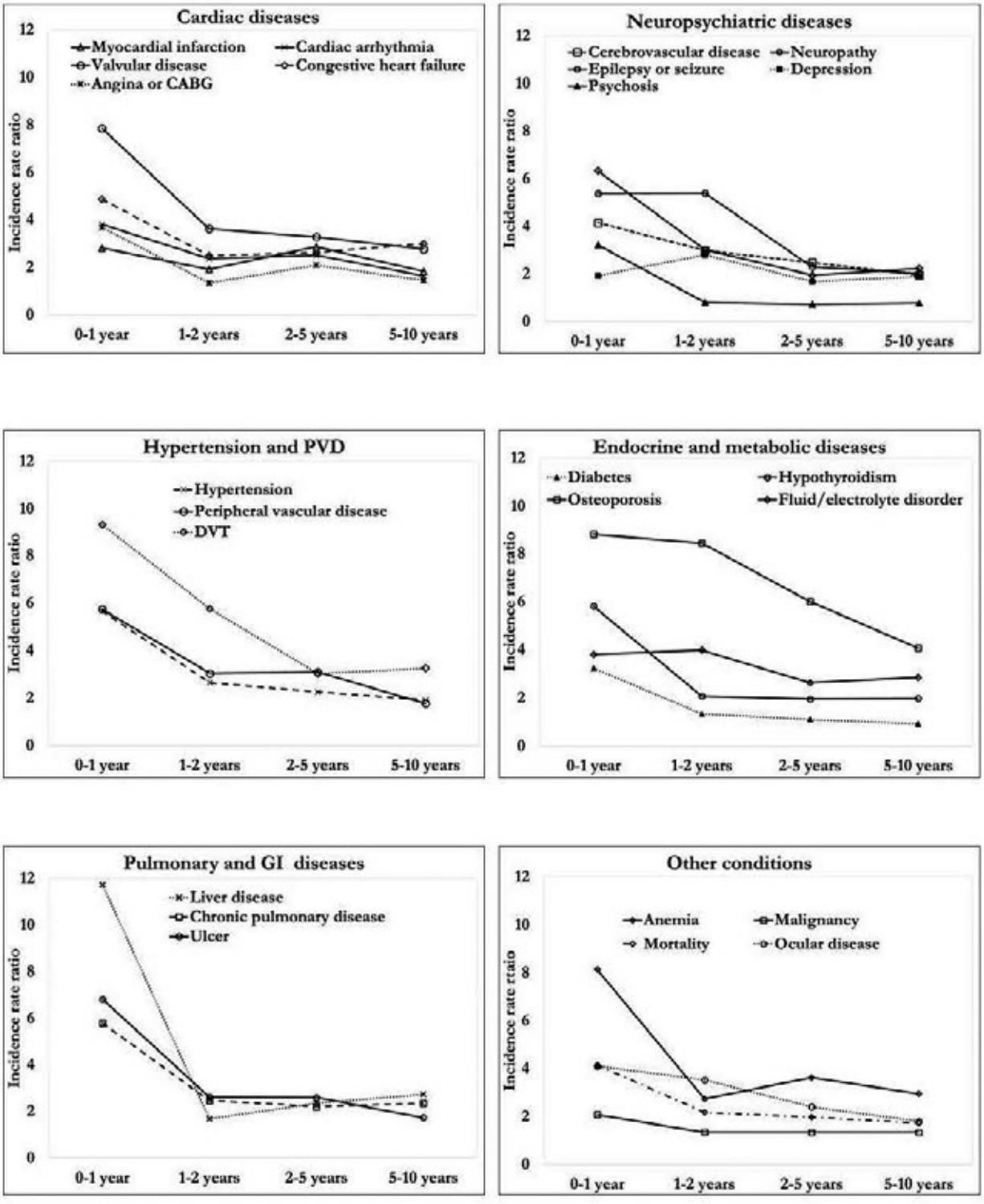

Figure. Incidence rate ratios adjusted for gender and age at baseline of frequent Charlson, Elixhauser and SLICC-ACR damage index comorbidities (per 1000 person-years) during 0-1, 1-2, 2-5 and 5-10 years post index date.

range of comorbidities featured by the SDI, Charlson and Elixhauser indices. These data may prove valuable for upcoming works on evaluating comorbidity and damage accrual in patients with SLE.

Disclosure: R. Hansen, None; **T. Falasinnu**, None; **J. Simard**, None; **M. Faurschou**, None; **S. Jacobsen**, Bristol-Myers Squibb, 2.

Abstract Number: 1581

Impact of Diabetes on Risk of End Stage Renal Disease in Danish Nationwide Cohort of Newly Diagnosed Patients with *Systemic Lupus Erythematosus*

Renata Hansen,[1] Julia Simard,[2] Mikkel Faurschou,[3] Søren Jacobsen,[4] and Titilola Falasinnu[5], [1]Copenhagen Lupus and Vasculitis Clinic, Denmark, Stanford, CA, [2]Stanford University School of Medicine, Palo Alto, CA, [3]Copenhagen Lupus and Vasculitis Clinic, Denmark, Copenhagen, Hovedstaden, Denmark, [4]Copenhagen Lupus and Vasculitis Clinic, Denmark, Copenhagen, Denmark, [5]Department of Health Research and Policy, Stanford School of Medicine, Palo Alto, CA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
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Background/Purpose: Risk of end stage renal disease (ESRD) is increased in patients with systemic lupus erythematosus (SLE). Due to lifestyle –related risk factors, inflammation, and medications such as steroids, SLE patients are also more likely to have diabetes mellitus (DM), the leading cause of ESRD in the world. We estimated the impact of DM on ESRD incidence in a large inception cohort of patients with SLE.

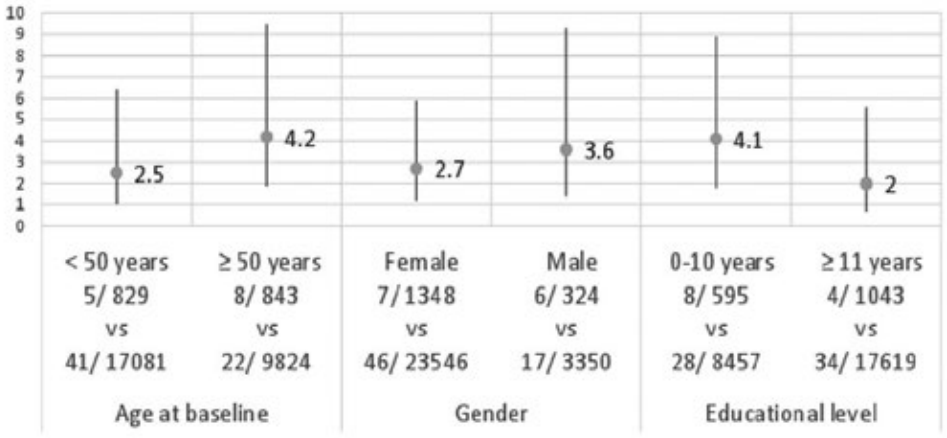
Methods: All adult patients registered with SLE International Classification of Diseases (ICD) codes in the Danish National Patient Register (DNPR) from January 1, 1996 to July 31, 2018 were identified. Individuals had no SLE ICD codes prior to 1996 (incident cases, n=3178). The date of this first SLE registration was set as SLE diagnosis date (baseline). DM was defined as the date of first DM ICD code or the date of first filled DM prescription (National Register of Medicinal Product Statistics). ESRD was defined as first registration of dialysis, renal transplant or terminal

Table 1. Characteristics of SLE inception cohort stratified by diabetes mellitus (DM).

	DM	non-DM
n	290	2859
Female (n, %)	224 (77.2 %)	2441 (85.4 %)
Age at SLE diagnosis (mean, SD)	53.4 (14.8)	46.2 (16.4)
Age at DM diagnosis (mean, SD)	54.3 (15.8)	
Mean duration from SLE to DM date, years (mean, SD)	6.4 (5.8)	
Prevalent DM	119 (41 %)	
Incident DM	171 (59 %)	
Educational level (n, %)		
Unknown	13 (4.5 %)	105 (3.7 %)
Primary and lower secondary education (0-10 years)	114 (39.3 %)	844 (29.5 %)
Upper secondary education (11-15 years)	110 (37.9 %)	1237 (43.3 %)
Higher education (>15 years)	53 (18.3 %)	673 (23.5 %)
Hypertension at baseline (n, %)	104 (35.9 %)	578 (20.2 %)

SLE: systemic lupus erythematosus

Figure 1. Incidence rate ratios (with 95% CI) of ESRD in SLE patients with diabetes compared with SLE patients with no diabetes; stratified by gender, age group at baseline and educational level at baseline (also showing number of ESRD/ person years in DM group vs non-DM group).



ESRD: end stage renal disease, SLE: systemic lupus erythematosus

(stage 5) kidney insufficiency using ICD codes. Patients with prevalent ESRD at baseline were excluded from the analyses (n=29). ESRD incidence was compared in those with DM vs those without DM (non-DM). Incidence rates per 1000 person years (IRs) and incidence rate ratios (IRRs) with corresponding 95% confidence intervals (95% CI) were estimated, stratified by gender, age at baseline (< 50 years vs >= 50 years) and educational level at baseline. Poisson regression estimated IRR.

Results: The DM group included 290 patients of whom 77% were female compared to 85% of the 2859 in the non-DM group. Those with DM were older at baseline (53 vs 46 years) (Table 1). Of those with DM at any time, DM was prevalent at baseline in 119 (41%) and incident in 171 (59%) of the patients. Mean duration from SLE to DM date for patients with incident DM was 6.4 years. Hypertension was more prevalent at baseline in those with DM compared with the non-DM group (35 % vs 20 %). Patients with DM had nearly 3 times higher incidence rate of ESRD compared with non-DM patients, adjusted for gender, age, and educational level (2.6 (1.4-4.9)). The rates were higher in females, patients aged ≥50 years, and those with lower educational level (Figure1). However, due to overlapping CIs these differences might not be significantly different from one another.

Conclusion: We found that DM greatly increased the risk of ESRD in SLE patients. Timely diagnosis and treatment of comorbidities like DM are essential to prevent long term complications and damage accrual in SLE patients.

Disclosure: R. Hansen, None; **J. Simard**, None; **M. Faurschou**, None; **S. Jacobsen**, Bristol-Myers Squibb, 2; **T. Falasinnu**, None.

Abstract Number: 1582

The Association of Lupus Nephritis Histopathologic Classification with Venous Thromboembolism Is Modified by Age at Biopsy

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that is associated with an increased incidence of venous thromboembolism (VTE). Lupus nephritis (LN) has been shown to be an independent risk factor for VTE. To our knowledge the risk of VTE has not been studied by International Society of Nephrology/Renal Pathology Society (ISN/RPS) LN class.

Methods: A cross-sectional analysis was performed using data from the Glomerular Disease Collaborative Network (GDCN). Patients with class V LN were compared to those with class III or IV (but not associated class V) LN. Classes I, II and VI were excluded from analysis due to their low prevalence. The outcome of interest was image-confirmed VTE. Logistic regression was used to calculate odds ratios and 95% confidence intervals, adjusted for age, sex, race, hormonal contraception use, serum albumin and use of hydroxychloroquine. Effect modification was assessed between the main effect and other covariates and considered if $p < 0.05$.

Results: Our cohort consisted of 533 patients; 311 (58.3%) with class III/IV and 222 (41.7%) with class V LN. Mean±SD age was 30.9±15.0 years (range 6-79 years), with an overall incidence of image-confirmed VTE of 54/533 (10.1%). In adjusted analyses, the odds of VTE were not significantly different for those with class III/IV compared to class V LN (OR, 95% CI: 1.00, 0.54-1.84). There was, however, evidence of effect modification of LN class on VTE by age at biopsy, as displayed in table 1.

Conclusion: VTE was common in LN patients in the GDCN, occurring in ~10%, and its incidence was similar among patients with class III/IV LN and those with class V LN. These findings suggest that the association between LN and VTE is not limited to class V-related nephrotic syndrome. Interestingly, however, age-specific analysis demonstrated increased odds of VTE with class III/IV LN diagnosed at a younger age and decreased odds ratio for VTE with class III/

Age, continuous	Effect	OR (95% CI)
Estimated at age 15 (-1SD)	Class III/IV vs V	5.38 (1.42-20.34)
Estimated at age 30 (mean)	Class III/IV vs V	1.19 (0.59-2.42)
Estimated at age 45 (+1SD)	Class III/IV vs V	0.26 (0.09-0.78)

Table 1

IV LN diagnosed at an older age. This may suggest the presence of an age-sensitive modulation of LN class-specific VTE risk.

Disclosure: I. Cooley, None; **V. Derebail**, Novartis, 5, Retrophin, 5, Retrophin, 2, Mallinckrodt, 2, Otsuka, 2, Chemocentryx, 2, Gilead, 2, Infla-RX, 2, American Society of Nephrology, 8, RTI International, 8, UpToDate, 8, University of North Carolina at Chapel Hill, 3; **K. Gibson**, Reata Inc, 5, Retrophin Inc, 2, Aurinia Inc, 2; **C. Alvarez**, None; **C. Poulton**, None; **L. Blazek**, None; **A. Love**, None; **S. Hogan**, None; **R. Falk**, None; **S. Sheikh**, GSK, 5.

Abstract Number: 1583

Prognostic Value of Urinary Biomarkers for the Developing of End Stage Renal Disease in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
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Background/Purpose: There is an increasing knowledge about the utility of urinary biomarkers for the diagnosis of lupus nephritis (LN) in patients with systemic lupus erythematosus (SLE). However, information as prognostic factors is more limited. Our aim was to evaluate a wide panel of urinary biomarkers in patients with SLE in order to assess their capability for prediction of progression to end stage renal disease (ESRD) in LN patients.

Methods: We conducted a prospective single center study including patients with SLE. Only those with LN criteria according ACR were included. A wide panel of urinary biomarkers were measured at the moment of study inclusion, then, a prospective follow up was made according daily clinical practice. We measured urinary levels of 6 different biomarkers including: monocyte chemoattractant protein 1 (MCP-1), neutrophil gelatinase-associated lipocalin (NGAL), TWEAK, Ceruloplasmin (CP), Transferrin (TF) and vascular cell adhesion molecule-1 (VCAM-1) using a commercial ELISA kits (R&D system and Assaypro, USA). In addition, serum anti C1q antibodies were measured by ELISA (Inova, USA).

Continuous data were summarized as means ± SDs and compared by an independent T test or Mann–Whitney test. Categorical data were expressed as number of patients and percentages and compared by Fisher's exact test. Receiver operating characteristic (ROC) curve analysis was used to explore discrimination between those with ESRD and determine the optimal cutoff point for different biomarkers. Survival curves were drawn using the Kaplan–Meier method. Statistical analyses were performed using IBM SPSS Statistics version 23.0.

	N=76 patients
Female patients (%)	85
Mean age at inclusion, years (SD)	29.3 ± 9.4
Biopsy proven LN (%)	56
Proliferative LN (%)	37
Mean 24 hours proteinuria, mg/dl (SD)	2310 ± 2779
eGFR , ml/min/1.73 m^2 (SD)	92.2 ± 36.4
Mean activity index (SD)	5.1 ± 4.2
Mean chronicity index (SD)	2.6 ± 5.1
Anti dsDNA positive (%)	77
Anti C1q positive (%)	65
Low C3 (%)	84
Low C4 (%)	77
SLEDAI at inclusion (SD)	11.2 ± 9.31

Table. General Characteristics of LN patients

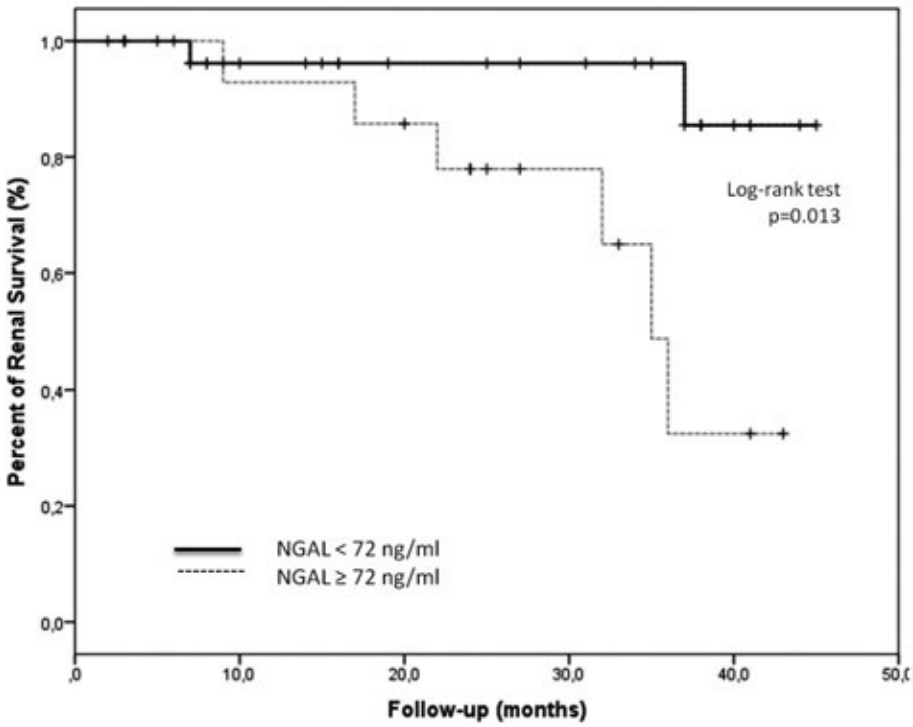

Figure. Kaplan–Meier survival curve for renal survival among SLE patients with LN according NGAL levels, Log rank test was used for analysis. p-value <0.05 were considered significant.

Results: From 120 patients with SLE, 76 (63%) had LN. The median age of patients at time of inclusion was 29.3 ± 9.4 years and the average follow-up period was 23.0 ± 13.1 months. Main clinical and serological characteristics are summarised in Table. During the follow-up 4 patients had LN progression (From class II to Class IV or V). Two patients had chronic renal disease at baseline. Eight out of 76 (10.5 %) progressed to ESRD, and 2 patients deceased. Urinary levels of NGAL (434.5 ± 193.0 vs 73.7 ± 21.5 ng/ml) and TF (8528.5 ± 234.2 vs 6780 ± 539 ng/ml) were significantly higher in those patients who progressed to ESRD. No differences were found with other urinary biomarkers or serum Anti C1q levels and risk of ESRD. The combination of these NGAL and TF compared to any of the urine

markers individually improved the prediction of future ESRD. AUC values were 0.71 and 0.63, respectively. Comparisons of renal survival grouped by the level of urinary NGAL at baseline were predictors for ESRD in LN patients (Figure).

Conclusion: In this cohort of patients with LN, around 10% of patients progressed to ESRD. High levels of Urinary NGAL levels at baseline were related with a higher risk of progression to ESRD.

Disclosure: J. Gómez-Puerta, None; **T. Urrego**, None; **B. Ortiz Reyes**, None; **A. Vanegas-García**, None; **C. Muñoz-Vahos**, None; **L. González**, None; **G. Vasquez**, None.

Abstract Number: 1584

Factors Associated with Accrual of Damage over Time in Patients with SLE: Results from a Multinational Latin American Cohort

Milena Mimica,[1] Oslando Padilla,[2] Felipe Aguilera,[3] Fernando Cavalcanti,[4] Eduardo Borba,[5] Marlene Guibert-Toledano,[6] Rosa Chacon-Diaz,[7] Gloria Vasquez,[8] Guillermo Pons-Estel,[9] Mario Cardiel,[10] Oscar Neira,[11] Mary-Carmen Amigo,[12] Eloisa Bonfa,[13] Graciela Alarcón,[14] Bernardo A. Pons-Estel,[15] and Loreto Massardo[16], [1]Centro de Biología Celular y Biomedicina, Facultad de Medicina y Ciencia. Universidad San Sebastián, Santiago, Chile., Santiago, Region Metropolitana, Chile, [2]Pontificia Universidad Católica de Chile, Santiago, Region Metropolitana, Chile, [3]Universidad San Sebastián, Santiago, Region Metropolitana, Chile, [4]Hospital das Clínicas da Universidade Federal de Pernambuco, Recife, Brazil, [5]Rheumatology Division, Hospital das Clinicas, Faculdade de Medicina da Universidade de Sao Paulo (HCFMUSP), Sao Paulo, Brazil., Sao Paulo, Brazil, [6]Servicio Nacional de Reumatología, Centro de Investigaciones Médico Quirúrgicas (CIMEQ), La Habana, Cuba, [7]Servicio de Reumatología, Policlínica Méndez Gimón, Caracas, Venezuela., Caracas, Venezuela, [8]University of Antioquia, Medellin, Antioquia, Colombia, [9]Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Rosario, Argentina, [10]Centro de Investigación Clínica de Morelia, SC, Morelia, México., Morelia, Mexico, [11]Sección Reumatología, Hospital del Salvador. Universidad de Chile. Unidad de Reumatología. Clínica Alemana de Santiago, Facultad de Medicina Clínica Alemana, Universidad del Desarrollo., Santiago, Chile, Santiago, Chile, [12]Servicio de Reumatología, Centro Médico ABC, Ciudad de México, México., Mexico, Mexico, [13]Rheumatology Division, Hospital das Clinicas, Faculdade de Medicina da Universidade de Sao Paulo (HCFMUSP), Sao Paulo, Brazil., Sao Paulo, Sao Paulo, Brazil, [14]University of Alabama at Birmingham, Birmingham, [15]Centro Regional de Enfermedades Autoinmunes y Reumáticas (CREAR), Grupo Oroño, Rosario, Rosario, Argentina, [16]Centro de Biología Celular y Biomedicina, Facultad de Medicina y Ciencia. Universidad San Sebastián, Santiago, Chile., Santiago, Chile

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with Systemic Lupus Erythematosus (SLE) are at risk of accumulating damage, having an impaired quality of life and experiencing a premature death. The different domains and items of the SLICC/ACR Damage Index (SDI) and the predictors of their development and progression in patients from a large multiethnic, multinational Latin American Lupus Cohort were studied.

Methods: 1,385 SLE patients, with a recent SLE diagnosis (< 24 months and >6 months to comply with SDI definition), were studied and followed-up for a mean of 47.0 (SD 25.1) months. Socio-demographic and clinical variables were assessed. The 41 items and 12 domains of SDI were evaluated annually. Kaplan-Meier (Log-rank test) and Cox frailty models as multivariate analysis were performed.

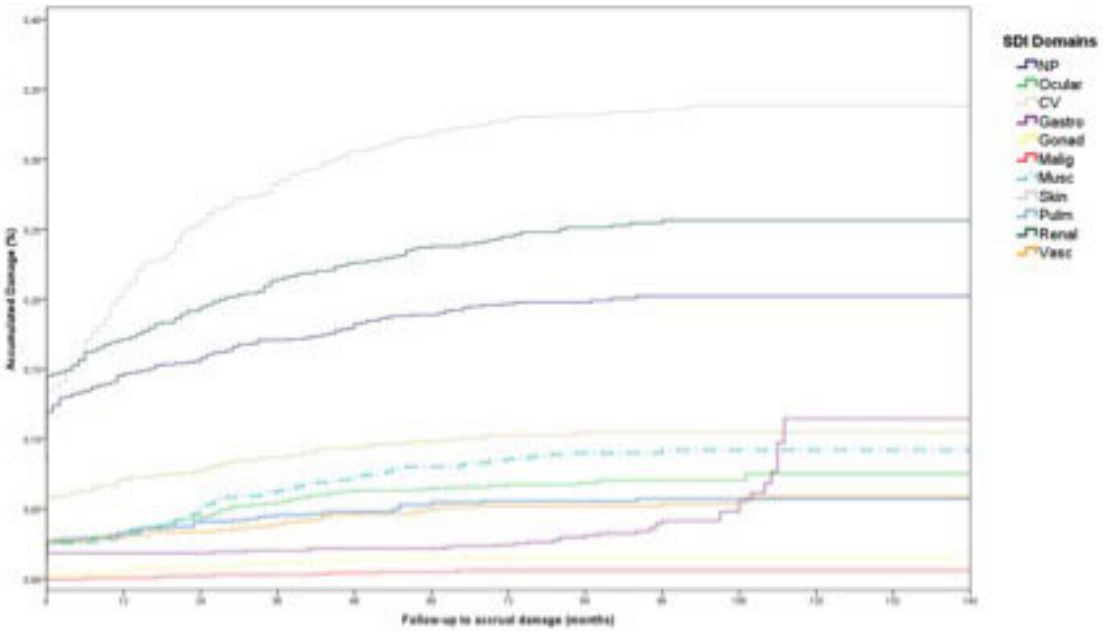

Figure 1: Accumulative damage curves in the 12 domains of the SDI during follow-up

Results: At cohort entry 565 patients (40.8%) had damage score ≥1, with a mean baseline SDI 0.66 (SD 1.01). During follow-up 658 patients (47.5%) accrued new damage ≥1, with a meantime between cohort entry and new damage of 33.2 months (SD 26.2). 11.3% accrued severe new damage (SDI ≥3 points).At last follow-up: 952 patients (68.7%) had a total damage score ≥1, with a mean final SDI of 1.57 (SD 1.67). 76 patients (5.5%) died during follow-up, at a mean time of 50.0 (SD 23.5) months from cohort entry; 56.6% of they had damage at baseline, with a mean SDI of 1,12 (SD 1.4). The highest proportion of new damage occurrence was in the skin domain, followed by renal and neuropsychiatric domains, and the lowest proportion were for gonadal and malignancy domains, as shown in Figure 1 of damage accrual for the 12 SDI domains. Multivariate analysis (including gender, age, medical coverture, country of origin, race, rural or urban residency, socioeconomic status, education years, SLE duration, and diagnosis delay), to investigate predictors of different damage domains, showed that higher baseline SLEDAI scores associated with a significant Hazard Risk for new damage in the neuropsychiatric, ocular, cardiovascular, skin, pulmonary and renal domains. There were differences according to country of origin, with more new damage occurring in patients from Perú and Argentina, and with less damage accrual occurring in those from Guatemala, Cuba and Brazil. No other differences were observed. At last follow-up: alopecia was the most frequent SDI item (30.4% SLE) followed by proteinuria >3.5g/d (11.2%), estimated glomerular filtration range < 50% (9.0%), and seizures requiring therapy for >6 months (7.5%). The other 37 SDI items were present in < 5% of the members of the cohort.

Conclusion: In this cohort, skin (mostly alopecia) was the most prevalent domain in damage accrual. SLEDAI predicts damage accrual in several domains, including major organs, reinforcing the need for early treatment intervention to minimize the inflammatory process and consequent damage. Relevant differences according to country of origin were identified.

Disclosure: M. Mimica, None; **O. Padilla**, None; **F. Aguilera**, None; **F. Cavalcanti**, None; **E. Borba**, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #306879/2018-2), 2; **M. Guibert-Toledano**, None; **R. Chacon-Diaz**, None; **G. Vasquez**, None; **G. Pons-Estel**, None; **M. Cardiel**, None; **O. Neira**, None; **M. Amigo**, None; **E. Bonfa**, Conselho

Nacional de Desenvolvimento Científico e Tecnológico (CNPq #305068/2014-8), 2, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4 and #2010/10749-0), 2; **G. Alarcón**, None; **B. Pons-Estel**, None; **L. Massardo**, None.

Abstract Number: 1585

Endothelial Dysfunction and Arterial Stiffness in Patients with Systemic Lupus Erythematosus: A Systematic Review and Meta-analysis

Claudia Mendoza-Pinto,[1] Adriana Rojas-Villarraga,[2] Nicolás Molano-González,[3] Pamela Munguía-Realpozo,[4] Socorro Méndez-Martínez,[4] Aurelio López-Colombo,[4] and Mario García-Carrasco[1], [1]Systemic Autoimmune Diseases Research Unit, Hospital de Especialidades, UMAE CMNMAC - CIBIOR, Instituto Mexicano del Seguro Social. Department of Rheumatology and Immunology, Medicine School, Benemérita Universidad Autónoma de Puebla, Puebla, Puebla, Mexico, [2]FUCS -Fundación Universitaria de Ciencias de la Salud, Bogotá, Distrito Capital de Bogota, Colombia, [3]Universidad del Rosario, Bogotá, Distrito Capital de Bogota, Colombia, [4]Instituto Mexicano del Seguro Social, Puebla, Puebla, Mexico

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Studies have reported increased cardiovascular (CV) morbidity and mortality in patients with SLE. In recent years, several non-invasive surrogates of CV disease risk have become available to assess en-

Table. Estimations of risks and mean differences of clinical variables and cardiovascular markers between SLE cases versus controls

Variable	Case/Controls		OR	MD	95% CI	P value
	%	Mean (95%CI)				
Female	94/91		1.54		1.16-2.03	0.002
Age		38.7 (36.2-41.2)/38.6 (36.1-41.1)		0.084	-0.61-0.77	0.81
Smoking	8/9		0.92		0.69-1.22	0.56
Hypertension	21/7		3.48		2.09-5.76	0
Obesity	8/5		1.74		0.72-4.20	0.21
DM	3/2		1.99		1.23-3.21	0.005
Dyslipidemia	10/5		1.91		1.05-3.47	0.03
FMD		7.28 (5.34-9.23)/ 11.59 (9.63-13.54)		-4.30	-6.13-2.47	0
NMD		18.38 (15.66-21.10)/ 21.06 (18.32-23.81)		-2.69	-6.00-0.62	0.11
PAT		1.61 (0.45-2.78)/ 2.02 (0.86-3.18)		-0.41	-0.86-0.05	0.07
MFR		2.41 (2.12-2.69)/ 2.73 (2.35-3.11)		-0.32	-0.79-0.15	0.18
AI		19.09 (13.70-24.47)/ 14.53 (8.90-20.16)		4.56	1.49-7.63	0.003
Any PWV		8.62 (7.53-9.72)/ 7.50 (6.38-8.61)		1.12	0.72-1.52	0
Central PWV		7.24 (6.58-7.90)/ 6.13 (5.41-6.85)		1.12	0.65-1.59	0
Peripheral PWV		10.59 (8.58-12.59)/ 9.06 (7.08-11.05)		1.52	0.82-2.23	0
Braquial-ankle PWV		10.89 (7.79-13.98)/ 10.88 (7.79-14.08)		-0.05	-0.91-0.81	0.91
Aortic MRI PWV		6.96 (6.04-7.87)/ (5.11-4.37)		1.84	0.66-3.02	0.0002

AI: augmentation index; CI: confidence interval; DM: diabetes mellitus; MRI: magnetic resonance imaging; FMD: flow-mediated dilatation; MD: Mean difference; MFR: myocardial flow reserve; NMD: nitroglycerin-mediated dilatation; PAT: peripheral arterial tonometry; PWV: pulse wave velocity; SD: standard deviation.

dothelial dysfunction (ED) and peripheral arterial stiffness (AS), which have been evaluated in SLE patients. The aim of this study was to systematically review and meta-analyze existing reports of CV disease (CVD) in SLE patients, as measured by ED and AS.

Methods: We performed a systematic review and meta-regression of studies evaluating the impact of SLE on the risk of ED and AS. Studies analyzing the relationship of SLE with ED (flow-mediated dilatation [FMD], nitroglycerin-mediated dilatation [NMD] and peripheral arterial tonometry [PAT]) and AS (augmentation index [AI], pulse wave velocity [PWV]) were systematically searched for in PubMed, EMBASE, Web of Science databases. Inclusion criteria included peer-reviewed publication, and report of original data in English. Mean differences (MD) and 95% confidence intervals (CIs) between SLE patients and controls were estimated using the random effect model.

The study was registered with PROSPERO, number CRD42019121068

Results: For the analysis of ED 21 studies were included. Compared with controls (n=644), SLE patients (n=943) showed a significantly lower mean FMD (MD= -4.30 %; 95% CI: -6.13%, -2.47%; $p < 0.001$). However, NMD did not significantly differ between SLE patients (n=404) and controls (n=265) (MD= – 2.68%; 95% CI -6.00, 0.62; p= 0.11). For the AS analysis 25 studies were included. A significantly-increased AS between SLE patients (n=1234) and controls (n=678) according to overall PWV (MD= 1.12 m/s; 95% CI 0.72-1.52; $p < 0.001$), central PWV (MD= 1.12 m/s; 95% CI 0.64, 1.59; $p < 0.001$), and peripheral PWV (MD= 1.52 m/s; 95% CI 0.82- 2.22; $p < 0.001$) was found, but not for the brachial-ankle PWV. AI (reported in 12 studies) was also increased in SLE patients (n=740) compared with healthy controls (n=411) (MD= 4.55%; 95% CI 1.48-7.63; $p = 0.003$).

Conclusion: SLE patients showed impaired FMD, an independent predictor of CV events. We also found a higher degree of AS in SLE patients compared with controls. The presence of ED and AS in SLE should be taken into account to plan adequate prevention strategies and therapeutic approaches.

Disclosure: C. Mendoza-Pinto, None; **A. Rojas-Villarraga**, None; **N. Molano-González**, None; **P. Munguía-Realpozo**, None; **S. Méndez-Martínez**, None; **A. López-Colombo**, None; **M. García-Carrasco**, None.

Abstract Number: 1586

All-cause Hospitalizations and Mortality in Systemic Lupus Erythematosus in the US- results from a National Inpatient Database

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

	N (weighted estimate)	% total SLE hospitalizations	mean LOS (se), days	mean cost (se), US $
1. SLE as primary diagnosis	**10195**	**5.85**	**6.86 (0.21)**	**16636 (742)**
Glomerular and tubulointerstitial nephropathy	3305	32.42	8.30(0.40)	20798 (1608)
Other organ involvement (Lupus myopathy, polyneuropathy, CNS lupus, Hemolytic anemia)	1060	10.40	11.24 (1.2)	28313 (2694)
Endocarditis, Pericarditis	615	6.03	7.73 (0.83)	24011 (3876)
Lung involvement in SLE	565	5.54	5.56 (0.79)	15474 (2571)
Unspecified organ involvement	95	0.93	6.79 (1.96)	16249 (5728)
SLE without mention of organ involvement	4555	44.68	4.48 (0.19)	10139 (532)
2. SLE as secondary diagnosis	**164040**	**94.15**	**5.52 (0.05)**	**14312 (186)**
Infection	28460	16.33	6.71 (0.11)	15701 (398)
AKI	4120	2.36	5.56 (0.22)	10948 (465)
GI disorders (esophagitis, gastro-duodenitis, PUD, IBD, UGIB)	3,740	2.15	4.65 (0.17)	11365 (632)
ACUTE HF	3650	2.09	5.79 (0.28)	13983 (1270)
ACS	3405	1.95	4.97 (0.21)	22601 (782)
Pulmonary (ARF, ILD, Pulmonary hemorrhage, PPH)	3095	1.78	7.09 (0.33)	20548 (1293)
Conduction blocks and arrhythmias	2745	1.58	4.36 (0.32)	13019 (656)
Stroke	2725	1.56	7.73 (0.69)	22780 (1634)
VTE	2635	1.51	4.76 (0.19)	11620 (607)
Seizure	1515	0.87	4.28 (0.22)	10569 (682)
Noninfectious enteritis, colitis and diarrhea	1235	0.71	3.97 (0.22)	7908 (508)
Avascular necrosis	630	0.36	3.63 (0.28)	16637 (1017)
Hematologic disorders (DIC, cytopenias)	620	0.36	6.46 (0.68)	17457 (2499)
Carditis (endo/myo/pericarditis) and cardiomyopathy	540	0.31	7.64 (0.90)	21117 (2553)
Pleural effusion NOS	530	0.30	5.32 (0.59)	12974 (1759)
Fatigue and generalized weakness	460	0.26	6.72 (0.67)	10902 (1759)
Valvular disease (mitral/aortic stenosis or regurgitation)	425	0.24	8.67 (1.15)	46041 (2739)
Toxic Hepatitis	410	0.24	6.05 (0.77)	17008 (2935)
Pathologic fractures	400	0.23	5.86 (0.38)	16299 (1201)
PVD	345	0.20	6.96 (0.98)	25770 (4281)
Pericardial effusion NOS	345	0.20	7.58 (0.76)	19561 (1875)
Other neurologic disorders (TM, NMO)	150	0.09	14.07 (3.62)	30562 (7717)
Thoracoabdominal aneurysm and dissection	140	0.08	9.71 (2.24)	48049 (9455)
Toxic colitis	90	0.05	4.06 (0.72)	8260 (1856)
None of these coded diagnoses	110,615	58.33	5.15 (0.05)	13410 (194)

Table 1: Primary diagnoses in hospitalizations with SLE

Abbreviations: PUD (peptic ulcer disease), IBD (inflammatory bowel disease), UGIB (upper gastro-intestinal bleeding), ARF (acute respiratory failure), ILD (interstitial lung disease), PPH (primary pulmonary hypertension), DIC (disseminated intravascular coagulation), NOS (not otherwise specified), TM (transverse myelitis), NMO (neuromyelitis optica)

Infection	1300 (38.18)
Pulmonary (ARF, ILD, Pulmonary hemorrhage, PPH)	205 (6.02)
Stroke	155 (4.55)
Acute coronary syndrome	150 (4.41)
SLE as a primary diagnosis	140 (4.11)
Acute heart failure	110 (3.23)
Conduction blocks and arrhythmias	90 (2.64)
Acute kidney injury	55 (1.62)
Venous thromboembolism	50 (1.47)
GI disorders (esophagitis, gastro-duodenitis, PUD, IBD, UGIB)	40 (1.17)

Table 2: Top 10 primary diagnoses among SLE hospitalizations who DIED (3405), N (%)

Abbreviations: ARF (acute respiratory failure), ILD (interstitial lung disease), PPH (primary pulmonary hypertension), PUD (peptic ulcer disease), IBD (inflammatory bowel disease), UGIB (upper gastro-intestinal bleeding)

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic multisystem autoimmune disorder with variable presentation. While several studies have outlined the risk factors for hospitalization and mortality in SLE, the frequency of these causes have varied among studies and over the years. We aimed to assess leading nationwide causes of SLE hospitalizations and mortality in the US in a recent year, 2016 using a large inpatient database.

Methods: We used the National Inpatient Sample (NIS) database from the year 2016 to identify hospitalizations with SLE using the previously validated International Classification of Disease (ICD-10) code M32. NIS is a part of the Healthcare Cost and Utilization Project (HCUP). It contains 20 % stratified sample of US hospital discharges (~ 7 million/year), the weighted estimate of which corresponds to about ~ 35 million/year. Hospitalizations with SLE in primary and secondary positions were identified. Among SLE as the secondary diagnosis, ICD-10 codes used to look for primary diagnoses associated with hospitalizations and mortality.

Results: We identified 174,235 SLE hospitalizations in 2016 among which 89% were females. The mean age of hospitalization for SLE was 52 years and mean length of stay was 5.6 days. SLE was the primary diagnosis in 10,195 (5.85%) patients, among which lupus nephropathy was the most common (32.42%). Among SLE as the secondary diagnosis, infection was the commonest primary diagnosis (16.33 %) followed by acute kidney injury (2.36%) and gastrointestinal manifestations (2.15%). Cardiac manifestations including acute heart failure (2.09%), acute coronary syndrome (1.96%) and conduction disturbances (1.58%) were other important causes of hospitalization **(Table 1)**. In-hospital mortality of SLE was 1.95% and infection was the leading cause of in-hospital mortality (38%) **(Table 2)**.

Conclusion: In our study using a large national database, we noted that SLE was the primary cause for hospitalization in 5.85 %, which is fewer than previously reported. Infection was the leading primary diagnosis associated with SLE hospitalization, which is in accordance with other recent studies globally. On 2016, the inpatient mortality for SLE was 1.95 %, which was fewer than the 3.15% reported by Krishnan et al. using the same NIS database (1998 – 2002), which suggests possible improvement in mortality in SLE hospitalizations in the recent years. In conclusion, infection was the leading reason for hospitalization and in-hospital mortality in SLE. Renal and cardiac involvements were other important causes of hospitalization.

Disclosure: R. Dhital, None; **D. Poudel**, None; **R. Pandey**, None; **P. Karmacharya**, None.

Abstract Number: 1587

Oxidized Human Serum Albumin Is Increased in Systemic Lupus Erythematosus, but Not in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

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Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are at high risk of atherosclerosis and have high mortality due to cardiovascular disease. Oxidative stress is involved in the progression of atherosclerosis, with the percentage of human non-mercaptoalbumin (HNA%), the oxidized form of human serum albumin, attracting considerable attention as a potential biomarker of oxidative stress. Although previous studies have shown increased HNA% in the elderly people and in patients with either chronic kidney disease, diabetes mellitus, or liver cirrhosis, there are no reports on HNA% in patients with rheumatic diseases. The aim of this study was to evaluate HNA% in patients with SLE or RA and to identify factors associated with this biomarker.

Methods: We measured HNA% in patients with SLE, RA, and healthy controls by using high-performance liquid chromatography. Analysis of covariance was used to compare HNA% between SLE and healthy controls, or RA and healthy controls. Factors associated with HNA% in SLE and RA patients were assessed by using multiple linear regression analysis.

Results: HNA% was measured in 89 SLE patients [age (mean ± SD), 44 ± 11 years; female, 97%], 51 RA patients [age (mean ± SD), 62 ± 13 years; female, 94%], and 65 healthy controls [age (mean ± SD), 55 ± 14 years; female, 58%)]. All participants were Japanese. Mean HNA% (SD) of SLE, RA, and healthy controls were 23.0% (5.0%), 23.7% (4.7%), and 21.8% (3.7%), respectively. The correlation between HNA% and age was significant in RA patients and healthy controls, but not in SLE patients (Figure 1). The age-adjusted mean difference in HNA% between the SLE patients and the healthy controls was 2.9% (95% CI, 0.96 to 4.9%; Bonferroni corrected p value = 0.001), and between the RA patients and the healthy controls, 0.84% (95% CI, –3.0 to 1.3%; Bonferroni corrected p value=1.0), respectively. In SLE patients, SLICC/ACR damage index (β=0.48, p< 0.001) and serum creatinine level (β=0.24, p=0.01) were significantly associated with HNA%. In RA patients, serum creatinine level (β=0.42, p< 0.001), age (β=0.37, p=0.002), and daily prednisolone dosage (β=0.29, p=0.006) were significantly associated with HNA%.

Conclusion: SLE patients have increased HNA% compared to the healthy controls, especially in association with the SLICC/ACR damage index. Patients with RA do not show this association. In SLE patients, increased HNA% might reflect excessive oxidative stress and possibly be associated with an increased risk of atherosclerosis.

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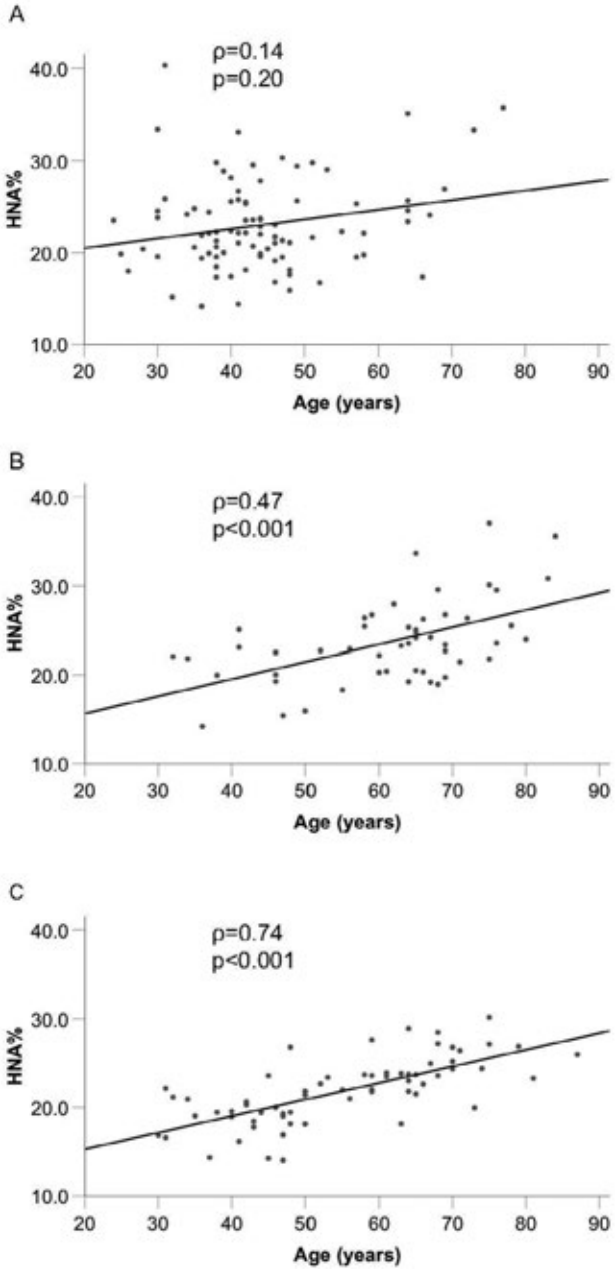

Figure 1. Correlation between HNA% and age (A) in SLE patients, (B) in RA patients, (C) healthy controls. The correlation was examined by calculating Spearman's rank correlation coefficients.

Co., 2, Mitsubishi Tanabe Pharma Corp., 2, Nippon Kayaku Co. Ltd., 2, Taisho Toyama Pharmaceutical Co. Ltd., 2, Takeda Pharmaceutical Co., 2, Takeda Pharmaceutical Co., Ltd., 2, Teijin Pharma Ltd., 2, 8, Teijin Pharma, Ltd., 2, 8.

Abstract Number: 1588

Disease Activity and Dysregulated Iron Metabolism: A Potentially Overlooked Mechanism for Anaemia in Patients with Systemic Lupus Erythematosus?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Haematological manifestations of SLE are common with anaemia reported in approximately 50% of cases, yet the role of altered iron metabolism is poorly understood. Key regulators of iron homeostasis include; 1. Hepcidin, which prevents iron release from stores (under the influence of IL6 and IL1β); 2, Ferritin, an iron carrier protein also implicated as a functional potent pro-inflammatory mediator; 3. Erythropoietin (EPO); 4. Lipocalin-2 (LCN2), released on innate immune activation that induces iron sequestration; 5. Transferrin, binds circulating iron and regulates transport to stores in the liver, spleen and bone marrow; 6. Soluble transferrin receptor (sTfR), a cleaved extracellular receptor; 7. Haptoglobin (Hp), binds free haemoglobin (Hb); 8. Natural resistance-associated macrophage protein 2 (NRAMP2), a metal ion transporter that facilitates transfer of iron into enterocytes.

In this study, we aimed to evaluate the changes in these regulators in patients with SLE and assess for the influence of disease activity for the first time.

	Healthy Control N=17	Low Lupus Disease Activity (SLEDAI ≤4) N=17	Active Lupus (SLEDAI >4) N=22	p-value
Hepcidin (ng/ml ± SD)	7.63 ± 5.0	14.56 ± 12.2	75.02 ± 103.7	<0.0001†
Interleukin-6 (pg/ml ± SD)	0.71 ± 0.4	1.60 ± 1.6	9.00 ± 8.8	<0.0001†
Interleukin-1β (pg/ml ± SD)	0.01± 0.02	0.19 ± 0.3	0.53 ± 0.8	<0.0001*
Ferritin (ng/ml ± SD)	40.3 ± 23.3	92.5 ± 95.9	345.2 ± 299.4	<0.0001†
Transferrin (ng/ml ± SD)	648.3 ± 204.0	729.7 ± 262.7	563.1 ± 203.8	0.08
Soluble transferrin receptor (µg/ml ± SD)	8.24 ± 2.3	15.02 ± 12.5	11.64 ± 6.3	0.04†
Lipocalin-2 (ng/ml ± SD)	46.7 ± 27.1	71.6 ± 32.1	35.0 ± 21.3	0.0004†
Haptoglobin (mg/ml ± SD)	1.20 ± 0.76	0.83 ± 0.56	1.32 ± 0.61	0.03†
Erythropoietin (IU ± SD)	4.79 ± 5.6	6.90 ± 5.7	14.64 ± 10.7	0.005*
NRAMP2 (ng/ml ± SD)	5.55 ± 4.0	18.38 ± 31.2	34.11 ± 36.6	0.0008*

SD, Standard Deviation; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLE, Systemic Lupus Erythematosus; NRAMP2, Natural Resistance-Associated Macrophage Protein 2
* significant difference between healthy control and lupus (irrespective of disease activity)
† significant difference between active and inactive lupus

Table 1: Differences in key regulators of iron metabolism between healthy controls, low disease activity and active lupus

Hepcidin	0.56**										
Interleukin-6	0.44**	NS									
Interleukin-1β	NS	NS	0.40*								
Ferritin	0.52**	0.52**	NS	NS							
Transferrin	-0.34*	NS	NS	NS	NS						
Soluble Transferrin Receptor	NS	NS	NS	NS	NS	NS					
Lipocalin-2	-0.43**	NS	NS	NS	0.40**	NS	NS				
Haptoglobin	0.39*	0.33*	0.32*	NS	NS	NS	NS	NS			
Erythropoietin	NS	NS	NS	NS	NS	NS	0.58**	NS	NS		
NRAMP2	NS	NS	NS	NS	NS	NS	0.34*	NS	NS	NS	
Haemoglobin	-0.38*	NS	NS	NS	-0.53**	NS	NS	NS	-0.34*	-0.55**	NS
* p<0.05 ** p<0.001	SLEDAI	Hepcidin	Interleukin-6	Interleukin-1β	Ferritin	Transferrin	Soluble Transferrin Receptor	Lipocalin-2	Haptoglobin	Erythropoietin	NRAMP2

Figure 1: Correlations between SLEDAI-2K, haemoglobin and regulators of iron metabolism. Results expressed as r values (*p<0.05; **p<0.01)

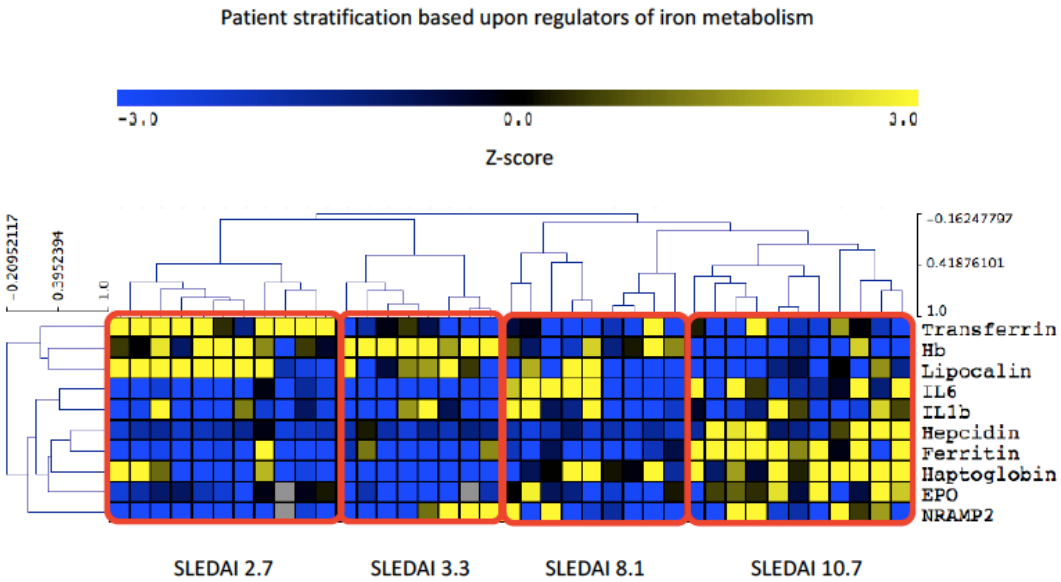

Figure 2: Heatmap representation of cluster analysis of key iron mediators in SLE. Normalised data is presented as Z-score with 3.0 being elevated and -3.0 reduced in comparison to the mean (0.0). Results presented as correlative clusters with mean SLEDAI expressed beneath each group.

Methods: Serum samples were collected from patients with SLE (n=39) attending University College London Hospital, UK, in addition to 17 healthy controls (HC). Patients with haemolytic anaemia were excluded. Clinical measures including Hb, dsDNA, complement C3 and SLEDAI-2K (where >4 was considered active disease; ≤4 classified in-

active / low disease activity) were recorded. Levels of IL6, IL1β, Hepcidin, Ferritin, LCN2, Transferrin, sTfR, EPO, Hp and NRAMP2 were measured by ELISA. Differences between groups were calculated by One-way ANOVA / Kruskal-Wallis and correlations by Spearman's / Pearson's. Following normalisation of significant variables, Z-scores were used in hierarchical correlate clustering performed using MeV software to present as a heatmap.

Results: Of the 39 patients recruited 90% were female (35/39) with a mean age of 27.8 (± 11.7) years. Results comparing HC, inactive / low disease activity SLE and active SLE are summarised in Table 1. Interestingly LCN2 levels were lower in active SLE, which is surprising given that elevated levels are commonly observed in systemic inflammation. SLEDAI-2K showed a strong positive correlation with hepcidin, ferritin, IL6 and Hp, whilst negatively correlating with both LCN2 and Transferrin. In SLE, ferritin and LCN2 correlated significantly regardless of disease activity ($p< 0.001$, $r=0.40$). Figure 1 summarises all correlations in SLE. Figure 2 demonstrates the results of hierarchical clustering. The cluster containing patients with a combination of reduced LCN2 and Hb with elevated Hp, Ferritin, Hepcidin and EPO showed the highest mean SLEDAI-2K (10.7) whilst higher Hb, LCN2 and Transferrin was observed in the group with the lowest mean SLEDAI-2K (2.7).

Conclusion: We have detailed the dysregulation of key mediators in iron homeostasis in SLE for the first time. Key findings include a paradoxical reduction in LCN2, which inversely correlates with ferritin. Further, reduced Transferrin with elevated EPO and Hepcidin in active disease suggests a state of functional iron deficiency with iron being held in stores and therefore not available for use in erythropoiesis thus representing a novel mechanism for anaemia.

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Abstract Number: 1589

Prevalence of Cognitive Impairment in an Inception Lupus Cohort as Assessed by a Comprehensive Neuropsychological Battery

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SESSION INFORMATION
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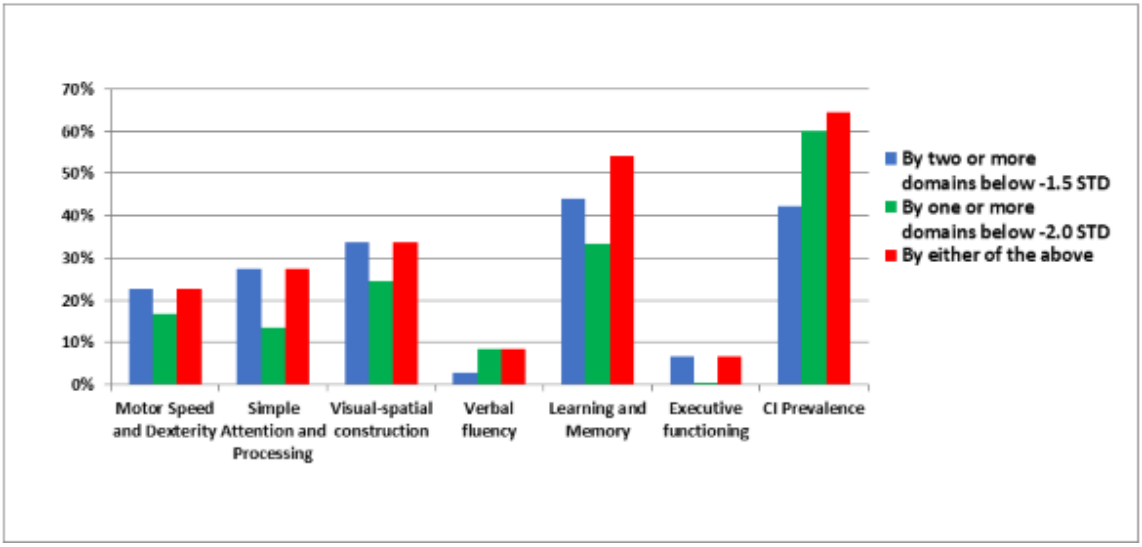
Background/Purpose: Systemic Lupus Erythematosus (SLE) can lead to a number of neuropsychiatric manifestations including cognitive impairment (CI). Previous meta-analyses have reported the prevalence of CI at 38% (95% confidence interval: 33-43%), with a range of 15-79%. We aim to report the prevalence of CI in a lupus cohort as assessed by a comprehensive neuropsychological battery (NB) of tests. Additionally, we were interested in exploring differences in demographic, clinical and serological characteristics of SLE patients in an inception cohort, with and without CI.

Figure 1. Prevalence of patients with domain z-scores of ≤ - 1.5 and ≤ - 2.0 (n=279)



Methods: Consecutive consenting patients aged 18-65 years, who attended a single center were enrolled (Jul 2016 – Mar 2019). Each patient completed a comprehensive NB evaluating six cognitive domains including: manual motor speed and dexterity, simple attention and processing, visual spatial construction, verbal fluency, learning and memory (verbal and visuospatial) and executive function. Using age- and gender-stratified normative data, patients were classified on the ACR NB as having CI if a z-score of ≤-1.5 was observed in ≥ 2 domains or z-score of ≤ -2.0 on ≥1 domain; otherwise non-CI. Further, patients with CI (z-score of ≤ -1.5 on ≥2 domains) were compared to non-CI patients.

Results: 279 patients were included in this study, 89.6% comprised of females. The average age and SLE duration at enrolment were 41.2 ± 12.2 and 14.1 ± 10.1 years, respectively. The prevalence of CI was 42.3% (z-score of ≤ -1.5 on ≥2 domains) and 60.2% (z-score of ≤ -2.0 on ≥1 domain).

The most affected domains were learning and memory, and visual spatial construction – prevalence of 44.1% (n=147/279,) and 33.3% (n=94/279,) respectively. Prevalence of impairment in visual spatial construction was 33.8% (n=94, z-score of ≤ -1.5 on ≥2 domains) and 24.5% (n=68, z-score of ≤ -2.0 on ≥1 domains). The least affected domains were verbal fluency, and executive function. Prevalence of impairment in verbal fluency was 2.9-8.6% (z-score of ≤ -1.5 on ≥2 domains, z-score of ≤ -2.0 on ≥1 domains). Prevalence of executive function impairment varied between 0.4-6.8% (z-score of ≤ -2.0 on ≥1 domains, z-score of ≤ -1.5 on ≥2 domains).

There were no differences in demographics, medication use, disease duration and activity, and serologic markers between those with and without CI [using the definition of CI as z-score of ≤ -1.5 on ≥2 domains].

Conclusion: The pooled prevalence of CI in this cohort varied with different definitions of CI (44.3%-60.2 % [z-score of ≤ -1.5 on ≥2 domains, z-score of ≤ -2.0 on ≥1 domains]). There is an unmet need to standardize the metrics and the definitions for CI. CI is identified across all cognitive domains with particularly high prevalence in learning and memory.

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Table 1. Patient Demographics and characteristics by cognitive impairment at enrollment

Characteristic	Overall (n=279)	Cognitive Impairment (z-score of ≤ 1.5 on ≥2 domains) (n=118)	No Cognitive Impairment (n=161)
Female (%)	250 (89.6%)	105 (89.0%)	145 (90.1%)
Mean age (years) (mean± SD)	41.2 ± 12.2	40.7 ± 12.5	41.5 ± 12.1
Disease duration (years) (mean± SD)	14.1 ± 10.1	12.8 ± 9.7	15.0 ± 10.3
Race (%)			
Chinese	25 (9.3%)	11 (10.0%)	14 (8.9%)
Black	54 (20.1%)	31 (28.2%)	23 (14.6%)
Caucasian	155 (57.8%)	56 (50.9%)	99 (62.7%)
Other	34 (12.7%)	12 (10.9%)	22 (13.9%)
Education Level			
Grade 8 or high school graduate	58 (21.4%)	29 (25.7%)	29 (18.4%)
College or university graduate	213 (78.6%)	84 (74.3%)	129 (81.6%)
Medication Use			
Glucocorticoid use at enrollment (%)	135 (48.4%)	60 (50.8%)	75 (46.6%)
Glucocorticoid dose at enrollment (mg)	8.5 ± 8.5	8.3 ± 8.7	8.6 ± 8.5
Hydroxychloroquine	229 (82.1%)	93 (78.8%)	136 (84.5%)
Immunosuppression	160 (57.3%)	66 (55.9%)	94 (58.4%)
Immunologic profile at baseline			
Anti-dsDNA	109 (39.6%)	40 (34.5%)	69 (43.4%)
Hypocomplementemia (C3,C4)	105 (38.2%)	39 (33.6%)	66 (41.5%)
Anti-U1RNP	165 (61.3%)	72 (64.3%)	93 (59.2%)
Anti-SSA/Ro60	141 (52.4%)	55 (49.1%)	86 (54.8%)
Anti-SSB/La	69 (25.7%)	21 (18.8%)	48 (30.6%)
Anti-Smith	127 (47.2%)	57 (50.9%)	70 (44.6%)
Anti-phospholipid	103 (38.9%)	36 (33.3%)	67 (42.7%)
Clinical profile at baseline			
SLE ACR criteria	6.4 ± 1.4	6.3 ± 1.5	6.5 ± 1.3
Adjusted mean SLEDAI	3.1 ± 3.4	3.3 ± 3.9	3.0 ± 3.1
SLICC Damage Index	1.1 ± 1.5	1. 0 ± 1.3	1.1 ± 1.6

5, Werfen International, 5; **M. Choi**, None; **M. Zandy**, None; **J. Su**, None; **M. Vitti**, None; **D. Bonilla**, None; **J. Wither**, None; **S. Lombardi**, None; **Z. Touma**, Janssen Research & Development, LLC, 2, Janssen Scientific Affairs, LLC, 2.

Abstract Number: 1590

Clinical and Sociodemographic Associates of Depression and Anxiety in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: In our recent systematic review, we have shown a high prevalence for depression (35%) and anxiety (25.8%) in Systemic Lupus Erythematosus (SLE)[1]. A better understanding of the SLE phenotypic manifestations associated with depression and anxiety may lead to enhanced early diagnosis and treatment strategies.

Objectives: To determine the overall prevalence of anxiety and depression in a cohort of SLE patients, stratified by SLE-implicated organ systems and to study their associations.

Methods: Patients attending the Toronto Lupus Clinic from August 2017 to January 2019 were studied. Depression and Anxiety were diagnosed with Center for Epidemiological Studies-Depression Scale (cut-off26), BECK Depres-

Table 1: Demographic and clinical description of patients at study visit (n=341)

Variables	Total patients n=341 (%)	Patients with neither anxiety or depression n=204 (%)	Patients with depression n=91 (%)	Patients with anxiety n=116 (%)	Patients with comorbid depression and anxiety n=70 (%)
Gender					
Female	306 (89.7)	181 (88.7)	86 (94.5)	104 (89.7)	65 (92.9)
Male	35 (10.3)	23 (11.3)	5 (5.5)	12 (10.3)	5 (7.1)
Age at Diagnosis [mean±SD]	29.4±15.6	28.7±11.8	28.3±10	31±21.5	28.7±10.7
Age at enrolment [mean±SD]	45.9±17.8	45.8±14.6	43.7±13.1	46.1±23.2	43.1±13.3
Disease duration at enrolment [mean±SD]	16.5±11.6	17.1±11.5	15.4±11.2	15.1±11.5	14.4±10.7
Ethnicity					
Caucasian	198 (58.1)	120 (58.8)	6 (6.6)	5 (4.3)	38 (54.3)
Black	62 (18.2)	28 (13.7)	25 (27.5)	26 (22.4)	17 (24.3)
Asian	32 (9.4)	26 (12.7)	48 (52.7)	68 (58.6)	5 (7.1)
Other	49 (14.4)	30 (14.7)	12 (13.2)	17 (14.7)	10 (14.3)
Inception Patient					
Yes	140 (41.1)	74 (36.3)	48 (52.7)	54 (46.6)	36 (51.4)
No	201 (59.9)	130 (63.7)	43 (47.3)	62 (53.4)	34 (48.6)
Education Level					
High School or Less	90 (26.9)	50 (25)	29 (32.2)	34 (29.8)	23 (33.3)
College/University	245 (73.1)	150 (75)	61 (67.8)	80 (70.2)	46 (66.7)
Employment status					
Employed	173 (50.9)	11 (55.7)	38 (41.8)	50 (43.1)	28 (40)
Retired	26 (7.6)	18 (8.9)	5 (5.5)	6 (5.2)	3 (4.3)
Homemaker	25 (7.4)	15 (7.4)	7 (7.7%)	9 (7.8)	6 (8.6)
Student	26 (7.6)	20 (9.9)	4 (4.4)	6 (5.2)	4 (5.7)
Disabled/Sick Leave	72 (21.2)	31 (15.3)	28 (30.8)	34 (29.3)	21 (30)
Looking for work	10 (2.9)	3 (1.5)	5 (5.5)	7 (6)	5 (7.1)
Other	8 (2.4)	3 (1.5)	4 (4.4)	4 (3.4)	3 (4.3)
Marital Status					
Single	145 (42.8)	84 (41.4)	45 (50.0)	52 (45.2)	36 (52.2)
Married/Common Law	162 (47.8)	103 (50.7)	36 (40.0)	49 (42.6)	26 (37.7)
Widowed/Divorced/Separated	32 (9.4)	16 (7.9)	9 (10.0)	14 (12.2)	7 (10.1)
AMS score [mean±SD]	4.2±3.2	4.2±3	4.6±3.6	4.3±3.3	4.5±3.5
SDI [mean±SD]	1.3±1.8	1.3±1.8	1.3±1.6	1.4±1.7	1.3±1.5

AMS: Adjusted-Mean-SLEDAI score (five years to study visit). SDI: SLE Damage Index score (up to study visit)

Table 2: SLE clinical manifestations stratified by organ systems of cumulative 10-year SLEDAI-2K

SLEDAI organ system involvement	Total patients n=341 (%)	Patients with neither anxiety or depression n=204 (%)	Patients with depression n=91 (%)	Patients with anxiety n=116 (%)	Patients with comorbid depression and anxiety n=70 (%)
Skin	191 (56)	101 (49.5)	62 (68.1)*	77 (66.4)*	49 (70)*
Skin rash	116 (34)	61 (29.9)	36 (39.6)	45 (38.8)	26 (37.1)
Alopecia	108 (31.7)	54 (26.5)	39 (42.9)	45 (38.8)	30 (42.9)
Mucosal ulcers	86 (25.2)	42 (20.6)	28 (30.8)	39 (33.6)	32 (32.9)
Central nervous system[b]	53 (15.5)	27 (13.2)	19 (20.9)	22 (19)	15 (21.4)
Musculoskeletal	131 (38.4)	66 (32.4)	47 (51.6)*	54 (46.6)*	36 (51.4)*
Arthritis	121 (35.5)	60 (29.4)	43 (47.3)*	50 (43.1)*	32 (45.7)*
Myositis	12 (3.5)	7 (3.4)	4 (4.4)	5 (4.3)	4 (5.7)
Internal organs					
Renal	126 (37)	73 (35.8)	34 (37.4)	45 (38.8)	26 (37.1)
Proteinuria	108 (31.7)	64 (31.4)	29 (31.9)	37 (31.9)	22 (31.4)
Renal Casts	46 (13.5)	30 (14.7)	12 (13.2)	12 (10.3)	8 (11.4)
Hematuria	68 (19.9)	38 (18.6)	19 (20.9)	24 (20.7)	13 (18.6)
Pyuria	65 (19.1)	34 (16.7)	20 (22)	25 (21.6)	14 (20)
Serosal	31 (9.1)	18 (8.8)	7 (7.7)	12 (10.3)	6 (8.6)
Pericarditis	18 (5.3)	12 (5.9)	3 (3.3)	8 (6.9)	2 (2.9)
Pleuritis	21 (6.2)	12 (5.9)	5 (5.5)	5 (4.3)	4 (5.7)
Hematologic[b]	93 (27.3)	67 (32.8)	19 (20.9)	22 (19)	15 (21.4)
Immunologic[c]	275 (80.6)	172 (84.3)	74 (81.3)	86 (74.1)	57 (81.4)
Constitutional[d]	0	0	0	0	0

[a]Encompasses seizure, psychosis, organ brain syndrome, cranial nerve involvement, visual disturbance, lupus headache, cardiovascular accident, and vasculitis. [b]Encompasses leukopenia and thrombocytopenia. [c]Encompasses low complements and positive anti-dsDNA antibodies. [d]Encompasses fever. *Statistically significant at $p < 0.05$ by Chi-square test or Cochran-Armitage trend test (reference group = patients with neither anxiety or depression).

sion Inventory-II (cut-off18), and the BECK Anxiety Inventory (cut-off19). Disease activity was measured with the SLE Disease Activity Index 2000 (SLEDAI-2K). The SLE phenotypic manifestations were stratified based on the organ systems of cumulative 10-year SLEDAI-2K – skin, musculoskeletal (MSK), ocular, neuropsychiatric, and internal organ manifestations (renal, pulmonary, immunologic, and haematologic). Separate multivariate logistic regression analyses (for depression [D], anxiety [A], and comorbid anxiety and depression [AD]) were performed to study the factors associated factors, including age at enrollment, sex, ethnicity, disease duration, inception status (enrolled in the clinic within 1 year of SLE diagnosis), fibromyalgia, and SLE phenotypic manifestations, comparing their significance to the group with neither A or D.

Results: 341 patients (89.7% female), with mean age 45.917.8 years were studied. The prevalence of A and D in the cohort was 34% and 27% respectively, while 21% of the total cohort was found to have AD. Among the 3 outcome groups, MSK system involvement has a significantly higher prevalence when compared to the group with neither A or D (p-values< 0.05). Skin system involvement was also significantly more prevalent among A, D, and AD groups, in comparison to the normal group. Patients with A had significantly higher odds of skin system involvement compared to the normal group (OR=1.8; 95% CI: 1.1, 3.0). Patients with D had higher odds of MSK (OR=1.9; 95% CI: 1.1, 3.5) and skin system involvement (OR=1.8; 95% CI: 1.04, 3.2) compared to the group with neither A or D. Additionally, the odds of skin system involvement was significantly higher among patients with AD, compared to the group with neither (OR=2.0, 95% CI: 1.2, 3.9). In all three models, employment and fibromyalgia were also significant. Age at enrolment was significant in the D and AD models, while inception patient status was significant in the D model exclusively.

Conclusion: SLE phenotypic manifestation, specifically those involving patients' skin or MSK systems, along with fibromyalgia, socio-demographic factors, and inception status were associated with anxiety or depression. Routine patient screening and evaluation, especially among patients with shorter disease duration, for these associated factors may facilitate the diagnosis of these mental health disorders, and allow for more timely diagnosis and intervention strategies.

Disclosure: D. Eldeiry, None; **M. Zandy**, None; **O. Tayer-Shifman**, None; **A. Kwan**, None; **S. Marzouk**, None; **J. Su**, None; **K. Bingham**, None; **Z. Touma**, Janssen Research & Development, LLC, 2, Janssen Scientific Affairs, LLC, 2.

Abstract Number: 1591

Anti-ovarian Antibodies Are Not Associated with Premature Menopause in SLE Treated with Cyclophophosphamide

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SESSION INFORMATION
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Session Title: SLE – Clinical Poster II: Comorbidities
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Background/Purpose: Treatment of systemic lupus erythematosus (SLE) with cyclophosphamide is associated with premature menopause, especially those at an older age of treatment and those receiving a higher cumulative dose. We hypothesized that reduced ovarian reserve caused by ovarian autoimmunity would be associated with premature ovarian failure among SLE patients treated with cyclophosphamide. We undertook this study to test this hypothesis. Treatment of systemic lupus erythematosus (SLE) with cyclophosphamide is associated with premature menopause, especially those at an older age of treatment and those receiving a higher cumulative dose. We hypothesized that reduced ovarian reserve caused by ovarian autoimmunity would be associated with premature ovarian failure among SLE patients treated with cyclophosphamide. We undertook this study to test this hypothesis.

Methods: All SLE women with a history of cyclophosphamide therapy were identified in the Lupus Registry and Repository (LFRR). The subjects met the revised ACR classification criteria. Spontaneous lack of menstrual periods prior to age 45 was defined as premature menopause. Anti-ovarian antibodies were measured by ELISA (Anti-Ovarian Ab ELISA, IBL, Minneapolis, catalog # IB9184). We used Student's T test and chi square testing for data analyses. Approval was obtained from local Institutional Review Boards.

Results: Among ~3000 SLE women enrolled in the LFRR, 258 had received cyclophosphamide. Of these 169 had menopause before age 45, while 73 underwent menopause after age 45. 16 patients were over age 45 and still having menstrual periods at the time of evaluation. Thus, there were a total of 89 SLE women who did not have premature menopause. Among the 169 with premature ovarian failure the mean anti-ovarian antibody level was 16.2 units (SD=20.3), while the mean among those without premature menopause was 17.4 units (SD=21.7). These values were not statistically different. Considering categorical results, 11 of 169 (6.5%) SLE women with premature menopause had a positive result while 8 of 89 (8.9%) without premature menopause were positive (X^2=0.53, p=0.46, OR=1.02 (95% CI 0.95-1.1)).

Conclusion: A small percentage of SLE patients treated with cyclophosphamide had anti-ovarian antibodies in their serum. Nonetheless, the presence of these antibodies was not related to premature menopause.

Disclosure: M. Tsaliki, None; **K. Koelsch**, None; **A. Chambers**, None; **M. Talsania**, None; **E. Chakravarty**, None; **R. Scofield**, None.

Abstract Number: 1592

Defining the SLE-Associated Pulmonary Arterial Hypertension Phenotype

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SESSION INFORMATION
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Background/Purpose: Pulmonary arterial hypertension (PAH) is a leading cause of death in SLE patients. Hypocomplementemia, antiphospholipid antibodies, and elevated antibodies to RNP and Ro are correlated with SLE-associated PAH. In this study, we sought to define the SLE phenotype associated with PAH.

Methods: 207 (8%) SLE patients with pulmonary hypertension (PH), defined as a right ventricular systolic pressure greater than 40 mmHg on transthoracic echocardiogram or as pulmonary artery dilatation noted on CT of the chest, were identified from a longitudinal SLE cohort (94% female, 56.5% African American, 39% Caucasian, mean age 45.6 years). All patients with SLE met either the revised ACR or SLICC classification criteria.

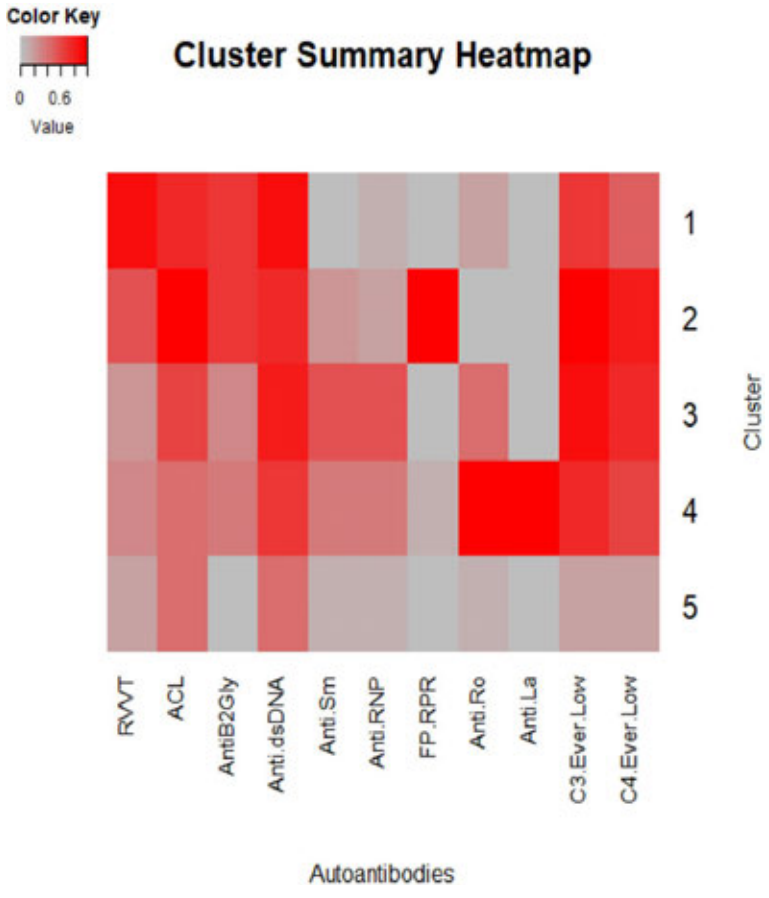

Figure. Clustering of Pulmonary Arterial Hypertension Patients by Autoantibodies

136 patients with SLE and PAH were eligible for the cluster analysis, as they had information available for all 11 selected autoantibodies (lupus anticoagulant, anticardiolipin, anti-beta2 glycoprotein 1, anti-dsDNA, anti-Sm, anti-RNP, false positive(FP)-RPR, anti-Ro, anti-La, and hypocomplementemia (C3 ever low or C4 ever low)). Agglomerative hierarchical clustering algorithm with Ward's method was used to cluster the patients who had PAH, based on their history of autoantibodies. All analyses were performed in JMP version 13.0 and R version 3.5.1 using package cluster and gplots.

Results: Five clusters were identified, representing five different phenotypes. Clusters 1 and 2 had high frequencies of hypocomplementemia, antiphospholipid antibodies, and anti-dsDNA. Cluster 2 additionally had a high frequency of FP-RPR. Cluster 3 had high frequencies of hypocomplementemia, anticardiolipin, anti-Sm, anti-RNP, and anti-dsDNA, but only moderate frequencies of anti-Ro. Cluster 4 had high frequencies of hypocomplementemia, anti-Ro, anti-La, and anti-dsDNA. Cluster 5 had only moderate frequencies of anti-dsDNA and anticardiolipin.

Conclusion: Our data indicate an important association in several, but not all, clusters between antiphospholipid and PAH in SLE. Elevated anti-dsDNA and hypocomplementemia in some clusters may represent an association with active SLE in these subsets. Two clusters were antiphospholipid antibody predominant and two clusters were extractable nuclear antigen predominant, which may represent different pathophysiology and associate with divergent responses to immunosuppressive therapy.

Disclosure: M. Mizus, None; **J. Li**, None; **D. Goldman**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 1593

Heart Rate Visit-to-Visit Variability in Patients with Systemic Lupus Erythematosus Is Associated with Increased Mortality

Tyler Reese,[1] Alyson Dickson,[1] Jocelyn Gandelman,[1] Sarah Bayefsky,[1] April Barnado,[1] Katherine Barker,[1] C. Michael Stein,[1] Vivian Kawai,[1] and Cecilia Chung[1], [1]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) have increased mortality compared to the general population. Heart rate visit-to-visit variability (HRVVV) has emerged as an adverse risk factor for long-term outcomes, particularly in patients with cardiovascular disease. SLE patients represent a high-risk population for cardiovascular disease; however, the relationship between HRVVV and all-cause mortality in patients with SLE has not been examined. We studied the association between increased HR visit-to-visit variability and all-cause mortality in patients with SLE.

Methods: We identified a cohort of patients with SLE using a previously validated algorithm (PPV 94%) from a de-identified version of an academic medical center's electronic health record that contains more than 2.8 million patients. Demographic variables (age, race, and sex), ICD9 codes, laboratory results, and HR measures were extracted. We excluded HR measures from inpatient admissions or emergency department visits, measures for individuals under 18, measures < 40 or >140 beats per minute, and individuals with fewer than three outpatient measures. HR variability was defined as the intraindividual standard deviation of all qualifying measures. The primary outcome was all-cause mortality with incident rate ratios (IRR) calculated using Poisson regression.

Results: A total of 687 patients with SLE met our inclusion criteria with 16,981 heart rate measures. The median intraindividual standard deviation was 12.1 (mean 12.51 ± 4.05). HRVVV correlated significantly with age and creati-

Table 1: Factors associated with heart rate visit-to-visit variability in SLE

Variable	Spearman coefficient	p-value
Age	-0.23	<0.001
Creatinine	-0.13	<0.001
C-reactive protein	-0.002	0.97
Charlson score	-0.03	0.34
C3	0.02	0.55
C4	0.005	0.91
Body mass index	-0.04	0.35

Table 2: Heart rate visit-to-visit variability and mortality in SLE

Variable	Incidence Rate Ratio (95% CI)	p-value
Unadjusted	1.10 (1.06-1.15)	<0.001
Adjusted for age, sex, race, and Charlson baseline score	1.14 (1.09-1.19)	<0.001

nine, but not with C-reactive protein, C3, C4, nor body mass index (Table 1). Over a median follow-up of 5.7 years, 66 patients died. One SD of HRVVV was associated with a higher risk of mortality (IRR: 1.10 95% CI: 1.06-1.15, p< 0.001). After adjustment for age, sex, race, and baseline Charlson comorbidity score, the association between HR variability and increased mortality remained significant (IRR: 1.14, 95% C.I.: 1.09-1.19, Table 2).

Conclusion: In patients with SLE, higher heart rate visit-to-visit variability was associated with increased mortality independent of age, sex, race, and baseline comorbidities.

Disclosure: T. Reese, Rheumatology Research Foundation, 2; **A. Dickson**, None; **J. Gandelman**, None; **S. Bayefsky**, Rheumatology Research Foundation, 2; **A. Barnado**, NIH/NIAMS 5K08AR072757-02, 2; **K. Barker**, None; **C. Stein**, None; **V. Kawai**, NIH K23GM117395, 2, NIH NIGMS K23GM117395, 2, NIH/NIGMS K23GM117395, 2, NIH, 2, NIH, 2; **C. Chung**, Lupus Research Alliance, 2, NCATS/NIH CTSA grant ULTR000445, 2, Rheumatology Research Foundation, 2, Veterans Health Administration CDA, 2.

Abstract Number: 1594

High Expression of CD38 on CD8 T Cells Predicts Increased Burden of Infections in Patients with SLE

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: We have previously reported that CD38 gene expression in the peripheral blood T cell from patients with SLE is increased. $CD8^{+}CD38^{+}$ T cells have impaired cytotoxicity leading to increased risk of infections.

The purpose of the current study was to further investigate whether the expansion of $CD8^+CD38^+$ T cells in patients with SLE predicts increased load of infectious episodes.

Methods: CD38 surface expression was measured by flow cytometry in fresh T cells from patients with SLE (n=43) over a period of time ranging from 6 to 24 months. The expression of CD38 on the surface of T cells was estimated my flow cytometry. Clinical parameters (SLEDAI, flare rate and medications) as well as rate and type of infections were recorded from patients with SLE for further analysis.

Results: CD38 surface expression was higher in CD8+ T cells from patients with SLE (30%±3, n=37) compared to normal controls (18.7% 1, n=18, p< 0.001). Within group of patients with SLE we identified two groups of patients: those with high (> 28.9%; mean +2 standard deviations of normal values) and those with low (< 28.9%) expression levels of CD38. We followed these patients longitudinally and recorded number of infections over the study period. 43 subjects were found to had two or more visits. Interestingly, 23 out of the 30 SLE patients with lower percentage of CD8+CD38+ T cells did not report any infections at the initial visit compared with 4 out of the 14 SLE with higher CD8+CD38+ percentages who reported at least one infectious episode (p< 0.01 using Chi-squared test). Even more, patients with SLE who had a higher percentage of CD8+CD38+ T cells (n=32) at their initial visit were more prone to developing subsequent infections (1.1 infections/year) compared to those with low percentage of CD8+CD38+ cells (n=14, 0.7 infection/year, p=0.05). Early analyses did not reveal an association with disease activity and treatment.

Conclusion: Our data indicate that increased percentage of $CD8^+CD38^+$ T cells in the peripheral blood of patients with SLE predicts increased numbers of infections. Identification of this subset of patients should alert care-takers to expect, identify and treat promptly in order to limit morbidity and mortality.

Disclosure: L. Mulki, None; **A. Suarez-Fueyo**, None; **E. Katsuyama**, GSK, Horizon Pharma, Exagen Diagnostics; **V. Kyttaris**, exagen diagnostics, 2, Exagen Diagnostics, 2, GSK, 5, gsk, 5, horizon pharma, 5, Horizon Pharma, 5; **G. Tsokos**, Janssen Research & Development, LLC, 2.

Abstract Number: 1595

Role of Aerobic Exercise in Modulating Fatigue in Women with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that predominantly afflicts women. One of the most debilitating symptoms experienced by SLE patients is persistent fatigue. We previously found that fatigue, as measured by the Fatigue Severity Scale (FSS), is independent of SLE disease activity, as measured by the Safety of Estrogen in Lupus Erythematosus National Assessment Group-Systemic Lupus Erythe-

Table-1-Demographics and SELENA-SLEDAI score of patients enrolled in Exercise Study	
Variables	***N=13***
Age (Years)	
Mean ±SD	42±10.7
Disease Duration (years)	
Mean ±SD	9.5±7.2
BMI	
Mean ±SD	28.9±5.5
Race/Ethnicity, N (%)	
African American	3 (23.1 %)
Asian	2 (15.4 %)
Caucasian	2 (15.4 %)
Hispanic	6 (46.2 %)
Gender, N (%)	
Female	13 (100.0%)
SELENA-SLEDAI	
Mean ±SD	1.4±1.9

Table-2- Fatigue Severity Scale (FSS) pre and post Exercise Study			
FSS Questions	**Pre-exercise median (Q1- Q3)**	**Post-exercise median (Q1- Q3)**	***p-value***
FSS LOW MOTIVATION	6(5--6)	4(2--7)	0.2109
FSS EXERCISE BRINGS	5(4--6)	3(2--4)	**0.0313**
FSS EASILY FATIGUE	5(4--6)	3(2--5)	**0.0469**
FSS INTERFERES PHYS FNCTN	5(4--5)	3(2--4)	**0.0156**
FSS CAUSE FREQ PROB	5(4--6)	2(2--3)	**0.0156**
FSS PREVNTS SUSTND PHYS FXN	5(2--6)	2(1--2)	**0.0156**
FSS INTERFERES DUTIES	6(2--6)	2(1--2)	**0.0313**
FSS AMONG 3 DISABLNG SX	6(6--6)	2(2--4)	**0.0313**
FSS INTERFERES WORK	6(2--6)	2(2--5)	0.1563
FSS Average	4.8(3.6--5.7)	2.2(2--3)	**0.0039**

matosus Disease Activity Index (SELENA-SLEDAI) scores. The purpose of this study is to characterize the response and adaptation to an aerobic exercise program in SLE patients with significant fatigue and minimal disease activity.

Methods: A cohort of 20 SLE patients with minimal to no disease activity (SELENA-SLEDAI < 4) and a FSS score of > 3 are being enrolled in a supervised, aerobic exercise training program that consists of vigorous walking on a treadmill for 30 minutes, three times a week for 12 weeks. The primary outcome measure is the time it takes the subjects to reach anaerobic threshold during a cardiopulmonary exercise test (CPET), which is performed pre and post exercise training. Vascular endothelial dysfunction and arterial stiffness are measured by non-invasive vascular studies. Secondary outcome measures such as the FSS, SELENA-SLEDAI scores and the Patient-Reported Outcomes Measurement Information System (PROMIS) survey assesses changes in disease activity and fatigue.

Table-3- Patient-Reported Outcomes Measurement Information System (PROMIS) pre and post Exercise Study			
PROMIS Domains	Pre-exercise Median (Q1--Q3)	Post-exercise Median (Q1--Q3)	*p-value*
Physical Function	4.5(4--4.8)	4.8(4.5--4.9)	0.0781
Anxiety	2(1.1--2.8)	1.5(1--2.4)	**0.0156**
Depression	1.6(1.3--1.9)	1(1--1.8)	0.0938
Fatigue	2.3(1.8--2.4)	1.8(1.3--2)	**0.0195**
Sleep Disturbance	2.6(2.4--2.8)	2.3(1.6--2.5)	0.0898
Satisfaction with Social Roles	1.3(1.1--1.8)	1.4(1--2.3)	0.7188
Pain Interference	2(1.1--2)	1(1--1.1)	0.1563
Pain Intensity	2(2--4)	1(1--2)	0.1211
P-Value (*) were obtained using Wilcoxon signed-rank test. Median; Q1, first quartiles; Q3, third quartile			

Results: So far, 13 SLE patients have been screened and enrolled into the protocol. Of the 13 patients enrolled, the average age is 42 years with the mean disease duration of 9.5 years. In the 9 patients that have completed the study so far, baseline average SLEDAI score was 1.4 and remained unchanged at the end of the study. All patients attended ≥ 80% of the exercise sessions, with no serious adverse events. The FSS average baseline scores was 4.8 and significantly decreased to 2.2 following the exercise program (p=0.0039). At the end of the study, the PROMIS survey also demonstrated an overall improvement most significantly in anxiety and fatigue.

Conclusion: Supervised aerobic exercise training improves patient-reported fatigue in SLE, without exacerbation of disease activity. These patients with SLE were able to tolerate vigorous exercise training, suggesting physical exercise may be a valuable intervention to consider for SLE patients with significant fatigue and minimal disease activity.

Disclosure: M. Chapman, None; **S. Gupta**, None; **J. Chu**, None; **M. Naqi**, None; **Z. Manna**, None; **M. Mazhar**, None; **A. Munday**, None; **M. Stockman**, None; **B. Dinkard**, None; **L. Chin**, None; **M. Kaplan**, None; **R. Keyser**, None; **L. Chan**, None; **S. Hasni**, None.

Abstract Number: 1596

Assessing the Validity of QRISK3 at Predicting Cardiovascular Events in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: It has been well established that patients with systemic lupus erythematosus (SLE) have an increased risk of developing cardiovascular disease (CVD). Traditional CVD risk calculators such as the Framingham risk score (FRS) have been shown to underestimate risk in this patient population. QRISK3 is unique in including SLE and corticosteroid use as risk factors and has been shown to enhance CVD risk detection in a cohort of SLE patients in the UK. The purpose of this study was to assess the validity of QRISK3 compared to other cardiovascular risk models (FRS, modified FRS and PREDICTS) in predicting CVD risk in a cohort of SLE patients in the United States.

Table 1: Comparison of Sensitivity and Specificity between Risk Calculators

	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)	PPV (%, 95% CI)	NPV (%, 95% CI)
QRISK3 >10%	46.0 (33.4-59.1)	80.9 (75.4-85.6)	38.2 (29.9-42.2)	85.4 (82.2-88.1)
FRS >10%	11.1 (4.6-21.6)	93.9 (90.1-96.6)	31.8 (16.6-52.3)	80.5 (79.0-81.9)
Modified FRS >10%	41.3 (29.0-54.4)	72.0 (66.0-77.5)	27.4 (20.9-35.0)	82.7 (79.3-85.7)
High PREDICTS	66.7 (53.7-78.1)	63.8 (57.5-69.8)	32.1 (27.1-37.5)	88.2 (83.9-91.5)

Table 2: Comparison of Area under ROC between Risk Calculators

	Area under ROC	Std Error	Asymptomatic Sig.	95% CI
QRISK3 >10%	0.635	0.042	0.001	0.553-0.716
FRS >10%	0.525	0.042	0.539	0.443-0.607
Modified FRS >10%	0.566	0.041	0.105	0.485-0.647
High PREDICTS	0.652	0.039	0.000	0.557-0.728

Methods: We studied a prospective cohort of 309 patients with SLE without prior history of any cardiovascular event, defined as coronary artery disease (CAD), myocardial infarction (MI), ischemic stroke, transient ischemia attack (TIA) or peripheral artery disease (PAD). Patients received care at an academic medical center and were followed over a 10-year period. Baseline data on demographic factors, diagnosis and clinical values were obtained via chart review and used to calculate QRISK3, FRS, modified FRS (FRS multiplied by 2, as described by Urowitz et al., 2016) and PREDICTS (Predictors of Risk for Elevated Flares, Damage Progression, and Increased Cardiovascular Disease in Patients with SLE) scores. Chi-squared test was used for dichotomous variables and Student's t-test for continuous variables. Receiver operator characteristic (ROC) curves were created using SPSS software to evaluate the diagnostic performance of QRISK3, FRS, modified FRS and PREDICTS using a threshold of risk greater than 10% for the first 3 calculators and "high-risk" categorization for PREDICTS.

Results: The cohort was composed of 98% females, and the mean age of all patients was 42.3 years. Sixty-three of the 309 patients (20.2%) experienced a cardiovascular event during the 10-year follow-up period. Forty-six percent of patients who had a cardiovascular event had a QRISK3 risk score greater than 10%, whereas 19.1% of patients who did not have an event had a QRISK3 score greater than 10% ($p< 0.001$). In comparison, 11% of patients who had a cardiovascular event had a FRS greater than 10%, whereas 6.2% who did not have an event had an FRS greater than 10% ($p=0.17$). The corresponding numbers for modified FRS and PREDICTS were 41.3% and 28.0% ($p=0.04$), and 67% and 36% ($p< 0.001$), respectively. A QRISK3 score greater than 10% had sensitivity of 46.0% and specificity of 80.9%, with comparison to other calculators shown in Table 1. The area under the ROC using QRISK3 greater than 10% was larger than that using FRS or modified FRS greater than 10%, though it was slightly smaller than that using high PREDICTS score (Table 2).

Conclusion: Both QRISK3 and PREDICTS demonstrated better performance at predicting risk of CVD in this cohort of SLE patients compared to FRS and modified FRS. These results indicate that QRISK3 may be a more useful risk assessment tool in this population compared to traditional calculators.

Disclosure: L. Zhu, None; **M. Singh**, None; **S. Lele**, None; **M. Liang**, None; **L. Sahakian**, None; **J. Grossman**, None; **M. McMahon**, None.

Abstract Number: 1597

Assessing Long-term Poor Outcomes in Systemic Lupus Erythematosus Patients with Acute Coronary Syndromes

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
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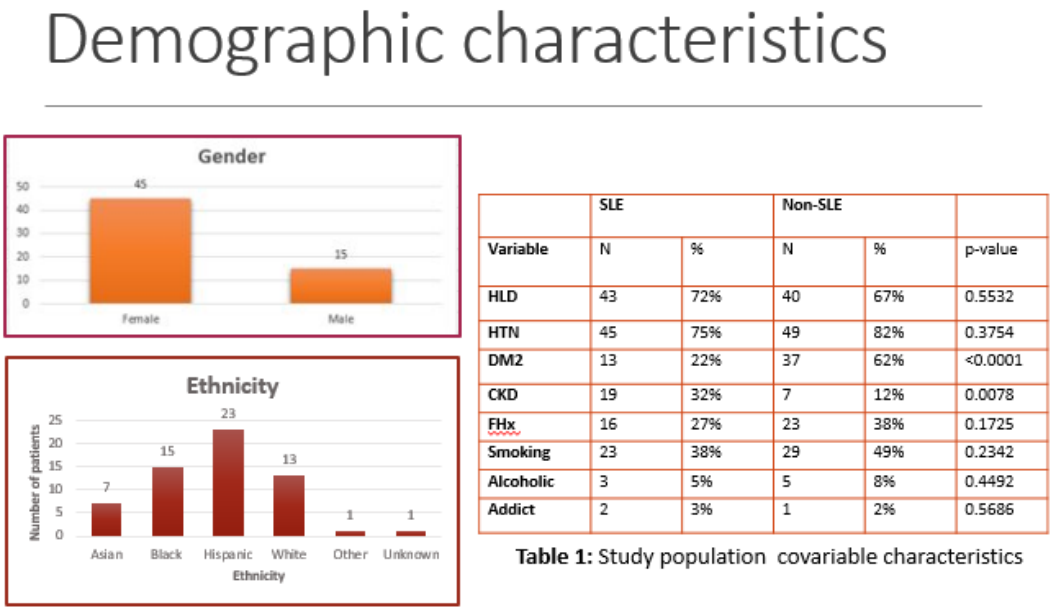
Background/Purpose: Systemic lupus erythematosus (SLE) is a significant risk factor for coronary atherosclerosis, independent of the classic risk factors. Previous studies have found poor acute outcomes in regard to in-hospital mortality and prolonged hospitalizations in SLE patients with acute myocardial infarction. This study aims to examine long term adverse events in lupus patients who have a first time acute coronary syndrome (ACS). We hypothesize that SLE patients with ACS are more likely than age and gender-matched controls to have worse outcomes.

Methods: This is a retrospective study conducted within time frame of 2007-2019 that involved adults above the age of 18. The study comprised of two groups including SLE and non SLE group with 60 patients in each. SLE group consisted of patients diagnosed with SLE who experienced a first time ACS. A second group (non SLE) comprised of randomly selected age, ethnicity, and gender-matched patients with ACS who have no history of SLE. A multivariate analyses was performed to adjust for the confounders. Primary outcome included major adverse clinical events (MACE), including 30-day readmit, 30-day CV readmit, CVA, CHF admission, ACS readmit, and CV death. Secondary outcomes evaluated included LV dysfunction, STEMI, and multivessel CAD.

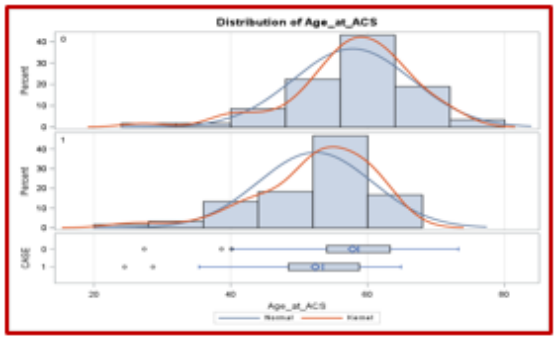
Results: Our results indicated that on average, the SLE patients develop ACS 5.5 years earlier than non SLE patients. There is evidence of more single vessel and more nonobstructive disease in the SLE patients (77% vs 47%, p=0.0003). SLE patients have more STEMI (35% vs 11%, p = 0.002) and less unstable angina (11% vs 42%, p =



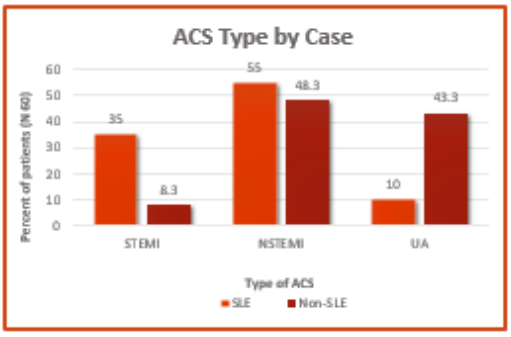
	SLE		Non-SLE		
Variable	N	%	N	%	p-value
HLD	43	72%	40	67%	0.5532
HTN	45	75%	49	82%	0.3754
DM2	13	22%	37	62%	<0.0001
CKD	19	32%	7	12%	0.0078
FHx	16	27%	23	38%	0.1725
Smoking	23	38%	29	49%	0.2342
Alcoholic	3	5%	5	8%	0.4492
Addict	2	3%	1	2%	0.5686

Table 1: Study population covariable characteristics

Demographic characteristic and traditional risk factor profile

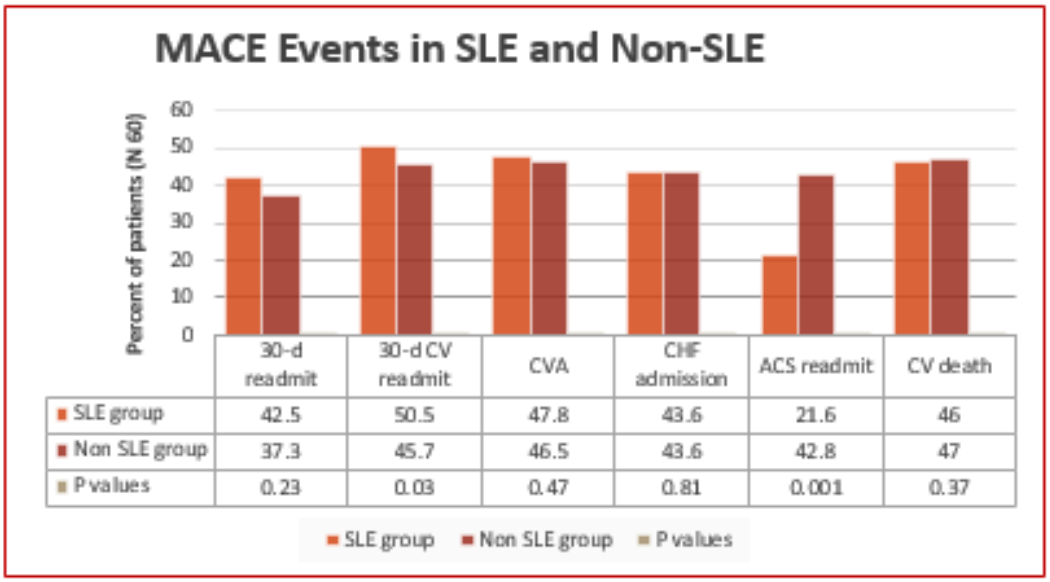


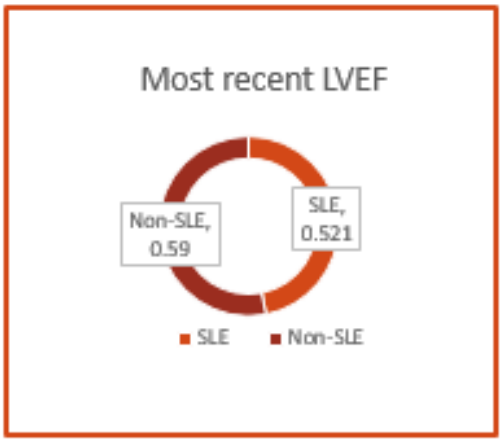
On average, the SLE patients develop ACS 5.5 years earlier than non SLE patients.



ACS type: SLE patients have more STEMI (35% vs 8%, p 0.002) & less unstable angina (10% vs 43%, p = 0.0001)

Distribution of age at ACS event and ACS type





MACE events and Left ventricular ejection fraction (LVEF) in SLE and Non SLE group

0.0001). For MACE, 30-day readmission, 30-day CV readmission, and CV death was more frequent although not statistically significant in patients with SLE. These findings may be statistically significant with bigger sample size that would increase the power of the study or an increased time frame of the study as MACE events of stroke or cardio-

vascular death may take longer to manifest. Based on propensity score balanced weights, SLE patients have worse LV systolic function and they have less rebound in LVEF during follow up (p value < 0.001).

Conclusion: Based on the results of our study, we conclude that SLE patients develop ACS much earlier than their age, gender, and ethnicity matched non SLE cohort. SLE group has less severe CAD lesions (shown by 1 vessel disease) but more acute events, manifested by STEMI. Inflammatory mediators likely contribute to plaque instability that lead to rupture, thrombosis, and vessel occlusion. Identification of risk factors in SLE patients may enable early and aggressive intervention and risk factor modification. The results of this study show that SLE as an atherogenic risk factor results in worse long-term outcomes for patients with ACS as compared to non-SLE patients including early onset of disease, worse LV function as well as worse 30 day CV readmit. Further directions of this study can implore into whether tighter control of inflammation will reduce the risks of acute ACS events in patients with SLE.

Disclosure: P. Singh, None.

Abstract Number: 1598

Disability Among Subtypes of SLE

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SESSION INFORMATION
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Background/Purpose: The rate of medical disability among patient with systemic lupus erythematosus (SLE) ranges from 20-40% and is associated with a number of socioeconomic, disease-related and clinical factors. Our group has developed a conceptual model of SLE symptoms reflecting the patients' experience: Type 1 SLE activity includes classic inflammatory manifestations of SLE such as arthritis and serositis, whereas Type 2 SLE activity includes fatigue, depression, widespread pain, sleep dysfunction and perceived cognitive dysfunction. We examined the socioeconomic status of patients within these SLE subtypes and factors associated with disability.

Methods: This was a cross-sectional study of SLE patients (SLICC classification criteria) at a university lupus clinic (September 2018 to March 2019). All patients completed Patient Health Quesionnaire-9 (PHQ-9), 2016 ACR fibromyalgia criteria and socioeconomic surveys. Patients were divided into 4 groups: active Type 1 SLE (SLEDAI ≥ 6, clinical SLEDAI ≥ 4, active lupus nephritis, or PGA ≥ 1.5); active Type 2 SLE (fibromyalgia severity score (FSS) ≥ 10); Mixed

	Total n=156	Type 2 SLE n=24	Mixed SLE n=29	Type 1 SLE n=33	Minimal SLE n=70	p-value
Black/African-American	91 (59%)	7 (30%)	16 (55%)	26 (79%)	42 (61%)	0.004
Disability or Doesn't Work	66 (42%)	15 (65%)	16 (62%)	7 (23%)	28 (41%)	0.004
Married or Living with Partner	75 (49%)	13 (57%)	15 (52%)	9 (27%)	38 (55%)	0.05
Social Support, > 2 people to rely on	110 (71%)	17 (74%)	22(76%)	25 (76%)	46 (67%)	0.7
College Education or More	85 (55%)	12 (52%)	11 (38%)	18 (55%)	44 (64%)	0.1
Lives with Children or Adults	117 (76%)	18 (78%)	20 (69%)	24 (73%)	55 (80%)	0.7
Medicare/ Medicaid or No Insurance	77 (50%)	15 (65%)	15 (54%)	14 (42%)	33 (48%)	0.4
Income ≤$15,000	31 (22%)	4 (18%)	3 (13%)	10 (31%)	14 (22%)	0.5

Table 1 Socioeconomic differences between SLE subtypes

		Disability/Not Working*	Working/Retired/ Student	p-value
	n	n=68	n=90	
Age	158	50.0 (13.6)	38.2 (11.6)	<0.0001
Female	158	64 (94%)	84 (93%)	1.0
Black	158	36 (53%)	55 (61%)	0.3
Social Support, > 2 people to rely on	158	41 (60%)	73 (81%)	0.004
College Education or More	158	29 (43%)	60 (67%)	0.004
Married or Living with Partner	158	37 (54%)	44 (49%)	0.5
Lives with Children or Adults	158	53 (78%)	70 (78%)	1.0
Black/African-American	158	36 (53%)	55 (61%)	0.3
Medicare/ Medicaid or No Insurance	157	56 (84%)	19 (21%)	<0.0001
Income, ≤$15,000	148	17 (26%)	13 (16%)	0.1
Patient-Reported Flare (moderate-severe)	144	26 (41%)	16 (20%)	0.006
Measures of Type 2 SLE Activity:		Mean (SD)		
ACR Fibromyalgia Severity Score (FSS)	156	10.8 (6.6)	7.2 (6.0)	0.0003
Areas of Pain	157	5.1 (4.3)	2.8 (3.3)	0.0005
ACR Symptom Severity Score (SSS)	156	5.7 (3.2)	4.2 (3.1)	0.004
Cognitive dysfunction (moderate-severe)	146	15 (23%)	13 (16%)	0.3
Fatigue (moderate-severe)	146	40 (62%)	37 (46%)	0.07
Sleep Dysfunction (moderate-severe)	147	36 (55%)	25 (31%)	0.004
Depression (PHQ-9 criteria)	131	7 (13%)	7 (9%)	0.6
Depression severity score (PHQ-9)	131	6.6 (4.8)	5.1 (4.9)	0.07
Measures of Type 1 SLE Activity:				
PGA	157	0.6 (0.6)	0.6 (0.6)	0.9
SLEDAI	146	3.1 (3.5)	3.7 (3.7)	0.3
Active Lupus Nephritis	151	7 (11%)	12 (14%)	0.6
SLE History:				
Length of SLE disease, years	131	17.9 (9.2)	13.1 (7.9)	0.002
Lupus Nephritis History	158	33 (49%)	59 (66%)	0.04
Inflammatory Arthritis History	158	46 (68%)	58 (64%)	0.7
Interstitial Lung disease (ILD) History	158	4 (6%)	8 (9%)	0.6
History of Cardiac Involvement	158	15 (22%)	16 (18%)	0.5
History of Gastrointestinal involvement	158	3 (4%)	3 (3%)	1.0
History of Hematologic	158	14 (21%)	19 (21%)	1.0
Anti-phospholipid antibody syndrome	158	6 (9%)	8 (9%)	1.0
Subacute and chronic cutaneous lupus	158	39 (57%)	45 (50%)	0.4

*missing work status data on n=6

Table 2 Clinical and socioeconomic differences between disabled and non-disabled groups

SLE (both Type 1 and 2); Minimal SLE (neither Type 1 nor 2). Differences were analyzed by Fisher's exact test. A step-wise regression analysis examined predictors for disability.

Results: 164 patients completed the surveys (93% female, mean age 43.5 years, 58% Black, 39% Caucasian, 2% Asian, average length of disease 15 years). The demographics of the SLE subtypes were similar, except that more patients with active Type 1 SLE were Black and more with active Type 2 SLE were unable to work (Table 1).

Disabled patients were older, less educated, had less social support, longer disease duration, less historical nephritis, and were more likely to be uninsured or be on Medicare/Medicaid insurance. Furthermore, disabled patients had greater Type 2 symptoms including a higher fibromyalgia severity score (FSS) (10.8 vs 7.2, p = 0.0007), symptom severity score (5.7 vs 4.2, p = 0.005) , more frequent sleep dysfunction (55% vs 31%, p =0.005), and more areas of pain (5.1 vs 2.8, p = 0.005).

There were no differences in current Type 1 SLE activity between patients with and without disability; these two groups had similar SLEDAI and physician's global assessment, as well as similar features of arthritis, cardiopulmonary, hematologic, or cutaneous SLE.

In multivariate analysis, patients on disability were older (OR 1.07 for every 1 year in age, 95% CI:1.03, 1.12), less educated (OR 2.72, 95% CI: 1.15, 6.45), had a lower income (OR 3.78, 95% CI 1.26, 11.40), and had a higher FSS (OR 1.08 for every 1 point in FSS, 95% CI: 1.00, 1.16).

Conclusion: The overall rate of disability mirrors that of other SLE cohorts, but this study provides evidence that Type 2 not Type 1 SLE that drives SLE patients' limitations in the workforce. As such, this study suggest that addressing pain, fatigue, and sleep dysfunction could improve health-related quality of life and the care of SLE patients. Incorporating the Type 1 and Type 2 categorization system into clinical practices encourages the provider to focus on all aspects of SLE, including the Type 2 symptoms, which contribute significantly to the high societal cost of SLE.

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Abstract Number: 1599

The Impact of Body Mass Index Variability in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: SLE is a chronic illness that carries both a physical and psychosocial burden, where the cumulative impact can lead to worse global outcomes. One outcome of interest is BMI especially with recent public health efforts highlighting the risk of BMI elevation to obesity and its affiliated metabolic risk factors. We examined the associated features and impact of BMI variability amongst SLE patients.

Methods: The Georgians Organized Against Lupus (GOAL) is a population-based research cohort of SLE patients in Atlanta derived from the Centers for Disease Control and Prevention supported by Georgia Lupus Registry who consent to and complete annual surveys encompassing multiple domains. The 2017 results included calculated BMI and the Patient-Reported Outcomes Measurement Information System (PROMIS) questionnaire for depression with T-score conversion, disease activity (Systemic Lupus Activity Questionnaire, SLAQ), perceived stress (Perceived Stress Scale), discrimination (Everyday Discrimination Scale), and self-assessment of continuity of care with a regular

Table 1. Characteristics of the Georgians Organized Against Lupus Cohort, 2017

Characteristics	Overall	BMI<25	BMI≥25	P-Value*
	n=795	n=265	n=530	
Sociodemographics				
Age, years (mean±SD)	48.1±13.99	46.3±15.5	48.9±13.1	0.0160
Sex				
male, n (%)	48 (6.04)	21 (43.75)	27 (56.25)	0.1143
female, n (%)	747 (93.96)	244 (30.69)	503 (63.27)	
Marital status				
married, n (%)	289 (36.35)	98 (33.91)	191 (66.09)	0.7943
not married, n (%)	506 (63.65)	167 (33.00)	339 (67.00)	
Educational attainment, years (mean±SD)	14.44±3.02	14.93±3.35	14.24±2.78	0.0042
Below Federal poverty level, n (%)	281 (35.93)	83 (29.54)	198 (70.46)	<0.0001
Race				
African American, n (%)	648 (81.41)	199 (30.71)	449 (69.29)	0.0491
white, n (%)	130 (16.33)	53 (4.77)	77(59.23)	
other, n (%)	26 (3.27)	6 (33.33)	20 (66.67)	
Work status				
unemployed, n (%)	376 (47.30)	136 (36.17)	240 (63.83)	0.2038
employed, n (%)	414 (52.08)	132 (31.88)	282 (68.12)	
Disease Characteristics				
Age at diagnosis, years (mean±SD)	32.00±11.9	30.47±12.61	32.76±11.54	0.0116
Disease duration. years (mean±SD)	16.11±10.38	15.91±10.37	16.23±10.32	0.6857
Disease activity, SLAQ (mean±SD)	14.68±8.6	13.61±8.39	15.24±8.68	0.0117
Disease damage, SA-BILD				
none (score=0), n (%)	100 (12.58)	46 (46.00)	54 (54.00)	0.0121
mild (score=1-2), n (%)	268 (33.71)	89 (33.21)	179 (66.79)	
severe (score≥3), n (%)	427 (53.71)	130 (30.44)	297 (69.56)	
Steroids				
no, n (%)	384 (48.98)	119 (30.99)	265 (82.25)	0.0066
yes, n (%)	398 (50.77)	142 (35.68)	256 (64.32)	

provider. Logistic regression evaluated the potential relationship between BMI and aforementioned factors. BMI was categorized as either non-elevated (BMI< 25) or elevated (BMI≥25).

Results: The 2017 GOAL survey comprised of 795 patients, of whom 265 (33.3%) had non-elevated BMI and 530 (66.6%) had elevated BMI. African Americans (AA) made up 81.4% of this cohort. The average disease duration was

16.11 ± 10.38 years. Univariate logistic regression analyses demonstrated that older age was linked to elevated BMI (p = 0.016, Table 1). Additionally, greater years of higher education was linked to non-elevated BMI, p=0.0042; whereas being below the federal poverty level and/or being AA carried greater association with elevated BMI (p< 0.001 and p=0.0491, respectively). While disease duration carried no impact on BMI, diagnosis at a later age was linked to higher incidence of elevated BMI, p=0.0116. Patients with elevated BMI had greater disease activity and damage and experienced more discrimination.

Conclusion: The variability of BMI amongst SLE can be associated with different clinical and behavioral impact. Patients with greater disease activity had elevated BMI. They were also likelier to experience more discrimination, but this may be affected by the greater proportion of AA's (81.4%) in the cohort. Poverty was associated with elevated BMI. Further research into understanding the prolonged impact of BMI variability in SLE needs to be investigated and can prove to be instrumental in the overall care of SLE patients.

Disclosure: X. Gao, None; **T. Vashi**, None; **S. Lim**, None.

Abstract Number: 1600

Frailty and Sarcopenia in Women with Systemic Lupus Erythematosus

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Table 1. Fried frailty classification

Components of Frailty	Definition	Participants (N=50), %
Unintentional weight loss	BMI ≤18.5 kg/m^2 Or self-report ≥10 lbs over the past year	14.3%
Exhaustion	3 items from the Center for Epidemiologic Studies Depression Scale	38.3%
Inactivity	<600 MET-minutes/week from the International Physical Activity Questionnaire	57.9%
Slowness	Slow 4-m walk test	12.5%
Weakness	Low grip strength normalized for BMI	60.8%
Overall		
Non-frail	0 criteria	8.2%
Pre-frail	1-2 criteria	74.0%
Frail	≥3 criteria	18.4%

Table 2. Characteristics of participants by frailty classification

Characteristic	Non-frail (N=4)	Pre-frail (N=37)	Frail (N=9)	p-value
Age, years, median [IQR]	55 [45, 60]	46 [31, 58]	54 [43, 59]	0.31
SLE disease duration, years, median [IQR]	9 [8, 38]	13 [7, 27]	16 [13, 19]	0.95
Charlson Comorbidity Index, median [IQR]	2.5 [1.5, 3]	2 [1, 3]	3 [3, 4]	0.14
Disease activity SELENA-SLEDAI, median [IQR]	0 [0, 2]	4 [1, 4]	6 [0, 7]	0.24
Disease damage SLICC/ACR index, median [IQR]	1 [0, 2.5]	0 [0, 2]	3 [1, 4]	0.18
Steroid dose, mg, mean [IQR]	2 [2, 10]	5 [5, 7.5]	5 [5, 6.5]	0.60
Race, %				0.71
Asian	0	2.8	0	
Black or African American	25.0	33.3	66.7	
Native Hawaiian or Pacific Islander	0	0	0	
White	50.0	36.1	11.1	
Other	25.0	25.0	22.2	
Declined to state	0	2.8	0	
Ethnicity, %				0.58
Hispanic	0	27.8	33.3	
Non-Hispanic	100	72.2	66.7	
Education, %				**0.03**
High school or less	0	12.1	22.2	
Some college	0	21.2	44.4	
College	25.0	54.6	22.2	
Graduate/professional school	75.0	12.1	11.1	
Insurance status, %				
Medicare	25.0	18.9	33.3	0.73
Medicaid	25.0	27.0	66.7	0.08
Private insurance	75.0	62.2	33.3	0.30
Uninsured	0	0	0	--
Other	0	2.7	0	--
Smoking status, %				1.00
Never	75.0	84.9	77.8	
Ever	25.0	15.2	22.2	
Concurrent fibromyalgia, %	25.0	18.2	22.2	0.30
Body mass index (BMI) kg/m^2, median [IQR]	22.0 [22.1, 30.1]	26.3 [22.9, 30.8]	27.4 [22.7, 32.4]	0.83
Sarcopenia*, %	0	5.4	33.3	0.10
Erythrocyte sedimentation rate (mm/hr), median [IQR]	28 [16, 55]	14 [8, 32]	22 [18, 30]	0.27
High-sensitivity C-reactive protein (mg/mL), median [IQR]	2.2665 [1.817, 2.716]	2.551 [0.515, 8.578]	2.014 [2.010, 4.162]	0.99

Background/Purpose: Frailty is a clinical phenotype that increases with age. However, frailty can occur in younger patients with chronic disease, including SLE. Based on few studies, frailty has been found in up to 27.5% of patients with SLE and is associated with increased mortality [1-2]. The prevalence of frailty in other cohorts of patients with SLE and its association with sarcopenia, an important related domain, or patient-centered domains, is unclear.

Methods: Adult women < 70 years old who fulfilled ACR criteria for SLE were recruited from a single center. Exclusions included pregnancy, dialysis, active malignancy, overlap autoimmune syndromes, or severe SLE disease activity. Frailty and pre-frailty were measured according to Fried frailty criteria [3] (Table 1). Patient-reported outcomes were measured using a) global Patient-Reported Outcomes Measurement Information System (PROMIS) computerized adaptive tests and b) the disease-specific LupusQOL. Disease activity was measured with the SELENA-SLEDAI, and damage with the SLICC/ACR index. DXA was used to compute sarcopenia [4] (Table 2). Differences between frail, pre-frail, and non-frail participants were evaluated using chi-square tests and Kruskal-Wallis tests as appropriate.

Results: 50 women enrolled from 8/2018-3/2019. Although median age was only 51 years, 74% and 18% were pre-frail and frail, respectively (Table 1). Frail women had increased disease activity and damage as compared to pre-frail and non-frail women; however, this did not differ significantly across the three groups (Table 2). Age and comorbidities, including fibromyalgia, were similar between non-frail, pre-frail, and frail women. Educational attainment differed significantly across pre-frail, frail and non-frail patients (p=.03), with a larger proportion of lower educational attainment among frail women. Significant differences in PROMIS mobility (p=0.004), physical function (p=0.014), pain interference (p=0.030), and fatigue (p=0.004) and LupusQOL physical health (p=0.008) and pain (p=0.008) were observed across frailty groups, with frail women reporting clinically meaningfully worse scores in all measures. While not statistically significantly different across the frailty groups, frail women were 6x more likely to be sarcopenic (Table 2).

Conclusion: The prevalence of frailty and pre-frailty is high in this cohort of mid-aged women with SLE. Frailty did not appear to be a proxy for comorbidity or fibromyalgia. Compared to pre-frail and non-frail women, frail women had poorer health-related quality of life and a higher proportion of sarcopenia. Data collection is ongoing to clarify the relationship between frailly and potential confounders. If frailty is associated with worse health outcomes, it could be a potential therapeutic target.

References

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3. Bandeen-Roche et al. 2006
4. Cruz-Jentoft et al. 2019

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Abstract Number: 1601

Prevalence of Peripheral Neuropathy and Its Electrophysiological Types in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Session Type: Poster Session (Monday)

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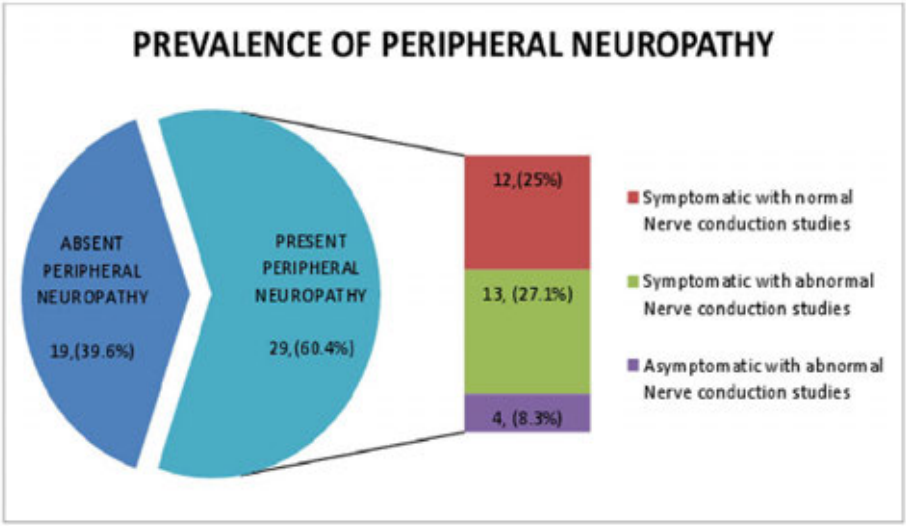

Figure 1: Prevalence of Peripheral Neuropathy and its presentation in the study participants (Sample population N=48)

Background/Purpose: Peripheral neuropathy (PN), one of the neuropsychiatric syndromes of SLE, occurs in 2% to 36% of patients. It has been associated with high disease activity indices and poor quality of life scores. The aim of this study was to determine the prevalence of peripheral neuropathy using clinical evaluation and Nerve Conduction Studies (NCS), to describe its electrophysiological types using NCS; and to correlate quality of life with presence of peripheral neuropathy among SLE patients

Methods: This was a crossectional study of SLE patients attending Rheumatology outpatient clinic. Fourty eight patients with a diagnosis of SLE as per the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria who were 18 years and above were consecutively selected for the study. Patients were excluded if they were Amputees, had history of traumatic involvement affecting the nerves, had foot ulcerations, those with other known causes of peripheral neuropathy such as mixed connective tissues disease, diabetes mellitus, and history of heavy alcohol consumption, chronic renal failure and pernicious anemia. Socio-demographic data and clinical information were obtained from the patient's medical records. Structured history and clinical examination was performed on all patients. All patients had NCS carried out and at least 5 nerves were tested: the median, the ulnar, the peroneal, the sural and the Tibial. Lupus quality of life questionnaire was administered to all patients.

Results: Prevalence of PN was suggestive in 29 out of 48 patients (60.4%). Of these 27.1% were symptomatic for peripheral neuropathy and had abnormal nerve conduction studies while 25 % were symptomatic for peripheral neuropathy and had normal nerve conduction studies. The other 8.3 % had abnormal nerve conduction studies despite being asymptomatic (figure 1). Numbness was the most common symptom complaint in 41.7% of patients. The most common nerve conduction abnormality was demyelination 9(52.94%). However excluding 5 patients found to have carpal tunnel syndrome, then demyelination was 4(23.52%), While axonopathy was found in 5(29.41%) of the patients. Motor neuropathy was the most prevalent nerve conduction syndromes in 9(52.94%) patients. There was a significant correlation between the presence of peripheral neuropathy with lower quality of life scores involving the domains of physical health ($p =< 0.001$), pain ($p=0.012$), planning ($p=0.003$), and fatigue ($p=0.005$).

Conclusion: There is a high prevalence of peripheral neuropathy among SLE patients, with variable clinical and electrophysiologic presentation. Quality of life is scores are lower in affected patients

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Abstract Number: 1602

Persistency in Platelet C4d and Thrombosis Risk Score Associate with Thrombosis in Systemic Lupus Erythematosus

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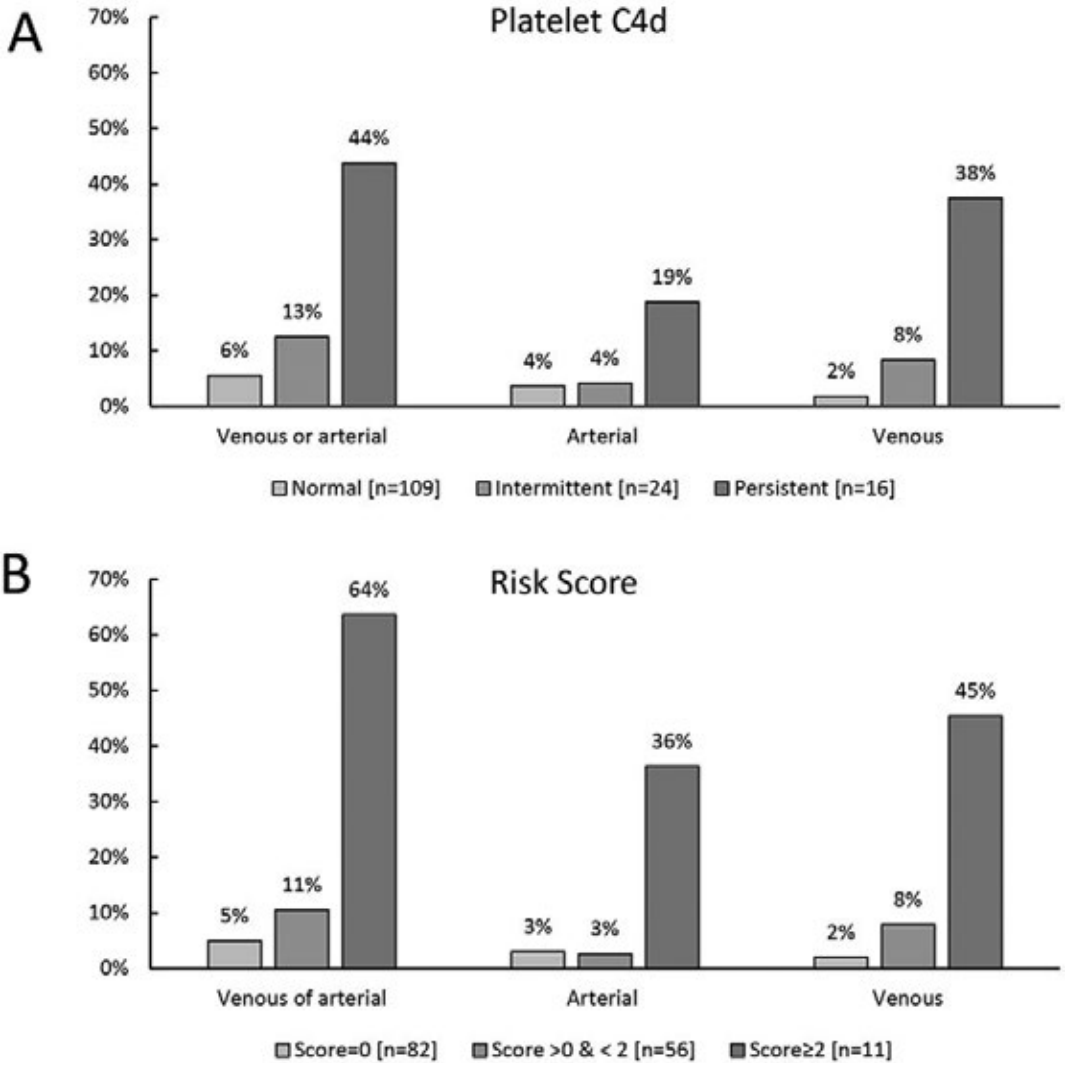
Background/Purpose: A thrombosis risk score containing abnormal Platelet-bound C4d (PC4d), low complement C3 and abnormal anti-phosphatidyl serine prothrombin (PS/PT) IgG antibody has been shown to associate with thrombosis in Systemic Lupus Erythematosus (SLE). Our objective was to evaluate the relationships between persistency in PC4d, risk score and thrombosis during follow-up (FU). A secondary objective evaluated the impact of whole blood Hydroxychloroquine (HCQ) levels in associating with thrombosis.

Methods: This was a longitudinal study of 149 SLE patients (mean age: 47±1 years, 86% female), with (n=16, 11%) or without (n=132, 89%) a history of thrombosis (venous or arterial) in the past 5 years. PC4d was measured using flow cytometry. Percent FU visits with abnormal PC4d status (>20 mean fluorescence intensity [MFI]) was calculated. Persistency in PC4d was defined as abnormal PC4d (>20 net MFI) status at baseline and all FU visits, intermittent PC4d was defined as abnormal PC4d status during at least one visit. Complement C3 (< 81 mg/dl) and anti-PS/PT IgG (>30 Units) were measured using immunoassays. Mean thrombosis risk score for each patient was calculated. Whole blood HCQ levels were measured using liquid chromatography and mean HCQ per patient was calculated. Statistical analysis consisted of Wilcoxon, Fisher's Exact and logistic regression. Odds Ratio (OR) with confidence intervals (CI) were calculated.

Results: 424 FU visits were collected (average 3 visits per patient). Persistent and intermittent PC4d status were observed in 16 (11%) and 24 patients (16%), respectively. Logistic regression analysis revealed that the percentage FU visits with abnormal PC4d status significantly associated with any thrombosis (OR range 11.7 CI 95%: 3.23-42.44) (p< 0.001), venous thrombosis (OR range= 33.4 CI95: 5.8-193.5) (p< 0.001) and approached significance with arterial thrombosis (OR=4.7 CI 95%: 0.9-25.4) (p=0.08) (Figure 1, panel A). During FU, the mean risk score per patient was 0.57±0.76 (n=149). Risk score at FU associated with any thrombosis (OR= 3.8 CI 95%: 2.0-7.2 per unit change, OR range = 53.9 CI 95%: 7.8-372.4) (p< 0.001), venous thrombosis (OR= 3.9 CI 95%: 1.9-8.2 per unit change, OR range = 60.3 CI95%: 6.5-560.8) and arterial thrombosis (OR= 3.0 CI95%: 1.4-6.4 per unit change, OR range = 26.5 CI95%: 2.7-259.4) (Figure 1, panel B). Among 133 patients treated with HCQ, median HCQ levels were 696 ng/ml (Interquartile range [IQR]: 537-989 ng/ml, n=15), 794 ng/ml (IQR: 628-1121 ng/ml, n=22), and 976 ng/ml (IQR: 675-1300 ng/ml, n=96) in the group of patients presenting with persistent, intermittent and normal PC4d status, respectively. Levels were significantly lower in the group of patients with persistent or intermittent PC4d status when compared to normal PC4d (p=0.028). Risk score did not associate with HCQ levels. Lower HCQ levels tended to associate with venous



thrombosis (median=916 ng/ml [IQR: 675-1300], n=10 vs 648 ng/ml [IQR: 382-929], n=123) (p=0.061) but not with arterial thrombosis (p >0.20).

Conclusion: Our data suggest that persistency in PC4d and the thrombosis risk score both associate with thrombosis. Lower HCQ levels may associate with venous thrombosis.

Disclosure: M. Petri, Eli Lilly and Company, 5, Exagen, 2, 5; **J. Conklin**, Exagen, 3; **T. O'Malley**, Exagen, 3; **J. Ligayon**, Exagen, 3; **L. Wolover**, Exagen, 3; **T. Dervieux**, Exagen, 1, 3, 4, 6.

Abstract Number: 1603

Stroke Clusters in SLE by Lupus Autoantibodies

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Cluster	Pts (N)	Pct	RVVT	ACL	anti-dsDNA	C3	C4	Anti-Sm	Anti-RNP	Anti-Ro	Anti-La
1	86	40.2%	0.59	0.67	0.79	1.00	0.84	0.00	0.17	0.16	0.00
2	22	10.3%	0.45	0.59	0.86	0.95	0.91	0.45	0.55	0.91	1.00
3	30	14.0%	0.43	0.67	0.77	0.83	0.73	1.00	0.83	0.37	0.00
4	44	20.6%	0.07	0.11	0.27	0.02	0.07	0.00	0.23	0.36	0.18
5	32	15.0%	0.78	1.00	0.50	0.16	0.00	0.00	0.03	0.31	0.09

1.00 – 0.75
0.74 – 0.50
0.49 – 0.25
0.25 – 0.00

ACR 2019-Stroke Clusters in SLE by Lupus Autoantibodies-Table1
Cluster Analysis of Stroke Patients without Anti-beta2 GP1

Cluster	Pts (N)	Pct	RVVT	ACL	Beta2 GPI	anti-dsDNA	C3	C4	Anti-Sm	Anti-RNP	Anti-Ro	Anti-La
3	44	20.6%	0.75	0.75	0.57	0.89	1.00	0.89	0.02	0.02	0.09	0.00
1	11	5.1%	0.36	0.55	0.36	0.64	0.64	0.55	0.00	0.27	1.00	1.00
2	35	16.4%	0.43	0.66	0.43	0.80	0.97	0.94	0.77	0.91	0.66	0.29
5	28	13.1%	0.11	0.18	0.11	0.18	0.25	0.07	0.00	0.18	0.25	0.00
4	27	12.6%	0.78	1.00	0.52	0.44	0.11	0.00	0.11	0.11	0.22	0.11

1.00 – 0.75
0.74 – 0.50
0.49 – 0.25
0.25 – 0.00

ACR 2019-Stroke Clusters in SLE by Lupus Autoantibodies-Table2
Cluster Analysis of Stroke Patients with Anti-beta2 GP1Cluster Analysis of Stroke Patients without Anti-beta2 GP1

Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Stroke is the most common arterial thrombotic event in SLE. It is known to be associated with antiphospholipid antibodies, but clinicians have additional concern about the contribution of SLE. We performed the first cluster analysis of stroke in a longitudinal SLE cohort.

Methods: There were 245 strokes in SLE patients confirmed by brain CT or MRI. Patients were 93.5% female, 50.5% Caucasian, and 45.3% African-American. Age at time of stroke was 41.5 ± 15.0 years (mean ± SD). Autoantibodies included lupus anticoagulant (dRVVT with confirmatory testing), anticardiolipin, anti-dsDNA, low C3, low C4, anti-Sm, anti-RNP, anti-Ro and anti-La. Analyses were done both without (Table 1, 214 patients) and with (Table 2, 145 patients) anti-beta2 glycoprotein 1, due to more missing data on anti-beta2 glycoprotein 1. Clustering was performed using Ward's Hierarchical Clustering method (JMP v 13.0.0, SAS Institute Inc).

Results: Five clusters were identified. Cluster 5 (Table 1) and cluster 4 (Table 2) are an antiphospholipid cluster without strong serologic activity. Cluster 4 (Table 1) and Cluster 5 (Table 2) are clusters without antiphospholipid and without serologic activity. Clusters 1, 2 and 3 (Table 1) and clusters 2, 3 and to some extent cluster 1 (Table 2) are

clusters with serologic activity. Clusters 2 and 3 (Table 1) and cluster 2 (Table 2) have strong anti-Sm and anti-RNP markers, and are associated with more African-American ethnicity compared to the other clusters combined (63.3% vs 42.3%, p=0.0136).

Conclusion: Stroke clustering identified 4 major serologic backgrounds for stroke in SLE: antiphospholipid alone, serologic markers alone, both antiphospholipid and serologic, and a group with neither. Some clusters represent stroke in predominantly African-American patients. These clusters may be helpful in formulating risk scores for stroke in SLE, in risk prevention, and eventually might be useful in treatment.
Disclosure: **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5; **D. Goldman**, None.

Abstract Number: 1604

The Systemic Lupus Erythematosus Cardiovascular Risk Equation

Michelle Petri,[1] Erik Barr,[2] and Laurence Magder[2], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]University of Maryland School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Accelerated atherosclerosis remains the major cause of late death (after 5 years) in systemic lupus erythematosus (SLE). Yet, the "traditional" cardiovascular risk equations (such as Framingham) consistently underestimate the risk. We revised our data-driven formula for cardiovascular risk in SLE, to base it on data collected during just the first year of follow up in a longitudinal cohort, versus two years.

Methods: We included 1,721 patients from a longitudinal cohort. They were assessed for cardiovascular adverse events (stroke, myocardial infarction [MI], angina or coronary procedures, claudication, or congestive heart failure), for traditional cardiovascular risk factors (age, sex, ethnicity, systolic blood pressure, total cholesterol, smoking, and diabetes mellitus) and for SLE-related risk factors (low C3 and C4, anti-dsDNA, proteinuria, SELENA SLEDAI score, and history of lupus anticoagulant and anticardiolipin) during the first year of follow up. Using Cox proportional hazards modeling, SLE formulas to calculate the 10-year risk of a subsequent cardiovascular event were derived and compared to the Framingham (for all outcomes) and to the American Heart Association/American College of Cardiology (AHA/ACC) formula (for MI and stroke).

	Hazard Ratio (95% CI)	P-value
Age (per decade)	1.41 (1.24, 1.60)	<0.0001
Male (vs. female)	1.56 (1.00, 2.45)	0.052
Systolic Blood Pressure (per 10 mmHg)	1.25 (1.12, 1.39)	<0.0001
Current or Past Smoking	1.74 (1.28, 2.38)	0.0004
Total Serum Cholesterol≥140 mg/dl	2.38 (1.16, 4.87)	0.018
Diabetes Mellitus	2.34 (1.61, 3.40)	<0.0001
SLEDAI (per unit increase)	1.10 (1.04, 1.17)	0.0024
History of Lupus Anticoagulant	1.67 (1.21, 2.31)	0.0021
Low Mean C3 (< 79)	1.89 (1.29, 2.76)	0.0011

ACR 2019-Development of SLE CV Risk Equation-Abstract-Table1
Association between predictors and risk of a cardiovascular event

Traditional Risk Factor[2]					SLE-related Risk Factors			Estimated 10-year risk	
Sex	Age	SBP	Chol	HDL	Mean SLEDAI	Low C3	Lupus anticoag.	Hopkins Lupus Cohort (% Risk, 95% CI)	Framing-ham[3] (% Risk)
Low Risk from Traditional Risk Factors, no SLE Risk Factors									
F	50	120	135	50	0	No	No	2.4 (0.5, 4.2)	2.5%
M	50	120	135	50	0	No	No	3.7 (0.4, 6.8)	4.7%
F	70	120	135	50	0	No	No	4.6 (0.7, 8.4)	5.4%
M	70	120	135	50	0	No	No	7.1 (0.4, 13.4)	12.7%
Moderate Risk from Traditional Risk Factors, no SLE Risk Factors									
F	50	145	240	40	0	No	No	9.5 (5.9, 12.9)	9.6%
M	50	145	240	40	0	No	No	14.4 (7.0, 21.2)	15.1%
F	70	145	240	40	0	No	No	17.9 (10.1, 25.1)	19.7%
M	70	145	240	40	0	No	No	26.5 (11.8, 3.9)	36.8%
Low Risk from Traditional Risk Factors, SLE Risk Factors									
F	50	120	135	50	3	Yes	Yes	9.6 (1.7, 16.8)	2.5%
M	50	120	135	50	3	Yes	Yes	14.5 (1.3, 25.9)	4.7%
F	70	120	135	50	3	Yes	Yes	18.1 (1.7, 31.7)	5.4%
M	70	120	135	50	3	Yes	Yes	26.7 (0.2, 46.2)	12.7%
Moderate Risk from Traditional Risk Factors, SLE Risk Factors									
F	50	145	240	40	3	Yes	Yes	34.2 (18.8, 46.6)	9.6%
M	50	145	240	40	3	Yes	Yes	47.9 (22.9, 64.8)	15.1%
F	70	145	240	40	3	Yes	Yes	56.3 (28.1, 73.4)	19.7%
M	70	145	240	40	3	Yes	Yes	72.5 (33.1, 88.7)	36.8%

[1]Risk of a broad cardiovascular outcome, i.e., coronary death, myocardial infarction, coronary insufficiency, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease, heart failure.
[2]Also assuming no smoking, no diabetes, and no treatment for hypertension
[3] Calculated at: https://www.framinghamheartstudy.org/fhs-risk-functions/cardiovascular-disease-10-year-risk/
SBP = systolic blood pressure
Chol = total cholesterol
HDL = high density lipoprotein

ACR 2019-Development of SLE CV Risk Equation-Abstract-Table2
Estimated 10-year risk of a cardiovascular event based on the formulas from the Hopkins Lupus Cohort and the Framingham cohort, given various risk factors

Results: Of the 1,721 patients, 168 had a cardiovascular event after the first year of cohort participation, and during cohort participation. Of these 168 events there were 70 strokes, 27 myocardial infarctions, 27 patients with angina or requiring coronary procedures, 14 patients with heart failure, 13 with peripheral artery disease, 11 with claudication, and 6 with more than one type of event. Table 1 shows the hazard ratios for rates of a cardiovascular event. Using the hazard ratios from Table 1, we compared the estimated 10-year risk based on our formula with the calculated risk using the Framingham formula (Table 2). We also derived a formula for a more restricted definition of cardiovascular event (cardiovascular death, MI and stroke) using hazard ratios from a separate Cox proportional hazards model and derived a formula that was compared with the AHA/ACC formula (Table 3). Using our formulas, which includes SLE-related risk factors, the risk was substantially higher than the estimated risk based on the formulas for the general population.

Conclusion: The excess cardiovascular risk among SLE patients varies substantially depending on the SLE-related risk factors, age, and traditional risk factors. Cardiovascular risk formulas based on individual data from SLE patients from the first year of their rheumatology followup may better estimate 10-year cardiovascular risk among SLE patients than the Framingham or AHA/ACC equations.

Traditional Risk Factor					SLE-related Risk Factors			Estimated 10-year risk	
Sex	Age	SBP	Chol	HDL	Mean SLEDAI	Low C3	Lupus anticoag.	Hopkins Lupus Cohort (% Risk, 95% CI)	ACC/AHA (% Risk)‡
Low Risk from Traditional Risk Factors, no SLE Risk Factors									
F	50	120	150	50	0	No	No	2.7 (1.5, 3.9)	0.8
M	50	120	150	50	0	No	No	3.4 (1.1, 5.6)	2.1
F	70	120	150	50	0	No	No	4.3 (1.8, 6.7)	7.9
M	70	120	150	50	0	No	No	5.4 (1.2, 9.4)	14.1
Moderate Risk from Traditional Risk Factors, no SLE Risk Factors									
F	50	145	240	40	0	No	No	6.6 (3.5, 9.6)	3.0
M	50	145	240	40	0	No	No	8.3 (3.0, 13.3)	7.0
F	70	145	240	40	0	No	No	10.4 (4.5, 15.8)	13.4
M	70	145	240	40	0	No	No	13.0 (3.8, 21.3)	26.2
Low Risk from Traditional Risk Factors, SLE Risk Factors									
F	50	120	150	50	3	Yes	Yes	11.3 (5.1, 17.1)	0.8
M	50	120	150	50	3	Yes	Yes	14.1 (3.8, 23.2)	2.1
F	70	120	150	50	3	Yes	Yes	17.4 (5.2, 28.1)	7.9
M	70	120	150	50	3	Yes	Yes	21.6 (3.1, 36.5)	14.1
Moderate Risk from Traditional Risk Factors, SLE Risk Factors									
F	50	145	240	40	3	Yes	Yes	25.8 (11.1, 38.1)	3.0
M	50	145	240	40	3	Yes	Yes	31.6 (9.8, 48.1)	7.0
F	70	145	240	40	3	Yes	Yes	38.0 (12.6, 56.0)	13.4
M	70	145	240	40	3	Yes	Yes	45.5 (9.9, 67.1)	26.2

Also assuming female, no smoking, no diabetes mellitus, and no treatment for hypertension

‡ As calculated at: http://www.cvriskcalculator.com/

SBP = systolic blood pressure; Chol = total cholesterol; HDL = high density lipoprotein; M = male; F = female

ACR 2019-Development of SLE CV Risk Equation-Abstract-Table3

Estimated 10-year risk of a hard cardiovascular event (cardiovascular death, myocardial infarction or stroke) based on the formulas from the SLE cohort

Disclosure: **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5; **E. Barr**, None; **L. Magder**, None.

Abstract Number: 1605

Homocysteinemia Predicts Renal Insufficiency in Systemic Lupus Erythematosus

Hakan Babaoglu,[1] Jessica Li,[2] Daniel Goldman,[3] Laurence Magder,[4] and Michelle Petri[2], [1]Gazi University School of Medicine, Ankara, Turkey, [2]Johns Hopkins University School of Medicine, Baltimore, MD, [3]Johns Hopkins University School of Medicine, Baltimore, MD, [4]University of Maryland School of Medicine, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Homocysteinemia is present 8-15% of patients with SLE and is associated with increased risk of atherosclerosis, arterial thrombosis and stroke in SLE patients. Recently, it was found to be an independent predictor of new damage accrual in Mestizo SLE patients. The aim of this study was to determine the association between homocysteinemia and episodes of renal insufficiency.

Patient Characteristic	Proportion (%) with Homocysteinemia	p-value
Sex		
Female	256/1550 (17%)	<0.0001
Male	42/135 (31%)	
Race		
Caucasian-American	116/860 (13%)	<0.0001
African-American	167/684 (24%)	
Other	15/141 (11%)	
Income		
<$25,000	118/412 (29%)	
$25,000-$50,000	58/357 (16%)	<0.0001
$50,000-$75,000	41/268 (15%)	
$75,000+	63/539 (12%)	
Education		
HS or less	129/524 (25%)	<0.0001
College	134/795 (17%)	
Some Graduate School	28/327 (9%)	
Ever Smoker		
No	171/1095 (16%)	0.0024
Yes	127/590 (22%)	
History of Malar Rash		
No	150/885 (17%)	0.39
Yes	148/708 (19%)	
History of Discoid Rash		
No	231/1340 (17%)	0.37
Yes	66/342 (19%)	
History of Photo Sensitivity		
No	154/804 (19%)	0.14
Yes	144/878 (16%)	
History of Oral Ulcers		
No	143/752 (19%)	0.21
Yes	155/931 (17%)	
History of Musculoskeletal manifestations		
No	71/474 (15%)	0.066
Yes	227/1209 (19%)	
History of Proteinuria		
No	102/957 (11%)	<0.0001
Yes	195/726 (27%)	
History of Serositis		
No	130/849 (15%)	0.010
Yes	168/836 (20%)	
History of Neurologic Manifestations		
No	249/1507 (17%)	0.0003
Yes	49/178 (28%)	
History of Hematologic Manifestations		
No	102/549 (19%)	0.50
Yes	196/1136 (17%)	
History of Immunologic Manifestations		
No	42/275 (15%)	0.25
Yes	256/1410 (18%)	
History of Anticardiolipin		
No	147/808 (18%)	0.58
Yes	148/863 (17%)	
History of prolonged RVVT		
No	201/1208 (17%)	0.060
Yes	96/467 (21%)	

ACR 2019-homocysteine-Table1
Table-1 Prevalence of Homocysteinemia by time-invariant patient characteristics

Methods: A total of 1,688 SLE patients, diagnosed according to the SLICC or ACR classification criteria, had at least one homocysteine measurement. Among these, 341 had two visits with homocysteine measurement, 572 had three or more. Patients were followed quarterly per protocol. First, patients were classified as having homocysteinemia if their average homocysteine level was above 15 umol/L. and demographic and clinical subgroups were compared

with respect to prevalence of homocysteinemia. Second, we used a longitudinal regression model to explore whether homocysteine levels were associated with serum creatinine levels longitudinally. Third, to assess whether a history of homocysteine was associated with episodes of renal insufficiency, we assessed whether there was a relationship between past measures of homocysteine and episodes of renal insufficiency (defined as serum creatinine exceeding 1.5 mg/dl). For each visit, we calculated the mean homocysteine level based on previous homocysteine levels and those with a mean level over 15 mg/dl were considered as a visit with previous homocysteinemia. We used a multivariable GEE model to assess the association between previous homocysteinemia and later renal insufficiency.

Results: 295 of the patients (17.7%) had homocysteinemia. Patients who were male, African-American, had a smoking history, proteinuria, and neurological manifestations were more likely to have homocysteinemia (Table 1). In the longitudinal analysis, we observed that those patients with generally higher levels of homocysteine tended to have higher levels of serum creatinine and that changes in homocysteine coincided with changes in serum creatinine. Specifically, a 1 umol /L increase in mean homocysteine levels was associated with a 0.04 mg/dl increase in serum creatinine (CI: 0.03, 0.04) ($p< 0.0001$). To assess the relationship between homocysteine and episodes of renal insufficiency, 10779 visits were identified after homocysteinemia, while 43651visits occurred following normal homocysteine levels. The proportion of visits with renal insufficiency was significantly higher in visits following a history of homocysteinemia (21% vs 3%). This association remained significant after adjusting for age, gender, ethnicity, hydroxychloroquine use, previous low C3, and previous proteinuria (CI: 2.7, 6.3) ($p< .0001$).

Conclusion: Homocysteinemia is a strong predictor of renal insufficiency even after adjusting for potential confounders. Homocysteine is a modifiable risk factor, as combination B-vitamins (B6, B12, and folic acid) can reduce it. Although treatment of homocysteinemia fell out of favor for prevention of cardiovascular outcomes, it should be reconsidered for the prevention of renal insufficiency. Longitudinal studies are needed.

Disclosure: H. Babaoglu, None; **J. Li**, None; **D. Goldman**, None; **L. Magder**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 1606

Association of African- American Ethnicity and Smoking Status and Total and Individual Damage Index in Systemic Lupus Erythematosus

Romy Kallas,[1] Jessica Li,[1] and Michelle Petri[1], [1]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Smoking and African- American ethnicity are risk factors for systemic lupus erythematosus (SLE). Smoking has been associated with increased prevalence of SLE, increased disease activity and decreased effectiveness of hydroxychloroquine in cutaneous lupus. The objective of the study was to determine the association between smoking status and total damage, as well as individual damage items, in SLE by ethnicity.

Methods: We analyzed data from a longitudinal Lupus Cohort. Damage was recorded using the Systemic Lupus Erythematosus International Collaborating Clinics/ American College of Rheumatology (SLICC/ACR) Damage Index. Poisson regression was used to model the total damage score against ever smoking. Cox regression was used to assess the relationship between time to damage items and ever smoking, stratified by ethnicity. Adjusted hazard ra-

	All		African American		Caucasian	
	HR[1] (95% CI)	p-value	HR[2](95% CI)	p-value	HR[2] (95% CI)	p-value
Angina OR coronary artery bypass	1.55 (1,2.39)	0.0498	1.41 (0.65,3.04)	0.387	1.84 (1.06,3.19)	0.0309
Myocardial infarction ever	1.75 (1.15,2.67)	0.0085	1.52 (0.79,2.91)	0.2117	2 (1.12,3.55)	0.0183
Pericarditis>6 months, OR pericardiectomy	0.51 (0.19,1.33)	0.1679	0.2 (0.04,0.91)	0.0378	2.02 (0.44,9.42)	0.3684
Claudication x6 months	2.74 (1.31,5.73)	0.0072	2.97 (0.9,9.79)	0.0735	2.54 (0.99,6.55)	0.0529
Venous thrombosis with swelling, ulceration, OR venous stasis	0.55 (0.3,0.98)	0.043	0.47 (0.19,1.19)	0.1129	0.58 (0.27,1.24)	0.1592
Muscle atrophy or weakness	1.47 (0.78,2.75)	0.2331	0.77 (0.31,1.93)	0.5834	2.51 (0.99,6.39)	0.0528
Scarring chronic alopecia	1.68 (0.95,2.98)	0.0734	1.67 (0.89,3.14)	0.1112	1.83 (0.47,7.08)	0.3827
Extensive scarring or panniculum other than scalp and pulp space	2.57 (1.2,5.5)	0.0152	2.9 (1.17,7.15)	0.0211	1.96 (0.47,8.24)	0.3569
Skin ulceration (not due to thrombosis) for more than 6 months	2.39 (1,5.75)	0.0508	2.72 (0.77,9.67)	0.1211	2.07 (0.61,7.07)	0.2446
[1]Adjusted for sex, race, age at diagnosis, and years of education [2]Adjusted for sex, age at diagnosis, and years of education						

Abstract- ACR 2019-RomyKallas-Table1
Table 1 - Adjusted Associations Between Damage Index Items and Smoking Status

tios (HR) and 95% confidence intervals were reported. For each damage item, patients who had a damage diagnosis prior to or at the date of SLE diagnosis were excluded in the analysis.

Results: The study included 2629 patients. The prevalence of ever smokers was 35.8%. There was no significant difference in total damage score between eve smokers and never smokers after adjustment. Table 1 summarizes the Damage Index findings.

Ever smokers had more atherosclerotic cardiovascular (angina, coronary bypass, myocardial infarction and claudication) damage and skin damage compared to non-smokers. Caucasian SLE patients who ever smoked were more likely to have muscle atrophy. African- American patients who ever smoked were more likely to have any skin damage.

Conclusion: Smoking is a modifiable factor for organ damage in SLE. Our analysis proved the major effect was on cardiovascular damage (angina, coronary bypass, myocardial infarction and claudication). Surprisingly, these cardiovascular damage items have higher hazard ratios in Caucasian smokers. Smoking also increased some skin damage items. These skin damage items hazard ratios were higher in African-Americans.

Disclosure: R. Kallas, None; **J. Li**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 1607

Risk Factors for Avascular Necrosis in SLE: A Multivariate Model

Romy Kallas,[1] Jessica Li,[1] and Michelle Petri[1], [1]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus patients, particularly those who received corticosteroids are at high risk of avascular necrosis (AVN). A past meta-analysis identified other risk factors including African-American ethnicity, active disease, Raynaud's, arthritis, cyclophosphamide use, and IgM anticardiolipin antibodies. In this analysis, we determined the predictors of AVN in a longitudinal lupus cohort in which Caucasian and African-American ethnicities were well represented.

Methods: We analyzed data from 1986 until April 2019. AVN was recorded using the Systemic Lupus Erythematosus International Collaborating Clinics/ American College of Rheumatology (SLICC/ACR) Damage Index. Cox regression was used to identify variables that were associated with time to AVN. First, we assessed the univariate relationship between each variable and time to AVN. Those variables with significant association with time to AVN were then entered into the multivariable model; the ones that remained significant were retained in the final model. Variables that were highly colinear with highest prednisone were not included in the same model. Hazard ratios (HR) and 95% confidence intervals were reported.

	HR (95% CI)	p-value
Highest dose of prednisone with duration		
None	Ref	
1-40 mg/day for <1 months	2.24 (0.5 ,10)	0.2911
1-40 mg/day for >=1 months	3.04 (0.9 ,10.3)	0.0736
40-60 mg/day for <1 months	2.02 (0.45 ,9.06)	0.3577
40-60 mg/day for >=1 months	5.61 (1.68 ,18.79)	0.0052
60+ mg/day for <1 months	10.17 (3.16 ,32.74)	0.0001
60+mg/day for >=1 months	9.79 (3.09 ,30.96)	0.0001
Ethnicity		
Caucasian	Ref	
African American	1.99 (1.48 ,2.68)	<.0001
Other	2.01 (1.15 ,3.51)	0.0138
Gender: male	1.66 (1.07 ,2.57)	0.0236
Year of SLE diagnosis (per 5 year difference)	0.90 (0.84, 0.96)	0.0008
History of vasculitis	1.57 (1.15 ,2.16)	0.0049
History of obesity	1.47 (1.1 ,1.97)	0.0102
Other variables not significantly predictive of AVN included education level, hypertension, low complement, anti-RNP, anti-Sm, history of lupus anticoagulant, ESRD, and cytotoxic drugs.		

ACR Abstract-AVN and SLE_MP_Table1
Predictors of Avascular Necrosis

Results: This analysis included 2477 patients who were 92.2% female, 39.1% African American, and 52.8% Caucasian. Non- Caucasian patients, male gender, obesity and history of vasculitis conferred a higher risk of AVN. Patients who received prednisone doses more than 60 mg had 10 times the risk of having an AVN, regardless of the duration of treatment, compared to patient who did not receive any prednisone. Patient who were on prednisone 40 mg daily had 6 times the risk of having AVN if the duration of treatment was more than 1 month compared to those who did not receive any prednisone (Table 1). The association between AVN and antiphospholipid antibodies (lupus anticoagulant) was only significant in the univariate analysis.

Conclusion: Prednisone dose remains the most important predictor of AVN. At doses below 60 mg, AVN occurrence is dependent on the duration of highest prednisone dose. However, for doses above 60 mg, the risk is independent of the duration. The major reduction in AVN incidence in later decades likely reflects lower use of such high prednisone doses. Particular attention should be paid to avoidance of prednisone at 60 mg doses in African-Americans, given the doubling of risk of AVN as compared to Caucasians.

Disclosure: R. Kallas, None; **J. Li**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 1608

Effect of the Metabolic Syndrome on Renal Function Decline in Four Rheumatic Diseases: An 8-year Longitudinal Analysis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To study the effect of the metabolic syndrome (MetS) on renal function decline in four rheumatic diseases.

Methods: Consecutive patients who fulfilled the ACR/SLICC criteria for systemic lupus erythematosus (SLE), EULAR/ACR criteria for rheumatoid arthritis (RA), ASAS criteria for spondyloarthritis (SpA) and the CASPAR criteria for psoriatic arthritis (PSA) were recruited in 2009/2010. At entry, patients recruited had measurement of body weight, height, waist circumference and blood pressure. MetS was defined by the updated joint consensus criteria, using the Asian criteria for central obesity, when ≥3 of the following were present: (1) waist ≥90cm in men or ≥80cm in women; (2) blood pressure ≥130/85mmHg or requiring therapy; (3) serum triglyceride level ≥1.7mmol/L; (4) serum HDL-chol ≤1.0mmol/L in men and 1.3mmol/L in women; and (5) fasting glucose ≥5.6mmol/L. Renal function of the participants was assessed by the 4-variable MDRD formula (eGFR). Patients were followed longitudinally for eGFR change. Change in eGFR was compared between those with and without the MetS at baseline. Regression analysis was performed for the effect of MetS on eGFR decline adjusted for other confounding factors.

Results: 1497 patients were studied (693 RA, 577 SLE, 121 SpA and 106 PSA). The age at entry was highest in RA (53.4±12.0 years) and lowest in SpA (39.0±11.9 years). Disease duration was longest in SLE (9.3±7.2 years) and shortest in PSA (3.6±3.2 years). MetS was present in 137 RA (20%), 85 SLE (15%), 13 SpA (11%) and 39 PSA (37%) patients. Patients were followed for 91.1±12.1 months. The mean decline of eGFR (ml/min/1.73m2) at last observation from baseline was 5.00±13.5 in RA, 4.16±11.6 in SpA, 3.95±12.3 in PSA and 8.93±16.4 in

SLE (p=0.03; one-way ANOVA). The proportion of patients with eGFR decline by ≥10% was also greatest in SLE (41%) compared with RA (29%), SpA (24%) and PSA (25%) patients (p< 0.001). Among patients with SLE, a significantly more profound drop in eGFR over 8 years was observed in patients with the MetS at baseline (-17.8±26%) than those without (-7.6±18%; p=0.002). The difference in last eGFR between patients with and without the MetS was significant after adjustment for baseline eGFR, age and sex (65.5±32.2 vs 88.4±24.4 ml/min/1.73m2; p< 0.001). In a linear regression model, eGFR at last follow-up was significantly associated with the baseline eGFR (slope 0.72 SE 0.03; Beta 0.77; p< 0.001), renal involvement (slope -4.36 SE 1.30; Beta -0.08; p=0.001) and the MetS (slope -6.88 SE 1.86; Beta -0.09; p< 0.001). In patients with RA/SpA/PSA, eGFR also showed a greater trend of decline over time in those with MetS than without, but the difference did not reach statistical significance.

Conclusion: Among patients with common rheumatic diseases, SLE showed the greatest decline in renal function over time. presence of MetS in SLE significantly accelerated renal function decline over time independent of the presence of renal disease. The MetS also unfavorably affected eGFR in patients with inflammatory arthritis. A more detailed analysis on the causes of eGFR decline in individual diseases and a longer period of follow-up of the renal function is needed.

Disclosure: C. Chu, None; **C. Mok**, None; **L. Ho**, None; **C. To**, None.

Abstract Number: 1609

Organ Damage Free Survival in Southern Chinese Patients with Active Lupus Nephritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical Poster II: Comorbidities
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To study the organ damage free survival and its predictive factors in patients with active LN.

Methods: Consecutive patients who fulfilled ≥4 ACR/SLICC criteria for SLE and with biopsy proven active LN between 2003 and 2018 were retrospectivey analyzed. Those with organ damage before LN onset were excluded. Data on renal parameters and treatment regimens were collected. Complete renal response (CR) was defined as normalization of serum creatinine (SCr), urine P/Cr (uPCR) < 0.5 and inactive urinary sediments. Partial renal response (PR) was defined as ≥50% reduction in uPCR and < 25% increase in SCr. Organ damage of SLE was assessed by the ACR/SLICC damage index (SDI). The cumulative risk of having any organ damage or mortality since LN was studied by Kaplan-Meier's analysis. Factors associated with a poor outcome were studied by a forward stepwise Cox regression model, with entry of covariates with p< 0.05 and removal with p >0.10.

Results: 273 LN patients were identified but 64 were excluded (organ damage before LN onset). 211 LN patients were studied (92% women; age at SLE 30.4±13.5 years; SLE duration at LN 1.9±3.1years). 47 (22%) patients had nephrotic syndrome and 60 (29%) were hypertensive. Histological LN classes was: III/IV±V (75.1%), I/II (7.8%) and pure V (17.1%) (histologic activity and chronicity score 7.0±4.2 and 1.8±1.5, respectively). Induction regimens were: prednisolone (33.1±17.5mg/day) in combination with intravenous cyclophosphamide (CYC) (21.4%; 1.0±0.2g per

pulse), oral CYC (8.6%; 96.4±37.8mg/day), azathioprine (AZA) (14.3%; 78.6±25.2mg/day), mycophenolate mofetil (MMF) (22.8%; 1.9±0.43g/day) and tacrolimus (TAC) (17.1%; 4.3±1.1mg/day). After a follow-up of 8.6±5.4 years, 94(45%) patient developed organ damage (SDI≥1) and 21(10%) patients died. The commonest organ damage was renal (36.3%) and musculoskeletal (17.9%), and the causes of death were: infection (38.1%), malignancy (19.0%), cardiovascular events (9.5%) and ESRF complications (9.5%). At last visit, 114 (55%) patients survived without any organ damage. The cumulative organ damage free survival at 5, 10 and 15 years after renal biopsy was 73.5%, 59.6% and 48.3%, respectively. The 5, 10 and 15-year renal survival rate were 95.2%, 92.0% and 84.1% respectively. In a Cox regression model, nephritic relapse (HR 3.72[1.78-7.77]), proteinuric relapse (HR 2.30[1.07-4.95]) and older age (HR 1.89[1.05-3.37]) were associated with either organ damage or mortality, whereas CR (HR 0.25[0.12-0.50]) at month 12 were associated with organ damage free survival. Baseline SCr, uPCR and histological LN classes were not significantly associated with a poor outcome. Among patients with class III/IV LN, the long-term organ damage free survival were not significantly different in users of MMF (reference) from CYC (IV/oral) (HR 1.45[0.76- 2.75]) or TAC (HR 1.03[0.26-1.62]) as induction therapy.

Conclusion: Organ damage free survival is achieved in 55% of patients with active LN upon 9 years of follow-up. CYC/MMF/TAC based induction regimens did not differ for the long-term outcome of LN. Targeting complete renal response and preventing renal relapses remain important goals of LN treatment.

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Abstract Number: 1610

Prediction of Organ Damage Accrual in Systemic Lupus Erythematosus Using a Frailty Index

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SESSION INFORMATION
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Background/Purpose: We previously constructed a frailty index (FI) as a measure of susceptibility to adverse outcomes among patients with systemic lupus erythematosus (SLE). In this work, higher baseline FI values were associated with increased mortality risk during follow-up. However, the association with other clinically important health outcomes has not been described. Therefore, the objective of the current study was to estimate the association of baseline FI values with the risk of subsequent organ damage accrual in a large, prospective, international, inception cohort of SLE patients.

Methods: Patients fulfilling ≥ 4 ACR classification criteria for SLE were recruited within 15 months of diagnosis and were assessed annually for medication use, comorbidities, disease activity (SLEDAI-2K), organ damage [SLICC/ACR Damage Index (SDI)], health-related quality of life [Short-Form 36 (SF-36)], and other measures.

For our analysis, the baseline visit was defined as the first at which both SDI and SF-36 data were available as both instruments, in addition to other variables, were used to generate the baseline FI scores. We determined organ damage accrual during follow-up by subtracting the baseline SDI score from the SDI score at the final study visit. Any change in SDI ≥ 1 defined damage accrual.

Multivariable negative binomial regression was used to estimate the association between baseline FI values and the rate of change in SDI scores per patient-year of follow-up, adjusting for relevant demographic and clinical characteristics. Model fit was evaluated using likelihood ratio (LR) tests and Akaike information criterion (AIC) values.

Results: The 1,549 SLE patients (84.8% of the cohort) eligible for this analysis were mostly female (88.7%) with mean (SD) age 35.7 (13.3) years and median (IQR) disease duration 1.2 (0.9-1.5) years at baseline. Mean (SD) baseline FI score was 0.17 (0.08) with a range from 0 to 0.51.

Over a mean (SD) follow-up of 7.2 (3.7) years, 653 patients (42.2%) had an increase in SDI score. Higher baseline FI values (per 0.05 increment) were associated with higher rates of change in SDI scores during follow-up (Incidence Rate Ratio [IRR] 1.19; 95% CI 1.13-1.25), after adjusting for age, sex, ethnicity/region, post-secondary education, baseline SLEDAI-2K, baseline SDI, and baseline use of corticosteroids, antimalarials, and immunosuppressives.

The addition of the baseline FI to the multivariable model was associated with significant improvement in model fit (LR test statistic 40.49 [p< 0.001]) and relative predictive quality (change in AIC = 3563.60 - 3602.09 = -38.49). Furthermore, the association between the baseline FI and subsequent damage accrual persisted when overlapping damage items were omitted from the FI (IRR 1.12; 95% CI 1.08-1.16) and when the analysis was restricted to the subgroup of patients without organ damage (SDI=0) at the baseline visit (IRR 1.21; 95% CI 1.14-1.30).

Conclusion: Frailty, measured using an FI, predicts organ damage accrual among SLE patients and provides added prognostic value when considered in addition to existing SLE measures. This further supports the FI as a valid and robust health measure in SLE.

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Abstract Number: 1611

Systemic Lupus Erythematosus Registries: Are the Measures Captured in the Real World Similar to Those in Clinical Trials?

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SESSION INFORMATION
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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease that causes connective tissue inflammation and can result in multiple organ damage. Registries may be a valuable source of real-world data that complements randomized clinical trial data.

To 1) identify SLE registries, 2) determine what measures are collected within the registries, and 3) determine which registries capture metric(s) and/or endpoints which have been collected within a SLE clinical trial.

Methods: Utilizing the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISM) guidelines, we conducted a systematic review of the literature search using PubMed, EMBASE, and Scopus databases between 2012 to the present and a gray literature search to identify SLE registries. We reviewed each registry for the following criteria: 1) population diagnosed with SLE, who were 16 years or older; 2) published in English language; and 3) contained content on any of the following measures or endpoints; Short-Form(SF)-36, SRI (SLE responder index),

Characteristic	Registries
Collect SLEDAI, PGA	Monash Lupus Clinic Hopkins Lupus Cohort Childhood Arthritis and Rheumatology Research Alliance (CARRA) International registry-unknown name Swiss Systemic lupus erythematosus Cohort Study (SSCS) Plaquenil LUpus Systemic: PLUS Study
Collect SLEDAI, BILAG	UK BIOGEAS Jiangsu Rheumatology Associates British Isles Lupus Assessment Group Biologics Registry UK Juvenile SLE Cohort Study
Collect SLEDAI, SF36	Asia Pacific Lupus Collaboration 1000 Canadian Faces of Lupus Lupus Outcomes Study
Collect PGA, SF-36	Lupus in Minorities; Nature vs. nurture (LUMINA)
Collect biobank data	UK Juvenile SLE Cohort Study Asia Pacific Lupus Collaboration SPOCS
Collect SF-36	Asia Pacific Lupus Collaboration Lupus Outcomes Study LuLa Study LUMINA 1000 Canadian Faces of Lupus

Table 1: Overview of SLE Registries

SLEDAI (SLE Disease Activity Index), PGA (physician global assessment), BILAG (British Isles Lupus Activity Group), Systemic Lupus Collaborating Clinics (SLICC) damage index, Lupus Quality of Life (LupusQoL), Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue, healthcare utilization, clinical outcomes (e.g. flares) or biobank information.

Results: A total of 41 SLE registries were identified. No registry captures all the components of the SRI-4, the SLEDAI, BILAG, and PGA. Ten registries collect 2 components of the SRI-4 (Table 1). Four SLE registries capture the SF-36 and 3 registries collect biobank data (Table 1). There is at least 1 SLE registry in each of the 4 main regions of the world; North America, Europe, Asia Pacific, and Latin America.

Conclusion: There is variability among the measures collected by SLE registries. Many of the SLE registries capture a subset of measures common to those collected by SLE clinical trials. It appears that measures collected by SLE clinical trials are not necessarily the same as those captured in real world settings. Additional research is needed to develop validated measures which may be captured within clinical trials as well as within real world settings such as registries.

Disclosure: J. Lofland, Janssen Scientific Affairs, LLC, 3; **E. Wan**, Janssen Scientific Affairs, LLC, 3, 9; **P. Berry**, Janssen Scientific Affairs, LLC, 3; **C. Karyekar**, Abbott, 3, BMS, 3, Janssen, 1, 3, Janssen Scientific Affairs, LLC, 3, Novartis, 3.

Abstract Number: 1612

Disease Activity and Cognitive Function in Systemic Lupus Erythematosus

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SESSION INFORMATION

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Session Type: Poster Session (Monday)

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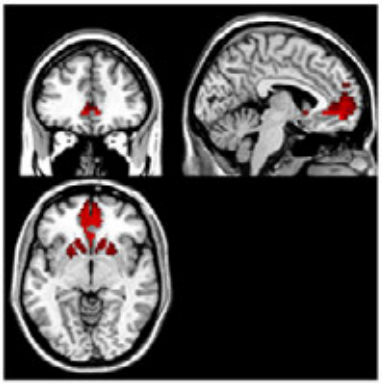
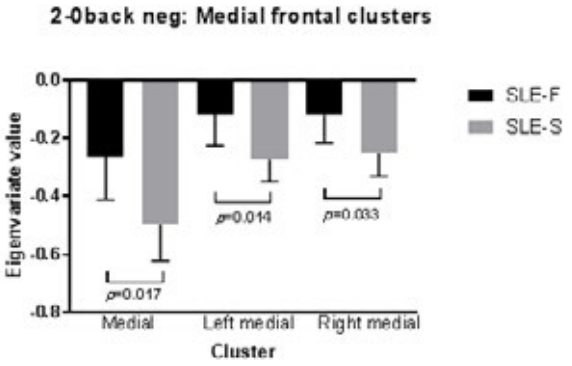
Background/Purpose: Cognitive dysfunction (CD) is a common symptom in systemic lupus erythematosus (SLE), that significantly affects quality of life but there are limited treatment options available. There are many factors causative of CD which are shared with other chronic diseases. However, CD is more prevalent in SLE than in other conditions, such as rheumatoid arthritis. This suggests a direct link between SLE and CD but the effect of disease activity on CD in SLE is still unclear. The aim of this study was to investigate the effects of active disease in SLE on CD. We compared cognitive measures in SLE patients with stable disease activity (SLE-S) to those with active disease (SLE-F).

Table 1: Baseline characteristics, SLE-S vs SLE-F

	Variable	SLE-F (n=24)	SLE-S (n=34)	p-value
		Mean (S.D.), Median (LQ, UQ) or n (%)		
Demographic and clinical	Age (years)	36 (12)	39 (11)	0.330
	Disease duration (years from diagnosis)	10 (8)	12 (7)	0.470
	BILAG global score	12 (9, 16)	1 (0, 2)	**<0.001**
	Oral corticosteroids (y/n)	15 (63)	12 (35)	0.061
	Current immunosuppressant use	18 (75)	14 (41)	**0.016**
	Current antimalarial use	18 (75)	19 (58)	0.261
	Biologic medication	4 (17)	3 (9)	0.432
Depression & anxiety	MADRS	8 (4, 12)	4 (1, 8)	**0.003**
	HADS – A	6 (5, 10)	6 (3, 10)	0.713
CANTAB® task scores (Higher is better except where indicated with *)	Visual memory* *(Total errors adjusted)*	28 (17, 75)	28 (19, 63)	0.897
	Verbal memory *(Maximum = 18)*	9 (2)	10 (3)	0.135
	Attention *(Maximum = 27)*	18 (15, 22)	13 (12, 20)	0.063
	Emotion processing *(Percentage correct)*	62 (10)	62 (9)	0.727
	Executive function* *(Mean choices to correct)*	1.3 (1.3, 1.6)	1.4 (1.3, 1.7)	0.981
	Spatial working memory* *(Between errors)*	107 (56)	112 (57)	0.793





The medial frontal cluster includes the medial frontal cortex, superior frontal cortex-medial segment, anterior cingulate gyrus and frontal pole.

The left and right frontal clusters include the putamen, accumbens, caudate and subcallosal area.

Figure 1 Differences in BOLD response between the SLE-S and SLE-F groups during the n-back (working memory task), 2-0back condition, negative main effect.

Table 2: Significant correlations for change in SLE-F results between v1 and v2 (v2 minus v1)

Variable	n-back task condition	Cluster	r_s	*p*-value
MADRS	2-0back positive main effect	Left angular gyrus	-0.670	0.004
		Right angular gyrus	-0.604	0.013
		Right middle temporal gyrus	-0.594	0.015
		Parietal	-0.656	0.006
BG-VRS		Parietal	0.567	0.022
IL-6		Frontal	-0.618	0.011
FSMC-Cog	2-0back negative main effect	Cingulate gyrus	0.509	0.044
VCAM-1		Cingulate gyrus	-0.541	0.030

MADRS: Montgomery Asberg Depression Rating Scale, BG-VRS: Basal Ganglia Virchow-Robin spaces, IL-6: Interleukin-6, FSMC-Cog: The Fatigue Scale for Motor and Cognitive Functions, VCAM-1: Vascular Cell Adhesion Molecule-1

Methods: 34 SLE-S and 24 SLE-F were recruited, all meeting 1997 ACR or SLICC criteria. Active disease was defined as BILAG A or B with a change in treatment. Stable disease was defined as SLEDAI-2K ≤4. 17/24 SLE-F patients were assessed again at a 2nd visit (v1 vs v2), approximately 4 months later. CD was measured using a computerized battery of tests (CANTAB®). fMRI was used to examine neuronal responses to a working memory and attention task (n-back) and a facial emotional processing task (FERT). Analyses compared the SLE-S to the SLE-F group and SLE-Fv1 to SLE-Fv2 for "responders" only. Responders were defined as having a decreased BILAG score at their second visit. Exploratory correlations were also undertaken, for all of the SLE-F group who had 2 visits, using delta scores. fMRI data were analysed using SPM12. All other data were analysed using SPSS 22.

Results: There were no differences between the SLE-S and SLE-F groups or between v1 and v2 on demographic and clinical measures except disease activity. The SLE-F group scored higher than the SLE-S group on the MADRS depression scale (p=0.003) but no other significant differences in psychiatric symptoms were observed. There were no significant differences on CANTAB® performance for either comparison (table 1). The fMRI showed a SLE-S vs

SLE-F difference in n-back related response in the medial prefrontal cortex (p=0.012; figure 1) but no differences on the FERT. There were no differences in the n-back or FERT for the SLE-F v1 vs v2 comparison. However, the exploratory correlations showed changes in BOLD signal response were associated with changes in the MADRS (depression score), BG-VRS (basal ganglia Virchow-Robin spaces), IL-6, vascular cell adhesion molecule-1 (VCAM-1) and FSMC-cognition (cognitive fatigue measure) (table 2).

Conclusion: Flares in SLE are associated with both increased inflammatory markers and depression scores. Compensatory brain mechanisms to maintain cognitive function may negatively affect mood during flares and this adversely affects overall cognitive function independent of the active phase response. Reduction in inflammation over time also influences cognitive function and so consideration of mood and disease activity is needed when treating flares.

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Abstract Number: 1613

LDL-cholesterol as a Risk Factor of Progression to ESRD in Patients with Lupus Nephritis

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SESSION INFORMATION
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Background/Purpose: There are few data on the effect of dyslipidemia in patients with lupus nephritis (LN). Thus, we investigated the effect of low-density lipoprotein-cholesterol (LDL-C) on the progression to end-stage renal disease (ESRD) in patients with biopsy-proven LN.

Methods: We followed 121 LN patients who underwent kidney biopsy and were subsequently treated with immunosuppressive drugs. Sociodemographic, clinical, laboratory (including lipid profile), and treatment-related data at the time of kidney biopsy and during follow-up were obtained by a review of patients' charts. Patients were divided into two groups related to the mean LDL-C level: < 100 mg/dL and ≥100 mg/dL. Cox's proportional regression analysis was performed to identify the independent predictors of progression to ESRD in LN patients.

Results: Seventy-one of 121 biopsy-proven LN patients (58.7%) showed more than 100 mg/dL of LDL-C at the time of LN diagnosis. The higher LDL-C group excreted more 24-hour urine protein (p=0.003), and showed a higher proportion of proliferative LN (p=0.013) and an activity score >12 (p=0.023). During a mean follow-up of 83.0 (range, 12–171) months, ESRD was more frequent in the higher LDL-C group than in the lower group (15.5% vs.

2.0%; *p*=0.012). In the multivariate Cox's proportional regression analysis, LDL-C ≥100 mg/dL (hazard ratio [HR], 171.340; *p*=0.012), estimated glomerular filtration rate during the renal biopsy (HR, 0.977; *p*=0.005), statin exposure during follow-up (HR, 0.163; *p*=0.031), relapse (HR, 9.752; *p*=0.036), and complete remission at 1-year of treatment (HR, 0.034; *p*=0.003) were significant predictors of progression to ESRD in LN patients.

Conclusion: Our findings suggest that dyslipidemia at the onset of LN is an independent risk factor for predicting the development of ESRD in LN patients. Therefore, lipid profile should be monitored carefully and managed aggressively to avoid the deterioration of kidney function in patients with LN.

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Factors Associated with Peripheral Neuropathies in Patients with Systemic Lupus Erythematosus: A Single Center Experience

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SESSION INFORMATION
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Table 1. Clinical Characteristics of lupus patients with peripheral neuropathies

	ANP n= 45 (49.5%)	MNP n=17 (18.9%)	DNP n= 20 (21.9%)	p value
Previous visit (3 months):				
Cumulative damage (SLICC/SDI), Md (IQR)	0.1 (0-0.3)	0(0-0.1)	0 (0-0.1)	0.011
Alopecia n(%)	3 (6.7%)	1 (5.9%)	7 (35%)	0.006
Nephropathy n(%)	26 (57.8%)	14 (82.4%)	8 (40%)	0.033
Hemolytic anemia n(%)	10 (22.2%)	0	0	0.009
At the time of PNP				
Age, years, Md (IQR)	48 (29.5-57)	31 (25-37.5)	35.5 (27.8-40)	0.003
Time (months) between SLE and the PNP, Md (IQR)	120 (18-179)	82 (9-118.5)	12 (2.5-80.2)	0.0001
SLEDAI -2k, Md (IQR)	4 (0-8)	8 (4.5-14)	4 (2-14.2)	0.009
Methylprednisolone, n(%)	4 (15.4%)	15 (88%)	13 (65%)	0.000
Cyclophosphamide, n(%)	3 (6.7%)	15 (88%)	6 (30%)	0.000

ANP: Sensory or sensory motor axonal neuropathy, MNP: Multiplex Mononeuropathy, DNP: Demyelinating neuropathy

Table 2. Logistic regression model (Dependent variable: APN vs. MNP + DNP)

	OR	IC 95%	p value
Cumulative damage, SLICC/SDI (previous visit)	1.89	1.096-3.259	0.022
Age (years)	1.054	1.007-1.103	0.23
Time between SLE diagnosis and the PNP* (months)	1.007	1-1.013	0.04

*PNP: peripheral neuropathies

Background/Purpose: The prevalence of peripheral neurological manifestations in Systemic Lupus Erythematosus (SLE) ranges between 1.5% and 27% and are a major cause of morbidity.

To determine associated factors with the different neurophysiological patterns in peripheral neuropathies in patients with systemic lupus erythematosus.

Methods: A retrospective study was performed. We included patients with SLE (ACR 1997 and SLICC 2012 criteria), who presented a PNP associated with SLE according to ACR 1999 nomenclature, from January 2014 to December 2018. Patients were classified according to the neurophysiologic pattern by the Neuromuscular Clinic Disorders at our Institute in 3 groups: 1. Sensory or sensory-motor axonal neuropathy (ANP). 2. Multiplex Mononeuropathy (MNP), and 3. Demyelinating neuropathy (DNP). Clinical information including demographics and SLE characteristics were gathered from the clinical chart and reviewed by an expert rheumatologist in three different moments: Previous visit (3 months before to PNP presentation); at the time of PNP presentation, and one year after. Demographic characteristics: gender, age, Body Mass Index (BMI), and comorbidities. Lupus characteristics: ACR criteria, the time between SLE diagnosis and PNP presentation, ACR / 2012 criteria, disease activity (SLEDAI-2K), cumulative damage (ACR/SLICC-DI), and treatment were compared. One year after, disease activity, cumulative damage, and treatment were reviewed. Statistical analysis: Mann-Whitney U, Chi-squared test and Fisher exact test were used as appropriate. Multiple comparisons and logistic regression analysis was made.

Results: Ninety one PNP were included, 45 (49.5%) ANP, 17 (18.9%) MNP, and 20 (21.9%) DNP. Demographics and comorbidities were similar between groups. At previous visit, the (SLICC/SDI) was higher in APN group compared with MNP and DNP (table 1). Patients with DNP presented more frequently cutaneous manifestations (alopecia) compared with MNP and ANP (table1). Patients with MNP had more nephropathy compared with ANP and DNP, and patients with APN had more hemolytic anemia compared with other groups (table 1).

At the time of PNP presentation, patients with ANP were older and had a long time between SLE diagnosis and the PNP presentation, compared with MNP and with DNP (table 1). Patients with MNP had higher disease activity compared with ANP and DNP groups (table 1). Pulses of methylprednisolone, cyclophosphamide, and higher doses of prednisone were used in the MNP compared with DNP and ANP group ($p < 0.05$). One year after, disease activity and cumulative damage were similar between groups. In the logistic regression analyses, older age, the time between SLE diagnosis and PNP presentation, and cumulative damage in the previous visit were factors independently associated with APN compared with MNP and DNP (table 2).

Conclusion: ANP was the most frequent PNP. Patients with MNP have more disease activity than the other groups. MNP and DNP considered more severe and received more aggressive treatment than APN. Factors independently associated with APN were older age, have a longer time between SLE diagnosis and the PNP presentation and have more damage 3 months previous the PNP presentation.

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Abstract Number: 1615

The Effects of Anti-glutamate Receptor Subunit Antiantibodies on Systemic Lupus Erythematosus Without Neuropsychiatric Involvement

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SESSION INFORMATION
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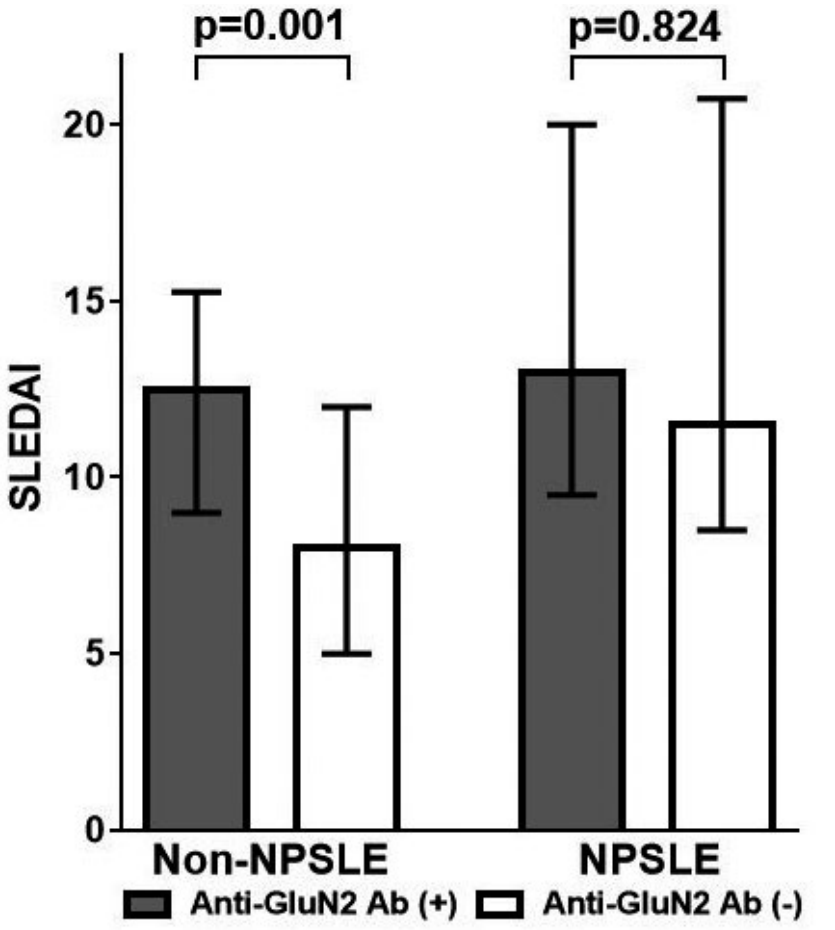

Fig.1 SLEDAI by anti-GluN2 Ab presence

Background/Purpose: Autoantibodies against N-methyl-D-aspartate receptor subunit GluN2 (anti-GluN2) in the cerebrospinal fluid are known to be related with the development of diffuse psychiatric/neuropsychological manifestations in NPSLE. However, relation with serum anti-GluN2 antibody (Ab) is unknown. The aim of this study is to clarify the association of damages due to SLE disease activity and serum anti-GluN2 Ab.

Methods: Sera were collected from SLE patients with active disease (N=132), anti-GluN2 Ab were measured in ELISA and clinical information was collected from the past medical history retrospectively.

Results: Patients were subdivided into those complicated with NPSLE (n=37) and those without NPSLE (non-NPSLE) (n=95). Among the NPSLE patients, anti-GluN2 Ab positivity and negativity made no difference in SLEDAI. Whereas, SLEDAI was significantly higher in patients with positive anti-GluN2 Ab (p=0.001) than those with negative within non-NPSLE patients (Fig. 1). In addition, there was significant positive correlation between SLEDAI and anti-GluN2 titers only in non-NPSLE patients (p< 0.001). In univariate analysis using components of SLEDAI, the positivity for anti-GluN2 Ab was a significant risk for complicating pleuritis, arthritis, fever, leukocytopenia, the positivity for anti-dsDNA Abs or hypocomplementemia. Multivariate analysis resulted with high odds ratio (OR) for fever (OR 9.19, 95% confidence interval (CI) 2.42-46.70, p=0.003) and hypocomplementemia (OR 12.74, 95%CI 2.37-103.28, p=0.007) in non-NPSLE patients with positive anti-GluN2 Ab.

Conclusion: Anti-GluN2 existing in serum can be pathogenic autoantibodies, causing damages related to lupus activity even in SLE patients without complicating NPSLE.

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Abstract Number: 1616

Do All Antiphospholipid Antibodies Confer the Same Risk for Major Organ Involvement in Systemic Lupus Erythematosus Patients?

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SESSION INFORMATION

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	Arterial thrombosis	Venous thrombosis	Small vessel thrombosis	Fetal death	≥3 pregnancy losses
LA	4.45 (3.2-6.3) p<0.001	4.9 (3.8-6.3) p<0.001	4.7 (3.2-7) p<0.001	1.7 (1.2-2.5) p<0.001	4.1 (2.2-7.3) p<0.001
aB2GP IgM	3.5 (2.3-5.2) p<0.001	1.8 (1.3-2.3) p=0.001	2.7 (1.6-4.3) p<0.001	2.2 (1.4-3.5)p=0.001	4.6 (2.3-9)p<0.001
aB2GP IgG	6.5 (4.4-9.5) p<0.001	3.2 (2.3-4.4) p<0.001	3.7 (2.3-5.8) p<0.001	1.8(1.1-2.9) p=0.024	5.2 (2.7-10) p<0.001
aCL IgM	2.4 (1.8-3.4) p<0.001	2.4 (1.9-3.0) p<0.001	4 (2.8-5.8) p<0.001	1.7 (1.2-2.4) p=0.006	3.1 (1.8-5.3) p< 0.001
aCL IgG	7.3 (5.2-10.2) p<0.001	4 (3.2-5.0) p<0.001	4 (2.8-5.7) p<0.001	1.9 (1.4-2.6) p<0.001	3.8 (2.2-6.6) p<0.001

Table 2 ACR

Background/Purpose: Antiphospholipid antibodies (aPL) have been associated with organ damage and certain features in SLE patients. Our aim is to investigate the association between the different aPL and SLE manifestations as well as to elucidate the influence of the load of antibodies.

Methods: Patients from the RELESSER-T registry were included. RELESSER-T is a multicenter, hospital-based registry, with retrospective cross-sectional collection of data from a large representative sample of adult non-selected patients with SLE attending Spanish rheumatology services from the public national health system.

Results: Out of a total of 3651 SLE patients, 1368 were aPL positive (24.8 % were positive for IgG anticardiolipin (aCL) antibodies, 20.1% for IgM aCL, 13.5% showed positivity for IgG antib2glycoprotein I (aB2GPI) and 13.8% for IgM aB2GPI. Lupus anticoagulant (LA) was positive in 24% of patients). Regarding the load of antibodies, 20.6%, 12.1% and 4.8% were positive for one, two and three antibodies respectively. The association between the different aPL, the number of positive antibodies and antiphospholipid syndrome related manifestations is showed in Table 1. Overall, all types of aPL were associated with classic APS manifestations, although LA, IgG isotypes, and patients with more than one aPL display a higher risk to develop clinical APS. Regarding specific lupus manifestations, all aPL types showed a negative association with cutaneous manifestations. LA and aCL were associated with an increased risk of haematological, ophthalmological and neuropsychiatric manifestations ($p< 0.001$). Furthermore, LA was also associated with an increased risk of renal disease ($p< 0.001$). IgG isotypes were associated with a higher risk of specific lupus manifestations compared with IgM. IgG aCL were associated with an increased risk of cardiac and respiratory manifestations. When evaluating the influence of the load of antibodies, we found that the risk of neuropsychiatric manifestations significantly increased with a higher number of positive antibodies (OR for one antibody was 1.19 and 1.7 for 2 and 3 antibodies). Inversely, the risk of cutaneous symptoms decreased while the number of positive antibodies increased (OR=0.9 for one antibody, OR=0.8 for double positivity and OR=0.7 for triple positivity).

Conclusion: There is a hierarchy for aPL and the risk of APS and SLE manifestations. aCL, and especially LA, confer a higher risk for major organ involvement in SLE patients. IgG isotypes seem to have a more important role. The load of aPL confer a higher risk for APS and certain SLE manifestations

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Platelet Bound Complement Split Product (PC4d) May Be a Marker of Platelet Activation and Cardiovascular Events in Systemic Lupus Erythematosus

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SESSION INFORMATION
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Background/Purpose: Cell-bound complement activation products (CB-CAPs), including platelet bound C4d (PC4d), are sensitive markers for diagnosis and evaluation of lupus activity. Presence of PC4d is associated with antiphospholipid antibodies and thrombotic events in SLE, but its role in cardiovascular (CV) disease is not fully understood. The current study investigates if PC4d is a biomarker for CV disease in SLE.

Methods: In a cohort of 96 SLE patients, we evaluated the association between PC4d and clinical and subclinical cardiovascular (CV) disease, defined by CV events and/or presence of coronary artery calcium (CAC), respectively. Blood was collected and PC4d levels, measured by flow cytometry, were reported as positive or negative, defined by a cutoff of 20 mean fluorescence intensity (MFI). CV events were defined as any medical record documentation or self-report of a myocardial infarction or ischemic cerebrovascular accident. Non-contrast CT chest, performed when required for routine clinical care, was used for calculating CAC scores. Demographics, disease characteristics, and cardiovascular comorbidities were ascertained. Disease activity was assessed using SLE Disease Activity Index 2000 (SLEDAI-2K).

Results: 96 SLE patients were included (41±13 years old, 91% female, 35% Caucasian, 31% Hispanic, 19% African American, disease duration 12±7 years). SLE patients met on average 6±2 ACR-SLE classification criteria. All were ANA+, 64% were dsDNA+, 31% antiphospholipid (aPL) antibodies positive. Average SLE disease activity was 6±5, 39% had lupus nephritis. CV comorbidities included: 19% had a history of smoking, 26% had hypertension, 7% were diabetic and 8% had hyperlipidemia. Average total cholesterol level was 173±53 mg/dL. A positive PC4d level was detected in 16% (n=15). 13% (n=12) had a history of a CV event while CAC >0 was detected in 37% of the 38 patients with available scores. There was no association between history of CV event and presence of CAC >0 (p=0.62). PC4d was associated with history of a CV event (OR 5.3 95% CI 1.4-19.9 p=0.008) but not with the presence of CAC >0 (35% vs 50%, p=0.62). Additionally, positive PC4d was associated with low complement levels (60% vs 21%, p=0.001), history of thrombocytopenia by ACR criteria (47% vs 15%, p=0.004), a lower platelet count (253±81 vs. 148±58 x cells/μL, p=0.0001) and a larger platelet volume (11±1.1 vs 12±1.4fL p=0.003) at the time of PC4d measurement. In a multivariable model, the association between CV events and PC4d, as well as between platelet count/volume and PC4d, remained significant and independent of aPL status or low complement.

Conclusion: In this pilot study, the presence PC4d was associated with history of CV events, lower platelet counts, and larger mean platelet volumes, suggesting that PC4d may be a marker for complement-mediated platelet activation and morphological change, as well as arterial thrombotic events in SLE. No association was found between

		SLE (n=96)		
	SLE (n=96)	PC4d NEG (n=81)	PC4d POS (n=15)	p-value*
Age, years	41 ± 13	42 ± 13	38 ± 12	0.38
Female, n(%)	87 (91%)	74 (91%)	13 (87%)	0.63
Race/ethnicity				
White, n (%)	34 (35%)	29 (36%)	5 (33%)	0.85
Hispanic, n (%)	30 (31%)	27 (33%)	3 (20%)	0.38
Black, n (%)	18 (19%)	13 (16%)	5 (33%)	0.12
Disease duration in years	12 ± 7	11 ± 7	15 ± 7	0.11
SLEDAI-2K	6 ± 5	5 (2-8)	8 (3-15)	0.13
ACR Criteria, total	6 ± 2	6 ± 2	6 ± 2	--
Malar rash	60 (63%)	51 (63%)	9 (60%)	0.83
Discoid rash	28 (29%)	25 (31%)	3 (20%)	0.54
Photosensitivity	49 (51%)	44 (54%)	5 (33%)	0.14
Mucositis	28 (29%)	22 (27%)	6 (40%)	0.32
Arthritis	81 (84%)	67 (83%)	14 (93%)	0.45
Serositis	36 (38%)	28 (35%)	8 (53%)	0.17
Renal disease	37 (39%)	31 (38%)	6 (40%)	0.90
Neurological	9 (10%)	7 (9%)	2 (13%)	0.63
Hematological	59 (62%)	45 (56%)	14 (93%)	**0.008**
Hemolytic anemia	5 (5%)	3 (4%)	2 (13%)	0.17
Leukopenia	25 (26%)	21 (26%)	4 (27%)	1.00
Lymphopenia	45 (47%)	37 (46%)	8 (53%)	0.59
Thrombocytopenia	19 (20%)	12 (15%)	7 (47%)	**0.004**
Low Serum Complement	26 (27%)	17 (21%)	9 (60%)	**0.002**
Platelet Count, x10^3 cells/μL	237 ± 87	253 ± 81	148 ± 58	**0.001**
Mean Platelet Volume, fL	11 ± 1.2	11 ± 1.1	12 ± 1.4	**0.003**
Antibodies				
ANA, n (%)	96 (100%)	81 (100%)	15 (100%)	-
ds-DNA antibody, n (%)	61 (64%)	49 (61%)	12 (80%)	0.15
SSA antibody, n (%)	40 (42%)	33 (41%)	7 (47%)	0.67
SSB antibody, n (%)	10 (10%)	8 (10%)	2 (13%)	0.65
Sm antibody, n (%)	33 (34%)	26 (32%)	7 (47%)	0.28
RNP antibody, n (%)	47 (49%)	37 (46%)	10 (67%)	0.14
Antiphospholipid antibodies, n (%)	30 (31%)	25 (31%)	5 (33%)	0.85
Hypertension, n (%)	25 (26%)	20 (25%)	5 (33%)	0.39
Diabetes, n (%)	7 (7%)	6 (8%)	1 (7%)	1.00
Ever smoker n (%)	18 (19%)	14 (17%)	4 (27%)	0.39
BMI, kg/m^2	28 ± 7	28 ± 7	27 ± 5	0.58
Total cholesterol, mg/dL	173 ± 53	176 ± 54	156 ± 42	0.20
HDL, mg/dL	56 ± 19	57 ± 19	51 ± 19	0.35
LDL, mg/dL	93 ± 42	96 ± 43	80 ± 34	0.23
Medication use, current				
Aspirin use, n (%)	29 (30%)	24 (30%)	5 (33%)	0.77
Statin use, n (%)	12 (14%)	8 (10%)	4 (27%)	0.07
Antimalarials, n (%)	81 (84%)	70 (88%)	11 (73%)	0.23
Non-biologic DMARDs, n (%)	44 (46%)	36 (45%)	8 (53%)	0.55
Biologics, n (%)	20 (21%)	16 (20%)	4 (27%)	0.58
Glucocorticoids, n (%)	32 (33%)	25 (31%)	7 (47%)	0.27
Cardiovascular disease				
Coronary artery calcium > 0	14/38 (37%)	12/34 (35%)	2/4 (50 %)	0.62
CVA or MI	12 (13%)	7 (9%)	5 (33%)	**0.008**

PC4d and subclinical atherosclerosis or CV events and subclinical atherosclerosis, further supporting that CV events in SLE are not entirely mediated through traditional CV risk factors.

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Abstract Number: 1618

Factors Associated with Damage Accrual in SLE Patients with No Clinical or Serological Disease Activity

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: SLE – Clinical Poster II: Comorbidities

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Accrual of irreversible organ damage is a major risk factor for death in SLE. While unmodifiable factors, such as age at disease onset and ethnicity, are associated with increased damage accrual in SLE, disease activity and medications, in particular glucocorticoids, are also associated. Understanding the independent contribution of glucocorticoid use to organ damage in SLE is confounded by the fact that glucocorticoid use is associated with active disease. We determined factors contributing to the risk of damage accrual in SLE independent of disease activity by studying patients who had no measurable disease activity.

Methods: SLE patients were prospectively recruited from 13 centres in 8 countries and followed longitudinally between 2013-2016. Disease activity (SLEDAI-2K) and treatment details were recorded at each visit, and organ damage measured annually (SDI). Cox-proportional hazards analyses were used to examine time-dependent associations of variables with damage accrual. The absence of disease activity was defined as time-adjusted mean (TAM)-SLEDAI-2K=0.

Results: 1707 patients were studied. Patient characteristics are shown in Table 1. 157 patients (9%) had no clinical or serological disease activity for the entire study period (TAM-SLEDAI-2K=0). Prednisolone exposure was 66% (103/157) in this group, with a median TAM-prednisolone dose of 2.0mg/day (0.0-5.9). Forty-one per cent (65/157) of patients had irreversible organ damage at baseline. Despite SLEDAI-2K=0 throughout, accrual of irreversible organ damage occurred in 13% of this subset, with 21 events captured over a median (IQR) 1.9 (1.0-2.3) years follow-up. In univariable analysis of time-adjusted mean variables, prednisolone exposure was associated with damage accrual (HR 1.1, 95% CI 1.0-1.3, p=0.05), as was physician global assessment (PGA) (HR 1.15, 95% CI 1.0-1.3, p=0.01). Baseline SDI organ damage, gender and ethnicity were not associated with damage accrual in this subset (Table 2). In multivariable analysis, damage accrual was independently associated with prednisolone exposure (HR 1.14, 95% CI 1.03-1.25, p=0.01), physician global assessment (PGA) (HR 1.13, 95% CI 1.03-1.23, p=0.01) and age at enrolment (HR 1.04, 95% CI 1.01-1.07, p< 0.02) (Table 3).

	SLEDAI-2K=0
	(n=157)
Patient characteristics at enrolment	
Age at enrolment (yrs)	49.1 (40.7, 57.3)
Age at diagnosis (yrs)	37.0 (27.0, 47.0)
Disease duration at enrolment (yrs)	9.0 (5.0, 16.0)
Study observation period (yrs)	1.9 (1.0, 2.3)
Total number of visits	5.0 (5.0, 7.0)
Female	149 (94.9%)
Asian ethnicity	143 (91.1%)
Current smoker at enrolment (%)	8 (6.2%)
Medication details	
No. patients on prednisolone ever	103 (65.6%)
Cumulative prednisolone (g)	1.2 (0.0, 2.7)
TAM prednisolone (mg/d)	2.0 (0.0, 5.0)
No. patients on immunosuppressants ever	74 (47.1%)
No. patients with anti-malarials ever	85 (54.1%)
Clinical indications	
TAM SLEDAI	0.0 (0.0, 0.0)
TAM PGA	0.2 (0.0, 0.4)
Baseline SDI score	0.0 (0.0, 1.0)
No. patients SDI>0 at baseline (n, %)	65 (41.4%)
No. patients with SDI damage accrual during study (n, %)	21 (13.4%)

Table 1. Baseline Patient and Disease Characteristics

	HR	(95% CI)	p-value
Age at enrolment	1.04	(1.01,1.07)	0.01
Female	1.15	(0.18,7.36)	0.88
Asian ethnicity	0.84	(0.22,3.21)	0.80
Current smoker	1.14	(0.16,8.04)	0.89
TAM prednisolone	1.13	(1.00,1.28)	0.05
Anti-malarials ever	1.24	(0.56,2.74)	0.59
Other immunosuppressants ever	0.55	(0.22,1.35)	0.19
TAM PGA	1.15	(1.04,1.28)	0.01
Baseline SDI damage	1.2	(0.54,2.67)	0.66

Table 2 Univariable associations of damage accrual in patients with no clinical or serological disease activity as measured by SLEDAI-2K throughout the study period (N=157)

Conclusion: Irreversible damage accrual occurs in SLE patients with no clinical or serological disease activity as captured by SLEDAI-2K. Glucocorticoid use contributes to the risk of organ damage in these patients. These findings confirm an independent contribution of glucocorticoid use to organ damage accrual in SLE.

	HR	(95% CI)	p-value
Age at enrolment	1.04	(1.01,1.07)	0.01
TAM prednisolone	1.14	(1.03,1.26)	0.01
TAM PGA	1.13	(1.03,1.23)	0.01

Table 3 Multivariable associations of damage accrual in patients with no clinical or serological disease acitivity measured by SLEDAI-2K throughout the study period (N=157)

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Abstract Number: 1619

Early Vascular Ageing as a Predictor of Future Cardiovascular Events and Mortality in Systemic Lupus Erythematosus Patients: A Prospective Cohort Study

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SESSION INFORMATION
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Background/Purpose: Systemic Lupus Erithematosus (SLE) is associated with increased cardiovascular (CV) risk compared with general population; an accelerated atherosclerosis is considered the main underlying mechanism. Arterial Stiffness (AS) is considered a reliable surrogate marker of arterial wall dysfunction and an independent predictor of cardiovascular events in the general population. Several studies showed that AS in SLE patients is abnormally in-

CV risk factor	N patients (%)
Smoking habit	20 (30.7%)
Diabetes	1 (1,6%)
Hypertension	21 (32.8%)
Dyslipidemia	17 (26.6%)
Antiphospholipids Syndrome	13 (20%)
Overweight (BMI≥25)	19 (29.2%)
Obesity (BMI≥30)	7 (10.8%)

Table 1 CV risk factors

creased with respect to healthy controls; however, the prognostic value of AS has not been fully evaluated in patients with SLE. The aim of the study was to evaluate the predictive value of AS for major cardiovascular events, mortality and poor renal outcome in SLE patients.

Methods: Consecutive SLE patients classified according to the 1997 ACR criteria were enrolled for this study. At baseline, demographics, clinical history, menopause status, cumulative dose of glucocorticoid (GC), traditional CV risk factors, disease activity and organ damage (according to SELENA-SLEDAI and SLICC/DI respectively) were recorded; AS was assessed by measuring carotid-femoral pulse wave velocity (PWV). The patients were prospectively followed, and the following outcomes were evaluated at last observation: major events (including IMA, PTCA, mortality due to CV events, overall mortality, stroke, TIA); poor renal outcome (end-stage renal disease, dialysis or renal transplantation).

Results: A total of 65 patients were included (63 Caucasian, %, 63 females, %). At baseline, median age was 41.5 ± 11.9 years, median disease duration was 14 years (IQR 9-24). As for cumulative organ involvement, the most prevalent was cutaneous involvement (n= 48, 75%), followed by renal (n=31, 48.4%), serositis (n=10, 15.6%) and neuropsychiatric (n=10, 15.6%). Cumulative median dose of GC was 16.75 g (IQR 10.25-30.00). Fifteen patients (23.1%) presented active disease (SLEDAI >4) at the time of enrolment, 19 (29.2%) had at least one organ damage (SLICC >0); in those patients the median SLICC-DI resulted 2 (IQR 1-3). The prevalence of traditional CV risk factors is reported in table 1. Overall, at baseline PWV resulted 7 (IQR 6.35-8.45) and vascular age 48 (IQR 39.3-60.0). During the observational period (mean duration of follow-up 4.5 ± 2.4 years), 7 major events occurred in seven patients (10.8%), namely: 5 patients suffered from IMA, 1 from stroke; one death also occurred, for non-CV cause (sepsis). Only one patient developed a poor renal outcome, requiring dialytic treatment and then renal transplant. CV events occurred at median age of 43.8±9.8 years. At univariate cox-regression analysis, baseline age (OR= 1.078) , PWV (OR= 1.71) and vascular age (OR= 1.08) all resulted predictors of future major events ($p< 0.01$; $p< 0.01$; $p< 0.02$ respectively); baseline SLICC was also predictive of major events ($p< 0.01$).

Conclusion: These data suggest that arterial stiffness could be considered a reliable marker of early vascular aging in patients with SLE and its predictive value for cardiovascular events was confirmed in this population. Thus, these data support the utility of the vascular ageing assessment to set-up preventive strategies tailored on the single patient.

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Abstract Number: 1620

T-cell Exhaustion in Prolonged Remission SLE Patients

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Background/Purpose: Cellular exhaustion is a cellular dysfunction characterized by the progressive loss of the effector function, and an increased expression of multiple inhibitory receptors. Exhaustion develops after repetitive stimulation and a high antigenic load. Remission in SLE can be defined as the lack of clinical and serological activity for a specific period, and it has been associated with less accrual damage, and number and severity of flares. Cellular exhaustion has been associated with a better outcome in autoimmune diseases, such as SLE and antibody associated vasculitis.

To identify exhausted CD8+ T-cells populations in prolonged remission SLE patients, active SLE patients, and in healthy subjects.

Methods: We performed a transversal exploratory study. We included patients classified with SLE according to the revised SLE ACR 1997 and SLICC 2012 criteria. Three groups were studied: 1. Prolonged remission SLE (PR SLE): patients with SLE in clinical remission of the disease, defined as a SLEDAI-2K of 0 (excluding hypocomplementemia and high anti-DNA titers), and absence of corticosteroid or immunosuppressant treatment for at least 10 continuous years. 2. Active SLE: patients with SLE with clinical activity measured with SLEDAI-2K. 3. Healthy controls: paired by gender and age ± 5 years with PR SLE group. Flow cytometry was performed to measure the expression of surface and intracellular markers associated to exhausted T CD8+ lymphocytes (Table 1). Percentage of T cells was determined using FlowJo software v10. Leukocyte counts and percent lymphocytes were used to determine the absolute lymphocytes subset counts (cells/μL) of the different subpopulations. Descriptive statistics and multiple comparisons were performed between groups.

Results: We included 15 patients in each group, with an age of 49 years (48 – 60) in the PR SLE patients, 33 (30 – 46) in active SLE, and 47 (44 – 48) in healthy controls. No difference was found between age of PR SLE and healthy controls. In PR SLE patients, disease duration of SLE was 308 (230 – 425) months, and in active SLE 111 (69 – 161) months. Duration of remission state in PR SLE was 203 (146 – 248) months. The exhausted CD8+ lymphocytes analysis between groups is shown in table 2. Comparing PR SLE patients with active SLE patients with Mann Whitney U test, differences were found in CD8+2B4+ % ($p = 0.049$), CD8+2B4+ a ($p = 0.014$), CD8+2B4+PD-1+ a ($p = 0.012$), CD8+PD-1+ a ($p = 0.040$), CD8+Tim-3+PD-1+ a ($p = 0.023$), CD8+T-bet+ % (PR SLE 65.4 [33.3 – 71.7] vs Active SLE 28.1 [10.7 – 59.2], $p = 0.010$), CD8+EOMES+ % (PR SLE 42.9 [21.1 – 68.5] vs Active SLE 13.9 [10.5 – 37.2], $p = 0.029$), CD8+EOMES+ a (PR SLE 111.6 [58.3 – 321.4] vs Active SLE 46.2 [22.3 – 133.7], $p = 0.024$), CD8+T-bet+EOMES+ % (PR SLE 25.0 [18.9 – 47.6] vs Active SLE 9.86 [4.44 – 20.7], $p = 0.010$), and CD8+T-bet+EOMES+ a (PR SLE 93.4 [48.1 – 161.7] vs Active SLE 24.3 [8.1 – 92.3], $p = 0.014$).

Table 1. Markers of exhaustion in CD8+ T cells.

2B4+	CD38+HLA-DR+PD-1+
PD-1+	T-bet+
2B4+PD-1+	EOMES+
Tim-3+	T-bet+EOMES+
Tim-3+PD1+	

Table 2. Exhausted CD8+ lymphocyte populations in PR SLE, Active SLE, and healthy subjects.

		PR SLE N = 15	Active SLE N = 15	Healthy Subjects N = 15	p
Lymphocytes	%	36 (27.2 – 40)	18 (12.9 – 32)	31.5 (27.2 – 38.8)	**0.003**
	cells/µL	1.67 (1.23 – 2.76)	1.12 (0.74 – 1.71)	1.77 (1.28 – 2.76)	**0.017**
CD3+CD8+	%	20.7 (12.3 – 25.3)	20.7 (19.1 – 22.2)	2.14 (1.60 – 2.39)	ns
	cells/µL	384.0 (222.63 – 565.0)	283.5 (224.0 – 434-92)	461.48 (322.26 – 507.78)	ns
CD8+2B4+	%	62.30 (43.20 – 77.30)	43.30 (22.20 – 56.70)	61.10 (50.30 – 77.90)	**0.023**
	cells/mL	73.82 (25.18 – 205.68)	22.49 (10.13 – 67.73)	70.63 (32.32 – 257.92)	**0.011**
CD8+PD-1+	%	36.50 (29.10 – 48.10)	28.50 (13.70 – 43.30)	30.90 (24.60 – 38.10)	ns
	cells/mL	74.05 (16.46 – 127.34)	18.01 (3.69 – 46.48)	38.52 (19.15 – 139.10)	ns
CD8+2B4+PD-1+	%	27.24 ± 13.31	19.14 ± 12.88	26.06 ± 11.07	ns
	cells/mL	98.49 (46.64 – 183.45)	39.44 (20.43 – 75.62)	99.75 (39.64 – 128.10)	**0.037**
CD8+Tim-3+	%	1.01 (0.28 – 2.91)	0.71 (0.37 – 2.66)	0.96 (0.57 – 2.22)	ns
	cells/mL	2.29 (0.57 – 8.59)	0.50 (0.038 – 5.04)	1.25 (0.55 – 7.57)	ns
CD8+Tim-3+PD-1+	%	0.77 (0.17 – 2.19)	0.21 (0.14 – 0.62)	0.13 (0.01 – 0.59)	**0.021**
	cells/mL	2.50 (0.77 – 11.08)	0.64 (0.45 – 2.02)	0.55 (0.044 – 1.98)	**0.021**
CD8+CD38+HLA-DR+PD-1+	%	5.78 (3.03 – 10.20)	4.74 (2.21 – 12.04)	2.07 (1.07 – 3.40)	**0.011**
	cells/mL	34.91 (9.73 – 62.53)	20.52 (6.08 – 57.14)	15.26 (5.40 – 17.47)	ns
CD8+T-bet bright	%	6.98 (4.41 – 12.00)	4.72 (0.48 – 9.65)	5.32 (2.77 – 12.20)	ns
	cells/mL	2.15 (1.07 – 3.59)	1.41 (0.32 – 2.65)	1.79 (0.85 – 4.33)	ns
CD8+T-bet dim	%	15.30 (10.40 – 19.00)	8.34 (4.69 – 23.80)	11.90 (8.04 – 17.70)	ns
	cells/mL	5.29 (2.40 – 9.74)	2.89 (1.10 – 9.11)	3.46 (2.32 – 5.24)	ns

ns = not statistically significant.
The lymphocytes populations are shown in Median and IQR, for both the percentage of CD8+ T cells (%) and in absolute lymphocytes counts (a). Kruskal – Wallis test was performed to compare between the three groups, a p value < 0.05 was considered statistically significant.

Conclusion: SLE patients in prolonged remission express more exhausted CD8+ T cells than patients with active SLE. These findings support that cellular exhaustion is inherent to a better clinical outcome.

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Abstract Number: 1621

The Impact of Disease Activity and Related Factors on Cognitive Dysfunction in SLE

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Table 1

Subject Characteristics		SLE (N = 74)	HC (N = 74)	*p*	Flare (N=23)	Stable Active (N=29)	Inactive (N=22)	*p*
Age *(mean # years +/- SD, range)*		37.6 +/- 9.6 (22 – 57)	36.2 +/- 9.4 (18 – 55)	p=0.377	37.3 +/- 10.9 (23 – 57)	38.8 +/- 8.4 (23 – 53)	36.5 +/- 9.8 (22 – 55)	p=0.705
Ethnicity (Hispanic/Latino)		13 (17.6%)	14 (18.9%)	p=0.831	6 (26.1%)	3 (10.3%)	4 (18.2%)	p=0.332
Race	Black	45 (60.8%)	41 (55.4%)	p=0.787	16 (69.6%)	17 (58.6%)	12 (54.5%)	p=0.165
	White	16 (21.6%)	19 (25.7%)		4 (17.4%)	4 (13.8%)	8 (36.4%)	
	Other	13 (17.6%)	14 (18.9%)		3 (13.0%)	8 (27.6%)	2 (9.1%)	
Education Level *(mean # years +/- SD, range)*		15.7 +/- 2.4 (10 – 22)	16.2 +/- 2.5 (7.5 – 21)	p=0.198	15.6 +/- 2.5 (11 – 20)	15.9 +/- 2.3 (12 – 19)	15.6 +/- 2.6 (10 – 22)	p=0.887
Computer Experience	Extensive	20 (27.0%)	34 (45.9%)	p=0.022	7 (30.4%)	7 (24.1%)	6 (27.3%)	p=0.644
	Moderate	41 (55.4%)	35 (47.3%)		11 (47.8%)	19 (65.5%)	11 (50%)	
	Some	13 (17.6%)	5 (6.8%)		5 (21.7%)	3 (10.3%)	5 (22.7%)	
Tobacco	Current	4 (5.4%)	3 (4.1%)	p=0.609	2 (8.7%)	1 (3.4%)	1 (4.5%)	p=0.233
	Ever	4 (5.4%)	7 (9.5%)		0	3 (10.3%)	1 (4.5%)	
Occupation	Executive/professional	14 (18.9%)	18 (24.3%)	p=0.008	4 (17.4%)	8 (27.6%)	2 (9.1%)	p=0.356
	Skilled worker	16 (21.6%)	19 (25.7%)		3 (13%)	8 (27.6%)	5 (22.7%)	
	Semi-skilled worker	16 (21.6%)	28 (37.8%)		7 (30.4%)	3 (10.3%)	6 (27.3%)	
	Unskilled worker	5 (6.8%)	2 (2.7%)		1 (4.3%)	1 (3.4%)	3 (13.6%)	
	Unemployed	23 (31.1%)	7 (9.5%)		8 (34.8%)	9 (31%)	6 (27.3%)	
Cognitive dysfunction self-report		33 (44.6%)	2 (2.7%)	p=0.000	13 (56.5%)	13 (44.8%)	7 (31.8%)	p=0.249
Pertinent History	Hypertension	28 (37.8%)	0	p=0.000	9 (39.1%)	10 (34.5%)	9 (40.9%)	p=0.885
	Thrombosis	11 (14.9%)	1	p=0.003	5 (21.7%)	3 (10.3%)	3 (13.6%)	p=0.508
	Psychiatric illness requiring medication	7 (9.5%)	0	p=0.013	2 (8.7%)	2 (6.9%)	3 (13.6%)	p=0.710

SESSION INFORMATION
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Background/Purpose: Attribution of cognitive dysfunction (CD) to SLE is compromised by potential confounders. Studies reveal conflicting results on the relationship between CD and disease activity, likely due to testing differences, subject demographics, comorbidities (NPSLE in particular), and small sample sizes. We assessed cognition in a large cohort of SLE subjects compared to healthy controls (HC) to determine the impact of disease activity.

Methods: Seventy-four adult SLE subjects that met ACR criteria, had no history of NPSLE or other CNS deficits, and 74 age, gender and racially matched HC underwent cognitive testing and assessments for depression, pain, fatigue, sleepiness, anxiety and anger. SLE subjects were assessed for disease activity and medication use. Exclusion criteria included alcohol or illicit drug dependence/abuse, infection, and current narcotic/psychiatric medication use.

Table 2

Cognitive and Behavioral Test Performance	SLE (N = 74)	HC (N = 74)	*p*	Flare (N=23)	Stable Active (N=29)	Inactive (N=22)	*p*
Automated Neuropsychological Assessment Metric (ANAM)							
Simple Reaction Time (SRT) *visuomotor processing speed, simple motor speed, attention*	363.8 +/- 88.0	321.1 +/- 65.4	p=0.001	366.6 +/- 94.4	347.7 +/- 76.8	382.0 +/- 95.0	p=0.407
Matching Grids (MG) *visuospatial processing*	29.6 +/- 9.9	34.0 +/- 11.8	p=0.022	31.1 +/- 11.0	30.0 +/- 10.5	27.5 +/- 7.7	p=0.476
Match to Sample (MS) *working memory, visuospatial processing*	25.5 +/- 8.6	31.8 +/- 12.0	p=0.001	26.4 +/- 9.6	26.4 +/- 8.5	23.4 +/- 7.5	p=0.455
Running Memory (CPT) *vigilance, sustained attention, working memory*	73.4 +/- 14.7	84.0 +/- 15.6	p=0.000	75.7 +/- 14.9	71.6 +/- 16.1	73.3 +/- 12.9	p=0.620
Spatial Processing Simultaneous (SP) *mental rotation, visuospatial skills*	24.0 +/- 7.0	26.3 +/- 8.8	p=0.257	23.7 +/- 5.9	25.3 +/- 7.1	22.6 +/- 7.8	p=0.377
2x2 array							
Non-Spatial Memory Test (NSM) *working memory*	1.8 +/- 0.6	2.1 +/- 0.7	p=0.001	1.7 +/- 0.5	1.9 +/- 0.6	1.8 +/- 0.5	p=0.437
Spatial Memory Test (SM) *spatial memory*	3.6 +/- 1.1	4.3 +/- 1.6	p=0.008	3.6 +/- 1.2	3.7 +/- 1.0	3.7 +/- 1.2	p=0.818
Behavioral tests							
Beck Depression Index (BDI) score, range: 0 – 63 Median +/- IQR (range)	9.0 +/- 12.3 (0 – 44)	1.5 +/- 3.0 (0 – 34)	p=0.000	10.0 +/- 12.0 (0 – 28)	10.0 +/- 13.5 (0 – 30)	2.5 +/- 8.0 (0 – 44)	p=0.002[a]
# BDI scores > 13 (%) (clinically significant scores)	19 (25.7%)	1 (1.4%)	p=0.000	9 (39.1%)	8 (27.6%)	2 (9.1%)	p=0.067
Pain Numerical Rating, range: 0 - 10 Median +/- IQR (range)	1.5 +/- 4.0 (0 – 8)	0.0 +/- 0.0 (0 – 7)	p=0.000	3.0 +/- 5.0 (0 – 8)	1.0 +/- 4.5 (0 – 8)	0.0 +/- 2.0 (0 – 8)	p=0.015[b]

SLE disease activity status was categorized as “Flare” (met SELENA SLEDAI Flare Index criteria), “Stable active” [clinical SLEDAI (all descriptors other than serology) > 0 or PGA > 0.5 or prednisone > 10 mg and lack of flare], and “Inactive” (clinical SLEDAI = 0 and PGA ≤ 0.5 and prednisone ≤ 10 mg and lack of flare). Differences in group characteristics and test performance were assessed between SLE and HC (t-test and/or Mann Whitney), and among the SLE disease activity groups (ANOVA with post-hoc Tukey’s). The impact of variables on individual test performance was determined by multivariable modeling for SLE versus HC and SLE only grouped by disease activity; variables on univariate screen ($p < 0.1$) were included.

Results: There were no demographic differences among SLE and HC groups (Table 1). Compared to HC, SLE scored worse on most tests and this poor performance was driven by increased reaction time rather than poor accuracy for most tests (Table 2). Among SLE subjects, disease activity did not impact test performance; unexpectedly, inactive SLE performed the worst compared to HC (Table 2). Multivariable models demonstrate significant impacts of 1) SLE, age (as expected), Black race, depression, anger, computer experience and history of psychiatric illness in SLE ver-

Table 3: Final results of multivariable models to determine predictors of test performance

Variables Significantly Impacting Test Performance	Individual Cognitive Tests*						
SLE versus HC	**SRT**	**MG**	**MTS**	**CPT**	**SP**	**NSM**	**SM**
Inactive SLE (versus HC)	X	X	X				
SLE (versus HC)				X			
Black race (versus Other)	X	X			X	X	X
Age	X	X	X	X	X	X	X
History of psychiatric illness requiring medication	X			X			
Depression score		X			X		
Anger score				X		X	X
Decreased computer experience (versus extensive)						X	X
SLE Only grouped by disease activity							
Age		X	X				X
History of psychiatric illness requiring medication	X		X			X	
History of thrombosis		X	X				
Decreased computer experience (versus extensive)						X	X
Increased platelet count	X	X			X		

*All of the test scores were significantly lower in SLE compared to HC except for the Spatial Processing test (SP)

sus HC and 2) age, increased platelets, history of psychiatric illness, computer experience and history of thrombosis in SLE only (Table 3).

Conclusion: Multivariable analyses suggest that poor cognitive performance is related to having SLE after controlling for other factors. Surprisingly, disease activity did not associate with performance, and unpredicted variables such as Black race, increased platelets, history of thrombosis and psychiatric illness did. Black race may be a surrogate for socioeconomic status. The potential of platelets as contributors to other neurodegenerative disease(1) supports further investigation in SLE. The paucity of associations between SLE cognitive performance and disease measures demonstrated in this study highlights the importance of continued study of biologic neurotoxic mechanisms for CD.

Reference

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Abstract Number: 1622

Cognitive Impairments in SLE Negatively Related to Participation and Quality of Life: A Systematic Review

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SESSION INFORMATION
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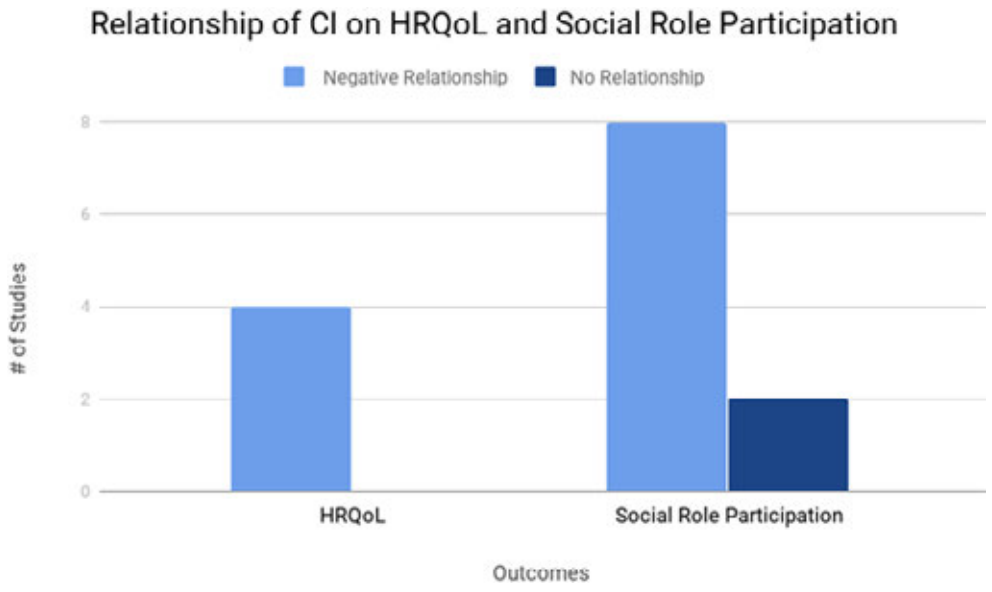
Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease affecting multiple organ systems. Approximately 33 to 43% of individuals with SLE experience cognitive impairments (CI) such as declines in attention/concentration, verbal fluency, visuo-spatial constructions, memory, processing speed and/or executive functions. Patients report significant effects of CI on Health Related Quality of Life (HRQoL), health status, and social participation roles. However, the quantitative data regarding the relationship of CI on these outcomes has not been synthesized. The objective of this review is to critically appraise and synthesize literature on the relationship of CI on HRQoL, health status, and social participation roles in individuals with SLE.

Methods: Six electronic databases were searched using a wide search strategy and the support of a librarian. Two reviewers (SA, LK) independently completed all phases of the review (title/abstract screening, full-article selection, quality rating, extraction), and a third reviewer resolved disagreement (LE). Forward and backward citation searches of included articles were completed to ensure relevant articles were identified. Fourteen articles were selected for this review.

Results: Five thousand six hundred fifty- two titles were identified and screened. Fourteen articles were included in the data extraction process. Twelve of the fourteen articles found the presence of CI negatively correlated with individuals' HRQoL and social participation roles such as employment status, academic performance and valued life ac-



tivities (**Figure 1**). The most common cognitive domains assessed in these studies were memory, attention, language and executive function. The two articles that did not find a relationship had a small sample size and unclear methodology. There was heterogeneity of measures used between studies: eight articles used different cognitive batteries, two articles used a self- report cognitive measure, and the remaining four articles used a brief cognitive screening measure to assess cognition. Three different HRQoL measures were used in the four articles examining HRQoL; all articles examining social role participation used different measures to assess social role participation. Studies were unable to be pooled for meta-analysis secondary to the heterogeneity across measures used.

Conclusion: Cognitive impairments are negatively related to HRQoL and social role participation in SLE patients. Healthcare professionals need to be aware of this relationship so that they are addressed in clinical practice. Further research is needed across different SLE patients using standardized metrics to enable pooling of data. Also, research examining a broader set of social participation roles, such as leisure, family and community roles, would provide more understanding of the effects of CI in SLE patients. Future research focusing on creating evidence-based treatment plans targeting CI, life roles participation, and/or HRQoL is needed.

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Abstract Number: 1623

Mortality in a SLE Inception Cohort of Hispanic Patients

Maria del Carmen Zamora Medina,[1] Jessica Roldan Ortega,[2] Mario Cesar Ocampo Torres,[3] Pilar Lara Reyes,[1] Ivon Bautista Mejia,[1] Alba Cicero Casarrubias,[1] and Juanita Romero-Diaz[4], [1]Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, MEXICO CITY, Mexico, [2]Monterrey Institute of Technology and Higher Education, MEXICO CITY, Mexico, [3]Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, MEXICO CITY, [4]Instituto Nacional de Ciencias Medicas y Nutricion Salvador, Zubiran Vasco de Quiroga, Mexico City, Mexico

SESSION INFORMATION
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Background/Purpose: To determine mortality and identify risk factors for mortality at 10 years in a mexican-mestizo SLE inception cohort at a tertiary care center in Mexico City.

Methods: In October 1999, an inception cohort of patients aged >16years, who were within 12 months of accrual ≥4 ACR classification criteria for SLE was assembled. At entry, patients had a standardized medical evaluation, and laboratory test. Every 3-6 months, patients were seen at the lupus clinic for medical care. Every year, information was updated, including irreversible damage index, any comorbidity and blood sample was drawn. For this purpose, we assessed disease characteristics, comorbidities, autoantibodies profile, medication, clinical and laboratory variables present at baseline and follow up (FU). Univariate and multivariate analysis were performed.

Results: Two hundred and twenty three patients were included (89.7% females, mean age 27.2±9.2 years), with a mean disease duration of 5.2 months at time of enrolment. Seventeen patients (7.62%) lost FU at our center before 10 years, so were excluded from the analysis. During FU, 34 (16.5%) have died at 10 years and 21 (61.73%) died in the first 5 years. Main causes of death were infection (35%), diffuse pulmonary hemorrhage (8.8%) and chronic renal failure (8.8%). Twenty five deaths were considered SLE related (SLE activity or morbidity). Among patients who died during first 10 years, hypertension (56% vs 39%, p=0.001), hematologic activity (97 vs 73%, p=0.002) and peripheral neuropathy (3% vs 0, p=0.02) were more prevalent. At baseline, lower serum albumin (2.8 ± 0.7 vs 3.1 ± 0.8, p=0.03),

higher proteinuria (2.6 ± 3.5gr vs 1.6 ± 2.6gr, p=0.05), C-reactive protein (4.5 ± 4.0 vs 2.8 ± 3, p=0.02) and cumulative dose of prednisone (6.3 ± 4.3gr vs 3.7 ± 3.4gr, p=0.0003) were observed in patients who died. Antimalarial use at inclusion (53% vs 26%, p=0.005) or during FU (77% vs 47%, p < 0.001) were more frequent in survivors. Male gender was not associated with an increased risk of death (10 vs 15%, p=0.41). SLICC damage index score ≥1 was more frequent in patients who died within first 10 years (8 vs 21%, p=0.03). In multivariate analysis, hematologic activity (HR 10.26, 95%CI 1.40-75.21, p=0.022) and cumulative prednisone dose at baseline (HR 1.14, 95%CI 1.06-1.23, p< 0.001) were associated with risk of death at 10 yrs. Antimalarial use or length of usage does not persist as independently associated with a protective effect for death however, only 50% of patients in the whole cohort were on antimalarials at baseline.

Conclusion: We identified baseline factors associated with 10 years mortality in a mexican-mestizo SLE inception cohort. Ten-year survival was 83.2% in the entire cohort. Almost two-thirds of deaths occurred during the first 5 years of FU. Hematologic activity and cumulative prednisone at baseline were the only factors associated with increased risk of dead at 10 years.

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Abstract Number: 1624

Progression and Factors Associated with Damage Accrual in a SLE Inception Cohort of Hispanic Patients

Maria del Carmen Zamora Medina,[1] Jessica Roldan Ortega,[2] Mario Cesar Ocampo Torres,[3] Pilar Lara Reyes,[1] Alba Cicero Casarrubias,[1] Ivon Bautista Mejia,[1] and Juanita Romero-Diaz[4], [1]Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, MEXICO CITY, Mexico, [2]Monterrey Institute of Technology and Higher Education, MEXICO CITY, Mexico, [3]Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, MEXICO CITY, [4]Instituto Nacional de Ciencias Medicas y Nutricion Salvador, Zubiran Vasco de Quiroga, Mexico City, Mexico

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Background/Purpose: The aims of our study were to determine the cumulative prevalence of damage at baseline, 5 years and 10 years of follow-up, to identify factors associated with damage accrual and incident damage in a mexican-mestizo SLE inception cohort.

Methods: Patients fulfilling the ACR classification criteria for SLE were enrolled at inception and followed-up to 10 years at a tertiary care center in Mexico City. SLICC damage index (SDI) was measured annually. Damage was defined as an SDI score ≥1 and progression or incident damage as an increase of ≥1 in SDI score compared to baseline. We assessed disease characteristics, comorbidities, medication, autoantibodies profile, clinical and laboratory variables at baseline and follow up (FU). Univariate and multivariate analysis were performed.

Results: Two hundred and twenty three patients were included (89.7% females, mean age 27.2±9.2 years), with a mean disease duration of 5.2 months at time of enrolment. At baseline, no damage was present in 200 patients (89.7%). During FU, 34 (15%) died and 48 (21%) were lost before 10 year assessment, so 141 were included for the analysis for incident damage. Eighty four (48.3%) and 88 patients (62.4%) accrued damage at 5 and 10 years,

respectively. Among patients without damage at baseline, 75 (58.6%) developed damage and 53 (41.1%) remained damage free at 10 yrs. Patients with damage at enrolment were more likely to accrue damage at 5 and 10 years FU (p< 0.001 and p< 0.003). Lupus nephritis at baseline (p=0.014 and p=0.01), lower C3 (p=0.004 and p< 0.008), lower serum albumin levels (p< 0.001 both), cyclophosphamide use (p=0.03) and a higher cumulative prednisone dose at 1 year (p=0.002 both) were more frequent in patients with damage at 5 and 10 years compared to patients with no damage. Patients with damage at 10 years showed at baseline higher SLEDAI-2K score (p=0.03), higher systolic blood pressure (p=0.006), lymphopenia (p=0.03) and lower antimalarial length usage (p=0.03), compared to patient with no damage. Patients with incident damage had higher systemic blood pressure (p=0.005), lymphopenia (p=0.03), low C3 levels (p< 0.002), higher baseline SLEDAI-2K score (p=0.03), renal activity (p=0.04) and higher prednisone cumulative dose at 1 year FU (p=0.0003). A higher prevalence of any anti-cardiolipin antibody positivity (< 0.001), low dose aspirin use (p=0.03), photosensitivity (p=0.03) and longer antimalarial use (p=0.03) were observed in patients free of damage at 10 years. In multivariate analysis, only photosenstivity (HR 0.52, 95% CI 0.3-0.90, p=0.02) and a higher GFR at baseline (HR 0.99, 95% CI 0.98-0.99) were inversely associated with incident damage at 10 years. Antimalarial usage was associated with a protective effect for damage accrual at 5 years (HR 0.99, 95% CI 0.98-0.99, p=0.01) but this effect did not persist at 10 years (HR 0.99, 95% CI 0.99-1.00, p=0.081) and for incident damage (HR 1.32, 95% CI 0.70-2.48, p=0.39).

Conclusion: Damage accrual was present in 10% of SLE patients at baseline, at 5 years of FU it progress to 48.3% and 62.4% at 10 years. Incident damage was observed in 58.6%. Photosensitivity and higher GFR at baseline were protective for incident damage in our cohort.

Disclosure: M. Zamora Medina, None; **J. Roldan Ortega**, None; **M. Ocampo Torres**, None; **P. Lara Reyes**, None; **A. Cicero Casarrubias**, None; **I. Bautista Mejia**, None; **J. Romero-Diaz**, None.

Abstract Number: 1625

Severe Infection Prior to Diagnosis of Systemic Lupus Erythematosus (SLE) Is Associated with Disease-Specific Attributes and Long-Term Comorbidities

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	Acute Rash	Discoid	Oral/Nasal Ulcer	Alopecia	Arthritis	Serositis	Renal	Neurological
All Prior Infections Coefficient	-0.21	-0.31	-0.33	0.17	0.31	0.32	0.05	-0.05
P-value	0.51	0.23	0.13	0.50	0.51	0.13	0.81	0.82
Prior Bacterial Coefficient	0.22	-0.32	0.15	0.62	0.05	0.59	0.19	-0.12
P-value	0.66	0.39	0.65	0.07	0.94	0.06	0.57	0.76
Prior Viral Coefficient	-0.39	-0.31	-0.64	-0.23	0.56	0.13	-0.03	-0.01
P-value	0.29	0.35	**0.02**	0.52	0.38	0.63	0.92	0.98

Table 1a: Association Between Prior Infections and Clinical SLICC Criteria

	Hemolytic Anemia	Leukopenia	Thrombo-cytopenia	Anti-dsDNA	Anti-Smith	Anti-Phospholipid	Complement	Coombs
Prior All Infections Coefficient	0.50	1.14	-0.55	0.18	0.21	0.12	0.37	-0.64
P-value	0.14	**0.03**	0.13	0.46	0.40	0.58	0.13	0.41
Prior Bacterial Infections Coefficient	0.43	0.95	-0.54	0.12	0.34	0.29	0.21	-15.96
P-value	0.39	0.20	0.32	0.57	0.34	0.40	0.55	0.99
Prior Viral Infections Coefficient	0.56	1.30	-0.55	0.16	0.12	0.02	0.51	0.17
P-value	0.17	**0.08**	0.23	0.61	0.72	0.96	0.11	0.83

Table 1b: Association Between Prior Infections and Laboratory Based SLICC Criteria

SESSION INFORMATION
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Background/Purpose: Lupus is a systemic autoimmune disease whose mechanism of development is largely unknown. Prior infection is a suspected sentinel event that may trigger disease in susceptible people and have an impact on disease development. In this exploratory study, we investigated if severe infections prior to SLE diagnosis were associated with specific SLE attributes and comorbidities.

Methods: We identified 469 patients with known SLE in a physician validated registry, the Chicago Lupus Database, with medical records in the Northwestern Medicine Enterprise Data Warehouse (NMEDW). Each patient was assessed for the Systemic Lupus International Collaborating Clinics classification (SLICC) criteria, via chart review, to determine the presence or absence of each criteria. We excluded ANA from the analysis because 15% patients had missing ANA values (likely due to tests being performed at an outside institutions). Prior severe infections (viral, bacterial, fungal and mycobacterial) and comorbidities (heart failure, stroke, sepsis, end stage renal disease and

	Heart Failure	Stroke	ESRD	Sepsis	Osteoporosis
All Prior Infections Coefficient	0.59	0.49	0.46	1.12	0.38
P-value	**0.04**	0.08	0.27	**0.0006**	0.09
Prior Bacterial Infections Coefficient	0.61	0.83	0.71	1.25	0.55
P-value	0.13	**0.02**	0.13	**0.004**	0.11
Prior Viral Infections Coefficient	0.59	0.20	-0.08	1.04	0.29
P-value	0.10	0.59	0.89	**0.009**	0.30

Table 2: Association Between Prior Infections and SLE Comorbidities

osteoporosis) were identified based on ICD9/10 codes in the NMEDW. The association between prior infections and SLE criteria and comorbidities were evaluated using multivariate logistic regression. Models were adjusted for age of SLE onset, sex and race/ethnicity. Severe viral and bacterial infections were also analyzed separately in relation to criteria and comorbidities to assess associations.

Results: Among 469 patients, 26% had severe infections prior to SLE diagnosis, including 71 with viral infections and 49 with bacterial infections. The average age of SLE diagnosis in our population is 30.1 years; 50% are white, 29% African American, 21% identified in other racial/ethnic categories; 92% are female. For SLE comorbidities, 14% developed heart failure, 15% had a stroke, 9% developed ESRD, and 58% developed osteoporosis. Association coefficients and p-values between infection prior to diagnosis of SLE and classification criteria are shown in Tables 1a and 1b and the relation between infections and comorbidities are shown in Table 2. Among classification criteria, prior infection is significantly associated with leukopenia (p=0.03). Among comorbidities, prior infection is significantly associated with heart failure and sepsis. When analyzing prior infections by viral and bacterial subgroups, bacterial infections had significant association with stroke (p=0.02) and sepsis (p= 0.004). Viral infections were significantly associated with oral ulcers (p=0.02) and sepsis (p= 0.009). Association between prior bacterial infection and alopecia (p= 0.07), serositis (0.06), as well as association between prior viral infection and leukopenia (p = 0.08) had borderline significance.

Conclusion: Our exploratory study shows severe infections prior to SLE diagnosis are associated with leukopenia, oral ulcers and an increased risk of heart failure, stroke and sepsis. These results suggest that prior infection could increase the likelihood of long term cardiovascular comorbidities, and that supportive care should be considered to minimize infections and cardiovascular complications for persons with SLE.

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Abstract Number: 1626

Baseline Serum Osteopontin (OPN) Level Is Associated with Early Coronary Artery-calcification and Its Progression in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
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Session Type: Poster Session (Monday)
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Background/Purpose: Background/purpose Premature atherosclerosis has been recognized as a major cause of morbidity and mortality in SLE patients. We aimed to determine 1) the incidence and progression of Coronary-Artery calcification (CAC) and 2) if OPN serum levels are associated with progression of CAC in SLE patients

Methods: Design: Inception Cohort. Since enrollment into the cohort, all patients had a standardized medical history, physical examination, and laboratory tests, including lipid profile, apoB, homocystein, high-sensitivity C-reactive

protein (hs-CRP), serum complement (C3 and C4), and autoantibodies. Every 3-6 months, patients have been seen at the lupus clinic for medical care, and assessments of disease activity using the SLE disease activity scores, and medications usage. Every year, information has been updated, including irreversible damage accrual, any co-morbidities, traditional cardiovascular risk-factors, and a blood sample has been drawn. In 2008, 104 lupus patients from the cohort (93% females) were screened for coronary-artery calcifications using Multidetector Computed Tomography, after first 5 years of follow-up. In 2018 a follow-up screening for CAC was carried-up. Progression of CAC was considered as positive if i) patients without CAC in 2008 were found with CAC+ in the second screening or ii) patients with CAC positive in 2008 were found with any increase of their Calcium Score. OPN plasma levels were measured by ELISA. Correlates for calcifications were analyzed. Cumulative incidence of CAC was calculated and risk factors for CAC progression were identified by multivariate analysis.

Results: At-enrollment, lupus patients were 27.2+9.1 years of age and disease duration 5.4+3.8 months.. On 2008 during the first screening, CAC were detected in 7. 2% patients, since age 23 years, and from three years of disease duration. At follow-up screening, progression of CAC was identified in 16. 3% (IC95% 10. 4-24. 6). Cumulative incidence of CAC was observed in 9%. Mean value of OPN level at baseline was 102.7 ng/mL (95% CI = 89.3-116.1 ng/mL). Earlier Risk factors associated with CAC were disease activity (p=0. 03) and disease duration (p=0. 03) while risk factors for progression of CAC were postmenopausal status (p=0. 01), apoB levels (p=0. 01) and OPN levels (p=0.009). There was a positive correlation for progression of CAC and adjusted mean SLEDAI at first 5 years of follow-up and baseline OPN levels (p=0.006).

Conclusion: Our findings suggest that in patients with SLE, early CAC is associated with disease severity while in the progression of CAC, traditional risk factors atherosclerosis and OPN level were adding

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Abstract Number: 1627

Bronchoalveolar Lavage Fluid Analysis and Mortality Risk in Systemic Lupus Erythematosus Patients with Pneumonia and Respiratory Failure

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Background/Purpose: To evaluate the pathogens from bronchoalveolar lavage fluid (BALF) and risk factors of mortality in SLE patients with pneumonia and respiratory failure.

Methods: Twenty-four SLE patients were enrolled. Clinical characteristics, laboratory profiles at admission, and microbiology from BALF were presented. We also performed univariable analyses for mortality risk.

Results: Among the 24 patients (21 women, median age: 46.5 years; duration of SLE: 11 years), 8 of them had septic shock, and 9 of them died within 30 days. All of them were supported with mechanical ventilations with a medial duration of 11 days (Table 1). Pathogens identified from BALF were *Pneumocystis jiroveci* pneumonia (PJP) in 12

Table 1 Characteristics of SLE patients with bilateral pneumonia and respiratory failure under mechanical ventilation

Parameter	All (N=24)
Age at admission, years	46.5 (31.53 – 53.19)
Female gender	21 (87.5)
Duration of SLE, years	11 (4.0 – 18.3)
Lupus nephritis	17 (70.8)
Background medication	
Prednisolone equivalent dose, mg/day	15 (10.0 – 20.0)
Azathioprine	5 (20.8)
Mycophenolate	7 (29.2)
Calcineurin inhibitors	8 (33.3)
Pulse MP within 1 months	2 (8.3)
Cyclophosphamide within 3 months	1 (4.2)
Rituximab within 6 months	7 (29.2)
Clinical status at ICU admission	
Septic shock at endotracheal intubation	8 (33.3)
APACHE II score	25 (20.0 – 28.8)
SOFA score	10 (8.0 – 10.8)
ECMO support	2 (8.3)
MV to BAL duration, days	3 (2.0 – 5.0)
Duration of MV, days	11 (7.3 – 15.0)
Laboratory finding	
WBC count, $10^3/\mu l$	9.65 (6.63 – 13.9)
Lymphocyte count, $10^3/\mu l$	0.58 (0.23 – 0.89)
Platelet count, $10^9/l$	156 (80 – 243)
Serum albumin, g/dl	2.6 (2.10 – 3.10)
Serum total bilirubin, mg/dl	0.6 (0.35 – 0.61)
Serum creatinine, mg/dl	1.5 (1.13 – 4.70)
Serum CRP, mg/dl	3.9 (0.95 – 13.10)
Serum procalcitonin > 0.5 ng/ml	11 (45.8)
Serum C3, mg/dl	64 (47.0 – 85.4)
Serum C4, mg/dl	17 (10.1 – 24.6)
Serum IgG, mg/dl	710 (431 – 1070)
30-day mortality	9 (37.5)
Hospitalization mortality	11 (45.8)

Values are presented as median (interquartile range) or number (percentage)

APACHE: Acute Physiology and Chronic Health Evaluation; BALF: bronchoalveolar

patients (50%), Cytomegalovirus in 7 patients (29.2%), bacteria in 11 patients (45.8%). Thirteen patients (54.2%) had blood stream infections, the leading causes were cytomegalovirus in 8 patients (33.3%) and *E. coli* in 5 patients (20.8%). Univariable analysis indicated that the presence of thrombocytopenia (odd ratio [OR]: 8.0, 95% confidence interval [CI]: 1.23–52.25), bacteremia before or after one month of endotracheal intubation (OR: 8.0, 95% CI: 1.23–52.5), and PJP (OR: 7.0, 95% CI: 1.04–46.95) were risk factors for 30-day mortality (Table 2). Kaplan-Meier analysis also confirmed the risk of 30-mortality in patients with thrombocytopenia and bacteremia (Figure 1).

Table 2 Risk factor analysis for 30-day mortality in SLE patients with pneumonia under mechanical ventilation

Variable	OR	95% CI	p value
Age	1.0	0.93 – 1.04	0.555
Lupus nephritis	0.3	0.05 – 1.94	0.212
Prednisolone > 10 mg/day	4.0	0.62 – 25.96	0.146
Mycophenolate	1.4	0.23 – 8.30	0.728
Calcineurin inhibitors	2.2	0.39 – 12.58	0.375
Rituximab within 6 months	1.4	0.23 – 8.30	0.728
APACHE II score ≧ 20	0.5	0.06 – 4.69	0.575
Septic shock at intubation	0.4	0.07 – 2.81	0.377
Platelet < 100 x 10^9/L	8.0	1.23 – 52.25	0.030
Serum CRP > 6 mg/dL	1.9	0.35 – 9.98	0.461
Serum PCT > 0.5 ng/ml	2.3	0.19 – 28.19	0.519
Low C3 or C4	5.3	0.52 – 54.34	0.158
Serum IgG < 751 mg/dL	8.0	0.71 – 90.00	0.092
Bacteremia[a]	8.0	1.23 – 52.25	0.030
Pathogen in BALF			
Pneumocystic jiroveci	7.0	1.04 – 46.95	0.045
Cytomegalovirus	3.2	0.52 – 19.84	0.212
Bacteria	1.9	0.35 – 9.98	0.461

APACHE, Acute Physiology and Chronic Health Evaluation; BALF, bronchoalveolar lavage fluid; CMV, Cytomegalovirus; Ig, immunoglobulin; OR, odds ratio; SOFA, Sequential Organ Failure Assessment; WBC, white blood cell

[a]within one month before or after endotracheal intubation.

SLE pneumonia BAL table 2

Table 2

Conclusion: The prevalence of cytomegalovirus and *Pneumocystis jiroveci* was high in BALF from SLE patients encountered pneumonia and respiratory failure. BALF analysis facilitated a pathogen-specific treatment, which may lower the overall mortality rate in such vulnerable patients. Thrombocytopenia, bacteremia, and PJP may indicate an increased 30-day mortality rate.

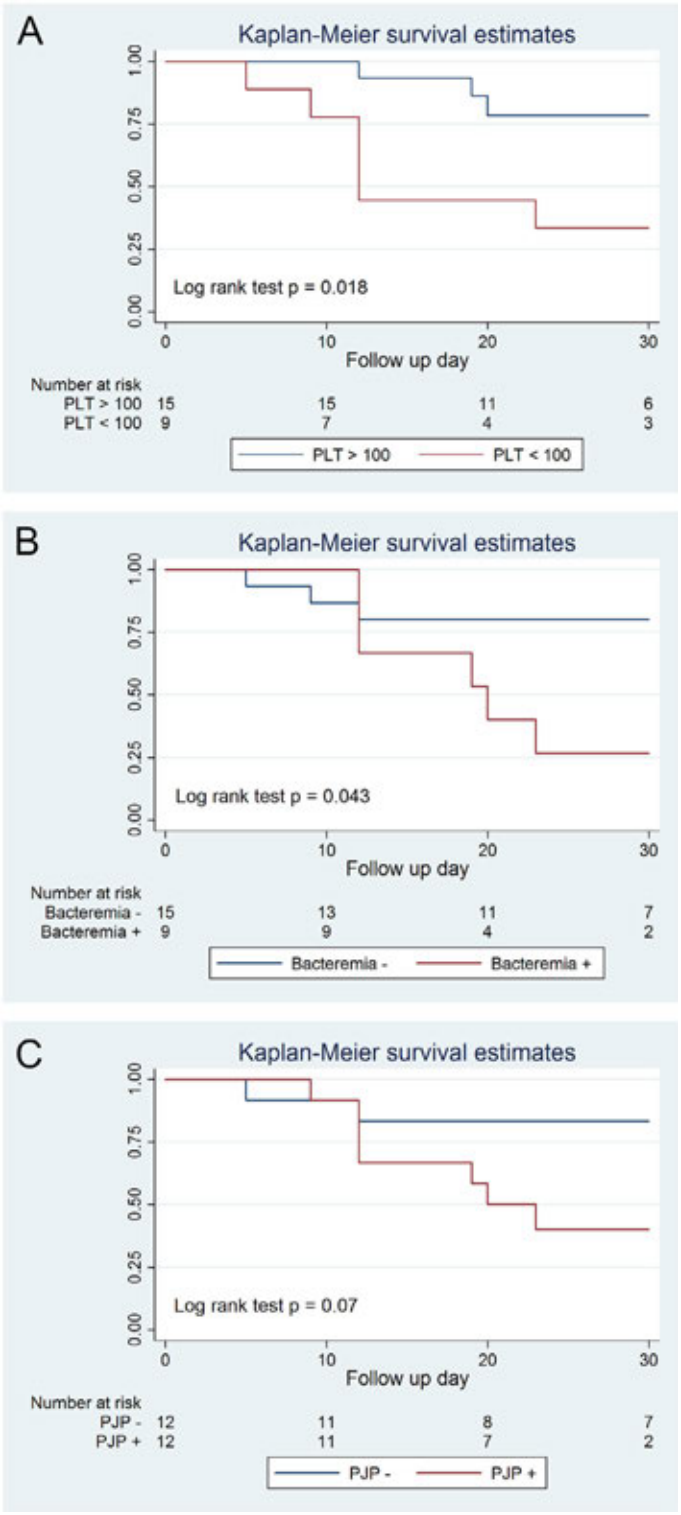

Figure 1

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Abstract Number: 1628

Lung Function Decline in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease in the SENSCIS Trial: Subgroup Analysis by Time Since First Non-Raynaud Symptom

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SESSION INFORMATION

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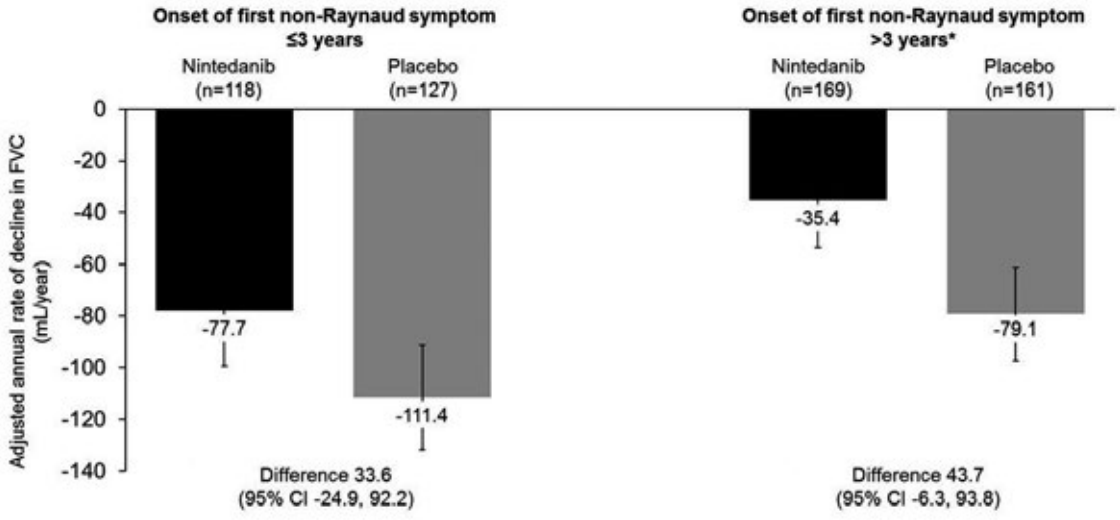
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a common and usually early manifestation of systemic sclerosis (SSc). Decline in lung function in patients with SSc-ILD is generally believed to be most rapid early in the course of the disease. In the SENSCIS trial, nintedanib reduced the annual rate of decline in forced vital capacity (FVC) vs

Figure. Annual rate of decline in FVC (mL/yr) over 52 weeks in the SENSCIS trial in subgroups by time since onset of first non-Raynaud symptom.



Treatment-by-time-by-subgroup interaction p=0.80

*Inclusion criterion was onset of first non-Raynaud symptom <7 years before screening. Actual maximum was 7.2 years.

placebo in patients with SSc-ILD. We analyzed outcomes in the SENSCIS trial in subgroups based on time since onset of first non-Raynaud symptom.

Methods: Subjects with SSc-ILD with onset of first non-Raynaud symptom < 7 years before screening, ≥10% fibrosis of the lungs on high-resolution computed tomography (HRCT) and FVC ≥40% predicted were randomized to receive nintedanib 150 mg bid or placebo. We analyzed outcomes in subgroups based on time (at randomization) since onset of the first non-Raynaud symptom (≤3 vs >3 years).

Results: Among 576 patients who received ≥1 dose of trial drug, the time since onset of first non-Raynaud symptom was ≤3 years in 118 (40.9%) and 127 (44.1%) of patients in the nintedanib and placebo groups, respectively. At baseline, in patients with onset of first non-Raynaud symptom ≤3 years and >3 years, respectively, 41% and 60% had diffuse cutaneous SSc, 59% and 62% were positive for anti-topoisomerase I antibody, mean (SD) modified Rodnan skin score (mRSS) was 9.8 (8.8) and 12.1 (9.0), C-reactive protein level (mg/dL) was 7.1 (20.1) and 5.8 (10.7), extent of fibrosis on HRCT (%) was 34.8 (21.0) and 36.9 (21.4), FVC (mL) was 2549 (819) and 2463 (744), and FVC % predicted was 73.1 (16.1) and 72.1 (17.1). In both the nintedanib and placebo groups, the rate of decline in FVC (mL/year) was numerically greater in patients with onset of first non-Raynaud symptom ≤3 than >3 years (Figure). Nintedanib reduced the rate of decline in FVC compared with placebo both in patients with onset of first non-Raynaud symptom ≤3 and >3 years, with a similar effect between subgroups (Figure). In the nintedanib and placebo groups, respectively, absolute declines in FVC >5% predicted were seen in 21.2% and 33.1% of patients with onset of first non-Raynaud symptom ≤3 years (OR 0.55 [95% CI 0.31, 0.98) and 20.1% and 24.8% with onset >3 years (OR 0.76 [0.45, 1.28]) (treatment-by-subgroup interaction p=0.41). The adverse event profile of nintedanib was consistent between the subgroups by time since onset of first non-Raynaud symptom.

Conclusion: In patients with SSc-ILD in the SENSCIS trial, the rate of FVC decline over 52 weeks was numerically greater in patients whose onset of first non-Raynaud symptom was ≤3 years than >3 years before randomization. The effect of nintedanib on reducing decline in FVC was consistent between subgroups of patients by time since first non-Raynaud symptom.

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Abstract Number: 1629

Significance of Abnormal Nailfold Videocapillarscopy Among Patients with Raynaud's Phenomenon And/or Suspected Connective Tissue Disease: A Cross-Sectional Single-Center US Experience

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SESSION INFORMATION
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Background/Purpose: Nailfold videocapillaroscopy (NVC) is a simple, non-invasive & highly sensitive tool to evaluate structural abnormalities of the microcirculation in vivo and considered a key clinical finding to help differentiate primary from secondary Raynaud's phenomenon (RP). It is available at limited centers across the US. We examined the significance of NVC patterns in an unselected cohort of patients with RP and/or suspected connective tissue disease (CTD) referred to a recently instituted NVC Clinic at our institution.

Characteristic	PRP (34) n (%)	SSc (35) n (%)	UCTD (42) n (%)	MCTD (15) n (%)	SLE (4) n (%)	Sjögren's (9) n (%)	DM (2) n (%)	APLS (2) n (%)
NVC Pattern								
Normal	34 (100)	2 (6)	22 (52)	5 (33)	2 (50)	7 (78)	1 (50)	1 (50)
Abnormal								
Non-specific	0	7 (20)	7 (17)	1 (7)	0	0	0	0
SSc pattern	0	26 (74)	13 (31)	9 (60)	2 (50)	2 (22)	1 (50)	1 (50)
Early	0	6 (17)	6 (14)	4 (27)	1 (25)	1 (11)	1 (50)	1 (50)
Active	0	12 (34)	7 (17)	2 (13)	0	1 (11)	0	0
Late	0	8 (23)	0	3 (20)	1 (25)	0	0	0
Raynaud's	34 (100)	33 (94)	41 (98)	14 (93)	3 (75)	6 (67)	2 (100)	2 (100)

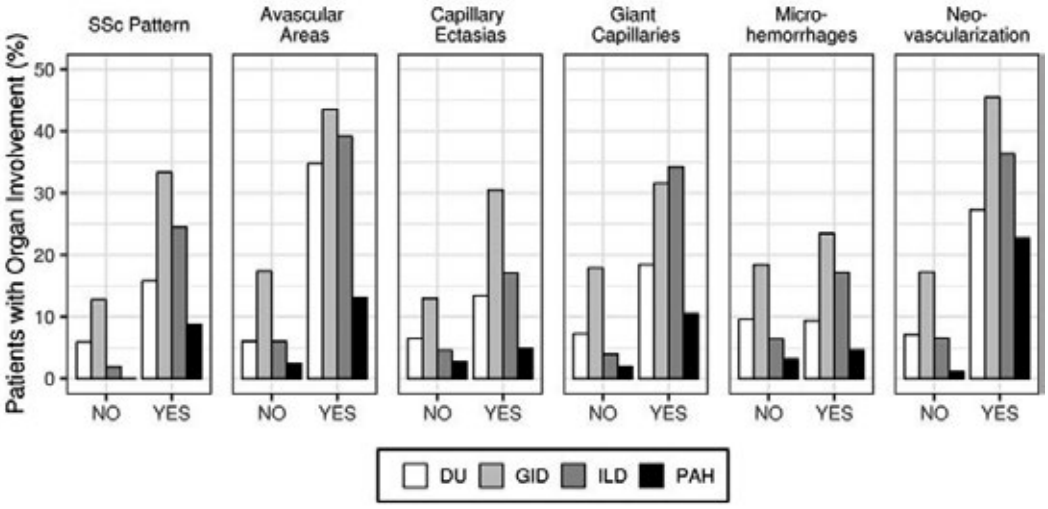
PRP=Primary RP; SSc=systemic sclerosis; UCTD=undifferentiated CTD; MCTD=mixed CTD
SLE=Systemic lupus erythematosus; DM=Dermatomyositis; APLS=antiphospholipid syndrome

Table 1. Nailfold Videocapillaroscopy findings in 190 patients in accordance with clinical diagnosis, with or without Raynaud's Phenomenon

Pattern	ILD (19) n (%)	PAH (7) n (%)	GID (39) n (%)	DU (18) n (%)	ANA (126) n (%)	Anti-scl70 Ab (20) n (%)	Anti-Centromere Ab (20) n (%)	Anti-RNA polymerase Ab (18) n (%)
NVC Pattern								
Normal	2 (11)	0	13 (33)	6 (33)	66 (52)	9 (45)	9 (45)	7 (39)
Abnormal								
Non-specific	3 (16)	2 (29)	7 (18)	3 (17)	18 (14)	4 (20)	3 (15)	3 (17)
SSC pattern	14 (73)	5 (71)	19 (49)	9 (50)	42 (34)	7 (35)	8 (40)	8 (44)
Early	2 (11)	0	5 (13)	1 (6)	16 (13)	3 (15)	2 (10)	3 (17)
Active	8 (42)	2 (29)	8 (21)	3 (17)	17 (13)	3 (15)	5 (25)	2 (11)
Late	4 (21)	3 (43)	6 (15)	5 (28)	9 (7)	1 (5)	1 (5)	3 (17)

ILD=interstitial lung disease; PAH=pulmonary arterial hypertension; GID=gastrointestinal dysmotility; DU=digital ulcers; ANA=Antinuclear Antibody

Table 2. Organ involvement, autoantibodies and nailfold videocapillaroscopy patterns among 190 patients with Raynaud's phenomenon and/or suspected connective tissue disease



DU=Digital ulcers; GID=gastrointestinal dysmotility; ILD=interstitial lung disease; PAH= pulmonary arterial hypertension

Figure. Association of "SSc pattern" and other nailfold videocapillaroscopy findings with organ involvement

Methods: Medical records of all patients referred to our NVC Clinic between 1/1/2017 to 3/31/2019 were retrospectively reviewed. Demographics, clinical diagnosis, major organ involvement that can been seen in systemic sclerosis (SSc) or CTDs (interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), digital ulcers (DU) and gastrointestinal dysmotility (GID)) and autoantibodies were abstracted. NVC results (Optilia, 200x; 2nd-5th Digits examined bilaterally) were classified as normal or abnormal (described as non-specific or SSc specific pattern- early, active, late). Fulfilment of ACR/EULAR 2013 SSc classification criteria and Very Early Diagnosis of SSc (VEDOSS) criteria was ascertained.

Results: 190 patients (mean age 46 ± 15 yrs, 81 % females, 93% white) underwent NVC during the study period. Indications for referral were RP (92%), positive autoantibodies (56%) and/or suspicion for underlying CTD (21%).

A normal NVC was noted in 102 (54%) patients, of whom 34 patients were considered to have Primary RP. Abnormal NVC was noted in 88 (46%) patients of which 57 (65%) had SSc pattern (39% early, 46% active, and 16% late). Among those with SSc NVC pattern, 26 (46%) met classification criteria for SSc, 48 (84%) fulfilled VEDOSS criteria

and 28 (49%) were diagnosed as other CTDs. Among patients met ACR/EULAR 2013 SSc diagnosis, NVC abnormalities were noted in 33 (94%). NVC abnormalities were also notable in patients with other CTDs (Table 1).

Organ involvement was observed more frequently with SSc NVC pattern (Table 2). Among the 13 patients with SSc NVC pattern (6 early, 7 active) that did not meet criteria for SSc or other CTDs, 3 had ILD, 1 DU and 2 had GID.

Among patients with SSc NVC pattern, 74% had a positive ANA, 37% had SSc specific autoantibodies (anti-centromere 14%, anti-Scl70 12% and anti RNA polymerase-III 14%), and 39% had a positive ENA (16% anti-Ro/SSA, 2% anti-La/SSB, 7% anti-Sm, 16% anti-RNP).

In absence of RP (n=13), SSc pattern was observed in 4 (31%) patients: 3 met VEDOSS, 2 met ACR/EULAR SSc criteria and 1 had Sjogren's syndrome; 2 had anti-RNA polymerase-III and 1 had anti-Scl70 antibody.

The association of NVC abnormalities (giant capillaries, dilatations, microhemorrhages and avascularity) with organ dysfunction is shown in the figure.

Conclusion: Our study underscores the importance of performing NVC for early diagnosis of SSc. This study supports the role of NVC as a valuable screening tool for evaluation of CTDs where abnormal NVC, particularly SSc pattern, may be associated with a high prevalence of disease-specific autoantibodies and internal organ involvement (particularly ILD and PAH), even in the absence of RP and may signal an evolving CTD.

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Abstract Number: 1630

Contribution of Chest Wall Muscle Atrophy to Decline of Forced Vital Capacity in Patients with Systemic Sclerosis-associated Interstitial Lung Disease

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

Background/Purpose: Interstitial lung disease (ILD) is the leading causes in patients with systemic sclerosis (SSc). Forced vital capacity (FVC) is routinely used for assessment of severity of SSc-ILD. Since FVC decline is shown to predict poor survival, serial FVC change is used as an outcome measure in clinical practice as well as in clinical trials. In general, FVC is decreased in the presence of restrictive lung diseases such as ILD, but also by neurologic and

muscle disorders that affect respiratory muscles[1]. Here, we have investigated whether chest wall muscle atrophy influences on FVC change in patients with SSc-ILD.

Methods: This is a retrospective study involving 36 patients with SSc-ILD, who were selected from our SSc database, based on fulfillment of 2013 ACR/EULAR classification criteria, disease duration from non-Raynaud's symptoms < 10 years, availability of at least 2 simultaneous measurements of pulmonary function test (PFT; FVC, FEV1, DLco) and chest high-resolution computed tomography (HRCT) at an interval of 1-3 years. Two independent examiners measured the extent of ILD according to Goh et al [2] and chest wall muscle volume at the level of 9th thoracic spine on HRCT by manual tracing in a setting of blinded patient identity, and the mean values were used for analysis. Serial changes of FVC, ILD extent, and chest wall muscle volume between two measurements (ΔFVC, ΔILD, and Δmuscle) were statistically assessed using Wilcoxon signed-rank test. Correlation coefficient was calculated by Spearman's rank sum test. Multiple regression analysis was used to evaluate independent roles of ΔILD, Δmuscle in contributing to ΔFVC, by incorporating various co-variables.

Results: Baseline characteristics of the patients included: 72% female, age of 54.9 ± 13.5 years, disease duration of 2.8 ± 3.0 years (range: 0-10 years), 53% dcSSc, 53% anti-topoisomerase I-positive, FVC of 2.37 ± 0.56 L (%predicted FVC of 86 ± 19%), %predicted DLco of 69 ± 21%, and ILD extent of 20.5 ± 16.1%. An interval between the first and second PFT/HRCT evaluations was 20.8 ± 6.9 months. Inter-examiner correlation coefficient was 0.79 for chest wall muscle volume and 0.61 for ILD extent. Sixteen patients (44%) were treated with cyclophosphamide, mycophenolate mofetil, tocilizumab, and/or nintedanib, while 19 (53%) received corticosteroids. There was no change in FVC ($P = 0.30$) or ILD extent ($P = 0.078$), whereas chest wall muscle volume reduced significantly with time (5232 ± 1416 to 4895 ± 1259 mm^2: $P = 0.0008$). ΔFVC was correlated negatively with ΔILD ($r = -0.48$, $P = 0.003$) and positively with Δmuscle ($r = 0.53$, $P = 0.01$), but ΔILD and Δmuscle were not correlated with each other ($r = -0.073$, $P = 0.67$). A variety of multivariate models consistently demonstrated that ΔILD and Δmuscle were independent contributors to ΔFVC (adjusted R-squared 0.50-0.59).

Conclusion: In patients with SSc-ILD, FVC decline might reflect not only ILD progression but also chest wall muscle atrophy, which potentially attribute to skeletal muscle involvement of SSc. Our finding may call our attention upon interpretation of serial FVC changes in SSc-ILD patients.

References

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2. Goh NS et al. Am J Respir Crit Care Med. 2008;177:1248-54.

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Abstract Number: 1631

Assessment of the Repeatability and Convergent Validity with Dermal Collagen of High Frequency Ultrasound in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

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Background/Purpose: There have been a number of recent negative clinical trials of SSc utilising the modified Rodnan Skin Score. High Frequency Ultrasound (HFUS) allows objective quantitative and qualitative assessment of dermal pathology and could be a useful surrogate measure of skin involvement in Systemic sclerosis (SSc). No previous studies have examined the convergent validity between HFUS features and dermal collagen in SSc. The repeatability of HFUS warrants further assessment before this method can be accepted in clinical practice. This study aims to assess the repeatability and convergent validity of HFUS parameters with dermal collagen deposition in SSc.

Methods: Fifty-three patients with SSc meeting ACR/EULAR 2013 criteria and 15 healthy controls (HC) underwent HFUS assessment of skin thickness (ST), echogenicity (as a reflection of cutaneous oedema) and Shear Wave Elastography (demonstrating skin stiffness, SWE) at the middle finger, hand, distal forearm and abdomen. Ten SSc patients and 10 HC underwent skin biopsies taken from the distal forearm. Dermal collagen was determined using Masson's Trichrome stain.

Results: Strong positive correlations were found between dermal collagen quantification and both ST (Spearman's rank correlation coefficient, ρ = +0.697, p=0.025) and SWE (ρ = +0.709, p=0.022) at the forearm in SSc, but not with echogenicity. Multiple linear regression analysis confirmed ST and SWE as significant predictors of localised skin collagen deposition in SSc (R^2 = 0.876). ST and SWE were highly reproducible across all 4

Intra-observer variability in HFUS parameters			
Anatomical region of interest	**Intra-class Correlation Coefficient (95% CI)**		
	Skin thickness (mm)	**Echogenicity (mean, Gray scale)**	**SWE (mean, kPa)**
Proximal Middle Finger	0.946 (0.913-0.967)	0.782 (0.642-0.866)	0.954 (0.926-0.972)
Dorsal Hand	0.970 (0.952-0.982)	0.744 (0.586-0.842)	0.953 (0.923-0.971)
Distal Forearm	0.978 (0.965-0.987)	0.648 (0.432-0.783	0.964 (0.941-0.978)
Abdomen	0.963 (0.940-0.977)	0.865 (0.781-0.917)	0.973 (0.955-0.983)

Table 1. Intra-Class Correlation coefficient demonstrating excellent reproducibility (intra-observer variability) for skin thickness and Shear Wave Elastography. Reproducibility for echogenicity was good, but marginally less so than the other HFUS parameters.

regions of interest for the combined cohort (SSc and HC combined) with Intra-class Correlation Coefficients (ICC) of 0.946-0.978 and 0.953-0.973 respectively (Table 1). Echogenicity reproducibility was good, but weaker than ST and SWE (ICC 0.648-0.865).

Conclusion: We have demonstrated for the first time that ST and SWE on HFUS reflect collagen deposition in affected SSc skin. However, whilst low echogenicity is felt to reflect cutaneous oedema, increasing echogenicity does not accurately reflect fibrosis. HFUS parameters were highly reproducible although notably more so for ST and SWE than echogenicity. Our findings strongly support the use of ST and SWE in particular as a surrogate marker for skin fibrosis in clinical trials.

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Evidence-based Consensus Statements for the Identification and Management of Interstitial Lung Disease in Systemic Sclerosis

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Background/Purpose: Guidelines are needed to aid early recognition and treatment of interstitial lung disease in systemic sclerosis (SSc-ILD). This study was conducted to develop expert consensus statements for the identification and management of SSc-ILD.

Methods: Evidence-based consensus statements were established using a modified Delphi process based on a systematic literature analysis. An expert panel of 27 European-based pulmonologists, rheumatologists and internists participated in three rounds of online surveys, a face-to-face discussion and a WebEx meeting, to establish statements and define an SSc-ILD management algorithm.

Results: The final evidence-based consensus included detailed statements on screening and risk stratification, diagnosis, assessment of severity, treatment options, monitoring, assessment of progression and treatment escalation. The consensus management algorithm is presented here in an abbreviated form for clinical use (figure).

Conclusion: These evidence-based expert consensus statements, developed using a modified Delphi process, provide important guidance for the identification and management of SSc-ILD in clinical practice**.**

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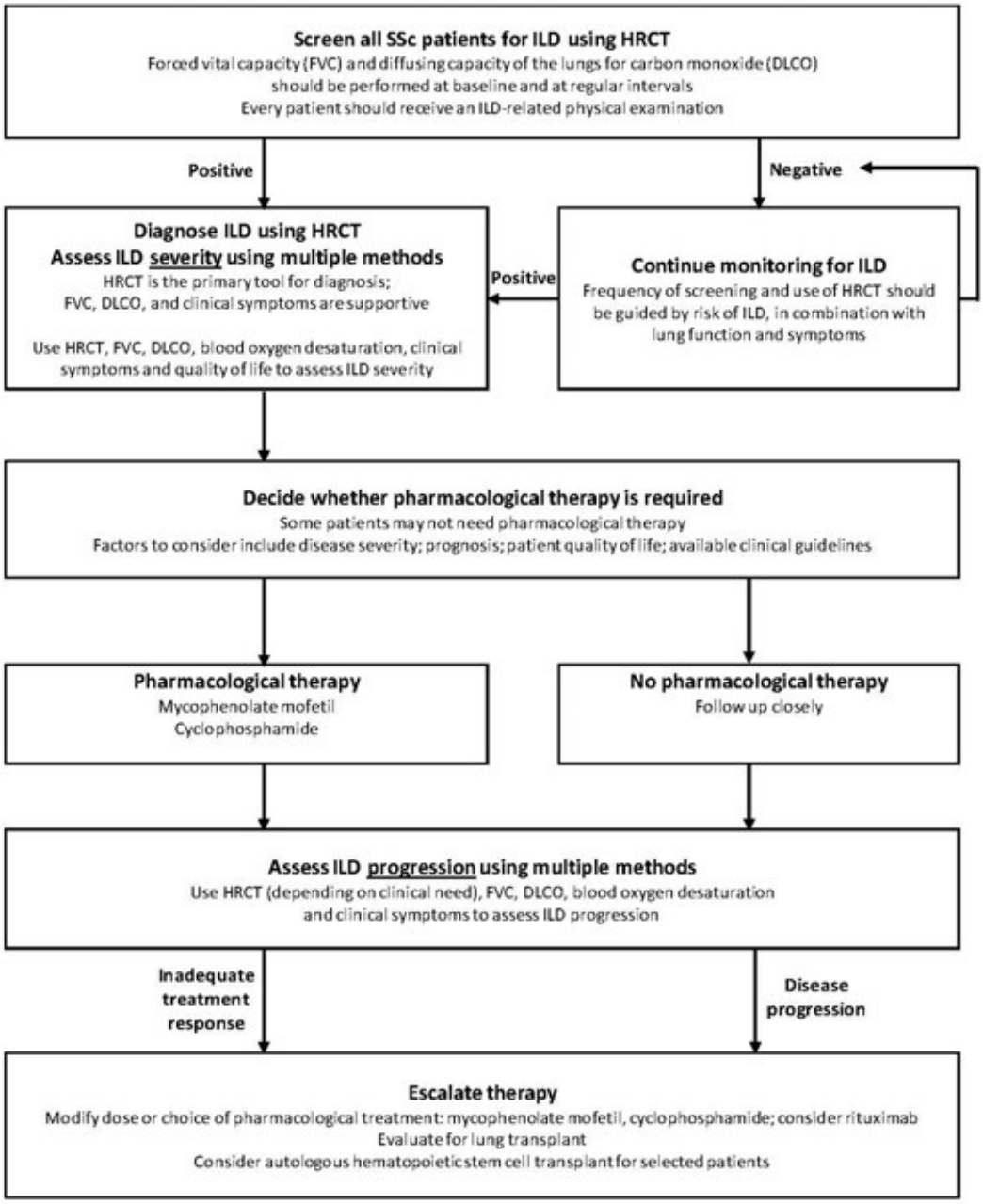

Figure. Clinical management algorithm for SSc-ILD

Bridget Griffiths; Alfredo Guillén-Del-Castillo; Abdul Monem Hamid; Bernhard Hellmich; Rudolf Horváth; Michael Hughes; Michael Kreuter; Belén López-Muñiz; Florentine Moazedi-Fuerst; Jacek Olas; Suman Paul; Cinzia Rotondo; Manuel Rubio-Rivas; Andrei Seferian; Michal Tomčík; Yurdagül Uzunhan; Ulrich A Walker; and Ewa Więsik-Szewczyk. The steering committee was chaired by John Cole (IQVIA, London, UK); the modified Delphi process was managed by Laura Wilson (IQVIA, Reading, UK). Medical writing support was provided by Rebecca Sutch, PhD, on behalf of AMICULUM Ltd, Oxford, UK.

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Abstract Number: 1633

Relationship Between YKL-40, VEGF, and IL-5 in Borderline mPAP and Pulmonary Hypertension in Systemic Sclerosis

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Background/Purpose: Systemic sclerosis (SSc) is an intractable connective tissue disease that causes skin and organ fibrosis, and its prognosis is affected by pulmonary hypertension (PH). Attention has been paid to borderline mPAP that does not lead to PH diagnosis at 21 ≤ mean pulmonary arterial pressure < 25 mmHg with a right heart catheter (RHC). In recent years, a mouse model of PH has been established by administering IL-33, which leads to pulmonary artery narrowing. In this model, PH was prevented by suppressing IL-5. Previous reports have demonstrated elevated serum YKL-40 levels in SSc and SSc-PH in Japanese patients with progressive pulmonary capillary lesions. The chitinase-like protein, YKL-40, has been implicated in inflammation, tissue remodeling, and angiogenesis in malignant tumors. We examined the relationship among YKL-40, VEGF, and IL-5 levels, which play an important role in SSc patients with borderline mPAP and PH.

Methods: We conducted a retrospective analysis of 64 SSc patients who were referred to our institution for treatment between August 2014 and April 2017. Group 1 included 47 patients without PH, group 2 included 6 patients with borderline mPAP, and group 3 included 11 patients with PH. Exclusion criteria were arthritis, infection, and malignant tumor complications. We measured serum YKL-40, VEGF, and IL-5 levels using ELISA and examined the correlation between YKL-40 age percentile, which was age-corrected for serum YKL-40 levels. The diagnosis of PH was made using an RHC.

Results: Age, sex (male:female), disease duration, and disease type (diffuse cutaneous SSc: limited cutaneous SSc) were as follows: group 1, 63.5 ± 12.8 years, 7: 40, 10. 2 ± 10.0 years, and 7: 40; in group 2, 66.0 ± 8.5 years, 1: 5, 13.7 ± 12.5 years, and 1:5; and in group 3; 60.7 ± 9.2 years, 1:10, 11.9 ± 11.2 years, 4: 7, respectively. The YKL-40 age percentile, VEGF (pg/mL), and IL-5 (pg/mL) results were as follows: in group 1, 44.2 ± 26.8, 307.8 ± 167.4, and 1.2 ± 0.3; in group 2, 93.3 ± 7.2, 401.0 ± 128.4, and 1.8 ± 0.6; and in group 3, 90.2 ± 11.2, 584.1 ± 387.3, and 1.3 ± 0.4, respectively. YKL-40 level was significantly elevated in groups 2 and 3, VEGF level was higher in group 3 that in group 1, and IL-5 level was higher in group 2 than in group 1. Moreover, a positive correlation was found between YKL-40 and IL-5 levels, with a correlation coefficient of r = 0.3.

Conclusion: YKL-40, a biomarker that reflects vascular lesions of SSc at an early stage, may be a useful biomarker for the early diagnosis of borderline mPAP as it was significantly elevated in groups 2 and 3. We found that IL-5 level was elevated in the borderline mPAP complex, indicating that it may be involved in the progression at an early stage of pulmonary artery injury. As VEGF was elevated in the PH complex, it may also contribute to the progression of the vascular injury. From these results, early therapeutic intervention may improve the survival prognosis.

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Comparison of Different Pulmonary Hypertension Screening Algorithms in Patients with Systemic Sclerosis

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Background/Purpose: Pulmonary hypertension (PH) is an important cause of morbidity and mortality in patients with systemic sclerosis (SSc). Different screening algorithms have been proposed for identifying patients who have a high probability of PH and require right heart catheterization (RHC), which is the gold standard for diagnosing PH. The aim of this study was to compare the performance of PH screening algorithms in patients with SSc.

Methods: Forty-eight consecutive pts fulfilling ACR/EULAR 2013 SSc criteria have been screened for PH until now, using the 2015 ESC/ERS, DETECT and ASIG algorithms. Pulmonary function tests (PFT), diffusing capacity of the lung for carbon monoxide (DLCO), trans-thoracic echocardiography, serum NT-proBNP, serum uric acid assay and

Table 1. Demographic and Clinical Features of Patients									
	All Patients n=33	ESC/ESR screen positive, n=8 (25%)	ESC/ESR screen negative, n=24 (7%5)	DETECT screen positive, n=9 (27%)	DETECT screen negative, n= 24 (63%)	ASIG screen positive, n=13(41%)	ASIG screen negative, n=19 (59%)	Any of the algorithms, n=14 (41%)	Any of the algorithms, n=20 (59%)
Age, median [IQR]	51 [46.75-59.75]	66.5 [59-69.75]	48 [38.75-52]	66.5 [58.25-69.75]	48 [38.5-51.5	61 [52.75-68.5]	48 [38-51]	57 [50.5-68]	48 [38-51
Male, n (%)	-	-	-	-	-	-	-	-	-
Female, n (%)	100 (100)	100 (100)	100 (100)	100 (100)	100 (100)	100 (100)	100 (100)	100 (100)	100 (100)
Duration of SSc symptoms, year [IQR]	13.5 [5 20.75]	52 [39 57]	65 [51 79.5]	24 [5 38]	12 [5.25 16.75]	14 [5 37]	13 [5 19]	14 [5.25 35.25]	12 [5 17.5]
SSc pattern, n (%)									
Diffuse	10/34 (29)	2/8 (75)	8/26 (31)	1/8 (13)	9/24 (27)	4/13 (31)	6/21 (29)	4/14 (29)	6/20 (30)
Limited	24/34 (71)	6/8 (75)	18/26 (69)	7/8 (87)	15/24 (63)	8/13 (69)	8/23 (61)	10 (71)	14/20 (70)
SSc related serology, n (%)									
Anti-Scl70 (+)	18/34 (69)	3/6 (50)	15/20 (75)	5/7 (71)	13/18 (72)	6/10 (60)	12/16 (75)	6/10 (60)	12/16 (75)
Anticentromere (+)	3/34 (9)	***3/7 (43)***	***0/20 (0)***	***2/5 (40)***	***1/20 (5)***	***3/10 (30)***	***0/17 (0)***	***3/10 (30)***	***0/17 (0)***
Presence of ILD, n (%)	17/34 (50)	4/8 (50)	13/23 (57)	4/9 (44)	12/24 (50)	7/13 (54)	10/21 (48)	7/14 (50)	10/20 (50)
Presence of digital ulcer(ever), n (%)	21/34 (66)	**4/8 (50)**	**17/24 (71)**	6/9 (67)	14/22 (64)	8/13 (62)	13/19 (68)	9/14 (64)	12/20 (60)
Presence of GIS involvement, n (%)	14/34 (41)	**6/8 (75)**	**8/22 (36)**	**4/9 (44)**	**12/24 (50)**	**7/13 (54)**	**7/21 (33)**	**7/14 (50)**	**7/20 (35)**
Presence of telangiectasia, n (%)	14/34 (41)	5/8 (63)	9/19 (47)	4/9 (44)	10/24 (42)	7/13 (54)	7/21 (33)	**7/14 (50)**	**7/20 (35)**
sPAP on TTE, median (mmHg) [IQR]	28.5 [23.5-33]	36.5 [29.25-46.25]	27 [21.75-31]	33 [29.5-44]	27 [21-31.	30 [25.5-40.5]	27 [19.5-31]	30 [25.75-40.25]	27 [18.75-31]
FVC, median (% predicted) [IQR]	86 [69.5-102.5]	**92 [58.25-115.25]**	**83 [70-99]**	92 [63.5-114]	79 [69.25-100]	92 [67-108.75]	76 [69.5-99]	90 [72-107.5]	74 [69.25-100]
DLCO, median (% predicted) [IQR]	53.5 [41.25 71]	**47 [33.75-56.5]**	**62 [45-78.5]**	55 [46 71]	52 [43 71.75]	50 [35.5 58.5]	63 [46 79]	51 [37.25 62.5]	62 [44 77
FVC / DLCO ratio, median [IQR]	1.4 [1.1-1.74]	**2.11 [1.58-2.18]**	**1.3 [1-1.4]**	1.6 [1.28-2.18]	1.40 [1.11-1.58]	1.78 [1.35-2.12]	1.35 [1-1.43]	1.71 [1.29-2.12]1.36 [1.4-1.44]	1.36 [1.04-1.44]
NT-proBNP, median (pg/mL) [IQR]	137 [63-258]	**284 [162-778]**	120 [52-165]	451 [210-887]	120 [52-158]	284 [124.25-695]	120 [38-158]	284 [124.25-695]	120 [38-158]
Presence of dyspnea, n (%)		7/8 (88)	7/26 (27)	**5/9 (56)**	**9/24 (38)**	**7/13 (54)**	**7/21 (33)**	**7/14 (50)**	**7/20 (35)**
WHO-FC, n (%)									
Class 1		1/14)	-	-	-	-	-	-	-
Class 2		5 (72)	7 (100)	4/5 (80)	9 (100)	6/7 (86)	7/7 (100)	6/7 (86)	7/7 (100)
Class 3		1 (14)	-	1/5 (20)	-	1/7 (14)	-	1/7 (14)	-
Class 4		-	-	-	-		-	-	-
GIS: Gastrointestinal system, ILD, Interstitial Lung Disease, Ssc: Systemic Sclerosis, TTE: Transtorasic Echocardiography, WHO-FC: World Health Organization Functional Capacity									

Table 2. Performance of the PAH screening algorithms

	Performance for 25-mmHg cut-off			Performance for 20-mmHg cut-off		
	ESC/ESR	ASIG	DETECT	ESC/ESR	ASIG	DETECT
Sensitivity, %	100	100	100	75	100	50
Specificity, %	54	9	40	67	17	0
PPV, %	37.5	23	33	75	61	44
NPV,%	100	100	100	67	0	0

high-resolution computed tomography (HRCT) were performed as needed. Pts with known PH, severe interstitial lung disease and severe left ventricular dysfunction (LVD) were not included. RHC was performed in all patients with positive screening according to any one of the screening algorithms. Pts with PH were classified according to the updated PH classification criteria. Sensitivity and specificity of the 3 screening algorithms were evaluated according to the estab-

lished cut-off value of 25 mmHg for mean systolic pulmonary artery pressure and for the recently proposed cut-off value of 20 mmHg.

Results: Among the 48 SSc pts, 15 were excluded due to already diagnosed PH (n=4), LVD (n=4), no measurable tricuspid regurgitation velocity (TRV) (n=5) and coexisting lung cancer (n=2). Among the remaining 33 patients, 14 required RHC according to at least one of the screening algorithms. Demographic and clinical features were summarized in Table 1. Number of patients who had suspected PH and required RHC according to ESC/ERS 2015, DETECT and ASIG algorithms were 8 (%25), 9 (%27), and 13 (%41) respectively (Figure 1). Among the 14 who had RHC, PH was present in 3 pts according to the 25-mmHg cut-off (Group1 in 1, Group 2 in 1, Group 3 in 1) and in 8 pts according to the 20-mmHg cut-off (Group 1 in 5, Group 2 in 2, Group 3 in 1). The sensitivity,specificity, positive and negative predictive values of each algorithm are presented in Table 2. Sensitivity was similar at 100% for the 3 algorithms, but the ESC/ERS algorithm had better specificity, when PH was diagnosed with the 25-mmHg cut-off. For the 20-mmHg cut-off, sensitivity was better with ASIG and the specificity was better with the ESC/ERS algorithm. For both cut-offs ESC/ERS had the best positive predictive value, and the best negative predictive value for the 20-mmHg cut-off. The negative predictive values were similar for the 3 algorithms.

Conclusion: The ESC/ERS algorithm seems to perform better in detecting PH in patients with SSc. However our numbers are still small for a firm conclusion. Another limitation of this study was that RHC was not performed in patients who did not fulfill criteria according to any of the screening algorithms. The sensitivities may be lower than what we propose, if there are patients with PH who are asymptomatic and not captured with any of the algorithms.

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Correlation Between Raynaud's Condition Score, Nailfold Videocapillaroscopy and Laser Speckle Contrast Analysis in Secondary Raynaud's Phenomenon Due to Systemic Sclerosis

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Background/Purpose: To evaluate any correlation between the Raynaud's Condition Score (RCS) and the morphological and functional methods available to evaluate microvascular damage in systemic sclerosis (SSc) patients (1-4).

Methods: Sixty-six SSc patients with Raynaud's phenomenon (RP) were enrolled during routine clinical assessment after informed written consent (60 women and 6 men, mean age 61±17 years, mean RP duration 11±9 years, mean disease duration 7±5 years). RCS, frequency and duration of Raynaud's attacks were assessed together. All patients had been on a stable drug regimen for at least two months, all vasodilator drugs had been suspended at least four week before evaluation (cyclic prostanoids, endothelin-1 receptor antagonists, ACE-inhibitors, calcium channel blockers). Patients were allowed to continue other treatments: hydroxychloroquine (5 patients), methotrexate (3 patients), cyclosporine A (10 patients), mycophenolate (6 patients), proton-pomp inhibitors (21 patients).

Nailfold videocapillaroscopy (NVC) was performed in each patient to assess any morphological microvascular damage and the microangiopathy evolution score (MES) was calculated (2). Blood perfusion (BP) was measured by Laser Speckle Contrast Analysis (LASCA) (3) at the level of fingertips, periungual areas, dorsum and palm of the hands. Statistical analysis was carried out by non-parametric tests.

Results: A positive correlation was observed between RCS and BP at the level of the fingertips, periungual areas and palms of the hand ($p< 0.01$, $r=0.85$, for all areas). There was no statistically significant correlation between RCS and BP at the dorsum hand level, whilst there was a positive correlation between RCS and MES ($p=0.03$, $r=0.79$).

RCS for RP activity (possible range 0-10) was 5±2, frequency (number of event during the day) was 2±1 and duration (in minutes) was 14±6 of Raynaud's attacks.

BP at the level of fingertips was 67±17 PU, periungual areas 60±16, palm of hands 59±18 and dorsum of hand 49±22. The MES average value was 3±2.

Conclusion: Our findings demonstrate a significant correlation between the RCS and the morphological and functional methods used to evaluate microvascular damage in SSc patients.

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Abstract Number: 1636

Effect of Anti-Topoisomerase I Antibody Status on Decline in Lung Function in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease: Data from the SENSCIS Trial

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session (Monday)

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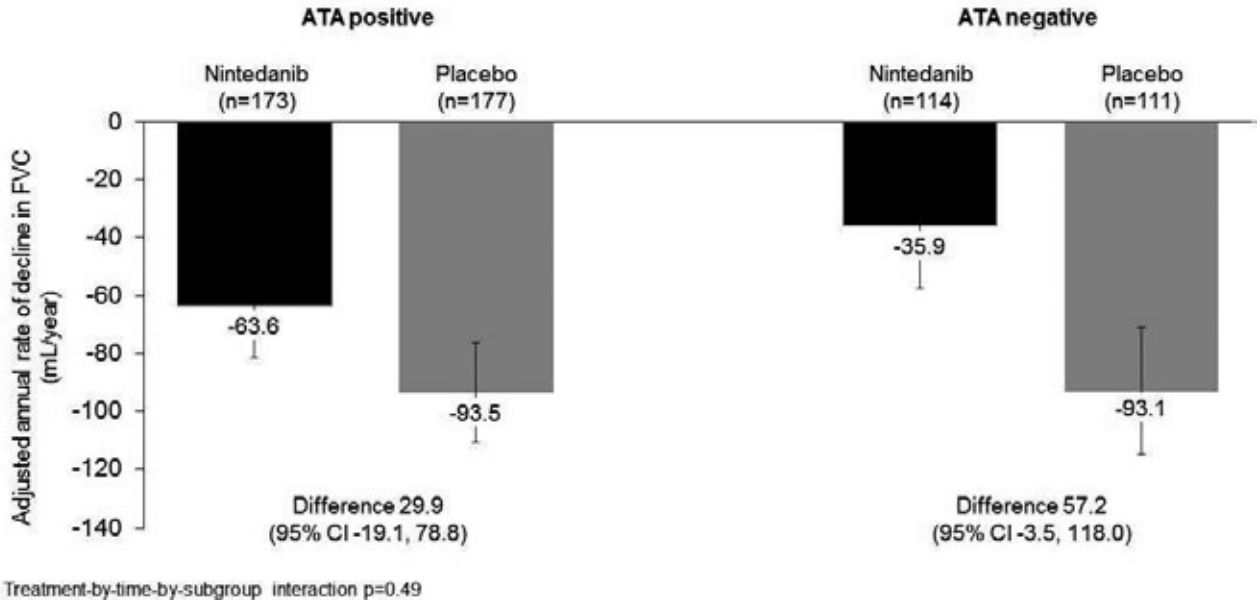
Background/Purpose: The presence of anti-topoisomerase I antibody (ATA) in patients with systemic sclerosis (SSc) has been associated with a greater risk of developing interstitial lung disease (ILD) and a greater rate of lung function decline in patients with early SSc. In the SENSCIS trial, nintedanib reduced the annual rate of decline in forced vital capacity (FVC) versus placebo in patients with SSc-ILD. We analyzed data from the SENSCIS trial in subgroups based on ATA status at baseline.

Methods: Patients with SSc according to the 2013 ACR/EULAR classification criteria, with ≥10% fibrosis of the lungs on a high-resolution computed tomography (HRCT) scan and with onset of the first non-Raynaud symptom < 7 years before screening were randomized to receive nintedanib 150 mg bid or placebo, stratified by the presence of ATA (based on historical information or, if not available, analysis at a central laboratory). We analyzed outcomes and adverse events over 52 weeks in subgroups of patients who were ATA positive or negative at baseline.

Results: Of 576 patients treated in the SENSCIS trial, 173 (60.1%) and 177 (61.5%) patients in the nintedanib and placebo groups, respectively, were ATA positive. In the subgroups that were ATA positive and negative, respectively, mean (SD) FVC (mL) was 2459 (773) and 2563 (781), and mean FVC % predicted was 71.4 (15.9) and 74.3 (17.7). Nintedanib reduced the rate of FVC decline compared with placebo both in patients who were ATA positive and negative. The treatment effect of nintedanib on reducing the rate of FVC decline was numerically greater in patients who were ATA negative than positive (Figure) (-63.6 vs -35.9 ml/year), but the treatment-by-time-by-subgroup interaction did not indicate heterogeneous treatment effects between the subgroups (p=0.49). In the nintedanib and placebo groups, respectively, absolute declines in FVC >5% predicted were seen in 23.1% and 30.5% of patients who were ATA positive (OR 0.69 [95% CI 0.43, 1.10]) and 16.7% and 25.2% who were ATA negative (OR 0.59 [0.31, 1.14]) (treatment-by-subgroup interaction p=0.73). Adjusted mean absolute changes from baseline in modified Rodnan skin score at week 52 in the nintedanib and placebo

Figure. Annual rate of decline in FVC (mL/yr) over 52 weeks in the SENSCIS trial in subgroups by ATA status at baseline.



groups were -1.5 and -1.7 in patients who were ATA positive (difference 0.2 [95% CI -0.7, 1.2]) and -3.2 and -2.4 in patients who were ATA negative (difference -0.8 [-2.0, 0.4]; treatment-by-visit-by-subgroup interaction p=0.18). The adverse event profile of nintedanib was consistent between patients who were ATA positive and negative.

Conclusion: In the SENSCIS trial in patients with SSc-ILD, the rate of FVC decline over 52 weeks in placebo-treated patients was similar between patients who were ATA positive and ATA negative. Nintedanib reduced the rate of FVC decline compared with placebo both in patients who were ATA positive and negative, with a numerically greater treatment effect in patients who were ATA negative.

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Abstract Number: 1637

The Clinical Features of Anti-RNA Polymerase III Antibodypositive Systemic Sclerosis with and Without Malignancy

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Systemic Sclerosis (SSc) patients with anti-RNA polymerase III (RNAP) antibody have been reported to have an increased risk of malignancy as compared with those with other disease-specific autoantibodies in Caucasian populations. The aim of this study was to investigate the relationship between disease-specific autoantibodies and malignancy, to examine the expression of RNAP in tumor tissues and to examine of the clinical features of cases with and without malignancy.

Methods: The study involved 208 Japanese patients with SSc consisting of 47 male and 161 female patients with a mean age of 63.1 ± 14.0 years. Of 208 patients, 52patients had diffuse cutaneous systemic sclerosis (dcSSc) and 156 had limited cutaneous systemic sclerosis (lcSSc). Fourteen patients (6.7%)had anti-RNAP antibody, 36 (17.3%) patients had anti-topoisomerase I (Topo I) antibody and 112 patients (53.8%) had anticentromere antibody (ACA), 19 patients had the other antibodies, and 27 patients had unknown antibodies. Malignant tumor tissues were stained using an anti-POLR3A antibody (Atlas antibodies, Sweden), which provided instructions for making the subunit A of RNA polymerase III.Statistical analysis: Statistical analysis was performed using the Mann-Whitney U test for determining the level of significance of differences between sample means. A p value less than 0.05 was considered statistically significant.

Results: The prevalence of malignancy was significantly higher in patients with RNAP antibody (8/14, 57.1%) than in those with Topo I antibody (2/36, 5.5%) and in those with ACA (5/112, 4.4%). Importantly, among 8 patients with RNAP antibody and malignancy, 5 patients (62.5%) developed malignancy from 2 years before to 1 years after SSc onset. Tumor tissues obtained from SSc patients with RNAP antibody complicated with

malignancy were stained using POLR3A antibody. Expression of POLR3A protein was observed in the tumor tissue.Regarding other clinical correlation, RNAP poisitive SSc patients with malignancy exhibited increased male/all ratio relative to those without malignancy (75% vs 33% p< 0.05). The mean age of RNAP SSc patients with maligncay was significantly higher than without malignancy (66.9 vs 52.8 years old p< 0.05). RNAP SSc patients with malignancy had average modified Rodnan skin score (MRSS) less than those without malignancy (7.38 vs 21.5 p< 0.05).

Conclusion: Japanese SSc patients with RNAP have an increased risk of malignancy as compared with those with other disease-specific autoantibodies. This result was similar to previous reports in Caucasian populations. In SSc patients with RNAP antibody complicated with malignancy, it was shown that POLR3A protein was expressed frequently in tumor tissues. SSc patients with RNAP could be considered to share the same pathological process among different ethnic groups. Furthermore, among SSc patients with anti-RNAP antibody, it was considered that male, relatively old, and patients with low MRSS should pay attention especially to the complication of malignancy.

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Abstract Number: 1638

Sexual Health in 60 Female Patients with Systemic Sclerosis

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SESSION INFORMATION
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Questionnaire: score range (meaning)	Systemic sclerosis (n=60)	Healthy controls (n=60)	p-value
FSFI: Female Sexual Function Index: 2(worst)-36(best)	14.9±1.5	26.2±1.5	p<0.0001
BISF-W: Brief Index of Sexual Function for Women: -16(worst)-75(best)	17.3±2.3	31.5±2.2	p<0.0001
SFQ28 Desire domain: Sexual Function Questionnaire: 5(worst)-31(best)	12.6±0.8	17.6±0.8	p<0.0001
PISQ-12: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form: 0(best)-48(worst)	13.8±0.8	8.6±0.6	p<0.0001
SQoL-F: Sexual Quality of Life Questionnaire – Female: 0(worst)-100(best)	52.1±3.4	81.6±2.6	p<0.0001
PFIQ7: Pelvic Floor Distress Inventory Questionnaire – short form 7: 0(best)-300(worst)	32.0±6.3	7.0±2.0	p<0.0001
FIS: Fatigue Impact Scale: 0(best)-160(worst)	63.1±4.5	31.9±4.0	p<0.0001
MAF: Multidimensional Assessment of Fatigue Scale: 1(best)-50(worst)	26.7±1.4	13.9±1.2	p<0.0001
BDI-II: Beck's Depression Inventory II: 0(best)-63(worst)	14.8 ±1.3	5.6± 0.8	p<0.0001
HAP: Human Activity Profile–adjusted activity score: 0(worst)-94(best)	50.0±3.0	81.5±1.3	p<0.0001
HAQ: Health Assessment Questionnaire: 0(best)-3(worst)	0.9±0.1	0.1±0.0	p<0.0001

Background/Purpose: Systemic sclerosis (SSc) is a chronic, multisystem, connective tissue disorder characterized by fibrosis of the skin and internal organ involvement, which can influence all aspects of life including sexual life. The aim of this study was to assess sexual functioning in female SSc patients compared to age-/sex-matched healthy controls (HC) and to determine the association between sexual health impairment and disease activity, treatment, physical and psychological aspects of the disease.

Methods: In total, 60 women (45 currently have a partner) with SSc (mean age: 49.5, disease duration: 6.2 years, lcSSc/dcSSc: 38/22, mRSS: 11.0, ESSG activity index: 2.4), who fulfilled the ACR/EULAR 2013 criteria, and 60 healthy controls (54 currently have a partner, mean age: 49.5) without rheumatic diseases filled in 12 well-established and validated questionnaires assessing sexual function (FSFI, SFQ28, BISFW, PISQ-12), quality of sexual life (SQoL-F), pelvic floor function (PFIQ-7), fatigue (FIS, MAF), physical activity (HAP), severity of functional impairment (SHAQ – only in SSc patients) and depression (BDI-II). A standard laboratory testing was performed. Data are presented as mean ± SEM.

Results: Patients with SSc had significantly higher prevalence and greater severity of sexual dysfunction (FSFI, BISF-W, SFQ28, PISQ-12 – in all subscales as well as total scores) and worse sexual quality of life (SQoL-F) compared to HC (table). Worse scores in SSc patients were associated with increased inflammation [CRP: FSFI (r=-0.260, p=0.0499), BISF-W (r=-0.273, p=0.0398), SFQ28 Pain Domain (r=-0.362, p=0,0056], disease activity [ESSG activity score: FSFI Pain Domain (r=-0.297, p=0.0210), FSFI Satisfaction Domain (r=-0.263, p=0.0423), PISQ-12 (r=0.403, p=0.0024)], more severe functional impairment [SHAQ: FSFI (r=-0.526, p< 0.0001), BISF-W (r=-0.477, p< 0.0001], greater fatigue [FIS: FSFI (r=-0.490, p< 0.0001), BISF-W (r=-0.458, p=0.0002), MAF: FSFI (r=-0.358, p=0.0011), BISF-W (r=-0.378, p=0.0030)], more severe depression [BDI-II: FSFI (r=-0.411, p< 0.0001), BISF-W (r=-0.419, p=0.0008)], deteriorated quality of life [HAQ: FSFI (r=-0.342, p=0.0073)], and worse ability to perform physical activities [HAP: FSFI (r=0.509, p< 0.0001), BISF-W (r=0.474, p=0.0002)]. No associations were found with disease duration, current prednisone equivalent dose or skin score.

Conclusion: Women with SSc reported significantly impaired sexual function and sexual quality of life and pelvic floor function than healthy controls with identical age. Worse scores in SSc were associated with disease activity, increased inflammation, more severe functional impairment, physical inactivity, fatigue, depression and decreased quality of life.

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Abstract Number: 1639

Endoscopic Findings in a Scleroderma Cohort with and Without Interstitial Lung Disease

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Table 1: Clinical characteristics of SSc patients with endoscopy and pulmonary disease

	HRCT: No Ground Glass Opacities N=34	HRCT: Ground Glass Opacities Present N=32	P-value*
Age (yrs), mean (SD)	59.1 (12.4)	58.9 (9.5)	0.956
Sex, n (%)	28 (82.4)	27 (84.4)	0.826
White race, n (%)	20 (58.8)	19 (59.4)	0.964
SSc Diffuse, n (%)	20 (58.8)	18 (56.3)	0.833
SSc Limited, n (%)	13 (38.2)	15 (46.9)	0.478
SSc Mixed, n (%)	9 (26.5)	8 (25.0)	0.891
SER ANA, n (%)	30 (88.2)	26 (83.9)	0.611
SER Scl70, n (%)	4 (11.8)	10 (31.3)	0.053
SER ACA, n (%)	8 (23.5)	4 (12.5)	0.246
SER RP3, n (%)	6 (17.6)	8 (25.0)	0.465
SER URNP, n (%)	3 (8.8)	3 (9.4)	0.938
Number of scope abnormalities, mean (SD)	1.9 (0.8)	1.7 (0.8)	0.242
Interstitial Lung Disease, n (%)	14 (41.2)	30 (93.8)	<0.0001
Forced Vital Capacity (%FVC), mean (SD)	79.5 (22.3)	70.9 (16.4)	0.080
Total Lung Capacity (%TLC), mean (SD)	80.5 (23.9)	67.0 (22.1)	0.020
Honeycombing, n (%)	5 (14.7)	15 (46.9)	0.004
Bronchiectasis, n (%)	4 (11.8)	16 (50.0)	0.001
Raynaud Duration (yrs), mean (SD)	15.3 (14.4)	17.7 (13.4)	0.488
Non-Raynaud Duration (yrs), mean (SD)	15.0 (13.6)	17.1 (10.8)	0.492
Gastritis vs. other scope abnormalities, n (%)	20 (58.8)	20 (62.5)	0.760
Esophagitis vs. other scope abnormalities, n (%)	18 (52.9)	8 (25.0)	**0.020**
Gastritis and esophagitis abnormalities only, n (%)			0.138
No Gastritis and no esophagitis	6 (17.6)	8 (25.0)	
Gastritis but no esophagitis	10 (29.4)	16 (50.0)	
Esophagitis but no gastritis	8 (23.5)	4 (12.5)	
Gastritis and esophagitis	10 (29.4)	4 (12.5)	

* P-values for Pearson chi-square tests for categorical variables and student's t-tests for continuous variables

Table 2: Odds of ground glass opacities in SSc patients with esophagitis and gastritis

	Odds Ratio	95% CI	P-value
Esophagitis but no gastritis	1.00 (referent)		
Gastritis but no esophagitis	3.20	0.76 – 13.47	0.1126
No Gastritis and no esophagitis	2.67	0.54 – 13.21	0.2296
Gastritis and esophagitis	0.80	0.15 – 4.25	0.7933

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Background/Purpose: Gastro-intestinal (GI) involvement is universal in systemic sclerosis (SSc) and may affect the entire length of the bowel, most commonly the esophagus (1). The pathogenesis is unknown but it is proposed that vasculopathy, immune-mediated abnormalities, fibrosis and atrophy, all contribute to disruption of GI function in SSc. Esophageal involvement has been associated with more severe scleroderma-related interstitial lung disease (SSc-ILD), which is a major cause of morbidity and mortality (2,3,4). Pulmonary function tests (PFT) and high resolution chest CT scan (HRCT) are commonly used to evaluate for SSc-ILD. Common HRCT findings may include potentially reversible changes such as ground glass opacities (GGO), and irreversible findings such as fibrosis, traction bronchiectasis and honeycombing (5). We sought to study the association of abnormal endoscopic and HRCT findings in our SSc cohort with ILD.

Methods: We examined the records of 140 SSc outpatients, all of whom met the 2013 ACR criteria for SSc (6). SSc-ILD was confirmed by HRCT associated with restrictive pattern on PFT. Descriptive HRCT findings included outcomes of honeycombing, bronchiectasis, and GGO. Pearson chi-square tests and student's t-tests were used to assess differences in distributions of clinical and sociodemographic variable across outcomes, respectively. Odds ratios of presence of honeycombing, bronchiectasis and GGO were estimated using logistic regression.

Results: A total of 140 SSc patients were enrolled, of whom 71 had endoscopies performed. Among those who were scoped, 68 (96%) had abnormalities detected, of which the majority were gastritis (n=40, 59%) and esophagitis (n=26, 38%). SSc patients with GGO on HRCT were less likely to have esophagitis than those without GGO (53% vs 25%, p=0.02; table 1). Patients with gastritis had 3.2 times higher odds of having GGO than patients with esophagitis (95% Confidence interval=0.76-13.41; table 2). We observed no significant differences in demographics, disease duration or serologic status between SSc patients with and without ILD who had abnormal endoscopies.

Conclusion: Abnormal endoscopies are common in SSc. Patients with SSc-ILD had a higher prevalence of gastritis relative to esophagitis, and those with gastritis had a higher likelihood of having GGO on HRCT. Larger prospective studies are needed to elucidate any causal relationship and to better understand the complex relationship between the upper GI tract and pulmonary findings in patients with SSc-ILD.

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Abstract Number: 1640

Cutaneous and Musculoskeletal Clinical Characterization of a Cohort of Patients with Chronic Graft-versus-host Disease

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Background/Purpose: Chronic graft-versus-host disease (cGVHD) is a major cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation (HCT). Clinically, cGVHD is a multiorgan syndrome involving

tissue inflammation and fibrosis that often result in permanent organ dysfunction with important repercussions at the systemic, cutaneous and musculoskeletal levels.

Objectives: To describe the musculoskeletal and connective tissue manifestations, in the first visit, of the patients with cGVHD treated in a multidisciplinary consultation (Hematology /Dermatology/Rheumatology).

Methods: Observational and prospective study to describe the clinical characteristics of patients with cutaneous and musculoskeletal cGVHD collected in the database. We describe the clinical characteristics of 58 patients with sclerodermiform GVHD well cutaneous, fascial and / or tendinous detected in the first visit. The usual variables, the transplant reason disease, the type of transplant, and the assessment of clinical manifestations according to NIH diagnostic and follow-up criteria: for skin involvement, ROM (range of motion) and P-ROM (scale of photographic range of motion) to objectify the degree of limitation of joint mobility. The descriptive and frequency statistical analysis is done through Microsoft Office Excel 2007.

Results: Sixty-three (67%) of the patients seen in the clinic had some type of non-lichenoid and / or musculoskeletal skin reaction. Five (7%) patients did not meet diagnostic or distinctive criteria of cGVHD (1 muscle cramps, 2 arthralgias and 2 polymyalgia). The cohort with sclerotic involvement (58 patients): 23 (40%) were women and 35 (60%) males, with a mean age of 52 years (r 7-78 years). The most frequent diseases that cause the transplant were acute myeloid leukemia (32%) and non-Hodgkin lymphoma (31%), and thirteen (22%) patients did not receive immunosuppressive treatment at the time of the visit. Ten (30%) patients were diagnosed by skin biopsy. The mean time from transplant to the initial visit was 3 years (r 8 months to 9 years). Seven (12%) had musculoskeletal sclerotic involvement (fascial / tendinous) detected by ROM without objective cutaneous involvement and the cutaneous involvement was severe in most cases (Tables attached)

Table 1: Skin and joint/fascia scoring

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
ECOG*	43 (74%)	12 (20%)	2 (3%)	1 (1,7%)
ROM^	43 (74%)	11 (19%)	3 (5%)	1 (1,7%)
Skin"	7 (12%)	0 (0%)	11 (19%)	40 (69%)

* ECOG Eastern Cooperative Oncology Group Perfomance status " ROM Range of mobility

Table 2: Clinical forms

	n= 58
Sclerodermiform	41 (70%)
Superficial Scl	11 (19%)
Deep Scl	21(36%)
Lipodermatosclerosis type	3 (5%)
Mixed (lichenoid + Scl)	6 (10%)
Eosinophilic fasciitis	10 (17%)
Soft tissue sclerosis without skin involvement	7 (12%)

Conclusion: Sclerodermiform affectation is very common in our cohort, with fascial and tendon affectation, mainly of the flexor tendons of the carpus, the most frequent and, sometimes, without cutaneous involvement, making it difficult to detect them, being necessary the use of scales of joint assessment systematically. Physiotherapy is a fundamental part of the treatment.

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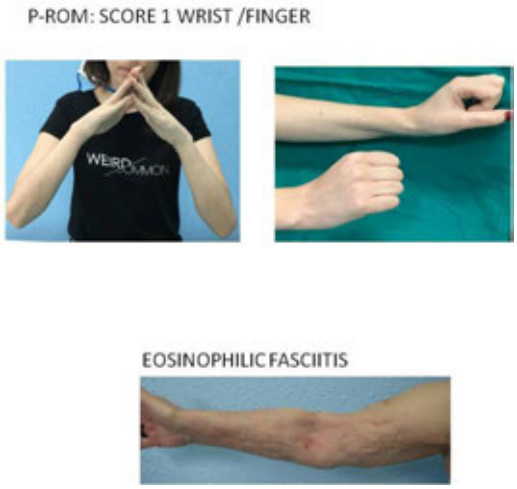

Abstract Number: 1641

Change in Calcinosis over 1 Year Using the SCTC Radiologic Scoring System for Calcinosis of the Hands in Patients with Systemic Sclerosis

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Background/Purpose: Calcinosis cutis is a debilitating complication of systemic sclerosis (SSc) affecting one quarter of patients, most frequently involving the hands. We previously developed and published a radiographic scoring system to assess severity of calcinosis affecting the hands in patients with SSc that is feasible with excellent inter- and intra-rater reliability. We sought to further validate our radiographic scoring system to assess for change over 1 year and to identify factors associated with improvement or progression.

Methods: Baseline and 1-year antero-posterior hand radiographs were obtained in 39 SSc patients with calcinosis who were prospectively enrolled at 6 centers within the US, Canada, Mexico and Australia. Two blinded readers scored all radiographs using the calcinosis scoring system. We defined progressive calcinosis as >10% increase in score from baseline at 1 year, stable calcinosis as change in score between -10% to 10%, and improvement of calcinosis as decrease in score by >10% (Figure 1).

Results: Our cohort was 85% female, 69% Caucasian, 28% Hispanic, and 3% Asian. 72% had limited cutaneous disease. Mean disease duration from first non-Raynaud phenomenon (RP) symptom was 16.9±11.4 years. Inter-rater reliability was high with intra-class correlation coefficient of 0.93 (0.89-0.95). The median percentage of change from

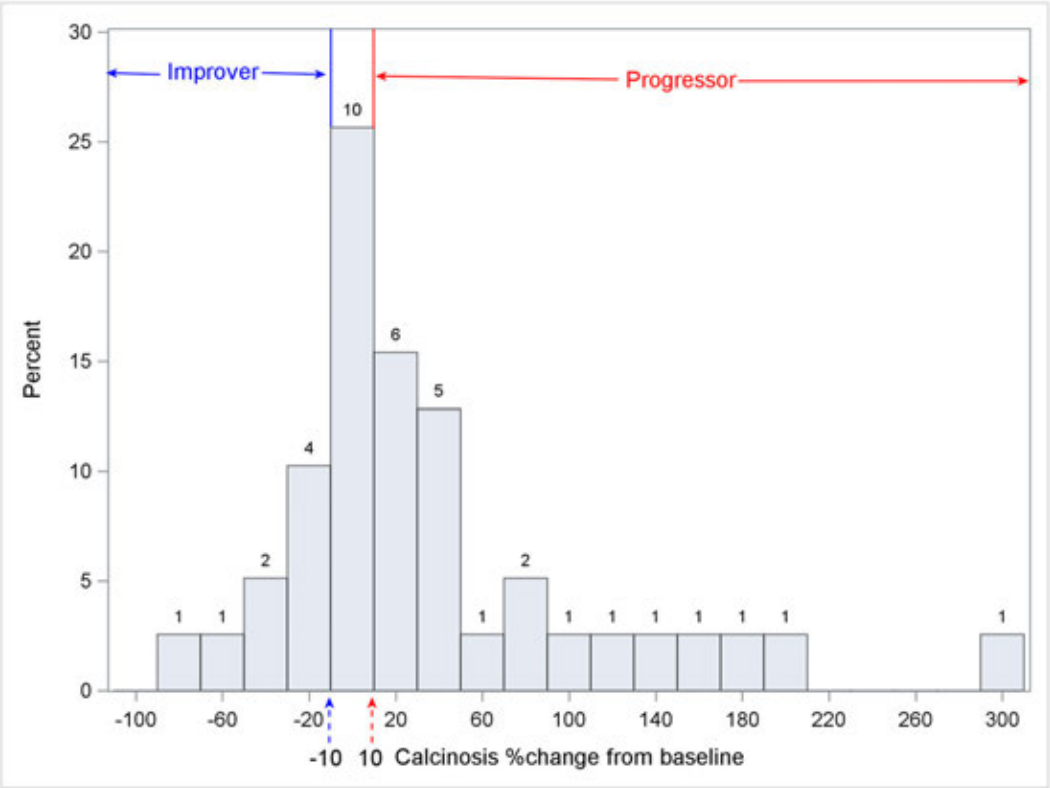

Figure 1. Distribution of change in calcinosis score over 1 year

baseline to 1 year was 12.8% (range -89.3-290.2%). Twenty-one patients (54%) experienced progression of calcinosis over 1 year with a range of 12.7-290.2% worsening from baseline; 10 (26%) remained stable; and 8 (20%) had improvement (range -89.3-7.4%)(Figure 1). Patients with progressive calcinosis had lower mean modified Rodnan skin score (mRSS) (3.81 vs. 6.5, p=0.0446) and lower prevalence of pulmonary artery hypertension (PAH) by right heart catheterization than patients who did not progress (0 % vs 23%, p= 0.022)(Table 1). They also exhibited a trend toward having more digital pitting scars (76% vs. 50%, p= 0.0892), and arthritis (52% vs. 34%, p= 0.0694). Patients whose calcinosis improved had higher mean mRSS (7.13 vs. 4.52, p=0.061), less arthritis (0 vs. 50%, p=0.0154) and greater prevalence of antibodies against PM-Scl (43 vs. 3%, p=0.018) than patients whose calcinosis did not improve. They also exhibited a trend toward having less gastrointestinal disease (50 vs. 84%, p=0.0651). In multivariable analysis, a trend for anti-PM-Scl antibodies to be a predictor of calcinosis improvement persisted (OR 13.5 (0.99 - 183.14), p=0.051)(Table 2).

Conclusion: We confirmed the excellent inter-rater reliability of our radiographic calcinosis scoring system and quantified changes in calcinosis severity over 1 year in a longitudinal cohort of SSc patients. More than half of patients experienced >10% progression of calcinosis over one year; however, 20% of patients improved and these patients were more likely to be positive for the PM-Scl antibody.

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	Not progressed n (%)	Progressed n (%)	p-value	Not improved n (%)	Improved n (%)	p-value
Total	18 (46.15)	21 (53.85)		31 (79.49)	8 (20.51)	
Age (mean years ± SD)	60.1 ± 9.8	58.3 ± 8.7	0.5353	59 ± 9	60 ± 10	0.8685
Female gender	17 (94.4)	16 (76.2)	0.1897	26 (83.9)	7 (87.5)	1
Race			0.8514			
Caucasian	12 (66.7)	15 (71.4)		21 (67.7)	6 (75)	0.1938
Asian	1 (5.6)	0 (0)		0 (0)	1 (12.5)	
Hispanic	5 (27.8)	6 (28.6)		10 (32.3)	1 (12.5)	
SSc Subtype			0.8514			
Diffuse	5 (27.8)	6 (28.6)		8 (25.8)	3 (37.5)	0.7354
Limited	13 (72.2)	15 (71.4)		23 (74.2)	5 (62.5)	
mRSS (mean ± SD)	**6.5 (5.2)**	**3.81 (3.8)**	**0.0446**	**4.52 (4.5)**	**7.13 (5.1)**	**0.0611**
Disease duration from first non-Raynaud Phenomenon (mean years ± SD)	16 (11.5)	17.7 (11.6)	0.6829	16.9 (11.25)	17 (13.00)	0.8483
Raynaud's phenomenon	18 (100)	20 (95.2)	1	30 (96.8)	8 (100)	1
Digital ulcers	5 (27.8)	10 (47.6)	0.323	14 (45.2)	1 (12.5)	0.1214
Digital pitting scars	**9 (50)**	**16 (76.2)**	**0.0892**	21 (67.7)	4 (50)	0.4237
Loss of digital pulp	5 (27.8)	9 (42.8)	0.3278	11 (35.5)	3 (37.5)	1
Abnormal nailfold capillary exam	14 (77.78)	17 (85)	0.821	24 (80)	7 (87.5)	1
Puffy fingers	10 (55.6)	14 (66.7)	0.4771	17 (54.8)	7 (87.5)	0.1214
Sclerodactyly	12 (66.7)	14 (66.7)	1	20 (64.5)	6 (75)	0.6942
Telangiectasias	15 (83.3)	20 (95.3)	0.3183	29 (93.6)	6 (75)	0.1803
Osteopenia or Osteoporosis	3 (25)	9 (45)	0.1175	9 (32.2)	3 (75)	0.42
PAH echocardiogram	3 (16.7)	2 (9.5)	0.8186	4 (12.9)	1 (12.5)	1
PAH RHC	**3 (23.1)**	**0 (0)**	**0.026**	2 (6.9)	1 (25)	0.5139
Pulmonary fibrosis	7 (38.9)	6 (28.6)	0.3969	10 (32.3)	3 (37.5)	1
Any GI involvement	12 (66.7)	18 (85.7)	0.2552	**26 (83.9)**	**4 (50)**	**0.0651**
Myositis	2 (11.11)	0 (0)	0.3911	2 (6.45)	0 (0)	1
Arthritis	**4 (23.5)**	**11 (52.4)**	**0.0694**	**15 (50)**	**0 (0)**	**0.0154**
Positive Scl-70	3 (18.8)	2 (9.5)	0.6419	3 (10)	2 (28.6)	0.3647
Positive Anti-centromere	9 (56.3)	11 (52.4)	1	15 (50)	5 (71.4)	0.7859
Positive PM-Scl	3 (20)	1 (4.8)	0.169	**1 (3.5)**	**3 (42.9)**	**0.0183**
Positive Anti-RNA polymerase III	1 (6.3)	3 (14.3)	0.8025	3 (10)	1 (14.3)	0.319
Positive U1 RNP	2 (13.3)	1 (4.8)	0.3966	2 (6.9)	1 (14.3)	0.3632
Positive ANA	14 (93.3)	20 (95.2)	0.6667	27 (93.1)	7 (100)	1

SD=Standard deviation, mRSS=modified Rodnan Skin Score, PAH=Pulmonary artery hypertension, RHC=Right heart catheterization

Table 1. Characteristics of patients whose calcinosis progressed and did not progress and whose calcinosis improved and did not improve.

	OR (95% CI)	p-value
Predictors for improvement		
Modified Rodnan Skin Score	1.1 (0.85 - 1.32)	0.6232
Positive PM-Scl	13.5 (0.99 - 183.14)	0.0511
Predictors for progression		
Modified Rodnan Skin Score	0.8 (0.72 - 1.03)	0.1103
Arthritis	3.6 (0.81 - 15.8)	0.0919

Table 2. Predictors for progression and improvement of calcinosis of the hands in multivariable analysis

Abstract Number: 1642

Automated Nailfold Capillary Counting System (AUTOCAPI) in Systemic Sclerosis Patients with Different Capillaroscopic Patterns

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SESSION INFORMATION

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Background/Purpose: Nailfold videocapillaroscopy (NVC) allows assessment of possible microvascular markers of severity and progression in systemic sclerosis (SSc), such as reduced capillary number, which has been associated with a high risk of developing disease complications (1-2). An automated capillary counting system (AUTOCAPI) has recently been validated in SSc patients (3). The aim of this study was to evaluate the performance of this automated software for absolute nailfold capillary number counting, in SSc patients with different NVC patterns of microangiopathy (Early, Active, and Late).

Methods: 183 SSc patients were random collected and enrolled at both Genova and Ghent Divisions of Rheumatology (LeRoy 2001 or ACR 2013 criteria, mean age 55±13 year, mean disease duration 5.5±6.8 years) and classified by NVC in one the following patterns: 28 "not specific", 37 "Early", 89 "Active", 29 "Late") (4). Eight fingers for each patient were analysed, counting the number of nailfold capillaries manually and by the AUTOCAPI software (DS Medica, Italy) along a millimetre in each finger image (3). The mean capillary number value from the eight finger images was calculated. The software reliability was assessed through calculation of the intraclass correlation coefficient (ICC) between automatic and manual counting.

Results: The mean number of capillaries assessed by manual vs automatic counting was as follows: 5.23±1.7 vs 5.47±1.3 in the total group of SSc patients, 5.91±1.2 vs 6.87±1.2 in the "not specific", 7.23±1.4 vs 5.67±1.1 in the "early", 4.67±1.1 vs 5.16±1.2 in the "active" and 3.72±1.5 vs 4.85±1.1 in the "Late" pattern of microangiopathy.The higher standard deviation observed for automatic counting was 1.23 in the "not specific" group. The following ICC's were obtained respectively for total patients, "not specific", "Early", "Active", and "Late" NVC patterns: 0.53, 0.51, 0.48, 0.50 and 0.66. The mean values for the manual versus automatic capillary counting assessed by the two centres in all SSc patients were respectively: 5.92±1.8 and 5.02±1.1 for Genova centre, and 4.71±1.5 and 5.83±1.4 for Ghent centre. The automatic counting confirmed that capillary number progressively reduces from "Early" to "Active" to "Late" NVC pattern of microangiopathy in SSc.

Conclusion: This study demonstrates the good reliability of AUTOCAPI software in nailfold capillary number counting in SSc patients with different patterns of microangiopathy. The use of automated counting software allows to standardize nailfold capillary assessment among different Rheumatologic centres.

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Disclosure: A. Sulli, None; **A. Vanhaecke**, None; **C. Pizzorni**, None; **G. Ferrari**, None; **V. Tomatis**, None; **M. Pendolino**, None; **V. Smith**, None; **M. Cutolo**, Boehringer, Actelion, Celgene, Bristol-Mayer Squibb, 2.

Abstract Number: 1643

Efficacy and Safety of Nintedanib in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease: Subgroup Analysis of the SENSCIS Trial by Corticosteroid Use

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SESSION INFORMATION

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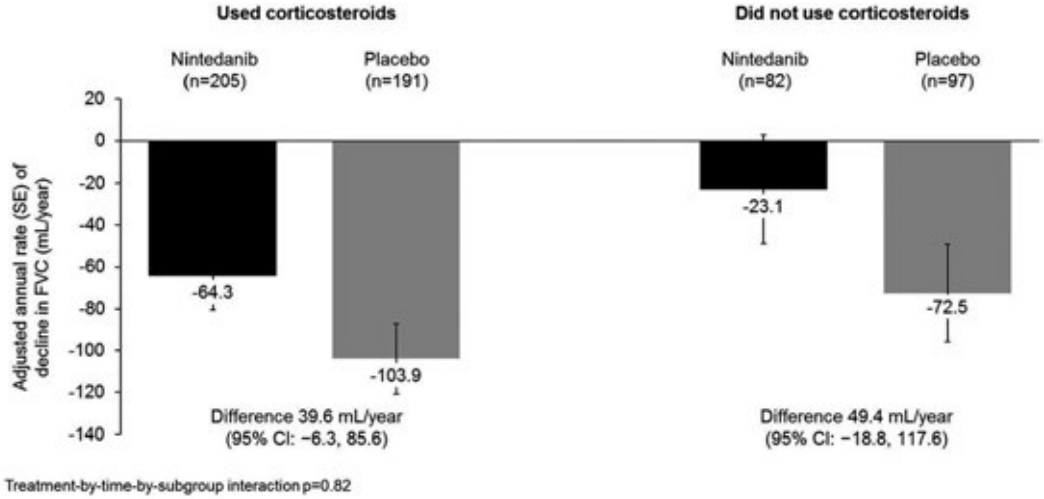
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In the SENSCIS trial in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD), nintedanib reduced the rate of decline in forced vital capacity (FVC) over 52 weeks compared with placebo (–52.4 versus –93.3 mL/year; difference 41.0 mL/year [95% CI 2.9, 79.0]; p=0.04), with adverse events that were manageable for most patients. Corticosteroids are commonly used in patients with SSc-ILD, despite a lack of evidence to support their efficacy. We assessed the efficacy and safety of nintedanib in patients who did and did not use corticosteroids in the SENSCIS trial.

Methods: Patients with SSc-ILD with ≥10% fibrosis of the lungs on HRCT were randomized to receive nintedanib 150 mg bid or placebo. Patients taking prednisone ≤10 mg/day or equivalent were allowed to participate. Lung function outcomes and adverse events (irrespective of causality) were analyzed in subgroups of patients who did and did not use corticosteroids. Corticosteroid use included use at baseline, during treatment with trial drug, and following discontinuation of trial drug (up to week 52).

Results: Of 576 patients who received trial drug, 206 (71.5%) and 191 (66.3%) patients in the nintedanib and placebo groups, respectively, used corticosteroids. Mean (SD) FVC (mL) at baseline was 2499 (814) in patients who used corticosteroids and 2501 (691) in patients who did not, and FVC % predicted was 71.9 (17.0) and 73.8 (15.9) in these

Figure. Annual rate of decline in FVC (mL/year) over 52 weeks in the SENSCIS trial in subgroups by use of corticosteroids



groups respectively. In patients who received placebo, the mean (SE) rate of decline in FVC over 52 weeks was numerically greater in patients who used corticosteroids than in those who did not [-103.9 (16.7) versus -72.5 (23.3) mL/year]. Nintedanib reduced the annual rate of decline in FVC (mL/year) versus placebo both in patients who did and did not use corticosteroids, with no difference in the treatment effect between subgroups detected (treatment-by-time-by-subgroup interaction p=0.82) (Figure). In the nintedanib and placebo groups, respectively, absolute declines in FVC >5% predicted were seen in 22.4% and 27.2% of patients who used corticosteroids (OR 0.78 [95% CI: 0.49, 1.23]) and 15.9% and 30.9% of patients who did not use corticosteroids (OR 0.42 [95% CI: 0.20, 0.87]) (treatment-by-subgroup interaction p=0.16). The adverse event profile of nintedanib was similar between the subgroups by corticosteroid use, but the proportions of patients with nausea or vomiting adverse events were lower, and the proportion with upper respiratory tract infection was higher, in those who used corticosteroids (Table). The proportion of patients treated with nintedanib who had adverse events leading to discontinuation of study drug was similar in patients who did and did not use corticosteroids. A limitation of these analyses is that they have not been adjusted for differences between the subgroups of patients taking and not taking corticosteroids at baseline.

Conclusion: In the SENSCIS trial in patients with SSc-ILD, over two-thirds of patients used corticosteroids. Nintedanib reduced the annual rate of decline in FVC irrespective of use of corticosteroids. The adverse event profile of nintedanib was similar in patients who did and did not use corticosteroids.

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Table. Adverse events by corticosteroid use in the SENSCIS trial

	Used corticosteroids		Did not use corticosteroids	
	Nintedanib (n=206)	Placebo (n=191)	Nintedanib (n=82)	Placebo (n=97)
Most frequent adverse events*				
Diarrhea	159 (77.2)	64 (33.5)	59 (72.0)	27 (27.8)
Nausea	59 (28.6)	27 (14.1)	32 (39.0)	12 (12.4)
Vomiting	45 (21.8)	21 (11.0)	26 (31.7)	9 (9.3)
Skin ulcer	42 (20.4)	38 (19.9)	11 (13.4)	12 (12.4)
Nasopharyngitis	27 (13.1)	33 (17.3)	9 (11.0)	16 (16.5)
Cough	27 (13.1)	35 (18.3)	7 (8.5)	17 (17.5)
Weight decreased	23 (11.2)	9 (4.7)	11 (13.4)	3 (3.1)
Upper respiratory tract infection	28 (13.6)	27 (14.1)	5 (6.1)	8 (8.2)
Abdominal pain	26 (12.6)	13 (6.8)	7 (8.5)	8 (8.2)
Fatigue	23 (11.2)	16 (8.4)	8 (9.8)	4 (4.1)
Decreased appetite	18 (8.7)	8 (4.2)	9 (11.0)	4 (4.1)
Adverse events leading to treatment discontinuation	31 (15.0)	15 (7.9)	15 (18.3)	10 (10.3)

Adverse events reported over 52 weeks (or until 28 days after last trial drug intake for patients who discontinued trial drug before week 52). Data are n (%) of patients with ≥1 such adverse event. Adverse events were coded according to preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA).
*Adverse events reported in >10% of patients in any of the subgroups shown.

5; **S. Johnson**, Bayer, 2, Boehringer Ingelheim, 2, 5, Corbus, 2, Ikaria, 5, Roche, 2; **S. Assassi**, Bayer, 2, Boehringer Ingelheim, 2, 5, 8, Integrity Continuing Education, 8, 9, Medscape, 8, 9, Momenta, 2; **L. Meng**, Boehringer Ingelheim, 3; **M. Quaresma**, Boehringer Ingelheim, 3; **M. Alves**, Boehringer Ingelheim, 3; **E. Clerisme-Beaty**, Boehringer Ingelheim, 3; **W. Wuyts**, Boehringer Ingelheim, 9, Roche, 9.

Abstract Number: 1644

Effects of Nintedanib in Patients with Diffuse and Limited Cutaneous Systemic Sclerosis and Interstitial Lung Disease: Subgroup Analysis of the SENSCIS Trial

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SESSION INFORMATION

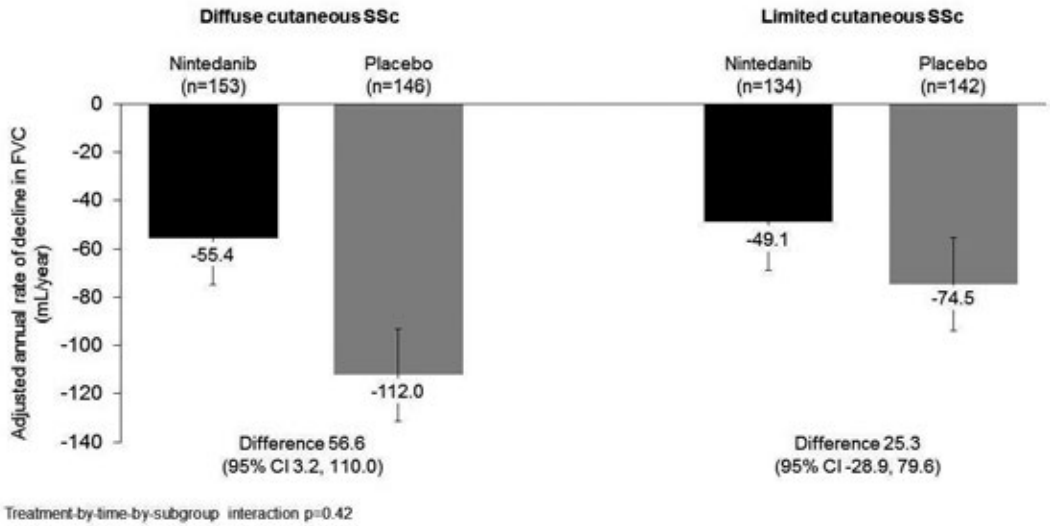
Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Figure. Annual rate of decline in FVC (mL/yr) over 52 weeks in the SENSCIS trial in subgroups with diffuse cutaneous SSc or limited cutaneous SSc.



Background/Purpose: Patients with diffuse cutaneous systemic sclerosis (dcSSc) are at greater risk of developing interstitial lung disease (ILD) than patients with limited cutaneous systemic sclerosis (lcSSc). In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) vs placebo over 52 weeks, with no difference between groups in the change from baseline in modified Rodnan skin score (mRSS). We analyzed data from the SENSCIS trial in subgroups of patients with lcSSc or dcSSc.

Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom < 7 years before screening and ≥10% fibrosis of the lungs on a high-resolution computed tomography (HRCT) scan were randomized to receive nintedanib 150 mg bid or placebo. We analyzed outcomes and adverse events over 52 weeks in subgroups of patients with lcSSc or dcSSc at baseline.

Results: Of 288 patients treated in each group, 153 (53.1%) and 146 (50.7%) in the nintedanib and placebo groups, respectively, had dcSSc. At baseline, in patients with dcSSc and lcSSc, respectively, mean (SD) FVC (mL) was 2461 (797) and 2542 (755), FVC % predicted was 70.5 (16.3) and 74.8 (16.8), and modified Rodnan skin score (mRSS) was 16.7 (8.8) and 5.2 (4.1). In the placebo group, the annual rate of FVC decline was numerically greater in patients with dcSSc than lcSSc (-112.0 vs -74.5 mL/year). Nintedanib reduced the rate of FVC decline both in patients with lcSSc and dcSSc. The treatment effect of nintedanib on FVC decline was numerically greater in patients with dcSSc than lcSSc, but no difference in the treatment effect between subgroups was detected (treatment-by-time-by-subgroup interaction p=0.42) (Figure). In the nintedanib and placebo groups, respectively, absolute declines in FVC >5% predicted at week 52 were seen in 22.2% and 28.8% of patients with dcSSc (OR 0.71 [95% CI 0.42, 1.20]) and 18.7% and 28.2% with lcSSc (OR 0.59 [0.33, 1.04]) (treatment-by-subgroup interaction p >0.05). Adjusted mean absolute changes from baseline in mRSS at week 52 in the nintedanib and placebo groups were -1.6 and -1.5 in patients with dcSSc (difference -0.2 [95% CI -1.2, 0.8]) and -2.7 and -2.5 in patients with lcSSc (difference -0.3 [-1.3, 0.8]; treatment-by-subgroup interaction p >0.05). The adverse event profile of nintedanib was similar between patients with dcSSc and lcSSc.

Conclusion: In the SENSCIS trial in patients with SSc-ILD, the rate of decline in FVC in patients who received placebo was greater in patients with dcSSc than lcSSc. Nintedanib reduced the rate of FVC decline both in patients with dcSSc and lcSSc. The treatment effect of nintedanib was numerically greater in patients with dcSSc than lcSSc,

but statistical testing did not indicate heterogeneity in the treatment effect between the subgroups. No effect of nintedanib was demonstrated on skin fibrosis assessed using the mRSS.

Disclosure: **M. Kuwana**, Abbvie, 2, 8, Actelion, 2, 8, Actelion Pharmaceuticals, 2, 8, Astellas, 2, 8, Bayer, 5, Boehringer Ingelheim, 5, Boehringer-Ingelheim, 5, Chugai, 2, 5, 8, Corbus, 5, CSL Behring, 5, CSL Berling, 5, Eisai, 2, 8, Eli Lilly, 2, Janssen, 8, Japan Blood Products Organization, 8, MBL, 7, 8, Ono, 2, 8, Pfizer, 2, Reata, 5, Tanabe-Mitsubishi, 2, 8; **K. Highland**, Actelion Pharmaceuticals, 2, 8, 9, Bayer, 8, Bayer Healthcare, 8, Boehringer Ingelheim, 2, 5, 8, 9, Eiger Pharmaceuticals, 2, Genentech, 2, 8, Gilead Sciences, 8, Reata Pharmaceuticals, 2, United Therapeutics, 2, 8; **M. Gahlemann**, Boehringer Ingelheim, 3; **C. Denton**, Actelion, 5, Actelion Pharmaceuticals, 5, Actelion, GlaxoSmithKline, Bayer, Sanofi, Inventiva, Boehringer Ingelheim, Roche, Bristol Myers Squibb, CSL Behring, UCB, Leadiant Biosciences, 5, Bayer, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Corbus Pharmaceuticals, 5, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, Leadiant Biosciences, 2, 5, Inventiva, 5, Pfizer, 5, Roche, 5, Sanofi, 5, UCB, 5; **A. Fischer**, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Hoffmann-La Roche, 5, Roche, 5; **M. Mayes**, Boehringer Ingelheim, 5, 8, 9, Corbus, 9, Corbus Pharma, 9, Eicos, 9, Eicos Sciences, 9, Galapagos, 5, 9, GlaxoSmithKline, 9, Mitsubishi Tanabe Pharma, 5, Mitsubishi-Tanabe, 5, Reata Pharma, 9, Reata Pharmaceuticals, 9, Sanofi, 9; **V. Steen**, Boehringer Ingelheim, 5, Corbus, 5, 9, CSL, 5, 9, CSL Behring, 2, 5, DSMB, 5, 9, Galapagos, 5, 9; **D. Khanna**, Acceleron, 5, 8, Acceleron Pharma, 5, Actelion, 5, 8, Actelion Pharmaceuticals, 5, Astra Zeneca, 5, Bayer, 2, 5, 8, Behring, 5, Blade, 5, Blade Therapeutics, 5, 8, Blade therapeutics, 5, BMS, 2, 5, 8, Boehringer Ingelham, 5, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Celegene, 5, Celgene, 5, 8, ChemomAB, 5, ChemomAb, 5, CiviBioPharma, Inc., 3, Corbus, 5, Corobus, 5, Corpus, 5, CSL Behring, 5, 8, Curizon, 5, Curzion, 5, Cytori, 5, 8, Eicos, 4, Eicos Sciences, 4, Eicos Sciences, Inc, 4, Eicos Sciences, Inc/ CiviBioPharma, Inc, 1, 4, Eicos Sciences, Inc/ CiviBioPharma, Inc., 1, Eicos, Inc, 4, Eicos, Inc., 5, 8, Eicos, INC., 4, Galapagos, 5, Genentech, 5, Genentech/Roche, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 2, 5, Mitsubishi Tanabe Pharma, 5, Mitsubishi Tanabe Pharma Dev America, 5, Mitsubishi Tanabe Pharma Development America, 5, Mitsubishi Tanabi, 5, NIH K24 and R01, 2, NIH / NIAMS K24 AR-063120, 2, NIH/NIAMS R01& K24, 2, Pfizer, 2, 5, Sanofi, 5, Sanofi Aventis, 5, Sanofi-Aventis, 5, 8, Sanofi-Aventis/ Genzyme, 5, UCB, 5, UCB Pharma, 5; **Y. Allanore**, Actelion, 2, 5, Alpine, 2, 5, Bayer, 2, 5, BMS, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 2, 5, Genentech Roche, 2, 5, Inventiva, 2, 5, Italfarmaco, 2, 5, Sanofi, 2, 5, Servier, 2, 5; **M. Girard**, Boehringer Ingelheim, 3; **M. Alves**, Boehringer Ingelheim, 3; **S. Stowasser**, Boehringer Ingelheim, 3; **O. Distler**, A. Menarini, 5, Abbvie, Acceleron, 5, Acceleron Pharma, 5, Actelion, 2, 5, 8, Actelion Pharmaceuticals, 2, 5, 8, 9, Amgen, 5, AnaMar, 2, 5, Bayer, 2, 5, 8, 9, Biogen Idec, 2, 5, Blade Therapeutics, 5, Boehringer Ingelheim, 2, 5, 8, 9, Catenion, 5, 9, ChemomAb, 2, 5, ChemomAB, 5, CSL Behring, 5, Ergonex, 5, espeRare Foundation, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 5, GSK, 2, 5, Holds Patent mir-29 for the treatment of systemic sclerosis, 9, Inventiva, 2, 5, iQvia, 5, Italfarmaco, 2, 5, Italfarmco, 5, Lilly, 2, 5, med, 5, 8, medac, 5, Medac, 2, 5, MedImmune, 2, 5, Medscape, 5, 8, 9, Menarini, 8, Mepha, 8, Mitsubishi Tanabe, 2, 5, Mitsubishi Tanabe Pharma, 2, 5, MSD, 5, 8, Novartis, 2, 5, 8, 9, Patent, 9, Patent issued, 9, Pfizer, 2, 5, 8, Pharmacyclics, 2, 5, Roche, 5, 8, 9, Sanofi, 2, 5, Sinoxa, 2, 5, Target Bio Science, 5, Target BioScience, 5, UCB, 2, 5, 9, UCB in the area of potential treatments of scleroderma and its complications, 2, 5.

Abstract Number: 1645

Comparison of Automated Capture and Analysis System of Sublingual Microvessels and Nailfold Videocapillarscopy for Microvascular Assessment in Systemic Sclerosis

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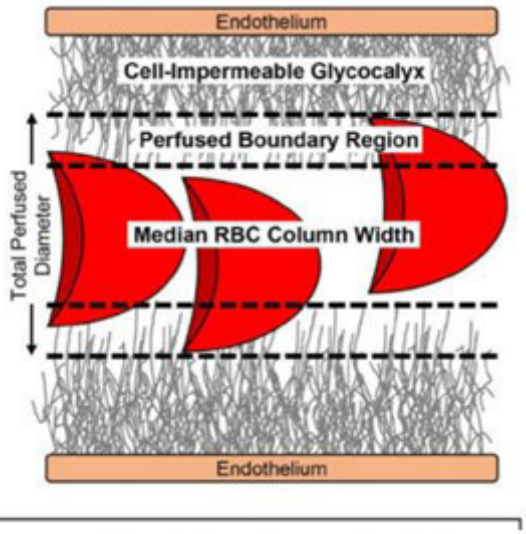

Figure. Sublingual intravital microscopy parameters

SESSION INFORMATION
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Background/Purpose: Similar to nailfold videocapillaroscopy (NVC), automated capture and analysis of sublingual microvessel segments (intravital microscopy) can define vasculopathy, and distinguish systemic sclerosis (SSc) patients from healthy controls. The aim of this study is to compare automated capture and analysis of sublingual microcirculation parameters with NVC derived scores for assessment of SSc-related vasculopathy.

Methods: Consecutive, consented SSc registry patients that met ACR/EULAR classification criteria had intravital microscopy of the sublingual microcirculation and NVC at the time of routine care. The following intravital microscopy parameters were captured: total microvascular density, median RBC width (RBCfract) and perfused boundary region (PBR) (Figure 1). The following NVC parameters were obtained: (1) capillaroscopy patterns (early, active and late); (2) degree of enlarged capillaries, giant capillaries, capillary hemorrhages, capillary density, disorganization of vascular array and capillary ramification assessed by a semi-quantitative method; and (3) microangiopathy evolution score (sum of capillary density, disorganization of vascular array and capillary ramification). Non-parametric tests were used for statistical evaluation.

Results: Thirty-nine SSc patients were enrolled (37 women and 2 men, mean age 59±21 years, mean SSc duration years 9.5±8.9, 30 limited cutaneous SSc and 9 diffuse cutaneous SSc). There was a statistically significant negative correlation between sublingual total microvascular density and microangiopathy evolution score (r=-0.532, p=0.0006). Furthermore, there was a highly significant inverse association between the total microvascular density and number of capillaries measured by NVC (r=-0.569, p=0.0002). There was significant, negative correlation between the total microvascular density and disorganization of vascular array and capillary ramification (r=-0.461, p=0.003) and degree of giant capillaries (r=-0.387, p=0.01). There was no correlation between RBCfract and PBR with NVC parameters.

Conclusion: This study confirmed a significant correlation between intravital microscopy of the sublingual microcirculation and NVC in terms of sublingual total microvascular density and microangiopathy evolution score. The two methods

did not correlate in all captured parameters. Consequently, in order to define progressive vasculopathy in SSc, intravital microscopy of the sublingual microcirculation could be a valuable tool in addition to NVC for longitudinal analysis.

Disclosure: M. Radic, None; **J. Thomas**, None; **T. Frech**, None.

Abstract Number: 1646

Incidence Rate and Prevalence of Valvular Heart Disease in Systemic Sclerosis: A Retrospective Cohort Study from a Single Institution

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SESSION INFORMATION

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Background/Purpose: Systemic sclerosis (SSc) associated heart involvement remains ill-defined, with non-ischemic systolic heart failure, conduction defects, and arrhythmias often included in the definition in clinical studies.

Table 1. Demographics and Characteristics at time of Baseline Echo

	Total (n=506) N (%)
Age, yrs, mean (SD)	59.7 (12.8)
Female sex	435 (86)
Race	
Caucasian	479 (95)
Non-Caucasian/Unknown	27 (5)
Subtype	
Limited/Sine	415/490 (85)
Diffuse	75/490 (15)
Autoantibodies	
ANA	418/451 (93)
Anti-centromere	210/392 (54)
Anti-Scl70	62/348 (18)
Anti-RNA Polymerase III	19/75 (25)
Disease duration, yrs, mean (SD)	0.8 (1.4)
Time between first and last echo, yrs, mean (SD)	5.6 (4.3)
Body Mass Index (BMI), kg/m^2, mean (SD)	27.8 (20.7)
Smoking Status	
Never smoker	267/503 (53)
Former smoker	210/503 (42)
Current smoker	26/503 (5)
Hypertension	180/503 (36)
Diabetes Mellitus	26/505 (5)
Coronary Artery Disease	27 (5)
Chronic Kidney Disease	43 (8)

Table 2. Prevalence and Incidence Rate of Valvular Heart Disease in SSc

Valve Disease Type & Severity	Prevalence at Baseline Echo, N (%)	Incidence Rate per 100 person-years (95% CI)
Aortic Regurgitation		
None/Trivial	467 (92)	
Mild	36 (7)	1.80 (1.31, 2.36)
Moderate	3 (1)	0.29 (0.12, 0.52)
Severe	0 (0)	0.00
Aortic Stenosis		
None/Trivial	500 (99)	
Mild	3 (1)	1.25 (0.87, 1.70)
Moderate	1 (0)	0.65 (0.38, 0.98)
Severe	2 (0)	0.28 (0.12, 0.51)
Mitral Regurgitation		
None/Trivial	385 (76)	
Mild	99 (20)	6.36 (5.24, 7.59)
Moderate	18 (4)	1.46 (1.03, 1.95)
Severe	4 (1)	0.04 (0.00, 0.13)
Mitral Stenosis		
None	505 (100)	
Mild	0 (0)	0.21 (0.08, 0.42)
Moderate	1 (0)	0.07 (0.01, 0.20)
Severe	0 (0)	0.04 (0.00, 0.13)

Valvular heart disease (VHD) in SSc has not been well studied. In this referral-based single-institution cohort, we evaluate the incidence rate (IR) and prevalence of VHD in SSc.

Methods: In this retrospective cohort study, medical records of 506 cases with SSc seen between 1/1/2000 and 11/10/2018, with at least two echocardiograms in the health care system, were manually reviewed. All cases included fulfilled ACR/EULAR 2013 classification criteria for SSc or 3/5 CREST criteria, and had a baseline echocardiogram within five years of diagnosis. Mild, moderate, and severe VHD was clinically defined at time of echocardiogram. IR of VHD, per 100 person-years, and prevalence of VHD were determined. Cox models were used to examine associations between incident VHD and SSc characteristics as well as cardiovascular disease (CVD) risk factors, adjusting for age and sex.

Results: Demographics, SSc characteristics, and baseline CVD risk factors are reported in table 1. Mitral regurgitation (MR) was most common, with 20% of cases having at least mild MR on baseline echocardiogram (table 2). The prevalence of at least mild aortic regurgitation (AR) or aortic stenosis (AS) was 7% and 1%, respectively (table 2). The highest IR (IR) (per 100 person-years) was 6.36 (95% CI 5.24 - 7.59) for mild MR, followed by 1.80 (95% CI 1.31 - 2.36) for mild AR and 1.25 (95% CI 0.87 - 1.70) for mild AS (table 2). Development of severe VHD was only observed for AS, with an IR of 0.28 (95% CI 0.12 - 0.51). On age- and sex-adjusted hazard models examining baseline SSc and CVD risk factors for incident VHD, age remained a significant risk factor for all VHD types (table 3). Coronary artery disease (CAD) was associated with incidence of at least mild MR (HR 2.20, 95% CI 1.04 - 4.65) (table 3). Anti-Scl70 antibody was associated with at least mild incident MR (HR 1.81, 95% CI 1.11 - 2.97) and was negatively associated with at least mild incident aortic stenosis (HR 0.18, 95% CI 0.04 – 0.87) (table 3). Anti-centromere antibody trended towards significance for at least mild incident AS (HR 2.02, 95% CI 0.92 - 4.47) (table 3).

Conclusion: MR was the most common VHD found at baseline echocardiogram in this retrospective cohort of patients with SSc, and was also the most common valve abnormality to develop, typically mild in severity. Development of any severe valve disease was less common, with severe aortic stenosis having the highest IR. Follow-up time was

Table 3. Age- and Sex-Adjusted Cox Models Evaluating Association Between Baseline Risk Factors and at least Mild Incident Valvular Heart Disease in Subjects with SSc

Characteristic	At least mild AR	At least mild AS	At least mild MR
	Hazard ratio* (95% CI)	Hazard ratio* (95% CI)	Hazard ratio* (95% CI)
Age (per 10 years)	2.05 (1.54, 2.74)	2.25 (1.60, 3.14)	1.27 (1.10, 1.48)
Female Sex	0.95 (0.40, 2.25)	1.10 (0.38, 3.18)	0.73 (0.44, 1.21)
Disease duration, yrs	0.99 (0.81, 1.21)	0.85 (0.65, 1.10)	1.06 (0.93, 1.20)
BMI, kg/m^2	1.00 (0.99, 1.01)	0.98 (0.91, 1.04)	0.99 (0.96, 1.02)
Ever smoker	1.34 (0.74, 2.43)	0.87 (0.43, 1.76)	1.43 (0.97, 2.10)
Diffuse vs Limited/Sine	0.66 (0.23, 1.89)	0.45 (0.10, 1.93)	0.97 (0.57, 1.65)
Anti-Centromere Ab	0.86 (0.44, 1.70)	2.02 (0.92, 4.47)	0.87 (0.55, 1.38)
Anti- Scl70 Ab	0.89 (0.35, 2.23)	0.18 (0.04, 0.87)	1.81 (1.11, 2.97)
Anti-RNA Pol III Ab	2.89 (0.17, 48.82)	--	0.52 (0.09, 2.89)
Anti-Nuclear Ab (ANA)	2.47 (0.34, 18.07)	1.42 (0.19, 10.59)	1.21 (0.56, 2.61)
Hypertension	1.56 (0.85, 2.87)	0.52 (0.25, 1.10)	1.25 (0.84, 1.86)
Diabetes Mellitus	0.52 (0.07, 3.77)	1.75 (0.40, 7.63)	1.04 (0.48, 2.27)
CAD	1.79 (0.60, 5.36)	1.32 (0.29, 6.03)	2.20 (1.04, 4.65)
CKD	1.82 (0.76, 4.36)	1.38 (0.41, 4.63)	1.69 (0.92, 3.13)

AR=Aortic Regurgitation; AS=Aortic Stenosis; MR=Mitral Regurgitation; Ab=Antibody; Anti-RNA Pol III=Anti-RNA Polymerase III; CAD=Coronary Artery Disease; CKD=Chronic Kidney Disease
*Age- and Sex-adjusted

relatively short at a mean of less than 6 years. As VHD may cause cardiac remodeling and cardiopulmonary hemodynamic changes, additional studies examining impact of VHD on cardiopulmonary outcomes in SSc and appropriate management strategies in this population are warranted.

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Abstract Number: 1647

The Collaborative National Quality and Efficacy Registry for Scleroderma: Data Completion Outcomes from a Multicenter United States Cohort Using Guideline-Based Registry Practices

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SESSION INFORMATION

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Background/Purpose: The Collaborative National Quality and Efficacy Registry (CONQUER) for Scleroderma is a multicenter US-based longitudinal study of patients with systemic sclerosis (SSc) within 5 years of first non-Raynaud's symptom. Supported by the Scleroderma Research Foundation, CONQUER is designed to provide linked bio-specimen and clinical outcomes data on a longitudinal cohort of SSc patients for validation of hypothesis driven research and to provide a platform for studying patient reported outcomes. The purpose of this analysis was to assess the effectiveness of guideline-based registry practices on database quality at 6 months.

Methods: The CONQUER registry was developed using the guidelines of the International Society for Biological Repositories. It was an iterative process between 13 physicians with an expertise in SSc, patient stakeholders, and information technology experts to ensure there is minimal missing data in 775 fields of data elements.

Results: During the first 6 months of the CONQUER Scleroderma study, 151 SSc patients with less than 5 years of disease duration (from first non-Raynaud's symptom) were recruited. The mean age is 51 ± 14 years, 83% are female and 60% of patients have diffuse disease. Data completion is shown in Table 1. Survey completion rates are above 88% for all patient reported outcome surveys. Bio-specimen collection rates are over 97% and disease severity score completion rates are over 98%.

Conclusion: As demonstrated by data completion, the CONQUER study demonstrates the value of guideline-based registries that are designed by physicians, patients, and information technology experts. CONQUER is a unique and growing resource for studying SSc in a longitudinal, US-based population.

Disclosure: V. Shanmugam, AbbVie, 2; **T. Frech**, None; **V. Steen**, Boehringer Ingelheim, 5, Corbus, 5, 9, CSL, 5, 9, CSL Behring, 2, 5, DSMB, 5, 9, Galapagos, 5, 9; **L. Hummers**, Boehringer Ingelheim, 2, 5, Boehringer-Ingelheim, 2, 5, Corbus, 2, Corbus Pharmacueticals, 2, CSL Behring, 5, Cumberland, 2, Cumberland Pharmaceuticals, 2, Cytori, 2,

Table 1: Clinical Data and Assessment Collection

	Overall (N = 151)
Baseline Form	151 (100.0%)
Social History	151 (100.0%)
Medications	151 (100.0%)
Vitals	151 (100.0%)
Samples[1]	144 (95.4%)
Serum	144 (100.0%)
RNA	140 (97.2%)
EDTA	141 (97.9%)
Other[2]	6 (4.2%)
Pulmonary Function Test	137 (90.7%)
Six Minute Walk Test	19 (12.6%)
Echocardiogram	121 (80.1%)
Right Heart Catheterization	19 (12.6%)
Electrocardiogram	49 (32.5%)
High Resolution CT	95 (62.9%)
Lab Assessments	148 (98.0%)
ANA	143 (94.7%)
Autoantibodies	141 (93.4%)
Rodnan Skin Score	151 (100.0%)
Musculoskeletal Assessment	148 (98.0%)
Vascular Assessment	151 (100.0%)
Gastrointestinal Severity Assessment	150 (99.3%)
Cardio Pulmonary Assessment	149 (98.7%)

[1] Percentages of Serum, RNA, EDTA and Other are out of the number of patients that had samples collected.
[2] Other samples could be skin or other specified sample.

Cytori Therapeutics, 2, GlaxoSmithKline, 2; **A. Shah**, Bristol Meyer Squibb, 5, Bristol-Myers Squibb, 5; **E. Bernstein**, None; **D. Khanna**, Acceleron, 5, 8, Acceleron Pharma, 5, Actelion, 5, 8, Actelion Pharmaceuticals, 5, Astra Zeneca, 5, Bayer, 2, 5, 8, Behring, 5, Blade, 5, Blade Therapeutics, 5, 8, Blade therapeutics, 5, BMS, 2, 5, 8, Boehringer Ingelham, 5, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Celegene, 5, Celgene, 5, 8, ChemomAB, 5, ChemomAb, 5, CiviBioPharma, Inc., 3, Corbus, 5, Corobus, 5, Corpus, 5, CSL Behring, 5, 8, Curizon, 5, Curzion, 5, Cytori, 5, 8, Eicos, 4, Eicos Sciences, 4, Eicos Sciences, Inc, 4, Eicos Sciences, Inc/ CiviBioPharma, Inc, 1, 4, Eicos Sciences, Inc/ CiviBioPharma, Inc., 1, Eicos, Inc, 4, Eicos, Inc., 5, 8, Eicos, INC., 4, Galapagos, 5, Genentech, 5, Genentech/Roche, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 2, 5, Mitsubishi Tanabe Pharma, 5, Mitsubishi Tanabe Pharma Dev America, 5, Mitsubishi Tanabe Pharma Development America, 5, Mitsubishi Tanabi, 5, NIH K24 and R01, 2, NIH / NIAMS K24 AR-063120, 2, NIH/NIAMS R01& K24, 2, Pfizer, 2, 5, Sanofi, 5, Sanofi Aventis, 5, Sanofi-Aventis, 5, 8, Sanofi-Aventis/Genzyme, 5, UCB, 5, UCB Pharma, 5; **J. Gordon**, Corbus, 2, Corbus Pharmaceuticals, 2, Cumberland, 2, Cumberland Pharmaceuticals, 2, Elcos, 2; **F. Castelino**, Boehringer-Ingelheim, 5, Corbus, 9, Cumberland, 9, Galapagos, 9, Scleroderma Research Foundation, 2; **L. Chung**, BMS, 6, 9, Boehrenger-Ingelheim, 5, Boehringer Ingelheim, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squib, 5, Eicos, 5, 6, 9, Eicos Steering Committee, 5, Mitsubishi Tanabe, 5, Reata, 5, 6, Reata DSMB, 5, Reatta, 5; **F. Hant**, None; **E. Startup**, None; **J. VanBuren**, None; **L. Evnin**, None; **S. Assassi**, Bayer, 2, Boehringer Ingelheim, 2, 5, 8, Integrity Continuing Education, 8, 9, Medscape, 8, 9, Momenta, 2.

Abstract Number: 1648

Systemic Sclerosis Auto-antibody Profiles Predict Interstitial Lung Disease Onset but Not Progression

Boyang Zheng,[1] Mianbo Wang,[2] Marvin Fritzler,[3] May Choi,[3] Murray Baron,[4] and Marie Hudson[5], [1]Jewish General Hospital, McGill University, Montreal, QC, Canada, [2]Lady Davis Institute, Jewish General Hospital, Montreal, QC, Canada, [3]Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, [4]Jewish General Hospital, McGill University, Montreal, Canada, [5]Jewish General Hospital, Lady Davis Institute for Medical Research, and Department of Medicine, McGill University, Montreal, QC, Canada

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Figure 1: Kaplan-Meier curves to compare the time to ILD onset between auto-antibody subsets

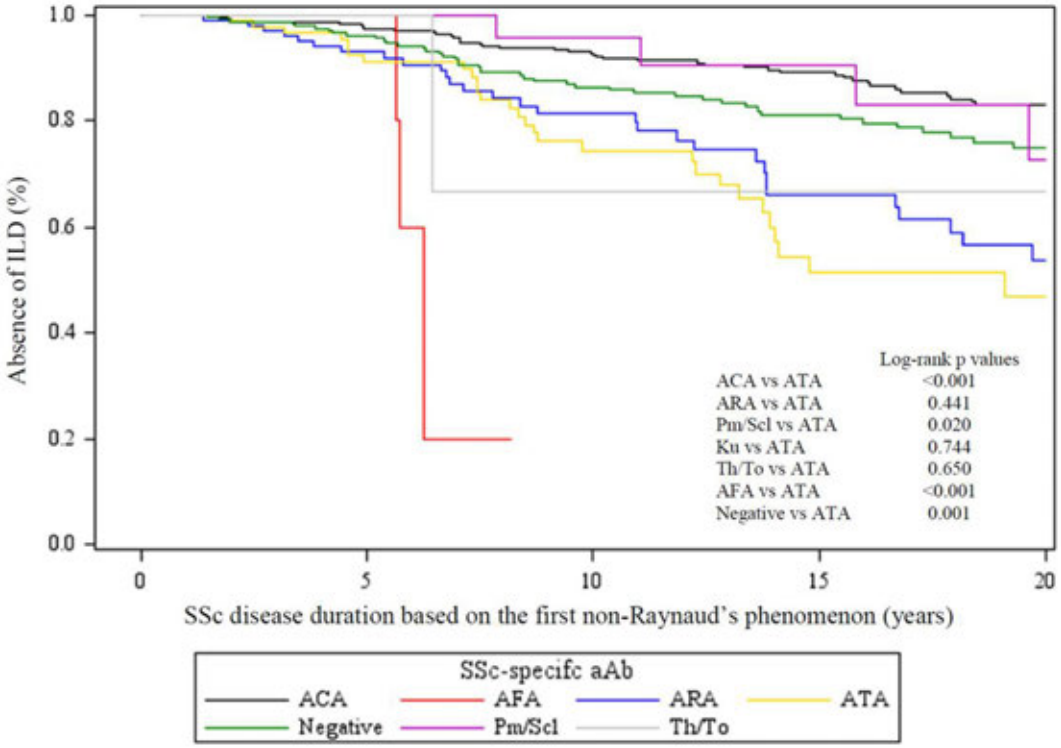
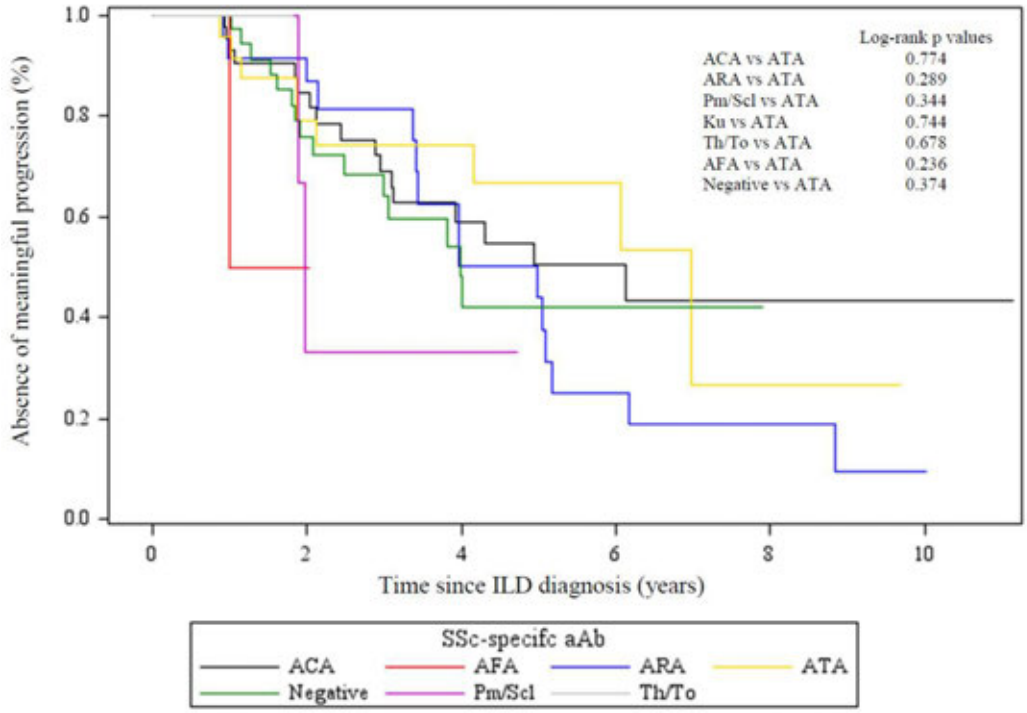


Figure 2: Kaplan-Meier curves to compare the time to clinically meaningful ILD progression between auto-antibody subsets after ILD diagnosis



Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is frequent manifestation and a leading cause of mortality in systemic sclerosis (SSc). Some SSc-related autoantibodies (aAbs), especially anti-topoisomerase I (ATA), are associated with an increased prevalence of ILD. In contrast, anti-centromere (ACA) may be protective. The association with other aAbs is unclear and it is unknown whether aAb profiles can predict the rate of ILD progression. Our goal was to examine the incidence of SSc-ILD and its subsequent progression between different aAb profiles. We hypothesized that while aAbs predict ILD development, all SSc-ILD progress similarly.

Methods: SSc subjects without pre-existing ILD in a large multi-center longitudinal cohort from 2004-2018 were included. ILD was defined by the presence of high-resolution computed tomography (HRCT) findings, or if no HRCT was available, then either a chest x-ray showing interstitial fibrosis, and/or the presence of "velcro like crackles" on exam. Clinically meaningful progression of ILD was defined using OMERACT criteria(1) of ≥10% relative decline in FVC, or ≥5% to < 10% relative decline in FVC and ≥15% relative decline in DLCO. Subjects were grouped based on single specificity aAbs: ATA, ACA, anti-RNA polymerase III (ARA), anti-PM/Scl, anti-Ku, anti-Th/To (hPOP1), anti-fibrillarin (AFA), or negative aAbs. The time to ILD onset was compared between groups using Kaplan Meier and multivariate Cox analyses adjusted for age, gender, diffuse (vs. limited) subset, physician global assessment of severity, immunosuppression exposure at or prior to baseline and presence of anti-Ro52/TRIM21 antibodies. In those with incident ILD, the time to clinically meaningful progression and mortality after ILD onset were examined. ATA served as the reference for all comparisons.

Results: Of 931 patients, 190 (20%) developed ILD: 60/429 (14%) ACA, 31/94 (33%) ATA, 32/114 (28%) ARA, 6/24 (25%) anti-Pm/Scl, 0/2 anti-Ku, 2/5 (40%) anti-Th/To, 4/5 (80%) AFA, and 55/258 (21%) negative aAb. Subjects with ATA developed ILD earlier than ACA, anti-PM/Scl and negative aAb groups (log rank $p < 0.01$, $p = 0.02$ and $p < 0.01$, respectively), although AFA group had the most rapid onset ($p < 0.01$) (Figure 1). In multivariate analyses, ACA and negative aAb groups were less likely (HR (95% CI) 0.36 (0.22, 0.57) and 0.53 (0.34, 0.84) respectively), whereas AFA was more likely (HR (95% CI) 4.12 (1.22, 13.86)) to develop ILD compared to ATA. On the other hand, no differences in the time to clinically meaningful ILD progression (Figure 2) or survival after ILD onset were found between groups.

Conclusion: Compared to patients with ATA, AFA conferred a higher risk of developing ILD, whereas ACA, anti-PM/Scl and the absence of SSc specific aAbs were associated with a lower risk. Nevertheless, ILD developed in all aAb sub-groups and, once present, the aAb profile was not associated with ILD progression or subsequent mortality.

Reference

1. Khanna D, Mittoo S, Aggarwal R, Proudman SM, Dalbeth N, Matteson EL, et al. Connective Tissue Disease-associated Interstitial Lung Diseases (CTD-ILD) - Report from OMERACT CTD-ILD Working Group. The Journal of rheumatology. 2015;42(11):2168-71.

Disclosure: B. Zheng, None; **M. Wang**, None; **M. Fritzler**, Alexion Canada, 7, BioRad, 5, Dr. Fooke Laboratorien GmbH, 5, Euroimmun GmbH, 5, 7, ImmunoConcepts, 7, Inova Diagnostics, 5, 7, 8, Inova Diagnostics Inc. San diego, CA, 5, Inova Dx, Mikrogen GmbH, 5, Werfen International, 5; **M. Choi**, None; **M. Baron**, None; **M. Hudson**, None.

Abstract Number: 1649

Mycophenolate Mofetil and Cyclophosphamide Improve Health-Related Quality of Life in Patients with Systemic Sclerosis Who Participated in SLS II

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Table 1. Changes in patient reported outcomes, as well as the proportion of participants meeting the minimum clinically important difference (MCID) for each patient reported outcome for SLS II participants randomized to mycophenolate (MMF) versus cyclophosphamide (CYC).

	Change from baseline to 24 months in CYC arm	Change from baseline to 24 months in MMF arm	Treatment group differences (P-value)	% Patients meeting MCID in CYC arm at 24 months	% Patients meeting MCID in MMF arm at 24 months
SF-36 PCS[a]	N=53 Mean change: 2.34 P=0.08	N=53 Mean change: 2.04 P=0.13	0.87	17%	17%
SF-36 MCS[a]	N=53 Mean change: 2.10 P=0.11	N=53 Mean change: 3.41 P=0.02	0.67	20%	21%
Total GIT 2.0[b]	N=53 Mean change: -0.04 P=0.39	N=52 Mean change: 0.05 P=0.33	0.19	13%	10%
HAQ-DI[c]	N=53 Mean change: -0.04 P=0.43	N=53 Mean change: 0.02 P=0.79	0.51	17%	14%
TDI[d]	N=39 Mean change: 2.09 P=0.0003	N=53 Mean change: 1.86 P=0.005	0.80	29%	24%
LCQ[e]	N=52 Mean change: 0.62 P=0.24	N=52 Mean change: 0.74 P=0.12	0.87	16%	10%
SGRQ[f]	N=53 Mean change: -5.53 P=0.029	N=52 Mean change: -3.36 P=0.43	0.34	28%	25%

[a] Postive change for the SF-36 Physical Component Summary (PCS) and Medical Component Summary (MCS) indicates improvement. The MCID for the SF-36 PCS and MCS domains is >= 5.
[b] Negative change for GIT 2.0 indicates improvement. The MCID for the total GIT 2.0 score is <= -0.21.
[c] Negative change for HAQ-DI indicates improvement. The MCID for the HAQ-DI score is <= -0.22.
[d] Postive change for the TDI indicates improvement. The MCID for the TDI score is >= 1.
[e] Positive change for LCQ indicates improvement. The MCID for the LCQ is >= 1.5.
[f] Negative change for SGRQ indicates improvement. The MCID for the SGRQ is <= -4.

Background/Purpose: Interstitial lung disease (ILD) is the leading cause of morbidity and mortality in systemic sclerosis (SSc). The majority of studies investigating novel therapies for SSc-ILD use the forced vital capacity (FVC) as the primary outcome. However, changes in the FVC may not consistently translate into clinically meaningful improvements from a patient's perspective. This study evaluated whether treatment with cyclophosphamide (CYC) and mycophenolate (MMF) improves health-related quality of life (HRQOL) among SSc patients with active ILD.

Methods: This study examined outcomes in patients (N=142) who participated in Scleroderma Lung Study (SLS) II (Tashkin et al. Lancet Resp Med 2016), a randomized controlled trial comparing mycophenolate (MMF) for 2 years versus oral CYC for 1 year followed by 1 year of placebo in patients with relatively early SSc-ILD. The following HRQOL outcomes were examined: Short Form 36 (SF-36), Health Assessment Questionnaire (HAQ) disability index (DI), Baseline and Transitional Dyspnea Index (BDI, TDI), the Leicester Cough Questionnaire (LCQ), St. George's Respiratory Questionnaire (SGRQ), and the Scleroderma Clinical Trials Consortium Gastrointestinal Tract (GIT) 2.0. The differences in HRQOL scores from baseline to 24 months were measured in each treatment arm. The proportion of subjects in each treatment group whose scores improved at >= the minimum clinically important difference (MCID) in HRQOL measures was assessed. Correlations between changes in HRQOL and those in FVC%-predicted were also examined using Pearson correlation coefficient.

Results: Treatment with CYC and MMF led to improvements in HRQOL outcomes, with no appreciable between treatment arm differences (Table 1). The TDI improved significantly in both treatment arms (CYC: P=0.0003; MMF: P=0.005), and 29% and 24% of CYC and MMF patients, respectively, met or exceeded MCID estimates. For the HAQ-DI, 17% and 14% of CYC and MMF patients, respectively, met or exceeded the MCID estimates. For Total SGRQ scores 28% and 25% of CYC and MMF patients, respectively, met or exceeded MCID estimates. At baseline, the FVC%-predicted did not correlate with any of the HRQOL outcomes (coefficients with HRQOL ranged from 0.01 to 0.11; data not shown) The 24-month change in the FVC-% predicted correlated weakly with only a few of the changes in HRQOL scores (HAQ-DI r=-0.30; TDI r=-0.40; SF-36 Physical Component Summary r=0.30).

Conclusion: Treatment with CYC and MMF improved overall HRQOL in patients with SSc-ILD, including a large proportion who improved in dyspnea and respiratory HRQOL by >= MCID estimates. The relationship between HRQOL measures and changes in the FVC was relatively weak, suggesting that changes in the PROs provide additional information about treatment efficacy not captured by changes in the FVC alone in this patient population. The overall improvement in FVC%, along with HRQOL in the SLS-II, supports the treatment of SSc-ILD with immunosuppressive therapies. Future SSc-ILD trials should include PROs as they directly measure how a patient feels and functions.

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2, NIH / NIAMS K24 AR-063120, 2, NIH/NIAMS R01& K24, 2, Pfizer, 2, 5, Sanofi, 5, Sanofi Aventis, 5, Sanofi-Aventis, 5, 8, Sanofi-Aventis/Genzyme, 5, UCB, 5, UCB Pharma, 5.

Abstract Number: 1650

Baseline Skin Score, Older Age and CD34-selection Influence the Outcome of Autologous Stem Cell Transplantation for Systemic Sclerosis – Results of a Prospective Non-interventional Study from the European Society for Blood & Marrow Transplantation (EBMT)

Joerg Henes,[1] Maria Carolina Oliveira,[2] Myriam Labopin,[3] Manuela Badoglio,[4] Hans Ulrich Scherer,[5] Nicoletta Del Papa,[6] Thomas Daikeler,[7] Marc Schmalzing,[8] Roland Schroers,[9] Thierry Martin,[10] Grégory Pugnet,[11] Belinda Simoes,[12] David Michonneau,[13] Erik Marijt,[14] Bruno Lioure,[15] Jacques Olivier Bay,[16] John Snowden,[17] Montserrat Rovira,[18] Anne Huynh,[19] Francesco Onida,[20] Lothar Kanz,[1] Zora Marjanovic,[21] and Dominique Farge[22], [1]University Hospital Tuebingen, Department of Internal Medicine II (Oncology, Haematology, Immunology and Rheumatology), Tuebingen, Germany, [2]Ribeirão Preto Medical School, University of São Paulo, Sao Paulo, Brazil, [3]EBMT Paris Study Office, Saint Antoine Hospital, Université Pierre et Marie Curie, Paris, France, [4]EBMT Paris Study Office, Hôpital St Antoine, Paris, France, [5]Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands, [6]Scleroderma Clinic, Osp. G. Pini, Department of Rheumatology, Milan, Italy, [7]University and University Hospital of Basel, Department of Rheumatology, Basel, Switzerland, [8]Universitätsklinikum Würzburg, Department of Rheumatology/ Clinical Immunology, Wuerzburg, Germany, [9]University Hospital of Bochum, Med. Klinik, Bochum, Germany, [10]Hôpitaux Universitaires de Strasbourg Service de Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Auto-Immunes Systémiques Rares Est-Sud-Ouest (RESO), Strasbourg, France, [11]CHU de Toulouse, Hôpital Purpan, Service de Médecine Interne, Toulouse, France, [12]Ribeirão Preto Medical School, University of São Paulo, Division of Hematology, Sao Paulo, Brazil, [13]Hôpital Saint Louis & Université Paris 7, Denis Diderot, Department of Hematology, Paris, France, [14]Leiden University Medical Center, Department of Hematology, Leiden, Netherlands, [15]Strasbourg University Hospital, Department of Hematology, Strasbourg, France, [16]CHU de Clermont Ferrand, Department of Hematology, Clermont Ferrand, France, [17]Department of Haematology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom, [18]Hospital Clínic of Barcelona, Department of Haematology, Barcelona, Spain, [19]UCT Oncopole, Department of Haematology, Toulouse, France, [20]Fondazione IRCCS Ca Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy, [21]Saint Antoine Hospital, Department of Haematology, Paris, France, [22]Hôpital Saint-Louis, AP-HP Assistance Publique des Hôpitaux de Paris, Centre de Référence des Maladies Auto-Immunes Systémiques Rares d'Ile-de-France, Filière 'FAI2R', Unité de Médecine Interne: Maladies Auto-immunes et Pathologie Vasculaire (UF 04), Université de Paris, EA 3518, Paris, France; Department of Medicine, McGill University, Montreal, QC, Canada, Paris, France

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Three randomized controlled trials in systemic sclerosis (SSc) demonstrated that autologous hematopoietic stem cell transplantation (aHSCT) is superior to standard cyclophosphamide therapy. This EBMT trial was a multi-center, prospective non-interventional study (NISCC1), designed to further decipher aHSCT efficacy and safety in real-life practice and to search for prognostic factors.

Methods: All consecutive adult patients, fulfilling the 2013 ACR/EULAR classification criteria for SSc, and undergoing a first aHSCT between December 2012 and February 2016 were included in the study. Primary endpoint was progression free survival (PFS) after two years. Secondary endpoints were overall survival (OS), non-relapse mortality (NRM) and response (RESP) to treatment, defined as >25% improvement in modified Rodnan skin score (mRSS) and/or ≥10% improvement in lung function test for Forced vital capacity (FVC) or diffusion capacity for carbon monoxide (DLCO) and with no need for further immunosuppression.

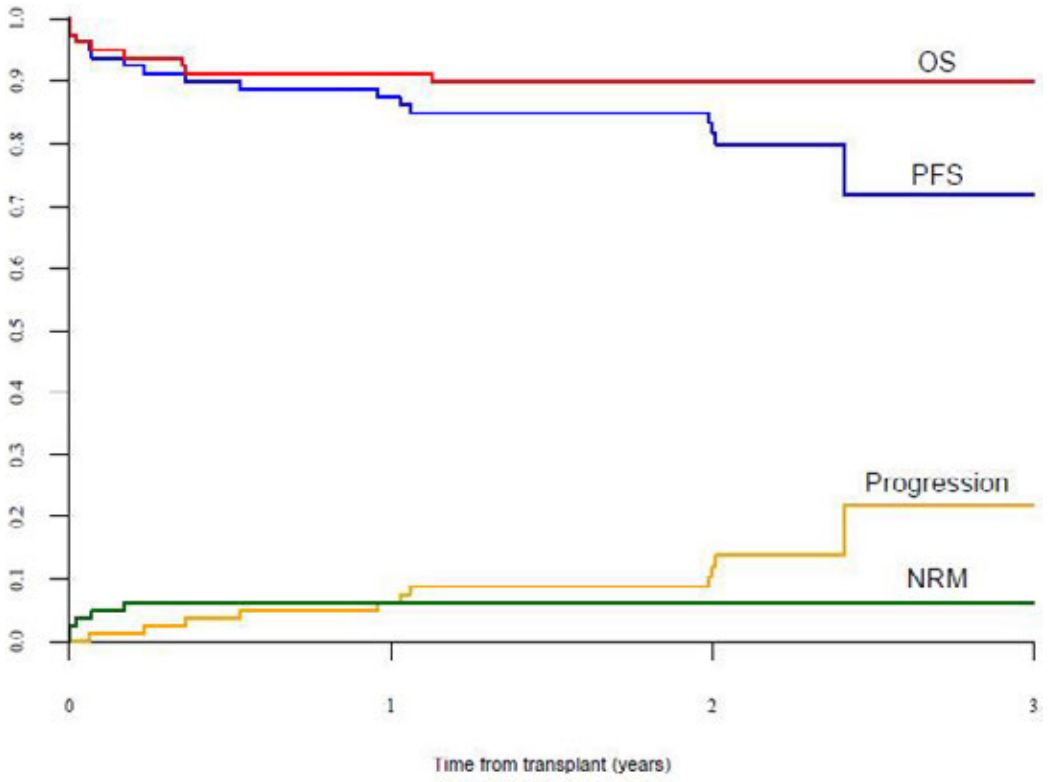

Figure. Kaplan-Mayer curves showing data for overall survival (OS), progression free survival (PFS), progression and non-relapse (treatment) related mortality (NRM) over time

Results: Eighty SSc patients were included. Median follow-up was 24 (6-57) months after aHSCT using cyclophosphamide plus antithymocyte globulin conditioning for all, with CD34+ selection in 35 (44%) patients. Following aHSCT, G-CSF was administered to 34 (43%) patients for a median duration of five (1-13) days. Median time following aHSCT to neutrophil engraftment was 11 (8-24) days and nine (1-25) days to platelet engraftment. There was an inverse correlation between the number of CD34+ cells infused and the time to engraftment (Spearman: r2= -0.31; p< .01), while the number of infused CD34+ cells or addition of G-CSF until aplasia recovery were not associated with a reduced number of infectious complications (p=0.32). At two years, PFS was 81.8%, OS was 90% and RESP was 88.7%. The 100 day NRM was 6.25% (n=5) with four deaths from cardiac events. Mean mRSS decreased from 23.9 at baseline to 14.2 at month 12 and 12.6 at month 24 (n=55, p< 0.001). Regarding lung function, mean FVC increased from 73.6% at baseline to 79.5% at month 12, and 80.6% at month 24 (n=37, p< 0.001); mean DLCO was 60.2% at baseline, 59.7% at month 12 and 60.4% at month 24 (n=35). By multivariate analysis, baseline mRSS >24 and older age at transplant were associated with lower PFS. CD34+-selection was associated with better RESP.

Conclusion: The NISCC1 study is the largest prospective cohort today demonstrating the efficacy and safety of aHSCT in eighty severe SSc patients in a real-life setting. NISCC1 showed superior response in patients with CD34+ graft selection with regard to response to treatment no increase in the rate of infectious complications.

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Abstract Number: 1651

Multicenter Double-Blind, Proof-of-Concept, Randomized Placebo-Controlled Trial of Riociguat in Systemic Sclerosis-associated Digital Ulcers

Vivek Nagaraja,[1] Cathie Spino,[1] Pei-Suen Tsou,[1] Robyn Domsic,[2] Robert Lafyatis,[2] Tracy Frech,[3] Jessica Gordon,[4] Virginia Steen,[5] and Dinesh Khanna[6], [1]University of Michigan, Ann Arbor, MI, [2]University of Pittsburgh, Pittsburgh, PA, [3]Division of Rheumatology, University of Utah and Salt Lake VAMC, Salt Lake City, UT, [4]Hospital for Special Surgery, New York, NY, [5]Georgetown University, Washington, D.C., USA, Georgetown, [6]Department of Medicine, University of Michigan, Ann Arbor, Michigan, USA, Ann Arbor

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The soluble guanylate cyclase stimulator riociguat (RIO) is a vasodilator with efficacy in patients with pulmonary arterial hypertension associated with connective tissue disease. Our objective was to evaluate the efficacy and safety of RIO in patients with systemic sclerosis-associated digital ulcers (SSc-DU) (NCT02915835).

Methods: Eligible subjects (with active or painful indeterminate DUs) were randomized in a 1:1 ratio to either placebo (PLA, n = 8) or RIO (n = 9) in individualized doses (maximum of 2.5 mg three times daily) during an 8-week titration period, followed by an 8-week stable dosing period.PDE5 inhibitors were not allowed. This was followed by an optional

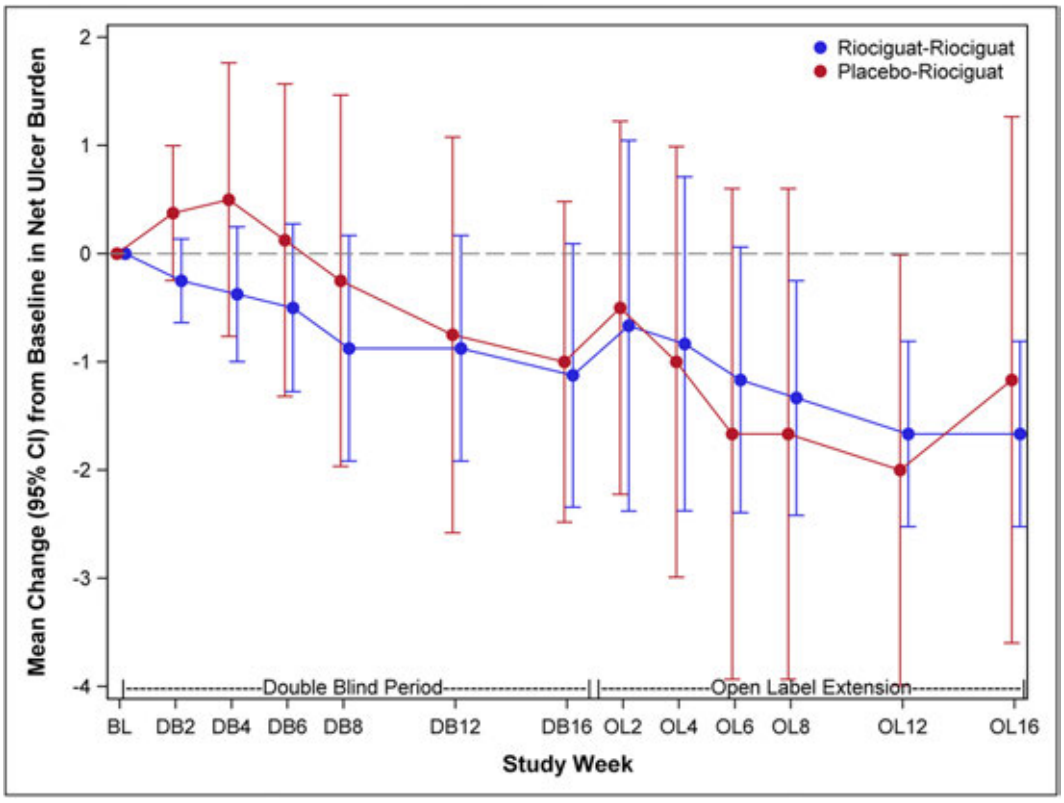

Figure 1: Mean Trend Over Time: Change in Net Ulcer Burden

	Placebo (N=8)	Riociguat (N=7)	Treatment Difference (95% CI)	p-value
Net Ulcer Burden, LS mean †*	-0.98	-1.22	-0.24 (-1.46 to 0.99)	0.706
Patient global assessment for overall disease, LS mean †	-1.19	0.31	1.50 (-1.30 to 4.30)	0.27
Patient assessment, LS mean †				
Severity of RP	-1.41	-3.47	-2.06 (-4.63 to 0.51)	0.11
Severity of DU	-4.00	-4.63	-0.63 (-3.68 to 2.41)	0.66
Pain during RP attack (0-100)	-7.01	-0.30	6.71 (-14.01 to 27.43)	0.49
Numbness during RP attack (0-100)	-15.44	-19.73	-4.28 (-33.44 to 24.87)	0.75
Tingling during RP attack (0-100)	-7.49	1.18	8.67 (-13.75 to 31.09)	0.41
Raynaud's condition score, LS mean†	-0.82	-1.15	-0.33 (-2.60 to 1.94)	0.76

Table 1: Changes from baseline to week 16 in primary and secondary efficacy endpoints

16-week open-label extension phase for participants with active DUs / reoccurrence of DUs within 1 month of the end of the main treatment phase. The primary endpoint was the change from baseline to week 16 in net ulcer burden (NUB), analyzed using ANCOVA. Other endpoints included plasma biomarkers and the proportion of participants with treatment-emergent adverse events (AEs).

Results: We randomized 17 participants with SSc-DUs at 5 US centers between January 2017 and March 2018. Six participants in each group progressed transitioned to the open-label extension phase. Baseline characteristics were comparable between treatment groups, except participants randomized to PLA were older (mean 61 vs. 43 yrs) with longer disease duration (mean 17.5 vs. 7.1 yrs). At baseline, the mean (SD) NUB was 2.5 (2.0) in the PLA and 2.4 (1.4) in the RIO. No significant difference was observed between RIO and PLA in change from baseline to 16 weeks in NUB [treatment difference -0.24 favoring RIO, p=0.70; Figure 1]. In the open-label extension, participants in the RIO-RIO arm had complete healing of their DUs.There were no statistically significant treatment differences in secondary efficacy endpoints, except for the eating component of HAQ-DI (Table 1). All 17 participants reported ≥1 adverse event, with the vast majority being mild or moderate. Four participants experienced 5 serious AE (4 in RIO and 1 in PLA); none was considered related to study medication. Statistically significant elevations of cGMP were observed at 16 weeks [treatment difference 157.3 nM, p=0.05, Figure 2]; no other biomarkers showed statistically significant changes.

Conclusion: In participants with SSc-DU, treatment with RIO did not reduce the number of DU net burden compared with PLA. Open-label extension suggests that a longer duration is needed to promote DU healing, which needs to be confirmed within a new trial.

The negative results may reflect a small number of patients, low number of NUB at baseline, moderate-to-severe vasculopathy with long term disease, and the difficulty to recruit patients in the era of widespread use of PDE5 inhibitors.

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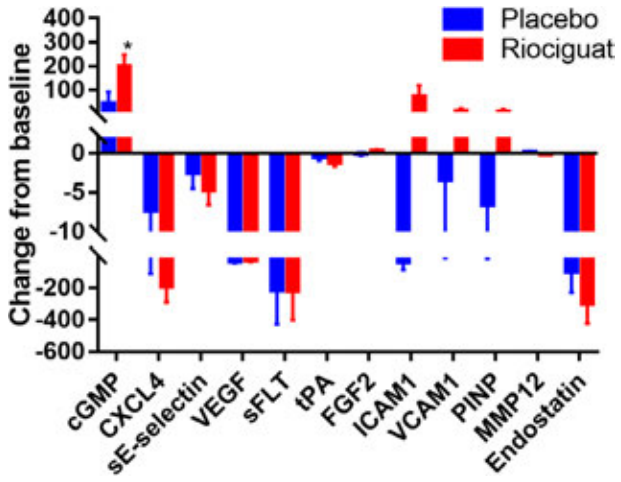

Figure 2: Plasma biomarker changes from baseline (week 0) to week 16

Khanna, Acceleron, 5, 8, Acceleron Pharma, 5, Actelion, 5, 8, Actelion Pharmaceuticals, 5, Astra Zeneca, 5, Bayer, 2, 5, 8, Behring, 5, Blade, 5, Blade Therapeutics, 5, 8, Blade therapeutics, 5, BMS, 2, 5, 8, Boehringer Ingelham, 5, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Celegene, 5, Celgene, 5, 8, ChemomAB, 5, ChemomAb, 5, CiviBioPharma, Inc., 3, Corbus, 5, Corobus, 5, Corpus, 5, CSL Behring, 5, 8, Curizon, 5, Curzion, 5, Cytori, 5, 8, Eicos, 4, Eicos Sciences, 4, Eicos Sciences, Inc, 4, Eicos Sciences, Inc/ CiviBioPharma, Inc1, 4, Eicos Sciences, Inc/ CiviBioPharma, Inc.1, Eicos, Inc, 4, Eicos, Inc., 5, 8, Eicos, INC., 4, Galapagos, 5, Genentech, 5, Genentech/Roche, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 2, 5, Mitsubishi Tanabe Pharma, 5, Mitsubishi Tanabe Pharma Dev America, 5, Mitsubishi Tanabe Pharma Development America, 5, Mitsubishi Tanabi, 5, NIH K24 and R01, 2, NIH / NIAMS K24 AR-063120, 2, NIH/NIAMS R01& K24, 2, Pfizer, 2, 5, Sanofi, 5, Sanofi Aventis, 5, Sanofi-Aventis, 5, 8, Sanofi-Aventis/Genzyme, 5, UCB, 5, UCB Pharma, 5.

Abstract Number: 1652

Anticentromere Antibody Levels and Isotypes Associate with Disease Severity in Systemic Sclerosis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Although some studies suggest a possible association between clinical characteristics and isotypes of anticentromere antibodies (ACA) in patients with systemic sclerosis (SSc), characteristics of ACA response have not been described thoroughly. Therefore, we evaluated whether ACA isotype expression and levels: 1.

Baseline characteristics and ACA isotype expression and levels in patients with very early SSc and SSc

	Very early SSc (n=90)	SSc without organ involvement (n=211)	SSc with organ involvement (n=144)
Female, n(%)	82 (94)	199 (94)	126 (87)
Age, mean (SD)	52 (15)	60 (11)	**62 (12)***
Since RP, median(IQR) in years	6 (3-13)	11 (6-18)	**12 (6-25)***
Since non RP, median(IQR) in years	NA	5 (2-11)	6 (3-13)
mRSS, median (IQR)	0 (0-0)	2 (0-4)	3 (1-6)
Digital ulcers, n(%)	0 (0)	0 (0)	73 (51)
ILD on HRCT, n(%)	0 (0)	0 (0)	64 (45)
PAH, n(%)	0 (0)	0 (0)	39 (27)
Renal crisis, n(%)	0 (0)	0 (0)	2 (1)
ACA characteristics			
IgA positivity, n(%)	53 (72)	145 (76)	105 (77)
IgA level [aU/mL], median (IQR)	78 (33-160)	75 (38-173)	**88 (44-181)***
IgM positivity, n(%)	57 (76)	**168 (87)***	**122 (89)***
IgM level [aU/mL], median (IQR)	105 (17-551)	142 (43-593)	**217 (69-1193)***
IgG level [aU/mL], median (IQR)	283 (92-658)	**455 (205-940)***	**678 (302-1146)***

Table 1. Baseline characteristics of the three groups, SSc=systemic sclerosis, RP=Raynaud phenomenon, mRSS= modified Rodnan Skin Score, ILD= interstitial lung disease, HRCT= high resolution computed tomography, PAH= pulmonary arterial hypertension.

* Significant difference compared to very early SSc group p< 0.05. Both groups were separately compared with very early SSc group. No significant differences were found between the SSc group without and the SSc group with organ involvement.

Table 2:Multivariate logistic regression: higher IgG levels independently associate with disease severity in SSc

	Very early SSc patients (n=90) vs. SSc patients (n=355)	SSc patients with organ involvement (n=144) vs. SSc patients without organ involvement (n=211.)
	OR (95% CI)	OR (95% CI)
High IgG level	**0.29 (0.15-0.58)***	**2.55 (1.48-4.40)***
High IgM level	1.22 (0.61-2.46)	0.80 (0.46-1.41)
High IgA level	1.79 (0.87-3.28)	0.96 (0.57-1.60)
IgM positivity	0.48 (0.21-1.08)	1.34 (0.63-2.84)

Table 2. All analyses were adjusted for age and disease duration since first Raynaud symptom.
* Significant p < 0.05

associate with disease severity, 2. differ between patients with very early SSc and SSc, and 3. can identify very early SSc patients that will progress to SSc.

Methods: All ACA IgG+ patients fulfilling the American College of Rheumatology (ACR) 2013 criteria for SSc and ACA+ IgG patients with very early SSc (based on ACA, Raynaud and puffy fingers or abnormal nailfold capillaroscopy but not fulfilling ACR 2013 criteria), from the prospective SSc cohorts from the Leiden University Medical Centre (LUMC), the University Hospital Zurich, and the Oslo University Hospital were included. Presence and levels of ACA IgM and IgA were determined by J.B. at the LUMC. Patients were categorized in three groups according to disease severity: very early SSc, SSc without organ involvement, and SSc with organ involvement. Organ involvement was defined as any of: digital ulcers, interstitial lung disease, pulmonary arterial hypertension, renal crisis and myocardial involvement. Associations between isotype presence and levels and disease severity were evaluated with logistic re-

gression, with adjustment for age and disease duration. ACA response characteristics were compared between very early SSc patients that progressed to ACR 2013 criteria and those who did not.

Results: ACA characteristics were measured in 445 ACA IgG + patients. Ninety patients (20%) had very early SSc and 355 (80%) fulfilled the ACR criteria, in which 41% (n=144) were classified as SSc with organ involvement (Table 1). At baseline, 86% of patients were ACA IgM+, and 75% were ACA IgA+. Very early SSc patients show lowest titers of IgM and IgG. In contrast, SSc patients with organ involvement most often express ACA IgM and show highest titers of all isotypes, indicating a more active, specific B cell responses (Table 1). With adjustment for disease duration and age, ACA IgG levels were significantly higher in SSc patients vs. very early SSc, and in SSc patients with organ involvement vs. SSc without organ involvement (Table 2). Of all very early SSc patients with follow-up (n=70; median FU 2.1 year) 30% progressed to SSc, mostly due to skin progression (88%), and 23% developed lung involvement, after a median period of 4.3 year. As age and follow-up duration were significantly higher in the progressors we were underpowered to analyse isotype characteristics by means of regression. However, again, we observed a trend for higher ACA IgG levels in the very early SSc patients progressing to SSc fulfilling ACR 2013 criteria.

Conclusion: Here we show in a large multicentre SSc cohort that ACA IgG levels increase with increasing disease severity, from very early SSc, to SSc without organ involvement and SSc with organ involvement. Our data indicate that ACA+ SSc specific B cell responses are potentially involved in disease-relevant pathogenic processes. In addition, ACA response characteristics might also be useful for risk stratification in clinical practice.

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Abstract Number: 1653

Efficacy and Safety of Romilkimab in Diffuse Cutaneous Systemic Sclerosis (dcSSc): A Randomized, Double-Blind, Placebo-Controlled, 24-week, Proof of Concept Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Table 1. Baseline Characteristics

Baseline Characteristics	Placebo (N=49)	Romilkimab (N=48)	All (N=97)
Age (years)			
Mean (SD)	47.2 (12.1)	52.3 (10.8)	49.7 (11.7)
Sex [n(%)]			
Male	11 (22.4)	9 (18.8)	20 (20.6)
Female	38 (77.6)	39 (81.3)	77 (79.4)
Race [n(%)]			
American Indian or Alaska Native	0	1 (2.1)	1 (1.0)
Asian	1 (2.0)	0	1 (1.0)
Black or African American	2 (4.1)	2 (4.2)	4 (4.1)
Native Hawaiian or other Pacific Islander	1 (2.0)	0	1 (1.0)
White	45 (91.8)	45 (93.8)	90 (92.8)
Ethnicity [n(%)]			
Hispanic or Latino	12 (24.5)	10 (20.8)	22 (22.7)
Not Hispanic or Latino	37 (75.5)	38 (79.2)	75 (77.3)
BMI (kg/m2)			
Mean (SD)	24.9 (5.3)	24.3 (4.4)	24.6 (4.9)
mRSS			
Mean (SD)	20.6 (7.0)	20.5 (6.1)	20.6 (6.5)
Predicted FVC (%)			
Mean (SD)	89.5 (15.8)	96.1 (17.4)	92.8 (16.9)
Predicted HGB Corrected DLCO (%)			
Mean (SD)	66.5 (14.6)	72.4 (14.2)	69.4 (14.7)
Disease duration from first non-RP manifestation (months)			
Mean (SD)	21.8 (10.7)	19.3 (9.2)	20.6 (10.0)
Stratified with history of SSc-ILD [n(%)]	18 (36.7)	18 (37.5)	36 (37.1)

Table 2. Outcome Measures

Outcome Measures @ Week 24 (vs. Baseline)	Placebo N = 49	Romilkimab N= 48	Difference (RKB – PBO)	P-value (one-sided)
PRIMARY (All)				
ΔmRSS	-2.45 (0.85)	-4.76 (0.86)	-2.31 (1.21)	0.029
No Background Therapy	-0.95 (1.34)	-3.64 (1.24)	-2.69 (1.83)	
Background Therapy	-3.43 (1.08)	-5.81 (1.17)	-2.38 (1.59)	
SECONDARY (All)				
ΔFVC (L)	-0.08 (0.04)	-0.01 (0.04)	0.07 (0.06)	0.096
ΔDLco (mmol/min/kPa)	-0.27 (0.10)	-0.12 (0.10)	0.15 (0.14)	0.135
ΔHAQ-DI	-0.12 (0.08)	-0.09 (0.08)	0.03 (0.11)	0.398
EXPLORATORY (Partial)				
ΔPain (SHAQ)	1.18 (3.44)	-6.94 (3.46)	-8.12 (4.91)	0.051
ΔRaynaud's (SHAQ)	-4.26 (3.24)	-8.46 (3.27)	-4.20 (4.64)	0.184
ΔDigital Ulcers (SHAQ)	0.08 (3.38)	-6.07 (3.41)	-6.15 (4.81)	0.102
ΔDisease Severity (SHAQ)	-7.30 (3.12)	-12.72 (3.16)	-5.42 (4.48)	0.115
ΔEQ-5D-5L	0.00 (0.03)	0.07 (0.03)	0.07 (0.04)	0.038

Background/Purpose: Systemic sclerosis (SSc) is a progressive, multi-organ disease with limited treatment options. Interleukin-4 (IL-4) and IL-13 have been implicated in the general fibrotic pathway and pathogenesis of SSc and are promising targets. Romilkimab (RKB) is an engineered humanized bispecific immunoglobulin-G4 antibody that binds and neutralizes both IL-4/IL-13. We report a Phase IIa randomized, double-blind, placebo-controlled trial (NCT02921971, Sanofi funded) employing RKB in SSc.

Methods: Patients with dcSSc (disease duration ≤36 months, mRSS 10-35) with or without immunosuppressive background therapy were randomized (1:1) to subcutaneous RKB 200mg or placebo (PBO) for 24 weeks and stratified based upon history of SSc-ILD. The primary endpoint was mean change in mRSS from baseline to Week 24 and FVC/DLco and HAQ-DI served as secondary endpoints. All analyses employed a 1-sided p-value < 0.05 as reaching statistical significance.

Results: Ninety-seven patients with similar baseline characteristics between arms (Table 1), including the use of background therapy (PBO 59.2% vs. RKB 52.1%) were randomized. Six (12.2%) and 4 (8.3%) patients discontinued study treatment early in the PBO and RKB arms, respectively. The primary endpoint showed an absolute change in mRSS of -2.45 (0.85) and -4.76 (0.86) for the PBO and RKB groups, respectively with a difference of -2.31 (1.21) favoring RKB (p-value = 0.029) (Table 2). Subgroup analysis based upon stratification criteria did not yield a significant difference (interaction p-value=0.731). Subgroup analysis based on background therapy showed a similar treatment

effect with a placebo subtracted difference in mRSS of -2.69 (1.83) and -2.38 (1.59) (Table 2), suggesting an additive effect between background therapy and RKB. Secondary endpoints did not show a statistically significant difference between RKB vs. PBO arms, although there was numerically less decline in FVC with RKB (Table 2). Exploratory endpoints suggested possible effect of RKB on overall pain, Raynaud's, digital ulcers, and EQ-5D-5L (Table 2). Adverse events (AE) were balanced between the two groups (PBO 83.7% and RKB 83.3%). There were 5 and 4 patients with serious AEs in the PBO and RKB arms, respectively. One death occurred in each arm (PBO – cardiomyopathy, RKB – scleroderma renal crisis).

Conclusion: Patients with dcSSc who were treated with RKB showed a statistically significant reduction in mRSS compared to those receiving placebo. None of the secondary outcomes were met, although RKB was associated with a smaller decline in FVC than placebo. Romilkimab was well tolerated with no major safety concerns.

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Abstract Number: 1654

Esophageal Dilation and Other Clinical Factors Associated with Pulmonary Function Decline in Patients with Systemic Sclerosis

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SESSION INFORMATION

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Table 1. Baseline characteristics (N = 138) in systemic sclerosis patients with vs. without clinically meaningful worsening of % predicted forced vital capacity (FVC)

Mean (SD) or N (%)	Total (N = 138)	Decline in % predicted FVC ≥5 (N=51)	No significant decline in FVC (N =87)	p-value
Age at time of HRCT, years	50.1 (11.1)	51.7 (9.4)	49.1 (12.0)	0.18
Sex, women	116 (84%)	40 (78%)	76 (87%)	0.17
Race, white	104 (75%)	39 (77%)	65 (75%)	0.48
Smoker, current or former	52 (38%)	22 (43%)	30 (35%)	0.31
Proton pump inhibition, current	81 (59%)	29 (57%)	52 (60%)	0.74
SSc disease subtype, diffuse	64 (46%)	27 (53%)	37 (43%)	0.24
SSc disease duration, years*	6.0 (8.0)	5.1 (7.3)	5.9 (8.5)	0.57
SSc-specific autoantibodies, positive (N=136)	107 (79%)	40 (78%)	67 (79%)	0.96
Anti-topoisomerase I (Scl-70)	50 (36%)	26 (51%)	24 (28%)	0.01
Anti-centromere	24 (17%)	7 (14%)	17 (20%)	0.38
Anti-RNA polymerase III (N=135)	34 (25%)	8 (16%)	26 (31%)	0.06
Erythrocyte sedimentation rate, mm/h	24 (23)	22.9 (17.7)	24.4 (25.3)	0.69
C-reactive protein	1.4 (3.8)	2.1 (6.0)	0.90 (1.3)	0.24
Modified Rodnan skin score	11 (9)	10.2 (7.6)	12.2 (9.7)	0.22
Medications, any use	64 (46%)	24 (47%)	40 (46%)	0.90
Mycophenolate mofetil	31 (23%)	13 (26%)	18 (21%)	0.51
Cyclophosphamide	6 (4%)	3 (6%)	3 (4%)	0.50
Prednisone	35 (25%)	12 (24%)	23 (26%)	0.70
Pulmonary hypertension present among those with RHC (N = 56)	19 (34%)	11 (42%)	8 (27%)	0.22
Radiographic ILD, present	100 (73%)	40 (78%)	60 (69%)	0.23
FVC % predicted	78 (17)	78.6 (16.5)	77.3 (16.9)	0.67
DLCO % predicted	61 (19)	59.1 (21.4)	60.4 (19.8)	0.73
Digital ulcers, present	52 (38%)	14 (28%)	38 (44%)	0.06
Widest esophageal diameter, mm	17.6 (8.2)	18.2 (8.5)	17.2 (8.0)	0.53

Legend. *SSc disease duration defined as the interval between first non-Raynaud SSc symptom and baseline HRCT date. WED=widest esophageal diameter; HRCT=high-resolution computed tomography of the chest; SSc=systemic sclerosis; ILD=interstitial lung disease; PAH=pulmonary arterial hypertension; RHC=right heart catheterization; FVC=forced vital capacity; DLCO=diffusing capacity of the lungs for carbon monoxide (adjusted for hemoglobin).

Background/Purpose: Prior work has shown that Scl-70 positive autoantibody status and baseline c-reactive protein (CRP) are associated with more rapid pulmonary function decline in patients with systemic sclerosis (SSc). We previously found that patients with esophageal dilation on chest high-resolution computer tomography (HRCT) scan had lower % predicted forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO) at baseline.

Table 2. Change over time in % predicted forced vital capacity (N=138) and diffusing capacity for carbon monoxide (N=99) in patients with systemic sclerosis, by Scl-70 and widest esophageal diameter, adjusted models* (95% CI)

	Positive Scl-70 autoantibody status (N=50)		Negative Scl-70 autoantibody status (N=86)		Widest esophageal diameter ≥19mm (N=64)		Widest esophageal diameter <19mm (N=74)	
PFT	FVC	DLCO	FVC	DLCO	FVC	DLCO	FVC	DLCO
Baseline	63 (52, 74)	46 (30, 61)	72 (60, 83)	52 (36, 68)	61 (50, 72)	45 (28, 61)	71 (60, 82)	50 (33, 67)
Modeled 5-year change	-6.3 (-9.9, -2.8)	-4.2 (-10.3, 2.0)	1.8 (-0.6, 4.2)	-3.4 (-6.6, -0.25)	-2.4 (-5.4, 0.5)	-6.1 (-10.4, -1.8)	0.7 (-2.0, 3.4)	-1.7 (-5.4, 2.0)

Legend. Scl-70= anti-topoisomerase 1; FVC = forced vital capacity; DLCO = diffusing capacity for carbon monoxide (adjusted for hemoglobin); PFT = pulmonary function test. PFT results shown as % predicted. *Scl-70 PFT means adjusted for sex, proton pump inhibitor use, prednisone use, SSc disease subtype, duration since first non-Raynaud (years), smoking history (current or former), widest esophageal diameter, and presence of digital ulcers. WED PFT means adjusted for sex, proton pump inhibitor use, prednisone use, SSc disease subtype, duration since first non-Raynaud (years), smoking history (current or former), Scl-70 autoantibody status, and presence of digital ulcers.

The purpose of this study is to identify clinical factors, including HRCT esophageal dilation, that are associated with pulmonary function decline in SSc.

Methods: Included participants were enrolled in the Northwestern Scleroderma Registry, fulfilled 2013 SSc criteria, and had ≥1 HRCT and ≥2 pulmonary function tests (PFT) obtained as standard of care. The widest esophageal diameter (WED) and radiographic interstitial lung disease (ILD) were assessed using published methods. The WED was dichotomized as dilated (≥19 mm) vs. not dilated (< 19mm) based upon published data. Clinically meaningful PFT change was defined as % predicted FVC ≥5-point difference and % predicted DLCO ≥15-point difference based upon published data. Clinical characteristics at the time of baseline HRCT scan were collected. Pulmonary arterial hypertension (PAH) was present if mean pulmonary arterial pressure was ≥25 mmHg on right heart catheterization. Linear mixed effect models were used to model PFT change.

Results: 138 SSc patients met study criteria. Radiographic ILD was present in 100 of 138 (73%) participants (Table 1). 51 of 138 (40%) patients demonstrated clinically meaningful FVC decline (median follow-up 2.8 years). In adjusted models, patients with (vs. without) esophageal dilation had statistically significant 5-year % predicted DLCO decline (-6.1; 95% CI -10.4, -1.8), however this change did not meet the 15-percentage point threshold for clinical significance (Table 2, Figure 1). There was no difference in the presence of PAH at baseline between those with vs. without DLCO decline (14% vs. 13%, p=0.51). Patients with positive (vs. negative) Scl-70 autoantibody status had statistically significant 5-year % predicted FVC decline (-6.3; 95% CI -9.9, -2.8) (Table 2, Figure 1). Esophageal diameter did not distinguish between those with vs. without significant FVC decline. There was no difference in baseline SSc disease duration, modified Rodnan skin score, smoking status, gender, age, baseline CRP, or race between those with vs. without clinically meaningful FVC change.

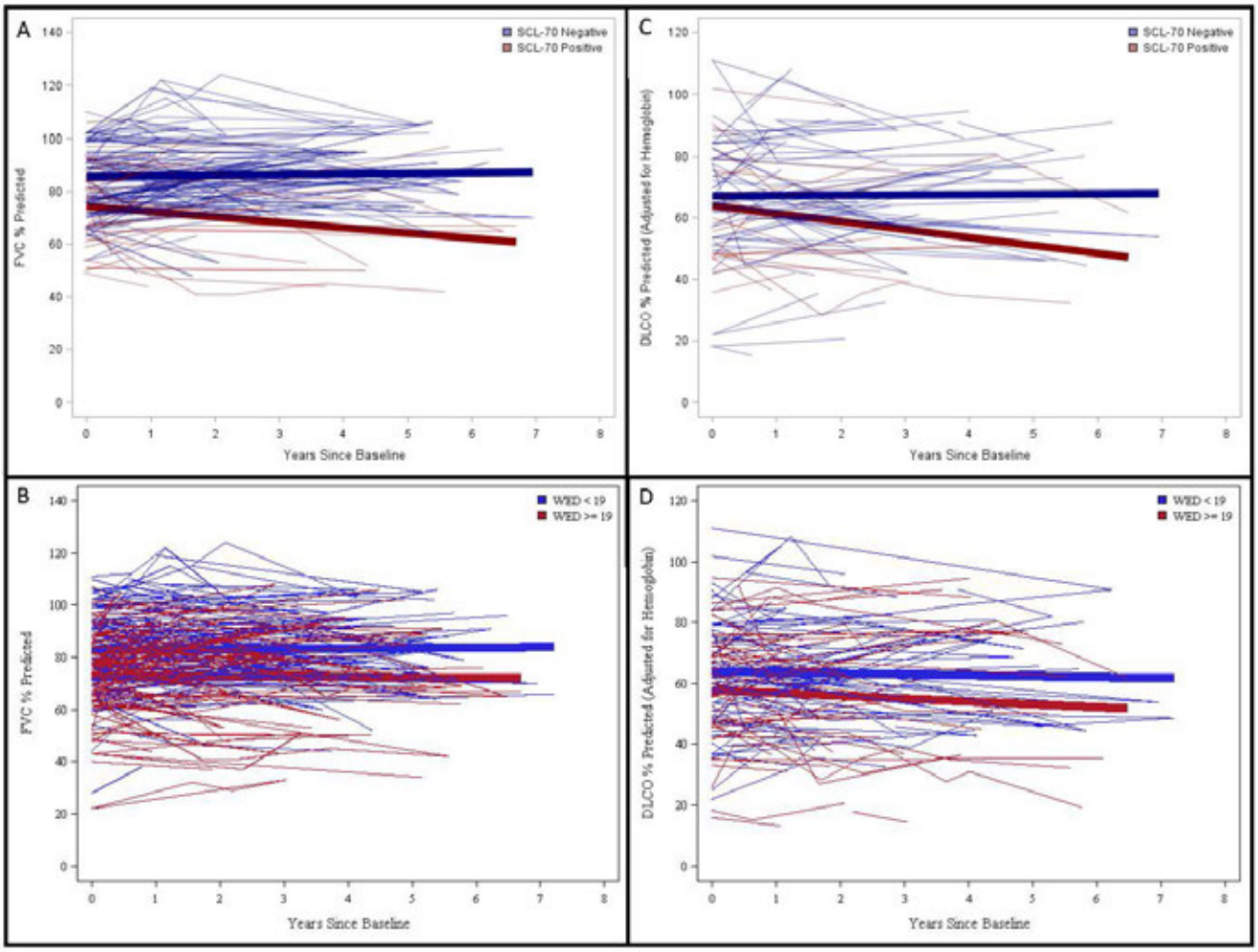

Figure 1. Change in pulmonary function by Scl70 and Widest Esophageal Diameter (WED) status. Change in forced vital capacity (FVC) % predicted (N=138) by Scl70 autoantibody status (A) and WED (B); and change in carbon monoxide diffusing capacity (DLCO) % predicted, corrected for hemoglobin (N=99) by Scl70 autoantibody status (C) and WED (D), unadjusted. Thin lines represent individual patient data. Thick lines represent estimated % predicted DLCO from statistical model using data from all patients.

Conclusion: Scl-70 positivity, but not elevated baseline CRP, is a risk factor for % predicted FVC decline. Esophageal dilation on HRCT was associated with a minimal, non-clinically significant 5-year decline in DLCO and no change in FVC during follow-up. These results have important prognostic implications for SSc-ILD patients with esophageal dilation.

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Abstract Number: 1655

Histologic Features Correlate with the Modified Rodnan Skin Score, Serum Inflammatory Markers, and Patient Reported Outcomes in Patients with Early, Diffuse Cutaneous Systemic Sclerosis

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SESSION INFORMATION
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Background/Purpose: The association between systemic sclerosis (SSc) skin histology and clinical findings is not fully characterized. In two SSc trials, we developed a scoring system to evaluate histologic change. The purpose of this study is to determine (1) the reliability of our histology scores and (2) if histologic features correlate with clinical findings.

Methods: Skin biopsies were assessed from patients enrolled in Nilotinib (n=7) and Belimumab (n=18) trials. Our skin histology scoring approach, developed with dermatopatholgist (CM) consultation, includes skin thickness (epidermis to subcutis), follicle count, and semi-quantitative (0-3) assessment of infiltrate, collagen density, alpha-smooth muscle actin (aSMA) and CD34 staining intensity, and global histologic severity. Blinded to prior scores, a dermatopathogist (CM) and second pathologist (YZ), oriented to our approach, analyzed a sub-sample of biopsies. Intraclass correlation coefficients (ICC) were calculated for inter- and intra-rater reliability. Spearman correlations were used to correlate histology scores (baseline, 52-weeks post-treatment, and overall) and clinical variables (local and total modified Rodnan skin score (MRSS), erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), 36-item Short Form Health Survey (SF-36), and physician global assessment (PGA)).

Results: 56 biopsies were analyzed from 26 diffuse SSc patients (median (IQR) disease duration 0.8 (0.54) years). Most were female (77%), Caucasian (73%), and RNA polymerase III positive (58%). Median (IQR) baseline MRSS was 25 (9). Reliability was excellent (ICC≥0.90) for follicle count and intra-rater CD34; good (0.75< ICC >0.90) for thickness, inter-rater CD34, intra-rater collagen density, and intra-rater global score; and moderate (0.5< ICC >0.75) for infiltrate, intra-rater collagen density, aSMA, and inter-rater global score.

Histologic scores correlated moderately with MRSS, ESR, CRP, and SF-36 (Table 1). Post-treatment local MRSS correlated with thickness (r=0.674, p< 0.001), collagen density (r=0.497, p=0.04), global histologic severity (r=0.467, p=0.02), follicle count (r=-0.550, p=0.01), and CD34 stain intensity (r=-0.653, p=0.001). However, local MRSS did not correlate with infiltrate score or PGA and weakly correlated with aSMA stain intensity (r=0.337, p=0.01). In strat-

Table 1. Correlation between clinical variables and histologic features in diffuse systemic sclerosis

Clinical Feature	Significant* Spearman's Correlation Coefficients (r_s) for Histologic Features	p-value
Local modified Rodnan skin score	Collagen density (0.470)	<0.001
	CD34 staining intensity (-0.518)	<0.001
	Post-treatment thickness (0.674)	<0.001
	Post-treatment collagen density (0.497)	0.04
	Post-treatment global histologic severity (0.467)	0.02
	Post-treatment follicle count (-0.550)	0.01
	Post-treatment CD34 staining intensity (-0.653)	0.001
Total modified Rodnan skin score	Collagen density (0.425)	0.001
	CD34 staining intensity (-0.460)	<0.001
	Baseline infiltrate score (0.435)	0.03
	Post-treatment thickness (0.486)	0.02
	Post-treatment collagen density (0.425)	0.04
	Post-treatment CD34 staining intensity (-0.487)	0.02
C-reactive protein	Thickness (0.409)	0.01
	Post-treatment thickness (0.655)	0.002
	Post-treatment global histologic severity (0.475)	0.04
	Post-treatment CD34 staining intensity (-0.539)	0.02
Erythrocyte sedimentation rate	Follicle count (-0.430)	0.001
	Baseline follicle count (-0.410)	0.04
	Post-treatment thickness (0.526)	0.01
	Post-treatment CD34 staining intensity (-0.501)	0.01
36-Item Short Form Health Survey (SF-36)	Post-treatment global histologic severity (-0.567)	0.004

Legend: If no time point specified, reported data are from combined baseline and post-treatment samples.
*$p \leq 0.05$ and $r_s \geq 0.4$.

ified analysis, collagen density correlated with local MRSS in patients with low (< 1) but not high (≥1) infiltrate score (r=0.578, p< 0.001 vs. r=0.253, p=0.256). Total MRSS correlated with collagen density (r=0.425, p=0.001) and CD34 stain intensity (r=-0.460, p< 0.001). Total MRSS and thickness correlated positively in patients with low infiltrate (r=0.326, p=0.05) but negatively in patients with high infiltrate (r=-0.456, p=0.03).

Conclusion: Our scores demonstrate moderate to excellent reliability, thus have potential to be used across centers. Histologic features correlate with MRSS, inflammatory markers, and patient reported outcomes. However, infiltrate does not correlate with MRSS and confounds the correlation of MRSS with collagen density and thickness. This supports further study of skin histology as an SSc outcome measure.

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Abstract Number: 1656

Health-Related Quality of Life in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD): Impact of Lung Function on Patient-Reported Outcomes in a Randomized Phase III Trial

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SESSION INFORMATION

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Background/Purpose: SSc-ILD is a major cause of morbidity and mortality in patients with systemic sclerosis. A subset of patients with SSc-ILD show a decline in lung function and increasing symptoms that interfere with daily activities and ultimately impair patients' health-related quality of life (HRQoL). The aim of this analysis was to evaluate the impact of lung function changes on HRQoL as measured by patient-reported outcomes (PRO) within the Phase III SENSCIS® trial.

Methods: In the SENSCIS® trial (NCT02597933), patients with SSc-ILD were randomized to nintedanib 150 mg twice daily or placebo. Patients in the nintedanib arm experienced a significantly lower adjusted annual rate of decline in forced vital capacity (FVC) (–52.4mL vs –93.3mL: difference 41.0 [95% CI 2.9–79.0]; P=0.04). PRO assessments were conducted at baseline, week 24, week 52 and study completion, with no differences between arms in changes from baseline to week 52 in the St. George's Respiratory Questionnaire (SGRQ). In this analysis, PRO scores and changes from baseline were assessed according to baseline lung function parameters, independent of treatment arm. PRO assessments included Functional Assessment of Chronic Illness Therapy (FACIT)-Dyspnea, Health Assessment Questionnaire Disability Index (HAQ-DI) and Scleroderma Health Assessment Questionnaire (SHAQ) visual analog scale (VAS).

Results: A total of 576 patients were randomized. In patients categorized by baseline FVC percent predicted (FVC %pred), those with FVC ≥70% pred had a mean SGRQ total score of 33.8 at week 52, whereas mean score for those with FVC < 70% pred was 45.1 (P< 0.0001) (higher scores indicate a worse quality of life). This pattern was also reflected for the subdomains of the SGRQ score, including activities, impacts and symptoms. Similarly, FACIT-Dyspnea, FACIT-Dyspnea functional limitations, HAQ-DI and SHAQ VAS breathing problems scores were lower in patients with FVC ≥70% pred than those with FVC < 70% pred (Table 1). When PRO assessments were compared in patients categorized by supplemental oxygen use at baseline, those using oxygen had a mean SGRQ total score of 51.2, compared with 39.0 in those not requiring oxygen (P=0.0005). Again, these differences were also evident for the

	FVC %pred groups				Mean difference (SD)	P-value
	FVC ≥70% pred		FVC <70% pred			
	N	Mean (SD)	N	Mean (SD)		
SGRQ total	257	33.8 (20.5)	242	45.1 (20.2)	−11.3 (20.4)	<.0001
FACIT-Dyspnea						
Dyspnea	249	44.6 (10.3)	240	48.7 (9.5)	−4.2 (9.9)	<.0001
Dyspnea-related functional limitation	251	45.0 (10.1)	242	48.8 (9.7)	−3.8 (9.9)	<.0001
HAQ-DI	255	0.5 (0.7)	245	0.7 (0.7)	−0.2 (0.7)	0.0043
SHAQ VAS breathing problems	252	2.5 (2.7)	240	3.6 (2.7)	−1.1 (2.7)	<.0001

Table 1. Week 52 HRQoL scores stratified by FVC %pred at baseline

	Supplemental oxygen use				Mean difference (SD)	P-value
	Yes		No			
	N	Mean (SD)	N	Mean (SD)		
SGRQ total	37	51.2 (18.0)	612	39.0 (20.7)	12.2 (20.6)	0.0005
FACIT-Dyspnea						
Dyspnea	38	52.1 (10.0)	608	45.9 (9.8)	6.2 (9.8)	0.0002
Dyspnea-related functional limitation	38	52.0 (10.2)	612	46.0 (9.5)	6.0 (9.5)	0.0002
HAQ-DI	37	0.7 (0.6)	610	0.6 (0.7)	0.1 (0.7)	0.2286
SHAQ VAS breathing problems	38	4.5 (3.3)	577	2.9 (2.7)	1.6 (2.8)	0.0006

Table 2. Week 52 HRQoL scores stratified by supplemental oxygen use at baseline

subdomains of the SGRQ score. FACIT-Dyspnea, HAQ-DI and SHAQ VAS breathing problems scores were also all higher in patients with oxygen use (Table 2). In patients with a moderate (5–10%) or large (>10%) improvement in FVC %pred from baseline to week 52, changes in SGRQ scores indicated improved HRQoL (–3.4 and –3.8, respectively). A moderate or large deterioration in FVC %pred was associated with worsening HRQoL (+1.4 and +5.5, respectively). Other PRO assessments showed a largely similar pattern (Table 3).

Conclusion: In the SENSCIS® trial, while there was no significant difference between arms in the change from baseline in SGRQ, patients with FVC < 70% pred or requiring supplemental oxygen had consistently worse PRO scores, independent of treatment arm. Improvements in lung function between baseline and week 52 were reflected in improving PRO scores, potentially indicating an association between lung function and HRQoL in patients with SSc-ILD.

HRQoL score	FVC changes from baseline to week 52							
	Large deterioration (decline >10% pred)		Moderate deterioration (decline 5–10% pred)		Moderate improvement (increase 5–10% pred)		Large improvement (increase >10% pred)	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
SGRQ								
Total	37	+5.5 (17.9)	81	+1.4 (13.8)	33	−3.4 (11.1)	9	−3.8 (6.9)
FACIT-Dyspnea								
Dyspnea	36	+3.1 (7.6)	82	+0.9 (6.3)	32	−1.2 (6.3)	8	+0.4 (6.2)
Dyspnea-related functional limitation	36	+2.9 (6.2)	82	+1.0 (6.2)	33	−0.5 (6.3)	8	+2.2 (5.0)
HAQ-DI	37	+0.2 (0.4)	79	+0.1 (0.4)	34	0.0 (0.4)	9	−0.1 (0.5)
SHAQ VAS breathing problems	31	+0.5 (1.9)	79	+0.4 (2.9)	32	+0.2 (2.0)	6	−1.8 (2.5)

Table 3. Change in HRQoL scores at week 52 in patients with a moderate (5–10% pred) or large (>10% pred) improvement or deterioration in FVC from baseline

Disclosure: M. Kreuter, Boehringer Ingelheim, 2, 5, 8, Roche, 2, 5, 8, Galapagos, 5; **A. Hoffmann-Vold**, Actelion, 5, 8, Boehringer Ingelheim, 2, 5, 8, GSK, 5, 8; **M. Matucci-Cerinic**, Actelion, 2, 5, 8, Bayer, 5, 8, BMS, 2, 5, Chemomab, 5, J&J, 2, J&J, Janssen, Lilly, MSD, Pfizer, 5, 6, Lilly, 5, Pfizer, 5; **L. Saketkoo**, None; **K. Highland**, Actelion Pharmaceuticals, 2, 8, 9, Bayer, 8, Bayer Healthcare, 8, Boehringer Ingelheim, 2, 5, 8, 9, Eiger Pharmaceuticals, 2, Genentech, 2, 8, Gilead Sciences, 8, Reata Pharmaceuticals, 2, United Therapeutics, 2, 8; **H. Wilson**, Boehringer-Ingelheim, 3, Evidera; **M. Alves**, Boehringer Ingelheim, 3; **N. Schoof**, Boehringer Ingelheim International GmbH, 3; **T. Maher**, Boehringer Ingelheim, 5, 8.

Abstract Number: 1657

Sarcopenia in Systemic Sclerosis

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Background/Purpose: Gastrointestinal tract involvement in systemic sclerosis (SSc) occurs in almost all patients varying in severity and affecting motility, digestion, absorption and excretion. These abnormalities can cause malnutrition and significant changes in body composition, perhaps the most important is the progressive and gradual loss

of the mass, function and strength of the skeletal muscle known as sarcopenia, which increases the risk of physical disability, worsening of the quality of life and risk of falls.

Methods: An observational, prospective, cross-sectional study was conducted in adult patients who met the ACR/EULAR 2013 classification criteria, evaluated by the rheumatology outpatient service of the British Hospital of Buenos Aires. Body composition was assessed by dual energy X-ray absorptiometry (DXA), grip strength using a Jamar dynamometer following the standardized Mathiowetz standards and performance by 4-meter gait speed. According to European Working Group on Sarcopenia in Older People (EWGSOP), skeletal muscle mass index (SMMI) was calculated as the sum of arms and legs fat and bone-free mass, in kilogram, and height squared meter. The cutoff values for sarcopenia were ≤5.5 kg/m2 in women and ≤7.26 kg/m2 in men, grip strength for women < 20 kg and men < 30 kg and for walking speed < 0.8 m/s in both genders.

Results: A total of 27 patients were included, 20 (74%) were females. The mean inclusion age was 52.5 (± 14.1) years and mean diagnosis age was 44.6 (± 12.8) years, with a mean time of disease evolution of 93.62 (± 83.68) months. LcSSc were reported in 16 (59.2%) patients. We found a mean Rodnan score of 7.2 (± 6.8), Medsger score of 2.3 (± 1.2), EUSTAR activity score of 0.5 (± 0.2), SHAQ of 1.2 (± 0.4) and EVA of 17 (± 14.5). The mean weight was 68.8 (± 12.5) kg, size 162.5 (± 7.9) cm and BMI was 26.1 (± 4.5) kg/m2. Mean lean appendicular mass was 17.92 (± 4.3) kg with an SMMI of 6.74 (± 1.16) kg/m2, grip strength in dominant hand of 22.8 (± 7.9) kg and non-dominant hand of 21.4 (± 9) kg, speed of 0.65 (± 0.57) m/s. Sarcopenia was found in 9 (33.3%) patients (lcSSc in 6/16 (37.5%) and dcSSc in 3/11 (27.2%) patients), among whom was found presarcopenia in 4 (14.81%) patients, mild sarcopenia in 4 (14.81%) patients and severe sarcopenia in 1 (3.7%) patient, with an average of physical activity of 2094 (± 2063) METS and risk of malnutrition with a median of 0.58 (range: 0-4).

Conclusion: Sarcopenia frequency was found in 33.3% of patients. The recognition of this condition has important therapeutic implications, due to the impact on the quality of life, morbidity and mortality. Strategies should include a focus on the nutritional aspects, improving the protein-rich diet intake with physical training program that aims to increase muscle mass and improve strength and performance, maintaining an adequate control of the disease and associated comorbidities.

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Abstract Number: 1658

Impact of Visceral Involvement in the Characterization and Prognosis of Patients Without Skin Involvement Classified as Systemic Sclerosis (SSc) According to 2013 ACR/EULAR Criteria in a Large Single Cohort

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Background/Purpose: The 2013 ACR/EULAR classification criteria for systemic sclerosis (SSc) allowed the inclusion of a subset of patients without skin involvement, not considered by the 1980 criteria. As the severity and the prognosis of these patients are still controversial, a pragmatic approach to characterize them according to the severity of visceral involvement is useful in the current daily practice.

Methods: Consecutive patients classified as SSc according to 2013 ACR/EULAR criteria attended in a single scleroderma outpatient clinic between 2010 and 2018 were included. Overlap syndromes were excluded. Patients with SSc skin involvement were classified as diffuse (dSSc) and limited (lSSc) according to LeRoy criteria. Patients without skin thickness were divided in two distinct groups: visceral sine-scleroderma (vsSSc) and non-visceral sine scleroderma (nvsSSc). VsSSc was considered in the presence of: a) Interstitial lung disease (ILD) [ground-glass > 10% in chest high resolution computed tomography (HRCT) or forced vital capacity < 70%]; b) Pulmonary arterial hypertension (PAH) confirmed by right heart catheterization; c) Heart (symptomatic arrhythmia, pericarditis or congestive heart failure); d) Kidney (scleroderma renal crisis). Clinical and laboratory data were obtained from an electronic register database. Proper statistics tests were applied and considered significant when $p< 0.05$. Log-Rank test was used to compare the survival curves.

Results: The cohort comprised 638 patients, 27.3% dSSc, 50.5% lSSc13.3% vsSSc, and 8.9% nvsSSc. Patients with skin involvement had longer disease duration and time of follow-up when compared to vsSS and nvsSSc ($p< 0.001$). As expected, patients with vsSSc presented a predominant clinical picture of ILD (85.9% of any ground-glass and 42.4% of >10% ground-glass in chest HRCT) or PAH (29.4%). Remarkably, the frequency of ILD in vsSSc was similar to dSSc($p=0.95$), and PAH was more common in vsSSc than in any other subset ($p< 0.01$). Although cardiac (23.5%) and renal (2.4%) involvement were observed, they were never referred as a SSc initial symptom in the vsSSc subgroup. In the other hand, nvsSSc also presented a lower frequency (36.8%, $p< 0.001$) of ILD (all with < 10% of ground-glass in chest HRCT). These nvsSSc patients were predominantly women with higher frequencies of SD pattern at the nailfold capillaroscopy (98.1%,$p=0.03$) and anticentromere antibody(70.9%,$p< 0.001$), presenting a similar frequency of peripheral vascular manifestations as the other subsets($p >0.05$) (table 1). At the end of follow-up, deaths represented 20.1% of dSSc 18.1% of vsSSc and 15.8% of limited SSc, with no death in nvsSSc ($p< 0.01$). The survival rate in vsSSc was similar to dSSc, but significantly higher than lSSc and nvsSSc (figure 1).

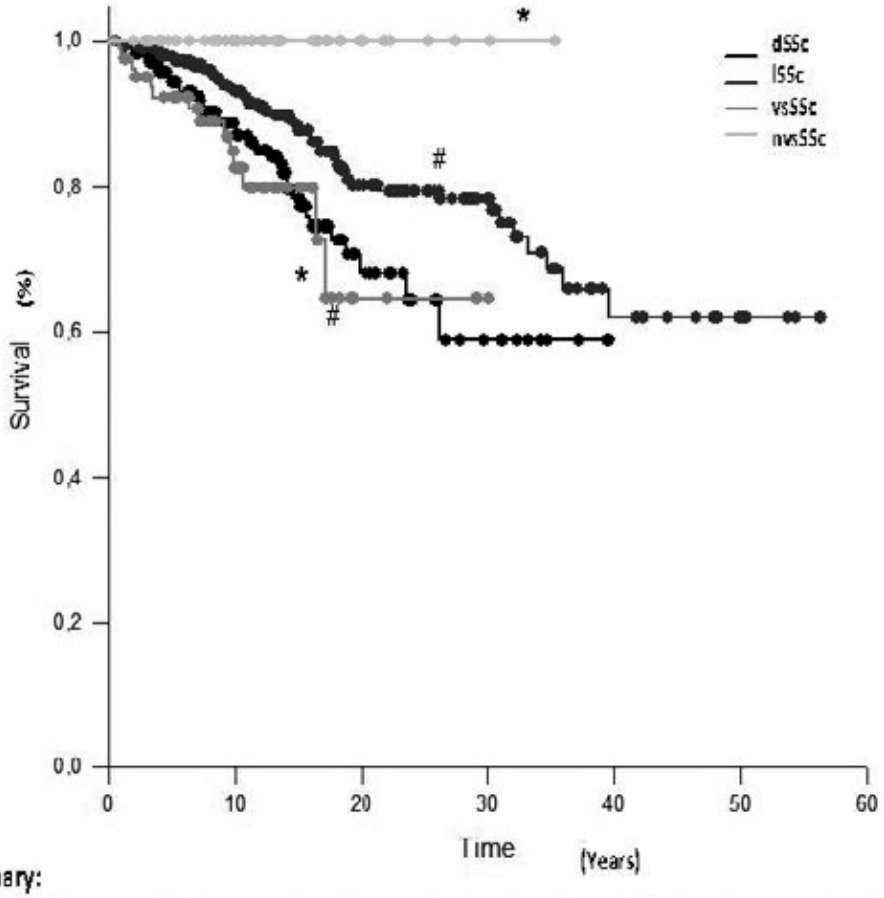
TABLE 1. DEMOGRAPHIC AND CLINICAL FEATURES OF SSc PATIENTS

Type(N)	dSSc (174)	lSSc (322)	vsSSc (85)	nvsSSc (57)	p	a	b	c	d	e	f
Female n (%)	141 (81)	286 (88.8)	73 (85.9)	54 (94.7)	0.02	**	-	**	-	-	-
Age, years	50.6 (13.2)	59.1 (11.4)	59(8.4)	55.2 (10.6)	<0.001	**	**	-	-	-	-
Age at onset, years	37.7 (13.5)	42.9 (11)	51.3(8.9)	47.4 (11.7)	<0.001	**	**	**	**	-	-
Disesase duration, years	12.9 (7.9)	16.2 (8.4)	7.7(3.8)	7.9 (4.1)	<0.001	**	**	**	**	**	-
Time of follow-up	9.3 (6.6)	9.7 (5.5)	4.9 (3)	5.2 (3.2)	<0.001	-	**	**	**	**	-
Caucasian race	110 (63.2)	207 (64.3)	54 (63.5)	40 (70.2)	0.81						
Environmental factor	20 (11.5)	40 (12.4)	11 (12.9)	6 (10.5)	0.96						
Smoking	55(31.6)	104(32.3)	35(41.2)	14(24.6)	0.20						
INITIAL SYMPTOMS											
Puffy hands	52 (29.9)	239 (74.2)	38 (44.7)	46 (80.7)	<0.001	**	**	**	**	-	**
Skin sclerosis	99 (56.9)	31 (9.6)	0	0	<0.001	**	**	**	**	**	-
Arthritis	18 (10.3)	27 (8.4)	5 (5.9)	4 (7)	0.64						
Esophageal disease	2 (1.1)	5 (1.6)	4 (4.7)	1 (1.8)	0.22						
ILD	0	8 (2.5)	24 (28.2)	0	<0.001	-	**	-	**	-	**
PAH	2 (1.1)	2 (0.6)	5 (5.9)	0	0.002	-	**	-	**	-	-
CLINICAL SYMPTOMS											
RF	173 (99.4)	321 (99.7)	85 (100)	57 (100)	0.84						
Puffy hands	141 (81)	292 (90.7)	54 (63.5)	49 (86)	<0.0011	**	**	-	**	**	-
Pitting scars	171 (98.3)	310 (96.3)	73 (85.9)	54 (94.7)	<0.001	-	**	-	**	-	-
Digital ulcers	66 (37.9)	109 (33.9)	19 (22.4)	15 (26.3)	0.057	-	**	-	**	-	-
Amputation	12 (6.9)	29 (9)	3 (3.5)	6 (10.5)	0.31						
Calcinosis	25 (14.4)	67 (20.8)	3 (3.5)	2 (3.5)	<0.001	-	**	**	**	**	-
Telangiectasias	96 (55.2)	212 (65.8)	40 (47.1)	35 (61.4)	0.007	**	-	-	**	-	-
Hand contracture	96 (55.2)	88 (27.3)	0	0	<0.001	**	**	**	**	**	-
Arthritis	32 (18.4)	36 (11.2)	8 (9.4)	5 (8.8)	0.061	**	-	-	-	-	-
Esophageal dysmotility	141(81)	273(84.8)	61(71.8)	23 (40.4)	<0.001	-	-	**	**	**	**
GERD	137(78.7)	147(80.1)	59(69.4)	26(45.6)	<0.001	-	-	**	**	**	**
Bowel disease	15(8.6)	17(5.3)	1(1.2)	0	0.047	-	-	**	-	**	-
ILD (ground glass > 10% at HRTC)	59 (33.9)	43(13.4)	36(42.4)	0	<0.0001	**	-	**	**	**	**
ILD (CVF < 70%)	71 (40.8)	65 (20.2)	27(31.8)	0	<0.0001	**	-	**	**	**	**
ILD (any ground glass)	150(86.2)	213(66.1)	73(85.9)	21(36.8)	<0.001	**	-	**	**	**	**
ILD (honeycombing)	31(17.8)	24(7.5)	15(17.6)	0	<0.001	**	-	**	**	**	**
PAH	18 (10.3)	51 (15.8)	25 (29.4)	0	<0.001	-	**	**	**	**	**
Heart	42(24.1)	69 (21.4)	20(23.5)	0	<0.01	-	-	**	-	**	**
Renal crisis	7(4)	1(0.3)	2 (2.4)	0	<0.01	**	-	-	-	-	-
Death	35 (20.1)	51 (15.8)	15 (18.1)	0	<0.01	-	-	**	-	**	**
NFC SD pattern	134(94.4)	233 (87.3)	70 (86.4)	51(98.1)	0.017	**	**	-	-	**	**
LABORATORY											
ANA	168 (96.6)	313 (97.2)	83 (97.6)	55 (96.5)	0.25						
ACA	8 (4.6)	105 (32.6)	19 (22.4)	39 (70.9)	<0.001	**	**	**	-	**	**
Anti-Scl 70	82 (47.1)	78 (24.2)	22 (25.9)	4 (7.3)	<0.001	**	**	**	-	**	**

P=referent to the multigroup comparison
a = diffuse (dSSc) *vs* limited (lSSc) scleroderma groups
b = dSSc *vs* visceral sine-scleroderma (vsSSc)
c = dSSc *vs* non-visceral sine scleroderma (nvsSSc).
d = lSSc *vs* vsSSc
e = lSSc *vs* nvsSSc
f = vsSSc *vs* nvsSSc
**p<0.05; - p≥0.05

Conclusion: The analysis of the visceral involvement permitted the characterization of two distinct subgroups without skin thickening (vsSSc and nvsSSc) with significant differences in survival. One subset is characterized by predominant visceral involvement (ILD or PAH), and worse prognosis (vsSSc), while the other had a significantly milder disease and higher frequency of anticentromere antibody (nvsSSc).

Figure 1. SSc Subsets Survival Analysis (since first non-Raynaud SSc symptoms)



Data Summary:

Group	Total	Missing	Events	Censored	Percent Censored	Survival time (years) mean (SD)
dSSc	174	0	35	139	80	29(1.6)
lSSc	322	0	51	271	84	41(2.2)
vsSSc	85	0	15	70	82	15.5(0.8)
nvsSSc	57	0	0	57	100	-
Overall	638	0	101	534	84	

Log-Rank Test: p <0.001, significant for the following comparisons: vsSSc vs. lSSc (# p=0.0003); vsSSc vs. nvsSSc (* p=0.0057)

Disclosure: A. Ribeiro, None; **A. Luppino-Assad**, None; **H. Silva**, None; **L. Prado**, None; **D. Andrade**, None; **P. Sampaio-Barros**, None.

Abstract Number: 1659

Linaclotide for the Treatment of Gastrointestinal Symptoms in Systemic Sclerosis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Gastrointestinal (GI) involvement is the most common internal organ affected in systemic sclerosis (SSc). Constipation is a common GI complication in SSc that affects over 50% of patients. It can be severe and impacts quality of life. We sought to examine the safety, tolerability, and efficacy of linaclotide, a selective agonist of guanylate cyclase C (GC-C) as an intervention for SSc patients with refractory constipation.

Methods: We performed a retrospective analysis of all patients seen at Johns Hopkins Scleroderma Center between August 2012 and January 2019 who were prescribed linaclotide as an outpatient for refractory constipation. All patients had data prospectively collected in our longitudinal database if they met criteria for systemic sclerosis. Patients were defined as linaclotide responders if they were to medication for at least 12 months and had documentation of clinical effectiveness documented by the treating physician. We examined the prescribed dose and frequency of the drug, rates of symptom improvement, duration of treatment, treatment response, and side effect profiles among linaclotide-treated patients.

Results: Thirty-one patients with SSc were treated for refractory constipation with linaclotide. We found that the majority of patients (90.3%; 28/31) had a favorable response to treatment and tolerated it well, while only three patients (9.7%) reported ineffectiveness or had intolerable side effects. Low-dose linaclotide achieved adequate symptom control in approximately 2/3 patients (58.1%; 18/31), though high-dose linaclotide (equivalent to at least 145 mcg daily dosage) was required in a subset (41.9%; 13/31). The most common side effects were diarrhea, cramping, or bloating, which was present in 8 patients (8/31, 25.8%). Ineffectiveness, cost, and abdominal pain were the complaints cited among those who discontinued therapy. We then evaluated the subset of linaclotide-treated SSc patients with objectively measured colonic transit times by whole gut scintigraphy. We found that 11/14 (78.6%) had delayed colonic transit and 3/14 (21.4%) had normal colonic transit. This demonstrated that while severely delayed colonic transit was present among a subset of patients treated with linaclotide, not all significant constipation in SSc is associated with delayed colonic . The presence of responders to linaclotide in both groups (8/11, 72.7%, with delayed transit; 3/3100%, with normal transit) suggests that SSc patients with refractory may respond favorably to linaclotide, independent of colonic transit abnormalities.

Conclusion: Linaclotide is a well-tolerated and efficacious prosecretory agent that can be used to manage refractory constipation in who have failed management with over the counter laxatives and/or stool softeners. We find that low-dose treatments with linaclotide are an effective option with a lower side effect profile than high-dose treatment regimens, though high doses are required for optimal symptom control in some patients.

Disclosure: E. Dein, None; **J. Clarke**, None; **F. Wigley**, None; **Z. McMahan***, None.

Abstract Number: 1660

Serial Sublingual Videomicroscopy in Systemic Sclerosis Clinic: Are the Microcirculation Measurements Correlated with Gastrointestinal Symptoms?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Intravital microscopy of the sublingual microcirculation provides estimates of perfused barrier region (PBR) and red blood cell fraction (RBCfract), which quantifies vasculopathy and, similar to nailfold capillaroscopy, may be valuable in serial assessment of systemic sclerosis (SSc) disease progression. In this report, we examine the longitudinal correlates of sublingual videomicroscopy with gastrointestinal symptoms of SSc.

Association of change in GIT 2.0 measures with change in RBC fraction		
GIT 2.0 Component	Beta coefficient for 1 point change PBR	p-value
Total score	-2.98 (-6.09, 0.13) *	0.06
Reflux	-3.52 (-5.83, -1.20)	0.003
Distention	-1.11 (-2.91, 0.68)	0.222
Fecal Soilage	-1.31 (-3.53, 0.90)	0.243
Diarrhea	-0.64 (-2.83, 1.55)	0.562
Social Function	-2.65 (-5.96, 0.67)	0.116
Wellbeing	-1.31 (-3.79, 1.17)	0.298
Constipation	-3.58 (-6.46, -0.70)	0.015
Association of change in GIT 2.0 measures with change in PBR		
GIT 2.0 Component	Beta coefficient for 1 point change	p-value
Total score	0.17 (0.03, 0.32)	0.02
Reflux	0.21 (0.10, 0.31)	<0.001
Distention	0.05 (-0.03, 0.14)	0.209
Fecal Soilage	0.08 (-0.03, 0.18)	0.141
Diarrhea	0.06 (-0.04, 0.17)	0.231
Social function	0.12 (-0.04, 0.28)	0.129
Wellbeing	0.08 (-0.04, 0.20)	0.188
Constipation	0.18 (0.04, 0.32)	0.01

Methods: Patients enrolled in a single center SSc (2013 ACR/EULAR Classification Criteria) registry, who completed the Scleroderma Clinical Trials Consortium Gastrointestinal Tract (GIT 2.0) questionnaire and had sublingual videomicroscopy are in this analysis. The GIT 2.0 includes 34 questions (assessing reflux, bloating/distention, diarrhea, soilage, emotional well-being, social function, and constipation), and provides a total score of GIT severity. Automated capture and analysis of sublingual microvessel segments provides detailed, objective microvascular structural (RBCfract) and functional data (PBR). To find the association between the GIT 2.0 and vascular outcomes (PBR and RBC fract), we ran 2 different models for a) Baseline vascular outcome vs baseline GIT score (total score and 7 individual scales + severity) and b) Delta vascular outcome vs delta GIT scores (Stable / improved GIT score vs worse GIT score; total score and 7 individual scales + severity). All models are adjusted by SSc disease duration, reflux medication, vasodilator, and immunosuppression use.

Results: There were a total of 116 participants with complete vascular outcomes, treatment data, and GIT scores at baseline visit and 55 participants with a second complete measurement set. These SSc patients were mostly female (n=100), white (n=110) with a SSc mean disease duration of 9.7 years (SD 8.3) and ANA/SSc-specific antibody positive (n=92). At baseline, GIT 2.0 total severity score significantly associated with PBR (p=0.01) and RBCfract (p=0.015); and the subdomains of reflux (p=0.02) and distention (p=< .001) were significantly associated with PBR. The association of vascular outcomes with change in GIT 2.0 components are shown in Table 1.

Conclusion: Gastrointestinal complaints are common in SSc and may be due to progressive vasculopathy. Intravital microscopy provides a bedside monitoring approach that can be correlated easily to clinical features and warrants further study.

Disclosure: T. Frech, None; **G. Wei**, None; **M. Murtaugh**, None.

Abstract Number: 1661

Circulating Cell Free DNA Released from Eosinophils Is a Practical Biomarker in Patients with Eosinophilic Granulomatosis with Polyangiitis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fragmented cell-free DNA (cfDNA) is released into blood circulation as results of damage or death of peripheral blood cells as well as organ tissues, and it is significantly increased in those of cancer patients to be used in monitoring disease activities. CfDNA was also reported as a potential biomarker in autoimmune diseases, such as rheumatoid arthritis and systemic lupus erythematosus.

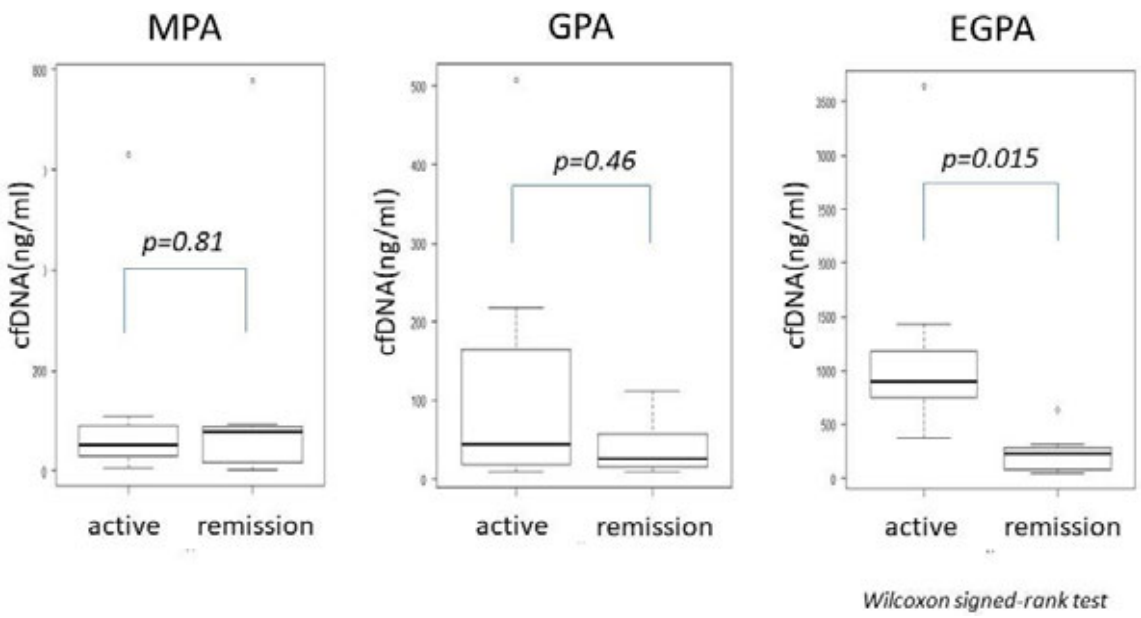

Figure 1. The concentration of cfDNA in patients with AAV before immunosuppresssive therapy and remission period

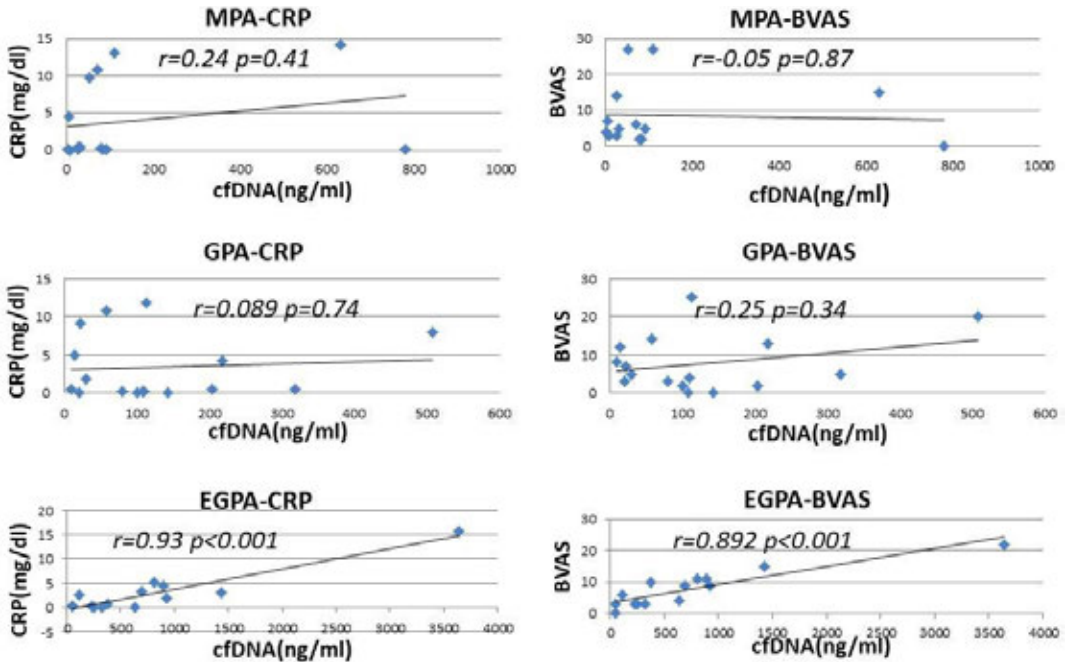

Figure 2. Correlation between cfDNA and disease activity in patients with AAV

The cfDNA sequence is identical to that of genomic DNA, since the DNA of each cell type possesses specific methylation patterns. In eosinophils, methylation levels of the loci, *interleukin 5 receptor alpha unit (IL5RA)* and *interleukin 4 (IL4)*, were reported to be lower as compared to other blood cells.

The purpose of this study is to evaluate the correlation between serum cfDNA and clinical disease activities in patients with Eosinophilic granulomatosis with polyangiitis (EGPA), and to examine tissue specific methylation patterns of cfDNA.

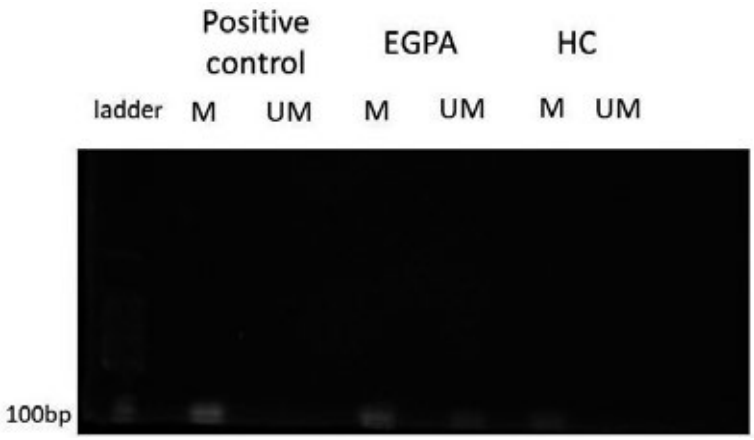

Figure 3. Representative analysis of MSP products amplified by IL5RA methylated specific primer (M) and unmethylated spesific primer (UM) positive control: Methylated HeLa gDNA

Methods: The study group included 24 patients with ANCA associated vasculitis (AAV), 8 patients with EGPA, 7 with microscopic polyangiitis (MPA) and 9 with granulomatosis with polyangiitis (GPA). CfDNA was extracted from serum using Qiamp MinElute cfDNA kit (QIAGEN). By quantitative real-time PCR, the concentration of cfDNA was measured twice retrospectively; before immunosuppressive therapy and remission period. CfDNA from 10 healthy controls (HC) was also measured. Then, we evaluated the correlation between cfDNA and the clinical disease activity, using Birmingham vasculitis score (BVAS) and C reactive protein (CRP).

Next, cfDNA from patients with EGPA and HC was treated with bisulfite to convert unmethylated cytosines to uracils. Methylation specific PCR was performed to evaluate two loci, *IL5RA* and *IL4*.

Results: The concentration of cfDNA in AAV was higher than HC ($p< 0.001$) before treatment, and cfDNA in EGPA was significantly higher than the other AAV ($p< 0.001$). After introduced immunosuppressive therapy, cfDNA was significantly decreased in EGPA ($p=0.015$), but not changed in MPA ($p=0.81$) and GPA ($p=0.46$) (fig.1). In patients with EGPA, cfDNA was strongly correlated with BVAS (EGPA; $r=0.89$, $p< 0.001$, MPA; $r=-005$, $p=0.87$ and GPA; $r=0.25$, $p=0.34$, respectively). CfDNA also strongly correlated with CRP in EGPA (EGPA; $r=0.92$, $p< 0.001$, MPA; $r=0.24$, $p=0.4$ and GPA; $r=0.09$, $p=0.74$, respectively) (fig.2). Methylated DNA of IL5RA and IL4 was detected in both EGPA and HC, while those of un-methylated DNA was detected in EPGA (fig.3).

Conclusion: CfDNA is expected to be a useful biomarker for EGPA, representing the lower methylation of *IL5RA* and *IL4* loci in eosinophils from patients with EPGA .

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Abstract Number: 1662

Does PR3-ANCA+ Eosinophilic Granulomatosis with Polyangiitis (Churg–Strauss)Really Exist?

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – ANCA-Associated Poster II

Session Type: Poster Session (Monday)

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Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) (Churg–Strauss) is a small-vessel necrotizing vasculitis characterized by blood and tissue eosinophilia and asthma. Only a third of EGPA patients are ANCA+, mainly directed against myeloperoxidase (MPO). ANCA+ patients have more neurological and renal involvements, while ANCA– patients have more cardiac manifestations. ANCA directed against proteinase (PR3) are rarely found in EGPA, and their interpretation remains unclear. We aimed to examine the significance of PR3-ANCA in EGPA.

Methods: We set up a multicenter, European, EGPA cohort including 845 patients who satisfied the American College of Rheumatology criteria, 2012 Chapel Hill Consensus Conference definitions and/or MIRRA trial criteria. Baseline characteristics and outcomes were analyzed and compared according to ANCA status.

Results: ANCA status and specificity were available for 734 patients: 508 (69.2%) ANCA–, 209 (28.5%) MPO-ANCA+ and 17 (2.3%) PR3-ANCA+. At diagnosis, PR3-ANCA+ patients, compared to those MPO-ANCA+ or ANCA–, respectively, had: less frequent asthma (71% vs 91% or 93%, P=0.004), especially steroid-dependent asthma (21% vs. 34% or 46%, P=007); more skin manifestations (65% vs. 38% or 34%, P=0.03); less frequent pulmonary infiltrates (41% vs. 40% or 58%, P=0.03) but more frequent nodules (25% vs. 10% or 8%, P=0.046); less frequent peripheral

neuropathy (29% vs. 72% and 47%, P< 0.0001); and lower median [IQR] eosinophil count/mm3(2015 [IQR 802–5826] vs. 5718 [2330–10444] or 3224 [1332–7570], P< 0.0001). Renal involvement did not differ between PR3-ANCA+ and MPO-ANCA+ patients.Median follow-up was74 [37–116] months for the whole cohort. PR3-ANCA+ vs. MPO-ANCA+ or ANCA– patients, respectively, experienced vasculitis relapses more frequently (47% vs. 34% or 24%; P=0.004). Moreover, vasculitis relapse-free survival was much shorter for PR3-ANCA+ [hazard ratio (HR) 7.32, 95% CI 2.02–26.5; P=0.002] and MPO-ANCA+ patients (HR 1.71, 95% CI 1.23–2.37; P=0.002) compared to those ANCA–. Also, median prednisone doses at 24 and 60 months, respectively, were significantly higher for PR3-ANCA+ than MPO-ANCA+ or ANCA– patients (P=0.02 and P=0.007). Finally, at 24 months of follow-up, PR3-ANCA+ vs. MPO-ANCA+ or ANCA– patients, respectively, had less frequent chronic asthma (38% vs. 51% or 60%, P=0.04) but more frequent renal damage (20% vs. 10% or 1%, P< 0.0001).

Conclusion: PR3-ANCA+ EGPA patients' characteristics differ from those MPO-ANCA+ or ANCA–, especially asthma and eosinophil counts, which are the cardinal features of EGPA. Since eosinophilia can be mild-to-moderate in granulomatosis with polyangiitis (GPA, Wegener's), we wonder if PR3-ANCA+ EGPA is not a third phenotype of EGPA but rather a particular form of GPA.

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Abstract Number: 1663

Assessments of Quality of Life in Patients with Eosinophilic Granulomatosis with Polyangiitis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – ANCA-Associated Poster II

Session Type: Poster Session (Monday)

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Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is characterized by asthma and other manifestations of vasculitis, some of which can be life-threatening, cause major organ damage, or become chronic. Data on health-related quality of life (HRQoL) and patient-reported outcomes (PRO) in EGPA are limited. This study aimed to describe HRQoL in patients with EGPA enrolled in a large cohort.

Table 1: Demographic and disease-associated factors at baseline and end of follow-up for patients with eosinophilic granulomatosis with polyangiitis

	Baseline	End of follow-up
Age, years (SD)	53.1 (13.8)	57.0 (14.1)
Disease duration, years, median (IQR)	3.11 (0.35-3.62)	6.1 (2.5-9.7)
Relapse after diagnosis (%)		63%
Duration of glucocorticoids, months, median (IQR)		12 (3-13)
Ever used cyclophosphamide (%)		41%
PROMIS Fatigue score (SD)	55.6 (9.6)	51.1 (11.1)
PROMIS Physical functioning score (SD)	43.5 (8.3)	46.3 (9.2)
SF36 PCS (SD)	40.7 (11.5)	42.6 (11.0)
SF36 MCS (SD)	48.2 (11.5)	50.0 (11.0)

SD = standard deviation; IQR = inter-quartile range; VDI=Vasculitis Damage Index; SF36=Short form 36; PCS =physical component summary; MCS=mental component summary

Table 2. Association of demographic and disease-associated factors with fatigue, physical functioning, and HRQoL in patients with eosinophilic granulomatosis with polyangiitis

	PROMIS Fatigue	PROMIS Physical functioning	SF36 PCS	SF36 MCS
Age, years	-0.07 (0.24)	-0.17 (0.001)	-0.16 (<0.001)	0.07(0.14)
Female	4.64 (0.01)	-2.42(0.11)	-0.38 (0.78)	-2.01(0.13)
Disease duration, years,	0.06 (0.68)	-0.09 (0.42)	0.07 (0.50)	0.04 (0.68)
ANCA-positive	-2.44 (0.21)	1.41 (0.37)	0.82 (0.57)	2.08 (0.15)
Duration of glucocorticoid use, months	0.08 (0.25)	-0.05 (0.41)	-0.02 (0.42)	-0.01 (0.87)
Ever flared after diagnosis	2.19 (0.24)	-0.80 (0.61)	-1.61 (0.24)	-0.31 (0.82)
Ever used cyclophosphamide	-2.96 (0.10)	0.18 (0.90)	0.87 (0.52)	1.94 (0.15)

Results are expressed as increased in PROMIS/SF36 measures per one unit increase in predictor variables with p-values within parenthesis. SD = standard deviation; IQR = inter-quartile range; VDI=Vasculitis Damage Index; SF36=Short form 36;
PCS =physical component summary; MCS=mental component summary

Methods: Retrospective analysis of HRQoL in patients with EGPA participating in a multicenter longitudinal study from 2003-2019. Demographic and disease-associated factors at baseline include age, sex, ANCA status, use of cyclophosphamide or not, and cumulative duration of glucocorticoid (GC) use. Fatigue and physical functioning were

assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS) instruments administered through computer adaptive testing (CAT). PROMIS instruments are calibrated so that scores are normally distributed with a mean of 50 and a standard deviation of 10 in the US population. Higher scores signify better physical functioning and increased fatigue. HRQoL was assessed with the SF36 with physical component summary (PCS) and mental component summary (MCS) scores calculated. SF36 summary scores are calibrated so that scores are normally distributed with a mean of 50 and a standard deviation of 10 in the US population. Continuous and categorical variables are presented as a percentage and continuous variable presented as means with standard deviations or medians with inter-quartile range (IQR). The association of demographic and disease-related factors with PROMIS and SF-36 measures were assessed at the end of follow-up using general linear models. Results are presented as an increase in measures per one unit increase in the predictor variables.

Results: Data from 276 patients with EGPA were included; 57% were female, with a mean age of 53.1 years (SD ±13.8) years. The median duration of follow-up was 3.1 (IQR 0.9-6.2) years. Table 1 shows demographic and disease-associated factors. At baseline, fatigue and physical functioning was assessed among 66 study patients and 151 patients at the end of follow-up. SF36 was assessed among all patients at baseline and at the end of follow-up. At baseline, patients had substantially increased fatigue scores 55.6 (SD 9.6) and reduced physical functioning scores 43.5 (SD 8.3) compared to the general population. The mean SF36 PCS scores were quite low 42.6 (11.0) but the mean SF36 MCS scores were the same as the population norm, 50.0 (11.0). At the end of follow-up, scores were closer to the population norms (Table 1). At the end of follow-up, female sex was associated with a 4.6 point higher fatigue score ($p=0.01$) and age was associated with reduced physical functioning and PCS and with reduction of 0.17 ($p=0.001$) and 0.16 ($p < 0.001$) for one-year increase in age, respectively (Table 2).

Conclusion: Compared to the general population, patients with EGPA have an increase in fatigue, reduced physical functioning, and substantially reduced HRQoL.

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Abstract Number: 1664

Reducing the Number of Rituximab Infusions at Onset of Maintenance Therapy for ANCA-associated Vasculitides: Results of a Post Hoc Analysis from a Randomized–controlled Trial

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SESSION INFORMATION

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Background/Purpose: Rituximab (RTX) superiority over azathioprine to maintain ANCA-associated vasculitis (AAV) remission was demonstrated.The MAINRITSAN2 trial was designed to compare an individually tailored RTX-infusion schedule to 5 RTX infusions at a predefined schedule. The tailored-regimen group received a 500-mg RTX infusion at randomization (day (D) 0), with reinfusion only when CD19 lymphocytes or ANCA had reappeared, or ANCA titer rose markedly, based on testing every 3 months until month (M) 18. The fixed-schedule group received RTX (500 mg) on D0 and D14, then at M6, M12 and M18. AAV relapse rates did not differ significantly between the 2 groups at M28. The objective of this post hoc analysis was to evaluate the effect of omitting the D14 500-mg RTX infusion on early AAV-relapse rates.

Methods: MAINRITSAN2-trial data were subjected to post-hoc analyses of M3, M6, M9 and M12 relapse-free survival rates in each arm as primary endpoints. Relapses were defined as reappearance or worsening of AAV symptoms, i.e., BVAS >0. Exploratory sub-group analyses were run according to cyclophosphamide or rituximab induction and newly-diagnosed or relapsing AAV. Other endpoints were ANCA status and titer, and CD19+ B-cell–count evolutions.

Results: At M3, M6, M9 and M12, respectively, among the 161 patients included, 79/80 (98.8%), 76/80 (95%), 74/80 (92.5%) and 73/80 (91.3%) from D0, and 80/81 (98.8%), 78/81 (96.3%), 76/81 (93.8%) and 76/81 (93.8%) from D0+D14 groups were alive and relapse-free. No between-group differences were observed. Results were not affected by cyclophosphamide or rituximab induction, or newly-diagnosed or relapsing AAV. On D0, a higher percentage of D0-infusion patients were ANCA-positive and that difference remained stable at M12. Median (IQR) circulating CD19+ B-cell counts/mm^3 on D0, and at M3, M6, M9 and M12, respectively, were: 14 (1–44), 0 (0–0), 0 (0–1), 0 (0-4) and 0 (0–2) for the D0-infusion group; and 9 (0–35), 0 (0–0), 0 (0–2), 0 (0–1) and 0 (0–2) for the D0+D14-infusion group. Those results remained unchanged in the sub-group analyses

Conclusion: Eliminating the D14 rituximab remission-maintenance dose did not seem to impact the relapse-free survival rate at M12.

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Abstract Number: 1665

Glucocorticoids in Incident ANCA-Associated Vasculitis (AAV) Patients - A Study of Routine Clinical Practice in the EU Demonstrates Prolonged Use and Temporal Relationship to Adverse Events and Infections

Dieter Goette,[1] and Peter Rutherford[1], [1]Vifor Pharma, Zurich, Zurich, Switzerland

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: AAV is a severe systemic vasculitis and rapid induction of remission is essential and high dose glucocorticoids (GC) are part of standard of care. Achieving control of AAV is critical but patients are also at risk from GC-related adverse events leading to long term organ damage as well as acute morbidity and mortality. This retrospective study aimed to examine GC prescribing patterns, AAV response and adverse events (AEs) in incident AAV patients managed in routine clinical practice in Europe.

Methods: 929 incident AAV patients (54% of patients had granulomatosis with polyangiitis, and 46% had microscopic polyangiitis; mean age was 56.82 years (SD 14.2) with 53.7% male) from 4 European countries (399 physicians) were diagnosed between 2014-17. Routine clinical data collected at baseline, 1, 3, 6 and 12 months following commencement of induction therapy were collected and analysed.

Results: Severity of vasculitis varied - 12% patients were mild/localized, 54% moderate systemic and 34% had severe, life threatening vasculitis. Overall 83% of patients received GCs initially – 49% IV followed by oral, 17% oral only and 17% IV only. 43% used a combination of cyclophosphamide and GC, 13% rituximab and GC, 10% only GC with the remainder using other regimes. As BVAS was not used routinely, full clinical response was assessed as no vasculitis activity and GC taper on track. Most patients remained on GCs over 12 months, AAV response was incomplete and AEs were common especially in first 3 months when GC dose highest. GC dose changes were performed

	1 month	3 months	6 months	12 months
Full response %	22	43	61	68
Still receiving GC %	82	79	67	61
Decrease/stop GC at visit %	38/1	45/4	38/5	26/8
At least one AE/infection %	64/46	42/28	35/23	30/20

variably and varied geographically - for instance more UK patients had GC reductions at 3 (55%) and 6 months (46%) compared to other countries. At 12 months, of the 61% patients still needing GCs, 34% were receiving < 5mg, 56% 5-10mg, 9% 10-20mg and 2% > 20mg. 67% had no vasculitis activity, 17% local disease only, 11% mild to moderate systemic disease and 6% moderate to severe systemic disease

Conclusion: Most incident AAV patients receive high dose GCs as part of remission induction therapy, commonly IV initially, and the majority remain on GCs over 12 months. AEs and infections are common especially in the first months when GC dose is high. Clinical response is variable and only a minority of patients at 12 months have full remission of AAV without the clinical need for steroids. New targeted therapeutic approaches are needed to address this unmet medical need in AAV.

Disclosure: D. Goette, Vifor Pharma, 3, 4; **P. Rutherford**, Vifor Pharma, 3, 4, Zytoprotec, 1.

Abstract Number: 1666

Maintenance Treatment in ANCA Associated Vasculitis in Real World Clinical Practice – Burden of Disease, Use of Glucocorticoids and Impact on Patient Functional Status Remain Major Problems

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Session Title: Vasculitis – ANCA-Associated Poster II
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Background/Purpose: After successful remission induction AAV is a relapsing remitting long term condition and patients are at risk of organ damage from both active AAV and therapy in particular from glucocorticoids (GC). The remission maintenance phase of AAV is critical for good long term outcomes. This retrospective study aimed to examine the definition of maintenance, therapies used and outcomes in AAV patients managed in routine clinical practice

Methods: AAV patients from 4 European countries (310 physicians) who completed induction therapy for organ or life threatening AAV and initiated maintenance therapy between 2014-16 were studied. Data were collected at the time maintenance was determined to begin by the physician and then at following 6, 12, 18 and 36 months

Results: 929 patients were studied - 51% of patients had granulomatosis with polyangiitis,; mean age 54 years with 54% male. 49% were studied from incident AAV and 51% from a relapse. Physicians defined the start of maintenance with mean of 5.6 months from induction start on basis of fixed time point 38%, starting of new drug for maintenance 27%, reaching full remission 26% and no specific criteria 9%. At this time 45% were in full AAV remission vs 49% in partial and 6% refractory. Over 36 months from when maintenance was defined, 84% were in remission but 10% had major relapse requiring re-induction therapy and left follow up, 6% died (in 2/3 of cases at time of relapse). There is variation in the drugs used for maintenance therapy in real world practice. At 36 months, 9% of AAV patients were receiving renal replacement therapy and CKD was reported in 17% of patients vs 7% at start of remission induction therapy and osteoporosis also increased 15% vs 7%. 55% of patients had no AAV activity, 28% positive ANCA serology but no clinical disease, 8% local AAV, 6% mild to moderate systemic disease and 3% moderate to severe systemic disease. Active AAV was see most commonly in kidney (29%), lung (13%) and sinuses (8%). There was

	Maintenance start	6 months	12 months	18 months	36 months
Remission n	929	817	789	777	742
Total relapse %/major %		12/46	10/53	6/51	7/66
GC/Azathioprine/Rituximab/ MMF %	62/37/19/18	59/37/20/19	49/31/17/18	40/28/15/16	33/23/13/12
GC dose > 7.5mg %		59	41	30	29
At least one infection %		43	34	28	26

negative impact on patient functional status after 36 months with 13% having reduced working hours, 13% restricted social life, 6% had to leave employment, 5% were registered as disabled and 2% had to leave full time education

Conclusion: Maintenance therapy in AAV has variable definitions but typically begins after 6 months of remission induction therapy. Relapse of varying degree is still a clinical problem and many patients require ongoing GC therapy to maintain remission. Infectious complications are a problem and there is significant negative impact on patient functional status over time. There is an ongoing need for new targeted therapies in AAV to improve clinical and patient functional status

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Disclosure: D. Goette, Vifor Pharma, 3, 4; **P. Rutherford**, Vifor Pharma, 3, 4, Zytoprotec, 1.

Abstract Number: 1667

Long Term Outcome of Hydralazine-Associated Vasculitis

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Background/Purpose: Hydralazine associated vasculitis (HAV) is rare but with potentially detrimental complications, affecting different organ systems. Most case series described short term disease course. Hence, data is sparse regarding long term management and outcome of HAV. The aim of this study is to determine long term outcome and whether variable duration of therapy has any impact on outcome.

Methods: We identified cases of HAV by searching electronic medical records for ICD codes of vasculitis and association of hydralazine intake from July of 2001 to July of 2017. Patients who received hydralazine after vasculitis onset were excluded. 23 patients were identified with diagnosis of HAV as deemed by the treating clinician. Data collected included demographics, hydralazine dose/duration, comorbid conditions, clinical presentation, laboratory, radiologic and pathological data, treatment strategies and outcomes. Continuous variables were summarized using means or medians, and categorical variables were summarized using frequencies and percentages. Outcomes were defined by full renal recovery, chronic kidney damage or relapse. Lung involvement was also registered.

Results: 23 patients (age 65.8±10.5 years, 65% males) with HAV were identified. Median duration of hydralazine use at onset of vasculitis was 34 months (5,170), with median total daily dose of 150 mg. Table 1 represents organ involvement, serological findings and treatment. The most commonly involved organs were the kidneys (100%) and lungs (48%). Majority of patients had positive serology (ANCA 100%, ANA 91%, anti-histone 71%, ds-DNA 63%).

Table 1: Organ involvement, serological findings and treatment

Factor	Total (N=23) Statistics
Organ involvement	
Constitutional	3(13)
Eye (iritis)	1(4)
Ear/Nose/Throat	3(13)
. Nose (ulcer, epistaxis)	2 (9)
. Throat ulcers	1 (4)
Lung	11(48)
. Diffuse Alveolar Hemorrhage	7 (30)
. Nodular opacities	4 (17)
Skin	2(9)
. Leukocytoclastic vasculitis	1 (4)
. Interface dermatitis	1 (4)
Kidney	23(100)
. Pauci-immune	11 (48)
. Crescents	9 (40)
. Immune complex deposition	4 (17)
Joint	5(22)
Hematological	11(48)
. Anemia	9 (40)
. Thrombocytopenia	1 (4)
. Pancytopenia	2 (9)
Serological Workup (antibodies)	
ANCA	23(100)
ANA	21 (91)
ds-DNA	14 (63)
Anti-histone	15 (71)
Therapy	
Induction	19 (83)
Induction and short-term maintenance	12 (52)
Induction and ongoing maintenance	4 (18)
No treatment	2 (8)
Relapse	0

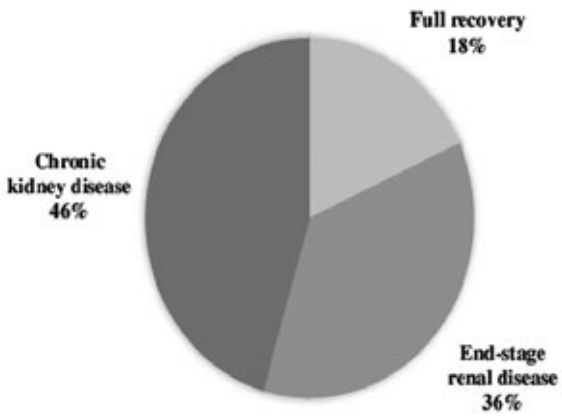
Statistics presented as Mean ± SD, Median (min, max) or N (column %)

Median follow up duration: 34 months (5,170)

Median duration of follow-up was 30 months. One patient was lost to follow up, 4 patients (18%) had complete renal recovery and 18 patients (82%) had chronic kidney damage (Figure 1). Higher serum Creatinine and need for dialysis at onset of the disease were associated with worse outcome (p=0.002, p=0, 0046 respectively). Overall death in the cohort was 6 (26%) patients, 3 of whom died within the first year of diagnosis due to complications related to vasculitis. 7 patients (30%) had diffuse alveolar hemorrhage, while 4 (17%) had nodular opacities, with resolution of both entities on follow up testing.

Most commonly used treatments were systemic steroids (83%), cyclophosphamide (34%) and rituximab (26%). 19 patients (83%) received induction therapy. 12 patients (52%) received induction and short-term maintenance therapy, with a median duration of 6 months. 4 patients (18%) received induction and are still on maintenance therapy to date. 2 patients (8%) did not receive any treatment. No relapse or progression of kidney disease was noted in the whole cohort despite variable treatment regimens, including patients who did not receive any treatment.

Figure 1: Long-term outcome of renal involvement



Conclusion: HAV mainly involves the kidneys and the lungs. Renal outcome is poor regardless of induction or maintenance therapy regimens. No relapse occurred in our series, which represents the longest follow up to date. Maintenance therapy may not be needed in these patients. Cohorts with longer follow up duration are needed to validate this observation.

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Abstract Number: 1668

Granulomatosis with Polyangiitis: Data from the French Vasculitis Study Group Registry

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – ANCA-Associated Poster II

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Background/Purpose: The long-term features of granulomatosis with polyangiitis (GPA), a systemic small-vessel ANCA-associated necrotizing vasculitis, have been mainly reported in small patient series. The aim of this study was to describe the main characteristics and long-term outcomes of patients entered in the nationwide French Vasculitis Study Group (FVSG) database.

Methods: Clinical and laboratory characteristics of patients with GPA, satisfying 1990 ACR criteria and/or revised Chapel Hill Nomenclature, enrolled in the FVSG cohort were collected. All patients had ANCA detection by immunofluorescence and/or ELISA determination of ANCA specificity at diagnosis or during follow-up. Estimated patients' overall and relapse-free survival rates were analyzed by Kaplan–Meier curves and Cox regression analysis.

Results: Between May 1983 and April 2018, 795 GPA patients were entered in the Registry: 181 (23%) before 2000, 419 (53%) 2000–2010 and 195 (24%) after 2010. They were followed for a mean ± SD of 4.6 ± 3.9 years. At diagnosis, mean ± SD age was 53 ± 16 years, with 52 (7%) >75 years old; their main clinical manifestations were: fever >38°C (43%); weight loss (45%); arthralgias/arthritis (52%); ENT involvement (80%), including rhinitis (54%), sinusitis (42%) and/or otitis (23%); lung involvement (68%), including nodules (41%) and alveolar hemorrhage (18%); neurologic (29%) involvement, including peripheral (21%) and central (10%) manifestations; and renal (56%) involvement. Median creatinine at diagnosis was 93 µmol/L, when 177/609 (29%) patients' had levels >150 µmol/L; between baseline and diagnosis those levels had already risen >30% for 193 (24%) patients. At diagnosis, 13 (2%) patients had subglottic stenosis; 55 (7%) had GPA limited to ENT and/or lungs (localized). Among the 728 available ELISA results, 546 (75.0%) patients were anti-PR3+ and 120 (16.5%) anti-MPO. Mean BVAS was 17.4 ± 8.8. To induce remission, glucocorticoids (GCs) were prescribed for 772 (97%) patients (median dose 60 [IQR 50–70] mg/day), combined with intravenous (76%) or oral (7%) cyclophosphamide, rituximab (6%) or methotrexate (4.5%). Among 729 (92%) patients achieving remission, 394 (54%) relapsed a mean of 2.7 ± 2.2 years after diagnosis. Kaplan–Meier estimated 5- and 10-year relapse-free survival rates, respectively, were 37% and 17% for the entire cohort, 35% and 14% for PR3+ patients, and 46% and 25% for those MPO+ (P=0.11). Univariable analysis identified PR3 positivity (HR 1.30; P=0.04) as the only factor associated with relapse, while oral cyclophosphamide use lowered relapse probability (HR 0.60; P=0.05). Multivariable analysis retained PR3 positivity (HR 1.29; P=0.05) as the only factor independently associated with relapse. Five- and 10-year overall survival rates were 90% and 85%, respectively. Among the 90 main severe side effects were 34 (4%) cancers, 32 (4%) opportunistic infections and 20 (3%) cardiovascular events.

Conclusion: Findings based on this large series showed good survival of GPA patients, with a low rate of side effects, and confirmed the higher probability of relapse among those PR3-ANCA+ at diagnosis.

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Abstract Number: 1669

Comparison of Mizoribine with Azathioprine in Efficacy and Safety for ANCA-Associated Vasculitis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – ANCA-Associated Poster II

Session Type: Poster Session (Monday)

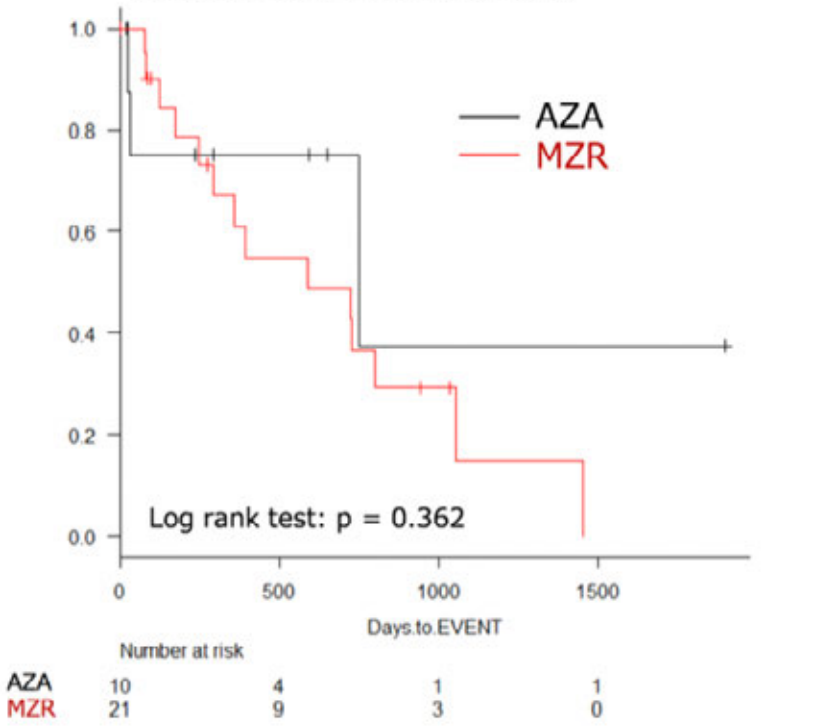
Session Time: 9:00AM–11:00AM

Background/Purpose: Mizoribine (MZR) is an immunosuppressant working as an inhibitor of purine synthesis, which mechanism of action is similar to mycophenolate mofetil. MZR is approved as the treatment of rheumatoid arthritis and lupus nephritis in Japan, and is reported to have effect in ANCA-associated renal vasculitis. But the data about the effect in remission maintenance and glucocorticoid dose reduction in patients with ANCA-associated vasculitis (AAV) are limited.

Table1. Baseline Characteristics and outcomes in patients treated with MZR and AZA

	Overall (n=31)	MZR (n=21)	AZA (n=10)	p value
Age	69 [58, 75]	70 [63, 74]	59 [54, 77]	0.281
Female (%)	18 (58.1)	12 (57.1)	6 (60.0)	1
BMI	23.4 (3.7)	24.1 [21.1, 25.3]	21.3 [20.1, 24.8]	0.403
Type of AAV				
MPA (%)	14 (45.2)	12 (57.1)	2 (20.0)	0.068
GPA (%)	7 (22.6)	3 (14.3)	4 (40.0)	0.172
EGPA (%)	9 (29.0)	6 (28.6)	3 (30.0)	1
Unclassified(%)	1 (3.2)	0 (0.0)	1 (10.0)	1
Blood Test				
MPO-ANCA (%)	12 (38.7)	12 (57.1)	0 (0.0)	0.004
PR3-ANCA (%)	5 (16.1)	1 (4.8)	4 (40.0)	0.027
RF (%)	13 (41.9)	10 (47.6)	3 (30.0)	0.452
CCP (%)	5 (16.1)	5 (23.8)	0 (0.0)	0.147
Remission Induction Therapy				
Cyclophosphamide (%)	9 (29.0)	5 (23.8)	4 (40.0)	0.417
Rituximab (%)	5 (16.7)	4 (19.0)	1 (10.0)	1
Steroid Pulse (%)	8 (25.8)	5 (23.8)	3 (30.0)	1
Steroid without pulse therapy(%)	20 (64.5)	13 (61.9)	7 (70.0)	1
Remission Maintenance Therapy				
1st Dose of MZR and AZA		150 [125, 150]	50 [25, 50]	
Concomitant PSL Dose	30 [10, 50]	40 [20, 50]	12.5 [9.0, 22.5]	0.051
Last Dose of MZR and AZA		150 [150, 300]	50 [50, 75]	
Concomittant PSL Dose	5 [2.5, 10]	5 [3, 10]	2.50 [0, 8.5]	0.111
Duration of MZR / AZA	596 [102, 1077]	924 [247, 1078]	265 [93, 637]	0.291
Concurrent immunosuppressants (%)	8 (25.8)	8 (38.1)	0 (0.0)	0.032
Outcome				
Flare of AAV (%)	17 (54.8)	14 (66.7)	3 (30.0)	0.121
Time to Flare of AAV (days)	375 [162, 734]	392 [247, 728]	33 [29, 393]	0.201
PSL dose at flare	5 [2.5, 15]	8 (25.8)	17.5 [11, 19]	0.114
Retention of medications (%)	16 (51.6)	10 (47.6)	6 (60.0)	0.704
Reason of discontinuation				
Insufficient Effects (%)	8 (32.0)	8 (38.1)	0 (0.0)	0.032
Adverse Event (%)	7 (28.0)	3 (14.3)	4 (40.0)	0.172
Flare or discontinuation of medication(%)	22 (73.3)	17 (85.0)	5 (50.0)	0.078
Time to flare or discontinuation of medication	294 [92, 728]	357 [126, 728]	265 [27, 637]	0.352
Adverse Events				
WBC decrease < 3000 /μL (%)	4 (14.3)	3 (16.7)	1 (10.0)	1
Anemia (Hb < 10 g/dl) (%)	10 (32.3)	9 (42.9)	1 (10.0)	0.106
Thrombocytopenia < 100 thousand /μL (%)	2 (6.5)	2 (9.5)	0 (0.0)	1
Grade1 Liver dysfunction	18 (62.1)	14 (73.7)	4 (40.0)	0.114
Grade2 Liver dysfunction	3 (9.7)	1 (4.8)	2 (20.0)	0.237
Serious infection (%)	4 (13.3)	3 (15.0)	1 (10.0)	1

Figure1. Flare-free survival curves in AAV patients treated with MZR and AZA



Methods: We retrospectively reviewed charts of patients with AAV who used MZR or azathioprine(AZA) at St. Luke's International Hospital, Tokyo, Japan from January 2004 to December 2018. We investigated basic demographics, types of AAV, results of blood tests, and medications used in the treatment of AAV including glucocorticoid and other immunosuppressants(IS). We defined flare of AAV as a new onset AAV-related symptom that required increase or initiation of glucocorticoids or IS. We calculated and flare-free rate and compare between MZR treatment group and AZA treatment group with Kaplan Meier curve by using log rank test. We also check the dose reduction effect in glucocorticoids before and after MZR treatment by using Wilcoxon signed-rank test.

Results: We identified 31 patients in total, and there were 21 and 10 patients who were primarily treated with MZR and AZA. Baseline characteristics are shown in Table1. 8 Patents (38.1%) in MZR-treatment group used concurrent IS (5: methotrexate, 1: azathioprine, 1: abatacept and 1: tacrolimus). Flare-up of AAV was seen in 14 (66.7%) in MZR and 3 (30.0%) in AZA-treated group, but there was no significant differences in the flare free rate (Figure 1). Dose of glucocorticoids significantly decreased after using MZR and steroid dose at flare is low (median 40mg [20, 50] vs 5 mg [3, 10]; $p < 0.01$, Wilcoxon signed-rank test). Mild liver dysfunction is common in MZR group, but just 3 (14.3%) patients discontinued MZR for adverse events(AE) (2: allergy, 1: infection) and major reason for discontinuation was insufficient effect, although 40% of patients treated with AZA had to discontinue due to bone marrow suppression and severe liver dysfunctions.

Conclusion: MZR seemed to have significant steroid-sparing effect in patients with AAV although rate of flare-up is high. Given the safe profile of MZR, MZR may be a useful agent can be used as alternative in patients who cannot continue AZA or other IS for AE, or in addition to regular IS for AAV.

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M. Kishimoto, AbbVie, 8; **K. Yamaguchi**, None; **M. Okada**, Abbott Japan, 8, Ayumi Pharmaceutical, 8, Mitsubishi Tanabe Pharma, 8, Ono Pharmaceutical,, 8, Pfizer, 8.

Abstract Number: 1670

Evaluation of Subclinical Coronary Atherosclerosis in ANCA-associated Small Vessel Vasculitides (AAVs) Compared to Matched Controls Through Visual Assessment of Coronary Arterial Calcium (CAC) Score Using Non-Gated Chest Computed Tomography (CT)

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – ANCA-Associated Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) is the most prevalent adult vasculitis and is associated with significant inflammatory burden; chest computed tomography (CT) is frequently obtained as part of the diagnostic work up and prognosis. Coronary calcium score (CCS) is a non-invasive modality used to evaluate the presence of coronary arterial calcium (CAC). Visual assessment of

Characteristic	GPA, EGPA, or MPA Number = 61	Controls Number = 61	P-value
Age (year)*	61.0 ± 16.3	61.7 ± 15.1	0.791
Female; n (%)	37 (60.7)	37 (60.7)	1.000
White race; n (%)	54 (88.5)	55 (90.2)	0.769
Disease duration (months)*	37.19 ± 25.85	NA	NA
BMI*	27.8 ± 6.2	28.6 ± 5.8	0.506
Smoking history; n (%)	28 (45.9)	29 (47.5)	0.856
Family history of CAD; n (%)	18 (29.5)	14 (23.0)	0.410
Hypertension; n (%)	36 (59.0)	32 (52.5)	0.466
Systolic blood pressure*	125.0 ± 18.0	127.3 ± 13.6	0.429
Diastolic blood pressure*	73.8 ± 9.7	74.3 ± 8.8	0.776
Hyperlipidemia; n (%)	31 (50.8)	31 (50.8)	1.000
Total cholostorol*	187.5 ± 40.8	185.8 ± 34.2	0.805
HDL*	54.9 ± 15.1	54.2 ± 16.2	0.804
LDL*	105.4 ± 29.5	106.7 ± 27.0	0.793
Creatinine*	1.41 ± 1.13	1.16 ± 1.32	0.028
BVAS*	6 ± 8	NA	NA

Table 1. Clinical characteristics of patients with GPA/MPA/EGPA and control group

* Plus–minus values are means ± standard deviation

GPA – granulomatosis polyangiitis; MPA – microscopic polyangiitis; EGPA – eosinophilic granulomatosis polyangiitis; BMI – body mass index; CAD – coronary artery disease; HDL – high density lipoprotein; LDL – low density lipoprotein; BVAS – Birmingham vasculitis activity score; NA – not applicable; n - number

Variable	GPA/MPA/EGPA Patients (N = 61)	Controls (N = 61)	P-value
CAC Score*	2.18 ± 2.46	1.46 ± 1.80	0.089
Distribution of CAC Score Severity			0.104
0	24 (39.3%)	28 (45.9%)	
Mild (1-4)	19 (31.1%)	23 (37.7%)	
Moderate (5-8)	10 (16.4%)	9 (14.8%)	
Severe (9-12)	8 (13.1%)	1 (1.6%)	
CAC Prevalence	37 (60.7%)	33 (54.1%)	0.464
Adjusted CAC Prevalence[a]	72.4%	55.5%	0.199

Table 2. CAC scores and CAC prevalence in patients with GPA/MPA/EGPA and control subjects

* Plus–minus values are means ± standard deviation

CAC – coronary artery calcification; GPA – granulomatosis polyangiitis; MPA – microscopic polyangiitis; EGPA – eosinophilic granulomatosis polyangiitis

[a] – adjusted for age, sex, race, body mass index, smoking, family history of coronary artery disease, and hypertension

CAC via previously validated ordinal scoring in routine non-gated chest CT accurately predicts CCS (in Agatston units) from electrocardiogram-gated CT. Studies have demonstrated increased CCS/CAC burden in rheumatoid arthritis and systemic lupus erythematosus, but none have studied vasculitides, specifically AAVs: granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), and microscopic polyangiitis (MPA). We evaluated the cardiovascular burden in AAVs through visual assessment of CAC, compared to matched controls.

Methods: In a single tertiary care center we performed a retrospective chart review (2006-2018) of all adults with GPA, MPA, and EGPA (identified by ICD-9 and ICD-10 code) who had routine non-gated chest CT within 1 year before, or any time after diagnosis, and cholesterol profile within 5 years of diagnosis. Exclusion criteria included a history of coronary artery disease (CAD), peripheral arterial disease, or stroke. Abstracted data included: demographics, AAVs characteristics including the Birmingham vasculitis activity score (BVAS), and CAD risk factors. One thoracic radiologist blindly reviewed the chest CTs of AAVs and control patients matched by age (within 5 years), sex, race, body mass index (BMI, within 3 units), and same year of chest CT. CAC was scored ordinally: 0 = none, 1 = mild, 2 = moderate, and 3 = severe, in each of the main four coronary arteries; total scores ranged 0-12. All chest CTs were done without intravenous contrast.

Results: We identified 61 AAV patients and 61 controls (Table 1). For the AAV group: disease duration (mean ± SD) until CT scan was 37.2 ± 25.8 months, subjects were mostly white (88.5 %), and female (60.7%); BVAS was able to be calculated within 6 months of CT scan in 53 (87%) of subjects with a mean score of 6. Creatinine was significantly

Variable	Disease Duration (0-12 months)		Disease Duration (13-36 months)		Disease Duration (≥ 37 months)	
	GPA, MPA, EGPA	Controls	GPA, MPA, EGPA	Controls	GPA, MPA, EGPA	Controls
Number of subjects	27	27	14	14	20	20
CAC Score*	2.48 ± 2.58	1.52 ± 1.99	1.29 ± 1.77	1.36 ± 1.82	2.40 ± 2.66	1.45 ± 1.61
CAC Score Severity						
0	9 (33%)	13 (48%)	0 (0%)	0 (0%)	8 (40%)	8 (40%)
Mild (1-4)	9 (33%)	8 (30%)	7 (50%)	7 (50%)	6 (30%)	10 (50%)
Moderate (5-8)	5 (19%)	5 (19%)	4 (29%)	5 (36%)	2 (10%)	2 (10%)
Severe (9-12)	4 (15%)	1 (4%)	3 (21%)	2 (14%)	4 (20%)	0 (0%)
CAC Prevalence	18 (67%)	14 (52%)	7 (50%)	7 (50%)	12 (60%)	12 (60%)

Table 3. CAC score and prevalence based on GPA/MPA/EGPA disease duration and matched control group comparison.
Data was not shown to be statistically significant ($p < 0.05$) in all groups
* Plus–minus values are means ± standard deviation
GPA – granulomatosis polyangiitis; MPA – microscopic polyangiitis; EGPA – eosinophilic granulomatosis polyangiitis; CAC – coronary arterial calcium

higher in the AAV group (*P* = 0.028). The mean CAC scores (AAV: 2.18 ± 2.46; control: 1.46 ± 1.80; *P* = 0.089) and prevalence of CAC (AAV: 60.7%, control: 54.1%; *P* = 0.464) in AAVs were not significantly different compared to controls (Table 2). The prevalence of CAC in AAVs, even when adjusted for CAD risks, was not significantly different compared to controls. 34 of the AAV patients (64%) had a BVAS > 0, but the CAC score was comparable to controls (*P* = 0.26). Longer disease duration was not associated with higher CAC score or prevalence (Table 3).

Conclusion: CAC interpreted through ordinal scoring is similar in patients with GPA, MPA, or EGPA, compared to control group. Though CAC score and prevalence were higher in the vasculitis group, they did not reach statistical significance (likely due to small sample size and retrospective nature of our study). Controlled prospective studies are needed to best analyze the cardiovascular risk and utility of CAC assessment in AAV.

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Abstract Number: 1671

Hospital Admissions and Mortality in Patients with ANCA-associated Vasculitis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) has a high rate of complications, both from disease itself and treatments. Hospital mortality rates for AAV range between 10-20%. There is a lack of information regarding reasons for hospitalization and outcomes of these hospitalizations. It is important to characterize the current state of treatment and outcomes in AAV in order to improve patient care.

Methods: A retrospective chart review was performed at a large academic medical center in which all hospitalizations were reviewed in adults with a diagnosis of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) from 10/1/2015 - 12/31/2018. The electronic medical record (EMR) was queried for in-patient visits with an ICD-10 code of M30.1, M31.30, M31.31, and M31.7. The diagnosis of vasculitis was made by the treating rheumatologist or nephrologist. Patients with eosinophilic granulomatosis with polyangiitis (EGPA), without AAV or an unclear diagnosis, and absent ANCA titers were excluded. Differences in outcomes between GPA and MPA patients were measured by Fisher's exact test and t-tests.

Results: There were 127 total hospitalizations amongst 54 patients (33 GPA, 21 MPA). Forty-one hospitalizations (35 patients) were for active disease: 25 had a new vasculitis diagnosis and 16 for recurrence or flare. Patients with new disease were most commonly admitted with simultaneous lung (n=15) and renal involvement (n=16); 8 of these patients had diffuse alveolar hemorrhage (DAH). Patients with recurrent disease were most commonly admitted for respiratory disease, 6 with lower respiratory and 5 with upper airway disease (1 required emergent tracheotomy).

Of the 86 hospitalizations in patients with inactive disease (n=31 patients), infection caused almost half of admissions (41%, n=36) with pneumonia and skin/soft tissue infections being most common. There were 24 admissions for cardiovascular related causes; 9 for blood loss (most commonly GI bleed (n=6)); 4 for a deep vein thrombosis; 4 for osteoporotic fractures, and only 1 patient had a new diagnosis of cancer (urothelial carcinoma with remote history of prior Cytoxan).

There were 27 ICU admissions among 21 patients (39% of all patients) attributed to respiratory failure in 56%, renal failure in 33%, and infection in 26% of cases. More than half (56%) were for active disease and 10 of these had new disease. Mechanical ventilation and vasopressors were required in nearly half of ICU admissions.

Overall mortality was 7% for hospitalized patients and 19% for those admitted to the ICU (3 GPA, 1 MPA). All 4 hospital deaths occurred in the setting of infection. An additional 5 patients died within 28 days of discharge, for a total mortality rate of 17% (n=9).

Conclusion: Patients with GPA and MPA can have frequent hospitalizations, many that are not related to active disease. Those hospitalized with new disease were more likely to have both pulmonary and renal involvement. Although outcomes have improved considerably, mortality rates for hospitalized patients with disease remain high.

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Abstract Number: 1672

Use of Rituximab for the Treatment of ANCA-Associated Vasculitis in Canada, 2010-2018

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SESSION INFORMATION
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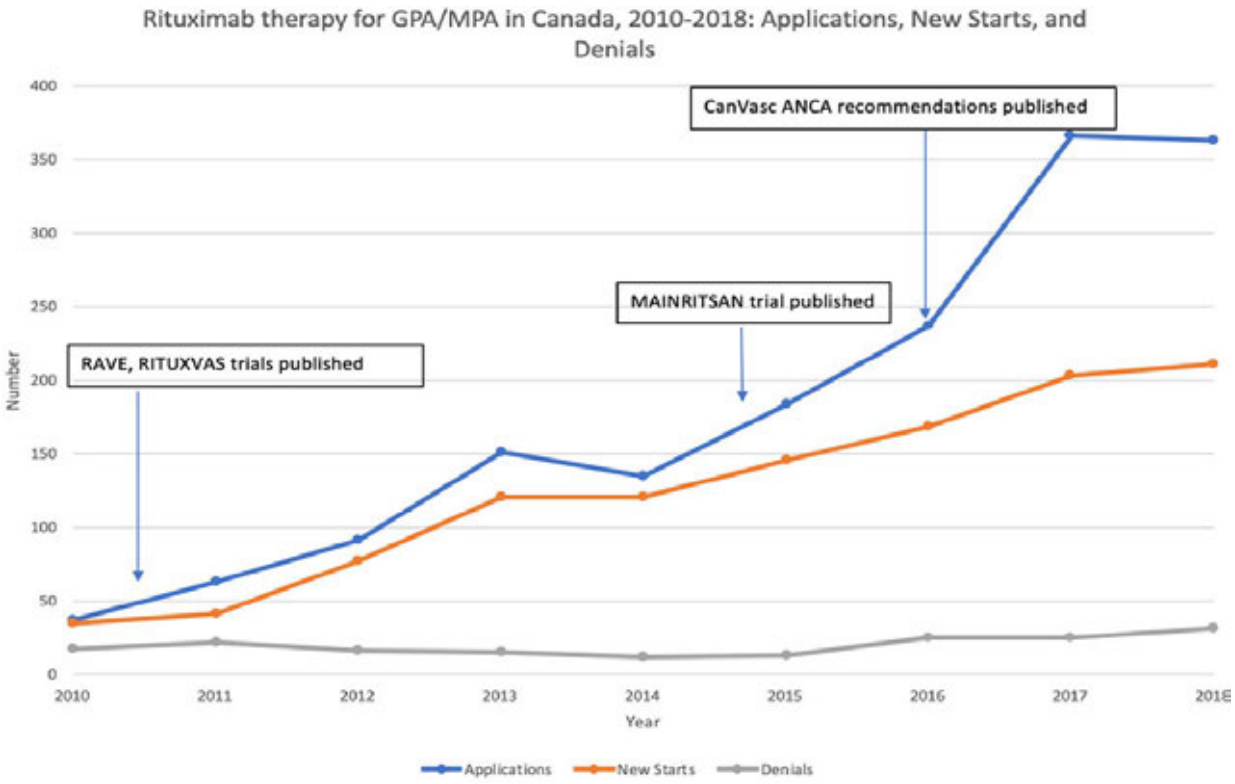
Background/Purpose: Rituximab (RTX) is an effective therapy for ANCA-Associated Vasculitis (AAV). The Canadian Vasculitis Research Network (CanVasc) recommends RTX for induction among patients with unacceptable risk of infertility or other contraindication to cyclophosphamide, and among those who have not responded or have relapsed after conventional induction therapy. RTX is also recommended for maintenance, where available. Our objectives were to (1) describe real-world use of RTX in AAV since the publication of the Rituximab in ANCA-associated vasculitis (RAVE) trial in 2010, and (2) compare current RTX use for AAV across regions, sexes, and age groups.

Methods: Anonymized, aggregate-level data on RTX use in AAV (Granulomatosis with Polyangiitis and Microscopic Polyangiitis) from January 2010-December 2018 were obtained from the national pharmaceutical-funded patient support program database, covering approximately 85% of RTX prescriptions for vasculitis in Canada and exclud-



RTX in Canada 2010-2018
Rituximab use in Canada, 2010-2018

ing inpatient infusions. RTX use was compared across sexes, age groups, geographic regions, and coverage type (private, public, or combination). The number of unique applications and denials (all funding sources), and new drug starts were assessed over time. Data on RTX indication (induction, relapse, or maintenance) were not available.

Results: From 2010, 1124 patients started RTX therapy for AAV (including new diagnosis, relapsing disease, or maintenance). New RTX starts increased 6-fold, from 35 in 2010 to 211 in 2018, while the number of application denials (from public and/or private funders) remained relatively stable (from 18 in 2010 to 32 in 2018). Applications for treatment of AAV represented only 11% of the total RTX applications for other disease indications. Among current RTX users (n=556), 306 (55%) patients were female and 115 (21%) were of reproductive age (18-39 years). Patients received public coverage more often in Quebec (51% [95% CI, 42-60]) and Western provinces (46% [38-53]) compared to Ontario/Atlantic provinces (26%[22-32]).

Conclusion: The use of RTX for AAV in Canada has increased substantially since clinical trials established its efficacy. Between provinces, there are significant differences in the proportion of patients covered publicly, although this could reflect practice variations in the use of RTX for maintenance (not currently covered publicly). Only 21 % of RTX users were in the reproductive age group, suggesting that RTX is used broadly for AAV treatment and is not being limited to those with fertility concerns.

Disclosure: A. Mendel, None; **S. Carette**, None; **C. Pagnoux**, ChemoCentryx, 5, Chemocentryx, 5, Genetech/Roche, 5, Genzyme/Sanofi, 5, GlaxoSmithKline, 5, Hoffman-La Roche, 2, 5, 8, Hoffman-LaRoche, 2, 5, 8, Sanofi, 5.

Abstract Number: 1673

Factors Associated with Overall and First-Year Mortality in Turkish Patients with ANCA-Associated Vasculitides: *Retrospective, Multicentre Trial*

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Overall mortality in ANCA-associated vasculitides (AAVs) over the last two decades has been reported to be decreasing with the use of immunosuppressive therapies. However, despite treatment, mortality rates remain high, particularly in the first year after diagnosis. In this study, we aimed to determine the prevalence of mortality in AAV patients and to investigate the factors that may be associated with first-year and overall mortality.

	GPA (n=137)	MPA (n=40)	EGPA (n=25)	RLV (n=30)	AAV (n=232)
Sex, male (n) (%)	77 (56)	21 (53)	10 (40)	15 (50)	123 (53)
Age at diagnosis, mean (SD) (years)	49.22 ∓ 15.62	59.53 ∓ 13.18	46.67 ∓ 14.99	54.13 ∓ 16.46	51.4 ∓ 15.75
ANCA					
Positive n (%)	116 (92)	27 (68)	11 (46)	26 (87)	180 (82)
Negative n (%)	10 (8)	13 (33)	13 (54)	4 (13)	40 (18)
ANCA subtype					
p/MPO-ANCA n (%)	24 (21)	23 (85)	8 (73)	20 (77)	75 (42)
c/PR3-ANCA n (%)	92 (79)	4 (15)	3 (27)	6 (23)	105 (58)
Organ/system involvements (n) (%)					
Kidney	90 (67)	39 (98)	8 (32)	30 (100)	167 (73)
Lung	98 (74)	31 (78)	18 (72)	0 (0)	147 (65)
ENT (ear-nose-throat)	102 (77)	2 (5)	16 (70)	0 (0)	120 (53)
Eye	27 (21)	1 (3)	1 (4)	0 (0)	29 (13)
Cardiac	4 (3)	3 (8)	4 (16)	0 (0)	11 (5)
GI	9 (7)	5 (13)	0 (0)	0 (0)	14 (6)
CNS	9 (7)	0 (0)	2 (8)	0 (0)	11 (5)
MNM	9 (7)	3 (8)	8 (32)	0 (0)	20 (9)
FFS (n=202); (n) (%)					
0	41 (37)	3 (8)	18 (72)	1 (4)	63 (31)
1	32 (29)	2 (5)	6 (24)	2 (7)	42 (21)
2	27 (24)	24 (63)	1 (4)	18 (67)	70 (35)
3	12 (11)	7 (18)	0 (0)	6 (22)	25 (12)
4	0 (0)	2 (5)	0 (0)	0 (0)	2 (1)
Maximum Creatinine level at diagnosis (mg/dl) (median, IQR)	1.75 (5.29)	4.64 (4.82)	0.80 (0.37)	4.66 (4.17)	2.51 (5.18)
ESRD development (n) (%)	27 (21)	8 (20)	0 (0)	17 (61)	52 (24)
Hemodialysis at diagnosis (n) (%)	31 (25)	22 (55)	0 (0)	19 (68)	72 (33)
Plasmapheresis at diagnosis (n) (%)	22 (18)	20 (50)	2 (8)	13 (48)	57 (26)
BVAS at diagnosis, mean (SD) (n=102)	18.56 ∓ 9.40	16.60 ∓ 9.07	14.23 ∓ 8.12	11 ∓ 2.64	16.91 ∓ 9.02
Overall Mortality (n) (%)	21 (16)	13 (33)	0 (0)	10 (33)	44 (19)
First-year mortality (n) (%)	11 (9)	8 (21)	0 (0)	3 (10)	22 (10)
Follow-up duration (months), median (min-max)	48.52 (1-244)	26.68 (0-106)	29.35 (3-226)	34.67 (2-155)	40.0 (0-244)

*ANCA: Anti-Neutrophil Cytoplasmic Antibody; AAV: ANCA-Associated Vasculitis; GPA: Granulomatosis with PolyAngiitis; MPA: Microscopic PolyAngiitis; EGPA: Eosinophilic Granulomatosis with PolyAngiitis; RLV: Renal Limited Vasculitis; MPO: Myeloperoxidase; PR3: Proteinase3; c-ANCA: Cytoplasmic-ANCA; p-ANCA: Perinuclear-ANCA; GI: Gastrointestinal; CNS: Central Nervous System; MNM: MonoNeuritis Multiplex; FFS: Five Factor Score; IQR: InterQuantile Range ; ESRD: End-Stage Renal Disease; BVAS: Birmingham Vasculitis Activity Score; SD: Standard Deviation

Table 1. Demographic and clinical characteristics of ANCA-associated vasculitis patients

Methods: AAV patients who were categorized according to the 2012 Chapel Hill consensus nomenclature, were included in this study from two university centers. Diagnostic subgroups were; granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA) and renal-limited vasculitis (RLV). Patients with only clinical renal involvement and diagnosed by renal biopsy were classified as RLV. The clinical and demographic characteristics of the patients were collected retrospectively. Factors predictive of mortality were evaluated by Kaplan-Meier method and the Cox proportional hazard model.

	Univariate analysis results for overall mortality			Univariate analysis results for first-year mortality		
	B	CI 95 %	p	B	CI 95%	p
Age at diagnosis[1]	1.07	1.04-1.10	<0.001	1.064	1.02-1.10	<0.001
ANCA subtype (p/MPO vs c/PR3)	1.96	1.01-3.81	0.046	0.98	0.39-2.44	0.97
AAV subgroups			0.008			0.197
GPA vs MPA	0.30	0.15-0.63	0.001	0.37	0.14-0.91	0.032
EGPA vs MPA	0	NA	0.96	0	NA	0.97
RLV vs MPA	0.74	0.32-1.72	0.49	0.46	0.12-1.75	0.25
Renal involvement, present vs none	16.30	2.24-118.43	0.006	7.90	1.06-58.76	0.043
Maximum Creatinine level at diagnosis[2]	1.10	1.04-1.16	<0.001	1.09	1.01-1.16	0.012
GFR at diagnosis[3]	0.96	0.94-0.98	<0.001	0.96	0.94-0.99	0.006
Proteinuria at diagnosis (≥500 mg/day vs <500 mg/day)	18.32	2.51-133.37	0.004	9.21	1.24-68.50	0.030
Microscopic hematuria at diagnosis (Present vs None)	7.79	2.38-25.46	0.001	3.74	1.10-12.66	0.034
ENT involvement, (Present vs None)	0.47	0.25-0.89	0.022	0.71	0.30-1.64	0.42
Cardiac involvement, (Present vs None)	3.50	1.36-8.99	0.009	5.16	1.72-15.44	0.003
FFS[4]	3.52	2.28-5.44	<0.001	2.95	1.79-4.86	<0.001
BVAS, at diagnosis[5]	1.17	1.06-1.29	0.001	1.19	1.04-1.36	0.008
ESRD development, (Present vs None)	4.06	1.96-8.41	<0.001	1.19	0.37-3.79	0.76
Plasmapheresis at diagnosis, (Present vs None)	2.22	1.15-4.31	0.017	1.96	0.83-4.59	0.12
Hemodialysis at diagnosis, (Present vs None)	5.26	2.65-10.43	<0.001	4.52	1.84-11.10	0.001

*ANCA: Anti-Neutrophil Cytoplasmic Antibody; AAV: ANCA-Associated Vasculitis; GPA: Granulomatosis with PolyAngiitis; MPA: Microscopic PolyAngiitis; EGPA: Eosinophilic Granulomatosis with PolyAngiitis; RLV: Renal Limited Vasculitis; MPO: Myeloperoxidase; PR3: Proteinase3; c-ANCA: Cytoplasmic-ANCA; p-ANCA: Perinuclear-ANCA; ENT: Ear-Nose-Throat; GFR: Glomerular Filtration Rate; ESRD: End-Stage Renal Disease; BVAS: Birmingham Vasculitis Activity Score; FFS: Five Factor Score; CI: Confidence Interval

** [1] One year increase in age; [2] 1 mg/dl increase in creatinine; [3] 1 ml/min/1.73m^2 increase in GFR; [4] One point increase in FFS; [5] One point increase in BVAS

Table 2. The results of Kaplan-Meier survival analysis: Factors associated with overall and first-year mortality

Results: In total 232 (123 [53%] male and mean age at diagnosis51.4±15.75 years) AAV patients (137 [59%] GPA; 40 [17%] MPA; 30 [13%] RLV and 25 [11%] EGPA) were included in the analysis. ANCA positivity was detected in 82%

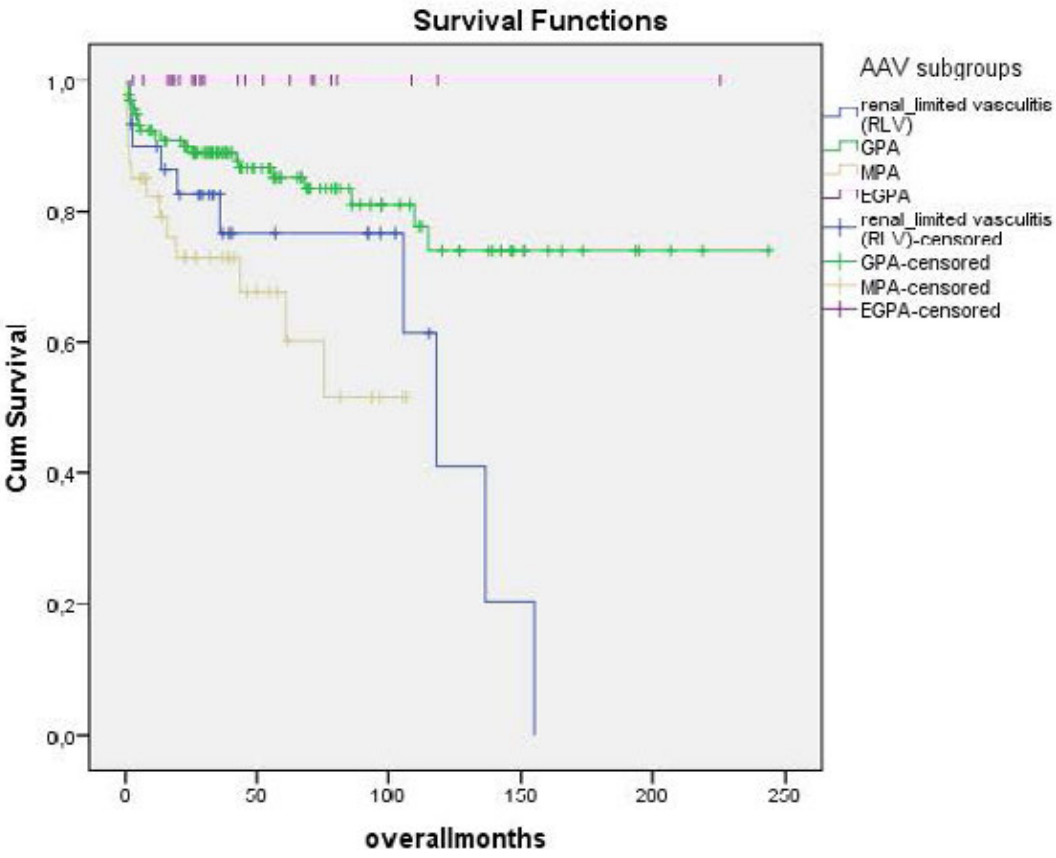

Figure. The results of the Kaplan-Meier analysis: Overall mortality was significantly different in ANCA-associated vasculitis subgroups

(180/220) patients with IIF and/or ELISA. 167 patients (73%) had renal involvement and among them, one in third patients (52/167) had developed end-stage renal disease (ESRD). Other clinical features are shown in table 1. Overall 44 patients (19%) died during a median 40 months (0-244) of follow-up. First-year and five-year mortality rates were 10% and 30% respectively. Overall mortality was significantly different in AAV subgroups ($p< 0.001$, Figure). Factors associated with overall and first-year mortalities that were detected with univariate analysis, including disease activity scores (Five Factor Score [FFS] and Birmingham Vasculitis Activity Score [BVAS]), are summarized in table 2. In the multivariate analysis age at diagnosis (Hazard ratio [HR] 1.05, 95 % Confidence interval [CI] 1.01-1.08, p=0.002) and cardiac involvement (HR 6.79, 95 % CI 1.97-23.32, p=0.002) were found to be the independent predictive factors of overall mortality. The same factors were also predictors of the first-year mortality (Age at diagnosis [HR 1.06, 95 % CI 1.02-1.10, p=0.001] and cardiac involvement [HR 5.45, 95 % CI 1.81-16.40, p=0.003]).

Conclusion: Our findings suggest that there could be some survival differences between AAV subgroups and, disease activity scores (both FFS and BVAS at diagnosis) are helpful to predict mortality. However, the age at diagnosis and cardiac involvement seems to be the only significant predictors of first-year and overall mortality in AAV patients.

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Abstract Number: 1674

Survival in ANCA-Associated Vasculitis in a Latin-American Center: 28 Years of Experience

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – ANCA-Associated Poster II

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To identify demographic and clinical risk factors for mortality in patients with ANCA-associated vasculitis (AAV) who were followed-up in a Latin-American Tertiary Referral Hospital.

Methods: Medical records of patients with AAV according to the 1990 ACR criteria, Chapel Hill 2012 consensus, EMEA criteria, or diagnosed by an experienced rheumatologist, and covering the period between January 1990 and December 2018, were reviewed. Granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) were included. Renal limited vasculitis (RLV) was considered separate from MPA. Features analyzed as potential predictors of mortality were demographic factors (age at diagnosis, gender), disease duration, clinical manifestations (per organ involvement), creatinine level at diagnosis (mg/dl), ANCA status [by method (ELISA or IIF)], diagnosis, and EULAR disease categorization (limited, early systemic, generalized

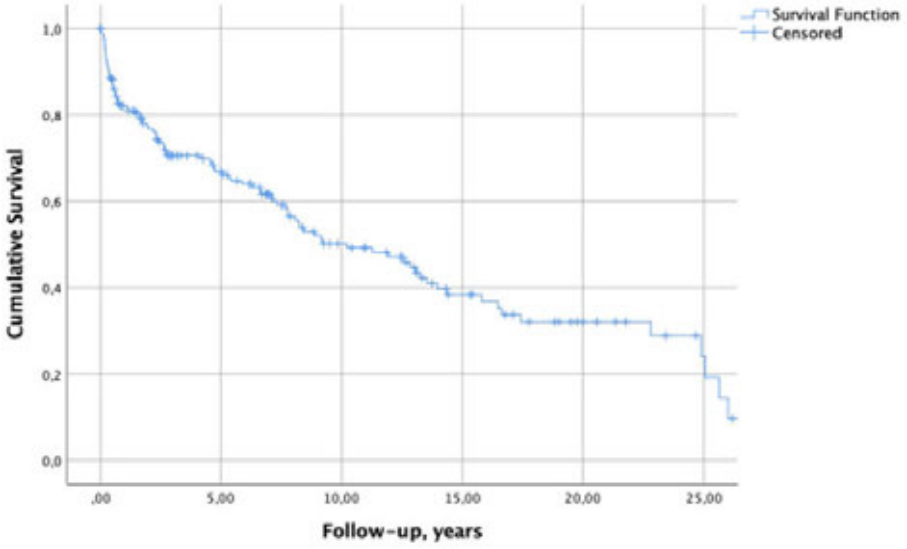

Figure 1. Kaplan-Meier survival analysis.

Variable	Univariable HR (95% CI)	p value	Multivariable HR (95% CI)	p value
Age at diagnosis (years)	1.02 (1.01-1.04)	0.010	1.02 (1.00-1.04)	0.031
Gender				
Male	Ref.			
Female	0.72 (0.48-1.09)	0.117		
Manifestations (per organ involvement)				
Renal	2.19 (1.42-3.40)	<0.001	2.24 (1.42-3.52)	0.001
Cutaneous	1.09 (0.72-1.65)	0.684		
Ocular	0.42 (0.21-0.87)	0.020	0.39 (0.19-0.81)	0.012
ENT	0.32 (0.13-0.79)	0.013		
Lung	1.75 (1.13-2.70)	0.011	1.60 (1.02-2.48)	0.039
Cardiovascular	0.83 (0.20-3.38)	0.789		
Neurologic	0.90 (0.57-1.42)	0.650		
Gastrointestinal	0.74 (0.27-2.01)	0.550		
Diagnosis				
RLV	Ref.			
GPA	0.58 (0.09-3.60)	0.561		
MPA	1.06 (0.26-4.36)	0.936		
EGPA	0.56 (0.12-2.64)	0.462		
ANCA-IIF				
Negative	Ref.			
Cytoplasmic	1.07 (0.60-1.93)	0.813		
Perinuclear	0.78 (0.37-1.66)	0.521		
ANCA-ELISA				
Negative	Ref.			
PR3	1.21 (0.68-2.14)	0.514		
MPO	0.93 (0.42-2.06)	0.864		
EULAR categorization				
Severe renal	Ref.			
Generalized	0.13 (0.02-1.01)	0.051		
Early systemic	0.33 (0.18-0.60)	<0.001		
Limited	0.55 (0.32-0.96)	0.035		

AAV: ANCA-associated vasculitis. ENT: Ear, nose and throat. GPA: Granulomatosis with polyangiitis. MPA: Microscopic polyangiitis. EGPA: Eosinophilic granulomatosis with polyangiitis RLV: Renal limited vasculitis.

Table 1. Variables predictive of mortality in AAV. Univariable and multivariable analysis

and severe renal). Categorical variables were summarized as frequencies and percentages while continuous variables were presented as medians and their interquartile ranges (IQR). Cox regression models were used to determine the risk factors for mortality. Univariable and multivariable analyses using a backward selection method with α-level to stay in the model set at 0.05 were performed. Statistical analyses were performed using SPSS v26.0.

Results: One hundred eighty-nine patients were included with a female/male ratio of 2:1 [127 (67.2%)/62 (32.8%)]. Their median (IQR) age at diagnosis and disease duration were 60.0 (51.5-68.5) and 4.7 (1.0-11.1) years, respectively. One hundred forty-six (77.2%) patients had MPA, 32 (16.9%) GPA, 5 (2.6%) EGPA and 6 (3.2%) RLV. One hundred seventy-eight patients had ANCA-IIF results [p-ANCA: 119 (66.9%), c-ANCA: 38 (21.3%), negative-ANCA: 21 (11.8%)] and 172 patients had ANCA-ELISA results [MPO: 117 (68.0%), PR3: 31 (18.0%), negative-ANCA: 24 (14.0%)]. According to EULAR categorization, 5 (2.6%) were limited, 67 (35.5%) were early systemic, 88 (46.6%) were generalized and 29 (15.3%) were severe renal. The last two categories had a median (IQR) creatinine level of 1.4 (0.9-2.7) and 8.0 (6.7-10.1). Until April 2019, 96 (50.8%) patients had died. The corresponding Kaplan-Meier survival curve is depicted in Figure 1; five-year survival was 66.9%, ten-year survival was 50.1% and twenty-year survival was 32.0%. Ocular involvement was protective [HR 0.39 (CI95% 0.19-0.81), p=0.012] while renal involvement [HR 2.24 (CI 95% 1.42-3.52), p=0.001], lung involvement [HR 1.60 (CI95% 1.02-2.48), p=0.039] and age at diagnosis [HR 1.02 (CI95% 1.00-1.04), p=0.031] were predictive factors of mortality (Table 1).

Conclusion: Ocular involvement was protective while age at diagnosis and renal and lung involvements were predictive factors of mortality in Latin-American AAV patients. At ten years of follow-up, the survival rate was 50%.

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Abstract Number: 1675

A Retrospective Cohort Study Using Clinical Notes and Latent Topic Modeling to Characterize the Natural History of ANCA-Associated Vasculitis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) is associated with end-organ damage, complications of treatment, and excess death. Retrospective studies on the clinical course of AAV, including the evolution of clinical manifestations, comorbidities, and complications before and after the diagnosis are limited to analyses of claims data and case series relying on chart review or coded fields in electronic health records. No study has used automated methods to evaluate the clinical notes documented in the patients' EHR as a data source to characterize AAV's natural history.

Characteristic[a]	Study cohort N=660 (%)
Age, mean (SD), years[b]	56.9 (18.1)
Sex, Female (n, %)	392 (59.4)
Race	
White	559 (84.7)
Black	18 (2.7)
Others	21 (3.2)
Unknown	62 (9.4)
Ethnicity	
Non-Hispanic	598 (90.6)
Hispanic	33 (5.0)
Unknown	29 (4.4)
Baseline BVAS/WG Score, mean (SD)	4.4 (2.2)
ANCA Type	
PR3-ANCA+	268 (41%)
MPO-ANCA+	392 (59%)
Renal Involvement	
Any Renal Disease	411 (63%)
End-Stage Renal Disease Ever	105 (16%)
Duration of follow-up in the PHS system, mean (SD), months[c]	124.3 (80.1)
Prior to the initial treatment	59.1 (68.7)
After the initial treatment	90.6 (64.7)
No. of clinical notes, n (%)	
Prior to the initial treatment	10,877 (15.4)
After the initial treatment	59,642 (84.6)

[a] Summary of the characteristics of patient demographics information and note events.
[b] Age was calculated at the time of diagnosis.
Abbreviations: BVAS/WG, Birmingham Vasculitis Activity Score/Wegener's Granulomatosis; PR3-, Proteinase-3; MPO, Myeloperoxidase

Table. Characteristics of the Study Cohort

Methods: The Partners AAV (PAAV) cohort is a consecutive inception cohort established at Partners HealthCare System (PHS), a large hospital system in New England, that has been previously described. All cases are PR3- or MPO-ANCA+. The clinical notes of this study cohort were obtained from PHS Research Patient Data Registry between the inception of the database and 08/23/2018. We then conducted automatic topic modeling to capture the trends of various themes mentioned in care provider notes three years prior to and five years after the initiation of AAV treatment. Each topic was manually labeled independently by two vasculitis experts; differences were resolved through consensus.

Results: This cohort analysis included 660 patients with AAV, with mean (SD) age of 56.9 (18.1) years and 392 (59.4%) female (**Table 1**). We generated 89 stable topics from a total of 70,519 notes. We studied the progression of the disease using topics that included AAV and treatment, cutaneous symptoms, psychiatric disorders, joint symptoms, and topics related to AAV complications of the kidneys and lungs like end-stage renal disease, renal transplantation, and bronchiectasis. Examples of topics are shown in **Table 2**. The temporal trends of selected topics are shown in **Figure 1**. Generally, AAV follows a prolonged clinical course with treatment mentioned for years following initiation (**Figure 1a**). Joint issues, skin lesions, and foot ulcers were frequently mentioned in the years preceding AAV, while these conditions appeared to be less commonly discussed following diagnosis and treatment of AAV (**Figure 1c**). Symptoms, including anxiety and stress, were often mentioned in the year prior to the disease diagnosis but then become less frequent (**Figure 1d**). Topics related to pulmonary and renal disease were common during the disease course but followed distinct patterns (**Figures 1e and 1f**). While pulmonary symptoms were common before and after diagnosis, renal disease (e.g., glomerulonephritis) was particularly common at the time of and following diagnosis.

Conclusion: Using the clinical notes of a large AAV cohort, we identified several topics relevant to the diagnosis, treatment, comorbidities, and complications of AAV. The patterns and trends of these topics support the notion that diagnostic delay is common and that some symptoms (e.g., cutaneous) may respond better to treatment than others

Groups	Topic Labels	Top 15 Probable Words
AAV	AAV	anca vasculitis rituximab renal skin prednisone ckd rituxan azathioprine wegener chest steroid chronic clear disease
	Wegener's Granulomatosis	anca wegener prednisone azathioprine rituxan clear granulomatosis normal month hypertension stable skin chest past allergy
	Churg-Strauss Syndrome	churg strauss stenosis asthma anca rituximab recurrent wegener cough syndrome steroid dose cell sputum treat
AAV Treatment	AAV Treatment	tablet anca rituximab prednisone cyclophosphamide steroid vasculitis positive skin chest start normal clear improve month
	Rheumatology Treatment	prednisone anca rheumatology gpa foot symptom rash swell joint vasculitis deny loss rituximab lab chest
	Arthritis Treatment	prednisone swell wegener hand normal joint knee methotrexate esr anca month negative crp vasculitis
Joint Issues, Skin Lesion, and Foot Ulcer	Skin Lesion	skin lesion area left rash cream dermatology scalp review include face exam apply cell discuss
	Foot Ulcer	grant foot mcg lesion pyoderma premphase dpm refer left toe start gangrenosum ultram normal Ditropan
	Joint Issues	left knee hip shoulder joint fracture spine ankle hand foot physical lumbar swell motion mild
Psychiatric disorders and Assessment	Psychiatric	disorder anxiety problem mood depression report support feel axis assessment cocaine current deny think treatment
	Neurology Evaluation	left normal head intact neurology weakness stroke headache brain nerve seizure exam hand sensation gait
Pulmonary Involvement in AAV	Bronchiectasis*	bronchiectasis culture hemoptysis specimen sputum walter chest neg neb negative lobe pneumonia pulmonary stable result
	Bronchiectasis*	bronchiectasis neg pseudomonas sputum flare oral nasal mucoid chest neb hyperlipidemia inhaler disease sen stable smear
	Pulmonary Findings	chest left lobe lung nodule upper lower find pleural pulmonary small effusion impression opacity pneumonia
	Pulmonary Symptoms	pulmonary lung cough disease chest prednisone anca oxygen dyspnea fev interstitial fvc mild ild increase
	Pulmonary Disease	arnold lung pulmonary derrick mcg vasculitis left chronic rituximab fax microscopic polyangiitis phone mmhg hemorrhage
Kidney Involvement in AAV	Glomerulonephritis*	renal negative anca urine positive antibody anti igg vasculitis result cell normal protein disease hematuria
	Glomerulonephritis*	renal anca vasculitis prednisone cytoxan anemia disease steroid failure creatinine cyclophosphamide admission dose start rpgn
	End Stage Renal Disease	renal esrd fistula transplant left disease folic acid buhle unit catheter nephrocaps access stage hemodialysis
	Renal Transplant	transplant renal tacrolimus prograf donor post cellcept mycophenolate disease bid immunosuppression cmv negative risk rejection
	Pulmonary-Renal Syndrome	renal pulmonary bruce left dvt anca urine positive lupus curtis ckd age seizure lasix mcdonough

* Topics with same labels were merged for trend analysis

Abbreviations: AAV: antineutrophil cytoplasm antibody-associated vasculitides; anca: antineutrophil cytoplasm antibody; mcg: microgram, gpa: granulomatosis with polyangiitis, esr: erythrocyte sedimentation rate, crp: C-reactive protein, neb: nebulizer, fvc: forced vital capacity, fev: forced expiratory volume, mmhg: millimeters mercury, igg: Immunoglobulin-G, rpgn: rapidly progressive glomerulonephritis, esrd: end stage renal disease, cmv: cytelomegalovirus, dvt: deep vein thrombosis, ckd: chronic kidney disease

Table Examples of Stable Topics, Labels, and Analysis Groups

(e.g., pulmonary). This method can therefore provide unique insights regarding signs and symptoms that are often not documented in EHR structured data fields. Future studies might evaluate the role of automated topic modeling in identifying possible AAV cases prospectively.

Disclosure: L. Wang, None; **E. Miloslavsky**, None; **J. Stone**, Genentech, 2, 5, Roche, 2, 5, Xencor, 2, 5; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5; **L. Zhou**, None; **Z. Wallace**, National Institute of Arthritis, Musculoskeletal, and Skin Diseases, 2, Rheumatology Research Foundation, 2.

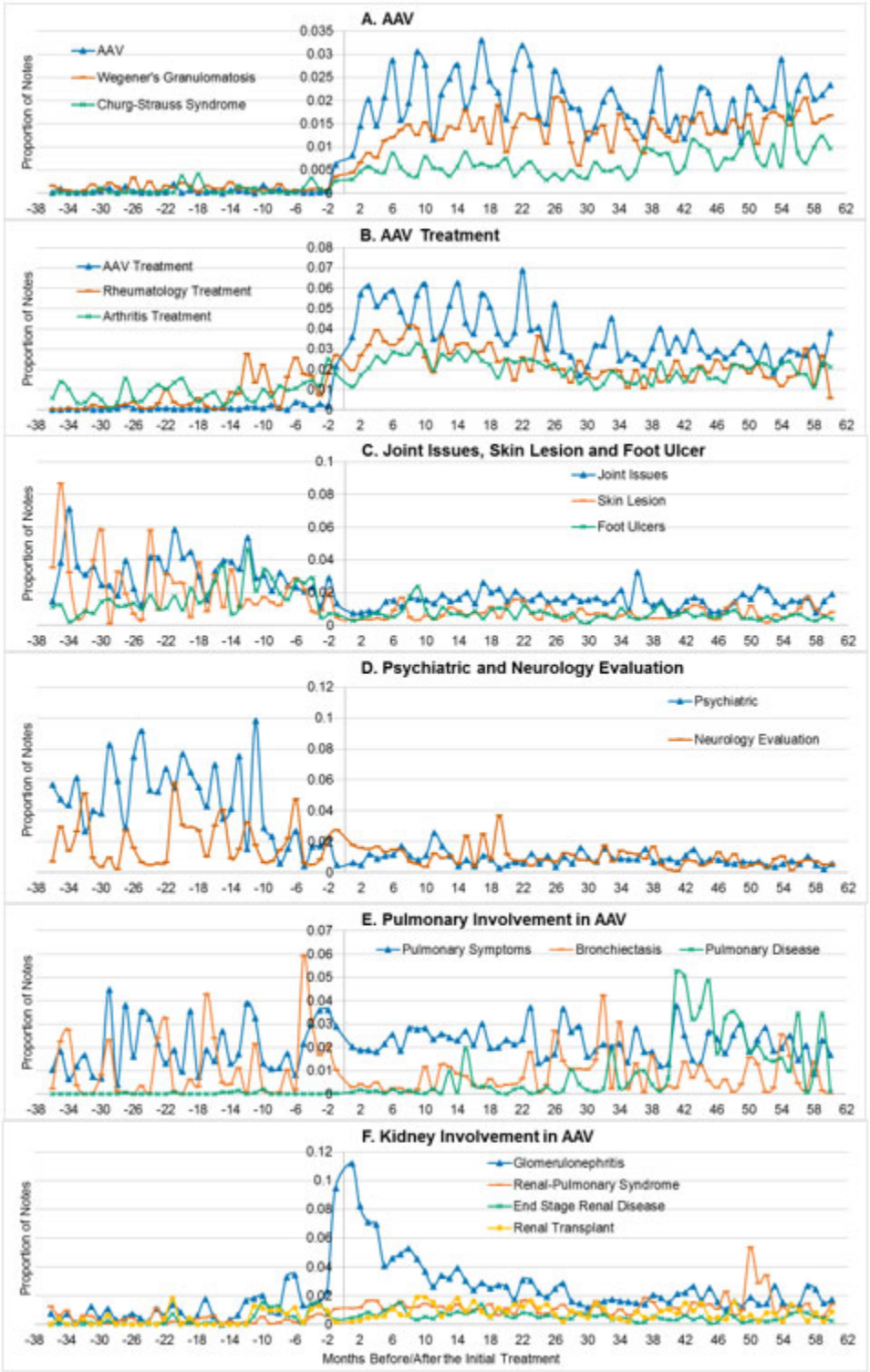

Figure. Trend analysis of different groups of topics 3-year prior to and 5-year after the initial treatment, including: A. AAV, B. AAV treatment, C. joint issues, skin lesion and foot ulcer, D. psychiatric and neurology evaluation, E. pulmonary involvement in AAV, F. kidney involvement in AAV.

Abstract Number: 1676

Does Pneumocystis Jiroveci Pneumonia (PJP) Prophylaxis Prevent Hospitalizations for Other Infections in Vasculitis Patients?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – ANCA-Associated Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatic diseases are often at risk for opportunistic infections given the combination of disease manifestations and immunosuppressive treatment regimens, but the rates of *Pneumocystis jiroveci* pneumonia (PJP) are fairly low in this population. Prophylaxis against *Pneumocystis jiroveci* is often recommend for immunosuppressed transplant, leukemia and HIV patients, but there are no guidelines for patients with rheumatic diseases. The purpose of this study is to review the number of PJP cases at our institution in vasculitis patients and compare the rates of hospitalizations for other infections for patients receiving PJP prophylaxis to those who are not.

Methods: Using Epic's Slicer Dicer tool, we selected microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) patients over the past ten years who received care at our institution. Patients under 18 years-old, and patients without documented MPA or GPA were excluded. We then reviewed the electronic charts for these patients and recorded demographic information, PJP prophylaxis, hospitalizations at our institution for infections, disease and

MPA		PJP Prophylaxis (n=10)	No PJP Prophylaxis (n=13)
	Age (Average)	62 years old	58 years old
	Sex		
	Female	7 (70%)	8 (62%)
	Male	3 (30%)	5 (38%)
	Cases of PCP	0	0
	Infection requiring hospitalization	5 (50%)	2 (15%)
	Lung involvement	7 (70%)	5 (38%)
GPA		PJP Prophylaxis (n=55)	No PJP Prophylaxis (n=76)
	Age (Average)	55 years old	61 years old
	Sex		
	Female	27 (49%)	43 (57%)
	Male	28 (51%)	33 (43%)
	Cases of PJP	1	0
	Infection requiring hospitalization	5 (9%)	5 (7%)

Figure 1 compares MPA and GPA patients with and without Pneumocystis jiroveci pneumonia (PJP) prophylaxis. Only one case of PJP was found in the GPA group with prophylaxis. The p-value for GPA patients for infection hospitalizations between prophylaxis and non-prophylaxis groups was 0.7415. For MPA patients, the p-value was 0.1688.

treatment information. Fisher's exact test was used to compare rates of hospitalizations for infections for the PJP prophylaxis group vs. the non-prophylaxis group for MPA and GPA.

Results: Initially, 287 charts were reviewed and 154 met our inclusion criteria. Of all MPA and GPA charts reviewed, there was only one reported case of PJP listed in the past medical history of a GPA patient's chart happened to be on PJP prophylaxis. This case was complicated by a history of renal transplant and it was unclear when PJP was contracted in relation to PJP prophylaxis timing. The PJP prophylaxis group for MPA and GPA together had more cases of hospitalizations due to infections. The majority of these infections were viral (influenza, CMV) and skin-related (abscesses and cellulitis). The p-value for GPA patients for infection hospitalizations between prophylaxis and non-prophylaxis groups was 0.7415 and was 0.1688 for MPA patients, neither of which were statistically significant.

Conclusion: The rate of PJP in our vasculitis population is low, as suggested by prior literature. Our results do not indicate that PJP prophylaxis decreases hospitalizations for infections in MPA or GPA patients, although our results likely underestimate the number of hospitalizations, since we were unable to include hospitalizations at other institutions. The next steps of this study will be to evaluate other diseases including EGPA, PM/DM, SLE, CTD-ILD for rates of PJP and hospitalizations for other infections.

Disclosure: V. Patel, None; **K. Trotter**, None.

Abstract Number: 1677

Management of Severe Renal Disease in Anti-Neutrophil-Cytoplasmic-Antibodies Associated Vasculitis: Role of Rituximab and Plasma Exchange?

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SESSION INFORMATION

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Background/Purpose: Induction therapy for severe ANCA-associated vasculitides (AAVs) is based on the combination of glucocorticoids and cyclophosphamide (CYC) or rituximab (RTX). For patients with severe acute renal impairment, use of RTX alone has not been evaluated in randomized–controlled trials and CYC is usually given in this situation. The additional benefit of plasma exchanges (PEs) is controversial. We compared the efficacies of glucocorticoid and RTX or CYC induction therapy for severe renal AAV flares and evaluated the potential benefit of PE adjunction to manage those flares.

Methods: This retrospective, multicenter study included patients with severe renal flares of granulomatosis with polyangiitis, microscopic polyangiitis or pauci-immune renal-limited vasculitis. The severity of renal impairment was defined as serum creatinine ≥350 μmol/L and/or an estimated glomerular filtration rate ≤15 mL/min/1.73 m^2. The primary endpoint was AAV remission at month (M) 3 and M6, and being dialysis-free at M3, M6 and M12. A propensity score and a double robust adjustment were used to compare groups.

Results: Between 2005 and 2017, 173 AAV renal flares occurred in the 161 patients included: 65 (40%) women and 96 (60%) men; mean (±SD) age at the time of the flare was 63 ± 13.1 years. Twenty-nine (17%) flares were treated with RTX and 144 (83%) with CYC. Remission rates did not differ between RTX- and CYC-treated groups, respectively, at M3 (93% vs 94%) and M6 (100% vs 92%). Although more RTX- than CYC-treated patients were dialysis-free at M12 (respectively: 91% vs 69%; odds ratio (OR) 4.59 [95% CI 1.02–20.6]), the difference was not significant after adjustment. At M12, 10 patients—all treated with CYC—had died.Because of too few RTX-treated flares, PE efficacy was evaluated only for CYC-treated patients. Among 144 CYC-treated flares, 81 (56%) also had PEs. M3 and M6 remission rates were comparable for the weighted CYC groups treated with or without PEs, respectively, at M3 (94% vs 95%) and M6 (92% vs 91%).The dialysis-free survival rates were significantly higher for CYC- and PE-treated patients vs no PE, respectively, in weighted groups (74% vs 65%; OR 2.91 [95% CI 1.11–7.62] at M6 and 73.2% vs 62.3%; OR 3.05 [95% CI 1.13–8.21] at M12). Significance was confirmed after double robust adjustment at M6 (OR 6.91 [95% CI 1.24–38.6]) but not at M12 (OR 5.37 [95% CI 0.90–32.1]).

Conclusion: According to the results of this retrospective study, RTX was apparently equivalent to CYC as induction therapy for patients with severe AAV renal flares. PE adjunction to CYC was associated with higher dialysis-free rates at M6. Despite the use of a propensity score, we were not able to overcome all the biases and these results need to be confirmed by prospective controlled trials. Subgroup analyses may be required to better identify the place of each treatment for AAV patients with severe renal involvement.

Disclosure: P. Morel, None; **A. Karras**, Roche, 8; **R. Porcher**, None; **X. Belenfant**, None; **V. Audard**, None; **C. Rafat**, None; **G. Hanouna**, None; **S. Beaudreuil**, None; **C. Vilain**, None; **A. Hummel**, None; **B. Terrier**, Grifols, 8, GSK, 8, LFB, 8, Roche, 8; **E. Pillebout**, None; **M. Groh**, None; **R. Jouenne**, None; **R. Dhote**, None; **O. Fain**, None; **M. Ponsoye**, None; **N. Noel**, None; **N. Limal**, None; **L. Guillevin**, None; **L. Mouthon**, None; **A. Régent**, None.

Abstract Number: 1678

Interstitial Lung Disease in ANCA Associated Vasculitis: A Single Center Retrospective Analysis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: ANCA associated vasculitis patients have a wide spectrum of pulmonary involvement in the form nodular disease (especially peri-bronchial nodules), cavitating lesions, diffuse alveolar hemorrhage and less commonly interstitial lung disease (ILD) either usual interstitial pneumonitis (UIP) or nonspecific interstitial pneumonia

Characteristic	Subcategory of AAV with ILD manifestations	GPA (N=1)	EGPA (N=2)	MPA (N=4)
Demographic characteristics	M:F ratio	0:1	2:0	1:3
	Mean BMI	36.1	29.8	23.4
	Mean age at diagnosis of ILD	26	59	57.5
	Hispanic or Latino ethnicity	1 (100%)	1 (50%)	1 (25%)
	White/Caucasian ethnicity	0	1 (50%)	1 (25%)
Associated symptoms	Presence of Cough	1 (100%)	2 (100%)	4 (100%)
	Cutaneous vasculitis	0	2 (100%)	3 (75%)
Other pulmonary disease associations	Pulmonary hypertension	1 (100%)	1 (50%)	1(25%)
	Chronic sinus disease	1 (100%)	1 (50%)	1(25%)
	Tracheobronchial disease	1 (100%)	0	1(25%)
	Asthma	0	2 (100%)	0
Other major organ involvement	Eye	0	1 (50%)	3 (75%)
	Kidneys (mainly decreased GFR)	1 (100%)	0	1 (25%)
	Nervous System (mainly peripheral neuropathy)	1 (100%)	1 (50%)	0
CT scan chest findings	NSIP	1 (100%)	1 (50%)	1 (25%)
	UIP	0	0	0
	Granulomatous disease on CT chest	0	1 (50%)	2 (50%)
PFTs findings	Restrictive Lung disease pattern	1 (100%)	1 (50%)	2 (50%)
Labs values and serology	RF (rheumatoid factor)	0	1 (50%)	1 (25%)
	c-ANCA/PR-3	0	0	0
	p-ANCA/MPO	0	0	4 (100%)
	hematuria	1 (100%)	0 (0%)	3 (75%)
	ESR/CRP	1 (100%)	1 (50%)	3 (75%)

Table 1. Comparison between ILD in GPA, EGPA and MPA patients' demographic characteristics, clinical symptoms, other major organ involvement, CT chest findings, pulmonary function tests findings and relevant serological values.

Characteristic	GPA (N=1)	EGPA (N=2)	MPA (N=4)
Smoking history	0	0	0
TB exposure	0	0	1 (25%)
Chemotherapy exposure	1 (100%)	1 (50%)	4 (100%)
Silica Exposure	0	1 (50%)	0
Asbestos Exposure	0	1 (50%)	0

Table 2. Comparison between ILD in GPA, EGPA and MPA patients in terms of environmental/ hazardous exposures.

(NSIP). ILD seems to be a rare manifestation mostly associated with MPA (Microscopic Polyangiitis). However, the disease characteristics, serologic findings, demographics and associated risk factors is not well described to date in this subset of patients.

Methods: We performed a single center analysis of patients diagnosed with ANCA associated vasculitis (diagnosed based on biopsy findings and/or appropriate lab criteria with typical clinical characteristics) followed in the vasculitis clinic at Loma Linda University Health from 2017 to current. A retrospective chart analysis was performed on patients with diagnosis of AAV and ILD. Epidemiologic, demographic, clinical, imaging and serological data for these patients were collected. ILD was diagnosed by typical findings on CT scan, lung biopsy or restrictive pattern on PFTs in the absence of other potential causes of restrictive lung disease.

Results: Thirty patients with AAV (M:F= 8:22, mean age at diagnosis 51.3) were enrolled. 15 patients (50%) had Granulomatosis with Polyangiitis (GPA), 11 patients (36.6%) had Microscopic Polyangiitis (MPA) and 4 patients (13.3%) had Eosinophilic Granulomatosis with Polyangiitis (EGPA). ILD was diagnosed in 1 out of 15 GPA patients (6.6%), 2 out of 4 EGPA patients (50%) and 4 out of 11 MPA patients (36.3%). Mean time of diagnosis of ILD from the time of AAV diagnosis was 7 years in GPA, 9 months in EGPA and 10 years in MPA. 42.8% were of Hispanic/Latino ethnicity and 28.5% patients were of White/Caucasian ethnicity. Mean age of ILD diagnosis for GPA was noted to be 26 years as compared to EGPA and MPA which was 58.2 years. NSIP was the most frequent CT pattern found in all AAV patients with ILD in our cohort. None of the patients had any smoking history. TB exposure was reported in 1 patient and occupational asbestos and silica exposures were reported in 1 patient. All 7 patients had some degree of chronic prednisone use. 6 out of 7 patients received treatment with Rituximab and 1 patient was treated with Cytoxan for their AAV. Of note the 2 patients that had associated kidney disease were found to have pauci-immune crescentic GN on kidney biopsy.

Conclusion: Our study revealed ILD is most seen in MPA and least common in GPA. It is strongly associated with MPO Abs. ILD tends to present earlier through the course of the disease in EGPA patients as compared to MPA and GPA patients. Chronic sinusitis and pulmonary hypertension were the most frequent concurrent pulmonary manifestations while cutaneous vasculitis and eye involvement seems to be the most common extra-pulmonary manifestations. None of the patients with AAV-ILD had a smoking history. Although hematuria was a common manifestation

observed in most AAV-ILD patients, decreased GFR was only observed in 2 patients. Further prospective studies in larger cohorts are required to clarify the clinical characteristics and prognosis of ILD in patients with AAV.

Disclosure: H. Youssef, None; **M. Hojjati**, Exagen, 2.

Abstract Number: 1679

Adaptive Study Design of a Randomized, Multicenter, 2-Part Phase 2 Trial of Replacement of Glucocorticoids by IFX-1, a C5a Inhibitor, in Active Granulomatosis with Polyangiitis and Microscopic Polyangiitis

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SESSION INFORMATION
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Background/Purpose: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) are life-threatening rare autoimmune diseases are both forms of anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV). Standard of care treatment includes high-dose glucocorticoids (GC) in combination with cyclophosphamide (CYC) or rituximab (RTX). There is a high unmet medical need to reduce or eliminate high-dose GC to prevent patients from experiencing severe side effects. Complement component 5a (C5a) is known to prime and activate neutrophils, which is a major contributor to the pathogenesis of AAV. IFX-1, a monoclonal antibody, specifically binds to C5a inhibiting C5a-induced biological effects.

Methods: This clinical trial uses an adaptive, stepwise approach to evaluate if GC can be replaced by IFX-1 in AAV.

Results: This is a randomized, double-dummy, double-blind, multicenter trial evaluating the efficacy and safety of IFX-1 in subjects with moderate to severe GPA or MPA (ClinicalTrials.gov NCT03895801). The trial consists of two parts (**Figure 1**). All subjects in both parts are treated with RTX or CYC. In Study Part 1, subjects are randomized to receive either IFX-1 plus a reduced-dose of GC (Group A) or placebo-IFX-1 plus high-dose GC (Group B). Following global clinical evaluation, the trial proceeds to Part 2 in which either additional subjects are randomized to Group B (as above) or subjects are randomized to Group C: IFX-1 and placebo-GC. Patients in Group B are used as the comparison group in both Parts. In total, about 80 subjects will be randomized at approximately 90 sites in Europe and Russia.

Major eligibility criteria are a diagnosis of new or relapsing GPA or MPA requiring treatment with CYC or RTX plus GCs, known positive test for ANCA, ≥ 1 major item or ≥ 3 minor items or ≥ 2 renal items on the Birmingham Vasculitis Assessment Score version 3 (BVASv3).

Intravenous IFX-1 or corresponding placebo is given on days 1, 4, 8, 15 and then every other week until Week 16. GC or corresponding placebo is given according to a standardized tapering scheme. The primary endpoint is the propor-

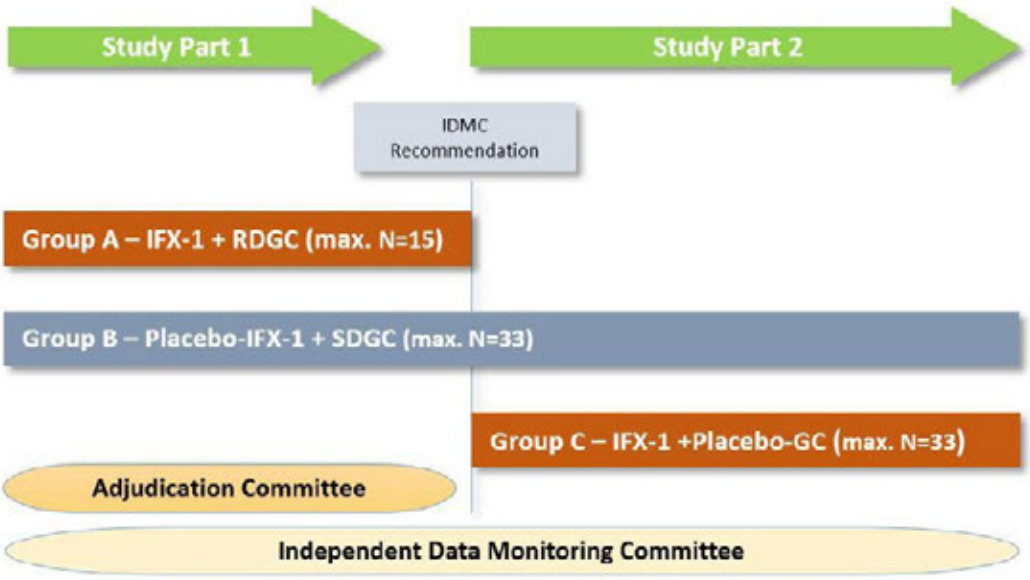

Figure 1. Adaptive, Two-Stage Study Design
IDMC: independent data monitoring committee;
RDCG: reduced-dose glucocorticoids;
SDGC: standard-dose glucocorticoids.

tion of subjects achieving clinical response, defined as ≥ 50% reduction in BVASv3 at Week 16 compared to baseline and no worsening in any body system. Key secondary endpoints include the clinical response at other time points, proportion of subjects with a clinical remission (BVASv3 = 0) at Week 16, adverse events, and pharmacokinetic and pharmacodynamics parameters.

An Adjudication Committee (AC) evaluates the treatment response of each subject after each study visit under blinded conditions. An unblinded Independent Data Monitoring Committee is responsible for continuous review of subject safety data and of reports from the AC to make a recommendation to continue with Study Part 2. Study enrollment started in April 2019.

Conclusion: This ongoing trial is designed to address the substantial unmet need for new therapies that allow for reducing the burden of GCs in the treatment of AAV. This adaptive design provides an innovative approach to investigating new agents in AAV that allows for testing smaller sample sizes in this rare disease while maintaining a strong focus on patient safety.

Disclosure: P. Merkel, Abbvie, 5, AbbVie, 5, AstraZeneca, 2, 5, AstraZeneca,, 2, 5, Biogen, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, Celegene, 2, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Genentech/Roche, 2, 5, Genetech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Kypha, 2, TerumoBCT, 2, UpToDate, 7; **B. Hellmich**, InflaRx GmbH, 5, Roche, 2, 8; **D. Jayne**, Astra Zeneca, 5, Boehringer-Ingelheim, 5, Celgene, 5, ChemoCentryx, 2, 5, GSK, 2, 5, Infla-Rx, 5, InflaRx GmbH, 5, Insmed, 5, Roche Genetech, 2, Sanofi Genzyme, 2, Takeda, 5; **S. Rückinger**, InflaRx GmbH, 2; **Z. Tamas**, InflaRx GmbH, 3; **C. Thielert**, InflaRx GmbH, 3; **O. Zenker**, InflaRx GmbH, 3, 4.

Abstract Number: 1680

Design of a Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial of 2 Different Dose Regimens of IFX-1, a C5a Inhibitor, as an Add-On Therapy for Granulomatosis with Polyangiitis or Microscopic Polyangiitis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Background/Purpose: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) are life-threatening rare autoimmune diseases to anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Standard of care (SOC) treatment includes glucocorticoids (GCs) in combination with cyclophosphamide (CYC) or rituximab (RTX). SOC is still associated with incomplete treatment response, disease relapses, and long-term side effects. Complement component 5a (C5a) is known to prime and activate neutrophils, which is a major contributor to the pathogenesis of AAV. IFX-1, a monoclonal antibody, specifically binds to C5a inhibiting C5a-induced biological effects. Observations in previous clinical studies of sepsis, hidradenitis suppurativa, and cardiac surgery indicate that IFX-1 is safe and well-tolerated. These data suggest that IFX-1 might be a safe, tolerable, and efficacious agent for the treatment of AAV.

Methods: We describe the design of an ongoing clinical trial evaluating the safety of two different doses of IFX-1 or placebo as add-on therapy to SOC in subjects with moderate to severe GPA or MPA.

Results: This randomized, placebo-controlled, multicenter trial is evaluating the safety of two different doses of IFX-1 in combination with SOC, including a standard tapering schedule for GCs (ClinicalTrials.gov NCT03712345). The trial will be performed in about 40 sites in the USA and Canada and will include a total of 36 subjects, 12 per arm. A pharmacokinetic (PK) substudy is planned to enroll 15 subjects. Participation could last for up to 26 weeks, including a 16-week treatment and an 8-week follow-up period.

Major eligibility criteria are a diagnosis of new or relapsing GPA or MPA that requires treatment with CYC or RTX plus GCs, positive test for ANCA, and ≥ 1 major item or ≥ 3 minor items or ≥ 2 renal items on the Birmingham Vasculitis Assessment Score version 3 (BVASv3). Intravenous IFX-1 or placebo will be given on days 1, 4, 8, 15 and then every other week until Week 16. Primary outcome is the number and percentage of subjects who experience at least one treatment-emergent adverse event (TEAE) per treatment group. Key secondary endpoints are IFX-1-related serious AEs and TEAEs, AEs of special interest, proportion of subjects achieving clinical response (reduction in BVAS of ≥50% at Week 16 and no worsening in any body system), proportion of subjects with clinical remission (BVAS = 0) at Week 16, and PK and pharmacodynamic (PD) parameters. The safety of subjects will be monitored continuously by an unblinded Independent Data Monitoring Committee.

Study enrollment in this trial began in October 2018.

Conclusion: This prospective Phase 2 trial of subjects with AAV is intended to demonstrate the safety, tolerability, and efficacy of IFX-1, a C5a blocking therapy, in two different dose regimens in comparison with placebo.

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Abstract Number: 1681

The Association of Reduced Low-Density Lipoprotein (LDL) Cholesterol Levels with ANCA-Associated Vasculitis (AAV)

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) is a small vessel vasculitis associated with an intense inflammatory state. AAV patients are at a 2-fold higher risk of cardiovascular disease (CVD) compared to the general population and CVD is the leading cause of death in this population. As such, CVD risk stratification, often with lipid levels, is recommended in AAV. However, the effect of inflammation on lipid levels in AAV is poorly understood and may impact the interpretation of risk stratification. We sought to evaluate the association between AAV and lipid levels.

Methods: The Partners AAV (PAAV) cohort is a consecutive inception cohort established in the Partners HealthCare System (PHS), a large hospital system in New England. The PAAV cohort has been previously described. All cases are PR3- or MPO-ANCA+. Each AAV case was matched to up to five controls from the PHS Research Patient Data Registry by age, sex, race, and index date (date of AAV treatment initiation). We identified matched cases and controls who had lipid levels (total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], and low-density lipoprotein cholesterol [LDL-C]) measured as part of routine care following the index date. The primary outcome of interest was the difference in lipid levels between cases and controls using the first available lipid level within one year of the index date. We also evaluated the difference in lipid levels between AAV cases and controls in the second and third years of follow-up after the index date. We compared lipid levels between cases and controls using linear regression after adjusting for relevant covariates.

Results: We included 217 cases and 538 matched controls with lipid levels measured in the first year following the index date. The mean age (65 vs 67) and proportion of males (57% vs 53%) and White persons (84% vs 82%) was similar in cases and controls. The majority of AAV cases were MPO-ANCA+ (155, 71%). Compared with controls,

	AAV Cases	Controls	P-Value
N	217	538	
Age (mean, SD)	65 (15)	67 (13)	0.06
Male (N, %)	123 (57)	287 (53)	0.4
Race (N, %)			0.07
White	183 (84)	443 (82)	
Black	6 (3)	27 (5)	
Asian	4 (2)	11 (2)	
Other/Unknown	24 (11)	57 (10)	
Statin Use (when 1st lipid measured) (N, %)	133 (61)	275 (51)	0.01
AAV Characteristics			
MPO-ANCA+ (N, %)	155 (71)	--	
PR3-ANCA+ (N, %)	62 (29)	--	
BVAS/WG (Median, IQR)	4 (4-6)	--	
Any Renal Involvement (N, %)	161 (74)	--	
BMI (kg/m^2, mean, SD)	28.4 (6)	28.7 (7)	0.8
SBP (mmHg, mean, SD)	133 (20)	128 (16)	0.02
DBP (mmHg, mean, SD)	73 (13)	76 (9)	0.08
A1C (%, mean, SD)	6.1 (1)	6.5 (1)	0.01

Table 1. Baseline Characteristics of PAAV Cases and Controls

	TC (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
Unadjusted Difference (AAV vs Control)	-2.3	+3.6	-11.0*
Age- & Sex-Adjusted Difference (AAV vs Control)	-4.2	+3.0	-12.5*
Age-, Sex-, & Race-Adjusted (AAV vs Control)	-4.1	+3.2	-12.7*
Age-, Sex-, Race, & Statin-Adjusted (AAV vs Control)	-3.9	+3.8	-12.2*

*P<0.05

Table 2. Differences in First Lipid Measurement After Index Date Among AAV Cases vs Controls

AAV cases were more frequently prescribed a statin prior to the lipid measurement (61% vs 51%). In unadjusted analyses, TC (187 mg/dL vs 189 mg/dL, P= 0.62) and HDL-C (57 mg/dL vs 52 mg/dL, P= 0.08) were similar between cases and controls. In contrast, LDL-C was significantly lower in cases compared with controls (98 mg/dL vs 109 mg/dL, P=0.006). In analyses adjusted for age, sex, race, and statin use, AAV cases had a significantly lower LDL-C compared with controls (β= - 12.2 mg/dL (95% CI: -20.0 to -4.4), P= 0.002). During follow-up, the difference in LDL-C between cases and controls were no longer significant (Year 2: β= -8.9 mg/dL (95% CI: -19.0 to +1.3), P=0.09; Year 3: β= -5.2 mg/dL (95% CI: -16.4 to +6.1), P=0.4).

Conclusion: We found that LDL-C levels are significantly lower in AAV cases compared to controls in the first year following treatment initiation and these differences appear to dissipate subsequently. We hypothesize that this reflects improvements in the inflammatory state among AAV cases. When screening for dyslipidemia in AAV and assessing CVD risk, one should consider the effect of inflammation on lipid levels. Future studies are necessary to understand if lipid levels, especially as part of risk stratification tools, accurately predict CVD events in this population.

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Abstract Number: 1682

Inpatient Epidemiology of Granulomatosis with Polyangiitis in the United States

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SESSION INFORMATION
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Session Title: Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session (Monday)
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Background/Purpose: Granulomatosis with polyangiitis (GPA, formerly known and Wegener's granulomatosis) is a major subtype of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis characterized by granulomatous inflammation of small- and medium- size vessels. Data on inpatient epidemiology, resource utilization, and healthcare expenditures of GPA are not well described. The aim of this study was to explore those characteristics using a large national inpatient database.

Methods: This retrospective cohort study used the data from the National Inpatient Sample (NIS), the largest public inpatient database in the US, in the year 2005-2014. Data for more than seven million individual hospitalization across all-payers from over 4,000 non-federal acute care hospitals across 40 states are recorded annually in the NIS data-

Table 1 – Adjusted odds ratios, means and additional adjusted means in patients with GPA compared to patients admitted with other medical conditions

Variable	Odds Ratio	95% Confidence Interval	p-value
Mortality	1.50	1.41 – 1.61	<0.01
Shock	1.65	1.53 – 1.78	<0.01
ICU	1.80	1.70 – 1.90	<0.01
AKI	2.55	2.45 – 2.66	<0.01
Multi-organ failure	2.38	2.30 – 2.48	<0.01
Arteriography	0.88	0.80 – 0.95	0.01
CT Scan	1.31	1.07 – 1.61	0.01
MRI	1.18	0.87 – 1.60	0.29
Mean Costs/Charges/LOS			
Costs ($USD)	$18,358		
Charges ($USD)	$61,317		
Length of Stay (days)	7.1		
Variable			
Additional Adjusted Costs	$5,125	4719-5531	<0.01
Additional Adjusted Charges	$16,841	15280-18403	<0.01
Additional Adjusted LOS (days)	1.8	1.6 – 1.9	<0.01

base. All patients with ICD9-CM diagnostic codes for GPA were included. None were excluded. The primary outcome was determining the inpatient prevalence of GPA. Secondary outcomes included determining inpatient mortality, morbidity, resource utilization, hospital length of stay (LOS), and inflation-adjusted total hospital costs and charges. Multivariate regression analyses were used to adjust for age, gender, Charlson Comorbidity Index, income in patient zip code, hospital region, location, size and teaching status.

Results: A total of 124,682 admissions of patients with a diagnosis of GPA occurred in the study period. The mean age was 60.2 years and 52.3% were female. For the primary outcome, the inpatient prevalence of GPA was 32.6 cases per 100,000 discharges. The most common reasons for hospitalization were GPA itself (38.3%) followed by pneumonia (13.7%), sepsis (8.4%), acute kidney injury (8.3%), and acute respiratory failure (4.8%). Patients with GPA displayed significantly higher odds of inpatient all-cause mortality compared to patients admitted for all other causes. Patients with GPA displayed significantly higher morbidity odds of shock, ICU stay, AKI, and multiorgan failure when compared to patients admitted for all other reasons. Patients with GPA were also found to have increased odds of utilizing special investigations, including CT, MRI, and arteriography. Patients with associated diagnosis of GPA displayed higher hospital costs, charges and LOS compared to patients with no GPA (Table 1).

Conclusion: The inpatient prevalence of GPA was higher than what would be expected from the overall incidence. Hospitalizations of these patients were associated with high morbidity and mortality. The mean total hospital costs, charges, and LOS for patients admitted with GPA were higher than patients without GPA.

Disclosure: P. Ungprasert, None; **M. Koster**, None; **W. Cheungpasitporn**, None; **K. Wijarnpreecha**, None; **C. Thongprayoon**, None; **P. Kroner**, None.

Abstract Number: 1683

Cardiac Involvement of Eosinophilic Granulomatosis with Polyangiitis (Churg–Strauss): Initial Manifestations and Outcomes Based on Data from a Monocenter Patient Cohort

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Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is a systemic necrotizing vasculitis characterized by blood and tissue eosinophilia, and asthma. Its cardiac involvement is a major concern that was previously described as the most important predictor of death; however, definitions of that involvement differ according to study. We aimed to describe the first EGPA cardiac manifestations and outcomes in recent decades.

Methods: This retrospective, monocenter study included all EGPA patients followed in our vasculitis center. Patients' and disease characteristics were recorded at diagnosis and throughout follow-up, especially cardiac assessments. Cardiac involvement was defined as clinical or extra-clinical signs of patent cardiopathy, with no other potential caus-

es identified.EGPA relapses, major cardiac-related events (i.e. acute and chronic heart failure, atrial fibrillation and/or ventricular tachycardia, ischemic cardiopathy) and causes of death were recorded.

Results: The 150 EGPA patients (78 men; mean±SD age 47.8±15.9 years) included were characterized by asthma (99%), eosinophilia (95%), sinonasal abnormalities (84%), pulmonary infiltrates (51%), peripheral neuropathy (57%) and eosinophil-rich infiltrates (19%); 39% were ANCA+. Median baseline BVAS was 17.5 [IQR 13–22].Sixty-five (43%) patients had cardiac involvement, 55 (85%) diagnosed at EGPA diagnosis and 10 (15%) during follow-up. The main clinical cardiac manifestations included chest pain (16%), peripheral edema (8%), palpitations (4%), cardiogenic shock (3%) and arrhythmia (1%). Patients with cardiac involvement, compared to those without, respectively, were less frequently ANCA+ (27% vs. 48%, P=0.02), had less frequent peripheral neuropathy (46% vs. 66%, P=0.02), and had higher eosinophil count (9748±7639 vs. 6346±5291/mm^3, P=0.004).Patients with cardiac involvement had abnormal ECG (70%), abnormal echocardiography [(68%; mainly pericardial effusion (42%) and left ventricular dysfunction (31%)] and cardiac MRI abnormalities [(98%; with left ventricular dysfunction (43%), myocardial edema (24%) and late gadolinium enhancement (74%)]. However, ECG, echocardiography and cardiac MRI, respectively, were also abnormal for 32%, 40% and 61% of the patients without patent cardiopathy.After mean follow-up of 121±97.2 months, 65 (43%) patients experienced EGPA relapses, with no between-group differences (37 vs 48%, P=0.19). However, 46% of patients with cardiac involvement had cardiac relapses. Major heart-related events occurred in 17/150 (11%) patients, most often those with known cardiac involvement (18% vs. 6%, P=0.02). Finally, 4 patients died but none from cardiac causes.

Conclusion: Cardiac involvement is frequent in EGPA in a tertiary referral center, especially in patients without ANCA, with higher eosinophil counts and no peripheral neuropathy. Long-term outcome was better than previously reported. However, in the absence of a consensual definition of cardiac involvement, comparisons among studies remains difficult.

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Abstract Number: 1684

Remission and Low Disease Activity State in Patients with Granulomatosis with Polyangiitis and Microscopic Polyangiitis: Prevalence and Impact on Damage Accrual

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Background/Purpose: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) require glucocorticoids (GCs) and immunosuppressants (IS) to induce and maintain remission. At the era of highly active drugs

and treat-to-target strategies, defining the goal to achieve in terms of remission could be beneficial for the long-term management. We aimed to assess the impact of prolonged remission or low disease activity state (LDAS) in GPA and MPA patients and its relationship with damage accrual.

Methods: Patients diagnosed with GPA and MPA, according to ACR criteria and/or Chapel Hill definitions, seen in our vasculitis center and followed-up for ≥5 years were included. Disease activity was assessed by BVAS , and damage accrual by the VDI. Three levels of remission were defined: complete remission (CR): BVAS=0 and negative ANCA in GCs-free and IS-free patients; clinical remission off therapy: no disease activity and positive ANCA in GCs-free and IS-free patients; clinical remission on therapy: no disease activity in patients with low dose GCs (≤5 mg/d) and/or IS. LDAS was defined as 0< BVAS≤3 without major organ activity, no new disease activity, low-dose GCs (≤7.5 mg/day) and well-tolerated IS. We defined remission or LDAS as prolonged when lasting ≥2 consecutive years. The effect of prolonged remission and LDAS on damage accrual was evaluated.

Results: 126 patients were included: 94 (75%) GPA, mean age 51.6±16.9 years. At 5-years, mean VDI was 2.6±1.9, mainly because of AAV-related items (2.0±1.7) rather than treatment-related items (0.6±0.9). During the 5-year follow-up, 8 (6.3%) patients achieved prolonged CR, 6 (4.8%) prolonged clinical remission off therapy, 62 (49.2%) prolonged clinical remission on therapy, 37 (29.3%) prolonged LDAS and 13 (10.3%) never achieved LDAS. Damage accrual at 5-years in patients with prolonged CR, clinical remission off therapy, clinical remission on therapy, LDAS or those never achieved LDAS was 1.8±1.3, 1.8±1.7, 2.2±1.7, 3.3±1.6and 3.8±2.7, respectively (P< 0.003). Damage was comparable between patients in prolonged remission off therapy and those in remission on therapy (P=0.44). In contrast, patients in prolonged LDAS or those never in LDAS had significantly more damage accrual (P=0.002 and P=0.048, respectively) than those in prolonged remission off therapy. The inability to achieve prolonged remission was associated with a VDI ≥3 at 5-years (OR 3.86, 95% CI 1.77-7.84, P=0.0005), and considering only prolonged CR or clinical remission off therapy did not had any benefit on damage accrual. In contrast, achieving prolonged LDAS had no benefit compared to spending no time in LDAS (P >0.99). Compared to patients achieving prolonged remission, those not able to achieve prolonged remission were younger (46±16 vs. 55±16, P=0.004), had more frequent GPA (P=0.0003) and ENT involvement (P=0.01).

Conclusion: Sixty percent of GPA and MPA patients achieved prolonged remission, which was associated with a better outcome in terms of damage accrual. In contrast, prolonged LDAS was associated with increased damage and was not a sufficient target to achieve in GPA and MPA.

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Abstract Number: 1685

Inpatient Burden, Expenditures and Comorbidities of Polyarteritis Nodosa: National Inpatient Sample 2014

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Due to the rarity of polyarteritis nodosa (PAN), no study has ever investigated inpatient characteristics, healthcare utilization and frequency of comorbidities of patients with PAN. The current study was conducted with the aim to better describe those information using data from a large national database.

Methods: Patients with PAN were identified from the Nationwide Inpatient Sample (NIS) database for the year 2014 using ICD-9 diagnostic codes. The primary outcome was determining the inpatient prevalence of PAN in hospitalized patients in the US. Secondary outcomes included determining inpatient mortality, morbidity, comorbidities, hospital length of stay (LOS) and expenditures. Expenditures were sub-divided into total hospitalization charges and hospital costs. Total hospital charges represent the amount of money that each hospital billed the payers for the service provided during each admission, while hospital costs represent the amount of money the hospital invested to provide care during each admission. A cohort of patients without PAN was also identified from the same database to serve as comparators for analysis of comorbidities. Multivariate regression analysis was used to adjust for age, sex, ethnicity and hospital characteristics.

Results: A total of 4,110 patients with PAN were included in the study. The mean age was 59.5 years and 61% were female. The inpatient prevalence of PAN was 11.6 cases per 100,000 admissions. The most common reasons for admission among patients with PAN in this database were as follows; PAN itself (17.6%), sepsis (6.9%), acute kidney injury (4.9%), acute respiratory failure (2.1%) and pneumonia (2.0%). During hospitalization, a significantly higher

Table 1: Adjusted odds ratios comparing the prevalence of comorbidities between patients with polyarteritis nodosa versus patients without polyarteritis nodosa

	Adjusted odds ratio	95% CI	*p*-value
Deep venous thrombosis	1.97	1.47 – 2.63	<0.01
Pulmonary embolism	1.93	1.41 – 2.65	<0.01
Acute myocardial infarction	1.13	0.64 – 2.00	0.66
Congestive heart failure	0.96	0.78 – 1.18	0.68
Arrhythmia	1.09	0.86 – 1.37	0.48
Acute kidney injury	3.73	3.15 – 4.42	<0.01
Chronic kidney disease	8.40	6.50 – 10.87	<0.01
End-stage renal disease	4.79	3.76 – 6.10	<0.01
Hepatitis B virus infection	5.85	3.17 – 10.80	<0.01
Hepatitis C virus infection	1.97	1.32 – 2.93	<0.01
Sepsis	1.87	1.51 – 2.32	<0.01

morbidity among patients with PAN was observed as indicated by a significantly higher risk of shock (adjusted OR 1.75; 95% CI, 1.23 – 2.50), admission to ICU (adjusted OR 1.88; 95% CI, 1.44 – 2.45) and multi-organ failure (adjusted OR 3.12; 95% CI, 2.64 – 3.69) although the odds of mortality was not significantly elevated (adjusted OR 1.35; 95% CI, 0.91 – 2.00). Patients with PAN also displayed significantly higher hospital costs (additional adjusted mean [aAM]: $9,693, p< 0.01), hospitalization charges (aAM: $34,273, p< 0.01) and LOS (aAM: 4.1 days, p< 0.01) compared to patients without PAN. Analysis of comorbidities found a significant association between PAN and several comorbidities as shown in table 1.

Conclusion: The inpatient prevalence of PAN is higher than what would be expected from the overall general prevalence. Hospitalizations of patients with PAN are associated with significantly higher rates of morbidity and expenditures.

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Abstract Number: 1686

Risk of Vasculitis Associated with Inflammatory Bowel Diseases: Evidence for a Role of TNF-α Blockers

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: An increased risk of side effects, especially infections, has been reported among patients receiving tumor necrosis factor (TNF)-α blockers. Some leukocytoclastic cutaneous vasculitides reportedly occurred under TNF-α blockers used to treat various inflammatory diseases, but the risk of vasculitis with TNF-α blockers remains uncertain, especially in comparison with other immunosuppressive agents.We aimed to assess the risk of vasculitis associated with thiopurines and TNF-α blockers prescribed to manage inflammatory bowel diseases (IBD).

Methods: This nationwide population-based study included patients (≥18 years old) affiliated with the French National Health Insurance (FNHI), with an IBD diagnosis based on long-term diseases listed and/or hospital-discharge diagnoses in the FNHI database from January 2010 through 2011, and followed until 31 December 2014. The risks of vasculitis associated with exposure to thiopurines or TNF-α blockers were compared using a Cox regression model adjusted for baseline sociodemographic characteristics and comorbidities. The primary outcome was incident vasculitis.

Results: Among the 193,663 IBD patients included in our analysis, 173 developed vasculitis, mainly IgA vasculitis (n=41), hypersensitivity vasculitis (n=41) and large-vessel vasculitis (n=39). Incidences per 100,000 person-years were 4.9 for IgA vasculitis, 4.9 for hypersensitivity vasculitis, 4.6 for large vessel vasculitis, 2.1 for ANCA-associated vasculitis and 1.2 for medium-sized–vessel vasculitis.

Compared with patients not exposed to TNF-α blockers or thiopurines during the study period, TNF-α blockers (hazard ratio [HR], 2.39; 95% confidence interval [95% CI], 1.49–3.84) were associated with a higher risk of vasculitis

but not thiopurines (HR, 0.72; 95% CI, 0.40–1.31). The magnitude of TNF-α-blocker–associated risk was higher for patients with ulcerative colitis (HR, 4.07; 95% CI, 1.96–8.47) than those with Crohn's disease (HR, 1.75; 95% CI, 0.95–3.22). The risk of vasculitis with TNF-α–blocker exposure was independently associated with older age (per 1-year increment, HR, 1.09; 95% CI 1.04–1.15), female sex (HR, 1.47; 95% CI, 1.08–2.00), cardiovascular disease (HR, 2.01; 95% CI, 1.33–3.04) and diabetes mellitus (HR, 1.77; 95% CI, 1.12–2.79).Finally, exploratory analyses showed that exposure to TNF-α blockers was not associated with a specific subtype of vasculitis: IgA vasculitis (HR, 3.11; 95% CI, 1.36–7.09), hypersensitivity vasculitis (HR, 3.48; 95% CI, 1.52–1.7.95), large-vessel vasculitis (HR, 2.56; 95% CI, 0.87–7.57) or ANCA-associated vasculitides (HR, 7.68; 95% CI, 1.99–29.7).

Conclusion: Based on a nationwide cohort study of IBD patients in France, TNF-α blockers were associated with an increased risk of vasculitis, unlike thiopurines. Cardiovascular disease and diabetes mellitus were also associated with the risk of vasculitis, suggesting relationships among atherosclerosis, chronic hyperglycemic state andinflammation.

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Abstract Number: 1687

Dramatic but Suspensive Effect of interleukin-1 Inhibitors on Persistent Urticarial Vasculitis

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Background/Purpose: Urticarial vasculitis (UV) is a rare disease characterized by dermal capillary inflammation responsible for long-lasting urticarial lesions. UV can be separated into 2 different entities according to complement fraction levels: hypocomplementemic urticarial vasculitis (HUV), associated with low C1q levels and inconstant anti-C1q antibodies, and normocomplementemic urticarial vasculitis (NUV).UV is characterized by frequent relapses or glucocorticoid (GC)-dependence. We report the efficacy of IL-1β inhibitors against relapsing and GC-dependent UVs.

Methods: This retrospective multicenter study included patients with relapsing and/or GC-dependent UVs treated with IL-1β inhibitors. Patients had to have biopsy-proven UV with long-lasting urticarial lesions and leukocytoclastic vasculitis in a skin biopsy, associated or not with systemic involvement. Relapsing and GC-dependent disease was defined as cutaneous lesions despite GCs at a dose >10 mg/day. For each patient, retrospectively collected data included clinical and biological characteristics, previous and concomitant treatments and theirevolutions, details on IL-1β inhibitors, and disease under IL-1β–inhibitor therapy at discontinuation. Clinical complete response (CR) was defined as total disappearance of cutaneous lesions and other systemic manifestations. Clinical partial response (PR) was defined as attenuation of disease activity without achieving CR. The primary endpoint was the CR rate.

Results: Six patients were included [3 men and 3 women, median age 41 (range 23–62) years], 4 with HUV and 2 with NUV. Median time from diagnosis to starting IL-1β inhibitors was 5.5 (range 1–16) years. All patients had cutaneous and joint involvement, and 2 had gastrointestinal manifestations. All patients received anakinra (100 mg/day); 5 had concomitant treatments, mostly GCs. Under IL-1β inhibitors, 5 (83%) patients achieved CR, within 7 days after starting treatment for 4 (80%) of them, and 1 had a PR. GC use was discontinued for 4 (80%).In the HUV subgroup, no normalization of complement-fraction levels was obtained. Progressive discontinuation of IL-1β inhibitors was attempted for 4 patients but was constantly associated with relapses within a few days. Safety was good, but 2 patients experienced reactions at the injection site, leading to an anakinra-to-canakinumab switch for 1, with CR persistence. No death, infection or neutropenia occurred.

Conclusion: IL-1β inhibitors had a dramatic—but only suspensive—effect on persistent UV and could be considered alternative agents to treat relapsing and GC-dependent UV.

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Abstract Number: 1688

Glucocorticoids Plus Rituximab versus Glucocorticoids Plus Placebo in Non-infectious Active Mixed Cryoglobulinemia Vasculitis: Results of a Placebo-Controlled Randomized Trial

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: A previous retrospective study suggested superiority of glucocorticoids (GCs) plus rituximab (RTX) compared to GCs alone to induce complete clinical response in non-infectious cryoglobulinemia vasculitis (CryoVas). However, GCs plus RTX regimen was associated with severe infections, whereas death rates did not differ between therapeutic regimens. The ESBAM trial (NCT02556866) aimed to evaluate the efficacy and safety of RTX in combination with GCs for the treatment of non-infectious active mixed CryoVas.

Methods: We conducted a multicenter, randomized, double-blind, superiority trial of RTX as compared with placebo for remission induction in non-infectious active mixed CryoVas. To be included, patients had to have an active CryoVas defined by positive serum cryoglobulin and an active vasculitis, and to be treatment-naive or relapsing patients. Patients were randomized to receive prednisone plus RTX administered by intravenous infusion at 375 mg/m^2 at day (D) 1, D8, D15 and D22, or prednisone plus placebo administered following the same schedule.GCs were tapered off.

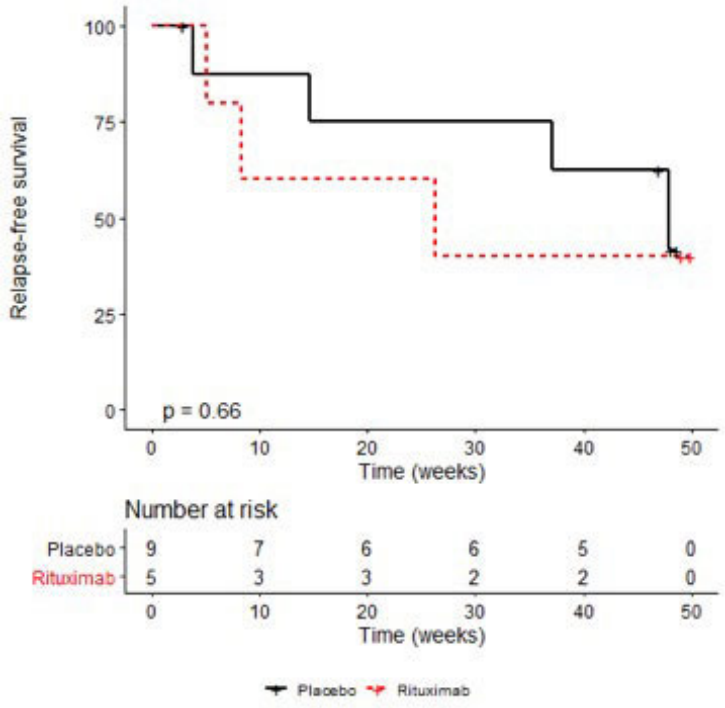

Figure. Relapse-free survival between the two groups of treatment

The primary endpoint was the remission of mixed CryoVas without the use of prednisone at week (W) 24. This study was initially planned to include 79 patients per group.

Results: Between July 2015 and July 2017, 15 patients were enrolled in the ESBAM trial and 14 were randomized (one patient died before randomization): 5 to receive RTX and 9 to the placebo-group. Their median age was 62 [45;71] years, 73% were women, and 73% relapsing-patients. Main CryoVas manifestations included: purpura (71%), neuropathy (43%), arthralgias (36%) and glomerulonephritis (29%). Patients' characteristics were comparable between groups.

At W24, 4/5 (80%) had an inactive vasculitis in the RTX-group compared to 6/8 (75%) in the placebo-group. A remission with no prednisone was achieved in 1/5 (20%) patient the RTX-group vs. 0/8 in the placebo-group. Cumulative doses of GCs at W24 and W48 were comparable in the two groups.

During the 48-week follow-up, 7 vasculitis relapses occurred, i.e. 3 in the RTX-group vs. 4 in the placebo-group. Relapse-free survival rates at W48 were 40.0% [13.7–100%] in the RTX-group vs. 41.7% [15.9–100%] in the placebo-group (**Figure**). The SF-36 physical health summary significantly improved in the RTX-group compared to placebo-group, especially at W36 and W48 (P=0.02 and P=0.04). Cryoglobulinemia remained positive in both groups for the majority of patients, and evolution of serum C4 fraction was comparable between groups during the 48 weeks. Twenty severe adverse events were recorded, 6 in the RTX-group and 20 in the placebo-group, including 1 patient in the RTX-group and 2 in the placebo-grouphaving severe infections. No patient died after randomization.

Conclusion: Combination of glucocorticoids plus rituximab and glucocorticoids plus placebo seemed to induce similar rates of remission at week 24 in non-infectious active mixed cryoglobulinemia vasculitis.

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Abstract Number: 1689

Off-Label Use of Biotherapies to Treat Relapsing And/or Refractory Polyarteritis Nodosa

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Polyarteritis nodosa (PAN) is a rare systemic necrotizing vasculitis of medium- and small-sized arteries, not associated with antineutrophil cytoplasmic antibodies (ANCA). Conventional treatments include glucocorticoids (GCs) for non-severe disease, and combined GCs and immunosuppressants for severe disease. Nevertheless, some patients have refractory and/or relapsing disease. We examined off-label biotherapy use for relapsing/refractory PAN.

Methods: This retrospective European collaborative study included patients with PAN meeting ACR criteria and/or Chapel Hill Consensus Conference 2012 definitions. Treatment efficacy and safety were recorded. Remission was defined as the absence of vasculitis manifestations (BVAS = 0) with ≤5 mg/day of prednisone. Partial response was defined as BVAS = 0, with 6–10 mg/day of prednisone.

Results: Fifty-two patients (24 men and 28 women; median age 51 years) were included. Nineteen (37%) patients received TNF-α blockers, 16 (31%) rituximab (RTX), 9 (17%) tocilizumab (TCZ), and 8 (15%) other biologics (i.e. alemtuzumab for 3, anakinra for 2, interferon-α for 2 and abatacept for 1). Previous treatments were: GCs for all, including methylprednisolone infusions (73%), cyclophosphamide (62%), azathioprine (54%), mycophenolate mofetil (48%) or methotrexate (46%). At inclusion, median BVAS was 5 (range 0-18), including 5 (2-12) for the TNF-α blocker group, 5 (2-12) for the RTX recipients and 4 (0-6) for those given TCZ.

At month (M) 6 and M12, respectively, median BVAS fell to 3 and 0 for TNF-α blockers group, to 3.5 and 0 for those given RTX, and to 0 and 0 for the TCZ group. Median GCs dose declined from baseline 17.5 mg/day to 10 at 6 months and 5 at 12 months for the TNF-α blocker recipient, from 15 to 10 and 5 mg/day for those given RTX, respectively, and from 15 to 7 and 5 mg/day for the TCZ group.

Nine (47%) patients stopped TNF-α blockers: for adverse events in 2 and/or refractory disease in 8. Refractory disease led 6 (38%) to stop RTX. Finally, 4 (44%) stopped TCZ: 2 for adverse events (testicular abscess and worsening renal failure), and 2 for refractory disease. Two additional patients had to decrease the dose because of cytopenias.

After median follow-up of 34.4 [IQR 21.5–59.5] months, remissions, partial responses, treatment failure and stop for adverse event, respectively, occurred in 43%, 5%, 47% and 5% for TNF-α blockers recipients, 31%, 13%, 56% and 0% for RTX recipients, and 56%, 0%, 22% and 22% for TCZ recipients. No remission was noted in patients treated with anakinra, alemtuzumab, interferon-α and abatacept.

Conclusion: These results suggest that TNF-α blockers and TCZ could achieve higher remission and GC-sparing rates for relapsing and/or refractory PAN than other biologics. Our findings warrant further study to confirm or refute them.

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Abstract Number: 1690

The Long-term Outcome of Patients with Arthritis of Behçet's Disease

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Behçet's disease (BD) is characterized by recurrent aphthous stomatitis, eye lesions, skin lesions, and genital ulcer. In addition to these symptoms, Behçet's disease is frequently complicated by joint symptoms, usually affecting large joints. Although glucocorticoid and NSAIDs are effective in subsiding each arthritis attack, they are unable to prevent recurrence of attacks. In 2018 EULAR recommendations, colchicine as well as other drugs, such as TNF inhibitors, IFN-alpha and azathioprine are recommended to control arthritis in BD. However, long-term outcome of patients with arthritis has not been determined. In fact, bone deformity and bone destruction are considered rare in BD in contrast with rheumatoid arthritis. In this study, we investigated the long-term outcome of joint symptoms in patients with BD.

Methods: Retrospective analysis of the clinical charts of 107 patients with BD was carried out, who visited the clinic of our hospital between 2017 and 2018. All the patients met the International Study Group for BD criteria. The pres-

ence and clinical course of joint symptoms were surveyed in these patients. The status of activity of daily living was evaluated using Steinbrocker's functional grade (Class I–IV) at the most recent visit.

Results: Of the 107 patients, 36 (15 men and 21 women) were treated for joint symptoms associated with BD. Arthritis attacks in most patients were successfully treated with glucocorticoid and/or NSAIDs. After the initial attacks, colchicine, methotrexate and infliximab were given to 18 patients, 10 patients and 2 patients, respectively, to prevent the relapse of arthritis attacks. The mean (± SD) duration from the onset of joint symptoms to the most recent check-up was 21.2±14.6 years (mean ± SD). The functional stages at the time of the most recent check-up were Class I in 30 patients and Class II in 6 patients, whereas there were no patients in Class III or IV. The functional stages at the evaluation were not significantly correlated with the duration of the disease or treatment with colchicine, methotrexate or infliximab. Thus, no major impairment in active daily living was noted throughout the long-term course in all the patients. Consistently, no patients showed bone erosion or destructive arthritis on radiography.

Conclusion: The results in the present study have disclosed that the long-term outcome of arthritis in BD is much better that that of RA, resulting in no patients with serious disability over Class III even after a long time of disease duration of 21.2 years in average. Although the final functional stages were not correlated with their use, further studies with a larger number of patients are needed to confirm whether colchicine, methotrexate and infliximab might have beneficial effects for arthritis in BD.

Disclosure: H. Kikuchi, None; **T. Tomizuka**, None; **K. Asako**, None; **H. Kono**, Celgene Corporation, 2; **S. Hirohata**, None.

Abstract Number: 1691

Efficacy of TNF α Inhibitors for Refractory Vascular Behcet's Disease: A Multicenter Observational Study of 27 Patients

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

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Session Time: 9:00AM–11:00AM

Background/Purpose: Vascular involvement is one of the major causes of morbidity and mortality in Behcet's Disease (BD) patients. Immunosuppressive (IS) agents are the mainstay of vascular BD (VBD) treatment, however up to one third of patients relapse under conventional ISs. In this case series, we present the results of tumor necrosis factor-alpha (TNFα) inhibitor use for the treatment of VBD patients who were refractory to conventional ISs and corticosteroids.

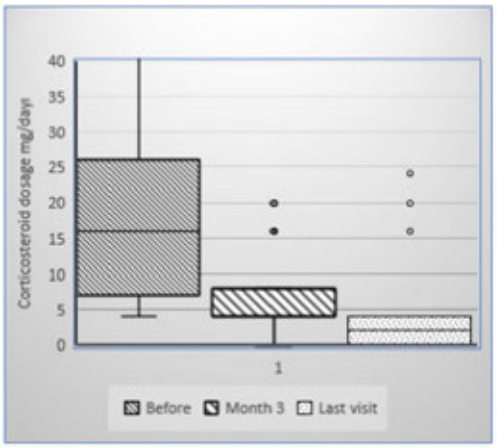

Figure 1: Corticosteroids sparing effects of TNF α inhibitors

Figure 1 Corticosteroids sparing effects of TNF α inhibitors (The median daily dose at baseline was 16 (4-64) mg vs 4 (0-20) mg at 3 months (p=0.000) and 2 (0-20) mg at last visit (p=0.000), respectively)

Methods: This retrospective multicenter study included 27 refractory VBD patients treated with TNFα inhibitor agents. All data were acquired from patient charts.Activity was assessed by the treating clinician according to clinical manifestations, imaging findings and acute-phase reactant results. Complete remission was defined as no new signs and symptoms of vascular disease assessed by physician and corticosteroid dose under 10 mg/day at the third month of treatment. Partial response was defined as an improvement of clinical and laboratory parameters and at least 50% reduction of initial corticosteroid dose at the third month.

Results: Infliximab was the first choice of TNFα inhibitor in 24 and adalimumab in 3 patients. Complete clinical remission was achieved in 22 (80%) patients within 3 months of the initiation of TNFα inhibitors. The median daily dose of corticosteroids significantly decreased at 3 months. (Figure 1) and stopped in 7 patients during follow-up without any relapse. Also, 89% of patients discontinued or maintained 4 mg or lower daily of methylprednisolone dosage at the last visit. Fifteen patients received concomitant immunosuppressive (all was azathioprine) together with a TNFα inhibitor. A trend towards a higher rate of complete remission was observed with concomitant IS use compared to monotherapy of TNFa inhibitors (93% vs 67%, p=0.09). Also, duration of first TNFα inhibitor drug survival was also 12.5 (1-43) months and 24 (4-67) months for monotherapy and concomitant IS user groups, respectively (p >0.05) (Figure 2) Three patient had vascular relapses under the treatment of TNFα inhibitors (2 Infliximab, 1 Adalimumab). Serious side effects were observed in 2 patients (1 pneumonia and 1 tuberculosis). TNFα inhibitors were stopped with sustained remission in 2 patients (after 24 and 37 months of treatment). One of the patients relapsed 6 months after cessation of TNFα inhibitor. After median 14 (3-67) months of follow-up period under TNFα inhibitors, 23 patients were still under TNFα inhibitors and all were in remission.

Conclusion: TNFα inhibitors seem a highly effective option for remission-induction of refractory VBD with an acceptable safety data. Concomitant IS use may achieve higher complete remission rates as compared to TNFα inhibitor monotherapy. Comparative efficacy and safety of biological agents for VBD require further prospective, randomized controlled studies with a longer duration of follow-up.

Table 1: Characteristics of patients

Patient	Drug initiation Age	Sex	Indication of TNF α inhibitors	Previous treatment
1	28	M	PAA, cardiac thrombi	CS, CYC, IFN
2	35	M	PAA, cardiac thrombi	CS, CYC
3	32	M	CVT, DVT, IVC	CS, AZA, IFN
4	35	M	Retinal vein, DVT	CS, CyS, IFN, AZA
5	30	M	CVT	CS, AZA, IFN
6	39	M	CVT, retinal vein thrombosis	CS, AZA
7	28	M	DVT (6 times)	CS, AZA
8	36	F	PAT	CS, AZA
9	38	M	PAT, cardiac thrombi	CS, AZA, CYC
10	35	M	PAT, DVT	CS, CYC, AZA
11	28	M	DVT, IVC	CS, CYC, AZA
12	33	M	CVT, DVT, renal vein	CS, AZA, CyS
13	28	M	DVT, PAT	CS, AZA, CyS
14	29	M	DVT	CS, AZA
15	42	M	Aorta aneurysm	CS, CYC, AZA
16	39	M	DVT, IVC	CS, CYC, AZA,
17	24	M	PAT (endarterectomy)	CS, CYC, AZA
18	55	M	Celiac-iliac artery, aorta aneurysm, SMA thrombi	CS, CYC, AZA
19	41	M	DVT	CS, CYC, AZA
20	35	M	DVT	CS, CYC, AZA
21	33	M	PAA	CS, CYC
22	29	F	PAT, cardiac thrombi	CS, CYC, AZA
23	30	M	PAT, cardiac thrombi	CS, CYC, AZA
24	40	M	DVT, SVC	CS, CYC, AZA
25	50	M	DVT	CS
26	46	F	DVT, Aorta aneurysm, femoral artery aneurysm	CS, CYC, AZA, CyS
27	41	M	CVT, thoracic aorta thrombi	CS, CYC, AZA

CS: corticosteroid, PAA: pulmonary artery aneurysm, DVT: deep vein thrombi, PAT: pulmonary artery thrombi , SVC: superior vena cava, CYC: cyclophosphamide, AZA: Azathioprine, CyS: cyclosporine, CVT: cerebral vein thrombi, IVC : inferior vena cava, IFN: Interferon , TNF α: Tumor necrosis factor alpha

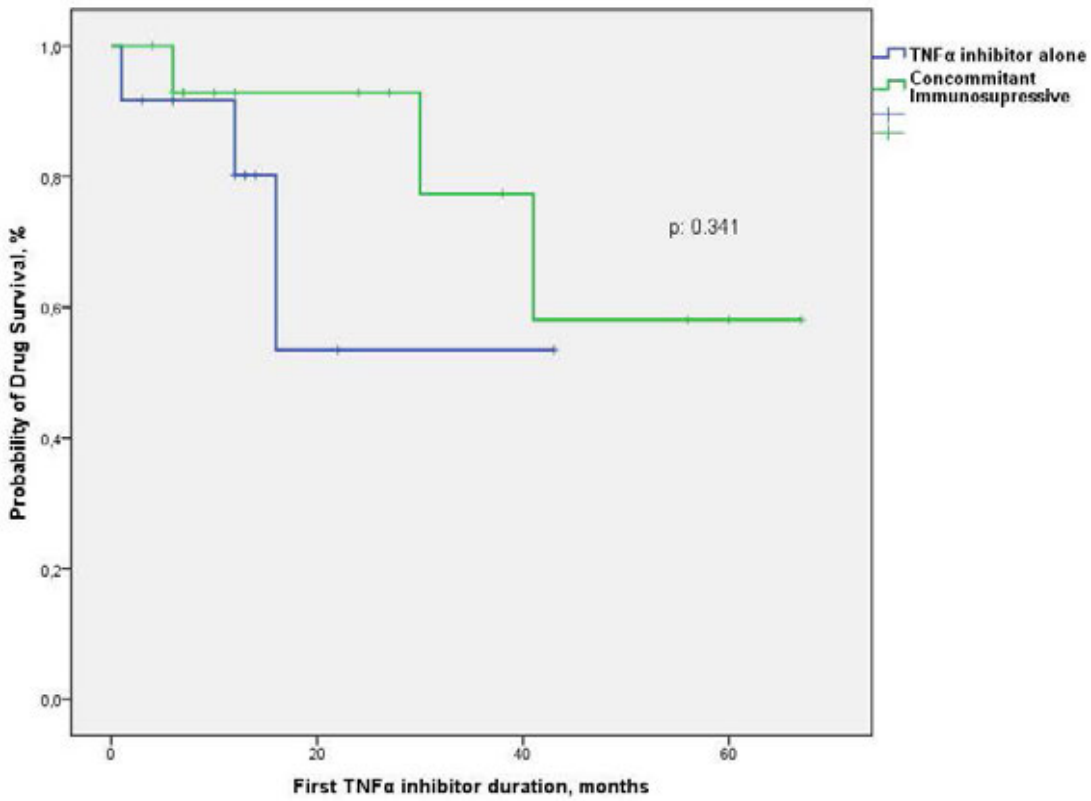

Figure 2: Event Free Drug Survival

Disclosure: A. Aksoy, None; **A. Yazici**, None; **A. Omma**, None; **A. Cefle**, None; **F. Onen**, Tofacitinib (Pfizer), 8; **U. Tasdemir**, None; **T. Ergun**, None; **H. Direskeneli**, None; **F. Alibaz-Oner**, None.

Abstract Number: 1692

Long-Term Follow-Up of Anti-IL6-Receptor Tocilizumab in Refractory Uveitis in Patients with Behçet Disease: Multicenter Study of 14 Patients in Clinical Practice

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

TABLE. Evolution of ocular parameters with TCZ therapy in a long-term follow-up.

	BASAL n=26	1 WEEK n=20	2 WEEKS n=24	1 MONTH n=24	3 MONTHS n=24	6 MONTHS n=20	1 YEAR n=17	2 YEARS n=11	3 YEARS n=7	4 YEARS n=4
BCVA	0.38±0.35	0.46±0.34*	0.56±0.36*	0.58±0.38*	0.61±0.37*	0.65±0.37*	0.61±0.38*	0.61±0.33	0.63±0.29*	0.93±0.12
AC CELLS	1 [0-3]	1 [0-2]*	0 [0-1]*	0 [0-0.75]*	0 [0-0.25]*	0 [0-0]*	0 [0-1]*	0 [0-0]	0 [0-0]	0 [0-0]
VITRITIS	1 [0-2]	1 [0-2]	0 [0-1]*	0 [0-1]*	0 [0-0]*	0 [0-0]*	0 [0-0]*	0 [0-0]*	0 [0-0]	0 [0-0]
OCT	339.9±110.1	329.3±109.1*	324.6±108.5	298.7±83.5	263.4±88.4*	251.8±87.4*	232.8±45.8*	245.8±29.9	247.25±6.2	247.25±6.2

*p< 0.05

Abbreviations: AC= anterior chamber; BCVA= best corrected visual acuity; n= number of available eyes; OCT= optical coherence tomography.

Background/Purpose: Ocular involvement in Behçet's disease (BD) is a potential severe and disabling complication. Anti-TNF-α agents have shown an improvement of visual outcome in BD-related uveitis refractory to conventional immunosuppressive (IS) drugs. However, these drugs do not achieve control of intraocular inflammation in all patients or are not well tolerated. Tocilizumab (TCZ) has shown efficacy in different refractory ocular inflammatory diseases. To assess the efficacy of long-term therapy with TCZ in refractory uveitis associated to extraocular manifestations due to BD.

Methods: Multicenter study of patients with BD refractory to standard systemic treatment.

Results: We followed up 14 patients (9 men/5 women) (26 affected eyes); mean age 40.8±19.5 years. Pattern of ocular involvement: panuveitis (10; 4 with retinal vasculitis), anterior (3) and posterior (1) uveitis; 8 recurrent and 6 chronic; 9 with cystoid macular edema. At TCZ onset the following extraocular manifestations were present: oral and/or genital ulcers (10), arthritis (6), folliculitis/pseudofolliculitis (6), erythema nodosum (3), livedo reticularis (1), intestinal affection (1) and neurological involvement (3).

Before TCZ, they had received corticosteroids (13 intraocular, 12 oral and 12 iv), conventional IS drugs and biologic agents: methotrexate (11), cyclosporine (8), azathioprine (10), colchicine (1), cyclophosphamide (2), mycophenolate mofetil (1), adalimumab (10), infliximab (6), golimumab (3), canakinumab (1), or etanercept (1). TCZ was used in monotherapy (7) or combined with conventional IS drugs (7) at 8 mg/kg/iv/4 w (11) or 162 mg/sc/w (3).

After a mean follow-up of 21.7±14.5 months using TCZ, all patients experienced ocular improvement, with complete remission in 10. However, TCZ was only effective in 5 of the patients with extraocular manifestations. TABLE shows the evolution of ocular parameters.

TCZ had to be withdrawn temporally in 1 case, due to an episode of cellulitis with sepsis, and definitely in 4 cases, due to a severe infusion reaction, arthritis impairment, persistence of oral ulcers or a new episode of uveitis (1 each). Prednisone dose was significantly reduced until suspension in all patients.

Conclusion: TCZ seams a useful and secure therapy in highly refractory BD-related uveitis.

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Abstract Number: 1693

Biological Therapy in Neurobehçet: Multicenter Study of 31 Patients

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SESSION INFORMATION
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Background/Purpose: Behçet's disease (BD) is a variable vessel vasculitis and typically presents with mucocutaneous involvement. However, any organ can be affected, being the neurological affectation (neurobehçet, NB) one of the most serious manifestations.

Our aim was to assess the efficacy and safety of biological therapy as treatment of NB.

Methods: We set up a multicenter observational study of 31 patients with NB on treatment with biological therapy (BT). NB diagnosis was made by neuroimaging, CSF analysis and/or suggestive clinical signs of central and/or peripheral nervous system involvement, excluding infectious causes or more prevalent pathology. Results are expressed as mean±SD or as median and interquartile range (IQR) as appropriate.

Results: 31 patients (16♂ / 15♀) with an average age of 39.7 ± 10.5 years. HLA-B51 was positive in 51.6% of the patients. **Table** shows the non-neurological manifestations. Regarding the neurological manifestations, 23 patients (74.2%) had parenchymal involvement (hemiparesis (n=6), brainstem involvement (n=1), encephalopathy (n = 4), optic neuropathy (n=3), dysphasia (n=1), polyneuropathy (n=6), cognitive impairment (n=4), and non-steroidal psychosis (n=1), while the remaining 8 patients (25.8%) presented aseptic meningitis as a non-parenchymal affectation (**Table**).

Prior to BT, patients had received the following treatment: oral prednisone (n=29), methylprednisolone bolus (n=9), CsA (n=10), AZA (n=17), MTX (n=16) and mycophenolate (n=2).

Demographical parameter	
- Patients, n	31
- Sex, n (%)	$16_{♀}/15_{♂}$ (51.6/48.4)
- Age, year (mean±SD)	39.7±10.5
- HLA-B51 +	16 (51.6)
Non Neurological manifestation	
- Oral ulcers	30 (96.8)
- Genital ulcers	25 (80.6)
- Uveitis	18 (58.1)
- Skin lesions	22 (70.1)
- Arthritis	7 (22.6)
- Arthralgia	21 (67.7)
- Venous/arterial thrombosis	7 (22.6)/3 (9.7)
Neurological manifestation	
Parenchymal Disease, n (%)	23 (74.2)
- Hemiparesis	6 (19.4)
- brainstem syndrome	1 (3.2)
- encephalopathy	4 (12.9)
- optic neuropathy	2 (6.5)
- dysphasia	1 (3.2)
- polyneuropathy	6 (19.4)
- cognitive dysfunction	4 (12.9)
- psychosis	1 (3.2)
Non-parenchymal Disease (aseptic meningitis), n (%)	8 (25.8)
Time from diagnosis to BT onset, months (median[IQR])	34 [10-72]
Previous immunosuppressants	
- Oral corticoids	29 (93.5)
- Bolus MTP	9 (29.0)
- Azathioprine	17 (54.8)
- Methotrexate	16 (51.6)
- Cyclosporine	10 (32.2)
- Mycophenolate	2 (6.5)
First Biological therapy	
- Infliximab	19 (61.3)
- Adalimumab	7 (22.6)
- Tocilizumab	2 (6.5)
- Golimumab	2 (6.5)
- Etanercept	1 (3.2)
Follow-up, months (median[IQR])	22 [18.5-74]
- 1st/2nd Switch, n (%)	9 (29.0) / 2 (6.5)
- Discontinued (inefficacy)	3 (9.7)
- Severe adverse events	0 (0)

After a median of 34 [10-72] months since the beginning of the neurological symptoms, the following BT was initiated: infliximab (IFX)(n=19), adalimumab (ADA)(n=7), tocilizumab (TCZ) (n=2), golimumab (GOL) (n=2) and Etanercept (ETN) (n=1). A first switch to ADA was necessary in 9 patients with IFX due to primary failure. In addition, 2 of them needed a second switch to TCZ, getting a partial response. The BT was discontinued in 5 patients, 2 of them for obtaining clinical remission and the remaining 3 for inefficacy.

After a median follow-up of 5.4±4.6 years, complete response was obtained in 15 patients, partial response in 11 and no response in the remaining 3. We observed an anaphylactic reaction and psoriasis induced by IFX, without other serious adverse events (**Table**).

Conclusion: BT, especially anti-TNF, seems effective and safe for treatment in NB.

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Abstract Number: 1694

Pharmacogenetics and Pharmacodynamics of Response to Apremilast in a Phase 3 Clinical Study in Subjects with Active Behçet's Disease

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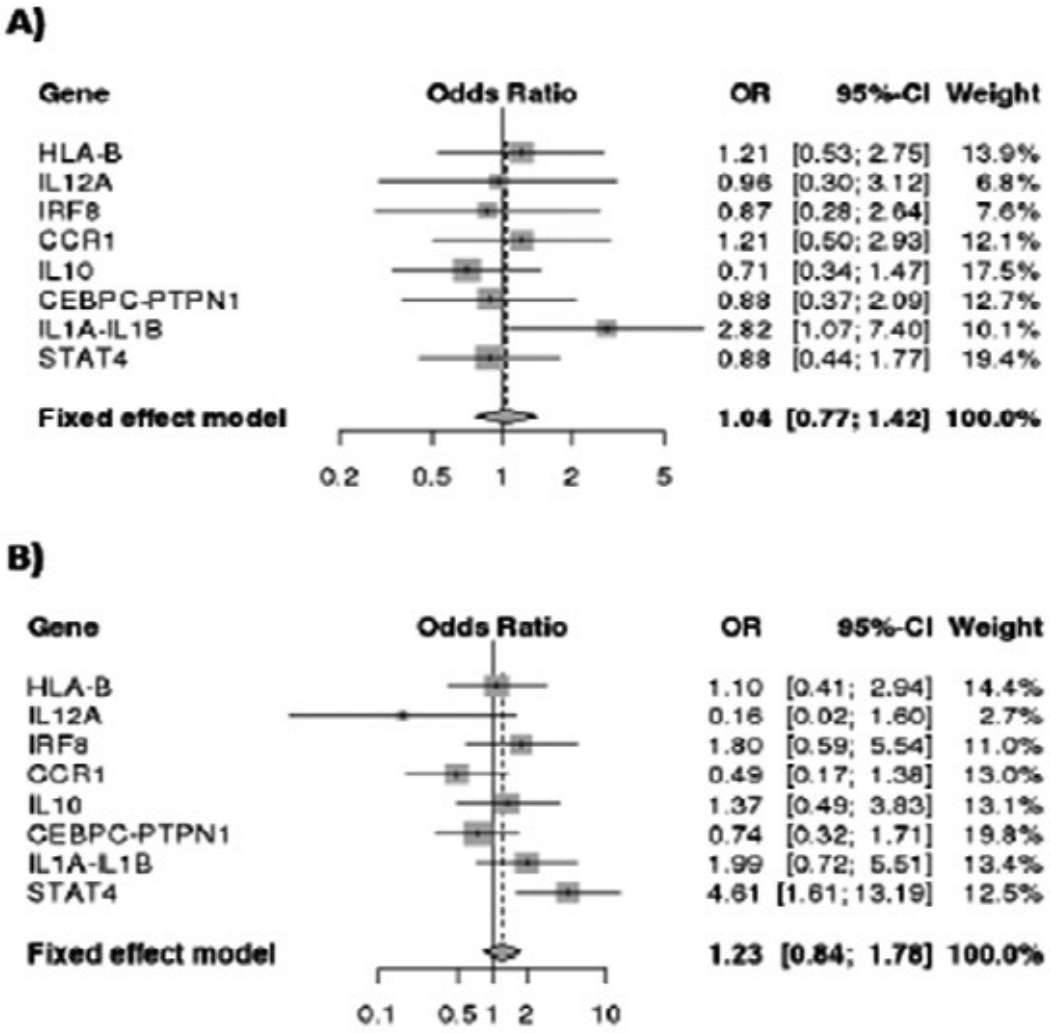
Background/Purpose: This was an exploratory analysis of genetic polymorphisms, plasma biomarkers, and blood leukocytes with clinical response in the phase 3 clinical study CC-10004-BCT-002 (NCT02307513).

Methods: Subjects with active Behçet's disease (BD) were randomized (1:1) to apremilast (APR) 30 mg BID or placebo (PBO). The primary clinical efficacy endpoint was the oral ulcer area under the curve from Week 0 to 12 (AUC_{Wk0-12}). Among 207 subjects enrolled, 140 provided consent for DNA genotyping, 116 for plasma biomarker testing, and 96 for leukocyte subset testing. Genotyping was performed on the Illumina Omni2.5 BeadChip (Covance Genomics Laboratory). TNF-α, IL-6, IFN-γ, and IL-17A levels were measured using Simoa Single Molecule Array; IL-8 and IL-23 were measured using the Human DiscoveryMAP multiplex panel (Myriad RBM). Th17, Treg, and CD3 T cells were counted using bisulfite-specific RT-PCR (Epiontis Gmbh). A rank ANCOVA model focused on between-treatment differences (APR vs. PBO) in % change from baseline for each biomarker/leukocyte subtype over the 12 weeks of treatment. Within each treatment group, the correlation of % change from baseline at Week 12 in biomarker/leukocyte subtype with the primary efficacy endpoint AUC_{Wk0-12} was examined using a univariate regression model. A separate regression model was used to assess the interaction between treatment and the biomarker/leukocyte subtype clinical response.

Results: Pharmacogenetic analysis of BD risk variants in HLA-B, IL-10, TLR2, ACE, TNF, GIMAP, PDGFRL, and UBAC2 + 55 genes associated with PDE4 biology yielded no candidate variants that were significantly associated with response to APR or PBO at a Bonferroni-corrected *P* value of 2×10^{-6}. Clinical response to APR with respect to

Figure 1. Forest Plots Showing Association With Response for Each Lead Polymorphism at a Behçet's Disease Genome-Wide Association Study Locus, and Results of a Fixed Effects Meta-analysis



Results for A) APR and B) PBO are plotted separately.

HLA-B51 yielded an OR of 1.21 (95% CI, 0.53-2.75), indicating no significant relationship (Figure 1). Pharmacodynamic changes for IL-6, IL-3, IL-17A, IL-23, and TNF-α were not statistically significant. APR treatment was associated with a significant change in IFN-γ (mean: +107.4%; median: –19.2%) vs. PBO (mean: +78.8%; median: +7.9%) (*P*=0.0077) (Table 1). Using a univariate regression model, TNF-α showed strong positive correlation with AUC_{Wk0-12} in the APR group (*r*=0.90; *P*=0.0140); IL-8 had weak positive correlation with AUC_{Wk0-12} in the APR group (*r*=0.04; *P*=0.0333). A significant negative correlation was observed between the % change from baseline in number of Th17 cells and AUC_{Wk0-12} in the APR group (*r*=–0.79; *P*=0.0392) and a significant positive correlation was observed with the % change from baseline in number of Treg cells and efficacy in the PBO group (*r*=0.94; *P*=0.0182). Of all the biomarkers and leukocyte subtypes examined in a regression model using treatment as a factor, only Treg had a statistically significant treatment interaction (*P*=0.0069) (Table 2).

Table 1. Percent Change From Baseline at Week 12 in Biomarker and Leukocyte by Treatment Groups (Rank ANCOVA, LOCF)		
	Week 12	
Biomarker Statistic	**PBO n=54**	**APR 30 mg BID n=62**
IL-6, % Δ from baseline		
Mean (SD)	83.9 (295.1)	218.4 (1608.1)
Median	−4.1	−22.2
P value		0.1236
IL-8, % Δ from baseline		
Mean (SD)	0.2 (25.8)	90.8 (624.2)
Median	0.0	0.0
P value		0.7410
IL-17A, % Δ from baseline		
Mean (SD)	21.1 (84.5)	2.4 (43.9)
Median	0.9	−5.3
P value		0.2327
IL-23, % Δ from baseline		
Mean (SD)	−3.2 (12.3)	−0.5 (16.2)
Median	0.0	0.0
P value		0.8621
IFN-γ, % Δ from baseline		
Mean (SD)	78.8 (251.5)	107.4 (695.4)
Median	7.9	−19.2
P value		0.0077
TNF-α, % Δ from baseline		
Mean (SD)	7.1 (35.0)	2.9 (28.8)
Median	0.0	0.0
P value		0.1499
	Week 12	
Leukocyte Subtype Statistic	**Placebo n=43**	**APR 30 BID (N=53)**
Total T cells, % Δ from baseline		
Mean (SD)	4.25 (31.460)	10.21 (35.247)
Median	0.56	3.37
P value		0.1079
Th17, % Δ from baseline		
Mean (SD)	4.10 (29.929)	11.23 (33.764)
Median	0.61	4.20
P value		0.2742
Treg, % Δ from baseline		
Mean (SD)	9.89 (38.627)	9.34 (36.392)
Median	0.00	0.00
P value		0.9364

ANCOVA=analysis of covariance; LOCT=last observation carried forward.

Table 2. Relationship Between AUC_{W0-12} for the Number of Oral Ulcers and Percent Change in Biomarkers from Baseline at Week 12							
	Univariate Regression Analysis						
	Placebo n=54			**APR 30 mg BID n=62**			
Biomarker	**Regression Coefficient**	**Standard Error**	***P* Value**	**Regression Coefficient**	**Standard Error**	***P* Value**	**Interaction *P* Value**
IL-6	0.04	0.050	0.4104	−0.00	0.007	0.4500	0.2996
IL-8	−0.42	0.659	0.5252	0.04	0.017	0.0333	0.4286
IL-17A	−0.18	0.179	0.3190	−0.04	0.245	0.8780	0.6600
IL-23	−0.17	1.267	0.8911	−0.00	0.652	0.9994	0.8971
IFN-γ	0.04	0.060	0.5557	−0.00	0.015	0.7439	0.4667
TNF-α	0.24	0.520	0.6453	0.90	0.361	0.0140	0.2851
Total T cells	0.02	0.497	0.9699	−0.08	0.342	0.8238	0.8716
Th17	0.08	0.536	0.8775	−0.79	0.376	0.0392	0.1761
Treg	0.94	0.391	0.0182	−0.44	0.329	0.1865	0.0069

Conclusion: Although there were no genetic predictors of clinical response to APR treatment, strong correlation was observed between the % change from baseline in plasma TNF-α with AUC_{Wk0-12} in the APR group. A negative correlation was observed between % change from baseline in Th17 cells and AUC_{Wk0-12} in the APR group and a positive association was observed between Treg cells and AUC_{W0-12} in the PBO group.

Disclosure: J. Maranville, Celgene Corporation, 3; **I. Medvedeva**, Celgene Corporation, 3; **R. Yang**, Celgene Corporation, 3; **M. Chen**, Celgene Corporation, 3; **L. Fang**, Celgene Corporation, 3; **S. Collazo**, Celgene Corporation, 3; **S. McCue**, Celgene Corporation, 3; **M. Hochfeld**, Celgene Corporation, 3; **P. Schafer**, Celgene Corporation, 3.

Abstract Number: 1695

Apremilast in Combination vs Monotherapy for Refractory Oral And/or Genital Ulcers in Behçet's Disease: National Multicenter Study of 51 Cases

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Background/Purpose: Oral and/or genital aphthous ulcers are the most common symptoms of Behçet´s disease (BD), and are often refractory to conventional treatment. The inhibitor of phosphodiesterase-4 apremilast (APR) has demonstrated efficacy in the treatment of this manifestations. Our aim was to compare the efficacy and safety of APR in monotherapy or combined with disease-modifying anti-rheumatic drugs (DMARDs) in BD patients with oral and/or genital ulcers refractory to conventional treatment.

Methods: National multicenter open-label study on 51 BD patients treated with APR at maintained standard dose of 30 mg twice daily. The main outcome was achievement of oral and/or genital ulcers remission.

Results: We included 51 patients (35 women/16 men), mean age of 47.7±13.2 years. Before APR, all patients had received several systemic conventional drugs. The main clinical symptoms for starting APR were oral (n=19) and genital (n=2) aphthous ulcers or both (n=30). Other manifestations present at APR onset were: arthralgia/arthritis (n=16),

	Combined group (N=20)	Monotherapy group (N=31)	p
Age, mean (SD) years	46.1 (12.6)	43.8 (13.8)	0.65
Sex, men/women, n/n	7/13	9/22	0.68
HLA-B51 positive, (%)	30	42	0.45
Months with Behçet disease before APR, mean (SD)	86.1 (82.6)	81.1 (72.9)	0.52
Treatment before APR onset, (%)			
Topical	53	48	0.74
Oral corticosteroids	100	90	0.15
Colchicine	100	97	0.42
NSAIDs	53	40	0.38
Methotrexate	55	52	0.81
Azathioprine	45	48	0.81
Adalimumab	30	20	0.41
Infliximab	30	13	0.13
Tocilizumab	20	3.2	**0.049**
Other treatments	65	42	0.27
Main clinical symptoms for starting APR, n (%)			
Oral ulcers	6 (30)	13 (42)	0.67
Genital ulcers	1 (5)	1 (3)	
Oral and genital ulcers	13 (65)	17 (55)	
Prednisone dose at APR onset, mean (SD), mg/d	14.4 (9.2)	13.8 (11.8)	0.68
Concomitant treatment			
Oral corticosteroids, n (%)	13 (65)	15 (48)	0.16
Colchicine, n (%)	11 (55)	14 (45)	0.38
NSAIDs, n (%)	5 (25)	10 (32)	0.57
Azathioprine, n	7	0	
Methotrexate, n	5	0	
Hydroxychloroquine, n	4	0	
Sulfasalazine, n	1	0	
Dapsone, n	1	0	
Tocilizumab, n	2	0	
Infliximab, n	1	0	
Adalimumab, n	1	0	
Follow-up on APR therapy, mean (SD), months	9.3 (7.8)	7.8 (6.3)	0.31
Side effects, (%)			
Diarrhea	21	23	0.85
Dyspepsia	21	20	0.92
Headache	26.3	13.3	0.25
Nausea	10.5	33.3	0.07
Abdominal pain	10.5	6.7	0.63
Others	0	19.4	0.62

TABLE 1. Main baseline features and follow-up of a series of 31 patients with refractory oral and/or genital ulcers due to Behçet's disease undergoing apremilast (APR) in combination or monotherapy.

folliculitis/pseudofolliculitis (n=14), asthenia (n=7), erythema nodosum (n=3), furunculosis (n=2), paradoxical psoriasis by TNFi (n=2), ileitis (n=2), deep venous thrombosis (n=2), erythematosus and scaly skin lesions (n=1), fever (n=1), eating disorder (n=1), fibromyalgia (n=1), unilateral anterior uveitis (n=1) and neurobehçet (n=1).

Excluding corticosteroids, colchicine or NSAIDs, APR was given in monotherapy in 31 cases or combined with conventional or biologic DMARDs in 20. There were not found statistically significant differences in baseline characteristics or sides effects, neither in previous treatment, except for tocilizumab that was more frequent in the combined group. The main demographic and clinical features are shown in TABLE 1.

Outcome of oral and/or genital ulcers n, (%)	Week 1-2		Week 4		Month 3		Month 6		Month 12		Month 18		Month 24	
	C n=19	M n=30	C n=19	M n=26	C n=13	M n=25	C n=12	M n=17	C n=7	M n=6	C n=3	M n=2	C n=1	M n=1
Complete resolution	8 (42.1)	11 (36.7)	12 (63.2)	20 (77)	10 (76.9)	22 (88)	7 (58.4)	14 (82.4)	3 (42.8)	3 (50)	2 (66.7)	1 (50)	1 (100)	1 (100)
Partial resolution	9 (47.4)	16 (53.4)	7 (36.8)	3 (11.5)	2 (15.4)	0	5 (41.6)	2 (11.7)	4 (57.2)	3 (50)	1 (33.3)	1 (50)	0	0
No response	2 (10.5)	3 (9.9)	0	3 (11.5)	1 (7.7)	3 (12)	0	1 (5.9)	0	0	0	0	0	0
p value	0.9		0.1		0.1		0.1		0.8		0.7		0.7	

C= combined; M= monotherapy; n= available data.

TABLE 2. Evolution of main symptoms with apremilast in combination vs monotherapy.

After a mean follow-up of 8.45±6.9 months, most of the patients experienced clinical improvement in both groups, without statistically significant differences. TABLE shows the evolution of the mucocutaneus manifestations in each group, combined vs monotherapy. In this period of time, 33 patients developed any side-effect (TABLE 1), 11 (55%) patients in the combined group and 22 (70%) patients in the monotherapy group), most of them mild and during the first 3 months of treatment.

Apremilast was discontinued in 11 patients due to: not obtaining the expected improvement (5), intense gastrointestinal adverse effects (n=4), desire of pregnancy (n=1) and development of neurological involvement (n=1).

Conclusion: Apremilast leads to a rapid and maintained improvement in many patients with highly refractory mucocutaneous ulcers of BD. This therapy seems as effective and safe in monotherapy as in combination with DMARDs.

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Abstract Number: 1696

Is the Risk of Tuberculosis Increased in Behçet's Disease Compared to Other Rheumatological Disorders After Anti-TNF-α Treatment?

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor necrosis factor (TNF)-α inhibitors are extensively utilized in the treatment of inflammatory rheumatic diseases. These agents increase the risk of tuberculosis (TB), especially in countries with a high incidence, such as Turkey. This study aims to evaluate the incidence of tuberculosis after anti-TNF-α treatment for Behcet's disease (BD) and to report the risk in comparison to other disorders in our center.

Methods: The data of 1302 patients who received anti-TNF-α treatment for more than six months between 2005 and 2018 were assessed retrospectively. Demographic features, type of aTNF-α treatment used, treatment duration, tuberculin skin test (TST) and Quantiferon results, use of isoniazid prophylaxis and the development of tuberculosis were recorded. We compared the disease characteristics of patients with and without tuberculosis after aTNF-α treatment.

Results: Among the 1302 patients (F/M: 698/604, mean age: 48.8±13.2 years), aTNF-α agents were most commonly used in ankylosing spondylitis (AS) patients (n=659, 50.9%). Median aTNF-α treatment duration in all patients was 32.5 months (Q1-Q3: 12-61). During the follow-up period, 13 patients developed tuberculosis. Seven (54%) of the TB patients had pulmonary and six (46%) had extrapulmonary TB. Median time from the initiation of aTNFα therapy to the diagnosis of TB was 40 months (Q1-Q3: 22-56). The characteristics of all patients receiving aTNFα therapy and developed TB were displayed in Table 1. The TNFα antagonists patients receiving were Etanercept in 4, Adalimumab in 5, Infliximab in 2 and Certolizumab in 2 patients.

TB was detected in 3 (7.5%) of 40 BD patients and 10 (0.8%) of 1256 non-Behçet's patients. There was a statistically significant increase in TB risk, in Behcet's patients after aTNF-α treatment when compared to the rest of the group (p=0.006). When we combined our patients with a large, multicenter cohort from Turkey, among 8320 patients who received aTNF-α treatment(1), TB developed in 8 (4.9%) patients among 161 BD and 75 (0.9%) patients in 8159 non-Behçet's patients (p=0.0002).

Conclusion: Comparable to the previous literature from Turkey, our results verified an increased risk of tuberculosis after aTNF-α treatment in patients with Behçet's Disease compared to other rheumatological disorders. Pro-inflammatory nature of BD with a higher risk for infections or concomitant therapies such as corticosteroids might

Table 1. Characteristics of The Patients Receiving Anti-TNF-α Therapy

	WHOLE GROUP	TB
N	1302	13
Mean Age ± SD, Years	48.8 ± 13.2	51.6 ±4
Male	604(46.4%)	10(77%)
Female	698(53.6%)	3(23.1%)
TST Positivity	806/ (1144) (70.5%)	7/12(58.3%)
Quantiferon Positivity	50/199 (25%)	2/2 (100%)
Isoniazid Prophylaxis	892(69%)	9(69%)
Anti-TNF-A Agent		
Etanercept	515 (39.6%)	7 (53.8%)
Adalimumab	524 (40.2%)	5 (38.5)
Infliksimab	384 (29.5%)	5 (38.5%)
Certolizumab	85 (6.5%)	2 (15.4%)
Golimumab	80 (6.1%)	0
DISEASE SUBTYPE		
Rheumatoid Arthritis	490 (37.6%)	4 (30.8%)
Ankylosing Spondylitis	659 (50.6%)	5 (38.5%)
Psoriatic Arthritis	98 (7.5%)	1 (7.7%)
Behçet's Disease	40 (3.1%)	3 (23.1%)
Takayasu's Arteritis	14 (1.1%)	0

Except where indicated otherwise, values are the number/total number (percent) of patients.
TNFα: tumor necrosis factor; TB: tuberculosis; TST: TB skin test; INH: isoniazid

influence the higher TB risk in BD. This observation should be taken into account when anti-TNF-a agents are used in refractory BD patients with major organ involvement.

Reference

1) Kisacik B, et al. Characteristics Predicting Tuberculosis Risk under Tumor Necrosis Factor-α Inhibitors: Report from a Large Multicenter Cohort with High Background Prevalence. J Rheumatol. 2016 Mar;43(3):524-9.

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Efficacy of Apremilast for Oral Ulcers Associated with Active Behçet's Syndrome over 64 Weeks: Long-term Results from the Japanese Subgroup in a Phase III Study

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SESSION INFORMATION

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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

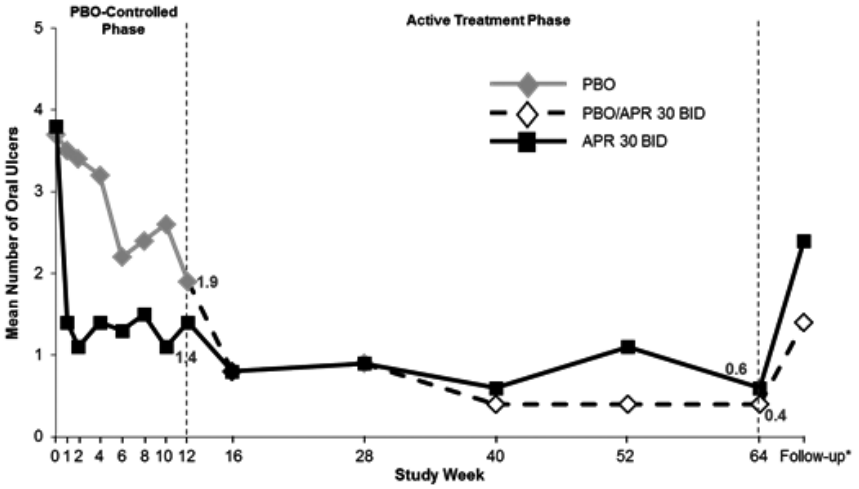
Background/Purpose: Behçet's syndrome is a chronic, multi-system, variable vessel vasculitis characterized by painful, recurrent oral ulcers (OU) that can be disabling and may impair quality of life. Apremilast (APR), an oral phosphodiesterase 4 inhibitor, demonstrated efficacy in the treatment of OU of Behçet's syndrome in a phase III, multinational, randomized, double-blind, placebo (PBO)-controlled study (RELIEF). Here, we report efficacy and safety of APR assessed over 64 weeks in the subgroup of Japanese patients in RELIEF.

Methods: Patients were randomized (1:1) to APR 30 mg BID or PBO BID for a 12-week PBO-controlled phase, followed by a 52-week active treatment extension. Patients were stratified by region (Japan/other). Eligible patients were ≥18 years of age, had active Behçet's syndrome, with ≥3 OU at randomization or ≥2 OU at screening and randomization and without active major organ involvement. The primary efficacy endpoint was area under the curve for the number of OU over 12 weeks (AUC_{Wk0-12}). Clinical improvement in OU was evaluated by assessments of OU number and pain (100 mm visual analog scale), disease activity (Behçet's Disease Current Activity Form [BDCAF], composed of the Behçet's Disease Current Activity Index [BDCAI] and Patient's and Clinician's Perception of Disease Activity, and Behçet's Syndrome Activity Score [BSAS]) over 64 weeks. An ANCOVA model was used to analyze the primary endpoint. In the Japanese subgroup, Week 12 variables were prespecified without multiplicity adjustment. Nominal *P* values are given. Data at Week 64 are as observed.

Results: Of the 207 randomized patients, 39 were Japanese (APR: n=19; PBO: n=20); 26 Japanese patients completed the active treatment phase (12 initially randomized to APR and 14 initially randomized to PBO). Consistent with the findings of the overall study population, the primary endpoint of AUC_{Wk0-12} was significantly lower for APR vs PBO (115.9 vs 253.3; nominal *P*=0.0168). At Week 12, significantly more Japanese patients had OU complete response with APR (57.9%) vs PBO (25.0%) (nominal *P*=0.0426); numerically greater reductions in OU pain were observed with APR vs PBO (–17.0 [95% CI: –39.1, 5.1]; nominal *P*=0.1273). Improvements in mean number of OU (**Figure 1**), OU pain (**Figure 2**), complete and partial response rates, as well as disease activity assessments (BDCAF and BSAS) were observed at Week 12 and generally maintained in Japanese patients continuing APR 30 mg BID treatment for up to 64 weeks and emerged in those who switched from PBO to APR. At 4 weeks after APR treatment discontinuation, worsening in measures of oral ulcer disease was observed in both treatment groups. Adverse event (AE) rates were similar in the 2 groups during the PBO-controlled period (APR: 73.7%; PBO: 75.0%). Common AEs were diarrhea, upper respiratory tract infection, nausea, and headache. No new safety concerns were identified up to 64 weeks.

Conclusion: APR demonstrated efficacy in the treatment of OU in a subset of Japanese patients with Behçet's syndrome from RELIEF. Benefits were sustained up to 64 weeks with continued APR treatment. Safety findings were consistent with the known AE profile of APR.

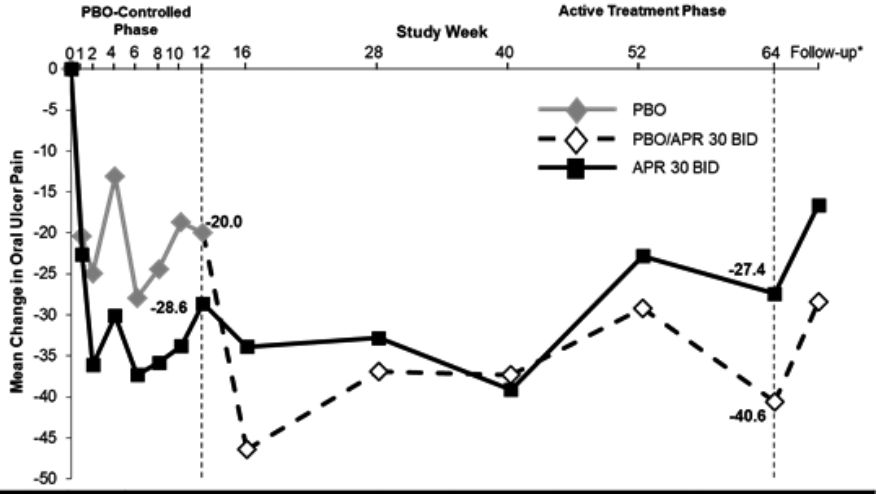
Figure 1. Mean Oral Ulcer Count Over 64 Weeks in Japanese Subgroup



Weeks	0	1	2	4	6	8	10	12	16	28	40	52	64	68
PBO, n	20	20	19	19	17	16	16	16						
PBO/APR, n									16	15	14	14	14	20
APR, n	19	18	18	17	18	17	17	17	17	17	15	12	12	17

ITT population; data as observed. *Patients entered a 4-week posttreatment observational follow-up phase following discontinuation of APR or before Week 64. n=number of patients.

Figure 2. Mean Change in Oral Ulcer Pain VAS Over 64 Weeks in Japanese Subgroup



Weeks	0	1	2	4	6	8	10	12	16	28	40	52	64	68
PBO, n	20	20	19	19	17	16	16	16						
PBO/APR, n									16	15	14	14	14	20
APR, n	19	18	18	17	18	17	17	17	17	17	15	12	12	17

Baseline mean OU pain VAS (0-100): PBO, 61.7; APR, 54.3.
ITT population; data as observed. *Patients entered a 4-week posttreatment observational follow-up phase following discontinuation of APR or before Week 64. n=number of patients.

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2, 8, Mitsubishi-Tanabe, Bristol-Myers, Eisai, Chugai, Takeda, Abbvie, Astellas, Daiichi-Sankyo, Ono, MSD, Taisho-Toyama., 2, Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, 2, Novartis, 8, Ono, 2, Pfizer, 5, 8, Pfizer Inc, 8, Roche, 5, Sanofi, 2, Takeda, 2, 8, Teijin, 8, UCB, 2, YL Biologics, 8; **H. Kono**, Celgene Corporation, 2; **S. Sugii**, None; **M. Kishimoto**, AbbVie, 8; **S. Cheng**, Celgene Corporation, 3; **S. McCue**, Celgene Corporation, 3; **M. Chen**, Celgene Corporation, 3; **M. Paris**, Celgene Corporation, 3; **H. Dobashi**, None.

Abstract Number: 1698

Development of Machine Learning Models (Artificial Neural Networks) for Prediction of Vision Threatening Behçet's Disease

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SESSION INFORMATION

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Background/Purpose: Ocular involvement in Behçet's Disease (BD) is associated with chronic damage and high morbidity; however, limited evidence is available on risk factors to recognize the subset of BD patients at jeopardy to develop vision-threatening disease (VTD). There is a clear need for identification of those patients early in order to reduce morbidity. Machine learning (ML), including Artificial Neural Networks (ANNs), have been used to forecast

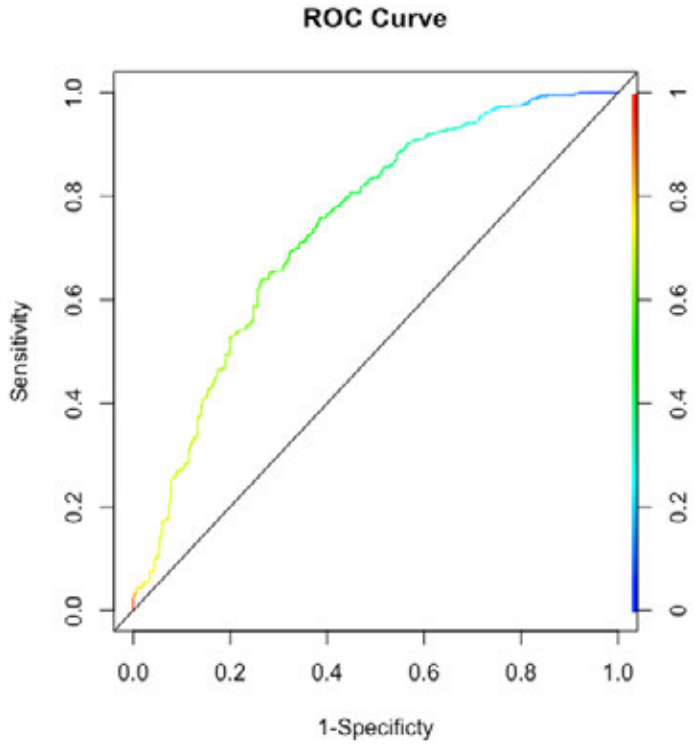

Figure 1. The ROC graph of the Logistic regression analysis for predicting vision-threatening outcomes in BD patients.

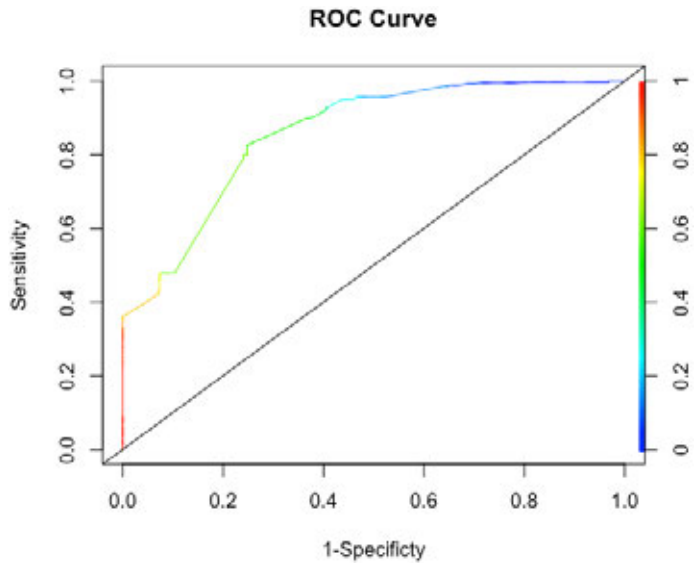

Figure 2. The ROC graph of the selected artificial neural networks for predicting vision-threatening outcomes in BD patients.

complex disease outcomes in the medical setting including rheumatology. Using the Egyptian College of Rheumatology (ECR) cohort data available, we aimed to develop a data-driven ECR-BD accurate model to predict the risk of VTD using ML techniques, with a combination of demographic, clinical, and biochemical information.

Methods: Out of an ECR-BD, a large multicentric cohort, 1094 patients fulfilling the 2014 International Study Group diagnostic criteria for BD were included. VTD was determined by the presence of retinal disease and/or optic nerve affection and/or occurrence of blindness. Twenty-seven variables including patient demographics, clinical manifesta-

tions, comorbidities, medications and laboratory data for each patient were used as predictors (inputs) for building-up and testing the ANNs. Prior to the training of the ANNs, the dataset was randomly split into training (80%), and testing (20%) data. The testing set was used to evaluate the final performance of the networks. Inputs were normalized before being entered in networks. Several networks with different properties were trained, and the performance of each network was evaluated. In order to evaluate and select the most accurate network, we used a confusion matrix (sensitivity, specificity, and accuracy), the receiver operating characteristic (ROC) curve and the area under the ROC curve(AUC) of each network and compared them to the logistic regression (LR) model results. R studio v. 3.5.0 software was used to design the neural networks and LR.

Results: A total of 1094 BD patients [71.5% were men, mean ± SD age; 36.1 ± 10 years; and median disease duration 72 months] had complete ocular manifestations data. The mean BD current activity form was 4.7±3.7. About 75% of the ECR-BD cohort had at least one form of ocular involvements, 49.8% of them had VTD. By applying ANNs, we obtained a model (2 hidden layer and 4 neurons) characterized by a sensitivity of 90%, a specificity of 64%, an accuracy of 77%, and AUC value of 0.86, able to predict VTD. These measures for the LR were 73%, 65%, 76.8%, and AUC value of 0.74 respectively. The ANNs results suggest that C-reactive protein is the most important positive predictor of VTD, followed by disease duration, oral ulcers, and presence of diabetes mellitus.

Conclusion: These findings suggest that the artificial neural network could be an accurate technique for prediction of vision-threatening BD. Therefore, building accurate ML models allowed to identify patients at risk to develop VTD in a large BD cohort. The application of this model on longitudinal data in future work is required.

Reference

1) Gheita TA, ECR-BD study group, et al. Behçet's Disease in Egypt: a multicenter nationwide study on 1526 adult patients and review of the literature. Clin Rheumatolo. 2019 May 22.

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Abstract Number: 1699

Disease Course of Behçet's Syndrome Patients Not Fulfilling International Study Group Criteria at Presentation

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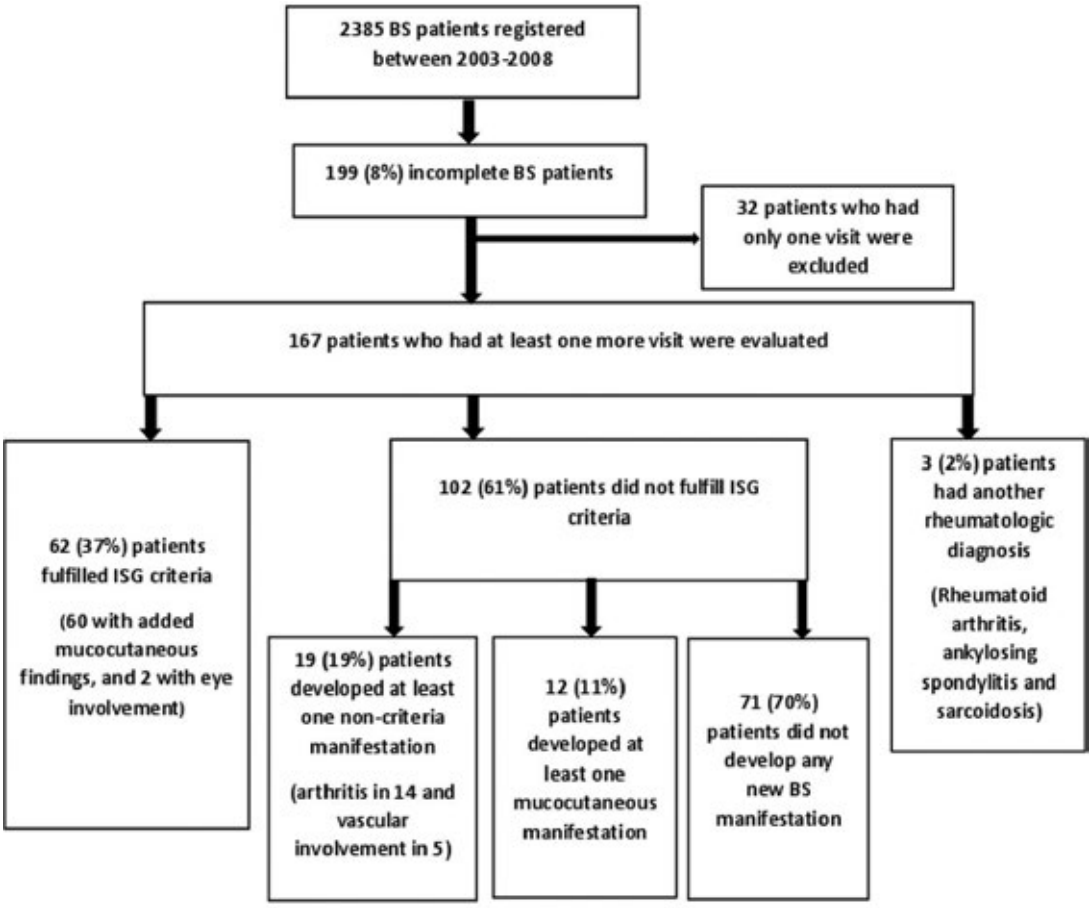

Figure Flowchart of the study population

SESSION INFORMATION

Session Date: Monday, November 11, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Behçet's syndrome (BS) shows a heterogeneous phenotype involving many organ systems and is diagnosed by recognizing the coexisting manifestations. Patients may have major organ manifestations before they fulfill the International Study Group (ISG) criteria and failure to recognize BS and treat promptly may lead to permanent damage in such patients. We aimed to determine the magnitude of this problem by identifying the presentation patterns and the outcome of patients who did not fulfill ISG criteria when they presented to our clinic but were followed and treated for manifestations strongly suggesting BS.

Methods: We conducted a retrospective chart review of all BS patients who were registered between 2003 and 2008. Among the 2385 patients, there were 199 (8%) patients who did not fulfill ISG criteria at their initial visit but had manifestations strongly suggesting BS. A standard form was used for recording data on demographic features, BS manifestations, and treatment at the initial visit and during follow-up. An attempt was also made to invite them to our dedicated clinic to assess the outcome.

Of these 199 patients, 6 died (massive hemoptysis due to pulmonary artery aneurysm in 1, pancreatic cancer in 1, lung adenocarcinoma in 1 and unknown reasons in 3), 32 including 3/6 patients who died due to unknown reasons had only 1 visit, 54 including 3/6 who died could not be reached but there were enough data in the charts for the purposes of this study, 71 were contacted by telephone and 42 were evaluated in the clinic. Overall, 167 patients who had at least one more visit with a median follow-up of 11 years (IQR: 7-12) were analyzed.

Results: Among the 167 patients (M/W: 77/90, mean age: 33.4 ± 11.4 years), 62 (37%) had major organ involvement (eye disease in 32, venous thrombosis in 22, arterial aneurysms in 8, nervous system disease and gastrointestinal disease in 1 patient each) at the initial visit. Eighteen (11%) did not have recurrent oral ulcers but had major organ involvement at the initial visit. Thirty-two patients (19%) had a family history of BS.

49/113 patients we could contact and 13/54 patients we could not reach but were being followed in our clinic had fulfilled ISG criteria. Thus, a total of 62 (37%) patients fulfilled ISG criteria after a median follow-up of 1.5 years (IQR: 1-4.5). Sixty of these 62 patients fulfilled ISG criteria with added skin-mucosa findings and 2 with added eye involvement.

Among the remaining 102 patients who did not fulfill ISG criteria during the follow-up, 19 (19%) patients had developed at least one non-criteria BS manifestation (arthritis in 14 and vascular involvement in 5) after a median follow-up of 4 years (IQR: 1-6). 12 (12%) had developed at least one mucocutaneous manifestations. Three patients had another rheumatologic diagnosis (Figure).

Conclusion: In this 10-year follow-up study among at least 167 BS patients not fulfilling ISG criteria at presentation, 62 of 167 (37%) patients had fulfilled ISG criteria after a median duration of 1.5 years. In 60/62 (97%) of these patients, this was additional skin-mucosa disease.

Disclosure: S. Esatoglu, None; **S. Bilgin**, None; **C. Sulu**, None; **V. Hamuryudan**, None; **Z. Kutlubay**, None; **M. Melikoglu**, None; **I. Fresko**, None; **H. Yazici**, None; **G. Hatemi**, Abbvie, Mustafa Nevzet, UCB, 8, Bayer, Eli Lilly, 5, BMS, Celgene Corporation, Silk Road Therapeutics, 2, Silk Road Therapeutics, 2.

Abstract Number: 1700

Clinical Characteristics and the Level Disease Activity of Behcet´s Disease in China: A Study Based on Smart System of Disease Management (SSDM)

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SESSION INFORMATION

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Background/Purpose: Behcet´s disease (BD) is a systemic autoimmune disease that affects multiple organ systems with recurrent oral ulcers, genital ulcers and skin lesions, which might be accompanied by psychological abnormalities such as anxiety or depression. Behcet´s Disease Current Activity Form (BDCAF) and Electronic Medical Record-based Activity Index (EMRAI) are commonly used internationally to evaluate the disease activity of BD; Hospital Anxiety & Depression Scale (HADS) is commonly used to evaluate patients' mental health.

This study aimed to analyze the clinical characteristics, the level of disease activity, and the incidence of anxiety and depression for Chinese BD patients. Patients can perform self-management of disease with Smart System of Disease Management (SSDM).

Methods: SSDM is a series of doctor-patient interactive applications for self-management of patients with chronic diseases. Patients can perform BDCAF, EMRAI and HADS self-assessment with SSDM and upload the self-assessment data to their authorized doctors. The SSDM patients' application system integrates the BDCAF and EMRAI into one scoring system. Patients could obtain scores of BDCAF and EMRAI by responding to one questionnaire through SSDM. Patients with a score ≥4, will be diagnosed as BD. HADS is divided into two sub-tables of HADS-Anxiety (HADS-A) and HADS- Depression (HADS-D). A patient's HADS score >10, will be diagnosed with anxiety or depression.

Results: From April 2017 to May 2019, 1,072 BD patients from 225 hospitals used SSDM, with a mean age of 38.78±12.23 (14~78) years old, and median disease duration of 21.77 months. 513 patients performed BDCAF and

Table 1. Clinical Characteristics of different systems in Chinese BD patients.

Presence of clinical features	Total	Males	Females	P value
Oral ulcer	76.29% (666)	80.27% (240)	74.22% (426)	0.046*
Genital ulcer	40.21% (351)	32.11% (96)	44.43% (255)	<0.001**
Epididymitis	4.70% (41)	10.03% (30)	0 (0)	<0.001**
Erythema	24.40% (213)	26.09% (78)	23.52% (135)	0.402
Skin lesions	24.28% (212)	28.09% (84)	22.30% (128)	0.058
Superficial thrombophlebitis	29.21% (255)	21.74% (65)	33.10% (190)	<0.001**
Headache	29.21% (255)	21.74% (65)	33.10% (190)	<0.001**
Joint pain	43.87% (383)	46.82% (140)	42.33% (243)	0.205
Arthritis	10.54% (92)	11.71% (35)	9.93% (57)	0.418
Gastrointestinal involvement	21.76% (190)	21.40% (64)	21.95% (126)	0.853
Nausea or vomiting or abdominal pain	16.95% (148)	17.39% (52)	16.72% (96)	0.803
Diarrhea with altered or frank blood	9.28% (81)	9.70% (29)	9.06% (52)	0.757
Ocular symptoms	48.11% (420)	61.87% (185)	40.94% (235)	0.316
Red eye	22.34% (195)	29.77% (89)	18.47% (106)	<0.001**
Painful eye	18.56% (162)	18.39% (55)	18.64% (107)	0.929
Blurred vision	31.73% (277)	36.45% (109)	29.27% (168)	0.03*
Reduced vision	29.90% (261)	25.75% (77)	32.06% (184)	0.054
Nervous involvement	21.42% (187)	22.74% (68)	20.73% (119)	0.492
Blackout	2.86% (25)	4.35% (13)	2.09% (12)	0.058
Difficulty with speech or hearing	6.76% (59)	7.69% (23)	6.27% (36)	0.428
Double vision	4.93% (43)	6.35% (19)	4.18% (24)	0.159
Weakness or loss of feeling in the face, arm or leg	4.93% (43)	6.69% (20)	4.01% (23)	0.082
Memory loss	9.74% (85)	10.03% (30)	9.58% (55)	0.831
Loss of balance	4.93% (43)	5.35% (16)	4.70% (27)	0.675
Vascular involvement	14.20% (124)	16.72% (50)	12.89% (74)	0.124
Chest pain	2.86% (25)	4.35% (13)	2.09% (12)	0.058
Breathless	6.76% (59)	7.69% (23)	6.27% (36)	0.428
Coughed up blood	4.93% (43)	6.35% (19)	4.18% (24)	0.159
Pain, swelling or discoloration of either the face, arm or leg	4.93% (43)	6.69% (20)	4.01% (23)	0.082

P values are for the comparison between the males and females.

EMRAI self-assessment 873 times, 130 patients repeat assessments for 360 times. The mean score of BDCAF and EMRAI are 3.69±2.25 and 3.60±2.03, respectively. The matching degree of the two score was 0.8818.

The most common clinical characteristics were oral ulcers (76.9%), joint pain (43.87%) and genital ulcer (40.21%). The comparative study between males and females revealed significant difference in the aspects of epididymitis (10.03% vs 0, $p< 0.001$), genital ulcer (32.11% vs 44.43%, $p< 0.001$), headache (21.74% vs 33.10%, $p< 0.001$), superficial thrombophlebitis (21.74% vs 33.10%, $p< 0.001$) and red eye (29.77% vs 18.47%, $p< 0.001$). Please see details in Table 1.

The incidence of anxiety and depression was 15% and 16%, among 134 patients assessed for HADS.

Conclusion: Chinese BD patients can effectively perform BDCAF and EMRAI self-assessment with SSDM. The results of the assessment conducted by the two scoring systems are similar. The clinical characteristics of Chinese BD were different depending on gender.

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Abstract Number: 1701

Amyloidosis in Behcet's Disease: Experience of a Vasculitis Centre at Silk Road

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Bechet's disease (BD) is a vasculitis characterized by oral aphtae, genital ulcers, skin lesions, uveitis and with less frequent involvement of the neurological, vascular and gastrointestinal tract. Amyloidosis is an uncommon but highly morbid complication of BD. This study is aimed to investigate frequency, clinicodemographic features and disease course of amyloidosis in Behcet's Disease.

Methods: Patients with vasculitis diagnosis have been recording at Hacettepe University Vasculitis Center (HUVAC) database since October 2014. Enrolled 451 Adult BD patients were searched in terms of clinically and histopathologically amyloidosis. Demographics, clinical features and treatment characteristics of patients were re-evaluated.

Results: Two hundred thirty seven (52.5%) patients were male and 211 (46.8%) of all patients had only mucocutaneous disease. Mean age at BD diagnosis was 30.9 ±8.2 years. Five patients (1.1%) had biopsy-proven AA-type amyloidosis diagnosis (Table). All BD-amyloidosis patients were male and presented with nephrotic-range proteinuria. Diarrhea was observed in two patients. There was no clinical evidence about familial mediterranean fever (FMF) and other rheumatic or infectious etiology for development of amyloidosis in any patient. All of five patients had genital ulceration. During follow-up time after amyloidosis diagnosis (median 51 month), end-stage kidney disease (ESKD) were developed in two patients (No: 4 and 5) and no death was observed. Interferon alpha and Tocilizumab were emerging drugs used in these patients. Proteinuria almost completely regressed in two patients (No: 2 and 3).

Conclusion: BD is one of the rare causes of the AA amyloidosis. Furthermore amyloidosis in BD is an important but it is relatively rare. Therefore other possible etiologies (e.g. FMF) should be excluded. Amyloidosis could result in life-threatening disease course. Amyloidosis-related symptoms and findings (e.g. proteinuria) may be treatable according to data from our cohort and literature. Definite predictors for development of ESRD are unknown in amyloidosis of

No	Age at Dx of BD, Gender	Age at Dx of Amyloidosis	Follow-up time (for Amyloid, Month)	Bx	Amyloidosis Type	MEFV gene	FMF Clinical Findings	HLA-B51 / B5	OA	GU	Skin		Skin Pathergy Test	Uveitis	Arthritis	GIS	Neu	Vasc	Other Symptoms (Related with amyloidosis)	First Cre/ Last Cre/ ESKD	Proteinuria at Amyloidosis Dx	Proteinuria at Last Visit	Comorbidity (Except CKD)	Death	Treatment
											Papulopustular	EN													
1	30, M	30	4	Kidney	AA	- / -	-	B5-B51+	+	+	+	-	-	+	-	-	-	+	-	F. Cre:0.6/ L.Cre:0.7/ HD: -	10269 mg	7959 mg	-	-	TCZ, COL, ACEi
2	30, M	50	162	Colon	AA	M694V/-	-	*Unk.*	+	+	-	-	-	+	-	-	-	+	-	F. Cre:0.88/ L.Cre: 0.98/ HD: -	11500 mg	83 mg	-	-	COL, IFN, ACEi
3	40, M	58	50	Kidney	AA	- / -	-	*Unk.*	+	+	+	+	-	-	-	-	-	-	-	F. Cre:0.71/ L.Cre: 1.0/ HD: -	8354 mg	156 mg	-	-	COL, TCZ, ACEi
4	27, M	55	51	Kidney	AA	*Unk.*	-	*Unk.*	+	+	-	+	-	+	+	-	-	-	Diarrhae	F. Cre:2.99/ HD: +	4700 mg	Anuria	-	-	COL, ACEi
5	53, M	53	84	Kidney	AA	*Unk.*	-	*Unk.*	+	+	+	+	-	-	-	-	-	-	Diarrhae	F. Cre: 1.0/ HD +	8611 mg	Anuria	HBV, Hypo-thyroidia	-	COL, AZA, TAL, IFX, ACEi

(**Abbreviations: ACEi:** ACE inhibitors, **AZA:** Azatioprine, **BD:** Behcet's Disease, **Bx:** Biopsy, **Cre:** Creatinin, **CKD:** Chronic Kidney Disease, **COL:** Colchicine, **Dx:** Diagnosis, **EN:** Erythema Nodosum, **ESKD:** End-Stage Kidney Disease, **GIS:** Gastrointestinal System, **GU:** Genital Ulcer, **F:** Female, **FMF:** Familial Mediterrenean Fever, **HBV:** Hepatitis B Virus, **HD:** Hemodialysis, **IFN:** Interferon-alpha, **IFX:** Infliximab, **M:** Male, **Neu:** Neurological involvement, **No:** Number, **OA:** Oral Aphtae, **TAL:** Talidomide, **TCZ:** Tocilizumab, **Unk.:** Unknown, **Vasc:** Vascular involvement)

Demographic Features and Disease Characteristics of BD Patients with Amyloidosis

BD. However early recognition of these patients and awareness of clinicians about this rare complication is quite important.

Disclosure: E. Bolek, None; **E. Erul**, None; **G. Yardımcı**, None; **L. Kilic**, None; **A. Akdoğan**, None; **O. Karadag**, None.

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Target Organ Associations in Polyarteritis Nodosa (PAN): Results of a Worldwide Collaboration Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Session Time: 9:00AM–11:00AM

Background/Purpose: Polyarteritis nodosa (PAN) is a rare type of the systemic vasculitides with heterogeneous presentations.There is a paucity of information on the current phenotypes, ethnic and geographic differences of PAN. A global PAN study group has been working for clinical subphenotypes and GWAS studies.

Methods: A retrospective survey of databases from centres was done for PAN patients fulfilling the EMEA Vasculitis Classification algorithm. Patients with typical angiographic and/or histopathologic findings consistent with PAN were enrolled. In addition to baseline clinical characteristics, treatment and outcome data was recorded.

Factor analysis was used to analyze target organ associations of these 229 patients. Four factors were identified by factor analysis of variables sex, ethnicity, disease onset age, pediatric-onset, monogenic disease relationship, HBV relationship, any cutaneous features, any musculoskeletal symptoms, any constitutional symptoms, any other

	Factors			
	Factor 1	**Factor 2**	**Factor 3**	**Factor 4**
Any of gastrointestinal findings	0,723			
Renal involvement	0,681			
Cutaneous involvement	-0,585			
Testicular involvement	0,541			
Any of musculoskeletal findings		0,822		
Any positive constitutional symptoms		0,647		
Any of neurologic findings			0,770	
Ear nose throat involvement			0,699	
Any monogenic relationship FMF or ADA				0,877

Note: Only loadings above 0.5 are displayed

Table Target organ associations in Polyarteritis Nodosa (PAN)

involved areas (abdominal, renal, testicular, neurologic, ear nose and throat (ENT), cardiac, pulmonary), positive angiographic findings and relapses.

Results: PAN Cohorts from 5 different countries were investigated in this study. (Japan: n=39, Mexico: n=29, Slovenia: n=14, TUR: n=100, UK: n=47). Totally 229 (M/F: 130/99 and Caucasian 70.3%, Asian 17.0%, and Hispanic 12.7%) patients were included in the study. Four were HBV-related, and 21 of TR patients had a monogenic form of disease (Familial Mediterranean Fever association in 14, deficiency of adenosine deaminase 2-DADA2- in 7).

20.5% of patients were cutaneous-only PAN patients. 45.4% of patients had radiologic, and 69.4% had biopsy-proven PAN. Median age at disease onset was 38.5 (IQR 24.0-57.0) years. During a median 60 (16-130) months follow-up, 23 patients died.

Factor analysis revealed 4 factors that explained 60% of the original information on the matrix as follows: Factor 1,represented the association between any of gastrointestinal findings, renal involvement, and testicular involvement which are negatively associated with any of cutaneous involvement; **Factor 2,**the association between any of musculoskeletal findings, and any positive constitutional symptoms; **Factor 3,**any neurologic involvement was associated with ENT involvement, **Factor 4,**any monogenic relationship FMF or ADA itself. The eigenvalues of the 4 factors were 1.853, 1.297, 1.164, and 1.085, in decreasing order, i.e., the highest contribution to the overall variance in the matrix came from the togetherness of the 3 clinical manifestations that made up Factor 1. Factors, their relative contributions to the total variance and the communalities for each of the variables are shown in Table.

Conclusion: The target organ associations found in this study could support the hypothesis of subphenotypes in PAN. Factor 1-more organ involvement with less cutaneous features seems to be the most severe form. Patients with any monogenic genetic background (FMF or DADA2) have distinct target organ associations. Even though ENT involvement was rare, its association with neurologic involvement might define a different subphenotype- looks like a ANCA negative medium vessel vasculitis.

Disclosure: O. Karadag, None; **S. Furuta**, None; **A. Hocevar**, None; **U. Gazel**, None; **A. Hinojosa-Azaola**, None; **S. Ugurlu**, None; **S. Gopaluni**, None; **E. Bolek**, None; **B. Armagan**, None; **F. Alibaz-Oner**, None; **M. Tomšič**, None; **G. Ayan**, None; **A. Yazici**, None; **E. Martin-Nares**, None; **S. Sánchez-Cubías**, None; **M. Nedim Tas**, None; **A. Cefle**, None; **K. Aksu**, None; **H. Kono**, Celgene Corporation, 2; **T. Kawakami**, None; **Y. Abe**, None; **T. Kaşifoğlu**, None; **M. Tezcan**, None; **O. Gercik**, None; **S. Kilickap**, None; **H. Direskeneli**, None; **S. Ozen**, Enzyvant, 8; **A. Ertenli**, None; **D. Jayne**, Astra Zeneca, 5, Boehringer-Ingelheim, 5, Celgene, 5, ChemoCentryx, 2, 5, GSK, 2, 5, Infla-Rx, 5, InflaRx GmbH, 5, Insmed, 5, Roche Genetech, 2, Sanofi Genzyme, 2, Takeda, 5.

Abstract Number: 1703

Increased Levels of IL-2 and IL-4 Promote Th17/Treg Immune Imbalance in Patients with Behcet's Disease

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Behcet's disease(BD) is a multisystem inflammatory disorder of unknown etiology.Improved understandings indicate the Th17/Treg immune imbalance may play a critical role in BD's pathogenesis, which was accompanied by an increased levels of IL-17 and IL-23.The aim of this study was to examine associations between levels of a broad selection of cytokines and Th17/Treg immune balance in patients with BD.

Methods: The study included 67 BD patients and 66 healthy controls. The circulating levels of lymphocyte subpopulations were detected by flow cytometry for all participants.Serum levels of the following 6 cytokines were determined in the same samples using a cytometric beads array: IL-2, IL-4,IL-6,IL-10,INF-γ and TNF-α for all BD patients.

Results: A significant increase in the Th1 cells and Th17 cells and the ratio of Th1/Th2 and Th17/Treg were observed. When patients with BD were divided into active (patient index score $\geq$ 2 in the BDCAF) and inactive groups, the absolute counts of Th17 cells and the ratio of Th17/Treg tended to be higher in patients with active BD, and this observation was statistically insignificant. A significantly positive correlation was found between the investigated cytokines and Th17/Treg:i.e.,IL-2(r=0.261,P=0.033) and IL-4(r=0.292,P=0.016)(P$\geq$0.2 for all other cytokines),and Th17 cells(r=0.246,P=0.045vs r=0.291,P=0.017).

Conclusion: The T cell homeostasis perturbation,especially Th1 and Th17 expansion and Th17/Treg immune imbalance,may serve as the cornerstone of BD pathogenesis.Immune responses associated with increased levels of IL-2 and IL-4 may promote Th17/Treg immune imbalance.

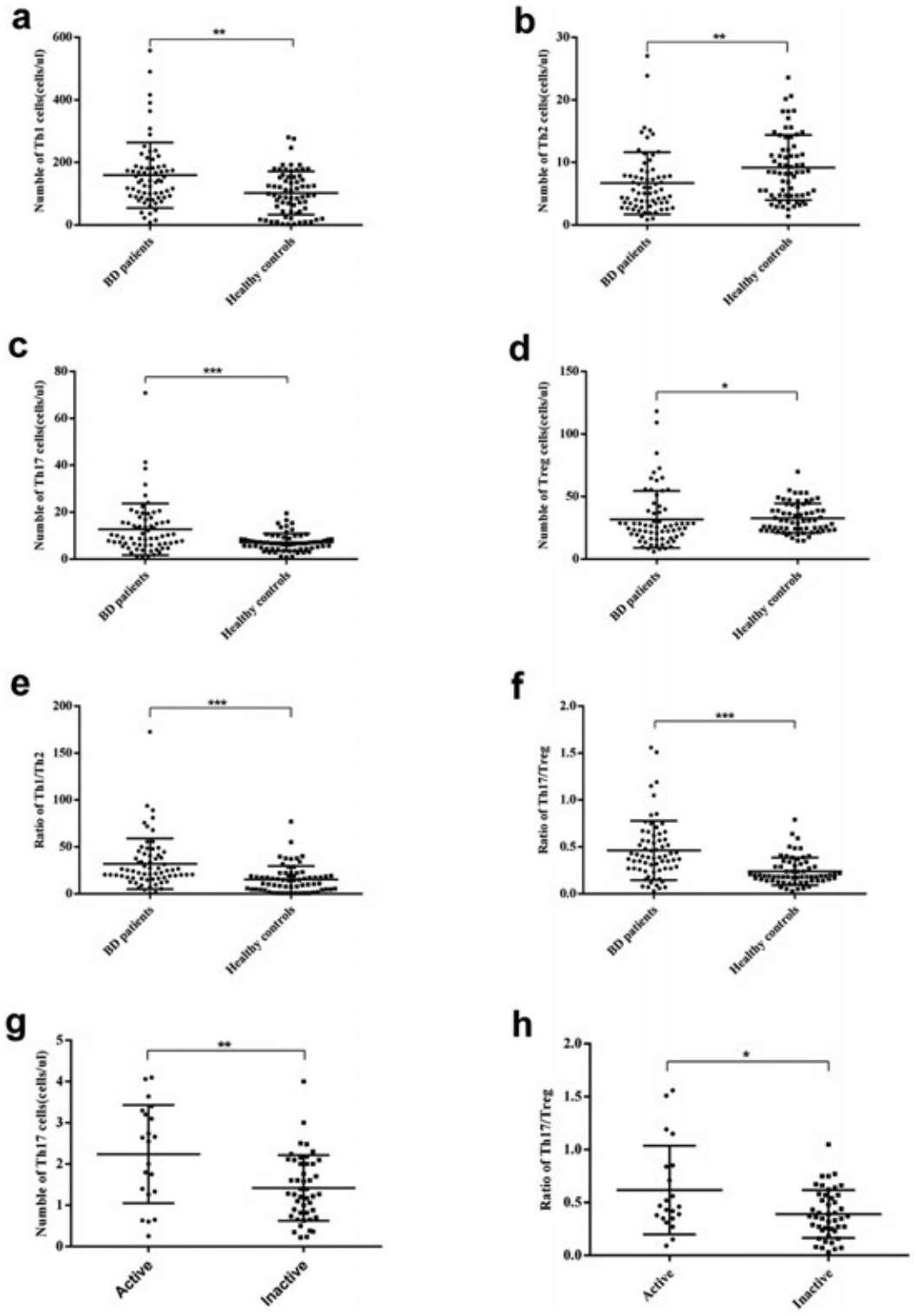

Figure 1 Characteristics of the absolute numbers proportions of CD4+ T cells in the PB of patients with BD. Lymphocytes in the PB of the healthy control (n=66) and BD group (n=67) were assessed by flow cytometry. (a and c) The absolute number Th1 cells and Th17 cells were significantly increased. (b and d) Reduction of Th 2cells and Treg cells were observed. (e and f)The ratio of Th1/Th2 and Th17/Treg were evidently increased.(g and h)The absolute counts of Th17 cells and the ratio of Th17/Treg in active BD patients were higher than inactive.*P<0.05; **P<0.01; ***P<0.001 vs healthy control group.

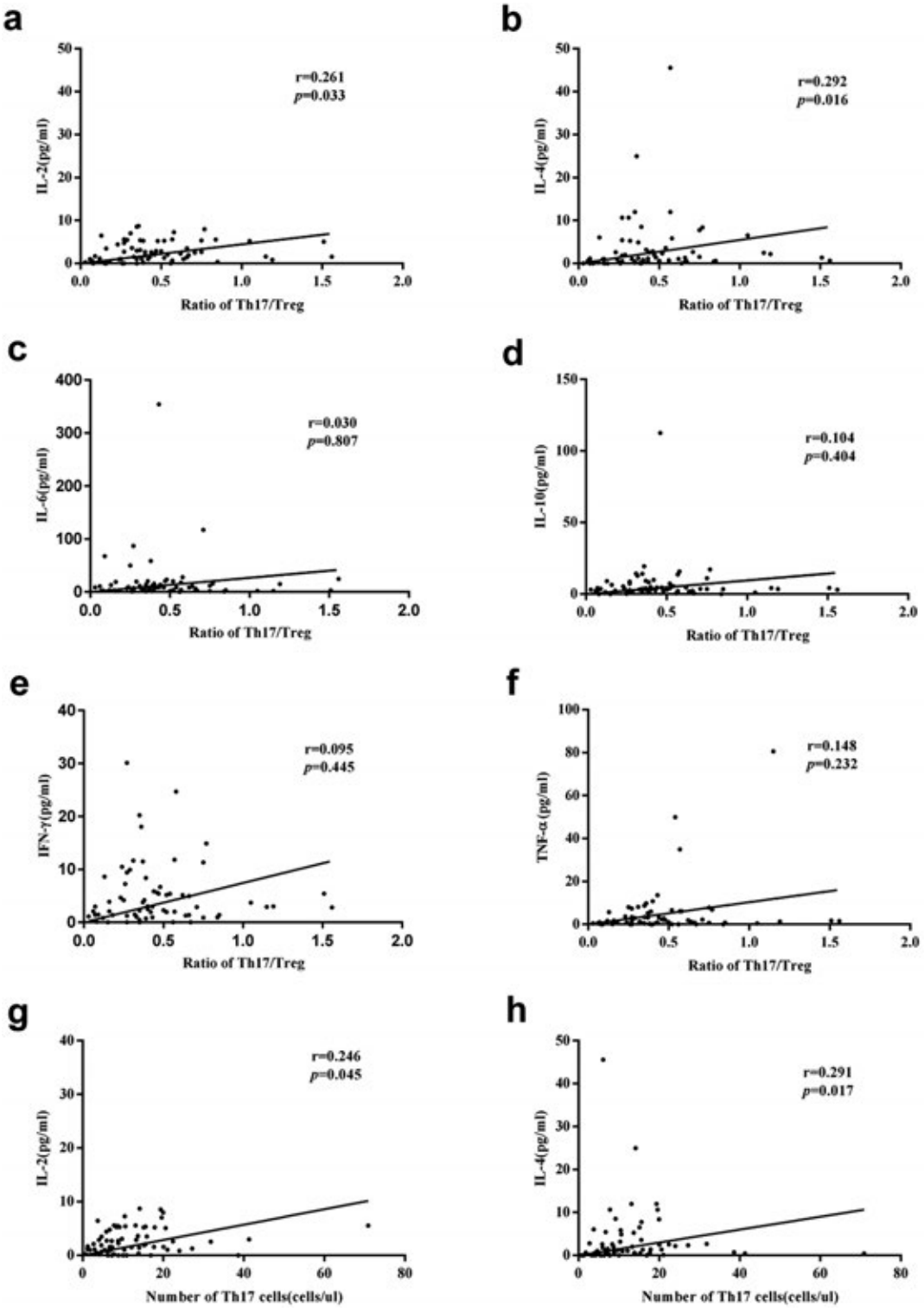

Figure 2 Correlation between the level of cytokines and the ratio of Th17/Treg,the absolute of Th17 cells in patients with Behcet's disease,which were calculated by Sperman's rank correlation.(a and b) Two cytokines were positively correlated with Th17/Treg:i.e.,IL-2(r=0.261,P=0.033) and IL-4(r=0.292,P=0.016)(P≥0.2 for all other cytokines).Th17/Treg was not correlated with IL-6,IL-10,IFN-γ and TNF-α.(g and h)The levels of IL-2 and IL-4 are positively associated with the absolute counts of Th17 cells(r=0.246,P=0.045vs r=0.291,P=0.017).

Disclosure: Y. Liu, None; **Y. Yang**, None; **R. Su**, None; **X. Zheng**, None; **X. Li**, None; **C. Wang**, None.

Abstract Number: 1704

Efficacy of Leflunomide for Treatment of Vasculitis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Table 1. Characteristics of patients who received leflunomide for treatment of vasculitis (n = 93).

Characteristics	Values
Demographic features	
Age at diagnosis, mean ± SD [range], years	48 ± 19.3 [4–80]
No. females	66 (71%)
Race	
Caucasian	73 (79%)
Asian	6 (7%)
Black or African American	4 (4%)
Vasculitis diagnosis	
Granulomatosis with polyangiitis	45 (48%)
ANCA-positive	31 (69%)
Microscopic polyangiitis	8 (9%)
ANCA-positive	8 (100%)
Eosinophilic granulomatosis with polyangiitis	12 (13%)
Takayasu's arteritis	9 (10%)
Giant cell arteritis	14 (15%)
Polyarteritis nodosa	5 (5%)
Previous treatments	
Glucocorticoids	87 (94%)
Oral or intravenous cyclophosphamide	65 (70%)
Methotrexate	64 (69%)
Azathioprine	51 (55%)
Rituximab	15 (16%)
Mycophenolate mofetil	12 (13%)
Infliximab	6 (7%)
Others*	21 (23%)

Data are n (%) of patients unless otherwise indicated.

*n= 4, hydroxychloroquine; n=4, intravenous immunoglobulin; n=3, plasma exchange; n=3, etanercept; n=2, tocilizumab; n=3, sulfasalazine; n=1, cyclosporine; and n=1, eculizumab (in a pediatric patient with severe refractory GPA).

Background/Purpose: Only a few small case series, case reports, and one small clinical trial suggested some benefit of leflunomide (LEF) in ANCA-associated vasculitis and other vasculitides. We analyzed the clinical efficacy and tolerability of LEF in a large cohort of patients with various vasculitides.

Methods: This was a retrospective analysis of patients who received LEF for treatment of their vasculitis enrolled in the Vasculitis Clinical Research Consortium (VCRC) Longitudinal Study and in 3 additional centers from the Canadian vasculitis research network (CanVasc). Efficacy was defined as a response to LEF at 6 months after its initiation, as per the treating physician, with the ability to taper glucocorticoids (GC), if applicable, the relief of symptoms for which LEF was started, or the maintenance of remission without the need to add or substitute another agent. Efficacy was further analyzed at 12 and 24 months. The validation of efficacy also required the absence of active disease, corresponding to a Birmingham Vasculitis Activity Score of 0.

Results: Data for 93 patients were analyzed. As shown in Table 1, 45 patients had granulomatosis with polyangiitis (GPA), 8 microscopic polyangiitis (MPA), 12 eosinophilic granulomatosis with polyangiitis (EGPA), 14 giant-cell arteritis (GCA), 9 Takayasu's arteritis (TAK) and 5 polyarteritis nodosa (PAN). The main reason for initiation of LEF was active disease (89%). The mean duration of treatment with LEF was 2.3±2.3 years; it was used with GC (mostly low-dose prednisone), at least initially, for 79% of patients; as monotherapy without GC for 18%; and in addition to another non-GC immunosuppressive sparing agent for 27%. As shown in Table 2, LEF was efficacious for remission induction or maintenance at 6 months for 62 (67%) patients (64% with GCA, 89% with TAK, 80% with PAN, 69% with GPA, 33% with EGPA); 20% discontinued LEF before achieving remission because of persistent disease activity. Five (5.4%) patients experienced nausea, vomiting, or diarrhea. Neuropathy was reported in 4, which resolved after cessation of LEF in 1 (3 had symptoms of minor sensory neuropathy and stopped LEF). Infections were reported in 4 patients (1 with GCA, also on GC, died from sepsis before month 6 of LEF) and mild transient elevation of transaminase levels in 3 patients. High blood pressure was reported in 1 patient after 12 months of use. Overall, 22 adverse

Table 2. Response to treatment with leflunomide among patients with vasculitis

	All patients	Type of vasculitis					
		GPA	MPA	EGPA	GCA	TAK	PAN
No. of patients (%)	93	45 (48.4%)	8 (8.6%)	12 12.9%)	14 15.1%)	9 (28.1%)	5 (5.4%)
Efficacy at 6 months	62 (67%)	31 (69%)	6 (75%)	4 (33%)	9 (64%)	8 (89%)	4 (80%)
Reason for treatment inefficacy							
Active disease	19 (20%)	7 (16%)	-	6 (50%)	4 (29%)	1 (1%)	1 (20%)
Adverse events	12 (13%)	7 (16%)	2 (25%)	2 (17%)	1 (7%)	0	0
Sustained remission at 12 months	54 (58%)	27 (63%)	6 (75%)	4 (33%)	7 (54%)	8 (89%)	3 (60%)
Sustained remission at 24 months	46 (50%)	23 (58%)	5 (71%)	4 (33%)	7 (54%)	7 (88%)	2 (40%)

Given percentages are for the proportion of patients in each type of vasculitis with available data, which was incomplete at 12 and/or 24 months for 7 individuals (2 lost to follow-up after 12 months [MPA and TAK]; 4 had not yet reached 12 and/or 24 months with LEF (3 GPA and 1 GCA); one with GPA died of natural causes before 24 months of LEF).

EGPA, eosinophilic granulomatosis with polyangiitis; GCA, giant cell arteritis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; PAN, polyarteritis nodosa; TAK, Takayasu's arteritis.

events led to drug discontinuation in 18 (19%) patients, of which 6 stopped LEF before month 12 and before showing any benefit in 8/12 of these patients.

Conclusion: LEF can be an effective therapeutic option for various vasculitides, especially for non-severe refractory or relapsing ANCA-associated vasculitis or large-vessel vasculitis, and for maintenance in GPA or MPA. No new safety signals for LEF were identified in this population.

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Abstract Number: 1705

Cyclophosphamide Therapy for the Neurologic Involvement of Behçet's Disease – Is It Superior to Azathioprine in Preventing Relapses?

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Neurologic involvement is one of the most serious cause of long-term morbidity and mortality in Behçet's disease (BD). To date, no controlled trials have assessed therapy for Neuro-BD and therapy is guided by expert opinion. It is usually recommended to treat active parenchymal Neuro-BD with 5-10 intravenous pulses of methylprednisolone and a course of high-dose glucocorticoids followed by azathioprine. Biologic agents such as interferon (IFN)α or TNF antagonists are used in refractory cases. However, Brazilian rheumatologists usually prescribe intravenous pulse therapy with cyclophosphamide to treat and prevent relapses of neuro-BD. Thus, the objective of this study is to compare the use of monthly intravenous pulse therapy with cyclophosphamide to azathioprine in preventing relapses of Neuro-BD.

Methods: An observational, retrospective cohort study was performed. Inclusion criteria were BD diagnosis according to the criteria of the International Study Group (ISG) or the International Criteria for Behcet's Disease (ICBD), neurologic involvement of BD and written informed consent. Neuro-BD was treated with high-dose glucocorticoids and at physician's discretion patients were treated either by a monthly course of intravenous cyclophosphamide pulse

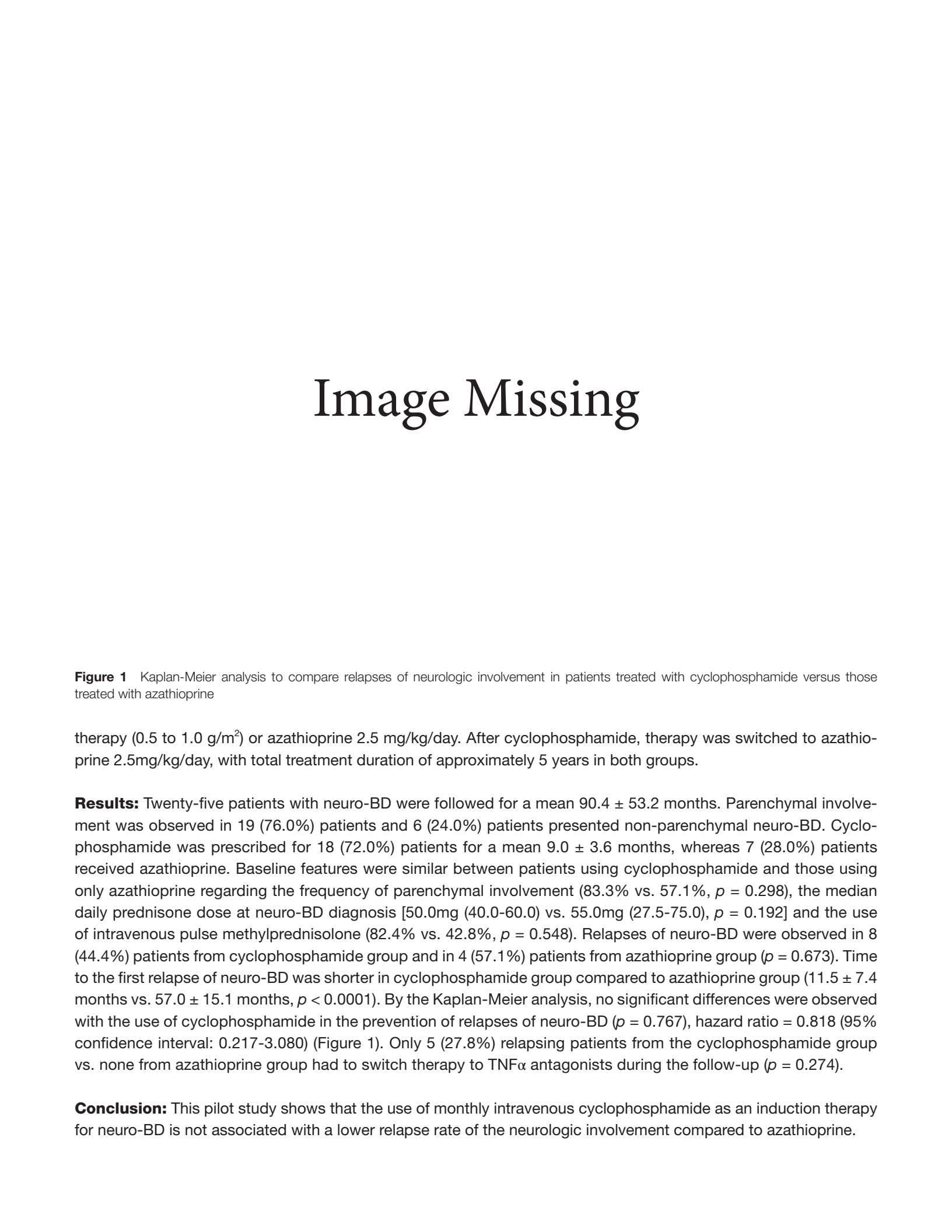

Figure 1 Kaplan-Meier analysis to compare relapses of neurologic involvement in patients treated with cyclophosphamide versus those treated with azathioprine

therapy (0.5 to 1.0 g/m^2) or azathioprine 2.5 mg/kg/day. After cyclophosphamide, therapy was switched to azathioprine 2.5mg/kg/day, with total treatment duration of approximately 5 years in both groups.

Results: Twenty-five patients with neuro-BD were followed for a mean 90.4 ± 53.2 months. Parenchymal involvement was observed in 19 (76.0%) patients and 6 (24.0%) patients presented non-parenchymal neuro-BD. Cyclophosphamide was prescribed for 18 (72.0%) patients for a mean 9.0 ± 3.6 months, whereas 7 (28.0%) patients received azathioprine. Baseline features were similar between patients using cyclophosphamide and those using only azathioprine regarding the frequency of parenchymal involvement (83.3% vs. 57.1%, p = 0.298), the median daily prednisone dose at neuro-BD diagnosis [50.0mg (40.0-60.0) vs. 55.0mg (27.5-75.0), p = 0.192] and the use of intravenous pulse methylprednisolone (82.4% vs. 42.8%, p = 0.548). Relapses of neuro-BD were observed in 8 (44.4%) patients from cyclophosphamide group and in 4 (57.1%) patients from azathioprine group (p = 0.673). Time to the first relapse of neuro-BD was shorter in cyclophosphamide group compared to azathioprine group (11.5 ± 7.4 months vs. 57.0 ± 15.1 months, $p < 0.0001$). By the Kaplan-Meier analysis, no significant differences were observed with the use of cyclophosphamide in the prevention of relapses of neuro-BD (p = 0.767), hazard ratio = 0.818 (95% confidence interval: 0.217-3.080) (Figure 1). Only 5 (27.8%) relapsing patients from the cyclophosphamide group vs. none from azathioprine group had to switch therapy to TNFα antagonists during the follow-up (p = 0.274).

Conclusion: This pilot study shows that the use of monthly intravenous cyclophosphamide as an induction therapy for neuro-BD is not associated with a lower relapse rate of the neurologic involvement compared to azathioprine.

Disclosure: P. Ribeiro, None; **E. Zarur**, None; **F. Campos Peixoto**, None; **P. Matos**, None; **P. de Alcantara Pedro**, None; **R. Medeiros Golebiovsk**, None; **L. Dutra**, None; **A. de Souza**, None.

Abstract Number: 1706

*HLA-B*51* and Its Subtypes in Brazilian Patients with Behçet's Disease

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SESSION INFORMATION
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Background/Purpose: *HLA-B*51* is considered the genetic marker mostly associated with Behçet's disease (BD), mainly in countries of the silk route, where its prevalence ranges from 40-80% in individuals with BD. To date, the frequency of *HLA-B*51* and its subtypes in Brazilian patients with BD and their associations with clinical manifestations of the disease are not known. The aims of this study are to evaluate the prevalence of *HLA-B*51, B*51:01* and *HLA-B*51:08* in Brazilian patients with BD and in healthy controls, to evaluate associations between *HLA-B*51* and its subtypes and a higher risk for BD in the Brazilian population and to evaluate associations with specific clinical manifestations BD.

Methods: We carried out a cross-sectional study with BD patients and healthy controls. The presence of *HLA-B*51* was investigated by sequence-specific polymerase chain reaction (PCR-SSP) and *HLA-B*51* positive samples were submitted to genetic sequencing by the Sanger method to evaluate their alleles at medium resolution.

Results: Eighty-three BD patients and 258 healthy controls were evaluated. The prevalence of *HLA-B*51* was 30.1% in DB patients and 15.5% in control subjects (p = 0.003). The most frequent alleles among DB patients were *HLA-*51:01* (18.1%), *HLA-B*51:08* (6.0%), *HLA-B*51:22* (2.4%), *HLA-B*51:29* (2.4%) and *HLA-B*51:02* (2.1%), while *HLA-B*51:01* (12.0%) and *HLA-B*51:55* (1.2%) were the most frequent subtypes in the control group. Each of the other *HLA-B*51* subtypes were observed in less than 1% of the control group. As for clinical manifestations, *HLA-B*51* was less frequent in BD patients with neurological involvement (8.0% vs. 29.3%; p = 0.034) while *HLA-B*51:01* was more frequently observed in BD patients with ocular involvement (93.3% vs. 60.3%; p = 0.014) and no BD patient with neurological involvement or vascular involvement had *HLA-B*51:01*. *HLA-B*51:08* was more frequent in patients with vascular involvement (60.0% vs. 15.4%; p = 0.012). In the multivariate analysis, the presence of *HLA-B*51* was an independent risk factor for BD (OR = 2.410; 95%CI: 1.332-4.361; p = 0.004) and *HLA-B*51:08* had an independent association with the development of vascular manifestations of BD (OR = 14.843; 95%CI: 1.550 - 142.115; p = 0.019). No independent associations were observed between *HLA-B*51* or with *HLA-B*51:01* and disease manifestations of BD.

Conclusion: *HLA-B*51* is more frequent in Brazilian BD patients compared to healthy controls and it is an independent risk factor for BD. The *HLA-B*51:08* subtype was independently associated with vascular manifestations of BD.

Disclosure: J. Belem, None; **A. Fraga**, None; **L. Andrade**, None; **A. de Souza**, None.

Abstract Number: 1707

IL-6 Promotes IgG4-related Disease by Inducing Fibroblast-dependent Tfh Cell and B Cell Differentiation Factors

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Background/Purpose: Considering the unsatisfied effect of conventional therapy, to investigate the pathogenesis of IgG4-related disease (IgG4-RD) is crucial to explore novel treatment strategies. This study aims to clarify the pathogenesis of interleukin 6 (IL-6) in IgG4-RD through the induction of fibroblast-dependent Tfh cell and B cell differentiation factors and find the new therapeutic target.

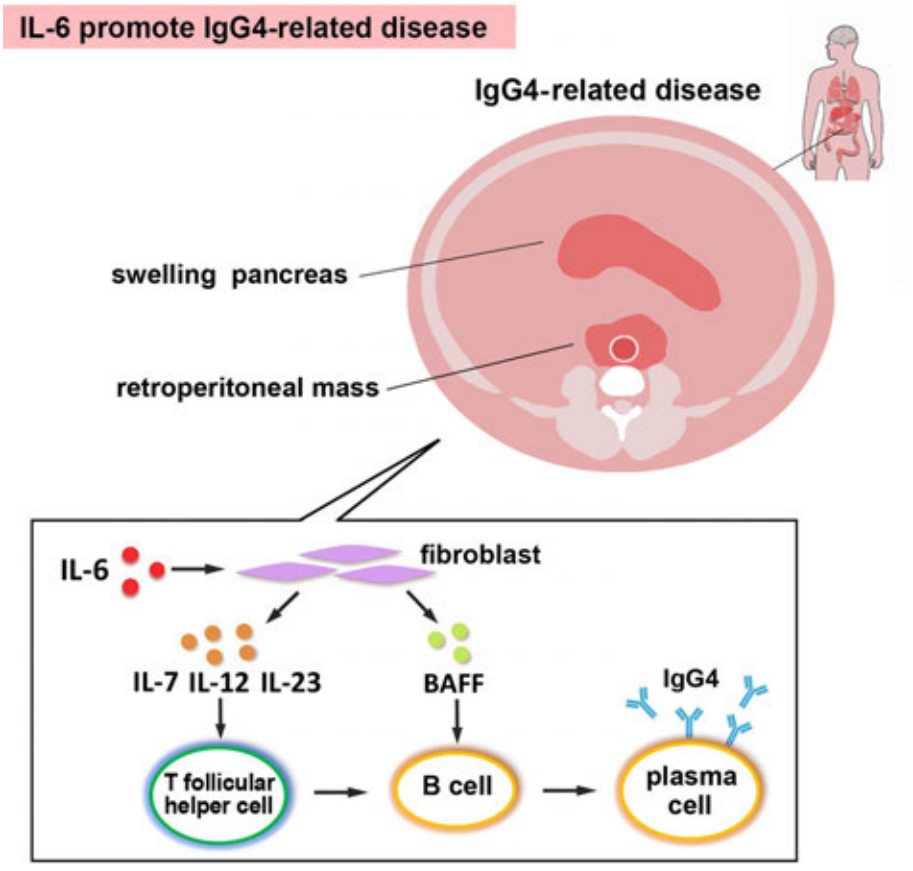

Figure. IL-6 promotes IgG4-related disease by promoting the production of B cell differentiation cytokine (BAFF), and Tfh cell differentiation cytokines (IL-7, IL-12, and IL-23) in fibroblast.

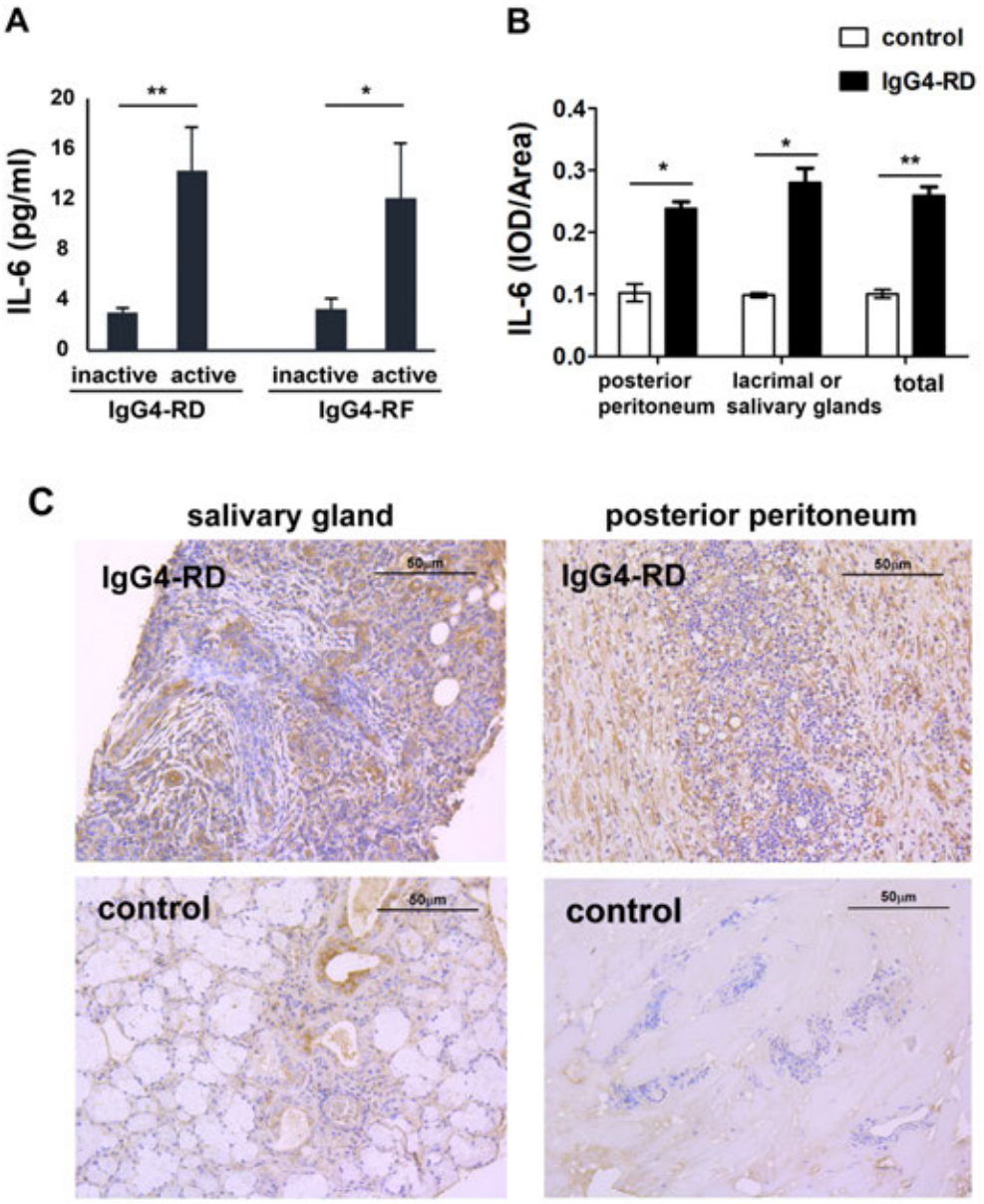

Figure. The level of serum IL-6 was elevated in active IgG4-RD patients. The expression of IL-6 in the tissue of IgG4-RD patients was also significantly higher than that in the normal tissue. *$p < 0.05$; **$p < 0.01$

Methods: The IL-6 expression in the serum and tissues of patients with IgG4-RD and healthy controls were detected by ELISA, immunohistochemistry, and immunofluorescence, respectively. Human aorta adventitial fibroblasts (AAFs) were cultured and stimulated with IL-6/IL-6 receptor (IL-6R). The effect of IL-6/IL-6R on AAFs was determined by CCK-8 and Luminex assays.

Results: The level of serum IL-6 was elevated in active IgG4-RD patients and was positively correlated with IgG4-RD reactive index (RI).The expression of IL-6 in the tissue of IgG4-RD patients was also significantly higher than that in the normal tissue. IL-6-producing fibroblasts were found to co-localize with $IgG4^+$ plasma cells in the tissue of IgG4-related retroperitoneal fibrosis (IgG4-RF). Co-localization of α-SMA and B cell differentiation cytokines (i.e., B cell activating factor (BAFF)), α-SMA and T follicular helper (Tfh) cell differentiation cytokines (e.g., IL-7, IL-12, and IL-23) were present in the local lesions. IL-6/IL-6R significantly promoted the production of BAFF, IL-7, IL-12, and IL-23 in AAFs in a dose-dependent manner. This effect was blocked by JAK1, JAK2, STAT3, and Akt inhibitors, respectively.

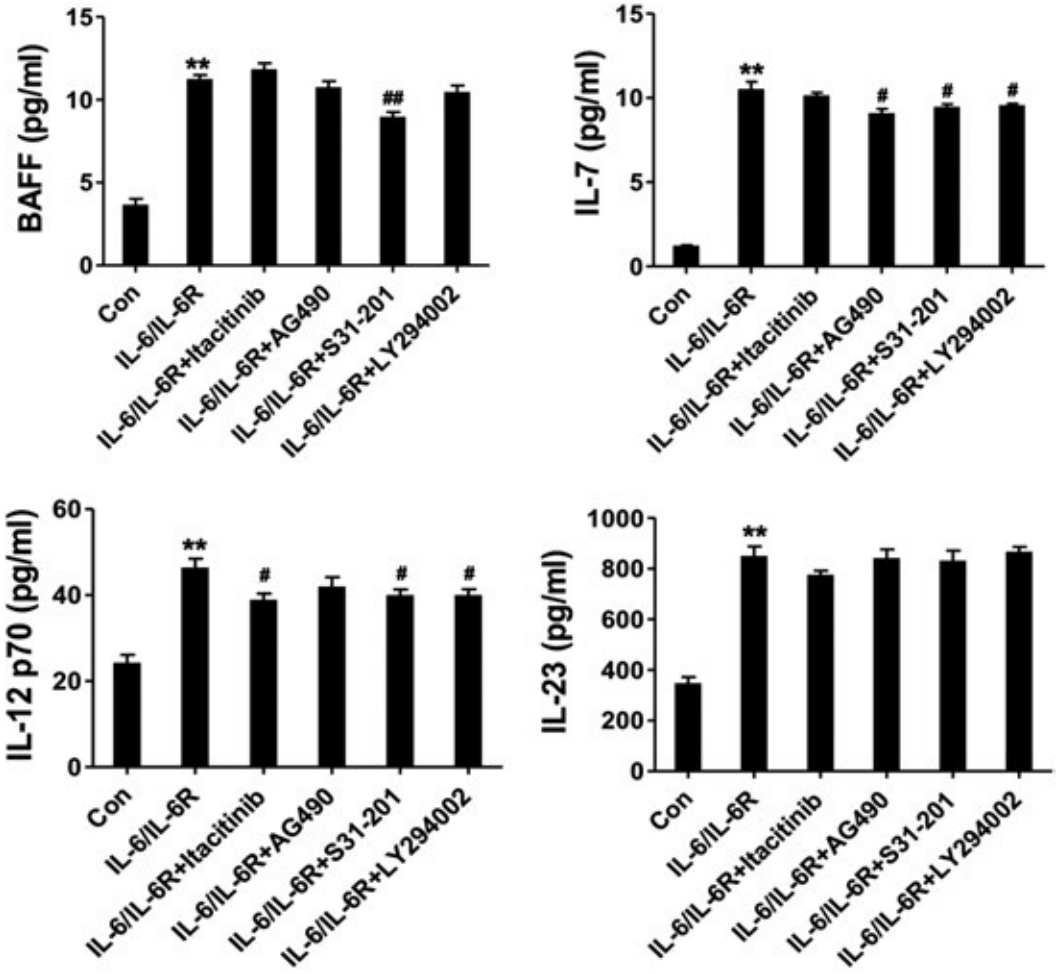

Figure. The secretion of cytokines (IL-7, BAFF, IL-12 p70, and IL-23) in the supernatant following stimulation with IL-6/IL-6R (50 ng/mL) with or without different inhibitors. **p < 0.01 versus control group; #p < 0.05 versus IL-6/IL-6R group.

Conclusion: IL-6 promotes IgG4-RD by inducing fibroblast-dependent Tfh and B cell differentiation factors via the JAK2/STAT3, JAK1/STAT3, and JAK2/Akt pathways. Thus, IL-6 and JAK1/2 inhibitors may be therapeutic targets for IgG4-RD.

Disclosure: Z. Ji, None; **R. Chen**, None; **X. Cui**, None; **L. Ma**, None; **X. Kong**, None; **L. Ma**, None; **Y. Sun**, None; **X. Dai**, None; **Z. Zhang**, None; **H. Chen**, None; **L. Jiang**, None.

Abstract Number: 1708

Azathioprine and Glucocorticoid Combination Might Be a Good Treatment Option to Achieve Remission in Patients with IgG4-related Disease

Aydan Köken Avşar,[1] Onay Gercik,[2] Gercek Can,[3] Berrin Zengin,[4] Sinem Burcu Kocaer,[5] Atilla Okan Kılıç,[6] Sadettin Uslu,[7] Ali Karakaş,[5] Merih Birlik,[5] Servet Akar,[8] and Fatos Onen[9], [1]Dokuz Eylul University School of Medicine, Rheumatology,, Türkiye, Izmir, Turkey, [2]Izmir Katip Celebi University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, İzmir, Turkey, [3]Dokuz Eylul University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Izmir, Izmir, Turkey, [4]Dokuz Eylul University School of Medicine, Rheumatology,, Turkey,Izmir, Izmir, Turkey, [5]Division of Rheumatology, Dokuz Eylül University School of Medicine, İzmir, Turkey, Turkey,Izmir, Izmir, Turkey, [6]Dokuz Eylul University School of Medicine, Internal Medıcıne, Turkey,Izmir, Izmir, Turkey, [7]Division of Rheumatology, Dokuz Eylül University School of Medicine, İzmir, Turkey, Izmir, Turkey, [8]Izmir Katip Celebi University, Faculty of Medicine, Division of Rheumatology, İzmir, Turkey, [9]Dokuz Eylul University School of Medicine, Division of Rheumatology, İzmir, Turkey

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Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4-related disease is a recently recognised inflammatory disease of unkown etiology, often seen in men over the age of 50 and may affect many organs and systems with elevated serum IgG4 levels and typical histopathological features.The aim of this study is to determine the demographic and clinical characteristics of patients with IgG4-related disease.

Table 1: Demographic and clinical features of patients

Parameter	Result
Age (year)*	51.49 ± 12.36
Gender (male) n (%)	37 (69.8)
Smoking (yes) n (%)	19 (35.8)
Comorbidity n (%) Hipertansiyon Diabetes mellitus Chronic renal failure Nephrolithiasis Asthma Coronary artery disease Chronic obstructive pulmonary disease Malignancy	 18 (34) 16(30.2) 7(13.2) 6(11.3) 6(11.3) 5(9.4) 4 (7.5) 3 (5.7)
ESH (mm/h) *	50.7 ± 29.7
CRP (mg/l) *	35.5 ± 51.9
Cree (mg/dl) *	1.37 ± 1.32
GFR*	78.3 ± 32.7
IgG4 concentration (mg/dl) *	581.6 ± 957.8

* *Continuous variables were presented as mean ±SD*

Table 2. Distribution of clinical findings and tissue/organ involvement (n=53)

Constitutional symptoms	12 (22.6)
Retroperitoneal fibrosis	29 (54.7)
Cardiovascular disease** *Periaortit* *Aortit* *Aortic aneurysm* *Pericardiyal effusion*	24 (45.3) *21 (39.6)* *3 (5.7)* *3 (5.7)* *1 (1.9)*
Dacryoadenitis	6 (11.3)
Pancreatitis	6 (11.3)
Sialadenitis	5 (9.4)
Sinusitis	5 (9.4)
Orbital pseudotumor	4 (7.5)
Lymphadenopathy	4 (7.7)
Arthritis	3 (5.7)
Fibrosing mediastinitis	3 (5.7)
Sclerosing cholangitis	3 (5.7)
Kidney disease *Tubulointersisyel nephritis* *Kidney mass*	2 (3.8) *1 (1.9)* 1 (1.9)
Thyroiditis	2 (3.8)
Esophagus disease	1 (1.9)
Lung disease	1 (1.9)

**two patients had periaortit and aortic aneurysm and one patient had periaortit and pericardiyal effusion together

Methods: Patients diagnosed as having Ig-G4-related disease by their typical histopathological findings and imaging features and/or increased serum IgG4 concentrations (> 135 mg / dl) from two university hospital in Izmir were included in the study.

Results: There were 53 patients with a mean age of 51.49 yrs (69.8% male). The most common involvement was retroperitoneal fibrosis (54.7%), followed by the cardiovascular system (CVS) involvement (45.3%) (Table 1). While 22 patients had at least two organ involvement, the most common association was retroperitoneal fibrosis and CVS involvement (15 patients). Serum IgG4 levels were studied in 36 patients (67.9%) and found to be higher levels in 20 patients. (55.5%) (Table 2). In 44 patients (83%), acute phase reactants (APRs) were increased at the time of the diagnosis. There was no correlation between the extent of the disease and serum IgG4 levels and initial erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) values. 28 patients (52.8%) were diagnosed by imaging, 9 (17%) by imaging and IgG4 elevation, 5 (9.4%) by imaging and histopathology, 10 (18.9%) by imaging, histopathology and IgG4 elevation and 1 patient (1.9%) by only histopathology. The most commonly (58.5%) used imaging method for diagnosis was computed tomography (CT). All the patients used initial glucocorticoid treatment.4 patients (7.5%)

recieved only glucocorticoid,others were underwent the following treatments combined with glucocorticoid: azathioprine (AZA) (60.4%); methotrexate (mtx) (11.3%), rituximab (RTX) + AZA (9.4%), mtx + AZA (5.7%), RTX (3.8%) and infliximab (1.9%). In the follow-up, a significant decrease in acute phase reactants was found in 62% of the patients at their last visits. While 27.3% of the patients had complete remission, 36.4% had partial remission, 20.5% had stable course, 13.6% had progression in the disease and 2.3% had recurrence. In 18 patients (64.3%) out of 28 patients who were in partial or complete remission, remission was achieved by using glucocorticoid and AZA combination treatment.

Conclusion: In conclusion, we have described a considerably large serie of patients with IgG4-related disease from Turkey. The results of the study suggested that AZA and glucocorticoid combination treatment was commonly used in Turkish patients with IgG4-related disease and it might be a good treatment option to achieve remission.

Disclosure: A. Köken Avşar, None; **O. Gercik**, None; **G. Can**, None; **B. Zengin**, None; **S. Kocaer**, None; **A. Kılıç**, None; **S. Uslu**, None; **A. Karakaş**, None; **M. Birlik**, None; **S. Akar**, Abbvie, 2, 5, Amgen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5; **F. Onen**, Tofacitinib (Pfizer), 8.

Abstract Number: 1709

Juvenile-Onset IgG4-Related Disease: A Systematic Review

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4-related disease (IgG4-RD) presenting in the pediatric age is rare. Natural history and outcomes are not well defined. The aim of this study was to describe the clinical characteristics and outcomes of juvenile-onset IgG4-RD.

Methods: We included patients with juvenile-onset IgG4-RD reported in the English literature that fulfilled de Comprehensive Diagnostic Criteria (CDC) for IgG4-RD and patients followed at two referral centers in Mexico City. Juvenile-onset IgG4-RD was defined as first manifestation of the disease < 18 years. We searched relevant articles on Medline and Pubmed. We extracted variables such as: demographics (sex, age), clinical (number and type of organs involved, clinical phenotype), serological and histopathological data, treatment and outcomes. The juvenile-onset cohort was compared with a published multi-ethnic cohort of adult-onset IgG4-RD patients.

Results: We found 53 articles describing 57 patients with juvenile-onset IgG4-RD. After screening, 49 cases in 46 articles fulfilled the CDC for IgG4-RD. Five new cases from our centers were included. A total of 54 patients with juvenile-onset IgG4-RD were analyzed. Thirty (55.6%) were female. Mean age at presentation was 11.62 ± 4.1 years. Single organ involvement was found in 33 (61.1%). Most frequently involved organs were: orbit (29.3%), lacrimal glands (14.8%), lymph nodes (14.8%), salivary glands (11.1%) and lung (11.1%) (Figure 1). Most frequent clinical phenotype was "head and neck-limited" in 31 (57.4%) patients, followed by "pancreato-hepatobiliary" in 11 (20.4%), "retroperitoneum and aorta" in 5 (9.3%) and "Mikulicz and Systemic" in 2 (3.7%) (Figure 2). Serum IgG4 level were elevated in 33 out of 37 (86.5%) patients tested; the median IgG4 level was 420 mg/dl (range: 4-1650). Forty two

Table 1.	Juvenile-onset IgG4-RD (N=54)	Adult-onset IgG4-RD (N=493)	P
Male, n (%)	24 (44.4)	322 (65.3)	0.003
Single organ, n (%)	33 (61.1)	120 (24.3)	<0.001
Multiorganic, n (%)	21 (38.9)	373 (75.6)	<0.001
Head and neck phenotype, n (%)	31 (57.4)	115 (24)	<0.001
Mikulicz/Systemic phenotype, n (%)	2 (3.7)	100 (22)	0.003
Retroperitoneum/Aorta phenotype, n (%)	5 (9.3)	114 (24)	0.07
Pancreato-hepatobiliary phenotype, n (%)	11 (20.4)	149 (31)	0.13
Unclassified phenotype*, n (%)	5 (9.3)	0	<0.001
Lacrimal gland, n (%)	8 (14.8)	128 (26)	0.07
Orbit, n (%)	16 (29.3)	32 (6.5)	<0.001
Salivary glands, n (%)	6 (11.1)	186 (37.7)	<0.001
Lung, n (%)	6 (11.1)	70 (14.2)	0.53
Pancreas, liver, biliary tract, n (%)	14 (25.9)	235 (47.4)	0.04
Retroperitoneum, n (%)	3 (5.5)	78 (14.2)	0.04
Aorta, n (%)	0	51 (10.3)	0.04
Kidney, n (%)	3 (5.5)	77 (15.6)	0.04
High IgG4, n (%)	33/37 (86.5)	388/478 (81.1)	0.38
*Unclassified phenotype: solitary lung involvement.			

Table 1 Clinical characteristics of Juvenile-onset VS Adult-onset IgG4-RD.

(77.8%) were biopsy proven. Forty six (85.2%) patients received glucocorticoids, 9 (16.6%) azathioprine, and 8 each (14.8%) mycophenolate mofetil and Rituximab. Nineteen (35.2%) patients had a surgical procedure. Thirty five (64.8%) achieved total and 12 (22.2%) partial remission. When we compare juvenile-onset VS adult-onset patients, the former were more frequently female, had single-organ involvement, orbital involvement and belonged to the "head and neck-limited" and less commonly to the "Mikulicz and Systemic" phenotype (Table 1).

Conclusion: Juvenile-onset IgG4-RD differs in demographics and clinical presentation compare to the adult counterpart. Juvenile-onset IgG4-RD patients are more frequently female and have a "head and neck-limited" phenotype.

References: Wallace ZS, Zhang Y, Perugino CA, et al. Clinical phenotypes of IgG4-related disease: an analysis of two international cross-sectional cohorts. Ann Rheum Dis. 2019 Mar;78(3):406-412.

Figure 1: Frequency of Organ Involvement in Juvenile-Onset IgG4-RD (n=54)

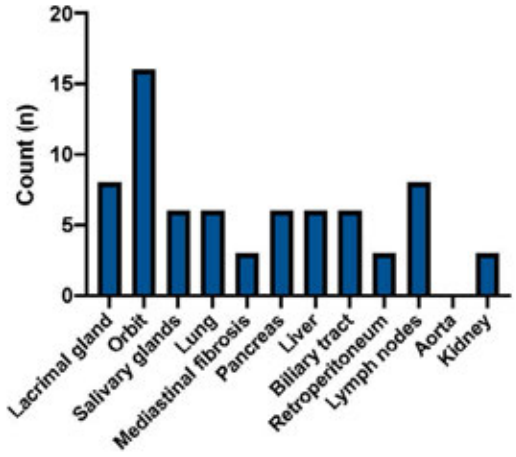
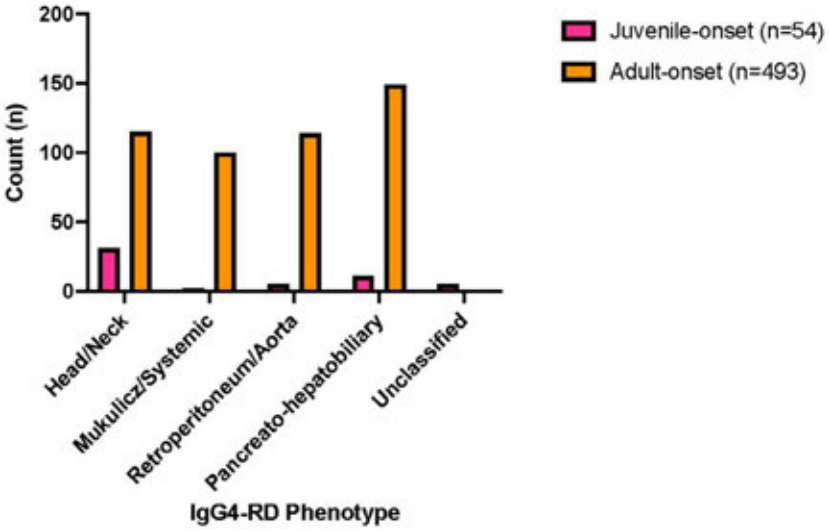


Figure 2: IgG4-RD Phenotype



Disclosure: E. Martin-Nares, None; **T. Díaz-Prieto**, None; **E. Faugier-Fuentes**, None; **L. Aparicio Vera**, None; **G. Hernandez-Molina**, None.

Abstract Number: 1710

Chemokine and Cytokine Tear Profile of Patients with IgG4-Related Disease

Eduardo Martin-Nares,[1] Luis Llorente,[1] Guadalupe Lima,[1] Diego Hernández-Ramírez,[1] Isela Chan-Campos,[1] Vanessa Saavedra-González,[1] and Gabriela Hernandez-Molina[1], [1]Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The lacrimal gland is frequently involved in both IgG4-related disease (IgG4-RD) and Sjögren's syndrome (SS) and presents with swelling and/or dry eye symptoms. Although a distinct chemokine and cytokine tear profile might distinguish SS from idiopathic dry eye, as of today no study has assessed this issue in IgG4-RD. Our aim was to evaluate and compare a set of chemokine/cytokine in the tears of patients with IgG4-RD and primary SS.

Methods: We included 11 patients with IgG4-RD according to the Comprehensive Diagnostic Criteria for IgG4-RD and 17 with primary SS according the AECG criteria, who attended a tertiary referral center in Mexico City. Schirmer-I test were performed using two standardized sterile tear strips, and then immediately frozen at -86°C until assayed. Once defrosted, the tears were extracted from the strips using a buffer containing 0.5 M NaCl and 0.5% Tween-20. Then, the amount (pg/mL) of the following selected chemokines and cytokines were measured by Luminometry: CCL11, G-CSF, IFN-γ, IL-12p40, IL-12p70, IL-13, IL-17A, IL-1α, IL-1β, IL-4, IL-7, CXCL10, CCL2, CCL3, CCL4 and TNF-α.

Results: Patients with IgG4-RD were younger (51.3±14.7 vs. 55.7±10.6) and more frequently men (45.5% vs. 5.9%) than SS patients. Regarding the IgG4-RD group, 7 (63.6%) had lacrimal gland involvement, 5 (45.5%) dry eye symptoms and 6 (54.5%) positive Schirmer-I test. We observed multi-organic involvement in 9 patients (81.8%), median number of involved organs of 5, 9 (81.8%) patients had active disease, median IgG4-RD responder index of 6 points, 8 (72.7%) patients had high IgG4 serum levels, and 9 (81.8%) biopsy proven diagnosis. We found higher levels of IL-7 and CCL2, and a trend for G-CSF in the IgG4-RD group. Conversely, primary SS patients had higher levels of IL-12p40, IL-1α, IL-1β, CCL3 and CCL4. At the logistic regression analysis, the variables that remained associated with IgG4-RD were IL-7 (OR 1.43 95% CI 1.06-1.93, p=0.01) and IL12p40 (OR 0.92, 95% CI 0.84-0.99, p=0.01).

In a sensitivity analysis, including only 7 IgG4-RD patients with dacryoadenitis, we also observed higher levels of IL-7 and G-CSF in the IgG4-RD group vs primary SS.

Conclusion: The chemokine and cytokine profile of tears of patients with IgG4-RD is characterized by a mixed immune response (Th1/Th2/Th17) compare with a predominantly Th1 response in primary SS. Our results also suggest a possible role of IL-7 in the pathogenesis of IgG4-RD.

Table 1.			
Chemokine/cytokine pg/mL, median(range)	IgG4-RD n=11	pSS n=17	*p*
CCL11	11.9 (3.7-34.4)	15.4 (3.7-33.0)	0.06
G-CSF	118.7 (14.5-325.9)	88.5 (14.5-226.5)	0.08
IFN-γ	1.3 (0.3-2.1)	1.7 (0.01-7.2)	0.19
IL-12p40	8.7 (1.3-35.5)	24.1 (1.3-69.3)	0.02
IL-12p70	0.5 (0.09-3.1)	1.6 (0.09-28.1)	0.05
IL-13	19.2 (4.6-84.9)	18.1 (2.4-75.0)	0.30
IL-17A	0.9 (0.2-1.7)	0.9 (0.08-4.9)	0.89
IL-1α	25.8 (10.5-166.8)	54.3 (21.6-119.1)	0.003
IL-1β	0.1 (0.1-1.5)	1.5 (0.1-7.2)	0.001
IL-4	11.0 (1.8-17.6)	8.2 (1.8-19.8)	0.45
IL-7	13.8 (6.6-65.1)	6.4 (1.27-15.0)	0.001
CXCL10	5399.5 (296.9-11394)	5368.1 (1205-11553.6)	0.51
CCL2	11.4 (1.1-104.4)	1.1 (1.1-166.3)	0.03
CCL3	2.4 (0.3-4.0)	3.4 (1.1-40.7)	0.01
CCL4	1.2 (1.2-27.6)	11.1 (1.2-164.3)	0.02
TNF-α	0.8 (0.1-5.4)	2.03(0.1-7.6)	0.06

Disclosure: E. Martin-Nares, None; **L. Llorente**, None; **G. Lima**, None; **D. Hernández-Ramírez**, None; **I. Chan-Campos**, None; **V. Saavedra-González**, None; **G. Hernandez-Molina**, None.

Abstract Number: 1711

Distinctive Imaging Features Between IgG4-Related Ophthalmic Disease and Graves' Orbitopathy: A Comparative Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: IgG4-related ophthalmic disease (IgG4-ROD) may present as a cause of orbital myositis leading to proptosis and diplopia. This clinical scenario can be mistakenly diagnosed as Graves' orbitopathy (GO), preventing a timely and adequately treatment. Our aim was to elucidate if there are specific radiological features that might differentiate between IgG4-ROD and GO by imaging.

Methods: We included 19 patients with diagnosis of IgG4-related disease (IgG4-RD) according to the Comprehensive Diagnostic Criteria for IgG4-RD. All had ophthalmic involvement and available computed tomography (CT) and/or magnetic resonance imaging (MRI) of the orbits. We also included 32 patients with GO with available CT and/or MRI of the orbits. Imaging studies were evaluated by a blinded head and neck radiologist for the following features: exophthalmos, extraocular muscles (EOM) size and morphology, lacrimal gland enlargement, orbital fat involvement, stretching of the optic nerve (ON), ON sheath thickening and orbital bone changes.

Results: Groups were similar in age (49.1±15.8 vs. 51.6±14.7, p=0.58) and gender (men 58.9% vs. 40.6%, p=0.23). In addition to ophthalmic involvement, 18 (94.7%) IgG4-RD patients had extra-ophthalmic involvement with a median number of organs involved of 7 (1-12). Three patients were misdiagnosed as GO before IgG4-RD diagnosis. Graves' disease was the underlying thyroid disorder in 28 (87.5%) GO patients, Hashimoto's thyroiditis in 2 (6.3%), papillary thyroid carcinoma in one (3.1%) and one patient was euthyroid with positive thyroid stimulating immunoglobulin. The prevalence of exophaltmos (78.9% vs. 93.8%), bilateral involvement (78.9% vs. 87.8%) and overall EOM involvement (47.4% vs. 68.8%) was similar between IgG4-ROD and GO groups. However, IgG4-ROD patients had a higher frequency of lacrimal gland involvement (73.7% vs. 10.7%, p=0.001) and a tendency for the lateral rectus to be the most frequently involved EOM (22.2% vs. 0%, p=0.07); conversely they had a lower prevalence for the inferior rectus to be the most frequently involved EOM, (33.3% vs. 72.7%, p=0.04), orbital fat involvement (47.4% vs. 81.3%, p=0.01), ON stretching (57.9% vs. 87.5%, p=0.02) and orbital bone changes (0% vs. 25%, p=0.02). EOM bellies were involved in all the IgG4-ROD and GO cases, whereas EOM tendon involvement was present in 9% of GO and in none of the IgG4-ROD group. Patients with IgG4-ROD had more frequently the combination of lacrimal gland and lateral rectus (31.6% vs. 3.1%, p=0.008) and less frequently the combination EOM and orbital fat involvement (21.2% vs. 59.4%, p=0.008).

At the logistic regression analysis we found an association of lacrimal gland involvement (OR 64.4.0, 95% CI 6.8-609.5, p=0.001) with IgG4-ROD. In a second model including combined variables, the combination of lacrimal gland and lateral rectus involvement was associated with IgG4-ROD (OR 62.5, 95% CI 3.31-1000), P=0.006), whereas the presence of EOM and orbital fat involvement was protective (OR 0.05, 95% CI 0.006-0.48, p=0.009).

Conclusion: Imaging features may reliably differentiate between IgG4-ROD and GO. The presence of both lacrimal gland and lateral rectus enlargement must alert clinicians to consider IgG4-ROD diagnosis.

Disclosure: E. Martin-Nares, None; **O. Amaya-Piña**, None; **R. Delgado Hernández**, None; **G. Hernandez-Molina**, None.

Abstract Number: 1712

Head and Neck Involvement of IgA Vasculitis: A Case-Control Study

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SESSION INFORMATION
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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: IgA vasculitis (IgAV) is an immune-complex mediated, small-vessel vasculitis which predominantly involves the skin on the lower extremities. Head and neck involvement is rarely reported. The purpose of this study was to describe the presentation and outcome of a series of patients with head and/or neck involvement in comparison to patients with cutaneous findings isolated to the lower extremities.

Methods: Patients with biopsy-proven IgAV from January 1, 1997 through December 31, 2016 were retrospectively identified through direct medical chart review. IgAV was diagnosed in accordance with the American College of Rheumatology (ACR) and the European League Against Rheumatism/ Paediatric Rheumatology European Society/ Paediatric Rheumatology International Trials Organisation (EULAR/PRINTO/PRES) criteria. Among this cohort, patients with documented clinical, photographic, or histologic descriptions of vasculitic skin lesions affecting the head or neck were compiled. Each patient with head/neck (H/N) involvement of IgAV (case) was matched to two age- and sex-matched control patients with IgAV for which the cutaneous features were isolated to the waistline or distal. Baseline characteristics, laboratory parameters, treatments and outcome were collected by a physician abstractor.

Results: Thirteen patients with H/N-IgAV involvement were identified. Baseline characteristics of the cases and controls are demonstrated in Table 1. H/N involvement included facial (cheeks, forehead) [n=6], perioral/oral/lip [n=6], auricular [n=2], nasal [n=2], and neck [n=1]. All patients in both groups had evidence of purpuric skin lesions. Patients with H/N-IgAV involvement more frequently had evidence of skin ulcerations (23% vs. 0%; p=0.01) [Figure 1]. Overall baseline renal involvement and microscopic hematuria were less commonly observed in patients with H/N-IgAV. Among H/N-IgAV cases, at last follow-up all had resolution of H/N lesions but 3 of 13 had persistent skin lesions on the lower extremities despite ongoing treatment. Long-term outcome between cases and controls did not identify any significant differences in the development of end-stage renal disease, time to resolution of hematuria or proteinuria, time to complete IgAV response, or time to first IgAV relapse.

Conclusion: This study reports the largest series of patients with head/neck involvement of IgA, a rarely reported entity. In this cohort, patients with H/N-IgAV had less frequent renal involvement compared to IgAV patients with lower extremity only skin lesions. Clinicians should be aware of atypical locations of IgAV involvement. Additional research is needed to further understand this clinical subset.

Disclosure: M. Villatoro-Villar, None; **D. Wetter**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **K. Warrington**, Eli Lilly, 2, GlaxoSmithKline, 2, roche, 2, 8, Roche, 2, 5, 8, Sanofi, 5, sanofi, 5; **M. Koster**, None.

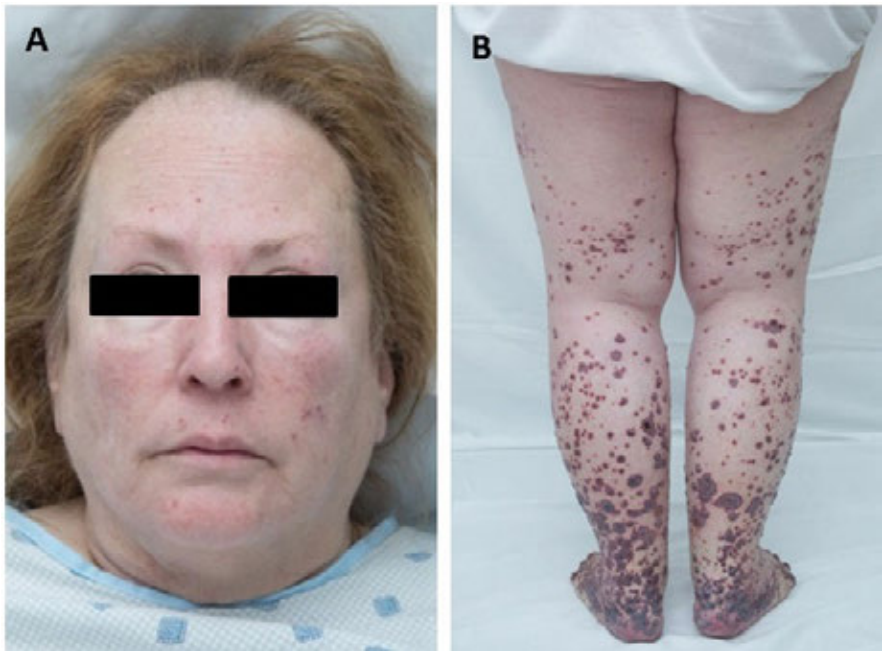

Figure 1 A) H/N involvement in IgAV (perioral, nasal, cheeks and neck). B) Severe PP in lower extremities with bullous, ulcerations and skin necrosis.

Characteristic, n (%)	H/N-IgAV (N=13)	LE-IgAV (N=26)	*p*-value
Age at diagnosis, years*	38 (24)	38 (24)	1.0
Male	7 (54%)	16 (62%)	0.65
Caucasian	13 (100%)	24 (96%)	0.47
Length of follow-up, years*	2.6 (3.5)	1.3 (2.0)	0.28
Body mass index, kg/m^2*	32 (17)	28 (10)	0.72
Hypertension	2 (15%)	8 (31%)	0.30
Infection within 4 weeks	7 (54%)	11 (42%)	0.50
Antibiotic exposure within 4 weeks	4 (31%)	6 (24%)	0.65
Abdominal ischemic symptoms	2 (15%)	3 (12%)	0.74
Palpable purpura	13 (100%)	26 (100%)	---
Skin ulceration	3 (23%)	0 (0%)	0.01
Any renal involvement	5 (38%)	19 (73%)	0.04
Microscopic hematuria	4 (31%)	17 (65%)	0.04
Proteinuria	4 (31%)	15 (58%)	0.11
C-reactive protein, mg/L*	28 (25)	22 (22)	0.61
Erythrocyte sedimentation rate, mm/hr*	20 (21)	27 (25)	0.80
eGFR (ml/min/1.73m^2)*	87 (41)	95 (42)	0.88

*mean (±standard deviation); H/N, head and/or neck; LE, lower extremity only

Table 1: Baseline characteristics of patients with head and neck involvement of IgA-vasculitis compared to those with lower extremity only skin lesions

Abstract Number: 1713

Drug-induced IgA Vasculitis: Data from the French Pharmacovigilance Network and the WHO VigiBase

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

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Session Time: 9:00AM–11:00AM

Background/Purpose: IgA vasculitis (IgAV) is an immune complex small-vessel vasculitis, with IgA1-dominant immune deposits. Drug-induced IgAV were rarely reported in the literature, but no systematic analysis was done so far. We used a novel approach combining the analysis of two pharmacovigilance (PV) databases to identify the main drugs associated with drug-induced IgA.

Methods: We used VigiBase, the WHO global individual case safety reports database, and the FPVD (French PV Database), to extract drug-induced IgAV using MedDRA terms compatible with the diagnosis of IgAV, between database inception and Jan 2019. Detailed narratives of cases from BNPV were analyzed by two investigators and then categorized into possible or definitive IgAV based on predefined criteria. Demographic and clinical data on IgAV, drugs class and chronological relationship with IgAV were described. Using VigiBase data, we evaluated the association between IgAV and drugs by conducting disproportionality analyses (case-noncase method) calculating reporting odds ratios (RORs). Significance was reached if RORs were >1.

Results: From the 466 cases extracted from the FPVD database, we finally included 113 definitive or possible IgAV cases (for which 177 drugs were suspected as potential triggers); and among 18,518,924 individual case safety reports from VigiBase, we included 1242 cases (associated with 40 drugs with significant RORs).

FPVD population was mainly male (58%), with a median age of 28 years. Main IgAV clinical characteristics were purpura in 100%, joint involvement in 55%, gastrointestinal involvement in 36% and renal involvement in 33%. No vasculitis-specific treatment was required in 67%, whereas 32% of patients received glucocorticoids, 3% colchicine, and 1% cyclophosphamide. Outcome was favorable in 60% of patients, but 16% had sequelae, most frequently mild to moderate (only 2 patients had chronic renal failure). No death was reported during follow up.

The drugs associated with the highest number of drug-induced IgAV were vaccines (23% of all treatments), antibiotics and others antimicrobial drugs (21%), and tumor necrosis factor (TNF)-α blockers (8%). Median interval between initiation of vaccines, antibiotics/antimicrobial drugs and TNF-α blockers and IgAV onset were 11 days, 10 days and 26.5 months, respectively.

Frequencies of drugs identified within the FPVD and their associated RORs calculated within VigiBase are summarized in the Table.

Conclusion: Our study enables the identification of the main drugs associated with drug-induced IgAV using a combined approach of the detailed narratives from the FPVD and the large international Vigibase. Main suspected drugs

Table 1 : Drugs frequencies in BNPV and associated RORs in Vigibase	FPVD %	n =	Vigibase RORs
Vaccines (41)	**23%**	**41**	
measles, combinations with mumps and rubella, live attenuated vaccine	5%	8	9,93
hepatitis B, purified antigen vaccine	3%	6	8,38
influenza, inactivated, split virus or surface antigen vaccine	3%	5	8,27
influenza A(H1N1)pdm09 vaccine	3%	5	9,13
diphtheria-pertussis-poliomyelitis-tetanus vaccine	3%	5	8,85
hepatitis A, inactivated, whole virus vaccine	2%	3	9,62
diphtheria-poliomyelitis-tetanus vaccine	2%	3	19,7
meningococcus C, purified polysaccharides antigen conjugated vaccine	1%	1	10,54
meningococcus A,C, bivalent purified polysaccharides antigen vaccine	1%	1	
pneumococcus, purified polysaccharides antigen conjugated vaccine	1%	1	5,65
papillomavirus (human types 6, 11, 16, 18) vaccine	1%	1	12,79
diphtheria-hemophilus influenzae B-pertussis-poliomyelitis-tetanus vaccine	1%	1	4,26
diphtheria-hemophilus influenzae B-pertussis-poliomyelitis-tetanus-hepatitis B vaccine	1%	1	
Antibiotics and other microbial drugs (38)	**21%**	**38**	
B-lactamines (14)	**8%**	**14**	
amoxicillin	2%	4	2,19
amoxicillin and beta-lactamase inhibitor	1%	2	2,43
ceftriaxone	2%	3	0,52
cloxacillin	1%	1	
piperacillinpiperacillin and beta-lactamase inhibitor	1%	1	0,92
ceftazidime	1%	1	
cefixime	1%	1	
cefpodoxime	1%	1	
Macrolides (3)	**2%**	**3**	
clarithromycin	1%	2	4,48
azithromycin	1%	1	1,44
Fluoroquinolones (4)	**2%**	**4**	
ciprofloxacin	1%	2	1,76
norfloxacin	1%	2	
Others (17)	**10%**	**17**	
sulfamethoxazole and trimethoprim	2%	3	0,86
doxycycline	1%	2	
pristinamycin	1%	2	
nitrofurantoin	1%	1	1,72
clindamycin	1%	1	0,99
tobramycin	1%	1	
spiramycin and metronidazole	1%	1	
rifampicin	1%	1	
isoniazid	1%	1	
rifampicin and isoniazid	1%	1	
ethambutol	1%	1	
atovaquone ; proguanil	1%	1	
oseltamivir	1%	1	
TNF alpha blockers (14)	**8%**	**14**	
adalimumab	5%	9	1,72
infliximab	3%	5	4,52
Antihypertensive agents (12)	**7%**	**12**	
furosemide	1%	2	0,7
spironolactone	1%	1	
buflomedil	1%	1	
troxerutin	1%	1	
bisoprolol	1%	1	
bisoprolol and thiazides	1%	1	
lercanidipine	1%	1	
diltiazem	1%	1	1,46
perindopril	1%	1	
ramipril	1%	1	
irbesartan and diuretics	1%	1	
Analgesics (10)	**6%**	**10**	
paracetamol	3%	5	1,32
paracetamol, combinations excl. psycholeptics	1%	2	
tramadol and paracetamol	1%	1	
codeine	1%	1	
morphine	1%	1	

were vaccines, antibiotics and TNF-α blockers in both databases. This list of suspected drugs may prove useful to physicians when confronted with potential IgAV cases.

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Abstract Number: 1714

Can We Predict Early Relapses in Adult IgA Vasculitis?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In adults, IgA vasculitis (IgAV) frequently takes a severe course in the acute phase of the disease. Data on long term outcomes is limited. It has been observed that a proportion of patients relapse. Our aim was to define potential predictors of relapsing IgAV in a cohort of unselected adult IgAV cases.

Methods: We analysed medical records of histologically proven IgAV cases diagnosed between January 2010 and September 2018, and prospectively followed until May 2019. The relapse was defined as a new development of skin purpura, joint or gastrointestinal tract (GIT) symptoms or laboratory signs of renal disease at follow-up visit after clinical/laboratory remission, after exclusion of other causes. We explored the differences in the baseline characteristics between the relapsing and non-relapsing IgAV cases. A multivariate logistic regression model included predictors that significantly differed between the groups.

Table 1. Baseline characteristic of IgAV

Characteristics*	Relapsing IgAV (30)	Non-relapsing IgAV (183)	p-value*
Male gender#	17 (56.7)	105 (57.4)	1.0
Age (years)$	51.7 (32.4-74.6)	64.6 (48.6-77.3)	0.032
Ever smoker#	5 (16.7)	83 (45.9)	0.003
Infection – recent#	9 (30.0)	63 (34.4)	0.683
New medication#	4 (13.3)	44 (24.0)	0.243
History of cancer#	3 (10)	24 (13.1)	0.775
Constitutional symptoms#	6 (20.0)	29 (15.8)	0.596
Joint involvement#	11 (36.7)	78 (42.6)	0.690
Generalized skin purpura&,#	13 (43.3)	91 (49.7)	0.559
Skin necroses#	7 (23.3)	86 (47)	0.017
GIT#	8 (26.7)	58 (31.7)	0.674
Renal#	11 (36.7)	81 (44.3)	0.552
Elevated serum IgA#	11/21 (52.4)	60/136 (44.1)	0.491
BVAS-3$	6 (2-12)	8 (3-15)	0.049

Legend: # - number (%) of patients; $ median (IQR); & - purpura above the waistline, GIT - gastrointestinal tract; BVAS-3 - Birmingham vasculitis activity score. *Fisher's exact test or Mann-Whitney U test

Results: During the 105-month observation period we identified 250 new IgAV cases. During the acute disease 4 patients died. 33 patients were lost to follow-up. Of the remaining 213 patients who were followed for a median 12.5 (IQR 6.8–24.2) months, 30 (14.1%) patients relapsed. 21 (70%), 5 (16.7%), and 4 (13.3%) patients relapsed once, twice, and three or more times, respectively. The relapse was limited to the skin in 24 (80%) patients, involved skin, joints, GIT and kidneys in 4 (13.3%), and was limited to the kidneys in 2 (6.7%) patients. The comparison of baseline characteristics between relapsing and non-relapsing IgAV subgroup is shown in Table 1. In a multivariate logistic regression model, the relapsing IgAV was associated with younger patient age (OR 0.98 (95% CI 0.96-0.99; p=0.024) and non-smoking status (OR 4.41 (95%CI 1.6-12.1), p=0.004).

Conclusion: Younger IgAV patients, who never smoked, tend to have a higher risk for early relapse and should be followed closely.

Disclosure: J. Ostrovrsnik, None; **Z. Rotar**, None; **M. Tomsic**, None; **A. Hocevar**, None.

Abstract Number: 1715

Predictors of Gastrointestinal and Renal Involvement in Adult IgA Vasculitis

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Background/Purpose: IgA vasculitis (IgAV) is a common vasculitis of adult population, yet the disease in adults is still poorly defined. The aim of our study was to determine the predictors of gastrointestinal (GI) or renal involvement in adult IgAV.

Methods: Medical records of histologically proven adult IgAV cases diagnosed between January 2013 and April 2019 at our secondary/tertiary rheumatology center were analyzed. The impact of 7 variables (age, gender, smoking, history of preceding infection, use of new medication prior IgAV, the extent of skin purpura (generalized above the waist vs. localized), and the presence of elevated serum immunoglobulin A (IgA) level) on the development of GI and renal involvement was evaluated using logistic regression models.

Results: During the 76-month observation period we identified 203 new adult IgAV cases (58.1% males, median (interquartile range) age 64 (47-76) years, 91 (44.8%) ever smokers). GI tract and renal involvement developed in 55 (27.1%) and 78 (38.4%) cases, respectively. Clinical characteristics of IgAV patients are presented in Table 1. In a multivariate logistic regression model generalized purpura increased (OR 5.45 (95%CI 2.56 - 11.59), p< 0.001) and elevated serum IgA level decreased (OR 0.45 (95%CI 0.21 - 0.95), p=0.037) GI tract involvement. Current smoking (OR 3.04 (1.34-6.89), p=0.008), generalized purpura (OR 1.97 (95%CI 1.06-3.65), p=0.032), elevated serum IgA (OR 1.96 (95%CI 1.02-3.74), p=0.041), and marginally also age (OR 1.02 (95%CI 1.01-1.04), p=0.012,) were associated

Clinical characteristics	*IgAV cases (203)*	*Clinical characteristics*	*IgAV cases (203)*
Male gender (%)	58.1	Necrotic purpura (%)	45.8
Age (years)*	58 (38-74)	Generalized purpura[&] (%)	51.2
Prior infection (%)	33.0	Joint involvement (%)	35.5
New medication (%)	24.6	Arthritis (%)	12.8
Current smoking (%)	19.7	GI tract involv. (%)	27.1
Past smoking (%)	25.1	Renal involv. (%)	38.4
Elevated serum IgA (%)	46.3	BVAS-3	6 (2-13)

Legend: * median (IQR); [&] purpura above the waistline; GI gastrointestinal; BVAS-3 Birmingham vasculitis activity score;

with an increased risk of renal involvement in our cohort. Gender and potential triggers of IgAV (i.e. prior infections, and the use of new medication) did not significantly influence the clinical presentation of adult IgAV.

Conclusion: Generalized purpura predicted both renal and GI involvement in adult IgAV, active smoking renal involvement, while the serum IgA level had a divergent effect on renal and GI involvement.

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Poor-Prognosis Factors of Systemic Vasculitides with Gastrointestinal Involvement: Data from a Large Retrospective Study

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SESSION INFORMATION

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Background/Purpose: Gastrointestinal (GI) involvement was described as a poor-prognosis factor of systemic necrotizing vasculitides. However, the prognostic impact of GI involvement may vary according to clinical manifestation and vasculitis subtype. We aimed to describe initial symptoms and outcomes of GI involvement of vasculitides and identify factors predictive of poor outcomes among systemic vasculitides.

Methods: Patients with systemic vasculitides as defined by the 2012 Chapel Hill Consensus Conference and with initial GI involvement were retrospectively included. Baseline characteristics, treatments received and outcomeswere recorded. The primary endpoint was a composite of intensive care unit (ICU) admission, emergency surgical procedure, GI-related sepsis or death.

Results: Among the 191 patients diagnosed between 2006 and 2019 included (67% men, mean±SD age 50±19 years), vasculitides were distributed as follows: 75 IgA vasculitis, 50 ANCA-associated vasculitis, 35 polyarteritis nodosa (PAN), 9 large-vessel vasculitis and 22 other vasculitides (including Behçet's disease). Seventy-four (39%) patients reached the composite primary endpoint after a median [IQR] of 10 [0–32] days.Sixty (31%) patients were admitted to the ICU, 34 (18%) required emergency surgery, 30 (16%) had GI-related sepsis. Twelve (6%) patients died of a GI cause after a median of 41 [24–68] days. Vasculitis subtype was associated with the primary endpoint: PAN diagnosis was associated with a poor outcome (hazards ratio [HR] 2.21 (95% CI 1.36–3.62); P< 0.001), while IgA vasculitis had a better outcome (HR 0.32 (95% CI 0.18–0.58); P< 0.001).

Baseline characteristics associated with the primary endpoint [HR (95% CI)] included: age [1.02 (1.0–1.03); P=0.007], fever [2.52 (1.56–4.08); P< 0.001], abdominal pain requiring morphine [3.05 (1.74–5.34); P< 0.001], abdominal guarding [2.76 (1.53–4.98); P=0.001], ileus [3.1 (1.79–5.36); P=0.001], melena [2.30 (1.33–3.98); P=0.003]and intestinal ischemia [3.95 (2.14–7.28); P< 0.001]. High serum C-reactive protein level, WBC count, lactate dehydrogenase levels, performance status, in-hospital admission SOFA score, low oxygen saturation, and hemoglobin and bicarbonate levels were associated with poor outcomes. Endoscopy-identified mucosal abnormalities were not associated with the primary outcome.

To identify patients requiring ICU admission, emergency surgery, GI-related sepsis or death, a score predictive of poor outcome is being developed.

Conclusion: Vasculitides with initial GI involvement, mainly PAN, had poor outcomes for >30% of the patients. We identified a set of clinical and biological factors present at diagnosis associated with this poor outcome. We are devising a predictive score based on these variables to identify patients requiring early supportive care.

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Abstract Number: 1717

Identifying Patterns of Histopathologic Presentation in CNS Vasculitis

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SESSION INFORMATION
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Background/Purpose: Primary central nervous system vasculitis (CNS-V) is vasculitis confined to the brain, spinal cord and meninges. It is a rare condition with unknown pathogenesis. Brain biopsy is the gold standard for the diagnosis of CNS-V, which histologically is marked by transmural inflammation of small and medium-sized leptomeningeal and parenchymal arterial vessels. This study aimed to analyze in depth other histopathologic features that may better distinguish CNS-V from other non-CNS-V conditions.

Methods: We identified patients who had brain biopsy and who were enrolled in the prospective CNS Vasculopathy Bioregistry at the Cleveland Clinic between 2012 and 2019. Registry participants are enrolled in both outpatient and inpatient settings based on differential diagnosis of CNS-V or a mimic of its symptoms. Out of 33 patients included, 19 were diagnosed with CNS-V according to (Calabrese and Mallek, 1988). Fourteen patients had uncertain diagnosis or diagnosis not consistent with CNS-V. Pathology reports were analyzed looking for documented inflammatory cell types (T cells, B cells, macrophages, reactive astrocytes, plasma cells, and giant cells) and other histological features (granuloma/epithelioid histiocytes, necrotizing vasculitis, infection, neuronal loss, myelin loss, and amyloid deposits), each categorized by the presence ('yes/no') of cell type or histological feature, abundance ('scant' or 'abundant'), confirmation by staining ('yes/no'), and localization ('transmural' or 'perivascular').

Results: Our cohort consisted of mostly white (~90%), male (≥50%) and middle-aged (48.6±15.8 years; age at biopsy) individuals who had undergone 1.15±0.44 biopsies. Both CNS-V and non-CNS-V cases had the right side (53% and 64%) and frontal lobe (35% and 29%) as the most affected sites. Patients with diagnosis of CNS-V were more likely to have vascular wall infiltration by T cells (33% vs 10%), B cells (20% vs 10%), macrophages (18% vs 0%), and reactive astrocytes (22% vs 0%), and more prevalence of necrotizing vasculitis (11.8% vs 0%). Perivascular distribution was conversely lower in CNS-V than non-CNS-V, noted in 42% vs 70% for T cells, 40% vs 60% for B cells, and 18% vs 20% for macrophages.

Conclusion: In this retrospective study, we took a broad approach of comparing brain biopsies of patients with or without CNS-V to identify histopathological features that may be unique or more predictive of CNS-V. Intramural infiltration of inflammatory cells was more specific to the diagnosis of CNS-V than findings of perivascular inflammatory process. The presence of perivascular inflammation is nonspecific and is more common in non-CNS-V specimens.

Reference

1 Calabrese, L.H. and Mallek, J.A. (1988) Primary angiitis of the central nervous system. Report of 8 new cases, review of the literature, and proposal for diagnostic criteria. *Medicine (Baltimore)* 67, 20–39

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Abstract Number: 1718

Geographic Disparities in Mortality Rates of Vasculitis in the United States: 1999 to 2017

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Background/Purpose: Earlier diagnosis and less toxic immunosuppressive therapies have improved the survival of patients with vasculitis. Current data on mortality rates of vasculitis are limited. We aimed to estimate the mortality rates of primary vasculitis using the most recent publicly available mortality data in the United States.

Methods: We used the CDC Wonder Underlying Cause of Death database and its query system to obtain mortality rates of vasculitis as the underlying cause of death from 1999 to 2017. We used the following ICD-10 codes: D69.0 (Allergic purpura) for Henoch-Schoenlein purpura, D89.1 (Cryoglobulinaemia) for cryoglobulinemia, M30.0 (Polyarteritis nodosa) for polyarteritis nodosa (PAN), M30.1 (Polyarteritis with lung involvement [Churg-Strauss]) for eosinophilic granulomatosis with polyangiitis (EGPA), M30.2 (Juvenile polyarteritis) for juvenile polyarteritis, M30.3 (Mucocutaneous lymph node syndrome [Kawasaki]) for Kawasaki's disease, M30.8 (Other conditions related to PAN), M31.0 (Hypersensitivity angiitis) for Goodpasture's syndrome, M31.3 (Wegener's granulomatosis) for granulomatosis with polyangiitis (GPA), M31.4 (Aortic arch syndrome [Takayasu]) for Takayasu's arteritis (TAK), M31.5 (Giant cell arteritis

Figure 1. Age-adjusted mortality rate for vasculitis as underlying cause of death by year.

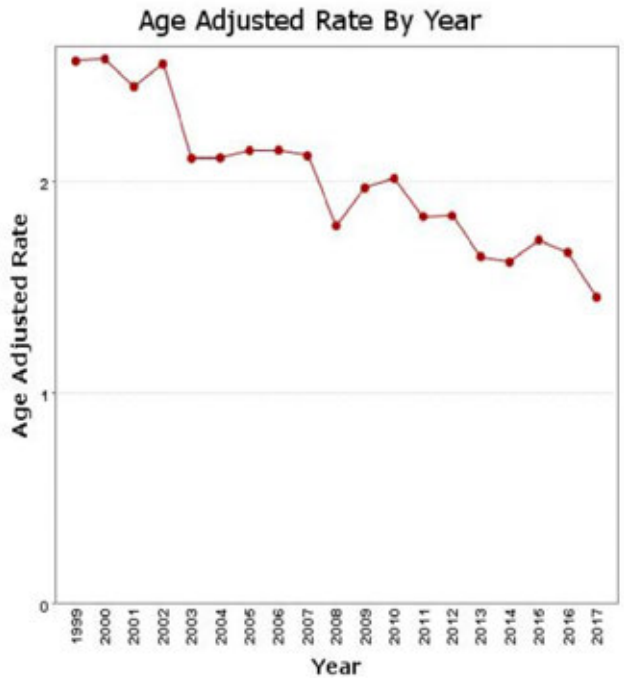

Table 1. Age-adjusted mortality rate per million for vasculitis as underlying cause of death, by race and gender.

Race	Gender	Deaths	Population	Age-Adjusted Rate (95% CI)	% of Total Deaths
White	Female	6,125	2,326,457,753	2.067 (2.015 - 2.120)	50.771%
	Male	4,906	2,275,993,219	2.159 (2.098 - 2.220)	40.666%
	Total	**11,031**	**4,602,450,972**	**2.122 (2.082 - 2.162)**	**91.437%**
American Indian or Alaska Native	Female	62	36,894,044	2.473 (1.863 - 3.219)	0.514%
	Male	35	37,044,572	1.624 (1.070 - 2.362)	0.290%
	Total	**97**	**73,938,616**	**2.087 (1.658 - 2.594)**	**0.804%**
Black or African American	Female	369	406,808,112	1.025 (0.919 - 1.131)	3.059%
	Male	319	372,183,341	1.142 (1.007 - 1.277)	2.644%
	Total	**688**	**778,991,453**	**1.063 (0.981 - 1.145)**	**5.703%**
Asian or Pacific Islander	Female	137	158,995,020	1.012 (0.839 - 1.185)	1.136%
	Male	111	147,089,506	0.993 (0.797 - 1.189)	0.920%
	Total	**248**	**306,084,526**	**1.003 (0.873 - 1.132)**	**2.056%**
Total		**12,064**	**5,761,465,567**	**1.989 (1.953 - 2.024)**	**100.000%**

CI: Confidence interval.

[GCA] with polymyalgia rheumatica [PMR]) for GCA with PMR, and M31.6 (Other GCA) for GCA, M31.7 (Microscopic polyangiitis [MPA]), and M35.2 (Behcet's disease). Mortality rates were obtained by year, gender, race, state and separately for the specific ICD codes. To obtain age-adjusted mortality rates we used year 2000 U.S. standard population. Mortality rates are given as number of deaths per million. A linear regression model was applied to evaluate trends over time.

Results: During the 19-year period, vasculitis was the underlying cause of death of 12,064 patients. Age-adjusted mortality rate was 1.99 per million (95% CI: 1.95-2.02). Since 1999, there has been a significant trend to the decrease ($p< 0.0001$) (Figure 1). The age-adjusted mortality rate was higher in males than in males (2.05 vs. 1.94 per million). Age-adjusted mortality rate was higher in Whites (2.12, 2.08-2.16) than in Blacks (1.06, 0.98-1.14) (Table 1). GPA accounted for 50.93% of all vasculitis deaths. Interestingly, there was only one death for GCA with PMR and only one for juvenile polyarteritis. There was geographic distribution in the mortality rates of vasculitis by estates. The estates with the highest age-adjusted mortality rates were Oregon, Maine, Vermont, Wyoming and Alaska (Table 2). The estates with the lowest rates were New York, North Dakota, Hawaii, New Jersey and Rhode Island. and.

Conclusion: Mortality by vasculitis remains very low, probably due to the low incidence of these disorders. There is a progressive decrease of the mortality rates. Age-adjusted mortality rate was higher in males and in Whites, which can

Table 2. The 12 states with the highest mortality due to vasculitis as underlying cause of death with age-adjusted rates and 95% confidence interval.

	Deaths	Population	Age-Adjusted Rate per 1,000,000 (95% CI)
Oregon	264	71,265,198	3.274 (2.876 - 3.671)
Maine	97	25,013,975	3.166 (2.562 - 3.870)
Vermont	42	11,801,177	3.085 (2.214 - 4.185)
Wyoming	32	10,296,319	3.077 (2.091 - 4.368)
Alaska	29	13,100,743	2.976 (1.907 - 4.428)
Montana	61	18,443,327	2.884 (2.201 - 3.712)
Idaho	76	28,525,825	2.751 (2.164 - 3.449)
New Mexico	107	37,679,448	2.735 (2.214 - 3.257)
Tennessee	327	117,660,805	2.609 (2.323 - 2.894)
Iowa	179	57,386,432	2.562 (2.181 - 2.942)
Kansas	147	53,312,917	2.552 (2.137 - 2.968)
Minnesota	270	99,446,183	2.535 (2.231 - 2.840)

CI: Confidence Interval.

be explained by the fact that GPA, which is more frequent in males and Whites, is responsible for half of the overall number of deaths. Investigation of the reasons for the geographic disparities is warranted. Our findings should be taken with caution until quality studies to determine the reliability of the data about these rare diseases available in national databases are performed.

Disclosure: A. Rodriguez-Pla, None.

Abstract Number: 1719

Clinical Phenotypes in Relapsing Polychondritis in a Prospective Cohort

Marcela Ferrada,[1] Kaitlin Quinn,[2] Wendy Goodspeed,[3] Jeffrey KIm,[4] Clint Allen,[4] Arlene Sirajuddin,[5] Marcus Chen,[5] K Bates Gribbons,[6] Joel S. Rosenblum,[7] Casey A. Rimland,[8] James Katz,[1] and Peter C. Grayson[9], [1]NIAMS, Bethesda, MD, [2]Georgetown University Hospital/National Institutes of Health, Washington, DC, [3]NIAMS, Bethesda, [4]NIDCD, Bethesda, [5]NHLBI, Bethesda, [6]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [7]National Institute of Arthritis, Musculoskeletal and Skin Disease (NIAMS), Bethesda, MD, Bethesda, MD, [8]National Institute of Arthritis, Musculoskeletal and Skin Disease (NIAMS), Bethesda, MD, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC, Chapel Hill, NC, [9]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) of the National Institutes of Health, Bethesda, MD, Bethesda, MD

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Relapsing polychondritis (RP) is a systemic inflammatory disease that can be fatal. The main clinical feature that typically leads to diagnosis is ear inflammation, however the disease is very heterogeneous and can involve multiple organs. Failure to recognize RP can lead to diagnostic delay and further complications. The study objective was to identify specific phenotypes in a prospective cohort of patients with RP.

Methods: Patients 18 years and older were selected from a prospective, observational cohort. All patients met McAdams or Damiani's diagnostic criteria for RP. Six clinical variables were used to identify clusters of patients using latent class analysis. Model selection was based on the akaike information criterion. Cases were assigned to a cluster based on probability of membership. The variables included in the model were saddle nose deformity, subglottic stenosis (SGS), tracheomalacia (TM), bronchomalacia (BM), ear inflammation and tenosynovitis/synovitis. SGS was defined as pathological narrowing of the subglottis visualized by laryngoscopy. TM was defined as antero-posterior and/or lateral flattening of the tracheal wall during expiration on dynamic CT of ≥50%. BM was defined as collapse of the bronchi during dynamic CT scan. Ear involvement was defined as physician-observed tender swelling of the pinna with associated redness. Differences were assessed by chi square or Kruskal-Wallis test. Median values are presented.

Results: A total of 73 patients were included. Three clusters were identified: Cluster 1 "Typical" (n=10, 14%); Cluster 2 "Airway Predominant" (n=21, 29%); and Cluster 3 "Mild' (n=42, 57%) (Table 1). Typical RP was characterized by saddle nose deformity (86%), SGS (78%), TM (98%) and ear involvement (98%). Compared to the other clusters, these patients were defined by the shortest time to diagnosis (median = 1 year) and the greatest frequency of weight loss, stridor, air trapping, tracheal wall thickening, decreased FEF 25-75% and FEV1/FVC, ICU admissions, and tracheostomy. Airway Predominant RP was defined by TM (98%) and BM (56%) without saddle nose deformity or SGS and with infrequent ear involvement (41%). Patients in this cluster had the longest delay to diagnosis (median = 10 years) and the greatest percentage of genital ulcers, a previous diagnosis of asthma, and disability. Mild RP was defined by ear involvement (55%) and inflammatory arthritis (41%) without saddle nose deformity, SGS, TM, or BM. These patients had the highest prevalence of skin disease (33%). There were no significant differences in sex, ethnicity, hearing loss, use of DMARDs or biologics between the three clusters. Comparisons between the three clusters are summarized in Table 2.

Table 1. Three subgroups of patients with relapsing polychondritis identified using unbiased, clustering algorithm.

	Mild n=42	Airway Predominant n=21	Typical n=10	p value
Variables Included in Latent Class Analysis				
Saddle nose n (%)	0	0	8 (86)	<0.001
SGS n (%)	0	0	7 (78)	<0.001
TM n (%)	0	21 (98)	9 (98)	<0.001
BM n (%)	0	12 (56)	5 (49)	<0.001
Ear involvement n (%)	22 (55)	9 (41)	9 (98)	0.001
Tenosynovitis/Synovitis n (%)	25 (60)	11 (51)	6 (60)	0.81
Demographic Characteristics				
Race (White n (%))	38 (90)	18 (86%)	7 (70%)	0.29
Sex (Female n (%))	36 (86%)	17 (81%)	9 (90%)	0.78
Age, symptom onset (yrs, IQR)	35 (26-43)	37 (31-46)	37 (22-40)	0.36
Age at diagnosis (yrs, IQR)	42 (31-50)	48 (43-56)	39 (23-49)	0.08
Diagnostic Delay (yrs, IQR)	4.5 (2-8.5)	10(3.5-20)	1 (0.6-5)	0.007
Clinical Symptoms				
Fever n (%)	9 (21)	7 (33)	2 (20)	0.55
Weight loss n (%)	4 (9)	0(0)	4 (40)	0.02
Oral ulcers n (%)	10 (24)	10 (48)	2 (20)	0.12
Genital ulcers n (%)	5 (12)	7 (33)	0 (0)	0.02
Audiovestibular n (%)	34 (80)	16 (76)	7 (70)	0.73
Eye inflammation n (%)	11 (26)	4 (19)	4 (40)	0.47
Sinonasal disease n (%)	40 (95)	19 (95)	9 (90)	0.82
Costochondritis n (%)	37 (88)	17 (80)	9 (90)	0.70
Dry cough n (%)	32(76)	20 (95)	10 (100)	0.09
Skin symptoms n (%)	14 (33)	5 (24)	0 (0)	0.02
Sicca symptoms n (%)	17 (40)	8 (28)	5 (50)	0.82
Wheezing n (%)	12 (28)	13 (62)	5 (50)	0.03
Stridor n (%)	3 (7)	0 0	7 (70)	<0.0001
Other Diagnosis prior to RP Diagnosis				
Asthma n (%)	12 (28)	13 (62)	5 (50)	0.009
Ear infections n (%)	6 (15)	1 (5)	2 (20)	0.36
Sinusitis n (%)	10 (24)	4 (19)	4 (40)	0.46

Conclusion: We identified three phenotypic clusters of patients with RP that differ in time to diagnosis, clinical and radiological characteristics, and complications. Recognizing a broader spectrum of clinical patterns of disease in RP, beyond cartilaginous involvement of the ear and upper airway, may reduce diagnostic delay and facilitate development of targeted management approaches.

Disclosure: M. Ferrada, None; **K. Quinn**, None; **W. Goodspeed**, None; **J. Klm**, None; **C. Allen**, None; **A. Sirajuddin**, None; **M. Chen**, None; **K. Gribbons**, None; **J. Rosenblum**, None; **C. Rimland**, None; **J. Katz**, None; **P. Grayson**, None.

Table 2. Differences in Imaging, Pulmonary Function Test, Treatment, and Outcomes Among Three Subgroups of Patients with Relapsing Polychondritis.

	Mild n=42	Airway Predominant n=21	Typical n=10	p value
Chest Dynamic CT Scan				
Airtrapping n (%)	13 (34%)	14 (67%)	8 (89%)	0.002
Tracheal wall >2 mm n (%)	4 (10%)	3 (14%)	9 (90%)	<0.0001
Pulmonary Function Test				
FVC Pre % (median, IQR)	91 (85-100.5)	90 (81-103)	94 (58-102)	0.92
FEV1 Pre % (median, IQR)	89 (81-89)	83 (67-97)	76 (26-84)	0.06
FEF 25-75 %Ref (median, IQR)	82 (65-97)	88 (47-92)	38 (15-66)	0.01
FEV1/FVC Pre% (median, IQR)	79 (75-81)	76 (66-80)	60 (43-71)	0.0006
VC% Ref (median, IQR)	96 (87-107)	94 (86-111)	91 (44-102)	0.55
TLC % Ref (median, IQR)	93 (89-99)	94 (87-105)	92 (66-97)	0.78
RV % Ref (median, IQR)	74 (61-83)	82 (66-97)	75 (51-101)	0.36
RV/TLC Ref (median, IQR)	72 (64-85)	87 (71-95)	80 (65-104)	0.12
DLCO Adj % (median, IQR)	19 (17-21)	18 (17-22)	18 (15-19)	0.25
Treatment				
DMARD's n (%)	25 (59)	16 (76)	8 (80)	0.25
Biologics n (%)	17 (40)	8 (38)	7 (70)	0.19
Complications				
Tracheostomy n (%)	2 (5)	0 (0)	5 (50)	<0.001
Disability n (%)	11 (26)	12 (57)	2 (20)	0.10
Hearing loss n (%)	13 (31)	9 (43)	5 (50)	0.43
ICU admission n (%)	5 (13)	1 (6)	5 (50)	0.02

Abstract Number: 1720

Pentoxifylline Gel for Oral Ulcers in Patients with Behçet's Syndrome

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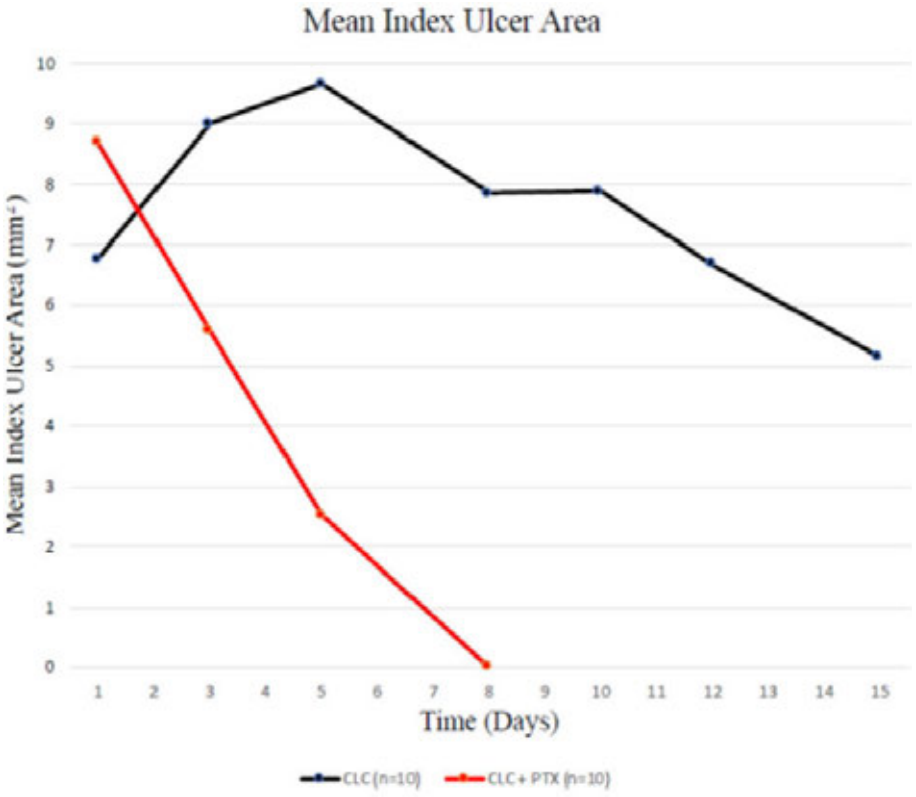
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Oral ulcers, the hallmark lesion of Behçet's syndrome (BS) can be disabling and impair eating, drinking and speaking. Despite recent advances in systemic medications for the treatment of oral ulcers, some patients do not achieve complete remission. Topical agents may help such patients by decreasing the pain and duration of oral ulcers. Pentoxifylline (PTX) is a methylxanthine derivative that inhibits phosphodiesterase and is thought to have immunomodulatory effects in addition to improving blood flow which is its main reason for use in peripheral vascular disorders. The aim of this study is to assess the efficacy and safety of PTX gel for oral ulcers in patients with BS. We also aimed to explore the best tools for the assessment of treatment response to topical agents in randomized controlled trials (Clinicaltrial.gov ID: NCT 03888846).

Methods: This was an open-label, randomized, parallel group study comparing PTX gel in addition to colchicine (PTX-COL) with colchicine alone (COL). Patients with BS who were treated with colchicine and not using any other systemic medications for BS, having at least one oral ulcer that appeared during the last 48 hours were included. PTX 5% gel with a dose of 1000 mg/day was applied in 4 divided doses per day for 14 days. Patients were contacted daily for 14 consecutive days. Photographs were taken every 24 - 48 hours and graphical processing software was used to calculate the area of the index ulcer. Duration of the index ulcer, time to start of index ulcer shrinkage, time to 50% reduction in oral ulcer pain on a 10 mm visual analog scale (VAS), change from baseline in the area of the index ulcer over time, total number of oral ulcers and adverse events were evaluated. A total of 60 patients are planned to be recruited. We present here results of the interim analysis of the first 21 patients.

Results: A total of 21 patients (ratio M:F 1:1.1, mean age:39.9 years), 11 in the PTX-COL group and 10 in the COL group have completed the study at the time of this analysis. One patient in the PTX-COL group withdrew from the study after day 1 and was not included in the current analysis. Mean duration of index ulcer, time to start of index ulcer shrinkage, time to 50% reduction in oral ulcer pain, and total number of oral ulcers during 14 days in each group were lower in the PTX-COL group as presented in the Table. Change from baseline in the area of index ulcer over time

	PTX-COL (n=10)	COL (n=10)	Difference of means (95% CI)	Effect size (Cohen's *d*)
Mean duration of index ulcer (days)	3.4 ± 2.01	7.5 ± 3.89	4.1 ± 9 (1.2 to 7)	1.32
Mean time to start of index ulcer shrinkage	1.2 ± 0.6	4.3 ± 3.5	3.1 ± 2.36 (0.74 to 5.46)	1.23
Mean time to 50% reduction in pain VAS (days)	2.8 ± 1.03	5.9 ± 3	3.1 ± 2.11 (0.99 to 5.21)	1.38
Mean total number of oral ulcers during 15 days	0.8 ± 0.48	1.97 ± 1.64	1.17 ± 1.14 (0.03 to 2.31)	0.97



is shown in the Figure. There were no serious adverse events. Seven patients in the PTX-COL group reported transient discomfort and nausea while they kept the gel in their mouth, 1 patient withdrew from the study for this reason.

Conclusion: The preliminary analysis of the first 21 patients of this open label, randomized trial showed that PTX gel may be a promising agent for decreasing the duration and pain of oral ulcers in patients with BS: However, caution is required when interpreting these results in a yet small number of patients. Duration of oral ulcers, time to start of ulcer shrinkage and 50% reduction in pain score seem to be relevant outcomes for studying topical agents in RCTs for oral ulcerations of BS.

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Abstract Number: 1721

Adult Primary Central Nervous System Vasculitis Treatment and Course: A Long-term Follow-up Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate long-term treatment and outcomes of a large cohort of patients with primary central nervous system vasculitis (PCNSV)

Methods: The study cohort consisted of 191 consecutive patients seen at Mayo Clinic (Rochester, MN) over 35-years (1983 to 2017). The follow-up and treatment of all PCNSV patients were updated until June 2018. The diagnosis of PCNSV was based on findings of brain or spinal cord biopsy, cerebral angiography, or both. Biopsy specimens were reviewed by a neuropathologist, and neurological imaging by a neuroradiologist. We used the treating physician's global opinion to assess response to therapy. Disability was defined using the modified Rankin scale. Outcomes, relapses, treatment response and ability to suspend treatment at last follow-up were analyzed (mean follow-up length: 54.2+73.6 months).

Results: Treatment at diagnosis in 186/191 patients were as follows: 72 prednisone (PDN) alone, 90 PDN and cyclophosphamide (CYC), 2 CYC alone, 13 mycophenolate mofetil (MMF) and PDN, 6 azathioprine (AZA) and PDN, 1 chlorambucil and PDN, 1 rituximab (RTX) and PDN and 1 infliximab and PDN. A favorable response was observed in 83.1% of patients treated with PDN alone, in 81.2% of patients treated with CYC and PDN, and in 94.7% of patients treated with MMF or AZA and PDN. Relapses were observed in 30.4% of patients (13.1% had at least 2 flares), and 34.6% of patients discontinued therapy by the time of the last followup visit. Patients with prominent gadoliniun-enhanced cerebral or meningeal lesions had more frequently relapses (OR 1.76), while no significant differences in relapse rates were observed comparing patients treated with only PDN versus those associating PDN and CYC. High disability scores (Rankin score of 4-6) were equally frequent at last followup in patients with relapsing disease (34.5%) and in those without relapses (30.1%). Large vessel involvement (OR 2.80) and cerebral infarction on imaging at diagnosis (OR 3.92) were associated with a poor treatment response. Cerebral infarction at diagnosis (OR 1.76) were also associated with continued treatment at last followup. Higher disability scores at last followup visit were associated with increasing age at diagnosis (OR 1.48) and cerebral infarctions on imaging (OR 2.09). No differences in mortality or in high disability scores at last follow-up (Rankin score 4-6) were observed comparing patients initially treated with PDN plus CYC (HR 0.740, OR 1.450) and PDN plus AZA or MMF (HR 0.538, OR 0.486) to those treated with PDN alone. 26 patients treated with MMF at the beginning or during followup had less frequent high disability scores (Rankin score of 4-6) at last followup than those treated with other drugs initially (15.3% vs 34.5%, $p = 0.06$), while patients given MMF had more relapses (53.8% vs 27.5%, $p = 0.01$). Three patients were treated with RTX for a disease flare and one as initial treatment. In 3 patients RTX was associated with a marked reduction in the number of flares (from 9 before starting RTX to 2 after).

Conclusion: The majority of patients with PCNSV responded to treatment. Cerebral infarctions at diagnosis were associated with poor response to treatment and worst outcomes. MMF and RTX appears to be effective therapy for PCNSV.

Disclosure: C. Salvarani, None; **R. Brown**, None; **T. Christianson**, None; **J. Huston III**, None; **C. Giannini**, None; **G. Hunder**, None.

Abstract Number: 1722

Mixed Cryoglobulin Immune Complex Proteomics: Analysis by Mass Spectroscopy

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Mixed Cryoglobulins (MCs) are cold precipitable Rheumatoid Factors (RFs) that provide a biomarker for immune complex formation, particularly associated with chronic Hepatitis C Virus (HCV) and Cryoglobulinemic Vasculitis (CryoVas) syndromes. Both the IgM and IgG components of MCs may span a spectrum of clonality, in type 2 >95% being IgMk and bearing Cross-reactive Idiotypes (CRIs) that can be revealed antigenically or by assessing specific heavy and/or light chain V-gene usage. Older studies indicated that C1q may be an integral part of MCs and that up to a third of the protein content is nonimmunoglobulin.

Objectives: We aimed to define the Immune Complexome of MCs by Mass Spectroscopy and protein sequence analysis (MALDI TOF) compared to existing data bases

Methods: MCs were isolated from the sera of patients with (a) HCV/CroVas before and after clearance of virus by Direct Acting Antivirals (DAAs), (b) persistent disease (purpura, nephritis) 2-15 years after HCV cure; (c) HIV-HCV coinfection, and (d) sjogrens or lupus patients with MCs consistently negative for HCV RNA . Isolated MCs were characterized by immunofixation and gel electrophoresis (SDS-PAGE) before being processed for MALDI-TOF. Specific gel bands identified by SDS-PAGE, including the IgM heavy chain, were excised and sequenced. In addition, serum obtained before cryoprecipitation was analyzed for the three pathways of complement activation and k/l by free and heavy-light chain immunoassays.

Results: In a prospective clinical trial (NTC0282512) the prevalence of complement abnormalities and an expansion of k light chains was demonstrated and the short-term effects of DAA, as well as SVR 24 were analyzed to assess biomarkers concomitant with viral clearance from blood and cryoprecipitates. Depression of C4/C1q was particularly apparent among the patients with persistent cryoglobulinemia, along with IgMk clonality. The validity of MALDI-TOF was reflected in the abundance of Ig heavy and light chain sequences, IgG subclasses, k/l ratios, V-region subgroups, and MC/monoclonal RF VH1-69, VH3-30, VK3D-15 and VK3D-20 MC CRI protein sequences In addition, complement (notably C1q) co-associated with the MC Igs, as well as other proteins relevant to known phlogistic activities of MCs, binding of IgM and the aggregation of proteins in the cold.

Conclusion: Our studies provide a platform for the analysis of MC immune complex proteomics as a laboratory biomarker relevant to CryoVas clinical syndromes

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Disclosure: P. Gorevic, None; **F. Eng**, None; **A. Branch**, None; **A. Elshamy**, None; **E. Doyle**, None; **T. Schiano**, None.

Abstract Number: 1723

Mixed Cryoglobulinaemia Since the Advent of New Direct-acting Antivirals for Hepatitis C Infection: Clinical Characteristics, Etiologies and Biological Features in 679 Patients

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Behçet's Disease & Other Vasculitides

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Previously chronic hepatitis C virus (HCV) infection was accountable for 80-90% of cases of mixed cryoglobulinemia (MC). The advent of direct-acting antivirals (DAA) has dramatically changed the management of chronic HCV infection. However, since their approval in 2011, data are very scarce on the prevalence of HCV-related MC. We aimed to study the main etiologies, clinical manifestations and immunological parameters of MC in the era of DAA agents.

Methods: Observational longitudinal cohort study that included 679 patients with MC at the Pitié-Salpêtrière Universitary Hospital, Paris, France, between 2011 and 2018. Demographic information (age at diagnosis, gender, year of diagnosis, etiology of MC) and laboratory data were recorded. Patients included were divided into two categories: HCV-related MC and non-HCV-related MC.

Results: The mean age of the patients was 55.5 (15.8) years, 54.5% were female, and 20.5% had vasculitis. Presence of vasculitis was not statistically different between HCV-related and non-HCV-related MC cases. Main clinical manifestations included skin involvement in 54.7%, neurological involvement in 49.6%, renal involvement in 21.6% and arthritis in 10.1% of patients. HCV-related MC cases had higher cryoglobulin levels (378 vs 369 mg/L, $p< 0.001$) and lower serum levels of complement C4 (0.16 vs 0.18, $p< 0.001$), whereas RF activity was higher in non-HCV-related cases (280 vs 261 UI/Lm $p< 0.001$).

Over the period of 2011 and 2018 chronic HCV infection accounted for 56% of cases of MC. The remaining causes of MC were autoimmune diseases (23%), hematological and neoplastic conditions (6%), infectious diseases other than chronic HCV infection (5%), whereas 10% of MC cases were identified as essential. In 2016-2017, HCV-related cases dropped with non-HCV-related cases representing the leading cause of MC. Indeed, in 2018, non-HCV-related represented 66.7% of MC.

Conclusion: DAA have changed the landscape of MC with HCV no longer being its leading cause in our cohort. Due to the safety profile and cure rates of DAA regimens, with HCV elimination being high on the world health agenda, we speculate that the incidence of HCV-related MC will dramatically decrease in the upcoming years.

Disclosure: G. Boleto, None; **P. Ghillani-Dalbin**, None; **L. Musset**, None; **P. Cacoub**, Abbvie, 5, AstraZeneca, 5, Bristol meyer squibb, 5, Gilead, 5, Glaxo Smith Kline, 5, Janssen, 5, Merck Sharp Dohme, 5, Roche, 5, Servier, 5, Vifor, 5; **D. Saadoun**, Abbvie, 5, AstraZeneca, 5, Bristol meyer squibb, 5, Gilead, 5, Glaxo Smith Kline, 5, Roche, 5, Servier, 5.

Abstract Number: 1724

Disease Manifestations and Impact on Quality of Life in Subjects with Pre-Pubertal Onset Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) can be a severe disease, especially when diagnosed in childhood. Onset prior to puberty (Tanner stage II) is rare, and less is known about the impact SLE has on this pediatric subpopulation. We assessed clinical and quality of life (QOL) measures in a pre-pubertal SLE onset cohort to better globally understand the burden of this disease in this group.

Methods: In a prospective, multicenter (10 Childhood Arthritis and Rheumatology Research Alliance sites), observational study, subjects with pre-pubertal onset of SLE were enrolled. Subjects either were still in Tanner I or no later than Tanner stage II at enrollment. QOL measures were collected in addition to comprehensive medical history, physical examination findings, laboratory assessments, SLEDAI-2K scores, and SLICC/ACR Damage Index. QOL measures were obtained by PedsQL™ 4.0 Core and PedsQL™ 3.0 Rheumatology Module surveys completed by the child at the enrollment visit. QOL data was available for 42 subjects (31 females, 11 males) and longitudinal QOL data was available for 25 subjects. QOL means were compared with disease manifestations by t tests.

Manifestations of Disease Activity	Number	Percent
Psychosis	1	2%
Organic Brain Syndrome	1	2%
Lupus Headache	1	2%
Vasculitis	3	7%
Arthritis	5	12%
Rash	10	24%
Alopecia	5	12%
Pleurisy	2	5%
Pericarditis	1	2%
Thrombocytopenia	1	2%
Hematuria	5	12%
Pyuria	9	21%
Urinary Casts	1	2%
Increased DNA Binding	25	60%
Low Complement	18	43%
Proteinuria	12	29%
No individuals affected by the following disease activity indices at baseline: seizure, visual disturbance, cranial nerve disorder, cerebrovascular accident, myositis, mucosal ulcers, fever, or leukopenia		

Table 1. Frequency of Manifestations of Disease Activity at Enrollment

Enrollment Quality of Life Responses				
Enrollment N=42	Child Response		Parent Response	
PedsQL™ Measure	% Affected	Mean Score	% Affected	Mean Score
PedsQL™ 4.0 Core	86%	83.8	74%	82.5
Physical Health	67%	85.4	50%	82.3
Emotional Functioning	69%	85.0	60%	82.2
Social Functioning	52%	88.3	52%	86.7
School Functioning	79%	76.4	71%	78.0
PedsQL™ 3.0 Rheumatology Module	81%	86.2	71%	87.7
Pain and Hurt	55%	82.6	48%	82.2
Daily Activities	24%	95.7	19%	96.0
Treatment	60%	86.5	62%	88.4
Worry	40%	84.1	45%	85.7
Communications	45%	82.1	45%	85.9

Table 2. Child and Parent Quality of Life Responses at Enrollment

Longitudinal Quality of Life Responses				
Child Response n=25	Enrollment		Follow Up	
PedsQL™ Measure	% Affected	Mean Score	% Affected	Mean Score
PedsQL™ 4.0 Core	92%	85.7	84%	85.2
Physical Health	68%	89.6	72%	83.2
Emotional Functioning	68%	87.0	56%	85.6
Social Functioning	48%	88.4	32%	92.2
School Functioning	84%	77.8	76%	79.6
PedsQL™ 3.0 Rheumatology Module	80%	89.6	64%	91.6
Pain and Hurt	44%	90.0	48%	87.7
Daily Activities	24%	98.0	16%	97.4
Treatment	48%	90.0	48%	93.0
Worry	32%	85.3	36%	88.7
Communications	40%	84.7	36%	91.3
Parent Response n=25	Enrollment		Follow Up	
PedsQL™ Measure	% Affected	Mean Score	% Affected	Mean Score
PedsQL™ 4.0 Core	80%	85.9	68%	87.5
Physical Health	44%	88.9	52%	87.3
Emotional Functioning	64%	84.6	52%	88.8
Social Functioning	44%	91.0	40%	90.4
School Functioning	76%	79.0	64%	83.6
PedsQL™ 3.0 Rheumatology Module	76%	89.4	56%	91.9
Pain and Hurt	40%	89.0	36%	88.8
Daily Activities	16%	97.8	12%	97.4
Treatment	60%	90.3	52%	92.9
Worry	48%	82.7	36%	88.3
Communications	40%	87.3	36%	92.0

Table 3. Child and Parent Quality of Life Responses Compared between Enrollment and Follow Up 12 Months Later

Results: At enrollment, the mean age of diagnosis was 9.9 years, with a mean disease duration of 1.2 years. Duration between enrollment and follow up QOL was a median of 12.3 months (IQR 11.7-13). Males were older at diagnosis than females (10.9 vs 9.5 years, p=0.023) with no difference in enrollment disease duration. The mean SLEDAI-2K score was 7 (range 0-18) with diverse manifestations of activity (Table 1). Disease activity and individual SLE manifestations did not vary by gender. Laboratory markers of activity were present more frequently on the SLEDAI-2K than clinical exam findings, of which rash (24%), alopecia (12%) and arthritis (12%) were the most common. Seven subjects had disease damage reported on the SLICC/ACR DI.

School functioning domain had the worst QOL measure with the greatest number of children impacted (Table 2). Active arthritis was associated with lower mean scores in Physical Health (p=0.007), PedsQL Core total (p=0.048), Pain and Hurt (p=0.002), Daily Activities (p=0.003), Treatment (p=0.002), Worry (p=0.036), and PedsQL Rheumatology total (p=0.001). There was no association with QOL measures for rash, alopecia, or laboratory markers. Disease damage on SLICC/ACR DI was associated with greater impact on the Worry domain (mean 64.3 vs 88.1, p=0.23). On examination of follow up QOL, change in quality of life was trending towards improvement while physician global assessment was stable (Table 3).

Conclusion: Children with pre-pubertal SLE onset report significant impacts on QOL regarding school. The disease manifestation affecting the most QOL domains was arthritis, whereas skin manifestations, while common, did not demonstrate an impact on QOL. This is the first study to specifically address quality of life for children who develop SLE prior to pubertal development.

Disclosure: B. Stevens, None; **M. Rodriquez**, None; **A. Rakestraw**, None; **K. O'Neil**, AbbVie pharma, 5, Eli Lilly Pharmaceuticals, 5.

Abstract Number: 1725

Disease Activity in Childhood-Onset Systemic Lupus Erythematosus: Initial Analysis of the Childhood Arthritis and Rheumatology Research Alliance Registry

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Substantial risk of early morbidity and mortality exists for patients with childhood-onset systemic lupus erythematosus (cSLE) despite widespread use of immunosuppressive therapy. There are limited studies describing predictors of longitudinal disease activity in cSLE. Our objective was to determine patient-level demographic and clinical predictors for high disease activity scores.

Methods: We performed a retrospective analysis of prospectively collected data from the Childhood Arthritis and Rheumatic Disease Research Alliance (CARRA) Registry. Eligible patients had symptom onset before 18 years, new diagnosis of cSLE or established cSLE with new onset lupus nephritis within 24 months of enrollment, and were less than 21 years at enrollment. Data was collected every 6 months, and patients were included if at least one follow-up visit was recorded in the Registry. The primary outcome was Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) at most recent visit, dichotomized into ≤ 4 (low disease activity) or > 4 (high disease activity). Predictor variables included sex, race, age at diagnosis, number of ACR classification criteria at diagnosis, presence of lupus nephritis, number of follow-up visits, time since enrollment in months, and SLEDAI-2K at enrollment. Descriptive statistics were calculated across the study population. Univariate analyses were performed using two-sample Student t test or Mann-Whitney U test for continuous variables and Chi-square for categorical variables.

Table 1. Demographic and Clinical Baseline Predictors of High vs Low Disease Activity at Follow-up for Patients with cSLE in the CARRA Registry

	Total Cohort (n = 268)	SLEDAI ≤ 4 (n = 188)	SLEDAI > 4 (n = 80)	*p* value
Female, n (%)	227 (85%)	162 (86%)	65 (81%)	0.4
Race, n (%)				
Black	84 (31%)	59 (31%)	25 (31%)	0.8
White	64 (24%)	42 (22%)	22 (28%)	
Hispanic	61 (23%)	41 (22%)	20 (25%)	
Asian	42 (16%)	32 (17%)	10 (13%)	
Other	17 (6%)	14 (7%)	3 (4%)	
Age at diagnosis, mean (SD)	13.7 (3)	13.6 (3)	13.9 (3.2)	0.5
Number of ACR classification criteria, median (range)	5 (1-10)	5 (4-6)	6 (5-7)	< 0.001
Lupus nephritis, n (%)	131 (49%)	92 (49%)	39 (49%)	1
Number of follow-up visits, median (range)	2 (1-4)	2 (1-4)	1 (1-4)	0.6
Time since enrollment, mean (SD) months	10.8 (5.2)	10.8 (4.9)	10.8 (5.9)	0.99
SLEDAI-2K at enrollment, median (range) score	3 (0-37)	2 (0-30)	6 (0-37)	< 0.001
SLEDAI-2K at most recent visit, median (range) score	2 (0-23)	1 (0-4)	8 (5-23)	

Results: We identified 268 cSLE patients enrolled in the CARRA Registry with a mean duration of 10.8 months and median of 2 follow-up visits (Table 1). This multiracial North American cohort was 85% female with a mean age at diagnosis of 13.7 years. Lupus nephritis was present in 49%. The median (range) SLEDAI-2K score at enrollment was 3 (0-37) and at most recent visit was 2 (0-23). At the most recent visit, 30% of patients had high disease activity. Statistically significant differences between the high and low disease activity groups were noted in the number of ACR classification criteria and the SLEDAI-2K at enrollment, with higher number of criteria ($p < 0.001$) and higher SLEDAI-2K at enrollment ($p < 0.001$) in the high disease activity group. Interestingly, in the high disease activity group, the median SLEDAI-2K was 2 points higher at the most recent visit compared to enrollment, which may indicate more disease activity flare in this subgroup.

Conclusion: This study provides an initial analysis of predictors of disease activity scores in cSLE patients enrolled in the longitudinal CARRA Registry. While the majority of patients had a low disease activity score at their most recent visit, there was still a substantial proportion of patients with high disease activity. The number of ACR classification criteria and SLEDAI-2K at enrollment were significant predictors of subsequent disease activity scores, highlighting the importance of including these factors in future longitudinal analyses. Additional investigation is needed to better understand modifiers of disease activity, such as early diagnosis and treatment, in order to identify targets for intervention and improved outcomes.

Disclosure: E. Smitherman, None; **M. Son**, None; **A. Knight**, None; **T. Beukelman**, CARRA, 6, UCB, 5; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **A. Hersh**, None.

Abstract Number: 1726

Disease Activity and Health Care Utilization Among Young Adults with Childhood-onset Lupus Transitioning to Adult Care: Follow-Up Data from the Pediatric Lupus Outcomes Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Table 1. Demographics, medication usage, healthcare utilization, comorbid disease and pregnancy

	Pre-transfer (n=47)	Post-transfer(n=38)	P-Value
Age, mean, years	19	24.5	<0.001
Female	87.2	94.7	NS
Recruited from Utah	34.8	97.3	<0.001
Non-White Ethnicity	74.5	29	<0.001
Disease Activity			
SLAQ score, mean	11.3	9.4	NS
Flare in Past-3 months	31.1	26.3	NS
Medication Usage			
Hydroxychloroquine	88.1	63.2	0.009
Any Steroid	74.4	18.4	<0.001
Immunosuppressants	88.4	34.2	<0.001
DMARDs	69.8	31.6	0.001
Always Take Medications as Prescribed	46.8	65.8	0.080
Forget Medications at Least Once a Week	26.1	5.6	0.014
Skip Medications at Least Once a Week	8.7	5.6	NS
Been Seen by Rheumatologist in Last Year	93	68.4	0.004
Have Health Insurance	95.4	89.5	NS
Trouble Obtaining Insurance	11.6	34.2	0.015
Lupus Medications Not Covered	5.3	6.1	NS
Comorbidities			
Hypertension	21.3	36.8	NS
Hyperlipidemia	0	10.5	0.02
Diabetes	2.2	0	NS
Anxiety	17.4	18.4	NS
Depression	17.4	13.2	NS
Osteoporosis	2.2	13.2	0.052
Ever Been Pregnant	0	38.9	<0.001

Values in % unless otherwise stated

Background/Purpose: Individuals with childhood-onset systemic lupus erythematosus (cSLE) must transfer from pediatric to adult health care as they enter adulthood. Previous analyses of the Pediatric Lupus Outcomes Study demonstrated significantly lower rates of medication usage and more frequent gaps in rheumatology care in a post-transfer cohort compared to a pre-transfer group, in spite of similar levels of disease activity. This study aims to further explore these findings by comparing transition readiness, illness perceptions, comorbid conditions, pregnancy, and insurance barriers to obtaining medication.

Methods: Data derived from the baseline interview of the Pediatric Lupus Outcomes Study, an annual telephone survey of 91 English- and Spanish-speaking participants age 18-30 with confirmed cSLE. Subjects were recruited from rheumatology clinics. To define a cohort undergoing transition from pediatric to adult care, we included respondents who received care from a pediatric rheumatologist currently or in the past (N=85). Transition readiness and illness perception were assessed using Transition Readiness Questionnaire (TRAQ) and Brief Illness Perception Questionnaire (IPQ-B). Patients answered questions related to medication compliance, insurance barriers, comorbidities, and

Table 2. Health Related Quality of Life and Illness Perception

	Pre-transfer	Post-transfer	P-Value
SF-36			
Physical Functioning	95	90	NS
Role limitations due to physical health	75	50	NS
Role limitations due to emotional problems	66.7	66.7	NS
Energy/Fatigue*	61.5	52.8	0.072
Emotional well-being	80	80	NS
Social Functioning	100	75	0.014
Pain	80	77.5	NS
General health*	58.2	47.1	0.016
IPQ-B			
Consequences	39.5	30	NS
Timeline	92	100	NS
Personal Control	79.5	75	NS
Treatment Control	87	90	NS
Identity	49	30	NS
Concern	70	55	NS
Understanding	80	70	NS
Emotional Response	42	40	NS

SF-36 = Short Form 36. Scores range from 0-100, correlating with increased health related quality of life
IPQ-B = Brief Illness Perception Questionnaire. Scores range from 0-100, with higher scores correlating with stronger agreement with question
*Mean results. Otherwise table reflects median values

Table 3. Transition Readiness

	Pre-transfer	Post-transfer	P value
Appointment Keeping	3.9	5	<0.0001
Tracking Health Issues	4.6	4	NS
Managing Medications	4.3	4.8	0.036
Talking With Providers	5	5	NS
Managing Daily Activities	5	5	NS
TRAQ total score	4.4	4.8	0.0001

Scores for each section range from 1-5, correlating to the following answers: 1. No, I do not know how; 2. No, but I want to learn; 3. No, but I am learning to do this; 4. Yes, I have started doing this; 5. Yes, I always do this when I need to
Scores reflect median values

reproductive health. Bivariate analyses were used to compare individuals currently cared for by pediatric vs adult rheumatologists.

Results: Mean age was 21 years; mean age at diagnosis was 13 years. 38 respondents (45%) had transferred to adult care. Post-transfer patients were more likely to report 100% medication compliance than the pre-transfer group (66 vs 47%), which neared significance. Pre-transfer patients were more likely to forget to take medications (26 vs 6%). Post transfer patients had significantly higher incidence of hyperlipidemia (11 vs 0%) and a trend towards higher incidence of osteoporosis (13 vs 2%). The rate of pregnancy was higher in the post-transfer (39%) vs pre-transfer (0%) patients. The post-transfer group scored lower on General Health (47 vs 58) and Social Functioning (75 vs 100) metrics of the Short-form 36 health survey. The post transfer group had significantly higher overall TRAQ scores (4.8 vs 4.4), with higher scores in the appointment keeping (5 vs 3.9) and medication management (4.8 vs 4.3) subcategories.

Conclusion: Both post- and pre-transfer groups demonstrated similar disease perceptions and quality of life, while the post-transfer group reported higher transition readiness. While previous findings showed that decreased immunosuppressant use in the post-transfer group could not be explained by differences in disease activity, this difference in medication utilization could be explained by higher pregnancy rates and medication side-effects/comorbidities. Despite lower rates of medication usage the post-transfer group reported better medication compliance, which may reflect both different prescribing practices between pediatric and adult providers and expected developmental changes during adulthood. Future studies will use longitudinal data to assess changes in disease activity and healthcare utilization as pre-transfer patients move to adult rheumatology care.

Disclosure: S. Haro, None; **E. Lawson**, None; **A. Hersh**, None.

Abstract Number: 1727

Worsening Disease Activity and Inability to Taper Corticosteroids in an Ethnically Diverse Cohort of Pediatric-Onset Lupus Patients After Transition to Adult Care

Marla Guzman,[1] B. Anne Eberhard,[1] and Joyce Hui-Yuen[1], [1]Cohen Children's Medical Center, New Hyde Park, NY

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Transition of pediatric lupus (pSLE) patients from pediatric to adult rheumatology care is historically difficult and challenging. Although our division routinely assesses for transition readiness, we do not administer a formal transition readiness questionnaire to evaluate ways in which transition preparedness can improve. We aim to investigate disease activity and medication use in pediatric lupus patients before and after transition to adult care.

Methods: A retrospective chart review was conducted of all patients who were seen in our pediatric rheumatology clinic between the years 2003-2019 who fulfilled 1997 ACR classification criteria, were diagnosed with pSLE, and transitioned to our institution's adult rheumatology division. Descriptive statistics and paired t-tests were used.

Results: Thirty three patients with pSLE had documentation of transition from pediatric rheumatology to adult rheumatology within our institution. Twenty-six patients were female. Twelve patients were Black (36%), 7 patients were White (21%), and 5 patients were Asian (15%). 6 patients reported race as unknown or other. Four patients (12%) reported Hispanic ethnicity. The mean age at diagnosis was 12.7 +/- 2.9 years. The mean age at the first adult visit was 20.8 +/- 1.6 (range 18-24) years. The average time between last pediatric visit and first adult visit was 6.7 (median 3.0) +/-7.9 months. The mean SLEDAI score at final pediatric visit was 3.44 (median 3.0) +/- 3.7, and the mean SLEDAI score at approximately 12 (range 4-24) months after first adult visit was 6.59 (median 6.0) +/- 5.7 (p= 0.0008). The mean daily dose of prednisone at final pediatric visit was 10.6 (range 0-60, median 2.5) +/- 16.2 mg, and the mean daily dose of prednisone approximately 12 (range 4-24) months after first adult visit was 9.2 (range 0-50, median 2.5) +/- 14.2 mg (p=0.5898). Nineteen patients were on at least one steroid sparing medication at final pediatric visit, and 4 additional patients were started on a steroid sparing medication approximately 1 year (range 4 months-2 years) after first adult visit. Fourteen patients had been diagnosed with nephritis and underwent induction treatment while under pediatric care, and 2 additional patients developed nephritis post-transition.

Conclusion: Disease activity in pSLE increases as early as within the first 4 months after transition to adult rheumatology in our primarily Black cohort of pSLE patients. Daily prednisone dosing in patients on prednisone during pediatric care did not significantly decrease post-transition, suggesting continued active disease. Similarly, 4 patients who were not on treatment with immunosuppressive medications were started on at least 1 immunosuppressive post-transition. Analyses are currently underway to determine whether demographic and socioeconomic factors affect disease activity and medication use after transition in this population. Use of a formal assessment of transition readiness to assist with areas of weakness prior to transition may be beneficial.

Disclosure: M. Guzman, None; **B. Eberhard**, None; **J. Hui-Yuen**, None.

Abstract Number: 1728

Persistent Disease Activity Is Associated with Avascular Necrosis Development in Juvenile Systemic Lupus Erythematosus

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SESSION INFORMATION
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Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Avascular necrosis (AVN) is a serious comorbidity of juvenile systemic lupus erythematosus (jSLE) associated with disability, impaired quality of life, and increased cost of care. Many factors have been been reported to be associated with AVN risk, with most studies focused on adult SLE. A recent meta-analysis found high maximum and cumulative glucocorticoids (GC) dosage, lupus nephritis (LN), central nervous system disorder, and Cushingoid body habitus to be associated with AVN (Nevskaya et al 2017; Clin Exp Rheumatol; 35:700). The aims of this study were to identify factors associated with AVN risk in jSLE.

Table: Univariate Comparison of jSLE Patients who had and did not have AVN				
Characteristic	**All Patients, n=49 n (%)**	**No AVN, n=42 n (%)**	**AVN, n=7 n (%)**	**P-Value**
Age at SLE Diagnosis (years)	13.1 (11, 14.6)	12.8 (10.9, 14.3)	15.1 (13.7, 16.1)	**0.016**
Age at Study entry (years)	18 (16, 21)	18 (16, 20)	20 (19, 22)	NS
Gender: Female	41 (83.67)	34 (81.0)	7 (100.0)	NS
Race				NS
Asian	7 (14.6)	7 (16.7)	1 (14.3)	
Black	13 (27.1)	11 (26.2)	2 (28.6)	
White	24 (50.0)	24 (57.1)	4 (57.1)	
Ethnicity: Hispanic	19 (38.8)	17 (40.5)	2 (28.6)	NS
Public Health Insurance	20 (40.8)	17 (40.5)	4 (57.1)	NS
SLE Manifestations				
Malar Rash	32 (68.1)	26 (65.0)	6 (85.7)	NS
Discoid-Lupus	6 (12.8)	4 (10.0)	2 (28.6)	NS
Photosensitivity	12 (25.5)	9 (22.5)	3 (42.9)	NS
Oral or Nasal Ulcers	9 (19.6)	8 (20.5)	1 (14.3)	NS
Nonerosive Arthritis	32 (68.1)	27 (67.5)	5 (71.4)	NS
Cytopenia	33 (71.7)	28 (71.8)	5 (71.4)	NS
Lupus Nephritis Class III, IV, or V	35 (71.4)	28 (66.7)	7 (100.0)	NS
LN Class III	6 (12.2)	3 (7.1)	3 (42.9)	**0.031**
LN Class IV	22 (44.9)	19 (45.2)	3 (42.9)	NS
LN Class V	10 (20.4)	7 (16.7)	3 (42.9)	NS
Neurologic or CNS Disorder	6 (12.8)	3 (7.5)	3 (42.9)	**0.035**
Other Major Organ involvement	6 (12.8)	3 (7.5)	3 (42.9)	**0.035**
Cushingoid Habitus	18 (41.86)	15 (41.67)	3 (42.86)	NS
Autoantibodies* and complement				
ANA positivity	48 (98.0)	41 (97.6)	7 (100.0)	NS
Anti-dsDNA positivity	41 (85.4)	35 (85.4)	6 (85.7)	NS
Antiphospholipid positivity	32 (66.7)	28 (68.3)	4 (57.1)	NS
Low C3	25 (55.6)	20 (52.6)	5 (71.4)	NS
Low C4	34 (75.6)	29 (76.3)	5 (71.4)	NS
Glucocorticoid Treatment				
GC Duration (months)	25.8 (15, 51.6)	30.4 (15, 52.6)	18 (13.5, 25.8)	NS
Initial oral GC dose (mg/day)	50 (25, 60)	44 (20, 60)	60 (60, 80)	*0.096*
Cumulative GC (mg)	25,173 (8720, 34450)	25,778 (8289, 37515)	22,620 (8720, 31053)	NS
Maximum oral GC (mg/day)	60 (50, 80)	60 (40, 80)	80 (60, 100)	*0.062*
Maximum oral GC (mg/kg/day)	1.1 (0.9, 1.7)	1.1 (0.9, 1.7)	1.3 (1.1, 1.7)	NS
Mean oral GC (mg/day)	17.1 (11.2, 24.7)	14.8 (10, 24.6)	21.7 (18.6, 29.8)	**0.038**
Mean oral GC (mg/kg/day)	0.4 (0.3, 0.5)	0.4 (0.3, 0.5)	0.5 (0.4, 0.7)	**0.044**
Methylprednisolone Pulses	0 (0, 3)	0 (0, 3)	3 (0, 5)	NS

Methods: We conducted a single center retrospective cohort study of jSLE patients seen between 2009-2010. Eligible patients had to fulfill 1997 American College of Rheumatology (ACR) classification criteria for SLE and/or have LN, and been treated with GC. Data was collected from disease onset to AVN development for AVN patients, and

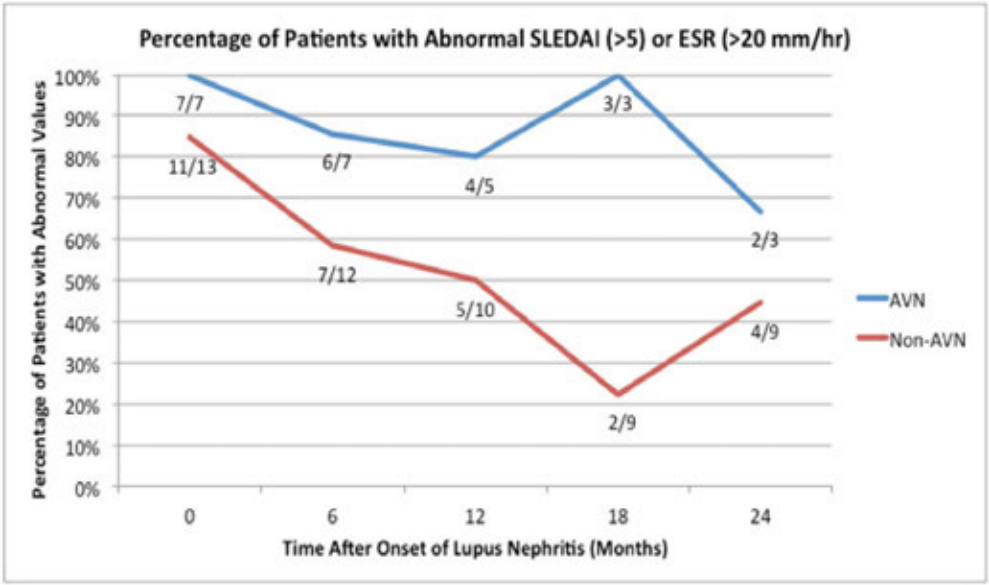

Figure Active disease following onset of lupus nephritis. Patients were censored after developing AVN (AVN patients), or at the end of the study period (non-AVN patients). At each timepoint, the number of patients with active disease (numerator), and total number of patients evaluated (denominator) are shown. Data was missing for 1 non-AVN patient at 18 months.

to 12/31/10 for non-AVN patients. Onset of LN was considered to be time of renal biopsy. For the subanalysis, the minimum age of disease onset for the comparator group was the youngest age of onset in the AVN group (11 years old). We calculated Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) scores for each 6-month timepoint following renal biopsy based upon reported clinical features and laboratory values within 2 months of timepoint. Active disease was considered to be SLEDAI score >5 and/or erythrocyte sedimentation rate (ESR) score >20. Univariate statistics, two-tailed Fisher's exact tests, and independent samples t-tests were performed. P values < 0.05 were considered to be significant.

Results: Of the 101 jSLE patients identified, 49 fulfilled study criteria, 7 (14.0%) of whom developed AVN. AVN patients had an older age of SLE onset, higher prevalence of LN class III, higher prevalence of neurologic or CNS disorder, and higher mean daily oral GC dose than non-AVN patients (Table). No significant differences were found for gender, race, ethnicity, mucocutaneous involvement, cytopenia, autoantibody pattern, Cushingoid habitus, cumulative GC dose, methylprednisolone pulse treatment, or other treatment (Table). To evaluate for additional factors associated with AVN risk, we did a sub-analysis of patients that had adolescent age of SLE onset and LN (adolescent LN)(Figure). Patients were censored after developing AVN (AVN patients), or at the end of the study period (non-AVN patients). Compared to adolescent LN who did not develop AVN, the AVN group were more likely to have persistently elevated SLEDAI scores and/or ESR values for up to 2 years following onset of LN.

Conclusion: We found older age of SLE onset, LN class III, neurologic/CNS disorder, and higher mean daily GC dose were associated with AVN risk. Patients with AVN were more likely to have persistently active disease following onset of LN than LN patients who did not develop AVN. This suggests that higher disease activity at certain times may also contribute to AVN risk in jSLE. Prospective studies are needed to assess these potential risk factors for AVN development and improve our ability to identify and manage at-risk patients.

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Abstract Number: 1729

Infections and Mortality in 230 Childhood Lupus Patients: A Single Center Experience from North India

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Children with systemic lupus erythematosus(cSLE) have more severe disease as compared to adults. Additionally, Asians in their geographic area have high burden of infections as well. There is paucity of data on infections & mortality in cSLE from India. We are a pediatric rheumatology referral center & have studied infections and mortality in cSLE at our unit.

Purpose
1 To study spectrum of infections in cSLE.
2 To study mortality in cSLE.
3 To compare infections & mortality with other centers.

Methods: Records of cSLE patients(onset < 18) from Jan09-Mar19 were reviewed. Data on infections & death collated. Patients who did not attend clinic for ≥1 year were considered lost to follow up & contacted via telephone. Serious infections:leading to hospitalization/ death/ required iv. therapy. Chi square test was applied as needed.

Results: 230 cSLE seen over 10 yrs. Thirty(13 %) infections: 25 girls, 5 boys. Median time to infections from diagnosis: 1.91 yrs. Median SLEDAI-2K at the time of infection:6. Eighty three percent of children with serious infection had SLEDAI >4 whereas 16.7% had SLEDAI < 4 (p=0.009). Patient details-table 1 Medications at the time of infection: 78% on steroids(low dose).Therapy details Table 2. INFECTIONS: Thirty(13%) children had 34 infectious episodes with 39 infections.Twelve (40%) had serious infection in 15 episodes. Ten improved & 2(16.6%) died-one with septicemia, second, invasive aspergillosis(pulmonary).Twenty patients had non-serious infections, commonest herpes zoster(30%).Details in Table 3. MORTALITY: Of 230 cSLE patients,156 were on regular follow up & 74 lost to follow up. Ten(4.3%) deaths in this cohort. Three of 156 patients(2%) who were on regular follow up died: mean follow up 1.91 yrs (0.5-4.25 yrs). Cause of death infections in 2, non infectious in one: Patient 1. Invasive aspergillosis(pulmonary),Patient 2. Adenoviremia with refractory septic shock(defaulted treatment 9 mths). Patient 3. Probable thrombotic thrombocytopenic purpura. Seven(9.4%) of 74 patients who were lost to follow up died: cause not known. Infectious complications(13%) & mortality(4.3%) in this cohort are far superior than those reported from other centers in the subcontinent(infections25%,mortality5-20%)(1,2). Mortality rates at this centre are comparable to other cohorts across the world(1.4-30%)(3-8).

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Table 1: Demographic features, organ involvement, disease burden and outcome of cSLE patients with infections.

Demographic details	
Total number of cSLE patients	230
Female to male	25:5
Total number of patients with infections	30
Number of episodes	34 in 30 patients
Total number of infections	39 in 34 episodes
Median age(years) at time of infection(n=33)	14.91(12.08-17.08)
Median time between diagnosis and infection(years)(n=33)	1.91(0.25-4.25)
Disease burden	
Median(IQR) SLEDAI-2K at the time of infection(n=31)	6(2-13.5)
Labs/Serology	
Median(IQR) Total leukocyte count(TLC)(thous/ul) at the time of infection(n=29)	7700(5800-10300)
Percentage of patients with low TLC(n=29)	14%
Median(IQR) C3 levels(mg/L) at the time of infection(n=29)	536(152-1044)
Percentage of patients with low C3(n=29)	72%
Median(IQR) C4 levels(mg/L) at the time of infection(n=26)	91(33.5-156.75)
Percentage of patients with low C4	77%
Organ involvement at the time of infection(n=33)	
No organ involved	11
Renal	13
Cutaneous	8
Arthritis	6
Gastrointestinal	5
Central nervous system	5
Vasculitis	4
Myositis	1
Hematological	0
Outcome(n=30)	
Improved	28
Death	2

SLEDAI2K: Systemic Lupus Erythematosus disease activity index-2K

Table 2: Treatment details of cSLE patients at the time of infection(n=32)

Disease modifying anti-rheumatic agents	
Hydroxychloroquine	29
Mycophenolate mofetil	12
Azathioprine	5
Cyclophosphamide	5
Methotrexate	3
Cyclosporin	1
Tacrolimus	1
Thalidomide	1
Steroids	
Intravenous steroids	2
Oral steroids	23(72%)
Median(IQR) dose of oral prednisolone(mg/kg/day) at the time of infection	0.2(0-0.55)
Biologic response modifiers	
Rituximab	3
Other medication	
Thalidomide	1

Table 3: Details of infections in the cohort of 230 cSLE patients

Infection	Number	% of cSLE patients of 230	Description
Total	30 patients(39 infections)	13%	---
Serious infections	12 patients(15 episodes) 19 infections	5.2%	4 bacterial sepsis,2 soft tissue infections,2 pneumonia(adenovirus/nocardia),3 CMV,3 dengue,2 UTI, 1 TB, 1 spontaneous bacterial peritonitis,1 invasive aspergillosis
Non serious infections	20 patients(20 episodes)20 infections	8.7%	9 herpes zoster,2 varicella,2 soft tissue infections, 2 UTI,2 TB,1 dengue,1 CMV,1 tinea corporis
All patients with >1 episode of infectious disease	3	1.3%	Patient1: Episode1: Soft tissue infection Episode2: Varicella Patient2: Episode1: Soft tissue infection Episode2: CMV Episode 3: Spontaneous bacterial peritonitis Patient3: Episode1: Soft tissue infection Episode2: CMV, bacterial sepsis,pneumonia(nocardia)
>1 infection in each episode	4	1.7%	Patient 1: Soft tissue infection,bacterial sepsis Patient 2: Pneumonia(adenovirus),UTI Patient 3: CMV,bacterial sepsis,pneumonia(nocardia) Patient 4: Bacterial sepsis, CMV, UTI

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Conclusion: Infections in cSLE occurred in 13%, 40% serious infections,6.6 % mortality. Of non serious infections, herpes zoster was most common. Infections occurred predominantly in patients with active disease (SLEDAI >4). Overall mortality was 4.3%. In addition to infections, irregular follow up was major contributor to death. Patients on regular follow up had a lower mortality(2%) when compared to those that were lost to follow up(9.4%). Mortality at this centre is comparable to the west and infection rate is lower than other centers in the region(1).

Disclosure: S. Mittal, None; **M. Agarwal**, None; **S. Sawhney**, None.

Abstract Number: 1730

Impact of Preceding and Co-existing Autoimmune Cytopenias on Severity of Childhood-onset Systemic Lupus Erythematosus: A Single-Center Retrospective Cohort Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune cytopenias may precede or occur with childhood-onset systemic lupus erythematosus (cSLE). Adult studies suggest that lupus patients with concurrent autoimmune cytopenias have relatively

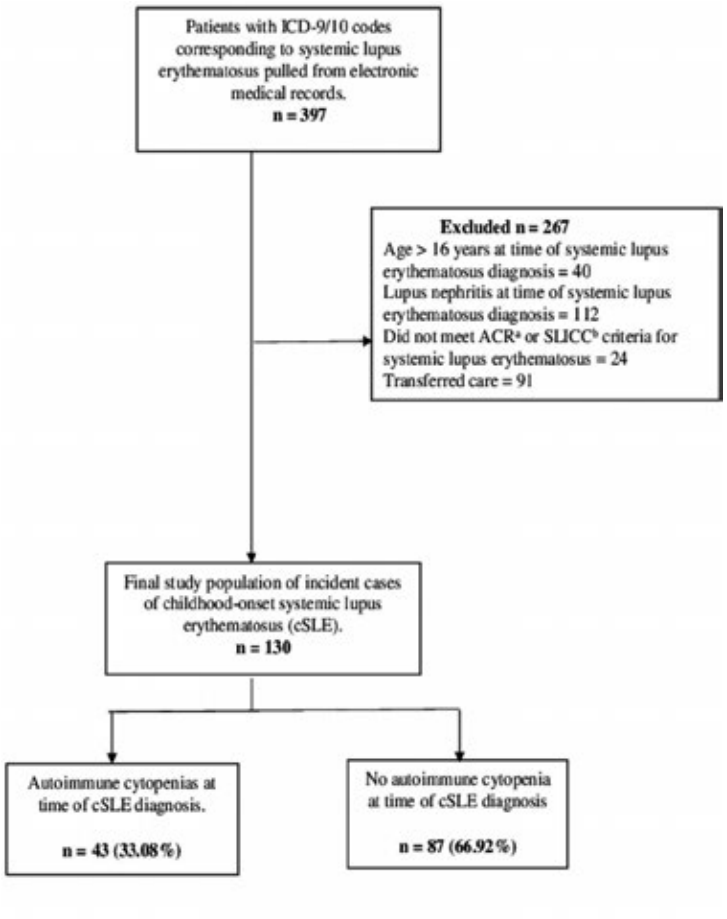

Figure 1: Flow diagram showing selection of study population

Abbreviations: [a]ACR = American College of Rheumatology; [b]SLICC = Systemic Lupus International Collaborating Criteria for Systemic Lupus Erythematosus

Figure 1 Flow diagram showing selection of study population

Table 1. Comparison of demographic, clinical and laboratory characteristics of 130 incident patients with childhood-onset systemic lupus erythematosus from January 1, 2000 and June 30, 2016 by baseline autoimmune cytopenia status.

	All cSLE (n=130)N(%)	cSLE with AC (n=43)N(%)	cSLE without AC (n=87)N(%)	P-value	Missing
Demographics					
Sex					
Female	107 (82.31)	35/43(81.40)	72/87(82.76)	0.848	
Race				0.6202	8
Black	81 (66.39)	26/41(63.41)	55/81(67.90)		
Other	41 (33.61)	15/41(36.59)	26/81(32.10)		
Age in years at cSLE diagnosis (mean (SD))[c]	12.28 (2.95)	12.65(2.51)	12.10(3.14)	0.3211	
Clinical features					
Fever	54(41.86)	21/42(50.00)	33/87(37.93)	0.1929	1
Malar rash	47(36.43)	10/42(23.81)	37/87(42.53)	0.0384[$]	1
Photosensitivity	47(36.43)	13/42(32.56)	34/87(39.08)	0.3687	1
Discoid lupus[a]	3(2.33)	1/42(2.38)	2/87(2.30)	1	1
Vasculitic rash	33(25.58)	13/42(30.95)	20/87(22.99)	0.3313	1
Raynauds[a]	14(10.85)	5/42(11.90)	9/87(10.34)	0.7704	1
Oral ulcers	31(24.03)	9/42(21.43)	22/87(25.29)	0.6308	1
Nasal ulcers[a]	4(3.10)	2/42(4.76)	2/87(2.30)	0.5956	1
Alopecia	21(16.28)	4/42(9.52)	17/87(19.54)	0.1487	1
Arthritis	64(50.00)	13/42(30.95)	51/86(59.30)	0.0026[$]	2
Angioedema[a]	8(6.30)	2/41(4.88)	6/86(6.98)	1	3
Pleural effusion	26 (30.59)	12/32(37.50)	14/53(26.42)	0.2826	45
Pericardial effusion	17(32.08)	7/19(36.84)	10/34(29.41)	0.5784	77
Neuropsychiatric symptoms[a]	8(6.15)	6/43(13.95)	2/87(2.30)	0.0159[$]	
Myositis*	20(28.99)	2/20(10.00)	18/49(36.73)	0.0264[$]	61
Laboratory features					
Positive ANA ≥ 1:40	130(100)	43(100)	87(100)		
Positive anti-dsDNA ≥ 1:10	88(69.84)	31/43(72.09)	57/83(68.67)	0.6918	4
Positive anti-RNP*	72(58.06)	24/43(55.81)	48/81(59.26)	0.7114	6
Positive anti-Smith*	71(57.26)	22/43(51.16)	49/81(60.49)	0.3175	6
Positive anti-SSA*	56(45.16)	20/43(46.51)	36/81(44.44)	0.8258	6
Positive anti-SSB*	20(16.26)	10/43(23.26)	10/80(12.50)	0.1232	7
Leukopenia ≤ 4,000/uL	59(46.09)	21/43(48.84)	38/85(44.71)	0.6579	2
Lymphopenia ≤ 1,500/uL	81(65.85)	29/42(69.05)	52/81(64.20)	0.5906	7
Neutropenia ≤ 1,500/uL	32(26.45)	14/42(33.33)	18/79(22.78)	0.2104	9
Positive Coombs test and anemia of hemoglobin ≤ 10g/dl	23 (18.11)	23/43(33.86)	0/84(0.00)	<0.0001[$]	3
Thrombocytopenia <100,000/uL	19(15.08)	19/43(44.19)	0/83(0.00)	<0.0001[$]	4
Low C3 complement*	63(52.50)	25/41(60.98)	38/79(48.10)	0.1804	10
Low C4 complement*	78(65.00)	29/41(70.73)	49/79(62.03)	0.343	10
ESR in mm/hr (mean(SD))[c]	62.96(40.53)	79.80(45.13)	55.21(35.95)	0.0026[$]	
eGFR < 90mL/min/1.73m2	35(30.43)	16/41(39.02)	19/74(25.68)	0.1362	
SLEDAI-2k (median(IQR, range))[b]	9(5.00, 2 - 32)	9.00(5.0, 4 - 32)	10.00(5, 2 - 23)	0.6554	
Prior Treatment					
Corticosteroids[a]	10(7.69)	10/43(23.26)	0	<0.0001[$]	
Cyclophosphamide	0	0	0		
IVIG[a]	7(5.38)	7/43(16.28)	0	0.0003[$]	
Rituximab[a]	2(1.54)	2/43(0.05)	0	0.1077	
2 year risk of lupus nephritis after cSLE diagnosis	16(12.31)	3/43(6.98)	13/87(14.94)	0.1934	
Follow-up period in years (mean (SD))[c]	4.03(2.24)	3.96 (2.15)	4.16(2.44)	0.641	

Abbreviations: AC = Autoimmune cytopenia; ANA = Anti-nuclear antibody; cSLE = childhood-onset systemic lupus erythematosus; CNS = Central nervous system; dsDNA = double-stranded DNA; ESR = Erythrocyte sedimentation rate; eGFR = Estimated glomerular filtration rate; IVIG = intravenous immunoglobulin; RNP = ribonucleoprotein; SLEDAI-2k = Systemic Lupus Erythematosus Disease Activity Index 2000; SS = Sjogren syndrome-related antigen; $ = significant with p value < 0.05; * By laboratory reference range, Comparisons were by chi square test except otherwise stated, [a] Fisher's exact test, [b]Wilcoxon Rank Sum test, [c]Student T test

Table 1. Comparison of demographic, clinical and laboratory characteristics of 130 incident patients with childhood-onset systemic lupus erythematosus from January 1, 2000 and June 30, 2016 by baseline autoimmune cytopenia status

lower prevalence of lupus nephritis (LN) and are a unique disease sub-population. The reason for this association is unclear. Also, it has not been well studied in cSLE which has a higher risk of LN. LN often occurs within 2 years of

cSLE diagnosis. Since autoimmune cytopenias are more common in cSLE and often occur early in this disease, assessing their impact on cSLE phenotype is important. In addition, the effect of treatment for idiopathic autoimmune cytopenias on subsequent cSLE has not previously been explored. Therefore, the objectives of our study were to assess whether in cSLE, autoimmune cytopenias decrease the 2-year risk and severity of LN; to assess associated serologic differences in those with and without autoimmune cytopenias at cSLE diagnosis; the effect of prior immune therapy for autoimmune cytopenias on 2-year risk of LN; and to perform descriptive analyses of these pediatric patients without LN at cSLE diagnosis.

Methods: We conducted a retrospective cohort study of incident cSLE cases at our institution from January 1, 2000 to June 30, 2016. We included patients aged less than 17 years who met American College of Rheumatology and/or Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. We excluded patients diagnosed outside our institution and those with LN at cSLE diagnosis. Our follow-up period was 2 years. We defined autoimmune cytopenias as either autoimmune hemolytic anemia, Coombs positive anemia without hemolysis, immune thrombocytopenia or Evan's syndrome before or at cSLE diagnosis.

Results: We had 130 incident cSLE patients who met our inclusion and exclusion criteria. Of these, 43 (33%) had autoimmune cytopenias (Figure1). At cSLE diagnosis, there was no serologic difference between those with and without autoimmune cytopenias. Those with autoimmune cytopenias had significantly more neuropsychiatric symptoms and higher mean ESR versus those without autoimmune cytopenias. However, they had less arthritis, malar rash and myositis (Table1). 2-year incidence of LN was 12% in our cohort. Patients with autoimmune cytopenias had lower 2-year risk of LN compared to other cSLE patients (7% vs 15%). Of the 16 patients that developed LN, those with autoimmune cytopenias had mostly class V (2 of 3 patients) versus mostly class III and IV in those without autoimmune cytopenias (6 of 12 patients). None of the 13 patients pre-treated for autoimmune cytopenias prior to cSLE diagnosis developed LN.

Conclusion: Patients with autoimmune cytopenias before or at cSLE diagnoses have statistically significant and clinically relevant differences in their presentation from other cSLE patients. Our findings call for further studies on the immunologic and genetic basis of these differences.

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Abstract Number: 1731

Validation of the 2017 Weighted Criteria in Pediatric Systemic Lupus Erythematosus (SLE)

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

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Background/Purpose: Different classification criteria for systemic lupus erythematosus (SLE) have been proposed over many years. The most widely used and accepted criteria have been the 1997 ACR criteria. In 2012, the SLICC criteria were published in an attempt to improve clinical relevance of SLE criteria and address concerns with the 1997 ACR criteria. In 2017, a weighted criteria were proposed at the ACR meeting. Our aim was to validate the 2017 weighted criteria for pediatric-onset SLE.

Methods: Retrospective chart review of patients with a clinical diagnosis of SLE diagnosed before the age of 19 years at our tertiary care center between 2003 and 2018. The 2017 weighted, 2012 SLICC, and 1997 ACR classification criteria were applied to these patients, and compared against a gold standard of physician diagnosis. Autoimmune controls were defined as patients who were referred for serologies positive for ANA only but who did not fulfill criteria for diagnosis of SLE at the initial visit, or were diagnosed with another autoimmune disease.

Results: There were 156 patients (82.7% female) who were diagnosed with SLE over the past 15 years. The mean age at diagnosis was 13.1±2.8 years, with 21.8% Asian, 27.6% Black, 26.9% Caucasian, 22.4% Other, and 1.3% Unknown; 23.1% also identified as Hispanic. pSLE patients had a median of 6 of 11 (range 2-9) positive domains and a median of 21 (range 6-41) points by 2017 weighted criteria. The most commonly met domains were antibodies and complement, and the most frequently met clinical criteria were hematologic and synovitis. The sensitivity for the 2017 weighted criteria was 97.4 (CI: 0.94-0.99) and specificity was 98.4 (CI: 0.97-0.99). The median score was 21. The sensitivity for the 2012 SLICC criteria was 97.4 (CI: 0.94-0.99) and specificity was 99.7 (CI: 0.99-1.00). The sensitivity for the 1997 ACR criteria was 87.2 (CI: 0.81-0.92) and specificity was 100 (CI: 0.99-1.00).

Conclusion: The 2017 weighted criteria and the 2012 SLICC were more sensitive, and similarly specific to the 1997 ACR criteria. There were no significant difference in sensitivity and specificity between the 2017 weighted and 2012 SLICC criteria. The sensitivity findings are comparable with the observed sensitivities in the adult population. Analyses are underway to further evaluate the performances of these criteria in a larger cohort of patients.

Disclosure: M. Ma, None; **J. Hui-Yuen**, None; **J. Cerise**, None; **S. Iqbal**, None; **B. Eberhard**, None.

Abstract Number: 1732

Evaluating the New 2018 ACR/EULAR SLE Classification in Pediatric Patients

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The traditional 1997 ACR SLE classification criteria classify a patient as having SLE if 4 of the 11 criteria have been met over time. In comparison, the 2018 ACR/EULAR SLE classification criteria uses a point system (2018-SLE-Score) for 22 clinical and immunologic domains (range:0-51; threshold score for SLE presence:10 points including an antinuclear antibody (ANA) titer of at least 1:80 on HEp-2 cells or an equivalent positive test). We

Table 1: Comparison of patients who met both, one or neither of the classification criteria

	2018+/ 1997+	2018+/ 1997-	2018-/ 1997-	2018-/ 1997+	Total
Total	**87**	**16**	**10**	**6**	**119**
Sex					
Female	70	16	7	4	**97**
Male	17	0	3	2	**22**
Ethnicity					
Hispanic	1	1	2	0	**4**
Not Hispanic	86	15	8	6	**115**
Race					
White	45	10	9	4	**68**
Black	30	3	1	2	**36**
Asian	7	0	0	0	**7**
Native Hawaiian/Pacific Islander	1	0	0	0	**1**
Multiracial	1	2	0	0	**3**
Other	3	1	0	0	**4**
SLICC Score					
SLICC=not done	17	4	10	5	**36**
SLICC= 0	45	10	0	0	**55**
SLICC>1	25	2	0	1	**28**

Table 2: Current cSLE patients that were diagnosed earlier using the 2018 criteria

	Patients that received treatment (n=6)	Patients not receiving treatment (n=3)
Average number of days between 2018 vs 1997 classification criteria	510.33	108.17

investigated the difference of classifying patients with childhood-onset SLE (cSLE) when using the 2018 vs. 1997 SLE criteria. Further, we explored the association between the 2018 Criteria and disease activity in cSLE.

Methods: We reviewed the electronic medical record of ALL patients treated at a tertiary referral center carrying a diagnosis of cSLE, undifferentiated (UCTD) or mixed connective tissue disease (MCTD) from 2008 – 2018, as per the assessment of the treating pediatric rheumatologist. Patient data were reviewed starting from the initial encounter at the medical center, with external data reviewed if available. Disease activity as measured by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score was recorded within 1 month of diagnosis, and the most recent SLICC damage index (SDI) score was collected. SLEDAI and SDI scores were compared with the 2018-SLE-Score at initial diagnosis, and the sensitivity of 1997 ACR criteria and 2018 ACR criteria was compared to the current diagnosis of the patient's pediatric rheumatologist.

Table 3: Sensitivity of the 1997 vs 2018 ACR criteria

	Current Diagnosis cSLE	Current Diagnosis Not cSLE
1997 ACR criteria +	93	0
1997 ACR criteria -	18	8

	Current Diagnosis cSLE	Current Diagnosis Not cSLE
2018 ACR criteria +	98	5
2018 ACR criteria -	13	3

Results: Our study consisted of 119 patients diagnosed with cSLE, UCTD, or MCTD: 87 (73.1%) were female with an average age at diagnosis of 14.56 years. These patients were predominantly white 68 (57.1%), black 36 (30.3%), and non-Hispanic 115 (96.6%; see Table 1). Of this cohort, the number of cSLE patients that were classified earlier using the 2018 criteria as compared to the 1997 SLE criteria was 9 out of 109 (8.3%) (See Table 2). The number of UCTD patients that were reclassified as SLE according to the 2018 criteria was 11 out of 33 (33.33%), and the number of MCTD that were reclassified was 4 out of 5 (80%). Our study found that there was neutral correlation between the SDI score and the 2018 SLE Score with a correlation coefficient= 0.28 and a median score of 22 that is associated with a patient SDI score > 1. The median 2018-SLE-Score that was associated with SLEDAI scores ≥ 6 during the first month post diagnosis was 16.5. 2018-SLE-Score and SLEDAI scores were moderately associated (r = 0.631; p= .000946). The sensitivity of the 1997 ACR criteria for our cohort was 83.78% and the 2018 ACR criteria was 88.29%. The 2018 ACR criteria were more sensitive but also produced more false positives (type I error; see Table 3). The median 2018-SLE-score of the 5 false positives was 10.8, close to the lower threshold for SLE presence.

Conclusion: Patients were found to be diagnosed earlier with cSLE using the 2018 ACR criteria among those carrying a current diagnosis of UCTD or MCTD . The 2018 ACR disease criteria proved to be more sensitive in detecting cSLE in our patient population than the 1997 ACR disease criteria. In addition, our study revealed that the 2018 criteria score did not correlate with patient disease damage as indicated by the recent SDI score.

Disclosure: C. Strahle, None; **A. Merritt**, None; **X. Niu**, None; **A. Mathur**, None; **A. Watts**, None; **H. Brunner**, ., 2, 5, 8, AbbVie, 5, AstraZeneca, 5, Bayer, 5, Bristol-Myers Squibb, 2, 5, EMD Serono, 5, Genentech, 2, 5, 8, GlaxoSmith-Kline, 5, Janssen, 5, Lilly, 5, Novartis, 5, 8, Pfizer, 2, 5, R-Pharm, 5, Sanofi, 5, UCB, 5.

Abstract Number: 1733

Long-term Renal Survival of Pediatric Onset Lupus Patients in a Population-Based Cohort

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Compared to adult-onset disease, pediatric-onset SLE (p-SLE) has more severe renal involvement. There are no population-based, long-term follow-up studies of pediatric lupus nephritis (LN) in the United States. This study characterized the long-term risk of end-stage renal disease (ESRD) in p-SLE.

Methods: The Georgia Lupus Registry is a population-based registry supported by the Centers for Disease Control and Prevention of validated SLE patients in 2 counties of Atlanta, Georgia. Trained abstractors reviewed medical

Table 1. Characteristics of Incident Pediatric-Onset SLE Patients at Baseline (2002-2004), stratified by ESRD status (through 2015)

Characteristic	All N=25	No ESRD N=19	ESRD N=6	P-value
Age at diagnosis, years [Median (25^{th}-75^{th})]	14.0 (12.1-15.8)	14.4 (12.5-15.8)	15.3 (14.0-16.9)	0.29
Age by 2004, years [Median (25^{th}-75^{th})]	24.3 (18.6-32.3)	16.3 (13.7-17.5)	17.1 (16.3-17.8)	0.43
Gender [N (%)]				
Female	132 (83%)	15 (79%)	5 (83%)	1.00
Race* [N (%)]				0.58
White	23 (14%)	1 (5%)	1 (17%)	
Black	131 (82%)	17 (89%)	5 (83%)	
Asian	5 (3%)	1 (5%)	0	
ACR Criteria [N (%)]				
Malar rash	82 (52%)	9 (47%)	1 (17%)	0.34
Discoid rash	33 (21%)	1 (5%)	1 (17%)	0.43
Photosensitivity	51 (32%)	7 (37%)	1 (17%)	0.62
Oral Ulcers	51 (32%)	5 (26%)	2 (33%)	1.00
Nonerosive Arthritis	125 (79%)	13 (68%)	4 (67%)	1.00
Pleuritis or Pericarditis	57 (36%)	3 (16%)	2 (33%)	0.56
Neurologic Disorder	37 (23%)	4 (21%)	1 (17%)	1.00
Hematologic Disorder	144 (91%)	16 (84 %)	6 (100%)	0.55
Immunologic Disorder	127 (80%)	14 (74%)	6 (100%)	0.29
Positive Antinuclear Antibody	148 (93%)	18 (95%)	6 (100%)	1.00
Final Diagnosis by [N (%)]				0.38
None	4 (3%)	0	0	
Dermatologist	86 (54%)	0	0	
Rheumatologist	2 (1%)	11 (58%)	2 (33%)	
Nephrologist	3 (2%)	0	0	
Rheumatologist and Nephrologist	64 (40%)	8 (42%)	4 (67%)	
Lupus Nephritis [N (%)]	86 (54%)	11 (58%)	3 (50%)	1.00
ACR renal criterion [N (%)]				
500 mg proteinuria/24 hours	65 (41%)	8 (42%)	3 (50%)	1.00
cellular casts	44 (28%)	6 (32%)	2 (33%)	1.00
≥3 grams proteinuria	70 (44%)	7 (37%)	3 (50%)	0.65
Anti-dsDNA antibodies [N (%)]	116 (73%)	12 (63%)	6 (100%)	0.14
Low C3 [N (%)]	96 (60%)	15 (79%)	5 (83%)	1.00
Low C4 [N (%)]	104 (65%)	15 (79%)	6 (100%)	0.54
Histological Class* [N (%)]				1.00
Non-proliferative (I, II, V, II/V)	13 (25%)	2 (29%)	0	
Proliferative (III, IV, III/V, IV/V)	39 (75%)	5 (71%)	2 (100%)	

P-value: Wilcoxon Rank-sum test for continuous variables and Chi-squared (or fisher's exact if cell count <5) for categorical variables.
*No other races or ethnicities were captured.
**There were no class VI.
Lupus Nephritis defined as meeting ACR renal criterion and/or kidney biopsy consistent with lupus nephritis

Table 2. End Stage Renal Disease Characteristics of Incident Cases Stratified by Presence or Absence of Baseline Lupus Nephritis				
	Overall	Baseline Lupus Nephritis	No Baseline Lupus Nephritis	P-value
Dialysis, n(%)	6 (100)	3 (50)	3 (50)	1.00
Age at Dialysis in Years, median (25^{th} – 75^{th} percentile)	19.6 (18.0-23.0)	23.0 (17.9-25.0)	19.5 (19.4-19.6)	0.66
Time from SLE Diagnosis to First Dialysis in Months, median (25^{th} – 75^{th} percentile)	50 (33-89)	89 (35-138)	33 (23-65)	0.19
P-value: Wilcoxon Rank-sum test for continuous variables or Chi-squared (Fisher's exact if cell count <5) for categorical variables. Baseline Lupus Nephritis defined as meeting ACR renal criterion and/or kidney biopsy consistent with lupus nephritis in 2002-04				

records to validate incident SLE cases in 2002-2004 (baseline), including p-SLE (diagnosed < 18 years of age) using the following criteria: ≥ 4 ACR classification criteria for SLE or 3 criteria with a final diagnosis of SLE made by a board-certified rheumatologist. Patients were matched to the United States Renal Data System through 2015. ESRD cases were defined as being on dialysis or having received a renal transplant. Wilcoxon rank-sum tests were used to analyze continuous variables and Chi-squared (or Fisher's exact) tests for categorical variables using SAS.

Results: The median age at diagnosis was 14 years (12.1–15.8), 82% were females, and 82% were black. Out of 25 incident cases, 6 (24%) developed ESRD through 2015. There were 14 (56%) who had LN at baseline, from which 3 (21.4%) developed ESRD. The other 3 ESRD cases had no record of renal involvement at baseline. There were no significant differences in baseline ACR criterion between those with and without eventual ESRD, including renal and immunologic parameters. Biopsy findings were not associated with ESRD (Table 1). The median age at first dialysis was 19.6 years, and the median time from SLE diagnosis to dialysis initiation was 50 months. Median age of dialysis initiation was 19.6 years. Those with baseline nephritis were slightly older (23.0 vs. 19.5 years, median) and had much longer time from SLE diagnosis to first dialysis (89 vs. 33 months, median) (Table 2).

Conclusion: This is the first population-based, long-term follow-up of validated p-SLE patients and their renal survival in an incident cohort. More than half had LN at baseline, with most maintaining renal survival during follow-up. However, after 12-14 years of follow-up, nearly a quarter of all p-SLE patients developed ESRD, and there were no associations between baseline clinical or immunologic characteristics and eventual ESRD. Various factors associated with p-SLE and the transition to adult care must be explored to improve long-term outcomes.

Disclosure: C. Park, None; **J. Figueroa**, None; **C. Drenkard**, None; **L. Plantinga**, None; **L. Greenbaum**, None; **S. Lim**, None.

Abstract Number: 1734

Low Bone Mineral Density Was Associated with Lupus Nephritis Irrespective of Duration on Steroid Treatment in a Large Observational Study of Juvenile Systemic Lupus Erythematosus Patients

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: An estimated 10-20% of all patients with systemic lupus erythematosus (SLE) develop clinical disease before the age of 18 years and are therefore classified as juvenile-onset SLE (JSLE). JSLE patients have a higher prevalence of lupus nephritis (LN) compared to adult-onset SLE and decreased long-term survival compared to JSLE patients without LN. We aimed to identify clinical and laboratory predictors of LN in JSLE patients by comparing the baseline characteristics of JSLE patients with and without LN.

Table 1: Baseline characteristics

	Lupus nephritis	Without Lupus nephritis	P value
Number of patients, n (%)	45 (36%)	89 (66.4%)	
Female	39 (86.7%)	73 (82%)	0.624
Age, years	22 (21- 26)	21 (19- 25)	0.092
Age at diagnosis, years	13 (10- 15)	13 (11.25- 15)	0.471
Age at menarche, years	12.75 (11.25- 15.75)	12.25 (11- 14.38)	0.543
Disease duration, years	10 (8- 14)	8 (6- 13)	0.012*
BMI, kg/m2	24.31 (20.41- 26.13)	23.96 (21.69- 28.5)	0.726
ANA	38 (84.4%)	85 (95.5%)	0.064
ENA	24 (53.3%)	51 (57.3%)	0.114
Anti- Ro	15 (33.3%)	31 (34.8%)	0.134
Anti- La	6 (13.3%)	14 (15.7%)	0.130
RF	3 (6.7%)	18 (20.2%)	0.114
Highest dsDNA levels ever	197 (32- 434)	48 (10- 294)	0.022*
Numbers are medians (interquartile ranges) unless otherwise stated. *p< 0.05 is significant			

Table 2: Clinical manifestations and complications

	Lupus nephritis	Without Lupus nephritis	P value
Number of patients, n (%)	45 (36%)	89 (66.4%)	
SLICC at last clinical assessment	0	0 (0- 0.5)	0.872
SLEDAI at last clinical assessment	2 (0- 4)	0 (0- 2)	0.123
BILAG at last clinical assessment	1 (0- 1.75)	1 (0- 1)	0.822
Constitutional symptoms	26 (80%)	67 (75.3%)	0.666
Mouth ulcers	31 (68.8%)	61 (68.5%)	0.258
Skin involvement	40 (88.9%)	73 (82%)	0.150
Arthritis	37 (82.2%)	71 (79.8%)	0.309
Myositis	5 (11.1%)	16 (18%)	0.451
Neuropsychiatric involvement	15 (33.3%)	19 (21.3%)	0.146
Cardiorespiratory involvement	12 (26.7%)	20 (22.5%)	0.669
Gastrointestinal involvement	8 (17.8%)	18 (20.2%)	0.724
Ophthalmic involvement	4 (8.9%)	9 (10.1%)	0.108
Haematological involvement	26 (57.8%)	44 (49.4%)	0.464
Hypertension	8 (17.8%)	6 (6.7%)	0.071
Stroke	1 (2.2%)	2 (2.2%)	1.000
Low bone mineral density	16 (35.5%)	11 (12.4%)	0.008*
Malignancy	1 (2.2%)	1 (1.1%)	1.000
Numbers are medians (interquartile ranges) unless otherwise stated. *p< 0.05 is significant			

Table 3: Treatment differences among JSLE patients			
	Lupus nephritis	Without Lupus nephritis	p
Number of patients, n (%)	45 (36%)	89 (66.4%)	
Hydroxychloroquine, n (%)	43 (95.6%)	88 (98.9%)	0.295
Steroid treatment duration, (months)	31 (1.5- 84.5)	29.5 (9- 54.8)	0.834
MMF, n (%)	39 (86.7%)	43 (48.3%)	0.000*
MMF, months	42 (18.75- 94.5)	0 (0- 44)	0.000*
Cyclophosphamide, n (%)	22 (48.9%)	17 (19.1%)	0.001*
Cyclophosphamide, number of courses	0 (0- 3)	0	0.000*
Rituximab, n (%)	27 (60%)	29 (32.6%)	0.003*
Rituximab, number of courses	2 (0- 2)	0 (0- 1)	0.000*
Azathioprine, months	2.5 (0- 48.5)	10 (0- 41)	0.868
Methotrexate, months	0	0 (0- 0.75)	0.529
Tacrolimus, months	0	0	0.219
Belimumab, months	0	0	0.310
Numbers are medians (interquartile ranges) unless otherwise stated. MMF= mycophenolate mofetil. *p< 0.05 is significant			

Methods: This is a single-center retrospective study that included JSLE patients reviewed in our young adult and adolescent clinics after transitioning from paediatric services. All data was analysed descriptively. Mann-Whitney U or Chi-square test were performed to compare the characteristics between patients with and without LN. In addition, we performed uni and multivariate analysis to investigate potential predictor biomarkers for LN.

Results: We identified 134 JSLE patients, 45 (34%) of which had LN. The baseline characteristics are detailed in **table 1.** As expected, the highest dsDNA levels ever were observed in patients with LN (p= 0.022).Patients with LN also had longer disease duration (p= 0.012). The overall clinical manifestations and complications did not differ between JSLE patients with or without LN, except for the prevalence of low bone mineral density (**Table 2**). Factors associated with low bone mineral density in a univariate logistic regression analysis were: the use of mycophenolate mofetil (p= 0.021) and the presence of LN (p= 0.007), while LN also associated with low bone density (p= 0.008) in a multivariate analysis. Skin involvement was the most common clinical manifestation in both JSLE patient groups. Treatment was more aggressive in patients with LN, including the use of cyclophosphamide, mycophenolate and rituximab, but there was no difference regarding the length of the steroid treatment (**Table 3)**. The majority of patients (67%) had one flare of nephritis. For the remaining patients, the number of flares ranged from 2 (13%) to 12 (2.2%). The class of nephritis was reported in 34 out of 45 patients, and focal lupus nephritis (class III) was the most common type (44%) reported. There were no statistically significant differences in the baseline characteristics or treatments among the different classes of LN.

Conclusion: Low bone mineral density in patients with JSLE is well described. However, this is the first study highlighting the association of low bone density with LN independent of total duration of steroid treatment or other clinical manifestations.

Disclosure: A. Madenidou, None; **Y. Mahfouz**, None; **O. Cheng**, None; **F. El-Sharnouby**, None; **C. Foley**, None; **C. Ciurtin**, None.

Abstract Number: 1735

Clinical Variables Influencing Prednisone Dosing Towards the Development of Corticosteroid Treatment Algorithms in Pediatric Proliferative Lupus Nephritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

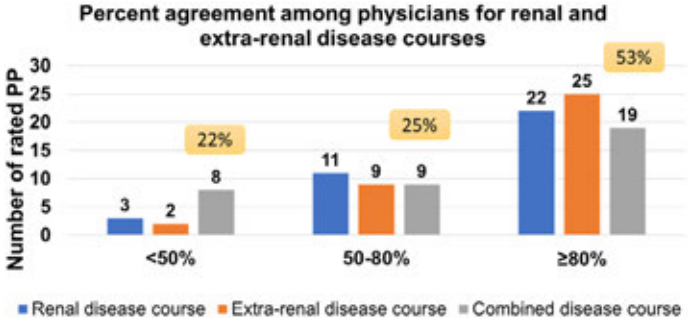
Session Type: Poster Session (Monday)

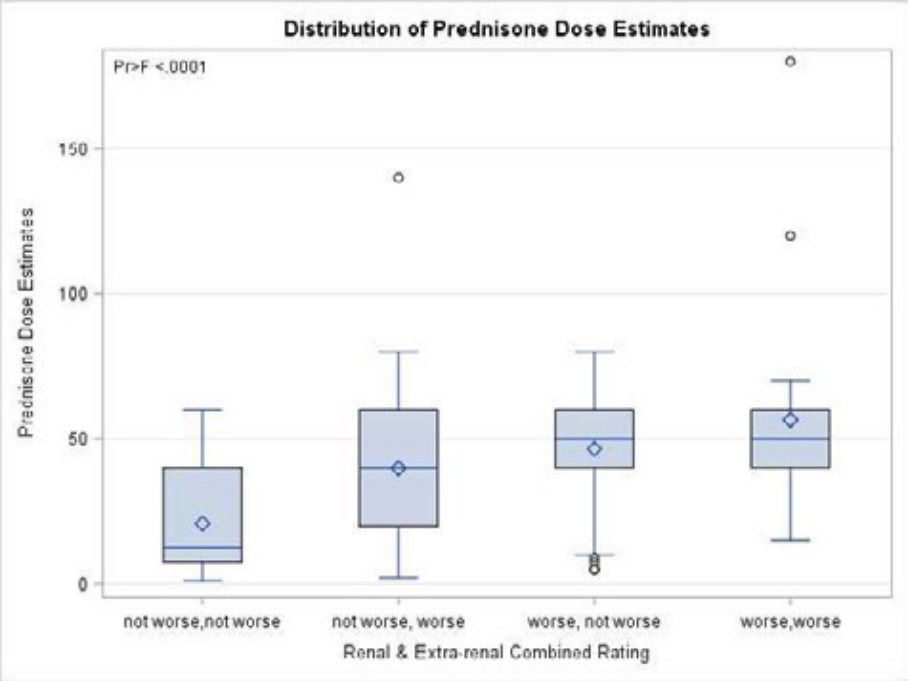
Session Time: 9:00AM–11:00AM

Background/Purpose: Corticosteroids (CS) are the mainstay of childhood-onset systemic lupus erythematosus (cSLE) and proliferative lupus nephritis (LN) therapy. However, there are no widely accepted CS dosing regimens for the treatment of LN. As a first step to establish CS dosing standards for cSLE and proliferative LN, we aimed to identify clinical variables influencing CS dosing with focus on oral prednisone dosing in children with newly diagnosed proliferative LN.

Methods: Consensus formation techniques were used. Patient profiles (PP) were generated using data from the medical records of children with proliferative LN at Cincinnati Children's Hospital Medical Center (CCHMC). Using the extracted data, an online survey was sent to rheumatologists (PP raters) at CCHMC and the University of Cincinnati Medical Center (UCMC) to adjudicate on renal and extra-renal clinical disease courses and estimate prednisone dosing for a given PP. Pearson correlation coefficients were computed to identify clinical variables that correlate with the estimated prednisone doses by PP raters. Mixed model analysis was performed to determine multivariable predictors of the estimated prednisone dose.

Results: Overall, the survey completion rate was 87% with a total of 291 completed PP. Each PP provides information about 2 subsequent visits (V1 and V2). PP survey responses showed a high level of agreement among raters for renal and extra-renal clinical disease courses when categorized into worsening vs non-worsening disease (Figure 1). The estimated prednisone dose by PP raters is found to be most strongly correlated with the pre-visit prednisone dose (r=0.70), and C3 level at V2 (r= -0.56). Proteinuria and SLEDAI-2K scores at V2 show moderate correlations with the estimated prednisone dose (r=0.49, and r=0.48 respectively). Using one-way ANOVA, the highest mean prednisone dose estimates are noted for worsening of the combined renal and extra-renal disease courses (57 ± 34 mg)





Prednisone dose estimate= β0 + β1 * (pre-visit prednisone dose) + β2 * (renal SLEDAI at V2) + β3 * (renal SLEDAI at V2-renal SLEDAI at V1) + β4 * (extrarenal SLEDAI at V2) + β5 * (extrarenal SLEDAI at V2- extrarenal SLEDAI at V1)

Renal and extra-renal clinical disease courses	β0	β1	β2	β3	β4	B5
Worse, Worse	44.87	0.14	0.35	0.77	-0.45	2.71
Not worse, Worse	3.28	0.95	0.35	0.77	-0.45	2.71
Worse, Not worse	17.53	0.70	0.35	0.77	-0.45	2.71
Not worse, Not worse	1.62	0.78	0.35	0.77	-0.45	2.71

and the lowest when the combined disease courses are not worse (21 ± 18 mg) (Figure 2). The pre-visit prednisone dose and the PP ratings of renal, extra-renal and combined renal and extra-renal clinical disease courses are found to be the best predictors of prednisone dose estimates using mixed model analysis (Table 1).

Conclusion: Prednisone dosing regimens in children with newly diagnosed proliferative LN depend on physicians' opinions of renal, extra-renal and the combined clinical disease courses as well as the pre-visit prednisone dose. The identification of clinical variables that correlate with and predict prednisone dosing regimens is key to the future development of CS treatment algorithms in children with proliferative LN.

Disclosure: N. Chalhoub, None; **T. Qiu**, None; **J. Deng**, None; **A. Merritt**, None; **B. Huang**, None; **H. Brunner**, ., 2, 5, 8, AbbVie, 5, AstraZeneca, 5, Bayer, 5, Bristol-Myers Squibb, 2, 5, EMD Serono, 5, Genentech, 2, 5, 8, GlaxoSmith-Kline, 5, Janssen, 5, Lilly, 5, Novartis, 5, 8, Pfizer, 2, 5, R-Pharm, 5, Sanofi, 5, UCB, 5.

Abstract Number: 1736

Cognitive Impairment in Childhood-Onset Systemic Lupus Erythematosus: Early Detection with MRI Spectroscopy and Its Association with MOG Antibodies

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

Session Type: Poster Session (Monday)

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic inflammatory disease characterized by the presence of various autoantibodies. Unnoticed and progressive cognitive impairment may develop in the course of disease even without overt neuropsychiatric (NP) features. Some authors attributed this mild impairment to the immune-mediated myelinopathy. Evidence exists that myelin oligodendrocyte glycoprotein (MOG) might act as a mediator of interactions between myelin and the immune system. We sought to detect the role of MOG-Ab in neurologic manifestations of childhood-onset SLE (cSLE) and to better delineate the actual grade of cognitive dysfunction by neurocognitive tests in patients without overt NP features (non-NPSLE). Moreover, we aimed to identify the localization of pathology at molecular level by analyzing the presence of any correlation between various metabolite peaks in MR spectroscopy (MRS) and the severity of cognitive dysfunction in non-NPSLE children.

Methods: MOG-Ab levels were studied in all healthy subjects (n=28) and in all patients with (NPSLE =9) and without (non-NPSLE=36) overt neuropsychiatric manifestations. All of the non-NPSLE group and healthy group underwent brain MR and MRS examination. However, only 20 subjects in each group met the MRS imaging standards for evaluation. In the non-NPSLE group, 29 cSLE patients were further evaluated by neurocognitive tests. Sixteen children with non-NPSLE were assessed by both MRS and neurocognitive tests.

Results: The mean age of the SLE patients at study time was 16.22±3.22 years. MOG-Ab was detected positive neither in cSLE nor in healthy group.

In children with non-NPSLE, verbal IQ ranged from 40 to 108 (mean: 79.06±17.66), performance IQ ranged from 42 to 111 (mean: 92.03±16.28), and full-scale IQ ranged from 40 to 106 (mean: 84.31±16.39). There were 15 patients (51%) in non-NPSLE group with a full-scale IQ under 85. There was no significant difference between the non-NPSLE group and healthy subjects in terms of choline, N-aspartic acid (NAA), creatine, NAA/creatine and choline/creatine.

A negative correlation was observed between the NAA/Creatine level of the left frontal white matter in MRS and the stroop test time (measures the ability to shift a perceptual set with changing demands which is a function of the frontal lobes) (p=0.015; r=0.596).

Conclusion: More than a half of our patients in non-NPSLE group were found to have a full-scale IQ under 85. Cognitive impairment may develop insidiously in cSLE children even without any overt symptom or sign. There was no association of MOG-Ab with cSLE, whether neuropsychiatric manifestations present or not. A causal relationship between immune-mediated myelinopathy and neuropsychiatric involvement/cognitive impairment could not be suggested, since there has been no patient with positive MOG-Ab and there has been no difference in choline, cholin/creatine between cSLE patients and healthy subjects. Decrease in the NAA/Creatine level of the left frontal white matter in MRS, which is a finding of neuronal loss, may be used as a first sign of cognitive impairment in patients with cSLE.

Disclosure: H. Kilic, None; **S. Sahin**, AbbVie, 2; **M. Toprak**, None; **G. Atay**, None; **K. Yilmaz**, None; **A. Adrovic**, AbbVie, 2; **K. Barut**, AbbVie, 2; **E. Isik**, None; **E. Tuzun**, None; **O. Kizilkilic**, None; **S. Saltik**, None; **O. Kasapcopur**, AbbVie, 2.

Abstract Number: 1737

Systemic Vascular Involvement in Kawasaki Disease: A Single Center Cohort

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
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Session Time: 9:00AM–11:00AM

Background/Purpose: Kawasaki disease is classically thought to be a monophasic disease that primarily targets the coronary arteries. The American Heart Association Kawasaki guidelines note that patient with severe coronary involvement may have peripheral aneurysms but does not specify which patients to image and how to follow peripheral involvement over time. Hoshino et al followed a cohort of twenty patients with peripheral aneurysms and concluded a diameter greater than 10 millimeters was associated with increased risk of development of stenotic lesions. The risks of additional radiation and sedation to image pediatric patients' peripheral vessels must be weighed against the benefit of detection peripheral lesions that may cause hemodynamically significant lesions as the patients grow. In this case series, we discuss the presentation and outcome of seven patients found to have peripheral artery aneurysms at a single institution.

Methods: With approval from the Baylor College of Medicine institutional review board, a retrospective review of the medical records of KD patients identified to have peripheral vessel disease was performed. Data including ethnicity, sex, age at diagnosis, total days of fever, day of illness first intravenous immunoglobulin (IVIG) received, coronary aneurysms, peripheral aneurysm characteristics and medications received were abstracted by chart review.

Results: The median age was 9 months, with range of 2 months to 7 years. Most patients described are Hispanic in ethnicity, with one Asian and one African American. Four of the patients described were male and three were female. The median days of fever was 13 days with range of 6 to 34 days. The median day of illness that first IVIG was

received was day 10 with range from day 4 to day 34. Six of seven patients had giant coronary aneurysms at some point in the disease course. The peripheral arteries involved were axillary, subclavian, aorta, iliac and femoral. All of the patients received intravenous methylprednisolone in addition to the first IVIG. Three of the seven received a second IVIG, five received infliximab, three received anakinra, and three received cyclophosphamide. Median duration

Patient	Age at diagnosis	Sex	Ethnicity	Day of illness at first IVIG	Initial fever duration	Other Treatment	Coronary disease second echo	Coronary disease at 6-week echo	Day of illness of peripheral imaging	Peripheral vascular disease	Duration of follow-up	Coronary outcome at last follow-up
1	2 m	Female	Hispanic	34	34	IVMP	Normal LMCA, LAD and RCA with giant aneurysms	left coronary aneurysm 4.7 mm, smaller RCA aneurysm of 3.7 mm	49	Irregular contours to the lateral portions of the axillary arteries, right femoral artery is more conspicuous than the iliac artery, similar finding to a lesser degree for left femoral artery	1 y + 6 m	No coronary aneurysm
2	3 m	Male	Asian	10	9	IVMP, infliximab	Small aneurysm in LMCA, medium in LAD and RCA	No coronary aneurysm	14	Mild aneurysmal dilation of distal abdominal aorta with significant dilation of bilateral proximal iliac arteries with abrupt transition in caliber to distal common iliacs	2 m	No coronary aneurysm
3	9 m	Male	Hispanic	15	15	IVMP, infliximab, cyclophosphamide	Small aneurysm in LMCA, giant in LAD and RCA	Giant aneurysm of LAD	21	Bilateral aneurysms of internal iliac with bulbous dilation at the common iliac bifurcation	1 y + 5 m	No coronary aneurysm
4	9 m	Male	African-American	11	11	Second IVIG, IVMP	Normal at outside hospital	Fusiform aneurysm of RCA, diffuse dilation of left coronary arteries	39	Focal large aneuryms of the bilateral subclavian and axillary arteries, at least 3 on each side with areas of stenosis in between	8 y + 4 m	No coronary aneurysm
5	1 y + 2 m	Male	Hispanic	6	16	Second IVIG, IVMP, infliximab, anakinra, cyclophosphamide	Dilation only in all 3 vessels	Severe dilation of LMCA and LAD, giant saccular aneurysm of RCA	18	Fusiform aneurysmal dilations in bilateral internal iliac arteries	1 y + 10 m	Giant fusiform aneurysm of the LAD, moderate to large aneurysm in RCA
6	1 y + 3 m	Female	Hispanic	4	6	Second IVIG, IVMP, infliximab, anakinra, cyclophosphamide	Normal	Severe diffuse dilation of RCA, severe dilation with irregular contoured appearance of left main and LAD	54	Mildly ectatic proximal course of the right subclavian artery over length of 1.5 cm, focal 5 mm aneurysm of subscapular division arising from the axillary artery	1 y + 6 m	Large aneurysm in distal RCA
7	7 y + 4 m	Female	Hispanic	9	13	IVMP, infliximab, anakinra, cyclophosphamide	Small aneurysm in LMCA, medium in LAD and giant in RCA	Large fusiform in RCA (proximal and mid), Large fusiform in LAD (mid and distal)	32	Focal aneurysms (5 to 7.8 mm) involving the proximal aspect of the thoracoacromial branch of both axillary arteries as well as the proximal lateral thoracic division arising from the distal right axillary artery.	4 m	Large fusiform aneurysm in LMCA and LAD. Giant fusiform in RCA.

Legend	
LMCA	Left Main Coronary Artery
LAD	Proximal Left Anterior Descending
RCA	Proximal Right Anterior Descending
IVMP	Intravenous methylprednisolone
IVIG	Intravenous Immunoglobulin

KD peripheral aneursym table
Individual characterisitics of patients

of follow-up was 18 months with range from 2 months to 8 years. Notably, the youngest four of the seven had no coronary aneurysms observed on echo at last follow-up.

Conclusion: Patients described in this cohort had severe disease and often required aggressive multi-modal immunomodulation due to persistent systemic inflammation and extra-coronary involvement. It is reasonable to obtain peripheral imaging in patients that have severe coronary involvement at the second echo or 6-week echo. It is the practice of our center to obtain such imaging when the patients are undergoing cardiac computed tomography. More research is required to understand the frequency of clinically relevant peripheral changes in patients with Kawasaki disease. From this small case series, young patients under 18 months appear to be at increased risk. It is also important to gather information about the normal size of peripheral vessels for very small body sizes. It is possible that this is an under recognized aspect of the disease.

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Abstract Number: 1738

Tracking Whole-Brain Volumetric Trends in Childhood-onset Systemic Lupus Erythematosus Patients in the Clinical Setting by Magnetic Resonance Imaging

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The course of childhood-onset Systemic Lupus Erythematosus (cSLE) commonly includes neurocognitive dysfunction, a manifestation with poor prognosis. It has been challenging to diagnose and categorize CNS involvement in cSLE due to its heterogeneity, especially in early stages. As part of development of a comprehensive patient-centered care approach, we are collecting clinical MRI in cSLE patients, including specialized protocols for CNS lupus assessment. Here, we focus on whole-brain volumetric measures from our protocol. We have previously identified multiple areas of gray matter (GM) loss on structural MRI in cSLE patients with neurocognitive deficits. This work is part of our overall aim to identify clinical neuroimaging signatures for patient-specific categorization of CNS involvement and to allow tracking of disease course and treatment response.

Methods: The first 12 cSLE patients referred for a specialized clinical lupus MRI evaluation were analyzed. Appended to a routine clinical brain MRI protocol were sequences for diffusion-weighted imaging, resting-state functional MRI, and so-called synthetic MRI (synMRI). Using multiple weightings, synMRI provides quantitative mapping of tissue magnetic relaxation properties permitting segmentation of gray matter (GM), white matter (WM), cerebrospinal fluid, and myelin tissue classes. Our initial analyses focused on whole-brain volumes, specifically tissue class volumes as percentage of total intracranial volume (%ICV). We assessed the association of GM, WM, myelin, and parenchyma (GM+WM) as %ICV with SLE severity (SLEDAI) and neurocognitive performance via the Pediatric Automated Neuropsychological Assessment Metrics (PedANAM), principle component (PCA) and Multiscore summary scores.

Results: The 12 cSLE patients included 10 females and 4 African Americans, with mean age 16.6 ± 3.1 years. Mean SLEDAI score at the time of the MRI was 4.8 ± 3.2 (range 0 to 12). On the PedANAM, mean PCA was -2.3 ± 3.8 (range -11.7 to 1.4), and mean Multiscore was 7.3 ± 5.3 (range 1.6 to 21.4). One patient lacked SLEDAI data and another lacked PedANAM indices, resulting in 11 available for correlative analyses. Regression results are summarized in Table 1. Total parenchymal volume as %ICV was found to significantly decrease as the Multiscore index increased (Figure 1). This relationship was driven by decreases in GM (Figure 2) rather than myelin (WM). Lack of correlation between parenchymal volume and PCA or SLEDAI could be at least partly explained by counterbalanced dependencies on GM and myelin volumes. WM and myelin volumes were highly correlated (R^2=0.79) and gave similar outcomes. Age, gender, and race covariates were tested individually and found to not contribute significantly.

Table 1: Correlation of Brain Volumes to Patient Assessment

Brain Tissue Volume[a]	Patient Assessment[c]	coefficient	R^2	p-value
GM	SLEDAI*	0.526	0.297	0.083
	PCA*	0.437	0.290	0.087
	Multiscore**	-0.387	0.428	0.029
Myelin[b]	SLEDAI*	-0.138	0.333	0.063
	PCA**	0.140	0.442	0.026
	Multiscore	0.030	0.039	0.562
Parenchyma	SLEDAI	0.125	0.016	0.712
	PCA	0.090	0.015	0.719
	Multiscore**	-0.350	0.424	0.030

a. expressed as % intracranial volume (ICV), b. Myelin content highly correlated with WM volume, c. PCA and Multiscore are PedANAM indices.
* trending $p < 0.1$, ** $p < 0.05$.

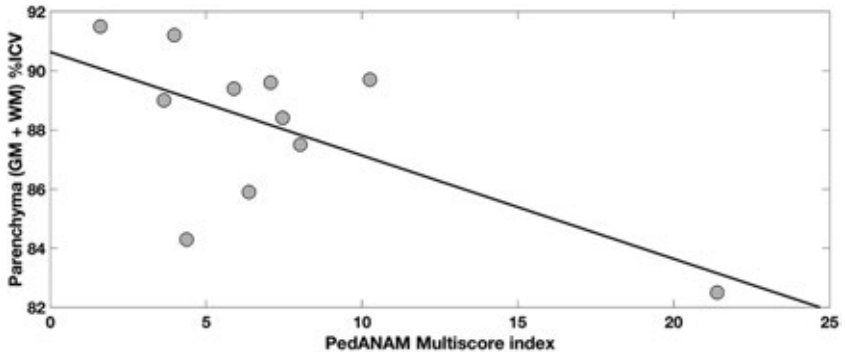

Figure 1 Regression of Total Parenchyma %ICV against PedANAM Multiscore index

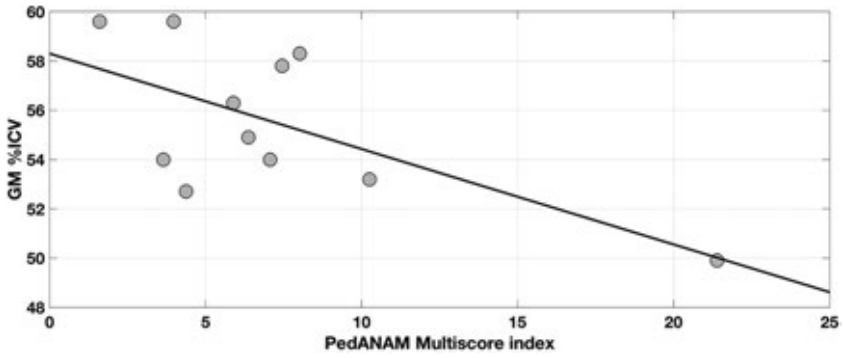

Figure 2 Regression of Total GM %ICV against PedANAM Multiscore

Conclusion: We present the results of whole-brain volumetric analysis in an initial group of cSLE patients referred for clinical brain MRI showing a significant association between neurocognitive measures and brain tissue class volumes. These outcomes motivate continued collection of clinical MRI data using our specialized protocol extensions with the aim of developing specific neuroimaging signatures for SLE for application to patient-centered care.

Disclosure: H. Brunner, ., 2, 5, 8, AbbVie, 5, AstraZeneca, 5, Bayer, 5, Bristol-Myers Squibb, 2, 5, EMD Serono, 5, Genentech, 2, 5, 8, GlaxoSmithKline, 5, Janssen, 5, Lilly, 5, Novartis, 5, 8, Pfizer, 2, 5, R-Pharm, 5, Sanofi, 5, UCB, 5; **A. Mathur**, None; **W. O'Brien**, None; **M. DiFrancesco**, None.

Abstract Number: 1739

Kawasaki Disease Shock Syndrome - More Common Than We Think: Our Experience at Chandigarh, North India

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SESSION INFORMATION
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Background/Purpose: Approximately 5% patients with Kawasaki disease (KD) can present with cardiovascular collapse-the KD Shock Syndrome (KDSS). This is an unusual presentation of KD and is often confused with septic shock. As a result, the diagnosis can be easily missed. We report the profile of patients with KDSS from a cohort of 810 KD patients at Pediatric Rheumatology Clinic, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, North-West India.

Methods: 810 children were diagnosed to have KD during the period January 1994-December 2018. Case files of patients with KDSS were retrieved and clinical details recorded.

Results: Of the 810 cases, 28 (15 boys; 13 girls) had hemodynamic instability. Median age at diagnosis was 7 years (range 6 months-14.5 years). All patients required inotropic support. Infection triggered KD was seen in 6 patients and most common organism was *Staphylococcus aureus*. Initial diagnosis of toxic shock syndrome (TSS) had been given in 15 (53.6%) patients. Thrombocytopenia was seen in 12 (42.9%). We were able to perform NT-proBNP in 11 patients and median value was 921.5 (225-9450) pg/mL. First line treatment was intravenous immunoglobulin (IVIg) therapy. Second line therapy was required in 9 patients - infliximab in 3; second dose IVIg in 2 and glucocorticoids in 4. Coronary artery abnormalities (CAAs) were seen in 5 (17.8%) - of these, one had giant aneurysms in left anterior descending coronary artery and right coronary artery. Six had severe myocardial dysfunction secondary to myocarditis. We recorded one death amongst the patients with KDSS.

Conclusion: Both KDSS and TSS can present to the Emergency Room with fever, rash, and shock. Clinical differentiation between the two entities is crucial as management protocols for the 2 conditions are completely different. Delays in recognition of KDSS are not uncommon and may result in avoidable morbidity and occasional mortality. Patients with KDSS are at an increased risk of developing CAAs.

Disclosure: R. Kumar, None; **H. Chaudhary**, None; **M. Singhal**, None; **S. Singh**, None.

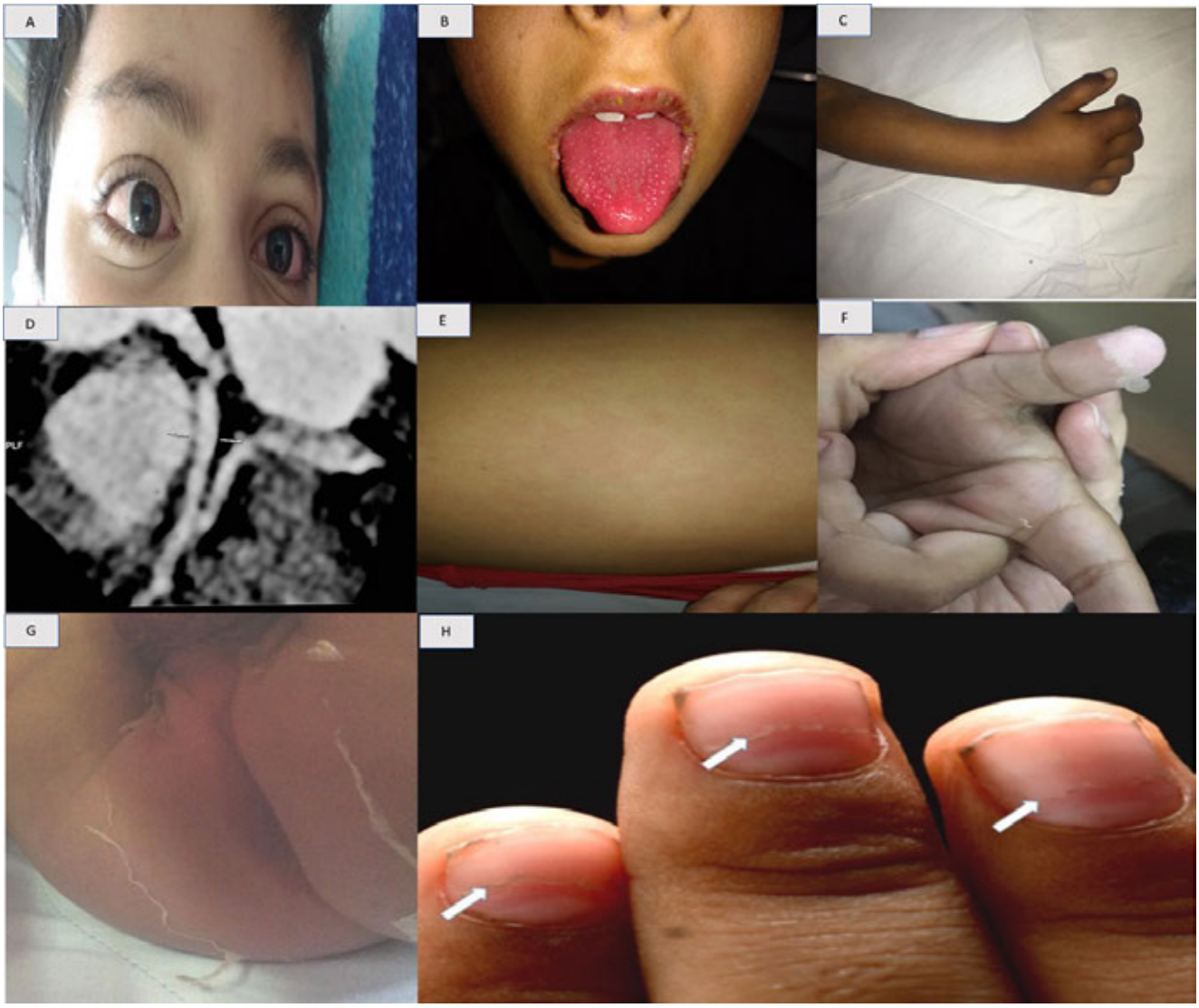

Figure 1 Images panel patients showing A: conjunctival injection; B: Strawberry tongue; C: Dorsal edema over hand; D: CTCA LAD aneurysm in Image panel patient; E: Erythematous macular rash; F: Periungual desquamation; G: Perineal desquamation; and H: Beau's line

Abstract Number: 1740

Orange Brown Chromonychia in Kawasaki Disease: A Clinical Sign That Merits Greater Attention

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

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Session Time: 9:00AM–11:00AM

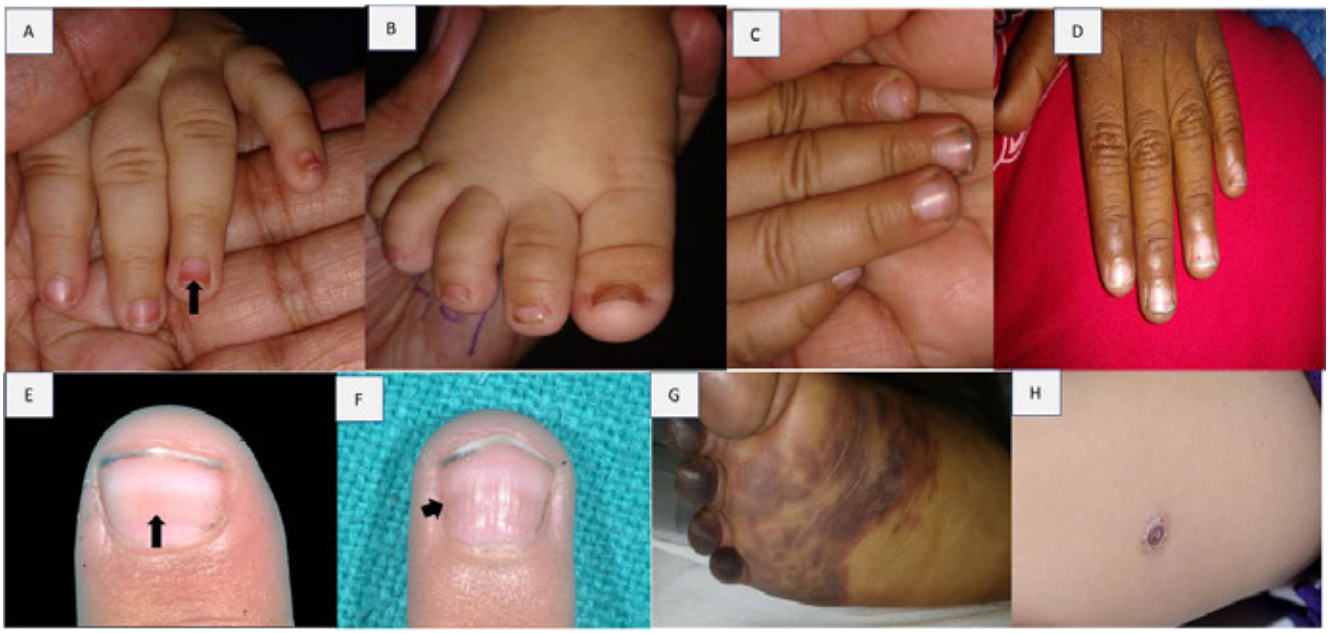

Figure 1 A, B: Shows orange brown transverse lines (chromonychia) on all nails in patient 1 C: Chromonychia in patient 2 D: Chromonychia in patient 3 E, F: Orange brown chromonychia in convalescent phase patient 4 G: Peripheral gangrene in patient 5 F: BCG reactivation in patient 1

Background/Purpose: Peripheral signs in Kawasaki disease (KD) include erythematous swelling of hands and feet during acute phase, periungual desquamation and Beau's lines on nails in convalescent phase. Orange–brown discoloration of nails has, however, not been frequently described in KD.

Methods: Although chromonychia was described by Pal et al way back in 2010, we had not been looking prospectively for this sign until very recently. We report 20 patients with KD and orange-brown chromonychia that were seen during the period May 2017 - February 2019.

Results: Median age at diagnosis in these patients was 1.4 years (range:3 months-4 years). Seven patients were below 1 year. Eleven patients developed chromonychia in acute phase of KD, while in 9 this finding was identified in convalescent phase. Associated atypical features that were seen in these patients included BCG reactivation in 2; macrophage activation syndrome in 2; uveitis in 1; peripheral gangrene in 1; bilateral parotidomegaly in 1; HIN1 pneumonia in 1. Ten (50%) children required second line therapy - infliximab in 6; second dose of IVIg in 1; methylprednisolone in 3. Coronary artery abnormalities were seen in 5 patients and 2 had giant aneurysms - one in left main coronary artery; another in left main, left anterior descending and left circumflex coronary arteries.

Conclusion: Transverse orange brown chromonychia is a useful clinical sign in KD and may be seen in both acute and convalescent phases of the disease. This sign can be easily missed if not looked for carefully. It appears to be more common in infants and young children and may be a marker of more severe disease. Presence of this sign may help pediatricians in arriving at a diagnosis of KD, especially in situations where the presentation is incomplete.

Disclosure: R. Kumar, None; **A. Jindal**, None; **H. Chaudhary**, None; **S. Singh**, None.

Abstract Number: 1741

Depression and Anxiety Symptoms in Childhood-Onset Systemic Lupus Erythematosus

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Background/Purpose: Depression and anxiety disorders are common in patients with childhood-onset systemic lupus erythematosus (cSLE). It is unclear if they are due to central nervous system involvement, secondary to a chronic illness or to treatment. We aimed to determine the prevalence and risk factors for clinically elevated depression and anxiety symptoms in a cohort of children with SLE.

Methods: Eligible participants for this cross-sectional study were all patients ≥8 years old who were seen in the cSLE clinic at The Hospital for Sick Children between July 2017 and January 2019, with cSLE or incipient SLE (iSLE) per ACR or SLICC classification criteria. Non-English speakers were excluded. Participants completed demographic questionnaires, the Center for Epidemiologic Studies Childhood Depression Scale (CES-DC), the Screen for Childhood Anxiety Related Disorders (SCARED), and Quality of My Life (QoML) scales. Medical history, SLE features, and medications were collected via chart review and clinic database. Clinically significant depression and anxiety symptoms were indicated by scores of >15 for CES-DC and >25 for SCARED, respectively, and prevalence was compared to general North American population data from the National Comorbidity Survey Study– Adolescent Supplement[1]. Anxiety subtypes were tabulated. CES-DC and SCARED scores were analyzed with Spearman correlation for association with SLEDAI-2K score, disease duration, global and health related QoML score.

Results: There were 51 patients recruited (48 cSLE and 3 iSLE; mean age 14.9 years, SD 2.1), 84.3% females (Table 1). Mean disease duration was 4.6 years (SD 0.4), history of anti-phospholipid antibodies was present in 41.1% (21/51), lupus nephritis 39.2% (20/51), CNS lupus in 21.6% (11/51), and SLEDAI-2K median was 1, IQR (0,2). Mean CES-DC score was 13.5 (SD 9.8), child-reported SCARED score 20.2 (SD 9.9) and parent-reported SCARED score was 13.6 (SD 8.2) (Table 2). Compared with NCS-A population data, cSLE patients had a higher prevalence of clinically significant depression on the CES-DC (29.5% vs 11%; x2=15.2, 95% CI 7.1-22.1, p =0.0001), and anxiety (36.4% vs 12%; x2= 24.5, 95% CI 11.8-39.2; p< 0.0001) by child report. Past history of depression or anxiety was reported in 9.8% (5/43); past or current psychological treatment in 3.9% (2/43), and mood or anxiety disorder in a first degree relative in 35.3% (18/43). CES-DC scores correlated with global QoML score (r=-0.55, p< 0.001), health related QoML

Total N = 51	N (%)
Diagnosis	
Systemic Lupus Erythematosus (SLE)	48 (94.1)
Incipient SLE	3 (5.9)
Age in years, mean (SD)	14.9 (2.1)
Female Sex	43 (84.3)
Race/Ethnicity N (%)[1]	
Black or African American	2 (3.9)
White/Caucasian	8 (15.6)
East Asian	11 (21.6)
South Asian	6 (11.7)
Hispanic/South American	9 (17.6)
Mixed	4 (7.8)
Other	3 (5.8)
First degree relative with mood disorder[1]	18 (35.3)
History of depression and/or anxiety (previously or currently)[1]	5 (9.8)
Past or current treatment for depression and/or anxiety (counselling or medication)[1]	2 (3.9)
Disease duration in years, mean (SD)	4.6 (0.4)
History of CNS lupus (other than depression/anxiety)	11 (21.6)
History of Anti-phospholipid antibodies (Lupus anticoagulant, Anti-cardiolipin antibodies)	21 (41.1)
History of Lupus Nephritis	20 (39.2)
History of severe skin disease (discoid lupus, annular erythema, panniculitis, or severe hypopigmentation)	2 (3.9)
SLEDAI-2K Score, median (IQR)[2]	1 (0,2)
Quality of my life global score, mean (SD)[3]	70.0 (17.4)
Health Related Quality of My Life Score, mean (SD)[3]	63.3 (21.0)
Current Medications:	
Hydroxychloroquine	47 (92.6)
Low-dose steroids (1-10 mg/day)	12 (23.5)
High dose steroids (>=10 mg/day)	2 (3.9)
Disease-Modifying Anti-Rheumatic Drugs (DMARD)[4]	23 (45.1)
Anti-depressant or Anti-anxiety medication	2(3.9)
History of Cyclophosphamide treatment	8 (15.7)
History of Rituximab treatment	5 (9.8)

[1]Incomplete data: n= 8 (17.5%); [2]Incomplete data: n= 2 (3.9%); [3]Incomplete data: n = 9 (17.6%)
[4]DMARD= Methotrexate, Azathioprine, Mycophenolate mofetil, Tacrolimus, Cyclosporine A

Table 1 Baseline Characteristics and Demographics in a Cohort of Patients with Childhood-Onset Lupus

	Patient-reported	Parent-reported
CES-DC score, mean (SD)	13.5 (9.8)	-
Positive screen for depression on CES-DC, N (%)	13 (29.5)	-
SCARED score, mean (SD)	20.2 (9.9)	13.6 (8.2)
Positive for screen for anxiety on SCARED, N (%)	16 (36.4)	3 (7.8)
Positive for screen anxiety subcategories on SCARED, N (%)		
Panic Somatic	6 (13.6)	1 (2.6)
Generalized Anxiety	17 (38.6)	2 (5.1)
Separation Anxiety	6 (13.6)	1 (2.6)
Social Anxiety	11 (25.0)	5 (12.8)
School Avoidance	4 (9.1)	2 (5.1)

Table 2 Prevalence of Depression and Anxiety Symptoms in a Cohort of Patients with Childhood-Onset Lupus

(-0.35, p=0.03), and both child (0.36, p=0.02) and parent-reported SCARED scores (0.47, p< 0.01). CES-DC and SCARED scores were not correlated with SLEDAI-2K or disease duration (Table 3).

Conclusion: Clinically significant depression and anxiety symptoms are prevalent in our cSLE group (with low rates of prior psychological treatment), and are not associated with current disease severity or treatment duration. Increased depression in cSLE patients is associated with decreased quality of life. Study of the longitudinal relationship between mood disorders and cSLE disease course, and optimal strategies for mental health intervention is warranted.

[1]Merikangas et al. J Am Acad Child Adolesc Psychiatry. 2010;49:980-989

	CES-DC Score Spearman's rho	SCARED Patient Score Spearman's rho	SCARED Parent Score Spearman's rho
SLEDAI-2K Score	-0.09	-0.04	0.26
Disease duration	-0.22	0.03	-0.05
QoML Global Score	-0.55***	-0.15	-0.07
Health Related QoML Score	-0.35*	-0.27	-0.02
SCARED Patient Score	0.36*	-	0.24
SCARED Parent Score	0.47**	0.24	-

*p<0.05
**p<0.01
***p<0.001

Table 3 Correlations between Depression and Anxiety Scores, and Disease-related Factors and Quality of Life

Disclosure: K. Neufeld, None; **F. Silverio**, None; **L. Ng**, None; **A. Danguecan**, None; **D. Dominguez**, None; **R. Schachter**, None; **M. Quilter**, None; **J. Couture**, None; **D. Korczak**, None; **D. Levy**, None; **L. Hiraki**, None; **E. Silverman**, None; **A. Knight**, None.

Abstract Number: 1742

Ethnicity and Neonatal Lupus Erythematosus Manifestations Risk in a Large Multi-Ethnic Cohort

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Background/Purpose: Neonatal Lupus Erythematosus (NLE) is an acquired autoimmune disorder of newborns secondary to the transplacental passage of maternal anti-Ro/La antibodies. Prior studies have suggested that children of non-European ancestry have a higher risk of cardiac disease compared to European ancestry children; however, this finding has not been consistently replicated. The risk of non-cardiac NLE manifestations by ethnicity is unknown. We aimed to evaluate the association between ethnicity and NLE risk and NLE manifestations in a large multi-ethnic population.

Methods: We conducted a cohort study of the children seen at the NLE clinic at SickKids. Children born to anti-Ro/La antibody positive mothers in the Greater Toronto Area were referred to the NLE clinic. All data was prospectively entered into a dedicated database. Beginning in 2011, families routinely reported ethnicity (Canada census categories). The cohort consisted of children ≤ 1 year of age seen between January 2011 and April 2019. The NLE patient cohort was divided into European and non-European groups according to the child's ethnicity. Outcomes were NLE and specific NLE manifestations (cardiac, dermatologic, cytopenias, transaminitis and macrocephaly). The frequency of NLE and specific manifestations were compared among ethnic groups with Fisher's exact test. Using separate logistic regression models, we tested the association between ethnicity and 1) NLE risk and 2) specific NLE manifes-

Table 1: Predictors of Neonatal Lupus Erythematosus Risk and Specific Manifestations (n=273)

Covariate	NLE OR (95% CI)* p-value	Cardiac OR (95% CI)* p-value	Dermatologic OR (95% CI)* p-value	Hematologic OR (95% CI)* p-value	Hepatic OR (95% CI)* p-value	Neurologic OR (95% CI)* p-value
Non-European Ethnicity	1.21 (0.73-1.99) 0.44	0.55 (0.21-1.46) 0.23	1.44 (0.65-3.18) 0.35	1.36 (0.72-2.54) 0.33	1.13 (0.64-2.00) 0.65	0.37 (0.10-1.38) 0.14
Sex - Male	0.62 (0.38-1.00) 0.06	0.42 (0.15-1.66) 0.09	0.87 (0.41-1.85) 0.73	0.63 (0.35-1.16) 0.14	0.50 (0.28-0.86) 0.01	4.42 (0.93-20.99) 0.06
Hydroxychloroquine use in pregnancy	0.80 (0.46-1.41) 0.45	0.99 (0.28-3.48) 0.99	0.57 (0.23-1.44) 0.24	0.94 (0.49-1.81) 0.85	0.59 (0.31-1.12) 0.11	1.24 (0.31-4.97) 0.75
Mother – Rheumatic disease status in pregnancy	0.97 (0.53-1.77) 0.93	0.33 (0.11-1.02) 0.06	0.82 (0.35-1.94) 0.66	2.71 (1.17-6.23) 0.01	1.02 (0.53-1.96) 0.93	1.57 (0.27-8.86) 0.60

*Effect of Child Non-European Ethnicity (vs. European Ethnicity) tested in multivariate models including covariates: Sex – Male (vs. female), maternal hydroxychloroquine use in pregnancy (taken or not taken), maternal rheumatic disease status (present or absent). Excluded for the analysis without information about pregnancy maternal hydroxychloroquine (n=2). NLE: Neonatal Lupus Erythematosus; OR: Odd Ratio; 95% CI: 95% confidence interval

tations, including covariates for child sex, maternal rheumatic disease status in pregnancy (present or absent) and maternal use of hydroxychloroquine during pregnancy, Bonferroni-corrected p-value < 0.002.

Results: Our study included 326 children born to anti-Ro/La antibody positive mothers. Median follow-up period was 12 months (IQR: 2,24months). We censored 51 children with mixed ethnicity (European and Non-European). The non-European group (59%) was comprised of East Asian (30%), South Asian (25%), African (20%), Latin American (6%) and Mixed non-European ancestry (18%). In comparing European and non-European children, there was no difference in the proportion of NLE in children of European (50%) vs. non-European (54%) ancestry (p 0.46). There was no significant association between Non-European ethnicity and NLE risk and frequency of specific NLE manifestations, in univariate of multi-variable adjusted models (Table 1).

Conclusion: In our large multi-ethnic cohort, there was no statistically significant association between the child's ethnicity and NLE risk, nor specific NLE manifestations. Future analysis will incorporate additional maternal medications during pregnancy and genetic analysis of NLE risk and specific NLE manifestations.

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Abstract Number: 1743

Kawasaki Disease: Is Intravenous Immunoglobulin Alone Adequate for the Child with Kawasaki Disease and Coronary Artery Lesions? A Retrospective Study of 65 Children with Kawasaki Disease from a Single North Indian Centre

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Steroid use in Kawasaki disease (KD)is controversial and has swung from contraindicated, to maybe & now perhaps "should be given to all."(1) Currently, standard practice is to use IVIg for *all* children with KD and add upfront steroids to IVIg only for those children who are at risk of non- response to IVIg , if such children can be identified. (2) There is data to support the use of steroids at 2mg/kg/day as an add on to IVIg for the child who is at high risk of non response to the 1st IVIg (3) At our center, over the last 18 years we have observed1. significant no. of children present with CALs & 2. These children often do not respond to 1st dose of IVIG. Thus, from 2017 we changed our practice & added steroids to IVIG as an upfront therapy to children presenting with CALs. We audited our practice & present the data on 65 children with KD.

Purpose
1 To study demographic & clinical profile of children with KD.
2 To study response rate of IVIg
3 To study the difference in response rate (if any) for the child with KD & CALs who was given only IVIg (pre 2017) or IVIg & steroids (post 2017) at first presentation

Methods: All children diagnosed with KD from Jan13 to Apr19 were included. Clinical & demographic details were recorded on predesigned proformas. CALs were defined by z score (Boston) of more than 2 in any coronary artery. Response to IVIG was defined as no fever 36 hours post IVIG completion. Patients given IVIG alone got high dose aspirin, with steroids only low dose was given.SPSS 17.0 was used for analysis.

Results: 65 KD patients reviewed. Clinical & demographic details in Table 1. CALs were present in 31(47.6%) children at diagnosis. Boys had more CALs at onset than girls(p=0.059) IVIg was given to all. Steroids as first line were given to 13(20%): All had CALs. A second dose of IVIG was required by 13(20%). Therapy detailed in Table 2. IVIg alone had a poor response in those presenting with CALs. Addition of steroids to IVIG upfront was associated with significant increase in response in those with CALs(p=0.001) Details in table 3. No factors predicted the response to IVIG alone(age, day of diagnosis, C reactive protein). A higher z score predicted poor response to IVIG alone(p< 0.005), thus reiterating the fact that steroids are helpful in KD patients with CALs Kawasaki shock syndrome was seen in 2(3%) and macrophage activation syndrome in 1(1.5%),requiring high dose methylprednisolone(10-30mg/kg/day). At median follow up of 14 months(IQR 8-15), CALs normalized in 27(86%),5 persisted to have abnormal CALs. (All had giant aneurysms at presentation, Z scores >10). There was no mortality in this cohort.

Table 1: Clinical and demographic characteristics

Characteristics	
Male: females	45:20
Median age at diagnosis(years)	2.77 years (IQR 1.28-5.24)
Median time to diagnosis(days)	9 days (IQR 7-13)
Complete KD	31(48%)
Incomplete KD	31 (48%)
Atypical KD *Seizures* *Jaundice* *Severe hemolytic anemia*	3 (4%) 1 1 1
Clinical features at presentation Oral cavity changes Non purulent bulbar conjunctivitis Rash Extremity changes(acute and subacute) Cervical lymphadenopathy Arthritis Irritability Urethritis BCG scar reactivation	 48 (74%) 48 (74%) 45 (69%) 42 (65%) 29 (45%) 19 (29%) 13 (20%) 3 (5%) 2 (3%)
Complications Kawasaki shock syndrome Macrophage activation syndrome Sensori neural hearing loss	 2(3%) 1(1.5%) 2 (3%)
Median C reactive protein	60.5mg/l(IQR 6-344)
Echocardiographic findings No CAL CAL at time of diagnosis	 33 (51%) 32 (49%)
Z scores(Boston criterion) <2 2-2.4 2.5-5 5.1-10 >10	 33 (51%) 4 (6%) 13 (20%) 9 (14%) 6 (9%)

References

1. Corticosteroids for the treatment of KD in children. Cochrane Review 2017.
2. Diagnosis, Treatment, and Long-Term Management of KD. 2017.
3. Efficacy of IVIG plus prednisolone for prevention of CALs in severe Kawasaki disease (RAISE study): Lancet 2012

Conclusion

1. 47% KD patients presented with CALs.
2. KD with CALs have poor response to IVIG alone vs IVIG with upfront steroids (p=0.001)
3. In addition to the well described scoring systems that predict a poor response to IVIG in the Japanese population, the presence of CALs and risk of non response to IVIG needs further study and replication in cohorts across the world.

Table 2: Details of therapy given per the echocardiographic finding

Patient profile	Upfront therapy with IVIG alone	Upfront therapy with IVIG and IV steroid	No of patients given second IVIG only	No of patients given rescue with steroids AND second dose of IVIG	No of patients given only steroid after 1st IVIG failure and no 2nd dose of IVIG	No of patients given additional anti inflammatory therapy ie Infliximab Azathioprine Cyclosporin Others	No of patients given additional antithrombotic therapy: Clopidegrol Low molecular weight heparin
KD with no CAL N=33	32	1* steroid for MAS	1	2	0	Infliximab 1** (for intolerance to IVIg)	0
KD with any CAL N=32	21	11	4	6	1	Infliximab 2 Azathioprine 1	LMW heparin 6 Clopidogrel 6
KD with CAL z 2-2.4 N=4	4	0	0	1	0	0	0
KD with CAL z 2.5-5 N=14	11	3	2	3	0	Infliximab 1	0
KD with CAL z 5.1-10 N=8	2	6	2	1	0	0	LMW heparin 2 Clopidogrel 2
KD with CAL z > 10 N=6	3	3	0	2	0	Infliximab 1	LMW heparin 3 Clopidogrel 4

Table 3: Response to IVIg(alone without steroids) and factors predicting response to IVIg

	Response to IVIg alone	No response to IVIg alone	p value
No CAL at onset	32(97%)	1(3%)	*0.001*
CAL at onset	20(62.5%)	12(37.5%)	
Age at onset <1 year	8 (66.7%)	4 (33.3%)	0.237
>1 year	44 (83%)	9 (17%)	
Diagnosis<day 10 of fever	33 (82.5%)	7 (17.5%)	0.524
Diagnosis >day 10 of fever	19 (76%)	6 (24%)	
Z scores <2	32(97%)	1 (3%)	<0.005
2-2.4	4 (100%)	0	
2.5-5	11 (78.6%)	3 (21.4%)	
5-10	2 (25%)	6 (75%)	
>10	3 (50%)	3 (50%)	

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Abstract Number: 1744

Serum Sickness Following Rituximab Treatment of Childhood-Onset SLE: A Single Center Experience

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
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Background/Purpose: Childhood-onset SLE (cSLE) is an autoimmune disease characterized by multiorgan involvement often necessitating a variety of immunolytic and immunomodulatory therapies to achieve adequate disease control and remission. One of these agents, in which effectiveness and safety has been well defined, is Rituximab, a chimeric monoclonal antibody that binds to CD20 expressed on B lymphocytes initiating B cell lysis and subsequent depletion of antibody burden. An uncommon adverse reaction is serum sickness (SS), an immune complex-mediated ("type III") hypersensitivity characterized as a triad of rash, fever and polyarthritis/arthralgias. Though not commonly documented, rituximab-induced SS has been noted in patients with underlying autoimmune diseases, and reported disorders including Sjogren's syndrome, chronic ITP, and rheumatoid arthritis.

Methods: With a local IRB approval, a retrospective review of the electronic health records of patients with cSLE from July 2011 to May 2019 was performed. Patients who developed SS following Rituximab treatment were included. Descriptive analyses were done to ascertain similarities amongst the patients, possible risk factors for the development of SS, response to treatment and use of other anti-CD20 medication use.

Results: At the time of this study, there were 210 cSLE patients being actively followed, 20 patients had received Rituximab as part of treatment. 6 patients developed SS after Rituximab treatment, 1 was excluded due to incomplete record. Of the 5 patients, 4 were female. The mean age of patients was 16.6 years old. All 5 were Hispanic. Mean disease duration was 3.8 years (Range: 2 to 6 years). Mean SLEDAI score at time of Rituximab treatment was 6.6 (Range: 4 to 11); 2 patients had polyclonal hypergammaglobulinemia and cSLE treatment included steroids (4/5), MMF (2/5), hydroxychloroquine (5/5). 3 patients had history of prior rituximab treatment with a mean dose of 858 mg/dose (575mg/dose to 1000 mg/dose) and mean interval from previous to most recent dose of 17.3 months. Mean time for drug exposure to SS manifestation was 9.8 days (Range: 7-13 days). Manifestations of SS included fever (4/5), acute polyarthritis (4/5), and rash (5/5). Anti-rituximab antibody was not determined at time of SS diagnosis. All patients required increased dose of glucocorticoids. 2 required hospitalization. 2 patients received and tolerated alternative B-cell depletion (ofatumumab).

Conclusion: We described a small cohort of cSLE who developed SS following rituximab treatment. It is important to recognize this adverse reaction as SS manifestations mimic that of active SLE features.

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Abstract Number: 1745

Exercise Improves Arterial Inflammation in Childhood-onset Takayasu Arteritis: A Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

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Background/Purpose: Childhood-onset Takayasu Arteritis (c-TA) is a rare primary systemic vasculitis that affects aorta and its major branches. This condition is associated with reduced wall thickness, stenosis, hypertension and high cardiovascular risk. In addition, these patients may display exacerbated inflammation and poor physical fitness. Evidence-based treatment in c-TA is limited by the absence of randomized controlled trials. Exercise training is a non-pharmacological strategy able to counteract several adverse effects related to c-TA, such as increased inflammation. We investigated the effects of an exercise-training program on arterial inflammation and pro- and anti- inflammatory cytokines in patients with c-TA.

Methods: This was a 3-center, prospective, randomized controlled trial (clinical.trials.gov: NCT03494062). Patients diagnosed with c-TA Takayasu Arteritis were randomly assigned (2:1) into the exercise training group (ET) or the non-exercised control group (CTRL). ET underwent a 12-week, 3-times-a-week, home-based exercises for the major muscle groups (squats, push-ups, sit-ups, lunges and front planks), with the support of an illustrated booklet and

	CTRL	ET	*P* value
Demographics			
Age (years)	20.4 ± 3.2	17.3 ± 3.6	0.12
BMI (kg/m²)	20.5 ± 2.0	22.2 ± 3.4	0.30
Disease time (years)	12.6 ± 3.0	8.0 ± 3.7	0.02
Age onset (years)	7.8 ± 5.1	9.9 ± 4.3	0.39
Hypertension n (%)	3 (60)	11 (92)	0.19
Medication, n (%)			
Methotrexate	1 (20)	7 (63.6)	0.29
Infliximab	0 (0)	2 (18)	1.00
Leflunomide	2 (40)	1 (9.0)	0.19
Adalimumab	1 (20)	1 (9.0)	0.51
Tocilizumab	0 (0)	1 (9.0)	1.00
Propranolol	2 (40)	3 (27)	0.60
AAS	3 (60)	7 (63)	1.00
Prednisone	1 (20)	3 (27.2)	1.00
Enalapril	2 (40)	3 (27.2)	0.60
Amlodipine	1 (20)	2 (18)	1.00
MRI features			
Arterial Occlusion, n			
Subclavian artery	1	1	0.51
Axillary artery	1	2	1.00
Brachial artery	0	1	1.00
Brachiocephalic artery	0	1	1.00
Arterial Stenosis, n			
Infrarenal segment	0	1	1.00
Renal artery	1	2	1.00
Axillary artery	2	0	0.07
Abdominal aorta	0	2	1.00
Iliac artery	0	1	1.00
Brachial artery	0	0	1.00
Common carotid artery	1	0	0.29
Celiac trunk	0	1	1.00
Upper mesenteric artery	0	1	1.00

Data are expressed as mean (SD). BMI (body mass index), AAS (acetylsalicylic acid), MRI (magnetic resonance imaging).

Table 1. Patients' characteristics at baseline

video, whereas CTRL received standard of care. A member of the research team (C.A.) monitored the compliance and adequacy to the exercises every two weeks. The exercise protocol comprised 3-4 sets of 8-12 repetitions maximum (RM), with a 60 to 90-second rest interval between sets and exercises. Adherence, adverse events, or signs and symptoms were self-reported. Before (PRE) and after 12 weeks of intervention (POST), the arterial inflammation (standard uptake value [SUV_{max}], as assessed by [^{18}F] fluoro-deoxy-D-glucose positron emission tomography/magnetic resonance imaging [FDG-PET/MRI]), inflammatory cytokines (as assessed by CRP, ESR, IFN-γ, IL-10, IL-12p70, IL-1ra, IL-1β, IL-6 and TNF-α) and clinical scores were evaluated. A complete-case analysis was conducted using delta scores (POST - PRE) and between-group differences were tested using unpaired T-tests.

Results: Twelve patients were assigned into ET and 5 into CTRL. Three individuals from ET dropped out for personal reasons. Adherence to exercise training was 93 ± 0.06%. It was not reported any adverse events. Baseline characteristics were similar between groups ($p > 0.05$, table 1). Importantly, ET showed higher decreases in SUV_{max} values in the ascending aorta (-1.37 ± 0.38 *vs* -0.9 ± 0.42, $p = 0.08$), aortic arch (-1.13 ± 0.21 *vs* -0.63 ± 0.19, $p < 0.01$), ab-

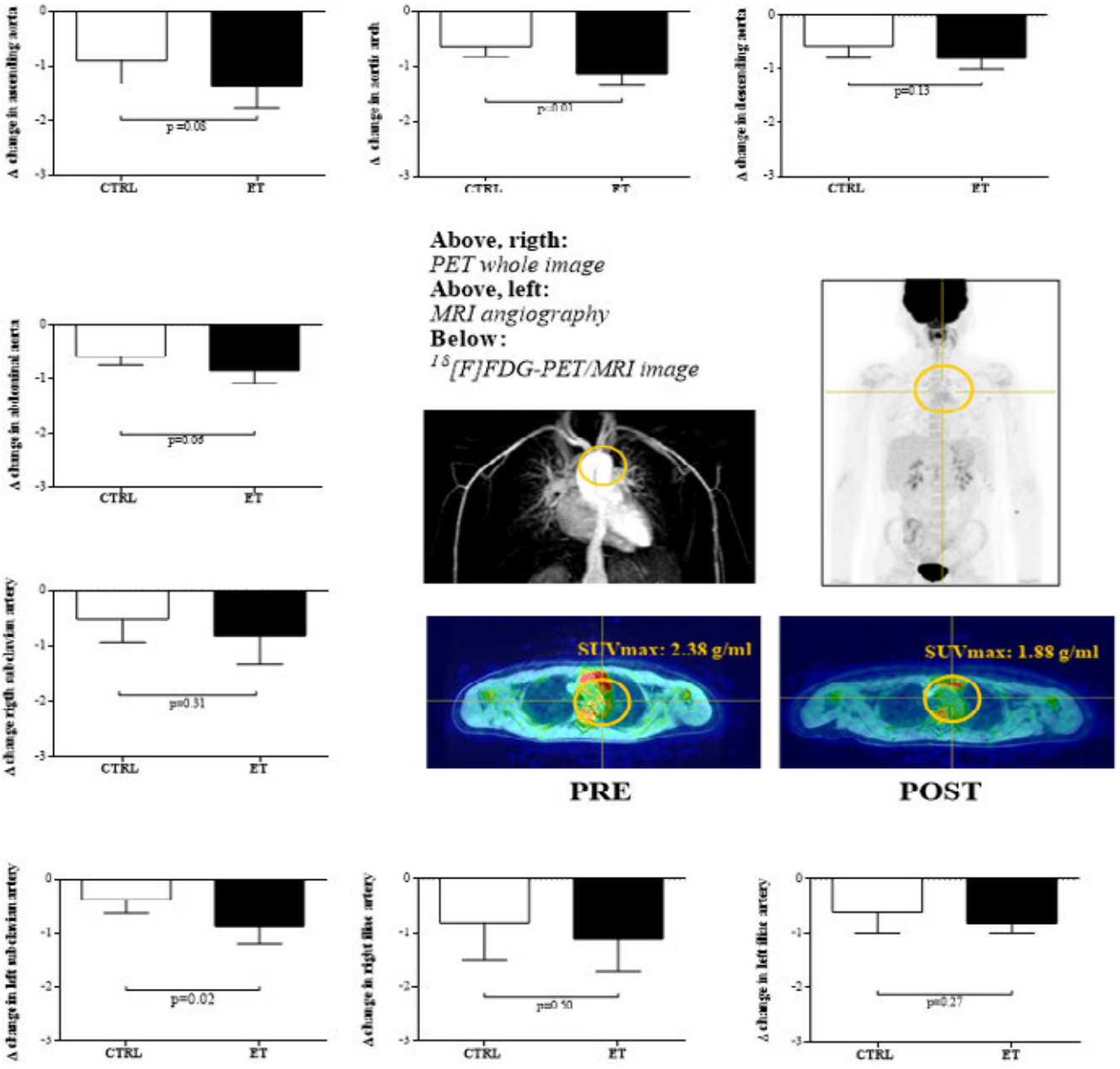

Figure 1. Changes in arterial inflammation (SUVmax), as assessed by [18F] fluoro-deoxy-D-glucose positron emission tomography/magnetic resonance imaging (FDG-PET/MRI), following 12 weeks of a home-based, exercise training program. A 12-year-old child SUVmax in the aortic arch pre (2.38 g/ml) and post exercise intervention (1.88 g/ml) (below).

dominal aorta (-0.85 ± 0.23 *vs* -0.59 ± 0.16, p = 0.06) and, left subclavian artery (-0.85 ± 0.33 *vs* -0.37 ± 0.24, p = 0.02) (Figure 1) *vs* CTRL. Inflammatory cytokines and clinical parameters did not change between groups (all p > 0.05).

Conclusion: In this first randomized controlled trial involving c-TA patients, a 12-week, home-based exercise training program was effective in reducing arterial inflammation in this disease. These findings provide evidence that exercise could be incorporated into the treatment routine of c-TA patients in order to mitigate their cardiovascular risk.

	CTRL		ET		Δ Difference (95% CI) after intervention	*P* value
	PRE	POST	PRE	POST		
Inflammatory markers						
CRP level, mg/liter	4.72 ± 7.61	4.40 ± 8.77	4.88 ± 6.53	3.52 ± 4.08	-0.52 (-4.25 to 3.20)	0.76
ESR, mm/hour	4.40 ± 2.07	3.40 ± 1.14	11.16 ± 10.3	7.37 ± 4.03	-2.33 (-11.91 to 7.24)	0.60
IFN-γ (pg/ml)	1.38 ± 1.01	2.20 ± 2.06	10.31 ± 14.98	5.34 ± 8.77	-7.72 (-24.90 to 9.45)	0.34
IL-10 (pg/ml)	16.18 ± 21.92	8.41 ± 4.51	14.34 ± 14.02	9.79 ± 9.12	3.55 (-17.87 to 24.98)	0.72
IL-12p70 (pg/ml)	2.75 ± 0.48	3.73 ± 1.57	6.58 ± 3.96	4.70 ± 3.09	-2.49 (-5.98 to 0.99)	0.14
IL-1ra (pg/ml)	110.7 ± 173.4	169.9 ± 294.7	128.9 ± 264.8	50.6 ± 36.7	-61.85 (-151.81 to 28.09)	0.15
IL1-β (pg/ml)	1.78 ± 0.56	2.70 ± 2.43	2.86 ± 1.33	2.50 ± 1.17	-1.76 (-3.57 to 0.03)	0.05
IL-6 (pg/ml)	12.96 ± 18.01	19.75 ± 34.03	25.4 ± 36.69	9.72 ± 12.27	8.31 (-51.39 to 68.02)	0.76
TNF-α (pg/ml)	15.78 ± 8.33	13.91 ± 2.93	14.75 ± 7.16	11.43 ± 3.44	1.77 (-8.79 to 12.34)	0.72
Disease scores						
ITAS score	0 (0-0)	0 (0-0.5)	0 (0-0)	0 (0-0)	-	0.15
PVAS score	0 (0-1)	0 (0-1)	0 (0-0)	0 (0-0)	-	1.00
VDI score	2 (1.5-2)	2 (1.5-2)	2 (1-2)	1 (1-2.5)	-	0.31

Data are expressed as mean (SD) or median (IQR), estimated a confidence interval for delta change for the difference between (post-pre) [95% confidence interval (95% CI)] and level of significance (p) between delta change c-TA *vs* c-TA+ET. * means $p < 0.05$, group difference. CRP (C-reactive protein), ESR (erythrocyte sedimentation rate), IFN (interferon), IL (interleukin), TNF (tumor necrosis factor), ITAS (Indian Takayasu's Arteritis Activity Score 2010), PVAS (Vascular Disease Assessment Score), VDI (Vasculitis Damage Index).

Table 2. Inflammatory markers and disease scores pre and 12-week post exercise training program in c-TA

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Abstract Number: 1746

Identifying Additional Risk Factors for Arterial and Venous Thrombosis Among Pediatric Antiphospholipid Antibodies Carriers

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SESSION INFORMATION

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Background/Purpose: Antiphospholipid antibodies (aPL) have been extensively reported in children; however, research on thrombotic risks associated with aPL among pediatric patients is scarce. Positive aPL are not uncommon in pediatric connective tissue diseases, but identification and management of these patients is challenging due to lack of validated criteria and a paucity of data. Misconceptions surrounding clinically significant aPL profiles may lead to missed diagnoses or incorrect diagnoses of APS, and many asymptomatic patients are managed with prophylactic ASA without a clear understanding of risk factors for thrombosis. Our aim is to identify additional risk factors for thrombosis in a unique cohort of pediatric aPL positive carriers.

Methods: Retrospective chart review was performed on 491 pediatric patients with connective tissue diseases seen in our institution from 2001 to 2019. Patients without persistently moderate to high titer aPL at least 12 weeks apart

Characteristics	aPL+ Patients with Thrombosis (n=14)	Percent	aPL+ Asymptomatic Patients (n=57)	Percent
Female	11	78.6%	51	89.5%
Ethnicity/Race				
Hispanic	9	64.3%	31	54.4%
African American	3	21.4%	17	29.8%
Caucasian	1	7.1%	6	10.5%
Asian	1	7.1%	2	3.5%
Native American	0	0%	1	1.8%
Age in years (mean ± SD)				
At diagnosis of CTD	12.7 ± 3.3		12.7 ± 2.5	
At first + aPL test	13.3 ± 2.6		13.3 ± 2.5	
At last follow-up visit	16.1 ± 2.5		17.2 ± 1.7	
Average duration of follow-up (years)	3.5 ± 2.2		4.5 ± 2.6	
Arterial Thrombosis	4	28.6%		
Venous Thrombosis	11	78.6%		
Recurrent Thrombosis	2	14.3%		
aCL IgG/IgM/IgA	8	57.1%	25	43.9%
aβ2GPI IgG/IgM/IgA	8	57.1%	41	71.9%
Lupus Anticoagulant	12	85.7%	35	61.4%
Triple positive	4	28.6%	14	24.6%

CTD: connective tissue diseases. aPL: antiphospholipid antibodies. aCL: Anti-cardiolipin. aβ2GPI: Anti-β2 Glycoprotein-I. Triple positive: positive aCL, aβ2GPI, and Lupus anticoagulant.

Table 1. Demographic summary of 71 aPL positive pediatric patients

were excluded. Univariate analysis was performed to evaluate the relationship between different risk factors and arterial/venous thrombosis.

Results: Seventy-one aPL positive children with underlying connective tissue diseases are included in this cohort (*Table 1*). The majority (87%) are female and of Hispanic ethnicity (56%). Mean age of the cohort at the diagnosis of connective tissue disease is 12.7 (SD 2.6) years, and mean age of first positive aPL is 13.3 (SD 2.5) years. Average length of follow-up is 4.3 (SD 2.5) years. Four (5.6%) patients had arterial thrombosis, and 11 (15.5%) had venous thrombosis. Fifty-seven (80.3%) patients did not have any thromboembolic events. Among traditional risk factors and signs of endothelial injury, only Raynaud's phenomena demonstrated significant association with arterial thrombosis (OR=8.4, 95%CI 1.13 – 111, P=0.039), and hypertension or antihypertensive use demonstrated significant association with venous thrombosis (OR=8.387, 95%CI 1.2 – 94, P=0.02) (*Figure 1*). Of the asymptomatic patients, forty-six (81%) were placed on long-term low dose ASA for primary thrombosis prophylaxis. Our investigation also identified several real-world clinical challenges, including variations in reference ranges for aPL studies over time and between reporting laboratories, inconsistencies in interpretation of aPL profiles by providers, over-identification of positive aPL, and subsequent over-utilization of prophylactic ASA without sufficient supporting evidence.

Conclusion: Data from our cohort suggests that Raynaud's phenomenon is a potential predictor of arterial thrombosis and the presence of hypertension or anti-hypertensive medication use is a potential predictor of venous thrombosis in aPL positive pediatric carriers. Due to lack of validated criteria and standardized clinical guidelines specifically for pediatric patients, identification and subsequent management of aPL positivity in this population remains problematic for clinicians. Further studies investigating pediatric aPL profiles and risk factors for development of thrombosis are needed to help guide clinicians in caring for these challenging patients.

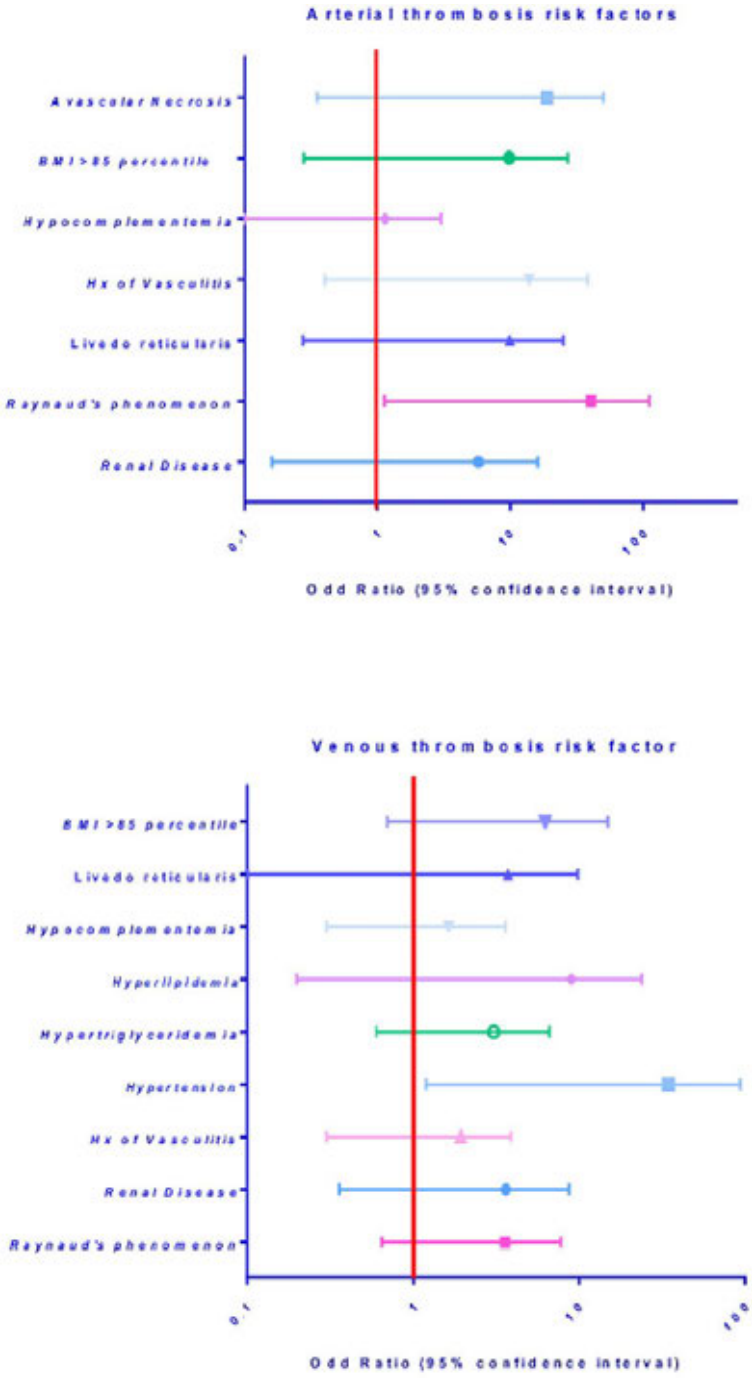

Figure 1. Logistic regression analyses for arterial thrombosis and venous thrombosis risk. Forest plots showing the results of univariate analysis for "second hit" arterial thrombosis risk (a) and venous thrombosis risk (b).

Disclosure: E. Sloan, None; **T. Wright**, None; **Y. Zuo**, None.

Abstract Number: 1747

Practice Variations in Treatment of Pediatric Anti-neutrophil Cytoplasmic Antibody (ANCA)-associated Vasculitis (AAV) with Renal Disease

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Renal disease is common in ANCA-associated vasculitis (AAV) and one of the goals of early treatment is to maximize renal function recovery. Corticosteroids are a cornerstone of induction treatment. However, the optimal dosing and weaning schedule is not known. The objectives of this study are to: 1) Describe practice variation in corticosteroid use in treatment of pediatric AAV with renal disease; 2) Assess for associations between baseline patient characteristics and corticosteroid dose at the time of diagnosis; and 3) Explore whether any variation in corticosteroid use at diagnosis is associated with outcomes at 12 months.

Methods: Patient data was obtained from an international pediatric vasculitis registry – PedVas. Patients followed for at least 12 months with AAV and biopsy confirmed pauci-immune glomerulonephritis were included. Patients' baseline characteristics such as dialysis requirement, glomerular filtration rate (GFR) and pediatric vasculitis activity score (PVAS) were examined for associations with the oral corticosteroid dose initiated at diagnosis. Outcomes ana-

Variables	Total	HiCS (>1.5mg/kg/day)	ModCS (0.5-1.5 mg/kg/day)	P-value
Diagnosis				0.855
- *GPA*	83 (78%)	31 (76%)	44 (77%)	
- *MPA*	23 (22%)	10 (24%)	13 (23%)	
Time to Diagnosis (median)	2 months (mos) (1,4 mos)	2 months (1,4 mos)	1 month (1,3 mos)	0.508
Country of Residence				0.160
- *Canada*	47 (44%)	13 (32%)	29 (51%)	
- *USA*	41 (39%)	20 (49%)	19 (33%)	
- *Other*	18 (17%)	8 (20%)	9 (16%)	
Year of Diagnosis (median)	2011 (2008, 2014)	2010 (2008, 2012)	2011 (2008, 2015)	0.246
Renal Disease				
GFR (ml/min/1.73m²)				0.064
- *≥60*	34 (37%)	16 (47%)	15 (31%)	
- *15-59*	36 (39%)	8 (24%)	24 (49%)	
- *<15*	22 (24%)	10 (29%)	10 (20%)	
Dialysis	26 (24%)	11 (27%)	15 (26%)	0.914
Disease Severity				
PVAS (median)	20 (18,24)	21 (18,24)	20 (18,24)	0.989
Plasmapheresis	36 (34%)	13 (32%)	23 (39%)	0.483
Treatment Choice				
Cumulative IV CS dose				0.221
- *>90mg/kg*	23 (25%)	10 (25%)	13 (25%)	
- *30-90mg/kg*	42 (46%)	19 (48%)	23 (45%)	
- *<30mg/kg*	27 (29%)	11 (27%)	15 (29%)	

Table 1 Baseline characteristics and association with corticosteroid dosing at diagnosis

Variables	HiCS (>1.5mg/kg/day)	ModCS (0.5-1.5 mg/kg/day)	P-value
GFR (12 months)			0.882
- *>60*	25 (66%)	37 (66%)	
- *15-59*	8 (21%)	10 (18%)	
- *<15*	5 (13%)	9 (16%)	
Oral corticosteroid dose at 12 months			0.435
- *< 0.2mg/kg/day*	28 (68%)	43 (75%)	

Table 2 12 month outcomes and association with corticosteroid dosing at diagnosis

lyzed for association with oral corticosteroid dose at diagnosis included GFR at 12 months, and the ability to wean to < 0.2mg/kg/day of oral corticosteroid. Statistical analysis was conducted using the Chi-squared test for proportions and the Mann-Whitney U Test.

Results: 106 patients were included in total. 83 (78%) patients were diagnosed with GPA, and 24 (21%) had MPA. 28 (26%) patients required dialysis at diagnosis, and 36 (34%) received plasmapheresis as part of induction treatment. 41 (38.7%) received >1.5mg/kg/day of oral corticosteroid (Hi-CS) and 57 (53.8%) received 0.5-1.5mg/kg/day of oral corticosteroid (Mod-CS) at diagnosis. No significant difference was found between oral CS dosing groups with regards to baseline patient characteristics (Table 1). Additionally, no associations were found between oral corticosteroid dose at diagnosis and 12 month outcomes such as renal function (Table 2).

Conclusion: Corticosteroid use in pediatric AAV with renal disease is highly variable, and with no associations between baseline patient characteristics and oral corticosteroid dose, it is unclear what guides physicians' use of corticosteroid at diagnosis. Furthermore, the results suggest that patient outcomes at 12 months were not improved for those treated with higher oral corticosteroid doses at diagnosis. This study highlights the need for prospective studies to further explore optimal corticosteroid dosing strategies in pediatric AAV.

Disclosure: A. Chen, None; **C. Mammen**, None; **J. Guzman**, None; **D. Cabral**, None; **K. Morishita**, None.

Abstract Number: 1748

Incidence of Retinopathy in Individuals Who Initiated Hydroxychloroquine Therapy During Childhood

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ), a medication used to treat Systemic Lupus Erythematosus (SLE), Discoid Lupus Erythematosus (DLE) and Sjogren's Syndrome (SS), reduces disease flare-ups, organ damage, and increases rates of remission[1,2]. While HCQ is relatively safe, recent research among adults has shown its long-term use to be associated with an increased risk of developing retinopathy[2]. The link between HCQ exposure during

childhood and the incidence of retinopathy has not been established. This study describes a contemporary cohort of pediatric patients who initiated treatment with HCQ for SLE, DLE or SS prior to their 18th birthday and assesses the incidence of retinopathy.

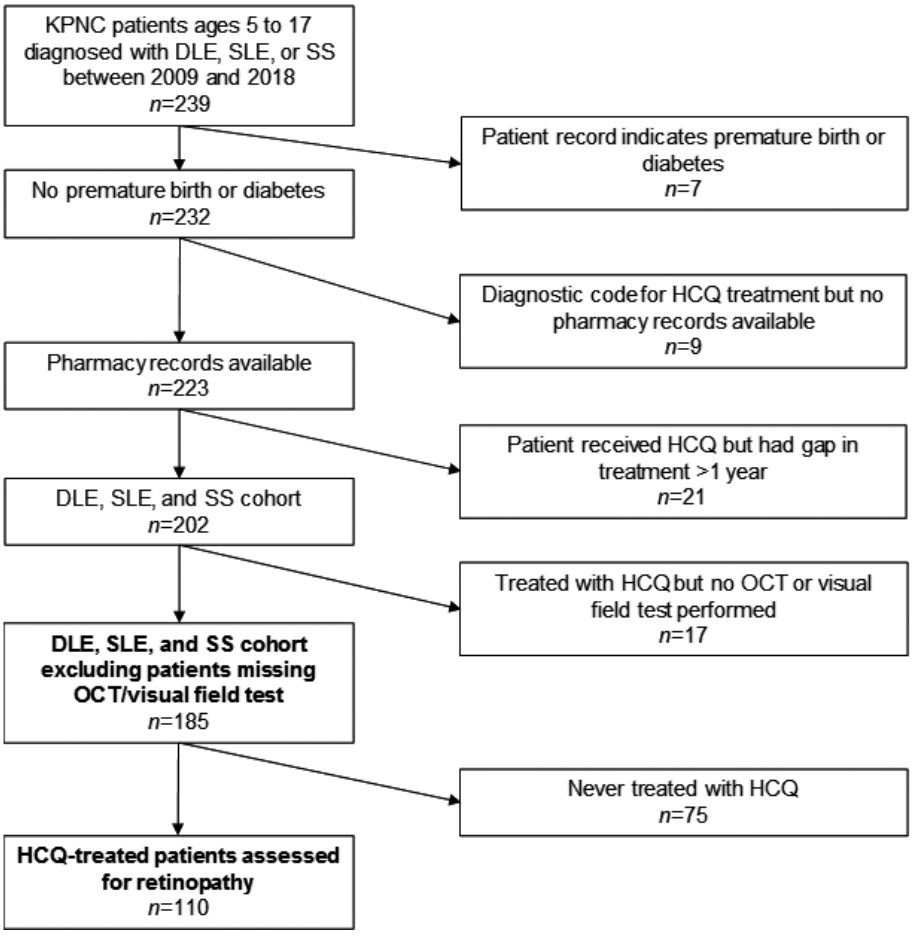

Figure 1 Flow chart of study identification, inclusion and exclusion criteria.

		HCQ treatment duration			
	Total sample (*n*=185)	Never treated (*n*=75)	<3 years (*n*=63)	≥3 years (*n*=47)	*p*-value*
Demographic characteristics					
Age at diagnosis, mean (s.d.)	13.80 (3.01)	13.87 (3.41)	13.62 (2.86)	13.91 (2.53)	0.853
Gender, *n* (%)					0.096
Female	148	55 (37%)	51 (34%)	42 (28%)	
Male	37	20 (54%)	12 (32%)	5 (14%)	
Race/ethnicity, *n* (%)					0.351
Non-Hispanic white	26	12 (46%)	6 (23%)	8 (31%)	
Black	35	13 (37%)	13 (37%)	9 (26%)	
Hispanic non-black	64	30 (47%)	18 (28%)	16 (25%)	
Asian/Pacific Islander	42	11 (26%)	21 (50%)	10 (24%)	
Other/Unknown	18	9 (50%)	5 (28%)	4 (22%)	
Clinical characteristics					
Retinopathy, *n* (%)†					—
No retinopathy	110	—	63 (100%)	47 (100%)	
Signs of retinopathy	0	—	0 (0%)	0 (0%)	

*F-test for continuous variables and chi-square test for categorical variables

†Retinopathy only assessed by OCT/VFT in patients who received HCQ treatment

Table 1 Demographic and clinical characteristics by HCQ treatment duration.

Methods: This is a retrospective descriptive analysis of patients receiving treatment within Kaiser Permanente Northern California (KPNC), who were diagnosed with SLE, DLE or SS between the ages of 5-17 years, and did not have evidence of premature birth or diabetes. Demographic information, as well as the age at diagnosis, were obtained from the electronic health record. The pharmacy database was queried for HCQ use. Chart review was performed to ensure patients met the American College of Rheumatology criteria for SLE and DLE, and the proposed criteria for juvenile SS. Further chart review was performed to determine evidence of retinopathy, defined by vision loss on the Humphrey Visual Field testing (HVF) and/or retinal thinning on the Spectral-domain optical coherence test (SD-OCT). Of the 232 patients who met the initial criteria, we further excluded those with no pharmacy record (n=9), those with treatment gaps greater than one year (n=21) and those with no evidence of a completed HVF or SD-OCT (n=17), resulting in a final study cohort of 185 patients and 110 patients with continuous HCQ exposure (Figure 1).

Results: The 185 individuals who met the initial study criteria had a mean age at diagnosis of 13.8 years (standard deviation: 3.01) and 80.0% were female. Of this cohort, 14.1% identified as non-Hispanic white, 18.9% black, 34.6% Hispanic non-black, 22.7% Asian/Pacific Islander and for 9.7%, the race/ethnicity was unknown. There were 75 patients who were never treated with HCQ, 63 who received less than three years of treatment, and 47 who were treated for three or more years (Table 1). HCQ treatment duration ranged from 0.1 to 9.6 years, with a median of 2.5 years and an interquartile range between 1.5 and 5.5 years. There were no demographic variations according to HCQ treatment duration. No patients developed retinopathy.

Conclusion: To the best of our knowledge, this is the first study to evaluate the incidence of retinopathy in a pediatric population exposed to HCQ for the treatment of SLE, DLE and SS. None of the patients developed retinopathy. Establishing a low risk of retinopathy for children taking HCQ is clinically relevant for treatment discussions in pediatric rheumatology, between providers, patients, and families. Further studies are needed to investigate risk in longer-term use.

References

1. Groot, N, de Graeff N, Avcin T, et al. Ann Rheum Dis 2017.; 76: 1788-1796.
2. Melles, R.B.,Marmor, M.F. The Risk of Toxic Retinopathy in Patients on Long-term Hydroxychloroquine Therapy. *JAMA Ophthalmology 2014; 132 (12): 1453-1460.*

Disclosure: S. Patrizi, None; **D. Stram**, None; **M. Weintraub**, None; **A. Aminoff**, None.

Abstract Number: 1749

Improving Eye Screening Among Pediatric Rheumatology Patients Receiving Hydroxychloroquine: Experience of a Quaternary Care Center

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is commonly used in the treatment of autoimmune diseases. However, its use is associated with progressive irreversible retinal damage and vision loss with an estimated overall prevalence of 7.5%. In 2016, the American Academy of Ophthalmology (AAO) published revised recommendations on eye screening for patients receiving HCQ. Only 65% of rheumatology patients receiving HCQ at Nationwide Children's Hospital (NCH) were screened in concordance with these recommendations. We developed a quality improve-

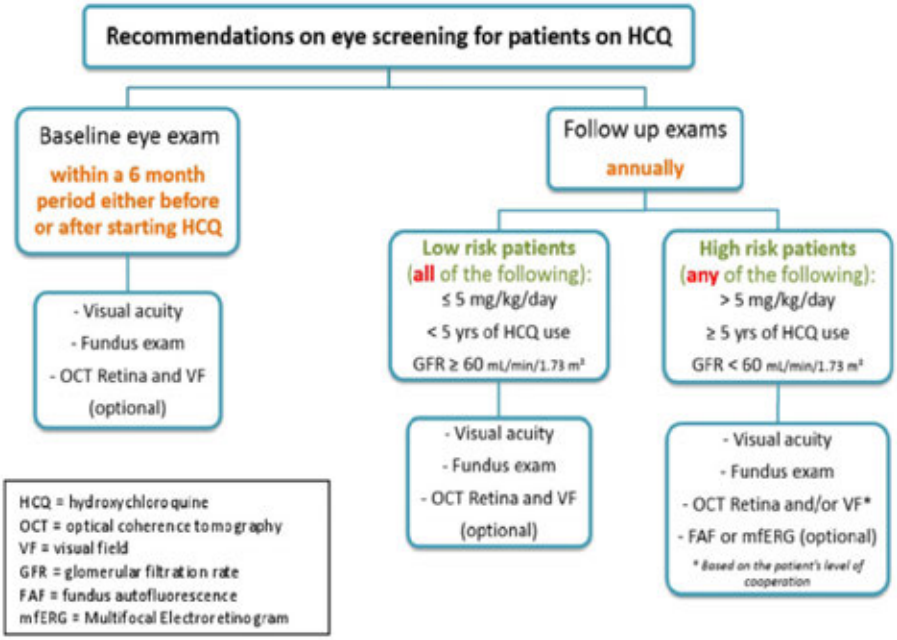

Figure 1 Consensus guidelines and risk-level-based algorithm based on the 2016 revision of the American Academy of Ophthalmology eye screening recommendations for patients receiving hydroxychloroquine

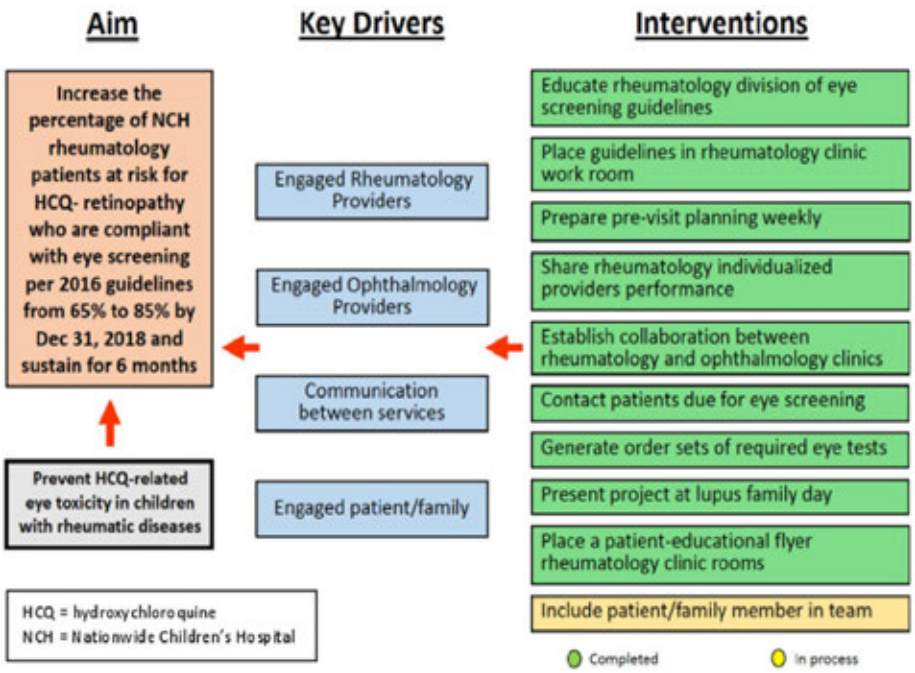

Figure 2 Key Driver Diagram showing the aim, key drivers and interventions to improve compliance with eye screening recommendations for rheumatology patients receiving hydroxychloroquine.

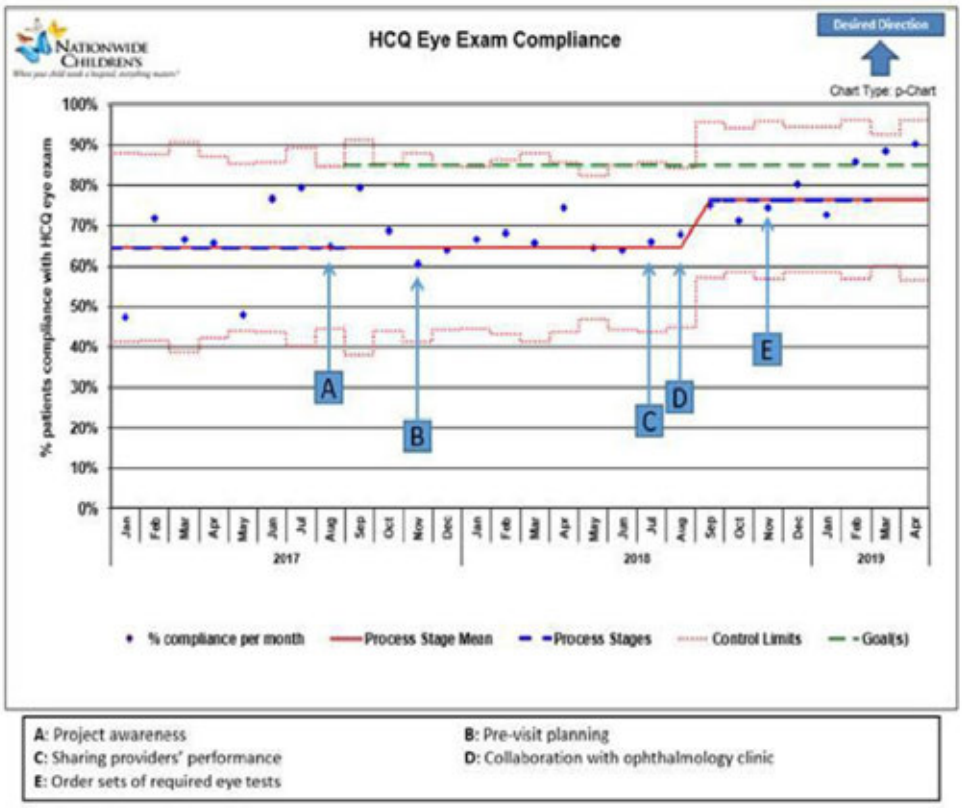

Figure 3 P-chart showing compliance with eye screening recommendations for rheumatology patients receiving hydroxychloroquine (HCQ) before and after the introduction of this quality improvement project.

ment (QI) initiative aiming to increase eye screening compliance in rheumatology clinic patients receiving HCQ from 65% to 85% by December 31, 2018 and to sustain the improvement for 6 months.

Methods: Our baseline analysis included patients receiving HCQ and were followed at NCH rheumatology clinic from 1/01/2017 to 8/31/2017. We formed a multidisciplinary team of rheumatologists, ophthalmologists, a clinical pharmacist, clinic nurses, a quality data technician and administrative staff. We developed consensus eye screening guidelines with risk-level stratification based on the AAO recommendations (Figure 1). A key driver diagram was utilized to identify barriers to compliance and determine possible interventions (Figure 2).

Results: Baseline performance data included 328 patients. Monthly performance assessment included an average of 41 patients on HCQ (range 30-51) (Figure 3). We reached our target of 85% compliance in February 2019 with a shift noticed in September 2018. We identified the following barriers to compliance: 1) Lack of knowledge among providers and patients, 2) Poor accuracy of data reports to reflect the population of interest, and 3) System barriers for interventions that involve another specialty with different locations and EHR systems. Major interventions included: 1) Educating providers and patients, 2) Preparing weekly pre-visit planning (PVP) to identify at-risk patients and provide screening recommendations, 3) Collaborating with ophthalmology clinic to facilitate same day eye screening, 4) Transparent sharing of provider-level data on a monthly basis showing individual performance, and 5) Implementing order-sets of specific eye tests in the EHR system.

Conclusion: This study is the first reported QI initiative to address the compliance with the 2016 eye screening recommendations for patients on HCQ. Our QI project highlights the following conclusions: 1) The usefulness of KDD in identifying root causes and planning interventions, 2) The importance of multidisciplinary team for large QI projects

that involve more than one department, 3) The role of PVP in QI projects in a busy clinic setting managing multisystem diseases, and 4) The advantage of implementing interventions such as order sets in the EHR system. Next steps will be directed at maintaining providers buy-in and recruit patient/family member in the QI team.

Disclosure: O. AlAhmed, None; **A. Way**, None; **S. akoghlanian**, None; **F. Barbar-Smiley**, None; **S. Lemle**, None; **D. MacDonald**, None; **K. Wise**, None; **S. Ardoin**, None; **V. Sivaraman**, None.

Abstract Number: 1750

Pediatric Sjögren Syndrome: A Single-Center Experience

Rachel Randell,[1] and Heather Van Mater[1], [1]Duke University, Durham, NC

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren syndrome (SS) is a chronic autoimmune disease of exocrine gland dysfunction that affects up to 4 million adults in the United States. Children are much less commonly affected, but have been reported to present with distinct, sometimes severe, manifestations. Little is known about clinical features, treatment and outcomes of SS in children.

Methods: An institutional web-based clinical research tool was used to identify patients with Sjögren or sicca syndrome diagnosis codes from year 2000-current in any child (< 18 years old at time of diagnosis). Query revealed 237 charts which were manually reviewed and narrowed to 25 cases of SS diagnosed by a pediatric rheumatologist, for whom in-depth chart review was performed.

Results: Of all 25 cases, 19 (76%) had primary SS and 6 (24%) had SS in the context of another autoimmune disease. Of those with primary SS, 10 (53%) had recurrent parotitis and 6 (32%) had sicca syndrome as predominant presenting symptom; 2 (10%) developed severe, persistent central nervous system symptoms. Of those with other autoimmune disease, 3 (50%) had a diagnosis of autoimmune disease prior to onset of SS, and 3 (50%) were initially diagnosed with SS and subsequently developed other autoimmune disease (undifferentiated connective tissue disease or systemic lupus erythematosus). Frequently reported symptoms included arthralgia, headache and fatigue. Nearly all (96%) had high ANA and SSA/Ro antibody titers. Shirmer test and salivary gland biopsy were less commonly used (44% and 36%, respectively). The most frequently prescribed systemic treatments were hydroxychloroquine, methotrexate, prednisone and methylprednisolone. Long-term outcome data were not available for the majority of cases, however there were no reports of malignancy or death, and only one case where the disease was not controllable with systemic medications.

Conclusion: In this single center study of 25 cases of SS in children, clinical presentation was variable and included recurrent parotitis, sicca syndrome and severe neurologic symptoms, both with and without other autoimmune disease. Although follow up data were not available for the majority of cases, it seemed that disease was controlled in nearly all cases using systemic therapies during treatment course. Long-term studies are needed to better understand the natural history and outcomes of SS in children.

Disclosure: R. Randell, None; **H. Van Mater**, None.

Abstract Number: 1751

A Systematic Literature Review of Efficacy and Safety of Biologic Agents for the Treatment of Juvenile Dermatomyositis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma

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Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile dermatomyositis (JDM) is a rare, chronic autoimmune illness characterized by symmetric, proximal muscle damages and involvement of the skin. While first line treatment is based on a combination of DMARDs (Methotrexate or cyclosporin) and glucocorticoids, there is limited evidence on treatment strategies for patients unresponsive to first-line treatment. We assessed the efficacy/effectiveness and safety of biologic agents in JDM.

Methods: A systematic literature review was conducted using Embase®, MEDLINE®, MEDLINE®-In Process and Cochrane library to identify studies on biologics agents in JDM published in English language as full-text articles (1975 to May 2019) or conference abstracts (2000 to May 2019).

Databases were searched with the key words "(juvenile dermatomyositis) crossed with "biologic agents OR tocilizumab OR rituximab OR adalimumab or INFLIXIMAB or anti TNF or baricitinib OR etanercept OR JAK inhibitors". Of note, we did not include children, age, or age limits in the search as medical subject headings terms because we may have been able to extract a sub cohort of children from studies including both children and adults

Results: Of the 1584 retrieved publications, 20 articles were identified for a total of 167 patients. 7 patients presented with a**nti**-signal recognition particle polymyositis. Only one RCT was identified for Rituximab; however, in the Rituximab in Myositis (RIM) trial no pediatric data could be extracted since they were reported as aggregate. In real-world studies, complete (CR) or partial response (PR) was often assessed, and their definitions and follow-ups (FUP) varied (table 1). JDM pts were most often treated with anti-TNF (90 pts); 11 pts received etanercept (ETA), 12 pts Infliximab (IFX), 1 pt adalimumab (ADA). Data regarding specific anti-TNFa agents were not available for the other 66 pts, as were not extractable. Rituxumab (RTX) was used in 76 pts. Single case reports reported the use of tocilizumab (TCZ), abatacept (ABA) e baricitinib (Table 1). Complete response was reported for 72% of pts treated with at least one anti-TNF and 64% for RTX, without statistical difference in head-to-head drug comparison. Anti-TNF were generally well-tolerated but 9 pts experience severe reactions (8 infusion-related adverse reaction; 1 infection). In the RTX group 6 patients experience severe events (3 infections; 1 infusion-related adverse reaction; 1 gastrointestinal perforation).

Table 1 . Main outcome measures and other data entered for each of the eligible studies.

References	Type of study	Number of patients	Biologics	dosage	Outcome	Clinical scales	Complete Response	Relapse	Follow-up lenght	Side effects
Case reports										
Luca et al.	case report	1 anti-SRP JPM (1F)	RITUXIMAB	500 mg/m2 x 2 doses	improved muscle strength, Muscle enzyme, MRI	MMT, CMAS	1	-	24 months	-
Vargas Lebrón et al.	case report	1 JDM (1F)	RITUXIMAB	375 mg/m2 weekly for 4 weeks	improvement in skin lesions, weakness, joint range of move	-	1	-	24 months	-
Tzaribachev et al.	case report	1 JDM (1F)	RITUXIMAB	375 mg/m2 weekly for 4 weeks (2 courses)	improvement in muscle lesions, CK, ALD	-	0	after 3 mo	24 months	-
Papadopoulou et al.	case report	1 JDM (1M)	BARICITINIB	6 mg twice a day	improvement in muscle and skin lesions, CK, decreased cor	CHAQ, MMT8, CN	1	after 12 mo	18 months	-
Arabshahi et al.	case report	1 JDM (1F)	ABATACEPT	10mg/kg at 0, 2, 4 weeks	improvement in muscle and skin lesions, LDH, decreased co	CHAQ, MMT8, CN	1	-	6 months	-
Chrong-Reen Wang et al.	case report	1 JDM (1M)	ADALIMUMAB	40 mg every 2 weeks for 88 weeks and 40mg	improvement in muscle lesions, CK, RM muscle edema, stat	MMT, CMAS	1	-	24 months	-
Cabrera et al.	case report	1 overlap syndrome (1F)	TOCILIZUMAB	8 mg/kg/4 weeks	joint manifestations	-	1	-		-
Case series										-
Dinh et al.	small series	1 JDM (1F)	RITUXIMAB	375 mg/m2 weekly for 4 weeks	improvement in skin lesions	-	1	-	20 months	transient flu sympotms
El-hallak et al.	moderate/large serie	1 JDM (1F)	RITUXIMAB	375 mg/m2 weekly for 4 weeks, repeated after	improved muscle strength, Muscle enzyme, fatigue	-	1	-	23 months	-
Holzer et al.	small series	2 JDM (2 F)	RITUXIMAB	375 mg/m2 weekly for 4 or 3 weeks	slight improvement / still active myositis	MMT, CMAS	0	-	32 and 49 months	-
Bader-Meunier et al.	open-label study	9 JDM (8 F, 1M)	RITUXIMAB		improvement in skin lesions, CK, aldolase	MMT	3	-	0.3-4 years	acute infusion-related event (1), GI perforation (1), bacterial infection (2) cmv pneumonia (1), bacterial infection (1).
Binns et al.	small series	3 anti-SRP JPM (3 F)	RITUXIMAB	750 mg/m2, repeated 2 weeks later	improved muscle strenght	MMT8, CMAS	3	-	4-12 months	-
Cooper et al.	moderate/large serie	4 JDM (3 F, 1M)	RITUXIMAB	375 mg/m2 weekly for 4 weeks	improvement in skin lesions, CK, aldolase	-	3	-	24 months	-
Rider et al.	moderate/large serie	5 JDM	RITUXIMAB	1 pt RTX at weeks 0 and 1 and placebo at week	improvement in muscle lesions, function measures, RM mus	MMT8, CMAS, DA	5	-	44 weeks	-
Riley et al.	moderate/large serie	5 JDM (3 F, 2 M)	INFLIXIMAB	3 mg/kg (weeks 0-2- 6 and every 8 weeks ther	improvement in skin lesions, weakness, joint range of move	CHAQ, CMAS, VA	3	1 pt	30 months	headaches (1)
Campanilho-Marques et al.	large series	66 JDM (41F, 25 M)	anti-TNFα		improvement in skin and muscle lesions, and global disease	MMT8, CMAS, DA	56	-	at least 3 months	reactions (7)
Rouster-Stevens et al.	moderate/large serie	9 JDM (7 F, 2 M)	ETANETCEPT	0.4mg/kg twice weekly		CMAS, DAS, Naill	3	-	after 24 weeks	
Rouster-Stevens et al.	small series	3 anti-SRP JPM (3 F)	INFLIXIMAB	3-3.5-4mg/kg	no clinical improvements	-	0	-		
De Oliveira et al.	moderate/large	4 JDM (3 F, 1M)	INFLIXIMAB /ETANERCE	IFX 4-6mg/kg (0-15-30-60 days); ETN 0.4-0.8	mg/kg 2 times weekly	-	1	-		Infusion-Related Adverse
Randomized controlled trial										
Oddis et al.	randomized, double	48 JDM	RITUXIMAB	-	≥ 20% improvement in 3 of any 6 CSM, with no more than	MMT8, CHAQ, ME	-	-		

Conclusion: Anti-TNF and RTX was efficacious in controlling disease in JDM in the studies assessed. However, response criteria and treatments were not directly comparable, thus more study are needed to determine the optimal treatment in the real-world setting

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Disclosure: e. marrani, None; **S. Abu Rumeileh**, None; **F. Tirelli**, None; **I. Maccora**, None; **G. Simonini**, None.

Abstract Number: 1752

Is Early Standardized Rituximab Therapy Sufficient for Toddlers with NMDAR Encephalitis?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-NMDAR encephalitis may be more prevalent than some forms of viral encephalitis in children. Pediatric rheumatologists are called upon to assist in the diagnosis and immuno-modulation of children with autoimmune encephalitides (AE). With prompt identification and early B cell depletion clinical outcomes may be robust in these disorders. Yet, children younger than 5 years of age with anti-NMDAR encephalitis may present differently than older patients and pose a diagnostic challenge. We present the presentation and outcomes of a cohort of young NMDAR encephalitis patients treated at a single center using a standardized step-up approach.

Methods:

- After obtaining approval from a local IRB we reviewed the charts of children diagnosed with Anti-NMDAR encephalitis between Jan 2012-April 2019 at a pediatric tertiary hospital. Diagnosis was based on clinical findings, and serum and CSF-Anti-NMDAR IgG antibodies. We reviewed all treatment modalities, adverse events of immunosuppression, and assessed disability at hospital discharge and last follow up using the Modified Rankin Scale (mRS) for children.

Results: Nine (20%) of children diagnosed with NMDAR encephalitis were ≤ 5 years of age at presentation (Median age 3 years, range 1.5-5 yr; 67% F). Presentations in younger children included gait disturbances, encephalopathy, reduction in speech, acute regression and severe movement disorders. Unlike older patients, seizures occurred in only one child. Median time to AE diagnosis was 5 days (range 4-99 days). Treatment followed a standardized institution protocol of: methylprednisolone, IVIG, and rituximab (2 doses at 500 mg/m2). Rituximab was administered 5-7 days after IVIG if a child did not show significant improvement. Children received rituximab at a median of 33 d, (range 16-128 d) from symptom onset. All children tolerated rituximab without infections or adverse events. All children with > 6 month follow-up re-populated their B cells, and none flared.

Prolonged hospitalizations were prevalent (median LOS 30 d, range 7-100 d) Five (55%) children required inpatient rehabilitation after initial hospital discharge. Modified Rankin Scale (mRS) scores improved from 4-5 (moderately severe-severe) at presentation to a mRS of 1 (mild symptoms) in one child (11%), a 2 (slight disability) in 5 children (56%), and a 3 in three children (33%) at their last visit (median f/u time 310 days, range 34-1219 d). Disability scores for younger children were higher than those of older patients (whose scores were predominantly 0-1). Deficits at time of last follow up related to language skills, and behavioral concerns.

Conclusion: Younger children with NMDAR encephalitis present differently than the "classic" phenotype of older children. Early B cell depletion practices were well tolerated in younger children. With rehabilitation, there were gradual and sustained gains in function in all children. It is unclear if greater disability of younger children was related to a shorter follow-up period or is a reflection of the vulnerability of toddlers to acquired CNS insults. There is a need for pediatric centers to share AE data so to answer questions regarding appropriate therapy and functional outcomes.

Disclosure: H. Amin, None; **M. Parnes**, None; **C. Niedzwecki**, None; **S. Risen**, None; **E. Muscal**, None.

Abstract Number: 1753

Are Patterns of Early Disease Severity Predictive of Grade 12 Academic Achievement in Patients with Childhood-onset Chronic Rheumatic Diseases?

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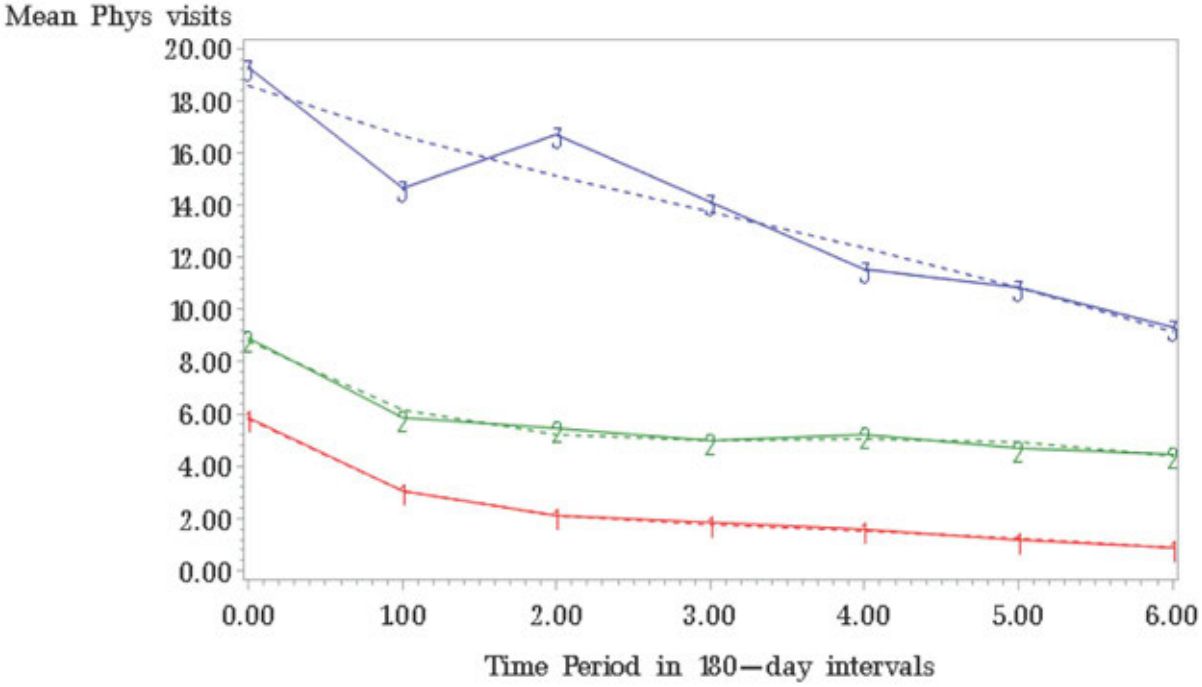
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Youths with childhood-onset chronic rheumatic diseases (ChildCRD), including juvenile arthritis (JA) and systemic autoimmune rheumatic diseases (SARD), have worse grade 12 standards tests results compared to their peers. SARD includes systemic lupus erythematous, dermatomyositis, Sjogren's syndrome and systemic sclerosis. We aimed to test if ChildCRD disease severity predicted the performance of ChildCRD patients on grade 12 standards tests.

Methods: Population-based longitudinal cohort study from one Canadian province. All ChildCRD patients had been captured in a registry since 1984. Data from ChildCRD patients born 1979-1998 (grade 12, 1996-2015) were linked to the administrative health (hospitalizations, physician billings, medications), education (grade 12 standards tests

Figure 1: Latent Trajectories of Physician Visits as an *Universal Disease Severity Indicator* in Childhood-onset Chronic Rheumatic Diseases



and enrollment) and social data (income assistance, child welfare involvement) housed in the provincial population data repository. *Outcomes:* Validated language and arts achievement index (LAI) and Maths achievement index (MAI) derived from grade 12 standards tests results and enrollment data. *Key predictor and covariates* : We constructed a universal disease severity indicator using latent class trajectory analysis (including disease groups: SARD, oligo- and non-oligoarticular JA, as membership covariate) of all physician visit within the first 3.5 years after diagnosis (early disease). Model covariates included an area-based socioeconomic factor index (SEFI2), maternal age at first child-birth, family ever on income assistance or involved with child welfare services, psychiatric morbidities pre-diagnosis and in the 12-months preceding tests. *Model***:** Effects of the severity indicator and covariates were tested in linear regressions for LAI and MAI; standardized coefficients (b) with standard errors (SE) and scaled deviance (DEV) were reported.

Results: 541 participants (474 JA, 44 SARD), of whom 70% were females were studied. The best fitting latent class model of disease severity, showed 3 latent trajectories: high (9%), moderate (54%) and low numbers of visit (37%) corresponding to severe, moderate and mild disease severities (Figure 1). The membership probabilities for the groups were 0.98 (severe), 0.97 (moderate) and 0.96 (mild). The severe group predicted LAI (b= –0.44, SE=0.17, p< 0.01) and MAI (b= –0.54, SE= 0.17, p< 0.01) in univariable models. After covariate adjustments, the severe disease group did not predict LAI, (b= –0.29, SE= 0.16, p=0.06, DEV=1.03) but predicted MAI (b= –0.41, SE=0.15, p< 0.01, DEV=1.03).

Conclusion: Longitudinal patterns of disease severity in early disease predicted grade 12 Maths standards tests results of ChildCRD patients, after covariate adjustment. Recognizing severe disease in early disease, in association

with sociodemographic and psychiatric histories can help identify ChildCRD patients who are at risk of reduced academic achievement and who may benefit from increased education support.

Disclosure: L. Lim, None; **O. Ekuma**, None; **R. Marrie**, None; **M. Brownell**, None; **C. Peschken**, None; **C. Hitchon**, Pfizer Canada, 2, UCB Canada, 2; **K. Gerhold**, None; **L. Lix**, None.

Abstract Number: 1754

Comorbidities and Treatments in United States Youth with Chronic Musculoskeletal Pain

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic musculoskeletal (MSK) pain has been associated with chronic illnesses, including mental disorders, and with high rates of pain medication use, often in referral centers, European populations, or studies focused on single drug classes. We aimed to characterize broad patterns of comorbidities and treatments associated with chronic MSK pain in a nationally representative sample of US youth.

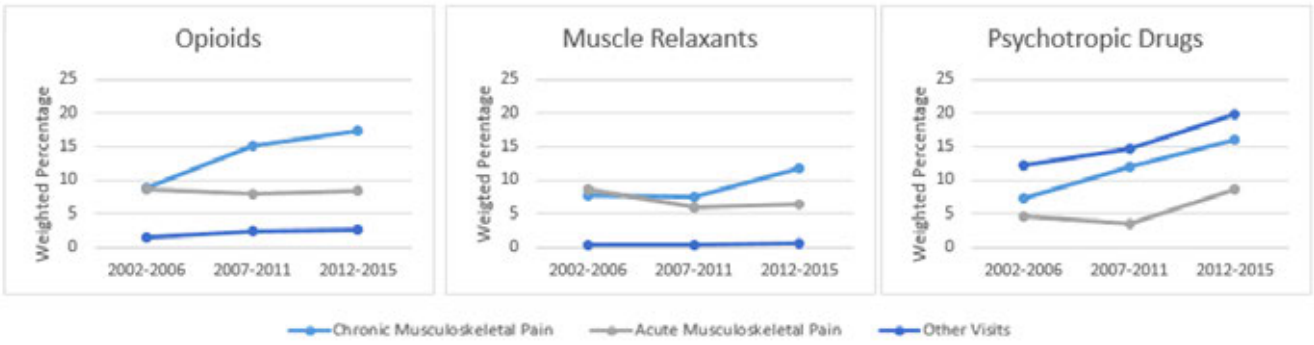
Methods: We used the National Ambulatory Medical Care Survey (2002-2015) and outpatient National Hospital Ambulatory Medical Care Survey (2002-2011), which contain national cross-sectional data on demographics, reasons for visit (RFV), diagnoses, and drugs ordered in visits to US office-based physicians. The study included all visits for youth age 8-24, excluding those for MSK pain of unknown duration or with diagnoses of malignancy or sickle cell disease. We identified visits for chronic (≥3mo) or acute (< 3mo) MSK pain based on the main RFV. We compared comorbidities and drugs ordered in visits for chronic MSK pain with (1) visits for any reason besides MSK pain (primary) and (2) visits for acute MSK pain (secondary), using chi-square tests and logistic regression, adjusting for age, sex, race, ethnicity, insurance, and setting of care.

Results: Chronic and acute MSK pain accounted for 1.3% and 4.1% of all visits, respectively. Chronic diseases besides mental disorders were more common among visits for chronic MSK pain (32.0%) in comparison to both visits for acute MSK pain (17.9%) and visits for other reasons (18.8%) (Table). Mental disorders and psychotropic drugs were more common in visits for chronic MSK pain than for acute MSK pain but not compared to visits for other reasons (Table). Nonsteroidal anti-inflammatories were more commonly ordered in visits for chronic MSK pain (23.9%) than in non-pain visits (4.7%) but not compared to acute MSK pain visits (31.3%) (Table). Opioids were also more common in visits for chronic MSK pain (13.5%) than non-pain visits (2.1%) and, to a lesser extent, acute MSK pain visits (8.4%) (Table). Orders for gabapentinoids and complementary and alternative medicine (CAM) were markedly higher in visits for chronic MSK pain (Table). Orders for opioids, muscle relaxants, and psychotropic drugs increased over time in visits for chronic MSK pain; similar trends were seen in other groups for psychotropic drugs but not pain medicines (Figure).

Table. Factors associated with chronic musculoskeletal (MSK) pain in multivariable models. 1 Odds ratios (ORs) from multivariable logistic regression models, adjusted for sex, race/ethnicity, year, region, insurance type, and survey setting (NAMCS vs. NHAMCS). 2 Non-steroidal anti-inflammatory agents. - denotes cell counts < 30, which may yield unreliable estimates. * P < 0.05; ** P <0.01; *** P < 0.001.

	Chronic MSK Pain vs. Other Visits [N = 116,913]		Chronic MSK Pain vs. Acute MSK Pain [N = 5,570]	
	OR[1]	95% CI	OR	95% CI
Comorbidities/Symptoms				
Any Mental Disorder	0.9	0.6-1.4	1.7*	1.03-2.8
Any Chronic Disease	2.5***	2.0-3.2	2.1***	1.6-2.7
Headache/Migraine	0.3***	0.2-0.5	0.7	0.4-1.5
Treatment				
NSAIDs[2]	6.9***	5.1-9.3	0.6***	0.5-0.8
Acetaminophen	0.3***	0.2-0.5	0.6	0.3-1.05
Opioids	4.2***	2.9-5.9	1.3	0.94-1.9
Acid-Blocking Agents	1.4	0.8-2.6	3.0**	1.3-6.7
Psychotropic Drugs	0.5**	0.4-0.8	1.4	0.9-2.3
Gabapentinoids	11.2***	5.6-22.4	-	-
Alternative Medicine	21.3***	9.5-48.1	-	-

Figure 1. Trends in opioid, muscle relaxant, and psychotropic drug orders in youth with and without chronic MSK pain (2002-2015)



Conclusion: Compared to youth without pain,youthwith chronicMSK weremore likely to have chronic non-psychiatric medical conditions but not mental disordersin a large ambulatory US population. Orders for gabapentanoids (unapproved for children with chronic MSK pain) and CAM were particularly common for those with chronic MSK pain, and orders for opioids and muscle relaxants rose over time in this group. Further research must clarify the effectiveness and safety of treatments commonly used to treat youth with chronic MSK pain.

Disclosure: M. Taylor, None; **S. Gmuca**, None; **L. Moorthy**, None; **A. Boneparth**, None; **D. Horton**, None.

Abstract Number: 1755

Improving Adolescent Health Care Transition: Piloting the Transition Readiness Assessment Questionnaire

Meghan Foster ,[1] Matthew Hollander,[2] Amanda Kennedy,[3] Laura Lewis,[4] Olivia Thompson,[3] Bradley Tompkins,[3] and Constance Van Eeghen[4], [1]UVMMC, Jericho, VT, [2]UVMMC, Burlington, VT, [3]UVMMC, Burlington, [4]UVM, Burlington

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Successful adolescent health care transition (HCT) is a vital process in providing developmentally appropriate care and minimizing negative outcomes, especially in adolescents with special health care needs. The purpose of this mixed-methods quality improvement project was to pilot the Transition Readiness Assessment Questionnaire (TRAQ) tool in a pediatric rheumatology clinic and assess its utility as a transition tool as well as to inquire about specific patient and family-based transition needs.

Methods: The TRAQ tool and follow-up survey were administered in dyads to all established pediatric rheumatology patients between the ages of 12-18, and one caregiver, who presented to the clinic during the two-month intervention period. A post-intervention interview with the treating team was also conducted to assess provider experience.

Results: 29/30 paired TRAQ and surveys returned with overall acceptance of the tool across adolescents, caregivers and providers. 84% of adolescents and 91.3% of caregivers agreed that they were seeking greater independence for themselves or their child and the skills listed on TRAQ would help them take care of themselves. Caregivers found the TRAQ easier to fill out, understand and more helpful as a transition tool than the adolescents. The treatment team reported the TRAQ was useful in starting a conversation about transition and highlighted the need for a structured transition process.

Conclusion: The TRAQ is an accepted and valuable HCT tool for adolescents, caregivers and providers. Future projects could be aimed at piloting the TRAQ or other readiness assessment tools in other sub-specialty clinics, building a transition framework to support utilization of transitional tools and addressing the transition themes identified by adolescents and their caregivers.

Disclosure: M. Foster, None; **M. Hollander**, None; **A. Kennedy**, None; **L. Lewis**, None; **O. Thompson**, None; **B. Tompkins**, None; **C. Van Eeghen**, None.

Abstract Number: 1756

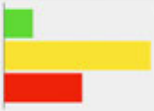
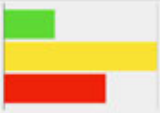
Health-related Social Media Use by Parents of Children with Rheumatic Diseases

Jonathan Hausmann ,[1] Vincent Del Gaizo,[2] Kara Magane,[3] Alexandra Marin,[4] Shannon Malloy,[5] Sanjay Mishra,[6] Tory Aquino,[7] Marc Natter,[8] Laura Schanberg,[9] and Elissa Weitzman[8], [1]Boston Children's Hospital / Beth Israel Deaconess Medical Center, Boston, MA, [2]Childhood Arthritis and Rheumatology Research Alliance, Whitehouse Station, NJ, [3]Boston Children's Hospital, Boston, MA, [4]Boston Children's Hospital, Boston, MA, [5]Cure JM Foundation, Seattle, WA, [6]Seattle Public Schools, Seattle, WA, [7]Hearing Life, Patterson Heights, PA, [8]Boston Children's Hospital / Harvard Medical School, Boston, MA, [9]Duke University Medical Center, Durham, NC

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Disease and treatment burdens are high for children living with rheumatic diseases. Pediatric patients and their families lack a mature evidence base to guide treatment decisions and often need greater levels of psychosocial support than may be available in traditional healthcare settings. In this context, engaging with others facing similar challenges and health problems via social media may be helpful and impactful for healthcare decision-making.

Table 1. Demographics of participants in the study. Disease activity is represented as the proportion of patients within each disease group in the following categories: remission (off medications) in green, stable (on medications) in yellow, and active disease (flare) in red.

Disease	N (%)	Age at diagnosis (SD)	Current age (SD)	Disease activity
Juvenile idiopathic arthritis	341 (32.5)	7.1 (4.2)	12.6 (5.4)	
Juvenile dermatomyositis	260 (24.8)	8.2 (4.2)	13.8 (6.3)	
Autoinflammatory disease	202 (19.2)	6.1 (4.2)	9.6 (5.1)	
Autoimmune encephalitis	79 (7.5)	10.2 (5.3)	14.1 (5.6)	
Systemic lupus erythematosus	71 (6.8)	14.5 (4.9)	18.5 (5.7)	
Vasculitis	26 (2.5)	14.9 (3.2)	19.0 (3.3)	
Scleroderma	25 (2.4)	9.8 (3.5)	12.0 (3.4)	
CRMO	20 (1.9)	9.4 (3.1)	12.1 (2.7)	
Sjogren's	14 (1.3)	11.5 (2.8)	14.4 (3.1)	
Other	12 (1.1)	9.2 (4.2)	12.7 (4.3)	
Total	1050 (100)	8.3 (4.9)	13 (5.9)	

In this study, we sought to understand attitudes, beliefs, and behaviors concerning social media use among parents of children with rheumatic diseases, and how such engagement might affect decision-making about their child's health care.

Methods: We worked with PARTNERS, a patient-powered research network, to disseminate an online survey through 9 different patient support organizations. The survey was distributed through email, website links, and on these groups' social media accounts.

Surveys were completed anonymously under implied consent. The survey was active between January 22 - April 2, 2019. The study was deemed exempt by the Boston Children's Hospital IRB.

Results: The survey was accessed 1,360 times and 1,050 surveys had non-missing data available for analysis. Participant characteristics are shown in Table 1. The mean age of children was 13; their mean age at diagnosis was 8.3 years. Only 11.1% of children were in remission and off medications, the rest had stable (44.5%) or active (44.3%) disease. Juvenile arthritis was the most common condition represented (32.5%).

Most parents (94.9%) used social media; of these, 97.8% had viewed content about other families with a child with a similar rheumatic condition on these platforms, and 92.9% had posted, shared, or commented on social media about their own child's rheumatic condition. Reading about other families was most helpful to learn how these families were living their lives in the setting of their child's disease. Other reasons for reading this content are shown in Figure 1. Social media use affected the child's medical care mainly by helping the parent manage their child's symptoms (67.7%) and medication side effects (64.3%). Other ways in which social media affected the child's medical care are shown in Figure 2.

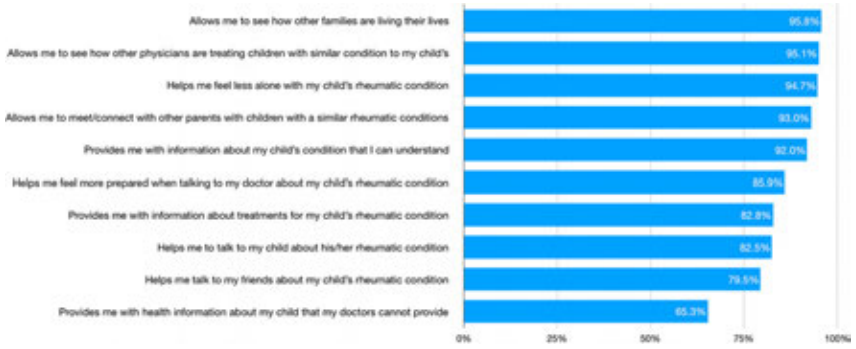


Figure 1. Proportion of parents who "agree" or "strongly agree" to the question: "Reading about other families who have a child with a rheumatic condition similar to your child's…" Denominators ranged from n=929 to n=933 across individual items.

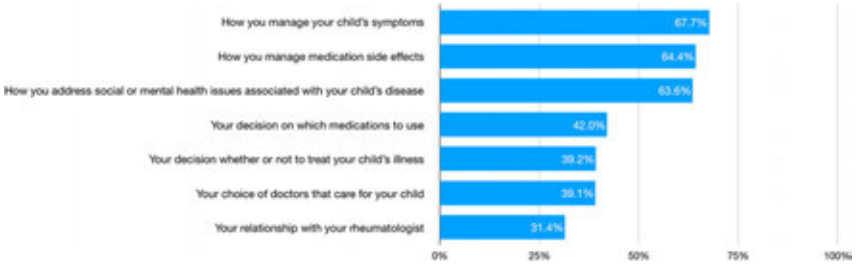


Figure 2. Proportion of parents who responded "somewhat" or "a great deal" to the question: "To what extent has what you learned about your child's rheumatic condition from social media affected…" Denominators ranged from n=862 to n=864 across individual items.

Conclusion: Health-related social media use by parents of children with rheumatic diseases was widespread in this large cohort of parents recruited online through patient support organizations. The greatest benefit from online interactions resulted from decreasing feelings of isolation of the parent and normalizing the diagnosis of a rheumatic illness in a child. While for most parents these online interactions did not have significant effects in the choices of medications used or the choice of doctors selected to treat their child's medical condition, they seemed to provide some utility in helping parents better manage their child's symptoms, medication side effects, and the mental and social challenges related to their diagnosis.

A better understanding of parental needs may allow us to create interventions that could help provide greater support for families and improve health outcomes for children with rheumatic diseases.

Disclosure: J. Hausmann, None; **V. Del Gaizo**, None; **K. Magane**, None; **A. Marin**, None; **S. Malloy**, None; **S. Mishra**, None; **T. Aquino**, None; **M. Natter**, None; **L. Schanberg**, CARRA, 9, Childhood Arthritis and Rheumatology Research Alliance, 2, Sanofi, 5, 9, SOBI, 5, UCB, 5; **E. Weitzman**, None.

Abstract Number: 1757

Review of Effectiveness of an Intensive Rehabilitation Programme in Managing Strength, Pain and Function in 123 Young People with Rheumatological Conditions

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – ePoster II: SLE, Juvenile Dermatomyositis, & Scleroderma – ARP
Session Type: Poster Session (Monday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Young people with Rheumatological conditions often experience ongoing pain, muscle weakness and reduced function despite modern medication. The unit at Great Ormond Street Hospital provides an intensive rehabilitation programme which focuses upon managing these symptoms. This review examines the immediate response and longer term follow up to the treatment.

Methods: A retrospective review of the notes was completed upon 123 children admitted for the intensive exercise therapy. Outcomes of specific muscle strength in the form of the Kendall scale grouped into the Manual Muscle Strength of 3 groups – gluteus maximus, gluteus medius and vastus medialis (MMT3) and the more extensive MMT8 are used, as well as a measure of pain and function (CHAQ). The outcomes were assessed at the admission and discharge of the rehabilitation programme and at the first follow up at 3 months.The treatment consists of focusing on a progressive resisted exercise programme completed 2x daily (2.5hrs per day) for 2 weeks (16 sessions in total) and primarily focuses upon correcting the biomechanics of the body as well as increasing aerobic fitness and education into managing pain and fatigue and learning to function despite pain. All the young people increased their exercises to 30 repetitions with the use of weights (max 3kg) focusing initially on specific muscle strengthening.

Results: The notes of 123 children were reviewed consecutively. 71/123 were female and the average age was 11.7 years (Range 4 – 17.5yrs). 44/123 had non-inflammatory pain, 10/123 has CRPS and the others had an inflammatory condition with 36/123 diagnosed with JIA. On admission the average pain score was 5.6/10 VAS and this reduced

Table 1. Muscle Strength Change Before and After Rehabilitation

	Initial assessment	D/C Assessment	Follow-up
Hip Abductor	6	9	9
Hip Extensor	6	9	8
Inner Range Quads	5	9	9
Plantar Flexors	1 rep	7 reps	6 reps
MMT 3	17/30	26/30	26/30
MMT 8	60/80	75/80	74/80

to 3.8/10 at follow up. The CHAQ reduced from 1.25/0.825. School attendance improved for most after the rehabilitation.

Conclusion: An intensive rehabilitation programme is effective in improving muscle strength and function as well as reducing pain and this is maintained for many months after discharge from the programme.

Disclosure: S. Maillard, None; **K. Noar**, None; **L. Stone**, None.

Abstract Number: 1758

Development of Ultrasound Detectable Arthritis Among ACPA Positive Subjects with Musculoskeletal Symptoms: The Risk RA Prospective Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Plenary II
Session Type: Plenary Session II
Session Time: 11:00AM–12:30PM

Background/Purpose: Studies have shown that anti-citrullinated protein antibodies (ACPA) are a risk factor for the development of arthritis. We aimed to nvestigate in a prospective setting whether ACPA and other biomarkers could predict the development of ultrasound detected arthritis

Methods: Subjects with positive ACPA-test referred from primary-care to the Rheumatology clinic, that lacked arthritis in the hands, feet and any other symptomatic joints by clinical and ultrasound examination (according to EULAR-OMERACT definition), were recruited into the Risk-RA research program during 2015-2016, and were followed-up to the end of January 2019. at inclusion, a detailed clinical examination was performed and blood samples were analyzed for 13 specific ACPA reactivities (using custom made peptide microarray) as well as 92 inflammation-associated protein biomarkers (using a multiplex immunoassay with Olink proximity extension technology). Presence of HLA-SE was analyzed using DR low-resolution kit. Univariate and multivariate analysis were used to investigate the association between clinical and laboratory parameters and development of ultrasound detected arthritis adjusting for the follow-up time.

Results: 46% (30 out of 65) of the Risk RA subjects developed ultrasound detectable arthritis during a median follow-up time of 11 months. The remaining 54% (35 out of 55) were followed for a median of 27 months (range 17-39) without any signs of ultrasound detectable arthritis. Those subjects that developed arthritis had a higher prevalence of HLA-SE (83% vs 55%) as well as an increased incidence of ultrasound detected tenosynovitis (40% vs 5%) as compared to those that did-not develop arthritis. ACPA reactivities to citrullinated vimentim peptides (cit vim 2-17: 20% vs 6%; and cit vim 60-75: 67% vs 44%) and citrullinated histone peptides (cit H4 31-50: 87% vs 47%; and cit H3 21-44: 47% vs 22%) were a more common occurrence in subjects developing ultrasound detectable arthritis.

Backward selection in Cox regression model showed that ultrasound detectable arthritis could be predicted in a model including HLA-SE, tenosynovitis and ACPA reactivity to cit H4 31-50. Hazard ratio (HR) for arthritis development were 2.2 (95% CI 0.8-6, p=0.13) for HLA-SE carriers and 2.9 (95% CI 1.3-6.5, p=0.01) for tenosynovitis, and 3.4 (95% CI 1.2-10, p=0.02) for Anti-citrullinated H4 31-50 positivity. Only modest differences were observed for few of the tested inflammatory markers in those developing as compared to those not developing ultrasound detectable arthritis: Interleukin- 6 (3.9 vs 3.3 AU/ML), Programmed death-ligand 1 (4.9 vs 5.2 AU/ML) and Chemokine (C-X-C motif) ligand 6 (9.2 vs 9.5 AU/ML).

Conclusion: Certain ACPA fine specificities, HLA-SE and tenosynovitis predicts the development of ultrasound detectable arthritis in seropositive individuals with musculoskeletal symptoms who are at risk for RA.

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Abstract Number: 1759

Methotrexate in Patients with Hand Erosive Osteoarthritis Refractory to Usual Treatments: A Randomized, Double-blind, Placebo-controlled Trial

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SESSION INFORMATION
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Background/Purpose: No studies have assessed the effect of methotrexate (MTX) in osteoarthritis of the hand (HOA). The purpose of our study was to examine the effect of MTX on pain and structural progression in symptomatic erosive HOA (EHOA).

Methods: This 1-year prospective, monocentric, randomized, double-blind, placebo-controlled study (NCT1968405) followed patients with symptomatic EHOA. Patients were randomized into two groups: 10 mg MTX per week or placebo. The primary endpoint was pain assessment at 3 months, and secondary endpoints were clinical features (pain

on visual analog scale (VAS)), radiographic features (Verbruggen anatomical radiographic score and Gent University Score System), and magnetic resonance imaging (MRI) at 12 months.

Results: Sixty-four EHOA patients were randomized to either the placebo or MTX group. At 3 months, there was no significant difference in the mean decrease in VAS pain score (mm) (MTX: 17.5 (28.4) vs placebo: 8.4 (25.2); p=0.2). Erosive joints progressed significantly more to a remodeling phase in the MTX group than in the placebo group (27% vs 15%) (p=0.03). Joints with joint space loss appeared to be less eroding in the MTX group than in the placebo group (8% vs 29%; p=0.2). Interleukin-6 level (p< 0.0001) and synovitis findings on MRI (p=0.02) at baseline were found to be predictive factors for erosive structural evolution of non-erosive joints.

Conclusion: Our study shows that MTX did not demonstrate superior efficacy over placebo on pain and function evolution at 3 and 12 months in subjects with EHOA.. However, MTX significantly reduced the progression of joint damage compared to placebo and seems to facilitate bone remodeling. The presence of systemic and local inflammations at baseline were predictors of erosive progression.

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Abstract Number: 1760

Six-week Treatment with Low-dose Prednisolone in Patients with Painful Hand Osteoarthritis (HOPE): Results from a Randomised Double-blind Placebo-controlled Trial

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Background/Purpose: Hand osteoarthritis (OA) is a prevalent joint disease with high disease-burden in need for effective therapeutic options. Studies have shown that synovial inflammation is often present in hand OA and a main determinant of pain and radiographic disease progression. Our aim was to investigate the efficacy and safety of short-term low-dose prednisolone in patients with painful hand OA.

Methods: This randomised, double-blind, placebo-controlled trial enrolled patients with painful hand OA, fulfilling American College of Rheumatology criteria, and signs of synovial inflammation. Patients with ≥4 interphalangeal joints (IPJ) with osteoarthritic nodes, ≥1 IPJ with soft swelling or erythema and ≥1 IPJ with positive power Doppler signal (PDS) or synovitis grade ≥2 on ultrasound, were eligible. Key exclusion criteria were chronic inflammatory rheumatic diseases, psoriasis, using immune modulating drugs within 90 days before baseline, and predominant thumb base pain. Eligible patients with visual analogue scale (VAS) finger pain ≥30 mm, flaring ≥20 mm upon non-steroidal

Table. Baseline characteristics and results of secondary endpoints at week 6 of HOPE study.

	Mean (SD) at baseline		Mean change (SD) from baseline to week 6		Adjusted mean between-group difference (95% CI)*	p-value
	Prednisolone	Placebo	Prednisolone	Placebo		
Pain						
AUSCAN pain, 0-20	11.3 (3.3)	10.2 (3.1)	–4.7 (3.5)	–1.1 (3.1)	–3.5 (–4.9 to –2.1)	<0.001
Function						
AUSCAN function, 0-36	18.6 (7.8)	19.0 (7.1)	–6.5 (7.4)	–2.7 (4.7)	–3.7 (–6.2 to –1.1)	0.01
FIHOA, 0-30	12.4 (5.4)	11.0 (4.7)	–2.6 (5.1)	–0.5 (4.0)	–2.1 (–4.0 to –0.2)	0.03
SF-36 physical component scale†	44.6 (7.9)	46.2 (6.8)	3.1 (6.7)	–0.3 (6.3)	3.5 (0.8 to 6.2)	0.01
VAS patient global assessment, 0-100	55.5 (21.7)	55.7 (22.0)	–23.6 (23.5)	–8.0 (25.3)	–15.4 (–25.6 to –5.2)	0.003
Grip strength, kg	20.4 (11.3)	20.4 (11.8)	3.5 (4.1)	2.2 (5.5)	1.2 (–0.8 to 3.2)	0.24
Ultrasound (sum scores)						
Synovitis, 0-90	16.4 (6.3)	17.8 (6.3)	–2.8 (4.7)	–0.3 (5.0)	–2.5 (–4.5 to –0.5)	0.02
Power Doppler Signal, 0-90	5.3 (4.1)	7.0 (4.3)	–1.7 (4.3)	–1.3 (4.2)	–0.4 (–2.2 to 1.4)	0.68

*Adjusted for baseline value and study center. †Norm-based scores with a standardized mean of 50 and SD of 10 using age- and sex-specific Dutch population-based norms. AUSCAN=Australian/Canadian Hand Osteoarthritis Index. FIHOA=Functional Index for Hand Osteoarthritis. SF-36=Short Form-36. VAS=visual analogue scale.

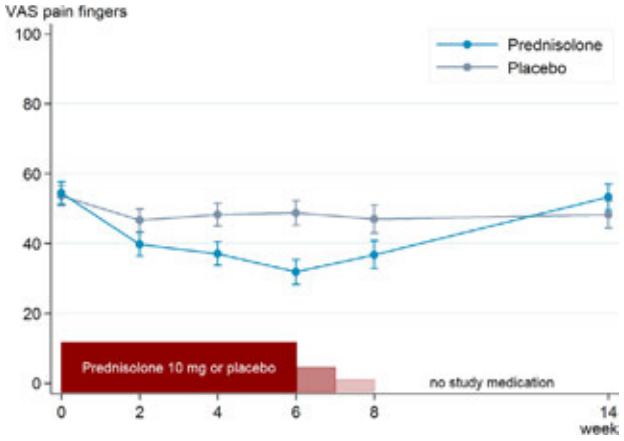

Figure. Results from primary endpoint (VAS pain) at week 6 of HOPE study.

anti-inflammatory drug washout, were randomised to receive prednisolone 10 mg daily for 6 weeks or placebo, followed by a two-week tapering scheme and 6 weeks without study medication. Outcomes were assessed at 2, 4, 6, 8 and 14 weeks. Primary endpoint was VAS finger pain at week 6 in intention-to-treat analysis. Secondary clinical endpoints included fulfilment of OMERACT-OARSI responder criteria, Australian/Canadian Hand OA Index (AUSCAN) pain/function, Functional Index for Hand OA (FIHOA), VAS patient global assessment, Short-Form 36 and grip strength. Imaging endpoints included ultrasound synovitis and PDS.

Results: Of 92 patients (mean (SD) age 63.9 (8.8), 79% women) randomised to prednisolone (n=46) or placebo (n=46), 42 patients in each group completed the study. Baseline characteristics were well-balanced between the groups. The mean (SD) change from baseline to week 6 in VAS finger pain was -21.5 (21.7) in the prednisolone and -5.2 (24.3) in the placebo group, with a mean between-group difference of -16.5 (95% confidence interval (CI) -26.1 to -6.9; figure). At week 6, 33 (72%) patients in the prednisolone versus 15 (33%) in the placebo group fulfilled OARSI responder criteria (odds ratio 5.3, 95% CI 2.0 to 13.6, p=0.001). In analogy with the primary endpoint, prednisolone was superior to placebo in most other secondary clinical endpoints (table). Ultrasound synovitis significantly improved at week 6 in the prednisolone compared to the placebo group, while no difference was observed in PDS (table). After tapering, between-group differences disappeared. Adverse events were mostly mild and comparable between groups.

Conclusion: Six-week treatment with low-dose oral prednisolone led to a substantial improvement of symptoms in patients with painful hand OA and signs of inflammation. This trial provides evidence that local inflammation is a suitable target for drug-treatment in hand OA.

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Abstract Number: 1761

The Prospective Open Label Preventive Approach to Congenital Heart Block with Hydroxychloroquine (PATCH) Study Demonstrates a Reduction in the Recurrence Rate of Advanced Block

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Background/Purpose: Based on encouraging bench to bedside results including experimental evidence supporting Toll-like receptor signaling in the pathogenesis of CHB, a case control study demonstrating CHB risk reduction in hydroxychoroquine (HCQ) exposed fetuses of anti-Ro positive SLE women, and a historical cohort study supporting a reduction in recurrence rate, an open label single arm Phase 2 clinical trial was initiated to evaluate whether HCQ reduces the CHB recurrence rate (π) below the historical recurrence rate of 18%.

Methods: A two-stage trial design (N=19 first stage; N=54 second stage) using Simon's optimal approach was employed to allow for early stopping due to absence of treatment efficacy. The null hypothesis, H_0:$\pi \geq 18\%$, would be rejected and HCQ considered efficacious at the end of the trial if ≤ 5 of 54 mothers with anti-Ro and a previous CHB child had a subsequent child with 2nd or 3rd degree block (primary outcome). The protocol required HCQ initiation or maintenance at 400mg by 10 wks gestation. Mothers underwent serial echocardiograms, with bloods drawn each trimester and delivery for cord blood to measure antibody and HCQ levels.

Results: Sixty five mothers (all with previous CHB child and anti-Ro52 or Ro60 > 1,000 EU; 47.9% with anti-La; 71.4% White; 47.6% SLE and/or SS; 42.9% started HCQ solely for CHB prevention; 41% prior CHB child died, 3.2% had > 1 CHB child) signed consent. Ten were considered screen failures (2 miscarriages < 12 wks, 7 wherein dating of conception placed HCQ initiation at > 10 wks, 1 given dexamethasone (dex) 1mg at 10 wks) and 1 was lost to follow up before delivery leaving 54 pregnancies evaluable with serial fetal echos and birth or one yr EKG or echo results known. In Stage I, 2/19 fetuses had CHB, and the study proceeded to Stage II. By intention to treat analysis, 4/54 pregnancies resulted in CHB (7.4%; p = 0.02 for H_0), all at 19-20 wks. Three presented with 2nd degree block, one reverted to NSR at birth following dex and two progressed to 3rd degree despite dex and IVIG (one electively terminated). One presenting with 1st degree was treated with dex prophylactically (eliminating this case from evaluating HCQ exposure alone), progressed to 2nd but reverted to NSR at birth. At 2 yrs, the 2 in NSR had intermittent 2nd degree on Holter monitor. In 8 mothers potentially confounding medications, IVIG and/or dex, were prescribed after enrollment for lupus flare, cardiac concerns apart from advanced block (APCs, echo brightness, 1st degree block), and/or phy-

sician decision to consider additional prophylaxis. To evaluate HCQ alone, 9 additional mothers were enrolled, one whose fetus developed 3rd degree block at 19 wks. Including only pregnancies exposed to HCQ alone prior to confirmed 2nd or 3rd degree block, 4/54 developed CHB (7.4%; p = 0.02). In total 5/63 pregnancies (7.9%) resulted in advanced block. HCQ levels in the second trimester confirmed a 98% adherence rate. Anti-Ro levels remained > 1,000 EU (considered vulnerable for CHB) throughout pregnancy. No CHB developed in any of the 7 mothers screened out because of low dose or delayed start of HCQ.

Conclusion: These prospective data from a single-arm clinical trial support that HCQ significantly reduces the recurrence of CHB below the historical rate.

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Abstract Number: 1762

UV Light Induces Acute Type I Interferon Production in the Skin and Blood Which Is cGAS Dependent

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SESSION INFORMATION
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Background/Purpose: Interferon response genes (ISG) are strongly expressed in the skin of many patients with systemic lupus erythematosus (SLE). Since plasmacytoid dendritic cells (pDC) are also found in the skin of SLE patients with rashes, it is assumed that type I Interferon (IFN-I) activation in the skin is caused by immune complex activation of pDC. We previously showed that UV responses were blunted in mice deficient in the DNA sensing adapter protein STING. Since cyclic cGAS acting upstream of STING is implicated in Aicardi Goutieres Syndrome patients with skin manifestations, and a proportion of SLE patients have elevated cGAMP in their blood, we examined the role of cGAS in UVB light mediated skin injury.

Methods: Mice (B6 female (f) and male (m), B6.*cGAS*-/- f, and B6.*Ifnar*-/- f, 3-4mo) were exposed to a single dose of UVBL (500mJ/cm2). Blood draws and skin biopsies were performed prior to and at different times after UVB light injury. For experiments looking at non-lesional ISG expression, mice were irradiated along one half of the back (UVB) while the other half was shielded from exposure (non-UVB). Biopsies in the non-UVB region were performed ~0.5 cm away from the UVB area. ISG (*Mx1, Isg15, Isg20, Ifit1, Ifit3, Irf7, Ifi44)* and inflammatory genes (*TNFα, Il6, Il1β)* transcripts were quantified by QPCR and normalized to 18s.

Results: A single high dose of UVB light triggered rapid (6hr) and sustained (48hr) cutaneous ISG expression in B6 mice (~10 fold increase), with significantly greater early ISG upregulation in female mice compared to their age-matched male counterparts. Local cutaneous IFN-I response was accompanied by early (6hr) increase in circulating IFNβ protein levels and upregulation in ISG expression in the peripheral blood cells. Female mice deficient in cGAS

showed no ISG expression in the skin 6hr after UVB light exposure, while ISG expression at 24hr, though present, was significantly lower than in the B6 controls (45.7% - 84.1% less). ISG expression in peripheral blood cells was also significantly reduced in the absence of cGAS. In contrast to ISG, rapid gene expression of inflammatory cytokines TNFα, IL6, and IL1β (6hr) in the skin following acute UVB light exposure was not impacted by the loss of cGAS. Of note, ISG expression in non-lesional skin covered during irradiation was detected at 6 and 24hr after injury. The ISG expression in non-lesional skin was cGAS-dependent at 6hr and partially at 24hr after UVB light injury.

Conclusion: Acute skin exposure to UVB light triggers rapid and sustained ISG expression in both skin and blood. The early cutaneous response is higher in the females and is cGAS dependent, while blood ISG expression is partially dependent on cGAS. The requirement for cGAS in UVB light-mediated IFN-I response in the skin is temporally regulated: i) cGAS is required for early (6hr after UV) ISG expression and ii) cGAS contributes to, but is not the sole player in late (24hr after UV) ISG induction. Presence of IFN-I signature in both the non-lesional skin as well as in peripheral blood cells, together with increased circulating IFNβ levels, provide a model by which skin exposure to UVB light drives systemic activation of the IFN-I response.

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Abstract Number: 1763

A Phase 3 Randomized Controlled Trial of Anifrolumab in Patients with Moderate to Severe Systemic Lupus Erythematosus

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Background/Purpose: In a phase 2 study in SLE patients (pts), substantial efficacy was observed with anifrolumab, a human monoclonal antibody that binds the type I IFN receptor subunit 1. TULIP-1, a phase 3 randomized, double-blind, placebo-controlled trial (NCT02446912), evaluated efficacy and safety of anifrolumab in pts with moderate to severe SLE.

Methods: SLE pts meeting ACR criteria with SLEDAI-2K ≥6 and BILAG ≥1 A or ≥2 B were randomized 2:1:2 to receive IV anifrolumab 300 or 150 mg or placebo (PBO) Q4W and background standard-of-care (SOC) therapy. Stable SOC was required throughout the study except for mandatory attempts at oral corticosteroid (OCS) tapering for pts receiving ≥10 mg/d prednisone or equivalent at entry. The primary endpoint was the difference between Week (W) 52 SRI(4) rates for anifrolumab 300 mg and PBO. Key secondary endpoints included OCS dosage reduction (baseline ≥10 mg/d to ≤7.5 mg/d), W12 CLASI response, and annualized flare rates. BICLA, joint counts, IFN gene signature

Table. Baseline Demographics and Disease Characteristics

Patient characteristic	Anifrolumab 300 mg (n=180)	Anifrolumab 150 mg (n=93)	PBO (n=184)
Age, years, mean (SD)	42.0 (11.99)	40.8 (12.05)	41.0 (12.30)
Female, n (%)	165 (91.7)	86 (92.5)	171 (92.9)
Time from SLE diagnosis to randomization, months, median (min, max)	88.0 (0, 450)	87.0 (6, 458)	79.5 (4, 503)
SLEDAI-2K global score, mean (SD)	11.3 (4.04)	11.0 (3.50)	11.5 (3.50)
BILAG-2004 ≥1 A, n (%)	93 (51.7)	40 (43.0)	84 (45.7)
BILAG-2004 no A and ≥2 B, n (%)	79 (43.9)	48 (51.6)	84 (45.7)
PGA score, mean (SD)	1.87 (0.399)	1.84 (0.446)	1.84 (0.383)
CLASI activity score, mean (SD)	8.5 (7.26)	7.7 (6.71)	8.1 (6.66)
SDI global score, mean (SD)	0.7 (1.16)	0.5 (0.96)	0.6 (0.98)
Swollen joint count, mean (SD)	7.4 (5.79)	7.4 (6.20)	7.0 (4.80)
Tender joint count, mean (SD)	11.7 (7.50)	11.3 (8.03)	10.6 (7.17)
High type I IFNGS, n (%)	148 (82.2)	76 (81.7)	151 (82.1)
Elevated anti-dsDNA antibodies, n (%)	81 (45.0)	44 (47.3)	82 (44.6)
Abnormal complement concentration, n (%)			
C3	58 (32.2)	34 (36.6)	65 (35.3)
C4	35 (19.4)	21 (22.6)	39 (21.2)
Key baseline SLE treatments			
OCS (prednisone or equivalent), n (%)	150 (83.3)	78 (83.9)	153 (83.2)
OCS dosage ≥10 mg/d, n (%)	103 (57.2)	48 (51.6)	102 (55.4)
Immunosuppressants, n (%)	85 (47.2)	38 (40.9)	91 (49.5)
Antimalarials, n (%)	124 (68.9)	76 (81.7)	134 (72.8)

Abbreviations: anti-dsDNA = anti–double-stranded DNA; BILAG = British Isles Lupus Assessment Group; CLASI = Cutaneous Lupus Erythematosus Disease Area and Severity; IFNGS = interferon gene signature; OCS = oral corticosteroid; PBO = placebo; PGA = Physician's Global Assessment; SD = standard deviation; SDI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SLE = systemic lupus erythematosus; SLEDAI = SLE Disease Activity Index.

(IFNGS), and safety were assessed. Post hoc analyses used modified restricted medication rules that were revised after unblinding to be more clinically appropriate.

Results: All 457 randomized pts received ≥1 dose of study drug and were included in the analyses (anifrolumab 300 mg, n=180; anifrolumab 150 mg, n=93; PBO, n=184). Baseline characteristics (**Table**) and treatment completion rates (~80%) were similar across groups. No difference in W52 SRI(4) response rates was observed for anifrolumab 300 mg (36.2% [65/180]) vs PBO (40.4% [74/184]); SRI(4) rates in the IFNGS test–high subgroup were 35.9% (53/148) and 39.3% (59/151), respectively. In prespecified analyses, any increase in NSAID dose or new NSAID use inadvertently resulted in nonresponse classification. Post hoc analyses, therefore, used modified restricted medication rules. In these post hoc analyses, W52 SRI(4) rates were 46.9% (84/180) for anifrolumab 300 mg vs 43.0% (79/184) for PBO; SRI(4) rates in the IFNGS test–high subgroup were 48.2% (71/148) vs 41.8% (63/151), respectively. Differences favored anifrolumab 300 mg over PBO for BICLA in all pts (46.1% [83/180] vs 29.6% [54 /184], diff: 16.4%; 95% CI: 6.7, 26.2) and in the IFNGS test–high subgroup (45.9% [68/148] vs 27.5% [41/151], diff: 18.4%; 7.7, 29.1). Differences favoring anifrolumab 300 mg vs PBO also occurred for OCS dosage reduction (48.8% [50/103] vs 32.1% [33/102], diff: 16.7%; 95% CI: 3.5, 29.8) and CLASI (43.6% [25/58] vs 24.9% [14/54], diff: 18.7%; 1.4, 36.0) as well as joint activity and flare reduction. IFNGS was suppressed with anifrolumab 300 mg but not PBO. Serologic changes showed trends toward normalization for anifrolumab 300 mg. Serious AEs occurred in 13.9% and 10.8% of pts with anifrolumab 300 and 150 mg vs 16.3% with PBO. Herpes zoster was more common in the anifrolumab groups vs PBO (5.6% and 5.4% vs 1.6%).

Conclusion: Although the primary endpoint, SRI(4), was not achieved in TULIP-1, numeric improvements achieving thresholds associated with clinical benefit were observed for BICLA, OCS, and other organ-specific endpoints. Anifrolumab 300 mg suppressed IFNGS and was generally well tolerated.

Writing assistance by Ellen Stoltzfus, PhD (Fishawack).

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Abstract Number: 1764

CCL25, a Novel Fibroblast and Macrophage Chemoattractant That Potentiates RA Bone Erosion

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Cytokines & Cell Trafficking
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: CCL25 and its receptor CCR9 have been detected in the inflamed joint; however their role is undefined in rheumatoid arthritis (RA). Hence studies were conducted to characterize the expression and functional significance of CCL25 and CCR9 in the inflammatory & erosive phases of RA.

Methods: For this purpose, expression pattern of CCR9 was determined in RA, osteoarthritis (OA) and normal (NL) synovial tissues (STs) as well as in RA ST fibroblasts (FLS) & *in vitro* differentiated macrophages (Mφ). Protein levels of CCL25 were quantified in synovial fluid (SF) and plasma from RA, OA and/or NL donors. Next role of CCL25 was evaluated in RA FLS and Mφ trafficking & inflammatory response in addition to identifying the signaling pathways linked to these functions. Last CCL25 potency was examined in the remodeling of RA naïve cells into mature osteoclasts.

Results: We show that CCR9 is highly expressed on RA ST lining, sublining and endothelial cells compared to OA and NL STs. While CCL25 expression is markedly elevated in RA & OA ST lining, sublining and endothelial cells relative to NL ST counterparts. Consistent with this notion, we found that CCR9 was expressed on unstimulated RA FLS (35%) and activation with IL-1β, TNF, IL-6 and RA SF can further accentuate its cell surface expression by 4-5 fold. In contrast, these inflammatory mediators did not impact CCR9 cell surface expression on RA Mφs. Nevertheless, we demonstrate that CCR9 cell surface expression is enhanced by 10 fold when RA monocytes (4%) are differentiated into Mφs (48%). Corroborating the histological findings, we reveal that CCL25 protein levels are comparable in RA and OA SF; which was significantly higher than those detected in RA and NL plasma. Interestingly, we showed that CCL25 present in RA SF can dose responsively attract RA FLS and monocytes into the joint and this process was suppressed by ERK and p38 inhibitors. On the contrary, stimulation with CCL25 did not instigate phagocytosis in fully differentiated RA Mφ. Next impact of CCL25 was examined on RA FLS and RA Mφ inflammatory response. We demonstrated that unlike RA FLS that were unaffected by CCL25 activation; stimulation of RA Mφ with CCL25

enhanced IL-8 production by 2 fold which was dependent on p38 and ERK signaling. However addition of RA FLS to RA Mφs in culture did not amplify CCL25's inflammatory response detected in myeloid cells. We also established that in later stages of disease, CCL25 was capable of remodeling RA myeloid progenitor cells into mature osteoclasts potentially by IL-8 induction.

Conclusion: We have uncovered that elevated levels of CCL25 in RA SF trigger infiltration of CCR9+ RA fibroblast and monocyte into the joint and accelerates transformation of myeloid cells into bone eroding osteoclasts. Our results suggest that CCL25 and CCR9 play an important role in the early and the later phases of RA pathology.

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Abstract Number: 1765

Interferon-gamma Supports Transcriptional Activity of BIRC5 in CD4+ T Cells in Established Rheumatoid Arthritis

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SESSION INFORMATION
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Session Title: Cytokines & Cell Trafficking
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Session Time: 2:30PM–4:00PM

Background/Purpose: It is known that rheumatoid arthritis (RA) should be treated early and a delay in treatment increases the rate of treatment non-response, joint damage, and disability. This is often explained by a diversity of molecular processes in the early and established phases of RA. The purpose of this study was to assess cytokine-dependent change in DNA methylation in CD4+ T cells of patients with early and established RA.

Methods: A cross-sectional RA cohort was analysed by comparing patients with the disease duration < 3y (mean 1.7y, n=23), 3-10y (mean 5.6y, n=94) and >10y (mean 19y, n=68). Serum levels of cytokines were measured by ELISA. Genome-wide DNA methylation was performed in sorted and activated CD4+ T cells of early (mean 1.3y, n=10) and established (mean 12.6y, n=14) RA patients using Infinium MethylationEPIC BeadChip (Illumina). Chromatin was immunoprecipitated with survivin (BIRC5) of CD4+T cells and coupled with high throughput sequencing (Hiseq2000, Illumina). False discovery rate was calculated using the Benjamini method.

Results: The groups differed with respect to the serum levels of IFNg, IL9, and IL6. The patients with RA< 3y had low cytokine levels and high serum survivin, while the patients with RA >10y had high IFN, IL9, and BIRC5 mRNA, suggesting IFNg and IL9 to be important for maintaining disease activity in patients with the established RA. The differential DNA methylation in CD4+ T cells of early and established RA (p< 10-5) identified IFNg- and IL9-dependent change in CpG rich areas. In dominating majority of CpG areas, an increase of cytokines was associated with a reduction of DNA methylation, which is known to precede the initiation of gene transcription. Since patients with established RA frequently combined high cytokines with high BIRC, we analyzed if this affects DNA methylation. Comparing CD4 with high and low BIRC5, we found that 85% of IFNg-dependent and 67% of IL9-dependent DNA

methylation changes occurred in presence of high BIRC5. To study if BIRC5 is found attached to chromatin, we performed chromatin immunoprecipitation in CD4+T cells. Analysis of the BIRC5-bound chromatin revealed enrichment for IRF-specific sequences where IRF1- and IRF8-binding sequences, but not IRF3 and IRF2 were predominantly found. We also found enrichment with complex sequences specific for binding bZIP-IRF (and not IRF-bZIP) and IRF-BATF sequences.

Conclusion: IFNg and IL9 are important for maintaining disease activity in patients with the established RA. In collaboration with intracellular survivin (BIRC5), these cytokines change the DNA methylation and gene transcription in CD4+ cells.

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Abstract Number: 1766

GM-CSF Is a Pro-Inflammatory Cytokine in Experimental Vasculitis of Medium and Large Arteries

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SESSION INFORMATION
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Session Title: Cytokines & Cell Trafficking
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Giant Cell Arteritis (GCA) is a granulomatous vasculitis with tissue tropism for medium and large arteries. Macrophages are a key cellular component of the granulomatous infiltrates and contribute to the disease process through the production of cytokines, growth factors and tissue-injurious proteases. Lesional macrophages can fuse to form the typical giant cells, the namesakes of the disease. To which extent the number of macrophages in the vasculitis lesions affects the intensity of inflammation is unknown. We have tested whether granulocyte-macrophage colony-stimulating factor (GM-CSF), a soluble cytokine involved in the generation the survival and the activation of macrophages has a role in exacerbating vascular inflammation. In a preclinical animal model of vasculitis, we have injected recombinant GM-CSF (rGM-CSF) or blocked GM-CSF activity by treating with Mavrilimumab (KPL-301), a monoclonal antibody, which inhibits the GM-CSF receptor-α.

Methods: Vasculitis was induced in human artery mouse chimeras by engrafting medium-sized human arteries and adoptively transferring peripheral blood mononuclear cells from patients with GCA. One group of mice received 50 ug of recombinant GM-CSF. Another group of mice was treated with control IgG or anti-GM-CSF. Another group of mice was treated with control IgG or anti-GM-CSFRα antibody intraperitoneally over one week. Arteries were harvested and examined by Hematoxylin and eosin staining and tissues transcripts.

Results: Compared to treatment controls, recombinant GM-CSF intensified and KPL-301 reduced tissue inflammation in the arteries. The numbers of tissue-residing T cells doubled after rGM-CSF injection and was reduced by about 50% after treating with the blocking antibody. Changes in the density of inflammatory cells were accompanied by parallel changes in he tissue gene expression of IL-1β, IL-6 and IFN-γ. the tissue expressions of IL-17 and TNF-α transcripts were unaffected by either intervention.

Conclusion: We conclude that GM-CSF has a role as an inflammatory cytokine in medium vessel vasculitis. The density of inflammatory cells in the lesions appears to be GM-CSF dependent. the effect of GM-CSF seems selective, with IL-17 and TNF-α being independent of GM-CSF signaling in this model.

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Abstract Number: 1767

Biomarker Profiling Reveals Novel Mechanistic Insights into Ustekinumab Therapeutic Responses in Systemic Lupus Erythematosus

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SESSION INFORMATION
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Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogenous autoimmune disease that causes progressive organ damage. The cytokines type I interferon (IFN-I), IL-12 and IL-23 have all been shown to contribute to SLE pathogenesis. We previously reported that treatment with ustekinumab (UST), an anti-IL-12/23 p40 neutralizing monoclonal antibody, improved global and organ-specific measures of disease activity in a randomized, placebo (PBO)-controlled study of patients with active SLE (NCT02349061)[1]. Here, we utilized biomarker data from this clinical study to elucidate the mechanism of action of UST in SLE.

We aimed to determine whether modulation of IL-12, IL-23, or both cytokines was associated with clinical efficacy, and to ascertain whether UST treatment could modulate IFN-I or improve disease activity in patients exhibiting an elevated IFN-I signature at baseline.

Methods: A Phase 2, placebo (PBO)-controlled study enrolled 102 patients with seropositive SLE and active disease despite standard-of-care therapy[1]. Patients were randomized 3:2 to receive UST IV ~6 mg/kg or PBO at week 0, then subcutaneous injections of 90mg UST q8w or PBO. Whole blood RNA from PAXgene tubes and serum were collected over 24 weeks. Age and sex-matched healthy controls were also studied. Serum IFN-g, and IL-17A, IL-17F and IL-22 levels were quantified by ELISA as indicative of the IL-12 and IL-23 pathways, respectively and an IFN-a ELISA was utilized to quantify the IFN-I pathway. Whole blood RNA was assessed for gene expression by microarray. Two Th17[2,3], an IFN-g[4] gene signature and 21-gene IFN-I signature (IGS)[5] were analyzed. SLE Responder Index (SRI)-4 at week 24 was used to define UST response (UST-R) and non-response (UST-NR).

Results: Serum IL-17A, IL-17F and IL-22 levels and Th17 gene signature levels in blood remained largely stable over the course of 24 weeks in all treatment groups. In contrast, UST-R was associated with a durable reduction in IFN-g protein and IFN-g gene signature levels relative to baseline, which was not observed in UST-NR or PBO patients. IGS levels were elevated in 67% of patients at baseline versus healthy controls. Serum IFN-a levels and IGS levels in blood were not modulated by UST treatment through week 24. Baseline IFN-I signature status did not associate

with response to UST, as the treatment effect size (UST vs PBO) was similar in IGS low (Δ=27%) and high (Δ=28%) patients.

Conclusion: Response to UST was associated with reductions in IFN-g levels, whereas IL-17A, IL-17F, IL-22 and IFN-I remained largely unchanged. While these findings require confirmation in an ongoing Phase 3 study, these data implicate the involvement of the IL-12 pathway and suggest a novel mechanism of action for UST-R in SLE.

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Abstract Number: 1768

A First-in-class Selective and Potent IRAK4 Degrader Demonstrates Robust *in Vitro* and *in Vivo* Inhibition of TLR/IL-1R Activation and Inflammation

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SESSION INFORMATION
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Background/Purpose: IL-1R/TLR activation plays a central role in the pathophysiology of multiple autoimmune and inflammatory diseases driven by the IL-1 family of cytokines and by TLR ligands. Full signaling from IL-1Rs and TLRs through the Myddosome is dependent on both the kinase and scaffolding functions of Interleukin-1 receptor associated kinase 4 (IRAK4) (De Nardo et al. JBC 2018, De et al. JBC 2018). Therefore, hetero-bifunctional molecules that selectively target IRAK4 for degradation and elimination by the ubiquitin proteasome pathway have greatest po-

tential to abrogate IL-1R/TLR signaling and shut down both the production of and response to TLR and IL-1 family cytokines.

Methods: Heterobifunctional degraders were designed to selectively target IRAK4 protein. Degradation selectivity was assessed in relevant human PBMC population by unbiased tandem mass tag proteomics. *In vitro,* PBMC flow cytometry and cytokine release assays were established to determine degradation potency (DC_{50}) and inhibition of R848, LPS and IL-1β induced pro-inflammatory cytokines. IRAK4 degrader was dosed orally in the mouse monosodium urate (MSU) air pouch model of gouty arthritis. *In vivo,* degradation was measured in mouse spleen tissues by targeted mass spectrometry.

Results: Unbiased proteomics with a depth >10,000 proteins showed exclusive degradation of IRAK4 in human PBMCs. *In vitro*, selective IRAK4 degraders led to potent and greater than 90% degradation in both lymphocytes (DC_{50}= 1.5nM) and monocytes (DC_{50}=0.4nM). Pre-treatment with IRAK4 degraders achieved potent single digit nanomolar inhibition of R848, LPS and IL-1β induced pro-inflammatory cytokines (TNF-α, IL-6) and chemokines (CCL3). Importantly, IRAK4 degradation led to more effective inhibition of cytokine and chemokine induction compared to a selective IRAK4 kinase inhibitor. Oral administration of an IRAK4 degrader in the mouse MSU air pouch model led to dose-dependent IRAK4 degradation in spleen tissue and a marked decrease in neutrophil infiltration (p=0.002 unpaired t test, two-tailed).

Conclusion: Selective and potent targeted IRAK4 degradation led to marked inhibition of both TLR- and IL-1R-mediated pro-inflammatory cytokine and chemokine production. By removal of both scaffolding and kinase functions, IRAK4 degradation demonstrated greater activity compared to kinase inhibition alone across multiple TLR/IL-1R stimuli. Promising *in vivo* mouse data showed that oral administration of an IRAK4 degrader can be achieved and have an effect on TLR/IL-1β-driven inflammation in a gouty arthritis model. Together, these data show the potential for IRAK4 degraders to treat TLR/IL-1R-driven inflammatory and autoimmune diseases.

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Abstract Number: 1769

Myosin Regulation of TNF Receptor 2 Signaling May Contribute to Anti-TNF Therapy Response

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SESSION INFORMATION
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Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Anti-TNF agents have revolutionized the clinical outcomes of patients with rheumatoid and psoriatic diseases. However, up to 40% of patients do not respond or partially respond, or lose efficacy of therapeutic response over time. There are no clinical tests available to predict responsiveness to anti-TNF therapy ahead of time. Small studies have supported that patients carrying TNFR2-M196R, (approx. 20% prevalence in general population) demonstrate a higher risk of being an inadequate responders to anti-TNF drugs, however, the underlying mechanisms are unclear. We have shown previously that non-muscle myosin (myosin) functions as a negative regulator of TNFR2 activation. Here, we test the hypothesis that a defect in myosin binding to TNFR2-M196R causes a TNF-independent proinflammatory activity and that leads to reduced responsiveness to anti-TNF agents.

Methods: We expressed equal levels of recombinant TNFR2-M196R or TNFR2 in primary endothelial cells and Jurkat T cells using lentiviral approach. To test whether myosin binds with TNFR2-M196R, we immunoprecipitated the recombinant TNFR2-M196R from the cells and probed for myosin by immunoblot. Proinflammatory gene induction in response to TNF in cells expressing TNFR2-M196R was measured at mRNA and Protein level by Q-PCR and ELISA, respectively. ROCK1 activity, which cause the release of myosin from TNFR2 were measured using Immunoprecipitated ROCK1 followed by MYPT1 phosphorylation.

Results: Our co-immunoprecipitation studies demonstrate that TNFR2-M196R variant does not bind to myosin as opposed to TNFR2. We also found TNFR2-M196R expressing cells show TNF-independent, ROCK1 activity and proinflammatory gene induction (e.g. ICAM1, CXCL10) in endothelial cells and Jurkat T- cells. Importantly, a TNF-neutralizing antibody failed to inhibit this constitutive gene induction in TNFR2-M196R expressing cells. ROCK1 inhibition blocks this TNF-independent activity. Furthermore, elevated proinflammatory gene induction upon TNF is sustained for longer time period in TNFR2-M196R expressing cells is (8 -10 hour) compared to TNFR2 expressing cells (4-6 hour). Mechanistically, TNFR2-M196R drives cells to a constitutive proinflammatory statepotentially due to a defect in myosin binding. Since this constitutive activity is TNF-independent, and given that ~20% of the general population carry TNFR2-M196R polymorphic variant, our findings may potentially explain in part, why a significant percentage of patients do not adequately respond to anti-TNF therapy.

Conclusions: Our mechanism-based approach implicating TNFR2-M196R could be tested in patients that are candidates for anti TNF therapy. Our approach not only may help to predict anti-TNF responsiveness but may also reveal novel pathways that can be targeted to treat inadequate responders of anti-TNF therapy in a subset of patients with rheumatoid and psoriatic diseases.

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Abstract Number: 1770

Experimental Rheumatoid Joint Ameliorated by CRISPR Interference Targeting Long Non-coding RNA H19 Through Wnt Signaling Inactivation

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SESSION INFORMATION
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Background/Purpose: Long non-coding RNAs (lncRNAs) participate in the rheumatoid arthritis (RA) pathogenesis. The aim of this study was to examine the lncRNA H19 and HOTAIR expression in RA patients, and whether delivery of CRISPR interference (CRISPRi) with catalytically dead Cas9 (dCas9) targeting H19 can ameliorate the experimental rheumatoid joint.

Methods: Synovial tissue (ST) and venous blood samples were obtained from RA and osteoarthritis (OA) patients. Synovial fibroblasts (SFs) were purified from ST, and normal SFs were acquired commercially. To generate CRISPRi-H19 and CRISPRi-HOTAIR, guide RNA spacer sequences targeting H19 or HOTAIR were cloned into the CRISPRi vector containing the dCas9/Krüppel-associated box repressor domain with an efficient transcription repression ability. SFs and 293T cells were transduced with CRISPRi-H19 and CRISPRi-HOTAIR, respectively, to create stable transfectants. Therapeutic effects of intra-articular CRISPRi-H19 injection were assessed in a rat model of collagen-induced arthritis. LncRNAs expression were examined by quantitative real-time PCR. Cell invasion was assayed by Transwells with membrane coated with Matrigel.

Results: Increased synovial and peripheral H19 levels were found in RA patients with decreased H19 expression in venous mononuclear cells (MNCs) after a TNF blockade (adalimumab) therapy as compared with OA counterparts. There were higher HOTAIR levels in MNCs from RA patients, but no differences after the anti-TNF therapy. H19 levels in SFs were enhanced by the TNF stimulation. Reduced H19, pGSK-3β (Wnt signaling), EZH2 and Snail expression, cell invasion and IL-6 production with increased Nkd1 (Wnt inhibitor) expression were identified in H19-silenced SF transfectants. Decreased Tri-Methyl-H_3K_{27} expression were found in HOTAIR-silenced 293T transfectants. Lower arthritis indexes and histological scores with less erosion on cartilage/bone were demonstrated in the CRISPRi-H19-injected joints with enhanced NKd1 and decreased H19, pGSK-3β, EZH2, Snail and IL-6 expression, suggesting silencing H19 to ameliorate experimental rheumatoid joint through inactivating the Wnt signaling.

Conclusion: Our results demonstrate that intra-articular delivery of CRISPRi targeting lncRNA can alleviate the experimental rheumatoid joint. Such findings might contribute to the development of lncRNAs-related therapeutics in RA patients.

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Abstract Number: 1771

MyD88 S209R Enhances Inflammation in Mouse Models of Arthritis

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Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: MyD88 is a critical adaptor protein that connects Toll-like and IL-1 receptor signaling to activation of NF-kB. We previously reported a heterozygous *de novo* gain-of-function mutation in *MYD88* (S222R) in a patient with a progressively deforming arthritis characterized by marked bony overgrowth in arthritic lesions. To further investigate the contribution of MyD88 to arthritis pathogenesis, we created a novel *Myd88* gene-edited (S209R) mouse using CRISPR/Cas.

Methods: We induced arthritis with collagen (CIA) in wild-type (WT), *Myd88*$^{S209R/WT}$, and *Myd88*$^{S209R/S209R}$ C57BL/6 mice to assess differences in incidence, duration, and severity of arthritic phenotype. Arthritis was assessed via clinical scoring, caliper measurements of limb swelling, and H&E and safranin-O staining of limb sections. Since CIA elicits a directly-pathogenic adaptive immune response, anti-collagen antibodies were quantified from serum samples. To bypass the role of MyD88 in collagen-antibody production, we induced arthritis with anti-collagen antibodies (CAIA) in WT, *Myd88*$^{S209R/WT}$, and *Myd88*$^{S209R/S209R}$ mice and assessed arthritis severity as above. *In vitro* assays were conducted to determine the effect of the mutation on T cells, including supernatant cytokine quantification, and measurement of proliferation rates by dye dilution.

Results: Mice harboring the *Myd88*-S209R mutation did not develop a spontaneous arthritic phenotype. CIA was achievable in 75% of *Myd88*$^{S209R/S209R}$ mice, 56% of *Myd88*$^{S209R/WT}$, and 38% of WT mice. *Myd88*$^{S209R/S209R}$ mice produced significantly higher amounts of anti-collagen antibodies than WT mice. Histological scoring revealed significantly more bone overgrowth in *Myd88*$^{S209R/S209R}$ and *Myd88*$^{S209R/WT}$ mice compared to WT. All mice that received exogenous anti-collagen antibodies developed arthritis, however arthritis in *Myd88*$^{S209R/S209R}$ and *Myd88*$^{S209R/WT}$ persisted longer than WT mice. Data from these experiments indicate enhancement of both the lymphocyte-dependent production of antibodies and their downstream pathogenic effects. *In vitro* analysis showed that *Myd88*$^{S209R/WT}$ T cells secreted more GM-CSF, IL-1b and CCL4 in response to stimulation. Additionally, naive T cells from *Myd88*$^{S209R/S209R}$ and *Myd88*$^{S209R/WT}$ mice showed increased rates of proliferation.

Conclusion: The *Myd88*-S209R mutation impacts CIA and CAIA models by increasing the incidence and duration of the arthritic phenotype, as well as changes suggestive of new bone formation. This is the first description of a mouse model harboring the *Myd88*-S209R mutation, which will allow for further investigation of the mechanism(s) by which innate and adaptive immune activation through MyD88 contributes to the complex phenotype of arthritis.

Disclosure: S. Bakshi, None; **A. Lindstedt**, None; **M. Waschmann**, None; **W. Tsai**, None; **R. Colbert**, Eli Lilly and Company, 2, 9; **K. Sikora**, None.

Abstract Number: 1772

Chronotherapy Using Baricitinib Attenuates Collagen-induced Arthritis in Mice

Arisa Yaekura ,[1] Kanta Morii,[2] Yuto Oketani,[3] Ikumi Okumura,[2] Kenta Kaneshiro,[4] Kohsuke Yoshida,[2] Yoshiko Kawasaki,[5] Nao Shibanuma,[5] Yoshitada Sakai,[6] and Akira Hashiramoto[2], [1]Kobe University Graduate School of Health Sciences, Kawanishi, Hyogo, Japan, [2]Kobe University Graduate School of Health Sciences, Kobe, Hyogo, Japan, [3]Kobe University Graduate School of Health Sciences, Himeji, Hyogo, Japan, [4]Kobe University Graduate School of Health Sciences, Osaka, Osaka, Japan, [5]Kobe Kaisei Hospital, Kobe, Hyogo, Japan, [6]Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Animal Models

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

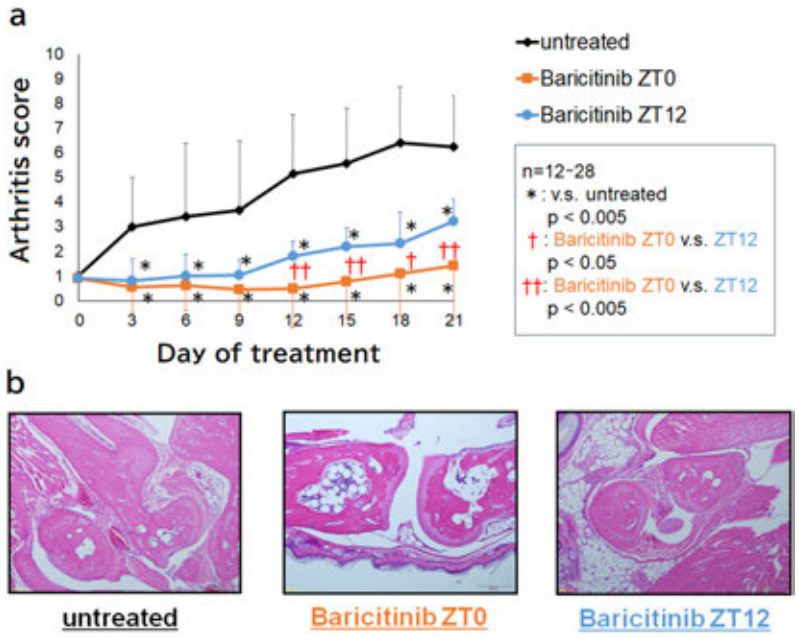

Figure 1. Arthritis score of ZT0/12 group decreased from day3 as compared to the untreated group, and those of ZT12 group rose significantly higher than those of ZT0 group from day12 (a). Joint destructions with synovial hyperplasia were observed in untreated group and ZT12 treated group, while those were suppressed in ZT0 group (b).

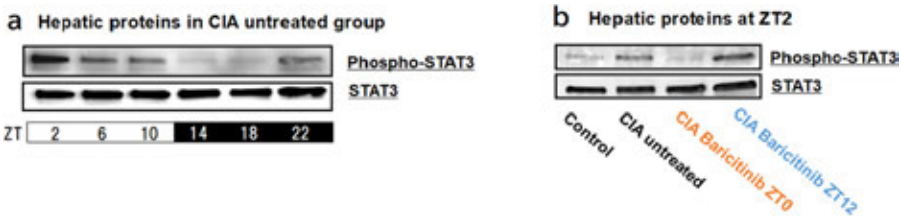

Figure 2. In CIA mice, STAT3 was highly phosphorylated from ZT22 to ZT10 (a). Phosphorylation of STAT3 was suppressed in ZT0 group at ZT2 (b).

Background/Purpose: Diurnal variations are observed in symptoms of rheumatoid arthritis (RA). Among them, “morning stiffness of joints” is closely reflects the daily medical condition of RA patients. The diurnal variation is also present in the production of inflammatory cytokines that interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) or interferon-gamma (IFN-γ) show peak concentrations in sera of RA patients during mid night, and similarly, those of collagen-induced arthritis (CIA) mice are reported to increase from morning to evening. A Janus kinase (JAK) inhibitor Baricitinib, orally administrated once a day, competitively inhibits phosphorylation of JAK1/2 bound of type 1/2 cytokine receptors, and suppresses productions of wide range of inflammatory cytokines derived from JAK/ signal transducers and activator of transcription (STAT) pathway. As reference to a recent report that chronotherapy using modified-release prednisone effectively suppresses “morning stiffness” of RA patients, in this study, differences in efficacy according to oral administration time of Baricitinib, targeting peaks of cytokine secretion, were examined in CIA mice.

Methods: CIA mice were administered a dose of 3 mg/kg of Baricitinib once a day at zeitgeber time (ZT) 0 or ZT12 for 21 days. Mice paws and ankles were scored on a scale from 0-4, as the cumulative value for all paws with a maximum possible score of 16, every third day. On day21, Hind limbs were examined by hematoxylin eosin staining.

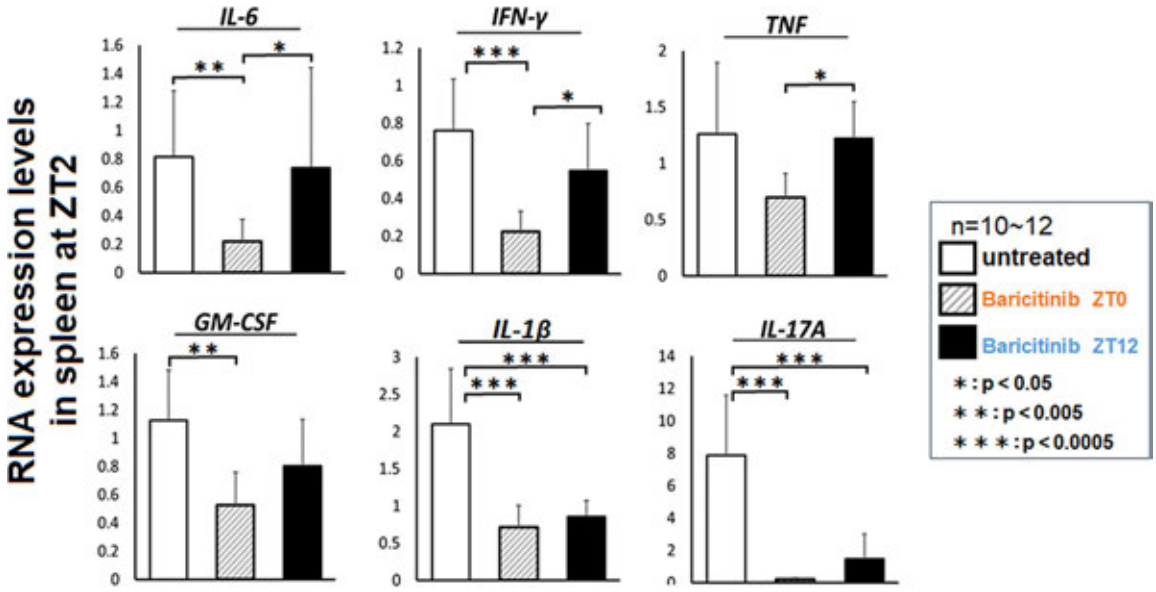

Figure 3. RNA expression levels in spleen at ZT2.

Hepatic proteins at ZT2, 6, 10, 14, 18 and 22 were analyzed for phosphorylation of STAT3 by western blotting. Splenic lymphocytes were isolated at ZT2, 6, 10, 14, 18 and 22 to measure expressions of *IL-1β*, *IL-6*, *IL-17A*, *TNF*, *IFN-γ* and *Granulocyte Macrophage Colony-Stimulating Factor* (*GM-CSF)* by Real-time PCR.

Results: Arthritis score of ZT0/12 group decreased from day3 as compared to the untreated group, and those of ZT12 group rose significantly higher than those of ZT0 group from day12 (Fig. 1a). Joint destructions with synovial hyperplasia were observed in untreated group and ZT12 treated group, while those were suppressed in ZT0 group (Fig. 1b). In CIA mice, STAT3 was highly phosphorylated from ZT22 to ZT10 (Fig. 2a), and it was suppressed in ZT0 group (ZT2) (Fig. 2b). The expressions of *IL-1β*, *IL-6*, *TNF*, and *GM-CSF* reached maximum levels at ZT2 in untreated group, and that of *IFN-γ* reached maximum level at ZT22. At ZT2, the expressions of *IL-6*, *IFN-γ*, *TNF* and *GM-CSF* in ZT0 treated group were significantly decreased as compared to untreated mice, whereas those of ZT12 group were not. The expressions of *IL-1β*, *IL-17A* in lymphocytes were significantly decreased by Baricitinib treatment as compared to untreated group (Fig. 3).

Conclusion: Administration of Baricitinib at ZT0 significantly attenuated the progression of arthritis in CIA mice. Results show that chronotherapy targeting cytokine secretions is far more effective than previously considered, and clinical application of chronotherapy using Baricitinib can be expected to enhance the drug efficacy by appropriate administration.

Disclosure: A. Yaekura, None; **K. Morii**, None; **Y. Oketani**, None; **I. Okumura**, None; **K. Kaneshiro**, None; **K. Yoshida**, None; **Y. Kawasaki**, None; **N. Shibanuma**, None; **Y. Sakai**, None; **A. Hashiramoto**, None.

Abstract Number: 1773

The Card9-Neutrophil Signaling Axis Is Critical to Induction of Th17-Mediated Arthritis in SKG Mice

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Animal Models
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Caspase recruitment domain-containing protein 9 (CARD9) is an adaptor protein downstream of C-type lectin receptor signaling within myeloid cells. CARD9 is critical for anti-fungal immunity; yet also linked to inflammatory diseases including ankolysing spondylitis and Crohn's Disease. Here, we investigated the role of Card9 in autoimmunity as modeled in SKG mice, which develop T cell-mediated arthritis in response to microbial triggers.

Methods: SKG and Card9$^{-/-}$SKG mice,were injected with zymosan (1.5 mg), clinically monitored for arthritis, and histologically analyzed for joint pathology. At 8 wk post-zymosan, CD4^{+} T cells from draining lymph nodes were stimulated *in vitro* with PMA/ionomycin and Th effector subsets were quantified by intracellular cytokine staining and flow cytometry. For adoptive T cell transfers, splenic CD4^{+} T cells purified from naïve mice by immunomagnetic selection were intravenously injected (4x10^{6}) into nude (*nu*/*nu*) recipients who were injected 24h later with zymosan. For lavage studies, peritoneal fluid collected 4h post-zymosan was analyzed for cellular (ie. neutrophils) and non-cellular (ie. chemokine/cytokine) content by flow cytometry and ELISA. Neutrophils were depleted in SKG mice with anti-Ly6G (1A8) or isotype control (2A3) beginning 24h prior to zymosan and every 2d for 11d. For all studies, three independent experiments were performed (n=5-6 mice/genotype), and data analyzed using non-parametric statistics.

Results: After zymosan injection, SKG mice developed chronic arthritis while Card9$^{-/-}$SKG mice developed no detectable arthritis. Card9$^{-/-}$SKG mice had reduced numbers of T cells in pLN including reduced CD4^{+} T effector cells (Th17, Th1, Th22), and decreased IL-17A in synovial fluid. The mechanism by which Card9 suppresses arthritis is T cell-extrinsic since Card9-deficient and –sufficient T cells had similar abilities to induce arthritis. Given the known anti-fungal role for Card9 within myeloid cells we examined acute myeloid cell responses to zymosan. Within 4h of zymosan injection Card9$^{-/-}$SKG mice had dramatically reduced proportions of peritoneal neutrophils, whereas the dendritic cells and macrophage responses were comparable in Card9$^{-/-}$SKG vs. SKG mice. Neutrophil chemoattractants (CXLC1, CXCL2) or inflammatory cytokines (IL-1b, IL-6, IL-23) levels in the peritoneum were not altered by Card9-deficiency. However, Card9-deficient neutrophils had significant reduction in activation status (CD62L) and in their ability to undergo degranulation as determined by mobilization of secondary (CD66b) and primary granules (CD63). Neutrophil depletion during the priming stage delayed arthritis onset.

Conclusion: These data reveal a previously unconsidered role for Card9-signaling within neutrophils in response to environmental triggers in conferring susceptibility to arthritis in SKG mice.

Disclosure: R. Napier, None; **E. Lee**, None; **E. Vance**, None; **B. Steffen**, None; **S. Sakaguchi**, None; **H. Rosenzweig**, None.

Abstract Number: 1774

Potential Involvement of OX40 Expressing Tfh Cells on Regulation of Autoantibody Sialylation in Experimental and Rheumatoid Arthritis

Izumi Kurata ,[1] Isao Matsumoto,[1] Natsuko Mikami,[1] Ayako Ohyama,[1] Atsumu Osada,[1] Yuya Kondo,[1] Hiroto Tsuboi,[1] and Takayuki Sumida[1], [1]Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Animal Models
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Recently, IL-23-Th17 cells axis and hyposialylation of antibodies were proved to be linked to experimental and rheumatoid arthritis. However it remains uncertain how Tfh, including IL-17 producing Tfh (Tfh17) cells, behaves as regulator of antibody hyposialylation. The aim of this study is to explore the molecular mechanisms of Tfh17 cells-associated autoantibody hyposialylation using glucose-6-phosphate isomerase (GPI) induced arthritis (GIA) model and peripheral blood of RA patients.

Methods:

1) Fluctuation of Tfh cells and their cytokine production in draining lymph nodes were analyzed in GIA. Cell surface molecule expression of Tfh cells was examined.

2) Expression of *st6gal1*, the responsible enzyme for sialylation, in plasmablasts (PBs) was followed during arthritis course. Sialic acid in purified anti-GPI antibodies obtained at the arthritis onset (day 7) and resolving phase (day 28) was quantified by mass spectrometry. Dendritic cells (DCs) were stimulated with anti-GPI antibodies from both phases. Artificial sialic acid removal/supplement was performed *in vitro* and *vivo*.

3) Expression of *st6gal1* in co-cultured PBs with Tfh cells was measured. OX40-OX40 ligand (OX40L) pathway was blocked with mAbs both *in vivo* and *vitro*.

4) Correlation between circulating Tfh17 cells, ACPA titers and *st6gal1* expression in PBs were analyzed in treatment-naïve patients with RA. OX40 expression of Tfh17 cells was analyzed.

Results:

1) Tfh cells, especially IL-17 producing Tfh17 cells were increased at day 7 in GIA. They highly expressed OX40.
2) *St6gal1* expression in PBs was significantly decreased at day 7 and 14 (arthritis peak) and gradually recovered. Mass spectrometric analysis revealed significant hyposialylation of day 7 antibodies. DCs produced more TNFα and CXCL1 when stimulated with day 7 antibodies than with those of day 28. Sialic acid-removed antibodies became stronger stimulants for DCs and GIA was ameliorated when sialic acid was supplied to mice.
3) Decreased expression of *st6gal1* was observed in PBs co-cultured with Tfh cells. OX40-OX40L pathway blockade rescued this decrease *in vitro*. By the blockade, GIA was ameliorated accompanied by sialylated anti-GPI antibodies and diminished Tfh17 cells *in vivo*.
4) Proportion of circulating Tfh17 cells had positive correlation with ACPA tiers in RA patients. Moreover, they negatively correlated with the *st6gal1* expression in RA patients (R^2= -0.596). OX40 was highly expressed in their Tfh17 cells.

Conclusion: Our findings suggested Tfh, including Tfh17 cells could have a crucial role in the development of arthritis via regulation of autoantibody sialylation through OX40-OX40L axis in experimental and rheumatoid arthritis.

Disclosure: I. Kurata, None; **I. Matsumoto**, None; **N. Mikami**, None; **A. Ohyama**, None; **A. Osada**, None; **Y. Kondo**, None; **H. Tsuboi**, None; **T. Sumida**, None.

Abstract Number: 1775

Cholesterol Sequestering in Macrophages Contributes to the Lipid Paradox in Chronic Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Animal Models
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Patients with active rheumatoid arthritis (RA) have increased cardiovascular mortality, paradoxically associated with reduced circulating lipid levels. Several disease-modifying antirheumatic drugs (DMARDs), such as the JAK inhibitor tofacitinib, ameliorate disease activity along with an increase in serum lipids. We previously demonstrated *in vitro* that tofacitinib favored cholesterol efflux from macrophages through an ABCA1-dependent mechanism. Furthermore, tofacitinib-treated chronic arthritic rabbits showed increased circulating lipids and decreased lipid accumulation within the synovium. Our aim was to explore *in vivo* whether inflammation impedes cholesterol efflux from macrophages, and whether tofacitinib restores macrophage cholesterol release during chronic arthritis. For that purpose, we assessed the ability of intraperitoneally-injected ^{3}H-cholesterol labelled macrophages to efflux cholesterol to circulating lipoproteins in collagen-induced arthritis (CIA) mice treated with tofacitinib or placebo, as compared to healthy controls.

Methods: DBA/1J mice were randomly assigned to healthy controls (Control, n = 9), CIA (CIA, n = 6) and CIA mice receiving 50 mg/kg/day tofacitinib, orally, for three consecutive days, starting on day 39 after CIA induction and coinciding with disease peak (CIA+TOFA, n = 6). The day after, ^{3}H-cholesterol labeled RAW264.7 macrophages were intraperitoneally injected into mice and tracer appearance was monitored in plasma lipoprotein subfractions, synovium, liver, bile and feces.

Results: The CIA group showed higher C-Reactive protein levels (CRP, *μg/ml*; Control: 10.90±0.49, CIA: 13.86±1.05, p=0.03 *vs.* Control) and lower circulating ^{3}H-cholesterol levels (*% of injected disintegrations per minute (dpm)/ml;* Control: 1.29±0.11, CIA: 0.92±0.11, p=0.04 *vs.* Control). Both serum CRP and ^{3}H-cholesterol –particularly the HDL fraction– were restored to baseline after the treatment with the JAK inhibitor (CIA+TOFA: 10.97±0.67 *μg/ml* and 1.37±0.20 *% of injected dpm/ml*, respectively, p=0.05 *vs.* CIA). Concomitantly, we observed an upward trend in ^{3}H-cholesterol accumulation within the synovium of CIA animals as compared to controls, which tended to normalize with the treatment.

Conclusion: Systemic inflammation induces cholesterol sequestering within macrophages *in vivo* by acting on cholesterol efflux transporters. Tofacitinib favors cholesterol release to plasma lipoproteins, hence increasing circulating cholesterol. This is not only due to a decrease in inflammation –an effect very likely shared with some other biologic DMARDs–, but also to a direct mechanism on ABCA1 transporters that favors cholesterol efflux. To our knowledge, this is the first report suggesting that cholesterol dynamics in the macrophage may contribute to the overall circulating cholesterol levels, especially considering that this phenomenon may occur in other cell types, such as adipocytes.

Disclosure: S. Pérez-Baos, None; **J. Arakawa**, None; **R. Largo**, None; **K. Ikewaki**, None; **G. Herrero-Beaumont**, None.

Abstract Number: 1776

Causal Effect of TNF-α, IL-12p70, IL-17 Levels on the Risk of Psoriatic Arthritis: A Mendelian Randomization Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Biologic agents targeting cytokines including TNF-α, IL-12p70 and IL-17 have been proven to be very effective in treating psoriatic arthritis (PsA). Nonetheless, whether these cytokines are causally associated with PsA is uncertain. The study aims to compare causal associations between genetically predicted cytokine level and risk of psoriatic arthritis via a two-sample Mendelian Randomization approach.

Methods: We used the publicly available summary-level findings from genome-wide association studies (GWAS) for identification of loci influencing concentrations of circulating cytokines (PMID: 27989323, n=8 293) as exposure and a GWAS for non-cancer illness code self-reported: PsA from the individuals included in the UK Biobank (total n = 462 933; case = 900, control = 462 033) as the outcome. A two-sample Mendelian randomization (MR) analysis was performed using the inverse-variance weighted (IVW), weighted median, and MR-Egger regression methods. Sensitivity analysis and MR-Egger regression analysis were performed to evaluate the heterogeneity and pleiotropic effects of each variant.

Table 1. MR estimates from each method of assessing the causal effect of three cytokines on the risk of PsA

Exposure	MR method	No. of SNPs	Beta	SE	Association p-value	Cochran Q statistic	df	Heterogeneity p-value	Horizontal pleiotropy
Tumor necrosis factor alpha levels (SD units increase)	MR Egger	6	0.000	0.001	0.959	0.9251	4	0.9209	
Tumor necrosis factor alpha levels (SD units increase)	Weighted median	6	0.000	0.000	0.647				0.67
Tumor necrosis factor alpha levels (SD units increase)	Inverse variance weighted	6	0.000	0.000	0.306	1.135	5	0.9509	
Tumor necrosis factor alpha levels (SD units decrease)	MR Egger	3	0.000	0.001	0.762	0.81	1	0.3681	
Tumor necrosis factor alpha levels (SD units decrease)	Weighted median	3	0.000	0.000	0.593				0.981
Tumor necrosis factor alpha levels (SD units decrease)	Inverse variance weighted	3	0.000	0.000	0.571	0.8109	2	0.6667	
Interleukin-17 levels (SD units increase)	MR Egger	7	-0.002	0.001	**0.087**	5.414	5	0.3674	
Interleukin-17 levels (SD units increase)	Weighted median	7	-0.001	0.001	**0.014**				0.513
Interleukin-17 levels (SD units increase)	Inverse variance weighted	7	-0.001	0.000	**0.002**	5.952	6	0.4286	
Interleukin-17 levels (SD units decrease)	MR Egger	5	0.001	0.001	0.651	1.127	3	0.7706	
Interleukin-17 levels (SD units decrease)	Weighted median	5	0.000	0.001	0.487				0.721
Interleukin-17 levels (SD units decrease)	Inverse variance weighted	5	0.000	0.000	0.685	1.28	4	0.8647	
Interleukin-12p70 levels (SD units increase)	MR Egger	9	-0.002	0.002	0.400	9.047	7	0.2493	
Interleukin-12p70 levels (SD units increase)	Weighted median	9	-0.001	0.001	0.162				0.558
Interleukin-12p70 levels (SD units increase)	Inverse variance weighted	9	-0.001	0.000	0.242	9.536	8	0.2991	
Interleukin-12p70 levels (SD units decrease)	MR Egger	5	-0.001	0.001	0.631	5.021	3	0.1703	
Interleukin-12p70 levels (SD units decrease)	Weighted median	5	0.000	0.001	0.692				0.821
Interleukin-12p70 levels (SD units decrease)	Inverse variance weighted	5	0.000	0.001	0.516	5.122	4	0.275	

Results: Single-nucleotide polymorphisms (SNPs) at genome-wide significance from GWASs on TNF-α (6 and 3 SNPs for increased and decreased TNF-α levels respectively), IL-12p70 (9 and 5 SNPs for increased and decreased in IL-12p70 levels respectively), IL-17 (7 and 5 SNPs for increased and decreased IL-17 levels respectively) were identified as the instrumental variables (IVs). Our results provided evidence to support a causal association between elevated level of Il-17 (IVs: rs117556572, rs141312283, rs149738638, rs17282552, rs187475560, rs57920188, rs62191444) and PsA (MR Egger, p = 0.087; Weighted median: p=0.014; Inverse variance weighted: p= 0.002). All three methods did not show any causal association between PsA and increased and decreased TNF-α and IL-12p70, and decreased IL-17 level (Table 1). Cochran's Q test and the funnel plot indicated no evidence of heterogeneity and asymmetry, indicating no directional pleiotropy.

Conclusion: Our findings provided strong evidence on the causal association of genetically elevated circulating IL-17 levels with the risk of developing psoriatic arthritis. IL-17 blockade might prevent the transition from psoriasis to psoriatic arthritis that warrants testing in suitably powered randomized trials.

Disclosure: D. WU, None; **P. Wong**, None; **S. Lam**, None; **I. Cheng**, None; **E. Li**, None; **L. Qin**, None; **L. Tam**, None.

Abstract Number: 1777

The Deubiquitinase TRABID Is a Potential Therapeutic Target in Spondyloarthritis

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SESSION INFORMATION
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Background/Purpose: Interleukin 12 (IL-12) and 23 (IL-23) may play a pivotal role in the pathogenesis of inflammatory diseases, including Spondyloarthritis (SpA). In mice, the deubiquitinase Trabid, encoded by Zranb1, participates to the epigenetic regulation of *IL-12* and *IL-23* genes via the stabilization of the histone demethylase JMJD2D. TRABID also regulates the methyltransferase EZH2, involved in the epigenetic control of the inflammatory response in human.

This study aims to assess the expression and the functional relevance of TRABID in controlling the inflammation and activation of IL-12/IL-23 axis in SpA.

Methods: TRABID expression was assessed in synovial tissue (ST) (n=10), Peripheral blood (PBMCs) (n=10), Bone Marrow (BM) (n=5) and Gut (n=20) of SpA patients with active disease and matched healthy by immunohistochemistry (IHC) and quantitative PCR.

Gene expression of *ZRANB1*, *JMJD2D*, *EZH2*, *IL-23*, *IL-12a*, *IL-17a* in ST was further investigated in the Pathobiology of Early Arthritis Cohort (PEAC) in DMARDs naïve RA (n= 91) and SpA (n=14) patients via RNA sequencing.

Ultrasound-guided synovial biopsies of clinically active joints from twenty-five patients (11 males) with active (DAS: mean 4.3; SD 1.1) SpA, were also studied. The degree of synovitis was histologically assessed by hematoxylin and eosin staining. Immunohistochemistry (IHC), followed by semi-quantitative scoring, was also performed to determine the degree of $CD20^+$ B cells, $CD3^+$ T cell, $CD68^+$ macrophage and $CD138^+$ plasma cell infiltration.

Accordingly, STs were categorized STs into fibroid, myeloid and lymphoid-myeloid pathotypes and TRABID, IL-23p19 and IL-23R expression were assessed by IHC.

Results: The expression of ZRANB1 was increased in SpA PBMCs and ileal samples ($p< 0.001$). In particular, the highest expression of *ZRANB1* was observed in chronic inflamed gut samples of SpA patients, being its expression directly correlated with IL-23p19 ($r=0.49$, $p< 0.05$) and IL-23R ($r=0.67$, $p< 0.001$). Within the early arthritis cohort the expression of *ZRANB1* in STs was higher in PsA versus Rheumatoid arthritis (RA) ($p< 0.05$) and expression of the TRABID target *EZH2* correlated with the levels of *IL12A* ($r= 0.46$; padj < 10-5), *IL23A* ($r= 0.45$; padj< 10^{-5}) and *IL-17A* ($r= 0.23$; padj< 0.05). The number of $TRABID^+$ cells was significantly increased in SpA ST ($p< 0.001$), gut ($p< 0.001$) especially among infiltrating inflammatory mononuclear cells, and BM ($p< 0.001$). In ST the number of $TRABID^+$ cells was particularly increased in the lymphoid and myeloid pathothypes compared to the pauci-immune fibroid ($p< 0.01$) and correlated with the synovitis score ($r= 0.48$; $p< 0.05$), CD68 in the sub-lining ($r= 0.69$; $p< 0.001$), CD3 ($r= 0.57$; $p< 0.01$), and CD20 ($r= 0.64$; $p< 0.01$). Finally, $TRABID^+$ cells were enriched in the STs rich in IL-23p19 versus the low expressing IL-23p19 STs ($p< 0.05$) and correlated with the number of IL-23R expressing cells ($r= 0.58$; $p< 0.05$).

Conclusion: ZRANB1/TRABID levels are increased in the synovial tissue, bone marrow and gut of SpA patients and correlated with specific histologic pathothypes, the degree of synovitis and the levels of IL-23 and IL-23R. In conclusion, this study may pave the way for future TRABID therapeutic inhibition in the treatment of SpA.

Disclosure: D. Mauro, None; **F. Macaluso**, None; **A. Nerviani**, None; **M. Boutet**, None; **A. Rizzo**, None; **R. Alessandro**, None; **G. Guggino**, None; **C. Pitzalis**, AbbVie, 2, astellas, 2, astra Zeneca, 2, BMS, 2, Janssen, 2, mad, 2, pfizer, 2, roche, 2, cub, 2, AbbVie, 5, astellas, 5, astra Zeneca, 5, bus, 8, Celgene, 5, Grunenthal, 5, ask, 5, Janssen, 5, mad, 5, pfizer, 5, Sanofi, 5, roche, 5, cub, 5, AbbVie, 8, astra Zeneca, 8, bus, 8, Janssen, 8, mad, 8, pfizer, 8, roche, 8, cub, 5; **F. Ciccia**, None.

Abstract Number: 1778

Entheseal CD90+ SOX9+ Cartilage-like Cells Initiate Spinal Ankylosis in Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Enthesitis is characterized by inflammation at the interface where tendon or ligament attaches to the bone and is a representative symptom of ankylosing spondylitis(AS). The enthesitis is primarily responsible for the initiation and progression of AS. However, it is not known which cellular and molecular characterizations

of enthesitis contribute to cartilage fusion and enchondral ossification causing ankylosis. Here, we hypothesized that inflammatory stimuli to cartilage-like cells in spinal ligaments cells are a pivotal driver of ankylosis.

Methods: The bone and ligament tissues of the facet joint of 5 patients with AS and 7 disease control obtained from spinal surgery were assessed by histology and immunofluorescence. Primary bone and ligament cells were isolated by outgrowth and collagenase type I&II-digested method, respectively. Isolated bone or ligament cells of both AS and control were analyzed by FACS for CD90 and SOX9 and used for further experiments. Both bone and ligament cells stimulated by TNF and/or IL-17A as inflammatory stimuli were assessed by qPCR, immunoblotting, immunostaining, human MMP antibody array, and ELISA. We also examined the differences in the response to osteogenic activity and differentiation status under identical conditions. Furthermore, distinct expressions in AS patients were confirmed by immunostaining at spinal ligaments in Curdlan-injected SKG mice.

Results: Histological results show that granulation tissues and blood vessels were frequently eroded in subchondral bone area of AS facet joints, as previously reported. Additionally, there is strong CD34 expression of the blood vessels in subchondral bone of AS joint. Ectopic cartilage-like cells were seen in granulation tissues eroding the subchondral bone. Intriguingly, SOX9+ cartilage-like cells were co-localized in the granulation tissues expressing MMP13 of AS. SOX9 level by FACS analysis was statistically higher in primary AS bone cells. When we analyzed cell surface markers of primary ligament cells by FACS, expression of CD90+ was determined as a ligament marker. In particular, high frequency of SOX9+ and CD90+ were found to be expressed in AS ligaments, but not in controls. Furthermore, expressions of MMP1, 3, and 13 were obviously increased and secreted more in AS ligament cells with co-stimulation of TNF and IL-17A than that in controls. The co-stimuli condition under osteoblast differentiation boosted calcium deposit and hydroxyapatite formation in AS ligament cells. Consistent with the above data, co-expression of MMP13 and SOX9 were markedly increased at spinal ligament in curdlan-treated SKG mice compared to controls.

Conclusion: Collectively, our findings reveal that entheseal CD90+ SOX9 cartilage-like cells contribute to the progression of spinal ankylosis.

Disclosure: S. Jo, None; **Y. Lee**, None; **T. Lee**, None; **Y. Park**, None; **T. Kim**, None.

Abstract Number: 1779

CLEC5A/MDL-1 Is Critical for Inflammatory Arthritis and Skin Inflammation

Cuong Nguyen ,[1] Dai Hui,[1] Ran Gu,[1] Trevor Chan,[2] Alina Marleev,[3] Emanual Maverakis,[3] Vijay Kuchroo,[4] Shie-Liang Hsieh,[5] Ilias Tagkopoulos,[2] Christopher Ritchlin,[6] and Iannis Adamopoulos[1], [1]Division of Rheumatology, Allergy and Clinical Immunology, University of California at Davis, Sacramento, CA, [2]University of California, Davis, Department of Computer Science, California, USA, Davis, CA, [3]Department of Dermatology, School of Medicine, UCD, Sacramento, California, USA., Sacramento, CA, [4]Center for Neurologic Diseases, Brigham and Women's Hospital, Harvard Medical School, MA, USA, Boston, MA, [5]Genomics Research Center, Academia Sinica, 128 Academia Road, Section 2, Nankang, Taipei, Taiwan, Taipei, Taiwan (Republic of China), [6]Division of Allergy, Immunology and Rheumatology, Center for Musculoskeletal Research, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA, Rochester, NY

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Interleukin-23 (IL-23) and its cognate receptor interleukin-23R (IL-23R):IL-12Rβ1 plays a critical role in the pathogenesis of autoimmune diseases including psoriasis and psoriatic arthritis. Although significance of IL-23 signaling in adaptive immunity has been well-studied, the role of IL-23 in myeloid cell activation remains unknown.

Methods: To investigate role of CLEC5A/MDL-1 in psoriatic arthritis-like pathology, we performed *in vivo* gene transfer of IL-23 in WT, IL-23R^{GFP} reporter, and *Mdl-1*$^{-/-}$ mice. qRT-PCR, RNAseq, Western blot, flow cytometry, ELISA, H&E stain, and immunofluorescence staining methods were used to analyze the phenotype of WT and transgenic mice.

Results: Herein, we show in the IL-23R^{GFP} reporter mice, that IL-23 induces the expansion of myeloid cell populations including an epidermal myeloid DNAX activation protein 12 (DAP12)-associating lectin-1 (MDL-1)$^{+}$CD11b^{+}Ly6G^{+}IL-23R^{+} cell population associated with epidermal hyperplasia and an MDL-1^{+}CD11b^{+}Ly6C^{high}IL-23R^{+} associated with bone destruction. Mechanistically, genetic ablation of MDL-1 prevented IL-23-gene transfer elicited myelopoiesis and showed a marked reduction of skin inflammation markers (*K16*, *S100a7, S100a8, S100a9*, *Cxcl-1*, *Cxcl-2*) and bone destruction markers (*Acp5*, *Ctsk*, *Mmp9*) compared to wildtype mice. Moreover, we found that *Mdl-1*$^{-/-}$ mice had significantly higher bone mass and impaired osteoclast differentiation *in vitro* and *in vivo* as well as reduced joint inflammation in IL-23 gene transfer induced arthritis. Mechanistic data through of flow cytometry, Western blotting and co-immunoprecipitation experiments revealed that a trimeric complex of IL-23R/DAP12/MDL-1 elicited the associated pathologies in our murine model. Furthermore, we performed RNAseq analysis of murine skin following IL-23 gene transfer and revealed 297 differentially expressed genes (DEGs) affected by MDL-1 deletion. Specifically, these DEGs are associated with myelopoiesis, neutrophil proteases, DAP12, cell survival and apoptosis. We correlated our findings with RNAseq meta-analyses derived from human psoriatic skin (135 patients vs 133 controls), which showed elevation of *MDL-1* in psoriatic patients and positive correlation for *IL-23* versus *MDL-1* and *IL-23R* versus *MDL-1.*

Conclusion: Collectively, our data demonstrate that MDL-1 is a critical component of IL-23 signaling that dictates synovial and skin inflammation *in vivo*, and could be targeted for the treatment of PsA.

Disclosure: C. Nguyen, None; **D. Hui**, None; **R. Gu**, None; **T. Chan**, None; **A. Marleev**, None; **E. Maverakis**, None; **V. Kuchroo**, None; **S. Hsieh**, None; **I. Tagkopoulos**, None; **C. Ritchlin**, AbbVie, 2, 5, 9, Amgen, 2, 5, BMS, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Lilly, 5, Novartis, 5, Pfizer, 2, Pfizer Inc, 5, UCB, 2, 5; **I. Adamopoulos**, None.

Abstract Number: 1780

Microbiome in Offspring of Ankylosing Spondylitis Patients

Matthew Stoll ,[1] Kimberly DeQuattro,[2] Zhixiu Li,[3] Henna Sawhney,[4] Maria Castillo,[4] Pamela F. Weiss,[5] Peter Nigrovic,[6] Lynn Punaro,[7] Kenneth Schikler,[8] Barbara Edelheit,[9] John Reveille,[10] Matthew Brown,[3] and Lianne Gensler[11], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of California, San Francisco, San Francisco, CA, [3]Queensland University of Technology, Queensland, Australia, [4]University of California in San Francisco, San Francisco, CA, [5]Children's Hospital of Philadelphia, Philadelphia, PA, [6]Boston Children's Hospital, Boston, MA, [7]Texas Scottish Rite Hospital, Dallas, TX, [8]University of Kentucky, Louisville, KY, [9]Connecticut Children's Medical Center, Hartford, CT, [10]University of Texas McGovern Medical School, Houston, [11]University San Francisco California, San Francisco, CA

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

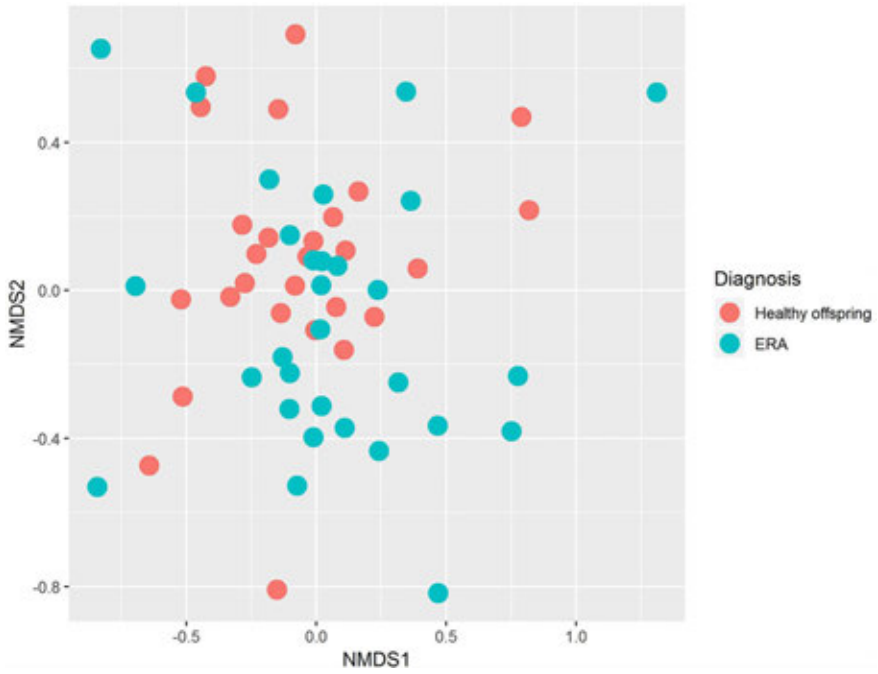

Figure 1. Visualization of the microbiota of healthy offspring (red) compared to ERA patients (blue). NMDS = nonmetric multidimensional scaling, an ordination method similar to principal coordinates analysis.

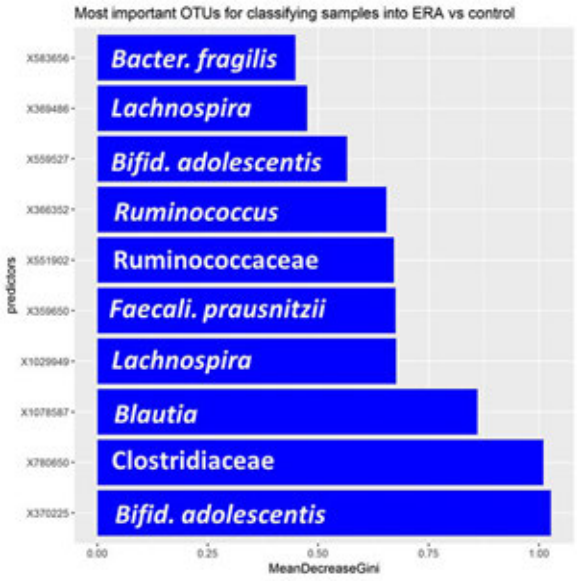

Figure 2. Results of Random Forests analysis evaluating the microbiota as a Predictor of arthritis. The top 10 most important OTUs (as reflected by the MeanDecreaseGini are shown.) The higher the MeanDecreaseGini, the more important the variable (in this case, OTU) is for classification of the sample. Two of the organisms were each represented by two different OTUs.

Background/Purpose: Spondyloarthritis (SpA) results from the interplay between genetic and environmental factors. An emerging factor is the human intestinal microbiota, which multiple studies in children and adults have shown to be abnormal in SpA patients, including enthesitis-related arthritis (ERA) and Ankylosing Spondylitis (AS). Considering the microbiota pathogenic, we may have the opportunity to both identify an at-risk population and consider ways to modify their microbiota. The purpose of this study was to analyze the microbiota of healthy children at risk for SpA, stratified by HLA-B27, and to compare these healthy children to HLA-B27+ ERA patients.

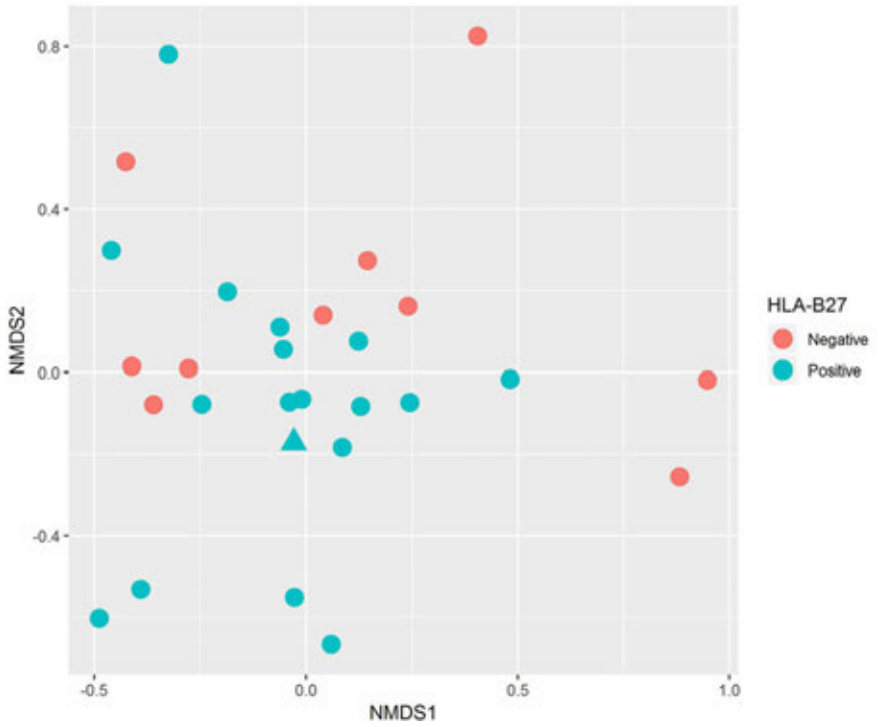

Figure 3. Visualization of the microbiota of HLA-B27- offspring (red) compared to HLA-B27+ offspring (blue) using NMDS. The microbiota of the child diagnosed with SpA is depicted as a triangle.

Methods: Children age 5 – 18 years (along with their AS parent) were examined by a rheumatologist for evidence of SpA. Human DNA as well as fecal specimens were collected from both parent and children. Microbiota specimens were subject to amplification of the V4 region of the ribosomal RNA gene, which was sequenced on the Illumina MiSeq device. Host SNP genotyping was performed with the Illumina Global Screening Array, a single nucleotide polymorphism (SNP) microarray with 760,000 markers, from which HLA types were imputed using SNP2HLA. The Quantitative Insight into Microbial Ecology was used for quality control as well as clustering into operational taxonomic units (OTUs) using uclust. The OTU table was imported as a phyloseq object for further processing, visualization, and diversity analysis. DeSeq2 was used for FDR-corrected comparisons of abundances of the major taxa, and the Random Forest algorithm was used to predict the development of arthritis based upon the microbiota contents.

Results: Fecal specimens were obtained on 28 offspring of AS patients, of whom 18 were HLA-B27+; one had a SpA diagnosis at study enrollment. Healthy offspring were compared to 29 additional children with HLA-B27+ ERA (ILAR criteria) recruited from 6 sites. Among ERA patients, clustering by diagnosis was present (Figure 1; $p = 0.004$, adonis). Following transformations and adjustment for multiple comparisons, 20 OTUs were significantly associated with diagnosis state, of which four (*Bifidobacterium adolescentis*, Ruminococcaceae, and Clostridiaceae higher in controls; *Bacteroides fragilis* higher in ERA) were identified among the top 10 most associated with the diagnosis in the Random Forest model (Figure 2). Comparison of the HLA-B27+ to negative offspring revealed clustering by genotype (Figure 3; $p = 0.05$) and demonstrated that several of the OTUs that distinguished healthy offspring from patients (e.g. *Ruminococcus gnavus*, higher in ERA vs offspring and HLA-B27+ vs HLA-B27- offspring) were also significantly associated with genotype.

Conclusion: Our data identified several bacteria associated with HLA-B27 in healthy at-risk children and ERA patients, and thus may identify a high-risk population that could be the target of future preventative efforts.

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Lilly, 2, 5, 8, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 5, Pfizer, 2, 5, UCB, 5; **M. Brown**, None; **L. Gensler**, AbbVie, 2, 5, Abbvie, 2, 9, Amgen, 2, Amgen, AbbVie and Novartis, 2, Center for Disease Control, 8, Division of Vaccine Injury Compensation, 8, Eli Lilly, 5, 9, Eli Lilly and Company, 9, Galapagos, 5, 9, Galapagos, Janssen, Eli Lilly, Novartis, Pfizer, and UCB, 5, Janssen, 5, 9, Novartis, 2, 5, 9, Pfizer, 2, 9, Spondylitis Association of America, 6, Spondyloarthritis Research and Treatment Network (SPARTAN), 6, UCB, 2, 5, 9, UCB Pharma, 2, 9.

Abstract Number: 1781

Cytokine Dependence of Enthesis-resident Lymphocytes in Murine Spondyloarthritis

Mederbek Matmusaev,[1] **Emma Haley** ,[1] Imtiyaz Hossain,[1] and Joerg Ermann[1], [1]Brigham and Women's Hospital, Boston

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Enthesis-resident CD4-CD8- double-negative (DN) T cells have been implicated in the pathogenesis of spondyloarthritis. Overexpression of IL-23 in adult mice activates these cells to produce IL-17A and other pathogenic cytokines leading to spondyloarthritis-like disease. Many innate lymphocytes require IL-1 for IL-23-induced production of IL-17A in vitro. We therefore investigated the role of IL-1 receptor signals on CD4-CD8- DN T cell homeostasis and induction of murine spondyloarthritis.

Methods: Lymphocytes were isolated from the spleen and Achilles enthesis of wildtype, Il23r-/-, Il1r1-/- and Il23r-gfp reporter mice (C57BL/6 background) and analyzed in vitro. Disease was induced by hydrodynamic injection of IL-23 minicircles (System Biosciences) in B10.RIII mice. To block IL-1 signals, animals were injected ip. with a cocktail of three monoclonal antibodies against IL-1α, IL-1β and IL-1R1. Animals were monitored every other day for arthritis development. Animals were euthanized two weeks after disease induction for tissue harvest and analysis.

Results: Enthesial CD4-CD8- DN T cells comprise $\gamma\delta$ T cells and DN $\alpha\beta$ T cells. Both $\gamma\delta$ T cells and DN $\alpha\beta$ T cells secreted IL-17A upon in vitro stimulation with IL-23 + IL-1β but not IL-23 alone. Cell frequencies were not substantially different in Il23r-/- or Il1r1-/- mice compared with wildtype mice. Disease induction in Il1r1-/- mice could not be tested as C57BL/6 wildtype mice do not develop arthritis upon IL-23 minicircle injection. Antibody blockade of IL-1 signals in susceptible B10.RIII mice had no impact on disease incidence but ameliorated arthritis severity.

Conclusion: IL-23 and IL-1 receptor signals control the function but not the development of enthesial $\gamma\delta$ T cells and DN $\alpha\beta$ T cells. Antibody-mediated blockade of IL-1 in susceptible B10.RIII mice reduced arthritis severity but not disease incidence suggesting that mediators other than IL-1 may provide a second signal for IL-23-induced IL-17A production in vivo. The lack of arthritis development in C57BL/6 mice injected with IL-23 minicircles diminishes the utility of this model for studies of spondyloarthritis pathogenesis.

Disclosure: M. Matmusaev, None; **E. Haley**, None; **I. Hossain**, None; **J. Ermann**, Boehringer Ingelheim, 2, Eli Lilly, 5, Novartis, 5, Pfizer, 2, UCB, 5.

Abstract Number: 1782

A Human SLE Variant *NCF1*-R90H Drives Lupus-like Kidney Disease in a Pristane-induced Murine Lupus Model

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Animal Models
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: We previously identify a p.Arg90His (p.R90H) substitution encoded in phagocyte neutrophil cytosolic factor (*NCF1*) as a novel risk variant for SLE, with decreased and increased*NCF1*copy numbers predisposing to and protecting against SLE, respectively. Our data highlights the pathogenic role of reduced reactive oxygen species (ROS) production in SLE. To study how reduced ROS promotes lupus, we established a C57BL/6 (B6) mouse model with a knock-in (KI) 90H mutation in *Ncf1*locus by CRISPR/Cas9 genome editing.

Methods: We compared 90H KI and wild-type (WT) R90 littermates for R90H genotypic effects on ROS production, type I interferon (IFN-I) signature and immune cell subsets in splenocytes, autoantibody production by ELISA and slide-based antigen array, renal IgG and C3 deposition and pathology. Pristane was injected intraperitoneally twice as an environmental trigger (0.1ml at 8wks and 0.5ml at 10wks), and lupus-like features were assessed at 30-36 wks.

Results: Compared with R90 WT littermates,untreated 5-week-old 90H KI mice exhibited reduced phorbol myristate acetate-induced extracellular ROS in splenocytes (n=5, p=0.03), splenomegaly (n=5, p=0.02),elevated IFN-I scores (p=0.047), as well as increased numbers of $CD4^{+}CXCR5^{++}PD\text{-}1^{++}$follicular helper T cells (Tfh, p=0.045) and $CD19^{+}CD23^{high}CD21^{int}$follicular B cells (p=0.005). Because KI mice had no spontaneous kidney disease at one-year old, we used pristane injection to induce lupus. Compared with pristane-treated female WT mice (n=10), 30-36-week-old female KI littermates (n=8) developed lupus-like manifestations including splenomegaly (p=0.02), increased IgG anti-RNP (p=0.02) and total IgG (p=0.004) levels, glomerulonephritis with increased glomerular score (p=0.046), elevated renal deposition of IgG (p=0.005) and C3 (p=0.04). IgG autoantibody profiles confirmed elevated IgG anti-Sm, dsDNA and RNP in those female KI mice. Increased numbers of $B220^{+}IgD^{low}CD95^{high}GL7^{high}$germinal center B cells (p=0.03) and $CD4^{+}CXCR5^{++}PD\text{-}1^{++}$(p=0.04) or $CD4^{+}Bcl\text{-}6^{+}$(p=0.02) Tfh were found in 30-36-week-old pristane-treated KI mice.

Conclusion: A single nucleotide polymorphism p.Arg90His (p.R90H) in the *Ncf1*gene resulted in reduced oxidative burst, elevated IFN-I scores, splenomegaly, and increased cell numbers of Tfh and follicular B cells in 5-week-old 90H KI C57BL/6 mice. Pristane treatment caused increased IgG autoantibodies and kidney disease development in 30-36-week-old female 90H KI C57BL/6 mice. The disease development might be attributed to increased cell numbers of Tfh, facilitating germinal center formation and autoantibody production.

Disclosure: L. Geng, None; **I. Molano**, None; **L. Xu**, None; **Q. Sun**, None; **P. Ruiz**, None; **Q. Li**, None; **G. Gilkeson**, None; **B. Tsao**, None.

Abstract Number: 1783

Reversible Dysregulation of Renal Circadian Rhythm in Lupus Nephritis

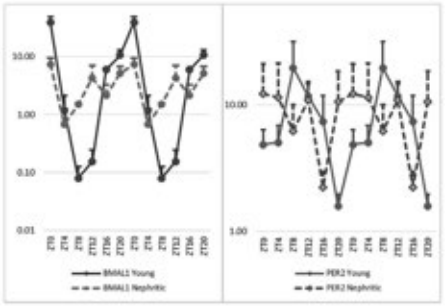
Rakesh Mishra,[1] Ramalingam Bethunaickan,[1] Celine Berthier,[2] Zhengzi Yi,[3] Joshua Strohl,[1] Patricio Huerta,[1] Weijia Zhang,[4] and **Anne Davidson** [5], [1]Feinstein Institute for Medical Research, manhasset, NY, [2]University of Michigan, Ann Arbor, MI, [3]Mount Sinai School of Medicine, New York, [4]Mount Sinai School of Medicine, New York, NY, [5]Feinstein Institutes for Medical Research, Manhasset

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Animal Models
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Circadian rhythm is a universal phenomenon that governs homeostasis of overall organism functioning as well as of individual organs. Circadian regulation of homeostatic functions in the kidneys regulates multiple renal functions including GFR, electrolyte excretion and blood pressure control. The effect of renal pathologic processes such as glomerulonephritis on circadian rhythms is not well described. In the course of genomic profiling of lupus kidneys from several mouse models of lupus nephritis we found abnormal expression of several master transcriptional regulators of circadian rhythm. Our goal was to determine how renal circadian rhythm is disrupted in lupus nephritis and the consequences of this disruption.

Methods: Perfused kidneys were obtained for molecular profiling at 4 hrly intervals over a 24hr period from groups of 5-9 young and nephritic NZB/W F1 mice. Genes with a circadian pattern of expression were identified using RAIN test. The enriched biological functions of the genes with circadian rhythm pattern at different time intervals were determined using REVIGO program. Dysregulated expression of transcriptional regulators Bmal1 and Per2 was confirmed by ELISA of renal lysates. Renal sodium and potassium excretion, urine pH and glucose, serum and urine aldosterone and blood pressure were measured at 4 hrly intervals. The effect of remission induction on gene expression and renal function was evaluated using the same assays.

Results: We found a major effect of circadian dysregulation on renal metabolic functions in nephritic mice that was not simply due to age or altered sleep-wake cycles including a change in diurnal regulation of fatty acid metabolism, a switch in carbohydrate metabolism from gluconeogenesis to the pentose phosphate pathway, loss of diurnal variation of multiple tubular transporters, altered diurnal sodium excretion, acquisition of a high aldosterone state, increased expression of genes that mediate diurnal control of vascular constriction and reverse blood pressure dipping. This circadian dysregulation was partially reversed by remission induction therapy with correction of the abnormalities in



PCR confirmation of dysregulated expression of master circadian transcriptional regulators Bmal1 and Per2 in kidneys of young and nephritis NZB/W F1 mice.

fatty acid and carbohydrate metabolism and of abnormal blood pressure dipping phenotype but significantly less effect on the dysregulation of tubular transporters.

Conclusion: There is a profound alteration of renal circadian rhythms in mice with lupus nephritis leading to multiple adverse effects on renal homeostasis and metabolism as well as blood pressure dipper status that are only appreciated upon multiple sampling of kidneys at sequential intervals. Our study indicates the role of inflammation in causing renal circadian disruption and suggests a potential role for circadian agonists in the treatment of lupus nephritis.

Disclosure: R. Mishra, None; **R. Bethunaickan**, None; **C. Berthier**, None; **Z. Yi**, None; **J. Strohl**, None; **P. Huerta**, None; **W. Zhang**, None; **A. Davidson**, None.

Abstract Number: 1784

Single Cell Analysis of Renal Myeloid Cells from NZB/WF1 Mice with Lupus Nephritis Reveals Multiple Subsets with Altered Functions

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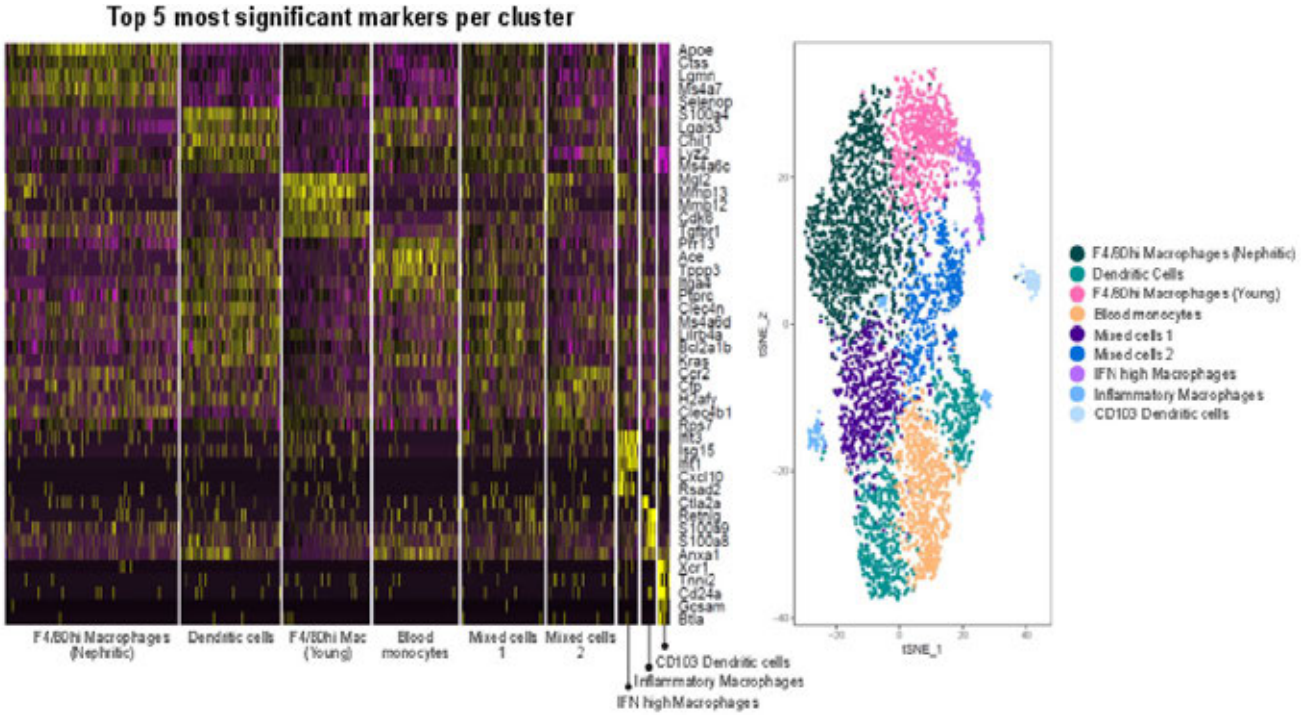
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Animal Models
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Renal infiltration with macrophages and dendritic cells is associated with poor prognosis in humans with lupus nephritis (LN). However, the precise pathogenic and/or protective functions of these cells in the LN context are still unknown.

Methods: To characterize the myeloid subsets infiltrating the LN kidney we performed RNASeq of 4 subsets of isolated renal macrophages and dendritic cells from kidneys of nephritic (classical DCs, CD103 DCs, F480hi macrophages, F4/80lo monocytes) and prenephritic (F4/80hi macrophages only) NZB/W mice and Ly6Clo peripheral monocytes of nephritic mice. Single cell RNASeq was performed on renal CD11b+/CD11c+ cells from 2 nephritic and 3 young NZB/W mice and peripheral blood monocytes from nephritic mice using 10X genomics technology and labeling with hashtag olionucleotides to allow subsequent deconvolution of samples. Doublets and cells with >1 hashtag, < 500 expressed genes and/or >15% mitochondrial content were excluded.

Results: Different cell subpopulations clustered separately by PCA analysis, confirming differences in gene expression between each subset and between young and nephritic mice. Functional analysis of gene expression using GO analysis showed a molecular profile of infiltrating myeloid DCs in nephritic mice that supports lymphoid neogenesis and lymphocyte activation suggesting that these cells help to organize and regulate the inflammatory infiltrates. The profile of F4/80hi macrophages reflects cell metabolism and repair; nevertheless macrophages from nephritic mice had a more inflammatory profile than those from young mice. Single cell analyses were performed on 2096 renal and 1091 blood cells from nephritic and 1449 renal cells from young NZB/W mice. Cluster analysis revealed 9 clusters of myeloid cells of which 7 could be identified as myeloid and CD103 DCs, F4/80hi macrophages (young and nephritic clustered separately), inflammatory macrophages, blood monocytes and a small subset of macrophages with a high IFN signature. The other two subsets comprising < 25% of the cells appeared to contain a mixture of subpopula-



Cluster analysis of all myeloid cells from NZB/W F1 kidneys

tions including CD209a expressing DCs. Subclustering of the larger clusters revealed that the blood cells and young F4/80hi macrophages were quite homogeneous, whereas F4/80hi macrophages from nephritic mice could be separated into 3 subclusters. Myeloid dendritic cells could be split into 3 subclusters and the two unknown subsets could also each be split into 3 further subclusters. Importantly a significantly higher percentage of IFN high macrophages expressed inflammatory chemokines than the other subsets.

Conclusion: We found several subsets of renal macrophages in nephritic mice whereas those in young mice were more homogeneous. An interferon high macrophage subset may contribute disproportionately to renal inflammation. Dendritic cells appear to play an important role in lymphoid neogenesis but also displayed considerable heterogeneity. An understanding of the heterogeneity of infiltrating myeloid cell types in LN may allow more precise targeting of those cells that are most likely to be causing renal damage while preserving the protective function of resident cells.

Disclosure: R. Mishra, None; **C. Berthier**, None; **H. Geiger**, None; **W. Zhang**, None; **A. Davidson**, None.

Abstract Number: 1785

The Pathogenic Potential of Choroid Plexus T Cells in Neuropsychiatric Lupus

Erica Moore ,[1] Michelle Huang,[1] Cara Reynolds,[1] and Chaim Putterman[2], [1]Albert Einstein College of Medicine, Bronx, NY, [2]Albert Einstein College of Medicine, New York, NY

SESSION INFORMATION

Session Date: Monday, November 11, 2019
Session Title: SLE – Animal Models
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

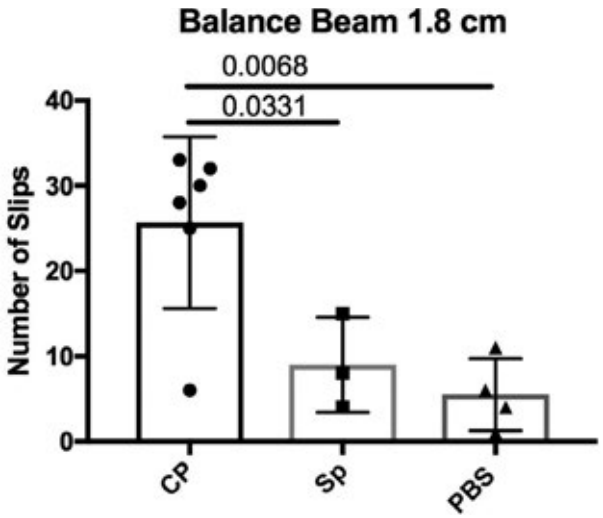


Figure 1A. Motor coordination assessment counting number of slips while crossing a balance beam, CP = choroid plexus, Sp = splenic T cell group, PBS = PBS group.

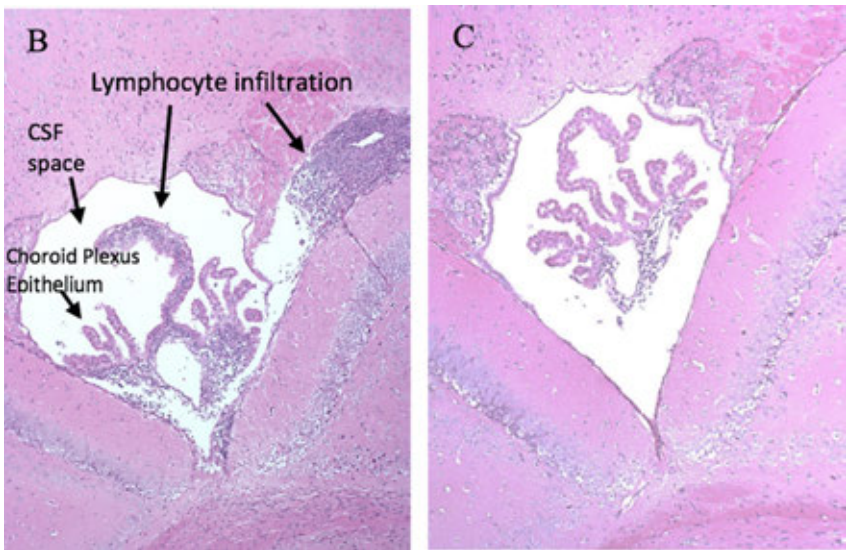


Figure 1B. H&E image of the third ventricle choroid plexus in MRL/lpr CP T cell recipient mouse; Figure 1C: H&E image of the third ventricle choroid plexus in MRL/lpr PBS recipient mouse.

Background/Purpose: The pathogenesis of neuropsychiatric Systemic Lupus Erythematosus (NPSLE) is incompletely understood, but is considered to be complex and multifactorial. Additionally, there is a wide range of possible NPSLE manifestations, including cognitive abnormalities, mood disorders, confusion, psychosis, and seizures. We have recently proposed that the blood-cerebrospinal fluid barrier at the brain choroid plexus (CP), rather than the blood-brain barrier, is the entry site for lymphocytes and other neuroinflammatory mediators into the brain. Indeed, the choroid plexus in the spontaneous MRL/lpr lupus mouse model is heavily infiltrated with predominantly T follicular helper CD4+ T cells and B cells, while preliminary imaging studies in human NPSLE have similarly revealed inflammation in the region of the CP. However, the function of CP-infiltrating T cells has not been studied as a potential contributor to the pathogenesis of NPSLE.

Methods: Six week old female MRL/lpr mice were intracerebroventricularly (ICV) injected with either MRL/lpr choroid plexus CD3+ T cells (n=6), MRL/lpr splenic CD3+ T cells (n=5), or PBS (n=4). The T cells were pooled from the choroid plexus of 16 week old MRL/lpr mice (n=7) and from the spleen of 6 week old MRL/lpr mice (n=2). The cells were stimulated and expanded with anti-CD3/CD28 antibodies (1 ug/mL) and mIL-2 (10 U/mL) for 4 days. About ~200,000

cells were injected into the lateral ventricle from the bregma at AP -0.34 mm, ML -1.0 mm, and depth -2.0 mm. Mice were sacrificed 4 weeks post-injection, with behavioral assessments and histology performed to assess features of NPSLE.

Results: In this pilot study, we found that CP T cell recipient mice had increased cognitive and depressive deficits compared to PBS controls and the MRL/lpr splenic T cell recipient mice. Additionally, the CP T cell recipient mice had a significantly compromised motor function, as assessed by the number of slips while crossing a balance beam ($p = 0.0068$), when compared to the splenocyte injected groups and the PBS controls (Figure 1A). Histological assessment and immunohistochemical staining revealed an increase in lymphocytic infiltration, the number of proliferating cells (Figure 1B-C), as well as in IgG and complement deposition, in the choroid plexus of CP T recipient mice compared to the PBS group.

Conclusion: Our result indicate that T cells can migrate to and proliferate in the CP following ICV injection, and that brain infiltrating MRL/lpr T cells may be a key contributor to the pathogenesis of NPSLE.

Disclosure: E. Moore, None; **M. Huang**, None; **C. Reynolds**, None; **C. Putterman**, Equillium, 5, Equillium, Inc, 2, 5, Exagen, 2.

Abstract Number: 1786

Surrogate Pathways of Complement Activation in Novel Polygenic SLE-like Models of Kidney Injury

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Animal Models
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Lupus nephritis (LN) is a major contributor to morbidity and mortality in systemic lupus erythematosus (SLE). Defective clearance of apoptotic cells (AC), autoantibodies, and low complement levels are three hallmarks of SLE pathogenesis that have not yet been captured in a single disease model. We posit that such a model will allow us to elucidate the clinically relevant mechanisms of kidney injury in SLE and shed light on the multifaceted role of complement in this disease.

Methods: To investigate mechanisms of kidney injury in a disease model that mimics the polygenic nature of human SLE, we generated C57BL/6 mice that produced anti-chromatin antibodies (*Sle1*), had defective clearance of AC (*Mfge8*-/-) and were deficient in either C1q [C1q Triple mutant (C1qTM)] or C3 (C3TM). Kidney injury was evaluated by urine albumin/creatinine ratio (UACR), PAS staining, immunofluorescence (IF) staining and electron microscopy (EM). The effect of thrombin inhibition with argatroban on kidney injury in *Mfge8*-/-*C3*-/- (C3 double mutant, DM) mice was studied in the nephrotoxic-nephritis (NTN) model of kidney injury.

Results: C1qTM and C3TM mice, but not any double mutant controls, developed spontaneous membranoproliferative glomerulonephritis (MPGN) with PAS positive deposits, glomerular hypercellularity and variable mesangial and endocapillary proliferation at ~10 months of age. EM revealed features reminiscent of human LN: “wire loop”

and glomerular mesangial immune deposits in fibrillary organized structures. MPGN in C1qTM and C3TM mice was accompanied by increased glomerular deposition of IgG and AC. At 5 months of age, C1qTM and C3TM mice spontaneously developed high anti-dsDNA and anti-chromatin IgG titers as well as marked antigen spreading, including antigens previously implicated in LN pathogenesis.

Remarkably, IF staining revealed membrane attack complex (MAC) deposition in both TM strains. In C1qTM mice MAC deposition was associated with glomerular deposition of C3/C3d. Terminal complement activation in C3TM kidneys was accompanied by increased glomerular deposition of the thrombin substrate, fibrin. We also observed increased thrombin enzymatic activity in the plasma of C3TM mice, relative to C1qTM controls. Using the NTN model of kidney injury in *Mfge8-/-C3-/-* mice, the thrombin inhibitor, argatroban, significantly reduced glomerular MAC deposition and UACR, compared to vehicle treated controls.

Conclusion: In the context of reduced clearance of AC (*Mfge8-/-)* and non-pathogenic autoantibodies (*Sle1)*, early complement component deficiencies (C1q or C3) have two distinct effects: i) their absence leads to B cell activation and epitope spreading and ii) surrogate pathways allow terminal complement MAC activation. In C1qTM mice, increased glomerular C3/C3d deposition suggests activation of the lectin or alternative complement pathways, in the absence of C1q. Increased fibrin deposition in C3TM and rescue of proteinuria in NTN C3DM mice by a thrombin inhibitor, suggest that thrombin acts as a C5 convertase in low C3 states. These data encourage surrogate pathway evaluation in SLE patients with low complement states and offer new potential targets for therapy.

Disclosure: S. Skopelja-Gardner, None; **X. Sun**, None; **Y. Peng**, None; **L. Colonna**, None; **P. Hermanson**, None; **L. Tanaka**, None; **J. Tai**, None; **D. Salant**, None; **K. Elkon**, None.

Abstract Number: 1787

The Glucocorticoid-Induced Protein GILZ Represent a Checkpoint in the IFN Program in SLE

Eric Morand ,[1] Champa Nataraja,[1] Melissa Northcott,[1] Wendy Dankers,[1] Jacqueline Flynn,[1] Wendy Zhu,[1] Taylah Bennett,[1] Mehnaz Pervin,[1] Brendan Russ,[1] James Harris,[1] and Sarah Jones[1], [1]Monash University, Melbourne, Victoria, Australia

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Animal Models
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Given the primacy of Type I interferon (IFN) pathways in SLE pathogenesis, and the near-ubiquity of glucocorticoid (GC) use in SLE treatment, clarifying the intersection between these two domains is required. IFN activation in SLE appears largely GC-resistant, suggesting a permissive defect in GC-mediated regulatory events in SLE. GC-induced leucine zipper (GILZ) (*TSC22D3*) is one of the most exquisitely GC-sensitive genes in the genome, has endogenous effects which limit activation of T cells, B cells, macrophages and dendritic cells, but is underexpressed in SLE. We investigated the effect of GILZ on the IFN program in SLE.

Methods: Wildtype and GILZ deficient mice, and isolated cells, were stimulated using TLR ligands, and the effects of GILZ deficiency measured by qPCR, ELISA, Luminex, bioassay, and FACS. IFN effects on GILZ expression were studied in human PBMC and in public gene expression datasets. Mechanisms of regulation examined by ChIP.

Results: GILZ overexpression in human cells suppressed IFNα-induced gene expression. Conversely, loss of GILZ permitted unregulated expression of IFNs and other pro-inflammatory cytokines, including in vivo, in response to TLR ligands. GILZ directly suppressed TLR-stimulated expression of IRF7, the transcription factor that drives production of IFNα, by binding at the IRF7 locus. In parallel, IFNα suppressed GC induction of GILZ in PBMC, through direct binding of STAT1 at the GILZ promoter. Correspondingly, GILZ expression was significantly lower in IFN-positive SLE patients. Murine lupus and IFN activation were exacerbated when GILZ was deleted.

Conclusion: This work establishes GILZ as a key regulator of the IFN program that is in turn suppressed by IFN, a finding which may provide the explanation for GC resistance in high-IFN SLE. Restoring GILZ expression and activity represents a potential therapeutic opportunity to interrupt the IFN program in SLE, without the use of GC.

Disclosure: E. Morand, AstraZeneca, 2, 5, 8, Bristol Myers Squibb, 2, Eli Lilly, 5, Janssen, 2, 5, Merck Serono, 2, 5, UCB, 2; **C. Nataraja**, None; **M. Northcott**, None; **W. Dankers**, None; **J. Flynn**, None; **W. Zhu**, None; **T. Bennett**, None; **M. Pervin**, None; **B. Russ**, None; **J. Harris**, None; **S. Jones**, None.

Abstract Number: 1788

Anti-neutrophil Extracellular Trap (NET) Autoantibodies in Primary Antiphospholipid Syndrome

Yu Zuo ,[1] Srilakshmi Yalavarthi,[2] Kelsey Gockman,[2] David Karp,[3] Quan-Zhen Li,[4] and Jason Knight[5], [1]University of Texas Southwestern, Dallas, TX, [2]University of Michigan, Ann Arbor, MI, [3]UTSouthwestern Medical Center, Dallas, TX, [4]Department of Immunology & Internal Medicine/University of Texas Southwestern Medical Center, Charleston, [5]Division of Rheumatology, Department of Internal Medicine, Michigan Medicine, Ann Arbor, MI

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Antiphospholipid Syndrome
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Neutrophil extracellular traps (NETs) are prothrombotic tangles of chromatin and microbicidal proteins ejected from neutrophils in response to a variety of stimuli. In antiphospholipid syndrome (APS), recent work has demonstrated high levels of NETs in the blood of APS patients; that antiphospholipid antibodies can engage neutrophils to trigger NET release; and that APS serum degrades NETs poorly. Here, we hypothesized that APS might be perpetuated by crosstalk between NETs and anti-NET autoantibodies.

Methods: Purified, partially-digested NETs were used to coat ELISA plates. Levels of anti-NET IgG and IgM (OD at 450 nm) were determined. A positive cut-off was established as mean OD+2 SD of healthy-control samples. For a subset of patients, we also measured autoantibody formation with a microarray platform that included 120 potential autoantigens (48 NET-associated antigens and 72 other autoantigens). Univariate logistic regression was performed to determine clinical associations. Non-parametric Mann-Whitney U-test was used to compare levels of anti-NET autoantibodies and plasma NET remnants (myeloperoxidase-DNA complexes) between groups.

Results: As compared with controls (n=46), primary APS (n=78) was characterized by marked elevations in IgG (0.51 ± 0.36 vs. 0.29 ± 0.09; p< 0.0001) and IgM (0.76 ± 0.50 vs. 0.26 ± 0.23; p< 0.0001) anti-NET autoantibodies. Importantly, levels of anti-NET antibodies did not correlate with levels of anti-β2GPI (R2 < 0.01). By univariate logistic regression, positive anti-NET IgG/IgM was significantly associated with arterial thrombosis (P< 0.0001 for IgG / P<

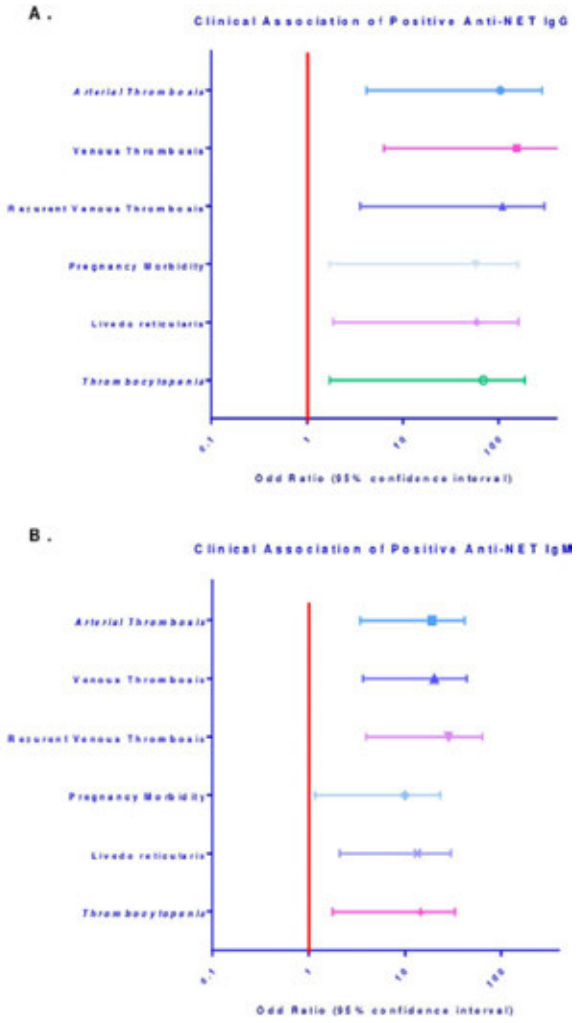

Figure 1. *Clinical association of anti-NET IgG (A) and IgM (B).*

Fig 1

0.0001 for IgM), venous thrombosis (P< 0.0001 for IgG / P< 0.0001 for IgM), and pregnancy morbidity (P=0.02 for IgG / P=0.03 for IgM). Intriguingly, positive anti-NET IgG/IgM was also associated with non-criteria features such as thrombocytopenia and livedo reticularis (Figure 1). Higher circulating NET remnants were observed in primary APS patients with venous thrombosis (P=0.0007) and recurrent venous thrombosis (P=0.0003) as compared with healthy controls (Figure 2). In pursuit of the antigen specificity of anti-NET autoantibodies, 20 of the primary APS samples were analysed by autoantibody microarray and compared with 20 matched controls. IgG/IgM autoantibodies against the following NET-relevant antigens were significantly elevated in primary APS: anti-citrullinated-histone H3, anti-chromatin, anti-nucleosome, and anti-bactericidal/permeability-increasing protein (BPI).

Conclusion: Patients with primary APS have high levels of anti-NET autoantibodies. Anti-NET IgG/IgM is associate with both criteria and some non-criteria APS clinical features. Autoantigen microarray reveals a marked enrichment of various specific citrullinated /non-citrullinated anti-NET autoantibodies in patients with primary APS. Anti-NET activity may associate with specific antigens present in NETs such as citrullinated-histone H3 and BPI. Interestingly, anti-NET autoantibodies do not correlate with anti-β_2GPI, suggesting their potential as a novel, independent, and clinically-relevant biomarker.

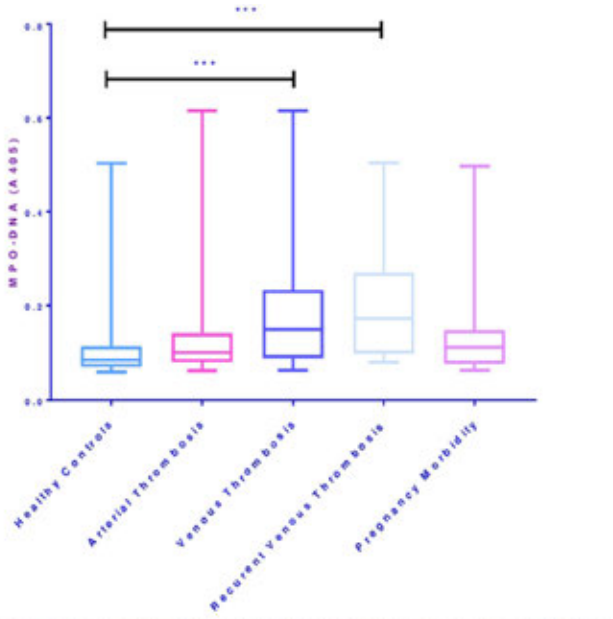

*Figure 1. Measurement of plasma MPO-DNA complexes in various groups. *** P<0.001*

Fig 2

Disclosure: Y. Zuo, None; **S. Yalavarthi**, None; **K. Gockman**, None; **D. Karp**, None; **Q. Li**, None; **J. Knight**, None.

Abstract Number: 1789

Defibrotide Inhibits Antiphospholipid Antibody-Mediated NET Release and Endothelial Cell Activation

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Antiphospholipid Syndrome
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Defibrotide is a mixture of phosphodiester oligonucleotides derived from porcine intestinal mucosa, currently approved for treatment of hepatic sinusoidal obstruction syndrome. Defibrotide has been considered a “multi-target compound,” and may have a particular role in limiting endothelial cell activation. Having said that, older literature also demonstrates anti-leukocyte and anti-neutrophil properties, with all of that work done prior to the first descriptions of neutrophil extracellular traps (NETs) in 2004. Our group and others have recently revealed a role for neutrophils and particularly NETs in the thrombotic complications of antiphospholipid syndrome (APS). Although defibrotide has been suggested as a possible treatment for APS, especially the microangiopathic variant known as catastrophic APS (CAPS), this possibility has not been investigated in the laboratory. Here, we hypothesized that defibrotide may act at the thromboinflammatory neutrophil-endothelium interface to neutralize APS-relevant NET release and endothelial cell activation.

Methods: Human neutrophils were prepared from healthy volunteers and stimulated with total IgG isolated and pooled from three CAPS patients (CAPS IgG). Stimulation was in the presence or absence of different concentrations of defibrotide, and NET release was quantified via the enzymatic activity of NET-associated myeloperoxidase.

In parallel, primary human umbilical vein cells (HUVECs) were isolated from human umbilical cord, and stimulated with 10% plasma pooled from three CAPS patients (CAPS plasma) in the presence or absence of defibrotide. Gene expression of ICAM-1, VCAM-1, and E-selectin were measured by real-time PCR. At this early stage of the study, statistical corrections were not made for multiple comparisons. P-values are therefore nominal, speaking to the scientific meaningfulness of the results, rather than statistical significance.

Results: We first assessed the effect of defibrotide on CAPS IgG-mediated NET release. As compared with control IgG, CAPS IgG triggered a significant increase in NET release from control neutrophils (~3-fold; $p< 0.05$). At doses ranging from 1 to 10 μg/ml, defibrotide significantly suppressed CAPS IgG-mediated NET release (40-50% suppression; $p< 0.05$). Interestingly, defibrotide also inhibited NET release induced by the canonical protein kinase C activator, phorbol 12-myristate 13-acetate (PMA). Regarding HUVEC activation, CAPS plasma significantly increased gene expression of ICAM-1 (~3-fold), VCAM-1 (2-fold), and E-selectin (2.5-fold), as compared with control plasma ($p< 0.05$ for each). Importantly, treatment with defibrotide returned the expression of all three genes essentially to baseline/control levels.

Conclusion: We demonstrate for the first time that defibrotide attenuates NET release and endothelial cell activation in the context of IgG and plasma derived from CAPS patients. Studies are underway to fully characterize defibrotide's mechanism of action and to assess its therapeutic potential in preclinical models of APS.

Disclosure: R. Ali, None; **H. Shi**, None; **S. Yalavarthi**, None; **J. Knight**, None.

Abstract Number: 1790

The Epidemiology of the Antiphospholipid Syndrome in the UK, 1990 – 2016

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Antiphospholipid Syndrome
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterised by recurrent vascular thrombosis and/or pregnancy morbidity in the presence of persistently positive antiphospholipid autoantibodies. It is estimated to account for 6% of all pregnancy morbidity, 13.5% of stroke, 11% of myocardial infarction and 9.5% of all deep vein thromboses. One small population-based study of APS has been reported and included only 33 individuals. This study aimed to estimate the incidence of APS and its complications in a large UK population.

Methods: A cohort study was conducted using the UK Clinical Practice Research Datalink. This is a database of primary care records kept by general practitioners in the National Health Service. It is deemed to be generally representative and contains active records for around 7% of the UK population. Data for all recorded cases of APS were included in this study. The incidence and prevalence of APS in the general population and the occurrence of venous thromboembolism (VTE), coronary heart disease (CHD), stroke and miscarriage in APS patients were estimated. The standardised mortality ratio was calculated to compare the mortality of APS patients to that of the UK general population.

Figure 1 - Age-specific incidence rates of APS for men and women

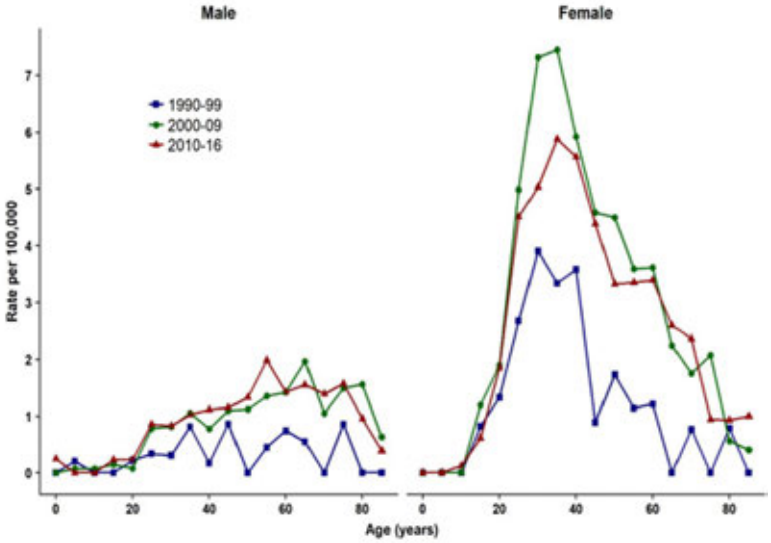

Figure 1. Age-specific incidence rates of APS for men and women

Table 1 - The incidence of complications in APS patients before and after diagnosis

	Before diagnosis		After diagnosis*	
	N	Incidence per 1,000 per year (95% CI)	N	Incidence per 1,000 per year (95% CI)
Miscarriage				
Women	247	19.0 (16.8 - 21.5)	84	10.4 (8.4 - 12.9)
Venous Thromboembolism				
Men	121	27.2 (22.7 - 32.5)	35	21.1 (15.2 - 29.4)
Women	213	15.6 (13.6 - 17.8)	10	13.4 (11.1 - 16.2)
			7	
Coronary Heart Disease				
Men	33	7.0 (5.0 - 9.9)	21	12.3 (8.0 - 18.8)
Women	41	2.8 (2.0 - 3.8)	41	4.9 (3.6 - 6.6)
Stroke				
Men	41	8.5 (6.2 - 11.5)	15	8.5 (5.1 - 14.1)
Women	76	5.2 (4.1 - 6.5)	31	3.7 (2.6 - 5.2)

*recurrent events were included after diagnosis if they were more than one year after last recorded event

Results: Data were analysed for 2,606 participants recorded with APS. In women, a peak incidence of 7.5 (95% confidence interval (CI) 6.2 to 8.9) APS cases per 100,000 person-years was observed at 35-39 years; in men, incidence reached a maximum of 2.2 (95% CI 1.2 - 3.5) per 100,000 at 55 to 59 years. Prevalence peaked at 50 (95% CI 49 - 55) in females in 2011 and 9.8 (95% CI 8.6 - 11.1) per 100,000 in males in 2012. Overall female to male ratio was 4:1. Before diagnosis, APS patients showed elevated incidence of miscarriage (19.0); VTE (men 27.2; women 15.6); CHD (men 7.0; women 2.8); and stroke (men 8.5; women 5.2) per 1,000 per year. The rate of miscarriage was lower after APS diagnosis (10.4 per 1,000 per year, 95% CI 8.4 – 12.9). There was no significant change in the rate of thrombotic complications after APS diagnosis. SLE was found in 20% of APS cases (SLE-APS). Female to male ratio was higher in this group compared to APS patients without SLE (10:1 and 4:1, respectively) and there was no significant difference in the rate of miscarriage or thrombotic manifestations. The overall standardised mortality ratio was 1.49 and 1.33 in females and males respectively.

Conclusion: This is the largest cohort of APS patients published to date. The overall estimated incidence is 1.8 and point prevalence of 43 per 100,000 persons in 2015. APS patients have elevated rates of thromboses, miscarriage and death compared to the general population.

Disclosure: M. Rodziewicz, Pfizer, 9; **D. D'Cruz**, AstraZeneca, Bristol-Myers Squibb, 2, 5, Eli Lilly, Eli Lily, 2, 5, GlaxoSmithKline, 2, 5, Human Genome Sciences, 5, Idorsia, Merck Serono, 2, 5, Pfizer, Roche, 5, TEVA, 2, 5; **M. Gulliford**, None; **N. Hazra**, None.

Abstract Number: 1791

Antiphospholipid Antibody Profile Stability over Time: Prospective Results from AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository ("Registry")

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SESSION INFORMATION
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Session Title: Antiphospholipid Syndrome
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Background/Purpose: APS ACTION "Registry" was created to study long-term outcomes in persistently antiphospholipid antibody (aPL)-positive patients with and without other systemic autoimmune diseases. Our primary objective was to determine whether clinically significant aPL profiles at baseline remain stable over time.

Methods: A web-based data capture system is used to store patient demographics and aPL-related medical history. Inclusion criteria are positive aPL, based on the Updated Sapporo APS Classification Criteria, tested at least twice within one year prior to enrollment. Patients are followed every 12±3 months with clinical data and blood collection. For this prospective analysis of available follow-up (f/u) aPL tests, *clinically significant aPL profile* was defined as

Table: Baseline Clinical and Laboratory Characteristics of 420 Patients with Stable or Unstable aPL Profile at Follow-Up Included in APS ACTION Clinical Database and Repository ("Registry")

	Total (n=420)	Clinically Significant aPL Profile		p-value
		Stable (n=366)	Unstable (n=54)	
Female	305 (73%)	267 (73%)	38 (70%)	0.74
Age Median (IR)	48.9 [48.1, 50.4]	48.6 [47.9, 49.4]	48.6 [48, 50]	0.09
White	279 (78%)	238 (77%)	41 (87%)	0.3
Non-Latin American	165 (39%)	137 (37%)	28 (52%)	0.46
Smoking History	46 (11%)	42 (11%)	4 (7%)	0.66
Autoimmune Disease				
aPL/APS Only	278 (66%)	244 (67%)	34 (63%)	0.76
Other SAIDx	148 (35%)	128 (35%)	20 (37%)	
aPL-Related History				
Vascular Event (any)	285 (68%)	245 (67%)	40 (74%)	0.35
Venous Event (any)	183 (64%)	153 (62%)	30 (75%)	0.16
Arterial Event (any)	125 (44%)	115 (47%)	10 (25%)	*0.01*
TIA (any)	38 (9%)	37 (10%)	1 (2%)	*0.04*
aPL Tests				
Lupus Anticoagulant (+)	319 (80%)	288 (83%)	31 (58%)	*<0.001*
aCL IgG ≥ 40U	202 (48%)	183 (50%)	19 (35%)	0.06
aCL IgM ≥ 40U	93 (22%)	89 (24%)	4 (7%)	*0.004*
aβ_2GPI IgG ≥ 40U	139 (33%)	130 (36%)	9 (17%)	*0.005*
aβ_2GPI IgM ≥ 40U	81 (19%)	76 (21%)	5 (9%)	0.06
≥ 2 Positive aPL Tests	244 (58%)	226 (62%)	18 (33%)	*<0.001*
Medications (Baseline)				
Aspirin	201 (48%)	187 (51%)	14 (26%)	*<0.001*
Warfarin	223 (53%)	192 (52%)	31 (57%)	0.68
Hydroxychloroquine	194 (46%)	168 (46%)	26 (48%)	0.82

IR: Interquartile Range, **aPL:** Antiphospholipid Antibody, **APS:** Antiphospholipid Syndrome, **SAIDx:** Systemic Autoimmune Diseases, **TIA:** Transient Ischemic Attack, **aCL:** Anticardiolipin Antibody, **aβ_2GPI:** Anti-β_2-Glycoprotein-I Antibody

positive lupus anticoagulant (LA) test and/or aCL/aβ_2GPI IgG/M ≥40U. *Stable aPL profile* was defined as a clinically significant aPL profile in at least two-thirds of f/u measurements. Univariate and multivariable generalized linear mixed models with logit link were used to assess the effect of time and other variables of interest on odds of clinically significant aPL profile. Wilcoxon rank-sum and Fisher's exact tests were employed to compare clinical characteristics of patients with stable versus unstable aPL profiles.

Results: As of January 2019, 796 patients were enrolled from 26 centers worldwide, 482 had f/u visits with aPL results, and 472 patients had a clinically significant aPL profile at baseline. Based on aPL profiles at f/u visits (median follow up: 5.1 years [interquartile range [IR]: 4.3, 5.8]; median number of f/u visits with aPL profiles: 2 [interquartile range: 1, 3]), 366/472 (78%) patients had stable aPL profiles over time (54 [11%] unstable; 52 [11%] inconclusive). Time did not affect odds of maintaining a clinically significant aPL profile at f/u (p=0.906). In multivariable analysis, time, age, concomitant systemic autoimmune disease (mainly lupus), smoking history, and hydroxychloroquine use did not affect odds of maintaining a clinically significant aPL profile at f/u. Based on crude unadjusted comparisons, patients with stable aPL profiles, compared to those with unstable profiles, were more likely to have baseline positive LA test, aCL IgM ≥ 40U (positive trend for IgG), aβ_2GPI IgG ≥ 40U (positive trend for IgM), two or more positive aPL tests, and history of arterial events and aspirin use (Table).

Conclusion: In approximately 80% of patients with a baseline clinically significant aPL profile (LA test and/or aCL/aβ_2GPI IgG/M ≥40U), aPL profiles remain consistently significant (stable) during five years of follow-up. Further mul-

tivariate analysis will investigate predictors of aPL profile stability over time, and guide future validation studies of stored samples through APS ACTION core laboratories.

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Abstract Number: 1792

Cognitive Dysfunction (CD) and Serum Levels of Brain-Derived Neurotrophic Factor (BDNF) in Primary Antiphospholipid Syndrome (PAPS)

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SESSION INFORMATION
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Background/Purpose: Cognition dysfunction (CD) is a poorly understood non-stroke central neurologic manifestation of antiphospholipid syndrome, whose diagnosis involves a specific neuropsychological (NP) evaluation. Brain-derived neurotrophic factor (BDNF) is a protein that plays an important role in neural plasticity, and could potentially be a biomarker of CD in primary antiphospholipid syndrome (PAPS). Our aim was to assess CD in PAPS patients and to evaluate its association with clinical data, antiphospholipid antibodies and serum BDNF levels.

Methods: This is a cross-sectional study that compared 44 PAPS patients (according to Sydney´s criteria) and 20 healthy controls matched for age, gender and education. PAPS patients and controls underwent a standardized cognitive examination. The demographic, clinical, and laboratorial characteristics of patients were recorded. Serum BDNF was measured by sandwich ELISA.

Results: Fourteen of the 44 (31,8%) PAPS patients had cognitive impairment compared with only 1 (5%) healthy control (p=0.019). The most common cognitive domains involved were verbal memory, executive function and attention. PAPS patients presented lower serum levels of BDNF compared to controls (p=0.007) and it was associated

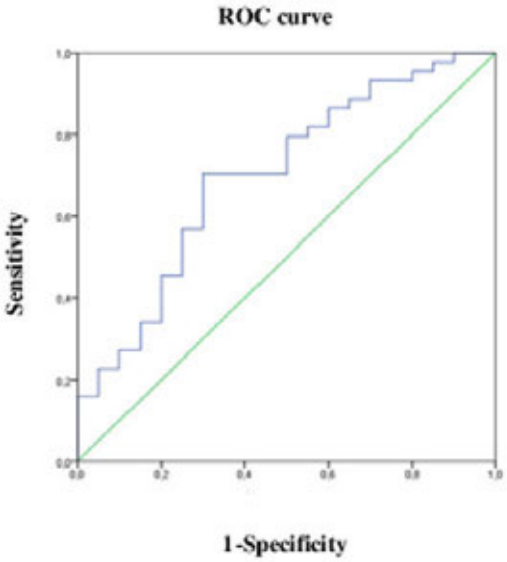

Figure 1: Receiver-operation characteristic (ROC) curve for determination of the cut-off for serum BDNF between PAPS and Control groups (Area under the curve = 0.700 ± 0.071; p=0.011; cutoff=736.5 ng/mL, sensitivity:70.5%, specificity: 70.0%).

with CD (p=0.032). The calculated cut-off value of serum BDNF was 736.5 ng/mL with sensitivity of 70.5% (CI95% 0,54-0,83), specificity of 70.0% (CI95% 0,45-0,88) and accuracy of 70.3% (CI95% 0,57-0,81)(Figure 1)**.** In a multivariate logistic regression stroke (OR 137.06; 95%CI, 4.73-3974.32; p=0.004), seizure/ epilepsy (OR 15.25; 95%CI, 0.65-356.37;p=0.090) and serum BDNF (OR 0.66; 95%CI, 0.41- 1.07;p=0.091) were independently associated with CD in PAPS.

Conclusion: Cognitive dysfunction is frequently diagnosed late in PAPS patients. The association of CD and low serum BDNF levels suggests that this neurotrophin can be a potential biomarker for predicting early cognitive dysfunction.

Disclosure: R. Rosa, None; **M. Remião Ugolini-Lopes**, None; **A. Gandara**, None; **K. Campanholo**, None; **L. Dutra**, None; **D. Andrade**, None.

Abstract Number: 1793

Descriptive Analysis of Biopsy-proven Antiphospholipid Antibody-associated Nephropathy Patients Included in the AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository (“Registry”)

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Background/Purpose: Antiphospholipid antibody (aPL) nephropathy is a distinct entity that can be challenging to recognize and treat; it remains unknown if uniform pathologic criteria are used to characterize this diagnosis world-wide. The primary aim of this project was to evaluate how aPL nephropathy lesions as described in renal biopsy reports of APS ACTION registry patients with "biopsy-proven aPL nephropathy".

Methods: APS ACTION "Registry" was created to study long-term outcomes in persistently aPL-positive patients with and without other systemic autoimmune diseases. The registry includes adults aged 18 to 60 years with positive aPL, based on the Updated Sapporo APS Classification Criteria, tested on two occasions at least twelve weeks apart within one year prior to enrollment. We descriptively reviewed the results and conclusion sections of the renal biopsy reports of APS ACTION registry patients with biopsy proven aPL nephropathy. For biopsies not reported in English, translation was provided by specific APS ACTION centers. We categorized patients based on whether the biopsy report conclusion specifically stated "acute" versus "chronic" aPL nephropathy. We compared the terminology used

Description of aPL-Nephropathy Biopsy Reports of Patients in APS ACTION Registry (2000-2019)

	"Acute" aPL-Nephropathy n: 3	"Chronic" aPL-nephropathy n: 8	"aPL" Nephropathy* n: 14	
Sapporo aPL Nephropathy Terminology				*Alternative Definitions Representative of Sapporo Terminology*
Thrombotic Microangiopathy	3	3 **	5 ***	
Fibrous Intimal Hyperplasia	1	7	8	*Intimal sclerosis, intimal fibrosis with/without mucoid intimal edema, and, fibro-intimal thickening (14 of 16 biopsies)*
Recanalization	0	3	0	-
Organized Microthrombi	1	2	0	*Chronic thrombi (1 of 3 biopsies)*
Fibrous/Fibrocellular Occlusions	0	1	0	*Arteriole with obliteration of lumen by intimal expansion (1 of 1 biopsy)*
Focal Cortical Atrophy	2	8	12	*Scarring, tubular atrophy, interstitial fibrosis, and ischemic glomeruli (19 of 22 biopsies)*
Thyroidization	0	2	0	-
Other Terminology				
Fibrin Thrombi	3	0	4	-
Focal Segmental Glomerulosclerosis	0	6	1	--
Membranous Glomerulonephritis	0	1	5	-

*Acute vs chronic status not reported (4 did not use the term "aPL nephropathy"); **reported as "chronic TMA" (n: 1); ***: reported as "chronic TMA" (n: 2).

in the biopsy reports to the aPL-nephropathy definitions from the 2006 APS Sapporo Classification Criteria (thrombotic microangiopathy [TMA] involving both arterioles and glomerular capillaries, fibrous intimal hyperplasia involving organized thrombi with/without recanalization, fibrous/fibrocellular occlusions of arteries and arterioles, focal cortical atrophy, and tubular thyroidization). Under the guidance of a team of experts in aPL-nephropathy (MT, MT, SS), we used our clinical judgement in the interpretation of "alternative" biopsy report terms representative of the Sapporo criteria terms. Based on our literature review of terminology used to define aPL nephropathy, we also included "other" biopsy findings that may be associated with aPL.

Results: Of 804 patients included in the registry as of Jan 2019, 23 patients (3%) had "biopsy-proven aPL nephropathy". Twelve (52%) patients had primary APS, and 11 (48%) fulfilled the ACR lupus classification criteria. Two patients had kidney biopsies twice; thus 25 biopsy reports, performed between 1997 and 2018 were reviewed. Majority of biopsies (14/25) did not specify "acute" versus "chronic" aPL nephropathy. The number of biopsy reports with aPL-nephropathy related terms (Sapporo, alternative, and other) is shown in Table; four out of 7 Sapporo terms were also represented by alternative terminology . While "TMA" was reported in 11/25 (44%) of the biopsies: a) 9/11 (82%) used the term in the conclusion; b) 3/11 (27%) used the term "chronic TMA"; and c) 2/11 biopsies did not report the type of TMA (glomerular: 6; arterial/arteriolar: 2; both: 1; and unspecified: 2).

Conclusion: The use of aPL-nephropathy related terms varies among pathologists while reporting the biopsy findings of kidney involvement in aPL-positive patients. An international effort/consensus is needed to update and harmonize the terminology used to describe aPL-nephropathy.

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Abstract Number: 1794

An Evaluation of Burnout Among U.S. Rheumatology Fellows: A National Survey

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SESSION INFORMATION
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Session Title: Education
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Session Time: 2:30PM–4:00PM

Background/Purpose: Physician and trainee retention is critical given the significant projected workforce shortage of rheumatologists. While previous studies have reported significant burnout among physicians and trainees as a

Table 1. Burnout, Depression, and Quality of Life of U.S. Rheumatology Fellows by Training Year.			
Characteristic	PGY4 (n=39)	PGY5, PGY6 (n = 66)	*P* value
Burnout Index, no. (%)*			
Burned out ¹	11 (28.2)	7 (10.6)	0.021
Emotional Exhaustion, high score	11 (28.2)	7 (10.6)	0.021
Depersonalization, high score	9 (23.1)	6 (9.1)	0.048
Screened positive for depression, no. (%)	5 (12.8)	1 (2.44)	0.016
Quality of life^, mean (standard deviation [SD])			
• Overall	6.87 (1.87)	7.79 (1.28)	0.004
• Mental	6.95 (1.95)	7.83 (1.33)	0.007
• Physical	6.28 (1.67)	7.56 (1.31)	<0.001
• Emotional	6.92 (2.22)	7.54 (1.59)	0.099
Fatigue^			
• Mean (SD)	5.67 (1.95)	6.81 (1.92)	0.004
• High fatigue, no. (%)	20 (51)	21 (32)	0.048

*We assessed burnout using the single-item measures for emotional exhaustion and depersonalization adapted from the full Maslach Burnout Inventory.

¹We used a high emotional exhaustion or depersonalization score on the Maslach Burnout Inventory indicating a frequency of weekly or more often to categorize a respondent as "burned out".

^ Quality of life and fatigue range 0-10 with a lower score indicating worse fatigue or quality of life.

Table 2. Multivariate Models of Burnout Unadjusted and Adjusted for Covariates.		
Characteristic	Unadjusted OR (95% confidence interval)	Adjusted^ OR (95% confidence interval)
Training year		
• PGY4	Reference	Reference
• PGY5 & PGY6	0.30 (0.11, 0.86)*	0.47 (0.14, 1.50)
Age		
• 26-30	Reference	Reference
• >31	0.19 (0.06, 0.57)*	0.23 (0.06, 0.82)*
Gender		
• Male	Reference	
• Female	1.51 (0.49, 4.63)	
Race		
• White	Reference	
• Asian	1.42 (0.48, 4.21)	
• Non-white, non-Asian	2.36 (0.40, 14.04)	
Relationship Status		
• Single	Reference	
• Married/Partnered	0.72 (0.24, 2.14)	

¹We used a high emotional exhaustion or depersonalization score on the Maslach Burnout Inventory (indicating a frequency of weekly or more often to categorize a respondent as "burned out")

*p<0.05

^Adjusted for all variables listed in table with p-value <0.05 in bivariate analysis

whole, there have not been any national studies of burnout among rheumatology trainees. The objective of this study is to evaluate levels of burnout among U.S. rheumatology fellows.

Table 3. Thematic Analysis of Open-ended Responses on Factors that Improve and Worsen Burnout.	
Factors Leading to Increased Burnout	Factors Leading to Reduced Burnout
Pager	Exercise
Documentation	Family/friends
Long hours	Sleep
Demands of patient care	Hobbies
Presentations and expectations	Support from colleagues and superiors

Methods: This is a cross-sectional study of U.S. rheumatology fellows conducted anonymously via an electronic survey tool from January to February 2019. The survey was disseminated to fellows at ACGME-accredited adult and pediatric rheumatology programs via the ACR program directors' listserv and ACR Fellows-In-Training Google group. Participants were given an incentive for participation in form of raffle of an Amazon gift card. Survey instruments included the Maslach Burnout Inventory (MBI) and the Patient Health Questionnaire 2 (PHQ2) to measure depression. We also measured burnout using the single-item measures for emotional exhaustion and depersonalization adapted from the full MBI. Measures of fatigue, quality of life, demographics (age, gender, ethnicity, marital status), and training year were also collected. We included open-ended questions about perceived factors to promote resiliency and reduce burnout and factors that worsen or lead to increased levels of burnout. Bivariate and multivariate regression analyses were used to examine correlates of burnout using STATA statistical software (STATA Corp. 2017). Open-ended responses were analyzed using thematic analysis.

Results: Response rate was 18.5% (105/567 total pediatric and adult rheumatology fellows) based on most recent data of trainees from 2017-2018. Survey responders were 64.8% female, 69.5% between 31-35 years, 59% white, and 61.9% married. When utilizing the MBI, 28.2% of PGY4 and 10.6% of PGY5/6 rheumatology fellows were found to have at least one symptom of burnout (p = 0.021). 12.8% of respondents in PGY4 year met criteria for depression compared with 2.4% in PGY5/6. In addition, PGY4 fellows reported worse fatigue and poorer quality of life compared with PGY5/6 (table 1). In multivariable models that controlled for training year and gender, higher age was associated with decreased odds of burnout (table 2). Additionally, PGY5/6 training year was associated with reduced odds of burnout in unadjusted models, but this effect was attenuated in adjusted models.

In thematic analysis of open-ended survey responses, participants identified factors to promote resilience and reduce burnout including: exercise, family/friends, sleep, support at work, and hobbies. Factors that contribute to burnout included pager, documentation, presentations/expectations, long hours, and demands of patient care.

Conclusion: This national survey of U.S. rheumatology fellows reveals that early trainee level and younger age are associated with worsened levels of fatigue, quality of life, and burnout. While awareness of and strategies to reduce burnout are needed for all fellows, targeted interventions for younger fellows and those in their first year of training may be of highest yield.

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Abstract Number: 1795

Education of Rheumatology Faculty: Evaluation of an Interactive Team Based Approach versus Traditional Didactic Teaching

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Background/Purpose: Medical schools have been moving from traditional teaching to interactive approaches. Team-based learning (TBL) is a conceptual model that focuses on learner engagement, and the current literature focuses on the use of TBL in health profession learners. The impact of interactive small group sessions on attending physicians has not been well elucidated (Reimschisel et al, Medical Teacher, 2017), nor has the application of TBL in rheumatology topics been well studied. The major aim of this study was to determine if TBL can be used effectively to increase topic specific competency and comfort with management among a group of faculty learners when compared to didactic lecture.

Methods: Informed consent was obtained from all participants, the majority of whom were clinical faculty rheumatologists. There were 2 sessions on various aspects of osteoporosis: A 1-hour lecture and a TBL session. Knowledge based multiple choice questions were administered pre and post each session. For TBL, a pre-reading assignment was given and participants completed individual readiness assurance tests and group application exercises. Pre and post surveys assessing learning preferences and comfort with diagnosing and treating osteoporosis were completed. Comfort was measured on a 5-point Likert scale (1: not comfortable and 5: very comfortable). Paired and independent samples t-tests were used for analyses.

Results: There were 17 participants in each group. For the lecture group, there were significant improvements in pre and post session test scores (0.2±0.4 vs 1.4±0.6, p = p < 0.001), comfort with diagnosis (3.3±1.3 vs 3.9±0.8, p = 0.045) and treatment (2.9±1.3 vs 3.8±0.9, p = 0.006), moving from neutral to comfortable ranges. The lecture was helpful for 88% and liked by 82%. For the TBL group, there were no significant changes in pre and post test scores (1.4±1.1 vs 1.5±0.07, p = 0.525), comfort with diagnosis (3.2±1.1 vs 3.5±1.1, p = 0.160) or treatment (3.0±0.8 vs 3.5±1.1, p = 0.128), though comfort moved from neutral to comfortable ranges. TBL was helpful for 82%, liked by 88% and 82% completed the pre-reading. When comparing groups, the lecture group had greater improvement in test scores (p = 0.016), but there were no differences in comfort with diagnosis (p = 0.459) or treatment (p = 0.326). Preferences for combined learning methods increased from 53% to 88% after TBL completion.

Conclusion: In an era emphasizing interactive learning, this study shows that traditional lecture formats remain effective in increasing topic specific knowledge, as well as comfort with diagnosis and treatment. Both sessions were well liked, leading to a considerable change in learning preferences for the TBL group. High rates of pre-reading completion possibly contributed to baseline differences between the groups and lack of change in test scores. Comfort did increase within the TBL group. The addition of an interactive session to a lecture-based curriculum may further refine knowledge and augment comfort levels. Additional research is needed regarding potential differences in knowledge retention between the groups.

Disclosure: A. Kwiatkowski, None; **N. Shakoor**, None; **A. Ruthberg**, None; **J. Block**, Abbvie, 2, ACR, 6, Agios, 7, Daiichi-Sankyo, 7, GlaxoSmithKline Consumer Healthcare, 5, Jannsen, 2, Medivir, 5, Novartis, 2, OARSI, Omeros, 7, Pfizer, 2, TissueGene, 2, Zynerba Pharma, 5; **S. Khandelwal**, None.

Abstract Number: 1796

Identifying Educational Themes and Knowledge Gaps Through Analysis of Electronic Consultation (eConsult) Communication Between Primary Care Physicians and Rheumatologists

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Education
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Despite advancements in management of rheumatologic diseases, barriers still exist for timely access to care. Electronic consultation (eConsult) use has increased in response to positive outcomes such as increased ability for primary care physicians (PCPs) to manage patient care, decreased wait time for

Table 1. Question type queried by PCP to Rheumatology eConsultant, n= number of questions

n=	139	
Questions regarding specific further work up required to understand a patient's constellation of symptoms	60	43.2%
Questions on specific treatment recommendations for symptoms (mainly medication)	27	19.4%
Question of confirmation of their suspected diagnosis	21	15.1%
Question of whether Rheumatology evaluation is required	18	12.9%
Question of whether expedited or routine Rheumatology evaluation required	13	9.4%

Table 2. PCP question content themes, n= number of identified themes

n=	106	
Questions centered around joint pain/arthralgias	48	45.3%
Abnormal serology or CRP/HsCRP (27)		
Normal serology or CRP/HsCRP (9)		
Serology or CRP/HsCRP not checked (12)		
Question regarding abnormal laboratory tests	25	23.6%
Abnormal serologies such as ANA/RF (20)		
Elevated CPK/Aldolase (5)		
Question on management of established rheumatic disease	12	11.3%
Confirmation of a diagnosis based on stated clinical characteristics (i.e. Relapsing Polychondritis,? Gout, ? autoimmune disease)	11	7.5%
Question on rash or biopsy	7	6.6%
Question on imaging	3	2.8%

Table 3. Rheumatology eConsultant teaching themes, n= number of identified themes

	n= 119	
Education on specific rheumatic disease	39	32.8%
PMR (9)		
Crystalline arthropathy (8)		
Myositis (7)		
Sjogren's syndrome (4)		
Spondyloarthropathy (3)		
Scleroderma (3)		
Relapsing Polychondritis (1)		
Fibromyalgia (2)		
Sweet's syndrome (1)		
Retroperitoneal fibrosis (1)		
Laboratory test interpretation	34	28.6%
Autoantibodies in rheumatic disease (24)		
HsCRP vs CRP value (10)		
Education on differential diagnoses of rheumatic diseases	27	22.7%
Non-inflammatory versus inflammatory arthropathy (18)		
Rheumatic causes of skin rash (6)		
Membranous nephropathy causes (1)		
Migratory arthritis (1)		
Elevated CPK/Aldolase (1)		
Management of specific rheumatic disease	16	13.4%
Radiographic/Imaging findings in rheumatic disease	3	2.5%

subspecialty visits, and satisfaction of PCPs. Studies have also investigated common eConsult diagnoses along with which types of questions were associated with recommendations for subsequent Rheumatology outpatient consultations.

eConsults also provide a forum of education by providing immediate feedback and by developing educational content based on common themes stemming from PCP questions. The objective of our study was to identify these themes and knowledge gaps in PCP's understanding of rheumatic diseases which may be used to improve patient care.

Methods: We performed a qualitative analysis of eConsult encounters from 2018-2019. Conventional content analysis was used to explore themes in eConsult communication from 1) questions posed by the PCP and 2) the recommendations provided by the Rheumatologist eConsultant. Each eConsult question and response could contain multiple themes. We also investigated if the Rheumatologist eConsultant recommended a visit following the eConsult.

Results: We reviewed 102 eConsult communications, 18% provided recommendations without a need for a face-to-face rheumatology appointment. The most common question types by the PCP were: further work up required to understand a patient's constellation of symptoms (43%), treatment recommendations for patient's symptoms (19%), and diagnosis confirmation based on patient's clinical history (15%). Within these question types, the following themes in question content were the most prevalent: joint pain/arthralgias (45%), abnormal autoantibody or inflammatory markers (24%), and management of an established rheumatic disease (11%). Table 2.

The most common educational recommendations provided by the Rheumatology eConsultant included: education on specific rheumatic diseases (33%, PMR most common), laboratory test interpretation (29%, autoantibody analysis most common), and differential diagnoses of rheumatic diseases (23%, features of non-inflammatory vs. inflammatory arthritis most common). Table 3.

The following knowledge gaps were identified: overdiagnoses of PMR, use of CRP and HsCRP interchangeably, and differentiation between inflammatory and non-inflammatory arthritis prior to lab testing.

Conclusion: This analysis of eConsult communication revealed common themes in both PCP questions and Rheumatologist recommendations. This knowledge may lead to focused educational opportunities, with greater understanding of rheumatic diseases and reduction in unnecessary lab testing. A larger proportion of eConsult questions required an outpatient visit than previously reported at other institutions. This highlights the importance of a detailed physical exam and subtle history in rheumatic disease diagnosis which often requires face to face visits with patients rather than relying solely on lab testing. This was a common teaching theme seen in our eConsults.

Disclosure: R. Jain, None; **A. Broder**, None; **S. Rikin**, None.

Abstract Number: 1797

Rheumatology Mechanism Madness: A Pilot Collaborative Learning Activity for Rheumatology Trainees

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SESSION INFORMATION
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Session Title: Education
Session Type: ACR Abstract Session
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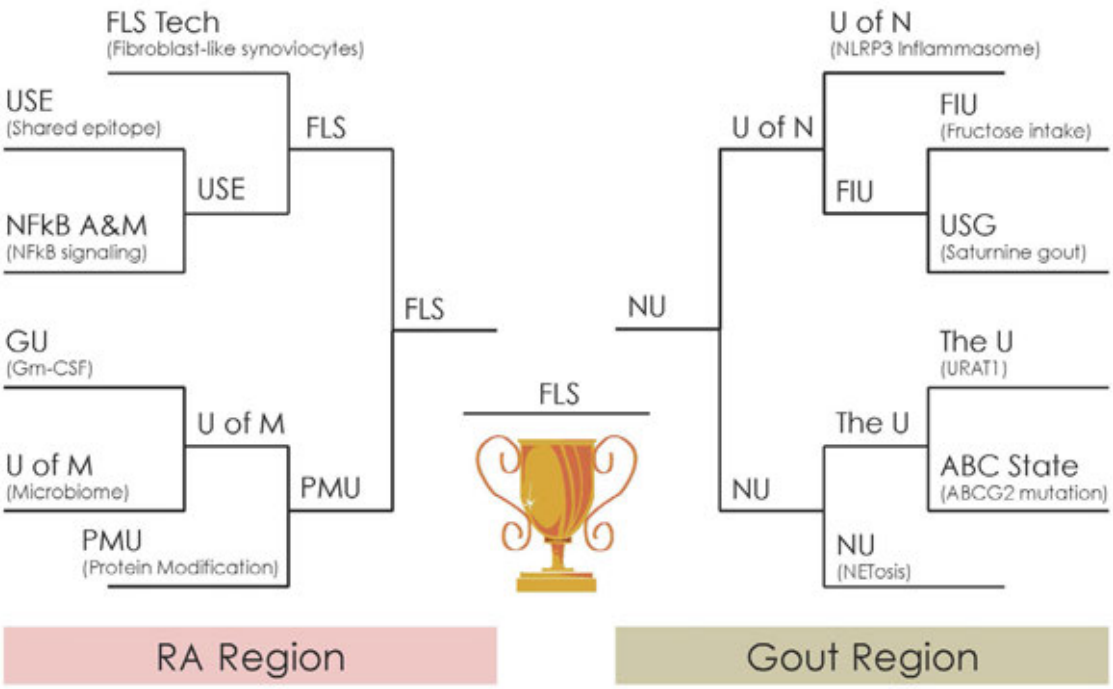
Figure 1: Rheumatology Mechanism Madness Bracket
(including winners of each matchup)



Background/Purpose: The Community of Inquiry (CoI) is a framework to understand how a group of individuals learns together and includes concepts of social, teaching, and cognitive presences. Inspired by the popular Neph-Madness online educational tournament that mimics the NCAA "March Madness" basketball tournament, we piloted Rheumatology Mechanism Madness (RMM) at our institution. Our primary goals were to test feasibility and assess the activity's educational impact using the CoI framework.

Methods: In two core curriculum sessions, fellows together identified and chose key disease mechanisms in RA and gout to include as individual "teams" in the RMM bracket. Fellows then wrote half page "scouting reports" reviewing each mechanism and presented topic overviews at one divisional grand rounds. The Division was invited to complete brackets and attendees voted for the winner of each matchup during grand rounds. We reviewed metrics on tournament engagement and distributed a modified validated CoI survey to the fellows who participated in RMM. In the CoI survey, cognitive presence describes learners' progression through four stages of cognitive processing: triggering, exploration, integration, and resolution; teaching presence describes the oversight of the learning activity. Our modified CoI survey included questions relating to the cognitive and teaching presences but omitted social presence as our fellows had already developed a social community. Each question was rated on a 5-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree). Data was analyzed using descriptive statistics.

Results: Fellows created a bracket with 12 mechanisms related to RA and gout (Figure 1). Out of 32 possible participants in our division, 19 (59%) submitted a bracket. The winning pathogenic mechanism was fibroblast-like synoviocytes in RA, and one participant correctly predicted every matchup outcome. All 6 fellows who participated in RMM responded to the post-survey. The average Likert score for questions relating to the cognitive presence was 4.1; subdomain scores were: triggering 4.6, exploration 3.9, integration 4.2, and resolution 4.1 (Table 1). The average Likert score for questions relating to the teaching presence was 4.5; subdomain scores were: design and organization

Table 1: Cognitive Presence Survey Results

Survey Questions by Community of Inquiry Domain	Total Reporting Each Score on 5-point Likert Scale (n) 1 Strongly Disagree	2 Disagree	3 Neutral	4 Agree	5 Strongly Agree	Average Likert Score
Triggering Event						
Problems posed increased my interest in course issues.	0	0	0	2	4	4.7
Course activities piqued my curiosity.	0	0	0	2	4	4.7
I felt motivated to explore content related questions.	0	0	0	3	3	4.5
Overall Triggering Event	0	0	0	7	11	4.6
Exploration						
I utilized a variety of information sources to explore problems posed in this course.	2	0	1	2	1	3.0
Brainstorming and finding relevant information helped me resolve content related questions.	0	1	0	3	2	4.0
The discussions were valuable in helping me appreciate different perspectives.	0	0	0	2	4	4.7
Overall Exploration	2	1	1	7	7	3.9
Integration						
Combining new information helped me answer questions raised in course activities.	0	0	2	2	2	4.0
Learning activities helped me construct explanations/solutions.	0	1	0	2	3	4.2
Reflection on course content and discussions helped me understand fundamental concepts in this class.	0	0	0	3	3	4.5
Overall Integration	0	1	2	7	8	4.2
Resolution						
I can describe ways to test and apply the knowledge created in this course.	0	0	5	0	1	3.3
I have developed solutions to course problems that can be applied in practice.	0	1	3	2	0	3.2
I can apply the knowledge created in this course to my work or other non-class related activities.	0	0	1	3	2	4.2
Overall Resolution	0	1	9	5	3	3.6
Total Cognitive Presence	2	3	12	26	29	4.1

Table 2: Teaching Presence Survey Results

Survey Questions by Community of Inquiry Domain	Total Reporting Each Score on 5-point Likert Scale (n) 1 Strongly Disagree	2 Disagree	3 Neutral	4 Agree	5 Strongly Agree	Average Likert Score
Design and Organization						
The instructor clearly communicated important course topics.	0	0	0	2	4	4.7
The instructor clearly communicated important course goals.	0	0	0	1	5	4.8
The instructor provided clear instructions on how to participate in course learning activities.	0	0	0	1	5	4.8
The instructor clearly communicated important due dates / time frames for learning activities.	0	0	0	0	6	5.0
Overall Design and Organization	0	0	0	4	20	4.8
Facilitation						
The instructor was helpful in identifying areas of agreement and disagreement on course topics that helped me to learn.	0	0	0	1	5	4.8
The instructor was helpful in guiding the class towards understanding course topics in a way that helped me clarify my thinking.	0	0	0	2	4	4.7
The instructor helped to keep course participants engaged and participating in productive dialogue.	0	0	0	1	5	4.8
The instructor helped keep the course participants on task in a way that helped me learn.	0	0	1	1	4	4.5
The instructor encouraged course participants to explore new concepts in this course.	0	0	1	1	4	4.5
Instructor actions reinforced the development of a sense of community among course participants.	0	0	0	2	4	4.7
Overall Facilitation	0	0	2	8	26	4.7
Direct Instruction						
The instructor helped to focus discussion on relevant issues in a way that helped me learn.	0	0	1	1	4	4.5
The instructor provided feedback that helped me understand my strengths and weaknesses relative to the course's goals and objectives.	0	1	2	2	1	3.5
The instructor provided feedback in a timely fashion.	0	1	1	3	1	3.7
Overall Direct Instruction	0	2	4	6	6	3.9
Total Teaching Presence	0	2	6	18	52	4.5

4.8, facilitation 4.7, and direct instruction 3.9 (Table 2). Every respondent agreed or strongly agreed that they enjoyed RMM (average score 4.7) and would be interested in participating in a future version that included fellows from other institutions (4.7).

Conclusion: The pilot RMM activity was feasible and enjoyable for fellow participants. CoI survey results provided evidence of effective cognitive and teaching presences within the activity. In the cognitive domain, this activity was most effective to trigger interest, and least effective in knowledge applicability. Next steps include adapting the initiative to include trainees at other institutions, adding steps to enhance applicability and further evaluating the CoI framework as a tool for studying this initiative, including the social presence.

Disclosure: D. Leverenz, None; **L. Criscione-Schreiber**, None.

Abstract Number: 1798

Time to Bridge the Gap in Rheumatology Education: Interactive Team Based Learning Is Most Effective in Increasing Internal Medicine Residents' Knowledge

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Education
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Medical education curricula have evolved to more interactive approaches. Fully interactive, team-based learning (TBL) is a flipped classroom model that has been well studied at the pre-graduate level. The impact of TBL in post graduate populations, especially on Rheumatology specific topics, has not been well explored (Reimschisel et al, Medical Teacher, 2017). How TBL compares to a more moderately interactive session is also not clear. The major aim of this study was to evaluate the efficacy of TBL versus a moderately interactive teaching approach and traditional lecture in increasing rheumatology specific topic competency in medical trainees.

Methods: Three 1-hour sessions on various rheumatology topics: a didactic, a moderately interactive lecture and a TBL session were performed. Three knowledge based multiple choice questions were administered pre and post each session. For the moderately interactive session, the group was asked open ended questions at regular intervals. For TBL, a pre-reading assignment was given and participants completed individual readiness assurance tests and group application exercises. Pre and post rotation surveys assessing learning preferences and to what degree the sessions enhanced comfort with diagnosis and treatment were completed. Comfort was measured on a 5-point Likert scale (1: not comfortable and 5: very comfortable). Paired and independent samples t-tests were used for analyses.

Results: There were 29 participants in the lecture, 27 in the moderately interactive and 46 in the TBL group. The majority were medical residents PGY 1-3. For the lecture, there were *decreases* in post test scores (1.7±0.6 vs 0.8±0.8, $p < 0.001$), though comfort with diagnosis (3.2±0.8 vs 4.0±0.7, $p < 0.001$) and treatment (2.5±0.7 vs 3.5±0.8, $p < 0.001$) improved. For the moderately interactive, there were improvements in test scores (0.8±0.8 vs 1.32±0.8, $p = 0.049$), comfort with diagnosis (2.9±0.7 vs 3.9 ±0.9, $p < 0.001$) and treatment (2.5±1.0 vs 3.5±1.0, $p = 0.011$). For TBL, there were improvements in test scores (1.0±0.6 vs 2.1±0.8, $p < 0.001$), comfort with diagnosis (2.7±1.0 vs 3.3±1.0, $p = 0.001$) and treatment (2.3±0.9 vs 3.2±1.1, $p < 0.001$). When comparing changes in test scores between groups, there were significant differences between TBL and lecture ($p < 0.001$), TBL and moderately interactive ($p = 0.019$) and between moderately interactive and lecture ($p < 0.001$). All increases in comfort went from uncomfortable or neutral to comfortable ranges and there were no significant differences in change in comfort between groups. The majority of residents preferred mixed learning formats.

Conclusion: Though residents prefer mixed learning models and all formats subjectively increased comfort with diagnosis and treatment, this study shows that TBL yields a significantly greater increment in rheumatology specific knowledge than moderately interactive and non-interactive sessions. Interestingly, knowledge scores after traditional lecture-based teaching actually decreased. Post graduate curricula should reflect the trends seen in pre-graduate education, by utilizing interactive small group formats.

Disclosure: A. Kwiatkowski, None; **N. Shakoor**, None; **A. Manadan**, RUSH University Medical Center, 3; **M. Grant**, None; **J. Block**, Abbvie, 2, ACR, 6, Agios, 7, Daiichi-Sankyo, 7, GlaxoSmithKline Consumer Healthcare, 5, Jannsen, 2, Medivir, 5, Novartis, 2, OARSI, Omeros, 7, Pfizer, 2, TissueGene, 2, Zynerba Pharma, 5; **S. Khandelwal**, None.

Abstract Number: 1799

Wellness and Resiliency Among Recent Rheumatology Fellowship Graduates: A Qualitative Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Education
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: The recent ACR workforce projections suggest that there will be a significant shortage of rheumatologists by 2030. Retirement of senior physicians, an increase in part-time providers and increased demand for rheumatologic care are cited as major reasons for this shortage. This has implications for recent rheumatology fellowship graduates, who are entering this challenging environment with an eye towards building preserving well-being and bolstering resiliency. Indeed, studies demonstrate that young physicians as a whole have the lowest career satisfaction, highest frequency of personal conflicts and highest rates of depersonalization. In this qualitative study, the investigators explore the characteristics of wellness and resiliency among newly board-certified rheumatologists.

Methods: We performed a qualitative study using semi-structured phone interviews of rheumatologists who completed fellowship in 2017. Participants were recruited through purposive sampling. Eight questions were devised by the investigators, covering wellness, resiliency, and burnout and probing their perceived challenges, motivations, and opportunities for improvement.

Interviews were recorded and transcribed independently and verified for consistency. Discrepancies were resolved through mutual consensus. The two investigators used grounded theory to sequentially code the transcripts line-by-line. These codes were then compiled and organized into larger themes and subthemes. We continued to analyze these data until reaching theoretical sufficiency.

Results: 24 rheumatologists were interviewed, of which 12 were in private practice and 12 were in academic practice. Five themes were identified: (1) work-family balance as a dynamic equilibrium changing over time, (2) inadequacy of formal training in addressing self-doubt over independence and autonomy, (3) uncertainty over career development and progression, and (4) excessive burden of documentation and billing, and (5) protective nature of longitudinal patient-physician relationships. These themes overlapped in both groups, although subthemes were unique (e.g. concerns over extramural funding in academics vs. developing a patient panel in private practice).

Conclusion: New rheumatologists face a series of challenges as they enter the workforce. This qualitative study empowers participatory research to understand the needs of this unique and vulnerable population. Investments into their well-being can help reduce the risk of burnout and enlarge our community. Our results highlight priorities as identified by recent fellowship graduates and provide suggestions to training program leaders to enable successful transitions to independent practice.

Disclosure: P. Iyer, None; **B. Kumar**, None.

Abstract Number: 1800

Safety and Humoral Immunogenicity to Herpes Zoster Vaccine in Patients with Rheumatoid Arthritis (interim Analysis)

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Infection-Related Rheumatic Disease

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: To evaluate the safety and humoral immunogenicity of a live attenuated herpes zoster (HZ) vaccine in patients with rheumatoid arthritis (RA) compared with healthy controls (HC).

Methods: This is a prospective multicenter study of a live attenuated HZ vaccine in 132 patients with RA receiving conventional disease-modifying anti rheumatic drugs (cDMARD) and/or low-dose glucocorticoids (GC), candidates to receive biologics or tofacitinib. The control groups was composed of 35 HC. All the subjects, above the age of 50 years. Clinical and laboratory assessments were performed at baseline and after 6 weeks. Each assessment included RA disease activity score (DAS-28) for RA patients, recording of side effects and blood samples for the evaluation of immunogenicity for each subject. At week 2 and 4 after vaccination, patients were contacted by phone and asked for adverse events. The immunogenicity was assessed using varicella zoster virus (VZV)-specific ELISA (Serion)

Results: 132 RA patients (median age 66, range 50-89, 81% women) and 35 HC (median age 67, range 51-100, 69 % women) were vaccinated with the Zostavax (MSD) vaccine. Safety: 67 (52%) of the RA patients and 12 (32%) of the HC developed vaccine related side effects. In the HC, all were local reactions to the vaccine which resolved after a few days. In the RA group, the adverse events included: 56 local reactions, 11 systemic reactions such as fever, 2 mild rash, and 1 event of herpes zoster. Seven RA patients reported worsening of the RA Effect on disease activity :No change in disease activity was observed . DAS28-ESR at baseline was (median [min, max], n (out of 132)) (4 [2,8], n=126/132) and (4, [1,9], n=121/132) after 6 weeks. Immunogenicity: The number of patients with non-protective titer at baseline was 1 (RA=0, and controls=1). The titer increased from (median [min, max], n) (877 [101, 3153], n=129/132) to (1327 [99, 4836], n=126) for RA and from (962 [54, 1650], n=35) to (1533 [222, 3564]) in the control group. The increase in each group was statistically significant (pv< 0.0001 for both groups, Wilcoxon signed-rank test, n.RA=124, n.Control=35). The degree of humoral response was similar in the 2 groups (p=0.238, Mann-Whitney Test, n.RA=124, n.Control=35)

Conclusion: In RA patients treated with cDMARDs, vaccination with a live attenuated vaccine against herpes zoster was safe and induced an adequate booster response

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Disclosure: O. Elkayam, Pfizer, 2, 5, 8; **I. Rosner**, None; **D. Zisman**, Pfizer, 5, 8; **M. Lidar**, Pfizer, 5, 8; **R. Mader**, None; **A. Bieber**, None; **A. Balbir-Gurman**, Pfizer, 5, 8; **M. Amit**, None; **S. Gertel**, None; **V. Furer**, None.

Abstract Number: 1801

Comparison of Infection-Related Hospitalization Risk and Cost in TNFi-Experienced Medicare Beneficiaries with Rheumatoid Arthritis Treated with Abatacept or Other Targeted Disease-Modifying Anti-Rheumatic Drugs

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Infection-Related Rheumatic Disease
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: The risk and cost of infection-related hospitalizations in tumor necrosis factor inhibitors (TNFi)-experienced patients with rheumatoid arthritis (RA) receiving subsequent targeted disease-modifying antirheumatic drug (tDMARD) is unknown in the Medicare population. This study compared the risk and cost of infection-related hospitalization costs between TNFi-experienced patients receiving abatacept, TNFi and other non-TNFi.

Methods: A retrospective cohort study using 100% Medicare fee-for-service (FFS) claims (Parts A/B/D) was designed to identify TNFi-experienced patients with RA who initiated a subsequent treatment with abatacept, TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab) or other non-TNFi (anakinra, sarilumab, rituximab, tocilizumab, tofacitinib) between January 2010-December 2017. The date of the new tDMARD therapy

Table. Baseline characteristics and unadjusted infection-related hospitalization costs

Variable	Abatacept (N = 6,343)	TNFi (N = 5,054)	p-Value Abatacept - TNFi	Other Non-TNFi (N = 5,250)	p-Value Abatacept – Non-TNFi
Mean Age, Years	73.0	73.1	0.25	72.7	0.02
Mean CCI Score	4.9	4.8	0.01	5.0	0.14
Mean Duration of Follow-up, Days	441.9	402.8	<0.0001	460.0	0.05
Follow-up Infection-related Hospitalization Costs, PPPM	$77.3	$107.7	0.11	$141.4	0.01
Genitourinary*	$41.8	$54.6	0.45	$59.9	0.03
Pneumonia*	$37.5	$54.7	0.12	$74.0	0.06
Sepsis*	$34.3	$49.1	0.44	$69.0	0.19
Skin & Soft Tissue*	$8.7	$20.6	0.37	$23.2	0.05
Joint*	$4.3	$11.4	0.32	$10.5	0.18
Bacterial Respiratory*	$4.2	$3.8	0.73	$9.5	0.96

CCI = Charlson comorbidity index, PPPM = per-patient per month

*Type of infections were not mutually exclusive

initiation was the index date. Patients were included if age 65+, ≥2 claims with a diagnosis code for RA, continuous enrollment 12-months pre- and post-index date, and no evidence of cancer and other auto-immune conditions. Follow-up ended at the date of disenrollment, death, end of study period, or end of index treatment, whichever occurred first. Infections included pneumonia, bacterial respiratory, sepsis, skin and soft tissue, joint or genitourinary. A two-part generalized linear model controlling for baseline demographics, comorbidities, infections, healthcare resource use and costs was used to examine differences in per-patient per month (PPPM) Medicare payments (2019 USD). A Cox regression model was used to compare the risk of infections.

Results: Of the study population, 6,343 patients were treated with abatacept, 5,054 with TNFi, and 5,250 with non-TNFi. At baseline, abatacept group had the highest proportion of patients with infection-related hospitalization (9.8% vs. 7.1% vs. 9.7%, P< 0.05). However, the risk of infection-related hospitalizations during follow-up was lower in patients treated with abatacept compared with TNFi (7.5% vs. 8.1%, P=0.21) and other non-TNFis. (7.5% vs. 10.7%, P< 0.0001). After adjusting for differences in patient characteristics, Cox regression analysis showed that the risk for an infection-related hospitalization was significantly higher for RA patients treated with TNFi's (HR: 1.48; 95% CI: 1.26-1.75, P< 0.0001) and other non-TNFi's (HR: 1.46; CI: 1.28-1.66, P< 0.0001) than in those treated with abatacept. During follow-up, after controlling for potential confounding variables, infection-related hospitalization PPPM cost was significantly higher in patients treated with a TNFi's (difference: $93; 95% CI: $51-$134) and other non-TNFi's (difference: $84; 95% CI: $52-$116) than in those treated with abatacept.

Conclusion: Medicare FFS beneficiaries with RA who initiated abatacept following the exposure of TNFi, had lower infection-related hospitalization costs compared to patients who switched to a different TNFi or other non-TNFi.

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Abstract Number: 1802

Utility of Repeat Latent Tuberculosis Testing in Patients Taking Biologics

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Infection-Related Rheumatic Disease
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Guidelines for repeat Latent Tuberculosis Infection (LTBI) testing while on biologics are not clearly defined. The American College of Rheumatology recommends repeat LTBI screening only in persons with risk factors for tuberculosis(TB) whereas the National Psoriasis Foundation recommends repeat annual LTBI screening in all patients on biologics. Furthermore, recommendations for annual LTBI screening for patients on biologics have been incorporated into the Medicare Merit-Based Incentive Payment Systems and will impact physician reimburse-

Table 1: Patient Characteristics of entire study cohort

Characteristics	Value
Total cases	5212
Age (years), mean	40.9
Most common medical diagnoses, N (%)*	5925 (100)
• Inflammatory bowel disease	1868 (31.52)
• Rheumatoid Arthritis	1722 (29.06)
• Psoriasis	1505 (25.40)
Average number of biologics per patient	1.80
Duration(months)of biologic therapy, mean	63.76
Most common biologics administered, N (%)*	9412 (100)
• Adalimumab	3107 (33.01)
• Etanercept	1630 (17.31)
• Infliximab	1561 (16.58)
No of QFT tests, mean	3.17

**The Medical diagnoses and biologics are more than total cases since some patients had more than one medical diagnoses and some received more than one biologic*

Table 2: Comparative characteristics of patients with indeterminate and positive QFTs

Characteristic	Indeterminate QFTs group	Positive QFTs group	P value
Number of patients	479	172	
Age(years), mean (SD)	40.99 (18.23)	44 (17.27)	0.0601
Most common medical diagnoses, N (%)*	575 (100)	196 (100)	
o Inflammatory bowel disease	235 (40.86)	65 (33.16)	
o Rheumatoid Arthritis	163 (28.34)	65 (33.16)	
o Psoriasis	85 (14.78)	34 (17.34)	
No of QFT tests, mean(SD)	3.68 (2.77)	3.46 (1.63)	0.0667
Latent TB treatment, N (%)	4(0.83)	83(48.25)	<0.00001
Biologic discontinued, N (%)	92(19.20)	12(6.97)	0.000173
Duration(months)of biologic therapy, mean(SD)	20.99(21.29)	75.08(52.15)	0.0001
Risk Factors for TB present, N (%)	61(12.73)	73(42.44)	<0.00001

**The Medical diagnoses are more than total cases since some patients had more than one medical diagnoses*

ment. However, little evidence supports that this practice of repeat annual screening is clinically valuable and/or cost-effective in patients on biologics.

Objective: To determine the value and cost-effectiveness of serial LTBI screening in patients taking biologics and to identify risk factors in patients who convert from negative to positive QuantiFERON TB test (QFT) results while on biologics.

Methods: We retrospectively reviewed LTBI screening results in patients treated with biologics for chronic inflammatory/autoimmune conditions at a single, tertiary care center between August 2007 and March 2019. For each patient, we collected demographic information, primary underlying diagnosis, biologics used, length of biologic therapy, number of QFTs and QFT results. Patients without repeat QFT results following biologic initiation and/or all QFTs outside the treatment period with biologics were eliminated from the study.

Results: Of 10,914 patients treated with biologics and with QFT results, 5212 had ≥1 repeat QFT result after starting biologic therapy (mean 3.2 per patient) and were included in our study (Table 1). The most common medical diagnosis in the study cohort were Inflammatory Bowel Disease (31%), Rheumatoid Arthritis (29%) and Psoriasis +/- Psoriatic Arthritis (25%). Majority patients had all negative QFTs (87.5%, n=4561), 9.2 % patients (n=479) had ≥1 indeterminate QFT and 3.3% patients (n=172) had ≥1 positive QFT (Table 2). Amongst patients with positive QFTs, only 61 patients converted from a negative to a positive QFT after initiation of biologic therapy. Importantly, only one case of active TB was found in the entire study cohort and this patient had a significant risk factor in the form of recent travel to a TB endemic area.

Conclusion: This represents the largest single institution study evaluating rates of QFT test positivity/conversion in patients taking biologics. Repeat LTBI testing in patients taking biologics revealed a low rate of conversion (1.17%), suggesting low clinical value and an undesirable cost-benefit ratio. Additionally, a high percentage of positive QFT converters had risk factors for TB exposure. Our results suggest clinical utility and cost-effectiveness of repeat LTBI screening in patients on biologics may be more valuable if not performed routinely, but driven by a focused review of TB exposure risk factors in each patient.

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Abstract Number: 1803

Performance of the RABBIT Infection Score in a Prospective Multicenter Cohort of Rheumatoid Arthritis Patients from Argentina

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SESSION INFORMATION
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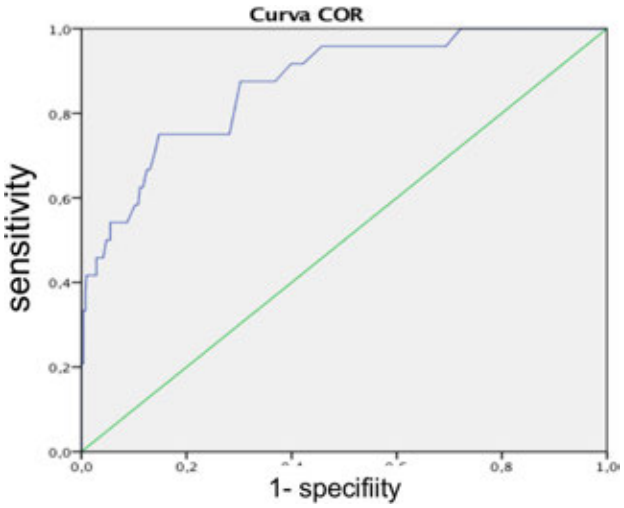
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: The biologics therapies in rheumatoid arthritis (RA) implies a well-known risk of infection. It is of utterly importance to count with predictive models to define risk factors for infection. Objectives: Validate the RABBIT risk score for serious infections in a cohort of RA patients followed for 12 months. Evaluate which variables of our population could be of relevance to optimize the score.

Methods: Patients ≥18 years old fulfilling 2010 ACR/EULAR criteria for RA were included and followed for 12 months. Basal sociodemographic data, comorbidities, RA characteristics and vaccination was consigned . Basal RABBIT score was calculed. Serious infections were consigned, describing site and time since enrollment. Statistical analysis: Categorical variables were compared using x2 test and continual variables using Student´s t test or Mann Whitney. Cumulative survival of infection was assessed using Kaplan Meier curves. Variables associated serious infections were evaluated using Cox proportional regression model.

Results: 605 patients were included. 83.5% female, mean age 52.8±12.8 years, 96.2% urban residence, 83% GRAFFAR III/IV (middle, middle-low class), median years of formal studies 10 (IQR 7-13) years. 70% had health insurance. Median time of RA evolution 84 (36-168) months, 90% RF+, 80% ACPA+, median DAS-28 3.5 (2.4-4.8), median CDAI 10 (3-19) and median HAQ 0.87 (0.37-1.50). Comorbidities: 7% Previous infection, 10% lung disease, 1% chronic kidney disease, 6% diabetes. Vaccination status: 67% antiinfluenza, 66.5% antipneumococcal, 47% antiHBV. Treatment: 75% patients were on MTX. 60% were on csDMARDs alone and 40% on bDMARDs (60% TNFi, 20% Tocilizumab, 13% Abatacept, 7% Tofacitinib). 15.6% had a prior history of bDMARDs use. Mean dose of prednisone was 3.6 mg/day and 75% of patients received under 7.5 mg/day. Incidence of serious infection was 5% (CI95% 3-7). Most frequent sites were respiratory and urinary (90%). Mean time to serious infection was 3.5 mont. Variables associated with serious infection: High disease activity by CDAI 4.1 (1.8-9.5) and DAS-28 3.2 (1.3-7.3), previous serious infection 19.3 (8-47), pulmonary disease 5.2 (2.1-13), diabetes 6.4 (2.3-17.6), prednisone >20mg/day 14.3 (4.8-42.5), Tocilizumab treatment 12.4 (3-53) and current use of DMARDs 0.24 (0.1-0.6). Cox regresión model (serious infection): Previous serious infection (expB:10.6 p:0.00001), diabetes (expB:4.8 p:0.02), Tocilizumab treatment (expB: 11.4 p:0.012), high dose of corticoids (expB: 9.3 p:0.008) and current use of DMARDs (expB: 0.3 p:0.04) were



independently associated. Performance of RABBIT score: Patients with no infection during follow up had a median score of 1.2 (IQR 0.8-2.1) and patients with infection a median score of 5.1 (IQR 2.15-12.6)(p=0.00001). ROC curve analysis: AUC 0.86 (CI95% 0.8-0.94), best cut-off 2.85 (sensibility 75%, specificity 85%).

Conclusion: The RABBIT score performed excellently in our patients. Serious infections was 5% during the 12 months, mean time to serious infection was 3.5 months and it was independently associated with previous serious infection, diabetes, use of Tocilizumab, prednisone dose >20 mg/day and negatively with current use of DMARDs.

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Abstract Number: 1804

Safety of the Zoster Vaccine Recombinant, Adjuvanted in Rheumatoid Arthritis and Other Systemic Rheumatic Disease Patients: A Single Center's Experience with 400 Patients

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Infection-Related Rheumatic Disease
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Patients with rheumatoid arthritis (RA) and other systemic diseases (SD) are at an increased risk of developing Herpes Zoster (HZ) due to either the nature of the diseases or the medications used to treat them. Zoster Recombinant Adjuvanted (ZRA) is a novel vaccine that can be used in immunosuppressed populations and was approved by the FDA in 2018. ZRA provides >90% efficacy in non-immunosuppressed patients older than 50. However, concern has been raised that ZRA may trigger disease flares and cause more side effects in immunocompromised patients. We investigated the impact of the new ZRA vaccine in RA and other SD patients, and measured the incidence of flares and side effects.

Methods: We performed a retrospective chart review of patients with RA and SD seen at BWH who received the ZRA vaccine between 2/1/2018 and 2/1/2019. Co-variates of interest were collected. A flare was defined as occurring within 12 weeks of vaccine administration by either: 1) documentation of RA flare in the rheumatologist office notes, telephone encounter or patient portal communication, or 2) new prednisone prescription, or an increase in dose of existing prednisone prescription. Vaccine side effects were defined as muscle soreness or rash at the injection site, redness, mild swelling, fatigue, fevers, myalgias, headaches, nausea, and abdominal pain. All potential flares were independently reviewed, adjudicated, and confirmed by three rheumatologists (EM, MEW, and SD).

Results: 402 (236 RA and 166 SD) patients who received the new ZRA vaccine between 2/1/2018 and 2/1/2019 were identified. Mean follow up was 13.2 weeks ranging from 1-50 weeks following administration. Patient characteristics are identified in **Table 1**. We identified 6.7% (n=27) patients who experienced a flare, lower than the observed background six-month flare rate of 30% in RA patients at our center (Bykerk VP et al., 2014). Of these patients 5.7%

Table 1: Characteristics of Subjects to Study the Safety of the Zoster Vaccine Recombinant

Total N	402
Mean Age (STD)	67 (10.9)
Females (%)	304 (75.6)
White (%)	344 (85.6)
Received 2nd Vaccine (%)	149 (37.1)
RA (%)	236 (58.7)
Other*	166 (41.3)
Medications	
MTX (mean dose=17.1mg/week)	134 (33.3)
Prednisone (mean dose=4.7 mg/day)	106 (26.4)
Tofacitinib (%)	50 (12.4)
TNF inhibitors (%) -Adalimumab, Certolizumab pegol, Etanercept, Golimumab, Infliximab	106 (26.4)
Other biologic therapy (%) -Abatacept, Tocilizumab, Rituximab, Sarilumab	50 (12.4)
Other immunosuppressants (%) -Azathioprine, Cyclophosphamide, Mycophenolic acid, Leflunomide	45 (11.2)

*Psoriatic Arthritis(28), SLE(16), Spondylitis(12), Sjogren's(12), GCA(10), and other(88)

(n=23) of flares occurred following the first dose and 3.4% (n=5) occurred following the second dose. One patient flared after both doses. All flares were mild, self-limited, responded to treatment with low dose glucocorticoids, and did not warrant a change in immunosuppressive therapy. 13.4% (n=54) patients experienced side effects. Of the patients who experienced side effects, 11.4% (n=46) occurred after the first dose and 8.7% (n=13) occurred following the second dose. Five patients experienced side effects after both doses. All side effects were regarded as mild. No cases of HZ were reported.

Conclusion: In 402 patients who received the new ZRA vaccine, the incidence of disease flares was ≤7% and side effects were 13.4%, which is lower than that observed in the general population. Both flares and side effects were mild, self-limited, and did not require a change in DMARD therapy. No cases of HZ were reported. Formal studies of patients exposed to the vaccine are required to confirm this conclusion. Immunosuppressive therapies may reduce the effectiveness of vaccines. Studies are needed to determine the immune response to the vaccine, and its efficacy in rheumatology patients. We encourage the use of the ZRA vaccine in RA and other SD patients.

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Abstract Number: 1805

Perioperative Anti-rheumatic Medications Are Not Associated with 30-day Odds of Infection in Rheumatoid Arthritis Patients Undergoing Surgery: A Retrospective Cohort Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Infection-Related Rheumatic Disease

Session Type: ACR Abstract Session
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Background/Purpose: Perioperative management of anti-rheumatic drugs in rheumatoid arthritis (RA) patients undergoing surgery remains controversial. Previous studies produced conflicting results, and data on non-orthopedic surgeries in RA patients are limited. The objective of the current study was to measure the impact of perioperative anti-rheumatic medication management on the 30-day odds of infection among RA patients undergoing surgery.

Methods: We conducted a retrospective cohort study of seropositive RA patients who underwent musculoskeletal or major organ surgery within the Fairview Health System in Minnesota between January 1, 2010 and December 31, 2017. Each surgical event was identified through the electronic medical record and manually reviewed by two trained clinicians for demographic variables, perioperative medication management, and outcomes. Surgeries were classified into three groups according to anti-rheumatic medication use during surgery: 1. neither DMARD nor biologic (either not prescribed or held for a pre-specified period of time, based on each medication's dosing schedule and mode of action); 2. DMARD with no biologic; 3. biologic with or without DMARD. The perioperative use of corticosteroids and antibiotics was also recorded. The primary outcome, post-operative infection, included surgical site infections, urinary tract infections, pneumonia, and blood stream infections occurring within 30 days of surgery as defined by CDC criteria. ANOVA, Chi-square tests and logistic regression were used for analyses.

Results: 154 seropositive RA patients underwent 244 surgeries (165 musculoskeletal and 79 major organ). Patients were predominantly female (78%), white (94%), overweight or obese (73%) with a mean age of 62 years, and a mean Charlson comorbidity index of 2.3. Of the 244 surgeries, 116 (47.8%) were performed on no anti-rheumatic medications, 95 (39.1%) on a DMARD with no biologic, and 32 (13.2%) on a biologic with or without a DMARD. The groups were well-balanced on age, sex, race, baseline BMI, Charlson comorbidity index, surgery type, perioperative steroid use, antibiotic use and expected duration of surgery ($p \geq 0.1$ for all comparisons). In total, 28 surgeries (11.5%) among 23 patients were complicated by a post-operative infection within 30 days: 14 (12%) in the no-medication group, 10 (11%) in the DMARD group, and 4 (13%) in the biologic group ($p = 0.9$). Of the other examined predictors, higher Charlson comorbidity index and longer expected duration of surgery were associated with infection ($p < 0.05$). After adjustment for these two predictors, overall and for musculoskeletal and major organ surgeries separately, perioperative use of anti-rheumatic drugs was not associated with increased odds of post-operative infection (table 1).

Conclusion: Perioperative use of anti-rheumatic medications was not associated with 30-day odds of post-operative infection in RA patients undergoing musculoskeletal or major organ surgery. Rather, higher Charlson comorbidity index and longer expected duration of surgery predicted postoperative infections in this RA population.

Table 1. Odds of developing infection 30-days post-surgery among seropositive RA patients by perioperative anti-rheumatic medication use status.

	Overall n=244		Musculoskeletal Surgery n= 165		Major Organ surgery n=79	
	OR	95% CI	OR	95% CI	OR	95% CI
DMARD with no Biologic†						
Crude	0.87	(0.37 - 2.05)	0.81	(0.25 - 2.61)	0.86	(0.24 - 3.15)
Adjusted*	1.1	(0.42 - 2.86)	1.01	(0.28 - 3.73)	1.28	(0.29 - 5.66)
Biologic with or without DMARD†						
Crude	1.05	(0.32 - 3.44)	1.54	(0.37 - 6.40)	0.48	(0.05 - 4.52)
Adjusted*	0.76	(0.20 - 2.93)	0.70	(0.12 - 4.06)	0.40	(0.03 - 5.31)

OR, Odds Ratio; 95% CI, 95% Confidence Interval, DMARD, Disease-Modifying Antirheumatic Drug.
† OR estimates shown vs "Neither DMARD nor Biologic" reference group.
*Adjusted for Charlson comorbidity index and expected duration of surgery.

Disclosure: M. Kerski, None; **P. Boersma**, None; **E. Miller**, None; **A. Brenner**, None; **G. Melton**, None; **A. Shmagel**, None.

Abstract Number: 1806

Inflammatory Arthritis Induced by Immune Checkpoint Inhibitor Therapy: A Distinct Clinical Entity and Immunologic Phenotype

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease II: Checkpoint Inhibitors-Induced & Other Rheumatic Conditions
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Immune checkpoint inhibitors (ICIs) are being used in the treatment of a variety of malignancies. ICIs target cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), programmed cell-death protein 1 (PD-1) and its ligand PD-L1, which negatively regulate T-cell activation. ICIs can induce widespread manifestations of autoimmunity, which are called immune-related adverse events (irAEs). Rheumatic irAEs have been increasingly reported, with inflammatory arthritis (IA-irAE) being the most common. IA-irAE symptoms can be severe and persistent, even after discontinuation of ICI. We sought to clinically and immunologically characterize a cohort of patients with IA-irAE.

Methods: From patients on ICI therapy for any malignancy, we recruited 15 cases of *de novo* IA-irAE. IA-irAE had physician-confirmed inflammatory arthritis supplemented by laboratory or imaging studies. As controls, 8 patients with seronegative rheumatoid arthritis (**Rh-control**), 4 ICI-treated cancer patients without any irAE (**ICI control**), and age and sex-matched healthy controls (**HC**) were included. Biospecimens including serum and peripheral blood mononuclear cells (PBMCs) were collected. Fifteen-parameter flow cytometry panels were used to profile T cell exhaustion and senescence phenotypes in PBMCs and serum cytokine levels were measured using Luminex technology.

Results: The majority of IA-irAE patients were treated with pembrolizumab (86.6%). The average onset of inflammatory arthritis was 4.36 months after ICI initiation. The predominant pattern of inflammatory arthritis was polyarticular/symmetric, as well as large joint involvement (66.6%), although patterns seen in spondyloarthopathies were observed as well. Four patients (27%) had positive serologies after the onset of symptoms, without having pre-existing symptoms of arthritis. IA-irAE patients had significantly reduced PD-1 expression on CD8 and CD4 T cells compared to ICI-controls ($p = 0.02$) and HC ($p < 0.0001$). In IA-irAE, the senescent T cell population was significantly increased in frequency compared to HC ($p = 0.01$) and tended to be increased compared Rh-control ($p = 0.05$). Finally, IA-irAE had elevated levels of pro-inflammatory cytokines IL-6, MIG and IP-10 compared to controls ($p = 0.02$, 0.001 and 0.007, respectively) and a similar trend was observed in comparison to Rh-controls.

Conclusion: Our preliminary findings suggest that IA-irAE is a distinct clinical entity with a heterogeneous clinical presentation and distinct immune phenotype. The latter suggests that ICI therapy may lead to over-activation of T cells, and sustained inflammation. Further, there is a tendency for these patients to have increased pro-inflammatory cytokines compared to Rh-controls. Increased sample sizes are needed to more definitively conclude whether these alternations can distinguish Rh-irAE from Rh-control, and these studies are ongoing. To our knowledge, this is one of the first studies addressing the immunological basis of IA-irAE, and the connection between IA-irAE and rheumatoid arthritis.

Disclosure: U. Thanarajasingam, None; **X. Zhu**, None; **X. Zhou**, None; **J. Jaquith**, None; **Y. Li**, None; **H. Zeng**, None.

Abstract Number: 1807

Teprotumumab, a Novel Biologic for Active Thyroid Eye Disease

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease II: Checkpoint Inhibitors-Induced & Other Rheumatic Conditions
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Thyroid eye disease (TED) is a debilitating autoimmune disorder characterized by inflammation and exophthalmia along with significantly altered appearance and vision changes. TED is predominately associated with Graves' disease, that can coexist with other autoimmune disease commonly managed by rheumatologists such as RA and SLE. Herein, we report results from the pooled 24-week randomized, double-masked, placebo-controlled, parallel-group, multicenter, Phase 2 (NCT01868997) and Phase 3 (NCT03298867) studies of teprotumumab, an insulin-like growth factor 1 receptor (IGF-1R) monoclonal antibody, in adults with active, moderate-to-severe TED.

Methods: Patients (Pts) with recent onset of TED (< 9 months) were treated with a teprotumumab or placebo infusion every 3 weeks for a total of 8 infusions. Primary and secondary endpoint data were pooled between the two studies and included: the % of patients with a reduction in proptosis of ≥2 mm at week 24 in the study eye without similar fellow-eye worsening, overall responder rate (% of patients with ≥2 mm proptosis reduction AND ≥2-point clinical activity score [CAS] reduction in a 7-point scale) at week 24, CAS responder rate (% of patients with a CAS value of 0 or 1) at week 24, % of patients with an improved diplopia score at week 24, average proptosis and GO-QoL (TED specific quality of life questionnaire) score change from baseline through week 24, as compared with placebo.

Results: 171 pts were included in the intent-to-treat analyses (84 teprotumumab, 87 placebo). The demographics were as follows: mean age of 51.5 years (teprotumumab) vs 51.4 (placebo), 69% female (teprotumumab) vs 77% (placebo) and 76% non-smokers (teprotumumab) vs 70% (placebo). Significantly more teprotumumab pts had reductions in proptosis of ≥2 mm (65/84 [77.4%] vs 13/87 [14.9%], p< 0.001) and an overall response (% of pts meeting proptosis AND CAS outcome) (62/84 [73.8%] vs 12/87 [13.8%], p< 0.001) at week 24. The reduction in average change from baseline through week 24 in proptosis, was significantly greater in pts who received teprotumumab (-2.63 mm) than in those who received placebo (-0.31 mm, p< 0.001). The % of pts with absent TED activity (CAS of 0 or 1) was greater with teprotumumab at week 24 (52/84 [61.9%] vs 19/87 [21.8%], p< 0.001). The diplopia responder rate (% pts improved 1 or more grades) was significantly higher with teprotumumab (69.7%) vs placebo (30.5%; p< 0.001) in those with baseline diplopia (66 and 59 pts, respectively). Improvements in average change from baseline through week 24 in GO-QoL in overall score and subscales were significantly greater in the teprotumumab group (overall 15.55 vs 5.92, p< 0.001; visual functioning 16.81 vs 6.10, p< 0.001; appearance 13.51 vs 5.78, p=0.002).

Conclusion: In the largest placebo-controlled evaluation of active TED thus far conducted, teprotumumab reduced inflammation, proptosis, and diplopia resulting in clinical and quality of life improvements as compared with placebo over 24 weeks. Teprotumumab is a promising infused biologic option for TED, with implications for rheumatologists involved in managing patients with TED.

Disclosure: G. Kahaly, None; **S. Sile**, Horizon, 3, 4; **E. Thompson**, Horizon, 3, 4; **T. Vescio**, Horizon, 3, 4; **R. Perdok**, Horizon, 3, 4; **J. Sherman**, Horizon, 3, 4, 6; **T. Smith**, UCLA and Los Angeles Biomedical Research Institute, 9; **R. Douglas**, Horizon, 5.

Abstract Number: 1808

Immune Checkpoint Inhibitor-Induced Inflammatory Arthritis Persists After Immunotherapy Cessation

Tawnie Braaten ,[1] Julie Brahmer,[1] Patrick Forde,[1] Dung Le,[1] Evan Lipson,[1] Jarushka Naidoo,[1] Megan Schollenberger,[1] Lei Zheng,[1] Michelle Jones,[1] Ami Shah,[2] Clifton Bingham,[3] and Laura Cappelli[3], [1]Johns Hopkins, Baltimore, MD, [2]Johns Hopkins Hospital, Baltimore, MD, [3]Johns Hopkins University, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease II: Checkpoint Inhibitors-Induced & Other Rheumatic Conditions

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: The use of immune checkpoint inhibitor (ICI) therapy for malignancy is growing. Various autoimmune and inflammatory syndromes, known as immune-related adverse events (irAEs) have been reported, including inflammatory arthritis (IA). Despite its growing incidence, the clinical features and optimal treatments of IA are not well defined, and long-term outcomes are unknown. This study aims to investigate long-term outcomes of patients (pts) who develop IA due to ICIs and to evaluate those with symptom persistence after ICI cessation, the need for immunosuppressants, and the impact of these medications on underlying malignancy.

Methods: This is a prospective observational study of pts referred to the Johns Hopkins Arthritis Center for IA due to ICIs recruited from 6/2015 to 12/2018 with data available after ICI cessation. ICIs were discontinued for cancer progression, treatment completion, or severe irAEs. Baseline demographics, cancer type, specific ICI treatment, tumor response, personal and family history of autoimmunity, other irAEs, labs, and clinical exam were obtained. Follow up occurred at varying intervals for up to 24 months (mo) from ICI cessation to assess the clinical status of IA and malignancy. Active IA was defined as active joint disease or the need for continued immunosuppression. Kaplan-Meier curves were developed to evaluate pts with persistent IA. A Cox proportional hazards model was used to assess the influence of various factors on IA persistence.

Results: A total of 60pts (53.3% female) were monitored with a median follow up after ICI cessation of 9 mo (1-24 mo). Pts had a wide range of cancers and 50% had other irAEs. Combination ICI therapy was used in 30% of patients. There were low rates of seropositivity (RF 1.8%, CCP 5.5%, ANA 14.3%) and 7pts had a family history of autoimmune disease. Immunosuppressive treatment was required in 75%. Forty-eight pts (80%) were treated with systemic/intraarticular steroids. csDMARDs were used in 19 pts and bDMARDS in 11. A majority (53.1%) had active IA at most recent follow up. Three-month follow up data after ICI cessation was available in 51pts, with 6mo data for 41. At 3mo, 70.6% had active disease; 48.8% had active disease at 6 mo. Among the 20 pts with persistent arthritis at 6 mo, 14 continued to have active disease at last follow up. IA was less likely to improve in those with longer duration of ICI use (hazard ratio 0.93, 95% CI 0.87 to 0.99; p=0.02), in those receiving combination therapy (hazard ratio 0.29, 95% CI 0.12 to 0.72; p=0.008) and in pts with other irAEs (hazard ratio 0.61, 95% CI 0.39 to 0.95, p=0.03). Although not significant, a better tumor response was associated with persistent IA. Tumor response did not appear to be impacted by immunosuppression.

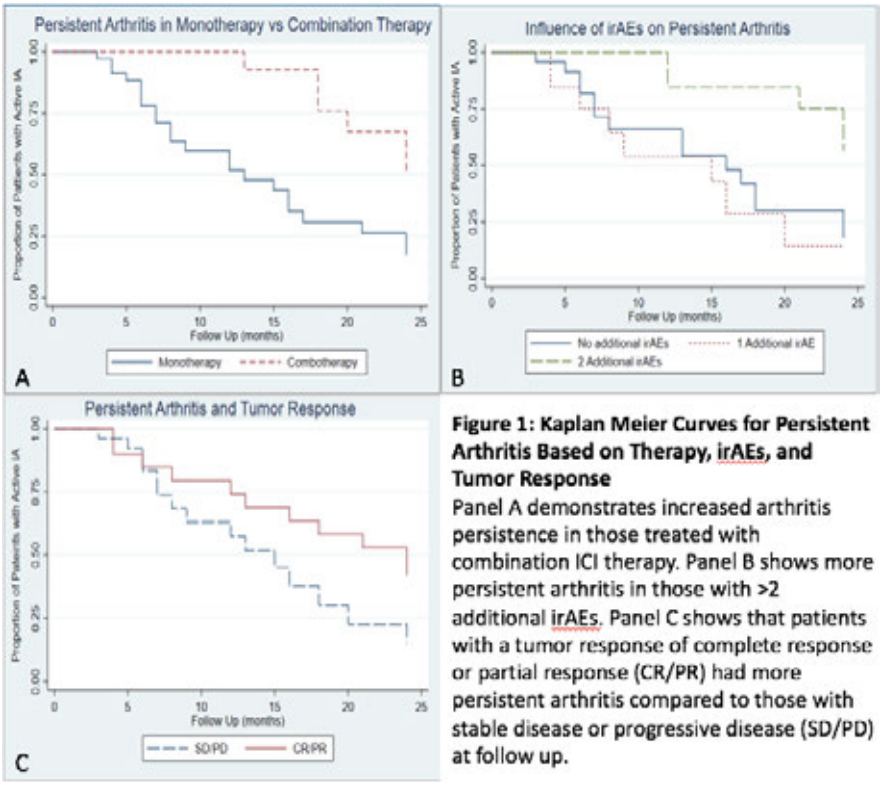

Figure 1: Kaplan Meier Curves for Persistent Arthritis Based on Therapy, irAEs, and Tumor Response
Panel A demonstrates increased arthritis persistence in those treated with combination ICI therapy. Panel B shows more persistent arthritis in those with >2 additional irAEs. Panel C shows that patients with a tumor response of complete response or partial response (CR/PR) had more persistent arthritis compared to those with stable disease or progressive disease (SD/PD) at follow up.

Conclusion: This study demonstrates that a significant number of pts developing ICI-induced IA have persistent arthritis at 3 and 6mo. Specific factors such as longer ICI exposure, combination ICI therapy, and other irAEs increase the risk of persistence. Immunomodulatory treatments were efficacious for symptomatic control while having no apparent effect on tumor response at follow up and persistent arthritis may associate with better tumor response.

Disclosure: T. Braaten, None; **J. Brahmer**, Bristol-Myers Squibb, 2, 5, Merck, 2, 5, MedImmune/AstraZeneca, 2, Syndax, 5, Janssen Oncology, 5, Amgen, 5, Genentech, 5, Lilly, 5, Celgene, 5; **P. Forde**, AstraZeneca, 2, 5, Bristol-Myers Squibb, 2, 5, Corvus, 2, Kyowa, 2, Novartis, 2; **D. Le**, Bristol Myer Squibb, 2, 5, Merck, 2, 5, 8, Aduro Biotech, 2; **E. Lipson**, Bristol-Myers Squibb, 2, 5, Novartis, 5, EMD Serono, 5, Array BioPharma, 5, Macrogenics, 5, Merck, 2, 5, Millennium, 5, Sysmex, 2; **J. Naidoo**, Merck, 2, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 5, 8; **M. Schollenberger**, None; **L. Zheng**, Halozyme, 2, iTeos, 2, Bristol-Myers Squibb, 2, Merck, 2, Amgen, 2, Biosynergics, 5, NovaRock Biological, 2, 5, Alphamab, 5, Mingrui, 1, 5, Foundation Medicine, 5, Datareve, 5, Aduro, 7; **M. Jones**, None; **A. Shah**, Bristol Meyer Squibb, 5, Bristol-Myers Squibb, 5; **C. Bingham**, Abbvie, 5, AbbVie, 5, BMS, 2, 5, Bristol Meyer Squibb, 2, 5, Bristol Myers-Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Eli/Lilly, 5, Genentech/Roche, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Pfizer Inc, 5, Regeneron/Sanofi, 5, Sanofi/Regeneron, 5; **L. Cappelli**, Bristol Meyer Squibb, 2, Bristol-Myers Squibb, 2, Regeneron/Sanofi, 5, Regeneron/Sanofi Genzyme, 5.

Abstract Number: 1809

A Quarter of Patients Treated with Checkpoint Inhibitors Develop Immune-Related Adverse Events: A University Center Experience

Celine Zhou,[1] **Whitney Elg-Salsman** ,[1] Sonam Kiwalkar,[2] Nishad Sathe,[1] Marcia Friedman,[1] and Atul Deodhar[2],
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SESSION INFORMATION
Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease II: Checkpoint Inhibitors-Induced & Other Rheumatic Conditions
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Immune checkpoint inhibitors (ICIs) are increasingly becoming the mainstay of management of advanced malignancies, but can result in immune related adverse events (irAEs) affecting nearly every organ system. The purpose of this retrospective study is to determine the incidence and nature of irAEs in patients treated with ICIs at our single center university hospital. The primary objective was to assess risk factors for development of irAEs. Secondary objectives included determining 1) incidence of rheumatic and non-rheumatic irAEs; 2) time to onset of irAEs; 3) proportion required to discontinue ICIs due to irAEs; 4) comparative risk of specific ICIs causing irAEs.

Methods: Patients over age 18 were identified by electronic chart review with oncologist-diagnosed cancer who were prescribed ICIs between March 31, 2011 to December 31, 2018. ICIs included cytotoxic T-lymphocyte-associated protein 4 inhibitors (CTLA-4), programmed death-1/programmed death-ligand 1 inhibitors (PD-1/PD L-1) or combination therapy. We performed a detailed chart review to collect patient demographics, type of cancer, ICI(s) utilized, time to onset of irAEs, type of irAEs, treatment, and outcome. Cases were defined as patients who either developed new irAEs or experienced a flare of their pre-existing autoimmune disease after initiation of ICI. Controls were defined as those without any irAEs. The Fisher test and the Kruskal-Wallis test were used to compare categorical and continuous variables, respectively.

Table 1. Comparison of patients with (cases) and without (controls) immune-related adverse events (irAEs) after treatment with immune checkpoint inhibitors (ICIs). The "other" category under ICIs denotes the remaining FDA-approved ICIs (durvalumab, avelumab and atezolizumab). Fischer tests were completed for categorical variables and Kruskal-Wallis tests were completed for continuous variables.

Column1	irAEs (Case)	non-irAEs (Control)	p value
Number	207	615	
Females (%)	91 (44.0)	270 (43.9)	0.87
Mean age in years (SD)	65.64 (13.5)	64.99 (13.7)	0.55
Race (%)			0.32
Caucasian	192 (92.8)	548 (89.1)	
Hispanic	1 (0.5)	12 (2.0)	
African American	4 (1.9)	12 (2.0)	
Others	10 (4.8)	43 (7.0)	
Type of malignancy (%)			<0.001
Advanced melanoma	98 (47.3)	121 (19.7)	
Advanced head/neck squamous cell carcinoma	6 (2.9)	21 (3.4)	
Advanced lung cancer	49 (23.7)	226 (36.7)	
Other	54 (26.1)	247 (40.2)	
Immune check point inhibitor (%)			<0.001
Ipilimumab	24 (11.6)	32 (5.2)	
Nivolumab	58 (28.0)	200 (32.5)	
Pembrolizumab	49 (23.7)	271 (44.1)	
Other	9 (4.3)	55 (8.9)	
Other Treatments (%)			<0.001
Resection	44 (21.3)	59 (9.6)	
Chemotherapy	16 (7.7)	84 (13.7)	
Radiation	2 (1.0)	13 (2.1)	
Combination	136 (65.7)	435 (70.7)	
None	9 (4.3)	24 (3.9)	
Mean time toICI (mean (SD))	25.56 (34.1)	25.99 (38.9)	0.88
Mean duration of ICI use in months (SD)	8.50 (9.0)	6.26 (6.7)	<0.001
Response to malignancy (%)			<0.001
Yes	113 (54.6)	157 (25.5)	
No	80 (38.6)	420 (68.3)	
Unknown	14 (6.8)	38 (6.2)	
Personal h/o autoimmune diseases (%)	25 (12.1)	67 (10.9)	0.73
Family h/o autoimmune diseases	35 (31.0)	66 (27.5)	0.58
Smoking (%)			0.11
Current smoker	19 (9.2)	52 (8.5)	
Former smoker	103 (49.8)	357 (58.0)	
Never	85 (41.1)	206 (33.5)	
Alcohol use (%)			0.06
Current	73 (35.3)	167 (27.2)	
Former	32 (15.5)	128 (20.8)	
Never	99 (47.8)	300 (48.8)	
Unknown	3 (1.4)	20 (3.3)	

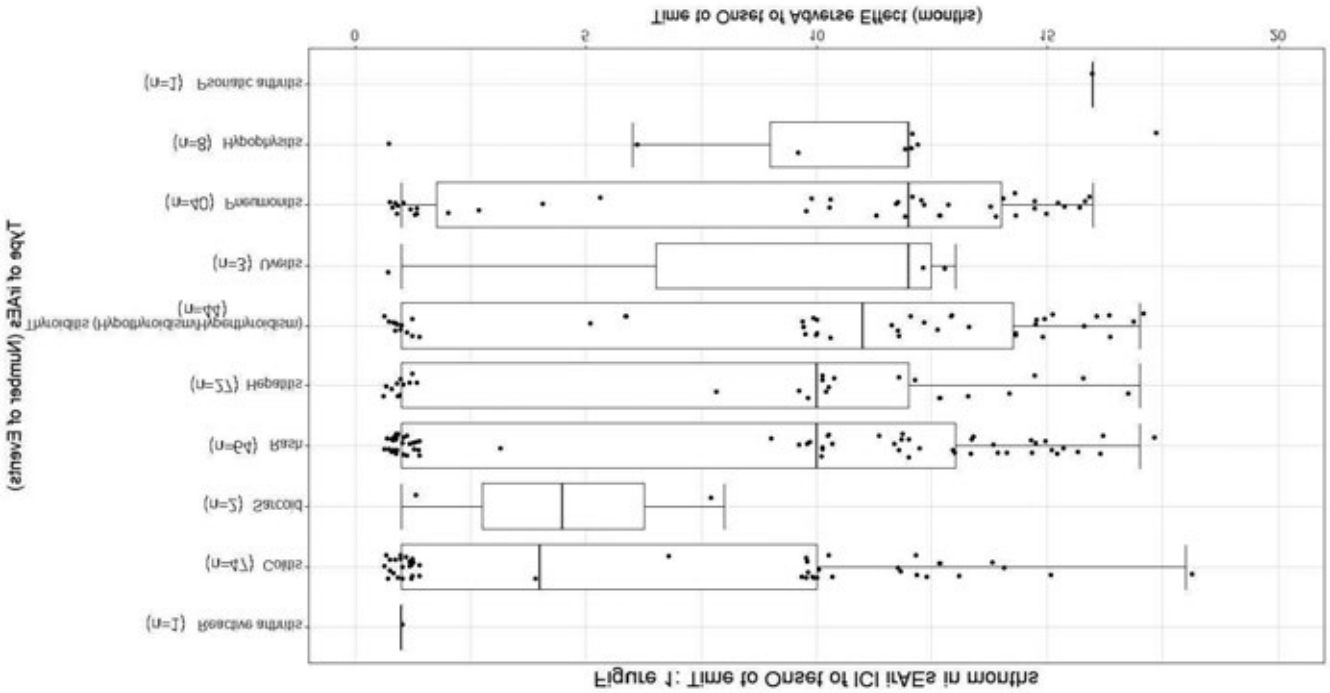

Figure 1. Time to diagnosis of immune-related adverse events (irAEs) since onset of immune checkpoint inhibitor therapy. The X-axis shows time in months and the Y axis shows the type and number of irAEs. Each dot represents an event. Each box shows the range of values within the 25th to 75th percentile while the vertical line in the box denotes the median.

Results: A total of 827 patients were prescribed ICIs, of which 209 (25%) developed 264 independent irAEs. A comparison of those who developed irAEs and those who did not is shown in Table 1. Sixteen patients (6%) developed rheumatic irAEs. Seven patients developed inflammatory arthritis. Less common rheumatic irAEs included uveitis, myositis, psoriatic arthritis, reactive arthritis and sarcoidosis. The majority were treated with oral prednisone. Time to onset of select irAEs since initiation of ICIs is shown in Figure 1. Of the 209 with irAEs, 145 (69.4%) required temporary/permanent discontinuation of ICIs due to irAEs. The odds of developing irAEs were 3.6 times higher with CTLA-4 compared to PD-1/PD-L1 agents. Odds for developing irAEs were also 1.5 times higher with combination therapy than CTLA-4 monotherapy, and 5.2 times higher than PD-1/PD-L1 alone.

Conclusion: We found that a quarter of patients treated with ICIs developed irAEs, and that non-rheumatic irAEs were much more common than rheumatic irAEs. Type of malignancy, type of ICI agent and nature of previous cancer therapies factored into the development of irAEs. The odds of developing irAEs were higher with usage of combination ICI compared to the single agents. However, in our study no rheumatic irAEs were attributed to CTLA-4 use alone. This could be explained by sample size. Data continues to remain scarce on treatment and long-term follow up of rheumatic irAEs. Partnering with oncologists, expediting patient referral to a dedicated ICI-rheumatology clinic and establishing multicenter registries will provide more robust data on these heterogenic irAEs.

Disclosure: C. Zhou, None; **W. Elg-Salsman**, None; **S. Kiwalkar**, None; **N. Sathe**, None; **M. Friedman**, None; **A. Deodhar**, AbbVie, 2, 5, 9, Abbvie, 5, 8, Abbvie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, and UCB Pharma, 5, 8, AbbVie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GSK, Galapagos, Janssen, Novartis, Pfizer and UCB, 5, AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Glaxo Smith and Klein, Janssen, Novartis, Pfizer, UCB, 5, Amgen, 5, 8, 9, BMS, 2, 5, 8, BMS, Eli Lilly, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, 2, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, UCB Pharma, 2, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, 8, Bristol Myers Squibb, 2, 5, Bristol-Myers

Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, 9, Eli Lilly and Company, 2, 5, Eli Lilly,, 5, Eli Lilly, GSK, Novartis, Pfizer and UCB, 2, Galagagos, 5, Galapagos, 5, 8, 9, Glaxo Smith & Klein, 2, Glaxo Smith & Kline, 2, 5, 8, Glaxo Smith Klein, 5, Glaxo SmithKlein, 2, 5, GlaxoSmithKlein, 2, 5, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, Janssen, 2, 5, 8, 9, Janssen Pharmaceutica, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9.

Abstract Number: 1810

Rheumatic Toxicities Associated with Immune Checkpoint Inhibitors: An Observational, Retrospective, Pharmacovigilance Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease II: Checkpoint Inhibitors-Induced & Other Rheumatic Conditions
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Monoclonal antibodies targeting co-inhibitory immune checkpoints (PD-1/PDL1 axis or CTLA-4) showed unprecedented clinical activity in several types of cancer by restoring antitumor immune responses. We recently described that vasculitis (giant cell arteritis) was a rheumatic immune-related adverse event (irAE) but the description of other rheumatic adverse events remains sparse.

Methods: Using WHO's global database of individual case safety reports, we compared rheumatic adverse events reporting in immune checkpoint inhibitors (ICI) exposed patients with the reporting in the full database. All rheumatic irAEs (except vasculitis) were included (according to the Medical Dictionary for Regulatory Activities). The association between ICI and rheumatic adverse events was analyzed using the reporting odds ratio (ROR) and the information component (IC: an indicator value for disproportionate reporting observed vs expected values). A positive IC_{025} (the lower end of the IC 95% credibility interval) is considered to be significant.

Results: We identified 54,416 adverse events reported in patients treated with ICI (14,988,450 adverse events reported in patients treated with any drugs, full database since 2008). Compared to the full database, ICI treatment was associated with higher reporting of arthritis (121,811 reports for the full database vs 606 for ICI, ROR 1.4 [1.3-1.5]; IC_{025} 0.34), myositis (26,722 vs 465, ROR 4.9 [4.5-5.4]; IC_{025} 2.12), sarcoidosis (2,772 vs 94, ROR 9.6 [7.9-11.9]; IC_{025} 2.85), polymyalgia rheumatica (1,504 vs 76, ROR 14.6 [11.6-18.4]; IC_{025} 3.34), Sjogren's syndrome (2,000 vs 49, ROR 6.9 [5.2-9.2]; IC_{025} 2.24) and scleroderma (2,385 vs 17, ROR 2.0 [1.2-3.2]; IC_{025} 0.17). Myositis patients were more frequently male (70.4%; $p< 0.0001$ vs 56% in other rheumatological irAE patients) and treated with anti-PD1/L1 (ROR 2.8 [1.9-4.0] vs anti-CTLA4) or with ICIs combination (ROR 2.0 [1.6-2.6] vs monotherapy). Myositis occurred earlier compared to other rheumatic irAEs (time to onset: 31 IQR [19.5-58.5] days) and were associated with the highest mortality rate (30.3%, $p< 0.0001$). Arthritis and Sjogren's syndrome had similar time to onset (78.5 [25-166.5] and 88 [47.8-145.8] days, respectively), and were associated with a mortality of 6.9 and 0%. Arthritis and Sjogren's syndrome occurred more frequently in patients with anti-PD1/L1 (vs anti-CTLA4; ROR 2.1 [1.6-2.8] or 4.4 [1.0-18.1]) with

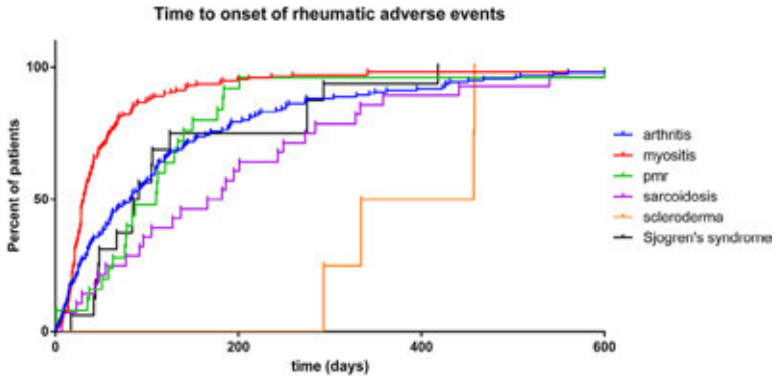

Figure 1. Delay between the first immune checkpoint inhibitor infusion and the onset of the rheumatic adverse events.

ICI combination (vs monotherapy; ROR 1.6 [1.3-2.0] and 2.9 [1.5-5.6]) whereas polymyalgia rheumatica was more frequently reported in patients with anti-PD1/L1 monotherapy (ROR 5.6 [1.8-17.7]). Sarcoidosis occurred in younger patients (57 [48-65.3] years) and with a longer time to onset (174 [71.5-275.8] days; p< 0.001). Scleroderma had the longest time to onset (395.5 [323.8-457.2] days; p< 0.001).

Conclusion: Among rheumatic disorders in addition to vasculitis: arthritis, myositis, sarcoidosis, polymyalgia rheumatica, Sjogren's syndrome and scleroderma have a higher reporting. Patients characteristics, type of ICI, time to onset, and patient outcome depend on the type of rheumatic irAEs. Myositis is the most severe.

Disclosure: C. Anquetil, None; **O. Benveniste**, None; **J. Moslehi**, None; **D. Johnson**, None; **B. lebrun-vignes**, None; **O. Lambotte**, None; **J. Selam**, None; **J. Spano**, None; **Y. Allenbach**, None.

Abstract Number: 1811

Commonly Used Drugs in Rheumatology May Alter Anti-Tumoral Response to Immune Checkpoint Inhibitors

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease II: Checkpoint Inhibitors-Induced & Other Rheumatic Conditions

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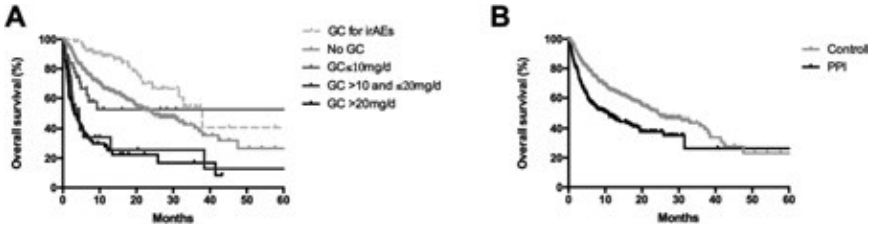
Session Time: 2:30PM–4:00PM



Background/Purpose: Immune checkpoint inhibitors (ICIs) are revolutionizing the treatment of some advanced cancers. Gut microbiota has emerged as an important component of anti-tumoral response and can also be related to the occurrence of immune-related adverse events (irAEs). It has recently been shown that antibiotic treatment given at the initiation of ICI therapy had a dramatic impact on microbiota that compromised the anti-tumoral effect of ICIs.

The objective of this study is to evaluate whether co-medications known to have a potential impact on gut microbiota may alter ICI efficacy and/or irAE occurrence when given at ICI onset.

Methods: This was a retrospective cohort study including all cancer patients who received ICIs at our institution from May 2015 to September 2017. Co-medications given to the patients within one month before or one month after the first administration of ICI were extracted from medical records on the basis of a predefined list of medications known to impact gut microbiota. The tumour response, occurrence of irAEs and patient outcomes were assessed on a regular basis. Overall survival (OS) has been considered from the start of ICI therapy.

Results: 635 patients (70% male, mean age 64.5 years) were included, of whom 293 had melanoma, 150 had advanced non-small cell lung cancer and 83 had renal carcinoma. A previous autoimmune disorder was present in 8% of patients, mainly rheumatic and endocrine diseases. Psychotropic drugs (41.1%), proton pump inhibitors (PPIs) (37.3%), angiotensin-converting enzyme (ACE) inhibitors and/or angiotensin II receptor blockers (ARBs) (32%), glucocorticoids (GC) (24.2%), antibiotics (21.4%), statins (20.8%) and morphine (20.6%) were the most co-prescribed medications. Baseline GC use, when ≥ 10mg of prednisone equivalent, was associated with significant decreased OS (median 4.5 months versus 24.3 months; p< 0.0001) and a less frequent tumour response (55% versus 73% ; p=0.0001). When given after ICI onset for the management of irAEs, GC did not influence ICI efficacy (Figure A). Baseline PPI use also altered both OS (median 10.9 versus 24.3 months; p< 0.0001) and tumour response (62% versus 71%; p=0.02) (Figure B). We confirmed the detrimental impact of antibiotics when given at ICI onset, and also found worse outcomes for patients receiving baseline psychotropic drugs (median OS 9.3 versus 19.4 months; p=0.0001). No significant difference was observed with baseline use of NSAIDs, aspirin, statins and ARBs/ACE. Furthermore, co-medication with antibiotics, GC, PPIs, morphine, NSAIDs, aspirin and psychotropic drugs was associated with decreased occurrence of irAE.

Conclusion: As many of these treatments are used by rheumatologists, one should be aware of their potential detrimental effect when used at ICI initiation, that sometimes could have been avoided.

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Abstract Number: 1812

Delineating Early Response Trajectories to Biologics in Polyarticular Course Juvenile Idiopathic Arthritis

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SESSION INFORMATION
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Session Title: Pediatric Rheumatology – Clinical II: JIA
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Most biologic trials in juvenile idiopathic arthritis (JIA) treat all participants with the biologic under study for 12 to 16 weeks before randomizing responders into a withdrawal phase. This implies that patients are expected to respond quickly to biologics. If treatment response can be predicted from early response patterns (< 12-16 weeks), this information may be applied to identify likely responders from likely non-responders early during clinical care, allowing earlier termination of ineffective treatment. We aimed to delineate the early treatment response trajectory of JIA patients to biologics.

Methods: Longitudinal data from early treatment phase (12-16 weeks) from 3 JIA trials: 1) Tocilizumab (Roche), 2) Etanercept (Amgen) and 3) the Trial of Early Aggressive Therapy TREAT (Etanercept), were obtained and combined. Primary outcome is the ACR response states: ACR50, 70, 90. Clinically significant minimal improvement was defined as attaining at least an ACR50 state. Secondary outcome was the clinical juvenile arthritis disease activity score (cJADAS): inactive, low, moderate and high disease states. Longitudinal responses (ACR states and cJADAS) were modelled using the Markov multistate model, corrected for interval censoring and allowing heterogeneous transition rates.

Results: 342 patients (188 Tocilizumab, 69 Etanercept, 85 TREAT) with polyarticular course JIA were studied. 27% (92/341) were males, median age at baseline (25 th -75 th percentile P) was 10.0 (5.7- 15.0) years and median (25 th – 75 th P) duration of disease was 3.6 (1.0- 8.7) years. Baseline median (25 th -75 th P) active joint counts was 15 (7-24). Pateints were on methotrexate (46%) and corticosteroids (34%) at baseline. 87% patients were on biologics (Tocilizumab 188, Etanercept 111). At week 4, the probabilities of transitioning from active disease to ACR50, 70 and 90, was 0.29, 0.13, 0.03. Probabilities of transition continued to increase from week 4 to 16, without plateau. At week 16, the probabilities of transition to ACR50, 70, 90 were: 0.19, 0.32, 0.25. By week 16, the mean durations of time spent in ACR50, 70, 90 were 0.91, 0.76 and 0.43 months. Even if no clinically significant minimal improvement was achieved by week 4, the probabilities of attaining this was substantial by weeks 12 (0.55) and 16 (0.67). At week 4, the probabilities of transition from a high cJADAS state to a moderate state was 0.20, to low state was 0.01, and to inactive disease < 0.01. At week 16, the probabilities for a moderate cJADAS state was 0.36, for low state was 0.10 and for inactive disease was 0.11. By week 16, the mean durations of time spent in low and inactive disease states were 0.15 and 2.37 months.

Conclusion: Patients treated with biologics continued to improve over the first 12-16 weeks, without plateau. Lack of early (4 weeks) clinically significant minimal response did not preclude attaining such response by 16 weeks. Our work suggests that response to biologics (Tocilizumab, Etanercept) continues to improve over the first 16 weeks of treatment. Therefore, patients should not be switched out of biologics before 16 weeks for a lack of effectiveness.

Disclosure: L. Lim, None; **A. Lokku**, None; **S. Ringold**, Childhood Arthritis & Rheumatology Research Alliance, 2, 6; **E. Pullenayegum**, None.

Abstract Number: 1813

New Medications Are Needed for Children with Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – Clinical II: JIA

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Existing legislation in the United States (US) promotes the study of new medications in children. Biologic disease-modifying-drugs (bDMARDs) and small molecules proven effective and safe in adults with rheumatoid arthritis and other forms of inflammatory arthritis require testing in children with juvenile idiopathic arthritis (JIA) to establish proper dosing, effectiveness, and safety. Several bDMARDs have been approved for the treatment of JIA in the US, but not all children with JIA have a complete clinical response to the available medications and are treated with medications off-label (i.e., anakinra, golimumab, infliximab, rituximab, secukinumab, tofacitinib, ustekinumab). The *purpose* of this research was to document the continuing medical need for new approved medications for the treatment of JIA.

Methods: The electronic medical record of JIA patients (n= 1599) treated at Cincinnati Children's Hospital Medical Center (CCHMC) since 2008 were reviewed for medication use and disease activity over time. JIA patients enrolled in the Childhood Arthritis & Rheumatology Research Alliance (CARRA) Registry (n=7,379) were assessed for medication use and disease activity at the most recent Registry visit. Medication need was defined as active JIA despite sequential use of ≥2 bDMARDs. Active JIA was defined as either a) physician-global assessment of JIA activity (MD-global; 0-10; 0 = inactive) ≥3 OR b) number of active joints (AJC) ≥3 OR c) patient-global assessment of well-being (Pt-global; 0-10; 0=very well) ≥3. Medication failure was only assessed for patients with complete data (a-c).

Results: At CCHMC, polyarticular-course JIA (40%), systemic JIA (9%) and juvenile psoriatic arthritis/enthesitis-related arthritis (JPSA/ERA; 17%) were common, and only 16% had persistent-oligoarticular JIA. Overall, use of bDMARDs (n=829; 53%) was common. Systemic JIA (85%) and jPSA/ERA patients (79%) were most commonly treated with bDMARDs. At least 5% (25/1599) of patients had failed ≥5 bDMARDs. Of 829 biologic users in the CCHMC cohort, 304 (37%) children were exposed to non-approved bDMARDs. Among 278 CCHMC patients

Table 1

	CCHMCJIA Registry – over time			CARRA Registry –most recent visit		
Patients	*Total N*	*Failure of bDMARD N (%)*	*Not Failing N (%)*	*Total N*	*Failure of bDMARDs N (%)*	*Not Failing N (%)*
All JIA*	487	255 (52%)	112 (23%)	1159	527 (45%)	300 (26%)
Irrespective of disease duration						
2 Biologics used	239 (48%)	113 (44%)	65 (58%)	731 (63%)	283 (54%)	224 (75%)
3 Biologics used	174 (37%)	97 (38%)	37 (33%)	282 (24%)	149 (28%)	57 (19%)
4 Biologics used	49 (10%)	31 (13%)	6 (5%)	87 (8%)	56 (11%)	15 (5%)
≥5 Biologics used	25 (5%)	14 (5%)	4 (4%)	59 (5%)	39 (7%)	4 (1%)
<3 years disease duration	104 (22%)	43 (17%)	52 (46%)	335 (29%)	164 (31%)	84 (28%)
2 Biologics used	62 (60%)	19 (44%)	36 (69%)	258 (77%)	125 (76%)	67 (80%)
3 Biologics used	34 (32%)	17 (40%)	15 (29%)	64 (19%)	31 (19%)	15 (18%)
4 Biologics used	7 (7%)	5 (11%)	1 (2%)	10 (3%)	7 (4%)	1 (1%)
≥ 5 Biologics used	1 (1%)	2 (5%)	0 (0%)	3 (1%)	1 (1%)	1 (1%)
≥3 and <6 years disease duration	143 (29%)	84 (33%)	28 (25%)	315 (27%)	131 (25%)	83 (28%)
2 Biologics used	68 (53%)	41 (49%)	13 (46%)	206 (65%)	68 (52%)	67 (81%)
3 Biologics used	56 (34%)	33 (39%)	10 (36%)	81 (26%)	47 (36%)	13 (16%)
4 Biologics used	9 (6%)	6 (7%)	3 (11%)	20 (6%)	13 (10%)	3 (4%)
≥5 Biologics used	10 (7%)	4 (5%)	2 (7%)	8 (3%)	3 (2%)	0 (0%)
≥6 years disease duration	240 (49%)	128 (50%)	32 (29%)	509 (44%)	232 (44%)	133 (44%)
2 Biologics used	109 (45%)	53 (41%)	16 (50%)	267 (52%)	90 (39%)	90 (68%)
3 Biologics used	84 (35%)	47 (36%)	12 (38%)	137 (27%)	71 (31%)	29 (22%)
4 Biologics used	33 (14%)	20 (16%)	2 (6%)	57 (11%)	36 (16%)	11 (8%)
≥5 Biologics used	14 (6%)	8 (7%)	2 (6%)	48 (9%)	35 (15%)	3 (2%)

*** with complete data Row %; column %**

with jPSA /ERA 27 (9.7%) had failed ≥2 bDMARDs. In the CARRA Registry, 46% of JIA patients had polyarticular disease course, 8% systemic JIA, and 18% jPSA/ERA; 4766 (65%) children had received a bDMARD with 1122 (24%) of these children receiving bDMARDs off label. Among 1351 jPSA/ERA patients in the CARRA Registry, about 10% failed ≥2 bDMARDs with active disease at their most recent visit. **Table 1** summarizes medication failures in both cohorts.

Conclusion: Data from a population-based cohort and a large national registry demonstrate a profound medical need for additional therapies to control JIA signs and symptoms, despite the availability of several approved biologic DMARDs. Given FDA approval ensures bDMARD access, the testing of new medications in JIA as they become available to treat adults is critical to further improve JIA outcomes.

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Abstract Number: 1814

Long-term Outcome of Juvenile Idiopathic Arthritis: From the Methotrexate to the Biologic Era

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SESSION INFORMATION
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Background/Purpose: After nearly two decades from the start of the Biologic era, systematic analyses of patients with juvenile idiopathic arthritis (JIA) have shown a high frequency of attainment of inactive disease (ID) and satisfactory levels of physical function and quality of life. However, whether and to what extent the disease prognosis has improved in comparison with the methotrexate (MTX) era is still uncertain.

Purpose of the present study was to compare the long-term disease state, in terms of activity and damage, of children with JIA who had their disease onset in MTX or Biologic eras.

Methods: Patients were included in MTX or Biologic era cohort depending on whether their disease presentation occurred before or after January 2000. Patients in the MTX era cohort and part of the patients in the Biologic era cohort were taken from a previous cross-sectional study published by our group,[1] which enrolled 310 patients with disease onset between December 1986 and December 2002. An additional sample of patients with onset in the Biologic era was enrolled in a subsequent prospective cross-sectional study, which included all consecutive patients meeting the ILAR criteria for JIA, who were seen consecutively at the Istituto Gaslini of Genoa, Italy, between January 2015 and June 2017. All patients had disease duration ≥ 5 years and underwent a prospective cross-sectional assessment, which included measurement of disease activity and damage. ID and low disease activity (LDA) states were defined according to Wallace, JADAS10 and cJADAS10 criteria. Articular and extra-articular damage was assessed with the Juvenile Arthritis Damage Index (JADI).

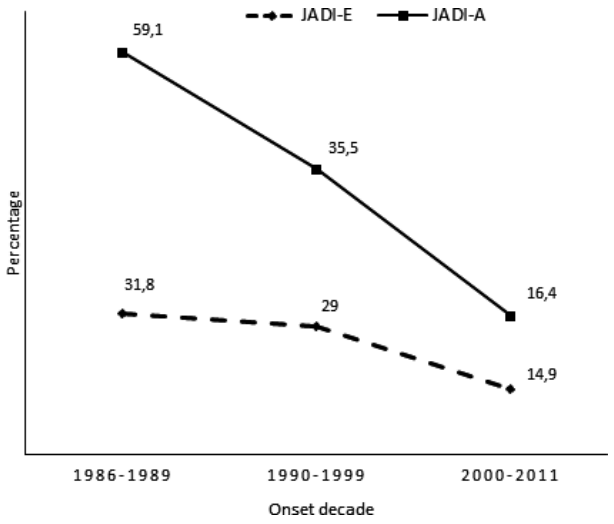

Figure 1. Trend in disease damage (JADI-A and JADI-E) over time. JADI-A: articular Juvenile Arthritis Damage Index; JADI-E: extra-articular Juvenile Arthritis Damage Index.

Results: MTX and Biologic era cohorts included 239 and 269 patients, respectively. Patients were divided in the "functional phenotypes" of oligoarthritis and polyarthritis. At cross-sectional visit, patients in the Biologic era cohort with either oligoarthritis or polyarthritis had consistently higher frequencies of ID and LDA than patients in the MTX era cohort. The measurement of disease damage at cross-sectional visit revealed that the frequency of impairment of > 1 JADI-Articular items was higher in MTX than in Biologic era cohort (17.6% versus 11% in oligoarthritis and 52.6% versus 21.8% in polyarthritis). Likewise, frequency of involvement of > 1 JADI-Extraarticular item was higher in MTX than in Biologic era cohort (26.5% versus 16.2% in oligoarthritis and 31.4% versus 13.5% in polyarthritis). The sole JADI items that were detected in more than 5% of patients in the Biologic era cohort were temporomandibular damage in oligoarthritis and polyarthritis, ankle damage in polyarthritis and leg-length inequality in oligoarthritis. The analysis of the temporal trend of damage development over the 25 years of our analysis (1986-2011) highlighted the marked decrease in damage over time and the more pronounced decline in the Biologic era (Figure 1).

Conclusion: Our study provides evidence of the remarkable prognostic improvement obtained with the recent therapeutic advance in JIA.

Reference

1. Solari et al. Arthritis Care Res. 2008;59:1571–9.

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Abstract Number: 1815

Subcutaneous or Intravenous Abatacept Monotherapy in Pediatric Patients with Polyarticular-Course JIA: Results from Two Phase III Trials

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SESSION INFORMATION

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Background/Purpose: In EU, abatacept (ABA) with MTX is approved in patients (pts) with polyarticular-course JIA (pJIA), as young as 2 years (SC) and 6 years (IV), intolerant or with an inadequate response to prior DMARDs, and can be used as monotherapy if MTX use is inappropriate.[1] In US, ABA can be used in combination with MTX or as monotherapy.[2] Here we report ABA efficacy and safety in pts without concomitant MTX or in pts with prior biologic use treated in an open-label, Phase III study of SC ABA (NCT01844518) and in a double-blind, Phase III study of IV ABA (NCT00095173).

Methods: Study design and eligibility criteria for both studies were reported previously.[3,4] In SC study, pts with pJIA and prior DMARD failure/intolerance were stratified by age cohort (2–5 and 6–17 years) to receive weight-tiered SC

Table 1. Baseline Demographic and Clinical Characteristics of Overall Patient Population by MTX Use in the SC and IV Abatacept Studies

Characteristic	SC abatacept (N=219)		IV abatacept (N=190)	
	ABA+MTX (n=173)	ABA (n=46)	ABA+MTX (n=138)	ABA (n=52)
Age, years	10.5 (11.0)	10.9 (11.5)	12.2 (12.0)	12.9 (13.0)
Female, n (%)	128 (74.0)	36 (78.3)	101 (73.2)	36 (69.2)
Disease duration, years	2.3 (1.0)	2.8 (2.0)	3.9 (3.0)	5.7 (5.0)
Prior biologic use, n (%)	32 (18.5)	24 (52.2)	30 (21.7)	27 (51.9)
Prior MTX use, n (%)	171 (98.8)	39 (84.8)	138 (100)	42 (80.8)
MTX dose, mg/m²/week	12.3 (11.8)	0	13.4 (18.3)	0
Prior DMARD use, n (%)	171 (98.8)	41 (89.1)	138 (100)	49 (94.2)
Number of active joints	12.3 (10.0)	9.8 (7.0)	16.5 (12.5)	15.3 (11.0)
Number of joints with LOM	10.9 (9.0)	8.0 (7.0)	17.2 (12.5)	14.1 (10.5)
CHAQ-DI	1.0 (1.0)	0.9 (0.9)	1.3 (1.3)	1.2 (1.1)
PaGA	45.0 (48.2)	40.8 (39.5)	44.7 (47.0)	44.0 (45.0)
PGA	48.9 (49.0)	45.6 (45.5)	52.8 (50.5)	57.8 (58.5)
CRP, mg/dL	1.3 (0.2)	1.2 (0.2)	3.5 (1.5)	2.4 (1.1)

Data are mean (median), unless indicated otherwise

ABA=abatacept, CHAQ-DI=Childhood Health Assessment Questionnaire-Disability Index; LOM=limitation of motion; PaGA=Parent Global Assessment; PGA=Physician Global Assessment

Table 2. Proportion of JIA-ACR Responders by Prior MTX Intolerance and Lack of Efficacy, and Safety Summary by MTX Use at Month 4

	SC abatacept (N=219)		IV abatacept (N=190)	
Prior MTX intolerance	**ABA+MTX (n=173)**	**ABA (n=21)**	**ABA+MTX (n=138)**	**ABA (n=21)**
JIA-ACR30	144 (83.2)	19 (90.5)	95 (68.8)	12 (57.1)
JIA-ACR50	129 (74.6)	16 (76.2)	70 (50.7)	10 (47.6)
JIA-ACR70	95 (54.9)	15 (71.4)	38 (27.5)	8 (38.1)
JIA-ACR90	60 (34.7)	8 (38.1)	17 (12.3)	5 (23.8)
Prior MTX lack of efficacy	**ABA+MTX (n=173)**	**ABA (n=14)**	**ABA+MTX (n=138)**	**ABA (n=23)**
JIA-ACR30	144 (83.2)	13 (92.9)	95 (68.8)	12 (52.2)
JIA-ACR50	129 (74.6)	12 (85.7)	70 (50.7)	9 (39.1)
JIA-ACR70	95 (54.9)	10 (71.4)	38 (27.5)	5 (21.7)
JIA-ACR90	60 (34.7)	5 (35.7)	17 (12.3)	1 (4.3)
Safety summary	**ABA+MTX (n=173)**	**ABA (n=46)**	**ABA+MTX (n=140)**	**ABA (n=50)**
SAEs	6 (3.5)	0	5 (3.6)	1 (2.0)
AEs	112 (64.7)	28 (60.9)	101 (72.1)	32 (64.0)
Related AEs*	41 (23.7)	15 (32.6)	39 (28.3)†	13 (25.0)‡

Data are n (%)

*Including possibly related; †overall n=138; ‡overall n=52

ABA=abatacept, SAE=serious AE

Table 3. Proportion of JIA-ACR Responders by Prior Biologic Use, and Safety Summary by MTX Use at Month 4

	SC abatacept (N=219)		IV abatacept (N=190)	
	Biologic exposed (n=56)	**Biologic naïve (n=163)**	**Biologic exposed (n=57)**	**Biologic naïve (n=133)**
JIA-ACR response				
JIA-ACR30	44 (78.6)	141 (86.5)	22 (38.6)	101 (75.9)
JIA-ACR50	39 (69.6)	126 (77.3)	14 (24.6)	80 (60.2)
JIA-ACR70	28 (50.0)	97 (59.5)	6 (10.5)	48 (36.1)
JIA-ACR90	11 (19.6)	65 (39.9)	1 (1.8)	23 (17.3)
Safety summary				
SAEs	1 (1.8)	5 (3.1)	3 (5.3)	3 (2.3)
AEs	30 (53.6)	110 (67.5)	38 (66.7)	95 (71.4)
Related AEs*	12 (21.4)	44 (27.0)	19 (33.3)	33 (24.8)

Data are n (%)

*Including possibly related

ABA=abatacept; SAE=serious AE

ABA (10 to < 25 kg [50 mg], 25 to < 50 kg [87.5 mg], ≥50 kg [125 mg]) weekly for 4 months (primary endpoint). JIA-ACR30 criteria responders at Month 4 could receive SC ABA for another 20 months.[3] In IV study, pts with pJIA and prior DMARD failure/intolerance received open-label IV ABA (10 mg/kg body weight) for 4 months (Period A); JIA-ACR30 criteria responders at Month 4 were randomized 1:1 to receive IV ABA (10 mg/kg body weight) or placebo every 4 weeks for 6 months or until flare (Period B). Pts could receive open-label ABA in a 5-year follow-up (Period C).[4] In this analysis, data were evaluated descriptively.

Results: Baseline characteristics were mostly balanced between the arms in both studies (Table 1). No additional numerical benefit in JIA-ACR responses was seen with ABA+MTX versus ABA monotherapy in either study at Month 4 (JIA-ACR90: SC ABA+MTX, 34.7% [60/173] vs SC ABA, 34.8% [16/46]; IV ABA+MTX, 12.3% [17/138] vs IV ABA, 13.5% [7/52]). Flare rates (95% CI) were comparable with ABA+MTX and ABA monotherapy in Period B of the IV study: 18.8% (7.7, 29.8) and 25.0% (0.5, 49.5), respectively. Efficacy responses of ABA+MTX and ABA monotherapy-treated JIA-ACR responders with prior MTX intolerance/lack of efficacy at Month 4 were similar in both studies (Table 2). As expected, ABA-treated biologic-naïve pts had a numerically greater clinical response than those with prior biologic use at Month 4 in both trials (Table 3); effect was independent of concomitant MTX use (data not shown). Rates of reported AEs were comparable for ABA+MTX- versus ABA-treated pts and for biologic-naïve versus those with prior biologic use across studies over 4 months (Tables 2, 3). No anti-drug antibodies (ADAs) were reported with ABA monotherapy in SC study; few pts receiving ABA monotherapy in IV study developed ADAs, with no impact on ABA efficacy seen (data not shown).

Conclusion: Abatacept (SC and IV) monotherapy was effective and well tolerated in pts with pJIA intolerant to MTX or when prior MTX was not effective. In addition, abatacept monotherapy can be considered for use in those with prior biologic therapy if MTX use is inappropriate.

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Abstract Number: 1816

Psoriasis Associated with Anti-Tumor Necrosis Factor-Alpha Therapies in Children with Inflammatory Bowel Disease, Juvenile Idiopathic Arthritis, and Chronic Noninfectious Osteomyelitis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology – Clinical II: JIA
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: TNF-alpha inhibiting therapies (TNFi) are a cornerstone of treatment for inflammatory conditions such as IBD, JIA, and chronic noninfectious osteomyelitis (CNO) but have been increasingly implicated in the development of psoriasis. The objective of this study was to compare the rate of psoriasis in children with IBD, JIA, and CNO with TNFi exposure to those without TNFi exposure and to the general pediatric population.

Methods: This was a single-center retrospective cohort study of electronic health record data from 2008 to 2018. Inclusion criteria were at least 2 ICD-9 or ICD-10 codes for JIA, IBD, or CNO, age at diagnosis of under 19 years, and at least 2 visits with a study center rheumatologist or gastroenterologist due to the frequent nature of one-time second opinion visits. Subjects with a listed past medical history or diagnosis code of psoriasis prior to the diagnosis of JIA, IBD, or CNO were excluded. TNFi exposure was defined as at least 1 prescription for either adalimumab, etanercept, or infliximab, and subjects were dichotomized as "ever" or "never" having TNFi exposure. The primary outcome was incident psoriasis which was defined as the first ICD-9 or ICD-10 code for psoriasis during a visit with a study center rheumatologist, gastroenterologist, or dermatologist. Subjects who had not developed psoriasis by their final recorded visit were considered censored. Incidence rates (IRs) were calculated as well as standardized incidence ratios (SIRs) comparing the observed to expected number of psoriasis cases in the general pediatric population according to previously published data. Univariate and multivariate Cox proportional hazards models determined by stepwise model selection were used to estimate the strength of association between TNFi exposure and incident psoriasis and to evaluate risk factors associated with psoriasis development.

Results: Between January 2008 and October 2018, 4403 children met inclusion criteria. Of these children, 1738 (39%) had TNFi exposure and 2665 (61%) did not with 5245 and 7365 person-years of follow-up, respectively. The IRs and SIRs for the entire cohort and for each condition are presented in **Table 1**. There were 64 (IR 1.2 per 100

	Person-years			Events			IR (per 100 person-years)			SIR[a] (95% CI)		
	All	TNFi unexposed	TNFi exposed	All	TNFi unexposed	TNFi exposed	All	TNFi unexposed	TNFi exposed	All	TNFi unexposed	TNFi exposed
All	12610.6	7365.3	5245.3	90	26	64	0.7	0.4	1.2	17.5 (14.2, 21.5)	8.7 (5.9, 12.7)	29.9 (23.4, 38.2)
IBD	8460.6	5052.9	3407.7	50	13	37	0.6	0.3	1.1	14.5 (11.0, 19.1)	6.3 (3.7, 10.9)	26.6 (19.3, 36.7)
JIA	3954.3	2206.3	1748.0	33	9	24	0.8	0.4	1.4	20.5 (14.5, 28.8)	10.0 (5.2, 19.2)	33.7 (22.6, 50.2)
CNO	195.7	106.1	89.6	7	4	3	3.6	3.8	3.3	87.7 (41.8, 183.9)	92.4 (34.7, 246.3)	82.1 (26.5, 254.5)

IR: incidence rate; SIR: standardized incidence ratio; CI: confidence interval; IBD: inflammatory bowel disease; JIA: juvenile idiopathic arthritis; CNO: chronic noninfectious osteomyelitis; TNFi: tumor necrosis factor inhibitor aSIRs were calculated as the ratio of observed psoriasis cases to expected psoriasis cases as estimated by the incidence in the general pediatrics population (40.8 per 100,000) (Tollefson, et al. Incidence of psoriasis in children: a population-based study. J Am Acad Dermatol. 2010; 62(6): 979-87). A SIR >1 indicates that more cases were observed than expected.

	Univariate model		Multivariate model	
Variable	HR (95% CI)	p value	HR (95% CI)	p value
TNFi exposure	3.54 (2.24, 5.59)	<0.001	4.23 (2.56, 7.01)	<0.001
Female	1.20 (0.79, 1.83)	0.39	--	--
Race[a]				
Black	0.46 (0.17, 1.25)	0.13	--	--
Other/unknown	0.80 (0.29, 1.67)	0.56	--	--
Age at diagnosis	1.03 (0.98, 1.08)	0.30	--	--
Family history of psoriasis	3.27 (2.03, 5.25)	<0.001	3.09 (1.83, 5.22)	<0.001
BMI $\geq$30 kg/m^2	0.71 (0.22, 2.24)	0.56	0.83 (0.26, 2.62)	0.75
Methotrexate exposure	1.32 (0.86, 2.03)	0.21	0.67 (0.42, 1.09)	0.11
Underlying diagnosis[b,c]				
JIA	1.38 (0.89, 2.16)	0.15	--	--

JIA: juvenile idiopathic arthritis; TNFi: tumor necrosis factor inhibitor; BMI: body mass index; HR: hazard ratio; CI: confidence interval aReference is white; bReference is IBD; cCNO removed from both models due to small sample size and low event rate.

person-years) and 26 (IR 0.4 per 100 person-years) cases of psoriasis in children with and without TNFi exposure, respectively. The SIR was 17.5 (95% CI 14.2, 21.5) for the entire cohort, 29.9 (95% CI 23.4, 38.2) for the TNFi exposed group, and 8.7 (95% CI 5.9, 12.7) for the TNFi unexposed group. When holding all other covariates constant, the hazard ratio for psoriasis comparing TNFi exposure to no TNFi exposure was 4.23 (95% CI 2.56, 7.01, p< 0.001) (**Table 2**). In children with TNFi exposure, family history of psoriasis was independently associated with an increased hazard of psoriasis (HR 3.09, 95% CI 1.83, 5.22, p< 0.001) (**Table 2**).

Conclusion: Children with IBD, JIA, and CNO had an increased rate of psoriasis compared to the general pediatric population, with the highest rate in those with TNFi exposure. TNFi treatment in children with IBD and JIA was associated with an increased hazard of developing psoriasis compared to those not treated with TNFi.

Disclosure: L. Buckley, None; **R. Xiao**, None; **M. Perman**, None; **A. Grossman**, None; **P. Weiss**, None.

Abstract Number: 1817

Arthropathy of Down Syndrome: An Under-diagnosed Inflammatory Joint Disease That Warrants a Name Change

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology – Clinical II: JIA

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Incidence and prevalence of arthropathy of Down syndrome (A-DS) is increased. It is rarely recognised at onset and remains under-diagnosed. Children with A-DS are therefore presenting with significant joint damage and disability at diagnosis.

The aim of this study was to identify undiagnosed cases of A-DS, document time to diagnosis, and describe clinical, laboratory and radiological features of A-DS at diagnosis.

Methods: Children with DS (0–21 years) were invited to attend a local, regional musculoskeletal screening clinic (figure 1). At this appointment a paediatric rheumatology clinical fellow performed a detailed musculoskeletal examination. A second physician at a further clinic confirmed suspected cases of A-DS. Investigations and treatment were instigated as per normal clinical practice for JIA. Data on a convenience sample of 21 newly diagnosed children with JIA was collected to create a comparison group.

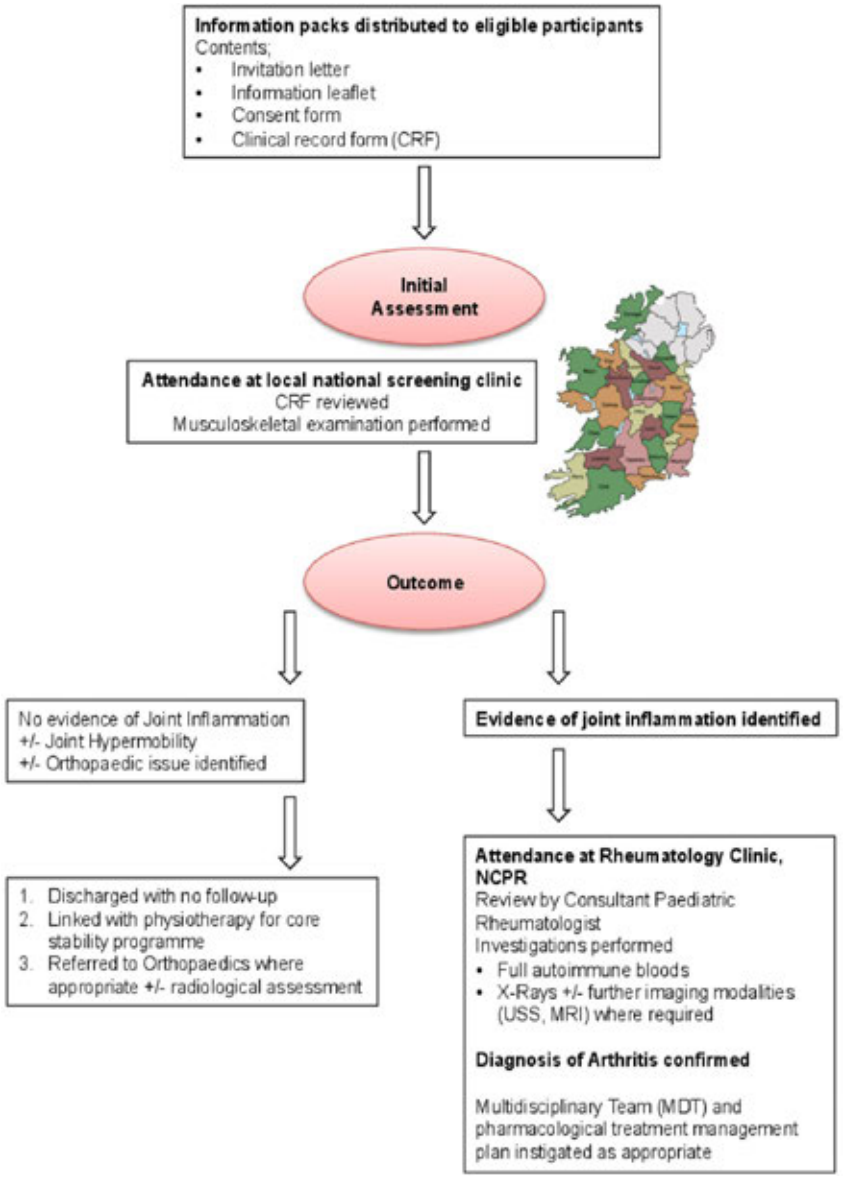

Figure 1. Flow diagram summarising the musculoskeletal screening process and follow-up provided to all children with Down syndrome that participated in the study.

Table 1. Demographic, clinical and laboratory features at diagnosis of A-DS (n=33) and JIA (n=21). Where data are presented as median and range, statistical significance was determined using the Mann-Whitney U-test. For data presented as a proportion of the total population, statistical significance was calculated using the Chi-square test or Fisher exact test. AJC = Active joint count; RJC = Restricted joint count, ESR = Erythrocyte sedimentation rate, CRP = C-Reactive Protein, ANA = Anti-nuclear antibody, RF = Rheumatoid factor. ϖSmall joint involvement is defined as evidence of active inflammation in the metacarpophalangeal (MCP), proximal (PIP) and/or distal (DIP) interphalangeal joints of the hands; ♯DA cohort of n = 25; ★DA cohort of n = 29 (n numbers less than total cohort as results missing)

Characteristic	A-DS n = 33	JIA n = 21	p value
Age, median in years (range)	11.4 (0.3 – 19.2)	6.3 (1.1 – 16)	p < 0.001
Gender, n male (% male)	18 (55)	11 (52)	ns
AJC, n (range)	3 (0 – 18)	4 (1 – 13)	ns
RJC, n (range)	4 (0 – 12)	1 (0 – 10)	p < 0.05
ϖSmall joint involvement, n (%)	28 (85)	9 (43)	p < 0.01
Raised ESR at diagnosis, n (%)	8♯ (32)	15 (71)	p < 0.01
Raised CRP at diagnosis, n (%)	3★ (10)	6 (29)	ns
ANA positive, n (%)	0 (0)	5 (24)	p < 0.01
RF positive, n (%)	0 (0)	1 (5)	ns

Results: Over an 18 month period, 503 children with DS were screened for arthritis and 18 new cases diagnosed. In total, 33 children were identified with A-DS (combining cases attending predating commencement of the study and those referred to our Centre during the study period) (Table 1). This suggests prevalence of A-DS is 20/1000. A significant delay in diagnosis of A-DS was observed. The majority of children presented with polyarticular RF negative arthritis, with predominance in the small joints of the hands and wrists. No children with A-DS were ANA positive. In the majority of cases, ESR and CRP were unhelpful in aiding diagnosis of A-DS. Erosive changes were reported on X-ray in a significantly ($p< 0.05$) greater proportion (42%) of children with A-DS than JIA (14%).

Conclusion: Studies of A-DS are limited. We describe a cohort of 33 children with A-DS. Comparable to previous reports, our results confirm an increased risk of arthritis in children with DS. However, we suggest that prevalence is at least 2–3 times greater than previously reported. We also observed a significant delay in diagnosis of A-DS, the reasons for this being multifactorial (figure 2). Children with A-DS most frequently present with a polyarticular RF negative arthritis, predominantly affecting the small joints of the hands and wrists. The arthritis is erosive in nature; a finding we do not believe is solely related to the observed delay in diagnosis.

Figure 5. corrected
Schematic highlighting challenges which may impede correct and timely diagnosis of A-DS (from top, clockwise). The first is lack of awareness about the increased risk of arthritis in children with DS among both the general public and healthcare professionals; Gradual functional loss over time rather than an acute presentation may go undetected by the child's carer. Frequently, delay in motor development is falsely attributed to intellectual disability, and changes in activities of daily living to behavioural problems associated with DS, rather than a possible diagnosis of arthritis. Hypermobility, a feature of DS may make musculoskeletal examination more challenging, as it may be difficult to appreciate loss of range of movement secondary to an inflammatory arthritis. Many children may be uncooperative when it comes to examination. This combined with poor verbal skills can make eliciting a clear history and thorough musculoskeletal examination challenging. Apparent differences in pain expression have been reported in children with DS. Children with DS often adapt to pain with reported observations such as slowing mobility, reluctance to hold a parental hand or behavioural change. Therefore, these are key features to try and elicit when taking a history from a child with a suspected diagnosis of A-DS.

This study highlights the importance of raising awareness about the increased risk of arthritis in children with DS to aid recognition and more timely diagnosis of A-DS. The addition of an annual musculoskeletal examination to the well recognised health surveillance guidelines for all children with DS would be an initiative of great benefit to this cohort. We propose a more appropriate clinical term that better reflects the inflammatory, erosive nature of the disease would be DS-associated arthritis (DA). In order to facilitate more cohesive clinical practice and future collaborative research, we would hope that this could become a universally accepted term among healthcare professionals and the general public. Future research to accurately define disease pathogenesis, identify a biomarker of disease and establish best practice in terms of treatment of A-DS would be of benefit.

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Abstract Number: 1818

Continuing versus Withdrawing Ixekizumab in Patients with Psoriatic Arthritis Who Achieved Sustained Minimal Disease Activity: Results from the SPIRIT-P3 Study

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical III: Miscellaneous

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory disease that may lead to serious disability if not appropriately treated. Data on the effect of treatment discontinuation and retreatment in the case of flare are scant. Ixekizumab (IXE), a high-affinity IL-17A antagonist, has demonstrated consistent efficacy in PsA for up to 3 years.[1] This study evaluated efficacy and safety of continuing vs. withdrawing IXE in PsA patients (pts) who achieved sustained minimal disease activity (MDA) on IXE and re-treating with IXE if required.

Methods: SPIRIT-P3 (NCT02584855) was a multicenter phase 3b study enrolling biologic-naïve pts with active PsA (diagnosis for ≥6 months, meeting Classification Criteria for Psoriatic Arthritis, ≥3/68 tender joints, ≥3/66 swollen joints) and previous inadequate response to conventional synthetic DMARDs (csDMARDs). Pts entered a 36-week, open-label (OL) treatment period with IXE every 2 weeks. Between Weeks 36–64, pts were randomized 1:1 to IXE or placebo (PBO) at the visit for which randomization criteria were met (sustained MDA for at least 4 visits over 3 consecutive months) and evaluated up to Week 104. Pts not meeting randomization criteria by Week 64 continued on IXE up to Week 104. Maintenance of treatment response was measured by the time to loss of sustained MDA (relapse) during the randomized withdrawal (RW) period. The proportion of pts who relapsed during the first 40 weeks of the RW period and time to regain MDA after re-treatment with IXE in relapsed pts were assessed. The Kaplan-Meier product limit method was used to estimate survival curves for time-to variables. Treatment comparisons were performed using a log-rank test adjusting for geographic region and csDMARD use as factors. Cumulative proportion of relapse was analyzed using a logistic regression model with treatment, geographic region, and csDMARD use as factors. Safety data were summarized for the entire study period for pts who received ≥1 dose of IXE.

Results: A total of 394 pts entered into the OL treatment period; 158 (40%) achieved sustained MDA criteria and were randomized to IXE (N=79) or PBO (N=79). Baseline characteristics were similar between groups (Table 1). The time to relapse for pts on PBO was significantly shorter than for pts on IXE ($p < 0.001$) during the RW period, with

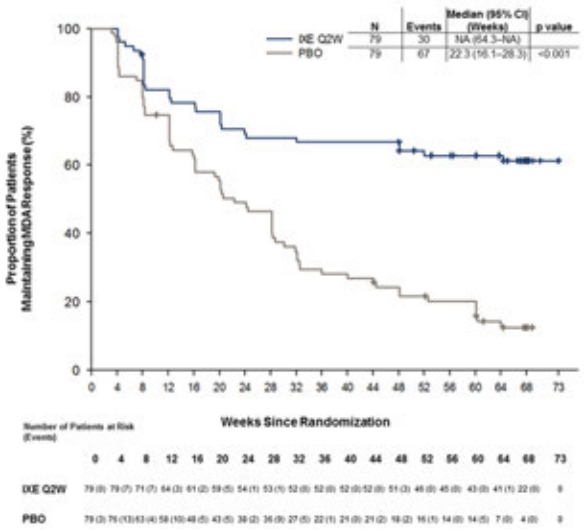
Table 1. Demographics and baseline characteristics

	Open-label population[a]	RW population[b]	
	IXE Q2W N=394	PBO N=79	IXE Q2W N=79
Age (years), mean (SD)	47 (11.4)	43 (10.5)	44 (10.8)
Male, n (%)	182 (46)	40 (51)	47 (60)
BMI (kg/m^2), mean (SD)	29 (6.3)	29 (7.2)	28 (5.0)
Time since PsA onset (years), mean (SD)	7.9 (7.1)	7.5 (7.5)	7.1 (6.3)
Current csDMARD use, N (%)[c]	291 (74)	60 (76)	59 (75)
TJC (68 joints), mean (SD)	21 (14.3)	16 (12.3)	17 (11.5)
SJC (66 joints), mean (SD)	10 (8.1)	9.0 (5.6)	9.4 (7.4)
HAQ-DI total score, mean (SD)	1.2 (0.6)	1.0 (0.5)	1.1 (0.6)
Pain VAS, mean (SD)	61 (18.0)	59 (18.9)	60 (19.4)
PatGA, mean (SD)	62 (18.9)	61 (19.5)	59 (18.3)
PASI total score[d], mean (SD)	7.1 (9.5)	7.6 (10.2)	8.4 (8.2)
BSA[e], mean (SD)	14 (17.6)	14 (17.8)	17 (18.2)
LEI total score, mean (SD)	2.6 (1.5)	2.5 (1.3)	2.4 (1.3)

[a]Week 0 to randomization or Week 64. [b]Randomization to relapse or Week 104. [c]Current csDMARD use reported at time of randomization. [d]In patients with baseline PASI >0. [e]In patients with baseline BSA >0.

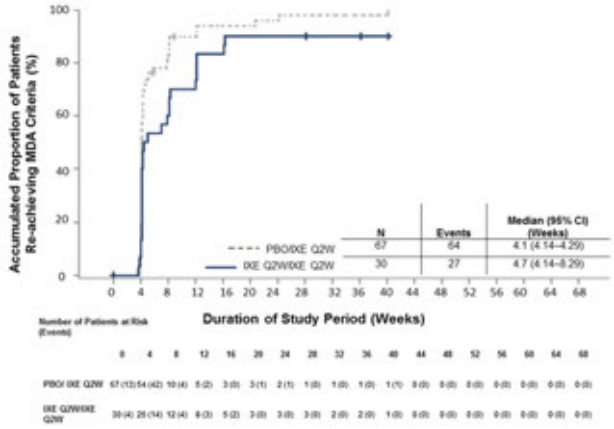
BMI=body mass index; BSA=body surface area; csDMARD=conventional synthetic disease-modifying anti-rheumatic drug; IXE Q2W=ixekizumab 80-mg every 2 weeks; HAQ-DI=Health Assessment Questionnaire-Disability Index; LEI: Leeds Enthesitis Index; N=number of patients in analysis population; PASI=Psoriasis Area and Severity Index; PatGA=Patient's Global Assessment of Disease Activity; PBO=placebo; RW=randomized withdrawal; SJC=swollen joint count; TJC=tender joint count; VAS=Visual Analog Scale.

Figure 1. Time to relapse (loss of MDA).



CI=confidence interval; MDA=minimal disease activity; IXE Q2W=ixekizumab 80 mg every 2 weeks; PBO=placebo. Time to relapse in weeks = (date of relapse – date of first injection of randomized dose of study treatment in the randomized double-blind withdrawal period +1)/7. Patients completing the withdrawal period without meeting relapse criteria were censored at the date of completion (the date of the last scheduled visit in the withdrawal period). Patients without a date of completion or discontinuation were censored at the latest non-missing date from the following dates: date of last injection of study treatment in the withdrawal period and date of last attended visit in the withdrawal period.

Figure 2. Time to re-achieving MDA following relapse.



CI=confidence interval; IXE Q2W=ixekizumab 80 mg every 2 weeks; PBO=placebo; RW=randomized withdrawal. The relapse population is defined as randomized patients who relapsed (no longer met criteria for MDA) after randomization and who received at least 1 dose of IXE after relapse.

a median time to relapse of 22.3 weeks in the PBO group (Figure 1). The cumulative relapse rate during the first 40 weeks of the RW period was 73% for PBO vs. 34% for IXE ($p < 0.001$). Of the patients who relapsed on PBO, 96% regained MDA following re-treatment with IXE. The median time to regain MDA was 4.1 weeks (95% CI 4.14–4.29) for PBO and 4.7 weeks (95% CI 4.14–8.29) for IXE (Figure 2). Safety data were consistent with previous IXE PsA studies with no unexpected safety signals.1

Conclusion: Continued IXE therapy was superior to PBO in maintaining MDA in biologic-naïve PsA pts who achieved sustained MDA on initial IXE treatment. A vast majority of pts who lost MDA after IXE withdrawal regained MDA with IXE re-treatment. Continuous IXE treatment is optimal for maintaining MDA; however, patients can regain MDA after re-treatment with IXE in case of treatment interruption.

1. Chandran V, et al. *Ann Rheum Dis.* 2018;77(Suppl 2): 385.

Disclosure: L. Coates, AbbVie, 2, 5, 8, Celgene, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Amgen, 5, 8, Galapagos NV, 5, Gilead Sciences, 5, Janssen Pharmaceutica, 5, UCB, 5, 8; **S. Pillai**, Eli Lilly, 1, 3, Eli Lilly and Company, 3; **L. Zhang**, Eli Lilly and Company, 1, 3, 4; **D. Adams**, Eli Lilly and Company, 1, 3; **L. Kerr**, Eli Lilly and Company, 1, 3; **M. Hojnik**, Eli Lilly and Company, 3, 4; **G. Gallo**, Eli Lilly, 1, 3, 4, Eli Lilly and Company, 1, 3, 4; **I. Valter**, Eli Lilly, 9, Eli Lilly and Company, 9; **H. Tahir**, AbbVie, Janssen, Eli Lilly, and Novartis, 8, Novartis, Eli-Lilly, 2; **V. Chandran**, Abbvie, 1, AbbVie, 1, 5, Abbvie, Amgen, Celgene, BMS, Eli Lilly, Janssen, Novartis, Pfizer, UCB, 5, Amgen, 5, Bristol Myers Squibb, 5, Celgene, 5, Eli Lilly, 3, Eli Lilly and Company, 5, 9, Janssen Pharmaceutica, 5, Novartis, 5, 8, Pfizer, 5, UCB, 5; **P. Mease**, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Boehringer Ingelheim, 5, Celgene, 2, 5, 8, Galapagos NV, 5, Genentech, 8, Gilead Sciences, 5, Janssen Pharmaceutica, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Sun Pharmaceutical Industries Ltd., 2, 5, UCB, 2, 5, 8; **A. Kavanaugh**, Abbott, 2, Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, 2, Amgen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 2, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, Pfizer Inc, 2, Roche, 2, UCB Pharma, 2.

Abstract Number: 1819

The Ankylosing Spondylitis Disease Activity Score Reflects and Predicts Response to Biologic Treatment in Axial Spondyloarthritis Patients with Coexistent Fibromyalgia Compared to the Bath Ankylosing Spondylitis Disease Activity Index

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical III: Miscellaneous
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Currently the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Spinal pain are used to assess whether a patient with Axial Spondyloarthritis (AxSpA) requires biologic therapy and their response to biologic therapy. However, the BASDAI does not just reflect inflammatory disease activity as it includes questions relating to fatigue (question 1) and musculoskeletal areas of tenderness (question 4) and therefore escalating treatment to biologic therapy, and/or stopping or switching biologic treatment based on a BASDAI may not improve symptoms or quality of life. We assessed the sensitivity of individual questions of the BASDAI, ASDAS and CRP against the response to biologics.

Methods: Data from 85 AxSpA patients were collected, including demographic characteristics, extraarticular manifestations and outcome measures. Patients were then analysed according to the following groupings: responder or non-responder to biologics. In each group, mean scores for individual questions of BASDAI, BASFI, ASDAS and CRP were calculated. Subjects were further analysed according to groups: Group 1 (BASDAI ≥4, ASDAS ≥2.1), Group 2 (BASDAI < 4, ASDAS ≥2.1) and Group 3 (BASDAI < 4, ASDAS < 2.1).

Results: There were n=65 male and n=20 female subjects. Mean (SD) age was 44.7 (13.3) years and AxSpA disease duration 9.5 (9.9) years. The mean BASDAI scores at baseline in patients receiving biologics were similar in respond-

Figure 1. Mean scores for Q1 and 4 of BASDAI

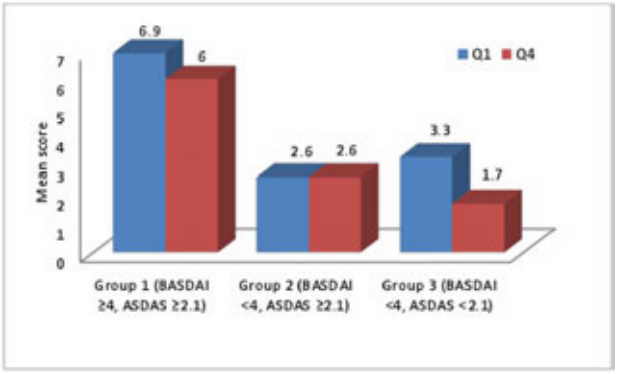
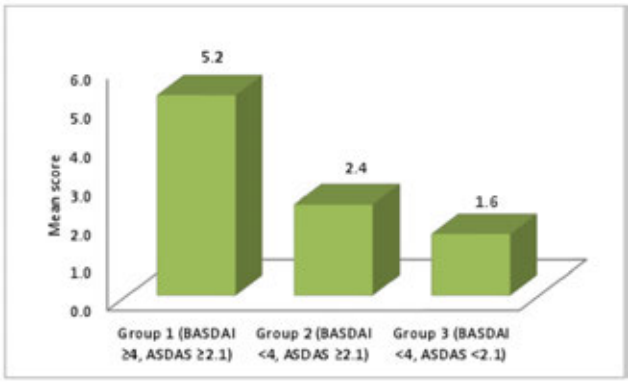


Figure 2. Mean BASFI score



ers 6.1 (1.8) and non-responders 6.2 (1.4). Post treatment with biologics, clinical non-responders had a higher mean score for Q1 and Q4 of the BASDAI (7.7 and 6.5) compared to responders (3.8 and 2.2). A similar trend was seen for BASFI (mean 5.9 in non-responders compared to 2.2 in responders). Further analysis using ASDAS, showed that patients in Group 1 had higher scores for Q1 and Q4 of the BASDAI (mean 6.9 and 6.0 respectively) and coexistent fibromyalgia compared to Groups 2 (mean 2.6 and 2.6) and 3 (mean 3.3 and 1.7), see Figure 1. This correlated with a high BASFI (mean of 5.2 in Group 1) compared to Group 2 (2.4) and 3 (1.6), see Figure 2. Patients in Group 2 had a higher CRP (mean 11.4) than the other groups (3.5 in Group 1 and 3.1 in Group 3), reflecting higher inflammatory burden. There was a lower proportion of females (16%) in Group 3 compared to the other groups (32% in Group 1 and 30% in Group 2). Furthermore, Group 3 had the highest percentage of patients with extra-articular manifestations (73%, compared to 51% and 58% respectively for Groups 1 and 2).

Conclusion: These findings support the hypothesis that fatigue and pain, as reflected by high scores for Q1 and Q4 of the BASDAI and coexistent fibromyalgia, are possible drivers of high perceived disease activity and non-response to biologics. This is correlated with a high BASFI. The elevated CRP seen in Group 2 suggests a higher burden of inflammation, in spite of low BASDAI scores, suggesting a need for more intensive therapy in this group. There was a trend for biologic responders to be males and with more extra-articular manifestions. ASDAS provides a means of incorporating more objective measures of disease activity, such as CRP, into clinical assessment, and therefore provides a useful adjunct to traditional Bath scores in assessing response to biologics.

Disclosure: S. Sacks, None; **K. Rigler**, None; **A. Chan**, Novartis, 8, UCB, 8, Abbvie, 8, Celgene, 8.

Abstract Number: 1820

Clinically Relevant Deficits in Performance Tests in Patients with Axial Spondyloarthritis(axSpA) – Collecting Questionnaires Is Insufficient

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical III: Miscellaneous

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Session Time: 2:30PM–4:00PM

Background/Purpose: Physical function in axial spondyloarthritis (axSpA) usually assessed by the BASFI questionnaire is an established core domain of that disease. There is evidence that self- reported physical function is not equivalent with the actual performance of patients. Physical performance can be assessed as a single task such as grip strength or single stance, or as a generic compound measure such as the short physical performance battery test (SPPB). SPPB comprises a chair rising test, a balance test and gait speed. The aim of the study is to investigate which performance tests are most frequently impaired in patients with axSpA.

Methods: Consecutive axSpA patients presenting to our tertiary hospital underwent a standardized assessment including patient and disease characteristics, patient-reported outcomes (ASDAS, BASFI, BASMI, ASAS Health Index (ASAS HI), PHQ-9) and performance tests (SPPB, grip strength and single stance). Structural damage was assessed by mSASSS. Validated cut-offs were used for SPPB, chair rise test, grip strength and gait speed. Impairment of performance tests as well as discrimination between subgroups was analysed.

Results: A total of 200 patients (r-axSpA 65.5%, nr-axSpA 34.5%) were included: 69% males, 44.3±12.5 years of age, mean symptom duration 17.9±12.6 years, mean ASDAS 2.5±1.1, BASFI 4.0±2.7, BASMI 3.5±1.8, ASAS HI 7.0±4.1, PHQ-9 8.8±6.2, mSASSS (n=157) 10.2± 18.8. A total of 132 patients were treated with bDMARDs (66.5%). The two most impaired performance tests were repeated chair rising and single stance (Figure 1). An impairment

Measure (n=200)	Patients with impairments	Mean (SD)	95% CI	Min-Max	Median	25-p75 percentile
SPPB (range 0-12), threshold ≤ 8	22 (11,0 %)	10,3 (1,8)	10,0-10,5	2-12	11	9-12
Repeated chair stand test, threshold > 15 s*	75 (37,5 %)	14,3 (5,9)	13,4-15,1	6,8-42,9	12,8	10,5-17,0
Gait speed, threshold ≤ 0,8 m/s	18 (9,0 %)	1,1 (0,3)	1,08-1,16	0,4-2,4	1,1	1,0-1,3
Grip strength male, threshold < 27 kg, n =138	11 (8,0 %)	42,2 (9,7)	40,5-43,8	15,0-66,0	43,0	36,4-48,0
Grip strength female, threshold < 16kg, n =62	6 (9,7 %)	24,0 (5,4)	22,6-25,3	12,0-38,0	24,0	21,8-27,0
Single stance, threshold ≤ 10 s, n =169**	25 (14,8 %)	66,6 (45,8)	59,5-73,6	2,2-120,0	60,2	19,9-120,0

*14 patients were not able to perform the test
** 4 patients were not able to do a single stance

Performance tests in patients with axSpA

in≥ 1 performance test was seen in 87 patients (43.5%). Patients with impairments, in comparison to those without, were older (48.9 vs. 40.8 years), more often obese (28.7 vs. 26.1%), more often depressed (PHQ 12.1 vs. 6.3%), had lower BASFI values (5.7 vs. 2.8), a decreased ASAS HI (9.6 vs. 5.0), and higher disease activity (ASDAS 3.0 vs. 2.1), all p< 0.01. The documented impairment in performance was irrespective of medication and structural damage on the group and the individual patient level. The correlation between BASFI and the performance test was moderate for SPPB (0.6), gait speed (0.5), chair rise (0.5) and single stance (0.4), while the correlation between BASFI and grip strength (0.2) and mSASSS (0.2) was rather limited.

Conclusion: n this consecutively recruited relatively young axSpA patients with limitations in physical function and health as assessed by established measures, we found a high prevalence of patients who didn't perform well in tests originally developed for older people. Importantly, a lot of impairment was seen when patients were asked to perform complex tasks requiring coordination and muscle strength. Impairment was present even though most patients received bDMARDs. Since such impairment is potentially influenced by physiotherapeutic interventions, we propose to perform studies to address these deficits. Our data strongly suggest to not only collect questionnaires but also do performance tests to better assess the 'real' physical capacity of patients.

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Abstract Number: 1821

Tildrakizumab Efficacy for Psoriatic Arthritis: 24-week Analysis of Swollen and Tender Joint Counts and Pain

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical III: Miscellaneous
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Tildrakizumab (TIL), a high-affinity anti–interleukin-23p19 monoclonal antibody, is approved to treat moderate-to-severe plaque psoriasis. A randomized, double-blind, multidose, placebo (PBO)-controlled, phase 2b study (NCT02980692) is evaluating the efficacy and safety of TIL for PsA. This analysis evaluated the efficacy of TIL on 66 swollen and 68 tender joint counts (SJC and TJC) and pain in patients with active PsA at week 24.

Table 1. Patient demographics and baseline disease characteristics. *For prior anti–TNF-α therapy, total patients analyzed (N) = 79, 78, 80, 78, and 76 for TIL 200 mg Q4W, TIL 200 mg Q12W, TIL 100 mg, TIL 20 mg, and PBO, respectively. BMI, body mass index; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; SD, standard deviation; TIL, tildrakizumab.

	TIL 200 mg Q4W (N = 78)	TIL 200 mg Q12W (N = 79)	TIL 100 mg Q12W (N = 77)	TIL 20 mg Q12W (N = 78)	PBO (N = 79)
Age, years, mean ± SD	50.1 ± 13.3	49.3 ± 11.2	49.2 ± 11.9	47.2 ± 13.4	48.1 ± 13.3
Female, n (%)	46 (59.0)	37 (46.8)	47 (61.0)	41 (52.6)	44 (55.7)
Race, n (%)					
White	76 (97.4)	78 (98.7)	75 (97.4)	75 (96.2)	74 (93.7)
Black or African American	0	0	1 (1.3)	1 (1.3)	3 (3.8)
Other	2 (2.6)	1 (1.3)	1 (1.3)	2 (2.6)	2 (2.5)
Weight, kg, mean ± SD	85.1 ± 19.7	87.1 ± 19.5	83.6 ± 18.9	85.1 ± 18.1	85.3 ± 20.2
BMI, kg/m², mean ± SD	30.1 ± 6.5	30.2 ± 6.5	29.5 ± 6.8	29.4 ± 5.2	29.5 ± 6.0
Duration of PsA, years, mean ± SD	6.9 ± 7.3	6.8 ± 6.3	6.3 ± 7.2	6.6 ± 6.7	7.3 ± 8.0
Prior anti–TNF-α therapy, n (%)*	18 (22.8)	17 (21.8)	19 (23.8)	19 (24.4)	18 (23.7)
Swollen joint count, mean ± SD	10.4 ± 7.4	10.0 ± 8.0	11.0 ± 8.2	9.4 ± 6.4	11.8 ± 9.8
Tender joint count, mean ± SD	16.6 ± 11.9	19.5 ± 13.9	21.3 ± 14.8	19.0 ± 13.0	19.7 ± 14.7
Pain, mean ± SD	55.4 ± 19.1	59.6 ± 23.5	59.2 ± 22.1	60.9 ± 19.7	64.2 ± 20.4

Methods: Patients with active PsA (Classification of Psoriatic Arthritis criteria),[1] stratified by prior anti-TNF use and baseline body weight (≤90 kg and ≥90 kg), were randomized 1:1:1:1:1 to receive TIL (200 mg once every 4 weeks [Q4W], 200 mg every 12 weeks [Q12W], 100 mg Q12W, 20 mg Q12W to week 24) or PBO Q4W to week 24. SJC and TJC were performed by an independent blinded assessor at baseline and Q4W through week 24. Patients rated pain using a visual analog scale (0–100 mm). Safety was assessed by monitoring treatment-emergent adverse events.

Results: Of 500 patients screened, 391 met the inclusion criteria with 77–79/treatment arm. Mean (SD) age was 48.8 (12.6) years, disease duration 6.8 (7.1) years, body mass index 29.7 (6.2), and 91 were TNF-α experienced (**Table 1**). At week 24, the least squares (LS) mean (standard error [SE]) reduction from baseline in SJC was 8.3 (0.5)/7.7 (0.5)/8.2 (0.5)/7.6 (0.5) in TIL arms vs 6.5 (0.5) in the PBO arm and statistically significant in TIL 100 mg Q12W and 200 mg Q4W vs PBO (P = 0.0189 and 0.0111, respectively, **Figure 1**). LS mean (SE) reduction in TJC was 11.9 (1.0)/12.6 (1.0)/13.0 (1.0)/12.0 (1.0) in TIL arms vs 9.4 (1.0) in the PBO arm; statistically significant for TIL 100 and 200 mg Q12W vs PBO (P = 0.0140 and 0.0234). LS mean (SE) reduction in patient pain was 35.2 (2.7)/31.7 (2.6)/32.2 (2.6)/28.9 (2.7) in TIL arms vs 21.5 (2.6) in the PBO arm; statistically significant for TIL 100, 200 mg Q12W, and 200 mg Q4W vs PBO (P = 0.0039, 0.0056, and 0.0003). Percent change from baseline for SJC (73.0%–79.8% TIL vs 59.3% PBO), TJC (62.1%–67.5% TIL vs 48.7% PBO), and pain (47.5%–63.5% TIL vs 33.5% PBO) at week 24 are shown in **Figure 2**. No malignancies, major adverse cardiac events, or deaths were reported.

Conclusion: At week 24, TIL 100 mg Q12W and 200 mg Q4W significantly reduced SJC vs PBO; TIL 100 and 200 mg Q12W significantly reduced TJC vs PBO. All TIL treatment arms had significant improvement in pain vs PBO in patients with PsA who were anti–TNF-naïve or experienced.

Editorial and writing support was provided by Marie-Louise Ricketts, PhD, of AlphaBioCom, LLC.

Reference:

1. Taylor W, et al. *Arth Rheum*, 2006; 54: 2665-2673

Disclosure: A. Orbai, AbbVie, 2, Celgene, 2, Eli Lilly, 2, 5, Horizon, 2, Janssen, 2, 5, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 5, UCB, 5; **R. Ballerini**, Sun Pharmaceutical Industries, Inc., 3; **R. Chou**, Sun Pharmaceutical Industries, Inc., 5; **S. Rozzo**, Sun Pharmaceutical Indsutries, Inc, 3, Sun Pharmaceutical Industries, Inc, 3, Sun Pharmaceutical Industries, Inc., 3; **A. Mendelsohn**, Johnson and Johnson, 1, 4, Sun Pharmaceutical Industries, Inc, 3, Sun Pharmaceutical Industries, Inc., 3; **L. Espinoza**, None.

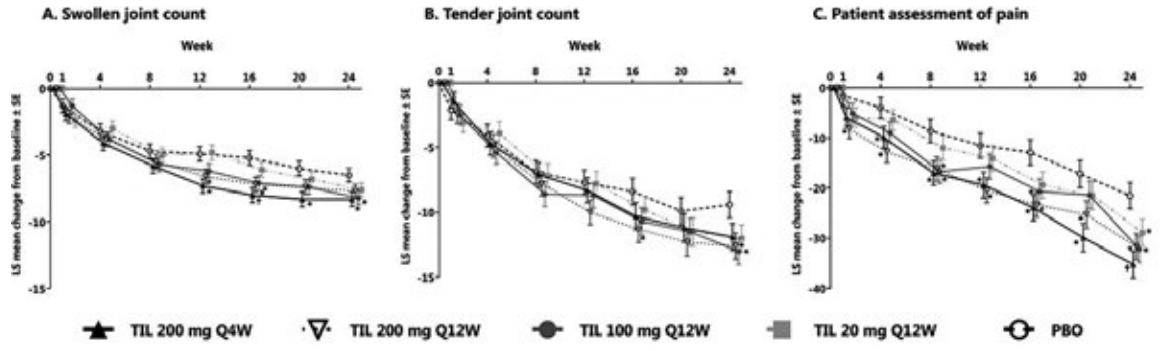

Figure 1. Mean Swollen (66) and tender (68) joint counts and pain through week 24. Shown for randomized patients who received ≥1 dose of study drug; values at week 0 represent baseline. *P <0.05; †P <0.001 vs PBO. LS, least squares; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; SE, standard error; TIL, tildrakizumab.

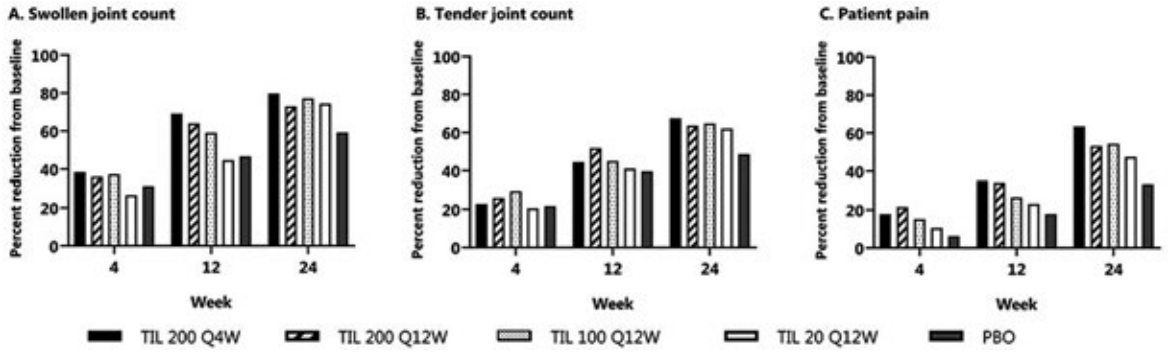

Figure 2. Percent change from baseline to 24 weeks in swollen (66) and tender (68) joint counts, and pain. Shown for randomized patients who received ≥1 dose of study drug. Swollen and tender joint count graphs were generated based on mean change from baseline; pain assessment graph is based on LS mean change in baseline. LS, least squares; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

Abstract Number: 1822

6 and 12-month Drug Retention Rates and Treatment Outcomes in 941 Patients with Axial Spondyloarthritis Treated with Secukinumab in Routine Clinical Practice in 12 European Countries in the EuroSpA Research Collaboration Network

Brigitte Michelsen ,[1] Johan Askling,[2] Catalin Codreanu,[3] Herman Mann,[4] Anne Gitte Loft,[5] Manuel Pombo-Suarez,[6] Ziga Rotar,[7] Tore Kvien,[8] Maria José Santos,[9] Anna Mari Hokkanen,[10] Florenzo Iannone,[11] Bjorn Gudbjornsson,[12] Fatos Onen,[13] Lennart Jacobsson,[14] Ruxandra IONESCU,[15] Karel Pavelka,[4] Carlos Sánchez-Piedra,[16] Matija Tomsic,[17] Joe Sexton,[18] Helena Santos,[19] Jenny Österlund,[20] Alberto Cauli,[21] Arni Jon Geirsson,[22] Servet Akar,[23] Adrian Ciurea,[24] Gareth Jones,[25] Irene van der Horst-Bruinsma,[26] Cecilie Heegaard Brahe,[27] Stylianos Georgiadis,[28] Lykke Midtbøll Ørnbjerg,[27] Mikkel Østergaard,[29] and Merete Lund Hetland[30], [1]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet Glostrup, Denmark/ Hospital of Southern Norway Trust, Kristiansand, Norway/ Diakonhjemmet Hospital, Oslo, Norway, Oslo, Norway, [2]Karolinska Institutet, Stockholm, Sweden, [3]Center of Rheumatic Diseases, University of Medicine and Pharmacy, Bucharest, Romania., Bucharest, Romania, [4]Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Prague, Czech Republic, Prague 2, Czech Republic, [5]Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark, Århus, Denmark, [6]Unit Research, Spanish Society of Rheumatology, Madrid, Spain, [7]UMC LJUBLJANA, DPT. OF RHEUMATOLOGY, LJUBLJANA, Slovenia, [8]Diakonhjemmet Hospital, Dept. of Rheumatology / University of Oslo, Faculty of Medicine, Oslo, Norway, [9]Rheumatology department, Hospital Garcia de Orta, Almada, Portugal, [10]Helsinki University Hospital, Helsinki, Finland, [11]Department of Emergency and Transplantation , Rheumatology Unit, University Hospital of Bari, Bari, Italy., Bari, Italy, [12]Centre for Rheumatology Research, Landspitali and Faculty of Medicine, University of Iceland, Reykjavik, Iceland, [13]Dokuz Eylul University School of Medicine, Division of

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SESSION INFORMATION

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Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

			All patients (n=941)	b/tsDMARD naïve patients (n=184)	1 prior b/tsDMARD (n=224)	2 or more prior b/tsDMARDs (n=533)	p-value*
Age (years), mean (SD) n available			47.5 (12.0) n=941	45.8 (12.3) n=184	47.7 (11.6) n=224	48.1 (12.0) n=533	0.08
Male, % n available			57.1% n=941	70.7% n=184	58.5% n=224	51.8% n=533	<0.001
Years since diagnosis, mean (SD) n available			10.4 (9.4) n=737	8.1 (9.7) n=174	10.9 (9.7) n=194	11.2 (8.9) n=369	<0.001
Current smokers, % n available			21.5 % n=888	22.5% n=173	22.2% n=212	20.9% n=503	0.87
Baseline C reactive protein (mg/L), median (25-75th percentiles) n available			9 (2-26) n=769	14 (5-32) n=147	9 (2-29) n=178	7 (2-24) n=444	<0.001
Baseline Erythrocyte sedimentation rate (mm/h), median (25-75th percentiles) n available			24 (10-45) n=618	26 (14-45) n=133	26 (9-43) n=149	21 (8-46) n=336	0.29
Baseline Pain (0-100), median (25-75th percentiles) n available			70 (50-81) n=708	80 (65-90) n=124	69 (41-80) n=160	70 (50-81) n=424	<0.001
Baseline Fatigue (0-100), median (25-75th percentiles) n available			70 (50-85) n=617	77 (65-90) n=111	65 (46-80) n=145	70 (50-86) n=361	<0.001
Average (95%CI) drug retention time in weeks, censored by 52 weeks n available			44.2 (43.3-45.1) n=941	47.5 (45.8-49.2) n=184	45.4 (43.6-47.1) n=224	42.6 (41.2-43.9) n=533	<0.001
Average (95%CI) time in weeks to secukinumab withdrawal in patients who withdrew due to loss of efficacy or adverse events before 12 months, n of events			22.9 (21.3-24.6) n=247	21.7 (17.5-25.9) n=27	23.7 (20.4-26.9) n=51	22.9 (20.8-25.0) n=169	0.82
Secukinumab retention rate, % (95%CI) *n at risk at 6/12 months*		6 months	82.4% (79.9-84.9%) n=756	89.5% (85.2-94.1%) n=184	85.9% (81.4-90.6%) n=224	78.4% (75.0-82.0%) n=533	0.001
		12 months	72.9% (70.1-75.9%) n=639	85.0% (80.0-90.4%) n=184	76.4% (70.9-82.3%) n=224	67.2% (63.3-71.4%) n=533	<0.001
BASDAI, median (25-75th percentiles) n available		Baseline	6.2 (4.5-7.7) n=780	6.4 (4.6-7.9) n=171	5.9 (4.2-7.2) n=189	6.2 (4.6-7.7) n=420	0.04
		6 months	3.9 (2.0-6.1) n=612	2.9 (1.5-4.3) n=120	2.8 (1.6-5.4) n=129	4.9 (2.5-6.7) n=363	<0.001
		12 months	2.8 (1.4-5.1) n=228	2.3 (1.0-3.4) n=85	4.0 (1.3-6.0) n=53	3.8 (1.8-5.4) n=90	<0.001
ASDAS, median (25-75th percentiles)		Baseline	3.6 (2.9-4.4)	4.2 (3.4-4.6)	3.6 (2.7-4.2)	3.5 (2.8-4.3)	<0.001
		6 months	2.6 (2.0-3.4)	2.2 (1.7-2.8)	2.5 (1.8-3.1)	2.8 (2.1-3.6)	<0.001
		12 months	2.2 (1.6-2.9)	2.2 (1.3-2.5)	2.5 (1.6-3.4)	2.8 (1.9-3.2)	0.001
BASDAI <2, % n available	6 months	Crude	24.2% n=612	32.5% n=120	32.6% n=129	18.5% n=363	<0.001
		LUNDEX adjusted**	16.4% n=612	26.5% n=120	23.0% n=129	11.5% n=363	<0.001
	12 months	Crude	33.8% n=228	43.5% n=85	30.2% n=53	26.7% n=90	0.051
		LUNDEX adjusted**	23.0% n=228	35.5% n=85	21.3% n=53	16.6% n=90	0.01
BASDAI <4, % n available	6 months	Crude	51.1% n=612	70.8% n=120	61.2% n=129	41.0% n=363	<0.001
		LUNDEX adjusted**	34.7% n=612	57.7% n=120	43.2% n=129	25.5% n=363	<0.001
	12 months	Crude	62.3% n=228	80% n=85	49.1% n=53	53.3% n=90	<0.001
		LUNDEX adjusted**	42.3% n=228	65.2% n=85	34.6% n=53	33.1% n=90	<0.001
ASDAS <1.3, % n available	6 months	Crude	7.9% 39/521	10.1% n=99	9.4% n=106	6.0% n=316	0.28
		LUNDEX adjusted**	5.1% n=521	8.2% n=99	6.6% n=106	3.7% n=316	0.19
	12 months	Crude	14% n=157	22.8% n=57	14.7% n=34	6.1% n=66	0.03
		LUNDEX adjusted**	9.5% n=157	18.6% n=57	10.4% n=34	3.8% n=66	0.04
ASDAS <2.1, % n available	6 months	Crude	23.4% n=521	31.3% n=99	26.4% n=106	19.9% n=316	0.047
		LUNDEX adjusted**	15.9% n=521	25.5% n=99	18.6% n=106	12.4% n=316	0.007
	12 months	Crude	32.5% n=157	42.1% n=57	23.5% n=34	28.8% n=66	0.13
		LUNDEX adjusted**	22.1% n=157	34.3% n=57	16.6% n=34	17.9% n=66	0.056

*Comparisons between b/tsDMARD naïve and non-naïve patients are performed with ANOVA for normally distributed data and with Kruskal-Wallis for skewed data. Drug retention is compared with Kaplan-Meier with log-rank test. **LUNDEX adjusted treatment outcome = (number of patients still treated at the respective timepoints / number of patients starting treatment) x (% of patients achieving the respective treatment outcomes)

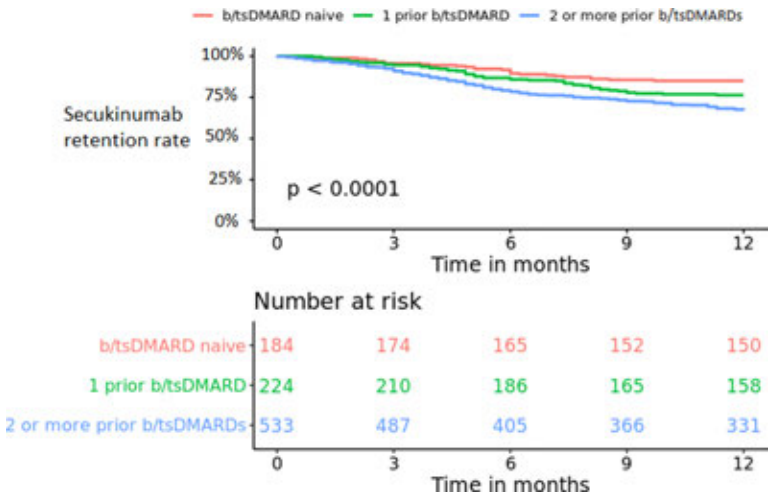

Figure. Pooled 12-month secukinumab retention rates for axSpA patients in EuroSpA stratified by previous b/tsDMARD treatment (log rank test; p<0.001).

Background/Purpose: Secukinumab is a fully human IgG1 monoclonal antibody targeting interleukin-17A. There is a lack of real-life evidence on secukinumab retention rates and treatment outcomes in axial spondyloarthritis (axSpA) patients. Hence, the aim of this study was to determine the 6- and 12-month secukinumab retention rates as well as the crude and LUNDEX corrected proportions of patients in remission after 6 and 12 months of treatment in Europe. This was assessed overall as well as stratified by prior biologic disease-modifying anti-rheumatic drug (bDMARD)/ targeted synthetic (ts)DMARD use.

Methods: Data from axSpA patients treated with secukinumab in routine care from 12 countries in the European Spondyloarthritis (EuroSpA) Research Collaboration Network were pooled. Time from treatment initiation to data cut was ≥ 12 months regardless of treatment durations and cover start date between May 2015 and April 2018. The following outcomes were calculated: Proportions of patients achieving Bath Ankylosing Spondylitis Disease Activity Score (BASDAI) < 2 / BASDAI < 4 and Ankylosing Spondylitis Disease Activity Score (ASDAS) < 1.3/ ASDAS < 2.1 at 6 and 12 months, including with LUNDEX1 adjustments. Group comparisons between b/tsDMARD naïve and 1 or ≥2 prior b/tsDMARD users were performed with ANOVA, Kruskal-Wallis or Chi-square test or with Kaplan-Meier analyses with log rank test, as appropriate.

Results: A total of 941 axSpA patients were included, thereof 6 who started treatment in 2015, 215 in 2016, 573 in 2017 and 147 in 2018. Overall 6/12-month secukinumab retention rate was 82%/73% and higher in b/tsDMARD naïve compared to non-naïve patients (table, figure). After 6/12 months treatment BASDAI < 4 was achieved by 51%/62%, BASDAI < 2 by 24%/34%, ASDAS < 2.1 by 23/33% and ASDAS < 1.3 by 8%/14% of the patients. b/tsDMARD naïve patients compared with patients treated with 1 prior or 2 or more prior b/tsDMARDs had shorter time since diagnosis, higher baseline disease activity and a higher proportion were men. Overall, LUNDEX adjusted 6 and 12 months' responses were achieved more often in b/tsDMARD naive patients than in patients who had received 1 or 2 or more previous b/tsDMARDs (table).

Conclusion: This study of >900 patients in 12 European countries provided real-world data on the effectiveness of secukinumab in patients with axSpA, adding evidence to existing RCTs. A majority of the patients were treated with 2 or more previous b/tsDMARDs and had long disease duration. Overall retention rate was 82%/73% at 6/12 months, respectively, with higher retention rates for b/tsDMARD naïve compared with patients treated with 1 or 2 or more previous b/tsDMARDs. Overall, a higher proportion of bionaïve than previous b/tsDMARD users achieved remission regardless of remission criteria.

Reference:

1. Kristensen et al. Arthritis Rheum 2006, 54(2):600-606

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Abstract Number: 1823

Magnetic Resonance Enterography as a Screening Tool to Detect Sacroiliitis in Crohn's Disease: Association with Clinical and Endoscopic Markers of Crohn's Disease Activity

Fardina Malik ,[1] Irvine Levine,[2] Gabrielle Castillo,[1] Brian Jaros,[2] Erin Alaia,[1] Justin Ream,[2] Jordan E. Axelrad,[1] David P. Hudesman,[1] and Jose Scher[3], [1]New York University School of Medicine, New York, NY, [2]New York University School of Medicine, New York, [3]Division of Rheumatology, New York University School of Medicine and NYU Langone Orthopedic Hospital, New York, NY

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical III: Miscellaneous

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Table 1. Baseline Patient Demographics Divided by Presence of Sacroiliitis

Table 1: Baseline Patient Demographics Divided by SI				
	Total (n=258)	No SI (n=213)	SI (n=45)	p-value
Age at MRE (years, median, IQR)	30.71 (25.24, 42.75)	30.24 (24.92, 41.16)	34.21 (26.86, 48.53)	0.232
Female	46.5% (120/258)	43.7% (93/213)	60% (27/45)	**0.046**
White	79.7% (204/258)	79.20% (168/212)	81.80% (36/44)	0.649
Back pain at the time of MRE	7.8% (20/258)	6.10% (13/213)	15.60% (7/45)	**0.031**
Seen by rheumatologist	13.6% (35/258)	9.90% (21/212)	31.10% (14/45)	**<0.001**
Personal history of Rheumatologic Disease	39.92% (103/258)	38.00% (81/213)	48.90% (22/45)	0.176
FHx of Rheumatologic disease	10.9% (28/258)	10.30% (22/213)	13.30% (6/45)	0.556
FHx of IBD	31.8% (82/258)	32.40% (69/213)	28.90% (13/45)	0.646
SI= sacroiliitis; MRE=Magnetic Resonance enterography; FHx=Family History				

Background/Purpose: Prevalence of sacroiliitis (SI) in Crohn's disease (CD) varies widely (range 4% -39%), depending on criteria utilized to define the disease (e.g. inflammatory back pain, plain radiographs or MRI). Sacroiliitis may remain underdiagnosed in CD patients given lack of association with clinical symptoms of back pain and CD activity. However, patients with CD often undergo magnetic resonance enterography (MRE) to assess extent, severity of small bowel CD and radiographic healing, affording clinicians the opportunity to evaluate for the presence of active and/or chronic SI. We sought to identify the prevalence of sacroiliitis in CD patients utilizing MRE and determine its relationship with CD activity, especially with concurrent biologic therapy.

Methods: All CD subjects undergoing MRE between years 2014-2018 at a large IBD referral center were identified. A musculoskeletal radiologist, blinded to clinical data, reviewed all MRE exams for the presence of acute bone marrow edema (BME) lesions and chronic lesions suggestive of acute and chronic SI, respectively. A second radiologist, also blinded, assessed MRE for mucosal CD activity using validated measures. Charts were reviewed for demographics, IBD characteristics, presence of back pain, clinical and endoscopic activity of CD, and Crohn's therapies within 3 months of MRE. Comparisons were made between CD subjects with and without SI using chi-square test. Univariate and multivariate logistic regression were used to determine risk factors of SI.

Results: 258 subjects with CD underwent MRE during the study period with a mean age of 35 years old, 53% (n=138) were male, and mean duration of CD at the time of MRE was 9 years. Few reported back pain (8%) and 14% had previously seen a rheumatologist. Overall, 17% (n=45) of patients had MR evidence of sacroiliitis (Table 1). Female gender, presence of back pain, and later age of CD diagnosis were associated with signs of sacroiliitis (p=0.05, p< 0.001, p=0.04 respectively; Table 2). Stricturing phenotype was associated with a lower rate of SI (7% vs. 24%; p=0.018), but inflammatory or penetrating phenotypes were not. CD location, activity as noted by clinical scores, endoscopic disease activity, or radiographic disease activity on MRE, were not associated with sacroiliitis (Table 2). On multivariable analysis, back pain was associated with the presence of sacroiliitis on MRE (OR 3.0, 95% CI 1.1- 5.6; p=0.04). Concurrent CD therapy with biologics did not lower the risk of sacroiliitis.

Conclusion: Although often underdiagnosed, SI is a common comorbid condition in CD. While recent history of back pain was associated with the presence of sacroiliitis visualized on MRE, no correlations were found with other clinical and endoscopic markers of CD activity. Moreover, concurrent CD therapy, especially biologics, was not associated with a lower risk of sacroiliitis on MRE. With limited clinical clues and CD characteristics to suggest sacroiliitis, gastroenterologists can utilize MRE as a screening tool to detect SI and refer CD patients to rheumatologists. Presence of SI on MRE in CD patients with back pain may help identify a subset of individuals likely to benefit from switching to therapies with proven efficacy in axial SpA.

Table 2. Crohn's Disease History and Activity Divided by Presence of Sacroiliitis

Table 2: Crohn's Disease History and Activity Divided by SI			
	No SI (n=213)	SI (n=45)	p-value
Age at Diagnosis, (years, median, IQR)	21.86 (15.52; 29.66)	27.82 (19.12; 36.39)	**0.04**
Montreal Age Classification			0.171
A1	31.46% (67/213)	20.00% (9/45)	
A2	54.93% (117/213)	57.78% (26/45)	
A3	13.62% (29/213)	22.22% (10/45)	
Disease duration at MRE (years, median, IQR)	7.52 (2.02; 14.11)	5.07 (1.29; 13.14)	0.528
Disease location			0.973
L3 (ileocolonic)	43.20% (92/213)	40.00% (18/45)	
L2 (colonic)	18.30% (39/213)	17.80% (8/45)	
L1 (small bowel/TI)	38.50% (82/213)	42.20% (19/45)	
upper GI involvement	7.00% (15/213)	13.30% (6/45)	0.161
Disease behavior			0.091
B1 (nonstricturing/nonpenetrating)	33.67% (67/199)	47.62% (20/42)	0.094
B2 (stricturing)	23.62% (47/199)	7.14% (3/42)	**0.018**
B3 (penetrating)	42.71% (85/199)	45.24% (19/42)	0.774
Perianal disease	32.90% (70/213)	26.70% (12/45)	0.417
Complications (abscess, obstruction)	39.10% (82/210)	34.10% (15/44)	0.846
Previous GI surgery	26.80% (57/213)	15.60% (7/45)	0.114
Current medications			
sulfasalazine	1.40% (3/213)	0% (0/45)	0.423
Biologics			
TNF-alpha inhibitor	37.10% (79/213)	33.30% (15/45)	0.634
Vedolizumab	3.30% (7/213)	0% (0/45)	0.218
Ustekinumab	7.50% (16/213)	8.90% (4/45)	0.754
Small Molecules	0.50% (1/213)	0% (0/45)	0.645
Methotrexate	4.70% (10/213)	4.40% (2/45)	0.942
Thiopurine	15.00% (32/213)	11.10% (5/45)	0.496
Systemic corticosteroids	23.90% (51/213)	24.40% (11/45)	0.943
Aminosalicylate	18.30% (39/213)	24.40% (11/45)	0.344
Most recent labs			
Fecal calprotectin (median, IQR)	105 (29, 278)	152 (60, 365)	0.642
CRP (median, IQR)	3.3 (1, 10)	5.2 (2, 9.6)	0.391
Clinical Scores			

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Abstract Number: 1824

Perceived Stress Independently Associates with Worse Type 2 Symptoms in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical II: Flares & Morbidity of SLE
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: A new posited framework for categorizing patients with systemic lupus erythematosus (SLE) is the division of symptomatology into two groups: type 1 manifestations represent classic signs and symptoms of lupus, link to immune-mediated inflammatory pathways, and respond to immunosuppressive therapy; type 2 manifestations represent symptoms such as fatigue, widespread pain, cognitive dysfunction, and self-reported disease activity that do not respond to the same treatments and are an area of major unmet need[1]. The pathogenesis and risk factors for type 2 symptoms remain poorly defined, and prior studies suggest a possible link between stress and disease severity in SLE. We examined whether high levels of psychological stress were associated with worse disease status in SLE and whether the association differed for type 1 and type 2 symptoms.

1. Pisetsky et al. A Novel System to Categorize the Symptoms of SLE. Arthritis Care Res 2018.

Table. Adjusted Means for Type 1 and Type 2 Lupus Symptoms by Perceived Stress

	Adjusted Mean* (95% CI)		
Disease Outcomes	High Perceived Stress**	Low/Moderate Stress***	P-value
Type I Symptoms			
Physician-assessed disease activity (SLEDAI) ‡	3.2 (2.5, 3.9)	2.9 (2.5, 3.3)	0.511
Type 2 Symptoms			
Self-report disease activity (SLAQ) ‡	13.2 (11.9, 14.6)	7.2 (6.5, 7.9)	<0.001
Cognitive function (PROMIS) †	44.6 (42.9, 46.3)	50.3 (49.4, 51.3)	<0.001
Pain (SF-36 Pain) †	42.2 (40.2, 44.3)	48.5 (47.4, 49.6)	<0.001
Fatigue (SF-36 Vitality) †	38.7 (36.5, 41.0)	50.7 (49.4, 51.9)	<0.001

*Adjusted means calculated based on multivariable linear regression adjusted for age, sex, race, education, income, smoking, disease duration, and disease damage (Brief Index of Lupus Damage score).
**Patients with scores in the top quartile of the 4-item Perceived Stress Scale (PSS) (range 8-16).
***Patients with scores in the three lower quartiles of the PSS (range 0-7).
‡ Higher score reflect worse status (more physician-assessed/self-reported disease activity)
†Higher scores reflect better status (better cognitive function, less pain/fatigue)
SLEDAI – Systemic Lupus Erythematosus Disease Activity Index
SLAQ – Systemic Lupus Activity Questionnaire
PROMIS – Patient Reported Outcomes Measurement Information System
SF-36 – Short Form 36 Health Survey

Methods: Participants in this sample, drawn from the California Lupus Epidemiology Study (CLUES), were at least 18 years old and met ACR criteria for SLE. In this cross-sectional study, stress was measured using the 4-item Perceived Stress Scale (PSS, range 0-16). No cut-points have been defined for the PSS and therefore participants with scores in the top quartile were identified as those with higher stress. Type 1 symptoms were represented by the physician assessed SLE disease activity index (SLEDAI) and type 2 symptoms by self-report disease activity (SLE Activity Questionnaire, SLAQ), cognitive function (PROMIS cognitive ability scale), pain (SF-36 Bodily Pain subscale), and fatigue (SF-36 Vitality subscale). We used multivariable linear regression to evaluate the associations of stress with SLEDAI and type 2 symptoms while controlling for potential confounders (age, sex, race, education, income, smoking, disease duration, and disease damage). We then calculated adjusted means for each outcome based on the multivariable regression.

Results: The sample (n=431) was 90% female, 30% white, 34% Asian, 22% Hispanic, and 11% African American; mean age 47 (± 14) years; 19% with poverty-level income; 73% with education beyond high school; mean disease duration 18 (± 11) years; and 38% on glucocorticoid therapy with ≥ 7.5 mg/day prednisone equivalent. The mean PSS score in the high stress group was 9.6 (± 1.9), compared with 3.5 (± 2.2) among the rest of the cohort. In the multivariate regression model, high stress was not associated with the Type 1 symptoms (worse scores for physician-assessed disease activity). However, high stress was associated with worse scores for each type 2 symptom: greater self-reported disease activity, lower cognitive function, more pain, and more fatigue (Table).

Conclusion: In a racially diverse sample of patients with SLE, high psychological stress was independently associated with worse type 2 symptoms including self-reported disease activity, cognitive dysfunction, pain, and fatigue. Evidence-based non-pharmacologic interventions to bolster stress resiliency, such as cognitive behavioral therapy, mindfulness-based stress reduction, and modified physical activity programs may be a strategy for improving outcomes in this patient population.

Disclosure: S. Patterson, None; **L. Trupin**, None; **C. Lanata**, None; **L. Murphy**, None; **W. Hartogenesis**, None; **M. Dall'Era**, Biogen,, 5, Genentech, 5, Janssen Pharmaceuticals, 5, Kezar Life Sciences, 2, Pfizer, 5; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2; **P. Katz**, None.

Abstract Number: 1825

Comparison of the Thrombosis Risk Score with Triple Positivity in SLE Thrombosis

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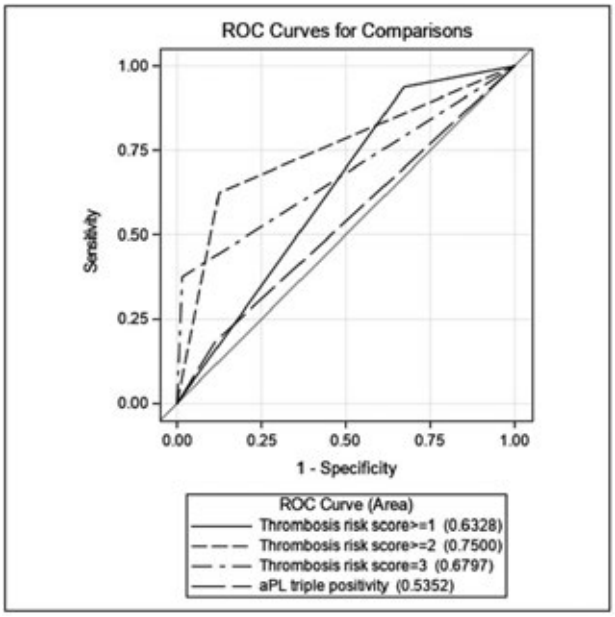
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical II: Flares & Morbidity of SLE
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: We previously developed a Thrombosis Risk Score, a sum of three factors: lupus anticoagulant (by RVVT confirm); low C3; and C4d bound to platelets. We now compare the Thrombosis Risk Score to a widely used risk score for APS thrombosis, "triple positivity", which is the presence of lupus anticoagulant, anticardiolipin, and anti-beta2 glycoprotein 1.



Discrimination performance according to area under the ROC curve

ROC Model	Area (95% CI)	p-value
Thrombosis risk score>=1	0.63 (0.56 ,0.71)	0.1041
Thrombosis risk score>=2	0.75 (0.62 ,0.88)	0.0207
Thrombosis risk score>=3	0.68 (0.56 ,0.8)	0.1276
APL triple positivity	0.54 (0.43 ,0.64)	Reference

Performance of different models

Methods: The study contained 149 SLE patients (85.9% female, 34.2% African American, 55.7% Caucasian). To evaluate the discriminatory performance of the fitted logistic models, the c-statistics, known as the area under the curve of the receiver operating characteristics (ROC curve), was calculated and 95% confidence intervals reported. The c-statistic is the proportion of predictions agreeing with the outcome (ability of the test to correctly classify those with and without thrombosis within the past 5 years).

Results: The area under the curves ranged from 0.54 (95% CI: 0.43-0.64) for the triple positivity model to 0.75 (95% CI: 0.62-0.88) for the model with thrombosis risk score >=2 (Figure 1, Table 1). The model with a thrombosis risk score of at least 2 points demonstrated better discrimination (AUC=0.75) while the model with triple positivity had the poorest performance (AUC=0.54). When comparing the thrombosis risk scores to triple positivity, the area of the thrombosis risk score >=2 ROC curve was significantly better.

Conclusion: The thrombosis risk score is superior to “triple positivity” in its association with any thrombosis (over the last 5 years) in SLE. The thrombosis risk score includes 2 pathways – low complement and platelets – not included in triple positivity.

Disclosure: M. Petri, Eli Lilly and Company, 5, Exagen, 2, 5; **J. Li**, None; **J. Conklin**, Exagen, 3; **T. O’Malley**, Exagen, 3; **J. Ligayon**, Exagen, 3; **L. Wolover**, Exagen, 3; **T. Dervieux**, Exagen, 1, 3, 4, 6.

Abstract Number: 1826

Describing Intra-Individual Cognitive Function Course over Time in Lupus Patients: Persistent and Fluctuating Cognitive Impairment, Affected Cognitive Domains, and Severity

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical II: Flares & Morbidity of SLE
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Cognitive impairment (CI) is a common manifestation of systemic lupus erythematosus (SLE). The course of CI in SLE patients has been described as persistent in some patients and fluctuating in others. **The objective was to describe the intra-individual course of CI over time, determine the severity of CI and the affected domains, over a 1-year period.**

Methods: One-hundred and eleven consecutive SLE patients, aged 18-65 years, from a single centre (July 2016-March 2019) were included. Patients were administered the American College of Rheumatology (ACR) Neuropsychological Battery (NB) at baseline (T0), 6 months (T1) and 12 months (T2). Patients' scores were compared to a normative data to obtain z-scores. CI was operationalized on the NB as a z-score of ≤-1.5 on ≥2 domains. Six domains were studied: *simple attention and processing speed, visual-spatial construction, verbal fluency, learning and memory, executive functioning* and *manual motor speed and dexterity.* Patients were defined as ***persistent CI*** if they had CI over 3 time-points (T0, T1 and T2), as ***stable non-CI*** if they did not have CI in any time-point, or as ***fluctuating CI*** if they had CI on 1-2 assessments. The severity of impairment of CI was determined based on the mean z-score of all 6 domains.

Fig 1: Mean z-scores of the six domains for each patient over time by the 3 groups: stable non-CI (green), fluctuating (orange) and persistent CI (red)

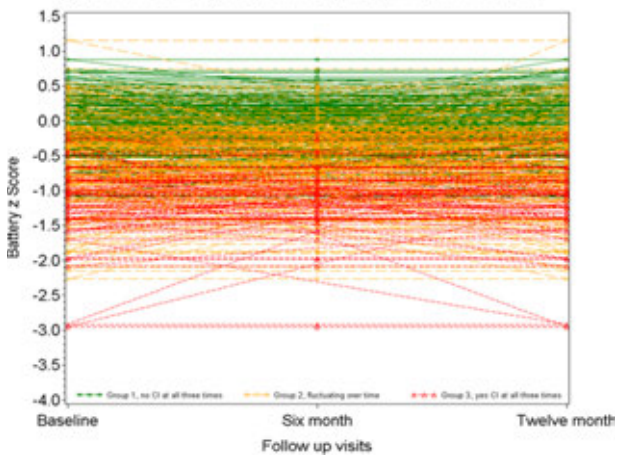
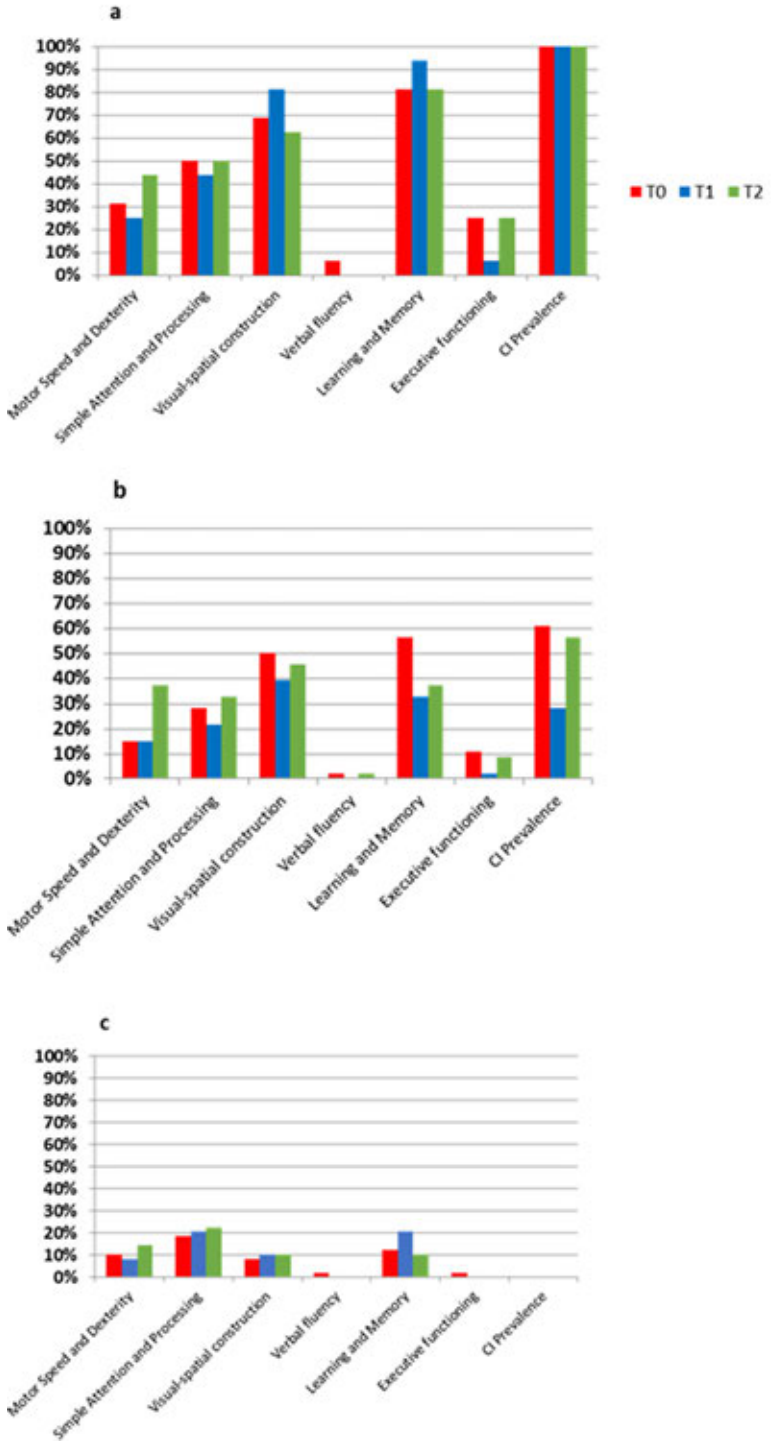


Figure 2: Percentage of impairment in each domain over 3 time points in the persistent CI group (a), fluctuating group (b) and stable non-CI group (c)



Results: One-hundred and eleven patients (90% female) completed 3 assessments at T0, T1 and T2. The mean age was 43.6 ± 12 years and SLE duration at enrolment was 15.2 ± 11 years. Fifty-six percent (62/111) experienced CI at some point over one year. The prevalence of CI was 39.6%, 26.1% and 37.8% at T0, T1 and T2 respectively. Sixteen patients (14.4%) experienced ***persistent CI***, 46 (41.4%) ***fluctuating CI*** and 49 patients (44.1%) were ***stable non-CI***. Mean z-score of all 6 domains for each patient at each time point by the 3 groups (**Fig. 1**) showed almost complete separation of the groups, with the persistent CI patients displaying lower mean z-score than the fluctuating CI pa-

tients – implying more severe CI. Percentage of impairment of the 6 different domains in the 3 groups (**Fig. 2**) revealed the most affected domain over time was *learning and memory* followed by *visual-spatial construction, simple attention and processing and motor speed and dexterity. Verbal fluency and executive functioning* were not significantly affected. ***There was no marked change over time*** in the domains involvement of the persistent CI group. The most affected domains in the fluctuating CI group were similar and there was more variation in the degree of impairment of the involved domains over time.

Conclusion: Fifty-six percent (62/111) of patients experienced CI at some point over a one-year period. While CI fluctuated in 74% (46/62) of patients, 26% (16/62) experience persistent CI across all time points. Although the same domains were affected in fluctuating and persistent CI groups, fluctuating patients displayed less severe CI with more variation in the affected domains compared to persistent CI patients. Our results support the close monitoring of cognition in patients with SLE and further research into the causes and nature of CI in SLE patients.

Disclosure: O. Tayer-Shifman, None; **D. Beaton**, None; **R. Green**, None; **L. Ruttan**, None; **J. Wither**, None; **M. Tartaglia**, None; **M. Kakvan**, None; **S. Lombardi**, None; **N. Anderson**, None; **J. Su**, None; **D. Bonilla**, None; **M. Zandy**, None; **M. Choi**, None; **M. Fritzler**, Alexion Canada, 7, BioRad, 5, Dr. Fooke Laboratorien GmbH, 5, Euroimmun GmbH, 5, 7, ImmunoConcepts, 7, Inova Diagnostics, 5, 7, 8, Inova Diagnostics Inc. San diego, CA, 5, Inova Dx, Mikrogen GmbH, 5, Werfen International, 5; **Z. Touma**, None.

Abstract Number: 1827

Clinical Implications of Neutrophil Extracellular Traps in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical II: Flares & Morbidity of SLE
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Neutrophil activation, including formation of neutrophil extracellular traps (NETs), is essential in host defense. However, NET formation has also been linked to inflammation and autoimmunity, such as systemic lupus erythematosus (SLE). We recently described that SLE-derived immune complexes (ICs) induced NET formation, with NETosis promoting lupus-like disease, including nephritis, in mice. However, whether these mechanisms would occur in human SLE, and the clinical implications of elevated levels of NETs in SLE has not been carefully addressed.

Methods: Levels of NETs (MPO-DNA complexes) were analyzed in plasma in four cross-sectional well-characterized SLE cohorts (n=44-142), and healthy individuals (n=100) using ELISA. Levels of immune complexes and calprotectin were determined by ELISA. Type I interferon (IFN) activity was analyzed using a cell reporter system. Endothelial-derived microparticles (EMPs) were measured by flow cytometry. To determine the capacity of NETs to predict disease flare, patients (n=47) were recruited at time-point of low disease activity and followed over three months, with 14 patients remaining in remission, and 33 patients developing worsening of disease. Statistical analyses were done using Mann-Whitney U test and logistic regression analysis.

Results: SLE patients had elevated levels of NETs in circulation as compared to healthy controls ($p< 0.01$). Consistent with prior in vitro studies, levels of NETs were associated with heightened type I IFN activity ($p< 0.05$) and levels

of immune complexes (r=0.40, p< 0.0001). In contrast to the neutrophil activation marker calprotectin (p< 0.01), levels of NETs (a marker of neutrophil cell death) were not associated with current disease activity (p=0.20), nor individual SLEDAI items. However, of note, levels of NETs predicted future increase in disease activity. Thus, patients with elevated levels of NETs at time-point of clinical remission, were likely to develop disease flare within a few months (OR=13.8, p=0.002). These results are consistent with NET formation occurring early in the disease development, prior to clinical manifest disease. As such, NET formation may be a promising therapeutic target. Further, elevated levels of NETs identified patients with a severe disease phenotype involving nephritis, independent on presence of anti-dsDNA antibodies (OR=1.25 per 1 U/mL NETs, p=0.03). Finally, we made the intriguing observation that levels of NETs were elevated in patients with arterial thrombosis, including myocardial infarction (OR=9.55, p=0.01), and associated with endothelial damage and EMPs (p< 0.0001).

Conclusion: NET levels are elevated in SLE patients, and associated with immune complex-driven disease involving nephritis and arterial thrombosis. NET levels provide significant clinical value in identifying patients at risk of flare and/or severe disease, which may allow for early preventive treatment interventions, reducing overall disease morbidity and mortality.

Disclosure: S. Moore, None; **H. Juo**, None; **C. Nielsen**, None; **H. Tyden**, None; **A. Bengtsson**, None; **C. Lood**, None.

Abstract Number: 1828

Avascular Necrosis Is Associated with APOL1 Variants in African Americans with Systemic Lupus Erythematosus

Kevin Yip ,[1] Elizaveta Efuni,[2] Yingzhi Qian,[1] Robert Clancy,[3] Jill Buyon,[2] and Ashira Blazer[1], [1]New York University School of Medicine, New York City, [2]New York University School of Medicine, New York, NY, [3]New York University School of Medicine, New York

SESSION INFORMATION
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Session Title: SLE – Clinical II: Flares & Morbidity of SLE
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: African Americans (AA) with systemic lupus erythematous (SLE) are at higher risk for both renal disease and avascular necrosis (AVN). The two Apolipoprotein L1 (APOL1) risk variants (RV), G1 and G2, have been associated with chronic kidney disease and atherosclerosis in AAs and are responsible for excess renal risk in this population. We therefore investigated the association between carriers of the risk variants and prevalence of AVN in AA SLE patients.

Methods: Our retrospective cohort study of 113 AA SLE patients addressed the hypothesis that APOL1 variants increase the risk of avascular necrosis. Subjects were recruited from three high volume urban SLE clinical sites. This IRB-approved study included patients over 18 years of age, of self-reported AA ancestry, meeting at least four of the American College of Rheumatology (ACR) revised criteria for SLE. PCR/sequencing was used to stratify subjects by APOL1 genotype. Medical charts including clinical notes and imaging reports were reviewed for documentation of avascular necrosis. Subjects were stratified into groups with zero, one or two risk alleles. Association between presence of AVN and APOL1 risk allele, basic demographic characteristics and duration of SLE disease were evaluated using logistic regression analysis via R statistical software.

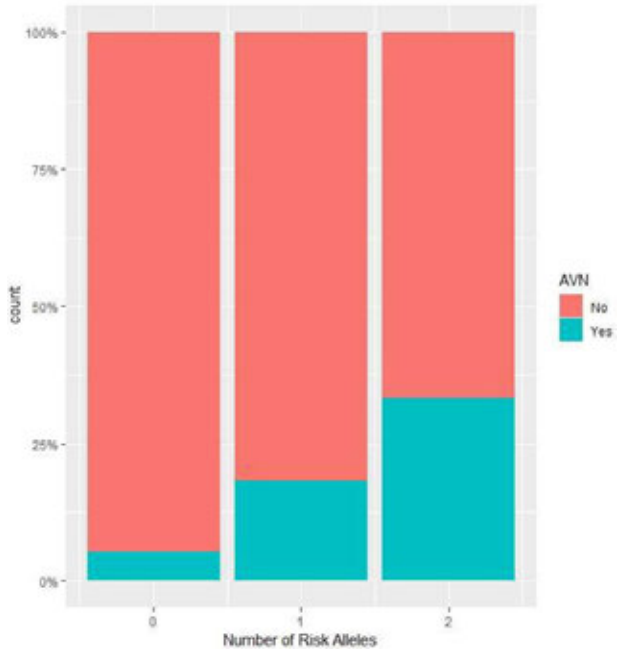

Figure 1. APOL1 risk alleles were associated with AVN with homozygotes variant carriers having the highest prevalence (OR 31.4 95% CI 3.25-303.63, p=0.003).

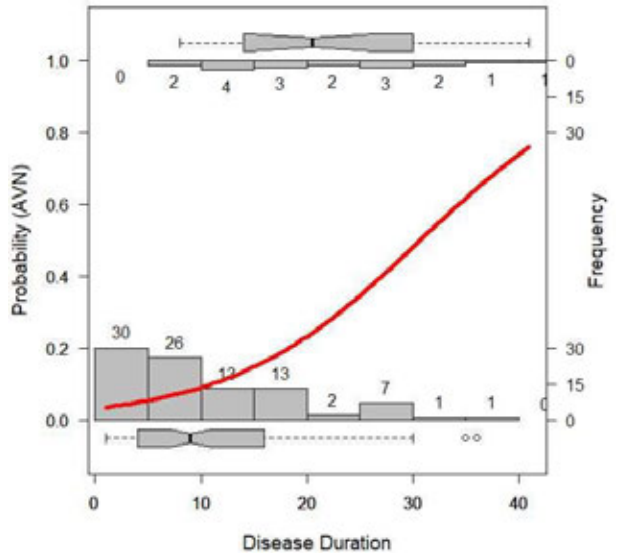

Figure 2. Longer disease duration was associated with increased risk of AVN (p<0.001).

Results: The frequencies of the G0, G1, and G2 alleles were 0.6, 0.22, and 0.18 respectively. Of the 113 patients 18 (16%) had documented AVN. Higher proportion of patients with documented AVN n = 16 (89%) had at least one risk APOL1 allele present vs those without AVN n = 59 (62%). There were no significant differences for age and gender between patients with and without AVN. Presence of one APOL1 allele trended towards increased risk of AVN (p=0.081), having two APOL1 risk alleles (p=0.016) and longer disease duration (p< 0.001) were associated with increased risk of AVN. Having one APOL1 risk allele (p=0.011) or two risk APOL1 risk alleles (p=0.003) and disease duration (p< 0.001) were significant when adjusted for age in multivariable logistic model. APOL1 variant alleles were associated with AVN in a dose dependent relationship with homozygotes variant carriers having the highest prevalence (OR 31.4 95% CI 3.25-303.63, p=0.003). BMI, average disease activity, corticosteroid use, presence of nephritis and ESRD were not associated with presence of AVN.

Conclusion: Our analysis suggests higher risk of avascular necrosis among African American SLE patients who are carriers of APOL1 risk allele. Given the high allelic frequencies of these variants in African Americans, this relationship may underpin the observed association of AVN with Black race. Further work is necessary to uncover the mechanism of this association.

Disclosure: K. Yip, None; **E. Efuni**, None; **Y. Qian**, None; **R. Clancy**, None; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **A. Blazer**, None.

Abstract Number: 1829

Ability of Inflammatory and Regulatory Soluble Mediators to Forecast Impending Clinical Disease Flare and Inform a Refined Lupus Flare Prediction Index in a Confirmatory Cohort of SLE Patients

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical II: Flares & Morbidity of SLE
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: SLE is marked by altered immune regulation linked to waxing and waning clinical disease activity. This study seeks to verify the alteration of inflammatory and regulatory mediators prior to clinical disease flare in a confirmatory cohort of SLE patients, seeking the best mediators to inform our Lupus Flare Prediction Index (LFPI).

Methods: Immune mediators were evaluated by xMAP assay in pre-flare (n=90) and "self" pre-nonflare (SNF) plasma samples (n=90) from the same female patients (49 European-, 41 African-American) with classified SLE (≥4 ACR criteria), as well as 48 race/age matched healthy controls (HC). Hybrid SLEDAI (hSLEDAI) scores, clinical features, medication usage, and the presence of SLE-associated autoantibody (AutoAb) specificities, including dsDNA, chromatin, Ro/SSA, La/SSB, Sm, SmRNP, and RNP, were also compared at pre-flare (100 ± 40 days prior to flare) vs. pre-SNF

Most Informative Soluble Mediators Altered Prior to Clinical Disease Flare

		BL Concentration (pg/ml)					BL Mediator vs. FU hSLEDAI score			LFPI Score Component						
		Pre-Flare		Pre-SNF						Pre-Flare		Pre-SNF				
RF Rank	Analyte	mean	SEM	mean	SEM	p value[a]	Spearman r	95% CI	P value[b]	median	SD	median	SD	OR[c]	95% CI	P value[d]
1	SCF	88.59	3.14	47.61	2.54	***<0.0001***	0.4674	0.3408 to 0.5773	***<0.0001***	0.3140	0.2900	-0.2701	0.4290	14.30	6.79 to 28.6	***<0.0001***
2	MCP-1/CCL2	410.4	25.41	214.0	18.65	***<0.0001***	0.5942	0.4872 to 0.6836	***<0.0001***	0.3353	0.482	-0.3497	0.496	14.10	6.74 to 29.6	***<0.0001***
3	TNFRI	2391	95.3	1306	59.59	***<0.0001***	0.5297	0.4120 to 0.6300	***<0.0001***	0.2956	0.380	-0.2807	0.488	10.20	5.14 to 19.6	***<0.0001***
4	IL-1RA	913.4	66.67	1843	176.60	***<0.0001***	-0.3234	-0.4519 to -0.1817	***<0.0001***	0.1597	0.296	-0.1418	0.279	4.23	2.25 to 8.02	***<0.0001***
5	MIP-1α/CCL3	290.8	13.26	183.8	7.42	***<0.0001***	0.3819	0.2455 to 0.5035	***<0.0001***	0.1170	0.324	0.0473	0.427	3.27	1.45 to 7.85	***0.0064***
6	TNFRII	4714	291.6	2682	211.4	***<0.0001***	0.4417	0.3119 to 0.5553	***<0.0001***	0.2198	0.332	-0.1524	0.461	9.10	4.65 to 17.2	***<0.0001***
7	IP-10/CXCL10	330.7	42.54	136.60	19.82	***<0.0001***	0.5238	0.4052 to 0.6250	***<0.0001***	0.1930	0.380	-0.2684	0.543	2.54	1.81 to 3.68	***<0.0001***
8	TGF-β (native)	15.44	8.09	32.23	14.04	***<0.0001***	-0.3001	-0.4312 to -0.1567	***<0.0001***	-0.0206	0.309	-0.1962	0.256	4.42	2.25 to 8.52	***<0.0001***
9	MIG/CXCL9	320.7	15.29	212.9	11.07	***<0.0001***	0.3768	0.2398 to 0.4990	***<0.0001***	0.1195	0.264	0.0848	0.454	2.59	1.16 to 5.71	*0.0309*
10	IFN-γ	65.91	7.65	33.89	2.18	***<0.0001***	0.3353	0.1946 to 0.4625	***<0.0001***	0.1537	0.305	0.0456	0.327	1.90	1.00 to 3.56	*0.0603*
11	TRAIL	86.18	0.36	58.61	2.77	***<0.0001***	0.3709	0.2334 to 0.4939	***<0.0001***	0.2005	0.349	-0.1677	0.337	4.69	2.47 to 8.54	***<0.0001***
12	MIP1-β/CCL4	395.9	15.16	284.9	11.57	***<0.0001***	0.4005	0.2661 to 0.5167	***<0.0001***	0.2185	0.356	-0.0067	0.387	2.46	1.32 to 4.55	*0.0059*
13	ICAM-1	634170	44086	447193	38150	***<0.0001***	0.2884	0.1441 to 0.4206	***<0.0001***	0.1204	0.278	0.0180	0.290	2.63	1.42 to 4.89	*0.0044*
14	TGF-β (total)	16692	1984	26331	2630	***<0.0001***	-0.2439	-0.3804 to -0.0969	***0.0010***	0.0869	0.228	-0.0727	0.239	3.87	2.06 tp 7.31	***<0.0001***

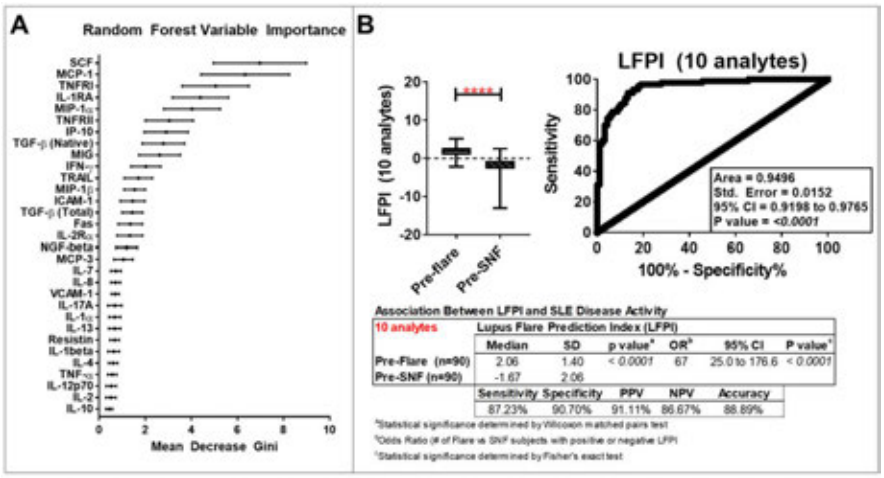
BL = Baseline; FU = Follow-up; hSLEDAI = hybrid SLEDAI; LFPI = Lupus Flare Prediction Index; RF = Random Forest; SNF = Self Non-flare

[a]Wilcoxon matched pairs test; Bonferonni corrected significant *p=0.0035* in **bold**

[b]Spearman rank correlation; Bonferonni corrected significant *p=0.0035* in **bold**

[c]Odds Ratio (# of Pre-Flare vs Pre-SNF SLE patients with positive or negative LFPI component value)

[d]Fisher's exact test; Bonferonni corrected significant *p=0.0035* in **bold**



Determination of the top soluble mediators (A) to inform the Lupus Flare Prediction Index (LFPI) and its ability to differentiate SLE patients with imminent clinical disease flare (Pre-Flare) from the same patients during a comparable "self" non-flare (Pre-SNF) period of clinical disease activity (B).

(96 ± 40 days prior to SNF) time points. A subset of 31, log-transformed, immune mediators were further evaluated using applied machine learning modeling approaches (random forest and XG Boost) to determine an optimal subset of mediators to inform the LFPI. The LFPI is the sum of log-transformed, standardized immune mediators, weighted by the Spearman r correlation coefficient of pre-flare/SNF immune mediator levels vs. hSLEDAI scores at disease flare/SNF.

Results: We did not observe differences with respect to hSLEDAI scores, clinical features, medication usage, or number and type of SLE-associated AutoAbs comparing pre-flare vs. pre-SNF time points, either in aggregate or by race. At follow-up, SLE patients experiencing a clinical disease flare (vs. SNF visit) had significantly elevated hSLEDAI scores ($p< 0.0001$), with an increased presence of arthritis ($p< 0.0001$), mucocutaneous ($p< 0.0001$), and serositis ($p=0.0066$) clinical features. Thirty-one immune mediators (**Figure [A]**) were altered in cases vs HC ($p\leq 0.05$), and altered in pre-flare vs. pre-SNF samples ($p\leq 0.02$ after adjusting for multiple comparison); inflammatory mediators were increased and regulatory mediators decreased in pre-flare samples. Variable importance of the 31 mediators was determined by random forest (**Figure [A]**) and confirmed by XG Boost. Forward selection/backward elimination drew 9-14 mediators that best differentiated pre-flare from pre-SNF (**Table**). A combination of the top 10 immune mediators best informed and maximized the performance of a newly refined LFPI (**Figure [B]**), achieving 87% sensitivity and 91% specificity. In addition to identifying impending clinical disease flare, the LFPI (and top mediators informing it) was significantly increased in SLE patients who went on to increased features of arthritis ($p< 0.0001$), mucocutaneous ($p< 0.0001$), or serositis ($p=0.0003$) clinical features at follow-up.

Conclusion: We verified the alteration of inflammatory and regulatory immune mediators with imminent lupus disease flare. A subset of mediators boosted the LFPI to identify SLE patients at risk of imminent flare who would benefit from early intervention strategies. Such an approach would be a game changer in prospective clinical trials and the management of lupus.

Disclosure: M. Munroe, Progentec Diagnostics, Inc., 2; **S. Kleckner**, None; **W. DeJager**, None; **S. Macwana**, None; **J. Guthridge**, DxTerity, 2; **E. Jupe**, Progentec Diagnostics, Inc., 3; **M. Purushothaman**, Progentec Diagnostics, Inc., 3; **S. Sharma**, Progentec Diagnostics, Inc., 3; **N. Redinger**, None; **T. Aberle**, None; **S. Kamp**, None; **C. Arriens**, AstraZeneca, 5, BMS, 2, 5, Exagen, 2, GSK, 2, 5; **E. Chakravarty**, None; **J. Merrill**, Abbvie, 5, Amgen, 5, Astellas, 5, AstraZeneca, 5, BMS, 2, 5, Celgene, 5, EMD Serono, 5, GSK, 2, 5, Idorsia, 5, ILTOO, 5, Immupharma, 5, Incyte, 5, Janssen, 5, Lilly, 5, Remegen, 5, Servier, 5, Xencor, Inc., 2; **J. James**, Abbvie, 5, Janssen, 5, Progentec, 2, Progentec Diagnostics, Inc., 2, Xencor, 2, Xencor, Inc., 2.

Abstract Number: 1830

Short- and Long-term Morbidity and Mortality Outcomes of African American Patients with Systemic Sclerosis-Related Interstitial Lung Disease

Elizabeth Volkmann ,[1] Virginia Steen,[2] Ning Li,[3] Michael Roth,[4] Philip Clements,[3] Dinesh Khanna,[5] Daniel Furst,[6] Shervin Assassi,[7] Grace Kim,[3] Jonathan Goldin,[3] Robert Elashoff,[3] and Donald Tashkin[3], [1]University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, [2]Georgetown University, Washington, D.C., USA, Georgetown, [3]University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, [4]University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA, [5]Department of Medicine, University of Michigan, Ann Arbor, Michigan, USA, Ann Arbor, [6]University of California, Los Angeles, CA, [7]Division of Rheumatology and Clinical Immunogenetics, University of Texas McGovern Medical School, Houston, Texas, USA, Houston, TX

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorder – Clinical II: Cardiopulmonary Involvement

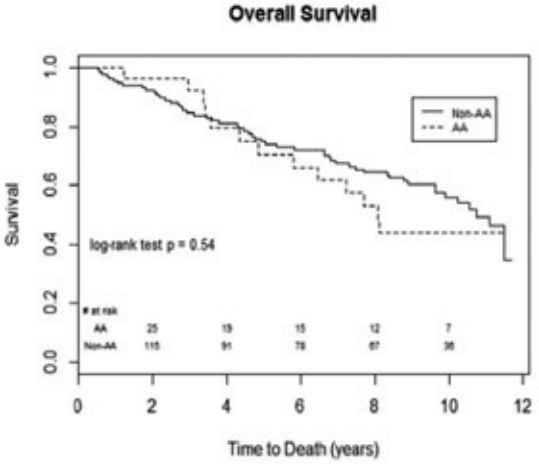


Figure 1a. Time to death in African American (dotted line) and non-African American participants of SLS I (solid line).

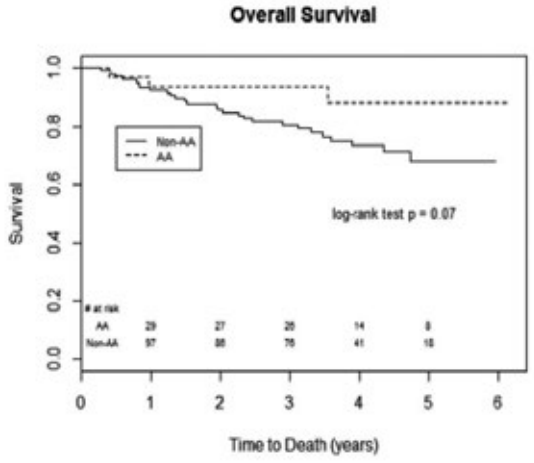


Figure 1b. Time to death in African American participants (dotted line) and non-African American participants of SLS II (solid line).

Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Observational studies have demonstrated that African American (AA) patients with systemic sclerosis (SSc) have a more unfavorable prognosis compared with non-AA. However, no studies have evaluated racial disparities using data from a randomized controlled trial (RCT) where all patients have equal access to care and standard treatment and follow-up during the trial. The objective of this study was to compare efficacy outcomes, as well as long-term morbidity and mortality, in AA and non-AA patients who participated in the Scleroderma Lung Study (SLS) I (Tashkin et al. NEJM 2006) and II (Tashkin et al. Lancet Resp Med 2016).

Methods: SLS I randomized 158 SSc participants (AA: N=26) with interstitial lung disease (ILD) from 13 US SSc centers to 1 year of oral CYC (cyclophosphamide) versus placebo, followed by 1 year off all treatment. SLS II randomized 142 SSc-ILD participants (AA: N=33) from 14 US SSc centers to 1 year of oral CYC, followed by 1 year of placebo, versus 2 years of mycophenolate (MMF). Both studies measured the forced vital capacity (FVC), diffusing capacity for carbon monoxide (DLCO) every 3 months during the study period. Up to 12 (SLS I) and 8 (SLS II) years after randomization, we contacted enrolled patients or designated surrogates to assess the following: mortality, cause of mortality, and development of organ failure. We created joint models to compare progression of ILD based on the course of the FVC and DLCO between AA and non-AA. We compared survival rates using a log-rank test and used Cox proportional hazard modeling to determine the variables associated with survival.

Results: Baseline demographic and disease characteristics of AA and non-AA were similar in SLS I and II, with the exception of age (AA were younger than non-AA [SLS I: 43.1 vs. 49.5 years; SLS II: 49.1 vs. 53.2 years], and extent of ILD (AA had a trend for more extensive quantitative radiographic ILD at baseline). In SLS I, there was no significant difference in the course of the FVC or DLCO over 24 months between AA and non-AA in CYC or placebo arms. In SLS II, AA had an improved course of FVC over 24 months compared with non-AA in the CYC arm (P=0.02); in the MMF arm, there was no difference in the course of the FVC. There was also no difference in the course of the DLCO over 24 months in either CYC or MMF arms. There was no difference in long-term survival (P=0.54; Figure 1a) or time to respiratory failure (P=0.37) between AA and non-AA in SLS I. There was a trend for improved long-term survival P=0.07; Figure 1b) and improved time to respiratory failure (P=0.10) in AA compared with non-AA in SLS II. The Cox models demonstrated AA race did not have any significant impact on long-term survival in SLS I or II participants.

Conclusion: Data from two large RCTs in SSc-ILD demonstrated that AA patients with SSc-ILD have similar morbidity and mortality outcomes compared with non-AA SSc-ILD patients when treated aggressively for SSc-ILD, even after adjusting for age and baseline disease severity. These findings contrast with the racial disparities described in previous observational studies and warrant further investigation.

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Pharma, 5; **D. Furst**, Actelion, 2, 5, Actelion Pharmaceuticals, 2, 5, Amgen, 2, 5, BMS, 2, 5, CME, 5, 8, Corbus, 2, 5, Galapagos, 2, 5, Galapogos Novartis, 5, GlaxoSmithKline, 2, GSK, 2, 5, NIH, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche/ Genentech, 2, 5, Sanofi, 2, 5; **S. Assassi**, Bayer, 2, Boehringer Ingelheim, 2, 5, 8, Integrity Continuing Education, 8, 9, Medscape, 8, 9, Momenta, 2; **G. Kim**, None; **J. Goldin**, None; **R. Elashoff**, None; **D. Tashkin**, None.

Abstract Number: 1831

Subtypes of Scleroderma Lung Involvement Associated with Burden of Disease and Outcomes

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Table 1. Cohort characteristics by subgroups of pulmonary involvement

	Isolated PAH (n=18)	Overlap ILD/PH (n=39)	Isolated ILD (n=146)	SSc w/o pulm involv (n=147)	P-value (whole cohort)	P-value (pulm vs no pulm involv)	P-value (PAH vs ILD/PH overlap)
Female, n (%)	17 (94.4%)	29 (74.4%)	117 (80.1%)	128 (88.3%)	*0.05	0.21	0.07
Age, mean (SD)	61.0 (13.7)	57.8 (13.4)	55.5 (12.6)	65.5 (9.8)	0.18	0.18	0.41
Current or former smoker, n (%)	3 (16.7%)	17 (43.6%)	46 (31.5%)	48 (32.7%)	0.25	0.13	0.07
Race							
Caucasian, n (%)	11 (61.1%)	20 (51.3%)	74 (51.0%)	94 (64.8%)	0.10	0.49	0.64
Hispanic, n (%)	2 (11.1%)	4 (10.3%)	14 (9.7%)	17 (11.7%)			
Black, n (%)	4 (22.2%)	6 (15.4%)	15 (10.3%)	8 (5.5%)			
Asian, n, (%)	0 (0%)	4 (10.3%)	25 (17.2%)	18 (12.4%)			
Other, n (%)	1 (5.6%)	5 (12.8%)	17 (11.7%)	8 (5.5%)			
Disease duration, median (IQR)	12.4 (16.0)	10.5 (7.2)	9.7 (10.9)	7.9 (13.5)	0.66	0.67	0.50
RP duration, median (IQR)	15.5 (12.1)	11.9 (9.9)	11.0 (12.5)	12.2 (15.4)	0.69	0.52	0.30
Disease duration at PH diagnosis, median (IQR)	9.0 (12.7)	7.5 (9.1)	n/a	n/a	-	-	0.36
Disease duration at ILD diagnosis, median (IQR)	n/a	3.2 (4.4)	2.7 (5.6)	n/a	-	0.39	-
Limited SSc, n (%)	15 (83.3%)	24 (61.5%)	86 (58.9%)	103 (71.5%)	*0.05	0.13	0.10
Centromere, n (%)	11 (61.1%)	3 (7.7%)	6 (4.2%)	68 (48.6%)	*<0.001	*<0.001	*<0.001
Scl70, n (%)	1 (5.6%)	11 (28.2%)	60 (42.0%)	16 (11.3%)	*<0.001	*0.003	0.08
RNA Poly III, n (%)	0 (0%)	7 (18.9%)	28 (20.3%)	27 (19.3%)	0.30	0.14	0.09
Worst mRSS, mean (SD)	5.7 (4.0)	6.2 (7.4)	7.1 (7.1)	7.2 (8.4)	0.78	0.58	0.77
BNP, median (SD)	65 (109)	118 (329)	48 (75)	70.9 (88)	0.09	0.13	0.38
Echo							
RVSP, mean (SD)	59.8 (20.5)	57.2 (21.9)	29.5 (11.9)	24.3 (7.6)	*<0.001	*<0.001	0.68
EF< 55%, n (%)	2 (11.1%)	2 (5.1%)	2 (1.4%)	5 (3.4%)	0.12	*0.05	0.41
RHC (at PH dx)							
mPAP, mean (SD)	40.5 (10.4)	35.8 (11.1)	19.2 (3.7)	16.4 (5.3)	*<0.001	*<0.001	0.15
PVR, mean (SD)	9.0 (5.4)	6.9 (4.8)	2.0 (0.8)	1.3 (0.04)	*<0.001	*<0.001	0.20
PFTs (at ILD dx)							P-value (ILD vs

SSc w/o pulm = SSc subjects without pulmonary involvement. Age = age at time of last follow up or death. Disease duration= 1st non-RP symptom to date of last follow up. Data from Echo and RHC closest to PH diagnosis and PFTs closest to ILD diagnosis were used. RHC was performed for 33 patients with ILD only and 9 patients without pulmonary involvement.

Table 2. Outcomes: PROs, supplemental oxygen use, exercise capacity, hospitalizations, mortality and transplant

	Isolated PAH (n=18)	Overlap ILD/PH (n=39)	Isolated ILD (n=146)	SSc w/o pulm involvement (n=147)	P-value (whole cohort)	P-value (pulm vs no pulm involv)	P-value (PAH vs ILD/PH overlap)
History supplemental O2 use, n (%)	2 (11.1%)	23 (59.0%)	8 (5.5%)	0 (0%)	*<0.001	*p<0.001	0.001
WHO Functional Class 3 or 4, n(%)	9 (50%)	29 (74.4%)	26 (17.8%)	5 (3.4%)	*<0.001	*<0.001	0.07
Worst 6MWT in meters, mean (SD)	361 (75)	281 (140)	388 (97)	479 (36)	*0.002	*0.006	0.07
Hospitalizations, n (%)	5 (27.8%)	15 (38.5%)	-	-	-	-	0.56
Mortality, n (%)	6 (33.3%)	8 (20.5%)	7 (4.9%)	1 (0.7%)	*<0.001	*<0.001	0.33
Lung transplant referral, n (%)	2 (11.1%)	27 (69.2%)	19 (13%)	1 (0.7%)	*<0.001	*<0.001	*<0.001
Lung transplant, n (%)	1 (5.6%)	13 (33.3%)	9 (6.2%)	0 (0%)	*<0.001	*<0.001	*0.04
Composite outcome (transplant or death)	7 (38.9%)	20 (51.3%)	16 (11.0%)	1 (0.7%)	*<0.001	*<0.001	0.38
modified borg dyspnea scale, mean (SD)	1.68 (1.5)	2.6 (2.5)	1.5 (1.6)	0.7 (1.2)	*<0.001	*0.005	0.18
UCSD SOB score, mean (SD)	46.2 (18.5)	52.1 (26.0)	30.9 (25.2)	19.1 (21.9)	*<0.001	<0.001	0.43
HAQ-DI score, mean (SD)	0.46 (0.51)	0.73 (0.59)	0.59 (0.61)	0.59 (0.66)	0.52	0.28	0.11
SHAQ_breath, mean (SD)	1.27 (0.86)	1.25 (0.78)	0.67 (0.73)	0.34 (0.58)	*<0.001	*<0.001	0.91
Disability due to scleroderma, n (%)	1 (5.6%)	13 (33.3%)	40 (27.4%)	24 (16.3%)	*0.01	0.07	*0.04
Duration follow up, median (IQR)	11.7 (16.6)	8.0 (8.4)	6.8 (10.3)	6.1 (11.5)	0.79	0.58	0.37

FC = WHO Functional Class. 6MWT = six-minute walk test. Duration of follow up is from SSc physician diagnosis to last follow up or death. HAQ= Health Assessment Questionnaire. SHAQ = Scleroderma HAQ developed by Steen and Medsger. VAS = visual analog scale. Fischer's exact test was used if observations <5. PRO scores were averaged for each patient if multiple questionnaires were completed over follow up.

SESSION INFORMATION

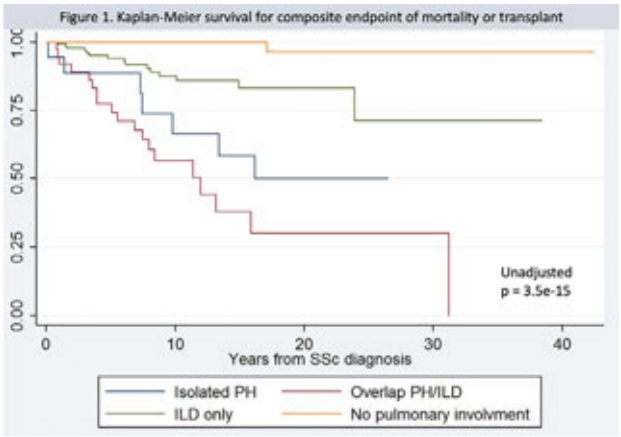
Date: Monday, November 11, 2019

Session Title: Systemic Sclerosis & Related Disorder – Clinical II: Cardiopulmonary Involvement

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Pulmonary disease is a leading cause of mortality in scleroderma (SSc). Previous studies indicate that the coexistence of pulmonary hypertension (PH) and interstitial lung disease (ILD) is associated with worse survival. However, this has not been uniformly confirmed, in part due to lack of refined categorization of ILD extent and PH assessment by invasive testing. In addition, the clinical burden of disease has not been fully explored



in different SSc lung disease subtypes. Therefore, we sought to define outcomes related to type and severity of lung involvement in a well characterized SSc cohort enriched for pulmonary disease.

Methods: A retrospective analysis was conducted on 355 SSc subjects stratified into the following subgroups: isolated ILD, isolated pulmonary arterial hypertension (PAH, WHO Group I), overlap ILD/PH (WHO Group I and/or Group III), or SSc without pulmonary disease. PH was confirmed by right heart catheterization according to standard definition. PH due to left heart disease (Group II) was excluded. ILD was confirmed by chest CT. Biannual assessments of clinical and functional data and patient reported outcomes (PROs) were included. Hospitalization for heart or respiratory failure and mortality were ascertained by medical record review. Continuous variables were compared by Student's *t*-test or Wilcoxon's rank sum test. Categorical variables were compared using chi-square. A composite outcome of mortality or lung transplant was assessed by Kaplan-Meier analysis and adjusted Cox proportional hazard models.

Results: Differences among pulmonary subtypes characteristics are shown in Table 1. A significantly higher proportions of males in ILD/PH, of limited SSc and centromere positivity in PAH, of SCL70 in ILD and ILD/PH were noted. Baseline hemodynamics and PH therapy did not differ significantly between PAH and overlap ILD/PH. Subjects with PH/ILD showed more severe restrictive lung disease at ILD diagnosis compared to ILD only (FVC 1.99±0.71 vs 2.48±0.72, p=0.002) with ILD preceding PH onset more commonly (89.7%). Among pulmonary SSc sybtypes, overlap ILD/PH was significantly associated with worse functional capacity (WHO Functional Class and 6-minute walk distance), greater requirement for supplemental oxygen, greater SSc-related disability, and higher mean dyspnea PRO scores (Table 2). Notably, ILD/PH subjects compared to PAH and ILD also showed significantly increased rates of referral for lung transplant (69% vs 11% vs 13; p=< 0.001) as well as of transplant itself (33.3% vs. 5.6% vs 6.2%; p=< 0.001). This may explain the lack of difference in mortality between PAH and ILD/PH in this cohort. In fact, death or transplant free survival was significantly worse in the PH/ILD group (Figure 1; p = 3.5e-15).

Conclusion: The disease burden of lung involvement in SSc is significant, particularly in subjects with concurrent PH (Group I and III) and ILD. This subset manifests more advanced respiratory symptoms and functional decline compared to PAH and ILD alone. Referral for lung transplantation is confirmed as a life-saving intervention for patients with SSc lung involvement.

Disclosure: S. French, None; **K. Taylor**, None; **S. Rush**, None; **F. Boin**, None.

Abstract Number: 1832

Reliability of Traditional Cardiovascular Risk Calculators in Predicting Risk of Cardiovascular Disease in Systemic Sclerosis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Systemic Sclerosis & Related Disorder – Clinical II: Cardiopulmonary Involvement
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Most cardiovascular (CV) risk calculators including the Framingham risk score (FRS) and American College of Cardiology (ACC) / American Heart Association (AHA) risk score underestimate CV risk in pa-

tients with chronic inflammatory diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and sarcoidosis. It is unclear how these scores perform in estimation of CV risk in patients with SSc.

Methods: Medical records of patients in a geographically well-defined area were reviewed to identify incident cases of SSc (defined by physician diagnosis) from Jan 1, 1980 to Dec 31, 2016. Fulfillment of the 1980 and 2013 SSc classification criteria was ascertained. Cardiovascular disease (CVD) events including coronary artery disease (CAD), congestive heart failure (CHF), cerebrovascular disease (transient ischemic attacks and cerebrovascular accidents), and peripheral arterial disease (PAD) were abstracted. The 10 year general FRS for CVD was calculated and the office-based 10 year FRS, which does not include laboratory values, was used when lipid values were unavailable. The ACC/AHA atherosclerotic CVD (ASCVD) pooled risk score was also calculated using the ACC/AHA risk calculator. Patients were followed until death, migration from Olmsted County or June 30, 2017. Observed follow-up was truncated at 10 years after SSc incidence. For patients with < 10 years of follow-up, the predicted risk for CVD was adjusted proportionately. The standardized incidence ratio (SIR) was estimated as the ratio of the predicted and observed numbers of CVD events.

Results: In order to apply FRS to this cohort of 78 patients with incident SSc, 21 cases were excluded to fit FRS age limits (30-74 years) as were 7 patients with prior CVD; therefore data was available in 44 of 50 cases. The mean FRS was 7.1% (SD 5.2%). Among SSc cases, 2.2 CVD events were predicted and 9 CVD events observed, for a SIR of 4.16 (95% CI 2.16 to 7.99, p< 0.001). Only subjects aged 40 to 79 years were included in the ACC/AHA risk calculator; two patients with prior myocardial infarction or stroke were excluded. Because of missing data on lipids, the ACC/AHA risk score could only be calculated in 22 out of the remaining 42 SSc cases. The mean ACC/AHA risk score was 8.9% (SD 7.8%). The predicted CVD events were 1.2 and 7 CV events were observed, corresponding to an SIR of 5.69 (95% CI 2.71 to 11.94, p< 0.001).

Conclusion: This is the first population-based study using comprehensive individual medical record review to investigate the performance of FRS and ACC/AHA risk score among patients with SSc, of which both are strongly underestimating the risk of CVD events by about 4-fold and 5-fold, respectively. The poor performance of these risk scores in SSc is consistent with their poor performance in other chronic inflammatory conditions such as RA and SLE. While CVD risk calculators are meant to assist the clinician in identifying high risk patients for appropriate preventive strategies, our study suggests that these scoring systems are inadequate and may misclassify high risk patients as low risk, depriving them of preventive CVD interventions. Better CVD risk assessment tools are needed for CVD risk prediction in patients with SSc.

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Abstract Number: 1833

Efficacy and Safety of Nintedanib in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease by Use of Mycophenolate at Baseline: Subgroup Analysis of the SENSCIS Trial

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SESSION INFORMATION

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Session Title: Systemic Sclerosis & Related Disorder – Clinical II: Cardiopulmonary Involvement

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Background/Purpose: In the SENSCIS trial in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD), nintedanib reduced the annual rate of decline in forced vital capacity (FVC) vs placebo (-52.4 vs -93.3 mL/year; difference 41.0 mL/year [95% CI 2.9, 79.0]; p=0.04), with adverse events that were consistent with the profile observed in patients with IPF. In many countries, mycophenolate is commonly used in the treatment of SSc-ILD. We analyzed the efficacy and safety of nintedanib in the SENSCIS trial by use of mycophenolate at baseline.

Methods: Subjects with SSc-ILD with ≥10% fibrosis of the lungs on HRCT were randomized to receive nintedanib 150 mg bid or placebo. Patients who had received stable therapy with mycophenolate for ≥6 months prior to randomization were eligible to participate. We analyzed lung function outcomes and adverse events over 52 weeks in subgroups of patients who were and were not taking mycophenolate at baseline.

Results: In the nintedanib and placebo groups, respectively, 139 (48.3%) and 140 (48.6%) of patients were taking mycophenolate at baseline. In patients taking and not taking mycophenolate at baseline, respectively, mean (SD) FVC

Figure. Annual rate of decline in FVC (mL/yr) over 52 weeks in the SENSCIS trial in subgroups by use of mycophenolate at baseline

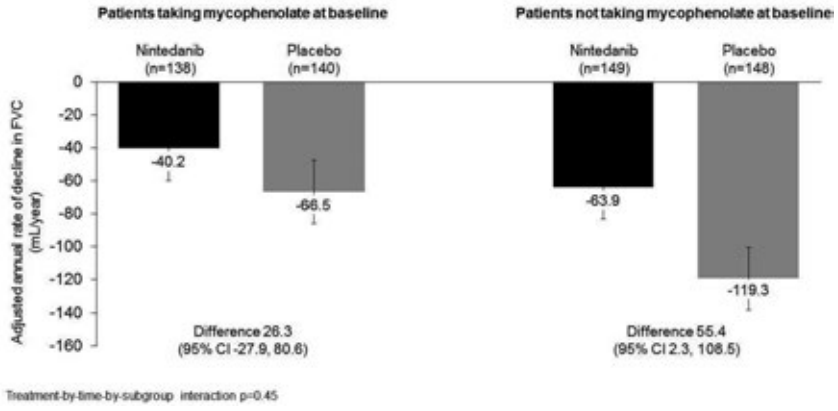

Table. Most frequent adverse events in the SENSCIS trial in subgroups by use of mycophenolate at baseline

	Patients taking mycophenolate at baseline		Patients not taking mycophenolate at baseline	
Adverse event	Nintedanib (n=139)	Placebo (n=140)	Nintedanib (n=149)	Placebo (n=148)
Most frequent adverse events*				
Diarrhea	106 (76.3)	48 (34.3)	112 (75.2)	43 (29.1)
Nausea	43 (30.9)	23 (16.4)	48 (32.2)	16 (10.8)
Skin ulcer	22 (15.8)	23 (16.4)	31 (20.8)	27 (18.2)
Vomiting	32 (23.0)	17 (12.1)	39 (26.2)	13 (8.8)
Cough	20 (14.4)	33 (23.6)	14 (9.4)	19 (12.8)
Nasopharyngitis	10 (7.2)	22 (15.7)	26 (17.4)	27 (18.2)
Upper respiratory tract infection	19 (13.7)	25 (17.9)	14 (9.4)	10 (6.8)
Abdominal pain	14 (10.1)	6 (4.3)	19 (12.8)	15 (10.1)
Fatigue	19 (13.7)	14 (10.0)	12 (8.1)	6 (4.1)
Headache	16 (11.5)	15 (10.7)	11 (7.4)	9 (6.1)
Urinary tract infection	16 (11.5)	11 (7.9)	8 (5.4)	12 (8.1)
Weight decreased	10 (7.2)	4 (2.9)	24 (16.1)	8 (5.4)
Decreased appetite	14 (10.1)	10 (7.1)	13 (8.7)	2 (1.4)
Adverse events leading to treatment discontinuation	15 (10.8)	9 (6.4)	31 (20.8)	16 (10.8)

Adverse events reported over 52 weeks (or until 28 days after last trial drug intake for patients who discontinued trial drug before week 52). Data are n (%) of patients with ≥1 such adverse event. Adverse events were coded according to preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). *Adverse events reported in >10% of patients in any of the subgroups shown.

(mL) was 2539 (770) and 2463 (784) and FVC % predicted was 70.8 (16.0) and 74.2 (17.1). In patients who received placebo, the mean (SE) rate of decline in FVC over 52 weeks was -66.5 (19.3) mL/year in patients taking mycophenolate at baseline and -119.3 (19.0) mL/year in patients not taking mycophenolate at baseline. Nintedanib reduced the rate of FVC decline both in patients who were and were not taking mycophenolate at baseline. The treatment effect of nintedanib was numerically greater in patients who were not taking mycophenolate at baseline, but statistical testing did not indicate heterogeneity in the treatment effect between subgroups (p=0.45) (Figure). In post-hoc analyses, in the nintedanib and placebo groups, respectively, absolute declines in FVC >5% predicted were seen in 15.2% and 25.7% of patients taking mycophenolate at baseline (OR 0.52 [95% CI 0.29, 0.95]) and 25.5% and 31.1% of those not taking mycophenolate at baseline (OR 0.76 [0.46, 1.26]). The adverse event profile of nintedanib was similar irrespective of mycophenolate use at baseline (Table). The proportion of patients treated with nintedanib who had adverse events leading to discontinuation of trial drug was no higher in patients taking mycophenolate at baseline than in those who were not (Table).

Conclusion: In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in FVC both in patients who had not taken mycophenolate and in patients who had taken a stable dose of mycophenolate for ≥6 months prior to randomization. The treatment effect of nintedanib was numerically greater in patients who were not taking mycophenolate at baseline. Careful interpretation of the data in the subgroups by use of mycophenolate is warranted as patients were not randomized by use of mycophenolate and the patients using mycophenolate at baseline had tolerated it for ≥6 months prior to entering the trial. The adverse event profile of nintedanib was similar irrespective of mycophenolate use.

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Abstract Number: 1834

Serum Interferon Chemokine Score Predicts Better Response to Immunosuppression in Systemic Sclerosis Related Interstitial Lung Disease

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SESSION INFORMATION

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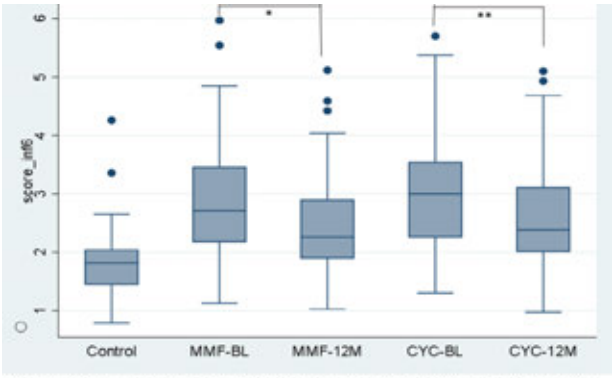
Background/Purpose: Response to immunosuppression is highly variable in systemic sclerosis (SSc) related interstitial lung disease (ILD), and there are no widely accepted clinical or biological parameters that predict response to treatment. The interferon (IFN) signature is the most prominent gene expression profile in the peripheral blood cells of SSc patients. We have previously identified 6 serum chemokines that highly correlate with the IFN transcript profile. Herein, we determined whether a composite serum IFN chemokine score has predictive significance for response to immunosuppression in SSc-ILD.

Methods: In the Scleroderma Lung Study (SLS) II (Tashkin et al. Lancet Resp Med. 2016), 142 SSc-ILD patients were randomized to receive either mycophenolate mofetil (MMF) for 2 years or oral cyclophosphamide (CYC) for 1 year followed by 1 year of placebo. The % predicted forced vital capacity (FVC%) was the primary clinical outcome and was measured every 3 months. Baseline serum samples were available in 135 participants. Serum from 45 unaffected controls matched for age, gender, and race in a 1 to 3 ratio to SLS II participants was also investigated. The serum levels of 6 IFN inducible chemokines (IP-10, MIG, MCP-2, B2M, MIP-3 beta, TNFR2) were measured using multiplex assays in a CLIA certified laboratory. A serum IFN composite score was calculated based on the levels of these six chemokines using a previously described method (Bauer et al. Arthritis Rheum. 2009). Similar to the primary outcome analysis in SLS II, a joint model of longitudinal measurements (serially obtained FVC%) and non-ignorable missing data was conducted in order to investigate the predictive significance of the baseline IFN chemokine score for response to treatment.

Results: In this study, 78 (57.8%) participants had diffuse cutaneous disease with a mean baseline FVC% of 66.3%. As shown in Figure 1, the IFN chemokine score was significantly higher in SSc-ILD (fold change= 1.62, $p< 0.001$) than in controls and decreased significantly in both treatment arms from baseline to 12-months. There was no significant correlation between baseline IFN chemokine score and baseline FVC% (p=0.197). As shown in Table 1, higher baseline IFN chemokine score predicted better response based on higher serial FVC% 3 to 12 months after initiation of treatment in CYC (b=0.91, p=0.009), and MMF (b=0.41, p=0.001) arms, after adjustment for baseline FVC%. In contrast, higher baseline CRP predicted progression of ILD based on significantly lower FVC% after treatment start in the CYC arm (b=-0.56, $p< 0.001$) and showed a similar trend for lower FVC% 3 to 12 months in the MMF arm (b=-0.15, p=0.091).



IFN chemokine score in controls, MMF patients at baseline (MMF-BL) and 12 months (MMF-12m), and CYC patients at baseline (CYC-BL) and 12 months (CYC-12M).
* P <0.05 in paired analysis
** p<0.001 in paired analysis

Figure 1. Boxplot of Interferon Chemokine Scores by Treatment

Table 1. Predictive Significance of IFN Chemokine Score for Subsequent Serial FVC%s

CYC Arm				
	Effect size	**2.5%**	**97.5%**	**P-value**
Predictive significance of baseline IFN chemokine score for serial FVC%s 3-12 months				
Baseline IFN sore	**0.91**	**0.56**	**1.13**	**0.009**
Baseline FVC%	0.87	0.84	0.9	<0.001
Predictive significance of 12-month IFN chemokine score for serial FVC%s 15-24 months				
12-month IFN score	**-0.61**	**-1.5**	**0.11**	**0.068**
12-month FVC%	1	0.96	1.08	<0.001
MMF Arm				
Predictive significance of baseline IFN chemokine score for serial FVC%s 3-12 months				
Baseline IFN score	**0.41**	**0.23**	**0.59**	**0.001**
Baseline FVC%	0.84	0.82	0.86	<0.001
Predictive significance of 12-month IFN chemokine score for serial FVC%s 15-24 months				
12-month IFN score	**0.28**	**0.11**	**0.69**	**0.029**
12-month FVC%	0.96	0.9	0.98	<0.001

Consistent with the different treatment approaches during the second year of SLS II, higher IFN chemokine score at 12 month showed a trend for predicting lower serial FVC% 15-24 months during the placebo treatment period of the CYC arm (b=-0.61, p=0.068) while it continued predicting better response to immunosuppression in the MMF arm (b=0.28, p=0.029).

Conclusion: Higher serum IFN chemokine score in SSc-ILD predicts better response to immunosuppression with MMF and CYC and could be potentially used for identify patients who may derive the most benefit from these two treatments.

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Frequency and Predictors of Meaningful Decline in Forced Vital Capacity During Follow up of a Large Cohort of Systemic Sclerosis Associated Pulmonary Fibrosis Patients

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Background/Purpose: Pulmonary fibrosis (PF) is common in systemic sclerosis (SSc) and serial pulmonary function tests (PFTs) are used for routine PF monitoring. Forced vital capacity (FVC) decline reflects progression in PF and FVC is frequently used as an endpoint in clinical trials assessing the effect of drugs on PF. We explore the changes in FVC over time in a cohort of patients with SSc-related PF receiving standard management, including immunosuppression.

Methods: Only SSc patients with CT-confirmed PF were included. FVC changes over the first 10 years from disease onset and the effects of age, sex, cutaneous subset and autoantibodies were assessed using linear mixed effect models. We analysed time to development of threshold FVC levels (FVC< 70% and FVC< 50%) on a time scale starting at first available FVC, if this was within the first 5 years of disease, using Kaplan-Meier estimates and Cox regression.

Results: From a single centre cohort of 1068 SSc patients with at least one PFT result available, we identified 505 (47.3%) who had PF. Of those 109 (21.6%) were male, average age of onset was 47 years and 249 (49.3%) had diffuse cutaneous subset (dcSSc). The most common autoantibody was anti-topoisomerase I (ATA) in 204 (40.4%) of the subjects, followed by anti-RNA polymerase in 59 (11.7%), anti-PmScl in 26 (5.2%), anti-centromere in 36 (7.1%) and anti-U3RNP in 15 (3.0%). In 83 (16.4%) of the patients ANA was positive, but no ENAs were identified (ANA+ENA-). FVC measurements on at least three occasions were available for 364 (72.1%) of the patients. Mean period between PFTs was 13 months.

Table 1. Multivariable mixed effect model for FVC

Fixed effects parameters	β	95% CI		p-value
Time, years (centred at 1 year)	-0.20	-1.15	0.13	0.151
Age at onset, years (centred at 48 years)	0.35	0.19	0.52	<0.001
Male	-3.58	-7.63	1.13	0.142
Male*Time (centred at 1 year)	-0.63	-1.19	-0.07	0.034
Diffuse cutaneous subset	-2.57	-4.54	-1.06	0.003
Antibodies				
Anti-RNA polymerase	ref.			
Anti-centromere antibody	-13.48	-23.86	-3.00	0.019
Anti-topoisomerase antibody	-14.03	-25.14	-8.87	<0.001
Anti-U3RNP antibody	-9.09	-20.63	5.48	0.152
Anti-PMScl antibody	-13.40	-23.84	-3.87	0.008
ANA+ ENA-	-12.13	-23.15	-8.35	<0.001
Other antibodies	-12.29	-23.44	-8.07	<0.001
Antibodies*Time (centred at 1 year)				
Anti-RNA polymerase	ref.			
Anti-centromere antibody	1.19	0.03	2.32	0.042
Anti-topoisomerase antibody	0.09	-0.83	0.80	0.118
Anti-U3RNP antibody	0.78	-0.70	2.26	0.301
Anti-PMScl antibody	0.97	-0.30	2.23	0.133
ANA+ ENA-	-0.70	-1.84	0.80	0.419
Other antibodies	1.01	0.18	1.82	0.017
Constant	32.20	29.48	101.25	<0.001
Random-effects parameters				
SD Time	1.79	1.28	2.03	
SD Constant	18.18	16.88	19.80	
Correlation (Time, Constant)	-0.16	-0.30	-0.02	
Residual SD	8.73	8.20	8.86	

Table 2. Multivariable mixed effect model for change in FVC prediction

Fixed effects parameters	β	95% CI		p-value
Anti-centromere antibody	ref.			
Anti-topoisomerase antibody	-1.78	-3.73	0.18	0.075
Anti-RNA polymerase	-1.84	-3.98	0.29	0.09
Anti-U3RNP antibody	-1.44	-4.37	1.49	0.335
Anti-PMScl antibody	-0.42	-3.10	2.27	0.761
ANA+ ENA-	-2.15	-4.27	-0.03	0.046
Other antibodies	-0.79	-2.90	1.32	0.463
Constant	1.19	-0.67	3.05	0.211
Residual SD	9.02	8.75	9.30	

Average FVC at 12 months from onset was 80.1% (SD 19.3). For most patients, FVC fluctuated over time, although there was a small but statistically significant absolute decline of approximately 0.32% per year (95%CI 0.09, 0.55; p=0.007) at a group level. There was no evidence for a significant correlation between baseline FVC

Table 3. Multivariable Cox regression analysis for predictors of time to development of FVC<70% and FVC<50% in systemic sclerosis patients with pulmonary fibrosis confirmed on CT.

	HR	95% CI		p-value
FVC<70% prediction				
Baseline FVC	0.84	0.79	0.89	<0.001
Male	1.92	1.16	3.16	0.011
Anti-topoisomerase antibody	1.68	1.05	2.69	0.030
Baseline FVC*Time (years)	1.02	1.01	1.03	<0.001
FVC<50% prediction				
Baseline FVC	0.91	0.89	0.94	<0.001

and subsequent change (correlation coefficient -0.13, 95%CI -0.26, 0.01). Multivariable analysis demonstrated significant associations between FVC and age at onset, sex, cutaneous subset and antibodies (Table 1).

In a multivariable model for change in FVC (difference between FVC measured in consecutive PFTs), only antibodies predicted future change with greatest drop observed in ANA+ENA- patients, followed by ARA+ and ATA+ ones (Table 2).

The proportion of PF subjects to develop FVC< 70%, if they had FVC≥70% at first available test, was 7.7% at 1 year, 13.6% at 2 years, 17.2% at 3 years, 18.7% at 4 years and 19.8% at 5 years from first FVC assessment. For FVC< 50% this was 2.1% at 1 year, 4.4% at 2 years, 5.8% at 3 years, 7.6% at 4 years and 10.5% at 5 years. In a multivariable model, factors that associated with increased risk for FVC drop below 70% were male sex, ATA positivity and low baseline FVC, while the only predictor of drop in FVC to 50% or lower was low baseline FVC (Table 3).

Conclusion: This study provides insight into long-term patterns of FVC change and develops a model that may help predict those most at risk of significant decline. We show that ATA positivity, male gender and diffuse subset are associated with greater long-term decline in FVC, while short-term change associated only with antibodies.

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Abstract Number: 1836

Clinical Outcomes of Patients with Giant Cell Arteritis with Polymyalgia Symptoms Only vs Cranial Symptoms Only Treated with Tocilizumab or Placebo in a Randomized Clinical Trial

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders II: Large Vessel Vasculitis Treatment

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: GiACTA, a randomized, double-blind, placebo (PBO)–controlled study, demonstrated the efficacy and safety of tocilizumab (TCZ) in patients with giant cell arteritis (GCA).[1] Growing evidence has shown that TCZ is also effective for the treatment of polymyalgia rheumatica (PMR); however, data on this are limited.[2,3] The purpose of this study was to evaluate the efficacy of TCZ in patients with GCA presenting with cranial symptoms only or PMR symptoms only in GiACTA.

Table 1. Patient Characteristics and Treatment at Study Baseline

	PMR Symptoms Only at Diagnosis (n = 52)	Cranial Symptoms Only at Diagnosis (n = 94)
Age, mean (SD), y	64.5 (8.3)	70.8 (7.8)
Female, n (%)	39 (75.0)	64 (68.1)
White, n (%)	51 (98.1)	91 (96.8)
Weight, mean (SD), kg	70.06 (14.09)	71.78 (16.10)
Body mass index, mean (SD), kg/m^2	24.81 (3.95)	26.36 (5.44)
GCA diagnosis, n (%)		
Newly diagnosed	27 (51.9)	41 (43.6)
Relapsing	25 (48.1)	53 (56.4)
Disease duration, mean (SD), days	327.04 (600.89)	239.05 (404.94)
ESR, mean (SD), mm/h	24.98 (20.21)	24.56 (19.92)
CRP, mean (SD), mg/L	6.51 (9.44)	7.73 (12.70)
Diagnosis, n (%)*		
Positive temporal artery biopsy	9/12 (75)	72/79 (91.1)
Positive imaging	44/52 (84.6)	31/94 (33.0)
Prednisone dose, n (%)		
≤ 30 mg/d	27 (51.9)	53 (56.4)
> 30 mg/d	25 (48.1)	41 (43.6)
Treatment group, n (%)		
TCZ†	31 (59.6)	58 (61.7)
Placebo‡	21 (40.4)	36 (38.3)

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PMR, polymyalgia rheumatica; TCZ, tocilizumab.
* Of patients with available results.
† TCZ 162 mg weekly or every other week with a 26-week prednisone taper.
‡ Placebo with a 26- or 52-week prednisone taper.

Table 2. Clinical and Safety Outcomes

	PMR Symptoms Only at Diagnosis (n = 52)		Cranial Symptoms Only at Diagnosis (n = 94)	
	TCZ* (n = 31)	Placebo† (n = 21)	TCZ* (n = 58)	Placebo† (n = 36)
Patients with ≥ 1 flare, n (%) with PMR symptoms, n/N (%) with cranial symptoms, n/N (%)	13 (41.9) 8/13 (61.5) 10/13 (76.9)	12 (57.1) 7/12 (58.3) 6/12 (50.0)	12 (20.7) 7/12 (58.3) 10/12 (83.3)	17 (47.2) 9/17 (52.9) 10/17 (58.8)
No. of flares with PMR symptoms, n/N (%) with cranial symptoms, n/N (%)	18 10/18 (55.6) 12/18 (66.7)	20 10/20 (50.0) 8/20 (40.0)	19 7/19 (36.8) 15/19 (78.9)	25 11/25 (44.0) 11/25 (44.0)
Annual flare rate, mean (SD)‡	0.64 (0.85)	0.95 (1.24)	0.40 (0.93)	0.93 (1.81)
Patients with flare following remission, n (%)	11 (35.5)	11 (52.4)	11 (19.0)	16 (44.4)
Cumulative prednisone dose, median, mg	1862.0	3671.5	1842.0	2965.5
Patients with ≥ 1 AE, n (%)§	30 (96.8)	20 (95.2)	55 (94.8)	36 (100)
Patients with ≥ 1 SAE, n (%)§	5 (16.1)	3 (14.3)	10 (17.2)	12 (33.3)

AE, adverse event; GCA, giant cell arteritis; PMR, polymyalgia rheumatica; SAE, serious adverse event; TCZ, tocilizumab.
* TCZ 162 mg weekly or every other week with a 26-week prednisone taper.
† Placebo with a 26-week or 52-week prednisone taper.
‡ Annualized flare rate is calculated as the number of flares between the first clinical assessment of GCA and the final clinical assessment prior to entry into Part 2, divided by the time period between the 2 days, multiplied by 365.25.
§ Multiple occurrences of AEs are included. Denominators are all AEs or SAEs.

Methods: GiACTA randomized 251 GCA patients to receive weekly or every other week TCZ plus a 26-week prednisone taper (TCZ + prednisone) or PBO plus a 26- or 52-week prednisone taper (PBO + prednisone).[1] In this post hoc analysis, baseline characteristics, sustained remission rate, number of flares, annual flare rate, time to flare, cumulative prednisone dose and safety were assessed in patients with PMR symptoms only and patients with cranial symptoms only at diagnosis. Disease flare was defined as the recurrence of signs or symptoms of GCA (including PMR) or an elevation in erythrocyte sedimentation rate attributable to GCA.

Results: Of 146 patients included in the analysis, 52 had PMR symptoms only and 94 had cranial symptoms only at diagnosis. Demographics and other patient characteristics are shown in **Table 1**. The hazard ratios for flare in patients receiving TCZ vs PBO were 0.77 (99% CI, 0.26-2.32) for patients with PMR symptoms only and 0.37 (99% CI, 0.13-1.01) for patients with cranial symptoms only. Of patients with PMR symptoms only, 18 flares occurred in 13/31 patients (41.9%) in the TCZ group and 20 flares occurred in 12/21 patients (57.1%) in the PBO group. Of patients with cranial symptoms only, 19 flares occurred in 12/58 patients (20.7%) in the TCZ group and 25 flares occurred in 17/36 patients (47.2%) in the PBO group (**Table 2**). For both the PMR and cranial symptoms only groups, annual flare rates were lower in patients receiving TCZ compared with those receiving PBO. The occurrence of adverse events and serious adverse events was similar between groups (**Table 2**).

Conclusion: TCZ improved clinical outcomes in patients who presented with PMR symptoms only or cranial symptoms only at diagnosis as indicated by a reduced incidence of flares. These findings suggest that TCZ is effective in patients with GCA with PMR or cranial symptoms.

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1. Stone JH, et al. *N Engl J Med*. 2017;377(4):317-328.
2. Lally L, et al. *Arthritis Rheumatol*. 2016;68(10):2550-2554.
3. Devauchelle-Pensec V, et al. *Ann Rheum Dis*. 2016;75(8):1506-1510.

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Abstract Number: 1837

Ustekinumab for the Treatment of Giant Cell Arteritis

Mark Matza ,[1] John Stone,[1] Ana Fernandes,[1] and Sebastian Unizony[1], [1]Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders II: Large Vessel Vasculitis Treatment
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Disease flare despite high cumulative glucocorticoid exposure is one of the hallmarks of giant cell arteritis (GCA). Tocilizumab is effective in controlling disease activity in most patients, but up to 35% of them fail this treatment due to inefficacy or side-effects. Thus, additional remission maintenance and glucocorticoid-sparing options are greatly needed in GCA. Interleukins (IL)-12 and 23 are thought to play a pathogenic role in this disease. Therefore, we evaluated the efficacy of the IL-12/23 antagonist ustekinumab (UST) in GCA patients.

Methods: We conducted a prospective, single center, open-label pilot study (ClinicalTrials.gov NCT02955147) to evaluate the efficacy and safety of UST in combination with prednisone for new onset and relapsing GCA patients with active disease. GCA diagnosis required positive temporal artery biopsy or vascular imaging. Active disease for study enrollment was defined as the presence of cranial or PMR signs/symptoms along with elevation of ESR (≥40 mm/hour) or CRP (≥10 mg/L) within 6 weeks of baseline. UST 90 mg was administered subcutaneously at baseline and weeks 4, 12, 20, 28, 36 and 44. All patients received a pre-specified 6-month prednisone taper starting at 60 mg, 40 mg, or 20 mg based on investigators' clinical judgment. The primary endpoint, prednisone-free remission, was defined as the absence of disease flare from induction of remission up to week 52 and the concurrent normalization of ESR (< 40 mm/hour) and CRP (< 10 mg/L), while adhering to the protocol prednisone taper. Disease flare was defined as the recurrence of signs/symptoms of GCA (e.g., cranial or PMR) that required treatment modification, regardless of ESR and CRP levels. A sensitivity analysis eliminating ESR and CRP from the definition of prednisone-free remission was also completed.

Results: A sample of 20 consecutive patients was planned for the study. However, the study was prematurely terminated due to inefficacy. Here we report the outcomes of the first 11 patients that completed 52 weeks of treatment. Baseline patient characteristics are shown in **Table 1**. The mean age of the patients was 71 years, 82% were females, 27% had new-onset disease, and 91% had a positive temporal artery biopsy. The initial prednisone dose was 60 mg in 2 patients, 40 mg in 8 patients and 20 mg in 1 patient. Results are shown in **Table 2**. All patients achieved disease remission within 4 weeks of baseline. Only 2 patients (18%) achieved the primary

Table 1. Patient Baseline Characteristics

	GCA patients (n = 11)
Age, years: mean (SD)	71 (7)
Female sex	9 (82)
Caucasian ethnicity	11 (100)
New onset disease	3 (27)
Biopsy-proven disease	10 (91)
Imaging-proven disease	3 (27)
Cranial signs or symptoms	11 (100)
PMR symptoms	8 (73)
ESR, mm/hour: mean (SD)	43 (14)
CRP, mg/L: mean (SD)	44 (29)

Values represent number and (%) unless otherwise specified
SD, standard deviation; PMR, polymyalgia rheumatica;
ESR, erythrocyte sedimentation rate; CRP, C-reactive protein

Table 2. Results

	GCA patients (n = 11)
Primary outcome achieved	2 (18)
Sensitivity analysis met	4 (36)
Disease flare	7 (64)
Clinical features at disease flare	
Cranial signs or symptoms	3/7 (43)
PMR symptoms	7/7 (100)
ESR, mm/hour: mean (SD)	49 (26)
CRP, mg/L: mean (SD)	40 (34)
Time to flare, weeks: mean (SD)	23 (7)
Number of UST doses received, mean (SD)	4 (1)
Prednisone dose, mg/day: mean (SD)	3 (3)

Values represent number and (%) unless otherwise specified
SD, standard deviation; PMR, polymyalgia rheumatica;
ESR, erythrocyte sedimentation rate; CRP, C-reactive protein
UST, ustekinumab

outcome. Of the 9 patients (82%) who failed to achieve the primary outcome, 7 patients had a flare after a mean period of 23 weeks and 3-6 UST injections. The mean (SD) prednisone dose at the time of flare was 3 (3) mg/day. The other 2 patients who failed to achieve the primary outcome did not have a disease flare, but their inflammatory markers were elevated at week 52. Four patients (36%) met the alternative definition of prednisone-free remission at week 52 (sensitivity analysis). UST was well tolerated. Only 1 patient developed pneumonia, which resolved with oral antibiotics.

Conclusion: UST in combination with 6 months of prednisone was not associated with clinically significant rates of sustained disease remission in this cohort of GCA patients.

Disclosure: M. Matza, None; **J. Stone**, Genentech, 2, 5, Roche, 2, 5, Xencor, 2, 5; **A. Fernandes**, None; **S. Unizony**, Genentech, Inc., 2.

Abstract Number: 1838

Time to Flare in Patients with New-Onset versus Relapsing Giant Cell Arteritis Treated with Tocilizumab or Placebo Plus Prednisone Tapering: 3-Year Results from a Randomized Controlled Phase 3 Trial

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders II: Large Vessel Vasculitis Treatment

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Tocilizumab (TCZ) administered subcutaneously every week (QW) or every other week (Q2W) with 26-week prednisone tapering was superior to placebo (PBO) plus 26-week (PBO+26) or 52-week (PBO+52) prednisone tapering for achievement of sustained glucocorticoid-free remission in patients with giant cell arteritis (GCA) in part 1 of the 52-week, double-blind GiACTA trial.[1] In part 1, among patients with new-onset GCA at baseline, TCZ QW and TCZ Q2W treatment reduced the risk for GCA flare compared with PBO+26, whereas among patients with relapsing GCA, TCZ QW but not TCZ Q2W treatment reduced the risk for flare compared with both PBO groups, and there was separation in the time to flare between the TCZ QW and Q2W groups. The objective of the current analysis was to report time to first flare over 3 years of the GiACTA trial (part 1 plus 2-year open-label part 2) among patients with new-onset or relapsing GCA.

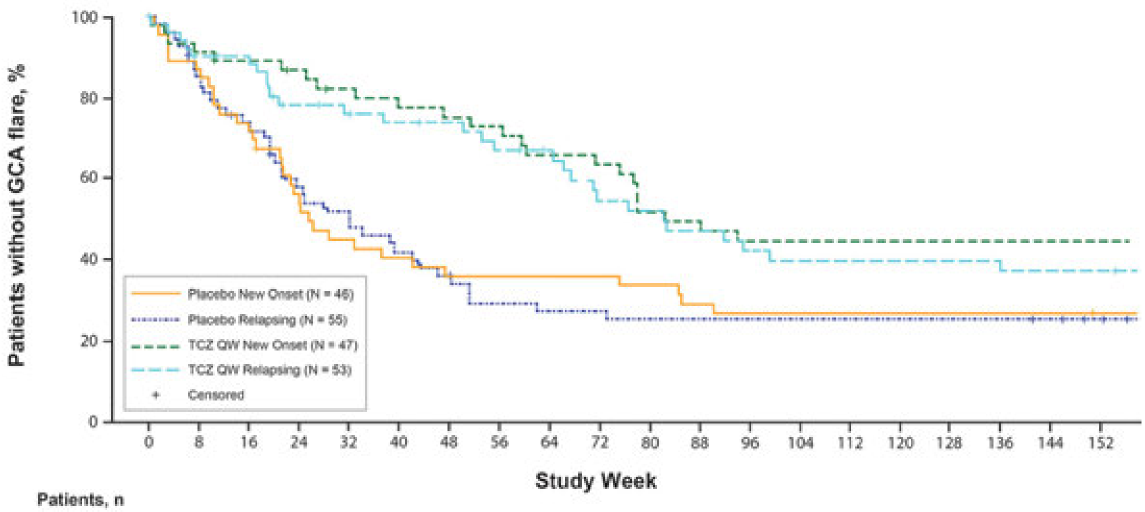
Methods: At the end of part 1, patients entered open-label part 2, in which GCA therapy (including initiation/termination of open-label TCZ and/or glucocorticoids) was given at the investigator's discretion according to disease status. Time to first GCA disease flare during the 3-year study period was assessed using Kaplan-Meier analysis for patients in the intent-to-treat population according to disease onset status at baseline (new-onset or relapsing) based on their originally assigned treatment groups: TCZ QW, TCZ Q2W, or pooled PBO (PBO+26 and PBO+52).

Table. Time to First Flare in Patients With New-Onset or Relapsing GCA

	TCZ QW		TCZ Q2W		Pooled PBO	
	New-Onset N = 47	Relapsing N = 53	New-Onset N = 26	Relapsing N = 23	New-Onset N = 46	Relapsing N = 55
Patients who experienced flare, n (%)	24 (51)	28 (53)	19 (73)	15 (65)	33 (72)	38 (69)
Time to flare, days, median (95% CI)	577 (499-NE)	575 (463-NE)	479 (341-778)	428 (162-645)	179 (149-331)	224 (148-322)

NE, not evaluable.
Treatment groups refer to originally assigned treatment in part 1.

Figure 1. Time to First Flare in Patients With New Onset or Relapsing GCA: TCZ QW Versus PBO Groups

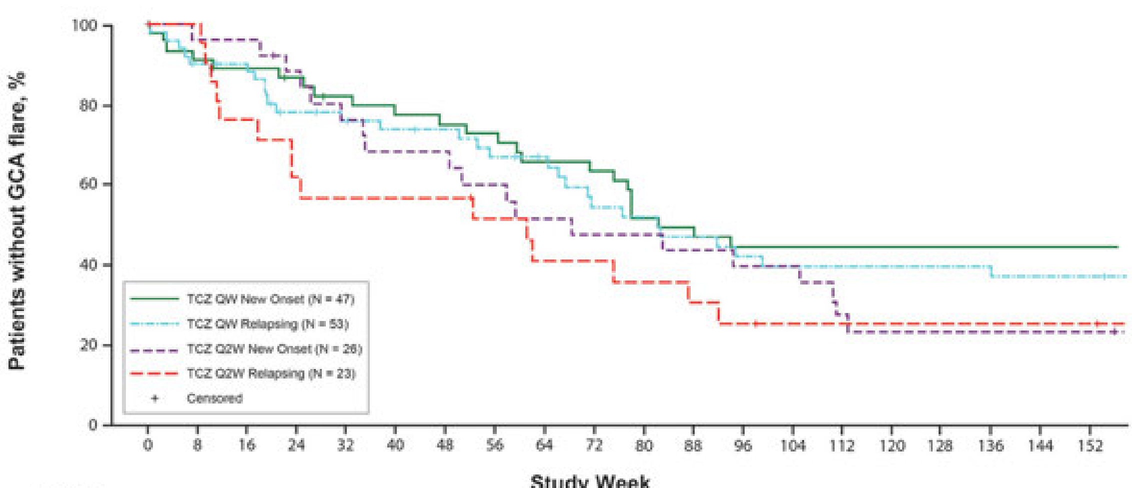


Patients, n

Placebo New Onset	46	41	40	35	33	30	25	21	20	19	18	17	16	16	16	16	16	16	16	15	15	15	13	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11
Placebo Relapsing	55	52	45	41	38	33	29	27	26	23	21	19	18	14	14	14	13	13	13	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	10	9
TCZ QW New Onset	47	43	42	40	40	40	38	36	35	34	33	33	32	31	31	29	28	28	27	26	22	21	21	20	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19
TCZ QW Relapsing	53	50	46	45	45	39	37	36	35	34	33	32	32	31	29	28	27	24	22	22	21	19	19	18	17	16	16	16	16	16	16	16	16	16	16	15	15	15	15

Treatment groups refer to originally assigned treatment in part 1. Patients who were never in remission were censored at day 1 and patients who withdrew were censored from the time of withdrawal.

Figure 2. Time to First Flare in Patients With New Onset or Relapsing GCA: TCZ QW Versus TCZ Q2W Groups



Patients, n

TCZ QW Onset	47	43	42	40	40	40	38	36	35	34	33	33	32	31	31	29	28	28	27	26	22	21	21	20	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19
TCZ QW Relapsing	53	50	46	45	45	39	37	36	35	34	33	32	32	31	29	28	27	24	22	22	21	19	19	18	17	16	16	16	16	16	16	16	16	16	16	15	15	15	15
TCZ Q2W New Onset	26	26	25	25	25	24	22	20	19	17	17	17	17	15	15	13	13	13	12	12	12	11	11	11	10	10	10	9	7	6	6	6	6	6	6	6	6	6	6
TCZ Q2W Relapsing	23	21	21	16	16	15	13	12	12	12	12	12	12	12	10	10	8	8	8	7	7	7	6	6	5	4	4	4	4	4	4	4	4	4	4	4	4	4	4

Treatment groups refer to originally assigned treatment in part 1. Patients who were never in remission were censored at day 1 and patients who withdrew were censored from the time of withdrawal.

Results: Among patients randomly assigned in part 1, 47 of 100 (47%) in the TCZ QW group, 26 of 49 (53%) in the TCZ Q2W group, and 46 of 101 (46%) in the pooled PBO group had new-onset GCA at baseline; the rest had relapsing GCA. Median time to first flare over 3 years was longer for patients assigned to TCZ treatment in part 1 than for those assigned to PBO. Among patients assigned to TCZ, it was longer with QW than Q2W dosing for both the new-onset and the relapsing subgroups (Table 1). Higher proportions of patients in the TCZ QW group (new-onset, 49%; relapsing, 47%) than the pooled PBO group (new-onset, 28%; relapsing, 31%) and the TCZ Q2W group (new-onset, 27%; relapsing, 35%) remained flare-free during the entire 3-year study. Kaplan-Meier analysis showed a clear separation

between the TCZ QW and pooled PBO groups over 3 years for patients with new-onset and relapsing GCA (Figure 1). Separation between the TCZ QW and TCZ Q2W groups was also observed over 3 years in patients with new-onset and relapsing GCA, although this was more evident in patients with new-onset GCA during year 3 (Figure 2).

Conclusion: In this 3-year analysis of GiACTA parts 1 and 2, time to first flare favored TCZ QW over TCZ Q2W in patients with new-onset and relapsing GCA. TCZ QW delayed time to first flare compared with PBO in patients with new-onset and relapsing GCA, supporting TCZ QW dosing in patients with GCA regardless of disease onset.

Reference:

1. Stone JH et al *N Engl J Med* 2017;377:317-328.

Disclosure: J. Stone, Genentech, 2, 5, Roche, 2, 5, Xencor, 2, 5; **H. Spotswood**, Roche, 1, 3; **S. Unizony**, Genentech, Inc., 2; **M. Aringer**, Abbvie, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, BMS, 5, 8, Boehringer Ingelheim, 5, 8, Bristol-Myers Squibb, 5, 8, Chugai, 5, 8, Hexal, 8, HEXAL, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, Sanofi-Aventis, 5, 8, UCB, 8; **D. Blockmans**, None; **E. Brouwer**, Roche, 5, 8; **M. Cid**, Roche, 9; **B. Dasgupta**, Abbvie, 2, BMS, 5, GSK, 5, Roche, 2, 5, 8, Roche Chugai, 5, 8, Sanofi, 2, 5, Sanofi Aventis, 5, Sanofi-Aventis, 5; **J. Rech**, AbbVie, 8, Biogen, 8, BMS, 5, 8, Celgene, 5, 8, Chugai, 5, MSD, 8, Novartis, 5, 8, Roche, 5; **C. Salvarani**, None; **R. Spiera**, BMS, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, ChemoCentryx, 2, 5, Chemocentryx, 2, Corbus, 2, CSL Behring, 5, Cytori, 2, Formation Biologics, 2, Genentech, Inc., 2, Genzyme/Sanofi, 2, 5, GlaxoSmith-Kline, 2, 5, GSK, 2, 5, Hoffman-La Roche Ltd, 2, Janssen, 5, Mitsubishi, 5, Roche, 2, Roche Genetech, 2, 5, Roche/Genetech, 2, 5, Roche-Genentech, 2, 5, Roche-Genetech, 2, 5, Sanofi, 5, Sanofi-Aventis, 5; **M. Bao**, Genentech, 1, 3, Genentech, Inc., 3, Roche, 4.

Abstract Number: 1839

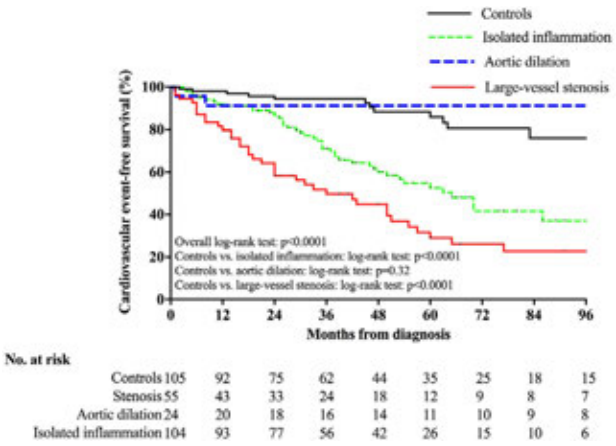
Different Patterns and Specific Outcomes of Large-Vessel Involvements in Giant Cell Arteritis

Hubert de Boysson ,[1] Eric Liozon,[2] Olivier Espitia,[3] Aurélie Daumas,[4] Mathieu Vautier,[5] Marc Lambert,[6] Jean-Jacques Parienti,[7] Alain Manrique,[7] David Saadoun,[8] Kim Heang Ly,[2] Christian Agard,[9] and Achille Aouba[10], [1]University Hospital of Caen, Caen, France, [2]Limoges University Hospital, Limoges, France, [3]Nantes University Hospital, Nantes, France, [4]Marseille AP-HM, Marseille, France, [5]Paris - Pitié salpétrière, Paris, France, [6]Lille University Hospital, Lille, France, [7]Caen University Hospital, Caen, France, [8]AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Department of Internal Medicine and Clinical Immunology, F-75013, Paris, France, Paris, France, [9]CHU Nantes, Nantes, France, [10]CHU Caen, Caen, France

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders II: Large Vessel Vasculitis Treatment
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Large-vessel involvements (LVI) in giant-cell arteritis (GCA) include different clinical and imaging patterns that are often pooled together in the published cohorts under the generic term “large-vessel vasculitis”. The analysis of the different imaging patterns in GCA patients with LVI and their relationships with patients’ cardiovascular prognosis have been poorly investigated.

Methods: We conducted a nationwide retrospective study and included GCA patients with LVI demonstrated on imaging at diagnosis between 2007 and 2017. We analyzed the prognosis of three different imaging patterns of LVI



Kaplan-Meier curves of cardiovascular event-free survival in patients with three patterns of giant cell arteritis-related large-vessel involvement on imaging at diagnosis and in control patients without large-vessel involvement on imaging at diagnosis.

present at diagnosis, with some of them overlapping but with the first one present in all patients: 1) inflammation of the aorta and/or its branches; 2) dilation of the aorta; and 3) stenosis of the aortic branches. A control group of GCA patients without LVI was constituted.

A Cox proportional hazards model was used to assess predictive factors associated with new cardiovascular complications, ischemic events and aortic dilation. Hazard ratios (HRs) and 95% confidence intervals (CI) were computed for each predictor in the univariate analysis and in the multivariate model using the backward stepwise approach using variables that reached $p < 0.1$ in univariate analyses. We analyzed the cardiovascular event-free survival in patients with each different pattern of LVI and in controls, using life tables and the Kaplan-Meier method, and these were compared using the log-rank test.

Results: We included 183 patients with LVI and 105 controls without LVI. Altogether, among the 183 patients who all showed inflammation of the aorta and/or its main branches, concomitant aortic dilation and large-vessel stenosis were observed in 27 (15%) and 55 (30%) patients, respectively. During the follow-up period, new cardiovascular events occurred in 49% and 11% of LVI patients and controls, respectively ($p < 0.0001$). Inflammation of the aorta and/or its branches (HR: 3.42 [2.09-5.83], $p < 0.0001$) and large-artery stenosis (HR: 2.75 [1.80-4.15], $p < 0.0001$) were independent predictive factors of new cardiovascular events. Conversely, the use of an immunosuppressant besides corticosteroids was a protective factor against new cardiovascular events (HR: 0.44 [0.29-0.66], $p < 0.0001$) and the development of aortic dilation (HR: 0.43 [0.23-0.77], $p = 0.005$).). The cardiovascular event-free survival in the three patterns and in controls is shown in the Figure. Patients with large-vessel stenosis showed the worst outcomes (log-rank test: $p< 0.0001$).

Conclusion: This study highlights that large-vessel involvement in GCA includes different clinical and imaging patterns that might influence cardiovascular outcomes. The involvement of the aorta and its branches at diagnosis may increase the risk of aortic dilation and dissection, whereas stenotic involvement of large vessels may favor the occurrence of ischemic events. In this study, the use of immunosuppressants in patients with LVI showed a protective impact on the occurrence of new cardiovascular events. A validation of this finding in other studies is required.

Disclosure: H. de BOYSSON, Chugai Pharma France, 5, Roche Chugai, 2, 5; **E. LIOZON**, None; **O. ESPITIA**, None; **A. DAUMAS**, None; **M. VAUTIER**, None; **M. LAMBERT**, None; **J. PARIENTI**, None; **A. MANRIQUE**, None; **D. Saadoun**, Abbvie, 5, AstraZeneca, 5, Bristol meyer squibb, 5, Gilead, 5, Glaxo Smith Kline, 5, Roche, 5, Servier, 5; **K. Ly**, None; **C. Agard**, None; **A. Aouba**, None.

Abstract Number: 1840

Risk Factors for Treatment Failure in Patients with Giant Cell Arteritis Treated with Tocilizumab Plus Prednisone versus Prednisone Alone

Sebastian Unizony ,[1] Min Bao,[2] Jian Han,[2] Yves Luder,[3] Páris Sidiropoulos,[2] Jinglan Pei,[2] and John Stone[1],
[1]Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA, [2]Genentech, South San Francisco, CA, [3]F. Hoffmann-La Roche, Basel, Switzerland

SESSION INFORMATION

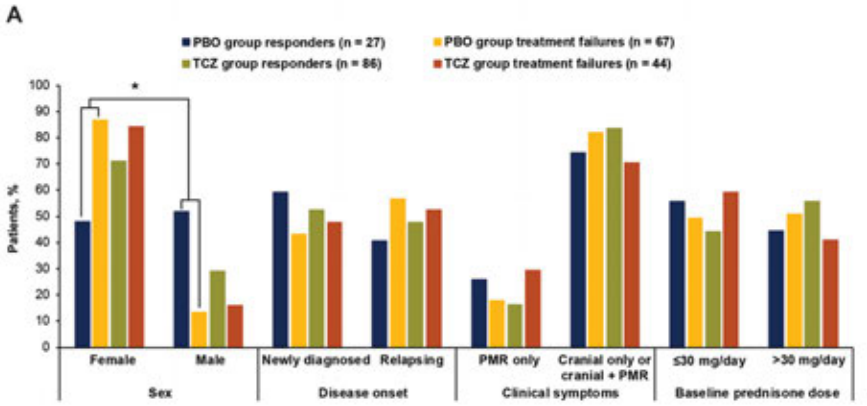
Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders II: Large Vessel Vasculitis Treatment

Session Type: ACR Abstract Session

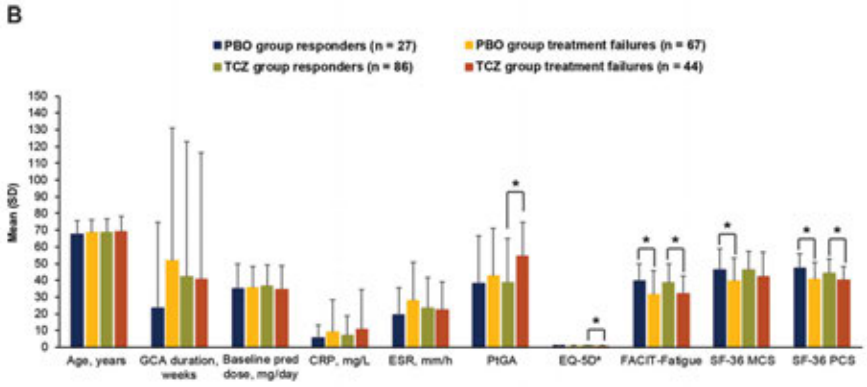
Session Time: 2:30PM–4:00PM

Figure 1. Univariate analysis of treatment failure according to categorical predictors (A) and continuous predictors (B)



p values (responders vs treatment failures)

PBO group	<0.0001	0.1606	0.3812	0.5802
TCZ group	0.0993	0.6197	0.0777	0.1077



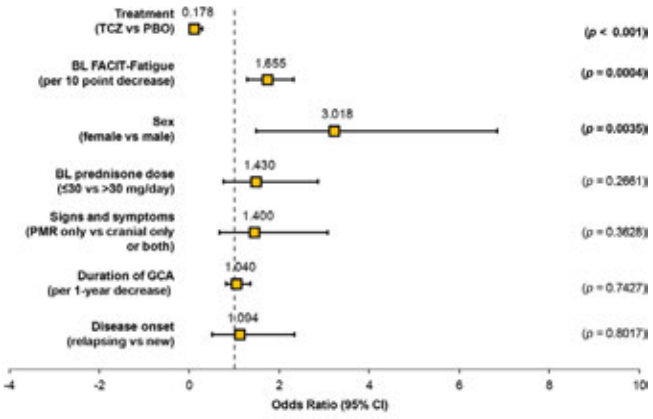
p values (responders vs treatment failures)

PBO group	0.4251	0.0929	0.8776	0.4021	0.0627	0.4610	0.1445	**0.0108**	**0.0332**	**0.0044**
TCZ group	0.7910	0.9192	0.4159	0.2058	0.7668	**0.0008**	**0.0271**	**0.0008**	0.1079	**0.0076**

Statistical significance was assessed by $\chi 2$ tests (A) or 2-sample *t* tests (B). Significant *p* values are indicated by the asterisk, and corresponding values are shown in bold.

*EQ-5D scores: PBO group responders, 0.8 (0.2); PBO group treatment failures, 0.7 (0.2); TCZ group responders, 0.8 (0.2); TCZ group treatment failures, 0.7 (0.2).

Figure 2. Multivariate analysis of treatment failure



Odds ratio >1 indicates the first group has higher odds of treatment failure than its comparator based on a multiple logistic regression model including all variables selected in univariate analysis plus all possible treatment by BL covariate interactions. Significant *p* values are shown in bold.

Background/Purpose: Risk factors for treatment failure in patients with giant cell arteritis (GCA) are poorly understood. The objective of this analysis was to identify predictors of treatment failure in GCA patients receiving tocilizumab (TCZ) or placebo (PBO) in combination with prednisone in a randomized controlled trial (GiACTA).[1]

Methods: Two hundred fifty GCA patients received weekly or every-other-week TCZ plus a 26-week prednisone taper (TCZ+pred) or PBO plus a 26- or 52-week prednisone taper (PBO+pred). Patients who achieved and maintained clinical remission (CR) from week 12 to week 52 while adhering to the protocol prednisone taper were classified as responders. CR, adjudicated by investigators, was defined as the absence of disease flare (GCA signs or symptoms, and/or ESR elevation attributable to GCA that required further treatment [eg, rescue prednisone]) regardless of C-reactive protein (CRP) level. Treatment failure was defined as failure to achieve CR by week 12 or occurrence of flare between weeks 12 and 52. Both TCZ groups and both PBO groups were combined for this analysis. Potential predictors investigated included baseline demographics, disease- and treatment-related factors, and health-related quality of life (HRQOL) measures. Univariate and multivariate analyses were performed.

Results: Overall, 45% (113/250) of patients were responders: 27% (27/101) in the PBO+pred groups and 58% (86/149) in the TCZ+pred groups. In contrast, 44% (111/250) of patients experienced treatment failure: 66% (67/101) in the PBO+pred group and 30% (44/149) in the TCZ+pred group. The other 10% (26/250) of patients were nonresponders for reasons other than treatment failure: 7 in the PBO+pred group and 19 in the TCZ+pred group. In univariate analysis, female sex and lower baseline SF-36 Physical Component Summary (PCS), Mental Component Summary, and FACIT-Fatigue scores were associated with treatment failure among PBO+pred–treated patients, whereas higher patient global assessment of disease activity scores and lower SF-36 PCS, FACIT-Fatigue, and EQ-5D scores were associated with treatment failure among TCZ+pred–treated patients (Figure 1). Among TCZ+pred–treated patients, no treatment response difference according to sex was observed. Age, previous relapse, starting prednisone dose, and GCA clinical features (cranial or polymyalgia rheumatica symptoms) were not associated with treatment failure in either group based on univariate analysis. Multivariate logistic regression demonstrated that PBO+pred treatment, female sex, and worse FACIT-Fatigue scores at baseline increased the risk for treatment failure (Figure 2).

Conclusion: Female GCA patients responded particularly poorly if treated with prednisone alone according to univariate analysis. Female sex, impaired HRQOL at baseline, and treatment with prednisone alone are risk factors for treatment failure in GCA. These factors may be considered when determining which treatment would be best for a particular patient.

Reference:

1. Stone JH et al. *N Engl J Med* 2017;377:317-328.

Disclosure: S. Unizony, Genentech, Inc., 2; **M. Bao**, Genentech, 1, 3, Genentech, Inc., 3, Roche, 4; **J. Han**, Genentech, 1, 3, Genentech, Inc., 3; **Y. Luder**, F. Hoffman-La Roche Ltd, 3, F. Hoffmann-La Roche, 1, 3; **P. Sidiropoulos**, Genentech, 1, 3, Genentech, Inc., 3; **J. Pei**, Genentech, 1, 3, Genentech, Inc., 3; **J. Stone**, Genentech, 2, 5, Roche, 2, 5, Xencor, 2, 5.

Abstract Number: 1841

Resolution of Vascular Inflammation in Patients with Giant Cell Arteritis Receiving Glucocorticoids, Methotrexate or Tocilizumab Treatment: Data from the Italian/German RIGA Study

Verena Schönau,[1] Jessica Roth,[1] Koray Tascilar,[2] Jürgen Rech,[3] Daniela Schmidt,[4] Torsten Kuwert,[4] Filippo Crescentini,[5] Luigi Boiardi,[6] Massimiliano Casali,[7] Annibale Versari,[8] Giulia Pazzola,[5] Georg Schett,[9] Carlo Salvarani,[10] and **Francesco Muratore** [11], [1]Rheumatology Unit, University of Erlangen, Erlangen, Germany, [2]Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg, University Hospital Erlangen, Erlangen, Germany, Erlangen, Bayern, Germany, [3]Department of Internal Medicine 3, Friedrich-Alexander-University Erlangen-Nuremberg (FAU) and Universitätsklinikum Erlangen, Erlangen, Germany, [4]Nuclear Medicine Unit, University of Erlangen, Erlangen, Germany, [5]Rheumatology Unit, Azienda Unita' Sanitaria Locale IRCCS di Reggio Emilia, Reggio Emilia, Italy, [6]Division of Rheumatology, Azienda Unita' Sanitaria Locale IRCCS di Reggio Emilia, Reggio Emilia, Italy, [7]Azienda USL-IRCCS di Reggio Emilia, REGGIO EMILIA, Italy, [8]Nuclear Medicine Unit, Azienda Unità Sanitaria Locale IRCCS di Reggio Emilia, Reggio Emilia, Emilia-Romagna, Italy, [9]Department of Internal Medicine 3, Friedrich Alexander University Erlangen-Nuremberg, Erlangen, Germany, [10]Division of Rheumatology, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy, [11]Division of Rheumatology, Azienda Unita' Sanitaria Locale IRCCS di Reggio Emilia, Reggio Emilia, Italy

SESSION INFORMATION

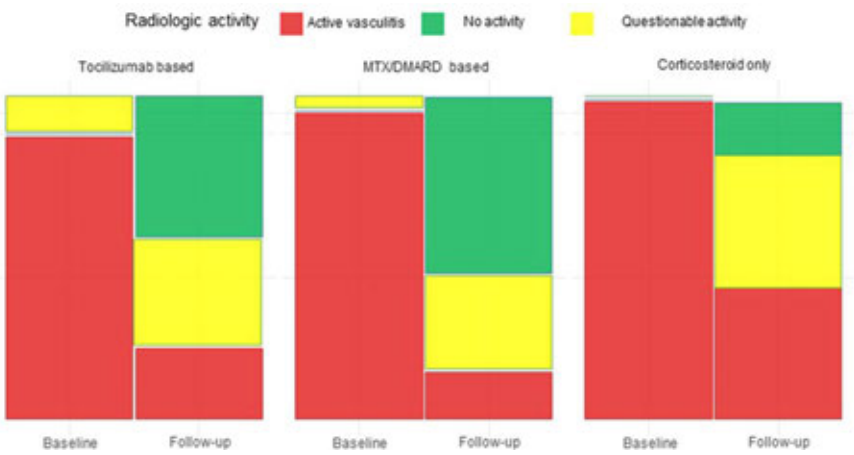
Session Date: Monday, November 11, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders II: Large Vessel Vasculitis Treatment

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: ^{18}F-FDG-PET/CT is a sensitive and comprehensive technique to diagnose giant cell arteritis (GCA). This technique may be also very useful to test whether vascular inflammation in GCA has disappeared or not, judging effectiveness of anti-inflammatory treatment. However, the role of ^{18}F-FDG-PET/CT in monitoring disease activity and judging disease remission is less well-established to date.



RIGA is an observational 2-center study that addresses the resolution of vascular inflammation in patients with new-onset GCA that are treated with either glucocorticoid monotherapy (GLC), GLC/methotrexate (MTX) or GLC/tocilizumab (TOC).

Methods: Patients with newly diagnosed GCA with large vessel involvement were clinically documented, subjected to sequential ^{18}F-FDG-PET/CT scanning and received treatment with GLC, MTX or TOC upon physicians' decision. Images were graded as active, questionable active and inactive according to nuclear medicine physician opinion and additionally graded by PETVAS score proposed by Grayson et al. (0-27) (1). We performed a mixed effects linear regression analysis to estimate the change in the PETVAS score adjusted by baseline CRP level and tested for treatment group interactions. We compared the proportion of radiologic activity states according to the activity tracer uptake in the follow up ^{18}F-FDG-PET/CT scan in three treatment groups with a chi-squared test.

Results: We included 48 patients (n=20 from Germany, n=28 from Italy) with a mean age of 66 years. At baseline, ^{18}F-FDG-PET/CT scan was graded as active in 46 patients while it was graded as questionable active in the remaining 2 patients. The mean CRP level was 66,8 mg/L (min 1,2; max 233,2 mg/l) and the mean PETVAS score was 21,1 (min=10 max=27). 12 patients received GLC, 27 MTX and 9 TOC as primary treatment. Follow-up PET/CT scans were graded as active in 11, questionable active in 16 and inactive in 21 patients. The mean CRP level at follow up was 12,4 mg/l (min 0,2; max 76,0) and the mean PETVAS score was 9,1 (min 0, max 27) with significant decreases in all 3 groups. The mean adjusted improvement in the PETVAS score (95%CI) was 13.0 (8.7 – 17.3) in GLC, 11.7 (8.9 – 14.6) in MTX and 11.8 (6.8 – 16.7) in TOC groups and interaction terms for treatment effect were not significant. However, only 17% of patients who received GLC showed no vasculitis activity in their follow up PET-CT compared to 53% of patients who received MTX or TOC (figure 1).

Conclusion: GLC, MTX and TOC significantly reduced vascular inflammation in GCA, but no significant differences between the three treatment strategies was found in this yet small population. However, when looking at complete resolution of vascular inflammation, MTX and TOC appear as being superior to GLC monotherapy, suggesting that addition of these agents right from the beginning of treatment of GCA may be beneficial to achieve complete control of vascular inflammation.

1. Grayson, P. C. et al, 18F-Fluorodeoxyglucose–Positron Emission Tomography As an Imaging Biomarker in a Prospective, Longitudinal Cohort of Patients With Large Vessel Vasculitis. Arthritis Rheumatol, 70: 439-449 https://doi.org/10.1002/art.40379

Disclosure: V. Schönau, Novartis, 8; **J. Roth**, None; **K. Tascilar**, None; **J. Rech**, AbbVie, 8, Biogen, 8, BMS, 5, 8, Celgene, 5, 8, Chugai, 5, MSD, 8, Novartis, 5, 8, Roche, 5; **D. Schmidt**, None; **T. Kuwert**, None; **F. Crescentini**, None; **L. Boiardi**, None; **M. Casali**, None; **A. Versari**, None; **G. Pazzola**, None; **G. Schett**, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, 8, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, UCB, 5, BMS, Celgene, GSK, Lilly, Novartis, 2; **C. Salvarani**, None; **F. Muratore**, None.

Abstract Number: 1842

Patients and Relatives Coping with Inflammatory Arthritis: Impact of Communication, Social Support and Relatives Burden on Patients Perceived Health

Morgane Brignon,[1] Catherine Beauvais,[2] Martine Beranger,[3] Jean-David Cohen,[4] Isabelle Griffoul,[5] Janine Sophie Le Quintrec,[6] Didier Poivret,[7] Corinne Thevenot,[8] Sonia Trope,[9] and **Anne-Christine Rat** [10], [1]Université de Lorraine, EA 4360 APEMAC, Nancy, France, [2]Saint-Antoine Hospital, Hôpitaux universitaires Est Parisien, AP–HP, Paris, France, [3]Orléans Hospital, Orléans, France, [4]Montpellier University hospital, Montpellier, France, [5]Tours University Hospital,

Tours, France, [6]Cochin University Hospital, Paris, France, [7]Metz Hospital, Metz, France, [8]Laon Hospital, Laon, France, [9]Andar, Montpellier, France, [10]CHU Caen, rheumatology department, Caen Normandie University, Université de Lorraine, EA 4360 APEMAC, Caen, France

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain, Anxiety, & Depression
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Relatives' and patients' adjustment to a chronic disease is complex, and there is room for improvement in the support provided to the dyad. So far, few studies have studied the impact of the characteristics of the caregiver and of the relationship within the couple simultaneously. Moreover, studies focused on rheumatoid arthritis (RA), not on spondyloarthritis (SpA), and were realized before biologics.

We aimed to analyze the impact of patient's caregiver and patient-caregiver relationship on functional impairment, mental health and self-efficacy of the patient with RA or SpA.

Methods: Study design: observational cross-sectional study.

Inclusion criteria: age ≥18 years old; diagnosis of RA or SpA; spouse consent. Exclusion criteria: major comorbidity. Participants were recruited by rheumatologists during their consultations in seven rheumatology departments and by a patient association.

Outcome criteria: functional impairment and mental health measured by the SF12 (Physical and Mental Component Summary scores) and self-efficay by the General Self-Efficacy Scale.

Potential determinants: Caregiver-patient relationship was assessed by the personal assessment of intimacy in relationships (PAIR) questionnaire (scores: communication, engagement, shared friends) and the Dyadic Adjustment Scale (DAS)(scores: degree of agreement, quality of the interactions), social support by the Social Support Questionnaire SQ6, burden by the Zarit questionnaire and comorbidities by the groll index.

Results: A total of 88 patient–relative dyads were included. Patients were mostly female (N=68, 77%), mean age 59 (SD 12.6) years old, 69% had RA, mean disease duration 16 (range 1-63) years, mean age of caregivers 60 (SD 13,5) years old, 35 (45%) were still in work.

	Patients Physical Component Summary Score (SF12)		Patients Mental Component Summary scores (SF12)		Patients General Self-Efficacy Scale [10,40]	
	Beta	P	Beta	P	Beta	P
Patients data						
Sex (women vs men)			-5,60	0,01		
IA (rheumatoid arthritis vs spondyloarthritis)	5,90	0,02	6,80	0,0002		
Comorbidities	-2,50	0,001			-0,8	0,04
Communication (PAIR)			0,50	0,04	0,4	0,04
Relatives data						
Social support (Satisfaction)			0,20	0,03		
Burden (ZARIT)					-0,2	0,003

In bivariate analyses, relatives' burden (and patients type of IA and comorbidities) were associated with patients functional impairment.

Patients' social Support (satisfaction scores), dyad relationship (PAIR communication and engagement scores, DAS degree of agreement and quality of the interactions scores assessed by patients) (and patients age, sex, IA), were associated with patients mental health.

Relatives burden, social support (satisfaction scores), relatives anxiety and depression, dyad relationship (PAIR communication score and DAS degree of agreement assessed by patients) (and patients comorbidities) were associated with self-efficacy.

In multivariate analyses (table), good communication in the couple, satisfaction with social support and low relative burden were independently associated with improved patients mental health and perceived self-efficacy.

Conclusion: This study has highlighted that mental health and self-efficacy of patients with IA are not only influenced by patient-relative relationship, but also by the perceived satisfaction of social support of the couple, the perceived burden of the relative and by relative anxiety and depression.

Intervention targeting relatives should be part of self-management programs of patients with IA.

Factors associated with functional impairment, mental health and self-efficacy of the patient with RA or SpA: multivariate analyses

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Disclosure: M. Brignon, None; **C. Beauvais**, None; **M. Beranger**, None; **J. Cohen**, None; **I. Griffoul**, None; **J. Le Quintrec**, None; **D. Poivret**, None; **C. Thevenot**, None; **S. Trope**, None; **A. Rat**, Pfizer, lilly, 5.

Abstract Number: 1843

Predictors of Mortality Among Black Women with Systemic Lupus Erythematosus: The Black Women's Experiences Living with Lupus (BeWELL) Study

Charmayne Dunlop-Thomas ,[1] Gaobin Bao,[2] Cristina Drenkard,[2] David Chae,[3] and S Sam Lim[2], [1]Emory University, Atlanta, Georgia, [2]Emory University, Atlanta, GA, [3]Auburn University, Auburn, AL

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain, Anxiety, & Depression
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Mortality continues to be disproportionately high in Black women with SLE living in the South region of the United States. Recent studies suggest that as in other chronic conditions, psychosocial and patient-reported health domains might have a strong influence on the mortality of people with SLE. We examined psychosocial, general health, health care access/utilization, and indicators of disease severity in relation to mortality among Black women with SLE.

Methods: We examined data from the BeWELL study. A sample of 438 self-identified Black women was recruited between April 2015 and May 2017, from the Georgian's Organized Against Lupus (GOAL) cohort, a large population-

Table 2: Predictive Factors for Mortality Risk, with Cox Regression Analysis				
	Univariate regression		Multiple regression*	
Description	Hazard Ratio (95%CI)	P value	Hazard Ratio (95%CI)	P value
Ever missed without rescheduling an appointment with rheumatologist during past 12 months	2.87 (1.29-6.42)	0.01	2.97 (1.30-6.80)	**0.01**
Overall current physical health: Poor/fair health	1.22 (0.55-2.72)	0.63	1.13 (0.45-2.84)	0.79
PROMIS Depression - T Score (per 5 points ?)	1.24 (1.01-1.53)	0.04	1.28 (1.01-1.62)	**0.04**
PROMIS Anxiety -T Score (per 5 points ?)	1.09 (0.89-1.34)	0.39	1.09 (0.87-1.38)	0.45
PROMIS Companionship – T Score (per 5 points ?)	0.78 (0.64-0.97)	0.022	0.78 (0.63-0.96)	**0.02**
PROMIS Pain – T Score (per 5 points ?)	1.23 (0.97-1.55)	0.082	1.22 (0.92-1.60)	0.16
PROMIS Fatigue – T Score (per 5 points ?)	1.09 (0.88-1.34)	0.43	1.07 (0.82-1.39)	0.63
Cohen's Perceived Stress (per 1 point ?)	1.16 (1.00-1.35)	0.049	1.20 (1.01-1.42)	**0.04**
*Multiple regressions were controlled for age, disease duration, education, insurance status, marital status, emergency room visit (yes/no), disease activity (SLAQ score) and organ damage (SA-BILD score)				

Table 2: Predictive Factors for Mortality Risk, with Cox Regression Analysis				
	Univariate regression		Multiple regression*	
Description	Hazard Ratio (95%CI)	P value	Hazard Ratio (95%CI)	P value
Ever missed without rescheduling an appointment with rheumatologist during past 12 months	2.87 (1.29-6.42)	0.01	2.97 (1.30-6.80)	**0.01**
Overall current physical health: Poor/fair health	1.22 (0.55-2.72)	0.63	1.13 (0.45-2.84)	0.79
PROMIS Depression - T Score (per 5 points ?)	1.24 (1.01-1.53)	0.04	1.28 (1.01-1.62)	**0.04**
PROMIS Anxiety -T Score (per 5 points ?)	1.09 (0.89-1.34)	0.39	1.09 (0.87-1.38)	0.45
PROMIS Companionship – T Score (per 5 points ?)	0.78 (0.64-0.97)	0.022	0.78 (0.63-0.96)	**0.02**
PROMIS Pain – T Score (per 5 points ?)	1.23 (0.97-1.55)	0.082	1.22 (0.92-1.60)	0.16
PROMIS Fatigue – T Score (per 5 points ?)	1.09 (0.88-1.34)	0.43	1.07 (0.82-1.39)	0.63
Cohen's Perceived Stress (per 1 point ?)	1.16 (1.00-1.35)	0.049	1.20 (1.01-1.42)	**0.04**
*Multiple regressions were controlled for age, disease duration, education, insurance status, marital status, emergency room visit (yes/no), disease activity (SLAQ score) and organ damage (SA-BILD score)				

based cohort of patients from metropolitan Atlanta Georgia with validated SLE, fulfilling 3 or more ACR classification criteria with a final diagnosis by a board-certified rheumatologist. Inclusion criteria: 18-79 years of age, and lack of significant visual or physical impairment that would prohibit being able to respond to questions on a computer. Mortality was assessed prospectively through April 2019 based on notices from family, obituaries or clinical notes. For this study, we explored the associations of the following measures: Patient-Reported Outcomes Measurement Information System (PROMIS) Companionship SF4, PROMIS Depression SF6, Cohen's Perceived Stress Scale, the Systemic Lupus Activity Questionnaire (SLAQ) and the Self-administered Brief Index of Lupus Damage (SA-BILD). Multivariate Cox regression analysis was used to examine predictors of psychosocial and health-related factors on death, controlling for demographics, healthcare, and disease-related confounders.

Results: Twenty-four participants (mean age at enrollment = 45.5 years) died within the observation period (mean years from study entry to death = 1.3) (Table 1). Multivariate analyses (Table 2) showed that depression, perceived stress, and missed health care appointments increased the risk of death with p values ranging from 0.01 to 0.04,

while perceived availability of someone with whom to share social activities was associated with lower risk after controlling for other covariates (p=< 0.02).

Conclusion: During the observation period, five percent of the sample of Black women unexpectedly died. Findings suggest that psychosocial factors, including depression, stress, and barriers to show up for medical appointments may serve as indicators of declining health and death. Companionship may be a potential protective factor, as studies have shown psychological benefits and longer life related to regular companionship.

Disclosure: C. Dunlop-Thomas, None; **G. Bao**, None; **C. Drenkard**, None; **D. Chae**, None; **S. Lim**, None.

Abstract Number: 1844

The Contribution of Disease Activity, Depression, and Anxiety to Health-Related and Non-Health-Related Quality of Life in US and Filipino Patients with SLE

Alexandra Watts ,[1] Desiree Azizoddin,[2] Shadi Gholizadeh,[3] Sarah Mills,[4] Geraldine Zamora,[5] Daniel Wallace,[6] Meenakshi Jolly,[7] Michael Weisman,[8] and Perry Nicassio[9], [1]University of California, Los Angeles, Los Angeles, CA, [2]Dana-Farber Cancer Institute, Boston, MA, [3]McGill University, Montreal, Canada, [4]Lineberger Comprehensive Cancer Center, Chapel Hill, NC, [5]Manila Doctors Hospital, Manila, Philippines, [6]Cedars-Sinai Medical Center/University California at Los Angeles, Los Angeles, CA, [7]Rush University Medical Center, Chicago, IL, [8]David Geffen School of Medicine at UCLA, Los Angeles, CA, [9]David Geffen School of Medicine, Los Angeles, CA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain, Anxiety, & Depression
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: It is well known that patients with SLE are often afflicted with deficits in quality of life and problems with physical impairment and psychosocial functioning. The present study sought to determine the variables associated with both health-related quality of life (HRQOL) and non-health-related quality of life (NHRQOL) in SLE.

Methods: Data from Patients with SLE from medical centers in an urban clinic in the United States and a rural-based clinic in the Philippines were analyzed. The US sample consisted of 136 patients from Los Angeles ages 18-81 (μ=49), and the Filipino sample was comprised of 100 patients ages 19-77 (μ=35) from Manila. Data on demographic factors (illness duration, age, income, and education), along with disease activity depression, anxiety, and quality of life (assessed using LupusPro) were collected. A series of multiple regression analyses were conducted to examine the contribution of demographic factors, disease duration and activity, and psychological factors to health-related quality of life (HRQOL) and non-health related quality of life (NHRQOL) in each sample.

Results: HRQOL. For the US sample, the regression equation was highly significant (F=22.88, p< .001), accounting for 57% of the variance. Anxiety (be=.-32, p< .001) and depression (be=-.46, p< .001) were each associated with lower HRQOL. No other variable was a significant predictor. For the Filipino sample, the regression equation accounted for 16% of the variance (F=2.49, p< .05). Depression was a significant predictor of lower HRQOL (be=-.28, p< .05). Disease activity (be=.20, p=.06) and anxiety (be=-.19, p=.08) both approached significance. NHRQOL. For the US sample, the regression equation accounted for 19% of the variance in NHRQOL (F=4.16, p< .001). Anxiety individually predicted lower NHRQOL (be=-.28, p< .001), while depression (be=-.16, p=.03) and age (be=-.19, p=.06) approached

significance. For the Filipino sample, the regression equation accounted for 10% of the variance in NHRQOL but was not significant (F=1.40, p=.22). Higher income was associated with higher NHRQOL (be=.23, p< .05) but since the overall model was not significant, the importance of income as an individual predictor could not be determined.

Conclusion: The findings illustrated the importance of depression in HRQOL for patients with SLE in the Philippines and the US, and anxiety for patients in the U.S. The results were more robust in general for the Cedars sample. More research on Filipino patients with SLE is needed to identify the predictors and potential intervention targets for quality of life in this population.

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Abstract Number: 1845

Physical Inactivity Is a Risk Factor for Incident Depression in Systemic Lupus Erythematosus

Laura Trupin ,[1] Sarah Patterson,[1] Louise Murphy,[2] Maria Dall'Era,[1] Jinoos Yazdany,[3] and Patricia Katz[1], [1]University of California, San Francisco, San Francisco, CA, [2]Centers for Disease Control and Prevention, Division of Population Health, Atlanta, [3]UCSF Division of Rheumatology, San Francisco, CA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain, Anxiety, & Depression
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Physical activity can prevent and reduce depression, but there is little research on the relationship between physical inactivity and subsequent onset of depression in lupus. We examined physical inactivity as a predictor of incident depression in a cohort of individuals with SLE.

Methods: Data derive from the California Lupus Epidemiology Study (CLUES), a longitudinal cohort of 431 patients in the San Francisco Bay Area with confirmed SLE diagnoses, drawn from a variety of clinical sources and prior SLE studies. Participants complete an annual interview that includes sociodemographic questions and validated self-report measures of depression (Patient Health Questionnaire; PHQ-8), physical functioning (in Patient Reported Outcomes Measurement Information System; PROMIS), disease activity (Systemic Lupus Activity Questionnaire; SLAQ) and damage (Brief Index of Lupus Damage; BILD). A subset of participants also had physician assessed disease activity (SLE Disease Activity Index; SLEDAI) and damage (SLICC Damage Index; SDI). Physical inactivity was

Table. Risk of incident depression over 2 years, by physical activity at baseline, among SLE cohort participants with no depression at baseline.

Physical activity	n	Baseline PHQ-8	Incident depression, over 2 years	
			Cumulative incidence	Adjusted hazard ratio*
		(mean±sd)	% (95% CI)	HR (95% CI)
Total non-depressed at baseline	276		15% (11-19%)	
Inactive	42	3.98±3.78	36% (21-50%)	2.4 (1.2-4.8)
Active	234	3.44±3.12	11% (7-15%)	Ref
p-value		0.24	<0.001	0.02

*From Cox proportional hazards model, adjusted for age, gender, race/ethnicity, education, diagnosis age, and self-reported baseline disease activity (SLAQ), damage (BILD), and physical functioning (PROMIS).

assessed at baseline from a single item: "I rarely or never do any physical activities." Respondents were categorized as not depressed at baseline if their PHQ-8 scores were < 10, a validated cut-point. In that group, those with scores ≥ 10 in either of the next two annual interviews were considered to have incident depression. Using Cox proportional hazards regression, we modeled incident depression over a 2 year period as a function of baseline physical inactivity, controlling for sociodemographics, baseline physical functioning and disease status.

Results: 366 participants had ≥1 follow-up interview, of whom 256 (70%) had 2 follow-ups. At baseline, mean age of the sample was 47±14, 90% were female, 66% racial/ethnic minority. Among the 90 (25%) with PHQ-8 ≥10 at baseline, 33% were inactive vs. 16% of the 276 without baseline depression (p< 0.001). Those with baseline depression were excluded from further analysis. Mean PHQ scores for those without depression at baseline did not differ by activity status, but those who were inactive at baseline were more than 3 times as likely to develop depression over the next two years. After adjusting for baseline disease activity and damage (either by patient or physician assessment), physical function, and sociodemographics, the association remained moderately strong (hazard ratio, HR=2.4; see Table). Using physician assessed activity and damage reduced the sample size to 216 but did not appreciably change the results (HR=3.0; 95% CI= 1.4-6.7).

Conclusion: In this diverse cohort of patients with SLE, a simple question about low levels of physical activity was highly predictive of incident depression over the subsequent 2 years, after adjusting for sociodemographic and disease-related risk factors. Results support the importance of even low levels of physical activity and suggest an urgent need for approaches to increase physical activity in this high-risk patient population, such as health care providers' recommendation of SLE-appropriate low impact activities (e.g., walking and swimming) and referral to community-based physical activity programs designed for individuals with SLE.

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Abstract Number: 1846

Does Cartilage Loss Cause Pain in Osteoarthritis?

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain, Anxiety, & Depression
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Treatment development in osteoarthritis continues to focus on chondroprotection, but it is unclear if delaying cartilage loss would reduce joint pain. In published studies, less cartilage in a knee has not been consistently associated with more pain in the knee. Studies have not tested whether cartilage loss over time is associated with worsening pain and have not adjusted for other sources of pain. Further they have not examined whether synovitis, induced by cartilage loss, might mediate any effect on pain. Using observational data from the FNIH cohort within the Osteoarthritis Initiative, we tested whether cartilage loss was associated with worsening knee pain after adjusting for coexistent bone marrow lesions (BMLs) and synovitis and examined whether the association of cartilage loss with pain was mediated by worsening synovitis.

Association of change in WOMAC knee pain over 24 months with change in cartilage thickness loss over 24 months, adjusted for change in synovitis and BMLs			
MOAKS Factors over 24 months	**Model** Adjusted for BML only **Mean change (95% CI)**	**Model** Adjusted for Synovitis only **Mean change (95% CI)**	**Model** Adjusted for both BML and synovitis **Mean change (95% CI)**
Cartilage Thickness Loss over 24 months	0.15(-0.02,0.33)	0.10(-0.08,0.27)	0.09(-0.08,0.27)
BML change over 24 months	0.13(0.01,0.24)	-	0.10(-0.01,0.21)
Synovitis change over 24 months		0.84(0.53,1.14)	0.80(0.50,1.10)
All models adjusted for age, sex, BMI, race, depressive symptoms (CESD).			

Association of change in WOMAC knee pain over 36 months with change in cartilage thickness loss over 24 months, adjusted for change in synovitis and BMLs		
MOAKS Factors over 24 months	**Model** Adjusted for Synovitis only **Mean change (95% CI)**	**Model** Adjusted for both BML and synovitis **Mean change (95% CI)**
Cartilage Thickness Loss over 24 months	0.04(-0.15,0.23)	0.05(-0.14,0.24)
BML change over 24 months	-	-0.02(-0.15,0.10)
Synovitis change over 24 months	0.74(0.41,1.08)	0.74(0.40,1.08)
All models adjusted for age, sex, BMI, race, depressive symptoms (CESD).		

Association of change in WOMAC knee pain with change in cartilage thickness loss and synovitis, in strata defined by change in synovitis over 24 months				
	Outcome: WOMAC pain change over 24 months		Outcome: WOMAC pain change over 36 months	
	Strata: synovitis increased over 24 months **n=176**	**Strata: synovitis unchanged or decreased over 24 months** **n=424**	**Strata: synovitis increased over 24 months** **n=176**	**Strata: synovitis unchanged or decreased over 24 months** **n=424**
MOAKS Factors over 24 months	**Mean change (95% CI)**	**Mean change (95% CI)**	**Mean change (95% CI)**	**Mean change (95% CI)**
Cartilage Thickness Loss over 24 months	**0.46(0.13,0.78)**	**-0.06(-0.26,0.14)**	**0.31(-0.07,0.68)**	**-0.05(-0.28,0.18)**
Synovitis change over 24 months	**0.70(-0.22,1.62)**	**0.65(0.07,1.24)**	**0.63(-0.44,1.70)**	**0.81(0.15,1.46)**
All models adjusted for age, sex, BMI, race, depressive symptoms (CESD), and BML change. Cartilage loss by synovitis strata: n=105 of 176, cartilage loss in strata of increased synovitis; n=178 of 424, cartilage loss in strata of unchanged or decreased synovitis. Of knees with cartilage loss 178 of 283(63%) were in the stratum where cartilage loss was unrelated to worsening pain.				

Methods: 600 knee MRIs were scored for structural features of OA using the MRI Osteoarthritis Knee Score (MOAKS) at the baseline, 12-month, and 24-month OAI visits. We focused on loss of cartilage thickness as our measure of cartilage loss, because extent of cartilage area loss was unassociated with pain in initial analysis. For each visit we created summary scores for synovitis (range 0-6, sum of Hoffa-synovitis and effusion scores), cartilage thickness loss (range 0-42, sum of 14 regions), and BMLs (range 0-45, sum of 15 region scores) and computed change scores for MRI features from baseline to 24 months. We used the WOMAC knee pain score (range 0-20) from each visit and calculated change from baseline to 24 and 36 months. Linear models calculated mean change in pain associated with cartilage thickness loss, adjusted for BMLs and covariates. We used approaches by VanderWeele to examine whether synovitis change mediated the cartilage loss-pain association longitudinally at 24 and 36 months. Analyses explored effects of cartilage loss on pain in strata defined by synovitis change.

Results: Mean age and BMI were 61.6 years (8.9) and 30.7(4.8), respectively. 59% were female. In cross-sectional analyses, cartilage thickness was significantly associated with WOMAC pain (mean change in pain score=0.2, 95%CI=0.1,0.3 per unit change in predictor) but this association weakened when BML score was taken into account (mean change=0.1, 95%CI=0.0,0.2). In analyses adjusted for BMLs but not those adjusted for synovitis, change in cartilage thickness was weakly associated with pain change over 24 months (see upper table). Cartilage thickness change over 24 months was not predictive of pain change over 36 months after adjustment for BML or synovitis change (middle table). Most of the association of cartilage loss with pain was mediated by synovitis change (me-

diation proportion 52%), and we found a significant interaction between cartilage loss and synovitis change such that loss of cartilage was associated with worse pain only in those with increasing synovitis over time (lower table). However, in most knees with cartilage loss, there was no increase in synovitis.

Conclusion: Cartilage loss is, at most, weakly associated with knee pain, and this association with pain appears to be mediated by change in synovitis.

Disclosure: K. BACON, None; **L. Michael**, None; **D. Felson**, None.

Abstract Number: 1847

A National Needs Assessment of Males with SLE: Assessing Medical, Psychosocial, Support & Coping Needs

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain, Anxiety, & Depression
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: SLE mostly affects women; however, males represent 4-22% of patients. Research shows men tend to seek medical attention & supportive care < women & are underrepresented at self-management/support services for coping with SLE, despite having higher disease severity. Limited research exists regarding the specific medical, psychosocial, & support needs of men with SLE. Our hospital conducted a national survey to identify self-reported needs & concerns for men with SLE, as well as their interest in male specific support forums.

Methods: An 85-item survey with Likert scale & opened-ended questions was disseminated nationally to males with SLE over 18. The survey was advertised via online forums, at major hospitals serving SLE patients in NYC & at local & national SLE groups. The survey assessed 4 core areas: health status & quality of life, health behavior & lifestyle, access to care & interest in male specific programming. Surveys were completed via an online link.

Results: A total of 112 respondents participated in the survey, 61% identified as White, 21% Black/African-American, 15% Hispanic & 31% other. Mean age was 26 & mean year since diagnosis (DX) was 10. 49% of males were employed/self-employed & 46% unemployed/unable to work. 53% had an annual income of ˃ 50K, & 59% had some college or advanced degree. 94% reported having health insurance. Almost half (45%) reported living in an urban/city area, 34% suburban area & 20% rural area. Almost all (92%) were being treated by a Rheumatologist.

When respondents rated their overall health, 65% reported their health as fair/good, while 21% reported poor health. The majority (76%) reported worrying more about their future since DX. Most males (83%) reported that SLE limits their activities of daily living. When asked about the single most important way SLE affected daily life, responses included fatigue & pain, with 48% reporting feeling pain daily. 53% of men reported SLE affects their sexual health: 52% reported less sexual desire & satisfaction, 45% limited motion, & 47% impotence. When asked how often they followed medical advice, 59% said always, however reasons for not following medical advice included: worry about treatment side effects (44%) & that treatment would not help (43%).

Over half (58%) reported feeling depressed for several days/more than half the days in the last 2 weeks. Regarding support & coping with SLE, 52% reported receiving no support. 84% had never taken a class to learn self-management & coping skills. When asked if they would be interested in receiving support to help cope with SLE, 40% were interested/very interested, 44% reported being unsure &15% were not interested. When asked about the type of support platform they would prefer, 77% indicated online, 71% lupus app, 69% social group & 67% support & education group. When asked how likely they would be to participate in a male only support group, 50% reported likely/very likely, 27% unlikely/very unlikely & 23% unsure.

Conclusion: Despite our small sample, this study provides important information about the physical & emotional health of males with SLE as well as their interest in psychosocial support. A next step would be to conduct focus groups with males with SLE to better understand their specific support needs.

Disclosure: P. Toral, None; **J. Rose**, None; **R. Horton**, None; **A. Tavera**, None; **N. Irvine**, None.

Abstract Number: 1848

Racial Disparities in Septic and Aseptic Total Knee Replacement Revision Risk: A Study Using Four State-wide Inpatient Databases

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Healthcare Disparities in Rheumatology
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Approximately 4% of total knee replacement (TKR) patients require revision within five years. Blacks are 40% more likely to undergo TKR revision than whites,[1] but whether racial disparities exist for both septic and aseptic TKR revision risk is unknown.

Methods: This study used patient-level data from four diverse states representing the Northeast (NY), Southwest (AZ), South (AR), and Gulf Coast (FL) with ≥ 5 years of revisit files available from the Healthcare Utilization Project State Inpatient Databases (HCUP-SID) and New York Statewide Planning and Research Cooperative System (SPARCS). The index cohort was defined as black or white patients undergoing their first primary TKR. The reason for TKR revision was determined using ICD-9-CM diagnosis codes and categorized as septic, fracture, mechanical ("aseptic") or other. Kaplan-Meier survival curves were generated to assess the association between race and time to septic or aseptic TKR revision. Cox proportional hazards models were used to evaluate the association between demographic and clinical characteristics and septic or aseptic TKR revision.

Results: We identified 607,798 patients who underwent primary TKR. Mean (SD) age was 67 (10) years, 63% were female and 8.9% were black. Compared to whites, blacks were younger, more likely to be female, to have diabetes, obesity, renal disease and inflammatory arthritis, to have experienced a surgical complication during the index TKR, and to have Medicaid insurance ($p< 0.001$ for all). Median [IQR] duration of surveillance was 5.25 [2.25, 8.75] years. 26,268 (4.3%) of the patients underwent TKR revision, 1.3% septic, 0.1% fracture, 2.6% mechanical ("aseptic") and

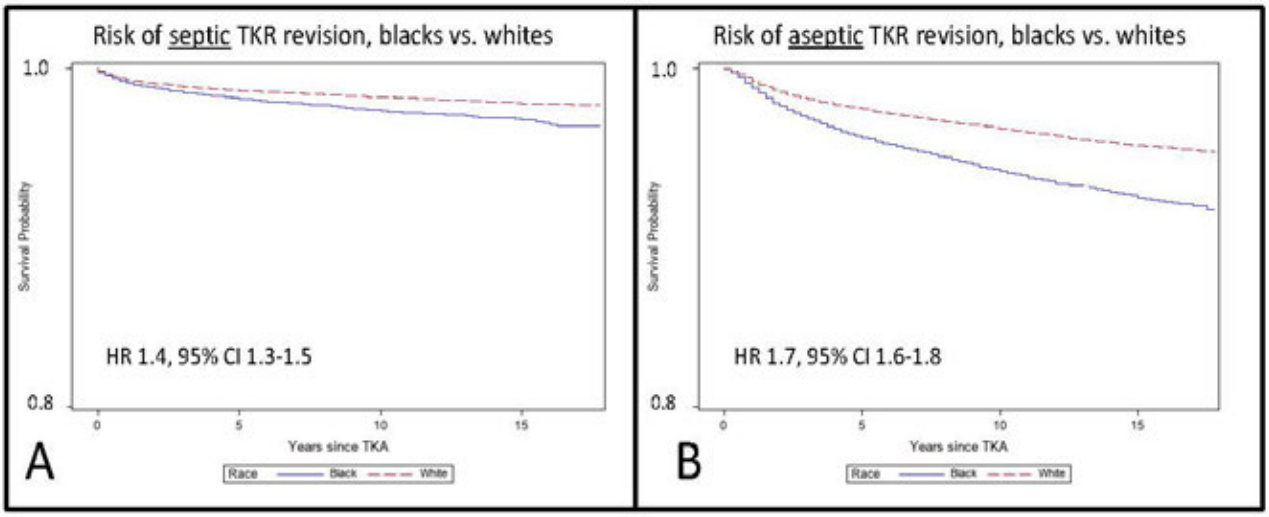

Figure 1. Kaplan-Meier survival analysis of septic and aseptic TKR revision risk, blacks vs. whites

Table 1. Cox proportional hazards models for risk of septic and aseptic TKR revision

	Septic TKR revision		Aseptic TKR revision	
Variable	**Hazard Ratio (95%CI)**	**p-value**	**Hazard Ratio (95%CI)**	**p-value**
Age (5 years)	0.8 (0.8-0.9)	<.0001	0.8 (0.8-0.8)	<.0001
Male	1.6 (1.5-1.6)	<.0001	1.0 (1.0-1.1)	0.3376
Black	1.2 (1.1-1.3)	<.0001	1.3 (1.3-1.4)	<.0001
State				
New York	reference		reference	
Arkansas	0.7 (0.7-0.8)	<.0001	1.0 (0.9-1.1)	0.9435
Arizona	0.7 (0.6-0.8)	<.0001	0.7 (0.6-0.8)	<.0001
Florida	0.7 (0.7-0.7)	<.0001	1.0 (1.0-1.0)	0.9547
Insurance				
Medicare	reference		reference	
Medicaid	1.3 (1.2-1.5)	<.0001	0.9 (0.8-1.0)	0.0766
Other	0.9 (0.8-1.0)	0.0135	1.3 (1.2-1.4)	<.0001
Private	0.8 (0.7-0.8)	<.0001	0.9 (0.9-1.0)	0.0002
Comorbidities				
Diabetes	1.3 (1.2-1.3)	<.0001	1.0 (1.0-1.0)	0.7244
Obesity	1.2 (1.1-1,3)	<.0001	0.9 (0.8-0.9)	<.0001
Renal Disease	1.5 (1.3-1.7)	<.0001	0.9 (0.8-1.1)	0.2836
COPD	1.2 (1.2-1.3)	<.0001	1.0 (1.0-1.1)	0.4852
Index surgery: diagnosis and complications				
Inflammatory arthritis*	1.5 (1.3-1.6)	<.0001	0.7 (0.7-0.8)	<.0001
Surgical complication**	2.1 (1.7-2.5)	<.0001	1.1 (0.9-1.3)	0.1962

*Rheumatoid arthritis, psoriatic arthritis, spondyloarthropathy

**Hemorrhage or hematoma complicating procedure, wound disruption, retained foreign body

0.3% other. In univariate analysis, the risk of septic revision was higher in blacks than whites, HR 1.4 (95% CI 1.3-1.5) (Figure 1a), as was the risk of aseptic revision, HR 1.7 (95% CI 1.6- 1.8) (Figure 1b). In multivariable models, the increased risk of TKR revision in blacks compared to whites was attenuated, but still present; HR 1.2, 95% CI 1.1-1.3 for septic and HR 1.3, 95% CI 1.3-1.4 for aseptic revision respectively (Table 1). In these models, Medicaid insurance

was a risk factor for septic TKR revision (HR 1.3; 95% CI 1.2-1.5) but not aseptic TKR revision (HR 0.9; 95% CI 0.8-1.0) (Table 1).

Conclusion: Blacks are at higher risk of both septic and aseptic TKR revision than whites. Medicaid insurance, a proxy for poverty, is associated with a higher risk of septic but not aseptic TKR revision. The interaction between race and poverty on the risk of septic TKR warrants study.

[1]Bass, AR et al. Higher Knee Arthroplasty Revision Rates among U.S. Blacks: A Systematic Literature Review and Meta-Analysis J Bone Joint Surg (Am) 2016; 98(24):2103-2108.

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Abstract Number: 1849

Cost-related Prescription Non-adherence Is Associated with Patient-reported Outcomes of Systemic Lupus Erythematosus Activity and Damage: The Michigan Lupus Epidemiology & Surveillance (MILES) Cohort

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Time: 4:30PM–6:00PM

Background/Purpose: Medication access and adherence play key roles in determining outcomes. We investigated whether cost-related non-adherence (CRNA) to prescription medications was associated with worse patient-reported outcomes in a population-based SLE cohort.

Methods: This study utilized baseline data from the Michigan Lupus Epidemiology & Surveillance (MILES) Cohort. We collected detailed clinical, medication, and sociodemographic data through structured interviews and validated questionnaires. We used validated patient-reported outcome measures of SLE activity (Systemic Lupus Activity Questionnaire, SLAQ) and damage (Lupus Damage Index Questionnaire, LDIQ). CRNA was based on questions derived from the National Health Interview Survey and considered positive if participants reported any of the following actions to save money in the last 12 months: skipping doses, taking less medicine, and/or delaying filling prescriptions. We performed multivariable linear regression to examine the associations between CRNA and lupus activity

Table 1. Multivariable regression results for cost-related deviation from taking medication as prescribed and lupus-related activity and damage.

	SLE Activity (SLAQ) β coeff (95% CI)	SLE Damage (LDIQ) β coeff (95% CI)
Cost-related non-adherence (CRNA)	2.7 (1.3, 4.1)***	1.42 (0.5, 2.4)**
Age (years)	0.0 (-0.0, 0.1)	0.00 (-0.0, 0.0)
Female (male referent)	3.1 (0.9, 5.2)**	-0.1 (-1.6, 1.4)
Self-identified race (white referent)		
Black	1.5 (0.3, 2.6)*	1.2 (0.4, 2.0)**
Other/unspecified [a]	4.4 (1.5, 7.2)**	2.9 (1.0, 4.9)**
Health insurance (private referent)		
Medicaid/Medicare	2.3 (1.0, 3.6)**	2.5 (1.6, 3.4)***
None	-2.6 (-6.5, 1.3)	-1.5 (-4.2, 1.2)
Education (<high school referent)		
High School Diploma/GED	-1.8 (-4.3, 0.7)	-1.3 (-3.0, 0.4)
Some College/Associate's	-0.2 (-2.2, 1.8)	-0.7 (-2.1, 0.6)
Bachelor's	-1.2 (-3.5, 1.2)	-0.4 (-2.0, 1.2)
Graduate/Professional	-1.4 (-3.8, 0.9)	-0.4 (-2.1, 1.2)
Unknown	-5.9 (-17.6, 5.8)	-1.4 (-9.4, 6.6)
Income <US median (above referent)	0.7 (-0.68, 2.0)	0.6 (-0.4, 1.5)
Unknown income	0.1 (-2.7, 2.8)	-0.9 (-2.7, 1.0)
PROMIS-Depression	0.1 (-0.0, 0.1)	0.4 (-0.0, 0.1)
PROMIS-Anxiety	0.1 (0.0, 0.2)	-0.0 (-0.1, 0.0)
FM survey criteria positive	6.8 (5.6, 8.0)***	2.5 (1.6, 3.3)***
SLE duration (years)	-0.1 (-0.1, 0.1)	0.1 (-3.1, 3.8)

*p<0.05, **p<0.01 ***p=<0.001
[a] Other/unspecified races include: AIAN (n=6); Asian (n=4); other/unknown (n=11)
Abbreviations: SLAQ=Systemic Lupus Activity Questionnaire; LDIQ=Lupus Damage Index Questionnaire; PROMIS=Patient-Reported Outcomes Measurement Information System; FM=fibromyalgia

and damage, adjusted for the following covariates: age, sex, race, health insurance type, education levels, household income below the US median, PROMIS-Depression, PROMIS-Anxiety, fulfillment of fibromyalgia survey criteria, and SLE duration.

Results: 462 SLE participants completed the study visit: 430 (93.1%) female, 208 (45%) black, and mean age 53.3 years. Of the 462 SLE cases, CRNA was reported by 100 (21.7%) for the preceding 12 months. Based on multivariable models, CRNA was associated with both higher levels of SLE activity and damage scores, after adjustment for covariates (Table 1): those reporting CRNA had SLAQ scores that were on average 2.7 points higher compared those not reporting deviation [β coeff 2.7 (95% CI 1.3, 4.1), p< 0.001] and LDIQ scores that were 1.4 points higher [β coeff 1.4 (95% CI 0.5, 2.4), p=0.003]. Non-white race, having Medicaid/Medicare (compared to private insurance), and fulfilling FM survey criteria were also associated with both higher SLAQ and LDIQ scores; female sex was further associated with higher SLAQ scores (Table 1).

Conclusion: SLE patients with CRNA in the last 12 months had higher disease activity and damage scores. Asking patients about financial barriers, using tools such as motivational interviewing to discuss medication adherence, and incorporating cost-related factors in shared decision making are likely meaningful avenues for improving patient outcomes.

Disclosure: D. Minhas, None; **W. Marder**, None; **S. Harlow**, None; **H. Saltzman**, None; **A. Hassett**, None; **S. Zick**, None; **L. Wang**, None; **K. Barbour**, None; **C. Helmick**, None; **C. Gordon**, Bristol-Myers Squibb, 5, 8, Centers for Disease Control and Prevention, 5, Eli Lilly, 5, 8, EMD Serono, 5, EMD Serono, UCB, 5, GlaxoSmithKline, 5, 8, Merck Serono, 5, 8, UCB, 2, 5, 8, Versus Arthritis/GSK, 2; **W. McCune**, None; **E. Somers**, None.

Abstract Number: 1850

Needs Assessment of Rheumatology Fellowship Program Directors on the Need for a Health Disparities Curriculum for Our Fellowship Programs

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SESSION INFORMATION
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Background/Purpose: Health disparities (HD) are pervasive in all fields of medicine including rheumatology. Low income patients as well as patients from racial and ethnic minority groups are disproportionately affected by the rheumatic diseases and have increased mortality. We previously conducted a needs assessment of rheumatology fellows that showed that while they felt the impact of the social determinants of the health on the well-being of their patients, they did not feel adequately trained to address these issues. Because of these findings, we now report a needs assessment of rheumatology fellowship program directors (PDs) to evaluate their views on the creation of a HD curriculum and to elucidate potential barriers to implementation.

Methods: We conducted an anonymous, survey-based study of rheumatology fellowship PDs at the annual PDs conference of the American College of Rheumatology held in March, 2019. Out of 74 unique fellowship programs that were registered to attend the conference, 49 completed the survey -- most from the Northeast (n=17) or Southeast (n=10). Our survey was modified from the 2016 survey that Cardinal et al. administered to internal medicine program directors assessing graduate medical education in disparities.

Results: 73% of the PDs reported that ≥ 10% of their fellows' patients are of limited English proficiency (LEP). 51% reported that ≥ 25% of patients were ≤ the US poverty level. At least 25% of the fellows' patients were from racial and ethnic minorities in 69% of programs and ≥50% in 39% of programs.

Overall 15 programs (30%) provided no training in cultural competency (CC), recognizing or addressing health disparities, or addressing health literacy in patients. Despite 51% of programs reporting that they train fellows to recognize (HD) in their populations, 71% give no training on how to address these HD. With regards to the care of LEP patients, 69% provided no training in how to care LEP patients, 75% offered no formal interpreter training, though interpreter services were widely available. In addition, 46% of PDs were neutral or disagreed with the statement that fellows had had prior training in HD and CC prior to fellowship, and 37% were unsure.

Barriers to the implementation of a curriculum that addresses CC, HD and LEP were:

- 78% of PD were neutral/disagreed that their faculty could assess their fellows providing CC care
- 88% were neutral/disagreed that they had the tools to assess fellows providing CC care

- 57% reported a lack of time in the curriculum
- 51% reported a lack of institutional resources

Conclusion: Our needs assessment of PDs shows that few programs are addressing HD and the social determinants of health despite the fact that HD are prevalent in rheumatology, and the fellows are caring for significant numbers of patients that are directly impacted by these disparities. While issues such as time and resources are commonly cited for many new initiatives, it is important to note that PDs feel that there is a paucity of faculty that can help address these issues. We, as a specialty, will need a two-pronged approach to implement a HD rheumatology curriculum, given we will have to train the faculty so that they can develop their skills in order to impart this education onto our trainees.

Disclosure: I. Blanco, None; **N. Barjaktarovic**, None; **C. Gonzalez**, None.

Abstract Number: 1851

The Association of Discrimination and Stress on Cardiovascular Disease in a Population-Based Cohort with Systemic Lupus Erythematosus

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Background/Purpose: African Americans (AA) are more likely to experience psychosocial and environmental stressors and develop SLE than whites. Increasing frequency of racial discrimination is associated with greater damage in SLE. Cardiovascular disease (CVD) is a leading cause of SLE morbidity and mortality. However, the increased CVD risk is not completely attributable to SLE activity and traditional CVD risk factors. We examined whether discrimination affects CVD risk after taking stress into account in patients with SLE.

Methods: The Georgians Organized Against Lupus (GOAL) is a population-based cohort of validated SLE patients in Atlanta derived from the Centers for Disease Control and Prevention supported Georgia Lupus Registry who consent to complete annual surveys across multiple domains. We analyzed 2 validated measures of psychosocial stress, Perceived Stress Scale (PSS) and Everyday Discrimination Scale (EDS), in the 2017 survey. Potential CVD events (ever) through 2016 were identified by patient report and by Georgia Hospital Discharge Database CVD-related codes. Medical records were reviewed by study physicians. CVD events (myocardial infarction, angina, transient ischemic attack, stroke, and/or peripheral vascular disease) were adjudicated using validated algorithms. Logistic regression was used to separately explore the association between PSS and CVD and EDS and CVD in univariate and multivariate analyses.

Results: The 2017 GOAL survey was comprised of 780 patients, of whom 621 (79.6%) were AA, 110 (14.1%) were white, and 49 (6.3%) from other racial/ethnic groups. A total of 179 (23%) patients were adjudicated as having had CVD. AA's had more CVD (24.8% vs. 15.7%, p=0.015), reported higher EDS score (1.8 vs 1.6, P=0.0002), but no difference in PSS level (6.4 vs 6.4, p=0.89) compared with non-AA's (Table 1). Multivariate logistic regression analysis demonstrated a significant association between both EDS and PSS with CVD after controlling for race; age; gender; SLE activity, dam-

Table 1. Descriptive Characteristics of the Georgians Organized Against Lupus Cohort, 2017

Characteristic	Overall	African American*	Non-African American*	P-Value*
	n=780	n=621	n=159	
Sociodemographics				
sex				
male, n (%)	53 (6.8)	42 (6.8)	11 (6.9)	0.94
female, n (%)	727 (93.2)	579 (93.2)	148 (93.1)	
marital status				
married, n (%)	247 (31.7)	155 (25)	92 (57.9)	**<0.0001**
not married, n (%)	533 (68.3)	466 (75)	67 (42.1)	
educational attainment, years (mean±SD)	14.5±3.0	14.2±2.9	15.6±3.3	**<0.0001**
below Federal poverty level, n (%)	303 (38.9)	279 (44.9)	24 (15.1)	**<0.0001**
Disease characteristics				
age at diagnosis, years (mean±SD)	32.6±12.1	32.6±117	32.7±13.5	0.92
disease duration. Years (mean±SD)	15.6±10.0	15.7±10.0	15.4±9.7	0.79
disease activity, SLAQ (mean±SD)	15.2±8.6	15.4±8.5	14.4±9.2	0.22
disease damage, SA-BILD				
none (score=0), n (%)	144 (18.5)	103 (16.6)	41 (25.8)	0.03
mild (score=1-2), n (%)	311 (40.0)	253 (40.9)	58 (36.5)	
severe (score≥3), n (%)	323 (41.5)	263 (42.5)	60 (37.7)	
on medications for				
cholesterol, n (%)	172 (22.8)	141 (23.4)	31 (21.3)	0.41
diabetes, n (%)	50 (6.6)	41 (6.8)	9 (5.8)	0.65
hypertension, n (%)	448 (58.0)	393 (64.0)	55 (34.8)	**<0.0001**
Adjudicated CVD				
yes, n (%)	179 (23)	154 (24.8)	25 (15.7)	**0.015**
no, n (%)	601 (77)	467 (75.2)	134 (84.3)	
Stress and Discrimination				
Perceived Stress Scale (mean±SD)	6.4±3.2	6.4±3.2	6.4±3.3	0.89
Everyday Discrimination Scale (mean±SD)	1.8±0.6	1.8±0.6	1.6±0.6	**0.0002**

SD=standard deviation, n=number, CVD=cardiovascular disease (myocardial infarction, angina, transient ischemic attack, stroke, and/or peripheral vascular disease). SLAQ=Systemic Lupus Activity Questionnaire, SA-BILD=Self-Administered version of the Brief Index of Lupus Damage

Table 2: Association of Cardiovascular Disease Risk with Selected Variables

Selected Variable	Univariate		Multivariate*	
	OR (95%)	P	OR (95% CI)	P value
Discrimination (per unit↑)	1.44 (1.10-1.87)	**0.0072**	1.43 (1.05-1.94)	**0.025**
Stress (per unit↑)	1.12 (1.06-1.18)	**<.0001**	1.16 (1.08-1.24)	**<0.0001**
Age at survey (per year↑)	1.03 (1.02-1.05)	**<.0001**	1.02 (1.01-1.04)	**0.013**
Disease duration (per year↑)	1.04 (1.02-1.06)	**<.0001**	1.02 (1.00-1.04)	0.055
Race (black vs. white)	1.58 (0.93-2.67)	0.089	1.52 (0.79-2.90)	0.21
Gender (female vs male)	0.58 (0.31-1.06)	0.078	0.50 (0.24-1.03)	0.06
Education (per year ↑)	0.92 (0.86-0.97)	**0.005**	0.97 (0.90-1.04)	0.42
Poverty	1.57 (1.11-2.21)	**0.011**	1.32 (0.84-2.07)	0.22
Disease activity (per unit↑)	1.04 (1.02-1.06)	**<.0001**	1.02 (0.99-1.04)	0.22
Organ damage Mild damage (vs. no damage)	2.02 (1.01-4.04)	**0.046**	1.24 (0.60-2.58)	0.12
Severe damage (vs. no damage)	6.37 (3.29-12.32)	**<.0001**	3.35 (1.64-6.87)	**<0.0001**
Taking medication for cholesterol	3.31 (2.28-4.82)	**<.0001**	2.37 (1.50-3.73)	**0.0002**
Taking medication for diabetes	2.62 (1.44-4.74)	**0.0015**	1.28 (0.63-2.60)	0.49
Taking medication for hypertension	1.91 (1.32-2.76)	**0.0006**	1.04 (0.67-1.62)	0.86
Currently smoking	1.79 (1.13-2.83)	**0.013**	1.29 (0.75-2.20)	0.36

Poverty: less than 100% Federal poverty level
*Logistic regression: multivariate model is adjusted by age, gender, race, disease duration, disease severity, education, poverty, currently smoking, and taking medication for high cholesterol, diabetes, or hypertension.

Table 3. Association of Cardiovascular Disease Risk with Discrimination and Stress

Model		Multiple regression*	
		OR (95% CI)	P value
Discrimination (per unit ↑)		1.43 (1.05-1.94)	**0.025**
Stress (per unit ↑)		1.16 (1.08-1.24)	**<0.0001**
Discrimination +	Discrimination (per unit ↑)	1.27 (0.91-1.76)	0.16
Stress	Stress (per unit ↑)	1.15 (1.07-1.23)	**0.0001**

*Adjusted by age, gender, race, disease duration, disease severity, education, poverty, currently smoking, and taking medication for high cholesterol, diabetes, or hypertension.
OR=odds ratio
Discrimination measured by the Everyday Discrimination Scale.
Stress measured by the Perceived Stress Scale.

age, and duration; being on medications for cholesterol, diabetes, and hypertension; currently smoking; and poverty (Table 2). The significance of the association was no longer present after including PSS in the model (Table 3).

Conclusion: Including PSS in the model of discrimination and CVD no longer made the association significant, suggesting the association between discrimination and CVD is principally through high stress levels. High stress is known to contribute to the development of atherosclerosis in the general population. In those with SLE, discrimination may result in greater CVD risk through higher stress rather than a result of being a certain race. In our study, the burden of psychosocial stress was higher in AA's than non-AA's, which may explain, in part, racial disparities in past CVD events along with poorer control of CVD risk factors. Including social determinants of health in the lupus health disparities framework provides a more comprehensive understanding of why low-income communities and communities of color experience poorer outcomes. Further research into related causal pathways, mitigating factors, and biologic mechanisms is also needed.

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Abstract Number: 1852

Community-level Deprivation Index: Impact on Discharge Destination After Elective Hip Replacement

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Background/Purpose: With the aging of the world population and the rising prevalence of Hip Osteoarthritis (OA), elective total hip arthroplasty (THA) has become one of the fastest growing procedures in the management of end-stage OA. Medicare, the largest payer in the US of joint replacement surgery, has introduced several payment reform models that target discharge destination and risk of readmission. In additional to clinical factors, social factors such as where one lives that might impact where patients go for post-op care and rehab following elective total hip replacement surgery.We sought to examine how the socioeconomic status of the community in which one lives influences discharge disposition and the odds of 90-day readmission after elective THA.

Methods: We used the Pennsylvania Health Care Cost Containment Council (PHC4) database to identify all patients who underwent elective THA between 2012 and 2016. We also derived Community level Area Deprivation Index

Table 1. Baseline characteristics and outcomes by Area Deprivation Index (ADI) and age group (N = 84 931).

Variable [a]	Years < 65 (N = 40 304)				Years ≥ 65 (N = 44 627)			
	Low ADI N = 14 681	Middle N = 18 741	High ADI N = 6882	p [b]	Low ADI N = 17 452	Middle N = 21 001	High ADI N = 6174	p [b]
Sex: Female	6808 (46.4)	8867 (47.3)	3295 (47.9)		10 568 (60.6)	12 928 (61.6)	3981 (64.5)	***
Race:								
White	14 126 (96.2)	17 341 (92.5)	4917 (71.4)	***	17 082 (97.9)	20 290 (96.6)	5223 (84.6)	***
African American	555 (3.78)	1400 (7.47)	1965 (28.6)		370 (2.12)	711 (3.39)	951 (15.4)	
Discharge Destination:								
Home or HH	13 230 (90.1)	16 308 (87.0)	5340 (77.6)	***	11 253 (64.5)	12 886 (61.4)	3446 (55.8)	***
Institution	1451 (9.88)	2433 (13.0)	1542 (22.4)		6199 (35.5)	8115 (38.6)	2728 (44.2)	
Insurance:								
Unknown/Uninsured	130 (0.89)	193 (1.03)	43 (0.62)	***	96 (0.55)	109 (0.52)	20 (0.32)	***
Medicare	1057 (7.20)	2332 (12.4)	1278 (18.6)		15 026 (86.1)	18 643 (88.8)	5550 (89.9)	
Medicaid	698 (4.75)	1696 (9.05)	1463 (21.3)		18 (0.10)	38 (0.18)	37 (0.60)	
Commercial	12 638 (86.1)	14 299 (76.3)	4036 (58.6)		2292 (13.1)	2168 (10.3)	552 (8.94)	
Government	158 (1.08)	221 (1.18)	62 (0.90)		20 (0.11)	43 (0.20)	15 (0.24)	
Metro area: Metro	14 662 (99.9)	17 469 (93.2)	6004 (87.2)	***	17 424 (99.8)	19 253 (91.7)	5125 (83.0)	***
Volume of cases (by facility and year):								
< 100/year	1735 (11.8)	3113 (16.6)	1460 (21.2)	***	2122 (12.2)	3954 (18.8)	1356 (22.0)	***
100 - 199/year	3570 (24.3)	4372 (23.3)	1832 (26.6)		4865 (27.9)	5199 (24.8)	1888 (30.6)	
200+/year	9376 (63.9)	11 256 (60.1)	3590 (52.2)		10 465 (60.0)	11 848 (56.4)	2930 (47.5)	
90-day readmission	1038 (7.07)	1641 (8.76)	743 (10.8)		1922 (11.0)	2443 (11.6)	821 (13.3)	
Elixhauser Index [c]:								
0	2820 (19.2)	3295 (17.6)	1109 (16.1)	***	3172 (18.2)	3428 (16.3)	1029 (16.7)	***
1-4	10 914 (74.3)	14 247 (76.0)	5346 (77.7)		13 230 (75.8)	16 224 (77.3)	4757 (77.0)	
≥ 5	947 (6.45)	1199 (6.40)	427 (6.20)		1050 (6.02)	1349 (6.42)	388 (6.28)	
Postoperative myocardial infarction	7 (0.05)	9 (0.05)	4 (0.06)		40 (0.23)	62 (0.30)	18 (0.29)	
Posthetic device complication	22 (0.15)	28 (0.15)	18 (0.26)		36 (0.21)	42 (0.20)	16 (0.26)	
Surgical wound infection	7 (0.05)	9 (0.05)	2 (0.03)		9 (0.05)	3 (0.01)	1 (0.02)	
Venous thromboembolism	6 (0.04)	3 (0.02)	3 (0.04)		22 (0.13)	29 (0.14)	11 (0.18)	

[a] Data are presented as n(%).

[b] Variables are compared by ADI for each age group (years < 65, ≥ 65) using Pearson χ2 test or fisher's exact test, as appropriate. Significance levels: * = p<0.05, ** = p<0.01, *** = p<0.001.

[c] Clinical comorbidities were identified based on coding algorithms developed by Quan and colleagues (enhanced Elixhauser version), using either the ICD-9-CM or the ICD 10 coding system, as appropriate. The Elixhauser co-morbidity index score is calculated based on the cumulative number of comorbidity conditions.

a Data are presented as n(%). b Variables are compared by ADI for each age group (years < 65, ≥ 65) using Pearson χ2 test or fisher's exact test, as appropriate. Significance levels: * = p<0.05, ** = p<0.01, *** = p<0.001. c Clinical comorbidities were identified based on coding algorithms developed by Quan and colleagues (enhanced Elixhauser version), using either the ICD-9-CM or the ICD 10 coding system, as appropriate. The Elixhauser co-morbidity index score is calculated based on the cumulative number of comorbidity conditions.

(ADI) from the American Census Survey. We used binary logistic regression models to test the association between community ADI and the discharge outcome of Institution vs. Home. We also modeled the risk of 90-day readmission for patients sent to an institution compared to home for post-op care and rehab. We adjusted for important clinical, demographic, and facility level covariates. To evaluate whether patient race affects this relationship, we included into the models an interaction term for community ADI and patient race.

Results: Our analytic sample consisted of 84, 931 who underwent THA between 2012 and 2016 within the State of Pennsylvania. The study sample is stratified by < 65 (n = 40, 304) and ≥ 65 (n = 44, 627) years of age groups. In the years < 65 group, 17.1 % came from high ADI communities (above Q3), 46.5% from middle strata ADI (within Q2 and Q3) and 36.4% from low ADI communities (below Q2). The distribution for high, middle, and low ADI among patients ≥ 65 years of age were 13.8%, 47.1%, and 39.1%, respectively. Compared to low ADI community patients, patients from high ADI communities were more likely to be discharged to an institution compared to home ($p < 0.001$ in both age groups), after controlling for patient and facility level characteristics. The interaction effect of race and ADI on discharge destination was statistically significant in those ≥ 65 years of age ($p < 0.05$), but not in patients < 65 years. The association of ADI on 90-day readmission was not statistically significant. The interaction of ADI and race on 90-day readmission was also not statistically significant.

Figure 1. Pennsylvania zipcode level area deprivation index (ADI) with individual THA patient discharge status.

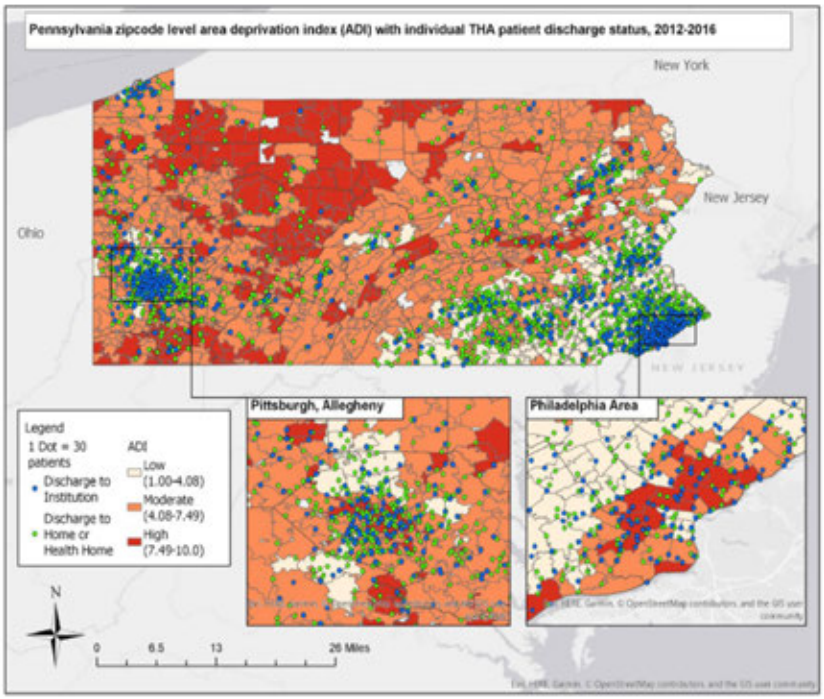
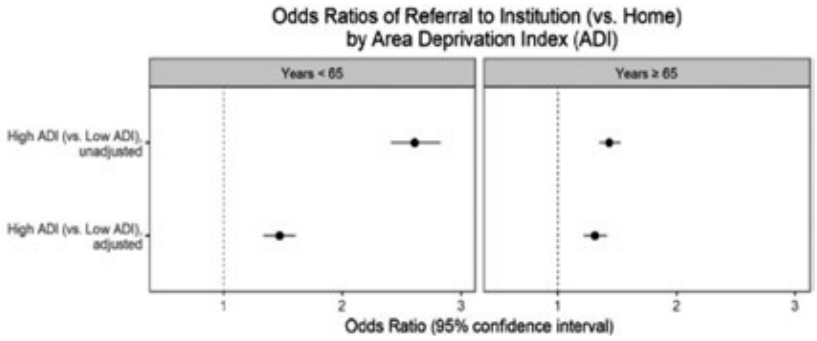


Figure 2. Odds ratio of referral to Institution for patients living in high area deprivation index (ADI) zipcode areas vs. low ADI areas.



Conclusion: In this large sample of patients who underwent THA in the State of Pennsylvania, the level of deprivation of the community in the patient resides influences where patients go for post-op care and rehab after elective THA disposition.

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Racial Differences in Highly Effective Contraceptive Use Among Medicaid Beneficiaries with SLE

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Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Highly effective contraception (HEC), which includes intrauterine devices, implants and sterilization, is safe for women with SLE and has a < 1% failure rate for preventing pregnancy. Prior studies have revealed low rates of contraceptive use among reproductive age women with SLE despite periods of high disease activity and frequent teratogenic medication use. Black and Hispanic women with SLE have higher rates of adverse outcomes, including pregnancy complications, compared to white women with SLE. Using U.S. nationwide data, we aimed to examine whether there are racial/ethnic differences in contraception use, and specifically HEC, among women with SLE.

Methods: Using Medicaid claims data from 2000-2010, we identified reproductive age women (18-50 years) with prevalent SLE (3 ICD-9 codes 710.0 separated by ≥30 days). We required 6 months of continuous enrollment prior to the 3rd SLE code (baseline) and 24 months of continuous enrollment after (follow-up). We excluded women ineligible for new contraceptive use (baseline codes for HEC, hysterectomy, or menopause). We examined uptake of contraception by race during follow-up. We used multivariable logistic regression adjusted for age, calendar year, region, and the SLE risk adjustment index (proxy for SLE severity), to estimate the odds (OR, 95% CI) by race/ethnicity of: A) any encounter for contraceptive management (vs. none), B) any contraception (vs. none), C) HEC (vs. no HEC), and D) HEC (vs. no HEC) in a subset with ≥1 teratogenic medication prescription during the baseline period. We also conducted sensitivity analyses excluding women with pregnancy codes.

Results: We identified 28,662 female Medicaid beneficiaries with SLE. The mean (SD) age was 36; 44% were black, 34% white, 15% Hispanic, 4% Asian, and 1% American Indian/Alaska Native. 15% had an encounter for contracep-

Figure. Racial/Ethnic Distributions of Contraceptive Methods and Encounters Over 24 Months Among Reproductive Age Female Medicaid Beneficiaries with SLE (N=28,662)

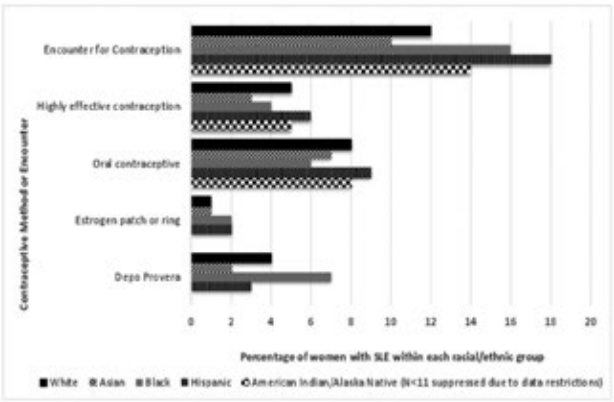

Table. Multivariable Logistic Regression Analyses Examining Factors Associated with Contraception Use Among Female Medicaid Beneficiaries with SLE, Aged 18-50 Years (N=28,662)

Race	A) Encounter for contraception# OR (95% CI)	B) Any Contraception use* OR (95% CI)	C) Highly Effective Contraception (HEC) Use OR (95% CI)	D) HEC Use in Setting of Teratogen** OR (95% CI)
White	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Asian	**0.65 (0.52-0.81)**	**0.59 (0.48-0.73)**	**0.54 (0.36-0.79)**	0.72 (0.28-1.89)
Black	**1.23 (1.13-1.34)**	**0.89 (0.82-0.96)**	**0.72 (0.63-0.82)**	0.89 (0.61-1.31)
Hispanic	**1.33 (1.20-1.48)**	0.91 (0.82-1.01)	1.01 (0.85-1.19)	1.07 (0.67-1.73)
AI/AN	1.30 (0.92-1.83)	0.94 (0.67-1.32)	1.07 (0.63-1.81)	0.67 (0.09-5.03)

Regression model adjusted for age, geographic region, calendar year and the SLE risk adjustment index
#ICD-9 codes of V25 ("Encounter for contraceptive management")
*Any contraception use includes sterilization, intrauterine devices, implants, oral contraceptives, estrogen patch, estrogen ring, and Depo Provera. Data on use of barrier methods was not available.
**Subpopulation (N=4,387) on methotrexate, mycophenolate mofetil, mycophenolic acid, cyclophosphamide, leflunomide, or warfarin

tive management, 16% received any form of contraception, and 5% received HEC (**Figure**). Among 4,387 women using a teratogenic medication, 4% received HEC. In multivariable models, compared to white women, despite 1.23 (95% CI 1.13-1.34) times higher odds of a contraceptive visit, black women had 0.72 (95% CI 0.63-0.82) times lower odds of HEC use. Asian women had significantly lower odds of both contraceptive visits and HEC use (**Table**). Younger age and living in the Midwest and South were associated with higher odds of HEC receipt; more severe SLE was associated with lower odds. Trends demonstrated significantly increased HEC uptake over time for white women, but not for other racial/ethnic groups. Findings were similar when women with pregnancy codes were excluded.

Conclusion: In this nationwide study of reproductive age women with SLE, HEC uptake was very low, even among women receiving teratogenic medications. Despite more encounters for contraception, black women had lower odds of HEC uptake; Asian women had fewer encounters and lower odds of HEC. With known disparities in pregnancy outcomes by race/ethnicity, further study is needed to understand whether racial/ethnic differences in HEC use among women with SLE are due to provider bias, patient preference, cultural factors, or variable access to reproductive counseling and care.

Disclosure: J. Williams, None; **C. Xu**, None; **K. Costenbader**, Astra-Zeneca, 2, Glaxo Smith Kline, 2, Janssen Scientific Affairs, LLC, 2, Lupus Foundation of America, 2, Lupus Research Alliance, 2, Merck, 2; **B. Bermas**, None; **L. Pace**, None; **C. Feldman**, None.

Abstract Number: 1854

The Utility of Fat Lesions in Close Relation to Other Structural MRI Lesions in the Sacroiliac Joints for Diagnosing Patients with Axial Spondyloarthritis

Sengül Seven ,[1] Mikkel Østergaard,[2] Lone Morsel-Carlsen,[3] inge Juul Sørensen,[1] Birthe Bonde,[4] Gorm Thamsborg,[5] Jens Jørgen Lykkegaard,[1] Oliver Hendricks,[6] Niklas Rye Jørgensen,[7] and Susanne Juhl Pedersen[8], [1]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark, Glostrup, Denmark, [2]Copenhagen Center for Arthritis Research, University of Copenhagen, Copenhagen, Denmark, [3]Department of Radiology, Rigshospitalet, Glostrup, Denmark, Glostrup, Denmark, [4]The Birthe Bonde Clinic of Physioterapy, Copenhagen, Denmark, Glostrup, Denmark, [5]Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark, Copenhagen, Hovedstaden, Denmark, [6]Danish Hospital for Rheumatic Diseases, Sønderborg, Denmark, Sønderborg, Denmark, [7]Department of Clinical Biochemistry, Rigshospitalet, Glostrup, Denmark, Glostrup, Denmark, [8]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark, Copenhagen, Hovedstaden, Denmark

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Imaging of Rheumatic Diseases I

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Bone marrow edema on MRI of the sacroiliac joints (SIJ) plays an important role in the ASAS (Assessment of Spondyloarthritis International Society) classification criteria for axial spondyloarthritis (axSpA). However, these lesions can also be seen in other conditions[1 2]. Structural SIJ MRI lesion characteristics may be of importance for differentiating patients with axSpA from other diagnostic entities with buttock/pelvic pain. The aim of this study was to investigate the diagnostic utility of the presence of fat lesions (FAT) in close relation to the joint space and other structural MRI lesions in order to differentiate patients with axSpA from other conditions.

Methods: This prospective cross-sectional study of 204 participants, included patients with axSpA (n=41), lumbar disc herniation (n=25), and women with postpartum buttock/pelvic pain (n=46) and a group of healthy participants consisting of women without postpartum buttock/pelvic pain (n=14), persons with hard physical work defined as hospital cleaning staff (n=26), long-distance runners (n=23) and healthy men (n=29). Participants with pain should all have VAS pain >2 (0-10) for ≥2 months. Non-axSpA participants were not allowed to have any clinical SpA features or rheumatological conditions. Participants underwent clinical, laboratory and MRI examination (semi-coronal STIR and T1W sequences) of the SIJs. MRIs were evaluated according to the SPARCC MRI definitions of lesions[1 2] by two independent readers. Analyses were based on "concordant reads", i.e. where both readers agreed on presence of the assessed pathology. In nine slices covering the entire cartilaginous compartment, each SIJ was separately assessed for the presence of FAT in relation to joint space (FAT@joint space), erosion (FAT@erosion), sclerosis (FAT@sclerosis) and ankylosis (FAT@ankylosis), respectively. Each of these "relation scores" had a total score range of 0-18 per patient.

Results: Table 1 shows the clinical characteristics of each group and table 2 shows the mean MRI FAT relation scores and the frequency of scores above various cut-off levels for each MRI relation score (concordant reads). FAT@joint space and FAT@sclerosis were seen in most groups, but higher scores were found in the axSpA group. FAT@erosion was almost only, and FAT@ankylosis exclusively, found in the axSpA group. A score above or equal to 1 (cut-

Table 1. Demographic, clinical and biochemical characteristics of the different groups of study participants

Table 1. Demographic, clinical and biochemical characteristics of the different groups of study participants

	AxSpA	Women with postpartum pain	Women without postpartum pain	Disc herniation	Cleaning staff	Long distance runners	Healthy men
Number of participants	41	46	14	25	26	23	29
Age (years)	30.9 (6.4) 30.0 (19; 44)	32.6 (3.3) 32.5 (26; 41) *	33.1 (4.1) 32.5 (27; 41)	35.2 (5.7) 37 (21; 43) **	39.1 (4.6) 39 (28; 45) ***	32.7 (6.2) 32 (22; 43)	30.9 (6.4) 30 (20; 45)
Male sex	26 (63.4)	0 ***	0 ***	11.0 (44.0)	0 ***	18 (78.3)	29 (100) ***
Childbirths, if woman	1.7 (0.8) 2 (0; 2)	1.5 (0.8) 1 (1; 4)	1.9 (0.8) 2 (1; 3)	1.6 (0.9) 2 (0; 3)	2.54 (1.1) 3 (0; 5)	0.5 (1.0) 0 (0; 2)	NA NA
Symptom duration (years)	8.4 (5.6) 8.4 (1.2; 23.8)	1.0 (0.8) (0.3; 6.0) ***	NA	1.0 (0.9) 0.7 (0.2; 3.6) ***	NA	NA	NA
Low back pain VAS (0-10)	3.8 (2.8) 3.7 (0; 10.0)	5.5 (2.4) 6.0 (0; 9.8) **	0.4 (0.7) 0 (0; 1.9) ***	5.5 (2.4) 6.2 (0.3; 9.6) *	0.8 (1.8) 0 (0; 6.8) ***	0.2 (0.5) 0 (0; 1.5) ***	0.1 (0.3) 0 (0; 1.2) ***
HLA-B27 positive	33 (80.5)	5 (10.9) ***	1 (7.1) ***	0 ***	0 ***	1 (4.3) ***	4 (13.8) ***
CRP >3 mg/l	24 (58.5)	8 (17.4) ***	3 (21.4) **	5 (20.0) **	4 (15.4) **	4 (17.4) **	1 (3.4) ***

Cells with 1 row: N (%). Cells with 2 rows: Mean (±SD) in upper row and median (min; max) in lower row.
Mann-Whitney test was applied, and all tests are patients with axSpA compared with the other groups. P<0.05*; p<0.01**; p<0.001***.
CRP: C-Reactive Protein; HLA-B27: Human Leukocyte Antigen-B27; VAS: Visual Analogue scale.

Table 2. FAT relation scores and proportion of participants with a score above a certain level. Results based on concordant reads

Table 2. FAT relation scores and proportion of participants with a score above a certain level. Results based on concordant reads								
		AxSpA	Women with postpartum pain	Women without postpartum pain	Disc herniation	Cleaning staff	Long distance Runners	Healthy men
FAT@	Joint space (0-18)	6.1 (5.3) 5.5 (0; 17.5)	0.3 (1.4) 0 (0; 8.5) ***	0.5 (1.5) 0 (0; 5.5) ***	0.3 (0.8) 0 (0; 3) ***	0 (0) 0 (0; 0) ***	0.5 (1.5) 0 (0; 6) ***	0.8 (2.8) 0 (0; 13) ***
	Sclerosis (0-18)	0.6 (1.2) 0 (0; 5.5)	0.1 (0.3) 0 (0; 1.5) ***	0.1 (0.3) 0 (0; 1)	0 (0) 0 (0; 0) ***	0 (0) 0 (0; 0) ***	0 (0.2) 0 (0; 1) ***	0.1 (0.6) 0 (0; 3) ***
	Erosion (0-18)	1.9 (2.7) 0 (0; 8.0)	0.0 (0.1) 0 (0; 1) ***	0 (0) 0 (0; 0) **	0 (0) 0 (0; 0) ***	0 (0) 0 (0; 0) ***	0 (0) 0 (0; 0) ***	0 (0) 0 (0; 0) ***
	Ankylosis (0-18)	1.7 (3.8) 0 (0; 16)	0 (0) 0 (0; 0) ***	0 (0) 0 (0; 0) *	0 (0) 0 (0; 0) ***	0 (0) 0 (0; 0) ***	0 (0) 0 (0; 0) **	0 (0) 0 (0; 0) ***
FAT@ Joint space	≥1	28 (68.3)	2 (4.3)	1 (7.1)	2 (8.0)	0	1 (4.3)	3 (10.3)
	≥2	25 (61.0)	2 (4.3)	1 (7.1)	2 (8.0)	0	1 (4.3)	2 (6.9)
	≥3	22 (53.7)	2 (4.3)	1 (7.1)	0	0	1 (4.3)	2 (6.9)
	≥4	20 (48.8)	2 (4.3)	1 (7.1)	0	0	1 (4.3)	2 (6.9)
	≥5	18 (43.9)	1 (2.2)	1 (7.1)	0	0	1 (4.3)	2 (6.9)
	≥10	9 (22)	0	0	0	0	0	1 (3.4)
FAT@ Sclerosis	≥1	3 (7.3)	0	1 (7.1)	0	0	0	1 (3.4)
	≥2	3 (7.3)	0	0	0	0	0	1 (3.4)
	≥3	2 (4.9)	0	0	0	0	0	0
FAT@ Erosion	≥1	11 (26.8)	0	0	0	0	0	0
FAT@ ankylosis	≥1	6 (14.6)	0	0	0	0	0	0

Cells with 1 row: Number (%) of patients with a score above a certain level. Cells with 2 rows: Mean (±SD) in upper row and median (min; max) in lower row.
Mann-Whitney test was applied, and all tests are patients with axSpA compared with the other groups. p<0.001***; p<0.01**; p<0.05*.
axSpA: axial spondylcarthritis; FAT: fat lesion; FAT@: fat lesions in relation to

off score ≥1) FAT@joint space was present in nearly all groups, however most frequent in the axSpA group followed by the group of healthy men. FAT@joint space was even present in both groups at high (≥10) cut-off scores. FAT@ sclerosis was present in axSpA, women with postpartum pain and healthy men, however, at higher thresholds, above ≥2, only in axSpA group.

Conclusion: Fat lesions in relation to other structural lesions were rarely recorded in the non-axSpA groups, in contrast to fat lesions in relation to the joint space. Assessment of structural sacroiliac joint lesions in anatomical relation to each other may be useful for differentiating axSpA from other conditions.

Referencer:

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2. Seven et al. annrheumdis-2018-eular.2586
3. Maksymowych et al. AR 2005;53(5):703-9.
4. Maksymowych et al. J Rheumatol. 2015;42(1):79-86.

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Abstract Number: 1855

Evaluating the OMERACT Definitions of Ultrasound Gout Structural Lesions in the Diagnosis of Gout

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging of Rheumatic Diseases I
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: To evaluate ultrasound (US) as a diagnostic tool for gout with positive urate crystal microscopy as the gold standard, using the OMERACT US working group definitions for crystal deposits.

Methods: US examinations (28 joints, 26 tendons) were performed in patients with clinically suspected gout. Joints (metacarpophalangeal, wrist, elbow, metatarsophalangeal, tibiotalar and knee joints) and tendons (extensor tendons of the wrist (scored as compartments (1-6)), triceps, quadriceps, patella, peroneus (longus and brevis scored as one), tibialis posterior and Achilles) were evaluated for the OMERACT gout structural lesions (double contour (DC), tophus, aggregates and erosions). Each of the structural lesions were registered as present/absent for each patient. The US assessment was compared to the gold standard reference for gout: presence/absence of monosodium-urate (MSU) crystals at joint fluid microscopy. The microscopies were performed by a rheumatologist blinded to US findings.

The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of each US lesion, with microscopy as gold standard, were evaluated.

Results: 82 patients (70 males, 12 females), mean age of 61 years (19-88) were included. 57 had a positive microscopy for MSU crystals, 23 patients had a negative microscopy and in 2 patients joint aspiration was not possible (table 1).

All four structural lesions were statistically significant more frequent in patients with positive MSU microscopy compared to patients with negative microscopy (Fisher's exact test with p-values from < 0.0001 to 0.0049), and all lesions

Table 1: Ultrasound findings in patients with suspected gout

		Microscopy gold standard reference No. 82							
			Microscopy positive	Microscopy negative/not done	Sensitivity	Specificity	PPV	NPV	Fisher's Exact Test
Ultrasound lesions		No.	57	25					P-values
Double contour	Present	49	46	3	0.81	0.88	0.94	0.67	<0.0001
	Absent	33	11	22					
Tophus	Present	47	45	2	0.79	0.92	0.96	0.66	<0.0001
	Absent	35	12	23					
Aggregates	Present	69	54	15	0.95	0.40	0.78	0.77	0.0002
	Absent	13	3	10					
Erosions	Present	55	44	11	0.77	0.56	0.80	0.52	0.0049
	Absent	27	13	14					

were found to have high sensitivities for gout (ranges from 0.77-0.95). DC and tophus showed high specificities for patients with microscopically verified gout (0.88 and 0.92, respectively) and were also found to have high PPV (0.94 and 0.96, respectively). Low specificities were found for both aggregates and erosions (0.40 and 0.56). Negative predictive values were low to moderate for all lesions (ranges from 0.52-0.77).

Conclusion: The OMERACT set of US definitions of structural gout lesions seems to be a valid tool for diagnosis of gout in clinical practice. Particularly, DC and tophi seem to have a high specificity and high PPV for the disease, when joint fluid microscopy is considered as gold standard.

Disclosure: S. Christiansen, None; **M. Østergaard**, AbbVie, 2, 8, 9, Abbvie, 2, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, UCB, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, 5, 8, Abbvie, Celgene, Centocor, Merck, and Novartis, 2, Abbvie, Celgene, Centocor, Merck, Novartis, 2, BMS, 2, 5, 8, 9, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8; **O. Slot**, None; **L. Terslev**, None.

Abstract Number: 1856

Tenosynovial Aspiration by Ultrasound Guidance: Correlation and Diagnostic Implications of Tenosynovial Analysis and Ultrasound Doppler Signal

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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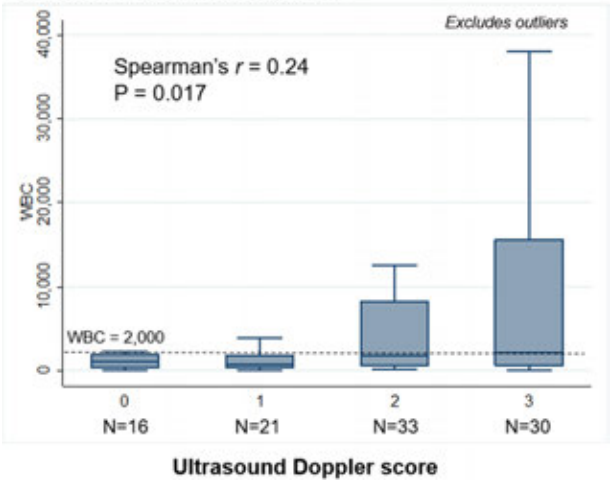
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Rheumatologists commonly use synovial fluid analysis and, more recently, US to establish a diagnosis in patients with joint effusions. Although tenosynovial (TS) effusions are common in rheumatic conditions, there is no guide on how to interpret the cell count of the fluid aspirated from tendon sheaths or how they correlate with US Doppler signal (DS). A multi-center collaboration was organized to prospectively analyze and correlate TS aspirate findings with US DS.

Methods: Patients with TS aspiration planned as part of routine care were enrolled. Tendon location, clinical diagnosis, synovial fluid analysis and Doppler US images were recorded. Doppler settings were standardized across sites and DS grading was performed blindly by 3 expert rheumatologists based on previously published methodology on a

Figure 1A. Correlation of Fluid WBC and Ultrasound Doppler Score in Tenosynovium

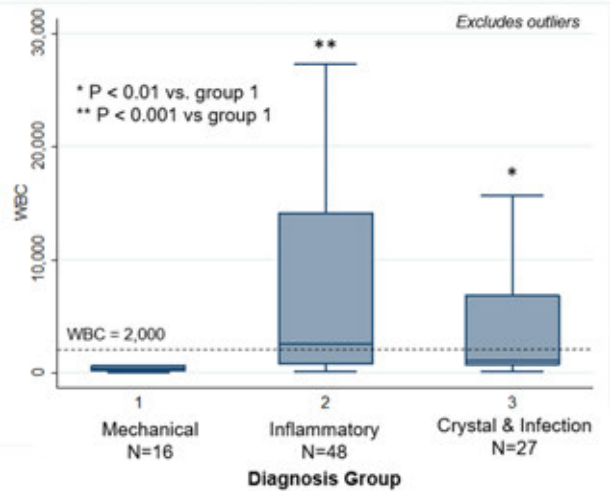


Correlation of tenosynovial fluid WBC count and ultrasound Doppler score in the tenosynovium

0-3 semiquantitative scale. Clinical diagnoses were categorized as non-inflammatory (group 1), inflammatory (group 2), or crystal/infection (group 3) related conditions. Inter-rater reliability was assessed using weighted kappa. Spearman's correlations of median DS with white blood cell (WBC) counts were determined. WBC counts and DS were compared between diagnostic groups using Kruskal-Wallis tests and logistic regression. Sensitivity and specificity calculations were used to discriminate between inflammatory and non-inflammatory conditions by WBC count or DS.

Results: 100 subjects with successful aspirations were enrolled at 14 participating sites. Subjects were primarily female (65%) and middle aged (mean 62 years). DS inter-rater reliability was substantial (kappa 0.74, 95% confidence interval 0.65-0.83). Fluid WBC count and DS correlated weakly (Figure 1A), and WBC counts were higher among diagnostic groups 2 and 3 (Figure 1B). There was substantial variability of TS WBC counts within diagnostic groups (ranges for groups 1, 2, and 3 were 4-7,734; 78-147,560; and 130-50,000 cells/μL respectively). Neither group 2 or 3 were significantly associated with higher DS, but notably, group 2 had only 3 (6%) subjects with a DS of 0. A DS of >1 had a sensitivity of 93.8% and specificity of 31.3% and a WBC count of >2000 cells/μL had a sensitivity of 58.3%

Figure 1B. Comparison of Tenosynovial Fluid WBC between Diagnosis Groups



Comparison of tenosynovial fluid WBC count between diagnosis groups

and specificity of 87.5% for discriminating group 2 vs. group 1. TS fluid WBC counts < 2000 cells/μL were observed in 41.7% of subjects with an inflammatory condition diagnosis (group 2). Crystals were observed in 22% of TS aspirates (CPPD 16% and monosodium urate 6 %).

Conclusion: DS and TS fluid WBC counts provide complementary information when evaluating TS effusions. DS may improve the sensitivity of detecting inflammatory tenosynovitis because TS fluid WBC counts from inflammatory arthritis are frequently in the range that would be considered non-inflammatory based on synovial fluid criteria for joints. While a negative DS strongly predicts a non-inflammatory condition, a positive DS is non-specific and should prompt aspiration for fluid analysis when possible. A TS fluid WBC count ≥2,000 cells/μL is highly specific for an inflammatory cause. TS fluid can also be used to identify crystal arthropathies.

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Abstract Number: 1857

High-resolution MRI Assessment of Flexor Tendon Pulleys in Psoriatic Arthritis for Disease Monitoring and Differentiation from Rheumatoid Arthritis Using a 16-channel Hand Coil

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging of Rheumatic Diseases I
Session Type: ACR Abstract Session
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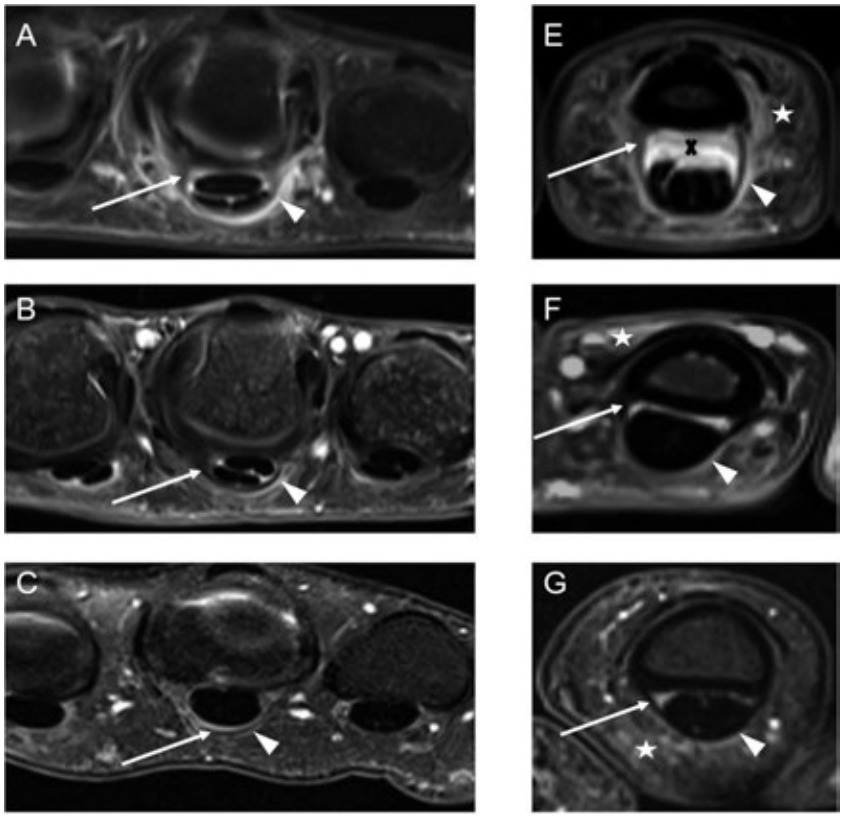
Background/Purpose: To evaluate the value of 3 Tesla (T) magnetic resonance imaging (MRI) changes of flexor tendon pulleys for the differentiation of psoriatic (PsA) and rheumatoid arthritis (RA), as well as for potential disease detection and monitoring.

Methods: A total of 17 patients with active PsA, 20 patients with active RA and 16 healthy controls (HC) were evaluated by high-resolution 3T MRI using a dedicated 16-channel hand coil. Images were analyzed by three independent readers for the degree of inflammatory changes, the thickness of flexor tendon pulleys and comparison to the outcome measures for RA clinical trials (OMERACT) PsA MRI score (PsAMRIS) and to its sub-scores: synovitis, flexor tenosynovitis, bone edema, bone erosion, periarticular inflammation and bone proliferation.

Results: Flexor tendon pulleys were thicker in PsA than in RA patients (mean difference 0.16 mm, p< 0.001) and HC (mean difference 0.2 mm, p< 0.001) and showed a higher degree of associated inflammatory changes (mean difference RA: 4.7, p=0.048; mean difference HC: 14.65, p< 0.001). Additionally, there was a strong correlation of



Transversal fat-saturated T1w images after iv contrast administration. A1 (A-C) and A2 (E-G) flexor tendon pulleys of D3 in PsA (A & E) and RA (B & F) patients and in HC (C & G). A & E: 25 year old male with PsA. Flexor tendon pulleys at A1 and A2 level (white arrows) with increased contrast enhancement surrounding each pulley in its course and at ist attachment sites of the pulley (white arrowheads). White asterisk indicates periarticular inflammation within the soft tissue. Black X marks intense flexor tenosynovitis. B & F: 29 year old female with RA. A1 and A2 Flexor tendon pulleys appear thinner (white arrows) than in A & E, with less contrast enhancement (white arrowheads). There is also periarticular inflammation in the surrounding soft tissue (white asterisk). C & G: 37 year old healthy male. Flexor tendon pulleys (white arrows) appear thinner than in PsA and RA. There is only minimal contrast enhancement surrounding each pulley (white arrowheads). White asterisk indicates minimal periarticular inflammation.

pulley inflammation and total PsAMRIS and its acute-inflammatory sub-scores, flexor tenosynovitis, synovitis and periarticular inflammation (digitus (D) 2: synovitis r=0.72, flexor tenosynovitis 0.7, overall PsAMRIS r=0.72; D3: flexor tenosynovitis r=0.91, periarticular inflammation 0.62, overall PsAMRIS r=0.81; D4: flexor tenosynovitis r=0.7, periarticular inflammation r=0.77; D5: synovitis r=0.83, flexor tenosynovitis 0.76, periarticular inflammation r=0.6, overall PsAMRIS r=0.8. $p < 0.05$).

Conclusion: The assessment of MRI changes of flexor tendon pulleys is potentially beneficial for disease detection and monitoring in PsA, as well as for its distinction from RA and HC.

Disclosure: P. Sewerin, AbbVie, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Celgene, 2, 5, 8, Chugai, 2, 5, 8, Hexal, 5, 8, Janssen-Cilag, 2, 5, 8, Lilly, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, Sanofi-Genzyme, 5, 8, Swedish Orphan Biovitrum, 5, 8, UCB, 2, 5, 8; **D. Abrar**, None; **D. McGonagle**, AbbVie, 9, Abbvie, 2, 8, BMS, 9, Celgene, 2, 8, 9, Janssen, 2, 8, Johnson & Johnson, 9, Lilly, 2, 8, MSD, 9, Novartis, 2, 8, 9, Pfizer, 2, 8, 9, UCB, 8, 9; **M. Frenken**, None; **K. Ratke**, None; **S. Vordenbaeumen**, None; **R. Brinks**, None; **M. Schneider**, None; **B. Ostendorf**, None; **C. Schleich**, None.

Abstract Number: 1858

Beta-2-Glycoprotein-I IgA Antibodies Predict Coronary Plaque Burden, Progression and Moderate the Effect of Inflammation on Atherosclerosis in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Imaging of Rheumatic Diseases I
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Background/Purpose: Beta-2-glycoprotein-I(b2GPI), an apolipoprotein abundant in plasma, is readily expressed in human atherosclerotic plaque. Anti-b2GPI-IgA antibodies (Ab) have been previously reported in both rheumatoid arthritis (RA) patients and controls;they independently predicted cardiovascular events in general patients. We explored whether a-b2GPI-IgA presence predicted coronary plaque burden, its progression and potential interactions between a-b2GPI-IgA and inflammation on atherosclerosis load increase in RA.

Methods: One hundred-one participants with a baseline coronary computed tomography angiography (CCTA) underwent follow-up assessment within 83±3.6 months. Numbers of coronary segments with plaque andcumulative plaque stenosis were recorded.Coronary artery calcium (CAC) was quantified by the Agatston method. Subclasses (IgG, IgM and IgA) of a-b2GPI Ab, anticardiolipin-Ab and lupus anticoagulant were assessed at baseline and confirmed 12-weeks later, if positive. Serum interleukin-6 (IL-6) was measured at baseline, while CRP was assessed on every visit from baseline through follow-up. Multivariable robust linear regression models evaluated the effect of a-b2GPI-IgA presence onbaseline CACandCAC change. Negative binomial regression assessed plaque progression, defined as number of segments with new plaque or increase in stenosis of existing plaque.The effects of interactions between a-b2GPI-IgA and time-averaged CRP or baseline IL-6 on plaque progression were also explored.

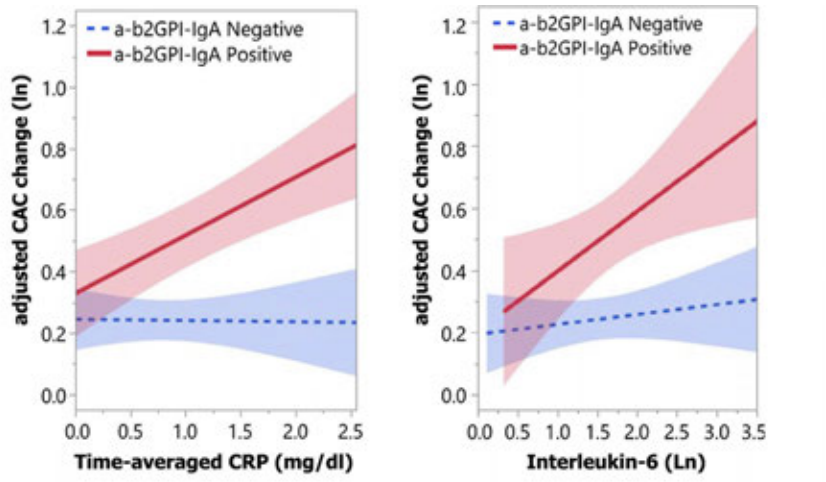

Figure 1. Associations of time-averaged CRP and baseline IL-6 with CAC change stratified by a-b2GPI-IgA presence. Models adjusted for age, hypertension, waist-to-height ratio, cumulative prednisone dose and time in-between scans.

Results: A-b2GPI-IgA was highly prevalent (34.7%) in contrast to other antiphospholipid-Ab subclasses (< 4%). Their presence predicted baseline CAC score independently of age, hypertension, statin use, and CRP [β=0.37 (0.04-0.71), p=0.029]. A-b2GPI-IgA further predicted CAC change [β=0.387 (0.06-0.71), p=0.019] and plaque progression [IRR=1.62 (1.03-2.56), p=0.039], independently of age, hypertension, time-averaged CRP, cumulative prednisone and methotrexate dose and duration of statin exposure. Similarly, Ab presence predicted incident CAC [OR=5.67 (1.10-29.23), p=0.038] as well as prevalent CAC progression [β=0.64 (0.02-1.26), p=0.044]. Notably, a-b2GPI-IgA moderated the effect of both time-averaged CRP and baseline IL-6 (Figure 1) on CAC change [p-interaction=0.01 and 0.017 respectively]; specifically, higher time-averaged CRP and higher baseline IL-6 promoted CAC progression only in a-b2GPI-IgA positive patients [β =0.47 (0.26-0.67), p< 0.001 and β=0.43 (0.05-0.81), p=0.028, respectively] but not negative ones [β=0.07 (-0.10-0.25), p=0.395 and β=-0.07 (-0.34-0.20), p=0.621, respectively].

Conclusion: A-b2GPI-IgA in RA independently contribute to higher baseline coronary atherosclerosis burden, accelerated plaque progression and remodeling, especially in the context of higher cumulative inflammation.

Disclosure: G. Karpouzas, Bristol Meyer Squibb, 8, bristol Meyer Squibb, 8, Bristol-Meyer-Squibb, 8, Pfizer, 2, 9, pfizer, 2, Sanofi, 5, 8; **S. Ormseth**, None; **E. Hernandez**, None; **V. Bui**, None; **M. Budoff**, None.

Abstract Number: 1859

Joint Tenderness and Ultrasound Inflammation in DMARD-naïve Early Rheumatoid Arthritis Patients

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SESSION INFORMATION
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Session Time: 4:30PM–6:00PM

Background/Purpose: A tender joint count is part of most disease activity scores and remission criteria in rheumatoid arthritis (RA). A recent study in established RA found that tender joint count might not reflect inflammatory activity assessed by ultrasound (1). Our objective was to explore if tender non-swollen joints is associated with subclinical inflammation, assessed by ultrasound, in DMARD-naïve early RA patients.

Methods: DMARD-naïve RA patients with < 2 years symptom duration from first swollen joint and indication for DMARD treatment were included in the ARCTIC trial (2). For the current analyses we used data from the baseline examination, including a tender joint count assessed by Ritchie Articular Index and a 44-swollen joint count. The Ritchie Articular Index treat certain joints as a single unit (as the MCP-joints), and scoring of tenderness in joints and joint groups is graded 0-3. All patients underwent an ultrasound examination of 32 joints, with a semi-quantitative 0-3 score for power Doppler in each joint. An ultrasound atlas was available for reference (3). We predefined the wrist and the MCP 1-5 joints as joint areas of interest since they are commonly involved in RA and were assessed both clinically and by ultrasound. We selected only joints that were clinically non-swollen, and assessed the association between joint tenderness and ultrasound power Doppler signal by mixed logistic regression models with patient-specific intercept to adjust for within-patient dependencies. The analyses were repeated using generalized estimating equations for robustness. The frequency and odds ratio (OR) of ultrasound power Doppler activity (yes/no) in tender

non-swollen wrists compared to non-tender non-swollen wrists were calculated. Similar analyses were performed for the MCP joints.

Results: A total of 222 patients with complete baseline data were included. 63% were female, median [IQR] age was 53.6 [41.2, 62.3] years, symptom duration 5.8 [2.9, 10.4] months, swollen joint count 9 [4, 15], joint tenderness 7 [4, 13] and power Doppler score 7 [3, 14]. Of 444 wrists, 268 were not swollen. The frequency of power Doppler signal >0 in tender non-swollen wrists were 50% (18/36), compared to 23% (53/232) in non-tender non-swollen wrists (p-value for comparison = 0.001). This corresponds to an OR of 4.32 (95% CI 1.47 to 12.65, p=0.008) for power Doppler signal if the wrist was tender but not swollen, compared to a non-tender non-swollen wrist. Similar results were found for the non-swollen MCP-joints (Table).

Table. The frequency and odds ratio (OR) of ultrasound power Doppler (PD) activity in Ritchie positive versus Ritchie negative non-swollen wrists and MCP joints.

	PD-signal positive if Ritchie positive	PD-signal positive if Ritchie negative	OR (CI)	p-value
Non-swollen wrist, n=268	18/36 (50%)	53/232 (23%)	4.32 (1.47 to 12.65)	0.008
Non-swollen MCP joints, n=165	15/35 (43%)	28/130 (22%)	4.84 (1.31 to 17.89)	0.02

Conclusion: Ultrasound power Doppler activity was more frequent in non-swollen wrists and non-swollen MCP joints if the joints had been scored as tender or painful by Ritchie Articular Index. Our findings indicate that in early RA patients, tenderness might reflect inflammation which is not detectable clinically.

Disclosure: N. Sundlisater, None; **A. Aga**, AbbVie, 2, 8, Eli Lilly, 8, MSD, 2, Norwegian Research Council, 2, Norwegian Rheumatism Association, 2, Norwegian South-Eastern Health Region, 2, Norwegian Women's Public Health Association, 2, Novartis, 8, Pfizer, 2, 8, Roche, 2, UCB, 2, 8; **H. Hammer**, None; **T. Uhlig**, None; **T. Kvien**, AbbVie, 2, 8, Biogen, 5, 8, Biogen, Egis, Eli Lilly, Hikma, Mylan, Novartis/Sandoz, Oktal, Hospira/Pfizer, Sanofi and UCB, 5, BMS, 8, Celltrion, 8, Egis, 5, 8, Eli Lilly, 5, 8, Hikma, 5, 8, Hospira/Pfizer, 2, 5, 8, MSD, 2, 8, Mylan, 5, 8, Novartis, 8, Novartis/Sandoz, 5, 8, Oktal, 5, 8, Orion Pharma, 8, Roche, 2, 8, Sandoz, 8, Sanofi, 5, 8, UCB, 5, 8; **E. Haavardsholm**, AbbVie, 2, 8, Cellgene, 8, Eli Lilly, 8, Janssen, 8, MSD, 2, Norwegian Research Council, 2, Norwegian South-Eastern Health Region, 2, Pfizer, 2, 8, Roche, 2, UCB, 2, 8; **S. Lillegraven**, AbbVie, 2, MSD, 2, Norwegian Research Council, 2, Norwegian South-Eastern Health Region, 2, Pfizer, 2, Roche, 2, UCB, 2.

Abstract Number: 1860

Using Electronic Visits (E-Visits) to Achieve Goal Serum Urate Levels in Patients with Gout in a Rheumatology Practice: A Pilot Study

Chio Yokose ,[1] April Jorge,[1] Kristin D'Silva,[1] Naomi Serling-Boyd,[1] Mark Matza,[2] Mazen Nasrallah,[2] Sarah Keller,[1] Amar Oza,[1] Hyon K. Choi,[1] Marcy Bolster,[1] and Deborah Collier[1], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Boston

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Measures of Healthcare Quality I: Digital Health Technologies – Tool for Improvement

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Gout is a highly prevalent form of inflammatory arthritis associated with increased morbidity and mortality, and the burden of gout on the healthcare system has continued to climb despite the widespread avail-

Figure 1. Gout E-Visit Questionnaire

Gout Questionnaire:

Overall, how have your gout symptoms been since your last visit (circle one)?
Better Same Worse

Have you experienced any gout attacks since your last visit? In the short term while you are being started on a medication to lower your uric acid, you are at an increased risk of a gout flare. Therefore, your doctor may also recommend taking another medication to prevent these flares.
Yes No

If yes, please answer the following 5 questions:
1. **How many flares have you had?** _____
2. **Which joints were affected?** _____
3. **How many days did the flares last, on average?** _____
4. **Did you have to visit the ER or hospital due to the flare?** _____
5. **How did you treat the flares (circle answers)** _____

Non-steroidal anti-inflammatory drugs (e.g., Indomethacin, naproxen(Aleve), ibuprofen (Motrin, Advil))
Colchicine (Colcrys, Mitigare)
Prednisone (Cortan, Orasone, Deltasone) or methylprednisolone (Medrol)
Ice packs
Other (please explain) _____
None of the above

Do you take a medicine to prevent gout flares? Yes No
If yes, which medicine do you take? _____ **Dose?** _____ **Number of times per day?** _____

General recommendations to ease or prevent gout attacks:
- Avoid foods that are high in purines (such as liver, organ meats, gravy, high-fat dairy products, tuna, anchovies).
- Avoid high-fructose corn syrup-sweetened beverages and foods.
- Drink plenty of water.
- Limit alcohol.
- Exercise regularly and maintain a healthy weight.
- If you're overweight, ask your doctor how to lose weight safely. Fast or extreme weight loss can raise uric acid levels.

Are you following these recommendations most of the time? Circle one. Yes No

Which uric acid-lowering drug are you taking for your gout? Select all that apply. Gout is caused by elevated uric acid levels in the blood. If the uric acid is lowered to target, then you can be cured of gout attacks. The medications listed below work by lowering uric acid levels. To be effective, they must be taken consistently and at the appropriate dose. Your doctor will adjust the dose of these medications to achieve the target uric acid level. The dose will likely need to be increased in several steps after lab checks over the next few months.
- Allopurinol (Zyloprim, Lopurin, Aloprim) Dose: _____
- Febuxostat (Uloric) Dose: _____
- Probenecid Dose: _____
- Other, please explain _____
- I have not been prescribed a uric acid-lowering drug

Are you taking the uric acid-lowering medication as prescribed?
Yes No

If no, then why? Select all that apply.
- Advice of another doctor. Please explain: _____
- Because my gout is mild and does not require preventive gout treatment
- Because I could not afford the treatment/medication co-pay
- Because I do not understand the medication instructions
- Because of side effects
- Other, please explain: _____

Are you experiencing any side effects from the medications?
Yes No
If yes, please explain: _____

Have there been any changes to your other prescription medications since your last visit?
Yes No
If yes, please explain: _____

Are you doing any non-medication therapy or taking any over-the-counter medicines for your gout?
Yes No
If yes, please explain: _____

Have you had your blood tests drawn since your last visit? It is important to have the uric acid level checked since this helps your doctor adjust the dose of your gout medication.
Yes No

Do you have other questions, concerns, or comments about your gout that you want your doctor to know?
Yes No
If yes, please explain: _____

Since your last visit, have you been: (Select all that apply)
- Told by a doctor that you have any new medical conditions? If yes, please explain: _____
- To the ER or hospital for a medical condition? If yes, please explain: _____
- None of the above

Table 1. Baseline Characteristics of Patients with Gout Enrolled in E-visits and Historical Controls

	E-visit Program (n=62)	Controls (n=62)
Age, years (mean, SD)[1]	58.3 (12.6)	56.5 (11.2)
Male sex (n, %)	52 (83.9%)	46 (76.7%)
White (n, %)	57 (91.9%)	52 (83.9%)
Black (n, %)	0	2 (3.2%)
Asian (n, %)	3 (4.8%)	4 (6.4%)
Other (n, %)	2 (3.2%)	4 (6.4%)
Hispanic (n, %)	3 (4.8%)	1 (1%)
Weight, kg (mean, SD)[1]	95.6 (18.9)	98.6 (20.7)
Height, cm (mean, SD)[1]	172.5 (10.8)	174.3 (10.6)
Body mass index, kg/m^2 (mean, SD)[1]	32.3 (6.7)	32.4 (6.3)
Creatinine, mg/dL (mean, SD)[1]	1.1 (0.3)	1.2 (0.4)
Mean glomerular filtration rate (mL/min/1.73m^2)[1,2]	103.4 (38.5)	99.0 (36.5)
Stage 3, 4, or 5 chronic kidney disease (n, %)[3]	11 (17.7%)	10 (16.1%)
New start of urate lowering therapy (n, %)	37 (59.7%)	29 (46.8%)

[1]Mean values are reported with standard deviation in parentheses
[2]Calculated by Cockroft-Gault Equation
[3]Stage 3 or worse chronic kidney disease defined as glomerular filtration rate < 60 mL/min/1.73m^2

Table 2. Comparison of Treat-to-Target in Gout Patients Enrolled in E-visits Compared to Historical Controls

	E-visit Program (n=62)	Controls (n=62)	P-value
Mean number of office visits in 6 months*	0.8 (0.8)	1.1 (1.0)	0.07
Mean number of E-visits in 6 months*	1.6 (1.5)	N/A	
Completed at least one E-visit (n, %)	43 (69.4%)	N/A	
Mean initial serum urate (mg/dL)*	8.3 (1.5)	8.1 (1.8)	0.50
Mean serum urate at 6 months (mg/dL)*	**5.5 (1.5)**	**6.6 (1.5)**	**<0.01**
Allopurinol (n, %)	55 (88.7%)	55 (88.7%)	1.00
Febuxostat (n, %)	6 (9.7%)	6 (9.7%)	1.00
Probenecid (n, %)	0	1 (1.6%)	0.5
Pegloticase (n, %)	1 (1.6%)	0	0.5
Mean allopurinol dose at 6 months (mg)*	273.5 (96.7)	263.2 (107.3)	0.58
Dose change/escalation over 6 months (n, %)	45 (72.6%)	40 (64.5%)	0.33
Achieved goal serum uric acid (n, %)**	**38 (61.3%)**	**18 (29.0%)**	**<0.01**

*All mean values are reported with standard deviation in parentheses
**Goal serum urate defined as <6 mg/dL
N/A not applicable

ability of effective medications. The American College of Rheumatology management guidelines for gout recommend a "treat-to-target" approach with a goal serum urate (SU) level < 6 mg/dL in most patients with gout with the use of urate-lowering therapy (ULT) such as allopurinol. However, achieving goal SU levels in patients with gout remains difficult in primary care and rheumatology practices. We hypothesized that an asynchronous electronic visit (E-visit) program could facilitate achieving a goal SU < 6 mg/dL among patients with gout on ULT.

Methods: Patients with rheumatologist-diagnosed gout and SU levels greater than 6 mg/dL either starting or continuing titration of ULT were eligible for the study and were enrolled in the E-visit program at the treating physicians' discretion between April 1, 2017 and May 31, 2018. The E-visit program consisted of an electronic questionnaire (Figure 1) that assessed medication compliance and recent symptoms and provided educational information on gout triggers and the "treat-to-target" approach for gout management. The E-visit also served as a reminder to the patient to have laboratory testing performed, as recommended by his/her physician. Once the E-visit was completed by the patient, the treating physician was notified to review the patient's responses (thus asynchronous) and recommend further action (including adjustment of ULT dose). We performed a retrospective cohort study, comparing patients who enrolled in the E-visit program with age- and sex-matched historical controls who received usual care and were seen within 12 months prior to E-visit program initiation. The primary outcome of interest was the proportion of patients achieving target SU level < 6 mg/dL at 6 months.

Results: Sixty-two patients were enrolled in the gout asynchronous E-visit program and were compared to 62 historical controls. Baseline characteristics including age, sex, body mass index, renal function, and initial SU were similar among patients enrolled in the E-visit program and controls (Table 1). At six months, E-visit patients had a lower mean SU level than the historical controls (5.5 mg/dL vs. 6.6 mg/dL, respectively, $p < 0.01$) (Table 2). The number of patients achieving a goal SU of < 6 mg/dL at the end of 6 months was higher in the E-visit group compared to control patients (61.3% vs. 29.0%, respectively, $p < 0.01$) (Table 2).

Conclusion: In this pilot study, a physician-initiated E-visit program led to a substantial improvement in the proportion of patients achieving goal SU in an academic rheumatology practice. E-visits may be a useful tool to improve gout management and achieve SU goals. Further studies should assess the generalizability and cost-effectiveness of an E-visit program in both academic and community rheumatology practice settings.

Disclosure: C. Yokose, None; **A. Jorge**, None; **K. D'Silva**, None; **N. Serling-Boyd**, None; **M. Matza**, None; **M. Nasrallah**, None; **S. Keller**, None; **A. Oza**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5; **M. Bolster**, Abbvie, 2, Corbus, 9, Cumberland, 9, Gilead, 5, Johnson & Johnson, 4, Johnson and Johnson, 4, Pfizer, 2; **D. Collier**, None.

Abstract Number: 1861

Use of a Novel Electronic Auto-notification Process to Manage Transitions of Care in Rheumatic Patients on DMARD Therapy

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Type: ACR Abstract Session
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Background/Purpose: Effective communication is essential in caring for medically complex patients with rheumatologic diseases. In our prior study of rheumatoid arthritis patients and hospital admissions, our rheumatologists were only notified 57.6% of the time. This project's goal was to integrate an auto-notification system into our clinical workflow, so that timely communication of sentinel events (Elective surgery, Hospital admission, or ER visit) in immunosuppressed rheumatic disease patients happens by design, not by accident.

Methods: We developed an algorithm that triggers an auto-notification to the Rheumatology Nurse Navigator when a patient of interest (POI) experiences a sentinel event. A POI has been seen by a rheumatologist at least twice within the past 14 months and takes a DMARD or glucocorticoid. The Nurse Navigator creates a telephone encounter that includes the event type, baseline glucocorticoid and DMARD therapy, and event date. That encounter is forwarded to the rheumatologist, who records recommendations based on current guidelines and returns it to the Nurse Navigator, who notifies the patient or other providers of the recommendations.

Results: During the four-month study period, 240 completed notifications were received - 57% for elective surgeries, 39% for ER visits, and 4% for admissions. The need for change in care plan was less common for ER visits (17%), but was 25% for hospital admissions and 44% for elective surgeries. A significant result is the time interval between receipt of the notification and the date of elective surgery. This is applicable to our patients taking biologic DMARDs and/or high dose glucocorticoids, as these medications may require holding or adjusting a dose weeks before surgery. The mean number of days in this interval was 23. Therefore, this notification process is useful in the case of medications that need to be held or adjusted three weeks or less prior to surgery. The time commitment by clinicians has been minimal. The nurse spent an average of 5 minutes for each patient and the physicians spent an average of 5.9 minutes. The percentage of time that clinicians were notified of sentinel events increased from 57.6% to 100%.

Conclusion: Without knowledge of the care team, and no communication process integrated into the clinical workflow, communication and care handoff failures are extremely common. We developed a process that "hardwires" notification of the specialist for a patient sentinel event, to facilitate timely and relevant care. The average number

of messages that clinicians received per week was 2.2. Since the average number of minutes clinicians spent per message was 5.9, this resulted in only 13 minutes of work for each clinician per week, making this a very manageable process. With this automated program, care communication failures fell from 42.4% to 0%. As changes to the care plan were needed 34% of the time, this notification is crucial to our patient care. The process is easy, reliable, and has been well-received. As the program has been effective in improving patient care and outcomes, other divisions in our institution, such as Pulmonary, are developing a similar program for their patient population.

Disclosure: M. Bielawski, None; **E. Newman**, None; **L. Schroeder**, None.

Abstract Number: 1862

Treat to Target Opportunities – Design, Testing, and Adoption of a Novel EHR-Integrated Electronic System to Engage Rheumatologists and Capture Decision Making

Eric Newman ,[1] Jonida Cote,[1] and Joseph Chronowski[1], [1]Geisinger, Danville, PA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Measures of Healthcare Quality I: Digital Health Technologies – Tool for Improvement
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

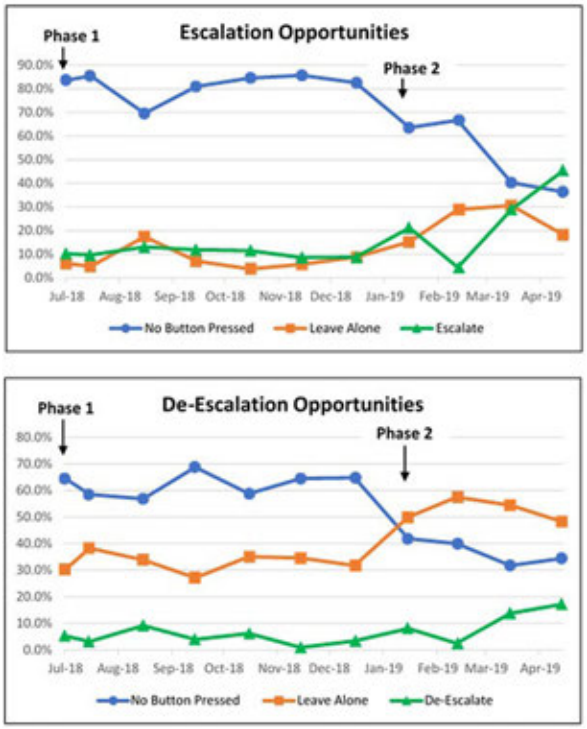
Background/Purpose: Treat to Target (T2T) opportunities and rheumatologist decision making are not defined, captured, or reportable within existing electronic health record (EHR) software. We developed a novel EHR-integrated electronic system that 1) signals rheumatologists in real time of an escalation or de-escalation treatment opportunity, 2) captures their decision making including exceptions, and 3) reports on those decisions.

Methods: Using the CDAI (Clinical Disease Activity Index - disease activity measure), we electronically defined an Escalation Opportunity (**E-Opp**) as the 2 most recent CDAIs in the moderate or high disease activity range and a De-escalation Opportunity (**D-Opp**) as every CDAI for the past year in the low or remission range.

Using EHR-integrated software that captures CDAI measures, we designed a T2T tab that displayed the E-Opp or D-Opp (Phase 1). The rheumatologist could choose to escalate/de-escalate therapy, or leave alone and why. The system then deactivated display of future T2T opportunities for that patient for a defined time period to minimize physician burden. Because of low adoption of navigation to the T2T tab, the software was redesigned (Phase 2) to give a visual cue upon completion of the CDAI, prompting in real time to address the T2T opportunity (Figure 1).

Figure 1. Clicking Treat to Target Opportunity displays "Escalate" or "Leave Alone" choices

Figure 2. Improvement in addressing T2T opportunities with Phase 2 redesign



Results: Between July 2018 and early May 2019, there were 1,428 T2T opportunities, representing 34.2% of the completed RA office visits during that time period. 11.3% of RA visits had an E-Opp and 22.9% of RA visits had a D-Opp. During Phase 1, rheumatologists used the T2T tab for only 18.1% of the E-Opp and 37.5% of the D-Opp. At the end of Phase 2, T2T tab use had risen to 63.6% for E-Opp and 65.5% for D-Opp (Figure 2). A decision to escalate rose from 10.2% to 45.5% of all E-Opp, and a decision to de-escalate rose from 5.3% to 17.2% of all D-Opp.

For opportunities where a decision was made, rheumatologists selected "leave alone" for 48.9% of E-Opp and 80.0% of D-Opp. When there was an E-Opp, reasons for "leave alone" included CDAI measure not accurate (33.9%), patient decision (14.5%), risk > benefit (14.5%), other (37.1%). When there was a D-Opp, reasons for "leave alone" included hard to control (46.1%), patient preference (29.4%), and poor prognostic factors (24.5%).

Conclusion: We designed and tested an EHR-integrated Treat to Target (T2T) tool that prompted rheumatologists about escalation/de-escalation opportunities and captured their medical decision making. Opportunities for escalation and de-escalation of therapy are common (34.2 % of RA visits), even in a well-managed RA population. Adoption of T2T tool use improved significantly with real-time visual notification. In parallel, decisions to escalate and de-escalate when opportunities existed also rose (10.2% to 45.5%, and 5.3% to 17.2%, respectively). Using this novel tool, the ability to reliably capture why escalation/de-escalation opportunities are deferred ("leave alone") will allow us to develop refined T2T care strategies. Now that it is embedded in routine RA care, next steps will be to use this tool to proactively drive value-concordant decision making and monitor the effect on disease control and cost of care.

Disclosure: E. Newman, None; **J. Cote**, None; **J. Chronowski**, None.

Abstract Number: 1863

Improving Pneumococcal Vaccination Rates in High Risk Rheumatology Patients

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: To improve Pneumococcal Vaccination rates in high risk Rheumatology patients on immunosuppressive therapy.

Methods: The study was a quality improvement project based on the pre-post-intervention design. The phase I of the project targeted all Rheumatoid Arthritis patients on immunosuppressive therapy for pneumovax vaccine (PV) seen in thirteen Rheumatology outpatient clinics (1/2013 to 7/2015). In the Phase II study (1/2015-10/2017) all Rheumatology patients on immunosuppressive medications irrespective of their diagnosis were intervened for pneumovax and prevnar vaccination as per current CDC guidelines. The electronic Best Practice Alert (BPA) for both PVs were developed with backend algorithm based on CDC guidelines. Based on patient eligibility checked electronically, the appropriate PV appeared on electronic medical records at the time of rooming of the eligible patient by the medical assistant. BPA was designed to inform the physician about vaccination status as well as enable physician to easily order PV or document refusal or deferral reasons (Figure 1). Education regarding vaccine guidelines, BPA, vaccination process, and regular feedback of results were important components of the project interventions. The vaccination rates during pre-post intervention phases during each study phase were compared using Chi square test.

Results: The PV rates reported as patients vaccinated among all eligible patients, improved significantly during both study phases. Phase I demonstrated 61.5% Pneumovax vaccination rate compared to pre-intervention rate of 27.9 % ($p < 0.0001$) (Figure 2). During Phase II 77% patients had received either pneumovax or prevnar compared to 49.6% patients in pre-intervention period ($p < 0.0001$) (Figure 3). The documentation rates (vaccine received, ordered, patient refusal and deferral reasons) also increased significantly in both phases.

Conclusion: Electronic identification of vaccine eligibility and implementation of BPA with capabilities to order and document reasons for non-compliance significantly improved PV rates. The process required minimal modification

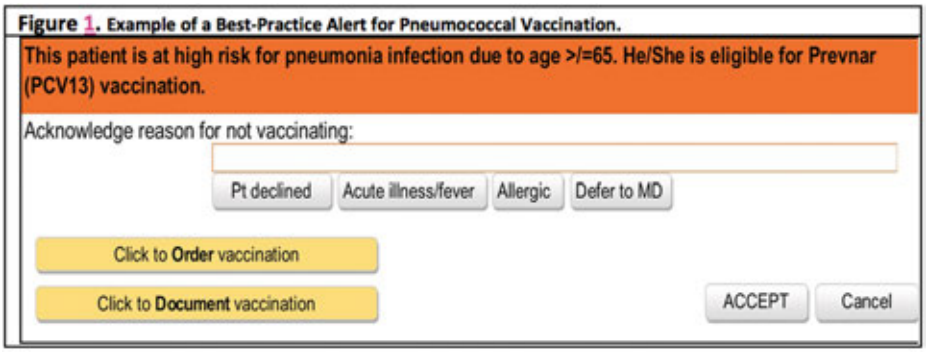

Figure 1. Pneumococcal Vaccine Best Practice Alert

Fig 2: Phase I Vaccination and Documentation Rates

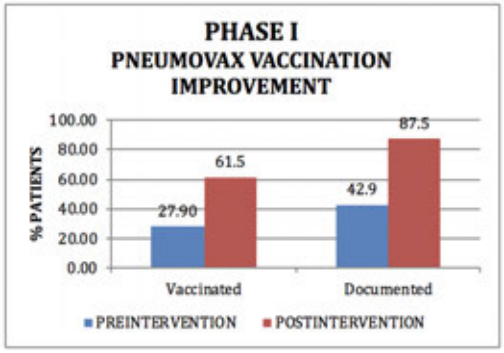

Figure 2. Pneumococcal Vaccination Improvement Rate Phase I

Fig 3: Phase II Vaccination and Documentation Rates

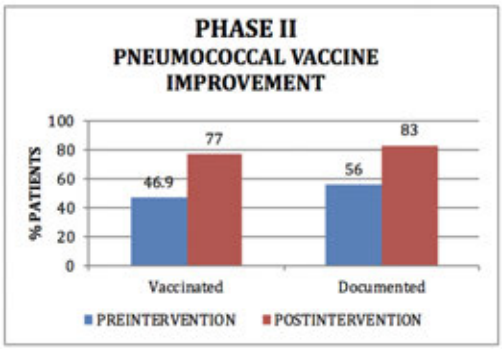

Figure 3. Pneumococcal Vaccine Improvement Rate Phase II

of clinic work flow, and did not increase physician time. The project was self- sustained during Phase II with initial education and thus has potential for self-sustainability and generalizability.

Disclosure: H. Sheth, None; **G. Vera**, None; **D. Rudge**, None; **G. Fischer**, None; **L. Moreland**, None; **R. Aggarwal**, Bristol Myers-Squibb, 2, 5, Pfizer, 2, Genentech, 2, Momenta, 2, Mallinckrodt, 2, 5, Octapharma, 5, CSL Behring, 5, AstraZeneca, 5, Corbus, 5, Kezar, 5.

Abstract Number: 1864

Gaps in Care for Patients with SLE: Data from the ACR's RISE Registry

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Measures of Healthcare Quality I: Digital Health Technologies – Tool for Improvement

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Although multiple national quality measures focus on the management and safety of rheumatoid arthritis, few measures address the care of patients with SLE. We used the ACR's RISE registry to assess na-

Table. Quality measures, number of eligible patients, and overall performance.

Quality measure	Number of patients eligible for the measure	Overall performance	Number of practices included in practice-level analysis†	25th-75th percentile practice-level performance
Proportion of patients with SLE with ≥1 documented urine study screening for lupus nephritis	22,171	26.2%	142	0 - 42.9%
Proportion of patients with SLE with ≥2 blood pressure readings recorded ≥30 days apart	22,171	90.3%	142	91.3 – 98.4%
Proportion of patients with SLE with blood pressure >140/90 mm Hg on ≥2 occasions ≥30 days apart	20,020	17.1%	131	8.1 – 24.7%
Proportion of patients with SLE prescribed ≥7.5 mg of prednisone (or equivalent) for > 90 days	22,171	14.9%	142	7.6 – 18.2%
Proportion of patients with SLE prescribed >6.5 mg/kg of hydroxychloroquine	2,176*	10.7%	35	5.6 – 14.4%

*Number of eligible patients, and therefore practices, is low because detailed HCQ prescription instructions could not be analyzed for many patients due to the unavailability of electronic prescription data.
† Practice-level analysis included only practices reporting on > 20 patients.

tionwide variations in SLE care around screening for renal disease; management of hypertension; medication safety related to prednisone and hydroxychloroquine (HCQ) use.

Methods: RISE is a national, EHR-enabled registry that passively collects data on all patients seen in participating practices, reducing the selection bias present in single-insurer claims databases. As of December 2017, RISE held validated data from 1,257 providers in 236 practices, representing ~36% of the U.S. clinical rheumatology workforce. Patients included this study were ≥18 years old and had ≥2 SLE codes ≥30 days apart between January 1 2017 and December 31 2017. Measures were assessed during this same period. We calculated 1) the proportion of patients with ≥1 documented urine study for screening for lupus nephritis (urinalysis; urine protein; or urine protein:creatinine ratio); 2) the proportion of patients with ≥2 blood pressure readings recorded ≥30 days apart; 3) the proportion of patients with systolic blood pressure >140 mm Hg or diastolic blood pressure > 90 mm Hg on ≥2 occasions, ≥30 days apart; 4) the proportion of patients prescribed ≥7.5 mg of prednisone (or equivalent) for > 90 days; 5) the proportion of patients prescribed >6.5 mg/kg of hydroxychloroquine. A practice-level analysis assessed performance on these measures among practices reporting on at least 20 patients. We also built a logistic regression model that included age, sex, race, insurance, and geographic region to assess independent predictors of performance on each measure.

Results: We included 22,171 unique patients from 142 practices; 92% were female, 51% white, with mean age 54±15. Additional characteristics of the SLE population included that 7,485 had at least 1 documented ANA (77.7% of these with titer > 1:40); 14,751 had at least 1 dsDNA Ab (46.4% of these with titer ≥ 1:40), and 9.7% had nephritis using ICD code definitions and 0.5% had ESRD. Performance on the proposed quality measures is shown in the Table: few patients had adequate screening for lupus nephritis. Although blood pressure screening was common, a meaningful fraction had untreated hypertension. Many were receiving long-term moderate-dose steroids, or excessive doses of hydroxychloroquine. Practice and regional variation were significant. Patients who were black were more likely to have uncontrolled hypertension (OR 1.79 (1.63, 1.97)) and high prednisone dosing (OR 1.35 (1.24, 1.49)) compared to whites.

Conclusion: Significant gaps in care exist for patients with SLE across the U.S. Although some performance variation may be explained by patient factors, dramatic differences suggest that developing quality measures to address these aspects of care in SLE may improve care.

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

Disclosure: G. Schmajuk, None; **Z. Izadi**, None; **M. Evans**, None; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2.

Abstract Number: 1865

Improving Lupus Care Index Documentation in Patients with Childhood-Onset Systemic Lupus Erythematosus (cSLE)

Fatima Barbar-Smiley ,[1] Stephanie Lemle,[1] Cagri Yildirim-Toruner,[1] Edward Oberle,[1] Darby McDonald,[1] Vidya Sivaraman,[2] and Stacy Ardoin[1], [1]Nationwide Children's Hospital, Columbus, OH, [2]Nationwide Children's Hospital and The Ohio State University, Columbus, OH

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Measures of Healthcare Quality I: Digital Health Technologies – Tool for Improvement

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Systemic lupus erythematosus (SLE) affects both adults and children with an estimated prevalence in children of 8/100,000. More than 1000 deaths related to SLE occur in a 5-year period, with most common causes attributed to active disease and organ failure. Adequate control of the disease reduces risk of organ damage, which is more common in children. Reliable measurement and documentation of disease activity is a key initial step for disease control. To achieve proper documentation of disease activity, our team developed a disease activity assessment tool called the Lupus Care Index (LCI). This index utilizes three existing metrics: SLE disease activity index (SLEDAI), Physician global assessment (PGA), and patient pain score. At our institution, we found that only one third of children diagnosed with SLE (cSLE) had proper documentation of all three components of LCI. We implemented a quality improvement (QI) project with aim to increase Lupus Care Index documentation, in children with SLE, from 38 % to 80%, by June 30, 2018.

Methods: We established a QI team including physicians, nurses, QI support staff. Patients with cSLE who received medical care in the pediatric rheumatology clinic from January 1, 2016 to November 31, 2016 were included in the baseline analysis. We excluded clinic visits scheduled for teaching purposes. Our process included a brainstorming session followed by development of a key driver diagram (Fig. 1). Our first PDSA cycle focused on establishing re-

Fig. 1

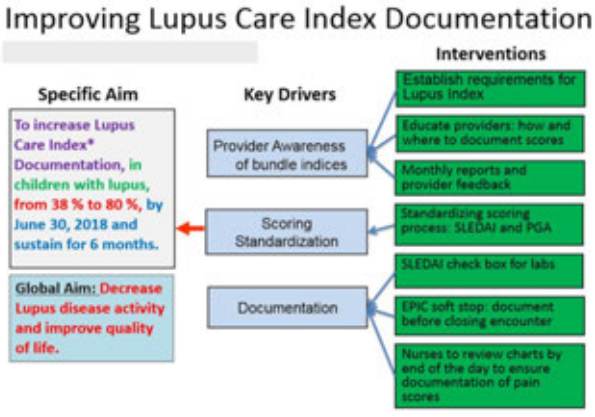

Figure 1. Key Driver Diagram (KDD)

Fig. 2

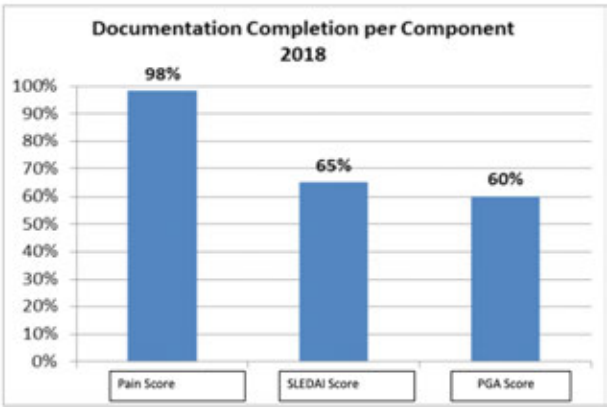

Figure 2. Pareto Chart

Fig. 3

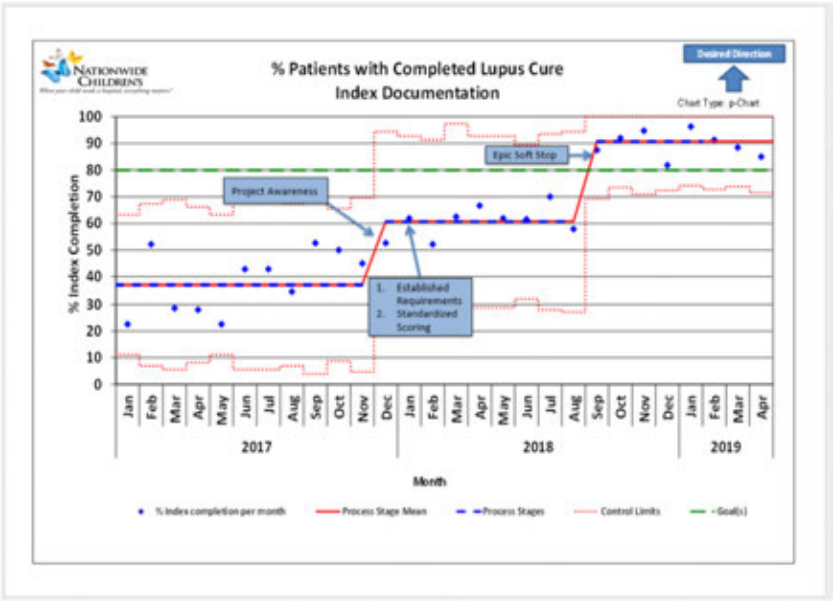

Figure 3. Control Chart

quirements for LCI and a team consensus for proper documentation. Next, we created a Pareto chart to assist with a targeted intervention approach focusing on least documented indices (Fig. 2). We ran monthly reports and provided timely feedback to providers, and developed EHR (electronic health medical record; EPIC) “soft stop” reminders for physicians to document disease activity prior to closing clinic encounters. We utilized control charts to show the monthly percentage of c-SLE patients who had complete documentation of all three components of LCI (Fig. 3).

Results: We noted initial improvement trend in documentation with project awareness, score standardization, and provider level monthly feedback. However, we were able to achieve and surpass our goal of 80% in Aug 2018 after establishing the EHR soft stop reminder. We have sustained the desired improvement for 8 months.

Conclusion: The results of this quality improvement initiative highlight the role of EHR reminders along with provider feedback and transparency in promoting quality of health care delivery. Future directions of this project aim at utilizing the documented disease activity indices to reduce disease activity and improve patient disease outcomes.

Disclosure: F. Barbar-Smiley, None; **S. Lemle**, None; **C. Yildirim-Toruner**, None; **E. Oberle**, None; **D. McDonald**, None; **V. Sivaraman**, None; **S. Ardoin**, None.

Abstract Number: 1866

Gene Expression Meta-Analysis Reveals Commonalities in Gene Activation and Enrichment of Immune Pathways and Cell Types in Dermatomyositis Target Tissues

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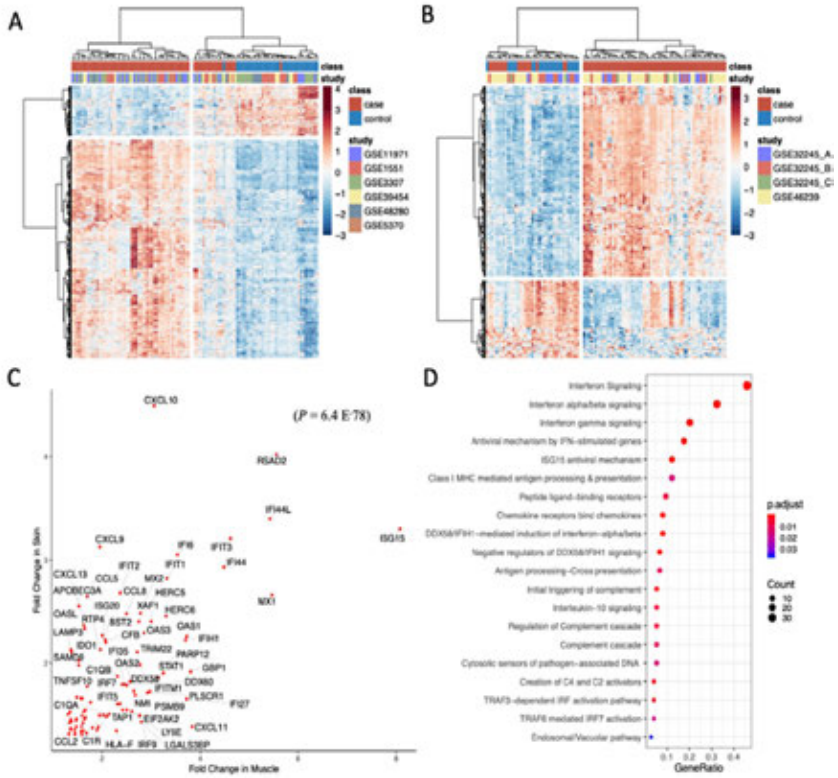
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Muscle Biology, Myositis & Myopathies I
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

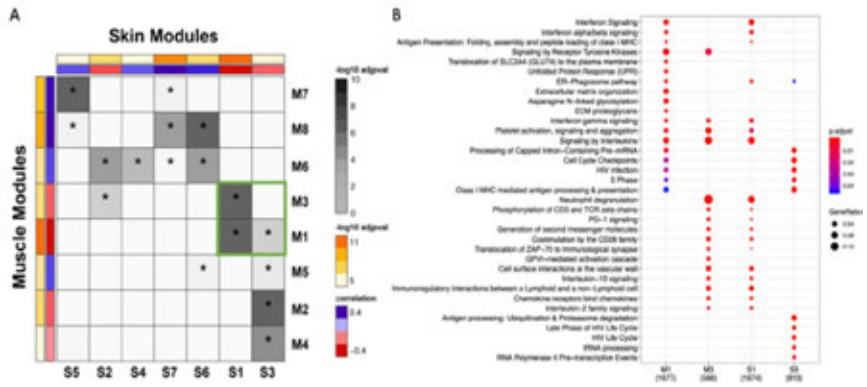
Background/Purpose: Dermatomyositis (DM) is a complex immune-mediated disease resulting in muscle and skin inflammation. Prior studies of gene expression in DM have revealed a type I interferon (IFN) signature, but less is known about alternative immune pathways involved. We conducted a comprehensive gene expression meta-analysis in DM muscle and skin to identify disease-relevant genes and pathways and elucidate a shared immune mechanism across tissues.

Figure 1



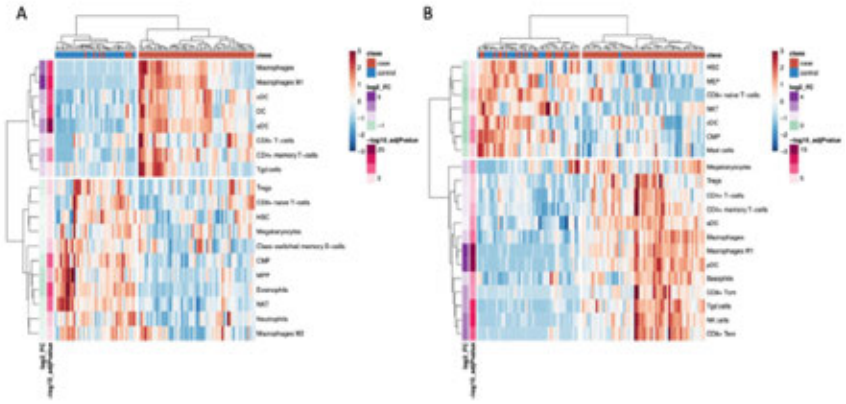
Heatmaps of differentially expressed genes (DEG) identified by SAM in muscle (A) and skin (B) using cut off of FDR p-value <0.05 and FC≥ 1.3. Hierarchical clustering demonstrates clustering of cases and controls and that the majority of DEGs in both tissues are up-regulated. C) Gene symbols of 94 overlapping differentially expressed genes plotted by fold change in muscle and skin. D) Enrichment of 94 overlapping genes by over-representation analysis using the Reactome Database. P-values are calculated using a hypergeometric distribution and corrected for multiple comparisons by the Benjamini Hochberg method.

Figure 2



A) Heatmap demonstrating hierarchical clustering of significant modules identified by WGCNA in each tissue based on gene overlap. Correlation between module eigengene and disease status is shown by the red to blue bar where red represents modules most positively-correlated with cases and blue represents modules negatively-correlated with cases. The color corresponds to a signed p-value: sign(correlation) * -log10(FDR p value). The -log10 adjusted p-value of this correlation is indicated by the yellow to orange bar. The degree of pairwise overlap in genes between muscle modules and skin modules computed using a hypergeometric test is denoted by grey coloring where modules with significant overlap in genes ($p < 0.05$) are denoted by an asterisk and the color range corresponds to –log10(pvalue) of the pairwise overlap. B) Plot showing over-representation analysis of pathways from the Reactome database across a cluster of highly overlapping and interesting modules (green box in pane A) in each tissue demonstrating enrichment of shared pathways across tissues.

Figure 3



Heatmaps of cell-type enrichment calculated using xCell demonstrates clustering of cases and controls based on cell types in both muscle (A) and skin (B). Enrichment was strongest for dendritic cells and M1 macrophages in both tissues.

Methods: Raw data from 6 publicly available datasets from DM muscle (71 cases, 36 controls) and 2 from skin (77 cases, 22 controls) were downloaded. Data were preprocessed, merged and batch-corrected, creating tissue-specific gene expression matrices. Significance Analysis of Microarrays was used to identify differentially expressed genes (DEG; cutoff FDR p-value < 0.05, FC≧1.3). A hypergeometric test was used to assess overlap between DEGs in skin and muscle. Weighted Gene Coexpression Network Analysis was used to construct muscle and skin networks and identify associations not detected on the single gene level. Disease-associated modules were identified by correlating module eigengene with case/control status. Network preservation was assessed by calculating gene overlap between muscle and skin modules using a hypergeometric test. Hub genes (gene significance >0.2 & module membership >0.8) in each network were identified. Cell type enrichment was performed using xCell.

Results: There were 544 significantly DEGs (FC≧1.3, q< 0.05) in muscle and 300 in skin (Fig 1A & 1B). There was significant overlap in upregulated genes across tissues with 94 shared genes (p=6.4xE-78) which were enriched in type I and II IFN signaling and MHC class I antigen processing pathways (Fig 1C & 1D). In a network analysis, we identified 8 significant muscle modules and 7 skin modules either positively or negatively correlated with case/control status (Fig 2A). Modules that were highly correlated with cases also shared significant overlap on the gene level (Fig 2A). These modules were enriched in pathways consistent with the single gene analysis and also in terms related to T cell activation and T cell receptor signaling (Fig 2B). Modules correlated with controls were enriched in processes related to energy metabolism. The top hub genes in each network included genes classically involved in type I IFN (STAT1, MX1, IFI44, ISG15), type II IFN (CXCL10, GBP1), class I MHC antigen processing (HLA-A, -B, -F, B2M, TAP1) and the immunoproteasome (PSMB8, PSMB9). In the cell type enrichment analysis, both tissues were enriched in antigen-presenting cells, including activated dendritic cells and M1 macrophages (Fig 3A & 3B).

Conclusion: This analysis demonstrates striking similarities in gene expression in target tissues in DM and simultaneous activation of innate and adaptive immune responses. Using an unbiased approach, we show enrichment of type I and type II IFN pathways, MHC class I antigen processing pathways, T cell activation, and antigen-presenting cells. These results suggest type II IFN contributes to the global IFN signature in DM and that altered autoantigen presentation through the class I MHC pathway may be important in disease pathogenesis.

Disclosure: J. Neely, None; **D. Rychkov**, None; **M. Paranjpe**, None; **M. Waterfield**, None; **S. Kim**, None; **M. Sirota**, None.

Abstract Number: 1867

Body Composition in Myositis Patients Is Negatively Changed Compared to Healthy Controls and the Changes Are Associated with Disease Activity and Duration, Skeletal Muscle Involvement and Physical Activity and Nutritional Status

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Muscle Biology, Myositis & Myopathies I

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Skeletal muscle, pulmonary and articular involvement in idiopathic inflammatory myopathies (IIM) limit the mobility/self-sufficiency of patients, and can have a negative impact on body composition. The aim of this study was to assess body composition and physical activity of IIM patients and healthy controls (HC) and the association with chosen inflammatory cytokines/chemokines and laboratory markers of nutrition and lipid metabolism.

Table 1: Body composition in IIM and HC.			
Parameters	**IIM (n=54)**	**HC (n=54)**	**p-value**
BF% (Body Fat %) (iDXA)	42.4±7.1	39.9±7.1	0.077
LBM (Lean Body Mass) (kg, iDXA)	40.6±7.2	45.6±8.1	0.001
LBM (Lean Body Mass) (kg, BIA)	48.7±9.0	52.6±8.8	0.023
ECM/BCM (Extracellular Mass/Body Cell Mass ratio)	1.44±0.42	1.06±0.15	<0.001
BMD (Bone Mineral Density) (g/cm^2)	1.1±0.1	1.2±0.1	<0.001

Table 2: Correlation of body composition parameters and clinical features of IIM: disease duration and activity, inflammation, muscle involvement, physical ability.		
Correlated parameters	**r**	**p-value**
BMD (Bone Mineral Density) (g/cm^2): Disease duration	-0.392	0.004
LBM (Lean Body Mass) (kg, BIA): Disease duration	-0.272	0.047
LBM (Lean Body Mass) (kg, BIA): MITAX; MYOACT	0.294; 0.335	0.031; 0.013
LBM (Lean Body Mass) (kg, iDXA): MITAX; MYOACT	0.341; 0.368	0.012; 0.007
BMR (Basal Metabolic Rate) (kcal): MITAX; MYOACT	0.336; 0.351	0.014; 0.010
FFM (Fat Free Mass) (kg): MITAX; MYOACT	0.338; 0.356	0.014; 0.009
BF% (iDXA); BF% (BIA): CRP (C-reactive protein) (mg/L)	0.276; 0.306	0.035; 0.025
ECM/BCM: MMT-8 (Manual Muscle Testing-8)	-0.385	0.006
BF% (iDXA): FI-2 (Function Index-2)	-0.311	0.026
BF% (iDXA): HAP (Human Activity Profile)	-0.292	0.032

Methods: 54 patients with IIM (45 females; mean age 57.7; disease duration 5.8 years; polymyositis (PM, 22) / dermatomyositis (DM, 25) / necrotizing myopathy (IMNM, 7)) and 54 age-/sex-matched HC (45 females, mean age 57.7) without rheumatic/tumor diseases were included. PM/DM patients fulfilled Bohan/Peter criteria for PM/DM. We assessed body composition (densitometry: iDXA Lunar, bioelectric impedance: BIA2000-M), physical activity (Human Activity Profile (HAP) questionnaire, serum levels of 27 cytokines/chemokines (commercial multiplex ELISA kit, Bio-Rad Laboratories) and serum levels of chosen parameters of nutrition and lipidogram. Disease activity (MITAX and MYOACT activity score) and muscle involvement (manual muscle test, MMT-8, and functional index 2, FI2) were evaluated. Data are presented as mean±SD.

Results: Compared to HC, patients with IIM had a trend towards significantly increased body fat % (BF%) as assessed by iDXA, but significantly decreased lean body mass (LBM) as assessed both by iDXA and BIA, and increased extracellular mass/body cell mass (ECM/BCM) ratio reflecting worse muscle predispositions for physical exercise, aerobic fitness/performance, and deteriorated nutritional status. Compared to HC, IIM patients had significantly lower bone mineral density (BMD) (Table 1). Disease duration negatively correlated with BMD and LBM-BIA. Disease activity assessed by both MITAX and MYOACT positively correlated with LBM (by BIA and iDXA), similarly as with basal metabolic rate (BMR) and fat free mass (FFM). CRP was positively associated with BF% (by iDXA and BIA). Higher BF%-iDXA was associated with worse physical endurance (Function Index-2, FI-2) and worse ability to perform physical activity (HAP). MMT-8 score negatively correlated with ECM/BCM ratio (Table 2). Serum levels of several inflammatory cytokines/chemokines (Table 3) and markers of nutrition and lipid metabolism were associated with alterations of body composition (Table 4 and 5).

Conclusion: Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our IIM patients, which are associated with their disease activity and duration, inflammatory status,

Table 3: Correlation of body composition parameters and serum levels of inflammatory cytokines/chemokines (pg/mL)		
Correlated parameters	**r**	**p-value**
IL-1ra: BMI (Body Mass Index); BF%; VF (Visceral Fat, kg)	0.359; 0.363; 0.409	0.009; 0.009; 0.003
MCP-1: ECM/BCM (Extracellular Mass/Body Cell Mass ratio)	0.387	0.005
IL-10: LBM	-0.473	0.014
Table 4: Correlation of body composition parameters and serum parameters of nutrition.		
Correlated parameters	**r**	**p-value**
Albumin (g/dL): ECM/BCM (Extracellular Mass/Body Cell Mass ratio)	-0.325	0.019
C3 (complement C3, g/L): FM (Fat Mass; kg, iDXA); FM (kg, BIA); BF% (Body Fat %, iDXA); BF% (BIA) VF (kg); A/G (Android/Gynoid ratio); BMI (body Mass Index)	0.590; 0,503; 0.500; 0.475; 0.505; 0.488; 0.471	<0,001; <0,001; <0,001; <0.001; <0,001; <0.001; <0.001
C4 (complement C4, g/L): BF% (BIA); ECM/BCM (Extracellular Mass/Body Cell Mass ratio)	0.284; -0.299	0.041; 0.031
Cholinesterase (µkat/L): VF (Visceral Fat, kg); A/G (Android/Gynoid ratio); FM (Fat Mass; kg, iDXA); FM (kg, BIA); BF% (Body Fat %, BIA)	0.475; 0.502; 0.298; 0.319; 0.308	<0,001; <0.001; 0.036; 0.021; 0.026
AMS (Amylase, µkat/L): LBM (Lean Body Mass; kg, iDXA); LBM (kg, BIA); FFM (Fat Free Mass; kg, iDXA); VF (Visceral Fat, kg)	-0.397; -0.461; -0.381; -0.344	0.004; <0.001; 0.006; 0.013
Insulin (µU/mL): FM (Fat Mass; kg, iDXA); FM (kg, BIA); BF% (Body Fat %; BIA); VF (Visceral Fat; kg, iDXA); A/G (Android/Gynoid ratio); LBM (Lean Body Mass; kg, iDXA); LBM (kg, BIA); FFM (Fat Free Mass; kg, iDXA); BMI (Body Mass Index)	0.654; 0.560; 0.488; 0.564; 0.563; 0.361; 0.412; 0.365; 0.518	<0.001; <0.001; <0.001; <0.001; <0.001; 0.010; 0.002; 0.009; <0.001
C-peptide (ng/mL): FM (Fat Mass; kg, iDXA); FM (kg, BIA); VF (Visceral Fat; kg, iDXA); A/G (Android/Gynoid ratio); LBM (Lean Body Mass; kg, iDXA); LBM (kg, BIA); FFM (Fat Free Mass; kg, iDXA); BMI (Body Mass Index)	0.396; 0.342; 0.348; 0.317; 0.341; 0.367; 0.349; 0.452	0.005; 0.014; 0.013; 0.025; 0.015; 0.008; 0.013; <0.001
Vitamin D (calcidiol, 25(OH)D, nmol/L): FM (Fat Mass; kg, iDXA); FM (kg, BIA); BF% (Body Fat %; BIA); LBM (Lean Body Mass; kg, BIA); BMI (Body Mass Index)	-0.386; -0.305; -0.290; -0.319; -0.374	0.006; 0.028; 0.036; 0.021; 0.006
Calcitriol (1,25(OH)D, pmol/L): ECM/BCM (Extracellular Mass/Body Cell Mass ratio)	-0.322	0.020
Orosomucoid (mg/dL): BF% (Body Fat %; BIA)	0.285	0.041
Table 5: Correlation of body composition parameters and serum parameters of lipid metabolism.		
Correlated parameters	**r**	**p-value**
TAG (Triacylglyceroles, mmol/L): FM (Fat Mass; kg, iDXA); FM (kg, BIA); BF% (Body Fat %, iDXA); BF% (BIA); VF (Visceral Fat; kg, iDXA); BMI (body Mass Index)	0.416; 0.357; 0.450; 0.424; 0.409; 0.291	0.003; 0.009; <0.001; 0.002; 0.003; 0.036
HDL (High-density Lipoprotein, mmol/L): FM (Fat Mass; kg, iDXA); FM (kg, BIA); BF% (Body Fat %, iDXA); BF% (BIA) VF (Visceral Fat; kg, iDXA); A/G (Android/Gynoid ratio)	-0.347; -0.368; -0.372; -0.366; -0.335; -0.355	0.013; 0.007; 0.007; 0.008; 0.016; 0.010
Atherogenic index (AI): FM (Fat Mass; kg, iDXA); FM (kg, BIA); BF% (Body Fat %, iDXA); BF% (BIA); VF (Visceral Fat; kg, iDXA); A/G (Android/Gynoid ratio)	0.400; 0.396; 0.421; 0.417; 0.393; 0.331	0.004; 0.004; 0.002; 0.002; 0.004; 0.018
ApoA (Apolipoprotein A, g/L): LBM (Lean Body Mass; kg, iDXA); LBM (kg, BIA); FFM (Fat Free Mass; kg, iDXA);	-0.353; -0.372; -0.347	0.012; 0.007; 0.014
ApoB (Apolipoprotein B, g/L): VF (Visceral Fat; kg, iDXA); BF% (Body Fat %, BIA)	0.283; 0.284	0.046; 0.043
Non-HDL (Non-High-density lipoprotein, mmol/L): BF% (Body Fat %, iDXA); BF% (BIA)	0.294; 0.285	0.036; 0.040

skeletal muscle involvement, and physical activity. These data could reflect their impaired nutritional status and predispositions for physical exercise, aerobic fitness and performance. Serum levels of certain inflammatory cytokines/chemokines and markers of nutrition and lipid metabolism were associated with alterations of body composition in IIM patients.

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Abstract Number: 1868

Clinical Correlations of Autoantibodies Against Heat Shock Cognate 71 kDa Protein in Patients with Juvenile Dermatomyositis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Muscle Biology, Myositis & Myopathies I
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Juvenile dermatomyositis (JDM) is an inflammatory myopathy characterized by prominent vascular and perivascular inflammation in affected skeletal muscles. The mechanisms of vessel injury in JDM remain unknown. Anti-endothelial cell antibodies (AECA) are frequently detected in inflammatory, infectious, and autoimmune diseases. We hypothesized that autoimmunity to blood vessel antigens may play a role in the pathology of JDM. We therefore, used proteomic approaches to identify target antigens for AECA in plasma from patients with JDM.

Methods: Proteins extracted from human aortic endothelial cells (HAEC) were separated by two-dimensional electrophoresis and transferred onto membranes. Western blotting using plasma from JDM and healthy controls was performed to detect antigens that were positive in JDM plasma, but not in healthy controls. Finally, the detected proteins were identified by peptide mass finger-printing. We next used ELISA assays to corroborate the mass spectrometry data, using plasma samples from 63 patients with JDM, 50 patients with polyarticular juvenile idiopathic arthritis (JIA) and 40 sex- and age-matched healthy controls. Nineteen patients with Kawasaki disease (KD) and 18 additional sex- and age-matched healthy controls were also used for ELISA assays. The differences in antibody levels and the frequency of autoantibodies between the groups were compared by Mann-Whitney U test and by Fisher's exact test, respectively. P values were determined with a two-tailed tests.

Results: Twenty-two proteins were identified as candidate targets of AECA in plasma from JDM patients. Among these antigens were molecular chaperones such as heat shock cognate 71 kDa protein (HSC70). On ELISA assays,

we found significant differences (p< 0.0001) in mean OD ± SD for autoantibodies against HSC70 when children with JDM were compared to healthy controls, and to children with JIA and KD. Autoantibodies to HSC70 were detected in 35% of patients with JDM, in 0% of healthy donors (P< 0.0001), 0% of patients with JIA (P< 0.0001), and 0% of patients with KD (P=0.002). The presence of autoantibodies against HSC70 correlated with the presence of other previously described myositis-associated autoantibodies (MAA). For example, antibodies against NT5C1A and Ro52 were more frequent in patients with autoantibodies against HSC70 than with these MAAs alone (69% vs. 29%, P=0.013 and 43% vs. 15%, P=0.027). The presence of skin ulcers was associated with autoantibodies against HSC70 (59% vs. 17%, P=0.0014). Use of wheelchairs and/or devices was associated with HSC70 autoantibodies (64% vs. 27%, P=0.007). We found significant differences (P=0.019) in mean serum levels of aspartate aminotransferase (AST) in JDM children with (32 ± 15 U/L) vs. without (25 ± 16 U/L) autoantibodies against HSC70.

Conclusion: Autoantibodies to HSC70 in the proteome of HAEC are present in the plasma of patients with JDM, implying that AECA may be involved in the pathophysiology of autoimmune inflammation of blood vessels in JDM. Larger studies will be required to determine the clinical utility of monitoring for these autoantibodies.

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Abstract Number: 1869

Myeloid Dendritic Cells (mDCs) Are Major Producers of Interferon-β in Dermatomyositis and Higher Numbers of mDCs Are Found in Hydroxychloroquine Nonresponders

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Muscle Biology, Myositis & Myopathies I
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Dermatomyositis (DM) is an autoimmune disease affecting the skin, skeletal muscle, lungs, and/or other organs. While the pathogenesis remains poorly understood, it is thought to be driven largely by type 1 interferons (IFN-β) and involve CD4+ cells and dendritic cells. Plasmacytoid dendritic cells (pDCs) are considered major producers of type 1 interferons. Our objectives were as follows: 1) to quantify inflammatory cells and Type 1 IFN expression in skin and correlate with the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) skin activity score, 2) to identify cells contributing to refractoriness to hydroxychloroquine (HCQ), 3) to identify the major dendritic cell type producing IFN-β in DM.

Methods: In Aim 1, we evaluated lesional skin biopsies from 12 patients with moderate-severe cutaneous DM at baseline and from a nearby skin site after 12 weeks of treatment with lenabasum or placebo added to stable standard of care. Immunohistochemistry (IHC) was performed to assess expression of Type 1 IFN and various cell types [CD4+,

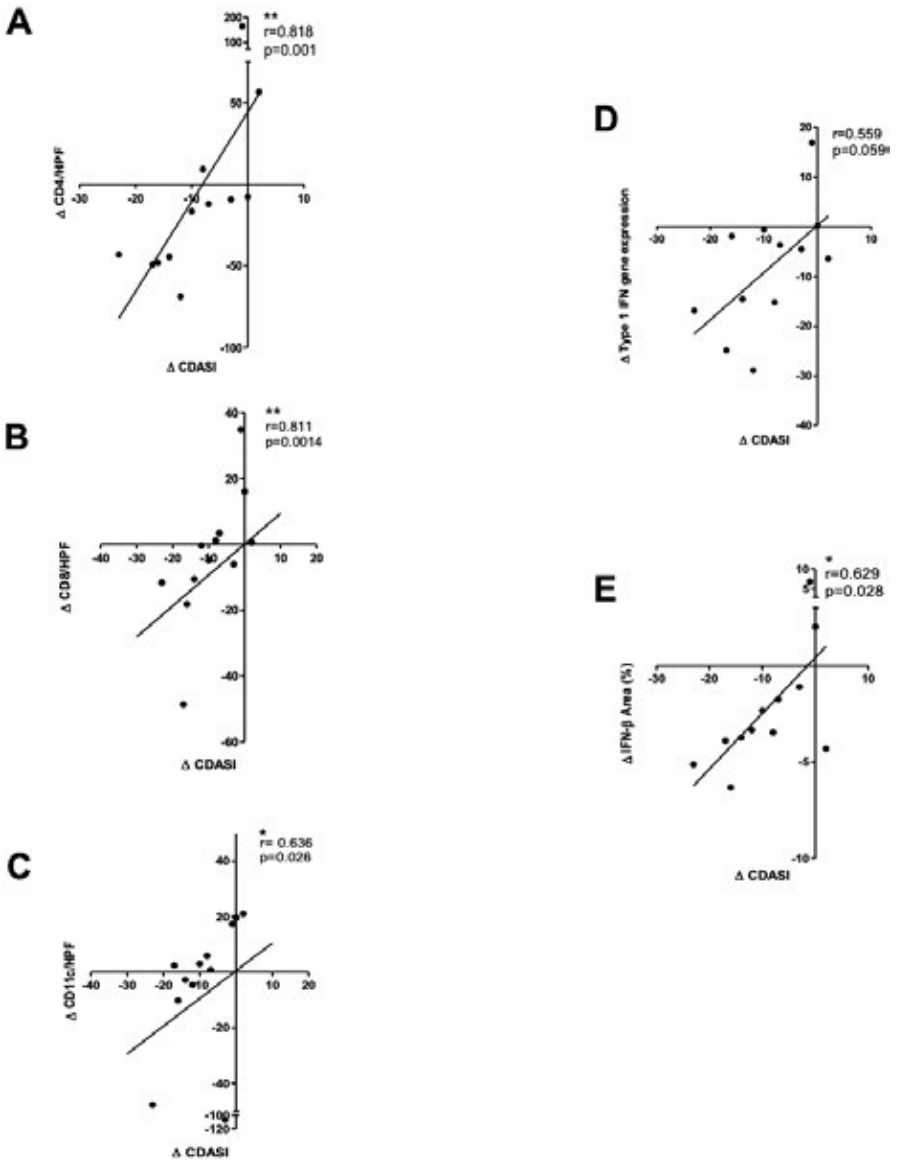

Figure 1. Change in CD4+/HPF, CD8+/HPF, and CD11c+/HPF significantly correlate with change in CDASI ($p < 0.05$). Change in Type 1 IFN gene expression and change in IFN-bβ protein expression correlate with change in CDASI.

macrophages, mDC (CD11c+), tissue-resident memory T (T_{RM}) cells (CD69+), CD8+, mast cells, and pDC (CD123+)] and relationship with CDASI activity scores. RT-PCR was performed to measure Type 1 IFN gene expression. In Aim 2, HCQ responders and HCQ nonresponders were identified from a longitudinal DM database where responsiveness to HCQ was defined as sufficient improvement in skin lesions so that further escalation of therapy was not needed. IHC was performed on lesional skin biopsies to compare mDC and pDC expression. In Aim 3, flow cytometry was performed on PBMCs from 5 healthy controls and 5 DM patients to identify whether mDCs or pDCs were predominant producers of IFN-β in the two study populations. PBMCs were stimulated with Resiquimod (R848). Analysis was performed using FlowJo software. Statistical analysis included the Spearman rank correlation test and the Mann-Whitney test.

Results: In Aim 1, we found CD4+, macrophages, mDCs, and T_{RM} cells were the most populous cells in DM lesional skin, followed by CD8+ cells, mast cells, and pDCs. Change in CD4+ cells/HPF, CD8+ cells/HPF, and mDCs/HPF significantly correlated with change in CDASI scores ($r = 0.818$, $p = 0.001$; $r = 0.811$, $p = 0.001$; $r = 0.636$, $p = 0.026$, respectively) (Fig. 1). Change in Type 1 IFN gene expression correlated with change in CDASI score ($r = 0.559$, p

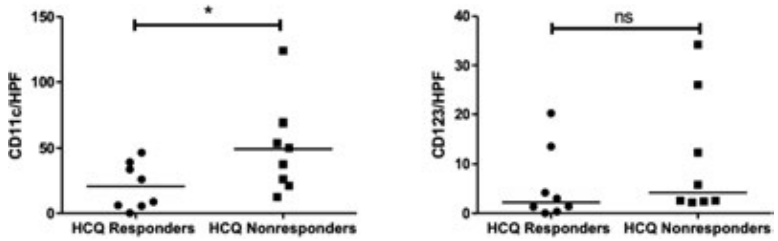

Figure 2. HCQ nonresponders have significantly more mDC (CD11c+)/HPF compared to HCQ responders ($p < 0.05$). There is no significant difference in pDC (CD123+)/HPF between HCQ responders and nonresponders.

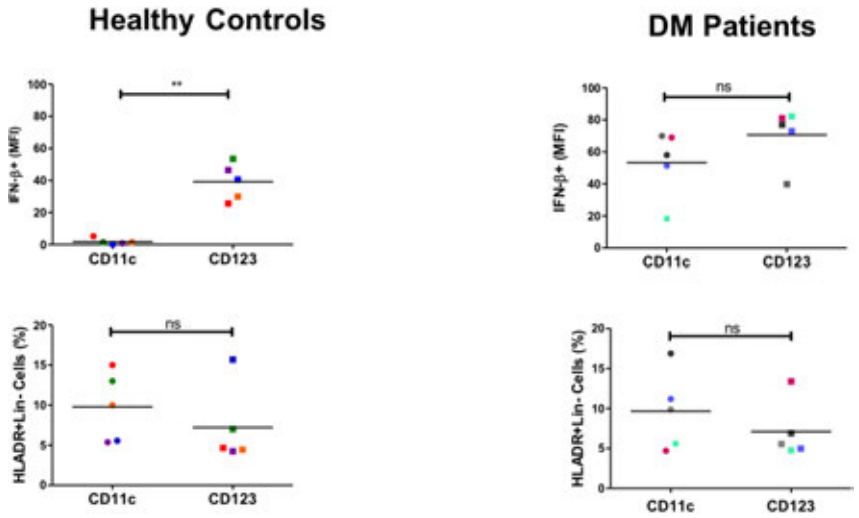

Figure 3. IFN-b β is produced by both mDCs (CD11c+)/HPF and pDCs (CD123+)/HPF in DM patients. IFN-bβ is produced predominantly by pDCs (CD123+)/HPF in healthy controls.

= 0.059) as did change in IFN-β protein expression ($r = 0.629$, $p = 0.028$) (Fig. 1). In Aim 2, significantly increased numbers of mDCs/HPF were found in skin of HCQ nonresponders ($p < 0.05$) (Fig. 2). In Aim 3, we found both mDCs and pDCs were major producers of IFN-β in DM patients; there was no significant difference in IFN-β production between the 2 cell types (Fig. 3). In contrast, in PBMCs from healthy controls, pDCs produced significantly more IFN-β compared to mDCs ($p < 0.01$) (Fig. 3). There was no significant different in percentage of mDCs vs. pDCs in healthy controls or DM patients (Fig. 3).

Conclusion: mDCs appear to play a significant role in DM pathogenesis. mDCs are major producers of IFN-β in DM patients but not in healthy controls. Increased numbers of mDCs are found in HCQ nonresponders.

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Abstract Number: 1870

NMR-Based Serum, Urine and Muscle Metabolomics in Inflammatory Myositis for Diagnosis and Activity Assessment: Serum Metabolomics Can Differentiate Active from Inactive Myositis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Muscle Biology, Myositis & Myopathies I

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

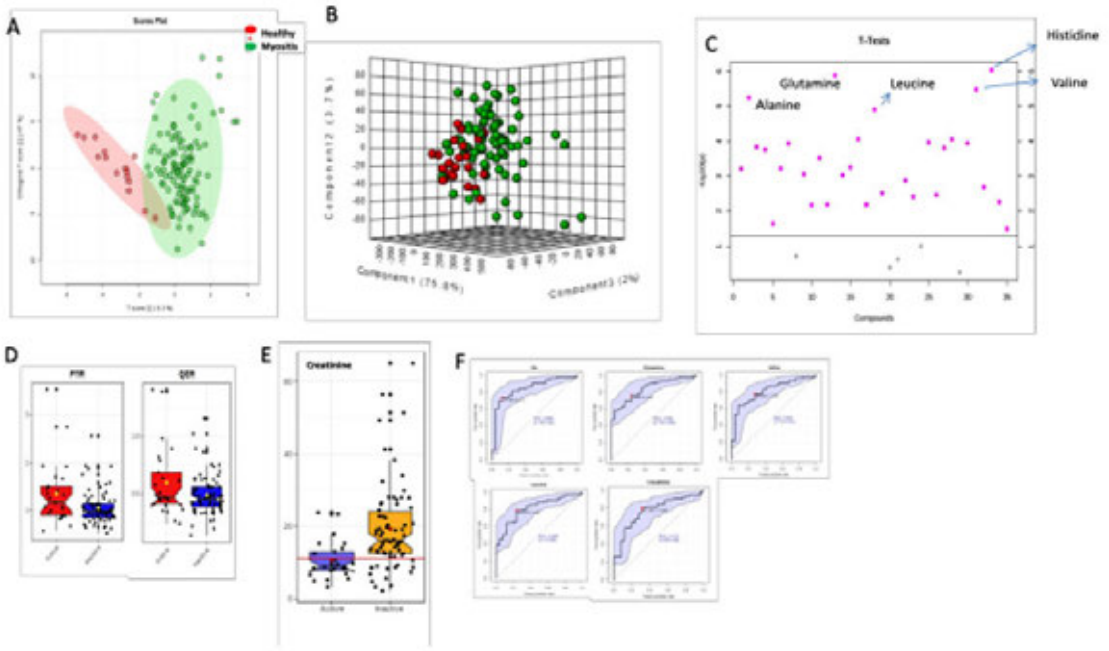

Figure 1: Serum metabolomics

(A) 3D score plot obtained from PCA analysis of 1D ^{1}H CPMG NMR based serum metabolic profiles showing clustering and separation between Healthy control and inflammatory myositis patients **(B)** 2D score plot after PCA analysis of sera from myositis patients with active and inactive disease **(C)** screening of metabolites responsible for the group separation in the score plot identified based on variable importance in projection (VIP) score > 2.0 **(D)** VIP projection suggesting elevated phenylalanine-to-tyrosine ratio (PTR) and Glutamate to Glutamine ration (EQR) **(E)** VIP projection suggesting creatinine is significantly decreased in the sera of active myositis patients **(F)** representative ROC curves of discriminatory metabolites

Background/Purpose: Differentiating smouldering disease activity from weakness due to fatty replacement of atrophied muscle can often be a challenge in Idiopathic Inflammatory Myositis (IIM). There is dearth of biomarkers that can distinguish active from inactive myositis.

To identify changes in metabolomics profiles in serum, urine and muscle of patients with myositis with active and inactive disease. Since we have previously found exquisite separation between paired serum samples obtained in fasting and non-fasting state, only sera collected in fasting state were taken for analysis.

Methods: Sera (n=116), urine (n=114) and muscle (n=11) from patients classifiable as myositis by the ACR-EULAR criteria [34 years (23.5 - 50.5 IQR), M/F 28:88] were compared with healthy controls [n=18 and 12 respectively, age= 44 (35-50) years, M/F-8:10]. For the muscle biopsies, two disease controls were used for comparison. To study effect of fasting state on urine metabolomics, 50 paired urine samples obtained in fasting and non-fasting states were analysed. Metabolic profiles were obtained at 800 MHZ NMR spectrometer and compared using multivariate partial least-squares discriminant analysis (PLS-DA). The discriminatory metabolites were identified based on variable importance in projection (VIP) statistics and further evaluated for statistical significance (p-value < 0.05). Paired T tests were done for metabolites in urine and muscle after normalizing for creatinine. MDAAT >=1 was used to define active myositis.

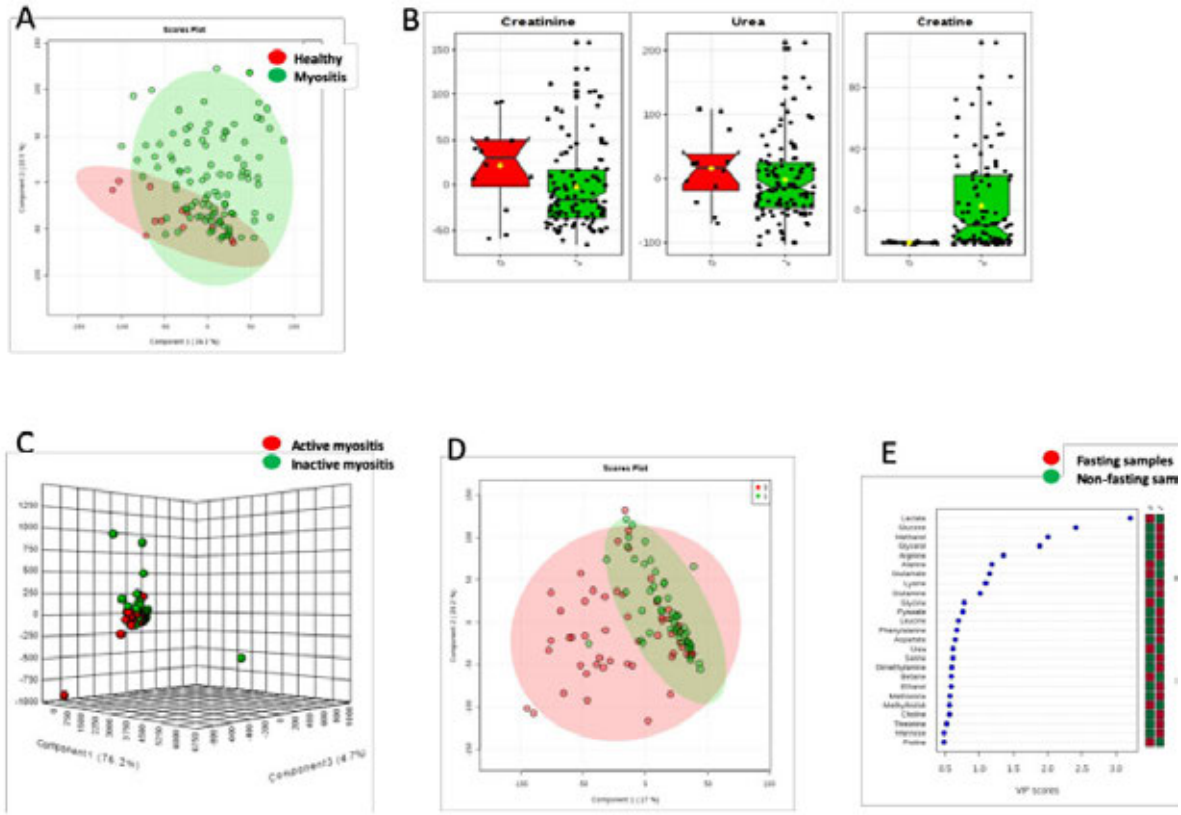

Figure 2: Urine Metabolomics
A) 3D score plot obtained from PCA analysis of 1D ^{1}H CPMG NMR based urine metabolic profiles showing clustering and separation between healthy control and inflammatory myositis patients **(B)** VIP projection suggesting elevated creatinine, and low urea and creatine in myositis versus healthy controls. **(C)** PCA suggests no differential clustering between active and inactive myositis. **(D)** In urine, paired samples obtained in fasting versus non-fasting state were fairly similar, **(E)** apart from differences in Creatine and Creatinine.

Results: Metabolomics profiles in IIM were distinct from healthy controls (Fig. 1A). Sera of patients with active myositis exhibited differential clustering from those with inactive myositis (Fig. 1B) with lower amino-acid metabolites (Fig. 1C) elevated phenylalanine-to-tyrosine ratio and glutamate to glutamine ratio (Fig. 1D) and low creatinine (Fig. 1E) with significant discriminatory potential (Fig. 1F). Urine of myositis patients exhibited higher creatine and lower urea and creatine than healthy controls (Fig. 1A, B). However, urine metabolomics exhibited similar clustering in active and inactive disease (Fig. 1C). In urine, paired samples in fasting and non-fasting state exhibited overlapping clustering (Fig. 1D) apart from higher creatine and creatinine (Fig. 1E) . Muscle of patients with inflammatory myositis exhibited almost absent levels of sucrose, mannose, uridine, histamine, inosineand carnitine compared with infection associated myositis.

Conclusion: Serum and urine metabolomics of myositis is distinctive. Serum metabolomic profiling using NMR has the potential to discriminate active from inactive myositis patients though urine metabolomics is largely non-contributory. Muscle metabolites holds potential to distinguish inflammatory myositis from infectious polymyositis.

Disclosure: L. Gupta, APLAR, 2; **D. Kumar**, None; **U. Kumar**, None; **A. Guleria**, None; **A. Zanwar**, None; **R. Raj**, None; **R. Misra**, None.

Abstract Number: 1871

Myositis-Specific Antibodies and Muscle Histopathology in Juvenile Dermatomyositis: New Insights into the Mechanism of Injury

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Muscle Biology, Myositis & Myopathies I
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Background/Purpose: Myositis-specific antibodies (MSAs) are identified in over half of children with JDM and are associated with distinct clinical phenotypes. MSA subtype, in combination with clinical or muscle histopathology findings, may have prognostic value and implications for disease monitoring and treatment. The aim of this study is to define the relationships between MSAs and muscle histopathology as well as clinical markers of disease activity in children with JDM.

Methods: A retrospective chart review of subjects with JDM followed in the pediatric rheumatology clinic at a single center between October 2016 and November 2018 was performed. Markers of JDM disease activity, including muscle enzymes (creatine kinase (CK), aldolase, lactate dehydrogenase, aspartate aminotransferase, and alanine transaminase) and other clinical data were obtained at the initial visit and at 6 months. MSA serum levels were measured at a single point during the disease course. Muscle biopsy samples, routinely obtained at diagnosis, were reviewed and scored independently by 2 neuropathologists using a visual analog scale. Mann-Whitney tests were conducted to detect differences between the most prevalent MSA subtypes. Pearson correlation coefficient (r) was conducted to analyze the correlation between MSA subtype and CK.

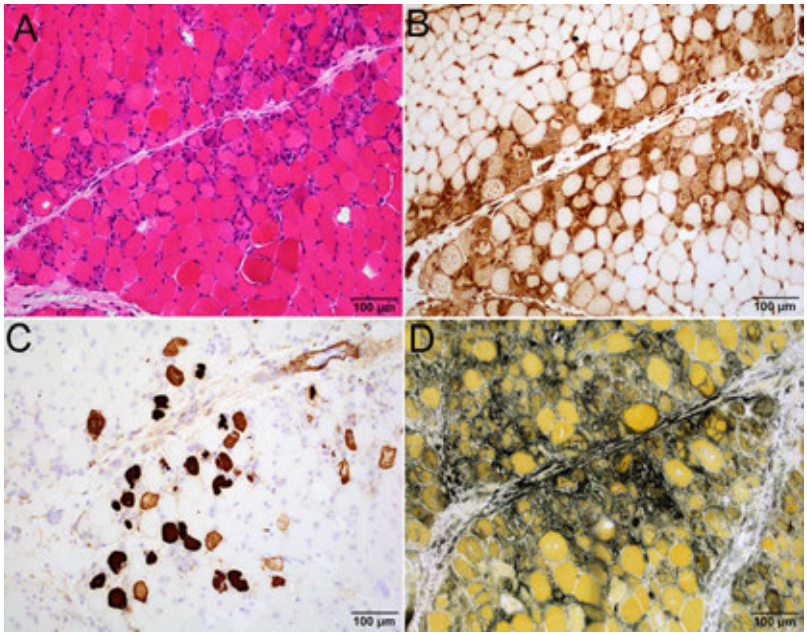

Figure 1. Twelve-year-old female with high anti-Mi-2 serum titer; quadriceps muscle shows prominent perifascicular necrotizing myopathy. (A) H&E shows abundant necrotic and regenerating fibers concentrated in perifascicular region. (B) MHC-1 is upregulated in perifascicular myofibers. (C) C5b-9 highlights necrotic fibers. There is no significant capillary deposition. (D) Alkaline phosphatase shows strong reactivity in regenerating fibers as well as in perimysial and endomysial connective tissue.

Results: Out of the 43 subjects in the study, 26 (60.5%) had a detectable MSA. The most common MSAs were anti-NXP-2 (13, 30.2%), anti-Mi-2 (7, 16.3%), and anti-MDA-5 (5, 11.6%). Other MSAs detected included anti-SRP, anti-Tif-1g, anti-OJ, and anti-PL-7.

Subjects with high titer anti-Mi-2 had more widespread perifascicular myofiber damage and perifascicular necrotizing myopathy (Figure 1). Subjects with high titer anti-NXP-2 had more prominent capillary C5b-9 deposition, indicative of vascular injury, and myofibers showed perifascicular atrophy and/or focal infarct but minimal perifascicular myofiber necrosis (Figure 2). All subjects with anti-MDA-5 had normal CK and normal muscle histology, consistent with previous reports of amyopathic or hypomyopathic disease. The subject with anti-PL-7 showed perifascicular necrotizing myopathy with diffuse MHC-1 upregulation on histopathology, consistent with the pattern seen in antisynthetase syndrome.

High titer anti-Mi-2 correlates with serum CK > 10,000 ($r=0.96$, $p=0.002$) (Figure 3). With the exception of a subject with anti-PL-7, no other MSA subtypes had a CK > 5000 at the initial visit. Anti-Mi-2 had a higher CK at initial visit compared to anti-NXP-2 ($p=0.04$) and anti-MDA-5 ($p=0.05$). In general, anti-Mi-2 was significantly associated with higher muscle enzymes, except for aldolase. There is no correlation between anti-NXP-2 titer and CK ($r=-0.21$, $p=0.49$) (Figure 3).

Conclusion: The mechanism of injury for patients with JDM differs based on MSA subtype: anti-Mi-2 is associated with direct myofiber damage; anti-NXP-2 is associated with vascular injury; and anti-MDA-5 is associated with minimal to no muscle injury. Serum CK, a clinical marker of disease activity, varies based on MSA subtype: anti-Mi-2 titer correlates with serum CK; anti-NXP-2 titer does not correlate with serum CK; and anti-MDA-5 is associated with normal serum CK.

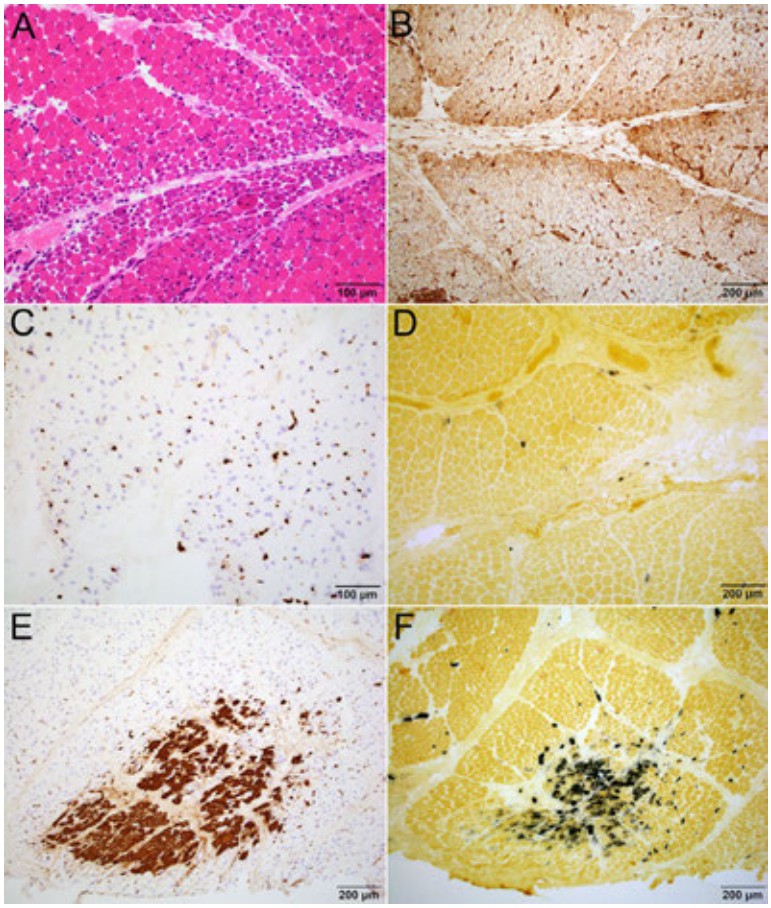

Figure 2. Two-year-old female with high anti-NXP-2 serum titer; thigh muscle shows prominent perifascicular atrophy, capillary C5b-9 deposition, and infarct. (A) H&E shows prominent perifascicular atrophy without significant myofiber necrosis. (B) MHC-1 is upregulated in perifascicular myofibers. (C) C5b-9 shows prominent capillary C5b-9 deposition. (D) Alkaline phosphatase shows no regenerating fibers or connective tissue reactivity. (E-F) Focal area of infarction is highlighted by C5b-9 stain (E) and alkaline phosphatase (F). The area of infarct is located in the center of a fascicle, and is composed of back-to-back, rather than scattered, necrotic fibers.

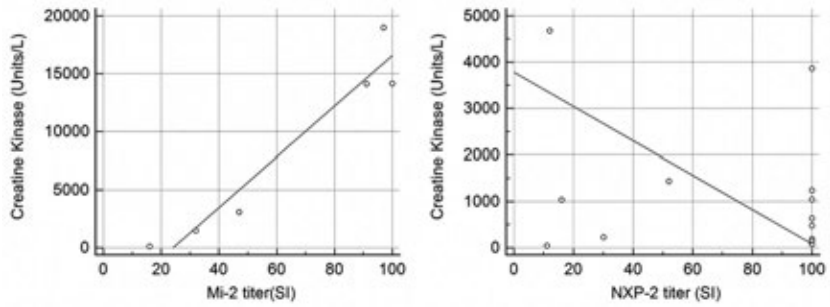

Figure 3. (left) Anti-Mi-2 titer strongly correlates with serum CK (r=0.96; p=0.002) and degree of myofiber damage. (right) Anti-NXP-2 titer does not correlate with serum CK (r=-0.21; p=0.49).

Disclosure: M. Nguyen, None; **V. Do**, None; **P. Yell**, None; **C. Jo**, None; **J. Liu**, None; **T. Wright**, None; **C. Cai**, None.

Abstract Number: 1872

Worsening Trends in Osteoporosis Management in the Medicare Population: 2010-2014

Jeffrey Curtis ,[1] Shanette G. Daigle,[2] Setareh A. Williams,[3] Richard Weiss,[3] Yamei Wang,[4] and Tarun Arora[2], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham, Birmingham, [3]Radius Health, Inc, Waltham, [4]Radius Health, Inc, Waltham

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Osteoporotic fractures are an important public health burden, and with an increasing aging population, the number of Americans at risk of fractures is projected to increase 33% by 2030. The objective of this study was to evaluate osteoporosis management in Medicare enrollees.

Methods: This study included Medicare fee-for-service (FFS) members with a closed fragility (or osteoporosis-related) fracture between 01/01/2010-12/31/2014. Cohort characteristics were computed yearly for 2010-2014 in order to examine secular trends in osteoporosis management. Inclusion criteria for cohort eligibility was age ≥65 at index date, continuous enrollment in Medicare FFS with medical and pharmacy benefits for ≥1 year before index date. Patients with Paget's disease or malignancy (except non-melanoma skin cancer) at baseline were excluded.

Results: Of 18,936,386 beneficiaries, 885,676 had fracture(s) and met eligibility criteria. Average age was 80.5(±8.4) years, 90.9% were white, and 93.8% female. Over half of patients in each yearly cohort had a comorbidity or a medication that increased fall risk, with approximately 50% of patients using opioids. Despite increased fall risk, osteoporosis diagnosis, screening, and treatment rates at baseline were low and decreased from 2010-2014: DXA: 25%, 24%, 23%, 22%,16%; diagnosis: 7%, 6%, 6%, 5%, 4%; treatment: 29%, 24%, 20%, 16%, 11%. A trend toward lower OP diagnosis and treatment utilization over time was observed.

Conclusion: These findings suggest continued and perhaps worsening osteoporotic fracture management over time. Opportunities exist to better identify and treat patients who have an increased risk of fracture.

Disclosure: J. Curtis, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **S. Daigle**, Radius Health, Inc., 9; **S. Williams**, Radius Health, Inc., 1, 3; **R. Weiss**, Radius Health, Inc., 1, 3; **Y. Wang**, Radius Health, Inc., 1, 3; **T. Arora**, Radius Health, Inc., 9.

Abstract Number: 1873

Geisinger HiROC Performance 2017-2018: Continuing to Narrow the Post-Fracture Treatment Gap

Thomas Olenginski ,[1] and Karen Mackiewicz[2], [1]Geisinger Medical Center, Danville, PA, [2]Geisinger, Danville, PA

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: The morbidity and mortality of osteoporotic fractures threaten our aging population. Despite advances in new therapies for osteoporosis and technology to more effectively communicate, fewer than 20 % of patients who break a bone will receive a medical evaluation and/or treatment for osteoporosis. Since 2008, Geisinger has operated a Fracture Liaison Service (FLS) termed HiROC (High-Risk Osteoporosis Clinic). Descriptions of our program and performance have been published (References 1,2,3). We report our 2017-2018 performance and summarize a decade of successful FLS care.

Methods: All inpatient HiROC fracture consultations seen by Rheumatology at Geisinger Medical Center-Danville or Geisinger Wyoming Valley- Wilkes Barre from 1/1/2017 through 12/31/2018 were identified in our database. An excel spreadsheet was constructed and the following demographic and clinical variables were extracted: mean age; sex; fracture site; Geisinger Health Plan (GHP) insurance (%); early death (up to 6 months post-fracture); later death (> 6 months post-fracture); osteoporosis treatment given. Specifically, we were held 'responsible' to initiate treatment in a High-Risk patient if they were seen in our outpatient HiROC clinical pathway post-discharge and did not have a medical contraindication, as this is the highest quality metric in post-fracture care. We report the outcomes of this retrospective analysis and summarize our first decade of HiROC care and performance.

Results: 740 inpatient consultations were seen, of which 74 % were women and 26 % men. Fracture sites were hip (femoral neck or intertrochanteric) 77.6 %; vertebrae 5.3 %; distal femur 3.5 %; mid shaft/subtrochanter 2.8 %; pelvis 2.4 %; wrist 1.9 %; periprosthetic 1.9 %; and other 4.6 %. Early deaths comprised 14 % of cohort and 7 % were later deaths. HiROC followup was accepted by 336 patients, 45 % of cohort. Of 288 patients drug eligible, 207/288 patients or 72 % of HiROC followed patients were initiated on an FDA-approved medication. Treatments utilized included intravenous zoledronic acid in 73 (35 %); oral bisphosphonates in 70 (34 %); denosumab in 54 (26 %); and anabolic agents in 10 (5 %). GHP insurance accounted for 256 (35 %) of entire cohort (Tables 1,3).

Conclusion: Geisinger HiROC reports treatment in 72 % of post-fracture patients who were followed in their outpatient clinical pathway. Prior performance analyses show HiROC treatment rates of 75-80 % (Table 2). Despite

Table 1. 2017-2018 HiROC Demographics

N = 740 patients
Mean Age 78
Women 545 (74 %)
Men 195 (26 %)
HiROC outpatient followup 336 (45 %)
HiROC treatment eligible 288
HiROC treated 207(72 %)
A) Zoledronic Acid 73 (35 %) B) Oral bisphosphonate 70 (34%) C) Denosumab 54 (26 %) D) Anabolic 10 (5 %)
Early Death 105 (14 %)
Later Death 53 (7 %)
GHP Insurance 256 patients (35 %)

Table 2. Geisinger HiROC Treatment Rates

2008-2011	80 %
2013-2015	75 %
2016	75 %
2017-2018	72 %

Table 3. Fractures Sites HiROC (2017-2018 and 2008-2018)

Fracture Sites	HiROC 2017-2018	HiROC 2008-2018
Hip	574	2183
Vertebrae	39	302
Mid-shaft/subtrochanter	21	190
Distal femur	26	144
Periprosthetic	14	152
Pelvis	18	142
Wrist	14	75
Other	34	512

our program's maturity, we face several ongoing barriers: patient activation/engagement and fear of FDA-approved medications; access to and/or cost of parenteral medications or anabolic agents; and inability to use database to capture care gaps in real time and correct/solve them. We hope that our work will inspire others in rheumatology to implement FLS care.

References:

1. Olenginski, TP et al. HiROC: improving osteoporosis and postfracture care with an organized, programmatic approach. Osteoporos Int 2015;26(2):801-810.
2. Dunn P et al. Geisinger HiROC: 2013-2015 FLS performance analysis. Osteoporos Int 2018; 29(2):451-457.
3. Olenginski TP et al. HiROC performance measurements:2016, presented at ISO/NOF meeting 2017

Disclosure: T. Olenginski, Amgen, 8, Radius, 8; **K. Mackiewicz**, None.

Abstract Number: 1874

Extensive Modeling-Based Bone Formation After 2 Months of Romosozumab Treatment: Results from the FRAME Clinical Trial

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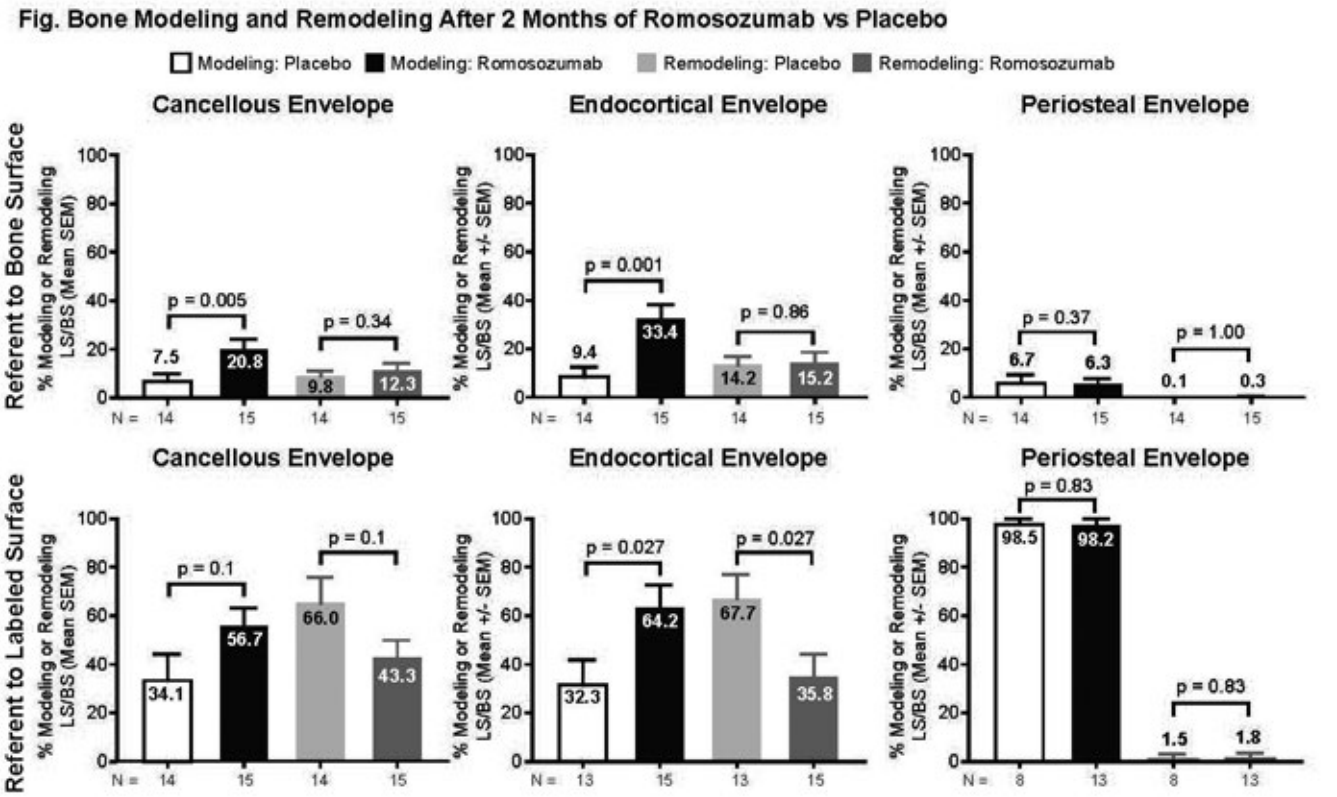
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: The bone-forming agent romosozumab (Romo) is a monoclonal antibody that binds to/inhibits sclerostin, leading to increased bone formation and decreased bone resorption. The highest levels of bone formation markers in human subjects are observed in the first 2 months of treatment (McClung, NEJM 2014). Studies in cynomolgus monkeys demonstrated that most new bone formation following Romo treatment was modeling-based (MBBF; Ominsky, JBMR 2014). Histomorphometric analysis of bone biopsies in a substudy of the FRAME trial (NCT01575834) showed an early significant increase in bone formation with concomitant decreased resorption (Chavassieux, ASBMR 2017). Here we analyzed bone biopsies from FRAME to assess the effect of 2 months of Romo vs placebo (Pbo) on the surface extent of MBBF and remodeling-based bone formation (RBBF) on cancellous (Cn), endocortical (Ec), and periosteal (Ps) envelopes.



N = Number of subjects with evaluable histomorphometry data at timepoint of interest. Nominal p-values are the treatment difference (romosozumab vs placebo) and are based on the Wilcoxon rank-sum test without multiplicity adjustment. BS, bone surface; LS, labeled surface; SEM, standard error of the mean.

(3.28.19 all p values) FRAME Modeling ASBMR 2019 Fig

Methods: In FRAME, postmenopausal women aged ≥55 years with osteoporosis (BMD T-score ≤–2.5 and >–3.5 at the total hip or femoral neck) were randomized 1:1 to 210 mg Romo or Pbo SC QM for 12 months, followed by 60 mg denosumab SC Q6M for 12 months. Subjects in the bone biopsy substudy who had a transiliac biopsy at month 2 received quadruple labeling (double labeling at baseline and prior to biopsy). Unstained, 7 μm bone sections were analyzed by fluorescence microscopy. Histomorphometric parameters were measured separately at the Cn, Ec, and Ps envelopes using an ocular linear test system, randomly rotated between fields of view for unbiased sampling of bone surfaces. At each line intersection of the ocular sampling grid with either single or double tetracycline labels administered at month 2, the underlying cement line was classified as smooth (signifying bone modeling) or scalloped (signifying bone remodeling). The effect of 2 months of Romo vs Pbo on MBBF/RBBF at each envelope referent to bone surface and labeled surface was compared using the Wilcoxon rank-sum test, without multiplicity adjustment.

Results: After 2 months of Romo, MBBF referent to bone surface was significantly increased on Ec and Cn, but not Ps, surfaces with no significant difference in the surface extent of RBBF vs Pbo (Fig.). Romo at month 2 reversed proportions of MBBF/RBBF from approximately 33%/66% in Pbo to 66%/33% in Ec and Cn envelopes.

Conclusion: These data show that stimulation of bone formation in the first 2 months of Romo treatment is predominately due to increased MBBF on the Ec and Cn surfaces.

Disclosure: E. Eriksen, Amgen, 2, 5, Takeda, 2, 5, 8, Ascendis, 5, Lilly, 5, 8, Merck, 5, 8, Mylan, 8; **R. Chapurlat**, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 5, Chugai, 2, MSD, 2, Pfizer, 5, UCB, 2, 5, UCB Pharma, 2, 5; **R. Boyce**, Amgen, 3; **J. Brown**, Amgen, 5, 8, Amgen Inc., 5, 8, Eli Lilly, 5, 8, Lilly, 5, 8, Mereo, 2, Radius, 2, Servier, 2, 5; **S. Horlait**, Amgen, 1, 3; **C. Libanati**, UCB Pharma, 1, 3; **Y. Shi**, Amgen, 1, 3; **R. Wagman**, Amgen, 1, 3; **P. Chavassieux**, Amgen, 2, UCB, 2.

Abstract Number: 1875

Subject Characteristics and Changes in Bone Mineral Density After Transitioning from Denosumab to Alendronate in the Denosumab Adherence Preference Satisfaction (DAPS) Study

David Kendler ,[1] Arkadi Chines,[2] Patricia Clark,[3] Peter R. Ebeling,[4] Michael McClung,[5] Yumie Rhee,[6] Shuang Huang,[2] Robert Kees Stad,[7] and Nick Freemantle[8], [1]University of British Columbia, Vancouver, BC, Canada, [2]Amgen Inc., Thousand Oaks, CA, [3]Hospital Infantil de Mexico Federico Gómez and National University of Mexico, Mexico City, Mexico, [4]Monash University, Melbourne, Victoria, Australia, [5]Oregon Osteoporosis Center, Portland, OR, [6]Yonsei University College of Medicine, Seoul, Republic of Korea, [7]Amgen Inc., Rotkreuz, Zug, Switzerland, [8]University College London, London, England, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: There are limited data on patients transitioning from denosumab (DMAb) to bisphosphonates (BPs). The Denosumab Adherence Preference Satisfaction (DAPS) study (NCT00518531) reported that alendronate (ALN) could maintain the gains in bone mineral density (BMD) achieved with 1 year of DMAb treatment (Freemantle *Osteoporos Int* 2012). Here, we investigate relationships between subject characteristics and their BMD responses after transitioning from DMAb to ALN.

Table. Selected baseline characteristics and percentage change in BMD for subjects who lost, maintained, or gained BMD after transitioning from denosumab to alendronate.

	Lumbar Spine (N = 82)			Total Hip (N = 92)			Femoral Neck (N = 92)		
Subjects stratified by BMD change category from M12 to M24[a]	Lost	Maintained	Gained	Lost	Maintained	Gained	Lost	Maintained	Gained
n (%)	13 (15.9)	52 (63.4)	17 (20.7)	7 (7.6)	75 (81.5)	10 (10.9)	20 (21.7)	56 (60.9)	16 (17.4)
Baseline characteristics	**n = 13**	**n = 52**	**n = 17**	**n = 7**	**n = 75**	**n = 10**	**n = 20**	**n = 56**	**n = 16**
Age (years), mean (SD)	63.8 (5.5)	65.5 (7.7)	64.3 (8.2)	66.4 (8.5)	64.5 (7.1)	68.5 (7.5)	67.1 (8.8)	64.2 (6.7)	65.8 (7.2)
BMD T-score, mean (SD)	−1.8 (2.0)	−2.1 (1.1)	−1.9 (0.8)[b]	−2.0 (0.5)	−1.4 (0.7)	−2.2 (0.7)	−1.9 (0.4)	−2.0 (0.5)	−2.2 (0.4)
History of fracture (yes), n (%)	7 (53.9)	23 (44.2)	10 (58.8)	4 (57.1)	37 (49.3)	3 (30.0)	7 (35.0)	26 (46.4)	11 (68.8)
M12 and M24 characteristics	**n = 12**	**n = 51**	**n = 14**	**n = 7**	**n = 71**	**n = 10**	**n = 19**	**n = 55**	**n = 14**
% change in BMD from M0 to M12, mean (SD)	7.1 (3.1)	5.9 (3.8)	3.1 (3.9)	6.2 (4.5)	3.0 (3.1)	2.8 (4.0)	7.0 (6.3)	2.7 (2.9)	0.6 (2.6)
	n = 12	**n = 51**	**n = 15**	**n = 7**	**n = 71**	**n = 10**	**n = 19**	**n = 55**	**n = 14**
BMD (g/cm^3) at M12, mean (SD)	1.0 (0.3)	0.9 (0.2)	0.9 (0.1)	0.8 (0.1)	0.8 (0.1)	0.7 (0.1)	0.7 (0.1)	0.7 (0.1)	0.6 (0.1)
	n = 12	**n = 51**	**n = 15**	**n = 7**	**n = 71**	**n = 10**	**n = 19**	**n = 55**	**n = 14**
BMD T-score at M12, mean (SD)	−1.2 (2.4)	−1.7 (1.2)	−1.7 (0.8)	−1.7 0.5)	−1.2 (0.7)	−2.1 (0.6)	−1.5 (0.6)	−1.9 (0.6)	−2.2 (0.5)
	n = 13	**n = 52**	**n = 17**	**n = 7**	**n = 75**	**n = 10**	**n = 20**	**n = 56**	**n = 16**
% change in BMD from M0 to M24, mean (SD)	2.1 (4.2)	6.7 (4.2)	7.7 (4.0)[b]	1.7 (4.1)	3.3 (3.2)	7.4 (3.8)	0.8 (5.4)	3.0 (2.8)	5.4 (2.3)
BMD at M24 below M0 value, n (%)	3 (23.1)	1 (1.9)	0 (0.0)[b]	2 (28.6)	5 (6.7)	0 (0.0)	10 (50.0)	8 (14.3)	0 (0.0)
ALN adherence at M24, n (%)	11 (84.6)	38 (73.1)	14 (82.4)	5 (71.4)	56 (74.7)	10 (100)	15 (75.0)	45 (80.4)	11 (68.8)

N = number of subjects with BMD values at M12 and M24; n = number of subjects in each BMD group with available data

BMD = bone mineral density; M = month; SD = standard deviation

[a] Based on a 3% BMD threshold. A BMD change ≤−3% indicated lost BMD; >−3% and <3% indicated maintained BMD; and ≥3% indicated gained BMD; [b] n = 16

Selected baseline characteristics and percentage change in BMD for subjects who lost, maintained, or gained BMD after transitioning from denosumab to alendronate.

Methods: DAPS was a 24-month, open-label, randomized, cross-over study designed to compare adherence to 12 months of DMAb treatment (60 mg Q6M SC) with ALN (70 mg QW PO) in treatment-naïve postmenopausal women with a T-score ≤—2.0 to ≥—4.0 at the lumbar spine (LS), total hip (TH), or femoral neck (FN). BMD was measured at baseline and months (M) 12 and 24. Here we evaluate subjects transitioning from DMAb to ALN at M12. A 3% BMD least significant change threshold identified subjects who lost, maintained, or gained BMD from M12 to M24 (change ≤—3%, >—3% and < 3%, or ≥3%, respectively); baseline, M12, and M24 characteristics were summarized using descriptive statistics.

Results: Of 126 subjects randomized to DMAb, 115 (91%) transitioned to ALN at M12. At baseline, subjects had a mean age of 65 years and mean BMD T-scores of —2.0, —1.6, and –2.0 at the LS, TH, and FN, respectively. BMD increased by 5.6%, 3.2%, and 3.1% with DMAb from M0 to M12 at the LS, TH, and FN, respectively, and changed by 0.6%, 0.4%, and –0.1% with ALN from M12 to M24. After transitioning from DMAb to ALN, most subjects showed maintained or increased BMD (Table); 15.9%, 7.6%, and 21.7% lost BMD at the LS, TH, and FN, respectively, and only 1 subject (1.2%) lost BMD at all 3 sites. Baseline characteristics, M12 BMD, and adherence to oral ALN showed no trend with the BMD change from M12 to M24. However, subjects who lost BMD from M12 to M24 on ALN showed greater gains in BMD from M0 to M12 on DMAb, and few who lost BMD fell below their pre-study baseline BMD value. No subject experienced clinical vertebral fracture.

Conclusion: ALN can effectively maintain the BMD gains accrued after 1 year of DMAb in most subjects. Those with larger BMD increases in year 1 are more likely to lose BMD in year 2, with other subject characteristics not predictive of the response in year 2. These data highlight the need for oral BP therapy following DMAb cessation and BMD monitoring of patients transitioning from DMAb to ALN.

Disclosure: D. Kendler, Amgen Inc., 2, 5, 8, Eli Lilly, 2, 5, 8, Pfizer, 5; **A. Chines**, Amgen, 1, 3, Amgen Inc., 1, 3; **P. Clark**, Pfizer, 2, 8, Amgen Inc., 8, Eli Lilly, 8; **P. Ebeling**, Amgen Inc., 2, 5, Eli Lilly, 2, Alexion, 5; **M. McClung**, Amgen Inc., 5, 8; **Y. Rhee**, Amgen Inc., 2, 8; **S. Huang**, Amgen Inc., 1, 3; **R. Kees Stad**, Amgen Inc., 1, 3; **N. Freemantle**, Ipsen, 2, PTC, 2, Allergan, 2, Sanofi Aventis, 2, 8, Astra Zeneca, 5, 8, Ionis, 5.

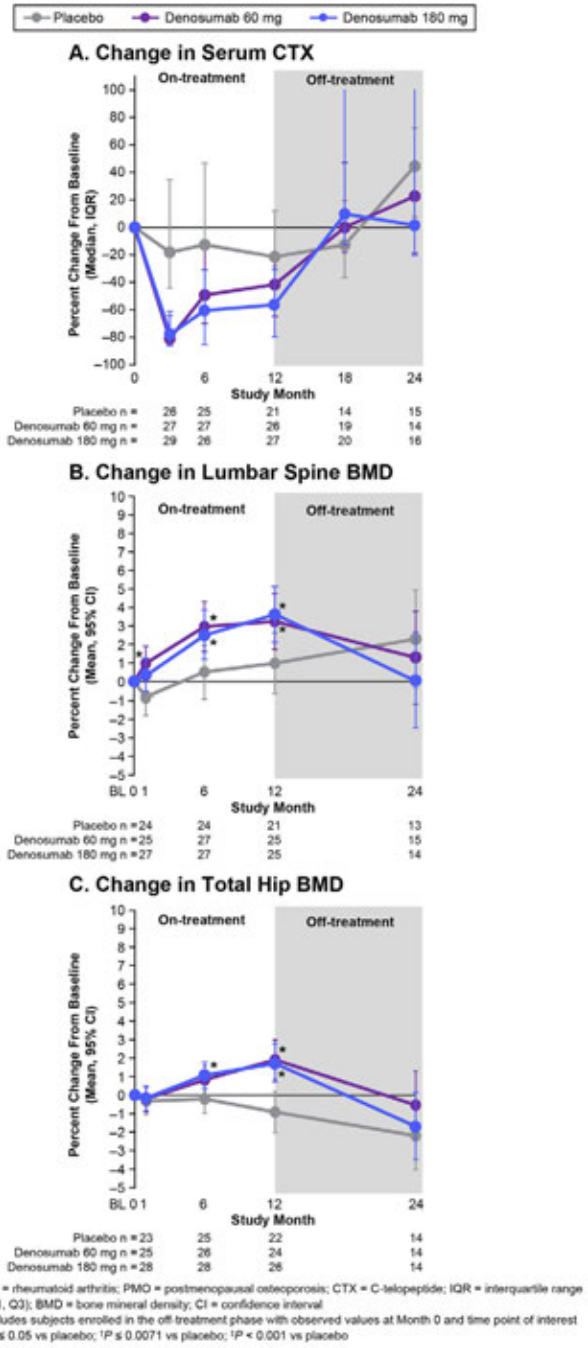
Abstract Number: 1876

Effect of Discontinuation of Denosumab in Subjects with Rheumatoid Arthritis Treated with Glucocorticoids

Kenneth Saag ,[1] Michele McDermott,[2] Jonathan Adachi,[3] Willem Lems,[4] Nancy Lane,[5] Piet Geusens,[6] Peter Butler,[2] Li Chen,[2] Daria Crittenden,[2] Robin Dore,[7] and Stanley Cohen[8], [1]University of Alabama, Birmingham, AL, [2]Amgen Inc., Thousand Oaks, CA, [3]McMaster University and St. Joseph's Healthcare Hamilton, Hamilton, ON, Canada, [4]VU University Medical Centre, Amsterdam, Netherlands, [5]University of California at Davis Medical Center, Sacramento, CA, [6]Maastricht University, Maastricht, Netherlands, [7]Robin K Dore Inc, Tustin, CA, [8]Metroplex Clinical Research Center, Dallas, TX

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Denosumab, a monoclonal antibody against RANKL, is approved for the treatment of glucocorticoid (GC) induced osteoporosis (GiOP). In postmenopausal women with osteoporosis, denosumab discontinuation leads to a transient increase in bone turnover above baseline, peaking at 12 months from the last dose, and a corresponding decline in bone mineral density (BMD). To better understand the effects of denosumab discontinuation



Change in CTX, Lumbar Spine BMD, and Total Hip BMD from Baseline Upon Denosumab Discontinuation in Patients with Rheumatoid Arthritis

in GC-treated patients, we analyzed a subgroup receiving GCs at baseline from a phase 2 study of denosumab in subjects with rheumatoid arthritis (RA), followed for 12 months after denosumab discontinuation, for changes in bone turnover and BMD. (Ann Rheum Dis, vol 8, suppl 2, yr 2019, pg A931)

Methods: This double-blind, placebo-controlled study enrolled subjects with RA who were randomized to receive denosumab 60 mg, denosumab 180 mg, or placebo subcutaneously for 12 months, and followed for progression of structural damage. Subjects were followed for an additional 12 months after denosumab discontinuation. Outcome measures in this subgroup analysis of subjects treated with GCs at study baseline included percent change from baseline in serum C-terminal telopeptide of type I collagen (CTX) and lumbar spine (LS) and total hip (TH) BMD on- and off-treatment. Baseline mean (SD) prednisone equivalent dose (mg/day) was 6.1 (2.4), 5.2 (2.1), and 6.1 (3.2) in

the placebo, denosumab 60 mg, and denosumab 180 mg groups, respectively. Data on CTX are reported as median and interquartile range. Percent changes in LS and TH BMD at each time point were assessed based on a repeated-measures model adjusting for treatment, baseline use of steroids, previous use of biologics, and baseline BMD value.

Results: Among 218 subjects in the phase 2 study, 82 (26 placebo, 27 denosumab 60 mg, and 29 denosumab 180 mg) were included in this analysis. After 12 months of denosumab treatment, CTX decreased from baseline in both groups (Figure); in the off-treatment period, CTX returned to baseline by 18 months and was overall similar to placebo at 24 months. BMD increased at the LS and TH at 12 months with denosumab treatment (Figure) and returned to baseline levels after 12 months of discontinuation.

Conclusion: Like all non-bisphosphonate medications for osteoporosis, denosumab is reversible with discontinuation. In this small subgroup of GC-treated subjects with RA, BMD gains achieved with denosumab were lost upon discontinuation, consistent with observations in postmenopausal women receiving denosumab for osteoporosis. In this analysis of short-term denosumab use in subjects with RA receiving GCs, bone turnover was reduced with denosumab and gradually returned to baseline upon discontinuation, without a clear increase to above-baseline levels in the off-treatment period.

Disclosure: K. Saag, Amgen Inc., 2, 5, Radius, 5, Roche, 5; **M. McDermott**, Amgen Inc., 1, 3; **J. Adachi**, Abbvie, 2, Amgen, 2, 5, 8, Amgen Inc., 2, 5, 8, Eli Lilly, 5, Lilly, 5, Pfizer, 2, UCB, 2; **W. Lems**, Amgen Inc., 8, Lilly, 8, Merck, 8, Pfizer, 8; **N. Lane**, Amgen Inc., 5, 8, GSK, 5, Radius Health, Inc., 8; **P. Geusens**, AbbVie, 2, 5, 8, Amgen Inc., 2, 5, 8, BMS, 2, 5, 8, Celgene, 2, 5, 8, Lilly, 2, 5, 8, Janssen, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB Pharma, 2, 5, 8, Will, 2, 5, 8; **P. Butler**, Amgen Inc., 1, 3, 9; **L. Chen**, Amgen Inc., 1, 3; **D. Crittenden**, Amgen Inc., 1, 9; **R. Dore**, AbbVie, 2, 5, 8, Amgen Inc., 2, 5, 8, Biogen, 2, Gilead, 2, 5, Lilly, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB Pharma, 2, 5, 8, BMS, 5, 8, Radius, 5, 8; **S. Cohen**, AbbVie, 2, 5, Abbvie, 5, Amgen, 5, Amgen Inc., 2, 5, AstraZeneca, 2, 5, Biogen-IDEC, 2, 5, Bristol Meyer Squibb, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5.

Abstract Number: 1877

Romosozumab Improves Lumbar Spine Bone Mineral Density and Bone Strength Greater Than Alendronate as Assessed by Quantitative Computed Tomography and Finite Element Analysis in the ARCH Trial

Jacques Brown ,[1] Arkadi Chines,[2] Roland Chapurlat,[3] Joseph Foldes,[4] Xavier Nogues,[5] Roberto Civitelli,[6] Tobias De Villiers,[7] Fabio Massari,[8] Cristiano A. Zerbini,[9] Wenjing Yang,[2] Chris Recknor,[10] and Cesar Libanati[11], [1]CHU de Quebec Research Centre and Laval University, Quebec, QC, Canada, [2]Amgen Inc., Thousand Oaks, CA, [3]INSERM UMR 1033, Université de Lyon, Lyon, France, [4]Hadassah Hebrew University Medical Center, Jerusalem, Israel, [5]IMIM Institut Hospital del Mar d'Investigacions Mèdiques, Barcelona, Spain, [6]Washington University School of Medicine, St. Louis, MO, [7]Stellenbosch University, Stellenbosch, South Africa, [8]Instituto de Investigaciones Metabólicas, Buenos Aires, Argentina, [9]Centro Paulista de Investigação Clinica, São Paulo, Brazil, [10]United Osteoporosis Centers, Gainesville, GA, [11]UCB Pharma, Brussels, Belgium

SESSION INFORMATION

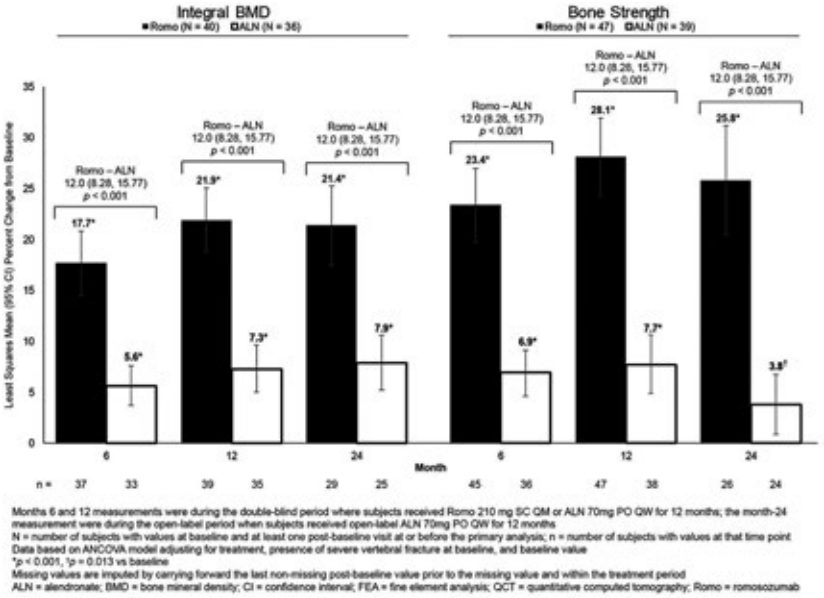
Session Date: Monday, November 11, 2019

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Recent evidence suggests BMD achieved during treatment is a reliable surrogate for fracture risk reduction (Bouxsein *JBMR* 2019). Romosozumab (Romo) is a bone-forming agent with a dual effect of



Percentage change from baseline and difference between romosozumab and alendronate treatment in integral BMD and bone strength at the lumbar spine through the primary analysis in ARCH

increasing bone formation and decreasing bone resorption. In ARCH (NCT01631214), Romo followed by alendronate (ALN) had greater efficacy in BMD gains and fracture risk reduction vs ALN alone (Saag *NEJM* 2017). Here we assessed improvements in lumbar spine (LS) BMD and bone strength with Romo vs ALN treatment by quantitative computed tomography (QCT) and Finite Element Analysis (FEA).

Methods: Postmenopausal women with osteoporosis and prior vertebral or hip fracture were randomized 1:1 to receive Romo 210mg SC monthly or ALN 70mg PO weekly for 12 months, followed by open-label ALN 70mg PO weekly. In an imaging substudy, LS BMD was assessed by QCT and vertebral-estimated bone strength by FEA using QCT images obtained at baseline and months 6, 12, and 24. Correlation analyses evaluated the relationship between changes in FEA, QCT, and DXA.

Results: This post-hoc analysis included 90 subjects (49 Romo, 41 ALN) with baseline and ≥1 post-baseline QCT/FEA assessment. At baseline, mean (SD) age was 73 (7) years; DXA T-scores were –3.08 (1.09), –2.70 (0.68), and –2.84 (0.45) at the LS, total hip, and femoral neck, respectively; and 97% had prior vertebral fracture, similar to core study subjects. 76 (40 Romo, 36 ALN) subjects had QCT assessments and 86 (47 Romo, 39 ALN) had FEA assessments at baseline and ≥1 post-baseline visit. Subjects in both groups experienced significant gains in integral and trabecular BMD from baseline at all time points (except ALN in trabecular BMD; Fig and data not shown). Differences between Romo and ALN were significant at months 6, 12, and 24. QCT BMD increases were accompanied by significant increases in LS bone strength in both groups at all time points, with significantly greater increases observed with Romo than ALN. With treatment arms combined, correlation between post-baseline percent change in FEA and BMD by QCT (integral and trabecular) and DXA was similar (r=0.69–0.87, all p< 0.001).

Conclusion: Compared with ALN, Romo significantly improved LS BMD by QCT and bone strength by FEA. These effects occurred rapidly (month 6), were sustained over 12 months, were preserved upon transition to ALN through 24 months—demonstrating maintenance of therapeutic effect achieved with Romo—and are consistent with greater fracture risk reduction observed in this trial with Romo-ALN vs ALN.

Disclosure: J. Brown, Amgen, 5, 8, Amgen Inc., 5, 8, Eli Lilly, 5, 8, Lilly, 5, 8, Mereo, 2, Radius, 2, Servier, 2, 5; **A. Chines**, Amgen, 1, 3, Amgen Inc., 1, 3; **R. Chapurlat**, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 5, Chugai, 2, MSD, 2,

Pfizer, 5, UCB, 2, 5, UCB Pharma, 2, 5; **J. Foldes**, None; **X. Nogues**, Amgen Inc., 5, Lilly, 5, UCB Pharma, 5; **R. Civitelli**, Mereo Biopharma, 2; **T. De Villiers**, Lilly, 5, Abbott, 8, Adcock Ingram, 8, Pfizer, 8; **F. Massari**, None; **C. Zerbini**, Amgen, 2, Amgen, GSK, Lilly, Merck, Novartis, Pfizer, Sanofi-Aventis, Servier and Roche, 2, Lilly, 2, Merck, Pfizer, Sanofi-Aventis, 5, 8, Pfizer, 2, Sanofi, 2; **W. Yang**, Amgen, 1, 3; **C. Recknor**, None; **C. Libanati**, UCB Pharma, 1, 3.

Abstract Number: 1878

Quantifying the Placebo Effect After Intra-Articular Injections: Implications for Trials and Practice

Sebastian Rodriguez-Garcia ,[1] Raul Castellanos-Moreira,[2] Jacqueline Uson-Jaeger,[3] ESPERANZA NAREDO,[4] and Loreto Carmona[5], [1]Rheumatology Department. Hospital Clínic Barcelona, Barcelona, Spain, [2]Rheumatology Department. Hospital Clínic Barcelona, Barcelona, Catalonia, Spain, [3]Hospital Universitario de Mostoles, Madrid, Spain, [4]Rheumatology Department, Joint and Bone Research Unit. Hospital Universitario Fundación Jiménez Díaz, Universidad Autónoma, MADRID, Spain, [5]Instituto de Salud Musculoesquelética - Inmusc., Madrid, Spain

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain Mechanisms – Basic & Clinical Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: In recent years, diverse compounds for intra-articular (IA) administration were brought into the market with a subsequent significant and heterogeneous literature production.

Understanding the efficacy of any drug to be delivered intra-articularly implies bearing in mind the placebo (PBO) effect of any medication that is placed where the pain is elicited, especially in the first weeks after the procedure. To date, most of the studies analyzing this effect were not focused specifically on the route of administration but on the treatment being administered. Thus, we aimed at evaluating the size of the PBO effect after IA injections.

Methods: For the upcoming EULAR recommendations/points to consider for IA therapies, an overview of systematic reviews (SR) was conducted, including SR of randomized-controlled trials (RCT) of IA therapies comparing an active treatment vs an IA control. We selected all SR in which the control arm was a saline solution. After assessing the risk of bias with the AMSTAR-2 tool, all SR showing high-confidence results were selected and the studies included in them, re-analyzed.

The analysis included data on the change in pain from the PBO arms, measured on continuous variables (different scales) from baseline to 3-6 and 12-16 weeks after the IA procedure. The standardized mean differences (SMD) from baseline were calculated as the ratio between the size of the intervention effect in each study and the variability observed in that study. A meta-analysis was performed using an inverse-variance random-effects model in Review Manager 5.3. The overall effect sizes obtained refer to versions of the SMD, which corresponds to the Hedges' (adjusted) g. e.g. a "g" of 1 indicates the two groups being compared differ by 1 standard deviation and so on.

Results: Two SR comprising 50 RCT were included, 44 had to be excluded: 26 due to not having PBO arms or not showing its data, 6 due to not measuring the target outcome or at the specified time-points, in 5 we could not obtain the target data, and 7 used a PBO different than saline.

Pain, measured by visual analog scale (VAS) and Lequesne index, was retrieved from 6 RCT. The effect of PBO IA administration from baseline to 3-6 weeks was pooled from 6 studies on VAS pain and 3 on Lequesne index; SMD

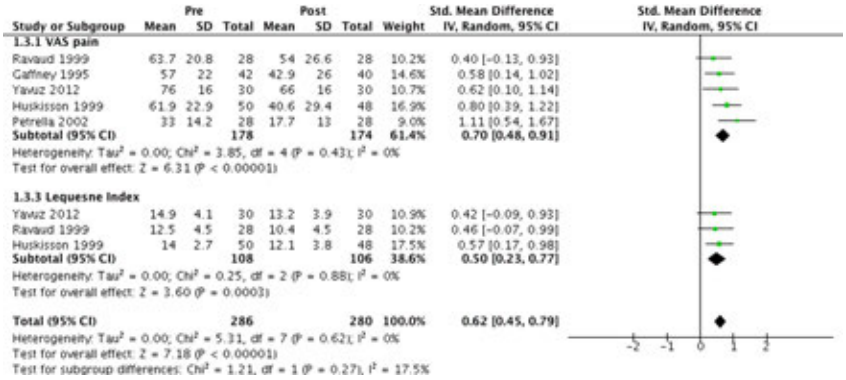


Figure 1. Forest plot for pooled effects of PBO arms on VAS pain and Lequesne Index at 3-6 weeks after injection.

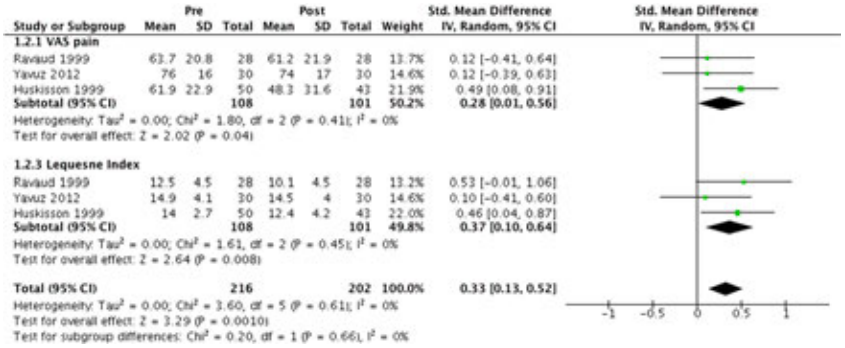


Figure 2. Forest plot for pooled effects of PBO arms on VAS pain and Lequesne Index at 12-16 weeks after injection

[95%CI] was 0,74 [0.47-1.00]. As one study had too large an effect, we performed a sensitivity analysis excluding it. This resulted in a notable reduction of overall heterogeneity both measured by I^2 and Tau^2 with a resultant SMD = 0.62 [0.45-0.79] (Figure 1).

The overall PBO effect at 12-16 weeks, measured by pooling data from 3 studies for VAS pain and for Lequesne, showed an SMD = 0.33 [0.14-0.52] (Figure 2).

Using the interpretation suggested by Cohen[1], our results would confirm a moderate to large effect of IA saline (PBO) at 3-6 weeks with a subsequent reduction to a small but persistent effect at 12-16 weeks. Therefore, IA PBO may have a clinically detectable and lasting effect.

Conclusion: Based on these findings we suggest that PBO effect should be taken into account not only when analyzing the efficacy of IA therapies in RCT but also in clinical practice, where this effect could be maximized, as well.

Reference:

1. Cohen J. *Statistical Power Analysis in the Behavioural Sciences*. 1988.

Disclosure: S. Rodriguez-Garcia, None; **R. Castellanos-Moreira**, None; **J. Uson-Jaeger**, None; **E. NAREDO**, None; **L. Carmona**, None.

Abstract Number: 1879

The Relation of Pain Sensitization and Conditioned Pain Modulation to Pain Patterns in Knee Osteoarthritis: The Multicenter Osteoarthritis Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain Mechanisms – Basic & Clinical Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Intermittent pain progresses to constant pain in some, but not all, individuals with knee osteoarthritis (OA). Differing pain mechanisms may underlie these transitions. Later onset constant pain may represent pain sensitization or inadequate descending inhibitory modulation, while earlier intermittent pain may be due to peripherally-driven nociceptive input. We sought to examine the association of pain sensitization and conditioned pain modulation (CPM) to patterns and predictability of knee pain.

Methods: Subjects from the Multicenter Osteoarthritis (MOST) study, a NIH-funded longitudinal prospective cohort of older adults with or at risk of knee OA, at the 144-month visit were included in this cross-sectional analysis. Mechanical pressure pain threshold (PPT) at the wrist and patella were assessed with a handheld algometer. Lower PPTs indicate greater sensitization. Weighted mechanical punctate probes were used to assess temporal summation at the wrist, an indicator of central sensitization. Efficiency of CPM was determined by assessing PPT at the patella (test stimulus, PPT1) with forearm ischemia as the conditioning stimulus, followed by reassessment of PPT at the patella (PPT2). Adequate CPM is operationalized as PPT2:PPT1 >1. Knee pain patterns were defined using the Intermittent and Constant OA pain (ICOAP) scale as no intermittent or constant pain; intermittent pain only; constant pain only; or a mix of both. Unpredictable pain was assessed with a question regarding pain onset without warning. We evaluated the relation of pain sensitization and adequacy of CPM to pain patterns using logistic regression with general estimating equations to account for 2 knees within an individual. Analyses were adjusted for age, sex, BMI, race, clinic site, depressive symptoms and catastrophizing.

Results: There were 2817 subjects included (mean age 64 yrs, 57% female, mean BMI 29.4 kg/m^2). Higher patellar PPT (less sensitivity) was associated with lower likelihood of constant +/- intermittent pain than intermittent only (OR 0.80 (95% CI 0.69, 0.93) or no pain (OR 0.69 (95% CI 0.60-0.81)) and less unpredictable pain (OR 0.88 (95% CI 0.79-

Table 1.

	ICOAP Pain Pattern constant+/- intermittent vs. intermittent only OR (95% CI)†	ICOAP Pain Pattern constant+/-intermittent vs. intermittent only or no pain OR (95% CI)†	ICOAP Pain Comes on Without Warning Sometimes/often vs. rarely/never OR (95% CI)†
*PPT - patella	**0.80 (0.69, 0.93)**	**0.69 (0.60, 0.81)**	**0.88 (0.79, 0.97)**
*PPT – wrist	**0.80 (0.66, 0.97)**	**0.70 (0.59, 0.84)**	0.97 (0.86, 1.10)
**Temporal Summation – wrist (Y vs. N)	1.14 (0.48, 2.67)	1.63 (0.76, 3.49)	1.33 (0.55, 3.21)
***Adequate CPM (> 1 vs.≤ 1)	**1.45 (1.09, 1.91)**	**1.36 (1.05, 1.78)**	1.00 (0.81, 1.23)

†Adjusted for age, sex, BMI, depressive symptoms, catastrophizing, race and clinic site.

*PPT: per unit SD increase; higher PPT indicates less pain sensitization
**TS: dichotomous; present if pain increases at end of stimuli train compared with baseline; TS indicates central sensitization
***CPM: dichotomous; adequate CPM indicates descending inhibitory modulation

0.97)) (**Table**). Similar findings were noted for wrist PPT, but were inverse for adequate CPM (**Table**). No associations were noted for temporal summation.

Conclusion: Lower levels of pain sensitization (by PPT) were associated with lower likelihood of constant +/- intermittent pain than intermittent pain or no pain, and less unpredictable pain. Adequate CPM was unexpectedly associated with greater likelihood of constant +/- intermittent pain, perhaps reflecting activation of this pathway when constant pain is present. These findings support the hypothesis that different pain mechanisms underlie intermittent vs. constant pain. Pain patterns noted over the course of OA appear to be related to peripheral +/- central facilitated ascending pain mechanisms.

Disclosure: L. Carlesso, None; **L. Frey Law**, None; **N. Wang**, None; **M. Nevitt**, None; **B. Lewis**, None; **T. Neogi**, MerckSerono, 5, Novartis, 5.

Abstract Number: 1880

Baricitinib 4 Mg and 2 Mg Once Daily Reduced Pain in Both Patients Who Were Opioid Users and Non-users in Active Rheumatoid Arthritis: A Post-hoc Analysis of Phase 3 Trials

Janet Pope ,[1] Yvonne Lee,[2] Jeffrey Curtis,[3] Daojun Mo,[4] Terence Rooney,[4] Li Xie,[4] Christina Dickson,[4] Douglas Schlichting,[4] Amanda Quebe,[4] Anabela Cardoso,[4] Lee Simon,[5] and Peter Taylor[6], [1]Western University, London, ON, Canada, [2]Northwestern University Feinberg School of Medicine, Chicago, [3]University of Alabama at Birmingham, Birmingham, AL, [4]Eli Lilly and Company, Indianapolis, IN, [5]SDG LLC, Cambridge, MA, [6]University of Oxford, Oxford, United Kingdom

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain Mechanisms – Basic & Clinical Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Opioid use in RA patients has increased over the past 2 decades in the US. Little is known about the combined effects of opioids and disease-modifying antirheumatic drugs (DMARDs) on pain in RA. To assess pain reduction in opioid users and non-users, we tested the effect of 1) 4 mg baricitinib (BARI), an oral JAK1/JAK2 inhibitor, vs. placebo (PBO) with data pooled from Phase 3 trials, RA-BEAM (NCT01710358, with RA patients with an inadequate response [IR] to MTX), RA-BUILD (NCT01721057, with those with IR to conventional DMARDs), and RA-BEACON (NCT01721044, with those with IR to ≥1 tumor necrosis factor inhibitors), 2) BARI 2 mg vs. PBO in RA-BEACON, and 3) subcutaneous 40 mg adalimumab (ADA) every other week vs. PBO in RA-BEAM.

Methods: Opioid users were patients who reported opioid use during the trials. The number of opioid users/the total number of randomized patients were: 171/891 BARI 4 mg and 153/892 PBO in the pooled analysis, 54/174 BARI 2 mg and 58/176 PBO in RA-BEACON, and 34/330 ADA and 50/488 PBO in RA-BEAM. Pain was measured by the Patient's Assessment of Pain visual analog scale (VAS, 0-100 mm). Last observation before treatment discontinuation or rescue was carried forward through Week 24. An ANCOVA model assessed differences in pain reduction at each time point between BARI 4 mg and PBO (pooled), BARI 2 mg and PBO (RA-BEACON), and ADA and PBO (RA-BEAM) by opioid users and non-users. Baseline pain VAS, age, BMI, and trial were covariates in the model. Heterogeneity of treatment effect (active vs. PBO) was evaluated across opioid users and non-users by interaction test. Analyses were not adjusted for multiplicity.

Results: BARI 4 mg had greater pain reduction vs. PBO in opioid users and non-users (P< 0.05) at all time points (Weeks 1, 2, 4, 8, 12, 14, 16, 20 and 24). Pain reduction in BARI 4 mg vs. PBO was similar between opioid users and non-users at all time points (interaction P >0.1 at all time points). At Week 24, the difference in pain VAS reduction between BARI 4 mg vs. PBO was -13.4 mm (95% CI: -19.0, -7.8) in opioid users and -14.3 mm (-16.7, -11.9) in non-users, interaction P=0.8. In RA-BEACON, BARI 2 mg had greater pain reduction vs. PBO in both opioid users and non-users (P< 0.05) starting at Week 12. Pain reduction with BARI 2 mg vs. PBO was similar between opioid users and non-users at all time points (interaction P >0.1 at all time points). At Week 24, the difference in pain VAS reduction between BARI 2 mg vs. PBO was -10.7 mm (-19.5, -1.9) in opioid users and -8.3 mm (-15.0, -1.6) in non-users, interaction P=0.8. In RA-BEAM, a significant difference in pain reduction was not observed for ADA vs. PBO in the opioid users; whereas, for non-users, a difference in pain reduction was observed for ADA vs. PBO at all time points (P< 0.05). At Week 24, the difference in pain VAS reduction between ADA vs. PBO was -4.9 mm (95% CI:-16.4, 6.6) in opioid users and -12.2 mm (-15.6, -8.9) in non-users, interaction P=0.2.

Conclusion: Pain reduction with BARI 4 mg was similar between opioid users and non-users and was observed at all time points. Pain reduction with BARI 2 mg vs. PBO was similar between opioid users and non-users from Week 12. In contrast, ADA did not result in pain reduction compared to PBO in opioid users.

Disclosure: J. Pope, AbbVie, 5, Abbvie, 5, Actelion, 5, Actellion, 5, Amgen, 2, 5, AstraZeneca, 2, Astra-Zeneca, 2, Bayer, 2, 5, BMS, 2, 5, Eicos Sciences, 5, Eli Lilly & Company, 5, Eli Lilly and Company, 5, EMERALD, 5, Emerald, 5, Genzyme, 5, Janssen, 5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8; **Y. Lee**, Cigna Corp, 1, Eli Lilly, 2, 5, Eli Lilly and Company, 2, Express Scripts, 4, Pfizer, 2; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corrona, 2, 5, Eli Lilly & Company, 2, 5, Janssen, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5; **D. Mo**, Eli Lilly and Company, 1, 3; **T. Rooney**, Eli Lilly and Company, 1, 3; **L. Xie**, Eli Lilly and Company, 1, 3; **C. Dickson**, Eli Lilly and Company, 1, 3; **D. Schlichting**, Eli Lilly and Company, 1, 3; **A. Quebe**, Eli Lilly & Company, 3, 4, Eli Lilly and Company, 1, 3; **A. Cardoso**, Eli Lilly and Company, 1, 3; **L. Simon**, Eli Lilly and Company, 5, AstraZeneca, 5, NuvoResearch, 5, Roche, 5, Pfizer, 5, Bayer, 5, Regeneron, 5, Gilead, 5; **P. Taylor**, AbbVie, 5, Abbvie, 5, Biogen, 5, Celgene, 2, 5, Eli Lilly and Company, 2, 5, Fresenius, 5, Fresenius SE & Co, 5, Fresnius, 5, Galapagos, 2, 5, Gilead, 5, GlaxoSmithKline, 5, Janssen, 2, 5, Lilly, 2, 5, Nordic Pharma, 5, NORDIC Pharma, 5, Pfizer, 5, Pfizer Inc, 5, Roche, 5, Sanofi, 5, UCB, 5.

Abstract Number: 1881

Association of Pain Centralization with DMARD Response in Active RA

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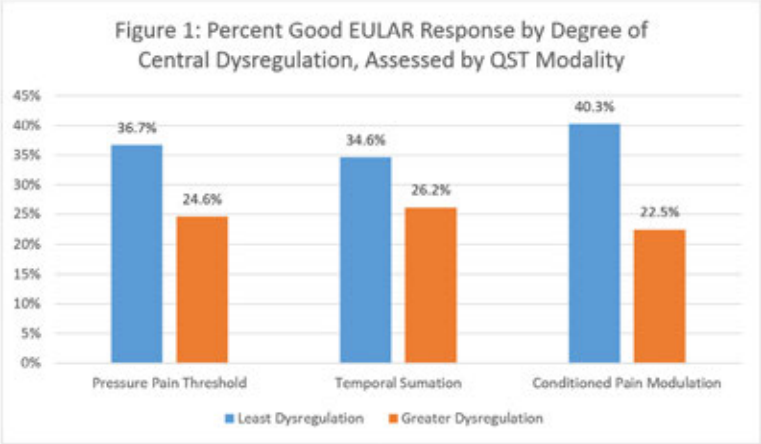
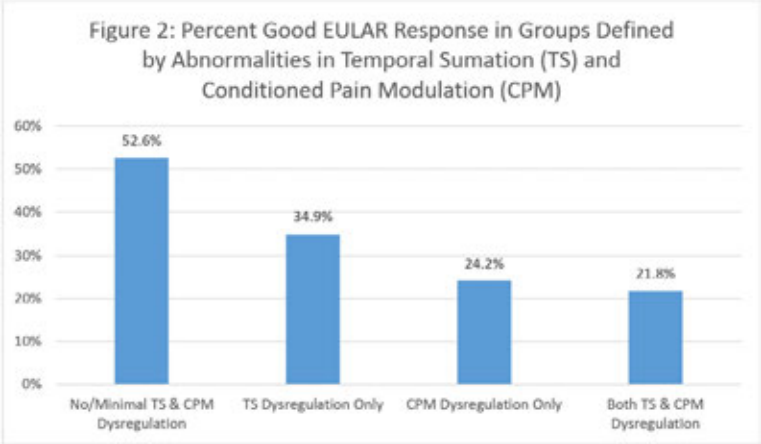
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain Mechanisms – Basic & Clinical Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Despite the availability of potent disease modifying anti-rheumatic drugs (DMARDs), a significant percentage of rheumatoid arthritis (RA) patients do not achieve low disease activity or remission de-





fined by composite disease activity measures (CDAMs). Although CDAMs are intended to reflect inflammation, non-inflammatory processes may also contribute to high scores. For instance, dysregulated central nervous system processing, termed “pain centralization”, is associated with high patient global assessment and tender joint count, both of which are components of CDAMs. The objective of this study was to assess the contribution of pain centralization to DMARD response.

Methods: One hundred and eighty-two RA patients with active disease necessitating DMARD initiation or change were included in this longitudinal prospective multicenter cohort. All patients met ACR criteria for RA. Patients were assessed before and approximately 12-weeks after DMARD initiation or change. The outcome was good response per the European League Against Rheumatism (EULAR) response criteria. Primary predictors were pain centralization assessed by quantitative sensory testing (QST). Overall pain centralization was measured by pressure pain thresholds (PPTs). Pain facilitation was assessed by temporal summation (TS). Impaired pain inhibition was measured by conditioned pain modulation (CPM). The secondary predictor was a combined measure of TS and CPM. Predictors were dichotomized into least central dysregulation and greater central dysregulation using a split between the 1st and 2nd sex-specific tertiles for each QST measure. Multiple logistic regression was used to calculate odds ratios (ORs) for good EULAR response.

Results: Mean age of the population was 55.2 years. 83% of patients were female, and 70.3% seropositive. Mean baseline Disease Activity Score in 28 joints (DAS28-CRP) was 4.3. Patients with greater central dysregulation had lower percentages of good EULAR response (PPT: 24.6% vs. 36.7%, TS: 26.3% vs. 34.6%, CPM: 22.5% vs. 40.3%) (Figure 1) and lower adjusted ORs of good EULAR response (PPTs: OR 0.59 (95% CI 0.28-1.23), TS: OR 0.60 (95% CI 0.27-1.34), CPM: OR 0.40 (95% CI 0.19-0.83)) than those with least dysregulation (Table 1). However, only the

Table 1: Odds Ratios (OR) for Good EULAR Response			
		Unadjusted OR (95% CI)	Adjusted[3] OR (95% CI)
Central Dysregulation Assessed by Individual QST Predictors[1]			
PPT	**Least**	1.00 (Referent)	1.00 (Referent)
	Greater	0.56 (0.29, 1.10)	0.59 (0.28, 1.23)
TS	**Least**	1.00 (Referent)	1.00 (Referent)
	Greater	0.67 (0.33, 1.34)	0.60 (0.27, 1.34)
CPM	**Least**	1.00 (Referent)	1.00 (Referent)
	Greater	**0.43 (0.22, 0.83)**	**0.40 (0.19, 0.83)**
Central Dysregulation Assessed by Combinations of TS and CPM[2]			
No/Minimal TS and CPM Dysregulation		1.00 (Referent)	1.00 (Referent)
TS Dysregulation Only		0.48 (0.16, 1.45)	0.49 (0.14, 1.67)
CPM Dysregulation Only		**0.29 (0.09, 0.96)**	0.31 (0.08, 1.13)
Both TS and CPM Dysregulation		**0.25 (0.09, 0.71)**	**0.23 (0.07, 0.73)**

1. Odds ratios are for good EULAR response for greater dysregulation compared to least dysregulation (referent) for each QST modality.
2. Odds ratios are for good EULAR response for each combination of dysregulation of TS and CPM compared to no/minimal TS and CPM dysregulation (referent).
3. Adjusted for age, sex, race, BMI, education, seropositivity, disease duration, PROMIS sleep disturbance, PROMIS depression, and modified Charlson comorbidity score.
* Bolded values indicate statistical significance.

OR for CPM reached statistical significance. Percent good EULAR response decreased with increasing number of abnormalities in pain centralization mechanisms (neither TS and CPM: 52.6%, only TS dysregulation: 30.8%, only CPM dysregulation: 24.4%, both TS and CPM dysregulation: 22.1%) (Figure 2). The adjusted OR for good EULAR response was 0.23 (95% CI 0.07-0.73) for patients with both TS and CPM dysregulation compared to those without TS and CPM dysregulation (Table 1).

Conclusion: In this study, high pain centralization, particularly impaired pain inhibition, was associated with poor DMARD response. Physicians should consider pain centralization as a possible reason why some patients fail to reach low disease activity or remission, despite treatment with DMARDs. Such patients may benefit from adjunctive therapy (e.g. serotonin norepinephrine reuptake inhibitors), rather than escalation of DMARD therapy.

Disclosure: A. Heisler, None; **J. Song**, None; **D. Dunlop**, None; **A. Wohlfahrt**, None; **M. Bolster**, Abbvie, 2, Corbus, 9, Cumberland, 9, Gilead, 5, Johnson & Johnson, 4, Johnson and Johnson, 4, Pfizer, 2; **W. Marder**, None; **C. Bingham**, Abbvie, 5, AbbVie, 5, BMS, 2, 5, Bristol Meyer Squibb, 2, 5, Bristol Myers-Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Eli/Lilly, 5, Genentech/Roche, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Pfizer Inc, 5,

Regeneron/Sanofi, 5, Sanofi/Regeneron, 5; **D. Clauw**, Aptinyx, 2, 5, Daiichi Sankyo, 5, Daiichi Snakyo, 5, Eli Lilly, 5, Intec Pharma, 5, Nix Paterson LLP, 8, Nix Patterson LLP, 8, Pfizer, 2, 5, Pfizer Inc, 2, 5, 8, Samumed, 5, Theravance, 5, Tonix, 5, Williams & Connolly LLP, 8, Williams and Connolly LLP, 8, Zynerba, 5; **T. Neogi**, MerckSerono, 5, Novartis, 5; **Y. Lee**, Cigna Corp, 1, Eli Lilly, 2, 5, Eli Lilly and Company, 2, Express Scripts, 4, Pfizer, 2.

Abstract Number: 1882

Anti-CCP Antibody and Pain Sensitization in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain Mechanisms – Basic & Clinical Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Many patients with RA report persistent pain in the absence of clinically appreciable inflammation. In a mouse model of inflammatory arthritis, mice injected with anti-cyclic citrullinated peptide (CCP) antibody exhibited increased pain sensitivity and more pain behaviors in the absence of histological evidence of joint inflammation. These findings raise the possibility of an inflammation-independent pain pathway mediated by anti-CCP antibodies. In this study, we investigated the association between anti-CCP antibody and pain, assessed by quantitative sensory testing (QST) and patient-reported measures, in RA patients with active inflammation.

Methods: This cross-sectional analysis included study participants who met the ACR/EULAR 2010 classification criteria for RA, had active inflammatory disease, and required initiation of a disease-modifying antirheumatic drug (DMARD). Serum levels of anti-CCP antibody and high sensitivity C-reactive protein (hsCRP) were measured. Subjects also underwent QST, including assessment of pressure pain thresholds (PPTs) at wrist and knee joints to quantify peripheral sensitization. Self-reported pain measures were obtained and included average pain intensity on a numeric rating scale (NRS) and pain interference score assessed by the Patient Reported Outcomes Measurement Information System computerized adaptive test (PROMIS® CAT). We examined the cross-sectional relation of anti-

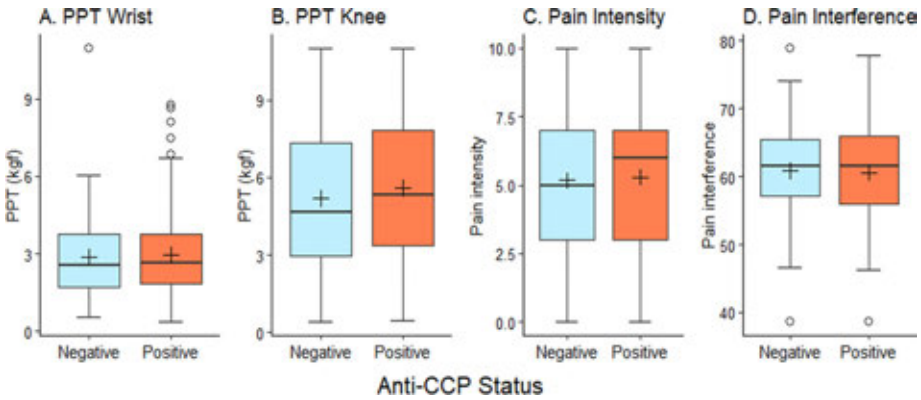

Figure 1. Pain sensitivity by QST and patient-reported pain measures grouped by anti-CCP seropositivity. The horizontal line in each box represents the median, the top and bottom of the boxes the interquartile range, and the whiskers the minimum and maximum observations within the lower and upper fences (1.5*IQR). The plus sign represents the mean.

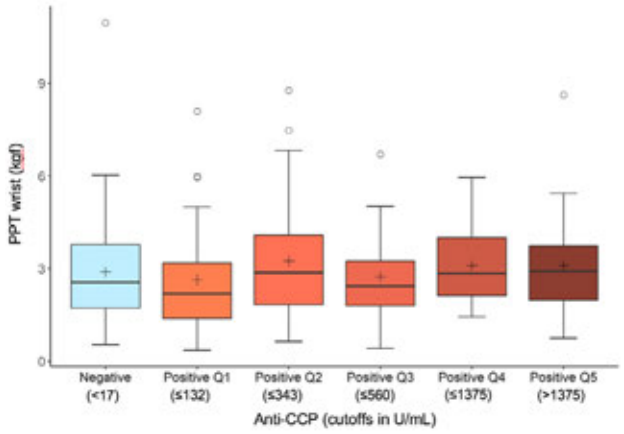

Figure 2. PPT at wrist grouped by anti-CCP-negative and anti-CCP-positive quintiles. The horizontal line in each box represents the median, the top and bottom of the boxes the interquartile range, and the whiskers the minimum and maximum observations within the lower and upper fences (1.5*IQR). The plus sign represents the mean.

Table 1: Association between anti-CCP positivity and pain measures

Outcome	Model	β coefficient	95% C.I.
Experimental Pain Sensitivity			
PPT, wrist	Unadjusted	0.07	-0.33 to 0.47
	Adjusted 1	0.16	-0.25 to 0.56
	Adjusted 2	0.16	-0.24 to 0.56
PPT, knee	Unadjusted	0.41	-0.31 to 1.13
	Adjusted 1	0.65	-0.06 to 1.37
	Adjusted 2	0.61	-0.10 to 1.31
Patient Reported Pain			
Pain intensity	Unadjusted	0.11	-0.46 to 0.68
	Adjusted 1	-0.14	-0.71 to 0.43
	Adjusted 2	-0.04	-0.58 to 0.50
Pain interference	Unadjusted	-0.31	-2.03 to 1.41
	Adjusted 1	-0.87	-2.63 to 0.88
	Adjusted 2	-0.52	-2.17 to 1.12

Adjusted 1: adjusted for age, race, gender, RA disease duration, current steroid/DMARD use, and study site. Adjusted 2: adjusted for covariates in Adjusted 1 + inflammation (hsCRP, swollen joint count) and fibromyalgia status.

CCP antibody seropositivity to PPT and self-reported pain measures using linear regression, adjusting for potential confounders. We also assessed for a dose-response relationship by categorizing anti-CCP as seronegative and as quintiles of seropositivity.

Results: There were 264 participants (mean age 54.6 years, average disease duration 10.2 years). On average, participants had 10.9 tender joints, 5.2 swollen joints, and a hsCRP level of 7.3 mg/L. Anti-CCP positivity was present in 164 patients (62.1%) and was not significantly associated with PPT at the wrist (b-coefficient 0.16, 95% confidence interval [CI] -0.24, 0.56) or knee (b-coefficient 0.61, 95% CI -0.10, 1.31) (Table 1, Figure 1). Similarly, there was no association between anti-CCP seropositivity and pain intensity (b-coefficient -0.04, 95% CI -0.58, 0.50) or pain interference (b-coefficient -0.52, 95% CI -2.17, 1.12). Categorizing seropositive anti-CCP into quintiles of increasing serum antibody did not show a dose-response relationship between anti-CCP and PPT at the wrist (Figure 2) or anti-CCP and any other pain measure (data not shown).

Conclusion: Among patients with active RA, anti-CCP seropositivity and higher levels of anti-CCP were not associated with experimental measures of pain sensitivity or patient-reported measures of pain. The possibility that untreat-

ed patients may demonstrate different findings cannot be ruled out. Nonetheless, these results contrast with data from animal models of inflammatory arthritis, as our data did not show evidence of an anti-CCP-antibody-mediated mechanism of joint pain as suggested in the animal models.

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Abstract Number: 1883

Elucidating Pain Mechanisms in Polyarticular Juvenile Idiopathic Arthritis Patients

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pain Mechanisms – Basic & Clinical Science
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Background/Purpose: Despite a broad range of available therapeutics, pain remains poorly treated in many juvenile idiopathic arthritis (JIA) patients[1-2]. For some patients, the level of pain is not commensurate with the magnitude of detectable joint pathology (i.e., synovitis). In order to elucidate pain mechanisms in JIA, we have investigated the functionality of CNS circuitry in polyarticular JIA (pJIA) individuals (>5 affected joints) alongside peripheral joint pathology, markers of inflammation, subjective measures related to pain and clinical status. This strategy is projected to facilitate the identification of pain biomarker signatures and define mechanisms that underlie the observed pain-inflammation disconnect in JIA.

Methods: Consented, male and female pJIA patients (8-16 years) with and without pain were assessed using functional magnetic resonance imaging (fMRI), musculoskeletal MRI, Patient Reported Outcomes Measurement Information System (PROMIS) questionnaires, fluid markers informing on inflammation (i.e., CRP and ESR levels) and clinical status. All evaluated patients had either past or ongoing hand joint abnormalities. Patient enrollment is currently active.

FMRI data collected during a hand motor task involved a visually cued, opening and closing of the right or left hand (depending on location of joint pathology or clinical pain) in a 30 second off/10 second on manner for 5 cycles. Evoked stimulation was subsequently performed by applying cold stimuli (10°C) to hand and knee joints also in a 30 second off/10 second on block design (Medoc LTD, Israel). Immediately following fMRI, patients underwent hand MRI (index hand only). All imaging was performed on a Siemens 3T scanner (Siemens, Germany). fMRI data was analyzed using FSL 6.0, while hand MRI was clinically evaluated by a musculoskeletal radiologist (KE). This study was approved by the Institutional Review Board at Boston Children's Hospital.

Results: Hand motor task fMRI showed differential CNS activation profiles amongst patients with No Pain + No inflammation, Pain + No Inflammation and Pain + Inflammation (**Figure 1)**. Of these states, the pain without inflam-

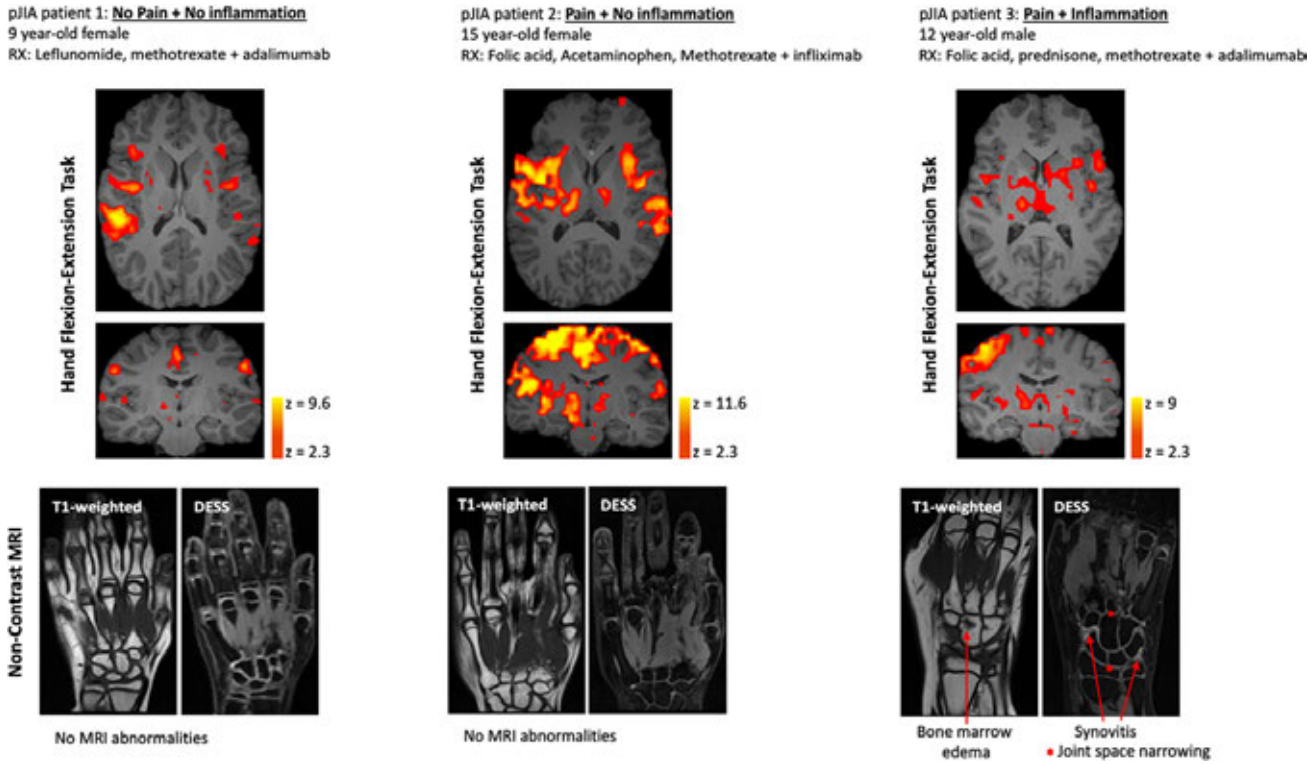

Figure 1. Evoked BOLD Response in pJIA Patients With and Without Pain During a Hand Motor Task. A. Single patient data showing CNS activity during a hand flexion and extension exercise. Statistical activation maps are depicted on axial (top row) and coronal (bottom row) planes on subject-specific, high-resolution anatomical MRI data. Patient 2 in particular reported pain and discomfort during the hand motor task. All pJIA patients had prior (Patient 1) or current (Patients 2 and 3) hand involvement in terms of clinical pain and/or inflammation. B. At the time neuroimaging evaluation, only one individual (Patient 3) had pathology detected in the hand as determined by non-contrast MRI. CRP and ESR levels were normal for Patients 1 and 2, but considered elevated in Patient 3 (CRP: 0.09 mg/dL and ESR: 24 mm/hr).

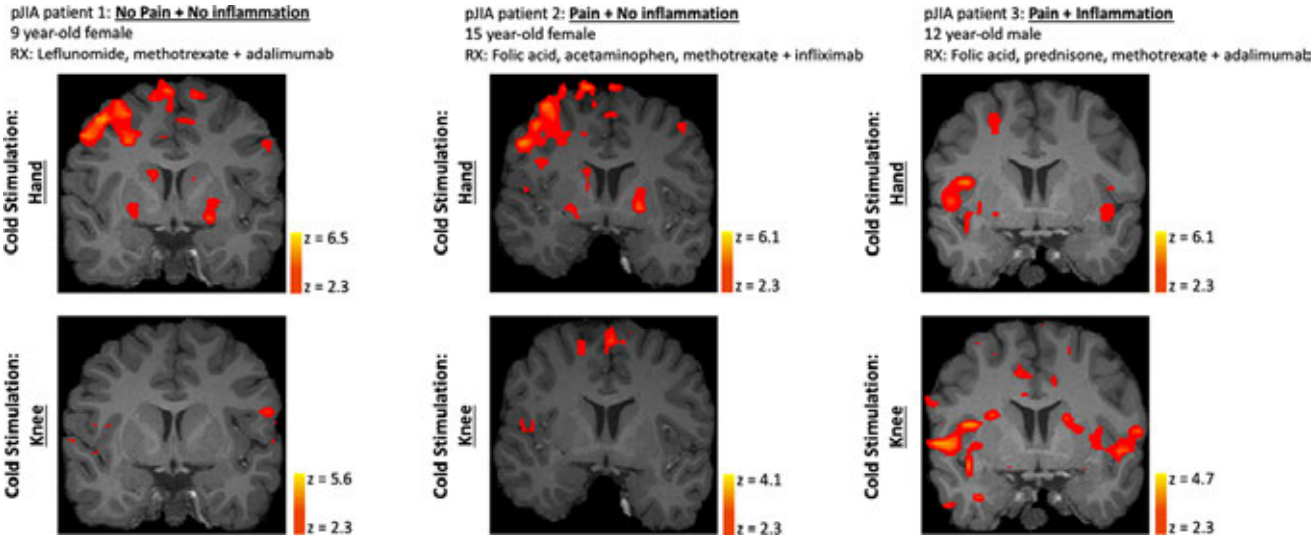

Figure 2. Evoked CNS Response in pJIA Patients With and Without Pain During Unilateral Cold Stimulation of the Hand (Top Row) and Knee (Bottom Row). Overall greater CNS activation was induced by cold stimulation of the dorsal side of the hand compared to the knee. Greater CNS activation for pJIA patient 3 for knee cold stimulation may have resulted from prior knee involvement. This patient reported pain during cold stimulation for both sites (hand and knee). Statistical activation maps are depicted on subject-specific, high-resolution anatomical MRI data.

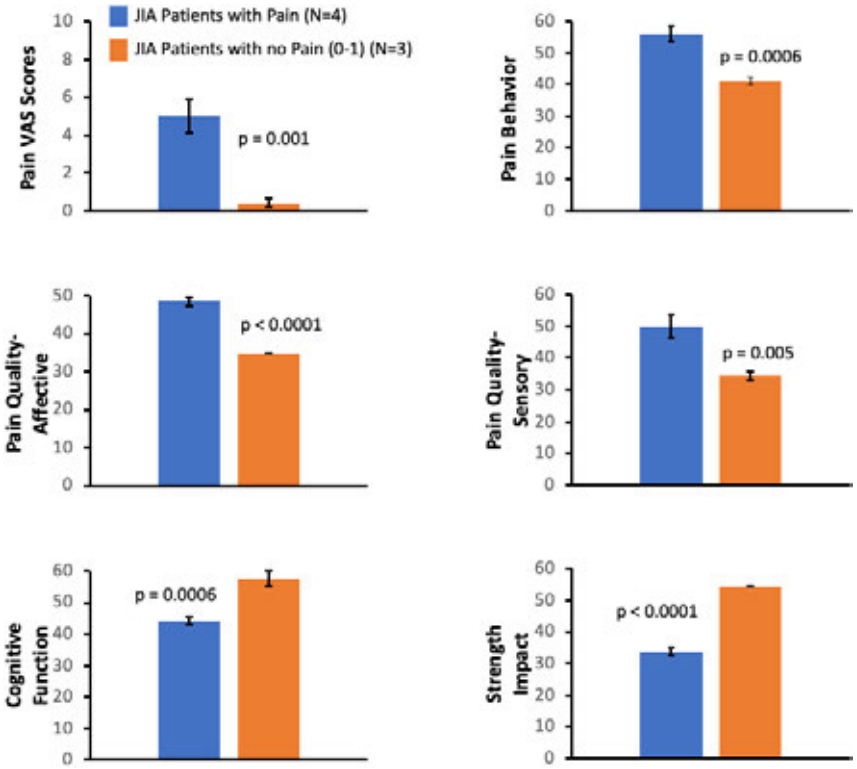

Figure 3. Group-Level Results Demonstrating the Impact of Pain in pJIA With and Without Pain. At the time of evaluation, pJIA patients reported clinical pain at a level of ~5 on a 0-10 scale. PROMIS-based questionnaires were used for all assessments, where higher T-score metrics represent more of the trait measured. The presence of pain in pJIA negatively impacted (loss of function) domains such as cognitive ability and strength. Two-tailed t-tests were performed for all comparisons.

mation (or other pathology) sub-type yielded the most robust CNS activation. MRI abnormalities detected in the hand in Patient 3 consisted of (teno-)synovitis, bone marrow lesions and joint space narrowing. Cold stimuli yielded comparable responses across pain and inflammation conditions (**Figure 2**). Interestingly, in the pJIA patient with current hand/wrist and past knee joint abnormalities, evoked CNS responses and pain scores to cold stimuli were similar at either site. Finally, from PROMIS-based questionnaires (**Figure 3**), pJIA patients with pain reported a greater extent of loss of functions (cognition) and gain of functions (behaviors altered by pain).

Conclusion: For the first time, a neuroimaging-based assessment of pJIA patients was executed. This allowed for novel insight to be gained regarding potential neurobiological factors driving pain in pJIA. The current multidisciplinary datasets are suggestive of non-inflammatory (centralized or neuropathic) and inflammatory pain mechanisms at play in pJIA.

1. Giancane, **Clin Exp Rheumatol.** (2017)
2. Shiff, **Pain**. (2018)

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Abstract Number: 1884

Autoantibodies to Malondialdehyde-acetaldehyde Preceding the Diagnosis of Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes III: Diagnosis & Prognosis

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Previous work has demonstrated that malondialdehyde-acetalehyde (MAA) adducts, resulting from oxidative stress, are formed in synovial and lung tissues of patients with rheumatoid arthritis (RA). Moreover, MAA co-localizes in these tissues with citrulline and generates robust anti-MAA antibody responses, suggesting a pathogenic role for MAA-adducted antigens in RA (Thiele GM et al. 2015, England BR et al. 2019). In this study, we sought to examine whether anti-MAA antibody responses were detectable in pre-clinical RA.

	Pre-diagnosis			Post-diagnosis
	Earliest Pre-RA diagnosis Sample	Midterm Sample	Closest Pre-RA diagnosis Sample	
RA cases, N	214	213	212	214
Time from Dx., yrs	-12.2 (15.7, 7.1)	-2.4 (3.0, 1.9)	-0.7 (1.1, 0.3)	+1.1 (0.7, 1.7)
IgA MAA	76 (29-149)	113 (54-212)	124 (74-247)	119 (63-202)
IgM MAA	215 (88-517)	347 (193-536)	359 (217-584)	366 (227-563)
IgG MAA	312 (149-600)	378 (237-733)	505 (301-877)	438 (251-774)
CCP2	0.5 (0.1, 1.5)	12.2 (0.9, 89.3)	58.8 (1.4, 216.2)	51.0 (2.7, 203.8)
CCP3.1	6.5 (4.4, 13.3)	43.7 (7.3, 261.7)	226.8 (13.3, 261.7)	255.0 (21.8, 261.7)
RF, IgM	5.4 (3.1, 11.4)	11.8 (4.1, 58.3)	29.3 (7.7, 104.7)	28.9 (7.6, 104.7)
Controls, N	210	208	207	109
IgA MAA	66 (30-129)	80 (43-155)	91 (53-165)	93 (60-204)
IgM MAA	255 (125-528)	335 (180-553)	360 (191-540)	368 (211-557)
IgG MAA	251 (148-435)	310 (200-591)	348 (206-568)	306 (207-574)
CCP2	0.3 (0.0, 0.7)	0.3 (0.0, 1.0)	0.3 (0.1, 1.0)	0.4 (0.1, 0.9)
CCP3.1	5.5 (3.8, 8.5)	5.9 (3.9, 8.3)	6.4 (3.8, 9.1)	8.5 (5.5, 10.5)
RF, IgM	4.2 (2.7, 7.8)	4.0 (2.0, 8.1)	3.8 (2.2, 7.0)	3.7 (2.2, 7.9)
P values, case v. control				
IgA MAA	0.572	**0.013**	**<0.001**	0.175
IgM MAA	0.409	0.816	0.486	0.741
IgG MAA	0.073	**0.004**	**<0.001**	**0.002**
CCP2	**<0.001**	**<0.001**	**<0.001**	**<0.001**
CCP3.1	**0.001**	**<0.001**	**<0.001**	**<0.001**
RF, IgM	**0.002**	**<0.001**	**<0.001**	**<0.001**

Table

*MAA antibody measured in AU/ml; CCP U/ml; RF IU/ml; significant p-values (case vs. control for given time point) shown in bold; values shown as median (interquartile range). **The identification of specific products or scientific instrumentation is considered an integral part of the scientific endeavor and does not constitute endorsement or implied endorsement on the part of the author, DoD, or any component agency. The views expressed in this abstract are those of the author and do not reflect the official policy of the Department of Army/Navy/Air Force, Department of Defense, or U.S. Government.

Methods: Using the Department of Defense Serum Repository, we identified 214 RA cases and 210 matched controls. We tested a mean of 3 serial serum samples from pre-RA diagnosis, and 1 post-RA diagnosis sample, for anti-MAA immunoglobulin (Ig) isotypes A, IgG, and IgM, anti-CCP antibody (CCP2 and CCP3.1), and RF (IgM). The relative timing and trajectories of autoantibody isotypes were evaluated. Case-control samples were compared for each time point using Wilcoxon rank-sum tests.

Results: RA cases and controls were similar in age, sex, race, and smoking status ($p > 0.05$). The timespan of oldest to newest sample was similar in RA cases (mean 12.8±5.6 years) and control (12.3±5.4 years) ($p=0.4$). Anti-MAA, CCP2, CCP3.1, and RF-IgM concentrations by sample in cases and controls are shown in the Table. CCP2, CCP3.1 and RF were significantly elevated in cases vs. controls in the earliest pre-RA diagnosis samples while anti-MAA (IgA, IgM) became significantly elevated in the midterm and closest samples pre-RA diagnosis.

Conclusion: IgA and IgG autoantibodies to MAA are increased pre-RA diagnosis, supporting a potential pathogenic role of immune responses targeting MAA in RA. In contrast to RF and anti-CCP, anti-MAA antibodies appear to be increased later in the pre-clinical period closer to the time of disease onset with higher IgA and IgG anti-MAA appearing, on average, at least 2-3 years prior to RA diagnosis. This suggests that anti-MAA responses may play a role in disease amplification and/or the transition to clinically-apparent RA, potentially after other autoantibodies (e.g. CCP and RF) have become elevated.

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Abstract Number: 1885

A Search to the Target Tissue in Which RA-specific Inflammation Starts: A Detailed MRI Study to Improve Identification of RA-specific Features in the Phase of Clinically Suspect Arthralgia

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes III: Diagnosis & Prognosis
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Based on a unique cohort of clinically suspect arthralgia (CSA) patients, we analysed which combinations of MRI-features at onset were predictive for Rheumatoid Arthritis (RA) development. This was done to increase our comprehension of locations of RA-onset and improve the predictive accuracy of MRI in CSA.

Methods: In the discovery cohort, 225 CSA-patients were followed on clinical arthritis development. Contrast-enhanced 1.5T MRIs were made of unilateral MCP(2-5), wrist and MTP(1-5)-joints at baseline and scored for synovitis, tenosynovitis and bone marrow edema. Severity, number and combinations of locations (joint/tendon/bone) with subclinical inflammation were determined, with symptom-free controls of similar age category as reference. Cox

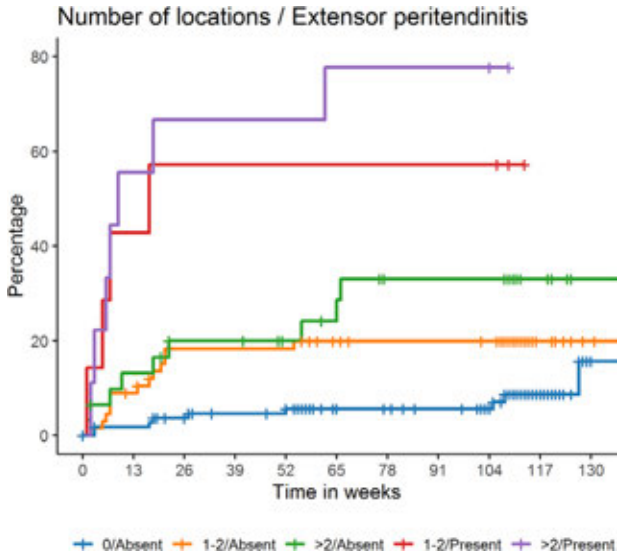

Figure 1. Kaplan Meijer curves showing the associations of the five risk-categories with inflammatory arthritis development in the discovery cohort. The five risk-categories are: 0/Absent: 0 locations with subclinical inflammation without MCP extensor peritendinitis; 1-2/Absent: 1-2 locations with subclinical inflammation without MCP extensor peritendinitis; >2/Absent: 3 or more locations with subclinical inflammation without MCP extensor peritendinitis; 1-2/Present: 1-2 locations with subclinical inflammation + MCP extensor peritendinitis; >2/ Present: 3 or more locations with subclinical inflammation + MCP extensor peritendinitis

regression was used for predictor selection. Predictive values were determined at 1-year follow-up. Results were validated in 209 CSA-patients.

Results: In both cohorts 15% developed arthritis < 1-year. The multivariable Cox model selected presence of MCP-extensor peritendinitis (HR 4.38 (2.07-9.25)) and the number of locations with subclinical inflammation (1-2 locations HR 2.54 (1.11-5.82); ≥3 locations HR 3.75 (1.49-9.48)) as predictors (Figure 1). Severity and combinations of inflammatory lesions were not selected. Based on these variables, five risk-categories were defined: no subclinical inflammation, 1-2 or ≥3 locations, with or without MCP-extensor peritendinitis. Positive predictive values (PPVs) ranged 5% (lowest category; NPV 95%)-67%(highest category). Similar findings were obtained in the validation cohort; PPVs ranged 4% (lowest category; NPV 96%)-63%(highest category).

Conclusion: Tenosynovitis, particularly MCP-extensor peritendinitis, is among the first tissues affected by RA. Incorporating this feature and number of locations with subclinical inflammation improved prediction making with PPVs up to 63-67%.

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Abstract Number: 1886

Antibody Systems Targeting Citrullinated, Carbamylated, and Peptidyl Arginine Deaminase Autoantigens Distinguish Rheumatoid Arthritis in Combination with Rheumatoid Factors

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SESSION INFORMATION

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Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Novel antibody systems including anti-carbamylated protein antibody (anti-CarP IgG) and anti-peptidyl arginine deiminase antibody (anti-PAD4 IgG) are emerging as independent diagnostic and prognostic biomarkers for rheumatoid arthritis (RA) and may add value to rheumatoid factor (IgM) and anti-citrullinated peptide antibody (ACPA IgG), the hallmark antibodies in RA. We evaluated the diagnostic performance of these markers in combination.

Methods: The cohort consisted of 638 consented subjects with RA (fulfilling the 1987 or 2010 ACR classification criteria, mean age: 59.8±0.5 years [SEM], 80% females) and a control group of 775 subjects (mean age: 44.7±0.5 years, 85% females, including systemic lupus erythematosus [n=369], primary Sjogren's syndrome [n=64], primary fibromyalgia [n=85], other connective tissue diseases [n=63], and a group of normal healthy donors [n=194]). Autoantibodies titers from serum were measured using fluoroenzyme immunoassays (IgM RF and anti-CCP [IgG]; Phadia, Upsala Sweden), ELISA (anti-CarP [IgG], research use only [RUO], Inova Diagnostics, San Diego) and bead-based Aptiva™ technology (anti-PAD4 [IgG], RUO, Inova Diagnostics) in a clinical laboratory accredited by the College of American Pathologists. For each positive antibody (above each cutoff) a score of 1 was assigned and the cumulative presence of the 4 antibodies was determined [range 0-4]. The ability of the biomarkers to distinguish RA from controls was calculated using sensitivity, specificity and interval likelihood ratio (LR). Predictive value (PPV) was estimated at 10% pre-test probability. Statistics consisted of Mann-Whitney and Chi-square test.

Results: In this cohort anti-CarP (>20 Units) yielded 33.5% sensitivity and 77.9% specificity. Anti-PAD4 (>1000 Units) yielded 35.0% sensitivity and 95.0% specificity. RF IgM (>5 Units/ml) and anti-CCP (>10 Units/ml) were 67.4% and 66.5% sensitive, respectively (87.5% and 97.0% specific, respectively). RA presented 5-fold higher 4-antibody system scores (2.02±0.05) than controls (0.42±0.02) (p< 0.01). Scores greater than 2 yielded 42% sensitivity and 98.8% specificity. A total of 82 subjects presented with full-house 4 antibodies (score = 4) and 81 of them had RA (99.9% specific). Interval LR and PV for each of the 4-antibody score are presented in the Table. There was no difference in the 4-antibody score between RA who fulfilled the 1987 ACR or 2010 ACR criteria (1.99±0.07 vs 2.08±0.09; p=0.40). In the subset of subjects newly diagnosed (less than one year), average 4-antibody system score for RA (n=33) was 1.72±0.22 (36.3% with score greater than 2) and 0.58±0.12 for other diseases (0% with score greater than 2, 100% specific) (p< 0.01).

Table 1. Combination of RF IgM, anti-CCP (IgG), anti-CarP (IgG), and anti-PAD4 (IgG)

Score	RA (%, N)	CTL (%, N)	Likelihood Ratio [CI 95%]	Pre-test PPV	Post-test PPV	Change
0	20.5% (131/638)	65.8% (510/775)	0.31 [0.27 to 0.37]	10%	3.4%	-6.6%
1	11.6% (74/638)	27.2% (211/775)	0.43 [0.33 to 0.54]	10%	4.5%	-5.5%
2	25.5% (163/638)	5.8% (45/775)	4.40 [3.22 to 6.02]	10%	32.8%	22.8%
3	29.6% (189/638)	1.0% (8/775)	28.70 [14.26 to 57.77]	10%	76.1%	66.1%
4	12.7% (81/638)	0.1% (1/775)	98.39 [13.73 to 705.04]	10%	91.6%	81.6%

Conclusion: This cumulative combination of antibody systems targeting citrullinated, carbamylated, PAD4 and RF is highly specific for RA. It may be useful in diagnosing and classifying RA even in symptomatic patients who present early in the course of disease.

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Abstract Number: 1887

Anti-Mitochondrial Antibodies Predict Severe Erosive Disease in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes III: Diagnosis & Prognosis
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Mitochondria are key regulators of metabolism, inflammation and cell death, with mitochondrial dysfunction being associated with several diseases. Though mainly found intracellularly, we recently made the observation that mitochondria (Mt) were extruded upon formation of neutrophil extracellular traps (NETs), a neutrophil cell death process commonly observed in autoimmune rheumatic diseases, including rheumatoid arthritis (RA). Other than the inflammatory potential of mitochondria, they are highly immunogenic, evoking an immune response with development of anti-mitochondrial antibodies (AMA). Anti-mitochondrial antibodies are also found in RA patients, with reactivity towards the mitochondrial-specific phospholipid cardiolipin having major clinical significance given the capacity to predispose to thrombosis and miscarriage. However, the potential pathogenic role of other AMAs in RA pathogenesis has not been carefully addressed. The aim of the current study was to investigate prevalence and clinical utility of AMAs in RA patients.

Methods: Mitochondria (Mt) were isolated from the human hepatic cell line HepG2 and analyzed for binding of AMAs using a state-of-the art flow cytometry-based method developed in-house. Two cohorts of healthy controls (HC) and RA patients were used: one cross-sectional (HC, n=30; RA, n=101) and one longitudinal inception cohort (HC, n=100; RA n=247). Purified whole Mt lysate was used to detect proteins targeted by RA AMAs via Western Blot.

Results: Using Western blot analysis, several mitochondrial proteins were identified to which RA patients, but not healthy individuals had reactivity. Of note, most RA patients (67%) recognized a 70 kDa mitochondrial protein ($p< 0.05$). Also by flow cytometry, assessing binding of RA IgG to highly purified mitochondria, AMA IgG levels were markedly elevated in the two RA cohorts as compared to HCs ($p< 0.0001$ and $p=0.02$). In the cross-sectional RA cohort, levels of AMAs were associated with a severe erosive disease ($p=0.01$). We next asked whether AMA positivity

could predict development of erosive disease using the longitudinal inception cohort with a median follow-up of 8 years. Consistent with prior studies, ACPA positivity predicted future erosive disease (OR=6.7, p< 0.0001). Of note, AMA positivity could also predict erosive disease independent of ACPA positivity (OR=4.6, p=0.006). Being positive for either of the autoantibodies further increased the odds ratio (10.4, p=0.002), suggesting additive value of the two markers. Further, in contrast to ACPA (OR=1.5, p=0.43), AMA could also predict joint space narrowing (OR=3.3, p=0.02).

Conclusion: Our results demonstrate the presence of an important, yet to be identified, novel mitochondrial autoantibody prevalent in RA patients. Further, these AMAs, by themselves, as well as in combination with established biomarkers, e.g. ACPA, provide significant clinical value in identifying patients at risk of developing severe erosive disease, allowing for preventative therapeutic strategies.

Disclosure: R. Moore, None; **T. Pan**, None; **J. Nelson**, None; **C. Lood**, None.

Abstract Number: 1888

Serum Calprotectin Is a Prognostic Marker for Drug-Free Remission in RA

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SESSION INFORMATION
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Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: The ability to accurately predict whether RA patients will flare following DMARD-tapering would open doors in clinical decision-making for achieving drug-free remission (DFR). Calprotectin (S100A8/A9 or MRP8/14), an inflammatory protein released locally by monocytes, is a marker of disease activity in RA[1]. We hypothesized that circulating calprotectin could indicate residual subclinical inflammation in patients who are in remission on DMARDs, and that patients with high calprotectin levels might thus be more prone to flare after DMARD-tapering. As such, we investigated the value of calprotectin levels as a marker for disease flare after DMARD-tapering.

Methods: We used data from two randomized controlled trials: the IMPROVED2 study and the RETRO3 study. The IMPROVED included early (< 2 years) untreated RA, was steered at disease activity score-remission (DAS44< 1.6), and, for those achieving remission at 8 months, rapidly tapered and stopped methotrexate to attempt drug-free remission. The RETRO randomized patients with long-standing RA in stable remission (DAS44< 2.6) to three arms: continue, taper by 50%, or stop (biological or conventional) DMARDs. Only patients in the taper or stop arms were included for this analysis. Circulating calprotectin at the tapering timepoint was determined using a diagnostic calprotectin kit (Inova Diagnostics, Research use only) in IMPROVED and using an in-house sandwich ELISA4 in RETRO. Logistic regression and area under the receiver operating characteristic curves (AUC) analyses were conducted

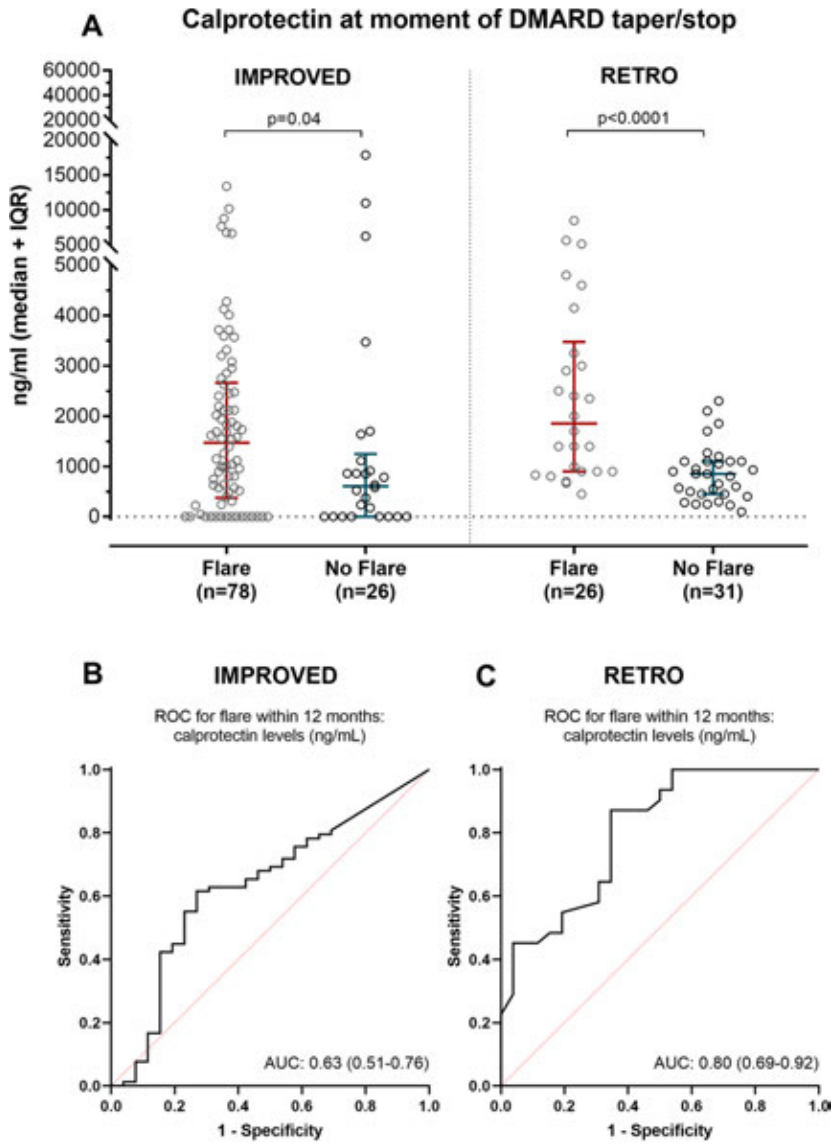

Figure 1. A) Circulating calprotectin levels (ng/mL) at the moment of DMARD tapering/stop, separated by whether patients experienced a disease flare within 12 months of tapering. p-values were calculated by Mann-Whitney-U tests. B-C) ROC-curves indicating the predictive value of circulating calprotectin levels (ng/mL) at the moment of DMARD-tapering/stop for disease flare within 12 months of tapering in the IMPROVED (B) and RETRO (C).

to evaluate the predictive value of calprotectin for flare (loss of remission) within 12 months of tapering/stopping DMARDs.

Results: In the IMPROVED and in the RETRO, respectively 104 and 57 patients were eligible to taper/stop DMARDs and had serum available. In both IMPROVED and RETRO, patients that flared within 12 months had higher calprotectin at the moment of DMARD-tapering/stop (Figure 1A). Two-fold higher calprotectin at the moment of DMARD-tapering/stop was associated with an increased risk (odds ratio) of flare of 1.1 (95% CI: 1.0-1.2) in the IMPROVED study and 3.6 (95% CI: 1.8-7.5) in the RETRO study. Correcting for clinical predictors of flare (body mass index, gender, anti-CCP2, and baseline DAS in IMPROVED; age and anti-CCP2 in RETRO) did not greatly alter these estimates: 1.1 (95% CI: 1.0-1.2) in the IMPROVED study and 4.0 (95% CI: 1.8 to 8.9) in the RETRO study. The AUC for

predicting flare within 12 months was 0.63 (95% CIs: 0.51-0.76) in the IMPROVED study and 0.80 (95% CIs: 0.69 to 0.92) in the RETRO study (Figure 1B-C).

Conclusion: Circulating calprotectin levels in RA patients in remission on DMARDs are associated with higher risk of disease flare upon DMARD-tapering. Calprotectin's ability to predict whether RA patients will flare following DMARD-tapering could aid in clinical decision-making for attempting drug tapering and discontinuation.

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4. https://doi.org/10.1136/annrheumdis-2011-200598

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Abstract Number: 1889

Biomarkers of Clinical Relapse and Radiological Progression in Patients with Rheumatoid Arthritis in Remission: Observational Study of 5 Years of Follow-up

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SESSION INFORMATION
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Background/Purpose: To search biomarkers of clinical relapse and radiological progression in patients with RA in clinical remission

Methods: RA patients in clinical remission (defined as DAS28-ESR < 2.6 for > 6 months) were selected. Clinical, epidemiological and serological data were analyzed. A MRI of dominant hand and an ultrasound assessment of knees and hands were performed at baseline and at 48 weeks. Serum levels of inflammation and angiogenesis biomarkers were determined by Quantibody® Human Array at baseline and 48 weeks. A synovial biopsy was performed in patients with subclinical synovitis. Patients were followed up for 5 years. Clinical and radiological data (hands and feet

X-rays) were collected. Clinical relapse was defined as loss of remission status (DAS28 > 2.6) leading to a therapeutic intervention. Treatment change was defined as the change in csDMARD or biological therapy of RA. Radiographic progression was defined as the change in the SvH index at 5 years >10.47 (SDD).

Results: 60 patients fulfilling ACR 2010 criteria for RA and DAS28< 2.6 were included. 1/3 also met remission criteria for SDAI (33.3%), CDAI (31.6%) and ACR (35%). 78.3% of the patients were women. Mean age was 53 years and the disease duration was 110 months. 81.6% were ACPA +. 26% were taking oral prednisone, 76% DMARDs and 45% biological therapies. At baseline, 67% had PD signal and 48% met a more stringent criteria for subclinical synovitis (UdAS: SH > 2 + PD). After 5 years of follow-up, 44 (73.3%), 11 (18.3%), 9 (15%) and 10 (16.6%) patients remained in remission according to DAS28, SDAI, CDAI and ACR criteria, respectively. 29 patients (48.3%) had flares at any time during the 5 years of follow-up. In the multivariate analysis, the variables that were related to clinical relapse were BMI (OR 1.8 CI 95% 1.2-2.7), TNFalpha levels at baseline (OR 32.4, CI 95% 1.9-546.2), the fisrt year change in CXCL16 levels (OR 1.05 CI 95% 1-1.1) and ESR (OR 2.48 CI 95% 1-6.1). Patients who flared during the follow-up had a significantly higher number of mast cells (p=0.02). Regarding to change in treatment, 20 patients (33.3%) changed DMARDs or biological therapy at any time during the 5 years of follow-up. In the logistic regression analysis, BMI (OR 1.3 CI 95% 1-1.7), biological therapy (OR 24.7 CI 95% 2.3-257.2), progression of erosions by MRI during the first year (OR 1.2, CI 95% 1-1.3) and the rate of progression of calprotectin serum levels during the first year (OR 2.8, CI 95% 1-8.2) were the main factors that predicted the change in baseline therapy after 5 years of follow-up . Finally, only 6 patients (10%) had X-Ray progression according to the SvdH index. The number of macrophages and T cells in synovial tissue at baseline was much higher in patients with radiological progression. Likewise, the first-year rate of bone edema was significantly higher in patients with structural progression (p = 0.04)

Conclusion: 27% of RA patients lost clinical remission (DAS28) after 5 years of follow-up. BMI, serum TNFa levels, and first-year rate of CXCL16 and VSG levels were predictors of joint flares. Baseline BMI, use of biological therapy, MRI erosions and calprotectin levels predicted the change of baseline therapy for RA. Only 10% of patients had radiological progression along the study.

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Abstract Number: 1890

Methotrexate Adverse Events in a Randomized Double-Blind Placebo-Controlled Trial:Results from the Cardiovascular Inflammation Reduction Trial (CIRT)

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SESSION INFORMATION

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Session Title: RA – Treatments III: Cardiovascular Disease & Readmissions

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Table 1: Frequency and Relative Risks of Adverse Events (AEs) During the Randomized Phase of CIRT				
	MTX N=2391	Placebo N=2395	p-value	Hazard ratio (95% CI)
	N (%)*			
All AEs of interest + laboratory AEs*	1968 (82.3)	1796 (75.0)	<0.01	1.27 (1.19, 1.35)
Mild	1911 (79.9)	1716 (71.7)	<0.01	1.28 (1.20, 1.37)
Moderate	729 (30.5)	579 (24.2)	<0.01	1.32 (1.18, 1.47)
Severe	205 (8.6)	156 (6.5)	<0.01	1.34 (1.09, 1.65)
All coded AEs**	2104 (88.0)	1998 (83.4)	<0.01	1.21 (1.14, 1.29)
Subtypes of adjudicated AEs of interest				
Gastrointestinal (including hepatic)	1091 (45.6)	682 (28.5)	<0.01	1.88 (1.71, 2.07)
Pulmonary	200 (8.4)	144 (6.0)	<0.01	1.41 (1.14, 1.75)
Infectious	602 (25.2)	528 (22.1)	0.01	1.16 (1.03, 1.31)
Hematologic (including hemorrhage)	1526 (63.8)	1393 (58.2)	<0.01	1.17 (1.09, 1.26)
Malignant	105 (4.4)	94 (3.9)	0.42	1.15 (0.87, 1.52)
Mucocutaneous	213 (8.9)	187 (7.8)	0.17	1.14 (0.93, 1.39)
Renal	44 (1.8)	49 (2.1)	0.61	0.89 (0.63, 1.26)
Neuro-psychiatric	78 (3.3)	83 (3.5)	0.70	0.96 (0.71, 1.31)
Musculoskeletal	155 (6.5)	135 (5.6)	0.22	1.16 (0.92, 1.46)
Notes: * N includes first events of a given type. The first mild, moderate, and severe are all included. As well, the first of each subtype of adverse event was included. ** The outcome labeled "all coded adverse events" includes all of the MedDRA coded events, not just the adjudicated events of interest.				

Background/Purpose: Prior observational studies have estimated the risk of adverse events with low dose methotrexate (MTX). However, prior randomized controlled trials (RCT) were too small to precisely estimate the risk of MTX-related adverse events (AEs). We investigated the risk of AEs in patients without rheumatic disease using MTX compared with placebo.

Methods: We conducted pre-specified secondary analyses of the CIRT randomized controlled trial (Ridker et al, NEJM, 2019). The trial was conducted in N. America among adults with known cardiovascular disease and diabetes or metabolic syndrome. Subjects were randomly allocated to low dose MTX (maximum 20mg/week) or placebo. All subjects received folic acid 1mg for six days/week. The "AEs of interest" were adjudicated blinded to study drug assignment; they included gastrointestinal (hepatic or other), pulmonary (COPD, bronchitis, or pneumonitis), infectious, hematologic (bleeding or cytopenias), malignant, mucocutaneous (skin, alopecia or oral lesions), renal (acute kidney insufficiency or nephrolithiasis), neuropsychiatric, and musculoskeletal. The frequency and relative rates of the specific AEs of interest, laboratory AEs (AST, ALT, and CBC) as well as all reported AEs were compared across treatment arms in intention to treat analyses. We estimated the hazard ratios (HR) using Cox proportional hazards regression. Skin cancers were further examined by sub-type using the same methods.

Results: 6,158 patients were enrolled and 4,786 randomized after a 5-8 week active run-in period and followed for a mean of 27 months on a median dosage of 16mg. Of the 2,391 subjects randomized to MTX, 2,104 (84.5%) experienced any AE and 1,968 (82.3%) experienced an AE of interest. This compared to 1,998 (78.0%) of the 2,395 randomized to placebo who experienced any AE and 1,796 (75.0%) who experienced an AE of interest. The relative rate of an AE of interest (**Table 1**) was 27% higher for those randomized to MTX (HR 1.27, 95% CI 1.19– 1.35) compared

Table 2: Frequency and Relative Risks of Skin Cancer Adverse Events (AEs) During the Randomized Phase of CIRT				
	MTX N=2391	Placebo N=2395	p-value	Hazard ratio (95% CI)
	N (%)*			
Skin Cancer Events	56 (2.3)	27 (1.1)	<0.01	2.20 (1.39, 3.50)
Basal cell	20 (0.8)	14 (0.6)	0.31	1.47 (0.74, 2.90)
Squamous cell	36 (1.5)	11 (0.5)	<0.01	3.55 (1.78, 7.05)
Melanoma	6 (0.3)	3 (0.1)	0.34	2.06 (0.52, 8.23)
* N includes first events of a given type.				

to placebo. The relative rates of gastrointestinal (HR 1.88, 95% CI 1.71-2.07), infectious (HR 1.16, 95% CI 1.03-1.31), pulmonary (HR 1.41, 95% CI 1.14-1.75), and hematologic (HR 1.17, 95% CI 1.09-1.26) events were elevated for those randomized to MTX. There was no difference between treatment arms for the risk of malignant, mucocutaneous, neuropsychiatric, musculoskeletal, or renal AEs. While there were no overall differences in malignancies, skin cancers were more common in patients randomized to MTX than placebo, with a composite skin cancer HR 2.20 (95% CI 1.39-3.50) and squamous cell cancer HR 3.55 (95% CI 1.78-7.05) (**Table 2**).

Conclusion: In this large RCT among patients with known cardiovascular disease, MTX was associated with a significantly increased risk of AEs compared with placebo. While the trial was conducted in non-rheumatic disease patients and only select adverse events were adjudicated, the elevated risks observed for infectious, pulmonary, gastrointestinal, hematologic and skin cancer events represent a broad range of clinical issues, requiring further examination. These results quantify risk of MTX for the many clinicians and patients considering treatment across the spectrum of systemic rheumatic diseases.

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Abstract Number: 1891

Hydroxychloroquine Use Is Associated with a Lower Risk of Major Adverse Cardiovascular Events in Medicare Recipients with Rheumatoid Arthritis

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SESSION INFORMATION

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Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Hydroxychloroquine (HCQ) has known immunomodulatory effects and mechanistic actions that may provide cardioprotective effects. To date, cardiovascular (CV) outcomes in elderly patients receiving HCQ in clinical practice have not been evaluated. This is important since the majority of patients with CV disease in the U.S. are adults ≥ 65 years. We hypothesized that the use of HCQ is protective for major adverse cardiovascular events (MACE) defined as acute admissions for stroke, myocardial infarction or heart failure.

Methods: We compared the risk of MACE in a retrospective cohort of Medicare beneficiaries aged ≥65 years with rheumatoid arthritis (RA) who initiated HCQ (exposed) and who did not initiate HCQ (non-exposed) between 2014 and 2016. RA was defined by the following ICD codes – 714.0, 714.2, M05.xx, M06.4 and M06.1. Data sources included Medicare Parts A, B, and D claims for a 5% random sample of beneficiaries. The index date for the exposed was defined by the date of the first HCQ fill. Each exposed user was matched to 2 non-users of HCQ using propensity score derived from patient baseline characteristics including demographics, comorbid conditions like prior CV disease, and other medication use (cardioprotective agents like ACE inhibitors, antiplatelets, statins and beta blockers, NSAIDs, opioids, steroids, methotrexate, and tumor necrosis factor alpha inhibitors [TNFi]) (Table 1). Patient follow-up started at the index date and continued until the first MACE, end of HCQ use or the end of the observation period (December 31, 2016). We compared incident MACE using Kaplan-Meier analysis on matched patients. The primary outcome was the occurrence of MACE, and the secondary outcome was the composite of MACE and all-cause mortality. Cox proportional hazards model was used to compare the hazards of MACE events between HCQ users to non-users.

Table 1. Demographics and Baseline Characteristics of HCQ users v/s non users

Table 1. Demographics and Baseline Characteristics of HCQ users v/s non users					
Characteristics	HCQ non users (n=233218)	Matched HCQ non - users (n=3264)	HCQ users (n=1632)	Standardized Difference (before matching)	Standardized Difference (after matching)
Demographics					
Age, mean (SD)	77.27(7.82)	74.33(6.73)	74.37(6.46)	0.404	0.006
Age groups					
1:65-74	40.92	57.18	56.74		
2:75-84	38.84	34.99	35.52		
3:85+	20.25	7.83	7.74		
Female gender (%)	74.43	72.53	75.41		
Race/ethnicity (%)					
White	81.16	82.33	81.21		
Black	9.81	7.52	8.05		
Hispanic	5.93	4.84	5.06		
Other	3.1	5.31	5.68		
Baseline health and comobidities					
Cardiovascular disease (%)	0.17	1.81	3.56	0.252	0.108
Pain	1.59	10.17	24.34	0.72	0.382
Steroids (%)	2.85	67.32	68.1	1.864	0.017
Methotrexate (%)	1.81	23.06	27.15	0.772	0.094
TNFi (%)	0.34	2.97	3.87	0.248	0.05
NSAID	2.65	49.59	47.32	1.264	0.046
Opioids	3.19	51.28	50.94	1.274	0.007
Biologic DMARDs	0.38	3.59	4.74	0.279	0.058
Non-biologic DMARDs	2.46	30.62	41.45	1.068	0.227
ARB/ACE	3.96	51.78	50.31	1.222	0.029
Antiplatelet	0.76	8.8	8.68	0.38	0.004
Antiarrhythmic	3.88	49.47	45.82	1.11	0.073
Statin	3.65	51.34	49.13	1.264	0.044
Beta Blocker	2.48	31.27	28.96	0.781	0.05

Results: We found 1602 eligible RA patients with incident HCQ use and matched them to 3204 RA patients who did not use HCQ over the study period. The mean age of HCQ user cohort was 74.37 years and of the non-users was 74.73. 75.41% of the HCQ users were females compared to 72.53% in the non-users. The mean follow-up time was 1.7 years in non-users and 1 year in HCQ users. During the observation period, 329 MACE events occurred, 54 in HCQ exposed (3.51 per 100 patient-years) and 275 in the non-exposed group (incidence rate of 5.38 per 100 patient-years. Multivariate Cox regression model showed a hazard ratio (HR) of 0.47 (95% CI: 0.35-0.63, p< 0.0001) for MACE for HCQ users versus non-users. Compared to people aged 85+ years, those aged 75 to <85 (HR 0.73, 95% CI: 0.51 – 1.04), or those aged 65 to <75 (HR 0.59, 95% CI: 0.42 – 0.84) years had a lower hazard of MACE. Similarly, the HR for composite outcome of MACE and all-cause mortality was 0.40 (95% CI: 0.32-0.51, p< 0.0001) for users compared to non-users.

Conclusion: Our study suggests that incident HCQ use is associated with a 53% lower risk of MACE events compared to non-users in an elderly population of patients with RA. Based on our study, future larger trials can be designed looking at the efficacy of a well-tolerated and relatively inexpensive drug on CV outcomes in the general population.

Disclosure: P. Iyer, None; **Y. Gao**, None; **S. Girotra**, None; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **M. Vaughan-Sarrazin**, None; **N. Singh**, None.

Abstract Number: 1892

Association Between Rheumatoid Arthritis Treatment and the Risk of Death or Readmission After Major Surgery

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SESSION INFORMATION
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Background/Purpose: The impact of immunosuppression on post-operative outcomes in rheumatoid arthritis (RA) has primarily been studied in patients undergoing joint replacement surgery. We aimed to evaluate the impact of glucocorticoids and biologics on outcomes after other major surgeries.

Methods: Using Medicare claims data 2006-2015 we identified adults with ≥2 diagnoses of RA who received methotrexate, a TNF inhibitor, abatacept, rituximab, tocilizumab, or tofacitinib within 6 months before major surgery and had 1 year of continuous prior Medicare enrollment (baseline). Hip fracture repair, abdominal surgeries (cholecystectomy, hysterectomy, hernia surgery, appendectomy, colectomy for diverticular disease), and cardiac surgeries (coronary artery bypass graft, mitral or aortic valve surgery) were identified based on primary ICD-9 procedure codes from inpatient hospitalization using established definitions. Patients with malignancy or HIV and patients with another major

Table 1: Select Cohort Characteristics

	Full cohort for glucocorticoid analyses	Biologic/tsDMARD or MTX within 8 weeks of surgery
N	13544	10677
Age, mean +/- standard deviation	72.3 +/- 11.3	72.5 +/- 11.2
Female	10840 (80.0%)	8549 (80.1%)
White	10694 (79.0%)	8448 (79.1%)
Hip fracture surgery	4328 (32.0%)	3559 (33.3%)
Abdominal surgery	6403 (47.3%)	4975 (46.6%)
Cholecystectomy elective	603 (4.5%)	443 (4.1%)
Cholecystectomy non-elective	2280 (16.8%)	1797 (16.8%)
Hysterectomy (all elective)	1022 (7.5%)	819 (7.7%)
Hernia surgery elective	625 (4.6%)	494 (4.6%)
Hernia surgery non-elective	470 (3.5%)	373 (3.5%)
Appendectomy (all non-elective)	434 (3.2%)	354 (3.3%)
Colectomy elective	400 (3.0%)	267 (2.5%)
Colectomy non-elective	569 (4.2%)	428 (4.0%)
Cardiac surgery	2813 (20.8%)	2143 (20.1%)
Coronary artery bypass graft elective	621 (4.6%)	459 (4.3%)
Coronary artery bypass graft non-elective	1017 (7.5%)	803 (7.5%)
Mitral/aortic valve surgery elective	638 (4.7%)	477 (4.5%)
Mitral/aortic valve surgery non-elective	537 (4.0%)	404 (3.8%)

Frequency (%) shown except where otherwise indicated

Table 2: Associations between glucocorticoids and biologics/tsDMARDs with mortality and readmission

	N	90-Day Mortality			30-Day Readmission		
		Mortality N (%)	Unadjusted OR (95% CI)	Propensity weighted OR (95% CI)	Readmission N (%)*	Unadjusted OR (95% CI)	Propensity weighted OR (95% CI)
Glucocorticoids							
None	7162	312 (4.3)	-	-	750/6688 (11.2)	-	-
≤5mg/day	3894	325 (6.0)	**1.41 (1.19-1.68)**	**1.27 (1.05-1.52)**	487/3596 (13.5)	**1.24 (1.10-1.40)**	1.11 (0.98-1.26)
5-10mg/day	1872	135 (7.2)	**1.70 (1.38-2.10)**	**1.44 (1.14-1.81)**	288/1710 (16.8)	**1.60 (1.38-1.86)**	**1.30 (1.11-1.53)**
>10mg/day	616	55 (8.9)	**2.17 (1.61-2.92)**	**1.63 (1.11-2.40)**	111/557 (19.9)	**1.97 (1.58-2.46)**	**1.51 (1.13-2.02)**
Biologics/tsDMARDs vs. Methotrexate							
Methotrexate	6194	401 (6.5)	-	-	781/5690 (13.7)	-	-
TNF	3523	134 (3.8)	**0.57 (0.47-0.70)**	0.83 (0.67-1.03)	367/3295 (11.1)	**0.79 (0.69-0.90)**	**0.86 (0.75-0.995)**
Non-TNF biologic/tsDMARD	1060	42 (4.0)	**0.60 (0.43-0.82)**	0.76 (0.49-1.20)	134/992 (13.5)	0.98 (0.81-1.20)	1.02 (0.78-1.33)

Propensity weighted odds ratios (OR) from inverse probability weighted logistic regression models. Both glucocorticoid and biologic propensity score models include age, sex, race, disability, region, urban, income, surgery type, number previous biologics, hydroxychloroquine/sulfasalazine/leflunomide, NSAIDs, opioids, antibiotics, Charlson score, extra-articular RA, diabetes, hypertension, congestive heart failure, lung disease, kidney disease, obesity, number hospitalizations past year, number emergency department visits past year, hospitalized infection past year, number outpatient visits past year, skilled nursing facility stay. Glucocorticoid propensity score models also include biologic/MTX exposure and time of last biologic/MTX infusion or prescription. Biologic propensity score models also include glucocorticoid dose past 90 days. Unbalanced covariates included in weighed models. Bold cells indicate $p < 0.05$.

* Readmission reported among patients discharged to home, home health, skilled nursing facility, or inpatient rehabilitation

Table 3: Associations between glucocorticoids and biologics with mortality and readmission by surgery type

	90-Day Mortality Propensity Weighted OR (95% CI)			30-Day Readmission Propensity Weighted OR (95% CI)		
	Hip Fracture Surgery	Abdominal Surgery	Cardiac Surgery	Hip Fracture Surgery	Abdominal Surgery	Cardiac Surgery
Glucocorticoids						
None	-	-	-	-	-	-
≤5mg/day	1.20 (0.91-1.50)	1.09 (0.79-1.51)	**1.55 (1.06-2.27)**	0.97 (0.76-1.25)	1.15 (0.95-1.39)	1.20 (0.94-1.53)
5-10mg/day	1.16 (0.77-1.76)	**1.52 (1.06-2.18)**	**2.04 (1.27-3.28)**	**1.59 (1.16-2.18)**	1.10 (0.86-1.40)	**1.50 (1.08-2.10)**
>10mg/day	1.38 (0.65-2.92)	1.22 (0.67-2.21)	**2.70 (1.18-6.18)**	1.56 (0.83-2.93)	**1.58 (1.06-2.35)**	1.24 (0.57-2.70)
Biologics/tsDMARDs vs. Methotrexate						
Methotrexate	-	-	-	-	-	-
TNF	0.82 (0.55-1.19)	0.87 (0.61-1.24)	0.95 (0.63-1.44)	0.80 (0.60-1.08)	0.88 (0.72-1.08)	0.93 (0.71-1.23)
Non-TNF biologic/tsDMARD	0.65 (0.31-1.39)	0.85 (0.41-1.75)	0.48 (0.21-1.08)	0.91 (0.48-1.72)	1.02 (0.69-1.50)	0.98 (0.58-1.65)

Odds ratios from inverse probability weighted logistic regression models. Propensity scores are re-calculated for each surgery type and include the same variables as the models shown in Table 2. Bold cells indicate $p < 0.05$.

surgery within 6 months were excluded. Inverse probability weighted logistic regression models assessed association between average glucocorticoid dose in the 90 days before surgery (none, ≤5mg, 5-10mg, >10mg) and risk of 90-day mortality and 30-day readmission (among patients discharged to home, skilled nursing facility, or inpatient rehabilitation). Propensity score models included surgery type, elective vs. non-elective surgery, demographics, and measures of healthcare utilization, comorbidities, and previous infection during the baseline period. Separate models with recalculated propensity scores compared risk of these outcomes in patients receiving a biologic or targeted synthetic DMARD (tsDMARD) vs. patients exposed to methotrexate without biologics/tsDMARDs, requiring patients to have an infusion or prescription within 8 weeks before surgery.

Results: We identified 13544 surgeries meeting all inclusion and exclusion criteria, including 4328 hip fracture surgeries, 6403 abdominal surgeries, and 2813 cardiac surgeries. Glucocorticoids were associated with a dose-dependent increase in the risk of 90-day mortality and 30-day readmission, although associations were partially attenuated in propensity weighted models (Table 2). Associations with mortality were strongest among patients undergoing cardiac surgery, while associations with 30-day readmission were similar across surgeries (Table 3). Among the 10677 (78.8%) of patients who received their biologic/tsDMARD or methotrexate within 8 weeks of surgery, we found no significant increase in the risk of 90-day mortality or 30-day readmission in patients receiving a TNF or patients receiving a non-TNF biologic/tsDMARD vs. patients receiving methotrexate, with similar results across surgery types (Tables 2-3).

Conclusion: Glucocorticoids are associated with greater risk of adverse outcomes after major surgery, especially at higher doses. Recent exposure to biologics/tsDMARDs, however, is not associated with increased mortality or readmission.

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Abstract Number: 1893

Statin Exposure Moderates the Effects of Chronic Inflammation on Coronary Atherosclerosis Progression and Cardiovascular Events in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
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Background/Purpose: Chronic inflammation yields higher risk of cardiovascular events (CVE) in patients with rheumatoid arthritis (RA). We recently reported that occult atherosclerosis burden on coronary computed tomography

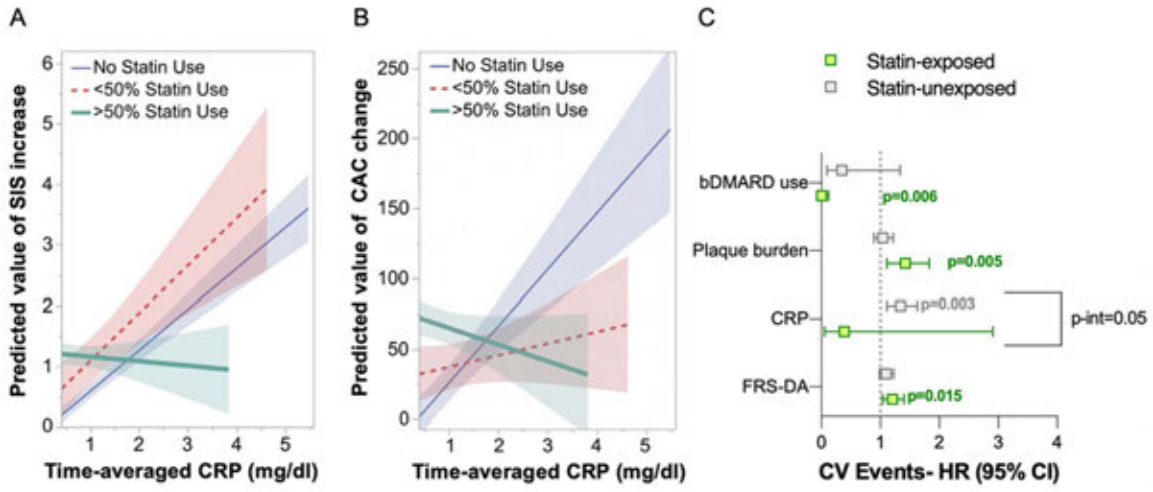

Figure 1. Statin exposure moderates the effect of cumulative inflammation on (A) coronary plaque, (B) CAC progression and (C) CVE risk in RA. FRS-DA: D'Agostino Framingham cardiovascular risk score.

angiography (CCTA) predicted CVE in RA beyond cardiac risk factors or scores. We further showed that that higher cumulative inflammation independently predicted coronary plaque progression. We here explored whether statin exposure impacted plaque progression or incident CVE in RA; we further evaluated potential interactions of statin treatment with cumulative inflammation on both outcomes.

Methods: One hundred-fifty RA patients underwent a baseline CCTA and followed thereafter; 101 had a repeat scan within 83±3.6 months. Coronary artery calcium (CAC) was reported as Agatston score. Segment involvement score (SIS) reported numbers of coronary segments with plaque; segment stenosis score (SSS) reflected the cumulative plaque stenosis. Plaque composition was defined as non-calcified (NCP), mixed or calcified. Cox proportional hazards regression models with time-varying covariates evaluated predictors of CVE. Negative binomial regression was used to assess count outcomes and a generalized linear model with a Tweedie (Poisson-Gamma) error distribution for CAC change.

Results: Longer statin exposure independently inhibited NCP progression [OR=0.72 (0.57-0.90), p< 0.01]. An interaction between cumulative inflammation and duration of statin exposure on total SIS increase (p=0.017) as well as CAC increase (p=0.006) was observed independently of age, dyslipidemia, total prednisone and methotrexate dose and bDMARD duration (Figure 1A and B respectively); higher time-averaged CRP yielded significant plaque progression in patients not on statin [RR=1.48 (1.05-2.09), p=0.025] or those receiving statins< 50% of the study period [RR=1.31 (1.01-1.69), p=0.040]. In contrast, in subjects with statin exposure >50% of study time, such risk was not observed [RR=1.07 (0.93-1.22), p=0.35]. Similarly for CAC, higher time-averaged CRP yielded greater progression risk in statin unexposed patients [OR=2.33 (1.29-4.22), p=0.005]; in contrast, any statin exposure mitigated that risk [OR=1.17 (0.81-1.68), p=0.41 for exposure< 50% and OR=0.96 (0.44-2.17), p=0.98 for exposure >50%]. Sixteen RA patients incurred 19 CVEs. Higher cumulative inflammation yielded significantly higher CVE risk in patients not receiving statins vs. those who do [HR=1.34 (1.11-1.63), p=0.003 and 0.39 (0.05-2.91), p=0.36 respectively, p-interaction=0.05, Figure 1C].

Conclusion: Statin exposure moderates the effect of cumulative inflammation on coronary atherosclerosis progression and CVE risk in RA. The atheroprotective effect of statins may highlight potential local anti-inflammatory attributes at the plaque level independently of systemic inflammation.

Disclosure: G. Karpouzas, Bristol Meyer Squibb, 8, bristol Meyer Squibb, 8, Bristol-Meyer-Squibb, 8, Pfizer, 2, 9, pfizer, 2, Sanofi, 5, 8; **S. Ormseth**, None; **E. Hernandez**, None; **M. Budoff**, None.

Abstract Number: 1894

Risk of Venous Thromboembolism in Rheumatoid Arthritis Patients Initiating Biologic and Non-biologic DMARDs, a Population-based Study

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SESSION INFORMATION

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Background/Purpose: Patients with rheumatoid arthritis (RA) have an increased risk of venous thromboembolism (VTE, which includes pulmonary embolism [PE] and deep vein thrombosis [DVT]) compared with the general population. However, population-based data on the risk of VTE among patients with newly diagnosed RA and new users of disease-modifying anti-rheumatic drugs (DMARDs) are limited. The objectives of our study were: 1) to estimate the incidence rate of VTE, PE, DVT among new users of biologic DMARDs (bDMARDs) and conventional DMARDs (cDMARDs) in RA patients. 2) To compare risk of VTE, PE and DVT between new users of bDMARDs and cDMARDs.

Methods: We conducted a population-based cohort study using administrative data that included all visits to physician and hospital from Jan 1990 until Mar 2015 and all dispensed medication from Sep 1995 to Mar 2015. Our sample included all patients with newly diagnosed RA using a previously validated case definition from physician billing data; and who were new users of a DMARD (no prior use in the 365 days before the first DMARD). Date of first DMARD use was considered the index date. For discontinuation, the exposure risk window for each DMARD extended until 30 days after the expiration of the last fill. Our outcomes of interest were first ever VTE, PE, and DVT based on ICD-9 or ICD-10 codes plus dispensation of an oral anti-coagulant. Follow-up began on the index date and continued until the earliest occurrence of: 1) DAMRD discontinuation; 2) leaving the province; 3) death; 4) the end of the study period; 5) the outcome of interest; or 6) switching to another DMARD. We calculated incidence rates per 100 person-years for

Table 1. Incidence rates of VTE by DMARDs use

Treatment	Total (N)	Events (n)	Person-Time (PY)	Follow-Up Time (Mean)	IR (95% CI) per 100 PY
All cDMARDs combined	14,809	40	10,965	0.74	0.36 (0.26, 0.50)
Leflunomide	2,799	5	1,381	0.49	0.36 (0.12, 0.84)
Methotrexate	14,610	37	10,714	0.73	0.35 (0.24, 0.48)
All bDMARDs combined	4,723	24	5,104	1.08	0.47 (0.30, 0.70)
Adalimumab	1,698	5	1,742	1.03	0.29 (0.09, 0.67)
Certolizumab pegol	212	<5	148	0.70	NA
Etanercept	2,785	19	3,629	1.30	0.52 (0.32, 0.82)
Golimumab	241	<5	212	0.88	NA
Infliximab	842	<5	373	0.44	0.54 (0.06, 1.94)
Anti-TNF biologics combined	4,444	22	4,972.7	1.12	0.44 (0.28, 0.67)
Rituximab	609	<5	99.2	0.16	1.01 (0.03, 5.62)
Tocilizumab	231	<5	209	0.91	0.96 (0.12, 3.46)
Abatacept	585	<5	439	0.75	0.46 (0.06, 1.65)
Tofacitinib	NA	NA	NA	NA	NA
Non-anti-TNF biologics combined	1,157	<5	605.2	0.52	0.66 (0.18, 1.69)

Table 2. Incidence rates of VTE by DMARDs use by age and sex groups

Treatment	Total (N)	%	Events (n)	Follow-Up Time Mean	Person-Time (PY)	IR (95% CI) per 100 PY
cDMARDs combined						
18-49 yrs.	4,223	28.5	<5	0.66	2,804	0.07 (0.01, 0.26)
50-59 yrs.	3,588	24.2	5	0.72	2,601	0.19 (0.06, 0.45)
60-64 yrs.	1,722	11.6	<5	0.77	1,332	0.23 (0.05, 0.66)
65+ yrs.	5,276	35.6	30	0.80	4,228	0.71 (0.48, 1.01)
Male	10,879	73.5	28	0.74	8,024	0.35 (0.23, 0.50)
Female	3,919	26.5	12	0.75	2,939	0.41 (0.21, 0.71)
bDMARDs combined						
18-49 yrs.	1,460	30.9	<5	0.93	1,364	0.15 (0.02, 0.53)
50-59 yrs.	1,306	27.7	<5	1.12	1,457	0.21 (0.04, 0.60)
60-64 yrs.	658	13.9	<5	1.26	830	0.36 (0.07, 1.06)
65+ yrs.	1,299	27.5	16	1.12	1,453	1.10 (0.63, 1.79)
Male	3,500	74.1	17	1.07	3,749	0.45 (0.26, 0.73)
Female	1,222	25.9	7	1.11	1,355	0.52 (0.21, 1.06)

Table 3. Relative risk of incident VTE, PE and DVT according to DMARDs use

	B-DMRADs	C-DMARDs
Venous Thromboembolism (VTE)	N = 4723	N = 14809
Cases, N	24	40
Incidence Rate/1000 Person-Years	0.47	0.36
Age-, Sex-, Entry Time-Adjusted Cox HR (95% CI)	1.58 (0.94, 2.65)	1
*Fully-Adjusted Cox HR (95% CI)	1.20 (0.67, 2.15)	1
Pulmonary Embolism (PE)	N = 4730	N = 14831
Cases, N	11	16
Incidence Rate/1000 Person-Years	0.21	0.15
Age-, Sex-, Entry Time-Adjusted Cox HR (95% CI)	1.76 (0.80, 3.85)	1
*Fully-Adjusted Cox HR (95% CI)	1.20 (0.49, 2.91)	1
Deep Vein Thrombosis (DVT)	N = 4730	N = 14826
Cases, N	16	31
Incidence Rate/1000 Person-Years	0.31	0.28
Age-, Sex-, Entry Time-Adjusted Cox HR (95% CI)	1.39 (0.75, 2.57)	1
*Fully-Adjusted Cox HR (95% CI)	1.04 (0.53, 2.04)	1

*adjusted for age, sex, number of outpatient and inpatient visits, charlson comorbidity index, obesity, alcoholism, hypertension, sepsis, varicosed vein, inflammatory bowel disease, trauma, fracture, surgery, glucocorticoid use, hormone replacement therapy, oral contraceptives, aspirin, cox-2 inhibitors

each outcome (Table 1). Incidence rates of VTE were also stratified by age and sex. Furthermore, we conducted Cox proportional hazard regression models to estimate the hazard ratio (HR) of incident VTE, PE, and DVT during periods of bDMARDs use relative to periods of cDMARDs use after adjusting for baseline covariates.

Results: 14,809 patients were new users of cDMARDs (74% female, mean age of 58 yrs) and 4,723 were new users of bDMARDs (74% female, mean age of 56 yrs). Among new users of cDMARDs and bDMARDs, 40 and 24 patients developed VTE, the incidence rate was 0.36 and 0.47 per 100 person-years (Table 1), respectively. Across cDMARDs and bDMARDs, risk of VTE increased with age and was also higher in men than women (Table 2). Comparing bD-

MARDs with cDMARDs, the fully adjusted HRs were 1.20 (95% CI, 0.67-2.15), 1.20 (95% CI, 0.49-2.91), 1.04 (95% CI, 0.53-2.04) (Table 3), for VTE, PE, DVT, respectively.

Conclusion: The incidence rate of VTE varies by age and sex among RA patients treated with different DMARDs. The point estimate suggests a potentially increased risk of VTE in bDMARDs compared to cDAMRDs, but the results were not statistically significant. Further studies with larger sample size and adjusting for confounding by indication are needed.

Disclosure: L. Li, None; **N. Lu**, None; **D. Lacaille**, None; **H. Xie**, None; **J. Esdaile**, None; **J. Avina-Zubieta**, None.

Abstract Number: 1895

Biologics Prevent Cardiovascular Events in Rheumatoid Arthritis by Inhibiting Non-calcified Coronary Plaque Progression and Stabilizing Vulnerable Plaques

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: RA – Treatments III: Cardiovascular Disease & Readmissions
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Biologic disease-modifying antirheumatic drugs (bDMARDs) may decrease cardiovascular events (CVE) in Rheumatoid arthritis (RA). We here evaluated whether bDMARDs reduce long-term CVE risk in RA; we further explored whether potential benefits were rendered by altering the trajectory of coronary plaque progression or stability.

Methods: One hundred-fifty patients without CV disease underwent a baseline coronary computed tomography angiography (CCTA) and followed thereafter; 101 underwent repeat CCTA within 83±3.6 months. Coronary artery calcium (CAC) was quantified by the Agatston method. Segment involvement score (SIS) reported numbers of coronary segments with plaque; segment stenosis score (SSS) reflected the cumulative plaque stenosis. Plaque composition

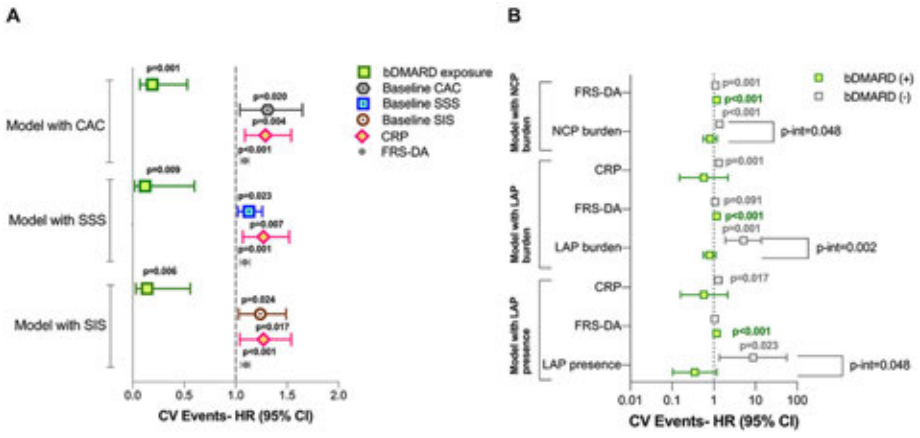

Figure 1. (A) bDMARD use independently lowers CV event risk in RA. **(B)** bDMARDs moderate the effect of soft, NCP burden as well as LAP presence and burden on long-term CVE risk.

was defined as non-calcified (NCP), mixed or calcified. Lesions containing necrotic cores (low attenuation plaques-LAP) were deemed vulnerable. Cox proportional hazards regression models with time-varying covariates evaluated predictors of CVE. Robust logistic regression was used to assess plaque progression, and a generalized linear model with a Tweedie (Poisson-Gamma) error distribution for CAC change.

Results: Sixteen RA patients incurred 19 CVEs. Use of bDMARDs lowered CVE risk independently of cardiac scores, baseline atherosclerosis burden and time-varying CRP (Figure 1A, all p< 0.009). bDMARD use moderated the effect of baseline NCP burden on CVE risk (p-interaction=0.048); higher NCP load yielded higher risk only in bDMARD unexposed patients [HR=1.37 (1.16-1.61)], but not in exposed ones [HR=0.82 (0.56-1.20), Figure 1B]. Indeed, longer bDMARD use inhibited NCP progression independently of statin exposure, cumulative prednisone and methotrexate doses [OR=0.77 (0.61-0.98)]. Moreover, bDMARD use moderated the effect of baseline LAP presence and burden on CVE risk [p-interaction=0.048 and 0.002 respectively, Figure 1B]. LAP presence yielded an 8.8-fold [(1.36-56.80)] higher risk of CVE in patients not on bDMARDs but not in those on bDMARDs [HR=0.35 (0.10-1.19)]. Similarly, higher baseline LAP burden yielded greater CVE risk exclusively in patients not on bDMARDs [HR=5.16 (1.90-13.99)] but not in those receiving bDMARD [HR=0.79 (0.56-1.10)]. Longer bDMARD use reduced the likelihood of LAP presence on follow-up [OR=0.22 (0.07-0.69)] after adjustment for cardiac scores. Indeed, patients with LAP loss or lower LAP burden on follow-up had longer exposure to bDMARDs compared to those without [differences of 3.75 years (0.46-7.04), p=0.028 and 6.08 years (3.02-9.13), p=0.001 respectively].

Conclusion: bDMARD use reduces CVE risk in RA, possibly by inhibiting non-calcified coronary plaque progression, remodeling and by stabilizing vulnerable plaques.

Disclosure: G. Karpouzas, Bristol Meyer Squibb, 8, bristol Meyer Squibb, 8, Bristol-Meyer-Squibb, 8, Pfizer, 2, 9, pfizer, 2, Sanofi, 5, 8; **S. Ormseth**, None; **E. Hernandez**, None; **M. Budoff**, None.

Abstract Number: 1896

Breastfeeding in Women with Rheumatic Diseases

Naira Ikram ,[1] Amanda Eudy,[1] and Megan Clowse[1], [1]Duke University, Durham

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: For many women, breastfeeding is a central aspect of motherhood, but many worry that their rheumatic disease or treatment will interfere. Fortunately, most anti-rheumatic medications are compatible with breastfeeding. This study sought to identify the frequency and predictors of the desire to and actually breastfeeding in women with a range of rheumatic diseases.

Methods: All pregnant patients with rheumatic disease in a single center between 2008-2018 in a prospective study of pregnancy and the post-partum period. Women were grouped into 4 diagnosis categories: systemic lupus erythematosus (SLE), undifferentiated connective tissue disease (UCTD), inflammatory arthritis (including rheumatoid, psoriatic, juvenile idiopathic arthritis, and spondyloarthropathies) and other rare rheumatic diseases. Breastfeeding intention was collected at study entry and breastfeeding was recorded at the post-partum visit. Infant feeding was divided into those who exclusively formula-fed, compared to those who exclusively breastfed or fed with a combination of breastmilk and formula.

Table 1. Maternal and Infant Characteristics by Method of Infant Feeding at the Post-partum Rheumatology Visit.

	Formula Only N=92 (35%)	Breastfeeding N=173 (65%)	P-value
Maternal Diagnosis			
SLE	38 (41%)	50 (29%)	0.081
UCTD	7 (8%)	26 (15%)	
Arthritis	30 (33%)	70 (40%)	
Rare rheumatic diseases*	17 (18%)	27 (16%)	
Maternal Demographics			
Race (black)	30 (33%)	29 (17%)	0.005
Mean age	29.6 (5.9)	32.2 (5.1)	0.0004
Education: at least college graduate	47 (52%)	137 (81%)	<0.001
Income under $50,000	40 (47%)	32 (20%)	<0.001
Single	21 (24%)	15 (9%)	0.002
Feeding Plan during Pregnancy			
Plan to breastfeed	53 (58%)	158 (90%)	<0.001
Plan to use formula	29 (32%)	5 (3%)	
Unsure	10 (11%)	12 (7%)	
Health of the Baby:			
Gestational age			
- Preterm (>37)	28 (30%)	27 (16%)	0.007
- Very preterm (<34)	8 (9%)	11 (6%)	0.5
Neonatal intensive care unit admission	27 (31%)	22 (14%)	0.003

* Rare Rheumatic Diseases: Antiphospholipid Syndrome=3, cutaneous lupus=8, mixed connective tissue disease=4, scleroderma=5, myositis=2, Sjogen's Syndrome=6, vasculitis=1, other=15.

Results: A total of 265 pregnancies were included in the study, 88 with SLE, 33 with UCTD, 100 with arthritis, and 44 with other rheumatic diagnoses. Overall, most patients were white (70%), had at least a college education (71%), lived with a spouse/partner (85%), and had private health insurance (76%). While pregnant, % of all women indicated a desire and plan to breastfeed their infant.

Post-partum, an average of 7.5 weeks after delivery, 92 (35%) were feeding exclusively with formula, 110 (42%) exclusively breastmilk, and 63 (24%) a mix of breastmilk and formula. Of the women who planned to formula-feed only, 85% did so. On the other hand, 25% of the women who planned to breastfeed were not. Of these, 81 had tried to breastfeed, but stopped. The most common reasons for having breastfeeding were having a low milk supply, the baby being unwell, and concerns over the mother's medications.

In univariate analysis, exclusively feeding with formula was not associated with maternal diagnosis, but was significantly more common in women who were black, younger, had less than a college education, had an income under $50,000/year, and live without a partner (see Table 1). Babies that were admitted to the neonatal intensive care unit or were born preterm were more likely to be formula-fed. In analysis, formula feeding was only associated with preterm delivery (OR 2.97 (1.39, 6.35)), younger maternal age (OR 0.94 (0.88-1.00)) and the mother having a college degree (OR 0.33 (0.17, 0.66)). Maternal education trumped race: only 30% of black women and 25% of non-black women with a college degree fed exclusively with formula.

Conclusion: The large majority of women with rheumatic disease in this cohort planned to breastfeed and were breastfeeding at follow-up. Maternal education and preterm birth were the primary predictors of breastfeeding, while diagnosis and race did not significantly impact the frequency of breastfeeding. The majority of women with rheumatic disease want to breastfeed and, given the safety of our medications for lactation, the large majority can do so successfully.

Disclosure: N. Ikram, None; **A. Eudy**, GSK, 2; **M. Clowse**, GSK, 2, UCB, 5.

Abstract Number: 1897

Sexual Function and Health-related Quality of Life in Male Patients with Systemic Lupus Erythematosus, the Untold Story

Martín Valdez-López ,[1] Jonathan Campos-Guzmán,[1] Ana Barrera-Vargas,[2] Samuel Govea-Peláez,[1] Diana Gómez-Martín,[1] Jorge Alcocer-Varela,[1] Eduardo Aguirre-Aguilar,[1] Diana Padilla-Ortíz,[3] and Javier Merayo-Chalico[1], [1]Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán", Mexico City, Distrito Federal, Mexico, [2]Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán", Mexico City, Mexico, [3]Universidad De La Sabana, Bogotá, Cundinamarca, Colombia

SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Reproductive Issues in Rheumatic Disorders

Session Type: ACR Abstract Session

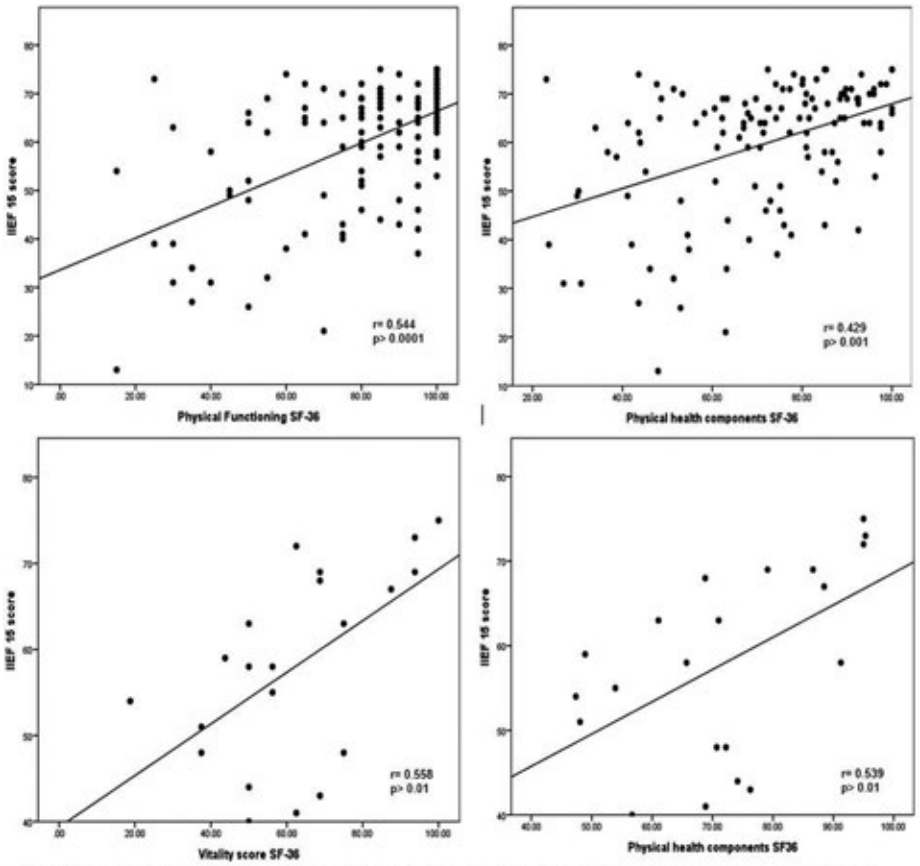

Image 1. All graphs show scatter plots comparing some of the different components of the Short Form-36 questionnaire, compared to the total International Index of Erectile Function. Pearson correlation coefficient r, and it's p value, are shown in each graph.

Table 1. Demographic, clinical and laboratory features (initial outpatient visit); p value <0.05 are shown in bold.

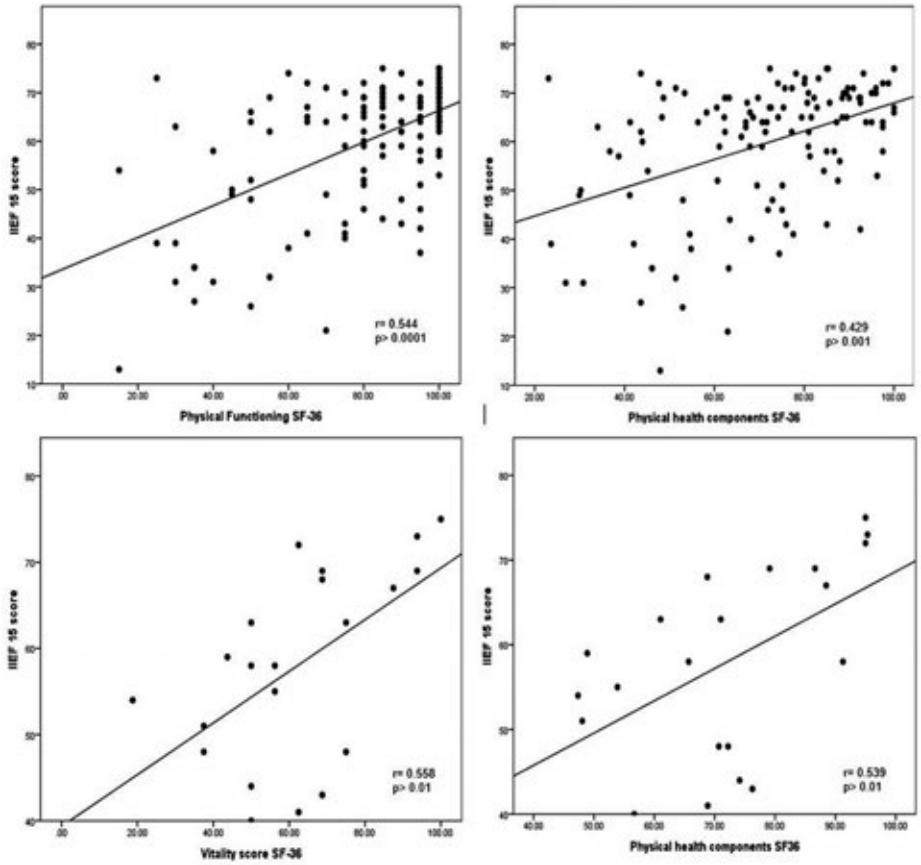

Figure 1. All graphs show scatter plot comparing some of the different components of the SF-36 questionnaire, compared to the total IIEF-15. Pearson correlation coefficient and p value, are shown in each graphic. The most representative graphs were selected (with the upper half being from the first visit, and the lower half corresponding to the third visit)

Session Time: 4:30PM–6:00PM

Background/Purpose: Although SLE is uncommon in men, the disease is usually more severe and requires more aggressive immunosuppression in male patients. There are multiple studies evaluating the association between SLE and sexual function in female patients and its impact on their quality of life, but information regarding male patients is practically non-existent.

Methods: We performed a longitudinal study in a referral center in Mexico City (2018- 2019). We included men aged ≥16 years who fulfilled ACR criteria for SLE and who were sexually active in the previous six months. All subjects answered the International Index of Erectile Function-15 (IIEF-15), the SF-36 (which determines generic health-related quality of life) and the HAQ questionnaire in the basal and subsequent visits. Other clinical, serological and demographic variables were measured. Statistical analysis was performed with SPSS v21.

Results: We included 124 male SLE patients. Mean age was 36.8 (±11.8) years and most patients (88%) were taking immunosuppressive therapy. There was some degree of sexual dysfunction in 58 (47.5%) of patients. Table 1 shows the different characteristics of patients with and without abnormalities in sexual function. Of note, men who presented some degree of sexual dysfunction had fewer years of schooling (p=0.010) and a higher HAQ score (p=0.011).

In the first visit, abnormalities in sexual function, as measured by IIEF-15, were associated with different spheres of the SF-36 score. The most relevant correlations between the different components of SF-36 and global IIEF-15 are shown in Fig 1. Other correlations were found between global IIEF-15 and the absolute neutrophil/lymphocyte ratio

(r= -0.259, *p*=0.004), as well as the SLICC score (r= -0.262, p= 0.003). Correlations between these same variables remained significant in subsequent visits.

When asked, 84.3% of patients said they would like to have specialized care if they were diagnosed with sexual dysfunction. Interestingly, only 22% of patients thought their disease could have repercussions on their sexual function.

Conclusion: To our knowledge, this is the first study to show that sexual function in male SLE patients seems to be closely associated with the patients quality of life, particularly with its physical aspects. Higher prevalence in patients with low education may reflect the importance of the psychological components in the development of this complication. The association of lymphopenia with an impaired sexual function could be related to its role in endothelial dysfunction and atherosclerosis. These findings highlight the need for rheumatologist to promote and coordinate a multidisciplinary approach for male SLE patients with sexual dysfunction.

Disclosure: M. Valdez-López, None; **J. Campos-Guzmán**, None; **A. Barrera-Vargas**, None; **S. Govea-Peláez**, None; **D. Gómez-Martín**, None; **J. Alcocer-Varela**, None; **E. Aguirre-Aguilar**, None; **D. Padilla-Ortíz**, None; **J. Merayo-Chalico**, None.

Abstract Number: 1898

Rheumatoid Arthritis in Pregnancy and Offspring School Performance. a Danish Nationwide Register-Based Study

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Rheumatoid arthritis (RA) during pregnancy is a risk factor for several adverse pregnancy and child outcomes. Studies have found higher incidences of neurological and psychiatric diseases, including childhood epilepsy and autism spectrum disorders, in children born to mothers with RA. However, the overall long-term cognitive development of children exposed to maternal RA has scarcely been examined.

In this study, we examine the overall cognitive development of children born to mothers with RA by comparing their results in national standardized school tests, to those of their peers. The Danish national school tests are mandatory, annual tests conducted in all Danish public schools since 2010.

Methods: All singleton children born in Denmark between 1995 and 2008, who were listed in the Danish national school test register were included in this study (n=738,862). Children exposed to maternal RA in utero were identified through linkage of national registers. In subgroup analyses, we classified exposure according to maternal RA serostatus, and also included a maternal preclinical RA group (defined as the mother receiving a diagnosis of RA up to 3 years after birth of the child).

The Danish National School Tests are standardized, adaptive computer-based tests. Children are tested in reading in grades 2, 4, 6 and 8, and in mathematics in grades 3 and 6. Results from all reading and mathematics tests, from 2010 until 2018, were included. We compared adjusted differences of means by maternal RA exposure separately for each test. We adjusted for potential confounders, i.e. maternal age, maternal educational level, nationality and smoking during pregnancy. We also compiled school test results from all tests, in reading and mathematics separately, and analysed them as repeated measurements for each child, using multilevel regression models. Missing data was handled by multiple imputations.

Results: In total, 816 (0.1%) children were exposed to maternal RA in utero.

There were no differences in test scores in any of the reading tests between maternal RA exposed and unexposed children in grades 2, 4, 6 and 8.

In mathematics, exposed children scored marginally worse in both grades 3 and 6, compared to their unexposed peers (adjusted mean differences were -0.15 Standard Deviations (SD) (95% CI: -0.24; -0.07) and -0.17 SD (95% CI: -0.26; -0.07), respectively).

Results did not change when combining the tests for all grade levels in multilevel regressions (adjusted mean differences were: reading: -0.01 SD (95% CI: -0.08; 0.06) and mathematics: -0.13 SD (95% CI: -0.20; -0.05)).

Children exposed to preclinical RA in utero showed the same pattern of test performance as children exposed to diagnosed maternal RA. There was no appreciable differences between children by maternal RA serostatus.

Conclusion: In this long-term national follow-up study of cognitive development in children, maternal RA exposed children performed similar to their peers in national reading tests. We observed a small, but consistent association with poorer performance on mathematics tests among the exposed children. This was comparable to children exposed to preclinical RA, indicating that RA treatment may not be the underlying cause.

Disclosure: S. Knudsen, None; **J. Simard**, None; **J. Christensen**, UCB Nordic, 5, 8, Eisai AB, 5, 8; **T. Lauersen**, None; **B. Deleuran**, None; **B. Bech**, None.

Abstract Number: 1899

sFlt-1, PlGF and VEGF in the Differential Diagnosis Between Active SLE Nephritis During Pregnancy and Preeclampsia

Guilherme De Jesus ,[1] Marcela Lacerda,[1] Bruna Rodrigues,[1] Flavia dos Santos,[1] Adriana Nascimento,[1] Luis Cristóvão Porto,[1] Nilson Ramires de Jesús,[1] Roger Levy,[2] and Evandro Klumb[1], [1]Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, [2]GlaxoSmithKline, Upper Providence, PA

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Pregnancy in patients with SLE is associated with significant morbidity and mortality. SLE activity during pregnancy, specifically nephritis, makes the differential diagnosis with preeclampsia (PE) troublesome

Table 1. Demographic and gestational results of patients with Inactive SLE, SLE nephritis and SLE with Preeclampsia.

	Inactive SLE (n = 41)	SLE Nephritis (n = 15)	SLE with Preeclampsia (n = 15)	p value (C.I. 95%) (ANOVA)
Age at inclusion Mean ± SD	27.2 ± 6	29.4 ± 4.4	30.1 ± 5.8	0.17
Gestational age at blood collection Mean ± SD	36.8 ± 1.7	33.7 ± 4.2	34.5 ± 2.5	**<0.001**
Gestational age at delivery Mean ± SD	38.7 ± 1.9	35.7 ± 3.8	35.8 ± 2.5	**<0.001**
SLICC Damage Index (SDI) Mean ± SD	0.3 ± 0.6	0.3 ± 0.5	0.1 ± 0.4	0.45
Birth weight Mean ± SD	2976.8 ± 532.4	2448.4 ± 759.2	2174.3 ± 834.6	**<0.001**
Small for gestational age (SGA) newborn n (%)	5 (12.1%)	4 (26.6%)	9 (60%)	NA

Table 2. Mean values of VEGF, PlGF and sFlt-1 for patients with Inactive SLE, SLE nephritis and SLE with Preeclampsia.

	Inactive SLE (n = 41)	SLE Nephritis (n = 15)	SLE with Preeclampsia (n = 15)	p value (C.I. 95%) (Mann-Whitney's U test)
VEGF (pg/mL) Mean ± SD	5.6 ± 7	12.3 ± 10.1	4.1 ± 5	Inactive SLE x SLE nephritis: **0.006** Inactive SLE x PE: 0.45 SLE Nephritis x PE: **0.009**
PlGF (pg/mL) Mean ± SD	189.8 ± 146.1	198.7 ± 134.8	61.4 ± 127.3	Inactive SLE x SLE nephritis: 0.83 Inactive SLE x PE: **0.003** SLE Nephritis x PE: **0.007**
sFlt-1 (pg/mL) Mean ± SD	1804.2 ± 668.3	1832.1 ± 760.9	2517.0 ± 431.9	Inactive SLE x SLE nephritis: 0.90 Inactive SLE x PE: **<0.001** SLE Nephritis x PE: **0.006**
Ratio sFlt-1/PlGF Mean ± SD	22.9 ± 25.1	23.3 ± 35.5	781.1 ± 1211.3	Inactive SLE x SLE nephritis: 0.96 Inactive SLE x PE: **0.02** SLE Nephritis x PE: **0.02**

in clinical practice. The use of angiogenic factors, like vascular endothelial growth factor (VEGF) and placental growth factor (PlGF), and antiangiogenic factors, such as soluble Fms-like tyrosine kinase-1 (sFlt-1), has been proposed to help differentiate these two conditions, but there is no available data about these cytokines in this scenario. The ob-

jective of this study was to evaluate circulating levels of VEGF, PlGF and sFlt-1 in SLE pregnant women with inactive disease, active lupus nephritis and PE.

Methods: Patients with SLE (ACR criteria) with singleton pregnancies followed at a high risk prenatal care, without any other autoimmune disease, were included. They were divided according to disease activity using SLE*P*DAI (SLE Pregnancy Disease Activity Index), clinical and laboratory evaluation by a rheumatologist experienced in evaluating pregnant SLE patients and the occurrence of PE. Blood samples were collected at the third trimester of pregnancy, within 3 weeks of delivery, and frozen for subsequent blinded analysis by ELISA kits (PlGF – DRG Instruments, Marbug, Germany; sFlt-1 and VEGF – R&D systems, Minneapolis, United States).

Results: Seventy one women were included. Forty one patients had inactive SLE (Group 1, SLEPDAI < 4), 15 had active lupus nephritis (Group 2, SLEPDAI >4, including renal criteria) and 15 had PE (Group 3). Mean gestational age at blood collection was of 36.8, 33.7 and 34.5 weeks, respectively and delivery at 38.7, 35.7 and 35.8 weeks, respectively; statistically significantly higher in patients with inactive SLE (Table 1). Mean levels of VEGF, PlGF and sFlt-1 of each group are reported on Table 2. Patients with SLE and PE had statistically significantly lower mean serum levels of PlGF than SLE patients without PE, while sFlt-1 was significantly higher in patients with PE compared to pregnant patients with inactive SLE or lupus nephritis. The sFlt-1/PlGF ratio was also significantly higher in patients of Group 3 (PE) compared to other patients with SLE (Groups 1 and 2). VEGF was higher in patients with SLE nephritis compared to inactive SLE and SLE with PE, while PlGF and sFlt-1 were similar when both groups without PE were compared.

Conclusion: In this study, pregnant SLE patients with PE had similar angiogenic and antiangiogenic profile of patients with PE without SLE – low PlGF and high sFlt-1, with high sFlt-1/PlGF ratio. This pattern differs from patients with inactive SLE or active lupus nephritis, the main differential diagnosis during gestation. Evaluation of angiogenic and antiangiogenic factors, specially PlGF and sFlt-1, can be a new tool to differentiate PE from lupus nephritis during pregnancy in clinical practice.

Disclosure: G. De Jesus, None; **M. Lacerda**, None; **B. Rodrigues**, None; **F. dos Santos**, None; **A. Nascimento**, None; **L. Porto**, None; **N. Ramires de Jesús**, None; **R. Levy**, None; **E. Klumb**, None.

Abstract Number: 1900

Assessing Commercial Titers of anti-Ro60 and Ro52 Antibodies to Risk Stratify Surveillance of Anti-Ro/SSA Antibody Positive Pregnancies

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Pregnancy counseling of all anti-Ro positive women includes advice regarding the development of congenital heart block (CHB), albeit the risk is only 2% for primigravida women or those with previously unaffected offspring. Despite this low risk, the prevailing surveillance recommendation is weekly echocardiography. While evidence from basic research laboratories support that "high" titers of antibodies confer clinically meaningful

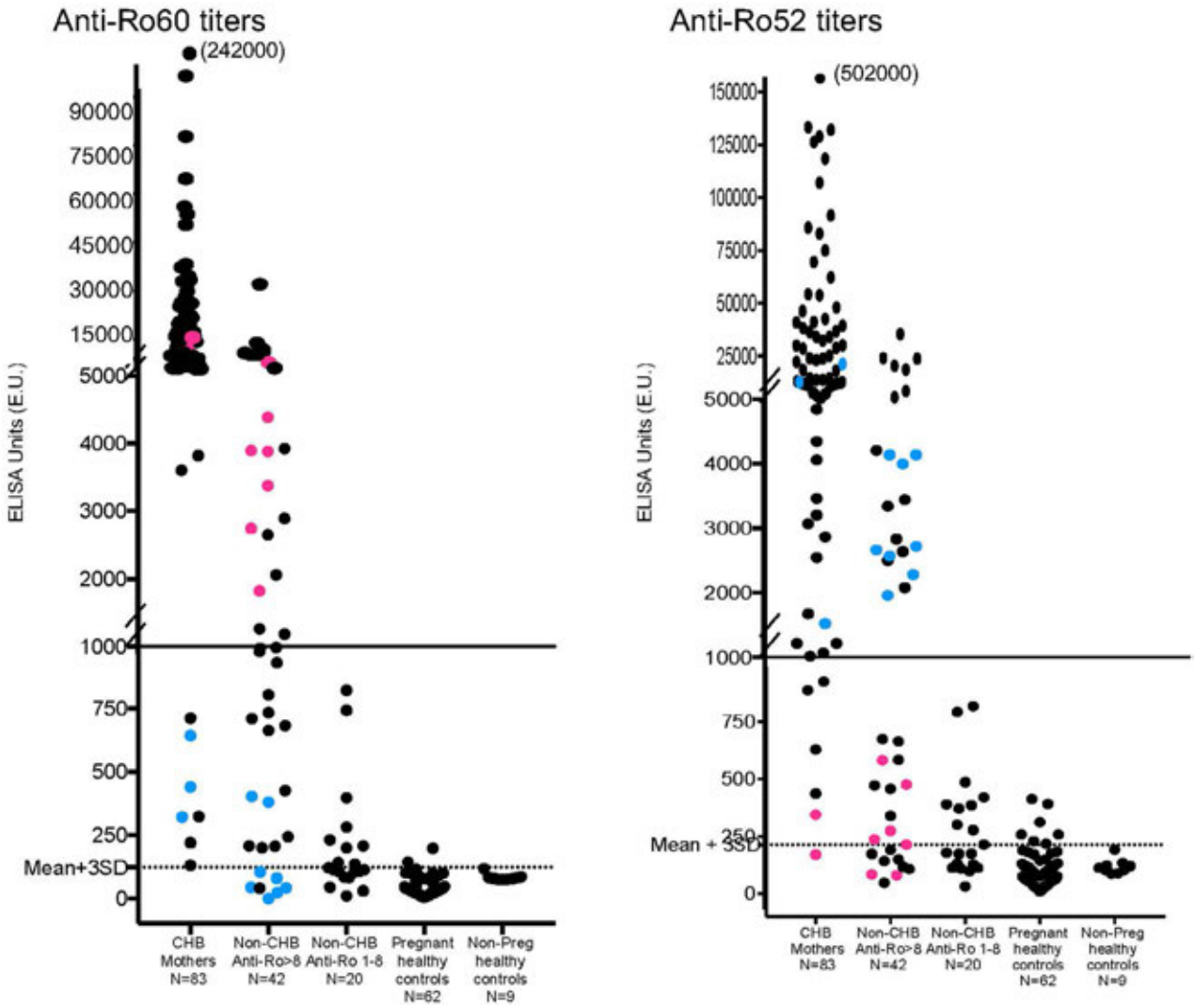

Figure 1. Anti-Ro60 and anti-Ro52 titers of mothers by CHB status and BioPlex assay results.

risk, unfortunately the majority of commercial laboratories use the BioPlex assay, which provides positive and negative values with limited information on actual levels because the sera or plasma are not diluted past a specified cutoff given cost (e.g. values of anti-Ro inclusive of Ro52 or Ro60 by laboratories such as Quest or LabCorp provide positive as 1-8 or > 8 units with no further information). The present study was initiated to assess whether the BioPlex assay used by many commercial laboratories provides adequate stratification of risk for counseling regarding management.

Methods: The study group comprised healthy non-pregnant donors (N = 9), healthy pregnant donors (N = 62), women testing positive for anti-Ro by commercial BioPlex but without CHB children (N = 60 SLE and 2 SS), and women with CHB children (N = 83). Anti-Ro60 reactivity was assessed using native antigen and anti-Ro52 using recombinant protein. Sera were applied to coated microtiter plates at serial dilutions ranging from 1:1000 – 1:50,000 for 1h at RT and run in duplicate. Tested samples were multiplied by the dilution factor which gives an OD in the range of 0.3-0.8. Results were considered positive at 123 ELISA units (EU) for Ro60 and 215 EU for Ro52 as this represented the mean +3 SD of the values obtained for healthy control sera.

Results: Of the 83 CHB mothers tested, 74 had titers of Ro60 and Ro52 > 1000 EU, in 1 anti-Ro60 was > 1000 EU and anti-52 Ro between 215 - 1000, in 3 anti-Ro52 was > 1000 EU and anti-Ro60 between 300 - 1000, and 1 mother had anti-Ro60 > 1000 EU and was negative for anti-Ro52. Albeit all positive, the sera from 4 CHB mothers obtained 15 years after the birth of the affected child were < 1000 EU for both anti-Ro60 and Ro52. With these results setting thresholds (> 1000 EU in either Ro60 or Ro52 for CHB risk), we assessed patients testing positive for anti-Ro based on the BioPlex assay. Of 42 patients with values of > 8 on BioPlex testing, 14 had titers > 1000 EU for both anti-Ro60 and Ro52, 7 had anti-Ro60 > 1000 EU, and 8 had anti-Ro52 > 1000 EU. Thus, 13 of 42 (25%) with commercial Ro > 8 did not meet the threshold EU for CHB risk. Of 20 patients considered positive for anti-Ro by BioPlex with values between 1-8, none had levels of either anti-Ro60 or Ro52 at 1000 EU. No patient or healthy control testing negative by the BioPlex assay was positive for CHB risk in our ELISA.

Conclusion: These data suggest that commercial testing using the BioPlex assay may fall short of stratifying risk for CHB. Women with positive values < 8 are not likely at risk, obviating the cost and burden of weekly fetal echo surveillance. Moreover, even those considered "high" titer on commercial testing may be at low risk supporting the need for more quantitative commercial testing than is currently available.

Disclosure: K. Robins, None; **R. Bhan**, None; **C. Trad**, None; **R. Cohen**, None; **M. Chang**, None; **B. Wainwright**, None; **M. Masson**, None; **S. Mehta-Lee**, None; **P. Izmirly**, GlaxoSmithKline, 5; **R. Clancy**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **B. Cuneo**, Philips Healthcare Products, 8; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2.

Abstract Number: 1901

Serious Infections in Offspring Exposed in Utero to Non-TNFi Biologics and Tofacitinib

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: ACR Abstract Session
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Background/Purpose: During pregnancy, maternal circulating immunoglobulins G (IgG) are actively transported across the placenta through their Fc portion. Thus, TNFi and other biologics harbouring an Fc part have the potential to transfer across the placenta, often reaching higher fetal than maternal levels. In addition, it is postulated that small-molecule drugs may cross the placenta, although this remains unconfirmed. As fetuses could be exposed to therapeutic (or potentially supra-therapeutic) levels of biologics and small molecules, there are concerns that these agents could cause immunosuppression in exposed offspring. We compared the risk of serious infections in children born to mothers with chronic inflammatory diseases who used non-TNFi biologics or tofacitinib during pregnancy, versus unexposed offspring and children exposed to TNFi in utero.

Methods: We identified all women with ≥1 hospitalization for delivery after a diagnosis of rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriasis (PsO), psoriatic arthritis (PsA), or inflammatory bowel diseases (IBD), and a randomly selected group of unaffected mothers, matched ≥4:1 for age, year of delivery, and state of residence, using MarketScan database (2011-2016). Only women continuously enrolled within MarketScan for ≥12 months prior to

delivery and with available child linkage were included. We defined tofacitinib, TNFi and non-TNFi biologic (i.e. abatacept, rituximab, tocilizumab, ustekinumab, vedolizumab) exposure based on ≥1 filled prescription and/or infusion procedure code during pregnancy and/or the preconception period. We ascertained serious infections in the offspring based on ≥1 hospitalization with infection as a primary diagnosis, within the first year of life. We also characterized all exposure groups according to maternal demographics, disease type, co-morbidities, pregnancy complications, and drug use (i.e. corticosteroids, DMARDs, biologics).

Results: We identified 16,490 offspring of mothers with RA (4,142), AS (381), PsO/PsA (5,743), and IBD (6,731), as well as 164,553 children born to unaffected matched mothers. Among offspring whose mothers had inflammatory diseases, 105 were exposed to tofacitinib or non-TNFi biologics (tofacitinib 4, abatacept 33, rituximab 4, tocilizumab 12, ustekinumab 42, vedolizumab 10) and 1,611 to TNFi during pregnancy. We observed 2 cases of serious infections in children exposed to tofacitinib or non-TNFi biologics (1.9%; 95% CI 0.3, 7.4): one case was exposed to tofacitinib, while the other was exposed to abatacept. The percent of serious infections in offspring of inflammatory disease mothers with no TNFi exposure was 2.1% (95% CI 1.9, 2.3), while for those with TNFi in utero exposure, it was 2.3% (95% CI 1.6, 3.0). In children born to unaffected mothers, the percent of serious infections was 1.6% (95% CI 1.6, 1.7).

Conclusion: In the largest cohort of inflammatory disease offspring ever assembled, we detected very few serious infections in children exposed to non-TNFi biologics or tofacitinib. More studies are necessary to precisely determine the specific effects of individual non-TNFi biologic and small-molecule drugs.

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Abstract Number: 1902

Systems Biology in 874 Patients with Primary Sjögren's Syndrome Indicates the Predominant Role of Interferon Alpha Compared to Interferon Gamma, Its Association with Systemic Complications, and a New Aspect of the Genetic Contribution of HLA

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SESSION INFORMATION

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Session Title: Sjögren's Syndrome – Basic & Clinical Science

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Session Time: 4:30PM–6:00PM

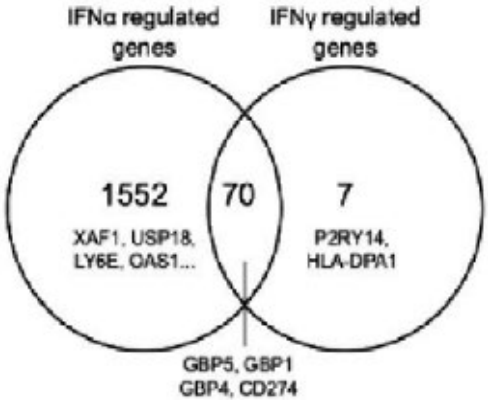

Figure.1 Venn diagram showing the number of genes transcriptionally controlled by IFNα, IFNγ, or both according to ultrasensitive digital ELISA of IFN alpha and IFN gamma

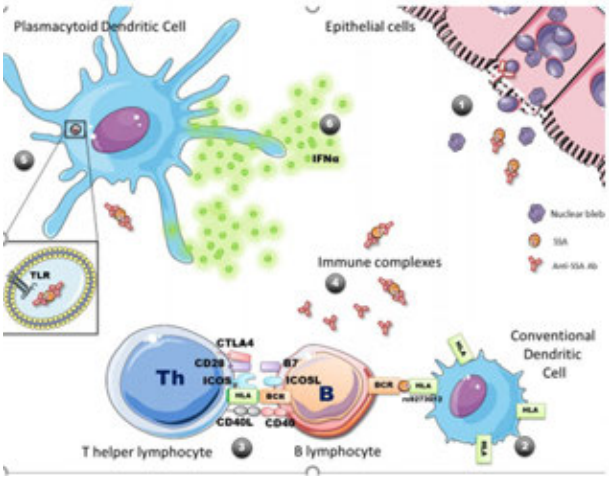

Figure 2. Proposed scenario underlying the association between HLA polymorphism and circulating IFNα. HLA predisposes to IFNα secretion by favoring classical presentation by cDCs of SSA peptides to T cells, leading to anti-SSA antibodies, and immune complexes stimulating IFNα secretion.

Background/Purpose: Primary Sjögren's syndrome (pSS) is the second most frequent systemic autoimmune disease affecting 0.1% of the general population. No specific immunomodulatory drug has demonstrated efficacy for this disease, and no biomarker is available to identify patients at risk of developing systemic complications. To enable a precision medicine approach, we explored the molecular stratification of the disease in an unsupervised systems biological manner.

Methods: Blood transcriptomes and genotypes of 351 pSS patients from a multi-center prospective clinical ASSESS cohort were analyzed. Clinical phenotype, immunological profile and yearly follow-up of disease course for 5 years of these patients were carefully assessed. Replication of the transcriptomic results was performed using 3 independent cohorts (n= 523 patients). Circulating IFN-alpha (IFNα) and IFN-gamma (IFNγ) protein concentrations were determined using ultrasensitive digital ELISA (SIMOA) and patients were genotyped using Immunochip in the ASSESS cohort.

Results: Transcriptomic analysis of the prospective cohort enabled patient stratification that matched clinical assessments, and showed a strong IFN gene signature in more than half of the patients. This finding was replicated in

three independent cohorts. As gene expression analysis did not discriminate between type I and II interferons, we applied digital ELISA to assess serum levels of IFNγ. The IFN transcriptomic signature was regulated by circulating IFNα, and not IFNγ, protein levels. 95% of the interferon-inducible genes (1552 genes) were specifically modulated by serum IFNα concentration, while only 7 genes were specifically regulated by serum IFNγ concentration. 70 genes were regulated by both IFNα and IFNγ concentrations (Figure 1).

IFNα protein levels, detectable in 75% of patients, were significantly associated with clinical and immunological features of disease activity at enrollment (association with anti-SSA: $p= 5.09*10^{-28}$, anti-SSB: $p= 2.45*10^{-14}$, RF: R=0.662, $p = 1.19 \times 10^{-41}$) . At enrolment, the mean ESSDAI was higher (4 [0-31] versus 2[1-18], p=0.0004) in patients with detectable IFNα blood levels. During the 5-year follow-up, patients with detectable IFNα blood levels more frequently developed systemic complications (OR 1.54 [1.14; 2.13]). Genetic analysis revealed a significant association between a specific MHC-II HLA-DQ locus genotype (HLA-DQA1*05:01 allele), anti-SSA antibody ($p=4.31 \times 10^{-12}$) and circulating IFNα protein ($p=1.70 \times 10^{-8}$). In multivariate analysis, both HLA DQA1*05:01 and anti-SSA positivity were independently associated with IFNα blood concentrations (OR 3.24 [1.78-5.88], p< 0.001, OR 3.08 [1.80-5.29], p< 0.001, respectively). Analyses in healthy controls, and in anti-SSA positive patients using Cytof, suggested that this HLA gene polymorphism acts through upregulation of HLA II molecules on conventional DCs (Figure 2).

Conclusion: This large systems biology analysis emphasizes the crucial role of circulating IFNα in pSS. In addition, we report a new pathogenic mechanism underlying the associations between HLA predisposition, autoantibody production, cytokine secretion and systemic complications of autoimmunity.

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Abstract Number: 1903

BTK Overexpression Is Associated with the Risk of Lymphoma in Primary Sjögren's Syndrome: Data from Whole Blood Transcriptome of 346 Patients Followed-up Prospectively for 10 Years

Pierre-Marie Duret ,[1] Tao Ye,[2] Wan-Fai Ng,[3] Alain Saraux,[4] Valérie Devauchelle Pensec,[5] Raphaele Seror,[6] Veronique Le-Guern,[7] Claire Larroche,[8] Aleth Perdriger,[9] Jean Sibilia,[10] Jessica Tarn,[11] Gaetane Nocturne,[12] Xavier Mariette,[13] and Jacques-Eric Gottenberg[14], [1]Hôpitaux civils de Colmar, COLMAR CEDEX, France, [2]GenomEAST platform / Institut National de la Santé et de la Recherche Médicale (INSERM), U1258, Institut de Génétique et de Biologie Moléculaire, IGBMC, Strasbourg, France, [3]Musculoskeletal Research Group Institute of Cellular Medicine Faculty of Medical Sciences Newcastle University, Newcastle, United Kingdom, [4]CHU de la Cavale-Blanche Brest, Brest, France, [5]University Hospital of Brest, Brest, France, [6]Hopitaux universitaires Paris Sud, Kremlin-Bicetre, France, [7]Department of Internal Medicine, Referral Center for Rare Autoimmune and Systemic Diseases, Hôpital Cochin, AP-HP, Université Paris Descartes, Paris, France,, Paris, France, [8]Internal Medicine, Paris, France, Paris, France, [9]Rheumatology department, Rennes University Hospital, France, Rennes, France, [10]CHU Strasbourg, Strasbourg, France, [11]Institute of Cellular Medicine Newcastle University, Newcastle, United Kingdom, [12]Center for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique – Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, Le Kremlin-Bicêtre, Université Paris Sud, INSERM, Paris, France., Paris, France, [13]Center for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique – Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, Le Kremlin-Bicêtre, Université Paris Sud, INSERM, Paris, France, [14]Department of Rheumatology, Strasbourg University Hospital, Strasbourg, France

SESSION INFORMATION
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Background/Purpose: To identify a molecular signature associated with lymphomagenesis in primary Sjögren's Syndrome (pSS).

Methods: Whole peripheral blood samples were collected from 346 well-phenotyped pSS patients enrolled in the ASSESS prospective cohort. A transcriptomic analysis was performed using Clariom S Human Arrays (Affymetrix). Patients with a pSS-related Non-Hodgkin lymphoma (NHL) (historic or incident NHL) were compared with 3 control populations: i) Patients without lymphoma and without any risk factor, among 9 validated predictive factors of developing lymphoma (systemic complications, parotid swelling, purpura, lymphocytopenia, CD4/CD8≤0.8, rheumatoid factors, cryoglobulinemia, monoclonal component and low C4 levels) (this comparator limits the risk of including patients who might develop lymphoma later during follow-up); ii) Patients without lymphoma but with moderate or high systemic disease activity at enrolment (ESSDAI≥5) (this comparator allows to identify relevant predictors in an at-risk population); iii) All patients without lymphoma. We focused on genes that were significantly differentially expressed in patients with lymphomas compared to each of these control populations.

Results: At enrolment, 13 patients had a history of lymphoma. During the 10-year follow-up, 9 patients developed an incident lymphoma. A total of 324 pSS patients had no lymphoma, including 110 patients with an ESSDAI≥5 and 61 patients without any risk factor of lymphoma. Gene Set Enrichment Analysis (GSEA) identified an over-expression of B-cell activation related genes in NHL-pSS, such as BAFF (p=0.007), APRIL (p=0.0009), BCMA (p=0.02) or BTK (p=0.0003) compared to patients without any risk factor of NHL. APRIL and BCMA were significantly up regulated when NHL-pSS patients were compared to all patients without NHL (p=0.002, p=0.04, respectively) but not BAFF (p=0.1). However, the gene expression profile of NHL-pSS patients compared to patients with an ESSDAI ≥ 5 did not show significant over expression of BAFF (p=0.3), APRIL (p=0.2) and BCMA (p=0.2). Conversely, the Bruton Tyrosine Kinase (BTK) gene was over expressed at enrolment, before the occurrence of lymphoma in patients with an incident NHL, in patients with a history of NHL, and in all NHL-pSS patients (either history of or incident) when compared to patients without any risk factor of developing lymphoma (p=0.006, p=0.005 and p=0.0003, respectively), to patients without lymphoma but with an ESSDAI ≥ 5 (p=0.03, p=0.02, p=0.003, respectively) and to all patients without lymphoma (p=0.02, p=0.01, p=0.0008 respectively).

Conclusion: BTK, a pivotal transducer of B-cell receptor, is over expressed in the peripheral blood of pSS patients before the occurrence of lymphoma. Conversely to BAFF, APRIL, and BCMA, BTK over expression is not related to a higher disease activity since BTK is up regulated in patients with lymphoma even when compared to patients with a moderate or high systemic disease activity and no lymphoma. BTK might therefore represent a pivotal pathogenic player in the transition from B-cell polyclonal activation to a monoclonal malignant proliferation. The present results suggest that BTK might represent a therapeutic target of interest in pSS.

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Abstract Number: 1904

IL-6 Receptor Inhibition in Primary Sjögren Syndrome : Results from a Randomized Multicenter Academic Double Blind Placebo-controlled Trial of Tocilizumab in 110 Patients

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SESSION INFORMATION
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Session Type: ACR Abstract Session
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Background/Purpose: IL-6 is suspected to play an important pathogenic role in primary Sjögren's syndrome (pSS) through its crucial roles in B-cell activation, and T-cell polarization, as shown in mice models and ex vivo studies. To investigate the relevance of IL-6 as a therapeutic target in patients with pSS, we performed a double- blind randomized placebo-controlled trial evaluating tocilizumab.

Methods: Inclusion criteria were pSS according to AECG criteria and an ESSDAI (score of systemic complications) ≥ 5. Patients received 6 monthly infusions of tocilizumab or placebo. Primary endpoint criteria was response to treatment evaluated at week 24. Response to treatment was defined by the combination of i) a decrease of at least 3 points in ESSDAI ; ii) no occurrence of moderate or severe activity in any new domain of the ESSDAI compared to enrollment ; iii) absence of worsening in physician's global assessment on visual numeric scale ≥ 1/10. Secondary endpoints included change in ESSPRI (mean of patient's fatigue, pain and dryness visual analogic scales), and in Schirmer's test. The data were analysed using Bayesian methods on an intent-to-treat basis.

Results: 55 patients (women : 98.2%, mean age : 50.9 [26 ; 76] years, anti-SSA antibody-positive : 84.7%) were randomized to tocilizumab and 55 patients to placebo (women : 90.3%, mean age : 54.9 [30 ; 80] years, anti-SSA positive : 87.6%). Mean ESSDAI was 11.5 [5 ; 25] and 12.4 [5 ; 39] and mean ESSPRI was 6.4 [2 ; 9] and 6.4 [1 ; 9] in the tocilizumab and in the placebo group, respectively.

The results on the primary outcome criteria were similar in both groups : 54.2% [41.3 ; 66.7%] of responders in the tocilizumab group, 62.1 %[49.0 ; 74.1] in the placebo group, OR = 1.6 [0.3 ; 3.3]

Mean ESSDAI at week 24 were 6.6 [4.7 ; 9.0] and 5.4 [3.7 ; 7.6] in the tocilizumab and placebo group, respectively, with a similar difference of the changes from baseline between groups (interaction, 0.9 [-1.3 ; 3.2]) (Figure 1).

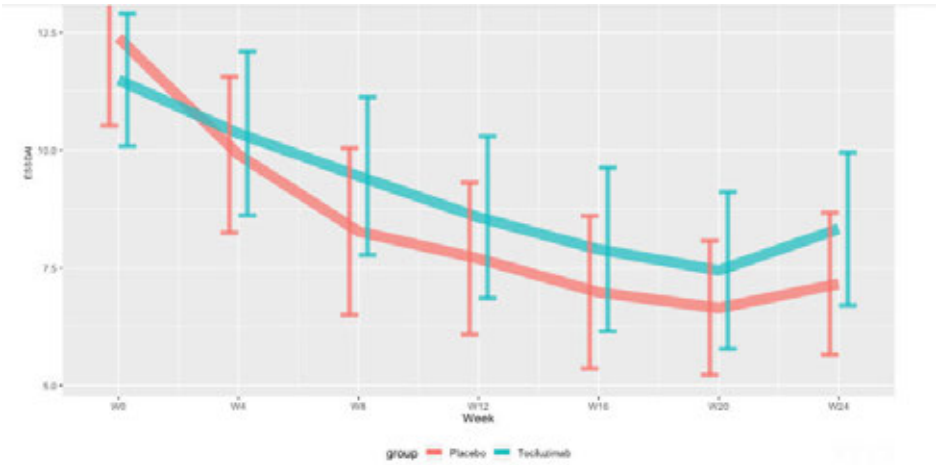

Figure 1. Change in ESSDAI.

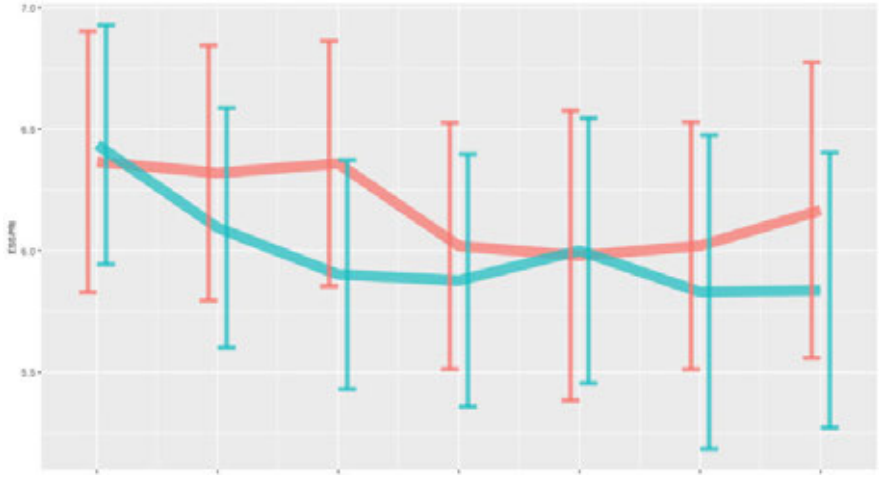

Figure 2. Change in ESSPRI

Mean ESSPRI at week 24 was 6.0 [5.0 ; 7.0] and 6.2 [5.2 ; 7.1] in the tocilizumab and placebo group respectivey, with a similar difference of the changes from baseline between groups (0.1 [-0.4 ; 0.7]) (Figure 2).

Change in Schirmer's test was similar in both groups.

Change from baseline in number of tender and swolllen joints was higher in the tocilizumab (from 7.4 [6.7 ; 8.1] to 3.6 [3.3 ; 3.9] and from 2.2 [1.8 ; 2.6] to 0.6 [0.5 ; 0.7], respectively) than in the placebo group (from 7.8 [7.1 ; 8.6] to 4.9 [4.6 ; 5.3] and from 2.4 [2.0 ; 2.8] to 1.3 [1.1 ; 1.5]) (interaction 1.2 [0.2 ; 2.7] and 0.8 [0.3 ; 1.4], respectively). Number of severe adverse events was similar in the 2 groups.

Conclusion: In this randomized placebo-controlled study, tocilizumab did not reach its primary outcome criteria and had no impact on main symptoms in pSS. Some improvement was observed in patients with articular involvement. Effect of tocilizumab on other subsets of patients and on immunological parameters is currently investigated and will be reported at ACR.

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Abstract Number: 1905

Sicca/Sjögren Syndrome Triggered by PD-1/PD-L1 Checkpoint Inhibitors: Data from the International ImmunoCancer Registry (ICIR)

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

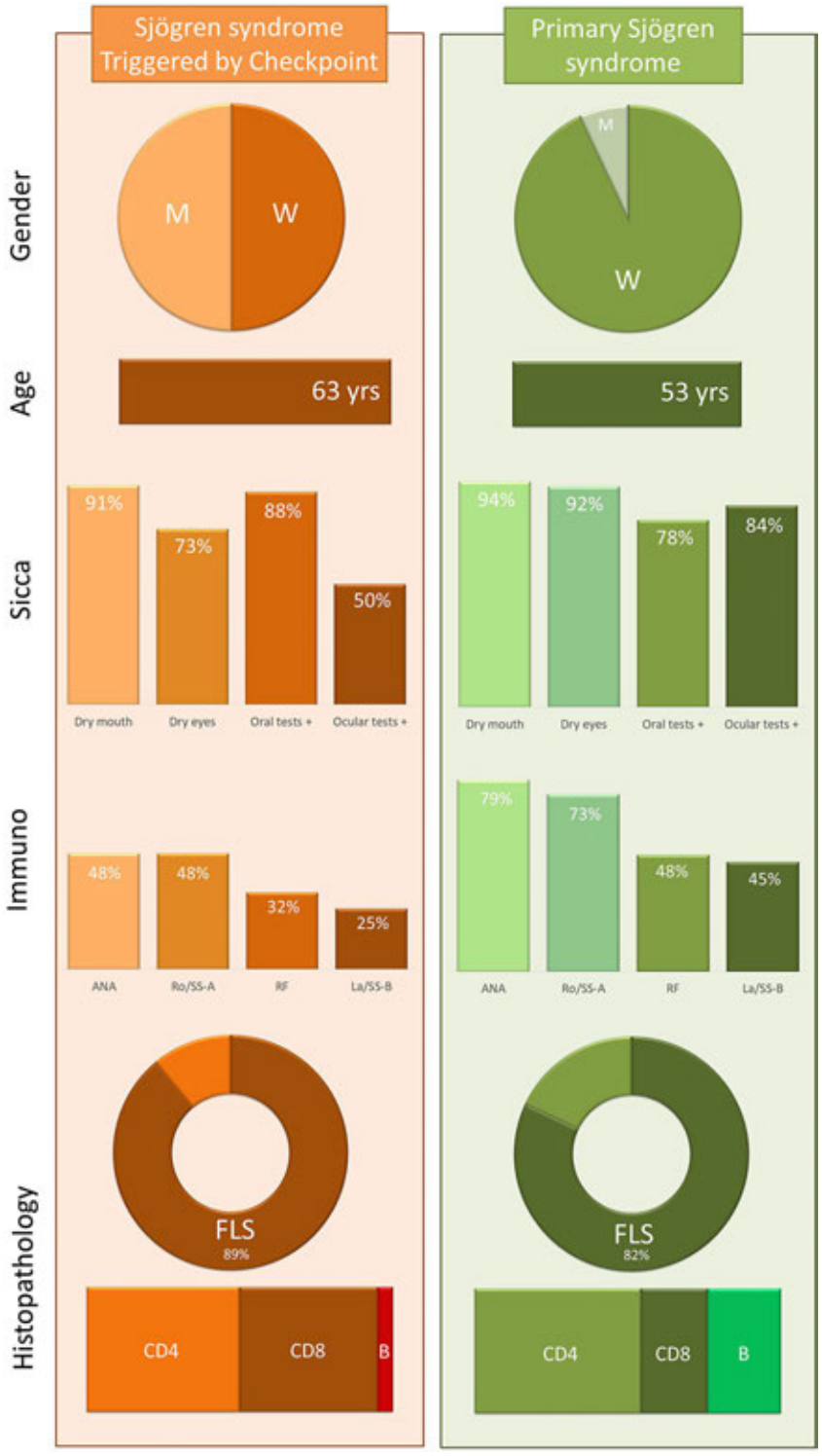
Session Title: Sjögren's Syndrome – Basic & Clinical Science

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: To analyse the worldwide occurrence of sicca/Sjögren (SjS) syndrome associated with the use of immune checkpoint inhibitors (ICI) in patients with cancer.

Methods: The ImmunoCancer International Registry (ICIR) is a Big Data-Sharing multidisciplinary network composed by 40 specialists in Rheumatology, Internal Medicine, Immunology and Oncology from 18 countries focused on the clinical and basic research of the immune-related adverse events (irAEs) related to cancer immunotherapies. For this study, patients investigating for a clinical suspicion of SjS after being exposed to ICI were included.



Results: We identified 26 patients (11 women and 15 men, with a mean age at diagnosis of 63,57 years). Underlying cancer included lung (n=12), renal (n=7), melanoma (n=4), and other (n=3) neoplasia. Cancer immunotherapies consisted of monotherapy (77%) and combined regimens (23%). In those patients receiving monotherapy, all patients were treated with PD1/PD1-L inhibitors (nivolumab in 9, pembrolizumab in 7 and durvalumab in 4); no cases associated with CTLA-4 inhibitors were identified. The main SjS-related features consisted of dry mouth in 25 (96%) patients, dry eye in 17 (65%), abnormal ocular tests in 10/16 (62%) and abnormal oral diagnostic tests in 12/14 (86%) patients. Minor salivary gland biopsy was carried in 15 patients: histopathological findings consisted of mild chronic sialadeni-

tis in 8 (53%) patients and focal lymphocytic sialadenitis in the remaining 7 (47%); a focus score was measured in 5 of the 6 patients (mean of 1.8, range 1 to 4). Immunological markers included positive ANA in 13/25 (52%), anti-Ro/SS-A in 5/25 (20%), RF in 2/22 (9%), anti-La/SS-B in 2/25 (8%), low C3/C4 levels in 1/17 (6%) and positive cryoglobulins in 1/10 (10%). Classification criteria for SjS were fulfilled by 10 (62%) out of 16 patients in whom the two key classificatory features were carried out. Among the 26 patients, there were only 3 (11%) who presented exclusively sicca syndrome without organ-specific autoimmune manifestations. Therapeutic management included measures directed to treat sicca symptoms and therapies against autoimmune-mediated manifestations (glucocorticoids in 42%, second/third-line therapies in 31%); therapeutic response for systemic features was observed in 8/11 (73%). No patient died due to autoimmune involvement.

Conclusion: Patients with Sjögren syndrome triggered by ICI display a very-specific profile different from that reported in idiopathic primary SjS, including more frequent occurrence in men, a higher mean age, a predominant immunonegative serological profile, and a notable development of organ-specific autoimmune involvement in spite of the poor immunological profile (Figure). The close association found between sicca/Sjögren syndrome and primarily PD1 blockade requires further specific investigation.

Disclosure: M. Ramos-Casals, None; **A. Maria**, None; **M. Suárez-Almazor**, Bristol-Myers Squibb, 5, Pfizer Inc, 5, Eli Lilly, 5; **O. Lambotte**, None; **B. Fisher**, None; **G. Hernandez-Molina**, None; **P. Guilpain**, None; **X. Pundole**, None; **S. Retamozo**, None; **A. Flores-Chávez**, None; **C. Baldini**, None; **C. Bingham**, Abbvie, 5, AbbVie, 5, BMS, 2, 5, Bristol Meyer Squibb, 2, 5, Bristol Myers-Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Eli/Lilly, 5, Genentech/Roche, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Pfizer Inc, 5, Regeneron/Sanofi, 5, Sanofi/Regeneron, 5; **P. Brito-Zerón**, None; **J. Gottenberg**, Abbvie, 8, BMS, 2, 5, Lilly, 5, 8, Pfizer, 2, 5, Roche, 8, Sanofi-Genzyme, 5, 8, UCB, 5, 8; **M. Kostine**, None; **T. Radstake**, None; **T. Schaeverbeke**, BMS, 5, Janssen, 5, Lilly, 5, Nordic Pharma, 5, Novartis, 5, Pfizer, 5, Roche Chugai, 5, Sanofi, 5; **H. Schulze-Koops**, None; **L. Calabrese**, AbbVie, 8, Amgen, 5, Bristol-Myers Squibb, 8, Crescendo, 8, Genentech, 8, GlaxsoSmithKline, 5, Horizon, 5, Janssen, 5, 8, Pfizer, 5, Sanofi-Regeneron, 5, UCB, 5, 8; **M. Khamashta**, None; **X. Mariette**, Biogen, 2, Bristol-Myers Squibb, 5, GlaxoSmithKline, 5, Janssen, 5, LFB Pharmaceuticals, 5, OSE Immunotherapeutics, 2, Pfizer, 2, 5, UCB Pharma, 5, 8.

Abstract Number: 1906

Using Multi-modal Ultrasound to Assess Disease Activity Within the Salivary Glands of Patients with Primary Sjögren's Syndrome Treated with Ianalumab (VAY736)

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: To use ultrasound (US) to demonstrate that ianalumab, a monoclonal antibody with dual mechanisms-of-action of BAFF:BAFF-R blockade and enhanced, ADCC-mediated B cell depletion, can modulate the inflammation and morphology within salivary glands of patients with primary Sjögren's syndrome (pSS).

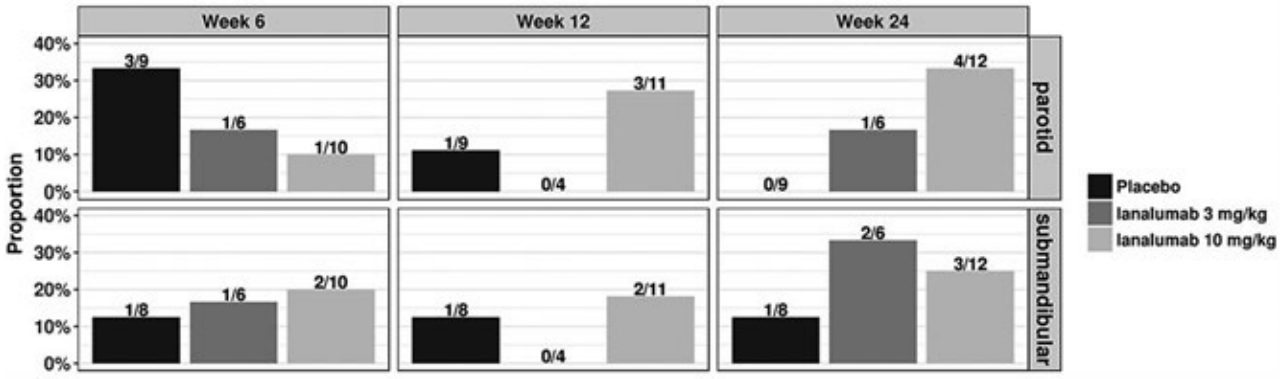

Figure 1. Proportions of de Vita responder by treatment group, week and gland type are shown in barchart. The responder is defined as one point reduction from baseline in de Vita score. The numbers on top of the bars, "m/n", indicates m responders out of n patients in a given group.

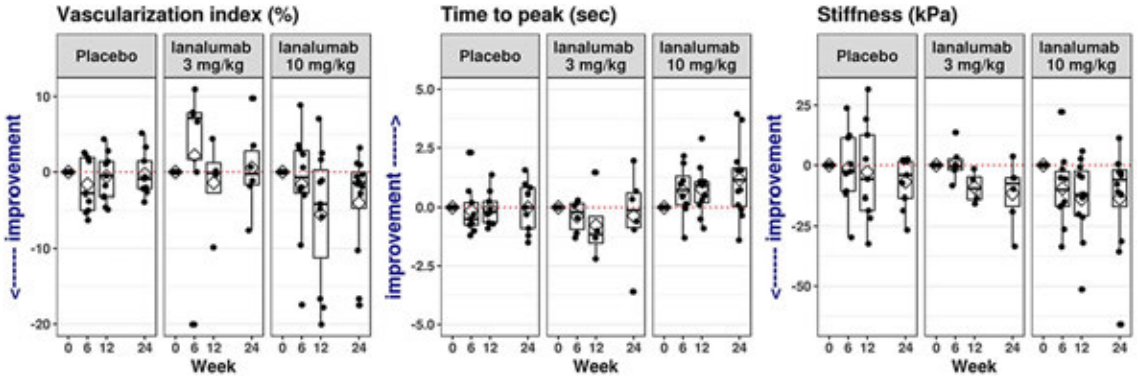

Figure 2. Change from baseline in a few ultrasound parameters are presented in boxplots by group over time, overlaid with individual data points. Median values are shown as the middle line within the boxes and mean values are indicated by diamonds. The direction of disease improvement is indicated by the arrow along the y axis. Two extreme data points greater than 70 are left out in the boxplot for the parameter of time-to-peak.

Methods: In a single-center study, 27 patients fulfilling the revised American European consensus criteria for pSS with stimulated whole salivary flow rate of >0 mL/minute and active disease (EULAR Sjögren's Syndrome Disease Activity Index; ESSDAI ≥6) were randomly assigned between three treatment groups in a 24-week double-blind treatment period to receive a single i.v. dose of either 3 mg/kg or 10 mg/kg ianalumab, or placebo[1]. Concurrent with clinical and laboratory outcomes that included ESSDAI, Physician's Global Assessment, and patient-reported outcomes for disease activity, fatigue and quality of life (EULAR Sjögren's Syndrome Patient Response Index, Multi-Dimensional Fatigue Index, Short Form-36, Patient's Global Assessment), multi-modal US images were acquired at baseline and weeks 6, 12, and 24. Using a single US device, applied modalities included: 1) echostructure by B-mode scored 0-4 in 5 categories according to de Vita classification[2,3], 2) large vessel blood flow by power Doppler (vascularity index, scored 0 for no vascularization and 1-3 for mild, moderate and high vascularization, respectively), and, limited to parotid glands (PG) only, 3) microvascularization using contrast-enhanced US (area under the curve, time to peak) and 4) gland stiffness by sonoelastography[4,5].

Results: The overall profiles of US data differed greatly between PG and submandibular glands (SMG) but were comparable between the respective left and right sides of these glands. A numerical improvement in both PG and SMG quality and declining inflammation in the glands were observed, including more de Vita responders (patients achieving ≥1 point reduction from baseline) in the VAY736 groups than in placebo (Figure 1), and changes in perfusion of both PG and SMG, as shown from large vessels and microvascular assessments (Figure 2), and a trend of decrease in PG stiffness (Figure 2). Change in some US parameters is observed to have correlation with some clini-

cal endpoints, including change in thickness with change in ESSDAI at week 12 (Spearman correlation coefficient = -0.63, p value = 0.0031), and change in TTP at week 12 correlated with change in patient global assessment (Spearmann cc=0.61; p=0.018) and with MFI-physical fatigue (Spearman cc = 0.61, p-value = 0.046).

Conclusion: Early signs of salivary gland improvement in response to an effective intervention can be shown using non-invasive, comprehensive, ultrasound-based approach at multiple time points without the need of biopsies.

Disclosure: T. Diekhoff, None; **M. Posch**, Charité Research Organisation, 3; **F. Wagner**, Charité Research Organisation, 3; **T. Fischer**, None; **Q. Schefer**, Charité Research Organisation, 3; **T. Dörner**, AbbVie, 5, Celgene, 5, Eli Lilly and Company, 5, 8, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Novartis Pharma AG, 5, Roche, 5, 8, Samsung, 5, 8, Sanofi, 2, UCB, 5, UCB Pharma, 2, 5; **D. Laurent**, Novartis Pharma AG, 1, 3; **Y. Li**, Novartis Pharma AG, 1, 3; **S. Oliver**, Novartis Pharma AG, 1, 3.

Abstract Number: 1907

Abatacept Reduces Serum CXCL13 and Disease-Relevant Immune Cell Phenotypes in a Double-Blind, Placebo-Controlled Primary Sjögren's Syndrome Clinical Trial

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Chemokine (C-X-C motif) ligand 13 (CXCL13), produced by follicular helper T (Tfh) cells, plays a pivotal role in B-cell homing and activation in germinal centers in salivary glands.[1,2] CXCL13 is associated with systemic disease activity and clinical activity in primary Sjögren's syndrome (pSS) and increased risk of lymphoma.[1,2] In patients with pSS, in an open-label trial (ASAP), abatacept (ABA) treatment decreased Tfh and CD4 memory T (TEM) cells.[1] In the Phase III, double-blind, placebo-controlled study (NCT02915159), ABA significantly impacted biomarkers of disease activity, but did not improve clinical disease measures, vs placebo.[3] This analysis aimed to assess serum CXCL13 levels and immune cell phenotypes of study patients.

Methods: Adult patients meeting the 2016 ACR/EULAR criteria for pSS with EULAR Sjögren's Syndrome Disease Activity Index ≥5 were randomized to receive ABA 125 mg SC weekly or placebo for 168 days. Serum and whole blood samples were collected at follow-up. Serum CXCL13 was measured using the SIMOA™ assay from Myriad RBM (all patients). Immune cell phenotyping of whole blood samples in a subgroup of patients from participating countries with available samples (cellular phenotyping population [CPP]) was assessed by flow cytometry, with data analyzed using BD FACSDiva™ software. Estimates of adjusted mean change from baseline (BL) in immune cells were from a repeated measures mixed model with statistical significance determined by the Benjamini–Hochberg procedure.

Results: In total, 187 (ABA, 92; placebo, 95)[3] patients were randomized and received ≥1 dose of study drug. At BL, CXCL13 levels were comparable between treatment arms. At Days 85 and 169, ABA reduced levels of serum

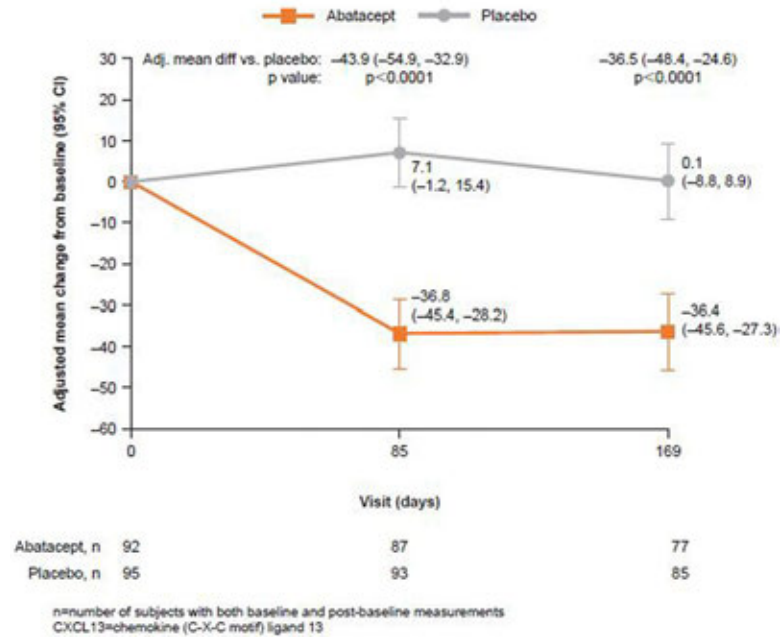
Table. Adjusted Mean Difference between Abatacept vs Placebo in Adjusted Mean Change From Baseline of Disease-Relevant Cell Subsets of Patients with pSS Treated With Abatacept, After 169 Days

Cell subtype	Adjusted mean difference from placebo (95% CI)	p value
Tfh	–1.38 (–2.23, –0.54)	0.0017*
ICOS-Tfh	–14.15 (–19.00, –9.30)	<0.0001*
Plasmablasts	–0.48 (–1.04, 0.09)	0.0957†
Treg	–1.80 (–3.00, –0.61)	0.0038*

*Statiscally significant based on Benjamini–Hochberg procedure with False Discovery Rate with alpha=10%; †nominal p-value

ICOS-Tfh=programmed death 1 inducible co-stimulator expressing activated follicular T helper cells; pSS=primary Sjögren's syndrome; Tfh=follicular T helper cells; Treg=regulatory T cells

Figure. Adjusted Mean Change From Baseline in Serum CXCL13



n=number of subjects with both baseline and post-baseline measurements
CXCL13=chemokine (C-X-C motif) ligand 13

CXCL3 from BL, and ABA-treated patients had significantly lower levels of serum CXCL13, compared with placebo ($p< 0.0001$; Figure). Seventy-eight (ABA, 32; placebo, 46) patients were included in the CPP, with no observed differences in BL characteristics between treatment groups or populations (CPP vs non-CPP). ABA-treated patients had significantly reduced proportions of disease-relevant cell subsets (Tfh, activated Tfh, CD4 TEM, helper T cell 1 [Th1] and regulatory T cells [Treg]) at Day 169 compared with BL (data not shown). At Day 169, there was a significant adjusted mean difference in adjusted mean change from BL for ABA vs placebo for Tfh, ICOS-expressing activated Tfh and Treg cells (Table), and CD4 TEM, Th1 cells and naïve CD4 T cells (data not shown), and a numerical difference for plasmablasts (Table).

Conclusion: A significant pharmacodynamic effect of abatacept was observed on disease-relevant serum (CXCL13) and pathogenic cell subpopulations. The disconnect between the effectiveness of abatacept in lowering serum CXCL13 (a relevant biomarker in pSS) and pathogenic cell subsets, and the previously-reported lack of demonstrable benefit (vs placebo) in clinical outcomes, warrants further investigation.

Reference

[1]Verstappen GM, et al. *Arthritis Rheumatol* 2017;**69**:1850–61.
[2]Nocturne G, et al. *Arthritis Rheumatol* 2015;**67**:3226–33.
[3]Baer AN, et al. EULAR 2019:abstract OP0039.

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Disclosure: J. Gottenberg, Abbvie, 8, BMS, 2, 5, Lilly, 5, 8, Pfizer, 2, 5, Roche, 8, Sanofi-Genzyme, 5, 8, UCB, 5, 8; **S. Mukherjee**, Bristol-Myers Squibb, 1, 4; **M. Nys**, Bristol-Myers Squibb, 1, 3; **R. Wong**, Bristol-Myers Squibb, 3, 4; **H. Bootsma**, Bristol-Myers Squibb, 2, 5, 8, GlaxoSmithKline, 2, 5, HarmonicSS, 2, MedImmune, 2, 5, Medimmune, 5, Novartis, 5, 8, Roche, 2, 5, UCB, 2, 5, Union Chimique Belge, 5; **N. Ray**, Bristol-Myers Squibb, 1, 3.

Abstract Number: 1908

Preliminary Identification of Arthritis-Associated Microbiota in Experimental Spondyloarthritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical IV: Axial Spondyloarthritis Translational Research
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Gut microbiota are strongly implicated in the pathogenesis of spondyloarthritis (SpA). Previous studies from our lab have documented extensive gut microbial dysbiosis in rats expressing HLA-B27 and human b2-microglobulin (HLA-B27 TG). The relative abundance of individual microbes is highly dependent on host genetic and environmental differences despite common immune dysregulation, indicating a complex ecological model of dysbiosis that precedes the development of arthritis. Here, we aimed to determine whether HLA-B27 TG rats that develop arthritis have a distinct gut microbial signature and host immune response.

Methods: Cohorts of mixed background (SDM) HLA-B27 TG and wild type (WT) littermates were generated by crossing HLA-B27 TG Lewis with WT Sprague-Dawley rats. SDM animals were monitored for the development of arthritis and euthanized at 4 to 6 months of age. Inflammation in the cecum and colon was assessed by histological scoring. Microbiota profiles were determined using DNA isolated from the cecum lumenal contents by 16S rRNA gene sequencing with primers specified by the Earth Microbiome Project (V4) and Illumina MiSeq. Data were quality-filtered using Quantitative Insights Into Microbial Ecology (QIIME 2). Host gene expression profiles were determined from the cecum tissue samples. RNA was isolated using a standard phenol–chloroform extraction and single-end sequencing of 50 bases was performed using an Illumina HiSeq 2000 system. Transcript expression levels (in reads per kilobase million [RPKM]) were generated and differentially expressed genes were defined for various comparisons.

Results: HLA-B27 TG SDM rats displayed early onset gut inflammation with ~30% developing arthritis by 4 months of age. No arthritis or gut inflammation was seen in WT SDM rats. Cecal and colon histology scores were similar in arthritic vs. non-arthritic HLA-B27 TG rats. There were distinct arthritis-associated microbial that were largely different from gut inflammation associated microbiota found by comparing HLA-B27 TG with WT SDM rats. Arthritic HLA-B27 SDM rats have increased abundance of phylum *Bacteroides* and *Parabacteroides* at the expense of *Firmicutes*. At

the species level, the relative frequency of *Akkermansia muciniphila* and *Blautia* was increased, while *Lachnospiraceae* and *[Ruminococcus] gnavus* were decreased compared to non-arthritic HLA-B27 TG rats. In contrast, cecal host gene expression between HLA-B27 TG arthritic and non-arthritic rats was not significantly different.

Conclusion: We provide a preliminary identification of arthritis associated gut microbiota in HLA-B27 TG rats, which is largely distinct from gut inflammation-associated microbiota. These results may provide valuable insights into the relationship between HLA-B27, gut microbiota, and arthritis in experimental SpA although further studies to determine cause-and-effect relationships are needed.

Disclosure: T. Gill, None; **T. Tran**, None; **S. Brooks**, None; **R. Colbert**, Eli Lilly and Company, 2, 9.

Abstract Number: 1909

miR-21-5p Expression as a Marker of Treatment Response in Psoriatic Arthritis Patients

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical IV: Axial Spondyloarthritis Translational Research
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Psoriatic arthritis (PsA) is an inflammatory arthritis occurring in patients with psoriasis. Links between altered miRNA expression with the pathogenesis of several autoimmune disorders have been reported. We previously demonstrated that miR-21-5p was upregulated in PsA compared to psoriasis without arthritis (PsC) and healthy controls (HC) and is thus a potential biomarker for PsA. We also demonstrated that miR-21-5p modulates inflammation in psoriatic disease (PsD = PsA & PsC) through IL-17/IL-23 axis and CXCL10 and is a marker of inflammation. We aimed to 1) validate the results in a new set of patients, 2) examine the expression of miR-21-5p before and after 24 weeks of methotrexate (MTX) treatment 3) determine if miR-21-5p expression differs depending on route of MTX administration.

Methods: Serum & whole blood RNA samples were collected from 40 patients with early PsA (< 2 years' disease duration and not receiving biologic therapy), 40 patients with psoriasis who have been confirmed by a rheumatologist not to have PsA (PsC, >10 years disease duration, not receiving biologic therapy, and matched to PsA patients on age, sex, psoriasis duration, and age of psoriasis onset), and 40 HC (matched to patients based on age, sex), 15 PsA patients before and after 24 weeks of treatment with MTX. An additional 15 PsA patient samples were collected to compare oral vs subcutaneous MTX. RNA was extracted using the Tempus Spin RNA Isolation Kit. miR-21-5p was measured by droplet digital PCR (ddPCR). Serum IL-17, CXCL10, IL-23, TGFβ1 were measured by commercially available ELISA kits. One-way ANOVA, Pearson Chi Square test, paired t-test and Spearman correlations were performed.

Results: miR-21-5p was upregulated in PsA compared to PsC (Fold Change(FC)=2.32, p=0.001) and HC (FC=15.7, p=< 0.0001), validating the results observed in our previous studies. In PsA patients we found a correlation between expression of miR-21-5p and swollen joint count (SJ) (r=0.367, p= 0.022) and actively inflamed joint counts (AJTOT) (r=0.326, p=0.043). miR-21-5p was significantly down regulated 24 weeks post-MTX treatment in 12 patients (p=0.021) and correlated with AJTOT (r=0.421, p=0.036), SJ (r=0.420, p=0.037), TJ (r=0.418, p=0.037) and clinical

Table 1: Demographic, Clinical and Relative Expression Data of Validation cohort

Variable	PsA (N=40)	PsC (N=40)	HC (N=42)	P Value
miR-21-5p*	121.1 (99.2)	52.06 (27.4)	7.74 (5.98)	<0.001
Sex Male	21(53%)	21(53%)	21(53%)	0.96
Female	19(47%)	19(47%)	19(47%)	
Age*	45.7 (10.3)	43.9 (9.2)	45.7 (10.3)	0.19
PASI*	5.03 (6.9)	5.09 (3.2)	N/A	0.29
AJTOT*	4.6(3.6)	N/A	N/A	N/A

*Mean (standard deviation); PASI-psoriasis areas severity index; AJTOT-total actively inflamed (tender or swollen) joint count; CRP-C reactive protein; PsA - psoriatic arthritis; PsC – cutaneous psoriasis without arthritis; HC- healthy controls

Table 2

Variable	PsA (N=15)	
Sex Male	8(47%)	
Female	7(53%)	
Age*	50.6(12.6)	
PASI*	2(2.2)	
AJTOT *	3.0(3.8)	
miR-21-5p*	Pre Treatment	Post Treatment
	104.4 (63.7)	67.2 (56.3)

*Mean (SD); PASI-psoriasis areas severity index; AJTOT-total actively inflamed (tender or swollen) joint count; CRP-C reactive protein; PsA - psoriatic arthritis

disease activity in PsA (cDAPSA) (r=0.549, p=0.004). 3 patients showed an upregulation of miR-21-5p. These 3 patients had treatment escalation at subsequent visit. We also observed significant downregulation of miR-21-5p and significant correlation with AJTOT (r=0.964, p=0.002) and cDAPSA (r=0.811, p=0.035) in patients taking subcutaneous MTX but no downregulation of miR-21-5p in patients taking oral MTX. The MTX dosage in both groups were not significantly different (avg dose 15.5 mg/wk).

Conclusion: We have determined a role of miR21-5p as a potential biomarker for inflammation in psoriatic disease and response to methotrexate treatment. miR-21-5p levels appear to decrease in patients taking subcutaneous but not oral MTX.

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Abstract Number: 1910

Inflammatory Processes in Experimental Spondyloarthritis Are Accompanied by Formation of Ectopic Lymphoid Structures and B Cell Lineage Alterations in the Bone Marrow

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical IV: Axial Spondyloarthritis Translational Research
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Tumour necrosis factor a (TNF) is important in immune-mediated inflammatory diseases such as spondyloarthritis (SpA). Transmembrane (tm)TNF-transgenic (tg) mice that overexpress tmTNF develop typical SpA symptoms, including inflammation, bone destruction and bone formation. Interestingly, these mice also develop lymphoid aggregates in the bone marrow (BM) of the axial and peripheral skeleton. We characterized the lymphoid aggregates in the context of angiogenesis and inflammation.

Methods: Ankles, femora, tibiae, vertebrae and spleens from tmTNF tg mice and wild-type (WT) littermates (6 weeks, 12 weeks, and 8 months old; n=5 per age per group) were dissected and analyzed by confocal microscopy. In addition, 12 week old mice (n=6 per group) were analyzed by flow cytometry. To study the importance of TNF-R signaling in these processes, tmTNF tg mice lacking TNF-RI (tmTNF tgxTNF-RI$^{-/-}$) or TNF-RII (tmTNF tgxTNF-RII$^{-/-}$) (n=5 per group) were investigated.

Results: Immunofluorescent (IF) evaluation demonstrated that BM of tmTNF tg mice contained extensive lymphoid aggregates, both in the vertebrae and the ankles, but not in the femurs. The aggregates in the BM progressed with age and contained characteristics of ectopic lymphoid structures (ELS) consisting of B220^{+} B cells, CD3^{+} T cells, expression of the germinal center marker peanut agglutinin (PNA) and FDC-M1^{+} follicular dendritic cells that are in close proximity of MECA79^{+} high endothelial venules (HEVs). Quantification showed a median of 2 aggregates per vertebra in the tmTNF tg mouse, while there were none in the WT (P=0.001). Flow cytometric analysis revealed that tmTNF tg vertebrae contained a significantly higher amount of B cells (P=0.002) and more IgD^{-}CD95^{+} germinal center B cells per B cell (P=0.002) with a higher expression of the costimulatory molecules CD80 (P=0.002) and CD86 (P=0.002) compared to vertebrae of WT animals. The vertebrae also contained significantly more CXCR5^{+}PD-1^{+}FoxP3^{-}CTLA4^{-} T follicular helper cells (P=0.026), CXCR5^{+}PD-1^{+}FoxP3^{+}CTLA4^{+} T follicular regulatory cells (P=0.02) and CXCR5^{-}PD-1^{-} FoxP3^{+} T regulatory cells (P=0.01) in tmTNF tg mice. Meanwhile, B cell development in the BM of tmTNF tg femurs and vertebrae was not altered. Furthermore, BM, spleen and vertebrae from tmTNF tg mice contained significantly more IgA^{+} plasma cells compared to WT littermates. Of note, tmTNF tgxTNF-RI$^{-/-}$ mice did not display lymphoid aggregates or HEVs in the BM, while tmTNF tgxTNF-RII$^{-/-}$ mice did, although to a lesser extent than tmTNF tg mice. Likewise, tmTNFa tgxTNF-RI$^{-/-}$ mice did not develop macroscopic inflammation in spine and ankle joints, while the tmTNF tgxTNF-RII$^{-/-}$ mice did.

Conclusion: tmTNF overexpression in mice induces ELS in BM and supports IgA^{+} plasma cell differentiation. These effects are critically dependent on TNF-RI signaling and may underlie SpA pathology, as BM edema and elevated serum IgA have also been described in SpA patients.

Disclosure: M. Kaaij, None; **J. van Hamburg**, None; **J. Rip**, None; **G. Kollias**, Biomedcode, 3, 6; **L. van Duivenvoorde**, None; **M. Nolte**, None; **D. Baeten**, UCB, 3; **S. Tas**, None.

Abstract Number: 1911

Targeting the Oxidative Stress Pathway in Experimental Spondyloarthritis Reduces Pro-inflammatory Response in Rat Macrophages and Modulates Their Metabolic Requirements

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical IV: Axial Spondyloarthritis Translational Research
Session Type: ACR Abstract Session
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Background/Purpose: HLA-B27 is associated with the development of spondyloarthritis (SpA) and has a tendency to generate ER stress due to misfolding which can activate the unfolded protein response (UPR). UPR may contribute to SpA pathogenesis by promoting the production of pro-inflammatory cytokines like IL-23 and TNF. Under ER stress cells produce more reactive oxygen species (ROS), which further can worsen the UPR and promote inflammation. Our preliminary data indicate that IFNg and LPS treatment increases ROS and cytokine production to a greater extent in HLA-B27-expressing macrophages compared to wild type cells or cells expressing the non-disease associated allele, HLA-B7. Another important aspect of inflammation is that upon inflammatory activation immune cells have to change their metabolic requirements in order to meet the adequate response like producing pro-inflammatory cytokines. Here we examined whether reducing oxidative stress in HLA-B27+ macrophages affects pro-inflammatory cytokine production and UPR gene expression. Furthermore, we were interested whether targeting the oxidative stress pathway will modulate the metabolic requirements of the cells upon inflammatory activation.

Methods: Bone marrow derived macrophages from HLA-B27 and human b_2m (hb_2m) transgenic rats were examined with and without IFNg and LPS treatment. ROS levels were meseared with the ROS-sensitive dye MitoSOX for mitochondrial ROS production and 2',7'-dichlorofluorescein diacetate (DCFDA) for cellular ROS level detection. N-acetylcysteine (NAC) was used as an antioxidant, and differential gene expression was determined by RNASeq. For cytokine secretion, ELISAs were used and in order to measure metabolic activity the Seahorse Assay was performed. Wild type (WT) and HLA-B7/hb_2m transgenic rat macrophages were used as controls.

Results: Bone marrow-derived macrophages from HLA-B27-transgenic (Tg) showed increased baseline mitochondrial ROS production in the absence of UPR compared to HLA-B7-Tg and wild type (WT) control rats. Further stimulation of HLA-B27-Tg macrophages with IFNg and LPS (stimulated) showed increased ROS production compared to HLA-B7-Tg and WT control rats.This was accompanied by robust activation of the UPR only in HLA-B27-expressing cells. Treatment with NAC, an ROS scavenger, significantly reduced ROS levels in HLA-B27+ macrophages and strongly decreased the transcription of many pro-inflammatory cytokines including Il-23, Il-12, Tnf, Il-6, Il-1a and Il-1b. The effect of NAC was further verified by ELISA assays available for rat IL-6 and TNF. NAC treatment had minimal effect on UPR gene expression, with partially reduction of BiP expression and no changes in HLA-B27 expression. Interestingly, NAC reduced metabolic activity in stimulated macrophages to levels similar to untreated control cells as measured by the Seahorse Assay.

Conclusion: Our data demonstrate that reducing ROS levels with NAC ameliorates ER stress-related pro-inflammatory effects of HLA-B27 misfolding. Alteration of the oxidative stress pathway should be further explored for therapeutic intervention in SpA.

Disclosure: F. Navid, None; **F. LiCausi**, None; **B. Nguyen**, None; **A. Cougnoux**, None; **P. Violet**, None; **M. Levine**, None; **R. Colbert**, None.

Abstract Number: 1912

High Dimensional Flowcytometric Profiling Distinguishes Psoriasis and Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical IV: Axial Spondyloarthritis Translational Research

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Background/Purpose: Psoriasis (Pso) is a common chronic inflammatory skin disease. About 30% of Pso patients develop psoriatic arthritis (PsA), a chronic inflammation of joints and entheses with an additional negative impact on quality of life. Early detection of PsA patients is important to ensure timely treatment and prevention of structural joint damage. Unfortunately, PsA is markedly under-diagnosed by dermatologists; an unmet need for biomarker-profiles to screen Pso patients at-risk is obvious. The aim of our study was to assess whether high dimensional flowcytometric profiling can distinguish Pso and PsA patients.

Methods: A cross-sectional and case-control study recruited 25 Pso patients without arthritis and 33 patients with PsA, both not using biological therapy at baseline. Psoriasis was diagnosed by a dermatologist and all the included Pso patients had a Psoriasis Epidemiology Screening Tool (PEST) score of 2 or lower. All PsA patients were clinically diagnosed by a rheumatologist.

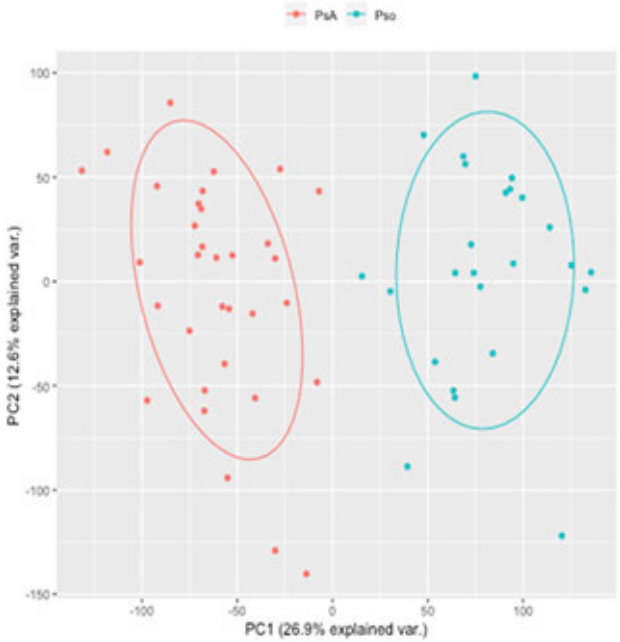

Figure 1. Semi-unsupervised clustering based on principal component analysis. Red dots represent PsA patients, blue dots represent Pso patients.

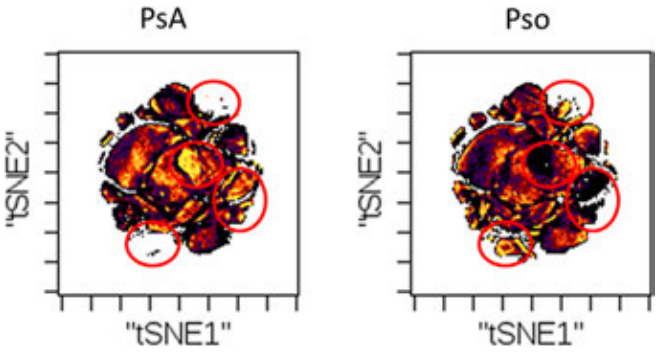

Figure 2. Density plots of different celsubsets in PsA and Pso based on viSNE analysis.

Peripheral blood samples were analyzed by high dimensional flowcytometry, consisting of five different and supplementary 10-color antibody panels, which enables the characterization of ~150 immune cell populations. Both semi-unsupervised and unsupervised computational flow cytometry analyses were performed. In case of semi-unsupervised analysis, the flow cytometry data was first manually analysed, followed by principal component analysis (PCA) and unsupervised hierarchical clustering of PCA (HCPC). For unsupervised computational flow cytometry, flowsom and viSNE analysis packages of Cytobank were used.

Results: The PsA and Pso population were comparable with regard to gender. In line with expectations, the PsA patients were slightly older compared to the Pso patients (57±15.4 vs 44±14.6). There was a significant difference in the use of methotrexate between the PsA patients (51%) and Pso patients (12%). Semi-unsupervised analysis of high dimensional flow cytometry data of peripheral blood from Pso and PsA patients clearly revealed differential clustering of Pso-vs-PsA patients as indicated by principal component analysis (Fig 1). This distinction between Pso and PsA patients was independent of age, gender, PASI scores and methotrexate use. Also unsupervised clustering showed a clear distinction between both diseases. Similar, unsupervised computational analysis utilizing flowsom and viSNE showed marked differences in the immune cell subset profiles between Pso and PsA patients (Fig 2).

Conclusion: High dimensional flowcytometric evaluation with semi-unsupervised and unsupervised analysis, can differentiate Pso and PsA patiens. Following validation, the obtained immune profiles might be used to support the timely diagnosis of PsA in Pso patients, as well as target finding to prevent this disease-shift.

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Abstract Number: 1913

Associations of HLA-B Alleles, Enthesitis and Peripheral Arthritis in Ankylosing Spondylitis

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SESSION INFORMATION

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Session Time: 4:30PM–6:00PM

Background/Purpose: Recent studies have suggested that peripheral arthritis in patients with spondyloarthritis is associated with HLA-B*15. Studies of white patients with psoriatic arthritis (PsA) have demonstrated associations with HLA-B*27, B*38, B*08 and B*37, whereas B*44 was associated with presence of milder disease. The purpose of this study was to examine HLA-B allele associations with peripheral arthritis and enthesitis in a longitudinal study of outcome in ankylosing spondylitis (AS) where these factors were assessed not only historically but also by systematic clinical assessments.

Methods: This study focused on white patients enrolled in a longitudinal study of outcome in AS. All patients met modified New York Criteria for AS. Study visits were conducted every 4-6 months, and at baseline and every two years a history of peripheral arthritis (and which joints involved), heel pain, plantar fasciitis and Achilles tendonitis. Hip and shoulder involvement was not included in this analysis. Clinical evaluation was carried out by the study rheumatologist at each visit, including joint pain/tenderness/swelling and entheseal involvement by the UCSF Enthesitis Index. HLA-B typing was carried out by single stranded conformational polymorphism (SSCP) analysis. Statistical

Table 1.

HLA-B Alleles and Peripheral Arthritis in Patients with AS by History

HLA	Peripheral Arthritis by History n=601	No Peripheral Arthritis N=408	P value	Odds Ratio
B*07	5.3%	6.0%	0.87	0.9
B*08	5.4%	5.6%	0.87	0.9
B*14	3.7%	2.5%	0.16	1.5
B*15	3.8%	2.2%	0.065	1.7
B*27	43.6%	45.6%	0.41	0.9
B*35	5.6%	5.2%	0.51	1.2
B*37	0.9%	0.6%	0.61	1.5
B*38	2.0%	1.8%	0.91	1.1
B*40	5.2%	4.0%	0.28	1.3
B*44	6.8%	7.8%	0.42	0.9
B*51	2.9%	3.3%	0.65	0.9
B*57	1.6%	0.7%	0.13	2.2

Table 2

HLA-B Alleles and Peripheral Arthritis in Patients with AS by Clinical Assessment

HLA	Peripheral Arthritis by Clinical Assessment n=261	No Peripheral Arthritis N=569	P value	Odds Ratio
B*07	5.9%	5.8%	1.0	1.0
B*08	5.9%	5.4%	0.83	1.1
B*14	3.6 %	3.1%	0.72	1.2
B*15	4.8%	2.6%	0.025	1.9
B*27	41.4%	45.2%	0.16	0.9
B*35	5.2%	5.8%	0.16	0.9
B*37	1.5%	0.5%	0.07	2.9
B*38	3.7%	3.7%	1.00	1.0
B*40	4.2%	4.3%	1.00	1.0
B*44	5.8%	8.2%	0.10	0.7
B*51	3.1%	3.3%	0.96	0.9
B*57	1.0%	1.1%	0.90	0.8

analyses were carried out by chi square analysis using the EPI-INFO statistical program. In order to control for the high frequency of HLA-B27, relative predispositional effect (RPE) analysis was carried out with HLA-B27 alleles.

Results: There were 1009 white AS patients with HLA-B typing available included in this analysis. Of these, 158 were seen only once and comprehensive musculoskeletal exam not carried out, though a history of peripheral arthritis, heel pain, plantar fasciitis and Achilles tendonitis attributed to AS recorded. In those patients followed longitudinally, there was an average of 7 study visits conducted. Peripheral arthritis (excluding hips and shoulders) attributed to AS occurred in 64.7% by history. Peripheral arthritis found on clinical evaluation was found in 25.9%. Heel pain by self report occurred in 25.9%, and plantar fascia/Achilles tendon tenderness on clinical evaluation at study visits in 32%. Entheseal tenderness as defined by the UCSF Enthesitis index was observed at least once in 65.5%. No HLA-B associations were encountered with heel pain, plantar fasciitis, Achilles tendonitis by history or plantar/Achilles tendon tenderness. Neither were any associations were observed on the UCSF Enthesitis index or with peripheral arthritis by patient history. HLA-B*15 was increased in frequency in those with peripheral arthritis seen on clinical evaluation (Table 2), which was confirmed on RPE analysis, where a weak negative association with HLA-B*44 was also observed (9.8 vs. 14.9%, p=0.04, OR=0.6).

Conclusion: These data in a large cohort of patients with AS confirms the association of HLA-B*15 with peripheral joint involvement in AS. The HLA-B associations with peripheral joint and entheseal involvement previously reported in PsA are not confirmed in AS suggesting that different mechanisms may be in play in the pathogenesis of peripheral joint and entheseal involvement between AS and psoriatic arthritis.

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Abstract Number: 1914

Increased Risk of Progression to Lupus Nephritis for Lupus Patients with Elevated Interferon Signature

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical IV: Lupus Nephritis
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Table 1. Patient Characteristics. 201 patients were included in the study. There were 113 patients with high IFN signature trait and 88 patients with low IFN signature trait. Gender, race, and age at SLE diagnosis are displayed for each group. The event of interest, development of lupus nephritis, is also included.

	All	IFN High	IFN Low
Total (n,%)	201 100%	113 56.22%	88 43.78%
Demographics			
Female (n,%)	180 89.11%	99 87.61%	81 92.05%
Race/Ethnicity (n,%)			
Asian	13 6.44%	12 10.62%	1 1.14%
Black/African American	47 23.27%	29 25.66%	18 20.45%
Hispanic/Latino	23 11.39%	17 15.04%	6 6.82%
Native American	23 11.39%	17 15.04%	6 6.82%
White/Caucasian	95 47.03%	38 33.62%	57 64.77%
Age at SLE Diagnosis (median, IQR)	32.00 [23.00-43.00]	27.65 [22.00-37.00]	37.5 [26.00-44.25]
Lupus Nephritis (n, %)	58 28.86%	48 42.48%	10 11.36%

Background/Purpose: The interferon (IFN) signature in SLE is well established, distinguishing lupus patients from healthy controls. Additionally, within lupus patients, higher levels of IFN-responsive gene expression associate with higher disease activity, elevated autoantibodies, greater number of SLE criteria, and higher damage indices. Despite these associations in SLE patients, an individual's IFN signature lacks responsiveness to acute changes in disease activity in longitudinal analyses. This stability is more reflective of a continuous trait, likely the result of known interferon pathway genetic associations. Elevated levels of IFN have been noted in lupus nephritis, which occurs in approximately half of SLE patients and is a major cause of morbidity and early mortality. Delay in diagnosis of lupus nephritis results in prolongation of renal inflammation, and often irreversible kidney damage. The ability to predict patients at greater risk of lupus nephritis may improve surveillance, reduce time to diagnosis and treatment, and potentially result in improved outcomes in lupus nephritis. We evaluated the prognostic significance of an individual having an elevated IFN-signature trait and progression to lupus nephritis.

Methods: The study included 201 lupus patients, all meeting both the ACR 1997 and SLICC 2012 classification criteria for SLE from a single institution. The open cohort had a median follow-up time of 14.14 years [IQR 10.96, 19.83]. Stored whole blood RNA (PAXgene) samples from the earliest longitudinal timepoint on these 201 patients were assessed for interferon signatures using an IFN-responsive four gene expression assay (Autoimmune Profile Assay, DxTerity Diagnostics) to define an individual's overall IFN-signature trait. Lupus nephritis status was defined by the date of attainment of the renal component of the SLICC SLE classification criteria. Cox proportional hazards modeling was utilized to determine the contribution of IFN signature trait, age at SLE diagnosis, gender, and race to the development of lupus nephritis.

Results: The cohort of 201 SLE patients included 58 patients who developed lupus nephritis and 113 with a high IFN signature trait. Characteristics of the complete group, as well as IFN-signature subgroups, are displayed in Table 1. High IFN signature trait was an independent predictor for earlier time to development of nephritis (Hazard Ratio 3.36, p=0.0008) after adjusting for age at SLE diagnosis, gender, and race (Figure 1). In our Cox proportional hazards model, younger age at diagnosis of SLE, male gender, and non-white race were also associated with higher likelihood of nephritis development. Racial subgroup analyses found that high IFN signature remained a significant predictor of earlier nephritis when evaluating either non-white patients (Hazard Ratio 3.41, p=0.021) or white patients (Hazard Ratio 2.97, p=0.031), adjusting for age at SLE diagnosis and gender.

Conclusion: Assessment of an individual's interferon signature phenotypic trait at the time of SLE diagnosis may be a useful tool to determine risk for development of lupus nephritis.

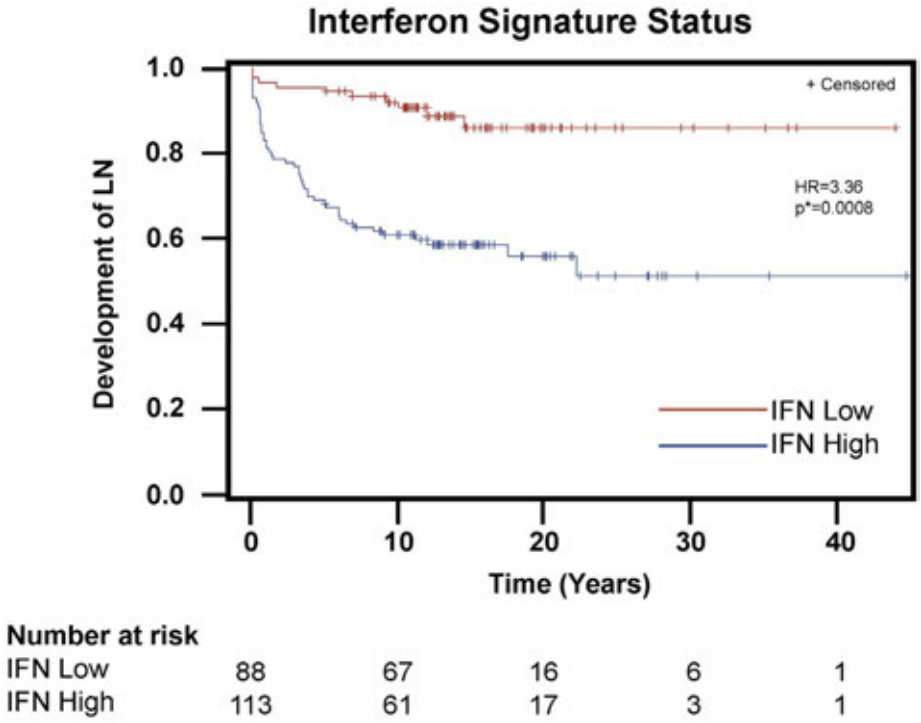

Figure 1. Kaplan-Meier Survival Analysis. Time to development of lupus nephritis is compared for patients with low interferon signature trait (red, upper) and those with high interferon signature trait (blue, lower). Cox Proportional Hazard Testing was utilized to adjust for covariates of age at lupus diagnosis, gender, and race (Hazard Ratio and p*).

Disclosure: C. Arriens, AstraZeneca, 5, BMS, 2, 5, Exagen, 2, GSK, 2, 5; **Q. Raja**, None; **S. Husain**, None; **B. George**, None; **M. Abedi**, DxTerity Diagnostics Inc, 1, 3, 4; **A. Jacobs**, DxTerity Diagnostics Inc, 1, 3, 4; **T. Guyon**, DxTerity Diagnostics Inc, 1, 3, 4; **H. Wijesuriya**, DxTerity Diagnostics Inc, 3, 4; **T. Aberle**, None; **A. Thanou**, Neovacs, 5; **S. Kamp**, None; **S. Macwana**, None; **E. Chakravarty**, None; **J. Merrill**, Abbvie, 5, Amgen, 5, Astellas, 5, AstraZeneca, 5, BMS, 2, 5, Celgene, 5, EMD Serono, 5, GSK, 2, 5, Idorsia, 5, ILTOO, 5, Immupharma, 5, Incyte, 5, Janssen, 5, Lilly, 5, Remegen, 5, Servier, 5, Xencor, Inc., 2; **J. James**, Abbvie, 5, Janssen, 5, Progentec, 2, Progentec Diagnostics, Inc., 2, Xencor, 2, Xencor, Inc., 2; **R. Terbrueggen**, DxTerity Diagnostics Inc, 1, 3, 4, 6; **J. Guthridge**, DxTerity, 2.

Abstract Number: 1915

Validation of a Serologic Antibody Biomarker Against a Candidate Gut Pathobiont for the Diagnosis of Lupus Nephritis

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SESSION INFORMATION
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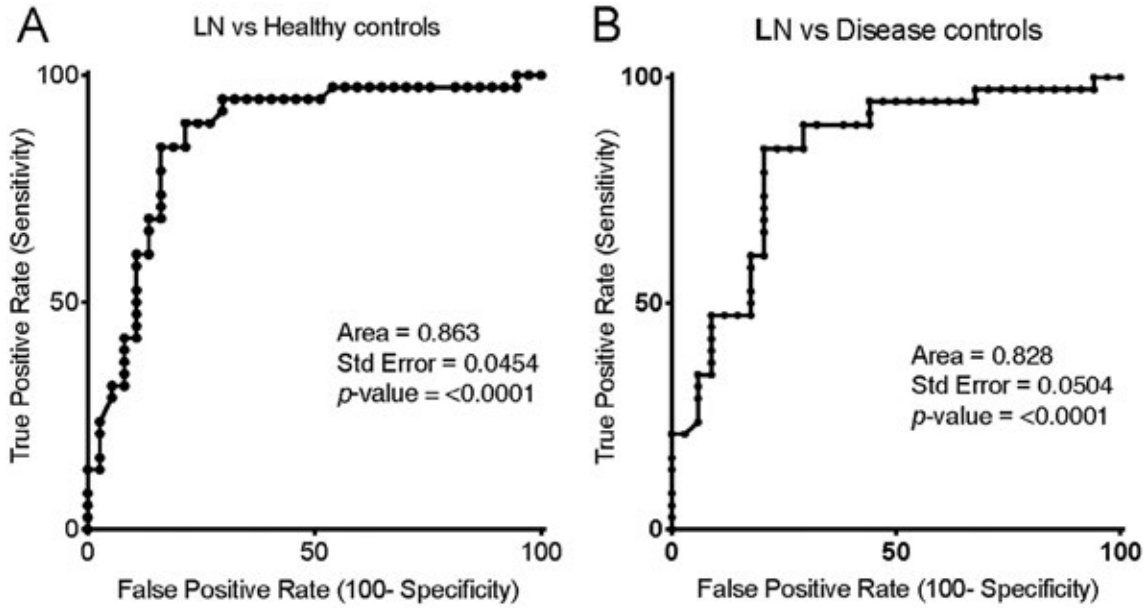
Background/Purpose: Systemic lupus erythematosus (SLE) is the archetypic systemic autoimmune disease, for which there is mounting evidence for roles for intestinal bacteria in the development of the systemic autoimmune responses, inflammation, and tissue injury. Whereas Lupus nephritis (LN) is amongst the most serious and potentially life-threatening complications of SLE, earlier diagnosis would speed clinical decision-making and initiation of definitive therapy. To characterize the interrelationships between Lupus host immunity and a candidate gut microbiome pathobiont, we have recently described an assay for detection of serum IgG responses to the commensal anaerobe, *Ruminococcus gnavus* (*RG*), for identification of individuals with active LN in three US adult Lupus cohort. In the current studies, we further validated this assay and investigated its potential utility in a Swedish cohort.

Methods: Patients were recruited and characterized at the Karolinska Hospital, based on ACR criteria, with 38 LN confirmed by renal biopsy, 38 non-renal SLE patients, with 37 age- gender- ethnicity- matched unaffected population (Healthy) controls, 20 ANCA-associated vasculitis (AAV) and 14 IgA Nephropathy (IgAN) patients, based on renal biopsy and/or standard clinical criteria. At our NYU lab, serologic studies were performed with a previously described custom bead-based serologic assay with nuclease-treated *RG2* extract and control analytes.

Results: LN patients had significantly higher levels of IgG anti-RG2 than Healthy subjects ($p < 0.0001$,) other non-renal Lupus patients ($p=0.0002$), or patients with IgAN ($p < 0.0001$) or AAV ($p < 0.0001$)(Wilcoxon rank-sum). There was a modest difference between non-renal Lupus patients, and Healthy subjects ($p=0.0283$), but no difference between Healthy with IgAN ($p=0.273$) or AAV ($p=0.433$). ROC analysis, when LN were compared to Healthy subjects gave an AUC of 0.863 and a Likelihood ratio (LR) of 5.6 at a cut-off of the mean+1 SD for control subjects ($p < 0.0001$); the LR was 5.8 for a cut-off of a mean+2SD ($p < 0.0062$), and LR of 7.8 for a cut-off of a mean+3SD ($p=0.0284$). For LN compared to the disease controls (AAV and IgAN) there was an AUC of 0.828 with a LR of 2.64 with a cut-off of a mean+1SD for disease controls ($p=0.01$), and the LR of 5.4 with a disease control mean+2SD ($p=0.0071$)(Figure 1A&B).

Conclusion: These findings further validate that serum IgG anti-*RG2* levels provide a robust biomarker for the identification of LN, unaffected by gender and age. Importantly, the assay displayed attractive performance characteristics



Area under the curve estimates for comparisons of Lupus nephritis patients to A) age- and gender-matched population (Healthy) controls, or B) Disease controls with AAV or IgA nephropathy that represent other forms of glomerulopathy often complicated by pathologic levels of proteinuria.

for discrimination of LN patients from population controls as well as those with pathologic proteinuria due to other forms of immune glomerulopathy (i.e., AAV and IgAN). Our findings also provide circumstantial evidence of a possible role for the *R. gnavus* pathobiont in patients in Sweden, suggesting this pathobiont may be involved in LN at sites geographically distant from the localities in which this association was first identified.

Disclosure: G. Silverman, NIH-NIAMS, 2; **D. Azzouz**, None; **C. Grönwall**, None; **I. Gunnarsson**, None; **E. Svenungsson**, None.

Abstract Number: 1916

Reduced DNASE1L3 Activity in Sporadic SLE Is Linked to Increased DNA Load of Microparticles, Reactivity to DNASE1L3-sensitive Antigens, and Lupus Nephritis

Johannes Hartl ,[1] Robert Clancy,[1] Peter Izmirly,[1] H Michael Belmont,[2] Catherine Trad,[1] Nicole Bornkamp,[1] Vanja Sisirak,[1] Benjamin Sally,[1] Jill Buyon,[1] and Boris Reizis[1], [1]NYU School of Medicine, New York, [2]NYU Langone Health, New York, NY

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical IV: Lupus Nephritis
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Null mutations in *DNASE1L3* cause severe familial SLE with prominent anti-DNA antibodies (Abs), suggesting that DNASE1L3 is a key driver of tolerance to DNA. Indeed, DNASE1L3-deficient mice rapidly develop anti-chromatin and anti-DNA Abs followed by renal involvement. DNASE1L3 is a secreted DNase that has the preferential capacity to digest DNA within nucleosomes and/or encapsulated by membranes. Our previous studies suggest that chromatin carried by circulating apoptotic microparticles (MP) is an important physiological substrate of DNASE1L3. Accordingly, the present study was initiated to address the hypothesis that dysfunction of DNASE1L3 and its downstream consequences contribute to the development of sporadic human SLE.

Methods: Reactivity to DNASE1L3-sensitive antigens on MP was measured by incubating plasma samples with control or DNASE1L3-treated MP and analyzing IgG binding to MP by flow cytometry. DNASE1L3 activity was measured based on its preferential capacity to digest complex DNA substrates with the readout expressed as the fraction of activity measured in healthy control subjects. The DNA load of MP was measured by qPCR of genomic DNA purified from the MP and MP-depleted fractions of plasma. In considering a spectrum from benign to clinical autoimmunity, subjects included those with active biopsy proven lupus nephritis as well as those with anti-Ro antibodies absent SLE.

Results: IgG-binding to MP was assessed in 116 SLE patients, 45 anti-Ro Ab-positive mothers whose children have neonatal lupus (17 asymptomatic or having an undifferentiated autoimmune syndrome, 2 SLE, 12 SS, 14 SLE/SS) and 16 healthy controls. IgG-reactivity to MP was not detected in any healthy controls. In contrast, 36% of SLE patients showed IgG binding to MP reversed by DNASE1L3 pretreatment (DNASE1L3-senstive reactivity). Only two of these patients were heterozygous for the known hypomorphic DNASE1L3 (R206C) variant. DNASE1L3-sensitive reactivity correlated with anti-dsDNA Abs ($p< .0001$) but did not overlap, indicating that reactivity is directed to more complex DNA. DNASE1L3-sensitive reactivity correlated with active proteinuria ($p=.0003$), low complement levels ($p=.01$) and overall SLEDAI ($p< .0001$). Among 45 anti-Ro-positive mothers, all were unreactive except the only 2 SLE mothers that developed lupus nephritis. The DNA load of MP and DNASE1L3 activity were assessed in a subset of SLE pa-

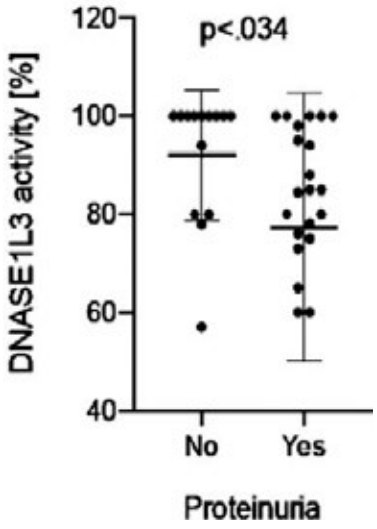


Figure 1. DNASE1L3 activity in SLE patients with and without proteinuria measured as a percentage of baseline activity in healthy controls.

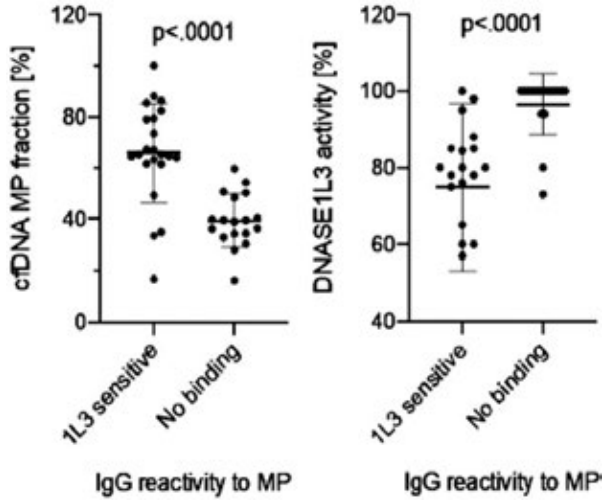


Figure 2. Cell-free DNA bound to microparticles (cfDNA MP fraction) as a percentage of total DNA in DNASE1L3-sensitive versus insensitive patient samples (left panel); DNASE1L3 activity in in DNASE1L3-sensitive versus insensitive patient samples measured as a percentage of baseline activity in healthy controls (right panel).

tients (n=40). Of these, patients with proteinuria showed lower plasma DNASE1L3 activity (p=.034) than those without proteinuria (Fig. 1). Moreover, increased partitioning of plasma DNA into MP correlated with reduced DNASE1L3 activity, and both parameters strongly correlated with DNASE1L3-sensitive IgG binding to MPs (p< 0.0001) (Fig. 2).

Conclusion: The activity of plasma DNASE1L3 is reduced in a significant fraction of SLE patients with renal disorder unrelated to a genetic explanation and is associated with DNA accumulation in MP targeted by Abs. Collectively, these data suggest that digestion of circulating chromatin by DNASE1L3 is a fundamental mechanism of tolerance to DNA which when disrupted may lead to sporadic SLE, particularly lupus nephritis.

Disclosure: J. Hartl, None; **R. Clancy**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **P. Izmirly**, GlaxoSmithKline, 5; **H. Belmont**, None; **C. Trad**, None; **N. Bornkamp**, None; **V. Sisirak**, None; **B. Sally**, None; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **B. Reizis**, None.

Abstract Number: 1917

Tubulointerstitial Inflammation Predicts Outcomes in Lupus Nephritis

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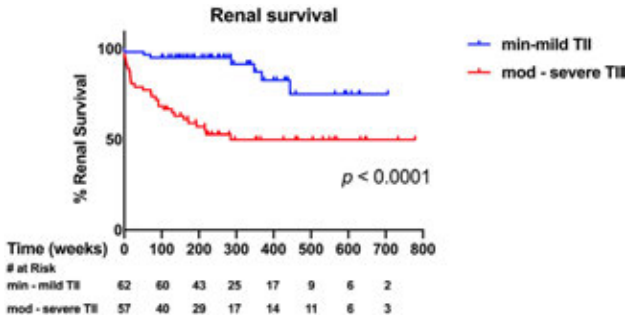
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical IV: Lupus Nephritis
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

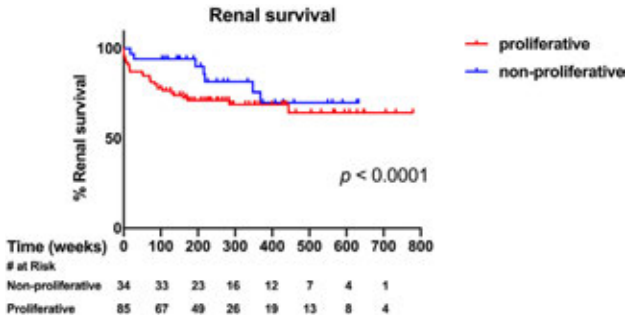
Background/Purpose: Lupus nephritis (LuN) causes significant morbidity and mortality, but predicting which patients will progress still remains imprecise. Current classification schema for LuN and its treatment are based exclusively or primarily on the glomerulus. Multiple studies have found that such classification schemes inconsistently predict outcomes, whereas tubulointerstitial inflammation (TII) has been shown to associate with poor renal survival. However, long-term data from a cohort with mostly African American (AA) patients with severe TII are still lacking. We aimed to determine the association between TII and long-term renal survival in LuN, and at-biopsy factors associated with moderate to severe TII.

Methods: Retrospective data from LuN subjects who had native kidney biopsies done from 2003 through 2014 were collected. Only those with at least 2 years of follow-up from the time of biopsy were included for analysis. Subjects were classified by International Society of Nephrology/Renal Pathology Society (ISN/RPS) criteria, and Class III and IV cases were combined into a proliferative class for analysis. TII was scored semi-quantitatively through light and immunofluorescence (CD45) microscopy by a blinded pathologist, and given scores from 0 – 3: 0 (< 10% of involvement, minimal), 1 (10 – 25%, mild), 2 (26 – 50%, moderate) and 3 (>50%, severe). Bivariate comparisons and multivariate logistic regression (MLR) analysis were performed to determine at-biopsy factors associated with moderate to severe TII. Renal survival analyses were done though Kaplan – Meier technique with time to end-stage renal disease (ESRD) with curves compared through the log-rank test.

Results: Among 122 subjects, 75.4% were AA, 84.4% were female, and 73.0% had proliferative LuN. The median follow-up period was 5.3 years (interquartile range 3.4 – 8.4 years). 60 subjects had moderate to severe TII, and they had higher percent of AA (91.7 vs 59.7%, $p < 0.0001$), higher median creatinine (1.5 vs 0.7 mg/dL, $p < 0.0001$), higher degree of proteinuria (3.8 g/day vs 1.8 g/day, $p < 0.0001$), and higher glomerular activity index ($p = 0.02$) and chronicity index (CI, both glomerular [$p = 0.0001$] and tubulointerstitial [$p < 0.0001$]) than those with minimal to mild TII. MLR analysis showed that moderate to severe TII was only associated with AA ethnicity (Odds Ratio [OR] 5.38, $p = 0.028$)



Higher degree of tubulointerstitial inflammation predicted worse renal survival



The ISN/RPS classification, stratified by proliferative (class III and class IV) vs nonproliferative, does not predict renal survival

and tubulointerstitial CI (OR 3.85, p = 0.001) but not with proliferative class or glomerular CI. Renal survival analysis found that subjects with moderate to severe TII had worse renal survival (approximately 50% with ESRD by 4th year) compared to those with minimal to mild TII (hazard ratio 5.01, $p < 0.0001$). There was no renal survival difference based on the presence of proliferative LuN (p = 0.2).

Conclusion: Higher degree of TII predicted worse renal survival, whereas ISN/RPS classification was not prognostic. Only AA ethnicity and tubulointerstitial CI were associated with moderate to severe TII at biopsy.

Disclosure: C. Oshinsky, None; **M. Siddiqui**, None; **V. Liarski**, None; **A. Chang**, Alexion, 5, 8, GlaxoSmithKline, 5, Amicus, 5; **M. Clark**, None; **K. Ko**, None.

Abstract Number: 1918

Urine CD163 Significantly Discriminates Active Lupus Nephritis and Strongly Correlates with Proliferative Glomerulonephritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical IV: Lupus Nephritis
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: CD163 is a marker for alternatively activated M2 macrophages, which have been implicated in the pathogenesis of lupus nephritis (LN). The potential of urine CD163 as a novel biomarker to reflect renal disease activities and pathological changes in LN was investigated.

Methods: Urine samples were obtained from LN patients with multiple ethnicities, assayed for CD163 using ELISA and then normalized to urine creatinine. Urine samples of healthy volunteers, inactive SLE, or active SLE patients without renal involvement were used as controls. CD163 was also measured in urine samples of an independent LN cohort with concurrent renal biopsies, and its correlation with renal pathology as well as clinical parameters were analyzed.

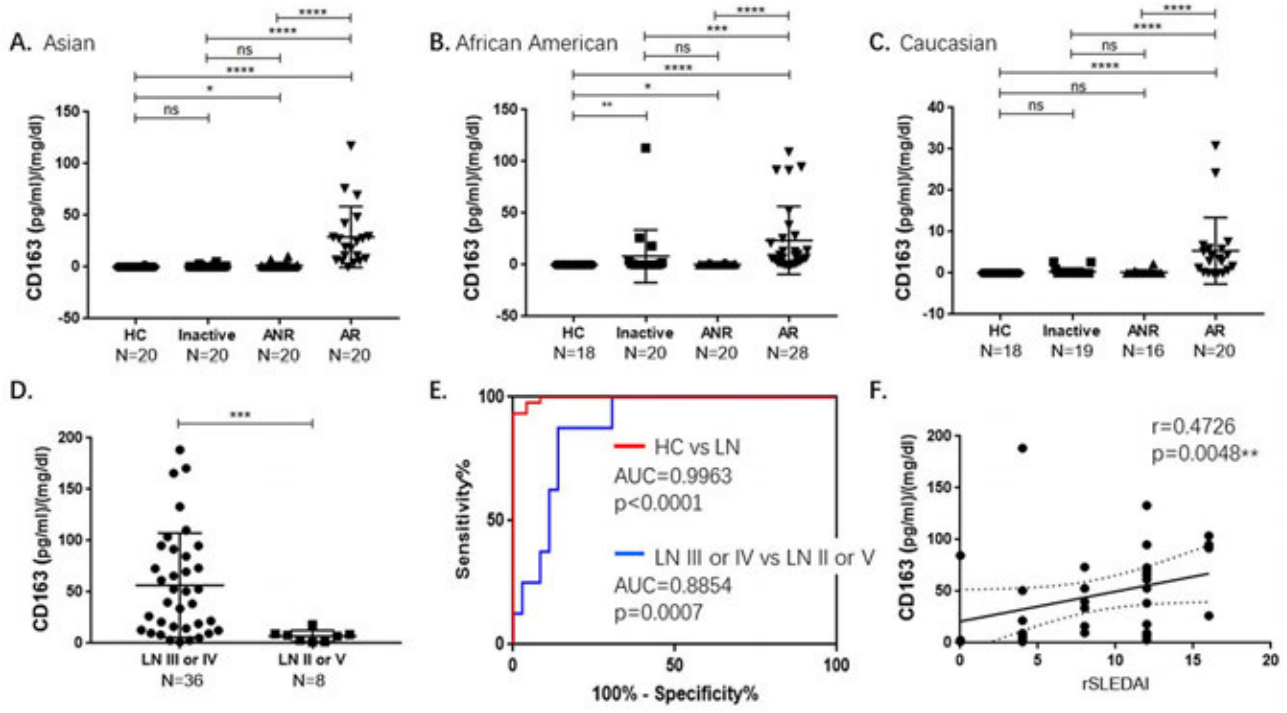

Figure 1. A-C, Cr-normalized urine CD163 was significantly elevated in active LN patients (AR) when compared with healthy controls (HC), inactive SLE patients or active SLE without renal involvement (ANR) in Asian, African American or Caucasian patients. D-E, Urine CD163 was significantly higher in LN patients with concurrent proliferative glomerulonephritis (LN III or IV). F, Urine CD163 significantly correlated with rSLEDAI.

Results: Urine CD163 was significantly elevated in active LN when compared with healthy controls, inactive SLE, or active SLE patients without renal involvement in Asian, Caucasian or African American patients (all $p< 0.001$). In 44 LN patients with concurrent renal biopsies, urine CD163 was dramatically increased in patients with proliferative glomerulonephritis (LN III or IV) when compared with that in other histological patterns (LN II or V) ($p< 0.001$) (Figure 1). Urine CD163 significantly correlated with SLEDAI, rSLEDAI, urine protein/creatinine and C3. It also strongly correlated with activity index of renal pathology, particularly fibrinoid necrosis, cellular crescents and interstitial inflammation (all $p< 0.01$).

Conclusion: Urine CD163 discriminates patients with active lupus nephritis from other SLE patients and is significantly elevated in LN with proliferative glomerulonephritis. It also excellently correlates with multiple clinical parameters reflecting lupus disease activities as well as renal pathological activity index.

Disclosure: T. Zhang, None; **R. Saxena**, None; **C. Mok**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5; **C. Mohan**, Equillium, 5, Equillium, Inc, 5.

Abstract Number: 1919

Development of a Multi-Modality Imaging Approach to Evaluate Lupus Nephritis

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SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: SLE – Clinical IV: Lupus Nephritis
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Lupus nephritis (LN) remains a significant cause of morbidity and mortality in subjects with Systemic Lupus Erythematosus (SLE). The gold standard for evaluation of LN remains the kidney biopsy, whereas renal function is usually evaluated by eGFR and urinary protein:creatinine ratio. More effective and sensitive methodology is needed to assess LN and also the response to treatment. Functional imaging of the kidney using quantitative techniques has great potential, as it can assess kidney function and pathologic changes non-invasively by evaluating perfusion, oxygenation, cellular density and fibrosis. The objective of this study was to develop a multi-modality imaging approach for the evaluation of the spectrum of pathologic changes in LN.

Methods: In this multi-center study (NCT03180021), subjects who were having a standard of care renal biopsy for LN were asked to participate in the imaging evaluation. Local Institutional Review Board approval was obtained, and subjects signed an Informed Consent Form. Dynamic contrast enhanced MRI (DCE-MRI) was employed to detect changes in vascularization and perfusion, Diffusion Weighted Imaging (DWI) to assess interstitial diffusion, T2*Map/BOLD to evaluate tissue oxygenation and T1rho to evaluate fibrosis (Figure 1). Regions of interest were identified in the imaged kidneys and imaging parameters were correlated with measures of renal function, including eGFR and urinary protein: creatinine ratio. In DCE-MRI, we specifically focused on mean Maximum Enhancement (ME), mean Time to Peak Enhancement (TTP) and mean Time of Washout (Twashout) as indicators of renal perfusion.

Results: Nine subjects have been evaluated to date and their imaging data assessed for quality. Evaluation of mean data from DCE-MRI has shown a significant correlation between renal perfusion and renal function. For example, the 24 hour protein concentration negatively correlated with ME (r_s=-0.81, p=0.015), TTP (r_s=-0.83, p=0.01) and Twashout (r_s=-0.81.p=0.01, Spearman rank correlation). In addition, the protein:creatinine ratio also negatively correlated with ME (r_s=-0.79, p=0.02), TTP (r_s=-0.74, p=0.04) and Twashout (r_s=-0.79, p=0.02, Spearman rank correlation).

Conclusion: These initial results have established the feasibility of multi-modality imaging as a tool to evaluate LN in a multi-center study. Moreover, changes in perfusion detected by DCE-MRI significantly correlate with proteinuria and urinary protein:creatinine ratio. These results suggest that multiparameter imaging may contribute useful data in the evaluation of subjects with LN.

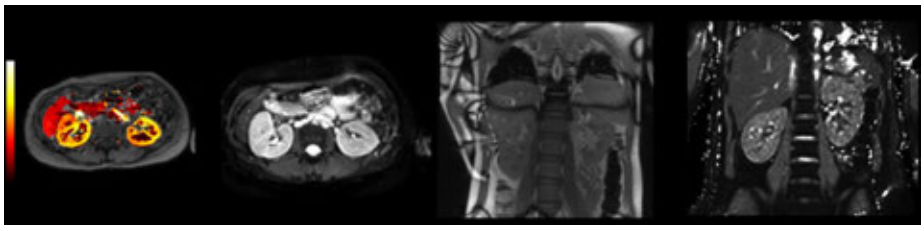

Figure 1. Multi-modality imaging from a representative LN patient. Left: Map of the initial rate of enhancement (DYNAMIKA™) from DCE-MRI showing the degree of perfusion (the white-yellow colors correspond to increased and the redder colors decreased perfusion) in which decreased perfusion can be seen in the anterior pole of the right kidney ; Left center: DWI sequence that shows diffusion; Right center: T1rho illustrating fibrosis; and Right:T2*Map/BOLD to investigate tissue oxygenation within the renal medullary tissue.

Disclosure: A. Saxena, AstraZeneca, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, GlaxoSmithKline, 5, GSK, 5; **D. Karp**, None; **B. Rovin**, Genentech, Inc., 9, Admirx, 5, Alexion, 5, Aurinia, 5, Biogen, 5, Biomarin, 5, Bristol Myers Squibb, 5, Callidates, 5, ChemoCentryx, 2, 5, Chugai Pharmaceuticals, 5, EMD Serono, 2, 5, Genentech, 5, Janssen, 5, Lupus Foundation of America, 5, Mallinckrodt, 5, MedImmune, 5, Morphosys, 5, Novartis, 5, Omeros, 3, Pfizer, 5, Ra Pharmaceuticals, 5, Retrophin, 2, 5, Rigel, 2, 5, Takeda, 5, AstraZeneca, 2, Hoffman-La Roche, 2, Human Genome Sciences Inc., a GSK Company, 2, NIH/NIDDK, 2, RILITE Foundation, 2; **M. Boesen**, Image Analysis Group, OAK Foundation, EUROSTAR, 2, AbbVie, AstraZeneca, Carestream, Celgene Corporation, Eli Lilly, Esaote, Pfizer, Roche, Siemens, UCB – consultant, 5, Image Analysis Group, 9; **O. Kubassova**, Image Analysis Group, 1, 3, 4; **C. Dykas**, None; **A. Yeo**, Horizon Pharma, 3; **P. Lipsky**, Horizon, 5, Janssen Research & Development, LLC, 2.

Abstract Number: 1920

School Nurse Education for Juvenile Idiopathic Arthritis

W. Blaine Lapin ,[1] Carleigh Kutac,[2] Danielle Guttman-Lapin,[3] Amanda Brown,[2] Eyal Muscal,[2] and Filiz Seeborg[2], [1]Baylor College of Medicine, Connecticut Children's Medical Center, Houston, TX, [2]Baylor College of Medicine, Houston, TX, [3]Aldine Independent School District, Houston, TX

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology: Outcomes & Quality of Life
Session Type: ACR/ARP Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: There is a paucity of literature on the challenges children with JIA face at school. Despite treatment advances, children with JIA often rate their Quality of Life (QoL) and school experience as lower than healthy peers. Absences due to disease flares, office visits, medication administration, or side effects may impact school experience. Training of school nurses on other chronic diseases has led to increased knowledge and management skills as well as improvement in children's QoL and school experience. Due to the lack of data on school nurses' awareness about the care of children with JIA, we aimed to improve their knowledge.

Methods: A pediatric rheumatologist presented to school nurses from two large, urban school districts attending a yearly educational seminar. The talk focused on JIA symptoms, course, and treatment, described challenges children with JIA face at school, and recommended accommodations/resources for families and school personnel. Pretest and posttest surveys were administered. Surveys assessed nurses' knowledge of JIA, any prior experience caring for children with JIA or other chronic conditions, assessed acquired knowledge, and responses to hypothetical cases. The study was approved by the primary institution's IRB and the local school districts.

Results: Two hundred and ninety-four school nurses attended the talks. Two hundred and sixty-one nurses (83%) completed both pre and posttest surveys. Most nurses were experienced (mean experience in school setting, 8.8 years, $\pm$ 8.7) and were predominantly located at elementary schools. They had variable exposure to other pediatric disorders (Table 1). Only 18.3% of nurses had ever met with a caregiver of a child with JIA, and only 11.8% had implemented a JIA health plan. Over 80% of nurses reported no experience in treating JIA, but reported experience treating Diabetes Mellitus (DM). Nevertheless, nurses identified other resources for managing children with JIA in school, such as supportive care and contacting parents. Seventy percent of respondents reported feeling more prepared to treat DM (vs JIA). After the presentation, nurses felt significantly more prepared to care for a child with JIA at a level that was comparable to DM knowledge (Table 2). Nurses' reported takeaways from the talk included "being

Table 1: Demographic data of participants

Characteristic	Frequency (%)
Type of school currently working in (may work in multiple types), total/frequency	
Early Childhood/Pre-K	26 (11.1%)
Elementary	148 (63.2%)
Middle	44 (18.8%)
High School	40 (17.1%)
Special needs children at nurses' schools	206 (93.2%)
Have you even taken a course/training program that covered improving school experience of children with arthritis?	4 (1.7%)
Have you used any published resources to learn more about a child with arthritis?	55 (23.8%)
Have you received any training about working with students who have other medical problems? number/frequency	
Total:	192 (85.3%)
Disease:	
Diabetes	104 (54.2%)
Seizures	48 (25.0%)
Asthma	41 (21.4%)
Food allergies	19 (9.9%)
Gastrointestinal Tube feeding	14 (7.3%)

Table 2: Reported feelings of preparedness of school nurses

How well prepared do you feel to care for a child who has…?	Diabetes Mellitus (Pretest)	JIA (Pretest)	JIA (Posttest)
Very well prepared	67 (27.92%)	7 (2.90%)	43 (17.84%)
Well prepared	109 (45.42%)	45 (18.67%)	130 (53.94%)
Somewhat prepared	54 (22.50%)	134 (55.60%)	49 (20.33%)
Poorly prepared	3 (1.25%)	41 (17.01%)	1 (0.41%)
Very poorly prepared	2 (0.83%)	10 (4.15%)	1 (0.41%)
Missing	5 (2.08%)	4 (1.66%)	17 (7.05%)
Total	240 (100%)	241 (100%)	241 (100%)

*$P < 0.001$. There was a significant relationship between the feelings of preparedness of school nurses in caring for a child with JIA vs caring for a child with diabetes when comparing the pre-test responses. There is a significant difference in feeling of preparedness of school nurses in caring for a child with JIA when comparing the pre-test and post-test preparedness responses.

more prepared," "more observant," and not "dismissing joint complaints in a child with JIA." The majority (86.3%) of school nurses found the educational session to be useful.

Conclusion: This study highlights school nurses' knowledge gap regarding JIA in school-age children. We demonstrated the effectiveness of a single educational session to increase knowledge of JIA and influence future care of children with JIA in school. Additional data is necessary to assess nurses' knowledge retention and practice changes over time. Similar educational interventions for teachers, social workers, or administrators could be used for other autoimmune and autoinflammatory disorders. Efforts to improve the QoL of patients with JIA should involve interdisciplinary "front-line" team members (e.g., medical, mental health, and school personnel). This project can be continued by future trainees to provide community education.

Disclosure: W. Lapin, None; **C. Kutac**, None; **D. Guttman-Lapin**, None; **A. Brown**, None; **E. Muscal**, None; **F. Seeborg**, None.

Abstract Number: 1921

Parent-Reported Medication Side-Effects and Their Impact on Health-Related Quality of Life in Children with Juvenile Idiopathic Arthritis: Results from the CAPRI Registry

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology: Outcomes & Quality of Life

Session Type: ACR/ARP Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children and many medications are available to control the disease. While physician-reported adverse events (AE) are captured in clinical trials and registries, perceptions of parents about side-effects (SE) of anti-rheumatic medications are not well studied.

Using data from the Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) JIA registry, we describe the frequency and incidence of parent-reported medication SE in children with JIA, compare them to physician-reported AE, and assess their impact on health-related quality of life.

Methods: All children with JIA enrolled within 3 months of diagnosis who had at least one visit documented in the Registry as of May 9, 2019 were included in this analysis. At every clinic visit parents were asked "Is your child having any side effects from medications taken for his/her arthritis?" They selected SE from a 17-item list, added any not listed, and rated their overall severity on a 21-point numerical rating scale from 0=no problem, to 10=very severe. Physicians reported AE that required additional visits, tests or treatments (irrespective of their cause) and used a standard 18-item list, similar to other registries. Health-related quality of life was assessed using the parent's global assessment from Singh's Childhood Health Assessment Questionnaire (CHAQ) "Considering all the ways that arthritis affects your child rate how your child is doing", from 0=very well, to 10=very poor; and the child's answer to Feldman's Quality of My Life questionnaire (QoML) "Considering my HEALTH my life is" from 0=the WORST, to 10=the BEST (if the parent felt the child could answer the question).

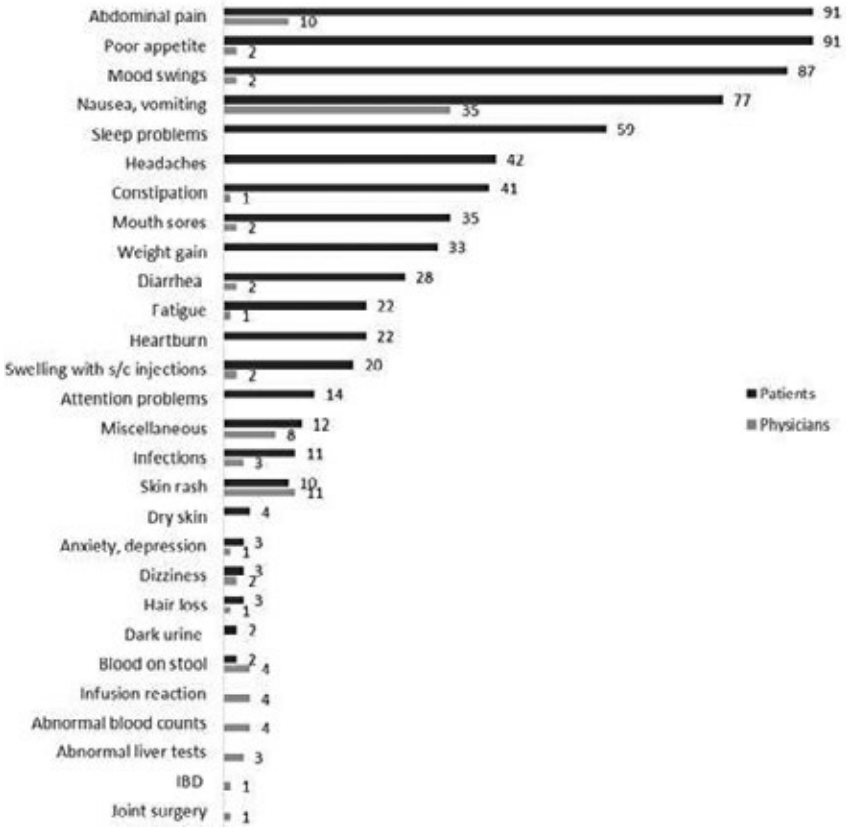
Results: The 226 included patients were typical of western JIA inception cohorts (Table 1). Parent reports were available for 718 of 760 visits (94.5%). Patients were receiving medications at 613 (85.4%) of those visits. Parents reported SE at 294 of 613 visits (48%) with a median of 2 SE per visit (IQR 1, 3). The corresponding incidence rate was 76 SE per hundred patient-years of follow-up with a 54% (CI 48-59) probability of experiencing at least one SE by 1 year after diagnosis. For physician-reported AE it was 25 events per 100 patient-years with a 24% (CI 19-30) probability of at least one AE by 1 year after diagnosis. The reported SE and AE are shown in Figure 1.

Table 1: Demographics

Number of patients	226
Median age at diagnosis, years (IQR)	8.1 (3.4, 12.5) *
Female sex	128 (59.3%) *
Median time diagnosis to enrollment, weeks (IQR)	4.6 (0, 9.3)
JIA subtype - number of patients (%)	
Oligoarticular	107 (47.3)
Polyarticular RF-	38 (16.8)
Polyarticular RF+	7 (3.1)
Psoriatic	10 (4.4)
ERA	37 (16.4)
Systemic	13 (5.8)
Undifferentiated	14 (6.2)
Medications - number of visits (%), out of 718 visits	
None	105 (13.8)
NSAIDs	446 (62.1)
Methotrexate	270 (37.6)
Other DMARDs	15 (2.1)
Biologics	71 (9.9)
Joint injections	95 (13.2)
Prednisone p.o.	79 (11)
Ocular corticosteroid	16 (2.2)

* Age information missing in 28 subjects and sex in 10 subjects.

Figure 1: Number of parent-reported SE and physician-reported AE in a total of 718 visits



The most common SE were gastro-intestinal. The severity of SE was a median of 3 out of 10 (IQR 1.5, 5) and 82% were mild with a score ≤ 5. The parent's global assessment was a median of 2 (IQR 0.5, 5.5) when SE were present, and a median of 0.5 (0, 2) when absent ($p < 0.0001$, median test). The patient's rating of their health-related quality of life was a median of 7 (5, 8.5) when SE were present, and a median of 8 (6.5, 9.5) when absent ($p < 0.0001$).

Conclusion: Parents of children with JIA report a very high frequency of medication SE, significantly higher than physician reported AE. SE have a measurable effect on the parent's global assessment and on the patient's assessment of health-related quality of life. Better addressing these SE may improve quality of life and adherence with medication regimens in children with JIA.

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Abstract Number: 1922

Improvement in Hepatitis B Screening Prior to Initiation of Biologic Therapy in the Pediatric Rheumatology Clinic

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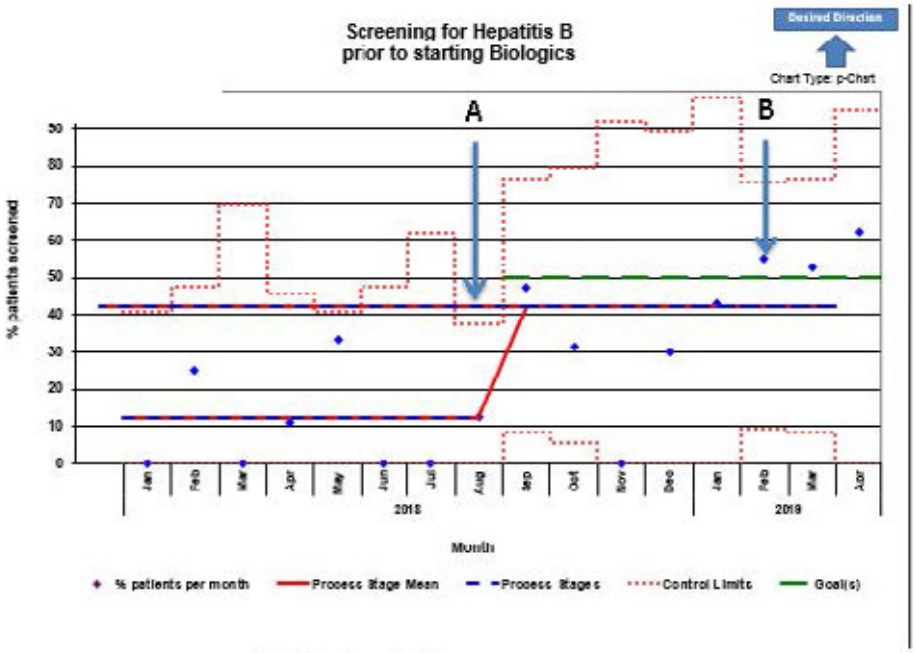
SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology: Outcomes & Quality of Life
Session Type: ACR/ARP Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Use of certain biologic medications increases the risk of reactivation of hepatitis B. Therefore, screening for hepatitis B viral (HBV) infection is recommended prior to initiation of biologic agents for the treatment of rheumatic diseases. Although children are routinely vaccinated for hepatitis B in the US, vaccine seroprotection may be reduced or lost in immunocompromised patients. We sought to evaluate our compliance with HBV screening before starting biologic therapies.

Methods: We used Quality Improvement methodologies with an aim to increase HBV screening rates in patients starting injectable biologic agents from 12.5% to greater than 50% in 6 months and to 80% in 1 year. Using a multidisciplinary team approach, we identified the root causes of incomplete HBV screening including: lack of provider awareness of guidelines, lack of access to vaccination records and prompts in the electronic health record (EHR), and concern about delay in therapy. To address these root causes, we performed multiple PDSA cycles including education of providers and engaging the clinical pharmacy staff, who were involved with the prior authorization for these Specialty medications. We created smart phrases for providers to use at the time of request for prior authorization for new injectable biologic medications, which included all required HBV screening tests. Another smart phrase enabled pharmacy staff to notify providers of patients missing screening. Flyers were posted in clinic rooms to remind prescribers and patients of the need to perform HBV screening.



A: Project Awareness
B: EPIC Smart phrase

Results: At the start of the project, only 1 of 7 providers (14%) stated that they routinely screened patients for HBV before starting a new biologic and only 12.5% of patients in the rheumatology clinic were screened for HBV with hepatitis B surface antigen prior to initiating biologic therapy. Through the PDSA cycles, monthly HBV screening rate for patients starting injectable biologics increased from 12.5% to 42.5% by 7 months. Further improvement is being seen with implementation of the EHR smart phrase. Since testing was incorporated in to the prior authorization process, initiation of therapy was not delayed.

Conclusion: Despite falling short of the initial project aim, our interventions resulted in a significant improvement in the number of patients screened for a potentially serious complication than in the pre-intervention period, as seen by the center line shift in the control chart (Fig 1). Inclusion of pharmacists in the improvement process was successful in reminding providers of missed opportunities for testing. Future directions include analysis for percentage of patients without evidence of immunity to hepatitis B with plans for booster vaccination when indicated.

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Abstract Number: 1923

Disability and Health-Related Quality of Life Outcomes in Patients with Systemic or Polyarticular Juvenile Idiopathic Arthritis Treated with Tocilizumab in Randomized Controlled Phase 3 Trials

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology: Outcomes & Quality of Life

Session Type: ACR/ARP Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Tocilizumab (TCZ) was approved for the treatment of systemic juvenile idiopathic arthritis (sJIA) and polyarticular juvenile idiopathic arthritis (pJIA) based on the results of 2 large phase 3 clinical trials.[1,2] Physical function, measured by the Childhood Health Assessment Questionnaire–Disability Index (CHAQ-DI), and health-related quality of life (HRQOL), measured by the Child Health Questionnaire (CHQ), were evaluated in both trials. The objective of this post hoc analysis of data from both phase 3 trials of TCZ was to examine measures of disability and HRQOL in patients with sJIA or pJIA treated with TCZ for up to 2 years.

Methods: Eligible patients aged 2 to 17 years of age diagnosed with active (≥6 months) sJIA or pJIA according to International League of Associations for Rheumatology criteria received TCZ IV or placebo every 4 weeks (pJIA) or every 12 weeks (sJIA). For sJIA patients, changes within 3 months of treatment initiation with TCZ (baseline) were compared between TCZ- and placebo (PBO)-treated patients using CHAQ-DI, pain-global assessment, physician (MD) global assessment, and patient global assessment using analysis of variance adjusted for treatment group. Changes in CHAQ-DI overall and domain scores from baseline to 2 years were compared for sJIA and pJIA patients treated with TCZ using the unpaired *t* test; similarly, for sJIA patients treated with TCZ, changes in CHQ domain and summary scores between baseline and 2 years were assessed.

Results: sJIA patients experienced clinically relevant improvement of physical function (CHAQ-DI) and reduction in pain (pain-global). Mean (SD) CHAQ-DI scores for patients treated with PBO and TCZ were 1.7 (0.8) for both groups at baseline and 1.2 (1.0) and 0.9 (0.8), respectively, at week 12 (week 12 mean difference, –0.2; median [range] change from baseline to week 12 difference, –0.3 [–0.6 to 0.0]). sJIA patients treated with TCZ had significantly improved socialization, behavior, mental health, and CHQ-psychosocial summary scores after 3 months compared with those receiving PBO (Table 1). Marked improvement in all CHAQ-DI domains over 2 years was observed with TCZ treatment in both sJIA and pJIA patients (Table 2); improvement rates in patient well-being (patient-global) were 87.7% in sJIA patients and 83.4% in pJIA patients. There was also significant improvement ($p < 0.05$) in most domains of HRQOL (CHQ-domain scores) in patients with sJIA; of note, sJIA patients experienced marked improvement in mean scores from baseline to week 104 for pain/discomfort (31.7 to 75.3), self-esteem (61.0 to 76.0), mental health (62.1 to 76.8), and social limitation-emotional (52.6 to 86.2).

Table 1. Change in HRQOL and Disability Within 3 Months of Starting Therapy in sJIA Patients*

Variable	Placebo n = 37		Tocilizumab n = 75		Difference	
	Baseline	Week 12	Baseline	Week 12	At Week 12	In Change From Baseline to Week 12[‡]
CHAQ-DI	1.66 (0.82)	1.17 (0.99)	1.74 (0.79)	0.94 (0.77)	–0.23	–0.31 (–0.62, 0.00)
Activity	1.86 (1.00)	1.30 (1.18)	1.93 (0.99)	1.19 (1.11)	–0.11	–0.18 (–0.61, 0.25)
Rising	1.51 (0.96)	1.00 (1.08)	1.55 (0.93)	0.79 (0.92)	–0.21	–0.25 (–0.67, 0.18)
Dressing and grooming	1.84 (1.09)	1.27 (1.19)	1.91 (1.02)	1.18 (1.00)	–0.09	–0.16 (–0.54, 0.22)
Eating	1.22 (1.18)	0.89 (1.02)	1.49 (1.06)	0.64 (0.76)	–0.25	–0.53 (–0.96, –0.09)
Grip	1.65 (1.03)	1.11 (1.10)	1.81 (0.91)	0.97 (1.00)	–0.13	–0.3 (–0.73, 0.13)
Hygiene	1.69 (1.04)	1.19 (1.17)	1.75 (1.00)	0.96 (1.08)	–0.23	–0.29 (–0.71, 0.14)
Reach	1.89 (1.05)	1.46 (1.14)	1.95 (0.96)	1.04 (0.94)	–0.42[†]	–0.47 (–0.86, –0.08)
Walking	1.62 (0.92)	1.11 (1.07)	1.52 (0.98)	0.76 (0.96)	–0.35	–0.25 (–0.62, 0.12)
VAS						
Pain-global	53.51 (22.35)	28.19 (27.17)	61.4 (23.98)	22.33 (24.21)	–5.86	–13.74 (–25.92, –1.56)
Physician-global	61.35 (21.12)	25.49 (24.01)	69.63 (15.65)	21.75 (19.20)	–3.74	–12.02 (–21.52, –2.51)
Patient-global	56.27 (21.2)	29.38 (25.93)	60.28 (23.78)	21.29 (21.88)	–8.09	–12.09 (–23.36, –0.83)
CHQ						
Global health	37.43 (28.06)	51.56 (21.98)	30.54 (25.66)	59.51 (26.57)	7.95	13.79 (0.34, 27.23)
Physical function	34.98 (25.56)	56.16 (34.18)	35.04 (27.78)	69.02 (29.56)	12.86	16.75 (4.16, 29.34)
Role/social limitation-physical	42.13 (30.21)	66.16 (35.47)	41.11 (33.37)	80.32 (26.59)	14.16[†]	16.2 (0.23, 32.18)
Role/social limitation-emotional	51.54 (34.24)	69.7 (34.5)	53.04 (34.20)	82.72 (25.49)	13.02	15.43 (–1.04, 31.91)
Pain/discomfort	34.72 (19.93)	54.85 (28.63)	30.27 (21.12)	65.56 (26.10)	10.71	15.94 (4.41, 27.46)
Behavior	64.00 (14.74)	61.36 (15.98)	63.72 (12.23)	69.12 (12.12)	7.76[†]	7.20 (1.75, 12.64)
Mental health	59.97 (15.65)	66.36 (17.91)	63.07 (19.12)	75.14 (17.58)	8.78[†]	5.64 (–1.62, 12.9)
Self-esteem	61.76 (20.91)	69.72 (23.7)	60.56 (20.92)	74.98 (18.81)	5.25	8.16 (–0.29, 16.61)
General health	41.76 (13.85)	45.08 (13.48)	42.20 (14.43)	39.96 (14.97)	–5.11	–4.59 (–10.19, 1.01)
Parental emotional	38.43 (20.44)	52.78 (26.24)	39.44 (25.24)	62.38 (25.64)	9.61	10.16 (–0.76, 21.07)
Parental time	57.72 (26.54)	69.02 (23.2)	60.59 (28.73)	72.99 (29.12)	3.97	2.08 (–10.83, 15)
Family activity	50.67 (22.26)	65.03 (23.87)	59.72 (23.92)	75.02 (25.51)	10	3.60 (–6.21, 13.41)
Family cohesion	75.97 (19.92)	69.24 (26.70)	70.33 (23.81)	75.56 (22.21)	6.31	10.66 (2.38, 18.94)
CHQ-PhS	19.47 (12.85)	31.85 (17.02)	18.68 (13.84)	36.97 (13.99)	5.12	7.31 (1.13, 13.49)
CHQ-PsS	40.64 (8.61)	43.57 (11.33)	41.38 (11.45)	48.44 (9.29)	4.87[†]	4.85 (0.42, 9.27)

*Data are mean (SD) unless otherwise specified. [†]ANOVA, $p < 0.05$. [‡]Median (min, max).
ANOVA, analysis of variance; CHAQ-DI, Childhood Health Assessment Questionnaire–Disability Index; CHQ, Child Health Questionnaire; HRQOL, health-related quality of life; PhS, physical summary; PsS, psychosocial summary; sJIA, systemic juvenile idiopathic arthritis; VAS visual analog scale.

Conclusion: TCZ treatment resulted in statistically significant and clinically relevant improvements in function and HRQOL in patients with sJIA or pJIA over 2 years.

References:

1. De Benedetti F et al. *N Engl J Med* 2012;367:2385-95.
2. Brunner HI et al. *Ann Rheum Dis* 2015;74;1110-7.

Table 2. Change in HRQOL and Disability From Baseline to Week 104 in sJIA and pJIA Patients*

Variable	pJIA			sJIA		
	Baseline n = 188	Week 104 n = 155	$p^{\dagger}$	Baseline n = 112	Week 104 n = 95	$p^{\dagger}$
CHAQ-DI	1.39 (0.74)	0.28 (0.45)	<0.001	1.71 (0.8)	0.58 (0.72)	<0.001
Activity	1.56 (0.97)	0.29 (0.58)	<0.001	1.91 (0.99)	0.80 (1.06)	<0.001
Rising	1.32 (0.88)	0.19 (0.48)	<0.001	1.54 (0.94)	0.39 (0.73)	<0.001
Dressing and grooming	1.60 (1.01)	0.30 (0.66)	<0.001	1.88 (1.04)	0.73 (1.07)	<0.001
Eating	1.16 (1.01)	0.25 (0.57)	<0.001	1.40 (1.10)	0.38 (0.70)	<0.001
Grip	1.53 (0.94)	0.43 (0.76)	<0.001	1.76 (0.95)	0.56 (0.87)	<0.001
Hygiene	1.30 (1.03)	0.26 (0.60)	<0.001	1.73 (1.01)	0.57 (0.88)	<0.001
Reach	1.57 (0.90)	0.35 (0.60)	<0.001	1.93 (0.98)	0.76 (1.01)	<0.001
Walking	1.11 (0.89)	0.15 (0.46)	<0.001	1.55 (0.96)	0.43 (0.78)	<0.001
Parent global pain assessment	52.32 (26.94)	9.79 (18.21)	<0.001	58.79 (23.65)	7.28 (11.76)	<0.001
Physician global assessment	61.36 (20.74)	5.88 (11.45)	<0.001	66.89 (17.98)	7.40 (10.36)	<0.001
Patient global assessment	52.91 (25.04)	8.77 (16.73)	<0.001	58.96 (22.94)	7.25 (10.86)	<0.001

*Data are mean (SD). †Paired *t* test.
CHAQ-DI, Childhood Health Assessment Questionnaire–Disability Index; HRQOL, health-related quality of life; pJIA, polyarticular juvenile idiopathic arthritis; sJIA, systemic juvenile idiopathic arthritis.

Disclosure: H. Brunner, ., 2, 5, 8, AbbVie, 5, AstraZeneca, 5, Bayer, 5, Bristol-Myers Squibb, 2, 5, EMD Serono, 5, Genentech, 2, 5, 8, GlaxoSmithKline, 5, Janssen, 5, Lilly, 5, Novartis, 5, 8, Pfizer, 2, 5, R-Pharm, 5, Sanofi, 5, UCB, 5; **C. Chen**, None; **A. Martini**, BMS, 9, GlaxoSmithKline, 9, Hoffman-La Roche, 9, Novartis, 5, 9, Pfizer, 5, 9, Sanofi Aventis, 5, 9, Schwarz Biosciences, 9, Abbott, 9, Francesco Angelini S.P.A., 9, Sobi, 9, Merck Serono, 9, Abbvie, 5, Boehringer, 5, Celgene, 5, CrescendoBio, 5, Janssen, 5, Medimmune, 5, NovoNordisk, 5, Vertex, 5, Servier, 5; **G. Espada**, None; **R. Joos**, None; **J. Akikusa**, None; **J. Chaitow**, None; **M. Gámir Gámir**, None; **Y. Kimura**, Novartis, 5, Sobi, 5; **C. Rietschel**, None; **D. Siri**, None; **E. Smolewska**, None; **H. Schmeling**, F. Hoffmann-La Roche Ltd, 2, Janssen, 2, Pfizer, 2, UCB Biosciences GmbH, 2; **D. Brown**, None; **F. De Benedetti**, AbbVie, 2, BMS, 2, Novartis, 2, Novartis, Novimmune, Hoffmann- La Roche, SOBI, AbbVie, Pfizer, 2, Novimmune, 2, Pfizer, 2, Roche, 2, Sanofi, 2, Sobi, 2, Swedish Orphan Biovitrum, 2, UCB, 2; **D. Lovell**, Abbott, 5, 9, AbbVie, 5, 9, Amgen, 5, 9, AstraZeneca, 5, Astra-Zeneca Pharm, 5, Biogen, 5, Boehringer Ingelheim, 5, Boeringher Ingelheim, 5, Bristol-Myers Squibb, 5, 9, Celgene, 5, Forest Research, 9, Forest Research Institute, 5, Genentech, 5, 8, GlaxoSmithKline, 5, Hoffmann-La Roche, 5, 9, Horizon, 5, Jannsen, 5, Janssen, 5, 9, Johnson & Johnson, 5, Novartis, 5, 9, Pfizer, 5, 9, Roche, 5, 9, Takeda, 5, 9, UBC, 5, Wyeth Pharm, 5, 8; **B. Huang**, None; **N. Ruperto**, AbbVie, 5, 8, Abbvie, 8, Ablynx, 5, 8, Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol Myers and Squibb, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, 8, AstraZeneca-Medimmune, 8, Astrazeneca-Medimmune, 8, AstraZeneca-MedImmune, 5, 8, Biogen, 5, 8, BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi., 2, Boehringer, 8, Boehringer Ingelheim, 5, 8, Boeringher Ingelheim, 8, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, Eli-Lilly, 8, EMD Serono, 5, 8, F Hoffmann-La Roche, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Hoffmann-La Roche, 8, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda, 8, Janssen, 2, 5, 8, Merck, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, R-Pharma, 5, 8, SanofiServier, 5, 8, Sinergie, 5, 8, Sobi, 2, 5, 8, 9, Takeda, 5, 8.

Abstract Number: 1924

Assessing Psychosocial Needs in Juvenile Dermatomyositis Patients Across the United Kingdom

Polly Livermore ,[1] and Lucy Wedderburn[2], [1]ICH/UCL, Arlesey, United Kingdom, [2]ICH/UCL, London, United Kingdom

SESSION INFORMATION
Session Date: Monday, November 11, 2019
Session Title: Pediatric Rheumatology: Outcomes & Quality of Life
Session Type: ACR/ARP Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Juvenile Dermatomyositis (JDM) is a rare, autoimmune inflammatory condition primarily affecting the muscles and skin. With a mean age of onset of 7 years of age, and research suggesting that 70-80% of young people will have ongoing treatment into adulthood, a significant proportion of children and young people will live with chronic disease for over 10 years of their childhood. Whilst it is acknowledged from studies asking carers that children and young people with JDM suffer from a significant impairment in their health related quality of life, there is no current published research asking young people what their psychosocial needs are and how we can improve their coping with this condition, even after disease remission.

Methods: We surveyed all 246 8-19 year old young people with JDM in the United Kingdom through the Juvenile Dermatomyositis Cohort and Biomarker Study and Repository (JDCBS). Young people were asked to complete measures which have proved significant from previous qualitative interviews, these included perception of uncertainty, quality of life, benefit, burden, and emotional distress, with the opportunity to answer qualitative questions with commentary.

Results: There were no differences in demographics or disease characteristics between the 123 responders and the 119 non responders. 40% of patients scored over the recommended cut-off for emotional distress, which suggested that they should be referred for further psychological assessment. Quality of life scores were lower in children with JDM compared with scores for healthy UK norms. JDM physical and psychosocial summary scores: (75.64 + 24.47 and 76.89 + 18.55) healthy physical and psychosocial summary scores: (88.51 +11.62 and 81.58 + 11.84). Regression analysis indicated that children with increased feelings of uncertainty about their disease and increased perception of burden had lower quality of life in all domains (P value < 0.001). Furthermore, uncertainty and burden were correlated (r= 0.64 P = < 0.001), but equally significant and therefore independently related to quality of life, however burden was more closely related to quality of life after adjusting for other factors. Importantly there was no evidence that quality of life varied by gender, age or years since diagnosis, and no relationship between benefit and quality of life or emotional distress was observed.

Conclusion: This study found that perception of uncertainty and feeling a burden in children and young people with JDM were significantly related to reporting a lower quality of life and higher emotional distress, and 40% of the UK cohort of JDM patients scored over the recommended threshold for emotional distress. These findings can be used by clinicians and allied health professionals to consider the impact of uncertainty and perception of being a burden on children and young people with JDM, and consider ways to lessen this uncertainty. From the qualitative comments, we have ideas about improving psychosocial support for the future, such as the creation of a book for teachers about JDM to improve their education experience.

Disclosure: P. Livermore, National Institute of Health Research, 9; **L. Wedderburn**, None.

Abstract Number: 1925

Discriminant and Predictive Ability of the Parent Version of the Juvenile Arthritis Disease Activity Score in Two Large Multination Cohorts of Patients with Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: Pediatric Rheumatology: Outcomes & Quality of Life

Session Type: ACR/ARP Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: The assessment of disease activity plays a pivotal role in the management of children with juvenile idiopathic arthritis (JIA). Most recent recommendations require that the parents' and children's perception is incorporated in the evaluation of disease course and of effectiveness of therapeutic interventions. A new disease activity tool, named parent Juvenile Arthritis Disease Activity Score (parJADAS), based only on parent-centered outcome measures, is currently under development**.** Aim of the study is to demonstrate, in 2 large multinational datasets, the discriminant and predictiveability of the parJADAS

Methods: The parJADAS (range 0-40) is the sum of 4 measures: 1) parent assessment of disease activity on a 21-numbered circle 0-10 VAS; 2) assessment of pain intensity on a 21-numbered circle 0-10 VAS; 3) proxy assessment of joint disease up to a maximum of 10 joints; 4) assessment of morning stiffness (MS) on a Likert scale, ranging from no MS (0 points) to > 2 hours of MS (10 points). Discriminat ability was assessed on a dataset of 8,656 children with JIA from 49 countries, enrolled in the study of Epidemiology, treatment and Outcome of Childhood Arthritis (Consolaro A et al. Lancet Child Adolesc Health. 2019), who had all the variables included in the parJADAS available. Discriminant ability was evaluated by comparing parJADAS median levels among patients with inactive disease (ID), low disease activity (LDA), moderate disease activity (MDA), and high disease activity (HDA) according to cJADAS10 and in patients whose parents were satisfied or not satisfied with disease status. To assess the influence of damage on the parJADAS, the levels of the score in patients with or without damage (Juvenile Arthritis Damage Index > 0) were compared in subjects in ID and with at least 2 years of disease course (n = 2,423). Predictive ability was assessed in a longitudinal dataset of subjects included in the PharmaChild Registry (Swart J, et al Arthritis Res Ther 2018). Patients (n = 98) were retained if they had 2 years of follow up and at least 4 visits with parJADAS available during the first year since enrolment. The AUC of the parJADAS in the first year of registry participation was calculated and compared

in subjects with/without reduced functional ability (Juvenile Arthritis Functionality Scale, JAFS > 0) at 2 years and in subjects who achieved or did not achieve clinically ID at 2 years.

Results: The median levels of parJADAS in patients in ID, LDA, MDA, and HDA were 0, 3.0, 6.0, and 4.5, respectively (Kruskal-Wallis test, $p < 0.001$). Median parJADAS in patients whose parents were satisfied or not satisfied with disease course were 1.5 and 13.0, respectively (Mann-Whitney test $p < 0.001$). ParJADAS was not different in JIA patients in remission with or without damage measured with the JADI (Mann-Whitney test $p = 0.08$). Subjects JAFS > 0 at 2 years had greater parJADAS AUC in the first year ($p < 0.001$). Subjects in remission at 2 years had smaller parJADAS AUC in the first year ($p < 0.001$)

Conclusion: The parJADAS showed excellent discriminant and predictive ability in 2 large multinational cohorts. The score was not relevantly influenced by disease damage in JIA patients in remission.

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Abstract Number: 1926

Characterization of *DOCK8* as a Novel Gene Associated with Macrophage Activation Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Macrophage activation syndrome (MAS), also known as secondary hemophagocytic lymphohistiocytosis (HLH), is a life threatening condition that commonly presents with unremitting fever and shock like multi-organ dysfunction (MOD). Laboratory studies show pancytopenia, elevated liver enzymes, elevated ferritin, and hemophagocytosis. Familial forms of HLH result from homozygous defects in genes involved in perforin mediated cytolysis by NK cells and CD8 T cells. As many as 30-40% of MAS patient cohorts studied have heterozygous defects in the same HLH genes resulting in decreased cytolytic function, prolonged interaction with antigen presenting cells, and subsequent increased pro-inflammatory cytokines resulting in MOD. Since NK cell dysfunction is common in MAS, there are likely other genes that contribute to MAS via decreased cytolysis. Using gene sequencing, mutations in potentially novel HLH genes present in 2 or more MAS patients were explored.

Table. *DOCK8* rare mutations and polymorphisms identified in MAS patients.						
#	Age (yrs)	Sex	Disease	Trigger	Mutation	Frequency
1	16	M	Hyper IgE syndr.	Bartonella	c.782C>T, p.Ala261Val	novel
2	19	M	T cell leukemia	?	c.54-1G>T (splice acceptor)	0.03%
3	24	M	Still disease	?	c.187G>A, p.Asp63Asn	12%
4	36	F	Polyarteritis nod.	Streptococcus	c.187G>A, p.Asp63Asn	12%

Table 1. Age, sex, disease, trigger, genetic mutation and its frequency of 4 MAS patients expressing DOCK8 mutations or a less common polymorphism.

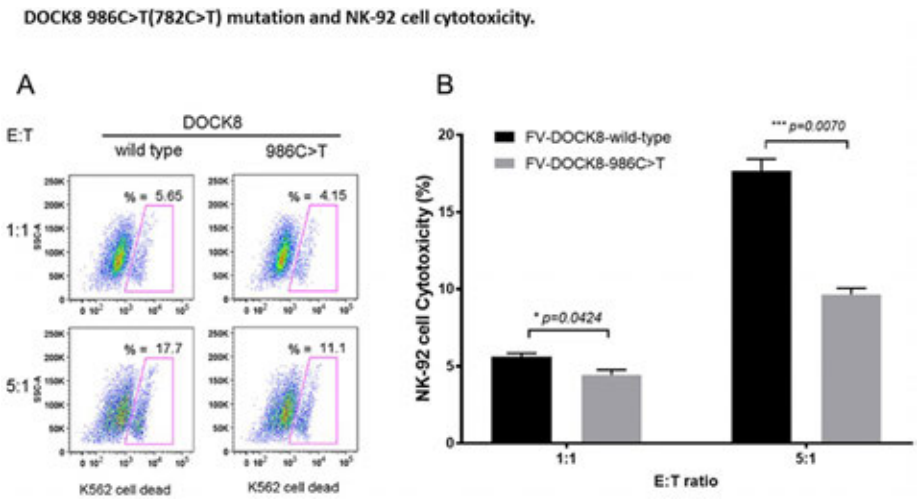

Figure 1. Cytolytic activity of NK-92 cell expressing (by foamy virus transduction) a novel DOCK8 mutation (c.782C>T, p.Ala261Val). A. A representative flow cytometry example of wild type (left columns) or mutant (right columns) DOCK8-expressing NK-92 cell lysis of K562 target cells at effector-to-target ratios of 1:1 (top row) and 5:1 (bottom row), with cell death noted along the X-axis. B. Mean +/- SEM cytoltyic activity of wild-type or mutant DOCK8-expressing NK-92 cells from 3 experiments.

Methods: Pediatric and adult patients with MAS at UAB were screened for genetic mutations, potentially contributing to MAS, via whole genome sequencing or a commercial immunodeficiency exomic genetic panel of 207 genes. Several patients were noted to have mutations in the guanine nucleotide exchange factor *DOCK8* critical to NK cell function. *DOCK8* mutations from this MAS cohort, or wild-type (WT) sequence controls, were introduced exogenously into human NK-92 NK cell lines by foamy virus (FV) transduction. Alternatively, the endogenous NK-92 *DOCK8* genes were cut and repaired to express WT sequence or patient derived *DOCK8* mutations by CRISPR/Cas9 technology. WT and mutant *DOCK8* expressing NK-92 cells were incubated with K562 target cells and compared for cytolytic activity, degranulation (CD107a), and cytokine [interferon-g (IFNγ), tumor necrosis factor (TNF)] production by flow cytometry.

Results: Two MAS patients were identified with rare heterozygous DOCK8 mutations, and 2 others with MAS were noted to have the same DOCK8 polymorphism (c.187G >A, p.Asp63Asn) present in 12% of the population (Table). One of the rare mutations was missense (c.782C >T, p.Ala261Val – novel), and one was a splice acceptor variant (c.54-1G >T, 0.03%). The novel DOCK8 mutant consistently decreased NK cell lytic activity when introduced by either CRISPR/Cas9 (n=2) or FV (n=3, decreased by ~50% compared to WT, p=0.007) (Fig. 1). Similarly, the novel mutant decreased degranulation by >50% (n=3, p=0.0129) (Fig. 2). During the incubation of the NK-92 cells with K562 targets, NK cells expressing the novel DOCK8 mutant increased expression of IFNγ and TNF by >200% (p=0.0192 & p=0.0027, respectively). Prolonged interaction of the DOCK8 mutant NK-92 cells with K562 cells is currently being explored as a cause of increased cytokine production. Also, the DOCK8 splicing mutation is currently being tested functionally by “exon trapping” to explore a potential hypomorphic mutation.

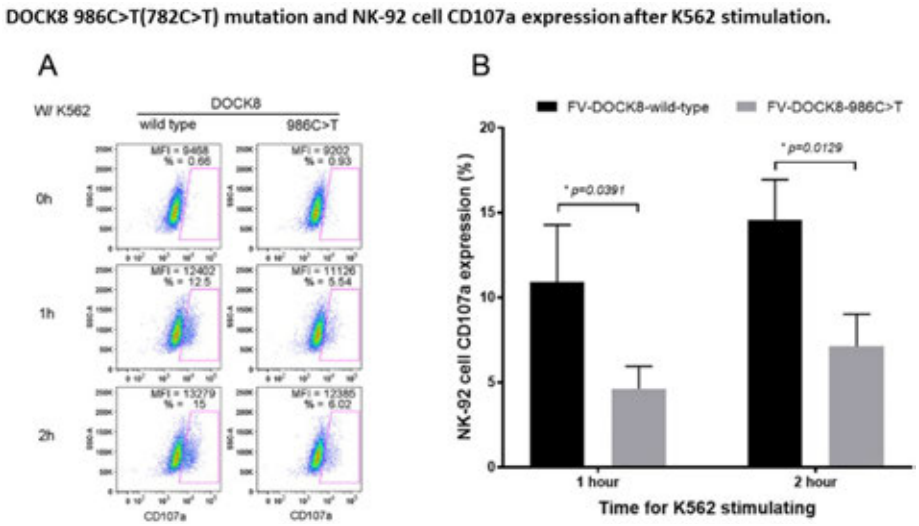

Figure 2. Degrantulation of NK-92 cell expressing (by foamy virus transduction) a novel DOCK8 mutation (c.782C>T, p.Ala261Val). A. A representative flow cytometry example of degranulation (CD107a expression) of wild type (left columns) or mutant (right columns) DOCK8-expressing NK-92 cells incubated with K562 target cells evaluated at 0 hr (top row), 1 hr (middle row), and 2hr (bottom row), with CD107a noted along the X-axis. B. Mean +/- SEM CD107a expression of wild-type or mutant DOCK8-expressing NK-92 cells from 3 experiments.

Conclusion: Heterozygous mutations in *DOCK8*, a novel MAS associated gene, likely contribute to pathology through a partial dominant-negative or hypomorphic effect resulting in decreased cytolysis and increased pro-inflammatory cytokine production.

Disclosure: M. Zhang, None; **R. Cron**, None; **D. Absher**, None; **C. Crayne**, None; **P. Atkinson**, None; **W. Chatham**, SOBI, 2; **R. Cron**, Novartis, 5, Pfizer, 9, SOBI, 2.

Abstract Number: 1927

Role of Mitochondrial DNA from OA Patients in Cellular Apoptosis, Senescence and Autophagy

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: With the redefinition of Osteoarthritis (OA) and the understanding that the joint behaves as an organ, OA is now considered a systemic illness with a low grade of chronic inflammation. Chondroptosis, chondrosenescence and autophagy contribute to cell death and tissue damage in OA. The mitochondria are related with these three process implicated in the cartilage degeneration. Mitochondrial dysfunction is well documented in OA and has the capacity to alter chondrocyte and synoviocyte function contributing to cartilage degeneration. Trans-mitochondrial cybrids are a useful cellular model to study mitochondrial biology *in vitro*, since they carry different mitochondrial variants with the same nuclear background

Purpose: The aim of this work was to study apoptosis, senescence and autophagy using cybrids with mtDNA from healthy (N) and OA donors.

Methods: Cybrids were developed using 143B.TK$^-$ Rho-0 cell line (nuclear donor) and platelets (mitochondrial donors) from healthy (N) and OA donors. The mitochondrial depolarized and morphology were evaluated incubating cells with DilC1(5) and MitoTracker Red® respectively and these parameters were analyzed using Flow Cytometer. The percentage of apoptotic cells was measured by Flow Cytometry using Annexin-V and PI. Senescence level was measured by real-time PCR method. Autophagy was evaluated through the developed of Microtubule-associated protein 1A/1B-light chain 3 (LC3) WB. The WB quantification was developed using Image J software. Appropriate statistical analyses were performed with GraphPad Prism v6.

Results: OA cybrids showed higher increment depolarized mitochondria under negative stimuli (2.57±1.20; 1.76±0.99; $p \leq 0.05$ respectively). Mitochondrial distribution showed that in OA cybrids mitochondria were concentrated around the nucleus whereas in N cybrids were organized in extended tubular structures. The quantification of staining reflected a decrease of fluorescence intensity in OA compared to N cybrids (14.31±3.16; 33.00±4.20 respectively, $p \leq 0.005$). When the cells were submitted for a positive stimuli and an inflammatory environment the analysis of apoptotic levels were developed and reflected that OA cybrids had an increase in positive cells for Annexin-V in comparison to N cybrids (2μM Staurosporine 15.68±6.39; 6.41±4.88 respectively, $p \leq 0.05$. 10ng/ml IL-1β 0.924±0.19; 0.47±0.24 respectively, $p \leq 0.05$). The gene expression corresponding to senescence marker protein (SMP30) showed higher levels in OA cybrids than in N (4.535±1.63; 1.21±0.42 respectively, $p \leq 0.0005$). Autophagy was analyzed studying LC3 a marker for autophagosome formation and the results showed that LC3 activation was reduced in OA cybrids (1.19±0.24; 1.41±0.21 respectively, $p \leq 0.05$).

Conclusion: Mitochondria from OA donors was involved in three relevant processes related with OA as cellular apoptosis, senescence and autophagy.

Disclosure: M. Fernandez-Moreno, None; **A. Dalmao-Fernández**, None; **U. Nogueira-Recalde**, None; **T. Hermida-Gómez**, None; **M. Vazquez-Mosquera**, None; **S. Relaño**, None; **I. Rego-Pérez**, None; **F. Blanco**, None.

Abstract Number: 1928

Identification of Immunological Processes Associated with the Response to Abatacept in Rheumatoid Arthritis Using Longitudinal Blood RNA-seq Analysis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Abatacept (CTLA4-Ig) is an approved biological therapy for the treatment of rheumatoid arthritis (RA). Similar to other biological agents, most patients (50-60%) respond significantly to this therapy. To date, however, the biological mechanisms underlying the lack of efficacy for this drug are unknown.The objectives of the present study were to generate insights into the biological processes that underly the differential response to abatacept and to evaluate the blood transcriptome as a valid source for drug response prediction.

Methods: A total of n=57 patients diagnosed with RA according to the ACR-EULAR criteria where recruited for this study from the rheumatology departments of 16 different university hospitals from Spain. All patients had >6 months of disease evolution and started therapy with a baseline DAS28 > 3.2. The primary clinical response was defined at week 12 of therapy using the EULAR criteria. Good and moderate responders were aggregated into a single response group and compared to the remaining (no response) group of patients. Whole blood RNA was collected from all patients at baseline using Paxgene tubes. From a subgroup of these patients (n=31), blood RNA was also obtained at weeks 12, 24 and 48 of treatment with abatacept. Gene expression levels were determined using paired-end RNA-seq with the NovaSeq 6000 platform (Illumina). Differential gene expression, association to biological processes, longitudinal association analysis and building of the multigenic predictor were performed using the R software. The Random Forest algorithm was used to build the predictor and the prediction accuracy was evaluated using the ROC AUC.

Results: From the 57 patients treated with abatacept, n=10 (17.5%) were good EULAR responders, n=24 (42%) moderate EULAR responders and n=23 (40.5%) non-responders at week 12 of therapy. Two significantly distinct biological profiles were identified between responders and non-responders to abatacept. In responders, we found an association to pathways associated with the effector phase of T cells (e.g. interleukin IL-15 and IL-22 signalling, adjusted $P < 0.05$). Non-responder patients showed instead a strong association to biological processes associated with antigen presentation and activation of T cells (adjusted $P < 0.005$). Using the baseline gene expression profiles, we built a multigenic predictor of response to abatacept with an AUC = 75%. In the longitudinal cohort, patients were stratified based on reaching an inactive state at week 48 (DAS28 < 3.2). Using this endpoint measure, the longitudinal analysis of the 4 time points corroborated the association with antigen presentation activation and the lack of response to this drug (adjusted $P < 0.01$).

Conclusion: The analysis of longitudinal blood RNA-seq profiles of RA patients starting abatacept therapy, has enabled the identification of specific immunological processes associated with the efficacy of B7 costimulation inhibition. Also, we demonstrate that blood expression profiles could be predictive of the response abatacept. The results

from this study contribute to the advancement of precision medicine in RA and the understanding of the underlying disease heterogeneity.

Disclosure: A. Julià, None; **M. Lopez Lasanta**, None; **A. Gómez**, None; **I. Bonafonte**, None; **R. Sanmartí**, None; **C. Marras**, None; **J. Pina**, None; **S. Romero-Yuste**, None; **R. Veiga**, None; **P. Navarro**, None; **C. Moragues Pastor**, None; **S. Martínez**, None; **F. De Toro**, None; **A. Sanchez**, None; **D. Cerdà**, None; **A. Prada**, None; **A. Erra**, None; **J. Monfort**, None; **A. Urruticoechea-Arana**, None; **N. Palau**, None; **R. Lastra**, None; **R. Tortosa**, None; **A. Pluma**, None; **S. Marsal**, Vorso Corp, 5.

Abstract Number: 1929

Identification and Validation of Transcriptional Genes Associated with Osteoporotic Vertebral Fractures by Microarray Study, in Community Elderly Women

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The pathogenesis of osteoporosis, a common disease with high morbidity[1], comprises genetic and environmental factors[2]. Recent studies demonstrated that blood samples are a source of reliable biomarkers which could serve as drug targets in treating of multiple age-associated diseases. The aim of this study was analyze transcriptomes of elderly women with osteoporotic Vertebral Frature, comparing with women with no Vertebral Fracture. Applying bioinformatical tools enabled us to identify such biomarkers for further validation.

Methods: We conducted microarray assays for comparing RNA expression of female vertebral fracture patients and no vertebral fracture controls. Age, bone mineral density (BMD) at lumbar spine, total hip and femoral neck and bone turnover markers were similar between the groups. In statistical analysis of microarrays we applied logistic regression model with age used as a covariate. Bioinformatic analysis involved interactome network analysis in Cytoscape software and enrichment analysis of biological processes regulated by the candidate genes. Special focus was put on identification candidate genes showing also age related changes in expression in bone and muscle tissue according

Table 1. Genes chosen using bioinformatic tools for validation

Genes	Top 10 UP regulate	Down regulate	Interaction genes	Muscle expression	Bone expression	Gene Ontology (Biological process and molecular function)	Aging related
SNTG2	Yes	-	-	Yes	-	Yes	-
TRAF3IP2	Yes	-	Yes	Yes	-	Yes	Yes
PNO1	Yes	-	Yes	Yes	-	-	-
CD248	Yes	-	Yes	Yes	-	-	-
TNXB	-	-	Yes	Yes	-	Yes	-
ITGA6	-	-	Yes	Yes	-	Yes	-
PRDX5	-	Yes	Yes	Yes	Yes	-	-
UBXN6	-	Yes	Yes	Yes	-	-	-

Table 2. Validation of gene expression using qPCR-RT

Gene	Fold change	SD	P
SNTG2	2.74	1.68	0.024
TRAF3IP2	1.83	0.66	0.010
PNO1	1.14	0.28	0.319
CD248	1.54	0.92	0.203
TNXB	0.96	0.50	0.845
ITGA6	1.62	0.45	0.007
PRDX5	1.04	0.35	0.783
UBXN6	1.42	0.53	0.093

to public available data (GTEX, String database). Expression changes were validated using SYBR green based qPCR-RT (quantitative real-time polymerase chain reaction). We used Pfaff method for relative expression quantification. The geometric mean of 2 control genes (RPL27 and RPL6) was used to compare the gene expression between the groups. Genes with p≤ 0.01 were considered statistically significant in microarray study and p≤ 0.05 in qPCR.

Results: We identified 142 differentially expressed transcripts, 57 up regulated, 85 down regulated in microarray analysis. The transcripts SNTG2, TRAF3IP2, PNO1, CD248, TNXB, ITGA6, PRDX5 and UBXN6 were chosen for validation due to their significance in the analysis of enrichment and genetic interaction. qPCR validation confirmed increased expression in Vertebral Fracture group of TRAF3 Interacting Protein 2 (TRAF3IP2 with fold change = 1.83, SD = 0.66, p = 0.01), Integrin Subunit Alpha 6 (ITGA6 with fold change = 1.62, SD = 0.45, p = 0.007) and Sintrophyn (SNTG2 with fold change = 2.74, SD = 1.68, p = 0.024).

Conclusion: TRAF3IP2 plays a role in various autoimmune and inflammatory diseases and interacts with TNF receptor-associated factor 3[3]. ITGA6 recently was found as upregulated and potentially involved in activity of osteoblasts of rheumatoid arthritis[4]. SNTGβ2 transcript that encodes a protein belonging to the syntrophin family, highly expressed in the musculoskeletal system[5].

Our data support the association of these transcripts with osteoporotic vertebral fracture in elderly women, independently of bone mineral density. These transcripts could be used as biomarkers or therapeutic targets in osteoporotic vertebral fracture in futures studies.

Disclosure: L. Jales Neto, None; **Z. Wicik**, None; **G. Torres**, None; **L. Takayama**, None; **N. Lopes**, None; **a. Pereira**, None; **R. Pereira**, None.

Abstract Number: 1930

Analysis of Lupus Nephritis Gene Expression Reveals Dysregulation of Pathogenic Pathways Activated Within Infiltrating Cells

Adam Labonte ,[1] Jackson Xu,[2] Sarah Heuer,[2] Robert Robl,[2] Prathyusha Bachali,[1] Michelle Catalina,[1] Peter Lipsky,[3] and Amrie Grammer[4], [1]AMPEL Biosolutions and the RILITE Research Institute, Charlottesville, VA, [2]AMPEL BioSolutions, Charlottesville, VA, [3]AMPEL BioSolutions, LLC, Charlottesville, VA, [4]AMPEL BioSolutions and RILITE Research Institute, Charlottesville, VA

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: LN is a serious complication of SLE that affects about 20-40% of all lupus patients and leads to kidney damage, end-stage renal disease, and patient mortality. Despite advances in therapy, progression to end stage renal disease has not been affected. Therefore, it is important to re-consider the pathogenic mechanisms involved in LN as a basis for development of more effective therapies. Here we present a multi-pronged approach to characterize LN via bioinformatic analysis of gene expression data obtained from kidney biopsies.

Methods: Genomic expression profiling data of LN patient biopsies, microdissected into glomerulus and tubulonterstitium (TI), was sourced from GSE32591 via the GEO database. Differentially expressed genes (DEGs) detected in LN-derived samples relative to samples from healthy individuals were interrogated for cell infiltrate composition using gene set variation analysis (GSVA) against a curated database of immune and non-immune cell type signatures (I-SCOPE, T-SCOPE). Weighted gene co-expression network analysis (WGCNA) was used to generate gene modules correlated to clinical variables. DEGs were further functionally characterized using a curated immunity-specific gene functional category database (BIG-C) and IPA signaling pathway analysis software. Queries of the perturbation database (LINCS, Library of Integrated Network-Based Cellular Signatures) were used to identify possible upstream regulators of altered gene expression patterns in LN samples as well as to identify drugs that could reverse abnormal gene expression profiles.

Results: WGCNA produced 6 gene modules (3 glomerulus, 3 TI) positively correlated with disease stage as measured by WHO class. These modules were enriched in signatures for several immune cell types, including granulocytes, pDC, DC, myeloid cells, $CD4^+$/$CD8^+$ T cells, and B cells. Additionally, the presence of both IG-κ and -λ as well as V_L genes and detection of pre- and post-switch PCs as indicated by IgM, IgD, and IgG1 Ig Heavy Chain genes indicate polyclonal PC infiltration. Podocyte signatures were detected as enriched in WGCNA modules negatively correlated with WHO class. Chemokines and pathways that mediate lymphocyte proliferation, organization and/or recruitment into lupus kidney tissue were detected as enriched via BIG-C and IPA analysis, including the cytokines TNF, IL1β, IL2, IL6, IL12, IL17, IL23, and IL27 and signaling pathways including CD40L, PI3K, NF-κB, NF-AT, and p70S6K. IPA upstream regulator analysis indicated ongoing signaling by cytokines such as TNF, IFNγ, IFNα, CD40L, IL1β, IL2, IL6, and IL17. Interestingly, connectivity analysis using LINCS elucidated high priority drug targets such as IFNβ (PF-06823859), IL12 (Ustekinumab), and S1PR (Fingolimod) that may prove to be good options for therapeutic intervention.

Conclusion: Bioinformatic analysis of LN gene expression highlights several dysregulated signaling pathways that can form the targets of novel therapeutic strategies, and further elucidation of these signatures may enhance clinical surveillance and diagnosis of LN to improve patient outcomes.

Disclosure: A. Labonte, None; **J. Xu**, None; **S. Heuer**, None; **R. Robl**, None; **P. Bachali**, None; **M. Catalina**, None; **P. Lipsky**, Horizon, 5, Janssen Research & Development, LLC, 2; **A. Grammer**, None.

Abstract Number: 1931

Comprehensive Characterization of the Immune Infiltrate of Skin Biopsies from Cutaneous Lupus Erythematosus Patients Using Single Cell RNAseq

Agnes Gardet ,[1] Thomas Carlile,[1] Will Chou,[1] Kejie Li,[1] Alex Pellerin,[1] Ravi Challa,[1] Will Chen,[1] Chao Sun,[1] Nathalie Franchimont,[2] Victoria Werth,[3] and Dania Rabah[1], [1]Biogen, Cambridge, [2]Biogen, Cambridge, MA, [3]Corporal Michael J. Crescenz VAMC, Philadelphia, PA, USA and Department of Dermatology, University of Pennsylvania, Philadelphia, PA, USA, Philadelphia, PA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The immune infiltrate of skin lesions of Cutaneous Lupus Erythematosus (CLE) patients is known to be rich and complex. Single cell RNAseq (scRNAseq) is a unique approach to understand the cell-specific transcriptional heterogeneity in a complex tissue. ScRNAseq analyses of CLE skin biopsies has the unique potential to improve our understanding of human disease tissues and provide critical biological insights into the CLE pathogenesis.

Methods: Skin punch biopsies were obtained from healthy skin or lesional skin from CLE patients. Skin storage conditions and tissue dissociation protocol were optimized using healthy skin biopsies. RNAseq protocol was tested with blood-sorted pDCs and monocytes. Skin biopsies were collected from patients with DLE or SCLE. After tissue dissociation and cell staining, single CD45+ immune cells were sorted using flow cytometry and scRNAseq was performed using the SMART-seq2 protocol for cDNA synthesis and library preparation prior to sequencing.

Results: The scRNAseq protocol showed a similar sensitivity as a state-of-the-art published protocol (Villani AC et al, Science 2017). Avoiding cryopreservation and digestion of the skin biopsies with collagenase provided the best immune cell yield. Approximatively 85% of the isolated single cells produced RNAseq data that passed quality control. Analysis of 5 biopsies provided transcriptomic characterization of B-cells, CD4 and CD8 positive T-cells, Macrophages, Dendritic cells, and pDCs from skin lesions and suggested immune infiltrate heterogeneity in CLE patients. RNAseq data was also leveraged to define cell type marker panel for scqPCR which allowed a more focused cost- and time- effective approach for follow-up/validation of gene expression analyses.

Conclusion: We developed a protocol that successfully identified and characterized the immune infiltrate from skin punch biopsies of CLE patients. Analyses from additional patients will be needed to further understand the immunological heterogeneity of CLE skin lesions.

Disclosure: A. Gardet, Biogen, 1, 3; **T. Carlile**, Biogen, 1, 3; **W. Chou**, Biogen, 1, 3; **K. Li**, Biogen, 1, 3; **A. Pellerin**, Biogen, 1, 3; **R. Challa**, Biogen, 1, 3; **W. Chen**, Biogen, 1, 3; **C. Sun**, Biogen, 1, 3; **N. Franchimont**, Biogen, 1, 3; **V. Werth**, Biogen, 2, 5, Corbus Pharmaceuticals, 2, 9, University of Pennsylvania, 9; **D. Rabah**, Biogen, 1, 3.

Abstract Number: 1932

Genetic Evidence for Recent Positive Selection of the *HLA-B*51:01* Allele in the Turkish Population, a Population with a High Prevalence of *HLA-B*51*-Associated Behçet's Disease

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

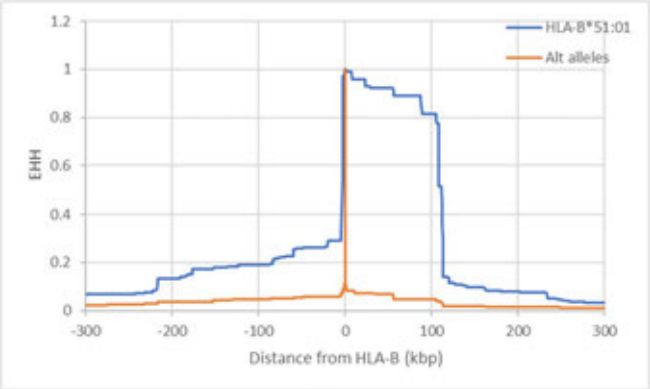


Figure 1. Extended haplotype homozygosity (EHH) of chromosome 6 markers flanking HLA-B*51:01. Decay of the ancestral HLA-B*51:01 bearing haplotype is shown by the frequency of chromosomes with the conserved haplotype at markers on either side of HLA-B, compared with haplotypes bearing all other HLA-B alleles (Alt alleles).

Background/Purpose: The Turkish population has one of the highest world-wide prevalence's of the genetically complex inflammatory Behçet's disease (BD), estimated as 4 affected per 1000 and also has one of the highest world-wide prevalence's of *HLA-B*51*, the strongest identified BD genetic risk factor, with the prevalence of *HLA-B*51:01* in healthy controls estimated as 25.6% and the prevalence in BD patients estimated as 55.6%. It has been proposed that the high frequency of *HLA-B*51* in this population is a result of a selective advantage that was provided to carriers of this HLA allele, for example, in response to some life-threatening infection. If recent positive selection occurred, haplotypes bearing the *HLA-B*51:01* allele should display unusually long-range linkage disequilibrium for their frequency, because selection would cause a rapid rise in the allele frequency over a short enough time that recombination does not substantially break down the selected haplotype. We looked for this genetic imprint of natural selection on *HLA-B*51:01* carrier chromosomes from the Turkish population.

Methods: Genome-wide SNP genotypes from 1,779 healthy Turkish subjects were obtained from a prior genome-wide association study. HLA alleles and MHC region SNP genotypes were imputed with the SNP2HLA application. Haplotypes were derived from genotypes with Eagle. Extended haplotype homozygosity (EHH) and frequency normalized iHS statistic values were computed for each marker in the combined marker set with the Selscan application.

Results: The chromosome 6 region flanking *HLA-B*51:01* exhibited extended haplotype homozygosity compared with other HLA-B alleles in the Turkish healthy control population (Figure 1). Of all the HLA-B alleles, *HLA-B*51:01* had the strongest evidence for recent positive selection with a frequency normalized iHS statistic = 3.87 (values greater than 2.00 are suggestive of recent positive selection).

Conclusion: *HLA-B*51:01* exhibits strong genetic evidence of recent positive selection in the Turkish population. An historical survival advantage provided by this allele could explain its current high frequency in the Turkish population, and as a strong BD risk factor, its high frequency could account for the high prevalence of BD in the Turkish population.

Disclosure: E. Remmers, None; **A. Gül**, None; **D. Kastner**, None.

Abstract Number: 1933

Tumorigenesis Related Gene Identification in Dermatomyositis Using Meta-Analysis

Jihad Aljabban ,[1] Saad Syed,[2] Sharjeel Syed,[3] Kalyn Hoffman,[4] Laith Hasan,[5] Nikhil Adapa,[1] Zahir Allarakhia,[6] Dexter Hadley,[7] Mohamad Aljabban,[8] and Wael Jarjour[9], [1]Ohio State University College of Medicine, Columbus, [2]Stanford School of Medicine, Stanford, [3]Stanford School of Medicine, Stanford, CA, [4]The Ohio State University College of Medicine, Columbus, OH, [5]Tulane School of Medicine, New Orleans, [6]Ohio State University College of Medicine, Columbus, OH, [7]Institute for Computational Health Sciences, San Francisco, [8]Genesys Health Systems, Grand Blanc, MI, [9]Ohio State College of Medicine, Columbus, OH

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Dermatomyositis (DM) is a progressive, systemic autoimmune disease-causing inflammatory changes in the skin and skeletal muscles. DM is associated with carcinomas of the ovary, breast, lung and GI tract in a significant number of patients.

Methods: We employed the STARGEO platform to search the Gene Expression Omnibus and conduct meta-analysis on muscle biopsy (71 DM vs 22 healthy). We then analyzed the signature using Ingenuity Pathway Analysis, restricting genes that showed statistical significance ($p< 0.05$) and an absolute experimental log ratio greater than 0.1. We focused our analysis on tumorigenic gene expression.

Results: Our data demonstrate activation of several tumorigenesis associated genes: a) Immunoglobulin lambda constant 1 (IGLC1; p-value 4.48e-10, log ratio 2.62) is part of the innate immune response but is also upregulated in chronic myeloid leukemia, T-cell lymphoma, and T-cell non-Hodgkin disease, b) IFI44 (p-value 0.0377, log ratio 2.40) upregulated in both cutaneous and muscle samples of DM, is also upregulated in T-cell non-Hodgkin disease, and in peripheral and cutaneous T-cell lymphomas, c) Periostin (POSTN; p-value 0.0359, log ratio 2.15) is a secreted extracellular matrix protein part of the FAS1 domain, binds to integrins to support adhesion and migration of epithelial cells, and plays a role in cancer stem cell maintenance and metastasis and d) the MYC (p-value 0.0414, log ratio 1.28) proto-oncogene. Further tumorigenesis pathways identified in our dataset include CD44 (p-value 0.0343, log ratio 0.886), NPM1 (p-value 0.0295, log ratio 0.462), and IDO1 (p-value 0.0109, log ratio 0.543). CD44 is a cell surface adhesion receptor that is overexpressed in cancer cells and regulates metastasis and is considered a stem cell marker in ovarian cancer and an indicator of poor prognosis. Overexpression of NPM1 is a marker for progression in solid tumors such as hepatocellular and ovarian carcinomas and in some breast cancers. Indoleamine 2,3-dioxygenase 1 (IDO1) is a tryptophan catabolic enzyme that is also implicated in tumorigenesis via promotion of immune tolerance to tumor antigens.

Conclusion: Our results demonstrate novel tumorigenesis related pathways that are upregulated in Dermatomyositis that have largely not been studied previously in this disease. Additional studies need to be carried out to determine if this tumorigenic gene overexpression can serve as a predictive biomarker of malignancy risk in DM. Moreover, since some of the genes (e.g. IDO) are being studied as target for anticancer therapy, this should be explored in patients with DM associated malignancy also.

Disclosure: J. Aljabban, None; **S. Syed**, None; **S. Syed**, None; **K. Hoffman**, None; **L. Hasan**, None; **N. Adapa**, None; **Z. Allarakhia**, None; **D. Hadley**, None; **M. Aljabban**, None; **W. Jarjour**, None.

Abstract Number: 1934

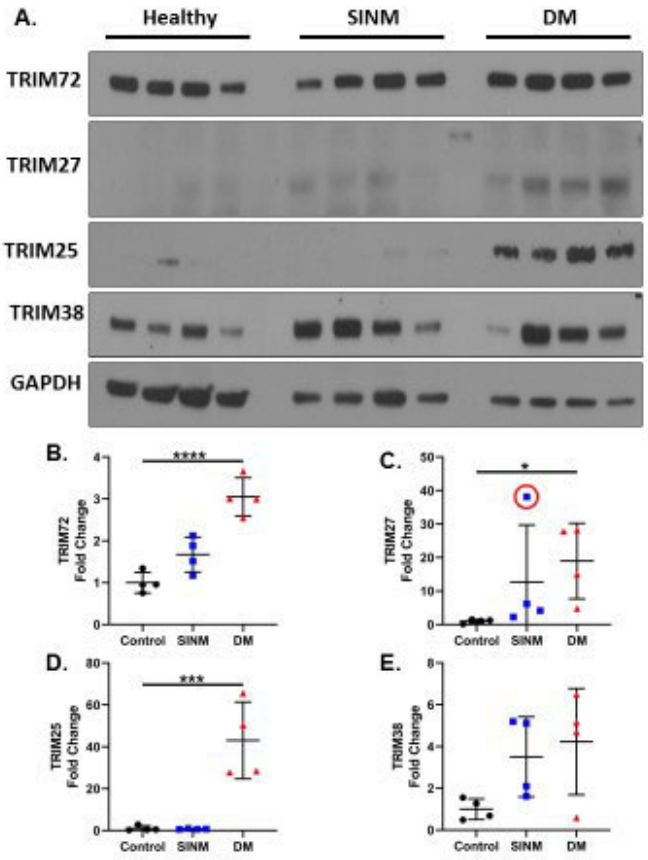
Tripartite Motif (TRIM) Gene Family Expression in Dermatomyositis

Jihad Aljabban ,[1] Sharjeel Syed,[2] Saad Syed,[3] Zarife Sahenk,[4] Noah Weisleder,[5] Kevin McElhanon,[5] Kalyn Hoffman,[6] Nikhil Adapa,[1] Zahir Allarakhia,[7] Laith Hasan,[8] Dexter Hadley,[9] Mohamad Aljabban,[10] and Wael Jarjour[11], [1]Ohio State University College of Medicine, Columbus, [2]Stanford School of Medicine, Stanford, CA, [3]Stanford School of Medicine, Stanford, [4]Department of Neurology, Research Institute at Nationwide Children's Hospital, Columbus, OH, [5]Dorothy M. Davis Heart and Lung Research Institute & Dept. of Physiology & Cell Biology, The Ohio State University Wexner Medical Center, Columbus, OH, [6]The Ohio State University College of Medicine, Columbus, OH, [7]Ohio State University College of Medicine, Columbus, OH, [8]Tulane School of Medicine, New Orleans, [9]Institute for Computational Health Sciences, San Francisco, [10]Genesys Health Systems, Grand Blanc, MI, [11]Ohio State College of Medicine, Columbus, OH

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Dermatomyositis (DM) is a progressive, systemic autoimmune disease causing inflammatory changes to the skin and skeletal muscles. TRIM family proteins are composed of approximately 80 E3 ubiquitin ligase proteins and some have a role in membrane resealing.

Methods: We employed the STARGEO platform to search the Gene Expression Omnibus and conduct meta-analysis on human skin (60 DM vs 34 healthy) and muscle biopsy (71 DM vs 22 healthy) samples. We analyzed the signature



using Ingenuity Pathway Analysis, restricting genes with significance ($p < 0.05$) and an absolute experimental log ratio greater than 0.1, focusing on TRIM family genes. We conducted similar analysis on rheumatoid arthritis (RA) blood (114 RA vs 90 healthy) and synovial samples (130 RA vs 68 healthy), sarcoidosis (SD) bronchoalveolar lavage (21 SD vs 20 healthy) and blood (216 SD vs 271 healthy) samples, systemic scleroderma (SSc) skin (63 SSc vs 31 healthy) biopsies, and Kawasaki (KA) blood (121 KA vs 40 healthy) for comparative TRIM activity analysis. Lastly, we conducted immunoblotting analysis on muscle biopsy specimens from 4 DM, statin-induced necrotizing myopathy, and healthy subjects. Bands of interest were visualized by chemiluminescence and fold change in TRIM72 protein levels evaluated by densitometry using ImageJ and Dunett's Test analysis.

Results: From our skin biopsy analysis in DM we found upregulation of TRIM genes TRIM5 (p-value 5.72e-12, log ratio 0.225), TRIM14 (p-value 3.36e-8, log ratio 0.132), TRIM34 (p-value 1.48e-6, log ratio 0.105), TRIM6 (2.97e-4, log ratio 0.212), TRIM21 (p-value 0.0111, log ratio 0.193), and TRIM38 (p-value 0.0189, log ratio 0.106). TRIM73 was downregulated (p-value 6.58e-13, log ratio -0.102). From our muscle biopsy analysis, we found upregulation of TRIM genes TRIM14 (p-value 0.0405, log ratio 1.02), TRIM22 (p-value 0.0361), TRIM25 (p-value 0.0287, log ratio 0.421), TRIM27 (p-value 0.00276, log ratio 0.298), and TRIM38 (p-value 0.0409, log ratio 0.949). Protein expression of TRIM 72, 25 and 27 protein expression were significantly upregulated and TRIM 38 trending although did not reach statistical significance in our DM cohort compared to healthy controls. Additional comparisons were made between DM and necrotizing myopathy and was significant for TRIM 25 only. Immunoblotting of human muscle proteins shown in Figure A and densitometry analysis shown in B-E. B.) TRIM72: Healthy vs. DM $p < 0.0001$. C) TRIM27: Healthy vs. DM $p=0.012$. D.) TRIM25: Healthy vs. DM $p=0.0006$. E.) TRIM38: Healthy vs. DM $p=0.064$. From our comparative analysis, there was no overlap in TRIM gene expression patterns in rheumatoid arthritis, sarcoidosis, systemic scleroderma, and Kawasaki with our skin and muscle biopsy DM analysis. The only overlapping expression was a similar upregulation of TRIM21 (p-value 3.97e-8, log ratio 0.158) in sarcoidosis blood samples.

Conclusion: TRIM protein family role in immune modulation is emerging. It has not been studied well in the context of DM. Our results suggest certain TRIM family members have a tissue and disease specific role in DM pathogenesis and may have diagnostic and therapeutic implications.

Disclosure: J. Aljabban, None; **S. Syed**, None; **S. Syed**, None; **Z. Sahenk**, None; **N. Weisleder**, None; **K. McElhanon**, None; **K. Hoffman**, None; **N. Adapa**, None; **Z. Allarakhia**, None; **L. Hasan**, None; **D. Hadley**, None; **M. Aljabban**, None; **W. Jarjour**, None.

Abstract Number: 1935

Multi-Organ System Meta-Analytic Approach to Investigating Sarcoidosis

Jihad Aljabban ,[1] Saad Syed,[2] Sharjeel Syed,[3] Nikhil Adapa,[1] Laith Hasan,[4] Zahir Allarakhia,[5] Dexter Hadley,[6] Mohamad Aljabban,[7] and Wael Jarjour[8], [1]Ohio State University College of Medicine, Columbus, [2]Stanford School of Medicine, Stanford, [3]Stanford School of Medicine, Stanford, CA, [4]Tulane School of Medicine, New Orleans, [5]Ohio State University College of Medicine, Columbus, OH, [6]Institute for Computational Health Sciences, San Francisco, [7]Genesys Health Systems, Grand Blanc, MI, [8]Ohio State College of Medicine, Columbus, OH

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis (SD) is a granulomatous inflammatory disease with a heterogenous presentation and no definite etiology. SD usually begins in the lungs, skin, or lymph nodes but can involve other organs such as the heart and lacrimal glands. A better understanding of pathogenesis can pave new therapeutic avenues.

Methods: We employed the STARGEO platform to tag samples from the Gene Expression Omnibus and performed three separate meta-analyses on 216 peripheral blood (216 SD vs 271 healthy), bronchoalveolar lavage (BAL; 21 SD vs 20 healthy), and lacrimal gland (22 SD vs 14 healthy) samples. We then analyzed the signature in Ingenuity Pathway Analysis.

Results: Lacrimal gland analysis revealed Th1 and Th2 activation and T helper cell differentiation as top canonical pathways. IFNG, TGFB1, and TNF were top upstream regulators. ADAMDEC1 was our top upregulated gene and is essential for dendritic cell differentiation. Additionally, we found upregulation of the metalloproteinase MMP12. MMP12 and ADAMDEC1 are potential markers of pulmonary SD activity and may be implicated in lacrimal glad involvement. GBP5, activator of the NLRP3 inflammasome, and osteopontin, associated in T cells in SD granulomas, were upregulated. Genes expressing antimicrobial peptides in secretions, such as HTN1 and STATH, were downregulated.

Blood analysis revealed TH1 activation, IFN, EIF2, TREM1, and pattern recognition receptor signaling as top canonical pathways. IRF7, IFNa, STAT1, and IFNL1 were top upstream regulators. We found upregulation of classical complement pathway related genes such as FCGR1B and SERPING1. Additionally, CARD17, regulator of IL1B, was upregulated and has activity linked to granulomatosis disease. The recently described transcription factor and immune regulator BATF2 was upregulated. Lastly, there was downregulation of TRABD2A, a metalloprotease and negative regulator or Wnt signaling.

BAL analysis revealed “role of macrophages, fibroblasts, and endothelial cells in rheumatoid arthritis” as the top canonical pathway, with TP53, hepatocyte growth factor, ERBB2, CTNNB1, and E2F7 as top upstream regulators. We found upregulation of sprout family gene SPRY2, a negative feedback regulator of tyrosine kinases. Additionally, there was downregulation of phospholipase D1, a regulator of signal transduction.

Conclusion: Sarcoidosis is a complex and likely multifactorial disease process. Our results emphasized the role of innate immune cell and Wnt activity in SD, among other signaling pathways, and suggest potential biomarkers and therapeutic targets. This approach to data analysis illustrates the importance of studying affected target organs to determine active pathways that are unique.

Disclosure: J. Aljabban, None; **S. Syed**, None; **S. Syed**, None; **N. Adapa**, None; **L. Hasan**, None; **Z. Allarakhia**, None; **D. Hadley**, None; **M. Aljabban**, None; **W. Jarjour**, None.

Abstract Number: 1936

The Expression of the Interferon Inducible Gene SERPING1 Is Reduced by Rituximab and Correlates with Clinical Response in Systemic Lupus Erythematosus

Liliana Santos Ribeiro ,[1] Mariea Parvaz,[2] Su-Ann Yeoh,[2] and Michael Ehrenstein[2], [1]University College London, London, United Kingdom, [2]University College London, London, England, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Abnormalities in B cells and the interferon alpha (IFN) pathway have been separately implicated in the pathogenesis of systemic lupus erythematosus (SLE). B cell depletion therapy with rituximab is used to treat SLE but clinical response varies between patients. We hypothesized that the IFN inducible gene response may explain the difference in clinical responses to rituximab.

Methods: RNA was isolated from whole blood collected into Tempus tubes. Gene expression of the IFN signature genes (STAT 1, SERPING1, S100) was analysed in whole blood from 13 active SLE subjects (before and 2 months after Rituximab), and on age/gender-matched healthy controls, using real time PCR normalized to GADPH. Disease activity was evaluated according to the SLE Disease Activity Index (SLEDAI) score. Complement component C3 was measured by Nephelometry and anti-dsDNA antibodies by ELISA. Analysis of variance (ANOVA) was used to identify significant differences.

Results: Gene expression of SERPING1, but not other interferon inducible genes, was significantly higher in SLE patients before rituximab compared to healthy controls (p=0.0002) (Figure 1). Rituximab treatment led to a 25% decrease in SERPING1 expression in SLE patients (p=0.0131) (Figure 1C) which correlated with clinical response measured by SLEDAI (p=0.054), a reduction in anti-dsDNA antibodies after rituximab (p=0.037), and a trend towards an increase in C3 (p=0.062).

Conclusion: These data suggest that assessment of SERPING1 gene expression, an IFN inducible gene, is strikingly increased in SLE patients and correlated with clinical response to rituximab. These results could support therapeutic targeting of IFN to improve the efficacy of rituximab.

Disclosure: L. Santos Ribeiro, None; **M. Parvaz**, None; **S. Yeoh**, None; **M. Ehrenstein**, None.

Abstract Number: 1937

Mononuclear Leukocyte DNA Methylome Imprinting of Networked Signaling and Immunity Regulatory Pathways in Gout

Zengmiao Wang,[1] Ying Zhao,[1] Amanda Phipps-Green,[2] Ru Liu-Bryan,[3] Arnold Ceponis,[1] David Boyle,[4] Jun Wang,[1] Tony Merriman,[5] Wei Wang,[4] and **Robert Terkeltaub** [6], [1]UCSD, La Jolla, CA, [2]University of Otago, Otago, Otago, New Zealand, [3]San Diego VA/UCSD, La Jolla, CA, [4]University of California, San Diego, San Diego, CA, [5]University of Otago, Birmingham, AL, [6]San Diego VA/UCSD, San Diego, CA

SESSION INFORMATION
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout encompasses acute arthritis flares mediated by innate autoinflammatory responses to urate crystals, chronic granulomatous tophi, and synovitis promoting bone erosion and soft tissue damage. Here, we probed gout mediators in the circulating mononuclear leukocyte (PBMC) DNA methylome.

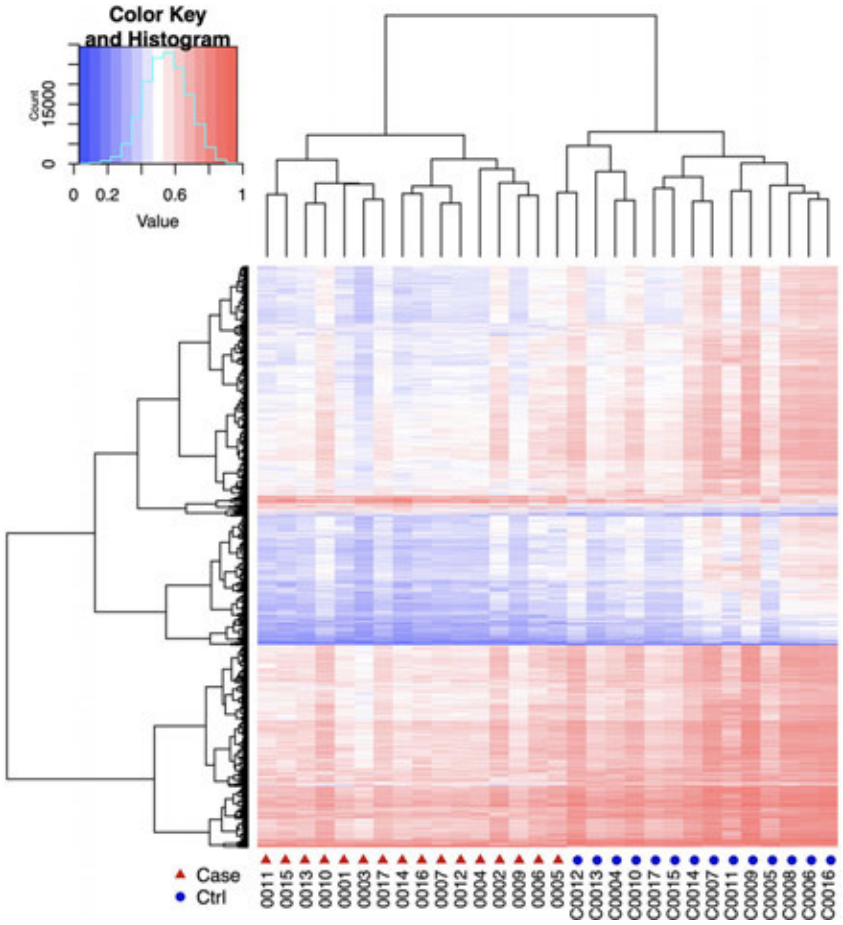

Figure 1. Hierarchical cluster analysis of gout vs. healthy controls in NA cohort.

Methods: PBMC DNA converted by Na+ bisulfite modification was hybridized to Illumina Infinium MethylationEPIC BeadChip arrays. Methylation data were processed with ChAMP in R. Our North American (NA) gout cohort (n=16), sampled between flares, all met ACR/EULAR criteria, and well-controlled urate overal. Healthy controls (n=14) were matched for age, gender, and BMI. Obese New Zealand (NZ) Maori, enriched in hypertension and diabetes, provided an independent validation cohort (n=13 gout; n=16 no gout). Transcription Factor (TF)-gene networks were built and combined from B and T cells, CD14+ monocytes, CD4+ and CD8+ T cells.

Results: By hierarchical clustering and PCA, gout DNA methylome signatures were significantly separable from controls in both the NA cohort (Fig. 1,2), and NZ validation cohort. Most (>85%) differentially methylated loci (DML) in gout were hypo-methylated in open sea regions, and gene body hypomethylation (which inhibits gene expression) was prominent. Gout DML included 23 from ~125 genetic risk loci from past GWAS (eg, urate transporter *SLC2A9* , B2 kinin receptor, and *IL-23R* , which bridges innate and adaptive immunity, and promotes granuloma formation). Numerous KEGG signaling pathways, but not the NLRP3 pathway, were enriched in DML (eg, circadian entrainment, and TRP ion channel signaling (which transduces pain in nerve fibers, and also activates phagocytes)), aligned with severe pain and nocturnal onset of background gout flares. We saw differential DNA methylation of myeloid cell signaling and function pathways (eg, FcgammaR phagocytosis, chemokine signaling, adhesion, PI3K-AKT, HIF-1), nutritional biosensing by NF-kB and NLRP3 inhibitor AMPK, and choline metabolism, which promotes gouty inflammation by modulating AMPK and mitophagy. In gout, *STAT2* , *IRF1* , nuclear factor of activated T cells (*NFATC2*), and major adaptive immunity pathways (T and B cell receptor signaling, Th17 differentiation) were differentially methylated. By far, most overlaps between gout cohorts were in transcription factors (TFs) with motifs enriched in hypo-methylated sequences, and enriched KEGG pathways based on TFs. Strikingly, DMLs of *NFATC2* , which blunts NF-kB hyper-

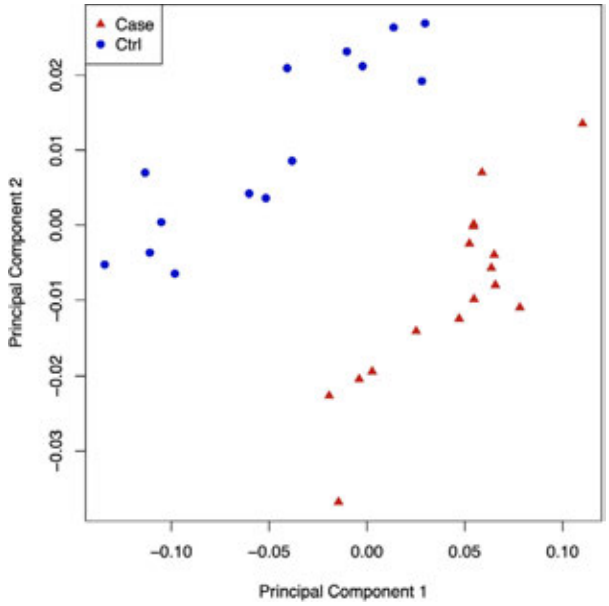

Figure 2. Principal component analyses of gout vs. healthy controls in NA cohort.

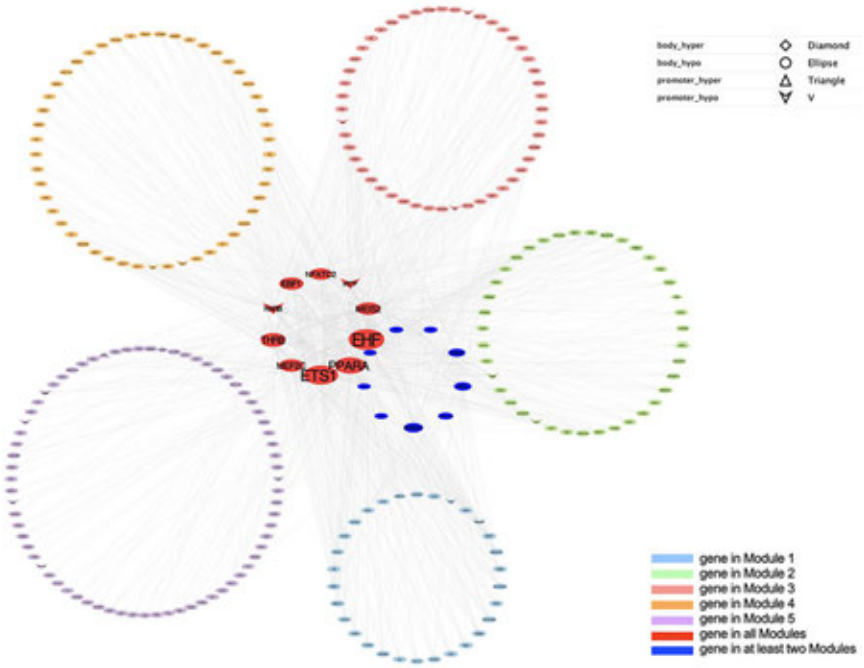

Figure 3. Integration of common gout-related DML-genes in both the NA and NZ cohorts with TF gene regulatory networks. Using ENCODE data, TF-gene networks were constructed in B-cells, T-cells, CD14+ monocytes, CD4+ helper T cells and CD8+ alpha-beta T cell respectively and then combined into one. After mapping common 361 DML-genes to the network, 256 DML-genes and 1053 edges were left (shown here). Five modules were identified using agmfit algorithm. The genes were colored based on the membership in a module. The 10 genes present in all Modules, which included NFAT2C and MEF2C, are depicted in red.

activation, and myocyte enhancer factor 2C *MEF2C* , which controls myeloid switching to granulocytopoiesis, were among 10 TFs propagated in all PBMC TF networks in both gout cohorts (Fig. 3).

Conclusion: A PBMC DNA methylome signature reflected trained immunity in gout, especially imprinting signaling and transcriptional pathways, and involving adaptive immunity. Such changes, and differential TF-gene network DNA methylation in all PBMCs, were in contrast to lack of NLRP3 pathway imprinting. The PBMC DNA methylome signature likely helps determine phenotypic outcomes of not only acute gouty arthritis, but also granulomatous tophaceous and chronic inflammatory synovitis, and potentially modulates comorbidities in the disease.

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Abstract Number: 1938

The Pre-pregnancy Rheumatoid Arthritis Gene Expression Signature Correlates with Improvement or Worsening of Disease Activity During Pregnancy: A Pilot Study

Amogh Pathi,[1] Mette Smed,[2] Lior Pachter,[3] Elizabeth Purdom,[4] Matthew Wright,[5] Nicholas Jewell,[4] J. Lee Nelson,[6] Jørn Olsen,[7] Merete Lund Hetland,[8] Vibeke Zoffmann,[9] and **Damini Jawaheer** [10], [1]UCSF Benioff Children's Hospital Oakland, Oakland, [2]Juliane Marie Center, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark, [3]Caltech, Pasadena, [4]University of California Berkeley, Berkeley, [5]UCSF Benioff Children's Hopsital Oakland, Oakland, [6]Fred Hutchinson Cancer Research Center, Seattle, [7]Aarhus University Hospital, Aarhus, Denmark, [8]DANBIO and Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Centre of Head and Orthopaedics, Rigshospitalet, Copenhagen, Denmark, [9]Juliane Marie Center, Copenhagen University Hospital, Rigshospitalet, Copenhagen, [10]UCSF Benioff Children's Hospital Oakland, Oakland, CA

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Background/Purpose: Pregnancy is known to induce a natural improvement of Rheumatoid Arthritis (RA) symptoms in 50-75% of patients as gestation progresses. However, the underlying mechanisms are not well understood and no biomarkers have been identified that predict whether a woman will improve or worsen during pregnancy. In this study, we aimed to identify RA-associated pre-pregnancy gene expression signatures to determine if they correlated with the subsequent improvement or worsening of RA during pregnancy.

Methods: Women with RA (n=11) and healthy women (n=5) were enrolled in our pregnancy cohort and followed prospectively. The women with RA were examined before pregnancy (T0) and at the third trimester (T3). Disease activity was assessed using Clinical Disease Activity Index (CDAI) scores. Blood was drawn from all women (RA and healthy) at both time-points. Total RNA was isolated and used to prepare cDNA libraries which were sequenced at an average depth of 60 million reads. The raw RNA sequencing (RNA-seq) data were pseudo-aligned to the reference Human transcriptome and quantified using kallisto. Genes differentially expressed between groups were identified with edgeR using a fold-change cutoff of 2 and significance threshold $q < 0.05$ (FDR corrected). Functional enrichment analysis was performed using Cytoscape.

Results: Of the 11 women with RA, 8 improved ($RA_{improved}$ group) by T3 while 3 worsened ($RA_{worsened}$ group). At the T0 baseline, however, the mean disease activity scores were similar in both groups of women ($RA_{improved}$: 3.2±0.7; $RA_{worsened}$: 3.5±1.4, p=0.7). When gene expression profiles of each RA subset was compared to the healthy women at T0, 94 genes were differentially expressed ($q< 0.05$; $FC\geq2$) between the $RA_{improved}$ and healthy women. These included CAMP, LGALS2, MAOA, S100A8, S100A9, S100A12 and a set of type I interferon inducible genes, many of which overlapped with previously reported RA expression signatures. A large proportion of the 94 differentially expressed genes clustered within 2 functional networks, one containing the over-expressed genes and the other containing the under-expressed genes. However, when the $RA_{worsened}$ women were compared to the healthy women at T0, a largely different RA-associated expression signature was identified. Of 83 genes that were differentially expressed, only 13 overlapped with those differentially expressed between $RA_{improved}$ and healthy women at T0. The majority of the 83 genes did not appear to be enriched in any relevant biological pathways.

Conclusion: In our pilot dataset, the RA-associated gene expression signatures identified before pregnancy correlated with, and were thus predictive of, subsequent improvement or worsening during pregnancy, even though mean disease activity scores at the pre-pregnancy baseline were similar between the two RA subsets. These different expression signatures suggest that there may be inherent genomic differences between women with RA that dictate how pregnancy can alter disease activity.

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Analysis of Discoid Lupus Erythematosus (DLE) Gene Expression Reveals Dysregulation of Pathogenic Pathways Associated with Infiltrating Immune/Inflammatory Cells

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Background/Purpose: DLE is a chronic, scarring inflammatory autoimmune disease of the skin. The precise molecular pathways underlying DLE pathogenesis have not been fully delineated. To obtain a more complete view of the pathologic processes involved in DLE, we undertook a comprehensive analysis of gene expression profiles from DLE affected skin.

Methods: Microarray gene expression data was obtained from skin biopsy samples of three studies (GSE81071, GSE72535, & GSE52471). Differentially expressed genes (DEGs) between DLE and control were identified by LIMMA analysis. Weighted gene co-expression network analysis (WGCNA) yielded modules of co-expressed genes. Modules correlating to clinical data were prioritized. Correlated modules were interrogated for statistical enrichment of immune and non-immune cell type specific gene signatures. Genes were functionally characterized using a curated immune-specific gene functional category database (BIG-C) and pathways elucidated using IPA®. Queries of a per-

turbation database (LINCS, Library of Integrated Network-Based Cellular Signatures) were used to identify drugs that could reverse the altered gene expression patterns in DLE.

Results: For each dataset, between 7-12 WGCNA modules had significant correlations to disease. Significant WGCNA module preservation was observed between all three datasets. Non-immune cell types (fibroblasts, keratinocytes, melanocytes) and also Langerhans cells are represented in WGCNA modules negatively correlated with disease. An immune cell signature was noted in WGCNA modules positively correlated to DLE, including DCs, myeloid cells, $CD4^+$ & $CD8^+$ T cells, NK cells, B cells as well as pre- and post-switch plasma cells (PCs). The presence of both Ig -κ & -λ as well as multiple VL genes suggests the presence of polyclonal PCs. Chemokines that mediate lymphocyte organization and/or recruitment into the skin were identified, including CCL5,7,8 & CXCL9-10,13. Cytokines (TNF, IFNγ, IFNα, IL1β, IL2, IL6, IL12, IL17, IL23 & IL27), signaling molecules (CD40L, PI3K, & mTOR) and transcription factors (NF-κB, NF-AT), as well as cellular proliferation, were evident. IPA® UPR analysis indicated that many of the expressed genes could be secondary to signaling by TNF, IFNγ, IFNα, CD40L, IL1β, IL2, IL6, IL12, IL17, IL23 & IL27. Interestingly, connectivity analysis using LINCS/CLUE identified high priority drug targets, such as IKZF1/3 (lenalidomide, CC-220), JAK1/2 (ruxolitinib) and HDAC6 (Ricolinostat) may prove to be options for therapeutic intervention.

Conclusion: Bioinformatic analysis of DLE gene expression has elucidated many dysregulated signaling pathways potentially involved in the pathogenesis of DLE that could be targeted by novel therapeutic strategies. Further investigation of these signatures may enhance our understanding of the pathogenesis of DLE.

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Abstract Number: 1940

Investigating the Post-Partum Flare in Rheumatoid Arthritis Using Transcriptome Analysis

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Background/Purpose: Women with Rheumatoid arthritis (RA) tend to have a predictable flare of disease activity in the months after childbirth. The mechanism(s) underlying this post-partum flare are as yet unknown. Using our pregnancy cohort, we (a) examined gene expression changes associated with a flare of RA disease activity post-partum, (b) determined how those changes compare to post-partum changes observed among healthy women, and (c) examined whether expression profiles by 3 months post-partum differed from those before pregnancy.

Methods: Ten women with RA and five healthy women were enrolled in our pregnancy cohort and prospectively followed. Data on joint counts and global scores were collected from the women with RA before pregnancy (T0), at the third trimester (T3) and every 3 months post-partum (PP), and used to assess disease activity. Blood samples were drawn from all women at each time-point. Total RNA was isolated and used for RNA sequencing (RNA-seq). Pseudo-alignment and quantification of the raw RNA-seq reads were performed using kallisto. Differentially expressed (DE) genes were identified with edgeR using a significance threshold of $q \leq 0.05$ and fold-change≥ 2. Longitudinal mixed linear models were also used to test for associations between gene expression and disease activity post-partum. Functional analyses were performed using Cytoscape and ClueGO.

Results: Among the women with RA, 133 genes were DE between T3 and 3 months PP, when there was a flare of disease activity. These included genes encoding cell surface receptors CD24, CD177 and PD-L1, defensins, immunoglobulin receptors, S100 calcium binding proteins, and TRIM proteins. Functionally, these genes were enriched in the Gene Ontology (GO) terms neutrophil activation (q=1.1e-16) and antimicrobial humoral response (q=1.4e-5). Of the 133 DE genes, 118 were also DE among healthy women between T3 and 3 months PP, with expression changing in the same direction in both RA and healthy women. Similar results were obtained when the PP time-point with maximal disease activity during the flare was used (instead of 3 months PP). In the mixed linear model, 64 genes had expression patterns significantly associated with RA disease activity post-partum; these were enriched in various immune-related pathways including complement and coagulation cascades and systemic lupus erythematosus. At 3 months PP, the gene expression profile among the women with RA differed from that at T0, with 61 genes DE between the 2 time-points. Among healthy women, however, there were no statistically significant changes in gene expression between T0 and 3 months PP, although some immune-related genes (n=24) were under-expressed by at least two-fold at 3 months PP compared to T0.

Conclusion: The large majority of gene expression changes between 3rd trimester and 3 months post-partum in RA reflect normal post-partum changes also seen among healthy women. Nonetheless, there are a set of immune-related genes whose expression appear to be influencing disease activity during the post-partum flare. Further, our results show that the RA expression profile at 3 months post-partum is distinct from that before pregnancy.

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Abstract Number: 1941

Interactions Between Genome-Wide Genetic Factors and Current Smoking in Determining SLE Risk

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Table 1. Demographics for SLE cases and matched controls		
	SLE Cases (673)	Matched Controls (3,276)
Age at SLE diagnosis or matched age (SD)	36.4 (15.3)	33.5 (14.3)
White (%)	75.2	79.9
Female (%)	92.3	93.7
Current smoking at diagnosis or quit within 4 years (%)	21.0	15.5
Number of ACR Criteria for SLE	5.0 (1.5)	--
Anti-dsDNA+ (%)	59.3	--

Table 2. Additive Gene-Smoking Interactions in SLE Risk and in dsDNA+ SLE Risk			
GRS*	Smoking	All SLE OR (95% CI)	dsDNA+ SLE OR (95% CI)
Low wGRS	Never/Past	1.0 (Ref.)	1.0 (Ref.)
Low wGRS	Current/Recent	1.17 (0.74-1.82)	1.18 (0.77-1.81)
High wGRS	Never/Past	**3.36 (2.67-4.22)**	**3.22 (2.60-4.00)**
High wGRS	Current/Recent	**5.58 (4.07-7.63)**	**5.24 (3.90-7.05)**
Additive Interaction: Current/Recent Smoking +wGRS			
Attributable Proportion (95%CI)		**0.37 (0.18-0.56)**	**0.35 (0.16-0.54)**
p for interaction		**0.00015**	**0.00027**
Multiplicative Interaction: Current/Recent Smoking x wGRS			
p for interaction		0.18	0.2
*wGRS includes 86 SLE SNPs + 10 HLA alleles, dichotomized at median from controls distribution			

Table 3. Multiplicative Interactions for Individual SNPs and Current/Recent Smoking (Strongest Associations)		
Interaction of Current/Recent smoking with (p-value):	All SLE	Whites-only SLE
HLA-DRB1-0102	**0.002**	**0.02**
SPATA8 (rs8023715)	**0.004**	0.10
DRAM1	**0.05**	**0.02**
GPR78 (rs13116227)	0.06	**0.01**
Weighted *HLA* GRS for SLE	0.06	**0.04**

Background/Purpose: We have previously reported that current smoking (or having recently quit within 4 years) was associated with elevated risk of SLE, in particular anti-dsDNA+ SLE. Genetic and environmental factors, such as smoking, may interact in determining SLE risk. We investigated whether interactions between smoking and genetic risk factors may influence SLE risk.

Methods: We identified subjects with validated SLE and DNA samples within the Nurses' Health Studies (NHS) and Partners Healthcare Biobank (PHB). 673 SLE cases were matched to 3,276 controls without SLE on age, sex and race (matched on self-report race in NHS and by 1st 3 principle components of GWAS in PHB). All subjects had data on smoking prior to SLE diagnosis date or the matched index date in controls. DNA samples were genotyped and imputed using Haplotype Reference Consortium (Michigan) and SNP2HLA for *HLA*. SLE risk alleles were identified from published GWAS studies (mainly from White and Asian populations): https://www.ebi.ac.uk/gwas/. After pruning for linkage disequilibrium, 86 SNPs and 10 *HLA* alleles with genome wide significance $p \leq 5\times10^{-8}$ were included in a new weighted genetic risk score (wGRS), weighted by log OR from published GWAS. The wGRS for all markers and for HLA alleles only were studied. Smoking was classified as current/quit within 4 years at SLE diagnosis vs. past/never smoker. wGRS was dichotomized as ≤ vs. > the median value in controls. We employed conditional logistic regression models for SLE or anti-double stranded DNA antibody + SLE (dsDNA+ SLE), conditioning on matching factors and controlling for cohort. We examined additive interactions using the attributable proportion (AP) due to interaction and tested for multiplicative interactions using a 1 d.f. χ^2 test, for the wGRS as well as for individual risk alleles. We repeated analyses for risk of anti-dsDNA+ SLE. We examined interactions among all subjects and among Whites only.

Results: Characteristics of the cases and controls are shown in **Table 1**. High wGRS (OR 1.4, p 5.6×10^{-52}) and current smoking (OR 1.5, p 0.0006) were individually both strongly associated with SLE risk. SLE risk was highest in those with high wGRS and current smoking, OR 5.58 (95% CI 4.1-7.6) (**Table 2)**. A significant additive interaction between high vs. low wGRS and current/recent vs. past/never smoking was found (AP 0.37, p 1.5×10^{-4}). Findings were similar for interactions associated with anti-dsDNA+ SLE risk. Significant multiplicative interactions between smoking and genotypes were found with specific genotypes, including *HLA-DRB1-0102* (p 0.002) (**Table 3**), the weighted HLA GRS for SLE, but not with overall wGRS (p 0.18). Findings were similar when limited to Whites only.

Conclusion: These findings support the hypothesis that smoking predisposes to SLE in the presence of genetic factors, with a greater than additive interaction with overall genetic risk and potentially greater than multiplicative interaction with certain genotypes. Studies should now investigate the mechanisms of these interactions and whether smoking influences the function of these genes in SLE pathogenesis.

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Genome-wide Association Study in a Japanese Population Revealed Novel Candidate Genes for Antineutrophil Cytoplasmic Antibody-associated Vasculitis

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Background/Purpose: Clinical and serological features of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are different across geographical regions and ethnicities, which strongly indicates significant roles of genetic factors in development of AAV. In AAV patients with Asian ethnicity, MHC and non-MHC genes associated with susceptibility or clinical characteristics of AAV were reported using the candidate-gene approach, but genome-

wide association study (GWAS) has not been reported. We implemented GWAS to identify single nucleotide variants (SNV) associated with AAV in the Japanese population.

Methods: GWAS was implemented using samples from 374 Japanese patients with AAV comprised of 214 with microscopic polyangiitis (MPA), 75 with granulomatosis with polyangiitis (GPA), and 45 with eosinophilic granulomatosis with polyangiitis (EGPA). Myeloperoxidase (MPO)-ANCA was positive in 300 patients and proteinase 3 (PR3)-ANCA was positive in 47 patients. Data were compared with those of 2,994 healthy Japanese owned by Japan PGx Data Science Consortium. The genotype data were obtained using HumanOmni 2.5-8 BeadChip Kits (Illumina, San Diego, CA, USA). From the genotypes of several SNVs around HLA regions, two alleles of each subject were predicted by HIBAG algorithm using the parameters tuned by Japanese population. The four-digit HLA alleles on six loci (HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DQB1, HLA-DPB1) for ANCA subjects were predicted. For JPDSC data, alleles of HLA-DQB1 were also predicted and other *HLA* loci were genotyped using the Luminex assay as four digits *HLA* allele.

Results: GWAS revealed substantially different associations from those reported from populations of European ancestry. SNVs rs2858331 in a region between HLA-DQB1 and HLA-DQA2 was associated with MPO-ANCA (OR=1.649, P=9.504E-09) at the genome-wide significance level, and tended to be associated with the phenotype MPA as well (OR=1.631, P=1.373E-06). HLA association test showed significant association of HLA-B*51:01-C*14:02 haplotype in addition to the previously reported HLA-DRB1*09:01-DQB1*03:03 haplotype with MPA and MPO-ANCA. SNV rs749873 in a region near CXCR4 gene showed a trend toward association with GPA (OR=8.058, P=6.755E-08).

Conclusion: GWAS demonstrated multiple association signals in MHC class I and class II regions, as well as potential associations in the non-MHC regions, not previously reported from European populations.

The authors are the members of Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis (JPVAS) and Research Committee of Progressive Renal Disease, Ministry of Health, Labour, and Welfare of Japan. This study was performed in collaboration with Japan PGx Data Science Consortium.

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The Emerging Regulatory Function of microRNA146a in Bone Biology and Osteoporosis

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

Methods: Systemic bone, tibiae and femur, of wt, miR-146a$^{-/-}$ and miR- 146a$^{-/-}$ TRAF6$^{+/-}$ animals was assessed histologically and via µCT analysis, over a period of 3 to 18 months of age. Serum cytokine levels were analysed by Elisa. MRNA expression levels in bone were analysed by qPCR. To induce osteoporosis, ovariectomy (OVX) induced bone loss was performed.

Results: When we analysed bone volume of long bones histologically as well as with µCT analysis we detected significantly increased trabecular as well as cortical bone mass in miR-146a deficient compared to wt animals, starting at an age of 6 months. Dose reduction of TRAF6, a main target of miR-146a, using miR-146a$^{-/-}$ TRAF6$^{+/-}$ animals could not change the observed bone phenotype. Analysis of serum in aged miR-146a deficient animals displayed elevated activity of bone resorbing osteoclasts as amounts of CTX I in miR-146a$^{-/-}$ mice were significantly increased compared to wt animals. Q-PCR analysis of important osteoclast as well as osteoblast marker genes in bones *ex vivo* displayed elevated expression of signature molecules of both cell types in aged miR-146a deficient mice, suggesting a regulatory role of miR-146a in both cell types. Moreover, expression level of Wnt5a, a known target of miR-146a, influencing bone forming as well as bone resorbing cells, was strongly elevated in miR-146a$^{-/-}$ bones, possibly responsible for this deregulated bone growth. When we induced osteoporosis using the OVX disease model, histological analysis of long bones showed significant trabecular bone loss in ovariectomized wt mice. In contrast, we could not detect trabecular bone loss in ovariectomized miR-146a knock out animals, suggesting that loss of miR-146a deficiency protects bone loss induced by estrogen deficiency.

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

Disclosure: V. Saferding, None; **M. Hofmann**, None; **J. Brunner**, None; **M. Militaru**, None; **A. Puchner**, None; **S. Hayer**, None; **M. Timmen**, None; **R. Stange**, None; **J. Smolen**, AbbVie, Amgen, Astra-Zeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, 8, AbbVie, Eli Lilly, Janssen, MSD, Pfizer, Roche, 2, ILTOO, Janssen, Medimmune, MSD, Novartis, Pfizer, Roche, Samsung, Sanofi, UCB, 8; **S. Blüml**, None.

Abstract Number: 1944

Two Biomarkers with Predictive Capacity to Diagnosis Pre-Radiographic Knee Osteoarthritis: Data from the Osteoarthritis Initiative

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
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Background/Purpose: Osteoarthritis (OA) is the most prevalent rheumatic disorder of the middle-age population. The lack of sensitive diagnostics methods led to an identification of the disease in advanced stages, where the only possible treatment is surgery. Therefore, the objective of this work was to validate and qualify the putative ability of 6 potential proteomic markers to predict the appearance of radiographic knee OA in the clinical routine.

Methods: In the *validation phase* 6 potential biomarkers were quantify in 540 sera at baseline belonging to participants from the Osteoarthritis Initiative (OAI) who will develop (incident group, n=209) or not (not-incident group, n=331) radiographic knee OA in a follow-up period of 96 months using custom sandwich immunoassays for bead-based xMAP technology. Non-parametric Mann-Whitney U test was carried out to look for statistical differences between the outcome groups. In the *qualification phase* significant association of the biomarkers with the risk of knee OA development was assessed by regression analysis. A clinical prognostic model was defined by stepwise

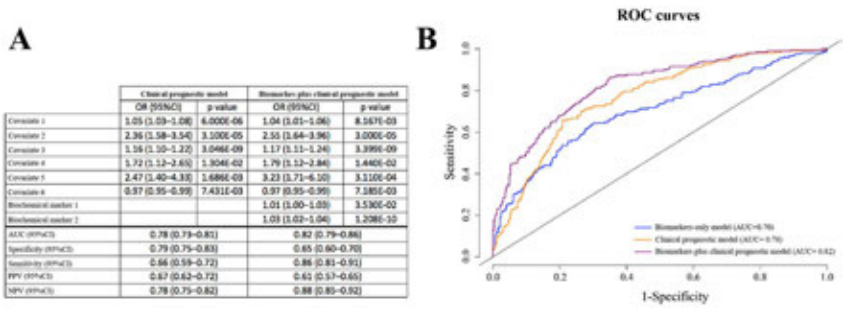

Figure 1. (A) Multivariate regression analysis comparing the clinical prognostic model with the biomarker plus clinical prognostic model. (B) Roc curves of the three models.

regression analysis using clinical non-radiographic variables significant associated with OA risk assessment. The utility of the potential biomarkers in the clinical routine, alone or in combination with other biomarkers included in the same multiplex sandwich immunoassay, was evaluated by comparing the Area Under the Curve (AUC) of the clinical prognostic model with the different biomarkers plus clinical models. Sensitivity, specificity and predictive coefficients were also assessed.

Results: The incident group showed significant higher serum concentrations of all the potential biomarkers analyzed ($p < 0.05$). We also found that 5 of the analytes were significant associated with the future appearance of radiographic knee OA, yielding Odd Ratios (OR) $\geq$ 10 per 10 µg/ml increase. Among all the possible combinations, the inclusion of 2 of the potential biomarkers to the clinical prognostic model showed a significant improvement of the predictive capacity (AUCs = 0.78 vs 0.82, p= 0,044) with 65% (60-70%) specificity and 88% (81-91%) sensitivity. The regression model and all metrics are listed in the Figure 1, comparing the biomarkers plus clinical model with the clinical prognostic model. The ROC curve of the biomarker-only model, clinical prognostic model and biomarker plus clinical model are also represented at the figure.

Conclusion: Significant association of higher concentrations of 5 of the potential biomarkers where found in people who are at risk of knee OA when analyzing 540 sera from the OAI cohorts by custom sandwich immunoassays. Among all of them, the combination of 2 of the analytes showed a putative utility in the clinical setting by improving the predictive capacity of a clinical prognostic model to predict who is in risk to develop radiographic knee OA.

Disclosure: M. Camacho-Encina, None; **V. Balboa-Barreiro**, None; **R. Paz-González**, None; **V. Calamia**, None; **L. Lourido**, None; **P. Fernández-Puente**, None; **C. Ruiz-Romero**, None; **F. Blanco**, None.

Abstract Number: 1945

Polymorphisms in Genes Involved in Methotrexate Pathway: Predictor of Response to Methotrexate Therapy in Indian Rheumatoid Arthritis Patients

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SESSION INFORMATION
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Background/Purpose: Methotrexate (MTX) is first line therapy to treat rheumatoid arthritis (RA) patients. However, the response is variable with 50-60% showing response and this variability could be related to single nucleotide polymorphisms (SNPs) in genes involved in MTX metabolism or action. Thus we studied association of eight polymorphisms [rs2236225 (MTHFD1 1958G >A), rs17602729 (AMPD1 G >A), rs1127354 (ITPA C >A), rs1431131 (TGFBR2 A >T), rs244076 (ADA T >C), rs2372536 (ATIC C >G), rs11188513 (ENTPD1 C >T), rs5751876 (ADORA2A T >C)] in the genes involved in MTX pathway with response to MTX therapy in Indian RA patients.

Table 1: Allelic and genotypic associations of polymorphism with response to MTX.

Gene	SNP	Allele frequency		Allele association, P value*; OR (95% CI)	Genotype frequency		Genotypic association, P value
		(R=172)	(NR=35)		R	NR	
ATIC	rs1372536 C>G	C= 0.50 G=0.50	C=0.63 G=0.37	**0.004** 4.1 (1.1-15.3) for allele G	CC=40 CG=92 GG=40	CC=14 CG=29 GG=2	**0.017**
AMPD1	rs17602729 G>A	G=0.95 A=0.05	G=0.87 A=0.03	0.44	GG=155 GA=17 AA=0	GG=33 GA=2 AA=0	0.53
ITPA	rs1127354 C>A	C=0.88 A=0.12	C= 0.66 A=0.34	0.11	CC=134 CA=37 AA=1	CC=15 CA=19 AA=1	**0.009**
TGFBR2	rs1431181 A>T	A=0.63 T=0.37	A=0.56 T=0.44	0.27	AA=69 AT=79 TT=24	AA=11 AT=17 TT=7	0.55
ENTPD1	rs11689513 C>T	C=0.37 T=0.63	C=0.3 T=0.7	0.28	CC=24 CT=80 TT=68	CC=3 CT=15 TT=17	0.29
ADORA2A	rs5751876 T>C	T=0.74 C=0.26	T=0.7 C=0.3	0.96	TT=94 TC=61 CC=17	TT=17 TC=15 CC=3	0.86
MTHFD1	rs2236225 G>A	G=0.48 A=0.52	G=0.51 A=0.49	0.45	GG=39 GA=81 AA=52	GG=9 GA=18 AA=8	0.72
ADA	rs244076 T>C	T=0.72 C=0.28	T=0.75 C=0.25	0.88	TT=89 TC=71 CC=12	TT=20 TC=12 CC=3	0.73

CI, confidence interval; R, responders; NR, non-responders; MTX, methotrexate; OR, odds ratio; SNP, single nucleotide polymorphism.
*P value calculated using $\chi 2$ test.

Allelic and genotypic associations of polymorphism with response to Methotrexate.

Methods: Genotyping of RA patients (EULAR/ACR 2010 criteria), DMARD naïve with active disease (DAS 28 >3.2) was done using by TaqMan 5' nuclease assay. MTX monotherapy was given to the patients by gradually escalating the dose to a maximum of 25mg/week or maximal tolerated dose. Four months after therapy, based on EULAR response criteria patients were classified into responder and non-responder group. The association of SNPs with response to MTX therapy was assessed using Chi-Squared test.

Results: Two hundred seven patients (85.5% females; median-age 40 [17] years); median duration of disease 24 (40) months; median DAS28-CRP 4.82 (1.51) were enrolled. At 4 months, based on EULAR response 172 patients were classified as responders and 35 as non-responders. Assuming C dominance, recessive model of ITPA C >T [P = 0.004; OR (95% CI= 1.44 (1.05-1.97) associated with response to MTX. Assuming C dominance, dominant model [P = 0.019; OR (95% CI) = 4.07 (1.03-16.06)] and recessive model [P = 0.04; OR (95% CI) = 1.28 (0.96- 1.7)] of ATIC C >G associated with response to MTX. On multiple logistic regression analysis, ITPA C >T and DAS28-ESR at baseline were independent predictors of response to MTX.

Conclusion: Two polymorphisms i.e. ITPA C >T and ATIC C >G were associated with response to MTX therapy in Indian RA patients. Along with clinical variables only ITPA C >T had independent association with response to MTX.

Disclosure: A. Singh, None; **H. Nair**, None; **V. Gupta**, None; **P. Sekhar**, None; **R. Misra**, None; **A. Aggarwal**, None.

Abstract Number: 1946

Metabolic Regulation in Cybrids Obtained from Healthy and Osteoarthritic (OA) Patients: Impaired Metabolic Flexibility in OA Process

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose:: Osteoarthritis (OA) is the most frequent joint disease.The OA is a heterogeneous disorder. With acceptance of the joint as an organ, the pathogenesis of OA has been viewed as a complex process that involves all the joint structures. There are several metabolic pathways involved in cell metabolism, including glycolysis, tricarboxylic acid (TCA) cycle and fatty acid (FA) oxidation. Metabolic flexibility has been described as the ability to adapt fuel oxidation by fuel availability. During OA, it has been established a relationship between mitochondrial dysfunction and cellular damage due to impairments in mitochondrial function and metabolic flexibility. Several studies have suggested that fatty acids may play an important role in OA development and progression.

Purpose: The aim of this work was to examine the differences in glucose and fatty acid metabolism, with special focus on metabolic flexibility, in cybrids from healthy (N) or OA donors.

Methods: Cybrids were developed using 143B.TK$^-$ Rho-0 cell line (nuclear donor) and platelets (mitochondrial donors) from healthy (N) and OA donors. Glucose and FA metabolism were measured using D-[^{14}C(U)]glucose and [1-^{14}C]oleic acid respectively. Metabolic flexibility was evaluated by co-culturing with glucose and oleic acid acutely by using inhibitors against glucose and FA oxidation, 20μM UK5099 and 10μM etomoxir, respectively. Incorporation of FA into lipid droplet (LD) was evaluated by thin layer chromatography and LDs were stained by LD540 and analyzed by confocal microscope and flow cytometry. Appropriate statistical analyses were performed with GraphPad Prism v6.

Results: There were no changes in basal glucose metabolism between cybrids. N cybrids had higher acid-soluble metabolites, reflecting incomplete FA β-oxidation than OA cybrids (N: 127.9±9.5 nmol/mg protein, OA: 91.58±7.17 nmol/mg protein, $p \leq 0.005$). Comparing glucose and FA metabolism showed that both types of cybrids preferred to oxidize glucose. Co-culturing with glucose and Oleic acid, increased total cellular uptake and oxidation of glucose in N (oxidation: 1.28±0.09, uptake: 1.22±0.09, $p \leq 0.05$) compared to basal condition but no in OA cybrids. Inhibition of FA oxidation by etomoxir increased complete glucose oxidation of N cybrids (1.14±0.02, $p \leq 0.0001$) compared to basal condition. Combine these data indicate that N cybrids are more metabolically flexible than OA. Cybrids presented different lipid distribution patterns; N cybrids had higher incorporation into phospholipids (N: 24.36±0.93, OA: 20.64±1.02, $p \leq 0.05$) but lower into TAG (N: 64.07±1.17, OA: 70.03±0.84, $p \leq 0.005$), compared to OA cybrids. Lipid droplet (LD) formation increased in both groups incubated in presence of FA (2.07±0.09, 2.61±0.17, $p \leq 0.0001$). Furthermore, N cybrids showed less LD formation than OA ($p \leq 0.005$).

Conclusion: The results indicated that cybrids from OA patients had reduced metabolic flexibility compared to N cybrids. Furthermore, the results indicate that this is associated with mitochondrial impairments.

Disclosure: A. Dalmao-Fernández, None; **J. Lund**, None; **T. Hermida-Gómez**, None; **M. Vázquez-Mosquera**, None; **I. Rego-Pérez**, None; **F. Blanco**, None; **M. Fernandez-Moreno**, None.

Abstract Number: 1947

Integrating Genetic Risk Scores and Pre-Diagnostic Metabolomics to Infer Dysregulated Mechanisms in Rheumatoid Arthritis in Women

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SESSION INFORMATION
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

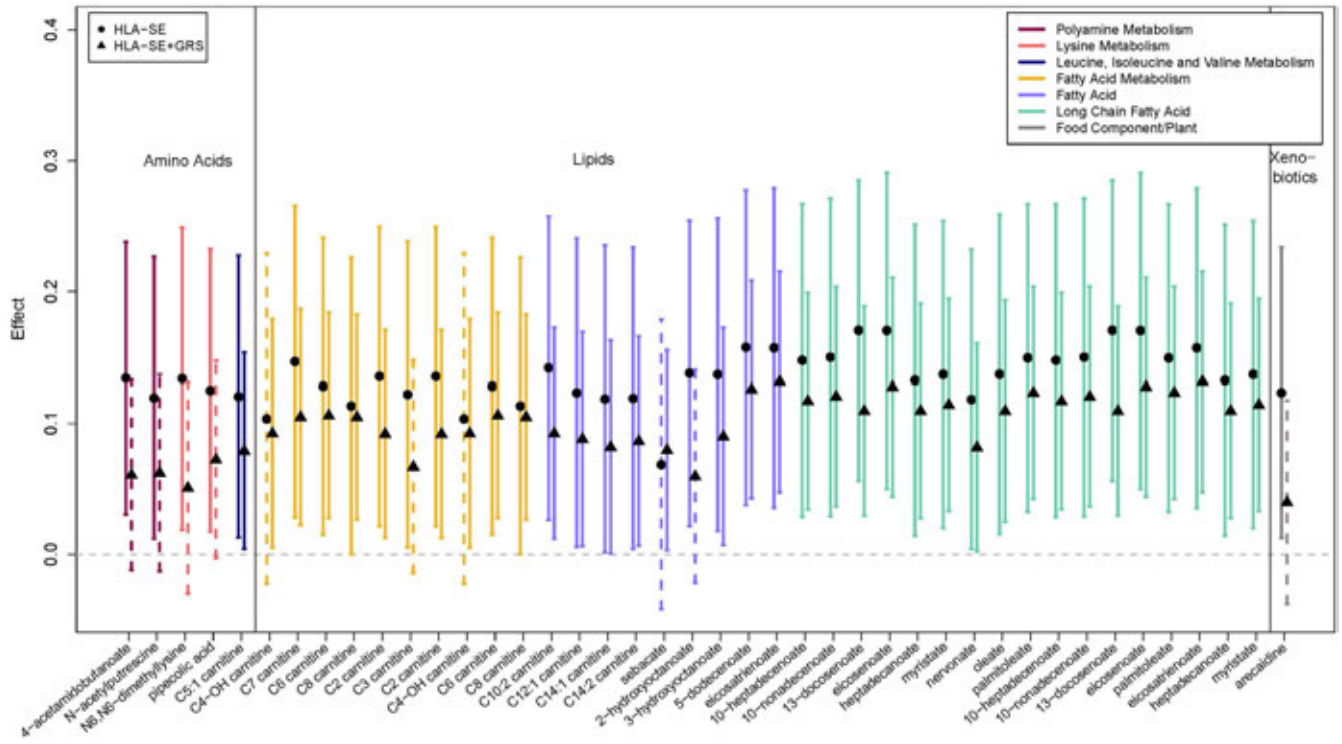
Background/Purpose: Rheumatoid arthritis genetic risk scores (RA-GRS) improve RA risk prediction, but the added predictive value over lifestyle risk factors is modest. Several human leukocyte antigen (HLA) haplotypes are strongly related to seropositive RA. Recently, we identified a number of metabolites, including short-chain acylcarnitines and metabolites involved in polyamine metabolism, associated with RA risk. Integrating RA-GRS and metabolomics may provide insight into RA pathogenesis.

Methods: Plasma samples obtained prior to disease onset from 254 female participants who later developed validated RA in the Nurses' Health Studies were 1) genotyped, imputed to the 1000 Genomes reference panel, and imputed HLA haplotype using SNP2HLA, and 2) analyzed using untargeted liquid-chromatography tandem mass-spectrometry for metabolomic profiling. Genetic risk measures included: 93 weighted non-HLA single nucleotide variants (wGRS93), and 18 weighted HLA (wHLA) haplotypes previously associated with RA risk. For metabolomic measurements, three complementary methods were applied to detect amines and polar metabolites, polar and non-polar lipids, and free fatty acids, bile acids, and metabolites of intermediate polarity. After quality control, 360 unique metabolites were included for analysis. Associations between wGRS93, wHLA, and the cumulative sum of wGRS93 and wHLA and individual metabolite levels were tested using ordinary least squares to identify putative genetically

Table 1. Characteristics of the pre-RA cases in the Nurses' Health Study sample.

Characteristics	Pre-RA Cases (N=254)
Age at Blood Draw	
Mean (SD)	51.3 (8.0)
Age at Diagnosis	
Mean (SD)	61.2 (10.3)
Seropositive Status*, N (%)	
Seropositive, At Blood Draw	39 (15.6)
Seropositive, Ever	158 (62.2)
Time to RA From Blood Draw (Years)	
Median (IQR)	10 (5-13)
Range	0.3-23
Menopause and PMH at Blood Draw, N (%)	
Premenopausal, No PMH	97 (38.2)
Postmenopausal, No PMH	50 (19.7)
Postmenopausal, Past PMH	76 (28.9)
Postmenopausal, Current PMH	31 (12.2)
Smoking Status, N (%)	
Ever	136 (53.5)
Pack Years Among Smokers	
Median (IQR)	30 (10-31)
Range	1-76
BMI	
Mean (SD)	25.8 (4.9)

SD: Standard deviation; IQR: Interquartile range; PMH: Post-menopausal hormone use



Putative associations of HLA-SE and cumulative HLS-SE and GRS93 with pre-RA plasma metabolites levels among 254 RA cases in the Nurses' Health Study. All metabolites reported above were significant at a false discovery rate adjusted p-value threshold of 0.1. Dashed lines indicate failure to meet nominal significance thresholds.

informed metabolites of RA. Adjustment for multiple comparisons was made using the pooled local index of significance, a false discovery rate approach which employs Hidden Markov Models to account for dependency structures in the data.

Results: After adjustment for multiple comparisons, no genetically informed metabolites for wGRS93 were found; however, 27 RA wHLA-SE associations were identified, including several short-chain acylcarnitines and metabolites involved in polyamine metabolism that we previously found to be associated with RA: C2 carnitine (β=0.120; p=0.018), C3 carnitine (β=0.122; p=0.007), C5:1 carnitine (β=0.120; p=0.016), 4-acetamidobutanoate (β=0.134; p=0.027), and N-acetylputrescine (β=0.119; p=0.011). In the combined wGRS93 and wHLA-GRS score, 21 associations were identified, also including several carnitines identified for wHLA-SE, as well as additional acylcarnitines: C4-OH carnitine (β=0.092; p=0.048) and C7 carnitine (β=0.105; p=0.017). In all results, higher genetic risk was associated with increased standardized metabolite expression levels.

Conclusion: We identified several novel associations between both 1) wHLA haplotypes and 2) combined wGRS93 and wHLA risk scores, with newly identified metabolite levels in pre-RA, but none for GRS93. These associations may point to new biologic pathways involved in RA development. However, further validation is required.

Disclosure: S. Chu, None; **J. Cui**, None; **J. Sparks**, None; **B. Lu**, None; **C. Clish**, None; **J. Lasky-Su**, None; **E. Karlson**, None; **K. Costenbader**, Astra-Zeneca, 2, Glaxo Smith Kline, 2, Janssen Scientific Affairs, LLC, 2, Lupus Foundation of America, 2, Lupus Research Alliance, 2, Merck, 2.

Abstract Number: 1948

The Mechanism of DC-STAMP-Mediated Signaling in Cell-Cell Fusion and Osteoclast Maturation

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SESSION INFORMATION
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Background/Purpose: Osteoclasts (OC) are bone-resorbing, multinuclear cells that originate from myeloid progenitor cells through repetitive cycles of cell-cell fusion. Dendritic cell-specific transmembrane protein (DC-STAMP) is essential for cell-cell fusion and formation of fully functional OC, resulting in mild-moderate osteopetrosis in DC-STAMP$^{-/-}$ mice; however the molecular mechanisms of its action is not well understood. We examined how the complete absence of DC-STAMP in the osteogenic progenitor cells (OCPs) affects their ability to participate in cell-cell fusion, alters calcium (Ca^{2+}) signaling, and gene and protein expression in response to osteoclastogenic stimuli: macrophage colony-stimulating factor (MCSF) and receptor activator of nuclear factor kappa-B ligand (RANKL).

Methods: We isolated bone marrow macrophages (BMMs) from wild type (WT) and DC-STAMP knockout (KO) mice. To analyze cell-cell fusion, we labeled DCSTAMP$^{+/+}$ and DCSTAMP$^{-/-}$ BMMs with red (CellVue® Red) and green (CellVue® Jade) membrane dyes respectively, cultured them with MCSF (30 - 50 ng/ml) and RANKL (30 - 50 ng/ml) and monitored cell-cell fusion with live cell imaging. Calcium signaling was examined using microspectrofluorimetry of Fura-2 loaded OC precursors. Activation of osteoclastogenic transcription factor NFATc1 was assessed using immunoblotting and immunofluorescence. The effect of DC-STAMP knockout on gene and protein expression was examined using RNAseq, quantitative PCR (qPCR), and immunoblotting.

Results: DCSTAMP$^{+/+}$ cells were essential to initiate cell-cell fusion events; however DC-STAMP$^{-/-}$ BMMs were successfully incorporated into forming OC. RANKL-induced Ca^{2+} oscillations were still present in DC-STAMP$^{-/-}$ precursors, and increased in intensity compared to DC-STAMP$^{+/+}$ OCPs during the later stages of differentiation. NFATc1 protein levels in DCSTAMP$^{-/-}$ OCPs increased with time following RANKL exposure and were comparable to WT. However, nuclear translocation of NFATc1 was significantly decreased in DCSTAMP$^{-/-}$ osteoclast precursors at day 3 of differentiation. We further observed decreased expression of key osteoclastogenic genes (CTSK, ATP6V0D2, ACP5) in DCSTAMP$^{-/-}$ cells. RNAseq analysis of DCSTAMP$^{-/-}$ and WT OCPs identified differentially expressed genes indicating alterations in key molecular pathways, including RELA, NFκB, FOS, PKC, and TREM1 signaling.

Conclusion: Our findings indicate that while DC-STAMP$^{-/-}$ OCPs cannot form multinuclear OCs, they do fuse with DCSTAMP$^{+/+}$ OCPs and are incorporated into maturing OCs. We demonstrate that even though calcium oscillations are present in DC-STAMP$^{-/-}$ OCPs, NFATc1 nuclear translocation is deficient, suggesting that DC-STAMP acts in the NFATc1 pathway, but downstream of calcium signaling. Our RNAseq analysis identified multiple differentially expressed genes that are potentially involved in cell-cell fusion and maturation of OCs.

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Abstract Number: 1949

The p.R321C Mutation in P62 Associated with Paget's Disease of Bone Leads to a Change of Localization of the Protein in Human Osteoclasts

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Session Time: 9:00AM–11:00AM

Background/Purpose: Paget´s disease of bone (PDB) is a chronic bone metabolic disorder. Currently, PDB is a focal disorder characterized by an increase in bone turnover in a disorganized way. Its cause is unknown, but it is clear that it is a multifactorial disease in which genetic and environmental factors are involved. The most important known genetic factor predisposing to PDB is mutation in Sequestosome1 (*SQSTM1*) gene. This gene encodes p62, a multifunctional protein involved in autophagy that binds ubiquitin and regulates activation of the nuclear factor kappa-B (NF-kB) signaling pathway, regulating autophagy. We detected for the first time the c.961C >T *SQSTM1* gene mutation localized in exon 6 of *SQSTM1* gene in three PDB patients. It causes the p.R321C mutation, localized in the LIR domain of p62 protein. The aim of this study is to characterize the effect of the p.R321C mutation in human osteoclasts.

Methods: First of all, the *SQSTM1* cDNA was cloned into the EcoRI site of the pCEFL-Flag vector to generate the pCEFL-Flag-cSQSTM1-321wt construct. The p.R321C mutation was introduced into this construct by mutagenesis using primers designed to introduce C >T base change at position +961 to generate pCEFL-Flag-cSQSTM1-321C construct. After that, PBMCs were isolated from venous blood samples for generating human osteoclasts in vitro, using Ficoll. Mononuclear cells were seeded in 6-well culture plates with glass cover slips and cultured with α-MEM medium supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin at 37ºC in a humidified 5% CO2 atmosphere. Cells were differentiated with fresh α-MEM containing M-CSF and RANKL every 3 days for 3 weeks. After that, the cells were transiently transfected with total plasmid DNA (pCEFL-Flag-cSQSTM1-321wt and pCEFL-Flag-cSQSTM1-321C). 72 hours after transfection cells were fixed and we performed a Confocal Co-Immunofluorescence Assay, using as primary antibodies anti-Flag M2 and anti-p62. Also, cells were stained with DAPI (4', 6-diamidino-2-phenylindole), to select the ones with at least 3 nuclei. Fluorescence images were captured with a confocal microscope.

Results: Our results showed that, while endogenous p62 remains scattered though the cytoplasm, p.R321C p62 is concentrated in the periphery of human osteoclasts. Transfection with WT p62 showed the same localization that endogenous WT p62. This change of localization caused by the mutation detected in PDB patients could result in an alteration in autophagy that can have an important role in the development of PDB, since autophagy is a catabolic process that occurs in the cytoplasm. In fact, previous studies have associated other mutations in autophagy genes with the physiopathology of PDB. To confirm the effect of this mutation in autophagy functional studies are ongoing.

Conclusion: The mutation p.R321C in the LIR domain of p62 protein leads to a change of localization of the protein in human osteoclasts, reinforcing the hypothesis that autophagy is involved in PDB.

Disclosure: N. Gestoso-Uzal, None; **R. Usategui-Martín**, None; **R. González-Sarmiento**, None; **J. Del Pino-Montes**, None.

Abstract Number: 1950

Apolipoprotein L1 Variant-Carrying Monocytes Exhibit Mitochondrial Respiration Defects

Ashira Blazer ,[1] Miao Chang,[1] Kimberly Robins,[1] Jill Buyon,[2] and Robert Clancy[2], [1]NYU School of Medicine, New York, NY, [2]NYU School of Medicine, New York

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In SLE Apolipoprotein L1 (APOL1) risk variants associate with cardiovascular and kidney damage. APOL1 is both a secreted and tissue intrinsic protein; the latter role mediates organ injury. Expression is driven by inflammatory stimuli which initially promotes survival through autophagy. At higher expression, APOL1 contributes to cell death partially by compromising mitochondria. The RV protein structure favors toxicity at lower thresholds. Macrophages express APOL1 and use metabolic plasticity to perform effector functions. We hypothesized that in activated macrophages, APOL1 expression impairs mitochondrial

Methods: Healthy controls were genotyped for APOL1 reference allele (G0) risk variants (RV) (n=15; G0/G0=8, RV/G0=4, RV/RV=3). Monocytes were isolated from PBMCs using a Miltenyi Biotec Pan Monocyte Isolation kit and differentiated into macrophages using GM-CSF. Cells were treated with SLE-relevant agonists ssRNA hY3 or IFNɣ; and APOL1 expression was observed by qPCR. As in-vivo correlates, APOL1 expression relative to IFN response gene, Siglec 1, in SLE patient monocytes (n=17); and expression in coronary artery tissue macrophages with (n=3) or without (n=3) atherosclerotic plaque were assessed through RNA seq data and immunohistochemistry respectively. To

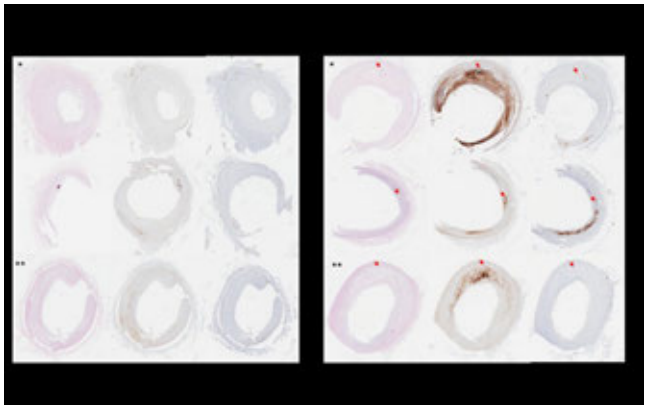

Figure 1. Axial sections of coronary arteries (explanted human hearts, magnification 1X). Sections denoted by * and ** represent samples taken from the same donor at a plaque free and plaque containing sites

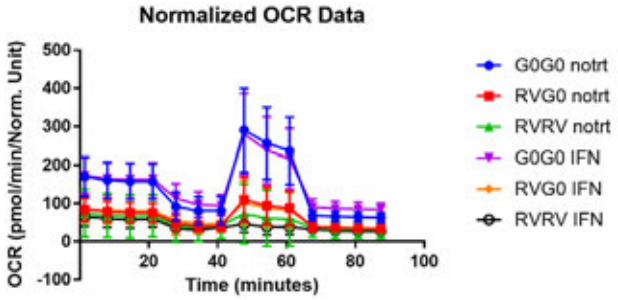

Figure 2. Representative mitochondrial oxygen consumption rate tracings by macrophage genotype and condition.

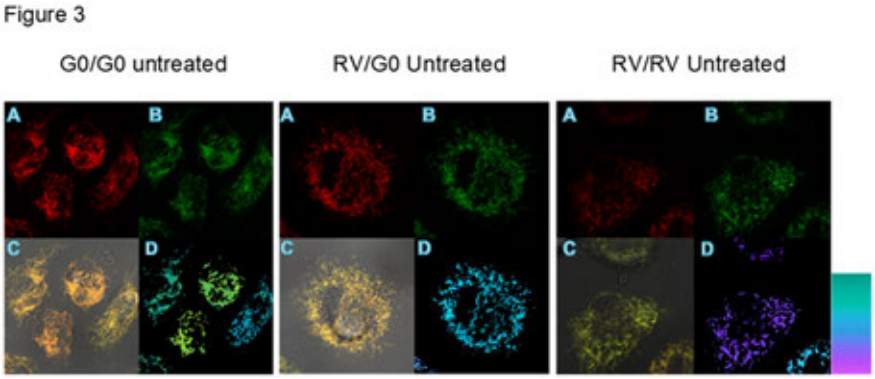

Figure 3. Representative montages of cells by genotype: A. MitoProbe Polarized mitochondria, B. MitoTracker All mitochondria, C. Composite Image. D. Masked Images showing MitoProbe/MiTotracker ratios.

test mitochondrial respiration, cultured HC macrophages were left untreated or IFNɣ treated, and bioenergetics were measured by the Seahorse assay. Confirmatory fluorescent microscopy was done by staining cells with Mitoprobe (polarized mitochondria) and Mitotracker (all mitochondria) and the ratio of Mitoprobe to Mitotracker staining was quantified using ImageJ software.

Results: Across the genotypes,hY3 and IFNɣ increased APOL1 mRNA expression 29.1±18.4 and 31.6±14.9 fold compared to untreated ($p< 0.001$ in each). In SLE monocytes, APOL1 significantly correlated with Siglec1 expression ($R=0.64$; $P=0.005$). APOL1 stained 4% of non-plaque containing and 18% of plaque-containing coronary arteries ($p=0.05$). APOL1 was apparent in multiple cell types including invading tissue macrophages (fig1). On the seahorse assay, there were genotype-dependent differences in Basal OCR (BO pmol/min), Spare Capacity (SC pmol/min), and total ATP production (ATP pmol/min) (G0/G0: BO: 99.4±11.3, SC:150.9±16.6, ATP: 88.1±9.5; RV/G0: BO: 46.1±4.5, SC: 52.1±8.8, ATP: 40.7±3.4; RV/RV: BO: 46±17.4, SC: 14.9±11.6, ATP: 36.7±9.5 each $p< 0.001$). Across genotype, these values fell with IFNɣ (G0/G0: BO: 73.9±6, SC: 129.4±17.3, ATP: 67.6±5.4; RV/G0: BO: 46±5.1, SC: 27.9±8.1, ATP: 39.5±3.9; RV/RV: BO: 42.1±8.6, SC: 9.5±8.3, ATP: 35.8±6.9) (fig2). Fluorescent microscopy confirmed findings with the mean respective MitoProbe/Mitotracker ratios in G0/G0, RV/G0, and RV/RV macrophages at rest 1.5±0.5, 0.86±0.3, and 0.89±0.3 and with IFNɣ 1.3±0.4, 0.74±0.3, and 0.6±0.2 (fig3).

Conclusion: Inflammation both in vitro and in vivo due to hY3, IFNɣ, and ischemia increase macrophage APOL1 expression across genotypes. In RV carrying macrophages, this results in diminished mitochondrial energy production—a potential underpin of variant-mediated toxicity.

Disclosure: A. Blazer, None; **M. Chang**, None; **K. Robins**, None; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **R. Clancy**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2.

Abstract Number: 1951

Transcriptomic Responses in CD4+ T Cells During Successful Therapy for Juvenile Idiopathic Arthritis

Tarbell Evan,[1] Kaiyu Jiang,[1] Tao Liu,[2] and **James N. Jarvis** [3], [1]University at Buffalo Jacobs School of Medicine, Buffalo, NY, [2]Roswell Park Cancer Instiyute, Buffalo, NY, [3]University at Buffalo, Jacobs School of Medicine and Biomedical Sciences, Buffalo, NY

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
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Session Time: 9:00AM–11:00AM

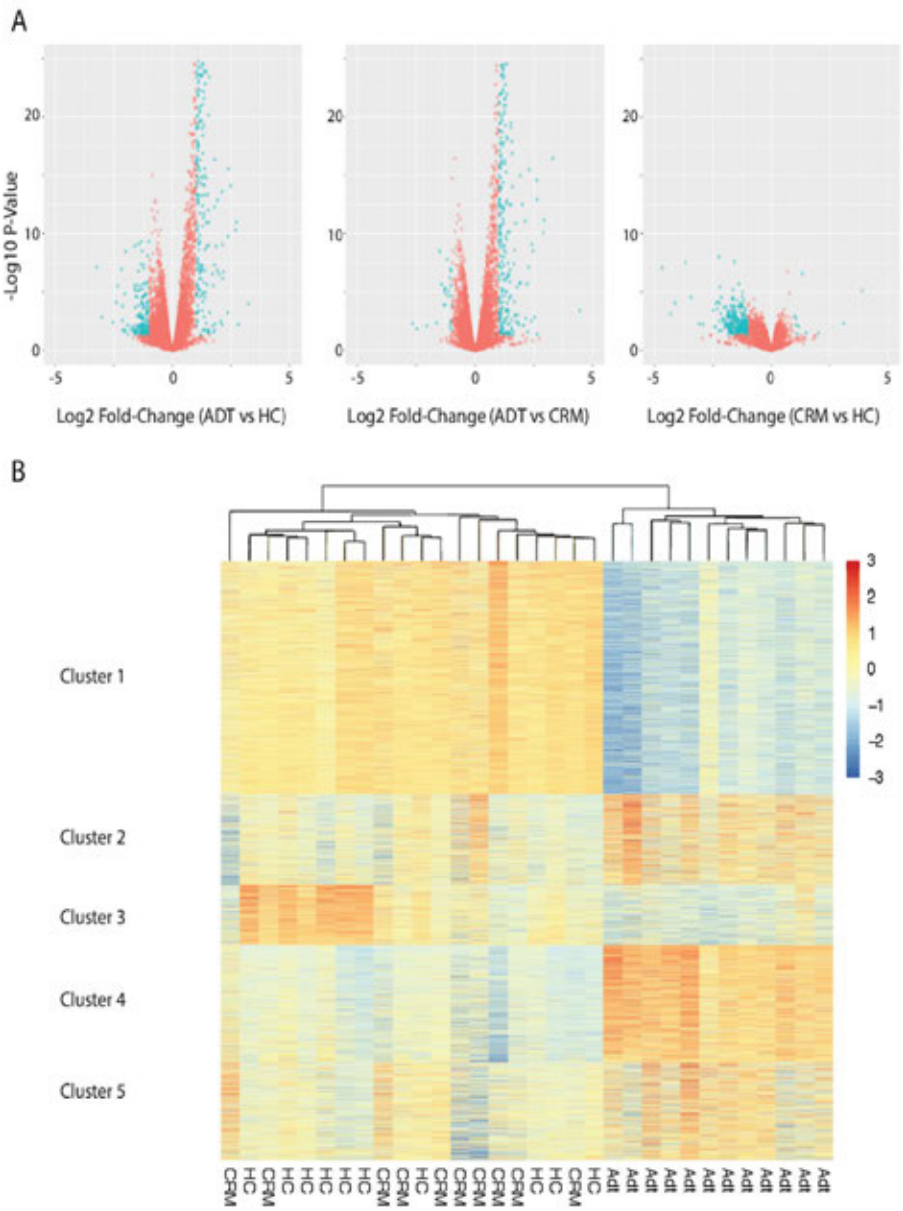
Background/Purpose: We have shown that therapeutic response in juvenile idiopathic arthritis (JIA) is a non-linear process invloving reorganization of gene expression networks. However, our earlier studies were performed on whole blood and neutrophils. Detailed descriptions of the lymphoid compartment have not been published. We undertook this study to gain a better understanding of treatment response in JIA using transcriptome analysis of peripheral blood CD4+ T cells.

Methods: This was a cross-sectional study of children with polyarticular, RF-negative JIA, who ranged in age from 5-13 years. Subjects included 12 patients with active disease on therapy with methotrexate (MTX) and etanercept (ADT), 10 patients also on MTX and etanercept who met crieria for clinical remission on medication (CRM),and 10 healthy control children (HC). CD4+ T cells were obtained from peripheral blood by positive selection and RNA purified and cDNA libraries prepared using conventional appproaches. Libraries were sequenced using 100 base pair (bp) paired-end reads on the Illumina HiSeq 2500 platform. We used standard statistical approaches to identify differentially expressed genes, and gene ontology (GO) analysis to identify common functional properties among groups of differentially expressed genes.

Results: We identified 4062 genes that were differentially expressed between ADT and HC, 3454 genes that demonstrated expression differences between ADT and CRM, and 22 genes that were expressed differently between HC and CRM. These findings differ from what we have seen in neutrophils, where transcriptional profiles of children who have achieved CRM differ significantly from those of HC. We next plotted all differentially expressed genes called between any pair of sample groups and used k-means clustering to group genes into gene clusters. We identified 5 distinct subgroups, representing different cellular functions. Cluster 1, which was characterized by increased expression in HC and CRM compared to ADT, was involved in metabolic processes. Clusters 2 and 4, representing genes that showed higher expression in the ADT group compared the HC and CRM groups, were enriched for genes involved in transcription and translation, indicating that in the active disease state, CD4+T-cells were more active in their transcriptional and translational processes. Cluster 3, which was characterized by higher expression in HC samples compared to CRM or ADT samples, was enriched for genes involved in immune activation and may represent genes that are suppressed by treatment. Cluster 5 contained genes that showed a wide variety of expression patterns across the samples but show a general increase in expression in the ADT samples compared to the CRM and HC samples; this cluster was represented by genes involved in RNA processing and RNA metabolism.

Conclusion: CD4+ T cells undergo significant re-organization of their transcriptional repertoires over the course of therapy. This re-organization involves fundamental cellular processes such as metabolism and the processing of RNA transcripts. Further research to determine whether these changes are necessary for or merely associated with therapeutic response is warranted.

Fig. 1



Volcano plots and hierarchical cluster analysis of RNAseq data from CD4+ T cells

Disclosure: T. Evan, None; **K. Jiang**, None; **T. Liu**, None; **J. Jarvis**, None.

Abstract Number: 1952

Genes Associated with Nucleotide Oligomerization Domain-Like Receptor Signaling Pathway Are Upregulated in Discoid Lupus Erythematosus

Irene Calderon ,[1] Inhan Lee,[2] and Rina Mina[3], [1]SCDS, Cincinnati, OH, [2]mcore, Ann Arbor, MI, [3]University of Cincinnati, Cincinnati

SESSION INFORMATION
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Background/Purpose: Background: Discoid Lupus Erythematosus (DLE) is disfiguring autoimmune skin disorder, associated with defects in the adaptive immune system. The innate immune system is likely involved as seen in the presence of interface dermatitis, observed in viral exanthem, and improvement of DLE using inhibitors to membrane-bound Pattern Recognition Receptors (PRR).

Hypothesis: Genes associated with defects in the innate immune system would be upregulated in DLE skin compared to normal controls.

Methods: Datasets selected from the Gene Expression Omnibus (GEO), GSE109248, GSE81071, GSE52417, GSE95474, and GSE72535 were analyzed using GEO2R to compare the gene expressions between DLE and normal controls. Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database, Gene Card, and Kyoto Encyclopedia of Genes and Genomes (KEGG) Pathway analysis were used to identify the interaction and function of specific genes.

Results: There were a total of 54 DLE skin samples and 37 normal controls. Genes associated with the Nucleotide Oligomerization Domain-Like Receptor (NLR) signaling pathway were consistently differentially expressed in DLE skin samples in all datasets (p-value < 8.74e-05). Five genes associated with the NLR signaling pathway, STAT1, OAS1, OAS2, OAS3, and AIM2, were found to be upregulated in skin samples of DLE patients compared to normal controls in all datasets. These five genes are associated with transcription activation, regulation of viral infection, and interferon response.

Table 1. Gene Functions, Source: Gene-Cards

Gene	Function	Relevance to Study
STAT1 (Signal Transducer and Activator of Transcription1)	Mediates cellular responses to interferons (IFNs), cytokines, and growth factors. Transcription activators of IFN-stimulated genes	Acts dysfunctionally in systemic lupus (SLE), related to DLE. IFN signature in monocytes in SLE is upregulated compared to normal
OAS (2'-5'-Oligoadenylate Synthetase) 1,2,3	Induced by IFNs. OAS 1 and 3 activate RNase L by catalyzing the 2', 5' oligomers of adenosine, which results in viral RNA degradation and the inhibition of viral replication. Related pathway: Toll-like Receptor (TLR) Signaling Pathway	Related to IFN-1. Isoforms may be suggestive of disease activity in SLE patients
AIM2 (Absent In Melanoma 2)	May control cell proliferation. Related pathway: TLR Signaling Pathway	Closely correlated with severity of disease in SLE patients. Upregulated in aberrantly activated macrophages

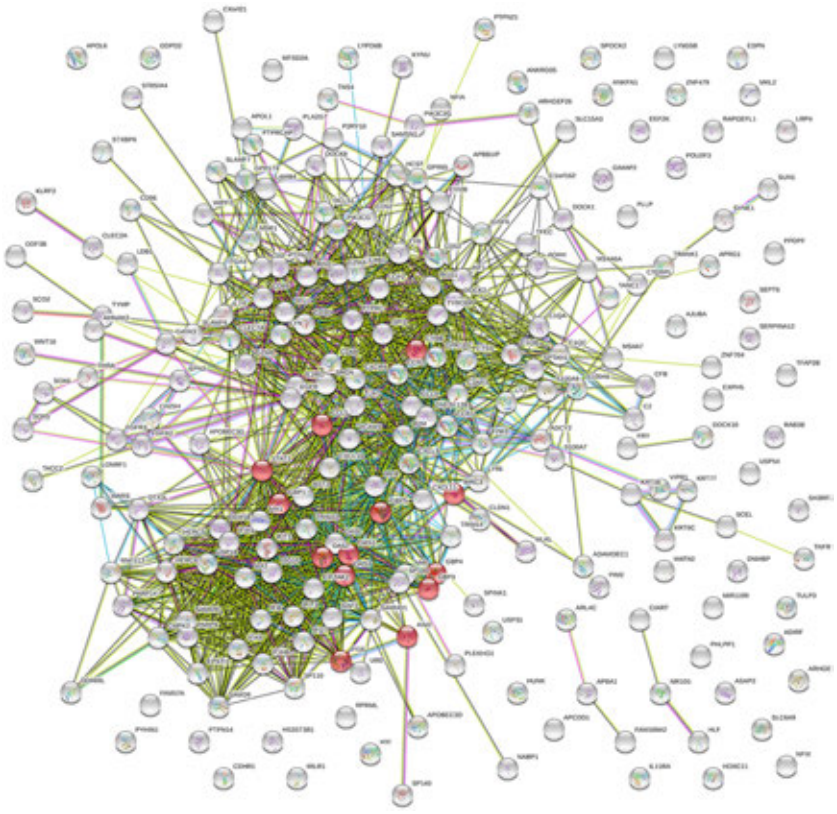

Image 1. NOD-Like Receptor Genes From GSE 81071

Conclusion: Genes associated with the NLR signaling pathway are differentially expressed in the skin of DLE patients compared to normal controls, supporting the role of the innate immune system in DLE. Further validation studies using experimental methods are needed.

Disclosure: I. Calderon, None; **I. Lee**, None; **R. Mina**, None.

Abstract Number: 1953

Estimating the Infiltration of Immune Cells in Synovium of Rheumatoid Arthritis Compared to Osteoarthritis and Healthy Control Using Transcriptomic Profiling

Mahmood Hachim ,[1] Noha Elemam,[1] Ibrahim Hachim,[2] Suad Hannawi,[3] Rifat Hamoudi,[4] and Azzam Maghazachi[1], [1]Sharjah Institute for Medical Research, College of Medicine, University of Sharjah, Sharjah, Sharjah, United Arab Emirates, [2]Sharjah Institute for Medical Research, College of Medicine, University of Sharjah, Sharjah, United Arab Emirates, [3]Ministry of Health and Prevention, Department of Rheumatology, Dubai, United Arab Emirates, [4]1Sharjah Institute for Medical Research, College of Medicine, University of Sharjah, Sharjah, United Arab Emirates

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Genetics, Genomics & Proteomics Poster

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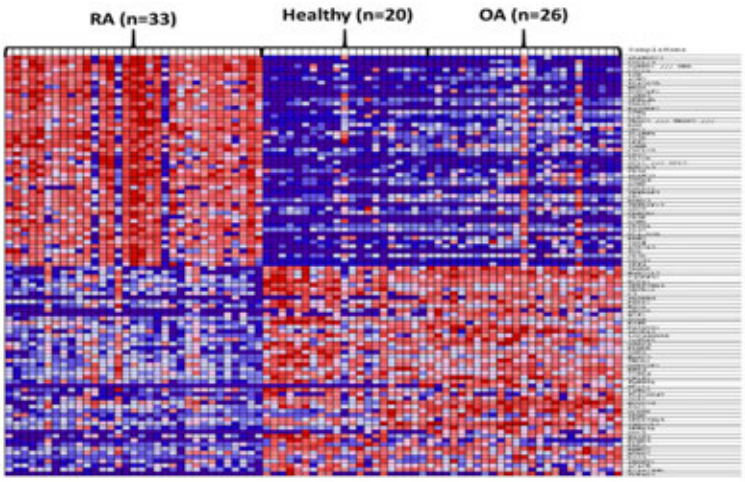

Figure 1. GSEA analysis on combined publicly available datasets (GSE55235, GSE55457, GSE55584) of synovium transcriptomic profiling showing the top 100 differentially expressed genes between RA (n=33), OA (n=26) and healthy controls (n=20). The figure was generated using GSEA software (http://software.broadinstitute.org/gsea)

Background/Purpose: Rheumatoid arthritis (RA) is one of the most prevalent autoimmune and prototypic inflammatory diseases. It is a heterogeneous autoimmune disease with local and systemic features. The molecular triggers for the synovium transition from healthy to inflammatory and then to rheumatoid arthritis are still not clearly defined. Recently, studying synovial tissue in RA is gaining more attention in order to have a better understanding of the early stages of the disease. Transcriptomic profiling of synovial samples is a promising approach to identify reliable biomarkers, assess the effects of medical interventions, and predict the outcomes. One limitation of such an approach is the masking effect of the local gene expression signature by the infiltrating immune cells, thus making it difficult to distinguish the trigger from the consequence. We aimed to establish a combined bioinformatical approach using in house pipeline to process, filter, and combine microarray transcriptomic data to identify novel synovium related biomarkers. The filtered transcriptomic profile was tested by ESTIMATE R package (Estimation of Stromal and Immune cells in MAlignant Tumor tissues using Expression data) to estimate the difference in immune cells infiltration in healthy, Osteoarthritis (OA) and RA.

Methods: Gene expression profile of synovial tissue from 33 RA, 26 OA, and 20 healthy controls from three datasets (GSE55235, GSE55457, GSE55584) were extracted using the Gene Expression Omnibus (GEO) public repository. Raw cell files were re-analyzed using in house pipeline for normalization and variant filtration. Gene Set Enrichment analysis was used to identify genes that are differentially expressed (DEG) between the three groups, as shown in Figure 1.

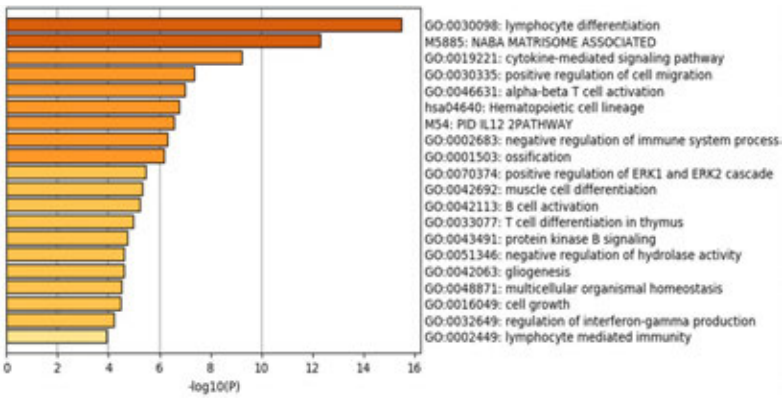

Figure 2. Top pathway enrichment for the top 100 Differentially expressed genes in RA synovium compared to OA and healthy controls. The figure was generated using metascape online tool (http://metascape.org)

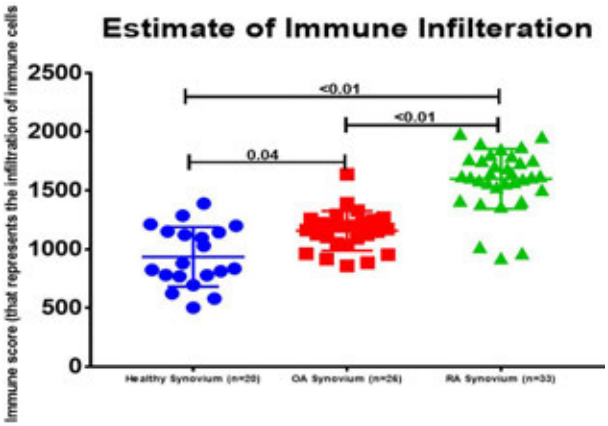

Figure 3. Using the transcriptomic profiling to estimate the infiltration of immune cells in synovium using ESTIMATE tool (https://bioinformatics.mdanderson.org/public-software/estimate/).

Results: In comparison to OA and healthy controls, RA synovium showed significant enrichment for immune-related pathways namely: lymphocytes differentiation, aβT cell activation, IL12 pathway, B cell activation, T cell differentiation, regulation of interferon-gamma production and lymphocytes mediated immunity, Figure (2). The most immune-related genes significantly altered in RA were chemokines (CXCL13, CXCL9, CCR2, CXCL10, XCL1, XCL2, and CXCL11), interleukins (IL7R, IL21R, IL32, and IRF4), and B cell related (TPD52, SLAMF8, IGHM, CD27, CD79A). Interestingly, NK related gene NKG7 (natural killer cell granule protein 7) was significantly upregulated in RA patients. Using ESTIMATE, it was shown that RA synovium contains more infiltrating immune cells than OA or healthy synovium, Figure (3). Healthy synovium contained the highest nonimmune cells (64±5%), compared to OA (58±2%), and RA (52±3%). One of the identified biomarkers to be synovium specific marker is CXCL13, a potent homing chemoattractant for B lymphocytes. CXCL13 was shown previously to be upregulated in RA synovium and can predict the recruitment of Follicular Dendritic Cells and synovial germinal centers formation, pathognomonic features in RA.

Conclusion: Using proper bioinformatical analysis of the synovium in RA to identify synovium specific biomarkers that are not masked by infiltrating immune cells may pave the way for understanding the molecular basis of RA.

Disclosure: M. Hachim, None; **N. Elemam**, None; **I. Hachim**, None; **S. Hannawi**, None; **R. Hamoudi**, None; **A. Maghazachi**, None.

Abstract Number: 1954

Association of Functional $(GA)_n$ Microsatellite Polymorphism in the *FLI1* Gene with Susceptibility to Human Systemic Sclerosis

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SESSION INFORMATION
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Background/Purpose: Susceptibility genes which can account for the characteristic features of systemic sclerosis (SSc) such as fibrosis, vasculopathy and autoimmunity remain to be determined. A series of extensive studies by Asano and colleagues using genetically engineered mice convincingly demonstrated that deficiency of a transcription factor Fli1 can play a causal role in the development of SSc with all these characteristic features. Although previous genome-wide association studies (GWAS) have not reported association of single nucleotide polymorphisms (SNVs) in the *FLI1* gene, *FLI1* contains $(GA)_n$ microsatellite in its regulatory region, which has been shown to be associated with expression level of FLI1. Because microsatellite polymorphisms are not usually captured by GWAS unless they are in tight linkage disequilibrium with SNVs, we thought it is possible that *FLI1* microsatellite may partly account for the "missing heritability" of SSc. In this study, we directly genotyped *FLI1* $(GA)_n$ microsatellite and examined whether it is associated with susceptibility to SSc.

Methods: Genomic DNA from 639 Japanese SSc patients and 851 healthy controls (HCs) was genotyped for $(GA)_n$ microsatellite using the fragment assay. In the discovery stage, the genotype distribution was compared between 479 patients and 573 HCs, and the cut-off repeat number for the susceptibility to SSc was determined by receiver operating characteristic (ROC) analysis to classify the alleles into L (long) and S (short) alleles. In the replication stage, 160 patients and 268 HCs were examined, and the data from both stages were combined using meta-analysis. Association with susceptibility and clinical characteristics was examined using logistic regression analysis with the adjustment for sex. *FLI1* mRNA levels were determined using quantitative RT-PCR.

Results: In the discovery stage, genotype distribution of the $(GA)_n$ microsatellite alleles in SSc patients showed a trend towards extension as compared with that in the HCs (Cochran-Armitage test for trend, P=0.045)(Figure 1). Based on the ROC analysis, (GA)n alleles with ≥22 repeats were collectively defined as L alleles, and alleles with ≤21 repeats as S alleles. The same trend was observed in the discovery and replication stages, and when combined, $(GA)_n$

Table 1. Case-control study of *FLI1* $(GA)_n$ microsatellite with systemic sclerosis

	n	Genotype frequency L/L	L/S	S/S	Allele frequency L	Additive model (L vs S) P	OR (95%CI)	power*
Discovery stage								
SSc	479	66 (0.138)	227 (0.474)	186 (0.388)	359 (0.375)	**2.0E-03**	**1.37 (1.12-1.67)**	0.945
HCs	593	58 (0.098)	252 (0.425)	283 (0.477)	368 (0.310)	referent		
Replication stage								
SSc	160	34 (0.213)	68 (0.425)	58 (0.362)	136 (0.425)	0.10	1.27 (0.96-1.70)	0.386
HCs	258	33 (0.128)	118 (0.457)	107 (0.415)	184 (0.357)	referent		
Meta-analysis						**5.0E-04**	**1.34 (1.14-1.58)**	

L alleles: $(GA)_{22}$ or longer alleles, S:alleles: $(GA)_{21}$ or shorter alleles.
SSc: systemic sclerosis, HCs: healthy controls, OR: odds ratio, CI: confidence interval.
Comparisons with P<0.05 are shown in bold.
*Power to detect statistical association at the significance level of 0.05.

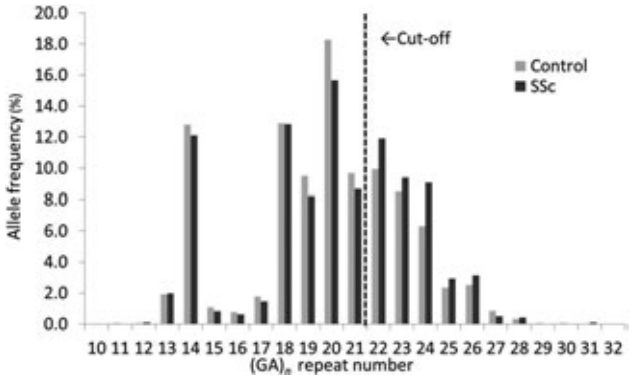

Figure 1. Distribution of FLI1 (GA)n microsatellite alleles in the patients with systemic sclerosis and healthy controls in the discovery stage. X and Y axes show the repeat number and allele frequency (%) of FLI1 (GA)n microsatellite, respectively. The distribution in SSc patients was significantly shifted to extended alleles when compared with healthy controls (Cochran-Armitage test for trend, P=0.045). The dotted line shows the cutoff value for the susceptibility to SSc derived from the receiver operating characteristic (ROC) analysis

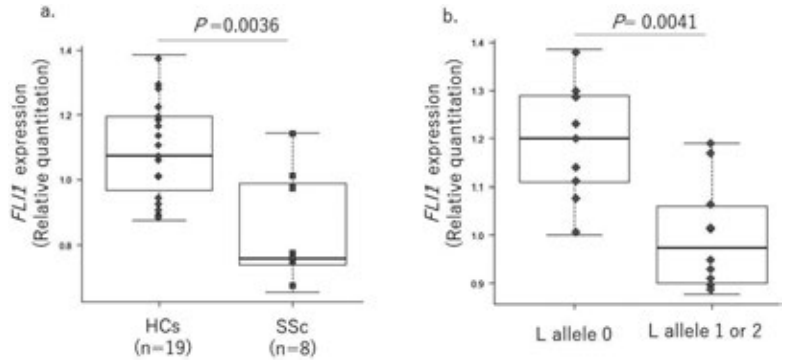

Figure 2. FLI1 mRNA expression in whole peripheral blood. The band and quartiles in the boxplot diagrams indicate median (Q2) and interquartile range (IQR) of FLI1 mRNA expression levels. P values were calculated by Mann-Whitney U-test. (a) Patients with SSc and HCs (all genotypes combined). HCs: n=19, Q2=1.07, IQR=0.23. SSc: n=8, Q2=0.76, IQR=0.24. (b) Healthy controls carrying (L alleles 1 or 2) and not carrying (L allele 0) (GA)n L alleles. (L allele 0: n=9, Q2=1.20, IQR=0.18, L allele 1or 2: n=10, Q2=0.97, IQR=0.14.)

L alleles were significantly associated with susceptibility to SSc (P=5.0E-04, odds ratio[OR]=1.34, 95% confidence interval 1,14-1.58, additive model)(Table 1). Significant association was observed both in diffuse cutaneous and limited cutaneous SSc. Among the SSc, $(GA)_n$ L alleles were significantly enriched in the patients with modified Rodnan total skin thickness score (mRSS)≥10 compared with those with mRSS< 10 (P=9.6E-03, OR=1.63). *FLI1* mRNA level in the whole blood was significantly reduced in SSc patients when compared with HCs(Figure 2a). When the mRNA levels were compared between the carriers and non-carriers of $(GA)_n$ L alleles among HCs, significant reduction was observed in individuals carrying $(GA)_n$ L allele (Figure 2b).

Conclusion: *FLI1* $(GA)_n$ microsatellite alleles with extended repeat numbers were associated with lower *FLI1* mRNA levels and susceptibility to human SSc.

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Abstract Number: 1955

Association of *TERT* and *DSP* Polymorphisms with Susceptibility to Myeloperoxidase-ANCA-Associated Vasculitis

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SESSION INFORMATION

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Background/Purpose: Epidemiology of ANCA-associated vasculitis (AAV) is substantially different between East Asian and European populations. Microscopic polyangiitis (MPA) and MPO-ANCA positive AAV (MPO-AAV) are prevalent in Japan, while granulomatosis with polyangiitis (GPA) and PR3-ANCA positive AAV (PR3-AAV) are dominant in Europe. In addition, high prevalence of interstitial lung disease (ILD), a severe complication and a prognostic factor in AAV, is a striking feature in the Japanese population, suggesting a role for genetic background in the development and clinical features of AAV.

A proportion of patients with idiopathic pulmonary fibrosis (IPF) are positive for MPO-ANCA, and some of these patients develop MPA, suggesting that ILD in AAV and IPF may share some pathogenic processes. Recently, we reported that 5% of MPO-AAV patients with ILD carry *MUC5B* single nucleotide variant (SNV) rs35705950T, the risk allele for IPF, as compared with 1% among healthy controls, indicating that *MUC5B* is a shared susceptibility gene between IPF and MPO-AAV associated ILD (Namba et al, Ann Rheum Dis 2019). However, the allele frequency of rs35705950T

Table 1. Association of AAV subphenotypes with *TERT* and *DSP*						
TERT rs2736100	total allele count	A allele	P (ILD+ vs. ILD-)	Pc	OR	95%CI
MPO-AAV with ILD	310	203 (0.655)	0.28	0.34	0.84	(0.61-1.15)
MPO-AAV without ILD	394	273 (0.693)				
			P (vs. HCs)	Pc	OR	95%CI
MPO-AAV	820	551 (0.672)	4.3E-05	5.2E-04	1.37	(1.18-1.60)
PR3-AAV	132	86 (0.652)	0.22	0.33	1.25	(0.87-1.80)
MPA	628	423 (0.674)	2.2E-04	0.0013	1.38	(1.16-1.64)
GPA	216	126 (0.583)	0.64	0.70	0.94	(0.71-1.23)
EGPA	136	94 (0.691)	0.029	0.070	1.50	(1.04-2.16)
Healthy controls (HCs)	8732	5230 (0.599)				
DSP rs2076295	total allele count	G allele	P (ILD+ vs. ILD-)	Pc	OR	95%CI
MPO-AAV with ILD	306	169 (0.552)	0.91	0.91	1.02	(0.75-1.37)
MPO-AAV without ILD	396	217 (0.548)				
			P (vs. HCs)	Pc	OR	95%CI
MPO-AAV	820	445 (0.543)	0.0026	0.0086	1.25	(1.08-1.44)
PR3-AAV	130	75 (0.577)	0.043	0.087	1.43	(1.01-2.03)
MPA	630	346 (0.549)	0.0029	0.0086	1.28	(1.09-1.51)
GPA	212	115 (0.542)	0.12	0.20	1.25	(0.95-1.64)
EGPA	136	73 (0.537)	0.26	0.34	1.22	(0.87-1.71)
HCs	8788	4286 (0.488)				

is much lower in general Japanese population as compared with European populations, and does not account for high prevalence of ILD in Japanese AAV. In this study, we performed association study of other IPF susceptibility genes, *TERT* and *DSP*, to examine whether these are associated with ILD in AAV patients.

Methods: The members of Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis (JPVAS) and Research Committee of Progressive Renal Disease, Ministry of Health, Labour, and Welfare of Japan contributed to this study.

Five hundred and twenty-three patients including 315 MPA, 108 GPA, 68 eosinophilic granulomatosis with polyangiitis (EGPA) and 32 unclassifiable AAV (412 MPO-ANCA positive [MPO-AAV] and 66 PR3-ANCA positive [PR3-AAV]) and 4394 controls were examined. Among MPO-AAV, 163 were positive for ILD and 264 were negative. Genotyping for *TERT* rs2736100 and *DSP* rs2076295 was performed by TaqMan SNP Genotyping Assays. Association was tested by chi-squared test.

Results: Allele frequencies of *TERT* rs2736100A and *DSP* rs2076295G were not significantly different between MPO-AAV with ILD and MPO-AAV without ILD (Table 1). However, when the association of *TERT* was tested in MPO-AAV regardless of the presence/absence of ILD, rs2736100A was significantly increased in MPO-AAV as compared with healthy controls (P=4.3E-05, Pc=5.2E-04, odds ratio [OR] 1.37). This association was also observed in MPA (P=2.2E-04, Pc=0.0013, OR 1.38). Similarly, *DSP* rs2076295G is increased in MPA (P=0.0029, Pc=0.0086, OR 1.28) and MPO-AAV (P=0.0026, Pc=0.0086, OR 1.25) as compared with healthy controls. Other AAV phenotypes were not significantly associated with both SNVs after correction for multiple testing, although a trend for association was observed between EGPA and *TERT* and between PR3-AAV and *DSP*.

Conclusion: *TERT* and *DSP* SNVs were found to be associated with MPO-AAV and MPA for the first time. These results suggest that some susceptibility genes to IPF may be associated with AAV regardless of the presence of ILD.

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Characterizing Arthritis Related to Immune Checkpoint Inhibitors Using Synovial Fluid and Matched Blood

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Monoclonal antibodies against CTLA-4 and PD-1 have revolutionized the field of immuno-oncology over the past decade. These therapies however are limited by immune related adverse events (irAEs) that can affect nearly every organ system. Inflammatory arthritis (irIA) is a common well-recognized irAE, but with a poorly understood pathophysiology that results in limited targeted treatments. Mechanistic insight into disease pathogenesis has been hampered by the lack of animal models, as mice treated with these drugs do not develop significant irAEs. We thus designed a translational study using human samples focused on identifying distinct cells types, and critical signaling pathways involved in promoting irIA.

Methods: We have established a specialty clinic that provides comprehensive clinical evaluation and long-term follow up of patients with suspected rheumatological irAEs. This clinic also enables serial sample collection of synovial fluid and matched blood samples at the time of the patient's first rheumatologic assessment and, when possible, serially before and after the initiation of immunosuppressive therapy. To define distinct cell populations that might be driving irIA pathogenesis and could be used as a diagnostic marker, we leveraged 10X Genomics droplet-based single-cell RNA-sequencing strategies that do not require an *a priori*knowledge of the specific cell populations or signaling components involved. Single-cell TCR analysis was performed in parallel on the same samples using the VDJ enrichment strategy.

Results: Approximately, 25,000 single cells from the synovial fluid of 5 patients with different irIA clinical phenotypes were analyzed. Findings shows that synovial fluid is highly heterogenous in composition and includes diverse

populations of myeloid and dendritic cells in high proportions. Furthermore, distinct CD8+ cytotoxic T cells across disease phenotypes were expanded. Paralleled single T cell receptor analyses identified diverse clonotypes within these expanded lymphocyte subsets, as well as clonotypic expansion within specific cytotoxic CD8+ populations across patients.

Conclusion: Our systems-level approach provides a better understanding of the biological basis of irIA. Importantly, because irIA provides a model to study mechanisms of immune-tolerance, we believe that our translational effort also represents a unique opportunity to study proximate events leading to autoimmunity in humans.

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Abstract Number: 1957

Aggregation of Functional Variants in *NOTCH4* Gene Increases SSc Risk

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SESSION INFORMATION

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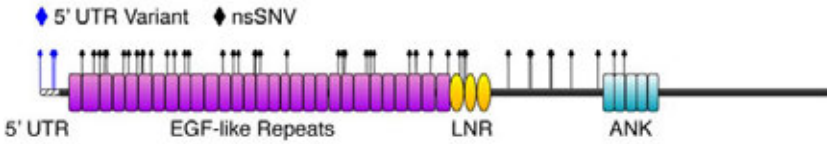
Background/Purpose: Genetic studies of common variants in scleroderma (systemic sclerosis, SSc) have identified several susceptibility loci increasing SSc risk. Most of these common variants are in the non-coding region and

Table 1. SKAT of the top 10 genes with functional variants in overall SSc

Chromosome	Gene Name	SKAT P-value	SKAT P-value$_{Corr}$	# Markers Used
6	NOTCH4	0.00099	0.032	49
12	SOX5	0.007	0.22	9
6	HLA-DQB1	0.01	0.3	33
6	HLA-DPA1	0.01	0.3	36
6	HLA-DRB1	0.01	0.3	2
6	ANKS1A	0.03	0.81	31
6	HLA-DPB1	0.03	0.81	27
6	PSORS1C1	0.05	1	29
6	HLA-DQA1	0.05	1	29
6	PRDM1	0.05	1	25

Figure 1. Schematic of NOTCH4 gene and the SSc associated variants



thus have a relatively minor effect size and are not able to fully account for the heritability of SSc. The risk accorded by rare and functional variants is presumed to be higher and could be part of the missing heritability.

Methods: We selected all SSc-associated loci at p-value< 0.00001 from the GWAS catalog, an NHGRI-EBI catalog of published genome-wide association studies and genes identified in candidate gene studies that were independently replicated. 26 genes were selected and sequenced using next generation sequencing technology in 379 SSc patients and 411 unaffected controls of Africa. Variants were selected for testing if they were missense, splice site or InDels and based on CADD score < 15 for synonymous and UTR variants. Association testing was performed using sequence kernel association test (SKAT). Significance threshold for p-value (P) was set at P< 0.002 after Bonferroni's multiple testing correction.

Results: After multiple testing correction only *NOTCH4* (Neurogenic Locus Notch Homolog Protein 4) gene was statistically significantly associated with SSc (P=0.00099, P_{corr}=0.03) with an increased burden of functional variants (Table1). We used CMC test to confirm the *NOTCH4* association and the P remained significant (CMC P=0.01, 100000 permutations). Majority of the variants were present on the extracellular domain of NOTCH4 (Figure 1). On comparing the phenotypic subsets of SSc, the *NOTCH4* association was strongest in the diffuse skin subset (P=0.001) and interstitial lung disease subset of SSc (P=0.0003).

Conclusion: Aggregation of functional variants in genes previously implicated with SSc provides new approaches to understand SSc pathogenesis. Understanding the functional role of these *NOTCH4* functional variants will increase our understanding of SSc and SSc-associated interstitial lung disease.

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Abstract Number: 1958

Contribution of *MOCS* on Xanthinuria Type III and Its Clinical Significance for Screening

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Xanthinuria is a rare inherited disorder of purine metabolism (1 in 69,000). In the first step, determination of serum and urinary uric acid and purine profile is

important to establish the diagnosis of xanthinuria. Second, xanthinuria is typed using urinary metabolomics. Finally, the results are confirmed by molecular genetics.[1] Here, we aimed to identify genetic variants in the xanthiuria patient using whole-exome sequencing (WES) and evaluated its functional variants.

To distinguish the types of HX, allopurinol loading test and invasive intestinal or liver biopsy have been traditionally used because XDH/XO activity in humans is expressed only in the small intestine and liver.

Methods: 43-year-old female (Roma ethnic group) visited the outpatient clinic. She was diagnosed as xanthinuria based on biochemical lab data (serum uric acid 70 μmol/L, FE-UA: 8.6%, urinary hypoxanthine 52.6 mmol/molCr and urinary xanthine 186.3 mmol/molCr). Conventional genotyping of *XDH*/*XO*, *AOX* and *MOCOS* does not find the causal variant. WES and corresponding downstream analyses were performed for the discovery of coding causal variants further evaluation and we compared the result to WES of 31 hypouricemia patients in Korean.

Results: Considering its prevalence and recessive inheritance, 34 candidate variants were identified after filtering out allele frequency threshold in Non-Finish European. Based on known gene list, homozygote mutation of p.Leu19Phe in *MOCS2* (MIM : 603708) was identified for the causal variants. Functional prediction tool indicated that the variants was found to be damaging (0.58, Polyphen2), disease causing (0.686, Mutation Taster) and CADD score of 16.62.

After investigating 31 hypouricemic Korean patients for the replication, we found a truncating p.Arg132* variant of *MOCS1* (MIM: 603707) in patients who have homozygous variants of *SLC22A12.*

Conclusion: This shows the value of *MOCS* genes for xanthinuria for the first time. Early genetic identification may prevent acute kidney injury or nephrolithiasis.

Disclosure: S. Cho, None; **B. Stiburkova**, None.

Abstract Number: 1959

Pleiotropy of Systemic Lupus Erythematosus (SLE) Risk Alleles: Association with Increased Risk for Type 1 Diabetes (T1D) Complications Through a *PTPN22* Polymorphism

Vivian Kawai ,[1] Mingjian Shi,[1] Qiping Feng,[2] Cecilia Chung,[1] Ge Liu,[2] Nancy Cox,[2] Dan Roden,[2] C. Michael Stein,[1] and Jonathan Mosley[2], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with SLE have increased risk of cardiovascular events and a higher prevalence of metabolic conditions compared to the general population. Inflammation is a strong component of the pathogenesis of SLE, cardiometabolic disorders, and other autoimmune diseases; thus, we examined the hypotheses that genetic predisposition to SLE may increase the risk for: 1) cardiometabolic outcomes and 2) other autoimmune diseases.

Methods: To test these hypotheses, we selected 47 independent SNPs ($R^2 < 0.10$) in 36 loci with significant associations with SLE ($P < 5x10^{-8}$) in the largest genetic study performed in Caucasians. In the Vanderbilt DNA biobank (BioVU), forty-one SNPs had a call rate ≥ 95% and were used to construct a weighted genetic risk score (wGRS) for SLE to: 1) test its association with 9 cardiometabolic disorders (Table 1) and 2) examine the relationship between the wGRS and all phenotypes present in 29,892 Caucasian patients in a global phenome wide association study (PheWAS) adjusting for median age in the electronic health record, sex, and 5 principal components. A P-value ≤ 0.006 was considered significant for the 9 selected cardiometabolic diseases, and a false discovery rate (FDR) < 0.1 was used in the global PheWAS. In addition, a set of independent SLE-associated SNPs ($R^2 < 0.05$) was used to perform a two-sample inverse-variance weighted regression (IVWR) meta-analysis using publicly available summary statistics

Table 1. Association of the wGRS for SLE with 9 clinical diagnosis (or proxies) using a PheWAS and IVWR approach

Table 1: Association of the wGRS for SLE with 9 clinical diagnosis (or proxies) using a PheWAS and IVWR approach								
	PheWAS				IVWR			
Disease	# cases	# controls	Odds Ratio [95% CI]	P-val	Study/Cohort	# SNP	Odds Ratio [95%CI]	P-val
Atrial fibrillation	5195	14453	0.96 [0.92, 0.99]	0.025	AFGEN	37	1.01 [0.99, 1.20]	0.310
Ischemic stroke	1399	23097	1.05 [0.99, 1.11]	0.092	METASTROKE	37	1.02 [0.99, 1.04]	0.143
Coronary atherosclerosis	8720	16746	1.00 [0.97, 1.03]	0.896	CARDIOGRAM	37	1.03 [1.00, 1.05]	0.066
Essential hypertension	16488	11767	0.99 [0.97, 1.02]	0.710	VMP (Systolic Blood Pressure)	37	1.08 [0.96, 1.21]	0.222
Hyperlipidemia	13038	15039	1.01 [0.98,1.04]	0.536	GLGC (LDL)	30	0.99 [0.97, 1.00]	0.076
Chronic renal failure	3486	21257	1.04 [1.00, 1.08]	0.038	CKD Gen	30	0.99 [0.96, 1.02]	0.520
Overweight	5325	22965	1.00 [0.97, 1.03]	0.834	GIANT (Waist circumference)	32	1.00 [0.99, 1.01]	0.671
Type 2 diabetes	6309	19612	1.03 [1.00, 1.06]	0.076	DIAGRAM	37	1.02 [0.99, 1.05]	0.204
Type 1 diabetes	1456	19571	1.07 [1.01, 1.12]	0.021	T1DGC	27	1.24 [1.02, 1.51]	0.028

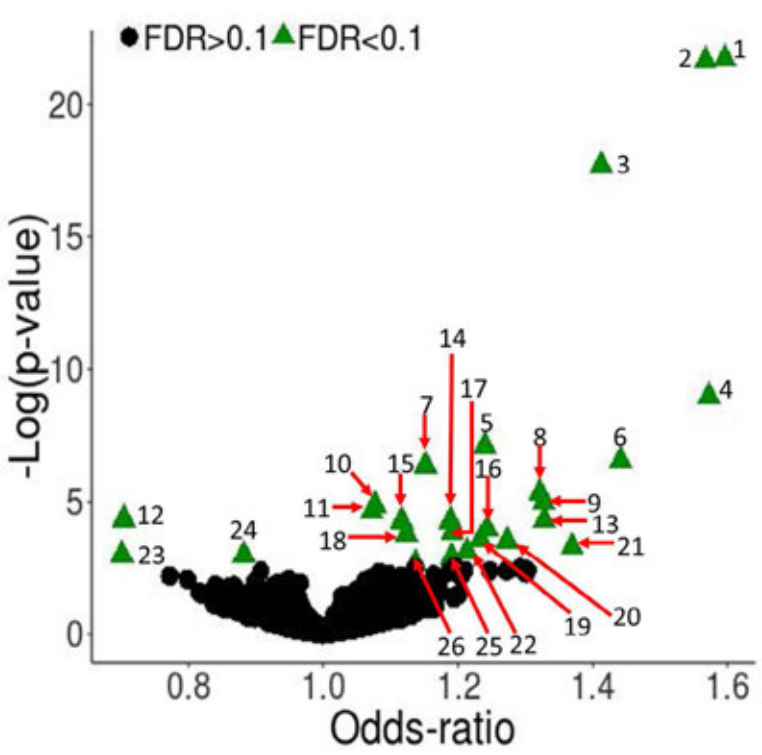

Figure 1: Clinical diagnoses associated with a wGRS for SLE

#	Condition	OR	P
1	Systemic lupus erythematosus	1.60	2.00E-22
2	Discoid lupus erythematosus	1.57	2.33E-22
3	Diffuse diseases of connective tissue	1.41	2.01E-18
4	Systemic sclerosis	1.57	1.07E-09
5	Other immunological findings	1.24	7.83E-08
6	Type 1 diabetic retinopathy	1.44	2.80E-07
7	Erythematous conditions	1.15	4.19E-07
8	Chronic hepatitis	1.32	4.56E-06
9	Raynaud's syndrome	1.33	1.00E-05
10	Hypothyroidism NOS	1.08	1.32E 05
11	Hypothyroidism	1.07	2.28E-05
12	Benign neoplasm of connective & soft tissue	0.70	4.31E-05
13	Sicca syndrome	1.33	4.85E-05
14	Diabetic retinopathy	1.19	5.03E-05
15	RA & related inflammatory polyarthropathies	1.12	5.13E-05
16	Chronic lymphocytic thyroiditis	1.24	1.07E-04
17	Thyroiditis	1.19	1.47E-04
18	Rheumatoid arthritis	1.12	1.62E-04
19	Chronic lymphocytic thyroiditis	1.23	2.53E-04
20	Type 1 diabetes nephropathy	1.27	2.86E-04
21	Acquired hemolytic anemias	1.37	5.01E-04
22	Graves' disease	1.21	7.47E-04
23	Chronic lymphoid leukemia	0.70	9.82E-04
24	Melanomas of skin	0.88	1.00E-03
25	Hypoglycemia	1.19	1.18E-03
26	Plasma protein metabolism disorder	1.14	2.09E-03

Figure 1. Clinical diagnoses associated with a wGRS for SLE

for the 9 cardiometabolic phenotypes of interest (or proxies). Egger regression was performed to test for horizontal pleiotropy with phenotypes in which the IVWR analysis was significant.

Results: There was no significant association between the SLE wGRS and the 9 selected cardiometabolic phenotypes (all P values >0.006, Table 1). In the global PheWAS the wGRS was associated with several autoimmune phenotypes including SLE (OR 1.6, $P=2x10^{-22}$), systemic sclerosis, hypothyroidism, Grave's disease, rheumatoid arthritis, and several T1D phenotypes (Fig. 1). The IVWR analyses comparing the genetics of SLE with that of the 9 selected phenotypes was significant for T1D (P=0.028, Table 1; Fig. 2). In the Egger analysis, the intercept term of the regression was not significant (P=0.49) suggesting no horizontal pleiotropy between SLE and T1D. Exclusion of the SLE-variant rs2476601, a SNP in *PTPN22*, in the T1D analysis (Fig. 2) attenuated the results of the IWVR analysis (P=0.06).

Conclusion: We found evidence suggesting pleiotropy between genetic predisposition for SLE and several autoimmune disorders as well as diabetic retinopathy and nephropathy. In the IVWR analysis, genetic predisposition to SLE was associated with increased risk of T1D, in part through a common missense variant in *PTPN22* known to be associated with several autoimmune phenotypes.

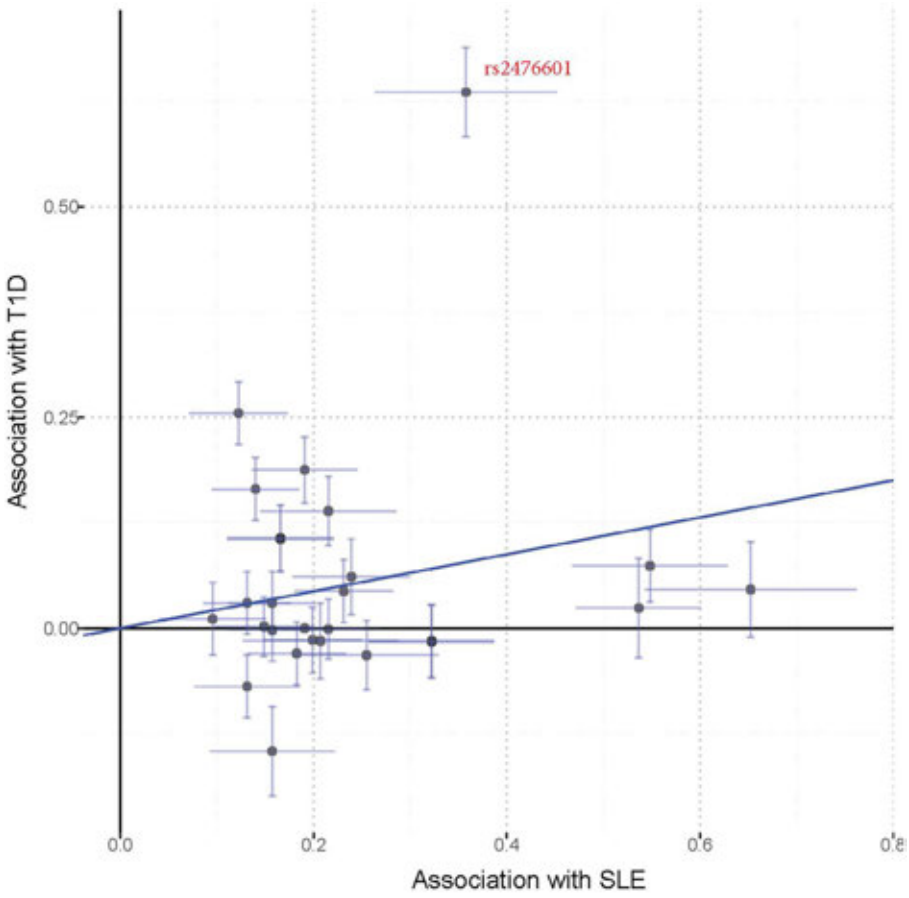

Figure 2. Scatter plot comparing the association between the genetic predisposition for SLE and the risk for T1D for 27 SNPs significantly associated with SLE in Caucasians.

Disclosure: V. Kawai, NIH K23GM117395, 2, NIH NIGMS K23GM117395, 2, NIH/NIGMS K23GM117395, 2, NIH, 2, NIH, 2; **M. Shi**, None; **Q. Feng**, None; **C. Chung**, Lupus Research Alliance, 2, NCATS/NIH CTSA grant ULTR000445, 2, Rheumatology Research Foundation, 2, Veterans Health Administration CDA, 2; **G. Liu**, None; **N. Cox**, None; **D. Roden**, American Heart Association (18SFRN342300)89, 2, American Heart Association (18SFRN342300)89, 2; **C. Stein**, None; **J. Mosley**, None.

Abstract Number: 1960

Pleiotropy of Genetic Predisposition to Rheumatoid Arthritis Increases the Risk for Autoimmune Disease

Vivian Kawai ,[1] Mingjian Shi,[1] Qiping Feng,[2] Cecilia Chung,[1] Ge Liu,[2] Nancy Cox,[2] Dan Roden,[2] C. Michael Stein,[1] and Jonathan Mosley[2], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville

Table 1: Association of the wGRS for SLE with 9 clinical diagnoses (or proxies) using a PheWAS and IVWR approach

Disease	PheWAS				IVWR			
	# cases	# controls	Odds Ratio [95% CI]	P-val	Study/Cohort	# SNP	Odds Ratio [95%CI]	P-val
Atrial fibrillation	5195	14453	0.98 [0.94, 1.02]	0.250	AFGEN	83	1.00 [0.98, 1.02]	0.969
Ischemic stroke	1399	23097	1.02 [0.97, 1.08]	0.392	METASTROKE	82	1.02 [0.99, 1.05]	0.273
Coronary atherosclerosis	8720	16746	0.99 [0.96, 1.02]	0.489	CARDIOGRAM	83	1.02 [0.99, 1.04]	0.181
Essential hypertension	16488	11767	0.98 [0.95, 1.01]	0.131	VMP (Systolic BP)	82	1.01 [0.92, 1.12]	0.817
Hyperlipidemia	5876	15039	1.00 [0.97, 1.03]	0.988	GLGC (LDL)	43	1.00 [0.98, 1.03]	0.710
Chronic renal failure	3486	21257	1.01 [0.97, 1.05]	0.580	CKD Gen	41	1.01 [0.97, 1.06]	0.547
Overweight	5325	22965	0.99 [0.96, 1.02]	0.542	GIANT (Waist circumference)	43	1.00 [0.99, 1.01]	0.886
Type 2 diabetes	6309	19612	1.02 [0.99, 1.05]	0.599	DIAGRAM	83	1.04 [1.02, 1.06]	<0.001
Type 1 diabetes	1456	19571	1.10 [1.04, 1.16]	<0.001	T1DGC	38	1.81 [1.51, 2.17]	<0.001

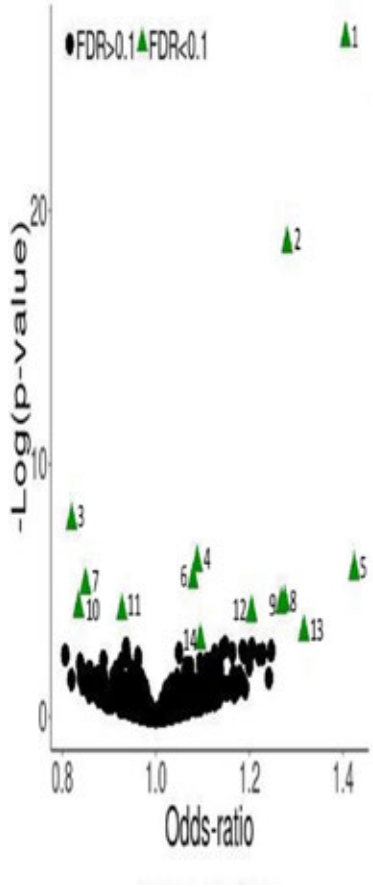

Figure 1: Clinical diagnoses associated with a wGRS for RA

#	Condition	OR	Pval
1	RA	1.41	1.54E-27
2	RA & related inflammatory polyarthrop	1.28	2.04E-19
3	Multiple sclerosis	0.82	1.73E-08
4	Hypothyroidism NOS	1.09	8.21E-07
5	Type 1 diabetic retinopathy	1.42	1.59E-06
6	Hypothyroidism	1.08	3.51E-06
7	Lack of coordination	0.85	5.95E-06
8	Chronic lymphocytic thyroiditis	1.28	3.22E-05
9	Chronic thyroiditis	1.27	3.69E-05
10	Other demyelinating diseases of CNS	0.82	4.55E-05
11	Palpitations	0.89	6.85E-05
12	Thyroiditis	1.20	7.27E-05
13	Systemic sclerosis	1.32	4.33E-04
14	Type 1 diabetes	1.10	9.82E-04

Figure 1. Clinical diagnoses associated with wGRS for RA

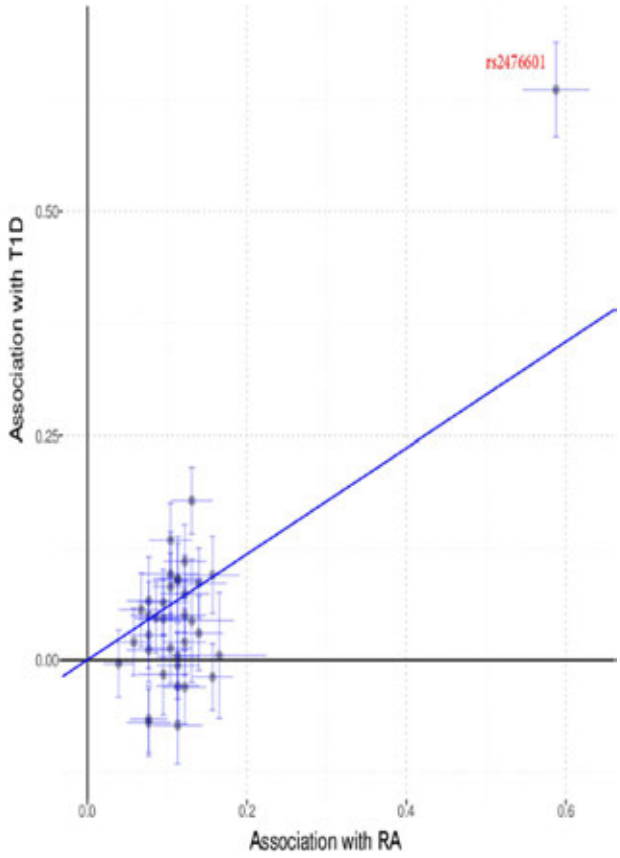

Figure 2. Scatter plot comparing the association between the genetic predisposition for RA and the risk for T1D for SNPs significantly associated with RA in Caucasians.

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disorder that is associated with increased risk of cardiovascular disease, cardiometabolic disorders, and autoimmune disease. Thus, we examined the hypothesis that genetic predisposition to RA increases the risk for cardiovascular disease, cardiometabolic disorders, and other autoimmune disorders.

Methods: To test this hypothesis, we selected 102 independent SNPs ($R^2 < 0.10$) that were significantly associated with RA ($P < 5x10^{-8}$) in the largest transethnic meta-analysis published. In the Vanderbilt DNA biobank (BioVU), ninety-five SNPs had a call rate ≥ 95% and were used to construct a weighted genetic risk score (wGRS) for RA to: 1) test its association with 9 cardiometabolic disorders (Table 1) and 2) perform a global phenome wide association study (PheWAS) examining the relationship between the wGRS and all phenotypes present in 29,892 Caucasian patients adjusting for median age in the electronic health record, sex, and 5 principal components. A P-value ≤ 0.006 was considered significant for the 9 selected cardiometabolic diseases and a false discovery rate (FDR) < 0.1 was used in the global PheWAS. In addition, a set of independent RA-associated SNPs ($R^2 < 0.05$) was used to perform a two-sample inverse-variance weighted regression (IVWR) meta-analysis using publicly available summary statistics for the 9 cardiometabolic phenotypes of interest (or proxies). Egger regression was performed to test horizontal pleiotropy with phenotypes in which the IVWR analysis was significant.

Results: Among the 9 cardiometabolic phenotypes selected, the wGRS for RA was significantly associated with type I diabetes (T1D) ($P=9.82x10^{-4}$, Table 1). In the global PheWAS, the wGRS was associated with increased risk for several autoimmune phenotypes including RA (OR=1.41, $P=1.54x10^{-27}$), thyroiditis, systemic sclerosis, and T1D phenotypes, and with protection against multiple sclerosis and demyelinating disorders (Fig. 1). In the IVWR analysis, RA was significantly associated with type 2 diabetes (T2D) ($P=4.04x10^{-4}$, Table1), but the association was abrogated when an RA SNP in the HLA region (rs9268839) was excluded from the analysis (P=0.133). T1D was also significantly associated with RA in the IVWR analysis ($P=1.93x10^{-10}$, Table 1, Fig. 2) with the Egger intercept term suggesting horizontal pleiotropy (P< 0.001). When rs2476601 (an RA SNP in *PTPN22*) was excluded, the IVWR analysis remained significant ($P=1x10^{-4}$) and the intercept term in the Egger regression no longer showed evidence of horizontal pleiotropy (P=0.611).

Conclusion: We found evidence suggesting pleiotropy between genetic predisposition for RA and several other autoimmune disorders including T1D. The IVWR analysis showed that genetic predisposition to RA was associated with increased risk of T1D, even after the exclusion of a common variant in *PTPN22* known to be associated with different autoimmune disorders.

Disclosure: V. Kawai, NIH K23GM117395, 2, NIH NIGMS K23GM117395, 2, NIH/NIGMS K23GM117395, 2, NIH, 2, NIH, 2; **M. Shi**, None; **Q. Feng**, None; **C. Chung**, Lupus Research Alliance, 2, NCATS/NIH CTSA grant ULTR000445, 2, Rheumatology Research Foundation, 2, Veterans Health Administration CDA, 2; **G. Liu**, None; **N. Cox**, None; **D. Roden**, American Heart Association (18SFRN342300)89, 2, American Heart Association (18SFRN342300)89, 2; **C. Stein**, None; **J. Mosley**, None.

Abstract Number: 1961

Mitochondrial DNA Sub-haplogroup H1 Influences the Risk of Rapidly Progressive Osteoarthritis of the Knee: Data from the Osteoarthritis Initiative

Alejandro Duran-Sotuela ,[1] Mercedes Fernandez-Moreno,[2] María E. Vázquez-Mosquera,[3] Paula Ramos-Louro,[1] Andrea Dalmao-Fernández,[3] Sara Relaño,[1] Natividad Oreiro,[1] Francisco J. Blanco,[1] and Ignacio Rego-Pérez[1], [1]Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). As Xubias, 15006. A Coruña, España, A Coruña, Spain, [2]Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). As Xubias, 15006. A Coruña, España. CIBER-BBM, A Coruña, Spain, [3]Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). As Xubias, 15006. A Coruña, España, A Coruña, Galicia, Spain

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: There is a need to identify the rapid progressive phenotype of Osteoarthritis (OA). Our aim is to analyze the effect of mitochondrial haplogroups in the risk of suffering rapid progressive knee OA in patients from the Osteoarthritis Initiative (OAI).

Methods: Caucasian patients from the OAI were classified into three groups based on previous criteria: i) Rapid progressors (RP), with baseline KL grade 0-I in at least one knee and increase up to KL≥III during 48 month follow-

Table 1. Regression model with two categories (Rapid vs Non-rapid pool) with all the variables influencing the rapidly progressive knee OA phenotype in Caucasian patients of the OAI

Variables	P-Value	OR	95% CI	
Gender (Female)	0,004*	1,644	1,176	2,297
Age	<0,001*	1,044	1,025	1,063
BMI	<0,001*	1,044	1,048	1,126
Contralateral OA at baseline	<0,001*	1,044	1,61	3,123
Previous injury	<0,001*	1,044	1,699	3,312
WOMAC (total)	<0,001*	1,044	1,006	1,02
H subtypes (N=2092)	0,31			
Non-H (1340)	Reference group			
H1 (264)	0,042*	1,573	1,017	2,435
H3 (83)	0,839	1,083	0,503	2,329
H5 (62)	0,835	0,894	0,311	2,571
H* (343)	0,832	0,953	0,611	1,487

WOMAC: Western Ontario and McMaster Universities Arthritis Index; BMI: body mass index; CI: Confidence Interval; OR: Odds Ratio; H*: includes minor haplogroup H subtypes; (*): statistical significance declared at $p < 0.05$

Table 2. Regression model with two categories (Rapid vs Non-rapid pool excluding Non-Progressors) with all the variables influencing the rapidly progressive knee OA phenotype in Caucasian patients of the OAI

Variables	P-Value	OR	95% CI	
Gender (Female)	0,924	0,98	0,651	1,476
Age	<0,001*	1,061	1,036	1,086
BMI	0,098	1,039	0,993	1,087
Contralateral OA at baseline	0,324	1,223	0,82	1,826
Previous injury	0,079	1,434	0,959	2,144
WOMAC (total)	0,074	1,008	0,999	1,017
H subtypes (N=502)	0,246			
Non-H (310)	Reference group			
H1 (72)	0,037*	1,797	1,036	3,117
H3 (19)	0,354	1,603	0,591	4,351
H5 (14)	0,684	0,776	0,228	2,638
H* (87)	0,943	1,019	0,6	1,732

WOMAC: Western Ontario and McMaster Universities Arthritis Index; BMI: body mass index; CI: Confidence Interval; OR: Odds Ratio; H*: includes minor haplogroup H subtypes; (*): statistical significance declared at $p < 0.05$

up; ii) Non-rapid progressors (NRP), with baseline KL grade 0-I in at least one knee and increase up to KL=II during 48 month follow-up; iii) Non-progressors (NP), with KL grade 0-I at baseline in at least one knee and bilaterally stable during the 48-month follow-up period.

Also, these groups were re-categorized into two groups: Rapid and Non-Rapid (pooling NRP and NP). Once selected, we performed regression models adjusting by clinical variables including gender, age, body mass index (BMI), contralateral OA, previous injury in the target knee and total WOMAC. mtDNA haplogroups and major H sub-haplogroups

(H1, H3, H5 and H*) were previously assigned using sequencing techniques. Analysis were performed with IBM SPSS Statistics v24.

Results: We analyzed data from 2092 patients splitted on 181 RP (8,7%), 321 NRP (15,3%) and 1590 NP (76%). The comparison between RP and NP revealed that all risk factors showed significant differences, including gender (female) (OR=1,934; 95%CI: 1,377 – 2,717; p< 0,001), age (OR=1,040; 95%CI: 1,021 – 1,060; p< 0,001), BMI (OR=1,113; 95%CI: 1,073 – 1,154; p< 0,001), contralateral OA (OR=2,710; 95%CI: 1,938 – 3,773; p< 0,001), previous injury of target knee (OR=2,849; 95%CI: 2,032 – 4,000; p< 0,001) and total WOMAC (OR=1,016; 95%CI: 1,008 – 1,023; p< 0,001); however, these significant differences were also observed between NRP and NP. Regarding mtDNA haplogroups, compared with haplogroup H, the haplogroup J showed a lower frequency in the RP in relation to NP, but this difference did not reach the statistical significance (OR=0,526; 95%CI: 0,251 – 1,101; p=0,088). When the analysis included major H subtypes, sub-haplogroup H1 appeared over-represented in the RP in relation to both NP (OR=1,533; 95%CI: 0,981 – 2,934; p=0,061) and NRP (OR=1,686; 95%CI: 0,984 – 2,889; p=0,057).

A second type of analysis included the re-categorized variable and, in addition to the significant association of the classical risk factors, the sub-haplogroup H1 appeared significantly associated as a risk factor for rapid progression (OR= 1,573; 95%CI: 1,017 – 2,435; p=0,042) (Table 1). Finally, we repeated this analysis but excluding NP from the Non-Rapid pool. Age was the only significant risk factor (OR=1,061; 95%CI: 1,036 – 1,086; p< 0,001), and the sub-haplogroup H1 remained significantly associated as a risk factor for rapid progression (OR=1,797; 95%CI: 1,036 – 3,117; p=0,037) (Table 2).

Conclusion: The mtDNA haplogroups, more specifically the major sub-haplogroup H1, increase the risk of rapidly progressive OA of the knee. The assignment of this mitochondrial genetic sub-haplogroup could be useful as complementary genetic biomarker for the early identification of this OA phenotype.

Disclosure: A. Duran-Sotuela, None; **M. Fernandez-Moreno**, None; **M. Vázquez-Mosquera**, None; **P. Ramos-Louro**, None; **A. Dalmao-Fernández**, None; **S. Relaño**, None; **N. Oreiro**, None; **F. Blanco**, None; **I. Rego-Pérez**, None.

Abstract Number: 1962

Whole Transcriptome Analysis Maps Proinflammatory and Procoagulant Pathways in aPL Treated HUVECs

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid syndrome is an autoimmune thrombophillia characterized by recurrent thromboembolism and or pregrancy morbidity in the presence of antiphospholipid antibodies (aPL), which recognize either a serum apolipoprotein, known as β2glycoprotein I (β2GPI), or other PL-binding proteins such as prothrombin. Complexes of anti-β2GPI/β2GPI activate platelets, monocytes and endothelial cells, probably by activating TLR4 and

TLR6 leading eventually to NFκB and MAPK activation resulting to Tissue Factor (TF) and proinflammatory cytokine expression. Therefore, we assessed the whole transcriptome of endothelial cells that have been stimulated with anti-β2GPI/β2GPI.

Methods: Human umbilical Vein Endothelial cells (HUVECs) were isolated from 4 Healthy control women upon delivery. Healthy donor HUVEC were stimulated with IgG isolated from APS patients with high anti-β2GPI titers or IgG from healthy individuals in the presence of β2GPI. Consequently, total mRNA was isolated, cDNA libraries were created and whole transcriptome sequencing (RNASeq) was performed. Gene expression data were validated in protein levels with immunocytochemistry and immunohistochemistry in placenta tissues from APS patients and healthy individuals. Data underwent KEGG Pathway Database and Gene Ontology analysis.

Results: Whole transcriptome analysis of HUVECs stimulated with anti-β2GPI/β2GPI complexes revealed 680 differentially expressed genes, among which 377 were upregulated and 303 downregulated in the aPL treated endothelial cells. Characteristic examples of the upregulated genes are IL-6, IL-8, VCAM1, SELE and TGFB2 and TGFBR1. Bioinformatics analysis revealed that the upregulated genes belong mainly to the cytokine-cytokine receptor interaction (hsa053323), MAPK signaling pathway (hsa04010), TNF signaling pathway (hsa04668) and NOD-like receptor pathway (hsa04621). Characteristic examples of the downregulated genes include the CBX4, CBX8, BCOR and HDAC7 genes. Several proteins encoded by these genes play role in the epigenetic modification of DNA. Immunohistochemical staining on placenta biopsies from APS patients and healthy individuals for IL-6, IL-8, IL-18, NFkB, TF, TNF-a, E-SELECTIN, MAPK8, TGFB2 and TGFBR1 showed increased intensity in the signal of endothelial cells on APS specimens validating thus the RNASeq results in the tissues.

Conclusion: RNASeq of endothelial cells treated with anti-β2GPI/β2GPI reveals a thoroughly analysed proinflamatory and procoagulant phenotype. Moreover, differential expression of DNA modifying proteins suggests the possible epigenetic regulation of gene expression on endothelial cells in APS syndrome. Ongoing experiments aim to analyze histone acetylation and methylation status of the promoters of the selected genes that were shown to be differentially expressed.

Disclosure: M. Patsouras, None; **P. Karagianni**, None; **M. Agelopoulos**, None; **S. Foutadakis**, None; **E. Alexopoulou**, None; **P. Vlachoyiannopoulos**, None.

Abstract Number: 1963

Combining Clinical and Candidate Gene Data into a Risk Score for Azathioprine-Associated Leukopenia in Routine Clinical Practice

Prathima Anandi,[1] Alyson Dickson,[2] Qiping Feng,[1] Wei-Qi Wei,[2] William Dupont,[2] Dale Plummer,[2] Ge Liu,[1] Katherine Barker,[2] Vivian Kawai,[2] Kelly Birdwell,[2] Nancy Cox,[1] C. Michael Stein,[2] Adriana Hung,[2] and **Cecilia Chung** [3], [1]Vanderbilt University Medical Center, Nashville, [2]Vanderbilt University Medical Center, Nashville, TN, [3]Vanderbilt University, Nashville, TN

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Azathioprine is a widely-used drug for the treatment of rheumatic diseases, inflammatory bowel disease, and for organ transplantation. However, treatment is often limited by serious adverse events, such

Table 1: Clinical characteristics: patients with leukopenia compared with controls

	Cases (n=216)	Controls (n=209)	Odds Ratio (95% CI)	p-value
Age in years, median (IQR)	46 (37 - 56)	51 (39 - 61)	0.97 (0.96-0.99)	0.001
Sex (Female), n (%)	125 (58%)	114 (54%)	1.17 (0.71-1.91)	0.54
Weight (in kilograms)	76 (65 - 89)	84 (68 - 101)	0.98 (0.97-0.99)	0.003
Indications				
SLE	22 (11%)	10 (5%)	Reference	
Autoimmune disease other than lupus	50 (23%)	88 (42%)	0.36 (0.15-0.86)	0.021
IBD	42 (19%)	58 (28%)	0.27 (0.11-0.69)	0.006
Organ transplant	95 (44%)	31 (15%)	1.82 (0.72-4.62)	0.21
Other indications	7 (3%)	22 (11%)	0.25 (0.07-0.83)	0.02
Azathioprine daily dose (mg/day), median (IQR)	100 (50 -150)	100 (50 - 150)	1.00 (1.00-1.00)	0.40
Concurrent use of allopurinol or febuxostat, n (%)	10 (5%)	3 (1%)	4.45 (0.97-20.50)	0.06
Concurrent use of other immunosuppressants[a], n (%)	58 (27%)	36 (17%)	1.11 (0.64-1.93)	0.70
TPMT intermediate metabolizer[b]	21 (10%)	14 (7%)	2.19 (1.01-4.76)	0.048

[a]Immunosuppressant: mycophenolate, leflunomide, tacrolimus, cyclophosphamide, methotrexate.
[b]*TPMT* haplotype, TPMT activity genotype

Table 2: Genetic variants included in the prediction of leukopenia

Gene	SNPs
TPMT	rs12663332, rs2842934, rs34889843, rs2518463, rs2518471, rs2842936, rs2842938, rs3898137, and rs9477634
NUDT15	rs12429348, rs17071168, rs2031775, rs7996580, rs7997347
XDH	rs17011368, rs207440, rs2295475, rs7575607, rs1884725, rs2163058, rs4407290, rs45523133
MOCOS	rs1057251, rs3744900, rs594445, and rs678560
ABCC4	rs4148437, rs11568681, and rs3765534
ITPA	rs8362, rs7270101, and rs9101
AOX1	rs2293525 and rs3731722
GST	rs1138272, rs2234951, rs1695, and rs2180314

as leukopenia. Our ability to predict azathioprine-associated leukopenia is limited to the evaluation of the enzyme thiopurine methyl transferase (TPMT), either by functional assays or by the identification of variants in the gene *TPMT* which encodes it. We hypothesize that a risk score composed of multiple clinical factors and variants in selected candidate genes—in addition to TPMT—could improve the prediction of azathioprine-associated leukopenia.

Methods: This is a case-control study that used de-identified records from BioVU, a clinical practice-based biobank at a tertiary medical center to identify 425 Caucasian patients who received prescriptions for azathioprine. Subjects with a leukocyte count of less than 4,000 WBC/μL while receiving prescriptions for azathioprine were classified as cases. Subjects receiving prescriptions for azathioprine who did not develop leukopenia were classified as controls.

We reviewed the clinical records, collected clinical variables (age, sex, weight, clinical indication for azathioprine use, concurrent prescription of other medications, and azathioprine daily dose) and genotyped 71 genetic candidates identified through literature and database review. Genotyping of 60 single nucleotide polymorphisms passed quality control. We built two scores using the coefficients from multivariate regressions; leukopenia was the dependent variable. The first model was a logistic regression including TMPT status, age, and sex. The second model included TPMT status, age, sex, additional clinical variables listed above, and genetic candidates. To avoid overfitting, we used ridge regression, which uses a standard cross-validated penalty to shrink the coefficients of the covariates.

Table 2: Genetic variants included in the prediction of leukopenia

Gene	SNPs
TPMT	rs12663332, rs2842934, rs34089943, rs2518463, rs2518471, rs2842936, rs2842938, rs3898137, and rs9477634
NUDT15	rs12429348, rs17071168, rs2031775, rs7996580, rs7997347
XDH	rs17011368, rs207440, rs2295475, rs7575607, rs1884725, rs2183058, rs4407290, rs45523133
MOCOS	rs1057251, rs3744900, rs594445, and rs678560
ABCC4	rs4148437, rs11568681, and rs3765534
ITPA	rs8382, rs7270101, and rs9101
AOX1	rs2293525 and rs3731722
GST	rs1138272, rs2234951, rs1695, and rs2180314
IMPDH1	rs2228075
IL6	rs2228043
CXCL2	rs9131
HLA-DQA1	rs2647087
FSTL5	rs3749598
CMAHP	rs1986731
ST3GAL1	rs2945770
FBLN2	rs9843344
NRXN3	rs17109516

Results: 216 patients had azathioprine-associated leukopenia and 209 were control subjects. Younger age, lower weight, a diagnosis of systemic lupus erythematosus or organ transplant, and being a carrier of the *TPMT* haplotype corresponding to intermediate metabolizer status were significantly associated with leukopenia (Table 1). The area under the ROC curve (AUC) of a score based on a regression that included TPMT status, age, and sex was 0.59 (95% C.I.: 0.54-0.64). After shrinkage, the ridge model included 11 clinical and 47 genetic candidates (Table 2); the AUC of the score from that model increased to 0.77 (95% C.I.:0.73-0.82).

Conclusion: This proof-of-concept study investigates the utility of adding clinical and genetic variables to TMPT to improve discrimination of the risk for azathioprine-associated leukopenia. After shrinkage, we were able to show that a combined model, including clinical and genetic variants, improved our ability to predict leukopenia. Further studies in larger populations with independent replications are needed to further develop prediction scores that are useful for routine clinical practice.

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Abstract Number: 1964

A Role for Microbiota in the Pathophysiology of Takayasu Arteritis (TAK) and Giant Cell Arteritis (GCA)

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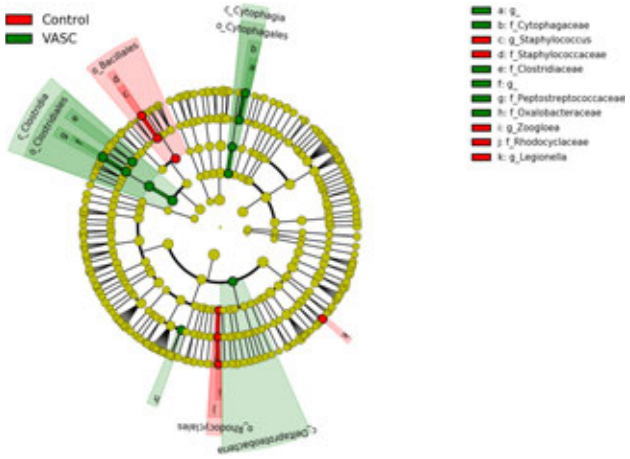

Microbiome profile of TAK patients compared to HD

Background/Purpose: The pathogenesis of Large Vessel Vasculitis (LVV) is not well understood. There is increasing evidence of a close link between intestinal dysbiosis and systemic inflammatory/autoimmune diseases. Gut microbiota has never been studied in LVV. We aimed at comparing the blood microbiota profile of patients with LVV (TAK or GCA) and healthy donors (HD).

Methods: We studied the blood microbiome profile microbiota of 20 patients with TAK, 11 with GCA and 16 HD. The microbiome profile microbiota was assessed by sequencing of the 16S rDNA blood bacterial DNA. Linear Discriminant Analysis (LDA) coupled with effect size measurement (LEfSe) was used to analyse the differences in the microbiome profile between groups.

Results: TAK and GCA patients had a mean age of 45 (23.1; 70.6) and 74.5 (58; 84) years, and were of female gender in 55% and 85%, respectively. Among TAK patients 10 had an active disease and 10 were inactive; among GCA patients, 6 were active and 4 inactive. TAK patients compared to HD showed a specific blood microbiota profile with a significant higher level of the phyla Clostridia (Clostridium saudiense), Cytophagia (Pseudarcella Hirudinis) and Delta-proteobacteria (Bdellovibrio bacteriovorus particularly), whereas Bacillus and Staphylococcus were significantly more abundant in HD ($p< 0.05$) (Figure). Active compared to inactive TAK patients had significantly lower levels of Staphylococcus. TAK microbiota compared to GCA showed significant higher levels of Bacteroidia (LDA >2; $p< 0.05$). In TAK patients, differences in the blood microbiome were also associated with a shift of metabolic functions. TAK patients compared to HD showed a significant increase of porphyrin and chlorophyll pathways. Active compared to inactive TAK patients showed increase of the same pathways. GCA patients did not show a specific blood microbiota profile compared to HD, except for lower levels of Bacteroidia.

Conclusion: patients with TAK showed a specific blood microbiome profile as compared to healthy controls and GCA patients. Among TAK patients, significant changes of blood microbiome profile were found in active as compared to inactive patients, and it was associated with specific metabolic functions.

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Abstract Number: 1965

Determining a Polygenic Risk Score in Pediatric Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a potentially life-threatening autoimmune disease with no cure. The onset of SLE is thought to be the result of environmental events in a genetically susceptible host, yet the underlying genetic architecture of the disease is not fully understood. Pediatric SLE (pSLE) patients have early disease onset and incur more organ damage than adults, and thus may have a larger genetic burden. Confirmed genetic associations with common variants have been demonstrated in many SLE genome wide association studies (GWAS). Examining the polygenic disease score allows us to capture both the number of common SLE risk variants and the magnitude of influence of each genetic variant on SLE predisposition. While a few studies have used a polygenic risk score to explore genetic burden differences in adult SLE patients, this measure has not been reported in pediatric onset SLE.

Methods: All SLE patients included fulfilled at least four of the 11 American College of Rheumatology classification criteria for SLE; pSLE subjects met criteria prior to age 18. Samples collected from 81 SLE patients were sequenced via whole genome sequencing using Illumina HiSeq X Ten. Baseline demographics are reported in Table 1. GWAS data from 1169 juvenile idiopathic arthritis patient genotypes were used as pediatric controls, and publicly available GWAS data from adult SLE women and healthy controls were used as a disease specific comparison group. 238 SLE risk single nucleotide polymorphisms (SNPs) tagging independent previously published and established SLE genetic susceptibility loci were assessed in the study. The risk variants were pruned for SNPs in linkage disequilibrium with PLINK 1.9 software using an r^2 value of 0.2, resulting in 183 SLE risk loci shared between pSLE and JIA controls.

Table 1. Demographic data

	Number of patients	African Ancestry %, (n)	European Ancestry %, (n)	Asian ancestry %, (n)	Amerindian ancestry %, (n)	Median age of onset (years)
Pediatric SLE	81	20 (16)	26 (21)	26 (21)	28 (23)	12
Adult SLE	216	0	100 (216)	0	0	NR
Juvenile Idiopathic Arthritis	1169	NR	NR	NR	NR	NR
Adult Healthy Control	81	0	100 (81)	0	0	NR

For adults, a limited number of 63 risk loci were shared and used to compare pediatric and adult risk. A polygenic risk score was calculated for each subject based on the sum of the product of the natural logarithm of the odds ratio for each association and the number of alleles present in each individual at each risk locus. Cumulative scores were calculated for all subjects. The case and control means and distributions of polygenic risk score were evaluated with the Wilcoxon rank-sum test.

Results: Pediatric-onset SLE patients have a high burden of SLE common risk SNPs, with mean polygenic risk score of 35.9. Comparing to other children with autoimmune diseases, pediatric onset SLE patients also have a significantly higher polygenic risk score than children with juvenile idiopathic arthritis (35.9 vs. 29.9, p value 2.2×10^{-16}). PSLE patients have a similar mean polygenic risk score (11.9) as adult SLE (11.9, p value NS) and higher than healthy adult subjects (11.4, p value 0.002)

Conclusion: Patients with childhood onset SLE have an increased burden of common risk SNPs for SLE when compared to children with non-SLE autoimmune disease. SLE Both childhood and adult-onset SLE have a higher polygenic risk score than adult healthy controls subjects. Childhood onset SLE patients have a polygenic risk score similar to adult onset SLE patient. This may be due to limited number of shared SNPs available for assessment or limited sample size for comparison.

Disclosure: L. Lewandowski, None; **M. Ombrello**, None; **I. Aksentijevich**, None; **Z. Deng**, None; **L. Hiraki**, None; **E. Silverman**, None; **C. Scott**, None; **A. Barrera-Vargas**, None; **S. Hasni**, None; **M. Kaplan**, None.

Abstract Number: 1966

A Genome-Wide Association Study of Copy Number Variations Identifies the Deletion Associated with Efficacy of TNF-Alpha Blocker Therapy in Korean Patients with Rheumatoid Arthritis

Ki-Nam Gu,[1] **So-Young Bang** ,[2] Hye-Soon Lee,[3] Youngho Park,[2] Juyeon Kang,[2] Ji-Soong Kim,[2] Bora Nam,[2] Hyun-Seung Yoo,[4] Jung-Min Shin,[2] Yeon-Kyung Lee,[2] Tae-Han Lee,[2] Sehwan Chun,[1] Soo-Kyung Cho,[2] Chan-Bum Choi,[2] Yoon-Kyoung Sung,[5] Tae-Hwan Kim,[2] Jae-Bum Jun,[2] DaeHyun Yoo,[2] Kwangwoo Kim,[1] and Sang-Cheol Bae[2], [1]Kyung Hee University, Seoul, Republic of Korea, [2]Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [3]Department of Internal Medicine, Hanyang University Guri Hospital,Hanyang University School of Medicine, Guri, Korea, Guri, Republic of Korea, [4]Hanyang University Hospital, Guri, Republic of Korea, [5]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Copy number variation (CNV) is the most common structural variation defined as large (>1 kb) genomic deletions and duplications and could yield a high impact on various traits including drug response. In this study, we performed a genome-wide association studies (GWAS) of CNV to investigate the efficacy of treatment with TNF-α blockers in patients with rheumatoid arthritis (RA).

Methods: The study was conducted in 357 Korean RA patients treated with TNF-α blockers. All the study subjects were classified into non-responders and responders based on the change in disease activity indexes at 6 months according to the EULAR response criteria. A multivariate logistic regression analysis performed to fit the response to

TNF-α blocker therapy with a CNV adjusting for the top 10 genetic principal components, body mass index, gender, baseline disease activity, and methotrexate use.

Results: The study subjects had 319 common CNVs with the frequency of abnormal-copy carrier ≥ 5% in autosomes and varied in their responses to TNF-α blockers with a wide range of 6-month changes in disease activity indexes. The CNV-response association analysis revealed that the copy number at 2q14.3 was associated with response to TNF-α blockers therapy in the patients with RA ($P \leq 3.2 \times 10^{-4}$) at a false discovery rate (FDR) threshold of 5%. The loss of copy number in the identified CNV was significantly more in the non-responders than in the responders ($7.3 \leq$ odds ratio ≤ 8.5), indicating worse response to TNF-α blockers in the deletion carriers. The 3.8-kb deletion at 2q14.3 is located in an intergenic region with the experimentally validated binding sites of two transcription factors, MAFF and MAFK.

Conclusion: This study conducted the first genome-wide CNV analysis to identify which structural variations associated with the varied response to the TNF-α blocker therapy. Here, we identified a novel CNV that explained a proportion of the inter-individual variance in efficacy of biologics based on the common response criteria.

Disclosure: K. Gu, None; **S. Bang**, None; **H. Lee**, None; **Y. Park**, None; **J. Kang**, None; **J. Kim**, None; **B. Nam**, None; **H. Yoo**, None; **J. Shin**, None; **Y. Lee**, None; **T. Lee**, None; **S. Chun**, None; **S. Cho**, None; **C. Choi**, Eisai Korea, 2; **Y. Sung**, BMS, Eisai, JW pharmaceuticals, Pfizer; **T. Kim**, None; **J. Jun**, None; **D. Yoo**, Celltrion Healthcare, 8, Celltrion, Inc., 2, 5, 8; **K. Kim**, None; **S. Bae**, None.

Abstract Number: 1967

Adenosine A2A Receptor Signals Through AMPK and SIRT1 to Increase Chondrocyte Homeostasis

Benjamin Friedman ,[1] and Bruce Cronstein[2], [1]Department of Medicine, Division of Rheumatology NYUSoM, NYC, [2]NYU Langone, New York

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: OA is characterized by loss of cartilage and chondrocyte dysfunction. Our lab has shown CGS21680 (CGS, 1μM) activation of adenosine A2AR leads to chondrocyte homeostasis. We have demonstrated *in vitro* and *in vivo* activation of FoxO1/3 in human TC28α2 chondrocytes and in obesity-OA mice treated with liposomal injections of adenosine or CGS. In this study, we sought to identify an upstream mechanism to explain A2AR related FoxO1/3 activation and cartilage homeostasis.

Methods: WB or IF was done for AMPK, phos-AMPK, LKB1, Sirt1, p53, Lys 382 Acetyl-p53, and Acetyl lysine in human TC28α2 cells ± CGS (1μM). Autophagy inhibitor hydroxychloroquine (HCQ, 25μM), Sirt1 inhibitor nicotinamide (NAM, 5mM) and peptide PKA inhibitor (15μM) were added *in vitro* as indicated. Sirt1 and acetyl lysine *in vivo* levels were measured by IHC in 1yr old A2ARKO, CD73KO, or WT mice.

Results: vs 1.0±0.2, p=0.02, n=4). Sirt1 is a homeostatic deacetylase that increases nuclear retention of deacetylated Foxo1/3. Further, it can indirectly activate AMPK via deacetylation of nucleus-sequestered LKB1 kinase so it can exit the nucleus to phosphorylate/activate AMPK. IF exhibited bimodal Sirt1 nuclear elevation based on average cell

intensity from 3 experiments both at 10m (5.3±0.4 vs 1.0±0.2, p=0.001) and 30m (8.2±0.8 vs 1.0±0.2, p=0.01). LKB1 cytoplasmic fraction increased with in vitro CGS at 15m (1.34±0.22 vs 1.0±0.14, p< 0.01, n=3) and 30m (1.5±0.2 vs 1.0±0.14, p< 0.01, n=3). Sirt1 proved to be a key mediator in the signaling pathway as its inhibitor NAM blocked CGS-induced activation of Sirt1 and Foxo proteins. In joint sections, Sirt1 was visibly decreased in A2ARKO and CD73KO mice (lower extracellular adenosine) with an increase in total cartilage acetylated lysine. To assess Sirt1 function we evaluated known target p53, which when deacetylated undergoes proteasomal degradation. Prior results in our lab show CGS decreases p53 in vitro. This decrease may be related to a chondroprotective increase in autophagy that occurs with A2AR activation, but we found cells treated simultaneously with starvation to induce autophagy plus autophagy inhibitor HCQ exhibited much higher p53 levels by IF and CGS treatment dramatically reduced p53 despite +HCQ. To test the alternative hypothesis that Sirt1 deacetylates and degrades p53, we performed IF for Ac-Lys-382 p53 and noted clear decrease at 30m post-CGS. Lastly, we identified an in vitro role for PKA in this A2AR pathway by demonstrating a PKA inhibitor blocked normal CGS-mediated activation of Sirt1 and FoxO1/3 assessed by IF.

Conclusion: These early results provide a viable mechanism by which A2AR can activate Sirt1 and AMPK through PKA, explaining the A2AR-associated chondroprotective effect with activation of FoxO1/3 and related increase in autophagy. Both AMPK and Sirt1, which reciprocally activate each other, are important for maintenance of healthy cartilage as evidenced by the fact that knockdown of these proteins is associated with OA. This AMPK/Sirt1 mechanism lends further support to the importance of A2AR activation in chondrocyte homeostasis that our lab has demonstrated *in vivo*.

Disclosure: B. Friedman, None; **B. Cronstein**, AstraZeneca, 5, CanFite Biopharmaceuticals, 4, Horizon Pharmaceuticals, 5, Regenosine, Inc., 4.

Abstract Number: 1968

A Drug Repurposing Story: New Therapeutic Tools Ready to Block Innate Immune Responses in Osteoarthritis

Eloi Franco-Trepat ,[1] Ana Alonso-Pérez,[1] Maria Guillán-Fresco,[1] Alberto Jorge-Mora,[2] Ana Lois Iglesias,[3] Oreste Gualillo,[4] and Rodolfo Gómez[1], [1]Institute IDIS - Musculoskeletal Pathology Group, Santiago de Compostela, Spain, [2]Institute IDIS - Musculoskeletal Pathology Group, Santiago de Compostela, [3]Institute IDIS - Musculoskeletal Pathology Group, Santiago de Compostela, Galicia, Spain, [4]Institute IDIS - NEIRID Lab - SERGAS, Santiago de Compostela, Spain

SESSION INFORMATION
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Background/Purpose: Rheumatic diseases, also known as musculoskeletal pathologies, are steadily rising their prevalence. This worldwide phenomenon is depriving our society of their life quality and has become a grave economic burden. Among musculoskeletal pathologies, osteoarthritis (OA) stands as the major rheumatic disease, in fact, the World Health Organization (WHO) included OA within the TOP10 most disabling diseases.

The activation of Toll-like receptors (TLRs) by damage-associated molecular patterns (DAMPS) promotes critical innate immune responses (IIR). Although TLR4 and OA IIR are linked, no drugs are available to block TLR4 in rheumatology. Interestingly, TLR4 share downstream signaling with interleukin 1 receptor (IL1R). The development of new

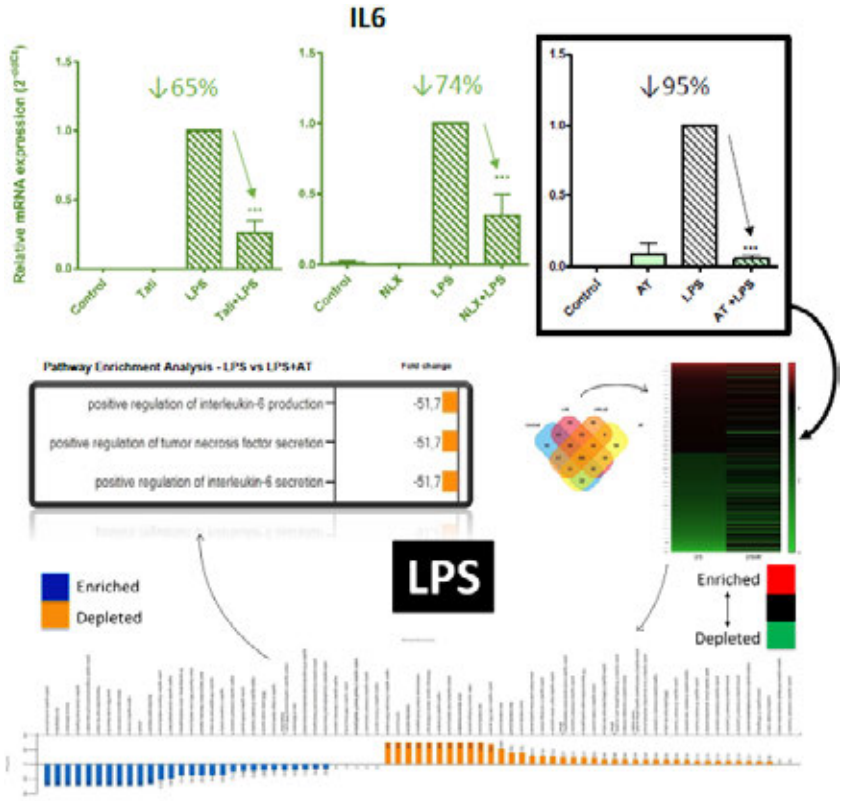

Figure 1. Effect of amitriptyline on TLR4-mediated and IL1R-mediated innate immune responses. OA human chondrocytes were stimulated with thalidomide (TALI) [500µM], naloxone (NLX) [100 µM] or amitriptyline (AT) [1µM], and TLR4 agonist LPS [100ng/ml] or the IL1R agonist IL1B [0,1ng/ml]. Pro-inflammatory factor interleukin-6 (IL6) was studied in human primary OA chondrocytes by RT-PCR and protein profiling MALDI/TOFF. A 4-way Venn diagram, differential Heatmap profile selection, a biological processes enrichment was done. Several cut-offs were carried out: 1st - false discovery rate (FDR) of 5% + p-value ±20% (Heatmap), 3rd augmented relevant immune IIR biological processes (Pathway enrichment analysis). Results are presented as mean ± SEM of four independent experiments. *p < 0.05; **p < 0.01; ***p < 0.001 versus stimulated control (LPS or IL1B). Statistical significance was determined by One-Way ANOVA analysis followed by a Tukey Post-Test.

drugs is necessary but requires decades of work and billions in investment. An alternative exists, the search for anti-TLR4 properties in currently available drugs.

Amitriptyline (AT) is a tricyclic antidepressant currently in-use for neuropathies. Naloxone (NLX) swiftly reverse opioid overdose thanks to its antagonist design. Thalidomide (TALI) initially used as a sedative was found to be teratogenic. In the present, it is used as an anti-neoplastic and to combat leprosy.

Recent studies indicate that AT, NLX and TALI might have anti-TLR4 activity, and could be repurposed to the rheumatology field.

Methods: AT [1µM], NLX [100µM] and TALI [500µM] effect on IIR was initially studied in mouse chondrocytes (ATDC5) and human synoviocytes (SW982) to evaluate the drug effects in the whole joint. Next, it was validated in human OA chondrocytes (hOAC) isolated from knee-joint replacements. Gene expression was evaluated by RT-PCR. Protein levels were determined by ELISA and MALDI/TOFF. Cell viability was evaluated by MTT assay.

Results: At the studied concentrations, AT reduced cell culture nitrite accumulation (Griess assay) and did not affect cell viability (MTT assay). NLX and TALI also reduced cell culture nitrite accumulation (Griess assay).

Stimulation with TLR4 agonist LPS [100ng/ml] or IL1R agonist IL1B [0,5ng/ml] increased IIR gene expression (LCN2, IL6, MCP1, COX2, NOS2, MMP9, MMP13, and ADAMTS4) in chondrocytes (hOAC & ATDC5) and synoviocytes (SW982). Inhibition of TLR4 by CLI95 [3μM] reduced IIR gene expression in LPS and IL1B-treated chondrocytes.

Upon treatment with AT, NLX or TALI, the observed IIR processes (mRNA) were significantly inhibited in synoviocytes and chondrocytes (Figure 1). AT showed the highest anti-TLR4 effect (↓95%) and was selected to perform a proteomic profile (MALDI-TOF) in hOAC. AT treatment depleted IIR-related pathways, including IL6 (Figure 1). To further validate the proteomic results, IL6 protein secretion was evaluated (ELISA) and showed reduced levels after AT treatment.

Conclusion:

We show in chondrocytes and synoviocytes

1. TLR4 receptor is involved in IL1β-mediated innate immune responses (IIR).
2. Amitriptyline, thalidomide, and naloxone blocked TLR4 and IL1R –mediated IIR gene expression.
3. Amitriptyline inhibited the expression of multiple TLR4 and IL1R –mediated IIR proteins.

The rheumatologists have a new therapeutic tool to manage innate immune responses in osteoarthritis.

Disclosure: E. Franco-Trepat, None; **A. Alonso-Pérez**, None; **M. Guillán-Fresco**, None; **A. Jorge-Mora**, None; **A. Lois Iglesias**, None; **O. Gualillo**, None; **R. Gómez**, None.

Abstract Number: 1969

FOXO1 Is Required for Human Osteoclast Differentiation

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Dysregulation of osteoclast differentiation and function is a feature of inflammatory arthropathies (IA). Multiple genes and signalling pathways have been associated with regulation of osteoclastogenesis. In particular, FOXO1, a member of the forkhead box O family of transcription factors, is implicated in many cell processes, including metabolism, signalling, ageing, stress, cell cycle, cell differentiation and as such is an intriguing candidate for osteoclast dysregulation in IA. Recent murine studies however provided conflicting data with regard to the role of FOXO1 in osteoclast differentiation (1, 2) and no data are available in human osteoclastogenesis. We therefore investigated the role of FOXO1 in human osteoclast differentiation.

Methods: Human CD14+ monocytes were isolated from human buffy coat samples using magnetic separation kit (Stemcell). Monocytes were differentiated into osteoclasts with M-CSF (25 ng/ml) and RANK-L (25 ng/ml) either in the presence or absence of a highly specific FOXO1 inhibitor (AS1842856; 0.5 uM for 3 days). To mimic

inflammation-driven osteoclastogenesis, monocytes were grown in suboptimal RANK-L (1 ng/ml) medium for 4 days and on the 4th day TNF or supernatants from activated CD3+ T cells, were added in the presence or absence of FOXO1 inhibitor. Mature osteoclasts were stained with tartrate-resistant acid phosphatase and quantified by light microscopy. Mineral-coated plates were used to assess the resorption activity. Gene expression was assessed by RT-qPCR.

Results: Inhibition of FOXO1 completely blocked both RANK-L driven and inflammation-driven (TNF or activated CD3^{+}supernatant), osteoclast differentiation of human CD14+ monocytes and strongly inhibited osteolytic activity. FOXO1 inhibited cells were viable and had a macrophage-like phenotype. Kinetic studies revealed that FOXO1 plays a role in both the early cell fate decision and the late commitment phase of osteoclastogenesis; both inhibition during the first three days (pre-osteoclast stage) or later stage (day 4-7; committed osteoclast pre-cursors) was observed. Moreover, selective addition of AS1842856 on only day 1, clearly implicated FOXO1 during the earliest stages of osteoclast differentiation. Finally, gene expression analysis of major osteoclastogenesis-associated genes (*M-CSFR*, *RANK* and *NFATC1*) showed reduction upon treatment with AS1842856.

Conclusion: Our results suggest that FOXO1 is an essential transcription factor for human osteoclast differentiation. The ability to inhibit inflammation-driven osteoclastogenesis and osteolytic function indicates that this pathway may be viable therapeutic target in inflammatory arthropathies.

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2. Tan P, Guan H, Xie L, Mi B, Fang Z, Li J, Li F. FOXO1 inhibits osteoclastogenesis partially by antagnozing MYC. Sci Rep. 2015 Nov 16;5:16835.

Disclosure: S. Chilaka, None; **Y. Degboe**, Celgene, 2; **I. McInnes**, Abbott, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, Roche., 2, 8, Abbvie, 5, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Astra Zeneca, 2, 5, AstraZeneca, 5, BI, 2, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 5, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Leo, 5, Lilly, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8; **C. Goodyear**, Celgene, 2, AstraZeneca, 2, 5, MedAnnex, 2, 5, UCB, 2, Jannsen, 2.

Abstract Number: 1970

Mechanism of Chondroprotective Effects of 4-Methylumbelliferone and 2-Deoxyglucose

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

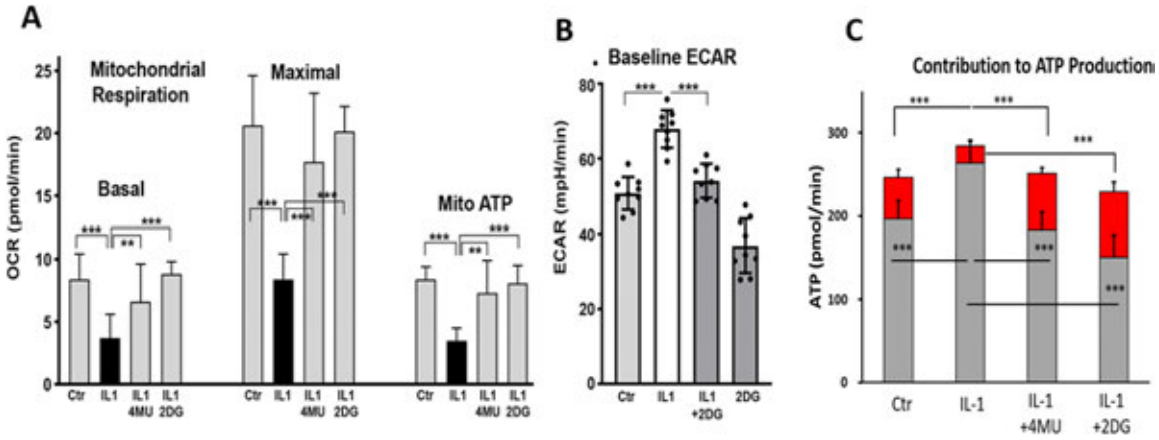

Figure 1. Bovine chondrocytes were incubated 24h ± IL1β (2 ng/ml) and without or with 4MU (1.0mM) or 2DG (2.0 mM). Panel A depicts a representative Mito Stress Test wherein bars represent basal and maximal mitochondrial respiration as a corrected OCR value. Panel B shows summaries of ECAR data representative of changes in basal glycolysis rates as labeled. Panel C shows a representative ATP rate assay wherein the contribution of glycolysis (grey bars) and mitochondrial respiration (red bars) to ATP production. (**: p<0.01 ***: p<0.001)

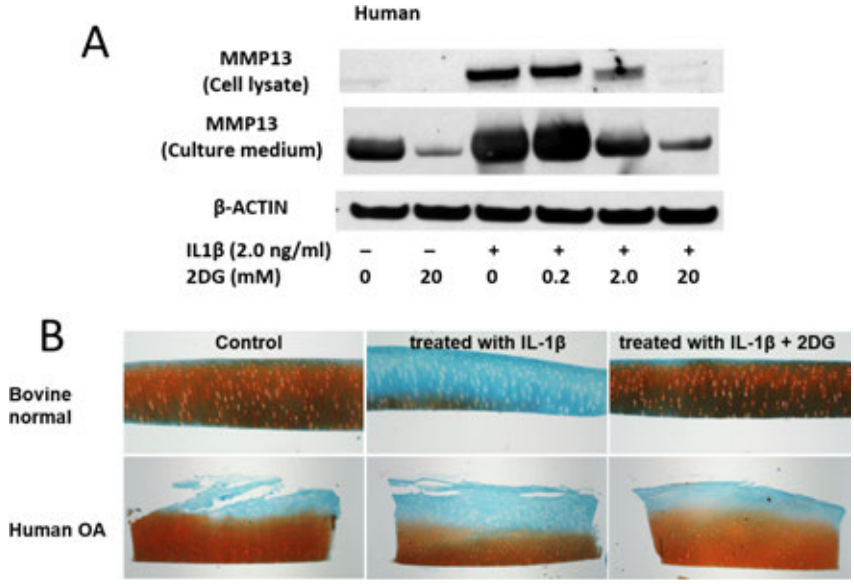

Figure 2. Effect of 2DG on chondrocytes activated with IL-β. Panel A represents the experiment with human OA chondrocytes treated ± 2 ng/ml IL1β in the absence or presence of 0.2, 2.0 or 20 mM 2DG for 24h. Panel B depicts representative examples of bovine and human OA cartilage explants stained by Safranin O.

Background/Purpose: We recently reported that the inhibitor of hyaluronan (HA) biosynthesis, 4-methylumbelliferone (4-MU) blocked IL-1β activation of MMP13 mRNA and protein expression in human osteoarthritic (OA), bovine as well as bovine or OA cartilage explants [1]. This was a somewhat counterintuitive observation because we have also demonstrated that the overexpression of HAS2 (HAS2-OE) exerted the same chondroprotective effects on human and bovine chondrocytes. Others [2] have reported that HAS2-OE in tumor cells generates a flux in intracellular UDP-sugar pools that resulted in changes in cell metabolism; switching from a dependence on glycolysis to aerobic respiration. HAS2-OE and 4-MU likely also cause dramatic fluxes in intracellular UDP-GlcUA pools. From these results, we hypothesized that the effect of HAS2-OE and 4-MU relate to changing metabolism and the possibility of inhibition of glycolysis induce chondroprotective effect. To determine that, we used the glycolysis inhibitor, 2-Deoxyglucose (2DG) as an alternative agent to change metabolism in chondrocytes.

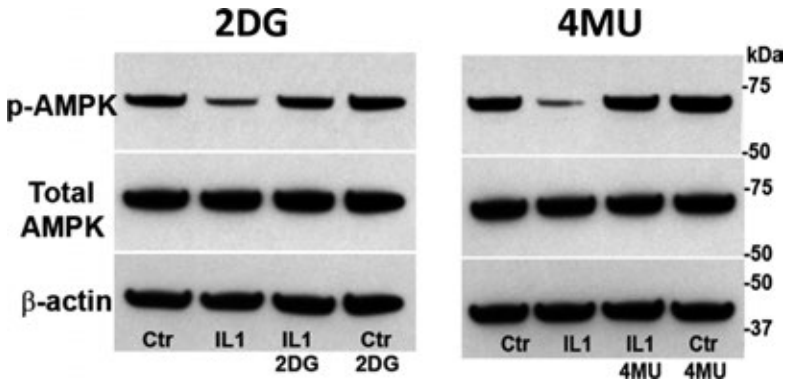

Figure 3. The effect of 4MU and 2DG on p-AMPK changes in IL1β activated chondrocytes. Bovine chondrocytes were treated for 24 h without (Ctr) or with IL1β (2 ng/ml) and ±2DG (2.0 mM), ±4MU (0.5 mM).

Methods: Bovine and human chondrocyte were stimulated with IL-1β (2ng/ml) in the presence or absence of 4MU (1.0 mM), 2DG (0.2-20 mM). Bovine chondrocytes were tested using Seahorse Flux Analyzer (Agilent Tech) to determine rate changes in medium accumulation of +H protons (indicative of lactic acid accumulation: ECAR) and for O2 consumption (indicative of mitochondrial respiration: OCR). Accumulation of MMP13 and phosphor AMPK (pAMPK) protein was quantified with Western blotting. Human and Bovine cartilage explants were cultured with L-1β in the presence or absence of 2DG (20 mM) for 7 days and stained with Safranin O.

Results: Reduced mitochondrial potential and enhanced dependence on glycolysis was observed in IL-1β stimulated chondrocytes. Co-treatment with 4-MU and 2DG returned the cell metabolism to levels at or below baseline (Fig 1A, B). The Seahorse ATP Rate Assay means the contributions of glycolysis and mitochondrial respiration to chondrocyte ATP production (Fig 1C). In control chondrocytes, the use of glycolysis contributes to the majority of ATP produced (grey bars) approximately 1/5th from the TCA cycle (red bars). IL1β-activated chondrocytes display increase in glycolysis and decrease in mitochondrial contributions. These changes are reversed by co-treatment with 4MU and 2DG. As shown in Figs 2A, 2DG reversed the IL1β-induced increases accumulation of MMP13 protein in human OA chondrocytes by Western blotting analysis. Although IL-1β lost safranin O staining in human and bovine samples, co-incubation with 2DG blocked in the loss of proteoglycan (Fig 2B). pAMPK is associate with energy homeostasis in chondrocytes. IL-1β treatment decreased accumulation of phosphor AMPK. Co-treatment with 4-MU and 2DG resulted in a rescue of the pAMPK status.

Conclusion: 4-MU and 2DG have chondroprotective effect by changing metabolism and upregulate AMPK. We propose that 4MU and 2DG become useful when these endogenous responses are not enough to rescue cells from a pro-catabolic phenotype.

References:

1. *J. Biol. Chem.* 291:12087, 2016;
2. *J. Biol. Chem.* 291:24105, 2016.

Disclosure: K. Terabe, None; **N. Takahashi**, AbbVie, 8, Asahi Kasei, 8, Astellas, 8, Bristol-Myers Squibb, 8, Chugai, 8, Chugai Pharmaceutical CO.,LTD., 8, Daiichi-Sankyo, 8, Eisai, 8, Eli Lilly, 8, Janssen, 8, Mitsubishi Tanabe, 8, Ono, 8, Pfizer, 8, Takeda, 8, UCB Japan, 8; **Y. Ohashi**, None; **T. Kojima**, AbbVie, 2, 8, Abbvie, 8, Astellas, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Chugai Pahrmaceutical, 2, 8, Chugai Pharmaceutical CO., LTD., 2, 8, Daiichi-Sankyo, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Janssen Pharmaceutical, 8, Lilly, 2, 8, Mitsubishi Tanabe, 2, 8, Novartis, 2, 8, Pfizer, 2, 8, Takeda, 2, 8, Tanabe Mitsubishi Pharma, 8; **N. Ishiguro**, AbbVie, 2, 8, Abbvie, 2, 8, Asahi Kasei, 2, 8, Astellas, 2, 8, Astellas Pharma, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Chugai Pahrmaceutical, 2, 8, Chugai Pharmaceutical CO.,LTD., 2, 8, Daiichi-Sankyo, 2, 8, Eisai, 2, 8, Eli Lilly, 2, 8, Janssen Pharmaceutical, 8, Kaken, 2, 8, Lilly, 8, Medical Corporation Sanjinkai, 2, 5, 8, Medical Corporation Toukoukai, 2, 5, 8, Mitsubishi Tanabe, 2, 8, Ono, 2, 8, Otsuka, 2, 8, Pfizer, 2, 8, Taisho Toyama, 2, 8, Takeda, 2, 8, Tanabe Mitsubishi Pharma, 2, 8, UCB, 8, Zimmer Biomet, 2, 8; **C. Knudson**, None; **W. Knudson**, None.

Abstract Number: 1971

CD39 Produced from Human Gingiva-Derived Mesenchymal Stem Cells Regulates the Balance of Osteoclasts and Osteoblasts Through Wnt / β-catenin Pathway in Osteoporosis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis led to severe bone-related diseases and increased mortality and health care costs. Existing treatments failed to reduce the risk of fractures in patients, so it is urgent to search new therapeutic methods for regulating bone resorption and formation.

Methods: 2×10^6 GMSC were intravenously injected to the ovariectomy (OVX) mice, trabecular bone parameters, dynamic bone formation and the frequency of osteoclasts were assessed. GMSC were pretreated with CD39 inhibitor, CD73 inhibitor or adenosine receptors to evaluate osteogenesis function in vitro and in vivo.

Results: OVX was performed in adult C57BL/6J mice after complete skeletal remodeling, and GMSC therapy was given 2 weeks after OVX. After 8 weeks of treatment, the distal femoral trabecular bone was sparse and discontinuous in OVX group, and GMSC treatment showed a clear therapeutic effect on bone density, trabecular BV/TV, trabecular numbers. GMSC treatment also resulted in a dramatically decreased frequency of osteoclasts and increased dynamic bone formation in vivo. To identify the mechanism, we found CD39 inhibitors (POM-1) inhibited the osteogenic potential of GMSC in vitro. Interestingly, POM-1 almost completely abolished the therapeutic effect of GMSC on osteoporosis. At the molecular level, we further observed that CD39 of GMSC exert their osteogenic capacity through Wnt / β-catenin pathway.

Conclusion: GMSC regulate the balance of osteoclasts and osteoblasts in osteoporosis by CD39 depending Wnt / β-catenin pathway. Our data suggests that application of GMSC represents a potential therapeutic approach for patients with osteoporosis, and highlight the key role of CD39 in the GMSC function.

Disclosure: W. Wu, None; **J. Wang**, None; **f. huang**, None; **l. Rong**, None; **S. Zheng**, None.

Abstract Number: 1972

Identification of Distinct Lipidomic Profiles in Synovial Membranes from Inflammatory Arthritis by Mass Spectrometry Imaging

Beatriz Rocha,[1] Berta Cillero-Pastor,[2] Cristina Ruiz-Romero,[3] Andrea Cuervo,[4] Ron M A Heeren,[2] Juan Cañete,[5] and Francisco J. Blanco[6], [1]Proteomics Group-ProteoRed/ISCIII, Grupo de Investigación de Reumatología, (GIR), INIBIC – Hospital Universitario de A Coruña, A Coruña, Spain, A Coruña, Galicia, Spain, [2]The Maastricht Multimodal Molecular Imaging Institute, (M4I), Division of Imaging Mass Spectrometry, Maastricht University, The Netherlands., Maastricht, Limburg, Netherlands, [3]Proteomics Group-ProteoRed/ISCIII, CIBER-BBN, Grupo de Investigación de Reumatología, (GIR), INIBIC – Hospital Universitario de A Coruña, A Coruña, Spain. A Coruña Spain, [4]Arthritis Unit, Rheumatology Department, Hospital Clinic, IDIBAPS, Barcelona, Spain. Barcelona, Catalonia, Spain, [5]Rheumatology Department, Hospital Clínic and IDIBAPS, Barcelona, Spain, [6]Servicio de Reumatología. Instituto de Investigación Biomédica de A

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Early diagnosis of inflammatory arthritis is associated with improved patient outcomes. However, accurate diagnosis can be challenging because of their complexity and heterogeneous nature. Synovitis is a common pathological event undergoing arthritis which causes severe histological changes in the synovium. In this work, we evaluated the lipid signature of the synovium from different forms of inflammatory arthropathies using mass spectrometry imaging, in order to identify novel biomarkers that may enable an accurate and differential diagnosis and patient classification.

Methods: Synovial membrane biopsies of patients affected by osteoarthritis (OA, n=13), rheumatoid arthritis (RA, n=6), psoriatic arthritis (PsA, n=12) and healthy controls (n=10) were compared by matrix-assisted laser desorption ionization mass spectrometry imaging (MALDI-MSI). Tissue sections were deposited on conductive slides and coated with different matrices for lipid extraction. Lipid measurements were acquired in duplicate on a rapifleX MALDI Tissuetyper™ time-of-flight instrument in both ion modes. On-tissue MS/MS was performed on a MALDI-enabled Orbitrap Elite to confirm the molecular identity of lipids. Principal component analysis (PCA) and discriminant analysis (DA) were employed to classify lipids specific for each disease. Statistically significant changes were established at $p < 0.05$.

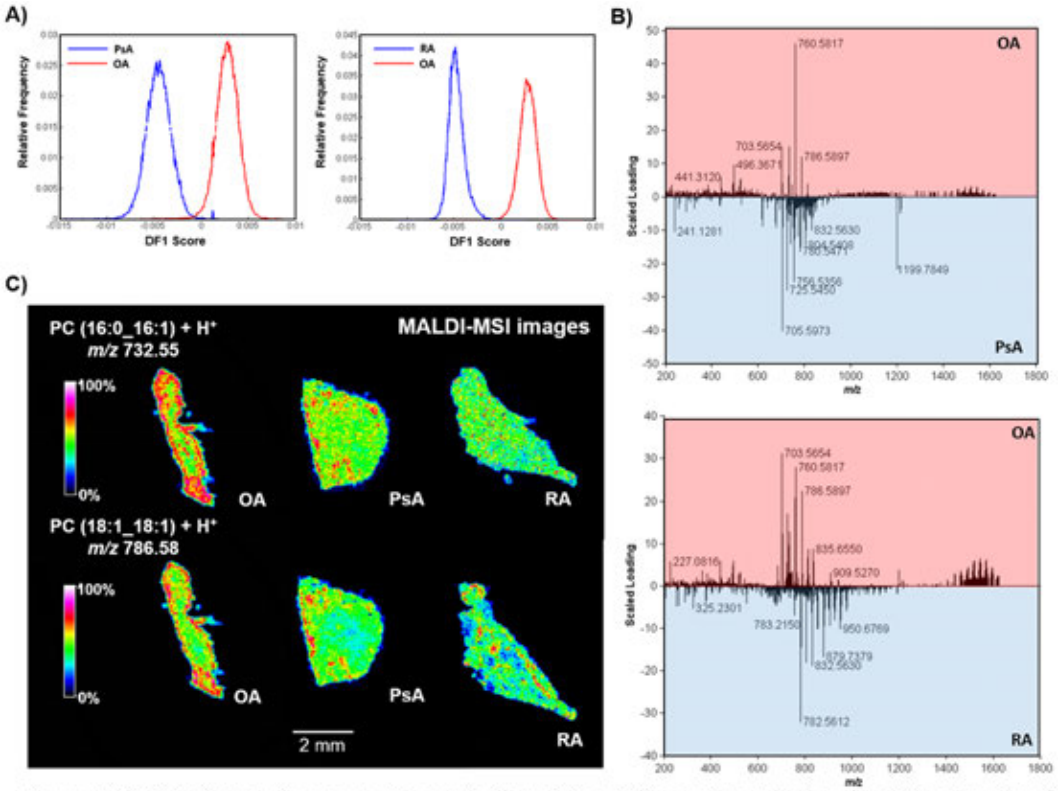

Figure 1. A) PCA-DA analysis separates OA samples from PsA and RA according to lipid profile. B) Loading plot of PCA-DA analysis representing the lipid masses characteristic to OA (positive side) and PsA/RA (negative side) samples given by MALDI-MSI. C) MALDI-MSI images showing the differences in the abundance and spatial distribution of two phosphatidylcholines (PC) in OA synovium compared to PsA and RA.

Results: MALDI-MSI in combination with PCA-DA showed a good separation of OA patients and controls pointing out a differential lipid profile between OA and control biopsies. OA tissues showed higher lipid content in the mass/charge (*m/z*) range 600-800, relative to controls. OA lipid intensities were normalized to healthy tissues to determine disease-associated lipidomic profiles of synovium. This analysis showed 35 phospholipids significantly different between OA and controls. These were mainly phosphatidylcholines (PC, 30%), phosphatidylethanolamines (PE, 26%), phosphatidylinositols (PI, 26%), phosphatidylserines (PS, 14%) and lysophosphatylcholines (LPC, 6%). PCA-DA analysis displayed a clear separation between OA and highly inflammatory arthritis (PsA and RA) based on lipid profiles (Figure 1A). Particularly, PC (*m/z* 732.5, 760.5 and 786.5) and sphingomyelins (*m/z* 703.5) were significantly upregulated in OA (Figure 1B). Some of them also showed a specific spatial distribution within the tissue. For instance, PC *m/z* 732.5 and *m/z* 786.5 were localized in the lining layer of hyperplastic OA synovium (Figure 1C). In contrast, most of PE were significantly more abundant in PsA, whereas phosphatidic acids distinguished RA synovium from OA.

Conclusion: OA synovial tissues were characterized by a higher content of PCs and sphingomyelins compared to healthy controls and other inflammatory joint diseases such as PsA and RA. These molecules may have an important role in the synovitis associated with the pathogenesis of OA, and constitute relevant molecular disease classifiers for the OA diagnosis.

Disclosure: B. Rocha, None; **B. Cillero-Pastor**, None; **C. Ruiz-Romero**, None; **A. Cuervo**, None; **R. Heeren**, None; **J. Cañete**, None; **F. Blanco**, None.

Abstract Number: 1973

Protective Effects of Intra-Articular Formulated Liraglutide in Osteoarthritis: Preclinical Studies

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SESSION INFORMATION
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Background/Purpose: Osteoarthritis (OA) is a degenerative joint disease affecting millions of individuals worldwide. Its development has been reported to be associated with cartilage degradation and inflammatory responses leading to pain, swelling and reduced function. Liraglutide, a Glucagon-Like-Peptide 1 Receptor (GLP-1R) agonist, is clinically used as a subcutaneous treatment for type 2 diabetes. Interestingly, immunomodulatory and anti-inflammatory properties of the GLP-1 pathway have been recently described in various diseases but its role in the pathogenesis of OA remains to be elucidated. The objective of this study was to evaluate the effects of intra-articular (IA) Liraglutide in *in vitro* and *in vivo* models of OA by evaluating surrogate markers of inflammation and cartilage matrix proteolysis, cartilage degradation and pain.

Methods: IL-1β-stimulated mouse articular chondrocytes were treated with different concentrations of Liraglutide for 24h. Production of matrix metalloproteinases (MMP) and prostaglandin E2 (PGE2) was measured by ELISA. IA injections of Liraglutide or vehicle were performed in two chemically-induced inflammatory knee OA models: the mouse

monosodium iodoacetate (MIA) model and the rat collagenase type II model. Paw withdrawal threshold and weight bearing distribution were performed for pain behavior assessment. Histopathological analyses (OARSI score) were conducted blindly by one observer in the rat collagenase OA model for evaluating cartilage degradation.

Results: Liraglutide significantly reduced the IL-1β-induced production of PGE2 (1341±86 vs 1766±145 pg/ml for vehicle, p≤0.05, 50nM dose) and cartilage matrix catabolic enzymes MMP-3 (294±23 for vehicle vs 204±15 ng/ml, p≤0.01, 3nM dose; vs 197±23 ng/ml, p≤0.001, 50nM dose) and MMP-13 with a dose response (127±14 for vehicle vs 90±18 pg/ml, p≤0.01, 3nM dose; vs 70±10 ng/ml, p≤0.001, 10nM dose; vs 52±6 ng/ml, p≤0.001, 50nM dose) in murine chondrocytes. In both *in vivo* OA models, Liraglutide IA injections significantly attenuated pain symptoms. Indeed, in the mouse MIA model, single injection of IA Liraglutide increased paw withdrawal threshold (0.37±0.39 vs 0.13±0.11 g for vehicle, p≤0.05, day 7) and improved weight distribution to the affected limb (80±7% at day 7 and 83±4% at day 10, p≤0.001) compared to vehicle (71±6% at day 7 and 74±4% at day 10). The response was found similar to the one after an IA injection of dexamethasone (79±8% at day 7 and 81±4% at day 10). In the rat collagenase OA model, repeated IA injections of Liraglutide improved weight bearing deficit at multiple time-points (50±4 at week 1, 66±5 at week 3 and 66±4% at week 6, p≤0.001) compared to vehicle (42±4 at week 1, 57±4 at week 3 and 59±3% at week 6). Histological assessment of rat collagenase-injected knee joint revealed a significant (p≤0.05) decrease of the total joint score in the IA Liraglutide treated group (8±4) compared to vehicle (11±4).

Conclusion: IA injection of Liraglutide has demonstrated anti-catabolic, anti-inflammatory and pain-relieving effects in preclinical OA models, opening the wave to considering now this molecule as a potential disease-modifying OA drug.

Disclosure: F. Berenbaum, 4P Pharma, 2; **C. Meurot**, 4P Pharma, 4; **M. Vieubled**, 4P Pharma, 3; **L. Sudre**, None; **c. bougault**, None; **r. rattenbach**, 4P Pharma, 1; **c. martin**, 4P Pharma, 4; **c. jacques**, 4P Pharma, 2.

Abstract Number: 1974

The Rat Homolog to FX201, a Gene Therapy in Development for the Treatment of Osteoarthritis, Demonstrates Dose-Dependent Decreases in the Severity of Cartilage and Bone Lesions Following Anterior Cruciate Ligament Transection

Rebecca Senter,[1] **Rogely Boyce** ,[2] Monika Chabicovksy,[3] Emily Walsh Martin,[1] Geneviève Langevin-Carpentier,[4] and Neil Bodick[1], [1]Flexion Therapeutics, Burlington, [2]Beechy Ridge ToxPath LLC, Clay, [3]MC Toxicology Consulting, Vienna, Austria, [4]Charles River Laboratories, Senneville, Canada

SESSION INFORMATION
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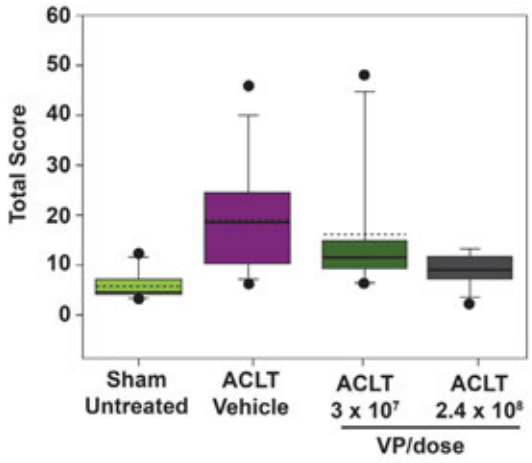
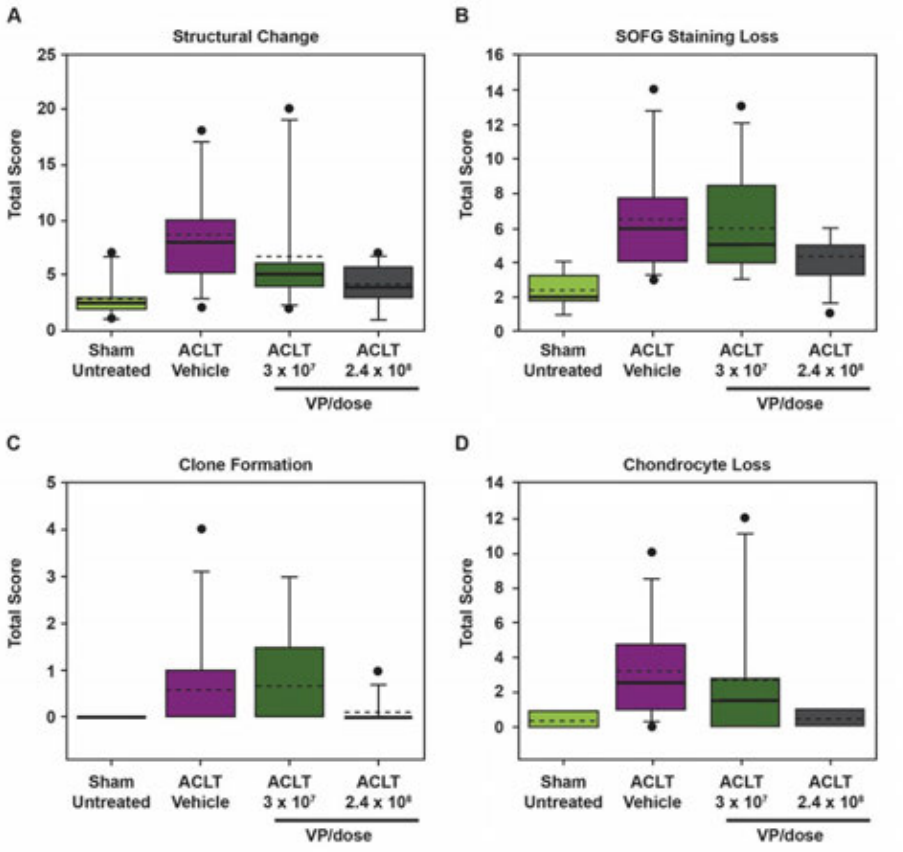
Background/Purpose: Acute injury to the anterior cruciate ligament (ACL) is a common cause of posttraumatic OA in humans, and ACL transection (ACLT) in rats is an established animal model of traumatic injury-induced OA. FX201, a helper-dependent adenovirus (HDAd)-based intra-articular (IA) gene therapy candidate designed to induce the production of an Interleukin (IL)-1 receptor antagonist (IL-1Ra) in the presence of inflammation, is in development as a potential therapeutic agent for OA. Here, we evaluated the effects of HDAd-ratIL-1Ra, the rat surrogate of FX201, when administered as a single IA injection in rats 1 week following ACLT surgery.



Dashed line = mean; solid line = median; dots = outliers; box extremities = quartile 1 (bottom) and quartile 3 (top); end of whiskers = min and max.
ACLT, anterior cruciate ligament transection; Min, minimum; Max, maximum; SOFG, Safranin O fast green; VP, viral particle.

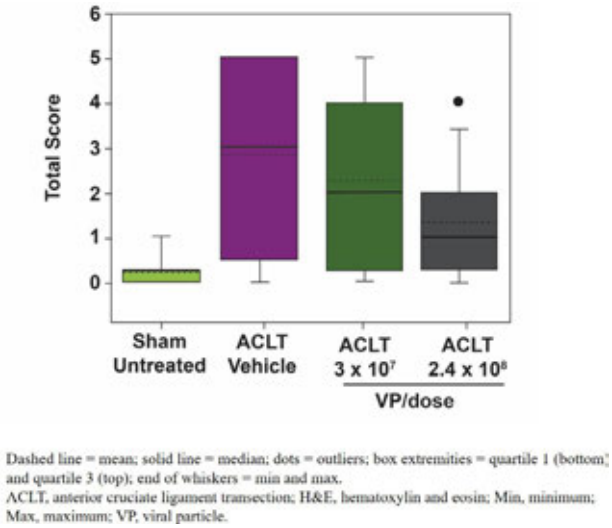
Figure 1. Composite (Total) Scores by Group for Cartilage/Bone Evaluation (SOFG Staining) in Sham- and ACLT-Operated Rats



Dashed line = mean; solid line = median; dots = outliers; box extremities = quartile 1 (bottom) and quartile 3 (top); end of whiskers = min and max.
ACLT, anterior cruciate ligament transection; Min, minimum; Max, maximum; SOFG, Safranin O fast green; VP, viral particle.

Figure 2. Total Scores by Group for (A) Structural Change (B) SOFG Staining Loss (C) Clone Formation and (D) Chondrocyte Loss in Sham- and ACLT-Operated Rats

Methods: A total of 46 Sprague Dawley rats were assigned to 1 of 4 study groups: high-dose HDad-ratIL-1Ra (ACLT/HDAd-ratIL-1Ra; 2.4×10^8 viral particles [VP]/dose; n=12), low-dose HDAd-ratIL-1Ra (ACLT/HDAd-ratIL-1Ra; 3×10^7



Dashed line = mean; solid line = median; dots = outliers; box extremities = quartile 1 (bottom) and quartile 3 (top); end of whiskers = min and max.
ACLT, anterior cruciate ligament transection; H&E, hematoxylin and eosin; Min, minimum; Max, maximum; VP, viral particle.

Figure 3. Composite (Total) Scores by Group for Synovial Membrane Evaluation (H&E Staining) in Sham- and ACLT-Operated Rats

VP/dose; n=12), vehicle (ACLT/vehicle; n=12), or sham/untreated (n=10). Rats underwent ACLT surgery in the right knee (except sham animals) under isoflurane anesthesia on Day -7. Seven days postsurgery (Day 1) rats received a single IA injection of HDAd-ratIL-1Ra or vehicle in the right knee joint under anesthesia. At Week 12, animals were sacrificed and whole right knee joints were harvested and analyzed for histopathology. For histopathological evaluation, whole right knee joints were stained with Safranin O fast green (SOFG) and hematoxylin and eosin and assessed using a semi-quantitative grading system (OARSI score) to score cartilage/bone and synovial membrane, respectively. Individual scores were recorded, and composite scores for each parameter were generated by the sum of all individual scores.

Results: In sham-operated rats, microscopic changes at Week 12 were limited to low incidence of superficial articular cartilage changes graded minimal in severity as assessed by surface irregularities with focal fibrillation/clefts/fissure, chondrocyte loss, and/or SOFG staining. All ACLT-operated rats developed OA microscopic changes that were minimal-to-severe in 1 or more of the examined articular compartments at Week 12. Among ACLT-operated rats, HDAd-ratIL-1Ra resulted in a dose-dependent decrease in composite scores for cartilage/bone compared with vehicle (**Figure 1**); these decreases are likely due to reduced severity of structural changes and chondrocyte loss with HDAd-ratIL-1Ra treatment compared with vehicle (**Figure 2**). Slight decreases in severity of SOFG staining loss and incidence of clone formation were also observed with HDAd-ratIL-1Ra treatment compared with vehicle (**Figure 2**). Furthermore, HDAd-ratIL-1Ra demonstrated dose-dependent decreases in composite scores of OA microscopic changes to the synovial membrane compared with vehicle (**Figure 3**); all synovial microscopic findings were minimal in severity.

Conclusion: A single administration of HDAd-ratIL-1Ra, the rat surrogate of FX201, resulted in a dose-dependent decrease in the incidence and severity of OA-related lesions to cartilage/bone and the synovial membrane 12 weeks postsurgery; these results support further development of FX201 as a potential therapeutic agent for OA.

Disclosure: R. Senter, Flexion Therapeutics, 3, 4; **R. Boyce**, Flexion Therapeutics, 5; **M. Chabicovksy**, Flexion Therapeutics, 5; **E. Walsh Martin**, Flexion Therapeutics, 3, 4; **G. Langevin-Carpentier**, Flexion Therapeutics, 5; **N. Bodick**, Flexion Therapeutics, 3, 4.

Abstract Number: 1975

Fibrates as Drugs with Senolytic and Autophagic Activity for Osteoarthritis Treatment

Uxia Nogueira-Recalde ,[1] Irene Lorenzo-Gomez,[2] Francisco J. Blanco,[3] María I. Loza,[4] Diego Grassi,[5] Valery Shirinsky,[6] Ivan Shirinsky,[6] martin lotz,[7] Paul D. Robbins,[8] Eduardo Domínguez,[4] and Beatriz Carames[2], [1]Grupo de Biología del Cartílago, Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña, Sergas, A Coruña, Spain, A Coruña, Spain, [2]Grupo de Biología del Cartílago, Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña, Sergas, A Coruña, Spain, A Coruna, Spain, [3]Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). As Xubias, 15006. A Coruña, España, A Coruña, Spain, [4]Biofarma Research Group, Center for Research in Molecular Medicine and Chronic Diseases (CIMUS), University of Santiago de Compostela, Santiago de Compostela, Spain, [5]Institute for Interdisciplinary Neuroscience (IINS), Bordeaux, Nouvelle-Aquitaine, France, Bordeaux, France, [6]Scientific Research Institute of Clinical immunology, Novosibirsk, Rusia, Novosibirsk, Russia, [7]Department of Molecular Medicine. Scripps Research, La Jolla, CA, USA, La Jolla, CA, [8]Institute on the Biology of Aging and Metabolism and Department of Biochemistry, Molecular Biology and Biophysics, University of Minnesota, Minneapolis, MN

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Increasing evidence suggest that osteoarthritis (OA) is associated with hallmarks of ageing, including cellular senescence or defective autophagy, that could promote disease onset. *The objective of this study was to identify small molecules with senolytic and pro-autophagy activity to prevent cartilage degeneration and OA.*

Methods: Senescence and defective autophagy were induced in human chondrocytes (T/C28a2) by treatment with IL-6, a SASP factor, at 20ng/ml for 72 or 18 hours, respectively. Chondrocytes were incubated with compounds from Prestwick Chemical Library to identify potential senotherapeutics, using SA-β-gal activity imaging as fluorescence reporter. To identify molecules activating autophagy flux, LC3 reporter stably expressed in chondrocytes was imaged and analyzed. Confirmatory assays for senescence, autophagy, FoxO signaling pathway and inflammation were performed in primary human chondrocytes. The potential protection from degeneration was evaluated by Safranin O staining and Nitric Oxide (NO) production in human cartilage. Moreover Senolytic index was determined. PPARα was evaluated as a target mechanism in both spontaneous aging and surgically-induced OA in mice and in blood and cartilage from human OA Cohort. Furthermore, the consequences of PPARα silencing was investigated in human chondrocytes.

Results: The cell-based screen yielded 279 potential senotherapeutic compounds, 14 of which show pro-autophagy activity. Fenofibrate (FN), a PPARα agonist approved for dyslipidemia was selected as a candidate. FN reduced senescence and increased autophagic flux ($p < 0.0001$) in response to IL-6, and protects against senescence, defective autophagy and inflammation in human OA and aging primary chondrocytes. This protective effect was confirmed in human aging articular cartilage explants by a reduction of proteoglycans loss and NO production ($p < 0.05$) in response to IL-1b. Interestingly, FN present a senolytic activity represented by a reduction of the senescent cells and the total number of cells ($p < 0.05$). Moreover, this selective elimination was mediated by apoptosis. Furthermore, FN upregulates key homeostasis markers, such as LC3 and FoxO1 and CPT1A, gen involved in mitochondrial fatty acid beta-oxidation. These effects were also observed for structurally distinct PPARα agonists, suggesting that pharmacological modulation of PPARα may provide therapeutic benefits in OA. Interestingly, PPARα silencing induced senescence, altered homeostasis mechanisms or increases inflammation at both basal conditions or in response to

IL-6 or IL-1b at 48 hours ($p < 0.05$). Moreover, PPARα expression was reduced with aging and OA in mice and in blood and cartilage from OA Cohort ($p < 0.01$). Remarkably, in a retrospective study, fibrate treatment improved OA clinical conditions in human patients from Osteoarthritis initiative (OAI) Cohort.

Conclusion: These results demonstrate that FDA-approved fibrate drugs targeting lipid metabolism protect against cartilage degeneration with aging and OA. Thus, these drugs could have immediate clinically utility for the treatment of OA and age-related cartilage degeneration.

Disclosure: U. Nogueira-Recalde, None; **I. Lorenzo-Gomez**, None; **F. Blanco**, None; **M. Loza**, None; **D. Grassi**, None; **V. Shirinsky**, None; **I. Shirinsky**, None; **m. lotz**, None; **P. Robbins**, None; **E. Domínguez**, None; **B. Carames**, None.

Abstract Number: 1976

Regulation of Interleukin-1β (IL-1β)-induced COX-2 Expression and IL-6 and MMP-1 Production in Human OA Synovial Fibroblasts by Guanylate Binding Protein 5

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a chronic degenerative joint disease caused by synovial inflammation and cartilage degradation primarily driven by interleukin-1beta (IL-1β). Studies suggest that TNF-stimulated gene 6 (TSG6) plays an important role in reducing IL-1β-induced tissue destruction in arthritis. In the present study, we evaluated the role of guanylate binding protein 5 (GBP5), an interferon gamma regulated gene, in regulating TSG6 expression, and IL-1β-induced COX-2 expression and IL-6 and MMP-1 production in human osteoarthritis synovial fibroblasts (OASFs).

Methods: Primary OASFs were isolated from synovial tissues obtained after joint replacement surgeries from OA patients under an approved IRB protocol and cultured in RPMI1640 with 10% FBS. Human OASFs were treated with IL-1β (10 ng/ml) or TNF-α (20 ng/ml) for 24 hours to study the expression of inflammatory proteins using Western immunoblotting, qRT-PCR, or ELISA method. The potential crosstalk and association of GBP5 with IL-1β stimulated signaling proteins was studied by the immunoprecipitation (IP) method. Small-interfering RNA (siRNA) mediated knockdown of GBP5 was conducted to study its effect on IL-1β-induced inflammatory mediators in human OASFs.

Results: Western blot analysis showed that the expression of GBP5 is significantly increased upon IL-1β or TNF-α stimulation in human OASFs ($p< 0.05$; n=3). Knockdown of GBP5 significantly increased the expression of IL-1β-induced COX-2 and the production of IL-6 and MMP-1 in human OASFs ($p< 0.05$; n=3). Our qRT-PCR and Western blotting results showed that the knockdown of TNF-stimulated gene 6 (TSG6) significantly upregulates IL-1β-induced MMP-1 expression in human OASFs ($p< 0.05$; n=3). Surprisingly, GBP5 knockdown by siRNA significantly lowered the expression of IL-1β-induced TSG6 at mRNA and protein levels ($p< 0.05$; n=3), which suggests GBP5 a novel reg-

ulator of TSG6 in human OASFs. Supporting evidence showed that the overexpression of GBP5 via lentiviral delivery resulted in the upregulation of TSG6 expression and a concomitant decrease in IL-1β-induced COX-2 expression and IL-6 and MMP-1 production in human OASFs ($p< 0.05$; n=3). Furthermore, the results from IP analysis showed that IL-1β stimulation led to enhanced association between TSG6 and GBP5 in human OASFs in vitro, thereby selectively amplifying phosphorylation of JNK/SAPK MAPK and its downstream substrate c-Jun.

Conclusion: Our study suggests that GBP5 suppresses IL-1β-induced tissue destruction primarily through TSG6, whereas it elicits anti-inflammatory actions that are independent of TSG6 in human OASFs.

Disclosure: M. Haque, None; **M. McDougal**, None; **A. Singh**, None; **S. Ahmed**, None.

Abstract Number: 1977

The Synthesis of Hydrogen Sulfide Is Impaired in Osteoarthritic Chondrocytes from Diabetic Patients and *in Vitro* in Cells Under High Glucose Environment

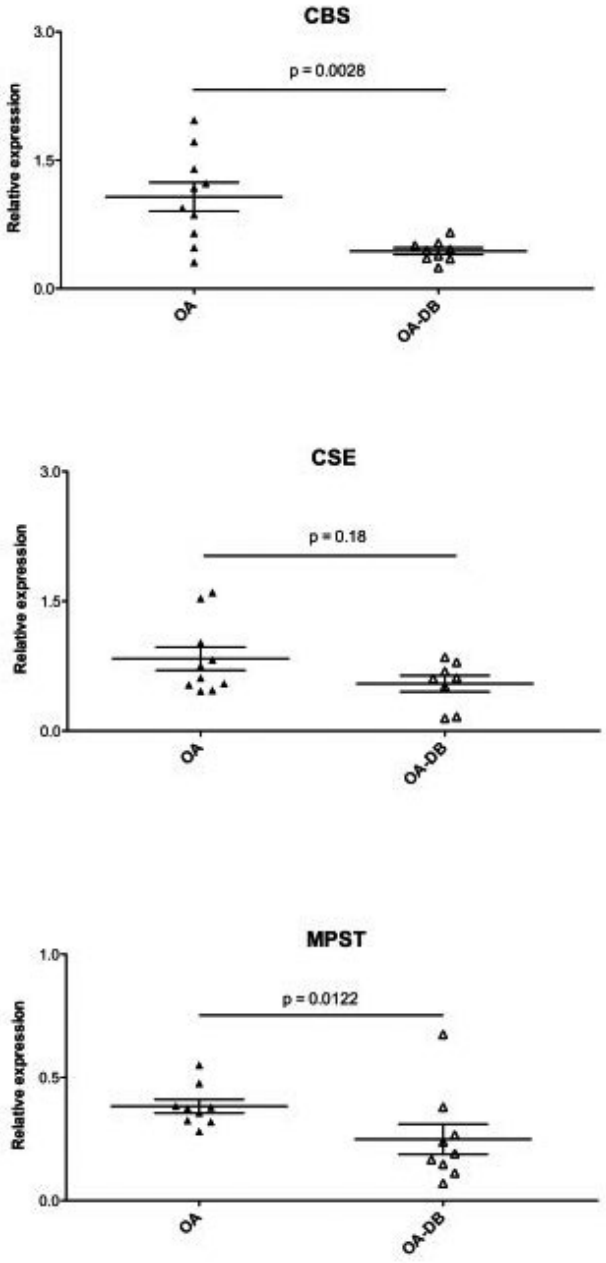
Carlos Vaamonde-García ,[1] Tamara Hermida-Gómez,[2] Francisco J. Blanco,[3] Elena F Burguera,[3] and Rosa Meijide-Faílde[1], [1]Tissue Engineering and Regenerative Medicine Group. University of A Coruña, A Coruña, Spain, [2]Unidad de Bioingeniería Tisular y Terapia Celular (GBTTC-CHUAC). Grupo de Investigación en Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC). Sergas. Centro de Investigaciones Científicas Avanzadas (CICA), A Coruña, Spain, [3]Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). As Xubias, 15006. A Coruña, España, A Coruña, Spain

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A growing number of findings indicates that type 2 diabetes is an independent risk factor of osteoarthritis (OA). However, the mechanisms underlying the connection between both diseases remain unclear. Hydrogen sulfide (H2S) plays an important role in the pathogenesis of diabetes and its complications. In relation, we and other authors have observed a protective impact of H2S induction on activation of pathological pathways in osteoarthritic chondrocytes. In this study we examined the modulation of H2S levels in serum and chondrocytes from OA/non-OA diabetic (DB) or non-diabetic (non-DB) patients and in cell under glucose stress, in order to elucidate whether impairment in H2S-mediated signaling could participate in the onset of diabetes-related OA.

Methods: Serum and chondrocytes were isolated from OA/non-OA cartilage of diabetic (DB) or non-diabetic (non-DB) patients. Serum levels of H2S were measured by an ion-selective microelectrode. Primary chondrocytes and T/C28a2 were stimulated w/o IL-1β (5 ng/mL) under a normal (5.5 mM; NG) or a high (25 mM; HG) glucose environment. Gene and protein expression of enzymes involved in H2S synthesis (cystationine γ-liase [CSE], cystationine β- synthase [CBS], and 3-mercaptopyruvate sulfurtransferase [3-MT]) and heme oxygenase 1 (HO-1) were assessed by RT-qPCR and WB, respectively. To determine the involvement of H2S in catabolic pathways activated by HG in chondrocytes, NaSH and GYY 4137 (500 μM), a fast and slow-releasing H2S donor respectively, were employed.

Results: H2S levels in serum from OA-DB patients were significantly lower than in those from non-OA-DB patients ($p< 0.05$). Likewise, fresh isolated chondrocytes from OA cartilage of diabetic patients showed lower levels of H2S synthesizing enzymes (CSE, CBS and 3-MT) than those of non-DB patients (Figure 1). T/C28a2 cells exposed to HG



Protein expression of enzymes involved in H2S synthesis in freshly isolated chondrocytes from OA or non-OA diabetic (DB) patients

stress expressed lower mRNA and protein levels of these 3 enzymes after 3 days of incubation than in those incubated in NG conditions (0.41- fold and 0.83-fold [CSE], 0.42-fold and 0.66-fold [CBS], and 0.52-fold and 0.79-fold [3-MT] for mRNA and protein expression, respectively; n=6, $p< 0.05$). Similar results were found in primary chondrocytes incubated in HG in the presence of IL-1β ($p< 0.05$). Additionally, the expression of IL-6 and COX-2 induced by IL-1β was significantly higher in primary chondrocytes under HG than NG condition (n=5, $p< 0.05$); whereas protein levels of anti-oxidant enzyme HO-1 were reduced in HG exposed cells. GYY 4137 and NaSH co-treatment recovered HO-1 expression and attenuated IL-6 and COX-2 expression in cells under HG+IL-1β condition (n=3; $p< 0.05$).

Conclusion: The results indicate a reduction of H2S synthesis as a critical feature involved in hyperglucidic-mediated dysregulation of articular chondrocytes. The impairment of H2S signaling could participate in the mechanisms un-

derlying the predisposition to OA development in diabetic individuals and may open new opportunities for treating patients with a diabetes-related OA phenotype.

Disclosure: C. Vaamonde-García, None; **T. Hermida-Gómez**, None; **F. Blanco**, None; **E. Burguera**, None; **R. Meijide-Faílde**, None.

Abstract Number: 1978

HSP90AA1, a Chaperone-mediated Autophagy Mediator, Is a Biomarker of Joint Damage in Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In osteoarthritis (OA) defects in Autophagy are evident and precede joint damage. *Therefore, identifying biomarkers associated with autophagy defects could facilitate the development of personalized therapeutic strategies to prevent OA progression.*

Methods: A comparative analysis of 35 autophagy genes was performed in blood from a Prospective OA Cohort of A Coruña (PROCOAC) of non-OA and knee OA patients. Non-OA patients (Age: 61,44 ± 1,16 years; BMI: 25,25 ± 0,52; Females, n=18) and Knee OA patients (Age: 65,50 ± 1,05 years; BMI: 29,55 ± 0,67; Females, n=18, OA grade III-IV) were profiled using an autophagy gene expression array. Confirmatory studies of the candidate genes were performed in blood from Non-OA patients (Age: 60,13 ± 1,12 years; BMI: 24,85 ± 0,59; Sex: Females; n=30) and Knee-OA patients (Age: 68,4 ± 1,11 years; BMI: 29,65 ± 0,55; Females; n=30, OA grade III-IV) by using Taqman Technology. Moreover, the candidate gene was evaluated as a potential biomarker in human cartilage from Normal (n=19) and OA (n=20) patients and in both spontaneous aging (2, 6, 12, 18, and 30 months old, n=3/each time) and surgically-induced OA (10 weeks after surgery, n=4/each) in mice by immunohistochemistry. Remarkably, the consequences of candidate gene silencing on autophagy, FOXO signaling, inflammation, senescence, oxidative stress and cell death by apoptosis was investigated by gene expression and flow cytometry.

Results: 15 autophagy-related genes were downregulated in blood from knee OA patients compared to non-OA patients ($p < 0.05$). No upregulation was found. although a trend towards upregulation was found for several genes involved in the mTOR signaling pathway. Importantly, key autophagy-related genes, including ATG16L2, ATG12, ATG4B and MAP1LC3B were significant downregulated in knee OA patients ($p < 0.05$). Interestingly, HSP90AA1 and HSPA8, chaperone-mediated autophagy genes involved in stress response and protein folding, were significant downregulated ($p < 0.001$). Confirmatory studies for MAP1LC3B and HSP90AA1, showed a significant downregulation ($p < 0.001$) in blood from knee OA patients. Remarkably, total proteome screening of human OA chondrocytes

with defective autophagy, showed a significant reduction of HSP90AA1 ($p< 0.05$). Moreover, pharmacological inhibition of HSP90 chaperone reduces chondrocyte homeostasis. Remarkably, HSP90AA1 expression was reduced in OA cartilage ($p < 0.01$) and in spontaneous aging and surgically-induced OA in mice ($p< 0.05$). Interestingly, HSP90AA1 silencing increased LC3 and FOXO1 expression ($p < 0.01$) and increased NFkB and p16 expression ($p< 0.05$) at 48h post-transfection. In addition, HSP90AA1 silencing increased cell death by apoptosis and mitochondrial ROS production 72h post-transfection ($p < 0.05$). These data indicate that HSP90AA1 might be a potential biomarker associated with defective autophagy in OA.

Conclusion: We identified biomarkers of defective autophagy as a mechanism of central homeostasis, which gives us a general vision of the disease mechanisms linked to OA clinical reality.

Disclosure: I. Lorenzo-Gomez, None; **U. Nogueira-Recalde**, None; **N. Oreiro**, None; **J. Pinto-Tasende**, None; **F. Blanco**, None; **B. Carames**, None.

Abstract Number: 1979

What Is the Pathogenic Meaning of Chondrocyte Hypertrophy in Osteoarthritis? Effect of Evc Deletion Through Hedgehog Signaling

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SESSION INFORMATION
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Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
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Background/Purpose: Osteoarthritis (OA) is mainly characterized by the progressive damage of articular cartilage, where chondrocytes acquire a hypertrophic-like phenotype. Indian Hedgehog levels are increased in OA cartilage. An induction of Hedgehog (Hh) signaling pathway induces OA-like cartilage lesions, whereas its pharmacological down-regulation prevents articular destruction in animal models. Mutations in *EVC* or *EVC2* genes disrupt Hh signaling, and are responsible for the Ellis-van Creveld skeletal dysplasia. Hence, *Evc* deletion would hamper the expression of Hh target genes, Runx2, ColX and MMP13 among others, preventing the expression of hypertrophic mediators and protecting cartilage against OA progression. Our aim was to study whether Hh pathway inhibition restrains chondrocyte hypertrophy and the effect of *Evc* deletion on joint damage in an Evc tamoxifen induced conditional knock out (cKO) ($Evc^{cKO-/-}$) model of OA in mice.

Methods: C57BL6 wild-type (WT) and $Evc^{-/-}$ primary murine chondrocytes were isolated from cartilage explants from E18.5 embryos and cultured in micromass. Hypertrophy was induced with insulin for 14 days ($n\geq6$). Cyclopamine (5-10 μM) was used for Hh pharmacological inhibition. Gene expression of hypertrophic markers and Hh genes was measured by qRT-PCR, and proteoglycan content visualized by Alcian Blue staining. To study the effect of Evc deletion *in vivo*, OA was induced by surgical knee destabilization in WT (n=6) and $Evc^{cKO-/-}$ (n=6) adult mice and let evolve for 8 weeks. Healthy WT (n=8) and $Evc^{cKO-/-}$ (n=3) mice were used as controls. Cartilage damage and chondrocyte size were evaluated in Safranin-O and haematoxylin/eosin stained joint sections. MMP levels were assessed by western blot and hypertrophic markers gene expression by qRT-PCR.

Results: Cyclopamine prevented the expression of ColX, alkaline phosphatase (ALP), Adamts5 and Runx2 ($p< 0.05$) and reduced proteoglycan content ($p=0.004$) evoked by insulin in cultured WT chondrocytes. $Evc^{-/-}$ chondrocytes showed a partial inhibition of insulin-induced hypertrophy, with a decrease in ALP and Runx2 gene expression ($p=0.03$) and in proteoglycan content ($p=0.02$). However, Evc deletion did not modify articular cartilage damage in OA mice, since similar OARSI scores were observed in OA WT and OA $Evc^{cKO-/-}$ mice ($p=0.64$). MMP13, MMP1 and MMP3 protein levels were increased in OA WT knees ($p< 0.01$ vs Healthy WT), and reduced levels of MMP3 ($p=0.09$) and MMP13 ($p=0.18$) were found in OA $Evc^{cKO-/-}$ mice when compared to OA WT. However, gene expression of Hh genes was induced in OA WT knees, and completely inhibited in OA $Evc^{cKO-/-}$. Furthermore, ColX ($p=0.002$), ALP ($p=0.13$) and Runx2 ($p=0.21$) gene expressions were decreased in OA $Evc^{cKO-/-}$ mice in comparison with OA WT. Likewise, chondrocyte size was increased in the OA WT calcified cartilage ($p=0.098$ vs. Healthy WT), while it was diminished in OA $Evc^{cKO-/-}$ ($p=0.11$ vs OA WT).

Conclusion: Although the inactivation of Hh signaling pathway prevented chondrocyte hypertrophy, it was not able to prevent cartilage damage progression in OA $Evc^{cKO-/-}$. Therefore, our results suggest that chondrocyte hypertrophy is not a pathogenic event in the progression of articular cartilage damage in OA.

Disclosure: A. Lamuedra, None; **P. Gratal**, None; **V. Ruiz-Perez**, None; **A. Palencia-Campos**, None; **S. Portal-Nuñez**, None; **G. Herrero-Beaumont**, None; **R. Largo**, None.

Abstract Number: 1980

Disorganization of Chondrocyte Columns in the Growth Plate During Experimental Osteoarthritis in Mice

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SESSION INFORMATION
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Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
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Background/Purpose: Osteoarthritis (OA) is a biomechanical joint disease mainly affecting articular cartilage and subchondral bone. A great variety of animal models, especially mice, are used trying to mimic human disease and its pathogenesis. Unlike in humans, mouse growth plates (GP) do not completely fuse and disappear. GP chondrocytes arrange in columns, where Hedgehog (Hh) pathway plays a key role orchestrating chondrocyte differentiation. In fact, we have previously shown that *Evc*$^{-/-}$ mouse embryos exhibit loss of columns in the GP, premature hypertrophy and shorter bones due to the disruption of the Hh pathway. In neonatal mice, an altered mechanical joint loading due to hemiplegia induces disorganization of chondrocyte columns in the GP. However, it is unclear whether joint biomechanical alteration modifies GP structure in adult mice. Our aim was to study whether OA can disturb GP organization in adult mice and to assess whether the GP alteration may have an additional deleterious effect on the articular cartilage damage.

Methods: Knee OA was induced by medial meniscus sectioning in wild-type (WT) adult mice and let evolve for 8 weeks. We used an Evc tamoxifen (Tx) induced conditional knock out (cKO) model to achieve intermediate (*Evc*$^{cKO+/-}$, +Vehicle) or null (*Evc*$^{cKO-/-}$, +Tx) Evc levels in adult mice, as a control for GP disorganization. Mice were randomly assigned to different groups: healthy WT (n=8), OA WT (n=6), healthy *Evc*$^{cKO+/-}$ (n=4), OA *Evc*$^{cKO+/-}$ (n=5), healthy *Evc*-

$^{cKO-/-}$ (n=3) and OA *Evc*$^{cKO-/-}$ (n=6). GP organization assessment was performed at the central region of the tibia, and expressed as Column Index (CI). CI was calculated as the percentage of GP chondrocytes in columns, with at least 3 cells less than 20 pixels apart, angles ranging from 155° to 180°, and corrected by column length[1]. Articular cartilage damage was evaluated by OARSI score and GP thickness measured in Safranin-O stained sections.

Results: GP column measurements revealed that CI decreased by 50% in OA WT mice, showing altered columnar structure and clusters of cells (Healthy WT: 2225±125; OA WT: 682±69; p=0.0001). Healthy *Evc*$^{cKO+/-}$ mice exhibited a low CI (1015±130; p=0.0004 vs Healthy WT) while a complete Evc deletion showed a significant loss of GP organization (Healthy *Evc*$^{cKO-/-}$: 462±76; p=0.005 vs Healthy *Evc*$^{cKO+/-}$). In *Evc*$^{cKO-/-}$ mice, OA drastically reduced CI (229±55; p=0.0002 vs OA WT). No changes were observed regarding GP thickness or proteoglycan content between groups. Neither a partial deletion nor a complete loss of Evc induced cartilage damage in mice (p=0.73 and 0.11 vs Healthy WT respectively). In addition, OA WT and OA *Evc*$^{cKO-/-}$ mice showed equally severe lesions in the articular cartilage (p=0.64).

Conclusion: Profound GP chondrocyte disorganization occurred in OA adult mice due to joint instability. However, the altered GP column structure in *Evc*$^{cKO/-}$ mice did not exacerbate articular cartilage damage. Although OA leads to the loss of GP chondrocyte column structure, this alteration in the GP does not seem to void mouse experimental models of OA. Further studies are needed to confirm the lack of interference of GP pathological state on articular cartilage damage in mouse OA.

[1] *Killion CH et al. Mol Biol Cell. 2017 Jul 7;28(14):1862-1870*

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Abstract Number: 1981

Functional Differences Between Osteoclasts and Osteoclast-like Cells Differentiated from Peripheral Blood Mononuclear Cells in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoclasts (OCs) are giant multinucleated cells formed from precursors of the monocyte/macrophage lineage and are believe to play a major role in the bone destruction associated with rheumatoid arthritis (RA). Previously, we have reported that osteoclast-like cells (OLCs) are differentiated from mouse bone marrow macrophages stimulated with TNFα and IL-6; they show bone resorption activity both *in vitro* and *in vivo*. The purpose of

the present study is to investigate the functional differences between OCs and OLCs differentiated from peripheral blood mononuclear cells (PBMCs) from patients with RA or healthy controls (HCs).

Methods: PBMCs and $CD14^+$ monocytes from 9 RA patients and/or HCs were stimulated with RANKL or TNFα and IL-6. The number of tartrate-resistant acid phosphatase (TRAP)-positive multinucleated cells (OCs/OLCs) and bone resorption activity were assessed. Quantitative RT-PCR was used to measure the mRNA expression levels of *cathepsin K* and *matrix metalloproteinases (MMPs)*. The relationship between the number of OCs/OLCs and the modified total Sharp score (mTSS) or whole-body bone mineral density (BMD) was also examined.

Results: The number of OCs/OLCs differentiated from PBMCs in RA patients was significantly higher than that in HCs (RA OCs, 30.7±7.3 vs. HCs OCs, 10.0±4.0, $p< 0.01$; RA OLCs, 16.0±6.1 vs. HCs OLCs, 2.3±0.7, $p< 0.01$). These cells showed bone resorption activity on dentin slices. Moreover, CD14+ monocytes-differentiated OCs and OLCs showed significantly increased expression of *cathepsin K* mRNA compared with osteoclast precursors (OCPs) (OCs 9.4±3.5-fold, OLCs 2.3±0.5-fold vs. OCPs 1.0±0.0-fold, $p< 0.01$, respectively). In addition, the expression levels of *MMP-3* mRNA was significantly higher in OLCs than in OCs and OCPs (OLCs, 35.7±12.8-fold vs. OCs 2.8±0.5-fold, OCPs 1.0±0.0-fold, $p< 0.01$, respectively). The number of OLCs differentiated from PBMCs in RA patients was significantly positively correlated with the mTSS, erosion score, and joint space narrowing score ($r=0.82$, $r=0.79$, and $r=0.68$, respectively, $p< 0.05$), while the number of OCs was not. On the other hand, the number of OCs was significantly negatively correlated with the whole-body BMD ($r=-0.67$, $p< 0.05$), while the number of OLCs was not.

Conclusion: Our results demonstrated that the PBMCs of RA patients showed a higher OC/OLC differentiation potential than those from HCs. The bone resorption activity of PBMC-differentiated OLCs could likely have a potential role in the joint destruction, whereas OC activity plays an important role in the development of osteoporosis in RA patients. OLCs could form a subpopulation of OCs; possibly, this is one of the functional differences between OLCs and conventional OCs.

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Abstract Number: 1982

Senescent Synoviocytes in Knee Osteoarthritis Correlate with Disease Biomarkers, Synovitis, and Knee Pain

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
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Background/Purpose: Cellular senescence is a natural state in which a cell permanently halts division through upregulation of a set of intracellular proteins including p16INK4A in response to various cellular stressors. Senescent cells secrete factors collectively referred to as the Senescence Associated Secretory Phenotype (SASP) that are proinflammatory and degradative in the local tissue environment. With aging, senescent cells accumulate in multiple tissues, and senolytic therapies are being developed to address age-related diseases. We conducted a clinical study

to evaluate the relationship between the accumulation of senescent cells in OA knee synovial tissue and SASP/OA biomarkers, OA severity, and knee pain.

Methods: This was a non-drug, cross-sectional, single-center study of 30 patients with symptomatic, radiographic, femoro-tibial knee OA (defined by a modified version of the American College of Rheumatology Criteria) for ≥6 months. Synovial biopsies were obtained arthroscopically and analyzed for the presence of p16Ink4A positive cells by immunohistochemistry. Blood, urine, and synovial fluid were collected for measurement of candidate biomarkers. Fixed-flexion, standing radiographs of the knees and gadolinium contrast-enhanced (CE)-MRI scans were performed and analyzed respectively for Kellgren-Lawrence (KL) grade and 11-point semiquantitative synovitis score. Patients completed the Knee Injury and Osteoarthritis Outcome Score (KOOS) Survey, from which were derived WOMAC pain subscale scores. Correlation analyses of senescence burden (i.e. percent of p16Ink4A positive synoviocytes) to candidate biomarkers in synovial fluid, plasma, serum and urine, and to MRI-based synovitis scores, KL grades, WOMAC pain scores, were done. Partial correlation coefficients after adjustment for age, BMI, and KL grade were determined.

Results: The study cohort had a mean age of 59 yrs, 47% were women, 77% white, and 93% had a KL grade of 2 or higher. Consistent with findings in ex vivo studies of human OA knee specimens and a surgically-induced OA model in mice, we detected p16Ink4A positive, senescent cells in synovial biopsies from OA patients. Moreover, the percent of p16Ink4A positive synoviocytes correlated significantly with a number of protein biomarkers in synovial fluid and plasma; the most strongly correlated was synovial fluid interleukin-6 (IL-6). Senescent synoviocytes also correlated significantly with the degree of synovitis (range 0-2) at the site of biopsy as assessed by the MRI-based synovitis score. A trend for the correlation between senescent synoviocytes and KL grade 1 to 4 was observed; when restricting to patients with KL grades 1 to 3, the correlation was statistically significant. Interestingly, the percent of senescent synoviocytes was also moderately correlated with pain as measured by the WOMAC-A pain subscale.

Conclusion: This cross-sectional study provides further evidence for a relationship between the accumulation of senescent cells in the OA joint, SASP secretion, pain symptoms, and structural changes of knee OA. It supports investigation of senolytics as a therapy for OA.

Disclosure: C. Yohn, UNITY Biotechnology, 1, 3, 4; **R. O'Brien**, UNITY Biotechnology, 1, 3, 4; **S. Lussier**, UNITY Biotechnology, 1, 3, 4, UNITY Biotechnology, 1, 3, 4; **C. Berridge**, UNITY Biotechnology, 3, 4; **R. Ryan**, UNITY Biotechnology, 3, 4; **A. Guermazi**, AstraZeneca, 5, BICL, 1, Boston Imaging Core Lab (BICL), 1, Galapagos, 5, Merck-Serono, 5, Pfizer, 5, Roche, 5, Shareholder BICL,LLC, 1, TissueGene, 5; **M. An**, UNITY Biotechnology, 1, 3, 4; **R. Laberge**, UNITY Biotechnology, 1, 3, 4; **B. Hsu**, UNITY Biotechnology, 3, 4; **C. Millward**, UNITY Biotechnology, 3, 4; **K. Doherty**, UNITY Biotechnology, 1, 3; **J. Dananberg**, UNITY Biotechnology, 1, 3, 4, 6.

Abstract Number: 1983

Preclinical Evaluation of Targeting TGF-beta Signaling and Senescence in *ex Vivo* Models of Human Knee and Spine Osteoarthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The absence of effective disease-modifying drugs remains an important unmet need in the treatment of osteoarthritis. In recent years, novel pharmacological treatments including targeting TGF-beta signaling in subchondral bone (Zhen *et al.*, Nat Med 2013) or senescence of joint tissues (Jeon *et al.,* Nat Med 2017) have demonstrated promising efficacy in experimental osteoarthritis. However, the translation from experimental models to humans has not been pursued to date. Here, we determined therapeutic and deleterious side effects of these treatment strategies in a preclinical explant model of human knee and facet joint osteoarthritis.

Methods: Osteochondral tissue explants of osteoarthritic human knee tibial plateaus (*n*=10) or lumbar facet joints (*n*=10) were cultured for one week in the presence and absence of an inflammatory stimulus (1 μg/mL LPS). Specimens were left untreated (control) or treated with a senolytic agent (4.5 mg/mL quercetin) or inhibitor of TGF-beta receptor signaling (10μm SB-505124). Subchondral bone turnover (Pro-Collagen-Iα) and tissue inflammation (IL-6, MCP-1) was assessed by ELISA. Tissue viability was determined by MTT staining. Data was analyzed by one-way ANOVA.

Results: Explanted tissues showed no appreciable loss of viability during culture and drug treatment. LPS challenge led to a 4- and 3-fold induction of IL-6 and MCP-1 tissue secretion, respectively. Subchondral bone turnover was not affected by inflammatory conditions. The therapeutic effect of TGF-beta signaling inhibition was revealed by a drastic reduction of pro-Col-I (~75%) and IL-6 (~50%) secretion. Unexpectedly, MCP-1 secretion was significantly elevated (~200%) revealing a TGF-beta-dependent negative feedback mechanism. This side effect was specific for knee osteoarthritis and not observed in facet joint specimens. Senolytic treatment with quercetin did not affect bone turnover, yet strongly induced IL-6 tissue secretion under control (~400%) and inflammatory conditions (~200%).

Conclusion: Taking advantage of a preclinical model of human osteoarthritis, we established therapeutic efficacy of TGF-beta signaling inhibition on subchondral bone turnover in knee and spine. Elevated MCP-1 secretion upon TGF-beta targeting and increased tissue inflammation using senolytic drugs prompt careful evaluation of these potential disease-modifying agents transitioning from experimental to human osteoarthritis. Osteochondral explant models are highly valuable for determining joint-specific tissue responses.

Disclosure: J. Geurts, None; **C. Netzer**, None; **S. Schären**, None; **T. Hugle**, None.

Abstract Number: 1984

Alendronate-CGS21680 Conjugates Prevent Bone Erosion in a Murine Osteolysis Model but Not in A_{2A} KO Mice

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
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Background/Purpose: Implant loosening due to loss of bone is the most common cause of total joint replacement revision surgeries. One of the main cause of osteolysis is the shed of wear particles from the implant as it causes an increased local inflammation and osteoclast number and activity. It is known that an A_{2A} adenosine receptor selective ago-

nist (CGS21680, CGS) prevents bone loss in wear particle-induced osteolysis model in mice. But frequent administration requirements and its potential to cause side effects make it a less than optimal treatment. We therefore generated and tested a novel alendronate-CGS conjugate (MRS7216) that specifically localizes to bone targeting the agonist to the site of tissue injury and thereby diminishing the frequency of administration and curtailing systemic side effects.

Methods: The conjugate was synthesized from CGS by sequential activation of the carboxylic acid moiety and reacting with the appropriate amino acid under basic conditions. A PEG_6 linker was incorporated to alendronic acid by direct coupling. Osteolysis in 6–8-week-old C57BL/6J (WT) or A_{2A} KO mice was induced by surgical implantation of 3mg of ultrahigh-molecular-weight-polyethylene particles over the calvaria. Mice received a weekly 10mg/kg intraperitoneal dose of MRS7216 conjugate, starting at the time of surgery. Other groups of mice were treated with equivalent weekly doses of alendronate-PEG_6 (AlenP) or saline respectively. An additional control group underwent sham surgery. New bone formation was studied by Calcein/Alizarin Red-labeling. After 2 weeks, animals were sacrificed and microCT and histology analyses were performed. The studies were approved by the Institutional Animal Care and Use Committee of NYU School of Medicine.

Results: Receptor binding studies demonstrate that the Ki for CGS, 7216 conjugates and the control AlenP molecules were 21.5 nM, 69.2 nM and >10,000 nM respectively, indicating that MRS7216 efficiently binds the A2A adenosine receptor. MicroCT studies showed that WT mice treated with weekly doses of MRS7216 had a significant reduction in bone damage of 40% (p=0.04) compared to saline treated mice. In contrast, AlenP molecules did not prevent bone erosion. Similarly in A_{2A} KO mice MRS7216 treatment did not prevent bone damage. Histological analysis of TRAP stained samples showed a significant decrease of osteoclast number/high-power field (HPF) of 55% (p=0.03) in AlenP treated WT mice compared to the saline treated group. The osteoclast depletion was more dramatic in MRS7216 treated group with an 81% reduction of osteoclasts number/HPF (p=0.002). Additionally alkaline phosphatase staining in MRS7216 treated group, showed a significant increase in osteoblast number per HPF compared to saline (55%, p=0.01) and to AlenP group (45%, p=0.03). Furthermore Double bone labeling with calcein/alizarin red showed a significant increase on femurs bone formation of MRS7216 treated group compared to saline and to Alendronate group (p=0.0092 and p=0.0345).

Conclusion: Alendronate-CGS conjugates represent a novel and specific therapeutic approach to inhibit osteolysis and stimulate new bone formation to prevent prosthetic failure in patients with prosthetic joints or other bone pathologies.

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Abstract Number: 1985

Divergent Mononuclear Cell Participation and Cytokine Release Profiles Define Hip and Knee Osteoarthritis

Ricardo Grieshaber-Bouyer ,[1] Till Kämmerer,[2] Nils Rosshirt,[2] Philipp Koniezke,[2] Sebastien Hagmann,[2] Elena Tripel,[2] Johannes Kirsch,[2] Tobias Gotterbarm,[2] and Babak Moradi[2], [1]Department of Medicine, Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; Department of Orthopedics, Heidelberg University Hospital, Heidelberg, Germany, Boston, MA, [2]Department of Orthopedics, Heidelberg University Hospital, Heidelberg, Germany, Heidelberg, Germany

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
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Background/Purpose: Osteoarthritis (OA) is a progressive joint disease driven by a blend of inflammatory and biomechanical processes. Studies using human samples to understand inflammatory mechanisms in OA frequently recruit OA patients with different affected joints, even though recent evidence indicates that OA is a heterogeneous disease which only culminates in a common end point. Differences in age of onset and the dynamics of disease progression suggest that different joints may represent different disease entities, thereby diluting the discovery potential in a combined analysis. We hypothesized that different OA joints may also differ in immunopathology within the synovium.

Methods: We profiled the immune cell composition (flow cytometry) and cytokine release profiles (ELISA) in purified mononuclear cells from the synovial membrane from 51 patients undergoing either hip (n = 34) or knee (n = 17) replacement surgery. Peripheral blood was collected simultaneously and profiled using flow cytometry. Overall, 48 different cytokines were assayed. Unsupervised computational approaches were used for disease deconstruction.

Results: Hip and knee osteoarthritis were not identical with respect to the inflammatory processes that take place in the synovial membrane. The mononuclear cell infiltration pattern in the synovial membrane was highly variable between individuals, ranging from a CD4+ T cell predominant phenotype to a macrophage predominant phenotype. When directly comparing hip and knee samples, we found that macrophages and CD8+ T cells were expanded fourfold in the synovial membrane of patients with knee OA compared to hip OA, while CD4+ T cells, B cells and NK cells were found at comparable quantities. In contrast, there were no differences in immune cell abundance in the peripheral blood.

Consistent with differences in mononuclear cell infiltration into the joints, we identified differences in the cytokine release profile of cultured cells. Upon isolation and culture of cells from synovial membrane over 24 hours, isolates from hip OA released higher concentrations of Eotaxin (CCL11), G-CSF, GM-CSF, IFN-γ, IP-10 (CXCL10), TNF-α, MIP-1α (CCL3), MIP-1β (CCL4), IL-4, IL-10, IL-17 and lower concentrations of stem cell factor (SCF), thereby highlighting the difference in nature of hip and knee osteoarthritis.

Conclusion: Osteoarthritis affecting different joints has often been regarded as the same disease. This study provides evidence that hip and knee OA are immunologically distinct types of OA, warranting further investigation of different subtypes of OA. Further, this public resource of the cytokine expression landscape and mononuclear cell infiltration pattern of patients with hip and knee osteoarthritis will help accelerate research on the immunobiology of osteoarthritis.

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Abstract Number: 1986

Insights into Osteoarthritis Progression by Gene Expression and miRNA Profiling of Mesenchymal Stromal Cells from Medial and Lateral Femoral Condyles

Clara Sanjurjo-Rodríguez,[1] Rachel Crossland,[2] Thomas Baboolal,[3] Monica Reis,[4] Agata Burska,[5] Frederique Ponchel,[5] Jehan El-Jawhari,[5] **Dennis McGonagle** ,[6] Hemant Pandit,[7] Xiao-nong Wang,[8] and Elena Jones[9], [1]Grupo de investigación en Terapia Celular y Medicina Regenerativa. Departamento de Fisioterapia, Medicina y Ciencias Biomédicas. Universidade da Coruña. Agrupación estratégica CICA-INIBIC. A Coruña, España; University of Leeds; Newcastle University, A Coruña, Spain, [2]2Institute of Cellular Medicine, Newcastle University, Newcastle, United Kingdom, [3]Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM) University of Leeds, Leeds, United Kingdom, [4]Department of Pediatrics, Harvard Medical School, Boston, MA, USA, Boston, [5]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, [6]University of Leeds, Leeds, United Kingdom, [7]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds. NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, [8]Institute of Cellular Medicine, Newcastle University, UK, Newcastle, United Kingdom, [9]University of Leeds, Leeds, England, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Bone marrow multipotential stromal cells (MSC) are widely used in clinical trials to treat bone and cartilage diseases. However, there is limited information on the role of MSC in the pathogenesis in humans. As osteoarthritis (OA) severity is often associated with an abnormal movement and load distribution on the medial compartment of the knee, the aim of this study was to determine differences in MSC topography and gene expression between the diseased medial and more "macroscopically normal" lateral femoral condyles. Also, we investigated the miRNA profiling of cargo from extracellular vesicles (EVs) secreted by medial OA MSCs (OAMSC-EVs) compared with the ones secreted by healthy MSCs (HMSC-EVs).

Methods: OA MSCs were obtained from femoral condyles of total knee replacement patients and were extracted from subchondral bone after digestion and sorted using the CD271+CD45- phenotype for gene expression analysis. MSCs from healthy donors were isolated from bone marrow aspirate by density gradient centrifugation using Lymphoprep and culture expanded for EV isolation. EVs were isolated from medial and healthy MSCs by differential centrifugation and characterized before miRNA profiling using NanoString technology.

Results: Medial condyles presented higher degree of cartilage damage (OARSI score 20) compared to lateral condyles (OARSI score 3) and sclerotic subchondral bone area was higher in the medial condyles (64.3±7.0% vs 27.6±7.4% area in lateral condyles). CD271+ cells in medial and lateral femoral condyles did not show differences in topography or numbers, and cultured MSCs also presented similar growth rates and trilineage capacities *in vitro*. Three genes were significantly upregulated in medial condyle CD271+ MSCs: GREM1 (lateral MSCs below detection), PTHLH (2.4-fold, p=0.02) and STMN2 (10.5-fold, p=0.02), all of them implicated in osteogenic differentiation and mineralisation. miRNA profiling showed 46 miRNA differentially expressed between OAMSC-EVs and HMSC-EVs.

Conclusion: Despite the apparent differences in cartilage damage and bone sclerosis, no major differences were found between medial and lateral condyles. However, there was upregulation of genes implicated in osteogenic differentiation and mineralisation in medial condyle MSCs that can be associated with sclerotic-plate formation. Also,

there was differences in miRNA between medial and healthy MSCs and MSC-EVs, for which the target genes and implicated pathways need further investigation.

Disclosure: C. Sanjurjo-Rodríguez, None; **R. Crossland**, None; **T. Baboolal**, None; **M. Reis**, None; **A. Burska**, None; **F. Ponchel**, None; **J. El-Jawhari**, None; **D. McGonagle**, AbbVie, 9, Abbvie, 2, 8, BMS, 9, Celgene, 2, 8, 9, Janssen, 2, 8, Johnson & Johnson, 9, Lilly, 2, 8, MSD, 9, Novartis, 2, 8, 9, Pfizer, 2, 8, 9, UCB, 8, 9; **H. Pandit**, None; **X. Wang**, None; **E. Jones**, None.

Abstract Number: 1987

CCN3 Regulates Macrophage Function in MSU-induced Inflammation

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is the most common metabolic disease in which monosodium urate (MSU) crystals form and deposit in the joints and soft tissues of patients. While several lines of evidence support the importance of MSU-induced macrophage activation in the inflammatory response in gout, the mechanism remains unclear. Recent studies implicate CCN3 matricellular signaling protein as emerging player in the regulation of inflammation, reactive oxygen species production and angiogenesis. Additional data suggest that CCN3 regulates macrophage polarization and foam cell formation in diabetes and atherosclerosis. However, information regarding the role of CCN3 in gout remains unclear. Therefore, the objective of this investigation was to decipher the role of CCN3 in the pathogenesis of gout.

Methods: A total of 41 gout patients and 41 healthy control subjects, matched for age and sex ratio, were enrolled. PBMCs and serum were harvested and subjected to real-time PCR and ELISA analysis. MSU-induced peritonitis was conducted in LysM-Cre CCN3$^{fl/fl}$ mice with a macrophage-selective deletion of CCN3. In addition, the IL-1β production of bone marrow derived macrophage (BMM) and peritoneal macrophage with CCN3 deletion or not were investigated.

Results: Levels of CCN3 were predominantly increased in gout patients when compared to healthy controls. Furthermore, the sera CCN3 levels showed a positive correlation with inflammatory response protein CRP, while no significant correlation with lipids level were observed. To further address the role CCN3 in the pathogenesis of gout, MSU-induced peritonitis was conducted in LysM-Cre CCN3$^{fl/fl}$ mice with a macrophage-selective deletion of CCN3. As expected, LysM-Cre CCN3$^{fl/fl}$ mice showed a decreased cell infiltration in the peritoneal cavity. In addition, decreased levels of IL-1β in the peritoneal lavage fluid and caspase1 activity in peritoneal macrophage were observed in LysM-Cre CCN3$^{fl/fl}$ mice. Similarly, bone marrow derived macrophage (BMM) and peritoneal macrophage with CCN3 deletion showed an impaired caspase1 activation and IL-1β production in vitro.

Conclusion: These results indicate that CCN3 in macrophage plays a critical role in the development of MSU-induced inflammation.

Disclosure: L. Duan, None; **J. Chen**, None; **J. Zhong**, None.

Abstract Number: 1988

Establishing an in Vitro Model of Hand Osteoarthritis by Generating Induced Pluripotent Stem Cells (iPSc) That Carry Single Nucleotide Polymorphisms Associated with Hand Osteoarthritis Risk

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Background/Purpose: Knowledge and research results in the field of hand osteoarthritis (hOA) are currently limited, mainly due to the unavailability of tissue samples to develop *in vitro* studies and lack of animal models of this disease. Cellular *in vitro* models are important tools to elucidate the molecular mechanisms and pathways that are involved in hOA, but current cell sources present disadvantages. Induced Pluripotent Stem cells (iPSc) generated by genetic reprogramming of somatic cells are considered ideal tools for these purposes, since they allow the use of unlimited cells with chondrogenic differentiation potential. Therefore, the aim of this study was to generate iPSc-lines from patients with hOA and healthy donors, to evaluate the presence of at-risk single nucleotide polymorphisms (SNPs), and to assess their chondrogenic differentiation potential in order to use them as cellular models of hOA.

Methods: Patients with hOA (non erosive hOA with thumb OA) and a healthy donor were selected for the study. Fibroblasts from 3mm skin biopsies of these patients were isolated. For the reprogramming, transcriptional factors Oct4, Sox2, Klf4 and c-Myc were introduced in these cells by using Sendai virus modified vectors. Cell lines obtained were morphologically, phenotypically and functionally characterized (Fig 1A). To evaluate weather these iPSc lines could be used as cellular model of hOA, presence of 10 SNPs within genes previously associated with hOA was studied by Sanger sequencing. Finally, chondrogenic differentiation capacity of the “healthy” and “ill” iPSc-lines was studied by means of histological techniques after 21 days in micromass culture.

Results: Fibroblasts were isolated from skin biopsies of two patients with radiographic hOA and one healthy donor. Embryonic stem cell-like colonies emerged in culture three weeks after reprogramming, which fulfilled the morphologic and phenotypic criteria to be considered pluripotent cells. This means, positivity for alkaline phosphatase activity (Fig 1B) and the pluripotency markers Tra1-81 and Nanog (Fig 1C), high relative expression levels of the pluripotency-related genes OCT4, SOX2, NANOG and CRIPTO, and capacity to give rise to cells from the three germ layers. Regarding SNPs studies, we found sequence variants in 6 out of the 10 genes studied. Interestingly, the at-risk allele within the genes SMAD3 and IL1-R1 was just detected in the “ill” iPSc-lines (Fig 1D). Finally, The “ill” iPSc-line

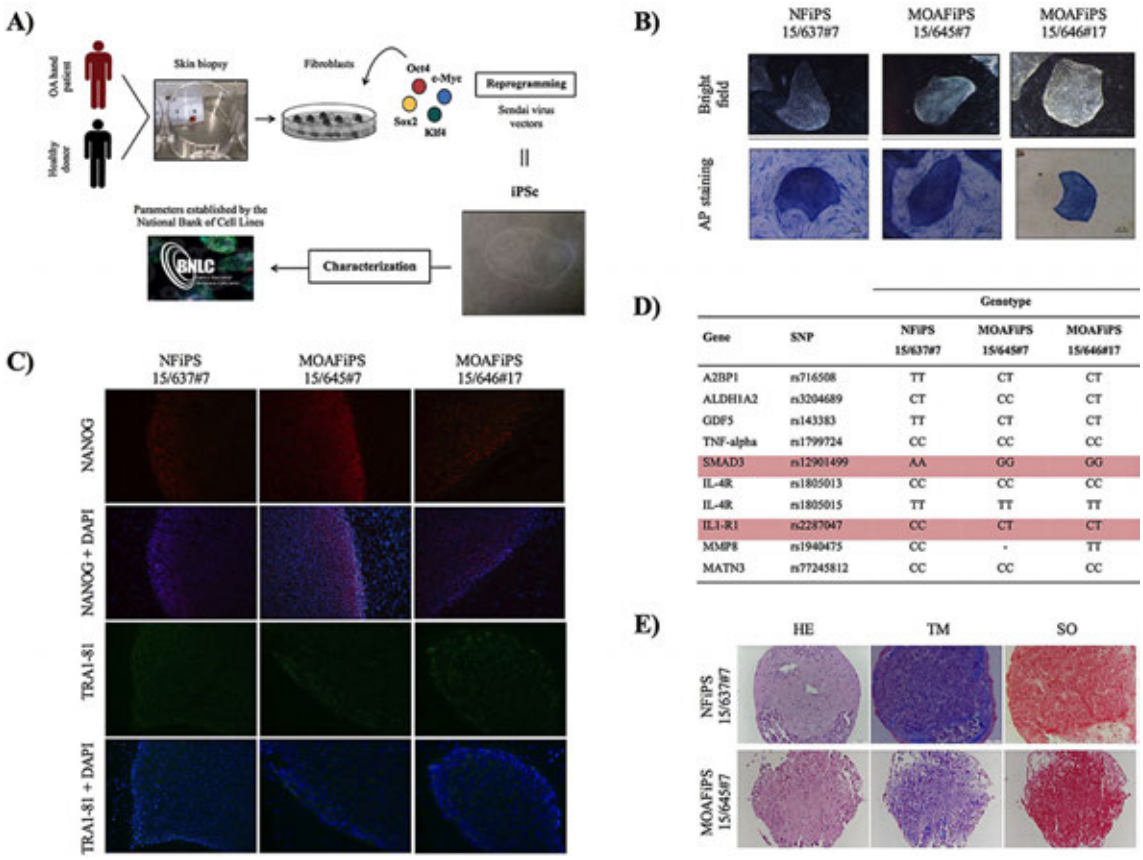

Figure 1. (A) General scheme of the followed process to generate iPSc-lines. (B) Bright field images of one representative iPSc-colonie from each donor and alkaline phosphatase (AP) activity staining. (C) Immunofluorescence images of pluripotency markers (NANOG and TRA-1-81) of representative clones from each cell line. Scale 100 μm. (D) Summarize of the results obtained after single nucleotide polymorphism analysis. (E) Haematoxilin-Eosin (HE), Masson's Tricromic (TM) and Safranin-O (SO) staining after chondrogenic differentiation of the iPSc lines. x10 magnification.

(MOAFiPS 15/645#7) showed worse chondrogenic differentiation than the "healthy" iPSc-line (NFiPS 15/637#7), as shown by the micromasses collagen and proteoglycan content (Fig 1E).

Conclusion: To our knowledge, the generation of iPSc-lines form patients with hOA is reported for the first time. The presence of sequence variants within the studied genes was maintained after fibroblast reprogramming. The generated iPSc-lines showed differences in their chondrogenic differentiation capacity, demonstrating their usefulness to model hOA *in vitro*, and to deeper study the role of these genetic variants in the pathogenesis of hOA.

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Abstract Number: 1989

Netrin-1 and Its Receptor Unc5B Mediates Tenofovir Induced Bone Loss and Dipyridamole, an Agent That Blocks Adenosine Transporter, Is Able to Modulate the Signal

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteopenia and fragility fractures have been associated with HIV infection. Tenofovir, a common antiviral in HIV treatment, also leads to increases in bone catabolism markers and decreased bone mineral density (BMD) in children and young adults. In murine models and human cell lines, tenofovir inhibits ATP release and decreases extracellular adenosine levels. We have recently reported that Netrin-1 is an autocrine and paracrine regulator of osteoclast differentiation with unique role for Netrin-1 in osteoclast biology and inflammation. We have also described that blosckade of adenoine uotaken with dipyridamole, prevent bone loss caused by tenofovir in mice. We hypothesized that Netrin1 might be involved in bone resorption induced by tenofovir, and if we increase adenosine levels, we could revert the deleterious effect of tenofovir.

Methods: Male C57Bl/6 mice were treated as follows: IP injection of saline (control), tenofovir 75mg/Kg/day, dipyridamole 25mg/Kg/day, combination tenofovir/dipyridamole (n=10, 4 weeks) and after sacrifice, long bones were prepared for histology. Primary murine M-CSF/RANKL-induced were challenge with Tenofovir 1mM alone or in combination with Dipyridamole 1mM, and expression of Netrin-1 and its receptors Unc5B and DCC were study by Western Blot.

Results: Mice treated with tenofovir showed an increased expression of Netrin-1 and its receptor Unc5b when compare to control mice, and treatment with Dipyridamole partially reverting the expression of these molecules. In vitro, tenofovir tenofovir increases Netrin1 expression (44±4% increased vs. basal, $p< 0.05$) and secretion (16±5% increased vs. basal, p=ns) and Unc5b expression (74±18% increased vs. basal, $p< 0.05$) 24 hours after stimulation, and pre-treatment with dipyridamole reverted the effect. No changes in DCC expression were observed.

Conclusion: These results suggest that Netrin-1/Unc5b might be involved in bone resorption mediated by tenofovir, and treatment with agents that increase local adenosine concentrations, like Dipyridamole, might prevent this bone loss.

Disclosure: A. Mediero, None; **P. Llamas-Granda**, None; **B. Cronstein**, Abbott, 4, Amgen, AstraZeneca, 5, Baxter, 4, Bristol-Myers Squibb, 4, CanFite Biopharma, 4, Eli Lilly & Co, 5, Gilead, 4, Horizon Pharmaceuticals, 5, NIH, Arthritis Foundation, Kairos, 2, Novartis, 4, Patent Pending for the use of adenosine receptor agonists for the treatment of OA, Patents pending for use of adenosine receptor agonist and antagonist for treatment of bone, liver diseases and wound healing, Regenosine, 4, Regenosine, Inc, 4, 6; **R. Largo**, None; **G. Herrero-Beaumont**, None.

Abstract Number: 1990

Tenofovir Modulates Semaphorin 4D Signaling and Regulates Bone Homeostasis, Which Can Be Counteracted by Dipyridamole and Adenosine A2A Receptor

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Semaphorins (Sema) are a family of proteins associated with neuronal development and guidance. Sema4D/CD100 was first identified as a regulator of immune response in resting T cells and NK cells. It has been recently found that loss of CD100 expression plays an important role in dysfunctional immunity in HIV infection. Osteopenia has been associated with HIV infection. Tenofovir, one of the most commonly used antivirals in HIV, increases in bone catabolism markers and decreased bone mineral density (BMD). Sema4D is secreted by osteoclasts (OC) in the presence of RANKL and binds to its receptor PlexinB1 on osteoblasts (OB) to inhibit their differentiation and function by activating RhoA/ROCK. Adenosine A2AR activation inhibits Sema4D-mediated OC activation and diminishes inflammatory osteolysis. We have recently described that treatment with agents that increase local adenosine concentrations, like dipyridamole, prevent bone loss following tenofovir treatment *in vivo* and *in vitro*. We hypothesized that Sema4D signaling might be regulated by tenofovir to alter bone turnover, and dipyridamole may counteract this effect.

Methods: Male C57Bl/6 mice were treated as follows: IP injection of saline (control), tenofovir 75mg/Kg/day, dipyridamole 25mg/Kg/day, combination tenofovir/dipyridamole (n=10, 4 weeks) and after sacrifice, long bones were prepared for histology. Primary murine M-CSF/RANKL-induced OC and stimulated OB were challenge with Tenofovir 1mM alone or with dipyridamole 1mM, and expression of Sema4D/PlexinB1, RhoA/ROCK and b-catenin were study by Western Blot and inmmunostaining (n=3-4). OB differentiation was studied by alizarin red staining.

Results: Mice treated with tenofovir showed an increased expression of Sema4D and its receptor PlexinB1 when comprare to control mice, and treatment with dipyridamole reverted the expression of these molecules. In vitro, tenofovir inhibits OB differentiation and treatment with dipyridamole reversed this effect. In OC, tenofovir increases Sema4D expression (1191±32% increase vs basal, $p< 0.05$) and secretion (51±20% increase vs basal, $p< 0.05$) 24 hours after stimulation, and pretreatment with dipyridamole reverted this effect. No changes in PlexinB1 expression were observed in OB. Both total b-catenin and de-phospho b-catenin (active) were increased in the cytoplasmic fraction and decreased in the nuclear fraction in OB 15 minutes after treatment with tenofovir and this was reverted in the presence of dipyridamole. Phosphorilation of RhoA was increased in OB by tenofovir 10 minutes after treatment (32±11% increase vs. basal, $p< 0.05$) and reverted by dipyridamole, and ROCK1 was increased by tenofovir 15 minutes after treatment (83±35% increase vs. basal, $p< 0.05$), and dipyridamole decreases the expression as well.

Conclusion: These results suggest that tenofovir increases bone loss by activation Sema4D/PlexinB1 signaling that inhibis OB differentiation. Treatment with agents that increase local adenosine concentrations, like dipyridamole, might prevent this bone loss following inhibition of the pathway and increase of OB differentiation.

Disclosure: A. Mediero, None; **P. Llamas-Granda**, None; **B. Cronstein**, Abbott, 4, Amgen, AstraZeneca, 5, Baxter, 4, Bristol-Myers Squibb, 4, CanFite Biopharma, 4, Eli Lilly & Co, 5, Gilead, 4, Horizon Pharmaceuticals, 5, NIH, Arthritis Foundation, Kairos, 2, Novartis, 4, Patent Pending for the use of adenosine receptor agonists for the treatment of OA, Patents pending for use of adenosine receptor agonist and antagonist for treatment of bone, liver diseases and wound healing, Regenosine, 4, Regenosine, Inc, 4, 6; **R. Largo**, None; **G. Herrero-Beaumont**, None.

Abstract Number: 1991

Inhibition of CD44 Intracellular Domain Production Suppresses Bovine Articular Chondrocyte De-differentiation Induced by Excessive Mechanical Stress Loading

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

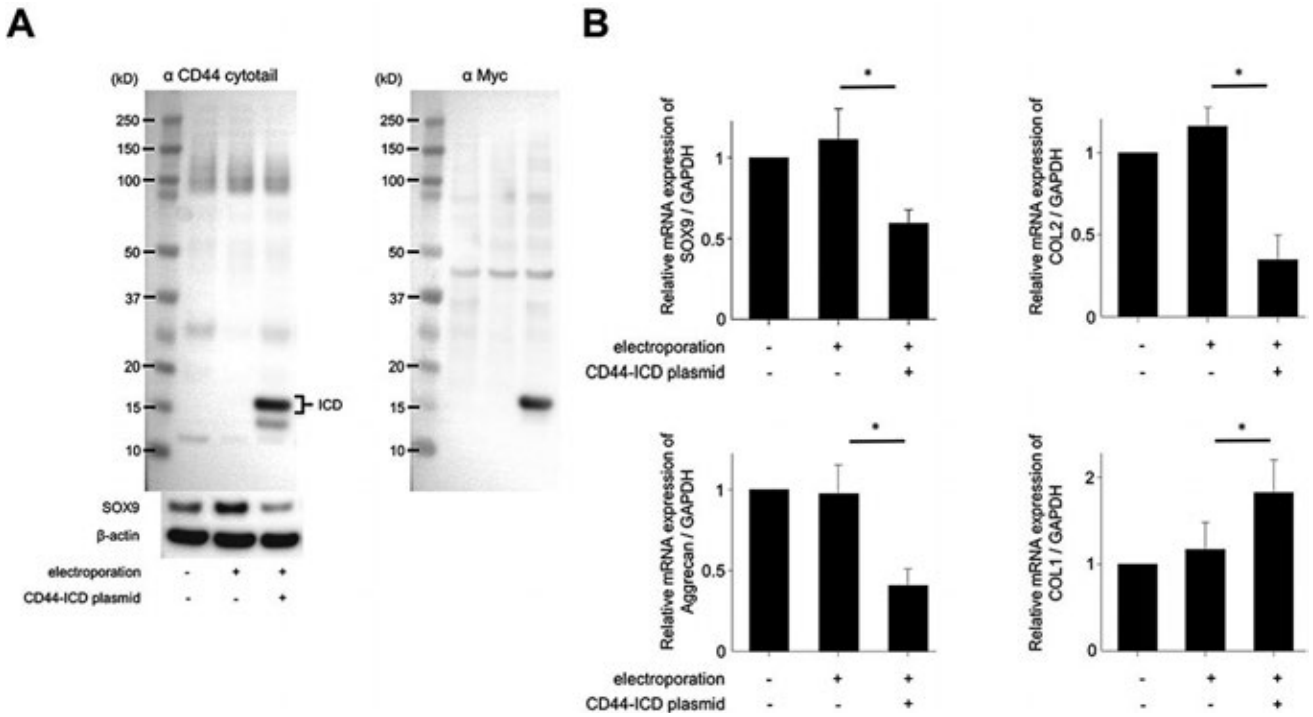
Background/Purpose: CD44 fragmentation is enhanced in chondrocytes of osteoarthritis (OA) patients. Excessive mechanical stress loading is a risk factor for OA, but the molecular mechanism underlying the relationship is unclear. We hypothesized that mechanical stress-induced enhancement of CD44-ICD production plays an important role in the de-differentiation of chondrocytes and OA. This study aimed to assess the relationship between CD44-ICD and chondrocyte gene expression.

Methods: Monolayer cultured primary bovine articular chondrocytes (BACs) were subjected to cyclic tensile strain (CTS) loading using a stretching system (STB-140) at various intensities. An ADAM10 inhibitor (GI254023X) and γ-secretase inhibitor (DAPT) were used to inhibit CD44 cleavage. In overexpression experiments, BACs were electroporated with a plasmid encoding CD44-ICD(pCMV/myc/cyto-CD44ICD).

Results: CTS loading increased the expression of ADAM10 and subsequent CD44 cleavage, while decreasing the expression of SOX9, aggrecan, and type 2 collagen (COL2) in an intensity-dependent manner. Both GI254023X and DAPT reduced the production of CD44-ICD upon CTS loading, and significantly rescued the reduction of SOX9 expression by CTS loading in a dose-dependent manner. Chemical inhibition of CD44-ICD production also rescued aggrecan and COL2 expression following CTS loading.

Induction of chondrocyte de-differentiation by CD44-ICD overexpression

The effect of CD44-ICD overexpression on the expression of chondrogenic differentiation-related genes was also assessed. As shown in Fig. A, two CD44-ICD bands of about 15 kD (a strong band and weak band) were observed in lysates of BACs transfected with the CD44-ICD plasmid by Western blot, while corresponding bands were absent in BACs that were not transfected or were transfected with control plasmid. SOX9 protein expression was reduced in BACs transfected with CD44-ICD, but not in controls (Fig. A). CD44-ICD significantly decreased the mRNA expression of SOX9, aggrecan, and COL2, while increasing the expression of COL1 mRNA (Fig. B). This suggests that the ability to maintain the chondrocyte phenotype was disrupted by CD44-ICD overexpression. These results suggest



Effect of CD44-ICD overexpression on bovine articular chondrocytes (BACs) de-differentiation. (A) BACs were transfected with plasmid DNA expressing CD44-ICD (pCMV/myc/cyto-CD44ICD) or empty plasmid as a control using an electroporator (NEPA21). A strong band of about 15 kD was observed in BACs transfected with the CD44-ICD plasmid, which was consistent with the addition of anti-Myc antibody, and SOX9 levels were reduced in these cells. (B) CD44-ICD overexpression significantly decreased the mRNA expression of chondrocyte differentiation markers (SOX9, aggrecan, and collagen type 2 [COL2]). In contrast, CD44-ICD overexpression significantly increased the mRNA expression of a chondrocyte de-differentiation marker (collagen type 1 [COL1]). N = 6, *p < 0.05.

that CD44-ICD overexpression or CD44-ICD production upon excess mechanical stress loading can promote the de-differentiation of articular chondrocytes.

Conclusion: Our findings suggest that CD44-ICD is closely associated with the de-differentiation of chondrocytes. Excessive mechanical stress loading promoted the de-differentiation of BACs by enhancing CD44 cleavage and CD44-ICD production. Suppression of CD44 cleavage has potential as a novel treatment strategy for OA.

Disclosure: Y. Sobue, None; **N. Takahashi**, AbbVie, 8, Asahi Kasei, 8, Astellas, 8, Bristol-Myers Squibb, 8, Chugai, 8, Chugai Pharmaceutical CO.,LTD., 8, Daiichi-Sankyo, 8, Eisai, 8, Eli Lilly, 8, Janssen, 8, Mitsubishi Tanabe, 8, Ono, 8, Pfizer, 8, Takeda, 8, UCB Japan, 8; **N. Ishiguro**, AbbVie, 2, 8, Abbvie, 2, 8, Asahi Kasei, 2, 8, Astellas, 2, 8, Astellas Pharma, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Chugai Pahrmaceutical, 2, 8, Chugai Pharmaceutical CO.,LTD., 2, 8, Daiichi-Sankyo, 2, 8, Eisai, 2, 8, Eli Lilly, 2, 8, Janssen Pharmaceutical, 8, Kaken, 2, 8, Lilly, 8, Medical Corporation Sanjinkai, 2, 5, 8, Medical Corporation Toukoukai, 2, 5, 8, Mitsubishi Tanabe, 2, 8, Ono, 2, 8, Otsuka, 2, 8, Pfizer, 2, 8, Taisho Toyama, 2, 8, Takeda, 2, 8, Tanabe Mitsubishi Pharma, 2, 8, UCB, 8, Zimmer Biomet, 2, 8; **T. Kojima**, AbbVie, 2, 8, Abbvie, 8, Astellas, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Chugai Pahrmaceutical, 2, 8, Chugai Pharmaceutical CO., LTD., 2, 8, Daiichi-Sankyo, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Janssen Pharmaceutical, 8, Lilly, 2, 8, Mitsubishi Tanabe, 2, 8, Novartis, 2, 8, Pfizer, 2, 8, Takeda, 2, 8, Tanabe Mitsubishi Pharma, 8.

Abstract Number: 1992

Adenosine A2A Receptor (A2AR) Stimulation Mitigates Mitochondrial Inflammaging, Enhances Mitochondrial Metabolism and Reduces Reactive Oxygen Species-Mediated Mitochondrial Injury *In Vitro* and *In Vivo* in Osteoarthritis

Cristina Castro ,[1] Carmen Corciulo,[2] Maria Solecio,[3] Benjamin Friedman,[4] Fengxia Liang,[5] Zhi Li,[6] Samson Jacob,[7] David Fenyo,[8] Evgeny Pavlov,[9] and Bruce Cronstein[4], [1]Immunology and Inflammation Training Program at Skirball Institute of Graduate Biomolecular Sciences, New York University School of Medicine (NYUSoM), NYC, [2]Division of Translational Medicine NYUSoM, NYC, [3]NYU College of Dentistry, NYC, [4]Department of Medicine, Division of Rheumatology NYUSoM, NYC, [5]Department of Cell Biology, NYU Langone Health, NYC, [6]Institute for Systems Genetics, Department of Biochemistry and Molecular Pharmacology, NYU Langone Helalth, NYC, [7]Institute for Systems Genetics, NYU Langone Health, NYC, [8]Institute for Systems Genetics, Department of Biochemistry and Molecular Pharmacology, NYC, [9]Basic Science and Craniofacial Biology, NYU College of Dentistry, NYC

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is the most common form of arthritis, affecting nearly 10% of the US population and one of the contributing factors in OA pathogenesis is inflammaging, chronic low grade inflammation. With injury and aging there is dysfunction of chondrocyte mitochondria, thought to be a central event in inflammaging, resulting in reduction of intracellular and extracellular ATP and extracellular adenosine. Reductions in extracellular adenosine or loss of A2AR leads to the development of OA. We therefore explored determined whether A2AR ligation regulates mitochondrial health *in vivo* and *in vitro.*

Methods: Primary murine WT and A2ARKO as well as primary human chondrocytes were isolated from neonatal mice or differentiated from surgical discard, treated with medium (CTRL) or IL-1β (5ng/mL for 4h) with and without the A2AR agonist, CGS21680 (1uM for 1h, CGS) or CGS alone and then stained with TMRM to evaluate mitochondrial length, network volumes and membrane polarity. RNAseq, RT-PCR and transmission electron microscopy (TEM) were performed in untreated murine chondrocytes and proteins of interest were evaluated by WB. Mitochondrial markers were also evaluated in rat post-traumatic OA (PTOA) and mouse obesity-induced OA (OB-OA) models*in vivo.* Human chondrocytic cells (T/C28-a2) were grown in culture, treated as stated above and submitted for TEM to study mitochondrial ultrastructure. Primary human chondrocytes were cultured from discarded surgical specimens.

Results: WT chondrocytes treated with CGS +/- IL-1β had increased mitochondrial lengths than cells that received medium or IL-1β alone ($p< 0.0001$, ONE-Way ANOVA). There were no significant differences in mitochondrial lengths of untreated WT or null chondrocytes but loss of A2AR signaling prevented mitochondrial length expansion after stimuli ($p< 0.04$, ONE-Way ANOVA). Depolarization upregulates total PINK1 expression in A2AR-/- ($p< 0.005$, unpaired, two-tailed t-test) but not Parkin levels. ROS burden was reduced and mitochondrial markers were improved in PTOA and OB-OA models in vivo. In fully differentiated human chondrocytes, A2AR ligation after stimulation with IL-1β increased TMRM and mitochondrial volumes ($p< 0.0001$, ONE-Way ANOVA). T/C28-a2 cells treated with CGS after IL-1β exposure had significantly reduced cristae widths ($p< 0.0001$) and an increased number of cristae junctions per mitochondria ($p=0.02$, ONE-Way ANOVA).

Conclusion: A2AR ligation enhances mitochondrial function and biomass in murine chondrocytes *in vitro*and *in vivo* in models of OA and, thereby diminishes the signs of inflammaging, maintains chondrocyte homeostasis and reverses OA *in vivo*.

Disclosure: C. Castro, None; **C. Corciulo**, None; **M. Solecio**, None; **B. Friedman**, None; **F. Liang**, None; **Z. Li**, None; **S. Jacob**, None; **D. Fenyo**, None; **E. Pavlov**, None; **B. Cronstein**, Abbott, 4, Amgen, AstraZeneca, 5, Baxter, 4, Bristol-Myers Squibb, 4, CanFite Biopharma, 4, Eli Lilly & Co, 5, Gilead, 4, Horizon Pharmaceuticals, 5, NIH, Arthritis Foundation, Kairos, 2, Novartis, 4, Patent Pending for the use of adenosine receptor agonists for the treatment of OA, Patents pending for use of adenosine receptor agonist and antagonist for treatment of bone, liver diseases and wound healing, Regenosine, 4, Regenosine, Inc, 4, 6.

Abstract Number: 1993

Inhibition of Choline Kinase Alpha Improves Synovitis and Cartilage Damage in Animal Models of Osteoarthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a disease of the whole joint, affecting cartilage, ligaments, menisci, bone and synovial tissue. We previously found that choline kinase alpha (ChoK) expression was upregulated in human OA synovial and cartilage tissues, and inhibition of ChoK decreased production of proinflammatory cytokines by OA synovial fibroblasts and inhibited chondrocyte catabolic responses to IL-1b *in vitro*. In this study, we evaluated the effects of ChoK inhibition on OA development *in vivo* in two animal models of OA.

Methods: Collagenase-induced osteoarthritis (CIOA) was done in 12-week old male C57BL/6 mice (intraarticular injection of 1 U of collagenase in left knee and PBS in the contralateral knee). MN58b (a ChoK inhibitor) was administered daily via intraperitoneal injection (i.p) at a dose of 2.5mg/kg. The control group received PBS i.p. Mice were sacrificed at 2 weeks. The destabilization of the medial meniscus (DMM) surgery-induced OA was performed in 12 weeks old male C57BL/6 mice on the right knee with sham surgery performed on the contralateral knee (control). PBS or MN58b (2.5mg/kg) i.p. was administered daily for 2 weeks and then every other day until 12 weeks when mice were sacrificed. Joints were graded for synovitis (1 none to 5 severe). Micro-computed tomography (μCT) at $(9\ \mu m)^3$ voxel size was used to evaluate associated bone damage in the DMM model. The medial and lateral femoral condyle (MFC, LFC) and medial and lateral tibial plateau (MTP, LTP) of the arthritic and contralateral knees were registered and visualized in tri-plane orthogonal views, centered in each region, and also in periodic 2-D planes (150 per knee). Joint sections were analyzed by histology with H&E and Saf-O/FG and scored for cartilage damage and osteophyte size and maturation, as well as by immunohistochemistry, probing for ChoK, CD86 and iNOS.

Results: In CIOA, synovitis was reduced from 2.0±1.5 (range 1–5, N=13) in control mice to 0.5±1.0 (range 0–3, N=11, p=0.03) in MN58b-treated mice. Compared to the control group, the MN58b-treated CIOA joints had a lower number of infiltrating cells in the synovial membrane that were positive for ChoK, iNOS and CD86. In the DMM model, cartilage damage in the control group (4.0±2.0, range 2–6, N=9) was reduced by MN58b treatment (1.8±1.3, range 0–4, N=10, p=0.018). Furthermore, medial osteophytes in the control group (1.04±0.59, range 0–1.9) tended to be reduced

in size by MN58b (0.72±0.6, range 0–1.7, p=0.1), although no difference was observed in the degree of maturation. μCT indicated that MN58b treatment reduced medial osteophyte size (by 28%, p=0.04) and medial subchondral plate thickness (by 12%, p< 0.01).

Conclusion: Our results show that ChoK inhibition reduces the degree of synovitis in CIOA animal model of OA, and cartilage damage and osteophyte size in the DMM model of OA. These findings suggest that ChoK may mediate multiple pathways of joint damage in the pathogenesis of OA and be a potential therapeutic target.

Disclosure: R. Coras, None; **L. Liu**, None; **S. Shi**, None; **A. Cheng**, None; **A. Stubelius**, None; **E. Sanchez-Lopez**, None; **R. Sah**, None; **R. Liu-Bryan**, None; **M. Guma**, None.

Abstract Number: 1994

Helicobacter Pylori Infection Among Korean Patients with Rheumatoid Arthritis and Its Interaction with Shared Epitope

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: While smoking is an important environmental risk factor for rheumatoid arthritis (RA) development, only a small proportion of Korean patients with RA were found to have tobacco exposure. Since Helicobacter pylori (HP) infection is not only highly prevalent among Korean adult population but also causes chronic gastric inflammation, we aimed to test potential interaction between shared epitope (SE) and HP infection for the risk of anti-citrullinated protein antibody (ACPA)-positive RA in a Korean population.

Methods: SE distribution and HP infection status were compared between ACPA-positive patients (n=202 for cases) who met 1987 ACR classification criteria for RA and age- and sex-matched healthy controls (n=187 for controls). SE

Table 1. Association between rheumatoid arthritis and shared epitope (SE) or Helicobacter pylori (HP) infection

Model 1[a]			Model 2[a]		
	OR [95% CI]	p		OR [95% CI]	p
SE	7.40 [4.60-11.90]	<0.0001	SE	7.08 [1.96-25.49]	0.003
HP infection	2.72 [1.42-5.21]	0.003	HP infection	2.62 [0.85-8.12]	0.093
			SE x HP infection	1.05 [0.27-4.15]	0.94

[a]Both models included age and sex in addition to the dependent variables presented above.

SE x HP infection is the interaction variable generated by a product of SE (0, 1) and HP (0, 1).

was considered positive for HLA-DRB1*01:01, *01:02, *04:01, *04:04, *04:05, *04:08, *04:10, *10:01, *14:02, and *14:06. HP infection was assessed by ELISA based anti-HP IgG titers (cut-off value of 20 U/mL). Logistic regression analysis was used to estimate the odds ratio (OR) and 95% confidence interval (CI). The relative excess risk due to interaction (RERI) based on OR was estimated to assess additive interaction.

Results: Patients with RA showed a mean (standard deviation, SD) age of 41 (11.7) years with 63.3% female. The anti-HP IgG titer was significantly higher among RA patients than controls (mean±SD, 6832±6406 vs. 3539±5238, $p < 0.0001$). RA patients showed a higher prevalence of HP infection and SE than controls (90.1% vs. 75.9%, $p < 0.0001$ for HP infection; 75.2% vs. 35.1%, $p < 0.0001$ for SE). SE and HP infection were independently associated with RA, adjusting for age and sex (Table 1, Model 1). The magnitude of association between HP infection and RA was similar between SE carriers (2.63 [1.17-5.88]) and non-carriers (2.72 [0.90-8.47], adjusting for age and sex. We found no multiplicative interaction between HP infection and SE for the risk of RA (measure of interaction [95% CI] = 1.05 [0.27-4.15, $p = 0.94$) (Table 1, Model 2). Although the additive interaction was positive ($RERI_{OR}$ [95% CI] = 9.87 [-3.73-23.48], $p = 0.15$), it was not statistically significant possibly due to limited power.

Conclusion: There was a significant association between RA and HP infection independent of SE status. We found no multiplicative interaction but positive, albeit statistically not significant, additive interaction between HP infection and SE for the risk of RA. Whether the association derives from causal relationship or merely suggests a higher susceptibility towards HP infection among RA patients remains to be determined.

Disclosure: E. Kang, Seoul National University Bundang Hospital, 3; **S. Bang**, Hanyang University, 3; **Y. Lee**, None; **Y. Ha**, Seoul National University Bundang Hospital, 3; **Y. Lee**, Seoul National University Bundang Hospital, 3; **Y. Song**, Astellas Pharma, Inc., 9; **S. Bae**, None; **E. Lee**, Seoul National University Hospital, 3.

Abstract Number: 1995

Gingival-Derived Mesenchymal Stem Cells Alleviate Cartilage Damage in Collagen-Induced Arthritis via Suppressing Activities of Inflamed Synovial Fibroblast

Ximei Zhang ,[1] Julie Wang,[2] Nancy Olsen,[3] Wael Jarjour,[4] and Song Guo Zheng[4], [1]Ohio State College of Medicine, Columbus, [2]Ohio State University, columbus, [3]Penn State University, Hershey, PA, [4]Ohio State College of Medicine, Columbus, OH

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Dysfunction of immunology and inflammatory responses is crucial in initiating and promoting bone/cartilage destruction in rheumatic arthritis (RA). Inflamed synovial fibroblast cells (ISFs) are the most prominent player in both inflammation and joint destruction in RA. ISFs not only produce pro-inflammatory cytokines that promote the differentiation and activation of osteoclasts and bone erosion but also expresses matrix metalloproteinases (MMPs) that contribute to matrix degradation. In addition, ISFs have a tumor-like behavior that directly attaches to articular cartilage and invades the extracellular matrix. Gingiva-derived mesenchymal stem cells (GMSC) are a unique population of mesenchymal stem cells(MSCs) with the intrinsic ability of self-renewal, potential for multilineage differentiation and potent immunoregulatory ability. Our preliminary data and many studies from other groups have demonstrated that infusion of MSCs significantly suppressed the disease development in various animal models of autoimmune diseases including RA model, nonetheless, it is unknown whether GMSC can target ISFs in rheumatoid arthritis.

Methods: To explore whether GMSCs suppress cytokines production of ISFs derived from patients with RA, ISFs were co-cultured with GMSC or control cells with different ratios (1:2-1:50 of GMSCs to ISFs) and the production of the pro-inflammatory factors TNF-α, IL-6, IL-12, IL-18, IL-1β, IL-11, IL-15, monocyte chemoattractant protein (MCP)-1, MMPs as well as anti-inflammatory cytokines IL-10, IL-1R were measured by qPCR or ELISA. ISFs were also co-cultured with GMSCs for 1-3 days and detected by CCK-8 (proliferation) or crystal violet staining (migration and invasion) to study whether GMSCs inhibit the tumor-like biologic behaviors of ISFs. To determine whether GMSC target ISFs in vivo, GMSC were adoptively transferred into CIA mice and humanized animal model.

Results: Our results showed that GSMC but not control cells significantly inhibited the production of the pro-inflammatory factors and matrix metalloproteinases, as well as proliferation, migration and invasion of ISFs isolated from RA patients in vitro. In line with these results in vitro, infusion of GMSCs reduced the activation of osteoclasts and bone erosion in CIA mice. ISFs isolated from CIA treated with GMSCs showed reduced expression of pro-inflammatory factors and matrix metalloproteinases and suppressed tumor-like biologic behaviors, with lower proliferation, migration and invasion. Moreover, infusion of GMSC markedly controlled the migration and invasion of RA-ISFs in a humanized animal model.

Conclusion: GMSC target RA-ISFs that implicates GMSC may have a potential promise to treat patients with RA.

Disclosure: X. Zhang, None; **J. Wang**, None; **N. Olsen**, None; **W. Jarjour**, None; **S. Zheng**, None.

Abstract Number: 1996

Bromodomain Inhibitor, I-BET762 Inhibits Production of Pro-inflammatory in Rheumatoid Arthritis Fibroblast-like Synoviocytes and Differentiation of Osteoclast

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Etiology & Pathogenesis Poster II

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disorder, characterized by joint inflammation and bone destruction. The fibroblast-like synoviocyte(FLS) contributes to the pathogenesis of RA through cellular proliferation and production of cytokines or chemokines. Recently, blockade of the bromodomain and extra-terminal domain (BET) family protein was reported to be a potential therapeutic target by inhibiting epigenetic interaction between bromodomains and acetylated histones. This study aimed to investigate the effects of bromodomain-

containing protein 4 (BRD4) inhibition on tumor necrosis factor (TNF)-α-stimulated RA-FLS and osteoclast using BRD4 inhibitor, I-BET762.

Methods: RA-FLSs were treated with TNF-α in the presence of I-BET762 for 48 h. The cell viability and proliferation were measured after 24, 48, and 72 h in I-BET762-treated RA-FLS using CCK-8 colormetric assay. We then screened pro-inflammatory mediators by using the human inflammation antibody array. The levels of interleukin (IL)-6, IL-8 and CXCL-10 were measured in culture supernatants of TNF-α-stimulated RA-FLS by ELISA. Migrations were analyzed by the wound healing assay. We compared the expression of BRD2, BRD3 and BRD4 level by BRD4 specific inhibition in RA. Expression of c-Myc was detected by using Western blot. PBMC isolated from buffy coat were cultured with M-CSF and RANKL for 14 days in the presence or absence of I-BET762. Cells were stained with tartrate-resistant acid phosphatase (TRAP) and the number was counted by light microscopy. The ability of actin formation in osteoclast was evaluated by immunofluorecent stain.

Results: I-BET762 had no effect on cytotoxicity and proliferation of RA-FLS. I-BET762 reduced the secretion of IL-6, CXCL-10 and regulated upon activation, normal T cell expressed, and secreted (RANTES) from RA-FLS in the antibody array. Level of IL-6, IL-8 and CXCL-10 were significantly decreased after treatment with I-BET762 by ELISA. The number of migrated cells decreased in response to I-BET762 compared with the vehicle. The expression levels of BRD2, BRD3 and BRD4 proteins did not change with I-BET762. Expression of the target molecule, c-Myc, was decreased in I-BET762 treated RA-FLSs. TRAP-positive multinucleated (more than three nuclei) cells were reduced in a dose-dependent manner. The actin formation of podosome, actin belt and actin ring were inhibited in the presence of I-BET762.

Conclusion: Inhibition of BRD4 by I-BET762 led to down-regulation of pro-inflammatory mediators, migration and expression of c-Myc in RA-FLSs. The differentiation of osteoclast and resorption activity was inhibited by I-BET762. These data suggest that the I-BET762 may have anti-inflammatory properties and prevent bone loss in RA.

Disclosure: R. Kim, None; **H. Yoo**, None; **S. Kang**, None; **J. Park**, None; **S. Kim**, None; **E. Lee**, None; **J. Park**, None; **Y. Song**, Astellas Pharma, Inc., 9.

Abstract Number: 1997

Histologic and Clinical Correlates of Ultrasound Measures of Joint Inflammation: Analysis of RA Tissue Obtained by Ultrasound Guided Biopsy in Phase 2 of the Accelerating Medicines Partnership RA Network

Diane Horowitz ,[1] Andrew Filer,[2] Jennifer Albrecht,[3] Arthur Mandelin,[4] Darren Tabechian,[5] Edward DiCarlo,[6] Brendan Boyce,[3] Ellen Gravallese,[7] Peter Gregersen,[8] Dagmar Scheel-Toellner,[9] Kevin Wei,[10] Katherine Liao,[11] Larry Moreland,[12] V. Michael Holers,[13] Michael Brenner,[14] Jennifer Anolik,[3] and Vivian Bykerk[15], [1]Northwell Health, Great Neck, NY, [2]Institute of Inflammation and Ageing College of Medical and Dental Sciences University of Birmingham, Birmingham, United Kingdom, [3]University of Rochester Medical Center, Rochester, NY, [4]Northwestern University Feinberg School of Medicine, Division of Rheumatology, Chicago, IL, [5]University of Rochester, Rochester, NY, [6]Hospital for Special Surgery, New York, [7]University of Massachusetts Medical School, Worcester, MA, [8]Feinstein Institutes for Medical Research, Manhasset, NY, [9]University of Birmingham, Birmingham, United Kingdom, [10]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [11]Brigham and Women's Hospital, Boston, [12]University of Pittsburgh, PITTSBURGH, PA, [13]University of Colorado Denver, Division of Rheumatology, Aurora, CO, USA, Denver, [14]Brigham and Women's Hospital:, Boston, [15]Hospital for Special Surgery, New York City, NY

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Etiology & Pathogenesis Poster II

Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The AMP-RA network applies cutting edge molecular single cell technologies to study synovial tissue obtained from rheumatoid arthritis (RA) patients using US guided synovial biopsy (USGSB). Ultrasound can provide objective joint level measures of synovial inflammation, including hypertrophy (greyscale ultrasound, GSUS) and hyperemia (Power Doppler ultrasound, PDUS). Phase 1 AMP-RA demonstrated that USGSB was effective and safe for obtaining synovial tissue in the United States in patients with RA. In Phase 2 RA patients with active disease were recruited based on treatment exposure. We examined the relationship between joint level US variables, clinical characteristics, and synovial histology in Phase 2 patients.

Methods: In this multi-center study, eligible AMP-RA Phase 2 subjects had classifiable RA, ≥2 actively inflamed joints including the biopsied "sentinel" joint, a CDAI >10, and a GSUS of ≥2 of the biopsied joint. Biopsies were done using either QuickCore™ needle or Portal and Forceps. Subject Groups defined by treatment exposure were: (1) DMARD naïve/ minimally exposed (≤ 4 weeks of MTX)((n=40), (2) MTX-IR despite ≥3 months of MTX (n=29), (3) TNF-IR despite ≥3 months of anti-TNF therapy. US scanned sentinel joints were scored using a 4-point semi-quantitative scale of GSUS and PDUS alongside composite RA disease activity measures. Retrieved tissue was fixed, stained and paraffin embedded, then sectioned and stained by H&E. Tissues were assessed for quality based on presence of and quantity of lining layer and synovium. Tissues were scored using 2 of 3 Krenn domains: lining layer (Krenn L) (0-3) and inflammatory infiltrate (Krenn I)(0-3) by three pathologists (BB, ED, EG).

Results: Of 119 synovial biopsies obtained from 13 sites across the USA and UK, 93 (83%) were of good quality. Clinical Groups 1, 2, and 3 had similar disease activity and US scores but the expected differences in disease duration (Table 1). GSUS, PDUS, CDAI, and Disease Duration were similar between the samples regardless of histology quality. Krenn scores differed between the Groups: Group 1 biopsies had higher mean Krenn(I) and Krenn(L) scores and a greater proportion with Krenn(L) and Krenn(I) scores of >1 (Table 2). PDUS grade correlated with the Krenn(L) and the Krenn(I) scores (p=0.003, r=0.32). GSUS grade failed to correlate with either histological measure (p=0.55, p=0.43 respectively).

Conclusion: In this cohort, the clinical and ultrasound characteristics did not correlate with tissue quality. Ultrasound measures of synovial hyperemia correlate with histologic joint infiltrates. Group 1 subjects had the shortest disease duration and least medication exposure. Despite such, Group 1 had higher mean Krenn(I) scores when compared to the MTX-IR (Group 2) and TNF-IR (Group 3) subjects.

Table 1. Clinical, Ultrasound and Histology correlates for 3 clinical groups.

Table 1: Clinical, Ultrasound and Histology correlates for 3 clinical groups.

	Number of Samples	CDAI Mean(SD)	Disease Duration Years Mean (SD)	GSUS Mean(SD)	PDUS Mean(SD)
Group 1	40	30.32(16.33)	1.30 (3.93)	2.03(0.76)	1.18(0.95)
Group 2	29	38.82(15.80)	9.02 (10.75)	2.23(0.65)	1.31(1.09)
Group 3	23	26.21(11.84)	11.69 (8.86)	1.89(1.08)	1.06(1.11)

Table 2. Krenn scores for 3 Clinical Groups

Table 2: Krenn scores for 3 Clinical Groups

	Number of Samples	% Krenn (L) > 1	% Krenn (I) > 1	Krenn (L) Mean(SD)	Krenn (I) Mean(SD)
Group 1	40	34.20%	62.50%	0.98(0.54)	1.66(0.78)
Group 2	29	24.14%	58.60%	0.96(0.54)	0.54(0.97)
Group 3	23	21.73%	39.10%	0.76(0.57)	0.57(0.86)

Disclosure: D. Horowitz, None; **A. Filer**, None; **J. Albrecht**, None; **A. Mandelin**, None; **D. Tabechian**, None; **E. DiCarlo**, None; **B. Boyce**, None; **E. Gravallese**, None; **P. Gregersen**, None; **D. Scheel-Toellner**, None; **K. Wei**, None; **K. Liao**, None; **L. Moreland**, None; **V. Holers**, AdMIRx, 1, 2, 4, 5, 6, Alexion, 7, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 5, Janssen R&D, 2, 5, Pfizer, 2; **M. Brenner**, None; **J. Anolik**, None; **V. Bykerk**, AbbVie, 5, Amgen, 1, 2, 3, 5, 8, Brainstorm Therapeutics, 1, 2, 3, 5, 8, Bristol-Myers Squibb, 5, Genentech, 5, Gilead, 5, NIH, 2, Pfizer, 1, 2, 3, 5, 8, Regeneron, 5, Regeneron Pharmaceuticals, Inc, 5, Sanofi, 5, Sanofi/Genzyme-Regeneron, 5, Sanofi-Genzyme/Regeneron, 1, 2, 3, 5, 8, Scipher, 1, 2, 3, 5, 8, The Cedar Hill Foundation, 9, UCB, 1, 2, 3, 5, 8, UCB Pharma, 5.

Abstract Number: 1998

Major Histocompatibility Antigen HLA-DQB1*0601 Is Associated with Rheumatoid Arthritis Among Indians in a Replication Study: Evidence of Gene-Environment Interaction with LPG Stove Use

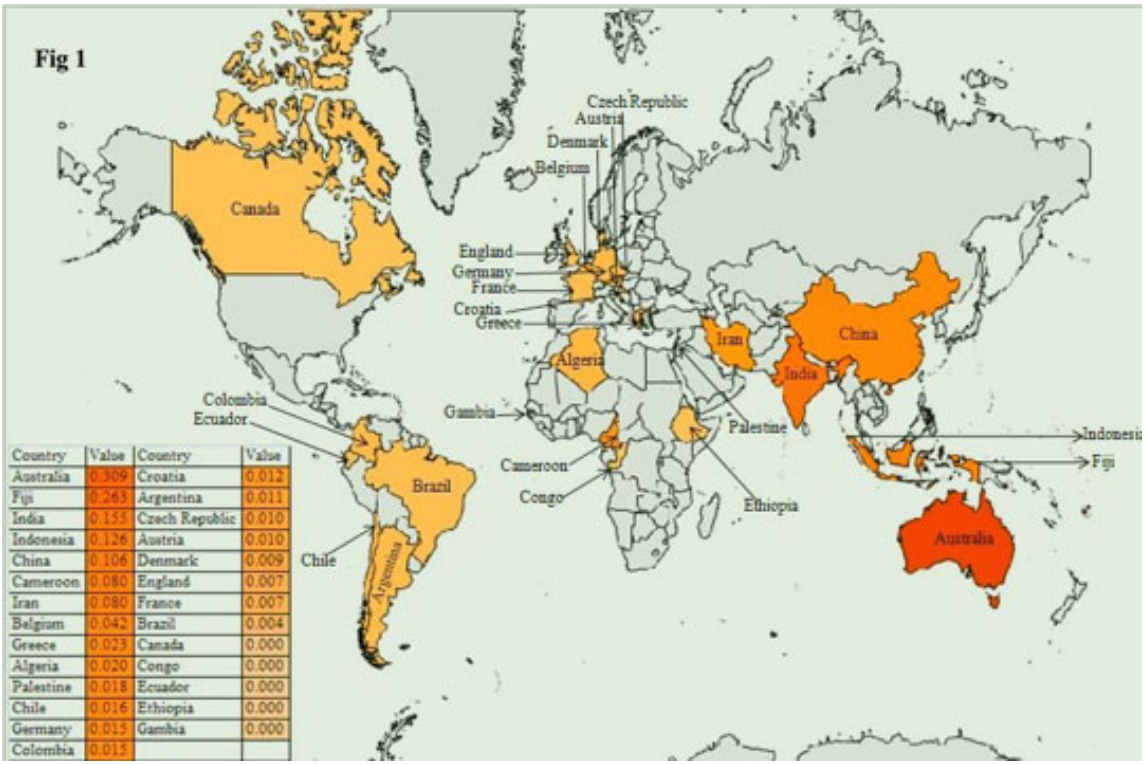
Able Lawrence ,[1] Anshul Dhar,[2] Swayam Prakash,[3] Suvrat Arya,[4] Amita Aggarwal,[5] and Suraksha Agrawal[6], [1]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Lucknow, Uttar Pradesh, India, [2]SGPGIMS, Lucknow, India, [3]Cellular and Molecular Immunology Laboratory University of California Irvine, School of Medicine USA, Irvine, CA, [4]Sanjay Gandhi Postgraduate Institute, Lucknow, India, Lucknow, India, [5]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, Lucknow, Uttar Pradesh, India, [6]SGPGIMS, Lucknow, Uttar Pradesh, India

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Shared epitope smoking interaction does not fully explain MHC association in Rheumatoid Arthritis (RA). We have previously shown HLA-DQB1*0601 (DQ6.1) to be a susceptibility allele in India1. It has a restricted geographic distribution being common in Japan, India and parts of middle-east while absent in Africa and western Europe (Fig 1 heat map of DQ6.1 distribution). In Pristane induced arthritis, susceptibility is determined by rat ortholog of DQ locus RT1-B. Thus it is possible that HLA-DQ6.1 may have an interaction with hydrocarbons. We therefore planned this study to confirm the association of DQ6.1 with RA and explore interactions with smoking and household fuel use.

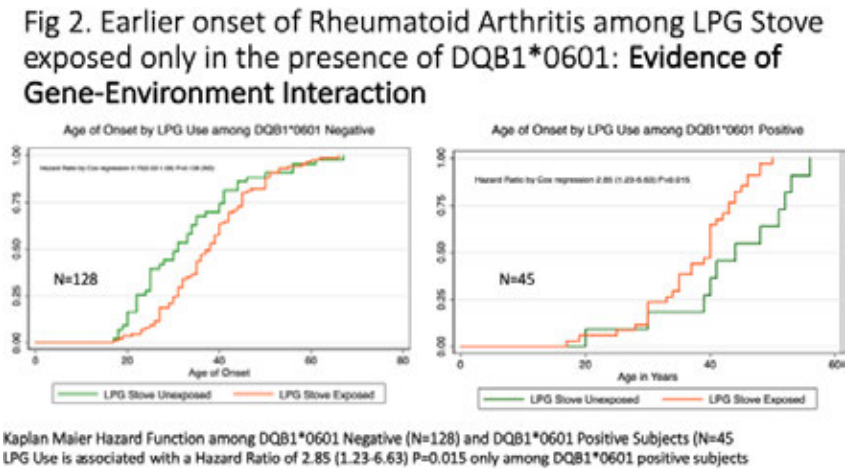
Methods: Patients with RA (ACR 2010 criteria) and healthy controls of similar ethnic background were included. Data on environmental exposure like tobacco use, active and passive smoking and exposure to household smoke during cooking including biomass fuels (wood, coal, cow-dung cake) and hydrocarbon fuels LPG and kerosene was collected. Patients sex, age of onset, duration of exposure, birth year, RF, anti-CCP were also recorded. HLA-DQB1*0601, DQB1*0603 and DQA1*0103 were typed using Sequence specific PCR. The association of Chi-squared test was used to test the strength of association. Gene environment interaction was studied using Cox regression after stratifying by genotype.

Results: 175 patients (21 males) and 263 healthy controls were included. The median age of onset of RA was 37(range 17-67 years) and median duration of disease was 9 years(range 2mo to 35 years). Of these 138/172 (80%) were RF positive and 104/126 (82.5%) were anti-CCP positive. Overall 165 were seropositive and 7 seronegative. Among patients DQB1*0601 was present in 45/175 (25.7%) while DQB1*0603 in 27/175(15.4%) and DQA1*0103 in 35/175(20%). Among controls, DQB1*0601 was present in 47/263 (17.9%) while DQB1*0603 was present in 31/263(11.8%) and DQA1*0103 in 42/263(16%). The putative risk allele DQB1*0601 was significantly associated with RA with an Odds Ratio of 1.59 (P< 0.005) confirming the association. There was no significant association be-



Country	Value	Country	Value
Australia	0.309	Croatia	0.012
Fiji	0.263	Argentina	0.011
India	0.155	Czech Republic	0.010
Indonesia	0.126	Austria	0.010
China	0.106	Denmark	0.009
Cameroon	0.080	England	0.007
Iran	0.080	France	0.007
Belgium	0.042	Brazil	0.004
Greece	0.023	Canada	0.000
Algeria	0.020	Congo	0.000
Palestine	0.018	Ecuador	0.000
Chile	0.016	Ethiopia	0.000
Germany	0.015	Gambia	0.000
Colombia	0.015		

Figure 1. Heat map of DQB1*0601 prevalence



Kaplan Maier Hazard Function among DQB1*0601 Negative (N=128) and DQB1*0601 Positive Subjects (N=45
LPG Use is associated with a Hazard Ratio of 2.85 (1.23-6.63) P=0.015 only among DQB1*0601 positive subjects

tween serological status with presence of DQ6.1. Smoking was rare among Females (4/154 versus 9/21 in males). 116/175 had exposure to biomass fuels (wood 107, cow-dung cake 72) while LPG stove was used by 121/175 subjects. Exposure to LPG was associated with earlier age of onset of RA (median 40 years versus 44 years) in the presence of DQ6.1 with a hazard ratio of 2.5 (CI 1.2-5, P=0.014, Figure 2) but not in DQ6.1 negative patients.

Conclusion: This replication study confirms the association of DQB1*0601 with RA. Smoking is rare among Indian women with RA. There is signal of gene-environment interaction between DQ6.1 and exposure to LPG stoves.

Lawrence A, Prakash S, Bharadwaj U, Aggarwal A, Misra R, Agrawal S. Major Histocompatibility Antigen HLA-DQ6.1 (DQA1*0103/DQB1*0601) Increases Rheumatoid Arthritis Risk Independent of Shared Epitope Among Indians [abstract].*Arthritis Rheumatol.* 2016; 68 (suppl 10). [ACR Annual Congress, 11-16 Nov 2016, Washington DC abstract no 1573]

Disclosure: A. Lawrence, None; **A. Dhar**, None; **S. Prakash**, None; **S. Arya**, None; **A. Aggarwal**, None; **S. Agrawal**, None.

Abstract Number: 1999

NADPH Oxidase 4 Regulates the Migration and Invasion of Synoviocytes in Rheumatoid Arthritis Through Pro-angiogenic Factor Secretion

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
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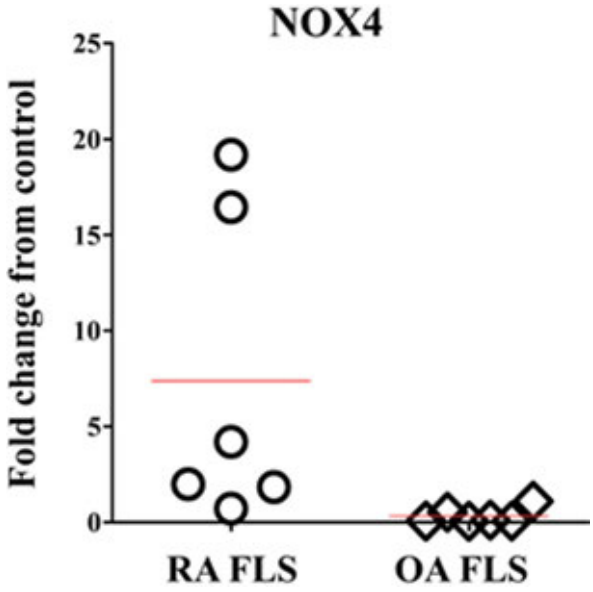
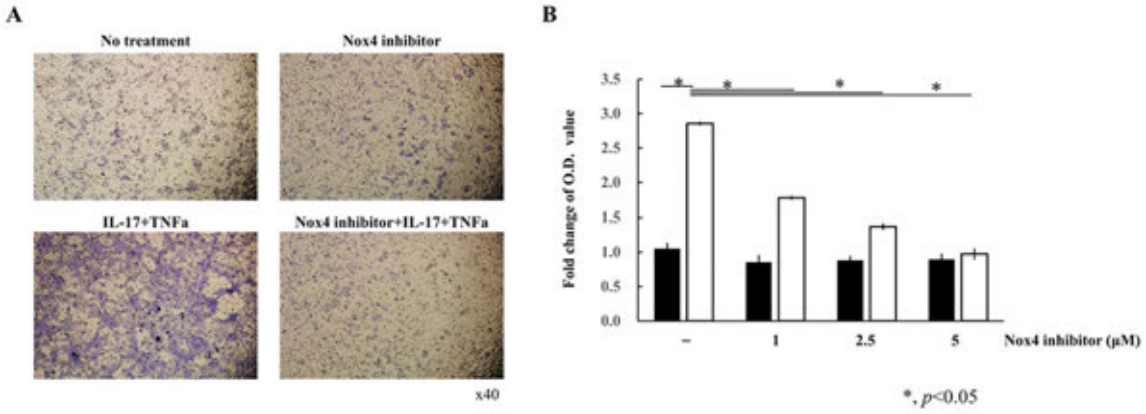
Background/Purpose: Fibroblast-like synoviocytes (FLS) are key effector cells in the pathogenesis of rheumatoid arthritis (RA) through the increased cell migration, degradation of extracellular matrix, and cartilage destruction. Reactive oxygen species (ROS) also have been known to be involved in the initiation and progression of RA, such as secretion of immunoregulatory and pro-angiogenic factors. Despite the important interrelationship between RA FLS and ROS, the mechanism of interaction and signaling is not clear.

Methods: In this study, the differential expression of six NADPH Oxidase subunits was analyzed after stimulation with recombinant interleukin-17 (IL-17) and tumor necrosis factor-alpha (TNFa) in FLS from RA and osteoarthritis (OA) patients. In particular, NADPH Oxidase 4 (NOX4) was highly increased by cytokine stimulation in RA FLS. So, we investigated whether Nox4 has a critical role in the migration and invasion of synoviocytes in RA. This study was performed according to the recommendations of the Declaration of Helsinki and approved by the Institutional Review Board of Chungnam National University Hospital in Republic of Korea. Synovial tissues were obtained from 5 RA patients (female 4, male 1, average age 55.6 ± 11.8) and 5 OA patients (female 4, male 1, average age 64.8 ± 16.1) who received synovectomy or joint replacement. For detection of ROS, MitoSox (mitochondria specific probe) was used according to the manufacturer's instructions. The cell migration assay was performed using transwell chamber (8 μm pore) and matrigel coating was added to transwell for the cell invasion assay. The migrated cells were stained with crystal violet and quantified.

Results: After the stimulation with recombinant IL-17 (10 ng/ml) and TNFa (10 ng/ml), the expression of Nox4 mRNA was higher by 8.73 folds in RA FLS compared to OA FLS. Following cytokine stimulation for 24 hours, the level of mitochondria-specific ROS was increased by 2 folds in RA FLS compared to OA. When the cells were treated with various concentrations of Nox4 inhibitor GLX351322 (1, 2.5, or 5 μM) for 1 hour, the level of ROS was significantly decreased in a dose dependent manner. On transwell migration assay, cytokines-stimulated RA FLS showed enhanced migratory ability by 3 folds compared to those without stimulation. Pretreatment with 5 μM of Nox4 inhibitor decreased the movement of RA FLS to the baseline level. The expression of pro-angiogenic factors, vascular endothelial growth factor (VEGF) and granulocyte macrophage colony stimulating factor (GM-CSF), was significantly reduced by Nox4 inhibition.



NADPH Oxidase 4 (NOX4) was the higher expression by cytokine stimulation for 1 hr in RA FLS than OA FLS.



Nox4 inhibition significantly decreased the cytokine-induced-migratory ability than no treatment in RA FLS

Conclusion: From these data, we suggest that Nox4 may modulate the migration and invasion of synoviocytes and contribute to progression of RA. Nox4 among NADPH Oxidase subunits can be an attractive therapeutic target of RA.

Disclosure: H. Lee, None; **S. Yoo**, None; **C. Park**, None; **J. Kim**, None; **I. Yoo**, None; **S. Kang**, None.

Abstract Number: 2000

Anti-inflammatory Effect of Novel Spleen Tyrosine Kinase Inhibitor, SKI-O-592, on Fibroblast-like Synoviocyte in Rheumatoid Arthritis and THP-1 Cell

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease characterized by bone and cartilage destruction with leukocyte infiltration and activation at synovial tissue. The fibroblast-like synoviocytes (FLS) have a central role in disease pathogenesis and in vitro FLS invasiveness which correlates with articular damage in RA patients. Spleen tyrosine kinase (SYK) is a non-receptor tyrosine kinase known to have a crucial role in immune receptor signaling. Recently, a number of studies have revealed that aberrant SYK activation is associated with diverse allergic disorders and antibody-mediated autoimmune diseases such as rheumatoid arthritis, asthma and allergic rhinitis. A novel small-molecule SYK inhibitor, SKI-O-592, was designed and synthesized. The aim of this study is to evaluate the inhibitory effect of SYK inhibitor on inflammation and migration in RA FLS and THP-1 cell.

Methods: Selectivity of SKI-O-592 was evaluated by KinaseProfiler platform consisting of 293 human purified kinases using ATP Km for each kinase. A series of concentrations of ATP ranged from 10 to 1,500 μM were simultaneously incubated with cell-free kinase reaction. FLS were isolated from synovial tissues of RA patients, and treated with SKI-O-592 under tumor necrosis factor alpha (TNF-α). FLS were stimulated with TNF-α for 48 hr after 1 hr treatment of SKI-O-592. After stimulation, cell viability were measured using CCK-8 assay. The levels of IL-6, CXCL10, MMP-3 and TNF-α were measured in culture supernatant of RA FLS and THP-1 cell by ELISA. Wound healing assay were performed to evaluate cell migration ability. The expression of α-tubulin, phosphorylated SYK and phosphoinositide 3-kinase (PI3K) were determined by Western blotting.

Results: SKI-O-592 inhibited the activity of recombinant human SYK enzymes with an IC_{50} of 5.1 nM. The kinases with more than 75% inhibition by 0.1 μM SKI-O-592 were SYK, YES and ROCK-II. The number of migrated cell to wound region was decreased in SKI-O-592 treated RA FLS without the change in cell viability. SKI-O-592 reduced the levels of cytokine and chemokine secretion including IL-6, CXCL10 and MMP-3 in RA FLS. Secreted TNF-α levels were decreased in THP-1 cell by SKI-O-592. Phosphorylation of PI3K was decreased after 30min of SKI-O-592 treatment. The viability and proliferation of the cells were not affected.

Conclusion: The novel SYK inhibitor, SKI-O-592 decreased the production of pro-inflammatory cytokine, chemokine and metalloproteinase in RA FLS. SKI-O-592 decreased the phosphorylation of PI3K. SKI-O-592 may provide a new therapeutic strategy in RA patients.

Disclosure: S. Kim, None; **H. Yoo**, None; **S. Kang**, None; **J. Park**, None; **R. Kim**, None; **J. Kim**, None; **H. Hwang**, None; **J. Park**, None; **E. Lee**, None; **Y. Song**, Astellas Pharma, Inc., 9.

Abstract Number: 2001

Survivin Controls the Transcriptional Activity by Changing the Pattern of Histone H3 Marks on Chromatin

Karin Andersson,[1] Malin Erlandsson,[1] Anastasius Damdimopoulos,[2] Robin Bremer,[1] Maja Jensen,[3] Maria-José Garcia-Bonete,[3] Gergely Katona,[3] and **Maria Bokarewa**[1], [1]Department of Rheumatology and Inflammation Research, the Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden, Gothenburg, Sweden, [2]Department of Biosciences and Nutrition, Karolinska Institute, Solna, Sweden, Stockholm, Sweden, [3]Department of Chemistry and Molecular Biology, the Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden, Gothenburg, Sweden

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The oncoprotein survivin coded by the BIRC5 gene was described as an important marker in rheumatoid arthritis (RA). Survivin participates in cell division being a member of the chromosomal passenger complex, while its role in gene transcription remains unknown. The purpose of this study was to identify survivin-specific transcription pattern in $CD4^+$ T-cells.

Methods: CD4+ T cells of RA patients and healthy females were isolated from the perpheral blood, activated and treated with a survivin inhibitor YM155. Chromatin was immunoprecipitated using polyclonal antibodies to survivin and to histone H3 trimethylation H3K27me3, H3K4me3 and acetylation H3K27ac marks. DNA libraries were prepared for all ChIP material using ThruPLEX (Rubicon) and **high throughput sequencing** was performed using Hiseq2000 (Illumina) and aligned to the human reference genome (Ensembl GRCh38) using the STAR aligner. Transcriptional analysis was done by RNAseq (Illumina) and conventional qPCR.

Results: Genome-wide analysis of survivin binding to chromatin in activated primary CD4+ T cells was enriched ($p< 10\text{-}5$) and annotated to RNA polymerase II-specific DNA binding transcription factor activity (GO:0000981) with known roles in developmental processes (GO:0032502), and cell communication (GO:0010646, GO:0098742). A search in the ENDCODE ChIP database identified colocalization of survivin with the enhancer of zeste homolog 2 (FDR< 10-33) and Suz12 (FDR< 0.001%), the subunits of the Polycomb-repressive complex 2 responsible for the trimethylation of H3K27. The analysis of histone H3 bound chromatin in CD4 cells revealed colocalisation of H3K27ac, H3K27me3 and H3K4me3 marks to 3784 common peaks. A surplus of the activation marks H3K4me3 and H3K27ac was found in 74%, while 25.6% genes had a surplus of the repressive mark H3K27me3, which was in agreement with the activated cell phenotype. Alignment of survivin peaks with histone H3 marks revealed a co-localization of survinin-ChIP with H3K27me3 (82.7%) mark rather than H3K4me3 (66%) ($p=0.042$). Depletion of survivin in cultured CD4 cells resulted in a significant general increase in deposition of the repressive H3K27me3 mark on chromatin (FC 1.98; $p< 10\text{-}24$) and shifted a balance from H3K27ac and H3K4me3 marks. Only 4% of the H3K4me3 surplus peaks kept it after survivin depletion. mRNA analysis of CD4 cells showed that survivin depletion changed the transcription of the genes controlled by H3K27me3 and EZH2. Among those we found the the genes of HOX-B cluster and their partners MEIS, PKNOX and PBX1 controlling the development of anatomical structures including joints.

Conclusion: This genome-wide study suggest that survivin has important transcription regulating function. It preserves optimal levels of the repressive histone H3K27me3 mark with a potential impact on the function of HOX genes and limb pathology in RA patients.

Disclosure: K. Andersson, None; **M. Erlandsson**, None; **A. Damdimopoulos**, None; **R. Bremer**, None; **M. Jensen**, None; **M. Garcia-Bonete**, None; **G. Katona**, None; **M. Bokarewa**, None.

Abstract Number: 2002

Presence of the MerTK Receptor on Human Synovial Tissue Macrophages Lowers Inflammatory Cytokine Production and Activation of the MerTK^{+}CD206^{+} Subpopulation Limits the Inflammatory Response of Synovial Fibroblasts

Samuel Finlay,[1] Stefano Alivernini,[2] Aziza Elmesmari,[3] Barbara Tolusso,[2] Luca Petricca,[2] Clara Di Mario,[4] Annunziata Capacci,[2] Andrew Filer,[5] Gianfranco Ferraccioli,[2] Iain McInnes,[1] Elisa Gremese,[2] and Mariola Kurowska-Stolarska[1], [1]Institute of Infection, Immunity & Inflammation, University of Glasgow, Glasgow, United Kingdom, [2]Division of Rheumatology - Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [3]Institute of Infection, Immunity & Inflammation, University of Glasgow, Glasgow, Scotland, United Kingdom, [4]Institute of Rheumatology - Università Cattolica del Sacro Cuore, Rome, Italy, [5]Institute of Inflammation and Ageing College of Medical and Dental Sciences University of Birmingham, Birmingham, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A substantial proportion of Rheumatoid Arthritis patients do not respond to treatment and only a small proportion achieve sustained disease remission. We showed previously that human synovial tissue macrophages (STMs) are heterogeneous; and a sub-population of CD206^{+}MertK^{+} positive STMs predominates in RA patients in sustained remission as compared to patients with active RA. Their surface receptors, *e.g.* MerTK, and distinct transcriptome suggest that they may play a role in re-enforcing joint homeostasis (1). *Thus, we hypothesise that activation of CD206^{+}MerTK^{+} human synovial tissue macrophages contributes to the resolution of inflammation.*

Objectives: We aimed to investigate whether activation of MerTK in STM sub-population promotes an anti-inflammatory environment in the synovium.

Methods: Using flow cytometric techniques and with a specific antibody panel design (1), STMs from digested RA synovial biopsies were phenotyped and/or harvested for functional studies. The study included patients with active disease and patients in remission (DAS28 ESR< 2.6 and power doppler negative). After excluding all other cell types, macrophages were gated based on the expression of CD64 and CD11b (CD45posCD64posCD11bposHLA-DRpos) (1). Two distinct subpopulations: CD206+MerTK+ and CD206-MerTK- were sorted and cultured on a collagen coated 96-well plate at 1000 cells per well in the presence of with LPS (10ng/ml) ± Gas 6, a MerTK ligand (100ng/ml), for 24h. Cytokine production was measured using a high sensitivity UPLEX assay. To test the role of MerTK expressing macrophages on the activation of synovial fibroblasts, a trans-well membrane coculture system was used. Macrophages were pre-treated with LPS (1ng/ml) ± MertK inhibitor (UNC1062, 100um-250um) for 4 and 2 hours respectively, and then co-cultured with fibroblasts for 48hours. MMPs production were measured by multiplex.

Results: As previously shown (1), RA patients in sustained remission have a majority $CD206^{+}MerTK^{+}$ STMs, whilst patients with active RA show an increased number of $CD206^{-}MerTK^{-}$ macrophages. The percentage of $CD206^{+}MerTK^{+}$ macrophages negatively correlated with the disease activity score in RA. Stimulation of FACS-Aria sorted $CD206^{+}MerTK^{+}$ and $CD206^{-}MerTK^{-}$ macrophages with TLR4 ligand induced a different cytokine pattern: the $CD206^{-}MerTK^{-}$ macrophages mostly produced TNF, IL-6 and IL-1b while $CD206^{+}MerTK^{+}$ produced IL-10. Inhibition of MerTK in macrophages increased the production of MMP1 and MMP3 by synovial fibroblasts in the co-culture system.

Conclusion: $CD206^{+}MERTK^{+}$ macrophages, which predominate in RA patients in remission, have Gas6-mediated negative feedback mechanism limiting inflammatory cytokine production and activation of synovial fibroblasts. Thus, Gas6/MerTK pathway in synovial tissue macrophages could drive the resolution of inflammation and synovial tissue homeostasis.

Reference:

1. Elmesmari A et al., Synovial tissue of RA patients in remission contains a unique population of regulatory macrophages. Annals of the Rheumatic Diseases, 2017;76 (Suppl2) 138-139.

Disclosure: S. Finlay, None; **S. Alivernini**, None; **A. Elmesmari**, None; **B. Tolusso**, None; **L. Petricca**, None; **C. Di Mario**, None; **A. Capacci**, None; **A. Filer**, None; **G. Ferraccioli**, None; **I. McInnes**, Abbott, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, Roche., 2, 8, Abbvie, 5, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Astra Zeneca, 2, 5, AstraZeneca, 5, BI, 2, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 5, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Leo, 5, Lilly, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8; **E. Gremese**, AbbVie, 5, 8, Abbvie, 5, 8, BMS, 5, 8, Bristol-Myers Squibb, 5, 8, Celgene, 5, 8, Jannsen, 5, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sandoz, 5, 8, UCB, 5, 8; **M. Kurowska-Stolarska**, None.

Abstract Number: 2003

Anti-Polygalacturonic Acid Antibody (PGA-Ab) Induced Bone Destruction in Rheumatoid Arthritis by Promoting Osteoclastogenesis via Integrin Beta 5

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-polygalacturonic acid antibody (PGA-Ab) is a new rheumatoid arthritis (RA)-related autoantibody first identified by our group. The sensitivity and specificity of PGA-Ab is even higher than anti-cyclic peptide containing citrulline (anti-CCP) and rheumatoid factor (RF). However, the pathogenesis of PGA-Ab has never been investigated.

Methods: Rabbits were immunized with PGA for PGA-Ab production followed by joint structure analysis by HE staining and micro-CT. Bone resorption index of RA patients were detected to analyze the comparation of PGA-Ab with bone loss. Osteoclasts were induced *in vitro* from peripheral blood mononuclear cells (PBMC) by M-CSF and RANKL with or without PGA-Ab treatment followed by RNA-Sequence for transcriptome analysis and then confirmed by real

Figure 1

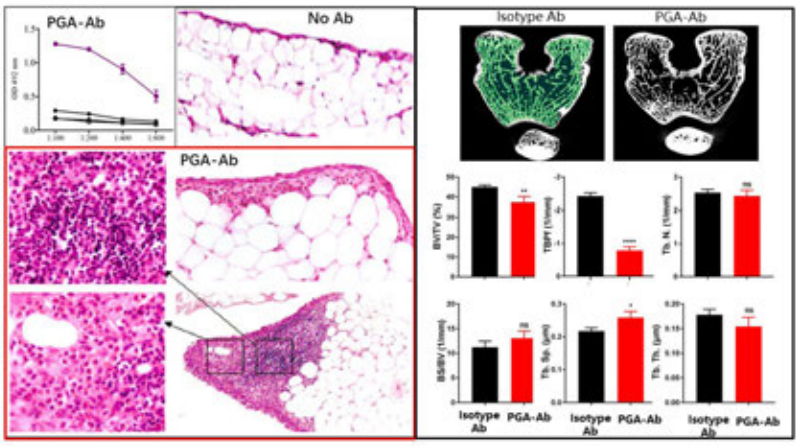

Figure 1 Knee joint inflammation and bone loss following induction of PGA-Abs in rabbits. Two month-old female white rabbits (3 per group) were subcutaneous injected with PGA and boosted 2 weeks and 4 weeks later. The mice were bled on 6th week and the sera were assayed for PGA-Abs. Hind knee joints from rabbits without PGA-Ab (B) and with PGA-Ab (C) were fixed with 4% formaldehyde solution and then decalcificated, followed by paraffin section preparation and HE staining. Microscopic observation found obvious inflammatory changes, including synovial hyperplasia, small vessels proliferation and inflammatory cell infiltration, in the joint sections from rabbits with PGA-Ab. (D) Micro-CT images of the distal femur and analysis of BV/TV, bone volume/tissue volume; BMD, bone mineral density; TbTh, trabecular thickness; TbN, trabecular number; Tb.sp, bone separation. Data are presented as the mean ± standard deviation (n=5 for each group). *P<0.05 vs. control.

Figure 2

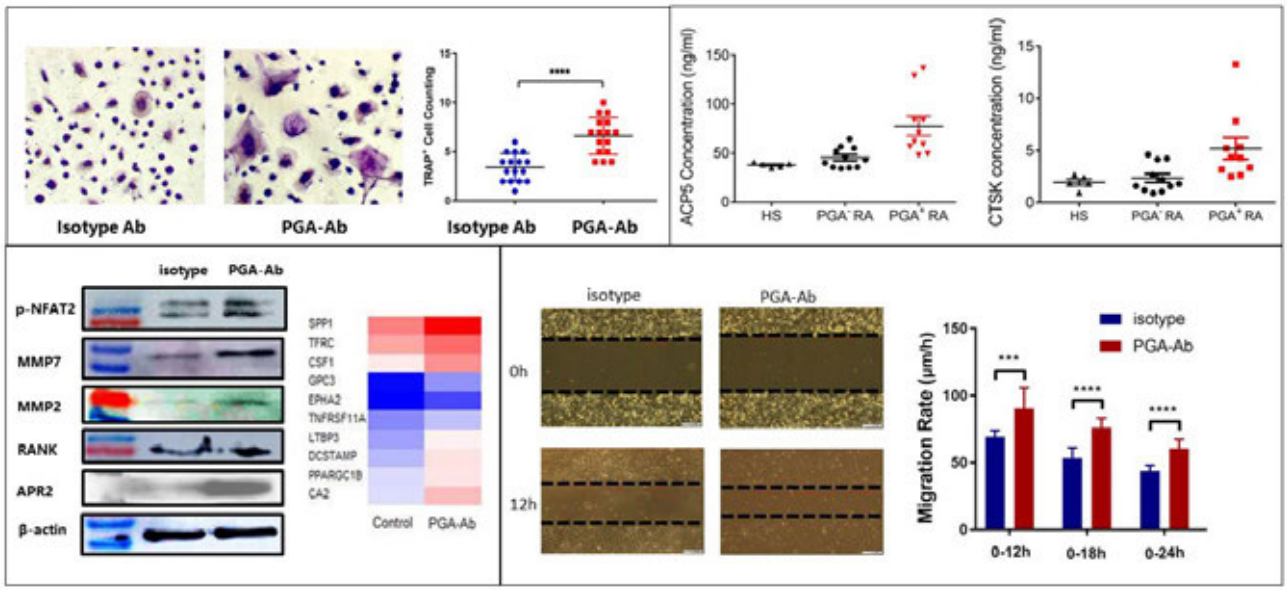

Figure 2 Effect of the PGA-Ab on osteoclastogenesis and migration (A) Osteoclasts were induced in vitro from peripheral blood mononuclear cells (PBMC) by M-CSF and RANKL with or without PGA-Ab treatment Representative images of osteoclastic TRAP staining and osteoclast cell number count were shown. (B) Bone turnover biomarker (ACP5 and CTSK) in healthy subjects and RA patients with or with PGA-Ab. (C) Protein extracts were isolated from osteoclasts after treatment with the isotype antibody or PGA-Ab (0.05mg/ml) for 48h and analyzed by immunoblotting with anti-NFAT2, beta-actin, and histone-1 antibodies. After treatment with isotype antibody or PGA-Ab for 48h, mRNA extracts were analyzed by RNA-seq for transcriptome analysis and representative heat map of osteoclastgenesis-related gene expression was shown. (D) Cells were treated by isotype antibody or PGA-Ab for 48h followed by migration assay by wound healing.

time quantitative PCR or western blot. Potential receptors were also identified by immunoprecipitation and protein spectrum sequencing (IP-MS).

Figure 3

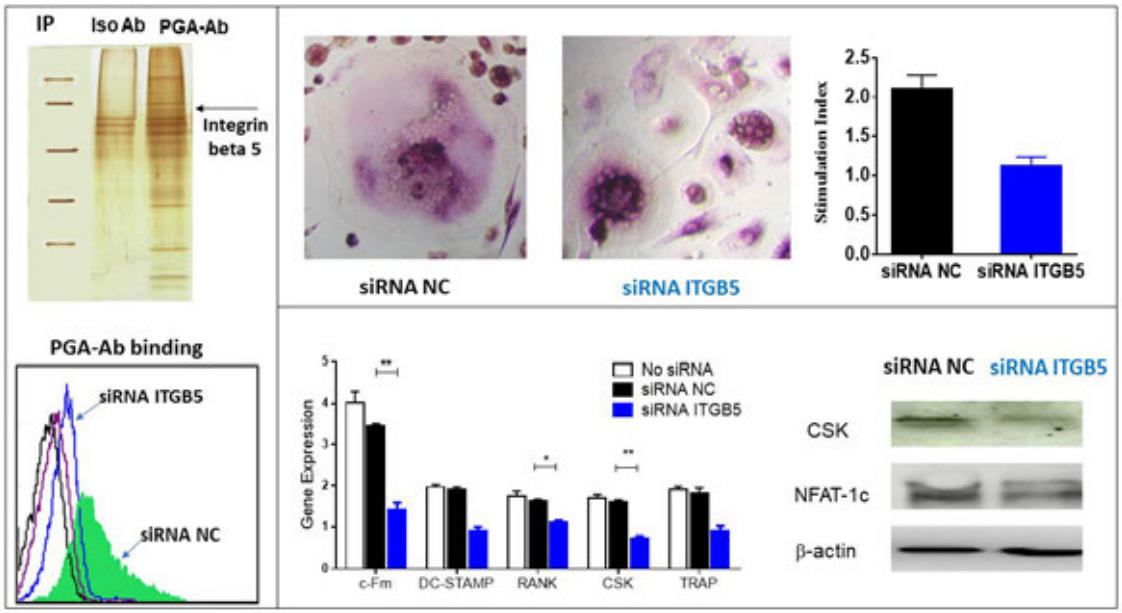

Figure 3 Integrin beta 5 was identified as a potential receptor of PGA-Ab on osteoclast (A) Protein extracts were isolated from osteoclasts followed by incubated with PGA-Ab or isotype Ab for immunoprecipitation. After protein spectrum sequencing for differential bands, integrin beta 5 was identified as PGA-Ab-binding protein. After knock down ITGB5 expression by siRNA, the binding of PGA-Ab and osteoclast were detected by flow cytometry. (B) ITGB5 knock down followed by osteoclastogenesis induced by M-CSF and RANKL. TRAP staining were used for osteoclast cell number count. (C) Gene and protein expression of osteoclasts after ITGB5 silence were detected by real time quantitative PCR and western blot, respectively.

Results: After PGA immunization, severe joint inflammation and damage were shown in PGA-Ab positive animals, including increasing synovium thickness, neutrophils and lymphocytes infiltration and reducing bone mineral density of femoral trabecula. Cathepsin k (CSK) and Tartrate Resistant (ACP5) in PGA-Ab positive RA patients were significantly higher than in PGA-Ab negative RA patients. *In vitro* culture, PGA-Ab treatment increased mature osteoclast numbers, CSK or metalloproteinases (MMPs) releasing and NFAT1c and AP-1 activation. Rho-GTPase signaling pathway-related protein RhoA, RhoD-GTP and ARP2 expression were also increased and PGA-Ab treatment increased wound healing, indicating increased cell migration and motility induced by PGA-Ab. Integrin beta5 (ITGB5) were identified as receptor of PGA-Ab on osteoclasts. Knockdown of ITGB5 eliminated the binding of PGA-Ab with osteoclasts and reduced PGA-Ab-induced osteoclastogenesis significantly.

Conclusion: PGA-Ab is a new RA-related autoantibody, which has pathogenic effect on arthritis bone erosion by inducing osteoclast differentiation through receptor integrin beta 5 via Rho-GTPase signaling pathway.

Disclosure: J. Xie, None; **H. Dai**, None.

Abstract Number: 2004

Protein Profiling and Network Enrichment Analysis in Individuals Before and After the Onset of Rheumatoid Arthritis

Mikael Brink,[1] Anders Lundquist,[1] Andrey Alexeyenko,[2] Kristina Lejon,[1] and **Solbritt Rantapää-Dahlqvist**[1], [1]Umeå University, Umeå, Sweden, [2]SciLife lab, Stockholm, Sweden

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Antibodies and up-regulated cytokines and chemokines predate the onset of symptoms of rheumatoid arthritis (RA). The aims with this study was to identify pathways related to the early processes leading to RA development, and potential novel biomarkers, using multiple proteins analysis.

Methods: A case-control study was conducted within the Biobank of northern Sweden. Plasma samples from 118 pre-symptomatic individuals (207 samples, median predating time 4.1 years), 79 early RA patients and 74 matched controls were analysed. The levels of 122 unique proteins with acknowledged relation to autoimmunity were analysed using 153 antibodies in a bead-based multiplex system (FlexMap3D, Luminex Corp.). Data was analyzed using ANOVA, Random Forest and Network Enrichment analysis (NEA), on the basis of the ten most significantly differentially expressed proteins for each two-by-two group comparison, using the MSigDB collection of Hallmarks.

Results: There was high agreement between the different statistical methods for identifying the most significant proteins. Levels of 22 proteins differed significantly between pre-symptomatic individuals and controls, 93 between RA-patients and controls and one between pre-symptomatic individuals and RA after adjustment for multiple testing. The area under curve for proteins discriminating pre-symptomatic individuals from controls was 0.75, between pre-symptomatic individuals and RA 0.80 and between RA and controls 0.93. Of the 30 proteins with the highest discriminatory capacity 27 differed between pre-symptomatic individuals vs. controls ($p< 1.9e-7$ to 0.05), 29 between RA-patients and controls ($p< 5.5e-26$ to $1.7e-4$) and 29 between pre-symptomatic individuals and RA ($p< 7.4e-4$ to 0.05). The Adipogenesis and Interferon alpha response hallmarks, included proteins involved in innate immunity, differentiated pre-symptomatic individuals from controls. Between pre-symptomatic individuals and RA-patients three hallmarks were identified, involving Apical Junction, Epithelial Mesenchymal Transition and TGF-β signaling including proteins suggestive of cell interaction, re-modulation and fibrosis. The Adipogenesis and Heme metabolism hallmarks differentiated RA-patients from controls.

Conclusion: We confirm the importance of Interferon alpha signaling as well as of lipids in the early phases of RA development. Network Enrichment Analysis provides a tool for a deeper understanding of molecules involved at different phases of the disease progression.

Disclosure: M. Brink, None; **A. Lundquist**, None; **A. Alexeyenko**, None; **K. Lejon**, None; **S. Rantapää-Dahlqvist**, None.

Abstract Number: 2005

Circulating Mitochondrial Danger-Associated Molecular Patterns as Novel Biomarkers of Disease Activity and Inflammation in Rheumatoid Arthritis

Bhargavi Duvvuri,[1] and Christian Lood[1], [1]University of Washington, Seattle

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) is an autoimmune inflammatory disease causing erosive and disabling joint damage. We recently found that mitochondria are extruded upon formation of neutrophil extracellular traps (NETs). The extruded mitochondria can be a source of danger-associated molecular patterns (DAMPs) that include highly unmethylated CpG motif content, oxidized mitochondrial DNA (mtDNA) and N-formylmethionyl (N-fMet) peptides. In RA, elevated levels of cell-free mtDNA have been reported in both synovial fluid and plasma. However, the clinical utility of mtDNA in RA is yet to be explored. Nothing has been reported on levels of N-fMet peptides in RA patients. The aim of the current study was to quantitate circulating levels of mitochondrial components in RA patients, and investigate their utility as novel non-invasive biomarkers in monitoring disease activity and severity in RA.

Methods: DNA isolated from plasma samples of healthy individuals (HC, n=20) and RA patients (n=100) was analyzed for mtDNA (Cytochrome C Oxidase Subunit II) and nuclear (nu) DNA (Ribosomal Protein Lateral Stalk Subunit P0) content using qPCR. NETs were analyzed by an in-house MPO-DNA ELISA. Levels of circulating human N-fMet and DNA damage (8-OHdG) were analyzed by ELISA.

Results: Seropositive RA patients had elevated levels of mtDNA compared to seronegative patients ($p=0.03$). However, no difference was observed for nuDNA ($p=0.11$). Further, RA patients had extensive DNA oxidation ($p=0.0009$). Oxidation, mainly seen in mtDNA, is known to increase the inflammatory capacity of DNA. Of note, cfDNA from RA patients had higher inflammatory potential upon in vitro incubation with PBMCs, as compared to cfDNA from HC ($p< 0.0001$). The inflammatory capacity of DNA correlated with mtDNA levels ($r=0.36$, $p=0.0004$), but not with nuDNA levels ($r=0.06$, $p=0.57$), suggesting circulating mtDNA as the pro-inflammatory component of cfDNA. Consistent with our hypothesis that NETs could be a potential source of mtDNA, we found a correlation between levels of cf-mtDNA and NETs ($r=0.025$, $p=0.03$). RA patients also had significantly elevated levels of circulating N-fMet as compared to controls ($p< 0.0001$). N-fMet levels correlated with markers of inflammation, including CRP ($r=0.56$, $p< 0.0001$), ESR ($r=0.32$, $p=0.01$), and calprotectin, ($r=0.42$, $p< 0.0001$). Both circulating mtDNA levels and N-fMet levels were elevated in patients with active disease ($p=0.001$ and $p=0.007$, respectively). Further, a distinct group of RA patients (n=20) with predominant levels of mtDNA, showed significant correlation between mtDNA levels and CDAI ($r=0.56$, $p=0.03$). Circulating N-fMet levels also correlated with joint involvement (N-fMet vs. swollen joints, $r= 0.23$, $p=0.03$; N-fMet vs. tender joints, $r= 0.22$, $p=0.04$).

Conclusion: Mitochondrial DAMPs are elevated in RA, indicating abnormal mitochondrial extrusion and/or clearance occurring in RA. Levels of mitochondrial DAMPs are related to inflammation and disease activity, suggesting an instrumental role in the RA pathogenesis. In all, pathways involved in mitochondrial extrusion could be considered as novel therapeutic targets as well as biomarkers in RA.

Disclosure: B. Duvvuri, None; **C. Lood**, None.

Abstract Number: 2006

Pyruvate Kinase M2 May Contribute to the Inflammation and Joint Destruction in Rheumatoid Arthritis

Dong Woo Han,[1] Yong Seok Choi,[1] **You-Jung Ha**,[2] Eun Hye Park,[2] Eun Ha Kang,[2] Yeong-Wook Song,[3] and Yun Jong Lee[1], [1]Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea, [2]Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea, Seongnam, Republic of Korea, [3]Seoul National University Hospital, Seoul, Republic of Korea

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Etiology & Pathogenesis Poster II

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Pyruvate kinase M2 (PKM2), one of glycolytic enzymes, is an emerging molecule that plays significant roles in tumor growth as well as inflammatory process. However, the role of PKM2 in the RA pathogenesis has not been well evaluated. The aim of this study is to investigate the expression of PKM2 in RA patients and to find their clinical implications. Also, we tried to determine the role of PKM2 in the biologic processes of RA fibroblast-like synoviocytes (FLSs) and osteoclast *in vitro*.

Methods: To determine expression and localization of PKM2 in RA synovial tissue, immunohistochemistry and double IF was performed. The levels of PKM2 in SF and plasma were measured by ELISA and their relations with clinical variables including modified Sharp/van der Heijde (SHS) scores and circulating levels of TNF-α, IL-6, and VEGF were analyzed. In RA FLSs and THP-1 cell lines stimulated with LPS, TNF-α, or IL-6, the PKM2 levels in the conditioned media were also investigated. The effect of recombinant PKM2 on osteoclast differentiation was examined in

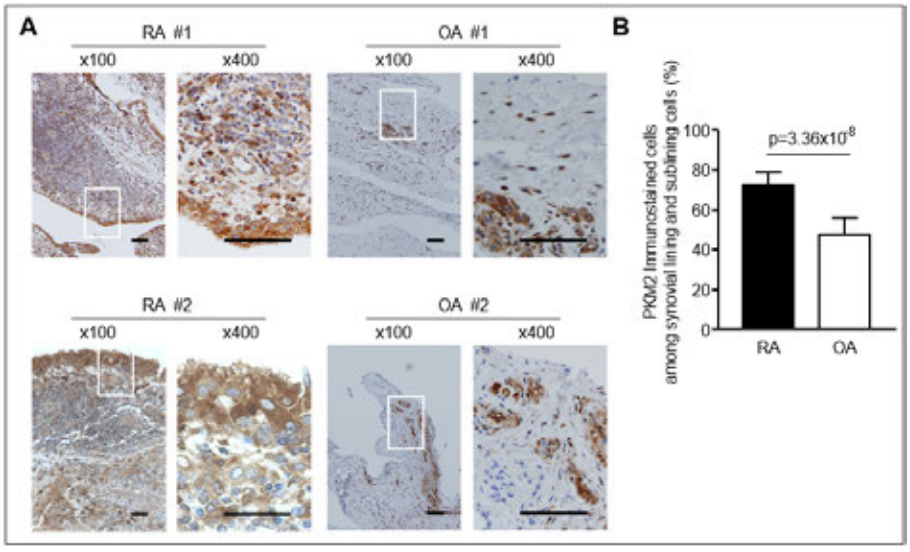

Figure 1. PKM2 expression in the synovial tissue. The number of PKM2 immunostained cells was significantly increased in RA synovium. RA = rheumatoid arthritis; OA = osteoarthritis.

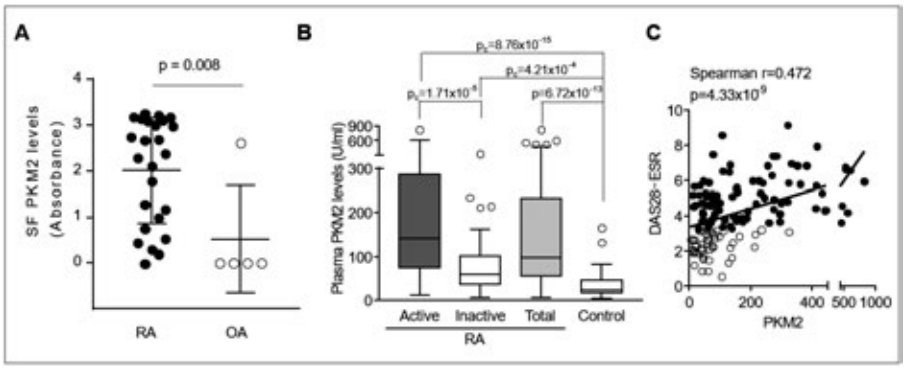

Figure 2. SF and circulating PKM2 levels in RA. (A and B) PKM2 levels in SF and plasma samples were significantly increased in RA patients, especially RA patients with active disease. (C) Plasma PKM2 levels were correlated with DAS28-ESR.

Raw264.7 cell line. Additionally, the impact of PKM2 down-regulation on migration and proliferation in RA-FLSs were determined using small-interfering RNA.

Results: In the synovial tissues of RA patients, PKM2 was more immunostained than in OA synovium and mainly expressed in the fibroblasts. The levels of SF PKM2 in RA patients were significantly higher than those in OA patients and correlated with SF inflammatory cell counts. Compared with healthy controls, the plasma PKM2 levels were significantly elevated in RA patients and correlated with DAS28. The circulating levels of PKM2 were positively correlated with IL-6 and VEGF levels, but not with TNF-α. Elderly onset RA patients with high PKM2 levels (≥ 90th percentile of the controls) were more likely to have radiographic progression (Δ SHS ≥1 unit/year) than those with low PKM2 levels. In early RA (disease duration ≤12 months) subgroup, plasma PKM2 levels were independent predictors for subsequent progression of radiographic damage. *In vitro*, PKM2 release was enhanced in stimulated macrophages, but not in stimulated RA-FLSs. The number of tartrate resistant acid phosphatase-positive multinuclear cells was dose-dependently increased by recombinant PKM2 in Raw264.7 cell, even without RANK ligand. PKM2 knockdown by siRNA transfection significantly decreased TNF-α induced migration and proliferation of RA-FLSs.

Conclusion: PKM2 was upregulated in RA synovium and the elevated PKM2 levels in plasma and SF were associated with inflammatory burden as well as radiographic progression. Intracellular PKM2 could be involved in the migration and proliferation of RA-FLSs, whereas extracellular PKM2 released from activated macrophages could promote osteoclastogenesis. These findings suggest that PKM2 might be a novel regulator in the pathogenesis of RA.

Disclosure: D. Han, None; **Y. Choi**, None; **Y. Ha**, Seoul National University Bundang Hospital, 3; **E. Park**, None; **E. Kang**, Seoul National University Bundang Hospital, 3; **Y. Song**, Astellas Pharma, Inc., 9; **Y. Lee**, Seoul National University Bundang Hospital, 3.

Abstract Number: 2007

Periodontal Pockets as a Potential Source of Circulating TREM-1 and Its Ligand PGLYRP1 in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Etiology & Pathogenesis Poster II

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: PGLYRP1, a member of peptidoglycan recognition proteins is a putative ligand as a ligand for triggering receptor expressed on myeloid cells-1 (TREM-1) which is involved in amplifying pro-inflammatory processes in chronic inflammatory diseases. However, the presence of circulating PGLYRP1 in patients with rheumatoid arthritis (RA) who suffer from periodontal disease is currently unknown.

The aim of the study was to investigate the association of circulating TREM-1 and its ligand PGLYRP1 with oral inflammatory/infection burden among patients with rheumatoid arthritis (RA).

Methods: The study population was recruited among individuals diagnosed with RA who were under sDMARD treatment for more than 6 months and never used biologic treatment (n=65, (F/M: 45/17) at the Department of Rheuma-

Table 1: Serum TREM-1 and Related Factors in Patients with RA and Controls

	RA		BD		HC				
	Mean	SD	Mean	SD	Mean	SD	RA-BD	RA-HC	BD-HC
TREM	167,11	95,0	102,84	44,4	90,75	56,57	**0.000**	**0.000**	**0.023**
PGLYRP1	156,57	228,83	52,4	26,01	68,88	37,75	**0.000**	**0.009**	**0.045**
	r	p	r	p	r	p			
TREM-1 and PGLYRP-1	0,52	**0.000**	0,62	**0.000**	0,53	**0.000**			
TREM-1 and DAS-28	0,30	**0,024**							
TREM-1 and Sedimantation rate	0,34	**0,012**							
TREM-1 and CRP	0,42	**0.001**							
PGLYRP-1 and CRP	0,33	**0.014**							
TREM-1 and DMFT	0,47	0,005							
PGLYRP-1 and DMFT	0,37	**0.036**							

Table 1. Serum TREM-1 and Related Factors in Patients with RA and Controls

Table 2: Oral Health in Patients with RA and Behçet's Syndrome and Healthy Controls

	RA (n=65)		BS (n=43)		HC (n=59)				
	Mean	SD	Mean	SD	Mean	SD	RA-BS	RA-HC	BS-HC
Number of teeth	18,67	8,45	24,02	3,7	25,36	3,83	**0.001**	**0.000**	**0.013**
DMFT	8,93	6,9	5,97	4,3	4,32	4,36	0.064	**0.000**	**0.044**
Total bacterial load	1E,↑09	2E,↑08	8E,↑08	8E,↑08	6E,↑07	7E,↑07	0.09	**0.009**	0.333
PI (Q-H)	1,26	1,3	1,3	1,11	0,82	0,87	0.540	0.125	**0.024**
BOP%	46,38	42,3	46,48	39,5	28,7	37,72	0.370	0.067	**0.020**
PPD mm	2,65	0,52	2,73	0,45	2,52	0,35	0.440	0.278	0.017
CAL mm	3,12	1,08	2,96	1,2	2,65	0,56	0.85	**0.021**	**0.007**
	n	%	n	%	n	%			
Severe periodontitis (+)	22	33,8	9	20,9	3	5,1	0.193	-	-
Severe periodontitis (-)	43	76,2	34	79,1	56	94,9			

DMFT: decay missing filled tooth PI: plaque index, BOP: bleeding on probing , PPD: periodontal pocket depth , CAL: clinical attachment level

Table 2. Oral Health in Patients with RA and Behçet's Syndrome and Healthy Controls

Table 3: Serum TREM-1 and PGLYRP-1 Levels According to Severe Periodontitis in RA

	Patients with RA (n=65)			
	Serum TREM-1		Serum PGLYRP-1	
	Mean	SD	Mean	SD
Severe periodontitis (+) (n=22)	219,17	52,0	265,68	336,75
Severe periodontitis (-) (n=43)	133,98	68,95	87,14	55,35
p	**0.001**		**0.035**	

Table 3. Serum TREM-1 and PGLYRP-1 Levels According to Severe Periodontitis in RA

tology, Faculty of Medicine, Marmara University, Turkey. 43 patients with Behcet syndrome (BS, F/M: 31/12) and 59 systemically healthy subjects (HC, F/M: 40/19) were assessed as controls. Serum and saliva samples were collected on the same day of oral health and musculoskeletal examination. RA disease activity was assessed using 28- joint disease activity score (DAS-28). Oral health was evaluated by dental and periodontal indices. Salivary levels of cumulative bacterial load and individual species including *S.oralis, A.oris, F.nucleatum, P.intermedia, A.actinomycetemcomitans, T.denticola, P.gingivalis,* and *T.forsthia* were analyzed by quantitative real-time polymerase chain reaction (qPCR). sTREM-1 and PGLYRP1 levels in serum were analyzed by ELISA.

Results: Elevated sTREM-1 and PGLYRP1 levels in serum was observed in RA (167,1±95,0 pg/ml; 157,5±228,8 pg/ml) than BD (102,8±44,4 pg/ml; 52,4±26,01pg/ml) and HC (90,7±56,5 pg/ml; 68,8±37,7 pg/ml) ($p< 0.05$)(Table 1). RA patients presented with significantly higher total bacterial load ($p< 0.05$) compared to the HC group. Tooth loss was significantly higher in RA (18.67±8.45) compared to those of BD (24.02±3.7) and HC (25.36±3.83)($p=0.001$ and $p=0.000$) (Table 2). In RA, sTREM-1 and PGLYRP1 levels were significantly higher in patients with severe periodontitis (219,1±107,9 pg/ml and 265,6±336,7 pg/ml) than the others (133,9±68,9 and 87,1±55,3 pg/ml) ($p=0.006$; $p=0.01$, respectively) (Table 3).

Conclusion: Serum sTREM-1 and its ligand PGLYRP1 levels were higher in patients with RA than BD and HC and especially were higher in patients with severe periodontitis. In addition, increased tooth loss and higher total bacterial load were associated with RA.

Disclosure: N. Inanc, None; **G. MUMCU**, None; **M. Can**, None; **H. Direskeneli**, None; **N. Bostanci**, None.

Abstract Number: 2008

Histone Lysine Methyltransferase MLL1 Regulates the Expression of Cytokines and Chemokines in Rheumatoid Arthritis Synovial Fibroblasts

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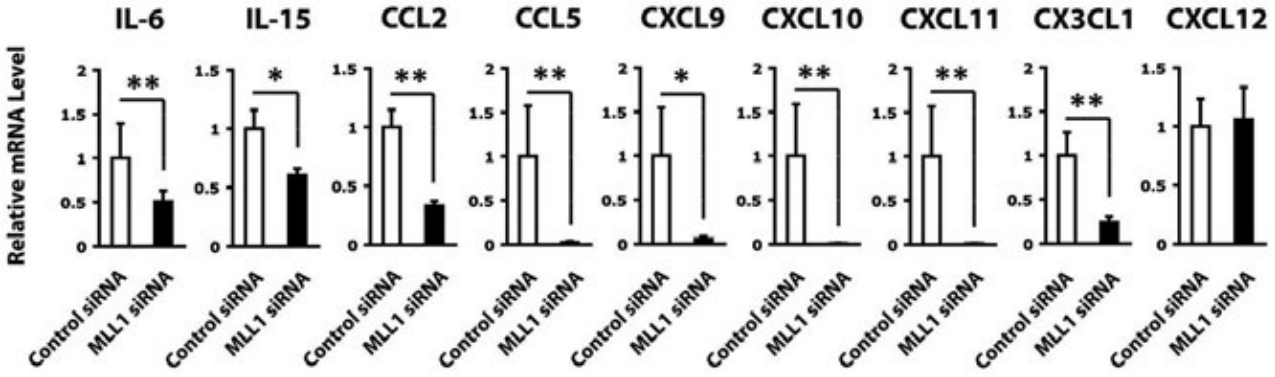
SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

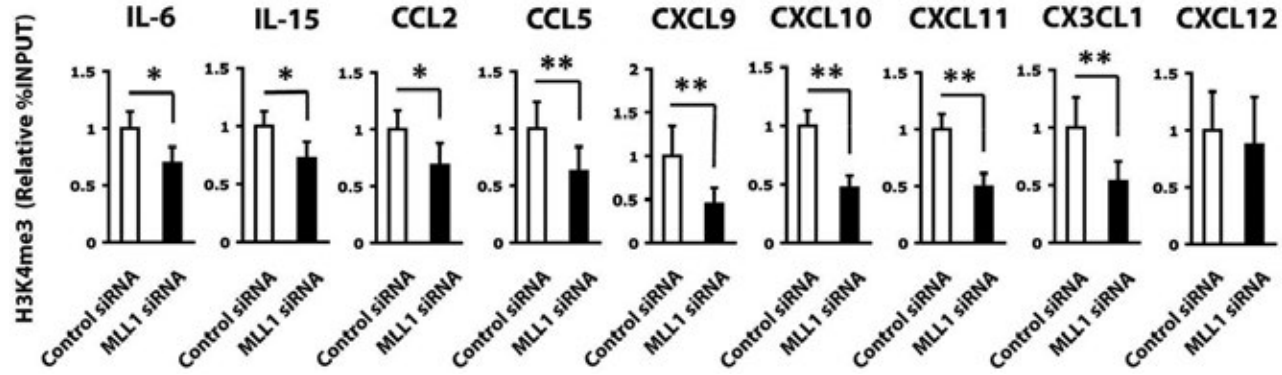
Session Title: RA – Etiology & Pathogenesis Poster II

Session Type: Poster Session (Tuesday)

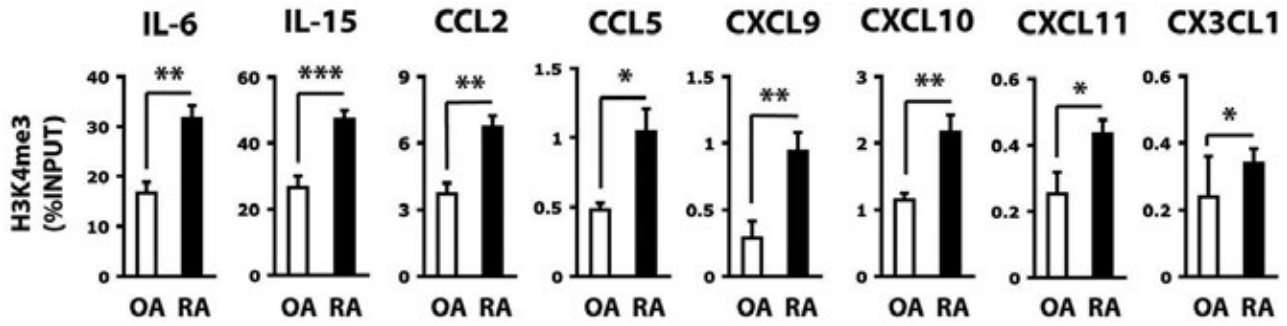
Session Time: 9:00AM–11:00AM



The silencing of MLL1 significantly decreased the mRNA levels of two cytokines (IL-6, IL-15) and six chemokines (CCL2, CCL5, CXCL9, CXCL10, CXCL11, and CX3CL1) in RASFs (N=12, *P<0.05, **P<0.01).



The H3K4me3 levels in two cytokines (IL-6, IL-15) and six chemokines (CCL2, CCL5, CXCL9, CXCL10, CXCL11, and CX3CL1) genes were significantly decreased in MLL1 siRNA-treated RASFs (N=7, *P<0.05, **P<0.01).



The H3K4me3 levels in two cytokines (IL-6, IL-15) and six chemokines (CCL2, CCL5, CXCL9, CXCL10, CXCL11, and CX3CL1) promoters were significantly higher in RASFs than OASFs (OA: N=8, RA: N=14, *P<0.05, **P<0.01, ***P<0.001).

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory disease that primarily affects the joints. The inflammatory process causes the activation of synovial fibroblasts (SFs) and the destruction of articular cartilage and bone, resulting in disability of the joints. Both genetic and environmental factors have been shown to be associated with the pathogenesis of RA. However, these factors are unable to explain the pathogenesis of RA completely. Epigenetic factors such as histone lysine methylation are suggested to be associated with the pathogenesis of RA. Epigenetics refers to heritable phenotypic changes that influence gene expression independently of the DNA sequence. Aberrant gene expression of MLL1, which catalyzes methylation of histone H3 lysine 4 (H3K4), has been reported in RASFs. The aim of this study is to elucidate the involvement of MLL1 in the pathogenesis of RA.

Methods: SFs were isolated from synovial tissues obtained from patients with RA or osteoarthritis (OA) during total knee joint replacement. MLL1 expression in the cultured SFs was evaluated after stimulation with tumor necrosis factor α (TNFα). We examined the changes in the expression of RA-associated genes, including matrix metalloproteinases (MMP-1, MMP-3, MMP-9, and MMP-13), cathepsins (CTSK and CTSL), cytokines (IL-6, IL-8, IL-15, and IL-23A), and chemokines (CCL2, CCL3, CCL5, CXCL1, CXCL5, CXCL6, CXCL9, CXCL10, CXCL11, CXCL12, CXCL13, and CX3CL1), as well as the trimethylation of H3K4 (H3K4me3) levels in the promoters upon siRNA-mediated depletion of MLL1 in RASFs. The changes in the gene expression were also investigated by the treatment with an MLL1 inhibitor MM-102. The H3K4me3 levels in the cytokine and chemokine promoters were also examined in RASFs and OASFs.

Results: The levels of MLL1 mRNA and protein were higher after TNFα stimulation in RASFs versus OASFs. The mRNA levels of IL-6, IL-15, CCL2, CCL5, CXCL9, CXCL10, CXCL11, and CX3CL1 genes were significantly decreased in MLL1 siRNA-treated RASFs. Correspondingly, the H3K4me3 levels in the promoters were significantly repressed. MM-102 significantly decreased CCL5, CXCL9, CXCL10, and CXCL11 mRNA levels in RASFs. MM-102 also repressed the H3K4me3 levels in the promoters in RASFs. In addition, the H3K4me3 levels in the IL-6, IL-15, CCL2, CCL5, CXCL9, CXCL10, CXCL11, and CX3CL1 promoters were significantly higher in RASFs than OASFs.

Conclusion: Study findings suggest that MLL1 regulates expression of the cytokines and chemokines that are involved in the pathogenesis of RASFs. MLL1 may be a new target for RA therapy.

Disclosure: Y. Araki, None; **K. Okamoto**, None; **Y. Aizaki**, None; **H. Oda**, None; **T. Mimura**, None.

Abstract Number: 2009

Biomarkers Identified by Serum Inflammatory Profile Analysis to Predict Biologic Treatment Response in Rheumatoid Arthritis Patients

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Etiology & Pathogenesis Poster II

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Biologic disease modifying antirheumatic drugs (b-DMARDs) have revolutionized the management of Rheumatoid Arthritis (RA). Despite this success, a high percentage of the patients undergoing biologic treatment respond insufficiently. There is thus an urgent need to identify effective biomarkers to guide treatment selection. The aim of this study was to identify several specific reliable clinical and molecular predictors of the response of RA patients to TNF-α inhibitors (TNFi) and to B-cell depletion by anti-CD20 antibody (Rituximab, RTX).

Methods: In a prospective RA cohort study, we collected serum from RA patients with moderate or high disease activity prior to treatment with TNFi or RTX and analyzed baseline levels of 27 proteins that constitute a multibiomarker test of inflammatory profile of these samples using a multiplex immunoassay. The patients' response was determined 24 weeks after starting bDMARDs treatment, according to the EULAR response criteria (good vs. moderate/no). We compared the inflammatory molecules between the response and non-response patient groups and analyzed their discriminative ability. Logistic prediction models were created to assess the added value of potential inflammatory predictors.

Results: Among 91 total RA patients, 45 of 66 patients in the TNFi group and 20 of 25 patients in the RTX group responded to the biologic treatment. As previously reported both, high DAS28 and CRP levels at baseline were predictive of response to TNFi. High rheumatoid factor titers and DAS28 at baseline were predictive of response to RTX. Instead, smoking habit and hyperlipidemia at baseline were predictors of a worse response to any of these b-DMARDs. Of the molecules analyzed by the multiplex assay, we identified seven molecules as potential predictors of TNFi response [fibroblast growth factor basic (FGFb), interleukin (IL)-10, IL-13, IL-15, IL-2, IL-8, and monocyte chemotactic protein -1 (MCP-1)] mainly involving molecules related to leukocyte's activation and recruitment to inflammatory tissues. On the other hand, three highly expressed cytokines/chemokines in RA serum were identified as predictors of RTX response [IL-9, interferon-inducible protein 10 (IP10) and macrophage inflammatory protein 1 beta (MIP1b)]. Receiver operating characteristic analyses for those multiple biomarkers revealed areas under the curve (AUC) ranging from 0.78 to 0.94, with a sensitivity of 100% and specificity varying from 80 to 90% for TNFi, and AUC

from 0,76 to 0,97 with a sensitivity of 96% and specificity varying from 79 to 88% for RTX. Combinations of these 7 and 3 biomarkers, respectively, significantly increased the accuracy of prediction.

Conclusion: By analysis of serum inflammatory profile, we identified specific and distinctive serum biomarkers that, in coordination with known clinical and serological profiles, have a high ability to predict the response of RA patients to TNFi or RTX treatments. Funded by PI-0285-2017, ISCIII, PI18/00837 and RIER RD16/0012/0015 co-funded with FEDER

Disclosure: **C. Lopez-Pedrera**, None; **N. Barbarroja**, None; **C. Perez-Sanchez**, None; **P. Font**, None; **A. Ibañez-Costa**, None; **M. Luque-Tevar**, None; **A. Patiño-Trives**, None; **I. Arias de la Rosa**, None; **M. Abalos-Aguilera**, None; **R. Ortega**, None; **A. Escudero**, None; **L. Pérez-Sanchez**, None; **J. Calvo-Gutierrez**, None; **R. Segura-Ruiz**, None; **C. Rodriguez Escalera**, None; **D. Ruiz-Montesinos**, None; **C. Romero Barco**, None; **N. Mena-Vazquez**, None; **J. Uceda Montañez**, None; **M. Toledo Coello**, None; **M. Aguirre**, None; **E. Collantes-Estevez**, None.

Abstract Number: 2010

Individual Functions of Histone-acetyltransferases CBP and p300 in Regulating Autophagy and Proteasomal Degradation in Synovial Fibroblasts

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Tight control of the two major catabolic pathways proteasomal degradation and autophagy is critical for the maintenance of cellular homeostasis and cell survival. Here we analyzed the individual functions of the two homolog histone acetyltransferases cAMP-response element binding protein binding protein (CBP) and p300 in regulating catabolic pathways in rheumatoid arthritis (RA) synovial fibroblasts (SF).

Methods: SF were obtained from knee, shoulder and hand joints of RA patients undergoing joint replacement surgery. The expression of CBP and p300 was silenced by transfection of antisense LNA gapmeRs (12,5 nM). 24 hours later, cells were stimulated with TNF-α (10 ng/ml, 24 hours). Transcriptomes were determined by RNA-seq (Illumina NovaSeq 6000, n=6). Pathway enrichment analysis (fold change >1.5, FDR < 0.05) was performed using DAVID Bioinformatic Resources. Autophagy was assessed by Western blotting using LC3B conversion and p62 as autophagy markers (n=5) in presence and absence of the lysosomal inhibitor bafilomycin A1 (100 nM, 4h). Cell death (n=6) was analyzed using the CytoTox-Glo cytotoxicity assay. Proteasome activities were analyzed using Proteasome-Glo chymotrypsin-like, trypsin-like and caspase-like cell-based assays (n=5).

Results: The top pathway identified after silencing of p300 in SF in presence (p=3.57-14) of TNF-α was 'proteasome', which was also among the top three pathways in unstimulated SF (p=6.77x10-5). The expression of most

genes encoding proteasome subunits was increased after silencing of p300 but unaffected by silencing of CBP. In contrast, chymotrypsin-like and trypsin-like proteasome activities were decreased by silencing of p300, indicating a compensatory upregulation of transcription of proteasome subunits under conditions of impaired proteasome function. Caspase-like proteasome activity was not affected by silencing of p300. Genes contributing to the biological process 'autophagy' (p=0.031) were enriched after silencing of CBP in presence of TNF-α, whereas genes contributing to 'regulation of mitophagy' were enriched after silencing of p300 in absence (p=0.02) and presence of TNF-α (p=0.06). In line with RNA-seq data, silencing of CBP reduced the conversion of LC3B and the protein expression of p62 in presence and absence of TNF-α. Results were similar in presence of bafilomycin A1, indicating a decrease in autophagosome synthesis. In contrast, the conversion of LC3B and p62 expression were increased after silencing of p300 in unstimulated SF, indicating increased autophagy. This effect was lost for LC3B after treatment with TNF-α, and LC3B conversion was even decreased in presence of bafilomycin A1. This indicates a late stage block of autophagy after silencing of p300 in TNF-α-stimulated SF. In line with this, silencing of p300 in SF ($p < 0.05$) increased cell death only in presence of TNF-α. Viability of SF was not affected by silencing of CBP.

Conclusion: Our data provide the first evidence that p300 but not CBP regulates proteasome activity in SF by post-translational modifications. CBP and p300 have diverging functions in regulating autophagy.

Disclosure: M. Krošel, None; **M. Gabathuler**, None; **M. Tomšič**, None; **O. Distler**, A. Menarini, 5, Abbvie, Acceleron, 5, Acceleron Pharma, 5, Actelion, 2, 5, 8, Actelion Pharmaceuticals, 2, 5, 8, 9, Amgen, 5, AnaMar, 2, 5, Bayer, 2, 5, 8, 9, Biogen Idec, 2, 5, Blade Therapeutics, 5, Boehringer Ingelheim, 2, 5, 8, 9, Catenion, 5, 9, ChemomAb, 2, 5, ChemomAB, 5, CSL Behring, 5, Ergonex, 5, espeRare Foundation, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 5, GSK, 2, 5, Holds Patent mir-29 for the treatment of systemic sclerosis, 9, Inventiva, 2, 5, iQvia, 5, Italfarmaco, 2, 5, Italfarmco, 5, Lilly, 2, 5, med, 5, 8, medac, 5, Medac, 2, 5, MedImmune, 2, 5, Medscape, 5, 8, 9, Menarini, 8, Mepha, 8, Mitsubishi Tanabe, 2, 5, Mitsubishi Tanabe Pharma, 2, 5, MSD, 5, 8, Novartis, 2, 5, 8, 9, Patent, 9, Patent issued, 9, Pfizer, 2, 5, 8, Pharmacyclics, 2, 5, Roche, 5, 8, 9, Sanofi, 2, 5, Sinoxa, 2, 5, Target Bio Science, 5, Target BioScience, 5, UCB, 2, 5, 9, UCB in the area of potential treatments of scleroderma and its complications, 2, 5; **C. Ospelt**, Kurt und Senta Herrmann Foundation, 2, Promedica Foundation, 2; **K. Klein**, None.

Abstract Number: 2011

Novel Somatic Mutations Identified by Whole Genome Sequencing of Rheumatoid Arthritis (RA) Fibroblast-Like Synoviocytes (FLS)

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Somatic mutations caused by reactive oxygen and nitrogen species in inflamed joints, have been implicated in the destructive nature of RA. Mutation analysis also helps identify mechanisms contributing to the aggressive behavior of RA FLS. However, previous analyses focused on candidate gene approaches. This work represents the first whole genome sequencing study of RA FLS.

Methods: Next generation sequencing of the whole genome was carried out for 10 RA and 10 osteoarthritis (OA) human FLS cell lines at 100X. Reads were aligned, sorted according to chromosome and position, duplicates and those with a MAQ score < 30 removed. Base quality score recalibration of aligned reads was then performed with GATK 3.8. Variant calling was performed using VarScan2 with low quality base calls of < Q20 filtered out. Finally, we removed low coverage and low confidence sites. To account for a lack of a germline reference for each line and potential culture effects, we used a novel approach by filtering for sequences with mutation frequencies (MF) in >2% and < 5-8% of reads and discarding those found in at least >92% of the reads to remove putative germline polymorphsms and identify somatic mutations. For each set of mutations, single nucleotide variants (SNV) and insertion/deletion (Indel) locations were overlapped with gene bodies and promoters to identify the associated genes or with gene exons only. Genes specific to RA were analyzed for enriched functions and pathways.

Results: Indel and Missense SNV somatic mutations in the range 2%< MF< 5% were overlapped with gene bodies and promoters. Mutated genes unique to RA were identified and ranked by the number of RA cell lines with the mutant gene. Only 43 genes had mutations in > 5/10 RA lines and 0/10 OA lines. The top ranking genes, which had 7/10 RA lines with intronic mutations included MTMR3, which plays a role in autophagosome formation and CLNK which plays a role in immunoreceptor signaling. Other RA-specific mutated genes included multiple E3 ubiquitin ligases and DNA repair genes. Using the same filter and overlapping somatic mutations only with exons yielded additional RA-specific genes. Of the 33 exon-only mutations in 3/10 or more RA lines and 0/10 OA lines, 5 are also unexpectedly involved ubiquitination. We then extended the mutation range to 2%< MF< 6% and only considered missense somatic mutations in exons. 260 and 207 genes unique to RA or OA, respectively, were identified. Pathway analysis on these gene sets identified 11 significant pathways ($p< 1 x10^{-5}$) for the RA genes but no significant pathways for OA suggesting that the latter were not functionally relevant. 3 of the mutant RA pathways involved antigen processing including “Antigen Presentation: Folding, assembly and peptide loading of class 1 MHC” ($p< 1 x10^{-16}$).

Conclusion: Whole genome sequencing of RA and OA human FLS lines identified somatic mutations unique to RA in genes consistent with immune deregulation. Our novel computational approach corrected for potential tissue culture effects and showed a high mutation rate in RA. The unbiased analysis showed significant mutant pathways enriched in RA and suggests that the mutations play a role in disease pathogenesis.

Disclosure: R. Ainsworth, None; **D. Hammaker**, None; **D. Boyle**, Janssen, 2; **R. Ai**, None; **J. Sokolove**, AbbVie, 3, 4; **W. Wang**, None; **G. Firestein**, Abbvie, 2, Janssen, 2.

Abstract Number: 2012

A Composite IFN-Based Signature Is Associated with a Filgotinib-Specific Clinical Response in bDMARD-Experienced Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL), an oral, selective, Janus Kinase 1 (JAK1) inhibitor was effective in Phase 3 studies of active RA in patients (pts) with inadequate response or intolerance to biologic DMARDs (bDMARD-IR;

Table. Filgotinib dose-dependent reduction of the composite IFN-based signature

Comparisons	Δ(SE)	*P* Value
Baseline		
FIL 100 mg vs Placebo	0.025 (0.22)	0.993
FIL 200 mg vs Placebo	0.22 (0.22)	0.58
FIL 200 mg vs FIL 100 mg	0.20 (0.22)	0.64
Week 4		
FIL 100 mg vs Placebo	-0.61 (0.22)	**0.016**
FIL 200 mg vs Placebo	-1.22 (0.23)	**<0.0001**
FIL 200 mg vs FIL 100 mg	-0.61 (0.22)	**0.015**
Week 12		
FIL 100 mg vs Placebo	-0.63 (0.22)	**0.011**
FIL 200 mg vs Placebo	-0.96 (0.22)	**<0.0001**
FIL 200 mg vs FIL 100 mg	-0.33 (0.22)	0.28

FIL, filgotinib, SE, standard error.

Table. Filgotinib dose-dependent reduction of the composite IFN-based signature

FINCH-2 ClinicalTrials.gov Identifier: NCT02873936). RA pts with high IFN scores have shown a diminished clinical response to first-line treatments (Rodríguez-Carrio *et al.* 2018; Cooles FAH *et al*. 2018) and differential responses to second-line treatments (Mavragani *et al*. 2010; Thurlings R *et al.* 2010). Baseline IFN scores have been associated with a week 12 FIL-specific ACR-N response in the DARWIN Phase 2 trials (Taylor *et al*. 2018). The value of baseline gene expression for predicting therapeutic response to FIL in a bDMARD experienced RA population was explored in an RNA sequencing study using FINCH-2 pts.

Methods: Blood samples from RA pts in FINCH-2 on either a stable dose of MTX and placebo (n = 144), or once daily FIL 100 mg (n = 151), or 200 mg (n = 143) were analyzed at baseline and weeks 4 and 12. To evaluate the relationship between baseline IFN activity and change in disease activity after 12 weeks, we tested two IFN-based signatures: a 4-gene panel (Rodríguez-Carrio *et al.* 2018) and a FINCH-2 composite score derived from IFN response genes and clinical assay results. The association of these two signatures at baseline with the week 12 change in disease activity score 28 CRP (DAS28-CRP) or ACR-N response were evaluated using a linear regression model. The main effect of signature activity on clinical response represents a prognostic effect (i.e. independent of treatment), while a multiplicative interaction between signature activity and FIL is predictive. A linear mixed-effects model determined the FIL-specific change in signature activity across 2 time-points post-baseline (weeks 4 and 12).

Results: Baseline Rodriguez-Carrio IFN signature score showed no significant association with week 12 clinical response ($P > 0.05$ for all comparisons). In contrast, the baseline FINCH-2 derived composite IFN-based signature was significantly associated with an increase of DAS28-CRP after 12 weeks ($P = 0.0026$), independent of treatment. The composite IFN-based signature score was significantly associated with a FIL-specific improvement in DAS28-CRP (FIL 100 mg, $P = 0.0045$; FIL 200 mg, $P = 0.0005$) and ACR-N responses (FIL 100 mg, $P = 0.036$) after 12 weeks. The composite signature was significantly reduced in a dose-dependent manner after FIL treatment at weeks 4 and 12 (Table).

Conclusion: Expression of 4 IFN-stimulated genes at baseline was not significantly associated with week 12 clinical response in FINCH-2, suggesting that IFN signalling alone is not sufficient to predict response to MTX in a bDMARD experienced population. However, an expanded FINCH-2 derived composite IFN signature demonstrated a treatment-specific significant association at week 12. Validation of this signature or its sub-components will be performed in the FINCH-1 (MTX-experienced) and FINCH-3 (MTX-naïve) clinical trials, and retrospectively in the DARWIN clinical trials.

Disclosure: P. Taylor, AbbVie, 5, Abbvie, 5, Biogen, 5, Celgene, 2, 5, Eli Lilly and Company, 2, 5, Fresenius, 5, Fresenius SE & Co, 5, Fresnius, 5, Galapagos, 2, 5, Gilead, 5, GlaxoSmithKline, 5, Janssen, 2, 5, Lilly, 2, 5, Nordic Pharma, 5, NORDIC Pharma, 5, Pfizer, 5, Pfizer Inc, 5, Roche, 5, Sanofi, 5, UCB, 5; **B. Downie**, Gilead Sciences, Inc, 3, Gilead Sciences, Inc., 1, 3; **E. Elboudwarej**, Gilead Sciences, 1, Gilead Sciences, Inc., 1, 3; **R. Hawtin**, Gilead, 1, 3, Gilead Sciences, Inc., 1, 3; **A. Mirza**, Abbott Laboratories, 1, Gilead, 1, 3, Gilead Sciences, Inc., 1, 3; **J. Liu**, Gilead, 1, 3, Gilead Sciences, Inc., 1, 3, Johnson & Johnson, 1, Johnson and Johnson, 1, Roche, 1.

Abstract Number: 2013

Increased Accumulation of Malondialdehyde-Acetaldehyde Modified HDL in Macrophage Without Decreased Cholesterol Efflux

Kevin Real,[1] Michael Duryee,[1] Patrick Opperman,[1] Evan Ryan,[1] Logan Duryee,[1] James O'Dell,[2] Ted Mikuls,[2] Daniel Anderson,[1] and Geoffrey Thiele[2], [1]University of Nebraska Medical Center, Omaha, NE, [2]VA Nebraska-Western IA Health Care System & University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Etiology & Pathogenesis Poster II

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) are approximately two-fold more likely to develop cardiovascular disease (CVD). Prior reports have suggested that "dysfunctional" HDL may explain at least part of this enhanced risk profile. It has been suggested that post-translational modifications of HDL, including those characteristic of RA, may attenuate relevant protective properties of this lipoprotein. Specifically, studies have suggested that the irreversible post-translational modification of proteins with malondialdehyde-acetaldehyde (MAA) that are prevalent in RA synovium are also present in atherosclerotic plaque. Moreover, antibodies to MAA correlate with the development and progression of both RA and CVD. Therefore, the purpose of this study was to examine the biologic effects resulting from the exposure of MAA-modified HDL to human macrophages that have been implicated in CVD pathogenesis.

Methods: HDL was incubated with 2mM malondialdehye and 1mM acetaldehyde for 3 days to form the MAA adduct. PMA activated human THP-1 macrophages were subjected to 0.1, 1, 10 μg/ml of native or modified HDL in via-

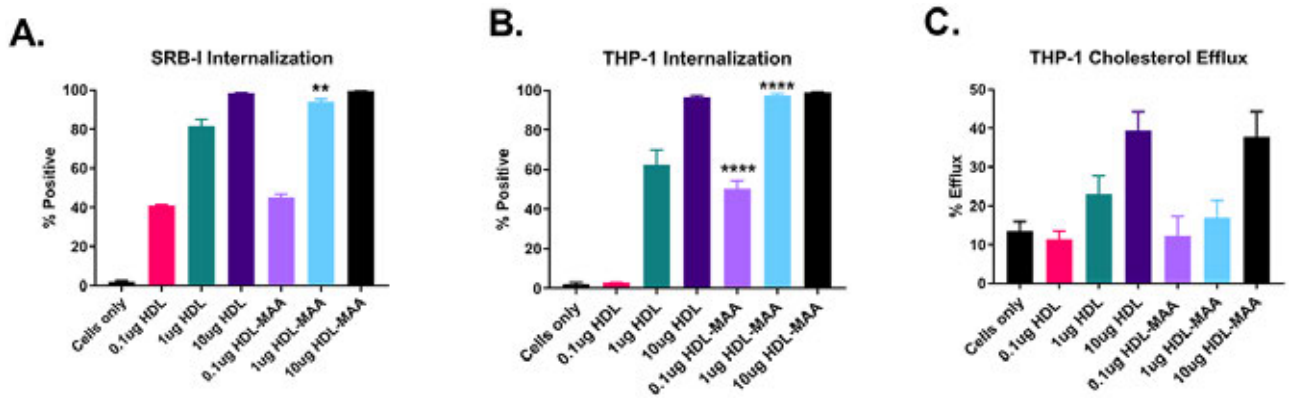

Figure 1 Internalization of MAA Modified HDL Proteins and Cholesterol Efflux. (A) CHO cells transfected with SRB-I internalize HDL-MAA significantly more ($p<0.01$) than native HDL at 1 ug. (B) THP-1 cells internalize HDL-MAA at 0.1 and 1 ug significantly more than native HDL ($p<0.0001$) (C) THP-1 cells demonstrated no significant change in the cholesterol efflux despite HDL particles being modified by MAA. (N=5)

bility assays for 4 hours and ligand internalization studies for 90 minutes. Internalization studies were also performed using Chinese Hamster Ovary (CHO) cells transfected with the B-I scavenger receptor (SRB-I) shown in prior studies to mediate cellular uptake of MAA-modified protein. Measurement of modified HDL function was tested using a fluorescent labeled cholesterol efflux assay using THP-1 cells.

Results: MAA modification of HDL was evident after 72 hours by fluorescence of the dihydropyridine ring at 398nm. THP-1 cell viability remained >95% after 4 hours of exposure to HDL-MAA. HDL-MAA was internalized at increasing concentrations compared to native HDL in both CHO cells transfected with the SRB-I receptor ($p< 0.01$) (A) and THP-1 cells ($p< 0.0001$) (B). However, cholesterol efflux (C) was not significantly different between native HDL and HDL-MAA, indicating that cholesterol binding is not MAA-dependent.

Conclusion: Post-translational modification of HDL may contribute to the development and progression of RA and CVD comorbidity. Increased internalization of HDL-MAA in the absence of meaningful effects on cholesterol efflux suggests that MAA modification does not alter the physiological rate of reverse cholesterol transport. However, the preferential accumulation of HDL in THP-1 cells following MAA modification suggests that this post-translational modification (demonstrated in RA to result from inflammation and increased oxidative stress) could impact the development and progression of comorbid CVD.

Disclosure: K. Real, None; **M. Duryee**, None; **P. Opperman**, None; **E. Ryan**, None; **L. Duryee**, None; **J. O'Dell**, None; **T. Mikuls**, BMS, 2, Horizon, 2; **D. Anderson**, None; **G. Thiele**, None.

Abstract Number: 2014

Loss-of-function of the DNA Repair Nuclease MRE11A Induces Mitochondrial Failure and Tissue Inflammation in Rheumatoid Arthritis

Yinyin Li,[1] Yi Shen,[1] Ke Jin,[1] Zhenke Wen,[1] Wenqiang Cao,[1] Bowen Wu,[1] Ru Wen,[1] Lu Tian,[1] Gerald Berry,[1] Jorg Goronzy,[1] and **Cornelia Weyand**[1], [1]Stanford University, Stanford, CA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
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Background/Purpose: Patients with rheumatoid arthritis (RA) accumulate tissue-invasive, pro-inflammatory $CD4^+$ T cells. Such T cells are metabolically reprogrammed, favoring cytokine production, lipogenesis and membrane formation while reducing ATP production. Also, such T cells have low expression of the DNA repair nuclease MRE11A, have a defect in DNA repair and are prematurely aged. How defective DNA repair, metabolic rewiring and the propensity to induce tissue inflammation are mechanistically linked is unknown.

Methods: $CD4^+$ T cells from seropositive RA patients and age-matched controls were isolated from human peripheral blood mononuclear cells. Nucleolytic activity of the DNA repair protein MRE11A was inhibited by gene knockdown or the pharmacologic inhibitor Mirin. Metabolic profiles and mitochondrial activity were examined by the Seahorse Analyzer and by quantifying metabolites. Inflammasome activation and lytic T cell death were measured by caspase-1 activation, IL-1β production and LDH release. Tissue inflammatory propensity of T cells was quantified in NSG mice engrafted with human synovial tissue and reconstituted with genetically or pharmacologically manipulated T cells.

Results: MRE11A^{low} CD4^{+} T cells from RA patients had low oxygen consumption and low ATP production, indicative of impaired mitochondrial function. The phenotype was reproduced with MRE11A knockdown in healthy T cells. Immunoblotting and imaging analysis localized MRE11A to the mitochondria. Pharmacologic and genetic inhibition of MRE11A resulted in leakage of mitochondrial DNA (mtDNA) into the cytoplasm, where it triggered assembly of the NLRP3 and AIM2 inflammasome and induced caspase-1-dependent pyroptotic cell death. Caspase-1 activation was a feature of T cells in lymph node biopsies of RA patients. MRE11A loss-of-function was associated with high propensity of T cells to induce synovial tissue inflammation in vivo, including the deposition of mtDNA in inflamed tissue sites. MRE11A overexpression was sufficient to restore mitochondrial function and prevent mtDNA leakage into the cytosol. Also, restoration of MRE11A expression suppressed pyroptotic T cell death and protected synovial tissue against inflammatory attack.

Conclusion: The DNA repair defect in RA T cells extends to mitochondrial DNA, impairing mitochondrial oxygen consumption and ATP generation and damaging mtDNA containment. The mitochondrial stress program associated with loss-of-function of the repair nuclease MRE11A triggers inflammasome assembly, caspase-1 activation and pyroptotic T cell death. The mechanistic connection between DNA repair, bioenergetic failure and pro-inflammatory T cell death provides novel therapeutic opportunities to manage immune aging and restore tissue homeostasis in rheumatoid arthritis.

Disclosure: Y. Li, None; **Y. Shen**, None; **K. Jin**, None; **Z. Wen**, None; **W. Cao**, None; **B. Wu**, None; **R. Wen**, None; **L. Tian**, None; **G. Berry**, None; **J. Goronzy**, None; **C. Weyand**, Kiniska Pharmaceuticals, 2.

Abstract Number: 2015

Methotrexate Treatment Is Associated with Reduction of Neutrophil Reactive Oxygen Species and CD177 in RA Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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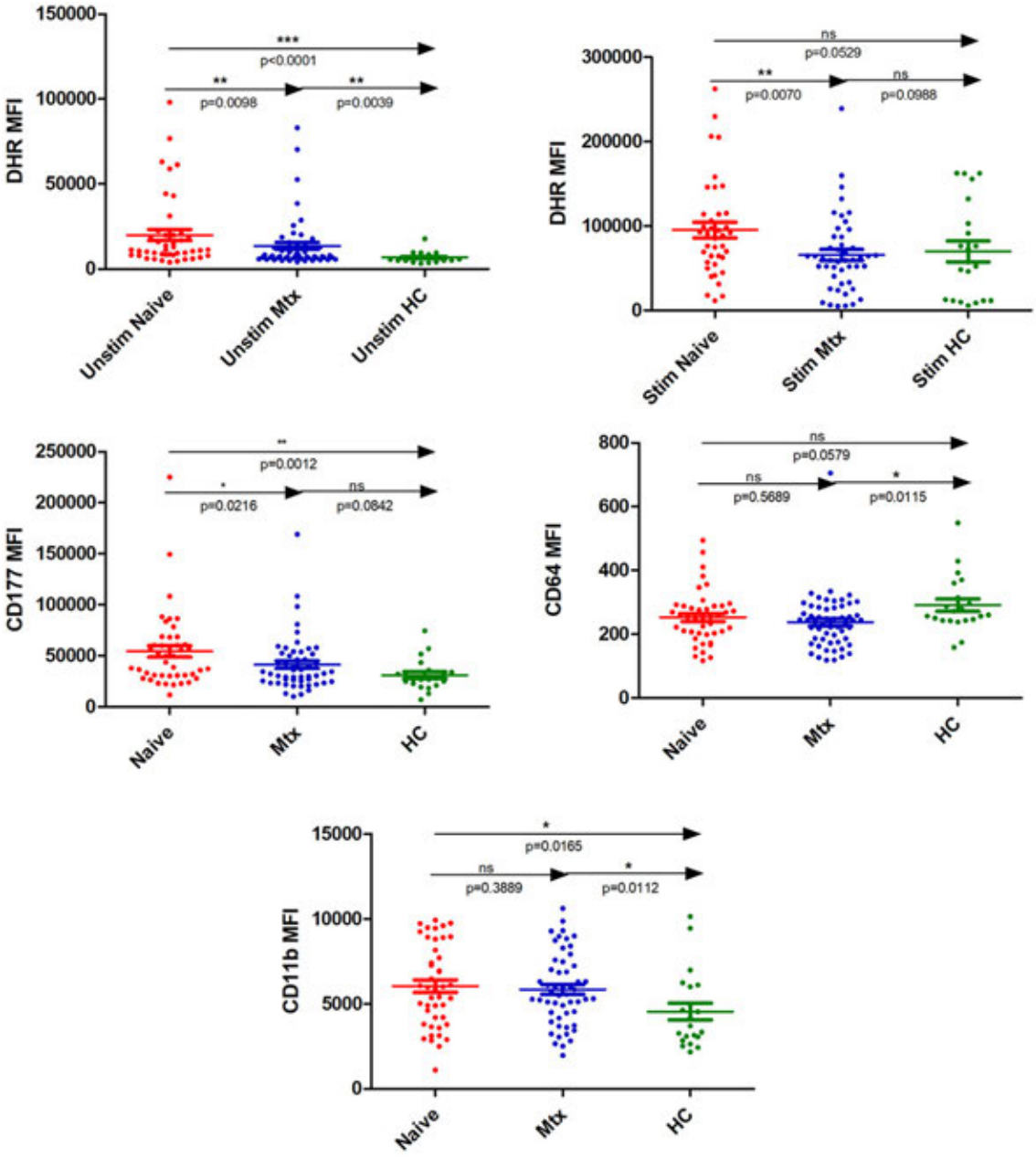
Background/Purpose: Methotrexate (MTX) is the gold-standard DMARD in rheumatoid arthritis, however, it is unclear how exactly it works. Its effects on neutrophils may involve reduction in ROS production and neutrophil activation markers like CD177, CD11b and CD64.

Methods: This was a single-center cross-sectional study, which recruited patients with rheumatoid arthritis (RA) and healthy controls. RA patients included naïve (could be on low dose steroids) and MTX treated patients (at least 15 mg/week for 6 months), labeled as naïve-RA and MTX-RA groups. Neutrophils were separated from blood using Hetasep and Ficoll density-gradient centrifugation. Reactive oxygen species (ROS) by dihydrorhodamine (DHR) was detected using flow cytometry after PMA stimulation (1.62 ug/ml) as Median Fluorescent Intensity (MFI). ROS by Luminol was detected after adding PMA (0.4 ug/ml) and Luminol (50 uM) and using a luminescence detector (area under curve over 30 mins). Activation markers CD177, CD11b and CD64 were detected by surface staining of neutrophils using FACS.



Top panel shows scatter-plots showing higher reactive-oxygen species detected using dihydrorhodamine in naive-RA than MTX-RA, but no differnce between MTX-RA and healthy controls (both unstimulated and pMA stimulated). Middle panel shows higher level of CD177 expression in neutrophils of naive-RA than MTX-RA, but no difference in CD64. Lower panel shows higher expression of CD11b in both RA groups than healthy controls.

Results: This study included 53 (F:M= 43:10) patients of rheumatoid arthritis on methotrexate (MTX-RA), 47 (F:M=39:8) naïve (naïve-RA) and 21 healthy controls. There was no significant difference in the mean age (44.5, 47.6 years, p=0.17) between RA groups. There was a significant difference in the DAS28-3 between the naïve-RA and MTX-RA group (6.2, 4.9., p< 0.001). At baseline, there was higher level of ROS by DHR (MFI) in neutrophils of naive-RA compard to MTX-RA (11049, 7301, p=0.009). ROS levels by DHR (MFI) remained higher in naive-RA than MTX-RA (88805, 59637, p=0.0070) even after PMA stimulation. However there was no significant between MTX-RA and healthy controls after PMA stimulation. No significant difference was found in ROS by luminol between Naive-RA and MTX-RA patients. CD177 was found higher expressed (MFI) in naïve-RA compared to MTX-RA patients (46620, 34475, p=0.0216) and healthy controls (46620, 26855, p= 0.0012). No significant change for CD11b and CD64 levels

was observed between naive and MTX treated patients. However, in comparison to healthy controls, MTX-RA patients had lower levels of CD64 (260, 241, p= 0.0115) while both MTX-RA and naïve-RA patients had higher levels of CD11b (3708, 5560, p= 0.0112 and 3708, 5978, p=0.0165).

Conclusion: MTX treatment in RA patients was associated with reduction (reaching healthy control levels) of ROS production in neutrophils. In addition, CD177 expression was also significantly reduced (reaching healthy controls) in MTX- treated patients. One of the ways MTX acts in RA may be through reducing neutrophil activation and ROS.

Disclosure: U. Kaundal, None; **V. Dhir**, None; **B. Saikia**, None; **A. Khullar**, None.

Abstract Number: 2016

Expression of Peptidyl-arginine Deiminases in Peripheral Blood Neutrophils and Its Association with Single Nucleotide Variants in Patients with Rheumatoid Arthritis

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Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
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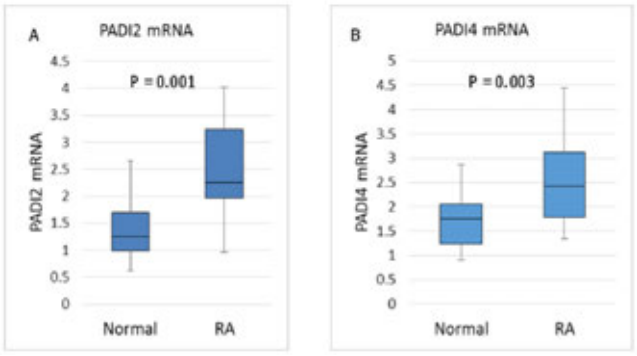
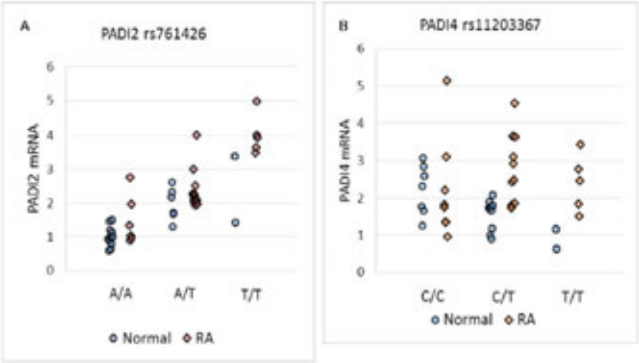
Figure 1. Expression of PADI2 and PADI4 mRNA in patients with RA and healthy controls



Peripheral blood neutrophils were separated by using magnetic beads and total RNA was extracted. PADI2 and PADI4 mRNA were measured by using real-time RT-PCR and normalized by beta-actin mRNA.

Figure 2. Expression of PADI2 and PADI4 mRNA in patients with RA and healthy controls stratified by the numbers of risk alleles



Patients and healthy controls were stratified by numbers of risk allele of the PADI2 or PADI4 single nucleotide variant, and mRNA levels of PADIs were compared across the groups.

Background/Purpose: Peptidyl-arginine deiminases (PADIs) are enriched in neutrophils and considered to be responsible for citrullination of proteins *in vivo*. Autoantibody against citrullinated proteins are frequently detected in patients with rheumatoid arthritis (RA) and are highly diagnostic for the disease. PADI activity is detected in synovial fluid, and citrullinated proteins are found in synovium of patients with RA. Genetic evidence has shown that single nucleotide variants (SNVs) of PADI2 and PADI4 genes are associated with RA susceptibility. We aimed to elucidate association of SNVs of PADIs and their expression in peripheral blood neutrophils from patients with RA.

Methods: We enrolled 23 patients who fulfilled the 2010 American College of Rheumatology / European League Against Rheumatism classification criteria for RA and 20 healthy controls. Peripheral blood neutrophils were separated by using magnetic beads and applied to *in vitro* culture and extraction of genomic DNA. Neutrophils were cultured with or without stimulation for 48 hours and supernatants were collected to measure PADI2 and PADI4 by using enzyme-linked immunosorbent assay. SNVs of PADI2 and PADI4 were determined by using TaqMan SNP Genotyping Assays. Quantitative real-time RT-PCR was used to measure mRNA levels of PADI2 and PADI4.

Results: Fresh neutrophils from patients with RA expressed significantly larger amounts of PADI2 (p = 0.001) and PADI4 (P = 0.003) mRNA, than healthy controls (Figure 1). Neutrophils spontaneously released PADI2 and PADI4. Upon stimulation with PMA (20 and 200 microM), secretion of PADI2 significantly increased in patients with RA (p = 0.003 for 20 microM; p = 0.001 for 200 microM), but not in healthy controls. On the contrary, secretion of PADI4 significantly decreased in healthy controls at both PMA concentrations (p = 0.001 for 20 microM; p = 0.003 for 200 microM), but only at 20 microM in patients with RA (p = 0.05 for 20 microM, p = 0.5 at 200 microM). Patients and healthy controls were stratified by numbers of risk allele in SNVs of PADI genes, and mRNA levels of PADIs were compared (Figure 2). Multiple linear regression analyses revealed that RA (versus healthy controls) [nonstandardized partial regression coefficient (NPRC) = 1.29, 95% confidence interval (95% CI) 0.67 – 1.91, p = 0.001] and numbers of the risk allele of PADI2 rs761426 (A - >T) (NPRC = 0.20, 95% CI = 0.010 – 0.39, p = 0.04) were significantly associated with the levels of PADI2 mRNA in neutrophils. RA (versus healthy controls) was also associated with the levels of PADI4 mRNA in neutrophils (NPRC = 0.95, 95% CI = 0.36 – 1.55, p = 0.002), but not numbers of the risk allele of PADI4 rs11203367 (C - >T).

Conclusion: Expression levels of PADI2 and PADI4 mRNA were higher in patients with RA compared to healthy controls, but their association with SNVs are different. Secretion of these PADIs upon stimulation with PMA were different, which may suggest their independent physiological and pathological roles *in vivo*.

Disclosure: M. Harigai, AbbVie Japan GK, 2, 8, Ayumi Pharmaceutical Co. Ltd., 2, Bristol Meyers Squib, 2, 5, 8, Bristol-Myers Squibb Co. Ltd, 2, 5, 8, Chugai Pharmaceutical Co. Ltd., 2, 5, 8, Chugai Pharmaceutical Co., Ltd., 2, 5, 8, Eisai Co. Ltd., 2, Eisai Co., Ltd., 2, Eli Lilly, 5, 8, Mitsubishi Tanabe Pharma Co., 2, Mitsubishi Tanabe Pharma Corp., 2, Nippon Kayaku Co. Ltd., 2, Taisho Toyama Pharmaceutical Co. Ltd., 2, Takeda Pharmaceutical Co., 2, Takeda Pharmaceutical Co., Ltd., 2, Teijin Pharma Ltd., 2, 8, Teijin Pharma, Ltd., 2, 8; **R. Sakai**, Ayumi Pharmaceutical Co. Ltd., 2, Bristol Meyers Squib, 2, Chugai Pharmaceutical Co. Ltd., 2, Mitsubishi Tanabe Pharma Corp., 2, Nippon Kayaku Co. Ltd., 2, Taisho Toyama Pharmaceutical Co. Ltd., 2; **T. Sugihara**, Ayumi Pharmaceutical, 9, Ayumi Pharmaceutical Corporation, 2, Chugai Pharmaceutical, 9, Chugai Pharmaceutical Co., Ltd., 2, CSL Behring, 9, CSL Behring K.K., 2, Japan Blood Products Organization, 2, 9, UCB Japan, 9, UCB Japan Co. Ltd., 2; **A. Ishigami**, None.

Abstract Number: 2017

Beyond Genes—a Multi-omic Analysis of Monozygotic Twins Discordant for Rheumatoid Arthritis

Julia Manasson,[1] Jeremy Sokolove,[2] Lauren Lahey,[2] Adriana Heguy,[1] Carles Ubeda,[3] and Jose Scher[1], [1]New York University School of Medicine, New York, NY, [2]Stanford University School of Medicine, VA Palo Alto Medical Center, Stanford, CA, [3]Centro Superior de Investigación en Salud Pública - FISABIO, Valencia, Spain

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Although a number of genetic factors, including susceptibility alleles, have been identified in rheumatoid arthritis (RA), the concordance rate in monozygotic (MZ) twins is only 15% (Silman AJ et al, Br J Rheumatol 1993). Given this relatively low rate, environmental factors (including smoking, the microbiome and others) likely play a significant role in disease pathogenesis. Several prior studies have highlighted this relationship. Two examples include oral *Porphyromonas gingivalis*, which has been implicated in the citrullination of peptides (Hitchon CA et al, J Rheumatol 2010), and intestinal *Prevotella copri*, which is significantly increased in new-onset RA (Scher JU et al,

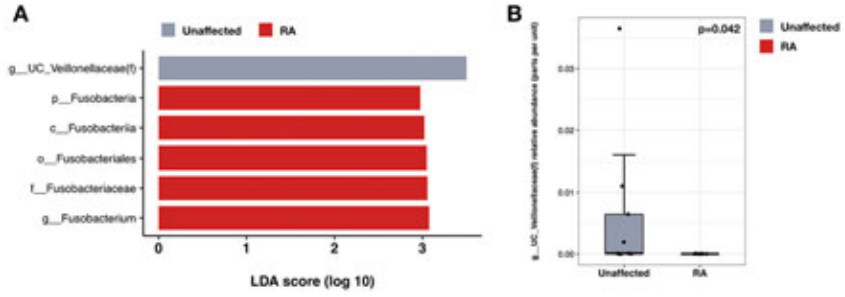
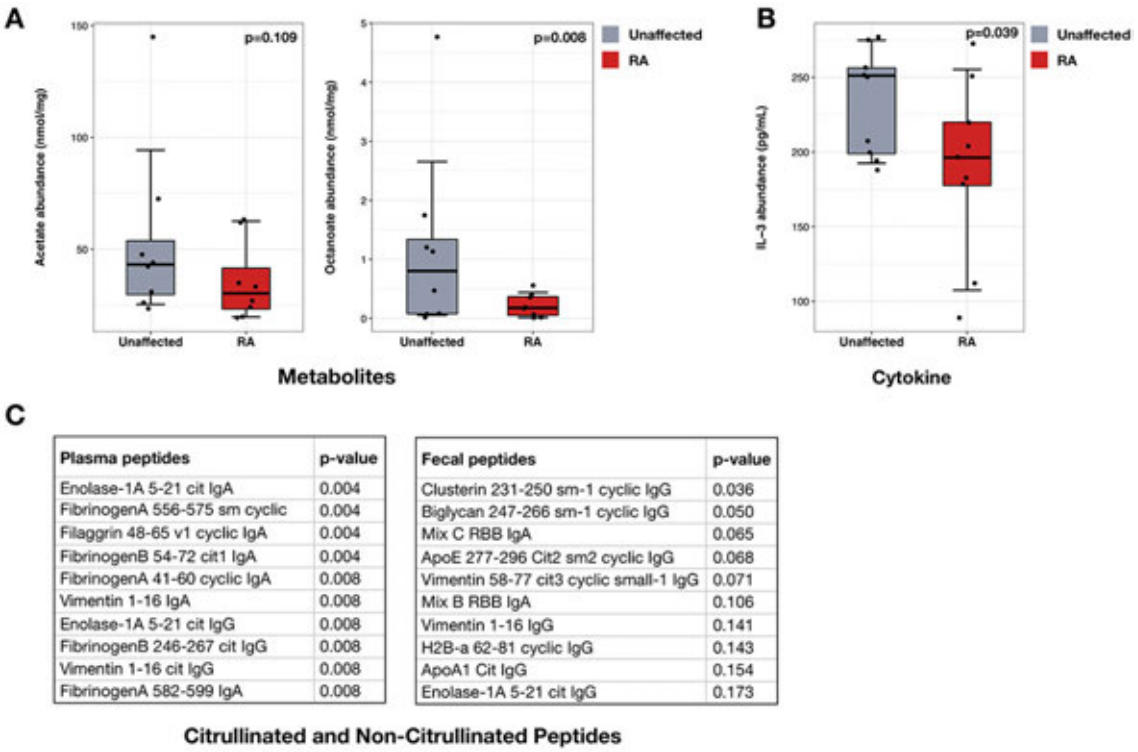


Figure 1 Linear discriminant analysis Effect size (LEfSe) identifies bacterial taxa that differentiate unaffected from RA twins. (A) Unaffected twins demonstrate differentially higher abundance of Unclassified Veillonellaceae, whereas RA twins demonstrate differentially higher abundance of Fusobacterium and other taxa within the Fusobacteria phylum. Linear discriminant analysis (LDA) score is on a log10 scale. Log10 LDA is >2 for all taxa. None of the identified taxa achieve FDR <0.1. (B) Boxplot of Unclassified Veillonellaceae relative abundance comparing unaffected and RA twins. Statistical significance calculated using the Wilcoxon signed-rank test.



Plasma peptides	p-value
Enolase-1A 5-21 cit IgA	0.004
FibrinogenA 556-575 sm cyclic	0.004
Filaggrin 48-65 v1 cyclic IgA	0.004
FibrinogenB 54-72 cit1 IgA	0.004
FibrinogenA 41-60 cyclic IgA	0.008
Vimentin 1-16 IgA	0.008
Enolase-1A 5-21 cit IgG	0.008
FibrinogenB 246-267 cit IgG	0.008
Vimentin 1-16 cit IgG	0.008
FibrinogenA 582-599 IgA	0.008

Fecal peptides	p-value
Clusterin 231-250 sm-1 cyclic IgG	0.036
Biglycan 247-266 sm-1 cyclic IgG	0.050
Mix C RBB IgA	0.065
ApoE 277-296 Cit2 sm2 cyclic IgG	0.068
Vimentin 58-77 cit3 cyclic small-1 IgG	0.071
Mix B RBB IgA	0.106
Vimentin 1-16 IgG	0.141
H2B-a 62-81 cyclic IgG	0.143
ApoA1 Cit IgG	0.154
Enolase-1A 5-21 cit IgG	0.173

Citrullinated and Non-Citrullinated Peptides

Figure 2 Unaffected twins demonstrate higher levels of octanoate and IL-3, whereas RA twins have significantly higher levels of fecal and plasma citrullinated/non-citrullinated peptides. (A-B) Boxplots of fatty acid metabolites and IL-3 abundance comparing unaffected and RA twins. (C) Tables of plasma and fecal citrullinated/non-citrullinated peptides comparing unaffected and RA twins. Only the top ten peptides by p-value are listed. For all panels, statistical significance calculated using the Wilcoxon signed-rank test.

Elife, 2013). In our study, we sought to further understand this relationship by exploring the microbial, metabolomic and cytokine differences in MZ twins with discordant disease.

Methods: Fecal and blood samples were collected from nine pairs of MZ twins where one sibling was diagnosed with RA and the other unaffected. Fecal samples underwent bacterial DNA extraction, amplification and 16S rRNA gene sequencing. Additionally, gas chromatography mass spectrometry (GC-MS) was used to quantify fecal metabolites and multiplex assays were used to quantify fecal and plasma ACPA autoantigens as well as other cytokines (Sokolove J et al, PLoS One, 2012.). Analysis was performed using R, Quantitative Insights into Microbial Ecology (QIIME) and Linear discriminant analysis Effect Size (LEfSe).

Results: Microbiome analysis revealed no significant differences in overall bacterial alpha or beta diversity between unaffected and RA twins. On average, RA twins had higher relative abundance of Bacteroidales (RA 56.6% vs Unaffected 47.9%) and lower abundance of Clostridiales (RA 34.5% vs Unaffected 42.8%). LEfSe analysis showed differentially higher abundance of *Unclassified Veillonellaceae* in unaffected twins ($p=0.042$). Unaffected twins also demonstrated higher levels of fecal octanoate ($p=0.008$), a medium-chain fatty acid with beneficial immune effects, as well as significantly increased levels of plasma IL-3 ($p=0.039$). Conversely, several fecal and plasma citrullinated/non-citrullinated peptides were significantly higher in RA twins compared to their unaffected siblings ($p< 0.05$).

Conclusion: We characterized differences in the bacterial microbiome, metabolites, cytokines and citrullinated/non-citrullinated peptides in MZ twins discordant for RA. We found changes in the abundance of particular taxa, as well as higher levels of octanoate and IL-3 in unaffected twins, further suggesting the possibility that the initial citrullination and autoimmune events in this disease may occur in the intestinal mucosa. Understanding the immune mechanisms

orchestrated by the gut microbiota and their downstream effects may ultimately shed light on the pathogenesis of RA beyond genetic susceptibility and allow us to potentially alter the course of disease development and progression.

Disclosure: J. Manasson, None; **J. Sokolove**, AbbVie, 3; **L. Lahey**, None; **A. Heguy**, None; **C. Ubeda**, None; **J. Scher**, Janssen, 5, Novartis, 5, UCB, Inc, 5, Pfizer, 5.

Abstract Number: 2018

Elevated Serum Levels of Tie-1 in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease that primarily affects patients' peripheral joints and can lead to severe personal disability from progressive articular joint destruction. The cause of RA is unknown. Recent studies have shown that collagen formation as well as angiogenesis are important in the pathophysiology of this disease. Specifically, serum vascular endothelial factor (VEGF) levels have been shown to be elevated in patients with RA and were correlated with the degree of radiographic joint damage. In addition to VEGF, a related angiogenic factor Tie-1 has been found to be elevated in RA synovial fluid. The objective of this study was to determine serum levels of Tie-1 in patients with RA and investigate associations with RA disease activity and RA clinical features.

Methods: 94 patients with RA and 21 healthy controls from the Penn State Hershey Investigation of Remission in Rheumatoid Arthritis (IRRA) cohort at Pennsylvania State M.S. Hershey Medical Center had measurement of serum Tie-1 levels using ELISA. High levels of Tie-1 were considered to be greater than 35,000. Mean Tie-1 levels were compared by T-test. Further analysis was performed using other available data including DAS 28 ESR/CRP, age, disease duration and mHAQ using Pearson's correlation and linear regression. Further chart review analysis was done to correlate radiographic findings. Data are expressed as mean (standard deviation).

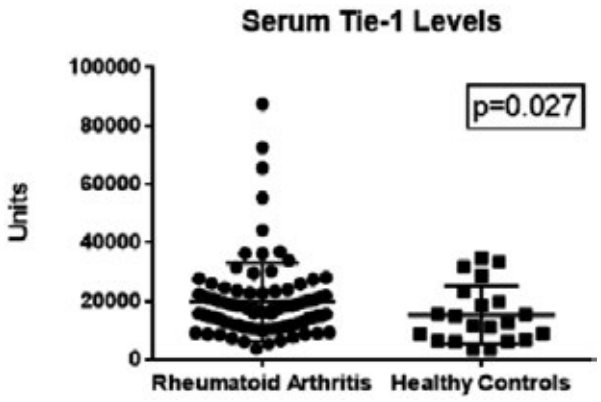

Figure 1. Serum Levels of TIE-1

Table 1a: Demographics			
	RA Patients (N=96)	Healthy Controls (N=21)	p-Values
Age (yrs)	55.57 (13.47)	48.48 (15.42)	0.035
Gender (% of female)	71 (74.0%)	16 (76.2%)	0.832
Seropositive for RF or CCP	89.4% (N=85)	-	-
DAS 28 CRP	3.33 (1.39) N=74	-	-
DAS 28 ESR	3.46 (1.59) N=64	-	-
Disease Duration (yrs)	11.09 (10.11) N=94	-	-
MHAQ (median, IQR)	0.125 (1.250) (N=90)	-	-
X-Ray erosions	41.8% (N=79)	-	-
BMI	29.57 (7.16)	25.15 (5.95)	0.010
Tie-1 level (units)	19794.91 (13373.99) N=94	15388.67 (9935.25)	0.027
Table 1b: High Tie-1 vs. Low-Tie 1			
	High TIE patients (levels >35,000) (N=8)	Low TIE patients (levels ≤35,000) (N=107)	p-Values
Age (yrs)	61.76 (7.82)	53.84 (14.20)	0.123
Gender (% of female)	7 (87.5%)	79 (73.3%)	0.390
Seropositive for RF or CCP	8 (100%)	67 (88.2%) (N=76)	0.590
DAS 28 CRP	3.97 (0.85) (N=6)	3.24 (0.17) (N=67)	0.209
DAS 28 ESR	4.21 (1.09) (N=5)	3.35 (1.60) (N=58)	0.246
Disease Duration (yrs)	17.96 (8.84)	10.50 (10.09) (N=84)	0.047
MHAQ	0.688 (0.625)	0.125 (1.250) (N=80)	0.036
X-Ray erosions	5 (83.3%) (N=6)	27 (38.0%) (N=71)	0.076
BMI	33.48 (8.25)	28.41 (7.04)	0.055
Tie-1 level (units)	54393.53 (19312.95)	16343.33 (7238.54)	<0.001

Results: The 94 subjects with RA had significantly higher serum Tie-1 levels compared to the healthy controls (19,794.91 (13,373.99) vs. 15,388.67 (9,935.25), p=0.027, Table 1a). There was a mild association between Tie-1 and DAS28ESR (β estimate 0.072; p=0.069). Eight subjects had high levels of Tie-1; 6 of these 8 patients had erosions on their x-rays (Table 1b). Patients with erosions had higher Tie-1 levels, but this was not statistically significant (P=0.125).

Conclusion: RA patients have higher levels of Tie-1 compared to healthy controls (Figure 1). High Tie-1 levels had a mild correlation with RA disease activity in this cross-sectional analysis. The etiology for the reason for higher levels of this angiogenesis factor in RA is unknown but may be related to synovial proliferation and other features of uncontrolled disease. Further research is needed to investigate the mechanism and source of the increase in serum and synovial fluid levels of TIE-1 and study as a biomarker of disease will be also of interest. These findings, combined with the previously described correlation between VEGF and RA activity, support the need to further understand the role of angiogenesis in the pathogenesis of RA.

Disclosure: D. Lee, None; **C. Mohan**, None; **D. Feger**, None; **N. Olsen**, None; **R. June**, None.

Abstract Number: 2019

Tenosynovitis at the Metatarsophalangeal Joints, a Novel Feature of RA: Results from an Anatomical and Large Magnetic Resonance Imaging Study of Tendon Sheaths of the Forefoot

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent magnetic resonance imaging (MRI)-studies revealed that tenosynovitis in the hands is associated with rheumatoid arthritis (RA). Although the forefoot is a preferential location for RA-inflammation, it is unknown whether MRI-detected tenosynovitis at the level of metatarsophalangeal (MTP)-joints is associated with RA. In addition anatomic literature leaves it undetermined if tendons at MTP-joints are surrounded by a synovial sheath. These questions were investigated.

Methods: Macroscopically, 14 forefeet of donated bodies were examined at the flexor-tendons and extensor-tendons for the presence and course of tendon sheaths. Tissue surrounding tendons was injected with blue-dyed resin or silicon. Presence of a sheath was also studied by light-microscopy. 624 persons (157 patients presenting with RA, 284 with other early arthritides and 193 symptom-free persons from the general population) underwent 1.5T MRI of unilateral MTP(1-5)-joints. Images were scored by two readers for tenosynovitis, synovitis and bone marrow oedema.

Results: Macroscopically, all extensor and flexor tendons crossing MTP-joints demonstrated clearly demarcated sheaths surrounding tendons. Microscopy revealed a synovial sheath. MRI-detected tenosynovitis occurred in 42% of RA-patients, 22% with other arthritidesand 1.6% of symptom-free controls. Compared to other arthritides, MRI-detected tenosynovitis was associated with RA, OR 2.38 (95%CI 1.5-3.8) for flexor and OR 3.13 (95%CI 1.9-5.2) for extensor tendons. The sensitivity of tenosynovitis in RA was 42%. The specificity compared to other arthritideswas 78%, and compared to symptom-free controls 98%.

Conclusion: Tenosynovium is present surrounding flexor and extensor tendons at MTP-joints. MRI-detected tenosynovitis of MTP-joints is specific for RA.

Disclosure: Y. Dakkak, None; **F. Jansen**, None; **M. DeRuiter**, None; **M. Reijnierse**, None; **A. van der Helm-van Mil**, None.

Abstract Number: 2020

Metabolic Changes Induced by Anti-Malondialdehyde Antibodies Promote Osteoclast Development

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Etiology & Pathogenesis Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Malondialdehyde (MDA) is highly reactive compound produced by lipid-peroxidation in situations associated with oxidative stress. MDA can irreversibly modify proteins (e.g. lysine, arginine and histidine residues), which can lead to the generation of immunogenic neo-epitopes that are recognized by autoantibodies. In fact, anti-MDA IgG antibodies are significantly increased in the serum of patients with autoimmune diseases, such as rheumatoid arthritis (1). Recently, anti-MDA IgG antibodies have been shown to promote osteoclast (OC) differentiation *in vitro* (1). In this study, we decided to further elucidate the molecular mechanisms triggered by these autoantibodies during osteoclastogenesis.

Methods: OCs were generated from monocyte-derived macrophages in the presence of the cytokines RANK-L and M-CSF. The development of OCs was monitored by light microscopy following tartrate-resistant acid phosphatase (TRAP) staining. Three different recombinant human monoclonal anti-MDA antibodies, generated by single-cells cloning from synovial RA B cells, or control antibodies were added to OC cultures. Cellular metabolism was monitored using Seahorse XF Analyzer (extracellular acidification rate and oxygen consumption) and a colorimetric L-Lactate assay. Genes expressions were assessed by RT-PCR.

Results: Lactic acid production correlated with stimulatory effect of anti-MDA antibodies on OCs, suggesting an antibody-mediated regulation of glycolysis. Moreover, extracellular acidification rate and oxygen consumption of the developing OCs were increased by the osteoclastogenic anti-MDA clone but not by control antibodies. We have also observed the upregulation of genes encoding the glucose transporter GLUT1 and the down-regulation of the pyruvate dehydrogenase kinase (PDK)2 and PDK4 enzymes by anti-MDA antibodies. The glycolysis inhibitor 2-deoxyglucose eliminated the stimulatory effect of anti-MDA clone on OCs at drug concentrations that did not influence baseline OC development.

Conclusion: Our study further confirmed that IgG autoantibodies against MDA/MDA-acetaldehyde posttranslational modifications might have pathological roles in RA. We showed that certain anti-MDA clones induced an early boost of glycolysis and mitochondrial respiration in developing OCs and these metabolic changes led to an increased OC differentiation. Our study thus described a new type of autoantibody-induced cellular mechanism that can contribute to bone abnormalities.

Reference:

1. C. Grönwall et al. Journal of Autoimmunity 84 (2017) 29-45.

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Abstract Number: 2021

Higher Genetic Risk Load in Patients with More Diverse Manifestations in a Korean Systemic Lupus Erythematosus Cohort

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multifactorial autoimmune disease with diverse heterogeneous phenotypes. Although many studies of SLE presented estimates of high heritability, impact of complex genetic variants on the clinical manifestations and antibodies profiles of SLE was not fully understood. The aim of this study is to identify the genetic load by genetic risk score (GRS) that influence the clinical and serological manifestations according to ACR criteria in patients with SLE.

Methods: A total of 781 Korean patients from the Hanyang BAE lupus cohort were genotyped by genome-wide association study array. Weighted genetic risk score (GRS) were calculated from 45 well-validated non-HLA SNPs and HLA SLE-risk loci. Individual GRS was tested for associations with the clinical subphenotypes based on ACR criteria of SLE and the development of autoantibody by using a multivariable linear regression or a logistic regression.

Results: We identified weighted GRS calculated from non-HLA and HLA SLE-risk loci with significant associations in various SLE subphenotypes defined by the ACR criteria (mean number 5.74) among 11 criteria. Individual's weighted GRS showed significantly positive correlation with the number of ACR criteria in a linear regression model (β coefficient = 0.13, $p = 9.00\times10^{-3}$). Consistently, a significant positive correlation with the number of ACR in both non-HLA GRS ($\beta = 0.11$, $p = 0.027$) and HLA GRS (β 0.06, $p = 0.021$) was observed, respectively.

In a clinical subphenotype analysis, weighted GRS from non-HLA and HLA risk loci were significantly related to malar rash (OR 1.23, $p = 2.68\times10^{-3}$), renal disorder (OR 1.15, $p = 4.41\times10^{-2}$), and thrombocytopenia (OR 1.21, $p = 7.55\times10^{-3}$) using a multivariable logistic regression. Weighted GRS were strongly associated with production of anti-DNA antibody (OR 1.38, $p = 2.18\times10^{-3}$).

Conclusion: In conclusion, genetic risk load of SLE is significantly higher in individuals with more diverse clinical and serological manifestations. Several subphenotypes (malar rash, renal disorder, thrombocytopenia and anti-dsDNA antibody) might be influenced by cumulative genetic risk load.

Disclosure: S. Bang, Hanyang University, 3; **E. Ha**, None; **H. Kwon**, None; **H. Yoo**, None; **J. Kang**, None; **J. Kim**, None; **B. Nam**, None; **J. Shin**, None; **Y. Lee**, None; **T. Lee**, None; **H. Lee**, None; **K. Kim**, None; **S. Bae**, None.

Abstract Number: 2022

Analysis of Gene Expression from Systemic Lupus Erythematosus Synovium Reveals Unique Pathogenic Mechanisms

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Arthritis is a common manifestation of SLE and the ability of a new lupus therapy often depends on its ability to suppress joint inflammation. Despite this, an understanding of the underlying pathogenic mechanisms driving lupus synovitis remains incomplete. We, therefore, interrogated gene expression profiles of SLE synovium to gain insight into the nature of joint inflammation in lupus arthritis.

Methods: Biopsied knee synovia from SLE and OA patients were analyzed for differentially expressed genes (DEGs) and also by Weighted Gene Co-expression Network Analysis (WGCNA) to determine similarities and differences between gene profiles and to identify modules of highly co-expressed genes that correlated with clinical features of lupus arthritis. DEGs and correlated modules were interrogated for statistical enrichment of immune and non-immune cell type-specific signatures and validated by Gene Set Variation Analysis (GSVA). Genes were functionally characterized using BIG-C and canonical pathways and upstream regulators operative in lupus synovitis were predicted by IPA®.

Results: DEGs upregulated in lupus arthritis revealed enrichment of numerous immune and inflammatory cell types dominated by a myeloid phentoype, whereas downregulated genes were characteristic of fibroblasts. WGCNA revealed 7 modules of co-expressed genes significantly correlated to lupus arthritis or disease activity (SLEDAI or anti-dsDNA titer). Functional characterization of both DEGs and WGCNA modules by BIG-C revealed consistent co-expression of immune signaling molecules and immune cell surface markers, pattern recognition receptors (PRRs), antigen presentation, and interferon stimulated genes. Although DEGs were predominantly enriched in myeloid cell transcripts, WGCNA also revealed enrichment of activated T cells, B cells, CD8 T and NK cells, and plasma cells/plasmablasts, indicating an adaptive immune response in lupus arthritis. Th1, Th2, and Th17 cells were not identified by transcriptomic analysis although IPA® predicted signaling by the Th1 pathway and numerous innate immune signaling pathways were verified by GSVA. IPA® additionally predicted inflammatory cytokines TNF, CD40L, IFNα, IFNβ, IFNγ, IL27, IL1, IL12, and IL15 as active upstream regulators of the lupus arthritis gene expression profile in addition to the PRRs IRF7, IRF3, TLR7, TICAM1, IRF4, IRF5, TLR9, TLR4, and TLR3. Analysis of chemokine receptor-ligand pairs, adhesion molecules, germinal center (GC) markers and T follicular helper (T_{fh}) cell markers indicated trafficking of immune cell populations into the synovium by chemokine signaling, but not *in situ* generation of fully-formed GCs. GSVA confirmed activation of both myeloid and lymphoid cell types and inflammatory signaling pathways in lupus arthritis, whereas OA was characterized by tissue repair/damage.

Conclusion: Bioinformatic analysis of lupus arthritis reveals a pattern of immunopathogenesis in which myeloid cell-mediated inflammation dominates, leading to further recruitment of adaptive immune cells that contribute to the ongoing inflammatory synovitis.

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Abstract Number: 2023

Gene-Expression Analysis of Male and Female SLE Patients Reveals Candidate Pathogenic Pathways

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The female predisposition for development of multiple autoimmune diseases is well recognized. The female to male ratio reaches a maximum during the reproductive years among SLE patients, suggesting a link between sexual development and disease. Additional epidemiologic data indicate an effect of sex chromosomes. To gain insight into molecular mechanisms of SLE, we investigated gene expression in PBMC of SLE patients and corresponding healthy donors of both genders using RNA-seq.

Methods: SLE samples were selected at a time of relative disease quiescence from a longitudinal cohort of patients. To minimize variation between male and female patients only demographically matched adults receiving low doses of steroids, hydroxychloroquine and mycophenolate motifil were selected and matched to healthy donors (HD). The analysis focused on identification of functional pathways affected in male and female SLE patients and abnormal gene expression from sex chromosomes.

Results: Principal component analysis differentiated the 4 donor groups, with PC1 and PC3 reflecting disease and PC2 reflecting gender. Male SLE patients received the highest score on PC1 and were placed closer to both SLE and healthy females than healthy males on PC2. We identified 796 and 99 differentially expressed genes in male and female SLE patients respectively, compared to HD ($p< 0.05$, logFC=1.5). Fewer genes (20 vs. 27) differed between genders in SLE vs. HD ($p< 0.05$, logFC=1.5). Weighted Gene Co-expression Network Analysis (WGCNA) identified 24 clusters of co-expressed genes in male and female patients. The most intriguing were clusters that differed in male and female HD and were upregulated in SLE of both genders. Those clusters include genes related to EGF receptor ligands (AREG, EREG, HBEGF), transcription factors (ATF3, NR4A1, NR4A2, NR4A3), cytokines and chemokines (CCL3, CXCL2, CXCL8, CCL3L3, IL1A, IL1B). We also identified a group of X-chromosomal genes strongly upregulated in male SLE patients, including CXorf21.

Conclusion: Despite being clinically similar, male SLE patients showed a higher level of affected genes and had a lower divergence from females based on gender-related genes. Male HD had the lowest basal level of pro-inflammatory genes and EGF receptor ligands. The signaling through the EGF receptor has been shown to modulate the type I interferon response and may predispose females to autoimmune disease. The effect of X-chromosomal genes, including those that can escape inactivation in females, should be further investigated. We propose that gender-specific differences in gene expression reveal immunopathogenic mechanisms in autoimmune disease.

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Abstract Number: 2024

Genetics of Longitudinal Kidney Function in Children and Adults with Systemic Lupus Erythematosus

Thai-Son Tang,[1] Declan Webber,[2] Jingjing Cao,[3] Daniela Dominguez,[4] Dafna Gladman,[5] Andrea Knight,[6] Deborah Levy,[7] Lawrence Ng,[4] Andrew D. Paterson,[8] Earl D. Silverman,[9] Zahi Touma,[10] Murray Urowitz,[10] Joan Wither,[11] Eleanor M. Pullenayegum,[12] and Linda Hiraki[13], [1]Dalla Lana School of Public Health, University of Toronto, Toronto, Canada, [2]University of Toronto, The Hospital for Sick Children, Toronto, Canada, [3]Genetics & Genome Biology, The Hospital for Sick Children, Toronto, Canada, [4]Division of Rheumatology, The Hospital for Sick Children, Toronto, Canada, [5]Toronto Western Hospital, Toronto, Canada, Toronto, ON, Canada, [6]Division of Rheumatology, The Hospital for Sick Children, Department of Paediatrics, University of Toronto, Toronto, ON, Canada, [7]Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, [8]Genetics & Genome Biology, The Hospital for Sick Children, Dalla Lana School of Public Health, University of Toronto, Toronto, Canada, [9]Division of Rheumatology, The Hospital for Sick Children, Department of Paediatrics, University of Toronto, Translational Medicine, Research Institute, The Hospital for Sick Children, Toronto, Canada, [10]University Health Network, University of Toronto, Toronto, ON, Canada, [11]University Health Network, Krembil Research Institute, Toronto, ON, Canada, [12]Child Health Evaluative Sciences, The Hospital for Sick Children, Dalla Lana School of Public Health, University of Toronto, Toronto, Canada, [13]Division of Rheumatology, The Hospital for Sick Children, Department of Paediatrics, University of Toronto, Child Health Evaluative Sciences, Research Institute, The Hospital for Sick Children, Toronto, Canada

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: SLE – Etiology & Pathogenesis Poster II

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Genetics influences kidney function (estimated glomerular filtration rate (eGFR)), systemic lupus erythematosus (SLE) and lupus nephritis (LN) risk. Genome-wide association studies (GWAS) have identified single nucleotide polymorphisms (SNPs) associated with eGFR in the general population as well as SLE. However, few loci have been identified and replicated for LN risk, in part due to heterogeneity with LN. Using quantitative, repeated eGFR measures as opposed to binary LN may be more informative in detecting LN genetic loci. Our objective was to demonstrate repeated eGFR measures as potentially informative measures in GWAS by showing an association exists between SNPs associated with eGFR and SLE on (1) mean and (2) variance of eGFR.

Patient-Level Covariates	All SLE Patients (n = 1167)	LN SLE Patients (n = 434)	Non-LN SLE Patients (n = 733)
Sex			
Female	1012 (86.7)	354 (81.6)	658 (89.8)
Age at Diagnosis (years)‡	19.61 [14.30, 31.71]	17.07 [13.21, 28.54]	21.92 [14.78, 33.64]
Total Follow-Up Time (years)‡	7.52 [3.92, 15.25]	8.72 [5.06, 16.25]	6.87 [3.52, 14.51]
Ancestry			
European	564 (48.3)	164 (37.8)	400 (54.6)
East Asian	236 (20.2)	105 (24.2)	131 (17.9)
African	111 (9.5)	56 (12.9)	55 (7.5)
South Asian	86 (7.4)	37 (8.5)	49 (6.7)
Amerindian/Hispanic	22 (1.9)	12 (2.8)	10 (1.4)
Admixed	148 (12.7)	60 (13.8)	88 (12.0)
Number of eGFR Measures	36,258	16,314	19,944
No. of aSLE Measures (CKD-EPI)	23,926 (66.0)	9,788 (60.0)	14,138 (70.9)
No. of cSLE Measures (Schwartz)	12,332 (34.0)	6,526 (40.0)	5,806 (29.1)
Within-Person No. eGFR Measures‡	24 [13, 41]	30 [17, 50]	21 [11, 35]
Within-Person Mean eGFR†	98.60 (21.86)	93.57 (26.75)	101.57 (17.72)
Within-Person eGFR Variance†	11.11 (5.95)	13.67 (7.40)	9.59 (4.23)

Categorical variables, frequency (proportion in %)
†Continuous variables, mean (standard deviation), ‡Continuous variables, median [interquartile range]
SLE = systemic lupus erythematosus, LN = lupus nephritis, eGFR = estimated Glomerular Filtration Rate, No. = number,
aSLE = adult-onset SLE, cSLE = childhood-onset SLE, CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration

Summary statistics of patient-level laboratory, demographic and clinical characteristics collected during follow-up between LN and non-LN patients.

Methods: We included 1167 patients followed in Toronto Lupus Clinics from SickKids and/or the Toronto Western Hospital. Patients met ≥4 ACR and/or SLICC criteria for SLE and were genotyped on the Illumina MEGA or Omni1-Quad arrays. Ungenotyped SNPs were imputed. Non-HLA additive genetic risk scores (GRS) were calculated for SLE, and for eGFR, using published GWAS weights for loci that met $p < 5x10^{-8}$. LN was confirmed by renal biopsy. Longitudinal, prospectively collected clinical and laboratory data, including serum creatinine, were extracted from lupus databases. eGFR was calculated using the CKD-EPI (≥18y), and Schwartz equations (< 18y). We tested the effect of SLE-GRS and eGFR-GRS with respect to (1) eGFR mean using linear mixed models and (2) eGFR variance through Gamma regression of squared-ordinary least squares jackknife residuals in R. Models included a time-varying indicator for eGFR taken as a child or adult.

Results: Our cohort included 567 (47%) patients with childhood-onset SLE (cSLE) and 615 (53%) adult-onset SLE (aSLE) with a total of 36,258 eGFR measures (23,926 measures (66%) during aSLE). Median follow-up time was 7.52 years [IQR: 3.92, 15.25 years] (Table). The majority were female (87%) and of European ancestry (48%). There was a median lag of 77 days [IQR: 0, 1193 days] between SLE diagnosis and first visit. Under a t-test of independence, we observed lower within-person mean eGFR ($p < 0.001$) and higher within-person eGFR variance ($p < 0.001$) in patients with LN compared to those without LN. From linear mixed models and Gamma regression, a unit increase in eGFR-GRS was associated with a 0.60 mL/min/1.73 m^2 increase in eGFR (0.60; 95% CI: [0.24, 0.96]; $p = 0.001$) and a 2% increase in eGFR variance (1.02; 95% CI: [1.02, 1.03]; $p < 0.001$). A unit increase in SLE-GRS was associated with a 1.28 mL/min/1.73 m^2 decrease in eGFR (-1.28; 95% CI: [-2.42, -0.13]; $p = 0.029$) and a 4% increase in eGFR variance (1.04 95% CI: [1.01, 1.06]; $p < 0.001$).

Conclusion: Using a large number of repeated eGFR measures taken from people with aSLE and cSLE, we observed that as expected, patients with LN had both lower mean eGFR and higher variability in eGFR, when compared to patients without LN. We demonstrated that eGFR and SLE loci are influencing (1) eGFR mean and (2) eGFR variance in SLE patients. This suggests that longitudinal eGFR measures may be more informative outcomes than binary LN categories for identifying genetics of kidney disease in SLE.

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Abstract Number: 2025

Ancestry Influences the Gene Expression Profile in Systemic Lupus Erythematosus and Contributes to Transcriptomic Heterogeneity in Lupus Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
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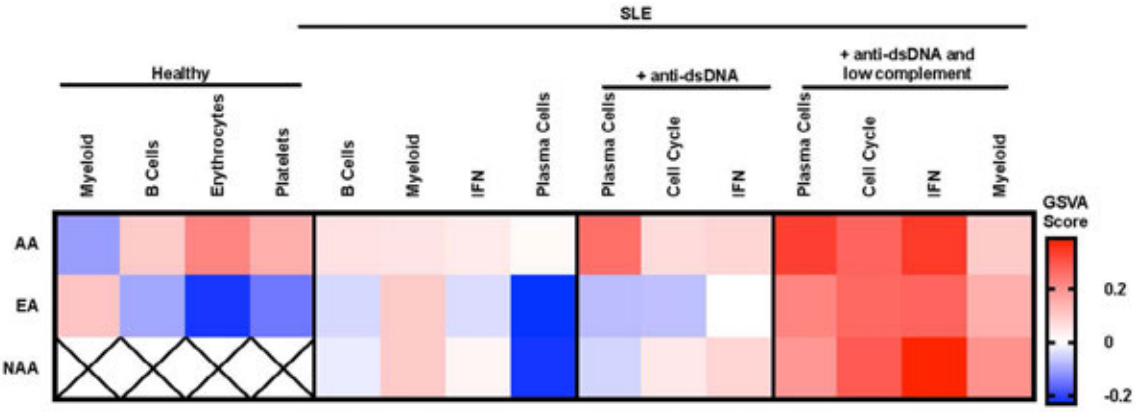

Figure 1. Gene Expression is Affected by Ancestry, SLE Autoantibodies and SOC Drugs. Average difference in GSVA enrichment scores are shown for Healthy. Average GSVA enrichment scores are shown for Lupus patients.

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease with both sex and ancestral bias. Gene expression analysis has revealed complex heterogeneity between SLE patients, making deconvolution of the data difficult and delineation of the impact of different disease drivers uncertain. We, therefore, sought to understand the individual contributions of ancestry, gender and medications to gene expression heterogeneity, as well as to determine the association of gene expression profiles with various SLE manifestations.

Methods: Bulk Differential Expression (DE) analysis and Gene Set Variation Analysis (GSVA) were carried out on 1903 SLE patients of African (AA), European (EA) and Native American (NAA) ancestry. Modules of genes defined by co-expression in patients and representing either functional or cell specific groups were used to determine the relationship between drugs, SLE manifestations and individual patient gene expression. Logistic regression analysis was used to understand the relative contribution of ancestry, drugs and SLE manifestations to gene expression signatures.

Results: Gene expression analysis between female disease-matched SLE patients of AA, EA, and NAA revealed thousands of DE transcripts between ancestries, but none within a single ancestry. AA, EA and NAA SLE patients had significantly different cellular contributions to gene expression and these differences were related to significantly different percentages of patients in each ancestry with specific signatures. GSVA showed an increase in plasma cells, B cells and T cells in the majority of AA patients and an increase in myeloid cells in most EA and NAA patients. Corticosteroids and immunosuppressives significantly changed gene expression and contributed to the disparate signatures between and within ancestries. Anti-dsDNA autoantibodies and low complement, but not other clinical features of SLE, were significantly associated with gene expression in AA, EA and NAA SLE patients. Despite the impact of medications, ancestry made a significant contribution to gene expression profiles. Notably, we found that differences between AA and EA SLE patients are similar to those between healthy people of these ancestries, and that there were fewer differences between males and females of the same ancestry, than between ancestries.

Conclusion: Combinations of different ancestries, specific medications and autoantibody production associate with gene expression profiles (Figure 1). Importantly, ancestry contributes unique features of gene expression, implying differences in the molecular basis of SLE in these populations. Understanding the contributions of the gene expression signature components may permit a better interpretation of the signatures and their relationship to disease status.

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Abstract Number: 2026

MicroRNA-27a Can Contribute to Interferon Signatures in Systemic Lupus Erythematosus via the Suppression of Tripartite Motif-containing Protein 27

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Background/Purpose: Type I interferons (IFN) contribute to antiviral innate immune responses. Upon viral infection, pattern recognition receptors trigger TANK-binding kinase 1 (TBK1) activation and lead to activation of the transcription factor IFN regulatory factor (IRF) 3 to induce type I IFN production. Because high expression of typeI IFN inducible genes, called IFN signature, is observed in systemic lupus erythematosus (SLE), the excessive IFN production has been thought to have the important role in SLE pathogenesis.

Recently, it has been reported that silica acid-binding immunoglobulin-like lectin (Siglec) 1 suppresses antiviral innate immune response by inducing TBK1 degradation by the E3 ubiquitin ligase, tripartite motif-containing protein (TRIM) 27. It has also been reported that type I IFN-induced downregulation of microRNA (miR)-27a can increase TRIM27 expression, and then inhibit the type I IFN production in antiviral innate response.

Here, we report that downregulation of TRIM27 by miR-27a can contribute to IFN signature in SLE.

Methods: Human peripheral blood mononuclear cells (PBMC) and sera were obtained from SLE patients and healthy controls (HC). All of the patients fulfilled the revised 1997 ACR Criteria for Classification of SLE. The quantitative real-

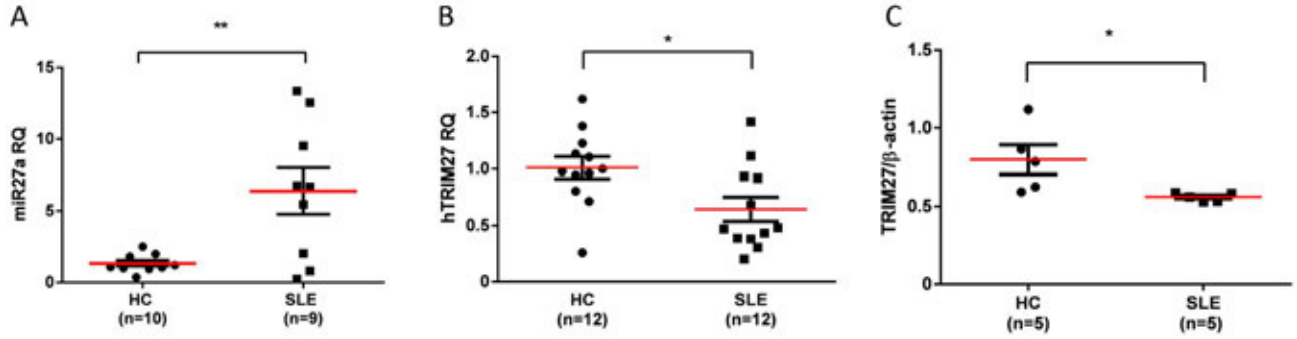

Figure 1 Increased miRNA-27a expression may induce downregulation of TRIM27 in SLE patients (A)The expression level of miR-27a in sera of SLE patients was higher than that of HC (p=0.0043). The expression levels of mRNA (B) and protein (C) of TRIM27 in PBMC of SLE patients were lower than those of HC (p=0.020, p=0.038, respectively). Data are presented as mean ± SEM. Statistically significant data (*, p< 0.05 and **, p < 0.01) by Student's t-test or two-tailed Mann-Whitney U test.

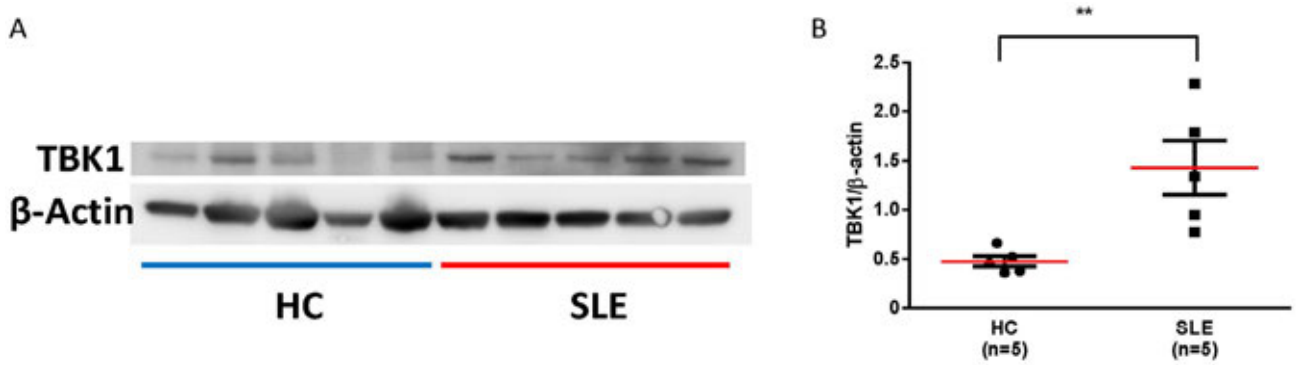

Figure 2. TBK1 protein level is higher in SLE patients. (A) Western blot analysis was performed with extracts from PBMC of SLE patients and HC using anti-TBK1 Ab. β-actin was used as a loading control. (B) TBK1 protein level was higher in SLE patients as compared to HC (n=5 in each groups). Data are presented as mean ± SEM. Statistically significant data (**, $p < 0.01$) by Student's t-test.

time PCR (qPCR) and western blotting were performed to assess the mRNA and protein expression levels of TRIM27 and TBK1, respectively. Serum miR-27a levels were investigated by qPCR. Statistical analysis was performed by using the GraphPad Prism. Data are presented as mean ± SEM. We used a Student's *t*-test or the two-tailed Mann-Whitney *U* test. The *p*-values < 0.05 were considered statistically significant.

Results: The expression level of miR-27a in sera of SLE patients was higher than that of HC (p=0.0043; Figure 1A). The expression levels of mRNA and protein of TRIM27 in PBMC of SLE patients were lower than those of HC (p=0.020, p=0.038, respectively; Figure 1B, C). On the contrary, TBK1 protein level was higher in SLE patients as compared to HC (p=0.0079; Figure 2A, B).

Conclusion: In SLE patients, increased miR-27a expression may induce downregulation of TRIM27, which leads to reduction of the TBK1 ubiquitination and degradation. The results suggest that miR-27a can contribute to interferon signatures in SLE via the suppression of TRIM27.

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Abstract Number: 2027

Dysregulation of Granulopoiesis in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
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Background/Purpose: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by autoantibody production and periods of elevated disease activity. Recent studies indicate that along with dysfunctional adaptive immune responses, neutrophils are also important in disease pathogenesis. SLE patients have higher numbers of low-density granulocytes (LDGs) in peripheral blood that express neutrophil markers and are hyper-

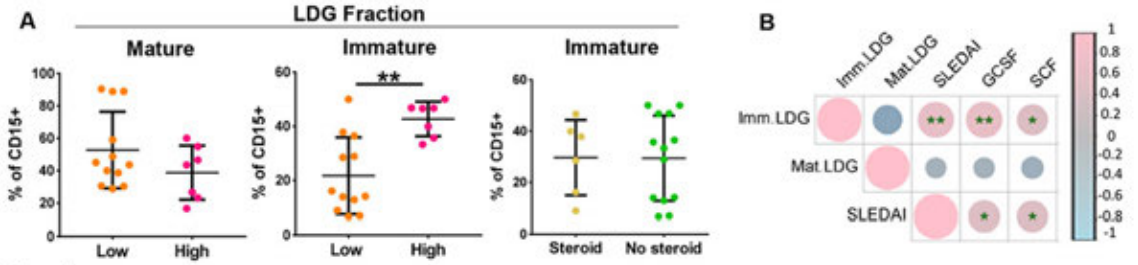

Figure 1

A. LDG fraction of SLE patients with elevated disease activity has higher frequencies of immature cells. PBMCs from SLE patients were enriched by density gradient centrifugation. Cells were stained, acquired on BD LSRII and analyzed by FlowJo. Low=SLEDAI<4 (*n=12*), High=SLEDAI>4 (*n=7*). **p<0.01* by Mann-Whitney. Immature neutrophil frequencies were independent of steroid use.

B. Immature LDGs correlate with SLEDAI, SCF, and GCSF. Spearman correlation coefficients were calculated and correlogram generated in R. The color represents direction and size of circles represents strength of association. **p<0.05, **p<0.01.* Imm.LDG=immature neutrophil in LDG fraction, Mat.LDG=mature neutrophil in LDG fraction. Pink=positive correlation, Blue=negative correlation.

responsive to external stimuli. LDGs also have an enhanced ability to form neutrophil extracellular traps (NETs), and are suggested to be pathogenic in lupus. This study was carried out to determine whether the LDG fraction consists of immature cells and whether these cells differ with disease activity.

Methods: Peripheral blood mononuclear cells from 19 SLE patients with varying disease activity and 11 controls were enriched by density gradient centrifugation. Neutrophils were enriched by dextran sedimentation and density gradient centrifugation. LDG numbers were determined by flow cytometry. Plasma cytokines were measured by xMAP assays. Neutrophils were cultured for 3h and cytokines in supernatants were measured by xMAP assays. Levels of microRNA (miRNA) were determined by quantitative PCRs. SLE disease activity indices (SLEDAI) were obtained from medical records. Immature and mature neutrophil frequencies in bone marrow from 9-11 months old B6.NZM/Sle1/Sle2/Sle3 (Sle123) or C57BL/6J (B6) mice were determined by flow cytometry.

Results: SLE patients with elevated disease activity had significantly higher frequency of immature LDGs as determined by surface marker expression (p=0.0053) (Figure 1A). The frequencies of immature LDGs correlated with the SLE disease activity index (SLEDAI) and plasma G-CSF (Spearman r=0.651, *p*=0.0025, r=0.663, *p*=0.002, respectively) (Figure 1B). Compared to their wild type B6 counterpart, the spontaneous lupus mice Sle123 showed increased immature neutrophils (p=0.0079), similar to our data from lupus patients. SLE neutrophils spontaneously secreted higher levels of BAFF (p=0.043) and IL-21 (p=0.0394), but not IL-8 or MMP9. SLE neutrophils expressed significantly different levels of select miRNA compared to healthy neutrophils, as was previously reported for neutrophils generated by G-CSF induced emergency granulopoiesis.

Conclusion: Our data suggest that SLE patients may have dysregulated development of myeloid cells in the bone marrow due to the cytokine milieu present during elevated disease activity. The functional responses of these newly generated neutrophils may differ due to differences in the bone marrow transit time. The dysregulation of granulopoiesis therefore may generate neutrophils that further exacerbate autoimmune response.

Disclosure: N. Jog, None; **T. Aberle**, None; **C. Arriens**, AstraZeneca, 5, BMS, 2, 5, Exagen, 2, GSK, 2, 5; **S. Galluccci**, None; **J. James**, Abbvie, 5, Janssen, 5, Progentec, 2, Progentec Diagnostics, Inc., 2, Xencor, 2, Xencor, Inc., 2.

Abstract Number: 2028

Inhibited Expression of Hematopoietic Progenitor Kinase 1 in Tfh Cells Contributes to Autoimmunity in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: T follicular helper cells (Tfh cells) are a newly discovered subset of $CD4^+$ T cells, which play a mainly role in inducing B cells to produce antibody. Tfh cells are over activated in systemic lupus erythematosus (SLE) patients, consequently bring about immune damages. Hematopoietic progenitor kinase 1 (HPK1) can inhibit T cell-mediated immune responses, but the role that HPK1 plays in Tfh cells from SLE patients remain elusive. The aim of this study is to investigate whether HPK1 plays roles in SLE Tfh cells.

Methods: Naïve $CD4^+$ T cells and B cells were isolated from healthy controls and SLE patients. Then Naïve $CD4^+$ T cells were induced to differentiate into Tfh cells by stimulating with anti-CD3 antibody, anti-CD28 antibody, IL-6, IL-12, IL-21, and TGF-β. HPK1 mRNA and protein levels in Tfh cells were determined by real-time RT-PCR and western blotting. Detection of IL-21, CXCL13, IFNγ, IL-17A, IgM, IgG1, IgG2a, IgG2b and IgG3 levels were performed by ELISA. Tfh cells proliferations were analyzed with MTT assay.

Results: We identified HPK1 mRNA and protein levels were significantly decreased in Tfh cells from patients with SLE. Moreover, HPK1 mRNA levels were found to negatively correlated with SLE disease activity as measured by SLE Disease Activity Index (SLEDAI). Down-regulation of HPK1 in healthy Tfh cells significantly accelerated Tfh cells proliferation and productions of IL-21, CXCL13, IFNγ, IgG1, IgG2a, IgG2b, and IgG3. There were no marked changes in IL-17A and IgM amounts. Consistent with these findings, overexpressing HPK1 in SLE Tfh cells caused significant decrease in Tfh cells proliferation and productions of IL-21, CXCL13, IFNγ, IgG1, IgG2a, IgG2b, and IgG3. And there were no significant alters in IL-17A and IgM levels.

Conclusion: Our results show for the first time that inhibited expression of HPK1 in SLE Tfh cells contributes to Tfh cells overactivation and B cells overstimulation, which lead to the development of SLE at last.

Disclosure: Q. Zhang, None; **H. Zhang**, None.

Abstract Number: 2029

Aberrant H3K9me3 Modification in Promoter Region Up-regulates cAMP Response Element Modulator Alpha in Systemic Lupus Erythematosus

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SESSION INFORMATION
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Background/Purpose: In recent years, accumulating evidences have demonstrated that increased cAMP response element modulator α (CREMα) which can inhibit IL-2 and induce IL-17A in $CD4^+$ T cells plays an essential role in the pathogenesis of systemic lupus erythematosus (SLE). However, the molecular mechanisms that result in CREMα over expression remain poorly understood. The aim of this study is to investigate the mechanisms that regulate CREMα expression in SLE.

Methods: $CD4^+$ T cells were isolated from healthy controls and SLE patients. Histone H3 lysine 9 trimethylation (H3K9me3, a hallmark associated with transcription inhibition) enrichments at various gene promoters in $CD4^+$ T cells from 5 healthy controls and 5 SLE patients were analyzed by chromatin immunoprecipitation (ChIP) microarray. Amounts of H3K9me3, H3K9 methyltransferases SUV39H1 and SUV39H2 within the CREMα promoter were subsequently assessed by ChIP and real-time PCR in $CD4^+$ T cells from 15 healthy controls and 15 SLE patients. And CREMα mRNA levels were determined by real-time RT-PCR.

Results: From the ChIP microarray data, we identified sharply decreased H3K9me3 enrichment at the CREMα promoter of SLE $CD4^+$ T cells compared to healthy controls. Then by ChIP and real-time PCR experiments, we confirmed this finding. In addition, H3K9me3 enrichment at the promoter was negatively correlated with CREMα mRNA level in SLE $CD4^+$ T cells. Moreover, a markedly decrease was observed in SUV39H1 binding, but no significant change in SUV39H2 enrichment at the CREMα promoter region in SLE $CD4^+$ T cells. We also proved SUV39H1 binding was positively correlated with H3K9me3 amount at the CREMα promoter, and negatively correlated with CREMα mRNA level in $CD4^+$ T cells from SLE patients.

Conclusion: Our findings suggest for the first time that decreased SUV39H1 binding down-regulates H3K9me3 enrichment at the CREMα promoter, which induces CREMα overexpression in SLE $CD4^+$ T cells, and results in the development of SLE at last.

Disclosure: H. Zhang, None; **Q. Zhang**, None.

Abstract Number: 2030

Staphylococcus Aureus Colonization Is Increased on Lupus Skin Lesions and Is Promoted by Interferon-Mediated Barrier Disruption

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Background/Purpose: Cutaneous inflammation is recurrent in systemic lupus erythematosus (SLE) and is often triggered by exposure to ultraviolet B (UVB) light. Type I interferons (IFN) play a critical role in SLE skin inflammation and are increased in non-lesional SLE keratinocytes. Mechanisms that drive cutaneous inflammation in SLE are not well-defined and may involve microbial dysbiosis, an underexplored source of cutaneous IFNs. *Staphylococcus aureus*, known to induce IFN production, could play a role in cutaneous inflammation in SLE. This study thus evaluated the colonization of lupus skin by *S. aureus* and the extent to which IFNs drive increased colonization rates by S. aureus.

Methods: Patients with SLE who fulfilled ≥4 ACR criteria for diagnosis were recruited from the Michigan Lupus Cohort. Nares, chest, and lupus related skin lesions were swabbed and analyzed for *S. aureus* colonization. To define the impact of IFNs on *S. aureus* colonization, we examined the effect of type I and type II IFNs (1000U/ml) on barrier gene expression in N/TERTs (a keratinocyte cell line) by real time quantitative PCR (RT-qPCR). Adhesion and invasion of log-phase *S. aureus* was assessed using confluent N/TERTs treated with IFNα or IFNγ. Adhered *S. aureus* were quantified by counting colony forming units (CFUs). Cells were treated with gentamicin (200 μg/ml) for invasion assays prior to CFU quantification. Keratinocytes were exposed to baricitinib (10 μg/ml) prior to IFN exposure to block IFN signaling. Primary keratinocytes were isolated from non-lesional skin of SLE patients and matched healthy adults and utilized for RNA-seq analysis as well as adhesion and invasion assays.

Results: We show here that active lupus lesions are highly colonized (~50%) by *S. aureus*. Microarray data from SLE lesional skin revealed lower expression of various cutaneous barrier genes such as filaggrin (FLG). IFN-exposed keratinocytes demonstrated lower expression of barrier related genes such as FLG, loricrin and involucrin. This repression of barrier genes was also seen in primary SLE keratinocytes without additional IFN treatment via RNA-seq. We next examined the role of IFN exposure on *S. aureus* colonization by adhesion and invasion assays. *S. aureus* adherence was significantly higher in keratinocytes that were exposed to IFNα but not IFNγ. RT-qPCR analysis showed higher expression of α-integrin in IFNα but not IFNγ exposed keratinocytes, indicating a possible mechanism for higher *S. aureus* adherence. In addition, IFNγ exposure appeared to inhibit invasion of *S. aureus* into keratinocytes. Confirming a role for IFNs in primary cells, *S. aureus* adhered better to SLE keratinocytes than healthy control keratinocytes. Exposure to baricitinib reduced IFNα-promoted *S. aureus* adherence, thus confirming specificity of the IFN activity.

Conclusion: SLE lesional skin is highly colonized by *S. aureus* and exhibits lower barrier gene expression indicating barrier compromise. IFN exposure inhibits barrier gene expression and IFNα promotes *S. aureus* adhesion. Together, these data suggest that chronic exposure to IFNs induces barrier disruption that allows for higher *S. aureus* colonization in SLE skin.

Disclosure: S. Sirobhushanam, None; **N. Parsa**, None; **T. Reed**, None; **C. Berthier**, None; **M. Sarkar**, None; **G. Hile**, None; **L. Tsoi**, None; **A. Horswill**, None; **J. Gudjonsson**, AbbVie, 2, Genentech, 2, genentech, 2, MiRagen, 5, Novartis, 5, Sun Pharma, 2, SunPharma, 2; **J. Kahlenberg**, AstraZeneca, 5, Bristol Myers Squibb, 5, Eli Lilly, 5.

Abstract Number: 2031

Interferon Alpha Promotes Caspase-Dependent Apoptosis Independently of Reactive Oxygen Species in Ultraviolet B-Exposed Keratinocytes

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by increased sensitivity to ultraviolet radiation (UVR). UVR can trigger cutaneous and systemic disease fares, yet mechanisms driving these responses are not well characterized. Type I interferons (IFNs), which have been previously implicated in driving apoptosis of cancer cells, are expressed at higher levels at baseline in non-lesional skin of SLE patients and drive hyperinflammatory responses after UVR. In addition, these type I IFNs promote increased death of SLE keratinocytes after UVR; however, the manner in which they regulate cell death after UVR is currently unknown. This study explores the cell death pathways activated in keratinocytes by type I IFNs and UVR.

Methods: Immortalized human keratinocytes (N/TERTs) were treated overnight with IFNα (0-1000 U/ml) prior to UVB exposure (0-50 mJ/cm^2). Reactive oxygen species (ROS) production was measured using the cell-permeable oxidative stress indicator CM-H_2DCFDA and fluorescence was measured 5 minutes post UVB exposure. Annexin V (AV) and propidium iodide (PI) staining was performed 4 hours post UVB exposure and cells were analyzed by flow cytometry. Cells were pretreated with apoptosis, necroptosis, and pyroptosis inhibitors to examine activated death pathways. Caspase-3 cleavage was measured by flow cytometry.

Results: Intracellular ROS were significantly increased by 5 minutes after UVB exposure. Surprisingly, priming with IFNα resulted in a dose-dependent decrease in ROS production. IFNα priming prior to UVB exposure also resulted in a significant increase in the percentage of AV^+PI^- cells, indicative of early apoptosis. In addition, IFNα treatment promoted apoptosis at a lower dose of UVB (20 mJ/cm^2). IFNα treatment prior to UVB exposure resulted in a significantly higher percentage of both cleaved-caspase-3^+ and AV^+PI^-, but not AV^+PI^+, cells compared to treatment with UVB alone. Pre-treatment with Z-VAD-FMK (pan-caspase inhibitor) or Z-IETD-FMK (caspase-8 inhibitor) significantly reduced AV^+PI^- cells following IFNα and UVB treatment while treatment with Z-LEHD-FMK (caspase-9 inhibitor) did not, suggesting enhanced activation of the extrinsic apoptosis pathway. Further, use of Necrostatin-1 (RIPK1 inhibitor) or AC-YVAD-CMK (caspase-1 inhibitor) showed no effect on death at 4 hours post UVB exposure in the presence of IFNα suggesting that enhanced death of type I IFN treated cells after UVB likely does not involve necroptosis or pyroptosis.

Conclusion: Treatment of keratinocytes with IFNα results in increased sensitivity to UVB-mediated cell death, which takes the primary form of caspase-8 driven apoptosis, independently of ROS. It is well documented that SLE skin is rich in type I IFNs and that high circulating IFNs are a feature of the disease. Together, these data suggest that pho-

tosensitive responses exhibited by lupus patients are likely due to type I IFN priming of keratinocytes that sensitizes the cells to undergo increased apoptosis after exposure to minimal amounts of UVB. Continued investigation into the mechanism by which IFN drives UVR-mediated cell death will be crucial for developing novel preventative strategies for photosensitivity.

Disclosure: S. Estadt, None; **J. Kahlenberg**, AstraZeneca, 5, Bristol Myers Squibb, 5, Eli Lilly, 5.

Abstract Number: 2032

Enhanced IFN a Production and STING Pathway in Monocytes in Systemic Lupus Erythematosus Is Suppressed by the Inhibition of mTOR Activation

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SESSION INFORMATION
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Background/Purpose: Interferona (IFNa) is increased and plays an important role in the pathogenesis of systemic lupus erythematosus (SLE). Overexpression of type I IFN regulated genes has been reported in patients with SLE. Plasmacytoid dendritic cells (pDCs) are thought as the main producer of IFNa upon activation of TLR pathway. However, IFNa producers by the stimulation of cyclic GMP-AMP synthase (cGAS) and stimulator of interferon genes (STING) in SLE still remains unknown. In this study, we investigated the IFNa producing capacity of myeloid cells under stimulation of cGAS-STING pathway.

Methods: Peripheral blood mononuclear cells from patients with SLE and healthy controls were stimulated with 2'3'c-GAMP, a stimulator of cGAS-STING pathway, or a TLR-7 agonist, imiquimod, and IFNa-producing capacity of myeloid cells was examined by intracellular cytokine staining and flow cytometry. The expression and co-localization of STING with TBK1 were examined by intracellular staining and flow cytometry or confocal microscopy. The effect of *in vitro* IFNa exposure on IFNa production and STING expression was examined. Monocytes were treated with rapamycin *in vitro*, and IFNa production and the expression of STING, pTBK1, IRF3 were examined.

Results: As previously reported, IFNa was produced from only pDCs upon activation of TLR7 pathway. However, IFNa was produced from monocytes, conventional dendritic cells (cDCs) and pDCs upon activation of cGAS-STING pathway. The frequency of IFNa-producing monocytes stimulated with 2'3'c-GAMP positively correlated with disease activity of SLE. The expression of STING and its co-localization with TBK1 were increased in lupus monocytes. Prior exposure to IFNa enhanced the IFNa-producing capacity of monocytes. Inhibition of mechanistic target of rapamycin (mTOR) pathway by using rapamycin suppressed IFNa production from monocytes and downregulated the enhanced expression of STING pathway.

Conclusion: We demonstrate that lupus monocytes are potent to produce IFNa in association with the augmentation of cGAS-STING pathway. Production of IFNa and enhancement of cGAS-STING pathway was suppressed by the

inhibition of mTOR pathway. These findings indicate that enhanced IFNa from lupus monocytes owing to augmented STING pathway is associated with the pathogenesis of SLE. The blockade of the cGAS-STING pathway may serve as a promising therapeutic target for SLE.

Disclosure: G. Murayama, None; **A. Chiba**, None; **A. Makiyama**, None; **T. Kuga**, None; **K. Yamaji**, ASAHI KASEI PHARMA, 2, Astellas pharma, 2, 8, bristol myers, 8, Chugai Pharma, 2, Janssen Pharma, 8, Mitsubishi-Tanabe Pharma, 2, 8, Sanofi Pharma, 8, Takeda Pharma, 2; **N. Tamura**, AbbVie GK, 8, AbbVie pharma, 8, ASAHI KASEI MEDICAL, 2, ASAHI KASEI PHARMA, 2, astellas pharma, 2, 8, Astellas Pharma Inc., 2, 8, AYUMI PHARMA, 2, AYUMI Pharmaceutical Corporation, 2, bristol myers, 8, Bristol-Myers Squibb, 8, Chugai Phamaceutical Co. Ltd., 2, Chugai Pharma, 2, Eisai Co., Ltd., 2, Eisai Pharama, 2, Janssen Pharma, 8, Janssen Pharmaceutical K.K., 8, Mitsubishi Tanabe Pharma Corporation, 2, 8, Mitsubishi-Tanabe Pharma, 2, 8, Sanofi K.K., 8, Sanofi Pharma, 8, Takeda Pharma, 2, Takeda Pharmaceutical Company Ltd., 2; **S. Miyake**, Bristol myers squibb, 2, Bristol-Myers Squibb, 2, Pfizer, 2, Pfizer Japan Inc., 2, Taiho pharmaceutical, 8, TAIHO PHARMACEUTICAL CO., LTD., 8.

Abstract Number: 2033

IRAK4 Inhibition Suppresses TLR7, TLR9, and SLE Serum-Induced IFNA Production in Primary Human Plasmacytoid Dendritic Cells

Angie Hammond,[1] Sean Parghi,[1] Nathan Wright,[1] Ethan Grant,[1] James Taylor,[1] and Matthew Warr[1], [1]Gilead Sciences, Inc., Foster City, CA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A hallmark of lupus is the presence of antinuclear autoantibodies, including those against RNA-protein complexes and double-stranded DNA (dsDNA).[1,2] FcγR-mediated internalization of these nucleic acid:autoantibody immune complexes results in endosomal activation of TLR7 and TLR9, respectively, and the production of IFNα from plasmacytoid dendritic cells (pDC).[3,4] The importance of this pathway is underscored by the majority of systemic lupus erythematosus (SLE) patients having a peripheral interferon-stimulated gene (ISG) signature.[5] IRAK4 is a serine/threonine kinase at the top of the signaling cascade downstream of TLRs, including TLR7 and TLR9. As such, inhibition of IRAK4 represents a promising therapeutic target for lupus. The objective of this study is to investigate the effect of a highly selective IRAK4 inhibitor on IFNα production from pDCs stimulated with TLR7 and TLR9 agonists, SLE serum, and nucleic acid:autoantibody immune complexes.

Methods: Primary human pDCs were precultured with an IRAK4 inhibitor followed by stimulation for 24 hours. Stimulation agents included TLR7 and TLR9 agonists, human SLE serum, and nucleic acid:autoantibody immune complexes. Culture supernatants were then assessed for secretion of IFNα by MSD.

Results: TLR7 and TLR9 stimulation of pDCs resulted in the secretion of IFNα from pDCs as expected. Treatment with an IRAK4 inhibitor resulted in dose-dependent inhibition of TLR7- and TLR9-induced IFNα with high potency. Human SLE serum was tested to extend findings to physiological SLE-relevant stimuli. Several SLE serum samples, which had positive ELISA titers to the antinuclear antibodies, stimulated production of IFNα in pDCs after 24 hours in culture. No induction of IFNα was observed with healthy volunteer serum samples. Treatment with an IRAK4 inhibitor effectively blocked secretion of IFNα from SLE serum-stimulated pDCs in a dose-dependent manner. Additional antigen (either RNP or dsDNA) was added to SLE samples that yielded titers for autoantibodies but failed to elicit IFNα

production. Addition of RNP or dsDNA to anti–RNP and anti–dsDNA-positive SLE sera induced strong IFNα production, and this response was blocked with IRAK4 inhibition. No induction was seen with SLE serum that was negative for both anti–RNP and anti–dsDNA.

Conclusion: This work demonstrates the effects of IRAK4 inhibition on IFNα production in primary pDCs downstream of disease-relevant stimuli and highlights the potential for IRAK4 inhibition as a promising treatment for lupus.

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5. Yao Y, et al. Hum Genomics Proteomics. 2009. 2009(374312):1-16.

Disclosure: A. Hammond, Gilead Sciences, Inc., 1, 3, 4; **S. Parghi**, Gilead Sciences, Inc., 3, 4; **N. Wright**, Gilead Sciences, Inc., 1, 3; **E. Grant**, Gilead Sciences, Inc., 3, 4; **J. Taylor**, Gilead Sciences, Inc., 3, 4; **M. Warr**, Gilead Sciences, Inc., 1, 3, 4.

Abstract Number: 2034

Identification of IL-17$^+$ and IL-10$^+$ TCR$\alpha\beta^+$ CD4$^-$ CD8$^-$ Double Negative (DN) T Cell Subsets in Lupus-prone Mice and Patients with SLE and Their Significance in Predicting Renal Involvement

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: We have previously shown that DN T cells are expanded in both lupus-prone mice and patients with SLE and we have demonstrated that this population is an essential component of the immunopathogenesis of the disease. It still remains unknown whether the DN T cell pool consists of functionally heterogeneous subpopulations. In this study we ask whether DN T cells comprise distinct functional subsets.

Methods: Flow cytometry analysis was applied for the expression of cytokines and T cell receptor (TCR) repertoire etc. IL-17-GFP B6 mice were crossed to MPL/lpr mice for 8 generations to generate IL-17-GFP MPL/lpr mice which were used to track IL-17$^+$ DN T cells *in vivo* and sort IL-17$^+$ DN T cells *ex vivo*. Cytokine capture assay was applied for *ex vivo* isolation of either IL-17$^+$ or IL-10$^+$ DN T cells from MPL/lpr mice and SLE patients. The mTOR pathway was assessed using RT2 profiler PCR array and verified by RT-PCR.

Results: Two distinct DN T populations were identified in both mice and humans based on the expression of two cytokines, IL-17 and IL-10. As expected, IL-17+ DN T cells were significantly increased in aging MRL/lpr mice (20 wks old) compared to either age matched control MRL/mpj mice or young MRL/lpr mice (12 wks old), a finding which is

consistent with our previous report that DN T cells contribute to lupus pathogenesis by producing IL-17. Interestingly, the numbers of IL-10+ DN T cells in aging (20 wks old) mice were reduced compared to young (12 wks old) MRL/lpr mice. Flow cytometry analysis revealed the different TCR V beta usage of V β 5, 6, 8.1/8.2, 12 in IL-17+ DN T cells while V β 14 and 15 in IL-10+ DN T cells. Consistently, increase of IL-17+ DN T cells (7.9 ± 0.7% vs 4.6 ± 0.6%, p=0.01) and reduction of IL-10+ DN T cells (1.5 ± 0.24% vs 4.6 ± 0.6%, P< 0.001) were observed in the peripheral blood from the subjects with SLE compared to healthy subjects. Interestingly, the ratio of IL17+/IL10+ DN T cells displayed a significant positive association with SLEDAI (p = 0.02) but negative association with C3 level (p = 0.01). Additionally, the ratio is found remarkedly higher in lupus patients with proteinuria (4.4 ± 1.2% vs 2.4± 0.4% p= 0.03) and positive anti- dsDNA (3.3± 0.3% vs 1.79 ± 0.2% p= 0.02). Of note, IL17+ DN Tc actively express most mTOR pathway associated genes compared to IL10+ DN Tc.

Conclusion: We present evidence that two distinct subsets exist within the DN T cell population in lupus prone mice and patients with SLE. The ratio of IL-$17^+/10^+$ DN T cells increases as the disease progresses in MRL/lpr mice, in lupus patients with more severe disease and renal involvement. The two subsets appear to utilize different TCR repertoire and metabolic enzyme patterns. We demonstrate that the ratio between the two subsets represents a valid disease biomarker and particularly of kidney involvement.

Disclosure: Y. Li, None; **H. Li**, None; **S. Yu**, None; **V. Kyttaris**, exagen diagnostics, 2, Exagen Diagnostics, 2, GSK, 5, gsk, 5, horizon pharma, 5, Horizon Pharma, 5; **G. Tsokos**, Janssen Research & Development, LLC, 2.

Abstract Number: 2035

Systemic Lupus Erythematosus (SLE) Is Caused by Expanded DOCK8-Positive Autoantibody-Inducing CD4 T (*ai*CD4 T) Cell

Shunichi Shiozawa,[1] Ken Tsumiyama,[1] Yumi Miyazaki,[2] Keiichi Sakurai,[3] Takahiko Horiuchi,[4] Motohiro Oribe,[5] Takashi Yamane,[6] Hidetoshi Kagawa,[7] and Kazuko Shiozawa[8], [1]Institute for Rheumatic Diseases, Ashiya, Japan, [2]Kyushu University Beppu Hospital, Tokyo, Japan, [3]Rheumatology and Allergology, St. Marianna University School of Medicine, Tokyo, Japan, [4]Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, Beppu, Japan, [5]Oribe Rheumatology Clinic, Oita, Japan, [6]Department of Rheumatology, Kakogawa Central City Hospital, Kakogawa, Japan, [7]Rheumatology, Red Cross Society Himeji Hospital, Himeji, Japan, [8]Rheumatic Diseases Center, Hyogo Prefectural Kakogawa Medical Center, Ashiya, Japan

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: We previously found in reproducible experiments in which the mice not prone to autoimmune disease were immunized repeatedly with antigen that overstimulation of CD4 T cells led to the development of autoantibody-inducing CD4 T cell (*ai*CD4 T cell) which had undergone TCR revision capable of inducing varieties of autoantibody and antigen-specific CTL *via* antigen cross-presentation, after which they caused SLE (Tsumiyama K et al. PLoS ONE 4(12): e8382, 2009). Here we show that the *ai*CD4 T cell is DOCK8-positive, and this DOCK8+CD4 T cell caused SLE in the mice not prone to autoimmune disease when adoptively transferred. Further, the SLE as induced in the mice was cured by anti-DOCK8 antibody treatment. The DOCK8+CD4 T cells were found to be expanded in association with patients' disease activity (SLEDAI).

Methods: The *ai*CD4 T cell was identified by transferring different CD4 T cell subsets of x12 OVA-immunized BALB/c mice into naïve mice and testing generation of autoantibodies in the recipients, where DOCK8 was identified by

extraction of membrane proteins, electrophoresis, mass spectrometry of isolated subsets. The DOCK8+CD4 T cell was then transferred into naïve mice to confirm generation of classical SLE features. The number of DOCK8+CD4 T cell was measured in the PBMC of SLE patients and evaluated with reference to clinical manifestation.

Results: Transfer of DOCK8+CD4 T cells into naïve mice induced autoantibodies including anti-dsDNA and anti-Sm antibodies and organ diseases such as WHO IV/V lupus nephritis, skin liquefaction degeneration, and splenic periarteriolar fibrosis with amyloid-like deposits known as Onion-skin lesion classical to SLE. The lesion such as pericholangitis, pneumonitis, thyroiditis, perineuritis or panniculitis was also induced. Such manifestations subsided after anti-DOCK8 Ab treatment. The DOCK8+CD4 T cell was a large lymphocyte with abundant ER and mitochondria, expressing ICOS, PD1, Ly6C and LFA1 but not CXCR5. The DOCK8+CD4 T cell produced increased amounts of IFNg, IL-4, IL-6, IL-17, IL-21 and IL-22, but not IL-2. The TCR repertoire of DOCK8+CD4 T cell was significantly deviated. In the PBMC of active patients with SLE, DOCK8+CD4 T cells were significantly increased, whereas they were negligible in inactive disease, other rheumatic diseases, or healthy control.

Conclusion: We prove the self-organized criticality theory explaining that autoimmunity, i.e., SLE, arises as a natural consequence of routine but exaggerated immune response against antigen when stimulated maximally beyond immune system's self-organized criticality, where expanded DOCK8+CD4 T cell was responsible for inducing SLE.

Disclosure: S. Shiozawa, None; **K. Tsumiyama**, None; **Y. Miyazaki**, None; **K. Sakurai**, None; **T. Horiuchi**, None; **M. Oribe**, None; **T. Yamane**, None; **H. Kagawa**, None; **K. Shiozawa**, None.

Abstract Number: 2036

Mitochondrial DNA: A Potential Trigger of Cyclic GMP-AMP Synthase Activation in Systemic Lupus Erythematosus

Jie An,[1] Bhargavi Duvvuri,[1] Xizhang Sun,[1] Lena Tanaka,[1] Christian Lood,[1] and Keith Elkon[1], [1]University of Washington, Seattle

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Approximately 70% of patients with Systemic Lupus Erythematosus (SLE) show a striking Type I Interferon (IFN-I) signature in peripheral blood. Although we have some understanding of how this signature can be generated *in vitro* (by immune complex activation of Toll-Like Receptors, TLRs), we have little understanding of mechanisms operative in SLE patients. Cyclic GMP-AMP (cGAMP) synthase (cGAS) is a cytosolic DNA sensor that is triggered by both microbial as well as self DNA and has been shown to be the most important cytosolic DNA sensor responsible for IFN-I production. Using PBMC samples from patients, we have shown that the cGAS-STING (stimulator of interferon genes) pathway is activated in ~15% of patients with SLE. In a separate study, we also reported that oxidized mitochondrial DNA (Ox-mtDNA comprising 8-hydroxydeoxyguanine or 8-OHdG) released from neutrophils undergoing NETosis stimulates IFN-I via the cGAS-STING pathway. The aim of our study was to determine the relationship between Ox-mtDNA and activation of the cGAS-STING pathway in SLE patients.

Methods: Cell-free DNA was isolated from the plasma of SLE patients (n=16) and Healthy Controls (HC, n=12) by standard procedures. Genes unique to mitochondria (COXII and MT-TL1, abbreviated MtDNA) in plasma were quantified by Real time qPCR. 8-OHdG was quantified by DNA Damage ELISA. Multiple Reaction Monitoring (MRM) by

Ultra-Performance Liquid Chromatogram coupled with tandem Mass Spectrometer (UPLC-MS/MS) was used to quantify cGAMP in peripheral blood mononuclear cells (PBMC). Disease activity was assessed using SLEDAI and defined as either low (SLEDAI< =2) or high (SLEDAI >4). Statistical analyses were performed with GraphPad Prism 7.

Results: Levels of mtDNA were increased in plasma from SLE patients compared to HC ($p< 0.01$), and related to disease activity, e.g. patients with active disease (n=8) had higher levels of mtDNA in plasma as compared to patients with low disease activity (n=8, $p< 0.05$) as well as HC ($p< 0.0001$). Further, SLE patients with active disease had higher concentrations of 8-OHdG DNA as compared to patients with low disease activity ($p< 0.05$) as well as HC ($p< 0.05$). Patients that were cGAMP+ (n=5) had higher concentrations of 8-OHdG compared to cGAMP- (n=11) SLE patients although the difference was not statistically significant. Of interest, the levels of mtDNA was significantly higher in cGAMP+ patients compared to HC ($p< 0.01$) whereas the levels of mtDNA in cGAMP- patients was not statistically different from HC ($p=0.1$).

Conclusion: SLE patients, in particular those with active disease, have elevated levels of mtDNA and 8-OHdG DNA in peripheral blood. The increased levels of mtDNA in cGAMP positive SLE plasma is consistent with a role of mtDNA in activation of the cGAS pathway in SLE patients although other ligands cannot be excluded.

Disclosure: J. An, None; **B. Duvvuri**, None; **X. Sun**, None; **L. Tanaka**, None; **C. Lood**, None; **K. Elkon**, None.

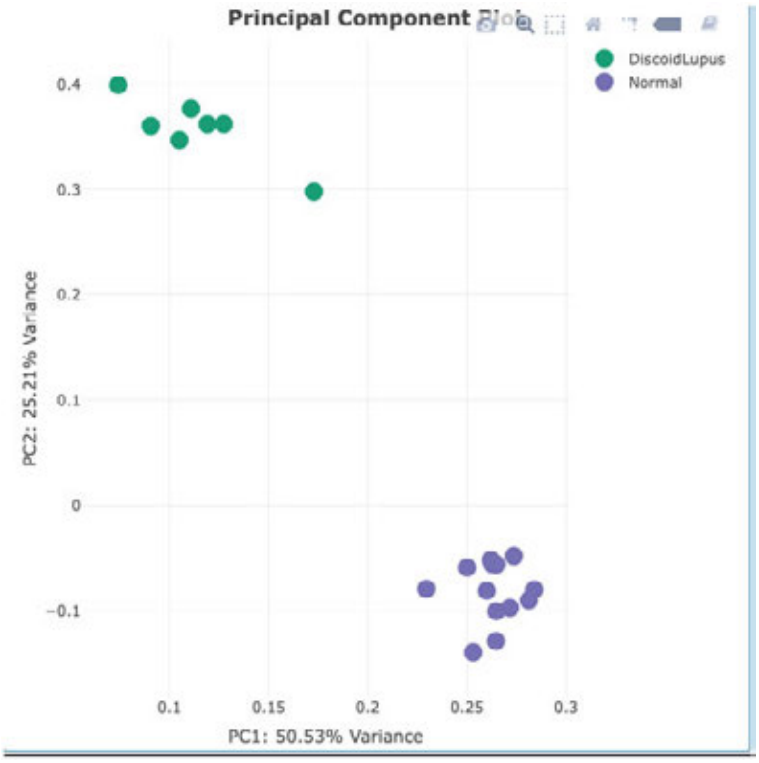
Abstract Number: 2037

Understanding Langerhans Cell ADAM17 Levels in Systemic Lupus Erythematosus: Potential Contributor to Photosensitivity

Theresa Lu,[1] Noa Schwartz,[2] Thomas Li,[2] William Shipman,[3] Dragos Dasoveanu,[3] Yong Liu,[4] Niroshana Anandasabapathy,[4] Henry Lee,[4] Ali Jabbari,[5] James Krueger,[5] Bebak Mehrara,[6] Keila Veiga,[2] Kira Minkis,[4] and David Oliver[2], [1]Hospital for Special Surgery, Weill Cornell Medicine (**Microbiology and Immunology)**, New York, [2]Hospital for Special Surgery, New York, [3]Hospital for Special Surgery; Weill Cornell Medicine, New York, [4]Weill Cornell Medicine (Dermatology), New York, [5]Rockefeller University, New York, [6]Memorial Sloan Kettering Cancer Center, New York

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Photosensitivity resulting in inflammatory skin lesions is a hallmark of cutaneous lupus. Lesions can be disfiguring and have a negative impact on patients' quality of life. Understanding photosensitivity is critical to developing better treatment. Prior research by our lab showed that ADAM17, a metalloprotease found on Langerhans cells (LCs), is activated by ultraviolet radiation (UVR) and is critical for limiting UVR-induced keratinocyte apoptosis and skin inflammation through cleavage and activation of epidermal growth factor receptor (EGFR) ligands. Two photosensitive lupus models showed reduced LC ADAM17 expression with evidence for dysfunction in human lupus, suggesting that photosensitivity is at least in part due to dysfunctional LCs. We propose a cross-sectional study to evaluate the hypothesis that LC ADAM17 expression and activity are reduced in the epidermis of lupus patients, contributing to photosensitivity. Our secondary hypothesis addresses whether reduced ADAM17 expression and increased photosensitivity is associated with lupus disease activity and severity. As part of our secondary hypothesis, we will correlate reduced ADAM17 levels with increased type I interferon (IFN) in lupus.

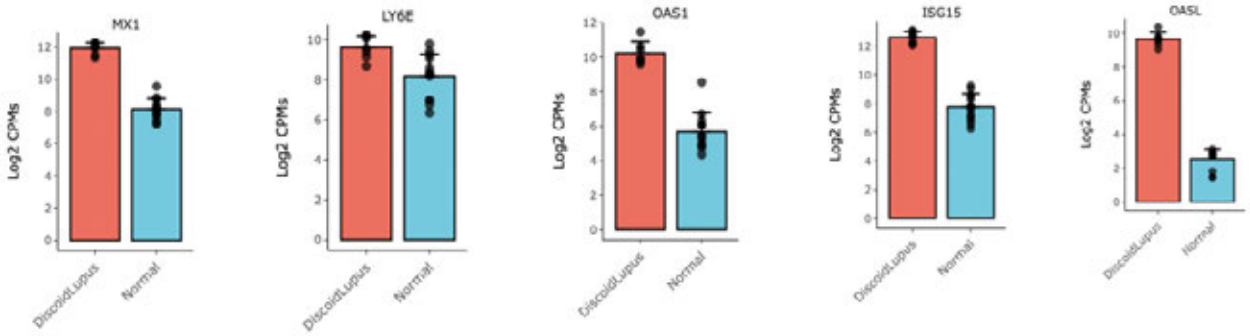


Principal Component Analysis comparing non lesional skin from discoid lupus patients (n=7) and controls (n=13)

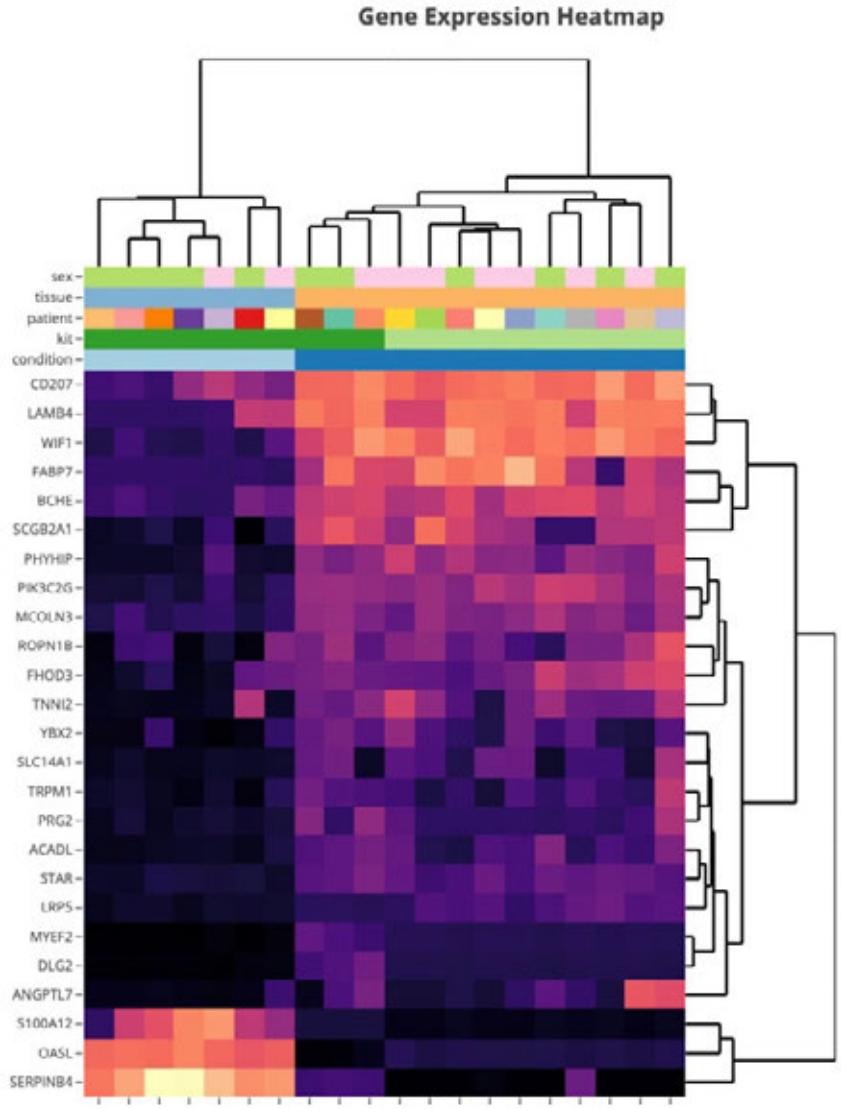
Methods: Transcriptomics of non-lesional skin from discoid lupus (DLE) and healthy controls were compared using microarray. Data was gathered from unpublished data from Krueger et al (2014) looking at immune related pathways present in DLE lesions compared to psoriasis and healthy skin. This study showed an enrichment of IFN gamma associated genes in DLE. We plan to collect punch biopsies of non-lesional, non-sun exposed skin from 10 patients who meet ACR/SLICC criteria for lupus nephritis as well as 5 healthy controls, at a single visit. We will perform flow cytometry on LCs from these biopsies to assess ADAM17 expression and activity. We will collect the SLE Disease Activity Index (SLEDAI) and will evaluate the correlation between ADAM17 activity with disease activity. Lastly, we will perform RNA sequencing to evaluate the IFN signature and correlate IFN expression with ADAM17 levels.

Results: Principal component analysis of microarray results demonstrated the variance between non lesional DLE skin and controls (Fig 1). Expression of IFN related genes were found to be elevated in non-lesional skin versus controls (Fig 2). Genes found to be highly expressed in non-lesional DLE skin included S100A12 and OASL(Fig 3). These results suggest an elevated IFN signature and inflammatory markers in non-lesional skin of DLE patients. We also demonstrate we can successfully assay for LC ADAM17 levels by 13 parameter flow cytometric analysis of human skin biopsies, and preliminary results from analysis of SLE patients are expected in the next several months.

Conclusion: Microarray results suggest an elevated IFN signature in non-lesional skin of DLE patients. If we find ADAM17 expression is reduced in non-lesional skin of SLE nephritis patients in comparison to controls, this would support a role of ADAM17 and perhaps type I IFN in SLE photosensitivity. These findings could lead to targeting of ADAM17 and potentially of type I IFN for treating the photosensitive rash seen in patients with lupus.



Expression of Interferon related genes in non-lesional skin from discoid lupus patients versus controls via microarray



Gene expression heat map showing elevated levels of S100A12, OASL and SerpinB4 in the skin of discoid lupus patients (N=7).

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Abstract Number: 2038

Antibodies to Malondialdehyde-acetaldehyde (MAA) Protein Adduct as a Biomarker for Cardiovascular Manifestations in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by devastating end-organ manifestations. Cardiovascular disease (CVD) is a leading cause for premature death in SLE patients across different ethnicities. While the traditional Framingham risk factors likely contribute to CVD in SLE, they cannot fully account for the highly increased risk of CVD in SLE. Malondialdehyde-acetaldehyde (MAA) protein adduct (a byproduct of oxidative stress) and antibodies to MAA have been suggested to mediate early inflammation in atherosclerotic disease. The purpose of this study is to determine whether SLE patients develop anti-MAA antibodies and whether anti-MAA antibodies identify SLE patients with cardiovascular manifestations.

Methods: 201 SLE patients who fulfilled the 1997 revised American College of Rheumatology criteria for the classification of SLE and 205 non-diseased healthy controls (matched in age, sex, and ethnicity) were recruited from the Dominican Republic for the study. Enzyme-linked immunosorbent assay (ELISA) was performed to determine the serum levels of anti-MAA IgG antibodies. Data were analyzed using Mann Whitney test. A p value of < 0.05 was considered significant.

Results: The mean anti-MAA IgG levels in SLE patients was 0.13 (in optical density units; SD 0.27, 95% CI 0.09-0.17), which is significantly higher than that in healthy controls (mean: 0.06; SD 0.07, 95% CI 0.05-0.07; p=0.041). SLE patients with pericarditis or myocarditis have higher levels of anti-MAA IgG antibodies than SLE patients without pericarditis or myocarditis (mean: 0.24 versus 0.07; p=0.018).Â SLE patients with vasculitis have significantly higher levels of anti-MAA IgG antibodies than SLE patients without vasculitis (mean: 0.22 versus 0.08; p=0.019).

Conclusion: SLE patients with CVD (such as pericarditis, myocarditis, or vasculitis) have significantly higher anti-MAA IgG antibodies than SLE patients without CVD. These results suggest that anti-MAA antibodies may be a biomarker for CVD in SLE. Future studies will determine if MAA and/or anti-MAA antibodies play a role in the pathogenesis of CVD in SLE.

Disclosure: Y. Yu, None; **M. Hearth-Holmes**, None; **T. Wang**, None; **P. Lopez**, None; **C. Tineo**, None; **G. Paulino**, None; **M. Duryee**, None; **G. Thiele**, None; **T. Mikuls**, BMS, 2, Horizon, 2; **E. Loyo**, None; **K. Su**, None.

Abstract Number: 2039

High Prevalence and Disease Correlation of Autoantibodies Against p40 Encoded by Long Interspersed Nuclear Elements (LINE-1) in SLE

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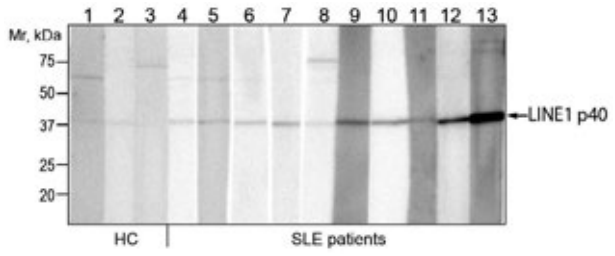
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

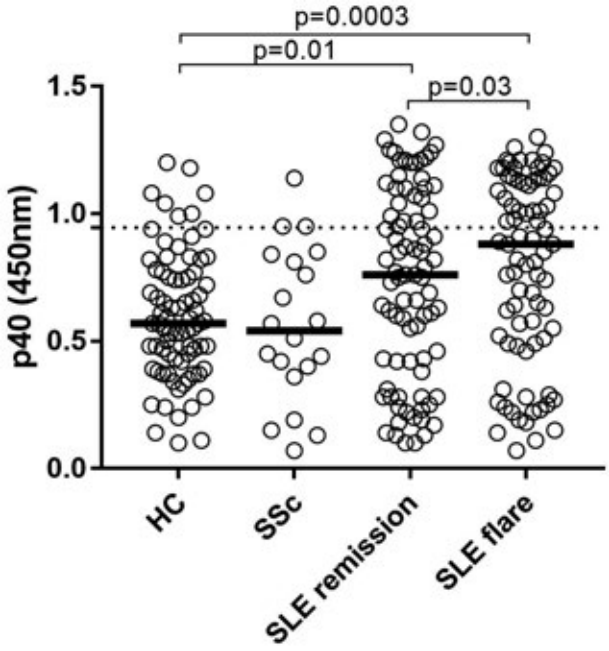
Background/Purpose: The long interspersed nuclear element 1 (LINE-1) has two major open reading frames (ORFs): ORF1 encodes the RNA-binding p40 protein, and ORF2 encodes the endonuclease and reverse transcriptase; both are required for LINE-1 to retrotranspose. In cells expressing LINE-1, these proteins assemble with the LINE-1 RNA and additional RNA-binding proteins, some of which are well-known autoantigens in patients with systemic lupus erythematosus (SLE). We asked whether SLE patients also make autoantibodies against the LINE-1 p40.

Methods: Highly purified p40 protein was used to quantitate IgG autoantibodies in the serum of SLE patients (n=172 total), disease controls (systemic sclerosis, n=20), and age-matched healthy subjects (n=78) by immunoblotting and ELISA. To determine the relationship between disease activity and LINE-1 p40 antibodies, the same SLE patients (n=80) were recruited at two time-points: low disease activity (median SLEDAI 2) and high disease activity (median SLEDAI 8.5). The patients were primarily female (89%), Caucasian (100%), with a median age of 44. An additional cross-sectional SLE cohort (n=12) was included to study LINE-1 p40 reactivity using Western blot. Preparations of p40 that also contained associated proteins were analyzed by immunoblotting with patient sera. Serum type I interferon (IFN) activity was analyzed using a cell reporter system (WISH). The 90th percentile of healthy controls was used as a cut-off for LINE-1 p40 positivity. GraphPad Prism and IBM SPSS were used for statistical analyses, and all analyses were considered statistically significant only if $p < 0.05$.

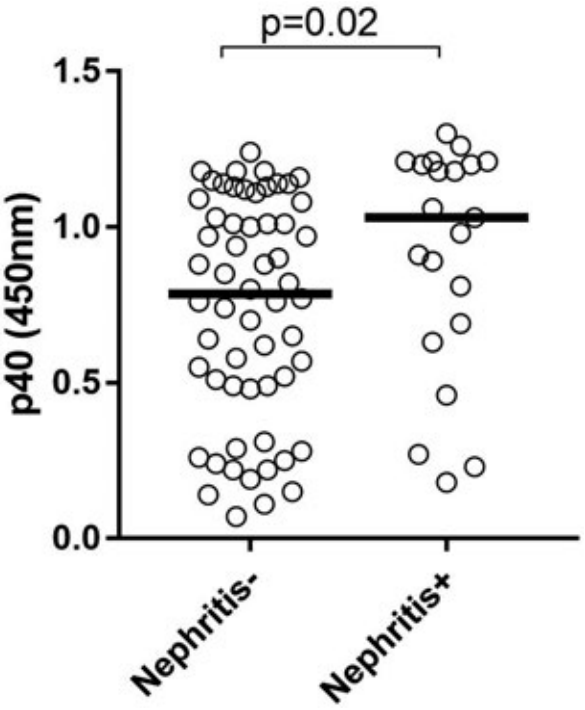
Results: Antibodies reactive with p40 were detected in the majority of patients and many healthy controls (Figure 1): they were higher in patients with SLE, but not systemic sclerosis, compared to healthy subjects (p=0.01, Figure 2). The anti-p40 reactivity was higher in patients during a flare than in remission (p=0.03, Figure 2), correlated with SLEDAI (p=0.0002), type I IFN score (p=0.006), complement C3 decrease (p=0.0001), anti-DNA antibodies ($p < 0.0001$), anti-C1q antibodies (p=0.004), current or past history of nephritis (p=0.02 and 0.003, Figure 3), and they correlated inversely with age (r=-0.49, $p < 0.0001$). SLE patient sera also reacted with p40-associated proteins.



Immunoblot



Disease State



Renal Disease Status

Conclusion: Autoantibodies reacting with LINE-1 p40 characterize a population of SLE patients with severe and active disease. These autoantibodies may represent an early immune response against LINE-1 p40 that does not yet by itself imply clinically significant autoimmunity, but may represent an early, and still reversible, step towards SLE pathogenesis.

Disclosure: K. Ukadike, None; **V. Carter**, None; **J. LaCava**, None; **M. Taylor**, None; **A. Bengtsson**, None; **C. Lood**, None; **T. Mustelin**, None.

Abstract Number: 2040

BATF2 Contributes to Interferon Dysregulation in SLE Keratinocytes

Jessica Turnier,[1] Celine Berthier,[1] Lam Tsoi,[1] Danielle Barnes,[1] Grace Hile,[1] Tamra Reed,[1] Jianhua Liu,[1] Johann Gudjonsson,[1] and J. Michelle Kahlenberg[1], [1]University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Skin inflammation can drive systemic disease in SLE, thus it is essential to understand the key regulators of the aberrant inflammatory response in lupus skin. We have previously identified BATF2 as a transcription factor that is highly overexpressed in lupus keratinocytes following type I IFN exposure. The objective of this study was to determine the role of BATF2 in regulating keratinocyte responses to type I and type II interferons.

Methods: After generating BATF2 knockouts (BATF2 -/-) in a human keratinocyte cell line (N/TERTs) using CRISPR/Cas9 technology, we treated both BATF2 -/- and control N/TERTs (CTL) with either media or 1000 units/milliliter of IFN alpha (α) or gamma (γ) for 6 hours. We subsequently isolated RNA from biological triplicates of each treatment condition and completed Illumina HiSeq analysis through the University of Michigan Sequencing Core. We performed RNA sequencing (RNA-seq) analysis to identify differentially expressed genes (DEGs; p-adjusted ≤ 10% and log2|FC| ≥ 1) and differences in transcriptional profiles between treatment conditions. We then utilized Ingenuity Pathway Analysis (IPA) to highlight enriched biological pathways within regulated genes and Genomatix Pathway System (GePS) to display transcriptional targets of regulated genes. To validate our RNA-seq findings, we performed RT-PCR of candidate genes and BATF2 immunostaining of cutaneous lupus (CLE) biopsies.

Results: RNA-seq analysis revealed an overall higher number of DEGs in CTL compared to BATF2 -/- with both type I and II interferon stimulation (905 and 1542 genes versus 536 and 947, respectively). DEGs unique to CTL upon IFNα stimulation included *IFNK*, *IL-16* and *HLA-DRB1*, and with IFNγ, *MX2*, *TNF*, *TLR5* and *CASP5*. Of identified DEGs, 408 were common to CTL and BATF2 -/- with IFNα and 744 with IFNγ stimulation, including the majority of IFN-responsive genes. Within common DEGs upon IFNα and γ stimulation, 127 and 215 genes were 1.5-fold increased or decreased in BATF2 -/- relative to CTL. IFN-responsive genes less expressed in BATF2 -/- with IFN stimulation compared to CTL included *CXCL10*, *OASL*, *CCL5*, *IFIT1/2/3, CASP1, IFI30 and ICAM1*, with some genes common and unique to IFNα and γ stimulation **(Figure 1)**. Not all IFN-responsive genes were differentially regulated by BATF2, and some were even more expressed in BATF2 -/- (*CXCL9*, *MX1*). Transcription factor analysis showed enrichment for key genes in the IFN response with a potential binding site for BATF2 in their promoter, including *CXCL9/10*, *IRF1*, *JAK2*, *MX1* and *TLR2,* many of which were identified as differentially regulated by BATF2. To validate RNA-seq data, we confirmed candidate differentially regulated genes between BATF2 -/- and CTL using RT-PCR, notably decreased *IFNK* expression in BATF2 -/-, and demonstrated increased BATF2 expression in CLE biopsies compared to healthy control skin.

Conclusion: BATF2 -/- keratinocytes respond similarly to CTL upon IFN stimulation with respect to expression of many IFN-responsive genes; however, critical genes dysregulated in CLE lesions, including *CXCL10, CCL5* and *CASP1* require BATF2 for peak induction by IFNs. Thus, BATF2 may be a specific target for blocking IFN-induced inflammatory responses in SLE skin.

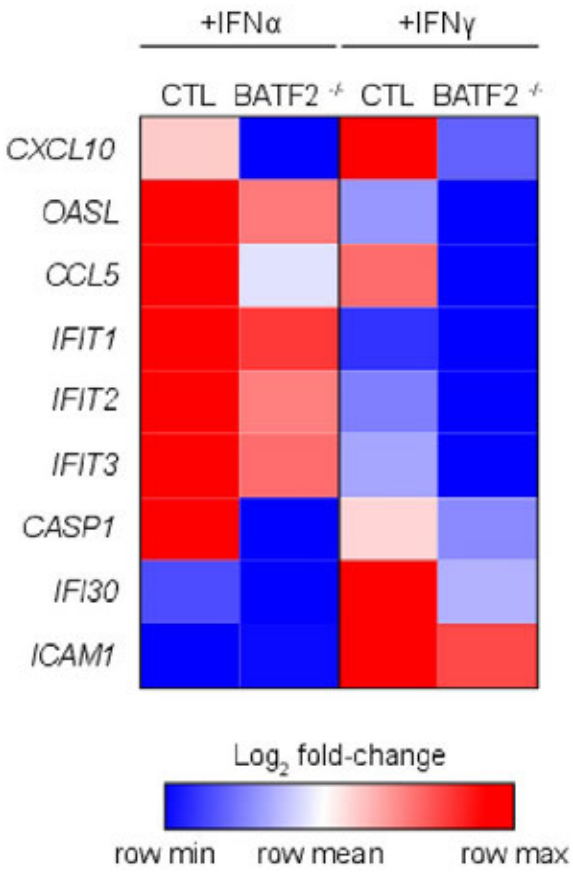


Figure 1 IFN-responsive genes less expressed in BATF2 -/- upon IFN stimulation compared to CTL

Disclosure: J. Turnier, None; **C. Berthier**, None; **L. Tsoi**, None; **D. Barnes**, None; **G. Hile**, None; **T. Reed**, None; **J. Liu**, None; **J. Gudjonsson**, AbbVie, 2, Genentech, 2, genentech, 2, MiRagen, 5, Novartis, 5, Sun Pharma, 2, Sun-Pharma, 2; **J. Kahlenberg**, AstraZeneca, Eli Lilly, Bristol Myers Squibb.

Abstract Number: 2041

Epigenome-wide Association Study Reveals Differential DNA Methylation in Systemic Lupus Erythematosus Patients with a History of Ischemic Heart Disease

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SESSION INFORMATION
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Background/Purpose: Patients with systemic lupus erythematosus (SLE) have an increased risk of ischemic heart disease (IHD). Altered methylation patterns have been reported both in SLE, including hypomethylation of interferon (IFN) regulated genes, and in individuals with a history of IHD in the general population. We performed a matched case-case epigenome-wide association study (EWAS) for IHD in patients with SLE to identify phenotype-specific differences in DNA methylation.

Methods: DNA methylation profiles from peripheral blood samples of 33 SLE patients with a history of IHD (myocardial infarction and or angina pectoris) and 66 matched (ethnicity and age) SLE patients without any prior cardiovascular events were generated on the HumanMethylation450k array (Illumina). All patients were female, fulfilled ≥ 4 ACR-82 SLE criteria and were recruited at the Uppsala, Linköping and Karolinska University hospitals, Sweden. Association was tested using a logistic regression model including age at sampling, blood cell type distribution and HM450k BeadChip as covariates. Differentially methylated CpG sites (DMCs) were defined as p< 1.3×10-7 based on Bonferroni correction and an absolute average difference in methylation beta of $|\Delta\beta| > 0.05$. Functional gene-set enrichment analyses were conducted using the ToppGene Suite database and for classification of IFN regulated genes the Interferome v2.01 database was queried.

Results: We identified 210 DMCs in SLE IHD, with a majority (84.3%) of DMCs showing decreased methylation levels in IHD. The strongest differentially methylated DMCs were located at Complement component 4 binding protein alpha (*C4BPA*) ($|\Delta\beta|$=-0.06, $p=1.1\times10^{-13}$), Membrane spanning 4-domains A3 (*MS4A3*) ($|\Delta\beta|$=-0.07, $p=3.7\times10^{-13}$) and Triggering receptor expressed on myeloid cells 1 (*TREM1*) ($|\Delta\beta|$=-0.07, $p=8.7\times10^{-13}$). Further, a differentially methylated region with multiple DMCs was observed in the promoter region of Programmed cell death 1 gene (*PDCD1*). DMCs in SLE IHD were annotated to 155 unique genes, of which 63.9% were characterized as interferon-induced. Gene-set enrichment analysis revealed response to oxidative stress ($p=1.0\times10^{-5}$), vesicle-mediated transport ($p=1.1\times10^{-6}$) and inflammasomes ($p=6.4\times10^{-6}$) as the most significantly enriched pathways in SLE IHD.

Conclusion: The results of this study highlight genes and pathways that may be implicated in the pathogenesis of and/or recovery from IHD in patients with SLE. The identified DMCs can serve as candidates for functional studies and as potential biomarkers for IHD in patients with SLE.

Disclosure: J. Imgenberg-Kreuz, None; **C. Sjöwall**, None; **M. Frodlund**, None; **I. Gunnarsson**, None; **E. Svenungsson**, None; **D. Leonard**, None.

Abstract Number: 2042

Intestinal Microbiota Alters Th1/Th17 Balance but Is Dispensable for the Development of Systemic Autoimmune Disease in BXD2 Mice

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SESSION INFORMATION
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Background/Purpose: Intestinal microbiota dysbiosis has been implicated in the pathogenesis of autoimmune disease. How the microbiota affects the peripheral immune system leading to the development of systemic autoimmune disease is elusive. Herein, we generated germ-free (GF) BXD2 mice, a complex lupus mouse model, to dissect the impact of microbiota on disease associated peripheral B and T cell signatures in these mice.

Methods: GF BXD2 mice were generated and maintained at UAB gnotobiotic core facility. Sera autoantibody levels were assessed by ELISA in special pathogen free (SPF) BXD2, GF BXD2, SPF B6, and GF B6 mice. The frequencies and absolute numbers of GC B ($CD19^+GL\text{-}7^+Fas^+$), Tfh ($CD4^+PD1^+ICOS^+$) and Treg ($CD4^+Foxp3^+CD25^+$) in spleen were determined by FACS. Immunostaining and confocal imaging were applied to assess the immune architecture of the spleens from each strain of mice. Antibodies against bacterial lysates from the intestine were measured by western blot. Histology was performed to evaluate disease development in the kidney, lung, liver and intestine. The microbiome in 4 strains of mice were comprehensively assessed by 16S rRNA V4 gene sequencing. GC B ($CD19^+GL\text{-}7^+Fas^+$) and Tfh ($CD4^+PD1^+CXCR5^+$) cells from SPF BXD2 and GF BXD2 were FACS sorted for RNA-seq transcriptome analysis.

Results: Deep 16S rRNA V4 gene sequencing revealed two distinctive clusters of microbiome compositions between GF and SPF. Serum levels of IgG against bacteria lysates of cecal content from SPF or GF BXD2 mice were lower in GF BXD2 than in SPF BXD2 mice. Surprisingly, the GF status did not diminish sera levels of IgG or IgM autoantibodies against dsDNA, BiP, histone, rheumatoid factor (RF), MARCO, SR-AI, and SSA in BXD2 mice. The differences of frequency and absolute numbers of GC B cells, $CD4^+$ T cells, Tfh cells were also undistinguishable between SPF BXD2 spleen and GF BXD2 mouse spleen although GF BXD2 mice exhibited a higher number of $CD19^+$ B cells, compared to the SPF counterpart. Interestingly, upstream pathway analysis of the transcriptomes of Tfh and GC B cells indicated that the GF status has favored the programs of Tfh-IFNɣ over Tfh-IL-17. There was also an increased *IL10RA* program in GF BXD2 Tfh cells and this was further supported by an increased follicular T-regulatory (Tfr) cells in GF BXD2 mice. Immunofluorescent staining demonstrated similar spleen follicle structures and enlarged GCs in both SPF and GF BXD2 mice, compared to normal B6 mice. Histologic study in the organs that are most affected in lupus showed similar disease scores in kidney and lung between SPF and GF BXD2 mice.

Conclusion: This study provided the fundamental evidence that the commensal microbiome is not the main driver for the development of systemic autoimmune disease in BXD2 mice. Since the Tfh-IFNɣ/Tfh-IL-17 balance and the Tfr programs were altered in GF mice, the results suggest that certain immune phenotypes may be modulated through leaky intestine, yet they are not sufficient to alter the autoimmune responses in BXD2 mice.

This work was supported by grants from VA grant (I01BX004049), NIH grants R01-AI-071110, R01 AI134023, and LRA Distinguished Innovator Award to J.D.M, the LRA Novel Research Award to H-C.H., and the P30-AR-048311 and the P30-AI-027767.

Disclosure: H. Hong, None; **Q. Wu**, None; **P. Yang**, None; **B. Luo**, None; **A. Essman**, None; **O. Ojo**, None; **M. Crowley**, None; **D. Crossman**, None; **C. Morrow**, None; **J. Foote**, None; **T. Schoeb**, None; **C. Elson**, None; **H. Hsu**, Lupus Research Alliance Novel Research Award, 2; **J. Mountz**, Lupus Research Alliance Distinguished Innovator Award, 2, NIH R01-AI-071110, R01 AI134023, P30-AR-048311, 2, R01-AI-071110, R01 AI134023, I01BX004049, 1I01BX000600, 2, VA Merit Review grant (I01BX004049), 2.

Abstract Number: 2043

Large Joint Arthritis in Systemic Lupus Erythematosus Is Characterized by TH17 Cells Rather Than B Cell Accumulation

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SESSION INFORMATION
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Background/Purpose: Arthritis is a common clinical feature of systemic lupus erythematosus (SLE), that can be present either at the onset or in later disease course. SLE-related arthritis is usually non-erosive and non-deforming as opposed to rheumatoid arthritis (RA). While RA synovial pathology has been extensively studied, little is known about the pathophysiology of arthritis in SLE. Here, we aimed to explore the cytokine and cellular compartments in synovial fluids (SF) of SLE patients with arthritic manifestations.

Methods: Paired synovial fluid mononuclear cells (SFMC) from large joint aspiration and peripheral blood samples (PBMC) from three SLE patients were analyzed by three different lineage-specific multicolor flow cytometry panels for B cells and T cells (cytotoxic and helper). SLE-derived SFMCs were further stimulated in vitro to measure T cell production of IFN gamma and IL-17. Since the majority of SF samples from SLE patients were not cellular, we analyzed the acellular SF samples (n=19) with cytokine bead array for Th1, Th17 and Th2 associated cytokines (BD Bioscience). The patients fulfilled the ACR 1982 classification criteria for SLE. Clinical records were reviewed in order to exclude the presence of comorbidities such osteoarthritis or overlap with RA.

Results: The overall frequency of CD4+ and CD8+ T cells among CD3+ T cells was similar across SFMC and PBMC samples, while CD19+ cells (B-lymphocytes) were scarcely present in the joint of SLE patients as opposed to the peripheral blood. In SF, we could identify an increased frequency of CCR6+ cells among CD4+ T cells, a marker associated with Th17 cells. IL-17-production could be validated in the (CD4+CCR6+) compartment following in vitro stimulation of SFMCs. Also, a strong IFN gamma production was seen, which may originate from the increased frequency of cytotoxic EOMES+ Granzyme A+ T cells that were also recorded in the SLE-SFMC. IFN gamma was not found in the acellular synovial fluid samples, while the TH17-associated cytokines IL-17 and IL-6 were abundant.

Conclusion: Although SLE is usually considered to be a B-cell driven disease, its common clinical features like arthritis could be driven in situ by T cells, namely TH17 cells and CD4+ T cells with cytotoxic profile.

Disclosure: N. Sippl, None; **F. Faustini**, None; **K. Chemin**, None; **I. Gunnarsson**, None; **V. Malmström**, None.

Abstract Number: 2044

Expression of SLAMF6 and Its Functional Significance in Podocytes of Lupus Nephritis: Report with Consideration Based on the Results of Microarray Analysis in Podocytes of MRL/*lpr* Mice

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

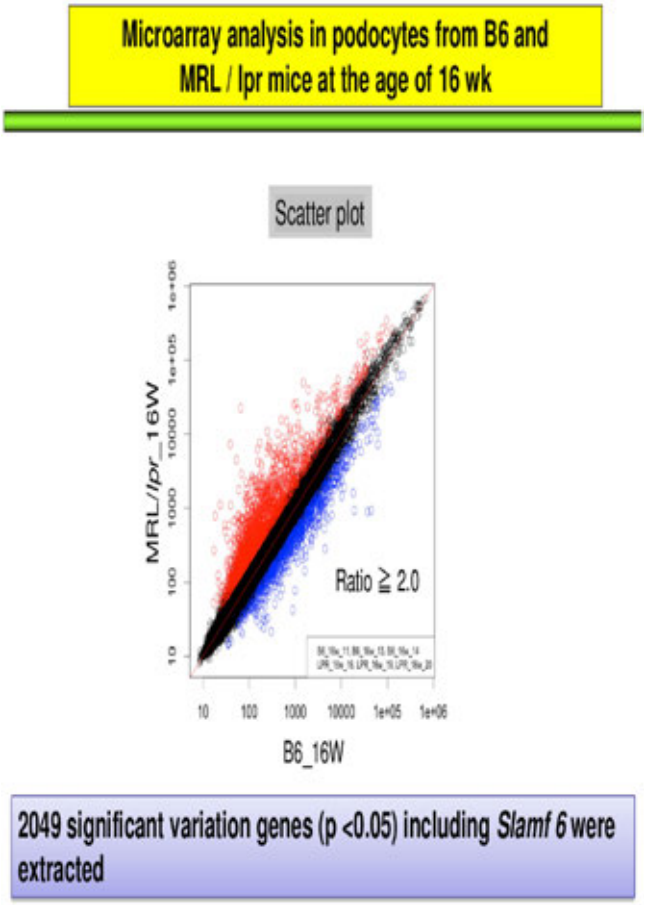

Figure 1 Microarray analysis in podocytes from B6 and MRL / lpr mice at the age of 16 wk

Background/Purpose: Lupus nephritis (LN) is one of the most serious complication of SLE. The alteration of the structural protein in podocytes is known as a mechanism of proteinuria in LN. The signaling lymphocyte activation molecule family(the SLAM family) of typeItransmembrane receptors consists of nine related members of the immunoglobulin superfamily and has been reported to mediate important regulatory signals between immune cells (Nat Rev Immunol. 2003 Oct;3(10):813-21).The 1q23 region on human chromosome 1 including the SLAMF cluster of genes, containing SLAMF6 has been identified as a lupus susceptibility locus(Nat Rev Rheumatol. 2010 Jun;6(6):348-57). We sought to examine the functional role of SLAMF6 in lupus podocytes.

Methods: We evaluated the co-expression of nephrin, a podocyte marker and SLAMF6 in kidney of normal controls and LN patients, also in B6 and MRL/*lpr* mice by immunofluorescence analysis. We also examined nephrin positive SLAMF6 expression in isolated podocytes from B6 and MRL/*lpr* kidneys. Then, we analyzed the expression of SLAMF6 in CD4+T cells of isolated kidney and spleen in B6 and MRL/*lpr* mice. We treated human podocytes with IgG from healthy individuals and LN patients for 24 h and 48h and analyzed the expression of SLAMF6 by real-time PCR. We isolated podocyte from B6 and MRL/*lpr* mice by cell sorter, then extracted mRNA, and performed microarray analysis.

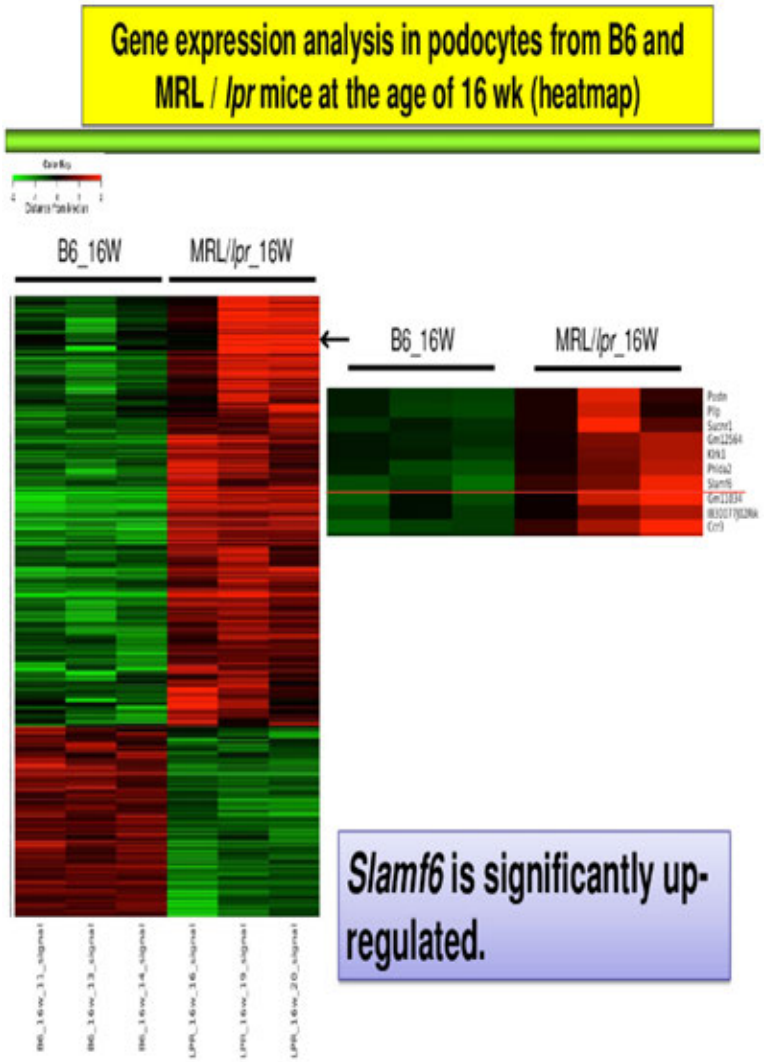

Figure 2 Gene expression analysis in podocytes from B6 and MRL / lpr mice at the age of 16 wk (heatmap)

Results: In the histopathology, the expression of SLAMF6 was increased in LN patients and MRL/*lpr* mice compared to control. Although the expression of nephrin in MRL/*lpr* mice kidney at 16 wk old decreased compared to B6 mice at same age, the expression of SLAMF6 in podocytes increased in diseased MRL/*lpr* mice compared to B6 mice. Similarly, the expression of SLAMF6 in CD4+ T cells increased in diseased MRL/*lpr* mice kidney and spleen compared to B6 mice. The level of SLAMF6 mRNA elevated in human podocytes exposed to LN-derived IgG compared to healthy control derived IgG.

When an arbitrary difference of 2.0-fold (or greater) change was selected, 1420 genes were identified as being up-regulated and 629 as down-regulated in podocytes derived from MRL/*lpr* mice as compared to B6 mice (Figure 1). Above all, the expression level of SLAMF6 in podocytes was significantly increased in MRL/*lpr* mice (ratio 3.22, P=0.0017) (Figure 2). The expression of the gene encoding the adapter protein, which is required for SLAMF signal transduction, was also confirmed in mice, and the fluctuation of some genes was confirmed. We also confirmed a decrease in several podocyte-related genes including *nphs1* (gene encoding nephrin) and an increase in apoptosis-related genes.

Conclusion: The expression of SLAMF6 is enhanced in LN podocytes, suggesting that the possibility of cooperating with CD4+T cells contributing to its dysfunction. Here, we compared the gene expression and signal transduction of podocytes in B6 mice and MRL /*lpr* mice by microarray. Further examination is needed to investigate in detail how SLAMF6 on downstream signals, specifically, the expression of nephrin and apoptosis markers are involved in the development of LN in the future.

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Abstract Number: 2045

RNA Sequencing of Plasma and Urine-derived Extracellular Vesicles from Lupus Nephritis Patients Identifies Disease-associated Small RNA Signatures and Putative Therapeutic Targets

Taylor Koenig,[1] Nicholas Young,[2] Giancarlo Valiente,[3] Ifeoma Okafor,[4] Emily Schwarz,[5] Peter Harb,[5] Caitlin Henry,[1] Kyle Jablonski,[6] Lai-Chu Wu,[4] Eli Roberson,[7] and Wael Jarjour[8], [1]Division of Immunology and Rheumatology, The Ohio State University Wexner Medical Center, Columbus, [2]The Ohio State University Wexner Medical Center, Division of Immunology and Rheumatology, Columbus, OH, [3]The Ohio State University, Columbus, [4]Ohio State College of Medicine, Columbus, [5]The Ohio State University Wexner Medical Center, Columbus, OH, [6]The Ohio State University Wexner Medical Center, Division of Immunology and Rheumatology, Columbus, [7]Washington University at St.Louis, St.Louis, MO, [8]Ohio State College of Medicine, Columbus, OH

SESSION INFORMATION
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Background/Purpose: Systemic lupus erythematosus is an autoimmune disease characterized by chronic inflammation. We have previously shown that TLR7 and TLR8 are significantly upregulated in PBMCs of Lupus patients. Recent studies have discovered that miR-21, mir-29a, and miR-29b packaged and secreted in extracellular vesicles (EVs) can also bind to these receptors.

Methods: Twenty four lupus patients meeting the revised ACR criteria and 15 healthy controls provided informed consent to participate in this IRB-approved study. Plasma- and urine-derived EVs were isolated from 16 lupus patients including lupus nephritis (LN) and 6 healthy subjects by differential ultracentrifugation and validated by Nanosight and ELISA. Moreover, urine and plasma EVs from an additional 5 LN patients and 9 healthy subjects were subjected to RNA sequencing to identify RNA species including lnRNA, miRNA, and mRNA. A novel human-mouse chimeric model for testing therapeutics in SLE was created by adoptively transferring PBMCs from 3 active lupus patients into immunodeficient mouse recipients. Prior to transfer, PBMCs were incubated with synthetic liposomal EVs containing miR antagonists to miR-21, mir-29a, and miR-29b, or a control. After 21 days, PBMCs were collected for immunophenotyping and ELISA; tissues were collected for histopathological analysis by H&E staining and immunohistochemistry (IHC) for human CD3.

Results: There was a significant upregulation of EVs detected in the plasma of lupus patients relative to healthy controls. Additionally, the lupus nephritis patients that had RNAseq data resulted in a collection of statistically significant small RNA reads, such as miR-142-3p and let-7b-5p. The unique RNA signature observed by volcano plots showed multiple RNA species significantly upregulated and downregulated in lupus nephritis plasma samples. Furthermore, principal component analysis of both plasma and urine derived EVs revealed distinct lupus nephritis and healthy populations. Finally, in the adoptive transfer model, human CD4+, CD8+, B-cells, monocytes, and NK cells were successfully recovered from whole blood of chimeric mice at similar levels, but levels of human IL-2, IL-6, IL-10, and TNF-α were reduced with miR inhibition. Moreover, miR inhibition significantly reduced the inflammatory histopathology in the small intestine, liver, and kidney, demonstrated by H&E and digital quantitation of positive human CD3 IHC staining.

Conclusion: Our data shows elevated levels of EVs in lupus patients and reveals unique EV-derived RNA signatures in both urine and plasma that may be targeted therapeutically or used as diagnostic biomarkers for Lupus.

Disclosure: T. Koenig, None; **N. Young**, None; **G. Valiente**, None; **I. Okafor**, None; **E. Schwarz**, None; **P. Harb**, None; **C. Henry**, None; **K. Jablonski**, None; **L. Wu**, None; **E. Roberson**, None; **W. Jarjour**, None.

Abstract Number: 2046

NMR Spectroscopy Reveals Alterations of Urinary Acetate and Citrate Levels Following Cyclophosphamide Therapy in Patients with Lupus Nephritis

Sujata Ganguly,[1] Umesh Kumar,[2] Anupam Guleria,[3] Sanjukta Majumder,[4] Sanat Phatak,[1] Smriti Chaurasia,[1] Nikhil Gupta,[5] Sandeep Kumar,[6] Amita Aggarwal,[7] Dinesh Kumar,[3] and Ramnath Misra[4], [1]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Lucknow, India, [2]Centre of Biomedical Research SGPGIMS, Raibareli Road, Lucknow-226014, India, Lucknow, Uttar Pradesh, India, [3]Centre for Biomedical Research, Sanjay Gandhi Post Graduate Institute of Medical Science, Lucknow, Uttar Pradesh, India, [4]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Lucknow, Uttar Pradesh, India, [5]Centre for Biomedical Research, Lucknow, DELHI, Delhi, India, [6]Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Post Graduate Institute of Medical Science, Lucknow, Uttar Pradesh, India, [7]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, Lucknow, Uttar Pradesh, India

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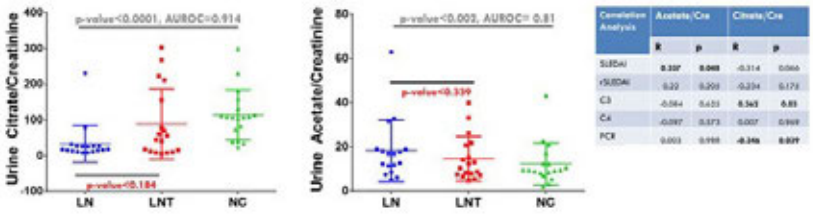

Correlation Analysis	Acetate/Cre		Citrate/Cre	
	R	p	R	p
SLEDAI	0.337	0.048	-0.314	0.066
rSLEDAI	0.22	0.203	-0.234	0.173
C3	-0.064	0.633	0.362	0.03
C4	-0.097	0.573	0.007	0.969
PCR	0.003	0.988	-0.346	0.039

Figure: The box plot representation of Urinary Citrate/Cre and Acetate/Cre ratios obtained for different study groups: LN (in blue), LNT (in red) and NC (green). The significantly higher p-values and area under the ROC curve (AUROC) between LN and NC groups demonstrated the diagnostic potential of these urinary ratios. The table on the right side shows the correlation analysis parameters between urinary metabolic profiles and clinical parameters.

Background/Purpose: Metabolomics, the study of global alterations in small metabolites is a useful tool to look for novel biomarkers. Recently, we reported a reprogramming of the serum metabolomic profile on nuclear magnetic resonance(NMR) spectroscopy following treatment in Lupus Nephritis (LN).(1)We explored urinary parameters using NMR Spectroscopy in patients with biopsy proven proliferative lupus nephritis. Change in parameters after 6 months Cyclophosphamide induction treatment and its correlation with disease activity was assessed.

Methods: Urine obtained from Lupus Nephritis (n=18, F=16,M=2) at diagnosis and following induction therapy with cyclophosphamide, and healthy controls (n=18, median age 35,all females) were stored at -80 °C. Metabolomic profiling was done using high resolution 800 MHz 1D 1H NMR spectroscopy. Urinary ratio of metabolites was calculated-(Metabolitex1000)/Creatinine. Disease activity was measured using SLEDAI. Metabolomic profiles were compared between groups and correlated with clinical parameters using SPSS

Results: Urinary metabolomic fingerprint of LN patients differed from healthy controls by having significantly raised urinary acetate/creatinine(LN=41.84±100.6, HC=12.36±9.40, p=< 0.002) and reduced urinary citrate/creatinine. (LN=34.22±54.8, HC=114.5±70.09, p=< 0.0001). Urinary citrate (88.68±98.33) increased after 6 months of Cyclophosphamide, while urinary acetate showed a trend towards decrease(14.77±9.98). AUC for urinary citrate/creatinine and acetate/creatinine were 0.9136 and 0.8086. The urinary acetate levels correlated with SLEDAI (r=0.337,p=0.048). Urinary citrate levels correlated with C3 (r=0.362,p=0.03) and negatively correlated with uPCR (r=0.346, p=0.039).

Conclusion: The decreased urinary citrate mirrors the finding seen in serum of the patients done earlier which reflects dampened aerobic glycolysis and oxidative phosphorylation.(1) Raised urinary acetate levels possibly reflects renal tubular injury and decreased entry into TCA cycle. Urinary metabolomics parameters are potential noninvasive biomarkers for diagnosis and monitoring treatment response in LN.

Reference:

1. Guleria A et al. NMR based serum metabolomics reveals reprogramming of lipid dysregulation following Cyclophosphamide based induction therapy in lupus nephritis. J **Proteome**Res. 2018, 17 (7), 2440–2448.

Disclosure: S. Ganguly, None; **U. Kumar**, None; **A. Guleria**, None; **S. Majumder**, None; **S. Phatak**, None; **S. Chaurasia**, None; **N. Gupta**, None; **S. Kumar**, None; **A. Aggarwal**, None; **D. Kumar**, None; **R. Misra**, None.

Abstract Number: 2047

Time-trends in Opioid Use Hospitalizations in Common Musculoskeletal Conditions: Gout, Osteoarthritis, Rheumatoid Arthritis, Fibromyalgia, and Low Back Pain

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rates of opioid abuse and associated mortality is a problem of epidemic proportion in the U.S. To our knowledge, limited data are available on opioid use disorder (OUD)-related hospitalizations in people with common musculoskeletal diseases

Methods: We used the U.S. National Inpatient Sample (NIS) data from 1998-2014 to examine the rates of OUD hospitalizations without opioid overdose, detoxification or rehabilitation services, based on the presence of any of the following International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes for opioid dependence or abuse in the primary diagnosis position: 304.0x, 304.7x, 305.5x, 965.0x, E850.0, or E935.05. Five key rheumatic diseases were assessed using the respective ICD-9-CM diagnostic codes in a secondary position: Gout, rheumatoid arthritis (RA), fibromyalgia, osteoarthritis (OA), and low back pain (LBP). Incidence of OUD claims was assessed per 100K NIS claims overall.

Results: The incidence of OUD-related primary hospitalizations was low in 1998-2000 for the five musculoskeletal conditions and increased over the 19-year study period (**Table1**). The increase was 3.5- fold higher in people with LBP to 24-fold higher in people with gout. Rates of OUD per 100K total NIS claims showed similar trends namely, with increased ranging 5-fold higher in people with LBP to 35-fold higher in people with gout (**Table 2**). There was a plateauing of OUD claims for LBP and gout, but the increase seems to continue for OA, fibromyalgia, and RA (**Figure 1**).

Conclusion: The rate of increase in OUD-hospitalizations occurred in all 5 musculoskeletal conditions, but the rate differed by the condition. Providers, policy makers and patients with these conditions need to be aware of these trends, so the OUD-associated morbidity and mortality can be prevented.

	Gout	OA	Fibromyalgia	RA	Low Back Pain
1998 - 2000	53	702	552	314	1,211
2001 - 2002	169	930	885	411	1,753
2003 - 2004	247	1,558	1,396	531	2,778
2005 - 2006	312	2,237	1,488	821	3,312
2007 - 2008	471	3,022	2,461	1,021	3,968
2009 - 2010	809	4,474	3,997	1,609	5,313
2011 - 2012	1,359	5,494	5,010	2,010	6,059
2013 - 2014	1,220	5,700	5,120	2,055	5,275
2015 - 2016	1,340	7,300	4,985	2,260	5,455
% change	2428.3%	939.9%	803.1%	619.7%	350.5%

Table 1. Number of Opioid use disorder (OUD) primary hospitalizations from 1998 to 2016 by top, five musculoskeletal diseases

	Gout	OA	Fibromyalgia	RA	Low Back Pain
1998 - 2000	0.05	0.68	0.53	0.30	1.17
2001 - 2002	0.23	1.28	1.22	0.57	2.41
2003 - 2004	0.33	2.09	1.87	0.71	3.73
2005 - 2006	0.41	2.95	1.96	1.08	4.36
2007 - 2008	0.62	3.96	3.22	1.34	5.20
2009 - 2010	1.08	5.96	5.32	2.14	7.08
2011 - 2012	1.85	7.48	6.82	2.74	8.25
2013 - 2014	1.72	8.03	7.22	2.90	7.43
2015 - 2016	1.88	10.22	6.98	3.16	7.64
% change	3568.5%	1408.8%	1210.3%	944.3%	553.6%

Table 2. Rate of Opioid use disorder primary hospitalizations from 1998 to 2016 by top, five musculoskeletal diseases per 100k total NIS claims

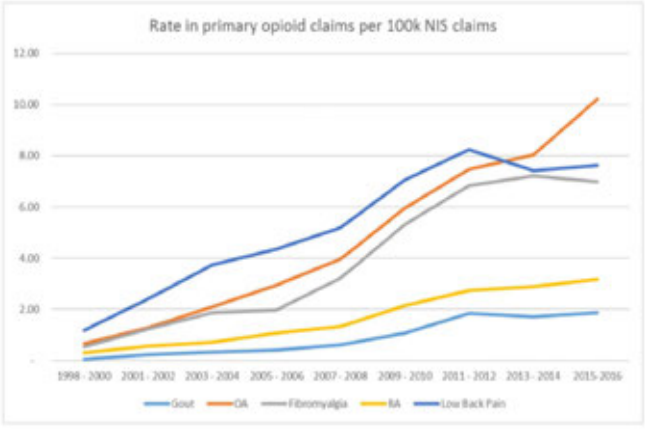

Figure 1 Trends in rates of primary OUD claims per 100K NIS claims, by five musculoskeletal conditions

Disclosure: J. Singh, Amarin pharmaceuticals, 1, 4, Clearview healthcae partners, 5, Clearview healthcare partners, 5, Clinical Care options, 5, Horizon, 5, Medisys, 5, OMERACT, 6, Putnam associates, 5, Spherix, 5, the American College of Rheumatology, 5, The American College of Rheumatology, 5, The National Institues of Health, 5, the National Institutes of Health, 5, Viking therapeutics, 1, 4, WebMD, 5; **J. Cleveland**, None.

Abstract Number: 2048

Opioid Prescription Use Among Patients with Rheumatic Disease: A Population Based Cohort Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatic diseases can be associated with pain and disability. An international opioid epidemic is ongoing, and prescription opioid use has been linked with increased risks of addiction, abuse, and mor-

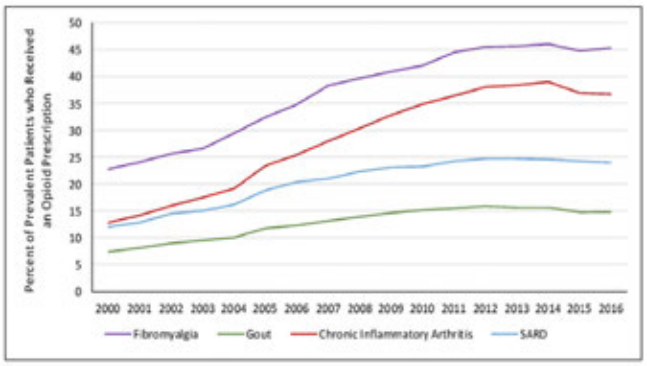

Figure 1 Annual Prevalent Opioid Prescriptions Among Patients with Rheumatologic Disease. Systemic Autoimmune Rheumatic Disease (SARD) includes systemic lupus erythematosus, Sjogren's syndrome, systemic sclerosis, dermatomyositis, polymyositis, mixed connective tissue disease, ANCA-associated vasculitis, and Behcet's disease. Chronic inflammatory arthritis includes rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis.

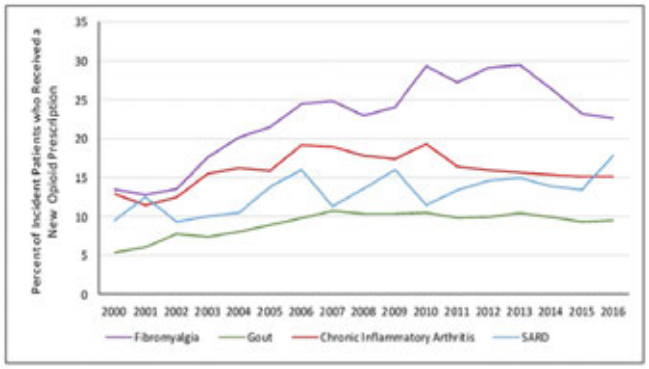

Figure 2 New Opioid Prescriptions Among Patients with Incident Rheumatic Disease. Systemic Autoimmune Rheumatic Disease (SARD) includes systemic lupus erythematosus, Sjogren's syndrome, systemic sclerosis, dermatomyositis, polymyositis, mixed connective tissue disease, ANCA-associated vasculitis, and Behcet's disease. Chronic inflammatory arthritis includes rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis.

tality. We assessed contemporary opioid prescription patterns among patients with rheumatic diseases in a general population context.

Methods: Using a United Kingdom general population database, we identified cohorts of fibromyalgia, chronic inflammatory arthritis (including RA, ankylosing spondylitis [AS], and psoriatic arthritis [PsA]), systemic autoimmune rheumatic diseases (SARDs) (including SLE, Sjogren's syndrome, systemic sclerosis, dermatomyositis, polymyositis, mixed connective tissue disease, ANCA-vasculitis, and Bechet's disease), and gout by Read codes and examined opioid prescriptions between January 1, 2000 and December 31, 2016 within these cohorts. We estimated the annual prevalence of opioid prescriptions among prevalent cases in each disease cohort. We also estimated the annual incidence of new opioid prescriptions among incident patients in each disease cohort, as determined by the percentage who received an opioid prescription within one year following their diagnosis and were free of opioid prescriptions in the antecedent 6 months. We examined secular trends by prescription opioid (e.g., tramadol, codeine) and strong opioids including morphine, oxycodone, fentanyl, hydromorphone, and methadone) within each disease cohort.

Results: Among incident cohorts, we identified 26,267 with fibromyalgia, 39,954 with inflammatory arthritis, 9,800 with SARDs, and 135,130 with gout. Prevalent opioid prescriptions increased in each disease cohort, reaching a plateau between 2012 and 2016 (**Figure 1**). In 2016, 45.2% of patients with fibromyalgia, 36.7% with inflammatory

arthritis, 24.0% with SARD, and 14.8% with gout received opioid prescriptions. Tramadol was the most commonly prescribed individual opioid (19.4%, 13.0%, 8.7%, and 5.2% prevalence, respectively), whereas 20.1%, 15.2%, 10.1%, and 3.6% of patients received strong opioid prescriptions, respectively. Patients with fibromyalgia were the most likely to receive new opioid prescriptions; annual rates rose from 12.8% in 2000 to 22.6% in 2016 (**Figure 2**). This was followed by incident inflammatory arthritis and SARDs, and the annual incidence was lowest among gout patients, rising from 5.3% to 9.5%.

Conclusion: In this general population-based study, we identified a substantial rise in the rates of opioid prescriptions among patients with rheumatic disease. Between 2012 and 2016, nearly half of patients with fibromyalgia, over one-third of patients with RA, PsA, and AS and nearly one-fourth of patients with SARDs received opioid prescriptions. These findings highlight the importance of increased awareness, as this population may be at risk for opioid-related complications.

Disclosure: A. Jorge, None; **N. Lu**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5.

Abstract Number: 2049

National Estimates of Pain Medication Use in Patients with Osteoarthritis

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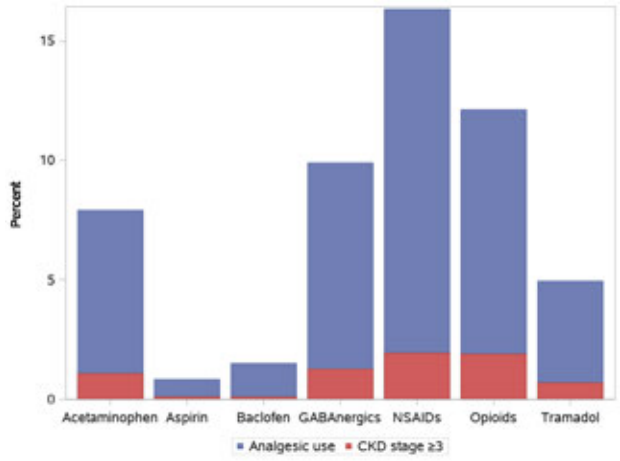
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The epidemiology of pain medication use among patients with osteoarthritis is not well explored. Chronic kidney disease (CKD) modifies choice of analgesics. The aim of this study was to explore real world use of pain medications in a nationally representative sample of patients with osteoarthritis.

Methods: The CDC's National Health and Nutrition Examination Survey (NHANES) 2013-2016 data were used, which is nationally representative of the non-institutionalized civilian resident population of the United States. The survey includes at-home questionnaires and health examination with laboratory testing. The study sample included adults (age ≥20 years) with a self-reported physician-made diagnosis of osteoarthritis. Prescription pain medication use in the past month was classified into groups: acetaminophen, aspirin, NSAIDs, tramadol, opioids, GABAnergics, and baclofen. eGFR was calculated using the CKD-EPI formula. Demographics including age and gender were identified. Survey-specific statistical methods were used to account for sample design and weighted frequencies and percentages were calculated with 95% confidence intervals (CI).

Results: There were 1,212 adults with osteoarthritis in the NHANES 2013-2016 sample, which represented 30,918,356 people when weighed. The sample was 65.0% female with a mean age of 61.5 years (95% CI, 60.6-62.4). eGFR was < 60 mL/min per 1.73 m2 (CKD stage ≥3) in 13.7% of study sample. The most commonly used prescription pain medications were NSAIDs, n=5,051,211 (16.3%); opioids, n=3,745,128 (12.1%); and GABAnergics, n=3,059,324 (9.9%). The prevalence of CKD stage ≥3 was 11.8% in NSAID users, 15.6% in opioid users, 12.8 in GABAnergic users, and 14.0% in tramadol users (See figure). Commonly used NSAIDs were meloxicam, n=1,648,619 (5.3%); celecoxib, n=965,139 (3.1%); and ibuprofen, n=947,035 (3.1%). Commonly used opioids were hydrocodone, n=2,088,939 (6.8%); oxycodone, n=967,814 (3.1%); and morphine, n=425,875 (1.4%). Use of more than one class of



Weighted Percentages of Prescription Pain Medication Use and CKD stage ≥3 in Patients with Osteoarthritis

Weighted Frequencies and Percentages of Prescription Pain Medication Use and CKD stage ≥3 in Patients with Osteoarthritis

	N (%)	CKD ≥3, N (Row %)
Acetaminophen	2,451,919 (7.9)	332,259 (13.6)
Aspirin	254,601 (0.8)	29,701 (11.7)
NSAIDs	5,051,211 (16.3)	594,373 (11.8)
Tramadol	1,529,572 (4.9)	214,330 (14.0)
Opioids	3,745,128 (12.1)	582,912 (15.6)
GABAnergics	3,059,324 (9.9)	392,824 (12.8)
Baclofen	462,480 (1.5)	29,136 (6.3)

pain medication included: NSAIDs and Opioids, n=1,158,653 (3.7%); NSAIDs and GABAnergics, n=1,136,693 (3.7%); Opioids and Gabanergics, n= 1,201,136 (3.9%); and NSAIDs, opioids, and GABAnergics, n=464,595 (1.5%).

Conclusion: Using nationally representative data, we described the epidemiology of prescription pain medication use, CKD prevalence, and use of combinations of pain medications in patients with osteoarthritis.

Disclosure: M. Saeed, None.

Abstract Number: 2050

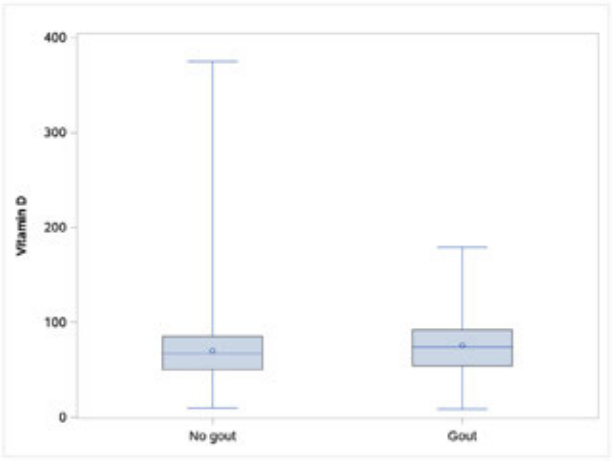
Association of Gout with Vitamin D: A Population-Based Study

Jinan Al-Naqeeb,[1] Mohammed Saeed,[2] Beata Dye,[3] and Mark Jeranko[4], [1]Ascension St John hospital, Grosse Pointe Park, MI, [2]Capital Health hopsital, Trenton, NJ, [3]Ascension St John Hospital, Detroit, MI, [4]Detroit Medical Center/ Wayne State University, Detroit, MI

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases



Mean vitamin D level in patients with gout compared to the nongout group

Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Prior research showed conflicting results about the association of vitamin D with gout. We aimed in this study to quantify vitamin D levels in patients with and without gout using nationally representative data.

Methods: The National Health and Nutrition Examination Survey (NHANES) is a nationally representative sample of the non-institutionalized population in the United States. We analyzed data from 2011 to 2014 for adults (age ≥20 years). Gout was defined as a "yes" to: "Has a doctor or other health professional ever told you that you had gout?". Gender, age, vitamin D level, and vitamin D supplement use in the past 30 days were identified. Vitamin D deficiency was defined as < 50 nmol/L and high vitamin D level was defined as >125 nmol/L. Survey-specific statistical methods were used to account for sample design. Mean vitamin D levels (with 95% CI) and low/high vitamin D prevalence were calculated for people with and without gout. The Chi-square test was used to test the difference between categorical variables with alpha=0.05.

Results: There were 10,907 adults in our sample, which represented 226,559,243 people when weighted. Gout was reported in 8,705,906 (3.8%) of the sample. The mean age was 60.8 (95% CI:59.0-62.6) in those with gout compared to 49.9 (CI:46.0-47.8) in those without gout. 67.3% of those with gout were male compared to 47.2% in those with no gout. Mean vitamin D level was 75.7 (95% CI:71.4-80.1) in people with gout compared to 69.9 (95% CI:67.8-72.1) in those without gout (see Figure 1). The prevalence of low vitamin D in people with and without gout were 25.2% and 27.7%, respectively (P value 0.3945). While the prevalence of high vitamin D level in people with and without gout were 6.4% and 4.3, respectively (P value 0.1265). Vitamin D supplement use was more common in people with gout (50.3%) compared to people without gout (40.4%, P value 0.0025). Among people with gout who took vitamin D supplements, 40.0% reported being advised by a doctor to take the supplement.

Conclusion: In this large nationally representative population-based cross-sectional study, vitamin D was not associated with gout. The prevalence of vitamin D deficiency was similar in people with and without gout. Vitamin D supplement use was more common in people with gout.

Disclosure: J. Al-Naqeeb, None; **M. Saeed**, None; **B. Dye**, None; **M. Jeranko**, None.

Abstract Number: 2051

Factors in Achieving Serum Uric Acid Target and the Occurrence of Gouty Arthritis: A Cross-sectional Study Based on Japanese Health Insurance Claim Data

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The number of gout attacks can be reduced by achieving and maintaining serum uric acid (sUA) at or below 6.0 mg/dL, a level uniformly recommended by international guidelines. However, although urate-lowering therapy (ULT) can reliably achieve such reductions, many gout patients fail to reach their sUA target, and such patients tend to experience recurring gouty arthritis in real-world clinical practice. The present study assessed factors related to achieving target sUA levels and the occurrence of gouty arthritis in Japanese clinical practice, to better understand the underlying reasons for suboptimal treatment of gout.

Methods: We analyzed Japanese health insurance claims and medical check-up data from April 2016 to March 2017, and assessed factors that were associated with target sUA in gout and asymptomatic hyperuricemia and with the occurrence of gouty arthritis in gout. We also conducted subgroup analysis of ULT prescriptions and outcomes, stratified by renal function, to determine effects on achieving target sUA. Data were obtained from the JMDC Claims Database, including diagnostic codes, names of prescription drugs prescribed, and data from physical examinations of company employees and their dependents.

Results: Patients who reached their target sUA tended to be older, to be female, to receive higher doses of ULT, to achieve higher treatment adherence (medication possession ratio), to have more comorbidities, and/or to be prescribed antidiabetic drugs. We found that renal dysfunction and/or diuretic prescriptions were predictive of reduced achievement of target sUA. This was obvious in severe renal dysfunction (OR 0.22 [95% CI 0.10-0.48] for < 15 and 0.15 [0.10-0.23] for ≥15 to < 30, compared with eGFR ≥90 mL/min/1.73m2) (Figure 1). Notably, the mean prescribed ULT dose was low (febuxostat 17.0-21.0 mg/day, allopurinol 123.1-139.6 mg/day) a cross all renal function categories. We also found that lower renal function was associated with lower achievement of target sUA for every ULT dosage category. Our data showed that gouty arthritis attacks occurred more often among patients with a prior history of gouty arthritis and less often in patients who had higher ULT adherence, sUA measured at medical facilities, and/or more comorbidities (Figure 2).

Conclusion: Our analysis showed renal dysfunction as an important predictor for failure to achieve target sUA; within our dataset, most renal dysfunction patients with gout or asymptomatic hyperuricemia did not reach target sUA. These findings imply suboptimal disease management, especially in this population. Our findings also suggested the importance of regular clinic visits and sustained adherence to ULT in the control of gouty arthritis attacks.

Disclosure: R. Koto, Teijin Pharma Limited, 3; **A. Nakajima**, Teijin Pharma Limited, 3; **H. Horiuchi**, Teijin Pharma Limited, 3; **H. Yamanaka**, Teijin Pharma Limited, 5.

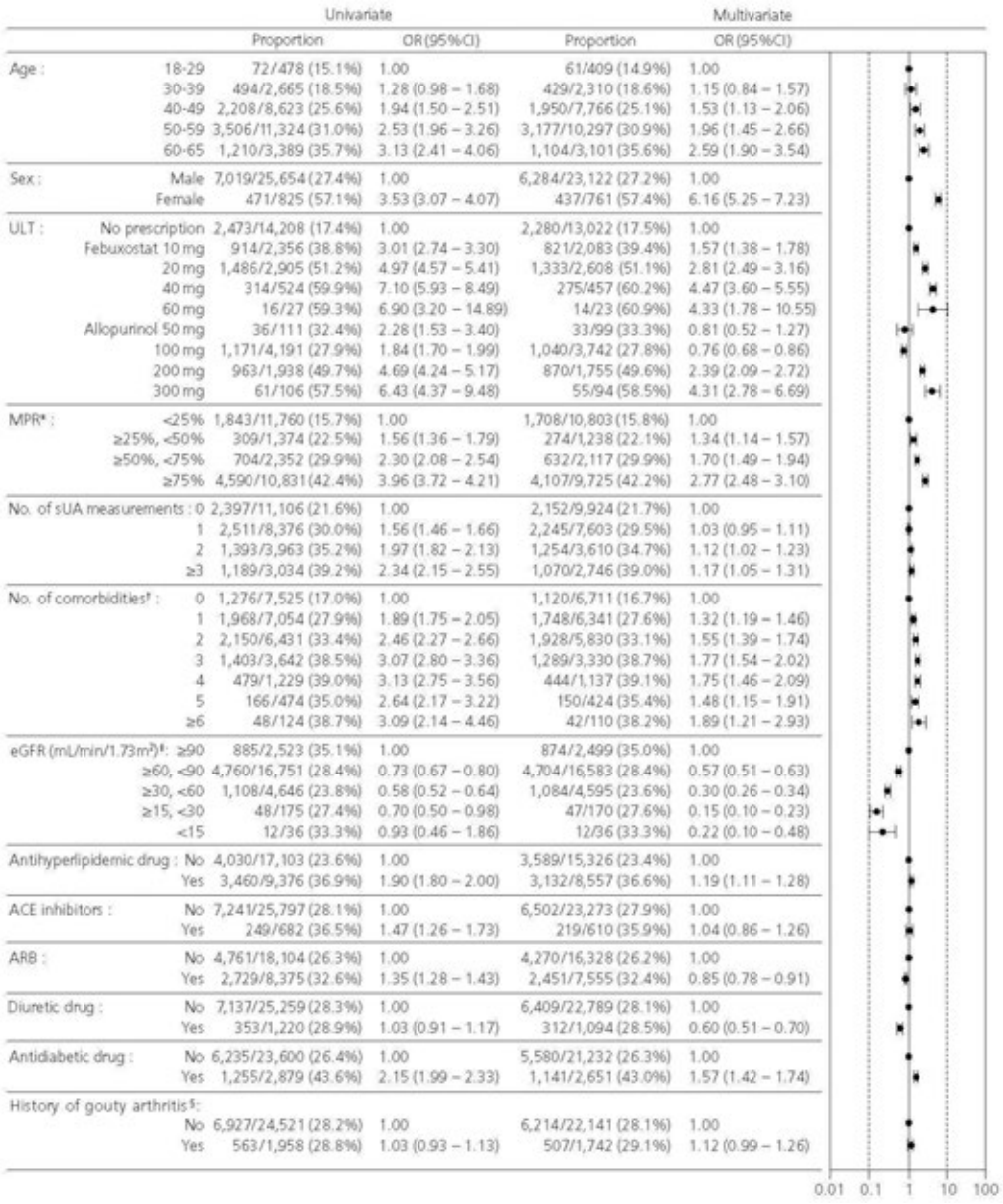

Figure 1 Factors associated with achievement of sUA target (6.0 mg/dL or below): logistic regression analysis The forest plot shows the point estimate and 95% confidence interval for the odds ratio in multivariate analysis. The objective variable was whether target sUA (6.0 mg/dL or below) had been achieved by the time of the medical check-up, and the explanatory variables were from data on sUA measurements during the 6-month period prior to the medical check-up. * MPR = Number of days ULT was prescribed from April 1, 2016 to March 31, 2017 / 365 days from April 1, 2016 to March 31, 2017 † Comorbidities: hypertension, type 2 diabetes, ischemic heart disease, heart failure, cerebrovascular disease, hyperlipidemia, renal dysfunction ‡eGFR was calculated using the following formula. eGFR (male) = 194×sCr-1.094×age-0.287, eGFR (female) = 194×sCr-1.094×age-0.287×0.739 § The most recent 6 months prior to the study period. OR, odds ratio; ULT, urate-lowering therapy; MPR, medication possession ratio; sUA, serum uric acid; eGFR, estimated glomerular filtration rate; ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker.

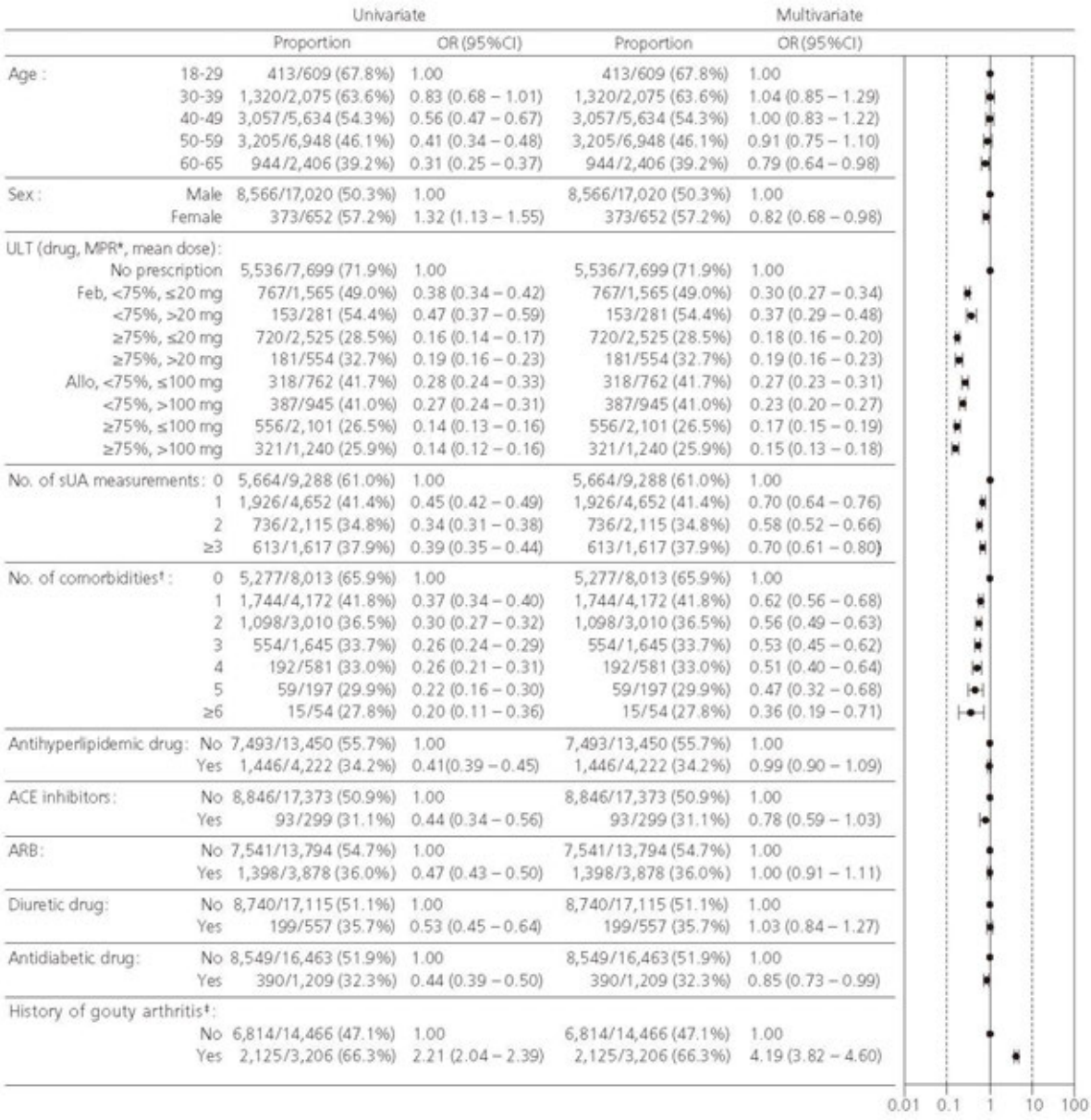

Figure 2 Factors associated with occurrence of gouty arthritis in gout patients: logistic regression analysis The forest plot shows the point estimate and 95% confidence interval for the odds ratio in multivariate analysis. The objective variable was whether gouty arthritis occurred between April 2016 and March 2017, and the explanatory variables were from data during the 6-month period between October 2015 and March 2016. * MPR = Number of days ULT was prescribed from April 1, 2016 to March 31, 2017 / 365 days from April 1, 2016 to March 31, 2017 † Comorbidities: hypertension, type 2 diabetes, ischemic heart disease, heart failure, cerebrovascular disease, hyperlipidemia, renal dysfunction ‡ The most recent 6 months prior to the study period. OR, odds ratio; ULT, urate-lowering therapy; MPR, medication possession ratio; Feb, febuxostat; Allo, allopurinol; sUA, serum uric acid ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker.

Abstract Number: 2052

Association of Traumatic Knee Injury with Knee Function, Symptoms, and Radiographic Osteoarthritis in Military Officers

Yvonne Golightly,[1] Kristin Shiue,[2] Maryalice Nocera,[3] Ali Guermazi,[4] John Cantrell,[3] Jordan Renner,[5] Darin Padua,[6] Kenneth Cameron,[7] Steven Svoboda,[7] Joanne Jordan,[8] Richard Loeser,[9] Virginia Kraus,[10] Stefan Lohmander,[11] Anthony Beutler,[12] and Stephen Marshall[3], [1]University of North Carolina at Chapel Hill Department of Epidemiology and Thurston Arthritis Research Center, Chapel Hill, NC, [2]University of North Carolina at Chapel Hill, Chapel Hill, NC, [3]University of North Carolina at Chapel Hill, Injury Prevention Research Center, Chapel Hill, NC, [4]Boston Medical Center, Boston, [5]University of North Carolina at Chapel Hill Department of Radiology, Chapel Hill, NC, [6]University of North Carolina at Chapel Hill, Department of Exercise and Sport Science, Chapel Hill, NC, [7]Keller Army Hospital, United States Military Academy, West Point, NY, [8]University of North Carolina at Chapel Hill Thurston Arthritis Research Center, Chapel Hill, NC, [9]UNC, Chapel Hill, NC, [10]Duke University School of Medicine, Durham, NC, [11]Department of Clinical Sciences Lund, Faculty of Medicine, Lund University, Lund, Sweden, Lund, Sweden, [12]Uniformed Services University, Bethesda, MD

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Traumatic knee joint injuries, such as injuries to the anterior cruciate ligament and menisci, are associated with early onset osteoarthritis (OA), but our understanding of the epidemiology of this association is limited. The effect of knee injury on patient-reported outcomes (PROs) of knee function and symptoms is understudied in military populations, despite their high risk of knee injury and knee OA. This study of a cohort of military officers examined the association of traumatic knee injury with knee function, symptoms, and radiographic OA (rOA).

Methods: Participants were recruited from an existing cohort of 6452 military officers enrolled between 2004 and 2009, at the time of their matriculation as cadets at the United States Air Force Academy, Military Academy, or Naval Academy. Officers with a history of ligament and meniscal injuries prior to, during, or after their 4-year academy career (knee injury subcohort; n=176) were compared to site-matched officers with no history of knee injury (non-injured subcohort; n=261). All participants completed a questionnaire between August 2015 and December 2017 that included PROs assessed with Knee Injury and OA Outcome Score (KOOS) scales (range 0-100=extreme to no deficits) and a single-item measure of knee symptoms (pain, aching, or stiffness in the past 30 days, 4-point Likert scale). Radiographic evidence of knee OA was evaluated using standardized fixed-flexion bilateral knee radiographs (available in n=117 injured, n=143 non-injured). These were read by a single highly-experienced musculoskeletal radiologist for Kellgren-Lawrence grade (KLG), presence of osteophytes (OST), and joint space narrowing (JSN). Data were analyzed using descriptive statistics, contingency table methods (radiographic data), and ANOVA (KOOS).

Results: Mean age was 28 years for both injured and non-injured participants; 39% were women (injured: 37%; non-injured: 40%). Mean weight was 78 kg and body mass index was 25 kg/m2. Mean time from first knee injury to follow-up assessment was 8.7 years. Among officers with a history of knee injury, 16% had knee rOA (KLG $\geq$ 2), 40% had OST, and 22% had JSN, compared to only < 1%, 9%, and 3% of non-injured participants ($p < 0.001$). Compared with non-injured participants, injured participants also had clinically relevant deficits on KOOS symptoms, KOOS pain, KOOS sports/recreation, and KOOS quality of life scales (mean score differences of -13.3, -9.6, -14.8, -19.6 respectively; all $p < 0.001$). Deficits on KOOS activities of daily living scale were also statistically significant (mean difference -4.6; $p < 0.001$) but were smaller and less clinically-relevant. Average scores on the single-item symptom scale were worse in the injured (1.1 vs. 0.4; $p < 0.001$).

TABLE 1. Mean Patient-Reported Outcome Measure Scores in Knee Injury and Non-Injured Subjects.

Patient-Reported Outcome Measure	Non-Injured Referent Subcohorts		Knee Injury Subcohort			
	All Non-Injured Subjects n=261	Non-Injured Knees of Injured Subjects n=127	All Injured Subjects n=176	Timing of Knee Injury		
				Before Academy n=79	During Academy n=73	After Academy n=24
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Single-Item Symptoms†	0.43 (0.64)	0.46 (0.68)	1.10 (0.83)	1.09 (0.83)	1.08 (0.85)	1.17 (0.82)
KOOS Subscale‡						
Symptoms	92.06 (10.86)	92.60 (10.34)	78.80 (17.82)	79.70 (17.32)	75.94 (19.04)	84.15 (14.57)
Pain	95.40 (7.77)	94.78 (9.32)	85.77 (13.55)	86.33 (13.08)	85.10 (14.58)	85.92 (12.31)
Activities of Daily Living	97.96 (5.19)	97.82 (5.59)	93.38 (10.28)	92.98 (10.38)	92.91 (11.00)	96.14 (7.23)
Sports & Recreational Activities	92.59 (13.31)	91.48 (14.74)	77.76 (22.38)	78.86 (23.19)	75.49 (22.03)	80.99 (20.84)
Quality of Life	89.05 (16.24)	88.65 (16.92)	69.48 (24.57)	71.12 (25.45)	68.26 (24.72)	67.71 (21.62)

†Knee symptoms in the past 30 days, including pain, aching, or stiffness, 4-point Likert scale
‡KOOS=Knee Injury and Osteoarthritis Outcome Score, score range 0-100=no to extreme deficits

Table 1. Mean Patient-Reported Outcome Measure Scores in Knee Injury and Non-Injured Subjects.

TABLE 2. Patient-Reported Outcome Measure Mean Differences in Knee Injury Vs. Non-Injured Subjects.

	Patient-Reported Outcome Measure	All Injured Subjects n=176			Timing of Knee Injury: Before Academy n=79			During Academy n=73			After Academy n=24		
		Mean Diff. (95% CI)		p-value	Mean Diff. (95% CI)		p-value	Mean Diff. (95% CI)		p-value	Mean Diff. (95% CI)		p-value
Non-Injured Subjects n=261	Single-Item Symptoms†	0.67	(0.53, 0.81)	<0.0001	0.66	(0.48, 0.84)	<0.0001	0.66	(0.47, 0.84)	<0.0001	0.74	(0.44, 1.04)	<0.0001
	KOOS Subscale‡												
	Symptoms	-13.26	(-15.83, -10.69)	<0.0001	-12.36	(-15.70, -9.01)	<0.0001	-16.12	(-19.62, -12.61)	<0.0001	-7.91	(-13.46, -2.36)	0.0053
	Pain	-9.63	(-11.61, -7.65)	<0.0001	-9.07	(-11.68, -6.47)	<0.0001	-10.30	(-13.00, -7.60)	<0.0001	-9.48	(-13.78, -5.18)	<0.0001
	Activities of Daily Living	-4.57	(-5.97, -3.18)	<0.0001	-4.97	(-6.80, -3.15)	<0.0001	-5.05	(-6.94, -3.15)	<0.0001	-1.82	(-4.85, 1.22)	0.2401
	Sports & Recreational Activities	-14.82	(-18.07, -11.57)	<0.0001	-13.73	(-18.00, -9.45)	<0.0001	-17.10	(-21.53, -12.67)	<0.0001	-11.60	(-18.69, -4.50)	0.0014
	Quality of Life	-19.57	(-23.30, -15.84)	<0.0001	-17.92	(-22.82, -13.03)	<0.0001	-20.79	(-25.87, -15.71)	<0.0001	-21.34	(-29.47, -13.21)	<0.0001
Non-Injured Knee of Unilateral-Injured Subjects n=127	Single-Item Symptoms†	0.63	(0.47, 0.80)	<0.0001	0.62	(0.42, 0.83)	<0.0001	0.62	(0.41, 0.82)	<0.0001	0.70	(0.39, 1.02)	<0.0001
	KOOS Subscale‡												
	Symptoms	-13.80	(-16.87, -10.73)	<0.0001	-12.89	(-16.63, -9.15)	<0.0001	-16.65	(-20.54, -12.77)	<0.0001	-8.44	(-14.24, -2.64)	0.0044
	Pain	-9.01	(-11.36, -6.66)	<0.0001	-8.45	(-11.35, -5.56)	<0.0001	-9.68	(-12.66, -6.70)	<0.0001	-8.86	(-13.34, -4.38)	0.0001
	Activities of Daily Living	-4.44	(-6.11, -2.77)	<0.0001	-4.84	(-6.88, -2.80)	<0.0001	-4.91	(-7.02, -2.81)	<0.0001	-1.68	(-4.85, 1.49)	0.2973
	Sports & Recreational Activities	-13.72	(-17.62, -9.81)	<0.0001	-12.62	(-17.41, -7.83)	<0.0001	-16.00	(-20.92, -11.07)	<0.0001	-10.49	(17.91, -3.07)	0.0057
	Quality of Life	-19.17	(-23.61, -14.74)	<0.0001	-17.52	(-22.98, -12.07)	<0.0001	-20.39	(-26.01, -14.77)	<0.0001	-20.94	(-29.42, -12.46)	<0.0001

CI=Confidence Interval; KOOS=Knee Injury and OA Outcome Score
†Knee symptoms in the past 30 days, including pain, aching, or stiffness, 4-point Likert scale
‡KOOS score range 0-100=no to extreme deficits

Table 2. Patient-Reported Outcome Measure Mean Differences in Knee Injury Vs. Non-Injured Subjects.

TABLE 3. Radiographic Evidence of Osteoarthritis in Knee Injury and Non-Injured Subjects.

Radiographic Measure Of Knee OA	Non-Injured Referent Subcohorts		Knee Injury Subcohort			
	All Non-Injured Subjects n=143	Non-Injured Knees of Injured Subjects n=92	All Injured Subjects n=117	Timing of Knee Injury		
				Before Academy n=49	During Academy n=51	After Academy n=17
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
rOA (KLG ≥ 2)						
Absent	142 (99)	92 (100)	98 (84)	42 (86)	41 (80)	15 (88)
Present	1 (1)	0 (0)	19 (16)	7 (14)	10 (20)	2 (12)
Osteophytes						
Absent	130 (91)	81 (88)	70 (60)	28 (57)	30 (59)	12 (71)
Present	13 (9)	11 (12)	47 (40)	21 (43)	21 (41)	5 (29)
Joint Space Narrowing						
Absent	139 (97)	86 (93)	91 (78)	41 (84)	35 (69)	15 (88)
Present	4 (3)	6 (7)	26 (22)	8 (16)	16 (31)	2 (12)

rOA=Radiographic Osteoarthritis; KLG=Kellgren-Lawrence Grade

Table 3. Radiographic Evidence of Osteoarthritis in Knee Injury and Non-Injured Subjects.

Conclusion: At the midpoint of an anticipated 20-year military career, officers with a history of ACL/meniscal injury have deficits in knee-related symptoms, QOL, and knee function. Approximately 1 in 6 officers with prior knee injury progressed to rOA before mean age 30. This progression rate is highly concerning given the physically-demanding nature of their profession and their young age.

Disclosure: Y. Golightly, None; **K. Shiue**, None; **M. Nocera**, None; **A. Guermazi**, AstraZeneca, 5, BICL, 1, Boston Imaging Core Lab (BICL), 1, Galapagos, 5, MerckSerono, 5, Pfizer, 5, Roche, 5, Shareholder BICL,LLC, 1, Tissue-Gene, 5; **J. Cantrell**, None; **J. Renner**, None; **D. Padua**, None; **K. Cameron**, None; **S. Svoboda**, None; **J. Jordan**,

None; **R. Loeser**, Bioventus, 5; **V. Kraus**, None; **S. Lohmander**, Pfizer, 8, Roche, 5, GSK, 5, Johnson & Johnson, 5, Galapagos, 5, Regeneron, 5; **A. Beutler**, None; **S. Marshall**, None.

Abstract Number: 2053

Risk of Non-vertebral Fracture in Gout Compared to Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Table 1. Baseline characteristics of study papulations in the 365 days before study entry

Variable	Gout (n=134,157)	RA (n=134,157)
Demographics*		
Age, year, mean (SD)	73.69 (6.52)	73.69 (6.52)
Female	94,456 (70.41)	94,456 (70.41)
Race, white	99,924 (74.48)	115,625 (86.19)
Osteoporotic fracture related comorbidities		
BMD test	13,922 (10.38)	33,274 (24.80)
Prior fall	5,953 (4.44)	5,810 (4.33)
Osteoporosis	16654 (12.41)	44135(32.90)
Obesity	23,598 (17.59)	9,802 (7.31)
Prior fracture†	2,649 (1.97)	3,426 (2.55)
Prior hip fracture†	753 (0.56)	1,246 (0.93)
Other comorbidities		
Comorbidity score, mean (SD)	2.03 (2.66)	1.03 (1.93)
Alcoholism	581 (0.43)	278 (0.21)
Dementia	8,879 (6.62)	8,172 (6.09)
Parkinson	1,602 (1.19)	1,772 (1.32)
Coronary heart diseases	55,635 (41.47)	39,839 (29.70)
COPD	38,012 (28.33)	35979 (26.82)
DM	67,909 (50.62)	37,643 (28.06)
Heart failure	33,290 (24.81)	14,758 (11.00)
Hypertension	126,632 (94.39)	101,379 (75.57)
Chronic Kidney diseases	46,420 (34.60)	13829 (10.31)
Stroke	24,349 (18.15)	18,855 (14.05)
Frailty index		
Robust, <0.15	35,902 (26.76)	41,942 (31.26)
Prefrail, 0.15-0.24	81,216 (60.54)	81,327 (60.62)
Mildly, 0.25-0.34	15,975 (11.91)	10,389 (7.74)
Moderate to severe, ≥0.35	1,064 (0.79)	499 (0.37)
Osteoporosis medication		
Bisphosphonate	10,061 (7.50)	29,866 (22.26)
PTH	191 (0.14)	941 (0.70)
Calcitonin	573 (0.43)	1,183 (0.88)
Denosumab	411 (0.31)	1,401 (1.04)
Raloxifene	1,640 (1.22)	2,294 (1.71)
Teriparatide	191 (0.14)	941 (0.70)
Other medications		
Prior cumulative dose of prednisolone equivalent, mg, mean (SD)	160.57 (540.52)	673.19 (1,096.69)
0	93,110 (69.40)	59,863 (44.62)
>0 and ≤224	20,503 (15.28)	12,786 (9.53)
>224	20,544 (15.31)	61,508 (45.85)
Steroid injection	10,357 (7.72)	18,893 (14.08)

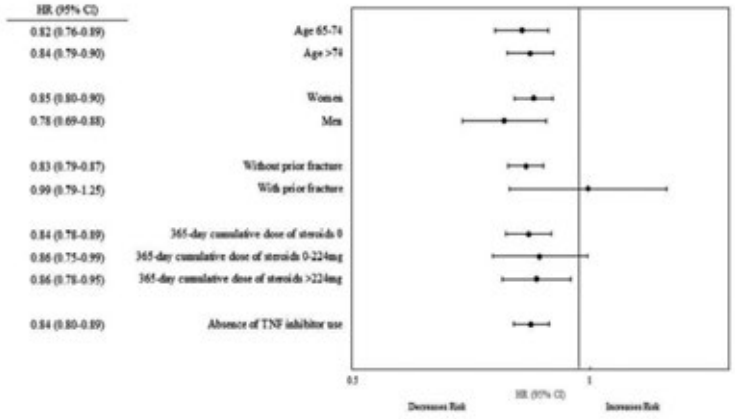
Table 2. Risk of non-vertebral or hip fracture in the gout group compared with the RA group

Adjustment	Hazard ratio (95% CI)
Non-vertebral fracture	
Model 1	0.69 (0.66-0.72)
Model 2	0.78 (0.75-0.82)
Model 3	0.75 (0.72-0.79)
Final model	0.84 (0.80-0.88)
Hip fracture	
Model 1	0.62 (0.59-0.66)
Model 2	0.72 (0.67-0.76)
Model 3	0.68 (0.64-0.73)
Final model	0.76 (0.71-0.82)

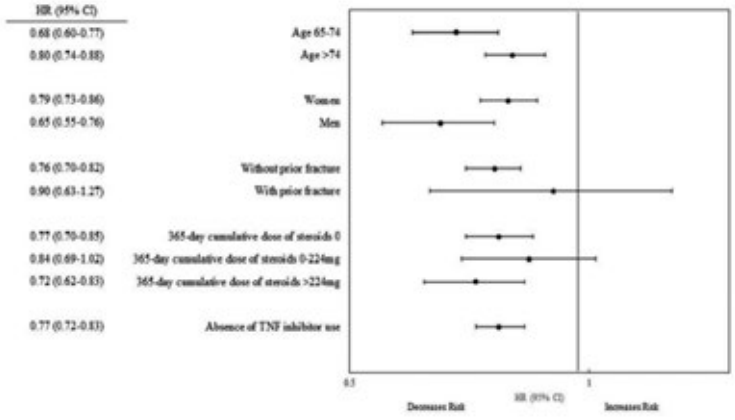
Model 1: Age, sex-adjusted
Model 2: Calendar year, bone mineral density test, Fall, obesity, prior fracture, bisphosphonates, use of non-bisphosphonate osteoporosis medications, recent use of steroids, and 365-day cumulative dosage of steroids in addition to model 1
Model 3: Race, frailty index, comorbidity index, and number of different prescriptions in addition to model 2
Final model: All other comorbidities, medication use, and intensity of health care utilization in addition to model 3

Figure. Risk of fracture in the gout group compared with the RA group according to stratification

A. Non-vertebral fracture



B. Hip fracture



Background/Purpose: Gout is a common inflammatory arthritis, characterized by hyperuricemia leading to crystallization of uric acid in joints. Proinflammatory cytokines have been known as an increasing factor for osteoporotic fractures, and chronic inflammatory diseases such as rheumatoid arthritis (RA) are considered to be a risk factor for

osteoporosis and fractures. However, association between hyperuricemia and osteoporotic fractures, and relationship between gout and osteoporotic fractures has shown conflicting results. We hypothesized that older patients with gout would have a similar risk of osteoporotic fracture compared with older patients with RA.

Methods: Using claims data from Medicare Parts A/B/D (2008-2015), we conducted a cohort study. We selected gout with ≥2 diagnosis codes and ≥1 dispensing for gout treatment. Similarly, RA were identified with ≥2 diagnosis codes and ≥1 dispensing for disease-modifying antirheumatic drugs. Gout patients were 1:1 matched to RA patients on age, sex, and index date. The primary outcome was non-vertebral fractures, a composite endpoint of humerus, wrist, pelvis or hip fracture, based on previously validated claims-based algorithms (PPV > 93%). The secondary outcome was hip fracture. We calculated the incidence rate (IR) of non-vertebral fracture and hip fracture in each group. Cox proportional hazards regression estimated the hazard ratio (HR) with 95% confidence intervals (CI) for the primary and secondary outcomes in gout versus RA, adjusting for 45 baseline risk factors for osteoporosis.

Results: We included a total of 134,157 matched pairs of gout and RA patients with mean age of 73.7 years. 70.4% were female. Risk factors of osteoporotic fracture such as receipt of a bone mineral density test, diagnosis of osteoporosis, prior fracture, use of osteoporosis medication, and steroid use were more prevalent in RA than gout. However, other comorbidities including obesity, coronary heart disease, heart failure, hypertension, hyperlipidemia, diabetes, and chronic kidney disease were more frequently noted in gout than RA (**Table 1**). Over the mean 2.8-year follow up, the IR per 1,000 person-year (PY) of non-vertebral fractures was 10.42 in gout and 15.01 in RA, and the IR per 1,000 PY of hip fracture was 4.86 in gout and 7.73 in RA. The IR of non-vertebral fractures was more than twofold higher in patients aged ≥75 years than patients aged 65-74 years, and about threefold higher in the patients with prior fracture than the patients without prior fracture in both groups. Multivariable HR associated with gout versus RA was 0.84 (95% CI 0.80-0.88) for non-vertebral fractures and 0.76 (95% CI 0.71-0.82) for hip fractures (**Table 2**). Subgroup analyses by age, sex, history of prior fractures, 365-day cumulative dose of steroids and absence of TNF inhibitor use showed similar results (**Figure**).

Conclusion: In this large cohort of older patients enrolled in Medicare, the absolute rate of non-vertebral fractures or hip fractures was high in both gout and RA. However, gout was associated with a decreased risk of non-vertebral and hip fractures regardless of age, sex, steroid use and prior fracture, compared to RA.

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Abstract Number: 2054

Epidemiology of Gout in South Korea with the National Health Insurance Corporation Database

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Table 1 Gout prevalence per 100,000 people per year and the gender ratio in 2002-2015

	Prevalence per 100,000			
year	total	male	female	Sex ratio
2002	388	588	193	3.0
2003	491	745	244	3.1
2004	569	876	270	3.2
2005	655	1,020	300	3.4
2006	743	1,169	326	3.6
2007	817	1,301	344	3.8
2008	918	1,460	389	3.8
2009	1,009	1,609	424	3.8
2010	1,143	1,813	490	3.7
2011	1,259	1,989	547	3.6
2012	1,428	2,223	653	3.4
2013	1,656	2,500	833	3.0
2014	1,801	2,727	899	3.0
2015	2,005	3,026	1,009	3.0

Background/Purpose: Gout is the most common inflammatory arthritis that results from chronic elevation of uric acid levels above the saturation point for monosodium urate crystal formation. However, data on gout incidence, prevalence and management, are sparse, especially in Korean populations. We reevaluated the recent prevalence and incidence of gout in Korean people after our previous study in 2011 (1).

Methods: The National Health Insurance Corporation (NHIC) Database was used to identify patients with gout. We selected the gout patients who were coded as having gout (KCD M10.0) from main diagnosis to 4th additional diagnosis. And we estimated the prevalence (from 2002 to 2015) and the incidence (from 2006 to 2015) for each calendar year.

Results: Prevalence of gout was 0.39% in 2002 and 2.00% in 2015. There was a 5.17 fold increased during over 13 years. Prevalence have increased at all ages, especially at the age of 80 and over. Also, incidence per 100,000 was 361 in 2006 and 797 in 2015, there was 2.21 fold increased during over 10 years. Sex ratio (male:female) was 3.0~3.8:1. When monthly incidence was examined, except for December, it increased as the day warmed and peaked in July and August. In the southern provinces, especially Busan, prevalence and incidence were high. Of those diagnosed with gout in 2012, a total of 30% of those who had been prescribed uric acid lowering agent (allopurinol or febuxostat or benzbromarone) within three years.

Conclusion: In Korea, prevalence and incidence of gout are rapidly increasing. Incidence was higher for males, for older age, for warmer days, and for southern regions. Management of gout in Korea is poor, with only three in ten affected people who have ever been treated with uric acid lowering therapy.

Disclosure: J. Park, None; **J. Song**, None; **M. Kang**, None; **C. Lee**, None.

Abstract Number: 2055

High Dietary Sodium Intake May Be Associated with Symptomatic Knee Osteoarthritis in a Korean Population: Korean National Health and Nutrition Examination Survey, 2010-2011

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Table 1. Comparisons of nutritional indices between subjects with and without symptomatic knee osteoarthritis (KOA)

	Subjects with symptomatic KOA (n = 2,193,783)	Subjects without symptomatic KOA (n = 10,711,213)	*p* value
Total energy intake	1718.6 ± 23.6	2012.1 ± 15.6	<0.001
Daily sodium intake	3198.6 ± 77.8	3809.0 ± 46.1	<0.001
Daily potassium intake	2938.8 ± 56.7	3270.2 ± 32.8	<0.001
The estimated 24-hour sodium excretion*	3353.3 ± 25.9	3255.5 ± 14.6	0.001

Data were described as mean ± SE
*Calculated by Tanaka equation

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A high sodium intake has been reported to adversely affect bone health and to be associated with an increased inflammatory response. However, the relationship between dietary sodium intake and OA has not been established. This study aimed to analyze the association between sodium intake and OA in Korean population using the fifth Korean National Health and Nutrition Examination Survey (KNHANES V).

Methods: We included participants aged 50 to 75 years who completed urinary sodium evaluation, plain knee radiographs, health interview and nutritional surveys in the 2010 to 2011 KNHANES V. Knee OA (KOA) was defined as the presence of radiographic features of Kellgren-Lawrence grade ≥2. We used the Tanaka formula to estimate 24-hour urinary sodium excretion from a fasting morning specimen as a surrogate for daily sodium intake. All of the statistical analyses were performed on the basis of a sampling weight to represent the entire Korean population. The association between symptomatic KOA and the dietary indices was statistically analyzed using univariate and multivariate logistic regression methods.

Results: Among study population, 10.5% (weighted n=1,214,665/11,610,574) had symptomatic KOA, of which 80.7% was female. Of the total, 86.8% of study participants had sodium intake levels well above the recommendation of World Health Organization (2,000 mg of sodium per day). Compared to the non-KOA group, the KOA group was older, more obese, less educated, and less earned. The percentages of subjects with depression or taking antihypertensive medications, and non-smokers in KOA were higher than those in non-KOA. Although total energy intake in KOA group was lower than in non-KOA group, the mean estimated 24-hour urinary sodium excretion level in KOA group was significantly higher than in non-KOA group. After adjusting for covariates, the statistical significance of the estimated 24-hour urinary sodium excretion was lost in total participants. However, subgroup analysis in subjects with high sodium intake (daily sodium intake ≥2,000 mg) demonstrate that 24-hr urinary sodium excretion was positively associated with symptomatic KOA even after adjustment with confounding factors (Odds ratio 1.165, 95% confidence interval 1.019-1.331, $p < 0.001$).

Conclusion: The present study suggested that sodium intake levels could be dose-dependently associated with symptomatic knee OA in subjects consuming dietary salt intake ≥2,000 mg/day.

Disclosure: Y. Ha, Seoul National University Bundang Hospital, 3; **E. Ji**, None; **E. Park**, None; **E. Kang**, Seoul National University Bundang Hospital, 3; **Y. Song**, Astellas Pharma, Inc., 9; **Y. Lee**, Seoul National University Bundang Hospital, 3.

Abstract Number: 2056

Opioids Use Among Medicare Beneficiaries with Knee Osteoarthritis: Prevalence and Correlates of Chronic Use

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) of the knee is prevalent among Medicare beneficiaries. Effective pain control is critical for managing this chronic disease. In the last decade, opioids became widely available for persons with knee OA. We sought to identify knee OA patients that use opioids chronically and occasionally, and determine factors associated with greater risk of occasional and chronic opioid use among knee OA patients ≥ 65years of age.

Methods: We used the Medicare Beneficiary Survey (MCBS) of a nationally representative sample of Medicare beneficiaries administered in 2015. MCBS survey data are linked to Medicare claims. We selected a knee OA cohort from community-dwelling MCBS respondents age ≥ 65 who had at least one outpatient visit in Medicare Parts A or B with an ICD-10-CM code of a) M17.9 or b) M25.569 (Pain in unspecified knee) plus M15.x or M19.90. We obtained data on demographics, smoking, marital status, comorbidities and prescribed medications from survey data and claims. We included all prescribed medication records classified as opioids under the First Databank therapeutic analgesics category. We stratified knee OA subjects into three opioid use groups: 1) none, 2) occasional (1-5 prescriptions/year), 3) chronic (6+ prescriptions/year). We built several multivariable logistic regression models to determine independent correlates of any opioid use vs non-use; chronic vs. non-use and chronic vs. occasional use.

Results: We identified a cohort of 620 persons with knee OA. Mean age was 78.5 (SD 7.3), 65% were female. 31% of the cohort had at least one opioid prescription during 2015. 10% of the overall cohort were identified as chronic opioid users, and 21% of the overall cohort as occasional users. Multivariable analyses that compared any opioid use to no use identified several patient features associated with greater risk of opioid use: ≥ 1 fall in the prior year (OR 1.96, 95% CI 1.16-3.30; ≥ 2 comorbidities (OR 2.62, 95% CI: 1.30, 5.29) and use of NSAIDS (OR 3.74, 95% CI: 2.09-6.71). Married beneficiaries had 0.50 odds of using opioids compared to those who were not married (95% 0.30-0.84). When we compared chronic opioid users to no users, features associated with chronic use included low household income (< 30K/annually; OR 6.13, 95% CI: 2.39-15.7; ≥ 2 comorbidities (OR 3.27, 95% CI: 1.25-8.55) and NSAID use (OR 2.77, 95% CI: 1.14-6.71). Comparing chronic users with occasional opioid users, features associated with chronic use included low income (OR 6.15, 95% CI: 2.04-18.44) and current smoking (OR 5.83, 95%CI: 1.15-29.45).

Conclusion: Over 30% of Medicare beneficiaries with knee OA use opioids and 10% use them chronically. Low income, NSAID use and higher burden of comorbidities are associated with greater risk of opioid use, while marriage was associated with lower risk of use. The causal relationship between prior falls, low income and marital status and risk of current opioid use requires further study. Efforts to find non-opioid regimens for knee OA would be especially useful for patients with risk factors identified in this study.

Disclosure: E. Losina, Flexion, 2, Flexion Therapeutics, 2, Pfizer, 2, Pfizer Inc, 2, Regeneron, 5, Regeneron Pharmaceuticals, 5, Roche/Genentech, 2, Samumed, 2, TissueGene, 2, Velocity, 5, Velocity Pharaceutical Development, 5, Velocity Pharmaceutical Development, 5; **S. Song**, None; **J. Katz**, Flexion, 2, Flexion Therapeutics, 2, Samumed, 2.

Abstract Number: 2057

Cross-sectional Associations of Multiple Joint Osteoarthritis in the Osteoarthritis Initiative

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

	Total	No MJOA	MJOA		Adjusted**
Variable	(n=3325)	(n=2392)	(n=933)	PR* (95% CI)	PR* (95% CI)
Demographics					
Age, years	60.9 (9.1)	58.6 (8.6)	66.7 (7.4)	**1.96 (1.86, 2.06)**	
Gender (n, %)					
Male	1438 (43.3)	1067 (44.6)	371 (39.8)	(ref)	
Female	1887 (56.8)	1325 (55.4)	562 (60.2)	**1.15 (1.03, 1.29)**	
Race (n, %)					
White	2731 (82.1)	1944 (81.3)	787 (84.4)	(ref)	
Black	513 (15.4)	387 (16.2)	126 (13.5)	0.85 (0.72, 1.00)	
Hispanic	81 (2.4)	61 (2.6)	20 (2.1)	0.86 (0.58, 1.26)	
BMI	28.2 (4.6)	28.0 (4.7)	28.7 (4.3)	**1.13 (1.07, 1.19)**	
WC > cutpoint (n, %)	2380 (73.5)	1625 (70.4)	755 (81.2)	**1.56 (1.35, 1.80)**	1.05 (0.89, 1.23)
BMD					
Baseline average cortical thickness (digits 2-5)	1.50 (0.28)	1.53 (0.28)	1.44 (0.30)	**0.80 (0.75, 0.85)**	**1.08 (1.01, 1.16)**
<65 years old					**0.85 (0.75, 0.97)**
65+ years old					1.02 (0.95, 1.11)
Femoral Neck BMD (g/cm2)	0.963 (0.147)	0.976 (0.137)	0.945 (0.159)	**0.88 (0.79, 0.99)**	1.09 (0.99, 1.20)
Medical History					
Comorbidity score	0.35 (0.82)	0.33 (0.80)	0.42 (0.86)	**1.07 (1.03, 1.12)**	
HTN (n, %)	1634 (49.1)	1061 (44.4)	573 (61.4)	**1.65 (1.47, 1.84)**	1.04 (0.92, 1.16)
Lipid disorder (n, %)	934 (28.1)	627 (26.2)	307 (32.9)	**1.26 (1.12, 1.41)**	0.94 (0.84, 1.04)
Diabetes (n, %)	209 (6.4)	135 (5.8)	74 (8.1)	**1.29 (1.06, 1.56)**	0.96 (0.80, 1.15)
Metabolic syndrome (n, %)					
None	452 (14.2)	380 (16.8)	72 (7.9)	(ref)	(ref)
1 criteria met	1119 (35.2)	847 (37.4)	272 (29.8)	**1.53 (1.21, 1.93)**	1.06 (0.85, 1.32)
2 criteria met	1015 (32.0)	668 (29.5)	347 (38.1)	**2.15 (1.71, 2.70)**	1.07 (0.85, 1.34)
3+ criteria met	591 (18.6)	370 (16.3)	221 (24.2)	**2.35 (1.85, 2.97)**	1.00 (0.78, 1.27)

Table 1 Cross-sectional associations of MJOA

Background/Purpose: Multiple joint osteoarthritis (MJOA) may represent a unique phenotype of osteoarthritis related to systemic factors associated with pathologic aging. We tested the hypothesis that metabolic syndrome and its components, frailty and its components and lower levels of bone density are associated with MJOA.

Methods: Participants in the Osteoarthritis Initiative (N=3325) had hand, hip and knee xrays performed and centrally read for osteoarthritis. Hand osteoarthritis (OA) was defined as at least one joint with Kellegren-Lawrence(KL) $\geq$2 on at least two rays; Hip OA was defined as modified Croft grade $\geq$2 in ether hip; Knee OA was defined as KL $\geq$2 in either knee. MJOA was defined as hand OA and either hip or knee OA. A metabolic syndrome score was developed based upon the presence of hypertension, diabetes, lipid disorder, and increased waist circumference. Frailty was defined as one positive on the Song Frailty index and evaluating waking speed, chair stands and self-reported energy. Cortical thickness of metacarpal bones digits 2-4 and femoral bone density (FMD) in a smaller sub-sample based upon DEXA estimated the effect of bone mineral density (BMD). Prevalence ratios and 95% confidence intervals were estimated using poisson regression.

Results: Of the 3325 participants, 933 had MJOA and 2392 did not. The average age of the analytic cohort was 60.9 years, 56.8% were female, 82.1% were white, 15.4% were black and 2.4% were hispanic, and 11% had incomes < $25,000. Age, female gender, BMI, abdominal circumference, hypertension, lipid disorder, diabetes, metabolic syndrome score, Song Frailty index, slow walking speed, using hands during chair stands were associated with higher prevalence of MJOA. Higher levels of physical activity,bone mineral density, walking speed, chair stand pace, extensor and flexor strength of lower extremities were inversely associated with MJOA. In multiple variate analysis adjusting for age, gender, and BMI metabolic syndrome and its components were no longer associated with MJOA, thinner cortical thickness was only associated with MJOA in those < 65 years of age, and only slow walking speed as a measure of Frailty was associated with MJOA. Faster chair stand pace and dominant lower extremity extensor strength remained inversely associated with MJOA. (See Table 1)

Conclusion: Age is a strongly associated with MJOA. Low bone density as measured by metacarpal cortical thickness at age less than 65, impaired walking speed, lower chair stand pace, decreased lower extremity extensor strength may reflect pathologic aging and are associated with MJOA in this cross-sectional analysis. Prospective analysis and exploring the underlying pathobiologic pathways associated with impaired BMD and muscle strength could lead to effective prevention and treatments of MJOA.

Disclosure: C. Eaton, None; **M. Roberts**, None; **J. Driban**, None; **M. Nevitt**, None; **J. Duryea**, None; **T. McAlindon**, None.

Abstract Number: 2058

Pharmacoepidemiology of Gout Treatment in Office-based Outpatient Care from 2009- 2016

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SESSION INFORMATION
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Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
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	Pharmacological treatment		Total	*P*-value
	No	Yes		
Sample size				
Unweighted sample	221	606	827	
Weighted visits	847,505	2,513,973	3,361,479	
Age				
18-44	6.8	11.74	10.5	0.574
45-64	43.7	38.6	39.9	
65-74	28.5	24.0	25.1	
75-84	15.1	18.7	17.8	
≥85	5.9	7.0	6.7	
Gender				
Female	31.6	21.0	23.7	0.044
Male	68.4	79.0	76.3	
Race/ethnicity				
Non-Hispanic White	63.0	74.2	71.4	0.116
Non-Hispanic Black	15.1	11.2	12.2	
Hispanic	16.5	7.0	9.4	
Other[a]	5.4	7.6	7.0	
Primary source of payment				
Private	48.6	46.9	47.3	0.990
Medicare	45.0	46.5	46.1	
Medicaid	2.8	3.2	3.1	
Other[b]	3.6	3.5	3.5	
Region				
Northeast	11.2	18.1	16.4	0.132
Midwest	15.5	23.4	21.4	
South	48.8	35.4	38.8	
West	24.5	23.1	23.5	
Reason for visit				
Acute problem	17.5	27.5	25.1	0.005
Routine chronic problem	55.8	63.1	61.3	
Physician specialty				
Primary care	67.9	67.7	67.7	0.979
Other[c]	32.1	32.3	32.3	
Office setting				
Private or group practice	94.2	87.0	88.8	0.030
Other	5.8	13.0	11.2	
Repeat of visits in the past 12 months				
0 visit	3.8	4.9	4.6	0.898
1-2 visits	31.7	33.7	33.2	
3-5 visits	44.7	40.2	41.3	
6+ visits	19.8	21.3	20.9	
Concomitant medications prescribed				
None	33.1	0.0	8.4	<0.001
1	15.3	10.8	11.9	
2-5	32.5	42.3	39.8	

[a] Asian, American Indian and Alaska Native, Native Hawaiian or Other Pacific Islander, or >2 reported racial or ethnic groups.

[b] Worker's compensation, self-pay, no charge, and others.

[c] Obstetrics and gynecology, cardiology, dermatology, urology, neurology, ophthalmology, otolaryngology, and others.

Table 1 Selected characteristics (weighted column %) of patients with gout by pharmacological treatment in office-based outpatient care visits

Background/Purpose: Studies show that gout treatment remains suboptimal in the United States (US). Despite clear benefits for urate-lowering therapy (ULT) for chronic gout, surveyed physicians in the US are less likely to continue prescribing ULT after the first prescription. Prophylactic therapy was also infrequently prescribed concurrently with initial ULT. Our study investigates rates and trends of pharmacological treatments for gout in ambulatory office-base care from 2009 to 2016, along with factors associated with use.

Methods: We used data from 2009-2016 National Ambulatory Medical Care Surveys (NAMCS), a nationally representative sample of US office-based outpatient care. We included visits in which gout was diagnosed among adults age 18 or older (n=827 unweighted). We estimated prevalence and trends from 2009 to 2016 for the following medication classes for pharmacological treatments of gout: non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, oral steroids, ULT, and opioids. Using a multivariable-adjusted logistic regression analysis, we examined associations between demographic and clinical characteristics and pharmacological treatments for gout.

Results: Between 2009-2016, there were 827 gout-diagnosed outpatient visits, representing 2.5 million office-based visits. Medication prescriptions occurred in 74.8% of these visits. Patients receiving prescriptions were predominantly aged 45 or older, male, and non-Hispanic white. When stratified by medication class, prescribing of opioids

	Years (%)				Overall	Trends (2009-2016)		
	2009-2010	2011-2012	2013-2014	2015-2016		OR	95% CI	*P*-value
Visits in which any gout-related medication prescribed	76.3%	69.4%	72.7%	80.1%	74.8%	1.08	0.76, 1.53	0.671
Stratified by physician specialty								
Primary care	74.8%	68.9%	72.9%	82.5%	74.7%	1.14	0.76, 1.71	0.528
Cardiovascular and orthopedic	83.8%	52.1%	46.2%	30.6%	61.4%	0.44	0.25, 0.78	0.005
Other[a]	78.8%	73.5%	81.1%	80.3%	78.5%	1.10	0.47, 2.55	0.831
Stratified by medication class								
Opiates[b]	9.1%	14.8%	17.8%	34.7%	19.2%	1.73	1.04, 2.88	0.034
Non-steroidal anti-inflammatory drugs[c]	26.4%	20.4%	22.5%	20.4%	22.5%	0.91	0.67, 1.24	0.552
Colchicine	25.5%	15.7%	27.2%	32.3%	25.3%	1.18	0.74, 1.87	0.485
Oral steroids[d]	10.7%	13.6%	17.3%	27.5%	17.3%	1.48	1.04, 2.08	0.028
Urate lowering therapy[e]	39.8%	41.9%	49.3%	49.5%	45.1%	1.16	0.92, 1.45	0.204
Sample Size						Total		
Unweighted sample	159	299	300	69		827		
Weighted visits	886,642	800,673	807,998	866,166		3,361,479		

[a] Obstetrics and gynecology, pediatrics, dermatology, urology, neurology, ophthalmology, otolaryngology, and others.
[b] Codeine, meperidine, methadone, alfentanil, hydromorphone, morphine, oxycodone, pentazocine, propoxyphene, sufentanil, opium, levorphanol, oxymorphone, butorphanol, nalbuphine, buprenorphine, hydrocodone, dihydrocodeine, remifentanil, tapentadol, tramadol, and their combined products
[c] Aspirin, diclofenac, ibuprofen, indomethacin, ketoprofen, ketorolac,naproxen, phenylbutazone, piroxicam, and tolmetin
[d] Prednisone, Methylprednisolone, Dexamethasone, Prednisolone, betamethasone
[e] allopurinol, febuxostat, probenecid, lenisurad, pegloticase

Table 2 National prescribing trends for gout treatment among adults with gout in office-based outpatient care visits

Characteristics *(Reference group in parenthesis)*	AOR	95% CI	*P*-value
Age (65-74)			
75-84	0.54	0.20, 1.46	0.223
85+	0.30	0.11, 0.85	0.023
Gender (Female)			
Male	2.36	1.20, 4.65	0.013
Race/ethnicity (Non-Hispanic White)			
Non-Hispanic Black	0.50	0.23, 1.10	0.084
Hispanic	1.11	0.34, 3.65	0.860
Other[a]	2.07	0.68, 6.29	0.199
Primary source of payment (Private)			
Medicare	1.38	0.67, 2.84	0.376
Medicaid	0.50	0.08, 3.15	0.458
Other[b]	1.00	0.23, 4.43	0.997
Repeat of visits in the past 12 months (Never)			
1-2 visits	0.66	0.19, 2.28	0.508
3-5 visits	0.76	0.22, 2.66	0.668
6+ visits	1.15	0.31, 4.34	0.833
Reason for visit (Acute problem)			
Routine chronic problem	0.50	0.22, 1.14	0.099
Pre- or post-surgery	0.12	0.02, 0.70	0.018
Physician specialty (Primary care)			
Cardiovascular or orthopedic	0.68	0.30, 1.51	0.339
Other[c]	1.78	0.78, 4.07	0.171
≥4 chronic conditions (< 4)	0.83	0.41, 1.71	0.619
≥6 medications (<6)	5.93	2.74, 12.82	<0.001
Office setting (Other)			
Private or group practice	0.39	0.16, 0.98	0.044

[a] Asian, American Indian and Alaska Native, Native Hawaiian or Other Pacific Islander, or ≥2 reported racial or ethnic groups.
[b] Worker's compensation, self-pay, no charge, and others.
[c] Obstetrics and gynecology, cardiology, dermatology, urology, neurology, ophthalmology, otolaryngology, and others.

Table 3 Multivariable-adjusted analysis of factors associated with gout-related medication prescribing among adults with gout in office-based outpatient care visits

has monotonically increased from 9.1% in 2009-2010 to 34.7% in 2015-2016 (odds ratio [OR] for trends=1.73; 95% CI=1.04, 2.88); prescribing of oral steroids similarly increased from 10.7% in 2009-2010 to 27.5% in 2015-2016 (OR for trends=1.48; 95% CI=1.04, 2.08). Over the same period, prescription of ULT remained steady OR=1.16; 95% CI=0.92, 1.45). Patient factors independently associated with a higher likelihood of prescribing medications for gout were being male (adjusted odds ratio [AOR]=2.36; 95% CI=1.20, 4.65) and those with six or more medications concomitantly prescribed (AOR=5.93; 95% CI=2.74, 12.82). Studied medications were also less likely prescribed during visits pre and post surgery (AOR=0.12; 95%CI=0.02, 0.70).

Conclusion: Opioids and oral steroids were increasingly prescribed at initial gout visits while prescriptions of ULT and colchicine were unchanged over time. This suggests a concerning trend toward use of opiates in gout patients. Also, despite surgical intervention being a risk factor for gout flare, ULT may be underutilized in this population. Overall, our findings support the need for better understanding of optimal gout treatment among US clinicians and further research is needed to support improved treatment of gout.

Disclosure: Y. Chock, None; **J. Ross**, Johnson & Johnson, 2; **L. Suter**, None; **T. Rhee**, None.

Abstract Number: 2059

Usage of Predicting Out-of-Office Blood Pressure Calculator in Hispanic Patients with Rheumatic Diseases

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Subjects with rheumatic diseases have an increased risk of cardiovascular (CV) morbimortality. Hypertension (HTN) is a key modifiable risk factor for CV events. A recently published and validated prediction model (Predicting Out-of-Office Blood Pressure, PROOF-BP) has been proposed as a tool to improve diagnosis of HTN, and detection of out-of-office HTN in subjects with a previous diagnosis, with a *c*-statistic (AUC) of 0.86 in non-rheumatic subjects. This model has not been explored in rheumatic patients. Therefore, the objective of this study was to evaluate the diagnostic performance of the PROOF-BP algorithm for the prediction of HTN in subjects with/without rheumatic diseases.

Table 1. Diagnostic performances.

	Sensitivity (%)	Specificity (%)	PPV (%)	NVP (%)
Low risk	100	55	58	100
High risk	29	95	80	68

Predicting Out-of-Office Blood Pressure calculator.TABLE
PPV- Positive predictive value; NPV- Negative predictive value.

Methods: A cross-sectional, observational trial was designed. Subjects with/without rheumatologic conditions were recruited at a rheumatology outpatient clinic. Complete history with somatometry of each subject was registered. BP was measured by a physician 3 times to each participant using current recommendations, with an OMRON HEM-7121 BP monitor. Calculations using the PROOF-BP online site were done, and risk categories were assigned to each subject: low (< 130/80 mmHg), medium (130/80-145/90 mmHg) and high risk (>145/90 mmHg). Subjects in the medium and high risk strata were then asked to return for further evaluation and additional BP measurement, to define each diagnosis of HTN. We used frequencies (%) and median (q25-q75) for descriptive analysis. Diagnostic accuracy of each category was determined using 2 x 2 tables.

Results: A total of 217 subjects were included. The most frequent rheumatic disease was RA (35.9%), followed by OA, SLE and Sjögren syndrome (13.4%, 2.8% and 2.3%, respectively). Using PROOF-BP, 84 (38.7%) subjects were stratified as medium or high risk. Of these, only 36 (42.8%) returned for evaluation. A final diagnosis of HTN was attained in 14 (38.8%) of those who returned. In 21 (67.7%) cases of the medium risk category the diagnosis of HTN was finally discarded, and in the remaining 10 (32.2%) diagnosis of HTN was finally ascertained. The high risk category had a specificity of 95% and a PPV of 80% for the diagnosis of HTN.

Conclusion: In a cohort of Mexican-mestizo subjects with rheumatic diseases, 38.7% were classified as medium or high-risk for HTN. Only 42.8% of patients that required further evaluation followed medical recommendations. More than 30% of patients in the medium-risk category had a final diagnosis of HTN. Using the BP-PROOF algorithm, none of the patients in the low-risk stratum had a final diagnosis of HTN (sensitivity= 100%); the high-risk category had a high specificity (95%) for the diagnosis of HTN.

Disclosure: D. Galarza-Delgado, None; **J. Azpiri-Lopez**, None; **I. Colunga-Pedraza**, None; **C. Martinez-Flores**, None; **M. Castro-Gonzalez**, None; **I. Reynosa-Silva**, None; **K. Cuellar-Calderon**, None; **R. Vera-Pineda**, None.

Abstract Number: 2060

The Current State of Big Data Use and Artificial Intelligence in RMDs: A Systematic Literature Review Informing EULAR Recommendations

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SESSION INFORMATION

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Background/Purpose: Big data are defined as data sets that are too large or complex for traditional data-processing application software to adequately deal with. Artificial Intelligence (AI) includes various statistical techniques which can deal with big data. The current use of these concepts in publications related to rheumatic and musculoskeletal diseases (RMDs) is unknown. Therefore, the aim of this literature review was to assess the current use of big data and AI in the field of RMDs.

Methods: A systematic literature review was performed in PubMed MEDLINE in November 2018, with key words referring to big data, artificial intelligence and RMDs. All original reports published in English were analyzed. A mirror literature review was also performed outside of RMDs on the same number of articles. The number of data analyzed, data sources and statistical methods used (traditional statistics, AI or both) were collected. The analysis compared findings within and beyond the field of RMDs.

Results: Of 567 articles relating to RMDs, 55 met the inclusion criteria and were analyzed, as well as 55 articles in other medical fields. The mean year of publication was 2014 for the RMDs SLR, with 72% of the articles published between 2013 and 2018; whereas the articles included in the mirror non-RMD review were all published in 2018 or 2019. Among RMDs, the most represented fields were inflammatory joint diseases (N=22, 40%) and osteoarthritis (N=16, 29%). The 3 most represented diseases were: knee osteoarthritis (N=13, 24%), rheumatoid arthritis (N=12, 22%) and post-menopausal osteoporosis (N=6, 11%). Outside of RMDs, the most represented medical fields were: oncology (N=14, 25%), neurology (N=8, 15%), infectious diseases (N=6, 11%), ophtalmology (N=5, 9%) and psychiatry (N=5, 9%).

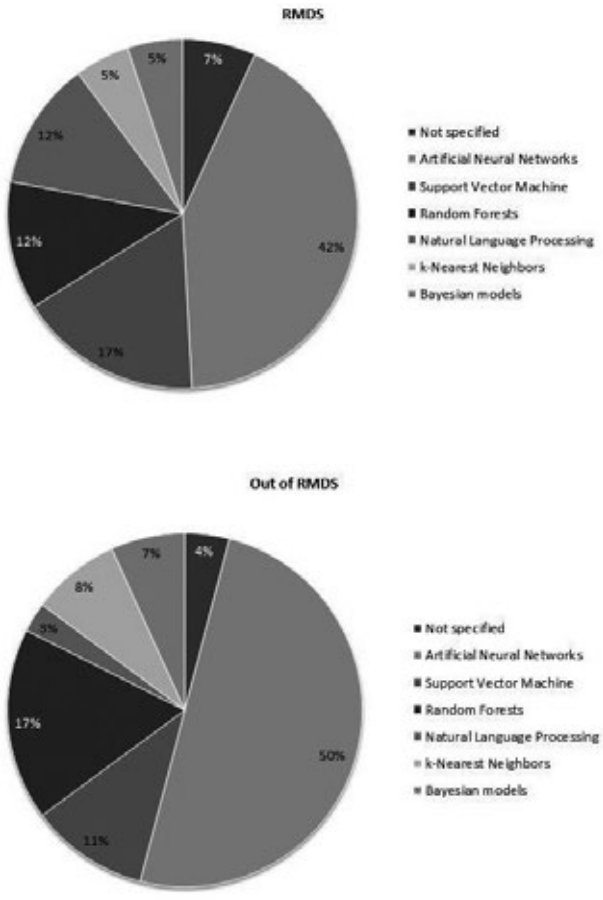

Figure 1 Distribution of machine learning methods in RMDs and outside of RMDs

Only two articles in the field of RMDs (4%) and seven articles out of the field of RMDs (13%) mentioned a clear definition of big data. The mean number of data points was 746 million [range 2000–5 billion] in RMDs, and 9.1 billion [range 100,000 – 200 billion] outside of RMDs.

Data sources were varied: in RMDs, 26 (47%) were clinical, 8 (15%) biological and 16 (29%) radiological; whereas outside of RMDs, the distribution was quite homogenous between clinical, biological and imaging sources (respectively 31%, 31% and 29%).

Both traditional and AI methods were used to analyze big data (respectively 10 (18%) and 45 (82%) in RMDs and 8 (15%) and 47 (85%) out of RMDs). Machine learning was used in almost all AI papers (44/45 in RMDs and 47/47 outside of RMDs), and among machine learning methods, the most represented was artificial neural network (20/44 in RMDs, and 24/47 out of RMDs). More details are provided in Figure 1.

Conclusion: Big data sources and types are varied within the field of RMDs, and methods used to analyze big data were heterogeneous. These findings informed a EULAR taskforce developing recommendations for big data in RMDs.

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Abstract Number: 2061

Association of Periodontitis with Rheumatological Disorders: NHANES III Analysis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The association between periodontal diseases, smoking, and some systemic diseases such as diabetes mellitusis is well established. Periodontitis and rheumatological disorders share common immunological features and there is some evidence of possible association between these diseases. The role of oral dysbiosis from

Table 1. Frequencies of study participants and the estimated population frequencies, by independent variables.

Disease	Frequency of cases		Weighted frequency	
	Number	%	Cases	Non-cases
Rheumatoid arthritis	415	2.75	3,844,209	135,784,851
Osteoarthritis	415	3.78	5,286,515	134,342,544
Osteoporosis	167	1.47	2,105,584	140,373,920
Gout	290	1.97	2,993,702	148,729,450
SLE	25	0.20	297,874	151,425,278
Smoking	6,540	50.60	76,772,736	74,950,416
Diabetes (HbA1c>=6.5)	890	3.78	6,027,904	153,538,909

Table 2. Linear regression analysis of the association of periodontal attachment loss (calculated as mean mm) with rheumatic diseases and adjusting for demographic variables.

Variables	Coefficients	Standard Error	P
Intercept	-0.49	0.06	<0.0001
Age	0.04	0.001	<0.0001
Gender:Male	0.23	0.03	<0.0001
Race:African-American	0.30	0.04	<0.0001
Race:Mexican-American	0.11	0.06	0.07
Smoking	0.43	0.03	<0.0001
HbA1c >6.5%	0.32	0.08	0.0002
Rheumatoid arthritis	-0.08	0.08	0.3
Osteoarthritis	-0.27	0.09	0.003
Osteoporosis	-0.04	0.10	0.7
Gout	-0.05	0.15	0.7
SLE	0.43	0.50	0.4

Table 3. Multivariable logistic regression analysis showing the odds ratio of the relationship between rheumatic disease and periodontitis.

Rheumatic diseases	OR*	CI	P
Rheumatoid arthritis	1.2	0.8-1.8	0.45
Osteoarthritis	0.7	0.5-0.97	0.03
Osteoporosis	0.8	0.6-1.2	0.2
Gout	1.1	0.6-1.9	0.8
SLE	2.1	0.5-8.3	0.3

OR= Odds Ratio, CI: 95% Confidence interval
*: Adjusted for age, gender, race-ethnicity, smoking, and history of diabetes mellitus.

key oral bacteria may play a role in the pathogenesis of autoimmune diseases. This study aims to determine the association between periodontal health and various rheumatic diseases by examining data from the Third National Health and Nutrition Examination Survey (NHANES III).

Methods: The NHANES III is a nationally representative survey of U.S. noninstitutionalized civilians and was conducted from 1988-1994. We included participants aged 13 years and older who had a periodontal examination (Table 1). We used assessments of self-declared physician diagnosis of the following diseases: RA, osteoarthritis (OA), gout, osteoporosis,and systemic lupus erythematosus (SLE). We also included smoking and diabetes mellitus as these have been shown to be significant risk factors for periodontitis. Periodontitis was defined using criteria recommended by the American Academy of Periodontology.

Results: The prevalence of periodontitis and the mean attachment loss increased with age and was significantly higher in males, African-Americans, smokers, and in persons with high HbA1c (Table 2). The regression analysis using mean periodontal attachment loss showed that the association of periodontitis with rheumatic diseases, including rheumatoid arthritis, was not statistically significant except for osteoarthritis (p=0.003). Similarly, using the diagnosis of periodontitis as the outcome variable, the logistic regression model showed no significant relationship between periodontitis and rheumatic diseases, except for osteoarthritis which showed a negative relationship with periodontitis (OR= 0.7, p=0.03), after controlling for the effect of other co-variates (Table 3).

Conclusion: This study shows positive associations of periodontitis with known risk factors, such as demographics, smoking, and diabetes mellitus, but it failed to show statistically significant positive association with systemic rheumatic diseases including RA. This is in contrast with other studies showing positive association of many rheumatic diseases especially RA with periodontitis. There was a trend toward an association of periodontitis with SLE but the number of SLE patients was very small. The negative association between osteoarthritis and periodontitis is unexplained. More prospective studies are needed to confirm or refute the association between periodontitis and rheumatic diseases.

Disclosure: V. Tiwari, None; **L. Brent**, None; **J. Albandar**, None; **C. Hsiao**, None; **S. Shah**, None.

Abstract Number: 2062

Arthritis, Physical Function, and Disability Among Older Mexican Americans over 20-Years of Follow-up

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hispanics are the fastest growing group of older adults in the US, with older Mexican Americans the largest segment of US Hispanics (65%), a population with high rates of disability. The objective of this study was to examine the effect of arthritis on physical function and disability among non-disabled older Mexican Americans over time.

Methods: Data are from a 20-year prospective cohort study of 2254 non-institutionalized Mexican American aged 65 years and older from the Hispanic Established Population for the Epidemiological Study of the Elderly (1993/94-2012/13) who were non-disabled at baseline. Data on self-reported arthritis, socio-demographic variables, medical conditions (hypertension, diabetes, stroke, heart attack, cancer or hip fracture), pain on weight-bearing, activities of daily living (ADLs), instrumental activities of daily living (IADLs), short physical performance battery (balance, repeated chair-stand, and timed walk tests), handgrip muscle strength, body mass index (BMI), and Mini Mental State Examination (MMSE) were collected at each the eighth waves of interview. Any ADL disability was defined as limitation in one or more of the seven ADL activities, and any IADL disability was defined as limitation in one or more of the IADL activities. General equation estimation were fitted to estimate the odds ratio (OR) of ADL and IADL disability and as a function of arthritis. General linear mixed models were performed to estimate change in short physical performance battery (SPPB) tests and handgrip muscle strength. All variables were used as time-varying except for gender and education.

Results: Thirty eight percent of the participants reported arthritis at baseline, 58% were female, and the mean years of education was 4.9. Participants with arthritis were at greater risk of any ADL [OR=1.37, 95% Confidence Interval (CI)=1.12-1.67) and IADL disability over time (OR=1.31, 95% CI=1.16-1.48) after controlling for all covariates. The total SPPB score declined 0.23 points per year among those with arthritis compared with those without arthritis (p-value =0.0105) after controlling for all covariates. The decline in handgrip muscle strength as a function of arthritis was not statistical significant.

Conclusion: Older Mexican Americans with arthritis were at higher risk of developing ADL and IADL disability and experience decline in physical function over 20-years of follow-up. Early prevention of disability will improve the quality of life in this at risk and underserved population.

Disclosure: M. Rodriguez, None; **L. Chou**, None; **J. Sodhi**, None; **K. Markides**, None; **K. Ottenbacher**, None; **S. Al Snih**, None.

Abstract Number: 2063

Arthritis, Upper-Lower Extremity Functional Limitations, and Disability in American Older Adults: Findings from the National Health and Aging Trends Study (NHATS)

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To examine the effect of arthritis on upper-lower extremity (UE-LE) functional limitations and disability over 6-years of follow-up among American older adults.

Methods: Data are from a 6-year prospective cohort study of 5716 American older adults aged 65 years and older residing in the community from the National Health and Aging Trends Study (NHATS 2011-2016). Data on self-reported arthritis, socio-demographic variables, medical conditions (hypertension, diabetes, stroke, heart attack, cancer or hip fracture), overall pain, activities of daily living (ADLs), body mass index (BMI), and UE-LE activities (able to put a heavy object or reach above the head, able to open a jar or grasp small objects, able to carry 20 or 10-pounds, able to walk 6 or 3-blocks, able to walk up 20 or 10-stairs, get down on knees, and able to bend over) were collected. UP-LE functional limitation was defined as limitation in one or more of the four activities for UE and one or more of the six activities for LE. ADL disability was defined as limitation in one or more of the six ADL activities. General estimation equation model was fitted to test the effect of arthritis on UE-LE disability over time. All variables were analyzed as time-dependent variable except gender, education and race/ethnicity. Analysis for any UE-LE functional limitations where performed among those who reported no limitations in UE-LE at baseline. Analysis for any ADL disability were performed among those who reported no ADL disability at baseline. Interaction effect between arthritis and race/ethnicity was performed.

Results: At baseline, 53% reported arthritis, 54.8% were female, 85.3% were Non-Hispanic White, 8% were Non-Hispanic Black, 7% were Hispanic, 17.8% reported UE functional limitations, 68.9% reported LE functional limitations, and 10% reported ADL disability. Participants with arthritis were at greater risk for any UE functional limitations [OR=1.72, 95% Confidence Interval (CI)=1.44-2.06), any LE functional limitations (OR=1.47, 95% CI=1.17-1.83), and any ADL disability (OR=1.59, 95% CI=1.32-1.90) after controlling for all covariates. Hispanics with arthritis were at greater risk for any ADL disability (OR=2.84, 95% CI=1.34-6.01) compared with Non-Hispanic Whites.

Conclusion: American older adults with arthritis were at higher risk of developing upper and lower extremity functional limitations, and ADL disability than those without arthritis over 6-years of follow-up. Hispanic older adults were at higher risk of developing ADL disability than Non-Hispanic White older adults.

Disclosure: M. Rodriguez, None; **J. Sodhi**, None; **S. Al Snih**, None.

Abstract Number: 2064

Evaluation of Methods to Account for Differential Follow-up When Comparing Clinical Trial Data to Observational Data

Vibeke Norvang,[1] Espen Haavardsholm,[1] Sara K. Tedeschi,[2] Houchen Lyu,[3] Tore Kvien,[1] Maria Dahl Mjaavatten,[4] Daniel Solomon,[5] and Kazuki Yoshida[6], [1]Diakonhjemmet Hospital, Dept. of Rheumatology / University of Oslo, Faculty of Medicine, Oslo, Norway, [2]Brigham and Women's Hospital, Div. of Rheumatology, Immunology and Allergy, Boston, MA, [3]Brigham and Women´s Hospital, Div. of Rheumatology, Immunology and Allergy, Boston, [4]Diakonhjemmet Hospital, Dept. of Rheumatology, Oslo, Norway, [5]Brigham and Women´s Hospital, Div. of Rheumatology, Immunology and Allergy, Boston, MA, [6]Brigham and Women's Hospital, Div. of Rheumatology, Immunology and Allergy, Boston

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Comparing the outcomes of an intervention in a clinical trial versus an observational study might help identify challenges in translating results from clinical trials to clinical practice. We aimed to describe differences in follow-up data of a clinical trial and an observational study using an empirical example and to evaluate selected methods to account for differences in missing data patterns.

Methods: We used data from two Norwegian rheumatoid arthritis (RA) cohorts, the ARCTIC randomized controlled trial (RCT) and the NOR-VEAC observational study. Both included treatment-naïve patients, implementing treat-to-target strategies. The outcome in the current study was achievement of remission according to the Disease Activity Score in 28 joints at 6, 12 and 24 months. For all analyses, we balanced the cohorts on baseline covariates using inverse probability of treatment weights. As a naïve analysis, we used unadjusted logistic regression in a subset of patients with complete follow-up data. Then, we analyzed the full dataset, combining multiple imputation by chained equations (MICE) to handle missing variables at existing visits and inverse probability of censoring weights (IPCW) to handle missing data due to drop-out. Further, we used three different approaches to handle intermittent missing visits, i.e. missing visits in patients with subsequent study visits: I) Censoring each patient at the first missing visit, II) Ignoring the missing data from single intermittent missing visits and III) Imputing the outcome variables of intermittent missing visits using MICE.

Results: We included 183 patients from the ARCTIC trial and 277 patients from the NOR-VEAC study. During follow-up, missing data in the ARCTIC trial were mainly a result of missing visits due to patients dropping out of the study, whereas missing data in the NOR-VEAC study were a result of missing variables at existing visits, intermittent missing visits or missing visits due to drop-out (**Figure 1**). The naïve complete case analyses resulted in estimates favoring outcomes in the ARCTIC trial at all study visits during follow-up (**Table 1**). Combining MICE and IPCW with three different approaches to handle intermittent missing visits yielded similar estimates at 6 months and attenuated estimates at 12 and 24 months (**Table 1**). At 24 months, odds ratios (ORs) with 95% confidence intervals for reaching remission in the ARCTIC trial vs. the NOR-VEAC study were 1.6 (0.9-2.7) for the complete case analyses and for the combination of MICE and IPCW, 1.4 (0.8-2.6) for the strict censoring approach, 1.6 (0.9-2.8) for the approach ignoring intermittent missing visits and 1.4 (0.8-2.5) (**Table 1**).

Conclusion: We observed more complex missingness patterns during follow-up in an observational study than in a RCT. The use of methods to account for missing data became more important with longer follow-up time. Compared to complete case analyses, the precision of the effect estimates improved using MICE and IPCW in combination with

Figure 1 Patterns of missing data in the ARCTIC trial and the NOR-VEAC observational study

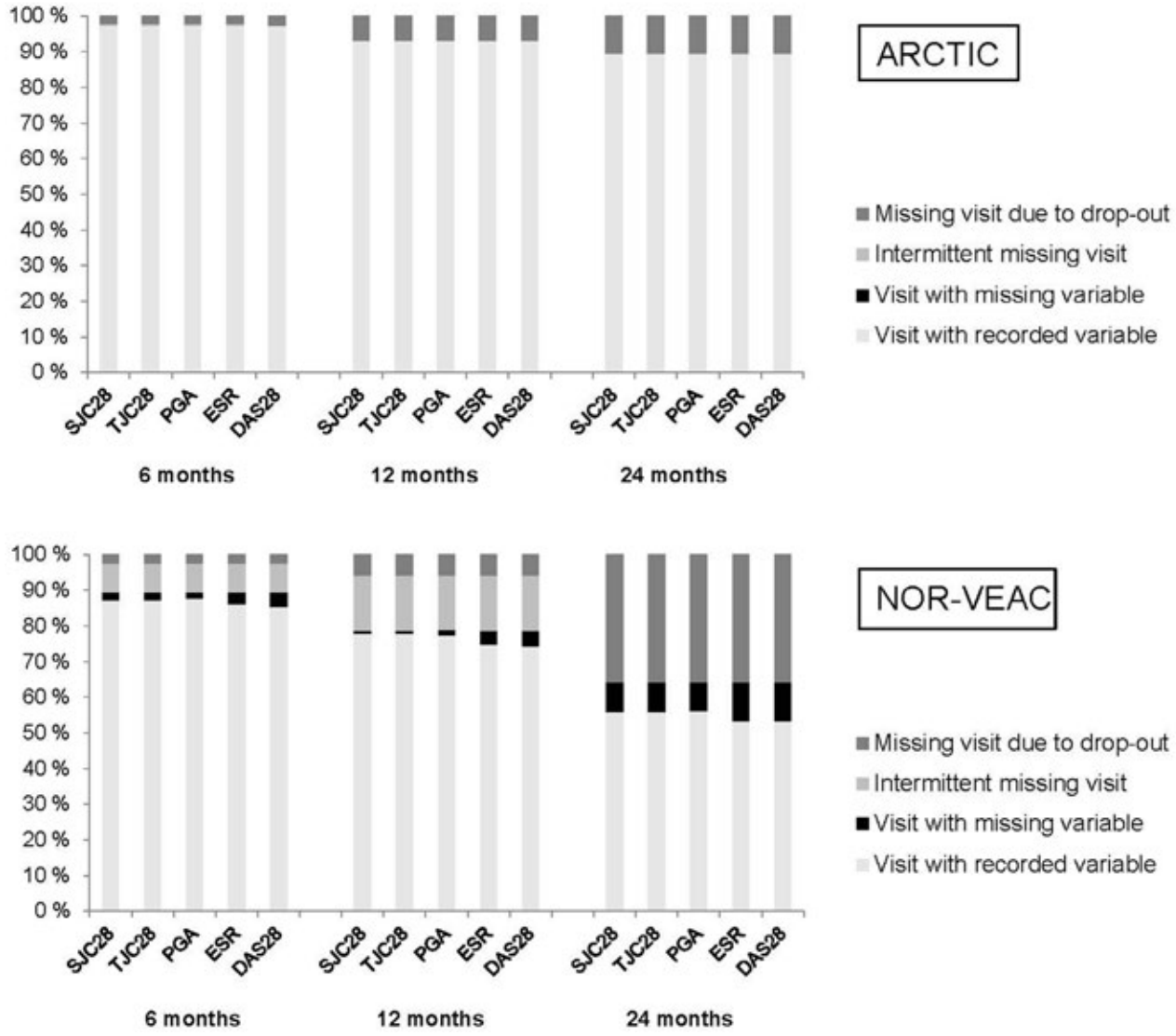

Figure 1 Patterns of missing data during follow-up in the ARCTIC trial and the NOR-VEAC observational study

three different approaches to account for intermittent missing visits. The strict censoring approach might be preferable due to the balance of more precise estimates and simplicity of implementation.

Table 1 Achievement of DAS28 remission at 6, 12 and 24 months in the ARCTIC trial compared to the NOR-VEAC study[3]

	6 months		12 months		24 months	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Complete case analyses[2]	1.46 (0.96 – 2.21)	0.08	2.15 (1.30 – 3.56)	0.003	1.60 (0.93 – 2.74)	0.09
Combining MICE and IPCW with 3 approaches for intermittent missing visits:[3]						
I: Strict censoring	1.43 (0.91 – 2.26)	0.13	1.73 (1.03 – 2.91)	0.04	1.42 (0.79 – 2.55)	0.24
II: Ignoring intermittent single missing visits	1.47 (0.94 – 2.29)	0.08	1.72 (1.04 – 2.84)	0.04	1.60 (0.93 – 2.76)	0.09
III: Imputing intermittent missing visits	1.45 (0.94 – 2.23)	0.10	1.67 (1.01 – 2.76)	0.05	1.42 (0.83 – 2.45)	0.20

[1]All analyses were performed after balancing the cohorts on baseline covariates using inverse probability of treatment weighting on the propensity scores.
[2]Unadjusted logistic regression model.
[3] Logistic regression models with inverse probability of censoring weights (IPCW). Multiple imputation by chained equations (MICE) was used to impute missing variables at existing visits. Approaches to account for intermittent missing visits: I, censoring at first missing visit; II, ignoring single intermittent missing visits by only including a missing indicator, but censoring if >1 subsequent intermittent visits missing; III, imputing intermittent missing visits using MICE.
DAS28, Disease Activity Score 28 joints; OR, odds ration; CI, confidence interval.

Table 1 Achievement of DAS28 remission at 6, 12 and 24 months in the ARCTIC trial compared to the NOR-VEAC study

Disclosure: V. Norvang, None; **E. Haavardsholm**, AbbVie, 2, 8, Cellgene, 8, Eli Lilly, 8, Janssen, 8, MSD, 2, Norwegian Research Council, 2, Norwegian South-Eastern Health Region, 2, Pfizer, 2, 8, Roche, 2, UCB, 2, 8; **S. Tedeschi**, None; **H. Lyu**, None; **T. Kvien**, AbbVie, 2, 8, Biogen, 5, 8, Biogen, Egis, Eli Lilly, Hikma, Mylan, Novartis/Sandoz, Oktal, Hospira/Pfizer, Sanofi and UCB, 5, BMS, 8, Celltrion, 8, Egis, 5, 8, Eli Lilly, 5, 8, Hikma, 5, 8, Hospira/Pfizer, 2, 5, 8, MSD, 2, 8, Mylan, 5, 8, Novartis, 8, Novartis/Sandoz, 5, 8, Oktal, 5, 8, Orion Pharma, 8, Roche, 2, 8, Sandoz, 8, Sanofi, 5, 8, UCB, 5, 8; **M. Mjaavatten**, None; **D. Solomon**, AbbVie, 2, Abbvie, 2, Amgen, 2, AstraZeneca, 2, Corrona, 2, Genentech, 2, Janssen, 2, Lilly, 2, Pfizer, 2; **K. Yoshida**, None.

Abstract Number: 2065

Association Between Anemia and Hyperuricemia: Korean National Health and Nutrition Survey 2016-2017

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Hyperuricemia and anemia may be related in terms of sharing comorbidities such as chronic kidney disease (CKD) and cardiovascular disease. However, to our knowledge, no studies have been conducted on the relationship between two conditions. The purpose of this study was to investigate the association between hyperuricemia and anemia using data from Korean National Health and Nutrition Examination Survey (KNHANES VII; 2016-2017), which is representative of the Korean population.

Methods: The present study included 10794 participants aged ≥ 19 years from KNHANES VII. Logistic regression was used to examine the association between anemia and hyperuricemia. Subgroup analysis was performed to confirm whether the association between two conditions varies according to participant characteristics.

Results: Because there were significant differences in baseline characteristics with and without hyperuricemia between subjects with CKD and subjects without CKD, we analyzed the association between hyperuricemia and anemia separately in subjects with and without CKD. The association between anemia and hyperuricemia was not evident in subjects without CKD, but the risk of hyperuricemia in patients with CKD was 2.2 times higher in patients with anemia. This association was also maintained when the glomerular filtration rate was adjusted (HR 2.34, 95% CI 1.20-4.56). In subgroup analysis, the association of anemia with hyperuricemia was significant in subjects aged 65 years and older, in men, in subjects with diabetes or hypertension, and in subjects with CKD. Subgroup analysis of subjects with CKD showed similar results.

Conclusion: In a Korean representative sample, the association of anemia with hyperuricemia was evident in CKD patients, which remained significant when GFR was adjusted. In addition, anemia and hyperuricemia were well correlated with older age, men, and comorbidity such as diabetes or hypertension.

Disclosure: S. Lee, None; **Y. Eun**, None; **J. Hwang**, None; **H. Cha**, None; **E. Koh**, None; **J. Lee**, None; **H. Kim**, None.

Abstract Number: 2066

Clinical, Serologic and Morphologic Features of Interstitial Pneumonia with Autoimmune Features (IPAF): A Single Center Experience

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Background/Purpose: Interstitial lung disease (ILD) encompasses a group of disorders that are classified together based on similar clinical, radiographic and pathologic findings. ILD is highly associated with autoimmune connective tissue diseases (CTD), and the diagnosis of ILD necessitates investigation into the possibility of an occult CTD. In a substantial number of cases, this investigation reveals evidence of autoimmunity, serologically, clinically or in both domains, without fulfilling criteria of a specific CTD. This disease category has been termed interstitial pneumonia with autoimmune features (IPAF). The goal of this study was to describe the characteristics of a cohort of ILD patients that fulfil the IPAF criteria.

Methods: The study patients were identified from a Mount Sinai Hospital-Department of Pulmonary Medicine registry of patients with ILD. All of the patients were diagnosed with ILD based on either a high resolution CT (HRCT) of the chest or a lung biopsy. The electronic medical records were reviewed to determine if they fulfilled clinical and/or laboratory IPAF criteria. The radiology report from each patient's HRCT was reviewed as well as pathology reports from lung biopsies when available. Patients were excluded if they fulfilled classification criteria for a specific autoimmune CTD, or if there was insufficient data to evaluate their case in each of the three domains in which IPAF is assessed (clinical, serologic, morphologic).

Results: Of 429 patients in the ILD registry, 32 met criteria for IPAF. Nineteen were female (59%) and 13 were male (41%). Twenty-nine out of 31 patients (91%), met serologic criteria for IPAF, with the most common being an ANA >1:320 in a diffuse, speckled or homogeneous pattern (16/32). The next most common serologic criterion was anti-

CCP positivity (6/32). Other serologic criteria that were present in the study cohort included anti-Ro positivity (4/32), anti-RNP (3/32), ANA< 1:320 in a nucleolar pattern (2/32) and anti-tRNA synthetase (1/32). Fifteen of the 32 patients (47%) met clinical criteria for IPAF. Presence of Raynaud's phenomenon was the most common (11/32) followed by inflammatory arthritis (5/32), digital edema (2/32) and palmar telangiectasia (2/32). Twenty-eight of the 32 patients (88%) met morphologic criteria for IPAF. Non spesific interstitial pneumonia (NSIP) on HRCT or on biopsy was the most common morphologic criterion (20/32). Other morphologic criteria included unexplained: pleural thickening (3/32), intrinsic airway disease (2/32), pulmonary vasculopathy (1/32), diffuse lymphoplasmacytic infiltrates on lung biopsy (1/32), and pericardial effusion or thickening (1/32).

Conclusion: In a single center, retrospective cohort of patients who meet the IPAF criteria, the great majority of patients have serologic and morphologic findings that support the diagnosis (91% and 88%, respectively). However, less than half of the patients in this cohort (47%), demonstrated clinical features of a systemic autoimmune disease. Identifying patients with IPAF early during the disease course may be important since there is evidence of a favorable response to immunosuppressive therapy.

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Comparison of Medication New User Definitions in Multi-Specialty EMR Data

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: New user designs are typically preferred in pharmacoepidemiology to avoid bias. The optimal implementation of a new user design in electronic medical record (EMR) data, where the concept of 'enrollment' does not necessarily exist, has not been well studied.

Methods: We used data from PCORnet, a large U.S. comparative effectiveness research network consisting of multiple EMR data sources from both academic and community practices, to compare various new user definitions in 5 PCORnet datamarts, focusing mainly on rheumatoid arthritis (RA) but examining other conditions (e.g. vasculitis) as exemplar use cases. The first prescription appearing in the data for medications of interest (e.g. methotrexate [MTX], biologic, targeted therapy) was identified in the EMR prescribing data. Five new user definitions with varying requirements for the amount and type of prior EMR data needed to construct a 'baseline' period were evaluated. New user definitions tested included 0) no requirement for any prior data; 1) >6 months (m) from first medical inpatient or outpatient medical encounter of any type; 2) >6m from first prescription [Rx] for any medication; 3) >6m from first medical encounter for disease indication (e.g. RA, vasculitis); 4) >6 m from first prescription for any disease-specific

rheumatologic therapy. The rate of hospitalized infection, where a time-dependent hazard was expected, and herpes zoster, where minimal time-dependent hazard was expected, was examined according to various new user definitions. Infections were ascertained over 6- and 12-month follow-up periods, using a first-exposure carried forward approach.

Results: A total of 6621 RA patients initiated one of 9 unique DMARDS, biologics or targeted medications. Mean (SD) age was 55(16) years, 78% women, 43% MTX, 38% TNFi biologics; 19% non-TNFi therapy, 38% oral glucocorticoids. The proportion of person-time represented in the new user analysis across the five definitions was: 100% (base case, 1st Rx is index date with no prior data required), 83% (>6m from first visit), 57% (>6m from first Rx of any type), 71% (>6m from first RA visit), and 29 % (>6m from first RA drug), respectively. The rate of hospitalized infection generally was numerically higher, although < 1-2/100py difference, using 6 month vs. 12 month followup. The crude rate of serious infections by exposure was sometimes but not always numerically higher using the more specific new user definitions (3 and 4) but meaningfully reduced exposure time, especially for 1st line therapies (e.g. methotrexate) and in diseases where sample size was small to begin with (e.g. vasculitis). In contrast, rates of herpes zoster varied minimally by new user definition.

Conclusion: A range of tradeoffs exist in how to best apply new user definitions to multi-specialty EMR data that will affect patient selection and outcome ascertainment. More rigorous and specific definitions are likely preferred for most pharmacoepidemiology studies to avoid bias but must be balanced against feasibility and may need to differ by disease and by outcome.

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Body Mass Index and Systemic Corticosteroid Use as Indicators of Disease Burden and Their Influence on the Safety Profile of Certolizumab Pegol Across Indications

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Certolizumab pegol (CZP) is an anti-TNF drug approved for rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), psoriatic arthritis (PsA), psoriasis (PSO) and Crohn's disease (CD). Older age, comorbidities and corticosteroid (CS) use have been linked to increased risk of serious infectious events (SIEs) in CZP-treated patients (pts) with RA.[1] However, the impact of overall disease burden on the risk of serious adverse events (SAEs) has not been fully examined for other CZP indications. High body mass index (BMI) has been linked to systemic inflammation and comorbidity risk.[2,3] Greater disease burden in these pts may lead to increased CS use – a known risk

Table: Cox proportional hazards models of time to first SAE of interest

		SIEs		Malignancies		MACE	
Covariate		HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
Indication	RA	Ref.		–		Ref.	
	axSpA	0.64 (0.38–1.10)	0.1053	–		0.27 (0.04–1.99)	0.2001
	PsA	0.59 (0.38–0.93)	0.0216	–		1.11 (0.50–2.47)	0.8035
	PSO	0.48 (0.30–0.79)	0.0038	–		0.44 (0.15–1.25)	0.1211
	CD	2.22 (1.69–2.91)	<.0001	–		0.38 (0.15–0.98)	0.0457
Sex	Male	Ref.		–		Ref.	
	Female	1.15 (0.97–1.35)	0.1112	–		0.54 (0.35–0.82)	0.0036
Age (yrs)	<45	Ref.		Ref.		Ref.	
	45–<65	0.92 (0.77–1.09)	0.3245	4.32 (2.68–6.96)	< 0001	4.61 (2.05–10.39)	0.0002
	≥65	1.68 (1.33–2.12)	< 0001	11.41 (6.80–19.13)	<.0001	13.40 (5.73–31.34)	<.0001
Disease duration (yrs)	<1	Ref.		Ref.		–	
	1–<5	1.10 (0.87–1.39)	0.4494	0.69 (0.45–1.06)	0.0883	–	
	5–<10	1.23 (0.96–1.56)	0.1038	0.60 (0.38–0.95)	0.0297	–	
	≥10	1.36 (1.07–1.73)	0.0135	0.61 (0.39–0.95)	0.0290	–	
CS use + BMI (kg/m²)	No + <18.5	1.01 (0.66–1.55)	0.9765	–		–	
	18.5–<25	Ref.		–		–	
	25–<30	0.91 (0.71–1.16)	0.4415	–		–	
	≥30	1.04 (0.80–1.34)	0.7702	–		–	
	Yes + <18.5	0.99 (0.58–1.68)	0.9636	–		–	
	18.5–<25	1.34 (1.08–1.68)	0.0091	–		–	
	25–<30	1.07 (0.82–1.41)	0.6101	–		–	
	≥30	1.72 (1.33–2.22)	<.0001	–		–	
BMI (kg/m²)	<18.5	–		–		1.93 (0.67–5.51)	0.2226
	18.5–<25	–		–		Ref.	
	25–<30	–		–		0.97 (0.57–1.64)	0.9008
	≥30	–		–		1.74 (1.06–2.84)	0.0284
CS use	No	–		–		Ref.	
	Yes	–		–		1.30 (0.87–1.94)	0.2092
Concomitant MTX use	No	Ref.		Ref.		–	
	Yes	1.19 (0.93–1.50)	0.1629	0.72 (0.53–0.99)	0.0405	–	
Prior anti-TNF use	No	Ref.		Ref.		–	
	Yes	1.20 (1.00–1.44)	0.0558	1.46 (0.98–2.18)	0.0605	–	

The above variables result from a stepwise selection procedure with p>0.25 for entry and retention into the model. A covariate was defined as a risk factor if p≤0.05. All p values are nominal and should be interpreted in an exploratory manner. axSpA: axial spondyloarthritis; BMI: body mass index; CD: Crohn's disease; CI: confidence interval; CS: corticosteroid; HR: hazard ratio; MACE: major adverse cardiovascular events; MTX: methotrexate; PsA: psoriatic arthritis; PSO: psoriasis; RA: rheumatoid arthritis; Ref.: reference category used as denominator in the hazard ratio calculations; SIE: serious infectious event; yrs: years.

factor for SAEs.[1] This study aimed to examine the contribution of BMI and CS use to the risk of SIEs, malignancies and major adverse cardiovascular events (MACE) in CZP-treated pts across indications.

Methods: Safety data were pooled across 49 CZP clinical trials (27 RA, 1 axSpA, 1 PsA, 5 PSO, 15 CD). SAEs of potential concern were medically reviewed by an external expert committee using predefined case rules.[4] Incidence rates (IR) were calculated per 100 pt-years (PY). Multivariate Cox modeling was used to estimate relative risk (hazard ratio [HR]) of time to first SIE, malignancy or MACE by baseline BMI (< 18.5, 18.5–< 25, 25–< 30, ≥30 kg/m^2) and CS use (yes, no). The model was adjusted for baseline age, sex, disease duration, methotrexate (MTX) use, prior anti-TNF drug use, and CZP indication.

Results: Across indications, 11,317 pts received CZP (21,695 PY total exposure; max: 7.8 years [yrs]; exposure for RA: 13,542 PY; axSpA: 978 PY; PsA: 1,316 PY; PSO: 1,481 PY; CD: 4,378 PY). Mean BMI was 27.8 kg/m^2 in RA, 27.6 kg/m^2 in axSpA, 29.8 kg/m^2 in PsA, 30.1 kg/m^2 in PSO, and 24.0 kg/m^2 in CD. Overall, 4,132 pts (37%) used CS at baseline, more so in RA (46%) and axSpA (51%). Across indications, IRs were 0.82/100 PY for all malignancies (0.66/100 PY excluding non-melanoma skin cancer [NMSC]), 0.47/100 PY for MACE, and 3.62/100 PY for SIEs. According to the Cox model, age ≥45 yrs, disease duration < 1 yr (compared with ≥5 yrs), and no MTX use were risk factors for malignancies (including NMSCs); BMI and CS use did not have a detectable impact (**Table**). MACE risk was higher in RA and PsA; BMI ≥30 kg/m^2 was a risk factor for MACE, in addition to age ≥45 yrs and male sex (**Table**). Compared with RA, SIE risk was higher in CD and lower in PSO and PsA; key risk factors included age ≥65 yrs, disease duration ≥10 yrs and CS use. Without CS use, BMI did not impact SIE risk, but among CS users, SIE risk was higher for obese pts (**Table**)

Conclusion: In CZP-treated pts across indications, malignancy risk was not influenced by BMI or CS use. As expected, obesity and CS use increased the risk of MACE. The SIE risk associated with CS use was compounded in obese pts, which may reflect the contribution of comorbidities, disease activity or other factors not examined here.

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Alcohol Consumption Is Not an Independent Predictor of Fatigue Severity over Time

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Background/Purpose: Alcohol consumption is a common, but declining, lifestyle behaviour of UK adults. Previous research has shown that among people with rheumatoid arthritis (RA) moderate drinkers report reduced symptom severity (e.g. pain) compared to non-drinkers, leading some to argue that moderate alcohol consumption may be beneficial for the management of chronic pain conditions. Little is known whether alcohol consumption may also reduce fatigue severity despite fatigue and pain sharing a number of common risk factors and possible mechanisms. This study sought to determine whether alcohol consumption was associated with levels of fatigue severity.

Methods: 270 participants recruited to the QUAlity of life, Sleep and rheumatoid ARthritis study (QUASAR) recorded fatigue and pain severity, measured on an ordinal scale from 1 (none) to 5 (very severe), daily for 30 days using a smartphone app. Average weekly alcohol consumption (in units) was reported at baseline and categorised as none- (0), moderate- (1-15) and heavy-drinkers (16+). Participants also reported an assessment of disease activity (Routine Assessment of Patient Index Data 3; RAPID-3), number of co-morbidities and medications and mental health (Hospital Anxiety and Depression (HAD) scale). Ordinal probit models with random effects tested the independent relationship between alcohol consumption and fatigue severity over time. The model was cumulatively adjusted for disease activity, pain, medications and co-morbidities, and mental health, and marginal effects were calculated. Results are presented as percentage point change in the probability of reporting severe or very severe fatigue and 95% confidence intervals (95%CI).

			Model 1†	Model 2‡	Model 3‡	Model 4‡	Model 5‡
No fatigue	Alcohol, units/wk†	1-15	**0.04 (0.01-0.06)**	0.01 (-0.02-0.04)	0.01 (-0.02-0.04)	0.01 (-0.02-0.04)	0.01 (-0.02-0.04)
		16+	0.04 (-0.02-0.11)	-0.001 (-0.05-0.05)	-0.001 (-0.05-0.05)	0.001 (-0.05-0.05)	0.001 (-0.05-0.05)
	RAPID-3			**-0.01 (-0.01—0.01)**	**-0.005 (-0.01—0.003)**	**-0.004 (-0.006-0.001)**	-0.001 (-0.004-0.001)
	Pain				**-0.07 (-0.08—0.06)**	**-0.07 (-0.08-0.06)**	**-0.07 (-0.08—0.06)**
	No. Medications					**-0.01 (-0.02—0.03)**	**-0.01 (-0.02-0.002)**
	No. Comorbidities					0.0002 (-0.01-0.01)	0.0003 (-0.01-0.01)
	Depression						**-0.01 (-0.01—0.003)**
	Anxiety						-0.0003 (-0.01-0.01)
Low fatigue	Alcohol, units/wk†	1-15	**0.14 (0.05-0.22)**	0.02 (-0.04-0.07)	0.02 (-0.03-0.06)	0.02 (-0.03-0.06)	0.02 (-0.03-0.06)
		16+	0.15 (-0.01-0.31)	-0.001 (-0.10-0.10)	-0.001 (-0.09-0.09)	0.001 (-0.08-0.08)	0.002 (-0.08-0.08)
	RAPID-3			**-0.02 (-0.02—0.02)**	**-0.01 (-0.01—0.01)**	**-0.01 (-0.01—0.003)**	-0.002 (-0.01-0.002)
	Pain				**-0.12 (-0.13—0.10)**	**-0.12 (-0.13—0.10)**	**-0.11 (-0.13—0.10)**
	No. Medications					**-0.02 (-0.03—0.01)**	**-0.02 (-0.03—0.004)**
	No. Comorbidities					0.0003 (-0.02-0.02)	0.001 (-0.02-0.02)
	Depression						**-0.01 (-0.02—0.01)**
	Anxiety						-0.0005 (-0.01-0.01)
Moderate fatigue	Alcohol, units/wk†	1-15	**-0.05 (-0.09—0.01)**	-0.01 (-0.02-0.01)	-0.01 (-0.02-0.01)	-0.01 (-0.02-0.01)	-0.01 (-0.02-0.01)
		16+	-0.06 (-0.17-0.05)	0.001 (-0.03-0.03)	0.001 (-0.03-0.03)	-0.0003 (-0.29-0.28)	-0.001 (-0.03-0.03)
	RAPID-3			**0.01 (0.004-0.01)**	**0.008 (0.002-0.005)**	**0.002 (0.001-0.004)**	0.001 (-0.001-0.002)
	Pain				**0.05 (0.03-0.06)**	**0.05 (0.03-0.06)**	**0.05 (0.03-0.06)**
	No. Medications					**0.01 (0.002-0.01)**	**0.01 (0.001-0.01)**
	No. Comorbidities					-0.0001 (-0.01-0.01)	-0.0002 (-0.01-0.01)
	Depression						**0.005 (0.002-0.01)**
	Anxiety						0.0002 (-0.004-0.005)
Severe fatigue	Alcohol, units/wk†	1-15	**-0.11 (-0.18—0.03)**	-0.02 (-0.07-0.03)	-0.01 (-0.06-0.03)	-0.02 (-0.06-0.03)	-0.01 (-0.05-0.02)
		16+	**-0.12 (-0.22—0.01)**	0.002 (-0.09-0.09)	0.001 (-0.08-0.08)	-0.001 (-0.08-0.08)	-0.002 (-0.07-0.07)
	RAPID-3			**0.02 (0.02-0.02)**	**0.01 (0.01-0.01)**	**0.01 (0.003-0.01)**	0.002 (-0.001-0.01)
	Pain				**0.11 (0.10-0.12)**	**0.10 (0.10-0.11)**	**0.10 (0.09-0.11)**
	No. Medications					**0.02 (0.01-0.03)**	**0.02 (0.004-0.03)**
	No. Comorbidities					-0.0003 (-0.02-0.02)	-0.0005 (-0.02-0.01)
	Depression						**0.01 (0.01-0.02)**
	Anxiety						0.0005 (-0.01-0.01)
Very severe fatigue	Alcohol, units/wk†	1-15	**-0.01 (-0.02—0.002)**	-0.004 (-0.02-0.01)	-0.004 (-0.02-0.01)	-0.005 (-0.02-0.01)	-0.005 (-0.02-0.01)
		16+	**-0.01 (-0.02—0.001)**	0.001 (-0.03-0.03)	0.0003 (-0.03-0.03)	-0.0002 (-0.03-0.03)	-0.001 (-0.03-0.03)
	RAPID-3			**0.01 (0.003-0.01)**	**0.008 (0.001-0.004)**	**0.002 (0.001-0.003)**	0.001 (-0.001-0.001)
	Pain				**0.03 (0.03-0.04)**	**0.04 (0.03-0.04)**	**0.04 (0.03-0.04)**
	No. Medications					**0.01 (0.001-0.01)**	**0.01 (0.001-0.01)**
	No. Comorbidities					-0.0001 (-0.01-0.01)	-0.0002 (-0.006-0.006)
	Depression						**0.004 (0.002-0.01)**
	Anxiety						0.0002 (-0.004-0.004)

Table – Marginal effects for the probability of fatigue severity reporting (95% confidence intervals) †Referent category 0 units. ‡adjusted for age, sex and day(time). Bold denotes statistical significance

Results: Of 267 participants who provided alcohol and fatigue data, 107 (40%) were non-drinkers, 139 (52%) were moderate-drinkers and 21 (8%) were heavy-drinkers. Compared to non-drinkers, moderate- and heavy-drinkers were 11 (95%CI:-0.18—0.03) and 12 (-0.22—0.01) percentage points less likely to report severe fatigue, respectively. Both groups were 1 percentage point less likely to report very severe fatigue compared to non-drinkers (-0.02—0.002; -0.02—0.001, respectively). The relationship between alcohol consumption and fatigue severity was attenuated and became non-significant upon adjustment all co-variates. Fatigue severity was predicted by concurrent pain reports, depressive mood and the number of medications, but not RAPID-3 (Table).

Conclusion: In contrast to previous research, we did not find alcohol consumption, at a moderate or heavy level, to be independently associated with fatigue severity over time. It is unlikely that moderate consumption of alcohol will be directly beneficial for those seeking to manage fatigue. Instead, greater benefits may be obtained through the use of management strategies which target pain, medication use, and mood.

Disclosure: K. Druce, None; **B. Yimer**, None; **L. Cordingley**, None; **M. Lunt**, None; **S. Kyle**, None; **W. Dixon**, None; **J. McBeth**, None.

Abstract Number: 2070

Co-morbidities in Patients with OA and RA: Results from a Large US Rheumatic Disease Registry

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The burden of co-morbid conditions can impact the overall quality of life in patients with RA and OA. However, the presence of common co-morbidities in inflammatory and degenerative arthritis is not well described. We sought to compare overlapping co-morbidities in the two patient groups.

Methods: We identified patients with physician-diagnosed OA and RA in FORWARD, The National Databank for Rheumatic Diseases, a large US registry with comprehensive 6-month questionnaires from 1998 through 2018, with patients primarily recruited through rheumatology clinics. Each patient with OA was age- and sex-matched to two patients with RA at study entry. We compared demographics, clinical characteristics and current and past co-morbidities between the OA and RA groups. Patient status at the last observation was further categorized as active (if they had a full follow-up questionnaire collected in the last 2 years), not active, or lost to follow-up/deceased. *T*-tests and Chi-square tests were used as appropriate to assess differences.

Results: Overall, 9463 patients with OA were matched to 18,926 patients with RA. Patients with OA experienced more pain compared with patients with RA (4.6 vs 4.2), but patients with RA had slightly worse HAQ scores (1.0 vs 1.1; Table 1). Higher use of NSAIDs was reported for patients with OA. Except for pulmonary and liver disorders,

Table 1. Clinical Measures and Treatment of Patients With OA and Age- and Sex-Matched RA, Characterized at Last Observation

Variable	Patients with OA n=9463	Patients with RA n=18,926	p value
Age, years	67.1 (12.4)	67.4 (12.2)	0.08
Male Sex, %	17.3	17.3	0.99
Year of questionnaire	2009.1 (6.1)	2008.8 (6.4)	<0.001
HAQ score (0–3)	1.0 (0.7)	1.1 (0.8)	<0.001
Pain VAS (0–10)	4.6 (2.8)	4.2 (2.9)	<0.001
Fatigue VAS (0–10)	4.7 (3.1)	4.7 (3.1)	0.58
Disease duration, years	17.7 (12.5)	17.7 (12.7)	0.85
Overlapping autoimmune disease (excluding RA), %	8.4	3.1	<0.001
Rheumatic Diseases Comorbidity Index (0–9)	2.3 (1.7)	2.1 (1.7)	<0.001
History of smoking, %	41.9	48.5	<0.001
History of DMARD use, %	12.8	70.3	<0.001
History of MTX use, %	3.7	50.1	<0.001
History of biologic use, %	1.8	38.7	<0.001
History of prednisone use, %	8.2	31.1	<0.001
History of any NSAID use, %	52.3	47.5	<0.001

*Data are mean (SD), except when indicated otherwise

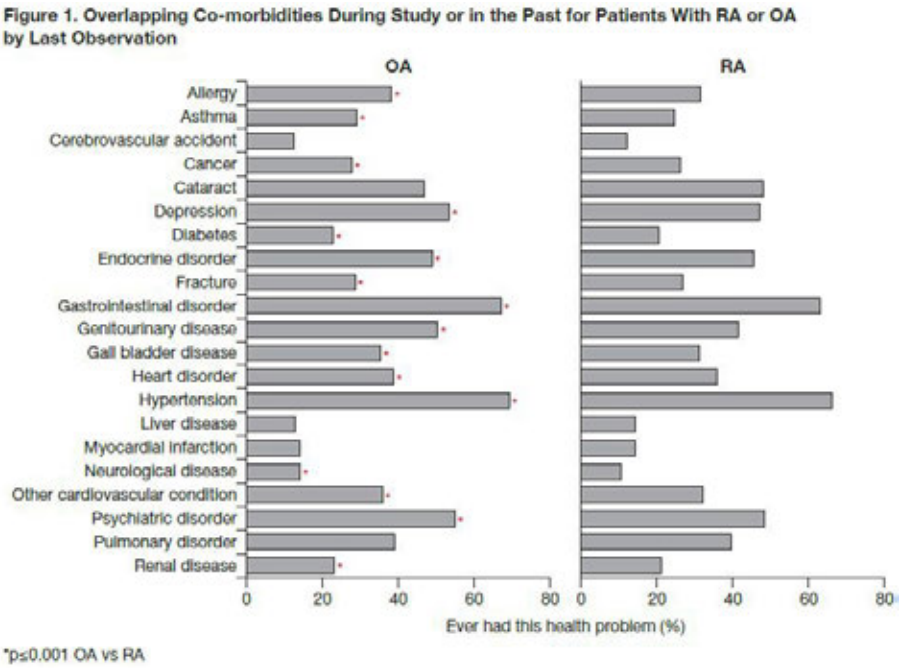
VAS=visual analog scale

Table 2. Overlapping Co-morbidities During Study or in the Past for Patients With OA and Age- and Sex-Matched RA by Last Observation and Active Status

Last observation	Patients with OA			Patients with RA			p value
	Not active (n=4510)	Lost to follow-up/death (n=3383)	Active (n=1570)	Not active (n=8280)	Lost to follow-up/death (n=7407)	Active (n=3239)	RA vs OA
Patients with each disease, %	47.66	35.75	16.59	43.75	39.14	17.11	
Hypertension	61.0	81.0	74.5	57.2	75.0	72.1	<0.001
Gastrointestinal disorder	61.4	74.5	71.8	57.4	68.1	68.3	<0.001
Psychiatric disorder	52.9	56.9	58.1	45.6	49.2	53.9	<0.001
Cataract	30.6	69.1	60.2	30.4	68.2	57.2	0.11
Depression	51.7	54.9	57.0	44.5	47.1	52.5	<0.001
Endocrine disorder	41.3	58.6	57.0	38.0	52.3	53.2	<0.001
Genitourinary disease	43.7	60.5	54.7	35.0	47.7	46.7	<0.001
Pulmonary disorder	33.7	45.3	45.6	30.3	50.1	45.8	<0.001
Heart disorder	27.9	56.2	45.6	24.5	51.2	39.7	<0.001
Other cardiovascular condition	25.7	51.0	43.6	21.8	45.4	36.9	<0.001
Allergy	34.2	41.6	45.3	26.8	33.3	39.2	<0.001
Gall bladder disorder	29.8	44.6	38.7	25.8	37.7	33.8	<0.001
Fracture	21.7	38.5	35.5	18.6	37.7	30.9	<0.001
Cancer	18.0	43.5	35.5	16.1	38.4	31.8	<0.001
Asthma	26.0	32.3	34.1	20.4	27.7	30.1	<0.001
Renal disease	17.4	31.9	28.5	16.5	25.8	26.6	<0.001
Diabetes	18.3	30.7	25.9	16.0	25.8	23.5	<0.001
Myocardial infarction	8.7	25.4	15.7	8.3	23.6	15.5	0.82
Liver disease	9.7	15.7	18.4	11.6	14.6	19.5	<0.001
Cerebrovascular accident	8.3	20.0	16.6	7.4	18.9	14.2	0.18
Neurological disorder	10.0	16.4	23.5	7.5	11.7	15.1	<0.001

which were more prevalent among patients with RA, patients with OA had a higher prevalence of the majority of co-morbidities, with an average overall disease co-morbidity index of 2.3 vs 2.1 for patients with RA. Presence of overlapping autoimmune disease was also higher for patients with OA (OA vs RA: 8.4% vs 3.1%). The most frequently reported co-morbidities (OA vs RA) were hypertension (69% vs 66%), gastrointestinal disorders (67% vs 63%) and psychiatric disorders (55% vs 48%) (Figure 1). As expected, patients who were lost to follow-up/deceased had worse outcomes and more co-morbidities than active and non-active patients both with OA and RA. Patients who were not active had more co-morbidities than active patients, revealing an informative drop-out (Table 2).

Conclusion: Patients with OA reported more overlapping co-morbidities than patients with RA, even after age- and sex-matching. Although RA has a much more complex etiology, affecting more organ systems, our data suggest that the burden of having OA in terms of overlapping symptoms and other problems is not negligible in comparison. It is possible that the advancement of medications for RA has aided in lessening the burden of disease or other co-morbidities when compared with OA. Also, this OA cohort may have increased disease severity due to seeking care from a rheumatologist.



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Disclosure: S. Pedro, FORWARD, the National Data Bank for Rheumatic Disease, 3, FORWARD, The National Data Bank for Rheumatic Diseases, 3; **R. Schumacher**, None; **A. Dominique**, Bristol-Myers Squibb, 1, 3, 4; **Y. Shaw**, Amgen, 2, MSD, 2, 8; **K. Wipfler**, Option Care, 3; **K. Michaud**, Pfizer, 2, Rheumatology Research Foundation, 2.

Abstract Number: 2071

The Prevalence of 78 Autoimmune Diseases in Catalonia (MASCAT-PADRIS Big Data Project)

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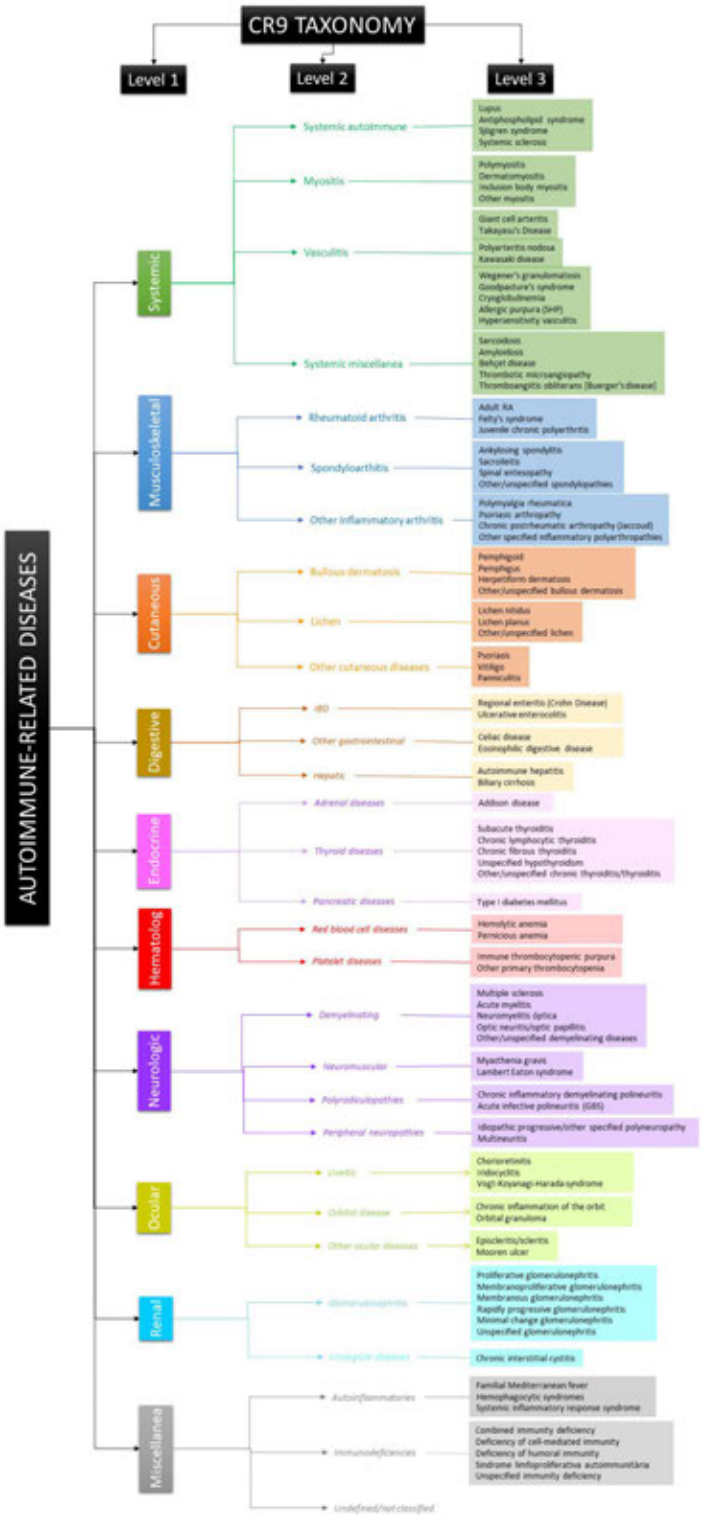
SESSION INFORMATION

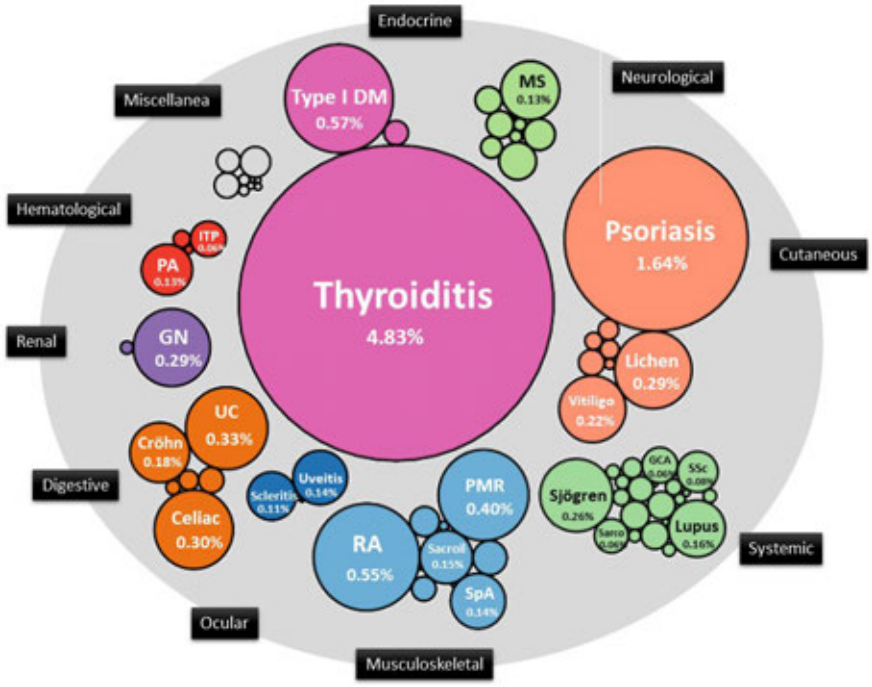
Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases

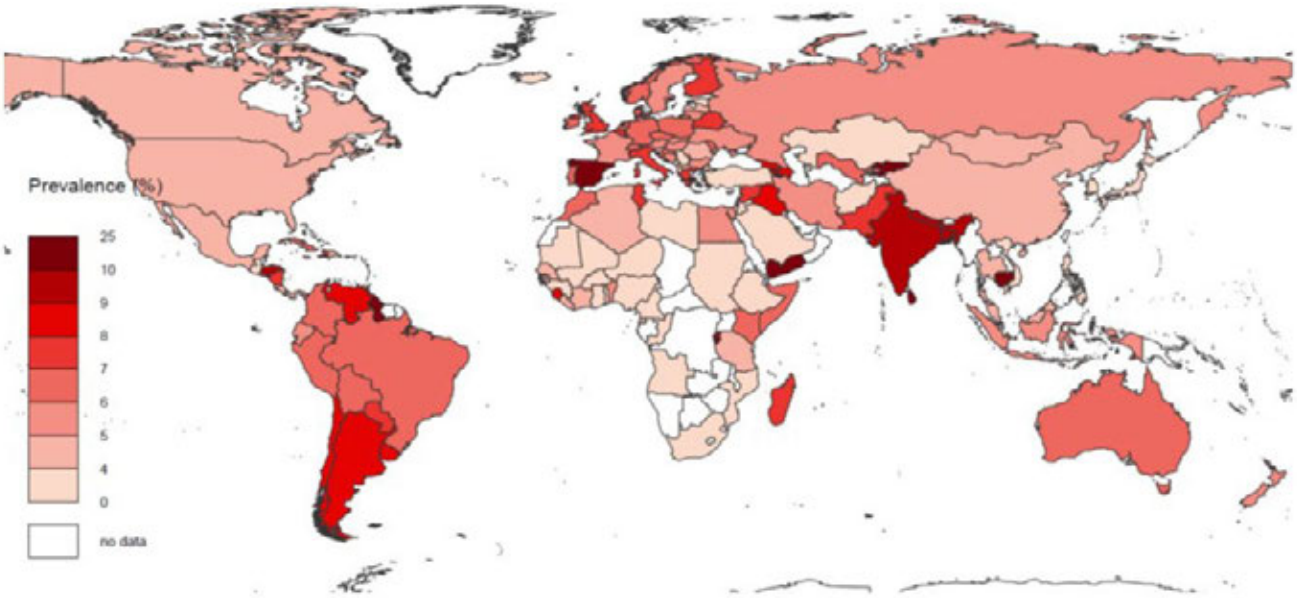
Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM





Prevalence by nationality (%) (population census > 0 habitants)



Background/Purpose: To analyze the prevalence of autoimmune diseases (ADs) in Catalonia, a Mediterranean region with nearly 8 million inhabitants using a public administrative big data program.

Methods: The MASCAT-PADRIS Project was designed in 2017 to take a "high-definition" picture of ADs in Catalonia. Individuals with ≥ 1 ICD-9-CM code for an AD recorded during the study period (January 1st, 2012 – December 31st, 2017) to be included. The prevalence rates were estimated for the main subgroups of ADs after grouping the 234 ICD-9-CM ADs codes into a 3-level taxonomy classification that included 78 individual diseases (Level 3), 28 AD subgroups (Level 2) and 10 main AD groups (Level 1) (**Figure 1**). We assumed that a patient with an AD will visit a primary care center and/or hospital at least once during the 6-year study period. Therefore, the lifetime prevalence for each individual AD was estimated as the number of individuals with ≥ 1 ICD-9-CM code during the study period divided by the mean number of people with public health coverage in Catalonia during the study period and expressed per 100,000 inhabitants.

Results: A total of 799,003 individuals had a diagnosis of AD during the 2012-2017 study period, representing a prevalence of 10.61%. Among the main individual ADs, 25 (32%) were classified as non-rare diseases (prevalence >5/10,000 inhabitants), 26 (33%) as rare diseases (prevalence 1-5/10,000 inhabitants) and the remaining 27 (35%) as very rare diseases (prevalence < 1/10,000 inhabitants). The 10 main individual ADs with the highest prevalence rates were thyroiditis (4.83%), psoriasis (1.64%), type I diabetes mellitus (1.90%), rheumatoid arthritis (0.58%), polymyalgia rheumatica (0.40%), ulcerative colitis (0.33%), lichen planus (0.31%), celiac disease (0.31%), glomerulonephritis (0.29%) and Sjögren syndrome (0.26%) (Figure 2). Of the 799,003 Catalans with ADs, 531,064 (66.46%) were women, with a female:male ratio of 2:1; only 20 (16 were rare diseases) out of the 78 main ADs (26%) were more frequently reported in men. The ADs most frequently reported in woman were Sjögren syndrome (ratio 6:1) biliary cirrhosis (ratio 5.5) and systemic lupus erythematosus (ratio 4.8:1), while ankylosing spondylitis (ratio 1.7:1), type I diabetes mellitus (1.3:1) and psoriasis (1.3:1) were more frequently reported in men. With respect to the country of birth, a south-to-north gradient of higher frequencies was found. For the main individual ADs, some countries had at least three ADs with a higher prevalence than native-born Catalans (India, Pakistan, Paraguay, Honduras, Morocco and the UK). Some ADs showed a geographically-driven higher prevalence: inflammatory bowel disease and multiple sclerosis in European countries, sarcoidosis in India, Pakistan, Morocco and Paraguay, vitiligo in India, Pakistan, Morocco and all Latin American countries, and thyroiditis in India, Honduras and Argentina (Figure 3).

Conclusion: Autoimmune diseases, although sharing a common etiopathogenic basis, are characterized by wide individual heterogeneity in their frequency, organ-specific phenotype, gender ratio, age predominance and ethnic influence.

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Abstract Number: 2072

Prevalence of Thyroid Dysfunction with Therapeutic Indication in Patients with Rheumatological Diseases

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases

Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

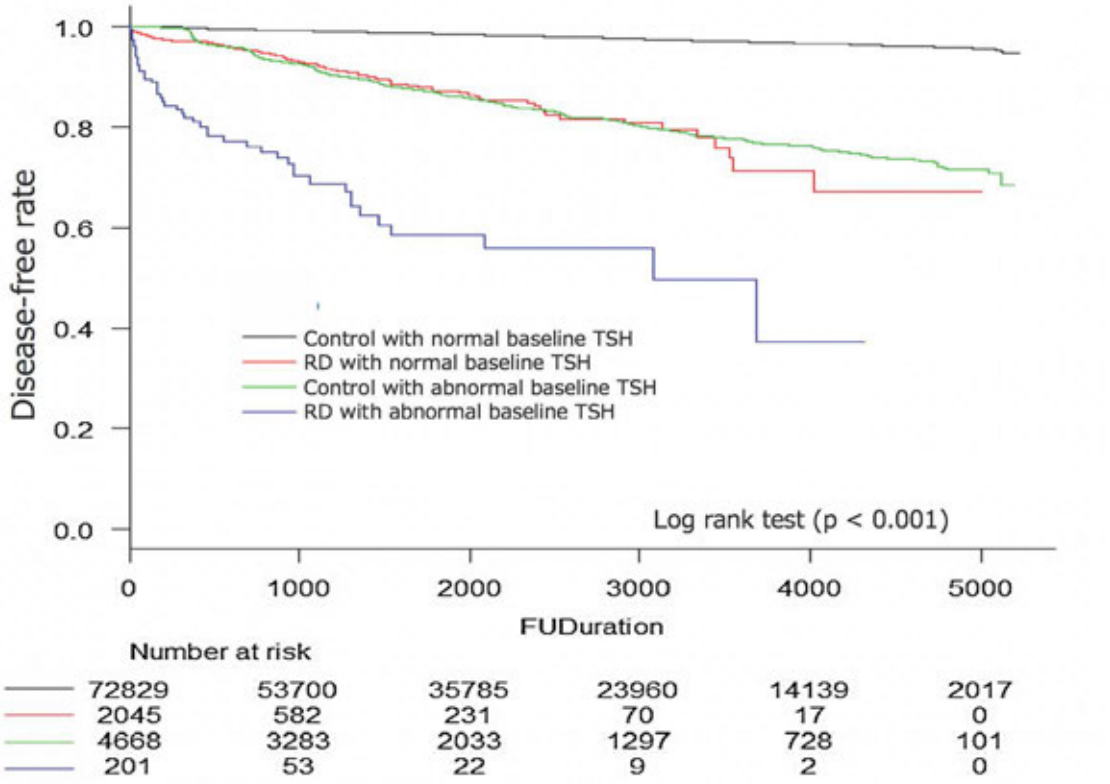
Background/Purpose: Thyroid dysfunction (TD) is known as a common complication of rheumatological diseases (RD). Treatment for TD is important not only in clinical TD for controlling symptom but also in some patients with subclinical ones especially for cardiovascular events in the future. But the data about prevalence of hypothyroidism or hyperthyroidism requiring treatment and it's changes with follow up in patients with RD is limited.

Methods: We retrospectively reviewed charts of consecutive patients with RD and healthy controls who checked TSH (thyroid stimulating hormone) level at least once at immuno-rheumatology center and preventive medicine center, in St. Luke's International Hospital, Tokyo, Japan, from January 2004 to July 2018. We investigated basic demographics, underlying diseases, blood tests including thyroid functions and treatment with thyroid hormone or antithyroid medications. We compared the number of TD requiring treatment (TSH ≧10 μU/mL, TSH ≦0.1 μU/mL or

Table1. Comparison of RD patients and controls

	Rheumatological Disease (n = 2007)	Control (n = 70251)	p value
Age(yr)	53.7 (16.2)	46.1 (11.9)	<0.001
FEMALE (%)	1826 (79.2)	38632 (49.4)	<0.001
BMI	22.74 (3.9)	22.41 (3.3)	<0.001
Blood Test			
Hb	12.1 (1.7)	13.9 (1.5)	<0.001
MCV	88.8 (6.72)	90.8 (4.04)	<0.001
Cre	0.57 [0.50, 0.68]	0.72 [0.61, 0.84]	<0.001
BUN	11.7 [9.5, 14.4]	12.9 [10.9, 15.1]	<0.001
TBil	0.4 [0.3, 0.5]	0.8 [0.6, 1.0]	<0.001
ALP	187 [150, 231]	180 [148, 218]	<0.001
AST	18 [15, 21]	20 [17, 24]	<0.001
ALT	14 [11, 18]	18 [14, 26]	<0.001
γ-GTP	19 [14, 32]	22 [15, 39]	<0.001
T-CHO	189 [163, 218]	199 [177, 223]	<0.001
L-CHO	105 [87, 125]	115 [95, 136]	<0.001
RF positive (%)	961 (41.7)	6734 (8.8)	<0.001
Baseline TSH Level(μU/mL)	1.76 [1.12, 2.69]	1.74 [1.20, 2.53]	0.953
Abnormal baseline TSH (%)	256 (11.1)	5422 (6.9)	<0.001
≧4.5 (%)	170 (7.4)	4061 (5.2)	<0.001
≧10 (%)	22 (1.0)	305 (0.5)	0.003
≦0.45 (%)	86 (3.7)	1371 (1.8)	<0.001
≦0.1 (%)	29 (1.3)	389 (0.5)	<0.001
Baseline FreeT4 Level(μU/mL)	1.15 [1.04, 1.28]	1.29 [1.18, 1.40]	<0.001
Times of TSH measurement	2 [1, 5]	5 [3, 9]	<0.001
Follow up (days)	117 [0, 1136]	1995 [866, 3562]	<0.001
Thyroid Dysfunction			
Thyroid dysfunction with indication of treatment (%)	214 (9.3)	2828 (3.8)	<0.001
At 1st check(%)	61 (2.6)	754 (1.0)	<0.001
Time to thyroid dysfunction requiring treatment (days)	190 [0, 1055]	769 [0, 2029]	<0.001
Hypothyroidism			
Hypothyroidism with indication of treatment (%)	146 (6.3)	1478 (1.9)	<0.001
At 1st check(%)	32 (1.4)	365 (0.5)	<0.001
TSH in follow up≧4.5 (%)	378 (16.4)	11099 (14.2)	0.003
TSH in follow up≧10 (%)	85 (3.7)	1220 (1.6)	<0.001
Treatment with hormone supplementation	129 (5.6)	718 (0.9)	<0.001
Time to hypothyroidism requiring treatment (days)	204 [17, 1088]	797 [237, 2142]	<0.001
Hyperthyroidism			
Hyperthyroidism with indication of treatment (%)	60 (2.9)	1350 (1.7)	<0.001
At 1st check(%)	29 (1.3)	389 (0.5)	<0.001
TSH in follow up≦0.45 (%)	231 (10.0)	3926 (5.0)	<0.001
TSH in follow up≦0.1 (%)	84 (3.6)	1379 (1.8)	<0.001
Treatment with Antithyroid Medication(%)	21 (0.9)	325 (0.4)	0.002
Time to hyperthyroidism requiring treatment (days)	32 [0, 955]	747 [0, 1864]	0.001

Figure1. Kaplan–Meier curve of TD with treatment indication and RD with or without baseline abnormal TSH level in patients without treatment indication at baseline



physician started treatment) and it's changes in follow up using univariate analysis and Kaplan–Meier method with log rank test. The risk of TD which needs treatments was assessed with Cox proportional hazard model in all subjects and logistic regression analysis in RD patients.

Results: 2307 RD patients and 78251 controls without past medical history of TD requiring treatments are included. Newly-detected TD requiring treatments are significantly frequent in RD patients (214, 9.3% vs 2828, 3.6%, P< 0.001). When focused on patients without TD requiring treatment at baseline, Kaplan–Meier method and Cox's proportional hazards model revealed hazard ratio of TD with indication of treatment is significantly higher in RD patients with baseline abnormal TSH(≦0.45 or ≧4.5 μU/mL) (HR=32.6; 95%CI 24.3-43.9, p< 0.001), RD with normal baseline TSH (HR=7.5; 95%CI 6.1-9.2, p< 0.001), control with abnormal TSH (HR=8.5; 95%CI 7.8-9.3, p< 0.001) when compared to controls with normal TSH at baseline after adjusting confounders. When focus on RD patients, female, patients with ANA(anti-nuclear antibody) related disease, baseline abnormal TSH level, and positive thyroid-related antibodies at baseline have statistically significant higher risk of TD requiring treatment after adjusting confounders in multivariate analysis.

Conclusion: TD with therapeutic indication are much more frequent in RD patients, especially with abnormal baseline TSH level, and about 1 out of 10 RD patients has TD requiring treatment. We encourage active routine measurement of thyroid function tests in RD patients especially with above risk factors.

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Abstract Number: 2073

The Association of Serum Uric Acid Levels and the Risk of Lower Urinary Tract Symptoms in Korean Healthy Adults

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Along the aging process, men frequently appeal lower urinary tract symptoms (LUTS). The impact of LUTS on quality of life and mental health was apparent regardless of the East and West. Recently, uric acid (UA) has emerged as a modulator of prostate cells. Because UA acts like two-faced Janus, antioxidants or pro-oxidants, depending on its chemical microenvironment, hyperuricemia has been proposed to link to various diseases independent of crystal formation. Although UA has been shown to play a role in prostate pathology, there has been scarce investigation between UA and LUTS, irrespective of prostatic hyperplasia and prostate cancer. Therefore, we performed this study to assess the relationship serum uric acid (SUA) levels and the incidence of LUTS using a large sample of Korean middle-aged men who underwent comprehensive health screening exams.

Uric acid level (mg/dl)	Person-years	Incident case	Incidence Density (per 1000 person-years)	Age-adjusted HR (95% CI)	Multivariate-adjusted HR[a] (95% CI)	
					Model 1	Model 2
<5.5	96,895.1	3,994	41.2	1.00 (reference)	1.00 (reference)	1.00 (reference)
5.5-6.4	125,703.0	4,715	37.5	0.98 (0.94-1.02)	0.99 (0.95-1.03)	1.00 (0.96-1.05)
6.5-7.4	88,701.7	3,134	35.3	0.96 (0.92-1.01)	0.97 (0.92-1.02)	1.00 (0.95-1.06)
7.5-8.4	35,049.3	1,216	34.5	0.98 (0.92-1.04)	0.99 (0.93-1.06)	1.03 (0.96-1.11)
8.5-9.4	9,626.9	291	30.2	0.88 (0.78-0.99)	0.90 (0.80-1.02)	0.98 (0.86-1.12)
≥9.5	3,006.6	74	24.6	0.73 (0.58-0.92)	0.74 (0.58-0.93)	0.77 (0.59-0.99)
P for trend				0.008	0.039	0.850

Hazard ratios (95% CI) of significant lower urinary tract symptom by uric acid level

Methods: A cohort study was performed in 101,091 Korean men, free of LUTS at baseline, who underwent health check-ups from 2011 to 2016. LUTS were assessed using the International Prostate Symptom Score (IPSS) and clinically significant LUTS were defined as an IPSS score ≥8. Men are divided into 6 groups according to SUA level in mg/dl (< 5.5, 5.5–6.4, 6.5–7.4, 7.5–8.4, 8.5–9.4, and ≥9.5). Hazard ratios (HRs) and 95% confidence intervals (95% CIs) for incident LUTS were estimated using Cox proportional hazards regression analysis. Stratified analyses were also conducted in pre-specified subgroups: age (< 50 vs. ≥50 years), smoking (none vs. ever smoker), alcohol consumption (< 20 g/day vs. ≥20 g/day), physical activity (health enhancing physical activity; no vs. yes) and body mass index (BMI) (< 25 kg/m^2 vs. ≥25 kg/m^2).

Results: During a total of 358,982.6 person-years of follow-up, 13,424 people developed significant LUTS (incidence rate, 37.3 per 1,000 person-years). In a multivariable model adjusted for age, center, year of screening examination, education level, BMI, alcohol intake, regular exercise, hypertension, diabetes mellitus, and estimated glomerular filtration rate, the highest level of SUA (< 9.5mg/dl) was associated with decreased risk of significant LUTS. The multivariable-adjusted HR for significant LUTS in the highest SUA categories compared with the reference category (< 5.5mg/dl) was 0.77 (95% CI 0.59-0.99). The association of the SUA levels with the risk of significant LUTS was examined by pre-specified subgroups, and the trend of decreasing risk for significant LUTS along the increasing SUA levels was predominant in age < 50 years.

Conclusion: In this large cohort of middle-aged men, higher SUA level was predictive of decreased risk of LUTS. This suggests another important role of SUA for preventing LUTS. A further study is warranted to elucidate the biological mechanisms underlying this association.

Disclosure: J. Hwang, None; **S. Ryu**, None; **J. Ahn**, None.

Abstract Number: 2074

Automated Diagnosis Extraction from Electronic Medical Records with Machine Learning Classifiers

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The use of Electronic Medical Records (EMR) for research purposes has led to an increasing interest in Natural Language Processing (NLP) for text classification. Little preparation is required as the NLP-methods are capable of automatically interpreting the data. Classification is often accomplished with naïve word-matching. An alternative to word-matching is the usage of a Machine Learning (ML) classifier. Rather than providing a set of patterns, an ML-model only requires the outcome and then formulates the patterns itself. The purpose of this study is to build a reliable classifier with machine learning techniques that can identify the Rheumatoid Arthritis (RA) cases based on the provided EMR entry.

Methods: Data was acquired from the HiX-EMR database consisting of 2,771 patients that visited the rheumatology outpatient clinic from the Leiden University Medical Centre between 2007 and 2018. This database featured a total of 38,216 entries. The first entry (if available) was selected per patient for annotation, resulting

Table 1: Overview of the different characteristics for each classifying method

Classifying Method	*Probabilistic*	*Multiclass*	*Description*
Naïve Bayes	+	+	Simple probabilistic model that treats every feature independently
Neural Networks	-	+	Utilizes multiple 'hidden' layers with weighted connections in between to form a 'response'
Gradient Boosting	+	+	Composition of multiple weak learners (decision trees in this case)
Decision Tree	-	+	Builds a flowchart-like structure and classifies based on multiple binary decisions
SVM	-	+	Defines the most optimal boundary (hyperplane) between classes

Note: Probabilistic = model returns probabilities, Multiclass= model can be applied to data with multiple classes, Description= classifying approach of model.

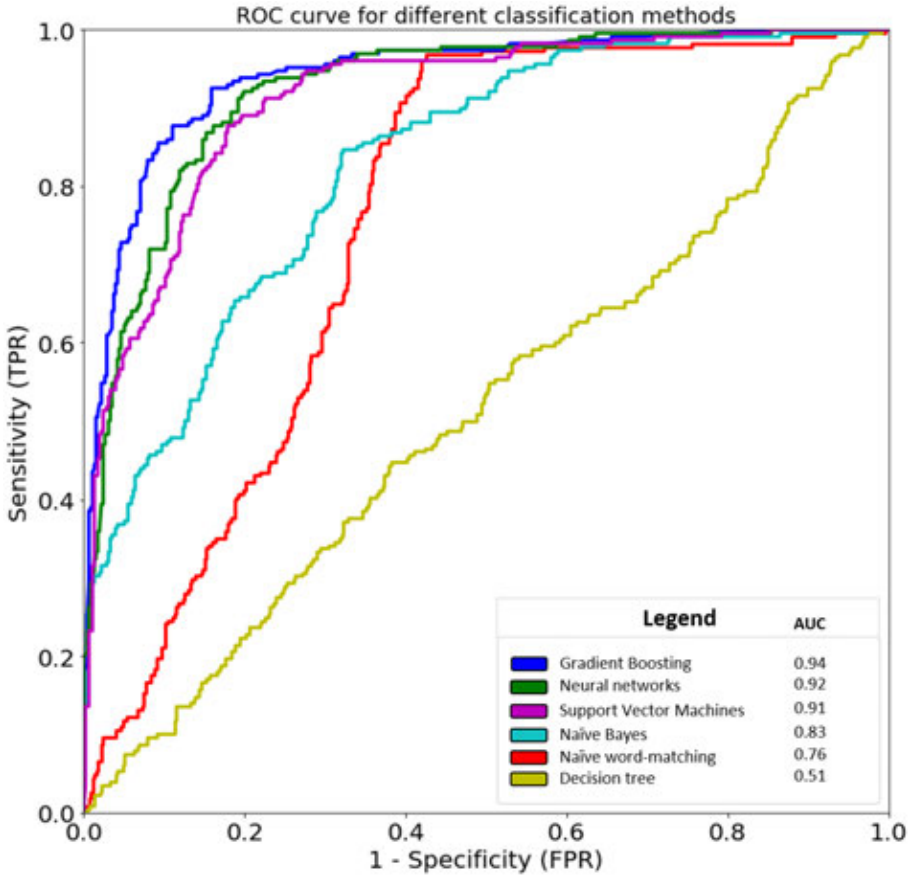

Figure 1: ROC-curve applied on both the Machine Learning models and the naïve word-matching method.

in a total of 1,361 entries. The annotated sample was then randomly split into an equally sized training and test set. Both sets were preprocessed and then classified with the following Methods naïve word-matching, Naive Bayes (NB), Decision Tree, Gradient Boosting (GB), Neural Networks and Support Vector Machines (SVM), see table 1 for more information. Default Scikit-learn implementations[2] were used to create the models, except for the word-matching model of which the classification is based on the presence of RA-defining strings like 'Reumatoide Artritis'.

Finally, the performance of the models was evaluated with a receiver operating characteristic (ROC) curve analysis via the pROC package[3]. The Delong test was used to assess the 95% confidence intervals (CI) and to determine the difference between the performance of the word-matching method and the ML-models.

Results: The naïve word-matching approach resulted in a high area under the curve (AUC=0.76). Likewise, the ML-models resulted in relatively high AUC-scores as well: NB=0.83, SVM=0.91, Neural Networks=0.92 and the GB-method with a 0.94. The Decision Tree showed the worst performance with an AUC-ROC of only 0.51. In comparison to the naïve word-matching ROC-curve, all the ML-models showed a significant difference: Decision Tree ($p< 2.2e-16$; CI=0.49-0.56), NB ($p= 4.4e-3$; CI=0.80-0.86), Neural Networks ($p< 2.2e-16$; CI=0.90-0.94), GB ($p< 2.2e-16$; CI=0.92-0.96) and the SVM ($p=4.0e-16$; CI=0.89-0.93).

Conclusion: The Gradient Boosting, Neural Networks, SVM and Naïve Bayes models all showcased a significantly better performance than the Naïve word-matching algorithm, which establishes these ML-methods as an efficient approach for data extraction from EMR.

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Abstract Number: 2075

Cross-sectional Study and Mendelian Randomization Analysis of Diet in Six Prevalent Autoimmune Diseases

Antonio Julià,[1] Sergio H Martinez,[2] Jesús Tornero,[3] Juan Cañete,[4] Antonio Fernández-Nebro,[5] Francisco J. Blanco,[6] Jesús Rodríguez,[7] Francisco Javier Lopez-Longo,[8] Benjamín Fernandez-Gutierrez,[9] Jordi Gratacós,[10] Jose J Pérez Venegas,[11] Carolina Pérez,[12] Ruben Queiró,[13] Alejandro Olivé-Marqués,[14] Mercedes Alperi-López,[15] Carlos Montilla,[16] José Luís Andreu,[17] Juan Carlos Torre-Alonso,[18] Mª Ángeles Aguirre-Zamorano,[19] Hèctor Corominas,[20] Paloma Vela,[21] Víctor Martínez-Taboada,[22] Sara Marique,[23] Joan M Nolla,[24] Isidoro Gonzalez,[25] Santiago Muñoz-Fernandez,[26] José Luís Marenco de la Fuente,[27] Carlos González,[28] Antonio Zea,[29] Maria Lopez Lasanta,[30] Daniel Roig,[31] Jose Maria Pego-Reigosa,[32] Mireia Lopez Corbeto,[33] Pedro Zarco,[34] Mercedes Freire González,[35] Alba Erra,[36] Elvira Díez,[37] Santos Castañeda,[38] Esther Rodriguez,[39] Alicia García,[40] Patricia Carreira,[39] Georgina Salvador,[41] Ricardo Blanco,[42] Cesar Diaz-Torne,[43] Alfredo Willisch Domínguez,[44] Joan Antonio Mosquera,[45] Simón Sánchez-Fernández,[46] Júlio Ramírez,[47] and Sara Marsal[48], [1]Rheumatology Research Group, Vall d'Hebron Hospital Research Institute, Barcelona, Spain., Barcelona, Catalonia, Spain, [2]Hospital Vall d'Hebron, Barcelona, Barcelona, Spain, [3]Hospital Universitario Guadalajara, Guadalajara, Spain., Guadalajara, Castilla-La Mancha, Spain, [4]Rheumatology Department, Hospital Clínic and IDIBAPS,, Barcelona, Spain, [5]Hospital Carlos Haya, Malaga, Spain, [6]Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). As Xubias, 15006. A Coruña, España, A Coruña, Spain, [7]Hospital Universitario de Bellvitge, Hospitalet, Spain, [8]Hospital Universitario Gregorio Marañón, Madrid, Madrid, Spain, [9]Hospital Clínico San Carlos, Madrid, Madrid, Spain, [10]Hospital Parc Taulí, Sabadell, Catalonia, Spain, [11]Hospital Jerez de la Frontera, Jerez de la Frontera, Spain, [12]Parc de Salut Mar, Barcelona, Barcelona, Spain, [13]Hospital Universitario Central de Asturias, Oviedo, Oviedo, Spain, [14]Hospital Universitari Germans Trias i Pujol, Badalona, Catalonia, Spain, [15]Hospital Universitario Central de Asturias, Oviedo, Spain, [16]Hospital Clínico Universitario de Salamanca, Salamanca, Spain, [17]Hospital Puerta de Hierro, Madrid, Madrid, Spain, [18]Hospital Monte Naranco, Oviedo, Spain, [19]IMIBIC/Reina Sofia Hospital/University of Cordoba, Córdoba, Spain, [20]Hospital de la Santa Creu i Sant Pau, Barcelona, Barcelona, Spain, [21]Hospital General Universitario de Alicante, Alicante, Spain, [22]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [23]Hospital Regional Univeristario de Málaga, Málaga, Spain, [24]Hospital Universitari de Bellvitge, Hospitalet, Spain, [25]Hospital Universitario La Princesa, Madrid, Spain, [26]Hospital Universitario Infanta Sofía, Madrid, Madrid, Spain, [27]Hospital Valme, Sevilla, Sevilla, Spain, [28]Hospital Universitario Gregorio Marañón, Madrid, Spain, [29]Hospital Universitario Ramón y Cajal, Madrid, Madrid, Spain, [30]Hospital Universitari Vall Hebrón, Barcelona, Barcelona, Catalonia, Spain, [31]Hospital Moisès Broggi, Barcelona, Sant Joan Despí, Barcelona, Singapore, [32]Complexo Hospitalario Universitario, Vigo, Spain, [33]Hospital Universitari Vall d'Hebron, Barcelona, Catalonia, Spain, [34]Hospital Universitario Fundación Alcorcón, Madrid, Madrid, Spain, [35]Hospital Universitario Juan Canalejo, La Coruña, Spain, [36]H Sant Rafael, Barcelona, Barcelona, Spain, [37]Complejo Asistencial Universitario de León, León, Castilla y Leon, Spain, [38]Rheumatology, Hospital Universitario La Princesa, Madrid, Madrid, Spain, [39]Hospital Universitario 12 de Octubre, Madrid, Spain, [40]Centro de Salud Virgen de los Reyes, Sevilla, Sevilla, Spain, [41]Hospital Mútua Terrassa, Terrassa, Spain, [42]Hospital Universitario Marqués de Valdecilla, Santander, Cantabria, Spain, [43]Hospital de la Santa Creu i Sant Pau, barcelona, Catalonia, Spain, [44]Complexo Hospitalario de Ourense, Ourense, Spain, [45]Complejo Hospitalario Hospital Provincial de Pontevedra, Pontevedra, Spain, [46]Hospital La Mancha Centro, Alcázar de San Juan, Alcázar de San Juan, Spain, [47]Hospital Clínic de Barcelona, Barcelona, Spain, [48]Vall d'Hebron Hospital, Barcelona, Catalonia, Spain

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune diseases (AD) are complex diseases associated with both genetic and environmental risk factors. In the last 10 years major advances have been made in the characterization of the genetic basis of AD. To date, very little is known on the environmental factors associated to AD. The objective of the present study was to characterize the dietary patterns of six of the most prevalent ADs, and evaluate the effect of disease on the observed changes.

Methods: A total cross-sectional cohort of 11,621 individuals from Spain encompassing six prevalent ADs (RA n=1,949; psoriasis (PS) n=2,186; PsA n=1,437; SLE n=699, ulcerative colitis (UC) n=1,415; Crohn's disease (CD) n=1,952) and healthy controls (n=1,983), was recruited through the IMID-Consortium from 2,007 to 2,012. Dietary habits were registered through a common epidemiological questionnaire, including biometric, socio-demographic and lifestyle information. For each individual, the weekly consumption frequency of 13 main food categories was recorded. Disease-specific main effects and moderation by disease activity were tested for statistical significance. Multivariate linear models were used to test for association with adjustment for main confounding covariates (e.g. age, gender, geographic region, BMI). In a subset of patients and controls with GWAS data (n=7,402) mendelian randomization (MR) was used to support the causality of disease on the observed diet variation.

Results: As expected, patients with ADs targeting the digestive system -UC and CD- showed the largest food consumption differences in comparison to healthy controls. This included a highly significant increase in bread, pasta and sweets ($P< 1e-8$ in CD, $P< 1e-5$ in UC). Like IBDs, SLE and PsA patients had a higher ingestion of sweets, and RA patients showed a higher consumption of bread ($P< 0.05$). Specifically, chronic arthritis RA and PsA had a reduced consumption of meat ($P< 5e-4$) compared to controls. RA and UC (but not CD) incorporated more fruit in their diet. Testing for association between disease activity in the three rheumatic diseases -SLEDAI for SLE and DAS28 for RA and PsA- did not support a direct association between the previous food groups with severity but revealed a positive association between dairy and disease activity in RA. Using a MR approach, we provide evidence that several of the observed dietary changes are caused by the disease. High smoking cessation rates were observed in UC, CD and SLE, but not in Ps, RA and PsA. Alcohol consumption was significantly lower in all ADs compared to healthy subjects. MR analysis showed that disease was the main cause for this change of habit in SLE ($P< 5e-11$) and RA ($P< 5e-7$), but not in PsA ($P=0.21$).

Conclusion: Using a large cross-sectional cohort of patients and controls from the Spanish population we provide, for the first time, a simultaneous analysis of the dietary habits of six autoimmune diseases. Our results confirm the high impact of IBD on diet alteration but also show multiple previously unreported associations with food categories and rheumatic ADs. Mendelian Randomization analyses support the causal effect of disease on multiple of the observed dietary changes but also suggest the presence of reverse causation.

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Abstract Number: 2076

The Opioid Epidemic: The Rheumatology Response to Management of Chronic Pain

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain is the hallmark symptom of many rheumatologic conditions and chronic pain management is a major part of clinical practice in rheumatology. Therefore, as the country and medical community evaluate and respond to the opioid epidemic, rheumatologists should be in the forefront of these discussions and response. In rheumatoid arthritis (RA), chronic opioid use doubled from 2002 to 2015, with peak use in 2010 (Curtis JR et al, *Arthritis Rheum*, 2017). However, it is still unclear in which diseases in rheumatology opioid use is most prevalent and how rheumatologists have changed their management in response to the crisis. Recent studies suggest an inclination for providers to seek alternate methods of pain control, and focus on the treatment of concomitant psychiatric disease (Yvonne LC et al, Arthritis Rheum, 2018). The purpose of this study was to evaluate changes in opioid and other medication use in the management of chronic pain for common rheumatologic conditions in an outpatient rheumatology clinic of an academic medical center.

Methods: Institutional review board approval was obtained and a retrospective electronic medical chart review was performed. Patients with the primary diagnosis of fibromyalgia (FMS), osteoarthritis (OA), and RA seen in the outpatient rheumatology clinic were randomly selected from 2011 and 2017. Records were reviewed to confirm primary diagnosis, demographic information, and medication use. Specifically, opioid use with consecutive prescriptions for at least 3 month duration, and gabapentin, pregabalin, tramadol, muscle relaxant, and selective serotonin reuptake

Table. Prevalence of Medication use for Chronic Pain in Rheumatology, 2011 vs 2017

Primary Diagnosis	Year	Opioid	Tramadol	Gabapentin	Pregabalin	SSRIs	Muscle relaxers
FMS	2011	11 (22%)	**17 (34%)***	**10 (20%)***	**17 (34%)***	36 (72%)	10 (20%)
	2017	5 (10%)	**8 (16%)***	**21 (42%)***	**6 (12%)***	32 (64%)	8 (16%)
OA	2011	**17 (34%)***	**22 (44%)***	5(10%)	3 (6%)	5 (10%)	6 (12%)
	2017	**7 (14%)***	**12 (24%)***	12(24%)	1 (2%)	8 (16%)	9 (18%)
RA	2011	15 (30%)	**10 (20%)***	4 (8%)	2 (4%)	5 (10%)	**1 (2%)***
	2017	8 (16%)	**1 (2%)***	6 (12%)	2(4%)	5 (10%)	**7 (14%)***
Total Pts	2011	**43 (29%)***	**49 (33%)***	**19 (13%)***	**22 (15%)***	46 (31%)	17 (11%)
	2017	**20 (13%)***	**21 (14%)***	**39 (26%)***	**10 (7%)***	45 (30%)	24 (16%)

*p less than or equal to 0.05 (when comparing 2011 to 2017)

inhibitor (SSRI) use were evaluated. Chi squared tests were used to analyze differences in medication use prevalence between 2011 and 2017.

Results: A total of 300 patients were evaluated, 50 in each diagnosis group from 2011 and 2017. Results are summarized in the Table. In 2011, prevalence of opioid use was 34% in OA, 30% in RA, and 22% in FMS. In the groups overall, there was a significant decrease in opioid ($p< 0.001$), tramadol ($p< 0.001$) and pregabalin ($p=0.022$) use from 2011 to 2017. There were also significant increases in gabapentin use ($p=0.028$). These trends were fairly similar for all groups. Interestingly, no significant changes in prevalence were found for SSRI use any group and muscle relaxant use significantly increased in the RA group only.

Conclusion: The opioid epidemic is a national crisis. In the medical community, rheumatologists are primary contributors to the management of chronic pain and directly affected by this crisis, considering that nearly 30% of these patients were on chronic opioids in 2011. It appears that the clinical community has responded to this epidemic quite dramatically over a 6 year period by decreasing use of opioids, and interestingly tramadol, by nearly 50%, as well as increasing gabapentin use by 50%. Notably, SSRI use did not increase, but remained relatively high at 30%. Rheumatologists should be major contributors to the discussions regarding management of chronic pain and we should continue to evaluate optimal chronic pain management regimens that provide improved quality of life for our patients without substantial risk.

Disclosure: M. Grant, None; **A. Kwiatkowski**, None; **N. Shakoor**, None.

Abstract Number: 2077

Population Impact Attributable to Modifiable Risk Factors for Hyperuricemia and the Fallacy of the Variance Explained

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases
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Session Time: 9:00AM–11:00AM

Background/Purpose: In a seminal *BMJ* paper (Prior 1986), the Tokelau Island migrant study for gout and hyperuricemia concluded preventive strategies to modify body mass, diet and patterns of alcohol use were needed to prevent gout in this migrant population living in urban New Zealand (9 times higher risk of gout vs. their non-immigrant counterparts). This and other multiple layers of epidemiologic and trial evidence suggesting the importance of obesity epidemics and lifestyle factors, are at odds with a recent *BMJ* paper (Major et al 2018) about minimal variance explained by isocaloric diets and an accompanying conclusion "Gout is genetic, and 'drinking too much beer' has very little influence on serum urate". To resolve this issue, we examined key modifiable risk factors in relation to the presence of hyperuricemia and estimated the theoretical proportion of hyperuricemia cases that could be prevented through risk factor modification. For comparison, we also estimated the variance explained for the same risk factors, which does not incorporate an exposure's prevalence in the population.

Methods: Using lifestyle, medical and diet data collected in NHANES III, we calculated adjusted prevalence ratios for hyperuricemia, adjusted population attributable risks (PAR) and the variance explained (partial R^2 from linear

Risk Factor	N of Individuals (%)	N of hyperuricemia	Multivariable prevalence ratios for hyperuricemia (95% CI)*	Multivariable serum urate level difference, mg/dL (95% CI)*
Body Mass Index (kg/m²)				
<25.0	5,789 (40)	607	1.0	0.0
25.0-29.9	5,133 (35)	1,090	1.85 (1.69 to 2.03)	0.48 (0.44 to 0.53)
30.0-34.9	2,378 (16)	729	2.72 (2.48 to 3.00)	0.84 (0.78 to 0.89)
≥35.0	1,324 (9)	508	3.53 (3.19 to 3.91)	1.11 (1.04 to 1.19)
DASH Diet Score				
1st Quintile	2,602 (18)	544	1.0	0.0
2nd Quintile	2,908 (20)	612	1.08 (0.98 to 1.19)	0.01 (-0.06 to 0.07)
3rd Quintile	3,499 (24)	706	1.11 (1.00 to 1.22)	0.04 (-0.02 to 0.10)
4th Quintile	3,075 (21)	593	1.16 (1.05 to 1.29)	0.07 (0.01 to 0.14)
5th Quintile	2,540 (17)	544	1.22 (1.09 to 1.37)	0.13 (0.05 to 0.20)
Alcohol Use (serving/day)				
0	7,564 (52)	1,555	1.0	0.0
0.01 to 0.09	1,428 (10)	237	0.95 (0.85 to 1.07)	0.00 (-0.07 to 0.07)
0.1 to 0.49	3,398 (23)	637	1.18 (1.09 to 1.28)	0.16 (0.11 to 0.21)
0.5 to 0.99	1,313 (9)	284	1.37 (1.23 to 1.53)	0.32 (0.25 to 0.40)
≥1	921 (6)	221	1.40 (1.23 to 1.58)	0.37 (0.29 to 0.46)
Diuretic Use				

Table 1. Multivariable serum urate level difference and prevalence ratio for hyperuricemia according to modifiable risk factors in the NHANES III

Modifiable Risk Factors	Exposure prevalence, %	PAR for hyperuricemia (95% CI), %	Serum urate variance explained, %	Serum urate variance explained, %*
BMI >25 kg/m²	60	44 (41 to 48)	8.3	8.9
DASH Diet Score (Bottom 4 Quintiles)	82	9 (3 to 16)	0.1	0.1
Alcohol Use	48	8 (5 to 11)	0.9	0.5
Diuretic Use	8	12 (11 to 14)	5.0	5.0

Abbreviations: BMI, body mass index. CI, confidence interval. DASH, Dietary Approaches to Stop Hypertension. PAR%, Population attributable risk percent.
*Calculated based on continuous variables except for diuretic use.

Table 2. Population attributable risk of hyperuricemia and serum urate variance explained for serum urate level according to modifiable risk factors in the NHANES III

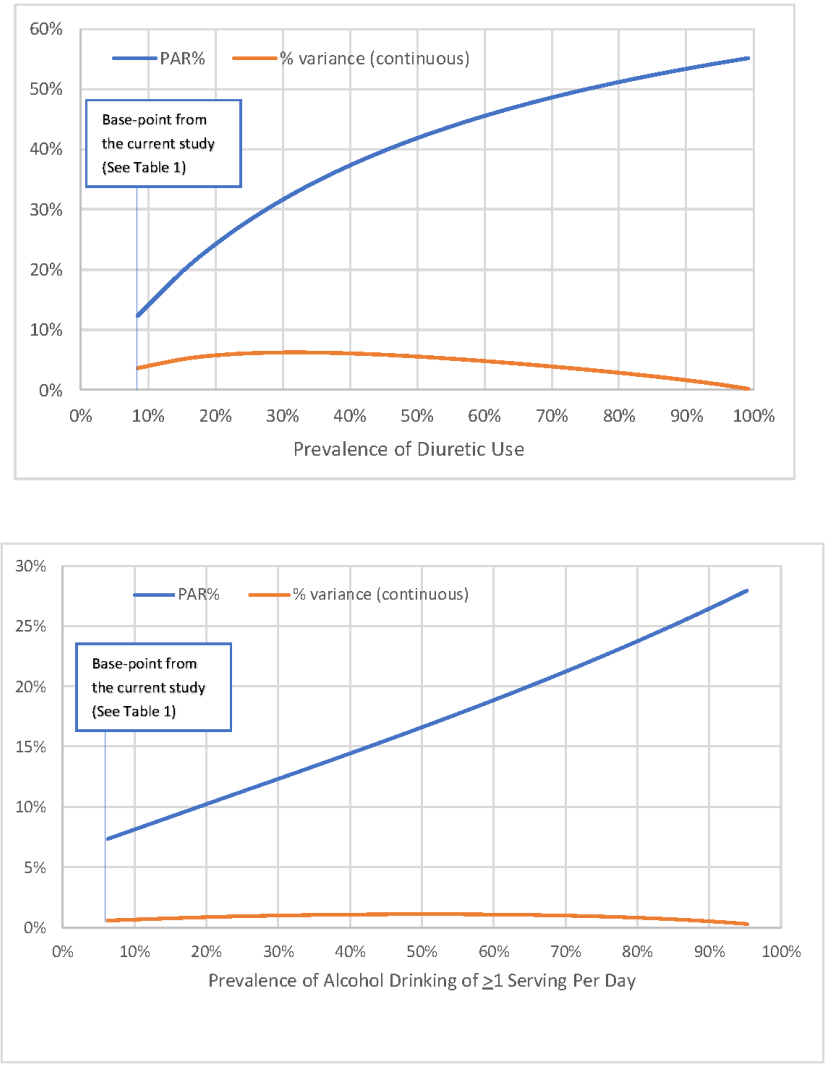

Figure 1. Population Attributable Risk vs Variance Explained According to the Prevalence of Diuretic Use (top) and Alcohol Use (bottom).

regression models) according to the following four factors: body mass index (BMI ≥25 kg/m^2), alcohol intake, non-adherence to a DASH-style diet (bottom 4 quintiles of the DASH diet score) and diuretic use. Hyperuricemia was defined as serum urate > 7.0 mg/dL among men and > 5.7 mg/dL among women. We also conducted simulation analyses to evaluate the impact on PAR and variance explained when varying the prevalence of exposure in the study population.

Results: We included 14,624 adults (mean age 47 years); 20% were hyperuricemic, 60% overweight/obese. BMI, alcohol intake, adherence to DASH-style diet, and diuretic use were all independently associated with serum urate levels and presence of hyperuricemia in a dose-response manner (**Table 1**). PARs of hyperuricemia cases for overweight/obesity, non-adherence to a DASH-style diet, alcohol use, and diuretic use were 44%, 9%, 8%, and 12%, respectively, while corresponding variances explained were 8.9%, 0.1%, 0.5%, and 5.0% (**Table 2**). Using the top half, decile and percentile of the DASH diet score as the reference group, PAR%s were 6%, 14% and 40%, respectively. Excluding those with self-reported history of gout or taking hyperuricemia drugs did not materially alter our results, nor did using an alternative definition of hyperuricemia (> 7.0 mg/dL in both sexes). Our simulation study showed the variance nearing zero with exposure prevalence's nearing 100% (**Figure**).

Conclusion: In this national sample of US men and women, four modifiable risk factors (BMI, DASH diet, alcohol use and diuretic use) independently accounted for a large proportion of hyperuricemia cases, suggesting a substantial role for modification intervention. However, the corresponding serum urate variance explained by these risk factors was far smaller and paradoxically masked their high prevalences, providing real-life empirical evidence for its limitations in assessing common environmental risk factors.

Disclosure: N. McCormick, None; **N. Lu**, None; **S. Rai**, None; **C. Yokose**, None; **Y. Zhang**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5.

Abstract Number: 2078

Transitions in Lumbar Spine Osteoarthritis: The Johnston County Osteoarthritis Project

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SESSION INFORMATION
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Background/Purpose: Spine osteoarthritis (SOA) has been defined by the presence of: 1) disc space narrowing (DSN) and vertebral osteophytes (OST), or 2) facet joint OA (FOA). Anatomical differences between these structures suggest they may have different etiologies. Furthermore, a current clinical paradigm is that SOA leads to lumbar spine instability and subsequent FOA, suggesting a transition pathway. The purpose of this study was to 1) describe the participants with SOA and FOA over time 2) describe the proportion that transitioned from neither SOA nor FOA at baseline to either FOA only or SOA only at follow-up and 3) describe the proportion that transitioned from FOA only or SOA only at baseline to both SOA and FOA at follow-up. Elucidating these transitions would improve our understanding of the underlying pathophysiological processes and may indicate the potential for separate clinical phenotypes.

Methods: These analyses used baseline (2006-2010) and follow-up (2013-2015) data from the Johnston County Osteoarthritis Project. Paired (baseline and follow-up) lumbar spine radiographs were graded using the Burnett Atlas for OST (0-3), DSN (grade 0-3), and FOA (present or absent). SOA was defined as the presence of at least ≥ 1 DSN and the presence of at least a ≥1 OST at the same lumbar level. Participants were categorized into those with 1) FOA only 2) SOA only 3) neither FOA nor SOA and 4) both FOA and SOA (excluded at baseline). Starting with neither FOA nor SOA at baseline, we describe the transition to SOA only and to FOA only at follow-up. Starting with prevalent FOA only or SOA only at baseline, we describe the transition to both SOA and FOA. Counts and percentages with 95% confidence intervals (CI) were used to describe the prevalence at baseline and incidence of transitions occurring at follow-up. The mean follow-up time was 5.5 years.

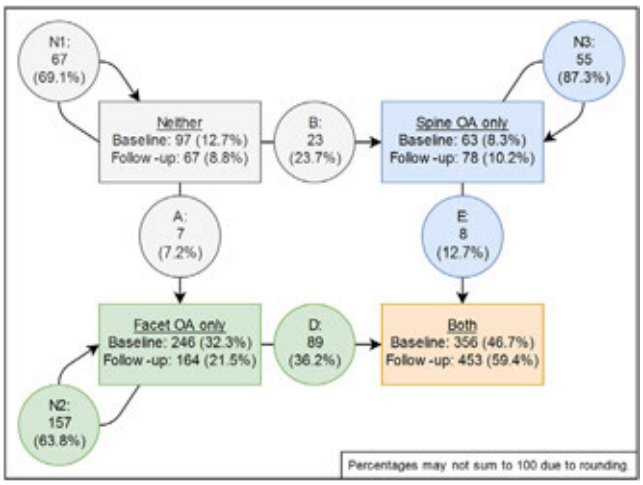

Figure illustrating the counts and percentages of participants that remain within subgroups (N1-3), transition to incident spine osteoarthritis (OA) or facet OA (A&B), or transition from prevalent facet OA or spine OA to both (D&E).

Results: A total of n=762 participants had complete data for these analyses. The mean age and body mass index (BMI) were 66.2 (SD 10.2) years and 30.9 (SD 6.5) kg/m2, respectively; 65.7% were women, and 32.6% were African American (AA).

The figure illustrates the counts and proportions of those with prevalent SOA only or FOA only at baseline and those that transition from either SOA (blue) or FOA (green) to both SOA and FOA (orange) at follow-up. At baseline, 13% of participants had neither SOA nor FOA, 32.3% had FOA only, 8% had SOA only, and 47% had both. At follow-up, a large proportion of participants remained within the same subgroup as baseline and did not transition: 69.1% neither SOA nor FOA (N1), 64% of those with FOA only (N2) and 87% of those with SOA only (N3). Among those with neither SOA nor FOA at baseline, 7% (95% CI 3% to 16%) transitioned to FOA only (A) and 24% (95% CI 16% to 36%) transitioned to SOA only (B). Among those with baseline SOA or FOA only, 36% (95% CI 30% to 42%) transitioned from FOA only to both (D) compared to 13% (95% CI 5% to 21%) that transitioned from SOA to both (E).

Conclusion: Participants in this study tended to remain within these subgroups over time. The most common transitions were from neither SOA nor FOA to SOA only and prevalent FOA only to both SOA and FOA. These findings suggest a different etiological process may exist between SOA and FOA and supports the potential for separate clinical phenotypes.

Disclosure: A. Goode, None; **D. Hu**, None; **R. Cleveland**, None; **S. George**, None; **V. Byers Kraus**, None; **T. Schwartz**, None; **R. Gracely**, None; **J. Jordan**, None; **Y. Golightly**, None.

Abstract Number: 2079

Impact of Eliminating the Bouted Minutes Requirement in the New 2018 Physical Activity Guidelines for Americans on Gender Disparity in Guideline Attainment for Persons with or at High Risk of Knee Osteoarthritis

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SESSION INFORMATION
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Background/Purpose: The 2018 Physical Activity (PA) Guidelines no longer require PA to occur in bouts of ≥ 10 minutes for meeting the weekly 150-min moderate-to-vigorous PA (MVPA) recommendations. In persons with lower limb joint symptoms, attaining 60-min weekly MVPA is linked to maintaining disability-free status over 4 years. This benchmark serves as an achievable intermediate step toward meeting guidelines and motivates those with chronic knee pain and/or function limitations to engage in PA. In persons with radiographic knee OA (KOA), 13% men and 8% women met the legacy 2008 PA Guidelines. It is unknown what proportions of men and women with or at high risk for KOA meet the updated 2018 Guidelines (150-min weekly MVPA) and the disability-free threshold (60-min weekly MVPA). Factors associated with meeting each threshold have not been examined. We aimed to (1) describe the prevalence of attaining ≥ 150-min and ≥ 60-min weekly MVPA; and (2) determine factors associated with attaining each of the PA recommendations, in persons with or at high risk for KOA.

Methods: 1922 OAI (Osteoarthritis Initiative) participants with valid accelerometer monitoring at 48-month OAI visit were included in the analysis sample. We computed weekly unbouted MVPA minutes for each participant. Radiographic KOA was defined as ≥ K/L 2 in at least 1 knee; symptomatic KOA defined as aching or stiffness for at least half of the days of a month (in the past year) in at least 1 knee. Descriptive summaries of weekly MVPA minutes are presented separately for men and women. To identify factors associated with attaining 150-min and 60-min MVPA respectively, we performed multivariate ordered logistic regressions, controlling for age, sex, BMI, race, education, depression, comorbidity, and radiographic/symptomatic KOA.

Results: In those with or at high risk for KOA, 44% men vs. 22% women had ≥ 150 weekly MVPA minutes; 67% men vs. 50% women had ≥ 60 minutes. In those with radiographic KOA, 41% men vs. 20% women had ≥ 150 minutes; 62% men vs. 47% women had ≥ 60 minutes. In those with symptomatic KOA, 41% men vs. 16% women had ≥ 150 minutes; 65% men vs. 45% women had ≥ 60 minutes (Table 1). Being a woman, older, obese, overweight, non-White, depressed; and having ≥ 2 comorbidities and both radiographic and symptomatic KOA was each associated with reduced likelihood of attaining the 150-min threshold. Being a woman, older, obese, overweight, non-college graduate, depressed; and having any comorbidity was each associated with reduced likelihood of attaining the 60-minute threshold.

Conclusion: The proportion of men and women meeting guidelines tripled based the updated 2018 PA Guidelines vs. the legacy 2008 Guidelines. The disparity between sexes widened; twice as many men attained the updated guidelines than women. PA interventions may explore strategies to engage women, non-Whites, and non-college graduates and target modifiable factors of BMI, depression, and symptom managements.

Table 1. Physical activity levels based on 150-min and 60-min weekly MVPA thresholds, among men and women

Characteristics (n)	Weekly time spent in MVPA		
	< 60 min	60 to 150 min	≥ 150 min
	n (row %)		
Men			
Overall (n=861)	283 (32.9%)	198 (23.0%)	380 (44.1%)
Age, years			
49-59 (n=315)	43 (13.7%)	83 (26.3%)	189 (60.0%)
60-69 (n=264)	79 (29.9%)	56 (21.2%)	129 (48.9%)
≥ 70 (n=282)	161 (57.1%)	59 (20.9%)	62 (22.0%)
BMI			
Normal (18.5-24.9 kg/m^2) (n=168)	41 (24.4%)	38 (22.6%)	89 (53.0%)
Overweight (25.0-29.9 kg/m^2) (n=389)	112 (28.8%)	92 (23.7%)	185 (47.6%)
Obese (≥ 30 kg/m^2) (n=304)	130 (42.8%)	68 (22.4%)	106 (34.9%)
Race			
White (n=763)	251 (32.9%)	169 (22.1%)	343 (45.0%)
Non-White (n=98)	32 (32.7%)	29 (29.6%)	37 (37.8%)
Education			
College graduate or above (n=779)	242 (31.1%)	182 (23.4%)	355 (45.6%)
Non-college graduate (n=82)	41 (50.0%)	16 (19.5%)	25 (30.5%)
Comorbidity score			
0 (n=589)	153 (26.0%)	140 (23.8%)	296 (50.3%)
1 (n=138)	66 (47.8%)	29 (21.0%)	43 (31.2%)
≥ 2 (n=134)	64 (47.8%)	29 (21.6%)	41 (30.6%)
Depressive Symptoms			
CES-D score < 16 (n=776)	248 (32.0%)	174 (22.4%)	354 (45.6%)
CES-D score ≥ 16 (n=85)	35 (41.2%)	24 (28.2%)	26 (30.6%)
Disease and Symptom State			
(-) RKOA + (-) SxKOA (n=246)	63 (25.6%)	59 (24.0%)	124 (50.4%)
(+) RKOA + (-) SxKOA (n=269)	100 (37.2%)	56 (20.8%)	113 (42.0%)
(-) RKOA + (+) SxKOA (n=94)	24 (25.5%)	26 (27.7%)	44 (46.8%)
(+) RKOA + (+) SxKOA (n=252)	96 (38.1%)	57 (22.6%)	99 (39.3%)
Women			
Overall (n=1061)	527 (49.7%)	298 (28.1%)	236 (22.2%)
Age, years			
49-59 (n=304)	82 (27.0%)	114 (37.5%)	108 (35.5%)
60-69 (n=381)	171 (44.9%)	124 (32.5%)	86 (22.6%)
≥ 70 (n=376)	274 (72.9%)	60 (16.0%)	42 (11.2%)
BMI			
Normal (18.5-24.9 kg/m^2) (n=320)	124 (38.8%)	93 (29.1%)	103 (32.2%)
Overweight (25.0-29.9 kg/m^2) (n=367)	189 (51.5%)	99 (27.0%)	79 (21.5%)
Obese (≥ 30 kg/m^2) (n=374)	214 (57.2%)	106 (28.3%)	54 (14.4%)
Race			
White (n=836)	410 (49.0%)	225 (26.9%)	201 (24.0%)
Non-White (n=225)	117 (52.0%)	73 (32.4%)	35 (15.6%)
Education			
College graduate or above (n=887)	417 (47.0%)	255 (28.7%)	215 (24.2%)
Non-college graduate (n=174)	110 (63.2%)	43 (24.7%)	21 (12.1%)
Comorbidity score			
0 (n=762)	344 (45.1%)	230 (30.2%)	188 (24.7%)
1 (n=192)	110 (57.3%)	43 (22.4%)	39 (20.3%)
≥ 2 (n=107)	73 (68.2%)	25 (23.4%)	9 (8.4%)
Depressive Symptoms			
CES-D score < 16 (n=917)	448 (48.9%)	258 (28.1%)	211 (23.0%)
CES-D score ≥ 16 (n=144)	79 (54.9%)	40 (27.8%)	25 (17.4%)
Disease and Symptom State			
(-) RKOA + (-) SxKOA (n=296)	128 (43.2%)	81 (27.4%)	87 (29.4%)
(+) RKOA + (-) SxKOA (n=348)	168 (48.3%)	98 (28.2%)	82 (23.6%)
(-) RKOA + (+) SxKOA (n=126)	63 (50.0%)	39 (31.0%)	24 (19.0%)
(+) RKOA + (+) SxKOA (n=291)	168 (57.7%)	80 (27.5%)	43 (14.8%)

MVPA = moderate-to-vigorous physical activity; BMI = body mass index; CES-D = Center for Epidemiological Study – Depression Scale; RKOA = radiographic knee OA; SxKOA = symptomatic knee OA

Disclosure: A. Chang, None; **J. Song**, None; **J. Lee**, None; **R. Chang**, None; **P. Semanik**, None; **D. Dunlop**, None.

Abstract Number: 2080

It Starts at Work: The Relationship Between Workplace Supports and Presenteeism Among Young Adults with Rheumatic Disease

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases – ARP

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Young adults with rheumatic disease who are employed frequently report presenteeism (i.e., working while unwell). Workplace supports including extended health benefits, job accommodations and work modifications have the potential to minimize presenteeism and promote long-term labor market engagement. Study objectives are to examine the most needed workplace supports reported by young adults with rheumatic disease, and to determine the relationship between meeting workplace support needs and presenteeism.

Methods: Baseline findings from an ongoing three-year longitudinal study of the transitional work experiences of Canadian young adults (18-35 years) with rheumatic disease are presented. Participants were recruited from rheumatology clinics, community-based patient organizations and a survey research firm. All participants completed an online survey that asked about sociodemographic (e.g., age, gender), health factors (e.g., pain, fatigue, disease activity) and work context (e.g., work hours, job demands). Participants were also asked about need for and use of twelve workplace supports. Participants were categorized as having workplace support needs met or exceeded when workplace supports used were equal or greater than the number of workplace supports needed, respectively. Presenteeism was assessed using one item from the Work Productivity and Impairment Questionnaire that asked about the effect of health on work (0= no effect; 10= completely prevented from working). A multivariable proportional odds model was used to examine the relationship between meeting workplace support needs and presenteeism.

Results: 412 young adult participants with rheumatic disease completed the baseline survey. Mean age of participants was 29 years (±4.2) and over half were female (51%). A majority of participants had rheumatoid arthritis (36%) or juvenile arthritis (20%). Participants indicated moderate pain, fatigue and disease activity. The most needed workplace supports included scheduling flexibility (92%), drug coverage (91%), paid sick leave (86%) and modified job duties (81%). Just over half of participants reported that their workplace needs were met (41%) or exceeded (16%); 43% reported unmet need. The sample's mean presenteeism score was 5.3 (±2.3). Those who reported that their workplace support needs were exceeded indicated significantly lower presenteeism (mean = 4.2 ± 2.8) compared to those who reported workplace support needs met (mean = 5.4 ± 2.5) or unmet (mean = 5.4 ± 2.4). When controlling for sociodemographic and health factors, those whose workplace support needs were exceeded showed 50% lower risk of reporting presenteeism (RR = 0.50, 95% CI 0.29-0.87). Having workplace needs met or unmet were not significantly associated with presenteeism.

Conclusion: For young adults, the workplace plays an important role in fostering work productivity. By providing diverse workplace supports and encouraging their use, employers can attenuate the relationship between rheumatic disease and presenteeism at the early career phase.

Disclosure: A. Jetha, None; **L. Tucker**, None; **J. Bowring**, None; **C. Backman**, None; **L. Proulx**, None; **V. Kristman**, None; **E. Hazel**, None; **L. Perlin**, None; **M. Gignac**, None.

Abstract Number: 2081

The Health-promoting Potential of Everyday Activities: Preliminary Results from an Exploratory Study of Adults with and Without Inflammatory Arthritis

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SESSION INFORMATION
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Background/Purpose: Inflammatory arthritis (IA) can disrupt a person's valued life activities but little is known about the potential health benefits of activities other than physical activity. This study explores (a) differences in activity characteristics between adults with and without IA, and (b) the relationships between activity characteristics and health and well-being. Understanding how people characterize their activities and how these activities impact health can help advance arthritis care.

Methods: We conducted a cross-sectional study (as the first phase of a larger longitudinal study) with 40 non-smoking adults, 20 with IA (confirmed by a rheumatologist) and 20 healthy controls (HC). Participants were recruited via clinic and community advertising. Demographic data included age, sex, diagnosis, and employment status. Activity characteristics were measured using Personal Projects Analysis: participants identify 10 salient, goal-directed activities and rate them on 19 characteristics (e.g., creative, absorbing, stressful) using a 11-point scale (e.g., 10=highly creative, 0=not at all creative). Health status indicators were the SF-36 health survey and telomere length (TL), measured from dried blood spots using the monochrome multiplex qPCR method. Descriptive statistics, t-tests, and correlation coefficients were calculated.

Results: Participants' mean age was 54 (SD=15.6); 82.5% were women. Mean age and proportion of women did not differ between groups. In the IA group 65% had RA, 20% lupus, 5% JIA, and 10% had both RA and lupus. In the IA group the highest ranked activity characteristics were value, time adequacy, and outcome, and in the HC group they were outcome, progress, and challenge. Significant between-group differences include creativity, value, control, and absorption. See Table 1. In the total sample, the SF-36 physical component score (PCS) was most strongly associated with value ($r = -0.56$, $p < 0.001$) and creative ($r = -0.38$, $p = 0.02$) activity characteristics. The SF-36 mental component score (MCS) was most strongly associated with stress ($r = -0.48$, $p = 0.002$) and difficulty ($r = -0.43$, $p = 0.006$). TL was most strongly associated with importance ($r = -0.33$, $p = 0.04$) and value ($r = -0.33$, $p = 0.04$). The correlation between TL and MCS ($r = -0.36$, $p = 0.02$) was stronger than TL and PCS ($r = 0.22$, $p = 0.17$). PCS score was significantly higher in the HC group than the IA group. See Table 2 for health outcomes between groups.

Conclusion: There are differences in how adults with and without IA characterize their daily activities. Our results show that people with IA engage in more activities of positive characteristics than those without IA. Perhaps having arthritis compels patients to engage in more valued activities; however, this requires further exploration. A better understanding of these differences may provide insight to future activity recommendations to support physical and

Activity characteristic	IA		HC		t	p
	Mean	SD	Mean	SD		
Value	7.9	2.7	5.2	3.2	-2.9	*<0.01*
Time Adequacy	7.5	2.7	5.9	3.0	-1.8	0.08
Outcome	7.4	2.9	6.4	2.8	-1.1	0.27
Progress	7.0	2.6	6.1	2.9	-1.0	0.31
Challenge	6.9	2.5	6.0	2.9	-1.1	0.30
Creativity	7.2	2.2	4.8	2.7	-3.0	*<0.01*
Control	7.4	2.9	5.2	2.8	-2.4	*0.02*
Absorption	7.2	2.5	4.1	3.5	-3.3	*<0.01*

Table 1. Activity characteristics between groups.

Health outcome	IA		HC		t	p
	Mean	SD	Mean	SD		
PCS	39.9	10.9	52.7	6.7	4.5	*<0.01*
MCS	48.5	11.6	50.5	9.9	0.6	0.56
TL	8.5	1.2	8.8	1.5	0.7	0.49

Table 2. Health outcomes between groups.

mental health. Although preliminary, the finding that TL is associated with ratings of activity importance and value, while self-reported MCS was associated with activity stress and difficulty, suggests interesting hypotheses for future studies examining how certain activity characteristics accrue different health benefits.

Disclosure: F. To-Miles, None; **S. Forwell**, None; **E. Puterman**, None; **C. Backman**, None.

Abstract Number: 2082

Activity in Work and Life: The Association Between Physical Activity and Employment Status with Future Slow Walking in Knee Osteoarthritis

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Background/Purpose: Knee osteoarthritis (OA) is the leading cause of functional limitation in older adults, e.g., slow walking. Physical activity (PA) is beneficial for those with knee OA, as those who walk more or engage in more moderate-to-vigorous PA (MVPA) have better physical function than their less-active counterparts. However, it is unclear to what extent work may modify this association. Over half of all PA occurs in a work context, i.e. preparing for

Table 1: Descriptive statistics and risk ratios for incident slow gait speed by PA and employment

	Baseline Gait Speed, mean ± SD	Incident Slow Gait Speed Proportion, n/N (%)	RR [95% CI], unadjusted	RR [95% CI], adjusted*
Steps Active (≥6000 steps/day)	1.46 ± 0.15 m/s	90/639 (14.1%)	1.0 (REF)	1.0 (REF)
Steps Inactive (<6000 steps/day)	1.40 ± 0.13 m/s	140/474 (29.5%)	**1.2 [1.1 - 1.3]**	**1.1 [1.0 - 1.2]**
Employed	1.44 ± 0.15 m/s	154/822 (18.7%)	1.0 (REF)	1.0 (REF)
Unemployed	1.40 ± 0.13 m/s	76/291 (26.1%)	1.1 [1.0 - 1.1]	1.0 [0.9 - 1.1]
MVPA Active (≥45 min/week)	1.45 ± 0.15 m/s	144/872 (16.5%)	1.0 (REF)	1.0 (REF)
MVPA Inactive (<45 min/week)	1.37 ± 0.11 m/s	86/241 (35.7%)	**1.3 [1.2 - 1.4]**	**1.2 [1.0 - 1.3]**
Employed	1.44 ± 0.15 m/s	154/822 (18.7%)	1.0 (REF)	1.0 (REF)
Unemployed	1.40 ± 0.13 m/s	76/291 (26.1%)	1.1 [1.0 - 1.1]	1.0 [0.9 - 1.1]

*adjusted for baseline age, sex, BMI, presence of knee pain, presence of radiographic knee OA

Table 1. Descriptive statistics and risk ratios for incident slow gait speed by PA and employment

work, commuting, and engaging in employment-based tasks. Therefore, the purpose of this study was to determine to what extent employment status may modify the association of physical activity with incident slow walking in adults with or at risk for knee OA.

Methods: We used data from the Osteoarthritis Initiative (OAI), a large cohort study of individuals with or at risk for knee OA. Objectively-measured PA (steps/day and MVPA) and employment status (yes or no) were collected at the 48-month visit (baseline). PA was measured with an Actigraph GT1M accelerometer worn at the hip for at least 4 days, 10 hours/day and MVPA was defined as ≥ 2020 counts/min. Employment status was obtained from the Physical Activity Scale for the Elderly (PASE) when asked whether they worked for pay or as a volunteer in the past 7 days. Gait speed from a 20m walk test was collected at the 48-month and 96-month visits. PA metrics were separately dichotomized into Active and Inactive using 6000 steps/day and 45 min/week of MVPA. Gait speed was dichotomized using 1.22 m/s as the cutoff to identify slow gait speed as walking less than that represents the inability to safely cross a timed street intersection. To determine to what extent employment status modifies the association between PA and incident slow gait speed at the 96-month visit, we first used binary logistic regression to calculate risk ratios and 95% confidence intervals (95% CI), adjusting for potential confounders at baseline. Next, we evaluated the interaction effect of PA and employment status on FL in a separate binary logistic regression model.

Results: Of the 1305 individuals with valid accelerometry data who were free of FL at the 48-month visit (age: 63.4 ± 8.6 years old, sex: 51.6% female, BMI: 28.0 ± 4.5 kg/m^2), 1133 had gait speed data at the 96-month visit. For both steps/day and MVPA, inactive individuals had greater risk of incident slow gait speed relative to active individuals. Risk for incident slow gait speed was similar based on employment status in both models. In a separate model, the interaction effect of PA and employment status on FL was not significant (p = 0.11).

Conclusion: Regardless of employment, those who were inactive throughout the day, either in terms of daily walking or MVPA, had greater risk for incident slow walking relative to those who were active. This suggests that PA is a driving factor in the development of slow walking habits and that simply whether an individual was previously employed does not impact future slow walking.

Disclosure: J. Jakiela, None; **L. Thoma**, None; **H. Master**, None; **D. Voinier**, None; **M. Christiansen**, None; **L. Neely**, None; **D. White**, None.

Abstract Number: 2083

Understanding Knee Function and Symptom Management in Individuals with Risk Factors for Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases – ARP
Session Type: Poster Session (Tuesday)
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Background/Purpose: Worse knee function and frequent use of knee symptom management strategies are common in people with symptomatic knee osteoarthritis (SxOA). There are several risk factors for SxOA, with the most common being overweight/obese (OW/OB) or having a previous knee injury/surgery (KISHx). Prior to the onset of SxOA, individuals likely are not seeking care, however the presence of risk factors may help identify those experiencing signs of early knee dysfunction and need for symptom management. Therefore, the purpose of this study was to describe the association of knee OA risk factors with knee function and symptom management. We stratified by frequency of knee pain since this is strongly related to knee function and use of symptom management strategies.

Methods: We used data from the Osteoarthritis Initiative (OAI). Our analytic sample was limited to those who had at least one risk factor for knee OA and were free of SxOA at baseline. Risk factors were: OW/OB as determined by age- and sex-specific cutoffs for weight, KISHx, family history (FmHx) of end-stage knee OA, presence of bilateral Heberden's nodes, frequent knee bending, and knee symptoms in the past 12 months. Outcomes were obtained from self-report questionnaires, including: knee function via the WOMAC Physical Function score and symptom management strategies, i.e. activity limitation due to knee symptoms in the past 30 days (yes/no), use of medications in the past year due to knee symptoms (yes/no). To assess the associations of the risk factors with each outcome, we used a general linear model and logistic regression to calculate effect estimates/odds ratios with 95% confidence intervals (CI). Analyses were stratified by knee pain frequency and adjusted for potential confounders.

Results: Of the analytic sample (n=2987, age 61.1 ± 9.3 years old, 59% female, BMI 28.3 ± 4.7 kg/m^2), 988 were OW/OB, 1475 had KISHx, 500 reported knee OA FmHx, 755 had bilateral Heberden's nodes, and 2182 reported frequent knee bending. Regardless of frequency of knee pain, those who were OW/OB or with KISHx had significantly worse knee function than those without each risk factor (Table). In those with infrequent knee pain, KISHx was associated with use of both symptom management strategies, while FmHx was only associated with activity limitation and presence of bilateral Heberden's nodes was only associated with use of medications. In individuals with frequent knee pain, OW/OB and KISHx were associated with use of both symptom management strategies.

Conclusion: KISHx and OW/OB were consistently associated with worse knee function regardless of the presence and frequency of knee pain. KISHx was also consistently associated with use of knee symptom management strategies when any knee pain was present, yet OW/OB was only associated in the presence of frequent knee pain. Other risk factors were not independently related to knee function, and inconsistently related to symptom management. These results emphasize the two most common risk factors for knee OA, OW/OB and KISHx, are also the most strongly related to knee function and symptom management. Early monitoring of people with these risk factors may allow for early intervention when symptoms present and delay the consequences of knee OA.

Table: Associations of risk factors with knee function and symptom management strategies, stratified by frequency of knee pain

	Outcome					
	Knee Function (WOMAC)		Activity restriction to manage knee symptoms		Medication use to manage knee symptoms	
	Mean diff.* (95% CI)	p-value	% with the outcome (n/N)	Odds Ratio* (95% CI)	% with the outcome (n/N)	Odds Ratio* (95% CI)
No Knee Pain						
Overweight/Obese						
No	**1.1 (0.1, 2.2)**	**0.03**	3% (8/323)	DNC	3% (10/323)	1.0 (REF)
Yes			1% (1/145)		4% (6/145)	1.4 (0.4, 5.1)
History of Knee Injury or Surgery						
No	**1.4 (0.5, 2.3)**	**0.0025**	1% (2/288)	DNC	3% (8/288)	1.0 (REF)
Yes			4% (7/176)		5% (8/176)	1.6 (0.5, 5.2)
Family History						
No	0.8 (-0.3, 1.9)	0.14	2% (7/377)	DNC	4% (13/377)	1.0 (REF)
Yes			2% (2/90)		3% (3/90)	1.3 (0.3, 5.0)
Heberden's Nodes bilaterally						
No	0.5 (-0.4, 1.5)	0.24	1% (4/283)	DNC	3% (9/283)	1.0 (REF)
Yes			3% (5/181)		4% (7/181)	1.4 (0.4, 4.4)
Frequent knee bending						
No	-0.4 (-1.4, 0.7)	0.47	0% (0/91)	DNC	8% (7/91)	1.0 (REF)
Yes			2% (8/375)		2% (9/375)	0.4 (0.2, 1.3)
Infrequent knee pain						
Overweight/Obese						
No	**1.2 (0.4, 2)**	**0.003**	13% (137/1095)	1.0 (REF)	8% (89/1093)	1.0 (REF)
Yes			9% (60/455)	1.1 (0.8, 1.6)	9% (39/455)	1.2 (0.8, 1.8)
History of Knee Injury or Surgery						
No	**1.4 (0.7, 2.2)**	**<0.001**	9% (68/785)	1.0 (REF)	6% (44/783)	1.0 (REF)
Yes			17% (128/758)	**2.2 (1.6, 3.1)**	11% (84/758)	**2.6 (1.7, 3.9)**
Family History						
No	0.2 (-0.7, 1.2)	0.60	12% (157/1282)	1.0 (REF)	8% (99/1280)	1.0 (REF)
Yes			16% (40/254)	**1.4 (1.0, 2.1)**	9% (23/254)	1.3 (0.8, 2.2)
Heberden's Nodes bilaterally						
No	0.8 (-0.1, 1.6)	0.08	13% (150/1164)	1.0 (REF)	7% (84/1162)	1.0 (REF)
Yes			12% (45/379)	1.2 (0.8, 1.8)	12% (44/379)	**2.2 (1.4, 3.5)**
Frequent knee bending						
No	-0.2 (-1, 0.6)	0.60	13% (59/444)	1.0 (REF)	9% (41/443)	1.0 (REF)
Yes			13% (137/1096)	1.0 (0.7, 1.3)	8% (87/1095)	0.9 (0.6, 1.4)
Frequent knee pain						
Overweight/Obese						
No	**4.2 (2.6, 5.8)**	**<0.001**	36% (207/576)	1.0 (REF)	33% (190/576	1.0 (REF)
Yes			42% (161/387)	**1.3 (1.0, 1.8)**	40% (155/388)	**1.3 (1.0, 1.8)**
History of Knee Injury or Surgery						
No	**2.9 (1.3, 4.4)**	**<0.001**	30% (126/417)	1.0 (REF)	32% (134/419)	1.0 (REF)
Yes			45% (241/542)	**2.1 (1.5, 2.8)**	39% (210/541)	**1.6 (1.2, 2.1)**
Family History						
No	-0.7 (-2.7, 1.3)	0.50	38% (300/793)	1.0 (REF)	36% (288/794)	1.0 (REF)
Yes			39% (61/156)	1.1 (0.8, 1.6)	33% (52/156)	1.0 (0.7, 1.4)
Heberden's Nodes bilaterally						
No	1.2 (-0.8, 3.1)	0.30	39% (296/762)	1.0 (REF)	36% (272/762)	1.0 (REF)
Yes			36% (69/194)	1.3 (0.9, 1.9)	36% (71/195)	1.2 (0.8, 1.7)
Frequent knee bending						
No	1.0 (-0.7, 2.7)	0.30	38% (94/245)	1.0 (REF)	36% (87/245)	1.0 (REF)
Yes			38% (270/711)	1.0 (0.7 - 1.3)	36% (254/712)	1.0 (0.7, 1.4)

*compared to not having the risk factor and adjusted for age, sex, race, and education
DNC, did not converge due to no outcome for one of the risk factors

Disclosure: J. Jakiela, None; **D. White**, None; **H. Master**, None; **M. Christiansen**, None; **D. Voinier**, None; **L. Neely**, None; **L. Thoma**, None.

Abstract Number: 2084

Why so Fast? A Focus on Reasons for an Increase in Arthritis-Attributable Activity Limitation Trends, 2002-2017

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases – ARP
Session Type: Poster Session (Tuesday)
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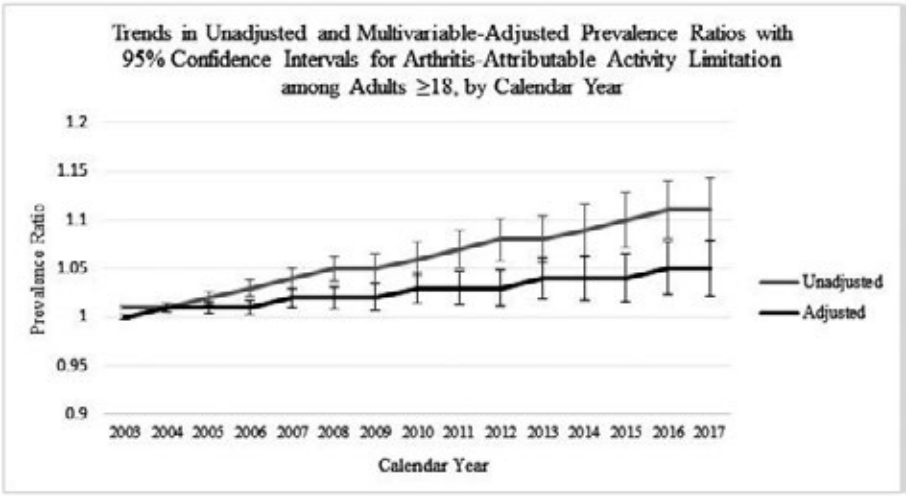
Background/Purpose: "Arthritis-attributable activity limitation" (AAAL) is linked to many potentially modifiable characteristics (e.g., work disability, physical inactivity, obesity). By 2015, prevalence of AAAL among adults ≥18 with arthritis had increased by almost 20% compared with that reported in 2002, and the observed annualized prevalence of AAAL in 2010 had outpaced projections for 2020 (22.7 vs. 22.1 million). Our objective was to investigate the extent to which trends in AAAL prevalence can be explained by changes in characteristics associated with AAAL among U.S. adults with arthritis.

Methods: Cross-Sectional data were obtained for participants ≥18 years from years 2002-2017 of the National Health Interview Survey (NHIS, average unweighted sample n=30,076), an ongoing, multistage probability survey designed to be nationally representative of the civilian, non-institutionalized U.S. population. Analyses were restricted to those with self-reported doctor-diagnosed arthritis. AAAL was defined as "yes" to "Are you now limited in any way in any of your usual activities because of arthritis or joint symptoms?" Demographic, health, function, and health care access measures were assessed across 30 variables.

We used unconditional logistic regression to estimate prevalence ratios (PR) with 95% confidence intervals (CI) to examine the associations between *a priori* selected variables and AAAL, modeled the prevalence of AAAL (dependent variable), and estimated a prevalence ratio (PR) for each independent variable in a model containing only that variable and (continuous) calendar year. Next, for 7 variables significantly associated with AAAL (identified with the overall Wald test of model coefficients) we estimated 2 PRs for AAAL trend: 1) average annual increase in AAAL, and 2) overall AAAL increase, (2017 prevalence less 2002 prevalence). Finally, we calculated a series of multivariable-adjusted (MV) models to test changes in the estimated effect of calendar year on AAAL post-adjustment, i.e., addition of a covariate which reduced the significance of the existing trend identified a variable with a significant role in the observed trend relationship.

Results: Between 2002 and 2017, prevalence of AAAL among adults with arthritis significantly increased (37.6% (95% CI=36.1-39.1) to 42.9% (41.4-44.4), p-value < 0.0001 test for trend). Initial model PR=1.11 (1.08-1.15). Only 4 variables reduced the PR, driven by: comorbidities (increased number), employment status (increased retired and not in labor force), body mass index (increased overweight), and race/ethnicity (increased non-Hispanic White). The final MV PR was 1.05 (1.02-1.08). The temporal trend in AAAL is largely explained by the temporal trends of the characteristics accounted for in this analysis (Figure).

Conclusion: In addition to identifying specific variables which explain some of the trend in increased AAAL between 2002-2017, we rejected many others as contributors. Still, unknown/unmeasured variables (e.g., zip code, urbaniza-



Adjusted for: Number of comorbidities, employment status, body mass index, and race/ethnicity.

tion, neighborhood) may account for some of the trend. Meanwhile, interventions can be directed at the subgroups identified here to reduce AAAL impact.

Disclosure: K. Theis, None; **M. Boring**, None; **R. Wilkie**, None.

Abstract Number: 2085

Too Soon to Say: Promising Results from a Community-Delivered RCT Examining Work-Related Outcomes of the Chronic Disease Self-Management Program

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SESSION INFORMATION

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Background/Purpose: More than two-thirds of U.S. adults with arthritis are working-age (< 65), and arthritis is a leading cause of work disability. The Chronic Disease Self-Management Program (CDSMP) has evidence for improving physical and mental health outcomes, but few studies specifically address employment. We examined work-related outcomes following participation in CDSMP.

Methods: From 6/2016-9/2017, we recruited participants through flyer, e-mail, and digital advertisements in communities, worksites, and other channels. No reference was made to CDSMP; participation was described in either a “health self-management program” or a “financial self-management program” (FSMP). Potential participants consented and enrolled through a website which screened for age (40-64 years), being employed, income, ≥1 chronic condition, English fluency, and living/working in the study area (5 North Carolina counties). Study design was a randomized controlled trial: intervention group=CDSMP, attenuated attention-control group=FSMP. Our primary study outcome was percent work productivity loss due to health-related presenteeism using the Work Limitations Ques-

tionnaire (WLQ) 4 Question Time Loss Module and the WLQ 25 Item Online Version. Baseline sample characteristics were summarized using descriptive statistics. Analyses of primary outcomes were conducted using simple t-tests, paired t-tests, and multivariate generalized linear models using an intent-to-treat (ITT) approach. We also did a post hoc analysis comparing CDSMP completers (attended ≥4 of the 6 sessions) to the FSMP group using α=0.10 due to the small sample size of CDSMP completers (n=41).

Results: A total of 327 enrolled and were randomized to CDSMP (n=160) or FSMP (n=167). The sample was predominantly white (54%), female (89%), and college educated (73%), with an average 2.89 chronic conditions, and average household income of $62,009. There were no significant group differences at baseline. Participation rates (attending any portion of program) were 35% (n=56) CDSMP and 25% (n=41) FSMP.

ITT analysis: There were no significant between-group differences in work-related outcomes (e.g., percent work productivity loss, time management, work output, or work self-efficacy) from baseline to 6 or 12-month follow up. In the CDSMP group (vs FSMP) depressive symptoms improved at 6 months (p=0.04) but not at 12 months; general health significantly improved at 12 months (p=0.02) but was clinically negligible.

CDSMP Completer Analysis: Compared to the FSMP group, CDSMP completers reported a greater reduction in percent work productivity loss (p=0.06) and subscales mental/interpersonal tasks (p=0.05) and work output (p=0.07) using α=0.10.

Conclusion: Low participation rates decreased power to find significant differences in the ITT analysis. However, the CDSMP completer analysis suggested a positive effect of CDSMP on work productivity among those who completed ≥4 sessions. A larger sample size of CDSMP completers is necessary to confirm these promising findings.

Disclosure: K. Theis, None; **T. Brady**, None; **S. Kneipp**, None.

Abstract Number: 2086

Arthritis-Attributable Work Limitation Variation by U.S. County Classifications and Selected Characteristics, 2017

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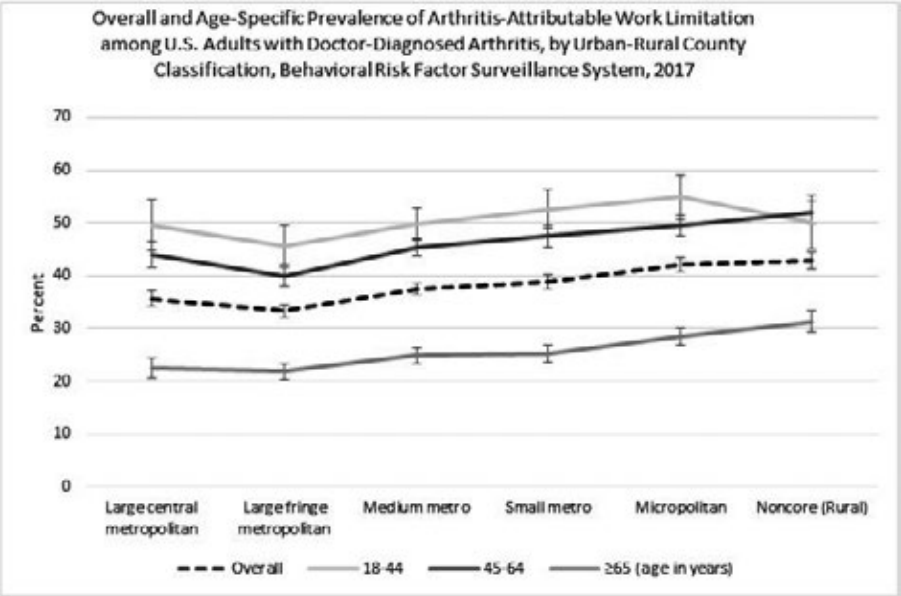
Background/Purpose: Arthritis prevalence ranges from 1-in-5 to 1-in-3 across U.S. counties, and its prevalence and effects vary by county economic grouping, metropolitan status, and uneven population density. It is a leading cause of work disability, which research suggests is sometimes linked to specific occupations/industries or job tasks. We examined the prevalence and variation of arthritis-attributable work limitation (AAWL) by overall county classification and selected characteristics.

Methods: Cross-Sectional data were from the 2017 Behavioral Risk Factor Surveillance System, an annual, state-based, random-digit–dialed landline/cellphone health survey of non-institutionalized U.S. adults ≥18 years. Among



adults with self-reported, doctor-diagnosed arthritis (145,776 respondents in 50 states and D.C.), AAWL was defined as "yes" to "In this next question, we are referring to work for pay. Do arthritis or joint symptoms now affect whether you work, the type of work you do, or the amount of work you do?" Analyses were restricted to those with AAWL, age, and county data (n=141,183). The National Center for Health Statistics 2013 Urban-Rural Classification Scheme for Counties was used to classify respondents in counties from most-urban to most-rural: large central metropolitan; large fringe metropolitan; medium metropolitan; small metropolitan; micropolitan; and noncore (smallest rural). Age-Specific estimates of AAWL prevalence by urban-rural status and selected characteristics were calculated with 95% confidence intervals (CIs). Pairwise comparisons tests for statistically significant differences between county classifications were conducted at α=0.05.

Results: Overall prevalence of AAWL among adults with arthritis ranged from 36% in large central metropolitan to 43% in the smallest rural (noncore) counties, with considerable variation by age group (Figure). Among 18-44 year olds, AAWL prevalence varied little by county classification, e.g., no statistical differences for less than high school education, unable to work/disabled, or having 0 or 1 comorbid conditions. For those ages 45-64, unemployed respondents in the 3 smallest county classifications reported higher prevalence of AAWL (range: 70-72%) vs the 3 largest county classifications (range: 54-57%). Prevalence of AAWL was highest among those 45-64 unable to work/disabled in noncore (rural) counties (76%) vs the 3 largest county classifications (69.0%, 70.8%, and 71.8%, respectively). AAWL prevalence and significance by county varied for physical activity obesity in this age group. Magnitude of AAWL prevalence was lowest among those ≥65, but all characteristics examined displayed variations by county classification.

Conclusion: Observed variations in AAWL prevalence are not fully understood. Some may be explained by distributions of arthritis-associated industries/occupations in more rural areas (e.g., farming, forestry), demographic shifts, and limited access to health care. Overall, county-specific AAWL prevalence was ≥1-in-3, indicating widespread need for evidence-based interventions to reduce negative personal and societal economic consequences of arthritis.

Disclosure: K. Theis, None; **Y. Liu**, None; **M. Boring**, None; **K. Souza**, None.

Abstract Number: 2087

Prevalence of Corticosteroid Use in Incidental Vertebral or Hip Fractures

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Background/Purpose: Non-traumatic vertebral and hip fractures are detrimental complications of osteoporosis and those with a previous fracture have double the risk of subsequent fractures. The objective of this quality improvement (QI) project was to determine the baseline characteristics that may have contributed to the vertebral or hip fracture and determine if bone health was optimized subsequent to the fracture. As corticosteroids can increase the risk of osteoporotic fractures, the initial focus of this analysis was on patients who had an outpatient prednisone prescription prior to admission.

Methods: Data was retrospectively collected from the electronic health record for patients aged 45 and older admitted to UF Health Jacksonville for an active vertebral or hip fracture diagnosis between January 1, 2017 and January 31, 2019. Traumatic injuries were excluded. Retrospective chart review could occur dating back to January 2014 for completeness. Data on patient demographics, any medication that may affect bone health (e.g. steroids, calcium and vitamin D products, bisphosphonates, etc.), DEXA scans, and pertinent labs were collected.

Results: A total of 287 patients were admitted 296 times between January 1, 2017 and January 31, 2019. Of these, 24 patients (8.4%) had an outpatient order for prednisone on at least one occasion prior to admission. Over half of the patients, 58.3%, had an outpatient order for prednisone with an associated diagnosis of chronic obstructive pulmonary disease. A majority, 79.2%, were female with a median age of 70.5 years old (range: 57 – 98 years old). More admissions were due to hip fractures (54.2%) than vertebral fractures (45.8%). Chronic prednisone use ≥ 15 mg/day prior to admission was noted in 9.1% of patients. The remaining 22 patients had prednisone bursts with 9.1% of patients having cumulative burst doses between 10-100 mg, 68.2% patients between 101-500 mg, 18.2% patients between 501-1000 mg, and 4.5% patients > 1000 mg. Of the 24 patients, six patients had a DEXA scan prior to admission and of these DEXA scans, 2 showed osteoporosis and 3 showed osteopenia in the affected fracture area at baseline. Only 8.3% of patients were on a bisphosphonate prior to admission. Baseline Vitamin D 25-OH levels were available in 12 patients with an average level of 30.365 ± 11.35 ng/mL.

Conclusion: In this convenience sample of patients who had an outpatient order for prednisone prior to admission, more hip fractures occurred than vertebral fractures. A small percentage of patients (9%) were on prednisone chronically. The rate of baseline DEXA scan was low as only 25% of patients had one available despite approximately 68% of patients having a cumulative prednisone dose exposure between 101 – 500 mg. The rate of bisphosphate use prior to admission was also low at 8.3%. Data collection for the patients not on prednisone is ongoing. The goal of this QI project is to create a care pathway for patients admitted to the hospital for vertebral or hip fractures to optimize bone health by mitigating modifiable risk factors and increasing appropriate osteoporosis medication prescriptions to reduce the future risk of fractures. No correlation can be made at this time between prednisone use, osteoporosis, and fracture incidence.

Disclosure: G. Kaeley, None; **J. Ferm**, None; **L. Dang**, None.

Abstract Number: 2088

When It Just Won't Stop: Chronic Pain and High Impact Chronic Pain Among U.S. Adults with Arthritis

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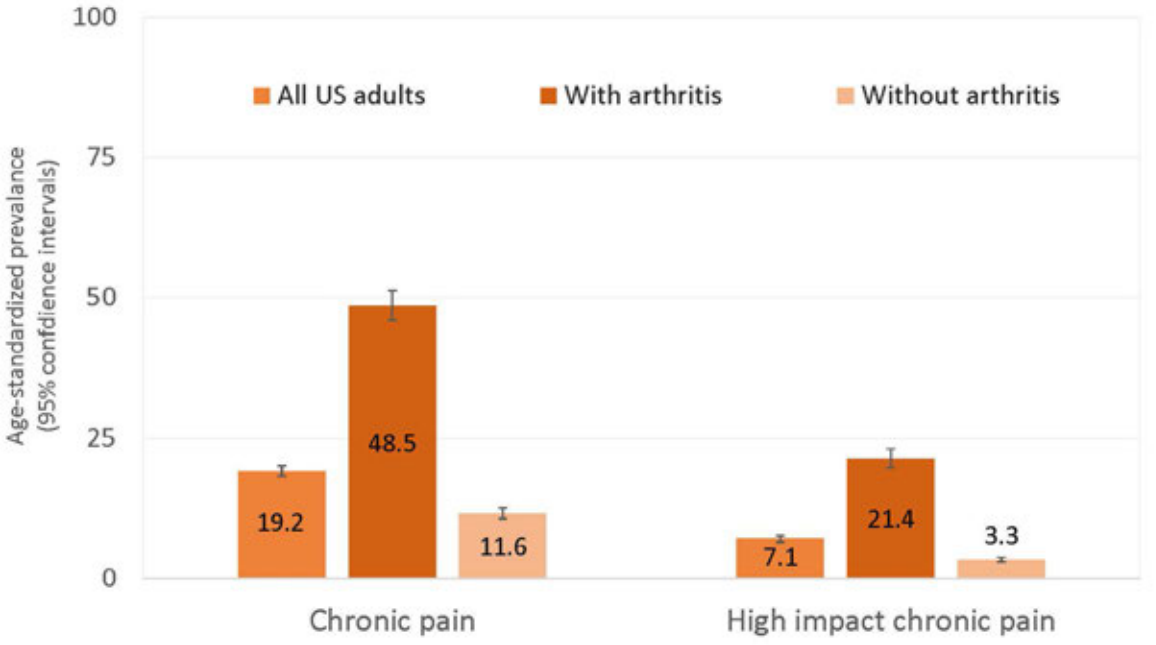
Background/Purpose: Pain is a hallmark of arthritis. Despite growing attention to chronic pain (CP), surprisingly little is known about its magnitude and impact among the 54.4 million US adults with arthritis. We studied two pain outcomes, CP and high impact chronic pain (HICP), among US adults age ≥18 years with a focus on those with arthritis.

Methods: We analyzed 2016/2017 data from the population-based US National Health Interview Survey (NHIS) (59, 696 participants). Arthritis was a "yes" (n=16,732) to "Have you **ever** been told by a doctor or other health professional that you have some form of arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia?" We calculated crude and age-standardized prevalence of CP (pain most/all days in past 6 months) and HICP (CP that limited life or work

Figure: Age-standardized prevalence of chronic pain and high impact chronic pain among US adults age ≥ 18 years, overall and by arthritis status, 2016-17 National Health Interview Survey



Crude chronic pain prevalence: all US adults (20.3%), adults with arthritis (48.4%), and adults without arthritis (11.5%)
Crude high impact chronic pain prevalence: all US adults (7.6%), adults with arthritis (21.6%), and adults without arthritis (3.2%)

Table: Multivariable-adjusted prevalence ratios (PR) for associations between each pain outcome and 14 selected chronic conditions*

	Chronic pain		High impact chronic pain	
Chronic Condition	PR	95% CI	PR	95% CI
Low back pain	2.2	(2.1 - 2.3)	2.3	(2.1 - 2.5)
Arthritis	**2.1**	**(2.0 - 2.2)**	**2.2**	**(2.0 - 2.4)**
Neck pain	1.8	(1.7 - 1.9)	1.9	(1.7 - 2.1)
Serious psychological distress	1.6	(1.5 - 1.7)	1.7	(1.6 - 1.9)
Asthma	1.2	(1.2 - 1.3)	1.2	(1.1 - 1.3)
Chronic obstructive pulmonary disease	1.2	(1.1 - 1.3)	1.2	(1.1 - 1.4)
Hypertension	1.2	(1.1 - 1.2)	1.2	(1.1 - 1.4)
Liver	1.2	(1.1 - 1.4)	1.2	(1.1 - 1.4)
Cancer	1.1	(1.1 - 1.2)	1.0	(0.9 - 1.2)
Diabetes	1.1	(1.0 - 1.2)	1.1	(1.0 - 1.1)
Heart disease	1.1	(1.1 - 1.2)	1.1	(1.0 - 1.2)
Hepatitis	1.1	(1.0 - 1.2)	1.1	(1.0 - 1.3)
Kidney	1.1	(1.0 - 1.2)	1.1	(1.1 - 1.2)
Stroke	1.1	(1.0 - 1.2)	1.2	(1.1 - 1.3)

*Multivariable logistic regression model for each pain outcome contained 14 chronic conditions and age, sex, race/ethnicity, highest educational attainment, employment status, sexual identity

CI, confidence interval

activities on most/all days in the past 6 months) among US adults overall and by arthritis status. Then, among all US adults, we estimated the multivariable-adjusted association with prevalence ratios (PR) from logistic regression models between each pain outcome and 14 chronic conditions and 6 socio-demographic characteristics. Finally, we calculated CP and HICP prevalence among adults with arthritis across socio-demographic characteristics, health status, and comorbidities.

Results: Crude CP and HICP prevalence among adults with arthritis was 48.4% and 21.6%, respectively (Figure). Both CP and HICP age-standardized prevalence for adults with arthritis was higher than for US adults overall and those without arthritis, respectively (CP=48.5%, 19.2%, and 11.6%; HICP=21.4%, 7.1%, and 3.3%). In multivariable modelling, across all conditions examined, arthritis had the second strongest association with CP (PR=2.1; 95% CI=2.0-2.2) and HICP (PR=2.2; 95% CI=2.1-2.4); low back pain was the most strongly associated with CP (PR=2.2; 95% CI [confidence interval]=2.1-2.3) and HICP (PR=2.3; 95% CI=2.1-2.5) (Table). Among adults with arthritis, 5 subgroups had CP prevalence >70%: serious psychological distress (82.2%), unable to work/disabled (80.8%), neck pain (74.1%), fair/poor self-rated health (73.3%), and arthritis-attributable activity limitations (71.7%). At least 40% in these 5 subgroups had HICP: unable to work/disabled (63.4%), serious psychological distress (59.7%), American Indian/Alaskan Native (43.0%), kidney disease (41.1%), and neck pain (40.3%).

Conclusion: Approximately one in two and one in five adults with arthritis live with CP and HICP, respectively; among them, both CP and HICP prevalence was even higher for those living with other challenges, including work disability and psychological distress. Despite unknown temporality, our study results combined with clinical evidence suggests that arthritis may be a leading cause of CP and HICP among US adults. Integrated approaches to pain management that include evidence-based non-pharmacologic strategies (e.g., cognitive behavioral therapy, physical activity, and self-management education) can reduce CP and its adverse effects, such as psychological distress, and may help reduce prescribed opioid use.

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Abstract Number: 2089

Restricting Activity to Evade Knee Symptoms Is Associated with Worse Physical Function and Radiographic Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases – ARP
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Activity restriction (i.e. limiting or avoiding normal activity) is a common strategy to reduce, and sometimes eliminate, knee symptoms. Knee symptoms, such as pain, aching, or stiffness, may be indicative of knee osteoarthritis (OA), thus are a common reason that individuals seek health care services. One concern is that activity restriction may indicate in deteriorating function and development of OA, even if the knee remains symptom free. It is unclear how activity restriction is associated with physical function and knee OA, in the presence or absence of knee symptoms. The purpose of this analysis was to examine the associations of pain and activity restriction with physical function and OA in adults with or at risk for knee OA.

Methods: We conducted a cross-sectional analysis using baseline data from the Osteoarthritis Initiative, a cohort study of individuals with or at risk for knee OA. We defined people using activity restriction to manage knee symptoms as those who reported that they "avoid/reduce pain, aching, or stiffness by changing or cutting back on normal activities" in the past 30 days. We defined people with knee symptoms as people reporting "knee pain, aching, or stiffness on more than half of the past 30 days". We created a four-category exposure by combining the answers to activity restriction (yes/no) and knee symptoms (yes/no). The outcomes of interest were physical function and radiographic knee OA (ROA). Physical function was assessed with the Short Form 12 Physical Component Score (SF-12 PCS), Western Ontario and McMaster Universities Osteoarthritis Index for function (WOMAC-function), and gait speed (m/s) from the 20-m walk test. ROA was defined as Kellgren-Lawrence grade ≥ 2 in either limb. To examine the association of the exposure groups with physical function, we used a general linear model to calculate effect estimates with 95% confidence intervals (95% CI), adjusting for potential confounders. To examine the association of

	Group	n	Mean ± SD	Mean difference* (95% CI)
SF-12 PCS ,	Neither	2156	52.5 ± 6.8	REF
(Range 0 – 100 with higher	Activity restriction only	567	48.6 ± 8.3	-3.6 (-4.3, -2.9)
scores indicating better	Knee symptoms only	808	49.2 ± 8.1	-2.3 (-2.9, -1.7)
function)	Both	1177	41.9 ± 10.2	-9.0 (-9.6, -8.4)
WOMAC Physical Function,	Neither	2167	4.1 ± 6.5	REF
(Range 0 – 68 with lower	Activity restriction only	571	10.3 ± 10.1	5.7 (4.8, 6.5)
scores indicating better	Knee symptoms only	815	13.5 ± 11.5	8.0 (7.3, 8.8)
function)	Both	1194	21.2 ± 13.1	14.8 (14.1, 15.4)
Gait Speed, (m/s)	Neither	2172	1.36 ± 0.20	REF
	Activity restriction only	572	1.33 ± 0.21	-0.03 (-0.04, -0.01)
	Knee symptoms only	817	1.31 ± 0.21	-0.02 (-0.03, 0.00)
	Both	1196	1.25 ± 0.24	-0.07 (-0.08, -0.06)

*Adjusted for age (years), sex (men vs. women), BMI (kg/m^2), race (white vs. non-white), education (college graduate vs. some college or less), comorbidity (none vs. at least 1), ROA in either knee(yes vs. no)

Table 1. Association of Exposure Groups with Physical Function

Group	n	% with ROA (n)	Odds Ratio* (95% CI)
Neither	2174	50% (1081)	1.00 [REF]
Activity restriction only	174	54% (309)	1.27 (1.04, 1.54)
Knee symptoms only	817	59% (482)	1.33 (1.12, 1.28)
Both	1202	66% (790)	1.85 (1.58, 2.2)

*Adjusted for age (years), sex (men vs. women), BMI (kg/m^2), race (white vs. non-white), education (college graduate vs. some college or less), comorbidity (none vs. at least 1)

Table 2. Association of Exposure Groups with ROA

the exposure groups with ROA, we used binomial logistic regression to calculate odds ratios with 95% CI, adjusting for potential confounders.

Results: Of the full sample (N=4796, 58% women, 61±9 years old, 28.6±4.8 kg/m^2), 45% reported neither activity restriction nor knee symptoms, 12% reported activity restriction only, 17% reported knee symptoms only, and 25% reported both activity restriction and knee symptoms. Compared to people reporting no activity restriction or knee symptoms, those who reported activity restriction and/or knee symptoms had worse self-reported and performance-based physical function (Table 1). Similarly, those reporting activity restriction and/or knee symptoms had higher odds of more (unilateral or bilateral) ROA compared to those reporting no activity restriction or knee symptoms (Table 2).

Conclusion: Individuals who restrict normal activities to avoid knee symptoms, or have knee symptoms, have worse physical function and higher prevalence of ROA compared to those who have neither. Identifying people who restrict normal activities to avoid pain may be a marker of early symptomatic progression.

Disclosure: L. Thoma, None; **J. Jakiela**, None; **H. Master**, None; **D. Voinier**, None; **M. Christiansen**, None; **D. White**, None.

Abstract Number: 2090

Differences in Stepping and Standing Based on Self-reported Exercise Identity in Persons Following Total Knee Replacement

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health Poster III: OA, Gout, & Other Diseases – ARP
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Following knee replacement, patients see an improvement in both function and pain, but physical activity often remains at pre-operative levels. One possible influence on an individual's physical activity may be their exercise identity. Exercise identity is the degree to which one views themselves as an exerciser. This is used to assess the importance of identifying with exercise as an integral part of each person's self-concept. Those who identify themselves as exercisers could potentially be more active than those who do not identify with exercise. The purpose of this study was to determine if there is a difference in objectively measured steps per day and minutes

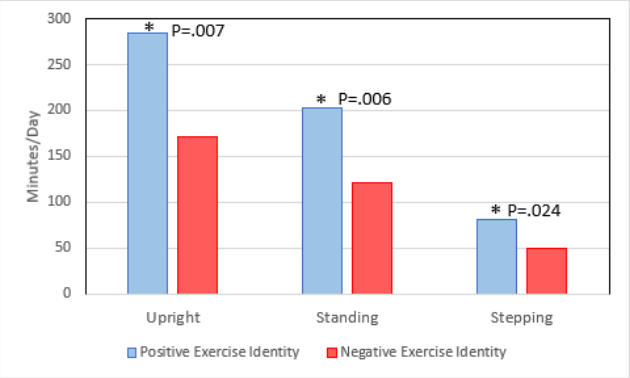

Figure 1. Means by group of time/day spent upright, standing, and stepping based on exercise identity categorization.

per day spent upright, standing, and stepping between participants with positive exercise identity and those with negative exercise identity.

Methods: Participants were aged 40-79 years and were recruited at their first out-patient physical therapy appointment following knee replacement. Participants completed an online self-reported exercise identity survey and wore an activPAL monitor for 7 days. The activPAL monitor assessed the number of steps/day and average minutes/day spent upright, standing, and stepping. Only valid days consisting of 24 hours of wear time were used for analyses. The self-reported exercise identity survey (Wilson & Muon, 2008) asked participants 9 questions to rate their feelings about exercise on a 1 (Strongly Disagree) to 5 (Strongly Agree) Likert scale. All 9 items were summed to create an exercise identity score. Participants median score of exercise identity (29) was used to separate the sample into groups. Analysis was done comparing the two groups as those who have a positive exercise identity (30) and those who have a negative exercise identity (≤29). Independent t-tests were used to compare means of the two groups to see if there was a difference in objectively measured physical activity outcomes based on exercise identity.

Results: Participants (n=19) were an average age of 63.0±7.4 years and body mass index of 32.8±6.2 kg/m^2. As a full sample, participants averaged 5.6±1.4 valid days with the activPAL. Participants in the positive exercise identity group (n=9) had significantly higher steps/day (5145±2034 vs 3128±1578; p=.027), time spent upright (283.9±96.8 vs 170.7±61.4 mins/day; p=.007), time spent standing (203.4±70.2 vs 121±40.8 mins/day; p=.006), and time spent stepping (80.6±31.6 vs 49.7±22.3 mins/day; p=.024) compared to the negative exercise identity group. (Figure 1).

Conclusion: Participants with knee replacement with positive exercise identity took significantly more steps and spent more time per day upright, standing, and stepping than those with negative exercise identity. Future researchers should consider using this information to tailor physical activity interventions based on the participant's exercise identity. If a participant identifies negatively with exercise, different strategies may be required to increase activity than if the participant identified positively with exercise.

Disclosure: N. Mook, None; **K. DeVivo**, None; **D. Brown**, None; **A. Rebar**, None; **C. Pellegrini**, None.

Abstract Number: 2091

The High Dose Influenza Vaccine Increases Immune Protection in Both Adults and Elderly Seropositive RA Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The high dose trivalent inactivated influenza vaccine (HD-TIV) contains four times the antigen dose per strain of the standard-dose inactivated influenza vaccines. HD-TIV is licensed only for persons aged 65 years and older based on immunogenicity and efficacy data. In seropositive RA, HD-TIV substantially improves

	Age (<65)			Age (65+)			Difference between two Strata
	SC (yes/no)	OR (95% CI)	p-value	SC (yes/no)	OR (95% CI)	p-value	
Hemagglutination-inhibition antibodies							
A/Hong Kong/4801/2014							
SD-QIV	9/68	**3.56 (1.15-10.91)**	**0.027**	3/56	**4.11 (1.02-16.53)**	**0.047**	0.1159
HD-TIV	22/63			9/44			
B/Brisbane/60/2008							
SD-QIV	23/54	**2.73 (1.41-5.28)**	**0.003**	17/42	1.30 (0.54-3.12)	0.563	**0.0001**
HD-TIV	46/39			16/37			
A/California/7/2009 (year 1)							
SD-QIV	13/28	**3.07 (1.27-7.40)**	**0.012**	5/25	1.85 (0.43-7.97)	0.408	0.1284
HD-TIV	31/20			5/13			
A/Michigan/45/2015 (year2)							
SD-QIV	12/24	2.65 (0.96-7.34)	0.061	5/25	**6.33 (1.48-26.99)**	**0.013**	**0.0698**
HD-TIV	18/16			14/21			
Microneutralisation antibodies							
A/Hong Kong/4801/2014							
SD-QIV	24/53	**2.24 (1.16-4.36)**	**0.016**	21/38	0.97 (0.43-2.18)	0.94	**0.0001**
HD-TIV	43/42			18/35			
B/Brisbane/60/2008							
SD-QIV	16/61	**3.84 (1.87-7.87)**	**0.0001**	10/48	2.55 (0.98-6.63)	0.055	**0.0293**
HD-TIV	42/43			16/38			
A/California/7/2009 (year 1)							
SD-QIV	15/26	1.85 (0.78-4.39)	0.163	5/25	**5.19 (1.22-22.1)**	**0.025**	**0.0002**
HD-TIV	28/23			9/9			
A/Michigan/45/2015 (year2)							
SD-QIV	18/18	2.26 (0.80-6.38)	0.122	8/21	**3.44 (1.14-10.44)**	**0.028**	**0.0001**
HD-TIV	22/12			21/15			

SC: seroconversion. SD-QIV: standard-dose quadrivalent inactivated vaccine. HD-TIV: high-dose trivalent inactivated vaccine. The difference between two strata was calculated by prevalence fraction.

Table-Age

the immune response to vaccination compared to a quadrivalent standard dose influenza vaccine (SD-QIV). It is unknown whether among RA patients, the increased immunogenicity of the HD-TIV is restricted to a specific age subgroup.

Methods: Between 2016 and 2018, we conducted a treatment-stratified, randomized, modified double-blind, active-controlled trial in adult seropositive RA patients (rheumatoid factor and/or anti-cyclic citrullinated peptide antibodies) to assess antibody responses to either SD-QIV (15 μg of hemagglutinin per strain) or HD-TIV (60 μg of HA per strain) (NCT02936180). Seroconversion (SC) rates were assessed using pre- (Day 0 – D0) and post-vaccine (D28) titers determined by serum hemagglutination inhibition (HI) and microneutralization (MN) assays. In both cases, SC was defined as at least a four-fold HI or MN antibody titer increase from D0.The effect of age (adults versus elderly, cutoff age 65+ years) on SC rates were evaluated using logistic regression analysis.

Results: A total of 279 seropositive RA patients were enrolled. 140 (50.2%) received SD-QIV and 139 (49.8%) received HD-TIV. The mean age (±SD) was 61.0±12.9 and 80% were female. Results of seroconversion rates based on hemagglutination and microneutralization assays, per vaccine strain and according to RA age groups are presented in Table 1.

Conclusion: The benefit of the HD-TIV regarding immune protection is not restricted to elderly seropositive RA patients. The HD-TIV substantially improves immune responses to all influenza strains in adults living with RA.

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Abstract Number: 2092

Efficacy and Safety of the Adjuvanted Recombinant Zoster Vaccine in Adults with Pre-existing Potential Immune Mediated Diseases: A Pooled Post-hoc Analysis on Two Parallel Randomized Trials

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The increased risk of herpes zoster (HZ) in older adults is attributable to age-related decline in immunity. In 2 pivotal studies, ZOE-50 (NCT01165177) and ZOE-70 (NCT01165229), the adjuvanted recombinant zoster vaccine (RZV) proved to be efficacious against HZ in adults ≥50 years of age (YOA), with no identified safety concerns, irrespective of the pre-existing medical conditions at enrollment.[1] This post-hoc analysis was performed to evaluate the impact of any pre-existing potential immune mediated diseases (pIMDs) on RZV efficacy (VE) against the first or only episode of HZ and on RZV safety. pIMDs included autoimmune diseases and other inflammatory and/or neurologic disorders of interest, which may or may not have an autoimmune etiology.

Methods: The ZOE-50 and ZOE-70 studies were phase 3, observer-blind, placebo-controlled, randomized trials conducted in 18 countries. Adults ≥50 YOA (ZOE-50) and ≥70 YOA (ZOE-70) received 2 intramuscular doses of RZV or placebo 2 months apart. This post-hoc analysis was performed on the pooled ZOE 50/70 population to evaluate

Conditions	n	RZV group (N=983) % (95% CI)	n	Placebo group (N=960) % (95% CI)
At least 1 condition	983	100 (99.6–100)	960	100 (99.6–100)
Psoriasis	215	21.9 (19.3–24.6)	239	24.9 (22.2–27.8)
Spondyloarthropathy	109	11.1 (9.2–13.2)	89	9.3 (7.5–11.3)
Rheumatoid arthritis	96	9.8 (8.0–11.8)	94	9.8 (8.0–11.8)
Coeliac disease	41	4.2 (3.0–5.6)	34	3.5 (2.5–4.9)
Vitiligo	37	3.8 (2.7–5.2)	33	3.4 (2.4–4.8)
Polymyalgia rheumatica	36	3.7 (2.6–5.0)	37	3.9 (2.7–5.3)
VIIth nerve paralysis	36	3.7 (2.6–5.0)	32	3.3 (2.3–4.7)
Lichen planus	33	3.4 (2.3–4.7)	24	2.5 (1.6–3.7)
Ulcerative colitis	31	3.2 (2.2–4.4)	30	3.1 (2.1–4.4)
Type I diabetes mellitus	31	3.2 (2.2–4.4)	36	3.8 (2.6–5.2)
Autoimmune thyroiditis	27	2.7 (1.8–4.0)	33	3.4 (2.4–4.8)
Raynaud's phenomenon	27	2.7 (1.8–4.0)	29	3.0 (2.0–4.3)
Sjogren's syndrome	23	2.3 (1.5–3.5)	21	2.2 (1.4–3.3)
Sarcoidosis	22	2.2 (1.4–3.4)	16	1.7 (1.0–2.7)

pIMD, potential immune mediated disease; TVC, total vaccinated cohort; N, number of participants included in each group; n, number of participants reporting the specific condition; 95% CI, 95% confidence interval.

Table 1. Most frequently reported pre-existing pIMDs at enrollment (TVC, pooled ZOE 50/70 population with pre-existing pIMDs at enrollment)

Age group	RZV group (N=936)				Placebo group (N=923)				Vaccine efficacy (%, 95% CI)
	N	Confirmed cases (n)	Person-year	Number/1000 person-year	N	Confirmed cases (n)	Person-year	Number/1000 person-year	
Overall (≥50 YOA *)	936	4	3611.7	1.1	923	38	3408.8	11.1	90.5 (73.5–97.5)
50–59 YOA **	222	1	885.6	1.1	201	11	775.6	14.2	92.8 (50.5–99.8)
60–69 YOA **	159	0	638.3	0.0	151	8	588.8	13.6	100 (54.9–100)
70–79 YOA **	427	2	1623.0	1.2	450	13	1647.3	7.9	84.4 (30.8–98.3)
≥80 YOA **	128	1	464.8	2.2	121	6	397.0	15.1	86.2 (-13.5–99.7)

mTVC, modified total vaccinated cohort; YOA, years of age; N, number of participants included in each group; n, number of participants with one confirmed herpes zoster (HZ) episode; person-year, cumulative follow-up period (censored at the first occurrence of a confirmed HZ episode) expressed in years; number/1000 person-year, incidence rate of participants reporting at least one event. Efficacy (VE) was calculated by means of the Poisson method. *VE adjusted by age strata and region; **VE adjusted by region.

Table 2. Vaccine efficacy against first or only HZ episode during the entire study period overall and by age strata (mTVC, pooled ZOE 50/70 population with pre-existing pIMDs at enrollment)

VE overall and by age strata, and safety in participants that had at least 1 pIMD at enrollment. Participants with pre-existing pIMDs were identified by querying the global medical history of the participants included in the total vaccinated cohort (TVC) with a customized MedDRA query for pIMDs.[2] VE was estimated in the modified TVC, which excluded participants who did not receive the second RZV dose or who had a confirmed HZ episode within 1 month after the second dose. Safety was evaluated in the TVC, which included all participants who received at least 1 RZV dose or placebo. Here, we present serious adverse events (SAEs) and SAEs with fatal outcome reported up to 1 year post-last vaccination.

Results: The pooled TVC included 14,645 RZV and 14,660 placebo recipients. Of TVC, 983 (RZV) and 960 (placebo) participants had pre-existing pIMDs, the majority of these (59.9%, RZV; 60.8%, placebo) were females. Table 1 summarizes the most frequent pIMDs in both groups at study enrollment. VE for participants ≥50 YOA with at least 1 pIMD at enrollment was 90.5% (95% confidence intervals: 73.5–97.5%) for the modified TVC (Table 2). High VE against HZ was maintained in all age groups: 50–59 YOA (92.8%), 60–69 YOA (100%), 70–79 YOA (84.4%) and ≥80 YOA (86.2%) (Table 2). SAEs were reported by 144 (14.6%) RZV and 112 (11.7%) placebo recipients and SAEs with

	n	RZV group (N=983) % (95% CI)	n	Placebo group (N=960) % (95% CI)
SAEs*	144	14.6 (12.5–17.0)	112	11.7 (9.7–13.9)
Infections and infestations				
Pneumonia	9	0.9 (0.4–1.7)	9	0.9 (0.4–1.8)
Urinary tract infections	5	0.5 (0.2–1.2)	5	0.5 (0.2–1.2)
Cardiac disorders				
Myocardial infarction	7	0.7 (0.3–1.5)	3	0.3 (0.1–0.9)
Cardiac failure	5	0.5 (0.2–1.2)	1	0.1 (0.0–0.6)
Fatal SAEs**	12	1.2 (0.6–2.1)	9	0.9 (0.4–1.8)

N, number of participants with at least 1 administered dose; n/%, number/percentage of participants reporting the event at least once. SAEs are presented by System Organ Class and Preferred Term. *Only events reported by ≥0.5% of RZV recipients are presented here. None of the fatal SAEs were reported by >0.5%. **RZV = 1 of each of the following events: acute myocardial infarction, myocardial infarction, large intestinal obstruction, sudden death, neutropenic sepsis, pneumonia, skull fracture, ovarian cancer, prostate cancer, rectal adenocarcinoma, cerebrovascular accident, pneumonia aspiration, and 2 pancreatic carcinomas. Placebo = 1 of each of the following events: acute myocardial infarction, chronic hepatic failure, large cell lung cancer, metastases to central nervous system, cerebrovascular accident, azotemia, pulmonary fibrosis, and 2 pancreatic carcinomas.

Table 3. Serious adverse events (SAEs) and SAEs with fatal outcomes reported up to 1 year post-last vaccination (TVC, pooled ZOE 50/70 population with pre-existing pIMDs at enrollment)

fatal outcome were reported for 12 (1.2%) RZV and 9 (0.9%) placebo recipients with pre-existing pIMDs at enrollment (Table 3).

Conclusion: This analysis demonstrated that RZV efficacy in adults ≥50 YOA is not impacted by the presence of pre-existing pIMDs at enrollment. There were no differences in the proportion of reported SAEs or fatal SAEs between RZV and placebo recipients with pre-existing pIMDs.

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[1]López-Fauqued et al., Vaccine, 2019
[2]Tavares Da Silva et al., Vaccine, 2013

Disclosure: A. Dagnew, GSK group of companies, 3; **D. Rausch**, GSK group of companies, 3; **C. Hervé**, GSK group of companies, 3; **T. Zahaf**, GSK group of companies, 1, 3; **A. Schuind**, GSK group of companies, 1, 3, GSK group of companies, 3.

Abstract Number: 2093

Safety of Adjuvanted Herpes Zoster Subunit Vaccine (HZ/su, Shingrix) Among Patients with Autoimmune Inflammatory Diseases

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Disease severity comparison before and after vaccine:

	No of patients with available data for comparison	Before vaccine (mean)	After vaccine (mean)	P value (Paired T test: 2-tailed)
CRP	40	6.960	5.270	0.168
Rapid 3 Score	21	13.557	14.590	0.297
Rapid 3 Score - RA	16	15.175	16.431	0.318
Prednisone used (mg)	47	1.79	1.63	0.529

Demographics Percentage shown in parenthesis
Participants: 47
Gender:
Female 38 (80.9)
Male 9 (19.1)
Age: 65.9 ± 7.7
Ethnicity:
Caucasian 27 (57.4)
African American 20 (42.6)
Others 0 (0)
Mean follow up after second vaccine: 4.78 months
Diagnosis:
RA 36 (76.6)
SLE 5 (10.6)
FMS 3 (6.4)
Vasculitis 2 (4.2)
Sjogrens 2 (4.2)
Conventional synthetic DMARDs use: 28 (59)
Methotrexate 13 (37.6)
Leflunomide 10 (21.3)
Hydroxychloroquine 5 (10.6)
Azathioprine 1 (2.1)
Tacrolimus 1 (2.1)
Biologic/targeted DMARDs use: 23 (49)
Anti TNF 15 (31.9)
IL-6 Inhibitors 3 (6.4)
Abatacept 2 (4.2)
Rituximab 1 (2.1)
Tofacitinib 3 (6.4)
Both conventional and biologic/targeted DMARDS use: 12 (25)

Background/Purpose: HZ/su has been in use since 2017 and is recommended by the advisory committee on immunization practices (ACIP) as the preferred shingles vaccine due to more than 90% efficacy in preventing shingles and postherpetic neuralgia. Centers for Disease Control and Prevention (CDC) recommends that healthy adults 50 years and older get two doses of HZ/su separated by 2 to 6 months. However, patients with immune-mediated inflammatory diseases were all excluded from HZ/su trials. HZ/su is reported to have high reactogenicity due to the presence of a novel adjuvant which has never been used before in humans. Given the high immunogenicity, rheuma-

tologists are concerned about the aggravation or potentially induction of autoimmune inflammatory diseases. Given the sparsity of data regarding the safety of HZ/su among rheumatology patients, we looked at the safety of the vaccine among subjects who are being treated with synthetic and biologic DMARDs.

Methods: This a retrospective study involving subjects from university-affiliated rheumatology practice who received HZ/su in 2018. Data were extracted from the electronic medical record. In addition to demographic details and medication use, Rapid 3 score and CRP level (mg/dl) before and after the series of vaccine administration were recorded. Any patient-reported adverse reactions related to HZ/su and provider documented flare-up of disease, after vaccination, were also recorded. Statistical analysis using paired T-test was conducted in order to see if there was a difference between Rapid 3 and CRP scores before and after vaccination. The analysis was done with SPSS 25.0.

Results: A total of 47 patient had received both doses of HZ/su. The mean age of patients was 65.9 and of all 76.6 % of the patients had rheumatoid arthritis as a primary diagnosis. The CRP, Rapid 3 for all patients, and Rapid 3 for RA patients were compared before and after vaccinations and were found to have no statistically significant differences. Average prednisone dose was similar before and after vaccination. Of all patients, 6.4% reported adverse reactions. Adverse reactions were non-severe and included fever, myalgia, fatigue, and stomach upset. None of the adverse events led to hospital admission, major organ failure or death. There were 4 events of underlying rheumatic disease flare-ups. All of the 4 patients had RA, and the 2 had self-discontinued the DMARDs (Methotrexate and Leflunomide). There was one event of herpes zoster occurred in a patient with SLE on Hydroxychloroquine and rituximab after receiving the first dose of vaccine.

Conclusion: HZ/su was well tolerated in our subjects. There was no statistically significant difference in CRP values in all patients, Rapid 3 scores in all patients, and Rapid 3 scores among rheumatoid arthritis patients before and after the HZ/su.

Disclosure: S. Acharya, None; **S. Raza**, None; **D. Pattanaik**, None; **A. Howard**, None.

Abstract Number: 2094

Evaluation of Influenza and Pneumococcal Vaccination Rate in Patients with Rheumatoid Arthritis and Spondyloarthritis, and the Attitudes of Rheumatologists About Vaccination

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Infection-Related Rheumatic Disease Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with inflammatory arthritis have increased risk of infections which may lead to morbidity and mortality. Some of those infections could be prevented by vaccination. The main objectives of the present study were to investigate (a) the uptake rate of influenza and pneumococcal vaccination among patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA) attending a rheumatology outpatient clinic, (b) the factors associated with their vaccination rate and, (c) the attitudes of Turkish rheumatologists about vaccination.

Methods: Patients, followed-up in a tertiary rheumatology outpatient clinic with the diagnosis of RA and SpA, volunteered for participating to study, were included in this cross-sectional study. Data regarding the socio-demographic and disease-related characteristics (including disease duration, medications used, and comorbid conditions) of the patients, vaccination history, the knowledge about the vaccination, and the factors potentially associated with the uptake of vaccination were collected by face-to-face interview using a standardized questionnaire. 102 out of 345 rheumatologists have participated in a web-based survey.

Results: In total, we collected data from 199 patients (145 with SpA and 54 with RA; 101 [50.8%] female and mean age 45.4 ± 12.2 years) (Table 1). Only 55 (27.6%) of our patients were responded that their disease or treatment might be related to the increased risk for infectious diseases. Influenza and pneumococcal vaccines were administered to 38 (19.1%) and 8 (4%) patients, respectively. Vaccination for influenza was recommended by family physicians in 16 patients and by rheumatologists in 6 patients. Rate of influenza vaccination was significantly higher in patients >65 years (p=0.031) and with any co-morbid conditions (p=0.027). The main reasons reported by unvaccinated patients were (a) the belief that they did not need the vaccine (58.4% for influenza and 30.9% for pneumococcal vaccine), (b) the absence of recommendation from their physicians (24.8% for influenza and 25.1% for pneumococcal vaccine), (c) fear of adverse event of vaccination (24.8% for influenza and 4.7% for pneumococcal vaccine), and (d) lack of knowledge vaccination (3.7% for influenza and 14.6% for pneumococcal vaccine). Even though 50% of rheumatologists who responded to the survey were aware of the presence of national vaccination recommendations, all of them stated that patients with inflammatory arthritis need to be vaccinated for both influenza and pneumococcal infections.

Conclusion: Although the knowledge and awareness about influenza and pneumococcal vaccinations were seemed to be high among rheumatologists, vaccination rates for both were insufficient in RA and SpA patients. There remains significant effort to improve vaccination rates and to prevent morbidity and mortality due to vaccine-preventable infections in inflammatory rheumatic diseases.

Disclosure: ???. Kurut Aysin, None; **M. Aysin**, None; **D. Solmaz**, None; **N. Baş Tomas**, None; **F. Koç**, None; **E. Durak Ediboğlu**, None; **G. Kabadayi**, None; **O. Gercik**, None; **S. Gücenmez**, None; **S. Akar**, Abbvie, 2, 5, Amgen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5.

Abstract Number: 2095

A Quality Improvement Intervention to Improve Influenza and Pneumococcal Vaccination Rates in Immunosuppressed Inflammatory Arthritis Outpatients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The ACR and CDC recommend influenza ("flu") and 23-valent pneumococcal polysaccharide (PPSV23) vaccination for inflammatory arthritis (IA) patients on immunosuppression. This study aimed to: 1). assess barriers to vaccination and 2). increase PPSV23 (5 yearly) and "flu" (annual) vaccination uptake in immunosuppressed IA outpatients through a multifaceted quality improvement (QI) intervention.

Methods: The primary outcome was adequate "flu" and PPSV23 vaccination uptake of immunosuppressed IA outpatients. Consecutive outpatients in 2017 were invited to complete an anonymous 23 question paper questionnaire including demographic, diagnostic, medication and vaccination (knowledge, status and barriers) data. Patients taking oral steroids, biologic disease modifying antirheumatic drugs (bDMARDs) or immunosuppressant conventional synthetic agents (csDMARDs) were included. Simultaneously, a low cost multifaceted QI intervention was performed (Figure 1).

In 2018, post-intervention, the clinic was re-assessed. Binary logistic regression analysis was used to assess for independent predictors of up-to-date vaccination.

Results: In 2017-2018, 163 and 262 patients, respectively, met inclusion criteria. Patients were typical of an IA clinic (74% women; 45.4% ≥60 years old; 72.7% RA; 61.1% using csDMARDs; 46.6% using bDMARDs; 23.1% using combination csDMARD plus bDMARD; 32.5% using oral steroids).

In 2017, 104 (65.4%) knew of the increased infectious risk with IA. In 2018, 168 (65.6%) were aware. In 2017, 111 (69.8%) were aware of increased infection risk with medications;172 (66.9%) in 2018.

Vaccination awareness was higher for "flu" (Table 1). General practitioners (GPs) informed and vaccinated most patients. The most common reason for non-vaccination was lack of awareness. This decreased post intervention. 70% of patients had smart phone access. 78% were willing to use this for vaccination reminders.

PPSV23 vaccination rates increased from 41.0% to 47.2% (P=0.29. Pearson Chi squared), and "flu" from 61.8% to 62.1% (P=0.95, Pearson Chi squared).

Age, bDMARD use and up-to-date influenza vaccination were significant predictors of PPSV23 vaccination (Table 2). Only, up-to-date PPSV23 vaccination predicted "flu" vaccination.

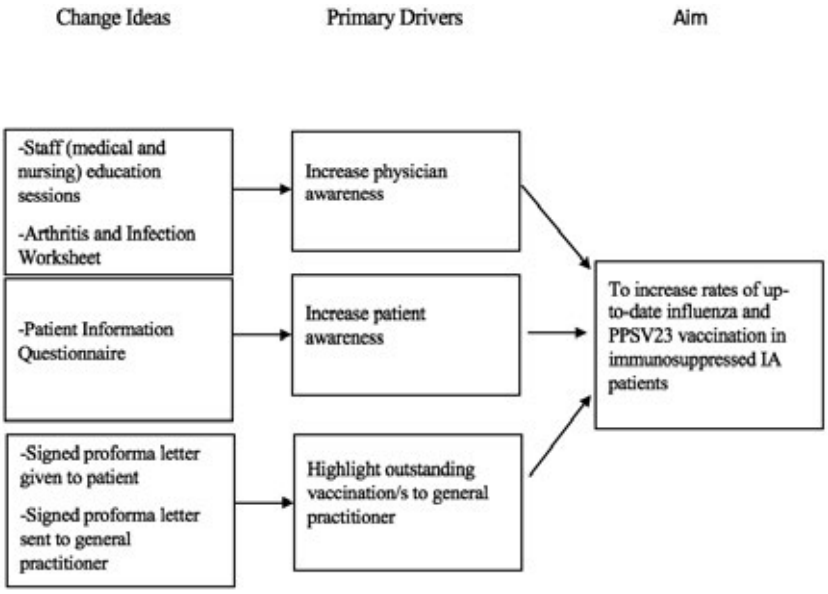

Figure 1. Quality improvement intervention

	Influenza		PPSV23	
	2017	2018	2017	2018
Vaccination awareness	128 (80%)	212 (81.9%)	60 (38%)	118 (46.8%)
Aware of frequency	133 (99.3%)	219 (99.1%)	59 (75.6%)	98 (65.8%)
Source of awareness				
GP	92 (73%)	146(71.2%)	49 (75.4%)	87 (70.2%)
Hospital	29 (23%)	44 (21.5%)	15 (23.1%)	27 (21.8%)
Clinical Nurse Specialist	0	12 (5.9%)	0	8 (6.5%)
Public Health/Ward Nurse	0	8 (3.9%)	0	1 (0.8%)
Radio	6 (4.8%)	9 (4.4%)	1 (1.5%)	1 (0.8%)
Television	5 (4%)	6 (2.9%)	0	0
Internet/Social Media	1 (0.8%)	3 (1.5%)	0	0
Site of last vaccine				
GP	93 (78.8%)	149(77.2%)	53(89.8%)	98 (90.7%)
Work	7 (5.9%)	14 (7.3%)	0	0
Pharmacy	6 (5.1%)	3 (6.7%)	0	1 (0.9%)
Public Health Nurse	6 (5.1%)	10 (5.2%)	1 (1.7%)	3 (2.8%)
Hospital	4 (3.4%)	5 (2.6%)	3 (5.1%)	4 (3.7%)
Other	2 (1.7%)	2 (1.0%)	2 (3.4%)	3 (2.8%)
Reason not vaccinated				
Unaware	18 (36.7%)	26 (34.2%)	69 (82.1%)	94 (76.4%)
Fear of side effects	12 (24.5%)	18 (23.7%)	7 (8.3%)	10 (8.1%)
Too busy	6 (12.2%)	10 (13.2%)	0	1 (0.8%)
Cost	2 (4.1%)	2 (2.6%)	0	1 (0.8%)
Other	13 (26.5%)	22 (28.9%)	8(9.5%)	17 (13.8%)

Table 1. Vaccination awareness, provision and reasons for non-compliance

	Influenza		PPSV23	
	OR (95% CI)	p value	OR (95% CI)	p value
Female	0.54 (0.26-1.13)	0.100	1.73 (0.84-3.56)	0.139
Age, years (vs ≤39)				
40-59	0.89 (0.33-2.43)	0.821	7.26 (1.93-27.23)	0.003
60-79	1.11 (0.37-3.30)	0.855	10.33 (2.61-40.86)	0.001
≥80	1.18 (0.08-15.64)	0.903	41.66 (3.69-469.8)	0.003
Education level (vs university)				
Primary	2.82 (0.86-9.30)	0.088	0.70 (0.24-2.06)	0.511
Secondary	1.05 (0.50-2.20)	0.897	0.97 (0.45-2.09)	0.933
Diagnosis (vs RA)				
Psoriatic arthritis	0.36 (0.13-1.00)	0.050	2.50 (0.88-7.07)	0.084
Ankylosing spondylitis	0.68 (0.12-3.89)	0.661	0.28 (0.02-3.66)	0.335
Medications				
bDMARD (vs not)	0.99 (0.45-2.21)	0.987	2.80 (1.24-6.32)	0.013
cDMARD & bDMARD (vs not)	1.49 (0.61-3.67)	0.386	0.71 (0.30-1.70)	0.444
PPSV23 up to date	8.93 (4.39-18.17)	0.000		
Influenza up to date			9.01 (4.40-18.42)	0.000
Smart phone				
Access	1.03 (0.38-2.77)	0.952	0.74 (0.28-1.99)	0.555
Willing to use for reminders	1.45 (0.56-3.80)	0.445	0.64 (0.23-1.77)	0.392

Table 2. Predictors of adequate vaccination

Conclusion: "Flu" and PPSV23 vaccination rates were suboptimal and increased marginally post intervention. Overall, < 5% of vaccinations were in hospital. New strategies to increase vaccination including point-of-care vaccination in clinic and guidelines advocating specialists sharing responsibility with GPs are required.

Disclosure: K. Murray, None; **C. Low**, None; **F. Young**, None; **A. O'Rourke**, None; **I. Callanan**, None; **E. Feeney**, None; **D. Veale**, Health Beacon, 1.

Abstract Number: 2096

An Intervention Bundle Increases Uptake of Influenza Vaccine by Rheumatoid Arthritis Patients

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Infection-Related Rheumatic Disease Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Annual vaccination with inactivated influenza vaccine is recommended for adults with rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA). Despite this, influenza immunization coverage among those patients is suboptimal. Interventions proven to enhance immunization rates in other at-risk groups include letters to patients, physician reminders, and home visits providing vaccines. We tested the effectiveness of an intervention bundle to enhance influenza vaccination uptake among adults living with RA and JIA.

Methods: Between 10/2018 and 12/2018, an influenza vaccine intervention bundle was implemented at a large academic center in North America. This consisted of: (i) a letter from the Division of Rheumatology mailed to RA/JIA patients reminding them of the benefits of vaccination and need to plan for it; (ii) providing influenza vaccine at the rheumatology clinics; and (iii) placing posters in rheumatology clinics targeting patients and their providers. Between 01/2019 and 05/2019, a post-intervention anonymous survey was completed by RA/JIA patients at the time of a routine rheumatology appointment. Baseline influenza vaccination rates had been established in 2015 using the same survey. The effectiveness of the intervention was determined by comparing patient reported vaccination rates in 2015 and 2019. During the intervention period, there were no changes in the public health program promoting vaccination in RA/JIA. Multivariate logistical regression analyses were performed to evaluate reasons of non-vaccination.

Results: On 10/2018**,** 254 letters were mailed to RA/JIA patients who had a rheumatology appointment in the previous 4 months. During the intervention period in which 343 RA/JIA patients had rheumatology appointments, 116 received the influenza vaccine. Most (107/116, 92.2%) were vaccinated at the time of a previously scheduled appointment while the remainder (9/116, 7.7%) presented for vaccination in response to the mailed letter. The post-intervention survey conducted in 2019, showed that the influenza vaccination rate in RA/JIA was 62.6% (67/107) increased from 48.5% (65/136) in 2015 (p=0.03). Over a third (26/67, 38.8%) of the surveyed patients received the vaccine at the rheumatology clinic in 2019. In multivariate analysis, age (OR 1.07, 95% CI 1.03-1.11), and biologic use (OR 3.45, 95% CI 1.04-11.4) independently predicted vaccination uptake. Physician recommendation was the strongest independent predictor of vaccination (OR 6.56, 95% CI 1.54-27.97). Vaccine hesitancy and refusal were reported reasons for non-vaccination in 35.5% (38/107) of the patients that completed the 2019 post-intervention survey.

Conclusion: An influenza vaccine bundle, with recall interventions directed at both patients and providers, and that facilitated vaccination access, was associated with an increase in vaccine coverage among adults with RA/JIA. Vaccine hesitancy and refusal remain high among RA/JIA patients. Rheumatologists have a key role in promoting vaccination in this population.

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Abstract Number: 2097

Tuberculin Skin Test and Quantiferon®-TB Gold In-Tube Test for Latent Tuberculosis Before Biologic Treatments: Lower Agreement Rate in Spondyloarthropathies Compared to Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Infection-Related Rheumatic Disease Poster

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Session Time: 9:00AM–11:00AM

Background/Purpose: Screening for and the treatment of latent tuberculosis is recommended in patients with inflammatory arthritides prior to biologic treatments, particularly the TNF inhibitors. The aim of this study is to evaluate the performance of tuberculin skin test (TST) with respect to Quantiferon®-TB Gold In-Tube test (QFT-GIT) in patients with rheumatoid arthritis (RA) and spondyloarthropathies (SpA) who are candidates for biologic treatments in a BCG-vaccinated population.

Methods: Data were collected from TReasure, a national-scale, multicenter registry of patients with inflammatory arthritis under biologic treatments[1]. Patients older than 18 years of age, with a diagnosis of RA or SpA, meeting 2010 ACR/EULAR and ASAS criteria, respectively, who had both TST and QFT-GIT prior to initiation of biologic treatments were included in the study. Exclusion criteria were the presence of active tuberculosis, HIV infection, diabetes, chronic kidney disease, chronic obstructive pulmonary disease or asthma, and malignancy. Sensitivity, specifity, and positive and negative predictive values of TST with respect to QFT-GIT were calculated at 5, 10, and 15 mm cutoffs in RA and AS groups.

Results: Among 2690 patients with RA and 4995 patients with SpA, 3468 (45.1%) and 3922 (51%) patients underwent testing with TST and QFT-GIT, respectively. Numbers of eligible patients with both tests performed were 206 for RA, and 392 for SpA. Features of these study groups were given in Table 1. Although the positivity rates of QFT-GIT did not differ substantially between RA and SpA groups, rates of positive TST at 5, 10, and 15 mm cutoffs were signif-

		n	RA	n	SpA	p
Sex, n(%)	Female	206	160 (77.7)	392	154 (39.3)	**<0.001**
	Male		46 (22.3)		238 (60.7)	
Age, years		206	49±15	392	43±11	**<0.001**
Education status, n(%)	Primary or lower	201	91 (45.2)	379	85 (22.4)	**<0.001**
	Secondary or high school		71 (35.3)		150 (39.6)	
	Higher education		39 (19.4)		144 (38)	
Smoking status, n(%)	Never smoked	202	130 (64.4)	369	154 (41.7)	**<0.001**
	Ex-smoker		35 (17.3)		63 (17.1)	
	Active smoker		37 (18.3)		152 (41.2)	
Disease duration, years		202	11.8±8	392	8.7±6	**<0.001**
Steroid use, n(%)		206	113 (54.9)	392	73 (18.6)	**<0.001**
cDMARDuse, n(%)		206	172 (83.5)	392	245 (62.5)	**<0.001**
	Methotrexate		137 (66.5)		89 (22.7)	**<0.001**
	Hydroxychloroquine		93 (45.1)		38 (9.7)	**<0.001**
	Sulfasalazine		110 (53.4)		217 (55.4)	0.647
	Leflunomide		76 (36.9)		18 (4.6)	**<0.001**
TST, mm		206	5.7±5.8	392	9.3±6.4	**<0.001**
TST, n(%)	>5 mm	206	91 (44.2)	392	271 (69.1)	**<0.001**
	>10 mm		38 (18.4)		154 (39.3)	**<0.001**
	>15 mm		16 (7.8)		60 (15.3)	**0.009**
QFT-GIT, n(%)	Positive	206	21 (10.2)	392	59 (15.1)	0.075
	Negative		185 (89.8)		333 (84.9)	
Treatment for LTB, n(%)		206	92 (44.7)	382	230 (60.2)	**<0.001**

Continuous variables were given as means±SDs. cDMARD = conventional DMARD; TST = tuberculin skin test; QFT-GIT = Quantiferon®-TB Gold In-Tube; LTB = latent tuberculosis

Table 1. General features of the study groups

	RA (n=206)			SpA (n=392)		
TST cutoff	**5 mm**	**10 mm**	**15 mm**	**5 mm**	**10 mm**	**15 mm**
QFT+TST+	5%	3%	2%	13%	10%	6%
QFT-TST-	51%	75%	84%	29%	56%	75%
QFT+TST-	5%	7%	8%	2%	5%	9%
QFT-TST+	39%	15%	5%	56%	29%	9%
Disagreement	44%	22%	13%	58%	34%	18%
Sensitivity	52%	33%	23%	88%	68%	40%
Specifity	56%	83%	94%	34%	65%	89%
PPV	12%	18%	31%	19%	26%	40%
NPV	91%	91%	91%	94%	92%	89%
Cohen's κ	0.02	0.09	0.16	0.08	0.19	0.29

TST = tuberculin skin test; QFT-GIT = Quantiferon®-TB Gold In-Tube; PPV = positive predictive value; NPV = negative predictive value

Note that a TST cutoff of 10 mm in SpA gave slightly better results compared to a 5 mm cutoff in RA in terms of sensitivity, specifity and agreement with respect to QFT-GIT (grey columns)

Table 2. Performance of TST with respect to QFT-GIT in the study groups

icantly higher in SpA group. Treatment rate of latent tuberculosis was also higher in SpA group (Table 1). Distributions of steroid and conventional DMARD use were different between groups (Table 1).

Performance of TST with respect to QFT-GIT for 5, 10, and 15 mm cutoffs were represented in RA and SpA groups in Table 2. The two tests poorly agreed in both groups at a TST cutoff of 5 mm. Increasing the TST cutoff only slightly increased the agreement between the two tests at the expense of decreased sensitivity (Table 2). For all cutoffs, SpA group had higher disagreement rates as compared to RA. Notably, a TST cutoff of 10 mm in SpA gave slightly better results compared to a 5 mm cutoff in RA in terms of sensitivity, specifity and agreement with respect to QFT-GIT (Table 2, grey columns).

Conclusion: Agreement of TST with QFT-GIT for latent tuberculosis was poor in patients with RA and SpA before the initiation of biologic treatments. TST positivity and the disagreement rates were more pronounced in SpA. Increasing the TST cutoff only slightly increased the agreement between the two tests at the expense of decreased sensitivity.

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Disclosure: U. İlgen, None; **S. Turan**, None; **H. Emmungil**, None; **A. Sarı**, None; **A. Erden**, None; **L. Kilic**, None; **???. Karadağ**, None; **S. Kiraz**, None; **A. Ertenli**, None; **O. Küçükşahin**, None; **???. Erten**, None; **Z. Akar**, None; **B. Öz**, None; **S. Koca**, None; **C. Bes**, None; **N. Alpay-Kanitez**, None; **E. Tekgöz**, None; **S. Çolak**, None; **M. Çınar**, None; **S. Yılmaz**, None; **V. Yazısız**, None; **M. Terzioğlu**, None; **A. Keleşoğlu Dinçer**, None; **A. Ateş**, None; **R. Mercan**, None; **O. Gercik**, None; **S. Akar**, Abbvie, 2, 5, Amgen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5; **M. Atagündüz**, None; **G. Kimyon**, None; **E. Gönüllü**, None; **E. Ersözlü**, None; **M. Aydın Tufan**, None; **B. Yağız**, None; **B. Coşkun**, None; **Y. Pehlivan**, None; **E. Dalkılıç**, None; **U. Kalyoncu**, UCB, 5.

Abstract Number: 2098

Distinctive Pattern of LTBI Screening Parameters in Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA) in Endemic Areas

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite late tuberculosis infection (LTBI) screening before anti-TNF treatment, TB reactivation/new exposure in endemic areas remains a relevant problem. The specific analysis of Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA) screening parameters has not been evaluated previously and may provide clues to improve risk assessment for these diseases. Our objective is to evaluate retrospectively the efficacy of LTBI screening for anti-TNF therapy in AS and PsA in endemic areas and further determine the possible distinguishing features of the LTBI parameters in each disease.

Methods: A total of 218 Spondyloarthritis patients (135 AS and 83 APS) were screened for LTBI before receiving anti-TNF treatment using the tuberculin skin test (TST), chest X-ray and history of previous TB exposure. Patients were regularly followed assessing infectious symptoms/new exposure every 2-3 months. LTBI patients were treated with isoniazid for 6 months.

Results: From June 2014 to June 2018, 135 AS and 83 PsA were referred to Immunotherapy Infusion Center to initiate anti-TNF treatment. LTBI screening was more often positive in AS than in PsA (42% vs. 30%, p=0.043). LTBI parameters were distinct in both diseases with a higher frequency of TST-positive (93% vs. 64%, p=0.002) and lower frequency of history of exposure (18% vs. 52%, p=0.027) and previous TB (0.7% vs, 6%, p= 0.03) in AS than PsA. During follow-up, 7 (4%) AS (71% LTBI-) and 4 (5%) PsA (50% LTBI-) patients developed active TB (ADA, INF and ETA) and 45% were extrapulmonary. Four cases (3 AS and 1 PsA) occurred within the first year of anti-TNF and 2 (50%) in LTBI+ patients, suggesting reactivation. Seven cases (4 AS and 2 PsA) occurred after the first year (4 AS and 1 PsA were LTBI-) probably due to re-exposure.

Conclusion: We report a distinct pattern of LTBI screening parameters in AS and PsA, with a higher frequency of LTBI in the former, mainly identified by TST. For PsA, TST and a history of exposure have similar relevance for LTBI diagnosis. The frequency of screening failure remains a problem and it was comparable in AS and PsA. Availability of non anti-TNF therapies, that are not associated with an increased risk of TB reactivation, may be safer for patients with high risk of TB. Furthermore the annual periodic rescreening may benefit the re-exposure group.

Disclosure: A. Shimabuco, None; **A. Ribeiro**, None; **R. Miossi**, None; **K. Bonfiglioli**, None; **J. Moraes**, None; **C. Gonçalves**, None; **P. Sampaio-Barros**, None; **C. Goldenstein-Schainberg**, None; **F. Souza**, None; **L. Prado**, None; **M. Remião Ugolini-Lopes**, None; **E. Yuki**, None; **E. Bonfa**, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #305068/2014-8), 2, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4 and #2010/10749-0), 2; **C. Saad**, None.

Abstract Number: 2099

Comparison of Single and Dual Latent Tuberculosis Screening Strategies Before the Initiation of Biologic and Targeted Therapy in Rheumatological Patients in Hong Kong

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Screening for latent tuberculosis infection (LTBI) before the initiation of biologic and targeted synthetic disease modifying anti-rheumatic drugs (b/tsDMARDs) is recommended internationally especially in tuberculosis (TB) endemic areas like Hong Kong. However, there is no gold-standard. The local guideline recommends the use of either tuberculin-skin-test (TST) or interferon-gamma-release-assay (IGRA) before starting b/tsDMARDs for rheumatic diseases. Both tests have reduced sensitivity in immunosuppressed patients and a previous local study has demonstrated that the two tests had fair level of agreement only. We conducted this study to determine whether the dual LTBI screening strategy could reduce the incidence of TB.

Methods: This is a retrospective cohort study. Consecutive patients who have received b/tsDMARDs for rheumatic diseases in a regional hospital in Hong Kong from July 2007 to December 2018 were reviewed. All patients underwent LTBI screening, either with single testing by TST/ IGRA or dual testing by both. They were categorized into single or

dual testing group. Background demographics, concurrent medications and choices of biologic were documented. All patients were followed-up regularly since the initiation of biologic agents for at least 6 months. Isoniazid chemoprophylaxis was prescribed if the patient was tested positive for LTBI. The primary outcome of this study was the incidence of TB during the b/tsDMARDs therapy in the single and dual testing groups. The secondary outcomes included the associated factors of TB, the agreement between TST and IGRA, and the safety of the TB chemoprophylaxis.

Results: Two hundred and seventeen patients were included in this study. One hundred and twenty one patients underwent single LTBI testing with either TST (115) or IGRA (6) and 96 patients underwent dual testing. There was no significant difference in the demographic variables between the two groups. The major indication of biologic agents was rheumatoid arthritis (57% in the single test group and 56% in the dual test group). TB occurred in 9 patients in single testing group and one patient in dual testing group (7.43% versus 1.09%, p=0.045 by Fisher's exact test). Thirty five patients in the single testing group and 36 patients in the dual testing group were tested positive for LTBI and given isoniazid chemoprophylaxis (28.9% versus 45.8%, p=0.007). The agreement between IGRA and TST was 74.5% with the Cohen's kappa value 0.413. However, in patients on prednisolone at screening, the kappa value was reduced to 0.378 and further to 0.346 in patients on at least 10mg prednisolone daily. Among all the b/tsDMARDs, infliximab use was significantly associated with the incidence of TB (p< 0.001). Reversible hepatotoxicity occurs in 7 out of 71 courses of isoniazid given, which was not significantly different between the two groups.

Conclusion: Dual testing strategy with both TST and IGRA appears to be an effective and safe way to reduce the incidence of TB in patients on biologic agents for rheumatic diseases. It should be considered in TB endemic areas especially in patients who are on prednisolone when undergoing LTBI screening or if infliximab therapy is anticipated.

Disclosure: Y. Tang, None; **H. So**, None; **W. Lao**, None; **H. Pang**, None; **T. Wong**, None; **T. Luk**, None; **M. Yip**, None.

Abstract Number: 2100

Screening for Hepatitis B Surface Antigen and Core Antibody Prior to Administration of Rituximab in Rheumatology Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab is used to treat a variety of rheumatic diseases. In 2015, the American Gastroenterological Association (AGA) categorized rituximab as high-risk in terms of hepatitis B virus (HBV) reactivation. Specifically, patients that are hepatitis B surface antigen (HBsAg) negative and total hepatitis B core antibody (anti-HBc) positive or HBsAg and anti-HBc positive are at high risk of reactivation when receiving rituximab, and therefore, should receive antiviral prophylaxis. This study aims to evaluate rates of HBV screening prior to rituximab.

Methods: A retrospective chart review was conducted on 228 patients at a single tertiary center. Patients were included who had received rituximab for a rheumatologic indication, were seen by the rheumatology department, and received the first rituximab infusion between January 1, 2008 and February 28, 2019. Charts were reviewed for dates of HBsAg, anti-HBc, IgM antibody to hepatitis B core antigen (IgM anti-HBc), and hepatitis B surface antibody (anti-HBs) laboratory tests. If patients were found to be HBsAg or anti-HBc positive, charts were reviewed for any referral to hepatology or infectious disease specialties as well as for any antiviral prophylaxis initiation.

Results: Out of 228 patients meeting criteria, indications for rituximab varied, with the majority being rheumatoid arthritis (65 [28.5%]) and granulomatosis with polyangiitis (44 [19.3%]). One hundred ninety (83.3%) had HBsAg tested and 133 (58.3%) were tested for anti-HBc before first rituximab infusion. Out of these patients, all 190 were HBsAg negative and eight of the 133 tested for anti-HBc were positive. Six of these patients were referred to either infectious disease or hepatology and initiated on tenofovir or entecavir for antiviral prophylaxis. No action was taken on the remaining two patients with positive anti-HBc. An additional two patients were found to be anti-HBc positive after receiving rituximab and both were started on entecavir. No documented HBV reactivation occurred in any of the patients.

Conclusion: This chart review identified inadequate screening of HBV prior to the administration of rituximab. The majority of patients were properly screened for HBsAg; but only slightly more than half had testing for anti-HBc prior to first rituximab infusion. This study identifies areas to implement system changes to improve rates of HBV screening.

Disclosure: R. Moran, None; **J. Beatty**, None; **J. Ternus**, None; **M. Krause**, None.

Abstract Number: 2101

Hepatitis C Affects More Than Just the Liver: A Retrospective Chart Review on the Prevalence of Connective Tissue Diseases and Autoantibodies in Hepatitis C Virus Infections in an Academic Rheumatology Clinic

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic Hepatitis C virus infection (HCV) has been shown to be associated with connective tissue diseases (CTD). It has been hypothesized that HCV can itself induce a clonal B-cell expansion leading to extrahepatic manifestations of HCV such as arthralgia which brings the question of whether the HCV or CTD is the cause of the arthritis. This determination is very important to help guide treatment decisions. Prior studies of CTD in Patients with HCV was on interferon-based immunomodulator therapy, which has inherent immunogenicity resulting in autoimmune diseases. Current therapy for eradication of HCV includes Direct-Acting Antivirals (DAA) which are not immunomodulators. Hence, we wanted to explore the association between HCV and CTD in the current era of DAA therapy.

Methods: This study is a retrospective chart review of 619 patients seen in the Rheumatology Clinic at Ochsner LSU Helath Hospital in Shreveport, LA with a diagnosis of HCV and CTD.

Results: Out of the 9,604 patients seen in Rheumatology clinic, 619 were found to have a positive Hepatitis C Antibody (6.4%), but only 61 patients had chronic HCV infection determined by a positive viral load. In the 61 patients with HCV, the CTD was Osteoarthritis (OA) in 36 % of cases, Rheumatoid Arthritis (RA) in 21.3%; Psoriatic Arthritis (PSA) in 13.1%; Systemic Lupus Erythematosus (SLE) in 6.5% and Seronegative Inflammatory arthritis in 4.9%. There

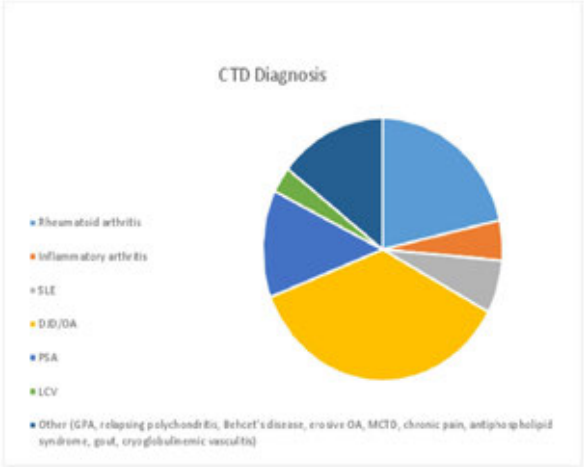

Figure 1. CTD Diagnosis in patients with HCV. SLE = Systemic Lupus Erythematosus; DJD = Degenerative Joint Disease; OA = Osteoarthritis; PSA = Psoriatic Arthritis; LCV = Leukocytoclastic Vasculitis; GPA = Granulomatosis with Polyangiitis; MCTD = Mixed Connective Tissue Disease

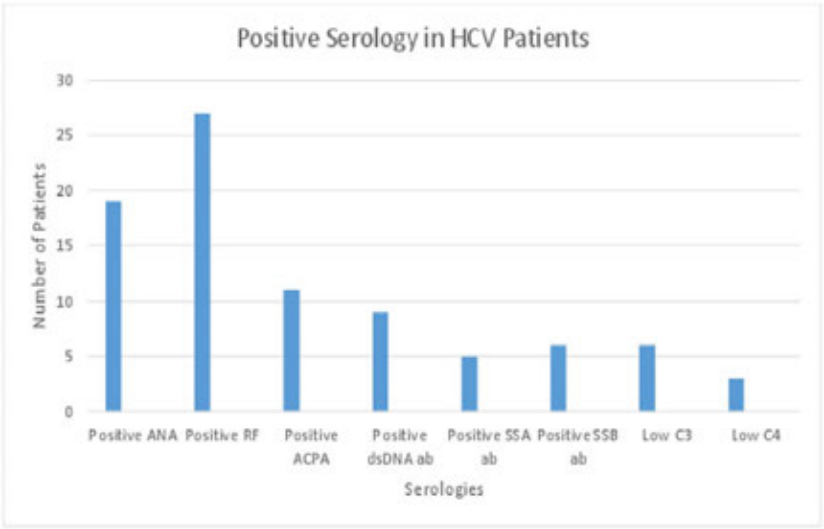

Figure 2. Positive serologies in patients with CTD and HCV.

were 1-2 cases of HCV associated with other CTDs (Figure 1). Positive Rheumatoid Factor (RF) and Antinuclear Antibody (ANA) were the most prevalent positive serological markers present in 44% and 31%, respectively (Figure 2). The RF was found to be a false positive (patients did not meet American College of Rheumatology-ACR diagnostic criteria for RA) in 25% of cases with the highest level being 106 IU/ml. Two out of 13 patients diagnosed with RA had a poor response to therapy and both patients were noted to have a high viral load and high anti-citrullinated protein antibody (ACPA). The HCV genotype most commonly associated with CTD was 1A in 61 % of patients. Joint pain was the presenting symptom in 51% of patients that were subsequently diagnosed with HCV. Hydroxychloroquine and Sulfasalazine (18%) were the most commonly prescribed Disease modifying agents and Tumor Necrosis Factor inhibitors (Etanercept and Adalimumab) were used in 16% of patients without relapse of HCV (Figure 3). Corticosteroids were used in 18% of patients.

Conclusion: HCV infection even without the interferon based therapy is associated with a variety of CTDs with RA and OA being the two most prevalent. Patients with CTD would benefit from a 2-stage HCV screening with HCV anti-

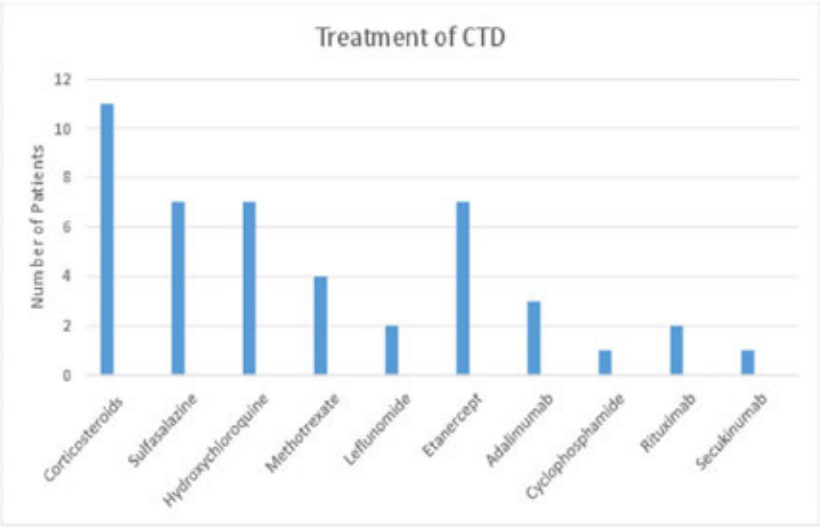

Figure 3. Treatments used for CTDs in patients with HCV.

body followed by HCV RNA on same serum sample due to high false positive antibody test in this subset of population. The presence of ACPA and erosions in addition to the ACR diagnostic criteria help diagnose RA in patients with HCV that have a higher incidence of false positive RF and joint pain. Further long term studies are needed to study the response of treating HCV with DAA to the disease course of CTD.

Disclosure: M. Malus, None; **L. Pham**, None; **H. Samant**, None; **M. Katikaneni**, None.

Abstract Number: 2102

First-line Antiretroviral Therapy with Tenofovir Produces Deleterious Effects on Bone and an Increase in Proinflammatory Cytokines Expression After 12 Months of Treatment in Naïve HIV Patients

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SESSION INFORMATION
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Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: For almost two decades, bone alterations have been observed in the course of HIV infection, characterized by a marked decrease in bone mineral density (BMD) and an increase in the frequency of fractures as a result of fragility. It is not clear if it is HIV infection per se that contributes to the decrease in BMD, osteoporosis and bone fagility, or if the risk factors associated with the disease (malnutrition, low body weight, high smoking rate and alcohol consumption or low vitamin D levels). In adults, the decrease in BMD has also been associated with prolonged treatment with antiretrovirals and more specifically therapy with tenofovir. The aim of this study was to evaluate the deleterious effects in bone metabolism, produced by tenofovir vs other HIV treatment in naïve patients.

	Table 1: BONE MARKERS (pg/ml)			
	TDF	*TAF*	*PI*	*ADL*
Variable	*Median (Q1, Q3)*	*Median (Q1, Q3)*	*Median (Q1, Q3)*	*Median (Q1, Q3)*
CTX	92.3 (17.9, 140.0)	28.5 (3.9, 84.9)	77.0 (44.1, 122.3)	53.8 (16.4, 122.6)
P1NP	81.4 (47.5, 98.8)	17.9 (4.5, 55.5)	44.3 (11.8, 70.7)	28.1 (4.0, 59.7)
OC	49.6 (42.7, 77.5)	1.6 (-10.0, 50.7)	87.6 (43.2, 126.4)	25.6 (-1.5, 63.5)
TRAP	51.1 (23.1, 84.9)	120.0 (31.5, 244.1)	44.1 (28.6, 56.5)	56.2 (22.2, 107.4)
PTH	35.8 (12.3, 67.7)	37.1 (-9.1, 54.2)	60.1 (37.4, 82.8)	20.8 (-9.6, 41.6)
FG	-18.7 (-22.8, -10.1)	-3.7 (-10.3, -0.2)	-6.5 (-11.3, 0.0)	-7.8 (-16.3, -2.8)
DKK1	67.4 (-18.2, 166.8)	-12.3 (-50.5, 17.8)	-36.1 (-49.3, -17.7)	-16.5 (-42.7, 35.1)
OPG	20.1 (-12.2, 87.6)	0.7 (-38.5, 54.1)	10.4 (-4.6, 67.8)	-5.9 (-30.6, 16.4)
OPN	63.5 (16.5, 169.4)	23.4 (-19.0, 39.5)	-19.8 (-35.6, 5.5)	-2.9 (-29.1, 21.2)
SOST	20.2 (-30.0, 88.2)	16.9 (-37.3, 95.5)	45.6 (10.8, 78.6)	12.2 (-16.0, 80.2)
RANKL	979.5 (587.7, 1397.0)	302.0 (-72.2, 1425.0)	482.3 (-52.3, 1619.3)	1017.1 (81.5, 2029.8)

Bone markers measured by ELISA on serum samples for HIV-patients. Median (% increment) and interquartile range (Q1 and Q3) are represented.

	Table 2: CYTOKINES (pg/ml)			
	TDF	*TAF*	*PI*	*ADL*
Variable	*Median (Q1, Q3)*	*Median (Q1, Q3)*	*Median (Q1, Q3)*	*Median (Q1, Q3)*
GM CSF	-35.1 (-57.7, -25.4)	7.5 (-28.3, 42.7)	-34.6 (-45.5, 56.9)	-37.8 (-60.1, 18.4)
IFNg	19.2 (-39.2, 69.6)	30.5 (-10.4, 62.4)	18.3 (-27.4, 78.9)	-11.1 (-44.6, 55.9)
IL10	-20.3 (-56.2, 15.0)	-7.0 (-39.4, 90.3)	-38.1 (-58.2, 8.8)	-44.1 (-65.0, 2.3)
IL12	-4.0 (-44.8, 33.7)	-15.1 (-43.4, 34.4)	-39.6 (-57.5, 67.2)	-36.0 (-59.0, 3.5)
IL13	13.6 (-61.6, 81.3)	32.6 (-35.9, 112.2)	-21.8 (-63.9, 102.1)	-43.5 (-81.4, 34.0)
IL1 b	-1.9 (-39.2, 17.1)	28.9 (-32.9, 64.0)	10.1 (-34.4, 87.3)	-12.4 (-56.4, 30.7)
IL2	33.6 (-6.2, 113.4)	62.1 (6.9, 106.6)	48.3 (-15.5, 69.2)	21.7 (-17.5, 77.8)
IL4	-35.7 (-62.9, -3.4)	-59.4 (-74.2, -46.9)	-51.0 (-73.9, -42.1)	-51.1 (-65.3, -18.0)
IL5	-17.2 (-53.3, 35.6)	78.4 (-31.5, 160.7)	34.7 (-38.7, 165.7)	-25.0 (-53.6, 54.3)
IL6	55.3 (-2.9, 213.6)	129.9 (4.0, 222.1)	-1.6 (-31.8, 69.0)	2.4 (-49.3, 119.6)
IL7	56.2 (-7.0, 192.9)	-26.4 (-41.0, 12.7)	-42.7 (-65.7, -28.6)	-2.9 (-35.9, 58.0)
IL8	41.0 (-1.5, 152.5)	108.5 (45.4, 207.3)	183.8 (-8.9, 363.3)	27.9 (-31.3, 129.1)
TNFa	-5.6 (-23.1, 33.6)	44.8 (3.2, 81.3)	42.2 (-28.1, 101.5)	1.8 (-29.0, 42.3)

Cytokines measured by ELISA on serum samples for HIV-patients. Median (% increment) and interquartile range (Q1 and Q3) are represented.

Methods: A cohort of 114 HIV-naïve patients were included in the study. Patients were separated by treatment: 1) Tenofovir Disoproxil Fumarate (TDF), 2) Tenofovir Alafenamide (TAF), 3) Abacavir/Dolutegravir/Lamivudin combo (ADL), 4) Protease Inhibitors (PI). Epidemiological, immunological, and metabolic parameters, as well as BMD were evaluated. Bone markers, proinflammatory and anti-inflammatory cytokines were analyzed in serum at basal and 12 months post-treatment by MILLIPLEX® MAP Luminex® Technology. The diagnosis of osteopenia/osteoporosis was made according to the WHO criteria.

Results: The mean age was 34.7 years (range 19-50 years). 91% was on CDC stage A. The median CD4 was 481 cell/μL (IQR=339.5), 10% had CD4 under 200 cell/μl, and 42% had CD4/CD8 under 0.4. 71% (71/143 p) had low Vitamin D levels, 4% low BMI (< 18.5). Osteopenia or osteoporosis was found in 53% and 11% respectively. In the serum/plasma we found differences at molecular level among different treatments (Table 1). We observed that both TDF and TAF presented a more aggressive resorptive profile than other antiretroviral drugs. We observed that there are no significant differences between the TDF and TAF group at 12 months. However, we have observed an increase in CTX, P1NP and DKK1 for TDF being greater than for TAF and the other treatments. All antiviral presented a pro-inflammatory profile with no significant differences among groups (Table 2).

Conclusion: HIV-naïve patients under 50 years have a high prevalence of bone fragility and osteoporosis, and patients treated with tenofovir (both TDF and also TAF) had greater bone deterioration and proinflammatory state than other patients at 12 months of treatment.

Disclosure: F. Conesa-Buendia, None; **P. Atencio**, None; **A. Cabello**, None; **P. Llamas-Granda**, None; **I. Mahillo-Fernández**, None; **R. Largo**, None; **G. Herrero-Beaumont**, None; **M. Gorgolas**, None; **A. Mediero**, None.

Abstract Number: 2103

Anti-TNF Therapy in Patients with HIV Infection

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with Human Immunodeficiency Virus (HIV) infection may benefit from the use of anti-Tumor Necrosis Factor (TNF) therapy in the setting of inflammatory disease, but the safety of this therapy in patients with HIV infection has not been well established.

Methods: All patients seen at an academic medical center with HIV infection who were prescribed anti-TNF therapy from 1/1/2014-5/1/2019 were identified through retrospective chart review. 11 patients met these criteria. Clinical characteristics, CD4 counts, HIV viral loads, and adverse outcomes including Emergency Department visits, hospitalizations, major infections, malignancies, and death are reported. IRB approval was obtained.

Results: The mean age of patients in this cohort was 48.4, and 90.9% of these patients were male. Indications for anti-TNF use included inflammatory bowel disease (45.4%), psoriatic arthritis (27.2%), rheumatoid arthritis (27.2%), psoriasis (9.1%), and hidradenitis suppurativa (9.1%). The mean duration of anti-TNF use was 52.3 months (range 7-168 months, standard deviation 54.9 months). There were 13 uses of anti-TNF therapy among 11 patients. There were 4 uses of infliximab, 4 uses of etanercept, 4 uses of adalimumab, and 1 use of certolizumab.

All patients were on antiretroviral therapy (ART) at the time of initial anti-TNF prescription, and remain on ART. 72.7% of patients received at least one DMARD in conjunction with anti-TNF use.

There was no significant change in CD4 count during anti-TNF therapy (mean change 103, $p = 0.34$). At the initiation of anti-TNF therapy, 72.7% of patients had undetectable HIV viral loads and 27.3% of patients had detectable viral loads. At the most recent check, all patients had undetectable viral loads. There were no instances of development of a detectable viral load once it became undetectable.

No major infections occurred over 47.9 person-years on anti-TNF therapy. There were 20 ED visits and 10 hospitalizations over this time course, but none were for infections, heart failure, or other complications of anti-TNF therapy.

Two malignancies were diagnosed over 47.9 person-years: an abdominal leiomyosarcoma diagnosed after 12 months of infliximab therapy for Crohn's disease, and a metastatic cholangiocarcinoma diagnosed after 168 months on etanercept for rheumatoid arthritis.

Conclusion: In 11 HIV-infected patients receiving anti-TNF therapy along with ART, anti-TNF therapy did not impact CD4 counts or viral load. No major infections were seen in this population. Two malignancies developed but they not clearly related to HIV infection, anti-TNF therapy, or the underlying disease requiring anti-TNF therapy. We suggest that with appropriate monitoring and consistent use of ART, patients with HIV infection may safely receive anti-TNF medications.

Disclosure: J. Marco, None; **A. Bays**, None.

Abstract Number: 2104

Vasculitis in HIV-Infected Individuals: Making the Case for an Antigen Driven Process

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A large spectrum of vasculitides affecting small, medium, and large vessels have been reported in HIV-infected individuals. Although vasculitis is a rare manifestation of HIV, it is a clinically important complication to recognize that requires immunosuppressive treatment. The purpose of this study was to examine the clinical features and treatment outcomes of HIV-infected individuals with vasculitis referred to a rheumatic disease clinic specialized in the treatment of HIV-related disorders.

Features of HIV-Associated Vasculitis

Age At Diagnosis	Gender/ Ethnic	Diagnosis	Treatment	Year of Diagnosis	Absolute CD4/ HIV viral load	Last Seen/Status
46	M/Black	Polyarteritis Nodosa	None	1996	Unknown	1997 - Deceased
51	F/Hisp	Polyarteritis Nodosa	Prednisone 60mg taper	2006	220/136,270	2019 - Alive, remission
57	M/White	Polyarteritis Nodosa	Prednisone 40 mg taper /Azathioprine	2008	187/208,571	Followed until 2015 – Lost to follow-up
21	M/Hisp	IgA Vasculitis (Henoch-Schoenlein purpura)	Prednisone 40 mg taper	2007	Unknown	2019 – Alive, remission
46	M/Hisp	Primary Angiitis of the CNS	Prednisone 60 mg taper	1998	Unknown	2019 – Alive, remission
53	F/Hisp	Primary Angiitis of the CNS	Prednisone/Mycophenolate Mofetil	2005	60/158,182	2012 - Deceased
44	F/Black	Granulomatosis with Polyangiitis	Prednisone 60 mg taper/Cyclophosphamide	1997	Always CD4 >500. (CD4 1767, viral load <400 in 2002)	2003 – Deceased
38	F/Hisp	Granulomatosis with Polyangiitis	Prednisone 60mg taper,azathioprine, cyclophosphamide	2002	146/ <400	2017 – Deceased
42	F/Hisp	MPO-associated Vasculitis	Prednisone 40 mg taper/Azathioprine	2006	27/ >750,000	2018 – Alive, remission
39	M/Black	HCV-related cutaneous vasculitis	Prednisone 40 mg taper	2007	511/10,176	2019 – Alive, remission

Methods: A retrospective chart review of HIV-infected patients evaluated at an outpatient rheumatology clinic from 1994-2019 was performed. Pertinent demographic data, disease features, laboratory data, treatment, and adverse events were collected.

Results: Ten of 1127 HIV-infected patients were diagnosed with the following: systemic vasculitis/polyarteritis nodosa (n=3), granulomatosis with polyangiitis (n=2) primary angiitis of the CNS (n=2), MPO-associated vasculitis (n=1), IgA vasculitis (n=1), HCV-associated cutaneous vasculitis (n=1). Ten patients were treated with prednisone, and 5 patients required additional immunosuppression with azathioprine (n=3), cyclophosphamide (n=2) and mycophenolate mofetil (n=1). Nine patients had sustained remission for several years. Five patients are currently alive, 3 patients died of non-vasculitis related complications, and 1 vasculitis-related death occurred in a patient who did not undergo treatment. One patient is lost to follow up. Of particular interest, no new cases of vasculitis were referred or diagnosed after 2008, despite no changes on the clinic physicians and no alternative clinical referral sites having become available.

Conclusion: Patients treated for vasculitis in the setting of HIV do well with sustained remission suggesting this is a milder form of disease. Additionally, the absence of new cases over the past 10 years is likely result of more effective antiretroviral treatment. This supports the hypothesis that the development of vasculitis in HIV-infected individual is an antigen or viral (i.e. HIV) driven process

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Abstract Number: 2105

The Comparative Efficacy of Pneumocystis Pneumonia Prophylactic Regimens in Patients with Connective Tissue Diseases Receiving Prolonged High-dose Glucocorticoids

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Trimethoprim-sulfamethoxazole (TMP-SMX) is recommended as a first-line agent of pneumocystis pneumonia (PCP) prophylaxis for those who receive prolonged high-dose glucocorticoids. Alternative agents can be used, but relative efficacy of PCP prophylactic regimens are unknown. We investigated the prophylactic effect of TMP-SMX and other agents for PCP in patients with connective tissue diseases (CTDs) receiving high-dose glucocorticoids.

Methods: Patients with CTDs aged ≧ 18 years who were treated with a prolonged course (≧ 4 weeks) of steroids (≧ 20 mg/day prednisone) in a Japanese tertiary center between January 2013 and December 2017 were included. The

Table1. Baseline characteristics of connective tissue diseases patients receiving high-dose glucocorticoids

	No prophylaxis (n=69)	TMP-SMX (n=296)	Other prophylactic drugs (n=115*)	P value
Male gender, n (%)	17 (24.6)	103 (34.8)	34 (29.6)	0.84
Age, years, mean ± SD	49.3 ± 18.5	55.8 ± 18.5	59.4 ± 18.2	<0.01
Disease duration, years, mean ± SD	8.8 ± 10.6	3.9 ± 7.0	4.2 ± 6.6	<0.01
Diagnosis, n (%)				
Systemic lupus erythematosus	25 (36.2)	25 (8.4)	28 (24.3)	
Polymyositis / Dermatomyositis	3 (4.3)	60 (20.3)	27 (23.5)	
ANCA-associated vasculitis	7 (10.1)	54 (18.2)	21 (18.3)	
Rheumatoid arthritis	8 (11.6)	25 (8.4)	10 (8.7)	
Aortitis**	2 (2.9)	21 (7.1)	4 (3.5)	
Behçet disease	6 (8.7)	6 (2.0)	2 (1.7)	
Adult onset Still's disease	3 (4.3)	6 (2.0)	5 (4.3)	
IgG4-related disease	5 (7.2)	20 (6.8)	5 (4.3)	
Mixed connective tissue disease	4 (5.8)	3 (1.0)	4 (3.5)	
Others	6 (8.7)	38 (12.8)	9 (7.8)	
Initial predonisone dose, mg/day, mean ± SD	26.7 ± 9.8	42.0 ± 15.6	46.5 ± 13.6	<0.01
Concomitant treatment, n (%)				
Steroid pulse therapy	7 (10.1)	39 (13.2)	33 (28.7)	<0.01
Cyclophosphamide	2 (2.9)	37 (12.5)	23 (20.0)	<0.01
Biologics	4 (5.8)	30 (10.1)	8 (7.0)	0.80
Underlying disease, n (%)				
HbA1c ≧ 6.5%	9 (13.0)	86 (29.1)	30 (26.1)	0.09
Lymphocyte ≦ 800/ml	28 (40.6)	161 (54.4)	86 (74.8)	<0.01
Chronic lung disease	10 (10.5)	115 (38.9)	60 (52.2)	<0.01

Categorical values were analyzed using Mantel-Haenszel chi-square test.
Continuous values were analyzed using one-way ANOVA.
*In other prophylactic drugs group, 107 cases received atovaquone and 8 cases received aerosolized pentamidine.
**Including Takayasu's arteritis and giant cell arteritis.
TMP-SMX, trimethoprim-sulfamethoxazole; ANCA, anti-neutrophil cytoplasmic antibody.

patients were categorized into three groups; TMP-SMX, other prophylactic drugs (atovaquone or aerosolized pentamidine), and no prophylaxis group. One-year incidence rate of PCP among the three groups was compared using a cox proportional hazards model.

Results: A total of 480 patients were identified. Two hundred ninety six patients received TMP-SMX while 115 received other prophylactic drugs (107 atovaquone and 8 aerosolized pentamidine). Compared with the no prophylaxis group, patients in the TMP-SMX and other prophylactic drugs group were older, more likely to have chronic lung disease and to be treated with cyclophosphamide and higher dose of glucocorticoids. During a total of 418.95 patient-years, 11 PCP cases (2 in the TMP-SMX, 6 in other prophylactic drugs, and 3 in the no prophylaxis group) occurred with a mortality rate of 54.5%. As compared with no prophylaxis, TMP-SMX significantly reduced the PCP incidence (adjusted HR=0.009, 95%CI 0.0005 to 0.15, p< 0.01) while other prophylactic drugs also reduced the PCP incidence (adjusted HR=0.034, 95%CI: 0.003-0.47, p=0.01).

Conclusion: Not only TMP-SMX but other PCP prophylactic drugs, atovaquone and aerosolized pentamidine, significantly reduced the PCP incidence in CTDs patients receiving prolonged high dose glucocorticoids. TMP-SMX seems to be more effective as a primary prophylaxis against PCP than other prophylactic drugs.

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Abstract Number: 2106

Features of Pneumocystis Jirovecii Pneumonia in Juvenile Idiopathic Inflammatory Myopathy

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Infection-Related Rheumatic Disease Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Approximately 6% of adults with idiopathic inflammatory myopathy (IIM) develop Pneumocystis jirovecii pneumonia (PJP), and PJP confers higher mortality in IIM patients compared to other connective tissue diseases. There are few studies examining PJP in juvenile IIM (JIIM). Our purpose was to characterize the clinical features associated with PJP infections in JIIM.

Methods: An electronic REDCap survey of 215 questions regarding JIIM disease course, medication usage, and PJP infection was sent to members of the Pediatric Rheumatology Bulletin Board, an electronic list-serv, and members of the Childhood Arthritis and Rheumatology Research Alliance. Retrospective chart review of JIIM patients who developed PJP was completed by the primary treating physician.

Results: Survey data were completed for nine juvenile dermatomyositis and one juvenile polymyositis patients who developed PJP infection between ages 1.7-18 years. Of these, 6/10 were male and the median age of IIM disease onset was 5.9 years (range 1.6-17.2 years). At IIM disease onset, 9/10 had weakness, 8/10 had Gottron's papules or heliotrope rash, 6/10 had dysphonia, and 5/10 had skin ulcers. Myositis specific autoantibodies (MSA) were obtained in 9 patients: 4 were positive for anti-MDA5, 1 was positive for anti-p155/140, and 4 were MSA negative. Anti-Ro (SSA) autoantibodies were present in 5/9 patients. The median duration from IIM onset to PJP diagnosis was 3.7 months (IQR 1.7-6.9 months). At PJP diagnosis, IIM disease severity was moderate in 7/10 and severe in 2/10 patients. At the time of PJP infection, 2 patients had interstitial lung disease, one of whom also had pulmonary hypertension. The average white blood cell count at PJP diagnosis was 12.7 thousand cells/μl and 3/10 patients had a low absolute lymphocyte count (range 76-590 cells/μl). Symptoms at PJP presentation included dyspnea on exertion (10/10), hypoxia (9/10), fever (8/10), cough (8/10), and tachycardia (8/10). Mean time from symptom onset to initiation of treatment for PJP was 1 week. The average daily dose of oral prednisone was 30mg (1.1 mg/kg/day) with 8/10 patients on ≥20mg prednisone daily, and 7/10 receiving IV pulse steroids the month prior. Only 2 patients received cyclophosphamide and/or rituximab prior to PJP. Eight patients required ICU admission and 6/10 required mechanical ventilation for an average of 49 days. Two patients required extracorporeal membrane oxygenation, both of whom died secondary to complications of PJP infection. None of the patients had received PJP prophylaxis prior to infection.

Conclusion: PJP affects JIIM patients receiving systemic immunosuppression. Most patients with PJP had moderate to severe disease at diagnosis. Skin ulcerations and anti-MDA5 autoantibodies were commonly reported. Infection with PJP occurred in the first 6 months of disease in the majority of patients, and most patients were receiving high doses of prednisone (≥20 mg) and IV pulse steroids. Due to the high mortality associated with PJP, prophylaxis may be warranted in a subset of JIIM patients with these disease features, especially early in the disease course when higher doses of steroids are required to control disease.

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Abstract Number: 2107

Comparison of the Management and Prognosis of Pneumonia in Patients with and Those Without Rheumatoid Arthritis Using the Japanese Diagnosis Procedure Combination Database

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Infection-Related Rheumatic Disease Poster

	RA	non RA	P value
Background			
Age (median) (year)	75	79.3	<0.01
Severity class of pneumonia			<0.01
mild (%)	691 (23.8)	28166 (16.2)	
moderate (%)	1724 (59.3)	104484 (60.1)	
Sever (%)	285 (9.1)	25219 (14.9)	
Very severe (%)	206 (7.1)	15844 (9.1)	
Sex (male) (%)	1087 (37.4)	102882 (59.2)	<0.01
BMI (mean)			0.11
Smoking (%)	814 (30.7)	74219 (42.7)	<0.01
Barthel index at admission (median)	87.8	68.3	<0.01
Comorbidity			
Diabetes mellitus (%)	584 (20.1)	30450 (17.5)	<0.01
Lung disease (%)	655 (22.5)	27982 (16.1)	<0.01
Heart disease (%)	436 (15.0)	37440 (21.6)	<0.01
Renal disease (%)	115 (4.0)	11149 (6.4)	<0.01
Organic brain disease (%)	74 (2.5)	11721 (6.7)	<0.01
Cancer (%)	174 (6.0)	22483 (16.9)	<0.01
Emergency admission via ambulance (%)	625 (21.2)	51946 (29.5)	<0.01

Clinical characteristics

Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Pneumonia is a common cause of death not only in the general population but also in patients with rheumatoid arthritis (RA). In particular, patients with RA have an increased risk for pneumonia due to rheumatoid lung disease and the use of some DMARDs. No studies have assessed differences in the management and prognosis of pneumonia in patients with RA compared to the general population. This study aimed to examine the prognosis of pneumonia and its management in patients with RA compared to the general population.

Methods: This study utilized the Diagnosis Procedure Combination database, a nationwide inpatient database in Japan. We reviewed abstract data and medical procedures to identify patients with pneumonia with or without RA between 2014 and 2016. We assessed differences in medical actions: examinations (such as imaging examination, bacteria culture, and antigen testing), interventions (such as oxygen supplementation, use of mechanical ventilation, and ICU admission), and treatment (such as type of antibiotic and duration of antibiotic therapy) between patients with and without RA. We compared the prognosis of pneumonia (mortality, length of hospitalization, aggravation of activities of daily living (ADL), and readmission) between patients with RA and those without RA. We examined the association between RA and pneumonia prognosis using multivariate analysis, adjusting for patients' background data, comorbidities, and pneumonia severity at admission.

	RA	non RA	P value
Test			
CT scan (%)	2549 (84.6)	142924 (82.3)	<0.01
Blood culture (%)	1548 (53.3)	86062 (49.5)	<0.01
Sputum culture (%)	2351 (80.9)	82807 (47.7)	<0.01
Antigen test (%)	1729 (59.5)	101947 (58.7)	0.38
Management			
Oxygen supplementation (%)	1500 (51.6)	100817 (58.0)	<0.01
Mechanical Ventilation (%)	97 (3.3)	7332 (4.2)	0.19
Use of ICU (%)	27 (0.9)	2182 (1.2)	0.11
Antibiotic			
Carbapenem (%)	467 (16.1)	22910 (13.2)	<0.01
Quinolone (%)	229 (7.9)	12315 (7.1)	0.1
Antipseudomonal therapy (%)	1409 (48.5)	60719 (35.0)	<0.01
Duration of antibiotic (median) (day)	8.9	7.6	<0.01
Rehabilitation (%)	1228 (42.3)	70219 (40.4)	0.46
Outcome			
30-day in-hospital mortality (%)	81 (2.7)	8920 (5.1)	<0.01
Length of stay (median)	12.6	11.4	<0.01
Aggravation of ADL at discharge (%)	49 (1.7)	2310 (1.3)	0.1
Readmission within two weeks (%)	130 (5.0)	9106 (6.6)	<0.01

	Severity class											
	mild			moderate			Sever			Very severe		
Death / total patients (%)	104 / 28857 (0.4)			3317 / 106208 (3.1)			2592 / 25504 (10.2)			2842 / 16050 (17.7)		
	OR (95%CI.)		p	OR (95%CI.)		p	OR (95%CI.)		p	OR (95%CI.)		p
RA	0.35	3.79	0.82	0.79	1.50	0.6	0.61	1.59	0.95	0.86	2.14	0.19
Sex (female)	0.41	0.98	0.04	0.54	0.64	<0.01	0.60	0.74	<0.01	0.59	0.74	<0.01
Age	1.03	1.08	<0.01	1.01	1.02	<0.01	1.01	1.02	<0.01	1.03	1.04	<0.01
BMI	0.86	0.95	<0.01	0.89	0.91	<0.01	0.90	0.92	<0.01	0.92	0.94	<0.01
Smoking	0.80	1.86	0.37	0.77	0.91	<0.01	0.76	0.93	<0.01	0.85	1.06	0.39
Barthel index at admission	0.96	0.97	<0.01	0.98	0.98	<0.01	0.98	0.98	<0.01	0.98	0.98	<0.01
Diabetes mellitus	0.45	1.47	0.49	0.91	1.12	0.9	0.73	0.96	0.01	0.75	1.01	0.08
Lung disease	0.83	2.43	0.20	1.31	1.58	<0.01	1.00	1.27	0.04	0.95	1.25	0.23
Heart disease	0.88	2.78	0.13	1.46	1.71	<0.01	1.12	1.35	<0.01	1.06	1.30	0.00
Renal disease	0.38	3.04	0.89	1.35	1.74	<0.01	1.32	1.74	<0.01	1.25	1.69	<0.01
liver disease	0.17	1.71	0.29	0.82	1.26	0.9	0.83	1.49	0.49	0.59	1.15	0.26
Cancer	4.18	9.26	<0.01	2.42	2.87	<0.01	1.86	2.38	<0.01	1.51	1.98	<0.01

Association of patients' background with 30-day hospital mortality

Results: For this study, 178,994 patients from 1,570 hospitals were eligible. Of these patients, 2,951 (1.6%) were diagnosed with RA. The severity of pneumonia in patients WITH RA was mild-to-moderate compared with patients without RA (p< 0.01). Patients with RA had more CT scans performed (84.6% vs 82.3%, p< 0.01) and more sputum culture tests (80.9% vs 47.7%, p< 0.01). Furthermore, broad-spectrum antibiotics (e.g., carbapenem) were frequently administered (16.1% vs 13.2%, p< 0.01) and the antibiotic administration period was slightly longer (8.9 days vs 7.6 days, p< 0.01) in these patients. Patients with RA had lower 30-day in-hospital mortality than those with RA (2.7% vs 5.1%, p< 0.01), but the length of hospital stay was longer (12.6 vs 11.4, p< 0.01). Multiple logistic regression analysis revealed that patients with RA did not have an associated increased risk of in-hospital mortality after adjusting for covariates in each pneumonia severity class (OR 1.36, 95% CI: 0.86-2.14). Lengthened hospitalization period was observed in patients with RA by Cox regression analysis (OR 0.78, 95% CI: 0.75-0.82).

Conclusion: Although pneumonia in patients with RA is not as severe as that in general patients, the rates of examination were high and broad-spectrum and long-term antibiotic treatment were administered more frequently in patients with RA. RA does not affect the prognosis of pneumonia but affects the hospitalization period. It is necessary to consider the implementation of appropriate medical practices according to the severity and the patient background for pneumonia in patients with RA.

Disclosure: E. Uechi, None; **K. Fushimi**, None.

Abstract Number: 2108

Risk Factors for Pulmonary Nontuberculous Mycobacterial Disease in Rheumatoid Arthritis Patients

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Infection-Related Rheumatic Disease Poster

Session Type: Poster Session (Tuesday)

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Background/Purpose: Rheumatoid arthritis (RA) patients have increased susceptibility to infection by pulmonary nontuberculous mycobacterial disease (pNTM) compared with the healthy population. The reason for this increased susceptibility to pNTM in RA patients is still unclear and few studies have been conducted to identify risk factors.

Methods: Medical records for all the RA patients who attended our hospital from March 2017 to March 2018 were retrospectively reviewed. pNTM was diagnosed by the criteria of the American Thoracic Society and the Infectious Diseases Society of America. Clinical factors such as age, gender, BMI, smoking history, diabetes, Charlson Comorbidity Index (CCI), rheumatoid factor (RF), anti-citrullinated protein antibody (ACPA), DMARDs, and chest CT findings were collected and compared between RA patients with and without pNTM.

Results: Data from 868 RA patients (205 males, 663 females) were analyzed. Among those patients, 37 patients were diagnosed with pNTM. Patients with pNTM were significantly older and had lower BMI than those without (72 +/- 10.6 vs 66.9 +/-13.5, p=0.014, and 20.0 +/-3.9 kg/m^2 vs 22.5 +/-4.5 kg/m^2, p=0.016, respectively). RF positivity was significantly higher in patients with pNTM (100% vs 83.6%, p=0.014). Percentages of MTX or bDMARDs use were significantly lower in patients with pNTM (48.9% vs 69.0%, p=0.016, 10.8% vs 30.0%, p=0.020). For chest CT findings, consolidation, cavitary lesion, pleural effusion, nodular lesion, and bronchiectasis were significantly higher among patients with pNTM (71.4% vs 8.0%, 14.3% vs 1.1%, 17.1% vs 2.0%, 85.7% vs 16.2%, and 62.9% vs 14.2%, respectively, with all p< 0.001). Multiple logistic regression analysis revealed ACPA and lower BMI to be independent risk factors of pNTM in RA patients (OR=4.9, 95% CI 1.1-21.0 and OR=0.8, 95% CI 0.7-0.9, respectively).

Conclusion: As is consistent with patients without RA, lower BMI is a risk factor for pNTM in RA patients. We identified ACPA positivity as a novel risk factor for pNTM in RA patients.

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Abstract Number: 2109

Are Immunosuppressants a Risk Factor Associated with *Mycobacterium Tuberculosis* Infection in Colombian Patients with Systemic Lupus Erythematosus? A Case-control Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Infection-Related Rheumatic Disease Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

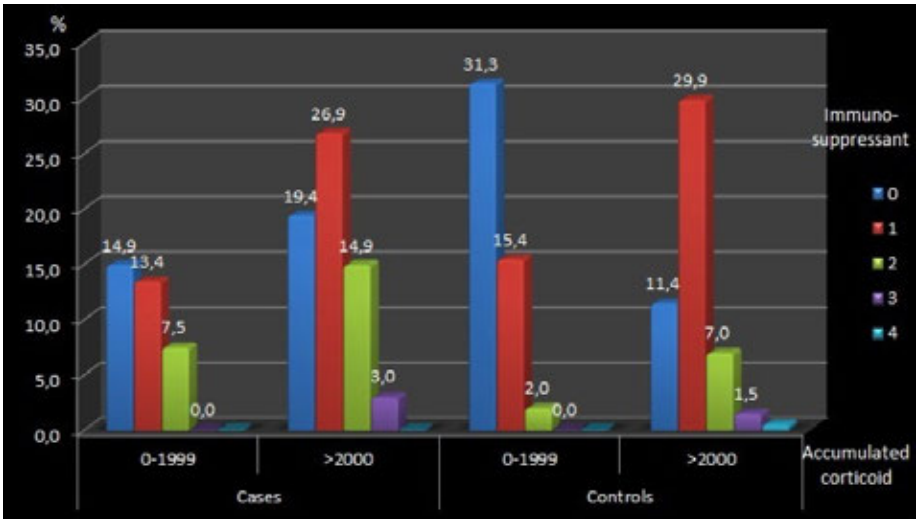

Figure 1. Number of immunosuppressants received within the last year in both, cases and controls, discriminated by the cumulative dose of glucocorticoids (<2 grams or ≥2 grams).

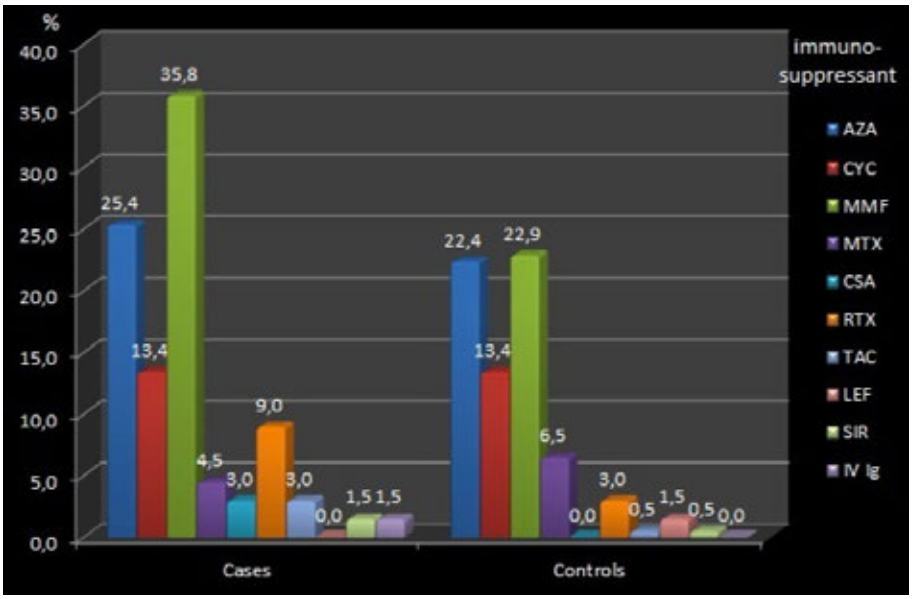

Figure 2. Frequency of immunosuppressants used in cases and in controls. AZA: azathioprine. CYC: cyclophosphamide. MMF: mycophenolate mofetil. MTX: methotrexate. CSA: ciclosporin A. RTX: rituximab. TAC: tacrolimus. LEF: leflunomide. SIR: sirolimus. IV Ig: intravenous immunoglobulin.

Background/Purpose: Tuberculosis (TB) infection is an important cause of morbidity and mortality in systemic lupus erythematosus (SLE) patients, especially in developing countries. Previous studies have shown that higher cumulative doses of glucocorticoids within the last year are a risk factor for *Mycobacterium tuberculosis* infection. However, the role of conventional immunosuppressants in TB development is controversial. The aim of this study was to identify the factors associated with TB infection in SLE patients.

Methods: A retrospective case-control study. From January 2007 to December 2017, a total of 268 patients who met the 1997 ACR revised classification criteria for SLE were included. Cases were SLE patients diagnosed with TB by clinical, radiological, microbiological, molecular and/or histopathological criteria (SLE-TB). TB infection was classified as pulmonary, extrapulmonary or disseminated. Controls were SLE patients without TB infection (SLE-non-TB). In

total 67 cases and 201 controls were assessed. The quantitative variables are expressed as means or medians with their respective measure of dispersion and the qualitative variables as absolute number and percentage. Univariable and multivariable logistic regression analyses were performed.

Results: Females were more frequent in cases (83.5%) and controls (86%). The mean age was 34 years (range 13-84 years) for cases and 36 years (range 10-87 years) for controls. No significant differences in the frequency of comorbidities [diabetes, cirrhosis and Charlson comorbidity index (CCI)], disease duration and disease activity (SLEDAI) between cases and controls were found. Pulmonary TB occurred in 46.3%, extrapulmonary TB in 16.4% and disseminated TB in 37.3% of cases. Miliary pattern on chest X-ray was found in 23.8% of cases. In the univariable analyses, kidney transplantation, cumulative glucocorticoid dose (>2 grams) and ≥2 immunosuppressants received within the last year were associated with TB infection (11.9% in cases vs. 4.4% in controls; p= 0.04; 3.7 grams in cases vs. 2.1 grams in controls, p = 0.02; 22.7% in cases and 8.9% in controls, p= 0.02, respectively) (figure 1). By multivariable analysis, after adjusting for age, gender, disease duration, nephritis, antimalarials, immunosuppressants and CCI, cumulative glucocorticoid dose (OR 1.00; 95% CI 1.00-1.01; p=0.02) and kidney transplantation (OR 4.1; 95% CI 1.06-16.1; p=0.04) were significantly associated with TB infection occurrence. The most commonly immunosuppressants used were mycophenolate mofetil (MMF), azathioprine and cyclophosphamide, with a higher prevalence of MMF and rituximab in SLE-TB compared with SLE-non-TB patients (35.8% vs. 22.9% and 9% vs. 3%, respectively) (Figure 2).

Conclusion: Besides cumulative glucocorticoid dose (>2 grams), kidney transplantation was found to be significantly associated with an increased risk of Mycobacterium tuberculosis infection. Although, the exposure to ≥2 immunosuppressants was more than twice in cases than in controls, it was not significant in multivariable analysis. Prospective studies are needed to clarify the potential risk of immunosuppressants for TB infection development in SLE.

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Abstract Number: 2110

Invasive Aspergillosis in Rheumatologic Patients in Tertiary Care Hospital in Mexico

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Fungal infections are an important cause of morbidity and mortality in patients with rheumatic diseases. Invasive aspergillosis (IA) is a fungal infection potentially fatal, which has been primarily described in patients with profound neutropenia such as those with hematologic malignancies. There is limited information in patients with rheumatic diseases. We describe herein clinical characteristics and outcomes of IA diagnosed in patients with rheumatic diseases.

Methods: At first, we identified from microbiological records of a national referral center for rheumatic diseases, patients with *Aspergillus spp.* isolated and/or positive galactomannan (January 2014-December 2018); then patients

Table 1. Demographical, clinical characteristics, treatment and relevant laboratory parameters from the population.

DEMOGRAPHIC CHARACTERISTICS N=33	
Female sex (%)	23 (70)
Age	51 (28-59)
Disease duration, years	2 (1-9)
Disease activity status (%)	26 (78.8)
Patients with severe disease activity	20 (60.6)
COMORBID CONDITIONS	
Chronic kidney disease (%)	9 (27.3)
Diabetes mellitus 2 (%)	5 (15.1)
LABORATORY PARAMETERS	
Leucocyte count	7.9 (4.2-12.3)
Neutrophils count	4488 (2964-8764)
Lymphocite count	560 (344-852)
Hemoglobine	8.3 (7.5-9.6)
Platelets count	109 (66-282)
C reactive protein	5.6 (1.7-13.8)
Serum creatinine	1.2 (0.57-2.87)
DISEASE RELATED TREATMENT (PREVIOUS THREE MONTHS)	
Steroides use (%)	28 (85)
Prednisone dose	50 (20-60)
Metilprednisolone pulses	7 (25)
Immunosuppresor non steroid	28 (85)
Plamapheresis	2 (6)

Data presented as median, IQR unless otherwise indicated.

Table 2. Clinical presentations, radiological findings and treatment.

CLINICAL PRESENTATION N=33	
Respiratory symptoms	27 (81.8)
Fever	23 (69.7)
CLINICAL SYNDROME	
Pulmonary disease	28 (84.9)
Sinopulmonary	5 (15)
RADIOLOGICAL CT FINDINGS	
Nodules/micronodules	30 (91)
Consolidation with ground glass opacieites	19 (58)
Single or multiple cavitations	6 (18)
Only ground glass	7 (21)
TREATMENT	
Time to initiate antifungal therapy, median (IQR)	10 (4-20)
Duration of treatment, median (IQR)	42 (35-56)
Voriconazole definitive therapy	13 (43.3)
Itraconazole definitive therapy	11 (36.7)
Posa vs Voriconazole trial therapy	4 (13.3)
Ampho B definitive therapy	1 (3.3)

Data presented as N (%), unless otherwise indicated.

with a defined rheumatic disease were selected. The charts from all the patients were reviewed and they were classified as with proven or probable IA according the EORTC/MSG criteria or putative IA with modified AspICU algorithm. In addition, relevant demographic, clinical, treatment (in previous three months) and laboratory characteristics were

Table 3. Six week mortality risk factors associated.

Characteristic	All N=33	Dead N=9	Alive N= 24	p	OR adjusted
Female sex (%)	23 (70)	6 (66.7)	17 (70.8)	0.8	
Age, median (IQR)	51(28-59)	45(32-59)	51(27.5-58)	0.7	
Pulmonary disease	28 (84.9)	6 (66.7)	22 (91.6)	0.09	
Platelets count, Median (IQR)	109 (66-282)	51(26-110)	156(85-375)	0.05	**0.98 (0.97-0.99) p 0.03**
Lymphonenia	26 (78.8)	9 (100)	17 (70.8)	0.00	
Steroids, (%)	28 (84.8)	7 (77.8)	21 (87.5)	0.00	
Immunosuppresor non steroid, n (%)	28 (84.8)	7 (77.8)	21 (87.5)	0.00	
Activity disease	26 (78.8)	8 (88.9)	18 (75)	0.39	
Hepatic failure	12 (36.4)	3 (33.3)	9 (37.5)	0.8	
Time to initiate antifungal therapy, median (IQR) days	10 (4-20)	9(3-21)	10(4-20)	0.8	

obtained, including the disease activity status and its severity. Descriptive statistics was used along with multivariate analysis to investigate 6-weeks mortality predictors.

Results: Thirty-three patients with a rheumatic disease and IA were identified; of them, 14 patients (42.4%) had SLE, 9 (27.3) had polyangiitis with granulomatosis, 4 (12%) had dermatomyositis, 3 (9.1%) had RA, 2 (6%) had adult onset Still disease and 1 patient (3%) has primary antiphospholipid syndrome. The majority of the patients (29 [87.9%]) had probable IA, meanwhile, 3 (9%) had putative IA and 1 patient left (3%) had proven IA; also, 14 patients (42.4%) had a bacterial co-infection. Demographical, clinical characteristics, treatment and relevant laboratory parameters from the population are summarized in **Table 1. Table 2** summarizes IA clinical presentations, radiological findings and treatment. Fifteen (45.4%) patients had ≥1 culture with *Aspergillus* growth, the most frequent species were: *A. fumigatus* 10 /19 (53%), *A. niger* 3 (15.7%), *A.flavus* 1 (5%) and 5(26.3%) *Aspergillus sp*. Galactomannan antigen was tested on 27 (82%) of which 20/27 (74%) were positive: 14(70%) serum, 12(60%) in broncoalvoelar lavage samples and 3 cases had both. Six-week mortality was 27%. **Table 3** summarizes risk factors associated to mortality. In the multivariate analysis platelets counts below 100.0 K/uL was the only risk factor identified.

Conclusion: In this study we found specifics characteristics among the rheumatologic patients. The six week mortality of 27% was lower than has been reported in non neutropenic patients. Finally only thrombocytopenia was found as a risk factor of mortality in this group. It is necessary an increased knowledge of IA characteristics in these group of patients for early diagnosis and treatment.

Disclosure: G. Guaracha-Basañez, None; **C. Román-Montes**, None; **M. González-Lara**, None; **A. Ponce-de-León**, None.

Abstract Number: 2111

Symptomatic Coccidioidomycosis Infections in Patients on Biologic Therapies

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Studies have shown an increased risk of *coccidioidomycosis* infection in immunosuppressed patients. However, relationship of *coccidioidomycosis* infections with different immunosuppressive medication is not well established. This study was aimed to examine the characteristics of symptomatic *coccidioidomycosis* infections in patients with rheumatic diseases on biologic infusions.

Methods: A retrospective study was conducted between 2013 and 2017 at two infusion centers affiliated with the University of Arizona. Patients with rheumatic diseases on biological infusions for the diagnosis of symptomatic *coccidioidomycosis* were identified. The data related to method of infection identification, subsequent management, and concurrent steroid.

Results: Out of 548 patients, 21/548 (3.8%) had symptomatic *coccidioidomycosis.* Mean age was 54 years. 15/21 (71.4%) were female and 6 (28.6%) were male. 1/21 had disseminated disease, 17/21 had primary pulmonary disease, and 3/21 had unclear disease status. 6/21 (28.6%) patients were on rituximab therapy, 4/21 (19%) were on infliximab, 4/21 (19%) were on tocilizumab, 2/21 (9.5%) were on abatacept, 2/21 (9.5%) on golimumab 1/21 (4.8%) on canakinumab, and 1/21 (4.8%) on IVIG. Total of 15/21 (71.4%) patients used glucocorticoids with average dose being 14.5mg. 7/15 (46.7%) of patients were on chronic glucocorticoids treatment.

10/21 (47.6%) were diagnosed with a positive qualitative immunodiffusion assay. 4/21 (19%) patients had a serum enzyme-linked immunosorbent assay with positive titers > 1:2. 4/21 (19%) patients had a positive complement fixation test. 3/21 (14.3%) patients were diagnosed with a positive fungal culture, 2/3 being from a respiratory source.

15/21 (71.4%) patients had an abnormal chest x-ray, with the most common finding being a nodule (6/15). 12/21 (57%) patients had an abnormal chest CT, with the most common finding being a nodule as well (6/12). 17/21 (80.9%) were started on antifungal therapy, with 16/17 (94%) being started on fluconazole. 9/21 (42.9%) patients had their biologic therapy stopped, with 3/9 (33.3%) eventually having their biologic therapy restarted. 12/21 patients continued their therapy without interruption.

Conclusion: This study showed that occurrence of symptomatic *coccidioidomycosis* infection was more prevalent in patients using concurrent glucocorticoids with biologics. Among biologics, rituximab had the highest rate of symptomatic infections. Qualitative immunodiffusion assay was commonly utilized test to diagnose coccidioidomycosis infection. The vast majority of patients were treated with fluconazole, but continued the antirheumatic therapy.

Disclosure: A. Peck, None; **E. Starobinska**, None; **G. Ortega**, None; **T. Maestas**, None; **J. Leong**, None; **P. Saligrama**, None; **J. Bilal**, None; **D. Sudano**, None.

Abstract Number: 2112

Real Life Serious Infections in Patients with Chronic Inflammatory Arthritis on Treatment with TNF Inhibitors

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SESSION INFORMATION
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Session Type: Poster Session (Tuesday)
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Background/Purpose: To study frequency and associated factors for serious infections in patients with inflammatory arthritis treated with TNF inhibitors

Methods: All the medical records of the patients with inflammatory arthritis being treated with TNF inhibitors at the beginning of 2016 were reviewed. All seroious infections suffered for these patients until the end of 2018 were recorded. Serious infections were defined as those which required to admitted at the hospital for intraveous treatment. Potential variables associated with the development of these infections including: demographic and clinical characteristics, concomitant treatments or comorbidity (by Charlson index) were studied. Standard statistical tests for descriptive and univariate analyses were used and a multivariable logistic regression model was built to check independent associations.

Results: Overall 334 patients (50.3% women) with a mean age of 56.67 (±12.853) were studied: 140 (41.92%) Rheumatoid arthritis (RA), 55 (16.46%) psoriatic arthritis (PsA) and 138 (41.62%) spondyloarthritis (Sp). Forty five serious infections were observed in 30 patients, being respiratory (40%) and urinary (8.8%) the most frequent localizations. Only one patient died. By univariate analysis, disease duration, age, concomitan use of glucocorticoids (GC) (but not of synthetic DMARDs), Charlson index and specifically Diabetes Mellitus were associated with infection ($p< 0.05$). The type of arthritis was not associated and the results in the subset of RA patients were overall similar. In the multivariate analysis the use of GC [OR: 5.31 (1.98.14.26)] and the Charlson index [OR:2.48 (1.70;3.60)] were found to be independently associated to infection.

Conclusion: In patients with inflammatory arthritis and treated with TNF inhibitors around a 10% developed any serious infection along three years of follow up. Use of GC and comorbidity emerged as the main risk factors for this complication.

Disclosure: A. Ruiz, None; **J. De Dios**, None; **B. Alvarez**, None; **M. Vasques Rocha**, None; **C. Stoye**, None; **S. Gil**, None; **O. Pompei Fernández**, None; **J. Calvo-Alen**, None.

Abstract Number: 2113

Biological Therapy Is Associated with Faster Recovery and Lower Frequency of Switch Treatment in Patients with Chikungunya Fever

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SESSION INFORMATION

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Background/Purpose: The first chikungunya fever outbreak in Brazil had its peak in the first half of 2016 and many patients with rheumatologic disease using biological disease-modifying antirheumatic drugs (bDMARD) and conventional synthetic disease-modifying antirheumatic drugs therapy (csDMARD) were affected by the disease. Although there was initially concerns about the use of drugs with immunosuppressive potential in patients with a viral infection, the clinical practice and a few case reports demonstrated that there were no major complications and the clinical course seems to be similar to healthy population. The aim of this study was to compare the clinical course of rheumatic patients with rheumatic diseases treated with bDMARD or csDMARD.

Methods: The patients included in this study was select from two centers in Pernambuco, participating in the Brazilian cohort of patients with rheumatic diseases using bDMARD or csDMARD. Data about the disease therapy for the rheumatic disease and the symptoms of Chikungunya fever were collected. All the patients had the rheumatic disease diagnosis before the Chikungunya fever Brazilian outbreak and underwent serologic testing for chikungunya virus (CHIKV) IgG. The clinical data and blood sample for serology testing was taken from July 2017 until July 2018.

Results: We included 103 patients in the study and 74.7% were women; the most frequent previous rheumatologic diagnosis was rheumatoid arthritis (76.1%); 50.5% of the sample was on bDMARD therapy combined or not with csDMARD, of which 21% exclusively on biological use. The overall soroprevalence of CHIKV IgG was 40.8%; on bDMARD patients it was 36.5% and on csDMARD 46.4% (p=0.437). Among patients with positive CHIKV IgG, 26.2% had no typical Chikungunya fever symptoms (fever and joint pain). No differences were observed among the two groups regarding the number of patients with asymptomatic infection. There was no clinically significant difference in acute phase symptoms between the two groups of patients. Regarding the persistence time of Chikungunya fever musculoskeletal symptoms in CHIKV IgG positive group, 85.7% of patients using bDMARD recovered up to 3 months compared to 47.1% in the non bDMARD group (p=0.029). In addition, the bDMARD group switched the treatment less frequently after CHIKV infection (p=0.0001).

Conclusion: The bDMARD seems to be associated with a shorter period of Chikungunya fever symptoms and lower frequency of flare triggered by CHIKV infection comparing to csDMARD. No difference was observed between the severity of the symptoms in both groups.

Disclosure: A. Razolin, None; **C. Marques**, None; **L. Rocha Jr**, None; **H. Lima**, None; **L. Martins**, None; **A. Almeida**, None; **P. Oliveira**, None; **A. Duarte**, None; **M. Rego**, None; **M. Pitta**, None; **I. Laurindo**, None.

Abstract Number: 2114

Risk Factors for Cytomegalovirus Infection in Patients with Autoimmune Diseases

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SESSION INFORMATION

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Background/Purpose: Intensive immunosuppressive treatment is often required for patients with autoimmune diseases, and those who are thus treated have a high risk of opportunistic infections. It is therefore important to investigate the risk of opportunistic infections to ensure appropriate management of patients with autoimmune disease. Cytomegalovirus (CMV) infection is one of the most common opportunistic infections. Since 2011 we have been performing routine weekly evaluation of CMV pp65 antigen for such patients. Here we investigated the predictive risk factors for CMV infection under remission-induction therapy in patients with autoimmune disease.

Methods: We enrolled 96 patients (male 34, female 62) with autoimmune disease who received remission-induction therapy with prednisolone at over 0.5 mg/kg/day in Niigata University Hospital between January 2017 and December 2018. We retrospectively analyzed their clinical features and laboratory data at the baseline, the treatment regimens used, and the results of CMVpp65 antigen analysis. The presence of more than 5 CMVpp65 antigen-positive cells/2 slides was defined as a positive result. We conducted univariate and multivariate analyses to identify risk factors for CMV positivity.

Results: The enrolled patients included 26 systemic lupus erythematosus (SLE), 18 anti-nucleolar cytoplasmic antibody-associated vasculitis (AAV), 8 interstitial pneumonia with anti-aminoacyl tRNA synthetase antibody, 6 mixed connective tissue disease (MCTD), 6 rheumatoid arthritis, 5 clinically amyopathic dermatomyositis (CADM), 5 adult-onset Still's disease (AOSD), 5 Takayasu's aortitis, and 17 other conditions. Methylprednisolone pulse therapy, intravenous cyclophosphamide, oral calcineurin inhibitor, methotrexate, azathioprine, and mycophenolate mofetil were applied in 36 (37.5%), 17 (17.7%), 7 (7.29%), 4 (4.17%), 4 (4.17%), and 3 (3.13%) patients, respectively. The median follow-up duration was 62.5 days, and 21 patients became CMV antigenemia-positive (SLE 9, AOSD 4, AAV 2, CADM 2, MCTD 2, and others 2). Univariate analysis showed that the positivity was associated with a low total lymphocyte count (TLC) (710/μl vs 1330/μl; $p< 0.001$), a low serum albumin level (2.70 g/dl vs 3.50 g/dl; $p< 0.001$), a high HbA1c level (6.4% vs 5.9%; $p< 0.001$), and a high initial prednisolone dosage (0.97 mg/kg/day vs 0.86 mg/kg/day; $p< 0.001$). Fifteen of the 21 patients in the positive group received steroid pulse therapy ($p< 0.001$). The Cox hazard regression model indicated that a higher age by decade (OR; 1.46 [95%CI 1.06- 2.00]), a lower TLC per 100/mL (OR; 0.827 [95%CI 0.731-0.935]), a higher HbA1c level per 1% (OR; 2.37 [1.25-4.53]), and mPSL pulse therapy (OR; 3.92 [1.33-11.5]) were independent risk factors for CMV positivity.

Conclusion: Lower TLC, lower serum albumin, higher HbA1c, and receiving steroid pulse therapy were risk factors for CMV pp65 antigen positivity. Careful monitoring is therefore necessary for such patients.

Disclosure: D. Kobayashi, None; **S. Takamura**, None; **Y. Wada**, None; **T. Kuroda**, None; **I. Narita**, None.

Abstract Number: 2115

BK Polyomavirus Viremia and Viruria in Patients with Autoimmune Connective Tissue Diseases: Impact of Immunosuppressants

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Background/Purpose: The human polyomaviruses, such as the BK and JC virus, are highly prevalent in humans but appear to cause clinical disease only in immunocompromised patients. BK virus (BKV) is the primary cause of tubulointerstitial nephritis and ureteral stenosis in kidney transplant recipients and hemorrhagic cystitis in bone marrow transplant recipients. Among transplant recipients, it has been hypothesized that the intensity of immune suppression, rather than the specific immunosuppressive agent used, determines the risk for BKV replication and progression to clinically significant disease.

Patients with autoimmune connective tissue diseases (CTD) like Systemic Lupus Erythematosus (SLE) and Rheumatoid arthritis (RA) have been shown to have increased polyomavirus levels in blood and urine. The treatment for these autoimmune diseases include medications like corticosteroids and disease modifying anti-rheumatic drugs (DMARDS), including biologics and cytotoxic agents which have been shown to increase the frequency of virus reactivation/excretion in prior studies. The purpose of this study was to determine the prevalence of BK virus in the blood and its excretion in urine in immunosuppressed patients with CTDs. We hypothesized that subjects on DMARDS plus steroids would have the highest prevalence of BKV viremia and viruria.

Methods: Sixty-six patients with CTD on various immunosuppressive regimens (including Prednisone, Mycophenolate Mofetil, Methotrexate, Leflunomide, Azathioprine, Sulfasalazine, Hydroxychloroquine, Tumor necrosis factor inhibitors, Tocilizumab, Rituximab, Cyclophosphamide) and control subjects were enrolled after informed consent was obtained. Urine and serum specimens were collected at each clinic visit and analyzed qualitatively and quantitatively for BK virus by PCR. Subjects' demographic data, diagnosis and medications were recorded at the time of each clinic visit. The frequency of BKV viruria and viremia was compared for clinical and demographic factors using Chi-square analysis. Multivariate analysis is planned once the study population reaches 100.

Results: The average age of study subjects was 53.5 +/- 12.4 years and 46 (69.7%) were African-American. Fifty-six (84.8%) subjects were female. Twenty subjects had RA, 15 had SLE, 31 had other diagnosis like Psoriatic arthritis, myositis, scleroderma. Serum and Urine specimens were collected from study subjects at 239 clinical visits. 155 (64.8%) of 239 urine specimens and 106 (45.1%) of 239 serum specimens were positive for BKV. There was no difference in the frequency of BKV viremia or viruria based on the subject's diagnosis (RA (49.2% and 62.9%) vs SLE (43.1% and 68.4%) vs other (43.6% and 69.6%)) Figure 1, or medication regimen (none vs. steroids vs. DMARDS vs. DMARDS + steroids) Figure 2.

Conclusion: Contrary to our hypothesis, there was no statistical difference between the frequency of BK-positive serum or urine by medication group. Likewise, there was no statistical difference in the frequency of BKV viremia or

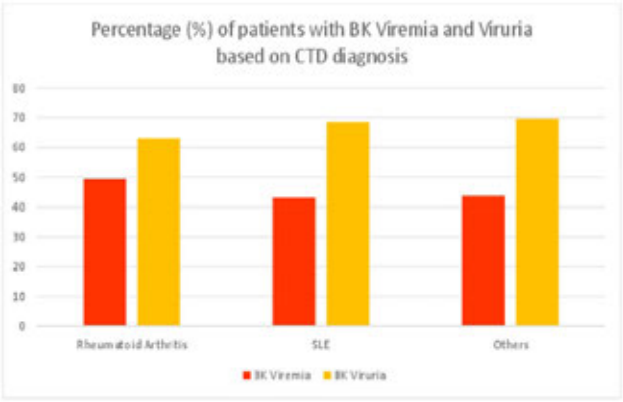

Figure 1. Percentage (%) of patients with BK Viremia and Viruria based on CTD diagnosis

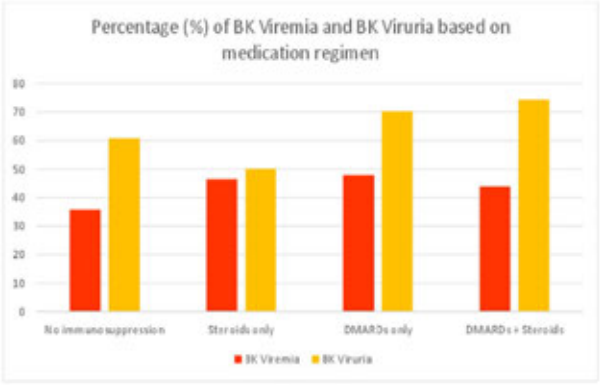

Figure 2. Percentage (%) of BK Viremia and BK Viruria based on medication regimen

viruria by subject's CTD diagnosis. These data suggest that immunologic control of BKV viremia and viruria may be dysregulated in CTD, independent of immunosuppressive regimens.

Disclosure: M. Katikaneni, None; **M. Davis**, None; **C. Smith**, None; **J. Vanchiere**, None.

Abstract Number: 2116

Serious Infection in Patients with Systemic Lupus Erythematosus, Lupus Nephritis and Rheumatoid Arthritis Compared to the General Population: Incidence Rates Using Real-World Claims Data

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Infection-Related Rheumatic Disease Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE), lupus nephritis (LN) and rheumatoid arthritis (RA) are at risk of serious infections (SIs) due to the impact of the disease itself and treatments that modulate immune function. Rates of SIs resulting in hospitalization among these patients have not been compared to the general population. The objective of this study was to compare the rates of SIs resulting in an inpatient claim in adult patients with SLE/LN, RA and the general population using population-based claims data.

Methods: We conducted a retrospective cohort study using the US-based Truven Healthcare MarketScan® Claims database for individuals aged 18-64 years enrolled between January 2007 and September 2015. Patients were required to have continuous enrollment for ≥ 90 days pre- and ≥ 365 days post-index date. Patients with SLE/LN (including non-renal SLE and LN) and RA were identified using modifications to algorithms developed for use in registry and/or claims data. The general population included individuals without SLE/LN or RA. Index date for the SLE/LN and RA cohorts was the date when patients fulfilled the diagnostic algorithms for SLE/LN, or RA. Index date for the general population occurred after 90 days of continuous enrollment. Patients were excluded from all cohorts if they had: an auto-immune (AI) condition other than SLE/LN or RA; cancer; received a solid-organ transplant; or HIV/AIDs. First incident SIs were identified as those that resulted in an inpatient claim for a pre-specified set of ICD-9 codes within 365 days of index date. Incidence rates (IRs) and standardized incidence ratios (SIRs) were calculated along with 95% confidence intervals (CI) adjusted for age, gender, index year, prevalent SI and glucocorticoid use.

Results: The SLE/LN, RA, and general population cohorts included 58,105, 183,229, and 50,530,269 patients, respectively. Table 1 provides a summary of cohort-specific patient characteristics. As anticipated, the SLE/LN and RA cohorts were predominantly female. The RA cohort was generally older than the other cohorts. Index date was fairly consistent across study year and cohort. In all cohorts, the unadjusted SI IRs increased with age, were higher among patients who had a prior SI (claim ≤ 90 days prior to the index date), and were slightly increased in patients who received systemic glucocorticoids ≤ 365 days after their index date. Adjusted SI IRs (95% CIs) were 21.2 (21.1, 21.2) in SLE/LN patients, followed by 15.8 (15.8, 15.8) in RA patients, and 3.8 (3.7, 3.8) in the general population

Table 1. Description of study population.

	SLE/LN* (n=58,105) n (%)	RA** (n=183,229) n (%)	General Population (n=50,530,269) n (%)
Age (years)			
18-34	11,177 (19.2)	17,298 (9.4)	18,790,240 (37.1)
35-44	14,389 (24.8)	31,873 (17.4)	11,218,925 (22.2)
45-54	18,352 (31.6)	63,702 (34.8)	11,677,603 (23.1)
55-64	14,187 (24.4)	70,356 (38.4)	8,837,501 (17.5)
Gender			
Female	52,316 (90.0)	136,341 (74.4)	26,188,302 (51.8)
Male	5,789 (10.0)	46,888 (25.6)	24,341,967 (48.1)

* SLE/LN = patients with non-renal systemic lupus erythematosus and lupus nephritis

** RA = patients with rheumatoid arthritis

Table 2. Adjusted* incidence rate (IR) and standardized incidence ratios (SIR) (95% confidence interval) for serious infections (SIs) for individuals with systemic lupus erythematosus(SLE) / lupus nephritis (LN), rheumatoid arthritis (RA) and the general population.

	SLE/LN**	RA***	General Population
SI event within 365 days of index	1,435	3,360	189,602
Person-years	57,037.10	180,919.70	50,433,745.24
Direct adjusted rate per 1000 person-year (95% CI)	21.2 (21.1, 21.2)	15.8 (15.8, 15.8)	3.8 (3.7, 3.8)
Adjusted SIR (95% CI)	4.4 (4.2, 4.6)	2.8 (2.7, 2.9)	Ref

* Adjusted for age, gender, index year, prevalent SI and glucocorticoid use within 365 days of index date.
** SLE/LN = patients with non-renal systemic lupus erythematosus and lupus nephritis
*** RA = patients with rheumatoid arthritis

(Table 2). Adjusted SIRs were 4.4 and 2.8 times higher among patients with SLE/LN and RA compared to the general population, respectively.

Conclusion: In this population-based analysis of claims data, adjusted SI IRs were highest in SLE/LN patients. Both AI cohorts experienced excess SI rates compared to the general population. These rates were based on inpatient claims from patients with varying disease severity and treatment patterns. Further characterization of the role of treatment and type of infection is warranted. Findings demonstrate the important contribution of SIs on the burden of disease among SLE/LN and RA patients.

Adjusted incidence rate (IR) and standardized incidence ratios (SIR) (95% confidence interval) for serious infections (SIs) for individuals with systemic lupus erythematosus(SLE)/lupus nephritis (LN), rheumatoid arthritis (RA) and the general population.

Disclosure: L. Lindsay, Genentech, Inc., 3, 4; **C. Chuo**, Genentech, Inc., 3, 4; **N. Jones**, Genentech, 1, 3; **J. Galanter**, Genentech, a member of the Roche Group, 1, 3; **A. McGregor**, Genentech, Inc., 3; **K. Tuckwell**, Genentech, Inc., 3, 4.

Abstract Number: 2117

Impact of Tapering Targeted Therapies (bDMARDs or Jakinibs) on the Risk of Adverse Events of Special Interest in Patients with Rheumatoid Arthritis or Spondyloarthritis: A Systematic Analysis of the Literature and Meta-analysis

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SESSION INFORMATION

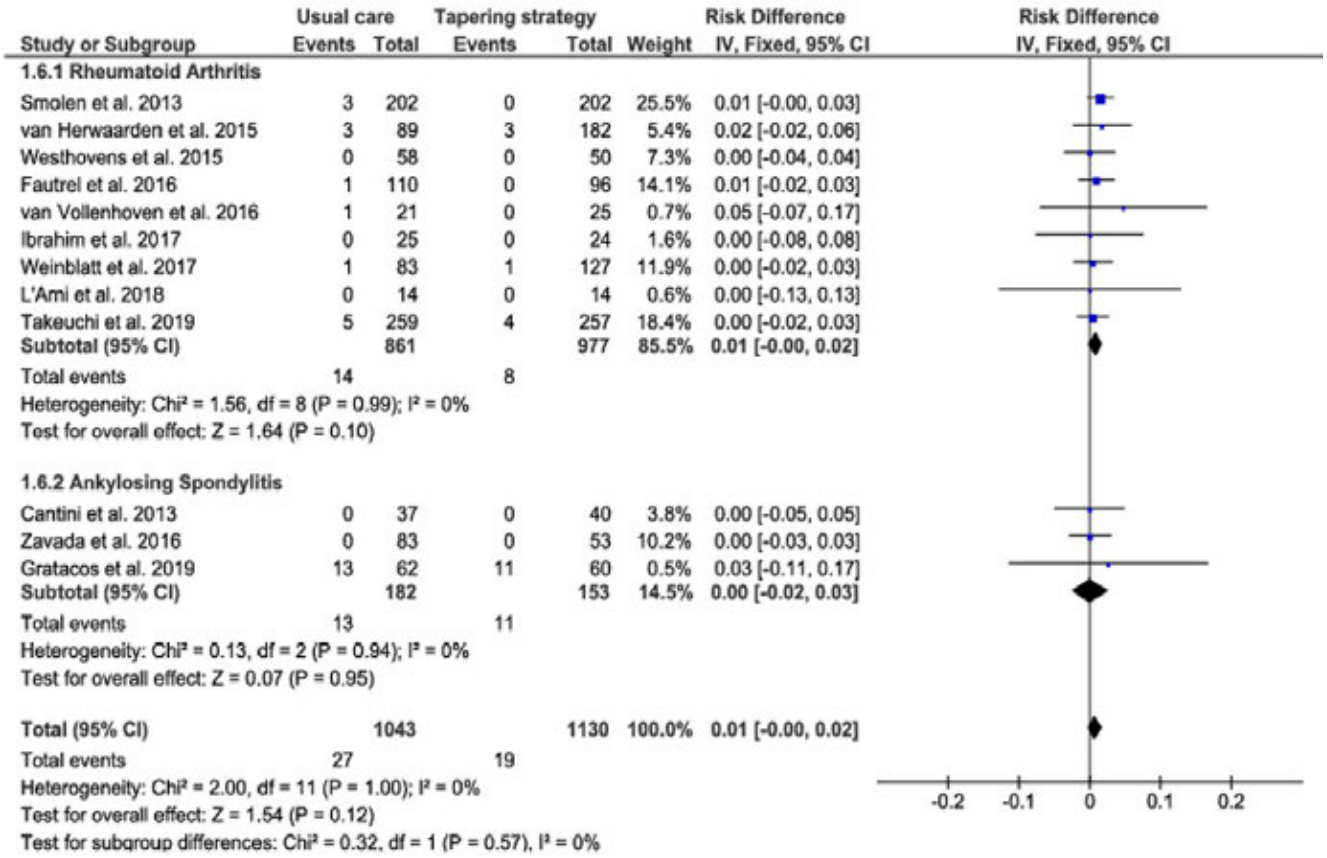
Session Date: Tuesday, November 12, 2019

Session Title: Infection-Related Rheumatic Disease Poster

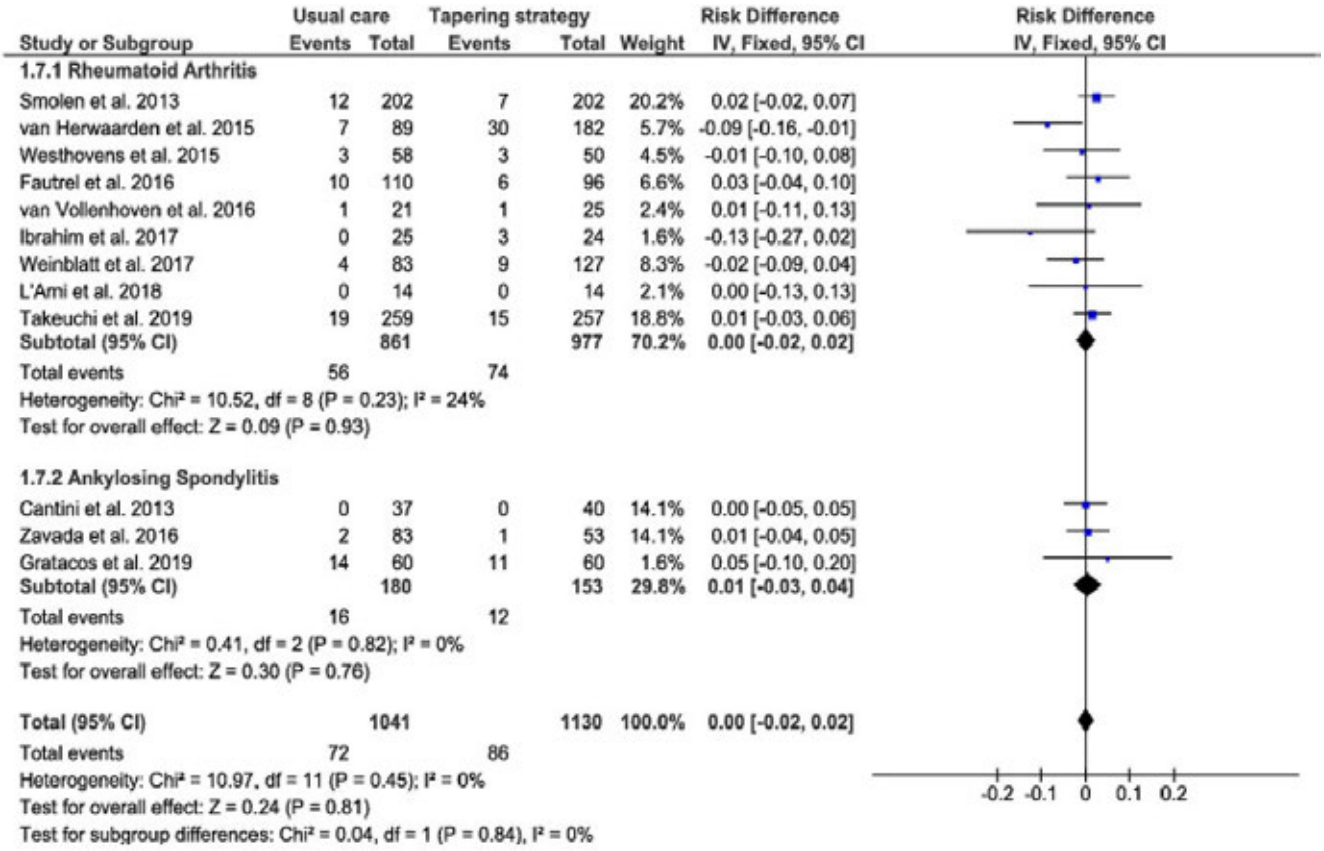
Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: A previous meta-analysis[1] showed that tapering of bDMARDs does not increase the risk of relapse in rheumatoid arthritis (RA) patients with remission or low disease activity (LDA). In the present meta-analysis



Risk difference of serious infections



Risk difference of serious Adverse Event

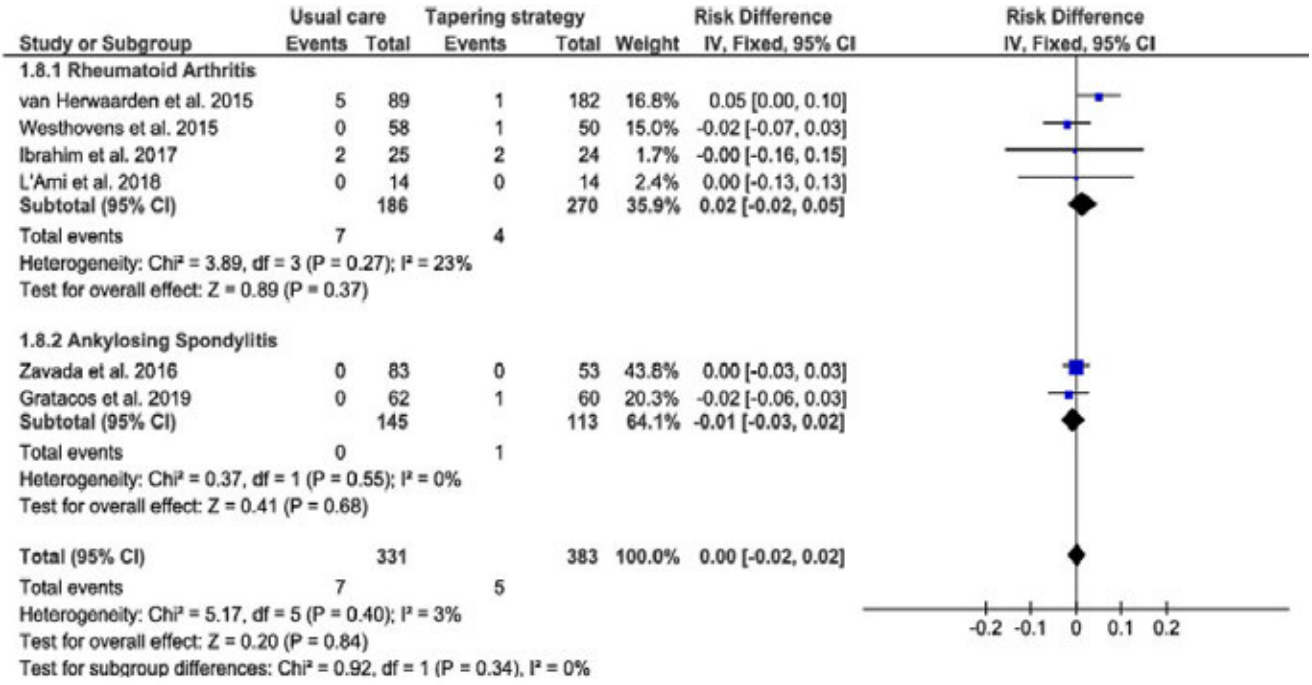
we assessed the impact of tapering targeted therapies (bDMARDs or Jakinibs) on the risk of adverse events (AEs) of special interest in patients with RA or spondyloarthritis (SpA) in remission or (LDA).

Methods: A systematic literature analysis was carried out through May 2019 on PubMed, Embase, Cochrane and international meeting databases, selecting controlled trials comparing tapering (dose reduction or spacing) versus continuation of the initial treatment regimen, in patients with RA or SpA in remission or LDA. The meta-analysis assessed the risk difference and 95% confidence interval (95%CI) of serious infections, serious AEs, malignancy or cardiovascular AEs after tapering versus continuation of bDMARDs or Jakinibs.

Results: 1922 records were screened in our systematic analysis of literature. 1826 records were excluded after title and abstract reading leaving 96 articles eligible. After full text assessment, 84 references were excluded. Twelve references were finally included in our systematic review and meta-analysis among which 9 trials refered to RA and 3 trials to SpA.

There were 1129 patient-year studied in the targeted therapy tapering group (TG) versus 1041 in the usual care group (UC). The study period lasted 6 months in 2 trials, 12 months in 7 trials and around 18 months in 3 trials. Mean years from diagnosis was 8 years and extended from 2.6 years to 16.6 years, the sex ratio was 67% and mean age was 51 years in both groups.

The meta-analysis comparing targeted therapy tapering versus continuation performed on twelve trials showed no decreased risk of serious infections (Risk difference (95% CI) = 0.01 (-0.00 to 0.02), P = 0.12), serious AEs (Risk difference (95% CI) = 0.00 (-0.02 to 0.02), P = 0.81), malignancy (Risk difference (95% CI) = -0.01 (-0.02 to 0.01), P



Risk difference of Cardiovascular Adverse Event

= 0.33) or cardiovascular AEs (Risk difference (95% CI) = 0.00 (-0.02 to 0.02), P = 0.84). There was no difference in subgroup analysis (RA and SpA).

Conclusion: In this meta-analysis focused on controlled trials in RA and SpA patients in remission or LDA, tapering bDMARDs or Jakinibs does not lead to a decreased risk of serious infections, serious AEs, malignancy or cardiovascular AEs in comparison with continuation of the initial treatment regimen.

Reference:

1. Henaux S, et al. Ann Rheum Dis 2018;77:515-22.

Disclosure: D. VINSON, None; **L. MOLLET-BENHAMOU**, None; **Y. Degboe**, Celgene, 2; **T. Pham**, Abbvie, 8, Amgen, 8, Biogen, 8, BMS, 8, Celgene, 8, Fresenius-Kabi, 8, Janssen, 8, Lilly, 8, Medac, 8, MSD, 8, Nordic, 8, Novartis, 8, Pfizer, 8, Roche-Chugai, 8, Sandoz, 8, Sanofi, 8, UCB, 8; **T. BARNETCHE**, Lilly, 5; **A. Constantin**, Novartis, 8, Pfizer, 5, Sanofi, 5, SANOFI, 8, UCB, 5, 8; **A. Ruyssen-Witrand**, None.

Abstract Number: 2118

Efficacy and Safety of Tocilizumab Treatment for Anti–human T Lymphotropic Virus Type I Antibody–positive Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Infection-Related Rheumatic Disease Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The asymptotic individuals with the human T lymphotropic virus type I (HTLV-I) infection rarely develop adult T cell leukemia/lymphoma (ATL) or HTLV-I–associated myelopathy (HAM). In addition, HTLV1 infection is also associated with rheumatic disease such as HTLV-I–associated arthropathy, rheumatoid arthritis (RA), and Sjogren's syndrome. The HTLV-I virus infects not only primarily CD4+ T lymphocytes but also synovial fibroblasts and salivary gland epithelial cells, and the HTLV-I infections modify the functions of these cells and induce various inflammatory conditions. Therefore, it is important clinical issue whether HTLV-I infection changes the pathological condition and the therapeutic response in patients with rheumatic disease.

Our previous study has showed that the efficacy of tumor necrosis factor inhibitor (TNFi) was attenuated in anti–HTLV-I antibody–positive patients with RA. However, no previous reports have examined the comparative efficacy and safety between anti–HTLV-I antibody–negative and –positive RA patients when they are treated with non-TNFi biologics.

We aimed to evaluate the efficacy and safety of tocilizumab (TCZ) in anti–HTLV-I antibody–positive patients with RA compared with those negative patients using a multicenter retrospective cohort.

Methods: The present study reviewed Japanese RA patients who TCZ was newly introduced as a first biologics between April 2008 and September 2018 at 7 participating rheumatology centers in Nagasaki and Miyazaki Prefecture in Japan, which are known as endemic areas of HTLV-I infection. Patients with unclear anti–HTLV-I antibody status and patients with remission at baseline were excluded. Overall, the outcomes of 184 patients treated with TCZ were analyzed. The primary end point was the change in the patients' clinical disease activity index (CDAI) between entry and 6 months after the initiation of TCZ treatment. We also analyzed the occurrence of ATL or HAM during TCZ treatment periods for 6 months.

Table 1. Baseline participant characteristic by positivity or negativity of anti–HTLV-I antibody (univariate analysis)

Variables	All patients (n = 184)	Anti–HTLV-I antibody–negative patients (n = 167)	Anti–HTLV-I antibody–positive patients (n = 17)	p-value
Patient characteristics at baseline				
Age (years)	62.5 (55.0 – 71.0, n = 184)	62.0 (54.0 – 71.0, n = 167)	70.0 (62.5 – 78.0, n = 17)	0.009
Disease duration (month)	68.5 (15.0 – 175.7, n = 184)	68.0 (15.0 – 180.0, n = 167)	72.0 (11.5 – 145.8, n = 17)	0.86
Male gender (%)	45/184 (24.5%)	41/167 (24.6%)	4/17 (23.5%)	1.00
Medication at baseline				
Concomitant prednisolone use (%)	114/184 (62.0%)	105/167 (62.9%)	9/17 (52.9%)	0.44
Doses of concomitant prednisolone (mg/day)	3.0 (0.0 – 5.0, n = 184)	3.0 (0.0 – 5.0, n = 167)	2.5 (0.0 – 6.3, n = 17)	0.67
Concomitant methotrexate use (%)	81/184 (44.0%)	70/167 (41.9%)	11/17 (64.7%)	0.08
Doses of concomitant methotrexate (mg/week)	0.0 (0.0 – 8.0, n = 184)	0.0 (0.0 – 8.0, n = 167)	8.0 (0.0 – 9.0, n = 17)	0.04
Laboratory findings at baseline				
Baseline RF positive (%)	147/184 (79.9%)	133/167 (79.6%)	14/17 (82.4%)	1.00
Baseline ACPA positive (%)	144/176 (81.8%)	29/159 (81.1%)	15/17 (81.2%)	0.74
Clinical disease activity at baseline				
Tender joint count in 28 joints	5.0 (2.0 – 10.0, n = 184)	5.0 (2.0 – 9.0, n = 167)	9.0 (5.0 – 14.0, n = 17)	0.02
Swollen joint count in 28 joints	4.0 (2.0 – 6.0, n = 184)	4.0 (2.0 – 6.0, n = 167)	6.0 (3.5 – 9.5, n = 17)	0.09
ESR (mm/hour)	43.0 (27.0 – 69.0, n = 181)	41.0 (26.3 – 67.8, n = 164)	62.0 (41.5 – 80.5, n = 17)	0.06
CRP (mg/dl)	1.2 (0.4 – 2.9, n = 184)	1.2 (0.3 – 2.9, n = 167)	1.8 (0.56 – 2.65, n = 17)	0.37
Patient's global assessment score (1–100-mm VAS)	50.0 (20.3 – 68.0, n – 184)	50.0 (20.0 – 68.0, n – 167)	50.0 (29.0 – 65.0, n – 17)	0.77

Table 1. Baseline participant characteristic by positivity or negativity of anti–HTLV-I antibody (univariate analysis)

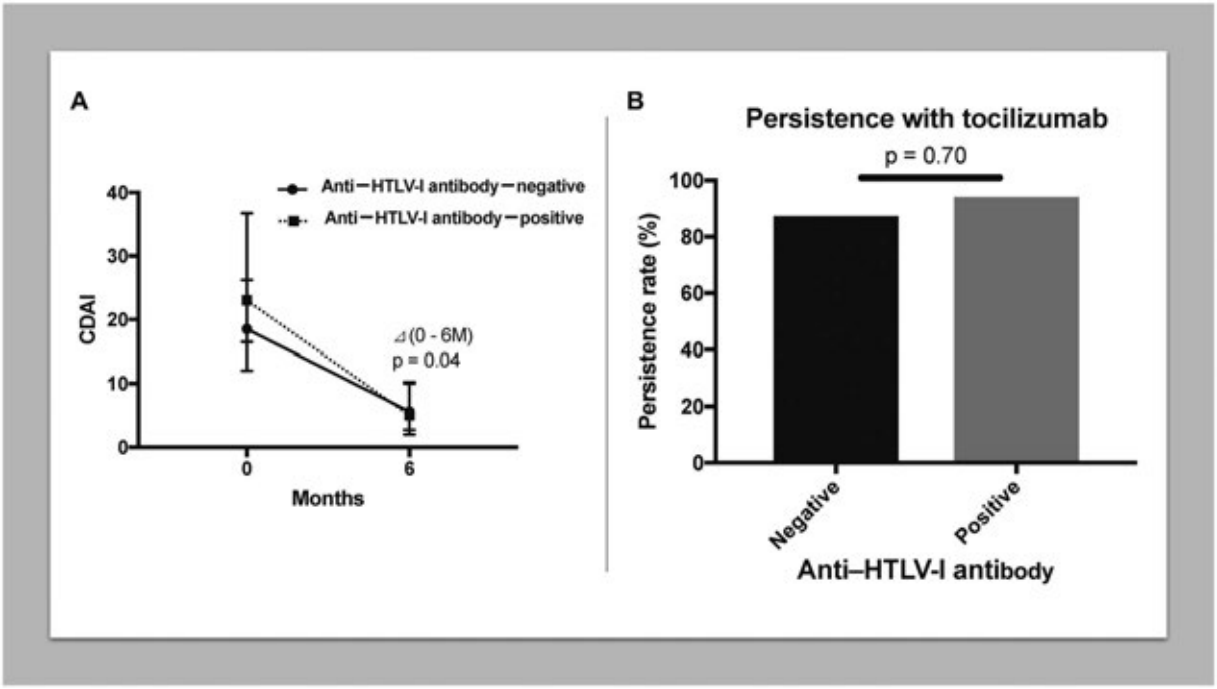

Figure 1. Clinical disease activity index and persistence with tocilizumab at 6 months by positivity or negativity of anti–HTLV-I antibody (univariate analysis)

Results: Enrolled total 184 patients were divided into anti–HTLV-I antibody–negative and –positive groups of 167 (90.8%) and 17 (9.2%). The median age at baseline and doses of concomitant methotrexate were significantly higher in anti–HTLV-I antibody–positive group ($p = 0.009$, $p = 0.04$, respectively). In addition, each indicator of clinical disease activity score at baseline was also significantly higher in anti–HTLV-I antibody–positive group. The CDAI score decreased significantly at 6 months in anti–HTLV-I antibody–positive group compared with anti–HTLV-I antibody–negative group ($p = 0.05$), and persistence with TCZ tended to be higher in anti–HTLV-I antibody–positive group. Multiple regression analysis demonstrated that anti–HTLV-I antibody status tended to be associated with the CDAI score's improvement but was not significant. No patients developed ATL or HAM during TCZ treatment periods for 6 months.

Conclusion: Our results indicate that TCZ treatment tend to confer prefer response in anti–HTLV-I antibody–positive patients with RA, but further investigations are desired.

Disclosure: Y. Endo, None; **K. Umekita**, None; **H. Nakamura**, None; **S. Fukui**, None; **T. Suzuki**, None; **J. Miyamoto**, None; **T. Shimizu**, None; **T. Koga**, None; **S. Kawashiri**, None; **N. Iwamoto**, None; **K. Ichinose**, None; **M. Tamai**, None; **T. Origuchi**, None; **A. Okada**, None; **K. Fujikawa**, None; **A. Mizokami**, None; **N. Matsuoka**, None; **T. Aramaki**, None; **Y. Ueki**, None; **K. Eguchi**, None; **Y. Kariya**, None; **Y. Hashiba**, None; **T. Hidaka**, None; **A. Okayama**, None; **A. Kawakami**, None.

Abstract Number: 2119

Impact of Day of Admission and Time to Diagnostic Arthrocentesis on Mortality and Other Outcomes in Septic Arthritis: A Nationwide Analysis

Gustavo Contreras,[1] Ana B Arevalo,[1] Shane Murray,[1] Faris Haddadin,[1] and Yiming Luo[1], [1]Mount Sinai St. Luke's - West/ Icahn School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Multiple studies have been done assessing the "weekend effect" and outcomes for hospitalized patients [1,2,3,4], however, there is no data evaluating the outcome of patients with septic arthritis of a native joint (SANJ) who are admitted on the weekend compared to the rest of the week. We evaluated whether important outcomes in SANJ, including in-hospital mortality, differ between patients admitted on weekends versus weekdays and the time to diagnostic arthrocentesis.

Methods: The National Inpatient Sample (NIS) database of the year 2016 was utilized for patients admitted to the hospital with a principal discharge diagnosis of SANJ. This was a retrospective cohort study of patients hospitalized in 2016 with SANJ in hospitals across the US. Patients were included if they were adults with a principal diagnosis of SANJ based on ICD-10 codes. Admissions between midnight Friday and midnight Sunday were classified as weekend admissions. Early arthrocentesis was defined as percutaneous arthrocentesis performed within 24 hours of admission. The proportion of patients with SANJ admitted over weekends versus weekdays was determined. Odds ratios (OR) were calculated for primary and secondary outcomes including in-hospital mortality rate, rates of diagnostic arthrocentesis and early arthrocentesis, length of stay and total hospital charges, These

results were compared after multivariable logistic regression adjusted for age, gender, race, day of admission, Charlson comorbidity index and median household yearly income in the patient's zip code. We used STATA-15 for statistical analysis.

Results: The study included 12819 patients with SANJ. Compared with patients admitted on weekdays, patients with SANJ admitted on weekends had increased in-hospital mortality rates (adjusted odds ratio[aOR] 3.67; 95% [CI] 1.52 – 8.86, p< .005), but similar early arthrocentesis rates ([aOR] 1.14; 95%, [CI] 0.90 – 1.45 p >0.05), length of stay (p >0.05) and hospital charges ($ 2751.11; 95% [CI] -4449.6 – 9951.8; P >0.05). However, regardless of the day of admission those who received an early arthrocentesis had lower length of stay (-1.46, p< 0.05), and lower total hospital charges ($ -6527 $; p< 0.05).

In-hospital mortality rates based on day of admission					
	Total	Weekend	Weekday	*Weekend as independent predictor of mortality	P value
SANJ	105/12819	46/105 (43.8%)	59/105 (56.2%)	(aOR 3.67; 95% CI 1.52 – 8.86)	P <0.005
*Adjusted for age, gender, race, day of admission, Charlson comorbidity index, median household yearly income in the patient's zip code; aOR= Adjusted odds ratio.					

Table 1

Adjusted* total hospital charges based on day of admission and time to arthrocentesis					
	Mean total hospital charges	Adjusted difference for arthrocentesis within 24 h	P value	Adjusted difference for arthrocentesis > 24 h	P value
SANJ	$ 64699.27; 95% CI (61321.48 – 68077.06)	$ -6527; 95 % CI (-13090.00 – -165.00)	P <0.05	$ 2751.08; 95% CI (-4449.6 – 9951.8)	P >0.5
*Adjusted for age, gender, race, day of admission, Charlson comorbidity index, median household yearly income in the patient's zip code					

Table 2

Adjusted* median length of stay (days)				
	Arthrocentesis within 24 h of admission	Arthrocentesis > 24 h after admission	P Value	Difference in length of stay (P value)
SANJ	7.11 (6.61 – 7.61)	8.61 (7.51 – 9.71)	<0.05	-1.46 (< 0.05)
*Adjusted for age, gender, race, day of admission, Charlson comorbidity index, median household yearly income in the patient's zip code				

Table 3

Conclusion: This study showed that compared with patients admitted on weekdays, patients with SANJ admitted on weekends had increased mortality rates but similar length of stays and total hospital charges. However, patients who received an early arthrocentesis had significantly lower length of stay and hospital charges regardless of the day of admission. This results add weight to the hypothesis of negative outcomes in weekend admissions. Moreover, we believe that our findings require further investigation to establish the role of early arthrocentesis in the management of septic arthritis.

Disclosure: G. Contreras, None; **A. Arevalo**, None; **S. Murray**, None; **F. Haddadin**, None; **Y. Luo**, None.

Abstract Number: 2120

No Evidence of an Increased Risk of Serious Infections Among 3 Classes of Biologics for Psoriasis or Psoriatic Arthritis: A Retrospective Real-World Cohort Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The real-world risk of serious infections associated with interleukin (IL) and tumor necrosis factor-alpha (TNF-α) inhibitors for patients with psoriasis (PsO) and psoriatic arthritis (PsA) is unclear. The objective of this study was to examine whether initiation of IL-17, IL-12/23, or TNF-α, was associated with increased risk of serious infection among PsO and PsA patients.

Methods: We built a cohort of commercially insured adults diagnosed with PsO or PsA between 2015–2018 using data from the OptumLabs® Data Warehouse. Exposure was new use of IL-17 (ixekizumab or secukinumab), IL-12/23 (ustekinumab), or TNF-α (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab). The main outcome was hospitalized infection after date of biologic initiation. Incidence rates (IR) per 100 person-years were computed, and hazard ratios (HR) with 95% confidence intervals (CI) were estimated using Cox proportional hazards regression models, adjusted for inverse probability of treatment weighted propensity scores to control for confounding. In sensitivity analyses, we varied the permissible gap between prescriptions, and to restrict to infection listed as the first diagnosis code position.

Results: A total of 11,560 new treatment episodes were included (19% IL-17, 25% IL-12/23, 56% TNF-α inhibitors). Overall, 190 serious infections (2% of treatment episodes) were identified in 9,264 person-years of follow-up (Table). Class-specific IR were similar among IL-17 and TNF- α, and significantly lower for IL-12/23. After adjustment for propensity scores, there was no evidence of an increased risk of serious infections with IL-17, as compared to either TNF-α (HR=0.89, 95% CI 0.48-1.66) or IL-12/23 (HR=1.12, 95% CI 0.62-2.03). By contrast, IL-23/23 were associated with a lower risk of infections than TNF-α (HR=0.59, 95% CI 0.39-0.90). In the subgroup of patients with PsA, we observed a similar risk of serious infections between the three biologics exposure groups. Indeed, compared to the PsA cohort, the PsO cohort patients were younger, more likely to be male, had fewer comorbidities, fewer physician

Table. Incidence of serious infections among biologic users with psoriasis or psoriatic arthritis, overall and by drug class.

	All biologic classes	IL-17	IL-12/23	TNF- α
Total cohort				
Number of treatment episodes	11,560	2,148	2,882	6,530
Total person-years of follow-up	9,264	1,528	2,461	5,275
Incident serious infections, n (%)	190 (2%)	32 (1%)	32 (1%)	126 (2%)
Incidence rate (95% confidence interval), per 100 person-years	2.1 (1.8-2.4)	2.1 (1.5-2.9)	1.3 (0.9-1.8)	2.4 (2.0-2.8)
Psoriasis				
Number of treatment episodes	9,691	1,903	2,644	5,144
Total person-years of follow-up	8,010	1,406	2,311	4,293
Incident serious infections, n (%)	156 (2%)	26 (1%)	29 (1%)	101 (2%)
Incidence rate (95% confidence interval), per 100 person-years	2.0 (1.7-2.3)	1.9 (1.2-2.7)	1.3 (0.9-1.8)	2.4 (1.9-2.8)
Psoriatic arthritis				
Number of treatment episodes	5,517	944	888	3,685
Total person-years of follow-up	4,159	605	647	2,907
Incident serious infections, n (%)	105 (2%)	14 (1%)	13 (1%)	78 (2%)
Incidence rate (95% confidence interval), per 100 person-years	2.5 (2.1-3.1)	2.3 (1.3-3.7)	2.0 (1.1-3.3)	2.7 (2.1-3.3)
Biologic-naive				
Number of treatment episodes	5,995	332	1,344	4,319
Total person-years of follow-up	5,019	237	1,217	3,565
Incident serious infections, n (%)	*	*	11 (1%)	80 (2%)
Incidence rate (95% confidence interval), per 100 person-years	2.0 (1.6-2.4)	3.4 (1.6-6.3)	0.9 (0.5-1.6)	2.2 (1.8-2.8)
Biologic experienced				
Number of treatment episodes	5,565	1,816	1,538	2,211
Total person-years of follow-up	4,246	1,292	1,244	1,710
Incident serious infections, n (%)	91 (2%)	24 (1%)	21 (1%)	46 (2%)
Incidence rate (95% confidence interval), per 100 person-years	2.1 (1.7-2.6)	1.9 (1.2-2.7)	1.7 (1.1-2.5)	2.7 (2.0-3.5)

*As per OptumLabs data confidentiality policies, cells with 10 or fewer events are not reported.

office visits, lower proportions of DMARD use, and less glucocorticoid exposure during baseline. Nevertheless, we note that the effect estimate even in the PsA patients for IL-12/23 exposure was numerically lower (0.74 , 95% CI 0.40 - 1.36) and compatible with the significantly protective association observed in the psoriasis patients (0.59, 95% CI 0.38 - 0.92).

Conclusion: We did not find empirical evidence of an increased risk of serious infection with the IL-17 inhibitors, and observed a significantly lower infection risk with IL-12/23 biologics, compared to TNF- α therapy. Given the relatively small magnitude of absolute effect (difference less than 1 per 100 person-years) yet strong relative risk reduction compared to TNF-a, these results may inform clinical decision-making regarding the safety of the available choices.

Disclosure: X. Li, None; **K. Andersen**, National Heart, Lung and Blood Institute (NHLBI) Pharmacoepidemiology T32 Training Program (T32HL139426-01)., 2, National Heart, Lung and Blood Institute Pharmacoepidemiology T32 Training Program (T32HL139426-01)., 2; **H. Chang**, None; **G. Alexander**, Chair of FDA's Peripheral and Central Nervous System Advisory Committee, 9, Monument Analytics, a health care consultancy whose clients include the life sciences industry as well as plaintiffs in opioid litigation, 4, 5, OptumRx's National P&T Committee, 6, Serves as a

paid advisor to IQVIA, 5, This arrangement has been reviewed and approved by Johns Hopkins University in accordance with its conflict of interest policies.; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5.

Abstract Number: 2121

Hospitalization Trends for Bacterial Septic Arthritis in the United States from 1997 to 2014

Soumyasri Kambhatla,[1] Estefania Gauto-Mariotti,[2] and Augustine Manadan[3], [1]John H. Stroger Hospital of Cook County, Chicago, [2]Cook County Health, chicago, [3]Rush University Medical Center, chicago

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Bacterial septic arthritis is a serious cause of morbidity and mortality, constituting one of the true musculoskeletal emergencies. In this abstract, we describe hospitalization trends for patients with bacterial septic arthritis in the USA over multiple years.

Table: Septic Arthritis Trends

Year	Total number of discharges: N	Rate of discharges per 100,000 persons	Age (mean)	LOS (length of stay), days (mean)	Charges, $ (mean)	In-hospital deaths: N	In-hospital deaths: %
2014	25,065	7.9	53.2	6.5	52,878	115	0.46
2012	24,875	7.9	53.13	6.5	49,899	125	0.5
2005	24,852	8.4	48.21	7.2	29,840	217	0.87
2013	24,200	7.7	52.94	6.6	52,341	120	0.5
2010	23,755	7.7	51.19	7.1	45,851	108	0.46
2011	23,716	7.6	53.4	7.1	51,019	160	0.67
2006	23,640	7.9	50.71	7.2	33,178	183	0.78
2008	23,443	7.7	52.74	7.1	39,332	157	0.67
2009	22,802	7.4	52.46	6.7	40,535	175	0.77
2007	22,726	7.5	51.47	7.2	35,901	198	0.87
2003	22,460	7.7	50.12	7.3	27,849	239	1.06
2004	22,371	7.6	50.6	7.4	28,642	242	1.08
2002	21,091	7.3	50.65	7.7	25,814	259	1.23
2001	20,596	7.2	50.73	7.9	22,391	321	1.56
2000	19,364	6.9	49.67	7.7	20,543	238	1.23
1999	18,626	6.7	48.09	7.3	17,168	196	1.05
1998	18,345	6.7	47.45	7.1	15,323	208	1.13
1997	17,300	6.3	47.38	7.5	15,381	184	1.07

Methods: Data were abstracted from the National Inpatient Sample Databases. This database is the largest longitudinal collection of inpatient admission data in the USA. It is a nationally representative sample of 20% of admissions from approximately 1000 hospitals pertaining to approximately 7 million inpatient hospital admissions. The numbers in the databases are weighted to optimize both national estimates and longitudinal analysis. The databases were searched for patients admitted from 1997 to 2014 with an ICD-9 septic arthritis codes 711.0 -711.09 listed as the principal diagnosis. Codes for fungal, mycobacterial and viral arthritis were not included. The total number of septic arthritis discharges, number of in-hospital deaths, percentage of in-hospital deaths, rates of discharges, length of stay (LOS), hospital charges and ages were recorded.

Results: An average of 22,179 hospital discharges per year (range 17,300-25,065) had an ICD-9 bacterial septic arthritis code listed as the principal diagnosis from 1997 to 2014. The average rate of discharges was 7.45/100,000 persons (range 6.3-8.4). The average age was 50.8 years. The average hospital charges was $33,549 (range 15,323-52,878). The average LOS was 7.2 days (range 6.5-7.9). The in-hospital deaths averaged 0.87% of those admissions. The annual trend for in-hospital deaths for septic arthritis seemed to both improve and parallel the overall improvement for deaths for all hospital discharges during same time period. This type of analysis is greatly limited by inability to determine actual cause of death.

Conclusion: This data gives us valuable information on the magnitude, cost, and temporal trends of septic arthritis hospitalizations in the USA. Our analysis shows septic arthritis resulted in an average of 22,179 hospital admissions per year. The rate of discharges per 100,000 was very low and stable from 1997 to 2014. Septic arthritis admissions averaged a LOS of 1 week and had an average hospital charge of $33,549. For a condition thought of as a rheumatologic emergency, it had a surprisingly low in-hospital mortality and has been trending in a favorable direction.

Disclosure: S. Kambhatla, None; **E. Gauto-Mariotti**, None; **A. MANADAN**, None.

Abstract Number: 2122

Outcomes and Risk Factors in Septic Arthritis with Underlying Rheumatic Conditions

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
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Background/Purpose: Septic arthritis is known to cause significant morbidity due to joint destruction and mortality if timely and adequate treatment is not given. In this study, we aim to describe outcomes of septic arthritis, focusing on comparison between the patients with and without underlying rheumatic disease.

Methods: Using the National Inpatient Sample database from 2016, we identified patients admitted with a principal diagnosis of septic arthritis based on ICD10 codes. Separate cohort was created for patients with secondary diagnoses of various rheumatic conditions including rheumatoid arthritis, psoriatic arthritis, osteoarthritis, osteonecrosis, lupus, ankylosing spondylitis, gout, polyarteritis nodosa, dermatopolymyositis, scleroderma, and

Descriptive data of septic arthritis patients with and without rheumatologic disease

Variable	Patients with septic arthritis and underlying Rheumatologic process	95% Confidence interval/ p-value	Patients with septic arthritis without rheumatologic disease	95% Confidence Interval/p-value
Mean age(years)	62.6	61.1-64.2	56.6	55.7-57.4
Proportion of females	40.9%	35.8%-46.1%	38.6%	36.4%-40.9%
Mean Length of stay(days)	5.30	4.9-5.6	5.74	5.4-6.02
Mean total hospitalization charge ($)	48,075	P<0.05	53,683	P<0.05
Mortality	0%	P<0.05	0.004%	P<0.05

Descriptive data for septic arthritis

Multivariable regression model to build adjusted risk factors

Risk factors for development of septic arthritis	Odd's ratio	P-value
Age- with increase in 1 year	1.028	<0.001
Race (compared to Caucasian)		
African American	1.004	0.94
Hispanic	1.11	0.16
Asian/ Pacific Islander	0.68	0.02
Native American	1.72	0.03
Obesity	1.24	0.006
Female sex	0.49	<0.001
Rheumatoid arthritis	3.77	<0.001
Psoriatic arthritis	3.13	<0.001
Osteonecrosis	7.74	<0.001
Osteoarthritis	2.41	0.002
SLE	1.93	0.006
Ankylosing Spondylitis	0.85	0.016
Diabetes without complications	1.12	0.058
History of arthroplasty	2.13	<0.001
PMR	0.80	0.634

Multivariable regression model

vasculitis. We identified risk factors for development of septic arthritis and compared the outcomes of patients admitted for septic arthritis with and without underlying rheumatic disease. STATA software was used to analyze the data.

Results: Study included 10,808 patients admitted in the year 2016 with septic arthritis, of which 1759 patients had underlying rheumatic disease and 9049 patients did not. For patients who did not have underlying rheumatic disease the mean age was 56.6 years, mean length of stay (LOS) was 5.74 days, and mean charges for hospitalization was $53,683. In comparison, for patients with underlying rheumatic disease, the mean age of patients was 62.6 years, mean LOS was 5.3 days and mean charges of $48,075. Both groups had higher proportion of Caucasians compared to other races (68.3% in those with rheumatic disease vs 69.1% in those without, both $p< 0.05$). There were no deaths in septic arthritis group with rheumatic disease whereas mortality rate was 0.004% in septic arthritis without rheumatic diseases. The following factors increased the risk of overall septic arthritis with the multivariable regression model: Obesity (OR=1.2), Rheumatoid arthritis (OR=3.7), Psoriatic arthritis (OR=3.13), Osteonecrosis (OR=7.7), Osteoarthritis (OR=2.4), SLE (OR=1.9), Arthroplasty (OR=2.13) with P values < 0.05. Female sex, Asian race and ankylosing spondylitis seemed to lower the risk (OR=0.49, 0.68 and 0.8 respectively) with P values < 0.05. Gout, PAN, Dermatopolymyositis, CKD and smoking were removed in the final analysis as they were found to be collinear variables.

Conclusion: In patients with septic arthritis, those with underlying rheumatic conditions seemed to be older with slightly higher proportion of females compared to those without. People with underlying rheumatic disease are more likely to develop septic arthrits but when they do, they seemed to have lower mortality, LOS and hospitalization charge compared to those without a rheumatic disease. This is likely because of better interdisciplinary care. Further studies are needed to establish various factors resulting in this outcome.

Disclosure: S. Kambhatla, None; **E. Gauto-Mariotti**, None; **A. Manadan**, RUSH University Medical Center, 3.

Abstract Number: 2123

Clinical Features of Prosthetic Joint Infections in Patients with Rheumatic Diseases vs Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatic disease (RD) patients are at increased risk for prosthetic joint infections (PJI), however, diagnosis is challenging because active RD may mimic joint infection and definitive microbiologic diagnosis may be delayed. We aimed to identify the clinical and microbiological features of total hip (THA) and total knee arthroplasty (TKA) PJI in RD and OA patients, using an institutional PJI registry and compare the incidence of culture negative (CN) PJI in RD vs OA. Baseline clinical differences between CN-RD and culture positive (CP)-RD and OA PJI as well as the relationship of infection free survivorship of the prosthesis were also evaluated.

Methods: A retrospective cohort of THA/TKA PJIs, from 2009 to 2016, were identified by ICD codes, and confirmed by chart review. RD cases were also confirmed by use of RD-specific medications. CN cases were defined as PJIs with no evidence of microbial growth in intraoperative cultures and CP PJI cases were defined by positive microbial growth in intraoperative cultures. Treatment failure was defined as subsequent surgical treatment for infection after the index procedure- debridement, antibiotics and implant retention (DAIR), one stage or two stage exchange. Demographics, medications, microbiology, surgical therapy and outcome were abstracted. Baseline characteristics were evaluated using Fisher's exact and Chi-Square tests.Kaplan-Meier estimates were used to calculate infection free survivorship.

Results: 807 PJI cases were identified including 36 RD (33 RAand 3 SLE) and 771 OA. A higher proportion of RD PJI were CN (N=10, 27%) vs. OA PJI (N=109, 14%, p=0.02). Fewer CN-RD cases met PJI histopathology criteria compared to CN-OA, (p=0.08). On average, RD-CN were younger than OA-CN (59 vs 69, p=.01), but no different than RD-CP cases. One year survivorship of CN-OA and CN-RD were 87% and 66%, respectively and 47% for CP-RD. Comparing CN-RD vs. CP-RD, no difference was observed in age, smoking, diabetes, or Charlson comorbidities, but a trend towards higher prevalence of prior PJI in the CN-RD group. No differences were found in surgical treatment (p=0.92) or use of biologics and DMARDs (p=0.12) between CN and CP RD patients. Among CP cases, there was no difference in diabetes, comorbidities, smoking, or history of PJI, but more RD were female (p=.0003) and used glucocorticoids (p=.0001). Across all CP cases, 57.4% were Staphylococcal, with no differences between groups.

	CN-RD (N=10)	CP-RD (N=26)	CN-RD vs CP-RD p-value	CP-OA	CP-RD vs CP-OA p-value
Age	59.04 (10.21)	58.35 (12.02)	0.986	66.33 (12.16)	.0003
Body mass index	25.88 (9.81)	27.16 (12.23)	0.697	28.31 (9.73)	.904
Sex			.842		.0003
Female	8 (80)	20 (76.92)		275 (41.54)	
Male	2 (20)	6 (23.08)		387 (54.46)	
Joint			0.285		.509
Knee	6 (60)	10 (38.46)		298 (45.02)	
Hip	4 (40)	16 (61.54)		364 (54.98)	
History of Smoking	1 (10)	3 (11.54)	1.000	78 (11.78)	1.000
Diabetes	0 (0)	5 (19.23)	0.293	137 (20.73)	.8535
History of prior PJI	2 (20)	0 (0)	0.071	49 (7.4)	.247
Glucocorticoids	2 (20)	8 (30.77)	.518	31 (4.68)	.0001
DMARD			.397		
Biologic	5 (50)	9 (34.62)		NA	
Synthetic only	5 (50)	17 (65.38)		NA	
Surgical Therapy			0.791		.760
One Stage Exchange	0 (0)	1 (3.85)		30 (4.53)	
Two Stage Exchange	7 (70)	17 (65.38)		360 (54.38)	
DAIR	3 (30)	8 (30.77)		262 (39.58)	

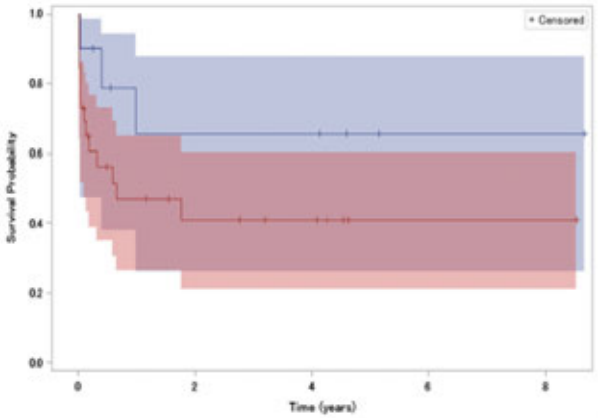
RD- rheumatic disease; CP- culture positive; CN-culture negative; DAIR- debridement, antibiotics and implant retention; PJI -prosthetic joint infection; DMARD – disease-modifying anti-rheumatic drugs

Table 1. Baseline Characteristics

Overall surgical treatment included 2-stage exchange (54.8%), DAIR (39.24%) and 1-stage exchange (4.51%), with no differencebetween groups (p=0.76). Treatment failure was more frequent for CP-RD (30.4% vs 42.3%), but the difference was not significant (p=0.19).

Conclusion: RD PJIs are more likely to be culture negative than OA PJIs, but small numbers limit our analysis. Prior PJI, histopathology and better outcomes suggest biologic differences between CN and CP PJI that should be explored further.

Figure 1 The Kaplan-Meier curve representing implant survivorship after prosthetic joint infection treatment for rheumatic disease(RD) was 66% at 1 year for culture negative (red) and 47% for culture positive (blue), p=0.163.



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Abstract Number: 2124

Screening and Follow-up of Patients with Rheumatic Diseases and Rheumatological Treatments Infected with Trypanosoma Cruzi (American Trypanosomiasis or Chagas' Disease). Is It Possible a Reactivation?

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Infection-Related Rheumatic Disease Poster

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Background/Purpose: American Trypanosomiasis or Chagas Disease (CD) is a zoonotic infection, endemic in Latin America. It is a major cause of morbidity, mortality and economic burden in developing countries. Because of population movements, it has spread out around the globe. CD behavior has been well-described in patients with HIV infection, oncologic and organ transplant-related immunosuppression, but little is known in rheumatic diseases (RD) with rheumatologic treatments (RT).

The purpose of this research is to screen and follow up (clinical and serologically) patients with RD under RT, with concomitant CD. To detect clinical and serological reactivation.

Methods: Prospective, observational study. A systematic screening for CD in the Rheumatology and Internal Medicine Departments was conducted for eighteen months in a third-level Hospital in Argentina. Patients with CD and concomitant RD under RT were included for follow up. Assessments were done before and after RT and if it was already established, subsequently. Clinical features were examined by anamnesis, physical examination, Electrocardiogram, Echocardiogram and Chest X-ray. In order to detect parasitemia, two methods were performed: Strout and Polymerase chain reaction (PCR). Levels of antibodies were evaluated by three techniques: enzyme-linked immunosorbent assay (ELISA), indirect hemagglutination assay (IHA) and indirect immunofluorescence assay (IFA). Every patient received, at least, two assessments. A descriptive analysis was performed.

Results: From the population screened, 46 patients with RD under RT, infected with Trypanosoma Cruzi were detected by two of three techniques (ELISA, IHA, IFA).

Table 1:

Demographics	N=46 (%)	N=46 (%)
Sex	Females	41 (89,13%)
	Males	5 (10,87%)
Mean Age (standard deviation)	51 years (SD:10)	
Birthplace	Argentina	42 (91,30%)
	Other countries	4 (8,70%)
Rheumatic Diseases	Rheumatoid Arthritis	26 (56,52%)
	Systemic lupus erythematosus:	4 (8,70%)
	Systemic Sclerosis	5 (10,87%)
	Vasculitis	2 (4,35%)
	Psoriatic Arthritis:	2 (4,35%)
	Uveitic	1 (2,17%)
	Other rheumatic diseases (Sjogren, Osteoarthritis, Mixed Connective Tissue Disease, Overlap Syndrome):	6 (13,14%)
Treatment (n and % do not reach 100%)	Classic DMARD	40 (68,98%)
	Biologic DMARD	4 (8,70%)
	Synthetic DMARD	2 (4,35%)
	Azathioprine	3 (6,52%)
	Cyclophosphamide	2 (4,35%)
	Steroids < 20 mg/day (prednisone equivalent)	22 (47,83%)
	Steroids > 20 mg/day (prednisone equivalent)	2 (4,35%)

Disease modifying antirheumatic drugs (DMARD). Classic: Methotrexate, Leflunomide, Hydroxychloroquine. Biologic: Adalimumab, Certolizumab, Abatacept. Synthetic: Tofacitinib.

Table 2:

Clinical aspects		First evaluation (n=46)	Follow up (n=46)
With Demonstrable Disease	Chagas Cardiomyopathy	5 (10,87%)	5 (10,87%)
	Gastrointestinal Disease	0 (0%)	0 (0%)
	Neurologic Disease	0 (0%)	0 (0%)
Without Demonstrable Disease		41 (89,13%)	41 (89,13%)
Serological aspects			
Strout and PCR	Positive	2 (4,35%)	0* (0%)
	Negative	44 (95,65%)	46* (100%)

* After Trypanosoma Cruzi Treatment

Table 1: Population characteristics, Rheumatic Diseases and Treatments.
Table 2: Clinical and Serological Follow up.

In search of reactivation, two patients with parasitemia (both Strout and PCR positive) and concomitant signs and symptoms were detected. They had chagasic cardiomyopathy. A 64-years old lady with Microscopic Polyangiitis, under prednisone 60 mg/day and a 57-years old lady with Systemic Lupus Erythematosus under prednisone 40 mg/day and hydroxychloroquine. They developed high fever, myalgias, arthralgias and asthenia. Other infections were ruled out. They received Benznidazole and Nifurtimox respectively. After one-week treatment, Strout and PCR became negative, with clinical improvement.

Conclusion: Of the 46 patients detected in the screening, 2 (4,35%) had parasitemia and clinical features suggestive of reactivation, in context of high doses of steroids. As they were sisters, a genetic relationship may be present. In the rest of the patients, no clinical or serological variation in the follow up was recognized, considering all treatments. As reactivation is possible, parasite´s screening before and during rheumatologic immunosuppression should be performed routinely in endemic countries and suspected in non-endemic countries with epidemiological nexus. CD specific antibodies determination, Strout and PCR are economic and practical techniques. The benefits of this measures would outweigh morbidity and mortality costs. Further studies are required to broaden our knowledge and make recommendations.

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Abstract Number: 2125

Rheumatic Fever in a Tertiary Medical Center - 25 Years of Follow Up

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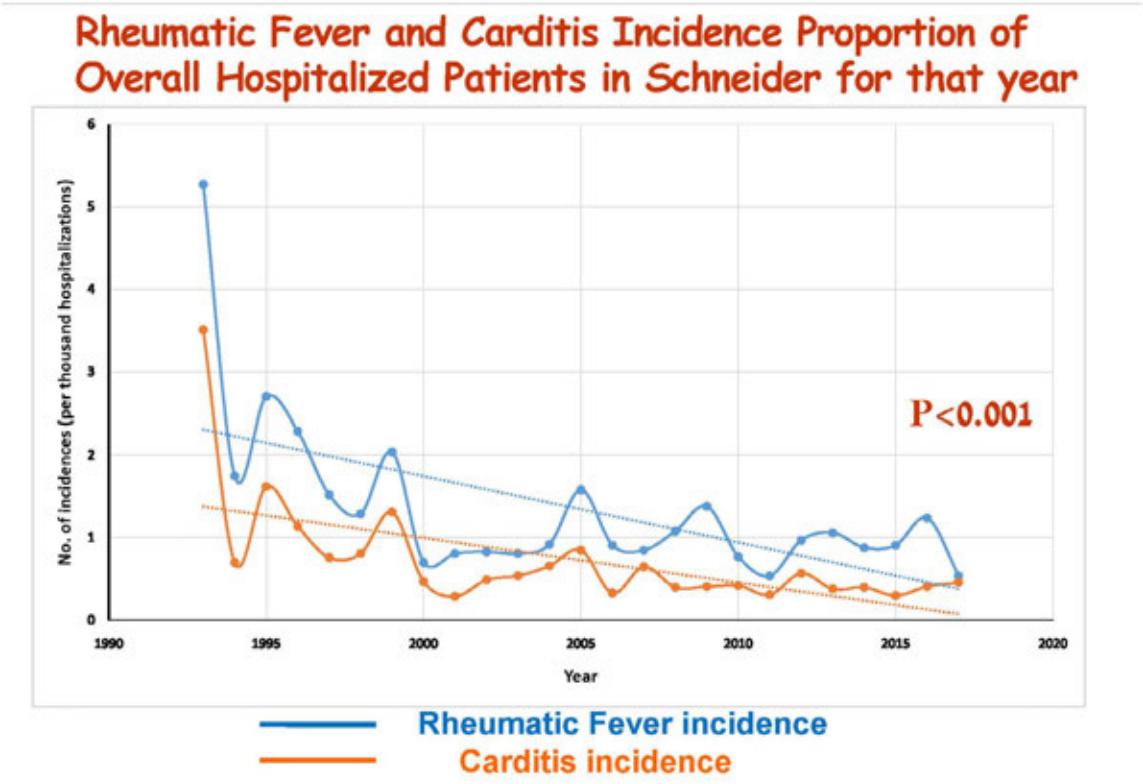
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

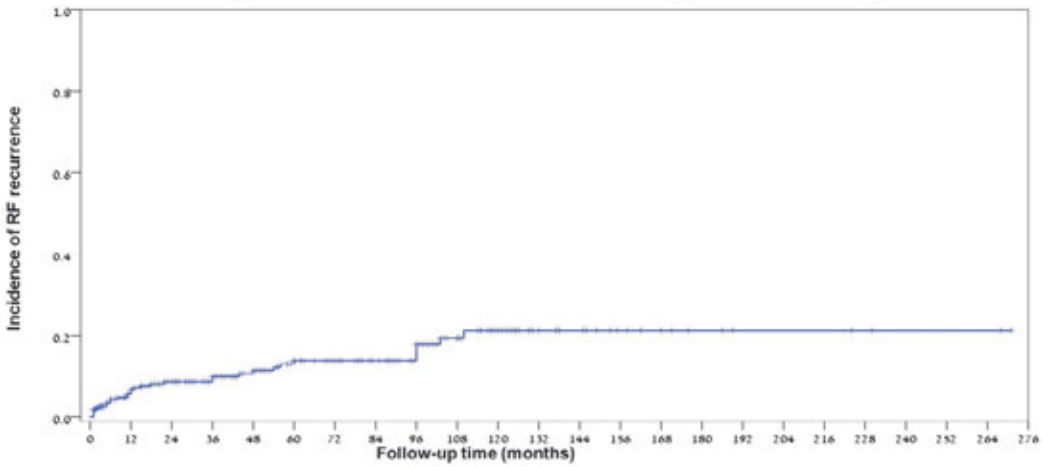
Background/Purpose: Rheumatic Fever (RF) occurs after a pharyngeal infection caused by group A-B-hemolytic streptococci.Its principal clinical significance is causing carditis at the acute phase of the disease, and valvular impairment, leading to a significant hemodynamic disturbance, as a late sequela.

Aim: To examine the number of cases of Rheumatic fever in Schneider Children's medical center, and to find whether it has declined during the years of its existence. In addition, to characterize the patient population, clinical characteristics, risk factors and asses the course of the disease. In addition, we will address the relapse rates, with an emphasis on cardiac relapses, with a correlation to preventive treatment.



Rheumatic Fever - Overall Recurrence Rate

•12% developed disease recurrence (32 of 268)

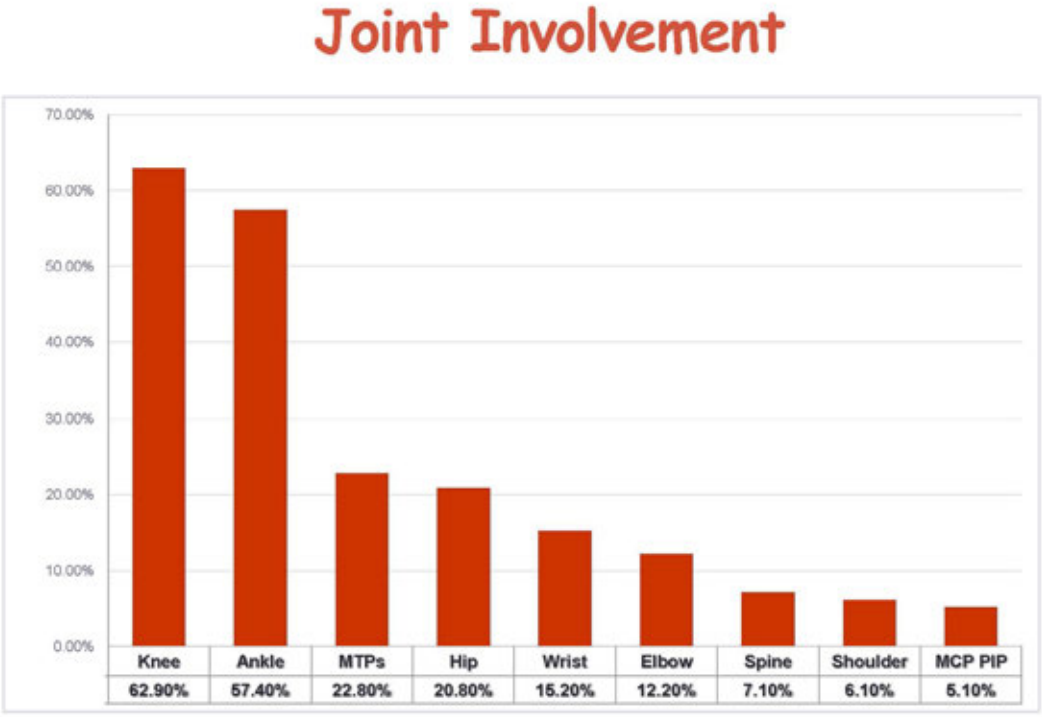


•15% of the children receiving oral prophylaxis developed recurrences, compared with 9% receiving IM injections [HR (IM) = 0.5 , 95% CI 0.25-1.06, P=0.076]

Methods: Retrospective cohort study was conducted, collecting data of patients with rheumatic fever who were admitted to the Schneider Medical Center from 1993 to 2017.

Results: 307 patients met the inclusion criteria. During the acute phase,64% presented with arthritis, 52% carditis, 15% chorea, 5% erythema marginatum, and 0.7% with subcutaneous nodules. 19.5% developed severe carditis, 13% of whom developed heart failure signs. There was a decrease in incidence of rheumatic fever and rheumatic heart disease during the study period. Median follow-up time was 49 months, 12% of all patients developed a relapse of the disease and 11 of whom (4% of all patients) developed a cardiac relapse. 15% of the patients who received oral prophylaxis experienced relapse, compared to 9% of those who received intramuscular injection therapy.

Conclusion: Despite the reduction in incidence of rheumatic fever and rheumatic heart disease during the study period, the disease remains a significant cause of general and cardiac morbidity among children despite being completely preventable, therefore, It should remain in the mind of every doctor, pediatricians in particular.



Disclosure: m. hammad saied, None; **L. Harel**, None; **G. Amarilyo**, None; **r. tal**, None; **R. Zidani**, None.

Abstract Number: 2126

Combined Detection of Cytokines and Biomarkers Improve the Diagnostic Performance of Bacteria Infection in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) suffer a high susceptibility to infection, and many inflammatory cytokines are prognostic in RA, but currently the role of cytokines in identifying infection individuals is rarely studied. We assessed the performance of serum inflammatory cytokines to discriminate bacteria infection from non-infections in RA, and setted up a bioscore system to evaluate the significance of these biomarkers in identifying bacterial infection.

Methods: A total of 168 RA patients were enrolled and divided into the bacterial infection (INFE) group and non-INFE group from January 2018 through January 2019, and were quantitatively measured the expression level of cytokines

Table 1. The demographic data and biomarkers of the INFE and the non-INFE group in RA patients

	INFE group (n=76)	Non-INFE group (n=92)	*P value*
Age (years)	60.28±10.87	51.21 ± 11.04	<0.001
Gender (female/male)	52/24	66/26	0.640
Weight (kg)	59.73±9.78	60.54±12.38	0.660
BMI	23.33±3.17	23.61 ± 3.52	0.609
Smoke (yes/no)	21/55	20/72	0.376
WBC (*10^9/L)	7.53±4.20	6.64 ± 1.90	0.09
PLT	279.24±111.28	300.49 ± 93.46	0.18
ESR (mm/h)	75.51±34.94	49.57 ± 32.31	<0.001
C3 (g/L)	1.05±0.33	1.05 ± 0.32	0.990
C4 (g/L)	0.22±0.09	0.22 ± 0.07	0.987
CRP (mg/L)	53.40 (14.65, 85.10)	15.15 (6.23, 30.98)	<0.001
T (cells/μL)	1020.73(809.50, 1483.78)	1209.32 (938.74,1695.80)	0.031
T cell (%)	72.11±10.01	71.58 ± 7.92	0.708
B (cells/μL)	141.71 (98.56, 213.18)	212.76 (142.81, 277.66)	<0.001
B cell (%)	11.31±6.94	12.58 ± 5.14	0.727
NK (cells/μL)	216.56 ± 137.82	240.83 ± 164.55	0.071
NK cell (%)	14.53 ± 8.05	13.59 ± 7.60	0.895
DAS28-3 (ESR)	5.16 ± 0.19	5.18 ± 0.17	0.909
IL-2 (pg/mL)	5.66 (3.37, 9.37)	4.84 (2.85, 8.00)	0.206
IL-4 (pg/mL)	6.59 (2.32, 15.93)	5.04 (2.20, 10.64)	0.249
IL-6 (pg/mL)	54.53 (19.30,105.96)	31.79 (12.69, 58.08)	0.006
IL-10 (pg/mL)	9.64 (7.14, 16.47)	8.07 (5.61, 13.29)	0.019
IL-17 (pg/mL)	43.08 (13.63, 91.66)	53.22 (7.03, 91.90)	0.084
IFN-γ (pg/mL)	12.67 (6.82, 32.22)	8.98 (4.51, 25.55)	0.033
TNF-α (pg/mL)	9.00 (4.95, 21.61)	9.04 (3.92, 18.48)	0.437

***All data were described as the medians (IQR) or M ± SD except gender and smoke**

by flow cytometry. The discriminating value of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood cell count (WBC), lymphocyte subsets, complement C3 and complement C4 also were assessed. Bacterial infection was confirmed through bacterial culture, image study, response to antibiotic therapy and typical clinical symptom. The diagnostic value for bacterial infection was evaluated by the areas under the receiver operating characteristic (ROC) curves (AUC) and a novel bioscore system combining multiple biomarkers.

Results: In INFE group, the levels of IL-6 (p=0.006), IL-10 (p=0.019), IFN-γ (p=0.033), CRP (p< 0.001), ESR (p< 0.001), B cell (p< 0.001) and T cell (p=0.031) were higher than in non-INFE group. The IL-2, IL-4 and TNF-α also increased in INFE group, but no statistical significance (IL-2, p=0.206; IL-4, p=0.249; TNF-α, p=0.437), IL-17 decreased (p=0.084). However, it was remarkable that the AUC yielded 0.820 (95%CI: 0.753, 0.876), with sensitivity of 64.38%

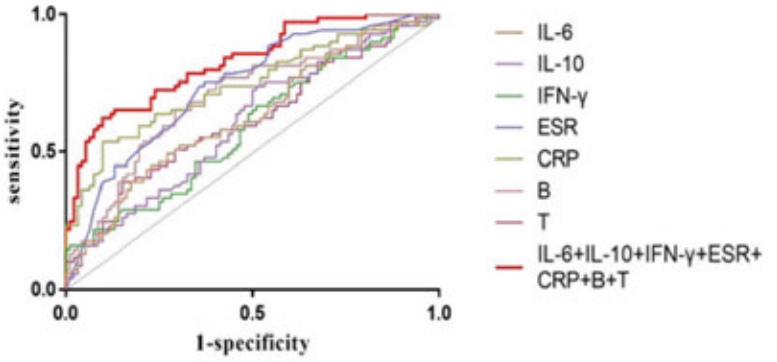

Figure.1 Receiver operating characteristic curves (ROC) of IL-6, IL-10, IFN-γ, ESR, CRP, B cells, T cell and their combination. ROC curves of the above biomarkers were plotted based on the differentiation between bacterial infection and non-infection in RA patients.

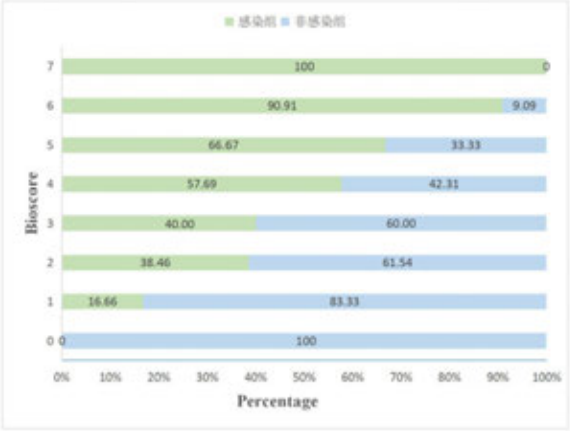

Figure.2 Distribution of the INFE group and the non-INFE group in bioscore range 0-7. As the score went up, so did the infection rate.

and specificity of 88.03%, when combined with IL-6, IL-10, IFN-γ, ESR, CRP, B and T cell. The above seven biomarkers were included in the bioscore system, the whole of patients with bioscore of 0 (n=18) were in the non-INFE group. When the score was 7, all patients (n=6) were in the INFE group.

Conclusion:

Serum cytokines are markers for detection of bacterial infection in RA. The combination of ESR, CRP, IL-6, IL-10, IFN-γ, B and T cell may be a valuable diagnostic score to early diagnose infection in RA, and provide certain reference basis for clinical treatment and prognosis evaluation.

Disclosure: Y. Qin, None; **X. Zhao**, None; **J. Luo**, None.

Abstract Number: 2127

Diagnosis of Inflammatory Rheumatic Diseases: Preliminary Approach by Urine Metabolomics

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Infection-Related Rheumatic Disease Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Early diagnosis of inflammatory rheumatic diseases (IRD), as axial Spondyloarthritis (axSpA), Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE) represents in our days a major clinical challenge. Increasing evidence has determined that early diagnosis, prompt treatment initiation and early achievement of remission are the main predictors of long-term clinical, functional and radiographic outcomes. Therefore, identification of sensitive markers is important for the early detection and precise therapy for IRD patients. Taking into consideration that metabolomics is a post-genomics technology that offers the closest characterization of the phenotype, this methodology can constitute a key tool for discriminating patients with IRD. This study aims to identify differences in the urinary metabolic profile and develop a feasible clinical approach for axSpA, RA and SLE diagnosis.

Methods: A cross-sectional non-targeted mass spectrometry-based metabolomics study was performed in 111 individuals composed by: axSpA (n=27, according to ASAS criteria), RA (n=22, according to ACR/EULAR criteria for RA) and SLE (n=23, according to ACR classification criteria for SLE) patients and healthy controls (HC; n=39). Patients with co-occurrence of other IRD or having received biotechnological therapies were excluded. Urine samples were analyzed by liquid chromatography high-resolution mass spectrometry (LC-HRMS) and data was subsequently preprocessed with the open-source software MZmine. The resulting matrix was normalized by total area and analyzed by multivariate analysis with the SIMCA software.

Results: Patients with RA were significantly older than controls [RA: 58±12 years old (yo); HC: 43±13yo; axSpA: 36±7yo; SLE: 49±12yo]. RA and SLE groups contained significantly more women (RA: 90%; SLE: 91%; HC: 49%; axSpA: 33%). However, Principal Component Analysis showed that the metabolic profile was not influenced by gender or age. Additionally, metabolic differences were identified between RA and SLE *vs* HC, but not between axSpA and HC. Importantly, the metabolic profile of SLE and RA patients was significantly different from the one displayed by axSpA patients.

Conclusion: Urine metabolomics demonstrated to be a useful tool to discriminate SLE and RA patients from axSpA patients. Further studies will validate the potential use of urine metabolomic profile for Inflammatory rheumatic diseases diagnosis in clinical practice.

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Abstract Number: 2128

Anti–MDA5 Antibody Positive Dermatomyositis Is Not Always Associated with Recalcitrant Lung Disease or Mortality

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Individuals with autoantibodies against melanoma differentiation-associated protein 5 (MDA-5) are reported to have a significant risk of developing rapidly progressive and fatal interstitial lung disease (ILD). It is important that as new DM-specific antibodies emerge, the associated phenotype be carefully defined as this can greatly impact the choice of treatment and prognostication of patients. The goal of this study is to describe the clinical and radiologic features of anti-MDA-5 antibody-positive patients in a North American cohort, and in doing so, we contrast the existing literature by highlighting that ILD was less severe than previously reported and most patients had more favorable outcomes with treatment.

Methods: This retrospective study characterized the clinical characteristics, lung function, HRCT findings, treatment and outcomes of MDA5-positive patients seen at at Emory University and affiliated hospitals.

Results: Fourteen MDA5-positive and two borderline-positive cases were identified between 2013 to 2019. Median disease duration is 18 months (range: 4-84). 15/16 (92%) had clinically amyopathic dermatomyositis, 7/16 (40%) had cutaneous ulcers and 14/16 (87%) had ILD. 6/16 subjects (37%) developed severe ILD of which 3 died from hypox-

Patient	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Patient 12	Patient 13	Patient 14	Patient 15	Patient 16
Gender	Female	Male	Female	Female	Female	Male	Male	Female	Female	Female	Female	Female	Male	Female	Female	Female
Race	African American	African American	Hispanic	Caucasian	African American	Hispanic	Asian	African American	African American	African American	African American	African American	Caucasian	African American	Caucasian	African American
Age at symptom onset, y	37	44	47	58	20	33	38	34	58	47	31	48	27	42	53	60
Disease duration, m	18	4	84	55	30	33	17	4	32	8	15	9.5	6	13	30	32
Tobacco use (pack-years)	No	No	No	50	No	No	No	No	No	No	No	No	No	No	No	10
Co-morbidities	None	None	Hypertension	None	None	None	None	None	Hypothyroidism	None	DM-II	None	None	Retinitis pigmentosa	Hypertension	Glaucoma
Initial presentation	Rash, exertional SOB	Joint pain, rash	Facial swelling, rash , joint pain	Rash	Diffuse body pain, fatigue	Joint pain, rash	Facial swelling, rash	Facial swelling, rash, sob	Hoarseness, sob	Rash	Facial swelling, hoarseness, SOB	SOB, generalized weakness	Joint pain, exertional SOB	Rash	Shortness of breath, cough	Facial swelling, fatigue
Clinical features																
ILD	yes	yes	yes	yes	no	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	none
Rapidly progressive or steroid non-responsive	yes	yes	no	no	-	no	no	no	no	no	yes	no	no	no	no	-
ILD flare requiring hospitalization, n	yes	yes	no	no	-	no	yes	no	yes	yes	yes	no	no	no	yes	-
Hand swelling	+	+	+	-	+	+	+	+	-	-	-	+	+	-	-	-
Arthritis/arthralgias	+	+	+	-	+	+	-	+	-	-	-	+	+	-	-	-
Amyopathic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Clinically amyopathic	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
Skin ulceration	+	+	+	+	+	-	-	+	-	+	-	-	-	-	-	-
Palmar papules	+	+	-	+	+	-	-	+	-	-	-	-	-	-	-	-
Mechanics hand	+	+	-	-	+	-	-	+	-	-	-	+	-	-	-	-
Panniculitis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Calcinosis cutis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Alopecia	+	-	+	-	-	-	-	+	-	-	-	-	-	+	-	-
Heliotrope rash	+	-	+	+	+	+	+	+	-	-	-	+	-	+	-	+
Gottron's papules	+	+	+	+	+	+	+	+	-	-	-	+	+	+	-	-
Periungual telangectasias	+	+	+	+	+	-	-	+	-	-	-	+	-	+	-	-
Pruritis	-	-	+	-	+	-	-	+	-	-	-	-	-	-	-	-
Oral ulcers	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-
Weight loss	+	+	-	+	+	+	+	+	-	-	-	+	+	-	-	-

Table 1. Clinical Characteristics

Patient	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Patient 12	Patient 13	Patient 14	Patient 15	Patient 16
Serologies																
ANA	1:160 (speckled)	1:160 (homogenous)	N/A	1:320 (homogenous)	1:40 (speckled)	<1:80	< 1:80	1:320 (speckled)	<1:80	<1:80	N/A	<1:80	1:320 (nucleolar)	1:80 (speckled)	N/A	1:10240 (speckled)
ENA	SSA > 240	Negative	Negative	Negative	SSA 24	dsDNA 40	SSA > 240	SSA >240	Negative	Negative	Negative	Negative	Negative	Negative	Negative	SSA >240, SSB 119
C3	63 - 66	99-136	N/A	182	110-195	N/A	120	133	N/A	63	N/A	71	134	127	N/A	63 -110
C4	40-48	30-23	N/A	33	13-14	N/A	39	36	N/A	26	N/A	30	30	27	N/A	16-24
RF (IU/mL)	N/A	60	N/A	N/A	<20	N/A	<20	21	<20	N/A	<20	<20	<20	N/A	N/A	N/A
CCP (unit/mL)	4.5	76	4.5	N/A	2.7	N/A	0.8	1.3	<0.4	N/A	<0.4	3	1.6	N/A	N/A	N/A
Anti-Ro52 (AU/ml)	117	1	68	6	11	5	230	3	3	20-25	150	14	11	7	33	94
Anti-synthetase antibodies	Negative	Negative	Negative	Negative	Negative	Negative	anti-TIF 1 gamma	anti-fibrillarin	Negative	Negative	Negative	Negative	Negative	Negative	anti-fibrillarin	Negative
ANCA	N/A	N/A	N/A	N/A	N/A	N/A	<1:20	N/A	<1:20	N/A	N/A	N/A	1:320	N/A	Negative	N/A
Lab tests																
CPK (unit/L) min, max	17 - 649	48-856	43-82	29-31	65-207	178-134	66-798	36	33-121	65	44-122	32-106	63-65	116-138	22-27	47
Ferritin (ng/mL)	83-636	N/A	590	N/A	20	N/A	2,662	194	311 - 6453	N/A	1300	N/A	1,023	N/A	204	N/A
AST (unit/L)	156 - 86	133-329	32-91	21-53	25-113	97-162	25-136	27-56	30-112	39-82	21-31	20-24	54-109	23-24	15-50	16-25
ALT (unit/L)	102-189	111-332	54-90	13-50	21-106	66-163	29-155	18-51	23-81	61-110	'11- 30	17-44	62-91	12-13	45-18	12-14
Aldolase (unit/L)	11.9 -173	N/A	6.9	6.1 - 8.8	2.4-6.3	8.2-9.3	5.8	14.2 - 9.1	9.8	N/A	6.2-8.3	4.7-6.8	7.2	3.3	7.6	N/A
LDH (unit/L)	437-735	N/A	N/A	N/A	N/A	321	475	N/A	433	N/A	335-371	N/A	N/A	N/A	22-27	N/A
Pulmonary function tests																
FVC-initial to last available (% predicted)	51	N/A	N/A	74 - 79	79	N/A	62-88	N/A	58 - 65	N/A	47-49	88-92	40	106	40	N/A
TLC – initial to last available	59	N/A	N/A	73 - 81	94	N/A	94-90	N/A	51 - 49	N/A	52	74	43	95	45	N/A
DLCO – initial to last available	N/A	N/A	N/A	51 - 60	66	N/A	76 - 44	N/A	32 -35	N/A	42	41-23.6	38	81	39	N/A
HRCT abnormalities	+	+	+	+	-	+	+	+	+	+	+	+	N/A; CXR Bibasilar opacities	N/A; CXR normal	+	-
GGOs	+	+	+	+	-	+	+	+	+	-	+	-			+	-
Consolidation	+	-	-	+	-	+	+	+	+	+	+	-			+	-
Reticulations	+	+	-	+	-	-	-	-	+	+	+	+			+	-
Bibasilar-predominance	+	+	+	-	-	+	+	-	+	-	-	+			+	-
Honeycombing	-	-	-	-	-	-	-	-	-	-	-	-			-	-
Pneumomediastinum	-	-	+	-	-	-	+	-	-	-	+	-			-	-
Bronchiectasis	-	-	+	+	-	-	+	-	+	+	+	-			+	-
Echocardiogram																
EF (%)	60-65	55	60	55-60	50	55	50-55	60-65	65	20-25	50-55	N/A	N/A	N/A	65	N/A
Estimated RVP (mmHg)	35	N/A	N/A	N/A	N/A	28.66	N/A	N/A	30.4	N/A	N/A	N/A	N/A	N/A	33.2	N/A
Mechanical Ventilation	+	-	-	-	-	-	-	-	-	+	+	-	-	-		

Table 2. Serological Profile, HRCT characteristics, PFTs

Patient	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Patient 12	Patient 13	Patient 14	Patient 15	Patient 16
Therapeutic regimen																
Pulse-dose corticosteroids	+	+	+	-	-	-	+	+	+	+	+	-	-	-	-	-
Mycophenolate mofetil	-	+	-	-	-	-	+	-	-	+	-	+	-	-	+	-
Tacrolimus		-	-	-	+	-	+	-	-	-	-	-	-	-	+	-
Cyclophosphamide	-	+	-	+	-	-	-	+	-	-	-	+	+	-	-	-
Rituximab	+	-	-	+	+	-	+	-	-	-	-	-	-	-	-	-
Intravenous immunoglobulins	+	-	+	+	+	-	+	-	-	-	+	-	-	-	-	-
Hydroxychloroquine	-	-	+	+	+	+	-	-	-	+	-	+	-	+	-	+
Azathioprine	+	-	+	+	+	+	-	-	+	-	+	-	-	-	-	-
PLEX	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cyclosporine	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-
Xarelto	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-
Disease course																
Time from disease onset to IS (months)	0.5	3	3	1	3	1	7	1	2	1	3	0.5	3.5	1	1	1
Time from disease onset to high-dose CS (months)	0.5	3	3	12	3	1	7	1	4	1	3	7	-	-	1	-
Time from disease onset to pulse steroids (months)	11	3.5	-	-	3	-	9	1	-	1.5	15	-	-	-	-	-
Time from disease onset to death (months)	18	4	-	-	-	-	-	-	-	-	15	-	-	-	-	-
Time from immunosuppression to death (months)	18	1	-	-	-	-	-	-	-	-	12	-	-	-	-	-

Table 3. Therapeutic regimen and Disease Course

emic respiratory failure. Of the three patients that died from hypoxemic respiratory failure, one had severe pneumomediastinum.

Conclusion: Our data supports that MDA5 Ab-associated ILD can be severe and/or progressive in a significant number of patients, however, it is can be treatable and stabilized in most cases. Borderline positive anti-MDA5 patients manifest a phenotype consistent with strong positive MDA5 patients. Finally, an association with spontaneous mediastinum may contribute to mortality rates in more severe cases.

Disclosure: D. Soni, None; **D. Maniscalco**, None; **S. Veeraraghavan**, None; **J. Cheeley**, None; **A. Khosroshahi**, Exagen, 2.

Abstract Number: 2129

Thyroperoxidase Antibodies in Patients with Positive ANA

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune thyroid disease, which is defined by the presence of thyroid antibodies, is the most common organ specific autoimmune disorder, affecting 11% of the general population[1]. There is a reported higher prevalence of thyroiditis in older women, and patients with systemic lupus (SLE), Sjogren's, or RA. Antinuclear antibodies (ANA) are present in 45% of patients with thyroid antibodies, but there are no studies looking at the prevalence of thyroiditis in ANA positive (ANA+) patients. Our goal was to report the prevalence of thyroperoxidase antibodies (TPO ab) in ANA+ patients, and define associations with disease specific autoantibodies, gender, age, and thyroid dysfunction.

Methods: Lab data from 1/1/2010 to 8/1/2018 on ANA+ rheumatology patients followed at an academic center was evaluated for the presence of the most recent TPO, dsDNA, Smith, RNP, Ro/SSA, La/SSB, RF, and CCP antibodies, and for the highest or maximum thyroid stimulating hormone (TSH) level reported for each patient over the study period . Antibody positivity, existence of elevated highest TSH, and gender were compared between TPO ab groups by Chi square or Fisher's exact test. ANA titers within 1 year of TPO ab testing, and age were analyzed relative to TPO ab titers using regression analyses or Kruskal-Wallis. Upper reference values for TPO ab were >35 or 61 IU/mL depending on year of testing and >5 mU/L for TSH.

Results: Of 690 ANA+ adults who had TPO ab testing, 196 (28.4%) had positive TPO ab (+TPO), and consisted of 184 (93.9%) females at a mean age of 47.5 years, see Table 1. There was no age difference between +TPO and -TPO groups. There was no significant difference in the prevalence of autoantibodies between TPO groups, Table 2. There was no relationship between ANA titer (p=0.265) or age (p=0.136) to TPO titer. There was a significant correlation between +TPO status and history of elevated TSH.

Table 1. Characteristics of 690 Adult Rheumatology patients with positive ANA.

	Positive TPO	Negative TPO	P
Female, n (%)	184 (30.0)*	428 (69.9)	*0.007
Male, n (%)	12 (15.4)*	66 (84.6)	
Age, years(sd)	47.5 (14)	49.1(16)	0.21
Max TSH >5 mU/L** N (%)	68 (59.7)	46 (40.3)	<0.0001

*p value for comparing female +tpo to male +tpo patients.

**Max TSH –the highest thyroid stimulating hormone level observed over the study period for each patient.

Antibody (Ab)	+Ab/+TPO n(%)	-Ab/+TPO n(%)	+Ab/-TPO n(%)	-Ab/-TPO n(%)	P
dsDNA	7 (11.3)	55 (88.7)	7(4.2)	160(95.8)	0.06
RNP	5(4.3)	111(95.7)	10(3.1)	307(96.9)	0.56
Smith	14(11.2)	111(88.8)	29(8.8)	299(91.2)	0.44
Ro/SSA	11(8.9)	112(91.1)	20(6.3)	298(93.7)	0.33
La/SSB	4(3.3)	118(96.7)	9(2.9)	304(97.1)	0.76
RF	21(12.4)	149(87.6)	48(11.5)	369(88.5)	0.77
CCP	12(11.4)	93(88.6)	19(6.5)	271(93.5)	0.11

Table 2. Autoimmune antibodies and Thyroperoxidase (TPO) antibody status in patients with positive ANA.

Conclusion: TPO antibodies, which are specific for thyroiditis, were present in 30% of ANA+ female patients, higher than the 16-20% prevalence reported in the general female population for the same age group[1]. Serologic markers for RA, Sjogrens, and SLE, were not higher in the +TPO group despite reports of increased TPO ab prevalence in these autoimmune conditions; additional workup for these autoimmune markers should not be routine in +TPO ab patients due to the low yield. This study did not compare the presence of TPO ab in patients with or without positive ANA, therefore no conclusion can be drawn as to the effect of ANA positivity on TPO ab positivity, although this study found no correlation between TPO and ANA titers. The strong association between TPO ab and TSH elevation justifies screening ANA+ patients for thyroiditis due to the increased risk of hypothyroidism. Future work will look at the presence of TPO ab and symptoms that may define thyroiditis with subclinical hypothyroidism.

Reference:

1. Hollowell JG, et. al., J Clin Endocrinol Metab 87: 489-499, 2002.

Disclosure: C. Lau, None; **S. Legunn**, None; **A. Nevares**, None; **T. Osler**, None.

Abstract Number: 2130

Enrichment of IL-17-producing CD4$^+$ T Cells in Synovial Fluid from Patients with Arthritis After anti-CTLA-4 and anti-PD-1 Combination Therapy

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) are associated with immune-related adverse events (irAEs), including arthritis (arthritis-irAE). Understanding the pathophysiology of arthritis-irAE is critical to treating it without impeding antitumor immunity; however, these mechanisms remain elusive. As a first step in elucidating these mechanisms, we characterized functional immune cell profiles in synovial fluid from patients with arthritis-irAE.

Methods: We collected and performed immunoprofiling of synovial fluid from seven patients with active arthritis-irAE who received ICIs and three control patients with osteoarthritis who did not receive ICIs.

Results: Four patients developed arthritis after PD-1 inhibitor monotherapy and three after combination therapy with CTLA-4 and PD-1 inhibitors. Two patients in the combination therapy group required interleukin (IL)-6 receptor inhibitor therapy in addition to steroids, compared with one patient in the monotherapy group (sulfasalazine). IL-17-producing $CD4^+$ T cells (Th17) were enriched in the combination therapy group (1.01±0.73% live $CD4^+$ T cells in the monotherapy group compared with 3.19±0.31% in the combination therapy group; P=0.005). Synovial fluid levels of IL-6 and IL-17A, key cytokines for Th17 cell differentiation and function, were higher in the combination therapy group than in the monotherapy group, although this difference was not statistically significant.

Conclusion: Our results demonstrate that combination therapy with CTLA-4 and PD-1 inhibitors may result in enhanced incidence of steroid-resistant arthritis-irAE. Th17 cells were enriched in the synovial fluid of arthritis-irAE patients with combination therapy, suggesting their role in disease pathophysiology. Further studies with more cases and controls are needed to better understand the mechanisms underlying arthritis-irAE.

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Abstract Number: 2131

Rituximab Safety and Persistence in Patients with Systemic Autoimmune Diseases

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

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Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab (RTX), an anti-CD20 monoclonal antibody inducing B cell depletion, is used as therapy for diverse systemic autoimmune diseases (SAIDs), but is associated with adverse events (AE) such as infusion reactions, infections and others, which may lead to therapy suspension. We aim to evaluate the safety profile and persistence of RTX in SAIDs and factors that influence on the development of infections in real-life practice.

DISEASE	N (%)
Rheumatoid arthritis (RA)	24(40%)
Vasculitis	11(18.3%)
Systemic lupus erythematosus (SLE)	9 (15%)
Systemic sclerosis (SSc)	5 (8.3%)
Antisynthetase syndrome	3 (5%)
Mixed connective tissue disease (MCTD)	2 (3.3%)
Overlap syndrome	2 (3.3%)
Others	4 (6.7%)

Methods: A retrospective observational study was conducted including patients diagnosed of SAIDs treated in a tertiary hospital between 2007 and 2018, who received at least 1 RTX infusion. At RTX initiation we collected clinical and demographic data including: age, sex, Charlson score, comorbidities, previous use of immunosuppressants (IM), biologic therapy and/or JAK inhibitors, use/dose of concomitant glucocorticoids (GC) and/or immunosuppressants and RTX dose. During treatment we analyzed: serum immunoglobulin (Ig) levels, number of RTX cycles and adverse events.

Results: 60 patients were included (73.3% women, mean age 52.8 ± 14.9 years), with median Charlson score of 3 (P25–75 1-4) and median disease evolution of 7.5 years (P25–75 1.2-12.6). Table 1 shows distribution of SAIDs.

Prior to RTX 85% of patients received IM, 48.3% biologic agents (16.7% >1) and 5% JAK inhibitors. Associated to RTX 58.3% of patients received IM and 81.7% GC (median dose 12.5mg, P25–75 7.5-15). Total RTX cycles registered were 215.5 with a median of 2.25 (P25–75 1.3-5) cycles per patient.

In terms of AE: 18 patients presented infusion reaction (72.2% were mild, 61.1% related to first cycle and 27.8% had recurrent infusion reactions). 28 patients presented infections (75% had >1), total number of infections was 64 (35 respiratory, 11 urinary, 6 skin and soft tissue, 4 gastrointestinal, 3 non-diseminated herpes zoster, 2 septic shock, 1 Pneumocystis Jiroveci pneumonia, 1 head and neck and 1 gynecological), 10 of them were serious and 1 was an opportunistic infection. There were 4 neoplasia (2 non-melanoma skin cancer, 1 bladder carcinoma and 1 ampullary carcinoma). 2 patients presented neutropenia and 1 presented an intersticial pneumonitis.

During RTX treatment 35% of patients had low Ig G and 48.3% low Ig M levels. None developed low Ig A levels. RTX was suspended in 26 patients (10 AE and 16 other reasons). 5 deaths were reported (2 infections, 2 unknown and 1 pulmonary fibrosis progression).

Low Ig G levels during RTX treatment were associated with the presence of infection ($p< 0.042$). Patients who had infection received more RTX cycles and higher doses of GC than those who did not, but there wasn't association on statistical analysis.

Kaplan Meier analysis showed less probability of continuing RTX therapy among SSc patients ($p< 0.0095$).

Conclusion: RTX therapy was safe and the presence of serious AE infrequent. Low Ig G levels were associated with the presence of infection. SSc patients showed less probability of continuing RTX than the rest of SAIDs.

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Abstract Number: 2132

Complement Component 3 as Biomarker of Cardiometabolic Risk in Rheumatic Diseases: Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriatic Arthritis and Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatic diseases have an increased risk of cardiovascular disease (CVD). Cardiometabolic disease includes an alteration in metabolic organs and CV system that might contribute to the development of CVD. Complement factors have recently been associated with metabolic events such as metabolic syndrome.

Objectives: 1) To evaluate the levels of complement C3 in rheumatic diseases with increased prevalence of cardiovascular risk and 2) to analyze the relationship of the complement C3 with the different cardiometabolic risk factors in patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE).

Methods: 570 subjects: cross-sectional study including 200 RA, 150 AS, 60 PsA, 60 SLE patients and 100 healthy donors (HD) recruited from the Rheumatology department of Reina Sofia Hospital, Cordoba (Spain). The prevalence of traditional cardiovascular risk factors was analyzed in the different rheumatic diseases. Inflammatory markers (C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), complement C3 and insulin resistance (HOMA-IR) was measured. Serum glucose, insulin, triglycerides (TG), total cholesterol, low density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, apolipoprotein A (apo-A), apoliprotein B (apo-B) were measured in overnight fasting conditions.

Kruskall wallis tests were performed for multiple comparisons. Chi-squared test were performed to analyze qualitative data. ROC analysis was carried out to identify biomarkers for cardiometabolic comorbidities. Spearman's rho correlation coefficient was used for correlation studies.

Results: All patients had significant increase in the prevalence of obesity, insulin resistance, hyperlipidemia and hypertension. PsA patients showed the worst cardiometabolic profile followed by RA, SLE and AS. Levels of complement C3 were significantly elevated in RA, AS and PsA patients. Although complement C3 levels were not increased in SLE patients, complement C3 levels were associated with HOMA-IR index in all the diseases, due to the strong correlation with insulin levels. ROC analyses showed that C3 levels could be a marker of IR in RA, PsA and SLE patients. Besides, complement C3 levels were strongly correlated with CRP in all the diseases. On the other hand,

in RA, AS and PsA patients, levels of complement C3 correlated with ERS and altered lipid profile. Hard clustering analysis identified two distinctive phenotypes in our cohort of rheumatic disease patients depending on the complement C3 levels. Patients from cluster 1 presented higher levels of complement C3 alongside increased prevalence of cardiometabolic comorbidities (obesity, diabetes, IR, hyperlipidemia, hypertension, apoB/apoA ratio, atherogenic risk) compared to cluster 2.

Conclusion: 1) Complement C3 could be a marker of IR in the rheumatic diseases most associated with cardiometabolic risk. 2) Complement C3 could be considered a cardiometabolic risk factor in RA, PsA and AS.

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Abstract Number: 2133

Acute Myocardial Infarction in Rheumatoid Arthritis, Gout, and Osteoarthritis: A Retrospective Study Using the National Inpatient Sample from 2002-2016

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies
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Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammation is a risk factor in the development of cardiovascular disease. The proposed etiology centers around accelerated atherosclerosis involving various cytokines in the TNF and IL families. As a result, chronic inflammatory diseases such as RA and gout are thought of as risk factors for the development of cardiovascular disease. There is limited data on comprehensive nationwide analysis of mortality, incidence, and demographic features in patients admitted for acute myocardial infarction (AMI) with underlying RA and gout. Our objectives are to describe the demographics associated with these admissions and report any differences between the inflammatory conditions of RA and gout to the non-inflammatory disease, OA.

Methods: We used the national inpatient sample (NIS) to capture all adult patients (> 18 years) hospitalized between 2002-2016. Using ICD-9 and -10 codes, we identified hospitalizations with primary diagnosis of AMI and further delineated these patients as having secondary diagnosis of RA, gout, or OA. The NIS is the largest publicly available multi-year hospital care dataset. Incidence and mortality rates were calculated and means/medians were used to describe demographic features. SAS v9.4 was used for all analyses and $p < 0.05$ was used to determine statistical significance.

Results: We identified 603,359 hospitalizations between 2002-2016 with a primary diagnosis of AMI and secondary diagnoses of RA, gout, or OA. Patients with AMI and secondary diagnosis of RA or gout had higher incidence of ad-

Table 1. Characteristics for Acute Myocardial Infarction Admissions Stratified by Rheumatic Disease			
	Rheumatoid Arthritis	Gout	Osteoarthritis
Sample Size	74,867	153,896	374,596
Age (years)		%	
18-24	<0.1	<0.1	<0.1
25-34	0.1	0.2	0.1
35-44	1.8	1.9	0.8
45-54	8.3	7.9	5.2
55-64	19.8	18.2	14.1
65-74	27.6	26.6	22.3
75-84	28.6	28.3	30.2
85+	13.8	16.9	27.3
Gender		%	
Male	35.7	74.4	43.3
Female	64.3	25.6	56.7
Race and Ethnicity		%	
Non-Hispanic White	80.0	72.6	81.5
African American	9.4	14.9	8.9
Hispanic	6.5	4.8	5.8
Other	4.1	7.7	3.8
Insurance		%	
Medicare	72.7	69.9	78.0
Medicaid	4.6	4.0	3.6
Private	19.2	21.1	14.9
Self-Payer	1.6	2.4	1.7
Other	1.9	2.6	1.8
Hospital Region		%	
Northeast	19.2	20.7	17.4
Midwest	20.0	18.2	22.9
South	41.8	38.2	41.1
West	19.0	23.0	18.6
Hospital Location and Teaching Site		%	
Rural	11.9	10.3	14.1
Urban Teaching	45.4	41.1	46.5
Urban Non-Teaching	42.7	48.6	39.4
Average Age in Years			
Average Age of Admission in Years (95% Confidence Interval)	70.9 (70.0-71.1)	71.7 (71.5-71.9)	75.4 (75.3-75.6)
Average Age of Death in Years (95% Confidence Interval)	77.2 (76.5-77.9)	79.0 (78.4-79.6)	82.4 (82.1-82.8)

Table 1. shows characteristics of admissions with acute MI and underlying RA, gout, and OA.

mission at a younger age and significantly younger average age of admission for AMI (RA 70.9, 95% CI [70.0-71.1], gout 71.7, 95% CI [71.5-71.9]) compared to those with secondary diagnosis of OA (75.4, 95% CI [75.3-75.6]). Hospitalizations associated with African American race had disproportionally higher incidence of admission for AMI with secondary diagnosis of gout compared to other races. There was a female predominance in those with admission for AMI and secondary diagnosis of RA and OA. The average age of death in those with admission for AMI was significantly lower in those with secondary diagnosis of RA (77.2, 95% CI [76.5-77.9]) or gout (79.0, 95% CI [78.4-79.6]) compared to OA (82.4, 95% CI [82.1-82.8]). Full demographic data is found in Table 1.

Conclusion: Patients with an underlying diagnosis of RA or gout are admitted for AMI at a younger age compared to those with a secondary diagnosis of OA; these same patients also die at a younger age compared to their counterparts with OA. This could reflect the pro-inflammatory disease state in RA and gout predisposing them to accelerated atherosclerosis. A Cleveland Clinic study showed increased prevalence of suboptimal treatment in the African American population likely leading to a higher vascular risk which may contribute to the higher incidence of admission with

AMI as we saw in our subgroup. RA is usually diagnosed at an earlier age in women; this longer disease course may also contribute to higher vascular risk manifested by higher incidence of admissions for AMI. Continued awareness and modification of the cardiovascular risks through disease control agents is needed in those with RA and gout to optimize cardiovascular outcomes.

Disclosure: R. Sen, None; **S. Aurit**, None; **L. Sarsam**, None; **O. Bhatty**, None; **M. Kumar**, None; **J. Nahas**, None.

Abstract Number: 2134

Extracellular Adenosine Increases IL-6 Production by Aging Tenocytes and May Contribute to the Age-related Pattern of Polymyalgia Rheumatica

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SESSION INFORMATION
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Background/Purpose: Polymyalgia rheumatica (PMR) is a common disease preferentially affecting elderly patients. Characteristically, PMR involves large tendons and muscles around the hips and shoulders. While corticosteroids remain the mainstay of PMR therapy, IL-6 inhibitors have been shown to be effective alternatives to corticosteroids in PMR. Recent work suggests that IL-6 levels in hip and shoulder regions of PMR patients are higher than circulating levels, thus suggesting local IL-6 production. The factors stimulating IL-6 release in tendon and muscles of PMR patients are not well defined. An explanation of the strong association of PMR with age also remains unclear. Adenosine levels are higher with age in some tissues. In myocardial tissue, for example, dysfunction of cellular adenosine transporters leads to accumulation of adenosine in the extracellular space. While adenosine is often considered to be anti-inflammatory, extracellular adenosine increases IL-6 production in some connective tissue cells. We sought to determine if elevated levels of adenosine promote IL-6 production in tenocytes, whether this is age-dependent, and whether levels of the adenosine transporter, equilibrative nucleoside transporter 1 (ENT1), vary with age.

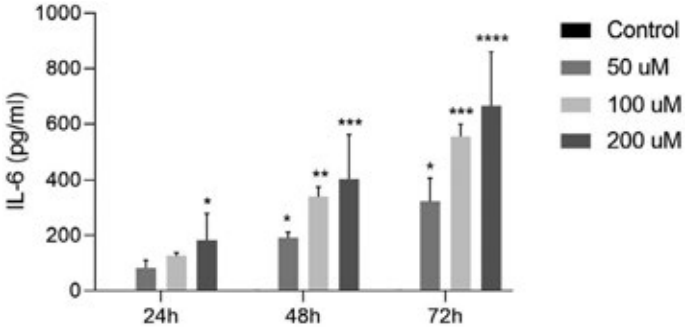

Figure 1. Effect of adenosine on tenocyte IL-6 levels. Old tenocytes were incubated with no additives (Control) or 50,100 or 200 uM adenosine. IL-6 levels were measured by ELISA in the media after 24-72 hours. IL-6 levels were not measurable at any time point in the controls. IL-6 levels were significantly increased at 24 hours by 200 uM adenosine (n=6, *= p<0.01) and at 48 and 72 hours by all concentrations of adenosine (n=6, **=p<.001, ***=p=.0002). IL-6 levels were not measurable in young tenocytes at any time point or with any concentration of adenosine (Data not shown.)

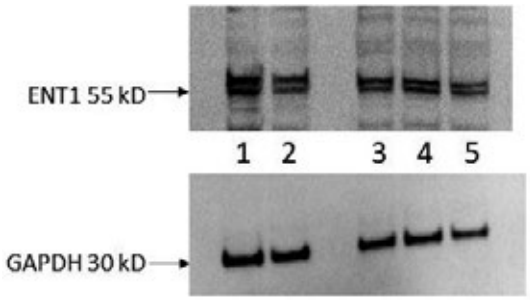

Figure 2. Levels of ENT1 in old and young chondrocytes. Two cultures of old and three cultures of young tenocytes were lysed with RIPA buffer, and similar quantities of protein were run on a 4-12 % Bis-Tris gel. Proteins were transferred to a nitrocellulose membrane and probed with ENT1 antibody. The loading control was GAPDH. There were no differences in the density of the ENT1 bands between old and young tenocytes. Lanes 1 and 2 are old tenocytes, Lanes 3,4 and 5 are young tenocytes.

Methods: Primary tenocytes were obtained from the patellar tendons of old (3-5 year old) and young (6 month old) pigs using digestion with collagenase. Cells were plated at $4.5x10^5$ cells/cm^2 in DMEM with 10 % fetal calf serum and used within 5 days of culture. After two days in culture, tenocytes were exposed to fresh DMEM with 0.35 % BSA with no additives (control) or 50 to 200 μM adenosine. IL-6 levels were measured in the conditioned media with both Western blotting using IL-17 as a positive control and an IL-6 ELISA (R&D Systems) with dose and time response. ENT1 levels were measured in the cell layer of young and old tenocytes using Western blotting and GAPDH as a loading control.

Results: In old tenocytes, 100 μM of adenosine and 10 ng/mL IL-17 increased media IL-6 levels by Western blot. The IL-6 ELISA showed no measurable amounts of IL-6 in the control of either young or old tenocytes. In old tenocytes, IL-6 levels rose to 666.3 +/- 194.3 pg/ml with 200 μM adenosine at 72 hours ($p< 0.002$) (Figure 1). In young tenocytes, there was no measurable IL-6 with any amount or time of adenosine exposure. (Data not shown.) Similar levels of ENT1 were present in both old and young tenocytes (Figure 2).

Conclusion: As tenocytes age, they may become increasingly responsive to adenosine leading to IL-6 production and an inflammatory response. While levels of ENT1 protein are similar in old and young tenocytes, additional work will be necessary to determine whether there are differences in adenosine metabolism in old and young tendon. Further studies of the pro-inflammatory effects of adenosine in older tissues may ultimately result in a better understanding of the pathways underlying the strong association of PMR with advanced age.

Disclosure: C. Shah, None; **T. Garvey**, None; **C. Gohr**, None; **E. Mitton-fitzgerald**, None; **A. Rosenthal**, None.

Abstract Number: 2135

Therapeutic Strategies and Survival in Patients with Interstitial Pneumonia with Autoimmune Features

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies
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Session Time: 9:00AM–11:00AM

Background/Purpose: Recently the term “interstitial pneumonia with autoimmune features” (IPAF) has been proposed to identify patients with interstitial lung disease and autoimmune characteristics, not fulfilling the criteria for specific connective tissue diseases (CTD). Until now, only few data are available about the clinical and serological features of IPAF patients, their survival and the possible evolution in a CTD.

The aim of the study was to investigate the therapeutic choices in IPAF patients, their efficacy and safety.

Methods: Fifty-two patients (mean age at diagnosis 65.5±11.0 years, female/male ratio 29/23) were consecutively enrolled and prospectively followed for 45±31.6 months. Data about therapies, disease onset, serological, clinical and therapeutic features, pulmonary function tests and high-resolution computed tomography were periodically repeated. A worsening of lung function was defined as a reduction of 10% compared to baseline of forced vital capacity (FVC) and diffusion lung capacity of CO (DLCO).

Results: An immunosuppressive therapy was prescribed in 15 patients (namely cyclophosphamide in 4, mycophenolate mofetil in 6 and azathioprine in 6, respectively), while 6 patients were treated with anti-fibrotic therapies (pirfenidone or nintedanib). Thirty-three patients taken corticosteroids, associated to other drugs in 18 patients, and alone in 15. Finally, no therapies were prescribed in 16 patients. At the end of follow-up FVC remained stable in 35% of patients, worsened in 50% and increased in 15%; DLCO remained stable in 25.8% of patients, worsened in 58.1% and increased in 16.1%. Mean survival was 94.2±8.5 months, and no differences were recorded according to the kind of therapy, while survival was significantly associated to the lung function at baseline (FVC and DLCO were confirmed to be significantly associated to death at multivariate analysis).

Conclusion: The therapeutic strategy in IPAF patients reflects the etherogeneity of the disease. Waiting for specific trial in this population, treatment is empyrical and based on the baseline features of the patients. Despite well tolerated, both anti-fibrotic and immunosoppressive therapies seem to not influence the evolution of the diseas.

Disclosure: M. Sebastiani, None; **G. Cassone**, None; **C. Vacchi**, None; **L. De Pasquale**, None; **S. Cerri**, None; **G. Della Casa**, None; **C. Salvarani**, None; **A. Manfredi**, None.

Abstract Number: 2136

Cardiovascular Risk Evaluation in Systemic Lupus Erythematosus and Rheumatoid Arthritis: Preliminary Results from the "Cardiovascular Obesity and Rheumatic DISease (CORDIS)" Study Group of the Italian Society of Rheumatology

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

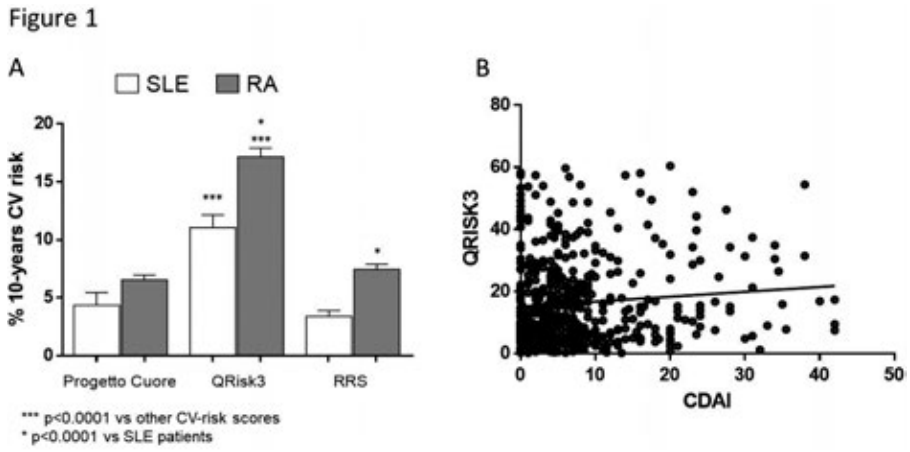
Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) patients present high cardiovascular (CV) morbidity and mortality. International guidelines suggest estimating CV-risk in these patients, but no indications about the strategy to use are specified. This multicentre cross-sectional study aimed to investigate the performance in real-life setting of three different 10-years CV-risk estimating algorithms in SLE and RA.

Methods: Data of 989 patients with SLE (140 patients; female 85.7%; age 40±16 years; disease duration 155±106 months) and RA (849 patients; female 79.3%; age 61±12 years; disease duration 133±110 months), according to specific classification criteria, were collected since January 2019 in 10 rheumatologic University Hospitals. Clinical and laboratory parameters were registered, and individual CV-risk was calculated using the "Progetto Cuore", QRisk3 and Reynolds risk scores (RRS), as stated by suitable algorithms. Statistical analysis was performed with appropriate tests using the Statistical System Prism (Graphpad Instat 6.0 - San Diego CA-USA).

Results: Fifty-six (6.6%) RA and 14 (10%) SLE patients had experienced a previous CV event (mainly myocardial- infarction). Among traditional CV-risks RA patients were significantly older ($p< 0.0001$), hyperlipidaemia was more prevalent in RA then SLE (57.8% vs 37.1%; $p< 0.001$), and similar prevalence of hypertension and diabetes was recorded. Mean BMI was not significantly different between groups, nevertheless a BMI >25 Kg/m2 was more prevalent in RA than SLE (47.8% vs 14.2% - $p< 0.0001$). RA patients were more frequently smokers (23.7% vs 13.6% - $p=0.007$). C-reactive protein was significantly higher in RA compared to SLE patients (6.8±1.1 vs 3.8±0.4 mg/l – $p=0.01$). Median (IQR) CDAI and SLEDAI were 7 (3-12) and 2 (0-2) in RA and SLE, respectively, and low-disease or remission according to CDAI (< 10) and SLEDAI (< 4) was similar. Sixty-eight percent of SLE patients were on a mean prednisone-dose of 5.9±2.6 mg/day whereas 41% of RA patients took 5.0±2.8 mg/day of prednisone ($p< 0.01$). All SLE patients were on



A. Estimated % 10-years cardiovascular risk in SLE and RA patients according to "Progetto Cuore", QRisk3 and Reynolds risk scores. B. Correlation between CDAI and QRisk3 score in RA patients.

hydroxychloroquine, 78 (55.7%) were co-treated with an immunosuppressant agent and 9 (6.4%) with belimumab or rituximab. Seventy percent of RA patients were on csDMARDs, mainly methotrexate, and 49.5% used also a biologic agent. CV-risk with QRisk3 results 2 to 3-fold higher compared to RRS and "Progetto Cuore" score in both patient groups. Moreover, QRisk3 and RRS resulted significantly higher in RA compared to SLE (Figure1A). Interestingly, only in RA a positive correlation between CDAI and QRisk3 (r=0.1; p=0.03) was detected (Figure1B).

Conclusion: This multicentre study showed a different performance in SLE and RA patients of the commonly used algorithms to estimate CV-risk in clinical practice. With a good disease activity control, traditional CV-risk factors may differently impact on predictable CV-risk using the "Progetto Cuore" scores, QRisk3 or the RRS. These findings should be considered when CV-risk is estimated routinely in such patients.

Disclosure: F. Cacciapaglia, None; **G. Erre**, None; **G. Sakellariou**, None; **O. Viapiana**, Abiogen; **M. Piga**, None; **E. Bartoloni**, None; **A. Manfredi**, None; **S. Colella**, None; **F. Castagna**, None; **G. Cafaro**, None; **M. Dessì**, None; **M. Fornaro**, None; **A. Giollo**, None; **S. Grignaschi**, None; **C. Vacchi**, None; **F. Spinelli**, None; **F. Atzeni**, None; **E. Gremese**, AbbVie, 5, 8, BMS, 5, 8, Celgene, 5, 8, Janssen, 5, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, UCB, 5, 8.

Abstract Number: 2137

Overall Survival in Patients with PD-1 Inhibitor-related Inflammatory Arthritis and Metastatic Melanoma

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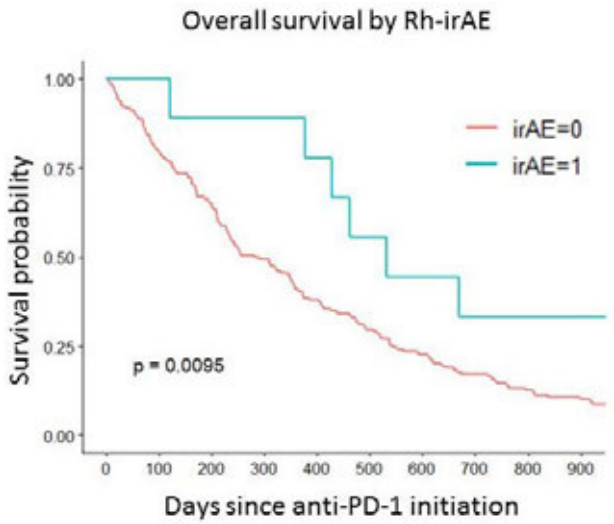
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM



Overall survival based on the development of inflammatory arthritis.Abbreviations: Rh-irAE; rheumatic immune-related adverse effect.

Background/Purpose: The development of *de novo* inflammatory arthritis (IA) occurs in 2-4% of all patients with cancer treated with programmed cell death protein 1 (PD-1) inhibitors. (1) Prognosis remains a major concern for managing physicians, particularly given the potential for immunosuppressive medications to impact the anti-tumor response. The objective of this study is to assess the overall survival of patients with melanoma who develop anti-PD-1 associated IA.

Methods: From a database of all patients who received any PD-1 inhibitor at the Mayo Clinic Rochester, Minnesota campus between January 1st, 2011 and May 1st, 2018, we identified those with metastatic melanoma and new-onset inflammatory arthritis using diagnostic codes, search terms, and manual chart review. A Cox proportional hazard model was used to examine overall survival using R statistical software.

Results: Of the 394 patients with stage IV melanoma who received any PD-1 inhibitor, 27 (6.9%) were diagnosed with inflammatory arthritis representing a rheumatic immune-related adverse effect (Rh-irAE). Mean age upon starting anti-PD-1 therapy was 62.4 (SD=13.9) and 39% of patient were female. There were no statistically significant differences in age or sex between patients with and without IA. Average duration of anti-PD-1 therapy was 225 days (SD=279) with no significant differences between groups. IA was most often polyarticular (74%) and was treated with systemic glucocorticoids in 82% of cases for a mean duration of 210 days (SD=221). Six patients (22%) were treated with disease modifying drugs and three patients (11%) required permanent anti-PD-1 discontinuation due to severe symptoms. The development of IA correlated significantly with increased overall survival (HR 0.39, 95% CI=0.19-0.81).

Conclusion: This study shows a significant survival benefit associated with the development of anti-PD-1 associated IA in patients with metastatic melanoma. The prevalence of IA was higher than previous reports on rheumatic irAEs.

Reference:

1. Richter MD, Crowson C, Kottschade LA, Finnes HD, Markovic SN, Thanarajasingam U. Rheumatic Syndromes Associated With Immune Checkpoint Inhibitors: A Single-Center Cohort of Sixty-One Patients. Arthritis Rheumatol. 2019;71(3):468-475.

Disclosure: M. Richter, None; **J. Orme**, None; **H. Finnes**, None; **U. Thanarajasingam**, None.

Abstract Number: 2138

Rheumatic Immune-related Adverse Effects from Checkpoint Inhibitor Immunotherapy in Patients with Solid Tumors in a Latin American Population

Alain Sánchez-Rodríguez,[1] Elina Alexandra Rodriguez-Melendez,[2] Alonso Turrent-Carriles,[3] Paola Bermúdez-Bermejo,[3] José Fabián Martínez-Herrera,[2] and Raquel Gerson-Cwilich[2], [1]Hospital General de Mexico, Mexico City, Distrito Federal, Mexico, [2]ABC Medical Center, Oncology Department, Ciudad de Mexico, Distrito Federal, Mexico, [3]ABC Medical Center, Rheumatology Department, Ciudad de Mexico, Distrito Federal, Mexico

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Cancer immunotherapy is a newly-approved approach in the management of advanced malignancies. Immune checkpoint inhibitors (ICIs) are the most commonly used type of cancer immunotherapy and have been associated with an increasingly number of immune-related adverse events (irAEs), including a variety of rheumatologic manifestations, however information regarding prevalence and incidence of irAEs in Latin American population is scarce.

Methods: We designed a retrospective, cross-sectional study to identify the prevalence of rheumatologic irAEs in patients with cancer receiving ICIs during the study period, ranging from January 2014 to February 2018 in a single center.

Results: Data from 140 subjects was included with a global prevalence of irAES of 38.6%, from which Rheumatic irAES were identified in 20 patients (14.3%). None of the patients had history of previous autoimmune disease. Mean age was 63 (+/- 11.3) years, 50% were female. The most common solid tumors were Lung and melanoma in 45 and 30%, respectively and 85% had metastatic disease. Patients received the following ICIs or combinations: Pembrolizumab in 45%, Nivolumab in 30%, Ipilimumab in 15% or Nivolumab + Ipilimumab in 10%. In order of frequency the following Rheumatologic irAEs were observed: Cutaneous (80%) (including lupus-like erythema), inflammatory arthritis (20%), myositis (5%), interstitial lung disease (5%), episcleritis (5%), nephritis (5%); Only four patients had available antinuclear antibodies with positive result. One patient developed a lupus-like syndrome with cutaneous, articular and renal involvement with negative antinuclear antibodies. Additionally, other concomitant non-rheumatologic irAES were observed: conjunctivitis in 4 patients, thyroiditis in 1 patient, and severe thrombocytopenia in 1 patient. Of notice, only 2 of the rheumatologic irAES were considered severe and 80% were mild or moderated. And most patients were treated with topic or low dose systemic glucocorticoids and symptomatic treatment and none required treatment with DMARDs.

Conclusion: We performed one of the first epidemiologic reports of rheumatologic irAES in a Latin American Population. Patients showed a predominantly mild and moderated cutaneous and articular involvement. Emphasis on serological assessment may improve identification of these newly described manifestations in Latin American populations.

Disclosure: A. Sánchez-Rodríguez, None; **E. Rodriguez-Melendez**, None; **A. Turrent-Carriles**, None; **P. Bermúdez-Bermejo**, None; **j. Martínez-Herrera**, None; **R. Gerson-Cwilich**, None.

Abstract Number: 2139

Rheumatic Immune-Related Adverse Events Associated with Treatment with Immune Checkpoint Inhibitors: A Multicenter Study of 38 Cases

Sebastian Rodriguez-Garcia,[1] David Lobo,[2] Fabiola Ojeda,[3] Raul Castellanos-Moreira,[4] Ana Laiz,[2] Roberto Gumucio,[4] Cesar Diaz-Torné,[2] Virginia Ruiz-Esquide,[5] Milena Millan,[2] Ivan Castellvi,[6] Patricia Moya Alvarado,[7] Berta Magallares,[2] Carolina Perez,[3] Hector Corominas,[8] and Jose Gomez-Puerta[9], [1]Rheumatology Department. Hospital Clínic Barcelona, Barcelona, Spain, [2]Rheumatology Department. Hospital Sant Pau, Barcelona, Catalonia, Spain, [3]Rheumatology Department. Hospital del Mar, Barcelona, Catalonia, Spain, [4]Rheumatology Department. Hospital Clínic Barcelona, Barcelona, Catalonia, Spain, [5]Department of Rheumatology, Hospital Clínic, Barcelona, Barcelona, Catalonia, Spain, [6]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [7]Hospital de la Santa Creu i Sant Pau, Barcelona, Catalonia, Spain, [8]Rheumatology Department, Hospital Sant Pau, Barcelona, Catalonia, Spain, [9]Department of Rheumatology, Hospital Clínic, Barcelona, Barcelona, Spain

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICI) against CTLA-4 or PD- 1/PD-L1 and more recently TIM3, have demonstrated efficacy in improving the survival of patients with diverse advanced malignancies including melanoma, lung and urothelial cancer, among others.

Because of its mechanism of action, ICI are prone to produce different immune-related adverse events (irAEs), including musculoskeletal manifestations.

Our aim was to describe the experience with rheumatic irAEs in three tertiary centers.

Methods: All adult patients referred to the rheumatology departments of three tertiary centers from 2015 to 2018 because of the onset of musculoskeletal symptoms following treatment with an ICI were included.

Data collected comprised demographic features as well as ICI indication and type, history of rheumatic disease, musculoskeletal manifestations at the irAE onset, laboratory tests, ultrasound findings and treatment. Diagnostic and treatment approach was done according to clinical judgment in daily clinical practice settings.

Results: 38 patients were included, 39.5% female, mean age was 64 years (range 32-83). The indication for ICI was lung cancer in 20 cases, 10 melanoma, 3 urothelial and 1 for acute myeloid leukemia, squamous skin, breast, head and neck and rectum cancer.

Pembrolizumab was the most used ICI with 17 cases (1 combined with epacadostat), 12 were treated with Nivolumab (4 combined with Ipilimumab), 6 Atezolizumab (1 combined with Ibatasertib) whereas Durvalumab, Ipilimumab and MBG453 (a TIM3 inhibitor) were used each in 1 patient.

A history of rheumatic disease was reported in 12 patients 3 gout, 2 chondrocalcinosis and 1 case for each RA, Spondyloarthritis, SLE, psoriasis, fibromyalgia and osteoarthritis.

The most frequent irAE presentations were arthritis with 20 cases (52.3%) and arthralgia in 12 cases (31.6%). After the assessment, 15 patients were diagnosed as undifferentiated arthritis, 4 psoriatic-like arthritis, 2 PMR-like,1

leukocytoclastic vasculitis, 1 small-vessel vasculitis, 1 tenosynovitis, 2 gout and 12 were classified as having non-inflammatory symptoms.

Antibody status was analyzed in 33 patients, ACPA were positive in 1 patient with known RA, ANAs were positive in 4 (including 1 patient with previous SLE) but without any specificities (i.e. ENAs) and ANCA were negative in one case with small-vessel vasculitis.

Ultrasonography assessment was performed in 11 patients, 3 did not show signs of inflammation. Among the remaining ones, 6 presented either synovial hypertrophy with/or positive power Doppler, 1 a peritendinous fluid collection and 1 an elbow joint effusion.

Most patients were treated with glucocorticoids and NSAID 23 (60.5%) and 13 (34.2%) respectively. Only 4 patients required csDMARD (Methotrexate or Hydroxychloroquine) and 4 had to withdraw ICI treatment due to irAEs.

Conclusion: Our results were in line with previous studies showing that MSK-irAEs associated with ICI may present as a flare of a previous known rheumatic disease or as a de novo symptom.

Most patients presented with asymmetric mono or oligoarthritis and responded to GC and NSAID with only a few requiring DMARD or ICI withdrawal

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Disclosure: S. Rodriguez-Garcia, None; **D. Lobo**, None; **F. Ojeda**, None; **R. Castellanos-Moreira**, None; **A. Laiz**, None; **R. Gumucio**, None; **C. Diaz-Torné**, None; **V. Ruiz-Esquide**, None; **M. Millan**, None; **I. Castellvi**, Actelion, 5, Boehringer -Ingelheim, 8, Gebro, 8, Kern, 5, Novartis, 8; **P. Moya Alvarado**, None; **B. Magallares**, None; **C. Perez**, None; **H. Corominas**, None; **J. Gomez-Puerta**, None.

Abstract Number: 2140

Preexisting Autoimmune Disease and Rheumatic Immune-Related Adverse Events Associated with Cancer Immunotherapy: A Case Series from the Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO)

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy by harnessing the immune system to fight cancer, but are associated with significant immune-related adverse events (irAEs). Limited data is available on the safety of ICIs in patients with preexisting autoimmune diseases and on concomitant use of immunosuppressive drugs. CanRIO is a network of Canadian rheumatologists with experience in the management of rheumatic irAEs secondary to ICIs. In this case series, we describe the clinical course of patients with preexisting autoimmune diseases who were treated with ICIs at 7 CanRIO sites.

Methods: Patients referred for rheumatological evaluation in the context of immunotherapy between 2013 and March 2019 at participating CanRIO sites with preexisting autoimmune disease were identified. Standardized data were extracted by retrospective chart review. Descriptive statistics were used to summarize the data.

Results: A total of 25 patients with preexisting autoimmune disease who received ICI treatment were identified. Their age was 62.9 ± 11.9 (mean ± SD), 13 (52%) were male, and 23 (92%) were White. Mean (SD) follow-up was 13.1 (9.2) months. The most common indications for ICI were advanced lung cancer (n=13, 52%) and melanoma (n=9, 36%); 96% had stage 4 disease. Most patients received ICI monotherapy (Pembrolizumab: n=17, 68%; Nivolumab: n=6, 24%).

Preexisting autoimmune diseases included rheumatoid arthritis (RA, n=8), psoriasis (n=4), psoriatic arthritis (n=3), axial spondyloarthropathy (SpA, n=3), systemic lupus erythematosus (SLE, n=2), dermatomyositis (n=1), polymyalgia rheumatica (PMR, n=1) and other non-rheumatic diseases (n=3).

Of 8 patients with RA, 71% (5/7) were seropositive (RF ±anti-CCP) and 43% (3/7) had erosive disease. 50% (4/8) were in remission at time of ICI initiation, 29% (2/7) had their DMARDs stopped, 29% (2/7) continued their DMARD(s) and 43% (3/7) had new DMARD(s) started prophylactically. Overall, 50% (4/8) experienced grade ≤ 2 flares of their polyarthritis, 13% (1/8) developed PMR *de novo*and 38% (3/8) did not have any rheumatic irAE. Of those who developed rheumatic irAEs, 80% (4/5) received Nivolumab, 80% (4/5) had seropositive disease, 63% (5/8) were on DMARDs at time of ICI initiation and 80% (4/5) events occurred after a single dose of ICI.

Of 4 patients with psoriasis but without arthritis, 3 (75%) experienced a flare (both mild and major) of their skin disease and 3 (75%) developed *de novo* arthritis (grade 2-3) within the first 4 months of ICI treatment. Of 3 patients with axial SpA, two experienced new peripheral arthritis (grade 2) after receiving ICI.

Inflammatory arthritis responded to oral corticosteroids (up to 50 mg, tapered over 4-9 months) and/or addition of DMARDs (methotrexate, hydroxychloroquine and/or sulfasalazine), and required ICI discontinuation in 27% (3/11) of patients. Two patients with SLE remained in remission (on hydroxychloroquine).

Conclusion: This is the largest multicentered study of patients with rheumatic autoimmune diseases exposed to immunotherapy. Arthritis flares in patients with RA exposed to ICI are frequent despite DMARD background therapy. New onset of peripheral arthritis is frequent in SpA and psoriatic patients.

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Abstract Number: 2141

Rituximab Therapy for Interstitial Pneumonia with Autoimmune Features (IPAF): A Case Series of Nineteen Patients

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

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Session Time: 9:00AM–11:00AM

Characteristic	IPAF Patients (N=19)
Age at diagnosis, years, mean (SD)	60 (13)
Female sex (%)	10 (53%)
White (%)	16 (84%)
Black (%)	2 (11%)
Current smoking (%)	1 (5%)
Past smoking (%)	9 (47%)
Prior diagnosis of	
Heart failure (%)*	2 (11%)
Chronic obstructive pulmonary disease (%)	1 (5%)
Obstructive sleep apnea (%)	3 (16%)
Pulmonary emboli (%)	2 (11%)
Oxygen requirements, fraction of inspired oxygen (FiO_2), mean % (SD)	42% (27%)
Clinical manifestations	
Inflammatory arthritis (%)**	**7 (37%)**
Myalgia (%)	**6 (32%)**
Esophageal symptoms (%)***	**13 (68%)**
Sicca symptoms (%)	**6 (32%)**
Raynaud phenomenon (%)	**7 (37%)**
Puffy hands (%)	1 (5%)
Mechanic's hands (%)	2 (11%)
Proximal muscle weakness (%)	3 (16%)
Abnormal nailfold capillaroscopy (%)	2 (11%)
Required hospital admission for hypoxemia (%)	9 (47%)
Required intensive care unit admission for hypoxemia (%)	4 (21%)
Required mechanical ventilation for hypoxemia (%)	3 (16%)
Radiographic pattern on chest CT	

Table 1. Baseline characteristics of 19 patients with interstitial pneumonia with autoimmune features (IPAF) treated with rituximab.

	IPAF patients (N = 19)	Laboratory Reference Ranges
Creatine kinase, units/L, mean (SD)	**161.4 (253.4)**	**40 - 150**
Aldolase, units/L, mean (SD)	**10.2 (4.7)**	**< 7.7**
Erythrocyte sedimentation rate, mm/h, mean (SD)	**40.4 (33.6)**	**< 13**
C-reactive protein, mg/L, mean (SD)	**32.3 (43.4)**	**< 8**
Positive ANA (%)*	**9 (47%)**	
Homogeneous pattern (%)**	5 (56%)	
Speckled pattern (%)**	3 (33%)	
Centromere pattern (%)**	1 (11%)	
Positive anti-dsDNA (%)	1 (5%)	
Positive anti-Ro 60 kDa isoform (%)	3 (16%)	
Positive anti-Ro 52 kDa isoform (%)	**7 (37%)**	
Positive anti-La (%)	2 (11%)	
Positive anti-Smith (%)	2 (11%)	
Positive anti-RNP (%)	2 (11%)	
Positive anti-Scl-70 (%)	2 (11%)	
Positive rheumatoid factor (%)***	**6 (32%)**	
Positive anti-PL-7 (%)	1 (5%)	
Positive anti-Ku (%)	3 (16%)	
Positive anti-NXP-2 (%)	1 (5%)	

*ANA considered positive if titer ≥1:320
**Percentage of patients with a given pattern out of the 9 patients with positive ANA.
***RF counted as positive if ≥2 times the upper limit of normal
****No patients had a positive ANA in a nucleolar pattern, ANCA, anti-RNA polymerase III, anti-CCP, anti-PM/Scl, anti-melanoma differentiation-associated protein 5, or other myositis-associated or myositis-specific antibodies except as noted in the table.

Table 2. Baseline laboratory values of patients with interstitial pneumonia with autoimmune features (IPAF) prior to treatment with rituximab.

Background/Purpose: Interstitial lung disease (ILD) is a major cause of morbidity and mortality in patients with connective tissue diseases (CTD). Approximately one-third of patients with ILD have autoimmune manifestations not classifiable as a CTD, designated as interstitial pneumonia with autoimmune features (IPAF). To our knowledge, there are no studies examining the efficacy of rituximab (RTX) in IPAF. Here, we describe a case series of 19 patients with IPAF treated with RTX.

Methods: An institution-wide registry of patients seen consecutively at a large academic medical center from 2000-2018 was queried for patients aged ≥18 years with diagnostic codes for ILD, treatment with RTX, and positive autoantibodies (including ANA, RF, anti-CCP, anti-dsDNA, anti-Ro, anti-La, anti-Smith, anti-Scl-70, anti-tRNA synthetase, anti-PM-Scl, anti-melanoma differentiation-associated protein 5). Patients included met the 2015 classification criteria for IPAF (N=19) (Fischer A, et al., *Eur Respir J* 2015; 46:976-87). Patients were excluded if they had received RTX for a known autoimmune disease or malignancy. Clinical data and pulmonary function tests (PFTs) were collected by medical record review. Chest computed tomography (CT) scans were reviewed independently by 2 radiologists. Clinical improvement was based on a composite of clinician assessment, oxygen requirements, hospitalization, and survival. Only those subjects with PFTs within 3 months prior to or 1 month after RTX initiation and 6-18 months af-

Outcome	Patients with IPAF (N=19 for clinical assessment, N=10 for pulmonary function testing)
Clinically improved (%)*	**8 (42%)**
Clinically stable (%)*	**8 (42%)**
Clinically worsened (%)*	3 (16%)
Absolute change in percent predicted of forced vital capacity, mean % (SD)	8% (13%)
Absolute change in percent predicted of diffusion capacity of carbon monoxide, mean % (SD)	3% (13%)
Pulmonary function testing improved (%)**	**5 (50%)**
Pulmonary function testing stable (%)**	**3 (30%)**
Pulmonary function testing worsened (%)**	2 (20%)
Tapered off corticosteroids completely (%)	6 (32%)

*Definition based on composite of clinician assessment, change in oxygen requirements, need for hospitalization, and survival.
**Improvement defined as ≥10% improvement in forced vital capacity. Stable defined as forced vital capacity within +/- 10% of prior measurement. Worsening defined as ≥10% decline in forced vital capacity.

Table 3. Outcomes after treatment with rituximab in patients with interstitial pneumonia with autoimmune features (IPAF).

ter RTX initiation were included in the PFT analysis (N=10); PFT improvement was defined as ≥10% improvement in forced vital capacity (FVC).

Results: To date, we have identified 19 patients with IPAF treated with RTX, with median follow up time of 24 months (**Table 1**). Several patients had inflammatory arthritis, myalgia, esophageal symptoms, and Raynaud phenomenon at the time of diagnosis. Sixteen patients had chest CT features of non-specific interstitial pneumonia (NSIP), organizing pneumonia (OP), or a combination of NSIP and OP. The creatine kinase, aldolase, ESR, and CRP levels were elevated (**Table 2**). The average number of RTX doses received was 7, over a median follow up time of 24 months (range 8-120 months).

After treatment with RTX, sixteen patients (84%) were improved or stable based on clinical parameters (**Table 3**). Among the ten patients with PFTs within the designated timeframe, the absolute changes in FVC percent predicted was +8% (SD 13%) and diffusion capacity of carbon monoxide (DLCO) was +3% (SD 13%). No patients stopped therapy due to adverse events. One patient died due to respiratory failure. Six patients were tapered off glucocorticoids completely after 1 year of treatment with RTX.

Conclusion: In this case series of 19 patients with IPAF treated with RTX, most patients appear to have had improvement or stability. These findings call for prospective studies, including potential randomized controlled trials, to further determine the risks and benefits of RTX use in IPAF.

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Abstract Number: 2142

Frailty in Systemic Rheumatic Diseases: A Systematic Review

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SESSION INFORMATION
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Background/Purpose: Frailty, a state of decreased homeostatic reserve, is well studied in the elderly and is independently associated with increased morbidity and mortality. Many systemic rheumatic diseases are increased in the elderly and can similarly be associated with poor outcomes. To our knowledge, there are no systematic reviews evaluating frailty in inflammatory rheumatic conditions. Thus, we performed a systematic review to evaluate the prevalence of frailty and the association of frailty with health-related outcomes in patients with systemic rheumatic disease.

Methods: A search of Ovid MEDLINE, Ovid Embase, the Cochrane Library, the Cumulative Index to Nursing and Allied Health Literature, AgeLine, and Scopus was conducted from database inception to January 2019 to identify original research articles and abstracts about frailty and inflammatory rheumatic conditions. Studies addressing frailty, using all definitions, and any inflammatory rheumatic disease were eligible. Data extracted included study design, patient characteristics, frailty instruments, and health-related outcomes. Risk of bias was assessed using the Newcastle-Ottawa scale for cohort and cross-sectional studies and the Cochrane Risk of Bias Tool for randomized controlled trials (RCTs). Two investigators reviewed each study. Disagreements were resolved by a third reviewer. The study was registered prospectively in PROSPERO and conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Figure 1. PRISMA flow diagram

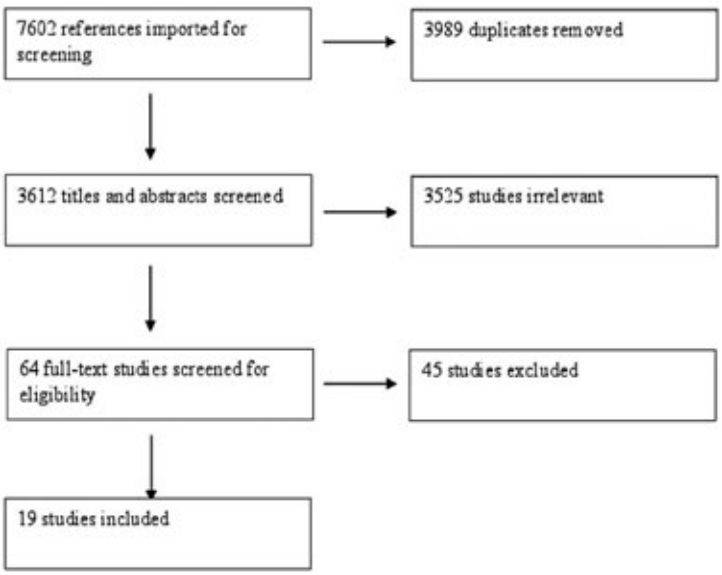

Table 1. Characteristics of included studies

Source	Study Design	N	Rheumatic Condition	Frailty Scale	Results
Andrews et al. 2017* (United States)	Cross-sectional study	124	RA	Fried phenotype	Frailty was associated with increased disability in RA as measured by Valued Life Activities after adjustment for confounders.
Bagshaw et al. 2016* (Canada)	Prospective cohort study	197	Rheumatoid/connective tissue disease	Canadian Study of Health and Aging Clinical Frailty Scale	Rheumatoid/connective tissue disease was associated with prehospital frailty in patients admitted to the intensive care unit.
Bernelli et al. 2015* (taly)	Case series	6	SSc	Not defined	Frailty was evaluated in all patients with SSc in whom transaortic valve implantation was performed.
Blunn KJ et al. 2010 (United Kingdom)	Prospective cohort study	207	RA	Subjective assessments in combination with age and Health Assessment Questionnaire	Frailty was identified as a reason for RA monotherapy or lack of therapy.
Cano-Garcia et al. 2014 (Spain)	Cross-sectional study	16	RA, SLE, SSc, PsA	Barthel Index	87.5% of participants with rheumatic diseases were frail.
Chang et al. 2010* (United States)	Cross-sectional study	620	RA	Fried phenotype	RA was associated with increased odds of frailty.
Cleutjens et al. 2018 (Netherlands)	Cross-sectional study	Unspecified	RA	Groningen Frailty Indicator	Frail patients with RA were more often female and reported lower health status and worse social and psychological domains.
Guler et al. 2017* (Canada)	Cross-sectional study	86	SSc-associated interstitial lung disease	42-Item Frailty Index	Dyspnea was associated with the frailty index

Results: Of 7602 abstracts identified, 64 full-text abstracts and articles were available for review, and 19 were included (Figure 1). These included 1 RCT, 9 prospective cohort studies, 7 cross-sectional studies, 1 retrospective cohort study, and 1 case series. Eleven studies included participants with RA, 4 studies included participants with SSc, 2 studies included participants with SLE, 3 studies included participants with vasculitis, 1 study included participants with PsA, and 2 studies included participants with non-specific “connective tissue disease.” Given study heterogeneity, meta-analysis was not conducted. Risk of bias varied across studies. Frailty was prevalent in multiple systemic rheumatic diseases and associated with poor clinical outcomes, including increased disability and mortality (Table 1).

Conclusion: To our knowledge, this is the first systematic review exploring the relationship between frailty and systemic rheumatic diseases. Frailty is prevalent in multiple systemic rheumatic diseases and is often associated with poor clinical outcomes. Further study is needed to determine risk factors for frailty in systemic rheumatic disease, including risks for progressing from pre-frail to frail. Using standardized frailty instruments will facilitate comparisons between diseases and patient populations.

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Abstract Number: 2143

Neuromyelitis Optica Overlaps Frequently with Systemic Rheumatic Diseases in African-Americans: Experience at a Large US Academic Medical Center

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SESSION INFORMATION
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Background/Purpose: Neuromyelitis optica (NMO) and neuromyelitis optica spectrum disorders (NMOSD) are immune-mediated demyelinating disorders of the central nervous system, primarily characterized by optic neuritis and longitudinal extensive transverse myelitis. Antibodies to aquaporin-4 (AQP4-IgG) are highly specific markers of NMOSD. The coexistence of NMOSD with systemic rheumatologic autoimmune disease has been well documented, especially systemic lupus erythematosus (SLE) and Sjogren syndrome (SS) [1]. Several recent studies have demonstrated that NMOSD may disproportionately affect black patients [2,3]. Our objective was to characterize African-Americans diagnosed with NMO at our academic medical center, and identify any associated systemic rheumatologic autoimmune diseases.

Methods: We conducted a retrospective chart review of adult African-American patients diagnosed with NMO at a single academic medical center between 2011 and 2017. The charts reviewed were identified using ICD codes for NMO, transverse myelitis and optic neuritis. The diagnosis of NMO was then confirmed as per the 2015 International Consensus Diagnostic Criteria. The diagnosis of SLE and SS were also confirmed based on existing diagnostic criteria.

Results: Of the 60 charts reviewed, 25 patients (41.7%) met criteria for NMO, and of those, 21 patients (84%) were African-American. Of the 21 African-American NMO patients, 89.5% (n=19) were AQP4-IgG positive, 95.2% were women, and 38.1% had an associated systemic rheumatologic autoimmune disease (SLE 62.5% and primary SS 37.5%). In 60% of the NMO patients with SLE, the diagnosis of NMO preceded the SLE diagnosis. Conversely, in 100% of the NMO patients with SS, the diagnosis of NMO either followed, or was made simultaneous to, the SS diagnosis. Notably, 80% of the SLE patients had primarily hematologic manifestations. ANA was positive in 78.6% of the African-American patients in whom ANA testing was performed (n=14), with anti-SSA (64.3%, n=14) and anti-SSB

(50%, n=11) the next most prevalent autoantibodies. Mean age of NMO onset was 46.7 years (SD 13.6). Transverse myelitis was the most common presenting manifestation (71.4%), followed by optic neuritis (61.9%).

Conclusion: Our population had a higher mean age of onset (46.7 vs 33 years) compared with other cohorts of seropositive NMO African-Americans [2]. Additionally, African-Americans with NMO at our institution had a higher female:male distribution than has been documented[3]. Not surprisingly, SLE was the most common associated systemic rheumatic disease in our cohort, however the frequency of SLE and ANA positivity in our NMO cohort was higher than has been reported (23.8% and 78.6%, respectively) [4]. Additional larger studies are needed to further explore how NMOSD in African-Americans may differ from other populations.

Disclosure: M. Belsky, None; **S. Dia**, None; **H. Amer**, None; **C. Collins**, Exagen, 2, 5; **K. Loupasakis**, Exagen, 2.

Abstract Number: 2144

Musculoskeletal Immune-Related Adverse Events After Immune Checkpoint Inhibitor Therapy: Single Center Experience

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Background/Purpose: Immune checkpoint inhibitors (ICI) are new anti-cancer agents used for lung cancer, melanoma, renal cell and urothelial carcinoma, and head and neck cancers. They activate anti-tumor immunity which hampers self-tolerance leading to many immune related adverse events (irAE) commonly affecting the skin, endocrine organs and GI tract. Historically, rheumatologists report limited experience and confidence in the management of irAEs. We report our single-center experience with musculoskeletal irAEs.

Table. Characteristics of melanoma patients and immune related adverse events

#	IrAEs	Grade	IrAE treatment	Interruption of ICI	Cycle	Freq	ICI	Combo or mono	Other IrAE	Prior autoimmune disease	Age	Sex	Race
1	Arthritis (Seronegative RA)	2	MTX	No	1	3 wks	Pembro	Mono	None	No	75	M	Caucasian
2	Arthralgia or arthritis	2	Prednisone	Yes	6	3 wks	Pembro	Mono	Rash, hyperthyroidism	No	81	F	Caucasian
3	Arthralgia or arthritis	2	Prednisone	No	7	3 wks	Pembro	Mono	Rash	No	81	M	Caucasian
4	Arthralgia	2	None	No	2	3 wks	Ipilumumab	Mono	Rash	No	26	F	Caucasian
5	Arthralgia	2	None	Yes	15	3 wks	Pembro	Mono	Rash, pneumonitis	No	62	M	Caucasian
6	Arthritis	2	Prednisone	No	4	2 wks	Ipilumumab	Mono	Autoimmune adrenalitis	No	73	M	Caucasian
7	Myalgia	2	Prednisone	Yes	1	3 wks	Ipi+Nivo	Combo	Hypothyroidism	No	80	M	Caucasian
8	Myositis	3	Prednisone	Yes	2	3 wks	Pembro	Mono	Hepatitis	Yes (MS)	66	M	Caucasian
9	Arthritis	2	Prednisone	No	4	3 wks	Pembro	Mono	Colitis, rash	Yes (RA)	62	F	Caucasian
10	Myalgia	2	None	Yes	19	3 wks	Pembro	Mono	Rash	No	62	F	Caucasian
11	Arthritis (Seronegative SPA)	3	Tocilizumab	Yes	9	2 wks	Nivolumab	Mono	Rash	No	45	F	Caucasian
12	Arthralgia	N/A	Prednisone	No	2	3 wks	Pembro	Mono	None	No	65	M	Caucasian

ICI: immune checkpoint-inhibitor, RA: rheumatoid arthritis, MS: multiple sclerosis, SPA: spondyloarthropathy, MTX: methotrexate, Pembro: pembrolizumab, Combo: combination, Ipi: ipilumumab, Nivo: nivolumab, N/A: not available, wks: weeks

Methods: University of Pittsburgh melanoma patients treated with ≥1 dose of a PD-1 inhibitor between 2011-2018 were analyzed. Demographic data, cancer diagnosis and treatment and the type and treatment of irAEs were obtained via retrospective chart review.

Results: The melanoma cohort included 130 patients with 12 (9.2%) developing ≥ grade 2 arthralgia, arthritis, myalgia or myositis. The mean age was 64.8 (± 16.1) and included 7 males and 5 females. Nine subjects developed ≥ grade 2 arthralgia/arthritis (6.9%) and two had grade 2 myalgias (1.5%) while there was 1 case of myositis (0.7%). Fifty percent of patients had their cancer treatment interrupted and the patient developing myositis was hospitalized. IrAEs occurred after a median of 4 (IQR 2-7.5) cycles and 66 (IQR 20.2-145) days after initiation of cancer treatment and was grade 2 in 81% of cases. Cancer treatment included pembrolizumab (n:8), ipilimumab (n:3) and nivolumab (n:1) in subjects with irAEs, and was single agent in 92% of the cases. Eighty-three percent of the cases developed other non-musculoskeletal irAEs, with rash (80%) the most common followed by thyroid abnormalities (20%). One melanoma patient with pre-existing rheumatoid arthritis (RA) flared with synovitis after 19 ICI cycles and was treated with a short course of prednisone. Treatment of the irAEs included prednisone alone in 58% and at least one additional agent in in 2 (17%) of the cases, all of whom significantly improved. Of the latter 2 cases, 1 was diagnosed with seronegative RA that responded to methotrexate while the other patient had a new diagnosis of seronegative spondyloarthropathy treated with sulfasalazine (discontinued due to rash), methotrexate (ineffective) and later responded to tocilizumab. The subject with myositis was hospitalized with muscle weakness and an elevated creatine kinase (CK) of 1058 U/L and responded to glucocorticoids. Two patients with myalgias and a normal CK improved with ICI discontinuation in one and a short course of prednisone with ICI monotherapy in the second case.

Conclusion: In summary, approximately 10% of melanoma patients receiving immunotherapy developed musculoskeletal irAEs with 50% requiring interruption in cancer treatment, and most (75%) requiring glucocorticoids or other immunosuppressive therapy. Musculoskeletal irAEs responded well to prednisone alone in 80% of cases, while 20% required an additional immunosuppressive agent. As more ICIs are used, it will be necessary to conduct prospective assessments of toxicity in order to better ascertain the frequency as well as to optimally manage the irAES to allow for continuation of effective cancer therapy.

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Abstract Number: 2145

Long-term Safety of Tildrakizumab in Patients with Moderate-to-Severe Plaque Psoriasis: Incidence of Severe Infections Through 3 Years (148 Weeks) from 2 Phase 3 Trials

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Background/Purpose: Tildrakizumab (TIL) is a high-affinity anti–interleukin-23p19 monoclonal antibody approved for the treatment of moderate-to-severe plaque psoriasis. The objective of this study was to evaluate severe infections in the phase 3 reSURFACE 1 (NCT01722331) and reSURFACE 2 (NCT01729754) trials.

Methods: This is a post hoc pooled analysis of adult patients with moderate-to-severe plaque psoriasis from two 3-part, parallel group, double-blinded, randomized, controlled trials; reSURFACE 1 (64 week) and reSURFACE 2 (52 week). Detailed methodology has been previously published.[1] Safety data over 148 weeks, pooled across trials and treatment groups, were included. Groups were defined as placebo, etanercept (until week 28), TIL 100 mg (100 mg-only in at least 1 part of the study), TIL 200 mg (200 mg-only in at least 1 part of the study), continuous TIL 100 mg (100 mg throughout the 3 double-blind parts plus open-label extension), continuous TIL 200 mg (200 mg throughout all parts), TIL 100/200 mg (any TIL dose in at least 1 part), and continuous TIL 100/200 mg (consistently exposed but dose could change throughout all parts). Severe infections were defined as any infection meeting the regulatory definition of a serious adverse event (SAE) or requiring intravenous antibiotics, irrespective of whether it was reported as an SAE. Exposure-adjusted incidence rates (EAIR) were reported.

Results: Overall, 928 patients on TIL 200 mg, 872 on TIL 100 mg, 316 on continuous TIL 200 mg, 352 on continuous TIL 100 mg, 543 on placebo, 1646 on TIL 100/200 mg, 808 on continuous TIL 100/200 mg, and 313 on etanercept were included. The EAIR of severe infections was 1.12/100 subject-years of exposure among TIL 200 mg, 1.14 (TIL 100 mg), 0.88 (continuous TIL 200 mg), 0.64 (continuous TIL 100 mg), 0.97 (placebo), 1.11 (TIL 100/200 mg), 0.86 (continuous TIL 100/200 mg), and 1.96 (etanercept). Most commonly reported types of severe infections included appendicitis, cellulitis, diverticulitis, and sinusitis.

Conclusion: Tildrakizumab had a favorable long-term safety profile as demonstrated by a low rate of severe infections (lower than etanercept and comparable to placebo) in patients with moderate-to-severe plaque psoriasis.

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Reference:

1. Reich et al., *Lancet*, 2017; 390(10091): 276-288

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Abstract Number: 2146

Complications of Immune Checkpoint Inhibitor Therapy in Patients with and Without Pre-existing Rheumatologic Disease

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) are effective therapies in the treatment of many cancers, but their use has been linked with immune-related adverse events (irAEs). As use of ICIs becomes more widespread, more patients are developing irAEs including rheumatologic manifestations. Thus, it is important that clinicians monitor for irAEs and identify patients who may be at increased risk for developing them. We sought to describe the prevalence and presentation of irAEs, both in general and specifically rheumatologic, in order to better characterize their clinical manifestations and recognize potential predisposing risk factors. We hypothesized that patients with preexisting rheumatologic disease would experience irAEs at an increased rate compared to those without preexisting conditions.

Methods: We performed an IRB approved retrospective review using an EMR database of patients treated with ICIs at our institution from January 2011 to April 2017. We reviewed charts to assess for the presence of preexisting rheumatologic disease as well as the development of irAEs during ICI treatment. In patients who experienced an irAE, we determined whether they required additional work up, glucocorticoid treatment, hospitalization, or cessation of ICI therapy. To see if there was an association between preexisting rheumatologic disease and developing irAEs, we did comparative analysis using the Fisher exact test.

Results: Of 420 patients treated with ICIs, 4.8% (n=20) experienced rheumatologic irAEs. As a result, 4 were referred for rheumatology consultation, 7 were treated with glucocorticoids, 3 had to delay or stop ICIs, and 0 required hospitalization. Preexisting rheumatologic disease was present in 4.8% (n=20). In this subgroup, 65% (n=13) developed any irAE compared to 43% (n=172) of those without preexisting rheumatologic disease (p=0.065). 15% (n=3) developed a rheumatologic irAE compared to 4.25% (n=17) of those without preexisting rheumatologic disease (p=0.063).

Conclusion: We did not detect a statistically significant difference in the rates of irAEs in patients with preexisting rheumatologic disease; however, this study was limited by its retrospective design and relatively small sample size. Given that p-values neared significance, it is possible that this study was underpowered to detect a true relationship and thus additional, larger studies would be beneficial to further investigate. Overall, the majority of rheumatologic irAEs did not require treatment or lead to cessation of ICI therapy. This suggests that even if there is found to be a significant relationship between preexisting rheumatologic disease and the development of irAEs, this risk factor should not preclude this population from receiving ICI therapy but would require careful monitoring and collaboration between these patients' oncologists and rheumatologists.

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Abstract Number: 2147

Musculoskeletal Ultrasound Enhances the Evaluation of Checkpoint Inhibitor Associated Musculoskeletal Immune Related Adverse Events

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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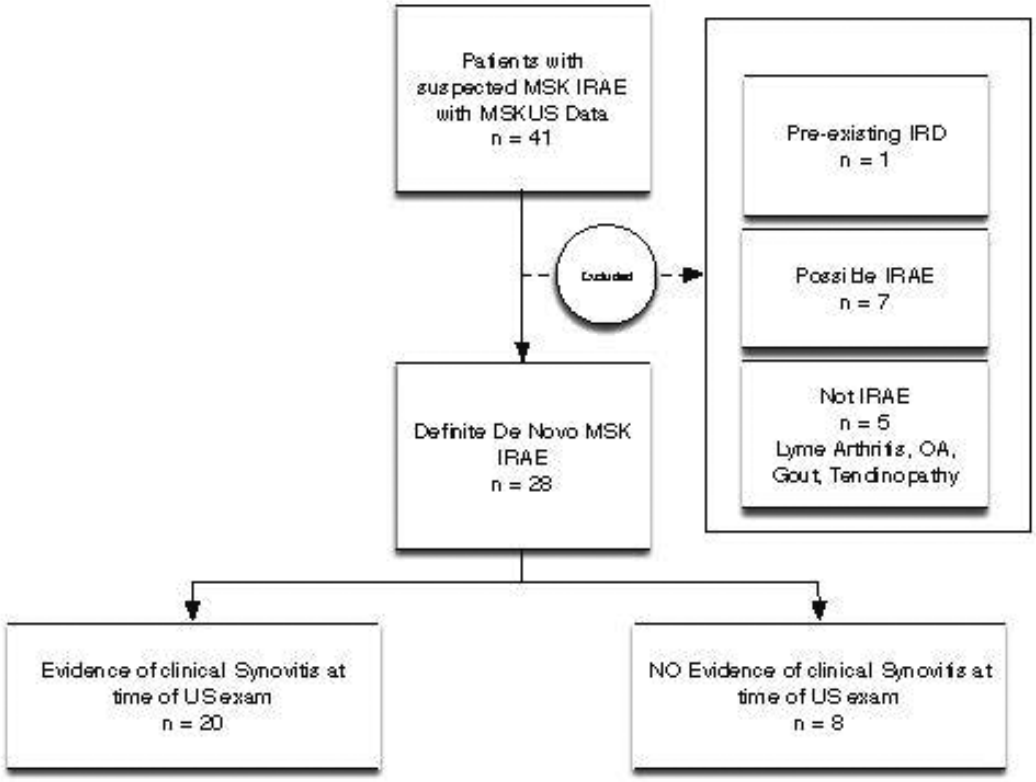
Background/Purpose: Cancer immunotherapy with monoclonal antibodies that antagonize molecular checkpoint pathways in immune activation, the PD-1/PDL1 axis and CTLA-4, have revolutionized the treatment of solid cancers. These therapies however are limited by immune related adverse events (irAEs), including inflammatory arthritis (irIA). Presentations can be subtle, and recognition delayed. Here we describe point-of-care musculoskeletal ultrasound (MSKUS) findings in patients with solid cancer treated with checkpoint inhibitors.

Methods: Patients >18 years treated with an ICI at our tertiary care center from 2011-2019 were seen by rheumatology for evaluation of musculoskeletal symptoms following ICI. Forty-one patients with suspected MSK irAEs had MSKUS performed and interpreted by the same ultra-sonographer. Findings were reviewed and confirmed by a blinded US reader. US findings in patients with confirmed de novo MSK irAEs were reviewed and correlated with the presence or absence of documented clinical synovitis and with available synovial fluid analysis.

Results: Twenty-eight out of forty-one patients had definite de novo MSK irAE, five patients had an alternative etiology identified with assistance of diagnostic MSKUS, 1 patient had pre-existing rheumatoid arthritis, and 7 patients were classified as possible MSK irAE when diagnosis was uncertain (Figure 1). Twenty out of the twenty-eight patients with definite de novo MSK irAE had clinical evidence of synovitis at the time of initial MSKUS examination, while 8 did not. Among patients with clinically evident synovitis, MSKUS examination confirmed inflammatory pathology in all patients. The most common MSKUS features identified were grade 2 or higher synovial thickening (80%), hyperemia measured by color power Doppler (CPD) signal (70%), tenosynovial proliferation (60%), and moderate or large effusion (45%). Among the 8 patients without clinically evident synovitis, the initial US examination identified inflammatory synovial or tenosynovial pathology in 6 patients (75%); in 2 patients, inflammatory features evolved only on follow up and were identified by MSKUS examination. Fourteen patients with definite de novo MSK IRAE had synovial fluid analysis; 6 patients had synovial fluid cell counts < 2000 cells/μl. Of these 6 patients with synovial analysis



NOT IRAE	An alternative explanation for patients symptoms and signs identified and more likely cause of symptoms.
POSSIBLE IRAE	MSK pathology potentially though not unequivocally correlating with ICI therapy and/or insufficient follow up data to assess for evolution in equivocal cases. Alternative diagnosis is felt to be equally possible.
DEFINITE IRAE	MSK pathology unequivocally correlating with ICI therapy and alternative etiology excluded based on history/exam/imaging/labs

Figure 1. Overview of Patients on Immunotherapy and MSK Symptoms with MSKUS Data

within the 'non-inflammatory' range, all patients had grade 2 or higher synovial thickening, 50% had moderate or large effusions, 50% had tenosynovial proliferation, and 33% had evidence of hyperemia (+CPD). All 6 patients required steroids (intra-articular or oral) and initiation of DMARD therapy at first or subsequent visits with improvement in symptoms.

Conclusion: Point-of-care MSKUS is a valuable tool for confirming inflammatory pathology and expediting early identification of subclinical synovitis or tenosynovitis among patients with ICI-therapy associated MSK symptoms. Additionally, MSKUS helps identify patients with inflammatory features when synovial fluid analysis is within the traditional non-inflammatory range and assists in excluding alternative etiologies.

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Abstract Number: 2148

Muscle Involvement Revealed by 18F-PET-CT in Polymyalgia Rheumatica

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Imaging techniques in polymyalgia rheumatica (PMR) have revealed mainly bursitis, tenosynovitis, capsulitis and enthesitis. This is also the case for 18F-FDG-PET-CT. This technique, which has shown its interest for the diagnosis of PMR, allows an assessment of the metabolic activity of the entire musculoskeletal system and in particular of muscle structures.

The aim of this study was to evaluate muscle damage using 18F-FDG-PET-CT in PMR.

Methods: This is a retrospective study including patients with PMR (ACR/EULAR 2012 criteria) seen in our department, who had an 18F-FDG PET-CT examination between September 2012 and November 2018. A control group consisting of subjects without rheumatologic manifestations who had such an examination as part of neoplastic research or neoplastic disease control was also evaluated. PET evaluation included 17 sites suggestive of PMR, as previously reported [1], leading to a global PET score ranging from 0 to 51. Muscle hyper metabolism areas were similarly rated according to the same Goerres classification [2](0 = no uptake; 1 = slight uptake, less than liver; 2 = uptake like liver; 3 = uptake higher than liver). Muscle activity sites have been identified. A comparison of PMR patients with and without muscle involvement was performed using the Mann Whitney or Fisher's exact test.

Results: 134 cases were reviewed, concerning 80 PMR (mean age 67.9) and 54 "controls" (mean age 68.1). Overall, PET muscle damage was observed in 27 cases (34%) in PMR and 6 cases (11%) in controls (p=0.004). The damage is bi or multi-focal in 16/27 cases. The affected muscular sites are: thighs and ischium-leg (n = 10), spinal (11), piriform/buttocks (7), pectoral (5), large serrated (4), subspinatus/subscapular (3), deltoid (1), trapezius (1). Fasciitis was found in 4 cases. As expected, PMR patients exhibited higher TEP scores than controls ($p< 0.001$). In PMR patients, PET muscle involvement was associated with higher ESR values ($p< 0.05$), but not with age, CRP or global PMR PET score.

Conclusion: Muscle involvement assessed by 18F-Fluorodeoxyglucose PET-CT is frequent in PMR (1/3 of cases), located at usual sites of symptoms of the disease, without association with age, CRP levels or global PET score for PMR. Muscle should be carefully evaluated during PET in cases of PMR; these pictures may be a new diagnosis feature of the disease.

References:

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2 Goerres GW, et al. Clin Nucl Med 2006;31:386-90.

Abstract Number: 2149

Principal Components Analysis as a Tool to Identify Lesional Skin Patterns in Cutaneous Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies
Session Type: Poster Session (Tuesday)
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Background/Purpose: Cutaneous lupus erythematosus (CLE) has multiple subtypes that account for a broad range of presentations. The preferential locations of skin lesions have only been described based on clinical experience, and statistical approaches are lacking. The principal component analysis is a dimension reducing test that seeks to describe variability amongst observed, correlated variables through a set of latent, or unobserved, variables called factors.[1] We propose that an analysis of this type will better characterize CLE subtypes in an objective way, particularly with regards to clinical aspects and location of skin lesions.

Methods: We conducted a cross-sectional analysis of patients enrolled in the Cutaneous Lupus Registry at the University of Texas Southwestern Medical Center from November 2008 to July 2018. Components of the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) were scored by one dermatologist (BFC) for 303 patients. We then ran a principal components analysis on these patients using IBM SPSS v. 25.

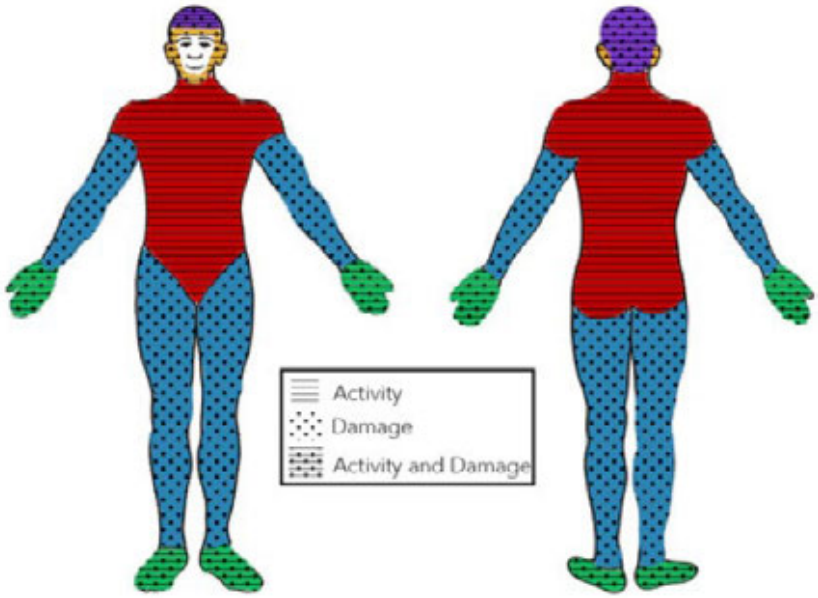

Figure 1. CLE skin lesion patterns identified by PCA. We extracted five factors with significant associations of body sites and clinical features in this cohort of CLE patients. Each color corresponds to the distribution described by each factor - red for factor 1, orange for factor 2, blue for factor 3, green for factor 4 and purple for factor 5. The overlying patterns represent the CLASI components that loaded highly for that factor – stripes for activity, dots for damage, and stripes and dots for both. Of note, factor 1 also had involvement of arms and factor 3 had involvement of chest, back and buttocks, which are not depicted here.

Results: Our results showed that around half of the variance was explained in the first five factors alone (F1 through F5). The factors correlated with well-known subtypes. F1 delineated patients with high CLASI activity scores in the neck, chest, arms and back, and resembled patients with subacute CLE, based on the trunk and arm preference with high activity scores (**Figure 1,** *red***).** F2 described patients with high CLASI damage scores on the scalp, ears and face (**Figure 1,** *orange***).** while F3 characterized patients with damage on the posterior neck, back/buttocks, arms and legs (**Figure 1,** *blue***)**. Because of their predilection for higher damage scores, F2 and F3 resembled localized and generalized discoid lupus, respectively. F4 characterized damage only predominately on acral surfaces, favoring chilblains lupus (**Figure 1,** *green***)**. F5 described patients with activity and damage in the scalp, which could resemble patients with discoid lupus limited to involvement of the scalp (**Figure 1,** *purple***)**.

Conclusion: The principal component analysis helps characterize where on the body lesions of CLE tend to occur, in terms of activity and damage, in certain patient demographics. These results further clinical knowledge about the nature of CLE lesions, and may help guide clinical decisions in the future.

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Abstract Number: 2150

Frequency of Polyautoimmunity in a Tertiary Hospital

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SESSION INFORMATION
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Background/Purpose: Polyautoimmunity (PAI) is the presence of more than one Autoimmune Disease (AID) in one patient. PAI have been reported in different AIDs as systemic lupus erythematosus (SLE) (33-45%), rheumatoid arthritis (RA) (13-23%), systemic sclerosis (SSc) (10-43%) or Sjögren Syndrome (SS) (32-52%). On the other hand, Multiple Autoimmune Syndrome (MAS) where three or more AIDs coexisting in one patient has been reported.

The aim of the present study is to determine PAI frequency in the context of AIDs reported in a tertiary hospital.

Methods: Cross-sectional observational study with systematic revision of patients' electronic clinical records with AIDs (from 2014 to 2018). We selected those patients who had two or more diagnosis of AIDs. Demographic, clinical and immunological data were collected.

Results: Of 1854 patients with AIDs, 96 (5.17%) had PAI. Mean age was 56±15 years and 93.75% were female. 7 patients from the 96 (0.4%) also had MAS.

The mean age at diagnosis of the first AID was 39.03±15.93 years and mean age at diagnosis of the second AID was 48.16±15.04 years. A mean difference of 9.17±10.18 years between first and second AIDs debut was observed.

RHEUMATIC AUTOINMUNE DISEASES	TOTAL CASES	POLYAUTOIMMUNITY CASES	FREQUENCY (%)
APS	70	23	32.86
SS	154	42	27.27
SLE	261	41	15.71
SSc	88	5	5.68
RA	926	46	4.97
Vasculitis	83	4	4.82
Psa	371	7	1.89

NON RHEUMATIC AUTOINMUNE DISEASES	POLYAUTOIMMUNITY CASES
IBD	12
AHyp	9
CD	7
DM-1	2
AHep	1

The most frequent AIDs registered are shown in table 1.

Antiphospholipid syndrome (APS), Sjögren syndrome (SS), Systemic lupus erythematosus (SLE), Systemic sclerosis (SSc), Rheumatoid arthritis (RA), Psoriasic arthritis (PsA), Inflammatory bowel disease (IBD), Autoimmune hypothyroidism (AHyp), Celiac disease (CD), Diabetes mellitus type 1 (DM-1), Autoimmune hepatitis (AHep).

The most frequent PAI cases registered were RA-SS (N=23), SLE-APS (N=17), SLE-SS (N=11), AR-IBD (N=7), RA-SLE (N=5), RA-CD (N=5), SS-SSc (N=4) and PsA-IBD (N=4).

In the total group of 1854 patients with AIDs, SLE with PAI was present in 41 (2.21%) patients, SS with PAI in 42 (2.26%), RA with PAI in 46 (2.48%) and APS with PAI in 23 (1.2%). Moreover, SS was present in the 4.21% of SLE patients and in the 2.48% of RA patients. In contrast, APS was present in the 6.51% of SLE patients, being de of 7.64 (17.62) years the difference between the onset of the first AID and the second AID.

In the MAS group an AHyp-SLE-APS in 2 patients was observed, as well as 1 patient with SLE-SS-Aps, 1 with SS-RA-APS, 1 with RA-vasculitis-AHyp and 1 with SS-Ahyp-Ahep.

Conclusion: A 5.17% frequency of patients with PAI in our group of AID patients was observed, mostly women. APS, SS and SLE respectively were the diseases that most PAI showed. The most frequent association of AID diseases in PAI cases were RA-SS, APS-SLE and SS-SLE.

We found a rather lower frequency compared with those published in the literature, possibly due to the putative bias of retrospective studies and the geographical differences of PAI patients.

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Abstract Number: 2151

Patient Reported Outcomes and Factors Predicting Clinical Disease Activity in Patients with Immune-Checkpoint Inhibitor Inflammatory Arthritis

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SESSION INFORMATION
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Background/Purpose: Immune checkpoint inhibitors (ICIs) enhance anti-tumor immunity by stimulating a patient's immune system to fight cancer. ICIs have demonstrated unprecedented response rates in a wide array of cancers, but have a unique side effect profile known as immune-related adverse events (irAEs) that can result in significant morbidity and mortality. Inflammatory arthritis (IA) is one of the most commonly encountered rheumatic irAEs and can persist after ICI cessation. Early recognition and appropriate treatment is critical to avoid erosive joint damage. Clinical Disease Activity Index (CDAI) is a commonly used scale for disease severity and guides therapeutic strategy in rheumatoid arthritis, which can also be utilized in ICI-induced IA to inform clinical approach. Additionally, other patient-reported outcome measures (PROs) are used to evaluate pain, physical function, and quality of life in rheumatic diseases. In this study, we evaluate PROs and disease activity to establish the impact of ICI-induced IA. We also evaluate the factors correlating with CDAI, so that management can be optimized to facilitate the goal of achieving remission.

Variable	Median (IQR)
Age	59 (IQR 52-69)
Patient Global Assessment (0-100)	35 (15-50)
Patient Fatigue (0-100)	40 (10-60)
Patient Pain (0-100)	50 (20-76)
Patient Stiffness (0-100)	53 (40-75)
mHAQ (0-3)	0.31 (0-0.72)
Physician Global Assessment (0-100)	24.5 (12.5-33.8)
Tender Joints (0-28)	2 (0.25-3.8)
Swollen Joints (0-28)	6 (2.3-10.5)
CDAI	14.2 (7.4-21.5) Remission: n =0 (0%) Low: n=21 (35%) Moderate: n= 26 (43.3%) High: n=13 (21.7%)

Oncologic diagnosis	Melanoma: 20 (33.3%) Non-SCLC: 11(18.3%). (Other tumor types included pancreatic cancer, basal cell carcinoma, endometrial cancer and renal cell carcinoma)
Cancer stage	Stage III: 14 (13.0%) Stage IV: 46 (86.8%)
ICI therapy	Anti-PD1 monotherapy: 39 (65%) Anti-CTLA4/PD1 combination: 15 (25%) Anti-CTLA4 monotherapy: 3 (5%) Anti-PDL1 monotherapy: 3 (5%)
Number of irAE	Median: 1 (IQR 1-3) • 1 irAE: 34 (56.7%) • >1 irAE: 26 patients (43.3%)

Methods: Patients evaluated at an academic Rheumatology clinic with confirmed ICI-induced IA who were enrolled in our prospective cohort study of rheumatic irAEs were included. Patient and physician data from questionnaires at the baseline visit were analyzed to obtain median and interquartile range (IQR) values. CDAI and Modified Health Assessment Questionnaire (mHAQ) scores were calculated. Univariate analysis was completed to assess factors that impacted CDAI score. Multivariate linear regression analysis was performed with variables that were significant in univariate analysis to identify the factors that yielded the greatest impact upon CDAI.

Results: Sixty patients were included in the analysis. 33 patients (55%) were female. Clinical characteristics and PROs are summarized in Table 1.

Oncologic history, immunotherapy regimen, and irAE are detailed in Table 2.

Univariate analysis revealed a significant relationship between CDAI and patient stiffness (p 0.001), patient fatigue (p 0.019), mHAQ score (p 0.03) and patient pain (p 0.0001), while age (p 0.212), cancer stage (p 0.9), number of irAEs (p 0.575) were not significant. In multivariate analysis, pain exerted a significant influence on CDAI (0.001).

Conclusion: Patients with ICI-induced IA have high levels of disease activity and experience significant impairment. The majority of patients have moderate or high disease activity. This is significant given the increasing incidence and prevalence of this disease entity. Furthermore, patient-reported pain, fatigue, and stiffness correlated with CDAI in these patients. Physicians should recognize and address these primary symptoms in order to optimize management. Assessment of a wider range of PROs may provide additional insight into the factors that could be modified to maximize health-related quality of life, enhance physical function, and reduce disease activity.

NSCLC:non-small cell carcinoma; anti-PD1: anti-programmed cell death protein-1; anti-PDL1: anti-programmed cell death ligand-1; anti-CTLA4: anti- cytotoxic T-lymphocyte-associated protein-4

Disclosure: C. Connolly, None; **T. Braaten**, None; **A. Shah**, Bristol Meyer Squibb, 5, Bristol-Myers Squibb, 5; **C. Bingham**, Abbvie, 5, AbbVie, 5, BMS, 2, 5, Bristol Meyer Squibb, 2, 5, Bristol Myers-Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Eli/Lilly, 5, Genentech/Roche, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Pfizer Inc, 5, Regeneron/Sanofi, 5, Sanofi/Regeneron, 5; **L. Cappelli**, Bristol Meyer Squibb, 2, Bristol-Myers Squibb, 2, Regeneron/Sanofi, 5, Regeneron/Sanofi Genzyme, 5.

Abstract Number: 2152

Safety of Immune Checkpoint Inhibitors in Patients Treated for Cancer with Pre-existing Autoimmune Diseases

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with pre-existing autoimmune diseases (AID) have been traditionally excluded from clinical trials of immune checkpoint inhibitors (ICI), so the data on risk of flare of pre-existing AID with ICI therapy is very limited. As we encounter more patients in clinical practice with pre-existing AID who have been treated with ICI therapy, there is a growing need for understanding the management of autoimmune complications from ICI therapies. The aim of our study was to investigate the safety of immune checkpoint inhibitors in patients who have pre-existing AID.

Methods: After approval from the University of Iowa Hospitals and Clinics (UIHC) IRB, we performed a retrospective chart review of all the patients with pre-existing AID who received any kind of ICI therapy at UIHC through September 1st, 2018. Data collection included- the nature of the pre-existing AID, treatments previously given or currently being given for the AID, type of ICI therapy given, course and duration of ICI therapy, effects of ICI therapy on the AID, timeline of development of flares of pre-existing AID (if applicable), grade and severity of any new immune related adverse events (irAE's) seen, progression free survival, overall survival and vital status at the time of last documentation available in the chart. Predictors of developing a flare were determined using logistic regression.

Results: A total of 42 patients with pre-existing AID were identified who received ICI therapy. Out of these, 25 patients had metastatic melanoma, 11 patients had lung cancer, four patients had genitourinary cancer, one patient had diffuse large B cell lymphoma and one patient had head and neck cancer. Twelve patients had flares of their pre-existing AID including three patients with rheumatoid arthritis (RA), two patients with psoriatic arthritis, two patients with polymyalgia rheumatica (PMR), and one patient each with skin psoriasis, Crohn's disease, bullous pemphigoid, inflammatory arthritis and myasthenia gravis. All of the flares were treated with oral or topical corticosteroids. In addition, one patient with RA flare was treated with tofacitinib and one Crohn's flare was treated with infliximab. Female sex, older age and non-smoker status were predictors of flare although these were not statistically significant **(Table 1)**. Five patients developed new irAE's, which were managed with corticosteroids as well. ICI therapy was stopped in four patients due to AID flare but continued in the rest. The median progression-free survival (PFS) in melanoma and lung cancer cohort was 943 and 158 days and median overall survival (OS) was undefined and 361 days respectively.

Table 1: Predictors of flare of pre-existing AID

Variable	Odds Ratio	95% Confidence intervals
Sex (F vs M)	1.394	0.33-5.83
Smoking status (Non vs ever smoker)	1.765	0.314-9.93
Age at start of ICI therapy (70.7 vs 66.9)	1.018	0.964-1.08

Conclusion: In patients with pre-existing AID treated with an ICI therapy, flare of AID happened in a small proportion of patients (28%). Even among those who flared, they were managed safely with corticosteroids alone or with additional disease modifying therapies. Immunotherapy could be safely continued in majority of the patients with close monitoring and multidisciplinary collaboration.

Disclosure: A. Kaur, None; **U. Swami**, None; **M. Fatima**, None; **M. Ginn**, None; **J. Stein**, None; **Y. Gao**, None; **Y. Zakharia**, None; **N. Singh**, None.

Abstract Number: 2153

Ocular Scleral Pathology and Relationship with Autoimmune Diseases: Study of 101 Patients from a Single Universitary Centre

Lara Sanchez-Bilbao,[1] Iñigo Gonzalez-Mazon,[2] Mónica Calderón-Goercke,[3] Diana Prieto-Pena,[2] Jose Luis Martín-Varillas,[1] Belén Atienza-Mateo,[1] Rosalia Demetrio,[4] Miguel A Gonzalez-Gay,[1] and Ricardo Blanco[1], [1]Rheumatology, Hospital Universitario Marques de Valdecilla, Santander, Spain, [2]Rheumatology, Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain, [3]Hospital Marqués de Valdecilla, Santander, Cantabria, Spain, [4]Hospital Universitario Marqués de Valdecilla, Santander, Spain

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies
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Session Time: 9:00AM–11:00AM

Background/Purpose: Ocular scleral pathology may be associated with autoimmune diseases. Our aim was to assess **a)** the epidemiological and clinical features and **b)** the relationship with immune-related diseases.

Methods: Observational study of unselected consecutive patients studied in a single reference University Hospital during the last ten years with**: a)** diagnosis of episcleritis and **b)** diagnosis of scleritis (Watson and Hayreh classification system, P. G. Watson, S. S. Hayreh, Br J Ophthalmol. 1976 Mar; 60(3): 163–191).

Patients were studied in a reference multidisciplinary unit (rheumatologist and ophthalmologist). Demographics features, clinical findings, complementary tests and treatment were recorded.

Results: We studied 101 (65 women/38 men) patients /202 eyes with diagnosis of scleral pathology (episcleritis=75; scleritis =26); mean age at diagnosis, 49.0±14.17 years. The mean follow-up was 3.68±5.30 years.Demographic baseline characteristics and clinical manifestations of these patients are shown in **TABLE 1.**

Diffuse anterior scleritis (n=17; 16.8%) was the most common type of scleritis, followed by nodular. In case of episcleritis, the most common was simple-form (n = 71; 70.3%).

Etiology was as follows: idiopathic (n=59, 58.4%), associated to systemic disease (SD-group) (n=32, 31.7%), and infectious (n=10, 9.9%). In SD-group, the main association was with Crohn's disease (n=8; 7.9%), rheumatoid arthritis (n=6; 5.9%) and psoriatic arthritis (n=4; 3.9%).

Laboratory tests were also performed in all patients, mainly as screening of systemic diseases. Antinuclear antibodies (ANA) and rheumatoid factor (RF) were positive in 9 patients, followed by HLA-B27 7; 6.9%).

	Patients diagnosed with episcleritis/scleritis (n=10)
DEMOGRAPHIC PARAMETERS	
Sex, n (%)	36 ♂ / 65 ♀ (35.6%,64.4%
Age at disease onset (years), mean ± SD	49.0 ± 14.17
Follow-up (years), mean ± SD	3.68 ± 5.30
Hyperuricemia, n (%)	7.0 (6.9)
Tuberculosis, n (%)	1.0 (0.9)
Ocular surgery, n (%)	5.0 (4.9)
SCLERA RELATED DATA	
Episcleritis	**75.0 (74.2)**
- Simple, n (%)	71.0 (70.3)
- Nodular, n(%)	4.0 (3.9)
Scleritis	**26.0 (25.7)**
- Diffuse anterior, n (%)	17.0 (16.8)
- Nodular anterior, n (%)	11.0 (10.9)
- Posterior, n (%)	0.0 (0.0)
- Necrotizing anterior scleritis	0.0 (0.0)
VA / IOP	
- VA left eye, mean ± SD	0.92±0.15
- VA right eye, mean ± SD	0.90±0.14
- IOP left eye, median [ICR]	15.0 [12.0-17.0]
- IOP right eye, median [ICR]	15.0 [12.5-16.7]
Phenylephrine	
- Positive, n (%)	76.0 (75.2)
- Negative, n (%)	25.0 (24.7)
Ocular involvement	
- Left eye limited, n (%)	36.0 (35.6)
- Right eye limited, n (%)	49.0 (48.5)
- Both, n (%)	16.0 (15.8)
Persistence / Recurrence	
- Persistent, n (%)	16.0 (15.8)
- Recurrent, n (%)	41.0 (40.6)
Complications, n (%)	**19.0 (18.8)**
- Keratitis, n (%)	6.0 (5.9)
- Uveitis, n (%)	5.0 (4.9)
- IOP, n (%)	5.0 (4.9)
- Cataract, n (%)	3.0 (2.9)
- Cystoid macular edema, n (%)	0.0 (0.0)
- Optic disc swelling, n (%)	0.0 (0.0)

Attending to the treatment, 100% of patients received topical treatment as first-line therapy and 81.2% (n=81) NSAIDs. Another conventional immunosuppressor and biological treatment were required in 27.7% (n=28) and 6.9 (n=7) respectively. The main indication for biological therapy was the presence of concomitant systemic disease.

Some complications were reported, being keratitis (n=6; 5.9%) the most common.

Conclusion: The results obtained are reproducible to those published in international series, except a more frequent of Crohn's disease and a less frequent of vasculitides. Scleral pathology is a frequent entity and it is necessary to exclude underlying systemic pathology.

ETIOLOGY	
Idiopathic, n (%)	**59.0 (58.4)**
Infectious, n (%)	**10.0 (9.9)**
- Herpes simplex virus, n (%)	8.0(7.9)
- Varicella zoster virus, n (%)	2.0 (1.9)
Systemic diseases	**32.0 (27.7)**
- Crohn's disease, n (%)	8.0 (7.9)
- Rheumatoid Arthritis, n (%)	6.0 (5.9)
- Psoriatic arthritis, n (%)	4.0 (3.9)
- Systemic lupus, n (%)	3.0 (2.9)
- Ankylosing spondylitis, n (%)	3.0 (2.9)
- Granulomatosis with polyangiits, n (%)	3.0 (2.9)
- Behçet, n (%)	1.0 (0.9)
- Recidivant polychondritis	1.0 (0.9)
- Sarcoidosis, n (%)	1.0 (0.9)
- Tireoiditis, n (%)	1.0 (0.9)
- Celiac disease, n (%)	1.0 (0.9)

LABORATORY TESTS	
CRP (mg/dl), median [ICR]	0.4 [0.2-0.9]
ESR (mm/1ªh), median [ICR]	8.0 [3.2-15.0]
Leukocytosis, n (%)	1.0 (0.9)
Hyperuricemia, n (%)	13.0 (12.9)
Renal function, n (%)	1.0 (0.9)
RF, n (%)	9.0 (8.9)
ACPAs, n (%)	2.0 (1.9)
ANAs, n (%)	9.0 (8.9)
Antiphospholipid ab, n (%)	3.0 (2.9)
ANCA, n (%)	4.0 (3.9) (PR3 +)
HLA-B27, n (%)	7.0 (6.9)
HLA-B51, n (%)	1.0 (0.9)
HLA-A59, n (%)	2.0 (1.9)

TREATMENT	
Topical treatment	**101 (100%**
- Corticosteroids, n (%)	75.0 (74.3)
- NSAIDs, n (%)	39.0 (38.6)
Oral/ev	
- NSAIDs, n (%)	**101 (100%)**
- Prednisone, n (%) / mean dose (mg/day), mean±SD	28.0 (27.7) / 8.35±15.23
- Bolus MTP, n (%)	2.0 (1.9)
Conventional immunosupressants	
- Methotrexate, n (%) / mean dosage (mg/week), mean±SD	15.0 (14.8) / 15.4±5.5
- Azathioprine, n (%) / mean dosage (mg/day), mean±SD	5 (4.9) / 91.6±32.2
- Salazopyrine, n (%) / mean dosage (mg/day)	4 (3.9)
- Hydroxycloroquine, n (%)	5 (4.9)
- Cyclophosphamide, n (%)	3 (2.9)
- Mycophenolate mofetil, n (%)	1 (0.9)
Biological agents	7.0 (6.9)
- Infliximab, n (%)	3.0 (2.9)
- Adalimumab, n (%)	2.0 (1.9)
- Etanercept, n (%)	0.0 (0.0)
- Golimumab, n (%)	1.0 (0.9)
- Tocilizumab, n (%)	0.0 (0.0)
- Rituximab, n (%)	0.0 (0.0)
- Secukinumab, n (%)	1 (0.9)

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Abstract Number: 2154

Role of Insulin Resistance and Inflammation on Resting Energy Expenditure in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies
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Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with rheumatoid arthritis(RA), elevated resting energy expenditure(REE) is associated with rheumatoid cachexia and protein catabolism driven by pro-inflammatory cytokines. IR is also associated with elevated REE in adults without RA, independent of inflammation. Given the high prevalence of IR in RA, our goal was to investigate the association between IR and REE in patients with RA.

Methods: 35 individuals meeting the 2010ACR/EULAR criteria for RA and 17 non-RA controls comparable in age, sex and race were selected. Body composition was determined by dual energy x-ray absorptiometry (DEXA). REE was measured using indirect calorimetry. Insulin sensitivity was measured using the Matsuda index. Linear regression model was used to study the relationship among REE, insulin sensitivity and CRP, as well as an interaction between IS and CRP. Statistical significance is defined by a p-value < 0.05.

Results: RA and non-RA controls had comparable body mass index, total fat free mass index, CRP and REE levels. Insulin sensitivity was lower in the RA group (median=2.9, IQR=5.4) compared to the non-RA group (median=5.9, IQR=4.1). The median DAS28-CRP among individuals with RA was 1.8 (IQR=1.7). Among individuals with RA, we found a statistically significant relationship between REE and CRP levels [R^2= 41.0 %, adjusted R^2=33.9%, estimate coefficient (SE)= 46.7 (13.7), p=0.0022], while insulin sensitivity was not significantly associated with REE after adjusting for CRP level [estimate (SE)=-57.4 (43.3), p=0.256]. Among individuals with RA, there was also no significant interaction between IR and CRP [estimate (SE)=-40.0976(22.746), p=0.146]. In the non-RA control group, neither insulin sensitivity nor CRP level were significantly associated with REE.

Conclusion: CRP was significantly and independently associated with REE among RA individuals, but not non-RA controls. IS was not independently related to REE in either group. These results suggest that, in RA, inflammation may be a common antecedent leading to both elevated REE and insulin resistance.

Disclosure: B. Hanaoka, None; **B. Gower**, None.

Abstract Number: 2155

The Spectrum of Interstitial Lung Disease Associated with Autoimmune Diseases: Data of a 3-Year-Prospective Study from a Referral Center of Lung Transplantation

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SESSION INFORMATION

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Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

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Background/Purpose: Interstitial lung disease (ILD) occurs in approximately 15% of patients with autoimmune diseases (AD) [1]. Its presence is associated with an increased risk of morbidity and mortality [2]. In the present study, we aimed to determine the frequency of ILD associated with AD (AD-ILD) among patients sent for assessment to a clinic of lung transplantation from a referral center. The different types of AD-ILD were described.

Methods: Clinical records of patients seen at the ILD clinic of Hospital Universitario Marqués de Valdecilla, Santander, Spain between May 2016 and May 2019 were reviewed. A diagnosis of ILD was made by the pneumologists based on clinical and radiological findings and pulmonary function test abnormalities. A definitive histological confirmation by transbronchial biopsy, surgical lung biopsy or cryobiopsy was performed according to the pneumologist consideration. All patients with ILD seen at the clinic were also assessed by an experienced rheumatologist to exclude the presence of an underlying AD.

Results: During the period of assessment, 384 patients were diagnosed with ILD in this referral clinic (**Table**). The diagnosis of ILD was histologically confirmed in 208 (54.2%) patients. Among the 384 ILD patients, 129 were diagnosed as having idiopathic pulmonary fibrosis (33.6%). Other frequent conditions unrelated to AD were chronic hypersensitivity pneumonitis (n= 40; 10.4%), non-classifiable interstitial pneumonia (n= 44; 11.5%) and non-specific interstitial pneumonia (n=20; 5.2%). Ninety-one (23.7%) of the ILD patients fulfilled definitions for AD. Most cases with AD-ILD were due to rheumatoid arthritis (n= 25/91; 27.5%); systemic sclerosis (n=24/91; 26.4%), antisynthetase syndrome (n= 16/91; 17.6%) and Sjogren's syndrome (n= 6/91; 6.6%). Interestingly, 15 of 91 patients with AD-ILD (16.5%) were diagnosed as having an interstitial pneumonia with autoimmune features. Other AD associated with ILD are shown in **Table**. The predominant radiological pattern in patients with rheumatoid arthritis was usual interstitial pneumonia. In contrast, a predominant non-specific interstitial pneumonia pattern was found in the remaining patients with AD.

Conclusion: Almost a quarter of patients with ILD seen at a referral clinic center have an underlying AD. Close assessment of patients with ILD by rheumatologists is of main importance to identify AD in patients with ILD.

Table. Characteristics of 384 patients with ILD unrelated and associated with AD included in this study.

					Pulmonary function tests			
	Women, n (%)	Age at study[1]	Age at diagnosis[1]	Smoking, n (%)	FVC, %[2]	FEV1, %[2]	FEV1/FVC, %[2]	DLCO, %[2]
ILD unrelated to AD (n=293,76.3%)	78 (26.6)	62 [56-67]	57 [48-63]	197 (67.2)	76.4 ± 22.9	72.0 ± 22.7	76.1 ± 12.4	35.2 ± 15.7
ILD associated with AD (n=91, 23.7%)	44 (48.3)	60 [56-67]	57 [50-63]	55 (60.4)	82.5 ± 23.3	79.4 ± 23.5	77.5 ± 8.4	37.2 ± 15.2
Rheumatoid arthritis (n=25, 27.5%)	8 (32.0)	66 [59-72]	59 [55-71]	19 (76.0)	91.1 ± 20.6	86.3 ± 18.7	75.6 ± 8.6	39.0 ± 16.8
Systemic sclerosis (n=24, 26.4%)	13 (54.2)	61 [59-65]	56 [44-63]	11 (45.8)	78.5 ± 24.1	74.8 ± 24.5	77.5 ± 9.7	35.0 ± 15.8
Anti-synthetase syndrome (n=16, 17.6%)	10 (62.5)	56 [47-61]	53 [46-57]	9 (56.3)	69.8 ± 24.4	69.2 ± 26.3	80.3 ± 6.9	35.7 ± 14.7
Interstitial pneumonia with autoimmune features (n=15, 16.5%)	5 (33.3)	57 [50-64]	56 [49-60]	10 (66.7)	81.8 ± 15.9	79.6 ± 17.9	78.3 ± 8.5	36.3 ± 17.4
Sjogren's syndrome (n=6, 6.6%)	5 (83.3)	71 [63-76]	71 [61-75]	3 (50.0)	99.3 ± 34.3	98.0 ± 37.4	78.0 ± 6.3	41.2 ± 7.3
Amyopathic dermatomyositis (anti-MDA-5) (n=2, 2.2%)	-	46	46	2 (100.0)	68.9 ± 10.1	79.0	82.0	46.0
Systemic lupus erythematosus (n=1, 1.1%)	1 (100.0)	59	58	-	103.0	94.5	77.3	43.2
Eosinophilic granulomatosis with polyangiitis (n=1, 1.1%)	1 (100.0)	52	51	1 (100.0)	65.0	53.7	70.1	23.9
Mixed connective tissue disease (n=1, 1.1%)	1 (100.0)	54	46	-	99.0	85.0	73.0	40.0

[1]Data shown in years, median [IQR].
[2]Data shown in mean ± SD.
AD: autoimmune disease; DLCO: diffusing capacity of the lung for carbon monoxide; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; ILD: interstitial lung disease; IQR: interquartile range; SD: standard deviation.

Reference:

1. Cottin et al. *Eur Respir Rev* 2018;27:180076; [2] Antoniou et al. *Eur Respir J* 2009;33:882-896.

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Abstract Number: 2156

Expanding the Phenotypic and Genotypic Spectrum in Yao Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies
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Background/Purpose: Yao syndrome (YAOS, OMIM 617321), formerly termed nucleotide-binding, oligomerization domain 2(*NOD2)*-associated autoinflammatory disease, has become increasingly recognized. The disease has been reported in America, Europe and Asia, and seems not uncommon. This study aimed to report novel phenotypic and genotypic findings in the disease.

Methods: This is a retrospective review of electronic medical records (EMRs) of 11 patients with YAOS, and the study was approved by the Stony Brook University (SBU) Institutional Research Board. These patients after an extensive workup without a unified diagnosis were referred to our Center of Autoinflammatory Disease at SBU, and followed up, and the charts were well documented by the lead author who has a vested interest in the disease. All

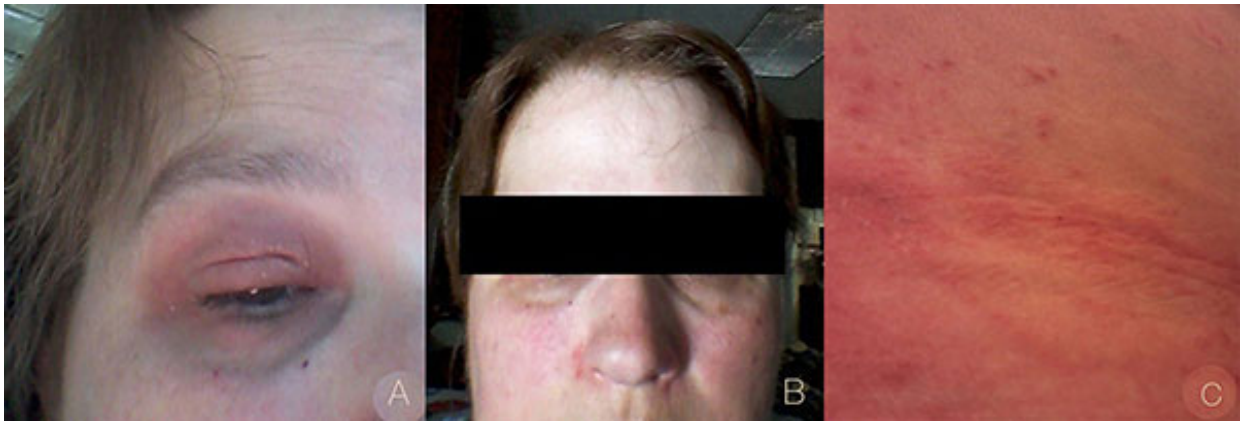
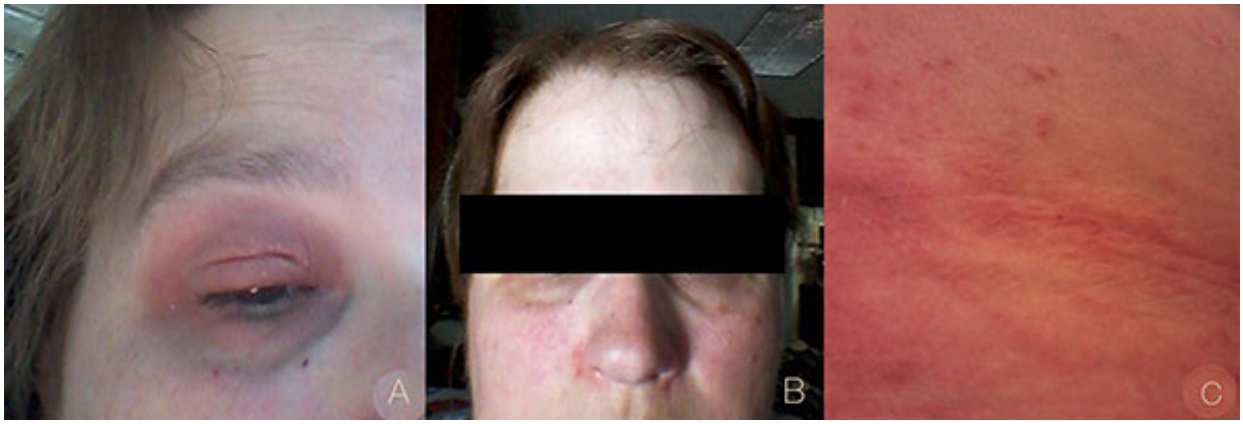


Table 1. Baseline Demographics, Clinical and Laboratory Characteristics of YAOS Patients



Eyelid swelling with discoloration and patchy erythema and plagues on the face and abdominal wall.

these patients underwent genetic testing for periodic fever syndrome 6-gene panel (MEFV, TNFRSF1A, NLRP3, MVK, NLRP12 and NOD2) or targeted gene sequencing for NOD2. These patients were included in the study because they fulfilled the diagnostic criteria for YAOS and had either eyelid swelling as corroborated by i-phone photographs and/or NOD2 variants that were not identified previously for the disease. Continuous variables were expressed as median, interquartile range, and frequency for descriptive statistics.

Results: All YAOS patients (10 females, 1 male) were Caucasians with the mean age of 25.9 at disease onset. They shared such known common phenotype for YAOS as fever, rash, arthritis/arthralgia, gastrointestinal, and sicca-like symptoms (Table 1). Three patients had a family history of the similar symptoms. Of note, 7 of the 11 patients developed unilateral or bilateral eyelid swelling with or without discoloration or eye redness (Figure 1). The symptom recurred and concurred with other clinical manifestations during disease flares and each episode lasted several hours to a few days with resolution. Six of the 7 patients carry the common NOD2 variants associated with YAOS. Of the 11 patients, 5 patients had clinical characteristics of YAOS and carry the rare NOD2 variants. These data support eyelid swelling as a new clinical feature of YAOS, and the spectrum of NOD2 variants associated with YAOS is extended.

Conclusion: This study indicates that the eyelid swelling and rare NOD2 variants are added clinical and genetic characteristics of YAOS. Recognition of the expanded disease spectrum will foster prompt diagnosis and management of the disease.

Disclosure: Q. Yao, None; **A. Kontzias**, Novartis, 5.

Abstract Number: 2157

Checkpoint Inhibitor-Associated Arthritis: Phenotype, Steroid Dose, Serology and Survival

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies suggest that steroid dose[1]and rheumatoid factor positivity[2] impact cancer survival in checkpoint inhibitor (CI)-treated patients (with CI-associated hypophysitis, and in all-comers with non-small cell lung cancer patients respectively). In this study we describe CI-associated arthritis phenotypes in patients enrolled in a CI registry, and measure the impact of phenotype, steroid dose, and serologic status on survival.

Methods: Patients referred to rheumatology at Hospital for Special Surgery (HSS) for CI-associated immune-related adverse events were enrolled in our registry. Demographics, cancer types, treatment and outcomes, musculoskeletal findings, labs and serologies were collected prospectively. We defined four categories of arthritis: (1) "small joint" swelling ± large joint involvement, (2) exclusively "large joint" swelling, (3) joint pain without joint swelling ("arthralgia"), and (4) polymyalgia rheumatica ("PMR"). For this analysis, we excluded patients with non-articular conditions, crystal disease, or mechanical disorders. Distribution of continuous variables was assessed using the Shapiro-Wilk test and summarized as median [IQR]; categorical variables are summarized as frequencies. Progression-free survival (PFS), measured from CI initiation until documented radiographic progression, is presented in Kaplan-Meier curves compared by 2-sided log rank test. Hazard ratios were estimated using Cox proportional hazards regression analysis.

Results: Of 50 registry patients enrolled between 5/1/18-4/1/19, 37 had articular complaints. Median [IQR] age was 67 [59,77], 22 (59%) were female, 17 (49%) had a smoking history, 14 (38%) had metastatic melanoma and 25 (68%) received anti-PD-1/PD-L1 monotherapy (**Table 1**). Median time to symptom onset was 2.8 [0.9,12] months after CI initiation. 22 (59%) had small joint involvement, 5 (14%) large joint, 8 (22%) arthralgia and 2 (5%) PMR. 9 (24%) had concomitant enthesitis/tenosynovitis and 11 (31%) were RFand/or CCP positive. The large joint phenotype was notable for prevalent combination CI (80%) and tenosynovitis (60%), high ESR of 90 [28,99], and no RF/CCP positivity. Overall, 17 (46%) patients required > 20mg prednisone, and 6 (16%) required a biologic DMARD (**Figure 1**). Overall median PFS was 100 [64,151] weeks, and did not differ between melanoma vs. non-melanoma, patients treated with >20mg vs. ≤20mg prednisone, RF/CCP pos vs. neg, or small joint vs. other phenotypes (**Figure 2**).

Conclusion: In our cohort, neither steroid dose nor seropositivity were associated with progression-free survival in CI-treated patients with symptomatic musculoskeletal syndromes. However, our findings are limited by the small size and heterogeneity of our cohort.

References:

1. Faje A. Pituitary 2016; 19:82–92
2. Toi Y et al. JAMA Oncol; Epub 12/27/18

Continuous Variables: median [IQR] Categorical Variables: n (%)	CI: Overall (N=37)	CI: Arthritis small joint (n=22)	CI: Arthritis large (n=5)	CI: Arthralgia (n=8)	CI: PMR (n=2)
Age	67 [59, 77]	70 [63,79]	65 [51,75]	57 [54,61]	78 [73,84]
Female	22 (59%)	13 (59%)	3 (60%)	6 (75%)	0 (0%)
Race					
White	33 (89%)	20 (91%)	5 (100%)	6 (75%)	2 (100%)
Black	1 (3%)	0 (0%)	0 (0%)	1 (13%)	0 (0%)
Smoker	17 (49%)	12 (57%)	1 (20%)	3 (43%)	1 (50%)
Malignancy					
Melanoma	14 (38%)	7 (32%)	3 (60%)	3 (38%)	1 (50%)
NSCLC[a]	4 (11%)	3 (14%)	0 (0%)	1 (13%)	0 (0%)
Renal cell	5 (14%)	2 (9%)	1 (20%)	2 (25%)	0 (0%)
Urothelial	3 (8%)	1 (5%)	0 (0%)	1 (13%)	1 (50%)
Other[b]	11 (30%)	9 (41%)	1 (20%)	1 (13%)	0 (0%)
Checkpoint Regimen					
Combination[c]	12 (32%)	5 (23%)	4 (80%)	3 (38%)	0 (0%)
PD-1 or PD-L1 alone	25 (68%)	17 (77%)	1 (20%)	5 (63%)	2 (100%)
Cancer Status					
Complete Remission	10 (27%)	5 (24%)	1 (20%)	3 (38%)	1 (50%)
Partial Remission	7 (19%)	6 (29%)	0 (0%)	0 (0%)	1 (50%)
Stable	10 (27%)	4 (18%)	4 (80%)	2 (25%)	0 (0%)
Progression	10 (27%)	7 (32%)	0 (0%)	3 (38%)	0 (0%)
Arthritis					
Time to symptom onset (months)	3 [1, 12]	2 [0, 4]	12 [8,21]	16 [2,22]	2 [0, 4]
Time to rheum referral (months)	5 [1, 10]	6 [1,10]	2 [2, 5]	9 [1,15]	2 [1, 3]
Max CDAI	17 [11, 24]	23 [15, 33]	15 [12,16]	11 [10, 11]	7 [7, 7]
Enthesitis/tenosynovitis	9 (24%)	1 (5%)	3 (60%)	5 (63%)	0 (0%)
Maximum steroid requirement					
Zero	3 (8%)	2 (9%)	1 (20%)	0 (0%)	0 (0%)
≤20 mg	17 (46%)	11 (50%)	1 (20%)	4 (50%)	1 (50%)
>20 mg	17 (46%)	9 (41%)	3 (60%)	4 (50%)	1 (50%)
Medications					
HCQ/SSZ[d]	22 (59%)	13 (59%)	3 (60%)	5 (63%)	1 (50%)
Methotrexate	8 (22%)	7 (32%)	1 (20%)	0 (0%)	0 (0%)
Biologic[e]	6 (16%)	5 (23%)	1 (20%)	0 (0%)	0 (0%)
Labs					
ANA+[f]	22 (67%)	12 (63%)	4 (80%)	4 (57%)	2 (100%)
RF and/or CCP[g]	11 (31%)	7 (33%)	0 (0%)	3 (35%)	1 (50%)
ESR[h]	30 [22, 46]	30 [17,49]	90 [28, 99]	37 [26, 41]	26 [22, 29]

[a]Non-small cell lung cancer
[b]Leiomyosarcoma (2); Merkel cell carcinoma (2); Breast cancer (1); Follicular lymphoma (1); High grade spindle sarcoma (1); Hodgkin lymphoma (1); Hepatocellular carcinoma (1); Pleomorphic sarcoma (1); Salivary gland cancer (1)
[c]Combination anti-cytotoxic T lymphocyte antigen 4(CTLA4) antibody and either anti programmed cell death-1 (PD-1) or anti programmed cell death-1 ligand (PD-L1) antibody
[d]Hydroxychloroquine/Sulfasalazine
[e]Infliximab, tocilizumab, rituximab
[f]Antinuclear antibody
[g]Rheumatoid factor and/or anti cyclic citrullinated protein antibody
[h]Erythrocyte sedimentation rate

Table 1. Demographics and tumor type

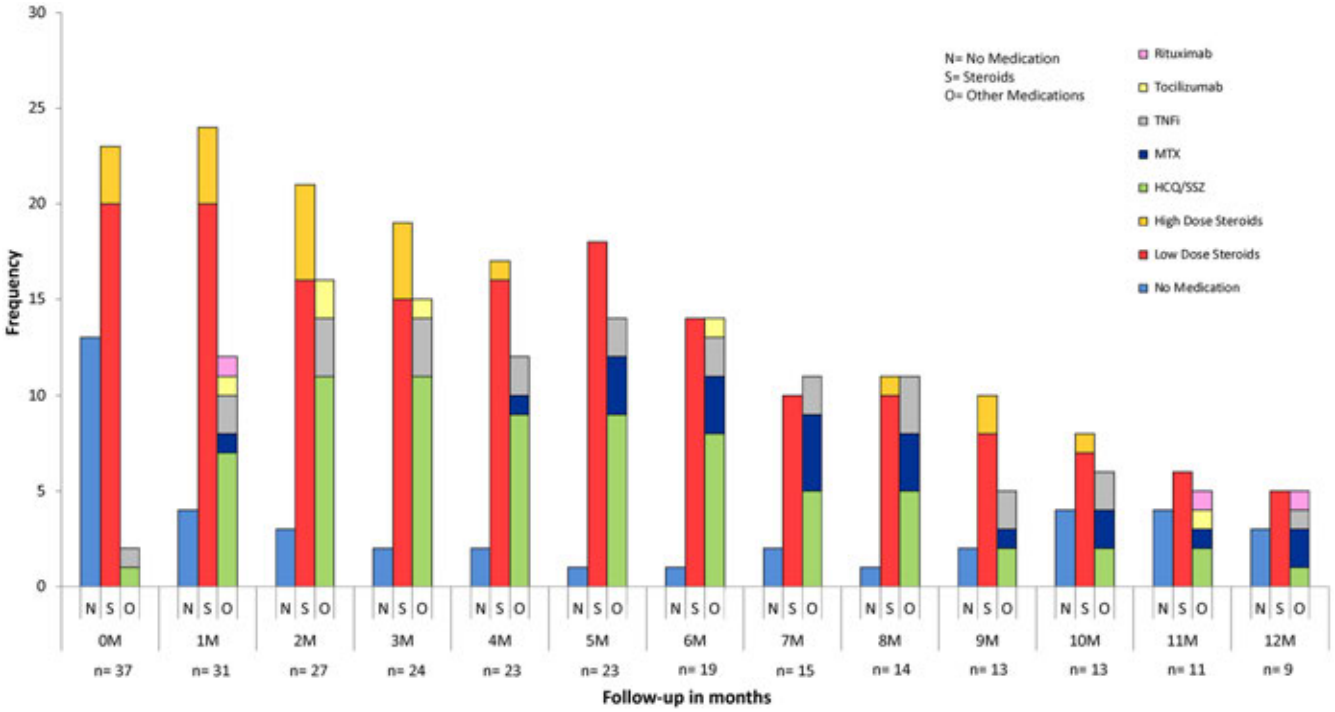

Figure 1 Characteristics of patients with musculoskeletal immune-related adverse events following checkpoint inhibitor therapy

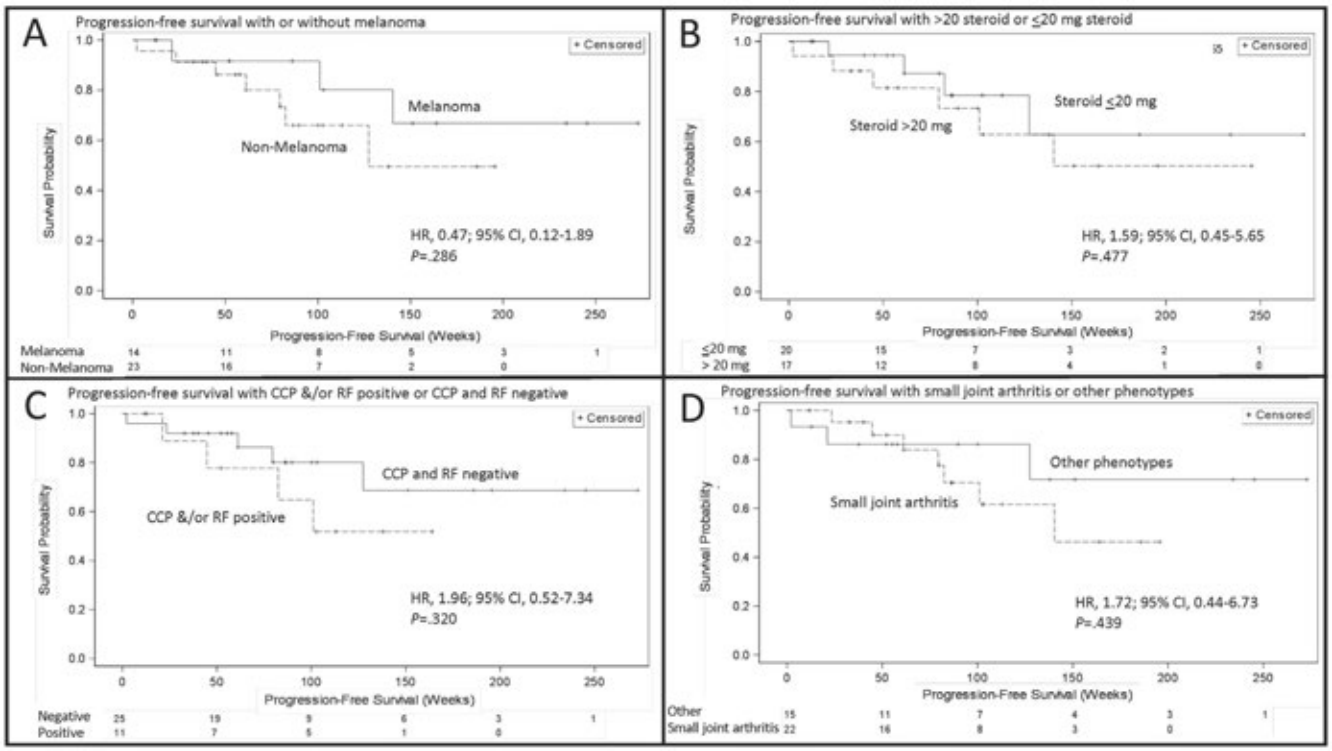

Figure 2. Progression-free survival. Kaplan-Meier curves are shown for progression-free survival among patients according to: (A) melanoma vs non-melanoma, (B) prednisone > 20 mg vs

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Rheumatic Immune Related Adverse Events Associated with Cancer Immunotherapy: A Nationwide Multi-centre Canadian Cohort from the Canadian Research Group of Rheumatology in Immuno-oncology (CanRIO)

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICI) have revolutionized cancer therapy by harnessing the immune system to fight cancer. They are associated with the development of autoimmune toxicities, referred to as immune-related adverse events (irAE). Rheumatic irAE (Rh-irAE), particularly arthralgias and arthritis are common and optimal management remains unknown. The Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO) is an emerging network of Canadian rheumatologists with an interest in Rh-irAE secondary to ICI.

Methods: Patients presenting with rheumatic symptoms associated with ICI therapy between 2013 and January 2019 at participating CanRIO sites were identified. Cases were stratified based on the presence or absence of pre-existing autoimmune disease (PAD). Standardized data were extracted by chart review. The data were pooled and analyzed descriptively.

Results: A total of 118 patients without PAD who developed 140 Rh-irAE were identified, 59% were male with a mean age of 62 years. The most common indications for ICI were melanoma (n=57, 48.3%), lung (n=30, 25.4%), and genitourinary (n=19, 16.1%) with stage 4 disease seen in 79%. ICI included nivolumab (n=30, 25.6%), pembrolizumab(n=38, 32.5%), ipilimumab (n=1, 0.9%), durvalumab (n=3, 2.6%), atezolizumab (n=4, 3.4%) or combination therapy (n=29, 24.8%). Common Rh-irAE included symmetric polyarthritis (n=45, 32%), arthralgias/myalgias or acute flare of

Characteristic, n (%)	Patients without PAD (n=118)	Patients with PAD (n=20)
Age, mean (SD)	62.3 (13.9)	63.9 (9.2)
Female	48 (40.7)	10 (50.0)
White	105 (89.0)	18 (90.0)
Tumor Type		
Melanoma	57 (48.3)	8 (40.0)
Lung	30 (25.4)	10 (50.0)
Genitourinary	19 (16.1)	0 (0)
Gynecological	3 (2.5)	0 (0)
Lymphoma	2 (1.7)	0 (0)
Sarcoma	1 (0.8)	0 (0)
Other	6 (5.1)	2 (10.0)
Stage 1	1 (0.9)	0 (0)
Stage 2	2 (1.7)	2 (10.0)
Stage 3	21 (18.1)	0 (0)
Stage 4	92 (79.3)	17 (85.0)
Tumor progression on ICI	14 (11.9)	7 (35.0)

PAD = pre-existing autoimmune disease; SD = standard deviation

Table 1. Demographics and tumor type

Characteristic	Patients without PAD (n=118)	Patients with PAD (n=20)
CTCA Grade for Rh-irAE (%)		
1 (asymptomatic/mild)	36 (25.7)	1 (25.0)
2 (moderate)	55 (39.3)	1 (25.0)
3 (severe)	45 (32.1)	2 (50.0)
4 (life threatening)	3 (2.1)	0 (0)
5 (death)	0 (0)	0 (0)
Time to first Rh-irAE, mean (SD) (months)	6.8 (8.6)	1.8 (1.9)
ICI therapy stopped	62 (52)	7 (35)
Investigations at diagnosis (%)		
ANA positive	13 (11.0)	NA
RF positive	7 (5.9)	NA
Anti-CCP positive	3 (2.5)	NA
X-ray abnormalities	30 (25.0)	2 (33.3)

PAD = pre-existing autoimmune disease; CTCA = common terminology criteria for adverse events; SD = standard deviation; ICI = immune checkpoint inhibitors; ANA = anti-nuclear antibody; RF = rheumatoid factor; anti-CCP = anti-cyclic citrullinated peptide

Table 2. Rh-irAE and selected Investigations

osteoarthritis (n=20, 16.9%), polymyalgia rheumatica-like presentation (n=17, 12%), tenosynovitis/enthesitis (n=17, 12%), sicca (n=11, 9.3%) and myositis (n=9, 7.6%).

The majority of cases experienced at least one other non-rheumatic irAE (O-irAE) (n=63, 53%). Mean time from first ICI exposure to onset of Rh-irAE was 6.8 months. ICI was either held or discontinued in 65% (n=77). Despite this, (n=81, 68.6%) had favorable tumor response, while (n=14, 12%) had tumor progression. There were no deaths related to Rh-irAE.

Characteristic	Patients with PAD (n=20)
Autoimmune disease	
Rheumatoid arthritis	8 (40.0)
Systemic lupus erythematosus	2 (10.0)
Spondylitis	2 (10.0)
Psoriasis/Psoriatic arthritis	6 (30.0)
Inflammatory bowel disease	3 (15.0)
Other connective tissue disease	1 (5.0)
Vasculitis	0 (0)
Other	3 (15.0)
PAD Response to ICI	
Unchanged	9 (45.0)
Mild Flare	7 (35.0)
Major Flare	3 (15.0)
Treatment of PAD Flare	
Responded to low dose prednisone	1 (10.0)
Responded to increasing DMARD	1 (10.0)
Required high dose Prednisone	2 (20.0)
Required change in DMARD	5 (50.0)
New Rh-irAE events	4
New O-irAE events	7

PAD = pre-existing autoimmune disease; ICI = immune checkpoint inhibitors; DMARD = disease-modifying antirheumatic drug; Rh-irAE = Rheumatic immune-related adverse events; O-irAE = other immune-related adverse events

Table 3. Effects of ICI on pre-existing autoimmune disease

The majority of patients without PAD had either a partial or complete response to either mono- or combination therapy with oral prednisone (n=77; maximum dose 60 mg/d), non-steroidal anti-inflammatories (NSAID; n=52), intra-articular corticosteroids (n=29), hydroxychloroquine (n=26), methotrexate (n=17), or tumor necrosis factor alpha inhibitors (n=9).

Twenty patients with pre-existing autoimmune diseases were identified 70% of whom were in remission prior to starting ICI. 50% (n=10) had flares, 15% (n=3) developed a new Rh-IrAE and 20% (n=4) developed O-irAE.

Conclusion: This is the largest multi-centered cohort of Rh-irAE described to date. Seronegative inflammatory polyarthritis was the most common Rh-IrAE although a broad range of conditions were identified. The most common first-line treatment was systemic corticosteroids followed by NSAID and intra-articular steroid injections. Prednisone was effective, however high doses were required. Disease-modifying antirheumatic drugs (DMARD) and biologic therapy were well tolerated and effective, with hydroxychloroquine being the most commonly used DMARD. Despite moderate to high doses of immunosuppression, the majority of patients had favorable tumor responses.

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Abstract Number: 2159

Pachymeningitis in Rheumatic Disease

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Miscellanous Rheumatic & Inflammatory Disease Poster III: Autoimmune Conditions and Therapies
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Pachymeningitis is a rare complication of rheumatic disease. Patients present with hearing loss or other neurologic complications. Diagnosis is made by thickening of dura or leptomeninges on MRI-imaging or histopathologically with biopsy of the dura. The prevalence pachymeningitis in rheumatic disease is unknown, and there is no standard of care.

Methods: We retrospectively identified nine patients diagnosed with pachymeningitis based on clinical symptoms, MRI findings, and in three cases, dural biopsy. We assessed the rheumatologic diagnoses, presenting symptoms, treatment modalities, and outcomes.

Results: There were two males and seven females, with a mean age of 63 for males and 60 for females. Five patients had rheumatoid arthritis, two had sarcoidosis, one had undifferentiated connective tissue disease and Sjogren's syndrome, and one had blastomycosis who developed rheumatoid arthritis one year later. The presenting symptoms were hearing loss (three), unilateral weakness (two), unilateral numbness (two), seizure (two). Additional symptoms included headache, confusion, memory loss, tinnitus, scleritis, optic neuritis, unilateral hemineglect, foot flaccidity, and gait disturbance. Diagnosis was confirmed in three patients with dural biopsy. MRI images were obtained on all patients. Six patients were treated solely with prednisone or pulse-dose methylprednisolone. Two patients were treated with anti-TNF agents and one patient with rituximab. Pre- and post-treatment MRI demonstrated resolution of leptomeningeal abnormality in two patients. Six out of nine patients reported resolution of symptoms with treatment. Three had persistent deficits, including hearing loss, visual impairment, and slight residual hemiplegia.

Conclusion: Rheumatoid arthritis was the most common rheumatological diagnosis, and hearing loss was the most common presenting symptom. Most patients had resolution of symptoms with prednisone, pulse methylprednisolone, anti-TNF agents, or rituximab. We hope this case series will assist clinicians with the diagnosis and management of pachymeningitis.

Age	Sex	Dx	Presenting Symptoms	Treatment and Outcomes
68	M	RA	R-sided hearing loss Synovitis, Scleritis	HD Prednisone Partial improvement in hearing loss
56	M	SD	R foot flaccidity	HD Prednisone Resolution of symptoms
51	F	RA	Optic neuritis L sided hearing loss	PD methylprednisolone Mild improvement but persistent visual loss
65	F	RA	Unilateral L hemiparesthesias and weakness	PD methylprednisolone Prednisone taper Leflunomide Rituximab Improvement in symptoms
51	F	RA	Headache, Tinnitus, R sided hearing loss	HD Prednisone Improvement in symptoms, chronic R hearing loss
67	F	BM UC	Focal seizure L sided numbness	Voriconazole Dx with RA one year after treatment
63	F	UCTD CREST SJ	Gait disturbance Memory loss	
47	F	SD	Ptosis	PD methylprednisolone Prednisone taper Remicaide Resolution of symptoms
76	F	RA	Acute Confusion, seizure, L hemiplegia, L sensory loss, L hemineglect	HD Prednisone Remicaide Slight residual hemiplegia

Table 1. Age, sex, rheumatologic diagnosis (Dx), presenting symptoms, outcomes and treatments of nine patients identified to have pachymeningitis based on clinical symptoms, magnetic resonance imaging (MRI) findings, and in three instances, dural biopsy. Rheumatologic diagnoses include rheumatoid arthritis (RA), Sarcoidosis (SD), Undifferentiated Connective Tissue Disease (UCTD), Limited cutaneous Systemic Sclerosis (CREST), Sjogren's Disease (SJ), Blastomycosis (BM), Ulcerative Colitis (UC). Lateralization of deficits abbreviated by L (Left) and R (Right). Treatment of patients was typically with high dose (HD) prednisone defined as 50 to 60 mg daily, pulse dose (PD) methylprednisolone of 500 mg to 1000 mg daily for three to five days.

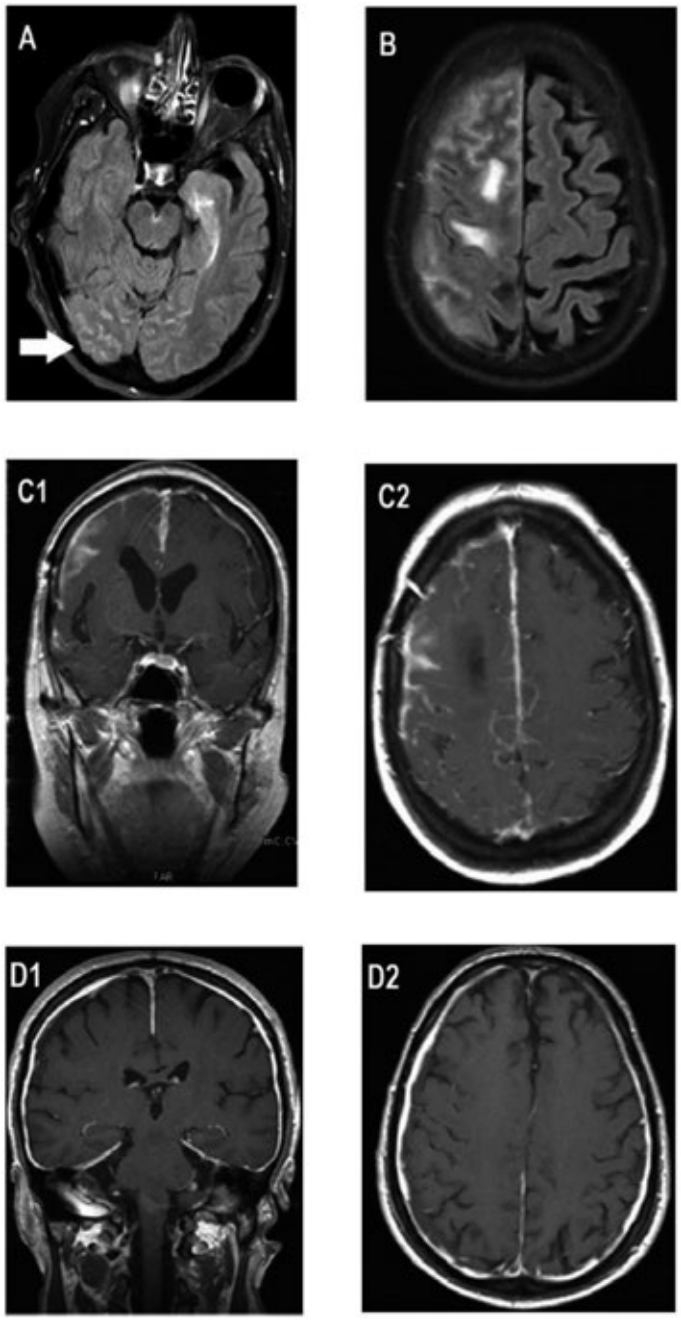

Figure 1. Magnetic resonance imaging (MRI) of the brain from individuals with pachymeningitis. (A) pachymeningitis with leptomeningeal enhancement overlying the occipital lobe (arrow) in a patient with RA presenting with optic neuritis; (B) Unilateral dural and leptomeningeal thickening and enhancement over superior R frontal lobe convexity and sulci extending into interhemispheric fissure in R medial frontal lobe in a patient with blastomycosis who developed focal seizure and L sided numbness who ultimately developed RA one year later; (C1, C2) Coronal and transverse plane images (respectively) demonstrating R cerebral dural, leptomeningeal enhancement seen in patient with RA presenting with acute confusion and L hemiparesis, L sided sensory loss, and L hemineglect; (D1, D2) Coronal and transverse plane images (respectively) demonstrating diffuse bilateral meningeal enhancement after gadolinium in a patient with RA presenting with R unilateral hearing loss, scleritis, and synovitis.

Disclosure: R. Kneeland, None; **J. Berry**, None; **S. Brandwein**, None; **M. Starosta**, None.

Abstract Number: 2160

Myopenia Is an Independent Risk Factor for Rotator Cuff Tear and Shoulder Dysfunction in Elderly People : Data from NAMGARAM Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster – ACR/ARP

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Background/Purpose: Myopenia refers to decline in muscle mass with age, causing significant impairment in the ability to carry out normal daily functions. Rotator cuff tear (RCT) is a localized tendon disease, however, it is known to be related with systemic inflammation. The aim of this study is to determine whether there is correlation between myopenia and RCT in elderly people. In addition, we investigate the relationship between myopenia and severity of shoulder dysfunction.

Methods: Using data from NAMGARAM cohort which consisted of a group of people living in three rural communities in Korea, 510 participants who were ≥ 60 years and who underwent bioimpedance analysis, magnetic resonance imaging of shoulder, and completed shoulder function questionnaire such as Korean shoulder score (KSS), Constant Shoulder Score (CSS) were enrolled. Myopenia was defined according to the criteria set by the Asia Working Group for Sarcopenia (7.0 kg/m2 in men and 5.7 kg/m2 in women). RCT was diagnosed by MRI

Results: The prevalence of RCT was 62.5 % (n = 319). Multivariate logistic regression analysis showed myopenia (OR 1.77, 95% CI 1.12-2.8), hand osteoarthritis (OR 1.96, 95% CI 1.25 - 3.07), and waist circumference (OR 1.05, 95% CI 1.01 - 1.1) were related with RCT after adjustment for age, education level, solitude, body mass index, grip strength, dyslipidemia, hand osteoarthritis, and waist circumference, and myopenia. Subgroup analysis among patients with RCT (n = 319), patients with myopenia showed more severe shoulder dysfunction (KSS, 83.73 ±16.44; CSS, 78.22 ± 14.30) than those of patients without myopenia (KSS, 87.88 ± 11.60; CSS, 81.25 ± 11.00, $P < 0.001$). These results remained after multivariate analysis.

Conclusion: Myopenia is an independent risk factor of RCT and it is related to severe shoulder dysfunction. Keeping skeletal muscle mass is important to maintain shoulder function.

Table 1. Characteristics of participants [a]

	Total (N=510)	RCT		p-value [*]
		Non-RCT (n=191)	RCT (n=319)	
Myopenia, n(%)	195 (38.2)	57 (29.2)	138 (70.7)	0.003
Female, n (%)	239 (46.9)	88(36.8)	151(63.2)	0.782
Age (years)	66.37 ± 4.7	65.54 ± 4.3	66.86 ± 4.9	< 0.001
Solitude, n (%)	441 (86.6)	173 (39.2)	268 (60.8)	0.043
Education, n (%)				< 0.001
≤ 6 years	219 (42.9)	62 (28.3)	157 (71.7)	
7-9 years	107 (20.9)	41 (38.3)	66 (61.7)	
≥ 10 years	184 (36.1)	88 (47.8)	96 (52.2)	
Current smoker, n (%)	58 (11.4)	25 (43.1)	33 (56.9)	0.345
Heavy alcoholics, n (%)	43 (12.0)	17 (39.5)	26 (60.5)	0.887
Trauma, n (%)	240 (47.2)	86 (35.8)	154 (64.2)	0.457
Hypertension, n (%)	199 (39.0)	70 (35.2)	129 (64.8)	0.396
Diabetes mellitus, n (%)	83 (16.3)	32 (38.6)	51 (61.5)	0.821
Metabolic syn., n (%)	116 (26.5)	41 (35.3)	75 (64.7)	0.697
Laboratory values				
Hemoglobin, mg/dL	13.93 ± 1.3	14.01 (1.2)	13.89 (1.4)	0.332
FBS, mg/dL	102.9 ± 25.7	104.1 (30.4)	102.1 (22.4)	< 0.001
Total cholesterol, mg/dL	191.3 ± 37.3	188.9 (35.9)	192.7 (38.1)	0.269
Triglyceride, mg/dL	128.7 ± 82.3	124.2 (67.6)	131.4 (89.9)	< 0.001
HDL, mg/dL	55.31 ± 15.5	56.04 (16.0)	54.87 (15.2)	0.412
LDL, mg/dL	126.6 ± 36.2	124.7 (34.0)	127.8 (37.4)	0.345
CRP,mg/dL	1.91 ± 6.3	1.33 (2.5)	2.25 (7.8)	< 0.001
HbA1c, mg/dL	6.06 ± 0.9	6.06 (0.9)	6.06 (0.8)	0.926
Free T4, mg/dL	1.22 (0.2)	1.22 (0.3)	1.22 (0.2)	< 0.001
MFPS, n (%)	314 (61.6)	111 (35.4)	203 (64.7)	0.215
Hand OA, n (%)	304 (59.6)	89 (29.3)	215 (70.7)	< 0.001
CONSTANT SCORE	81.78 (11.6)	84.86 (9.1)	79.94 (12.6)	< 0.001
KSS SCORE	87.43 (12.7)	89.67 (9.6)	86.08 (14.0)	< 0.001
Waist circumference, cm	85.88 (7.9)	84.91 (8.3)	86.47 (7.7)	0.032
Grip strength, kg	25.85 (10.3)	27.04 (10.1)	25.14 (10.4)	0.044
Low grip strength, n (%)	113 (22.2)	35 (30.9)	78 (69.0)	0.107
BMI (kg/m^2), n (%)	24.33 (2.9)	24.13 (2.7)	24.45 (2.9)	0.226
AMI (skeletal muscle/m^2 * 100, %)	6.98 (0.9)	7.04 (0.9)	6.95 (0.9)	0.337

[a] Categorical variables are presented as number (%), and continuous variables as mean ± SD, unless otherwise indicated. [*] *P* values are the results of comparisons between participants with RCT and participants without RCT. $P < 0.05$ was considered significant. AMI: appendicular

Table 2. Multivariate logistic regression analysis: risk factors for Rotator cuff tear

	Crude model		Adjusted model*	
	OR(95% CI)	p-value	OR(95% CI)	p-value
Myopenia	1.78(1.22,2.61)	0.003	1.77(1.12,2.8)	0.015
Gender				0.409
Female	Reference		Reference	
Male	0.95(0.66,1.35)	0.758	1.3(0.7,2.41)	
Age (years)	1.06(1.02,1.11)	0.003	1.04(0.99,1.09)	0.095
Spouse,				
No	Reference		Reference	
Yes	0.56(0.32,0.99)	0.045	0.49(0.25,0.96)	0.037
Education				
≤ 6 years	Reference		Reference	
7-9 years	0.64(0.39,1.04)	0.069	0.74(0.43,1.28)	0.287
≥ 10 years	0.43(0.28,0.64)	< 0.001	0.73(0.43,1.25)	0.254
CRP	1.04(0.99,1.1)	0.149	1.02(0.97,1.08)	0.421
Hand OA				0.003
No	Reference		Reference	
Yes	2.36(1.63,3.41)	< 0.001	1.96(1.25,3.07)	
CONSTANT	0.96(0.94,0.98)	< 0.001	0.92(0.88,0.96)	0.002
KSS	0.98(0.96,0.99)	0.002	1.1(1.05,1.15)	0.002
BMI	1.04(0.98,1.11)	0.235	0.98(0.87,1.11)	0.782

Predictors for increased rotator cuff terar were examined using multivariate logistic regression analysis. * $P < 0.05$ was considered significant. BMI: body mass index; CRP: C-reactive protein, FBS: Fast blood sugar; HDL: high-density lipoprotein; KSS: Korean shoulder score; LDL: low-density lipoprotein; MFPS = myofacial pain syndrome; RCT: rotator cuff tear

Table 3. Relationship between myopenia and shoulder dysfunction

	Total (n=319)	Normal (n=181)	Myopenia (n=138)	P-value
CONSTANT SCORE				< .0001
Mean (SD)	79.94(12.60)	81.25(11.00)	78.22(14.30)	
Median (IQR)	83.00(74.60, 88.28)	83.43(76.79, 89.00)	82.04(72.00, 88.00)	
(Min, Max)	(18.51, 100.0)	(41.26, 100.0)	(18.51, 100.0)	
KSS SCORE				< .0001
Mean (SD)	86.08(14.03)	87.88(11.60)	83.73(16.44)	
Median (IQR)	90.00(80.00, 97.00)	90.00(83.00, 97.00)	89.00(77.00, 97.00)	
(Min, Max)	(0.00, 100.0)	(47.00, 100.0)	(0.00, 100.0)	

*P values are the results of comparisons between participants with myopania and participants without myopenia. $P < 0.05$ was considered significant.

Disclosure: Y. Cheon, None; **Y. Suh**, None; **M. Kim**, None; **K. Park**, None; **S. Lee**, None.

Abstract Number: 2161

Perioperative Glucocorticoid Management in Patients with Rheumatologic Diseases Undergoing Elective Joint Surgeries

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster – ACR/ARP
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Over 7 million Americans are estimated to suffer from inflammatory rheumatologic diseases and the rate of joint arthroplasties are nearly 50 % higher among this population as compared to controls. Many of these patients are on glucocorticoids around the time of their joint surgeries. The optimum perioperative management of glucocorticoid dosing is not known and there is no established clinical practice. The most recent recommendation by American College of Rheumatology/ American Association of Hip and Knee Surgeons to continue home steroid dose rather than administer supraphysiologic stress dose for patients undergoing elective arthroplasties was based on a low level of evidence. The aim of our study was to compare the rates of peri- and postoperative outcomes after elective joint arthroplasties with continuing home glucocorticoid dosing versus administering stress dose steroid.

Methods: The study is a retrospective case-control study done at the Reading Hospital. Hospital records were used to select patients who were had elective joint arthroplasties (in 5 years period from February 2013- July 2018) and concomitant rheumatologic diseases on chronic steroids. The patients with rheumatologic diseases that received stress dose steroid in the perioperative period (cases) and did not receive stress dose steroid (control) were identified. Patient-specific demographic and clinical data and information on perioperative and postoperative outcomes were extracted.

	Overall (n=78)	Stress dose steroids (n= 38, 48.72%)	No stress dose steroids (n=40, 51.28%)	P value
Baseline demographic characteristics				
Age, Years- Mean (SD)	71.73 (10.56)	70.16 (12.18)	73.23 (8.65)	0.20
Sex, Female- n (%)	64 (82.05)	32 (84.21)	32 (80)	0.63
Race				
Caucasian- n (%)	73 (93.59)	36 (94.74)	37 (92.50)	0.32
African American- n (%)	2 (2.56)	0	2 (5)	
Hispanic- n (%)	3 (3.85)	2 (5.26)	1 (2.5)	
Baseline clinical characteristics				
BMI, kg/m^2- Mean (SD)	30.94 (7.18)	32.30 (7.06)	29.65 (7.16)	0.10
Current smoking- n (%)	11 (14.10)	4 (10.53)	7 (17.5)	0.38
Depression- n (%)	24 (30.77)	12 (31.58)	12 (30)	0.88
Hypertension- n (%)	47 (60.26)	22 (57.89)	25 (62.5)	0.68
HbA1c, % - Mean (SD)	6.58 (1.01)	6.45 (1.02)	6.69 (1.02)	0.49
Age adjusted CCI- Mean (SD)	5.04 (2.21)	4.61 (1.88)	5.45 (2.43)	0.09
Use of additional immunosuppressives - n (%)	36 (46.15)	19 (50)	17 (42.5)	0.51
Pre-procedure steroid dose- Mean (SD)	6.51 (4.49)	7.53 (4.99)	5.55 (3.77)	0.05
In-hospital steroid dosing				
DOS prednisone equivalent dose, mg- Mean (SD)	25.25 27.27)	47.62 (23.03)	4.01 (3.76)	< 0.001
Postop. prednisone equivalent dose, mg- Mean (SD)	8.77 (8.68)	12.38 (10.04)	5.35 (5.334)	0.0002
Hospitalization outcomes				
In hospital glucose level, mg/dl- Mean (SD)	143.31 28.77)	145.77 (26.98)	140.58 (31.2)	0.59
DOS glucose level, mg/dl- Mean (SD)	139.74 (34.4)	147.07 (36.9)	132.08 (30.53)	0.14
Postop. Glucose level - Mean (SD)	137.04 (32.65)	141.18 (30.65)	132.78 (6.01)	0.30
Hypoglycemia	0	0	0	
Infection- n (%)	4 (5.13)	2 (5.26)	2 (5)	0.96
Hypotension- n (%)	27 (34.62)	11 (28.95)	16 (40)	0.31
Intraoperative hypotension- n (%)	14 (17.95)	4 (10.53)	10 (25)	0.09
Disease flare- n (%)	2 (2.56)	1 (2.63)	1 (2.5)	0.97

Table 1. Comparison of baseline characteristics, steroid dosing, and perioperative outcomes after elective joint surgeries in patients with rheumatologic diseases

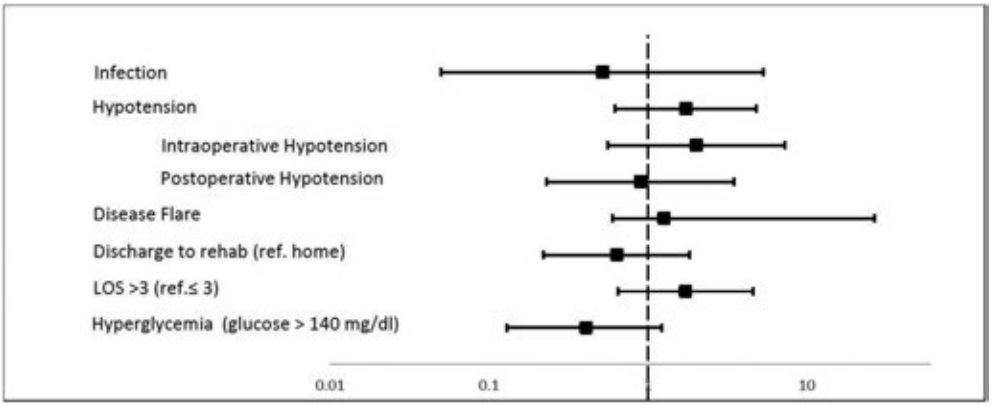

Figure 1. Odds of postoperative outcomes with no stress dose steroids (versus stress dosing) in the perioperative period * Odds adjusted for age, home steroid dose, use of other immunosuppressive and age-adjusted Charlson comorbidity index)

Results: 78 patients met the inclusion criteria, among which about 49 % received stress dose steroids perioperatively. Baseline characteristics were similar between the cases and controls (Table 1). The rate of peri- and postoperative outcomes were not significantly different between the two groups (Figure 1). Intraoperative hypotension was slightly higher in the control group versus those who received stress dose steroid (25 % vs 10.5%, p=0.09). Slight hyperglycemia was noted in the stress dose steroid group (mean in-hospital glucose 142 mg/dl vs 129mg/dl, p=0.07). No perioperative hypoglycemia was noted in either group (Table 1).

Conclusion: Although there is no clear guideline on perioperative glucocorticoid management for patients on chronic steroids, the recommended approach has been to treat patients with a high risk of secondary adrenal dysfunction (patients on > 20 mg prednisone equivalent daily for 3 weeks or with features of Cushing's syndrome). In our study of elective joint surgeries, no stress dose steroid group had a slightly increased tendency toward intraoperative hypotension and stress dose steroid group had increased hyperglycemia. No significant hemodynamic difference was noted between the two groups. Our study had a small size and is underpowered to make conclusions, however, the paucity of evidence necessitates more adequately powered studies to compare perioperative steroid strategies.

Disclosure: R. Dhital, None; **P. Sharma**, None; **I. Mir**, None; **A. Donato**, None.

Abstract Number: 2162

Characteristics of Patients with Rheumatoid Arthritis Undergoing Primary Total Joint Replacement: A 14-year Trend Analysis (2004-2017)

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Type: Poster Session (Tuesday)
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Background/Purpose: Total joint replacement (TJR) is performed when severe large joint destruction causes functional disability in patients with rheumatoid arthritis (RA). Biologics were approved in Japan for use in patients with RA in July 2003. We hypothesized that newer medications including biologics and more aggressive treatment strategies to suppress disease activity might have led to a delay in TJR in patients with RA. This study aimed to examine time

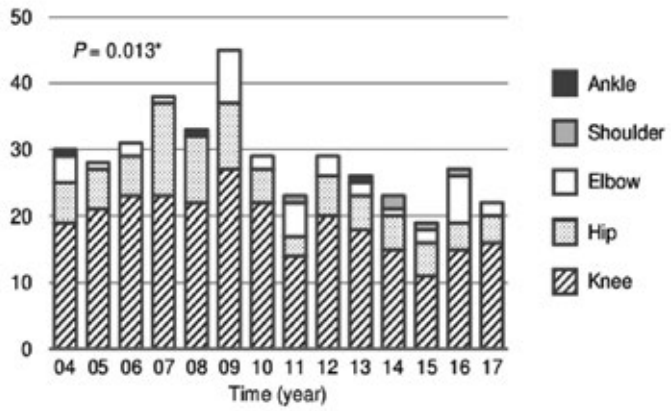
trends in the characteristics of patients with RA undergoing primary TJR since the approval of biologics, and to determine factors associated with time from RA onset to TJR.

Methods: A total of 403 large joints (266 knees, 89 hips, 40 elbows, 5 shoulders, and 3 ankles) in 282 patients who underwent TJR at our institute between January 1, 2004 and December 31, 2017 were retrospectively examined. Time trends over the study period were assessed using the Jonkheere-Terpstra trend test for continuous variables and the Cochran-Armitage trend test for categorical variables. Moreover, patients were divided into two groups according to year of surgery: 2004-2010 and 2011-2017. Data at the time of surgery were compared between the two groups with the Mann-Whitney U test for continuous variables and the chi-square test for categorical variables. Multiple regression analysis was performed to assess whether serum C-reactive protein (CRP) levels at surgery and age at RA onset were associated with time from RA onset to TJR, with sex as an additional variable.

Results: A significant decreasing trend was observed in the number of TJRs performed from 2004 to 2017 ($P = 0.013$) (Fig. 1). Both age at surgery and age at RA onset showed a significant increasing trend ($P = 0.002$ and 0.034, respectively) (Fig. 2A). Time from RA onset to TJR showed no significant trend ($P = 0.294$) (Fig. 2B). Serum CRP levels showed a significant decreasing trend ($P < 0.001$) (Fig. 2C), and the proportion of subjects with negative CRP (defined as ≤0.3 mg/dl) showed a significant increasing trend ($P < 0.001$) (Fig. 2D). Relative to the 2004-2010 group (n =234), the 2011-2017 group (n =169) was more likely to be older at surgery [median (IQR), 66 (60-73) vs. 63 (57-69) years, $P = 0.005$], older at RA onset [51 (41-61) vs. 48 (37-57) years, $P = 0.013$], have lower serum CRP levels [0.30 (0.07-0.95) vs. 0.88 (0.29-2.22) mg/dl, $P < 0.001$], and have a higher rate of negative CRP (50% vs. 27%, $P < 0.001$) (Table 1). With respect to RA treatment, a significant increasing trend was observed in the proportion of subjects receiving MTX ($P = 0.004$) and biologics ($P < 0.001$) (Figs. 2E, 2F). Multiple regression analysis revealed that negative CRP [partial regression coefficient (B) =1.56, $P = 0.046$] and age at RA onset (B =-0.51, for a 1-year increase, $P < 0.001$) were independently associated with time from RA onset to TJR.

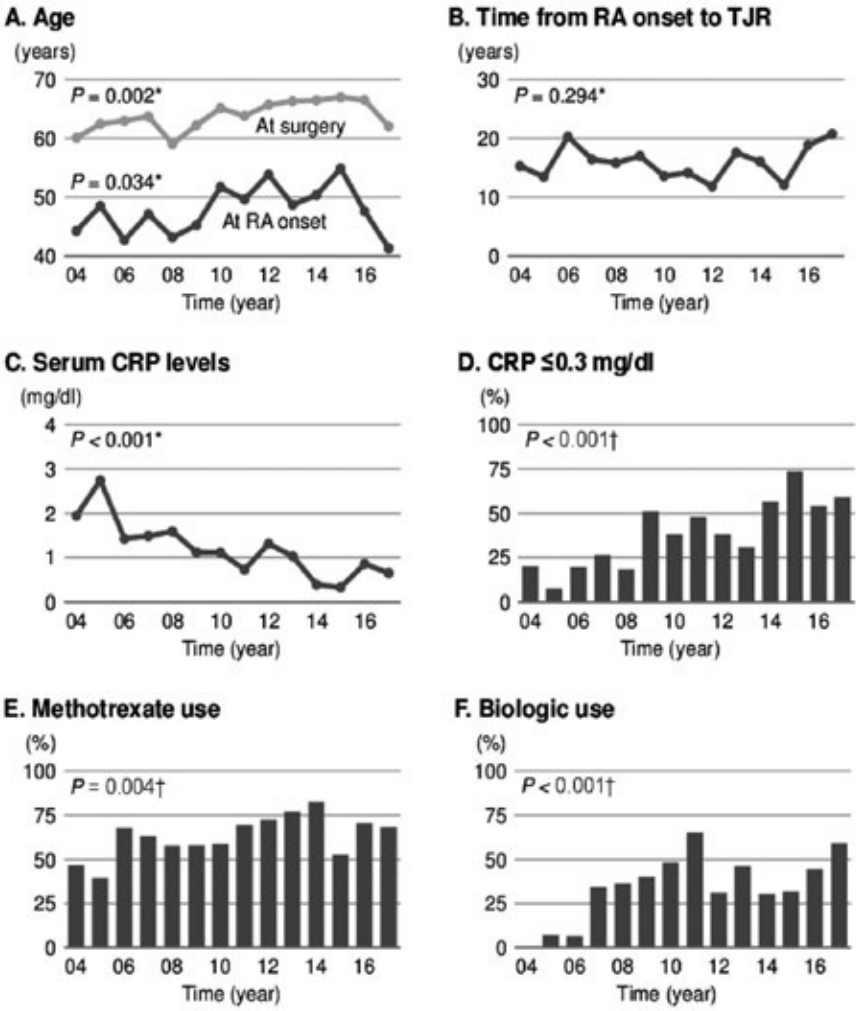
Conclusion: The number of TJRs decreased since the approval of biologics in Japan, and changes were observed in the characteristics of RA patients undergoing TJR. Negative CRP, defined as ≤0.3 mg/dl, was associated with longer times from RA onset to TJR independently of age. Newer medications and more aggressive treatment strategies to suppress disease activity can reduce the number of and delay TJR in patients with RA.

Figure 1



Time trends in numbers of total joint replacements.
*The Jonkheere-Terpstra trend test.

Figure 2



Time trends in age (A), time from rheumatoid arthritis onset to total joint replacement (B), serum C-reactive protein (CRP) levels (C), proportion of patients with CRP ≤0.3 mg/dl (D), methotrexate use (E), biologic use (F), glucocorticoid use (G), and osteophytes on radiograph (H).

Data are presented as mean values or percentage.

*The Jonkheere-Terpstra trend test; †The Cochran-Armitage trend test.

Table 1. Patient characteristics at the time of surgery

	Total	Year of surgery		P value
		2004-2010	2011-2017	
	(n=403)	(n=234)	(n=169)	
Female, %	83	85	82	0.498
Age at surgery, years	65 (58, 71)	63 (57, 69)	66 (60, 73)	0.005
Age at RA onset, years	49 (39, 59)	48 (37, 57)	51 (41, 61)	0.013
Time from RA onset to TJR, years	14 (8, 22)	14 (8, 22)	14 (8, 22)	0.619
Surgery site, %				0.024
Knee	66	67	64	
Hip	22	24	19	
Elbow	10	8	13	
Shoulder	1	0	3	
Ankle	1	1	1	
Previous large joint replacement, %	44	41	48	0.223
Use of methotrexate, %	63	56	71	0.003
Use of biologics, %	33	26	44	<0.001
Use of glucocorticoids, %	52	55	47	0.106
CRP, mg/dl	0.56 (0.17, 1.69)	0.88 (0.29, 2.22)	0.30 (0.07, 0.95)	<0.001
CRP ≤0.3 mg/dl, %	37	27	50	<0.001

Data are presented as median values (interquartile range) or percentage.
IQR: Interquartile range; SD: Standard deviation; RA: Rheumatoid arthritis;
TJR: Total joint replacement; CRP: C-reactive protein

Disclosure: S. Asai, AbbVie, 8, Abbvie, 8, Astellas, 8, Bristol-Myers Squibb, 8, Chugai, 8, Chugai Pahrmaceutical, 8, Chugai Pharmaceutical CO.,LTD., 8, Daiichi-Sankyo, 8, Eisai, 8, Janssen, 8, Janssen Pharmaceutical, 8, Pfizer, 8, Takeda, 8, Tanabe Mitsubishi Pharma, 8, UCB Japan, 8; **T. Kojima**, AbbVie, 2, 8, Abbvie, 8, Astellas, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Chugai Pahrmaceutical, 2, 8, Chugai Pharmaceutical CO., LTD., 2, 8, Daiichi-Sankyo, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Janssen Pharmaceutical, 8, Lilly, 2, 8, Mitsubishi Tanabe, 2, 8, Novartis, 2, 8, Pfizer, 2, 8, Takeda, 2, 8, Tanabe Mitsubishi Pharma, 8; **N. Takahashi**, AbbVie, 8, Asahi Kasei, 8, Astellas, 8, Bristol-Myers Squibb, 8, Chugai, 8, Chugai Pharmaceutical CO.,LTD., 8, Daiichi-Sankyo, 8, Eisai, 8, Eli Lilly, 8, Janssen, 8, Mitsubishi Tanabe, 8, Ono, 8, Pfizer, 8, Takeda, 8, UCB Japan, 8; **N. Ishiguro**, AbbVie, 2, 8, Abbvie, 2, 8, Asahi Kasei, 2, 8, Astellas, 2, 8, Astellas Pharma, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Chugai Pahrmaceutical, 2, 8, Chugai Pharmaceutical CO.,LTD., 2, 8, Daiichi-Sankyo, 2, 8, Eisai, 2, 8, Eli Lilly, 2, 8, Janssen Pharmaceutical, 8, Kaken, 2, 8, Lilly, 8, Medical Corporation Sanjinkai, 2, 5, 8, Medical Corporation Toukoukai, 2, 5, 8, Mitsubishi Tanabe, 2, 8, Ono, 2, 8, Otsuka, 2, 8, Pfizer, 2, 8, Taisho Toyama, 2, 8, Takeda, 2, 8, Tanabe Mitsubishi Pharma, 2, 8, UCB, 8, Zimmer Biomet, 2, 8.

Abstract Number: 2163

Prevalence of Postoperative Anemia in Patients with Rheumatoid Arthritis and Psoriatic Arthritis Undergoing Total Knee Arthroplasty: A Study of National Inpatient Sample 2010-2014

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster – ACR/ARP

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Total knee arthroplasty (TKA) is a valuable option for improving function and pain control in patients with end-stage arthritis, especially those with inflammatory arthritis like Rheumatoid arthritis (RA) or Psoriatic arthritis (PsA). RA and PsA have been associated with an overall increased risk of peri-operative complications, including infections and cardiovascular mortality. There is limited information comparing short-term inpatient complications like post-operative anemia and wound dehiscence in patients with RA or PsA. Anemia has been associated with delayed functional recovery for patients undergoing arthroplasty as well as higher postoperative morbidity and mortality. We aim to assess the prevalence of short term inpatient complications like post-operative anemia and wound dehiscence in patients undergoing TKA with RA and PsA.

Table 1: Comparison of hospitalizations for TKA: National Inpatient Sample 2010-2014

Characteristic	Adult TKA without RA or PsA	Adult TKA with RA	p value	Adult TKA with PsA	p value
Mean Age (in years)	65.985	64.852	<0.001	62.345	<0.001
Gender (%)			<0.001		
Male	38.2	22.17		37.67	
Female	61.8	77.83		62.33	
Race (%)			<0.001		<0.001
White	83.12	76.48		89.76	
Black	7.75	11.65		2.23	
Hispanic	5.22	7.33		4.94	
Asian or Pacific Islander	1.13	1.23		0.98	
Native American	0.51	0.7		0.36	
Other	2.26	2.6		1.73	
Mean Charlson Comorbidity Index	0.603	1.652	<0.001	0.803	<0.001
Total charges per hospitalization (in dollars)	52365	54808	<0.001	54141	0.05
Length of stay (in days)	3.0835	3.2257	<0.001	3.118	0.51

Methods: National Inpatient Sample (NIS)is the largest all-payer inpatient care database in the United States, with approximately 8 million hospitalizations each year. We extracted data for all the adult admissions for TKA from NIS database from 2010-2014 and stratified it into groups based on the status of RA and PsA; using ICD-9 CM diagnostic codes. The baseline characteristics, mortality, the prevalence of post-operative infections, wound dehiscence, and postoperative acute hemorrhagic anemia were compared, using appropriate statistical tools. Stata version 15 (College Station, TX) was used to perform the statistical analysis.

Results: An estimated total of 3172824 hospitalizations for TKA were identified, with around 3157706 TKA and 15117 revision TKA. Amongst these hospitalizations 108101 had an underlying diagnosis of RA and 7421 had an underlying diagnosis of PsA. No difference in postoperative mortality, postoperative infections, or risk of wound dehiscence was noted in these subgroups. But these subgroups were found to have significantly higher rates ($p< 0.05$)of postoperative acute hemorrhagic anemia. The Odds Ratio for patients admitted for TKA with an underlying diagnosis of RA was estimated as 1.295(95% confidence interval=1.249-1.342). 27.92% hospitalizations for TKA with underlying RA were found to have post-operative anemia (p-value < 0.001). The admissions for TKA with psoriatic arthritis also had significantly higher odds of post-operative acute hemorrhagic anemia (Odds Ratio 1.13, 95% confidence interval 1.012-1.282).

Conclusion: The study estimates that admissions for TKA with underlying RA or PsA have significantly higher rates of postoperative anemia. It may represent pre-existing anemia worsening with surgery, as RA and PsA are associated with anemia of chronic disease. Another explanation can be concomitant use of medications like NSAIDs, DMARDs, or steroids for treatment of RA and PsA. We suggest that besides pre-operative cardiovascular and infection risk assessment, patients with RA and PsA should also be screened for anemia, to avoid postoperative morbidity and mortality.

Disclosure: K. Jatwani, None; **K. Chugh**, None; **B. Bindra**, None; **S. Jatwani**, None.

Abstract Number: 2164

Lumbar Spinal Stenosis in Patients with Wild-type Transthyretin Cardiac Amyloidosis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster – ACR/ARP
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Background/Purpose: Senile systemic amyloidosis (SSA) derived from wild-type transthyretin (TTR) is a debilitating autosomal dominant disease leading to motor disability within 5 years and fatal within a decade without treatment. It is a common condition of old individuals, especially men. The main presentation is by cardiac involvement. SSA is, however, a systemic disease, and amyloid deposits may appear in many other tissues such as cartilage and ligaments[1]. Lumbar spinal stenosis is also a condition of elderly individuals in whom narrowing of the lumbar spinal canal leads to nerve compression of the lower extremities. Neuropathy caused by TTR amyloidosis had been frequently misdiagnosed as CIDP, paraproteinaemic peripheral neuropathy and other causes of acquired neuropathy[2].

Relation between Cardiac Amyloidosis and Lumbar Spinal Stenosis: adjusted for age, gender and race.				
Subgroup	n (%)	Odds Ratio (OR)	Confidence Interval (CI)	p value
Mean Age (years)	78.8	1.09 (per year of age)	95% CI 1.06-1.12	< 0.001
Female	25 (27.77)	0.028	95% CI 0.1-0.77	< 0.01
Race: -African American	25 (27.77)	3.8	95% CI 1.37-10.6	< 0.01
-Non-African American	65 (72.2)	2.07	95% CI 0.045-9.49	0.36
(n= 90; OR: 1.70; 95%-CI 1.03-2.82; p value <0.04)				

Table 1. Relation between cardiac amyloidosis and lumbar spinal stenosis, adjusted for age, gender and race.

Methods: This is a retrospective cohort study using the 2016 National Inpatient Sample (NIS) of adults hospitalized for Cardiac Amyloidosis (CA) as the admitting diagnosis and lumbar spinal stenosis (LSS) as a secondary diagnosis based on ICD-10 codes. Multivariate linear regression adjustment for confounders of age, gender and race was made. STATA 15 was used for data analysis.

Results: 1068 patients were admitted with cardiac amyloidosis in 2016, of which 90 patients had lumbar spinal stenosis (8.42%), 25 were females (27.77%), 65 males (72.2%), 65 were non-African American (72.2%) and 25 individuals were African American (27.77%). Mean age was 78.8 for those with CA and LSS, compared to 72.37 for CA and 68.3 for LSS alone. Univariate linear regression showed a significant relation between these two conditions (OR: 2.48; 95%-CI 1.49-4.12; p value: < 0.001). Multivariate linear regression adjusted to age, race and gender also showed a significant correlation (OR: 1.70; 95%-CI 1.03-2.82; p value: < 0.04). Subgroup analysis demonstrated an increased risk for developing LSS along with CA with the increase of age (OR: 1.09 per year of age; 95%-CI 1.06-1.12; p value: < 0.001) and for African-Americans (OR: 3.8; 95%-CI 1.37-10.6; p value: < 0.01). However, this association is less frequent in the female gender (OR: 0.028; 95%-CI 0.1-0.77; p value: < 0.01).

Conclusion: We conclude that LSS is quite frequent in patients with CA due to TTR-deposit therefore patients with lumbar back pain in the setting of restrictive cardiomyopathy deemed to be secondary to TTR, need a confirmatory tissue biopsy to avoid misdiagnosis because diverse treatment options are available, including tafamidis or patisiran, which all appear to be effective in early disease stages.

Relation between cardiac amyloidosis and lumbar spinal stenosis, adjusted for age, gender and race.

Disclosure: A. Arevalo, None; **F. Haddadin**, None; **S. Murray**, None; **G. Contreras**, None; **Y. Luo**, None; **Y. Ali**, None.

Abstract Number: 2165

Stakeholder Feedback on Novel Behavioral Intervention Targeting Comorbid Chronic Back Pain and Depression in Older Adults

Ailing Yang,[1] Wei Yuet,[2] LaDonna Saxon,[3] James LePage,[3] Liana Fraenkel,[4] Manney Reid,[5] and Una Makris[6], [1]UT Southwestern Medical Center, Dallas, [2]UNT Health Science Center, Fort Worth, [3]Dallas VA Medical Center and UT Southwestern Medical Center, Dallas, [4]Yale School of Medicine and VA Connecticut Healthcare System, New Haven, [5]Weill Cornell Medicine, New York City, [6]UT Southwestern Medical Center and Dallas VA Medical Center, Dallas

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster – ACR/ARP
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic low back pain (cLBP) is the 2nd most common reason for physician visits; annual related costs exceed $100 billion and are expected to rise with the aging population. Older adults with cLBP experience significant physical, psychological, and social consequences. We also know that depression frequently co-exists with cLBP and complicates management. A feasible, effective behavioral intervention targeting cLBP and comorbid depression in older adults is needed. Existing interventions are not adequate or sufficient, as they have not been specifically focused on older adults, nor have they targeted both cLBP and depression simultaneously.

We developed a novel 8-session, 12-week, telephone delivered behavioral intervention targeting older adults with cLBP and comorbid depression. MOTIVATE (Moving to Improve Chronic Back Pain and Depression in Older Adults) is delivered by a health coach who uses motivational interviewing and value concordant goal setting to capture individual motivations to increase physical activity. The ultimate goal is to improve both back pain-related disability and depression.

Table 1: Illustrative Quotes from Stakeholders Providing Feedback on MOTIVATE

Stakeholder	Theme	Illustrative Quotes
Veteran Participants	Rapport with health coach	"Before I had thoughts that stopped me from doing things. [Health coach] helped me overcome those thoughts." "Telephone calls were good. Some of the sessions were too long. I was fatigued, and [health coach] respected that and split the sessions up." "Being able to see my coach on video might be helpful."
	Motivation to follow through with goals related to physical activity	"[Health coach] motivated me a lot, once I got the idea and process of being more active to reduce depression and pain, then I got motivated by that." "This program helped me think differently about physical activity and depression…it changed me."
	Future role of health coaching within Patient Aligned Care Team	"It would be helpful to have someone who knows my values/goals call me and check in on me. Not every week! That would be a nuisance!"
Primary Care Providers including Clinic Director	Importance of health coach and goal setting in the context of pain and depression in primary care	"Goals would be valuable to know, especially if certain activities/modalities help alleviate their pain and improve their emotions. We could reinforce them." "It is very dependent on the health coach…They need to have the right personality." "Having adjunct health coach would be helpful, since we don't have time to do these types of sessions."
Health Coach	Perception of goal setting	"Goal setting … was the component the Veterans were most excited about…many at some point in their lives were very active…[this intervention] jump-started or augmented their current physical activity."
	Patient activation to improve outcomes	"Patient activation got patients out of the vicious cycle of severe depression and back pain."
	What successful implementation requires	"…requires education of staff and clinicians about what a health coach is and does…and examples of how they might help e.g. quit smoking, losing weight, exercising more."

Figure 1. Inelastic compression garment system

Methods: This single-arm pilot study of MOTIVATE was conducted to refine future intervention content, procedures, and delivery based on stakeholder feedback. The PARiHS (Promoting Action on Research Implementation in Health Services) framework was used to develop the discussion guide and facilitate individual in-depth interviews with the following key stakeholder groups: Veteran participants (n=4) over the age of 65 with comorbid cLBP and depression who received MOTIVATE, primary care providers (PCP) (n=4), clinic director (n=1), and health coach (n=1).

Results: We enrolled 8 Veterans in the pilot study who were predominately white (75%), male (87%), with a mean age of 70 years. The mean pain intensity score was 7.3/10; back pain-specific Roland Morris Disability Scale was 16.5/24; and depression (PHQ-9) score was 16.7/27. Upon completion of the intervention, semi-structured interviews with stakeholders provided valuable feedback on how to modify MOTIVATE moving forward (Table 1). Briefly, Veterans who completed MOTIVATE engaged well with the health coach, were motivated to walk with a pedometer and coaching, and felt that being more active reduced pain and depression. Of the four PCPs interviewed, all attributed the success of the intervention to the personal qualities and engagement of the health coach; we also learned about the variability in how PCPs would like results relating to patient-identified values and goals to be communicated to them. The health coach noted that Veterans were able to identify value concordant goals and easily link these to physical activities. All stakeholders stated that the individual health coach plays a critical role in activating and motivating older Veterans with complex medical and psychiatric issues.

Conclusion: This pilot study showed that we were able to effectively recruit older Veterans with cLBP and depression and deliver MOTIVATE via telephone. Feedback from key stakeholders regarding the iterative refinement of recruitment, study procedures, and content will aid the future evaluation and implementation of MOTIVATE.

Disclosure: A. Yang, None; **W. Yuet**, None; **L. Saxon**, None; **J. LePage**, None; **L. Fraenkel**, None; **M. Reid**, None; **U. Makris**, None.

Abstract Number: 2166

Multimodal Edema Management After Total Knee Arthroplasty: A Pilot Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster – ACR/ARP
Session Type: Poster Session (Tuesday)
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Background/Purpose: The ideal treatment of swelling after TKA is unclear. The purpose of this pilot study was to determine the feasibility and initial efficacy of a multimodal edema management (MEM) program including inelastic gradient compression garment, manual lymph drainage massage and home exercise for patients presenting with swelling after TKA.

Methods: This was a prospective pilot study with retrospective historical cohort comparison. Ten patients (mean ± SD, 68 ± 2 years; 6 female) were consecutively enrolled 2 weeks prior to primary TKA. Patients were excluded if they: (1) had a chronic lower extremity swelling condition including congestive heart failure; (2) had BMI > 40; (3) had a history of thrombolytic therapy > 14 d. The multimodal therapy consisted of using an inelastic compression garment (Figure 1) 12 hours daily, self-administered manual lymph drainage massage once daily for 10 minutes, and a home exercise

program (toe curling, calf pumps and knee range of motion exercises). The daily MEM program continued for 3 weeks. Primary outcomes were MEM adherence, patient satisfaction, and knee swelling quantified by bioelectrical impedance spectroscopy (BIS). Outcomes were assessed preoperatively and at 2 and 3 weeks. Secondary outcomes included quadriceps strength and activation. These outcomes were assessed preoperatively and at 3 weeks. All outcomes were

Figure 1. Inelastic compression garment system.

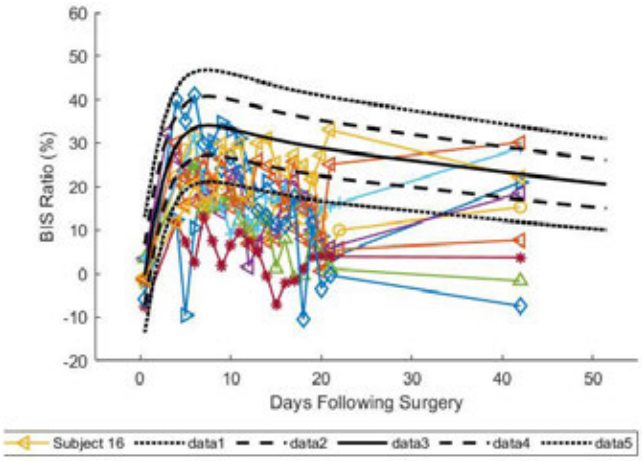

Figure 2. Plotted swelling percentiles of MEM intervention group vs. historical Controls (expected values for swelling after TKA at the 10th, 25th, 50th, 75th and 90th percentiles shown.)

re-assessed at 6 weeks. Data were compared to an historical Control group (n = 56) who met the same inclusion and exclusion criteria and who received standard physical therapy twice weekly. MEM and Control outcomes were compared using independent-samples t-tests. Preliminary effect sizes were obtained by calculating Cohen's d statistic.

Results: Mean compression garment adherence was 81.5% for hours worn per 12-hour daily goal, and 98% for all possible days of wear. Adherence to manual lymph drainage massage and home exercise program were 100% in all patients. MEM patients were similar at baseline to Control for age, sex, body mass index, ROM, quadriceps strength and quadriceps activation (all, P >.05). Mean swelling measures for MEM were 12% lower than Control at 2 weeks (P < 0.005), and 8 of 10 patients were below the 10th percentile of Control swelling at the conclusion of the 3-week intervention period (Figure 2). At 6 weeks mean swelling reductions for MEM were 7% lower than Control (P < 0.033). Mean quadriceps activation for MEM improved 17.5% at week 6 compared to 9.4% for Control (P < 0.106) with effect sizes of 0.82 and 0.38 respectively. MEM showed smaller losses in postoperative quadriceps strength at 6 weeks compared to Control (8.2 N-m vs. 21.7 N-m; P < 0.529) with effect sizes of -0.15 and -0.40 respectively. Mean loss in active knee flexion ROM was greater for MEM than Control at 2 and 6 weeks (range 16.1 to 17.4 degrees; all, P < 0.03) but effect sizes for MEM and Control at 6 weeks for this outcome were similar at 1.11 and 1.05 respectively.

Conclusion: Use of the MEM program is feasible for treating swelling after TKA and produces improvements in swelling and quadriceps activation. Future larger randomized controlled trials are needed to determine efficacy of the MEM program and determine optimal patient characteristics for success.

Disclosure: J. Carmichael, None; **M. Bade**, None; **J. Stevens-Lapsley**, None.

Abstract Number: 2167

A Randomised Controlled Clinical Trial Comparing the Effectiveness of 6 and 12 Weeks of a Shoulder Specific Exercise Programme for Patients with Rotator Cuff Related Shoulder Pain

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Type: Poster Session (Tuesday)
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Background/Purpose: Research has shown loaded exercise programmes to be beneficial for patients with rotator cuff related shoulder pain in terms of improving shoulder function, self-reported disability and pain[1,2]. The optimal duration for which these patients should complete a loaded exercise programme to achieve beneficial effects remains unclear. The purpose of this study is to determine if 6 weeks of a supervised shoulder specific exercise programme is as effective as 12 weeks of the same programme, for improving shoulder function, self-reported disability and pain, in patients with rotator cuff related shoulder pain.

Methods: In this randomised controlled single-blinded study patients with a history of lateral upper arm pain with MRI confirmation of rotator cuff pathology or positive testing on a cluster of clinical rotator cuff tests were included. Patients with a recent history of shoulder surgery or a shoulder fracture were excluded. Participants were randomly assigned to complete either 6 weeks (short group) or 12 weeks (long group) of the exercise programme. Both groups performed the same specific set of loaded exercises daily at home and attended 6 clinic-based group exercise sessions. Participants were assessed by a blinded assessor at 6 weeks, 3 and 6 months. Shoulder function was assessed using the Constant-Murley (CM) score. Disability was assessed using the QuickDash and the Shoulder Pain and Disability Index (SPADI). Pain was assessed using a visual analogue scale. Group comparisons were made using univariate generalised linear models.

Results: 85 patients were included in this study as per Table 1. An independent samples *t* test showed the two groups did not differ significantly in any of the outcome measurements at baseline ($p > .05$). Within each group all outcomes improved significantly at 3 months ($p < .05$). The mean difference between groups for each of the outcome measures are shown in Table 2. Results indicated that the long group had significantly lower pain scores at 3 months ($p = .02$). At 3 months there was no significant difference between the two groups in the CM score ($p = .415$), the SPADI score ($p = .053$) and the QuickDash score ($p = .249$). However, at 6 months, the long group had significantly greater changes in both the CM score ($p = .007$) and the SPADI score ($p = .002$). The results at six months indicate that receiving a corticosteroid injection in the three months prior to inclusion in the study did not influence participants' results within each group ($p = .97$).

Conclusion: In the management of patients with rotator cuff related shoulder pain the findings of this study indicate that a 12 week exercise programme results in better outcomes for pain at 3 months and self-reported disability and shoulder function at 6 months.

Characteristics	Short group (n = 45)	Long group (n = 40)
Sex (male/female)	24/21	21/19
Age in years median months (IRQ)	57 (15)	57 (14)
Duration of symptoms median months (IQR)	19 (18)	24 (51)
Previous physiotherapy, yes (%)	23 (51.1)	14 (35)
Corticosteroid injection, yes (%)	28 (62.2)	19 (47.5)

Table 1. Background Characteristics Of Participants

	Three months	p	Six-months	p
CM score	-2.93 [-10.05, 4.2]	.415	Group by CM score interaction	.007
Quick Dash	5.33 [-3.81, 14.47]	.249	4.36 [-4.35, 13.07]	.319
SPADI	9.28 [-.13, 18.69]	.053	Group by SPADI score interaction	.002
NPRS	1.23 [.19, 2.28]	.02	1.31 [-.01, 2.62]	.051

Table 2. Mean Difference Between Groups For All Outcome Measures

References:

1. Littlewood C, et al. Exercise for rotator cuff tendinopathy: A systematic review. Physiotherapy. 2012; 98(2), 101 - 109.
2. Holmgren T, et al. Effect of specific exercise strategy on need for surgery in patients with subacromial impingement syndrome: randomised controlled study. Br J Sports Med. 2014; 48(19), 1456-1457.

Disclosure: S. Keyes, None; **N. Walsh**, None; **M. Phelan**, None.

Abstract Number: 2168

Early Start of Outpatient Physical Therapy After Knee Replacement Is Associated with More Objectively-measured Steps and Time Spent Upright

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SESSION INFORMATION
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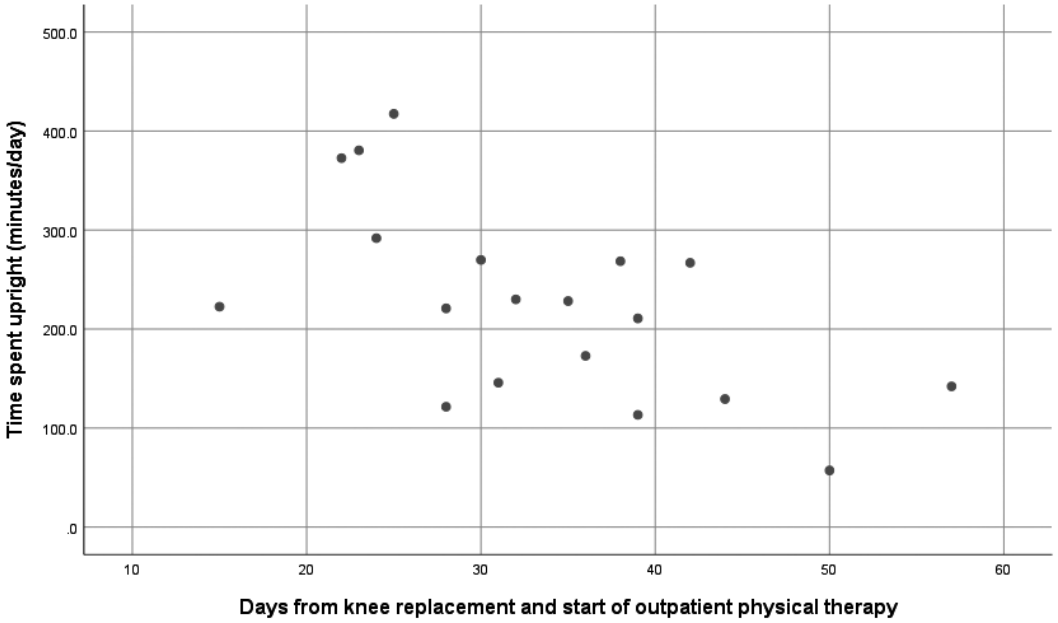
Background/Purpose: After knee replacement, patients often receive physical therapy in-home or at a rehabilitation facility shortly after surgery and then transition to outpatient physical therapy. Physical activity is typically limited at this time, but little is known about how much time is spent upright prior to the start of outpatient therapy. The purpose of this study was to determine whether the timing of outpatient physical therapy is associated with objectively-measured steps and upright time following knee replacement.

Methods: Adults 40-80 years were recruited at the first outpatient physical therapy visit following total knee replacement. Participants completed an online survey assessing demographics, a brief medical and surgical history, and wore an activPAL monitor for 7 days. The activPAL monitor assessed the number of steps/day and average minutes/day spent upright, standing, and stepping. Only valid days consisting of 24 hours of wear time were used for analyses. Linear regression, adjusting for age and body mass index (BMI) was used to determine whether the start of outpatient physical therapy was predictive of steps/day, upright, standing, or stepping time.



Relationship between the number of days from the start of outpatient physical therapy and time spent upright after knee replacement

Results: Participants (n=19) were 63.2% female, 57.9% white, with an average age of 63.0±7.4 years and body mass index of 32.8±6.2 kg/m2. Participants started outpatient physical therapy 33.6±10.3 days from surgery. On average, participants had 5.6±1.4 valid days of activPAL monitor wear. Over a 24 hour day, participants spent 224.3±97.1 minutes upright, with 160.0±30.7 minutes/day of that time standing and 64.3±30.7 minutes/day stepping. Participants took 4083.7±2038.5 steps/day. The start of outpatient physical therapy, adjusting for age and BMI, significantly predicted the time spent upright ($F(3,15) = 3.46$, $P< 0.05$, $R2 = 0.41$) (Figure 1) and stepping ($F(3,15) = 3.45$, $P< 0.05$, $R2 = 0.41$). The start of outpatient physical therapy, age, and BMI did not statistically predict the time spent standing ($F(3,15) = 3.07$, $P=0.06$, $R2 = 0.38$) and number of steps/day ($F(3,15) = 2.76$, $P=0.08$, $R2 = 0.36$).

Conclusion: The timing of the start of outpatient physical therapy predicts the number of steps/day and time spent upright in patients after knee replacement. Specifically, starting outpatient therapy sooner from surgery was associated with greater steps and time spent upright. Physical therapists may want to consider the timing of starting outpatient physical therapy in developing personalized activity plans especially among those who started late and take fewer steps/day and spent less time upright.

Relationship between the number of days from the start of outpatient physical therapy and time spent upright after knee replacement

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Disclosure: C. Pellegrini, None; **N. Mook**, None; **K. DeVivo**, None; **D. Brown**, None.

Abstract Number: 2169

Reporting of Adverse Events in Randomized Controlled Trials of Therapeutic Exercise for Knee Osteoarthritis: A Systematic Review

Johan vonHeideken,[1] and **Maura D. Iversen**[2], [1]Karolinska Institutet, Stockholm, Sweden, [2]Northeastern University, Boston

SESSION INFORMATION
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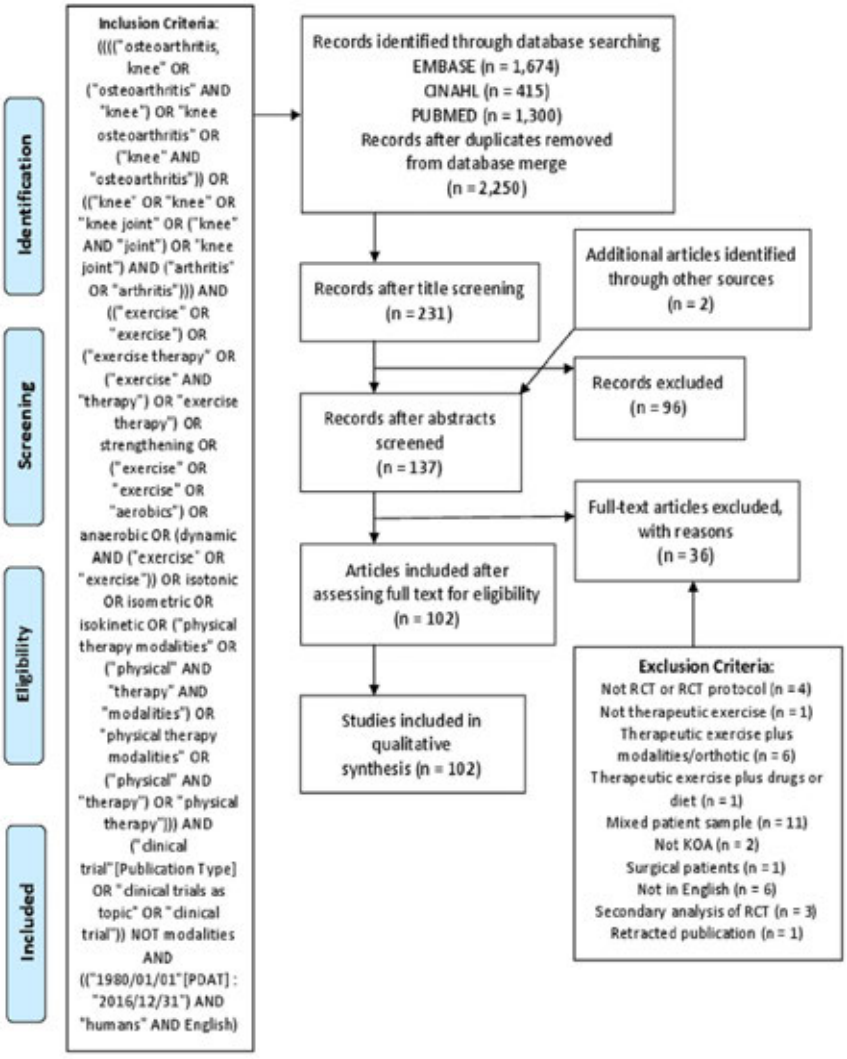
Background/Purpose: CONSORT guidelines recommend the reporting of adverse events (AEs) and drop outs, along with a description of each**.** However, the application of these guidelines in clinical trials of exercise is unknown. This study aimed to identify how AEs and drop outs are reported in clinical trials of therapeutic exercise for adults with KOA.

Methods: Cochrane Library, EMBASE, MEDLINE, and CINAHL databases were searched to identify randomized controlled trials of therapeutic exercise for patients with KOA published in English from January 1, 1980 through December 31, 2016. The American Physical Therapy Association operational definition of therapeutic exercise was used. Databases were searched using the following search terms: knee osteoarthritis AND exercise OR exercise therapy OR strengthening OR aerobics OR anaerobic OR dynamic OR isotonic OR isometric OR isokinetic OR strengthening OR aquatic OR physical therapy AND clinical trial NOT modalities. Studies which compared non-pharmacologic interventions to therapeutic exercise were eligible as long as the therapeutic exercise intervention arm included only therapeutic exercise. Studies which included patients with other forms of arthritis or with non-specified knee pain were excluded. We focused on studies which reported outcomes related to impairments, functional limitations and participation. Four researchers independently examined each study and eliminated studies which did not meet our inclusion criteria. The reference list for each chosen article was also screened for eligible studies. In instances where the eligibility of the study was unclear, the researchers deliberated and came to a consensus regarding inclusion. Using a standardized form, we extracted information regarding participant and intervention characteristics, whether there was a clear statement of AEs and drop outs and reasons for AEs and drop outs. Study quality was assessed using the PEDRO scoring method and descriptive and inferential statistics were used to characterize results.

Results: One hundred two studies from 21 countries met the inclusion criteria with 6,654 subjects exercising. Of these 102 studies, 32 studies (31%) included a statement of AEs and 14 of these studies (44%) reported AEs. Eighty-five studies (83%) had a clear statement regarding drop outs and 20 studies (23%) gave reasons for drop out that could be classified as AEs. Forty percent of studies published in North America and Western Europe had a statement of AEs compared to 25% of studies from the rest of the world (p=0.13). Adverse events were reported for 59 patients and 55 individuals dropped out for reasons that could be considered an AEs, yielding 114 patients (2%) experiencing an AE-related to exercise.

Conclusion: Overall the quality of included studies was good. Geographic variations existed in statements about AEs. AEs and drop outs may be underreported and not sufficiently represent the risk associated with therapeutic exercise. Greater clarity regarding definitions of AEs and adherence to the CONSORT reporting guidelines are needed to best determine safe dosing of therapeutic exercise for KOA.

Figure1: PRISMA Flow Diagram of Randomized Studies of Therapeutic Exercise for KOA



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement.* PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

TABLE 1: Summary of Adverse Event Reporting in Clinical Trials of Therapeutic Exercise (n=102)

Category	
Total number of subjects in exercise arm	6,664
Studies with a clear statement of adverse events	32 (31.4%)
Studies which reported adverse events occurring	14 (13.7%)
Total number of patients exercising in studies which had a clear statement of adverse events	2,484
Number of patients who had an adverse events related to exercise in studies that had a clear statement about AEs	59 (2.4%)
Studies which reported patients experiencing an adverse event NOT related to exercising	6 (14.3%)
Studies with a clear statement of drop outs	85 (83.3%)
Studies which reported drop outs	30 (29%)
Total number of patients exercising in studies which had a clear statement of drop outs	5,926
Studies in which reasons for drop outs could be considered adverse events (eg. Back pain, knee pain, neck pain, leg pain, wrist pain)	20 (23.5%)
Proportion of patients who dropped out where the reasons for drop out could be interpreted as an adverse event plus total # of adverse events reported	114 (2%)

** 30 studies had both a statement of AEs and drop outs

Disclosure: J. vonHeideken, None; **M. Iversen**, Pfizer, 2, Swedish Rheumatism, 2, Norrebacca Eugenia Foundation, 2.

Abstract Number: 2170

Risk Factors for Poor Outcomes After Hip Fracture Patients in the Robust Elderly: Are Patient Reported Outcomes Important?

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Background/Purpose: Low energy hip fractures are feared harbingers of morbidity and mortality. However, many older adults are high functioning and cognitively intact at the time of fracture, and thus death or loss of health-related quality of life post-hip fracture is unexpected and particularly devastating. Whether patient reported outcome meas-

TABLE 1. BASELINE DATA	
	Hip Fracture Patients (n=319)
Female (%)	70.9
White (%)	85.6
Age (years) [IQR]	81.7 [74.9, 87.3]
College educated or higher (%)	66.7
Pre-fracture Scores	**T-score**
PROMIS Physical Function [IQR]	45.3 [37.9, 56.9]
PROMIS Anxiety [IQR]	40.3 [40.3, 55.8]
PROMIS Depression [IQR]	41.0 [41.0, 51.8]
PROMIS Fatigue [IQR]	43.1 [33.7, 53.1]
PROMIS Sleep Disturbance [IQR]	48.4 [41.1, 52.4]
PROMIS Ability to Participate in Social Roles [IQR]	64.1 [51.6, 64.1]
PROMIS Pain Interference [IQR]	41.6 [41.6, 53.9]
PROMIS Pain Intensity* [IQR]	0 [0, 4]
*Pain Intensity = 0-10 Visual Analog Scale. All other PROMIS scores are T-scores (population mean=50). Higher PROMIS score = MORE of the domain being measured. PROMIS scores are reported as MEDIAN [INTERQUARTILE RANGE]	

ures (PROMs), collected at time of fracture, might provide risk stratification in these patients is unknown. This study evaluates the association of pre-operative PROMs with adverse events, death, and function in a cohort of robust, cognitively intact elderly patients 1-year after surgery for a low energy hip fracture.

Methods: Patients ≥ 65 at a single center who underwent surgical repair of a low trauma hip fracture were enrolled. Patients with active cancer, dementia, previous or bilateral hip fracture, or with a non-U.S. address were excluded. American Society of Anesthesiologists (ASA) risk score was recorded. The Lubben Social Networks Scale, a validated instrument designed to measure social isolation in the elderly, PROMIS29 and the Lower Extremity Activity Scale (LEAS) were administered 2-4 days post-op. to assess pre-fracture status, and again at 1-year. Adverse events (AEs) were recorded at 30 days, 3-months, and 1-year. Multivariable exact logistic regression was used to generate odds ratios and Wald 95% confidence intervals. Multivariable linear models were specified for each PROM of interest and each outcome, adjusting for confounders identified a priori using a directed acyclic graph approach. All analyses used SAS 9.4.

Results: 956 patients were screened; 140 excluded for dementia, 85 for cancer, 66 for previous/bilateral hip fracture, 211 for other reasons, and 319 consented to enroll. Subjects had less PROMIS29 anxiety, depression, fatigue, sleep disturbance, and better ability to participate in social roles than population means, though slightly worse physical function (Table 1). 31.9% were socially isolated pre-fracture. 19 subjects died, and of 189 patients eligible for follow up, 140 (74.1%) provided 1-year data.

There was no statistically significant association between pre-fracture social isolation and any PROMIS29 domain, or cumulative AEs at 1-year. In an analysis controlling for ASA score, social isolation predicted cumulative 1-year mortality, OR 2.9 (95% CI 0.95-9.4; p=0.06); this estimate is imprecise, however, as only 19 deaths were observed. In a multivariable linear regression controlling for PROMIS29 scores, age, race, sex, and ASA score, an increase in PROMIS29 physical function (β =0.18 p< 0.001) and male sex (β =1.4 p=0.03) were associated with an increase in 1-year LEAS function.

Conclusion: Although these results are imprecise due to the small number of deaths, our observations suggest pre-fracture social isolation could be associated with an almost 3x increase in 1-year mortality in these robust, cognitively intact, elderly hip fracture patients. Further research needs to verify these estimates. Identifying actionable risk factors, such as social isolation, which can be feasibly elicited at point of care, could help direct resource-intense interventions to high priority patients.

Disclosure: L. Mandl, Annals of Internal Medicine, 3, Annals of Internal Medicine- Associate Editor, 3, UpToDate, 7, Wolters Kluwer - Author at UptoDate, 7, Wolters Kluwer - Author at UpToDate, 7, Wolters Kluwer- Author at UpToDate, 7; **D. Sheira**, None; **M. Frey**, None; **J. Finik**, None; **K. Grueter**, None; **J. Lane**, None.

Abstract Number: 2171

Functional Exercise for Adults with Chronic Nonspecific Low Back Pain

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Table 1 Demographic and clinical characteristics at baseline

	EG (N=42)	CG (N=42)	p
Age (years)	39.5 ± 8.3	35.9 ± 9.7	0.069
Gender (female:male)	30:12	31:11	0.807
BMI in kg/m^2 (mean ± SD)	27.3 ± 5.5	26.4 ± 4.6	0.425
Schooling (years)	14.7 ± 2,6	15.3 ± 4.3	0.942
Employment n (%)			0.921
Formal work	26 (61.9)	24 (57.2)	
Self employed	9 (21.4)	8 (19.0)	
Work at home	2 (4.8)	2 (4.8)	
Not working	5 (11.9)	8 (19.1)	
Time of pain n (%)			0.354
3 Months to 1 year	9 (21.4)	5 (11.9)	
Between 1 and 3 years	6 (14.3)	12 (28.6)	
Between 3 and 5 years	6 (14.3)	5 (11.9)	
Less than 5 years	21 (50.0)	20 (47.6)	

Values are presented as the average ± standard deviation or percentage

Table 2. Between-groups four pain, functional capacity, kinesiophobia, general health and perceived exertion at all evaluation times

	Experimental Group				P intra-group	Control Group				P intra-group	p Value (GLM)
	T0	T6	T12	T24		T0	T6	T12	T24		
Numeric rating scale	6.2 (1.3)	3.1 (1.8)	2.3 (1.9)	2.3 (1.8)	<0.001	6.0 (1.7)	5.5 (1.7)	5.5 (1.8)	5.5 (1.6)	0.098	<0.001*
Oswestry	20.7 (10.8)	12.0 (7.0)	9.5 (6.3)	8.9 (6.4)	<0.001	25.5 (11.3)	22.1 (10.3)	22.5 (10.5)	22.8 (10.9)	0.025	<0.001*
Roland Morris	6.9 (5.0)	4.1 (3.3)	2.8 (2.6)	2.6 (2.4)	<0.001	8.4 (5.3)	7.6 (4.7)	7.3 (4.7)	8.1 (5.2)	0.136	<0.001*
6MWT	494.2 (57.5)	498.8 (63.5)	503.2 (55.3)	500.5 (44.2)	--	479.8 (73.1)	477.2 (70.4)	469.3 (64.8)	462.0 (69.6)	--	0.056
TUG	8.3 (1.1)	8.27 (1.94)	7.84 (1.08)	7.86 (0.83)	<0.001	8.7 (2.6)	8.69 (1.90)	8.99 (2.14)	9.08 (2.49)	0.084	0.005*
FABQ											
FABQ work	18.6 (15.7)	12.4 (9.0)	10.5 (9.3)	7.5 (7.4)	<0.001	17.6 (12.0)	16.8 (12.0	16.6 (11.1)	17.6 (11.4)	0.800	<0.001*
FABQ phys	11.9 (6.2)	7.1 (6.5)	7.0 (6.0)	6.9 (6.1)	<0.001	13.0 (6.3)	13.0 (7.1)	13.2 (7.3)	13.0 (7.5)	0.958	<0.001*
Short form-36											
Physical functioning	66.1 (21.3)	77.7 (16.5)	83.8 (13.8)	82.4 (14.3)	<0.001	60.1 (25.7)	61.8 (24.2)	58.2 (26.4)	60.1 (26.7)	0.374	<0.001*
Physical Role	55.4 (40.8)	78.1 (31.2)	86.3 (24.8)	87.7 (17.6)	<0.001	45.8 (39.8)	48.8 (38.2)	49.4 (42.9)	47.0 (39.9)	0.923	0.046*
Bodily pain	45.8 (17.0)	65.1 (19.8)	76.7 (16.0)	66.7 (21.6)	<0.001	40.0 (14.9)	55.7 (20.4)	62.0 (21.7)	61.1 (24.7)	<0.001	<0.001*
General health	64.8 (21.3)	68.3 (18.9)	77.2 (15.6)	76.0 (15.2)	<0.001	62.0 (20.1)	65.6 (17.2)	62.0 (17.2)	62.0 (17.4)	0.231	<0.001*
Vitality	46.4 (19.1)	58.8 (17.2)	64.1 (15.4)	62.7 (17.6)	<0.001	48.0 (22.3)	46.5 (21.2)	48.6 (18.9)	47.6 (19.9)	0.374	<0.001*
Social functioning	68.6 (24.7)	80.2 (18.6)	87.5 (17.0)	87.4 (17.1)	<0.001	65.7 (41.8)	64.8 (25.0)	69.6 (26.9)	68.3 (27.1)	0.393	<0.001*
Emotional Role	55.4 (41.5)	72.1 (36.8)	82.4 (29.8)	82.2 (27.0)	0.001	61.7 (41.8)	55.5 (42.1)	56.3 (46.3)	64.2 (43.2)	0.517	<0.001*
Mental health	62.7 (20.0)	70.9 (17.4)	74.6 (14.9)	72.3 (14.5)	<0.001	61.9 (21.0)	59.7 (22.8)	66.2 (20.4)	63.7 (21.1)	<0.001	0.074

Data are expressed as the mean (standard deviation); T0, baseline; T6, evaluation after 6 weeks – end of the treatment; T12, evaluation after 12 weeks; T24, evaluation after 24 weeks – follow-up.

Background/Purpose: To assess the effectiveness of a functional exercise program for pain, functional capacity, general health, kinesiophobia, medication consumption and patient satisfaction in adults with chronic nonspecific low back pain.

Methods: A randomized controlled clinical trial with intention-to-treat analysis and 24-week follow-up was performed. Eighty-four patients were randomly assigned to an experimental group (EG) or control group (CG). The EG participated in the functional exercise program performed twice a week for twelve weeks. The functional exercise program was composed of global exercises that worked the group of muscles in the trunk and lower and upper limbs with progression every 4 weeks. The two groups received an informative class on the disease and were advised to use analgesics if necessary. Evaluations were performed at baseline, after 6, 12 and 24 weeks by a blinded evaluator. The primary outcome was low back pain measured by the numeric rating scale (NRS). Secondary outcomes included functional capacity by the Oswestry and Roland-Morris questionnaires, 6-minute walk and TUG tests, kinesiophobia (FABQ), general health (SF-36), medication consumption and satisfaction with treatment (Likert scale). Sample size was calculated. The tests were used: Kolmogorov-Smirnov, Chi-square, Student's-T and Mann-Whitney. We used the Generalized Linear Models (GLM) with Bonferroni adjustments and the intention-to-treat analysis were performed.

Results: The groups were homogeneous for all parameters at baseline. Compared with the CG, the EG significantly improved pain ($p< 0.001$), functional capacity (Oswestry, Roland Morris ($p< 0.001$) and TUG ($p=0.005$), FABQ ($p< 0.001$) and most of the SF-36 parameters.

Conclusion: The functional exercise program was effective in improving pain, functional capacity, kinesiophobia and general health in adults with chronic nonspecific low back pain.

Disclosure: E. Moreira, None; **A. Jones**, None; **E. Lima**, None; **F. Jennings**, None; **J. Natour**, None.

Abstract Number: 2172

Depression of Vitamin D Levels After Adult Primary Posterior Spinal Fusion: Are We Adding Insult to Injury?

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster – ACR/ARP
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Vitamin D is a steroid hormone metabolized to its active form in the presence of parathyroid hormone in the kidney. Vitamin D is essential in the process of bone formation which in turn is vital for achieving spinal arthrodesis. Previous studies have indicated that 43% of patients who undergo orthopedic surgery are vitamin D deficient (Bogunovic et al. 2010). Animal studies demonstrated that vitamin D modulates consolidation of bone after grafting for spinal posterolateral fusion in rats (Metzger et al 2015). Low vitamin D levels and increased inflammatory markers have been found following total knee arthroplasty (Henriksen et al 2013). Studies have suggested that spinal fusion patients presenting with vitamin D deficiency achieved lower fusion rates and had higher rates of recurrent persistent back pain compared with patients with normal vitamin D levels (Rodriguez and Gromelski 2013). If patients are deficient in vitamin D preoperatively and their levels decrease postoperatively, do they ever attain the preoperative baseline and, if not, does this have any bearing on successful spinal fusion? To our knowledge no large prospective study has been published that measures changes in vitamin D levels immediately after surgical spinal fusion. We share this data as part of an ongoing study investigating the relationship between serum 25-hydroxyvitamin D 25(OH) D levels and spinal fusion outcomes 1 year after surgery.

Methods: In total, 103 participants were enrolled in this prospective cohort study of patients undergoing one or two-level primary posterior lumbar spinal fusion with four surgeons between 2016 and 2018. The current study describes a preliminary analysis of all patients who had serum 25(OH)D measured at baseline, postoperative day 1 (POD-1) and at a follow-up visit within six weeks after surgery (n=70, mean follow-up time=31.9 ± 20.0 days). Average age and BMI of participants were 64.1 ± 10.7 years and 28.7 ± 6.2 kg/m^2, respectively. 54% of patients were taking vitamin D supplements at baseline, and were on average older (p=0.005) and more likely to be female (p=0.001) than those who did not take supplements. Median differences in 25(OH)D were calculated at each time point and tested by Wilcoxon signed rank test.

Results: Median 25(OH)D was 35.3 ng/mL at baseline (range, 9.5-95.0 ng/mL) and 27.8 ng/mL at POD-1 (range, 7.0-63.5 ng/mL). Median change in 25(OH)D from baseline to POD-1 was -7.1 ng/mL or -20.9% (p< .0001). The majority (63%) of patients who had been taking vitamin D supplements at baseline had normal (>30ng/mL) levels at POD-1, while this was true for only 19% of patients who were not taking vitamin D (p=0.001).

Conclusion: The results of this study suggest that many patients who undergo posterior spinal fusion have inadequate 25(OH)D levels at the time of surgery. These results raise the question of whether or not ultimate success of fusion could be affected by low vitamin D levels. Given the high prevalence of vitamin D insufficiency and deficiency in patients not taking supplements as well as in those that do, we suggest that it might be beneficial to optimize 25(OH) D levels prior to surgery. Further research examining the effect of low 25(OH)D levels and 25(OH)D optimization on fusion success is recommended.

Disclosure: I. Smith, None; **S. Golenbock**, None; **G. Miley**, None; **S. Tromanhauser**, None.

Abstract Number: 2173

Descriptive Analysis of Patient-Reported Home Exercise and Physical Activity and Their Associations with Patient Baseline Characteristics Following Total Knee Replacement

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster – ACR/ARP
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Background/Purpose: Total knee replacement (TKR) is one of the most common elective surgeries and is effective for managing knee pain in osteoarthritis. However functional outcomes post TKR are variable. Exercise and physical activity (PA) improve functional outcomes post TKR, but little is known about the role of specific content and dosage of exercise and PA on outcomes. While most patients receive some physical therapy (PT) post TKR, PT exercise content and dosage vary widely and are poorly documented. Importantly, trends in healthcare show more patients are receiving less direct PT and are instructed to perform exercise and PA with no supervision or with "virtual" supervision at home. Our study describes the content and dosage of exercise and PA that patients performed at home post TKR and assesses patient attributes that may influence patient engagement in exercise and PA.

Methods: Patients from 3 US states and multiple outpatient PT sites post-TKR recorded home exercises and PA performed using daily logs. Logs included exercise name, repetitions, sets, resistance, perceived difficulty (RPE), and PA per day. Three independent reviewers identified exercise type, total and weekly average of exercises, total and weekly average of progressions and total and weekly average of PA. Patient demographics, health status and joint-specific symptoms were collected at baseline through patient-reported assessment surveys. Descriptive statistics of patient and exercise factors are reported. Chi^2 and Fisher's exact tests and linear regressions are used to identify patient factors associated with characteristics of exercise and PA.

Age (years)	66.1 (8.9)
Sex (% female)	66.1
BMI	31.0 (5.16)
Pain in other knee (% none/mild)	66.7
LBP (% none/mild)	82.1
Pre-operative MCS*†	58.5 (10.8)
Pre-operative PCS*†	32.4 (9.1)
Pre-operative KOOS (pain)* ‡	46.3 (19.0)

*Range 0-100, lower indicates more impairment
†Mental (MCS) and Physical (PCS) components of the SF12 Health Status Questionnaire
‡Pain scale of the Knee Injury and Osteoarthritis Outcome Score

Table 1. Patient characteristics (mean (s.d.)

Total strength volume (no. of ex X no. of days)	113.8 (74.19); 106.0 (103.5)
Ave strength volume per week	30.0 (18.8); 26.7 (27.75)
Total CC volume (no. of ex X no. of days)	38.8 (35.65); 28.5 (51.5)
Ave CC volume per week	10.2 (9.03); 7.6 (12.87)
Total OC volume (no. of ex X no. of days)	75.0 (51.8); 74.5 (79.0)
Ave OC volume per week	19.5 (13.2); 18.6 (19.83)
Ratio of CC to OC	0.76 (.96); 0.44 (.75)
Total number of strengthening Progressions	5.2 (4.1); 4.0 (6.0)
Ave strengthening progressions per week	1.4 (1.1); 1.1 (1.75)
Total flexibility exercise volume (no. of ex X no. of days)	59.2 (36.0); 57.0 (51.0)
Ave flexibility volume per week	16.4 (9.15); 15.6 (11.75)
Total number of flexibility progressions	2.0 (3.7); 1.0 (3.0)
Ave flexibility progressions per week	0.6 (1.0); 0.25 (0.75)
Ratio of strengthening to stretching volume	2.71 (2.55); 1.9 (2.7)
Total exercise volume (strength plus flexibility)	173.0 (90.6); 168.5 (115.5)
Average total exercise volume per week	45.39 (23.3); 43.25 (31.38)
Total progressions	7.2 (5.5); 6.0 (7.5)
Average progressions per week	1.95 (1.59); 1.5 (2.0)
Total PA volume in minutes	1040.0 (1063.9); 690.0 (940.)
Average PA minutes/week	264.0 (264.0); 189.2 (231.25)

Table 2. Exercise and Physical Activity Factors (mean (s.d.); median (IQR))

Results: 74 patients returned exercise logs, 15 were excluded for incomplete or unclear responses; 50 records included 4 weeks of exercise logs; 9 included < 4 weeks. Patient characteristics are similar to those in a national registry of total joint replacement patients (FORCE-TJR) (Table 1). Amount of weekly exercise and PA varied widely (Table 2). On average (s.d.) patients performed 45.4 (23.3) exercises weekly, more strengthening than stretching (30.0 (18.8) vs 16.4 (9.2)). More strengthening exercises were non-weight bearing (OC) than weight bearing (CC). Average PA was 264.0 (264.0) minutes per week. We found no statistically significant associations between patients' clinical attributes and types or quantity of exercise and PA, although trends existed suggesting sex, presence of low back pain (LBP) and pre-operative function may affect home exercise engagement**.**

Conclusion: Patient-reported amount of at-home exercise and PA varied widely. Exercise logs often overstate patient engagement, but our data show wide variations in quantity, with some patients reporting few exercises and little PA and others reporting extreme amounts. Patients' clinical attributes did not help explain this variation. As post TKR rehabilitation trends suggest more dependence on home exercise and PA than on face-to-face PT, it is essential that we understand the source of variation in the type and quantity of at-home exercise and PA. Future research will examine the influence of patient engagement and variation in home exercise and PA on long term functional outcomes post TKR in order to optimize functional outcomes.

Disclosure: C. Oatis, None; **N. Mendoza**, None; **W. Murray**, None; **B. Novak**, None; **W. Li**, None; **H. Zheng**, None; **P. Franklin**, None.

Abstract Number: 2174

Test-Retest Reliability and Validity of a Mobile Health Application to Automate the 30 Seconds Chair Stand Test – Preliminary Data to Create a Contemporary Instrument for Randomized Clinical Trials

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Contemporary technologies offer potential solutions to improve and automate data collection of randomized clinical trials by transitioning assessments from the clinic to the real-world. Mobile health (mHealth) applications (Apps) associated with smartphone embedded sensors offer the possibility to automate objective physical function tests by tracking, recording, and analyzing quantitative participant data. An automated mHealth app brings to clinicians and researchers the opportunity to reliably monitor physical function at more frequent intervals within a real-world setting. To create this tool, we collected preliminary data to establish the test-retest reliability and validity of an automated mHealth app to assess performance on a 30-second chair-stand test when compared with the gold standard assessment technique.

Methods: We recruited 10 healthy individuals to participate in two data collection sessions separated by 7 days. Individuals were at least 21 years old, able to comfortably walk 20 meters without an assistive device, and had an iPhone 5 or higher. We developed a mHealth App that uses algorithms associated with the smartphone's embedded motion sensors (gravitometer and accelerometer) to automate the count of the repetitions during the 30-seconds chair-stand test. During the test, the participant's smartphone was positioned inside an elastic strap at the chest level. Participants performed three trials in which they completed as many repetitions of standing and

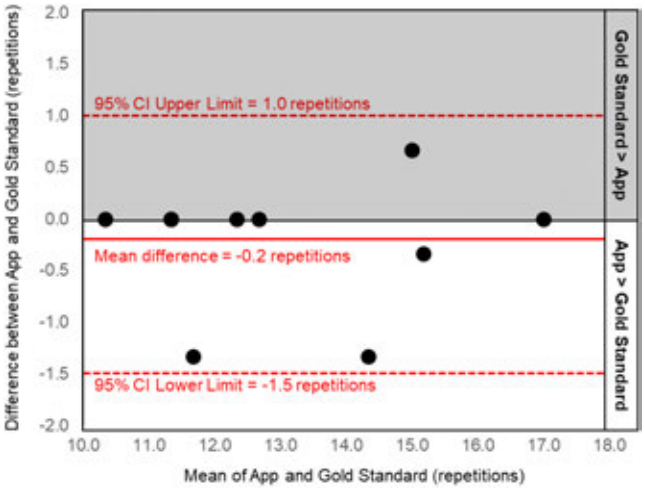

Figure 1. Bland-Altman Plot for the 30-second Chair Stand Test.

sitting from a standard chair during 30 seconds. For each trial, the mHealth app counted the number of repetitions completed by the participants. During the same three trials, an assessor manually counted the number of repetitions as the gold standard for assessing performance. The number of repetitions between the three trials was averaged for the mHealth app and the gold standard. Bland-Altman plots and Intraclass Correlation Coefficients (ICC) were used to establish agreement and inter-rater reliability between the gold standard and the mHealth app, respectively. ICCs were used to assess test-retest reliability between the two different sessions for the gold standard and the mHealth app.

Results: The majority of our sample was female (80%) with a mean ± standard deviation age of 30 ± 7 years, and body mass index of 24.7 ± 5.4 kg/m^2. The Bland-Altman plots demonstrate good agreement between the gold standard test and the mHealth app since no data points fell outside the 95% limits of agreement (upper limit:1.0 and lower limit -1.5 chair stands; **Figure 1**). Additionally, there is excellent reliability between the gold standard and the mHealth app ($ICC_{2,k}$ = 0.98). When comparing across the two different sessions, the gold standard ($ICC_{2,k}$ = 0.93) and mHealth app ($ICC_{2,k}$ = 0.89) demonstrate similar test-retest reliability.

Conclusion: The results suggest that our mHealth app is a reliable and valid tool to objectively quantify performance during the 30-second chair-stand test in healthy individuals. This data will lay the foundation for further development of algorithms to automate other objective physical function tests, as well as future implementation in clinical trials.

Disclosure: L. Dantas, None; **M. Harkey**, None; **A. Dantas**, None; **L. Price**, None; **J. Driban**, None; **T. McAlindon**, None.

Abstract Number: 2175

Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single Ascending Doses of the Anti-ADAMTS-5 Nanobody®, M6495, in Healthy Male Subjects: A Phase I, Placebo-Controlled, First-in-Human Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a serious disease characterized by progressive joint failure and cartilage degeneration. In OA, ADAMTS-5 protease is upregulated, resulting in enhanced cleavage of joint cartilage aggrecan into fragments (e.g. the aggrecan neo-epitope family [ARGS]) and subsequent stimulation of synovial inflammation. M6495 is an anti-catabolic, bivalent, bifunctional Nanobody® that selectively inhibits ADAMTS-5 *in vitro*, reducing aggrecan cleavage. This Phase I, single-center, randomized, double-blind, placebo-controlled, single ascending dose (SAD), first-in-human (FIH) study (NCT03224702) was conducted in healthy male subjects to explore the safety, tolerability, immunogenicity, pharmacokinetics (PK), and pharmacodynamics (PD) of single subcutaneous doses of M6495, with the aim to guide clinical development.

System Organ Class Preferred Term	Pooled Placebo N=18 (100%) n (%)	M6495 n (%) 1 mg N=6 (100%)	5 mg N=6 (100%)	20 mg N=6 (100%)	75 mg N=6 (100%)	150 mg N=6 (100%)	300 mg N=6 (100%)	All Doses N=36 (100%)	Overall N=54 (100%) n (%)
Subjects with at least one event	12 (66.7)	5 (83.3)	4 (66.7)	4 (66.7)	5 (83.3)	6 (100.0)	4 (66.7)	28 (77.8)	40 (74.1)
Nasopharyngitis	4 (22.2)	2 (33.3)	0 (0.0)	3 (50.0)	1 (16.7)	0 (0.0)	2 (33.3)	8 (22.2)	12 (22.2)
Headache	4 (22.2)	1 (16.7)	2 (33.3)	1 (16.7)	0 (0.0)	2 (33.3)	1 (16.7)	7 (19.4)	11 (20.4)
Injections site reaction	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	1 (16.7)	1 (16.7)	4 (11.1)	4 (7.4)
Dermatitis contact	4 (22.2)	1 (16.7)	0 (0.0)	0 (0.0)	1 (16.7)	1 (16.7)	0 (0.0)	3 (8.3)	7 (13.0)
Epistaxis	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (16.7)	1 (16.7)	3 (8.3)	3 (5.6)
Myalgia	1 (5.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	1 (16.7)	1 (16.7)	3 (8.3)	4 (7.4)

Table 1. Most common treatment-emergent adverse events by preferred term (safety analysis set)

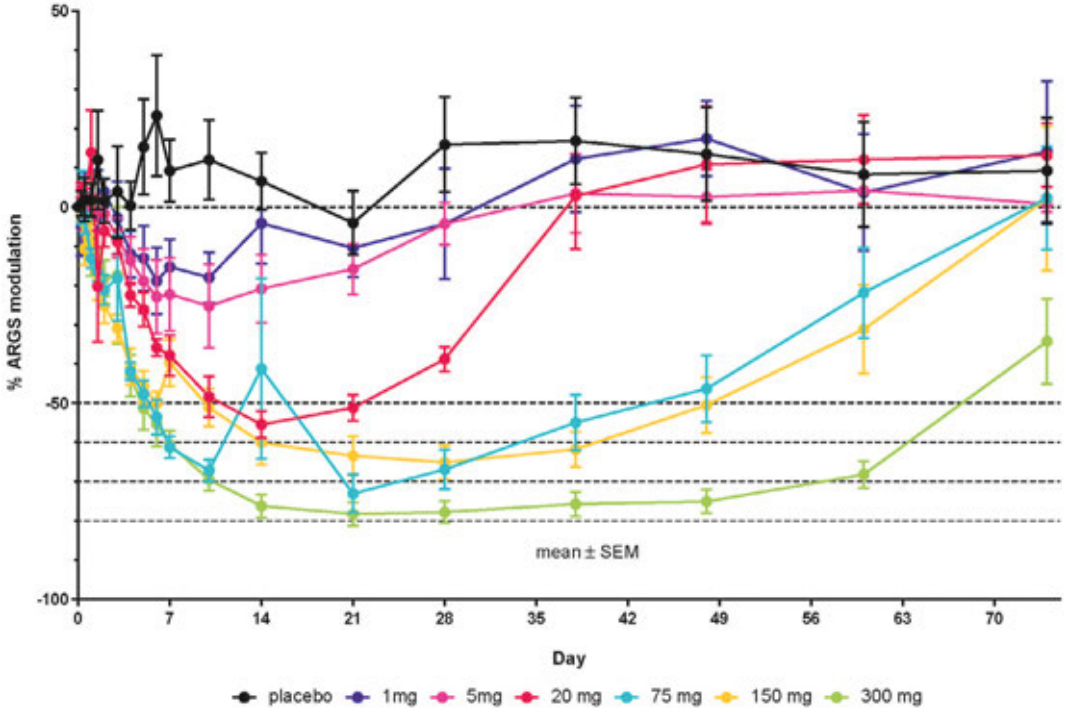

Figure 1. Mean M6495 serum-concentration profiles for all treatments (PK analysis set)

Methods: Male subjects (18–55 years old, body mass index of ≥18.5–≤29.9 kg/m^2) were randomized 2:1 to either M6495 or placebo in 6 dose-level (DL) cohorts (1 mg, 5 mg, 20 mg, 75 mg, 150 mg, 300 mg). Primary endpoints were safety and tolerability. Secondary endpoints were serum-based M6495 PK parameters and PD parameters, including percent change from baseline in ARGS. Exploratory endpoints included the effects of M6495 on versican degradation fragment (VCANM) and high-sensitivity C-reactive protein (hsCRP).

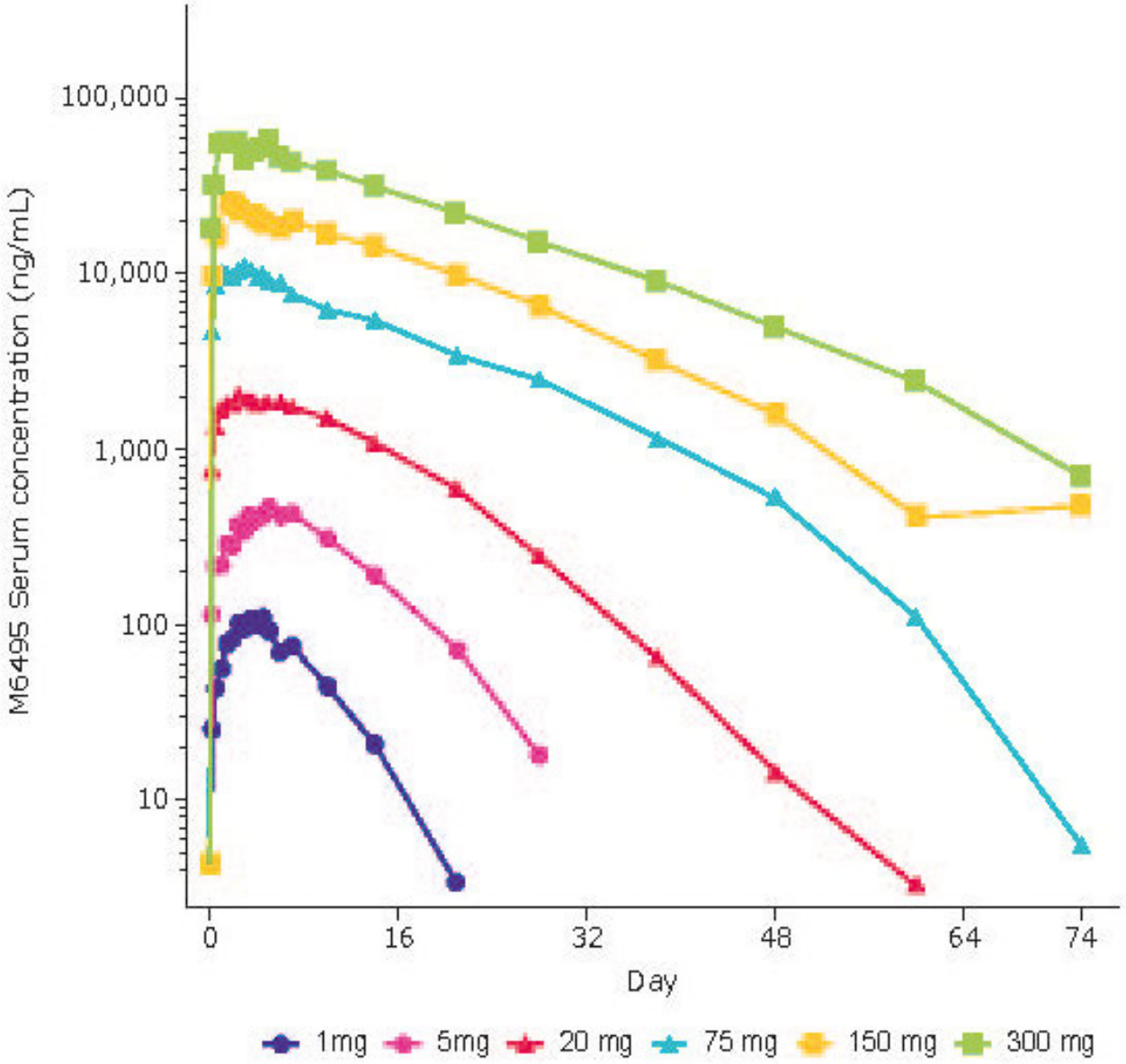

Figure 2. Mean (± standard error of the mean) percentage ARGS modulation (PD analysis set)

Results: 53/54 randomized healthy subjects completed the study; 1 discontinued due to an internship in Africa. Overall, there was minimal difference in treatment-emergent adverse event (TEAE) rate either between each M6495 DL cohort or between M6495 and placebo; 28 (77.8%) subjects receiving M6495 and 12 (66.7%) receiving placebo experienced TEAEs. The most common TEAEs are shown in **Table 1**; the majority were of mild intensity. Observed injection site reactions were mainly mild in nature and within expectations for a therapeutic protein. No deaths or safety signals emerged based on reported TEAEs or laboratory measurements. Based on serum AUC and C_{max}, M6495 exposure increased in a slightly greater-than-dose-proportional manner across the dose range (**Figure 1**). Median M6495 t_{max} ranged from 24–120 hours following administration of M6495. ARGS levels were reduced from baseline in a dose-dependent manner (**Figure 2**). Overall, 6 subjects had anti-drug antibodies (ADA); 2 in the placebo cohort and 1 each in the 5 mg, 20 mg, 75 mg and 300 mg cohorts. In 1 subject, ADA occurred at Day -1. Presence of ADA did not affect PK. In the 300 mg cohort, ARGS levels decreased by up to 78% vs baseline (95% CI = [54, 100]) and up to 93% vs placebo (mean [95% CI]: 93% [65, 120]) by electrochemiluminescence immunoassay. Following administration of 300 mg M6495, an ~45% decrease in mean percentage change from baseline

serum ARGS was maintained through 74 days (last planned time point) vs placebo, whereas reductions of >30% were maintained up to 60 days in the 75 mg and 150 mg cohorts. No significant modulation of hsCRP or VCANM were detected.

Conclusion: The observed safety profile of M6495 at single doses up to 300 mg appeared to be acceptable for further clinical development. M6495 dose-dependently inhibited release of the ARGS aggrecan fragment family.

Disclosure: H. Guehring, Merck KGaA, Darmstadt, Germany, 3; **T. Balchen**, DanTrials ApS, 3, 9; **K. Goteti**, EMD Serono Research and Development Institute, Inc., 3; **J. Sonne**, None; **C. Ladel**, Merck KGaA, Darmstadt, Germany, 3; **V. Ona**, Merck KGaA, Darmstadt, Germany, 3; **F. Moreau**, EMD Serono Research and Development Institute, Inc., 3, EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), 3; **A. Bay-Jensen**, Nordic Bioscience, 1, 2, 3; **A. Reinstrup Bihlet**, Nordic Bioscience, 1, 3.

Abstract Number: 2176

A Novel Composite Score Reflecting Disease Activity Predicts Future Knee Replacements: Data from the Osteoarthritis Initiative

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SESSION INFORMATION
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Background/Purpose: While knee osteoarthritis (KOA) leads to cumulative damage to a diarthrodial joint there are also more dynamic processes that fluctuate throughout the disease process (e.g., bone marrow lesions [BMLs], effusion-synovitis). To monitor the different constructs of structural progression, we recently validated 2 magnetic resonance (MR)-based composite scores. First, the cumulative cartilage damage score represents hyaline cartilage damage throughout the knee, relates to radiographic severity, and reflects the damage attributable to KOA over the

Table. Disease Activity is Associated with Knee Replacement Over the Subsequent 9 Years in Univariate Analyses

Variable	No Knee Replacement (REFERENCE) mean (SD)	Knee Replacement mean (SD)	Odds Ratio (95% CI) OR per SD
Primary Analysis: All Groups	**n = 355**	**n = 19**	
Baseline Cumulative Damage (SD = 3.65)	0.02 (3.62)	-0.34 (4.29)	0.91 (0.58 to 1.42)
Baseline Disease Activity (SD = 2.71)	-0.13 (2.24)	1.98 (6.95)	**1.47 (1.11 to 1.95)**
1-Year Change Cumulative Damage (SD = 0.61)	0.29 (0.58)	0.33 (0.99)	1.07 (0.69 to 1.66)
1-Year Change Disease Activity (SD = 4.61)	0.71 (3.16)	4.81 (14.81)	**1.51 (1.08 to 2.1)**
Sensitivity Analysis: Only AKOA Group	**n = 101**	**n = 18**	
Baseline Cumulative Damage (SD = 3.89)	0.01 (3.85)	-0.65 (4.19)	0.85 (0.52 to 1.38)
Baseline Disease Activity (SD = 3.82)	0.18 (2.83)	2.12 (7.13)	1.44 (0.96 to 2.16)
1-Year Change Cumulative Damage (SD = 0.79)	0.47 (0.74)	0.35 (1.01)	0.84 (0.49 to 1.46)
1-Year Change Disease Activity (SD = 7.31)	1.51 (4.53)	5.08 (15.19)	1.45 (0.93 to 2.25)

Note: SD = standard deviation, OR = odds ratio, AKOA = accelerated knee osteoarthritis

course of the disease. Secondly, the disease activity score is a composite of BMLs and effusion-synovitis volumes that relates to knee pain and reflects a patient's current state of disease and symptoms. It is unknown if these composite scores predict poor clinical outcomes (e.g., knee replacement). Hence, we assessed adults without radiographic KOA to determine if baseline and 1-year change in cumulative cartilage damage or disease activity predicted knee replacement over the subsequent 9 years.

Methods: We performed a secondary analysis using existing MR-based data from a sex-matched nested case-control study of 3 groups from the Osteoarthritis Initiative without radiographic KOA at baseline (Kellgren-Lawrence (KL)< 2): 1) accelerated KOA: developed KL 3 or 4 within 48 months; 2) typical KOA: increase in KL grade within 48 months; 3) no KOA: no change in KL grade within 48 months. We quantified tibiofemoral cartilage damage, BML volume, and effusion-synovitis volume with semi-automated programs. All MR-based measures were normalized to bone width and standardized, so all measurements were on the same scale. The cumulative cartilage damage score was the sum of standardized cartilage damage for the medial and lateral tibia and femur. The disease activity score was the sum of the standardized volumes of effusion-synovitis (single volumetric measure) and BML (4 locations: medial and lateral tibia and femur). The outcome was knee replacement (partial or total) that was reported or observed between the 1- and 9-year follow-up (>96% adjudicated). For the primary analyses we combined the 3 groups and used logistic regression models to assess if baseline or 1-year change in cumulative cartilage damage or disease activity predicted knee replacement. We performed a sensitivity analysis limited to those who developed accelerated KOA.

Results: The groups were mostly female (63%) and overweight, 33% reported frequent knee pain within a year of baseline, 23% developed radiographic KOA during the first year (KL >1), and 19 people received a knee replacement between the 1- and 9-year follow-up. Greater baseline and 1-year change in disease activity, but not cumulative cartilage damage, was statistically associated with greater chance of receiving a knee replacement (Table). These findings were consistent among adults who developed accelerated KOA.

Conclusion: Prior to the onset of radiographic KOA, disease activity was associated with a knee replacement over the subsequent 9 years. This supports the construct validity of disease activity, which relates to knees symptoms that are the main reason a person would receive a knee replacement.

Disclosure: J. Driban, Pfizer, Inc., 8; **M. Harkey**, None; **L. Price**, None; **G. Lo**, None; **J. Pang**, Pfizer, Inc., 3; **M. Zhang**, None; **T. McAlindon**, None.

Abstract Number: 2177

Sarcopenia and the Likelihood of Incident Knee Osteoarthritis and Knee Pain Among Older Adults in the Health ABC Study

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Background/Purpose: Osteoarthritis (OA) disproportionately affects older adults. Sarcopenia, or reduced muscle mass and strength, is strongly associated with reduced physical function and poor clinical outcomes among older adults. Prior studies of knee OA and sarcopenia used varied measures of muscle mass and strength, and results are conflicting. We tested whether two components of sarcopenia, lean mass and muscle strength, are associated with increased risk of incident knee OA and knee pain among older adults.

Methods: Data derived from the first 6 annual assessments of the Health ABC Study, a study of body composition and physical function in community dwelling adults aged 70-79 years. At baseline, appendicular lean mass (ALM) was measured by whole-body dual energy x-ray absorptiometry and grip strength by hand-held dynamometry. Incident OA by year 5 of follow-up was defined by participants' report A) that a doctor told them that they have osteoarthritis or degenerative arthritis of the knee, AND B) of having knee pain most days of the last month OR lasting >1 month in the past 12 months. Separate logistic regression analyses modeled the relationship of low ALM (low vs not low) (men < 19.75kg, women < 15.02kg[1]); and low grip strength (low vs not low) (men < 26kg, women < 16kg[1]) with the development of 1) incident knee OA and 2) incident knee pain (defined per B) above) over follow-up, adjusting for gender, race, baseline age, and baseline BMI. Participants who were lost or died prior to the end of follow-up were considered as not having developed the outcome, and those with the outcome at baseline were excluded. Secondary analyses modeled relationships of ALM and grip strength as continuous measures with the odds (per standard deviation (SD) decrement in exposure variable) of incident knee OA and knee pain.

Results: Table 1 presents baseline characteristics (n=2182). Forty-one (3.7%) and 300 (26.9%) men, and 94 (4.3%) and 367 (16.8%) women developed incident knee OA and knee pain, respectively. Neither low ALM (compared to not low ALM) nor low grip strength (compared to not low grip strength) was significantly associated with incident knee OA or incident knee pain. However, each SD decrement in grip strength was statistically significantly associated with increased likelihood of knee pain (OR per SD: 1.18, 95%CI: 1.03-1.35), Table 2); but the association between grip strength (as a continuous variable) and knee OA did not reach significance. ALM (as a continuous variable) was not significantly associated with either knee OA or knee pain.

Conclusion: Our findings suggest that weaker grip strength may be associated with development of incident knee pain, but not incident knee OA, in older adults. That those with low grip strength (compared to those without low grip strength) were not statistically more likely to develop incident knee pain suggests that published grip strength cut-points may be inadequate to identify older adults at increased risk of developing knee pain. Those with low ALM (compared to those without low ALM) were not statistically more likely to develop either incident knee OA or knee pain. Grip strength may, thus, be a useful tool to identify older adults at increased risk of knee pain.

Table 1: Participant Baseline Characteristics (n=2182)	
Age, years	73.6 ± 2.8
Female, n (%)	1067 (48.9%)
White, n (%)	1295 (59.3%)
BMI, kg/m^2	26.8 ± 4.5
ALM, kg	20.1 ± 5.0
Grip Strength, kg	30.5 ± 10.5
Low ALM[1], n (%)	547 (25.1%)
Low Grip Strength[1], n (%)	145 (6.6%)

All values are mean SD unless otherwise specified.
BMI: Body mass index
ALM: appendicular lean mass
[1]Low ALM: men <19.75kg, women <15.02kg; low grip strength men <26kg, women <16kg (McLean RR, Shardell MD, et al. Criteria for clinically relevant weakness and low lean mass and their longitudinal association with incident mobility impairment and mortality: the foundation for the National Institutes of Health (FNIH) sarcopenia project. J Gerontol A Biol Sci Med Sci. 2014;69(5):576-83)

Table 2: Odds ratios and 95% confidence intervals for the effect of appendicular lean mass (ALM) or grip strength on risk of incident knee osteoarthritis (OA) or knee pain over the first 5 years of follow-up in the Health ABC Study (n=2182)*

	Knee OA (n=2182)	Knee Pain (n=2182)
Low ALM[1] (y/n)	0.68 (0.41-1.14)	0.82 (0.64-1.07)
Low Grip Strength[1] (y/n)	1.15 (0.58-2.27)	1.31 (0.91-1.88)
ALM+ (kg)	0.88 (0.61-1.26)	0.88 (0.73-1.06)
Grip Strength+ (kg)	1.07 (0.80-1.41)	**1.18 (1.03-1.35)**

Bold font indicates p<0.05.
*All models are adjusted for gender, race, baseline age, and baseline body mass index (BMI).
+Odds ratios are expressed per SD decrement in the predictor variable.
[1] Low ALM: men <19.75kg, women <15.02kg; low grip strength men <26kg, women <16kg (McLean RR, Shardell MD, et al. Criteria for clinically relevant weakness and low lean mass and their longitudinal association with incident mobility impairment and mortality: the foundation for the National Institutes of Health (FNIH) sarcopenia project. J Gerontol A Biol Sci Med Sci. 2014;69(5):576-83)

Disclosure: J. Andrews, None; **L. Gold**, None; **M. Nevitt**, None; **P. Heagerty**, None; **P. Cawthon**, None.

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Associations Between Baseline and Longitudinal Quantitative Joint Space Width and Incident Hip Osteoarthritis: The Johnston County Osteoarthritis Project

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Background/Purpose: To quantify associations between baseline and change in computer-assisted hip quantitative joint space width (qJSW) with incident radiographic (rHOA) or symptomatic (sxHOA) hip OA.

Methods: The Johnston County OA Project (JoCoOA) is a longitudinal study of African American and white men and women. We analyzed individuals with anteroposterior pelvis x-rays from baseline and 3 follow up timepoints, approximately 6 years apart. Per protocol, women < 50 years did not have pelvis radiography. An expert musculoskeletal radiologist (JBR) assigned all hips a Kellgren-Lawrence grade (KLG). At all timepoints, participants reported presence of hip symptoms (On most days, do you have pain, aching, or stiffness in your (right, left) hip?"). Incident rHOA was KLG ≥ 2 at follow up, while incident sxHOA required both rHOA and symptoms in the same hip, among those without baseline rHOA or sxHOA, respectively. An independent reader (JD), blinded to all other data, measured qJSW (at 50 degrees, **Figure 1**) using a previously validated method. Analyses were in two steps. First, we used latent class modeling to identify clusters of hips with different patterns of qJSW change from baseline. Second, incident rHOA and sxHOA were modelled using logistic regression with generalized estimating equations to account for correlated hips; the independent relationship of baseline qJSW and identified cluster membership by sex with each outcome

Figure 1. Fixed location qJSW measurements

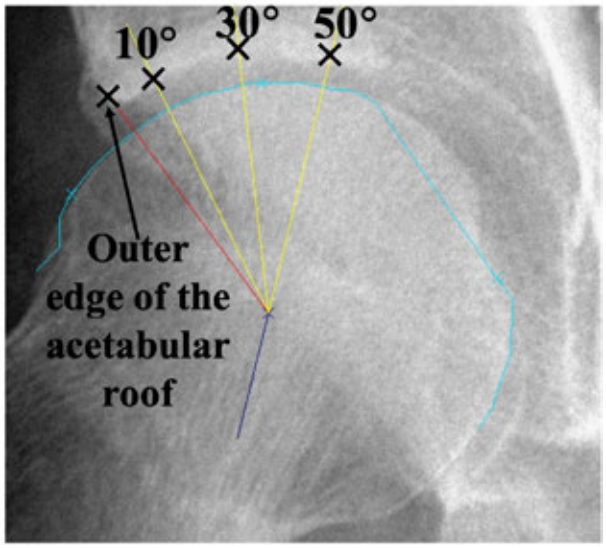
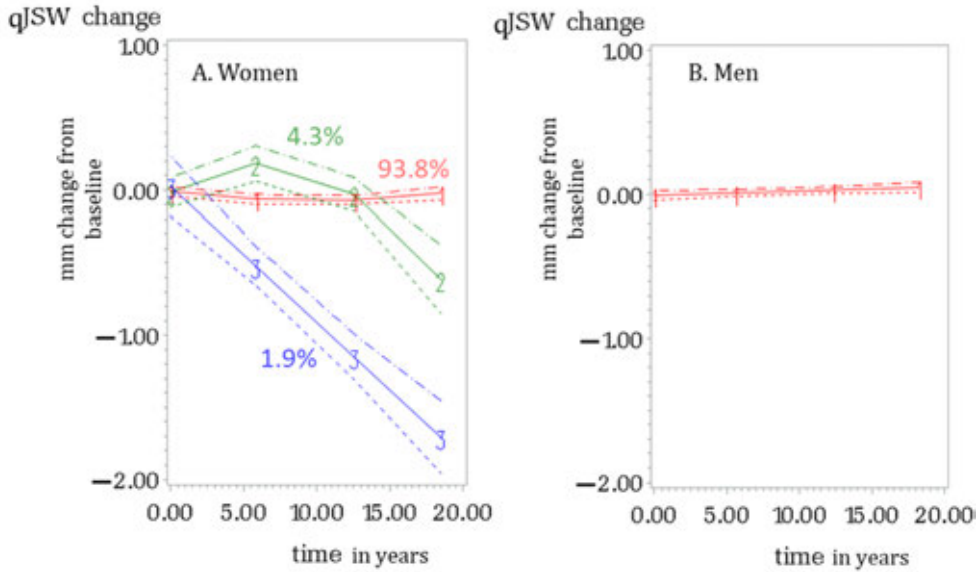


Figure 2. Identified groups and patterns of quantitative joint space width (qJSW) change over time among women (A) and men (B). Results are for the radiographic hip osteoarthritis (HOA) analytic samples (similar results were seen for the symptomatic HOA samples).



was estimated using adjusted (for age, race, education, height, body mass index [BMI], weight gain or loss [5% BMI change], and hip injury) odds ratios and 95% confidence intervals.

Results: Of 577 participants with 1154 hips meeting above criteria, 397 participants and 784 hips remained (59% women, 24% African American, average age 56 years) after excluding those missing hip films or with hip replacement. Baseline BMI was 28.6 (5.1) kg/m^2; 52% experienced >5% BMI increase over follow-up.

Among women, after exclusions for missing qJSW at 50 degrees and prevalent HOA, 360 and 410 hips were included in the incidence analysis of rHOA and sxHOA, resulting in an overall incidence of 25% and 13%, respectively. Three

Table 1. Adjusted* odds ratios and 95% confidence intervals [aOR (95% CI)] for the association of baseline quantitative joint space width (qJSW) and non-constant change in qJSW over time with incident radiographic (rHOA) or symptomatic hip osteoarthritis (sxHOA), separately for women (top) and men (bottom).

Sex	Main effect(s) for each model	Incident rHOA (H=number of hips in model)	Incident sxHOA (H=number of hips in model)
Women	*Overall effect*	*(H=360)*	*(H=410)*
	Loss of qJSW over time group (vs constant qJSW over time group)	**3.56 (1.73, 7.32)**	**3.28 (1.01, 10.7)**
	1 mm narrower (1SD) at baseline	**2.04 (1.43, 2.91)**	**2.71 (1.70, 4.33)**
Men	*Overall effect*	*(H=261)*	*(H=297)*
	1 mm narrower (1SD) at baseline	**1.63 (1.11, 2.37)**	**1.61 (1.04, 2.52)**

*Adjusted for: baseline age, race, education, BMI, height, 5% weight loss over time, any hip injury over time;
BOLD=statistically significant

patterns were seen in qJSW change over time; a constant qJSW group (**Figure 2.A**=1 red; n=394 [94%]), and two groups with loss over time (**Figure 2.A**=2 green and 3 blue; n=26 [6%]), combined for analysis. Narrower baseline qJSW and loss of qJSW over time were independently associated with increased odds of incident rHOA and sxHOA (**Table 1**).

Among men, after exclusions for missing qJSW at 50 degrees and prevalent HOA, 261 and 297 hips were included in the incidence analysis of rHOA and sxHOA, resulting in an overall incidence of rHOA and sxHOA of 21% and 10%, respectively. Men had only one qJSW pattern--constant over time (**Figure 2.B** red). In adjusted models, narrower qJSW at baseline was associated with increased odds of incident rHOA and sxHOA (**Table 1**).

Conclusion: Narrower qJSW at baseline predicts incident rHOA and sxHOA in both men and women, although more strongly in women; qJSW loss over time predicted incident HOA only in women. QJSW assessment may identify individuals at increased risk for HOA, allowing for earlier intervention to try to reduce HOA progression.

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Abstract Number: 2179

Erosive Hand Osteoarthritis, Metabolic Syndrome and Knee Osteoarthritis: A Cross-sectional Study Using Data from the PROCOAC Cohort

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Background/Purpose: Erosive hand osteoarthritis (EOA) is often considered a more severe form of hand OA. However, more data are needed regarding this phenotype to conclude if represents a different subset of hand OA or a different degree of affectation of the same disease. The purpose of this work is to compare the clinical pattern of patients with EOA with those that do not show this phenotype

Methods: This cross-sectional study was conducted in the Prospective Cohort of Osteoarthritis A Coruna (PROCOAC). The cohort consists of 1136 subjects, of which 877 were diagnosed of hand OA following ACR criteria. After reviewing the x-rays, we split the cohort into patients with and without EOA, and subsequently analyzed both clinical and demographic data within each group, together with the assessment of the AUStralian CANadian Osteoarthritis Hand (AUSCAN) index. The study consisted in a Univariate analysis comparing different variables between both groups, followed by a stepwise regression logistic regression analysis.

Results: The mean age of the cohort was 63.61±9.03 years and consisted of 718 females and 159 males. Of the 877 OA patients, 167 had EOA. The Univariate analysis revealed that patients with EOA were younger (59.85±7.95 vs 64.43±9.04;p< 0.001), smokers (p=0.008), with lower BMI (p=0.007), increased inflammatory episodes (p< 0.001), more presence of nodal OA (p=0.001), with family history or suffering psoriasis (p=0.046) and less number of damaged joints (p< 0.001), specially the knee (p< 0.001). In addition, despite the higher number of females suffering from hand OA, no significant differences between erosive and non-erosive phenotypes in terms of gender were detected.

The regression model (Table 1) confirmed the strong association of age (OR=0.964;95%CI=0.939-0.991;p=0.008), inflammatory episodes (OR=4.367;95%CI=2.489-7.663;p< 0.001) and increased prevalence of nodal OA (OR=2.249;95%CI=1.159-4.363;p=0.017) with the EOA. Interestingly, the model also showed MetS as a risk factor too, specifically over 64 years (OR=2.194;95%CI=1.249-3.854;p=0.006), with the tryglicerides content as the metabolic component most involved in this association (p=0.082). In addition, EOA patients show a lower prevalence of knee OA (OR=0.437;95%CI=0.259-0.739;p=0.002) and to carry this phenotype at baseline does not confer a significant increased risk for radiographic knee OA progression over time (p=0.515). The AUSCAN score showed significantly higher mean values in patients with the EOA: pain (58.66±28.78 vs 41.83±32.26; p< 0.001), function (56.19±27.44 vs 39.22±30.01; p< 0.001) and stiffness (55.47±32.34 vs 39.28±36.41;p=0.001).

Conclusion: EOA is associated with more inflammation in younger patients, and worst AUSCAN score. Contrarily to the non-erosive phenotype, the presence of erosions associates with a lower occurrence of other forms of OA,

Table 1. Logistic regression analysis describing all the variables influencing the erosive hand OA phenotype in the Spanish cohort PROCOAC

Variable	B	Adjusted OR	95% CI	p-value
Gender (female)	-0.250	0.779	0.423 – 1.433	0.422
Age	-0.036	0.964	0.939 – 0.991	**0.008***
BMI (Kg/m^2)	-0.017	0.983	0.939 – 1.030	0.477
MetS	0.786	2.194	1.249 – 3.854	**0.006***
Knee OA	-0.827	0.437	0.259 – 0.739	**0.002***
Nodular OA	0.810	2.249	1.159 – 4.363	**0.017***
Psoriasis[&]	0.156	1.169	0.730 – 1.872	0.515
Inflammatory symptoms	1.474	4.367	2.489 – 7.663	**<0.001***

B: Regression coefficient; BMI: body mass index; MetS: Metabolic syndrome; OR: Odds Ratio; CI: Confidence Interval; ([&]): Includes family history of psoriasis and/or psoriasis; (*): (**in bold**) statistical significance declared at p < 0.05

specially knee OA, as well as with no incidence on the radiographic knee OA progression. In our cohort, EOA seems to be more localized in the hand and it also seems to be associated with psoriasis and nodal OA.

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Abstract Number: 2180

High Molecular Weight Intraarticular Hyaluronic Acid for the Treatment of Knee Osteoarthritis: A Network Meta-Analysis

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Background/Purpose: The 2013 American Academy of Orthopaedic Surgeons (AAOS) clinical practice guideline (CPG) on the treatment of knee OA made a strong recommendation not in favor of the use of intraarticular hyaluronic acid (IAHA) because, though statistically significant, improvement in pain did not meet the threshold for a minimal clinically important difference (MCID). The AAOS CPG, and publications since, suggest there may be clinically important differences in the effectiveness of high vs. low molecular weight (MW) IAHA. We aimed to update the evidence-base since the guideline publication and use a network meta-analysis (NMA) to incorporate both direct and indirect evidence on this issue.

Methods: MEDLINE, Embase and CENTRAL were systematically searched to identify RCTs evaluating non-surgical interventions for people with knee OA. Trials were selected based on the AAOS CPG eligibility criteria. Effect sizes from each trial were computed using a pain measure hierarchy and longest follow up. The mean difference between intervention and comparator was converted to the standardized mean difference (SMD) before incorporating into the NMA using a random-effects Bayesian framework. To assess the impact of MW, high MW (HMW; defined as at least 6000 kDa) and low MW (LMW; < 750 kDa) nodes were created. Studies of IAHA which fell outside this definition were excluded. Sensitivity analyses were used to examine the robustness of the findings.

Results: The base-case analysis included a total of 14 RCTs (N=2,793), creating a network with 5 therapeutic nodes (Figure 1). Trials on NSAIDs, acetaminophen, and oral opioids were excluded as they lacked network connectivity. The results indicated that compared to IA placebo, HMW IAHA had a statistically significant effect on pain, which was "possibly clinically significant" according to the AAOS definition (SMD -0.57 [95% Credible Interval: -1.0, -0.11]) (Figure 2). In contrast, LMW IAHA resulted in a small, non-statistically significant improvement in pain relative to IA placebo (-0.23 [-0.67, 0.20]). The Bayesian model showed that HMW IAHA had the highest probability (71%) of ranking 1st with regard to improvement in pain score. Back-transforming the SMD to the WOMAC 0-100 pain scale indicated a 14.65 [13.93, 15.62] point improvement over IA placebo, substantially better than the AAOS minimum clinically important improvement threshold of 8.3. Sensitivity analyses confirmed these findings were robust.

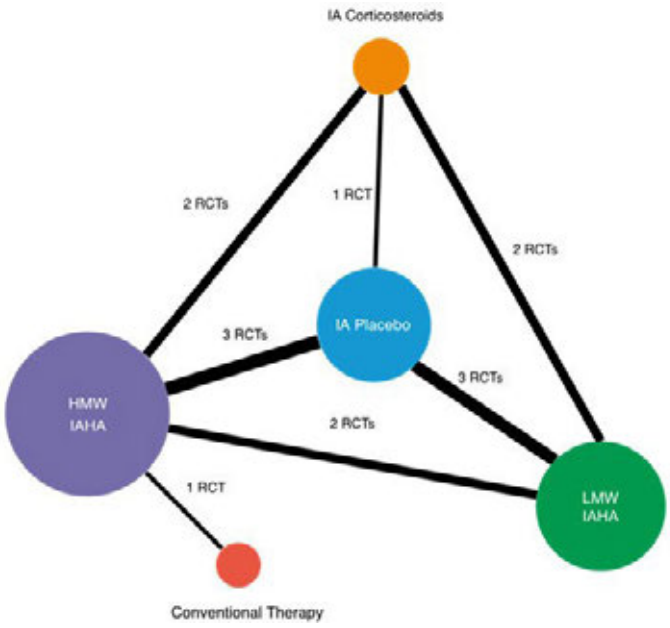

Figure 1. Network of trials comparing improvement in pain scores using nonoperative treatment for patients with knee osteoarthritis. The size of the nodes is proportional to the total number of participants and the width of the lines is proportional to the number of trials comparing every pair of treatments.

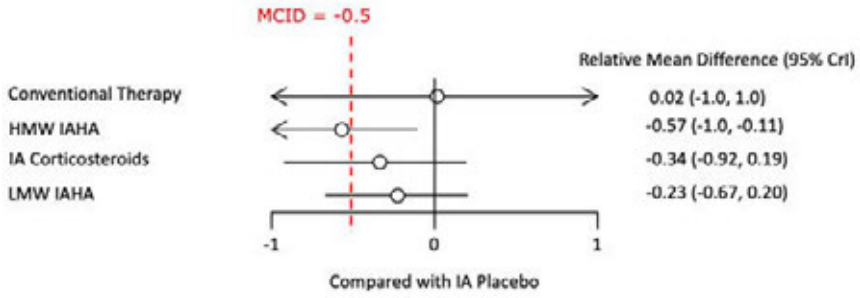

Figure 2. Relative standardized mean differences for each intervention compared to IA placebo based on network meta-analysis.

Conclusion: Based on direct and indirect evidence, stratified data of HMW IAHA (≥6000 kDa) revealed a pooled effect in pain relief which exceeded even the most conservative threshold for a MCID. Meaning, on average, the improvement can be subjectively perceived by the affected persons under therapy. In contrast, the pooled effect of LMW IAHA (< 750 kDa) is neither statistically significant nor clinically relevant. Amalgamation of data of LMW and HMW IAHA may have blurred the benefits of IAHA, which have led to negative therapy recommendations in the past. Differentiation according to the molecular weight offers refined insight into the IAHA treatment. The sub class of HMW IAHA's should be further evaluated in new focused RCTs.

Disclosure: C. Hummer, Flexion Therapeutics, 5, Sanofi, 5; **F. Angst**, None; **E. Schemitsch**, Sanofi, 5; **C. Whittington**, Doctor Evidence, 3; **C. Manitt**, None; **W. Ngai**, Sanofi, 1, 3, Sanofi US, 1, 3.

Abstract Number: 2181

Natural Disease Progression in Hand Osteoarthritis: Results from a Belgian Ten-years Prospective Cohort Study

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

Background/Purpose: Limited evidence is available about natural disease progression in hand osteoarthritis (HOA). A previous study of the Ghent HOA cohort showed a positive association between soft tissue swelling, tenderness upon pressure and pain with radiographic progression (1). The aim of the study is to study natural radiographic and clinical disease progression in HOA after 10 years of follow up.

Methods: From 2007 to 2009 (baseline, T0), 270 patients with HOA were included in a Belgian HOA register. On average, the disease was already ongoing for > 12 years at baseline. A first follow up visit (T1) occurred after approximately 5 years (n = 154) and a 2nd (T2) after 10 years (n= 106). Presence of tender and swollen joints was assessed. Grip strength was measured. FIHOA and AUSCAN were completed. Pain was scored on visual analogue scale (VAS pain, 0 -100). Radiographs of hands were taken and scored according to the scoring system by Verbruggen and Veys (2). Patients were categorized into 'non-significant radiographic progression', 'erosive ('E') progression only', "E' progression and remodeling ('R') occurring simultaneously' and "R' progression only'. Changes from N to S were considered non relevant. Longitudinal analyses were performed for patient related outcome measures from follow up (T1 or T2) to baseline (T0).

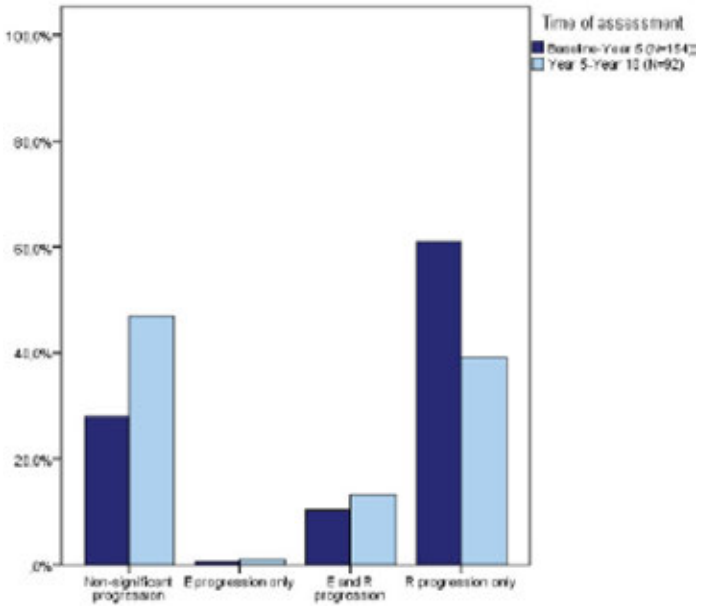

figure 1 Radiographic progression in HOA from baseline to T1 and T1 to T2

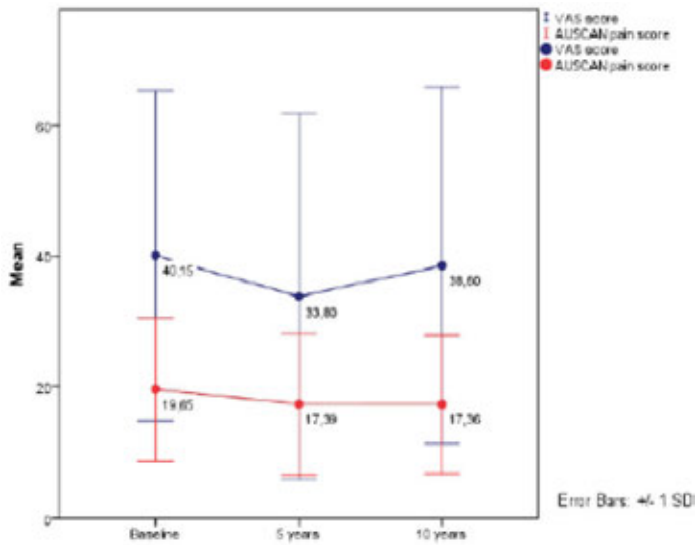

Figure 2 Longitudinal changes in functional status (FIHOA and AUSCAN function)

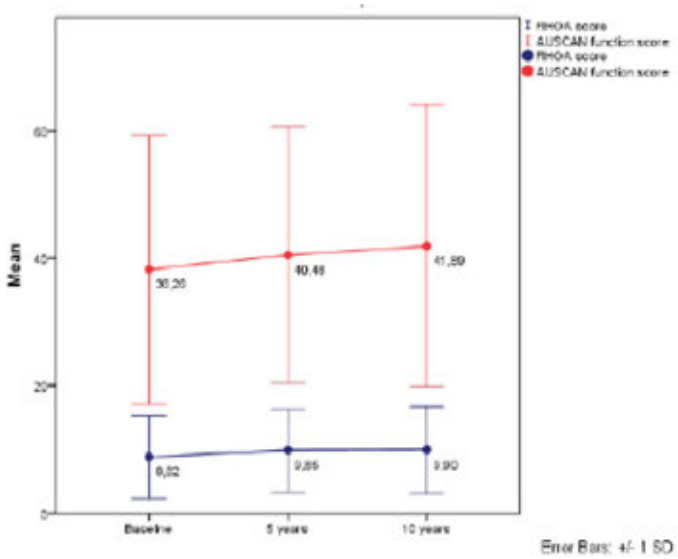

Figure 3 Longitudinal changes in pain (VAS pain and AUSCAN pain)

Results: After a mean follow-up of 9.7 years at T2, the majority of the patients (73.3%) showed any radiographic progression compared to baseline (figure 1). Exclusive 'E' progression is rare (0.6% from T1 to T0, and 1.1% from T2 to T1). Any 'E and R progression' is seen in 11% and 14.1%, resp. from T1 to T0, and T2 to T1. 'R' progression only is seen more often from T1 to T0 (61.1%) compared to T2 to T1 (39.2%)($p< 0.05$). FIHOA and AUSCAN, increased numerically over time and statistically significant after visit T2 ($p = 0.035$ for AUSCAN and $p = 0.017$ for FIHOA) (figure 2). Pain (measured by VAS and AUSCAN pain subscale) did not consistently nor significantly change over time (figure 3).After a mean follow-up of 9.7 years at T2, the majority of the patients (73.3%) showed any radiographic progression compared to baseline (figure 1). Exclusive 'E' progression is rare (0.6% from T1 to T0, and 1.1% from T2 to T1). Any 'E and R progression' is seen in 11% and 14.1%, resp. from T1 to T0, and T2 to T1. 'R' progression only is seen more often from T1 to T0 (61.1%) compared to T2 to T1 (39.2%)($p< 0.05$). FIHOA and AUSCAN, increased numerically over time and statistically significant after visit T2 ($p = 0.035$ for AUSCAN and $p = 0017$ for FIHOA) (figure 2). Pain (measured by VAS and AUSCAN pain subscale) did not consistently nor significantly change over time (figure 3).

Conclusion: HOA is a disease where significant radiographic progression is seen over time, with erosive progression being relatively rare and remodeling occurring frequently. While levels of pain remain similar over time, functional status does decrease. Future treatment goals in HOA should focus on preserving the functional status of HOA patients. Research is required to confirm this pattern of disease progression in a 'early' HOA cohort and amongst several subtypes of HOA.

References:

1. Meersseman P, et al. OAC 2015;23(12):2129-33.
2. Verbruggen G and Veys EM. A&R 1996;39(2):308-20.

Disclosure: L. Pardaens, None; **T. Vanhaverbeke**, None; **J. Vandercruyssen**, None; **R. Wittoek**, None.

Abstract Number: 2182

Relation of MRI-detected Structural Damage in the Knee to Anterior Knee Pain: The MOST Study

Joshua Stefanik,[1] Tuhina Neogi,[2] Mohamed Jarraya,[3] Ali Guermazi,[4] Irina Tolstykh,[5] John Lynch,[6] James Torner,[7] Cora Lewis,[8] and Erin Macri[9], [1]Northeastern University, Boston, [2]Boston University School of Medicine, Boston, MA, [3]Mercy Catholic Medical Center, Darby, [4]Boston Medical Center, Boston, [5]UCSF, San Francisco, [6]University of California at San Francisco, San Francisco, CA, [7]University of Iowa at Iowa City, Iowa City, [8]UAB, Birmingham, [9]Erasmus MC, Rotterdam, Netherlands

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
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Background/Purpose: Discordance between knee osteoarthritis (OA) and knee pain is common yet not well understood. Specifically, anterior knee pain (AKP) is widely held to be associated with patellofemoral (PF) joint structural damage. However, little is known about the relation of MRI-detected structural damage to AKP. A key challenge to identifying determinants of AKP relates to the high interpersonal variability in pain perception caused by psychosocial or central mechanisms, which can be difficult to account for with traditional methods. To address this challenge, we compared within-person, between-knee MRI-detected structural damage in individuals with unilateral frequent isolated AKP.

Methods: The Multicenter Osteoarthritis Study (MOST) is a NIH-funded cohort of individuals with or at risk for knee OA. Individuals were eligible if, in one knee only, they (i) reported pain, aching, or stiffness on most days of the 30 days prior to the study visit; and (ii) completed a knee pain map that indicated pain was isolated to the anterior knee (i.e., AKP). Frequent knee pain was absent in the contralateral knee. We used data from the 60-month visit, the first visit at which the knee pain map was available. If individuals were not eligible at 60-months but were at 84-months, we included eligible individuals from the 84-month visit. This within-person, knee-matched approach removes the effects of person-level characteristics that could otherwise explain pain variability between individuals (psychosocial factors, BMI, sex, genetics, etc.). 4 PF subregions (medial/lateral patella and trochlea) and 10 tibiofemoral subregions were scored semi-quantitatively using the WORMS method on bilateral MRIs. We assessed medial and lateral PF and TF compartments separately and dichotomized scores into: full-thickness cartilage damage, any bone marrow lesions (BMLs), small osteophytes, any infrapatellar synovitis, and at least moderate whole knee joint effusion. We

Table. Association between PFOA and TFOA features and frequent isolated anterior knee pain				
	Painful knee prevalence	Contralateral knee prevalence	Odds Ratio (95% CI)	p
Tibiofemoral joint				
Full thickness TF cartilage damage				
Medial	23/71 (32%)	19/71 (27%)	1.4 (0.6, 3.4)	0.40
Lateral	26/71 (37%)	20/71 (28%)	2.0 (0.8, 5.3)	0.17
Any TF BMLs				
Medial	25/71 (35%)	23/71 (32%)	1.2 (0.5, 2.5)	0.70
Lateral	17/71 (24%)	9/71 (13%)	3.0 (0.97, 9.3)	0.06
Def TF osteophytes				
Medial	57/71 (80%)	54/71 (76%)	1.5 (0.5, 4.2)	0.44
Lateral	33/71 (46%)	33/70 (47%)	0.9 (0.4, 2.1)	0.83
Patellofemoral joint				
Full thickness PF cartilage damage				
Medial	28/71 (39%)	28/71 (39%)	1.0 (0.5, 2.2)	1.00
Lateral	26/71 (37%)	26/71 (37%)	1.0 (0.4, 2.9)	1.00
Any PF BMLs				
Medial	29/71 (41%)	32/71 (45%)	0.8 (0.4, 1.7)	0.55
Lateral	34/71 (48%)	34/71 (48%)	1.0 (0.5, 2.2)	1.00
Def PF osteophytes				
Medial	35/71 (49%)	31/71 (44%)	1.4 (0.6, 3.2)	0.42
Lateral	35/71 (49%)	19/71 (27%)	5.0 (1.7, 14.6)	**<0.01**
Infrapatellar synovitis	21/69 (30%)	12/71 (17%)	2.8 (1.0, 7.8)	**0.05**
Moderate whole knee effusion	20/71 (28%)	9/71 (13%)	4.7 (1.3, 16.2)	**0.02**

evaluated the association between MRI-detected structural damage and the presence of AKP using conditional logistic regression.

Results: 71 individuals met eligibility criteria and had bilateral MRIs (mean [SD] age and BMI 69 [8] and 30.2 [5.3], respectively; 47 [66%] women). Lateral PF osteophytes were most strongly associated with AKP, followed by whole knee effusion and infrapatellar synovitis (see Table). PF cartilage damage and BMLs were not associated with AKP. There was no relation between TF MRI structural damage and AKP.

Conclusion: In individuals with unilateral frequent isolated AKP, odds of having AKP were higher in the presence of lateral PF osteophytes, joint effusion, and synovitis. AKP was not associated with PF cartilage or BMLs or any TF structural damage. While this within-person knee-matched design may limit generalizability, it does contribute to our understanding of which pathologic features of PFOA may contribute to AKP.

Disclosure: J. Stefanik, None; **T. Neogi**, MerckSerono, 5, Novartis, 5; **M. Jarraya**, None; **A. Guermazi**, AstraZeneca, 5, BICL, 1, Boston Imaging Core Lab (BICL), 1, Galapagos, 5, MerckSerono, 5, Pfizer, 5, Roche, 5, Shareholder BICL,LLC, 1, TissueGene, 5; **I. Tolstykh**, None; **J. Lynch**, None; **J. Torner**, None; **C. Lewis**, None; **E. Macri**, None.

Abstract Number: 2183

Relation of Intra-Articular Knee Mineralization on CT to Knee Pain in People with or at Risk of Knee Osteoarthritis

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Table: Relation of i.a. mineralization on knee CT to knee pain severity, frequent knee pain, and knee pain patterns

	WOMAC pain score beta **(95%CI)	Frequent knee pain OR (95% CI)	ICOAP Pain Pattern 3-level* OR (95% CI)
Any mineralization	0.11 (-0.28, 0.52)	1.11 (0.81, 1.53)	0.85 (0.59, 1.21)
Any Cartilage mineralization	0.12 (-0.30, 0.56)	1.20 (0.83, 1.74)	0.94 (0.52, 1.49)
Any meniscus mineralization	0.09 (-0.31, 0.50)	1.23 (0.87, 1.75)	0.87 (0.59, 1.28)

*ICOAP 3-level pain pattern: Constant+/- intermittent, intermittent only, or none
**per unit increase in WOMAC pain (0-20 scale) related to i.a. mineralization.

Background/Purpose: Intra-articular (i.a.) calcium crystal deposition is common in knee osteoarthritis (OA), particularly in end-stage disease. It is possible that low-grade inflammation related to crystals may contribute to knee pain, including pain fluctuation. However, in prior studies, results on this matter have been conflicting. Detection of chondrocalcinosis has relied on radiographs to date, which has low sensitivity, and this may have limited the ability to adequately assess the relation of chondrocalcinosis to knee pain. We used CT to identify i.a. mineralization to overcome this limitation.

Methods: The Multicenter Osteoarthritis (MOST) Study is a NIH-funded longitudinal cohort study of persons with or at risk of knee OA. Participants from the existing cohort underwent bilateral knee CT scans at the 144-months study visit (the first visit at which CTs were acquired), and completed standardized questionnaires to ascertain presence of frequent knee pain, knee pain severity using WOMAC, and patterns of knee pain using ICOAP (Intermittent and Constant OA Pain). A musculoskeletal radiologist scored multiplanar CT images (axial native images with coronal and sagittal 2D reformats) using a new CT scoring system that has high reliability, the Boston University Calcium Knee Score (BUCKS). The degree of mineralization in each of WORMS-defined subregions of cartilage and menisci was assessed using an ordinal score (0-3). Ligament and joint capsule mineralization were scored as present or absent. We evaluated the relation of presence of i.a. mineralization to WOMAC knee pain severity using linear regression, to presence of frequent knee pain with logistic regression, and to constant +/- intermittent pain versus intermittent pain only or no pain using ordinal logistic regression. Analyses were conducted with GEE and adjusted for age, sex, BMI, race, and KL grade.

Results: There were 633 persons (1261 knees) included (mean age 72, 57% female, mean BMI 29.9). Overall, 23.3% of knees had any i.a. mineralization; 16.7% had cartilage mineralization and 19.5% had meniscal mineralization. In terms of pain, 33% had frequent knee pain, 6.2% had constant +/- intermittent pain, 23.9% had intermittent pain only, and 46.2% had unpredictable knee pain that comes on without warning. Presence of i.a. mineralization anywhere in the joint, in the cartilage, or in the meniscus were not associated with WOMAC pain severity, frequent knee pain, or ICOAP pain pattern (i.e., constant +/- intermittent pain versus intermittent or no pain) (**Table**).

Conclusion: Despite greater sensitivity with CT, we did not find an association between i.a. mineralization and knee pain in these cross-sectional analyses. We were not able to differentiate type of crystal at this stage. Younger patients at earlier stages of disease may be a more relevant sample to study. Nonetheless, these cross-sectional analyses indicate that deposits of i.a. mineralization appear to be asymptomatic, though we cannot rule out subclinical inflammatory episodes not captured with these CT images that may contribute to symptoms.

Disclosure: T. Neogi, MerckSerono, 5, Novartis, 5; **J. Lynch**, None; **M. Jarraya**, None; **D. Felson**, None; **N. Wang**, None; **M. Nevitt**, None; **J. Torner**, None; **B. Lewis**, None; **A. Guermazi**, AstraZeneca, 5, BICL - Boston Imaging Core Lab, 1, 3, 4, 5, 6, 7, BICL, LLC., 1, Galapagos, 5, MerckSerono, 5, Pfizer, 5, Roche, 5, TissueGene, 5.

Abstract Number: 2184

A Flexion Contracture Is a Risk Factor for Radiographic Progression and Earlier Need for Arthroplasty in Knee Osteoarthritis: Data from the Osteoarthritis Initiative

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SESSION INFORMATION
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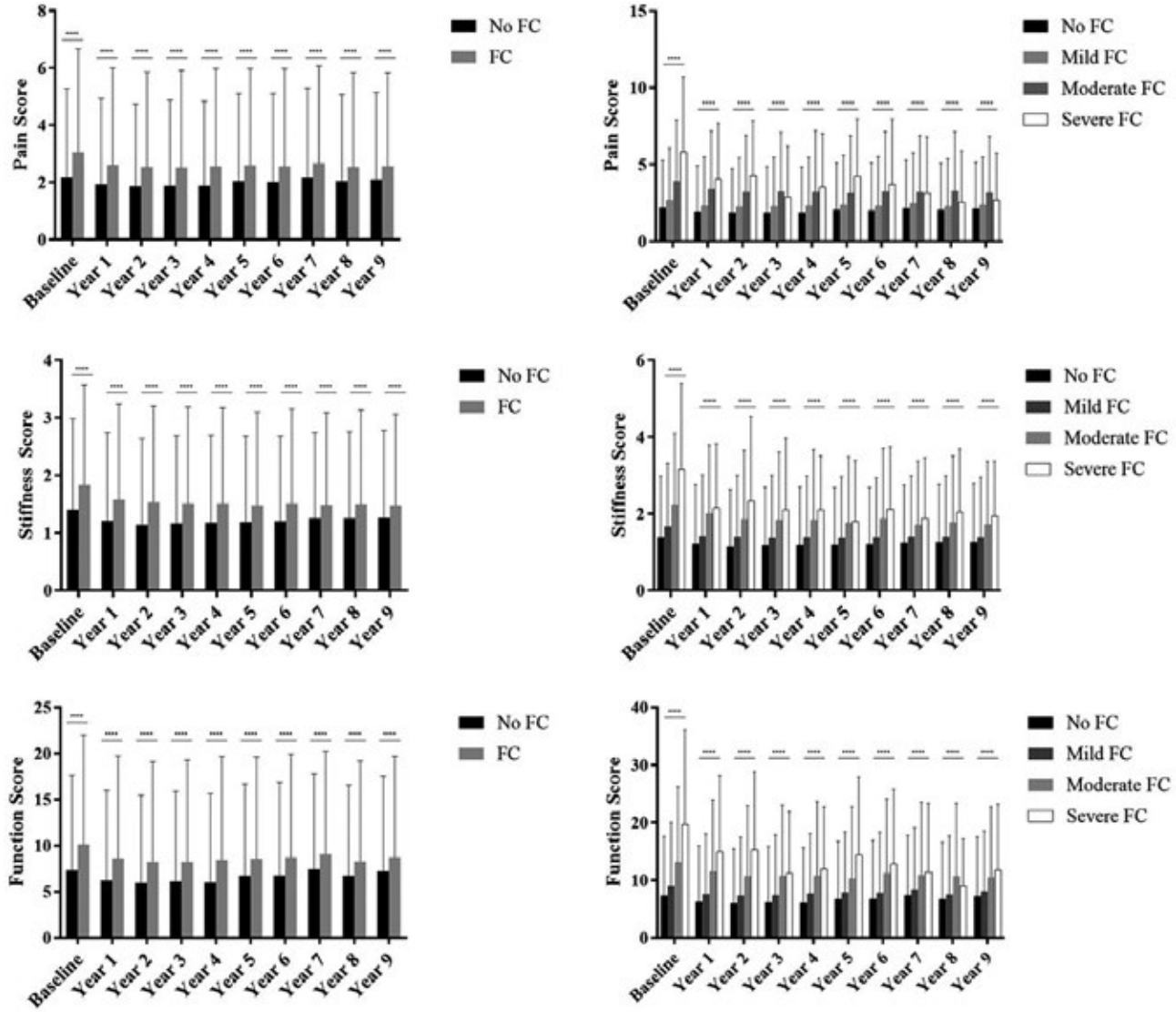

Figure 1. Clinical WOMAC outcome scores over 9-year timeline. Top: Pain subscores; middle: stiffness subscores, bottom: function subscores. Left: FC versus no FC; right: scoring by FC severity. All outcomes are worse in the FC group for each timepoint, with the majority following a dose-dependent relationship. FC: flexion contracture. ****p<0.001.

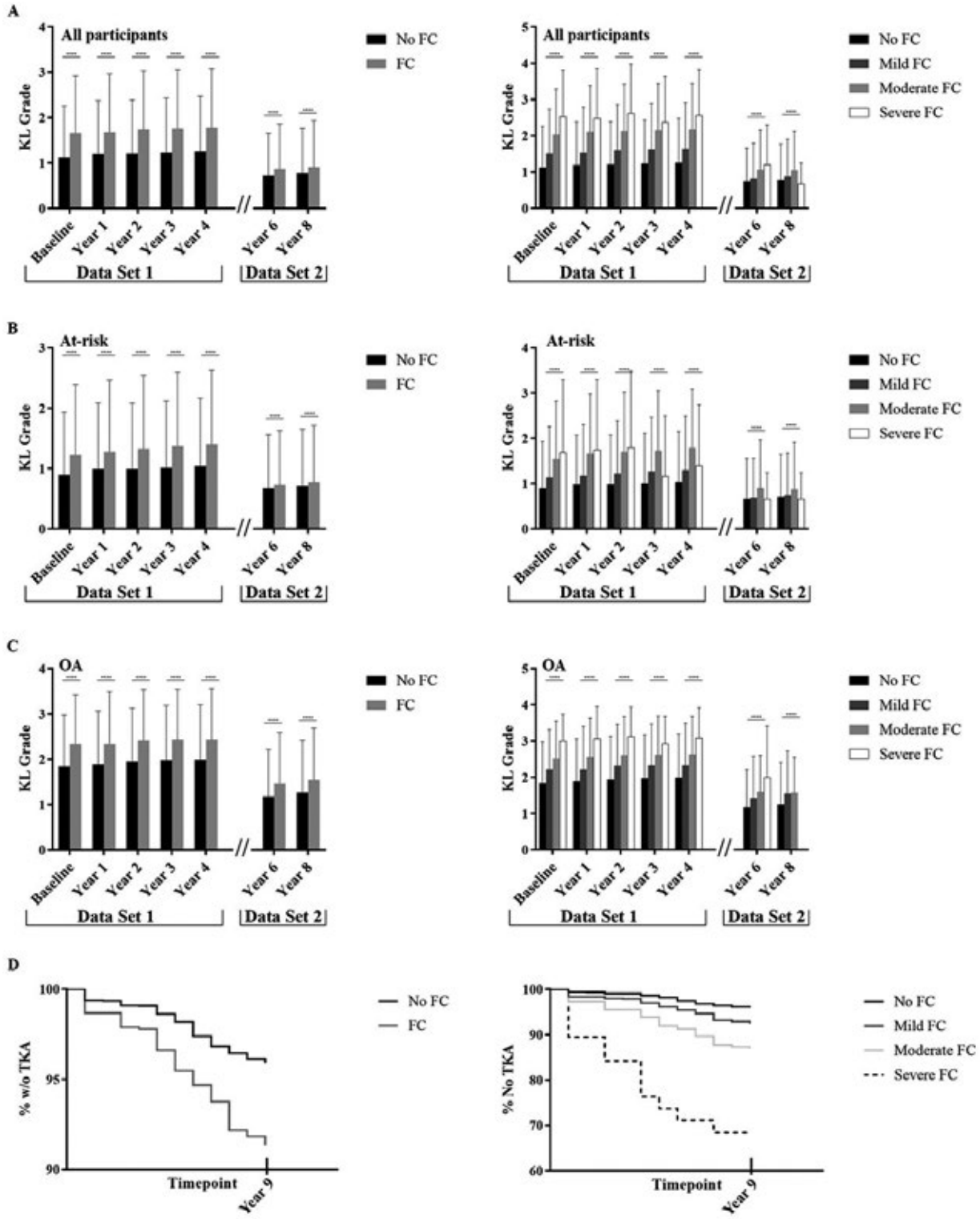

Figure 2. Radiographic scores and time to total knee arthroplasty for OAI participants over 9-year timeline. A) KL radiographic scores for all OAI participants. B) KL radiographic scores for at-risk OAI participants. C) KL radiographic scores for all OAI participants. D) Survival curves showing time to TKA for all OAI participants. For all panels - Left: FC compared to No FC group. Right: groups divided by FC severity. For OAI participants, all radiographic scores were worse over time, and worse for those with FC, in a severity dependent manner. The proportion of participants receiving TKA was increased and time to TKA was reduced for participants with FC, in a severity-dependent manner. FC: flexion contracture; KL: Kellgren and Lawrence. ****p<0.001.

Table 1 Flexion contracture and severity effect size on outcome measures

Outcome	Effect size	95% Confidence Interval	p-value
Clinical Outcomes			
Pain	0.17	0.12-0.22	All <0.001
Stiffness	0.12	0.09-0.14	
Function	0.64	0.48-0.80	
Incidence	-	-	>0.05
Radiographic K&L	0.38	0.35-0.41	<0.001
TKA			
FC	0.02	0.01-0.03	0.004
Severity			<0.001
Mild	0.14	0.06-0.21	
Mod	0.16	0.08-0.23	
Severe	0.16	0.09-0.24	
TKA timepoint			
FC	0.09	0.02-0.17	0.013
Severity			0.042
Mild	0.24	-0.28-0.75	
Mod	0.30	-0.21-0.81	
Severe	0.38	-0.13-0.88	

*Results of linear mixed regression model adjusting for repeated measures over time, age, BMI, sub-cohort, baseline radiographic OA severity, and contralateral knee score.

Background/Purpose: Osteoarthritis (OA) is the most common form of arthritis. Knee OA is often accompanied by a knee flexion contracture (FC), but the impact of FC on OA-related outcomes is not well-described. We evaluated whether the presence and/or severity of a knee FC were risk factors for increased OA incidence, clinical outcomes, radiographic progression and the need for and time to total knee arthroplasty (TKA).

Methods: The cohort design was based on 9-year longitudinal data from the osteoarthritis initiative (OAI) database. Participants (n=4,796) were divided into 3 sub-cohorts: at-risk of knee OA (n=3284), radiographically-established knee OA (n=1390), and low-risk controls (n=122). We categorized knee FCs as none, mild, moderate or severe, based on maximum knee extension at enrollment. The incidence of radiographic knee OA was based on those with Kellgren and Lawrence (KL) score < 2 at enrolment, but ≥2 on follow-up xray. Clinical outcomes (pain, stiffness and function) were evaluated using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale. KL radiographic scores, and time to TKA were extracted from the database. Effect size of FC was evaluated using a linear mixed regression model.

Results: Participants with knee FC without radiographic OA at enrolment did not have increased incidence of radiographic OA over the duration of data collection. The WOMAC pain, stiffness and function scores were worse in the FC group in a FC severity-dependent manner at nearly all timepoints (Figure 1). Effect estimates were significant for all 3 outcomes comparing FC vs no FC (0.17 [95% C.I. 0.12-0.22]) for pain, 0.12 [95% C.I. 0.09-0.14] for stiffness, 0.64 [95% C.I. 0.48-0.80] for function, all p< 0.001; Table 1). Those with knee FC had higher KL scores across all timepoints (effect size 0.38, p< 0.001, [95% C.I. 0.35-0.41]; Figure 2) with KL scores increasing with worsening FC severity (p< 0.001). Those with FC were more likely to undergo TKA (266/2819 or 9.4% with FC vs 246/5848 or 4.2% without FC, odds ratio 2.4 [95% C.I. 2.0-2.8], p< 0.001; Figure 2). After correcting for demographic variables, cohort, and baseline KL score, FC remained an independent predictor of TKA, in a severity dependent manner (Table 1). A FC was also a risk factor for having a TKA at an earlier timepoint (mean 279 days, p=0.024; Figure 2).

Conclusion: The presence of a knee FC at enrollment was a risk factor for worse clinical outcomes, radiographic progression, need for, and earlier time to TKA. Pain and OA-related structural changes may also lead to knee FC.

Further research using MRI to define the anatomic/structural factors that contribute to FC and the link to OA progression are needed. Early and aggressive treatment of a knee FC may represent a treatment option for improving clinical outcomes and slowing OA progression in knee OA. Longitudinal evaluation of such treatment is needed.

Disclosure: T. Campbell, None; **D. McGonagle**, AbbVie, 9, Abbvie, 2, 8, BMS, 9, Celgene, 2, 8, 9, Janssen, 2, 8, Johnson & Johnson, 9, Lilly, 2, 8, MSD, 9, Novartis, 2, 8, 9, Pfizer, 2, 8, 9, UCB, 8, 9.

Abstract Number: 2185

MRI-detected Abnormalities in Prediction Models of Incident Radiographic Knee Osteoarthritis over 10 Years of Follow-up

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Background/Purpose: MRI Osteoarthritis Knee Score (MOAKS) is a semi-quantitative scoring system used to assess MRI-detected structural abnormalities including over 100 raw scores representing multiple joint tissues, different ordinal grades and joint subregions or locations. Our objective was to compare 8 different representations of MOAKS in terms of prediction performance for time to incident radiographic OA over 10 years of follow-up.

Methods: We randomly selected 859 OAI participants with at least one knee at risk of developing ROA (i.e., KL 0,1 at baseline). 3T knee MRIs were assessed by expert readers using MOAKS. Radiographs were centrally read for KL grade, with ROA defined as KL³2. The 8 representations of MOAKS included features summarized at the whole knee level, the tibiofemoral and patellafemoral (PF) level, and the medial, lateral, subspinous, and PF level, with either maximum scores or sums for ordinal scores of the same feature/type (e.g., maximum number of BML lesions in a subregion (maxBMLLes]); additionally, raw scores as linear predictors and raw scores with indicators for each category were also included.

For each MOAKS representation, we fit lasso penalized Cox models and selected the penalty parameter that achieved a partial log-likelihood deviance within one standard error of the minimum in 10-fold cross validation. Performance of the optimal regularized model was then evaluated with a .632+ bootstrap estimate of the time-dependent Brier score, a weighted mean squared error for predicted survival probability and observed survival status, as well as area under the time-dependent ROC curve.

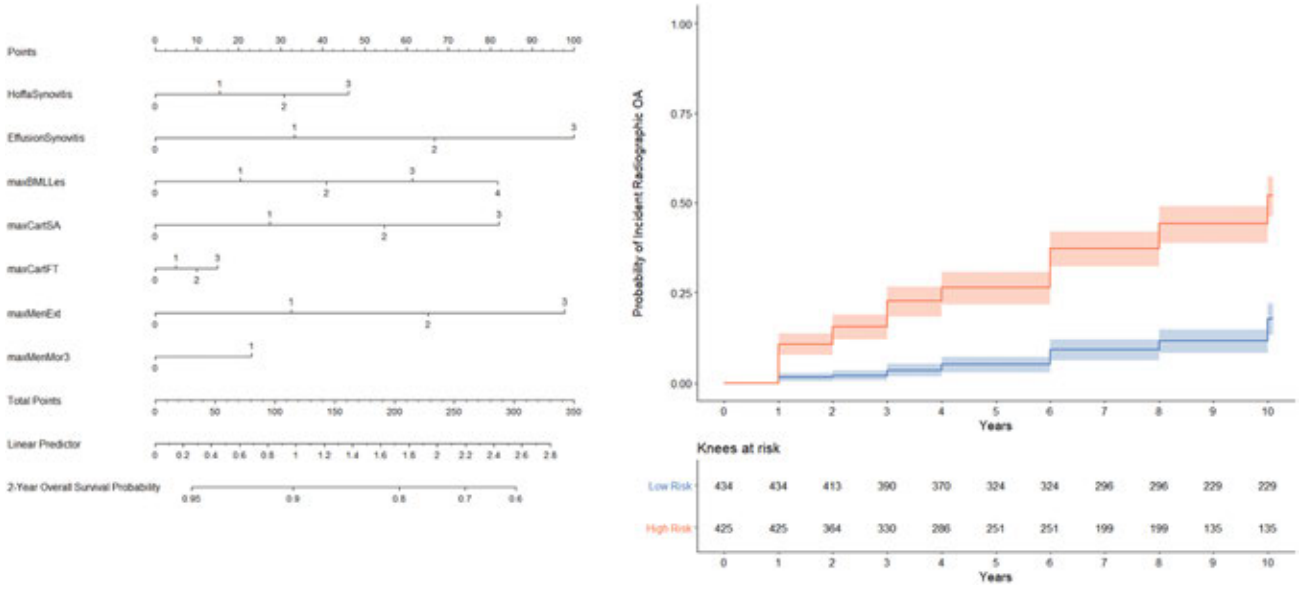
Results: A total of 244 knees developed incident ROA over the 10 year follow-up. Prediction error based on the area under the estimated prediction error curve was similar for the 8 representations of MOAKS. Variables selected under 6 of 8 representations of MOAKS are shown in Table 1. Performance and model interpretation for the whole knee maximum score model are shown in Figures 1 and 2. Prediction error increased over the course of follow-up (Figure 1a), with the greatest area under the time-dependent ROC curve achieved at 1 and 2 year follow-up (Figure 1b). The nomogram shows the MOAKS variables selected in the model, with the point values for each score, and the correspondence between the total points from these features out of a maximum

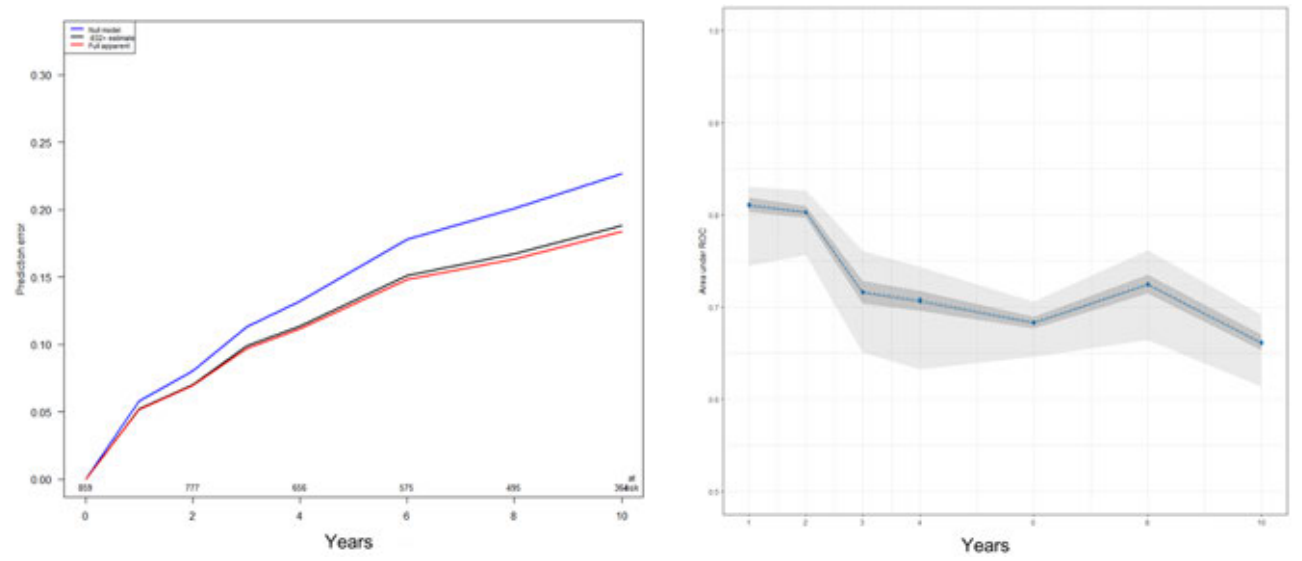
Whole Knee, maximum scores
Hoffa Synovitis
Effusion-Synovitis
Maximum number of bone marrow lesions (BML) in a subregion
Maximum surface area cartilage damage
Maximum full thickness cartilage damage
Maximum meniscal extrusion
Maximum meniscal morphology
Whole Knee, sums of scores (from 37 variables)
Hoffa Synovitis
Effusion-Synovitis
Sum of the total number of BMLs across all subregions
Sum of the surface area cartilage damage across all subregions
Sum of meniscal extrusion (medical and lateral)
Tibiofemoral(TF) or Patellofemoral(PF) compartment: maximum scores
Hoffa Synovitis
Effusion-Synovitis
Maximum BML size (TF)
Maximum number of BMLs (TF)
Maximum surface area cartilage damage (TF)
Maximum full thickness cartilage damage (TF)
Maximum surface area cartilage damage (PF)
Maximum meniscal extrusion
Maximum meniscal morphology
Tibiofemoral(TF) or Patellofemoral(PF) compartment: sums of scores
Hoffa Synovitis
Effusion-Synovitis
Sum of the total number of BMLs (TF)
Sum of surface area cartilage damage (TF)
Sum of surface area cartilage damage (PF)
Sum of meniscal extrusion (medical and lateral)
Medial TF, Lateral TF, Subspinous (SS), PF compartment: maximum scores
Hoffa Synovitis
Effusion-Synovitis
Maximum number of BMLs (SS)
Maximum surface area cartilage damage (medial TF)
Maximum surface area cartilage damage (PF)
Maximum meniscal extrusion (medial)
Medial TF, Lateral TF, Subspinous (SS), PF compartment: sums of scores
Hoffa Synovitis
Effusion-Synovitis
Sum of the total number of BMLs (SS)
Sum of surface area cartilage damage (medial TF)

Table 1 Selected Feature Scores for 6 of 8 representations of MOAKS

of 350 points and the 2 year probability of survival from ROA (Figure 2a). For example, a total of 260 points from the 7 variables in the whole knee maximum score model corresponds to a .7 probability of not having ROA 2 years later. Estimated probability of ROA over 10 years is shown for knees with risk scores above and below the median total risk score (Figure 2b).

Conclusion: Different representations of MOAKS, whether maintaining granular-level information or summarizing at the whole knee level with maximum scores or sums of scores, have similar prediction performance for





incident ROA. MRI-detected abnormalities provide the greatest discrimination between knees that do and do not develop ROA in the short term (1-2 years), while providing the greatest improvement in prediction over long-term follow-up.

1a Prediction error for whole knee maximum scores model The blue line is the estimated prediction error curve over 10 years based on the Kaplan-Meier survival estimate, without incorporating any MOAKS data The black line is the .632+ bootstrap estimate of prediction error based on the Cox model with MOAKS predictors The red line is the apparent estimate of prediction error (in the full sample) based on the Cox model with MOAKS predictors 1b Area under time-dependent ROC curve for whole knee maximum scores model with bootstrapped 95% confidence bands

2a Nomogram for whole knee maximum scores model 2b Predicted Probability of ROA for low risk and high risk knees based on the whole knee maximum scores model; knees with risk scores below the median are “low risk”, while knees with risk scores above the median are “high risk”.

Disclosure: C. Kwoh, Express Scripts, 5, GSK, 5, Kolon Tissue Gene, 5, MerckSerono, 5, Regeneron, 5, Regulus, 5, Taiwan Liposome Company, 5, Thusane, 5; **F. Roemer**, BICL, 1, Boston Imaging Core Lab, 1, 6, Shareholder BICL,LLC, 1; **E. Ashbeck**, EMD Serono, 5, MerckSerono, 5; **C. Hu**, None; **E. Bedrick**, None; **L. Sharma**, None; **A. Guermazi**, AstraZeneca, 5, BICL, 1, Boston Imaging Core Lab (BICL), 1, Galapagos, 5, MerckSerono, 5, Pfizer, 5, Roche, 5, Shareholder BICL,LLC, 1, TissueGene, 5.

Abstract Number: 2186

What Is an Important Difference in Gait Speed in Adults with Knee Osteoarthritis?

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

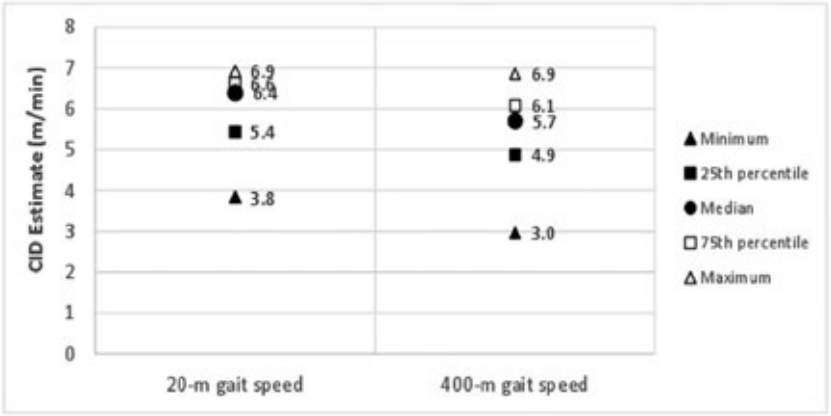
Background/Purpose: Little is known regarding what difference in functional performance measures are clinically significant in individuals with a chronic medical disease. This study examines the important differences in gait speed in adults with knee osteoarthritis.

Table: Baseline characteristics.

	All participants (n=2527)
Age (years), mean (SD)	62.6 (9.0)
Sex (% female)	57.8%
BMI[1] category (%)	
<25 kg/m²	16.6%
Overweight: 25-29.9 kg/m²	38.8%
Obese: >30 kg/m²	44.6%
K/L Grade (%)	
K/L Grade 2	53.6%
K/L Grade 3	35.0%
K/L Grade 4	11.4%
WOMAC function[3], mean (SD)	12.9 (12.7)
SF-12 function[4], mean (SD)	47.7 (9.3)
Chair stand rate (stand/sec)[5], mean (SD)	0.5 (0.1)
20-meter gait speed, mean (SD)	78.7 (12.9)
400-meter gait speed[6], mean (SD)	77.8 (13.0)

1. BMI: Body mass index, n=2523 participants
2. K/L Grade: Kellgren and Lawrence Grade, scale ranges from 0-4 with 0 no radiographic knee OA and 4 most severe radiographic knee OA
3. N=2521 participants. WOMAC physical function: Western Ontario and McMaster Universities Osteoarthritis Index range from 0 (best function) to 68 (most functional limitations)
4. N=2499 participants, SF-12 function: Medical Outcomes Study Short Form 12 Physical Component Summary Scale Score range from 0 (worst function) to 100 (best function)
5. N=2382 participants
6. N=2425 participants

Figure: Summary of usable* anchor-based important difference estimates



* An anchor was considered usable if the correlation between the anchor and gait speed was at least 0.3 and the corresponding effect size was within a plausible range of 0.2-0.8

Methods: Functional performance was objectively measured by gait speed using 20-meter and 400-meter walk tests among adults with radiographic knee osteoarthritis participating in the Osteoarthritis Initiative at baseline and 2 years later. Distribution-based methods were used to frame the range of gait speed likely to be considered important. We then utilized anchor-based methods using chair stand rate and self-reported physical function as anchors to calculate important gait speed differences.

Results: We included 2527 participants with radiographic knee osteoarthritis. Mean age was 62.6 years. Just over half (58%) of participants were female. Most participants were either overweight (39%) or obese (45%). Half (54%) had Kellgren Lawrence (K/L) grade 2 knee OA, 35% had K/L grade 3 knee OA and 11% had K/L grade 4 knee OA. Calculation of the distribution-based estimates resulted in a range from 4.1 to 6.4 meters/minute for 20-meter walk and 2.9 to 6.5 meters/minute for 400-meter walk. Anchor-based estimates ranged from 5.4 to 6.9 meters/minute for 20-meter walk and 3.0 to 6.9 meters/minute for 400-meter walk. Combining distribution-based and anchor-based methods we found the important gait speed difference for 20-meter walk is between 4.1 and 6.9 meters/minute and for 400-meter walk is between 2.9 and 6.9 meters/minute.

Conclusion: Our results found the important difference in gait speed for 20-meter walk and 400-meter walk are consistent with previous important difference estimates for older adult populations. These findings can provide benchmarks for assessing and understanding functional performance outcomes when comparing exposure groups and can be used in designing future studies targeting adults with knee osteoarthritis.

Disclosure: J. Song, None; **D. Cella**, AbbVie, 5, Alexion Pharmaceuticals, 5, Astellas Pharma, 5, Bayer AG, 5, Board of Directors for PROMIS Health Organization, 6, Bristol-Myers Squibb, 5, Clovis Oncology Inc, 5, Clovis Oncology Inc., 5, Evidera, 5, Exelixis Inc., 5, FACITtrans LLC (FACIT.org), 4, Functional Assessment of Chronic Illness Therapy (FACIT.org), 4, Horizon Pharma Inc., 5, Janssen Pharmaceuticals Inc, 5, Janssen Pharmaceuticals Inc., 5, Merck/Schering-Plough Pharmaceuticals, 5, National Academy of Sciences, 5, Novartis Pharma K.K. (Japan), 5, Pfizer Inc, 5, Pfizer Inc., 5, Pled Pharma, 5, PROMIS Health Organization, 6, Regeneron Pharmaceuticals Inc., 5; **A. Gilbert**, None; **R. Chang**, None; **D. Dunlop**, None.

Abstract Number: 2187

A Low Cartilage Formation & Repair Endotype Predicts Radiographic Progression in Symptomatic Knee Osteoarthritis Patients and Identifies Optimal Responders to a Potential OA Treatment

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a highly heterogeneous disease, which suggest that multiple endotypes exist. Identification and characterization of such endotypes may assist in precision medicine for identification of faster progressors whom may benefit from a given type of intervention. Recent published data have shown that SNPs in growth factors such as TGFbeta and GDF are associated with OA, which indicate that cartilage formation and repair play an important role in progression of OA. The aim was to determine whether a biomarker of type II collagen formation measured in serum, as a potential surrogate measure of cartilage formation, could predict radiographic progression in knee OA population. Subsequently, we investigated if such a proposed low cartilage formation/repair endotype was more responsive to a potential treatment of OA.

Methods: hsPRO-C2, a measurement of the type II collagen pro-peptide, was measured in blood samples of two independent knee OA cohorts: 106 recruited at New York University (NYU cohort) and 147 from the phase III OA trial SMC021-2301 (clinicaltrial.gov: NCT00486434) evaluating the efficacy and safety of oral salmon calcitonin. Patients were dichotomized based on their baseline level of hsPRO-C2 and the mean difference in two-year radiographic progression (joint space narrowing (JSN)) was analyzed using ANCOVA adjusting for baseline demographics and clinical characteristics.

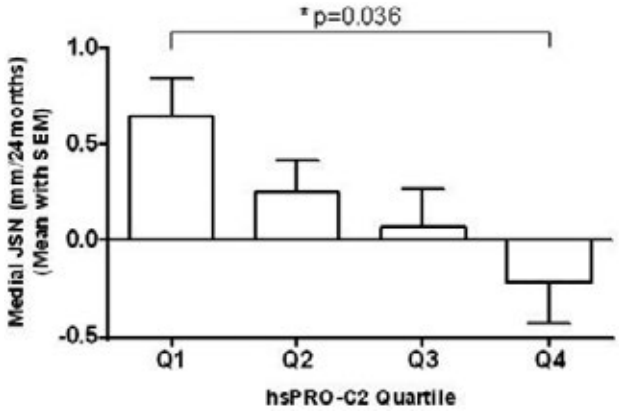

Figure 1. Two-year joint space narrowing in OA patients divided into quartiles based on baseline levels of plasma PRO-C2.

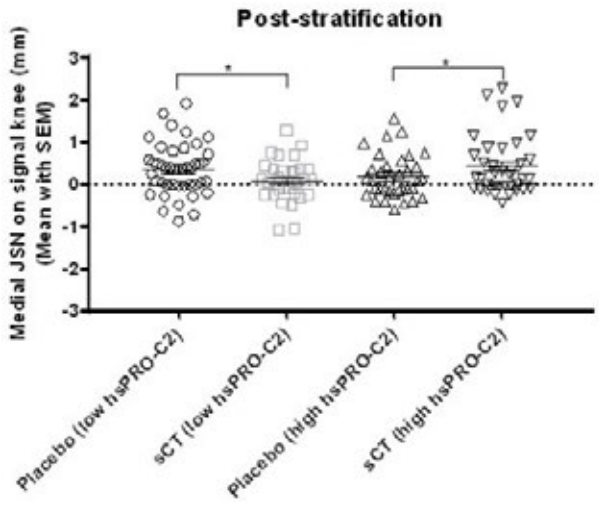

Figure 2. Two-year joint space arrowing in stratified patients treated with placebo or sCT.

Results: In the NYU cohort, baseline plasma hsPRO-C2 levels were negatively correlated with the progression of radiographic JSN ($r = -0.26$, $p = 0.009$). Quartile analysis demonstrated a significant difference in mean JSN from quartile 1 to 4 (0.51 mm versus -0.07 mm, $p = 0.036$, fig. 1). Knee OA patients with low hsPRO-C2 levels ($\leq$ 1.48 ng/mL) revealed significantly larger JSN compared to the individuals with high hsPRO-C2 levels (> 1.48 ng/mL) at 24 months (0.37 mm vs 0.02 mm, $p = 0.042$). In the SMC cohort, there was no significant treatment effect on the medial JSN over 2 years before stratification by hsPRO-C2; however, as observed in the NYU cohort, JSN was on average higher in the low hsPRO-C2 ($\leq$ 1.96 ng/mL) group compared to the high group (> 1.96 ng/mL). Furthermore, in the low baseline hsPRO-C2 subgroup, sCT-treated patients on average had a lower JSN compared to placebo patients ($p < 0.05$, fig. 2). The opposite trend was observed in patients with high baseline hsPRO-C2.

Conclusion: Here we show that low levels of cartilage formation, measured by PRO-C2, were associated with radiographic progression and greater likelihood of response to a salmon calcitonin. Low PRO-C2 may provide a measure of an OA endotype with low background cartilage formation (at baseline) and higher capacity for repair when treated with a potential cartilage anabolic drug.

Disclosure: Y. Luo, None; **J. Samuels**, None; **S. Krasnokutsky**, None; **I. Byrjalsen**, Nordic Bioscience, 3, Nordic Bioscience Clinical Development, 3; **J. Andersen**, Nordic Bioscience, 1, 3, 6; **A. Bihlet**, Nordic Bioscience, 1, 3, Nordic Bioscience Clinical Development, 3; **Y. He**, Nordic Bioscience, 3; **M. Karsdal**, Nordic Biosceince, 1, 3, Nordic Bioscience, 1, 2, 3, 4, 5; **S. Abramson**, None; **M. Attur**, None; **A. Bay-Jensen**, Nordic Bioscience, 1, 2, 3.

Abstract Number: 2188

The Association of Plasma Fatty Acids Levels with Hand and Knee Osteoarthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Obesity is one of the most important risk factors for osteoarthritis, and is strongly associated with increased levels of circulating fatty acids, which may result in lipotoxicity. However, our knowledge about the effect of different fatty acids on osteoarthritis is sparse. Therefore we aimed to investigate the association of plasma saturated fatty acids (SFAs), monounsaturated fatty acid (MUFAs), polyunsaturated fatty acids (PUFAs), omega-3 and omega-6 PUFAs with clinically defined hand and knee osteoarthritis.

Methods: In the population-based Netherlands Epidemiology of Obesity study, hand and knee osteoarthritis were defined by the ACR clinical classification criteria. Clinical hand and knee OA were defined by the ACR clinical classification criteria. Hand OA, knee OA and concurrent hand and knee OA were defined in 7%, 10% and 4% of participants, respectively. Plasma was sampled fasted and after a standardized meal (containing 600kCal, with 16% of energy (En%) derived from protein, 50 En% from carbohydrates and 34 En% from fat), and subsequently analysed using a nuclear magnetic resonance metabolomics platform. Since we are in a postprandial state most of the day, the postprandial samples were used for the primary analyses. All fatty acid concentrations were standardized (mean 0, SD 1). We excluded participants who reported to have inflammatory rheumatic disease or fibromyalgia, with missing physical examination, who were non-fasting at baseline, or reported using lipid-lowering medication. Logistic regression analyses were used to investigate the association between total fatty acids, SFAs, MUFAs, PUFAs, omega-6 PUFAs and omega-3 PUFAs and clinical osteoarthritis phenotypes. All analyses were stratified by sex and corrected for age, education, ethnicity and total body fat percentage.

Table 1. Characteristics of the weighted study population (n = 5,328), stratified by clinical OA phenotype

	No OA	Hand OA	Knee OA	Hand and knee OA
	79%	7%	10%	4%
General patient characteristics				
Age (year)	54.8 (6.1)	57.7 (5.3)	56.8 (5.1)	57.9 (4.5)
Women (%)	54	76	63	90
Ethnicity (% Caucasian)	95	93	95	91
Education (% high)	49	42	39	38
Body morphology measures				
Height (cm)	174 (10)	170 (9)	172 (10)	168 (7)
Weight (kg)	78.2 (15.5)	75.8 (16.0)	81.8 (17.4)	76.7 (15.1)
BMI (kg/m^2)	25.8 (4.1)	26.2 (4.6)	27.5 (5.2)	27.0 (4.8)
Total body fat (%)	30.5 (8.5)	34.4 (7.7)	33.8 (9.3)	37.3 (7.2)

Patients with missing physical examination, who were non-fasting at baseline, reported inflammatory rheumatic diseases or fibromyalgia or using lipid lowering medication are excluded. Numbers represent mean (SD) unless otherwise specified. † = median (IQR), BMI= body mass index.

Table 2. Association between postprandial plasma fatty acids and clinical OA phenotypes

		Clinical		
		Hand OA	Knee OA	Hand and knee OA
		OR (95% CI)	OR (95% CI)	OR (95% CI)
Total FA	(SD=2.41)			
		1.10 (0.94; 1.29)	0.92 (0.81;1.05)	0.86 (0.65; 1.13)
	Men	1.24 (1.01; 1.53)	0.93 (0.78; 1.12)	1.21 (0.76; 1.90)
	Women	1.05 (0.85; 1.30)	0.88 (0.74; 1.05)	0.83 (0.61; 1.13)
SFA	(SD=0.85)			
		1.09 (0.93; 1.29)	0.94 (0.82; 1.07)	0.80 (0.61; 1.04)
	Men	1.23 (1.00; 1.50)	0.99 (0.83; 1.19)	1.19 (0.80; 1.75)
	Women	1.05 (0.84; 1.31)	0.86 (0.72; 1.03)	0.76 (0.56; 1.04)
MUFA	(SD=0.99)			
		1.02 (0.87; 1.19)	0.95 (0.84; 1.08)	0.80 (0.60; 1.05)
	Men	1.20 (0.96; 1.50)	0.92 (0.76; 1.12)	1.12 (0.64; 1.98)
	Women	0.98 (0.80; 1.20)	0.92 (0.78; 1.08)	0.81 (0.60; 1.10)
PUFA	(SD=0.75)			
		1.21 (1.02; 1.42)	0.90 (0.78; 1.03)	0.95 (0.74; 1.21)
	Men	1.26 (1.00; 1.58)	0.90 (0.74; 1.09)	1.31 (0.84; 2.04)
	Women	1.13 (0.91; 1.41)	0.88 (0.73; 1.06)	0.86 (0.64; 1.14)
Omega-3 PUFA	(SD=0.13)			
		1.17 (0.99; 1.38)	0.94 (0.82; 1.09)	1.02 (0.81; 1.29)
	Men	1.24 (1.01; 1.52)	1.06 (0.86; 1.29)	1.24 (0.83; 1.85)
	Women	1.13 (0.90; 1.40)	0.85 (0.70; 1.04)	0.96 (0.74; 1.26)
Omega-6 PUFA	(SD=0.67)			
		1.19 (1.01; 1.40)	0.90 (0.78; 1.03)	0.94 (0.73; 1.20)
	Men	1.24 (0.98; 1.56)	0.87 (0.72; 1.06)	1.29 (0.85; 1.97)
	Women	1.12 (0.91; 1.39)	0.89 (0.74; 1.08)	0.85 (0.64; 1.13)

Results are based on weighted analyses of the study population. Fatty acid levels have been standardized (mean = 0, SD = 1), OR represents increased odds for every increase in SD. Analyses have been adjusted for age, fat percentage, education and ethnicity. Abbreviations: SFA= saturated fatty acid, MUFA= monounsaturated fatty acid, PUFA= polyunsaturated fatty acid.

Results: In the current analysis 5,328 NEO participants were included, with a mean age of 56 years and 58% were women (table 1). Unstratified analyses showed positive associations with OR (95% CI) of total PUFA concentrations 1.21 (1.02; 1.42), omega-3 1.17 (0.99; 1.38) and omega-6 PUFA concentrations 1.19 (1.01; 1.40) with clinical hand OA, but not with clinical knee OA. In men, total fatty acids 1.24 (1.01; 1.53), SFA 1.23 (1.00 – 1.50), total PUFA 1.26 (1.00 – 1.58) and omega-3 PUFA levels 1.24 (1.01 – 1.52) were positively associated with clinical hand OA. Similar effect estimates were observed with concurrent hand and knee OA, but not for clinical knee OA alone. In women no associations were seen of any of the fatty acids with clinical hand or knee OA (table 2).

Conclusion: Quantitively measured plasma postprandial SFA and PUFA levels were significantly associated with hand OA in men. Intriguingly, although SFA and omega-3 PUFAs are deemed to have opposing effects on inflammation, both were positively associated with hand OA. Future research is warranted for replication and to determine whether there is a causal role for plasma fatty acid levels in hand OA.

Disclosure: M. Loef, Innovative Medicines Initiative Joint Undertaking, 2; **A. Ioan-Facsinay**, None; **D. Mook-Kanamori**, Metabolome, 5; **K. Willems van Dijk**, None; **R. de Mutsert**, None; **M. Kloppenburg**, AbbVie, 5, APPROACH-IMI, 2, Dutch Arthritis Foundation, 2, Dutch Arthritis Society, 2, GSK, 5, Levicept, 5, Merck-Serono, 5, Pfizer, 2, 5; **F. Rosendaal**, None.

Abstract Number: 2189

Reference Curves for the Knee Injury and Osteoarthritis Outcome Score in the Middle-aged Dutch Population

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The Knee injury and Osteoarthritis Outcome Score (KOOS) questionnaire is a widely used patient-reported outcome tool, developed to evaluate short- and long-term knee symptoms and function. Previous studies evaluating knee complaints in the general population have shown that individuals in the general population do not report the best possible score on knee-specific questionnaires, stressing the need for benchmarks for adequate interpretation of these patient-reported scores. Therefore, we aimed to improve the interpretation of the KOOS by developing reference curves in a large population-based cohort.

Methods: We used cross-sectional data of middle-aged individuals from the Netherlands Epidemiology of Obesity study. We obtained questionnaires regarding demographic and clinical characteristics, including previous knee injuries and surgery, as well as the KOOS questionnaire. In addition, a standardized physical examination of the knee was performed, allowing the classification of participants with clinical knee osteoarthritis according to the ACR criteria, which were fulfilled in 15% of participants. Associations of demographic and clinical characteristics with KOOS were explored using ordered logistic regression and sex- and body mass index-specific reference curves were developed using quantile regression with fractional polynomials. Subsequently, KOOS scores of participants classified with knee osteoarthritis were compared to the reference curves.

Results: The NEO study population consisted of 6,643 participants (56.4% women) with a mean (SD) age of 55.7 (6.0) years. KOOS subscale scores (median; IQR) were high: pain (100; 94-100), symptoms (96; 86-100), ADL (100; 96-100), sport (100; 80-100), QOL (100; 75-100). Age was not independently associated with KOOS scores. We observed that scores of all KOOS subscales were lower in women compared to men, and in individuals with a higher body mass index. A history of leg fractures or knee surgery was not associated with KOOS scores. In contrast, knee osteoarthritis was associated with lower KOOS scores on all subscales. Plotting the scores of participants with knee OA shows that these scores are low relative to the general population.

Conclusion: In the middle-aged Dutch population KOOS subscale scores were generally high and were lower in women and in individuals with a higher body mass index. Reference curves developed in the general population can be used as benchmarks in research and clinical practice to aid the appropriate interpretation of scores from patients with knee complaints.

Table 1. Characteristics of the weighted study population (n = 6,643), stratified by sex

	Men	Women
General patient characteristics		
Prevalence, %	43.6	56.4
Age, year	56.1 (6.0)	55.4 (6.0)
Ethnicity, % Caucasian	95.0	94.6
Education, % high	47.7	44.0
BMI, kg/m^2	26.9 (3.7)	25.9 (4.9)
Clinical knee OA, %	10.4	18.3
Self-reported inflammatory rheumatic disease, %	4.5	3.7
Self-reported fibromyalgia, %	0.3	3.0
History of knee surgery, %	20.8	13.8
History of leg fracture, %	9.3	6.2

Numbers represent mean (SD) unless otherwise specified, † = median (IQR).
KOOS subscores are transformed to a 0–100 scale, with zero representing extreme knee problems and 100 representing no knee problems.
BMI= body mass index

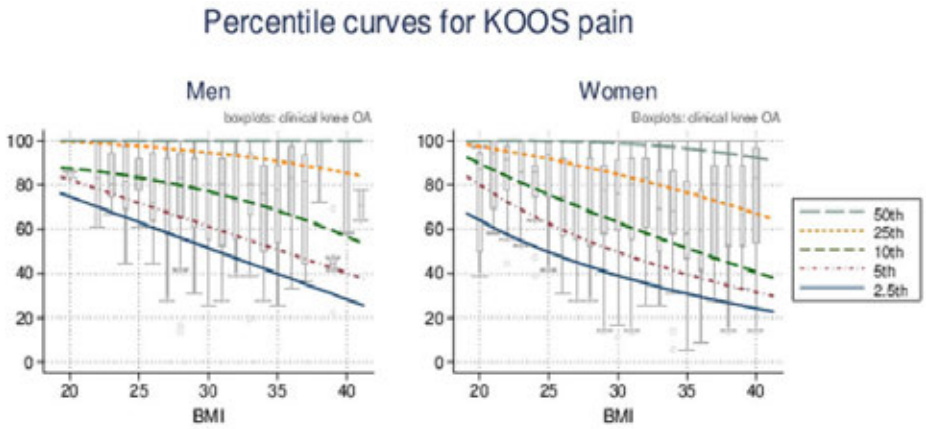

Figure 1. Sex- and BMI- specific reference curves for the Knee injury and Osteoarthritis Outcome Score pain subscale. Boxplots represent scores of participants classified with knee osteoarthritis.

Disclosure: M. Loef, Innovative Medicines Initiative Joint Undertaking, 2; **F. Kroon**, None; **S. Böhringer**, None; **F. Rosendaal**, None; **M. Kloppenburg**, AbbVie, 5, APPROACH-IMI, 2, Dutch Arthritis Foundation, 2, Dutch Arthritis Society, 2, GSK, 5, Levicept, 5, Merck-Serono, 5, Pfizer, 2, 5.

Abstract Number: 2190

Multi-vendor Multi-site $T_{1\rho}$ and T_2 Quantification of Knee Cartilage

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a degenerative joint disease characterized by deterioration of articular cartilage in the joints. MRI $T_{1\rho}$ and T_2 relaxation times have been proposed as potential biomarkers for early detection of cartilage degeneration. However, few studies examined their reliability in a multi-site multi-vendor setting, which is critical for future large-scale trials and clinical translation of such quantitative measures. The purpose of this study was to evaluate the intra-site repeatability and inter-site reproducibility of knee cartilage $T_{1\rho}$ and T_2 data acquired by multiple sites and multiple vendors in phantoms and human subjects.

Methods: Four 3T MR systems from four different sites and three vendors (Siemens, GE, and Philips) with dedicated knee coils were used for this study (**Table 1a**). Five subjects were scanned with same day rescan at each site, includ-

Table 1. a) MRI system and coil setup. **b)** imaging parameters used for each sequences. **c)** TE (T_2) and spin lock time ($T_{1\rho}$) used in each site.

a)

	Site 1	Site 2	Site 3	Site 4
MR systems	Siemens Prisma	Siemens Prisma	GE MR750 wide bore	Philips Ingenia wide bore
Software version	VE11C	VE11C	DV26	5.3.1
Coil	QED 1Tx/15Rx	QED 1Tx/15Rx	InVivo 1Tx/8Rx	InVivo 1Tx/16Rx

b)

	3D T2	3D T1rho	GRE/DESS	3D TSE
FOV (mm^3)	140 x 140 x 80 (Phantom) 140 x 140 x 96 (In-vivo)		140 x 140 x 112	
Imaging matrix	256 x 128 x 20 (Phantom) 320 x 160 x 24 (In-vivo)		384 x 307 x 160	320 x 280 x 160
Resolution (mm^3)	0.55 x 0.55 x 4 (Phantom) 0.44 x 0.44 x 4 (In-vivo)		0.36 x 0.36 x 0.7	0.44 x 0.44 x 0.7
# of echo	8		1	

c)

	Site 1	Site 2	Site 3	Site 4
3D T2 TEs (ms)	1.86, 11.58, 23.17, 34.75, 46.34, 57.92, 69.50, 81.09	5, 10, 20, 30, 40, 50, 60, 70	0, 8.847, 17.695, 26.542, 35.39, 44.237, 53.085, 61.932	1.6, 8.432, 16.864, 25.296, 33.728, 42.16, 50.592, 59.024
3D T1rho TSLs (ms)	0, 10, 20, 30, 40, 50, 60, 70			

ing two traveling volunteers whose knees were scanned at all four sites. The imaging protocol included 3D $T_{1\rho}$ and T_2 imaging, high-resolution gradient echo (GRE) imaging or dual echo steady state (DESS), and 3D turbo spin echo imaging (**Table 1b**). Data were transferred to one site for centralized data post-processing using in-house developed software. For all relaxation time fitting, two-parameter mono-exponential fittings were performed. The echo time or spin lock times used for fitting are listed in **Table 1c**. Cartilage was segmented semi-automatically into six compartments (medial/lateral femur [MFC/LFC], medial/lateral tibia [MT/LT, trochlea [TRO], and patellar [PAT]) using high-

Table 2. Intra- and inter-site CV of a) $T_{1\rho}$ and b) T_2 in phantoms. The MAPSS only inter-site CV was calculated using the mean values of site 1, 3 and 4.

a)

	Phantom	2% - 1	2% - 2	3% - 1	3% - 2	4% - 1	4% - 2
Intra-site CV (%)	Site 1	1.22	0.90	1.01	1.04	1.12	1.23
	Site 2	2.42	2.89	3.06	2.62	2.56	3.04
	Site 3	1.75	4.14	3.03	5.42	3.30	0.67
	Site 4	1.50	1.39	1.66	1.25	5.34	1.23
Inter-site CV (%)		6.93	6.64	5.83	7.44	8.91	10.27
Inter-site CV (%) (MAPSS only)		8.78	8.15	6.28	8.02	6.42	8.19

b)

	Phantom	2% - 1	2% - 2	3% - 1	3% - 2	4% - 1	4% - 2
Intra-site CV (%)	Site 1	2.15	1.48	1.40	1.77	2.03	1.83
	Site 2	2.59	2.97	3.00	2.63	2.54	3.12
	Site 3	3.08	1.75	1.31	1.81	3.40	2.08
	Site 4	2.72	3.20	3.25	5.72	2.39	2.55
Inter-site CV (%)		8.43	6.66	10.37	9.39	12.42	13.98
Inter-site CV (%) (MAPSS only)		8.88	5.79	7.50	4.91	5.33	7.32

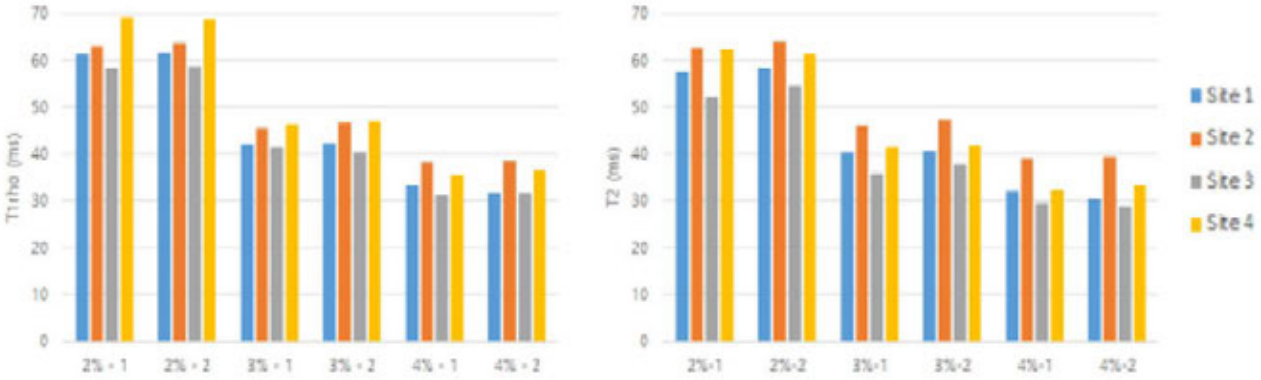

Figure 1. Bar graph of mean $T_{1\rho}$ and T_2 of the phantoms.

Table 3. Intra- and inter-site CV of a) $T_{1\rho}$ and b) T_2 in human subjects. The MAPSS only inter-site CV was calculated using the mean values of site 1, 3 and 4.

a)

	Cartilage	MFC	MT	LFC	LT	TRO	PAT
Intra-site CV (%)	Site 1	1.27	2.78	2.70	5.09	1.56	4.15
	Site 2	1.13	0.92	0.82	1.73	2.59	2.40
	Site 3	2.44	2.42	2.62	0.63	3.45	0.91
	Site 4	3.15	5.48	3.18	2.10	1.57	6.45
Inter-site CV (%)		9.85	12.01	13.06	11.73	16.50	17.13
Inter-site CV (%) (MAPSS only)		6.33	8.22	7.85	7.19	7.44	8.17

b)

	Cartilage	MFC	MT	LFC	LT	TRO	PAT
Intra-site CV (%)	Site 1	1.14	3.74	2.36	6.13	4.03	7.06
	Site 2	0.93	1.26	1.48	0.77	2.21	1.99
	Site 3	3.01	4.13	2.35	1.87	2.04	2.03
	Site 4	3.02	4.51	1.02	3.14	4.12	4.91
Inter-site CV (%)		15.49	18.30	19.73	18.60	23.41	24.45
Inter-site CV (%) (MAPSS only)		6.01	8.43	8.75	9.66	10.65	13.85

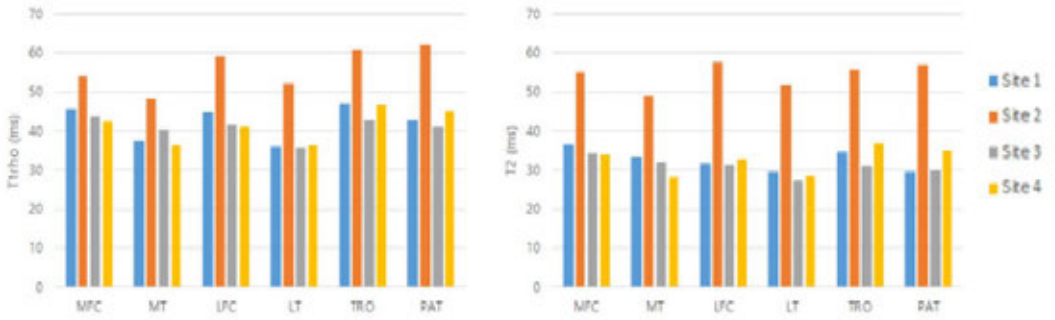

Figure 2. Bar graph of mean $T_{1\rho}$ and T_2 values of the traveling volunteers in each ROI. Note: Site 2 used a $T_{1\rho}$ and T_2 imaging sequence with segmented GRE and constant flip angle; while the other three sites used MAPSS $T_{1\rho}$ and T_2 imaging sequence with variable flip angles and RF cycling.

resolution DESS/GRE images, and the segmentation was overlaid on $T_{1\rho}$ and T_2 maps after registration to calculate means and standard deviations of $T_{1\rho}$ and T_2 values in each compartment.

Results: For phantoms, all sites showed excellent intra-site repeatability of $T_{1\rho}$ and T_2 values with an average CV of 2.24% for $T_{1\rho}$ and of 2.53% for T_2 (**Table 2, Fig. 1**). The average inter-site CVs were 7.67 % and 10.21 % for $T_{1\rho}$ and T_2 respectively with both sequences included (four sites); and 7.64% and 6.62% for $T_{1\rho}$ and T_2 respectively with the MAPSS sequence only (three sites).

For human subjects, excellent intra-site repeatability was observed for all sites with an average CV of 2.33% for $T_{1\rho}$ and of 2.91% for T_2, **Table 3**. The average inter-site CVs were 13.50% and 28.15% for $T_{1\rho}$ and T_2 respectively with both sequences included (four sites); and 8.2% and 10.17% for $T_{1\rho}$ and T_2 respectively with MAPSS sequences only (three sites). **Fig. 2** shows the $T_{1\rho}$ and T_2 values of each defined cartilage compartment for the traveling volunteers.

Conclusion: Cartilage $T_{1\rho}$ and T_2 imaging, after standardization of data acquisition and post-processing, demonstrates excellent intra-site repeatability, and inter-site reproducibility, suggesting great promise that $T_{1\rho}$ and T_2 may serve as reliable imaging biomarkers for future multi-site and multi-vendor studies, after standardization of data acquisition and post-processing. Factors that could introduce variations in $T_{1\rho}$ and T_2 values such as temperature, B0 and B1 inhomogeneity will be investigated further in future studies.

Disclosure: J. Kim, None; **K. Mamoto**, None; **R. Lartey**, None; **K. Xu**, None; **M. Tanaka**, None; **E. Bahroos**, None; **C. Winalski**, None; **T. Link**, None; **P. Hardy**, None; **Q. Peng**, None; **A. Botto-van Bemden**, None; **K. Liu**, Siemens Healthcare, 3; **R. Peters**, GE Healthcare, 3; **C. Wu**, Philips Healthcare, 3; **X. Li**, None.

Abstract Number: 2191

Construct Validity of OMERACT Ultrasound Knee Scores with Pain, Other Symptoms, Radiographic and MRI Findings

Win Min Oo,[1] James Linklater,[2] Kimberly Bennell,[3] Shirley Yu,[1] Xia Wang,[1] Vicky Duong,[1] and David Hunter[1], [1]Rheumatology Department, Royal North Shore Hospital and Institute of Bone and Joint Research, Kolling Institute, University of Sydney, Australia, Sydney, New South Wales, Australia, [2]Department of Musculoskeletal Imaging, Castlereagh Sports Imaging Center, St. Leonards, Sydney, Australia, Sydney, New South Wales, Australia, [3]Centre for Health, Exercise and Sports Medicine, Department of Physiotherapy, School of Health Sciences, Faculty of Medicine Dentistry & Health Sciences, The University of Melbourne, Melbourne, VIC, Australia., Parkville, Victoria, Australia

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the construct validity of Outcome Measures in Rheumatology (OMERACT) ultrasound scores for knee osteoarthritis (OA) with pain, other symptoms, and OA severity on radiographs and magnetic resonance imaging (MRI) counterparts.

Methods: A subgroup of community-recruited participants with symptomatic and mild-moderate radiographic knee OA participating in a randomized controlled trial of platelet-rich plasma were included in this study. At baseline, participants underwent dynamic ultrasound assessment using Aplio Platinum 500 machine, Toshiba, with a multi-frequency linear transducer (6-18MHz) according to the OMERACT scanning protocol. Using the published ultrasound image atlas by OMERACT group, a physician operator obtained semi-quantitative scores for synovitis, cartilage thinning, osteophytes and medial meniscal extrusion, and a dichotomous score for power Doppler (PD) signals, effusion and synovial hypertrophy. Clinical outcomes included the severity of pain on an 11-point numerical rating scale and Knee Injury and Osteoarthritis Outcome Score (KOOS) symptoms and pain sub-scores. The Likert responses of KOOS ranged from “none” to “extreme”. and scores ranged from 0 to 100, with lower scores indicating worse symptoms. OA severity was assessed using the Kellgren-Lawrence grade (KLG) on plain radiograph.

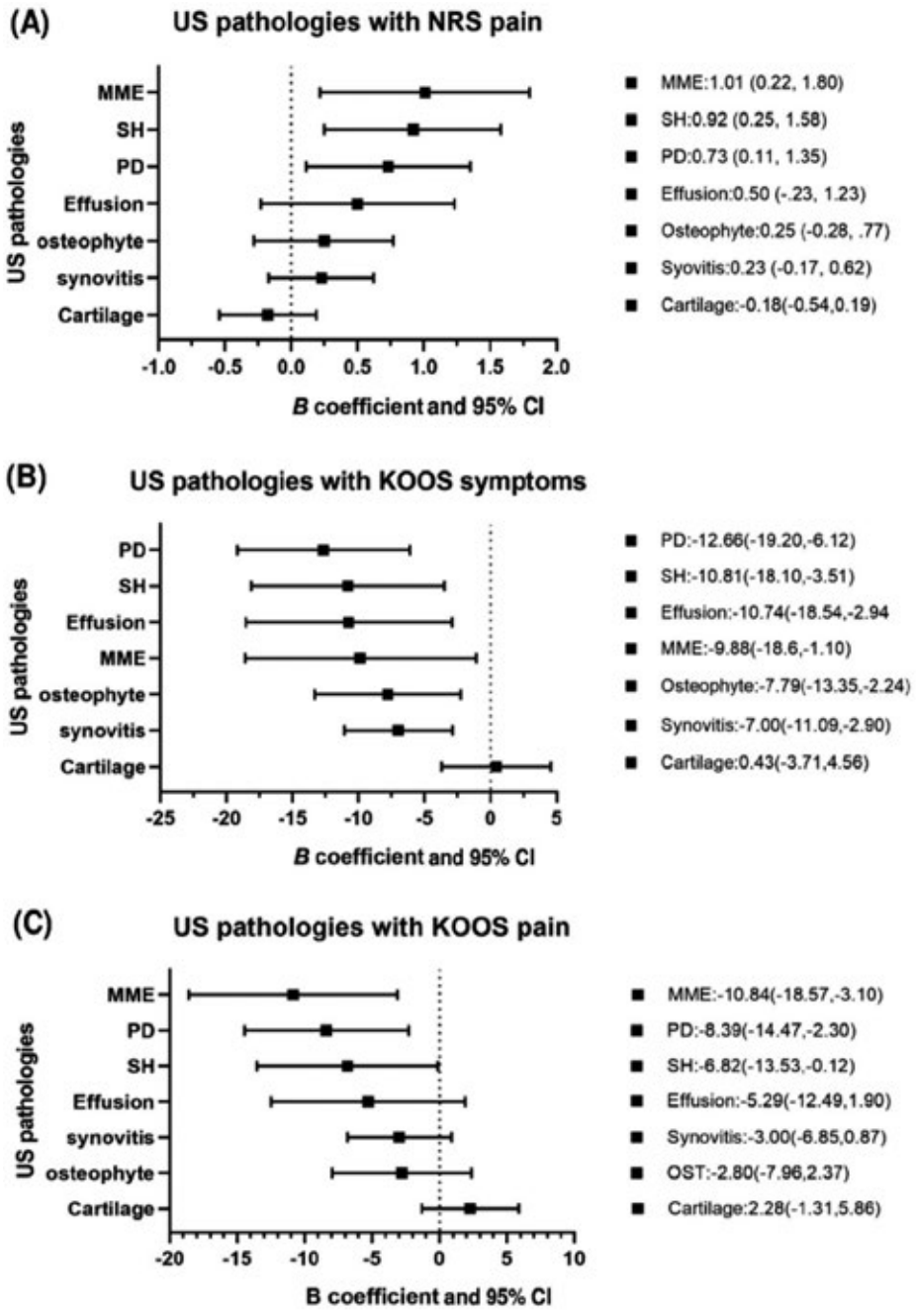

Figure 1. The association of OMERACT ultrasound OA scores with (A) NRS pain (B) KOOS symptoms (C) KOOS pain

KOOS= Knee Injury and Osteoarthritis Outcome Score; MME=Medial Meniscal Extrusion; NRS=Numerical Rating Scale; OST=Osteophyte; PD=Power Doppler; SH= Synovial Hypertrophy; US=ultrasound; CI=Confidence interval

MRI osteoarthritis knee score (MOAKS) was used on non-contrast-enhanced MRI sequences to evaluate cartilage loss (any or full thickness) from patellofemoral, medial and lateral tibiofemoral compartments, osteophytes from 12 different sites, medial meniscal extrusion, effusion-synovitis and Hoffa's synovitis. Linear regression was used to determine the associations of ultrasound OA pathologies with pain and KOOS sub-scores adjusting for confound-

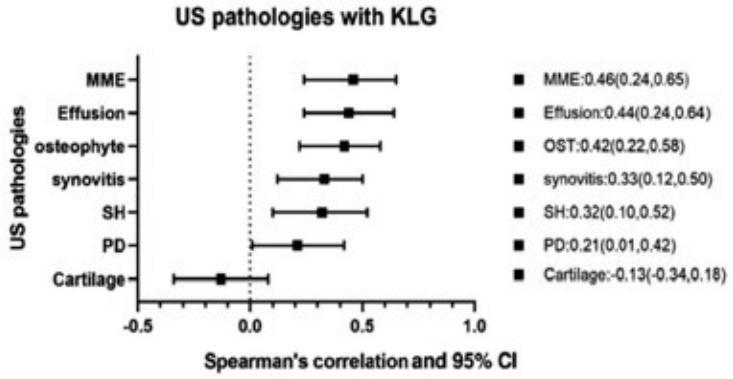

Figure 2. The association of OMERACT ultrasound OA scores with KLG on radiograph

KLG= Kellgren and Lawrence grade; MME=Medial Meniscal Extrusion; PD=Power Doppler; SH= Synovial Hypertrophy; US=ultrasound; CI=Confidence interval

ers such as age, gender, disease duration and KLG as appropriate, and Spearman's correlation was used for the relationship with KLG and MOAKS.

Results: Eighty-nine participants (female, 53.9%; body mass index, mean= 27.5±6.4) were included in the analysis. Synovial hypertrophy, PD signals and meniscal extrusion scores were associated with increased pain severity (*B* = 0.92, 95% confidence interval CI 0.25, 1.58); *B* = 0.73(95% CI 0.11, 1.35) and *B* = 1.01(95% CI 0.22, 1.80) respectively (**Figure 1A**). All ultrasound scores, except for cartilage grade, demonstrated associations with KOOS symptoms (**Figure 1B**) while only PD signals and meniscal extrusion were associated with KOOS pain (**Figure 1C**). All ultrasound scores, except for PD signals, were significantly correlated with KLG (**Figure 2**). Most ultrasound pathologies revealed moderate to good correlation with their MRI counterparts with ultrasound synovitis having the greatest correlation [0.69(95% CI 0.60, 0.78)] (**Figure 3**).

Conclusion: OMERACT ultrasound scores revealed good construct validity against commonly used measurement tools such as pain, function, and radiographic and MRI features, providing evidence to support its use as a standardized tool for determining ultrasound OA phenotypes.

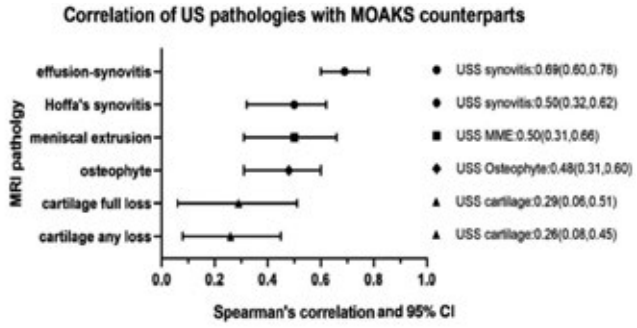

Figure 3. The association of OMERACT ultrasound OA scores with MOAKS on magnetic resonance imaging

MME=Medial Meniscal Extrusion; MOAKS= Magnetic Resonance Imaging Osteoarthritis Knee Score; MRI=Magnetic Resonance Imaging; PD=Power Doppler; SH= Synovial Hypertrophy; USS=ultrasound; CI=Confidence interval

Disclosure: W. Oo, None; **J. Linklater**, None; **K. Bennell**, None; **S. Yu**, None; **X. Wang**, None; **V. Duong**, None; **D. Hunter**, Pfizer, 5, Lilly, 5, Merck Serono, 5, TLC bio, 5.

Abstract Number: 2192

Stabilization of Patellar Bone-Shape Correlates Significantly with Reduced Knee Pain Frequency After IA TPX-100 in Subjects with Bilateral Patellofemoral OA

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Based on data from the Osteoarthritis Initiative (OAI), MRI-based analyses of bone shape changes in the knee predict symptomatic and radiographic progression of knee OA and risk of joint replacement (Neogi 2013; Barr 2016). In a 12-month, double-blind, placebo-controlled trial of MRI-confirmed bilateral patellofemoral OA, TPX-100, administered in 4 weekly injections (200 mg/injection), markedly improved knee physical function (KOOS/WOMAC) compared with identical placebo injections (McGuire 2017). At 12 months, there were no significant treatment differences in overall knee pain; however, pain frequency significantly decreased in TPX-100-treated knees compared with placebo-exposed knees, and overall analgesic use declined by >60%. In the current retrospective study, we investigated patellar bone-shape change from baseline to 12-months among subjects who participated in TPX-100-1 and analyzed the strength of association between patellar bone shape change and changes in knee pain frequency.

Methods: Patellar bone shape changes from baseline were analyzed centrally by an automated method (Imorphics, Inc.) blind to treatment assignment and clinical results. MRI image quality permitted analysis in 79 of 93 subjects (85%) using active appearance model (AAM). Bone shape scores were computed to discriminate normal (non-OA) shapes versus bone surface deformations associated with radiographic and symptomatic OA. Changes in pain frequency were determined using Question 1 from the KOOS pain domain: "How often do you experience RIGHT/LEFT knee pain?" Spearman analysis was performed to investigate correlations between patellar shape change and change in knee pain frequency.

Results: Pain frequency was significantly improved in TPX-100-treated knees compared with placebo-exposed knees. Patellar bone shape delay correlated significantly with pain frequency reduction (r=.411; p=.0002; Table 1). Knees with stabilized or reduced bone-shape changes at 12 months had the greatest reductions in pain frequency, with statistically significant differences between quartiles (Fig 1).

Conclusion: In subjects with MRI-confirmed bilateral PFOA, a single series of IA TPX-100 is associated with statistically significant and clinically meaningful reductions in knee pain frequency at 12 months, significantly correlated with reduced or stabilized pathologic patellar bone shape change compared with placebo. Quartile analysis suggests a "dose-response" relationship between reduced patellar bone shape change and reduced knee pain frequency in TPX-100-treated knees. These concordant structural and symptomatic benefits support

development of TPX-100 as a candidate DMOAD as well as further study of bone shape change as an imaging biomarker in knee OA.

References:

1. Neogi T, et. al. *Arthritis Rheum*. 2013;65(8):2048–2058
2. Barr AJ, et. al. *Rheumatology (Oxford)*. 2016;55(9):1585–1593

Table 1. Pain Frequency and Pathological Patella Bone Shape Change

12-Months	n	Patella Bone Shape Change Reduction Spearman Analysis	
		Correlation (r)	p-value
Pain Frequency Reduction	79	0.411	***0.0002***

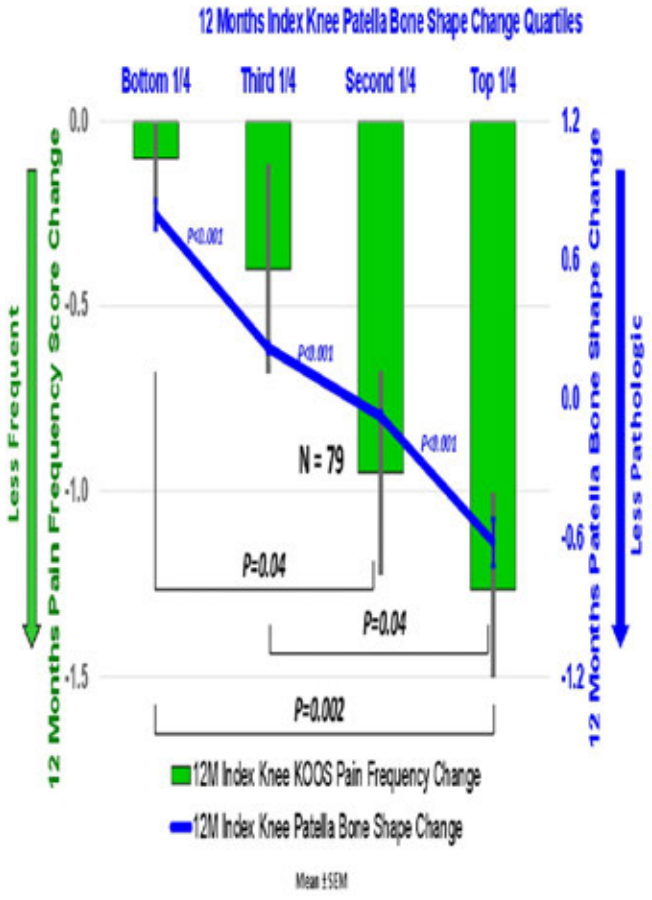

Fig 1. Stratified Analysis of KOOS Pain Frequency Change and Patella Bone Shape Change from Baseline to 12 Months in TPX-100-treated (Index) Knee

Disclosure: D. McGuire, OrthoTrophix, 3, 4, OrthoTrophix, Inc, 3, 4; **M. Bowes**, Imorphics (Stryker), 3, OrthoTrophix, 9; **A. Brett**, OrthoTrophix, 9, OrthoTrophix, Inc, 9; **N. Segal**, University of Kansas Medical Center, 3; **M. Miller**, OrthoTrophix, 3, 4, OrthoTrophix, Inc, 3, 4; **D. Rosen**, OrthoTrophix, 3, 4, OrthoTrophix, Inc, 3, 4; **Y. Kumagai**, OrthoTrophix, 3, 4, OrthoTrophix, Inc, 3, 4.

Abstract Number: 2193

"If It Was Unicorn Dust I'd Have It Again." Patient Experiences of Hip Osteoarthritis and Treatments in the Hip Injection Trial

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Evidence of the effectiveness of intra-articular corticosteroid injection for hip osteoarthritis (OA) is limited and conflicting. The HIT trial compared the clinical effectiveness of an ultrasound-guided intra-articular hip injection (USGI) of triamcinolone acetonide and 1% lidocaine hydrochloride combined with best current treatment (BCT) with (i) BCT alone (primary objective) and (ii) an USGI of 1% lidocaine only combined with BCT (EudraCT: 2014–003412-37). BCT comprised advice and written information on exercise, weight loss, footwear, walking aids and pain management. This qualitative study investigated patient experiences of hip OA and impact of trial treatments.

Methods: Semi-structured interviews were undertaken with a purposeful sample of participants in each arm after 2-month follow-up. Interviewers knew whether participants had received an injection but were unaware of which injection (to minimise patients becoming un-blinded to treatment allocation). Sampling ceased when inductive thematic saturation had been achieved. Thematic analysis was undertaken blind to the clinical results to facilitate an interpretive and inductive approach.

Results: 34 trial participants were interviewed (males n=13, females n=19, aged 53 to 83 years). 13 participants were in USGI triamcinolone/lidocaine group, 11 in the lidocaine only arm and 8 in BCT. Preliminary findings indicate wide-ranging impacts of living with hip OA. Participants in all arms talked of physical, social, psychological and work-related impacts and difficulties with sleep and undertaking valued activities. Participants in BCT reported receiving an examination, information/explanation and exercises, providing evidence of intervention fidelity in this arm. Despite this, most felt that they had not received any treatment indicating that advice/exercise was not perceived as treatment for hip pain. Adherence was low in this group. Participants described little or no benefit in pain or function. Thoughts about the future were negative, focusing on inevitable decline and future need for surgery.

Experiences of having an injection were positive overall, and impacts described in both injection groups included "getting my life back" and having "a new lease of life". Perceived benefit appeared to be greater in the triamci-

nolone/lidocaine group, although length of benefit varied in both injection groups and there was uncertainty about the longer-term benefits of injection. Participants in the injection groups were more hopeful and optimistic about the future than those in BCT only.

Conclusion: Hip OA remains burdensome, affecting many aspects of life. The findings complement the trial results that showed superiority of USGI of triamcinolone/lidocaine combined with BCT over 6 months compared with BCT alone, but no significant difference between injection groups raising the possibility of a placebo effect. Participants' narratives outlined benefit in pain and function in both injection groups, strengthening the interpretations of the trial clinical results. Importantly, participants in BCT reported receiving BCT but did not feel they had treatment, indicating the need for future work highlighting the value of self-management.

Disclosure: C. Jinks, None; **A. Hawarden**, None; **E. Roddy**, None; **Z. Paskins**, None; **C. Mallen**, None; **M. Holden**, None.

Abstract Number: 2194

Surgical and Medical Weight Loss Threshold Dictates Decreases in Knee Osteoarthritis Pain but Not Reductions in Inflammatory Biomarkers

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Weight loss in obese patients can reduce knee osteoarthritis (OA) pain, even when physical therapy and intra-articular injections have failed. The impacts of either non-surgical or surgical weight loss on knee OA pain have been reported separately, but few studies have assessed them conjointly. While the decrease in mechanical load helps, the contribution of metabolic changes is less clear. We aimed to compare biomarker changes with weight loss as predictors of knee pain improvement, and consider a threshold of total weight loss necessary for these changes.

Methods: Patients from the NYU Langone Weight Management program were screened for knee pain prior to bariatric surgery or the start of a medical weight loss (MWL) regimen. We excluded patients with autoimmune disease, recent malignancy, recent intra-articular knee injections, and lack of OA by Kellgren-Lawrence (KL) x-ray grading. The BMI, Knee Injury and Osteoarthritis Outcome Score (KOOS) for pain, and blood samples were obtained at baseline and 1, 3, 6 and 12 months for evaluation of pain and biomarker levels.

Results: Of 140 patients screened, 81 were eligible and enrolled (82.7% female; BMI 45.2±9.6 kg/m2, 31-74; age 52±12 years, 30-80). A total of 49 patients had surgery (10 bypass, 30 sleeve, 9 LapBand) and 24 medical weight loss. 33 patients completed visits up to 6 months (2 bypass, 18 sleeve, 6 LapBand, 7 MWL). By 1 month, the surgical patients had lost much more total weight than the MWL group (9.8% vs 4.1 %, p=0.001), and realized marked pain relief (p< 0.001). By 6 months both groups had continued to lose weight, proportionately greater for surgical patients with further pain improvement. (Figure 1) Leptin levels dropped at 1 and then 6 months with both methods of weight loss.

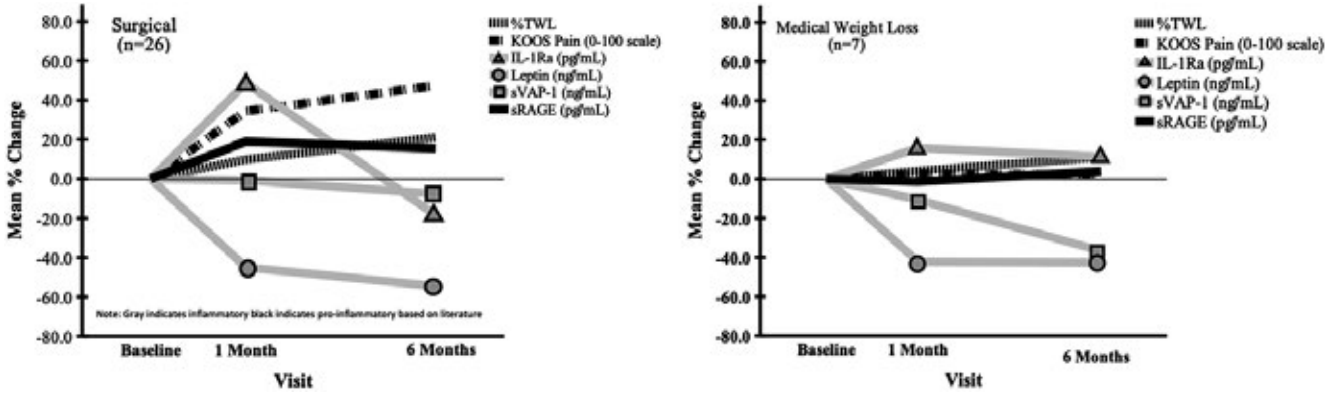

Figure 1. Surgical and medical outcomes for % total weight loss (TWL), knee pain and biomarkers

	Baseline	1 Month	6 Month	p-value (between 0 &1)	p-value (between 0 & 6)	p-value (between 1 & 6)
Surgical (n=26)						
%EWL	0.0	24.0 ± 9.3	50.9 ± 19.7	**<0.001***	**<0.001***	**<0.001***
%TWL	0.0	9.8 ± 2.9	21.0 ± 6.4	**<0.001***	**<0.001***	**<0.001***
BMI (kg/m^2)	44.9 ± 7.4	40.6 ± 6.9	35.5 ± 6.2	**<0.001***	**<0.001***	**<0.001***
KOOS Pain (0=worst, 100=best))	48.7 ±16.1	62.7 ± 18.9	67.8 ± 18.8	**<0.001***	**<0.001***	0.159
IL-1Ra (pg/mL)	940.7 ± 463.2	1284.4 ± 655.3	661.4 ± 206.5	**0.010***	**0.001***	**<0.001***
hsIL-6 (pg/mL)	2.4 ± 1.9	2.4 ± 2.1	2.9 ± 1.6	0.966	0.329	0.376
hsCRP (mg/dL)	4.7 ± 2.8	4.7 ± 2.2	5.1 ± 3.8	0.943	0.813	0.618
Leptin (ng/mL)	78.2 ± 20.9	44.2 ± 21.9	35.6 ± 21.0	**<0.001***	**<0.001***	0.187
sVAP-1 (ng/mL)	389.8 ± 78.9	384.8 ± 106.3	365.8 ± 138.7	0.781	0.323	0.288
sRAGE (pg/mL)	916.0 ± 534.7	1026.1 ± 571.2	1072.1 ± 615.0	**0.041***	0.051	0.895
Medical Weight Loss (n=7)						
%EWL	0.00	13.3 ± 8.9	37.4 ± 33.0	**0.007***	**0.024***	**0.043***
%TWL	0.00	4.1 ± 2.2	11.1 ± 9.8	**0.003***	**0.024***	0.060
BMI (kg/m^2)	38.8 ± 7.9	37.3 ± 7.6	34.8 ± 9.5	**0.002***	**0.028***	0.143
KOOS Pain (0=worst, 100=best)	58.7 ± 10.2	60.3 ± 14.7	59.9 ± 16.7	0.641	0.891	0.971
IL-1Ra (pg/mL)	614.4 ± 225.8	712.3 ± 215.4	684.4 ± 243.5	0.413	0.520	0.793
hsIL-6 (pg/mL)	2.4 ± 0.9	3.3 ± 2.2	3.4 ± 1.5	0.375	0.180	0.874
hsCRP (mg/dL)	3.6 ± 2.8	4.4 ± 2.5	5.7 ± 3.3	0.249	**0.021***	0.191
Leptin (ng/mL)	100.0 ± 19.9	57.8 ± 17.4	57.4 ± 25.0	**<0.001***	**0.001***	0.995
sVAP-1 (ng/mL)	436.4 ± 115.4	390.0 ± 168.4	275.6 ± 165.4	0.189	0.035*	0.135
sRAGE (pg/mL)	1068.8 ± 636.7	1054.5 ± 551.6	1110.7 ± 674.7	0.886	0.101	0.093

Table 1.

The pro-inflammatory protein IL-1Ra decreased significantly by 6 months in the bariatric patients, but increased with the medical regimen across both time points. Soluble vascular adhesion protein 1 (sVAP-1), another pro-inflammatory protein that facilitates leukocyte infiltration, decreased at both the 1 and 6 month intervals – but much more in MWL than in surgical patients. Consistent with the literature, the anti-inflammatory soluble receptor for advanced glycation endproducts (sRAGE) mirrored KOOS pain improvement only in surgical patients and stabilized after 1 month, but did not change in the MWL group. (Table 1) In a subgroup analysis, the 14 surgical patients who lost at least 10% of

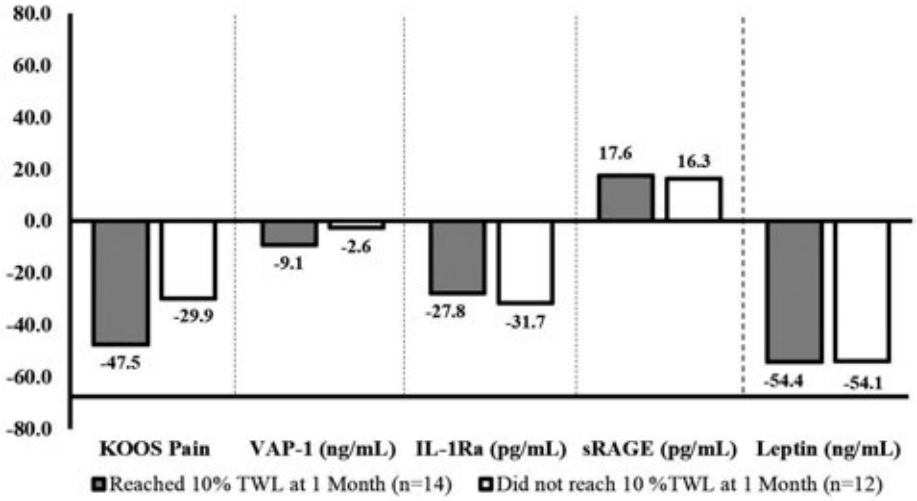

Figure 2. Percent change in biomarkers at 6 months in patients who reached threshold for one month total weight loss of 10%

total weight by 1 month had significantly less pain at 6 months than the 12 who did not meet the threshold (ΔKOOS 47.5 vs 29.9) but the biomarker levels were similar. (Figure 2)

Conclusion: Surgical and medically supervised weight loss both lead to significant decreases in adiposity, but only those having bariatric surgery realize significant pain relief. The anatomical changes of surgical (vs. medical) weight loss result in different metabolic cascades given divergent biomarker trends. Bariatric patients who lose more than 10 percent of total body weight within the first month are more likely to have better pain relief by 6 months, but the biomarker changes reflect anatomic intervention – and are not dependent on the degree of surgical weight loss.

Disclosure: F. Bomfim, None; **S. Chen**, None; **S. Zak**, None; **T. Jazrawi**, None; **M. Kundler**, None; **V. Qie**, None; **L. Peralta**, None; **J. Aleman**, None; **C. Ren-Fielding**, None; **H. Lofton**, None; **J. Patel**, None; **M. Attur**, None; **S. Abramson**, None; **J. Samuels**, None.

Abstract Number: 2195

BMI Has Minimal Effect on Reduction of Symptoms in Patients with Osteoarthritis of the Knee Treated with Diclofenac 1% Gel

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical trials demonstrate that diclofenac sodium gel 1% (DSG 1%), a topical NSAID, provides significantly better pain relief than vehicle placebo for patients with osteoarthritis (OA) of the knee. As patient BMI may affect the systemic availability and the volume of distribution of topical therapeutics, a post-hoc analysis was conducted to determine whether BMI has any clinical impact on the efficacy of DSG 1% in patients with OA of the knee.

Methods: This analysis pooled data from 3 vehicle-controlled studies of DSG 1%, VOSG-PN-304, VOSG-PN-310 and VOSG-PN-316, all double-blind studies with similar design and efficacy end-points, including Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) pain, function, and stiffness and pain on movement (POM). Efficacy data were analyzed as change from baseline and stratified by 3 BMI groups, (< 25, ≥25 to < 30, ≥30 kg/m2) at each visit (1, 4, 8 and 12 weeks). Populations included the Intention to Treat (ITT) efficacy population (all patients randomized and treated), and the Modified Efficacy Subset (MES) (patients with no decline in POM score between the screening and baseline visits and a score of 0-1 on the WOMAC abridged pain index for the contralateral knee). The treatment by BMI interaction from an analysis of covariance model was used for assessment.

Results: Improvement from baseline was larger for DSG 1% compared to vehicle in all 3 BMI groups for all 4 efficacy measures at each time point in both the ITT and MES populations. There were no significant differences in treatment effects between the 3 BMI groups at any time point for all 4 efficacy measures for both the ITT and MES population. Mean treatment effect (DSG 1% minus vehicle) at Week 12 and P-value for difference between < 25 (n=203), ≥25 to < 30 (n=460), ≥30 (n=751) kg/m2 BMI groups, respectively were: WOMAC pain, 1.01, 0.87, 0.79 (P=.94); POM, 9.66, 7.13, 6.06 (P=.71); WOMAC function, 2.38, 2.97, 3.77 (P=.78); WOMAC stiffness, 0.30, 0.47, 0.45 (P=.84) in the ITT population and WOMAC pain, 0.75, 1.48, 1.23 (P=.69); POM, 8.80, 10.39, 8.79 (P=.91); WOMAC function, 1.78, 4.99, 5.30 (P=.40); WOMAC stiffness, 0.22, 0.68, 0.66 (P=.37) in the MES population.

Conclusion: In this pooled analysis, patients treated with DSG 1% showed larger improvement from baseline in all 3 BMI groups, for all 4 efficacy measures, and at each time point compared to vehicle. There were no significant differences in efficacy between the 3 BMI groups, indicating that DSG 1% is efficacious regardless of BMI in patients with OA of the knee and that dose adjustments based on body size are not necessary.

Disclosure: J. Block, Abbvie, 2, ACR, 6, Agios, 7, Daiichi-Sankyo, 7, GlaxoSmithKline Consumer Healthcare, 5, Jannsen, 2, Medivir, 5, Novartis, 2, OARSI, Omeros, 7, Pfizer, 2, TissueGene, 2, Zynerba Pharma, 5; **B. Patel**, GlaxoSmithKline Consumer Healthcare, 3; **S. Yacoub Garas**, GlaxoSmithKline Consumer Healthcare, 3.

Abstract Number: 2196

Machine Learning Defines the Relationship Between Structural Knee Osteoarthritis and Patient-Important Outcomes: An 8-year Study of 47,858 Knee MRIs from the Osteoarthritis Initiative (OAI)

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a slowly progressing disease which may be asymptomatic for many years. Therapy development has been hampered by poor understanding of both structural progression and outcomes, largely based on imprecise radiographic assessment. A statistical shape model (SSM), a form of machine

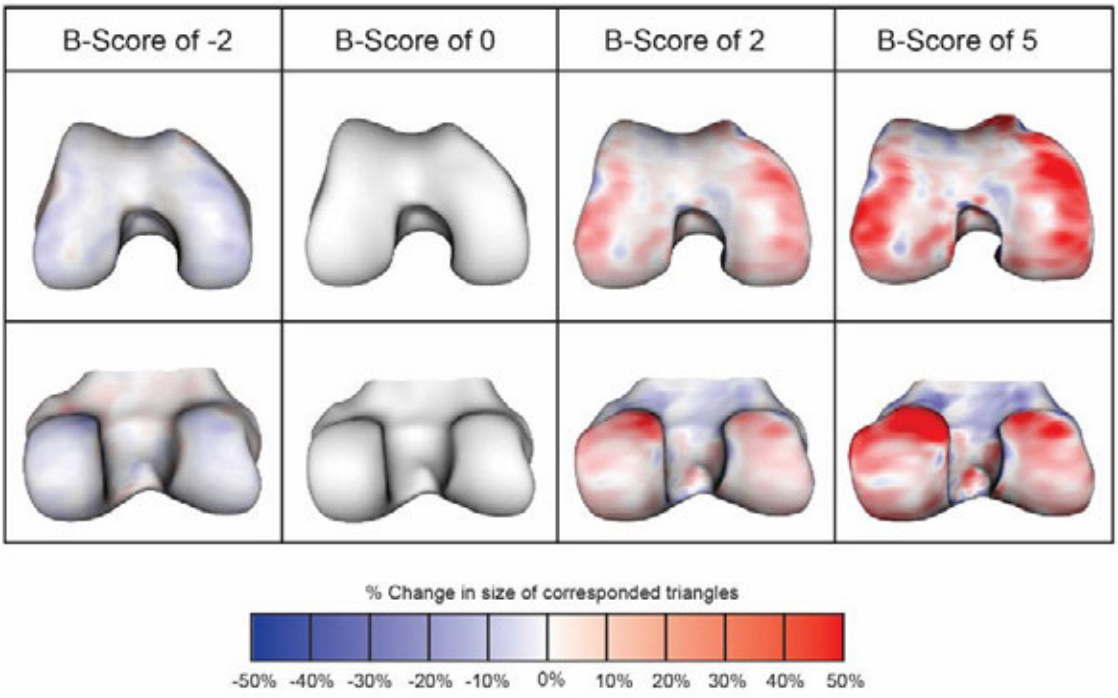

Figure 2. Change in Bone Shape with Increasing B-Score. Figure shows change in shape for the anterior femur (top row) and posterior femur (bottom row), for various B-scores. Red indicates where there is an increase in size, blue indicates decrease in size; scale shows percentage in local area size change.

learning, identified a characteristic 3D OA bone shape from MR images, enabling investigation of the relationship between structure and clinical outcomes in the largest musculoskeletal MRI study to date.

Methods: Construction of an SSM produces a "shape space," spanned by principal components used to describe the training set of examples. Within this space, we constructed an "OA vector" passing through the mean shape of an "OA Group" (all knees KLG ≥2 at all 0, 1, 2, and 4 years), and the mean shape for a "Non-OA Group" (KLG = 0 at the same time points). Distances along the OA vector are normalized to a z-score ("B-score"), with the mean shape of the Non-OA Group for each sex represented as the OA vector origin; 1 unit represents 1 SD of the Non-OA Group along the OA vector (+ve values toward the OA Group). Each femur bone shape was projected orthogonally onto the OA vector to specify the corresponding B-score. Representative examples of the femur bone shape are shown in Fig. 1.

The B-score was automatically measured at multiple time points up to 8 years in the OAI (9,433 knees; 5,031 without OA; 47,858 MRI images). WOMAC-A (pain) on the 20-unit scale was dichotomized, first by presence of moderate or higher pain (score ≥4) and then again by presence of severe pain (score ≥8). Knee Replacement Surgery (KRS) was defined as having either total or partial knee arthroplasty within the follow-up period, adjudicated using post-surgery radiographs. Logistic regression analysis was performed modeling any reporting of pain or KRS at any single time-point over the follow-up period for an individual knee by baseline B-score. This logistic regression was then repeated using baseline age.

Results: B-score was strongly associated with current and future pain; Fig. 2 displays the enhanced predictive power of B-score compared to age. Males and females were analyzed separately. However, an additional model combining both sexes was produced: for baseline B-scores of 0 and 6 (incipient and advanced disease), future risk of painful knee within an average follow-up of 5 years was 36.0% (95% CI: 34.9 to 37.1) and 75.1% (72.6 to 77.5), respectively. Males had 210 KRS, females had 318. Although both baseline B-score and baseline age were both sta-

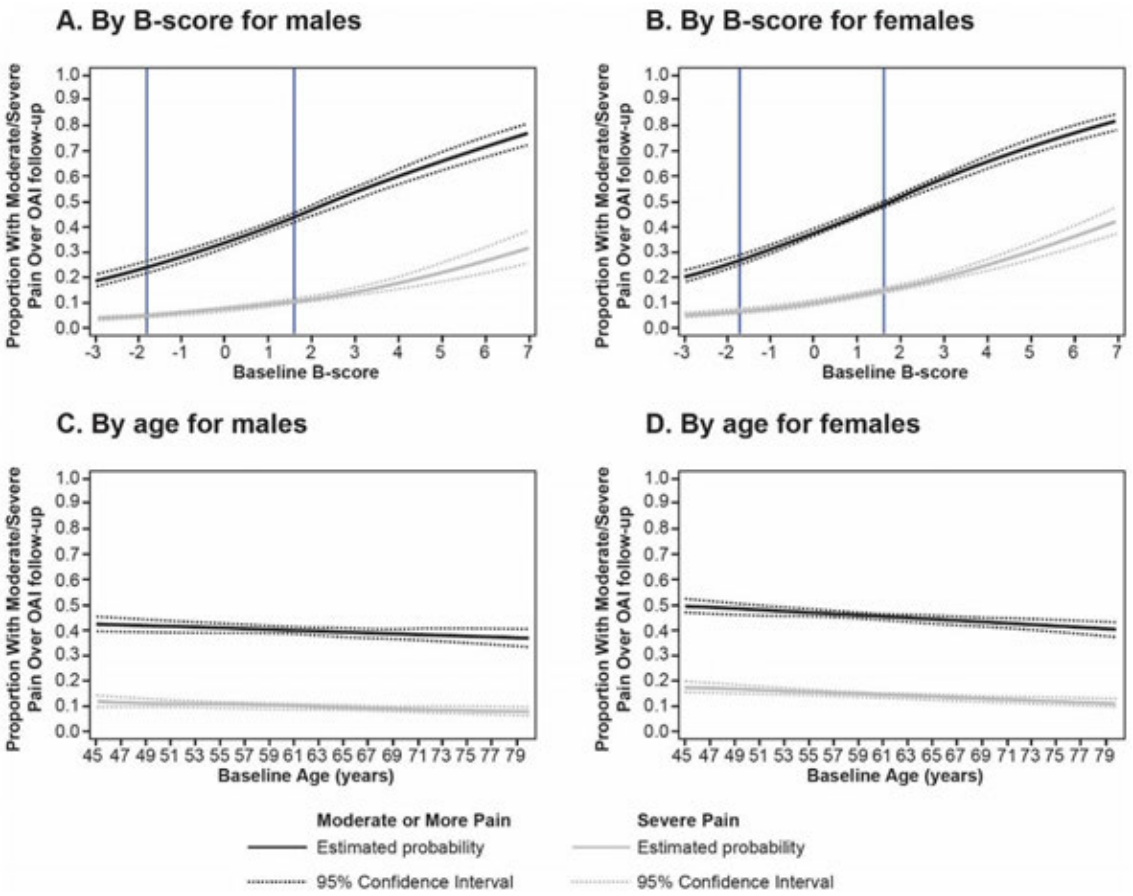

Figure 2. Knee Pain by B-Score for A) Males and B) Females and by Age for C) Males and D) Females. Moderate or more pain was defined as WOMAC-A (pain) ≥4 on the 20-unit scale; severe pain was defined as WOMAC-A (pain) ≥8 on the 20-unit scale. The average follow-up was 5 years. Vertical lines on B-score axis display Non-OA Range.

tistically significant at P< 0.001, Fig. 3 displays the enhanced predictive power of B-score compared to age for KRS. Using a combined model, future risk of KRS at B-scores of 0 and 6 was 2.3% (2.0 to 2.7) and 36.7% (32.5 to 41.1), respectively. Age had minimal utility in predicting pain or KRS.

Conclusion: By providing a continuous metric for OA, machine learning applied to a large dataset has for the first time demonstrated simple and strong relationships between bone shape and the current and future clinical outcomes. B-score provides accurate stratification for interventions and improved personalized assessment and is analogous to the T-score developed for osteoporosis.

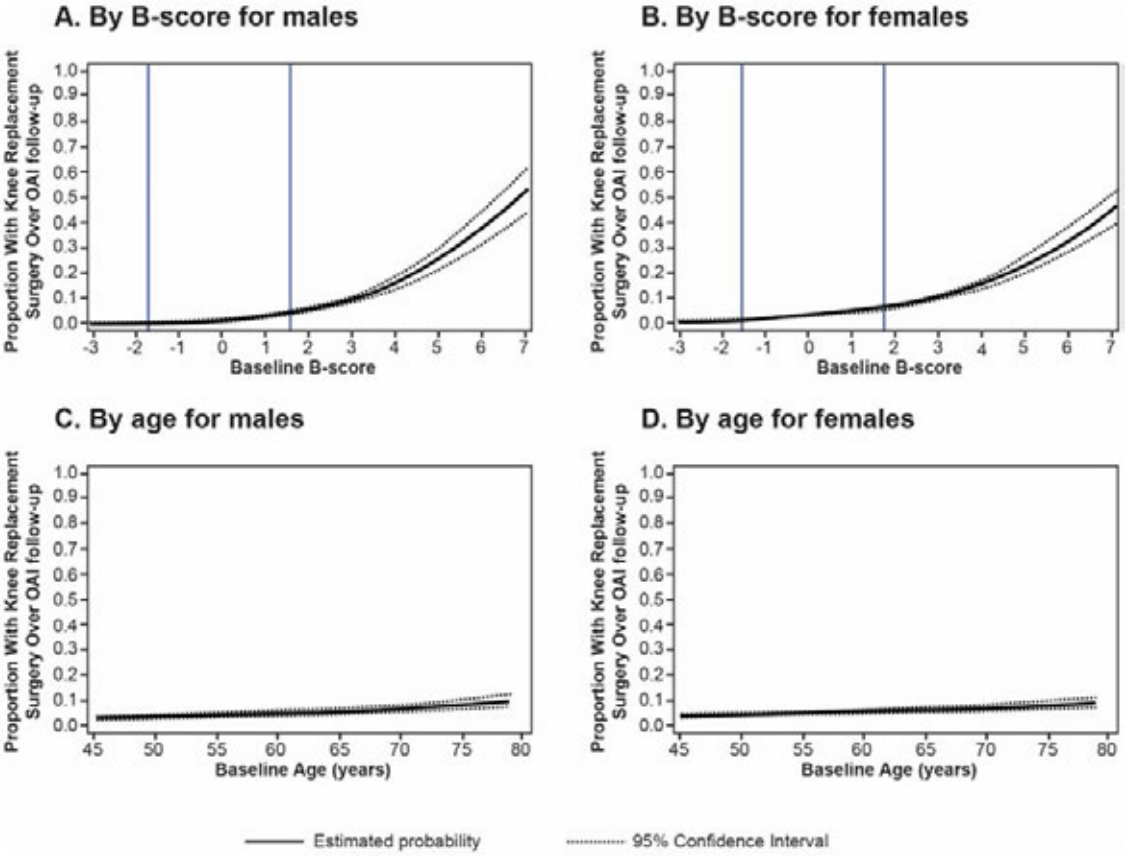

Figure 3. Risk of Knee Replacement Surgery by B-Score for A) Males and B) Females and by Age for C) Males and D) Females. Vertical lines on B-score axis display Non-OA B-score range.

Disclosure: M. Bowes, Imorphics (Stryker), 3, OrthoTrophix, 9; **K. Kacena**, Flexion Therapeutics, 5; **O. Alabas**, None; **A. Brett**, OrthoTrophix, 9, OrthoTrophix, Inc, 9; **B. Dube**, None; **N. Bodick**, Flexion Therapeutics, 3, 4; **P. Conaghan**, Abbvie, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, 8, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Eli Lilly, 8, EMD, 5, EMD Serono, 5, EMD Serono Research and Development Institute, Inc., 5, 8, Flexion, 5, 8, Flexion Therapeutics, 5, 8, Galapagos, 5, 8, Glaxo Smith Kline, 5, GlaxoSmithKline, 5, 8, Lilly, 8, Medivir, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Samumed, 5, 8, Serono, 5, Stryker, 5, 8.

Abstract Number: 2197

Clinically Relevant Improvements in Knee Osteoarthritis Pain with Diclofenac Sodium Gel 1%

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Topical agents are recommended for the initial treatment of patients with knee osteoarthritis (OA). Diclofenac sodium gel 1% (DSG 1%), a topical nonsteroidal anti-inflammatory drug (NSAID), demonstrated significant improvements in the signs and symptoms of knee OA and a higher percentage of patients meeting the Osteoarthritis Research Society International criteria for a response relative to a vehicle placebo in a trial of patients with OA of the knee. This post-hoc analysis was conducted to determine the percentage of patients in this study achieving a minimal clinically important improvement (MCII, the smallest improvement considered meaningful by an individual patient) in OA signs and symptoms.

Methods: This study was a 12-week, prospective, randomized, double-blind, multicenter, parallel group study that compared DSG 1% with placebo in subjects with OA of the knee. MCII responders were defined as having an improvement of ≥20% over baseline in Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) pain, function, and stiffness and in pain on movement (POM) per the definition used by Tubach F et al. (*Arthritis Care Res* (Hoboken). 2012;64(11):1699-707). The percentage of responders was analyzed using logistic regression with treatment and stratification factors (number of knees treated and Kellgren-Lawrence grade) included in the model. Time to MCII response was analyzed using the log-rank test with the same stratification factors.

Results: This analysis included 207 DSG 1%-treated and 212 vehicle-treated patients. Significant differences in the percentage of patients reaching an MCII were evident at Week 1 (DSG 1% vs vehicle, odds ratio [95% confidence limits]): WOMAC pain, 74.9% vs 61.8%, OR 1.87 [1.23, 2.85], *P*=.004; POM, 71.5% vs 59.9%, OR 1.71 [1.13, 2.59], *P*=.011; WOMAC function, 69.6% vs 58%, OR 1.70 [1.13, 2.56], *P*=.011; WOMAC stiffness, 75.4% vs 64.6%, OR 1.70 [1.11, 2.60], *P*=.015. Time to first MCII response was lower with DSG 1% for all measures: WOMAC pain, *P*=.001; POM, *P*=.013; WOMAC function, *P*=.018; WOMAC stiffness, *P*=.01. Significant differences in responder rates between groups were evident at most subsequent time points, with a higher percentage of patients with an MCII response with DSG 1% at Week 12 for all endpoints.

Conclusion: The MCII, a metric that considers patient perspectives on clinical improvements, was applied to data from a published clinical trial first time. In this analysis, most patients treated with DSG 1% achieved clinically meaningful relief within 1 week that was sustained for ≥12 weeks. Despite a relatively high vehicle response rate, a significantly higher percentage of patients had MCII responses with DSG 1%.

Disclosure: M. Hochberg, Bioiberica SA, 5, Bone Therapeutics, 5, BriOri Biotech, 4, Bristol Myers Squibb, 5, Eli Lilly, 5, Elsevier, 7, EMD Serono, 5, EMD Serono Research and Development Institute, Inc., 5, Galapagos, 5, Galapagos, IQVIA and Hoffman LaRoche, 9, IBSA Biotechniq SA, 5, Novartis Pharma AG, 5, Pfizer, 5, Pfizer Inc, 5, Plexxikon, 5, Regenosine, Samumed LLC, Symic Bio Inc., Theralogix LLC, TissueGene Inc., TLC Biopharmaceuticals, Inc., and Zynerba, 5, Rheumcon, Inc, 3, Samumed LLC, 5, Theralogix LLC, 4, 5, TissueGene Inc, 5, UpToDateTM, 7; **B. Patel**, GlaxoSmithKline Consumer Healthcare, 3; **S. Yacoub Garas**, GlaxoSmithKline Consumer Healthcare, 3; **R. Altman**, Sanofi US, 2, Flexion, 5, GSK, 5, Novartis, 5, Olatec, 5, Pfizer, 5, Sorrento, 5.

Abstract Number: 2198

Severe Acute Localized Reactions Following Intra-Articular Hyaluronic Acid Injections in Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Some concerns have been raised about subsequent severe acute localized reactions (SALR) (flares, pseudoseptic reactions, etc.) following hyaluronic acid (HA) injections for pain relief of knee osteoarthritis (OA). SALR has been speculated to be possibly related to the crosslink of hylan or an allergic reaction to hyaluronan of avian origin, but similar reactions have been reported following the use of non-crosslinked, non-animal, and/or naturally derived HA. We compared surrogate SALR measures between hylan G-F 20 and non-hylan G-F 20 patients and evaluated the corresponding risk factors for hylan G-F 20 patients in a real-world setting.

Methods: Knee OA patients were identified from the Optum Clinformatics (UnitedHealth Group private payer) dataset (Jan 2006-June 2016) and stratified into hylan G-F 20 and non-hylan G-F 20 users. The occurrences of surrogate SALR measures including inflammation/infection, corticosteroid (CS) injections, arthrocentesis/aspiration, and office visits were evaluated within three days of HA use. Logistic regression was used to evaluate risk factors.

Results: The study cohort involved 748,428 HA patients with 23.2% in the hylan G-F 20 group. Knee OA-related inflammation/infection rate was 0.001% for hylan G-F 20 and 0.002% for non-hylan G-F 20 groups (Fig. 1). Knee OA-related arthrocentesis/aspiration rate was 1.6% for hylan G-F 20 and 2.1% for non-hylan G-F 20 groups, with comparable risk for both groups ($p=0.201$; Table 1). The rate of CS injection (any diagnosis) was 0.48% for hylan G-F 20 patients compared to 0.41% for non-hylan G-F 20 patients, with 28% greater risk greater for hylan G-F 20 patients ($p< 0.001$), but the combined rates of CS injection and arthrocentesis/aspiration (any diagnosis) was comparable for both groups (hylan G-F 20: 2.2%; non-hylan G-F 20: 2.6%). The risk of any visit or studied responses was lower for the hylan G-F 20 cohort by 12% (unadjusted rate of 3.1% versus 4.3%; $p< 0.001$). Clinical characteristics, such as CS injections or arthroscopy within 1 week before HA and ultrasound imaging, were associated with 84%, 289%, and 35% increased risk of any studied clinical encounter, respectively. Concomitant CS and HA injections, and fluoroscopic imaging were associated with 35% and 42% lower risks, respectively (all $p< 0.001$).

Conclusion: Our study of almost 750,000 knee OA patients who had HA injections, of which about a quarter were only given hylan G-F 20, demonstrated that the diagnosis of inflammations or infections within three days of the HA injection was extremely rare. The occurrence was 1 out of 100,000 hylan G-F 20 patients and 2 out of 100,000 non-hylan G-F 20 patients for those events that had a corresponding knee OA diagnosis, and increased to 2 out of 10,000 for both cohorts when all inflammation or infections were included regardless of diagnosis. The overall risk of surrogate SALR measures was not greater for hylan G-F 20 patients.

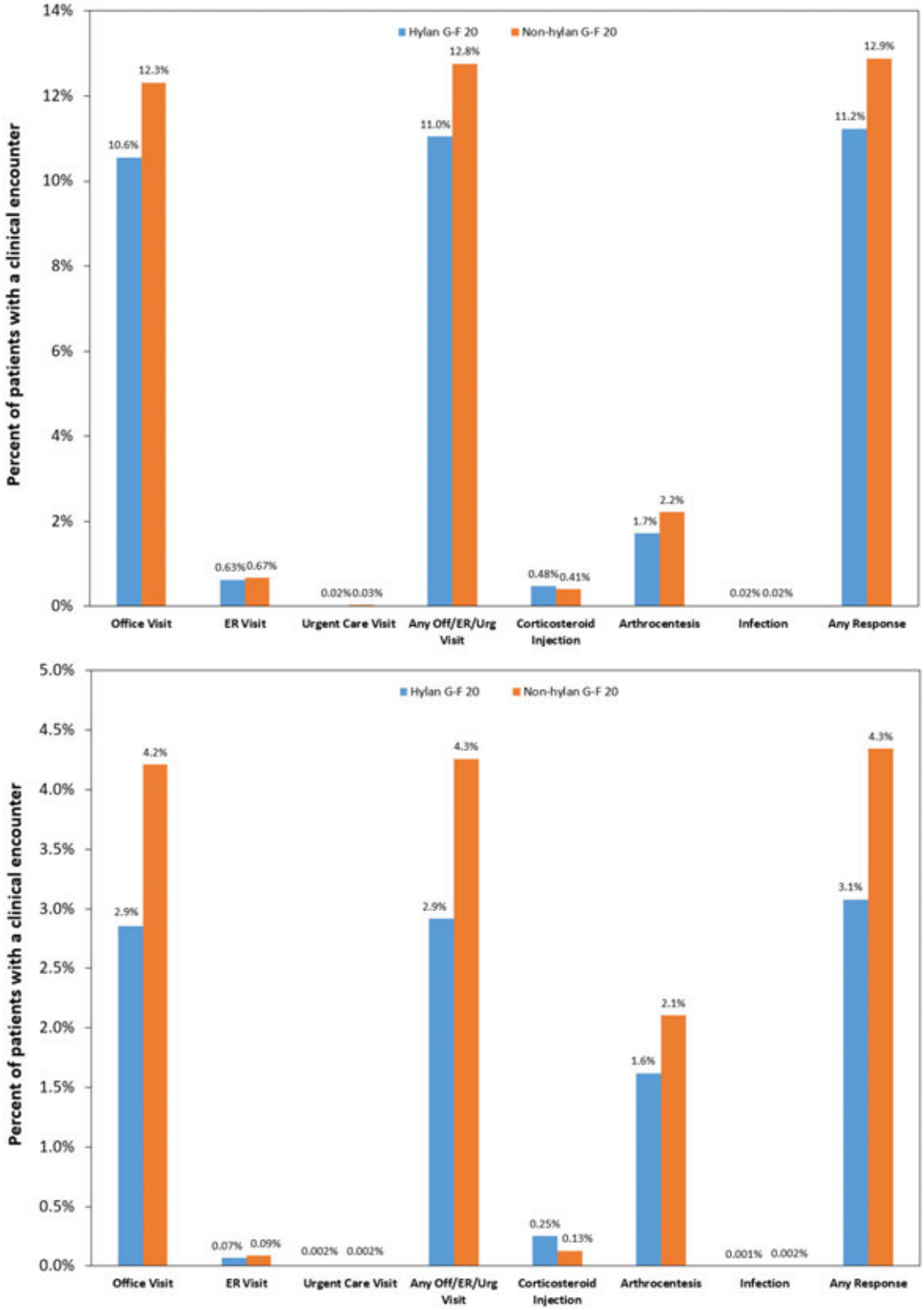

Figure 1. Clinical encounters (top: for any diagnosis; bottom: with knee OA diagnosis) within 3 days post-HA injection.

Table 1. Relative risk of clinical encounters within 3 days post-HA injection between hylan G-F 20 and non-hylan G-F 20 (reference) cohorts

		HR (Lower HR-Upper HR)	P-Value
Office Visits	Any visit	0.92 (0.90-0.93)	<0.001
	Knee OA related visit	0.84 (0.81-0.87)	<0.001
Emergency Room Visits	Any visit	0.99 (0.92-1.06)	0.689
	Knee OA related visit	0.94 (0.77-1.15)	0.560
Urgent Care Visits	Any visit	0.87 (0.62-1.23)	0.435
	Knee OA related visit	1.16 (0.35-3.87)	0.807
Any Office or ER or Urgent Care Visits	Any visit	0.93 (0.91-0.94)	<0.001
	Knee OA related visit	0.85 (0.82-0.88)	<0.001
Corticosteroid Injection	Any visit	1.28 (1.18-1.39)	<0.001
	Knee OA related visit	2.16 (1.91-2.44)	<0.001
Arthrocentesis	Any visit	0.98 (0.94-1.02)	0.322
	Knee OA related visit	0.97 (0.93-1.01)	0.201
Infection or Inflammation*	Any visit	n/a	n/a
	Knee OA related visit	n/a	n/a
Any Visits or Response	Any visit	0.94 (0.92-0.95)	<0.001
	Knee OA related visit	0.88 (0.85-0.91)	<0.001

*Incidence was too low

Disclosure: K. Ong, Sanofi US, 9, Medtronic, 9, Stryker Orthopaedics, 9, Ferring Pharmaceuticals, 9, Paradigm Spine, 9, Pacira Pharmaceuticals, 9, St Jude Medical, 9, Relievant Medsystems, 9, International Society for the Advancement of Spine Surgery, 9, Zimmer Biomet, 9, Joerns Healthcare, 9, SpineFrontier, 9, SI-Technology, LLC, 9, Ethicon, 9, DJO, 9, Ossur, 9, Karl Storz Endoscopy-America, 9; **M. Runa**, International Society for the Advancement of Spine Surgery, 9, Sanofi US, 9; **W. Ngai**, Sanofi, 1, 3, Sanofi US, 1, 3; **Z. Xiao**, Sanofi US, 1; **E. Lau**, Sanofi US, 9, Ferring Pharmaceuticals, 9, Medtronic, 9, Stryker Orthopaedics, 9, Relievant Medsystems, 9, Boston Scientific, 9, Alcon Corp, 9; **R. Altman**, Sanofi US, 2, Flexion, 5, GSK, 5, Novartis, 5, Olatec, 5, Pfizer, 5, Sorrento, 5.

Abstract Number: 2199

Is There an Association of Serum LDL, HDL and Total Cholesterol with the Development of Knee Osteoarthritis?

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent data have suggested an association between elevated serum cholesterol levels, particularly low density lipoprotein (LDL), and the development of osteoarthritis (OA). Within the joint, circulating LDL is taken up by the synovium and oxidized, activating macrophages and leading to the release of inflammatory medi-

ators. Further, mice with high LDL levels have high rates of OA compared with controls. In this study, we sought to comprehensively and longitudinally evaluate whether circulating total cholesterol, LDL, and high density lipoprotein (HDL) are associated with the risk of radiographic and symptomatic knee OA. We hypothesized that elevated levels of LDL increase the risk of developing knee OA.

Methods: We performed a nested case control study within the Multicenter Osteoarthritis study (MOST) cohort to examine the relationship between total cholesterol, LDL, and HDL and OA. MOST is an NIH-funded longitudinal study which followed 3,026 subjects with or at risk of developing OA for a seven year period, during which knee x-rays and MRIs were obtained and knee symptoms were queried at baseline, 30, 60, and 84 months. Baseline fasting blood samples were also drawn. We defined cases as those developing either radiographic OA (on plain film x-rays, N=283) or symptomatic OA (knee pain and radiographic OA, N=336) at follow-up. To identify cases with incident radiographic OA, we excluded those with prevalent radiographic OA at baseline and then followed subjects for the development of incident disease. Controls were selected randomly from those who were eligible to develop OA but did not. We carried out an identical case and control selection procedure for incident symptomatic OA. Additionally, we examined cartilage loss and synovitis on MRI and knee pain using the WOMAC scale. We carried out person-specific analyses using Cox Proportional Hazards regression adjusting for age, sex, BMI and educational attainment. When analyzing pain outcomes, covariates included depressive symptoms. We tested cholesterol as a continuous measure and did sensitivity analyses examining whether commonly used thresholds for high cholesterol (>=200mg/dl), LDL (>=130 mg/dl) or low HDL (< =60mg/dl) increased risk.

Results: Mean age at baseline was 62 years and 55% were women. The hazard ratio for incident radiographic OA and incident symptomatic OA according to total cholesterol, LDL, and HDL cholesterol levels as well as the mean cholesterol values showed no significant associations with OA (see table). Additionally, we found no significant association of total cholesterol, LDL and HDL with cartilage loss, worsening synovitis or worsening knee pain. We also examined whether persons with high cholesterol, LDL or low HDL had an increased risk of OA, and did not find a significant association.

Association of Cholesterol, LDL and HDL with Incident Knee OA in the MOST Study

	Mean (mg/dl)		HR with 95% CI (per SD)	P value
	Cases	Controls		
Incident Knee Radiographic OA(cases/controls=283/329)				
Total Chol	229	229	1.00 (0.88,1.14)	0.97
LDL	136	138	0.98 (0.87, 1.12)	0.80
HDL	62	61	1.11 (0.96, 1.29)	0.16
Incident Symptomatic Knee OA(cases/controls=336/559)				
Total Chol	224	229	0.91 (0.80, 1.03)	0.12
LDL	132	137	0.89 (0.79, 1.01)	0.06
HDL	62	61	1.09 (0.95, 1.24)	0.24

Conclusion: We did not find an association between LDL cholesterol, total cholesterol, or HDL cholesterol levels with incident osteoarthritis or other osteoarthritis outcomes. While LDL may have local deleterious effects on joint structure, elevated systemic levels do not confer risk of disease.

Disclosure: J. Barlow, None; **X. Sun**, None; **M. Nevitt**, None; **J. Torner**, None; **B. Lewis**, None; **N. Matthan**, None; **A. Lichtenstein**, None; **D. Felson**, None.

Abstract Number: 2200

Magnetic Resonance Imaging of Knee Joint Protection Following an Intra-Articular Injection of Lipid-Based Dexamethasone Sodium Phosphate Sustained Release Formulation on Subjects with Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The most commonly used intra-articular (IA) corticosteroid for osteoarthritis (OA) is triamcinolone acetonide (TA), but its potential chondrotoxicity restricts injection frequency to 3-4 injections per year. TLC599 is a liposomal formulation of dexamethasone sodium phosphate (DSP) designed for intra-articular injection in the treatment of knee osteoarthritis (OA). Based on a Phase 2a multi-center, randomized, double-blind, placebo-controlled clinical trial (ClinicalTrials.gov ID: NCT03005873), TLC599 has demonstrated durable pain relief and improved function over 24 weeks in patients with knee OA pain. Also, TLC599 possess the potential to protect articular cartilage from damage, making it potentially a beneficial therapy for OA with less risk of chondrotoxicity. To evaluate the effect of TLC599 on knee cartilage, magnetic resonance imaging (MRI) was utilized in this trial.

Methods: In the current Phase 2a study, subjects were eligible if they met the American College of Rheumatology Criteria for knee OA, with Grade 2 to 3 Kellgren-Lawrence severity. A total of 75 patients were randomized to receive 1 of the 3 regimens in the index knee in 1:1:1 ratio (TLC599 with 12 mg DSP and 100 μmol phospholipid (PL); TLC599 18 mg DSP with 150 μmol PL; or normal saline placebo). Patients were followed 24 weeks post injection. MRI was conducted on both knees before dosing and at the end of study, and cartilage was evaluated by a blinded radiologist at each center using the MRI Osteoarthritis Knee Score (MOAKS) instrument, with 14 articular subregions individually evaluated with 2 categorical scores, indicating the size of cartilage damage (surface area loss) and depth of cartilage damage (full thickness loss).

Results: Index knees were compared with non-index knees by number of sub-regions with worsening from baseline to the end of 24 weeks (≥ 2 sub-regions worsening representing significant worsening), regardless of the individual sub-region severity. Table 1 shows the MOAKS score pattern for placebo group index and non-index knees, representing the natural course of the disease, and the TLC599 group knees. For the placebo group, the index knee displayed similar or more significant cartilage damage (≥ 2 sub-regions with worsening) than the non-index knee, for both joint cartilage surface area and thickness. However, both TLC599 patient groups displayed lower proportions of significant cartilage damage in the index knee than the non-index knee. Figure 1 shows that the pattern of knee

Treatment group	Proportion of subjects with ≥2 cartilage sub-regions with worsening in:	Index knee	Non-index knee	Index knee minus non-index knee	Interpretation
Placebo (n=22)	Surface area loss	5%	5%	0%	Placebo group represents the natural course of cartilage degeneration. Assuming that index knee might be more severe and degenerate faster than non-index knee, the percentage with significant worsening was actually higher in the index knee than in the non-index knee.
	Full thickness loss	14%	5%	9%	
TLC599 12 mg (n=24)	Surface area loss	42%	50%	-8%	TLC599-treated subjects showed that the percentage of significant worsening was lower in index knee than non-index knee, which indicates that TLC599 might be able to slow down the natural course of cartilage degeneration.
	Full thickness loss	29%	33%	-4%	
TLC599 18 mg (n=21)	Surface area loss	14%	29%	-15%	
	Full thickness loss	5%	14%	-9%	

Table 1. Comparison of significant cartilage damage by MOAKS between placebo- and TLC599-treated patients

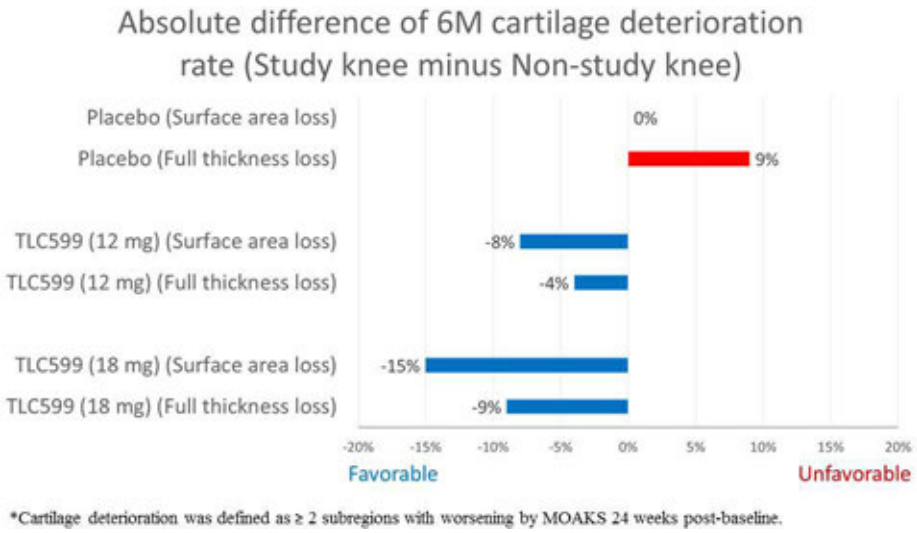

Figure 1. Difference in proportions with cartilage deterioration between index knee and non-index knee

joint cartilage damage change between treated groups was reflected by the difference between the proportions of subjects displaying ≥2 worsening cartilage sub-regions in index vs. non-index knee. These findings suggest there may be protection from cartilage degeneration by TLC599 IA injection.

Conclusion: The exploratory MRI evaluation of knee cartilage using semi-quantitative MOAKS indicated that, comparing index to non-index knees, patients treated with TLC599 IA injection displayed relatively less cartilage loss in the treated knee than placebo patients, suggesting a lack of cartilage damage or potentially a chondroprotective effect.

Disclosure: S. Shih, Taiwan Liposome Company, Ltd., 1, 3; **C. Brown**, Taiwan Liposome Company, Ltd., 1, 3; **T. Tai**, Taiwan Liposome Company, Ltd., 1, 3; **W. Chuang**, Taiwan Liposome Company, Ltd., 1, 3.

Abstract Number: 2201

Developing a Comprehensive Patient-Specific Disease Progression Prediction Model for Knee Osteoarthritis Using Machine/Deep Learning Methods

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Current assessment of knee osteoarthritis (OA) is primarily based on a patient's personal and familial history, clinical features, and on radiographies. However, such information does not provide enough evidence to lead to a robust prediction/prognosis of OA fast progressors. This study aims to identify early significant predictors of knee OA progression using advanced machine learning (ML) and deep learning (DL) algorithms and propose a prediction model based on a short number of selected predictors and outcomes.

Methods: We used six feature selection models, including LASSO (Least Absolute Shrinkage and Selection Operator), Elastic Net, GBM (Gradient Boosting machine), RF (Random Forest), IG (Information Gain), and DL-based Multi-Layer Perceptron [MLP]. In addition, more than 100 classification methods were tested on five outcomes: incidence of cartilage volume loss in medial plateau at 48 and 96 months (Prop_CV_48-96), knee replacement (TKR) at 48-96 months, Kellgren-Lawrence (KL) grade ≥2 and medial joint space narrowing (JSN) ≥1 mm at 48 months. Data were retrieved from the Osteoarthritis Initiative and quantitative magnetic resonance imaging (MRI) assessment. This study included 1044-1598 individuals/outcome, as well as 1107 variables and 135 MRI data at baseline. The classification was done using auto-ML tools by calculating the area under curve (AUC) and Matthews correlation coefficient (MCC) for the imbalanced TKR data. To prioritize the selected variables and outcomes, we used the multi-label Sparse Partial Least Square (sPLS) regression method.

Results: Feature selection and sPLS revealed MRI-based variable cartilage thickness and outcome cartilage volume loss at 96 months (Prop_CV_96) as the best predictors of knee OA progression. Moreover, medial joint space width along with pain were among the top predictors. The LASSO method outperformed other feature selection methods (AUC, 0.75-0.91). For the 1-label classification of top common variables between the models, MLP achieved the highest AUC in Prop_CV_96, KL, and JSN (0.80, 0.99, 0.95). For Prop_CV_48 and TKR outcomes, GBM was the best classifier (AUC, 0.70, 0.99).

Conclusion: This is the first time that such a comprehensive study is performed for identifying the best predictors of knee OA rapid progressors. Importantly, data showed that MRI-based variables and outcome have the most significant impact in identifying OA progressors, and could be applied for early prognosis in clinical practice.

Disclosure: A. Jamshidi, None; **M. Leclercq**, None; **J. Pelletier**, ArthroLab Inc., 1, TRB Chemedica, 5; **A. Labbe**, None; **F. Abram**, ArthroLab Inc., 3; **A. Droit**, None; **J. Martel-Pelletier**, ArthroLab Inc., 1, TRB Chemedica, 5.

Abstract Number: 2202

Trends in Prescribing of NSAIDs and Opioids Among Osteoarthritis Patients in British Columbia, Canada, 1998-2014

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are commonly prescribed for patients with osteoarthritis (OA). However, both types of medication are associated with serious side effects. As a result, guidelines for the treatment of OA have changed substantially over the past 2 decades. Our purpose in this study was to describe the trends in prescribing of NSAIDs (including COX-2 inhibitors) and opioids among patients with OA in the general population.

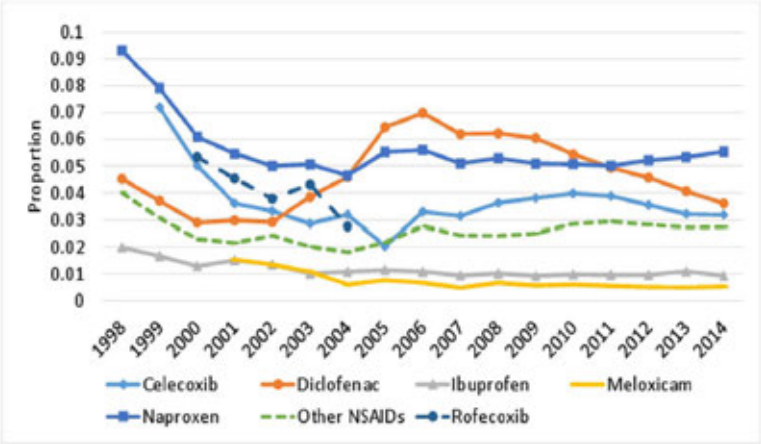

Figure 1. Prescriptions for NSAIDs in patients newly diagnosed with OA in British Columbia, Canada, 1998 - 2014

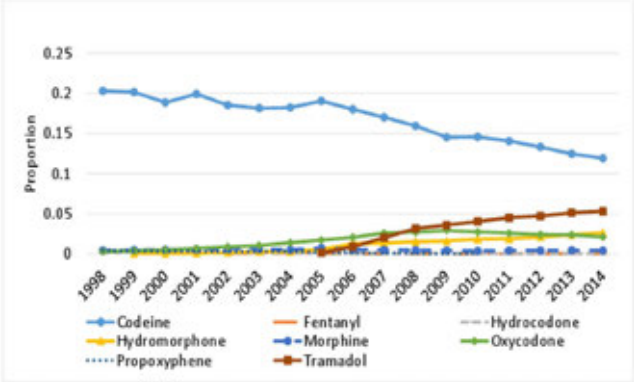

Figure 2. Prescriptions for opioids in patients newly diagnosed with OA in British Columbia, Canada, 1998 - 2014

Methods: We analyzed data from a large, population-based administrative database (PharmaNet) that included all prescriptions for persons aged 50+ processed by pharmacies in the province of British Columbia (BC), Canada, linked to diagnostic codes for visits to physicians and hospitalizations between 1990 and 2014. We identified all incident cases of OA, defined as at least 2 codes within 2 years, with a run-in period of 7 years. We identified all new prescriptions (no prescription in 6 months prior to diagnosis) for each NSAID and opioid available in BC and calculated the proportion of people starting NSAID or opioid medication. We performed similar analyses for prevalent (any) prescriptions among all prevalent cases of OA.

Results: Between 2000 and 2014, the proportion of new OA patients with an NSAID prescription declined from 19.8% to 16.5%. For most NSAIDs (Figure 1), prescriptions declined from 1998 till 2004 and were relatively stable until 2014, with the exception of diclofenac, which increased substantially from 2002 to 2006 and decreased afterwards. In 2014, the most common NSAID was naproxen (5.5%) followed by diclofenac (3.6%), celecoxib (3.2%), ibuprofen (0.9%) and meloxicam (0.5%). For opioids (Figure 2), the overall trend was relatively flat from 1998 to 2004, peaked in 2008 at 24.0%, and declined slightly thereafter. Codeine was by far the most commonly prescribed opioid throughout the study period, but declined from 20.3% of new OA patients in 1998 to 11.9% in 2014. Tramadol increased steadily from its introduction in 2005 and has been the second most common opioid since 2008, reaching 5.3% in 2014. Prescriptions for oxycodone started to decline around 2009 and reached 2.1% in 2014, whereas those for hydromorphone steadily increased to 2.6%. Other opioids were rarely prescribed in patients with OA. The results of prevalence analyses were essentially similar.

Conclusion: There have been important changes in the pattern of prescribing analgesics in BC during the study period. Declines in NSAIDs may have been compensated by increased prescriptions for opioids. This is likely to change as new guidelines discourage the long-term use of opioids as a consequence of the opioid crisis.

Disclosure: J. Kopec, None; **J. Cibere**, None; **N. Lu**, None; **H. Xie**, None; **J. Avina-Zubieta**, None; **J. Esdaile**, None.

Abstract Number: 2203

Impact of Hypothetical Changes in the Use of Analgesics on the Burden of Osteoarthritis: A Population-based Microsimulation Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Analgesics are the cornerstone of medical treatment of osteoarthritis (OA) but are associated with serious side effects. A more optimal use of analgesics in OA is one strategy to reduce the population health burden of OA. The purpose of this simulation study was to assess the impact of hypothetical changes in the use of analgesics on the quality-adjusted life years (QALYs) among persons with OA in the general population.

Methods: We used a previously validated population-based microsimulation model of OA in Canada, POHEM-OA. Model parameters were derived from a large administrative database in British Columbia, Canadian national surveys,

and the scientific literature. The model included data on OA incidence, frequency of use of 4 classes of medication (acetaminophen, traditional non-steroidal anti-inflammatory drugs [NSAIDs], COX-2 inhibitors [coxibs], and opioids), treatment benefits in terms of pain reduction, frequency and quality-of-life (QOL) impact of adverse effects associated with each medication type (dyspepsia, ulcer, cardiovascular disease [CVD], stroke, and "other") and overall QOL measured by the Health Utilities Index 3. We assessed the impact of changes in medication use on overall QALYs. In the base-case scenario we assumed that the relative risk of adverse effects due to medication is doubled among persons aged 70+ compared to those < 70 years of age. Alternative assumptions were tested in sensitivity analyses. The scenarios involved increases and decreases in the use of all medications and each medication type individually.

Results: Under the base-case scenario, an average person with OA accumulated about 13.3 QALYs from OA diagnosis till death. Increasing the odds of using analgesics by 50%, 100% and 200% resulted in incrementally greater improvements in overall QALYs. However, the improvements were small (0.05-0.15 QALYs) and were observed only for opioids and acetaminophen. Increasing NSAIDs had virtually no effect on overall QALYs. Targeting persons with moderate or severe pain (>2 or >3 on a 5-point scale) for aggressive treatment (increasing the odds of treatment 3-fold) achieved a greater overall benefit than targeting all OA patients. Reducing the odds of using all analgesics by 50% among older (70+) patients with OA did not affect QALYs, whereas eliminating NSAIDs in this group had a slight beneficial effect at the population level. These results were sensitive to the assumptions about the relative risk of adverse effects among the elderly.

Conclusion: We found a beneficial but relatively small impact on QALYs of more aggressive treatment of OA with acetaminophen and opioids, and no benefit from increasing NSAIDs. For coxibs, even though gastrointestinal complications were reduced compared to traditional NSAIDs, the benefits of pain reduction were virtually nullified by the increased risk of CVD and stroke. Overall, the results seem plausible and support the validity of the simulation model. A limitation of the current model is that it does not consider the long-term harmful effects of opioids, including addiction and overdose.

Disclosure: J. Kopec, None; **E. Sayre**, None; **A. Okhmatovskaia**, None; **J. Cibere**, None; **L. Li**, None; **N. Bansback**, None; **H. Wong**, None; **J. Esdaile**, None.

Abstract Number: 2204

Fragility Fractures in a Community Setting: Clinical Characteristics, Care Gaps, and Outcomes

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis-related fragility fractures contribute to significant morbidity and mortality. The risk of subsequent hip fracture is significantly increased after initial fracture, with some reports suggesting rates of recurrent fractures in hip and spine to be 41% and 45% at 1-year, respectively[1]. Hip fractures plateaued between 2002-2012, yet increased between 2013-2015 resulting in an estimated 11,000 additional fractures[2]. Despite widely available access to Dual-energy X-ray absorptiometry (DEXA) and treatment, this effect may be due to low rates of

screening and treatment[3]. The purpose of this study was to identify the most common initial and secondary fractures, associated mortality, and frequency of screening and treatment.

Methods: Adults aged 65 and older diagnosed with fragility fracture at Lutheran General Hospital from January 2012 to January 2017 were included in this analysis. Fragility fractures, defined as wrist, humerus, vertebral, hip, and pelvis, were identified with ICD9/ICD10 codes, along with demographic and clinical characteristics from the Advocate Health Care EMR system. Univariate analysis for continuous and categorical variables were conducted. Logistic regression was applied to examine the association of demographic characteristics and risk of fragility fractures. A two-tailed *P* level of .05 was considered statistically significant in all analyses. All analyses were performed using SAS 9.4.

Results: A total of 1,424 initial and 137 secondary fragility fractures were identified. For initial fractures, vertebral was most common (607, 42.63%), closely followed by hip (592, 41.92%), and pelvis (153, 12.08%). The majority of initial fracture patients were females (1021, 71.7%), Caucasians (1209, 84.9%) and the mean age was 82.1-years-old (range: 66-105). DEXA and treatment with anti-resorptive medications were recorded at time of initial fracture among 17.6% and 1.9% of patients, respectively. DEXA and treatment for patients with recurrent fractures were recorded among 27% and 31% of patients, respectively. There were no statistically significant differences for in-hospital all-cause mortality among vertebral, hip, and pelvic fractures.

Conclusion: Vertebral, hip, and pelvic fractures are a common cause of initial fragility fracture in those over age 65. Pelvic fractures may represent an under-reported cause of initial fragility fracture with similar rates of morbidity com-

	All Initial Fractures (N=1424)	Vertebral (N=607)	Hip (N=592)	Pelvis (N=153)
Age	N (%) or mean (SD)			
	82.07	80.5 (7.78)	83.5 (7.94)	82.8 (8.68)
Sex				
Female	1059 (74.4%)	158 (45.4%)	154 (44.3%)	36 (10.3%)
Male	365 (25.6%)	449 (44.7%)	438 (43.6%)	117 (11.7%)
Race/Ethnicity				
White	1209 (84.9%)	505 (44.0%)	514 (44.7%)	130 (11.3%)
Black	8 (0.006%)	2 (25%)	6 (75%)	0 (0%)
East Asian	80 (5.6%)	44 (57.1%)	29 (37.7%)	4 (5.2%)
Other	61 (4.3%)	27 (45.8%)	17 (28.8%)	15 (25.4%)
Unknown/Declined	66 (4.6%)	29 (49.2%)	26(44.1%)	4 (6.8%)

Table 1. Demographic characteristics of top three most common initial fracture types. Abbreviations: % = percentage of patients within a particular fracture type for male and female and for all initial fractures (vertical summation) or percentage of patients within a particular race/ethnic group who sustained particular fracture types (horizontal summation), SD = standard deviation.

	Initial Vertebral (N=607)	Initial Hip (N=592)	Initial Pelvis (N=153)	*P*-value
	N (%) or mean (SD)			
Died at discharge or went into hospice	35 (54.5%)	25 (39.1%)	4 (2.6%)	0.19
Length of Stay (days)	4.81 (6.40)	5.86 (3.91)	4.51 (4.82)	0.0005

Table 2. Distribution of in hospital all-cause mortality death or referral to hospice among fracture types and mean number of days hospitalized (SD = standard deviation) among patients with the top three most common initial fractures.

pared to hip and vertebral fractures. Rates of screening and treatment are low after initial and recurrent fractures. Future studies aimed investigating barriers to primary and secondary fracture prevention and treatment are warranted.

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Disclosure: R. Kneeland, None; **K. Wahle**, None; **I. Gill**, None; **Y. Liu**, None; **M. Starosta**, None.

Abstract Number: 2205

Dual Femur Bone Density Measurements with Novel Sonographic Approach - Radiofrequency Echographic Multi Spectrometry

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A novel, non-ionizing approach - Radiofrequency Echographic Multi Spectrometry (REMS) was recently introduced for diagnosis of osteoporosis on both sites-lumbar spine and femoral neck. In the previous studies, bone mineral density (BMD) assessed by REMS technique highly correlated with BMD obtained by dual X-ray absorptiometry (DXA). However, there is no previous study, which investigated the diagnostic role of the dual femur BMD measurements based on REMS technology. The aim of this study is to compare the REMS-$_{based}$ BMD values of both femora-left and right in postmenopausal women and to identify the number of the women, in which the inclusion of bilateral hip in BMD measurement changed the diagnosis to more severe.

Methods: Dual femur was assessed in 72 postmenopausal women with mean age 61 years ± 13 standard deviations (SD), (range 40-66 years). Data was analyzed with SPSS version 21.0. Patients were classified as osteopenic if -2.5 SD < T-score< -1.0 SD, as osteoporotic if T-score ≤ -2.5 SD and healthy if T-score ≥-1.0. Linear regression analysis was used to compare the REMS-based BMD values of both femora.

Results: Based on the unilateral (left) hip BMD measurements, 22 women were diagnosed with normal BMD, 35- with osteopenia and 15 - with osteoporosis. The mean left femoral neck BMD was 0.879 g/cm^2 ± 0.100 g/cm^2 in the women with normal BMD, 0.685 g/cm^2 ± 0.056 g/cm^2 in the women with osteopenia and 0.507 g/cm^2 ± 0.054 g/cm^2 in the women with osteoporosis. The mean right femoral neck BMD was 0.873 g/cm^2 ± 0.095 g/cm^2 in the women with normal BMD, 0.677 g/cm^2 ± 0.046 g/cm^2 in the women with osteopenia and 0.507 g/cm^2 ± 0.054 g/cm^2 in the women with osteoporosis. A strong correlation between left and right femoral neck BMD values was observed (r^2=0.978, p=0.000), (figure 1). 63.6% (14/22) of the women with normal BMD had a T-score discordance equal to

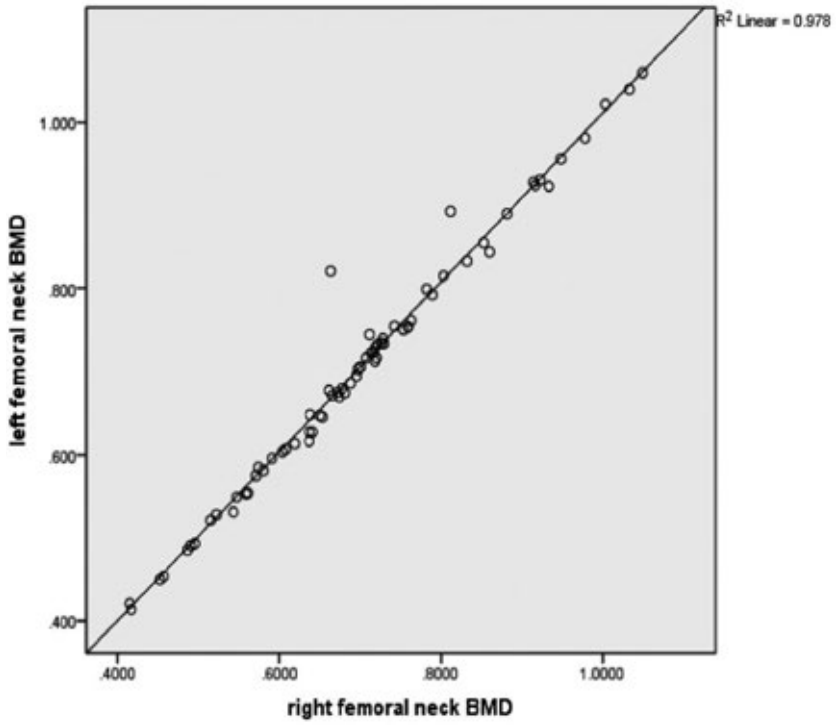

Figure 1. Linear regression analysis for comparison of the REMS-based BMD values of both femora.

0.1 and 4.6% (1/22) – equal to 0.2. 31.8% (7/22) of the women with normal BMD were attributed to a more severe diagnosis - osteopenia after assessing the dual femur. 48.6% (17/35) of the women with osteopenia had a T-score discordance equal to 0.1, 8.6% (3/35) – equal to 0.2 and 2.9% (1/35) – equal to 0.5. 2.9% (1/35) of the women with osteopenia were attributed to a more severe diagnosis – osteoporosis after assessing the dual femur. 33.3% (5/15) of the women with osteoporosis showed a T-score discordance equal to 0.1.

Conclusion: In women with femoral neck BMD values, which correspond to borderline T-scores, dual femur BMD measurements could be crucial for obtaining a more accurate diagnosis and decision about the treatment.

Disclosure: E. Kirilova, None; **N. Kirilov**, None; **M. Nikolov**, None; **N. Nikolov**, None; **I. Popov**, None; **S. Vladeva**, None.

Abstract Number: 2206

MRI-based Textural Analysis of Trabecular Bone: A Novel Method for the Opportunistic Screening of Bone Quality

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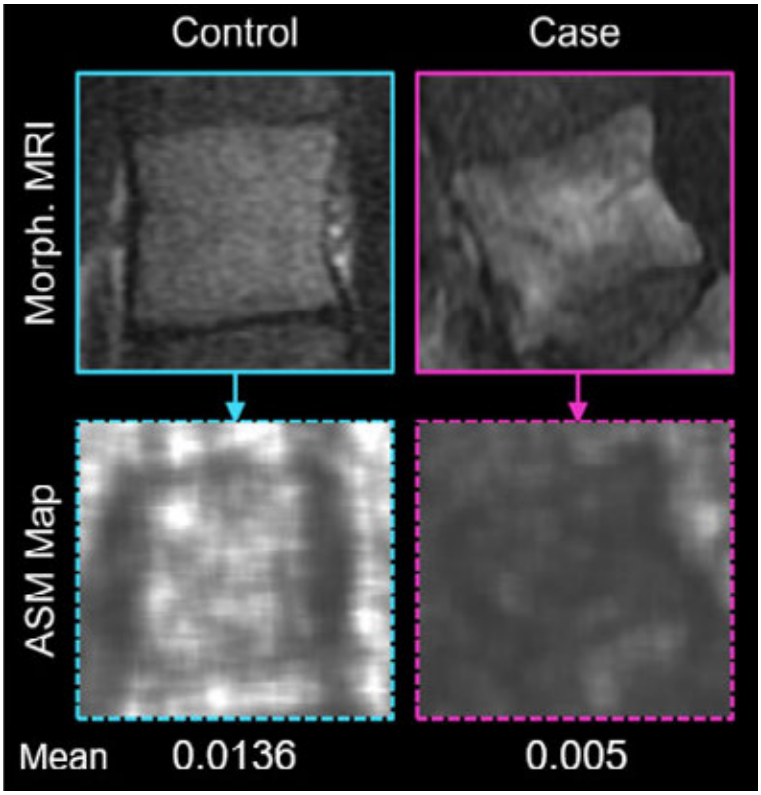
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A major obstacle to the treatment of osteoporosis and prevention of fractures is that many at-risk patients are never screened. Dual energy x-ray absorptiometry (DXA) measurements of bone mineral density, the gold standard for diagnosis of osteoporosis, are only performed in a minority of patients. Therefore, opportunistic methods using imaging obtained for other clinical purposes are needed to foster identification and treatment. The aim of this pilot study was to investigate textural analysis of MRI scans of the lumbar spine (LS) as a measure of bone quality. We hypothesized: 1) similar to trabecular bone score (TBS) derived from DXA, textural analysis of MRI would provide an assessment of bone quality based upon trabecular (Tb) bone distribution and 2) Tb bone heterogeneity measured by MRI texture analysis would be higher in those with a history of fragility fracture compared to healthy controls.

Methods: In this study, we analyzed LS MRI scans of 30 patients. Cases (n=15) were postmenopausal women with a radiographically confirmed fragility fracture. Controls (n=15) were healthy women aged 25-35 years. Tb bone from the lumbar vertebrae was segmented to create regions of interest (ROIs). Fractured or previously instrumented vertebrae were excluded. A gray level co-occurrence matrix (GLCM) was then created to quantify the distribution and spatial organization of pixels within the Tb bone ROI. Heterogeneity in Tb bone texture was assessed by the following independent parameters, both globally as well as in anatomic directions: contrast (variability), entropy (disorder) and angular second moment (homogeneity) [figure]. Texture measures were compared using the Wilcoxon rank-sum test.

Results: Measures of Tb bone heterogeneity were worse in fracture patients, who had 139% higher contrast, 14% higher entropy and 60% lower angular second moment compared to controls (all $p < 0.05$). Contrast was the measure that most effectively discriminated between groups: fracture patients had 128-161% higher values in the vertical, horizontal, diagonal and through planes (all $p < 0.05$).



Comparison of output map and mean value for angular second moment (ASM)

Conclusion: In summary, textural analysis of Tb bone discriminated between patients with known osteoporotic fractures and controls. Our results demonstrate the feasibility of applying this technique to MRI to evaluate Tb bone quality. Further investigation is required to validate this promising methodology, which has the potential to greatly expand the number of patients screened for skeletal fragility.

Disclosure: J. Cheah, None; **M. Koff**, Johnson & Johnson, 3; **R. Breighner**, None; **B. Lin**, None; **C. Jones**, None; **J. Havasy**, None; **M. Grewal**, None; **E. Stein**, Novartis, 2.

Abstract Number: 2207

Bone Mineral Density and Microarchitecture Among Chinese Patients with Rheumatoid Arthritis

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Table 1. Clinical Characteristics of patients with RA

	n = 81
Age at onset, y	48.6±11.1
Age at diagnosis, y	50.4±10.9
Duration of RA, y	5.7(1.4-11.2)
RF/CCP+, n(%)	74(91.4)
ESR, mm/h	17.0(10.0-33.0)
CRP, mg/L	2.19(0.92-7.23)
DAS28-ESR	3.4±1.5
DAS28-CRP	2.9±1.4
SDAI	8.2(3.2-16.2)
CDAI	7.0(3.0-15.8)
HAQ-DI	0.05(0.00-0.28)
Medications	
GC ever, n(%)	55(67.9)
Current dose, mg/d	5.6(5.0-10.0)
Maximum dose, mg/d	10.0(10.0-21.2)
Duration, m	17.0(6.5-58.0)
MTX ever, n(%)	57(70.4)
LEF ever, n(%)	31(38.3)
Sulfasalazine ever, n(%)	4(4.9)
HCQ ever, n(%)	20(24.7)
Tripterygium wilfordii Hook, n(%)	29(35.8)
bDMARDs ever, n(%)	14(17.3)

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate alterations of bone mineral density and microarchitecture in patients with rheumatoid arthritis (RA). We also aimed to identify potential factors associated with these alterations.

Methods: In this case-control study, patients with RA were recruited from the PUMC Hospital site of the Chinese Registry of rhEumatoiD arthrITis (CREDIT). The primary outcomes were high-resolution peripheral quanitative computed tomography (HRpQCT)-related measures at the distal radius and tibia (Scanco XtremeCT II), and data from age- and gender-matched healthy controls were included for comparison. Additional diagnostic imaging examinations included thoracolumbar X-ray and DXA. Data regarding demographic and clinical characteristics, osteoporosis-related risk factors, and RA-related diagnosis and treatment history were collected. Finally, grip srength, serum bone turnover markers, TNF-α and IL-6 were also measured. Correlation between HRpQCT parameters and potentially related covariates were analyzed using univariate and multivariate linear regression analysis.

Results: A total of 81 patients (69 women, aged 57.9±8.7y, RA duration 5.7(1.4-11.2)y) and 81 matched healthy controls were included. Compared with controls, patients had significantly larger bone area and lower total and trabecular vBMD at both distal radius and tibia. HRpQCT measures at the distal tibia also showed lower cortical bone thickness in patients with RA. Further analyses were conducted among RA patients. aBMD at both the lumbar spine and total hip was positively correlated with vBMD, trabecular bone volume fraction, trabecular number and cortical thickness, and was negatively correlated with trabecular separation and inhomogeneity. Trabecular thickness and

Radius	Patients n = 81	Controls n = 81	*P*
Geometry			
Tt.Ar,mm^2	280.8±66.9	253.1±51.5	**0.004**
Ct.Ar,mm^2	57.5±13.8	56.2±11.1	0.506
Tb.Ar,mm^2	227.2±64.6	200.425±48.5	**0.003**
Ct.Pm,mm^2	71.0±9.8	66.3±7.5	**0.001**
Volumetric BMD, mgHA/ccm			
Tt.vBMD	258.5±83.2	284.3±70.2	**0.034**
Ct.vBMD	882.9±111.6	911.7±58.7	**0.042**
Tb.vBMD	94.5±42.7	106.6±42.4	0.071
Microarchitecture			
BV/TV	0.144±0.056	0.160±0.057	0.073
Tb.Th,mm	0.219±0.019	0.219±0.016	0.864
Tb.N,1/mm	1.087±0.326	1.148±0.295	0.215
Tb.Sp,mm	1.042±0.538	0.931±0.393	0.136
Tb.1/N.SD	0.360(0.284-0.508)	0.318(0.268-0.508)	0.155
Ct.Th,mm	0.978±0.256	1.006±0.188	0.431
Ct.Po,mm	0.006(0.003-0.010)	0.005(0.003-0.009)	0.279

Table 2. HRpQCT parameters of patients and controls at distal radius

Table 3. HRpQCT parameters of patients and controls at tibia

Tibia	Patients n = 74	Controls n = 74	*P*
Geometry			
Tt.Ar,mm^2	712.4±128.5	679.3±110.4	0.081
Ct.Ar,mm^2	101.9±28.1	107.4±21.8	0.164
Tb.Ar,mm^2	615.6±124.3	577.2±110.0	0.039
Ct.Pm,mm^2	103.9±9.5	101.3±8.5	0.071
Volumetric BMD, mgHA/ccm			
Tt.vBMD	218.1±63.5	237.0±51.8	0.040
Ct.vBMD	859.8±89.8	869.5±77.4	0.465
Tb.vBMD	109.3±36.8	117.1±36.5	0.179
Microarchitecture			
BV/TV	0.179±0.047	0.189±0.047	0.196
Tb.Th,mm	0.241±0.019	0.240±0.019	0.627
Tb.N,1/mm	1.116±0.234	1.134±0.207	0.608
Tb.Sp,mm	0.939±0.239	0.902±0.194	0.281
Tb.1/N.SD	0.360(0.284-0.508)	0.318(0.268-0.508)	0.398
Ct.Th,mm	1.165±0.307	1.255±0.264	0.048
Ct.Po,mm	0.025(0.014-0.040)	0.030(0.015-0.039)	0.320

cortical porosity were not correlated with aBMD at any sites. vBMD was positively correlated with body mass index, grip strength and ever being treated with HCQ, and was negatively associated with age, RA duration and DAS28-ESR. Age and RA duration were significant factors in multivariate analysis. In contrast, parameters reflecting impairment of microarchitecture (trabecular inhomogeneity and separation) were negatively correlated with BMI and grip strength, and was positively related to age, disease duration and activity. Duration and activity remained significant in multivariate regression. Current treatment with glucocorticoids was related to decreased vBMD, trabecular number and increased trabecular separation and inhomogeneity. No correlations were observed with regards to dose or duration of GCs. Patients with fragility fractures had significantly lower vBMD in both trabecular and cortical bone, thinner cortical bone as well as impaired trabecular bone microstructure (fewer in number, larger separation and increased inhomogeneity). Bone turnover markers, TNF-α and IL-6 were not related to any HRpQCT parameters in this study.

Conclusion: Patients with RA have alterations in bone density and microarchitecture compared to healthy population, which may impair bone strength and lead to increased risk of fractures. Both traditional risk factors for osteoporosis and RA-associated factors need to be considered in the assessment of bone quality in RA.

Disclosure: S. Jin, None; **E. Hsieh**, None; **W. Xia**, None; **M. Li**, None; **Q. Wang**, None; **X. Zeng**, None.

Abstract Number: 2208

Mediators of Bone Metabolism (DKK1, OPG, Sclerostin and RANKL) in a Cohort of Patients with Elderly-onset Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with elderly-onset arthritis have greater comorbidity than young patients, with a higher incidence of osteoporosis (OP), probably mediated by increased bone resorption. However, there are few data on bone metabolism mediators in this population.

Methods: Longitudinal observational study that included patients with elderly-onset arthritis (> 65 years) without diagnosis of OP or on antiosteoporotic treatment. Phospho-calcium metabolism, quantification of bone remodeling mediators (DKK1, sclerostin, OPG and RANKL; ELISA, R&D systems) and bone densitometry were determined in all patients at diagnosis and at 12 months. The results were compared with a control group of the same age and sex (n=14). The statistical study was performed using SPSS.

Results: We included 73 patients (37F: 36M), with a mean age of 75±7 years. Most were diagnosed with rheumatoid arthritis (RA) (n=43), followed by polymyalgia rheumatica (n=16) and others (n=14). Fifteen patients were rheumatoid factor (RF) positive and 23 were ACA positive. Five patients had erosions at the diagnosis. 88.64% of patients with RA had an initial DAS28-ESR >5.1. Only 3 patients had previous fragility fractures (2 vertebral and 1 femur fractures). At diagnosis, patients with elderly-onset arthritis had higher levels of DKK1 and CTX than the control group, with no statistically significant differences in sclerostin, OPG, and RANKL values (table 1). In addition, DKK1 values were negatively correlated with sclerostin (r=-0.286, p=0.016) and OPG (r=-0.276, p=0.020). 31.9% had densitometric OP at baseline. We found no significant differences in bone remodeling mediators between patients with/without basal OP. At 12 months, DAS28-ESR was < 2.6 in 38.1%. The mean corticosteroid dose was 5.5 mg/day with a cumulative dose of 1630±426 mg. 45.8% received antiosteoporotic treatment (28 patients' bisphosphonates and 5 denosumab). The prevalence of OP at 12 months was 31.3% and 4 patients had new fractures (4 vertebral and 1 femur fractures). We observed a marked decrease in the values of DKK1 (-18.89%, p< 0.001) and sclerostin (-46.76%, p< 0.001) and an increase in OPG (11.97%, p=0.018). We didn´t found relationship between bone metabolism mediators and cumulative corticosteroid dose. There were not differences in terms of diagnosis (RA or PRM), ACA positivity, activity scores or treatment with bisphosphonates.

Conclusion: Patients with elderly-onset arthritis have higher Dkk1 values than the control group, and this correlate negatively with sclerostin and OPG. The marked decrease in Dkk-1 and sclerostin at 12 months, and the increase in OPG, suggests a role for these mediators in the bone metabolism of this population. It is important to note the high prevalence of OP in this group of patients.

Table 1: Clinical and analytical variables and values of bone metabolism mediators at baseline, at 12 months and in the control group.

Variables	Control N=14	Basal patients N=73	12 months patients* N=72
ESR (mm/h)	14 ± 10	55 ± 27 †	27 ± 18 †‡
CRP (mg/L)	3.6 ± 6.6	38,1 ± 50,6 †	4,9 ± 5,5 †‡
HAQ	-	1,6 ± 0,75	0,51 ± 0,57 ‡
DAS28-ESR (in RA){n=43}	-	6,32 ± 1,04	3,10 ± 1,30 ‡
CTX (ng/mL)	0,33 ± 0,18	0,49 ± 0,19 †	0,26 ± 0,13 ‡
OPG(pg/ml)	3127 ± 948	3319 ± 1134	3647 ± 1466 ‡
DKK-1(pg/ml)	1558 ± 555	2740 ± 1611 †	1516 ± 985 ‡
Sclerostin (pg/ml)	1299 ± 961	1189 ± 626	515 ± 333 †‡
RANKL (pg/ml)	122 ± 184	101 ± 102	-
RANKL indetectable n (%)	9 (64.3)	16 (22.5)	72 (100)

- We excluded patients treated with denosumab. † p<0.005 with respect to the control group. ‡ p<0.05 with respect to baseline.

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Abstract Number: 2209

Study of Vertebral Fracture Prevalence and Scanographic Bone Attenuation Coefficient of the First Lumbar Vertebra (SBAC-L1) in Patients with Rheumatoid Arthritis and Ankylosing Spondylitis vs. Controls

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SESSION INFORMATION
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Background/Purpose: Osteoporosis is a common disease whose prognosis can be seriously impacted by the development of fractures that lead to functional limitations and may even have life-threatening sequelae. This disease is often under-screened, especially in at-risk populations that require multidisciplinary care such as patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS). Moreover, a recent study showed that the scanographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1) with a threshold at 145 Hounsfield Units (HU) identified 96.6% of patients in the general population with a vertebral fracture (VF), whereas DEXA (with a T-score ≤ -2,5) identified only 39% of these patients.

The objective of the study was to identify the prevalence of vertebral fractures (VF) and to measure the scanographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1) based on CT-scan examinations of patients with rheumatoid arthritis (RA), patients with ankylosing spondylitis (AS) and in a control group.

Methods: This monocentric and retrospective study included patients who were evaluated between 2009 and 2017 with a diagnosis of RA based on the ACR/EULAR criteria, those with a diagnosis of AS based on the New-York criteria, and a RA-matched control group. All of the patients received a CT-scan. The osteoporosis risk factors, data from dual energy X-ray absorptiometry (DEXA) and clinical characteristics were collected. VFs were determined via CT-scans according to the Genant classification, and the SBAC-L1 was measured in Hounsfield units (HU). SBAC-L1 ≤ 145 HU (fracture threshold) defined patients at risk of VF.

Results: A total of 244 patients were included (105 RA, 83 AS, 56 controls). The AS group was younger and primarily consisted of males. Of the 4,365 vertebrae studied, 66 osteoporotic VF were found in 36 patients: 18 (17.1%) patients with RA, 13 (15.7%) patients with AS and 5 (8.9%) controls. The SBAC-L1 was 142.2 (±48.4) HU for the RA group and 142.8 (±48.2) for the AS group, both of which were significantly lower than that of the control group (161.8 (±42.7) HU). Of the 36 patients with VF and rheumatism, 28% had a T-score ≤ -2.5 SD, and 71.4% had a SBAC-L1 ≤ 145 HU. A T-score ≤ -2.5 SD and a SBAC-L1 ≤ 145 HU were associated with the presence of a VF (OR = 2.35 [CI95%: 1.12-4.92] and 2.06 [CI95%: 1.04-4.10]), respectively.

Conclusion: The SBAC-L1 was significantly lower in the RA and AS groups than in the control group. Furthermore, SBAC-L1 ≤ 145 HU was associated with a higher risk of VF, with an odds ratio similar to that of a DEXA.

Disclosure: M. Fauny, None; **E. Albuisson**, None; **E. Bauer**, None; **J. Perrier-Cornet**, None; **I. Chary-Valckenaere**, None; **D. Loeuille**, None.

Abstract Number: 2210

Relationship Between Structural Spine Involvement and the Scanographic Bone Attenuation Coefficient of L1 in a Population of 73 Patients with Ankylosing Spondylitis

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SESSION INFORMATION

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Background/Purpose: Thoracic and/or thoraco-abdomino-pelvic (TAP) Computed Tomography (CT) may be performed during the follow up of patients with ankylosing spondylitis (AS) and are able to assess vertebral fracture and recently to assess bone fragility thought the scanographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1).

The objective is to evaluate the correlation between the risk of bone fragility measured by the SBAC-L1 and spine structural severity assessed by the S (Modified stoke ankylosing spondylitis spinal score) in patients with AS.

Methods: This monocentric retrospective study included patients with spondyloarthritis followed from 2009 to 2017 at the University hospital of Nancy. Patients should fulfill New-York or ASAS 2009 criteria with radiographic sacroiliitis and a thoracic or TAP CT scan and radiographies (spine, pelvis) performed with a delay which did not exceed 2 years. Osteoporotic risk factors, Dual Energy X-ray Absorptiometry (DXA) measurements and clinical characteristics were collected. The mSASSS was performed by two readers with adjudications in case of discordance. The definition of structural spine involvement is retained for a mSASSS ≥ 2. Vertebral fractures were studied on sagittal spine radiographies according to Genant classification. The SBAC-L1 was measured in Hounsfield Units (HU) on axial L1 section in trabecular bone on CT. Intra- and inter-reader reliabilities for mSASSS and vertebral fractures were calculated. A SBAC L1 ≤ 145 HU (fracture threshold) defines patients at risk of VF.

Results: A total of 73 AS patients were included (age median: 60 (53-68.5) years, 8 women (11%)), disease duration median: 24 years (12-34)). Sixty patients (82.2%) have a mSASSS ≥ 2, with a mean score of 20.7 (±21.2). Presence of partial ankylosis is observed in 37 patients (50.7%). Fifty-three patients (72.6%) presented at least one clinical risk factor of osteoporosis. Assessment of osteoporosis was explored by DXA of the spine in only 16 patients (21.9%) and 3 (18.8%) of them presented a T-score ≤ -2.5 SD. T-score of AS patients with mSASSS + tended to be higher in comparison to AS patients with mSASSS – (p=0.051). Thirteen VFs were detected in 9 patients (12.3%) of the total population, 8 from them have a mSASSS ≥ 2 and 5 have de SBAC-L1 ≤ 145 HU. The mean SBAC-L1 was 141.1 HU (±45) in the whole population, 138.1 HU for mSASSS + and 154.8 for mSASSS – respectively. Forty-two patients (57.5%) presented a SBAC-L1 ≤ 145 HU: 60% in mSASSS + and 46.2% in mSASSS-. Patients with bone bridge have a lower SBAC-L1 (123.96 ± 41.1 HU) than patients mSASSS + without vertebral ankylosis (160.4 ± 41.9 HU) (p=0.02). The number of AS patients under the fracture threshold was higher in mSASSS+ in comparison to mSASSS - (73% vs 41.9%, p=0.006). The reproducibilities are very good (over 0.8) for mSASSS, poor to moderate for VF (0.3 to 0.6) and good to excellent for radiographic sacroiliitis.

Conclusion: There is no relation between the risk of bone fragility measured by the SBAC-L1 and spine structural severity assessed by the mSASSS in patients with AS, however patients with bone bridge have significantly lower SBAC-L1 and more of them are under the fracture threshold compared to patients without bone.

Disclosure: M. Fauny, None; **F. VERHOEVEN**, None; **E. Allado**, None; **E. Albuisson**, None; **C. Morizot**, None; **A. Pinzano-Watrin**, None; **I. Chary-Valckenaere**, None; **D. Loeuille**, None.

Abstract Number: 2211

What Are the Consequences of Spinal Ankylosis on the Bone Trabecular Fragility Assessed on CT- scan in Patients with Ankylosing Spondylitis?

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SESSION INFORMATION
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Table 1: Lumbar spine structural impairment

	L1		L2		L3		L4		L5	
	N	SBAC	N	SBAC	N	SBAC	N	SBAC	N	SBAC
No structural lesion	42	153.4	44	147.3	37	142.2	40	150	46	150.6
Syndesmophyte(s)	7	139.7	8	133.6	15	157.8	13	129.3	10	**151.9 ***
Partial Ankylosis	12	126	11	133.9	10	**108.4 ***	10	**96.2 ***	8	107
Total Ankylosis	12	**111.6 ***	10	**51.3 ***	11	**51.2 ***	10	**47.7 ***	9	**56 ***

***p<0.05 comparison with the control vertebrae status (vertebra without structural lesion),** L1, L2, L3, L4 and L5: lumbar vertebra 1, 2, 3, 4 and 5; N : number ; SBAC : Scanographic bone attenuation coefficient in Hounsfield units

Background/Purpose: Computed Tomography (CT) is sometimes performed during the follow up of patients with ankylosing spondylitis (AS) to screen comorbidities or complications. Thoracic or thoraco-abdomino-pelvic (TAP) CT have demonstrated their ability to depict vertebral fracture and recently to assess trabecular bone fragility though the scanographic bone attenuation coefficient (SBAC) on lumbar vertebrae (L1 to L5). To your knowledge, no study has assessed the impact of partial or complete vertebra ankylosis on the trabecular bone.

The principal objective was to characterize the SBAC on normal lumbar spine or spine with partial or total ankylosis.

Methods: This monocentric retrospective study included patients with AS followed from 2009 to 2017 at Nancy university hospital, fulfilling New-York criteria for AS and who underwent a thoracic or TAP CT and X-rays (spine, pelvis) within 2 years. Clinical characteristics were collected. Modified stoke ankylosing spondylitis spinal score (mSASSS) was scored by two readers, adjudication for one syndesmophyte discordance. Presence of one syndesmophyte defined mSASSS+ (mSASSS ≥ 2). Moreover, each lumbar vertebra was studied according to its level of ankylosis, 0: no lesion, 1: syndesmophyte(s), 2: partial ankylosis (superior or inferior) and 3: total ankylosis (both inferior and superior). The SBAC was measured in Hounsfield Units (HU) on L1 to L5 vertebrae, and a fracture threshold was defined at ≤145 HU.

Results: On 1503 spondyloarthritits, 73 AS patients were included (mean age: 60.3 (±10.7) years, 8 women (11%)). Sixty patients (82.2%) had a mSASSS ≥ 2, with a mean score of 20.7 (±21.2). Presence of ankylosis of at least one disco-vertebral unit in cervical or lumbar segments of the spine on mSASSS was observed in 37 patients (50.7%) and 6 (8.2%) have total lumbar spine ankylosis. Concerning the lumbar spine, the details of number of vertebrae without structural lesion, with syndesmophyte(s) or with partial and complete ankylosis are presented in table 1. The SBAC for each lumbar vertebra were not significantly different between patients with mSASSS < 2 versus mSASSS ≥ 2 (p = 0.24 to 0.99). However, the SBAC was lower for patients with mSASSS≥ 2 and bone bridge than for patients with mSASSS≥ 2 without bone bridge (p = 0.02 to 0.0001). The risk of SBAC ≤ 145 HU was higher in presence of total ankylosis on at least one lumbar vertebra (HR: 4.95(CI95% :1.104-17.36, p = 0.04 to 0.001)). Partial lumbar ankylosis of L3 and L4 affected also the SBAC with higher risk to have a SBAC ≤145 HU (HR :11.8 (CI95% :1.822-25.67) and 15 (CI95%: 2.54-30.85)) respectively.

Conclusion: Only AS patients with ankylosed vertebra on mSASSS presented lower values of SBAC. We showed that complete ankylosis of any lumbar vertebra and partial ankylosis of L3 and L4 were associated with lower values of SBAC, suggesting deterioration of the trabecular bone structure ankylosed.

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Abstract Number: 2212

Patients with Axial Spondyloarthritis Have Abnormal Microarchitecture Despite Normal Areal Bone Mineral Density and Trabecular Bone Score by DXA

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SESSION INFORMATION
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Background/Purpose: Axial Spondyloarthritis (axSpA) is characterized by abnormal bone formation that produces syndesmophytes, while paradoxically, inflammation causes increased bone resorption and skeletal fragility. Detection of osteoporosis using DXA can be challenging as syndesmophytes falsely elevate spine areal bone mineral density (aBMD). In contrast, high-resolution peripheral QCT (HRpQCT) measures volumetric BMD (vBMD) and microarchitecture and is not subject to this artifact. This study investigated skeletal health in a cohort with axSpA using aBMD, trabecular bone score (TBS), a method for estimation of spine trabecular bone quality, and HRpQCT. We hypothesized that TBS and HRpQCT would reveal skeletal abnormalities in axSpA, while aBMD by DXA would appear normal.

Methods: Patients fulfilling the imaging arm of the ASAS criteria who were enrolled as part of an ongoing longitudinal study had DXA measurements of aBMD of spine, hip and1/3 radius, and TBS. Trabecular (Tb) and cortical (Ct) vBMD and microarchitecture were measured by HRpQCT (Xtreme CT2, voxel size ~61 μm) at the distal radius and tibia. DXA in axSpA were compared with normative populations of age and sex matched individuals (Z-Scores). HRpQCT values were compared to a healthy reference population of young sex-matched adults. T-tests compared skeletal parameters in subjects and normative populations. Spearman correlations related skeletal parameters to disease features.

Results: 18 subjects were enrolled; 56% male, age 42+13 yrs. On average, subjects had symptoms for 14 yrs and had received a diagnosis of axSpA 6 yrs prior to study enrollment. BASDAI and other criteria reflected high disease activity (Table 1). The majority of subjects had normal aBMD by DXA. TBS was normal in the majority (67%). By HRpQCT at the radius, axSpA had lower Tb vBMD (-0.9 SD) and Tb thickness (-1.7 SD) than the reference population. At the tibia, axSpA had lower total (-0.9 SD), Ct (-1.5 SD) and Tb vBMD (-1.2 SD) and Tb thickness (-1.4 SD; $p< 0.01$ for all). Longer duration of symptoms was related to worse vBMD and microarchitecture, tibia: total vBMD ($r=-0.83$; $p< 0.0001$), Tb density ($r=-0.76$; $p< 0.0005$), Tb number ($r=-0.51$; $p< 0.04$) and Tb separation ($r=0.61$; $p< 0.01$) and radius: Tb density ($r=-0.64$; o< 0.1), Tb number (-0.50; $p< 0.04$) and Tb separation ($r= 0.57$; $p< 0.02$). Current disease activity did not relate to HRpQCT abnormalities.

Conclusion: Subjects with active axSpA had low vBMD and microarchitectural abnormalities by HRpQCT despite normal DXA and TBS. Abnormalities were most pronounced at the tibia and related to duration of symptoms. Larger studies are needed to confirm our findings, which suggest that long-term impairment in mobility may contribute to skeletal abnormalities in patients with axSpA.

Table 1. Disease Features, DXA and HRpQCT Measurements in Study Subjects

	Cohort (N=18)
Age (years) mean ± SD	42 ± 13
Sex, n (%)	
Male	10 (56%)
Ethnicity, n (%)	
Hispanic	4 (22%)
Race, n (%)	
Black	3 (17%)
American Indian/ Alaskan	1 (6%)
Asian	2 (11%)
White	10 (56%)
Other	2 (11%)
Symptom Duration (years), mean ± SD	13 ± 11
Disease Duration (years) mean ± SD	6 ± 9
HLA-B27 + n (%)	7 (39%)
Sacroiliitis n (%)	18 (100%)
BASDAI	4.98 ± 2.36
BASMI mean ± SD	3.29 ± 1.33
BASFI mean ± SD	3.66 ± 2.06
MDHAQ mean ± SD	2.19 ± 1.46
mSASSS mean ± SD	44.35 ± 18.64
DXA (Z-Score)	
Lumbar Spine (LS) mean ± SD	-0.80 ± 1.54
Total Hip (TH) mean ± SD	-0.28 ± 0.92
Femoral Neck (FN) mean ± SD	-0.24 ± 1.09
1/3 Radius (1/3R)	-0.22 ± 0.94
Trabecular Bone Score (TBS)	1.42 ± 0.13
HRpQCT (N=17)	
Tibial Total density (mgHA/cm3)	277 ± 49.9
Tibial Cortical Bone Density (mgHA/cm3)	851 ± 68.1
Tibial Trabecular density (mgHA/cm3)	148 ± 34.3
Tibial Trabecular number (1/mm)	1.87 ± 0.32
Tibial Trabecular Thickness (mm)	0.07 ± 0.01
Tibial Trabecular Separation (mm)	0.49 ± 0.09
Radial Total density (mgHA/cm3)	325 ± 65.1
Radial Cortical Bone Density (mgHA/cm3)	859 ± 73.5
Radial Trabecular density (mgHA/cm3)	153 ± 24.1
Radial Trabecular number (1/mm)	2.01 ± 0.23
Radial Trabecular Thickness (mm)	0.06 ± 0.01
Radial Trabecular Separation (mm)	0.44 ± 0.05

Disclosure: D. Ashany, None; **S. Goodman**, BMC Rheumatology, 5, 6, Calgene, 5, Celgene, 5, Current Rheumatology reports, 5, Current Rheumatology Reports, 6, Horizon, 2, 5, horizon, 2, Novartis, 2, 5, NYU College of Medicine, 3, NYU Langone College of Medicine, 3, Pfizer, 2, 5, Regenosine, 4, 9, Roche, 2, UCB, 5; **H. Tornberg**, None; **D. McMahon**, None; **D. Mintz**, Current Rheumatology Reviews Journal, 6, American Registry of Radiologic Technologists Registry Exam, 5; **L. Russell**, Arthritis Foundation, 6; **E. Stein**, Novartis, 2.

Abstract Number: 2213

Evaluation of Factors Associated with Bone Structure in an SLE Cohort Measured by Clinical 3T MRI and DEXA

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
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Background/Purpose: Osteoporosis and bone fractures are a frequent cause of morbidity in systemic lupus erythematosus (SLE), and are felt to be related both to disease activity and glucocorticoid (GC) exposure. Dual energy X-ray absorptiometry (DEXA) is the standard tool to assess bone density, but it does not measure bone quality or strength and is not a robust predictor of fractures in SLE. Clinical 3T MRI scans have been shown to assess information about bone not captured by DEXA. This study aims to evaluate factors associated with bone structure measured by DEXA and MRI in an SLE cohort.

Methods: DEXAs were performed on 31 women with SLE and 3T MRI of the non-dominant hip were performed on 29 of these cases. Results were associated with multiple demographic, clinical and laboratory measures. MRI parameters measured included trabecular plate width (PW), trabecular plate to rod ratio (PRR), plate volume fraction (PVF), rod volume fraction (RVF), trabecular bone thickness (Tb.Th), trabecular spacing (Tb.Sp) and trabecular network area (TNA). DEXA BMD was measured, and osteoporosis (OP) was defined as hip, spine or femoral neck Z score < -2.0 in premenopausal women, and T score < -2.5 in others, and low bone density (LBD) as Z score < -2.0 in premenopausal women and T score < -1.0 in others.

Results: By DEXA, 8/31 (25.8%) had OP and 12 (38.7%) had LBD. History of lymphopenia (75.0% vs. 31.8%, p=0.049) and lower concurrent HCQ dose (340 vs. 400 mg, p=0.006) associated with DEXA OP, while older age (48.3 vs. 36.3 y, p=0.024) associated with LBD. Higher ESR was inversely correlated with favorable bone structure (PW r(22) = -.49, p=0.025, PRR rs = -.51, p=0.018, PVF rs = -.51, p=0.018, RVF rs = .51, p=0.018, Tb.Th rs = -.58, p=0.005, Tb.Sp rs = .44, p=0.046, TNA rs = -.50, p=0.022). Higher CRP was likewise inversely correlated with favorable bone structure (PW r(20) = -.61, p=0.004, PRR rs = -.57, p=0.009, PVF rs = -.57, p=0.009, RVF rs =.57, p=0.009, Tb.Th rs = -.56, p=.011, Tb.Sp rs =.67, p=0.001, TNA rs = -.64, p=0.002). A history of lupus nephritis was associated with unfavorable bone structure (PW 705.3 vs. 833.3 μm, p=0.048, PRR 6.6 vs. 8.1, p=0.024, PVF 0.83 vs. 0.89, p=0.024, RVF 0.17 vs. 0.11, p=0.024, Tb.Th 178.1 vs. 193.4 mm, p=0.012, Tb.Sp 358.6 vs. 296.5 mm, p=0.056, TNA 0.41 vs. 0.54 (1/mm), p=0.009). ESR, CRP and history of lupus nephritis were not significantly associated with DEXA hip BMD, OP or LBD. MRI parameters for favorable bone structure were inversely correlated with DEXA hip BMD (PW r(28) = -.47, p=0.011, Tb.Th rs = -.53, p=0.003) and BMI (PW r(28) = -.54, p=0.003, TbTh rs = -.72, p< 0.001, TNA rs = -.44, p=0.017).

Conclusion: Higher ESR and CRP and a history of lupus nephritis associated with MRI parameters of unfavorable bone structure, but did not associate with DEXA abnormalities in SLE patients. MRI may be a more sensitive tool than DEXA to measure inflammatory effects on bone and potentially cumulative dose of steroid exposure. There were inverse correlations of MRI parameters with traditional osteoporosis risk factors and BMD measures on DEXA, and it

is possible that each tool evaluates different aspects of bone health. Further evaluation of MRI screening for fracture risk in SLE and GC exposed individuals is warranted to better quantify risk and guide treatment.

Disclosure: A. Saxena, Exagen, 2; **P. Izmirly**, GlaxoSmithKline, 5; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **S. Honig**, None; **X. Zhang**, None; **P. Saha**, None; **H. Belmont**, None; **G. Chang**, None.

Abstract Number: 2214

Assessment of Bone Quality by Trabecular Bone Score (TBS) in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
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Background/Purpose: Systemic lupus erythematosus (SLE) patients show an increased risk of low bone mass as a result of multifactorial events: physical inactivity, persistent inflammation, low vitamin D levels (protection to avoid photosensitivity) and glucocorticoid treatment. Trabecular Bone Score (TBS) is an index extracted from the dual-energy X-ray absorptiometry (DXA) that provides an indirect measurement of bone axial microarchitecture and allows to get information about bone quality in several rheumatic diseases (1-4).

The aims of this study was to examine the prevalence and risk factors for low bone mineral density (BMD) (osteoporosis or osteopenia) in female patients affected by SLE in comparison with matched healthy subjects (HS).

Methods: 60 female patients (mean age 45±16 years) affected by SLE and 60 age- matched CNT (mean age 47±5 years) were enrolled. Bone Mineral Density (BMD, g/cm2) of the lumbar spine (L1-L4) was analyzed using a DXA scan (GE, Lunar Prodigy). Lumbar spine TBS was derived for each spine DXA examination using the TBS index (TBS iNsight Medimaps).

Results: The mean BMD was 0.49±0.41 SD g/cm^2 at the lumbar spine and 0.59±0.62 g/cm^2 at the hip in SLE patients. The prevalence of osteopenia and osteoporosis in SLE patients was 39.0% and 16.4% respectively. Most of SLE patients (70%) presented a bone loss that was significantly lower when compared with control group ($p< 0.001$). Likewise, lumbar spine TBS score was found significantly lower in SLE patients compared with HS (0.797±0.825 vs

1.398±0.207, p< 0.001, respectively). An history of high-dose oral glucocorticoids (> 10 mg/day) was found associated with the preservation of BMD at the lumbar spine but not in spinal trabecular bone as observed by TBS analysis.

Conclusion: SLE is associated with significant trabecular bone loss, which might not be caused by glucocorticoid therapy. This study underlines the role of TBS as new and safe diagnostic tool for the quantification of the bone quality in chronic and systemic inflammatory rheumatic diseases, such as SLE.

References: 1 Cutolo M, et al. Ann Rheum Dis. 2009;68:446-7; 2 Dey M, et al. Lupus. 2018;27:1547-51; 3 Ruaro B, et al. Rheumatology (Oxford). 2018;57:1548-54. 4 Ruaro B, et al. Clin Rheumatol. 2018;373057-62.

Disclosure: A. Casabella, None; **S. Paolino**, None; **A. Sulli**, None; **E. Alessandri**, None; **V. Smith**, None; **B. Ruaro**, None; **C. Pizzorni**, None; **M. Cutolo**, Boehringer, Actelion, Celgene, Bristol-Mayer Squibb, 2.

Abstract Number: 2215

Modeling-Based Bone Formation Persists in the Femoral Neck Despite Remodeling Inhibition in Subjects Treated with Denosumab

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
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Background/Purpose: Denosumab (DMAb) is a potent antiresorptive agent, but findings in non-human primates suggest that modeling-based bone formation (MBBF) may persist despite DMAb treatment (Ominsky *JBMR* 2015). This study assessed whether MBBF in the femoral neck (FN) is preserved in the context of inhibited remodeling-based bone formation (RBBF) in subjects receiving DMAb (NCT02576652).

Methods: This open-label study enrolled ambulatory postmenopausal women and men with osteoporosis (OP) who had received ≥2 doses of DMAb (60 mg subcutaneously Q6M) per standard of care and were planning to undergo elective total hip replacement (THR) due to osteoarthritis of the hip. Transverse sections of the FN were obtained after THR surgery and analyzed histomorphometrically. The primary endpoint was the subject incidence of MBBF, based on fluorochrome labeling and the presence of smooth cement lines, in cancellous, endocortical, and periosteal surfaces of the FN. Secondary and exploratory analyses used histomorphometric parameters to characterize rates of MBBF and RBBF in the 3 envelopes in enrolled subjects and historical controls. Controls were from the placebo group of a prior study and were not treated with DMAb. All analyses were descriptive.

Results: Four of the 6 subjects enrolled were included in the analyses (all women, mean age 73.5 y, mean duration of DMAb use 1.8 y); one subject withdrew consent due to an allergic reaction to the tetracycline label, and one subject did not undergo THR. The 17 historical controls had a mean age of 68.3 y; 71% were women, and 47% had received OP treatment that did not include DMAb. All subjects in both groups exhibited MBBF in periosteal bone surfaces; in cancellous and endocortical surfaces, all DMAb-treated subjects and 88% and 82% of historical controls, respectively, showed evidence of MBBF (Table). Compared with historical controls, DMAb-treated subjects showed 792%

Table. Descriptive histomorphometric analysis of modeling- and remodeling-based bone formation in study subjects and historical controls.

	Historical Controls (N = 17)	Study Subjects (N = 4)
Modeling-based fluorochrome labeling at the femoral neck, n (%)		
Cancellous	15 (88.2)	4 (100.0)
Endocortical	14 (82.4)	4 (100.0)
Periosteal	17 (100.0)	4 (100.0)
Specialized histomorphometric parameters		
Cancellous, mean±SD		
Modeling-based formation unit (/mm)	0.013 ± 0.014	0.146 ± 0.210
Overfilled remodeling-based formation unit (/mm)	0.012 ± 0.013	0.004 ± 0.006
Remodeling-based formation unit including overfilled units (/mm)	0.135 ± 0.108	0.029 ± 0.017
Endocortical, mean±SD		
Modeling-based formation unit (/mm)	0.065 ± 0.063	0.222 ± 0.231
Overfilled remodeling-based formation unit (/mm)	0.018 ± 0.025	0.011 ± 0.014
Remodeling-based formation unit including overfilled units (/mm)	0.178 ± 0.091	0.032 ± 0.032
Periosteal, mean±SD		
Modeling-based formation unit (/mm)	0.250 ± 0.084	0.199 ± 0.141
Overfilled remodeling-based formation unit (/mm)	0.000 ± 0.000	0.000 ± 0.000
Remodeling-based formation unit including overfilled units (/mm)	0.004 ± 0.007	0.003 ± 0.007

SD: Standard deviation

and 242% higher values of MBBF in the cancellous and endocortical surfaces, respectively, while RBBF values were 79% and 82% lower. In the periosteal surface, MBBF and RBBF rates were similar between subjects and controls.

Conclusion: These results demonstrate the occurrence of MBBF in the adult human FN and suggest that DMAb preserves MBBF while inhibiting RBBF, consistent with previous findings. This effect may contribute to the continued increases in bone mineral density demonstrated with up to 10 y of DMAb treatment (Bone *Lancet Diabetes Endocrinol* 2017).

Disclosure: D. Dempster, Amgen Inc., 2, 5, 8; **P. Butler**, Amgen Inc., 1, 3, 9; **M. Bostrom**, NIH, 2, American Austrian Foundation, 2, Ines Mandi Research Foundation, 2, Smith & Nephew, 2, 5, 7; **J. Nieves**, Eli Lilly, 2; **H. Zhou**, None; **L. Chen**, Amgen Inc., 1, 3; **N. Pannacciulli**, Amgen Inc., 1, 3; **R. Wagman**, Amgen Inc., 1, 3; **F. Cosman**, RPharm, 5, Amgen Inc., 2, 5, 8, Eli Lilly, 2, 5, 8, Radius, 5, 8.

Abstract Number: 2216

Bone Mineral Density of the Spine, Hip, and Distal Radius in Patients with Postmenopausal Osteoporosis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
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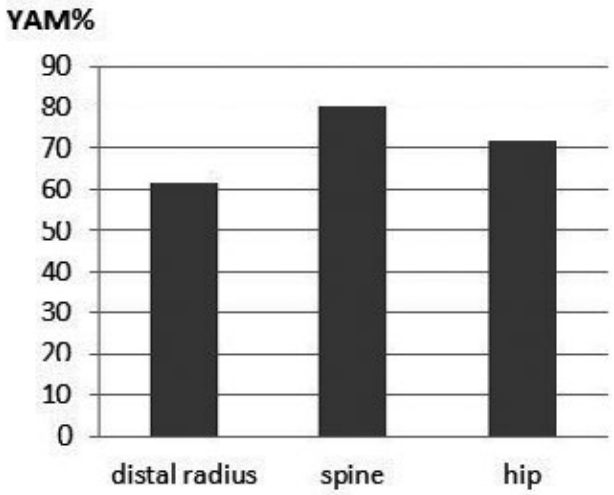

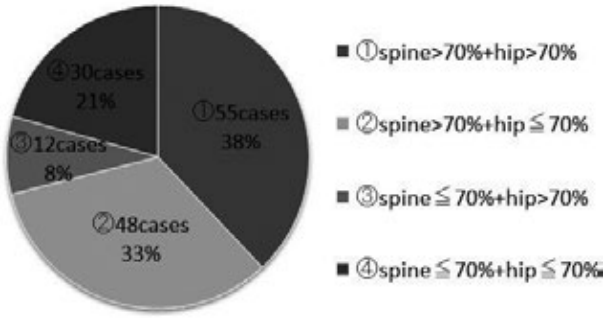

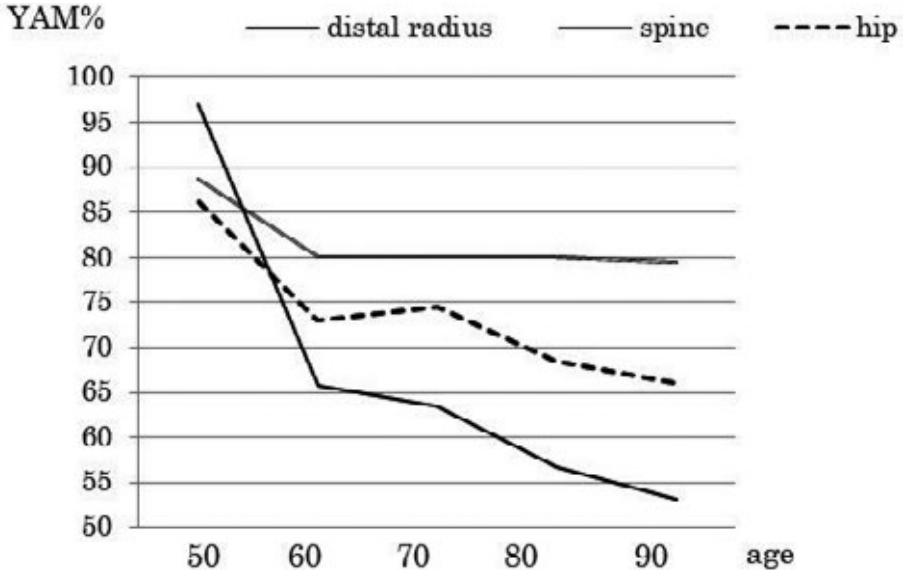

Background/Purpose: Bone mineral density (BMD) is used for the diagnosis of osteoporosis, predicting future fracture risk, and monitoring osteoporosis treatment. Osteoporosis is defined as BMD of at least 2.5 standard deviations below the young adult mean (YAM) (T-score ≦2.5) according to World Health Organization (WHO) criteria or a BMD of 70% or lower of YAM (YAM% ≦70) according to the Japanese Society for Bone and Mineral Research (JSBMR)

criteria in Japan. As is often the case, T-score or YAM% values of different skeletal sites are discordant. This means that making a diagnosis of osteoporosis may depend on measured sites. BMD of the spine and hip is usually measured for the diagnosis of osteoporosis; however, that of the distal radius is not always measured. The purpose of the present study was to clarify correlations of BMD among the three skeletal sites and evaluate whether measuring BMD of the distal radius is essential. In addition, BMD of the three skeletal sites based on patients' age was investigated.

Methods: Two hundred and one patients between the ages of 52 and 93 with postmenopausal osteoporosis were enrolled.

BMD of the spine, hip, and distal radius was measured using dual energy X-ray absorptiometry (DXA) (Prodigy, GE Healthcare UK Ltd.). The cut-off values for the diagnosis of osteoporosis according to JSBMR criteria were used. Analyses of correlations between BMD of two skeletal sites (i.e., hip and distal radius, spine and distal radius, and hip and spine) were assessed using the t-test.

Results: YAM% of the distal radius was 61.7%, being lower than that of the spine, 80.4%, and hip, 71.9% ($p > 0.001$) (Table 1). Correlation coefficients of BMD between the hip and distal radius, spine and distal radius, and hip and spine were 0.475965, 0.406596, and 0.415697, respectively. Among the 145 patients diagnosed as osteoporotic at the distal radius, 55 were not osteoporotic at either the spine or hip, 48 (33%) were osteoporotic at the hip but not spine, 12 (8%) were osteoporotic at the spine but not hip, and 30 (21%) were osteoporotic at both the spine and hip (Table 2). Among the 56 patients without osteoporosis at the distal radius, only one patient (1.8%) was osteoporotic at the spine and 12 (21%) were osteoporotic at the hip. YAM% of the three skeletal sites according to the patients' age is shown in Table 3.

Conclusion: BMD of the distal radius is significantly lower than those of the spine and hip. Sontag reported that the radius was frequently recognized as the site of initial osteoporotic fractures among women with osteoporosis. This report might support the present study and suggest the possible susceptibility of the radius to osteoporosis as the initial site compared with the spine and hip, especially in early osteoporotic generations. Among 145 patients diagnosed with osteoporosis at the distal radius, 55 (38%) were not osteoporotic at either the spine or hip. This means that a diagnosis of osteoporosis might not be made for some patients if only BMD of the spine and hip and not the distal radius is measured. Therefore, measuring BMD of the distal radius in addition to that of both the spine and hip is highly recommended to avoid underestimating the actual value of BMD for the diagnosis of osteoporosis, especially in early osteoporotic generations.

Disclosure: K. NAKASEKO, None.

Abstract Number: 2217

DEXA Does Not Accurately Reflect FRAX Score in Patients with Autoimmune Disease on Corticosteroids

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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Background/Purpose: Osteoporosis (OP) is a problem in the aging population. Patients with autoimmune disease are at increased risk for OP given their history of steroid use.

Methods: As part of a QI project on bone health, we reviewed female patients age ≥50 and male patients age ≥60. If the last DEXA scan was done prior to 2 years ago, a recommendation was made to order a new study. We collected data on risk factors for secondary OP and steroid doses within the past year, including most recent dose and average dose over one year. FRAX scores were calculated for all patients regardless of DEXA score, accounting for all of the standard risks for OP. We adjusted FRAX scores for steroid use based on the NEJM article recommendation to multiply the FRAX score by 15% for major OP fractures and by 20% for risk of hip fractures in patients who currently take >7.5mg of prednisone daily (1).

Results: 55 patients with autoimmune disease were studied, of whom 48 received prednisone at some time. 20/55 were on prednisone during the past year, average dose 14.6mg/d (range 2.8-30mg/d), 18/55 are currently on prednisone. Of the 20 patients on prednisone over the past year, mean age was 64.3y (range 50-83), 19 female (95%), 18 Black (90%), (full demographics in Table 1). Prednisone use was classified as low (< 2.5mg/d) n=0, medium (2.5-7.5mg/d) n=11, high (>7.5mg/d) n=9. DEXA results were not available in 7 patients. 5 patients had normal bone density, 6 were classified as osteopenia, and 2 were osteoporotic. Calculated FRAX scores were different from those anticipated by DEXA score (Table 2). FRAX ≥ 20% risk for major OP fractures was found in 5/20pts; of those, 2 had no DEXA available, 1 had normal BMD on DEXA, 1 was osteopenic and one had osteoporosis. Calculated FRAX of ≥3% risk for hip fractures was found in 7/20 pts, of whom 2 had no DEXA avail, 2 had normal BMD on DEXA, 2 were osteopenic and 1 was osteoporotic. Further adjustment for high dose prednisone use resulted in 2 additional patients at risk, 1 with FRAX ≥ 20% risk for major OP fractures and 1 with FRAX ≥ 3% risk for hip fracture.

Demographics	N= 20 pts
Mean age	64.3y (range 50-83)
Gender	19F (95%)
Race	18 Black (90%)
Ethnicity	1 Hispanic (5%)
Weight	177.8 (range 101-258)
BMI	30.6 (range 17.1-45.2)
RA	9 pts (45%)
SLE	9 pts (45%)
Other autoimmune disease	6 (30%) [vasculitis 2 (EGPA, GCA), MCTD (2), UCTD (1)]
Current smokers	3/20 (15%)
h/o nontraumatic fracture	4/19 (21%)
Premature menopause (<45y)	4/15 (26.7%)
PPI	3/19 (15.7%)
calcium suppl	7/19 (36.8%)
vit D suppl	7/19 (36.8%)
bisphosphonates	9 prior use/ 3 currently
Other antiresorptive agents	Prolia-2 pts, miacalcin-1 pt
Prednisone daily dose	Medium (2.5-7.5mg/d) 11pts (55%) High (>7.5mg/d) 9pts (45%)
DEXA results	No DEXA- 7 pts Normal BMD- 5 pts Osteopenia- 6 pts Osteoporosis- 2 pts

Table 1. Demographics

	DEXA unavailable	DEXA normal	Osteopenia	Osteoporosis
FRAX major OP ≥20	2	1	1	1
FRAX hip ≥3	2	2	2	1

Table 2. DEXA scores versus Calculated FRAX scores

Conclusion: There is a discordance between DEXA measured osteopenia/osteoporosis and FRAX risk. This is of particular concern in our demographically unique, largely Afro-Caribbean population with a high proportion of obesity, calcium-poor diets and comorbidities that can impact bone health. We recommend that FRAX scores be calculated on all patients even if no DEXA is available. We encourage smoking cessation and calcium/vitamin D supplementation for all. Just as weight gives only a partial glimpse of a patient's burden of adiposity and BMI is needed to fully understand the issue, so too DEXA parameters only provide a partial glimpse of bone health.

(1) Buckley L, Humphrey MB. Glucocorticoid-induced osteoporosis. N Engl J Med 2018;379:2547-56

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Abstract Number: 2218

1,25D3 Promotes Mineralization of Osteoblasts by Activating C/EBPβ-DKK1 Axis

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SESSION INFORMATION
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Background/Purpose: 1,25-Dihydroxyvitamin D3 (1,25D3) has a positive therapeutic effect on osteoporosis by activating osteoblasts. Bone formation is a dynamic and sequential process that comprises osteoblasts proliferation, increased ALP activity, collagen synthesis, and mineralization. In addition, the tight regulation between Wnt/β-catenin signaling and Dickkopf-1 (Dkk-1), Wnt antagonist, is critical for these series of steps to induce osteoblast differentiation and bone formation. Therefore, it is possible that 1,25D3 promote osteoblastic differentiation through Wnt activation; however, the potential role of Dkk1 in 1,25D3-induced osteoblastic differentiation is not fully elucidated.

Methods: Bone tissues were obtained from knee replacement surgery and primary preosteoblasts were isolated using outgrowth method. Preosteoblasts cultures underwent microarray analysis on day 14 either with stimuli for differentiation or without. The microarray data was verified using qPCR and ELISA. Also, the effect of 1,25D3 during preosteoblasts differentiation to osteoblasts was assessed by intracellular alkaline phosphatase (ALP) activity analysis, alizarin red (ARS) staining for calcium deposit, and hydroxyapatite staining. To investigate the indirect regulation of genes by 1,25D3 in unmineralized osteoblasts, preosteoblasts were incubated with ascorbic acid (AA) for 3 days and then exposed to 1,25D3 for 1 day. Subsequently, what happened at the molecular level by 1,25D3 was investigated using qPCR, Dkk1 promoter assay, immunostaining, immunoblotting, and Chromatin Immunoprecipitation (ChIP) assay.

Results: Gene expression microarrays revealed upregulation of DKK1 expression in differentiated osteoblasts. Increase in DKK1 expression and secretion in differentiated osteoblasts were confirmed by qPCR and ELISA, respec-

tively. 1,25D3 promoted osteoblast maturation of preosteoblasts and obviously induced the expression of C/EBPβ and DKK1 at day 7 during differentiation. Interestingly, mRNA and protein levels of C/EBPβ and DKK1 were markedly increased by 1,25D3 treatment following AA stimuli. To demonstrate the relationship between the two genes, we performed knockdown of C/EBPβ with siRNA, which reduced the up-regulation of DKK1 induced by 1,25D3. In contrast, overexpression of C/EBPβ boosted enhancement of DKK1 by 1,25D3. Furthermore, we also found that C/EBPβ bind to human DKK1 promoter in response to 1,25D3. Intriguingly, blocking DKK1 attenuated calcified nodule of mineralized osteoblasts, but not ALP activity and collagen synthesis.

Conclusion: Taken together, these observations suggest that 1,25D3 promotes the mineralization of osteoblasts through activation of DKK1 followed by an increase in C/EBPβ.

Disclosure: S. Jo, None; **S. Yoon**, None; **S. Nam**, None; **J. Yang**, None; **I. Sung**, None; **T. Kim**, None.

Abstract Number: 2219

Randomized Control Study in Glucocorticoid-Induced Osteoporosis Treated with Bisphosphonate or Denosumab (GOBID)

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: It has not been established which therapy, bisphosphonates or denosumab, is more effective for glucocorticoid-induced osteoporosis (GIO). The purpose of this study was to compare the therapeutic efficacy to GIO between bisphosphonate and denosumab on the basis of randomized control study (GIBID Study, UMIN000014341).

Methods: The inclusion criteria were as follows, glucocorticoids on, bone mineral density (BMD) < 80% in %YAM at the lumbar spine/femoral neck or fragile fracture at the spine, ≥1 year without bisphoshonates, ≥18 years old. The BMD was measured at the lumbar spine and femoral neck with GE Lunar iDXA. Incident fractures were evaluated with the semiquantative method (Genant) at the thoracic and lumbar spine. Medications, risedronate (17.5mg/W or 75mg/M, group B) or denosmab (60mg/6M, group P), were randomly assigned to the patients. The primary outcome was the changes in lumbar BMD (l-BMD) at 2 years.

Results: The included individuals were 28 rheumatoid arthritis (RA), 22 systemic lupus erythematosus (SLE), 17 polymyalgia rheumatic (PMR), other connective tissue diseases (CTDs) in total 89. The demographics of the group B and the group P were as follow, the number: 48/41 (B/P); female: 42/31; Age (mean): 66.0/70.6; prednisolone: 6.1/7.3mg/day; l-BMD; 0.959/0.928g/cm2; prevalent deformity at spine: 52/49%. No significant differences was observed between the groups. The change at 2 years in lBMD in group P (0.063+/-0.069 (mean+/-SD)) was significantly higher than that in group B (0.017+/-0.043) ($p< 0.001$). The numbers (rates) of incident fracture at 2 year were 6 (15%) in group B and 0 (0%) in group P ($p< 0.01$). Any serious adverse events due to the study drugs were not seen in the both groups.

Conclusion: These results suggest that denosmab is effective and safe for treatment of glucocorticoid-induced osteoporosis.

Disclosure: I. Tanaka, None; **M. Ushikubo**, None; **M. Konishi**, None; **Y. Hayashi**, None; **S. Hama**, None; **K. Izumi**, None; **Y. Okano**, None; **S. Tamaki**, None; **H. Ohshima**, None.

Abstract Number: 2220

Abaloparatide Followed by Alendronate on Bone Mineral Density and Fracture Incidence in Postmenopausal Women with Osteoporosis and Osteoarthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster

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Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis (OP) and osteoarthritis (OA) are often comorbid conditions in the elderly, with prevalence of OP in patients with OA reported as high as 30%. Previous studies have found significantly higher baseline BMD in OA patients than their non-OA counterparts, despite an increased risk for fracture, potentially contributing to delayed diagnosis and treatment in this population. In the ACTIVE phase 3 study of postmenopausal OP women, 18 months (M) of abaloparatide (ABL) treatment significantly increased bone mineral density (BMD) and reduced the risk of new vertebral, nonvertebral, clinical, and major OP fractures vs placebo (PBO) (NCT01343004). Women receiving ABL or PBO in ACTIVE were offered enrollment in the ACTIVExtend extension study in which both groups received 24M open-label alendronate (ALN) 70 mg weekly for a total of 43M (18M ABL or PBO, 1M for reconsent, and 24M ALN) (NCT01657162). The objective of this post hoc analysis was to evaluate efficacy and safety of ABL followed by ALN (ABL/ALN) vs PBO/ALN in the subgroup of patients with OA.

Methods: ACTIVExtend enrolled postmenopausal women with OP between the ages of 50 and 85; 558 were from the original ABL group and 581 from the PBO group of the ACTIVE study. Patients with the following terms in their medical history were included: “ongoing osteoarthritis” (including spine, knee, hand, foot, shoulder, and other sites), “spinal osteoarthritis”, “nodal/ hand osteoarthritis”, or “intervertebral disc degeneration”. New vertebral fracture incidence was evaluated using the modified intent-to-treat (mITT) population, other efficacy endpoints were evaluated using the ITT population. The percent mean changes in BMD from baseline to 43 months were calculated for the total hip (TH), femoral neck (FN), and lumbar spine (LS).

Results: A total of 395 ACTIVExtend patients with ongoing OA were identified (ABL/ALN, 190; PBO/ALN, 205). Most common sites of OA were at the knee (39.2%), and spine (38.5%). At baseline, 78 (19.7%) had a prevalent VF, 94 (23.8%) reported ≥1 prior NVF within the last 5 years, and 175 (44.3%) had no prior fractures. At 43M, 1.1% (2/186) ABL/ALN and 7.0% (14/201) PBO/ALN patients experienced ≥ 1 new vertebral fracture (P=0.004). Kaplan-Meier estimated cumulative incidence for other fracture endpoints was similar across treatment groups. Mean percent change in BMD were all significantly greater with ABL/ALN vs PBO/ALN at all timepoints assessed ($P < 0.001$). At 43M, BMD mean percent change from baseline was 6.0% ABL/ALN vs 2.3% PBO/ALN at the total hip, 4.9% ABL/ALN vs 1.4%

PBO/ALN femoral neck, and 14.3% ABL/ALN vs 6.7% PBO/ALN lumbar spine. Most common TEAEs overall were upper respiratory tract infection (9.0% vs 8.3%), arthralgia (7.9% vs 8.8%), worsening osteoarthritis (8.5% vs 6.4%), and back pain (7.9% vs 4.4%), for ABL/ALN vs PBO/ALN arms, respectively.

Conclusion: Improvements in vertebral fracture risk as well as significant gains in BMD were maintained through 43M with ABL/ALN vs PBO/ALN. This post hoc analysis suggests that ABL/ALN was effective in a subgroup of patients with OP and OA, with no new safety signals identified.

Disclosure: N. Lane, Amgen Inc., 5, 8, GSK, 5, Radius Health, Inc., 8; **R. Weiss**, Radius Health, Inc., 1, 3; **B. Mitlak**, Radius Health, Inc., 1, 3; **Y. Wang**, Radius Health, Inc., 1, 3; **G. Valenzuela**, AbbVie, 5, Bristol-Myers Squibb, 2, Celgene, 5, GSK, 5, Janssen, 5, Lilly, 2, 5, Merck, 2, 5, MLKCDT, 2, Novartis, 2, 5, Pfizer, 2, 5, Sanofi Regeneron, 2, 5, UCB, 5; **C. Deal**, Amgen, 5, 8, Eli LIlly, 5, 8.

Abstract Number: 2221

Bone Metabolism Impairment in Heart Transplant: Results from a Prospective Cohort Study

Luis Seguro,[1] Rosa Pereira,[2] Luciana Seguro,[3] Valeria Caparbo,[3] Monica Avila,[1] Sandrigo Mangini,[1] Iascara Campos,[1] Fabio Gaiotto,[1] Fabiana Marcondes-Braga,[1] and Fernando Bacal[1], [1]Instituto do Coracao (InCor), HCFMUSP, Sao Paulo, [2]Faculdade de Medicina da Universidade de Sao Paulo, São Paulo, Sao Paulo, Brazil, [3]Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Data on prevention of fractures after heart transplant (HTx) are controversial in the literature. Understanding the effects of HTx on bone may guide appropriate treatment in this high-risk population.

Methods: Seventy adult patients submitted to HTx were followed for 12 months. Clinical and laboratory parameters, bone mineral density (BMD), body composition, microarchitecture and vertebral fractures were assessed at baseline (intensive care unit discharge), 6 and 12 months. Patients received recommendations regarding calcium intake (1,000mg/day) and vitamin D supplementation (50,000U/week for 3 months, followed by 7,000U/week) after HTx.

Results: At baseline, 27.1% of patients had osteoporosis (T-score ≤-2.5), associated with the length of hospitalization before HTx (p=0.001). BMD decreased in the first 6 months, with partial recovery later. Bone microarchitecture deteriorated, mainly trabecular bone in the first 6 months and cortical bone in the subsequent 6 months. At baseline, 92.9% of patients had vitamin D level < 30ng/mL and 20.0% < 10ng/mL. Patients also had calcium at the lower limit of normal, high alkaline phosphatase, associated with low levels of vitamin D (15.5±9.1 ng/ml). These abnormalities were suggestive of impaired bone mineralization and normalized at 6 months with correction of calcium and vitamin D deficiency. The majority of vertebral fractures were identified at baseline (23.5% of patients). After multivariate analyses, only lower fat mass persisted as a risk factor for vertebral fractures (OR 1.23, 95% CI 1.04-1.47, p=0.012).

Conclusion: Present study showed a high frequency of densitometric osteoporosis, vitamin D deficiency, bone markers abnormalities sugestives of bone mineral defect and vertebral fractures shortly after HTx. Calcium and vitamin D supplementation should be the first step in correcting bone mineralization impairment, before specific osteoporosis treatment. Special attention should be given to patients with long length of hospitalization and low fat mass.

Disclosure: L. Seguro, None; **R. Pereira**, None; **L. Seguro**, None; **V. Caparbo**, None; **M. Avila**, None; **S. Mangini**, None; **I. Campos**, None; **F. Gaiotto**, None; **F. Marcondes-Braga**, None; **F. Bacal**, None.

Abstract Number: 2222

Bone Health: An Independent Predictor of Coronary Artery Disease

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: An association between low bone mineral density (BMD) and cardiovascular events has been shown. The calcification process observed in atherosclerosis and bone mineralization have a common patho-

Table 1. Baseline characteristics by FRAX HF score

	n	FRAX HF <3% n=92	FRAX HF >3% n=14	p-value
Age at DEXA, median (IQR)	106	65 (63, 67)	73 (70, 77)	**0.0003**
Women, n(%)	93	74 (80)	11 (12)	**0.097**
African American, n(%)	36	31 (86)	5 (14)	1
Vitamin D levels <20ng/mL, n(%)	44	38 (86)	6(14)	1
Smoker, n(%)	23	20 (6)	3 (3)	1
CKD III/IV, n(%)	37	33 (89)	7(19)	0.6
GFR <45mg/mmol, n(%)	26	25 (96)	1 (4)	0.52
CAD, n(%)	67	55 (82)	12 (18)	**0.000**
HTN, n(%)	82	71 (87)	11 (13)	0.13
DM, n(%)	58	51 (88)	7 (12)	0.21
LDL > 130mg/dL, n(%)	14	13 (93)	1 (7)	0.73

* DEXA: Dual-energy X-ray Absorptiometry. CKD: Chronic Kidney disease. GFR: Glomerular Filtration Rate. HTN: Hypertension. DM: Diabetes Mellitus. LDL: Low Density Lipoprotein.

Table 2. CAD risk by FRAX and T scores		
	CAD risk (OR)	P<
FRAX (adjusted for age) ≥3%	5.76	0.032
Osteoporosis (T score ≤-2.5)	1.36	0.45

Table 2. CAD risk by FRAX and T scores (2) CAD risk by FRAX and T scores

genesis pathway. Bone health parameters are not yet incorporated in the cardiovascular risk assessment scale. The objective of our study was to look for an association between standard bone health scores and coronary artery disease (CAD) in our patient population.

Methods: A retrospective chart review of 1,134 patients who underwent cardiac catheterization between 2011 and 2017 at Jacobi Medical Center was performed. Patients between the age of 40 and 90 years who had a bone densitometry done within three years of the cardiac catheterization were included in the study. 106 patients met the inclusion criteria. Their baseline demographics, cardiac risks, and bone mineral density data were analyzed. Patients were categorized to have CAD if any of the epicardial coronary artery had ≥50% stenosis. Bone density levels were categorized by standard WHO classification. FRAX (Fracture risk assessment tool) scores were calculated using a validated online tool. Standard 10-year risk of hip fracture cut-off of 3% was used. Multivariate Logistic regression modeling was used to quantify the association between FRAX score and occlusive CAD. Variables were included in a multivariate model if they modified the association between the two by greater than 10%.

Results: Median age of the patients was 66.3 +/- 8.5 years and 91% were female. Thirteen percent of patients had a FRAX score ≥3%. Both groups were identical with respect to their demographic, metabolic, and cardiovascular risk profiles (Table 1). Standard secondary causes of osteoporosis were not different between the groups. Patients with FRAX score of ≥3% were 5.76 times more likely to have occlusive CAD in at least one of the coronaries than those with score of < 3% (OR 5.76; 95%CI 1.16-28.5, p< 0.032) after adjusting for age which is incorporated in the calculation of FRAX score. There was no association between bone densitometric T score and occlusive CAD (Table 2).

Conclusion: Bone health has shown to be an independent risk factor for angiographic CAD when adjusted for age in our patient population. Although the T score was not found to be significant, FRAX score adjusted for age of ≥3% was found to be strongly associated with significant angiographic coronary artery disease based on our data. Patients with FRAX score of ≥3% should be screened for CAD. Our observation warrants further research in this field.

Disclosure: L. Bizzocchi, None; **M. Salgado**, None; **B. Chokshi**, None; **N. Kaur**, None; **O. Mena**, None; **M. Packman**, None.

Abstract Number: 2223

Attenuated Association Between Proton Pump Inhibitor Use and Fracture Risk After Consideration of Chronic Comorbidities

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session (Tuesday)
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Background/Purpose: Proton pump inhibitors (PPI), which are often recommended in patients with rheumatic diseases due to frequent use of high risk medications such as NSAIDs or high dose steroids, have been associated with an increased risk for fractures. However, it is unknown whether associated chronic comorbidities contribute to the fracture risk observed from PPI use.

Methods: Using a unique medical records linkage system available in our community to undertake population-based studies, we identified 3433 community residents age ≥ 50 yrs (2269 [66%] women; 1164 men; mean age 70 yrs) who had any fracture during a 3-year period (2009-2011) and an equal number of age- and sex- matched controls from the same population who had no fractures in this time period. All fractures were validated and their antecedent cause determined by trained nurse abstractors through review of complete (inpatient and outpatient) community medical records. Using our unique resources enabling access to all medical records in the community, we identified PPI use as well as the Elixhauser Comorbidity Index (ECI) and its components in the 5 yrs prior to fracture/index date for both cases and controls. To determine whether the use of PPIs was higher among fracture cases than non-fracture controls after accounting for comorbidity differences, propensity score methodology was used to estimate inverse probability weights (IPW). The IPW were used with a weighted logistic regression model, further adjusted for age and ECI, to examine the association between PPI use (of at least 2 yrs) and fracture risk.

Results: PPI use was more common among fracture cases than non-fracture controls (35% vs 27%). Comorbidities were not only more common among fracture cases than controls (45% vs 33%, with at least 5 Elixhauser comorbidities), they were also more frequent among those who had used a PPI compared with those who had not (63% vs 34% in fracture cases, 51% vs 26% in controls). While the association between PPI use and increased fracture risk was attenuated in adjusted analyses, when compared with unadjusted analyses, it remained persistent but modestly elevated (unadjusted vs adjusted odds ratios (OR), respectively: OR: 1.50 [95% CI: 1.33-1.69] vs 1.18 [95% CI: 1.02-1.37] for any fracture; OR: 1.72 [95% CI: 1.44-2.05] vs 1.25 [95% CI: 1.01-1.55] for any major osteoporotic site [hip, spine, wrist, shoulder] fracture). We found similar results when considering only moderate trauma fractures (i.e. fractures due to a fall from a standing height or less) or any PPI use (data not shown). Using similar methods, we found no association between H2-blocker use and fracture risk (data not shown).

Conclusion: While we found an association between PPI use and increased fractures, this risk was more modest after accounting for associated chronic comorbidities, which is relevant when weighing the risks vs benefits of continuing PPI use.

Disclosure: L. Wang, None; **E. Atkinson**, None; **H. Liu**, None; **S. Amin**, None.

Abstract Number: 2224

Parkinson's Disease and Risk of Fractures : A Meta Analysis of Cohort Studies

marion louvois,[1] stéphanie Ferrero,[1] Thomas Barnetche,[2] Christian Roux,[1] and Véronique Breuil[1], [1]university of nice, nice, France, [2]university of bordeaux, bordeaux, France

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
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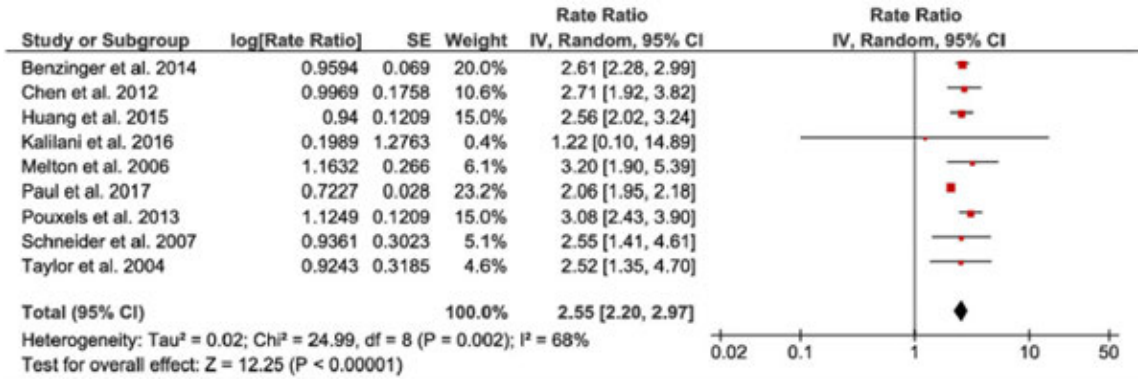
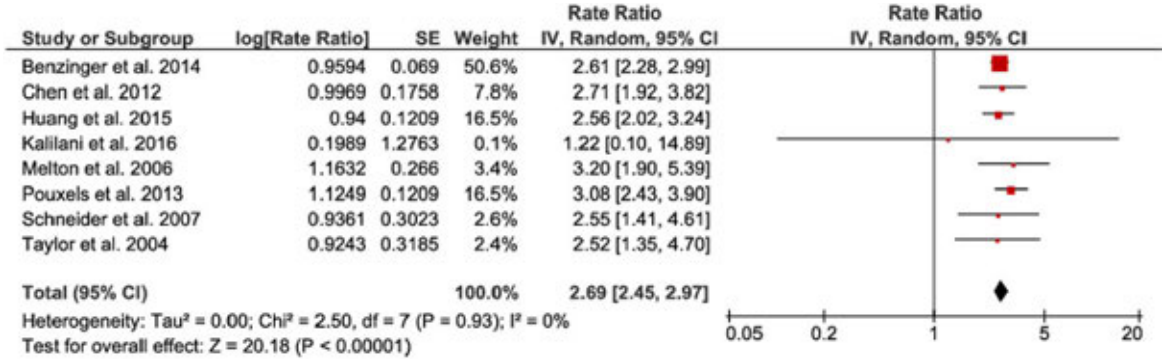
Background/Purpose: Parkinson's disease is a common neurodegenerative disorder in older adults. Parkinson's patients have an increase risk of falls. More over, previous studies have shown a reduced bone mineral density related to multifactorial factors. A meta-analysis performed in 2014 suggested an increased risk of fracture in Parkinson's disease. The aim of this study is to update this previous meta-analysis to evaluate the association between Parkinson's disease and fracture's risk.



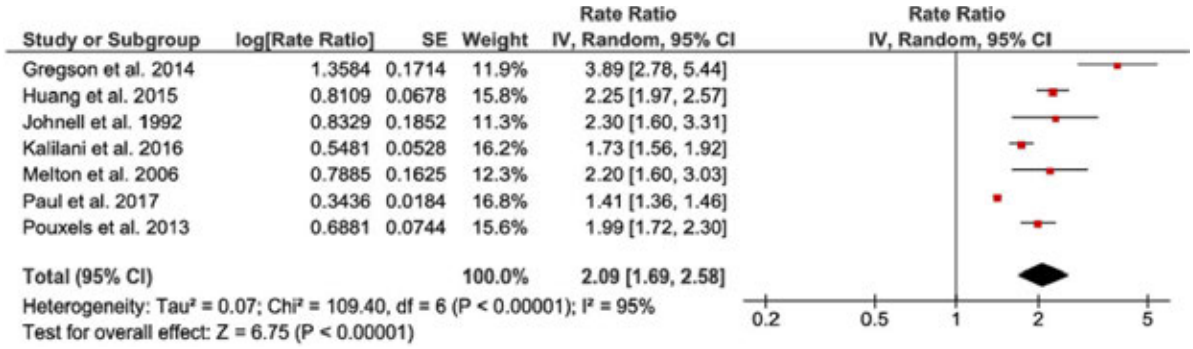
total fracture's risk

A Forest Plut of the association between Parkinson's disease and risk of fractures. The diamond represents the pooled RR and, the squares and the horizontal lines respectively represent the RR and 95% CI of each individual study.



sensitivity analysis hip's fractures

A Forest Plut of a sensitivity analysis of the the association between Parkinson's disease and hip fractures. The diamond represents the pooled RR and, the squares and the horizontal lines respectively represent the RR and 95% CI of each individual study.



total fracture's risk

A Forest Plut of the association between Parkinson's disease and risk of fractures. The diamond represents the pooled RR and, the squares and the horizontal lines respectively represent the RR and 95% CI of each individual study.

Methods: Eligible studies were search on PubMed, and Embase databases up to February, 2, 2019. Cohort studies, controlled or not, were selected. For each study, the authors extracted the risk of fracture for each anatomic site, or estimated it based on sample size and number of patients with fracture. Single risk ratios were then pooled to estimate a global risk ratio of fracture within a meta-analysis procedure using the inverse variance approach. Heterogeneity analysis was also performed with Cochran's Q-test and I^2value. RevMan software was used and p-value less than 5% was defined as significant.

Results: We included 13 retrospectives and propsectives cohort studies from the litterature's review. They involved 975646 participants. Parkinson's disease patients showed an increase fracture risk (RR globales fractures 2,09 $(1,69\text{-}2,58)_{95\%}$; I^2=95%). Especially hip fracture seems to be more frequent in Parkinson's disease population (RR hip fracture 3,13 $(2,36\text{-}3,15)_{95\%}$; I^2=68%). A sensitivity analysis was performed, excluding the study of Paul et al. which enrolled exclusively patients having fallen. This sub-analysis confirmed the increase of hip fracture risk with a negligible level of heterogeneity (RR 2.49 (2.45-2.97) $IC_{95\%}$; I^2=0%).

Conclusion: Our results confirmed the previous meta-analysis of an increased risk of fracture in Parkinson's disease, especially hip fracture recognized as a severe fracture associated with an increased morbidity and mortality. Currently, assessment of fracture's risk is not included in guidelines for Parkinson's disease patients care. Taking into account the increase risk of fracture, fracture's risk assessment should be recommended in Parkinson's disease adults.

Disclosure: m. louvois, None; **s. Ferrero**, None; **T. Barnetche**, None; **c. roux**, None; **V. Breuil**, None.

Abstract Number: 2225

Systematic Osteoporosis Screening in Chronic Obtructive Pulmonary Disease (Study of Correlation Between Pulmonary Functions Tests and Bone Parameters): Emphysematous Status Is Linked to Low Bone Density and Osteoporosis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
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Background/Purpose: Chronic obstructive pulmonary disease (COPD) is usually considered as a risk factor for osteoporosis. However, COPD is an heterogeneous disease with different phenotypes, based on clinical and/or pulmonary function test classification. Our objectives are (1) to analyze the efficiency of a systematic osteoporosis screening in a COPD population (2) to analyze the clinical risk factor for OP in this population and (3) to correlate pulmonary function tests with bone parameters.

Methods: 90 consecutive COPD patients followed in pneumology ambulatory care were systematically included to have DEXA, VFA, blood analysis and pulmonary functiontests.

Results: 62% of the COPD patients were male, with a median BMI of 24.1kg/m2(14.5-44). 69% had a frequent use of glucocorticoids (maintenance inhaled or systemic and > 2 courses of systemic). 44% were active smokers. 26% of the COPD patients were identified as osteoporotic and VFA demonstrated an unknown vertebral fracture in 9%. Anti-osteoporotic drug was prescribed (or modified) in 32% after bone status investigation.

A low BMI was strongly associated with a low bone mineral density (BMD) and osteoporotic condition in lumbar spine, femoral neck and total hip (p< 0.0001). Active smokershad significant lower BMD and were more osteoporotic than ex-smokers at the three sites studied (p< 0.01). Female gender was associated to lower BMD for total hip and femoral neck only. Biologic bone turnover and D-vitamin levels were not associated with BMD, while glucocorticoid use (as defined by the FRAX) was only associated to total hip osteoporosis.

COPD severity based on FEV1 and FEV1/FVC ratio were not associated with bone weakness, with no link between FEV1 stratification and BMD. However, COPD phenotype modulated the bone strength: patients with complete emphysematous status (DLCO< 70%, DLCO/VA< 80% and CPT >115%) had significant lower BMD at lumbar spine, femoral neck and total hip (p< 0.05), with more osteoporosis at the hip (p< 0.01) and less normal condition (versus osteopenic and osteoporotic) at the lumbar spine and the femoral neck (p< 0.01). Of interest, there were more vertebral fracture on VFA and more history of hip fracture when DLCO was < 70%.

Conclusion: (1) Systematic screening for osteoporosis in COPD patients is efficient, with osteoporosis detection in 1/4, new vertebral fracture in 1/10 and a therapeutic intervention with anti-osteoporotic drug prescription in 1/3.

(2) Low BMI and active smoking were associated to osteoporosis in COPD patients. (3) COPD severity was not associated with bone loss, while the emphysematous status (association of 3 functional emphysematous characteristics: DLCO< 70%, DLCO/VA< 80% and CPT >115%) was correlated to bone weakness and osteoporosis. The “pink puffer” phenotype in COPD is at high risk for osteoporosis and should be particularly screened.

Disclosure: O. Malaise, None; **C. André**, None; **L. Seidel**, None; **F. Schleich**, None; **R. Louis**, None; **M. Malaise**, None.

Abstract Number: 2226

Factors Contributing to Fracture in Pernicious Anemia Patients Presenting with Symptomatic Subacute Vertebral Compression Fractures

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Pernicious anemia (PA) has been associated with both low spine BMD and increased fracture risk in retrospective cohort studies. The cause of these observations is obscure. The purpose of this study is to describe and compare the clinical details of a cohort of PA patients who presented with subacute vertebral compression fractures (SVCF) to one without PA.

Methods: A retrospective cohort study was conducted from a population of 165 patients presenting with SVCF to an outpatient fracture clinic. The clinical characteristics of 30 PA patients diagnosed at the time of presentation, based on low vitamin B12 levels and the presence of either intrinsic factor (IF) or anti-parietal cell antibodies (APCA), was compared to the remaining 135 without PA. A complete history and physical exam including review of past medical records and current and past radiographs was performed. CBC, sedimentation rate, chemistry profile, TSH, urinalysis, vitamin B12, PTH, 25-OH vitamin D, and serum protein electrophoresis was done in all patients.

Results: There were 23 female and 7 male PA patients, ranging in age from 66-96 (mean 79.8 years) with a BMI of 15-31 (mean 25.3). 15 patients were taking thyroid hormone and 10 were on protein pump inhibitors (PPI). 16 patients had previous fractures. Fractures occurred after falling in 22, lifting in 3, and were spontaneous in 5. The location of the fracture was between T-11 and L-2 in 65% of the cases and 8 patients presented with multiple fractures. 25 out of the 30 patients with PA had evidence of peripheral neuropathy. IF was present in 17 patients, APCA in 5, and 8 had both. 25-OH vitamin D was < 20 ng/ml in 8 patients and PTH was >65 pg/ml in 6. A monoclonal gammopathy of undetermined significance (MGUS) was found in 6 PA patients. There was an increased incidence of peripheral neuropathy (p=0.002), 25-OH vitamin D < 20 ng/dl (p=0.01), use of PPI (p=0.006), thyroid disease (p=0.01), and MGUS (p=0.05) in the patients with PA. Age, gender, diabetes, previous fractures, BMI, PTH, fracture location, occurrence of multiple fractures, spontaneous fractures and those occurring with falling or lifting did not differ between the two cohorts.

Conclusion: This cohort of SVCF patients with PA had a higher incidence of peripheral neuropathy, vitamin D deficiency, PPI use, thyroid disease, and MGUS than SVCF patients without PA. These observations may explain the higher incidence of fractures and low BMD found in previous studies of PA patients.

Disclosure: M. Lovy, None; **N. Ben-Shlomo**, None; **J. Hattenbach**, None.

Abstract Number: 2227

Can We Predict Hypophosphatasia-Mutation Result Based on Alkaline Phosphatase Serum Levels?

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SESSION INFORMATION
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Background/Purpose: Hypophosphatasia (HPP) is caused by mutations in *ALPL,* resulting in low alkaline phosphatase (ALP) levels. The determination of ALPL mutation may not be accessible in clinical practice. In this case, an alternative simple method to predict the presence or absence of the mutation would be very useful. This study aimed to characterize the main clinical and laboratory features associated with the presence (HPP + GT) or absence (HPP – GT) of mutations in the *ALPL* gene among subjects with persistently low ALP levels.

Table 1. Demographic characteristics of study participants in each genetic group.

	HPP+ GT (N = 38)	HPP– GT (N = 45)	Total (N = 83)	*p* value
Age, Mean (SD) years	50.1 (14.9)	44.5 (10.5)	47.1 (13.0)	0.049
Female sex, No. (%)	22 (57.9%)	38 (84.4%)	60 (72.3%)	0.007
Race, No. (%)				
Caucasian	37 (97.1%)	45 (100.0%)	82 (98.8%)	0.274
Hispanoamerican	1 (2.6%)	0	1 (1.2%)	
Black	1 (2.6%)	0	1 (1.2%)	
BMI, kg/m^2 (SD)	25.9 (4.4)	22.7 (3.1)	24.2 (4.0)	0.0004

Methods: During this cross-sectional study, the laboratory reports from 386,353 people attending a Tertiary University Hospital from 2009 to 2015 were screened. 109 adult subjects with persistently low ALP values (≥2 measurements below or equal to 35 IU/L and none above 45 IU/L) were enrolled and 85 gave their consent for genetic testing. During one visit, a systematized questionnaire was performed to retrieve demographic, clinical and laboratory data and a genetic test to detect HPP was performed. Comparisons between groups were performed using the Student's *t*-test for unpaired data, if normally distributed; or Mann-Whitney U test, if not normally distributed. Logistic regression models adjusted for confounders were employed to investigate the association between clinical and laboratory characteristics and the presence/absence or ALPL mutation.

Results: Forty-seven percent (40/85) of subjects showed mutations in ALPL: 75% (30/40) were heterozygous for a pathogenic variant, 17.5% (7/40) for a likely pathogenic variant, 5% (2/40) for a variant of unknown significance (VUS) and one patient diagnosed of infantile HPP harbored compound heterozygous mutations. Demographic characteristics are shown in table 1. The presence of mutation was significantly associated with the presence of musculoskeletal pain (OR: 5.9; 95% IC: 1.7-20.5) and orthopedic surgery (OR: 4.8; 95% IC: 0.7-33.3). Metatarsal stress fractures were also more frequent in the HPP + GT group (4 vs 0, p=0.007). In terms of laboratory paramethers, ALP levels were lower in the HPP + GT group compared with HPP –GT group (24.2 vs 29.1 IU/L, $p < 0.0001$; respectively). Interestingly, levels below 25 UI/L showed a specificity of 97.8% and a positive predictive value of 94.4% to detect a positive genetic test.

Conclusion: In our cohort, ALP levels below 25 IU/L were identified as a very good predictor for the presence of mutations in ALPL. Furthermore, the presence of musculoskeletal pain and previous orthopedic surgery were also associated to a positive genetic test.

Association between clinical manifestations and genetic status.

Clinical feature	OR	95% IC	*p* value
Musculoskeletal pain	5.9	1.7 - 20.9	0.005
Fractures			
Peripheral fractures	1.5	0.5 - 4.2	0.444
Family history of fractures	0.8	0.2 - 3.1	0.751
Orthopedic surgery	4.8	0.7 - 33.3	0.041
History of premature teeth loss	4.7	0.4-60.1	0.234
Dental abnormalities	3.6	0.9-13.4	0.053
Family history of dental problems	1.2	0.4-3.9	0.704
Muscle weakness	2.5	0.4-18.7	0.356
Calcific periarthritis	1.2	0.1-10.1	0.896

Biochemical variables of study participants in each genetic group.

Biochemical variables	HPP+ GT (N=38)	HPP– GT (N=45)	Total (N=83)	*p* value
ALP, IU/L (N=36,45, 81)	24.2 (6.7)	29.1 (3.2)	26.9 (5.6)	<0.0001
< 20 IU/L	6 / 38 (16%)	0 (0%)	6 / 83% (7%)	
< 25 IU/L	17 / 38 (44%)	1 / 44 (2%)	18 / 83 (22%)	
< 30 IU/L	31 / 38 (82%)	25 / 45 (56%)	56 / 83 (67%)	
< 35 IU/L	36/38 (94.7 %)	44/45 (97.7%)	83/83 (100%)	
Calcio, mg/dl (N=34, 44, 78)	9.4 (0.4)	9.3 (0.3)	9.4 (0.4)	0.182
Phosphate, mg/dl (N=20,24,44)	4.1 (0.8)	3.6 (0.6)	3.8 (0.7)	0.018
Creatinine, mg/dl (N=36, 39,75)	1.6 (3.9)	0.8 (0.2)	1.2 (2.7)	0.246
Urinary calcium excretion, mg/24h (N=4, 1, 5)	68.4 (44.1)	123.0	79.2 (45.4)	0.349
Urinary phosphate excretion, mg/24h (N=3, 0, 3)	238.5 (354.6)	--	238.5 (354.6)	-

Table 4. Assessment of sensitivity (S), specificity (E), positive and negative predictive value (PPV and NPV) and likelihood ratio (LR + and LR-) for different thresholds of ALP

ALP levels	S	E	PPV	NVP	LR +	LR -
< 20 IU/L	15.8	100	100	58.4	Infinity	0.84
<25 IU/L	**44.7**	**97.8**	**94.4**	**67.7**	**20.3**	**0.57**
<30 IU/L	81.6	44.4	55.4	74.1	1.47	0.41
< 35 IU/L	94.7	2.2	45	33.3	0.97	2.41

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Abstract Number: 2228

Rheumatoid Arthritis Disease Activity Is Associated with Low Femoral Neck Bone Mineral Density in a Diverse Cohort of Patients

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SESSION INFORMATION

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Table 1. Multivariable linear regression model evaluating the association of mean RA disease activity (DAS28ESR) on the outcome of femoral neck bone mineral density (gm/cm^2). (n=166, r^2=0.32).

Variable	β	95% CI	p-value
RA Disease Activity (DAS28ESR)			
Remission/Low	ref	--	--
Moderate	-0.054	-0.107 to -0.001	0.047
High	-0.052	-0.124 to 0.019	0.151

-95% CI = 95% confidence interval, RA = rheumatoid arthritis, DAS28ESR = Mean Disease Activity Score 28 Joints with Erythrocyte Sedimentation Rate.
-DAS28SER cut points: Remission/Low (<3.2), Moderate (3.2-5.1), High (>5.1).
-Analysis included the following covariates: age, sex, race/ethnicity, RA disease duration, high positive anti-CCP (defined as >60 units), weight, osteoporosis medication use (ever), mean prednisone dose, and use of biologic medications (proportion of visits where biologics were noted). Biologics include: TNF inhibitors, anti-IL6 agents, anti-CD20 agents as well as CTLA-4Ig.

Background/Purpose: Rheumatoid arthritis (RA) is an independent risk factor for osteoporosis (OP) and fracture. Although several OP risk factors are well-described in RA, many mechanisms by which the disease impacts bone mineral density (BMD) remain unknown. Measuring the direct contribution of RA disease activity on BMD is complicated by concomitant risk factors for BMD loss such as glucocorticoid treatment, inactivity and systemic inflammation. We evaluated the association of RA disease activity as measured by the Disease Activity Score 28 Joints with Erythrocyte Sedimentation Rate (DAS28ESR) and femoral neck BMD by dual energy x-ray absorptiometry (DXA), after controlling for known osteoporosis (OP) risk factors.

Methods: Data were from the University of California, San Francisco RA Cohort, an observational cohort established in 2006. In this cross-sectional analysis, all participants with femoral neck BMD and at least 1 DAS28ESR measurement were included. Mean DAS28ESR from study entry to date of DXA was calculated, and participants were placed into disease activity categories, based on validated cut-points (Remission/Low, Moderate and High). Mean values for other time-varying exposures from enrollment to DXA date were also calculated. Multivariable linear regression was performed to identify the independent association of DAS28ESR with BMD, controlling for age, race/ethnicity, RA duration, body weight, RA and OP medications, and high positive anticyclic citrullinated peptide (CCP) status (previously identified as an independent predictor of low BMD in RA).

Results: 166 participants with a mean age of 63±10.3 years; 87% female; 46% Latino and 35% Asian; and mean RA duration of 15±8 years were included. The majority were rheumatoid factor (RF) (n=145, 87%) and high anti-CCP positive (n= 109, 65%). The mean prednisone dose was 3.9±3.6 mg/day, 58% (n=97) were exposed to biologics and 57% (n=95) were exposed to OP medications over the course of the study. BMD categories based on femoral neck BMD were: 45% Normal BMD (n=76), 45% Low BMD (n=75), 10% OP (n=16). The distribution of DAS28ESR categories was: 20% low/remission (n=37), 60% moderate (n=100) and 18% high (n=30). In the multivariable model, moderate and high disease activity were both independently negatively associated with femoral neck BMD (β=-0.054 and -0.052 g/cm2 respectively), but only moderate disease activity achieved statistical significance ($p< 0.05$).

Conclusion: Controlling for known OP risk factors, higher RA disease activity is independently associated with lower BMD. These results suggest that treating RA patients to achieve the target of low disease activity or remission may improve BMD. Longitudinal studies are needed, however, to further explore these associations.

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Differences in Fracture Risk Assessment (FRAX) and Osteoporosis Treatment Cutoffs with and Without Bone Mineral Density Are Greater in Anti-Cyclic Citrullinated Peptide Positive Rheumatoid Arthritis

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Background/Purpose: FRAX (Fracture Risk Assessment Tool) is the most commonly used tool to estimate 10-year fracture risk. FRAX estimates are performed with and without bone mineral density (BMD) measures; the BMD-adjusted FRAX (BMD-FRAX) provides a more sensitive estimate. In the United States, if FRAX major osteoporotic fracture (MOF) risk is ≥20% or the hip fracture risk is ≥3% or the T-score is ≤-2.5, then osteoporosis (OP) treatment is recommended. Rheumatoid arthritis (RA) is a risk factor for fracture in FRAX; however, RA is a heterogenous disease so it is important to identify which disease characteristics influence fracture risk. Anti-cyclic citrullinated peptide (CCP) positivity is thought to be a risk factor for lower BMD in RA. Our aim was to evaluate the difference in FRAX and BMD-FRAX estimates and OP treatment categories based on anti-CCP status.

Methods: Data were from the University of California San Francisco RA Cohort. All participants who had complete FRAX variable data and a DXA with a femoral neck BMD measure were included. Because OP medications improve BMD, thereby altering the risk of fracture, only OP medication naïve patients were included in the analysis. Participants were stratified by high positive anti-CCP status (dichotomized at >60 units to minimize heterogeneity of this group). Differences between FRAX and BMD-FRAX risk estimates were calculated for MOF and hip fracture. FRAX and BMD-FRAX based OP treatment categories were also compared.

Table 1: Average 10-year fracture risk assessment (FRAX) for major osteoporotic fracture (MOF) or hip fracture by anti-cyclic citrullinated peptide (CCP) status. FRAX calculations made with and without femoral neck bone mineral density (BMD). Osteoporosis (OP) treatment discordance and concordance comparing FRAX cutoffs[c] with and without BMD in the entire cohort as well as by anti-CCP status.

		High Positive anti-CCP[a]		
	All (N=56)	Yes (N=37)	No (N=19)	p-value[d]
10-year Fracture Risk by FRAX (%)				
MOF	8.0±5.9	7.9±6.2	8.2±5.4	0.83
MOF with BMD	8.6±9.2	9.4±10.8	7.2±4.3	0.42
Difference (MOF)[b]	0.6±5.2	1.5±6.1	-1.0±2.3	0.09
Hip	1.8±2.2	1.6±2.2	2.1±2.2	0.43
HIP with BMD	2.1±5.9	2.6±7.2	1.2±1.6	0.41
Difference (Hip)[b]	0.3±4.7	0.9±5.6	-0.9±1.6	0.16
Treatment threshold based on FRAX[c]:				
No Treatment Indicated for either	39 (69%)	26 (70%)	13 (68%)	--
No Treatment Indicated only with BMD-FRAX	3 (5%)	1 (3%)	2 (10%)	--
Treatment indicated only with BMD-FRAX	7 (13%)	6 (16%)	1 (5%)	--
Treatment Indicated for either	7 (13%)	4 (11%)	3 (16%)	--

CCP: cyclic citrullinated peptide; FRAX: Fracture Risk Assessment; MOF: Major Osteoporotic Fracture, BMD: Bone mineral density.
[a]- Anti-CCP positivity set at >60 units (3 times the upper limit of normal) to minimize heterogeneity in this group.
[b]- FRAX risk (%) with BMD minus FRAX risk (%) without BMD.
[c]- Osteoporosis treatment indications based on World Health Organization (WHO)- based FRAX 10-year risk cutoffs of ≥3% for hip fracture and ≥20% for MOF or a T-Score of ≤-2.5.
[d]-p-values derived from t-tests comparing groups with and without high positive anti-CCP.

Results: 56 OP medication naïve RA patients were included in this analysis. Subjects were 61.5±8.5years of age, 79% (n=44) were female and the majority were Hispanic (48%, n=27) or Asian (23%, n=13). Average disease duration was 11.9±8.9 years and mean Disease Activity Score 28 Joints with Erythrocyte Sedimentation Rate (DAS28ESR) was 3.9±1.2. The average prednisone dose was 3.3±4.5 mg/day. 66% (n=37) were categorized as high positive anti-CCP. No significant differences in RA disease characteristics were noted based on anti-CCP status. Individuals with high positive anti-CCP had a greater estimated fracture risk (MOF: +1.5±6.1%, Hip: +0.9±5.6%; See table) when FRAX was adjusted with BMD. Conversely, the group with lower anti-CCP values had decreased estimated fracture risk when BMD was added to FRAX (MOF: -1.0±2.3%, Hip: -0.9±1.6%), although these differences did not reach statistical significance. Changes in treatment category based on BMD-FRAX was supported in 18% (n=10) individuals; escalation of therapy was supported in 16% (n=6) of high positive anti-CCP individuals compared to 5% (n=1) in those with lower anti-CCP levels.

Conclusion: Adding BMD adjustment to FRAX scores increases the risk estimate in persons with high-positive anti-CCP levels but decreases the risk estimate in others. BMD-adjusted FRAX supports changes in OP treatment recommendations in nearly 1/5 of RA patients. Our data suggest that high positive anti-CCP individuals may represent a subset of the RA population who have an elevated risk for fracture that is not accurately captured in FRAX scores without BMD adjustment. Further studies in larger populations of OP medication naïve RA patients are needed to confirm these findings.

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Abstract Number: 2230

Applicability of FRAX in Clinical Practice: 10-year Results

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Background/Purpose: Applicability of FRAX in Clinical Practice. Results at 10 years

To evaluate the applicability of: 1) the fracture risk thresholds that we proposed in 2013 and 2) a new decision algorithm based on fracture risk calculated by FRAX.

Methods: In 2008, 853 women between 40 and 90 years old referred from Primary Care to the Bone Densitometry Unit were asked to complete a fracture risk factor questionnaire and underwent a bone density scanning (DXA). With FRAX, their absolute risk in the following 10 years of major fracture (MFR) and hip fracture (HFR) was calculated in the following 10 years.

In 2013, we published a proposal of thresholds of high (MFR ≥ 10%) and low (MFR ≤ 3.6%) fracture risk to identify the patients with medium fracture risk in whom a DXA would be indicated.

In 2018, the clinical course of the computerized history of Primary Care was reviewed to identify all bone fractures that occurred in 10 years. In case of doubts about the existence of a fragility fracture, its location or its mechanism of production, the emergency report and/or the bone X-ray was checked.

Results: The final sample is 837 patients; in 10, the follow-up is incomplete and 58 died. In 2008, the mean age of the patients was 61.95 (8.61) years. Eighty percent had at least one fracture risk factor. Twenty percent had normal BMD, 55% osteopenia and 25% osteoporosis. The mean MFR was 6.21% (5.39) and the HFR, 2.08% (3.20).

We identified 243 fractures (168 fragility and 75 traumatic fractures) in 153 patients. 124 patients had a MF (66 vertebral, 39 distal forearm, 10 hip and 9 humerus). Expected MF: 52. 64% of the patients who had MF did not have osteoporosis. 12 patients had a HF. Expected HF: 17.

The area under the ROC curve for MF prediction was 0.643 (95% CI: 0.592-0.694), low prediction capacity. For HR, 0.740 (95% CI: 0.632-0.849), moderate prediction capacity. For BMD in the three locations evaluated, the area was < 0.500, null predictive capacity.

The application of the proposed thresholds classifies appropriately the population with **low** (331 patients, 40% of the sample, incidence of fracture: 9.36%, 95% CI: 6.22-12.5), **medium** (357 patients, there would be recommended to perform a DXA in 42% of the sample; incidence of fracture: 16.25%, IC 95%: 12.42-20.07) and **high** (149, 18%, incidence of fracture: 23.49%, 95% CI: 16.68-30.30) fracture risk defined according to CAROC (< 10%, 10-20%, > 20%).

In patients with medium risk, reclassification to high risk was performed if they had osteoporosis or if the recalculated MFR including the BMD in FRAX calculation algorithm was ≥ 7%.

The result of the application of the algorithm was the classification of 574 patients (69%) as low risk (incidence of fracture: 10.98%, 95% CI: 8.42-13.53) and 263 (31%) as high risk (incidence of fracture: 23.19%, 95% CI: 18.09-28.29). The negative predictive value of fracture in patients classified as low risk is 89%.

Conclusion: The Spanish version of FRAX predicts adequately the HFR and can be used in clinical practice. On the contrary, it underestimates the MFR and should not be used to calculate it. However, in our series, the application of the proposed decision algorithm identifies properly the population with low, medium and high risk of fracture and could be used in clinical practice.

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Abstract Number: 2231

Improving Compliance with Screening for Osteoporosis in Elderly Women

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Background/Purpose: US Preventive Task Force (USPSTF) recommends screening for osteoporosis in women ≥ 65 years of age with dual-energy X-ray absorptiometry (DEXA) scan. There was inconsistent pattern of ordering DEXA scans for screening of osteoporosis at our internal medicine clinic (IMC) at Conemaugh Memorial Medical Center. The main aim of this study was to improve the compliance with screening for osteoporosis with DEXA scan at our IMC as per recommendations by USPSTF.

Methods:

- This is a quasi-experimental study with a pre and post intervention observational periods.
- Patients' medical charts from IMC at Conemaugh Memorial Medical Center were reviewed before an intervention period during which residents and clinic staff were educated regarding the importance of screening for osteoporosis and role of DEXA scans.
- Resident education sessions emphasizing the importance of screening for osteoporosis with DEXA scan were conducted twice a month for a period of 3 months. The need of DEXA screening in women ≥ 65 years, the correct interpretation of DEXA scans and the medication options for women diagnosed with osteoporosis or those with osteopenia who qualify for treatment were emphasized.
- Post intervention data was collected by reviewing patients' medical charts. Pre and post intervention data was compared to see if the above interventions resulted in improvement in compliance with screening for osteoporosis.

Results

- Data from our pre intervention phase showed that 72 women met criteria for osteoporosis screening. Based on our analysis, 32% (23/72) women appropriately received osteoporosis screening with DEXA scan.
- Post intervention data revealed that 58% (134/229) of patients that qualified for screening received DEXA scans.
- This observed 26% increase was statistically significant (P = .0002, z-test for significant difference between two independent proportions).

Conclusion: DEXA scans have been identified as the most sensitive screening test for osteoporosis. Based on the results of DEXA scans, patients can be started on medications like bisphosphonates which have been associated with a decreased incidence of fragility fractures. Our post intervention data has demonstrated a significant improvement in the osteoporosis screening practices of the IMC residents. The intervention measures used by us were simple, proved to be effective, and can be readily implemented in other primary care settings.

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Abstract Number: 2232

Results of the Implementation of a Bone Health Program in Patients with Rheumatoid Arthritis to Improve the Evaluation of Osteoporosis

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Session Type: Poster Session (Tuesday)

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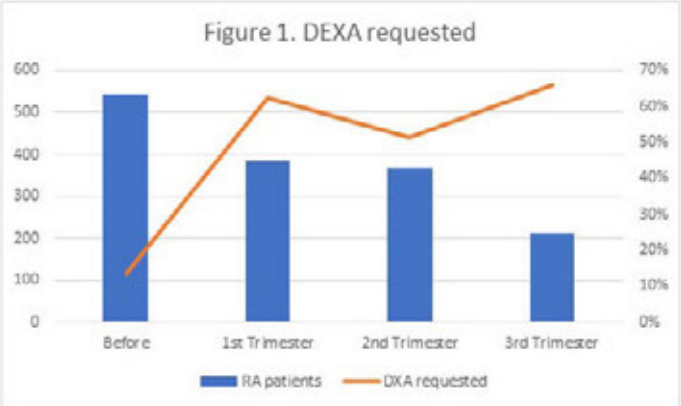
Background/Purpose: Osteoporosis is a generalized skeletal disorder characterized by compromised bone strength and deterioration of quality, often leading to fragility fractures (1). People with rheumatoid arthritis (RA) are at increased risk of osteoporosis for many reasons (inflammation, use of glucocorticoids, inactivity, etc.) (2). Dual-energy x-ray absorptiometry (DEXA) is the recommended test for osteoporosis screening among patients with RA (3). As part of the "Integral Attention Program in Rheumatologic Patients" a program of "Bone Health" was developed. The purpose of this study is to describe the screening strategies implemented as part of this program and the results after implementation.

Methods: An algorithm was developed for the diagnosis and treatment of patients with risk factors for osteoporosis and was distributed among all the rheumatology fellows in the rheumatology clinic of the University Hospital "Dr. José Eleuterio González" in Monterrey, Mexico. To evaluate the diagnosis implementation of these algorithm among

Table 1. DEXA requested and reported among RA patients

	Before	1st Trimester	2nd Trimester	3rd Trimester
RA patients, N	543	384	369	211
DEXA requested, n (%)	73 (13.4)	240 (62.5)	190 (51.5)	139 (65.8)
DEXA reported, n (%)	-	44 (60.2)	146 (60.8)	114 (60)



RA patients, the electronic medical record (EMR) was consulted from February 2018 to January 2019 and data was grouped in trimesters (one trimester before the implementation and the next three afterwards) to get the number of DEXA requested among RA patients. To evaluate the accomplishment of requested DEXA, we obtained the number of reported DEXA registered in the EMR and divided between the number of requested DEXA the last trimester. From the total of RA patients every trimester, we subtracted the number of DEXA requested the last trimester. The results are reported as frequency and percentage.

Results: Before the Bone Health program was applied, of the 543 RA patients consulted, only 73 (13.5%) DEXA studies were requested. During the first trimester of the program from 384 RA patients, 240 (62.5%) DEXA were requested and 44 (60.2%) were reported. During the second trimester among 369 RA patients, 190 (51.5%) DEXA were requested and 146 (60.8%) were reported. Finally, during the third trimester among 211 RA patients, 139 (65.8%) DEXA were requested and 114 (60%) were reported. (Table and Figure 1).

Conclusion: The development and implementation of a bone health program with a systematic methodology and the diffusion of these strategies among the rheumatology fellows improved three-fold osteoporosis screening. We should continue working to guarantee that all the patients with risk factors for osteoporosis get a complete evaluation.

Disclosure: G. Figueroa-Parra, None; **R. Pineda-Sic**, None; **J. Rodriguez-Hinojosa**, None; **C. Gamboa-Alonso**, None; **A. De-Leon-Ibarra**, None; **J. Riega Torres**, None; **I. Hernández-Galarza**, None; **D. Galarza-Delgado**, None; **C. Skinner Taylor**, None.

Abstract Number: 2233

Hip Fracture Incidence in a Teaching Hospital: Intervention for the Prevention of Second Hip Fracture

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Since March 2009, every patient who was admitted in the Orthopaedic Surgery Department for a hip fracture (HF) was evaluated during the admission period by a Hip Fracture Unit (HFU). The assessment included the risk of fracture and diseases related to bone fragility other than osteoporosis. In the discharge report, a mention of the risk of fracture and the previous treatments as well as a treatment recommendation were done. An electronic prescription was made for the advised treatment. An appointment in the next 3 months in the HFU outpatient clinics was set to monitor treatment adherence.

Purpose: To evaluate the incidence of HF in an 18 year period and the efficacy of the intervention made by the HFU in the incidence of second hip fracture (SHF).

Methods: From the area hospital discharge database of a teaching hospital between 1st of January of 2000 and 31st of December of 2017, the admissions for HF and SHF from the patients that lived in the reference area of the hospital were analyzed. A SHF was defined as the contralateral HF to a previous HF. SHF were only included if data from the previous HF was available. Two periods of study about 9 years long each were defined: a control period and an intervention period, before and after 1st of March 2009, the date when HFU started working. The rest of the items of the study were: sex, age, age at the time of HF and time of follow-up until SHF or the end of the study. Data about the reference population were accessible in the website of IDESCAT (Catalonian Institute of Statistics: http://www.idescat.cat/pub/). During the period of study, the subjects older than 65 years increased a 33%, from 48,606 to 64,396 inhabitants (31% women, 35% men).

Results: During the 18 years of the study, there were 2,625 patients > 65 years old admitted because of a HF (1,952 women and 673 men, ratio 2.9:1). The annual incidence of HF in this period was 257 fractures for 100,000 inhabitants and year (x 100 K/y) (333 x 100 K/y in women and 154 x 100 K/y in men).

The absolute number of hip fractures increased during the study period in women and in men with significant statistical difference ($p < 0.05$ women, $p < 0.001$ men). The incidence of HF has been stable in women and has increased in men ($p < 0.05$).

The patients included in both study periods were different in age and sex: in the intervention period there were more men (29% vs. 26%, $p < 0.05$) and they were older (83 ± 7 years, $p < 0.001$).

In the study period, 133 SHF were admitted (5.06% of fractures). There were 87 SHF which took place in the 1,143 patients who presented a HF during the control period (7.61%) and 46 in the 1,313 (3.50%) during the intervention period (p: ns). There were 244 patients who died during the admission and were excluded from the SHF study.

There were no differences in sex between patients who presented a SHF or those who did not. Patients with SHF were older than patients without SHF (86 ± 7 years vs. 83 ± 7 years, $p < 0.001$).

Conclusion: In a teaching hospital, the incidence of HF has remained stable in the last 18 years in women and has increased in men. After 9 years of a HFU intervention, we could not demonstrate a reduction in the incidence of SHF.

Disclosure: X. González-Giménez, None; **C. Gomez-Vaquero**, None; **L. Valencia-Muntala**, None; **A. Zacarias**, None; **I. Martin**, None; **C. Tramunt**, None; **A. Redondo**, None.

Abstract Number: 2234

Osteoporosis Screening in a Resident-Driven Clinic of a Large Academic Hospital

Anam Umar,[1] Titilope Olanipenkun,[1] Hiu Sze Kwong,[1] Chelsy Harris,[1] Amber Faquih,[2] Muhammad Bilal,[1] and Chinedu Ivonye[1], [1]Morehouse School Of Medicine, Atlanta, [2]Emory University School Of Medicine, atlanta

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis is associated with fragility fractures and represents a significant public health problem. The United States Preventive Services Task Forces (USPSTF) recommend dual-energy x-ray absorptiometry (DEXA Scan) of the hip and lumbar spine for osteoporosis screening in females aged 65 years and older. However, despite these recommendations, studies show that the screening rate remains suboptimal. Additionally, African-American females relative to other ethnic groups have been shown to have lower screening rates despite the higher risk of mortality following hip fractures. In teaching hospitals, internal medicine resident form an integral component of patient care and provide consultations to a significant proportion of patients in the primary care clinic. Hence, the objective of this study was to determine the screening rate for osteoporosis and identify factors that affect screening in a resident-driven clinic.

Methods: We selected through simple random sampling, 1,118 female patients aged 65 and older that visited one of the out-patient departments of Grady Memorial Hospital, Atlanta between July 1, 2017, and June 30th, 2018. Data was extracted from the electronic medical record (EMR) system. Osteoporosis screening rate was determined. Patients were asked to complete a questionnaire on reasons for not getting screened. We surveyed 20 internal medicine residents regarding their knowledge of osteoporosis screening and factors that influence their decisions. Two-sided P-value < 0.05 was considered statistically significant.

Results: Osteoporosis screening rate using DEXA scan was 37%(n=402). However, there was a disparity in screening rates by ethnic groups; African Americans (33%), Asians(78%), Caucasians(69%) and Hispanics(80%). Patients aged 65-75 years were more likely to have screening compared with age >75 (AOR 1.47 CI 1.04-3.16, P value< 0.005). Caucasians, Asians, and Hispanics were more likely to have screening compared to African Americans (AOR 1.29, CI 1.16-4.23, P value < 0.005). 81% (n=583/716) of the patients without screening did not have a scan ordered by their physicians. In cases where the scan was ordered but not done, identified reasons included lack of patients' knowledge regarding importance of screening (43%), scheduling and transportation issues(52%), and inability to afford the test (3%). More than 50% of surveyed residents cited inadequate knowledge of the screening recommendations and not remembering to discuss screening with patients and subsequently placing the order.

Conclusion: Our study provides information on the osteoporosis screening rate in a resident-driven clinic of a large academic hospital. We found the presence of racial disparities consistent with what has been previously reported in the literature. Interestingly, it appears that resident physician provider-related factors primarily drive the sub-optimal osteoporosis screening rates. We propose that education on the screening guidelines should be consistently provided to resident physicians involved in the care of these patients. Also, incorporating reminder alerts and patient education materials in the EMR system might improve the screening uptake and rate.

Disclosure: A. Umar, None; **T. Olanipenkun**, None; **H. Kwong**, None; **C. Harris**, None; **A. Faquih**, None; **M. Bilal**, None; **C. Ivonye**, None.

Abstract Number: 2235

Osteoporosis Screening in African American Patients of Rheumatoid Arthritis Patients: Are We Doing Enough?

Anam Umar,[1] Eric Chang,[1] Martin Campbell,[1] Hiu Sze Kwong,[1] Elyse Steven,[1] Amber Faquih,[2] Muhammad Bilal,[1] and Ivonye Chinedu[1], [1]Morehouse School Of Medicine, Atlanta, [2]Emory University School Of Medicine, atlanta

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster – ARP

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis is a well-known extra-articular complication in rheumatoid arthritis (RA) patients It is more common in patients with RA than in the general population, due to active systemic inflammation, the use of corticosteroids, and lack of mobility. The prevalence of concurrent osteoporosis in RA patients is 50% The International Society for Clinical Densitometry (ISCD) and National Osteoporosis Foundation (NOF) has recommended dual-energy x-ray absorptiometry (DEXA) testing for all adult RA patients due to their high-risk status. However, a significant percentage of RA patients do not undergo DEXA scan despite these recommendations. Our aim was to assess osteoporosis screening rates in African American patients with RA.

Methods: Patients with a diagnosis of RA who visited a primary care clinic of Grady Memorial Hospital between July 1, 2017, and June 30th, 2018 were included (n=132) Data were extracted from the electronic medical record (EMR) system. We obtained data regarding the diagnosis of low bone marrow density in terms of osteoporosis and osteopenia through dual-energy x-ray absorptiometry (DEXA Scan) of the hip and lumbar spine. Medication use included steroids, methotrexate, leflunomide, azathioprine, hydroxychloroquine, adalimumab, and any other disease-modifying antirheumatic drugs. STATA software was used and two-sided P-value < 0.05 was considered statistically significant.

Results: Out of 132 patients (74% females, 98% African American, median age 55), only 60 patients had a DEXA scan on file. Of these 60 patients, 50% had low bone marrow density. Osteoporosis and osteopenia prevalence were 40% (24/60) and 10% (n= 6/60) respectively. 43% (N =57 people) were on steroids at the time of data collection and had indications for osteoporosis screening based on the American College of Rheumatology's guidelines but only 30% had a DEXA scan on file. Out of 24 patients, who had osteoporosis, 50% (n=12/24) were on bisphosphonates and 33% of them had repeat DEXA scan in 2 years. The patients who were on steroids were more likely to have screening done as compared to patients who were not on steroids. (OR=2.29 CI 1.1-4., p=0.0234). The patients' age 50-60 were less likely to have DEXA scan on file compared to patients age > 60 (OR=0.29 CI 0.1-0.7 P = 0.01). There was no statistically significant difference in DEXA screening rates between patients with multiple comorbidities versus patients with RA only or patients with low vitamin D versus normal vitamin D.

Conclusion: Our study provides information on osteoporosis screening in predominantly African American RA patients. About half of RA patients for whom treatment was indicated never received an Osteoporosis medication. Our study shows the improper implementation of guidelines in our high-risk patient population which is consistent with previous studies. The results of this audit will make us more vigilant to identify those patients who need DEXA scanning to ensure that treatment is efficacious. Future goals are to set up a resident-driven intervention to not only educate providers about the increased risk of osteoporosis in RA patients but to also increase guideline compliance rates.

Disclosure: A. Umar, None; **E. Chang**, None; **M. Campbell**, None; **H. Kwong**, None; **E. Steven**, None; **A. Faquih**, None; **M. Bilal**, None; **I. Chinedu**, None.

Abstract Number: 2236

Strength Training for People with Rheumatoid Arthritis: Barriers, Facilitators, and Tailoring Considerations

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Strength training (ST) rates in people with rheumatoid arthritis (RA) are remarkably low (1-14%), reducing the potential health benefits of ST for this population (e.g., decreased fatigue, pain, muscle wasting, and inflammation). Compared to studies of factors that affect physical activity more broadly, studies on factors that affect ST in the general population are sparse; these studies are non-existent in RA. The purpose of this study was to examine patient-identified barriers, facilitators, and tailoring considerations for designing interventions to improve ST participation among people with RA.

Methods: Purposive sampling was used to include people with varying age (< /=40 vs >40), gender (male vs female), geographic location (rural vs urban), ST experience (none, less than the general population guidelines, meeting or exceeding the guidelines), and perceived RA severity (well-controlled/mild, moderate, severe). Semi-structured interview questions were co-developed with nine patient partners. Questions were iteratively modified to reflect new knowledge gleaned from interviews that were coded at mid-way points throughout data collection. Interviews were recorded and transcribed verbatim. We performed inductive thematic coding with the de-identified interview transcripts. Peer checking amongst researchers and patient partners was conducted to ensure credibility. We continued the interviews until content saturation was reached in the analysis.

Results: 13 participants were recruited through social media and email advertising across Canada (age range=25-70, male=3, rural=2, no ST experience=5, moderate-severe self-reported RA severity=6). Participants identified two barriers that were unique to the RA population. First, cognitive demand was an important barrier that was exacerbated by both disease/medication side-effects (e.g., 'brain fog' and poor memory) and increased focus required to perform ST compared to aerobic exercise (e.g., counting sets, reps, remembering the individual exercises and their techniques). Second, participants identified a knowledge gap in how much ST can be safely performed given their disease and how to distinguish between ST pain and RA pain. Several participants suggested the use of memory aids (e.g., videos, written programs) could assist in clarifying the steps to performing ST. Many also felt that RA-specific ST guidelines would be useful to improve understanding of how much ST is appropriate. When developing tailored programs, participants highlighted the need to understand their unique situation by probing for goals, motivators, barriers, available time and resources, abilities and limitations, and preferred environment, activities and communication style.

Conclusion: Our results revealed challenges to ST that were unique to people with RA. Participants also identified potential opportunities for developing tailored interventions for supporting ST participation. These findings have also provided a foundation for testing hypotheses that explore the mechanisms for improving ST behaviour in this population.

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Abstract Number: 2237

Gathering Patients' and Physicians' Perceptions to Improve Outcomes in Systemic Autoimmune Myopathies

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

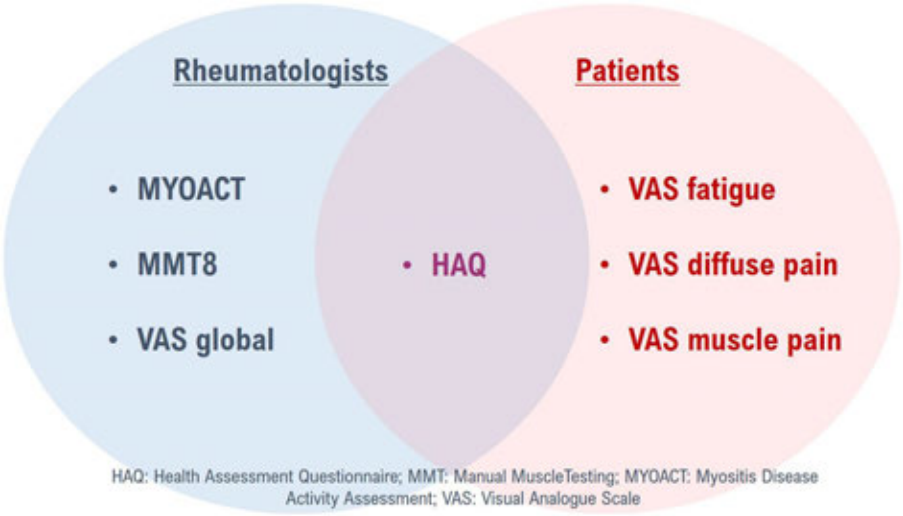
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Treat-to-target (T2T) strategy has become the best approach to treat several rheumatic disorders. However, most targets are only based on specialists' opinions, which may not reflect exactly the main patients' concerns during treatment. There is evidence that switching to a more patient-centered healthcare system seems to enhance treatment adherence and improve outcomes. Therefore, the purposes of this research were: a) to assess the concerns of the patients with systemic autoimmune myopathies (SAMs) during follow-up and compare to the rheumatologists' concerns; b) to gather patients' and physicians' concerns to develop a SAMs outcome standard set.

Methods: From 2018 to 2019, total of the 93 consecutive adult patients with SAMs (49 dermatomyositis and 11 polymyositis - EULAR/ACR 2017, and 33 anti-synthetase syndrome - Connors et al., 2010) and 51 rheumatologists from a tertiary center were invited to answer a standardized questionnaire. Initially, an open questionnaire was applied in order to assess unbiased concerns of both groups. Thereby, the top 10 answers were selected and applied a multiple-choice questionnaire, inquiring the top 3 major concerns. Answers of each group were plotted into charts



and frequencies were compared. The agreement rate was calculated by the sum of lowest frequency of each concern. Concerns were gathered in a SAMs outcome standard set, following the methodology proposed by the International Consortium for Health Outcomes Measurement (ICHOM). We also evaluated if the patients' concerns were associated with any current clinical features, previous manifestations or comorbidities.

Results: The top three concerns raised among the patients were: to avoid side effect of medication (51%), to improve muscle weakness (49%) and to prevent loss of functionality (35%). The top three concerns among rheumatologists were: prevent loss of functionality (71%), ensure quality of life (63%) and achieve disease remission (63%). The agreement rate between both groups was 41%.The patients' concerns that rheumatologists did not mention were respectively the improvement of: muscle pain (33% vs. 0%, P=0.001), diffuse pain (25% vs. 0%, P=0.001), skin lesions (23% vs. 0%, P=0.001) and fatigue (18% vs. 0%, P=0.001) - all symptoms related worries. The rheumatologists' concerns that patients did not mention were respectively the: achievement of disease remission (63% vs. 0%, P=0.001) and prednisone dose (0% vs. 22%, P=0.001). The concerns of pain and fatigue were not associated with other diagnosis such as fibromyalgia or depression/anxiety. Gathering both point of view, we developed a SAMs outcome standard set **(Figure 1)**.

Conclusion: Even though functionality and muscle weakness are still major concerns for physicians and patients, there are additional patients' concerns that should be assessed routinely during SAMs treatment and follow-up. Patients consider that controlling pain and fatigue are important outcomes to be pursued in SAMs and rheumatologists should be aware of these to provide a better assistance and ensure treatment adherence.

Disclosure: I. Bertoglio, None; **G. Abrahão**, None; **M. Remião Ugolini-Lopes**, None; **F. Souza**, None; **R. Miossi**, None; **S. Shinjo**, None; **E. Bonfa**, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #305068/2014-8), 2, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4 and #2010/10749-0), 2.

Abstract Number: 2238

Role of Clinical Impact, Disease-specific Knowledge and Beliefs About Medication on Therapeutic Adherence in Rheumatoid Arthritis: An Integrative Structural Equation Modeling Approach

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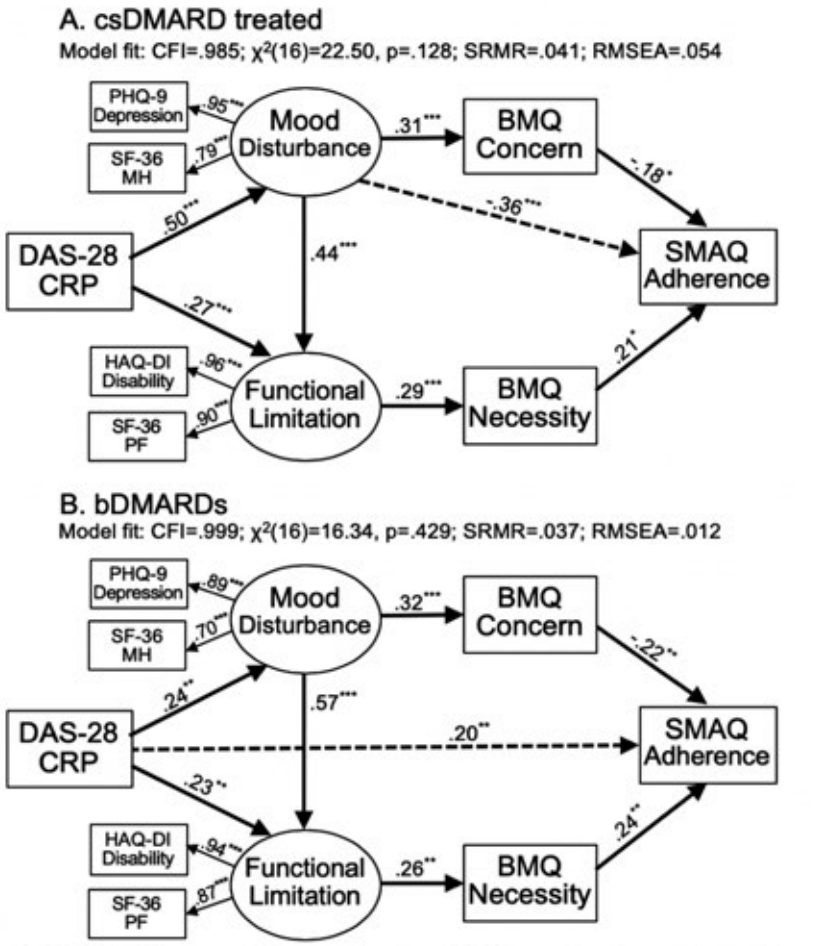
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment of rheumatoid arthritis (RA) to remission optimally ensures control of symptoms, prevention of structural damage, optimization of function and quality of life. Adherence to medical treatment is, therefore, critical for a comprehensive and successful management of RA. We interrogated the influence of distinct domains of RA clinical impact (disease activity, functional limitation, mood disturbance), RA-specific knowledge and patients' beliefs about medications on treatment adherence.

Figure 1: Contributions of clinical RA impact and beliefs about medication on therapeutic adherence.



DAS28-CRP: Disease activity score based on 28-joint count and c-reactive protein, PHQ-9: 9-item patient health questionnaire, SF-36 MH: Short Form 36 Health Survey mental health scale, HAQ-DI: health assessment questionnaire-disability index, SF-36 PF: Short Form 36 Health Survey physical function scale, BMQ: beliefs about medication questionnaire, SMAQ: Short medication adherence questionnaire.
*p<0.05, **p<0.01, ***p<0.001.

Methods: We evaluated 285 patients from a single center. In the proposed model, disease activity (DAS28CRP),mood disturbance (Patient Health Questionnaire-9 depression scale and SF-36 Mental Health domain), functional limitations (Health Assessment Questionnaire Disability Index and SF-36 Physical Function domain) and RA-specific knowledge (Patient Knowledge Questionnaire) were expected to predict beliefs about the necessity of RA medications and concerns about them (Beliefs about Medicines Questionnaire); in turn, those would impact adherence (Simplified Medication Adherence Questionnaire). Cross-sectional multi-group structural equation modeling evaluated the model separately in patients on bDMARDs on csDMARDs.

Results: RA-knowledge was not associated with medication beliefs or adherence and therefore dropped from the model. Addition of two supplementary paths (dashed lines) improved the model fit for both treatment groups (Figure 1). RA activity, functional limitations and mood disturbance influenced adherence via multiple, often competing pathways, directly or indirectly through a necessity/ concerns evaluation by the patient. RA activity directly promoted adherence in patients on bDMARDs ($p< 0.01$). In contrast, in patients on csDMARDs, RA activity had an indirect, net negative effect on adherence ($p< 0.01$), mainly through worsening mood disturbance ($p< 0.01$). Therefore, the experience of disease activity in patients on bDMARDs may be sufficiently impactful to independently promote med-

ication adherence.In contrast, RA activity may be largely experienced as depressed mood in patients on csDMARDs, overwhelming their capacity to adhere. Mood disturbance adversely influenced adherence directly in patients on csDMARDs ($p< 0.01$); yet there was no significant direct or net indirect effect of mood disturbance on adherence to biologics. Functional limitations fostered adherence through enhanced awareness of medication necessity ($p< 0.05$).

Conclusion: Distinct domains of clinical RA impact influence treatment adherence directly or indirectly through a necessity/ concerns framework. Mood disturbance and medication concerns may represent complementary yet salient intervention targets of RA management promoting adherence; the former may be more relevant in patients on csDMARDs whereas the latter in those on bDMARDs.

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Abstract Number: 2239

Reproductive Health Awareness and Needs: Assessment of Parents, Female Adolescents, and Young Adults with Pediatric Rheumatic Diseases

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The diagnosis of a pediatric rheumatic disease comes with worries for both parents and patient; one that may be overlooked is the impact on long- and short- term reproductive health, including the impact of the disease and treatment on fertility, pregnancy, and contraception. Little exploration has been done to assess the reproductive health needs and concerns of this population. We sought to identify areas of concern regarding reproductive health, topics in which pediatric patients/parents need more information, barriers to current knowledge, current sources of knowledge, and suggestions for ways to distribute information.

Methods: Females 15-20 years old diagnosed with any rheumatic condition and their parents were recruited from a children's hospital rheumatology clinic. Participants completed a survey collecting demographics, diagnosis, rheumatic medications, sexual activity, and contraception use and engaged in one of three focus groups: two age-specific patient groups and one parent group. Each audio-recorded focus group was professionally transcribed and coded using constant comparative analysis.

Results: A total of 9 patients and 7 parents participated. The majority of patients were Caucasian (n=7; 78%) and carried the diagnosis of JIA (n=6; 67%), with a small representation of systemic lupus (n=2; 22%) and vasculitis (n=1; 11%). Two-thirds of participants were on teratogenic medications. 11% of patients were sexually active, 55% of total subjects were using contraception. In the parent group, over 50% had some level of college education and household incomes over the median national average.

All focus groups expressed concerns about the interaction of rheumatic medications with contraception and fertility. Worry surrounding the effect of rheumatic conditions and medications on fertility, repercussions of future pregnancy on patients' and potential offspring's health, and motherhood was widespread. Participants reported varied levels of reproductive health education, ranging from none to in-depth discussions with fertility specialists, with a general agreement of dissatisfaction with currently available resources and the attention to rheumatic disease and reproductive health. Overall, rheumatology providers were not named by any of the focus groups as a consistent resource for reproductive health information.

Conclusion: Reproductive health is an important topic to female adolescents and young adults with rheumatic diseases, and their parents. The most prominent concern for all groups was medications' impact on many aspects of reproductive health. Young women and their parents were dissatisfied with the availability, quantity, and quality of reproductive health information related to pediatric rheumatic disease. Rheumatologists should re-consider our role in the reproductive health discussion, and seize the opportunity to improve the communication and education of this issue in our clinical practice.

Disclosure: V. Mruk, None; **K. Carandang**, None; **M. Clowse**, GSK, 2, UCB, 5; **S. Ardoin**, None; **E. Berlan**, Merck, 9; **C. Edens**, None.

Abstract Number: 2240

Mining Social Media Data to Investigate Patient Perceptions Regarding DMARD Pharmacotherapy for Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences
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Session Time: 9:00AM–11:00AM

Background/Purpose: Our hypothesis is that patients have a positive opinion regarding the newer, biologic DMARDs and a negative sentiment towards the conventional synthetic agents. We sought to analyse discussions on social media platforms regarding DMARDs so understand the collective sentiment expressed towards these medications.

Methods: Treato data analytics were utilised to download all available discussions on social media about DMARDs in the context of Rheumatoid arthritis. Strict filters were used to ensure that only user (patient) generated content was downloaded. The sentiment (positive or negative) expressed in these posts was analysed for each DMARD using the Natural Language Processing technique of Sentiment Analysis. We then further analysed the reason for this sentiment for each DMARD, looking specifically at the categories of efficacy and side effects.

Results: Sophisticated computer generated algorithms analysed hundreds of millions of posts and finally included 54,742 social media discussion about csDMARDs and bDMARDs. The overall ratio of positive comments to negative comments was higher for bDMARDs (1.296) than for csDMARDs (1.079). Tofacitinib had the highest ratio of positive to negative comments (1.71) whereas sulfasalazine had the lowest (.97). Methotrexate was the only other agent with an overall negative ratio (0.995), primarily due to concerns regarding side effects. Efficacy was the main reason for a positive sentiment and lack of efficacy was the most common reason for a negative sentiment. Side effects however also played a significant role in generating a negative sentiment especially about the csDMARDs. Most common emotions associated with a negative sentiment were a sense of hopelessness along with fear and uncertainty.

Conclusion: Public opinion as expressed on social media is generally positive about the bDMARDs. Lack of efficacy is the biggest reason for a negative sentiment towards a medication, which often leads to a sense of hopelessness. A sense of fear and uncertainty play a role in generating this sense of hopelessness. Clinicians should be aware of this when dealing with patients who have failed a DMARD and provide cognitive reassurance to mitigate the pessimistic feelings that the patient might be experiencing.

Disclosure: C. Sharma, None; **S. Whittle**, None; **P. Haghighi**, None; **F. Burstein**, None; **R. Sa'adon**, None; **H. Keen**, None.

Abstract Number: 2241

Parent Perspectives on Addressing Emotional Health for Youth with Juvenile Myositis: A Qualitative Focus Group Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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Background/Purpose: While juvenile myositis (JM) can negatively affect quality of life, studies of the emotional health needs of youth with JM are limited. We examined parent perspectives on emotional health needs and interventions for youth with JM.

Methods: Six focus groups (60 minutes each, audio-recorded, transcribed verbatim) of parents of youth ages 6-21 years old with JM were conducted at the 2018 CureJM National Family Conference. Parents were grouped by their child's age (6-12yo, 13-17yo, 18-21yo), with 2 focus groups per age range. Note takers in each focus group assisted with documentation of nonverbal cues by participants. At the start of each focus group, parents listed 3 words/phrases encapsulating JM-related emotional health challenges, which were then discussed in detail. Screening approaches and desired interventions were discussed. Using an a priori coding scheme, interview transcripts were independently coded using the constant comparison method and Dedoose software, with subanalysis by age group. Preference for emotional health interventions was also assessed via Likert scale (1 = very undesirable, 5 = very desirable). The study was approved by Children's Hospital of Philadelphia Institutional Review Board (IRB 18-015225).

Table 1: Parent demographics and reported child characteristics

Parents (n = 45)*	
Female, n (%)	38 (84%)
Race/Ethnicity, n (%)	
• White	43 (96%)
• Non-White**	2 (4%)
• Hispanic/Latino	4 (9%)
Child (n = 39)**	
Female, n(%)	29 (74%)
Mean age, years (SD)	13.7 (4.6)
Age group, n (%)	
• 6 to 12 years old	17 (44%)
• 13 to 17 years old	13 (33%)
• 18 to 21 years old	9 (23%)
Mean age disease onset, years (SD)	7.9 (4.6)
Mean disease duration, years (SD)	5.8 (4.7)
*Six parent couples participated total **non-white included: Asian (n = 1), other (n = 1); youth Asian (n = 1), other (n = 4)	

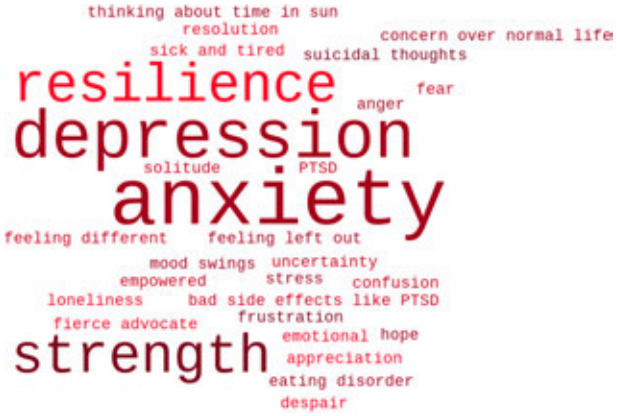

Figure 1. Parent-reported emotional health experiences of youth with juvenile myositis (word cloud, with size of word/phrase corresponding to listed frequency)

Results: Demographics are shown in Table 1. Parents commonly reported depression/anxiety as challenges, though strength/resiliency also emerged especially in older groups (Figure 1). Themes from the focus groups related to emotional challenges included impact of JM diagnosis, impact of JM on siblings/family dynamic, resiliency, and parental emotional health. Themes related to screening/intervention included perceptions that youth with JM may not always openly report distress, barriers to treatment (e.g. lack of access), desired interventions (e.g. technological modalities, peer support), and the role providers play in eliciting a history of emotional distress and providing access to emotional health resources. Parents strongly desired counseling and peer support groups for their children with JM (Figure 2).

Conclusion: Youth with JM and their family members experience substantial emotional challenges, with limited access to interventions. Resiliency in older age groups suggests coping may occur over time. Further studies should assess youth perspectives on emotional health in JM, as well as preferences for and efficacy of interventions.

Disclosure: K. Ardalan, None; **O. Adeyemi**, None; **D. Wahezi**, None; **A. Caliendo**, None; **M. Curran**, None; **J. Neely**, None; **S. Kim**, None; **C. Correll**, None; **E. Brunner**, None; **A. Knight**, None.

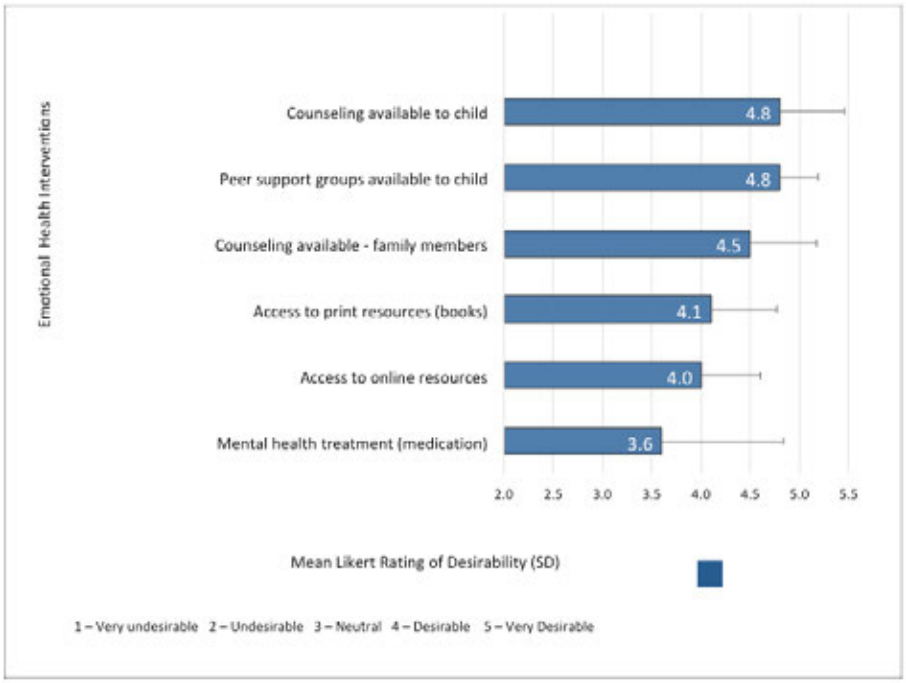

Figure 2. Emotional health interventions desired by parents of young adults with juvenile myositis

Abstract Number: 2242

Evaluating Important Change in Cutaneous Disease Activity as an Efficacy Measure for Clinical Trials in Dermatomyositis

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Background/Purpose: The FDA uses near or total clearance in cutaneous disease in inflammatory skin conditions as an endpoint in clinical trials. However, patients may experience improvement in their quality of life (QoL) without achieving complete clearance of their skin disease. A previous study has shown that the Cutaneous Dermatomyositis Disease Area and Severity Index-Activity (CDASI-A) score correlates with the Symptoms and Emotions subscales of the Skindex-29, a skin specific measure of QoL, down to CDASI-A scores of 7 and 10, respectively. Our goal is to define an important change in disease activity, as measured by CDASI-A, that results in meaningful change in QoL in patients with dermatomyositis (DM).

Methods: In 103 patients seen in the outpatient Autoimmune Disease Clinic at the University of Pennsylvania, we assessed the percent change and actual change in CDASI-A needed to achieve a meaningful improvement in QoL using linear regression models.

Results: Comparing the Skindex-29 to the Dermatology Life Quality Index (DLQI), we found that meaningful improvement in the Symptoms and Emotions subscales of the Skindex-29 is 7.86 (P< .0001) and 10.29 (P< .0001) points, respectively. For patients with initial CDASI-A scores >14, a 40% change in CDASI-A between the first two visits suggests a meaningful change in the Skindex-29. In patients with moderate initial CDASI-A (15-26), the change in CDASI-A score needed to achieve a meaningful change in Symptoms and Emotions was 6 (P=.0002) and 7 (P=.0007), respectively. For initial CDASI-A scores in the severe range of 27-35, an improvement in CDASI-A by 11 (P=.0301) and 9 (P=.0212) points is needed to result in meaningful change in Symptoms and Emotions, respectively.

Conclusion: In patients with an initial CDASI-A of >14, a 40% change in CDASI-A can be used to indicate meaningful change in QoL in future DM trials.

Disclosure: S. Ahmed, None; **S. Chakka**, None; **R. Krain**, None; **R. Feng**, None; **V. Werth**, Biogen, 2, 5, Corbus Pharmaceuticals, 2, 9, University of Pennsylvania, 9.

Abstract Number: 2243

Knowledge, Needs and Expectations Among Systemic Lupus Erythematosus: Preliminary Results from the INTEGRATE Pilot Project

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic inflammatory disease characterized by multi-organ involvement and a complex clinical picture, with a wide range of manifestations with and unpredictable relapsing and remitting course. Evidence suggests that discordance between patients and physicians could negatively affect patient care, adherence to treatment and outcomes of the disease. In particular, physicians' and patients' assessments of disease activity and health status in SLE are shown to differ considerably, suggesting the need to better understand patients' perspective to bridge the gap in information and communication.

The aim of the present study is to assess knowledge, needs and expectations among SLE patients to shine a light on patients' perspectives. The research was part of the INTEGRATE Pilot project assessing patients' and clinicians' perspectives to develop a strategy for the monitoring and treatment of chronic diseases aligning the integration of patient driven data with the traditional clinical evaluation.

Methods: A web survey was designed to assess knowledge, needs and expectations among SLE patients. LUPUS EUROPE and partner clinicians were invited patients to participate in the survey. Furthermore, two focus groups involving 15 patients from 12 European countries were then organized into two-hour sessions to delve deeper into survey's results.

Results: Overall 554 SLE patients (mean age 44.3±13.1 years; 94.2% female) participated to the survey. Responders were mainly from Italy (28.7%) and UK (30.9%), but answers came from almost all European countries.

Data from the survey suggested that about 50% of the patients had good to very good knowledge of disease related issues. The main needs highlighted from responders were related to the involvement in decisions about treatment and disease management (74.2% reported high to extreme need), improvement of participation in social activities (77.3% declared moderate to extreme need) and maintenance of relationship with friends (64.8% reported high to extreme need). During the focus groups many patients reported that they were not adequately informed about treatment, side effects and lifestyle choices. All patients reported problems of communication about their disease with others including loved ones, friends, the wider community and in some cases specialists and GPs. There was a particular emphasis on improving their relationship with their specialists and other healthcare professionals. Patients highlighted the need to receive more "understandable" and personalized information, even suggesting the possible role of a specialized nurse in providing practical support.

Conclusion: Patients inputs collected from both the survey and focus groups suggested specific areas of unmet needs and also provided ideas in relation to the practical strategies to adopt in order to fill existing gaps. These results, combined with the assessment of clinicians' perspectives, could serve to design an integrated strategy for disease management.

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Abstract Number: 2244

What Are the Prescribing Trends and Satisfaction Levels with Analgesics for Osteoarthritis as Reported by US Rheumatogists, Orthopaedic Surgeons, and Primary Care Physicians?

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Session Date: Tuesday, November 12, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences
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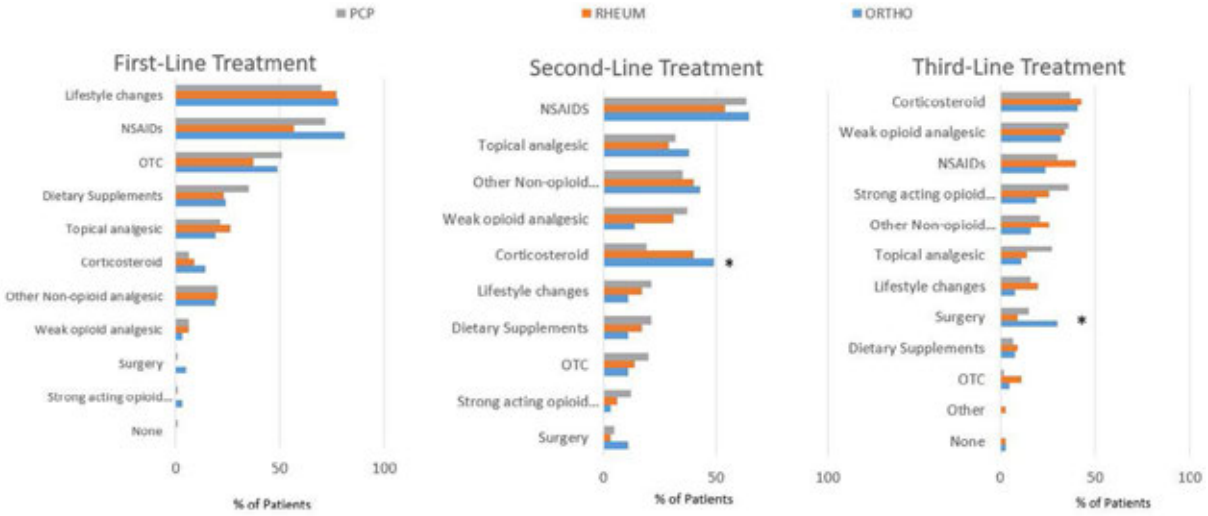
Background/Purpose: To describe patterns of care and physician satisfaction with prescribed treatments for osteoarthritis (OA).

Methods: Data were collected from February-May 2017 using US Adelphi Disease Specific Programme, a cross-sectional survey of 81 (52.9%) primary care physicians (PCP), 35 (22.9%) rheumatologists (RHEUM), and 37 (24.2%) orthopedic surgeons (ORTHO). Specialties were compared based on reported use and satisfaction with prescribed treatments using Likert-type scales: -2 (not satisfied) to +2 (very satisfied) for overall satisfaction; and -3 (performs very badly) to 3 (performs very well) for drug class attributes of efficacy, safety, quality of life (QoL), costs, and convenience. Specialties were compared using Fisher-Freeman-Halton exact tests and analysis of variance tests.

Results: Physicians were mostly male (72.5%), with private (84.7%) and office/outpatient (87.2%) practices and had been in practice over 15 years (77.8%). All specialty comparisons are listed as PCP, RHEUM, ORTHO, respectively. First-line treatment included predominantly lifestyle changes and NSAIDs (Figure 1), and rates for each treatment did not differ by specialty. Second and third-line medication use only differed by specialty for injectable corticosteroids and surgery, prescribed more frequently by ORTHOs. Affirmation from physicians that any guidelines were routinely followed differed by specialty (28.4%, 51.4%, 48.6%; $p< 0.05$). Slightly less than one-third of physicians had ever recommended cannabinoids (28.4% 28.6%, 27.0%). Among those physicians, the frequency of cannabinoid recommendations was reported as rare (60.4%), sometimes (34.9%), and frequent (4.7%). Physicians' satisfaction across all medications was mostly positive for mild patients (71.6%, 65.7%, 62.2%), but lower for moderate to severe patients (56.8%, 34.3% 51.4%) with mean satisfaction rated lowest among RHEUMs ($p< 0.05$, Table 1). When assessing performance across all 5 drug attributes evaluated, efficacy, cost considerations, and QoL differed by specialty (all $p< 0.05$; Table 2). Efficacy rating for overall medications, opioids, and other non-opioid analgesics were rated highest by PCPs and lowest by ORTHOs. Cost considerations differed for injectable corticosteroids which were most favorable among RHEUMs, and QoL was rated lowest among ORTHOs for opioids. Ratings for each medication by safety and convenience were similar across specialties. Opioids had the lowest mean performance ratings for efficacy (weak only), safety, and QoL.

Conclusion: Few differences by physician specialty were found in reported rates of first, second, and third line use of therapies for OA. Physicians rated satisfaction with overall medications as positive when treating patients with mild OA, but ratings were lower for moderate to severe patients. Variability by specialty was most pronounced in the performance ratings for efficacy and QoL; most noteworthy, opioids were reported highest by PCPs and lowest by ORTHOs. These data indicate more similarities than differences in OA treatment among physician specialties despite potential variations in physician specialty training and populations served.

Figure 1. Treatment Strategy for Patients with Moderate to Severe Osteoarthritis by Physician Specialty



*p<0.05

Table 1. Overall Satisfaction with Current Treatments Options by Patient Disease Severity and Physician Specialty

Overall satisfaction with current treatment options	Total (N=153)	PCP (N=81)	RHEUM (N=35)	ORTHO (N=37)	P-value
For Mild patients					
Mean±SD	**0.82±0.81**	**0.86±0.75**	**0.83±0.79**	**0.7±0.94**	**0.6012**
Negative (-2, -1)	7 (4.6%)	3 (3.7%)	1 (2.9%)	3 (8.1%)	0.705
Neutral (0)	42 (27.5%)	20 (24.7%)	11 (31.4%)	11 (29.7%)	
Positive (1, 2)	104 (68.0%)	58 (71.6%)	23 (65.7%)	23 (62.2%)	
For Moderate-severe patients					
Mean±SD	**0.44±0.91**	**0.57±0.79**	**0.11±1.08**	**0.46±0.93**	**0.0461**
Negative (-2, -1)	18 (11.8%)	6 (7.4%)	7 (20.0%)	5 (13.5%)	0.143
Neutral (0)	58 (37.9%)	29 (35.8%)	16 (45.7%)	13 (35.1%)	
Positive (1, 2)	77 (50.3%)	46 (56.8%)	12 (34.3%)	19 (51.4%)	

ORTHO=orthopaedic surgeon; PCP=primary care physician; RHEUM=rheumatologist; SD=standard deviation

Table 2. Mean Satisfaction with Treatments Attributes by Physician Specialty

Mean (SD)	Medication Type	Total (N=153)	PCP (N=81)	RHEUM (N=35)	ORTHO (N=37)	P-value
Efficacy	Overall medications	0.2 (0.82)	0.3 (0.74)	-0.0 (0.80)	-0.1 (0.92)	0.019
	NSAIDs	0.2 (0.96)	0.3 (0.95)	0.0 (1.00)	0.0 (0.90)	0.100
	Other Non-opioid analgesics	-0.1 (1.01)	0.1 (1.02)	-0.2 (0.92)	-0.4 (1.01)	0.041
	Weak opioids	-0.1 (1.11)	0.2 (0.95)	-0.2 (1.10)	-0.5 (1.32)	0.012
	Strong opioids	0.3 (1.19)	0.5 (1.03)	0.2 (1.23)	-0.1 (1.40)	0.024
	Injectable Corticosteroids	1.0 (1.00)	1.1 (1.04)	0.8 (0.97)	0.9 (0.94)	0.357
	Topical Analgesics	-0.5 (1.23)	-0.3 (1.19)	-0.6 (1.14)	-0.6 (1.38)	0.254
Safety	Overall medications	0.3 (0.86)	0.3 (0.79)	0.3 (0.99)	0.3 (0.88)	0.958
	NSAIDs	0.1 (1.09)	0.1 (1.03)	-0.1 (1.15)	0.2 (1.14)	0.422
	Non-opioid analgesic	0.4 (1.15)	0.4 (1.09)	0.4 (1.22)	0.5 (1.22)	0.976
	Weak opioids	-0.2 (1.19)	-0.2 (1.17)	-0.1 (1.23)	-0.5 (1.19)	0.226
	Strong opioids	-0.5 (1.16)	-0.4 (1.09)	-0.3 (1.27)	-0.8 (1.18)	0.135
	Injectable Corticosteroids	0.8 (1.07)	0.7 (1.03)	0.8 (1.26)	0.9 (0.97)	0.459
	Topical Analgesics	1.6 (1.07)	1.6 (1.00)	1.5 (1.17)	1.7 (1.13)	0.828
Convenience / Acceptability	Overall medications	1.4 (0.87)	1.4 (0.82)	1.3 (0.91)	1.4 (0.96)	0.959
	NSAIDs	1.7 (0.97)	1.8 (0.94)	1.5 (0.98)	1.7 (1.03)	0.325
	Non-opioid analgesic	1.6 (1.03)	1.6 (0.99)	1.5 (1.04)	1.6 (1.12)	0.894
	Weak opioids	1.3 (1.11)	1.3 (1.06)	1.3 (1.13)	1.2 (1.21)	0.917
	Strong opioids	1.1 (1.14)	1.1 (1.07)	1.2 (1.03)	1.1 (1.37)	0.810
	Injectable Corticosteroids	1.0 (0.97)	0.9 (0.99)	1.1 (1.02)	1.0 (0.90)	0.661

Disclosure: T. Schnitzer, AbbVie, 2, Aptinyx, Astellas, Calibr, Eli Lilly and Company, 2, 5, Flexion, 2, Galapagos, 2, GlaxoSmithKline, Grunenthal, 2, Kolon TissueGene, 2, Pfizer, 2, 5, Regeneron, 2, Sanofi, Vertex; **R. Robinson**, Eli Lilly and Company, 3, 4; **L. Viktrup**, Eli Lilly and Company, 1, 3, 4; **J. Cappelleri**, Pfizer Inc, 1, 3, Pfizer Inc., 1, 3; **A. Bushmakin**, Pfizer Inc, 1, 3; **L. Tive**, Pfizer, 1, 3; **J. Mellor**, Pfizer, 2; **N. Williams**, Pfizer, 2; **P. Hubanova**, Pfizer, 2; **J. Jackson**, Pfizer, 2.

Abstract Number: 2245

Polymyositis (PM) and Dermatomyositis (DM) Symptom Flares and Associated Impact from the Patient Perspective

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Background/Purpose: Flare activity or worsening symptoms are not well defined for myositis. This analysis characterizes PM and DM flares from the patient perspective and reports the corresponding disability and rates for emergency department or urgent care visits and hospitalizations.

Methods: An online survey was conducted with volunteer patients recruited from The Myositis Association and Johns Hopkins Myositis Center. Survey questions included sociodemographics, flare symptoms, Health Assessment Questionnaire Disability Index (HAQ-DI) and HAQ-Pain index, Work Productivity and Activity Impairment (WPAI), myositis related emergency department and urgent care (ED/UC) visits and hospital admissions during the past year. Flare frequency was assessed with two sequential questions, "Have you ever had a flare or worsening myositis symptoms?" if yes, "How many times in the past 12 months?".

Results: A total of 564 patients with self-reported diagnoses of PM (n=243) or DM (n=321) completed the survey between December 2017 and May 2018 (86.3% Caucasian, 78.2% female, 42.9% employed, mean age 56). There were 524 who recalled periods with or without worsening symptoms or flares (demographic profile similar to total sample) and those individuals are reported on here. There were 33 (6.3%) that reported never experiencing a flare, 113 (21.6%) reported 0 flares in the past year, 244 (46.6%) reported 1-3 flares, and 134 (25.6%) reported 4 or more

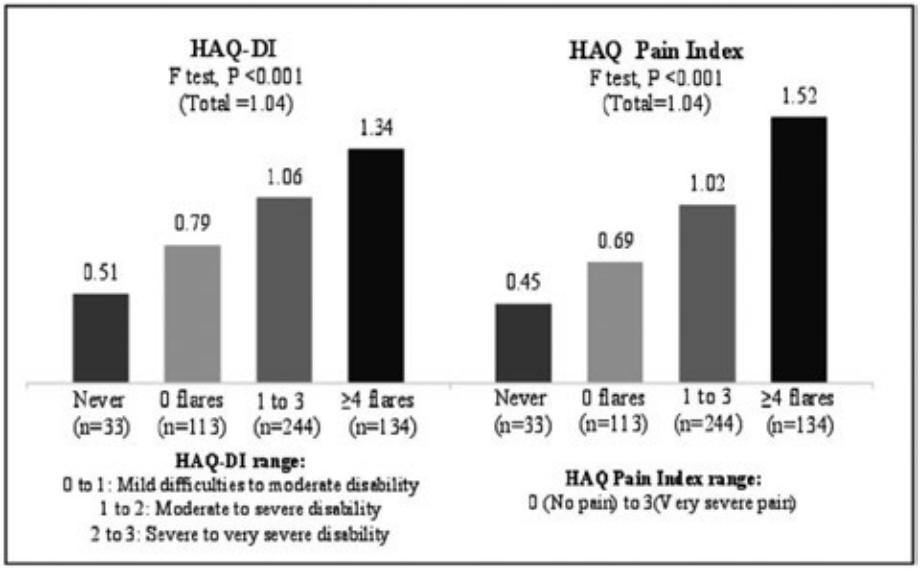

Figure 1. Mean HAQ-DI and HAQ Pain Index Scores for Never and Past Year Flare Groups.

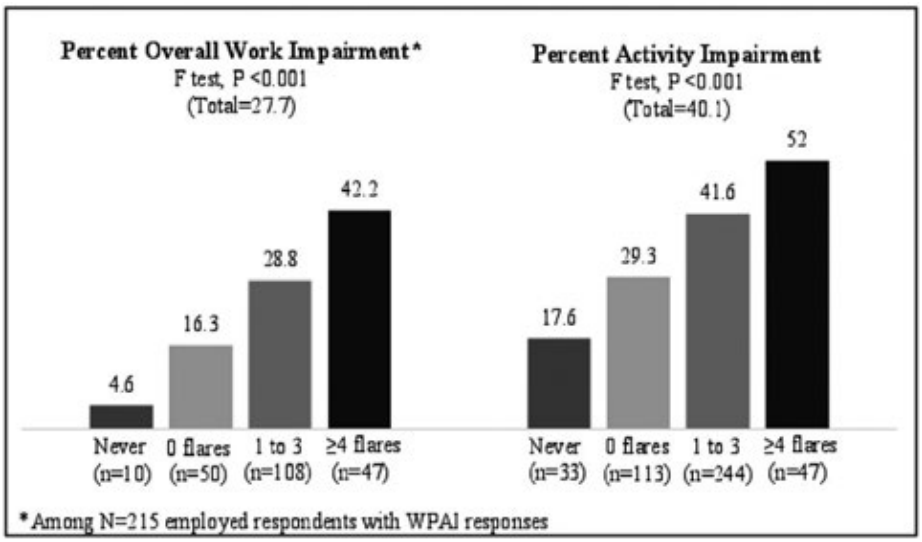

Figure 2 . Mean WPAI Work and Activity Impairment Percents for Never and Past Year Flare Groups.

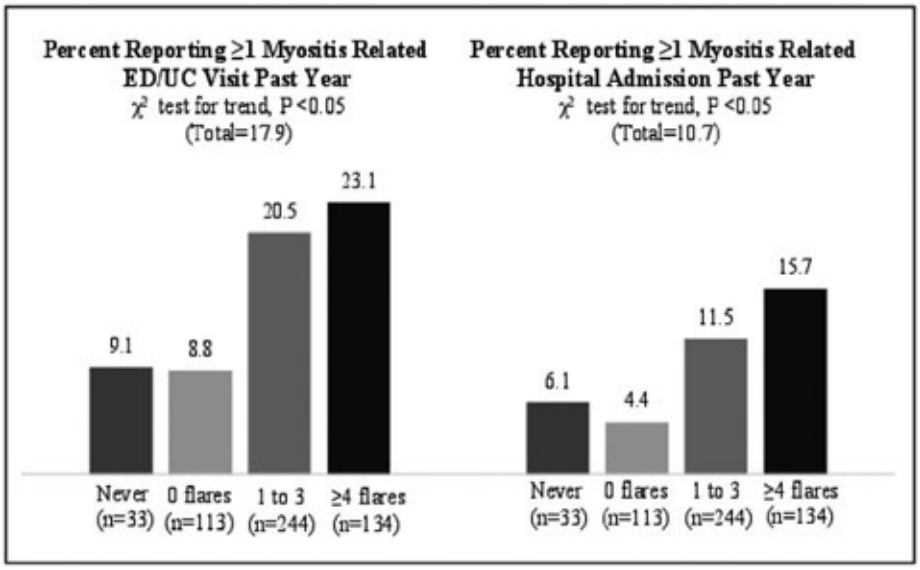

Figure 3. Myositis Related ED/UC Visits and Hospital Admissions for Never and Past Year Flare Groups.

flares in the past year. The pattern of flare frequency was similar for PM and DM respondents. Among those with past year flares or periods of worsening symptoms (n=378) the most common symptoms were muscle weakness (83%), extreme fatigue or exhaustion (78%), muscle pain/discomfort (64%), trouble climbing stairs (62%), trouble standing from a seated position (50%), and skin rash (45%). Dysphagia occurred for 27%. Increasing flare frequency was associated with greater mean HAQ-DI ($F=17.653$, $P < .001$), HAQ-Pain ($F=28.291$, $P < .001$) (**Figure 1**), greater mean percent of WPAI activity impairment ($F=20.109$, $P < .001$) and for the employed, greater mean percent of missed work time ($F=2.716$, $P < .05$), as well as greater impairment at work ($F=8.242$, $P < .001$), and overall work impairment ($F=9.933$, $P < .001$) (**Figure 2**). Percent with one or more past year myositis related ED/UC visits were found to be related to flare frequency ($\chi^2=11.634$, $P < .05$). The percent with one or more myositis related hospital admissions was also associated with flare frequency ($\chi^2=9.03$, $P < .05$) (**Figure 3**).

Conclusion: PM/DM-related flares or worsening symptoms are common, with 72% of respondents reporting one or more flare occurrence in the past year. Exacerbations of muscle weakness and fatigue were the most common flare symptoms, and flare frequency was associated with greater disability, more pain, more overall work impairment,

and more activity impairment. Past year ED/UC visits and hospital admissions were also more likely to occur as flare frequency increased. Higher frequency of patient-reported flares may serve as a marker of worsening physical functioning and intensifying health care needs, and therefore suggests their importance in the clinical assessment of patients with PM/DM.

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Abstract Number: 2246

Symptoms and Impacts in Psoriatic Arthritis: Findings from Qualitative Patient Interviews

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory disease resulting in significant symptom burden.[1] Over time and without adequate treatment, PsA can lead to disability and reduced patient quality of life.[2] Fatigue is among the most common symptoms,[1] but is complex and difficult to measure. The most burdensome symptoms that impact PsA patients need to be better understood in order to select patient reported outcomes (PRO) tools that adequately capture these concepts.

Objectives

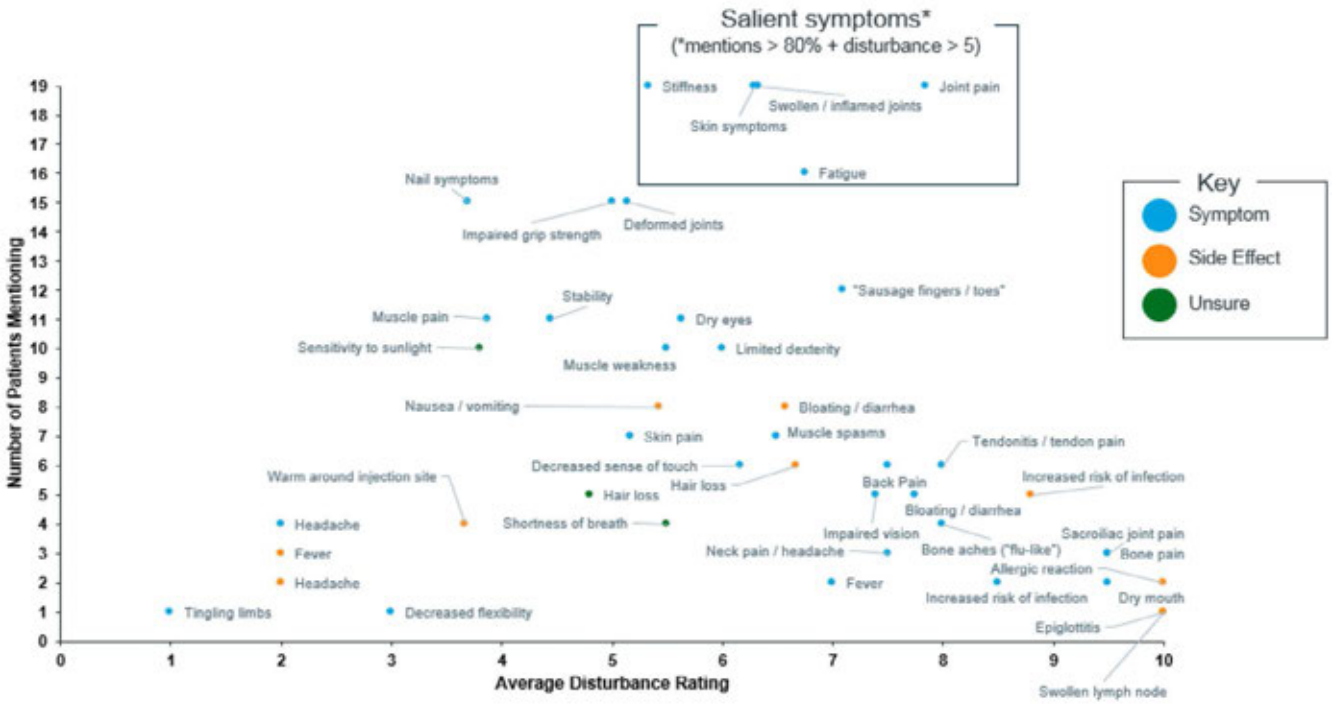
1. Identify the signs and symptoms of PsA experienced by patients, with a focus on fatigue, and how the disease and its treatment(s) impact patients' lives.

2. Assess the content validity of select PRO instruments and items to measure fatigue.

Methods: Qualitative interviews were conducted among patients with PsA recruited through the FORWARD databank, all of which satisfy the ACR classification for PsA. The most frequently experienced symptoms and impacts of PsA and the degree to which they disturbed patients' lives, were tabulated. Disturbance was evaluated on a scale from 0 (not at all) to 10 (greatly disturbs). Patients reporting fatigue were probed to describe the experience in their own words, and descriptors were recorded. Interviews were conducted and assessed on a rolling basis and recruitment continued until concept saturation was achieved.

Results: Nineteen PsA patients were interviewed for this study. A core set of PsA symptoms were identified by nearly all patients and with moderate to high average disturbance ratings (Figure 1): joint pain, skin symptoms, stiffness,

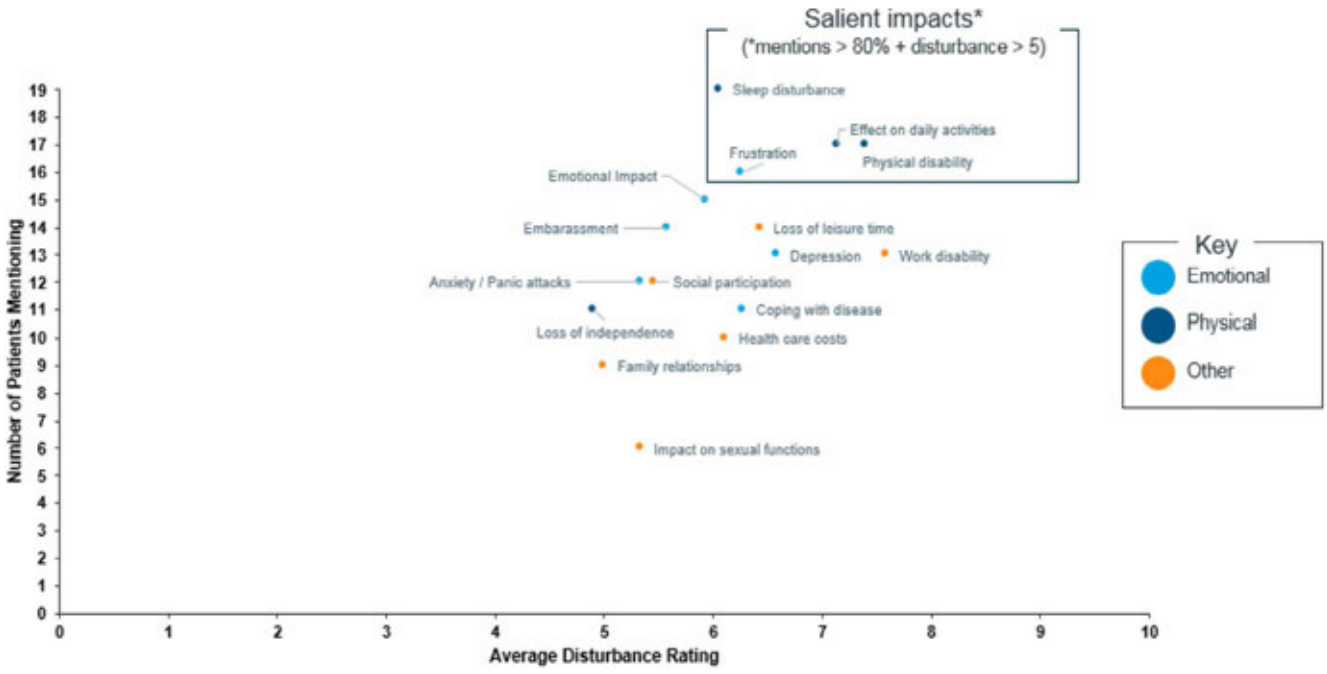
Figure 1. Salient Symptoms Reported by Patients in Qualitative Interviews (n=19)



swollen/inflamed joints, and fatigue. The most salient impacts (Figure 2) were sleep disturbance, physical disability, effects on daily activities, and feelings of frustration. Most common descriptors of fatigue included “fatigue,” “tiredness,” “lack of energy,” “mental fatigue,” and “exhaustion.”

Conclusion: Salient symptoms were consistent with those previously reported, along with a broader range of symptoms and impacts, which included fatigue. In addition to physical disability, others such as sleep disturbance, frustration, and effect of daily activities were common high impact themes that emerged.

Figure 2. Salient Impacts Reported by Patients in Qualitative Interviews (n=19)



Disclosure: K. Michaud, FORWARD, The National Databank for Rheumatic Diseases, 3, Pfizer, 2, Pfizer & Rheumatology Research Foundation, 2, Rheumatology Research Foundation, 2, University of Nebraska Medical Center, 3; **E. Alemao**, Bristol Myers Squibb, 1, 3, 4; **M. Nowak**, Bristol-Myers Squibb, 1, 3, 4; **R. Bruce**, Eisai, Inc., 5; **S. Cantor**, None; **C. Hintzen**, None; **P. Mease**, Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, Roche, UCB, 2, 5, Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB, 8, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Abbvie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer and UCB., 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB, 2, Abbvie, Amgen, Brsitol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Brsitol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Brsitol Myers Squibb,Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, Amgen, 2, 5, 6, 8, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, and UCB, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 2, 5, Boerhinger Ingelheim, 5, Bristol Myers Squibb, 2, 5, 8, Bristol Myers Squibb Co., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8, Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8; **K. DeBusk**, Roche, 1, 3, 4, Bristol-Myers Squibb, 1, 3, 4, Seattle Genetics, 1, 3, 4; **A. Ogdie**, Pfizer, 2, 5, Abbvie, 5, 8, Amgen, 5, 8, BMS, 5, Celgene, 5, 8, Corrona, 5, Lilly, 5, Novartis, 5, Novartis, 7.

Abstract Number: 2247

Patient Factors Associated with Willingness to Change Rheumatoid Arthritis Medications

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Evidence-based guidelines recommend escalation of therapy in patients with rheumatoid arthritis (RA) with inadequately controlled disease. However, some patients are hesitant to change therapies despite significant symptom burden. Understanding the patient factors that are associated with willingness to change therapy may inform the design of behavioral interventions to improve appropriate escalation of treatment in patients with RA.

Methods: Adult patients with self-reported RA who were enrolled in the ArthritisPower patient registry with a RAPID3 > 4 (range 0-10), treated with DMARDs in the past 6 months, and without potentially confounding conditions (e.g. fibromyalgia) were eligible to participate in the Confident Treatment Decisions for Living with Rheumatoid Arthritis (CONTROL RA) clinical trial. Patients were recruited by email to complete a compensated online survey. Participants' willingness to change RA treatment was determined at enrollment using the validated choice predisposition scale that reflects preference for changing RA therapies. Patients were asked "If at your next visit, your rheumatologist recommends that you change RA medication(s), would you be willing to do so?" This item was coded on an 11-point scale anchored by "Not willing at all" and "Extremely willing". Patients who answered 7-10 were categorized in the "more willing to change treatment" group, while those with a score of 0 - 6 were classified in the "less willing to change treatment" group. Bivariate tests and multivariable logistic regression evaluated the following characteristics associated with these two levels of willingness to change treatment: sociodemographic characteristics, biologic DMARD or conventional DMARD use, patient global assessment of disease activity (PGA), patient satisfaction with RA control, (yes vs no) personal attitudes favoring RA medications (calculated by surveying participants' agreement with 5 positive and 5 negative statements about use of medications in RA. Higher score represents more favorable attitude towards RA medications), patient-physician discussion on RA treatment goals occurring in the past year, subjective characterization of general health (5 point scale anchored by "excellent" and "poor"), and subjective readiness to change (Precaution Adoption Process Model). Subjective health literacy calculated by asking patients about their confidence in filling out medical forms.

Results: A total of 208 U.S. patients were recruited. Study participants were 90% Caucasian, 90% women, with high subjective health literacy and a mean (SD) age of 50 (11) years. In adjusted models, we found that compared to the less willing group, participants in the more willing to change group were more likely to have a higher PGA (OR 1.4 p = 0.0006, CI 1.1 – 1.6), and more likely to have a favorable attitude towards RA medication than those in the less willing group (95.1% vs 81.4%, p = 0.0042; OR 7.0, p = 0.0008, CI 2.2 – 21.8).

Table 1. Characteristics of patients with RA by willingness to change treatment status

Patient factors		Less willing to change (n = 86)	More willing to change (n = 122)	p value
Favorable attitude towards RA medication (higher score = more favorable attitude)		70 (81.4%)	116 (95.1%)	0.0042
Patient global assessment of present condition (0 = very well, 10 = very poorly)		4.9 (2.25)	6.0 (2.23)	0.0005
Age		48.8 (12.6)	50.1 (9.99)	0.67
Sex	Male	8 (9.4%)	13 (10.7%)	0.77
Race	White	76 (88.4%)	112 (91.8%)	0.41
Ever used biologics or conventional DMARDs		39 (45.3%)	57 (46.7%)	0.85
Patient satisfied with RA control	Yes	36 (41.9%)	45 (36.9%)	0.47
Treatment goals discussed in past year		64 (74.4%)	94 (77.0%)	0.66
General health	Excellent/Very good/Good	49 (57.0%)	58 (47.5%)	0.18
Readiness to change	Change not needed/haven't considered change	24 (27.9%)	23 (18.9%)	0.13

Table 2. Likelihood of willingness to change treatment status by associated patient factors

Patient factors	Variables	Odds Ratio	p value
Attitudes favor RA medication use	More agree vs More disagree/Neutral	6.986 (2.241 - 21.773)	0.0008
Patient global assessment of present condition	Continuous: 0 = very well, 10 = very poorly	1.362 (1.143 - 1.623)	0.0006
Age	Continuous	1.017 (0.988 - 1.048)	0.25
Sex	Female vs Male	0.913 (0.312 - 2.675)	0.87
Race	White vs Other	1.017 (0.343 - 3.014)	0.98
Ever used biologics or conventional DMARDs	Yes vs No	0.911 (0.490 - 1.695)	0.77
Patient satisfied with RA control	Yes vs No	2.141 (0.934 - 4.910)	0.07
Treatment goals discussed in past year	Yes vs No	0.895 (0.389 - 2.060)	0.79
General health	Excellent/Very good/Good vs Other	0.869 (0.422 - 1.790)	0.70
Readiness to change	Have considered/Not decided/Am changing/Already changed vs Change not needed/haven't considered change	1.843 (0.884 - 3.843)	0.10

Conclusion: Our study suggests that among patients with self –reported RA, having attitudes that favored RA medications and a higher patient global assessment of disease activity were independently associated with an increased willingness to change RA medications.

Disclosure: R. Vachhani, None; **L. Chen**, None; **R. O'Beirne**, None; **J. Melnick**, None; **E. Ruderman**, Pfizer, 2; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **M. Danila**, Pfizer, 2, Regeneron, 5.

Abstract Number: 2248

Legal Matters: Attitudes Regarding Marijuana for Medical Use Among Patients with Rheumatic and Musculoskeletal Disease

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: While there have been significant improvements in quality of life among people living with rheumatic and musculoskeletal disease (RMD) with the introduction of biologics and targeted therapies, patients often seek non-pharmacological alternative and complementary treatments, such as marijuana for medical use (MMU), to help manage their condition and symptoms. An understanding of patient use and perceptions of MMU is necessary to inform future research and care.

Methods: A 77-item cross-sectional survey was developed in partnership with RMD patient partners and administered online via CreakyJoints and the ArthritisPower research registry. Participants (pts) were eligible if they were ≥19 years of age, resided in the US and reported physician-diagnosed RMD. Pts reported on their current health status (NIH PROMIS Global Health), use and perceptions of MMU, and related information needs.

Results: A total of 1,059 pts completed the survey. A majority of pts were female (88%) and white (92%), with mean (SD) age of 57 (11) (Table 1). Of the total pts, 37% (n=387) reported use of MMU, either currently or in the past. Of those, a majority (93%) used it to manage a specific condition: 51% for rheumatoid arthritis, 46% for osteoarthritis, and 35% for fibromyalgia. Nearly two-thirds (62%) of current MMU users report using it at least once a day. Most current or past MMU users live in a state where marijuana is legal for medical reasons (77%), but only 40% have used a medical marijuana card to purchase it, with 60% citing the desire for use to be legal as a reason for using the card (Table 2). Top reasons for not using a medical marijuana card were marijuana not being legal for medical use where pt lives (42%), cost being more expensive through a medical dispensary (19%) and difficulty getting a card (18%). Among the 63% of all pts who had never used MMU, illegality (40%), potential impairment (24%), and not knowing where (21%) or how (20%) to obtain MMU were cited as top reasons for not using it. When asked about the likelihood of using MMU if it were legal where the pt lives, half of pts responded that they were likely to use it. The majority of pts (84%) living in states where marijuana is medically legal correctly identified their state as legal, whereas 66% of pts living in a state where medical marijuana is illegal knew that this was so. Overall, two-thirds of current or past MMU users informed their HCP about using MMU, but only 42% perceived that their HCP integrated it into their care (e.g. considering MMU part of pts' treatment regimen and advising on dosage). Of pts who live in states where marijuana is medically legal, 68% had informed their health care provider (HCP) of using MMU, whereas only 54% (p=0.02) informed their HCP in non-legal states.

A majority (62%) of participants expressed interest in participating in a trial on MMU treatment of RMD. Pts' top concern about a trial was ensuring participation would be legal (36%) (Table 3).

Table 1. Participant Characteristics, by Marijuana (MMU) Use

	Non-MMU Users (N=672)	Current and Past MMU Users (N=387)	p-value
Age, mean (SD)	57.8 (10.5)	56.0 (10.9)	0.007*
Female, n (%)	592 (88.1)	341 (88.1)	0.993
White, n (%)	616 (91.7)	362 (93.5)	0.269
College degree or higher, n (%)	332 (49.4)	172 (44.4)	0.120
Employed (full-time, part-time, self-employed), n (%)	268 (39.9)	142 (36.7)	0.305
Married, n (%)	416 (61.9)	211 (54.5)	0.056
Top 5 main conditions, n (%)+			
Rheumatoid arthritis	316 (47.0)	171 (44.2)	0.372
Osteoarthritis	149 (22.2)	85 (22.0)	0.937
Psoriatic arthritis	67 (10.0)	31 (8.0)	0.289
Fibromyalgia	54 (8.0)	38 (9.8)	0.321
Ankylosing spondylitis	24 (3.6)	26 (6.7)	0.020*
Time since diagnosis, years, mean (SD)	14.3 (10.7)	14.8 (11.2)	0.446
Current therapy, n (%)			
Biologic DMARDs	252 (37.5)	137 (35.4)	0.495
Targeted synthetic DMARDs only	21 (3.1)	6 (1.6)	0.118
Conventional synthetic DMARDS only	115 (17.1)	53 (13.7)	0.143
Corticosteroids only	29 (4.3)	19 (4.9)	0.655
No treatment or NSAIDS only	232 (34.5)	159 (41.1)	0.033*
Greater than a year on current therapy, n (%)	473 (70.4)	240 (62.0)	0.056
Satisfied with current therapy, n (%)	485 (72.2)	230 (59.4)	<0.001*
Living in state with legalized medical marijuana, n (%)	393 (58.5)	297 (76.7)	<0.001
PROMIS Global Physical Health, mean (SD)[1]	38.6 (7.6)	37.2 (7.1)	0.002*
PROMIS Global Mental Health, mean (SD)[1]	43.5 (8.8)	42.0 (8.6)	0.008*

*Statistically significant, p=0.05

+Not mutually exclusive

[1]Continuous scale from 20 (poor) to 80 (excellent)

Table 2. Reasons for medical marijuana card use among those currently using it (N=154)*

	n (%)
I want my marijuana use to be legal	93 (60.4)
It's the only way to access marijuana for medical use in my state	90 (58.4)
I want to know the chemical composition of what I'm receiving	65 (42.2)
I want to know that the chemical composition of what I'm receiving is the same each time	48 (31.2)
The medical dispensary has the chemical compositions that I want to try	41 (26.6)
The cost of purchasing marijuana is cheaper through a medical dispensary	23 (14.9)
Other	15 (9.7)

+Not mutually exclusive

Table 3. Concerns about clinical trial participation to examine marijuana for rheumatic and musculoskeletal disease treatment (N=1,059)[+]

	n (%)
I would want to be sure it is legal for me to be part of a marijuana trial	384 (36.3)
It might cost me money to participate	265 (25.0)
A trial might disrupt the prescribed treatment of my disease (not marijuana use)	250 (23.6)
I don't have concerns [exclusive choice]	244 (23.0)
I might receive a placebo drug	243 (23.0)
There might be side effects of the treatment	193 (18.2)
The treatment might not work	116 (11.0)
Other	110 (10.4)
A trial might take up too much of my time	97 (9.2)
A trial might disrupt my marijuana use	75 (7.1)
Participating in medical trials makes me uncomfortable	53 (5.0)

[+]Not mutually exclusive

Conclusion: Despite the lack of quality evidence to guide MMU, and regardless of its legality, many patients are using MMU to manage their RMD. Trials to inform MMU for RMD are urgently needed and patients are interested in participating in such studies.

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Abstract Number: 2249

Evaluation of Rheumatoid Arthritis Patients' Preferences Using Discrete Choice Experiment

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Background/Purpose: Rheumatoid arthritis (RA) exerts multifaceted burden through medical expenditures, productivity losses, disability, and intangible costs of pain, fatigue, and loss of functional capacity. Patient preference measures how they value a health outcome and it can be elicited by the trade-offs they place on different levels of the health outcomes. The study objective was to evaluate patients' preferences for pain/fatigue, functional capacity, disability and joint replacement surgery, employment losses, and out-of-pocket cost using a discrete choice experiment (DCE).

Table 1. Average Importance of Outcomes

Attribute	Importance	Lower 95% CI	Upper 95% CI
Chances of being disabled and require joint replacement surgery	23	21	24
Out of pocket treatment cost	23	21	25
Limitations in daily activities	20	19	21
Number of days missed work due to RA	19	18	20
Joint pain, swelling and tiredness	16	14	17

Table 2. Average Patient Preferences

Attribute	Attribute Level	Preference	Lower 95% CI	Upper 95% CI
Joint pain, swelling and tiredness	None	78	76	80
	Moderate	77	75	79
	Severe	Reference Level		
Limitations in daily activities	None	99	97	101
	Moderate	81	79	84
	Severe	Reference Level		
Chance of being disabled and require joint replacement surgery	Low (5%) or 5 in 100 chance	114	111	117
	Medium (40%) or 40 in 100 chance	88	86	91
	High (90%) or 90 in 100 chance	Reference Level		
Number of days missed work due to RA	1 day each month	95	92	97
	8 days each month	63	61	65
	24 days each month	Reference Level		
Out of pocket treatment cost	$20 per Month	114	110	118
	$500 per Month	81	79	82
	$2,500 per Month	Reference Level		

Methods: A DCE was conducted in a prospective cohort of adult (18+ years) RA patients on methotrexate treatment, identified from the member population of Kaiser Permanente Southern California health plan. The web-based DCE survey varied the following 5 conjoint attributes with 3 levels in each: (1) Joint pain, swelling and tiredness (None, Moderate, Severe) (2) Limitations in daily activities (None, Moderate, Severe) (3) Chances of being disabled and require joint replacement surgery (Low (5%); Medium (40%), High (90%)) (4) Number of days missed work due to RA (1 day/month, 8 days/month, 24 days/month) (5) Out of pocket treatment cost ($20/Month, $500/Month, $2,500/Month). After initial pilot testing, graphical representation of levels was used to convey magnitude to patients. The choice profiles for each respondent were randomly sampled from the full-choice design ensuring level balance and near-orthogonality within each respondent's profile. After completing 2 training tasks (not

analyzed), each respondent completed 12 random choice tasks that provided trade-offs to varying levels of the 5 outcomes. Hierarchical Bayesian models were used to evaluate individual patient preferences accounting for inter-patient heterogeneity.

Results: The DCE completion rate was 53% (237/448) and the mean age of the sample was 53 (±16) years with the majority (84%) of female. Of the 5 attributes, chance of disability and joint replacement surgery was tied with out-of-pocket treatment cost as the most important attributes (Table 1) and loss in functional capacity was deemed more important compared to missing work and pain/tiredness. The average preference was 114 (95% CI 111-117) higher for low (5%) vs. high (90%) chance of being disabled and require joint replacement surgery (Table 2). In contrast, the average preference of moderate vs. no joint pain, swelling and tiredness was just one-unit difference (Table 2).

Conclusion: Treat-to-target approach based on swelling/tenderness/pain activity indices can be made more effective by shared decision making to incorporate patient preferences which value functional capacity and treatment cost higher. Better understanding of patient preferences can inform gaps in the existing evidence-base to inform practice guidelines.

Disclosure: A. Kawatkar, Medac Pharma, Inc., 2, Bristol-Myers Squibb, 2, Shire, 2, Novartis, 2.

Abstract Number: 2250

Contribution of Personality Traits, Psychological Factors and Health Related Quality of Life on Medication Adherence in Patients with RA

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Non-adherence to long-term treatment is important in Rheumatoid arthritis (RA), as it can result in inadequate disease control and make rheumatologist to change the treatment strategy. Personality refers to individual differences in characteristic pattern of thinking, feeling and behaving. However, it is not clear that personality could predict medication non-adherence in patients with RA. The aim of this study is to investigate the association between personality traits and medication adherence and to identify the predictors of good medication adherence in RA patients including personality traits, psychosocial factors, disease activity, pain and health related quality of life (HRQoL).

Methods: Total 207 RA patients using disease-modifying antirheumatic drugs (DMARDs) was invited for an interview and questionnaire study from rheumatology outpatient clinics in Bucheon St. Mary's hospital in Korea. Medication adherence was measured with the Compliance Questionnaire of Rheumatology (CQR). Personality traits was analyzed with the five-factor model (neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness) with Korean version of Big Five Inventory 10 (K-BFI-10). A high level of each personality trait represents high scores (≧4 average score) of each personality item of five factor models. Psychological factors were also assessed

Table 1. Multivariate logistic regression on medication adherence

	OR	95% C.I.	
		Lower	Upper
Diabetes Mellitus	2.57	1.03	6.42
The number of prescribed medication	1.21	0.98	1.51
Total glucocorticoid dose (mg/month)	1.00	1.00	1.01
High conscientiousness	2.37	1.24	4.53

OR; odds ratio, C.I.; confidential Interval

with Patient Health Questionnaire (PHQ-9), General Anxiety Disorder 7(GAD-7) and the British Columbia Cognitive Inventory (BC-CCI), respectively. HRQoL and functional disability were evaluated with EuroQoL dimension (EQ5D) and health associated quality (HAQ). Multivariate logistic regression analyses were performed to investigate predictors of good medication adherence.

Results: A total of 207 RA patients (Female 83.1%, mean age 57 years, mean RA duration, 8.0 years) were participated. Non adherence to their DMARD prescription (CQR < 80) was reported in 66.2%. The number of daily prescribed pills was higher in the medication adherence group (P = 0.03). Concomitant oral glucocorticoids use and the dose was significantly associated with medication adherence. The personality trait, high level of conscientiousness and comorbid with diabetes mellitus were associated with better medication adherence (odds ratio [OR], 2.37; 95% confidence interval [CI, 1.24-4.53 and OR,2.57; 95% CI, 1.03-6.42, respectively) (Table 1). There were no significant differences in psychological factors and HRQoL between medication adherence and nonadherence group.

Conclusion: The personality traits were associated with medication adherence; conscientiousness was a predictor of medication adherence, among the five personality traits. Patients with diabetes mellitus showed higher medication adherence.

Disclosure: K. Ko, None; **S. Moon**, None; **J. Koh**, None; **J. Min**, None.

Abstract Number: 2251

Understanding Vulnerabilities in Diagnosis and Care of Childhood and Adult-Onset Lupus: A Qualitative Study

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SESSION INFORMATION

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Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences

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Background/Purpose: Systemic lupus erythematosus (SLE) poses complex diagnostic and management challenges, which may differ depending on whether SLE was diagnosed in childhood (cSLE) or in adulthood. We used qualitative methods to explore these issues with participants with childhood and adult-onset SLE to identify modifiable influences and coping strategies that could be leveraged to reduce areas of vulnerability and improve care.

Methods: Participants were recruited from two large academic medical centers, one with a Lupus Registry of individuals ≥18 years old with ≥4 1997 ACR classification criteria for SLE, and the other with a pediatric centralized data repository of cSLE patients. Three focus groups were held to explore potential vulnerabilities in SLE diagnosis and care including psychosocial aspects, medication use, the doctor-patient relationship, and the transition from pediatric to adult care. Focus groups were led by a trained moderator using a guide developed a priori, and were recorded and transcribed verbatim. A pediatric and adult rheumatologist reviewed transcripts and agreed upon preliminary concepts for coding. Codes were clustered into themes and transcripts were re-reviewed. A five-person study team adjudicated discrepant themes and chose key quotes. Qualitative software (Dedoose) was used for coding and thematic analysis of deidentified transcripts.

Results: Thirteen adults, 6 (46%) with cSLE, participated in three focus groups. The mean age was 35 (range 18-66); 5 participants identified as White, 5 Black, 2 Asian and 1 Hispanic. Themes were categorized into two domains: (1) challenges with SLE diagnosis and management and (2) patient coping strategies and modifiable factors of the SLE experience (**Table**). Participants identified five primary challenges: diagnostic odyssey, public versus private face of SLE ((discrepancy between the way one feels and the way one appears to others), SLE-related stresses, medication adherence, and transitioning from pediatric to adult care. Participants also offered specific strategies to address challenges, such as reducing stress and increasing sleep, and recognized modifiable factors in managing SLE and transitioning from pediatric to adult care including social support, open communication about SLE, and strong patient-provider relationships (**Figure**). Several participants with cSLE highlighted positive lessons learned through their experiences with SLE as part of their coping strategies, including empathy, resilience, and self-care skills.

Conclusion: Patients with childhood and adult-onset SLE identified common challenges, modifying influences and coping strategies based on their personal experiences. A strong patient-provider relationship emerged as a key modifiable factor improving the patient experience of living with SLE. Participants highlighted the importance of the human connection and trust in their medical team. The focus on optimism and empathy derived from their experience

Table: Description of themes and selected quotes		
Theme	**Description**	**Selected Participant Quotes**
Challenges in SLE		
Diagnostic Odyssey	The journey from onset of symptoms to diagnosis with SLE, including trauma of diagnosis	"I kept goin' back to the hospital, back to the hospital, back to the hospital.....When I say my chest was in excruciating pain, they was taking x-rays and everything. Then I finally had saw a different doctor, and the doctor saw that my lungs were completely dark. I'm like, I been comin' to you people for weeks.'"
Public vs. Private Face of SLE	Impact of SLE on life and identity, process of acceptance and sharing publicly, and coping with external changes in appearance and stigma and shame around SLE	"I kept the lupus hidden for a long time or as long as I could because I didn't wanna be thought of the lupus girl."
Medication Adherence	Side effects, system issues (ex: refills), changes in routine, forgetfulness, gap between knowing and doing	"Patients lie, and I think most patients overestimate when they answer to their doctor, "Have you been taking your medication?" "Yeah." "What percent?" "Like half the time," when it's not true. I do that ...sometimes, too, and I catch myself."
Transition from Pediatric to Adult Care	Logistics (ex: records transfer), difference in environment, patient responsibility, fear of losing relationship with first provider	"It's really all about the connection with your doctor. Cuz yeah, switching your medical records and things like that is—there's the whole logistics of it. I think it's just the relationship that you have with your doctor and then they haven't known you for such a long time. Having to switch to a new doctor who doesn't necessarily know you or know your medical record, but know you as a person."
SLE-Related Stress	Triggering disease flares, contributing to medication non-adherence	"I know sleep definitely affects me. My freshmen and sophomore years at university were really difficult with just stress. I would stress then I wouldn't eat well. I would just feel like I can't eat. Then I lost a lot of weight because of that, and then because of that I couldn't sleep. It's just like a cycle of stressing about my work, getting my work done, stressing about not being able to sleep, then not being able to sleep more. I would just walk in like a zombie and my professors would be like, 'Oh, you look really tired.' I'm like, 'I know.'"
Patient Strategies/Modifiable Factors		
Patient-Provider Relationship	Trust, two-way communication, role of research, bond with first rheumatologist	"I think it might be hard to stay motivated to take your prescription every day if you have a doctor you don't trust because then you might question whether or not they have your best interest in mind, or you may think that they're not aware of what the side effects are or compromises you need to make in order to keep taking this particular prescription. I think the doctor/patient relationship's very important."
Social Support	The role of parents, friends, social support networks, and technology	"I think my family has been real good about it and they just know—can kinda predict ahead what situations will bother me, so they try to help me with that. My brother was moving, my job was to watch the truck, so I didn't actually move anything. ... My mom is really supportive about taking me to doctor's appointments. She worries so much, so it can be—I know having lupus is hard, but sometimes I have to tell her, "You gotta keep it together."

with SLE was unique to several patients with cSLE. Leveraging factors that have improved the participants' experiences living with SLE may be used in future studies to address vulnerabilities in care.

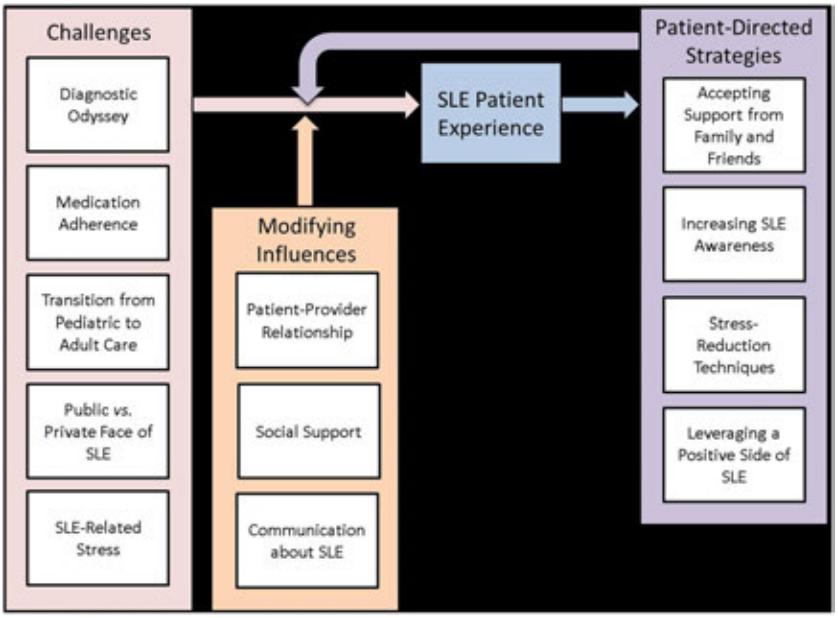

Figure: Interplay of themes and patient-directed strategies to cope with SLE

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Abstract Number: 2252

The #Worldlupusday 2019 Across Twitter: An Explorative Analysis of Spreading Concepts and Sentiment Perceptions on Social Media

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Social media nowadays has the capacity to disclose sentiments and opinions difficult to obtain elsewhere. This is of valuable importance in the healthcare sector as social networks mechanism can offer clues for health professionals coming from patients communities who reveal and express their needs, sentiments, as well indicators of self-reported quality of life [1]. The present study aims at illustrating the potential of using data from social media to unlock feelings and social network dynamics related to Systemic Lupus Erythematosus (SLE). SLE is still challenging because of the variety and complexity of symptoms, its impact on patients' quality of life. This study aimed at (1) collecting and analyzing tweets content using the (#) WorldLupusDay or #Lupus or #SLE released

Figure 1: Words cloud of tweeter frequency hashtags.

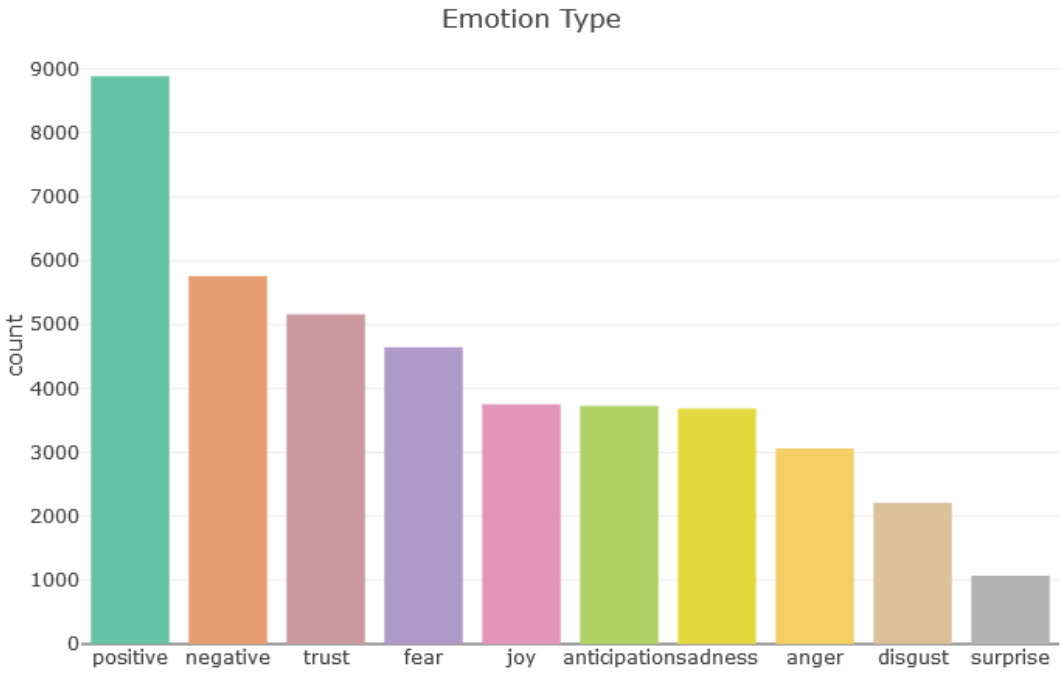

Figure 2: Tweets emotion distribution.

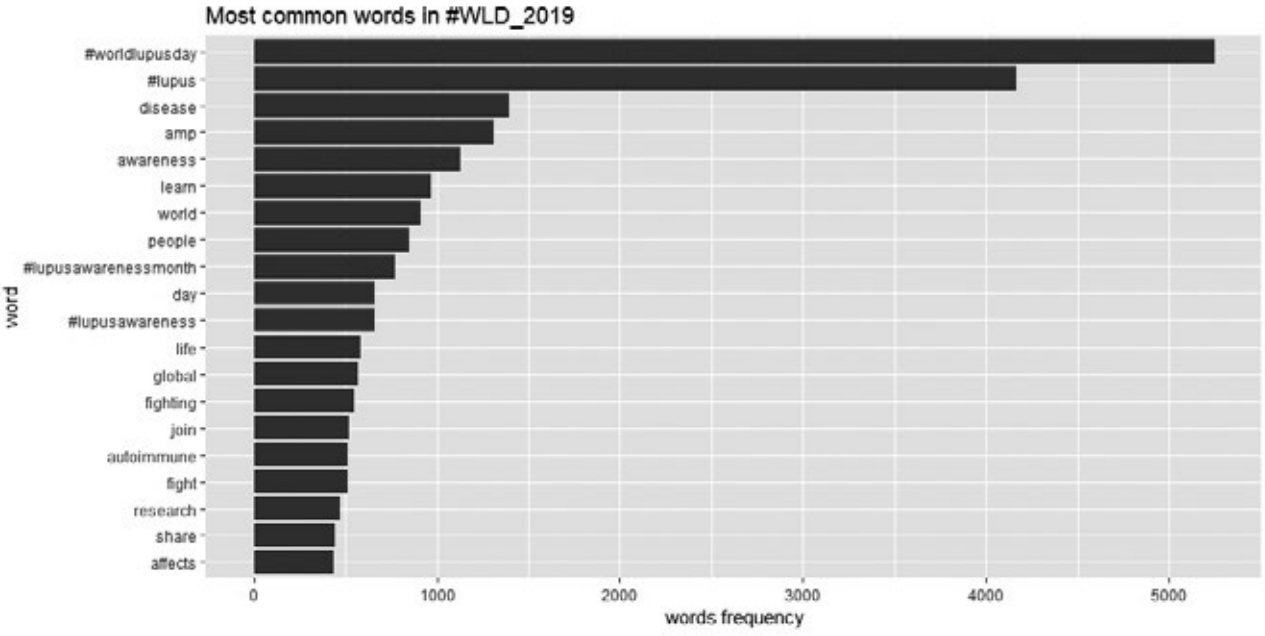

Figure 3: Top 20 most common words.

the 10th of May 2019; and at (2) using tweets text to compute sentiment score, explore main concepts and emotions, look at the most influencers' sentiment score and the trends shared about SLE disease.

Methods: As hashtags are the way that Twitter users categorize messages, promote ideas, and follow topics, using Twitter's public streaming API, all tweets released on the 10th of May 2019 worldwide and contain the hashtags #WorldLupusDay, #lupus and #SLE were used for the present analysis. Overall 6.162 tweets texts and account information (such as time, location, sources, followers count, friends count) created by 2.903 unique users account were extracted and used to perform a quantitative and qualitative analysis. The unique anonymous users' id identification number was used to gather the tweets text for each user and sentiment score values (anger, anticipation, disgust, fear, joy, sadness, surprise, trust, negative, positive) for each user were calculated using the NRC Emotion Lexicon[2] analysis. R software was used to analyze the retrieved tweets data.

Results: The most frequently words were Worldlupusday (*n* = 5247) lupus (*n* = 4165), disease (*n* = 1398) and amp (Accelerating Medicine Partnership; *n* = 773). The content analysis based on tweets text detected *awareness*, *research/share* and *more than my SLE* as frequently mentioned concepts in lupus world day tweets. Computed emotions values for all the tweets text collected revealed higher score in *positive* emotion (total score 8883; mean score = 1.4), and the lowers score in *surprise* emotion (total score 1068; mean score = 0.17). The overall distribution of the sentiment score tended to be more positive than negative with an average score of 0.57.

Conclusion: This study explored the potentiality of the social media network, in this case twitter, as a tool to identify users unmet needs and insights for sharing experience and feelings. Analyzing the emotions and sentiments score value evoked by terms identified in the users tweets text, a valuable picture of how users expressing themselves openly about their illness and perceptions on social media emerges, offering a possibility for gaining valuable insights of information missed using traditional tools for data collection.

Reference:

[1] W. C. Crannell, et. al. *A pattern-matched Twitter analysis of US cancer-patient sentiments*. J.of S. Res. (2016).
[2] Saif Mohammad, Peter Turney. *Crowdsourcing a Word-Emotion Association Lexicon*. C.. Intell; (2013).

Disclosure: S. Pirri, None; **V. Lorenzoni**, None; **L. Trieste**, None; **R. Talarico**, None; **I. Palla**, None; **C. Tani**, None; **E. Elefante**, None; **S. Cannizzo**, None; **I. Triulzi**, None; **S. Ticciati**, None; **G. Turchetti**, None; **M. Mosca**, None.

Abstract Number: 2253

Comparing Patient and Provider Perspectives on Long Term Biologic Use and Tapering in Stable, Well-Controlled Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: The 2015 American College of Rheumatology (ACR) and 2013 European League Against Rheumatology (EULAR) guidelines for management of rheumatoid arthritis (RA) conditionally recommend consider-

Table 1: Patient Demographic (n=30)	
Age, years	60(47-66)
Sex, females	21(70%)
Race, Caucasian	26(87%)
Seropositive (RF and/or ACPA)	15(52%)
Erosive disease on imaging	10(33.3%)

Table 2: Comparison of top concerns between well-controlled RA patients and their providers

Question	Patient Responses (n=20*)	Provider Responses (n=11)
Likelihood of considering tapering biologic (yes, %)	12 (60%)	4 (36%) [Always 1, Very likely 3]
Top concern about continuing biologic therapy long term	No concerns [10]	Clinical risk of long term biologic therapy [7]
	Infection [7]	Patient's coverage/affordability [3]
	Cancer [3]	Patient preference [1]
		Cost to healthcare system [0]
Top concern about reducing or stopping biologic therapy	Worsening Pain [9]	Flare [6]
	Loss of functional capacity/status [5]	Failed multiple therapies previously [2]
	Flare [4]	Patient preference [2]
	Medications less effective when restarting [1]	Risk of radiographic progression [1]
	No concerns [1]	Recapturing remission would be difficult [0]

ation of tapering biologic regimen in stable RA patients in remission with due consideration of patients' values and preferences. Given the paucity of data on perspectives, in this study we sought to explore and compare the patient and providers' perspectives on long term biologic use and biologic tapering.

Methods: Our study was performed using a survey instrument of adult patients with RA who were being followed at Allegheny Health Network Rheumatology between 01/01/2018 and 12/01/2018. The study included patients who have been on a biologic >6 months and clinically stable per review of their medical record (i.e. had no more than 1 RA flare in last 6 months, no change in DMARD or biologic dose in last 6 months). These patients were contacted to complete a questionnaire via a telephone survey designed to gather qualitative data on their perspectives about long term biologic therapy. A similar questionnaire was administered to their providers. Aggregate responses to each question were analyzed to compare patients and providers' perspectives, and to identify and predict patients' likelihood of considering tapering.

Table 3: Comparison of patients interested and not interest in biologic tapering			
	Patients interested in taper (n=13)	Patients not interested in taper (n=16)	p-value
Age, years	59(44-61)	61(55-68)	0.21
Duration of years	7.5(3-9)	16(8.5-27)	0.022
Duration on biologic, years	4(2-6)	4.5(2-8)	0.29
patient global assessment, at time of diagnosis (scale of 0-10; 10=worst)	9.5(8-10)	9.5(8-11)	0.88
patient global assessment, current (scale of 0-10; 10=worst)	3.5(2-4)	6.0(4.5-8.0)	0.005
On daily glucocorticoid, # patients	2(14%)	7(47%)	0.11
On DMARD therapy, # patients	10(77%)	11(79%)	0.9
Erosive Disease, # patients	4(29%)	6(38%)	0.71
RF/CCP positive, # patients	4(31%)	11(69%)	0.066
Well controlled RA per patient, yes	13(93%)	7(44%)	0.007
Previous biologic taper trial, yes	1(7.1%)	0	0.5
Previously failed biologics, yes	6(43%)	6(38%)	0.77
Concerns about long term biologic therapy, yes	9(64%)	7(44%)	0.26

Results: A total of 122 patients met our inclusion criteria. Of these, manual EHR review validated stable RA in 65 patients who were contacted for the telephone survey. 30 patient questionnaires were completed in entirety. Our cohort had the following characteristics: mean age of 55 years, 70% female, 86.7% Caucasian, 53.3% seropositive and 33.3% erosive disease (table 1). 20 of these 30 patients felt their RA was well controlled. 60% of the well controlled patients and 36% of the providers responded that they would consider biologic tapering as an option (table 2). Patients that would consider biologic tapering felt their RA was well controlled with lower patient global assessment scores and had a shorter duration of RA compared to those who did not consider tapering (table 3). The top concern of stable RA patients and their providers about long term biologic therapy was risk of infection and malignancy. Top concern of tapering biologics among both groups was risk of worsening RA (flare, function, pain). Of note, 10 patients (50%) had no concern about being on long term biologic therapy (table 2).

Conclusion: Patients on long term biologic therapy and stable, well-controlled RA were found to be more likely to consider tapering biologic therapy compared to their providers (60% versus 36%) in our survey-based study. Patients and providers shared the same top concerns about continuing or tapering biologic therapy. Patients with well-controlled and a shorter duration of RA were more likely to consider tapering as an option. This information is paramount in designing and implementing our divisional RA Biologic Tapering Initiative (RABTAP), but also to have a more effective and informed shared-decision with patients regarding continuing or tapering long-term biologic therapy in well-controlled RA.

Disclosure: P. Webster, None; **N. Wilson**, None; **C. Payne**, None; **K. Shields**, None; **T. Sharma**, None.

Abstract Number: 2254

The Urge for Mobile Apps in Rheumatology – a German Patient Perspective

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Background/Purpose: Mobile health applications have the potential of saving costs, empowering patients and improving treatment outcomes. Furthermore, the use of medical apps in routine care is increasing among rheumatologists[1]. In order to turn digitalization and all its benefits into practice it is crucial to include the main stakeholders. We therefore wanted to explore the needs and attitudes of patients with rheumatic diseases concerning mobile apps.

Methods: Between December 2018 and January 2019, 224 consecutive patients with rheumatoid arthritis, psoriatic arthritis and spondyloarthritis were seen at one rheumatology outpatients clinic and asked to complete a paper-

Table 1: patient demographic information

Factor		n (total = 224)	Mean, %
Age			
	<30	14	6
	30-39	35	16
	40-49	37	17
	50-59	65	29
	60-70	61	27
	>70	12	5
Gender			
	Male	90	40
	Female	134	60
Diagnosis			
	RA	127	57
	SpA	40	18
	PsA	57	25
Years since diagnosis		224	18
Patient global disease activity (VAS 0-10)		220	4

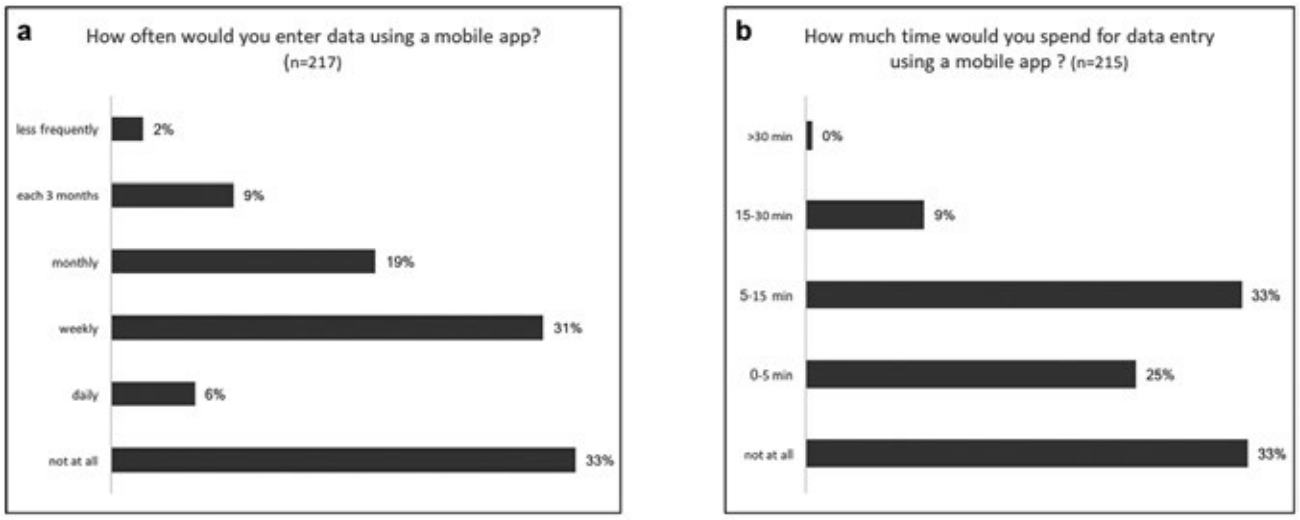

Figure 1

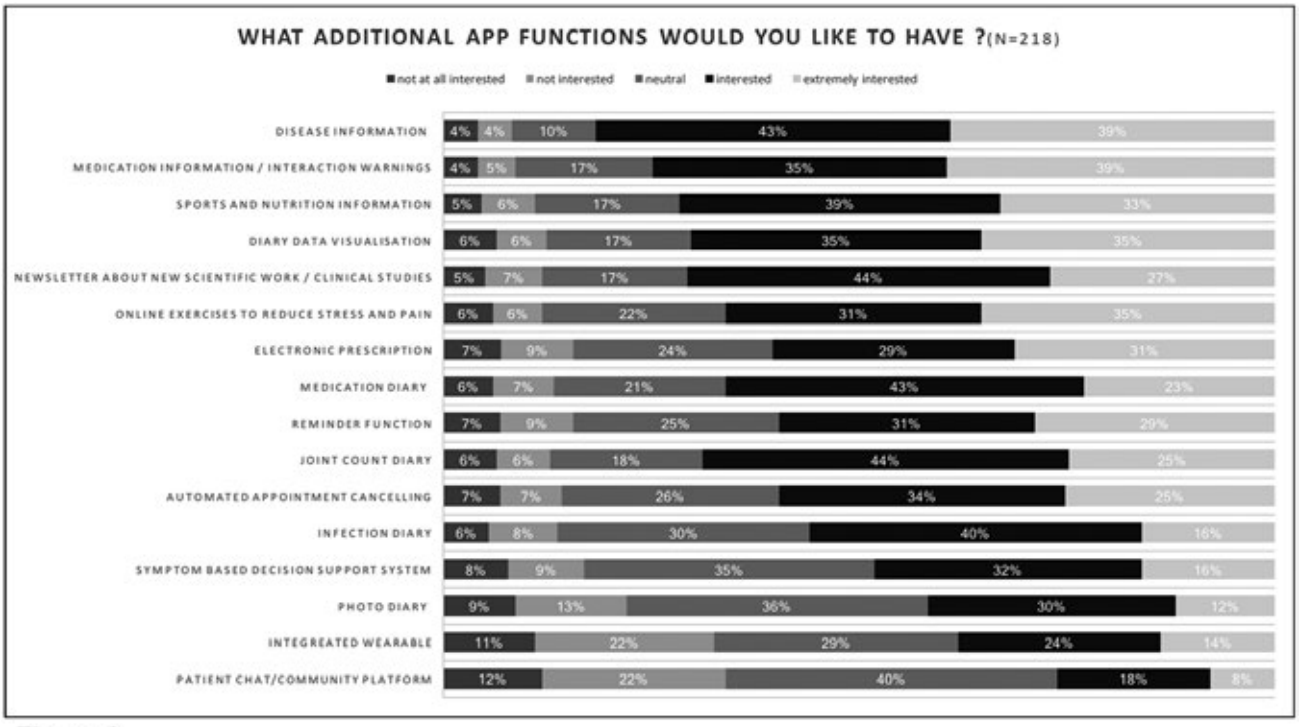

Figure 2

based survey. This survey evaluated the individual mobile app experiences, preferences and attitudes. This study was approved by the Ethics committee (No. 418-18B) and all patients consented to the study.

Results: Patient demographics are displayed in Table 1. 198 patients (90%) regularly used a smartphone, 103 patients (46%) regularly used social media. 144 (65%) patients believed that using medical apps could be beneficial for their health. Only 9 patients (4%) were currently using medical apps and only 24 patients (11%) stated that they knew useful rheumatology websites / mobile apps. 211 patients (96%) would agree to share their mobile app data

for research purposes if data was transferred by a secure and anonymized / pseudonymized method. 166 patients (76%) would welcome official mobile app recommendations from the national rheumatology society. Only 33% would not consent to future data entry (Figure 1), whereas average time for entry should not exceed more than 5 minutes. The most popular three app features desired were information about the disease, medication and sports and nutrition (Figure 2).

Conclusion: Most patients possessed smartphones and believed that using medical apps could be beneficial for their health. They were also willing to share data for research purposes. However only a small minority were currently using medical apps or knew useful apps. Patients stated that they would welcome app recommendations and information provided by apps. We could successfully identify unmet needs and patient priorities to accelerate and guide the way of mobile apps into routine rheumatology care.

References:

1. Knitza, J. et al. *[Use of medical apps and online platforms among German rheumatologists : Results of the 2016 and 2018 DGRh conference surveys and research conducted by rheumadocs].*Z Rheumatol, 2018.

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Abstract Number: 2255

Adherence to Subcutaneous Anti-tnf Therapies in Chronic Inflammatory Rheumatism and Therapeutic Education

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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The treatment options for chronic inflammatory rheumatism (CIR) have grown over the last few years with the emergence of anti-tumor necrosis factor (anti-TNF) agents. Patients' adherence to this treatment, however, appears suboptimal (Smolen et al, 2019). Given that therapeutic patient education (TPE) is now a recognized factor for improving treatment compliance, we sought to evaluate adherence to subcutaneous anti-TNF therapies by means of the Morisky Medication-Taking Adherence Scale-4 items (MMAS-4©) (Morisky and al, 1986; Morisky and al, 1990; Morisky & DiMatteo, 2011) among patients with CIR (rheumatoid arthritis [RA], ankylosing spondyloarthritis [AS], and psoriatic arthritis [PsA]) benefiting from different models of TPE.

Methods: This is a retrospective, observational monocentric study of current care practices. We evaluated patients receiving subcutaneous anti-TNF agents and benefitting from TPE from 2009 to 2013, categorized according to educational model (M1:individual informative consultation; M2: individual TPE; M3: individual and group TPE sessions). For all educational models, the patients were informed of the potential benefits and risks of the treatments. Adher-

ence was assessed by means of the MMAS-4© as follows: good adherence (MMAS-4© = 4), moderate adherence (MMAS-4© = 2-3), and poor adherence (MMAS-4© = 0-1).

Results: In total, 193 patients were included, comprising 124 women. The mean population age was 53.3 ± 14.8 years old; the mean CIR duration was 10 years [5; 18], with 113 patients suffering from RA, 73 from AS, and seven from PsA. Of the 193 patients, 107 (55.4%) received etanercept, 58 (30.1%) adalimumab, 11 (5.7%) certolizumab, and 17 (8.8%) golimumab. A total of 146 (75.7%) patients presented good adherence, 34 (17.6%) moderate adherence, and 13 (6.7%) poor adherence. The M1 model was followed by 92 patients, M2 by 80, and M3 by 21, with lower adherence observed in the M3 group compared to M1 and M2 (p=0.04). Old age was the only factor correlating with good adherence (p = 0.005). Level of knowledge had no significant impact on adherence (p=0.91). In this study, a similar rate of good adherence (70.6% - 74.1%) was found to that of the European-wide study by Smolen involving 3,390 CIR patients using the MMAS-4©. We found that the older subjects of our study presented the best treatment adherence, as was also observed by Smolen. As regards the specific educational model, we demonstrated that adherence dropped in patients receiving both individual and group TPE compared to those attending only individual TPE sessions or simple informative consultations. We were unable, however, to refer to other works from the literature, and it is possible that the group TPE analyzed in our study generated false beliefs introduced by certain patients. Actually, fear of treatment was shown to be inversely correlated to treatment compliance in CIR.

Conclusion: Our study demonstrated good adherence to anti-TNF treatment in patients receiving treatment education, particularly when it took the form of individual sessions.

Disclosure: F. Fayet, None; **A. Fan**, None; **M. Rodere**, None; **C. SAVEL**, None; **B. Pereira**, None; **M. SOUBRIER**, None.

Abstract Number: 2256

Patient Beliefs and Perceptions of Methotrexate for the Treatment of Rheumatoid Arthritis and Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate (MTX) is a frequently used therapy in both Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) due to its beneficial effects in both populations. Despite the well-known benefits of MTX, it is associated with a number of potential side effects and tolerability issues including nausea and fatigue, gastrointestinal toxicity, skin reactions, headaches, mouth sores and more serious, though rare, side effects such as liver toxicity and bone marrow suppression. The combined risks of rare but potential adverse events along with frequently reported side effects such as nausea and fatigue may add to patient burden of dealing with a chronic disease. Furthermore, many RA and PsA patients discontinue MTX with or without their physicians' knowledge (Mease, 2013). Currently, there is a gap in patient-centered studies focusing on patients' experience with MTX and how this relates to adherence and consequently patient outcomes. The purpose of this ongoing study is to examine patient beliefs and perceptions relating to methotrexate therapy for the treatment of RA and PsA.

Table 1: Participant Characteristics by Current or Previous Methotrexate (MTX) Treatment (N=121)

Characteristics	Participants (N=121)	Currently on MTX (n=49)	Previously on MTX (n=72)
Female, n (%)	108 (89.3)	42 (85.7)	66 (91.7)
Age, years, mean (SD)	57.2 (8.8)	56.5 (8.5)	57.8 (9.0)
White, n (%)	113 (93.4)	45 (91.8)	68 (94.4)
Bachelor's degree or higher, n (%)	58 (47.9)	30 (61.2)	28 (38.9)
Employment Status, n (%)			
Employed (full-time, part-time, self-employed	41 (33.9)	23 (46.9)	18 (25.0)
Not employed (unemployed, student, disabled, retired)	80 (66.1)	26 (53.1)	54 (75.0)
Current RA/PsA therapy, n (%)			
No treatment or NSAIDS only	3 (2.5)	0 (0.0)	3 (4.17)
Corticosteroids only	1 (0.8)	0 (0.0)	1 (1.4)
Non-biologic DMARDs only	46 (38.0)	21 (42.9)	25 (34.7)
Biologic DMARDs	72 (59.5)	28 (57.1)	44 (61.1)
Duration of current methotrexate use, years, mean (SD)	6.2 (5.9)	6.2 (5.9)	-
Current folic acid use, n (%)	52 (98.1)	48 (98.0)	-
BMI, mean, (SD)	31.2 (7.7)	32.7 (8.6)	30.1 (6.8)

Table 2: Side Effects Related to Methotrexate (MTX) (N=121), n (%)

Side Effect	Participants (N=121)	Currently on MTX (n=49)	Previously on MTX (n=72)
Any	83 (68.6)	26 (53.1)	57 (79.2)
Fatigue/tiredness	51 (42.1)	21 (42.9)	30 (41.7)
Nausea	42 (34.7)	10 (20.4)	32 (44.4)
Hair thinning	37 (30.6)	12 (24.5)	25 (34.7)
Hair loss	37 (30.6)	11 (22.4)	26 (36.1)
Brain fog	34 (28.1)	15 (30.6)	19 (26.4)
Flu-like feeling	32 (26.4)	11 (22.4)	21 (29.2)
Mouth sores or ulcers	29 (24.0)	10 (20.4)	19 (26.4)
Other	27 (22.3)	7 (14.3)	20 (27.8)
Abdominal pain	21 (17.4)	1 (2.0)	20 (27.8)
Diarrhea	21 (17.4)	6 (12.2)	15 (20.8)
Loss of appetite	20 (16.5)	6 (12.2)	14 (19.4)
Difficulty sleeping	16 (13.2)	3 (6.1)	13 (18.1)

Methods: Adult US patients in the ArthritisPower registry with self-reported rheumatoid arthritis RA or PsA taking or previously taking MTX were invited to participate in the survey via email invitation. Participants (pts) were either current or past users of MTX who completed a brief online survey. Recruitment for this study is ongoing. Descriptive statistics were conducted on data collected to date.

Results: As of May 2019, the survey had been completed by 121 pts of whom 88.4% were living with RA and 22.3% with PsA, not mutually exclusive. Mean age was 57.2 (8.8) years, 89.3% female, 93.4% White, with mean BMI 31.2 (7.7) (Table 1). Mean duration of MTX treatment among current users was 6.2 (5.9) years. Among respondents, 49

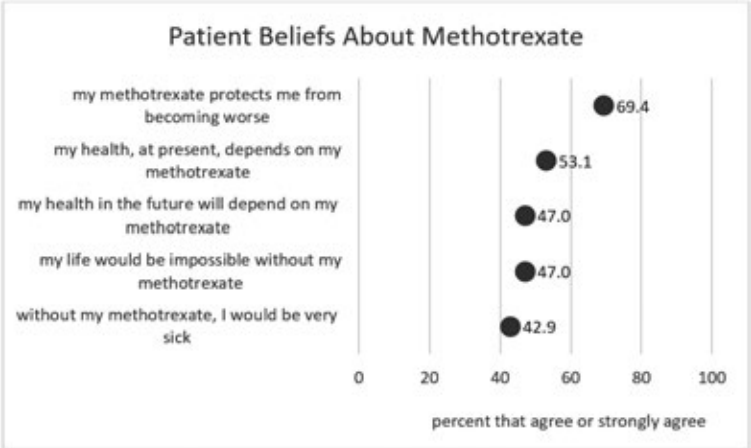

Figure 1: Patient Beliefs Among Current Users of Methotrexate (n=49)

(40.5%) were currently taking oral MTX and 72 (59.5%) had taken it previously but stopped. The majority of pts reported experiencing side effects on MTX: 26 (53.1%) among current users of MTX, 57 (79.2%) among those who previously discontinued MTX (Table 2). Fatigue was the most common symptom among current users, while nausea, abdominal pain, hair thinning, and difficulty sleeping were more common among discontinuers. When asked specifically, 57.1% of current users and 69.4% of discontinuers stated that they experienced fatigue within a day of their MTX dose. Nevertheless, among those currently taking MTX, most (69.4%) felt that MTX protects them from becoming worse and 47.0% agreed that their life would be impossible without MTX (Figure).

Conclusion: A majority of patients experience side effects such as fatigue, nausea and brain fog that they attribute to MTX. Importantly, people living with RA or PsA acknowledge the importance of taking MTX to manage their condition.

Disclosure: W. Nowell, AbbVie, 1, Allergan, 1, Biogen, 1, BMS, 1, CVS, 1, Eli Lilly, 1, Global Healthy Living Foundation, 3, GSK, 1, Merck, 1, Pfizer, 1, Stryker, 1; **E. Karis**, Amgen, 1, 3, Amgen Inc., 3, 4; **K. Gavigan**, Global Healthy Living Foundation, 3; **L. Stradford**, Global Healthy Living Foundation, 3; **S. Stryker**, Amgen Inc., 3, 4, Amgen, Inc, 3, 4; **S. Venkatachalam**, Global Healthy Living Foundation, 3; **G. Kricorian**, Amgen Inc., 1, 3, 4; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5.

Abstract Number: 2257

Patient and Clinical Characteristics Associated with Increased Willingness to Adopt RA Treatment After an Educational Intervention: An Analysis of the Confident Treatment Decisions for Living with Rheumatoid Arthritis (CONTROL-RA) Trial

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences

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Background/Purpose: The treat to target (T2T) treatment strategy is associated with better clinical outcomes in patients with rheumatoid arthritis (RA). We have previously found that a direct-to-patient video intervention aimed to increase knowledge about T2T was associated with increased willingness to adopt RA treatment. The goal of this study was to evaluate patient and clinical characteristics associated with improved willingness to adopt treatment.

Methods: The CONTROL-RA trial, as previously reported, enrolled participants with self-reported RA, with RAPID 3 >4 (range 0-10) and without potentially confounding conditions or who had been using disease modifying anti-rheumatic drugs (DMARDs) in the past 6 months. Outcomes were collected using compensated surveys. Participants completed a baseline survey, viewed the educational intervention and completed the follow up survey immediately after. Intervention group participants viewed up to 6 videos (minimum of 2, mean duration 2 min) on topics relevant to T2T. We performed a multivariate analysis, where the primary outcome was pre-post difference in patient-reported

Table 1: Patient characteristics by level of engagement with the intervention videos

	High Engagement (N=80)	Low Engagement (N=24)	p
Age, mean (SD), years	50.4 (10.09)	45.8 (12.26)	0.06
Race, white, N (%)	71 (88.8%)	21 (87.5%)	0.88
Sex, female, N (%)	72 (90.0%)	20 (83.3%)	0.37
Biologic disease modifying antirheumatic drug (DMARD) use, ever, N (%)	23 (28.8%)	6 (25.0%)	0.72
Conventional DMARD use, ever, N (%)	26 (32.5%)	7 (29.2%)	0.76
General health, good or better, N (%)	40 (50.0%)	13 (54.2%)	0.72
Health literacy, excellent, N (%)	78 (97.5%)	24 (100.0%)	0.44
Familiar with T2T, N (%)	40 (50.0%)	14 (59.3%)	0.48
Baseline willingness to adopt treatment, mean (SD)	7.1 (2.26)	5.5 (2.62)	0.01
Change in willingness to adopt treatment after intervention, mean (SD)	0.6 (1.83)	0.3 (1.37)	0.57
Baseline decision conflict, mean (SD)	33.6 (17.06)	29.4 (15.85)	0.25

Table 2: Characteristics associated with improved willingness to adopt RA treatment

Variable	β	p	95% CI
Baseline willingness to adopt treatment	-0.49	<0.0001	-0.63 , -0.35
High engagement with intervention	0.53	0.14	-0.17 , 1.24
Age	0.03	0.04	0.00 , 0.06
Female sex	-0.62	0.16	-1.49 , 0.25
Biologic DMARD use, ever, yes	0.64	0.08	-0.08 , 1.37
Conventional DMARD use, ever, yes	0.11	0.76	-0.59 , 0.81
General health, good or better	0.20	0.57	-0.49 , 0.88
Health literacy, excellent	-1.49	0.14	-3.48 , 0.49
Familiarity with T2T, yes	0.30	0.32	-0.30 , 0.90
Patient global assessment	0.07	0.42	-0.10 , 0.25
Patient acceptable symptom state, yes	-0.75	0.07	-1.57 , 0.07
Decision conflict about treatment change	0.02	0.09	0.00 , 0.04
Readiness for treatment change	0.28	0.48	-0.52 , 1.08
Personal attitudes favoring medications	0.08	0.05	0.00 , 0.16

willingness to adopt treatment. The following factors were considered: extent of engagement (e.g. high engagement group watched >80% of each of the 6 videos vs low engagement group watched less), age, sex, race, prior biologic/DMARD use, general health, health literacy, familiarity with T2T, patient global assessment, patient acceptable symptom state (PASS), decision conflict about treatment change (decision conflict scale, lower score is better), readiness for treatment change (precaution adoption process model) and personal attitudes favoring medications (10 items surveying patient attitudes regarding acceptable medication risks vs benefits; higher score is more favorable).

Results: Responses of 104 participants in the intervention group were analyzed (Table 1). Participants were 92% white, 92% women, with a mean age of 49 years. A total of 80 (77%) participants were classified in the high engagement group. Participants classified in the high engagement group had higher baseline willingness to adopt treatment than those in the low engagement group (7.1 vs 5.5, p=0.006). The pre-post difference in willingness to adopt treatment was 0.6 in the high engagement group and 0.3 in the low engagement group (p = 0.57). In multivariable models the level of engagement with the intervention was not associated with improved willingness to adopt treatment (p=0.14). Lower baseline level of willingness to change RA treatment, older age and personal attitudes favoring medications were associated with improved willingness to adopt RA treatment (Table 2).

Conclusion: We observed a high level of engagement and were thus not able to discern a dose-response relationship between our intervention and improved willingness after the intervention. Interestingly, those with higher willingness to change treatment were more likely to view the educational intervention, suggesting that those who are less open to treatment change may need additional support to get involved with this type of educational program.

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Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **M. Danila**, Pfizer, 2, Sanofi Regeneron, 5.

Abstract Number: 2258

Causes of Influenza Vaccine Hesitancy in Rheumatoid Arthritis and Adults with Juvenile Idiopathic Arthritis

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

Background/Purpose: Vaccine hesitancy -the reluctance or refusal to vaccinate despite the availability of vaccines- is one of the threats to global health set by the World Health Organization in 2019. Adults with rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA) have a greater risk of influenza-related morbidity and mortality, however in this population, vaccine uptake remains suboptimal. This study evaluated the underlying reasons for influenza vaccine hesitancy among RA and JIA patients.

Methods: Between 2016 and 2018, 4 focus groups (FG) of RA and JIA patients were conducted at a large Canadian teaching university hospital. In addition, 8 individual telephone-based semi-structured interviews were done with patients who refused to both get the influenza vaccine and participate in the FG. Barriers of influenza vaccination were discussed. All encounters were transcribed verbatim, uploaded into MAXQDA 12, and thematically analyzed.The analytic strategy was guided by an existing theoretical hesitancy model proposed by the Strategic Advisory Group of Experts (SAGE) on immunization.

Results: Participants wereRA (n=23) and adult JIA (n=5) patients, 48±17.3 years-old (mean ± SD, age range= 20-74), English speakers, and mostly women (82%). Identified barriers to vaccination pertained to three main levels, namely: patients, health care-providers and health-care system. At the patient level, limited knowledge about the value and mechanisms of action of inactivated vaccines and the increased risk of infection associated with RA/JIA, as well as poor overall health literacy, were identified as causes of concerns, misconceptions or fears about influenza vaccination. Negative influence from relatives, peers and media, and in some cases the perception that vaccines are promoted to benefit the pharmaceutical industry were also reasons of hesitancy. At the level of health care provider, RA/JIA patients indicated that the limited time to discuss about vaccines is a key cause of vaccine hesitancy. Aspects related to the health-care system mainly revolved around organization, including waiting time and accessibility to vaccines as causes of vaccine hesitancy.

Conclusion: The causes of influenza vaccine hesitancy among RA/JIA patients are multiple. Vaccine specific issues, contextual and individual influences affect RA/JIA patients' vaccination decisions. Specific multi-level approaches

enhancing knowledge-awareness and facilitating communication with health care providers could reduce vaccine hesitancy.

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Abstract Number: 2259

Physical Challenges in RA: A Qualitative Study of an Online Patient Support Group

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Background/Purpose: Patients with rheumatoid arthritis (RA) face a number of challenges which adversely affect their quality of life. The objective was to qualitatively evaluate content of online discussions on their perceived physical challenges posted by patients with RA.

Methods: Participants were adults 18 years or older, living the United States or Canada, diagnosed with RA and enrolled in a trial assessing the effects of social networking on chronic disease management in RA, using a private patient support group on Facebook. Different topics for discussion were posted weekly by a moderator. We collected the discussions posted by the participants on their perceived physical challenges and compiled them into a database. The data was coded using Dedoose, an online application for qualitative data analysis. We used a grounded theory approach and thematic content analysis to synthetize and categorized the codes into major themes.

Results: The group had 92 registered members. Sixty-four members comprising 60 females and 4 males participated actively by contributing to the discussion. They ranged in age from 24 to 71 years, 93.8% were non-Hispanic white, 68.8% were married or living with a significant other or partner and 61% had a Bachelor's degree or higher educational level. Participants had been diagnosed with RA between 1 and 9 years prior to the study. A total of 356 posts were found including 25 by the moderator. Number of posts per active participant ranged between 1 and 60. The major themes identified included: i) Perceived physical challenges, ii) Psychological manifestations, iii) Social effects of living with RA, and iv) Coping mechanisms.

Specific physical challenges commonly identified by participants included fatigue, pain, stiffness and inability or difficulty in carrying out simple daily tasks. Psychological manifestations included insomnia, brain fog, frustrations particularly from being misunderstood, and depression. Social effects included disruptions in their social engagements, family lives, difficulty in keeping up with friends and demands of work life. Coping mechanisms included use of medical therapies including pharmacotherapy and surgery, attitudinal changes, lifestyle modifications such as

going slowly in the mornings, getting up a bit early and not scheduling appointments before 10 am, and using social support.

Conclusion: Patients with RA face a myriad of physical challenges which may take a toll on their social lives and mental states. Our evidence suggests a beneficial effect for interventions designed to increase education or conversation between patients and their health care providers to address the identified issues.

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Abstract Number: 2260

Patients' Journeys Through Giant Cell Arteritis: A Qualitative Study

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SESSION INFORMATION
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Background/Purpose: Diagnosis of giant cell arteritis (GCA) is difficult due to multiple presenting symptoms, and access to care may be delayed because often multiple providers are involved in the diagnosis of GCA and disease management. Treatment with high-dose glucocorticoids (GCs) can relieve symptoms and prevent vision loss, but GC-related adverse events are common; GCA often relapses once GCs are tapered. The purpose of this study was to understand the GCA patient care pathway and unmet needs in GCA through in-depth patient interviews.

Methods: US patients with GCA were recruited through outreach to physicians and The Vasculitis Foundation. Extensive individual interviews with patients were conducted by qualitative researchers by phone or in person and explored patients' perspectives and experiences from the onset of GCA symptoms to diagnosis and disease management. The qualitative data collected were analyzed using human-centered design methodology, including patient typologies (personas: optimist, fearful, stoic or despondent), forced temporal zoom (journey maps), forced semantic zoom (stakeholder system mapping) and affinity mapping for pattern recognition of unmet needs.

Results: A total of 28 patients were interviewed; 23 (82%) were women and mean age was 69 years (**Table**). The number of patients in each persona category is shown in the **Table**. Stoic and optimist personas had medium to high levels of self-advocacy and a positive/engaged attitude about their condition, while fearful and despondent personas had low levels of self-advocacy with disengaged/negative attitudes toward their condition. Patients often ascribed their milder GCA symptoms to causes such as stress and did not consult a physician until they developed moderate to severe symptoms. After diagnosis of GCA, all patients received GCs with little information on the chronicity of GCA or treatment alternatives to GCs. Overall, patients managed their GCA independently, and sought to balance relief of GCA symptoms with the adverse effects of GCs. Patients concentrated on tapering and discontinuing GCs, with less concern about relapse. Furthermore, patients who were most uncomfortable with the adverse effects of GCs often waited until their GCA symptoms became debilitating before telling their physician. Almost all patients reported searching for a support group after the diagnosis.

Table. Demographics of Patients With GCA Who Participated in Interviews and Personas Based on Analysis of Qualitative Interview Data

	Patients N = 28
Age, mean, years	69
Women, n (%)	23 (82)
Interview type, n (%)	
Phone	15 (54)
In person	13 (46)
US region, n (%)	
Midwest	10 (36)
Northeast	6 (21)
South	5 (18)
Mid-Atlantic	4 (14)
West	3 (11)
Persona, n (%)*	
Optimist	9 (32)
Despondent	9 (32)
Fearful	8 (29)
Stoic	6 (21)

* Some interviewees fit into multiple personas.

Conclusion: Patients with GCA experience adverse effects from GCs and want a clearer understanding of treatment options; they remain focused on reducing their GC dose and need access to support groups. For those with inflammatory comorbidities, GCA diagnosis is another burden in a debilitating journey resulitng in a sense of disempowerment and resignation toward their condition and limited treatment options. Patients' attitudes and self-advocacy vary depending on their personas; recognizing these personas may help HCPs coordinate patient care. Increased awareness of GCA among patients and HCPs may accelerate the path to diagnosis and treatment, and emerging therapies may help reduce GC burden.

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Abstract Number: 2261

Post Traumatic Stress Disorder in Patients with Rheumatoid Arthritis

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Session Date: Tuesday, November 12, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: There is growing evidence that complex interactions between individual's genetic susceptibility, immunological processes, and environmental factors such as stress , increase the risk of developing Rheumatoid Arthritis (RA). For this reason, disorders associated with severe stress such as post-traumatic stress disorder (PTSD) have been implicated in various autoimmune pathologies.

Objectives: To estimate the frequency of traumatic events prior to the diagnosis of RA. To determine the frequency of PTSD in patients with traumatic events prior to the diagnosis of RA. To compare demographic, clinical, serological characteristics, existence of depression and anxiety, according to the presence or absence of PTSD.

Methods: Observational, analytical, cross-sectional study. Patients with a diagnosis of RA according to ACR (1987) and ACR EULAR (2010) criteria were included, from the Rheumatology Service of a public hospital in Buenos Aires, Argentina. They were recruited between October 2016 and August 2018. All Patients with another rheumatic or chronic disease were excluded. To determine the presence of PTSD, the Traumatic Experiences Questionnaire was used in its version validated in Spanish. To assess the severity of PTSD, the Davidson Trauma Scale was used in its Spanish version validated for Argentina. The continuous variables were described as mean and standard deviation (SD) or median and interquartile range (IQR), according to distribution and sample size. The categorical variables were expressed in percentages.In the bivariate analysis we used, for the continuous variables, the Student or Mann Whitney test, according to distribution and sample size. The categorical variables were analyzed using Chi square or Fisher's exact test, according to the expected frequency distribution table. A logistic regression model was performed taking PTSD as a dependent variable.

Results: 128 patients were included, 86.72% were female, with a mean age of 52.23 years (± 12.39). The mean time of evolution of RA was 12.96 years (± 9.66). 55.47% of the patients reported having experienced at least 1 traumatic event prior to the diagnosis of RA. The most frequently reported traumatic events were: unexpected death of a family member or close friend (39.5%). 32.39% of the patients who had experienced a traumatic event presented PTSD. 43.48% of patients with PTSD experienced a severe disorder.63.49% had some degree of depression and 55.56% of anxiety.

Statistically significant differences were found between the patients who presented PTSD vs those without PTSD in: female sex (100% vs 83.81%, $p = 0.04$), anxiety (median 12, IQR: 4-18 vs 6, IQR: 0-11 $p < 0.01$) depression (median 14, IQR: 6-19 vs 6, IQR: 0-12 $p < 0.01$). The main variable that showed an independent association with PTSD was depression (OR: 1.13, 95% CI: 1.05-1.20, $p < 0.01$).

Conclusion: We observed that more than half of the patients had experienced at least 1 traumatic event prior to the diagnosis of RA and 32.39% of them presented PTSD. PTSD was found associated with the female sex, the presence of anxiety and, independently, with depression. RA is probably product of the influence of various factors, with stress being one more determinant, within many existing ones.

Disclosure: M. Bejarano, None; **A. Secco**, None; **M. mamani**, None; **F. Romanini**, None; **N. Tamborenea**, None.

Abstract Number: 2262

Evaluation of Illness Perception in Systemic Sclerosis Patients with Pulmonary Involvement

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Lung disease is the current leading cause of death and the most common severe complication of systemic sclerosis (SSc), causing a significant adverse impact in quality of life. Due to its severity in the context

Table 1: Pearson correlation coefficient IPQR and SF36, HAQ, CAT

IPQR	SF 36								HAQ	CAT
	Physical Function	Role Physical	Pain	General Health	Vitality	Social Function	Role Emotional	Mental Health		
Timeline acute/chronic	-0,124	-0,126	-0,105	-0,115	-0,121	0,026	-0,124	-0,615	0,04	-0,012
Consequences	-0,357*	-0,257*	-0,436*	-0,510*	-0,505*	-0,456*	-0,252*	-0,431*	0,499*	0,460*
Cyclical	-0,456*	-0,396*	-0,466*	-0,530*	-0,472*	-0,444*	-0,403*	-0,369*	0,501*	0,482*
Personal Control	0,212*	0,255*	0,117	0,286*	0,201*	0,207*	0,364*	0,162	-0,375*	-0,270*
Treatment Control	0,144	0,0558	0,137	0,233*	0,207*	0,240*	0,0713	0,222*	-0,01	-0,279*
Coherence	-0,361*	-0,240*	-0,233*	-0,287*	-0,256*	-0,295*	-0,175*	-0,216*	0,297*	0,243
Emotional Representations	-0,443*	-0,277*	-0,355*	-0,541*	-0,596*	-0,499*	-0,320*	-0,646*	0,297 *	0,243*

*p<0.05

Table 2: Correlation between IPQR and General Health, HAQ and CAT

IPQR	Better General Health (SF36)	Worse General Health (SF36)	HAQ ≤ 1.25	HAQ > 1.25	CAT ≤ 20	CAT > 20
Timeline acute/chronic	17.8 ± 2.8	17.8 ± 1.9	17.8 ± 2.1	17.8 ± 2.6	17.8± 2.4	17.8 ± 2.4
Consequences	18.1 ± 0.9	21.0 ± 2.4 *	17.8 ± 2.6	20.4 ± 3.0 *	17.9± 2.6	20.3 ± 3.1*
Cyclical	11.0 ± 3.3	14.5 ± 2.6 *	11.2± 3.6	13.6 ± 3.1*	10.4± 3.2	13.8± 3*
Personal Control	18.0 ± 3.1	14.7 ± 3.1 *	18.3 ± 2.9	16.9 ± 3.5*	18.5± 2.7	16.9 ± 3.2*
Treatment Control	15.0 ± 1.8	14.7 ± 1.4	14.9± 1.7	14.8 ± 1.6	15.6± 1.9	14.6 ± 1.4*
Coherence	14.4 ± 2.7	15.5 ± 3.0 *	14.2 ± 2.8	15.4± 2.9*	14.6± 3.1	15.2± 2.8
Emotional Representations	16.4 ± 3.9	19.9 ± 2.8 *	16.8 ± 3.7	18.9 ± 3.7*	16.6± 4.3	18.9± 3.5*

*P<0.05

of SSc, we decided to focus on SSc patients with pulmonary involvement to determine their perception about the disease and correlate with quality of life, degree of disability and symptoms, as well as expectations.

Methods: This cross-sectional study included SSc patients with symptomatic lung involvement who signed an informed consent. Demographic, clinical and laboratory information were collected from an electronic register database. Revised Illness Perception Questionnaire (IPQR), 36-Item Short Form Health Survey (SF-36), Health Assessment Questionnaire Disability index (HAQDI), COPD Assessment Test (CAT) and three direct questions regarding quality of life, expectations about treatment and survival were applied to patients. IPQR score have negative domains (higher score means negative perception) and positive domains (higher score means positive perception). Correlations between questionnaires were made to evaluate patient perception measured by IPQR and if those perceptions would affect their opinion.

Results: 130 consecutive SSc patients were included, 55 (42%) with limited SSc, 64 (49%) diffuse and 11 (8%) sine scleroderma. Mean age was 54±12.5 years and mean disease duration 12±9 years. All domains of IPQR statistically correlated with SF36, HAQ and CAT, except the perception of chronicity. The Pearson linear correlation was negative between SF36 and negative IPQR domains (meaning worse quality of life and higher negative perception); and positive between SF36 and positive domains (meaning higher quality of life and higher positive perception). Higher HAQ and CAT indicated higher disability and dyspnea, presenting a linear positive Pearson correlation ($p < 0.0001$) (Table 1). A higher perception score was found comparing patients with moderate to severe disability (HAQ >1.25) or advanced dyspnea scores (CAT > 20) to patients with lower grade of disability or pulmonary symptoms. (Table 2). The relation between age, disease duration and IPQR had no statistical significance. Regarding the subjective opinion of the patients, established by direct questions, they presented optimistic answers as such 86.9% classified their quality of life as good, 45% expected cure or improvement with treatment in progress, and 85% believed that they would live more than 5 years. But no correlation between the IPQR domains and their opinion was found.

Conclusion: SSc patients with impaired quality of life, disability and major symptoms of dyspnea have higher perception of their disease by IPQR. However, the degree of perception does not appear to influence their opinion, suggesting an optimistic psychological profile with more positive attitude and effective coping strategies.

Disclosure: B. Bunjes, None; **P. Sampaio-Barros**, None; **A. Luppino-Assad**, None.

Abstract Number: 2263

A Qualitative Study Evaluating Near-Patient Tools Including a Mobile Application for Earlier RA Referral; Potential to Reduce Chronic Disease Burden

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences
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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic, debilitative autoimmune disease. Patients who are treated with disease modifying therapy within 6-12 weeks of symptom onset have better outcomes which leads to a reduced economic burden of disease.[1] Technology that enables near-patient blood testing coupled with digital health

applications may increase the proportion of patients treated within this window. This study aimed to assess the perceived unmet need for early treatment amongst clinicians and patients as well as their perceptions of a near-patient blood test and digital health mobile application.

Methods: 74 participants, approximately half from each of Canada (n=18) and the US (n=20) participated in a combination of in-depth interviews and surveys for 40-50 minutes. 38 of the 74 subjects, consisted of 16 rheumatologists, 14 primary care physicians (PCPs) and 8 RA patients. To supplement the patient study-sample, 36 additional patients completed an online survey of quantitative and open-ended questions focused on diagnosis and perspectives of a described near-patient blood test and mobile application. Rheumatologists who were in full-time practice and PCPs who see at least 15 RA patients a month were included. Patients were between 18 and 60 years old, had an RA diagnosis and experience using apps for health management.

Results: Almost all Rheumatologists and PCPs indicated that the time between symptom onset and treatment initiation (currently 6-18 months) could be improved and agreed that difficulty diagnosing is still one of the biggest unmet needs. Referrals to a Rheumatologist range from 6 weeks to 3 months. Patients indicated that it took 8 months to 2 years before treatment initiation. Most Rheumatologists said the longest delay is due to inconclusive PCP clinical exams and blood work, leading to repeated visits before patients are referred. Most clinicians and patients welcomed new tools with 33% of patients willing to pay for the near-patient blood test and mobile application. Clinicians had few concerns about a near-patient blood test and indicated that it should be available in the clinic, not the pharmacy. Patients reported the appeal of an easy to use near-patient blood test that could have meant an earlier diagnosis over a traditional laboratory blood test.

Conclusion: RA is difficult for PCPs to identify for early referral and treatment within 6-12 weeks of symptom onset. The clinicians and patients we surveyed reported positive perspectives regarding near-patient blood tests and mobile applications and welcome their use to assist with earlier referral and treatment. With the emergence of innovative near-patient technologies, opportunities exist to intervene earlier and potentially reduce the social and economic burden of chronic diseases.

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Reference:

[1]Nell VP, Machold KP, Eberl G, et al. Benefit of very early referral and very early therapy with disease-modifying anti-rheumatic drugs in patients with early rheumatoid arthritis. Rheumatology 2004;43:906–14.10.1093/rheumatology/keh199

Disclosure: N. Biln, Augurex Life Sciences Corp, 1, 3, 6; **S. Chahal**, Augurex Life Sciences Corp, 3; **B. Clarke**, Augurex Life Sciences Corp, 9; **A. Warner**, Augurex Life Sciences Corp, 9.

Abstract Number: 2264

Prescribing Exercise: Facilitators and Barriers to the Successful Implementation of Physical Activity Guidelines in Inflammatory Arthritis

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Table 1: Baseline Patient Characteristics and Comorbidities			
	Active (N=43)	Inactive (N=65)	p-val
Age (yrs), SD	51 (14)	50 (12)	0.71
BMI (kg/m^2)	27	31	0.002
ESR (mm/s)	23	20	0.72
CRP (mg/dL)	8.4	5.9	0.73
RAPID3	6.6	9.5	0.02
Diagnosis , N (%)			
Rheumatoid	26 (60%)	35 (54%)	0.45
Psoriatic	3 (7%)	10 (15%)	
Ankylosing Spondylitis	12 (28%)	19 (29%)	
Other	2 (5%)	1 (2%)	
Female, N (%)	27 (63%)	46 (71%)	0.60
Osteoarthritis, N (%)	21 (49%)	32 (49%)	0.97
Thyroid Disease , N (%)	3 (7%)	6 (9%)	0.63
Heart Disease, N (%)	9 (14%)	5 (12%)	0.74
HLD, N (%)	16 (37%)	22 (34%)	0.72
Hypertension, N (%)	9 (21%)	22 (34%)	0.15
Diabetes, N (%)	2 (5%)	13 (20%)	0.02
Using Tobacco, N (%)	1 (2%)	10 (15%)	0.03
Anxiety/Depression, N (%)	6 (14%)	18 (27%)	0.09
Fibromyalgia, N (%)	2 (5%)	9 (14%)	0.12
Arthroplasty, N (%)	4 (9%)	9 (14%)	0.48
Sleep Apnea, N (%)	1 (2%)	11 (17%)	0.02

Table 1: Baseline Patient Characteristics and Comorbidities

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Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Physical Activity (PA) is beneficial for people with inflammatory arthritis (IA). In 2018, EULAR published the first recommendations for guiding PA in patients with IA.[1]These endorsed the American College of Sports Medicine-American Heart Association Public Health Recommendations, which encourage participation in four domains of PA: Aerobic, Resistance, Flexibility, and Balance. They also included provider recommendations

Table 2: Factors Influencing Patient Physical Activity and Exercise Habits				
		Active N (%)	Inactive N (%)	p-val
Self-Efficacy	I am as active or more active than most other people my age.	34 (79)	20 (30)	<0.001
	I know I can exercise if I want to do it.	39 (91)	39 (60)	<0.001
	I consider exercise a priority.	38 (93)	40 (65)	0.001
General Motivators and Facilitators	Exercise gives me more energy.	40 (95)	52 (81)	0.037
	I exercise to control my weight.	35 (81)	29 (46)	<0.001
	Exercise helps people to look better.	42 (98)	59 (94)	0.34
	People who exercise are healthier in general.	41 (95)	61 (95)	0.99
General Obstacles and Barriers	Financially I cannot afford the kind of exercise I want to do.	4 (10)	19 (30)	0.014
	Exercise is a waste of my time.	0 (0)	1 (2)	0.41
	I find exercise boring.	9 (21)	22 (34)	0.15
	I don't have time to exercise regularly.	10 (24)	24 (37)	0.16
Health-Related Motivators	I know I will be healthier if I exercise.	41 (95)	61 (95)	0.99
	I know my arthritis will be less painful if my weight is healthy.	38 (93)	56 (90)	0.68
	People with arthritis who exercise are healthier than people with arthritis who do not exercise.	39 (90)	52 (83)	0.24
	Exercise is as important as taking medication for my arthritis.	38 (91)	50 (79)	0.13
Health-Related Barriers	Exercise is dangerous for someone with my type of arthritis.	2 (5)	9 (14)	0.12
	My arthritis is too painful for me to exercise.	11 (26)	30 (47)	0.026
	Fatigue prevents me from exercising.	8 (19)	34 (52)	<0.001
	Exercise will make my arthritis worse in the future.	1 (2)	11 (17)	<0.001
Health-Related Behaviors	I wish my doctor would talk to me more about exercise.	17 (41)	13 (20)	0.031
	I was physically active before my diagnosis.	37 (86)	40 (64)	0.011
	I have become less physically active after my diagnosis.	22 (54)	46 (73)	0.043
	I have become more physically active after my diagnosis.	8 (19)	3 (5)	0.019

ACRFIGURE2
Table 2: Factors Influencing Patient Physical Activity and Exercise Habits

for PA promotion and delivery to patients with IA. Objectives of our study were to 1) Describe levels of participation in the four PA domains in an IA population; 2) Identify barriers/facilitators to PA; 3) Explore patient views on importance of PA; and 4) Investigate if EULAR recommendations for promotion/delivery of PA are being incorporated into care.

Methods: Patients with IA from a university rheumatology practice were invited in person or via the medical record to take an 81-question, 15-minute survey. The survey asked in which PA domains they participated, about facilitators/barriers to PA, and whether the recommendations for PA promotion had been addressed during their care. Respondents reporting minimum aerobic exercise for 20 minutes three times weekly plus at least one other domain were categorized into an "Active" group, others were categorized as "Inactive." Patient characteristics and survey responses were compared between groups using t-test for continuous and Chi-squared or Fisher's-Exact Test for categorical variables.

Results: Of 1,113 patients invited, 108 participated. Sixty (43%) reported aerobic exercise, 44 (41%) flexibility, 42 (39%) resistance, and 18 (17%) balance. Forty-three (40%) were categorized as active and 65 (60%) as inactive. The

Table 3: Utilization of EULAR PA Promotion/Delivery Recommendations by Providers				
EULAR PA Promotion/Delivery Recommendation[1]	**Pertinent Survey Question**	**Active N (%)**	**Inactive N (%)**	**p-val**
1: Promoting PA should be an integral part of standard care.	Has your rheumatologist emphasized the importance of PA?	32 (76)	53 (84)	0.31
2: All HCPs should take responsibility for and cooperate to promote PA, including making necessary referrals, to ensure that people receive appropriate PA interventions.	Has another physician emphasized the importance of PA?	33 (79)	49 (78)	0.92
3: Competent providers should deliver PA interventions.	Have you received a referral for help with PA?	17 (43)	28 (44)	0.90
4: HCPs should evaluate PA to identify which of the four domains of exercise can be targeted for improvement.	Has a HCP explained the four recommended domains of PA to you?	8 (19)	12 (19)	1.0
5: General and disease-specific contraindications should be identified and taken into account.	Has a HCP /specialist discussed types of PA you should NOT do due to arthritis?	11 (26)	18 (28)	0.83
6: PA interventions should have clear, personalised aims.	Has a HCP/specialist worked with you to develop aims and goals for PA?	14 (33)	23 (37)	0.74
7: General and disease-specific barriers and facilitators related to performing PA should be identified and addressed.	Has a HCP/specialist helped you to identify barriers to PA related to your general life?	7 (17)	14 (22)	0.51
	Has a HCP/specialist helped you to identify barriers to PA related to your arthritis?	17 (41)	20 (31)	0.33
8: Necessary adaptations to general PA should be based on a comprehensive assessment of patient factors.	Has a HCP/specialist helped you create an exercise program tailored to your health-related and personal needs?	17 (40)	20 (31)	0.33
9: HCPs should plan and deliver interventions that include behavioural change techniques, self-monitoring, goal setting, action planning, feedback and problem solving.	Has a HCP/specialist helped you to monitor or self-monitor your PA?	12 (29)	16 (25)	0.68
	Has a HCP/specialist discussed with you techniques to overcome barriers to PA?	11 (26)	18 (28)	0.33
10: Healthcare providers should consider different modes of delivery of PA in line with people's preferences.	Has a HCP/specialist discussed with you different PA options based on your preferences /needs?	14 (33)	18 (28)	0.57

Abbreviations: HCP = Healthcare Provider; PA = Physical Activity
1: Rausch Osthoff A-K, et al. 2018 EULAR recommendations for PA in people with Inflammatory Arthritis and Osteoarthritis. Ann Rheum Dis. 2018:1251–60.

active group had lower BMI and lower RAPID3 Scores, and fewer people with diabetes, sleep apnea, and tobacco use (Table 1). A larger proportion of the active group reported self-efficacy for exercise ($p< 0.001$), prioritizing exercise ($p=0.01$), exercising for weight control ($p< 0.001$) and improved energy with exercise ($p=0.04$). A larger proportion of the active group (86%) also reported PA engagement prior to arthritis diagnosis ($p=0.01$). More patients in the inactive group compared to the active group cited finances ($p=0.01$), pain ($p=0.03$), fatigue ($p< 0.001$), and concern that PA worsens arthritis ($p >0.001$) as barriers . Most patients (in both groups) understood the health-related benefits of PA (Table 2). A minority of patients in both groups perceived recommendations about PA were addressed in clinical care (Table 3).

Conclusion: While about half of patients with IA reported aerobic exercise, most do not engage in resistance, flexibility, or balance training despite recommendations. Overall, patients acknowledge the benefits of PA, but do not perceive that they receive advice regarding PA from doctors and most habits are formed without instruction from rheumatologists. With new EULAR guidelines, there is an opportunity for providers to have more prescriptive discussions about exercise.

References:

1. Rausch Osthoff, et al. 2018 EULAR recommendations for PA in people with Inflammatory Arthritis and Osteoarthritis. Ann Rheum Dis. 2018:1251–60.

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Abstract Number: 2265

The Effects of Message Framing on Patients' Perceptions and Willingness to Switch to a Biosimilar

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Patient Preferences, Beliefs, & Experiences
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Background/Purpose: Patients may hold negative perceptions towards biosimilars which can create barriers to their uptake. Physicians also report uncertainty in how best to explain biosimilars. The aim of this study was to measure the effect of differently framed explanations on patients' perceptions of and willingness to switch to a biosimilar.

Methods: Ninety-six patients with rheumatic diseases taking an originator biologic were randomised to receive one of four biosimilar explanations delivered by video- positive framing with and without an analogy, and negative framing with and without an analogy. The same physician was featured in each video explanation to ensure consistency.. The positive explanation employed a positive valence attribute frame, whereby the *similarities* between the biologic and biosimilar were emphasised. The physician featured in the video used positive body language and verbal cues (e.g. nodding and smiling) to promote a positive interaction. Comparatively, the negatively framed explanation focused on the *differences* between biologics and biosimilars, and the physician used negative body language and verbal cues (e.g. less confident vocal tone) to imply uncertainty regarding efficacy and safety. The analogy used focused on the concept of baking bread, using a cheaper yeast from a different brand. Willingness to switch to a biosimilar, perceptions about biosimilars, and the effectiveness of the explanation were measured after the information delivery.

Results: Positive framing led to more participants being willing to switch (67%) than negative framing (46%). Framing significantly predicted willingness to switch to a biosimilar, with participants in the positive framing group being 2.36 times more willing to switch ($P = 0.041$). The positive framing group also reported significantly greater perceived efficacy of biosimilars ($P = 0.046$), and thought the explanation was more convincing ($P = 0.030$). The analogy did not enhance willingness to switch or understanding ($P > 0.05$).

Conclusion: Positive framing can improve perceptions of and willingness to switch to a biosimilar in patients currently taking biologic medications.

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Abstract Number: 2266

Treatment Preferences in Patients with Axial Spondyloarthritis

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Session Time: 9:00AM–11:00AM

Background/Purpose: Due to the increasing tendency of involving patients in decisions regarding their health care and knowing the need for further research on patients' preferences about treatment and adherence, the aim of this study was to evaluate the treatment preferences of patients with Axial Spondyloarthritis (axSpA) and to identify the factors associated with their choice.

Methods: Patients diagnosed with axSpA (ASAS 2009 criteria) were included. Sociodemographic data, disease characteristics, disease activity and treatments received were recorded. A specially designed questionnaire was administered to evaluate patient preference for the drug administration, doses frequency, the favorite site and the person chosen for the drug administration. Also the attributes and disadvantages of the chosen rout were assessed, as well as the characteristics and compliance with the current treatment. Statistical analysis: Student's T-test, Chi2 test and multiple logistic regression analysis.

Results: Seventy patients were included with a median age (*m*) of 46.5 years (IQR 38-57), 55 males (78.6%) and a median disease duration of 13.5 years (7.75-23.25).

According to the patients, the relevant aspects in decreasing order of frequency for choosing a treatment were: the ability to improve quality of life (32.9%), improvement in joint inflammation (22.9%), pain (21.4%) and physical function (14.3%). Sixty-three patients (90%) chose to receive the medication at home, and 55 (78.6%) chose to self-administrate the drug. The most chosen mode of administration was oral (51.4%), following by subcutaneous (SC) (41.4%), intramuscular (IM) 4.3% and intravenous (IV) 2.9%. The preferred frequency of oral administration was one tablet per week (61.1%) and SC administration, once a month (34.5%). The main advantages of oral administration were: the easy administration (58.3%), no need for a special skill (33.3%) and no requirement of refrigeration (16.7%), and in the case of SC: the easy application (44.8%), the efficacy (27.6%) and the safety (13.8%). The choice of oral route was associated with: preference for self-administration (88.9% vs 11.2%, p = 0.05), preference for receiving the medication at home (97.2% vs 2.8%, p = 0.02) and higher level of education (14.5 ± 4.2 years vs 11.5 ± 4.7 years, p = 0.009). These last two variables remained significant in the multivariate analysis.

The choice of the SC route was independently associated with the type of axSpA (46.7% in ankylosing spondylitis (AS) vs 10% in non-radiographic axSpA (nr), p = 0.038).

The patients with greater adherence to treatment were receiving more frequent biological SC treatment (52.7% vs. 13.3%, p = 0.008), and had lower disease activity, higher functional capacity and better quality of life. In the multiple logistic regression model, being receiving biological SC treatment and having lower disease activity remained significantly associated with the treatment compliance according to the patient.

Conclusion: The most preferred way of administration by patients with axSpA was the oral route, with a weekly frequency and self-administration at home, followed by the subcutaneous route, with monthly infusion.

Disclosure: D. Capelusnik, None; **E. Schneeberger**, None; **L. Macias Oviedo**, None; **J. Sevillano Gutierrez**, None; **G. Citera**, AbbVie, 5, 8, Abbvie, 2, 5, 8, BMS, 5, BRISTOL MYERS SQUIBB ARGENTINA, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, Gema Biotech, 2, 5, 8, Genzyme, 5, Janssen, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi Genzyme, 5, 8.

Abstract Number: 2267

The Association Between Non-restorative Sleep and Diurnal Patterns of Cognitive Function and Fatigue in People with Fibromyalgia and Matched Controls

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SESSION INFORMATION
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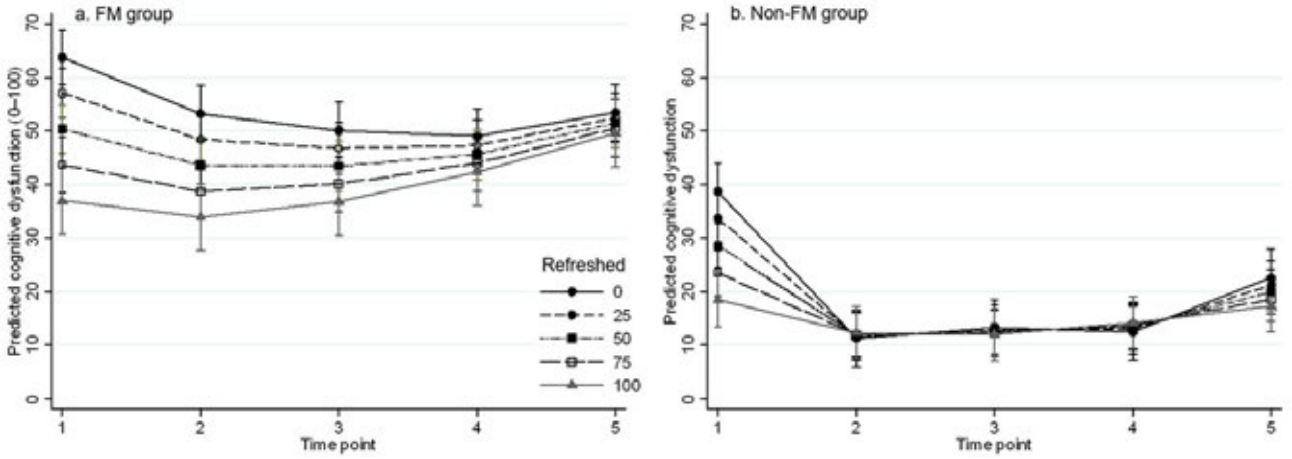
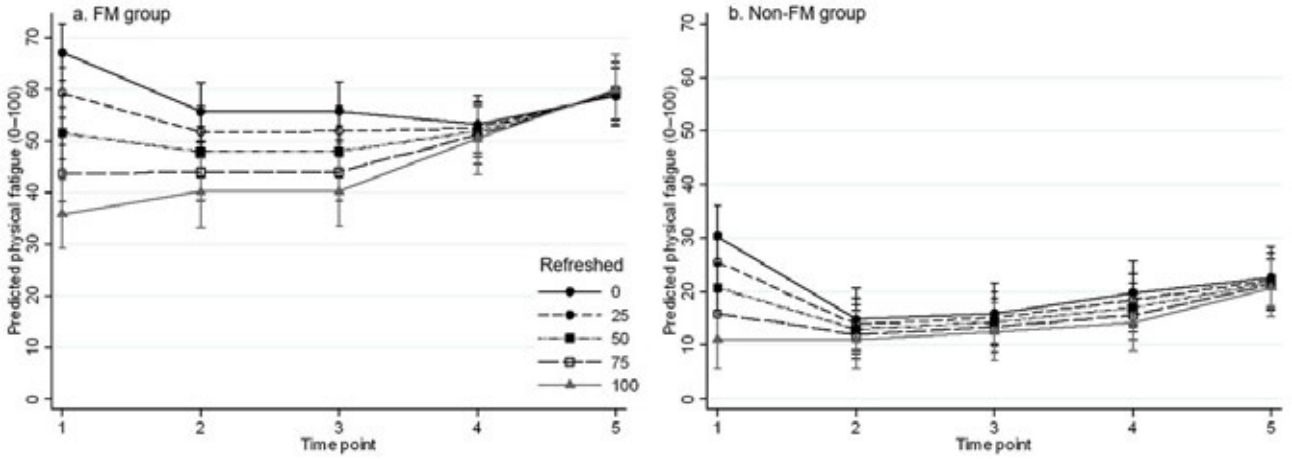
Background/Purpose: Non-restorative sleep is associated with poorer cognitive function and greater fatigue, not only in people living with fibromyalgia (FM), but also in the general population. Whether the extent of non-restorative sleep impacts on diurnal patterns of cognitive function and fatigue, and whether this differs based on FM status, has yet to be established.

Methods: This secondary analysis used data collected from 100 participants recruited to an ambulatory study conducted in real-world settings (50 participants who met 2016 ACR FM diagnostic criteria and 50 age-, sex- and education-matched non-FM controls). Participants reported the degree to which they felt refreshed upon awakening (0–100 scale, higher scores representing more restorative sleep). Ecological momentary assessments of self-reported cognitive function (perceived clarity and speed) and mental and physical fatigue (all measured using 0–100 numeric rating scales) were administered five times per day for eight days using a smartphone app. Multilevel linear regression models were used to investigate whether perceived level of refreshment on awakening was associated with diurnal symptom patterns of cognitive function and physical and mental fatigue.

Results: Mean age of the sample was 45.1 years (SD 13.9); 88% were female. A total of 756 days of data were available for analysis. Compared to the non-FM group, the FM group reported higher aggregate levels of cognitive dysfunction (mean difference: 31.5, 95%CI 25.2–37.8), physical fatigue (mean difference: 36.3, 95%CI 29.6–43.0), and mental fatigue (mean difference: 32.0, 95%CI 24.8–39.2). For both groups, non-restorative sleep was associated with greater cognitive dysfunction and fatigue (both mental and physical) on awakening. For the FM group, the effects of non-restorative sleep were sustained across the course of the day; for the non-FM group, recov-



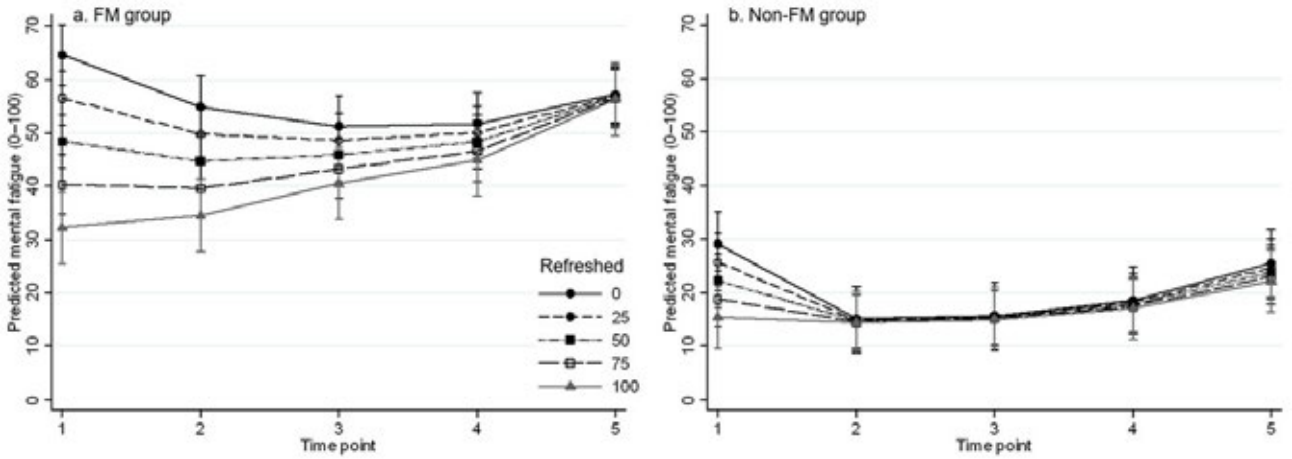
The impact of non-restorative sleep on diurnal pattern of cognitive function



The impact of non-restorative sleep on diurnal pattern of physical fatigue

ery was swift (Figures 1–3). There was a significant interaction between Group membership and impact of non-restorative sleep on diurnal symptom patterns for both physical and mental fatigue ($p < 0.01$), but not cognitive function ($p=0.07$).

Conclusion: Nights of non-restorative sleep exert negative effects on cognitive function and fatigue that persist longer into the day for those with FM compared to non-FM controls. If supported by further investigation, the diurnal patterns observed in the FM group may indicate optimal times for task planning and therapeutic engagement in response to subjective feelings of refreshment on morning awakening.



The impact of non-restorative sleep on diurnal pattern of mental fatigue

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Abstract Number: 2268

Preferences and Insights for Rheumatoid Arthritis Clinical Prevention Trial Participation

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SESSION INFORMATION
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Background/Purpose: In rheumatoid arthritis (RA) development, autoantibodies to citrullinated protein antigens (ACPA) are elevated in the blood before clinically-apparent synovitis develops. These findings underpin the development of several prevention trials in RA where individuals with elevated ACPA are studied to prevent or delay the development of clinically-apparent synovitis. Understanding the decision-making processes of individuals with such autoantibodies who are offered enrollment in a clinical prevention trial could provide important insights into optimizing participation in such trials. To address this, the Research Participation Influences (RPI) Study is an IRB-approved project that examines factors that influence the decision to participate in an ongoing RA clinical prevention trial.

Methods: Individuals with elevated serum levels of ACPA in absence of synovitis were notified of their ACPA results indicating risk for future RA development. Following this, subjects were provided a description of an interventional clinical trial and what their participation would entail. After each individual agreed to or refused participation, they were given a survey that gathered limited demographic information, first-degree relative (FDR) status, and 11 influences on trial participation which were rated on a Likert scale. In addition, 2 open response questions asked why individuals initially had their ACPA tested and to list any additional influencing factors. The responses were statistically compared between groups, and the qualitative data from open response questions were transcribed and sectioned by relevant meaning units. These units were used to build common themes using a language processing application.

Results: 62 surveys were collected; 37 'Yes' responses (agreed to trial) and 25 'No' responses (refused trial). Key findings in both the Likert and open response questions were that 'Yes' respondents expressed higher perceived risk for RA and higher perception of benefit to themselves or others (Table 1). 'No' respondents expressed more concern about adverse effects of the medication and had less personal or family experience with RA. There was a higher rate of FDRs agreeing to the trial (56.8%) than non-FDRs. Furthermore, 7 codes of high frequency were derived from the

Table 1: RPI Study Subject Demographics and Likert Scale Ratings Among Yes and No Groups

Characteristic	Agreed to Clinical Trial		Declined Clinical Trial		p-value
N = 62	37		25		
Age: mean±sd	51.6±13.6		58.2±14.1		0.08
Gender: N (% female)	28 (75.7)		21 (84.0)		0.53
Education: N (% beyond high school)	34 (91.9)		24 (96.0)		0.64
Income: N (%)					0.10
Less than $10,000	2 (5.4)		0 (0.0)		
$11,000-$30,000	6 (16.2)		2 (8.0)		
$31,000-$50,000	3 (8.1)		2 (8.0)		
$51,000-$75,000	4 (10.8)		5 (20.0)		
Greater than $75,000	17 (45.9)		6 (24.0)		
Prefer not to answer	5 (13.5)		10 (40.0)		
First-Degree Relative: N (% yes)	**21 (56.8)**		**4 (16.0)**		**0.002**
Likert Scale Ratings (0=not at all – 4=very much)	**Agreed to Clinical Trial**		**Declined Clinical Trial**		
N = 52*	31		21		p-value (median)
Reasons That Influenced Participation	**Mean**	**Median (IQR)**	**Mean**	**Median (IQR)**	
Potential benefit to me or my health	**3.5**	**4 (3-4)**	**2.0**	**2 (0-4)**	**0.002**
Potential benefit to my family	**2.9**	**3 (3-4)**	**1.3**	**0 (0-3)**	**0.0003**
Potential benefit to others	**3.6**	**4 (4-4)**	**2.0**	**2 (0-4)**	**<0.0001**
Time Required to Participate	1.7	2 (0-3)	1.9	2 (0-3)	0.95
Personal Risk of Developing RA	**3.2**	**4 (3-4)**	**1.9**	**2 (0-4)**	**0.001**
Compensation Offered	0.6	0 (0-3)	0.9	0 (0-2)	0.35
Moral feeling of obligation to help	2.6	3 (2-4)	1.8	2 (0-3)	0.05
Potential Positive Effects of Trial Medication	**2.7**	**3 (1-4)**	**1.7**	**2 (0-3)**	**0.01**
Potential Adverse Effects of Trial Medication	**1.9**	**2 (0-3)**	**3.7**	**4 (4-4)**	**<0.0001**
Potential to learn more about RA	2.8	3 (0-4)	2.3	3 (0-4)	0.40
Potential to be assigned placebo	1.7	2 (0-3)	2.3	3 (0-4)	0.19

*10 of the 62 total surveys were excluded because they were collected under V1 instead of V2; V1 lists "Potential Effects of Trial Medication" and V2 lists as above; separated into two influences

Table 2: RPI content analysis from survey Questions 5 and 7a

Codes derived from content analysis	Agreed to Trial N=37		Declined Trial N=25		Total Meaning Units
	Q5	*Q7a*	*Q5*	*Q7a*	
To support research for RA prevention To help those who suffer from RA	**18**	**5**	**4**	**1**	**28**
Personal Risk for Developing RA	**13**	**1**	**3**	**1**	**18**
Convenient/Easy to do	**5**	**1**	**11**	**0**	**17**
Established trust of Research institution/study team or recommendation by physician	7	3	4	3	17
Negative perception of trial or any medication/ Participant does not know enough about trial medication	**0**	**0**	**3**	**12**	**15**
Currently experiencing joint symptoms/seeking access to care/seeking close monitoring of RA risk	8	1	6	1	16
Family or personal experience with RA	11	1	1	0	13

Q5: In your own words, why did you decide to come here today to be screened and have your blood tested?
Q7a: Is there a reason not listed in the chart above that most influenced your decision to decline/participate in the clinical trial?

open response questions, revealing a general theme of support for research among the 'Yes' group and a negative perception of study medication among the 'No' group (Table 2).

Conclusion: 'Yes' respondents were more likely to be FDRs and exhibited a stronger concern for personal risk for RA than 'No' respondents. Given that all subjects were provided similar estimates of risk based on ACPA levels, further exploration is needed to determine why these differences in perception of risk were present, and whether these were due to other factors such as the presence of symptoms or an individual's interpretation of their risk for RA given family history. Understanding these and other underlying issues that influence participation, including perceptions of medications, will better inform researchers and individuals who are candidates for prevention.

Disclosure: C. Fleischer, None; **M. Feser**, None; **E. Bemis**, None; **C. Striebich**, None; **L. Moss**, None; **V. Kormendi**, None; **S. White**, None; **V. Holers**, AdMIRx, 1, 2, 4, 5, 6, Alexion, 7, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 5, Janssen R&D, 2, 5, Pfizer, 2; **M. Harrison**, None; **K. Deane**, Bristol-Myers Squibb, 5, Inova, 9, Janssen, 2, 5, Janssen R&D, 2, Microdrop, 5, Pfizer, 2.

Abstract Number: 2269

Major Stressors in the Year Prior to Diagnosis Affects RA Characteristics at Presentation and 1 Year

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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Session Time: 9:00AM–11:00AM

Background/Purpose: Although many RA patients attribute their disease onset to recent life events, results from retrospective studies remain unclear. We compared characteristics of newly diagnosed RA patients who did and did not report significant stressful life events (+*stress*) in year prior to diagnosis at baseline and 12 months.

Methods: Data were from early RA patients (symptoms < 1 year) enrolled in the Canadian Early Arthritis Cohort (CATCH) from 01-2007 to 03-2017 with ≥ 12 months of follow-up. Patients were asked about major psychological (death, divorce/separation, family, financial, other) and physical (motor vehicle accident, surgery, major illness/infection, other) stressors in previous year. We used independent t-tests and chi square to compare characteristics by sex and stress classification and multivariable regression to examine the impact of stress on disease activity and patient reported outcomes (PROs) at 1 year after adjusting for age, sex, education, and baseline fibromyalgia diagnosis and swollen joint count.

Results: The 1933 adults were mostly female (72%), with a mean (SD) age of 55 (15) years. At baseline, 52% reported one or more stressors in previous year; family (48%), financial stress (36%), death (35%), surgery (28%), and major illness (26%) were the most common stressors. Patients with +*stress* were more likely to be women, were significantly younger, had more comorbidities, slightly higher mean DAS28, and were more likely to have fibromyalgia (Table 1). Patients with +*stress* also reported significantly baseline higher pain, fatigue, depression, sleep disturbance, patient global, and HAQ-DI scores.

At 1 year, swollen joint counts and the proportion of patients in DAS28 REM was similar between groups. However, PROs remained higher in those with a history of +*stress*, with some evidence of a dose-response relationship (Table 2). The greatest impacts were on mood, sleep disturbance, and fatigue.

Conclusion: In this pan-Canadian early RA cohort, stressful life events were common in the year prior to diagnosis and were associated with significantly worse depression, fatigue, sleep disturbance, pain, patient global and disability scores at diagnosis; 1 year later effects on PROs persisted even though disease activity was similar between groups. Newly diagnosed RA patients with a history of recent stressors may benefit from emotional support to optimize how they feel and function.

Table 1. Patient characteristics at enrolment by stress status in year prior to RA diagnosis (N=1933).

Mean (SD) or N (%)	No Stress (N=928; 48%)	Physical Stress (N=131; 7%)	Psychological Stress (N=658; 34%)	Both (N=216; 11%)	SIG
Age	**56 (15)**	**56 (15)**	**53 (14)**	**52 (15)**	**<0.0001**
Women	622 (67%)	82 (63%)	512 (78%)	174 (81%)	**<0.0001**
College Education	464 (50%)	76 (58%)	345 (52%)	126 (58%)	0.0772
Rheumatic Disease Comorbidity Index	**1.1 (1.2)**	**1.4 (1.4)**	**1.1 (1.3)**	**1.4 (1.3)**	**0.0018**
OA or Spinal pain	**168 (18%)**	**35 (27%)**	**117 (18%)**	**55 (25%)**	**0.0086**
Current Smoking	157 (17%)	25 (19%)	131 (20%)	33 (15%)	0.3142
Body Mass Index	27.8 (5.6)	27.9 (6.3)	28.5 (6.9)	28.3 (6.4)	0.4099
Fibromyalgia diagnosis	**15 (2%)**	**2 (2%)**	**13 (2%)**	**11 (5%)**	**0.0140**
RA Characteristics					
Symptom duration (month)	5.6 (3.0)	5.7 (3.0)	5.9 (3.0)	5.9 (3.0)	0.0837
RF+ or ACPA +	607 (78%)	87 (74%)	466 (81%)	153 (83%)	0.1013
DAS28 – mean	**5.0 (1.4)**	**5.1 (1.5)**	**5.0 (1.5)**	**5.2 (1.4)**	**0.0511**
REM/LDA (DAS28 ≤3.2)	91 (10%)	10 (8%)	69 (10%)	13 (6%)	
Moderate (>3.2 and ≤ 5.1)	369 (42%)	52 (42%)	251 (40%)	82 (39%)	0.4549
Very active (>5.1)	427 (48%)	63 (50%)	314 (50%)	116 (55%)	
MTX ±csDMARDs	679 (73%)	100 (76%)	489 (74%)	166 (77%)	0.6536
Oral Steroids	295 (32%)	40 (31%)	215 (33%)	55 (25%)	0.2468
Patient Reported Outcomes					
Pain (0-10)	**5.3 (2.8)**	**5.5 (2.9)**	**5.7 (2.8)**	**6.2 (2.8)**	**0.0001**
HAQ-DI	**1.0 (0.7)**	**1.2 (0.7)**	**1.1 (0.7)**	**1.3 (0.7)**	**<0.0001**
Fatigue (0-10)	**4.7 (3.1)**	**5.0 (3.0)**	**5.7 (2.9)**	**5.9 (2.9)**	**<0.0001**
Patient Global (0-10)	**5.6 (2.9)**	**6.0 (2.9)**	**6.0 (2.9)**	**6.4 (3.0)**	**0.0011**
Depression (SF12 MCS < 45.6)	**329 (35%)**	**54 (41%)**	**356 (54%)**	**123 (57%)**	**<0.0001**
Poor sleep (0-10)	**4.5 (3.4)**	**4.8 (3.3)**	**5.3 (3.2)**	**6.0 (3.1)**	**<0.0001**

Table 2. Effect of stress in year prior to diagnosis on outcomes at 12 months (N=1933).*

	Pain	Fatigue	Patient Global	Depression	Poor Sleep	HAQ-DI	DAS28 REM	Swollen Joints
Any Stress	**0.27 (0.02, 0.53)**	**0.39 (0.12, 0.66)**	0.25 (-0.01, 0.51)	**1.55 (1.24, 1.95)**	**0.49 (0.21, 0.76)**	0.05 (-0.01, 0.11)	1.02 (0.82, 1.27)	0.12 (-0.19, 0.42)
Total stressors	**0.24 (0.12, 0.37)**	**0.32 (0.18, 0.45)**	**0.24 (0.11, 0.37)**	**1.30 (1.17, 1.45)**	**0.37 (0.24, 0.51)**	**0.05 (0.02, 0.08)**	1.00 (0.90, 1.12)	0.05 (-0.10, 0.20)
0 (n=928, 48%)	REF	REF	REF	REF	REF	REF	REF	REF
1 (n=575, 30%)	-0.02 (-0.31, 0.28)	0.14 (-0.17, 0.46)	-0.04 (-0.34, 0.26)	**1.31 (1.00, 1.71)**	0.18 (-0.14, 0.50)	0.00 (-0.07, 0.06)	1.12 (0.87, 1.43)	0.06 (-0.29, 0.42)
2 (n=295, 15%)	**0.54 (0.17, 0.92)**	**0.59 (0.19, 0.99)**	**0.54 (0.16, 0.92)**	**1.79 (1.29, 2.48)**	**0.80 (0.40, 1.20)**	**0.10 (0.02, 0.18)**	0.99 (0.72, 1.35)	0.20 (-0.25, 0.65)
3 (n=88, 5%)	**1.06 (0.45, 1.66)**	**0.73 (0.08, 1.39)**	**0.81 (0.19, 1.44)**	**1.90 (1.15, 3.16)**	**0.72 (0.06, 1.38)**	**0.18 (0.04, 0.32)**	0.90 (0.53, 1.52)	0.23 (-0.50, 0.96)
4+ (n=47, 2%)	0.75 (-0.11, 1.61)	**1.78 (0.84, 2.72)**	**1.02 (0.12, 1.91)**	**3.45 (1.70, 6.99)**	**2.10 (1.16, 3.04)**	**0.19 (0.00, 0.38)**	**0.46 (0.21, 1.03)**	0.03 (-0.99, 1.05)

*Multivariable linear regression coefficient adjusted for age, sex, education, baseline fibromyalgia diagnosis and swollen joints.

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5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8; **G. Hazlewood**, None; **L. Bessette**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, Amgen, BMS, Janssen, Roche, UCB Pharma, AbbVie Inc, Pfizer, Merck, Celgene, Sanofi, Eli Lilly, and Novartis., 2, 5, 8, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Bristol-Myers-Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5; **C. Hitchon**, Pfizer, 2, UCB, 2, UCB Canada, 2; **D. Tin**, None; **C. Thorne**, Abbvie, 2, 5, Amgen, 2, 5, CaREBiodam, 2, Celgene, 2, 5, Centocor, 5, Janssen, 5, Lilly, 5, Medexus/Medac, 5, 8, Merck, 5, Novartis, 2, 5, Pfizer, 2, 5, Sandoz, 5, Sanofi, 5; **E. Keystone**, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 5, Astra-Zeneca, 5, Biotest, 5, BMS, 2, 5, 8, Celltrion, 5, Crescendo, 5, Crescendo Bioscience, 5, F. Hoffmann-La Roche Inc, 2, 5, 8, Genentech, 5, Genentech Inc., 5, Genzyme, 5, Gilead, 2, 5, Gilead Sciences, Inc., 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 5, 8, Pfizer, 2, 5, 8, Pfizer Pharmaceuticals, 2, 5, 8, Roche, 2, 5, 8, Sandoz, 5, Sanofi, 2, 5, 8, Sanofi-Aventis, 2, 8, UCB, 5, 8; **V. Bykerk**, AbbVie, 5, Amgen, 1, 2, 3, 5, 8, Brainstorm Therapeutics, 1, 2, 3, 5, 8, Bristol-Myers Squibb, 5, Genentech, 5, Gilead, 5, NIH, 2, Pfizer, 1, 2, 3, 5, 8, Regeneron, 5, Regeneron Pharmaceuticals, Inc, 5, Sanofi, 5, Sanofi/Genzyme-Regeneron, 5, Sanofi-Genzyme/Regeneron, 1, 2, 3, 5, 8, Scipher, 1, 2, 3, 5, 8, The Cedar Hill Foundation, 9, UCB, 1, 2, 3, 5, 8, UCB Pharma, 5; **S. Bartlett**, Abbie, 2, Abbvie, 2, 5, Bayer, 5, International Society of QOL Research, 6, Janssen, 5, 8, Lilly, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, Pfizer Inc, 8, PROMIS International, 6, UCB, 5, 8; **C. (CATCH) Investigators**, Amgen, 2, Pfizer Canada, 2, AbbVie Corporation, 2, Medexus Inc., 2, Eli Lilly Canada, 2, Merck Canada, 2, Sandoz Canada Biopharmaceuticals, 2.

Abstract Number: 2270

A Pilot Study of the Psychosocial Impact of Undifferentiated Connective Tissue Disease

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

Background/Purpose: Despite increased awareness related to the diagnosis and treatment of Undifferentiated Connective Tissue Disease (UCTD), there is a dearth of research on the psychosocial impact of the disease. The objective of this qualitative pilot study was to better understand the psychosocial impact of UCTD on patient well-being.

Methods: We identified UCTD patients using the newly established Undifferentiated Connective Tissue Disease (UCTD) and Overlap Registry and the electronic medical record (EMR) clinic schedule of our specialty hospital. We recruited, consented and assembled for participation a convenience sample of patients diagnosed with UCTD, based on the presence of persistent antinuclear antibodies and CTD symptoms not meeting other classification criteria (*Mosca et al, Clin Exp Rheumatol 1999;17:615*). Baseline data on race and ethnicity, education level and disease duration were collected. A licensed clinical social worker administered a 30-minute structured interview by telephone. The standardized questionnaire consisted of demographic and 14 open-ended questions related to understanding and experiences related to UCTD. Grounded Theory was utilized to analyze the qualitative data and identify themes with a team of physicians, research coordinators and a social worker.

Table: Emerging Themes, Categories, and Illustrative Quotes Obtained from Structured Interviews by the Clinical Social Worker with Undifferentiated Connective Tissue Disease (UCTD) Patients (October 2018 – March 2019, n= 14)

Emerging Psychosocial Themes	Categories and Selective Illustrative Quotes
1. Acceptance of the disease	Validation by doctor and self • "I was in limbo, but they finally found out what was wrong with me, I wasn't crazy" • "I found a doctor who took me seriously" • "I may have to face the rest of my life with this, but it won't kill me" • "I don't accept that I have this"
2. Experience many symptoms	Extreme fatigue, loss of muscle strength and mobility, inflammation, joint and body pain and aches, skin changes and rashes: • "a disease that has no boundaries"
3. Uncertainty about future	Unknown future: • "My future is hard to predict. I'm not incapacitated now, but I know that one day I will be" • "I'm conflicted about my future" • "I don't want to be a burden on my family"
4. Importance of Self-management	Find ways to help yourself: positive attitude, exercise, good nutrition, rest, mindfulness, spirituality and prayer, gain knowledge: • "I exercise every day and eat right" • "I've learned to be strong; I focus on today" • "Make yourself a priority" • "Find a good rheumatologist you can talk to" • "Keep a positive attitude"
5. Value of professional support	Psychotherapy, social workers, counseling: • "Therapy helps me and my family cope" • "My family and friends don't always understand" • "Social workers should meet with patients in order to process a new diagnosis or for ongoing support" • A desire for support groups "help patients feel connected... meet each other...hear what someone else is going through"
6. Need to make accommodations	Work:

Results: We contacted 20 UCTD patients, of whom 14 participated (100% female, mean age 58 ± 13y [age range 27-74]). All patients had at least a Bachelor's degree and were predominantly white (64%), with other races included (21% African American, 7% Hispanic/Latina, and 7% Asian). Patients tended to have relatively long mean disease duration (12 ± 14yrs), and over half (64%) were currently engaged in counseling or mindfulness training. Nine specific psychosocial themes and categories emerged (Table), guided by data saturation. Patients expressed that profession-

al guidance and support for themselves, peers and family are necessary to increase awareness, reduce isolation and promote self-efficacy. They voiced a desire to “create support groups to connect to others”, with “patient education material” and to “have caregivers involved.”

Conclusion: This pilot study describes nine psychosocial themes expressed in structural interviews by women with UCTD at a major academic center, reflecting issues that may not be currently appreciated by health-care providers. Future studies will aim to recruit a larger, more diverse UCTD patient population, including those with recently diagnosed disease, to explore themes that may inform best practices for psychosocial interventions (e.g. patient support groups, educational materials, peer counselors) to support UCTD patients in better managing and coping with their illness.

Disclosure: J. Kleinman, None; **E. Sevim**, None; **M. Barbhaiya**, None; **J. Vega**, None; **C. Mancuso**, None; **M. Lockshin**, None; **L. Sammaritano**, None.

Abstract Number: 2271

Sexual Health, Intimacy and Rheumatology Practices

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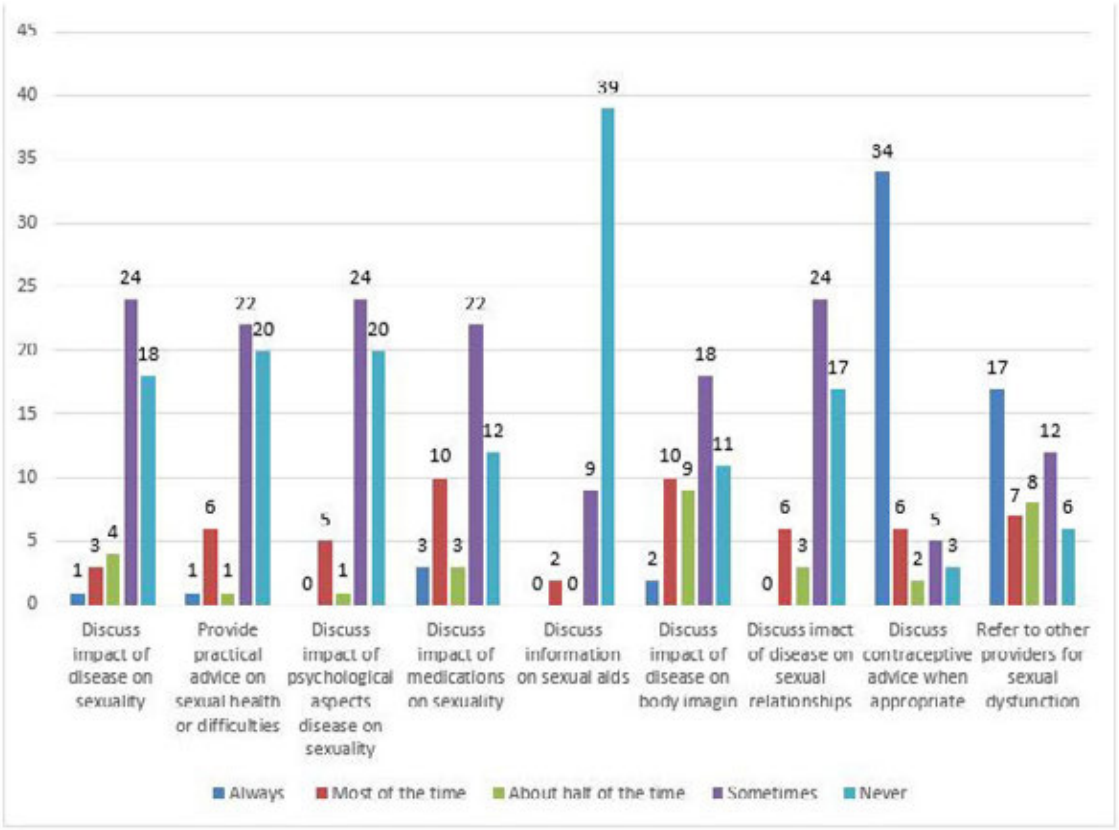

Figure 1. Rheumatology Provider Practices

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Psychology/Social Science Poster – ARP
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with chronic illness often face challenges with their sexual health and intimacy. The issues can be inherent to the disease state, self-image, or physiologic function. Sexual health, function and intimacy issues are rarely included in the health assessment questionnaires and disability indices used by Rheumatologists. In addition, Rheumatologists may be ill equipped to ask and respond to patients' inquiries about sexual function. Most providers acknowledge the impact of a patient's disease on their sexual health, but admitted this area is often neglected. The purpose of this study was to learn about rheumatology care providers' practices when speaking to patients about sexual health and intimacy. Despite the extensive data suggesting the widespread, negative impact of chronic illness on sexual health, we hypothesize that there is a lack of training for providers about how to address sexual health and intimacy issues. We intend to use this information to develop a provider education program so they may provide better care for patients.

Methods: Rheumatology Health Care Providers (HCPs), including Rheumatologists, Nurse Practitioners, and RNs, were asked to complete a 31 item questionnaire (N=50). The survey was designed to understand current practices and potential reasons why providers fail to address sexual health with patients. Ten questions addressed provider awareness of the effects of rheumatologic disease on sexual health, discussion of these topics, and if patients were

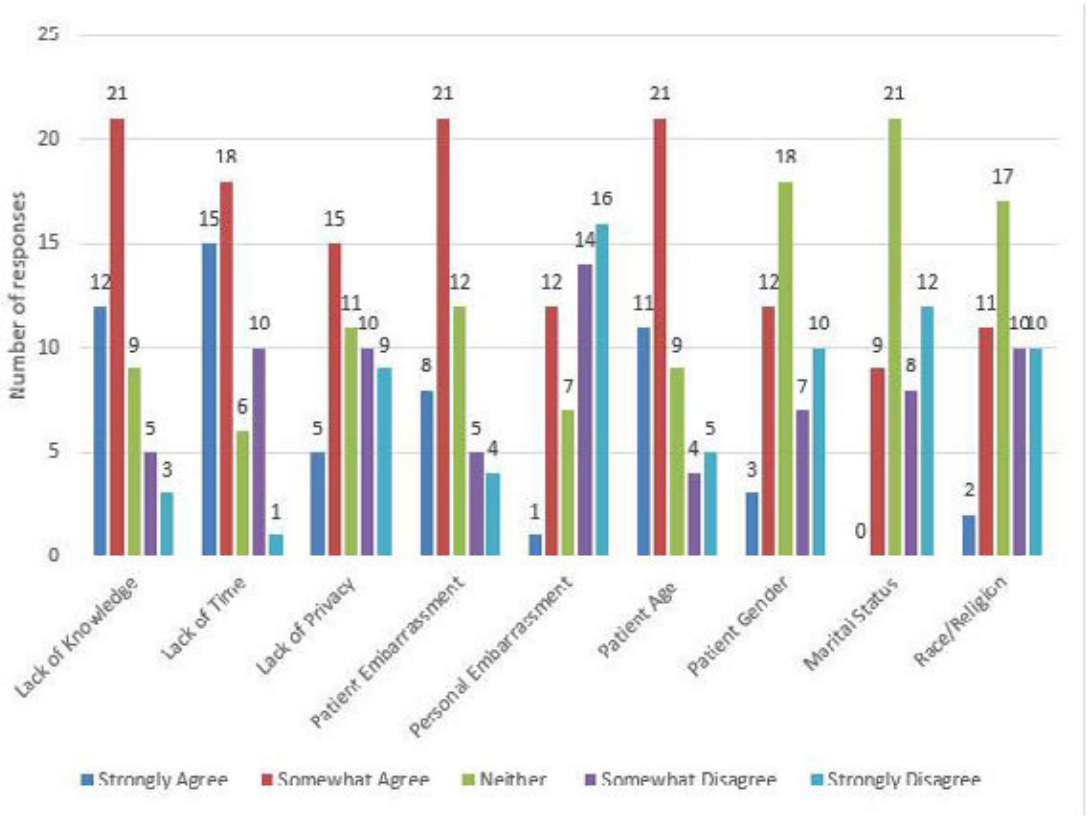

Figure 2. Issues that Influence the Decision to Discuss Sexual Health

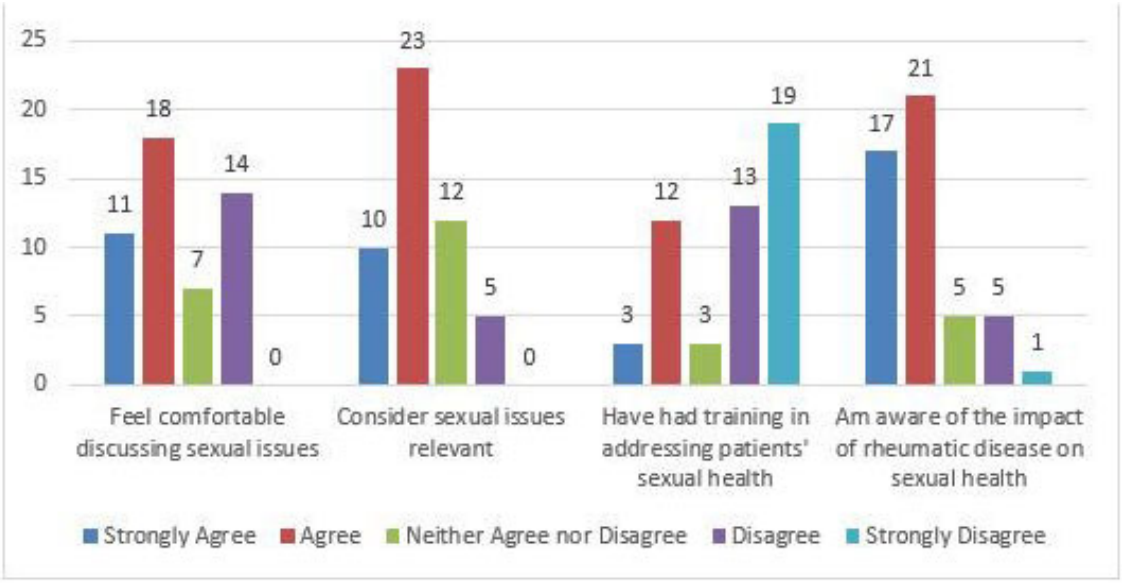

Figure 3. Care Provider Impressions

referred to other providers for assistance. Survey questions also assessed the effect of lack of time, and lack of training or experience in addressing sexual health issues. Each response was that of a five point Likert scale.

Results: Of the 50 HCPs who completed the survey, 48% reported that they discuss the impact of a patient's disease on their sexuality, and the impact of psychological aspects of disease on sexuality "sometimes." However, 36% and 40% of responders report that they "never" discuss either of the two topics, respectively. Additionally, 48% "sometimes" and 34% "never" discuss the impact of disease on patients' sexual relationships. Notably, 78% of HCPs never provide information about sexual aids. The majority of responders reported lack of skills/knowledge about sexual health, patient embarrassment, and patient age as barriers, while lack of time and privacy were noted to significantly interfere with providers' discussion of sexual health. Finally, 66% of HCPs agree or strongly agree that sexual health issues are relevant to rheumatology practice.

Conclusion: The impact of rheumatologic disease on sexual health cannot be underestimated. The results of this study highlight the barriers to discussing sexual health with patients, most significantly, a lack of knowledge about the topic. Additionally, more than half of survey responders agree that sexual health issues should be addressed, indicating an interest in the topic. We intend to use this information to develop a training program for rheumatology HCPs with the goal of educating providers about how to address and guide patients about their sexual health and intimacy issues.

Disclosure: J. Schwartzman-Morris, None; **A. Leo**, None; **P. Nandkumar**, None.

Abstract Number: 2272

Self-reported Anxiety, Depression and Levels of Physical Activity in Patients with Adult Idiopathic Inflammatory Myopathies

Kristofer Andreasson,[1] Helene Alexanderson,[1] and Heléne Sandlund[2], [1]Karolinska Institutet, Stockholm, Sweden, [2]Karolinska University Hospital, Stockholm, Sweden

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Psychology/Social Science Poster – ARP
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The adult idiopathic inflammatory myopathies (IIM) comprise dermatomyositis (DM), necrotizing myopathy (NM), antisynthetase syndrome (ASS), overlap myositis and inclusion body myositis (IBM). Impaired muscle endurance and strength, low aerobic capacity, and self-reported fatigue and pain are common features in patients with IIM. Quality of life is reduced compared to population-based reference values. To our knowledge self-reported levels of physical activity have not been studied within patients with IIM's. Further, anxiety and depression are common in other rheumatic diseases, such as systemic lupus erythematosus, but is less studied in myositis, and not previously in relation to levels of physical activity. Although, there is evidence for symptom reducing effects of exercise for depression and anxiety (Craft & Perna, 2004). The purpose of this study is to assess the levels of self-reported physical activity, depression and anxiety amongst adult patients with adult IIM and to and analyze possible relationships between physical activity and anxiety/depression.

Methods: All patients visiting the Rheumatology clinic at Karolinska University Hospital in Solna between February and May 2019 where asked to fill in questionnaires about their levels of physical activity, anxiety and depression using the International Physical Activities Questionnaire – short form (IPAQ) and Hospital Anxiety and Depression Scale (HADS) which is used for screening, not diagnosis. The questionnaires were distributed by the myositis team nurse. Spearman's rho was used for correlation analysis. HADS is scored in two separate scales, one for depression (HADS-D) and one for anxiety (HADS-A). The cut-off value for probable depression or anxiety is ≥8 of a maximum of 21 per scale. Physical activity was scored as 1 (low, < 150 min/w), 2 (moderate, ≥ 150 min/w) and 3 (high intensity, ≥ 300 min/w).

Results: So far, a total of 34 patients answered the questionnaires. 28 (82%) of the patients reported to be physically active on a health-enhancing level (HEPA) according to WHO's guidelines of 150 minutes of moderate physical activity every week. 12 of these patients reported to be active on a high level the last seven days. A total of seven patients

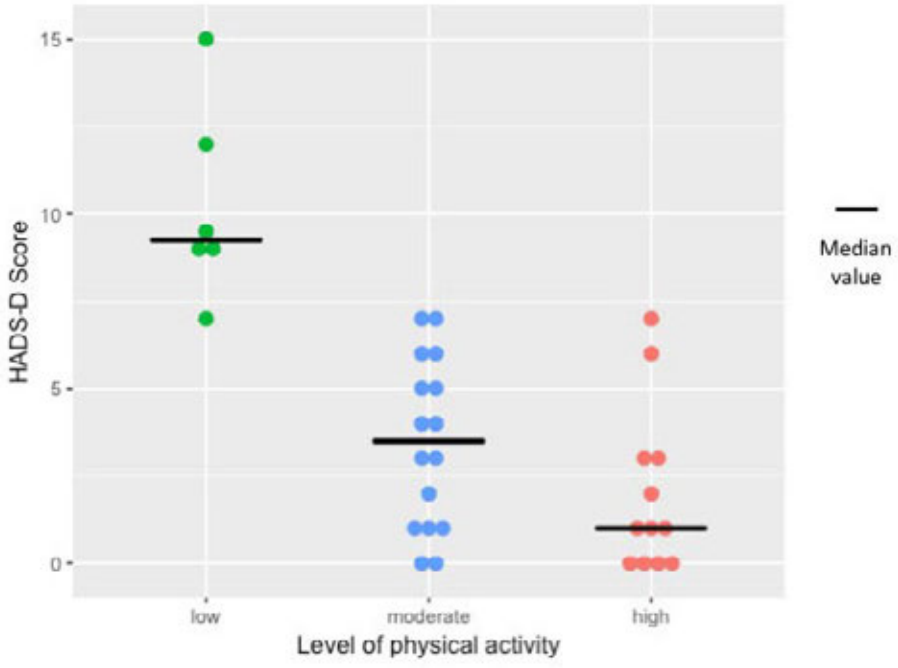

Figure 1. HADS-Depression score grouped by levels of physical activity by IPAQ

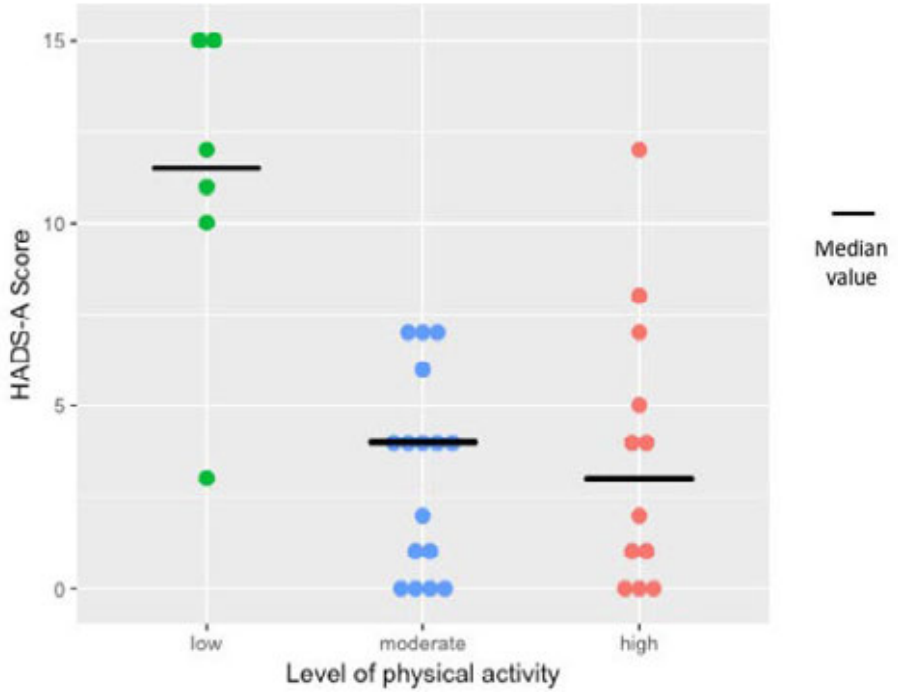

Figure 2. HADS-Anxiety score grouped by levels of physical activity by IPAQ

(21%) scored probable anxiety and/or depression, with five scoring ≥8 for both depression and anxiety. There was a moderate to strong negative correlation between Physical Activity and Depression (Fig. 1), rs=-0.63 (-0.8; -0.37) and a weak negative correlation between Physical Activity and Anxiety (Fig. 2), rs=-0.36 (-0.62; -0.02).

Conclusion: Self-reported data shows that most patients with IIM are physically active on a health-enhancing level and that higher levels of physical activity correlates well with less depression. However, anxiety showed a weaker correlation with physical activity. 82 % of the patients reported to reach HEPA which is a very high number. This can be due to frequent visits to physical therapists early in the disease and then yearly visits with focus on exercise and physical activity. This is preliminary data. Data collection will be ongoing throughout 2019 to confirm these results.

Disclosure: K. Andreasson, None; **H. Alexanderson**, None; **H. Sandlund**, None.

Abstract Number: 2273

Risk of Serious Infections in Offspring According to TNFi Subtypes

Evelyne Vinet,[1] Yvan St-Pierre,[1] Cristiano S. Moura,[1] Jeffrey Curtis,[2] and Sasha Bernatsky[3], [1]McGill University Health Centre, Montreal, QC, Canada, [2]University of Alabama at Birmingham, Birmingham, AL, [3]Research Institute of the McGill University Health Centre, Montreal, QC, Canada

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: Reproductive Issues In Rheumatic Disorders Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: TNFi subtypes have differential placental transfer, with some reaching higher fetal than maternal blood levels. Thus, certain TNFi subtypes could cause immunosuppression in the offspring. However, to date,

there is no data on the risk of serious infections according to TNFi subtypes. We evaluated serious infections in a large group of children born to mothers with chronic inflammatory diseases who used TNFi during pregnancy. Our comparators were unexposed offspring born to affected and unaffected mothers. We determined if the risk of serious infections differed according to TNFi subtypes.

Methods: We identified all women with ≥1 hospitalization for delivery after a diagnosis of rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriasis (PsO), psoriatic arthritis (PsA), or inflammatory bowel diseases (IBD), and a randomly selected group of unaffected mothers, matched ≥4:1 for age, year of delivery, and state of residence, using MarketScan database (2011-2016). We defined TNFi exposure based on ≥1 filled prescription and/or infusion procedure code during pregnancy and/or the preconception period. We further refined TNFi exposure based on potential for high (infliximab, adalimumab, golimumab) vs low (certolizumab, etanercept) placental transfer. We ascertained serious infections in offspring based on ≥1 hospitalization with infection in the 1st year of life. We performed multivariable analyses, adjusting for maternal demographics, disease type, co-morbidities, pregnancy complications, and drugs.

Results: We identified 16,490 offspring of mothers with RA (4,142), AS (381), PsO/PsA (5,743), and IBD (6,731), as well as 164,553 children born to unaffected mothers. Among offspring whose mothers had inflammatory diseases, 1,611 (9.8%) were exposed to TNFi during pregnancy, 338 (2.0%) were unexposed during pregnancy but exposed in the preconception period, and 14,541 (88.2%) were unexposed both during the pregnancy and preconception periods. The percent of serious infections in offspring of inflammatory disease mothers with no TNFi exposure (2.1%; 95% CI 1.9, 2.3) was similar to those with TNFi exposure (2.3%; 95% CI 1.6, 3.0), while the percent of serious infections in children born to unaffected mothers was 1.6% (95% CI 1.6, 1.7). In offspring exposed to TNFi with high placental transfer, the percent of serious infections was 2.3% (95% CI 1.6, 3.3), while for TNFi with low transfer, it was 1.7% (95% CI 1.0, 3.1). In multivariable analyses, we did not observe an increased risk of serious infections in TNFi-exposed offspring vs unexposed offspring of mothers with inflammatory diseases (OR 1.0; 95% CI 0.7, 1.5). Results were similar when we restricted TNFi exposure to the 3rd trimester (OR 1.1; 95% CI 0.7, 1.7). In multivariable analyses of children exposed to TNFi with high vs low placental transfer, our point estimate was consistent with increased risk, but the CI was wide, including the null value (OR 1.43; 95% CI 0.66, 3.08).

Conclusion: When we compared the risk of serious infections in offspring exposed to TNFi with high vs low placental transfer, we observed a potential trend for an increased risk, although the CI was wide and included the null value. Our findings stress the need to further study this issue.

Disclosure: E. Vinet, None; **Y. St-Pierre**, None; **C. Moura**, None; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **S. Bernatsky**, None.

Abstract Number: 2274

Targeted Education Improves Awareness of Reproductive Health Issues Among Women with Rheumatologic Diseases

Sonya Selvaraj,[1] Tanya Allawh,[2] Meagan Clark,[1] Sneha Patel,[3] Christina Payne,[4] and Arundathi Jayatilleke[1], [1]Drexel, Philadelphia, PA, [2]Hahnemann, Philadelphia, PA, [3]Einstein Montefiore, Bronx, NY, [4]Allegheny General, Philadelphia, PA

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Reproductive Issues In Rheumatic Disorders Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Managing rheumatologic conditions in women of childbearing age necessitates consideration of reproductive health issues. We studied reproductive health awareness in women with rheumatic disease by surveying them on the effectiveness of audiovisual (AV) and written educational interventions in improving their knowledge regarding pregnancy, fertility, lactation, and contraception.

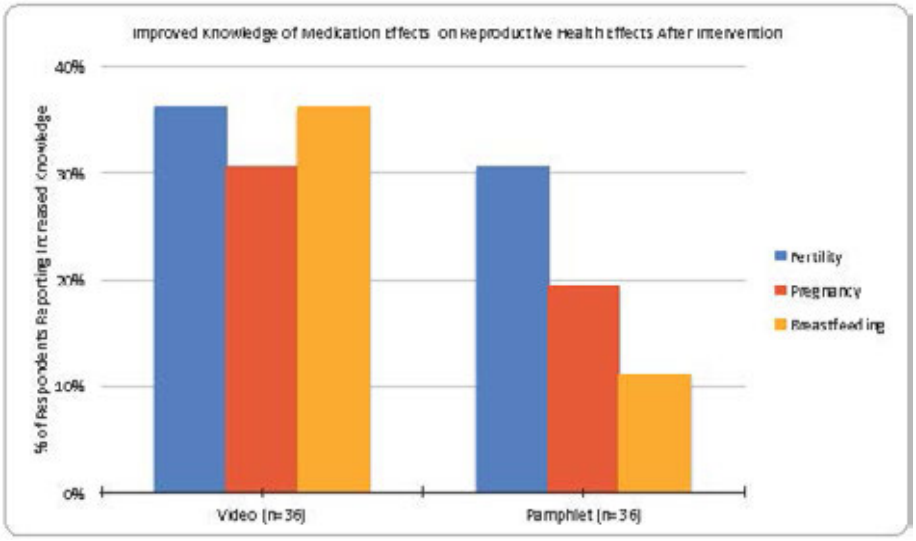

Figure 1 Survey respondents reported improved understanding of reproductive health issues after educational intervention.

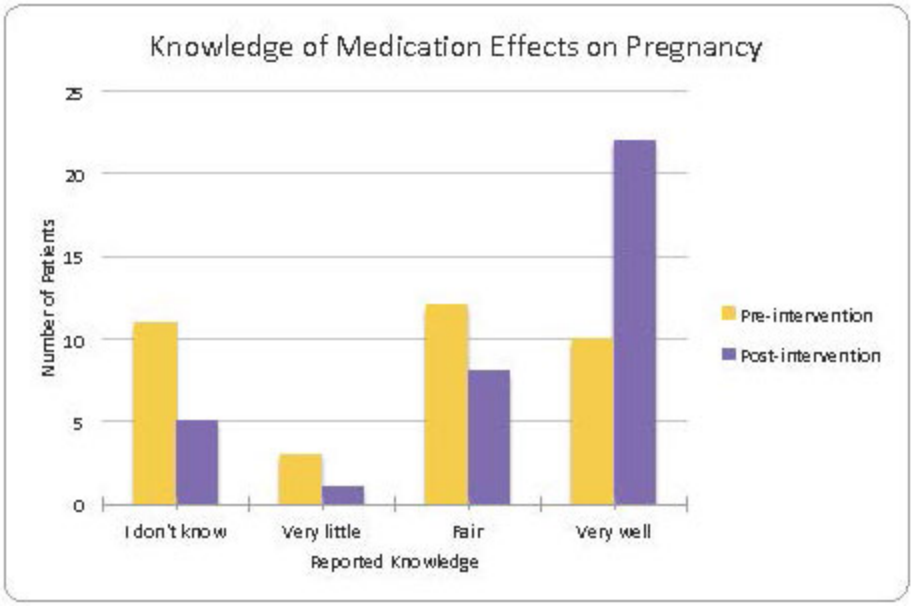

Figure 2 More women reported understanding the issue of medication effects on pregnancy after the intervention (n=36).

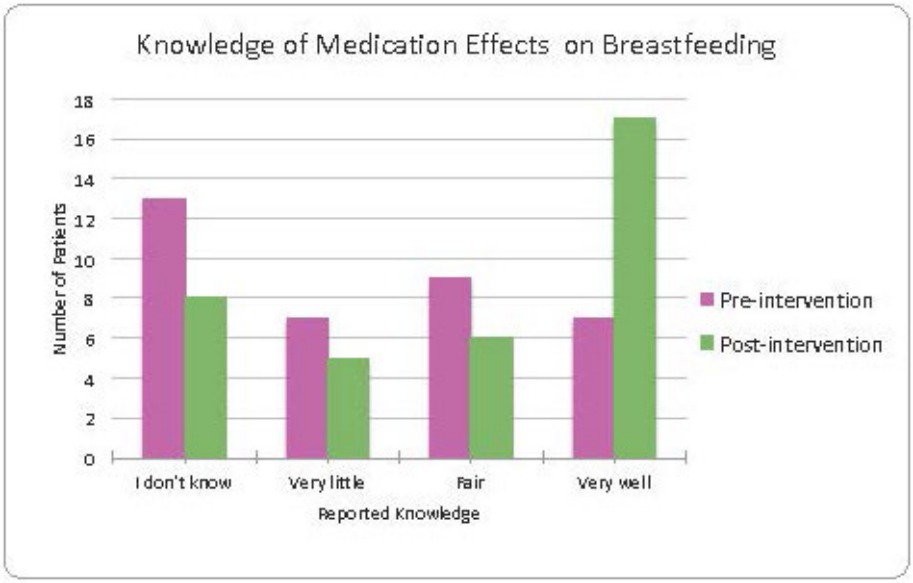

Figure 3 More women reported understanding the issue of medication effects on breastfeeding after the intervention (n=36).

Methods: We enrolled 101 women (ages 18-45) with rheumatic disease at our clinic and surveyed them on awareness of reproductive health issues as well as contraceptive practices. Respondents were randomized to view a video or receive a pamphlet with information on reproductive health issues and were surveyed again at a subsequent office visit.

Results: Pre-intervention surveys showed that of the 26 women who reported being sexually active with men and not using contraception (at risk of becoming pregnant), 19 (73%) were using teratogenic medications and thus at risk of adverse pregnancy outcomes. Furthermore, 32% of all participants reported not receiving any counseling previously regarding reproductive health.

74 (72%) received the intervention after an average of 6 months: 35 women (47%) watched the video and 39 (52%) received a pamphlet. 53 women (72%) returned a post-survey after an average of 9 months from time of intervention. 5 surveys were excluded from the final analysis due to not answering any post-survey questions.

Of the women who completed the post-intervention survey, 67% felt more knowledgeable about medication effects on fertility, 50% on pregnancy, and 47% on breastfeeding. 36%, 30%, and 36% reported improved awareness about fertility, pregnancy, and breastfeeding issues after the AV intervention compared to 30%, 19%, and 11% who received the pamphlet, although the difference did not reach statistical significance (see figure 1). After intervention, more women reported understanding these issues “very well” (see figures 2 and 3). In addition, fewer women (14/53; 26%) reported unprotected sex with men though many (11/14; 79%) were using teratogenic medications.

Conclusion: We previously reported that women with autoimmune diseases are not adequately counseled regarding reproductive health. Here, we show that women who received targeted education reported an increase in birth control use and knowledge about reproductive health, with a trend to better results in the AV arm. Women with rheumatic disease welcomed more information and conversation with providers regarding their reproductive health.

Disclosure: S. Selvaraj, None; **T. Allawh**, None; **M. Clark**, None; **S. Patel**, None; **C. Payne**, None; **A. Jayatilleke**, None.

Abstract Number: 2275

Effect of Race and Lupus Nephritis on Pregnancy Outcomes in Systemic Lupus Erythematosus: An Individual Participant Meta-analysis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Reproductive Issues In Rheumatic Disorders Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Individual cohort studies have found that Black and Hispanic women have worse pregnancy outcomes compared to their white counterparts. Additionally, this population of women has a higher prevalence of lupus nephritis. Therefore, this individual participant meta-analysis pooled data from multiple lupus pregnancy cohorts to assess the effect of maternal race and nephritis on pregnancy outcomes.

Methods: PubMed, Embase, and the Cochrane Database of Systematic Reviews were searched for prospective cohorts of pregnancies among women with lupus. Data from each cohort was collected and analyzed individually. Race was classified as white or non-white. Outcomes of interest included fetal loss, preterm birth (< 37 weeks gestation), preeclampsia, and high disease activity (PGA ever >1 or SLEDAI ever >4 during pregnancy). Pooled ORs were calculated in Review Manager. The analysis included one pregnancy per patient in women with a first trimester visit.

Results: The analysis included 312 pregnancies across three cohorts in the United States and Canada, of which 46% were to non-white mothers and 22% were to women with history of nephritis. Overall, there was an increased risk of fetal loss among non-white patients compared to white patients (OR: 1.96; 95% CI: 1.02,3.77). History of nephritis did not have an association with fetal loss. In patients with no nephritis history, non-white women had a higher rate of fetal loss (OR: 2.16; 95% CI: 1.03,4.52). There was no significant effect of race on preterm birth overall, nor when stratified by history of nephritis . Overall, there was no significant effect of race on preeclampsia. Among white women, a history of nephritis increased the risk of preeclampsia (OR: 3.57; 95% CI: 0.92, 13.92). Overall, non-white patients were at increased risk of high disease activity during pregnancy (OR: 1.74; 95% CI: 0.99, 3.05). Among non-

Association of Maternal Race with Poor Pregnancy Outcomes				
	Fetal Loss Pooled OR (95% CI)	Preterm Birth Pooled OR (95% CI)	Preeclampsia Pooled OR (95% CI)	High Disease Activity Pooled OR (95% CI)
Overall	1.96 (1.02, 3.77)	1.60 (0.90, 2.85)	1.57 (0.73, 3.37)	1.74 (0.99, 3.05)
LN History	1.06 (0.23, 4.84)	1.18 (0.34, 4.12)	0.69 (0.15, 3.11)	2.22 (0.71, 6.97)
No LN History	2.16 (1.03, 4.52)	1.61 (0.82, 3.18)	1.60 (0.65, 3.94)	1.26 (0.64, 2.48)

Table 1. Summary of pooled odds ratios for the association of maternal race with pregnancy outcomes

Association of Lupus Nephritis History with Poor Pregnancy Outcomes				
	Fetal Loss Pooled OR (95% CI)	Preterm Birth Pooled OR (95% CI)	Preeclampsia Pooled OR (95% CI)	High Disease Activity Pooled OR (95% CI)
Overall	1.01 (0.47, 2.22)	1.67 (0.87, 3.18)	2.20 (1.02, 4.75)	2.63 (1.43, 4.85)
White Women	1.29 (0.36, 4.58)	1.80 (0.60, 5.43)	3.57 (0.92, 13.92)	1.73 (0.66, 4.54)
Non-White Women	0.83 (0.31, 2.27)	1.37 (0.59, 3.17)	1.55 (0.50, 4.77)	3.22 (1.40, 7.43)

Table 2. Summary of pooled odds ratios for the association of maternal with pregnancy outcomes

white women, history of nephritis increased the risk of high disease activity during pregnancy (OR: 3.22; 95% CI: 1.40-7.43).

Conclusion: Race is not the only factor driving health disparities in pregnancy outcomes among women with lupus. Additionally, these differences are not entirely explained by the increased prevalence of nephritis in non-white women. When managing lupus in pregnancy, race and history of nephritis are important considerations. However, additional studies are needed to further elucidate why non-white women continue to have disproportionately worse outcomes.

Disclosure: R. Njagu, None; **A. Eudy**, GSK, 2; **S. Balevic**, UCB, 5, Rheumatology Research Foundation, 2, Thrasher Research Foundation, 2, NIH, 2; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, GSI, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5; **M. Urowitz**, Janssen Research & Development, LLC, 2, UCB Pharma, 9; **M. Clowse**, GSK, 2, UCB, 5.

Abstract Number: 2276

Impact of the Healthy Outcomes in Pregnancy with SLE Through Education of Providers (HOP-STEP) Program: A Mixed Methods Approach

Ravyn Njagu,[1] Amanda Eudy,[2] Amanda Snyderman,[1] Lisa Criscione-Schreiber,[2] and Megan Clowse[2], [1]Duke University, Durham, NC, [2]Duke University, Durham

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Reproductive Issues In Rheumatic Disorders Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: While centers have worked to optimize lupus pregnancy outcomes, additional efforts are required to have a broader impact on lupus pregnancy outcomes. The goal of this educational initiative was to create a multi-dimensional intervention to equip community rheumatologists with the needed skills, attitudes, and confidence to effectively manage contraceptive decisions and improve pregnancy outcomes.

Methods: Design of the HOP-STEP program included a needs assessment followed by development of a comprehensive program using mixed modalities to create lasting practice change. The program included an in-person di-

dactic, a simulated clinical experience, training in use of a comprehensive handout to guide open contraception and pregnancy conversations, and access to a website with additional resources including certified medical education. We assessed program impact using a mixed methods approach. A survey was emailed to 149 individuals before and after workshop completion. All attendees were invited to be interviewed about their experience integrating HOP-STEP resources into practice.

Results: We analyzed 68 pre-surveys (response rate 46%, 93% women, 66% attending-level rheumatologists) and 55 post-surveys (response rate 37%, 96% women, 64% attending-level rheumatologists). For qualitative analysis, 8 interviews were completed until thematic saturation was achieved. At program completion, the percentage of providers reporting a systematic approach to preparing a woman with lupus for pregnancy increased from 45.6% to 94.6%; $p< 0.0001$. When assessed using confidence scale (0=no confidence, 100=high confidence), median provider confidence in helping women with lupus choose appropriate contraception increased from 59 to 89; $p< 0.0001$ and confidence in choosing pregnancy compatible medications increased from 66 to 91; $p< 0.0001$. While participants demonstrated limited change in contraceptive knowledge, an emerging theme was use of the HOP-STEP contraception handout: "I'm not really comfortable recommending birth control method[s], but it was interesting to see that whole [contraception] chart…it did increase my confidence because I could just cheat and look at it and show [patients] visually." After the program more providers correctly identified azathioprine (74% to 98%, $p < 0.0001$) and tacrolimus (46% to 91%, $p < 0.0001$) as pregnancy compatible and mycophenolate as teratogenic (84% to 96%, $p=0.04$). Regarding comparative teratogenicity, a common theme was elucidated by the following quote: "That Cellcept is as high as it is on the list of drugs that are very bad for fetuses…I didn't realize that quite as much as I should've, everybody knows about methotrexate, but the fact that Cellcept is probably even worse than methotrexate I was not aware of…"

Conclusion: We have demonstrated successful creation and delivery of a new multi-modal educational program, HOP-STEP, that has improved provider confidence, skills, and knowledge in managing women with lupus who desire pregnancy. Providers may now access a unique curriculum and resources that encourage providers and patients to have open and accurate conversations about pregnancy, creating lasting clinical change.

Disclosure: R. Njagu, None; **A. Eudy**, GSK, 2; **A. Snyderman**, GSK, 2; **L. Criscione-Schreiber**, None; **M. Clowse**, GSK, 2, UCB, 5.

Abstract Number: 2277

Perspectives of Female Patients with Rheumatic Diseases Regarding Pregnancy Planning with Rheumatologists

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Reproductive Issues In Rheumatic Disorders Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose:: Women with rheumatic diseases may be at greater risk for adverse maternal, perinatal, and pregnancy outcomes. The American College of Rheumatology recommends that female patients who are contemplating pregnancy should discuss their individual pregnancy risks with rheumatologists. Little is known about patients' information priorities and preferences for such information, or their general attitudes about pregnancy planning in the rheumatology outpatient setting.

Table 1: Themes and Representative Quotations

Theme	Illustrative Quote
Rheumatologist Awareness of Reproductive Plans	*I think an initial conversation and opening the door to conversations about sexual and reproductive health on the initial visit is really helpful in building that relationship and that line of communication with the rheumatologist. (34 years old, Spondyloarthritis)*
	I would just say they should bring it up. I know with my doctor, they didn't bring it up, I brought it up. It made it even more uncomfortable when I brought it up because of my age and stuff I was still kind of shy... I think if they would bring it up once in a while it would make it open more. (29 years old, Systemic Lupus Erythematosus)
Rheumatologist Provides Clear Pregnancy and Family Planning Information	*I want doctors to be honest with me. I don't want them to sugarcoat it... I just want them to be honest with me and tell me what to expect and everything. Because some doctors, they try to make it sound better than what it is. (29 years old, Systemic Lupus Erythematosus)*
	What do I expect? Honestly, I just expect honest answers... You know, lupus is not a good disease; it's a really brutal, ugly disease that manifests in a lot of ways, this being one of them, and I want to be prepared for the future, so I appreciate that he's able to tell me what this is really going to look like, and what's going to help me have the smoothest pregnancy. (29 years old, Systemic Lupus Erythematosus)
Rheumatologist Provides Holistic Care	*I think people [rheumatologists] get so focused on their specialty, sometimes they're not thinking about how that can affect other aspects of someone's life... I think thinking holistically about their approach to an individual's care, they need to consider other parts of their life, mental, physical, and what your plans are, what your life is about. (34 years old, Rheumatoid Arthritis)*
Discontinuation of DMARDs in Pregnancy†	*I probably wouldn't want to take it. I don't know- I'd have to talk to the doctor. I know with my other pregnancies I did not take any type of medication while I was pregnant so it'd definitely be something I'd have to discuss with them. I'm kind of a person that errs on the side of caution that I would sacrifice, I guess, more of how I'm feeling for if the baby was safe. (43 years old, Systemic Lupus Erythematosus)*
Enhanced Communication Between Rheumatologist & ObGyn	*I expect her [rheumatologist] to advise my OBGYN when it comes time. To tell them what I have and what to watch out for. For instance, to watch out for lupus in the infant or in the womb... not all OBGYNs I've seen know about that. (35 years old, Systemic Lupus Erythematosus)*
	I think providers should be able to collaborate amongst themselves, so if I'm needing my gynecologist to communicate with my rheumatologist, I shouldn't be a middle person for that, but right now, how it's set up, I am the mediator for that plan of care. (34 years old, Rheumatoid Arthritis)

†DMARDs, Disease-Modifying Anti-Rheumatic Drugs.

Methods: Female patients ages 18-45 with at least one rheumatic disease were recruited to participate in semi-structured qualitative interviews that explored their priorities and preferences related to reproductive health care. Recruitment occurred in outpatient rheumatology clinics in Pittsburgh, PA. Interviews were conducted via telephone, and were audio-recorded and transcribed verbatim. A code book was inductively developed based on transcript

content. Two coders applied the code book to all transcripts (Cohen's Kappa= 0.69), and coding differences were adjudicated to full agreement. The finalized coding was used to conduct a thematic analysis.

Results: Interviews were conducted among 30 women, who were 35.1 years old on average (S.D. 5.84); 52% were married, 53% had children, and 73% were white. The most common diagnoses included rheumatoid arthritis (23% of sample), systemic lupus erythematosus (23%), Sjogren's syndrome (17%), undifferentiated connective tissue disorder (10%), and spondyloarthritis (7%). Five themes emerged: 1) Women wanted rheumatologists to initiate conversations about family planning repeatedly over time; 2) Women desired clear and complete information from rheumatologists regarding fetal, pregnancy, and infertility risks associated with their diseases and disease-modifying anti-rheumatic drugs (DMARDs); 3) Women wanted to be treated holistically, with family planning issues addressed in the context of their life circumstances and personal values as well as their diseases; 4) Women were reluctant to continue any DMARDs during pregnancy, even if compatible with pregnancy; 5) Women felt that they were often intermediaries between their rheumatologists and obstetrician-gynecologists (ObGyns), but preferred for their rheumatologists to communicate directly with their ObGyns in advance of and during pregnancy. Illustrative quotations are presented in Table 1.

Conclusion: Patients strongly desired for rheumatologists to play an active and continuous role in their family planning care. Patients specifically want for their rheumatologists to provide education, review DMARD- and disease-related risks related to pregnancy, and communicate directly with ObGyns before and during pregnancy to optimize a woman's chances for a healthy pregnancy. Prior studies indicate that family planning rarely occurs in the rheumatology outpatient setting; our results further suggest that some women with rheumatic diseases do not receive the family planning care that they desire. Further work is needed to clarify the role of rheumatologists in family planning, and how to enhance communication between rheumatologists and other women's healthcare professionals.

Disclosure: T. Wolgemuth, None; **M. Birru Talabi**, None; **A. Chodoff**, None; **S. Borrero**, None; **M. Talabi**, None.

Abstract Number: 2278

Perspectives About Contraception Among Reproductive-Aged Women with Rheumatic Diseases

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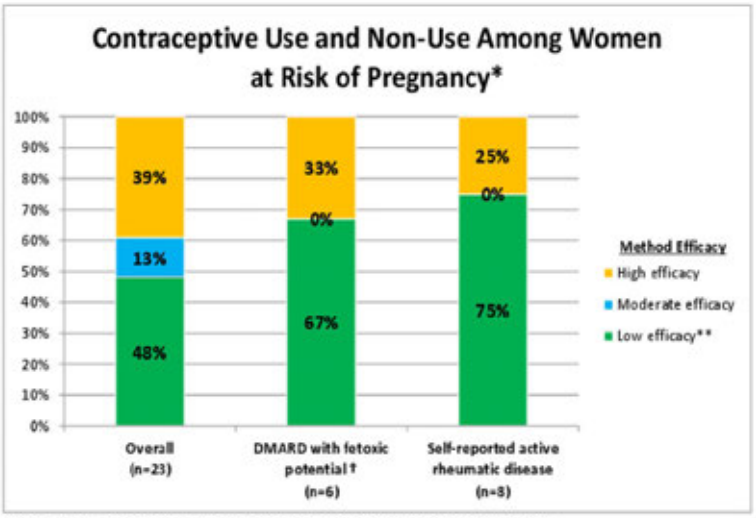
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Reproductive Issues In Rheumatic Disorders Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Prior work suggests that women with rheumatic diseases are rarely prescribed contraception. However, in addition to preventing undesired pregnancy, contraception may help these women to delay pregnancy until their diseases are well-controlled on pregnancy-compatible anti-rheumatic drugs— thus, optimizing their chances for healthy maternal and fetal outcomes. While hormonal contraception may augment thrombotic risks in diseases such as systemic lupus erythematosus and antiphospholipid antibody syndrome, most women with rheumatic diseases are able to use contraception safely. This qualitative study explored women's perspectives about contraception use in the context of their diseases, and their preferences for contraception care from their health care providers.

Figure 1. Contraception use and non-use among women with rheumatic diseases at risk of pregnancy (N=23).



*Not currently pregnant or trying to become pregnant and has not had a hysterectomy.

** High efficacy: tubal ligation, vasectomy, IUD, or implant. Moderate efficacy: oral contraceptive. Low efficacy: condom, withdrawal, abstinence, or no method.

† DMARD with fetotoxic potential: Methotrexate (n=4) and mycophenolate mofetil (n=2) (Gotestam Skorpen C, Hoeltzenbein M, Tincani A, Fischer-Betz R, Elefant E, Chambers C, et al. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. Ann Rheum Dis. 2016;75(5):795-810.)

Table 1. Distribution of Rheumatic Diagnoses and Disease-Modifying Anti-Rheumatic Drugs (DMARDs)

Five most common diagnoses	**N**	**%**
Rheumatoid Arthritis	7	23%
Systemic Lupus Erythematosus	7	23%
Sjogren's Syndrome	5	17%
Undifferentiated Connective Tissue Disease	3	10%
Spondyloarthritis	2	7%
DMARD use in the sample*		
Hydroxychloroquine	11	26%
Prednisone	8	19%
Azathioprine	4	9%
Methotrexate	4	9%
Leflunomide	3	7%
Mycophenolate	3	7%
Etanercept	2	5%
Intravenous immunoglobulin	2	5%
Sulfasalazine	2	5%
Abatacept	1	2%
Infliximab	1	2%
Ustekinumab	1	2%
Tocilizumab	1	2%

*Some patients used more than one DMARD.

Table 2. Major Themes and Illustrative Quotations

Theme	Illustrative Quotation
Women feared that hormonal contraception could exacerbate their diseases, irrespective of the disease	*"I used [combined estrogen-progestin oral contraceptive pill] for about three years. And after I was diagnosed with lupus, I didn't take any birth control whatsoever."* (Patient with systemic lupus erythematosus, uses withdrawal method) *"I was put on an oral contraceptive before I got diagnosed with my autoimmune disease, and then after just talking to the rheumatologist it seemed the risks outweighed the benefits of it, so we just switched to using condoms."* (Patient with mixed connective tissue disease, uses condoms)
Women were more concerned about theoretical risks of hormones than the efficacy of the contraceptive method	*"I've been nervous about taking hormonal contraception because I didn't have a provider that could guide me through the process who had an understanding of hormones and autoimmune disease, so I didn't really use any birth control for the past few years."* (Patient with spondyloarthritis, currently pregnant) *"With lupus there's a higher risk of blood clots... you don't want to compound that with a pill."* (Patient with systemic lupus erythematosus, uses condoms)
Women who used fetotoxic DMARDs or self-reported that they had active disease were not more likely to select a contraceptive method based on its efficacy than other women	*"On occasion it makes me a little uneasy... however, given my hormonal issues, odds are incredibly low that I would conceive even without the condom."* (Patient with rheumatoid arthritis, prescribed methotrexate and abatacept, uses condoms) *"My PCP... asks what I'm on and reiterates that, 'you should not become pregnant', that we should be using some type of birth control to prevent pregnancy with being on this medication."* (Patient with psoriatic arthritis, prescribed methotrexate and ustekinumab, uses condoms)
Patients rarely sought information on contraception from their rheumatologists but some women lacked access to a gynecologist or primary care provider	*"[My rheumatologist] seems like he's pretty conservative. It just seems it would make him uncomfortable to talk about it."* (Patient with granulomatosis with polyangiitis, uses condoms) *"I see my rheumatologist for the rheumatology... I would only get my rheumatologist involved if I wanted to get pregnant."* (Patient with spondyloarthritis, uses oral contraceptive pill)

Methods: Semi-structured interviews were conducted among women ages 18-45 diagnosed with at least one rheumatic disease, who were recruited from two outpatient rheumatology clinics in Pittsburgh, PA. Interviews were transcribed verbatim, and a code book was inductively developed based on transcript content. Two independent coders applied the code book to all transcripts, and coding differences were adjudicated to full agreement. The finalized coding was used to conduct a thematic analysis.

Results: Thirty women participated in interviews; the average age of the sample was 35.1 years (S.D. 5.8), and most women were white (73%), married (52%), and had at least one child (53%). Twenty-three women were at risk for preg-

nancy; others had a hysterectomy, were pregnant (n=2), or attempting to conceive (n=1). Table 1 presents the disease diagnoses and DMARDs used by women in the sample. Four major themes about contraception emerged from the interviews (Table 2): 1) Women feared that hormonal contraception could exacerbate their rheumatic diseases, irrespective of the disease; 2) Women were more concerned about theoretical risks of hormones than the efficacy of the contraceptive method; 3) Women who used fetotoxic DMARDs or reported that they had active rheumatic disease were not more likely to select a contraceptive method by its efficacy than other women; and 4) Patients rarely sought information about contraception from their rheumatologists but some women lacked access to a gynecologist or primary care provider. Figure 1 presents contraception methods used by women at risk of pregnancy and by women who used potentially fetotoxic DMARDs or who had active disease— i.e., elevated risk of adverse pregnancy outcomes.

Conclusion: Many women prioritized limiting their exposure to hormones rather than preventing pregnancy with hormonal contraception, including women who did not wish to become pregnant or had elevated risk of adverse pregnancy-related outcomes. Most women did not perceive that their rheumatologists were the appropriate providers to manage their contraception care, but some women lacked access to contraception providers. Our study suggests that women with rheumatic diseases may require counseling about the effects of exogenous hormones on their diseases, education about safe and efficacious contraception methods, and consistent access to contraception care.

Disclosure: O. Stransky, None; **T. Wolgemuth**, None; **A. Chodoff**, None; **M. Birru Talabi**, None.

Abstract Number: 2279

Pregnancy in Rheumatoid Arthritis: Continue, Reduce or Stop TNF Inhibitors? A Prospective Observational Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Reproductive Issues In Rheumatic Disorders Poster
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Background/Purpose: Women with active Rheumatoid Arthritis (RA) are more prone to relapses and complications during pregnancy. The potential risks of disease activation and treatment during gestation have to be weighed in a shared decision prior to conception. An increasing number of women who wish to conceive are being treated with TNF inhibitors (TNFi). Some want to discontinue or at least reduce therapy during pregnancy and require information on opportunities and risks. Therefore, we sought to explore the outcome of pregnancies in women with RA who either discontinued, reduced or maintained TNFi treatment after conception.

Methods:: Pregnancies of women from an outpatient pregnancy clinic were evaluated before conception, during each trimester and postpartum. Clinical characteristics, disease activity (DAS28-CRP), medication use and pregnancy outcome were analysed. A flare was defined as increase in DAS28 > 1.2 or an increase in DAS28 > 0.6 and DAS28 ≥ 3.2. All women received extensive counselling before pregnancy based on current knowledge and subsequently decided to continue or stop TNFi at conception. If they stayed on TNFi and were in remission, women received the suggestion to stretch the therapy intervals in a disease activity guided manner.

	TNFi exposure until conception (N=41)	Pregnancies with ongoing TNFi exposure (N=29)	
		Successful reduction (N=17)	No reduction possible (N=12)
Patient characteristics at conception			
Age (years), median (IQR)	32 (29-34)	34 (32-36)	36 (34.75-37.25)
Disease duration (months), median (IQR)	92 (48-216)	96 (84-168)	82 (58-121.5)
Seropositivity, n (%)	21 (51.2%)	11 (68.8%)	10 (83.3%)
DAS28, median (IQR)	2.9 (2.5-3.1)	2.5 (2.175-2.75)	2.8 (2.6-2.9)
Prednisolone (mg/day), (median, IQR)	5.0 (5.0-7.0)	5.0 (3.0-5.0)	5.0 (3.0-5.0)
Sulfasalazine, n (%)	2 (4.9%)	5 (29.4%)	1 (8.3%)
HCQ, n (%)	1 (2.4%)	4 (23.5%)	3 (25.0%)
Pregnancy outcomes			
DAS28-CRP ≤ 3.2, n (%)			
1st trimester	24 (58.5%)	17 (100%)	9 (75.0%)
2nd trimester	17 (41.5%)	14 (82.4%)	9 (75.0%)
3rd trimester	23 (56.1%)	14 (82.4%)	8 (72.7%)
3 months postpartum	18 (43.9%)	14 (82.4%)	8 (66.7%)
6 months postpartum	30 (75%)	13 (81.2%)	10 (83.3%)
Flare during pregnancy, n (%)	26 (63.4%)	3 (18.8%)	3 (27.3%)*
Odds ratio	1	0.06, 95% CI 0.01-0.57, p=0.01	0.12, 95% CI 0.02-0.61, p=0.01
Flare postpartum, n (%)	13 (32.5%)	2 (12.5%)	1 (9.1%)
Odds ratio	1	0.27, 95% CI 0.07-0.95, p=0.04	0.29, 95% CI 0.07-1.22, p=0.09
Preterm birth[*1], n (%)	11 (26.8%)	1 (5.9%)	1 (8.3%)
Low birth weight[*2], n (%)	7 (17.0%)	-	1 (8%)
Breastfeeding, n (%)	28 (68.3%)	15 (88.2%)	10 (90.9%)
Glucocorticoid use during pregnancy			
Prednisolone (mg/day), (median, IQR)			
1st trimester	10.0 (5.0-10.0)	5.0 (5.0-6.0)	5.0 (3.0-5.75)
2nd trimester	10.0 (10.0-15.0)	5.0 (5.0-6.0)	5.0 (3.0-7.75)
3rd trimester	10.0 (7.0-12.75)	5.0 (4.25-6.375)	5.0 (4.0-7.25)
Of those taking prednisolone – taking ≥ 10mg/d, n (%)			
1st trimester	17 (65.4%)	1 (11.1%)	2 (16.7%)
2nd trimester	24 (82.8%)	1 (10.0%)	3 (25.0%)
3rd trimester	19 (70.4%)	-	2 (18.2%)
Intraarticular steroid therapy, n (%)			
1st trimester	8 (19.5%)	-	2 (16.7%)
2nd trimester	12 (30.0%)	3 (17.6%)	2 (16.7%)
3rd trimester	3 (7.5%)	2 (11.8%)	2 (18.2%)

[*1]≤ 36+6 weeks of gestation, [*2] birth weight < 2500g, HCQ = hydroxychloroquine

Table 1

We applied a multivariate logistic regression model to assess the association between the use of TNFi throughout pregnancy and the occurrence of flares during pregnancy. Adjustment for potential confounders (age, disease duration, DAS28 at conception, sero-positivity, HAQ, previous therapy with methotrexate, previous joint surgery) was performed using logistic regression.

	No TNFi	Adalimumab	Certolizumab	Etanercept
Women on therapy at preconception				
All Groups, n (%)	10 (14.3%)	9 (12.9%)	22 (31.4%)	29 (41.1%)
Group 1, n (%)	10 (24.4%)	4 (9.8%)	7 (17.1%)	20 (48.8%)
Group 2a, n (%)	-	2 (11.8%)	8 (47.1%)	7 (41.2%)
Group 2b, n (%)	-	3 (25.0%)	7 (58.3%)	2 (16.7%)
Women of group 2a during pregnancy				
Therapy interval (weeks), median (min-max)	-	3.5 (3.0-4.0)	4.0 (4.0-5.0)	2.0 (1.5-6.0)

Table 2

Results: After exclusion of two miscarriages, 70 completed pregnancies were enrolled and grouped according to their decision to stop (group 1) or continue (group 2) TNFi therapy during pregnancy. The latter were subdivided into those who could stretch the therapy intervals (group 2a) and those who could not (group 2b). A significantly lower flare rate during pregnancy was observed in women who continued their TNFi, whether they could or could not stretch application intervals (OR 0.06 and 0.12, respectively). Postpartum, again both groups with continued TNFi showed a lower flare rate, but significance was only reached in those who were able to reduce TNFi with an OR of 0.27. In addition, a higher dose of oral prednisolone was reported in group 1 (Table 1).

About 59% of the women who chose to stay on therapy during gestation were able to stretch the injection interval of their TNFi, which was either Adalimumab (median every 3.5 [min 3.0, max 4.0] wks), Certolizumab (median every 4.0 [min 4.0, max 5.0] wks) or Etanercept (median every 3.0 [min 1.5, max 6.0] wks) (Table 2).

Conclusion: Women with RA who discontinue TNFi at conception face a higher risk of flares during pregnancy and often have an increased demand for steroids to control disease activity. When in remission under ongoing TNFi therapy during pregnancy, it seems possible and safe for women to reduce the frequency of injections in a disease activity guided manner. These real-world data will help to provide women with comprehensive advice on treatment options and risks regarding TNFi therapy at pregnancy counselling.

Disclosure: I. Haase, None; **S. Spaethling-Mestekemper**, None; **R. Brinks**, None; **M. Schneider**, None; **R. Fischer-Betz**, None.

Abstract Number: 2280

Reproductive Health Intention Screening in Women with Systemic Rheumatic Diseases: Low Uptake and Gender-Specific Provider Patterns Following a Standardized Intervention

Katherine Pryor,[1] Bill Albert,[2] Susan Ritter,[3] Laura Tarter,[3] Jonathan Coblyn,[3] Bonnie Bermas,[4] Caryn Dutton,[3] Lydia Pace,[3] Elizabeth Janiak,[3] and Candace Feldman[5], [1]Brigham and Women's Hospital, Brookline, [2]Power to Decide, Washington, DC, [3]Brigham and Women's Hospital, Boston, [4]UT Southwestern, Dallas, [5]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Reproductive Issues In Rheumatic Disorders Poster

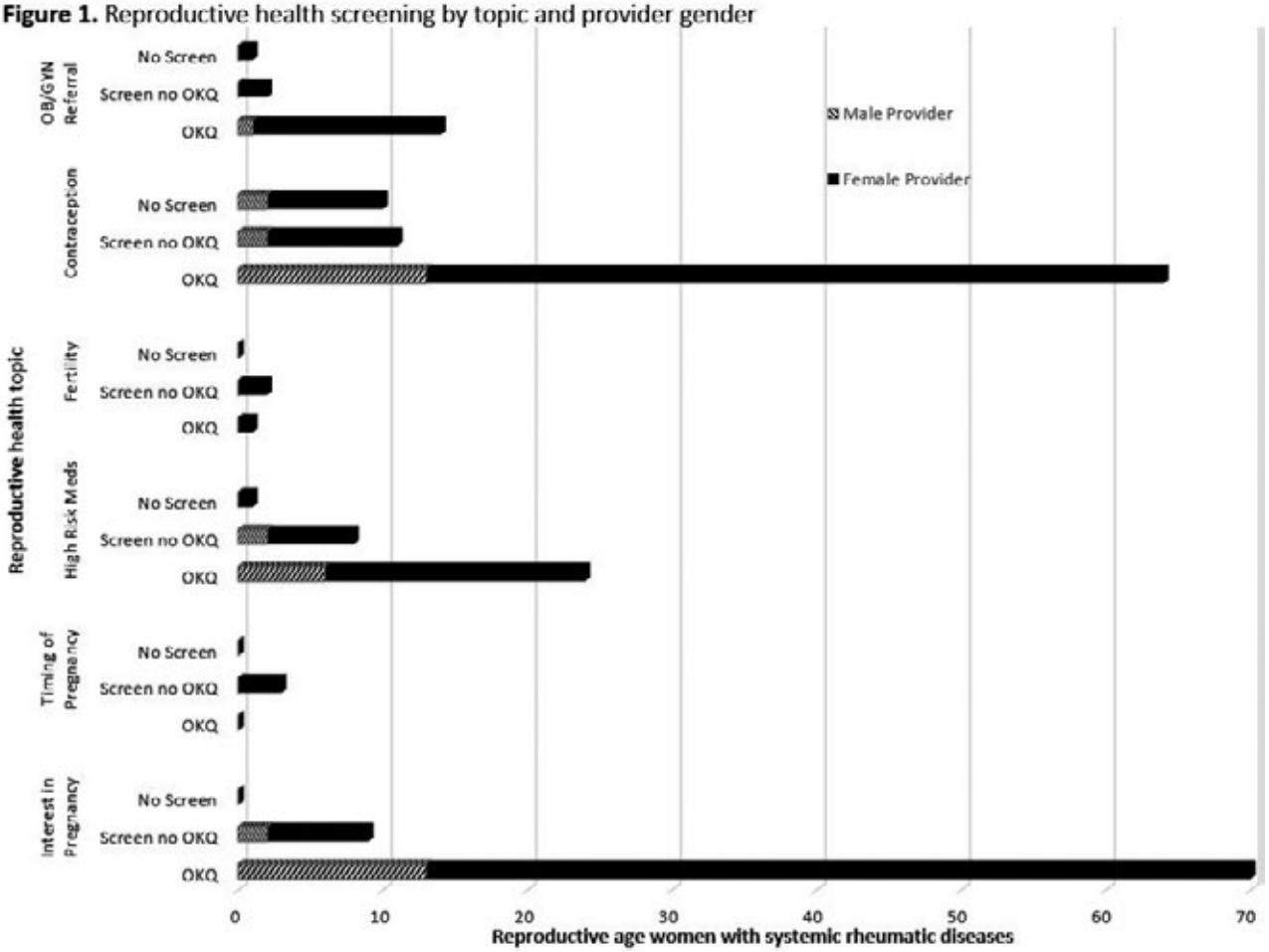
Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Table 1. Patient characteristics by reproductive health screen				
	OKQ used N=83 patients	OKQ not used, but reproductive health intention screening documented (N=18)	No OKQ or reproductive health preference screening* (N=78)	p-value**
Age (mean years ± SD)	33.3 ± 7.0	31.8 ± 8.9	37.0 ± 9.3	**0.02**
Race – N (%)				
• White	55 (71.4)	11 (64.7)	53 (72.6)	
• Black	12 (15.6)	2 (11.8)	8 (11.0)	0.06
• Asian	2 (2.6)	1 (5.9)	8 (11.0)	
• AI/AN	–	–	1 (1.4)	
• Other	8 (10.4)	3 (17.7)	3 (4.1)	
Insurance status – N (%)				
• Medicaid	18 (21.7)	3 (16.7)	12 (15.4)	
• Medicare	6 (7.2)	0 (0)	14 (18)	0.07
• Commercial	56 (67.5)	14 (77.8)	46 (59)	
• Uninsured	2 (2.4)	1 (5.6)	4 (5.1)	
• Other/Unknown	1 (1.2)	0 (0)	2 (2.6)	
Rheumatic disease – N (%)				
• RA	28 (33.7)	7 (38.9)	23 (29.5)	
• SLE	23 (27.7)	6 (33.3)	26 (33.3)	
• APS	3 (3.6)	3 (16.7)	2 (2.6)	
• MCTD	4 (4)	0 (0)	3 (3.9)	
• Psoriatic arthritis	4 (4.8)	0 (0)	6 (7.7)	0.92
• AS	5 (6.0)	0 (0)	3 (3.9)	
• Inflammatory arthritis+	5 (6.0)	1 (5.6)	5 (6.4)	
• Other	14 (16.9)	4 (22.2)	12 (15.4)	
Mean (SD) number of comorbidities	1.23 ± 0.9	1.17 ± 1.4	1.58 ± 1.6	0.09
High-risk medication use# - N (%)	38 (46.9)	6 (33.3)	27 (34.6)	0.22
Rheumatologist Gender - N (%)				
• Male	14 (16.9)	5 (27.8)	29 (37.2)	
• Female	69 (83.1)	13 (72.2)	49 (62.8)	**0.007**
Type of contraception- N (%)++				
• Highly effective methods	29 (34.9)	5 (27.8)	12 (15.4)	
• Other methods	30 (36.1)	1 (5.6)	9 (11.5)	
• Unknown	3 (3.6)	5 (27.8)	53 (68)	**<0.0001**
• None	21 (25.3)	7 (38.9)	4 (5.1)	
Ob/Gyn Referral – N (%)				
• Yes	10 (12.1)	1 (5.6)	0 (0)	**0.003**
• No	73 (88)	17 (94.4)	77 (100)	

Background/Purpose: Reproductive health intention screening is critical in women with systemic rheumatic diseases, as both disease activity and medication use can impact pregnancy outcomes. However, studies report that < 50% of patients with rheumatic diseases receive contraception counseling. We introduced a simple reproductive

Figure 1. Reproductive health screening by topic and provider gender



health intention screen, One Key Question ® (OKQ), to our academic rheumatology practice and examined subsequent practice patterns.

Methods: We developed an electronic medical record (EMR) smart phrase with OKQ ("Would you like to become pregnant in the next year?") with responses that would prompt documentation of contraception, teratogenic medication use and referrals for OB/GYN care when appropriate. Reproductive age (18-50 year-old), female patients with a systemic rheumatic disease were flagged in the EMR for screening before appointments. We introduced OKQ at Rheumatology Grand Rounds, in email notifications, and with exam room reminder cards. Documentation of OKQ was at the rheumatologists' discretion. We measured reproductive health intention screening over 6 months following introduction of OKQ, conducted chart reviews, and used descriptive statistics and a logistic regression model to compare patients who were screened (with OKQ or other documentation) vs. a randomly selected subset of patients who had been flagged for screening but did not have OKQ documented.

Results: Over the 6-month pilot with 43 rheumatologists (56% female), among 1092 reproductive age women with rheumatic diseases, 11 providers (82% female) used OKQ to document reproductive health preferences for 83 women (8%). In the subset of 96 charts flagged for screening but without OKQ documented, 15 providers (67% female) documented reproductive health screening (without OKQ) for 18/96 women (19%). Patients had 2.4 times higher odds of being screened if they saw a female vs. male rheumatologist (95% CI 1.21-4.85). OKQ use resulted in documentation of a broader range of reproductive health topics by rheumatologists of both gen-

ders (Figure 1). Adjusting for provider gender, a 1-year increase in patient age was associated with 5% lower odds of screening (95% CI 0.02-0.09). Highly effective contraception was associated with reproductive health screening (p< 0.0001). Although use of a high-risk medication was not associated with screening (p=0.22) (Table 1), rheumatologists who screened their patients were more likely to document risks of teratogenic medications (p< 0.0001).

Conclusion: Despite introducing a simple, standardized intervention, < 10% of reproductive age women with rheumatic diseases were comprehensively screened using OKQ, < 20% of an eligible subset were asked selected reproductive health-related questions, and >50% of unscreened patients had no documented contraception. Younger age and seeing a female rheumatologist resulted in higher odds of screening. While some providers may have screened patients without documenting the response, the data suggest that a high proportion of patients are not being screened. While uptake was suboptimal, this intervention improved the depth and breadth of reproductive health documentation among those who were screened.

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Abstract Number: 2281

The Vasculitis Pregnancy Registry (V-PREG): Information from the First 3 Years

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Reproductive Issues In Rheumatic Disorders Poster
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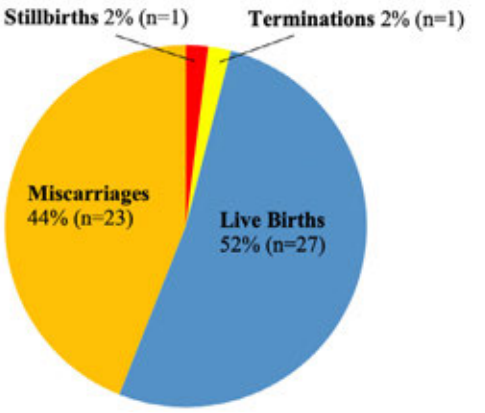
Background/Purpose: As outcomes for patients with vasculitis improve and treatments become less ovarian-toxic, more women with these diseases will become pregnant. How best to manage these pregnancies remains unclear

Table 1: Enrollment in V-PREG

Type of Vasculitis	Number of Patients
Granulomatosis with Polyangiitis	19
Microscopic Polyangiitis	2
Eosinophilic Granulomatosis with Polyangiitis	3
Takayasu's Arteritis	15
Behçet's Disease	5
IgA Vasculitis	4
Central Nervous System Vasculitis	3
Urticarial Vasculitis	3
Polyarteritis Nodosa	1
Other/Suspected	7

Figure 1: Outcomes of Pregnancies Prior to a Diagnosis of Vasculitis



and, given the rarity of these pregnancies, challenging to study. The Vasculitis Pregnancy Registry (V-PREG) is an online, patient-driven prospective pregnancy registry designed to collect observational data to increase our understanding of pregnancies in women with vasculitis [www.vpprn.org/VPREG].

Methods: V-PREG is imbedded within the online Vasculitis Patient-Powered Research Network (VPPRN), where members are asked to participate in this specific registry during pregnancy. Women with any form of vasculitis are eligible. All women indicate informed consent and are invited to complete online surveys at study entry, in each trimester, and post-partum. Women report pain, overall health, and vasculitis disease activity on a 0-10 visual analog scale (scores < 3 indicated minimal pain, vasculitis activity, or good health). Reminders to complete study surveys are sent to patients via repeated emails and phone calls.

Results: Between 11/2015-12/2018 62 pregnant women with one of several vasculitides enrolled in V-PREG (**Table 1**). Almost all women (95%) were diagnosed with vasculitis prior to conception and 67% (41/61) had been hospitalized for vasculitis at least once.

Twenty-one women reported 52 prior pregnancies **(Figure 1).** Of these, 44% (n=23) resulted in a miscarriage, with losses reported among several vasculitides. Additionally, 1 stillbirth and 1 elective termination were reported.

Of 36 pregnancies with data about the 3 months prior to conception, no women were hospitalized, 60% were taking immunosuppressive medications, 33% received glucocorticoids, and only one woman was taking a teratogenic medication (methotrexate). Self-reported vasculitis activity was generally low prior to conception with 83% reporting minimal pain, 75% good overall health, and 81% minimal vasculitis disease activity.

Of 32 pregnancies with first trimester data, 2 were hospitalized, 60% were taking immunosuppressive medications, and 40% received glucocorticoids. Self-reported vasculitis activity remained generally low with 78% reporting minimal pain, 72% good overall health, and 75% minimal or no vasculitis disease activity. There were no 1st trimester miscarriages.

Conclusion: V-PREG has successfully collected data on pregnancies among women with vasculitis. Women with vasculitis report an unusually high rate of prior miscarriage (>40%) compared to the average rate of approximately 15% for all pregnancies. The majority of current pregnancies occurred in women with minimal vasculitis activity and

off of teratogenic medications, suggesting they were well-timed for success. Given the small sample size and method of enrollment it is not yet clear if these findings are a result of disease itself, treatment, or possibly reporting bias. Future directions include continued patient enrollment, enhancing data return, and launch of planned translations of V-PREG to substantially increase the number of patients enrolled in the registry.

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Abstract Number: 2282

Reproductive Counseling Documentation Practices for Women Receiving Teratogenic Medications in an Academic Rheumatology Clinic Serving a Medicaid/Medicare Patient Population

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SESSION INFORMATION
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Background/Purpose: Women of reproductive age with rheumatic diseases are often prescribed teratogenic medications; thus, reproductive counseling is important. A prior study demonstrated improvement in counseling documentation from 30% to 45% after a quality improvement (QI) initiative [1]. In this study, we aimed (1) to determine the rate of reproductive counseling documentation within an urban, academic teaching clinic and (2) to determine patient factors associated with a lack of reproductive counseling documentation in female patients with rheumatic disease who are prescribed teratogenic medications.

Methods: Patients were identified from the Rheumatology Fellows' Teaching Clinic at the Hospital for Special Surgery, which serves individuals enrolled in Medicaid or Medicare. All patients who were female, 18 – 45 years-old, and prescribed mycophenolate mofetil, mycophenolic acid, methotrexate, leflunomide, or cyclophosphamide were included. The electronic medical record (EMR) was reviewed for age at last visit, self-reported race/ethnicity, rheumatic disease, duration of patient-physician relationship, marital status, and antiphospholipid (APL) antibody status. The outcome was reproductive counseling as documented in the EMR, defined as present if the physician referenced reproductive counseling in any encounter when the teratogen was prescribed. Patient characteristics were compared using Fisher's exact, Chi-squared, Wilcoxon rank-sum, and t- tests where appropriate. Logistic regression was used to determine if age, teratogen prescribed, or disease type were independent predictors of counseling documentation status.

Results: 45 women (mean (SD) age 34 (6.76) years old) met inclusion criteria (Table 1). 47% were Hispanic, 30% were Black, and 40% were diagnosed with systemic lupus erythematosus. Reproductive counseling was documented in 73% of patients over a median [IQR] physician-patient relationship of 1.3 years [0.44, 1.74]. Of 12 patients with-

Table 1. Patient Characteristics by Reproductive Counseling Documentation Status.

Patient Characteristic	Total (N=45)	Counseling Not Documented (N= 12)	Counseling Documented (N= 33)	p-value
Age (years), mean (SD)	34 (6.76)	37 (6.4)	33 (6.7)	0.11
Race/Ethnicity				0.70
White, not Hispanic	2 (4%)	1 (8%)	1 (3%)	
Black or African American	14 (31%)	4 (33%)	10 (30%)	
Hispanic	21 (47%)	6 (50%)	15 (45%)	
Other	8 (18%)	1 (8%)	7 (21%)	
Primary Language				0.17
English	39 (87%)	12 (100%)	27 (82%)	
Other	6 (13%)	0 (0%)	6 (18%)	
Disease				0.45
Rheumatoid Arthritis or JRA	16 (36%)	5 (42%)	11 (33%)	
Systemic Lupus Erythematosus	18 (40%)	3 (25%)	15 (45%)	
Other	11 (24%)	4 (33%)	7 (21%)	
Married (%)	14 (31%)	6 (50%)	8 (24%)	0.10
Disease duration (years), mean (SD)	12 (7.8)	13.5 (2.5)	11.8 (1.3)	0.52
Patient-physician relationship duration (years), median (IQR)	1.3 (0.44, 1.74)	0.48 (0.41, 1.47)	1.45 (0.55, 2.02)	0.17
APL antibody, positive* (among N=31 evaluated)	3 (7%)	0 (0%)	3 (9%)	0.42
Contraception use status				0.06
No current use	13 (29%)	5 (42%)	8 (24%)	
Current use	24 (53%)	3 (25%)	21 (64%)	
Not documented	8 (18%)	4 (33%)	4 (12%)	
Contraception Type (N= 24)				0.76
IUD (Copper or levonorgestrel)	7 (16%)	2 (17%)	5 (15%)	
Condoms alone	11 (24%)	1 (8%)	10 (30%)	
Combined oral contraceptive pill	2 (4%)	0 (0%)	2 (6%)	
Depo-Provera injection	2 (4%)	0 (0%)	2 (6%)	
Tubal ligation	1 (2%)	0 (0%)	1 (3%)	
Implant (Estrogen/Progesterone)	1 (2%)	0 (0%)	1 (3%)	
Medication Prescribed				0.49
Mycophenolate/Mycophenolic Acid	23 (51%)	5 (42%)	18 (54%)	
Methotrexate	18 (40%)	5 (42%)	13 (39%)	
Leflunomide	4 (9%)	2 (17%)	2 (6%)	
Cyclophosphamide	0 (0%)	0 (0%)	0 (0%)	

Legend. JRA= juvenile rheumatoid arthritis; APL=antiphospholipid.
*Positive APL status defined as anticardiolipin IgG or IgM >40, beta-2-glycoprotein IgG or IgM >40, or positive lupus anticoagulant on at least two occasions >12 weeks apart.

out reproductive counseling documented, 5 (42%) were not using contraception. There was no statistically significant difference in race/ethnicity, language, disease, marital status, teratogen prescribed, APL status, disease duration, or age between those with or without documented counseling. By univariate analysis, disease type, teratogen prescribed, and age were not independent predictors of reproductive counseling documentation status (Table 2).

Table 2. Predictors of Reproductive Counseling Documentation

Predictor Variable	Odds Ratio (95% CI)	p-value
Disease		0.43
Systemic Lupus Erythematosus	1.00 (Reference)	
Rheumatoid Arthritis or Juvenile Rheumatoid Arthritis	1.26 (0.24, 6.35)	
Other	1.69 (0.71, 4.05)	
Medication Prescribed		0.52
Leflunomide	1.00 (Reference)	
Mycophenolate/Mycophenolic Acid	3.60 (0.40, 32.40)	
Methotrexate	1.61 (0.53, 4.88)	
Age (years)	0.91 (0.81, 1.02)	0.10

Legend. Logistic regression was used to predict the odds of reproductive counseling documentation. Odds ratios and 95% confidence intervals are reported.

Conclusion: Reproductive counseling was documented in 73% of reproductive-aged women prescribed teratogenic medications. We identified no patient factors to predict the absence of counseling documentation in the remaining 27%. This underscores the need for additional work in larger samples to identify potential patient- and/or physician-related factors associated with a lack of reproductive counseling documentation as well as QI initiatives to improve documentation and counseling rates.

Reference:

[1] Sadun RE, et al. Increasing contraception use among women receiving teratogenic medications in a rheumatology clinic. BMJ Open Quality 2018;7:e000269

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Abstract Number: 2283

Improving Lactation Knowledge Among Providers Caring for Rheumatology Patients

Brooke Mills,[1] and Bonnie Bermas[1], [1]UT Southwestern Medical Center, Dallas, TX

SESSION INFORMATION
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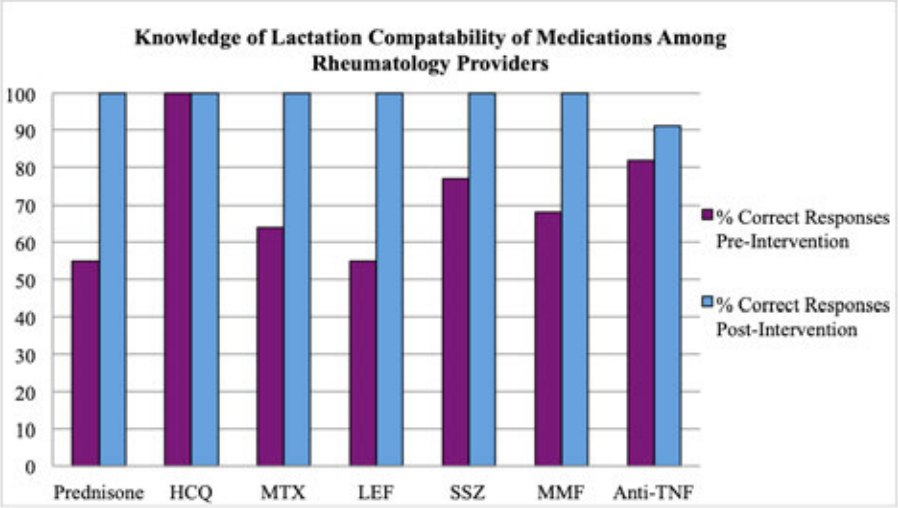
Background/Purpose: While the benefits of breastfeeding for both the mother and her infant are well established, available resources regarding medication compatibility with lactation are limited. Thus, providers may feel ill equipped to encourage breast-feeding amongst patients on anti-rheumatic drugs. We sought to improve knowledge of the lactation compatibility of medications used to treat rheumatic diseases amongst obstetric and rheumatology providers at an academic medical center that includes a safety net hospital.



Rheumatic Diseases and Lactation

- Women should be encouraged to breastfeed if desired
- There are no data to suggest that lactation worsens disease activity
- Risks/benefits should be reviewed with each patient for her particular situation

Medical therapy during lactation+

Compatible

- NSAIDs, ASA (81mg)
- Prednisone <20mg
- Hydroxychloroquine
- Sulfasalazine
- Colchicine
- Azathioprine
- Cyclosporine
- Tacrolimus
- TNF inhibitors
  - Infliximab
  - Etanercept
  - Adalimumab
  - Golimumab
  - Certolizumab
- Anakinra*
- Belimumab
- Abatacept*
- Tocilizumab
- Sekukinumab*
- Ustekinumab*
- Rituximab

"Pump & Dump"

- Prednisone > 20mg/day: delay breastfeeding or discard breast milk for the first four hours following steroid administration

Contraindicated

- Methotrexate
- Leflunomide
- Mycophenolate mofetil
- Thalidomide
- ASA (325mg)
- Apremilast **
- Tofacitinib**

+ Patient/provider resources: **MotherToBaby**; **LactMed**

*Medications unlikely to pass into breast milk in significant quantities due to molecule size but have not been studied

**Medications are likely to pass into breast milk due to molecule size but have not been studied

Methods: Baseline lactation knowledge was obtained via a multiple-choice survey. The survey was developed based on a literature review of rheumatology patients' concerns and knowledge gaps with regards to the lactation process. Providers were then given a laminated "lactation and rheumatic diseases" information card and asked to take the survey again. Improvement in knowledge was assessed. The survey will be re-administered three months after the initial survey date to test the sustainability of the intervention.

Results: Twenty-two rheumatology providers were surveyed, including fellows, attendings, nurse practitioners and physician assistants. All of the providers recommended women with rheumatic diseases breastfeed their children. Twenty-two of 22 providers responded that hydroxychloroquine (HCQ) was compatible with lactation. In contrast, 10/22 (45%), 8/22 (36%), 10/22 (45%), 5/22 (23%), 7/22 (32%), and 4/22 (18%) of providers were unsure or unaware of the lactation compatibility of prednisone, methotrexate (MTX), leflunomide (LEF), sulfasalazine (SSZ), mycophenolate (MMF), and anti-TNF medications, respectively. After administration of the information card, 100% of providers correctly answered questions regarding the compatibility of MTX, LEF, SSZ, and MMF with lactation. Ninety-one percent of providers correctly answered questions regarding the compatibility of TNF therapy with lactation.

Conclusion: There are knowledge gaps among rheumatology providers with regards to medication compatibility with lactation. Creating a simple structured information card helped to address these deficiencies. The sustainability of this intervention will be measured.

Knowledge of medication compatibility with lactation improved after administration of the "lactation and rheumatic diseases" information card.

This "Rheumatic Diseases and Lactation" information card was developed to assist providers in determining the compatibility of medications with lactation.

Disclosure: B. Mills, None; **B. Bermas**, None.

Abstract Number: 2284

The Titer of Anti-Double Stranded DNA Antibody Could Affect the Apgar Score of Newborns, Which Is Considered as the Predictive Clinical Index for Neurological or Physical Development

Hiromi Shimada,[1] Risa Wakiya,[2] Mai Mahmoud Fahmy Mansour,[2] Shusaku Nakashima,[2] Mikiya Kato,[2] Taichi Miyagi,[2] Tomohiro Kameda,[2] and Hiroaki Dobashi[1], [1]Kagawa University, Kagawa, Japan, [2]Kagawa University, Kagawa

SESSION INFORMATION
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Session Title: Reproductive Issues In Rheumatic Disorders Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Recently, the progression of treatment strategy enabled many systemic lupus erythematosus (SLE) women to become mothers. On the other hand, some reports have revealed another important problem about the associations between maternal SLE and neurological abnormalities including learning disorders and autism spectrum disorders among the children born to SLE mothers. However, it is unknown which factors influence neurological disorders on these children.

Table 1. Univariate analysis of risk factors for Apgar score

	Apgar score at 1 minute		Apgar score at 5 minutes	
Variable	Correlation Coefficient (r)	P-value	Correlation Coefficient (r)	P-value
SLEDAI				
First trimester	-0.288	0.09	-0.134	0.44
Third trimester	-0.624	<0.01*	-0.291	0.07
Positivity for autoantibody				
Anti SS-A antibody		0.99		0.34
Antiphospholopid antibody		0.54		0.20
Laboratory finding at the conception				
C3	0.281	0.10	0.220	0.20
C4	0.340	<0.05*	0.227	0.20
CH50	0.306	0.08	0.278	0.11
anti-dsDNA antibody	-0.808	<0.01*	-0.694	<0.01*
Mean dose of corticosteroid	-0.184	0.25	-0.014	0.93

Apgar scores is widely used as a common clinical index for assessing neonatal health status after birth. Especially, Apgar score at five minutes is demonstrated as a predictive index for neurological, cognitive, and psychological abnormalities of newborns. There is no report about the association between maternal SLE and Apgar score of newborns. The aim of this study is to identify risk factors for low Apgar scores of newborns from SLE mothers.

Methods: We investigated the data of 41 newborns who were delivered from SLE mothers from May 2006 to May 2019. SLE mothers were treated at Kagawa University Hospital from preconception counseling to pregnancy and delivery. We analyzed the association between SLE disease activities, autoantibody profiles, laboratory findings, treatment agents, and Apgar scores of newborns.

Results: In 41 newborns, the mean gestational weeks of delivery was 37.9 ± 2.8 weeks, and preterm birth occurred in nine cases (23.1%). The mean birth weight of newborns was 2754.0 ± 626.4 grams. Five newborns (12.8%) were light-for-date (less than the 10th percentile).

Table 1 showed univariate analysis of Apgar scores, which revealed that Apgar scores at one minute were related with SLEDAI score during the third trimester ($P< 0.01$), complement level of C3 ($P< 0.05$) and the titer of anti-double stranded DNA (ds-DNA) antibodies at the conception ($P< 0.01$). Additionally, Apgar scores at five minutes were associated with the titer of anti-dsDNA antibodies ($P< 0.01$). In multivariate analysis, there was a significant association between low Apgar scores at five minutes and high titer of anti-dsDNA antibodies ($P< 0.01$, Table 2).Other parameters including autoantibodies and corticosteroid dose were not associated with low Apgar score in either the univariate or the multivariate analysis.

Conclusion: In our retrospective study, high titer of anti-dsDNA antibodies at conception was a risk factor for low Apgar scores at both one minute and five minutes of newborns who were delivered from SLE mothers.

Table 2. Multivariate analysis of risk factors for Apgar score at 5 minutes

Variable	Standard β	P-value
SLEDAI at third trimester	0.340	0.06
C3 at conception	0.057	0.67
Anti-dsDNA antibody at conception	-0.913	<0.01*
		(R^2=0.538, P<0.001)

Variable	Standard β	P-value
SLEDAI at third trimester	0.356	0.06
C4 at conception	0.058	0.68
Anti-dsDNA antibody at conception	-0.922	<0.01*
		(R^2=0.540, P<0.001)

Variable	Standard β	P-value
SLEDAI at third trimester	0.410	0.03*
CH50 at conception	0.164	0.22
Anti-dsDNA antibody at conception	-0.941	<0.01*
		(R^2=0.566, P<0.001)

Variable	Standard β	P-value
SLEDAI at third trimester	0.306	0.09
Anti SS-A antibody	-0.056	0.66
Anti-dsDNA antibody at conception	-0.913	<0.01*
		(R^2=0.538, P<0.001)

Variable	Standard β	P-value
SLEDAI at third trimester	0.315	0.07
Antiphospholipid antibody	-0.072	0.57
Anti-dsDNA antibody at conception	-0.997	<0.01*
		(R^2=0.623, P<0.001)

Therefore, we speculate that high titer of anti-dsDNA antibodies might be a risk factor for children's physical or neurological development.

There is a need for long-term follow-up studies focusing on the neurological development of children born to SLE mothers.

* shows p-value of < 0.05 which is considered significant. SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, C3,C4,CH50: complement, anti-dsDNA antibody; anti-double-stranded DNA antibody

* shows p-value of < 0.05 which is considered significant. SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, C3,C4,CH50: complement, anti-dsDNA antibody; anti-double-stranded DNA antibody

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Abstract Number: 2285

Higher Than Expected Rates of Adverse Pregnancy Outcomes in Patients with Systemic Lupus Erythematosus from Three Tertiary Care Centers

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Reproductive Issues In Rheumatic Disorders Poster

Session Type: Poster Session (Tuesday)

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Table 1. Characteristics of SLE patients and pregnancies at three Southeastern tertiary care centers.

Number of SLE patients	Overall n = 131	Center 1 n = 41	Center 2 n = 38	Center 3 n = 52
Age at delivery				
Mean (SD)	29 (6)	31 (7)	29 (5)	27 (6)
Median (IQR)	29 (25-33)	32 (26-36)	29 (26-32)	27 (24-31)
Range	18-46	21-46	18-41	18-39
Race				
Asian	4 (3%)	2 (5%)	1 (3%)	1 (2%)
Black	74 (56%)	29 (71%)	25 (66%)	20 (38%)
Other	2 (2%)	2 (5%)	0 (0%)	0 (0%)
Unknown	4 (3%)	0 (0%)	2 (5%)	2 (4%)
White	47 (36%)	8 (19%)	10 (26%)	29 (56%)
Ethnicity				
Hispanic	7 (5%)	2 (5%)	1 (3%)	4 (8%)
Number of pregnancies*	**Overall n= 146**	**Center 1 n=45**	**Center 2 n= 39**	**Center 3 n= 62**
Stillbirth	7 (5%)	1 (2%)	1 (3%)	5 (8%)
Livebirth	139 (95%)	44 (98%)	38 (97%)	57 (92%)
Preterm Birth	58 (42%) of 137	19 (42%)	16 (41%)	23 (42%) of 55
Gestational Age				
Mean (SD)	35.7 (4.0)	36.2 (3.2)	35.9 (3.9)	35.2 (4.5)
Median (IQR)	37 (34-39)	37 (35-39)	37.5 (33-39)	37 (34-39)
Range	25-40	25-40	25-40	25-40
Preeclampsia	29 (24%) of 122	15 (38%) of 39	5 (17%) of 29	9 (17%) of 54
Preterm or Preeclampsia	58 (48%) of 122	22 (56%) of 39	12 (41%) of 29	24 (44%) of 54
Preterm Preeclampsia	23 (19%) of 122	10 (26%) of 39	5 (17%) of 29	8 (15%) of 54
C-section	74 (54%) of 138	20 (44%)	22 (56%)	32 (52%)

*Includes 3 twin and 1 triplet deliveries

Background/Purpose: Prospective cohort studies of pregnancies managed by experts demonstrate that up to 30% of systemic lupus erythematosus (SLE) pregnancies result in preterm birth. We assembled a real-world, multi-center, electronic health record (EHR)-based cohort of SLE births from three tertiary care centers in the Southeastern United States to assess the impact of race on adverse pregnancy outcomes.

Methods: Centers 1 and 2 selected subjects with at least 1 count of the SLE ICD-9 (710.0) or ICD-10 codes (M32.1*, M32.8, M32.9) and at least 1 ICD-9 or ICD-10 code for pregnancy-related diagnoses from 2013-2018. These subjects were reviewed by a rheumatologist to determine if the subject had SLE. Pregnancy outcomes were extracted as discrete variables through the EHR. Center 3 subjects had at least 4 counts of the SLE ICD-9 code or ICD-10 codes and at least 1 ICD-9 or ICD-10 code for pregnancy-related diagnoses. A subject was defined as a case if diagnosed with SLE by a rheumatologist, nephrologist, or dermatologist. Pregnancy outcomes were assessed through chart review for deliveries from 1993-2017. Only pregnancies that delivered at the academic center, had available pregnancy outcomes, and occurred after SLE diagnosis were included. Age-adjusted logistic regression models measured the association of maternal race with preterm birth and preeclampsia.

Results: Across the 3 centers, there were 131 women with SLE with 146 pregnancies. The mean age at delivery of 29 years was similar across the 3 centers (Table 1). The demographics were different between centers with more Black women at Center 1 (71%) and 2 (66%) compared to Center 3 (38%); there were very few Hispanic women. Overall, the rate of preterm birth was 42% with a mean gestational age of 35.7 weeks, which was similar in each center. More than half (54%) of all pregnancies were delivered surgically. Preeclampsia complicated 24% of all pregnancies, with the rate of preeclampsia twice as high in Center 1 (38%) compared to Centers 2 and 3 (17%). The large majority of preeclamptic deliveries occurred preterm (79%). When adjusting for maternal age, Black race was not significantly associated with preterm birth (OR = 1.28, 95% CI 0.62 – 2.62, p = 0.5) or preeclampsia (OR = 1.66, 95% CI 0.65 – 4.26, p = 0.3).

Conclusion: We observed higher than previously reported rates of preeclampsia, preterm birth, and Caesarean section at all 3 centers. Only slightly more than half of the deliveries were term and without preeclampsia. In the general population, preeclampsia is most common at term, whereas in this cohort 79% of preeclampsia occurred preterm. These findings likely reflect the severity of disease seen at large tertiary care referral centers in the Southeastern US. While the proportion of pregnancies to Black women was higher in this cohort than others, multivariate analysis demonstrated that race was not associated with adverse outcomes. We hypothesize that these findings reflect referral bias of the sickest SLE patients of all races to deliver at a tertiary care center. Our findings demonstrate that even at specialized, tertiary care centers, there is an unmet need for management guidelines that reduce adverse pregnancy outcomes in SLE.

Disclosure: A. Blaske, None; **A. Eudy**, GSK, 2; **K. Kirchoff**, None; **J. Oates**, None; **M. Clowse**, GSK, 2, UCB, 5; **A. Barnado**, NIH/NIAMS 5K08AR072757-02, 2.

Abstract Number: 2286

Mobile Responsive App – Useful Additional Tool for Data Collection in the German Pregnancy Register Rhekiss?

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Reproductive Issues In Rheumatic Disorders Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The German pregnancy register Rhekiss is designed as a nationwide, web-based longitudinal observational register established in 2015. The register follows women with inflammatory rheumatic disease prospectively from child wish through pregnancy until two years postpartum. During the observation, information on clinical and laboratory parameters, disease activity, comorbidities, flares, drug treatment, and (adverse) pregnancy outcomes are documented in pre-specified intervals. Physicians and patients (pts) report data for the same time periods via separated accounts and questionnaires (Qs) into a web-based application on personal computers, laptops, and notebooks. Due to the increasing use of mobile devices, a responsive App as a further documentation option and for facilitated patient-reported data entry was developed. We examined whether pts use an App for data entry in the pregnancy register.

Methods: The Rhekiss-App is available in German and can be downloaded for self-reported data retrieval since 08/2017 from App stores (Android and iOS). For the current analysis, Rhekiss register data were used from the time period October 2018 until April 2019 to ensure valid data on the applications modes.

Results: Within the analyzed period Rhekiss expected answers from 2207 Qs of 889 pts. Overall, 71.2% of the Qs were filled in. 49.9% of the Qs were sent from a browser installed on a desktop computer, ranging from 56% (January 2019) to 46% (April 2019), see table 1. Desktop users were on average 34±3.8 years old; the proportion of desktop users was highest in women after delivery (52%). The App installed on mobile devices was used for data entry of 760

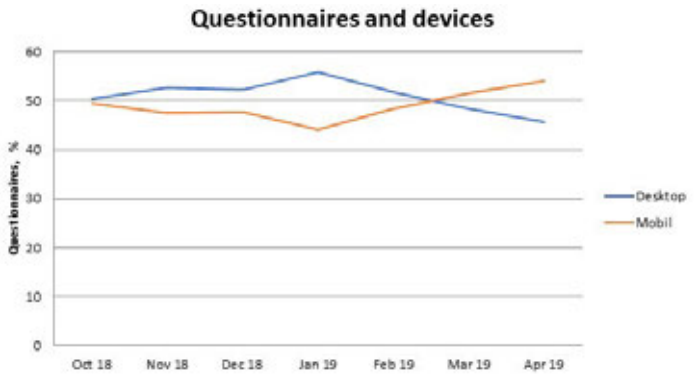

Figure 1 Progress of desktop and mobile documented questionnaires

	Desktop	Smartphone	Tablet/Phablet	Total
Number of questionnaires (%)	758 (49.9)	657 (43.3)	103 (6.8)	1518 (100)
Age of respondents years (SD)	33.9 (3.8)	33.1 (4.2)	33.8 (4.0)	33.5 (4.0)
Month				
October 2018	99 (50.5)	88 (44.9)	9 (4.6)	196 (100)
November 2018	102 (52.6)	81 (41.8)	11 (5.7)	194 (100)
December 2018	95 (52.2)	70 (38.5)	17 (9.3)	182 (100)
January 2019	85 (55.9)	56 (36.8)	11 (7.2)	152 (100)
February 2019	124 (51.7)	95 (39.6)	21 (8.8)	240 (100)
March 2019	73 (48.3)	66 (43.7)	12 (7.9)	151 (100)
April 2019	137 (45.8)	146 (48.8)	16 (5.4)	299 (100)

Table 1 Utilization of the various documentation routes over time

Qs (50.1%): Smartphone use ranged between 37% and 49%, tablet use was less frequent (up to 9%), and phablet use was neglectable, see table 1. Women with child wish had the highest smartphone App use (51%). Figure 1 depicts the progress of desktop and mobile documented Qs.

Conclusion: The responsive App is a useful additional tool for data collection in Rhekiss. It was used for data acquisition from approximately 50% of the questionnaires. While the use of the App on a smartphone was of high interest, the use of tablets/phablets for data collection seems negligible. Apart from desktop/browser developments, technological adoptions within observational cohorts and/or future (joined) registries need to take smartphone requirements and developments into account, especially when patient-reported data in young, mobile patients are collected.

Acknowledgement: The register's mobile App was implemented with software development from the IT partners Serrala, Berlin (Germany) and Questback, Köln (Germany)

Disclosure: J. Richter, None; **C. Bungartz**, None; **A. Weiß**, None; **R. Fischer-Betz**, None; **A. Zink**, Astra Zeneca, BMS, Lilly, Pfizer, Roche und UCB, 5, 8; **M. Schneider**, None; **A. Strangfeld**, AbbVie, BMS, MSD, Pfizer, Roche, Takeda and UCB, 8.

Abstract Number: 2287

Combined First-Trimester Serum BAFF and sFlt-1 Levels as an Early Biomarker of Spontaneous Abortion

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SESSION INFORMATION
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Background/Purpose: Immunologic, angiogenic, and anti-angiogenic factors have been associated with spontaneous abortion (SAB), yet early identification of those pregnant women who ultimately undergo SAB remains very limited. B-cell activating factor (BAFF; a vital B cell survival factor), a proliferation-inducing ligand (APRIL; a vital plasma cell survival factor), placental growth factor (PlGF; a vital angiogenic factor), and soluble fms-like tyrosine kinase-1 (sFlt-1; a vital anti-angiogenic factor) may play a role in the development of SAB and, hence, may serve singly or in

combination as an early biomarker of SAB. The present study was performed to evaluate serum levels of sFlt-1, PIGF, BAFF, and APRIL in the first trimester of pregnancy and to assess associations and predictive values of first-trimester levels of these factors with SAB.

Methods: In this prospective observational study, serum sFlt-1, PIGF, BAFF, and APRIL levels were measured in the first trimester of pregnancy in a medically-diverse group of women and in non-pregnant controls. Associations and predictive values of first-trimester sFlt-1, PIGF, BAFF, and APRIL levels with development of SAB were tested.

Results: Serum samples from 286 women (48 non-pregnant controls and 238 pregnant women) were evaluated. Median serum BAFF levels were significantly lower and median serum sFlt-1 levels were significantly higher in the first trimester of pregnancy than in non-pregnant controls (0.900 ng/ml versus 1.000 ng/ml, $p = 0.007$, for BAFF; 0.454 ng/ml versus 0.103 ng/ml, $p < 0.001$ for sFlt-1). No differences in serum APRIL or PlGF levels were appreciated. SAB developed in 27 of the pregnant women (11.3%). While first-trimester levels of APRIL and PIGF were not associated with SAB, first-trimester serum BAFF was significantly elevated and first-trimester serum sFlt-1 was significantly reduced in women with SAB compared to those who maintained their pregnancies ($p = 0.005$ and $p < 0.001$, respectively). Using the optimal cut-offs generated through receiver operating characteristics curves for BAFF and sFlt-1, respectively, the positive predictive values for SAB when taking serum levels of both BAFF and sFlt-1 into consideration were 0.3529 ($p < 0.0001$) for all subjects (N = 236), 0.4667 ($p < 0.001$) for subjects without an underlying chronic medical disorder (N = 131), and 0.3750 ($p = 0.0045$) for subjects with an underlying chronic medical disorder (N = 105; including 20 subjects with systemic rheumatic diseases). The corresponding negative predictive values for SAB were 0.9808 ($p = 0.0009$) for all subjects, 0.9706 ($p = 0.0140$) for subjects without an underlying chronic medical disorder, and 1.0000 ($p = 0.0362$) for subjects with an underlying chronic medical disorder.

Conclusion: The combination of serum first-trimester levels of BAFF and sFlt-1 greatly increases the ability to positively and negatively predict SAB. Identification of pregnant women at high risk for SAB through testing of serum BAFF and sFlt-1 levels could assist in their counseling and ultimately facilitate clinical trials that test candidate therapeutic interventions.

Disclosure: H. Stohl, None; **N. Yu**, None; **W. Stohl**, GlaxoSmithKline, 2, Janssen R&D, 5, Janssen Research & Development, 5.

Abstract Number: 2288

Pregnancy Outcomes in Women Exposed to Golimumab

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SESSION INFORMATION
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Background/Purpose: Rheumatologic disorders and inflammatory bowel disease can affect women of childbearing potential. Golimumab (GLM) is approved for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, nonradiographic axial spondyloarthritis, polyarticular juvenile idiopathic arthritis and ulcerative colitis (UC). To characterize pregnancy outcomes in patients treated with GLM, data obtained from maternal exposure to GLM are presented.

Methods: This dataset includes individual patient cases reported to the manufacturer through 06 April 2019. Cases included in the analysis were medically confirmed cases of maternal exposures to GLM during pregnancy or within 3 months prior to conception, and a reported pregnancy outcome. Both prospectively reported (ie, pregnancy outcome not known when first reported) and retrospectively reported cases (ie, pregnancy outcome known when first reported) were included. Cases originated from various sources, including spontaneous reporting, clinical studies, and registries.

Results: Two hundred eight pregnancy cases[1] (131 rheumatological[2]; 43 UC; and 34 other) with 211 reported birth outcomes were identified. Of these 208 pregnancy cases, 119 were prospective and 89 were retrospective (Table 1). Average maternal age was 31.9 years. Of the 119 prospectively reported pregnancy cases, 89 (74.8%) resulted in live births, 19 (16.0%) resulted in spontaneous abortion (of these, 42.1% (8/19) received GLM in combination with methotrexate [MTX]), 10 (8.4%) resulted in induced/elective abortion, and 1 (0.8%) resulted in ectopic pregnancy. Overall, 9 congenital anomalies were reported (2 prospective/7 retrospective cases).

Table 1: Summary of Pregnancy Outcomes in Patients Treated With GLM

Pregnancy Outcome	Count (%)	Rheum	UC	Other	Congenital Anomaly (CA)	MTX Use[a]
Prospective outcomes						
Live birth[b]	89 (74.8)	58 (73.4)	21 (75.0)	10 (83.3)	1[c]	9
Spontaneous abortion	19 (16.0)	15 (19.0)	3 (10.7)	1 (8.3)	0	8
Elective/induced abortion	10 (8.4)	6 (7.6)	3 (10.7)	1 (8.3)	1[d]	3
Ectopic pregnancy	1 (0.8)	0 (0.0)	1 (3.6)	0 (0.0)	0	0
Total	**119**	**79**	**28**	**12**	**2**	**20**
Retrospective outcomes						
Live birth[e]	54 (60.7)	29 (55.8)	9 (60.0)	16 (72.7)	5[f]	4
Spontaneous abortion	28 (31.5)	19 (36.5)	5 (33.3)	4 (18.2)	0	3
Elective/induced abortion	5 (5.6)	2 (3.8)	1 (6.7)	2 (9.1)	2[g]	1
Ectopic pregnancy	2 (2.2)	2 (3.8)	0 (0.0)	0 (0.0)	0	2
Total	**89**	**52**	**15**	**22**	**7**	**10**
Grand Total	**208**	**131**	**43**	**34**	**9**	**30**

Key: AE= Adverse Event; CA= Congenital Anomaly; GLM= Golimumab; MTX= Methotrexate; Rheum= Rheumatologic indications; UC= Ulcerative Colitis

a: Patient received MTX at the time of conception/during pregnancy.

b: Count includes 7 cases with pregnancy outcome live birth with AE: low birth weight baby (3), premature baby (3), jaundice (3), feeding disorder neonatal (1), immunodeficiency (1), and 1 case of live birth with CA. Additionally, 2 cases reported twin pregnancies.

c: One live birth with CA: fetal macrosomia.

d: One case of elective/induced abortion with CA: Down's syndrome.

e: Count includes 5 cases with pregnancy outcome live birth with AEs: premature baby (2), inadequate diet (1), bradycardia fetal (1), hematochezia (1), neonatal respiratory depression (1), ulcerative colitis (1), sepsis (1), fungal infection (1), low birth weight baby (1), milk allergy (1), rash generalized (1), and 5 cases of live birth with CA. Additionally, 1 case reported twin pregnancy.

f: Five live births with CA: atrial septal defect; cataract congenital, galactosemia; unspecified CA; hypoplastic left heart syndrome; heart disease congenital.

g: Two elective/induced abortions with CA: multiple congenital anomalies and unspecified CA.

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Table 2: Trimester Exposure and Pregnancy Outcome Reported in Pregnancies With GLM Use

		Pregnancy Outcome				
Reported Trimester of Exposure With GLM[a]	**Number of Pregnancies in Trimester**	**Live Birth**	**Spontaneous Abortion**	**Elective/Induced Abortion**	**Ectopic Pregnancy**	**MTX Use[b]**
Prospective						
0	10	7	2	1	0	6[c]
1st	72	49	15	7	1	13[d]
1st, 2nd	5	4	1	0	0	0
1st, 2nd, 3rd	18	18	0	0	0	1[e]
2nd	2	2	0	0	0	0
2nd, 3rd	1	1	0	0	0	0
3rd	2	2	0	0	0	0
Total	**110**	**83**	**18**	**8**	**1**	**20**
Retrospective						
0	4	3	1	0	0	0
1st	49	21	23	3	2	7[f]
1st, 2nd	5	4	0	1	0	0
1st, 2nd, 3rd	13	13	0	0	0	0
2nd, 3rd	1	1	0	0	0	0
3rd	1	1	0	0	0	0
Total	**73**	**43**	**24**	**4**	**2**	**7**
Grand Total	**183**	**126**	**42**	**12**	**3**	**27**

Key: AE= Adverse Event; CA= Congenital Anomaly; GLM= Golimumab; MTX= Methotrexate

a: 0, 1st, 2nd, 3rd= trimester 0 (<3 months before conception), first, second, third trimester, respectively.

b: Patient received MTX at the time of conception/during pregnancy.

c: Count includes 1 live birth without AE/CA, 2 live births with AE, 2 spontaneous abortions and 1 elective/induced abortion.

d: Count includes 4 live births without AE/CA, 1 live birth with AE, 6 spontaneous abortions and 2 elective/induced abortions.

d: Count includes 1 live birth with AE.

f: Count includes 1 live birth without AE/CA, 1 live birth with CA, 3 spontaneous abortions and 2 ectopic pregnancy cases.

For 183 of the 208 pregnancy cases with reported outcomes, the trimester of exposure to GLM was known (Table 2). Among the 110 prospectively reported cases, 82 (74.5%) were exposed during trimester 0 or 1. Of these, 19 had concomitant exposure to MTX, with the following birth outcomes: 8 live births, 8 spontaneous abortions, 3 elective/induced abortions. Eighteen of the prospectively reported cases (16.4%) were exposed to GLM throughout pregnancy (1st, 2nd and 3rd trimester) and all resulted in live births.

References:

1. Three cases reported twin pregnancies.
2. Rheumatological includes rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis.

Conclusion: The rates of congenital malformations and spontaneous abortions were consistent with published background rates for the general population. Persistent exposure throughout pregnancy was rare, but not associated with apparent clinical sequelae. Limitations of this analysis include the lack of a direct comparison group, the

variable amount of data available in the reports, and the possible bias towards reporting more negative outcomes in retrospective cases.

Disclosure: S. Esslinger, Johnson & Johnson, 3, 4; **S. Gabriel**, Johnson & Johnson, 1, 4; **M. Otero-Lobato**, Johnson & Johnson, 3, 4; **M. Clark**, Johnson & Johnson, 3, 4; **P. Sheridan**, Johnson & Johnson, 3, 4; **A. Geldhof**, Johnson & Johnson, 3, 4.

Abstract Number: 2289

Progesterone Decreases Gut Permeability Through Upregulating Occludin Expression in Primary Human Gut Tissues and Caco-2 Cells

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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Session Type: Poster Session (Tuesday)

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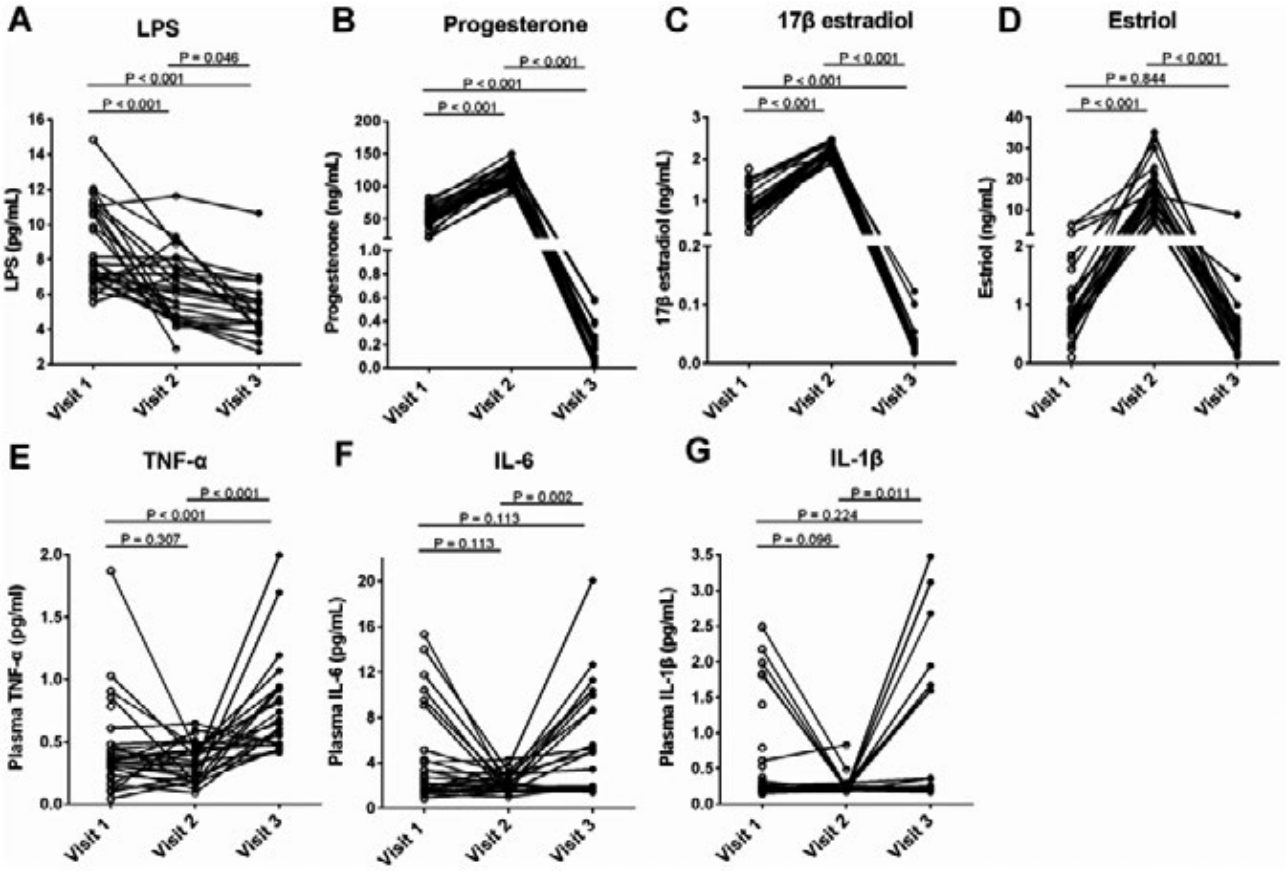
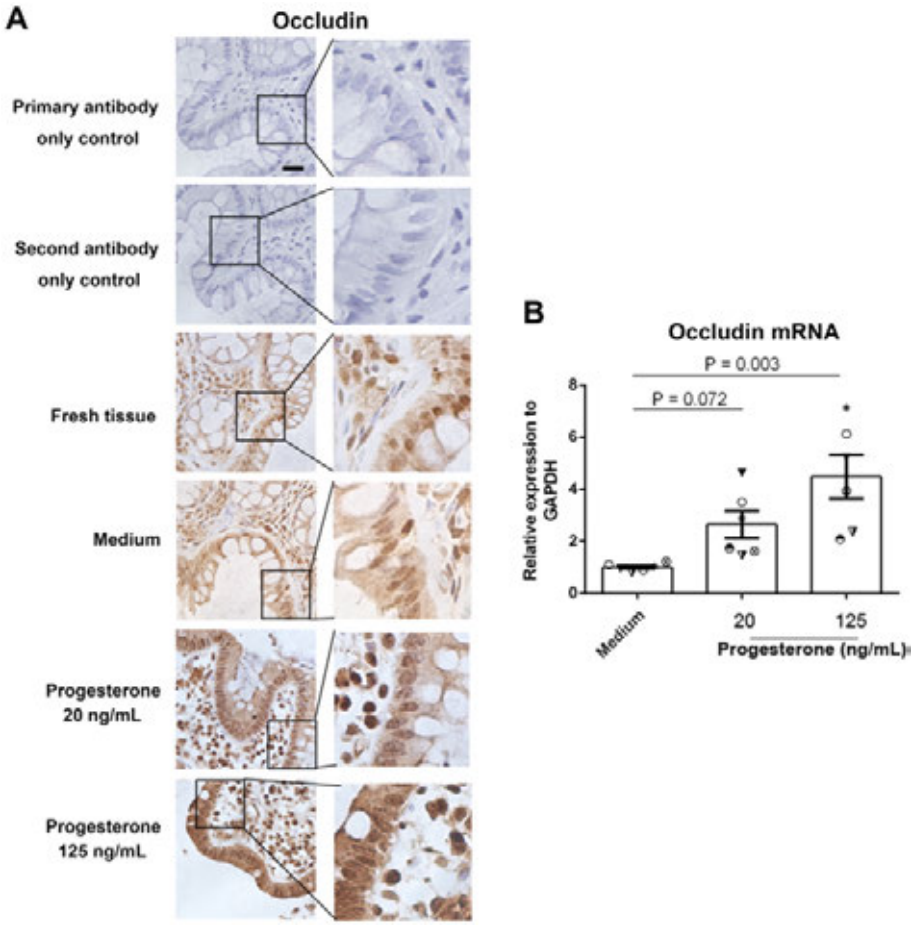
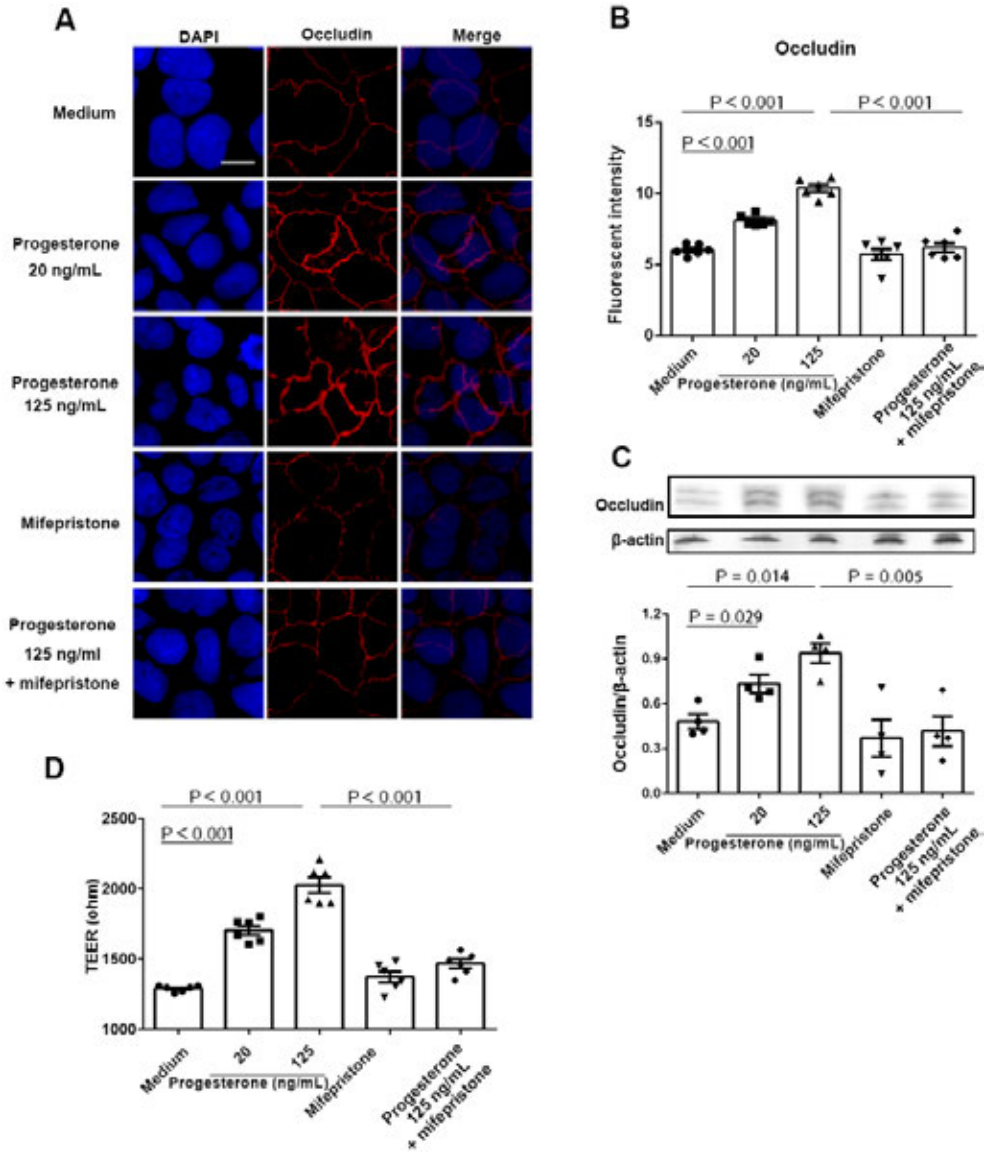




Background/Purpose: Progesterone plays a protective role in preventing inflammation and preterm delivery during pregnancy. However, the mechanism involved is unknown. Microbial product translocation from a permeable mucosa is demonstrated as a driver of inflammation.

Methods: To study the mechanism of the protective role of progesterone during pregnancy, we investigated the effect of physiologic concentrations of progesterone on tight junction protein occludin expression and human gut permeability *in vitro* and systemic microbial translocation in pregnant women *in vivo*. Plasma bacterial lipopolysaccharide (LPS), a representative marker of *in vivo* systemic microbial translocation was measured. Increased microbial translocation from a "leaky" gut has been shown to play a role in autoimmune diseases and pre-term delivery.

Results: We found that plasma LPS levels were significantly decreased from 24 to 28 weeks of gestation compared to 8 to 12 weeks of gestation ($P < 0.05$, ANOVA). The median plasma levels of LPS (pg/mL) were 7.76 (6.86 - 11.04) and 6.25 (4.53 - 7.55) and 4.88 (4.10 - 5.66) for 8-12 (visit 1), 24-28 weeks (visit 2) of gestation, and 6 to 8 weeks postpartum (visit 3), respectively. Plasma estriol and progesterone levels were increased at visit 2 compared to visit 1 but decreased at visit 3 ($P < 0.05$, non-parametric Mann-Whitney test). Moreover, plasma LPS levels were negatively correlated with plasma progesterone levels but positively correlated with plasma tumor necrosis factor-alpha (TNF-α) levels at visit 1 (Spearman correlation test) but not at visit 2. Progesterone treatment increased intestinal trans-epithelial electrical resistance (TEER) in primary human colon tissues and Caco-2 cells *in vitro* through upregulating tight junction protein occludin expression using IHC, qPCR, and TEER assays ($P < 0.05$, non-parametric Mann-



Whitney test). Furthermore, progesterone exhibited an inhibitory effect on nuclear factor kappa B (NF-κB) activation following LPS stimulation in Caco-2 cells by IHC, western blot and qPCR ($P < 0.05$, non-parametric Mann-Whitney test).

Conclusion: These results reveal a novel mechanism that progesterone may play an important role in decreasing mucosal permeability, systemic microbial translocation, and inflammation during pregnancy.

Disclosure: Z. Zhou, None; **G. Gilkeson**, None; **D. Kamen**, None; **J. Oates**, None; **W. Jiang**, None.

Abstract Number: 2290

A Multicentre Study of 244 Pregnancies in Women with Undifferentiated Connective Tissue Disease: Foetal/Perinatal and Maternal Outcomes and Disease Evolution Towards a Definite Connective Tissue Disease

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Background/Purpose: Undifferentiated connective tissue disease(UCTD) represents a common autoimmune condition in clinical practice, however, therapeutic strategies and follow-up are mostly based on clinician expertise. Little is known about the fetal and maternal pregnancy outcomes of women with UCTD. In this study, we aimed to investigate fetal/perinatal and maternal outcomes from a large multicentre cohort of women diagnosed with UCTD.

Methods: This multicenter study included patients diagnosed with UCTD ever pregnant, positive for antinuclear auto-antibodies and aged < 45 years old at study inclusion. Clinical data was collected retrospectively and complete laboratory profiles were assessed before conception, according to local standard of care adopted by all centers involved in the study.

Results: The study included a total of 133 women diagnosed with UCTD. Of the 224 pregnancies analysed,177 (79%) resulted in live births, 45 (20.1%) in miscarriages (defined as pregnancy loss before 12 weeks' gestation), 2 (0.9%) in stillbirths (pregnancy loss after 20 weeks' gestation) and six (2.7%) cases presented intrauterine growth restriction. Miscarriages and stillbirths were strongly associated with the presence of antiphospholipid antibodies (aPL) and extractable nuclear antigen antibodies (ENA).Maternal pregnancy complications were as follows: 5(2.2%) cases developed pre-eclampsia, 11 (4.9%) patients experienced gestational hypertension, and 12 (5.4%) women were diagnosed with gestational diabetes.

Joint involvement represented the most frequent clinical manifestation (57.9%), followed by Raynaud's phenomenon (10.6%), photosensitivity (32.3%) and haematological manifestations (27.1%).

The rate of disease evolution of our cohort from a diagnosis of UCTD to a diagnosis of definite connective tissue disease (CTD) was 12% within a mean time of 5.3 years (S.D. ±2.8). With a total follow-up after first pregnancy of

Patients characteristics	All (133)	%
Age at conception, mean (S.D.), years	32.5 (±5.2)	
Age at data collection, mean (S.D.), years	38.3 (±6.8)	
Ethnicity		
Caucasians, n	114	85.7
Africans, n	14	10.5
Asians, n	1	0.75
Other, n	4	3
Diagnosis		
UCTD, n	133	100
Disease duration at data collection, mean (S.D.), years	10.2 (±5.1)	
Mean follow-up at data collection, mean (S.D.), years	9.2 (±4.7)	
UCTD and aPL	33	24.8
UCTD and APS	6	4.5
Disease evolution during follow-up		
Mean time of follow-up for diagnosis evolution, years (S.D.)	5.3 (±2.8)	
Patients with diseases diagnosis evolution	16	12
SLE	7	5.3
MCTD	7	5.3
SSc	1	0.75
Sjögren's syndrome	1	0.75

Table 1. Demographic and diagnostic characteristics of the cohort

S.D. - standard deviation; UCTD – Undifferentiated connective tissue disease; aPL – Antiphospholipid Antibodies; APS – Antiphospholipid Syndrome; SLE- Systemic Lupus Erythematosus; MCTD-Mixed connective tissue disease; SSc- Systemic Sclerosis

1417 patient-years, we observed the evolution to a defined CTD in one for every 88 patient years. Demographic and diagnostic characteristics of the cohort are displayed in Table 1 and Table2 resumes pregnancy outcomes data.

Pregnancy characteristics	All (224)	%
Age at conception, mean (S.D.)	32.5 (±5.2)	
Mode of delivery		
Vaginal, n	127	71.8*
Vaginal Spontaneous/induced, n	99/28	
Cesarean section, n	50	28.2*
Outcomes		
Live births, n	177	79
Miscarriages (<12 weeks gestation), n	45	20.1
Stillbirths (>20 weeks gestation), n	2	0.9
Birthweight, mean (S.D.), grams	3192.4 (± 514)	
Gestation at delivery, mean (S.D.), weeks	36.2 (±.8.3)	
Delivery >37 weeks gestation, n	147	83.1*
Mild pre-term birth (34-36+6 gestation weeks), n	22	12.4*
Moderate pre-term birth (28-33+6 gestation weeks), n	7	4*
Severe pre-term birth (prior to 28 gestation weeks), n	1	0.4*
Maternal and foetal complications		
IUGR, n	6	2.7
Pre-eclampsia, n	5	2.2
Eclampsia, n	0	
Gestational hypertension, n	11	4.9
Gestational diabetes, n	12	5.4
Postpartum haemorrhage, n	2	0.9
Postpartum hypertensive crisis, n	1	0.4
Hypoxic-ischemic syndrome	1	0.4
Neonatal complications		
Birthweight below 10th percentile (Small for gestational age), n	21	11.9*
Birthweight between 10th-5th percentile, n	16	9.1*
Birthweight below 5th percentile, n	5	2.8*
Respiratory distress, n	1	0.4
Neonatal septicemia, n	2	0.9
Congenital heart block, n	2	0.9
Neonatal lupus, n	1	0.4

Table2. Pregnancy Outcomes

S.D. means standard deviation; IUGR– Intrauterine growth restriction;

**Percentages are calculated considering viable babies (total=177)*

Conclusion: Women with UCTD may warrant specialist follow-up when planning a pregnancy. ENA profiling and aPL testing should be mandatory in this setting, and further therapeutic approaches and management should be planned accordingly.

Therapy	Before pregnancy N (%)	During Pregnancy N (%)	After Pregnancy N (%)
Immunosuppressants			
Azathioprine	5 (3.8)	5 (3.8)	0
Cyclosporine-A	1 (0.75)	0	1 (0.75)
Mycophenolate mofetil	1 (0.75)	0	3 (2.3)
Methotrexate	5 (3.8)	0	12 (9)
Cyclophosphamide	2 (1.5)	0	4 (3)
Rituximab	1 (0.75)	0	0
Steroids	47 (35.3)	38 (28.6)	48 (36.1)
Other			
Low Dose Aspirin	20 (15)	63 (47.4)	18 (13.5)
Low molecular weight Heparin	1 (0.75)	19 (14.3)	6 (4.5)
Vitamin K antagonists	0	0	1 (0.75)
Hydroxychloroquine	57 (42.9)	58 (43.6)	77 (57.9)
Statins	4 (3)	0	7 (5.3)
Anti-hypertensive drugs	3 (2.3)	0	18 (13.5)

Table 3. Therapy undertaken by the patients before, during and after pregnancy.

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Abstract Number: 2291

Optimal Hydroxychloroquine Drug Levels in Pregnant Women with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Reproductive Issues In Rheumatic Disorders Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Pregnancies in women with systemic lupus erythematosus (SLE) often result in preterm birth. Active disease during pregnancy significantly increases the risks for these poor outcomes. Hydroxychloroquine (HCQ) reduces disease activity and flares in SLE, however, low serum levels may lead to treatment failure. Therefore, our objective is to evaluate HCQ levels during pregnancy and determine target serum levels to reduce maternal disease activity and preterm birth.

Methods: We performed a single-center observational study of women with SLE who were taking HCQ during pregnancy between 2013 and 2019. Serum samples were analyzed using validated high-performance liquid chromatography/mass spectrometry. Based on prior publications, we analyzed average HCQ exposure both continuously and

Characteristics	N (%) or Mean (SD)
	44 pregnancies, 39 women
Age (years)	31.2 (4.9)
Race	
White	25 (57%)
Black	17 (39%)
Other	2 (5)
Hispanic	3 (7%)
Average PGA	0.4 (0.4)
Pregnancy Outcomes	(n=40)
Live Birth	38 (95%)
Preterm Birth	9 (24%)
Gestational Age	37.6 (1.9)
Birthweight (grams)	3050 (708)

Table 1. Demographics (excluding lupus nephritis)

categorically: ≤ 100 ng/ml (low), 101-500 ng/mL (moderate), and > 500 ng/ml (high). The primary maternal outcome was disease activity, measured using the Physician Global Assessment (PGA) throughout pregnancy. The primary neonatal outcome was gestational age at birth. We excluded pregnancies in which the woman had lupus nephritis within the prior 3 years due to potential confounding between drug levels and preterm birth. We analyzed categorical outcomes using Fisher's exact test and continuous outcomes using linear regression models, Wilcoxon signed-rank test, Kruskal-Wallis test, t test, and ANOVA.

Results: We analyzed 172 samples from 52 pregnancies in 46 women (Table 1). HCQ concentration varied widely among individuals at each trimester. In addition, there was a non-statistically significant decline in HCQ concentrations throughout pregnancy, with a nadir in the 3rd trimester. Of live births (n=38), preterm birth was significantly more common in mothers whose average HCQ level was low (62.5%), compared to those with moderate levels (8.3%), and high levels (33.3%, p=0.005), Table 2. In addition, disease activity in these mothers was significantly higher in those with low HCQ levels (median [IQR]) PGA 0.67 [0.36-1.16], compared to those with moderate levels (0.06 [0-0.37]), and high levels (0.38 [0.25-0.5], p=0.006). The association between PGA and HCQ levels as a continuous variable was best characterized using a generalized linear model with a log function (figure 1, p=0.002).

	LOW HCQ HCQ ≤100 ng/mL	MODERATE HCQ HCQ 101-500 g/mL	HIGH HCQ HCQ >500 ng/mL	p-value*	p-value**
Neonatal Outcomes					
Gestational age	**n=8**	**n=24**	**n=6**		
Median (IQR)	36.5 (35-37.5)	38 (38-39)	36 (35-37)	**0.002**	**0.01**
Preterm Birth, n (%)	5 (62.5%)	2 (8.3%)	2 (33.3%)	**0.005**	**0.01**
Birthweight (grams)	n=6	n=23	n=6		
Median (IQR)	2596 (2515-2640)	3259 (2875-3785)	2465 (2040-2710)	**0.004**	0.08
Maternal Disease Activity					
All pregnancies	**n=9**	**n=28**	**n=7**		
Average PGA, median (IQR)	0.83 (0.50-1.25)	0.06 (0-0.50)	0.38 (0.25-0.50)	**0.003**	**0.002**
Average PGA >1, n (%)	3 (33%)	0 (0%)	0 (0%)	**0.009**	**0.006**
PGA ever > 1, n (%)	4 (44%)	1 (4%)	0 (0%)	**0.008**	**0.004**
Live births	**n=8**	**n=24**	**n=6**		
Average PGA, median (IQR)	0.67 (0.36-1.16)	0.06 (0-0.37)	0.38 (0.25-0.50)	**0.006**	**0.004**
Average PGA >1, n (%)	2 (25%)	0 (0%)	0 (0%)	0.06	**0.04**
PGA ever >1, n (%)	3 (38%)	1 (4%)	0 (0%)	**0.04**	**0.02**

*Comparing Low vs Moderate vs High HCQ
** Comparing Low vs Moderate and High HCQ combined

Table 2. Maternal and Neonatal Outcomes by Categorical HCQ Exposure (excluding lupus nephritis)

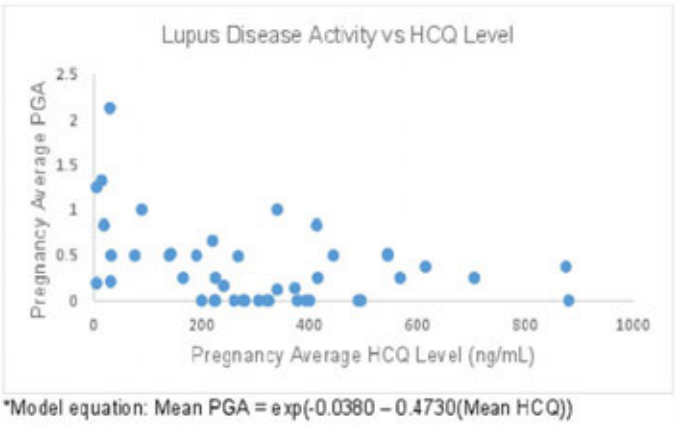

Figure 1: Lupus Disease Activity vs HCQ Level (all pregnancies, excluding lupus nephritis)*

Conclusion: Our data suggests that the optimal serum HCQ level in this cohort appears to be in the moderate range (101-500 ng/ml), with this group having the lowest maternal disease activity and the fewest preterm births. Women with the lowest HCQ levels, in the range concerning for medication non-adherence, had the highest lupus activity and rates of preterm birth. However, the relationship between HCQ drug levels and neonatal outcomes are complex and not linear, and some women with high exposure (levels >500 ng/mL) continue to experience SLE activity and preterm birth. Due to low sample sizes within subgroups, ongoing data collection and analyses will clarify the role of monitoring HCQ levels in lupus pregnancies, characterize the relationship between drug levels and medication adherence, and determine the need for HCQ dose adjustment through PK/PD modeling.

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Abstract Number: 2292

Disease Flares of Rheumatoid Arthritis During Pregnancy: What Is the Impact of Stopping bDMARDs at the Beginning of Pregnancy?

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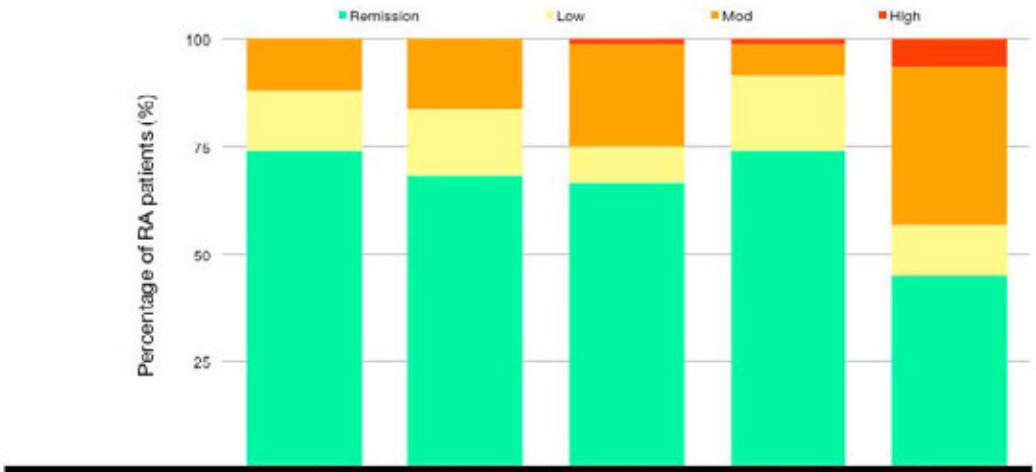
SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Reproductive Issues In Rheumatic Disorders Poster

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM



		PRECONCEPTION	FIRST TRIMESTER		SECOND TRIMESTER		THIRD TRIMESTER		POST-PARTUM	
Flare, n (%)		-	13 (18%)		10 (14%)		6 (9%)		24 (40%)	
PREDNISONE, mg/day, median (IQR)		5 (3.5-5)	5 (3.5-6.25)		5 (3.5-6..25)		5 (3.5-7.5)		5 (2.8-6)	
			overall	*start/ resume*	*overall*	*start/ resume*	*overall*	*start/ resume*	*overall*	*start/ resume*
csDMARDs	Hydroxychloroquine, n	26	36	10	38	2	35	0	34	9
	Sulfasalazine, n	8	5	3	5	0	4	0	6	2
	Cyclosporine-A, n	4	3	0	3	0	3	0	3	0
	Methotrexate/ Leflunomide, n	3	0	0	0	0	0	0	7	4
bDMARDs	ETANERCEPT, n	16	4	3	5	2	5	0	13	9
	CERTOLIZUMAB, n	5	1	1	6	5	6	0	7	2
	ADALIMUMAB, n	4	0	0	1	1	1	0	3	3
	GOLIMUMAB, n	4	0	0	0	0	0	0	1	1
	Other bDMARDs,n	2	0	0	0	0	0	0	3	2

Disease Activity, frequency of RA flares and changes in medications upon different time points.

Background/Purpose: During pregnancy, patients with rheumatoid arthritis (RA) can experience flares that might influence pregnancy outcomes. We aimed at assessing disease course during pregnancy and identifying possible risk factors of disease flares.

Methods: Data about RA patients prospectively followed in a pregnancy clinic were retrospectively collected before conception and during each trimester (T). Clinical characteristics, disease activity (DAS28-CRP3), medication use, and pregnancy outcomes were analysed. Flare was defined by an increase of DAS28-CRP3 >0.6 if the DAS28-CRP3 was >3.2 and by an increase of DAS28-CRP3 >1.2 if the DAS28-CRP3 was ≤3.2.

Results: Among 83 pregnancies (median age 35-IQR 30-38; median disease duration 66 months, IQR 36-156; ACPA+ 62.3%%, RF+ 60.2%) in 64 RA patients enrolled between 2010 and 2018, 8 pregnancies ended with early miscarriages, 1 with intrauterine foetal death and 1 with ectopic pregnancy. The remaining 73 pregnancies in 63 patients were analysed. Before conception, 54(74%) patients were in remission, 10 (14%) had low disease activity and 9 (12%) moderate disease activity (Fig.1). During pregnancy, a flare occurred in 27 (37%) patients (13 in T1, 10 in T2, 6 in T3; 2 patients had >1 flare). Flares during pregnancy were associated with the discontinuation of bDMARDs at positive pregnancy test (55% of patients with flare vs 30% of patients with no flare, p=0.034 OR 2.857, 95%CI 1.112-8.323). Flares during the course of pregnancy were also associated with a previous use of >1 bDMARDs (33% of patients with flare vs 10% of patients with no flare, p=0.019, OR 4.1, 95%CI 1.204-13.966). Fig.1 reports the use of drugs during each trimester and post-partum period (presented as overall use and start/resume of single drugs). Particularly, patients who stopped bDMARDs at the beginning of pregnancy resumed it during 2nd-3rd trimester (12/29, 41.4%) or after delivery (13/29, 44.8%). Twenty-four live births (33%) were complicated (9 preterm deliveries,

of which 3 < 34weeks; 12 premature rupture of membranes (PROM), 5 at term and 7 preterm; 10 "small for gestational age" newborns). Preterm pregnancies were characterised by higher values of CRP and DAS28-CRP3 at T1 compared with pregnancies at term (10 (5-11) vs 3 (2.5-5) p=0.01 and 4.2 (1.9-4.5) vs 1.9 (1.7-2.6) p=0.01, respectively). Preterm deliveries were associated with the occurrence of flare (flare 27% vs no-flare 7%, p=0.034, OR 4.625, 95%CI 1.027-20.829).

Conclusion: In a cohort of prospectively-followed pregnancies, 37% of RA patients experienced at least one flare during pregnancy despite the majority of the patients were in remission prior to conception. There was a 3-fold-increased chance of flare in patients who were on bDMARDs (and stopped the treatment early in pregnancy) as compared with bDMARDs-naïve patients. Patients with more aggressive RA (use of bDMARDs, especially if >1) may get benefit from continuing treatment beyond conception to ensure control of maternal disease and better pregnancy outcomes.

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Abstract Number: 2293

Pregnancy in Patients with Systemic Lupus Erythematosus After Cyclophosphamide Therapy

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) predominantly affects females of reproductive age. Cyclophosphamide, an alkylating agent, labelled category D for pregnancy, is used for induction in treatment of severe manifestations of lupus. Previous studies have shown increased rate of primary ovarian insufficiency causing infertility in patients who have received cyclophosphamide. But recent studies with cancer treatment suggest fair pregnancy outcomes in such patients. Now, with an earlier age at lupus diagnosis, increasing maternal age for pregnancy, and with treatment protocols using lower doses of medication, we have an increasing population of lupus patients who plan to conceive after having received cyclophosphamide. The objective of our study was to add to the available data in identifying the impact of cyclophosphamide exposure on fertility and pregnancy outcomes.

Methods: Using diagnostic codes, we searched for female patients fulfilling ACR criteria for SLE who received cyclophosphamide in the time period from 2000-2018 in our academic institution. We have identified about 400 such patients and as a pilot project of an ongoing study, we performed a retrospective chart review on 100 of those patients. Each patient was evaluated for demographic and serological profile, age of patient at the time of cyclophosphamide infusion and pregnancy and subsequent maternal and fetal outcomes or infertility. We compared these variables using two sample T-test. This is part of an ongoing study and more patients are expected to be added to our final analysis.

TABLE 1

	Patients with successful pregnancy (n=10)	Patients with spontaneous pregnancy loss (n=4)	Premature ovarian failure (n=7)
Mean age at SLE diagnosis (years)	22.3	27.7	23.7
Race			
African American (%)	8 (80%)	3(75%)	5 (71.4%)
Caucasian (%)	0	0	1 (14.3%)
Hispanic (%)	1 (10%)	0	0
Asian (%)	0	0	1 (14.3%)
Undisclosed (%)	1 (10%)	1 (25%)	0
SSA/SSB positive	5 (50%)	2 (50%)	1 (14.3%)
Antiphospholipid Antibody positive	4 (40%)	2 (50%)	4 (57.1%)
No of patients on mycophenolate mofetil prior to pregnancy	10 (100%)	2(50%)	2 (71.4%)
Maternal co-morbidities: CKD 4/5, ESRD	2 (20%)	0	4 (57.1%)
No of patients on an average steroid dose > 10 mg daily (%)	6 (60%)	3 (75%)	3 (42.8%)

Results: Of the 100 female SLE patients reviewed in this study, 82 were given cyclophosphamide for biopsy proven nephritis, 12 for cerebritis, 3 for vasculitis and 1 each for diffuse alveolar hemorrhage and severe cutaneous disease. Fertility counselling was documented in 54% of the patients at the time of medication initiation. 19 patients had subsequent pregnancies; 10 with healthy maternal and fetal outcomes, 5 underwent elective termination within first trimester and 4 had spontaneous miscarriages. Only 7 out of 100 females were identified to have premature ovarian failure which included 4 who also had end stage renal disease. (Table 1)

Average age (in years) at the time of cyclophosphamide administration was 24.9 in patients with successful pregnancy; 33.4 with spontaneous miscarriage and 32 with premature ovarian failure. Average duration (in months) between the last cyclophosphamide infusion and subsequent pregnancy was 53.5 in patients with successful pregnancy vs 19.3 in patients with a spontaneous miscarriage (p 0.144). Average cumulative dose of cyclophosphamide (in mg)

was 3733 in patients with successful pregnancy compared to 2000 with spontaneous miscarriage (p 0.1529) and 4375 with ovarian insufficiency (p 0.0403).

Conclusion: Our findings suggest that a longer time interval between the last cyclophosphamide infusion and pregnancy was more favorable for a successful pregnancy outcome. However, a higher cumulative dose is more likely to be associated with premature ovarian failure.

Disclosure: M. Sen, None; **A. Kurl**, None; **T. Vashi**, None; **A. Khosroshahi**, Exagen, 2.

Abstract Number: 2294

Contraception Documentation Rates in Women with Rheumatic Diseases on Teratogenic Medications in an Academic Rheumatology Clinic

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SESSION INFORMATION
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Session Title: Reproductive Issues In Rheumatic Disorders Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatic diseases are prevalent among women of childbearing age; their treatment often requires medications that potentially affect a woman's fertility and are teratogenic. Prior studies have shown minimal contraception counseling in women receiving high-risk medications and decreased contraception utilization. Our study explores rates of contraception counseling and documentation of contraception use, as well as their type of contraception.

Methods: A retrospective chart review was performed in a university-based Rheumatology clinic. Women ages of 18–50 years who were prescribed mycophenolate mofetil (MMF), methotrexate (MTX), and/or cyclophosphamide (CYC) over a 6-year period with any rheumatic disease were included. 372 of 485 charts reviewed met inclusion criteria. Subject demographics, documentation of contraception type, and counseling were recorded (Table 1). Contraception method was categorized as highly effective (permanent [hysterectomy, tubal ligation] or reversible [IUD, implants, female partners]), effective (OCPs, patch, ring, injection) and ineffective (none, abstinence, condoms). Categorical variables were compared using Fisher's exact test and ordered logit models were calculated.

Results: The most common teratogenic medication prescribed was MTX (56%), followed by MMF (39%), CYC (0.5%); 4% were taking a combination of these. Median age was 41 years, and majority were African American (51%). Lupus and other related connective tissue diseases (50%) were most represented. Across all rheumatic diseases, documentation of any contraception was 39% and the rate of counseling was 36%. There was a statistically significant relationship between age and race with respect to effectiveness of contraception ($p< 0.001$ and $p=0.010$, respectively) (Table 2). Multiple ordered logistic models demonstrated that for patients with contraception counseling, the odds of being on highly effective or effective contraception versus ineffective contraception compared to those without counseling documentation were increased (OR: 1.28, 95% CI: 0.86-1.93). For patients with a documented contraception method, they were more likely to be on highly effective

Table 1: Subject Demographics

	General
N	372 (%)
Age (years)	
18-25	39 (10)
26-35	85 (23)
36-45	153 (41)
46-50	95 (26)
Race	
African American	190 (51)
White	159 (43)
Other (Hispanic, Asian)	23 (6)
Teratogenic Medication(s)	
MTX	209 (56)
MTX/MMF	10 (3)
MMF	145 (39)
CYC	2 (<1)
CYC/MMF	6 (2)
Contraception Type	
Highly effective (permanent) -Hysterectomy, tubal ligation, vasectomy	58 (16)
Highly effective (reversible) -IUD, Implants, female partners	37 (10)
Effective -OCPs, Patch, Ring, Depo-Provera	72 (19)
Ineffective -None, abstinence, condoms, spermicide	205 (55)
Contraception Documented	
Yes	144 (39)
No	228 (61)
Contraception Counselling	
Yes	134 (36)
No	238 (64)

or effective contraception versus ineffective (OR: 5.83, CI: 3.72-9.13). Any reference to contraception (either type or counseling) were more likely to use highly effective or effective contraception (OR: 3.84, CI 2.44-6.04) (Table 3).

Conclusion: Our results demonstrate that a rheumatologist's recognition of a patient's need for contraception and clinical documentation of such while on teratogenic medications is the most important predictor of effective contraception method use; the magnitude of its impact is maintained after adjusting for age and race. This study reinforces the importance of increasing both provider and patient education surrounding awareness of contraception needs. Future QI measures to implement interventions that focus on these topics are needed to help improve contraceptive use in young females and increase use of more effective contraceptives in women of all ages on teratogenic medications.

Table 2: Contraceptive Effectiveness Stratified by Age, Race and Teratogenic Medication in all Rheumatic Diseases

	Highly Effective	Effective	Ineffective	P-value
Age N=372				<0.001
18-25	12 (11.9)	11 (16.9)	16 (7.8)	
26-35	18 (17.8)	22 (33.9)	45 (21.8)	
36-45	44 (43.6)	28 (43.1)	81 (39.3)	
46-50	27 (26.7)	4 (6.2)	64 (31.1)	
Race				0.010
African American	63 (62.4)	30 (46.2)	97 (47.1)	
Caucasian	35(34.7)	34 (52.3)	90 (43.7)	
Other *	3 (2.97)	1 (1.5)	19 (9.2)	
Teratogenic Medication(s)				0.76
CYC	0	0	2 (1.0)	
MTX	53 (52.5)	37 (56.9)	119 (57.8)	
MMF	45 (44.6)	24 (36.9)	76 (36.9)	
Combination**	3 (3.0)	4 (6.2)	9 (4.4)	
*Hispanic and Asian				
**Combination therapy: CYC/MMF or MMF/MTX				

Table 3: The Association of Contraception Effectiveness and Documentation of Contraception, adjusted for age and race

Contraception Effectiveness	Odds Ratio (95% CI)	P value
Documentation of Contraception Counselling	1.28 (0.83-1.98)	0.262
Documentation of Contraception Method	5.83 (3.72-9.13)	<0.001
Any Documentation (either counselling or method)	3.84 (2.44-6.04)	<0.001

Disclosure: J. Haritha, None; **C. Edens**, None; **I. Ventura**, None.

Abstract Number: 2295

Burden of Systemic Lupus Erythematosus Among Korean Women in Childbearing Years Based on the National Health Insurance Service Data

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SESSION INFORMATION

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Background/Purpose: Most women with systemic lupus erythematosus (SLE) are diagnosed with the disease in their reproductive ages, but the burden of SLE among women in childbearing years remains incompletely understood. We aimed to investigate the burden of SLE among Korean women in childbearing years in terms of prevalence and incidence of disease, prevalence of comorbidity, medication dispensing, and pregnancy and delivery rate.

Methods: From National Health Insurance Service data during 2009-2016, women between 20-44 years of childbearing years were identified. Among these women, the prevalence and incidence of SLE were estimated. Women without chronic diseases (CD) or rheumatic diseases including SLE, rheumatoid arthritis, and ankylosing spondylitis were defined as controls. Prevalence of CD including cancer (Ca), diabetes mellitus (DM), hypertension (HTN), and hyperlipidemia (HLD) was compared in SLE women and controls. Medication uses including NSAIDs, corticosteroids (CSs), and conventional (c) disease-modifying anti-rheumatic drugs (DMARDs), pregnancy and delivery rates in women with SLE were compared with controls.

Results: Total 12,756 women with SLE and 208,941 controls were identified. The overall prevalence of SLE during 2009-2016 was 138.5 (95% CI 136.1-140.9) per 100,000 and overall incidence of SLE was 49.1 (95% CI 47.7-50.5) per 100,000 females in childbearing years during 2011-2016. SLE women had significantly increased prevalence of CD compared with the controls in the same age group (60.4% vs 25.6%, odds ratio (OR) 5.4, p< 0.0001). Each chronic disease including Ca (6.3% vs 4.2%, OR 4.2), DM (9.7% vs 6.0%, OR 1.9), HTN (35.2% vs 8.2%, OR 8.0), and HLD (38.3% vs 16.6%, OR 3.6) were all more prevalent in SLE women compared with the controls (p< 0.001). The use of any rheumatic diseases related medications including NSAIDs, CSs, cDMARDs were more frequent in women with SLE than controls (NSAIDs; 53.6% vs 21.8%, CSs; 81.0% vs 4.3%, cDMARDs; 89.0% vs 0.4%, all p< 0.001). Although pregnancy rate showed no difference between SLE women and controls (22.1% vs 19.3%, OR=0.97, p=0.38), delivery rate was significantly lower in SLE women compared with controls (18.7% vs 20.3%, OR 0.8, p< 0.001).

Table 1. Prevalence of chronic diseases among women with SLE in childbearing age between 20-44 years during 2009-2016

	With SLE (12,756)		Without RD (n=208,941)		p-value	OR*	95% CI
	n	(%)	n	(%)			
Any CD	7,699	(60.36)	53,423	(25.57)	<.0001	5.43	5.22-5.65
Ca	808	(6.33)	8,845	(4.23)	<.0001	1.73	1.60-1.87
DM	1,232	(9.66)	12,606	(6.03)	<.0001	1.85	1.74-1.98
HTN	4,488	(36.18)	17,052	(8.16)	<.0001	8.03	7.69-8.40
HLD	4,884	(38.29)	34,672	(16.60)	<.0001	3.59	3.45-3.73

SLE, systemic lupus erythematosus; RD, rheumatic diseases; CD, chronic diseases; Ca, cancer; DM, diabetes mellitus; HTN, hypertension; HLD, hyperlipidemia; OR, odds ratio; CI, confidence interval

*Adjusted for age, income level, and habitation

Conclusion: High prevalence and incidence, increased rates of comorbidities and medication use, and decreased odds to have successful delivery are causes of a significant burden in Korean women with SLE during their childbearing years.

Disclosure: M. Chung, None; **J. Park**, None; **H. Lim**, None; **C. Lee**, None; **J. Lee**, None.

Abstract Number: 2296

Assisted Reproductive Technology in Patients with Inflammatory and Autoimmune Rheumatic Disease

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Reproductive Issues In Rheumatic Disorders Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Women with chronic inflammatory and autoimmune diseases increasingly solicit assisted reproductive techniques (ART) due to infertility, but there is little information about success rates of these techniques in such patients.

Objective: To analyze pregnancy rates after artificial insemination (AI) and *in vitro* fertilization-intracytoplasmic sperm injection (IVF-ICSI) in patients with inflammatory rheumatic disease.

Methods: Prospective study of 41 women with inflammatory rheumatic disease: 15 rheumatoid arthritis, 7 spondyloarthritis, 10 systemic lupus erythematosus, 4 Sjögren´s disease, 2 undifferentiated connective tissue disease, 1, dermatomyositis, 2 Behcet disease, monitored by our department. Mean age 33 years (range 24-41) and 5 ± 7 years from diagnosis of disease, currently inactive or with low clinical activity. Due to infertility, these patients underwent ART: 8 with AI and 33 with IVF-ICSI.

We analyzed pregnancy rate and live-birth rate per cycle in all women and by age.

Results: Pregnancy rate per cycle of AI was 14.9% with a cumulative rate of 33% after four cycles. In patients over 35 years the pregnancy rate per cycle was reduced to 7%.

The pregnancy rate per attempt using IVF-ICSI was 23.9% with a cumulative rate of 37% after three attempts. In women over 35 years the success rate was 23.2%.

The live-birth rate per-cycle was 74.9%; 73.3% in woman over 35.

Conclusion: The pregnancy rates of both AI and IVF-ICSI were a little lower in this series of patients with inflammatory rheumatic disease than those reported for the general population. However, the live birth rate per cycle was similar to the general population.

Disclosure: E. Trujillo, None; **E. Padrón**, None.

Abstract Number: 2297

Anti-TNF-α Exposure During Pregnancy: Impact on the Neonate's Immune System

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SESSION INFORMATION
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Session Title: Reproductive Issues In Rheumatic Disorders Poster
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Up to half of pregnant patients with rheumatic diseases experience disease activity which can increase the risk of pregnancy complications and poor disease outcomes. Treatment with anti-tumor necrosis factor-alpha (anti-TNF-α) is extendedly used in these patients to control disease activity. Placental drug barrier cross has been described for all anti-TNF-α, except for certolizumab. It occurs mainly during the third trimester of pregnancy. Few studies have evaluated the changes of newborn's immune system upon this exposure. The aim of this study was to evaluate the impact of anti-TNF-α exposure during pregnancy on the newborn's immune system, especially on lymphocyte subpopulations and innate immunity (IL-12 / IFN-γ pathway).

Methods: Prospective multicenter study which included newborns born to mothers with rheumatic diseases (including rheumatoid arthritis, spondyloarthropaties (ankylosing, psoriatic), juvenile idiopathic arthritis) , treated during pregnancy with anti-TNF-α. A control group of newborns not exposed to anti-TNF-α during pregnancy was included. All neonates underwent: a) clinical follow-up by a pediatric immunologist in search for infections, allergies or autoimmune disease; b) Umbilical cord (UC) and peripheral blood analysis at birth, 3, 6 and 12 months to record lymphocyte T and B subpopulations, analyze lymphocytes' proliferation capacity, as well as vaccine responses and innate immunity against mycobacteria. All patients signed informed consent.

Results: Fourteen newborns have been included, 10 exposed to anti-TNF-α (Certolizumab: 6, throughout pregnancy; Etanercept: 4, of which 3 during throughout pregnancy) and 4 not exposed. Cohort features are summarized in table 1.

One child developed atopic dermatitis in the non-exposed group; no other allergies or autoimmune diseases have been reported. 7 infections (anti-TNF-α exposed: 3 vs non-exposed: 4) were diagnosed during follow-up. In 3 cases, the patient required hospitalization (1 pyelonephritis, 2 bronchiolitis).

Conclusion: The preliminary results do not show an increase in the risk of infections or immune dysregulation in the anti-TNF-α exposed group.

Patient code	Mother rheumatic disease	Assisted reproductive techniques	Anti-TNF-α therapy	Anti-TNF-α exposure during third trimester	Prednisone during pregnancy (mean daily dose)	DMARDs during pregnancy	Active disease during pregnancy	Gestational age at birth (weeks)	Lactation	Weight at birth (Kg)
1	SAPHO syndrome	No	**Certolizumab**	**Yes**	5mg	None	No	38.4	Mixed	2,64
2	Juvenile idiopathic arthritis	No	**Certolizumab**	**Yes**	5mg	None	Yes	38.2	Mixed	3,05
3	Rheumatoid arthritis	In vitro fertilization + sperm donation	**Certolizumab**	**Yes**	10mg	None	Yes	36.3	Mixed	2,6
4										2,62
5	Juvenile idiopathic arthritis	In vitro fertilization	**Certolizumab**	**Yes**	none	None	No	41.2	Breast milk	3,82
6	Rheumatoid arthritis	No	**No**	**No**	6,25mg	None	No	40.1	Mixed	3,26
7	Juvenile idiopathic arthritis	No	**No**	**No**	none	None	No	37.3	Mixed	3,05
8	Juvenile idiopathic arthritis	No	**No**	**No**	none	Hydroxychloroquine	No	37	Mixed	2,28
9										2,33
10	Rheumatoid arthritis	No	**No**	**No**	No	None	No	38.3	Mix	3,02
11	Rheumatoid arthritis	No	**Etanercept**	**Yes**	7,5mg	None	Yes	39.2	Breast milk	2,83
12	Juvenile idiopathic arthritis	No	**Etanercept**	**Yes**	No	None	Yes	40.3	Formula	3,56
13		In vitro fertilization	**Etanercept**	**Yes**	none	Hydroxychloroquine	No	39.1	Breast milk	3,01
14	Ankylosing spondylitis	No	**Etanercept**	**No**	none	None	No	40.2	Infant formula	2,67

Table 1

No significant quantitative differences are observed in the lymphogenesis, but a more immature B population and a predominantly T memory population was found in newborns exposed to anti-TNF-α. These differences are attenuated at 3 and 6 months. Functional capacity of the IL-12 / IFN-γ pathway seems intact. The ongoing recruitment will give consistency to these results.

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Abstract Number: 2298

Interstitial Lung Disease Is Associated with Distinct Fine Specificities of Anti-Carbamylated Peptide/Protein Antibodies in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Table 1. **Demographic, Clinical and Therapeutic Features According ILD Status**

	Total Cohort N: 179	RA-ILD n:37	RA-No ILD n:142	p value
Female	141 (79%)	25 (68%)	116 (82%)	NS
Age at inclusion mean (SD)	59.7 (±13.0)	67.3 (±10.1)	57.7 (±12.9)	≤0.005
Age at RA onset mean (SD)	52.8 (± 13.0)	54.4 (±12.1)	52.4 (±13.3)	NS
Disease duration median (IQR)	5.4 (5.25)	9.9 (12.6)	4.8 (4.2)	≤0.005
Smoking history (ever)	83 (46%)	21 (57%)	62 (44%)	NS
Current Smoking	30 (17%)	7 (19%)	23 (16%)	NS
Tobacco cumulative exposure packs/year (SD)	24.1 (±13.0)	30.7 (±11.1)	21.8 (±12)	≤0.005
RA family history	22 (12%)	4 (11%)	18 (13%)	NS
Early onset RA	149 (83%	30 (81%)	119 (84%)	NS
ACPA positive (%)	128 (72%)	29 (78%)	99 (70%)	NS
ACPA titer mean (IC-95%) IU	813 (662-965)	1072 (705-1439)	746 (580-912)	NS
RF positive (%)	112 (63%)	28 (76%)	84 (59%)	NS
RF titer mean (IC-95%) IU	139 (108- 170)	212 (124-298)	120(89-151)	NS
Anti-FCS positive (%)	87 (49%)	26 (70%)	61 (43%)	≤0.005
Anti-FCS titer mean (IC-95%) AU	505 (399-610)	711 (448-974)	451 (337-565)	≤0.005
Anti-Fib positive (%)	100 (56%)	27 (73%)	73 (51%)	0.019
Anti-Fib titer mean (IC-95%) AU	322 (267-377)	393 (259-527)	304 (244-364)	NS
CFFCHP positive (%)	51 (29%)	18 (49%)	33 (23%)	≤0.005
CFFCHP titer mean (IC-95%) AU	332 (252-411)	520 (294-746)	283 (203-363)	0.016
Anti-CarP fine specificities mean (IC-95%)	1.3 (1.2-1.5)	1.9 (1.5-2.3)	1.2 (1.0-1.4)	≤0.005
≥ 2 positive Anti-CarP fine specificities	84 (47%)	27 (73%)	57 (40%)	≤0.005
Other extraarticular manifestation - Sicca syndrome - Rheumatoid nodules - Serositis	 33(18%) 21 (12%) 3 (2%)	 8 (22%) 7 (19%) 1 (3%)	 25 (18%) 14 (10%) 2 (1%)	 NS NS NS
Treatment: - Glucocorticoids - csDMARDs - MTX - bDMARDs	 106 (59,6%) 155 (86.9%) 115 (64.2%) 47 (26.3%)	 25 (67,6%) 33 (89.2%) 20 (54.1%) 11 (29.7%)	 81 (57.4%) 132 (85.9%) 95 (66.9%) 36 (25.4%)	 NS NS NS NS
Erosive disease	89 (50%)	26 (70%)	63 (44%)	≤0.005
Modified Larsen Score mean (IC-95%)	23.6 (20.5-26.7)	43.9 (34.1-53.8)	18.3 (15.9-20.6)	≤0.005
HAQ-DI mean (IC-95%)	0.39 (0.32-0.46)	0.69 (0.53-0.85)	0.31 (0.24-0.38)	≤0.005
Functional disability (HAQ ≥1)	27 (15%)	10 (27%)	17 (12%)	0.024

Background/Purpose: Interstitial lung disease (ILD) is a common and severe complication of rheumatoid arthritis (RA). It has been associated with the presence of ACPA. Anti-carbamylated peptides/proteins (anti-CarP) is a new family of RA autoantibodies associated with poor outcomes including an increased mortality due to respiratory disease (1). We aimed to analyze the prevalence of distinct anti-CarP fine specificities in an established RA cohort and determined whether anti-CarP are associated with ILD.

Methods: Cross sectional study. Patients with RA according to ACR/EULAR 2010 criteria with a disease duration of ≤ 10 years, and those with an associated ILD independently of the disease duration were included. ILD was diagnosed with a high-resolution CT according the American Thoracic Society/European Respiratory Society 2013 criteria, diagnosis confirmed by a multi-disciplinary committee. Demographic, clinical and radiological features were analyzed. Auto-antibody status (RF and ACPA) were also assessed. Three anti-CarP IgG autoantibodies were determined (anti-CarP fetal calf serum (FCS), anti-CarP fibrinogen (anti-Fib) and anti-CarP fibrine/filagrine homocitrulinated peptide (anti-CFFHP)) by home-made ELISA tests using as antigens either carbamylated proteins or a synthetic chimeric fibrin-filaggrin homocitrullinated peptide. Cut-off values were determined using ROC curves, with a specificity of 96% compared with a healthy population.

Results: 179 patients were included, 21% had an ILD. The mean age at ILD diagnosis was 64.2 (±9.7) years, the mean time from RA diagnosis until ILD diagnosis was 9.3 (IQR: 11.4) years. A significantly greater tobacco exposure (30.7 ±11.1 vs 21.8 ±12) and higher frequency of erosive disease (70% vs 44%) and disability (HAQ-DI >1: 27% vs 12%) was observed in patients with ILD. Total cohort demographic, clinical and radiological features are presented in *Table 1*.

Anti-CarPs prevalence in the total cohort was 49%, 56%, and 29% for anti-FCS, anti-Fib and anti-CFFHP peptide respectively. Positive Anti-FCS anti-Fib and anti-CFFHP peptide were found in 22%, 29% and 8% of ACPA negative patients respectively.

All anti-CarP fine specificities were significantly more prevalent in patients with ILD (anti-FCS 70% vs 43%; anti-Fib 73% vs 51%; anti-CFFHP 49% vs 23%), and significantly higher titers of Anti-FCS and anti-CFFCHP were observed in these patients.

A logistic regression model adjusted for age, disease duration, sex, smoking, erosive disease, RF and ACPA demonstrated that Anti-FCS (OR: 3.49; CI 95%: 1.16-10.50) and anti-CFFHP (OR: 4.82; CI 95%: 1.56-14.9) were independently associated with ILD.

Conclusion: In our cohort, the presence of anti-CarP ranges between 29-56% according to the antigenic specificity used. These autoantibodies were associated with ILD. Anti-CarP could be considered a more specific biomarker of ILD in patients with RA rather than ACPA.

Reference:

1. Vidal-Bralo L. Anti-carbamylated protein autoantibodies associated with mortality in Spanish rheumatoid arthritis patients. PLOS ONE. 2017;12(7):e0180144.

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Abstract Number: 2299

The Course of Disability in Early Rheumatoid Arthritis over 10 Years of Follow-up in Women and Men - Comparison with the General Population

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

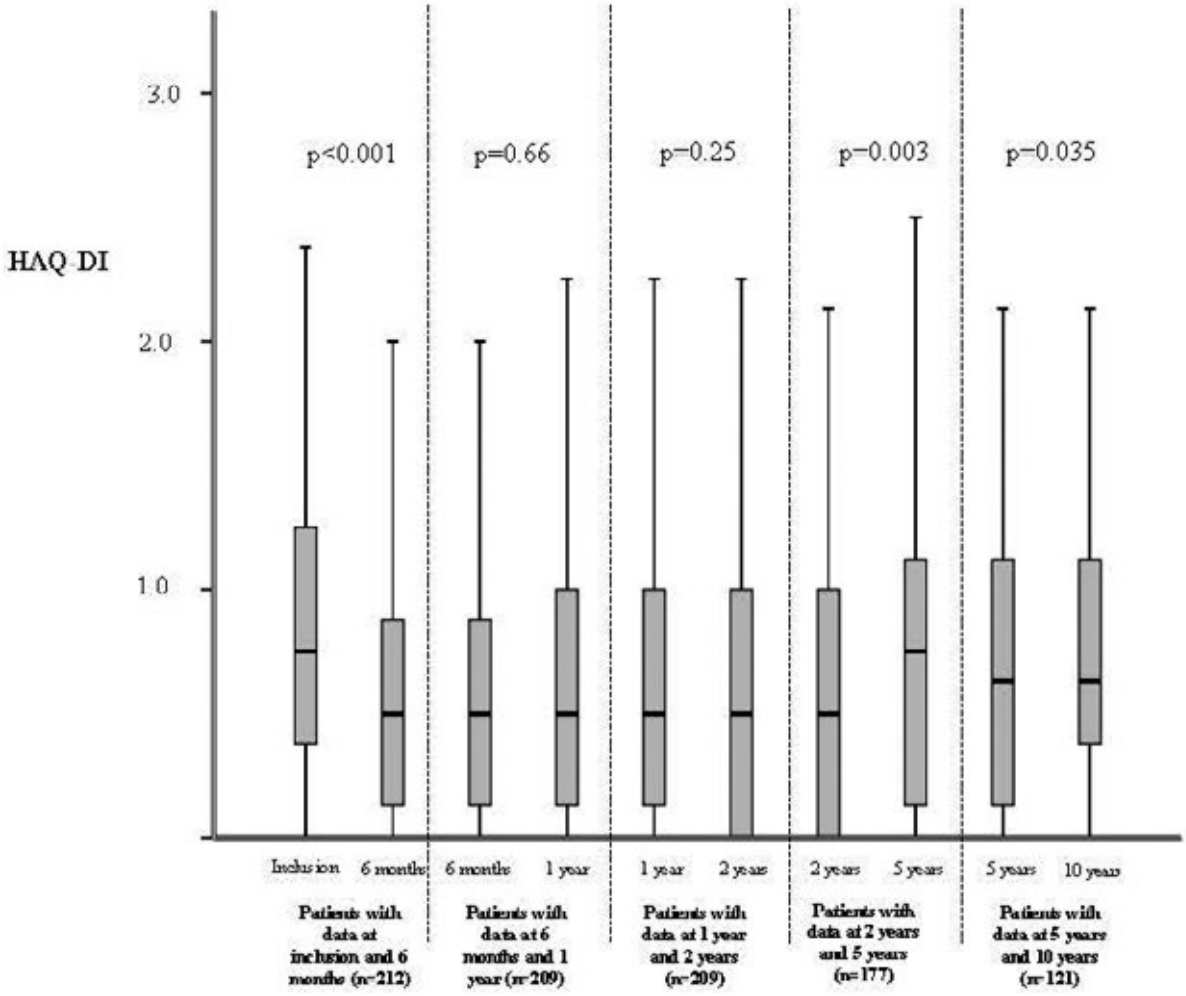
Background/Purpose: Patients with rheumatoid arthritis (RA) are known to have increased risk of disability. The aim of this study was to investigate the course of disability in early RA, and compare it to age- and sex specific reference values, overall and by sex.

Methods: An inception cohort of patients with early RA (symptom duration ≤12 months), recruited in Malmö 1995-2005, was followed in a structured program for 10 years. Patients were managed according to usual care, with no pre-specified protocol for pharmacotherapy or rehabilitation. Disability was assessed using the validated Swedish version of the Health Assessment Questionnaire (HAQ) and compared to expected age- and sex specific values from the literature (Krishnan et al. A&R 2004; 50: 953-60). Changes in HAQ disability index (HAQ-DI) between different time points were assessed using the paired t-test. Differences between observed and expected HAQ-DI over time after ≥6 months were investigated using linear mixed-effects models.

Table 1. HAQ-DI in the early RA cohort compared to the expected, based on age- and sex-specific reference values, at inclusion and each follow-up

		Inclusion	6 months	12 months	24 months	60 months	120 months
N		232	212	220	209	177	121
Female sex % (n)		70(163)	70(149)	70(155)	70(147)	71(126)	72(87)
Age (years) Mean (SD)		60.5 (14.6)	61.3 (14.2)	61.1 (14.6)	62.0 (14.8)	64.7 (14.3)	68.0 (13.3)
RF-positive % (n)		62 (143)	60 (128)	62 (136)	61 (127)	66 (116)	64 (78)
Anti-CCP positive % (n)		57 (116/202)	58 (108/187)	58 (110/190)	57 (104/181)	59 (92/155)	58 (61/105)
HAQ-DI overall Median (IQR)	Observed	0.75 (0.38-1.25)	0.50 (0.13-0.88)	0.50 (0.13-1.0)	0.50 (0-1.0)	0.75 (0.13-1.12)	0.63 (0.38-1.12)
	Expected	0.20 (0.10-0.34)	0.23 (0.13-0.34)	0.22 (0.13-0.34)	0.23 (0.15-0.49)	0.23 (0.17-0.68)	0.33 (0.18-0.77)
HAQ-DI women Median (IQR)	Observed	0.88 (0.38-1.25)	0.63 (0.13-0.94)	0.63 (0.25-1.0)	0.63 (0.25-1.12)	0.75 (0.38-1.16)	0.63 (0.38-1.25)
	Expected	0.23 (0.09-0.34)	0.23 (0.09-0.34)	0.23 (0.16-0.34)	0.23 (0.16-0.34)	0.33 (0.16-0.77)	0.33 (0.20-0.77)
HAQ-DI men Median (IQR)	Observed	0.75 (0.19-1.13)	0.38 (0-0.88)	0.38 (0-0.88)	0.19 (0-0.88)	0.38 (0-1.0)	0.56 (0.13-0.91)
	Expected	0.17 (0.10-0.49)	0.18 (0.13-0.49)	0.17 (0.12-0.49)	0.18 (0.13-0.49)	0.18 (0.17-0.49)	0.18 (0.17-0.68)

Figure 1. Changes in HAQ-DI between visits, in patients with data at both time points



Results: A total of 232 patients with early RA (70 % women, mean age 60.5 years, median symptom duration 7 months) were investigated. The HAQ-DI scores for all patients are reported in Table 1 together with the corresponding expected values. In paired analysis of those with available data at both time points, there was a significant decrease in HAQ-DI from inclusion to the 6 month follow-up (Figure 1). This was followed by a stable HAQ-DI through 24 months after diagnosis. Between 24 months and 60 months, and between 60 months and 120 months, there were significant increases in HAQ-DI. (Figure 1) The median HAQ-DI was higher for women than for men at every visit, both the observed and expected values (Table 1).

In linear mixed effect models, the estimated mean difference (EMD) over time from the 6 month follow-up through 10 years between observed and expected values was 0.29 [95% confidence interval (CI) 0.26 ; 0.33] for HAQ-DI. Estimated HAQ-DI values at 6 months, based on the intercept in the model, were higher than the expected (Table 2). Observed and expected values both increased significantly after the 6 month follow-up (Table 2), with no significant difference in the change per year (EMD0.004 (95% CI -0.008; 0.016). The EMD over time between observed and expected HAQ-DI scores were greater in women (mean 0.35; 95% CI 0.31; 0.39) than in men (mean 0.15; 95% CI 0.09; 0.22). In women, observed and expected HAQ-DI values increased over time (Table 2), with a trend towards a lesser increase in observed values (EMD for change over time 0.004/year (95% CI -0.01; 0.017). In men, there was a signif-

Table 2. HAQ-DI over time after ≥6 months of follow-up; linear mixed effect models

		Intercept		Change/year	
		Estimate	95% CI	Estimate	95% CI
HAQ-DI overall	Observed	0.64	0.56 ; 0.71	0.023	0.016 ; 0.030
	Expected	0.33	0.28 ; 0.38	0.032	0.029 ; 0.035
HAQ-DI women	Observed	0.69	0.60 ; 0.79	0.028	0.020 ; 0.037
	Expected	0.33	0.27 ; 0.39	0.034	0.030 ; 0.038
HAQ-DI men	Observed	0.50	0.38 ; 0.61	0.011	- 0.0030 ; 0.024
	Expected	0.32	0.23 ; 0.41	0.027	0.022 ; 0.033

Table 2

icant increase in expected, but not in observed values (Table 2). This difference did not reach statistical significance (EMD for change over time 0.006/year (95% CI -0.015; 0.028)).

Conclusion: Disability decreased during the first 6 months after diagnosis in patients with early RA. This was followed by a stable level of disability through 2 years, and a gradual increase after 2-10 years. The change in HAQ-DI after ≥ 6 months was similar to the expected based on data from the general population, suggesting that increasing disability over time in early RA is mainly explained by increasing age.

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Abstract Number: 2300

Risk Factors for Transfusion and Use of Tranexemic Acid in Patients with Rheumatoid Arthritis Undergoing Total Hip Arthroplasty and Total Knee Arthroplasty

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Utilization of total hip (THA) and total knee arthroplasty (THA) remains high for patients with RA, and most patients have moderate to high disease activity at the time of surgery. Risk of infection and transfusion are higher compared to OA, and transfusion at the time of surgery increases the risk of perioperative infection. Tranexamic acid (TXA), an anti-fibrinolytic, has gained widespread use in total joint arthroplasty to decrease transfusions, but benefits in RA has not been established. We aimed to determine the risk factors for transfusion for patients with RA undergoing THA/TKA, and assess the use of TXA in decreasing transfusions.

Table 1. Baseline Characteristics by TXA Yes and TXA No

Characteristic	TXA N=193	No TXA N=94	Combined N=287	p-value
Age, years (mean ± SD)	63.9± 10.7	62.9 ± 11.8	63.6 ± 11.0	0.68
Female, n (%)	161 (83.9)	73 (77.7)	234 (81.8)	0.20
Duration of RA diagnosis (mean ± SD)	13.4±11.9	15.5±12.3	14.2 ± 12.1	0.18
Type of surgery, n (%)				0.01
TKA	128 (66.3)	47 (50.0)	175 (61.0)	
THA	65 (33.7)	47 (50.0)	112 (39.0)	
Diagnosis, n (%)	164 (85.0)	88 (93.6)	252 (87.8)	0.04
RA				
OA	29 (15.0)	6 (6.4)	35 (12.2)	
Race, n (%)	122 (63.2)	65 (69.1)	187 (65.2)	0.69
White				
Black	18 (9.3)	65 (69.1)	187 (65.2)	
Asian	4 (2.1)	2 (2.1)	6 (2.1)	
Other	49 (25.4)	18 (19.2)	67 (23.3)	
Criteria, n (%)	73 (46.5)	28 (37.8)	101 (43.7)	0.07
Meet both criteria				
1987	19 (12.1)	13 (17.6)	32 (13.9)	
2010	41 (26.1)	13 (17.6)	54 (23.4)	
Included per PI	24 (15.3)	20 (27.0)	44 (19.1)	
Medication, n(%)				
NSAIDS	94 (61.8)	42(49.4)	136 (57.4)	0.06
Steroids	56 (35.9)	31 (36.1)	87 (36.0)	0.98
Methotrexate	74 (47.4)	43 (50.6)	117 (48.6)	0.64
Biologic	86 (55.4)	42 (49.4)	128 (53.3)	0.37
Pre-op hemoglobin, (mean ± SD)	12.7±1.4	13.1±1.9	12.8 ± 1.5	0.04
Platelet count (mean ± SD)	270.3±74.5	256.0±78.3	267.3 ±75.4	0.22
Hx of previous transfusion n (%)	5 (2.6)	4 (5.5)	9 (3.4)	0.26
Estimated blood loss , mL (mean ± SD)	190.6±64.9	183.6±52.9	189.2±62.6	0.79
IV TXA dose (mean ± SD)	988.7 ±68.7	-	988.7 ±68.7	-
Topical TXA dose (mean ± SD)	2942.3 ± 291.3	-	2942.3 ± 291.3	-
Surgery Duration, min (mean ± SD)	94.1±30.7	86.7±39.2	92.7 ± 32.4	0.01
Post op transfusion needed?, Yes n (%)	23 (11.9)	3 (4.1)	26 (9.8)	0.06
Indication, n(%)				
Hemoglobin < 7	5 (2.6)	0 (0)	5 (1.7)	0.17
Hemoglobin <8	12 (6.2)	0 (0)	12 (4.2)	0.01
Hypotensive	0 (0)	3 (3.2)	3 (1.1)	0.03
MDHAQ, (mean ± SD)	3.8±1.8	3.7±1.7	3.8 ± 1.7	0.94
DAS28 – ESR, (mean ± SD)	3.8±1.3	3.5±1.2	3.7 ± 1.3	0.19
CDAI, (mean ± SD)	18.7±11.5	17.6±9.4	18.4 ± 10.9	0.99
ESR result (mean ± SD)	20.5±18.7	20.6±21.5	20.5 ± 19.7	0.35
CRP (mean ± SD)	1.6±2.3	1.9±2.9	1.7 ± 2.5	0.53
CCP (mean ± SD)	199.3±393.8	134.8±101.8	178.2±329.1	0.09
RF (mean ± SD)	345.7±558.9	404.6±719.6	362.5±605.9	0.94

Methods: We retrospectively reviewed data from a prospectively collected cohort of 233 patients with RA and a convenience sample of 35 OA controls undergoing THA/TKA. Demographics, RA characteristics, and disease activity were systematically collected and hemoglobin and TXA use obtained by chart review. Disease activity was measured utilizing the DAS28 and CDAI, PROMs included HOOS/KOOS, and MDHAQ, and ESR, and CRP, and serologies

Table 2. Multivariate logistic regression to determine the risk of transfusion in 266 THA/TKA patients

Multivariate variable	Level	Odds ratio (95% CI)	p-value
TXA	No vs. Yes	0.585 (0.068, 5.06)	0.63
CDAI at baseline		1.079 (1.001, 1.162)	0.04
DAS28 – ESR at baseline		0.666 (0.313, 1.416)	0.29
Hemoglobin at baseline		0.394 (0.232, 0.669)	0.001
Duration of Surgery		1.022 (1.008, 1.037)	0.003

were drawn pre-op. Baseline characteristics were summarized using descriptive statistics and compared using Chi-squared, Fisher's exact test or two-sample t-test or Wilcoxon rank-sum test as appropriate. Logistic Regression analysis was performed to explore the relationship between transfusion (Yes or No) and predictors (including CDAI, DAS28, TXA received or not). Predictors that were found statistically significant ($p < 0.05$) in the univariate analysis were included in the multivariate analysis.

Results: RA cases were predominantly women (83%), with prolonged disease duration(14.1 +/-12 years), and active disease (mean DAS28= 3.7, CDAI=18.4±10.9), (TABLE 1). Transfusions were received by 26 RA(11.2%). TXA was given in 193 patients (67.3%, OA 83% vs RA 67%).There was no difference in blood loss or transfusion for those undergoing TKA vs THA (p=.32). Patients who received TXA required more transfusions than those who did not (11.9% vs. 4.1%, $p > 0.05$). In the univariate analysis, baseline hemoglobin, estimated blood loss, duration of surgery, baseline CDAI and baseline ESR increased the risk of transfusion. In the multivariate analysis to determine independent risk factors for transfusion (Table 2), a one g/dl decrease in baseline hemoglobin (OR=0.394, 95% CI (0.232, 0.669), p=0.001) , one-minute increase in surgical duration (OR=1.022, 95% CI (1.008, 1.037), p=0.003) and a one-point increase in CDAI (OR=1.079, 95% CI (1.001, 1.162) were significant. TXA was not associated with post-operative transfusion in either the univariate or multivariate analysis.

Conclusion: Pre-surgical optimization should include assessment and treatment of anemia in patients with RA who undergo total joint arthroplasty. This is important, as TXA was not associated with a lower transfusion rate as reported for patients with OA. Decreased pre-operative hemoglobin may be a modifiable risk factor, while increased disease activity as measured by CDAI and increased surgical time were risk factors for post-operative transfusion but may be more difficult to change in these patients with long standing RA.

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Abstract Number: 2301

Profile of Renal Function in Patient Suffering from Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

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Background/Purpose: Many medications used in the treatment of rheumatoid arthritis (RA) impact renal function. Some of these may be contraindicated in the presence of a certain degree of renal failure or may require dosage adjustment. Product monograph of different molecules such as hydroxychloroquine (HCQ), methotrexate (MTX), sulfasalazine (SSZ), tofacitinib (TOFA) address the issue with different nomenclature. A glomerular filtration rate (GFR) cut-off point of 60 mL/min/1.73 m^2 is often mentioned for dose adjustment or contraindication. The objective of this work is to evaluate the proportion of patients with impaired renal function at the moment of initiation of RA treatment.

Methods: The data of all patients affected by RA starting a csDMARD, bDMARD or tsDMARDS were extracted from the Rhumadata® registry. For those patients, the estimated GFR (eGFR) was assessed using the CKD-EPI equation and the MDRD formula. eGFR are presented in five years age groups for both men and women. Results are expressed as mean ± standard deviation, range, percentiles (5, 25, 50, 75 and 95) and the proportion of patients an impaired renal function (IRF) (i.e. an eGFR below 60 ml/min/1.73 m^2). Potential predictors of IRF include age at diagnosis, gender, disease duration, exposure to csDMARDS or b or ts DMARDs, hypertension, CVD, Charlson comorbidity index. The use of "contraindicated" molecules is explored.

Results: Overall eGFR was obtained for 609 men and 1853 women. In men, mean eGFR in the 25-29, 55-59 and 75-79-years age groups are 125±10, 92±15 and 69±16 ml/min/1.73 m^2. In women, these estimates are 115±14, 87±16 and 70±17 ml/min/1.73 m^2. No patients below 45 years of age has an IRF. After this age, the proportion of men with an IRF increases from 5.1% in the 45-49-years age group to 21.2% in the 75-79-years age group. In women, these same proportions are 2.3 and 24.2%. The results of a stepwise forward selection logistic regression predicting IRF retained age at diagnosis (OR and 95% confidence interval=1.093 (1.073, 1.112)), gender ((women vs. men) 1.929 (1.278, 2.913)), disease duration (1.111 (1.087,1.136)) and hypertension (3.271 (2.116, 5.056)). The CKD-EPI equation and the MDRD formula identically classified 99% of patients as having (6%) or not having (93.0%) IRF. MTX, SSZ, HCQ and Tofacitinib are respectively prescribed for 78%, 10%, 62% and 6% of patients without IRF. These proportions are 63%, 9%, 52% and 4% among patients with IRF, the differences being statistically significant for MTX and HCQ.

Conclusion: As expected, eGFR decreases with age in both groups. Patients in all age groups after 45 years old may have an eGFR inferior to 60 ml/min/1.73 m^2. Below 55 years old, less than 5% of our population has less than 60 ml/

min/1.73 m² of GFR as measure by CKD-EPI equation. Physicians prescribe less MTX, SSZ, HCQ and Tofacitinib to patients with IRF.

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Abstract Number: 2302

Comparison Between Fibromyalgia and Neuropathic Pain in Patients with Established Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Our objectives were (1) to identify similarities and differences of pain symptoms identified by fibromyalgia (FM) and neuropathic pain (NP) screening tool (2) to compare pain qualities and their relationship with rheumatoid arthritis (RA) disease activity.

Methods: 169 RA patients enrolled in the University of Pittsburgh Rheumatoid Arthritis Comparative Effectiveness Registry (RACER) underwent a clinical evaluation and fulfilled 3 self-report questionnaires (PainDETECT, Patient-

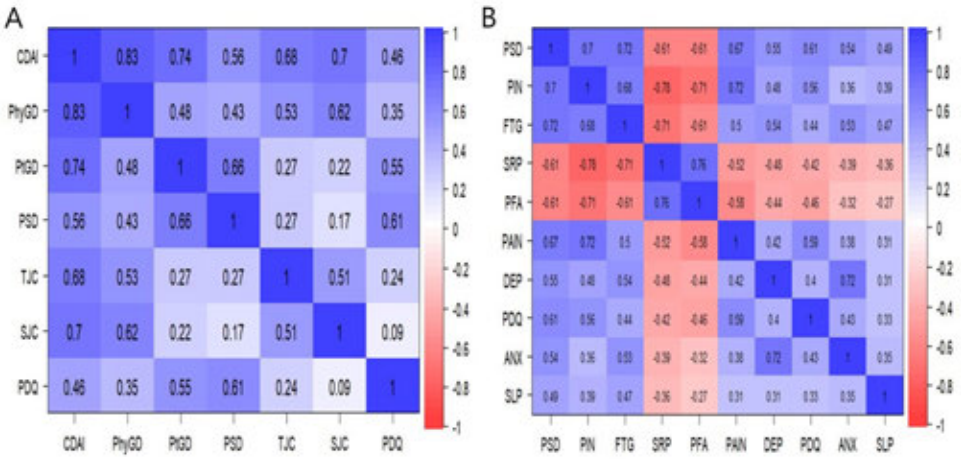

Table 1 Demographics and comparison of clinical characteristics of subgroups based on the fibromyalgia and PainDETECT categories (Mean (SD))

		Subjects			Fibromyalgia category			PainDETECT category			
		All	Pain>=4	Pain>=4 & SJC=0	Yes	No	p value	Neuropathic	Transitional	Nociceptive	p value
Demographic characteristics	Number of subjects	169	90	39	20	149		16	31	119	
	Age	64.26 (12.27)	64.89 (12.32)	65.34 (9.94)	59.81 (12.32)	64.85 (12.18)	0.085	61.98 (11.07)	62.91 (11.18)	64.94 (12.86)	0.532
	Disease duration	17.45 (10.55)	17.74 (11.00)	15.55 (8.64)	14.97 (9.53)	17.78 (10.67)	0.265	13.82 (7.65)	16.43 (10.57)	18.19 (10.84)	0.252
	Gender [Male (%)]	28 (16.6)	12 (13.3)	4 (10.3)	2 (10.0)	26 (17.4)	0.602	2 (12.5)	4 (12.9)	21 (17.6)	0.744
	Race [White (%)]	151 (89.3)	75 (83.3)	32 (82.1)	16 (80.0)	135 (90.6)	0.29	12 (75.0)	28 (90.3)	108 (90.8)	0.159
	BMI	29.33 (6.55)	30.06 (6.96)	30.97 (6.87)	30.64 (5.67)	29.15 (6.65)	0.342	30.86 (9.41)	29.91 (6.08)	29.08 (6.27)	0.535
Pain	Current pain (0-10)	3.49 (2.64)	5.21 (2.33)	5.33 (2.09)	4.15 (2.11)	3.40 (2.69)	0.231	6.75 (2.24)	4.65 (2.33)	2.77 (2.33)	<0.001
	1-week average pain (0-10)	4.04 (2.54)	6.04 (1.60)	6.03 (1.69)	5.20 (1.96)	3.89 (2.57)	0.029	7.44 (1.63)	4.90 (1.94)	3.40 (2.36)	<0.001
	PDQ (-1-38)	8.76 (7.11)	11.76 (7.44)	12.38 (8.07)	10.84 (6.10)	8.49 (7.20)	0.175	23.88 (4.60)	15.13 (1.75)	5.07 (3.44)	<0.001
	PSD (0-31)	8.51 (5.80)	11.62 (5.83)	12.08 (6.90)	11.70 (1.95)	8.08 (6.01)	0.008	16.12 (5.73)	11.00 (6.22)	6.91 (4.58)	<0.001
	Fibromyalgia (%)	20 (11.8)	15 (16.7)	5 (12.8)				3 (18.8)	4 (12.9)	12 (10.1)	0.57
	PDQ category (%)						0.57				
	Neuropathic pain	16 (9.6)	16 (18.0)	7 (17.9)	3 (15.8)	13 (8.8)					
	Transitional	31 (18.7)	22 (24.7)	13 (33.3)	4 (21.1)	27 (18.4)					
	Nociceptive	119 (71.7)	51 (57.3)	19 (48.7)	12 (63.2)	107 (72.8)					
RA disease activity	SJC	1.41 (2.66)	1.88 (3.13)	0.00 (0.00)	2.11 (3.67)	1.32 (2.46)	0.227	2.00 (4.21)	1.75 (3.13)	1.27 (2.30)	0.496
	TJC	1.59 (2.46)	2.25 (2.88)	1.03 (1.31)	1.84 (2.69)	1.55 (2.46)	0.634	3.21 (4.19)	1.61 (2.22)	1.41 (2.23)	0.038
	PhyGD	2.03 (1.69)	2.67 (1.86)	1.77 (1.67)	2.29 (1.62)	1.99 (1.70)	0.47	3.89 (2.62)	2.35 (1.67)	1.75 (1.36)	<0.001
	PtGD	3.67 (2.62)	5.26 (2.05)	5.06 (2.24)	4.83 (1.63)	3.52 (2.69)	0.036	3.03 (2.48)	4.71 (2.20)	6.72 (1.53)	<0.001
	CDAI	8.78 (7.06)	12.14 (7.15)	7.76 (3.74)	11.05 (7.39)	8.46 (6.96)	0.135	7.55 (6.28)	10.63 (6.97)	15.82 (8.57)	<0.001
	Discrepancy	2.14 (1.88)	2.84 (1.86)	3.22 (2.12)	2.53 (2.22)	2.08 (1.82)	0.333	1.94 (1.74)	2.44 (2.01)	3.04 (2.35)	0.078
PROMIS29 (T score)	Physical function	42.23 (6.88)	38.38 (7.47)	40.23 (7.70)	38.78 (6.08)	42.78 (9.11)	0.064	33.68 (3.14)	40.75 (6.89)	43.48 (9.11)	<0.001
	Anxiety	49.18 (9.65)	52.17 (10.08)	51.89 (9.59)	55.77 (8.68)	48.29 (9.46)	0.001	58.13 (12.61)	51.09 (8.28)	47.25 (8.64)	<0.001
	Depression	48.39 (8.87)	51.45 (9.55)	50.54 (9.29)	55.45 (6.60)	47.49 (8.74)	<0.001	56.59 (9.34)	49.25 (8.77)	47.05 (8.34)	<0.001
	Fatigue	51.66 (10.07)	55.73 (8.86)	55.19 (8.88)	57.19 (6.47)	50.92 (10.25)	0.009	63.93 (7.59)	53.10 (7.32)	49.83 (9.78)	<0.001
	Sleep disturbance	51.69 (8.20)	54.00 (8.13)	54.21 (7.67)	54.48 (7.39)	51.31 (8.25)	0.105	60.07 (8.45)	53.58 (6.36)	50.17 (7.94)	<0.001
	Social role participation	50.21 (9.22)	46.19 (8.42)	47.62 (9.73)	47.08 (7.59)	50.63 (9.36)	0.106	41.48 (6.56)	50.14 (6.35)	51.17 (9.53)	<0.001
	Pain interference	55.79 (9.01)	60.82 (7.24)	59.33 (8.18)	59.87 (5.89)	55.24 (9.23)	0.03	66.81 (4.93)	58.30 (4.97)	53.89 (9.00)	<0.001
Sensory profile	Burning*	1.19 (1.39)/21.6	1.46 (1.56)/32.5	1.46 (1.57)/31.8	1.30 (1.49)	1.17 (1.38)	0.695	3.38 (1.20)	2.39 (1.05)	0.56 (0.89)	<0.001
	Tingling*	1.14 (1.40)/23.4	1.57 (1.52)/34.8	1.46 (1.54)/31.8	1.60 (1.54)	1.08 (1.38)	0.121	3.44 (1.15)	2.42 (0.89)	0.49 (0.89)	<0.001
	Light touch*	0.86 (1.18)/12.6	1.19 (1.29)/19.0	1.26 (1.37)/23.1	1.26 (1.33)	0.81 (1.15)	0.114	2.56 (1.41)	1.23 (1.02)	0.54 (0.94)	<0.001
	Sudden attacks*	1.10 (1.40)/15.6	1.53 (1.55)/25.8	1.54 (1.47)/23.1	1.55 (1.43)	1.03 (1.39)	0.122	3.44 (1.26)	2.06 (1.24)	0.54 (0.92)	<0.001
	Cold/heat sensation*	0.72 (1.17)/9.6	1.11 (1.31)/32.6	1.23 (1.44)/21.5	0.80 (1.06)	0.71 (1.18)	0.759	2.56 (1.36)	1.26 (1.15)	0.34 (0.81)	<0.001
	Numbness*	0.96 (1.32)/16.2	1.42 (1.49)/27.0	1.67 (1.61)/35.9	0.90 (1.45)	0.97 (1.31)	0.818	3.19 (1.47)	1.90 (0.94)	0.42 (0.87)	<0.001
	Slight pressure*	1.71 (1.45)/30.6	2.39 (1.35)/49.4	2.46 (1.29)/51.3	2.45 (1.28)	1.61 (1.45)	0.015	3.75 (1.18)	2.32 (1.14)	1.28 (1.25)	<0.001

* Mean (SD) / % of sensory disturbances that were regarded as clinically relevant (i.e. score of >= 3), BMI: body mass index, PDQ: PainDETECT questionnaire, PSD: polysomatic distress score, SJC: swollen joint count, TJC: tender joint count, PhyGD: physician global disease assessment, PtGD: patient global disease assessment, CDAI: clinical disease activity index, Discrepancy: absolute value for discrepancy between PhyGD and PtGD, RA: rheumatoid arthritis, PROMIS: Patient-reported outcomes measurement information system

Reported Outcomes Measurement Information System (PROMIS) 29, Widespread Pain Index/Symptom Severity Scale). The results of the clinical evaluation and questionnaires were then compared.

Results: 20 patients (11.8%) met the fibromyalgia criteria, whereas 16 patients (9.6%) were found to have neuropathic pain. However, only three patients were categorized as FM among those patients who were classified as NP. PainDETECT and polysomatic distress score were significantly correlated with pain levels, RA disease activity, and all PROMIS domains. (Figure 1) No significant difference in the swollen joint count was found regardless of the presence or absence of FM or NP. Tender joint count, patient & physician global disease assessment (PtGD, PhyGD), and clinical disease activity index (CDAI) were significantly higher in patients with NP vs those without NP, whereas only PtGD was higher in patients with FM vs those without FM. (Table 1) Significantly higher scores were found for all PROMIS domains and sensory profiles in patients with NP, while anxiety, depression, fatigue, pain interference, and slight pressure-associated pain were increased in patients with FM. (Table 2)

Conclusion: This study highlights the differences between FM and NP in association with RA disease activity and PROMIS29 domains and demonstrates the PainDETECT can be a useful tool in identifying clinical phenotypes of RA patients.

A. Correlation matrix among painDEDECT, polysomatic distress score, and clinical disease activity index B. Correlation matrix among PainDETECT, polysomatic distress score, and patient-reported outcomes measurement information system 29 domains (PDQ: PainDETECT questionnaire, PSD: polysomatic distress score, SJC: swollen joint count, TJC: tender joint count, PhyGD: physician global disease assessment, PtGD: patient global disease assessment, CDAI: clinical disease activity index, Discrepancy: absolute value for discrepancy between PhyGD and PtGD, RA: rheumatoid arthritis, PROMIS: Patient-reported outcomes measurement information system, PFA: physical function, ANX: anxiety, DEP: depression, FTG: fatigue, SLP: sleep disturbance, SRP: Abilities to participate in social role, PIN: pain interference, PAIN: 1-wk average pain level)

Disclosure: Y. Hwang, None; **L. Zhu**, None; **L. Moreland**, None.

Abstract Number: 2303

Emotional and Social Determinants of Health Increase Office Communication for Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In RA patients, anxiety and depression are associated with higher disease activity and worse outcomes. We hypothesized that in RA patients, poorer mental health would also be associated with more frequent office communication.

Methods: Charts of RA patients who received care at a university arthritis center for at least 1 year between April and September 2018 were identified from 530 records consecutively ordered by MRN (any arthritis type). Patients completed Patient Reported Outcome Measurement Information System (PROMIS) 29-item profiles (depression, anxiety, fatigue, physical function, pain interference, sleep disturbance, participation in social roles and activities) at an index care visit and phone calls and patient portal messages to rheumatologists and other providers were summed from the preceding 12 months. Patients were stratified by telephone call volume (none vs >=1). Demographics, clinical char-

Table 1. Patient characteristics stratified by RA patients who called any provider in past year vs RA patients without telephone communication.

	>=1 Telephone Call N=62	No Telephone Calls N=92	p-value
Age, mean (SD)	60 (13)	56 (14)	0.078
Female sex (n, %)	72 (78)	38 (61)	0.022
White (n, %)	64 (70)	45 (73)	0.69
Disease Duration, (years) median (IQR)	9 (5, 16)	7 (4, 14)	0.29
CDAI, median (IQR)	8.3 (5, 21.25)	6.5 (3.5, 12.5)	0.082
Current Medications (n, %)			
Biologic	49 (53)	28 (45)	0.32
Methotrexate	47 (51)	40 (65)	0.099
Prednisone	21 (23)	13 (21)	0.79
Anti-Depressant	24 (26)	9 (15)	0.086
Benzodiazepine	15 (16)	15 (16)	0.24
Patient Portal Activated (% yes)	73 (79)	56 (90)	0.070
Patient Portal Messages, median (IQR)			
To Arthritis Center	0 (0, 6)	1 (0, 6)	.25
To Any Provider	2 (0, 10.5)	2 (0, 7)	0.98
Telephone Calls, median (IQR)			
To Arthritis Center	1 (0, 1)	0 (0, 0)	**<0.001**
To Any Provider	3 (1, 7)	0 (0, 0)	**<0.001**

acteristics, and frequency of communication were compared between groups using t-tests or chi-square; Poisson regression was used to evaluate the relationship between emotional distress and telephone frequency, controlling for age, sex, race, RA disease duration, clinical disease activity index (CDAI), and PROMIS physical function, social participation, sleep disturbance, pain interference, and fatigue. A sensitivity analysis was performed controlling for use of anti-depressants (AD) and benzodiazepines (BZD).

Results: 154 out of 185 RA patients met 2010 ACR criteria, completed PROMIS profiles, and had a complete CDAI; 1,452 office communications were accrued. Patients were mostly female (n=110, 71%) and white (n=109, 71%) with a mean age (SD) of 59 (14). The median RA disease duration (IQR) was 8 years (5, 16), and median CDAI (IQR) was low at 7.5 (4, 19). High anxiety was present in 24% of RA patients, and high depression symptoms in 18%. RA patients with >=1 versus no telephone calls were mostly female, tended to be older, have more disease activity, and take ADs (Table 1). In multivariable Poisson regression, age (IRR=1.04, p< 0.01), race (IRR=1.75, p=< 0.01), social participation (IRR=0.95, p< 0.01), sleep disturbance (IRR=1.02, p=0.01), and anxiety (IRR=1.03, p< 0.01) were significantly associated with telephone call volume (any provider) (Table 2). Depression was associated with call volume in univariate analysis (IRR=1.04, p< 0.01) with a trend in multivariable analysis (IRR=0.98, p=0.06). In sensitivity analysis when controlling for use of AD and BZD, anxiety and depression continued to significantly impact call volume.

Conclusion: Office communication is driven by emotional and social determinants of health and not RA disease activity, duration, or disability. Patients with high anxiety or depression symptoms telephoned significantly more often than those with low symptoms, although this was not necessarily directed towards the rheumatologist. Early identification of anxiety and depression symptoms may prompt implementation of multi-modal strate-

Table 2. Determinants of Telephone Call Volume.

	Univariate Model		Multivariable Model	
Determinants of Telephone Call Volume	**IRR**	**p-value**	**IRR**	**p-value**
Age	**1.03**	**0.00**	1.04	**0.00**
Sex	1.20	0.07	1.17	0.15
Race	1.44	**0.00**	1.75	**0.00**
Disease Duration	1.02	**0.00**	1.00	0.35
CDAI	1.02	**0.00**	1.00	0.35
Physical Function*	0.94	**0.00**	1.00	0.76
Social Participation*	0.94	**0.00**	0.95	**0.00**
Sleep Disturbance	1.04	**0.00**	1.02	**0.01**
Pain Interference	1.05	**0.00**	1.00	0.59
Fatigue	1.05	**0.00**	1.01	0.59
Anxiety	1.04	**0.00**	1.03	**0.00**
Depression	1.04	**0.00**	0.98	0.06

*Higher scores indicate better physical function, social participation. IRR=Incident Rate Ratio.

gies to address these symptoms and to provide additional information to alleviate patient concerns regarding their health.

Disclosure: D. DiRenzo, None; **M. Wu**, None; **T. Grader-Beck**, None; **S. Bartlett**, Abbie, 2, Abbvie, 2, 5, Bayer, 5, International Society of QOL Research, 6, Janssen, 5, 8, Lilly, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, Pfizer Inc, 8, PROMIS International, 6, UCB, 5, 8; **C. Bingham**, Abbvie, 5, AbbVie, 5, BMS, 2, 5, Bristol Meyer Squibb, 2, 5, Bristol Myers-Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Eli/Lilly, 5, Genentech/Roche, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Pfizer Inc, 5, Regeneron/Sanofi, 5, Sanofi/Regeneron, 5.

Abstract Number: 2304

Bone Microstructure of Patients with Rheumatoid Arthritis: A HR-pQCT Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In rheumatoid arthritis (RA), it has been reported that osteoclast are activated by immune complexes, anti-CCP antibodies (ACPAs), and inflammatory cytokines. The purpose of this study was to investigate the relationship between bone microstructure and joint involvement by imaging the distal radius using HR-pQCT.

Methods: Subjects were 127 female patients with RA, who were examined with X-ray and HR-pQCT. The patients were divided into the group with no RA change (erosion) in the wrist joint (E(-), Steinbrocker Stage I, N=80, 58+/-12 years old) and the group with RA change in the wrist joint (E(+), Steinbrocker Stage II and III, N=47, 59+/-15 years old). Seventy nine patients with APCA negative unclassified arthritis (UCA) (57+/-10 years old) was used as a disease control group. The distal radius, 9mm away from the distal end of the radius, was scanned with HR-pQCT. Parameters representing bone microstructure were measured separately in the cortical bone, trabecular bone, and the total bone. Statistical significant level was set at $p< 0.05$.

Results: The total volumetric bone mineral density (vBMD) and trabecular vBMD were significantly lower in E(-) and E(+) than in UCA. The cortical vBMD was significantly lower in E(+) than in E(-) and UCA. The cortical porosity and cortical pore diameter, measures of cortical microstructures, were significantly larger in E(+) than in E(-) and UCA. The trabecular measures such as trabecular bone volume fraction and trabecular number were lower in E(-) and E(+) than in UCA, while they were lower in E(+) than in E(-). Trabecular separation was larger in E(-) and E(+) than in UCA. There was no significant difference in trabecular thickness among the three groups.

Conclusion: In E(+) the porosity of the cortical bone was increased, and the cause of this was considered to be the effect of hand arthritis. In E(-) bone loss was observed in the trabecular bone but not in the cortical bone, suggesting the elevation of non-arthritic bone resorption.

Disclosure: I. Tanaka, None; **T. Kato**, None; **H. Mizuno**, None; **R. Hibi**, None; **M. Kai**, None; **K. Ogawa**, None; **H. Ohshima**, None; **S. Tamaki**, None.

Abstract Number: 2305

Multimorbidity May Worsen Fatigue in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fatigue is a pervasive problem for many patients with rheumatoid arthritis (RA) that often persists despite treatment with effective disease-modifying therapies. Recent studies have suggested that patients with RA have a high burden of multimorbidity, which could affect their disease experiences and treatment outcomes. We sought to determine whether multimorbidity is associated with fatigue in patients with RA.

Methods: This cross-sectional, prospective study of a population-based cohort from a geographically well-defined area included patients with prevalent RA who completed a questionnaire. Fatigue was assessed using the Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAF-MDQ, V1 27.08.10). Patients' medical records were reviewed for 25 chronic comorbidities from a combination of the Charlson Comorbidity Index, Elixhauser Comorbidity Index, and Rheumatic Disease Comorbidity Index prior to the date of BRAF-MDQ. Rheumatic comorbidities were not included. Linear regression models were used to estimate the change in fatigue outcome with multimorbidity adjusting for age, duration of RA, sex, obesity (body mass index ≥30 kg/m^2), current smoking status, C-reactive protein and RF/CCP positivity. Models were fit for the Total MDQ score and each subscore.

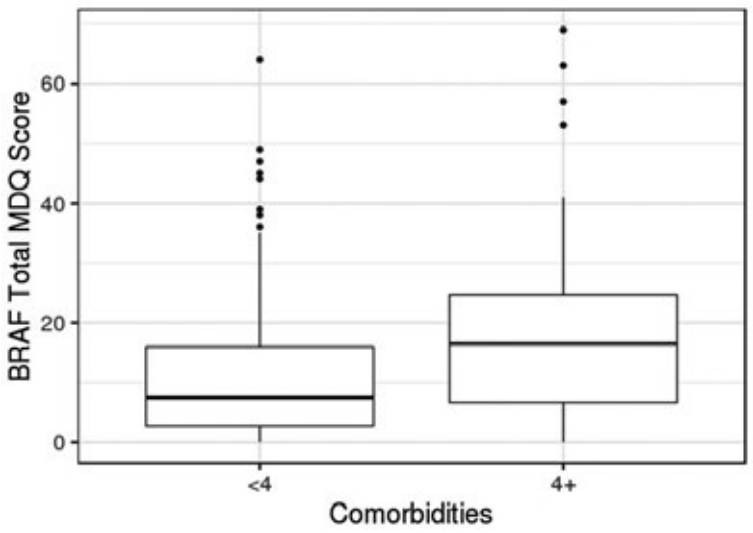

Figure. Total BRAF-MDQ score for patients with less than 4 versus 4 or more comorbidities

Results: The cohort included 192 patients (median age: 62 years, median RA duration: 13 years, 75% female, 46% obese, 6% current smokers, 69% RF/CCP positive). Multimorbidity was common with 93 (48%) patients having 2 or more comorbidities, and 27 (14%) having 4 or more comorbidities. Total BRAF-MDQ scores ranged from 0-69 (median [interquartile range (IQR)] 9 [3, 18]), with higher scores indicating greater fatigue. Patients with 4 or more comorbidities had higher total BRAF-MDQ scores (mean: 21.2; SD 20.2) than patients with less than 4 comorbidities (mean 11.2; SD 11.6; p=0.014; figure) Adjusted linear regression models revealed each additional comorbidity was associated with a 2.4 unit (95% confidence interval [CI]:1.0-3.7) increase in total BRAF-MDQ level (p< 0.001), and the presence of 4 or more comorbidities was associated with an 10.1 (95% CI: 4.3-15.9) unit increase in total BRAF score. Comorbidities were significantly associated with all 4 subscores in adjusted models. An association of this magnitude is likely to be clinically meaningful.

Conclusion: High levels of multimorbidity are associated with increased fatigue in patients with RA. The findings suggest that interventions targeting multimorbidity could help alleviate treatment-refractory fatigue in patients with RA and other rheumatic diseases.

Disclosure: J. Davis, Abbvie, 5, Pfizer, 2, 5, Sanofi Genzyme, 5; **E. Myasoedova**, Pfizer, 2; **T. Gunderson**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2.

Abstract Number: 2306

Prevalent and Incident Multimorbidity in Rheumatoid Arthritis: A Population-Based Cohort Study

Tina Gunderson,[1] Elena Myasoedova,[1] John Davis,[1] and Cynthia Crowson[2], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic Rochester, Rochester

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Multimorbidity is associated with increased risk of adverse outcomes in patients with rheumatoid arthritis (RA). Multiple studies have suggested increased burden of multimorbidity in patients with RA, but the extent of this increase and whether this excess in multimorbidity changes over time has not been well characterized.

Methods: In this retrospective, population-based cohort study, residents of a geographically well-defined area who met 1987 ACR criteria for incident RA in 1999-2013 were identified from a comprehensive medical record linkage system. Age and sex-matched non-RA comparators were selected from the same underlying population. Index date for each non-RA comparator corresponded to an incidence date of a matching patient with RA. Their medical records were then reviewed for 25 chronic comorbidities from a combination of the Charlson Comorbidity Index, Elixhauser Comorbidity Index, and Rheumatic Disease Comorbidity Index at index date and after index date. Rheumatic comorbidities were not included. Aalen-Johansen methods were used to estimate the cumulative incidence of multimorbidity (presence of 2 or more chronic comorbidities) or severe multimorbidity (5 or more) adjusted for the competing risk of death. Cox proportional hazards models with adjustment for age, sex, obesity (body mass index ≥30 kg/m^2) at index date, and calendar year were used to compare the rate of development of multimorbidity or severe multimorbidity between the RA and non-RA cohorts.

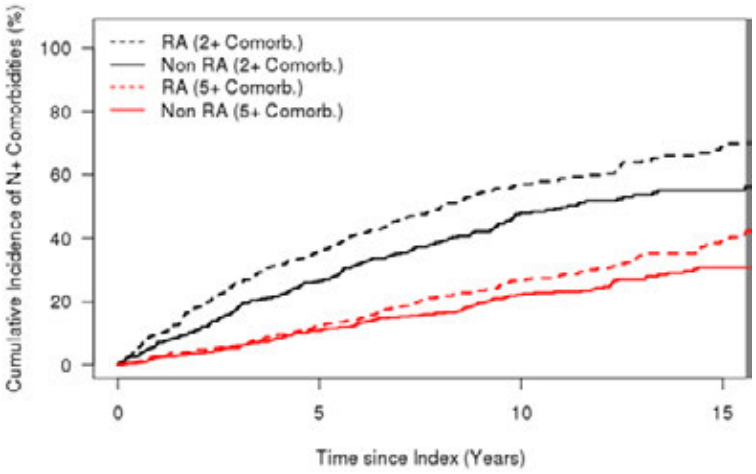

Figure. Cumulative incidence of multimorbidity in patients with and without rheumatoid arthritis.

Results: A total of 597 patients with incident RA (70% female; 90% Caucasian, 3% African-American; mean age 55.5 years) and 594 non-RA (70% female; 91% Caucasian, 3% African-American; mean age 55.4 years) were studied. By incidence/index date, RA patients had an increased prevalence of multimorbidity compared to non-RA subjects (38% RA vs. 32% non-RA, p=0.021) while prevalence of severe multimorbidity was similar (5% RA vs. 4% non-RA, p=0.68). The mean number of comorbidities (excluding rheumatic) by index date were 1.4 in RA patients and 1.2 in non-RA subjects. During follow-up (median 10.2 years RA patients, 10.3 years non-RA), RA subjects also showed an increased incidence of multimorbidity (214 RA vs. 188 non-RA; adjusted hazard ratio (HR): 1.41; 95% confidence interval (CI): 1.16–1.72). By 10 years after RA incidence/index, the cumulative incidence of multimorbidity among those without multimorbidity at index was 56% among the RA patients (95% CI: 51-62%) compared with 48% among the non-RA (95% CI: 43-54%; see figure). RA patients showed some increase in incidence of severe multimorbidity (167 RA vs. 139 non-RA; adjusted HR: 1.21; 95%CI: 0.96-1.51).

Conclusion: Patients with RA have both a higher prevalence of multimorbidity by the time of RA incidence as well as increased incidence thereafter. Studies investigating the underpinnings and implications of these findings are underway.

Disclosure: T. Gunderson, None; **E. Myasoedova**, Pfizer, 2; **J. Davis**, Abbvie, 5, Pfizer, 2, 5, Sanofi Genzyme, 5; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2.

Abstract Number: 2307

Intermetatarsal Bursitis Is Prevalent in Patients with Established Rheumatoid Arthritis and Is Associated with Anti-CCP and RF

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SESSION INFORMATION
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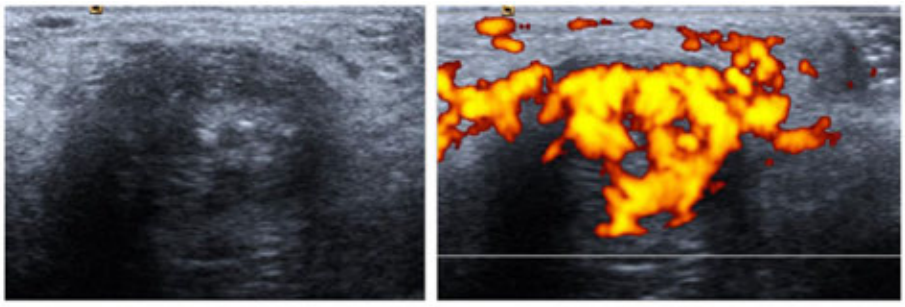
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

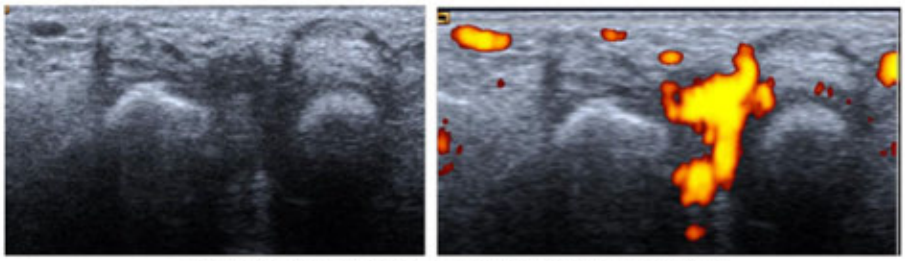
Background/Purpose: Ultrasound is sensitive for detection of inflammatory changes in patients with rheumatoid arthritis (RA). Intermetatarsal bursitis (IMB) may be detected by use of longitudinal dorsal scans between the metatarsophalangeal joints. The present objective was to explore the prevalence of IMB and its associations with subjective, clinical and laboratory assessments in established RA patients.

Methods: A total of 209 patients with RA (mean (SD) age 53 (13) years, disease duration 10 (9) years, 81% women, 79% anti-CCP positive) were included when initiating biological disease modifying antirheumatic drugs (bDMARD). The patients were assessed at baseline and after 1, 2, 3, 6 and 12 months with patient's global disease activity VAS, clinical examination (assessor's disease activity VAS, tender and swollen joint counts performed by a study nurse) and laboratory variables (ESR, CRP, anti-CCP and rheumatoid factor (RF)). Composite clinical scores (DAS28(ESR), CDAI and SDAI) were calculated. The presence of patient reported joint pain (PRJP) was assessed at joint level by use of a manikin (bilateral wrist, MCP1-5, PIP2-3, elbow, knee, ankle, MTP1-5). Each joint was scored 0-3 reflecting the level of spontaneous joint pain the last day. All ultrasound examinations (semi-quantitative scoring (0-3)) of grey scale synovitis (GS) and power Doppler (PD) (PIP 2-3, MCP 1-5, wrist, elbow, knee, talocrural, MTP 1-5 and extensor carpi ulnaris (ECU)/tibialis posterior (TP) tendons bilaterally) were performed by one rheumatologist (HBH) with high intra-reader reliability (Siemens Acuson Antares, excellence version, 5-13 MHz probe). In addition, both feet were at each examination assessed by dorsal longitudinal scan of all spaces between the MTP joints for IMB. Baseline GS and PD ultrasound and PRJP sum scores of MTP 1-5 bilaterally were calculated. Associations were explored by use of Mann-Whitney test and Odds Ratios (OR).

Results: A total of 43 patients (20.6%) had uni- or bilaterally IMB (27.8% right side, 41.9% left side and 23.3% bilaterally, while 7.0%.had no description of side). The patients had up to 4 IMB (n=1 in 72.1%, n=2 in 14.0%, n=3



Longitudinal, bursitis between MTP 3 and 4 joints



Transverse, bursitis between MTP 3 and 4 joints

UL av IMB for abstrakt

in 7.0% or n=4 in 7.0%. The figure shows a typical GS and PD ultrasound of an IMB. The locations of IMB (n=64) were: 4.7% between MTP1 and 2, 32.8% between MTP 2 and 3, 57.8% between MTP 3 and 4, 4.7% between MTP 4 and 5. The presence of IMB was not associated with sum score of baseline GS, PD or PRJP, and not with any of the clinical assessments. However, patients with versus without IMB had significantly higher MTP scores of GS and PD (p=0.05 and p=0.002, respectively), but no difference in PRJP. In addition, presence of IMB was associated with anti-CCP (OR (95% CI) 4.1 (1.2-14.0) and RF (3.7 (1.4-10.1), where 93% of patients with IMB were anti-CCP positive and 87% RF positive.

Conclusion: Intermetatarsal bursitis is quite common in established RA patients and was primarily found between MTP 2-3 and 3-4. It was associated with higher levels of ultrasound MTP joint inflammation and presence of anti-CCP and RF. Thus, ultrasound examination of forefeet should include exploring for this pathology which may indicate more severe disease.

Disclosure: H. Hammer, None; **T. Kvien**, AbbVie, 2, 8, Biogen, 5, 8, Biogen, Egis, Eli Lilly, Hikma, Mylan, Novartis/Sandoz, Oktal, Hospira/Pfizer, Sanofi and UCB, 5, BMS, 8, Celltrion, 8, Egis, 5, 8, Eli Lilly, 5, 8, Hikma, 5, 8, Hospira/Pfizer, 2, 5, 8, MSD, 2, 8, Mylan, 5, 8, Novartis, 8, Novartis/Sandoz, 5, 8, Oktal, 5, 8, Orion Pharma, 8, Roche, 2, 8, Sandoz, 8, Sanofi, 5, 8, UCB, 5, 8; **L. Terslev**, None.

Abstract Number: 2308

The Interaction Between Human Leukocyte Antigen Class II Alleles and Seroprotection to Seasonal Influenza Vaccination in Patients with Rheumatoid Arthritis: A *post-hoc* Analysis

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

Background/Purpose: There are few studies that have looked into the role of human leukocyte antigen (HLA) class II alleles in seroprotection to influenza, especially in subjects with rheumatoid arthritis (RA). We aimed to investigate the correlation between HLA class II polymorphism and the serologic response following seasonal influenza vaccination in patients with RA.

Methods: A total of 314 patients with RA were randomized to continue MTX (MTX-CONT) or to hold MTX (MTX-HOLD) for 2 weeks after vaccination with 2016–2017 seasonal quadrivalent influenza vaccine that contained H1N1, H3N2, B-Yamagata and Victoria (Clinicaltrials.gov NCT02897011). Positive vaccine response was defined as a ≥ 4-fold increase in the hemagglutination inhibition antibody titer, and a satisfactory vaccine response was defined to have a positive response in ≥ 2 of four vaccine antigens. Patients were typed for HLA-DRB1, -DQB1, -DQA1, and -DPB1 using the PCR sequence-based typing method, and its allele profiles were analyzed with the SBTengine soft-

ware. Antigen frequencies in percentage (AgF%) were compared in responder and non-responder groups using the Chi-square test.

Results: Baseline characteristics of both MTX-CONT (n= 155) and MTX-HOLD (n= 159) groups were comparable, as well as the AgF% of four HLA class II genes. In the MTX-HOLD patients, two alleles were associated with a satisfactory vaccine response: the HLA-DRB1*11:01 allele was detected at significantly higher frequencies in responders to H1N1 (p= 0.046, odds ratio, OR 6.33), H3N2 (p= 0.031, OR 9.87), and Victoria (p= 0.043, OR 8.29). The HLA-DQB1*03:02 allele frequency was significantly higher in responders to H3N2 (p= 0.017, OR 3.69) and Victoria (p= 0.047, OR 2.29). These AgF%-responder associations were nonexistent in the MTX-CONT group. There was no HLA class II antigen frequency associated with responders to B-Yamagata in both groups.

Conclusion: Our data indicate that holding MTX after influenza vaccination could lead to better seroprotection in RA patients with HLA-DRB1*11:01 or -DQB1*03:02. Further study is needed to elucidate the mechanisms of higher antibody response to influenza antigens in this subset of patients.

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2. Moss AJ, Gaughran FP, Karasu A, et al. Correlation between human leukocyte antigen class II alleles and HAI titers detected post-influenza vaccination.PLoS One. 2013 Aug 9;8(8):e71376.

Disclosure: M. Kim, None; **J. Park**, None; **E. Lee**, Seoul National University Hospital, 3; **K. Shin**, None.

Abstract Number: 2309

Clinical Study of Peripheral Blood Lymphocyte Subsets in Patients with Rheumatoid Arthritis Complicated with Osteoporosis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Rheumatoid arthritis(RA) is an autoimmune disease mainly manifested by aggressive polyarthritis.The incidence of osteoporosis(OP) has risen and the risk of fracture has further increased in parallel with the prolongation of the disease course,which seriously affects the prognosis and the quality of patients'lives.The purpose of this study is to investigate the incidence of OP in patients with RA and the status of peripheral lymphocyte subsets.

Methods: A total of 734 patients with RA and 81 healthy controls (HC) were enrolled in this study. All peripheral lymphocyte subsets of these participants were assessed by flow cytometry. Patients were divided to pure RA group and RA-OP group according to their bone mineral density (BMD) of lumbar or bilateral hip and the history of fragility

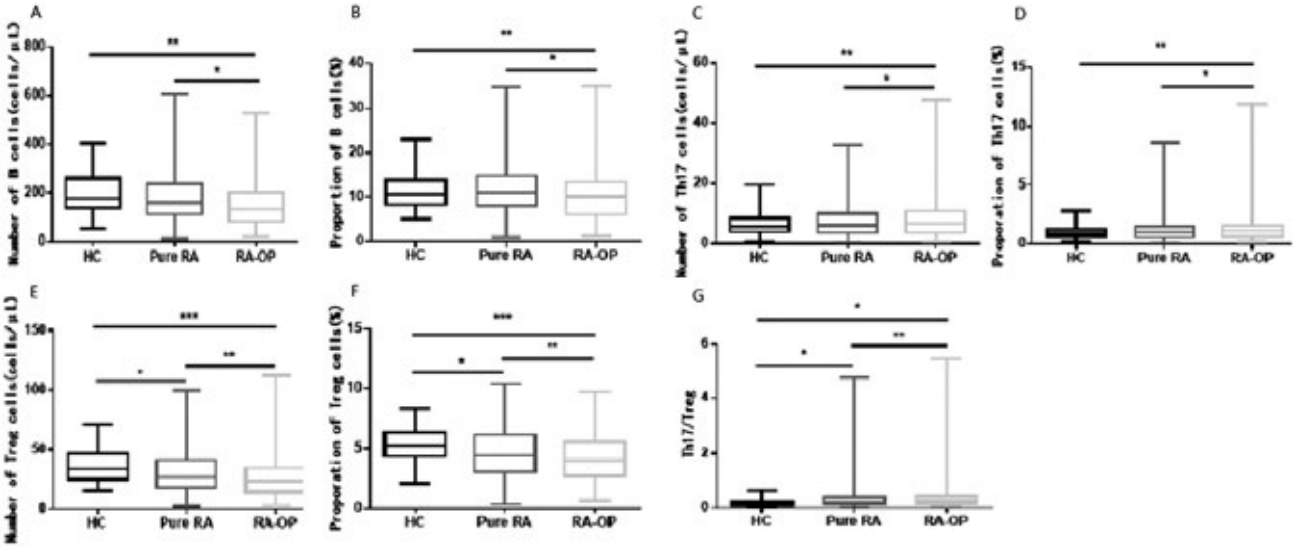

Figure1: The levels of B、Th17、Treg cells and the ratio of Th17/Treg among HC, pure RA and RA-OP group.(*P<0.05;**P<0.01;***P<0.001).

Table 1 The clinical characteristics of patients with or without osteoporosis in RA suffers (Mean±SD)

Parameters	Pure RA	RA-OP	*t*	*P*
Gender (Male/Female)	178/373	42/141	-	0.021
Age (year)	56.63±12.01	61.85±10.36	-12.896	<0.001
Disease duration (year)	5.28±6.33	7.17±5.82	3.645	<0.001
TJC	8.36±8.04	8.97±8.36	-2.023	0.043
SJC	4.57±6.22	5.24±6.37	-2.889	0.004
ESR (mm/h)	52.25±34.65	64.92±35.58	-9.662	<0.001
CRP (mg/L)	33.97±42.67	38.38±50.69	-2.456	0.014

fracture for further comparation of the general clinical data as well as the status of peripheral lymphocyte subsets among these participants.

Results: Among 181 (24.93%) RA-OP patients, there were more female (P=0.021), suggesting female is more susceptible to develop OP. Compared with pure RA patients, not only an older age (P< 0.001) and a longer disease dura-

Table 2 The absolute number and proportion of peripheral lymphocyte subsets among three groups

Parameters	HC	Pure RA	RA-OP
T(cells/μL)	1251.46±349.17	1172.43±455.33	1118.64±462.76[a]
T(%)	70.55±6.84	71.68±9.55	71.46±9.59
B(cells/μL)	201.99±83.28	186.71±111.55	160.31±108.70[ab]
B(%)	11.34±3.89	11.56±5.34	10.35±5.62[b]
NK(cells/μL)	295.51±163.92	230.96±153.67[a]	239.43±140.86[a]
NK(%)	16.23±6.35	14.75±8.89	16.31±8.84[b]
$CD8^+$T(cells/μL)	449.08±175.05	427.44±211.03	407.10±217.61
$CD8^+$T(%)	25.58±7.97	26.19±8.89	26.04±8.64
Th17(cells/μL)	6.41±3.52	7.36±5.36	8.35±6.99[ab]
Th17(%)	0.97±0.54	1.17±0.87	1.35±1.21[ab]
Treg(cells/μL)	35.92±13.03	31.20±19.22[a]	26.73±16.37[ab]
Treg(%)	5.33±1.41	4.69±2.08[a]	4.24±1.82[ab]
Th17/Treg	0.19±0.11	0.33±0.44[a]	0.41±0.58[ab]

([a] means $P<0.05$ compared with healthy control group, [b] means $P<0.05$ compared with pure RA group)

tion(P< 0.001) but also a higher disease activity was observed in RA-OP patients. Moreover, RA-OP patients suffered more joints swelling and pain (P< 0.05) as well as ESR(P< 0.001) and CRP(P=0.014) (Table 1). Compared with those of HC and RA group, the number of Th17 in RA-OP patients was significantly increased (P< 0.05), while Treg cells decreased (p< 0.05), leading to a higher ratio of Th17/Tregs (P< 0.05) (Table 2). In addition, the level of B cells in the pure RA or RA-OP group was significantly reduced, and this alteration was more obvious in patients with OP.

Conclusion: RA patients have a high incidence of OP, which was related to gender, age,disease duration and disease activity. Notably, immune disorder caused by Th17/Treg imbalance may also contribute to OP in RA patients. In addition, total B cells trended to decrease. Anti-osteoporosis treatment and immune regulation might be considered at the early stage of disease.

Disclosure: T. Cheng, None; **S. Zhang**, None; **X. Liu**, None; **J. Wang**, None; **C. Gao**, None; **X. Li**, None.

Abstract Number: 2310

Determinants of Cognitive Function in Rheumatoid Arthritis (RA) Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Table 1: Results of univariable regression models of determinants of log-transformed cognitive function.

Significant Predictors*:	Univariable Models Regression Coefficient (p-value)
Disease Activity: RADAI	0.047 (<0.001)
Pain VAS	0.040 (<0.001)
Current Disease Activity VAS	0.035 (<0.001)
Morning joint stiffness	0.024 (0.004)
Joint Count	0.045 (0.002)
Physical Function: HAQ	0.095 (0.029)
Number of comorbidities:	0.032 (0.009)
Respiratory	0.164 (0.041)
Hematological	0.211 (0.036)
Back Pain	0.162 (0.011)
Fibromyalgia	0.239 (0.004)
History of prior fracture	0.127 (0.047)
Depression: PDQ	0.042 (<0.001)
Quality of Life: SF-6D	0.039 (<0.001)
Sleep: PSQI	0.035 (<0.001)

*Alpha=0.05. Cognitive Function assessed with the global EMQ score, with higher scores associated with poorer cognitive function. Abbreviations: RADAI - RA Disease Activity Index; VAS - Visual Analog Scale; HAQ - Health Assessment Questionnaire; PDQ - Perceived Deficits Questionnaire, SF-6D - Medical Outcomes Study 6-Item Short Form, PSQI - Pittsburgh Sleep Quality Index.

Table 2: Results of multivariable regression model of log-transformed cognitive function.

Significant Predictors*	Multivariable Model Regression Coefficient (p-value)
Depression: PDQ	0.03430 (<.0001)
Physical Function: HAQ	-0.08653 (0.0659)
Quality of Life: SF-6D	0.02033 (0.0282)
Fibromyalgia as a comorbidity	0.11423 (0.1106)

*Alpha=0.15. Cognitive Function assessed with the global EMQ score, with higher scores associated with poorer cognitive function. Abbreviations: PDQ - Perceived Deficits Questionnaire; SF-6D - Medical Outcomes Study 6-Item Short Form; HAQ - Health Assessment Questionnaire.

Background/Purpose: Cognitive impairment (CI), or "brain fog" as rheumatoid arthritis (RA) patients often describe it, is prevalent in persons with RA and can significantly impact daily life1. Despite this, the cause of CI remains poorly understood in persons with RA. This study aimed to identify the determinants of cognitive function in RA to help gain a better understanding of what might contribute to CI in some individuals.

Methods: A cross-sectional study was conducted using 2018 data from an annual survey administered to an RA cohort, derived from a population-based cohort identified using administrative health data. Participants completed self-report questionnaires assessing sociodemographics, and RA-specific information (duration, disease activity, pain, fatigue, physical function), comorbidities including depression, lifestyle factors (alcohol, smoking, physical activity, sleep), BMI, and quality of life. Cognitive function was measured with the Everyday Memory Questionnaire (EMQ), 13 Item Version. Descriptive statistics were performed to characterize all the parameters. Associations between cognitive function and potential determinants were first explored using univariable linear models. Multivariable linear regression analyses were then performed with variables found to be associated with cognitive function in the univariable models, using a stepwise selection at alpha=0.15. Models were natural log-transformed to normalize residuals.

Results: The sample was comprised of 145 RA patients (all women, mean age = 73.7 years; RA duration; 31.3 years). The mean global EMQ score was 21.9, with 43 (30% of the sample) classified as having some level of CI (score above 25). Of these 43, 34 (79%) showed moderate impairment (score 26-38), and 9 (19%) showed severe impairment (score at or above 39). Significant predictors identified in univariable analyses are listed in Table 1. In the multivariable model, physical function, quality of life, depression, and having fibromyalgia as a comorbidity remained independently associated with impaired cognitive function, model R2 is 0.3758 (Table 2).

Conclusion: CI was prevalent among our sample of patients with RA. Our findings suggest that measures of RA severity, such as poor physical function, and comorbidities, such as depression and having fibromyalgia, are associated with impaired memory in RA. Interventions that target CI, as well as pain and depression, require evaluation to help improve how CI is managed in RA.

Szlachetka T, et al., Systematic review of studies reporting on cognitive function in rheumatoid arthritis compared to the general population [JRheum 2019 In press. Abstract from 2019 Canadian Rheumatology Association Annual Meeting)

Disclosure: T. Szlachetka, None; **L. Li**, None; **T. Liu-Ambrose**, None; **H. Xie**, None; **E. Sayre**, None; **D. Lacaille**, None.

Abstract Number: 2311

Association of Sexual Dysfunction and Depression in Rheumatoid Arthritis Female Patients

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic disease that affects joints and is associated with many aspects of the patients´ lives, including sexual function and psychiatric comorbidity, such as depression. This study aimed to assess sexual function and its association with depression in female RA patients and to analyze the factors associated with these conditions.

Methods: We conducted a cross-sectional study with 64 RA female patients. For clinical diagnosis of depression, the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders - 5th edition) was used and the BDI-II (Beck Depression Inventory II) was applied to evaluate the intensity of depression symptoms. Sexual dysfunction (SD) was evaluated using Female Sexual Function Index (FSFI) questionnaire. Clinical and sociodemographic data was collected. Thirty healthy women were included as controls.

Results: The mean age of patients was 52.6 years ($\pm$11.7) compared to a mean 52 years ($\pm$13) of the controls. None of the controls had SD associated with depression. Fifty-one patients had SD, in which 18 (28%) had depression associated with SD. Depression in patients with SD was associated with higher scores of the Health Assessment Questionnaire (p=0.05) and of visual analogue scale for fatigue (p=0.039). Of note, these patients correlated the prednisone dose negatively with domains of FSFI such as arousal (r= -0.5374; p= 0.043), lubrication (r= -0.5032; p= 0.048), orgasm (r= -0.5374; p= 0.043) and satisfaction (r= -0.6197; p=0,03). Patients with SD and no depression (n=33) showed positive correlation of height with arousal (r= 0.3480; p=0.047), lubrication (r= 0.3524; p= 0.044), orgasm (r= 0.3655; p= 0.036) and pain (r=0.3809; p=0.029). Overall, there were no associations of the domains of FSFI with presence of depression or intensity of depression symptoms.

Conclusion: There was high prevalence of sexual dysfunction and depresson in RA patients. Sexual dysfunction and depression might be present concomitantly in RA patients and are suggested to be associated with worse clinical aspects. There is no association of the aspects of sexual function with depression or with the intensity of depression symptoms.

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Abstract Number: 2312

Lymphoproliferative Disorders in Patients with Rheumatoid Arthritis: Results from Japanese Multi-institutional Study Using Research Electronic Data Capture

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SESSION INFORMATION

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Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

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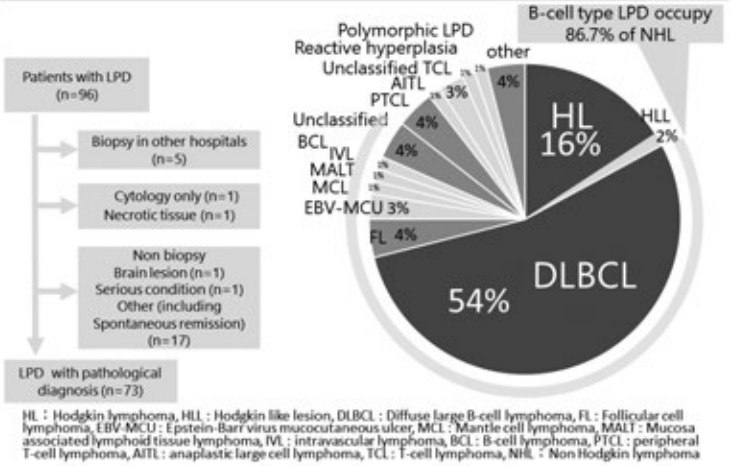
Session Time: 9:00AM–11:00AM

Background/Purpose: The risk of lymphoma is higher among patients with rheumatoid arthritis (RA) compared to general populations [1]. Methotrexate (MTX), the anchor drug for RA, is considered to be associated with development of lymphoproliferative disorders (LPD) [2]. Although a substantial proportion of the cases are reported from Japan, a large-scale epidemiological study on LPD in patients with RA has not been conducted. Thus, the purpose of this study is to investigate epidemiological and clinical characteristics, and risk factors of LPD in Japanese patients with RA.

Methods: This is a multi-institutional retrospective observational study. We enrolled patients who were aged 20 or older, met the 1987 American College of Rheumatology / European League against Rheumatism classification criteria

Figure 1 Histopathological type (n=73)



HL : Hodgkin lymphoma, HLL : Hodgkin like lesion, DLBCL : Diffuse large B-cell lymphoma, FL : Follicular cell lymphoma, EBV-MCU : Epstein-Barr virus mucocutaneous ulcer, MCL : Mantle cell lymphoma, MALT : Mucosa associated lymphoid tissue lymphoma, IVL : intravascular lymphoma, BCL : B-cell lymphoma, PTCL : peripheral T-cell lymphoma, AITL : anaplastic large cell lymphoma, TCL : T-cell lymphoma, NHL : Non Hodgkin lymphoma

Table 1 Clinical characteristics

	Patients without LPD (n = 10716)	Patients with LPD (n=96)	P value
Age (median [quartile])	63 [54, 71] (n=10716)	68 [62, 74] (n=96)	<0.001†
Sex (female %)	79.3 (n=10716)	69.5 (n=96)	0.008‡
Onset of age in RA (median [quartile])	53 [41, 62] (n=9843)	55 [47, 66] (n=94)	0.024†
Disease duration (year) (median [quartile])	6 [2, 14] (n=10476)	11 [4, 17] (n=94)	0.004†
History of MTX treatment before observations (%)	71.1 (n=10716)	91.7 (n=88)	<0.001‡
Duration of MTX treatment before observations (median [quartile])	39 [19, 72] (n=5639)	60 [24, 93] (n=67)	0.003†
Mean dose of MTX at observations (mg/w)	7.4 ± 2.8 (n=6302)	8.1 ± 2.9 (n=75)	0.011†
Sjogren's syndrome	6.8%	3.1%	0.153
At least any one of conventional synthetic DMARDs	84.8%	95.8%	0.003‡
Methotrexate	58.3%	82.3%	<0.001‡
Tacrolimus	7.9%	10.4%	0.372‡
Mizoribine	1.6%	5.2%	0.006‡
Bucillamine	9.9%	8.3%	0.610‡
Salazosulfapyridine	16.3%	17.7%	0.714‡
Iguratimod	0.1%	0%	0.817‡
Leflunomide	0.5%	1.0%	0.496‡
Corticosteroids	48.0%	53.7%	0.658‡
At least any one of Biologic DMARDs	24.8%	22.1%	0.550‡
Infliximab	4.8%	9.4%	0.035‡
Etanercept	8.3%	5.2%	0.269‡
Adalimumab	2.7%	3.1%	0.820‡
Certolizumab pegol	0.3%	0%	0.586‡
Golimumab	0.2%	0%	0.657‡
Tocilizumab	5.1%	3.1%	0.378‡
Abatacept	1.0%	2.1%	0.283‡
Tofacitinib	0.3%	0%	0.586‡
ESR(mm/hr)	22 [10, 41] (n=7738)	28 [14, 52] (n=75)	0.021†
CRP (mg/dl)	0.2 [0.06, 0.75] (n=9128)	0.4 [0.1, 1.2] (n=87)	0.004†
LDH (U/L)	196 [172, 227] (n=8432)	209 [178, 243] (n=70)	0.025†
A number of swollen joints ※	2.2 ± 3.3 (n=6321)	2.6 ± 2.9 (n=63)	0.013†
A number of tender joints ※	2.0 ± 3.5 (n=6302)	1.5 ±1.9 (n=62)	0.823†
Patient VAS (mm) (mean ± SD)	28.6 ± 24.0 (n=3930)	40.8 ± 25.5 (n=39)	0.01†
Physician's VAS (mm) (mean ± SD)	19.0 ± 18.0 (n=2845)	25.1 ± 21.6 (n=30)	0.036†
DAS28-CRP(3)	3.22 ± 0.98 (n=5912)	3.28 ± 0.80 (n=57)	0.203†

LPD : lymphoproliferative disorder, RA : rheumatoid arthritis, MTX : methotrexate, DMARDs : disease modifying anti-rheumatic drug, ESR : erythrocyte sedimentation rate, CRP : C reactive protein, LDH : lactate dehydrogenase, VAS : visual analog scale
† : Mann-Whitney U test, ‡ : chi-squared test

for RA, and visited the registered hospitals for rheumatology training program of Japan College of Rheumatology at least once between 1st April 2011 and 31st July 2011. We excluded patients who had been diagnosed as having lymphoma before the enrollment. The first visit of each patient during the above 4 months was defined as the start of the observation with a follow-up period of 3 years onward. A patient who fulfilled the definition of LPD during the observation were followed for up to 5 years from the onset of LPD. LPD of this study included lymphoma with pathological diagnosis, LPD other than lymphoma with pathological diagnosis, and clinical LPD without pathological diagnosis. We calculated proportion of patients with LPD, and investigated risk factors for LPD using a logistic regression model, and described pathological features, vital prognosis, and cause of death in patients with LPD. We used a REDCap toll for collecting data.

Table 2 Risk factors of LPD

	Standard error	Odds ratio	Confidence interval of odds ratio†		P value
			Lower limit	Upper limit	
Age by decade	0.010	1.553	1.293	1.877	<0.001
Sex (female vs. male)	0.001	1.003	1.001	1.005	0.008
Sjogren's syndrome	0.589	0.457	0.144	1.451	0.184
Methotrexate use	0.275	3.402	1.983	5.836	<0.001
Tacrolimus use	0.333	1.552	0.809	2.979	0.186
At least any one of Biologic DMARDs use	0.252	0.960	0.586	1.573	0.870
Corticosteroids use	0.195	1.162	0.792	1.704	0.443

LPD : lymphoproliferative disorder, DMARDs : disease modifying anti-rheumatic drugs
† : multivariate logistic regression model

Results: Of 11100 patients enrolled, 10812 were analyzed. At baseline, the mean age was 63 years old and 79.3% were female. The mean disease duration was 9.8 years, 6.8% of the patients had Sjogren's syndrome, and mean DAS28-CRP (3) was 3.22. Prevalence of MTX use and biological agent use was 58.6% and 22.8 %, respectively. The mean dose of MTX at baseline was 7.4 mg/week. Ninety-six patients (0.89%) developed LPD during the observation period. There were significant differences in patients' characteristics such as age, sex, disease duration, and use of MTX between those who did and did not develop LPD (Table 1). Multivariable logistic regression analysis showed that age by decade (odds ratio [OR] 1.55 [95% CI 1.29-1.88]) and MTX use at baseline (3.40 [1.98-5.84] were significant independent risk factors of developing LPD (Table 2). Of 73 cases with pathological diagnosis, diffuse large B cell lymphoma (DLBCL) was the most frequent (n = 41, 54%), followed by Hodgkin lymphoma (n=12, 16%) (Figure 1). Mortality rate was 20% (n=23/92). The major cause of death was lymphoma (n=18, 78.3%), followed by cardiovascular diseases (n=2, 8.7 %).

Conclusion: Conclusions: This nationwide study revealed risk factors and pathological subtypes of LPD, and vital prognosis in Japanese patients with RA for the first time.

References:

1. Arthritis Res Ther. 2015; 17: 212.

2. Am J Hematol. 2007; 82: 1106-9.

Disclosure: S. Honda, None; **R. Sakai**, Ayumi Pharmaceutical Co. Ltd., 2, Bristol Meyers Squib, 2, Chugai Pharmaceutical Co. Ltd., 2, Mitsubishi Tanabe Pharma Corp., 2, Nippon Kayaku Co. Ltd., 2, Taisho Toyama Pharmaceutical Co. Ltd., 2; **M. Majima**, None; **N. Konda**, None; **H. Takada**, None; **K. Yamamoto**, AbbVie GK, 8, Astellas Pharma Inc, 8, AYUMI Pharma Corporation, 8, Bristol-Myers Squibb, 8, Chugai Pharmaceutical Co. Ltd, 2, Eisai Co., Ltd, 8, Janssen Pharmaceutical K.K, 8, Mitsubishi Tanabe Pharma Corporation, 8, Ono Pharmaceutical Co., Ltd, 8, UCB Japan Co. Ltd, 8; **T. Takeuchi**, AbbVie, 2, 5, 8, AbbVie GK, 2, 9, Asahi Kasei, 2, Asahikasei, 2, Asahikasei Pharma Corp., 2, Astellas, 2, 8, 9, Astellas Pharma Inc, 2, Astellas Pharma, Inc., 2, 5, 8, 9, Astra Zeneca, 2, AstraZeneca, 8, AYUMI, 2, 9, AYUMI Pharmaceutical Corporation, 2, BMS, 2, 8, Boehringer-ingelheim, 9, Bristol–Myers K.K., 9, Bristol-Myers, 2, Bristol-Myers Squibb, 8, Chugai, 2, 8, 9, Chugai Pharmaceutical Co, Ltd., 2, Daiichi Sankyo, 2, 8, 9, Daiichi Sankyo Co., Ltd., 2, Eisai, 2, 5, 8, 9, Eisai Co., Ltd., 2, Eli Lilly, 2, 8, Eli Lilly Japan, 9, Gilead Sciences, Inc., 9, GlaxoSmithKline K.K, 9, GSK, 8, Janssen, 2, 8, Janssen Pharmaceutical K.K, 9, Mitsubishi Tanabe, 2, 9, Mitsubishi Tanabe Pharma Co., 2, Mitsubishi-Tanabe Pharma Corp, 2, 8, 9, Nippon Kayaku, 2, Nipponkayaku, 2, 9, Nipponkayaku Co.Ltd., 2, Novartis, 2, 8, Novartis Pharma K.K, 2, 9, Novartis Pharma K.K., 2, Pfizer, 2, 8, Pfizer Japan, 2, 9, Pfizer Japan Inc., 2, Sanofi, 8, Sanofi K.K, 9, Shionogi & Co., 2, Shionogi & Co., LTD., 2, Taiho, 2, 8, 9, Taisho, 9, Taisho Toyama, 2, 8, Takahashi Industrial and Economic Research Foundation, 2, Takeda, 2, 8, Takeda Pharmaceutical Co., Ltd., 2, Teijin, 2, 8, UCB, 8, 9, UCB Japan, 9; **M. Harigai**, AbbVie Japan GK, 2, 8, Ayumi Pharmaceutical Co. Ltd., 2, Bristol Meyers Squib, 2, 5, 8, Bristol-Myers Squibb Co. Ltd, 2, 5, 8, Chugai Pharmaceutical Co. Ltd., 2, 5, 8, Chugai Pharmaceutical Co., Ltd., 2, 5, 8, Eisai Co. Ltd., 2, Eisai Co., Ltd., 2, Eli Lilly, 5, 8, Mitsubishi Tanabe Pharma Co., 2, Mitsubishi Tanabe Pharma Corp., 2, Nippon Kayaku Co. Ltd., 2, Taisho Toyama Pharmaceutical Co. Ltd., 2, Takeda Pharmaceutical Co., 2, Takeda Pharmaceutical Co., Ltd., 2, Teijin Pharma Ltd., 2, 8, Teijin Pharma, Ltd., 2, 8.

Abstract Number: 2313

Patients with Rheumatoid Arthritis Have a Higher Risk of Bipolar Disorder: A Systematic Review and Meta-analysis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

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Background/Purpose: Patients with chronic autoimmune diseases may have a higher risk of psychiatric illness as a result of chronic neuro-inflammation and immune dysregulation. The current study was conducted with the aim to investigate the relationship between rheumatoid arthritis (RA) and bipolar disorder by identifying all available studies and summarizing their results together.

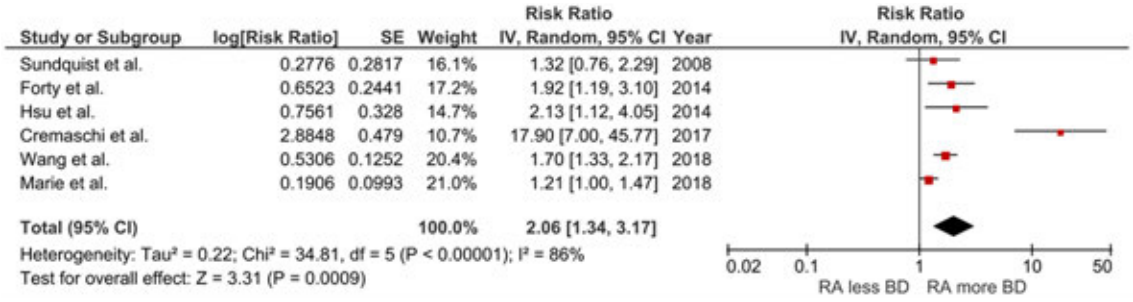

Figure 1: Forest plot of the current meta-analysis

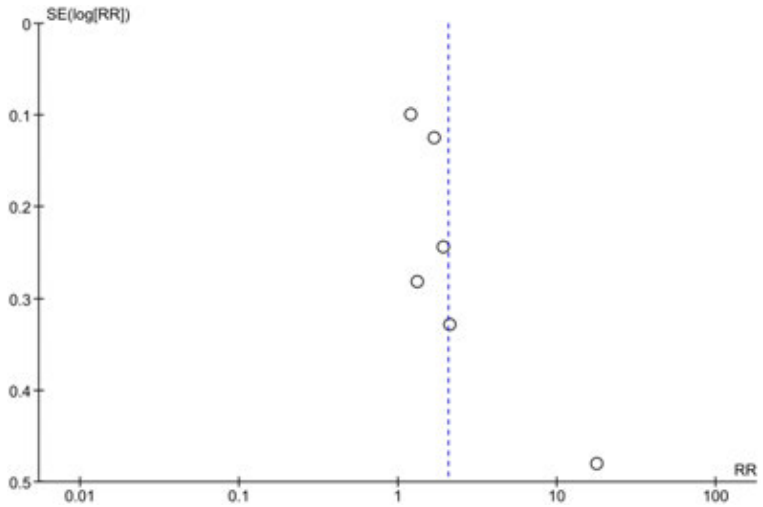

Figure 2: Funnel plot of the current meta-analysis

Methods: Potentially eligible studies that compared the risk of developing bipolar disorder between patients with RA and individuals without RA were identified from Medline and EMBASE databases from inception to May 2019 using search strategy that comprised of terms for "rheumatoid arthritis" and "bipolar disorder". Eligible studies could be either cohort studies or case-control studies. For cohort studies, they must recruit two groups of participants, patients with RA and individuals without RA. Then, the studies must follow their participants for incident bipolar disorder and report relative risk between the two groups. For case-control studies, they must recruit cases with bipolar disorder and controls without bipolar disorder. Then, the studies must explore their prior history of RA and report odds ratio comparing the two groups. Relative risk and standard error from each study were extracted and combined together using the random effect, generic inverse variance technique of DerSimonian and Laird. Odds ratio of case-control study was used as an estimate for relative risk to calculate the pooled effect estimate along with relative risk of cohort study.

Results: A total of 1,542 articles were identified using the aforementioned search strategy. After two rounds of independent review by two investigators, six studies with 420,458 participants fulfilled the inclusion criteria and were included into the meta-analysis. The risk of developing bipolar disorder was significantly higher among patients with RA than individuals without RA with the pooled relative risk of 2.06 (95% CI, 1.34 – 3.17; I^2 86%) (figure 1). Funnel plot was relatively symmetric and was not suggestive of presence of publication bias (figure 2).

Conclusion: A significantly higher risk of developing bipolar disorder among patients with RA was demonstrated in this study.

Disclosure: P. Ungprasert, None; **N. Charoenngam**, None; **B. Ponvilawan**, None.

Abstract Number: 2314

Improved Anxiety, Depression, and Emotional Distress for Rheumatoid Arthritis Patients Following the Completion of an Online Mental Health Intervention

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Anxiety and depression are common in people with rheumatoid arthritis (RA). These comorbidities are associated with worse disease outcomes including pain and functional disability. Thus, treating mental health comorbidity is an important component of RA care. Given access to clinical mental health resources are limited, we evaluated the potential benefit of an online mental health intervention (i.e., self-directed cognitive behavioral therapy/CBT) for reducing mental health symptoms and improving quality of life in individuals with RA.

Methods: RA participants with self-reported clinically significant anxiety (n=38, 89% female) were enrolled. Participants completed The Worry and Sadness program, a validated, 6-module course including psychoeducation and strategies for self-management developed by an Australian research group. The program was completed, at home, over 12 weeks. Mental health outcomes were assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS) scales for anxiety and depression, the Kessler Psychological Distress Scale (K-10) for emo-

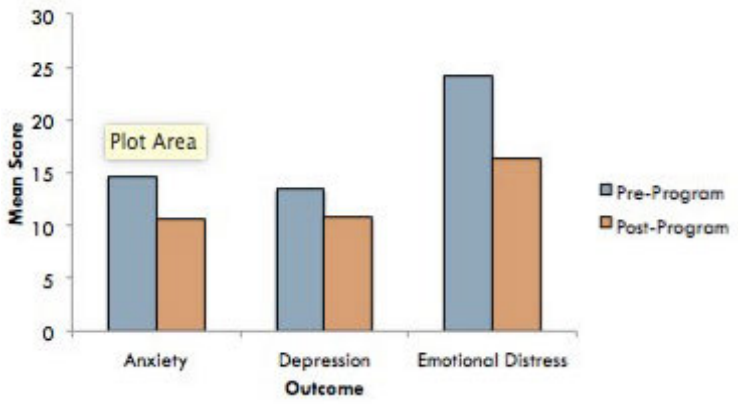

Figure: Pre-post comparisons of anxiety, depression, and emotional distress using the PROMIS Anxiety, PROMIS Depression, and Kessler Psychological Distress Scale (K-10).

tional distress, and the PROMIS scale for physical-health related quality of life. Arthritis outcomes were assessed with the modified health assessment questionnaire (mHAQ) for physical function, PROMIS scales for pain and fatigue, and a patient-reported verbal assessment for disease activity. Measures obtained before and after completing the program were compared using paired Student t-tests. Participants also rated the usefulness of the program.

Results: Participants who have completed the program (n=23) were predominantly female (mean age=59.4 years, standard deviation/SD=11.36). Immediately after completing the program, anxiety (mean difference pre-program versus post-program=4.13, SD=3.53, t(22)=5.61, p< 0.001), depression (mean difference pre-program versus post-program=2.57, SD=2.71, t(22)=4.54, p< 0.001), and emotional distress (mean difference pre-program versus post-program=7.81, SD=7.15, t(20)=5.01, p< 0.001) scores were all significantly reduced (Figure). Quality of life was unchanged, as were arthritis outcomes. Components of the program endorsed as useful to participants included identifying problematic thoughts, whereas reducing behavioural avoidance was considered less helpful.

Conclusion: Mental health symptoms experienced by RA patients improved after completing the Worry and Sadness online program, however, the program might benefit from adaptation to meet the needs of persons living with RA. Online tools are one feasible strategy to address the mental health needs of persons with RA, particularly in regions with limited clinical mental services.

Disclosure: C. Blaney, None; **C. Hitchon**, Pfizer, 2, UCB, 2, UCB Canada, 2; **R. Marrie**, None; **C. Mackenzie**, None; **P. Holens**, None; **R. El-Gabalawy**, None.

Abstract Number: 2315

Association of Rheumatic Autoimmune Disease, Including Rheumatoid Arthritis, with Post-Traumatic Stress Disorder but Not Traumatic Brain Injury in Veterans

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune diseases, including rheumatoid arthritis (RA) and systemic lupus erythematosus, are 2- to 3-fold more common among those with post-traumatic stress disorder (PTSD) than among matched controls. In US Armed Service personnel, PTSD is more prevalent among individuals with mild traumatic brain injury (TBI). For both PTSD and TBI there are immune changes that might predispose to autoimmune disease. We undertook this study in US veterans to investigate potential differences in risk of autoimmune rheumatic illness for TBI patients with versus PTSD those without PTSD.

Methods: We studied a cohort of 229 subjects (137 with PTSD) followed in a US Department of Veterans Affairs TBI clinic. Diagnoses were gathered from the electronic medical record. Clinical diagnosis of a rheumatic autoimmune disease was confirmed by chart review. Each subject with RA was evaluated for the 2010 ACR/EULAR RA Classification Criteria. We determined anti-CCP and rheumatoid factor by ELISA, anti-ENA by BioPlex and ANA by indirect immnofluorescence in a randomly selected subgroup of 40 veterans with TBI (20 with PTSD and 20 without PTSD), and without a prior diagnosis of RA, SLE, APL, or myositis.

Results: We found 11 of 137 (8%) TBI/PTSD subjects had RA. Each of these 11 met the 2010 ACR/EULAR criteria. Meanwhile, only 2 of 92 (2.1%) of those with TBI without PTSD had RA. Other rheumatic autoimmune disease in the PTSD/TBI group included polymyositis (3), SLE (1), undifferentiated connective tissue disease (1), and primary APL (1). Thus, a total of 17/137 (12.5%) in the PTSD/TBI group had a rheumatic autoimmune disease. Among those with only TBI, there were only 4/92 (4.3%) patients with a rheumatic autoimmune disease. This difference (17/137 versus 4/92) was statistically significant (p=0.02, Fisher's exact test). In the subgroup with serology, 6/20 sera from PTSD/TBI were ANA positive, while only 1/20 from TBI alone was ANA positive. Concerning anti-ENA, among PTSD/TBI subjects 1 had anti-Ro/SSA, one had anti-RNP and one had anti-RNP and anti-dsDNA. No TBI alone subjects had anti-ENA. Low positive RF was common but increased among those in the PTSD/TBI subgroup as compared to TBI alone (16/20 versus 10/20, p=0.04, Fisher's exact test).

Conclusion: There is an increased prevalence of autoimmune rheumatic disease, in particular rheumatoid arthritis, and positive rheumatic autoantibodies in TBI subjects with PTSD compared to those without PTSD. We conclude that TBI and autoimmunity are not associated, while autoimmunity – both clinically manifest and silent – is associated with PTSD. Studies investigating causality and mechanism are indicated in this at-risk population.

Disclosure: B. Kurien, None; **C. Prodan**, None; **R. Scofield**, None.

Abstract Number: 2316

National Trends in Hospitalizations and Mortality for Acute Myocardial Infarction in Patients with Rheumatoid Arthritis: Data from National Inpatient Sample 2010-2014

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

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Session Time: 9:00AM–11:00AM

Table 1: Trends in hospitalizations and demographics for AMI with RA: National Inpatient Sample (2010-2014)

	2010	2011	2012	2013	2014
Hospitalizations for Adult MI	601355	608695	604690	598845	605530
Hospitalizations for Adult MI & RA	8359	8814	9315	9225.003	9480
Mean Age (in years)	70.67	70.59	70.26	70.16	70.4
Sex (%)					
Male	36.15	36.09	37.36	36.04	38.66
Females	63.85	63.91	62.64	63.96	61.34
Race (%)					
White	80.03	77.65	80.81	79.67	79.29
African American	9.79	11.38	8.71	9.16	9.26
Hispanic	6.24	6.57	5.47	6.74	6.68
Asian/pacific islander	1.11	2.09	1.48	1.67	1.4
Native American	1.31	0.39	0.51	0.63	0.84
Other	1.51	1.92	3.02	2.13	2.53
Charlson Category (%)					
1	0	0	0	0	0
2	29.31	26.85	27.43	25.64	26
3	28.43	26.32	28.66	27.7	26.58
4	1752	17.99	18.36	18.05	18.35
5	11.33	12.92	11.54	13.33	12.39
>=6	13.41	15.91	14.01	15.28	16.67
Insurance status (%)					
Medicare	71.7	72.49	74.19	73.82	75.16
Medicaid	5.31	5.41	4.39	5.27	5.57
Private insurance	20.59	19.74	19.55	19.02	17.45
Self-pay	2.4	2.36	1.87	18.9	1.82
Median household income for patient's zip code (%)					
0-25th percentile	26.9	30.74	31.32	29.05	29.69
26th to 50th percentile (median)	27.48	23.57	7.03	27.45	28.88
51st to 75th percentile	25.71	25.73	22.53	24.04	22.36
76th to 100th percentile	19.92	19.96	19.12	19.46	19.07
Hospital location (%)					
Rural	11.7	10.4	12.08	11.22	9.92
Urban	88.3	89.6	87.92	88.78	90.08
Hospital size (%)					

Table 2: Trends in outcomes for hospitalizations for AMI with RA: National Inpatient Sample (2010-2014)

Patient Outcomes Studied	2010	2011	2012	2013	2014
Total charges per hospitalization (in dollars)	59011	66134	62826	72016	74721
Inpatient mortality (%)	5.54	5.55	6.12	4.72	4.22
Length of Stay (in days)	4.61	4.78	4.49	4.67	4.72

Background/Purpose: Rheumatoid arthritis (RA) has been associated with increased cardiovascular mortality. More intensive treatment with a focus on "treat to target" strategies are being developed, resulting in improved control of inflammation and lower levels of disability. Our literature review suggested that most of the studies were done to assess incident acute myocardial infarction (AMI) before 2010.

Our goal with this study was to evaluate recent (2010-2014) temporal trends of prevalence and mortality in AMI hospitalizations, with underlying RA in a nationally representative sample.

Methods: We reviewed the National Inpatient Sample (NIS) data over five years from 2010-2014 and identified adult AMI hospitalizations using validated ICD9-CM codes. These hospitalizations were stratified based on the secondary diagnosis of RA. Descriptive statistics were represented as means/medians for continuous and as frequencies and percentages for categorical variables. Using survey data-analysis, we calculated prevalence and in-hospital mortality.

Results: We identified 297192 hospitalizations with AMI from 2010 to 2014. Around 44557 patients had a secondary diagnosis of RA. Mean age of these patients was 70.41± 0.13 years (significantly higher than those without RA, p-value < 0.05), and 63.11% were females. There were 2315 estimated inpatient deaths from 2010-2014, with no significant difference in odds of mortality when compared to patients without RA (p value=0.75).

Conclusion: Trends in hospitalizations and inpatient mortality in RA patients hospitalized for AMI seems to have plateaued in recent years. RA patients were older and mostly females, as noted in previous studies as well. These findings are likely related to early disease recognition, improved disease control, as well as the implementation of cardiovascular risk factor modifications for patients with underlying RA. Further trends in mortality from other cardiovascular causes, such as stroke and congestive heart failure, will provide insight into other cardiovascular events.

Disclosure: S. Jatwani, None; **K. Jatwani**, None; **B. Bindra**, None; **K. Chugh**, None.

Abstract Number: 2317

Gut Dysbiosis Is Associated with Measures of Early Vascular Dysfunction in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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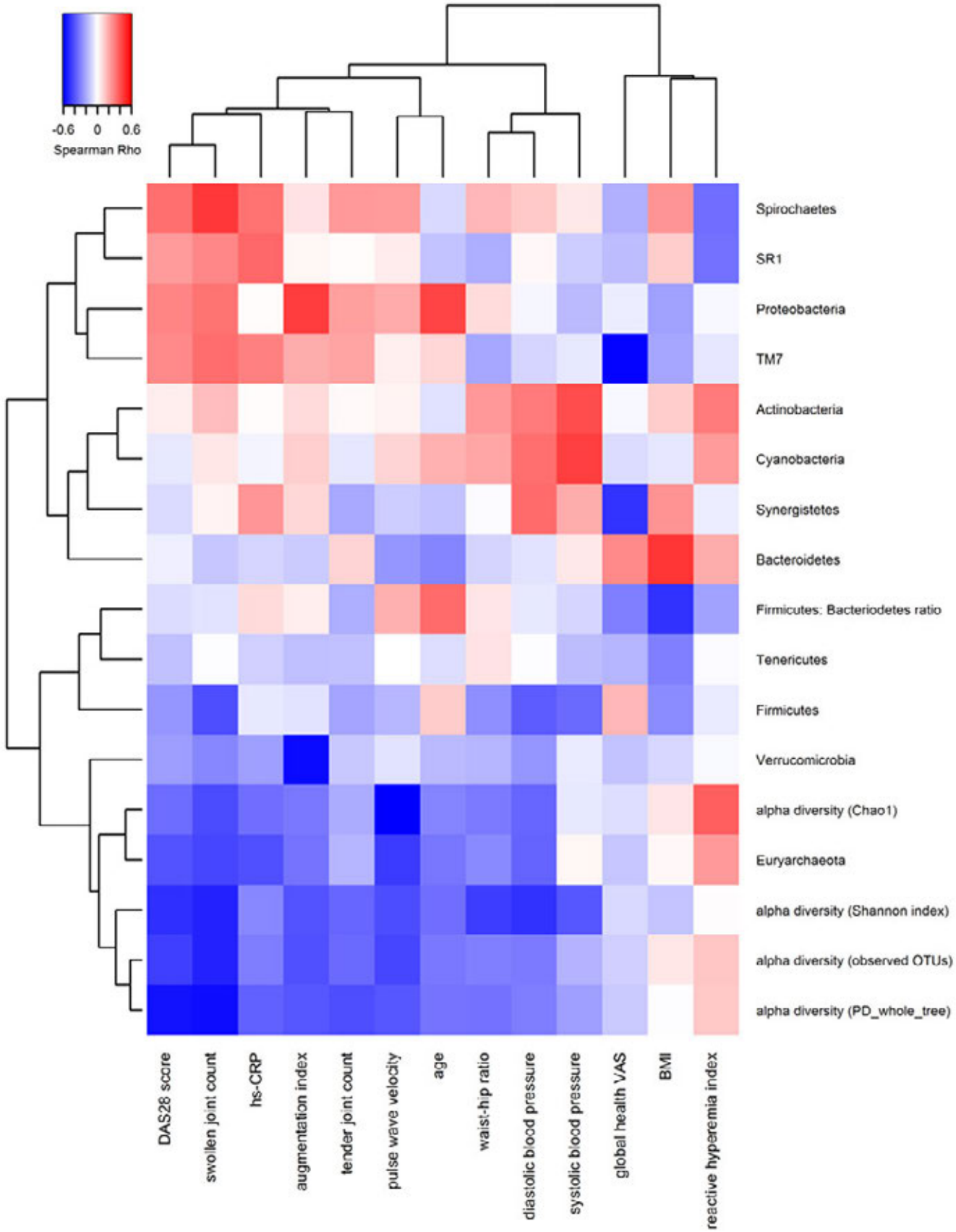

Figure 1 Heatmap with hierarchical clustering of gut microbiome alpha diversity and relative abundance of different phyla with measures of vascular function and clinical features in patients with rheumatoid arthritis.

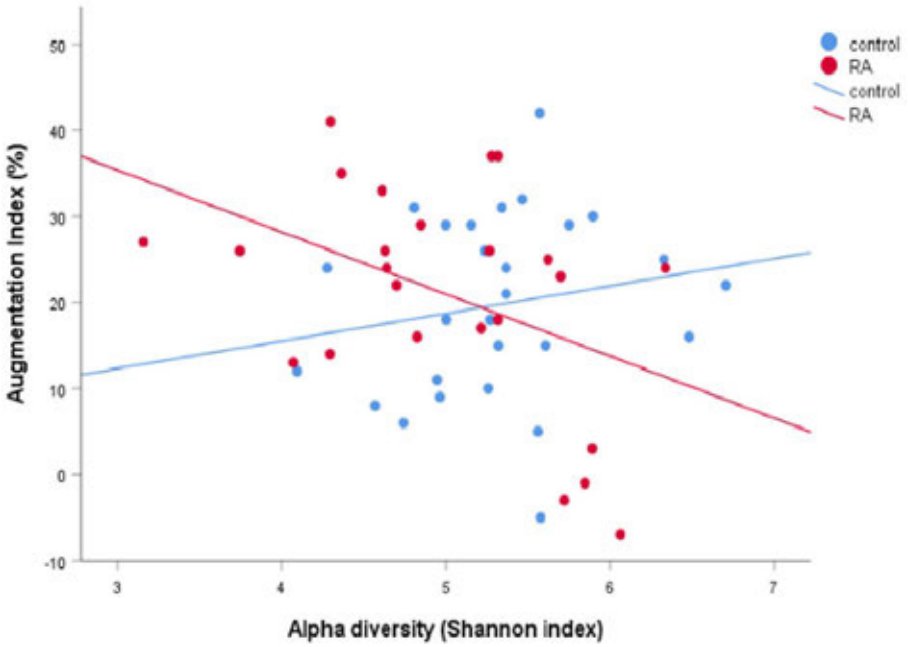

Figure 2. Rheumatoid arthritis modifies the association between Alpha diversity (assessed by Shannon index) and augmentation index. P=0.03 for interaction.

Background/Purpose: Patients with rheumatoid arthritis (RA) have accelerated cardiovascular disease independent of traditional risk factors. Previous studies demonstrate that the gut microbiome is altered in patients with RA and that the gut microbiota may play a role in development of cardiovascular disease in the general population. We tested the hypothesis that gut dysbiosis is associated with early vascular dysfunction in patients with RA.

Methods: Patients with RA (N=30) and control subjects (N=30), frequency matched for age, race and sex were recruited from the Nashville VA hospital and Vanderbilt University Medical Center. Measures of early vascular function including augmentation index, carotid-radial pulse wave velocity, and reactive hyperemia index as well as clinical data were obtained. Stool 16S rRNA gene sequencing was performed by Corebiome. The gut microbiome composition was compared in RA and control subjects with adjustment for false discovery rate. The primary analyses were determination of the association between alpha diversity (as a summary statistic of dysbiosis) and vascular measures in RA. Exploratory analyses included the association of phylum level relative abundance of microbes with vascular measures in RA.

Results: After adjustment for false discovery rate, there was no significant difference in gut microbiome composition, and a non-significant decrease in alpha diversity in RA versus control subjects. Among patients with RA, higher augmentation index and pulse wave velocity (both indicating increased vascular stiffness) were associated with lower alpha diversity (indicating increased dysbiosis) (Figure 1). However, these associations were not present among control subjects; and disease status (RA versus control) modified the association between Shannon index and augmentation index (P=0.03 for interaction, Figure 2). Among patients with RA higher augmentation index was associated with significantly greater proportion of gut Proteobacteria and lower proportion of Verrucomicrobia; and higher PVW was associated with less Euryarchaeota (Figure 1). Similarly, higher RA disease activity was associated with lower alpha diversity, significantly lower proportion of Euryarchaeota and more Fusobacteria in the gut (Figure 1).

Conclusion: Among patients with RA, but not control subjects, reduced gut microbiome alpha diversity was associated with increased vascular stiffness. Gut microbiome dysbiosis may be a contributor to accelerated atherosclerosis in RA.

Disclosure: M. Ormseth, None; **J. Solus**, None; **A. Oeser**, None; **C. Stein**, None.

Abstract Number: 2318

Elevated Pro-inflammatory Lipid Mediators Associate with Low Paraoxonase 1 Activity in Patients with Rheumatoid Arthritis and Arthritic K/BxN Mice

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

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Table 1: Circulating PON1 Activity and BLMs in RA Patients and K/BxN Mice Compared to Non-arthritic Controls

	RA-ATH	RA	HC
PON1 Activity			
Arylesterase (μmol/min/ml)	168 ± 71*	191 ± 79*	290 ± 66 #
Lactonase (units/ml)	6.5 ± 3.5 *	8.8 ± 3.0 #	10.7 ± 2.7 #
Paraoxonase (nmol/min/ml)	71 ± 39	131 ± 89 * #	74 ± 42
BLMs			
TXB2	6.5 ± 9.6	7.8 ± 8.8	4.1 ± 4.4
13 HODE	47.4 ± 104.9 *	11.6 ± 7.9 *	4.8 ± 2.4 #
9 HODE	56.9 ± 135.0 *	11.2 ± 10.0*	3.9 ± 2.3 #
17S-HDHA	15.4 ± 20.7	1.47 ± 0.76	0.96 ± 0.45
15 HETE	10.1 ± 27.8	1.87 ± 1.93 *	0.60 ± 0.45
14 S-HDHA	11.2 ± 15.9	13.4 ± 11.5	7.3 ± 9.4
11 HETE	10.65± 29.04	1.43 ± 1.63 *	0.32 ± 0.34
12 HETE	56.3 ± 103.1	55.8 ± 89.7	25.5 ± 23.2
5 HETE	113.3 ± 270.4	30.0 ± 60.4	4.0 ± 12.1
5-oxoETE	6.4 ±13.0	1.3 ± 2.3	0.24 ± 0.49
		K/BxN	**Ag7/KRN**
PON1 Activity			
Arylesterase (μmol/min/ml)		173 ± 56 *	242 ± 86
Lactonase (units/ml)		13.7 ± 5.3	15.0 ± 5.9
Paraoxonase (nmol/min/ml)		42 ± 16 *	63 ± 25
BLMs			
TXB2		4.7 ± 2.8 *	2.8 ± 1.6
13 HODE		16.1 ± 13.8 *	10.2 ± 6.8
9 HODE		7.6 ± 9.4	3.6 ± 2.9
17S-HDHA		131.4 ± 196.3*	7.9 ± 9.5
15 HETE		5.6 ± 7.4 *	1.4 ± 0.8
14 S-HDHA		79.0 ± 75.1*	25.8 ± 25.6
11 HETE		37.3 ± 21.3 *	14.5 ± 12.1
12 HETE		2.88 ± 3.93 *	0.67 ± 0.47
5 HETE		13.4 ± 25.5 *	1.8 ± 0.8
5-oxoETE		1.18 ± 2.22 *	0.22 ± 0.14

Table 2: Correlation Coefficients of PON1 Activity with BLMs

	Arylesterase	Lactonase	Paraoxonase
GROUP A: RA-ATH, RA, HC			
TXB2	**-0.50 ***	**-0.40 ***	0.04
13 HODE	**-0.36 ***	**-0.29 #**	0.02
9 HODE	**-0.39 ***	**-0.31 ***	-0.008
17S-HDHA	-0.13	-0.25	-0.21
15 HETE	**-0.37 ***	**-0.32 ***	0.11
14 S-HDHA	-0.10	-0.13	0.18
11 HETE	**-0.37 ***	**-0.38 ***	0.13
12 HETE	-0.17	-0.13	0.08
5 HETE	-0.21	**-0.31 ***	-0.02
5-oxoETE	0.03	-0.03	0.12
GROUP B: K/BxN, KRN, Ag7			
TXB2	**-0.30 ***	0.01	-0.05
13 HODE	**-0.22 #**	-0.18	-0.12
9 HODE	**-0.24 #**	-0.11	-0.13
17S-HDHA	-0.26	**-0.50 ***	**-0.46 ***
15 HETE	**-0.32 ***	-0.10	-0.18
14 S-HDHA	**-0.38 ***	**-0.30 ***	**-0.35 ***
11 HETE	**-0.48 ***	-0.17	-0.24
12 HETE	**-0.41 ***	-0.11	-0.23
5 HETE	-0.12	-0.12	-0.15
5-oxoETE	-0.13	0.04	-0.15

Background/Purpose: Paraoxonase 1 (PON1) is a high density lipoprotein (HDL)-associated enzyme, which promotes the anti-oxidant and anti-inflammatory properties of HDL. We previously associated low PON1 activity with increased atherosclerotic risk in patients with rheumatoid arthritis (RA). The current work investigates the relationship of PON1 activity to a lipidomics panel of pro-inflammatory bioactive lipid mediators (BLM) in patients with RA and arthritic K/BxN mice.

Methods: Group A included 16 RA patients with carotid atherosclerosis (RA-ATH), 16 RA patients without carotid ATH (RA), and 16 healthy controls (HC). Group B included 29 arthritic K/BxN mice, (9 weeks (n=10), 14 weeks (n=12), 21 weeks (n=7)), and 21 non-arthritic control mice, (14 weeks, KRN (n=10), Ag7 (n= 11)). Circulating PON1 activity was measured using 3 different substrates: phenylacetate (arylesterase assay), dihydrocoumarin (lactonase assay), and paraoxon (paraoxonase assay). Liquid chromatography–electrospray ionization, tandem mass spectroscopy was performed for a panel of 10 circulating BLM including TXB2, 13 HODE, 9 HODE, 17S-HDHA, 15 HETE, 14 S-HDHA, 11 HETE, 12 HETE, 5 HETE, and 5-oxoETE.

Results: PON1 activity was lower in patients with RA compared to HC and was significantly lower in the RA-ATH group compared to the RA group by both paraoxonase and lactonase assays. Similarly, PON1 activity was lower in arthritic K/BxN mice compared to KRN/Ag7 non-arthritic controls. Multiple BLMs were elevated in RA patients and K/BxN mice compared to controls, with trends for highest levels in the RA-ATH group compared to RA and HC groups (Table 1). Lower PON1 activity by arylesterase and lactonase assays correlated with higher levels of several BLMs in both humans and mice (Table 2).

Conclusion: Low circulating activity of the HDL-associated enzyme PON1 associates with higher pro-inflammatory BLMs in both RA patients and arthritic K/BxN mice. This work suggests a potential mechanism for increase atherosclerotic risk in patients with active RA via suppression of PON1 activity and elevation in pro-inflammatory lipid mediators. Further work is warranted to determine if PON1 represents a potential "dual" therapeutic target in patients with RA.

Lipidomics abstract Table 1 6-3-19.3

Values are mean ± SD. Units are ng/ml for all BLMs. *p<0.05 compared to HC or Ag7/KRN. # p<0.05 compared to RA-ATH.

Lipidomics Abstract Table 2 6-3-19.3

*p<0.05, # p ≤ 0.1 for Spearman correlation coefficient.

Disclosure: C. Charles-Schoeman, Abbvie, 2, AbbVie, 2, Amgen, 5, BMS, 2, Bristol Myers Squibb, 2, Gilead, 5, Octapharma, 2, 5, Pfizer, 2, 5, Regeneron, 5, Regeneron/Sanofi, 5, Sanofi, 5; **J. Wang**, None; **A. Shahbazian**, None; **J. Papesh**, None; **S. Reddy**, None.

Abstract Number: 2319

Are Vitamin D Metabolite Levels at Time of Diagnosis Associated with Long-term Severe Cardiovascular Events in Early Diagnosed Rheumatoid Arthritis Patients, Aggressively Treated During 10 Year Follow Up? Post-hoc Analyses of Observational Data from the CIMESTRA Cohort

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SESSION INFORMATION
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Background/Purpose: Cardiovascular disease is highly prevalent in Rheumatoid Arthritis (RA) and in non-RA subjects with low vitamin D levels. The aim of the present study was to evaluate the long-term risk of serious cardiovascular events (SCVE) RA patients having low vitamin D at time of diagnosis, compared to patients with normal vitamin D levels at RA diagnosis.

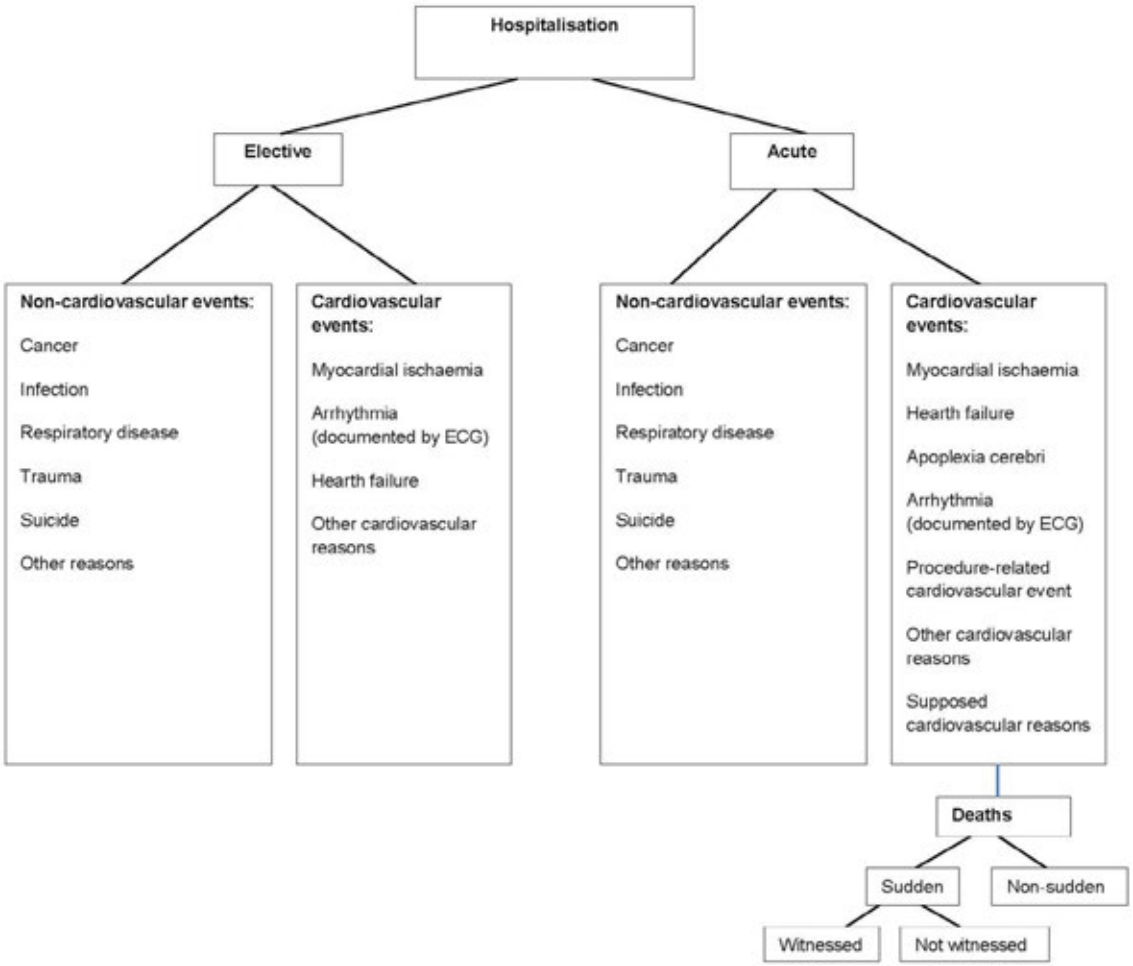

Figure 1 - SCVE adjudication CIMESTRA CVD
Figure 1 - Adjudication-strategy for SCVEs

Methods: The study is a longitudinal observational study with retrospective evaluation of outcomes using patient record adjudication, based on post-hoc evaluation of an Investigator-Initiated, Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study: The CIMESTRA Study (NCT00209859). Patients were recruited at 4 Danish University Clinics from October 1999 to October 2002**:** 160 early diagnosed, DMARD- and steroid RA-patients, fulfilling ACR 1987 criteria for RA were included in the original CIMESTRA study (NCT00209859). Eligibility criteria excluded most co-morbidities. The original CIMESTRA study treated all patients with methotrexate and intra-articular steroid, aiming at remission. Patients were further randomized to ciclosporine or placebo. Self-reported vitamin D intake was evaluated, and vitamin D supplemented according to national Danish Guidelines.

One-hundred-fifty-eight patients had vitamin D metabolites measured at time of diagnosis, prior to initiation of treatment and eventual vitamin D supplementation, and were included in the current study: Patients were allocated according to serum D_{total} (the sum of $25OHD_2$ and $25OHD_3$) at time of diagnosis, comparing "low" = $D_{total} < 50$ nmol/l to "normal" = $D_{total} \geq 50$ nmol/l. One-hundred-forty-two patients were alive without missing data for journal-adjudications after 10 years of follow-up. Primary outcome was a composite of fatal and non-fatal SCVEs. Secondary outcomes

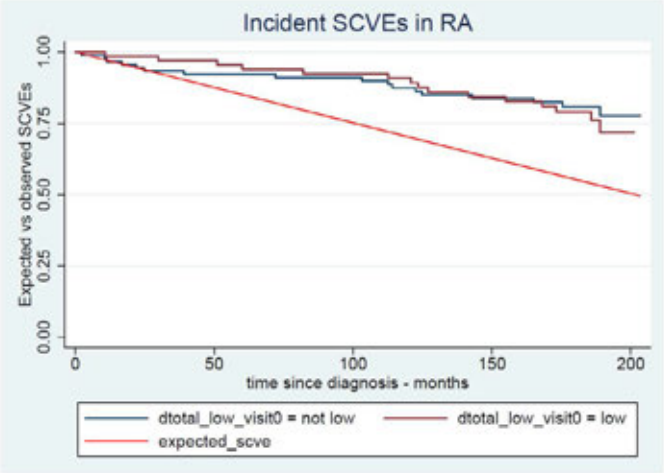

Figure 2 - Kaplan-Meier-plot - observed vs expected SCVE
Figure 2: Observed vs expected 10 years cardiovascular morbidity

	Low vitamin D_{total} (< 50 nmol/l) N=67	Normal D_{total} (≥50 nmol/l) N=91	Contrast between groups For all comparisons, the group having normal D_{total} (i.e. defined as "not low") was the reference.
Primary outcome: Any CSVE, no. (%)	9 (13.4 %)	13 (14.3 %)	Crude analysis[a]: OR=0.91, 95% CI (0.36; 2.28), p = 0.84 Logistic regression[b]: OR=0.94, 95% CI (0.37; 2.39), p=0.89 Adjusted logistic regression[c]: OR=0.76, 95% CI (0.25; 2.35) p=0.64 Adjusted logistic regression[d]: OR=0.86, 95% CI (0.23; 3.17), p=0.82
Cardiovascular death, no. (%)	1 (1.5 %%)	1 (1.1%)	Crude analysis[a]: OR=1.34, 95% CI (0.08; 21.8), p = 0.84. Logistic regression[b]: OR=1.04, 95% CI (0.06; 17.75), p=0.98* Adjusted logistic regression[c]:**
All-cause mortality, no. (%)	5 (7.5%)	7 (7.7 %)	Crude analysis[a]: OR=0.95, 95% CI (0.29; 3.13), p=0.93 Logistic regression[b]: OR=0.86, 95% CI (0.25; 2.93), p=0.81.*** Adjusted logistic regression[c]: OR=0.61, 95% CI (0.11; 3.34), p=0.57**** Adjusted logistic regression[d]:OR=0.41, 95%CI (0.05; 3.23), p=0.4

SCVE: Serious Cardiovascular Event, defined as hospitalisation or death owing to any cardiovascular event.
[a] Crude logistic regression; D_{total} as independent variable, no other covariates.
[b] Simple logistic regression, further containing Trial Center and ciclosporine group as fixed effects.
[c] Multiple logistic regression, further adjusted for age, sex, smoking, BMI-status and ACPA-status.
[d] Multiple regression analyses, further adjusted for baseline variables statistically associated with vitamin D_{total} levels at baseline.
Adjusting for Centre and ciclosporine in evaluation of SCVE death, two centers were omitted, leaving 88 observations for analyses.
** Adjusting for sex, smoking, adipositas and ACPA-positivity at time of diagnosis omitted women, non-smokers, ACPA-positive and patients not adipose, leaving no observations for comparison, and no further adjustments were performed.
*** Adjusting for Centre end ciclosporine, omitted patients from one centre, where no Deaths occurred, leaving 125 observations for the analysis
**** Further adjusting for age, gender, smoking, BMI and ACPA-status, omitted the 45 remaining non-smokes, as no deaths ccurred among them, and the final model comprised of 81 subjects.

Table 1 - Results of logistic regression
Table 1: Evaluation of outcomes after 10 years depending on baseline Dtotal level dichotomised at 50 nmol/l, in RA patients followed in the CIMESTRA trial (data as observed based on the ITT population).

were cardiovascular mortality and all-cause mortality. All events were evaluated through patient-record adjudication, using a validated adjudication process (See figure 1).

Odds for SCVE were evaluated using multiple logistic regression, adjusted for original trial group-allocation (ciclosporine or placebo), Trial Center, and the pre-specified, potential confounding variables sex, age at time of diagnosis, smoking, adipositas and ACPA-status, whereas the fully adjusted model further included weight and $1,25(OH)_2D$, both being statistical significant associated with D_{total}-status at time of diagnosis.

Results: Overall 10-year SCVE incidence was lower than expected (13.9% in patients with low D_{total}, 14.3% in patients with normal D_{total}) (See figure 2). There were no difference in SCVE between D_{total} groups in crude analysis OR=0.91, 95%CI (0.4; 2.3), or in fully adjusted model: OR=0.86, 95%CI (0.2; 3.2) (See table 1) Survival analyses showed no difference in SCVE according to baseline D_{total}, HR=1.15, 95 % CI (0.6; 2.3).

Conclusion: The 10-year SCVE incidence of 13.9% was unexpectedly low. Low vitamin D status at time of RA diagnosis was not associated with long-term SCVE in early diagnosed, aggressively controlled and DMARD treated RA patients.

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Abstract Number: 2320

Knowledge of Cardiovascular Disease Risk Among Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

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Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) have a significantly higher risk of cardiovascular disease (CVD) than general population. The Heart Disease Fact Questionnaire (HDFQ-RA 1 and 2) is a self-reported questionnaire that assesses the knowledge of general CVD risk and more specifically the related with RA and its treatment. The aim of this study was to validate the Spanish version of this questionnaire; and to assess the level of knowledge regarding CVD risk in a cohort of patients with RA.

Methods: Multicenter, observational, cross-sectional study. Translation and cross-cultural adaptation of the HDFQ-RA was performed according to the Beaton et al. guidelines. Consecutive patients ≥ 18 years old with RA (ACR/EULAR 2010) were included. Socio-demographic data, RA characteristics and traditional cardiovascular risk factors were recorded. All patients answered the questionnaire; a subgroup of them attended previously an informative meeting about CVD. A subgroup of patients completed the questionnaire again 10-15 days later. Statistical analysis: Demographic and disease characteristics were described. Internal consistency was assessed with Cronbach's alpha coefficient and inter-item correlation. Correlation of disease characteristics and questionnaire scores was evaluated with Student's T test, Chi^2 test and Fisher's exact test or Spearman correlation. Test-retest reliability was determined.

Results: A total of 787 patients from 25 centers across the country were included: 87.7% women, mean age 45 years (±12.7). Cronbach's alpha test was 0.83 and 0.93 for HDFQ-RA1 and HDFQ-RA2, respectively. There were no redundant questions. Test-retest reliability were 0.48 for HDFQ-RA1 and 0.42 for HDFQ-RA2. Median proportion for correct answers were 53.8% in HDFQ-RA1 and 62.7% in HDFQ-RA2; for incorrect answers 13.8% in HDFQ-RA1 and 0% in HDFQ-RA2; and for unknown responses 21.1% in HDFQ-RA1 and 22.1% in HDFQ-RA2. Sixty-six percent of patients did not know that RA increases the CVD risk, and a high percentage were unaware that NSAIDs and glucocorticoids magnify this risk even more. A higher level of instruction was associated with a higher number of correct answers ($p < 0.0001$). The subgroup of patients who attended the informative meeting about CVD had higher scores in both questionnaires ($p < 0.001$ for HDFQ-RA1 and $p = 0.001$ for HDFQ-RA2). Patients with a history of CVD had

higher scores (p = 0.01195 for HDFQ-R1 and p = 0.0114 for HDFQ-RA2) as well as those suffering from hypertension and those who were physically active.

Conclusion: HDFQ-RA1 and HDFQ-RA2 showed good internal consistency. Patients with a history of CVD and those who received previous instruction on CVD had higher scores, proving the construct validity of the questionnaire. This study demonstrates that a high percentage of RA patients neither know the higher risk of CVD caused by the disease nor the negative impact of NSAIDs and glucocorticoids on this risk. We consider that the use of these types of questionnaires would allow the implementation of targeted CVD prevention strategies as well as the ongoing assessment of their effectiveness over time.

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Abstract Number: 2321

Subclinical Myocardial Dysfunction Assessed by Strain Imaging in Patients with Rheumatoid Arthritis and Spondyloarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Although cardiovascular (CV) risk and mortality are increased in rheumatoid arthritis (RA) and spondyloarthritis (SpA), mechanisms resulting in CV risk excess and stratification are still unclear. Myocardial deformation imaging (expressed as myocardial strain) allows early detection of CV disease (CVD). The objective of the study was to assess subclinical myocardial dysfunction by 2D speckle tracking imaging in patients without known CVD and to compare to controls.

Methods: Two-dimensional and Doppler echocardiography with strain analysis was performed before initiating first biologic DMARD in patients with RA and SpA, and without CVD and CV risk factors (arterial hypertension, diabetes and known atherosclerosis). Myocardial strain measured by 2D speckle tracking echocardiography provides reliable

information about regional and global ventricular function. The strain is described as the deformation of an object normalized to its original shape and size. The strain can be analyzed in the longitudinal, circumferential and radial displacements of the left ventricle. Global Longitudinal Strain (GLS), used in this study, is negative due to left ventricular shortening in the course of contraction. The more the contraction is significant, the more the strain is negative. Abnormal GLS was defined by a value > -18.5 %. RA and SpA patients were compared to age- and sex-matched controls with normal echocardiography and no CVD or risk factors. Associations between GLS and disease characteristics were analyzed.

Results: 22 RA patients (mean age 55.9 ± 10.1 years, 77 % women, median disease duration 5.8 years, mean DAS28 4.4 ± 1.3) and 25 axial SpA (mean age 43.3 ± 0.3, 44 % men, mean disease duration 9 years, mean BASDAI 57 ± 12) were analyzed. At baseline, RA patients had worse GLS compared to controls (-20.1 ± 2.2 vs -21.5 ± 1.4, p=0.01). Moreover, GLS was not in the normal range in 5 RA (22.8%), while none of the controls had altered GLS (p=0.02). In SpA patients, mean GLS was not different from controls (-21.7 ± 0.68 vs -20.8 ± 1.7, p=0.60). However, 8 SpA patients (32 %) and 4 controls (16 %) had an abnormal GLS (p=0.01). Among these 8 patients, treatment with TNF inhibitor during 1 year improved GLS (-17.8 ± 1 vs -21.7 ± 1.9 p=0.002) and normalized the value in 6 of the 8 patients. For RA and SpA, no significant associations were found between baseline GLS and disease duration, activity (DAS28, BASDAI, ASDAS-CRP), disability (BASFI, HAQ), systemic inflammation (CRP). Patients with SpA and radiographic sacroiliitis (-19.9 ± 1 vs -22.6 ± 0.68 p=0.05) or HLA B27 positivity (-20.8 ± 0.67 vs -24.5 ± 1.34 p=0.05) had worse GLS.

Conclusion: This study confirms a subclinical myocardial dysfunction in active RA and SpA patients without known CVD and CV risk factors compared to controls. In SpA patients, strain abnormalities seem to be improved with anti-TNF treatment.

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Abstract Number: 2322

Toward Cardiovascular Risk Stratification in Rheumatoid Arthritis: Use of Regression Tree Analyses to Evaluate Impact of Serum Biomarkers and Cardiovascular Risk Factors on Carotid Intima Media Thickness

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SESSION INFORMATION

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Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

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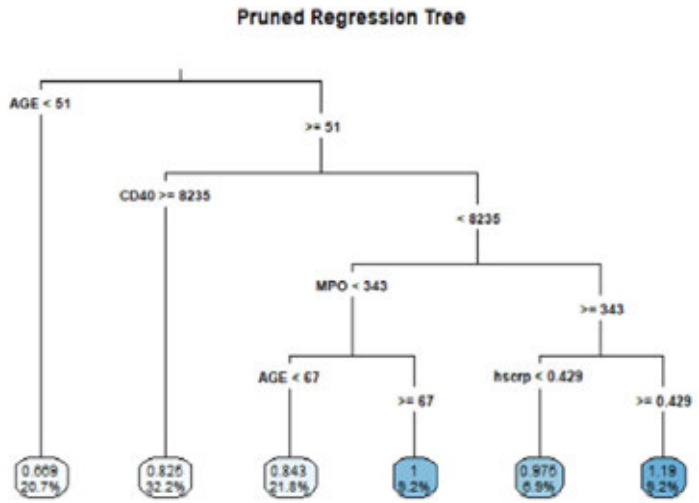
Session Time: 9:00AM–11:00AM

Background/Purpose: Both traditional cardiovascular (CV) risk factors and disease-related factors contribute to the increased risk of cardiovascular disease (CVD) in rheumatoid arthritis (RA). Mechanisms of atherosclerosis include (1) Endothelial dysfunction/activation mediated by intercellular adhesion molecules (e.g., ICAM-1, VCAM-1, E-selectin), nitrite (NO), and oxidative stress (e.g., via MPO activity); (2) Inflammation mediated by cytokines (e.g., IL-6); (3) Plaque

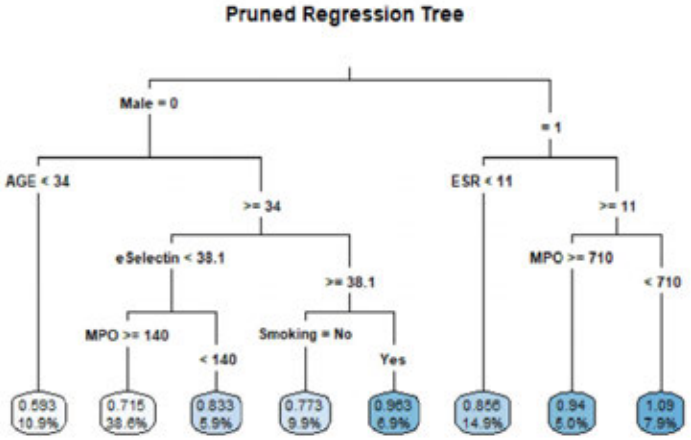
Figure 1 – Pruned Regression Tree for the RA Group



stability mediated by CD40-CD40L interactions; and (4) Proteolysis/Plaque rupture mediated by proteolytic enzymes (e.g. MMP-9). Inflammatory and immune biomarkers important in RA pathogenesis include erythrocyte sedimentation rate (ESR), C-reactive protein (hsCRP), and IL-17. This study seeks to develop easy to visualize decision rules for the differential effects of these serum biomarkers and CV risk factors on carotid intima-media thickness (cIMT) in RA vs. control subjects.

Methods: Carotid ultrasounds measured maximum cIMT and plaque presence, and serum biomarkers (ICAM-1, VCAM-1, E-selectin, NO, MPO, IL-6, CD40L, MMP-9, ESR, hsCRP, IL-17) were measured on 87 RA cases and 101 controls. All RA subjects met 2010 ACR classification criteria. CV risk factors (age, gender, race, obesity, hyperten-

Figure 2 – Pruned Regression Tree for the Control Group



sion (HTN), diabetes (DM), hyperlipidemia (HL), smoking (ever), personal and family history of CVD) were collected on all subjects. Regression tree models were applied with cIMT as the outcome measure, and all the serum biomarkers and significant (based on an unadjusted linear model) CV risk factors (age, gender, DM, smoking, personal history of CVD) as potential splits in the tree model. Tree models are built by identifying the best split across all values of all variables and partitioning the data into the two resulting subgroups (or nodes); within each subgroup the process is repeated until the nodes are too small (n< 10) to split further. The trees were also pruned by eliminating nodes (beginning with the lowest branches of the tree) that did not contribute significantly to model fit.

Results: Demographics were similar between RA and controls except for age (mean 59.6+/-12.0 in RA vs. 54.0+/-14.7 years in controls; p=0.005), as were CVD risk factors except for hypertension (46.4% in RA vs. 23.3% in controls). The tree models (Figures 1-2) display the mean cIMT (with the percent in that group) for each terminal node (e.g. final subgroups). For RA cases, Figure 1 shows that RA patients age 51 or older with CD40 < 8235 had the highest mean cIMT, especially for MPO ≥ 343 or for age 67 or older with MPO < 343 (0.98-1.19). In controls, males with ESR ≥ 11 and female smokers age 34 or older with eSelectin ≥ 38.1 had the highest mean cIMT (0.86-1.09).

Conclusion: This study reveals that RA and control subjects have differential contributing effects of various serum inflammatory and vascular biomarkers and traditional CV risk factors on subclinical atherosclerosis risk, as measured by cIMT. Results may inform future studies to develop additional CVD risk stratification algorithms in RA patients.

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Abstract Number: 2323

The Association Between Disease Activity with Coronary Microvascular Dysfunction in Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Inflammation accounts for much of the excess cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA). We hypothesize that increased systemic inflammation leads to vascular endothelial dysfunction and coronary microvascular dysfunction (CMD). CMD in the general population is associated with increased risk for cardiac mortality, however, there are limited data on CMD in RA. The objective of this study was to study the associations between RA clinical factors with CMD.

Methods: We used interim baseline data from the first 53 subjects enrolled in the Lipids, Inflammation, and CV Risk (LiiRA, ClinicalTrials.gov: NCT02714881) study. Briefly, the LiiRA study enrolls RA patients, age >35, about to

Table. Baseline clinical characteristics of LiiRA subjects

Clinical characteristics	All, n= 53
Age, years mean (SD)	54.9 (11.1)
Female, n (%)	83.0
RA disease duration, years mean (SD)	9.1 (9)
Seropositive, n (%)	70
CDAI*, mean (SD)	22.2 (13.6)
Low (%)	22.6
Moderate (%)	34.0
High (%)	43.4
ESR mm/h, mean (SD)	29.3 (44)
Baseline RA treatment (%)	
Methotrexate	67.9
Sulfasalazine	1.9
Hydroxychloroquine	22.6
Leflunomide	13.2
No DMARD	17.0
Prednisone (%)	37.7
Prednisone, mean dose (SD)	8.7 (6.8)
Comorbidities (%)	
Hypertension	26.4
Coronary artery disease	0
Diabetes mellitus	0
BMI, mean (SD)	29.4 (6.7)
Family history of CVD, n (%)	60.4
Ever smoker (%)	43.4
Abnormal stress test, n (%)	3 (5.6)

initiate tumor necrosis factor inhibitor (TNFi) therapy. Exclusion criteria include statin use, prednisone dose or equivalent >10mg, or biologic DMARD use in the past 6 months. Demographics, RA clinical factors, and clinical disease activity index (CDAI) were collected. All subjects underwent a stress myocardial perfusion PET scan (cardiac PET), a routine clinical stress test at our institution. The cardiac PET quantifies myocardial blood flow (MBF) at rest and during maximal hyperemia in response to a stress agent, regadenoson. Coronary flow reserve (CFR) is a ratio of MBF during maximal hyperemia over that at rest. A lower CFR in the absence of obstructive coronary artery disease (CAD) is indicative of CMD. We tested correlations between RA clinical factors with CFR. Our primary analysis tested the association between CDAI and CFR adjusted by age, gender, and smoking status.

Results: The mean age of subjects in LiiRA was 55 years, 83% were female, 70% seropositive, with a mean RA disease duration of 9.1 years (Table). No patients had history of CAD or DM, and 26% had a history of hypertension. Three patients (5.3%) had mildly abnormal perfusion scans at baseline. Higher CDAI was correlated with a lower CFR, r=-0.37, p=0.007 (Figure); this association remained significant after adjusting for age, gender, and smoking status (p=0.004). Other clinical factors associated with a significantly lower CFR were older age, r=-2.8, p=0.04, and a higher tender joint count, r=-0.34, p=0.01. We observed no correlation between DMARD or prednisone use at baseline with CFR.

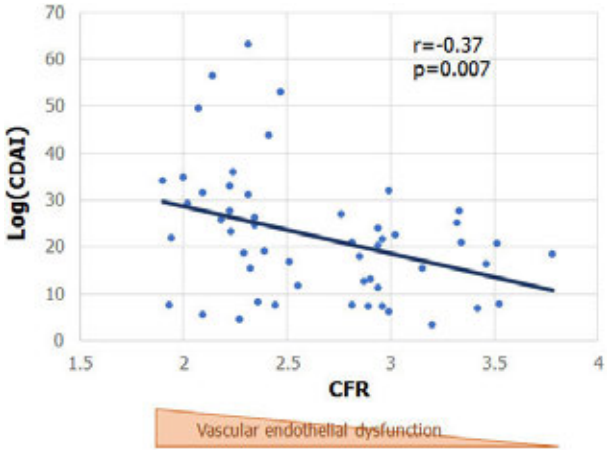

Figure. Correlation between RA disease activity as measured by CDAI with coronary flow reserve (CFR); a lower CFR indicates higher degree of vascular endothelial dysfunction and coronary microvascular disease (CMD).

Conclusion: Among RA patients with no history of overt CAD and low prevalence of CV risk factors, higher RA disease activity was associated with a higher degree of CMD. These findings support a mechanistic pathway whereby inflammation may lead to increased CV risk through microvascular dysfunction. Studies are underway to determine whether CMD is modifiable with RA treatments.

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Abstract Number: 2324

Metabolic Syndrome and Early Arthritis: Frequency, Association with Antibodies Profile and Disease Activity

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The Metabolic Syndrome (MetS) is an independent factor of cardiovascular morbidity and mortality and most studies show that its prevalence is higher in established Rheumatoid Arthritis (RA) than in the general population, which would be associated with systemic inflammatory activity. Few studies have evaluated this association in patients with Early Arthritis (EA) with different results. Objective: To study the frequency of MetS in patients with EA and its association with disease activity and antibodies profile.

Methods: We studied all the patients with diagnosis of EA who consecutively attended to Rheumatology Unit at Cordoba Hospital from August 2016 to February of 2018. EA was diagnosed by the presence of inflammation in 3 or more joints of less than 12 months duration. A non-RA population was a control group, matched by age and gender.

Table 1. Demographic and clinical characteristics of the 124 cases and controls

	Early Arthritis n=62	Controls n=62	P
Female sex	51 (82.3)	51 (82.3)	1.00
Age (years)	41.4 (12.2)	40.1 (9.7)	0.504
Weight (kg)	73.79 (16.64)	71.48 (15.15)	0.421
Height (meters)	1.62 (0.08)	1.65 (0.08)	**0.036**
Body Mass Index (kg/m²)	28.29 (6.05)	26.34 (4.95)	0.052
Waist circumference (cm)	89.73 (15.92)	87.26 (15.04)	0.377
Systolic blood pressure (mmHg)	121 (19.48)	111.8 (11.95)	**0.009**
Diastolic blood pressure (mmHg)	74.8 (12.03)	69.5 (10.6)	**0.011**
Total cholesterol (mg/dL)	188.4 (50.4)	187.8 (29.2)	0.678*
Triglycerides (mg/dL)	133.3 (80.7)	105.1 (78.9)	0.051

Table 2. Diagnosis of Metabolic Syndrome of the 124 cases and controls according to the 3 definitions used.

	Early Arthritis	Controls	p
ATP III	20 (32.3)	10 (16.1)	**0.036**
WHO	20 (32.3)	10 (16.1)	**0.036**
IDF	21 (33.9)	9 (14.5)	**0.012**

Table 3. Comparison of the 62 patients with EA according to the presence of metabolic syndrome using the IDF and/or ATP and/or WHO criteria

	EA/MetS+ n=25	EA/MetS- n=37	*p*
Age (years)	46.7 (10.2)	37.9 (12.2)	**0.004**
RF (IU/mL)	273.6 (558.3)	155.8 (256.6)	0.362*
RF >=14 IU/mL	16 (64.0)	20 (54.1)	0.436
ACPA (U/mL)	163.1 (192.5)	145.7 (217.6)	0.748
ACPA >=30 U/mL	15 (60.0)	22 (59.5)	0.966
ESR (mm/hour)	43.1 (29.2)	48.8 (35.5)	0.511
CRP (mg/dL)	1.1 (2.6)/24	1.4 (2.2)/36	0.609
DAS28-ESR	5.0 (1.5)	5.3 (1.0)	0.070*

Clinical and laboratory data were collected. The activity of the disease was evaluated by DAS28-ESR. The presence of MetS was evaluated according to 3 different international classification: World Health Organization 1998-1999 (WHO), Adult Treatment Panel III 2004 (ATPIII) e International Diabetes Federation 2005 (IDF). EA cases were analysed in to two groups according to MetS or not diagnosis (MetS+/MetS-). A chi-squared test and T-test or Mann–Whitney U test were applied for comparison of categorical and continuous variables as appropriate. $P < 0.05$ was considered statistically significant.

Results: Sixty-two EA patients were included. Demographic and clinical data are shown in table 1. Diagnosis criteria of MetS was more frequent in EA patients than in the control group according to the 3 definitions used (Table 2). In addition, EA patients with and without presence of MetS did not show statistically significant differences in ESR neither in CRP level. There was also no significant difference in level of RF and ACCP antibodies. On the other hand, there was no difference in DAS 28-ESR between EA patients with and without MetS. These results are shown in Table 3.

Conclusion: MetS seems to be more frequent in EA and its presence is not associated with disease activity and the presence of RF or ACCP antibodies. MetS is a known risk factor for cardiovascular disease, morbidity and mortality in systemic autoimmune diseases. A tight control of this condition in the early stages of disease should be recommended.

Note: all variables are expressed as mean and standard deviation (±SD) and compared using the T-test or Mann–Whitney U (*) except for females that are expressed in frequency and percentage (n (%)) and compared using the chi-squared test.

Note: all variables are expressed in frequency and percentage (n (%)) and compared using chi-squared test. ATP III: Adult Treatment Panel III. WHO: World Health Organization. IDF: International Diabetes Federation.

Note: continuous variables are expressed as mean and standard deviation and compared using the T-test or Mann–Whitney U (*). Categorical are expressed in frequency and percentage and compared using chi-squared test. MetS: Metabolic syndrome. RF: Rheumatoid Factor. ACPA: Anti-citrullinated cyclic peptide antibodies. ESR: Erythrocyte sedimentation rate. CRP: C Reactive Protein. DAS28-ESR: Disease Activity Score of 28 joints with ESR.

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Abstract Number: 2325

High Intensity Interval Training Improves Rheumatoid Arthritis Cardiorespiratory Fitness and Systemic Inflammation in Association with Alterations in Skeletal Muscle Metabolomic Profiles

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SESSION INFORMATION
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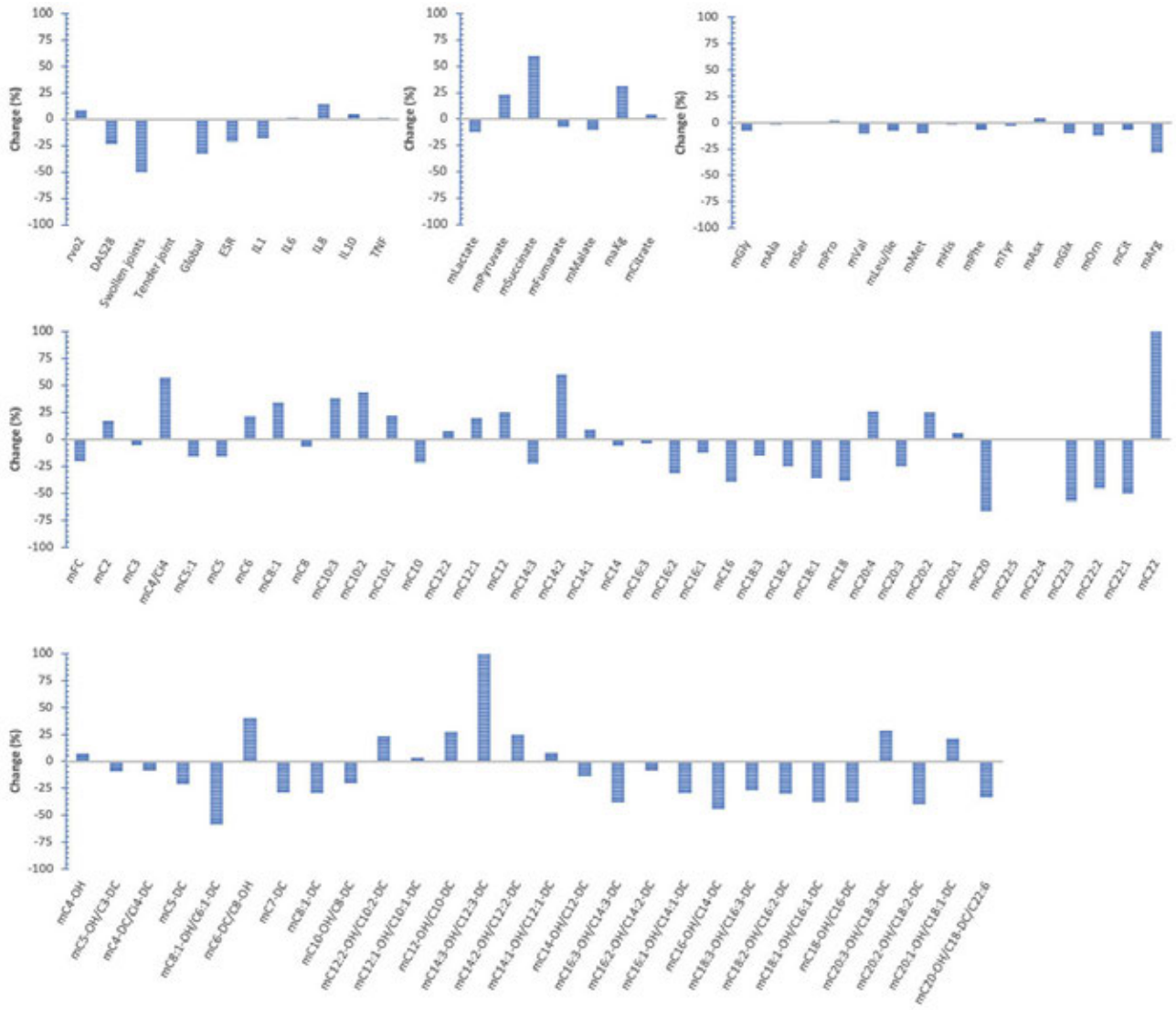

Figure 1. Change in cardiorespiratory fitness, disease activity, systemic inflammation, and skeletal muscle metabolites in RA following high intensity interval training. Bars represent median percent change from baseline for each variable for subjects with RA (n=11).
rVO_2 (relative maximal oxygen consumption), DAS28 (disease activity score-28), ESR (erythrocyte sedimentation rate), IL (interleukin), TNF (tumor necrosis factor), m (skeletal muscle), FC (free carnitine), C (acylcarnitine), OH (hydroxyl), DC (dicarboxyl)

Background/Purpose: Patients with rheumatoid arthritis (RA) are at greater risk for cardiometabolic disease and early death. It is unclear if current anti-inflammatory pharmacotherapies alone are enough to prevent RA comorbidities. In our previous work, in persons with established RA on stable medications, a high intensity interval training (HIIT) program improved both cardiorespiratory fitness and disease activity (Bartlett DB et al. Arthritis Res Ther. 2018; 20:127). To better understand the mechanisms by which exercise training improves RA inflammation and cardiometabolic risk, we evaluated relationships of HIIT-mediated changes in skeletal muscle metabolic profiles with improvements in cardiorespiratory fitness, disease activity, and systemic inflammation.

Methods: RA participants (n=11; mean age=64.0±7.5), who all satisfied 1987 ACR criteria, underwent clinical, physiologic, and biologic assessments before and after 10 weeks of supervised HIIT. Disease activity was assessed via Disease Activity Score-28 with ESR (DAS28). Cardiorespiratory fitness (relative VO_2 peak, mL/kg/min) was assessed via cardiopulmonary exercise testing. Plasma concentrations of cytokines (IL-1β, IL-6, IL-8, IL-10, and TNF-α) were quantified via immunoassay. Using *vastus lateralis*

biopsies, skeletal muscle (m) concentrations of metabolites (organic acids, amino acids, and acylcarnitines) were quantified via targeted mass spectrometry. Percent changes for clinical and metabolic intermediate data were calculated as follows: ([post-intervention variable minus pre-intervention variable]/pre-intervention variable) × 100. Correlations were evaluated with Spearman's rho.

Results: In RA participants, 10 weeks of HIIT improved peak VO_2 (median 8.2%) and DAS28 (median -23.8%). Changes in concentrations of plasma inflammatory cytokines and skeletal muscle organic acids, amino acids, and acylcarnitines are shown [Figure 1]. Among participants, improved peak VO_2 was associated with reduced muscle concentrations of leucine/isoleucine (r=-0.65, p=0.029) and phenylalanine (r=-0.61, p=0.047). Systemic inflammation improvements were inversely related to several muscle metabolic intermediates. Improved ESR, but not DAS-28, was associated with increased muscle pyruvate (r=-0.61, p=0.046). Plasma IL-8 reductions associated with increased muscle succinate (r=-0.61, p=0.047). Plasma IL-6 reductions associated with increases in muscle citrate (r=-0.65, p=0.028) and multiple muscle acylcarnitines, including mC2 (acetylcarnitine), mC12:1, mC12, mC20:1, mC6-DC/C8-OH and mC20:1-OH/C18:1-DC (r< -0.60, p< 0.05 for all).

Conclusion: In RA, HIIT-mediated improvements in fitness and inflammation were associated with muscle metabolic changes. Cardiorespiratory fitness improvement was associated with muscle amino acid reductions. RA systemic inflammation improvements were associated with greater muscle concentrations of multiple components of oxidative metabolic machinery. Thus, RA immune and metabolic function are likely improved with exercise training through systemic enhancement of protein synthesis and fat oxidation.

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Abstract Number: 2326

Prognostic Markers for Preclinical Cardiovascular Disease in Rheumatoid Arthritis and Correlation with Disease Activity

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Background/Purpose: Patients with rheumatoid arthritis (RA) have an elevated cardiovascular (CV) disease risk, explained both by an increased prevalence of traditional CV risk factors and the presence of chronic systemic inflammation that leads to (1) increased arterial stiffness, (2) thickening of the arterial wall and (3) impairs vascular function.

In this study we investigated the effect of anti-inflammatory treatment on prognostic markers for preclinical cardiovascular disease (arterial wall thickening and arterial stiffness) and the correlation of these markers with RA disease parameters.

Methods: Carotid ultrasound (using Artlab echotracking system) was used to determine far wall carotid intima media thickness (IMT) and pulse wave analysis was done with SphygmoCor tonometry to calculate carotid-femoral pulse

	n	Baseline	6 months	Mean difference (95% CI)
PWV (m/s)	39	8.0	7.3	0.7 (-0.2;1.5)
AIx (%)	45	27.4	26.6	0.8 (-6.4;7.9)
IMT (mm)	44	0.68	0.68	-0.007 (-0.03;0.02)

Table 1. Prognostic markers of atherosclerosis prior and after 6 months of anti-inflammatory therapy

wave velocity (PWV) and augmentation index (AIx). Paired t-test was used to compare PWV, AIx and IMT prior and after 6 months of therapy. Pearson correlation was calculated to investigated the correlation of PWV, AIx and IMT with (natural logarithm of) C-reactive protein (CRP), (natural logarithm of) erythrocyte sedimentation rate (ESR) and disease activity score-28 (DAS28). For correlations, data from both time points were pooled.

Results: In total 61 consecutive RA patients (50% early arthritis starting with csDMARD and 50% established RA starting with adalimumab) were asked to undergo arterial analysis just prior to start of therapy and after 6 months. PWV was performed in 45 patients at baseline and 39 at follow-up, IMT in 56 and 45 patients respectively and AIx in 51 and 44 patients respectively. Both signs of arterial stiffness (PWV and AIx) decreased after 6 months of therapy (mean difference 0.7 and 0.8 respectively; table 1), although this did not reach statistical significance. IMT remained stable during 6 months of therapy.

PWV (n=84) showed a significant correlation with ESR (0.262, $p< 0.02$) and DAS28 (0.269, $p< 0.02$). Both AIx (n=95) and IMT (n=101) showed a significant correlation with CRP (-0.223, $p< 0.05$ and 0.244, $p< 0.02$, respectively). Other correlation coefficients were not statistically significant (data not shown, $p >0.05$).

Conclusion: Arterial stiffness as measured with PWV tended to decrease after 6 months of anti-inflammatory treatment. Arterial stiffness and arterial intima media thickness correlated with serological inflammatory parameters. Altogether, these changes might suggest that effective anti-rheumatic therapy has favorable cardiovascular effects. Whether or not this ultimately leads to a significant reduction of clinical cardiovascular endpoints remains to be established in prospective studies.

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Abstract Number: 2327

Cardiovascular Disease in Rheumatoid Arthritis: Risk Factors and the Role of Auto-antibodies

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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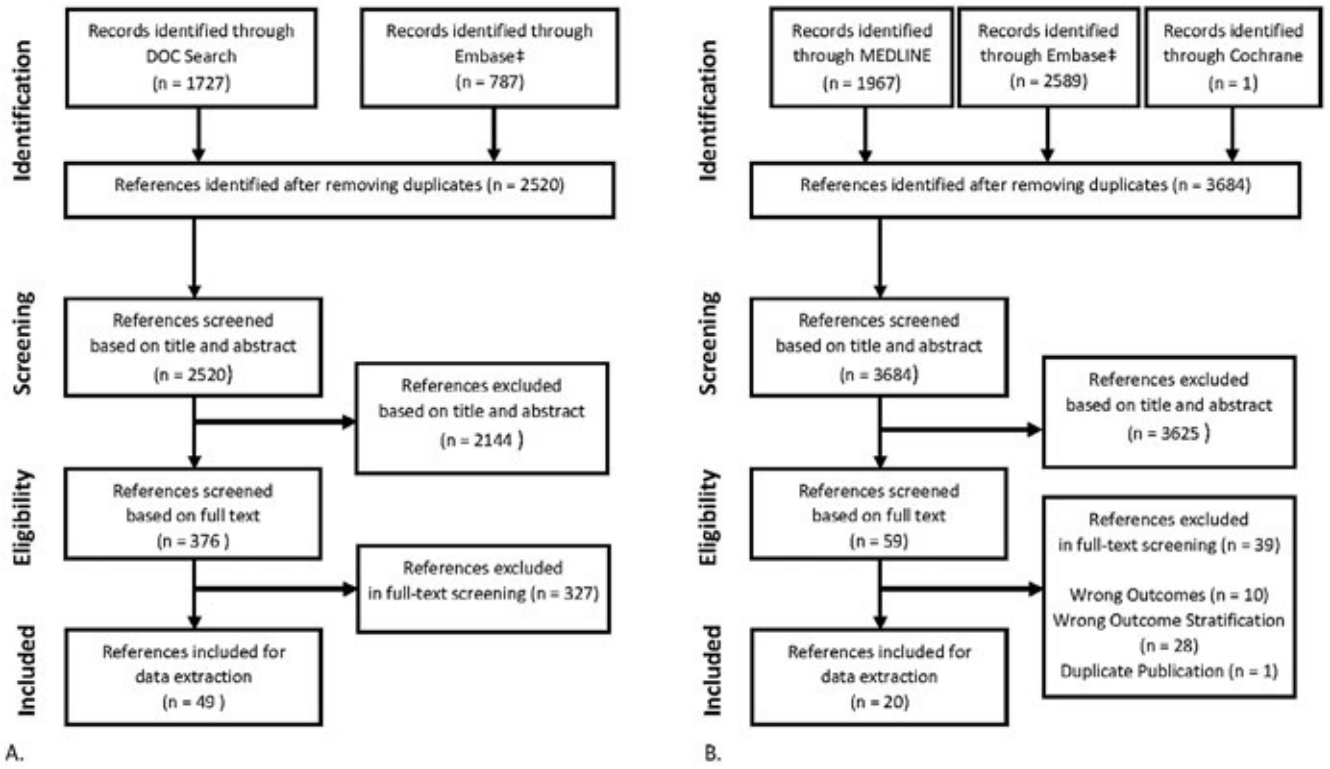

Figure: 1A PRISMA diagram for review on epidemiology and risk factors; 1B PRISMA diagram for review on auto-antibodies* ‡ For ACR and EULAR conferences, all proceedings were available through the Embase database, and were therefore included in the main Embase search results. * No additional record was idendified from the US and European clinical trials registries.

Background/Purpose: Shorter life expectancy in RA patients has in part been associated with an increased incidence of cardiovascular disease (CVD). This literature review summarizes the current understanding of CVD in the RA population, focusing on the role of risk factors and auto-antibodies.

Methods: A systematic literature review was conducted by searching MEDLINE, Embase, and Cochrane CENTRAL (inception-Jan 15, 2019) supplemented by a search in ACR, EULAR, and US and European clinical trial registries (2017 to 2019). Eligible studies included literature reviews, meta-analyses, clinical trials, and observational studies that investigated auto-antibody status related to CVD in the context of RA. This was supplemented by a comprehensive search using Doctor Evidence LLC's proprietary search platform (DOC Search) containing MEDLINE, clinicaltrials.gov, WHO-ICTRP, EPAR, Daily Med, and RSS feeds, targeting literature on epidemiology and risk factors associated with development of CVD in RA.

Results: The results of search and screening yielded 69 publications: 49 on CVD epidemiology and risk factors in RA, and 20 on cardiovascular outcomes stratified by auto-antibody status (Figure 1).

Eligible epidemiological studies reported higher risk of developing CVD and an increased burden of CVD comorbidities in RA patients compared to the general population, with a 48% increased CVD incidence, a 60% increased risk of cardiovascular death, and reduced life expectancy of 3 to 10 years or more in RA vs. non-RA. The reported prevalence of CVD in RA patients varied across countries. Eastern European populations report-

Traditional Risk Factors for CVD in RA	Novel Risk Factors for CVD in RA
Hypertension	Inflammation
Insulin resistance and diabetes	Atherosclerosis
Hyperhomocysteinemia	Neutrophil extracellular traps
Body weight	Phospholipids
RA treatment history (Non-steroidal anti-inflammatory drugs and corticosteroids)	Anti-citrullinated peptide antibodies and rheumatoid factors
Hyperlipdemia	Anti-apolipoprotein A1 antibodies
	Psychological risk factors including depression and anxiety

Table 1: Traditional and novel risk factors for CVD in RA

ed more than twice the prevalence of CVD in RA vs. US populations (21.3% vs. 8.5%); while India had a lower prevalence (5.6%). The risk of developing CVD was also significantly different between sexes, with men having a higher 10-year cumulative incidence of CVD compared to women (20.9% vs. 11.1%). However, the risk of CVD in women with RA increased following menopause. Specifically, women that underwent early menopause (< 45 yrs) were shown to be at significantly higher risk of CVD events compared to women who did not (HR 1.56, 95% CI 1.08-2.26).

The risk factors for CVD in RA can be separated into the traditional CVD risk factors as observed in the general population, and RA-specific risk factors (Table 1). Several studies noted that the risk factors for CVD often predate the onset of RA, suggesting that subclinical inflammatory processes facilitating both RA and atherosclerosis may be developing before patients become RA symptomatic.

Four types of auto-antibodies were identified showing association with cardiovascular events –RF, anti-CCP, aPL, and anti-lipoprotein auto-antibodies – with risk profiles varying across different types of auto-antibodies (Table 2).

Conclusion: Review of the current published literature suggests that a higher risk of CVD in RA populations is in part the result of shared inflammatory processes between the two, and that the presence of auto-antibodies could potentially be associated with increased risk of specific cardiovascular outcomes.

Outcome Categories	Hazard Ratio (95% CI), Incidence Rate, or Proportion of Patients with Cardiovascular Events/Diseases During Study Follow-up Auto-antibody Positive vs. Negative Status			
	RF	Anti-CCP	Anti-phospholipid	Anti-lipoprotein
Total Cardiovascular Events or Cardiovascular Diseases	2/5 studies with significance #1: 3.90 (95% CI: 1.99-7.65)* #2: 3.26 (95% CI: 1.86-5.71)*‡ #3: 1.11 (95% CI: 0.79-1.57) #4: 13.4% vs. 7.5% #5: 17.6% vs. 12.5%	0/3 studies with significance #1: 0.79 (95% CI: 0.23-2.85) #2: 16.02 vs. 23.41 per 1000 PPY #3: 11.15% vs. 8.22%, p=0.614	NR	2/2 studies with significance Anti-HDL #1: OR=4.49 (95% CI: 2.07-9.74)* Anti-Apo A1 #2: 4.7 (95% CI: 1.9-11.2)*
Cardiovascular Death	4/6 studies with significance #1: 1.30 (95% CI: 1.07-1.57)* #2: 1.73 (95% CI: 1.23-2.43)* #3: 1.62 (95% CI: 1.15-2.27)* #4: 2.82 (95% CI: 1.57-4.90)*‡ #5: 1.18 (95% CI: 0.46-4.18) #6: 5.2 vs. 4.2 per 1000 PPY	0/3 studies with significance #1: 1.01 (95% CI: 0.74-1.38) #2: 5.53 vs. 3.54 per 1000 PPY #3: 2.2% vs. 0.8%, p>0.05	NR	NR
Stroke	NR	0/2 studies with significance #1: 3.70 vs. 4.78 per 1000 PPY #2: 4.4% vs. 3.3%, p>0.05	0/2 studies with significance Anti-phospholipid #1: 7.7% vs. 1.2% Anti-cardiolipin (TNFi treated pts) #2: 3.4% vs. 0%	NR
Thrombosis	0/1 study with significance *Arterial thrombosis* #1: 5.4% vs. 5% *Venous thrombosis* #1: 6.8% vs. 5%	0/1 study with significance *Overall thrombosis* #1: 5.2% vs. 3.3%, p>0.05	1/3 studies with significance *Arterial thrombosis* Anti-phospholipid #1: OR=9.47 (95% CI: 1.82-49.12)* #2: 30% vs. 0% Lupus anticoagulant #1: OR=11.88 (95% CI: 1.98-71.30)* Anti-cardiolipin #3: 14.3% vs. 0% *Venous thrombosis* Anti-phospholipid #1: 0% vs. 0.9% #2: 36.7% vs. 3.6% Anti-cardiolipin #3: 20.0% vs. 12.1%	NR
Coronary Artery Disease	0/1 study with significance #1: 1.06 (95% CI: 0.83-6.39)	0/2 studies with significance #1: 9.17 vs. 11.01 per 1000 PPY #2: 9.5% vs. 8.6%	NR	NR
Heart Failure	1/1 study with significance #1: 3.29 (95% CI: 1.83-5.69)*‡	0/1 study with significance #1: 7.2% vs. 6.4%, p>0.05	NR	NR
Ischemic Heart Disease	NR	1/1 study with significance #1: OR=2.58 (95% CI: 1.17-5.65)*	0/1 study with significance Anti-phospholipid #1: 5.1% vs. 1.2%	NR
Peripheral Artery Disease	NR	NR	0/1 study with significance Anti-phospholipid #1: 2.6 vs. 0%	NR
Diastolic Dysfunction or Valvular Lesions	NR	1/1 study with significance #1: 72.2% vs. 25.0%, p=0.011*	NR	NR
Thromboembolism (thrombosis or embolism)	NR	NR	0/1 study with significance Anti-cardiolipin (TNFi treated pts) #1: RR=2.7 (95% CI: 0.8-4.6)	NR

Table 2: Studies reporting risk of cardiovascular events/diseases for auto-antibody positive vs. negative patients with RA Anti-Apo A1 = anti-apolipoprotein A1; Anti-CCP = anti-cyclic citrullinated peptide; Anti-HDL = anti-high density lipoprotein; CI = confidence interval; NR = not reported; OR = odds ratio; PPY = person-year; pts = patients; RF = rheumatoid factor; RA = rheumatoid arthritis; RR = relative risk; TNFi = tumor necrosis factor inhibitors * Statistically significant difference between auto-antibody positive vs. negative status ‡ Sub-group of patients exposed to glucocorticoids within the latest 3 months # Labeling of unique studies within each cell

Disclosure: L. Ferri, Bristol-Myers Squibb, 1, 3, 4, Bristol-Myers Squibb Company, 1, 3; **G. Crocket**, Bristol-Myers Squibb, 9, Rutgers University, 3; **Y. Kuang**, Doctor Evidence, 3; **B. Breznen**, Doctor Evidence, 3; **M. Fazeli**, Doctor Evidence, 3.

Abstract Number: 2328

In Rheumatoid Arthritis, New-onset Prednisone Use Is Associated with a Daily Dose, Cumulative Dose, and Duration-dependent Risk for Cardiovascular Events at 6 Months and 1 Year of Use

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SESSION INFORMATION
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Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory joint disease but also affects the cardiovascular (CV) system. Many patients are treated with corticosteroids. Corticosteroid use is associated with increased risk for cardiovascular events (CVE). We hypothesized that patients with RA who initiate corticosteroid therapy would have an increased risk for CVE related to dose and duration of corticosteroid use.

Methods: We investigated all RA patients enrolled in the Corrona registry between 10/2001-3/2018 who were not using prednisone at the time of enrollment and with at least one follow-up entry. Incident CVE were defined as physician-reported CVE captured in Corrona registry protocol (see Table 1). The enrollment visit date was the index date for estimating time to CVE. Survival analysis using Cox proportional hazard regression models were used to estimate adjusted hazard ratios (HR). Baseline covariables in the model adjusted for gender, age, race, duration of RA, history of CV disease, history of prednisone use, diabetes, hyperlipidemia, and/or hypertension, statin use, tobacco use, year of enrollment, the modified health assessment questionnaire score, and the clinical disease activity index (CDAI) for RA. Prednisone use and CDAI were included as time varying covariates. Several measures of prednisone use were considered: current dose; cumulative dose, and duration over the prior year and over the prior 6 months; weighted dose over 1 year and 6 months, with higher weights for more recent use. Data ranges for total dose and duration analyses were based on quartiles of prednisone use.

Results: 24,752 patients were eligible. 80,501 patient years of follow-up were analyzed. The overall rate of CVE was 1.75/100 person years (95% CI 1.66-1.84/100 person years). Table 1 shows HR and 95% confidence intervals (CI) for the various models. Current prednisone dose showed an increased risk at 5-9mg (HR=1.47) and ≥10mg (HR=1.56). Cumulative prednisone dose at 6 months showed increased risk at 811-1100mg (HR=1.42) and >1100mg (HR=1.55); weighted dose showed increased risk at 811-1100mg (HR=1.49) and >1100mg (HR=1.52). Cumulative prednisone duration at 6 months showed increased risk at >181 days (HR=1.48). Cumulative prednisone dose at 1 year showed increased risk at 1101-2100mg (HR=1.30) and >2100mg (HR=1.54); weighted dose shows increased risk for >2100mg (HR=1.69). Cumulative prednisone duration at 1 year showed increased risk for >360 days (HR=1.70).

Table 1

CVE* risk	Past 1 year		CVE* risk	Past 6 months
	HR [95% CI]			HR [95% CI]
Current Prednisone Dose			**Current Prednisone Dose**	
None	1 (ref)		None	1 (ref)
1-4mg	1.04 [0.70, 1.54]		1-4mg	1.04 [0.70, 1.54]
5-9mg	1.47 [1.17, 1.84]		5-9mg	1.47 [1.17, 1.84]
≥10mg	1.56 [1.11, 2.18]		≥10mg	1.56 [1.11, 2.18]
Total Dose			**Total Dose**	
None	1 (ref)		None	1 (ref)
1-500mg	1.0 [0.71, 1.41]		1-390mg	0.84 [0.57, 1.23]
501-1100mg	1.11 [0.82, 1.50]		391-810mg	1.26 [0.93, 1.70]
1101-2100mg	1.30 [0.99, 1.71]		811-1100mg	1.42 [1.09, 1.86]
>2100mg	1.54 [1.17, 2.03]		>1100mg	1.55 [1.12, 2.16]
Total Dose (wgt)†			**Total Dose (wgt) †**	
None	1 (ref)		None	1 (ref)
1-500mg	1.0 [0.72, 1.39]		1-390mg	0.79 [0.53, 1.17]
501-1100mg	1.16 [0.82, 1.64]		391-810mg	1.20 [0.87, 1.67]
1101-2100mg	1.00 [0.73, 1.37]		811-1100mg	1.49 [1.16, 1.92]
>2100mg	1.69 [1.34, 2.14]		>1100mg	1.52 [1.10, 2.10]
Total Duration			**Total Duration**	
None	1 (ref)		None	1 (ref)
1-100 days	0.98 [0.70, 1.37]		1-85 days	0.84 [0.56, 1.25]
101-220 days	1.27 [0.97, 1.65]		86-175 days	1.20 [0.81. 1.77]
221-360 days	0.87 [0.59, 1.29]		176-181 days	1.28 [0.84, 1.93]
>360 days	1.70 [1.33, 2.18]		>181 days	1.48 [1.20, 1.84]

Conclusion: For patients with RA who initiate corticosteroid use, there is an increased CVE risk associated with daily dose, cumulative dose over the last six months and one year, and duration of use. Physicians should counsel patients on the increased CVE risk and consider interventions to minimize risk.

RA and Steroids_ACR_Abstract_Table

*cardiac death, myocardial infarction, stroke, hospitalized for hypertension, revascularization procedures, ventricular arrhythmia, unstable angina, congestive heart failure, transient ischemic attacks, deep vein thrombosis, peripheral arterial thromboembolic event, urgent peripheral arterial revascularization, peripheral ischemia, pulmonary embolism, acute coronary syndrome, or other CV event; ref = reference value; †wgt = weighted for most recent dose

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Abstract Number: 2329

Do Myocardial Inflammation and Microvascular Dysfunction in RA Lead to Adverse Changes in Left Ventricular Structure and Function over Time? A Longitudinal Analysis of Participants from Rheumatoid Arthritis: Study of the Myocardium

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

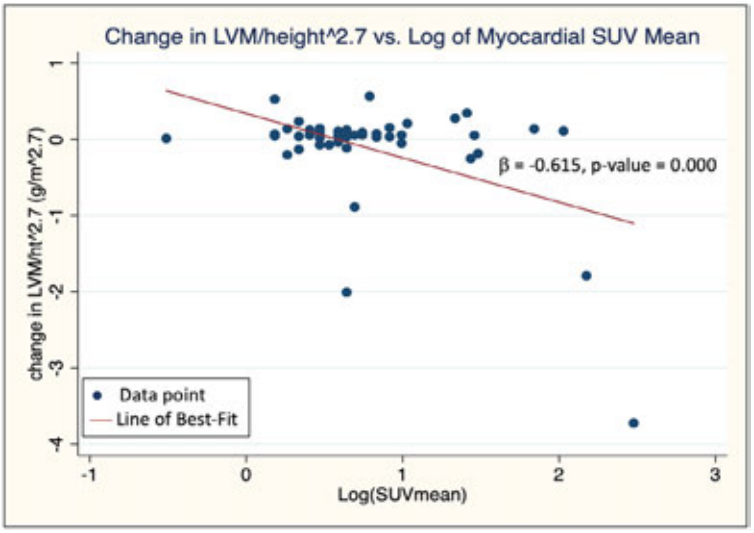
Session Time: 9:00AM–11:00AM

Background/Purpose: The risk of developing heart failure (HF) in RA patients as compared with non-RA subjects is significantly higher even when adjusted for traditional cardiovascular (CV) risk and presence of ischemic heart disease. HF in RA patients is characterized by preserved ejection fraction and diastolic dysfunction. A recent prospective study demonstrated more rapid declines in diastolic function and left ventricular mass (LVM) over time in RA patients compared with control subjects. In RA participants in the RHYTHM (RHeumatoid arthritis: studY of THe Myocardium) study, we observed a high prevalence of subclinical myocarditis (39% with visualized uptake on 18-Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography [18-FDG PET-CT]) as well as microvascular dysfunction (myocardial flow reserve reduced [MFR] in 29%). We hypothesized that RA patients with subclinical myocarditis and/or microvascular dysfunction would have greater decline in LV structure and function over time compared to RA patients without these features.

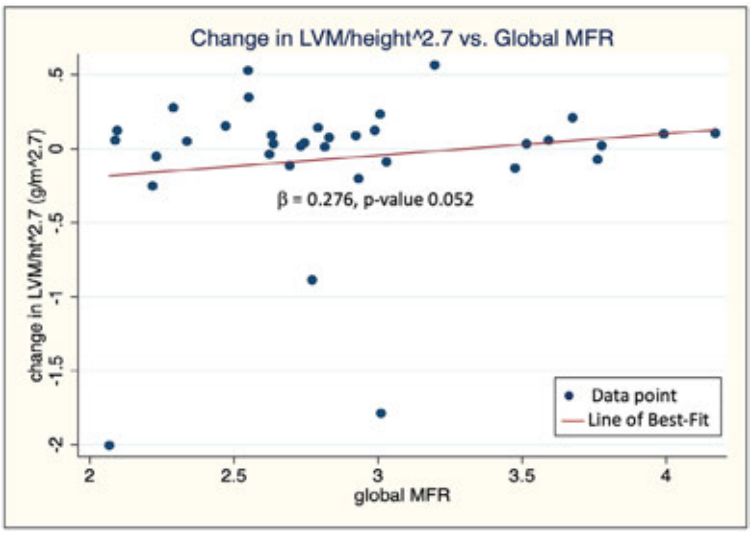
Methods: One hundred nineteen RA patients without clinical CV disease who were enrolled in RHYTHM underwent baseline 18-FDG PET-CT to measure myocardial FDG uptake as a measure of myocardial inflammation (assessed as standardized uptake value [SUV]), and MFR as a measure of microvascular function; in addition, 3-dimensional (3D) echocardiography was performed to assess LV structure and function. Forty-nine patients returned for a follow-up

Parameters	Mean (SD)	95% CI	Paired t-test p-value	Wilcoxon sign-rank test z-value
ΔLVMI, g/ht^2.7 (in $m^{2.7}$)	-0.11 (0.69)	[-0.31, 0.09]	0.14 (Δ<0)	0.12 (Δ<0)
ΔLVMI, g/BSA (in m)	-0.34 (1.48)	[-0.70, 0.09]	0.06 (Δ<0)	0.42 (Δ<0)
ΔLVEF	-0.001 (0.01)	[-0.005, 0.002]	0.19 (Δ<0)	0.31 (Δ<0)
ΔE/A	-0.02 (0.07)	[-0.04, 0.001]	0.03 (Δ<0)	0.06 (Δ<0)
ΔE/E'	0.06 (0.59)	[-0.10, 0.23]	0.22 (Δ>0)	0.79 (Δ>0)
ΔGLS, s^{-1}	0.32 (0.34)	[0.22, 0.42]	0.00 (Δ>0)	0.00 (Δ>0)

Table 1. Changes in selected echocardiographic parameters after 3-6-year time period, including left ventricular mass index (LVMI) adjusted for height^2.7 or body surface area (BSA), systolic function parameters including left ventricular ejection fraction (LVEF) and global longitudinal strain (GLS), and diastolic function parameters including E/A and E/E' ratios



Graph 1. Left ventricular mass (LVM) adjusted by height^2.7 decreases significantly with increasing myocardial inflammation represented by the log transformed mean standardized uptake value (SUV) on 18-FDG-PET scan.



Graph 2. Left ventricular mass (LVM) adjusted by height^2.7 decreases significantly with lower (less favorable) myocardial flow reserve (MFR) obtained with nuclear stress studies.

visit at 3-6-years post-baseline and underwent repeat 3D echocardiography. The mean changes in echo parameters were calculated and Wilcoxon sign-rank tests performed to assess statistical differences between groups. Multivariable regression models were created to assess associations between log transformed mean SUV and global MFR with change in selected echocardiographic parameters.

Results: Although in the overall group there was no significant change in the LVM index (LVMI) over time (Table 1), both higher baseline myocardial SUV (i.e., myocarditis) and lower (less favorable) MFR were associated with a greater decline in LVMI (Figures 1 and 2). In the overall group, although there was no decline in ejection fraction (EF) over

time, a significant decline in global longitudinal strain (GLS), a more sensitive measure of systolic dysfunction than EF, was observed. With regard to diastolic function, a decline in the E/A ratio, but not in the E/E' ratio, was observed over time. However, there were no statistically significant relationships in changes in systolic or diastolic function with baseline SUV or MFR.

Conclusion: These results suggest that subclinical myocardial inflammation and myocardial microvascular dysfunction may be risk factors for myocardial remodeling and decline in systolic and diastolic function in individuals with RA. Whether these subclinical features lead to clinical HF in RA is, as yet, unknown.

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Abstract Number: 2330

Factors Associated with Differing Types of Heart Failure in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: For patients with rheumatoid arthritis (RA), heart failure (HF) is a significant cause of morbidity and mortality. HF is further classified into 2 subtypes to guide management; HF with preserved ejection fraction (HFpEF) and HF with reduced ejection fraction (HFrEF). HFrEF is commonly observed after myocardial ischemia due to myocyte loss. Chronic inflammation is proposed to play a major role in HFpEF even in the absence of a chronic inflammatory condition. These HF subtypes have been traditionally difficult to study in RA due to the need for a large RA cohort with ejection fraction (EF) data. The objective of this study was to test existing approaches using natural language processing (NLP) to characterize HF subtypes in an electronic medical record (EMR) based RA cohort, and to study differences in clinical risk factors between the two HF subtypes in RA.

Methods: We used data from an EMR-based RA cohort from 2 tertiary care centers. Within this cohort we applied a published protocol using machine learning and natural language processing (NLP) to identify patients with HF. Among RA patients with HF, we further applied an NLP tool to extract EF data from cardiology reports. Incident HF cases (RA-HF) were identified and matched 1:3 by age, sex, and healthcare utilization to RA patients without HF. HF was classified using the EF data into HFrEF (EF< 40%) and HFpEF (EF >50%). The index date for HF patients was the date of the first EF measurement; thus, this study was limited to HF patients with EF in their records. For controls, the index date was the closest healthcare utilization date within a 6-month window for the EF date. We assessed covariates including RA clinical factors and traditional HF risk factors over the 3-year period prior to the index date.

Table 1. Clinical characteristics of RA patients with HF* compared to age, sex, and healthcare utilization-matched RA controls without evidence of HF.

Clinical characteristics	HF* (n=544)	Controls (n=1632)	p-value
Age (mean, sd)	76.4 (11.3)	76.4 (11.2)	1.00
Female gender (%)	68.0	68.0	1.00
Caucasian race (%)	82.5	79.6	0.15
Seropositive (%)	27.9	35.5	0.002
RA treatments			
Methotrexate (%)	19.3	26.2	0.001
TNFi (%)	8.3	16.3	<0.001
Other nbDMARDs (%)	23.7	21.6	0.34
Other bDMARDs (%)	2.2	3.6	0.16
Comorbidities			
MI (%)	31.8	3.9	<0.001
CAD (%)	56.1	14.2	<0.001
Valvular disease (%)	60.5	9.4	<0.001
Atrial fibrillation (%)	23.9	5.8	<0.001
Hypertension (%)	75.2	52.6	<0.001
Diabetes (%)	7.7	4.2	0.002
Dyslipidemia (%)	42.1	34.3	0.001
Peripheral vascular disease (%)	16.5	6.7	<0.001
Stroke (%)	20.4	10.1	<0.001
Charlson's comorbidity index (mean, sd)	2.64	2.03	<0.001

*With data on EF

TNFi, tumor necrosis factor alpha inhibitor; CAD, coronary artery disease; DMARD, disease-modifying anti-rheumatic drug (nbDMARD: non-biologic DMARD, bDMARD: biologic DMARD); EF, ejection fraction; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MI, myocardial infarction; RA, rheumatoid arthritis;

Table 2. Clinical factors associated with (a) HF, (b) HFpEF, and (c) HFrEF in RA compared to controls, matched by age, sex, and healthcare utilization*.

	All HF* (n=544)		HFpEF (n=395)		HFrEF (n=92)	
Covariate	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Methotrexate	0.61 (0.41-0.91)	0.015	0.52 (0.32-0.87)	0.012	0.67 (0.23-1.92)	0.45
TNFi	0.60 (0.37-0.98)	0.043	0.56 (0.30-1.06)	0.076	0.39 (0.12-1.28)	0.12
MI	3.10 (1.88-5.13)	<0.001	2.12 (1.11-4.04)	0.023	2.49 (0.71-8.79)	0.16
CAD	3.31 (2.23-4.89)	<0.001	2.92 (1.11-4.04)	0.0030	11.3 (2.86-44.6)	<0.001
Valvular disease	12.0 (8.45-17.1)	<0.001	18.5 (11.8-28.9)	<0.001	4.17 (1.53-11.3)	0.005
Atrial fibrillation	1.89 (1.22-2.93)	0.0041	2.25 (1.32-3.85)	0.0030	1.91 (0.37-9.79)	0.44
Dyslipidemia	0.72 (0.52-0.98)	0.035	0.83 (0.57-1.19)	0.31	0.34 (0.12-0.93)	0.036
Charlson's comorbidity index	1.17 (1.09-1.26)	<0.001	1.20 (1.11-1.31)	<0.001	1.25 (1.02-1.54)	0.034

*Only variables with significant associations shown. Conditional logistic regression adjusted by variables in Table 1.

TNFi, tumor necrosis factor alpha inhibitor; CAD, coronary artery disease; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MI, myocardial infarction; OR, odds ratio; RA, rheumatoid arthritis.

Using a case-control design, conditional logistic regression was performed to identify risk factors associated with the development of unclassified HF, HFpEF, and HFrEF.

Results: We identified 544 RA subjects with incident HF and EF data. Compared to age and sex matched controls, the RA-HF subjects were less likely to be seropositive or on methotrexate or TNF-α inhibitor (TNFi), and have more comorbid conditions (Table 1). Among RA clinical factors, methotrexate was associated with a lower

risk of any HF and HFpEF, and not HFrEF. TNFi use was also associated with reduced risk of any HF, with a stronger trend for reduction in HFpEF (Table 2). Traditional HF risk factors such as myocardial infarction (MI) and coronary artery disease (CAD) were associated with increased risk of any type of HF, with stronger association with HFrEF; valvular disease and atrial fibrillation were more strongly associated with increased risk for HFpEF, consistent with prior literature.

Conclusion: In this preliminary study, we observed that RA factors such as MTX and TNFi use was associated with reduced risk of HF, specifically HFpEF in the former. These differences may provide guidance on understanding the role of inflammation and HFpEF in RA, where anti-inflammatory therapies may provide benefit. Future work is needed to validate incident HF and EF definitions and to take into account the time-varying effect of DMARDs and disease activity on the risk of HF and its subtypes in RA.

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Abstract Number: 2331

Association of Rheumatoid Arthritis-related Autoantibodies with Pulmonary Function Test Abnormalities in a Prospective Rheumatoid Arthritis Registry

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
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Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary involvement in rheumatoid arthritis (RA), such as bronchiectasis, bronchiolitis, pleuritis, or interstitial lung disease (ILD), is associated with high morbidity and mortality. Pulmonary function testing (PFT) assesses for a wide range of pulmonary abnormalities, broadly characterized as restrictive or obstructive. Seropositive RA patients may be more likely to have restriction, commonly present in ILD. Obstruction may also be more common in seropositive RA related to smoking and airway mucosa as a possible initiating site for RA-related autoantibody development. Therefore, we aimed to determine whether RA-related autoantibodies were associated with abnormalities on PFTs.

Methods: We investigated RA serostatus and PFT abnormalities using a single center prospective RA registry. RA serostatus was assessed by commercial assays for cyclic citrullinated peptide (CCP) and rheumatoid factor (RF) obtained at baseline for research purposes. We used standard cutpoints to define presence and level of positivity for each autoantibody. Outcomes were abnormalities on clinically-indicated PFTs: restriction (% predicted

forced vital capacity [FVC] < 80), obstruction (ratio of forced expiratory volume in one second to FVC [FEV1/FVC] < 0.7), diffusion abnormality (% predicted diffusing capacity of the lungs for carbon monoxide [DLCO] < 70), and a composite of any abnormality. Logistic regression estimated ORs and 95%CIs for types of PFT abnormalities by RA-related autoantibody status, adjusted for possible confounders. We also analyzed only those who had PFTs performed.

Results: Among 1,272 analyzed subjects, mean age was 56.3 years (SD 14.1), 82.2% were female, 69.5% were seropositive (CCP+ or RF+), and 6.8% had ILD. There were 100 subjects with abnormal PFTs. Seropositivity was associated with increased odds of any PFT abnormality (multivariable OR 2.29, 95%CI 1.30-4.03, Table 1) compared to seronegativity. When analyzing by type of PFT abnormality, seropositivity was associated with restriction, obstruction, and diffusion abnormality; multivariable ORs were 2.48 (95%CI 1.26-4.87), 3.12 (95%CI 1.28-7.61), and 2.30 (95%CI 1.09-4.83), respectively. When analyzing by CCP and RF status, the associations were stronger for RF+ than for CCP+ (any PFT abnormality: OR 1.99, 95%CI 1.21-3.27 for RF+ vs. RF-; OR 1.67, 95%CI 1.03-2.69 for CCP+ vs. CCP-), with a dose effect of higher RF levels increasing odds for each PFT abnormality (p for trend< 0.05). Results were similar when only analyzing subjects who had PFTs performed (seropositivity: OR 2.40 (95%CI 1.07-5.35 vs. seronegativity, Table 2).

Conclusion: Seropositive RA patients had 2-fold increased risk for abnormalities on PFTs performed for clinical indications compared to seronegative RA. This association was present for all types of PFT abnormalities and was

Table 1. Multivariable adjusted* odds ratios for specified abnormalities on clinically-indicated pulmonary function testing according to RA-related autoantibody status (n=1,272).

RA serostatus	**Any PFT abnormality OR (95%CI)**	**Restriction (% predicted FVC <80) OR (95%CI)**	**Obstruction (FEV_1/FVC <0.7) OR (95%CI)**	**Diffusion abnormality (% predicted D_{LCO} <70) OR (95%CI)**
Seronegative	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Seropositive	**2.29 (1.30-4.03)**	**2.48 (1.26-4.87)**	**3.12 (1.28-7.61)**	**2.30 (1.09-4.83)**
CCP negative	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
CCP positive	**1.67 (1.03-2.69)**	**1.95 (1.09-3.47)**	**2.04 (1.00-4.15)**	1.47 (0.80-2.71)
CCP negative	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
CCP low+: >1 to ≤3x ULN	1.78 (0.89-3.57)	1.51 (0.62-3.67)	2.14 (0.79-5.79)	1.66 (0.68-4.01)
CCP high+: >3x ULN	**1.64 (1.00-2.69)**	**2.04 (1.14-3.68)**	2.01 (0.97-4.18)	1.43 (0.76-2.69)
p for trend	0.061	**0.016**	0.072	0.30
RF negative	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
RF positive	**1.99 (1.21-3.27)**	**2.34 (1.28-4.27)**	**2.60 (1.22-5.56)**	**2.01 (1.05-3.85)**
RF negative	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
RF low+: >1 to ≤3x ULN	1.32 (0.67-2.62)	1.67 (0.75-3.69)	1.52 (0.54-4.22)	1.32 (0.53-3.26)
RF high+: >3x ULN	**2.29 (1.37-3.84)**	**2.64 (1.42-4.90)**	**3.10 (1.42-6.76)**	**2.31 (1.18-4.53)**
p for trend	**0.001**	**0.002**	**0.003**	**0.012**
CCP-/RF-	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
CCP+/RF-	1.91 (0.75-4.87)	1.56 (0.48-5.13)	2.27 (0.54-9.54)	1.87 (0.55-6.29)
CCP-/RF+	**2.78 (1.20-6.44)**	2.46 (0.87-6.97)	**3.56 (1.03-12.29)**	**3.45 (1.23-9.65)**
CCP+/RF+	**2.28 (1.27-4.07)**	**2.61 (1.31-5.20)**	**3.17 (1.28-7.86)**	**2.20 (1.03-4.73)**

Numbers of outcomes in models: any PFT abnormality=100, restriction=74, obstruction=50, diffusion abnormality=55.

*Adjusted for age, sex, education, smoking, body mass index, and RA duration at study baseline.

CCP: cyclic citrullinated peptide antibody; CI; confidence interval; D_{LCO}: Diffusing capacity of the lungs for carbon monoxide; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; OR: odds ratio; PFT: pulmonary function test RA: rheumatoid arthritis; RF: rheumatoid factor; ULN: upper limit of normal

Table 2. Multivariable adjusted* odds ratios for abnormality on clinically-indicated pulmonary function testing according to RA-related autoantibody status, restricted to those who had PFTs performed (n=188).

RA serostatus	Any PFT abnormality OR (95%CI)
Seronegative	1.00 (Ref)
Seropositive	**2.40 (1.07-5.35)**
CCP negative	1.00 (Ref)
CCP positive	1.67 (0.80-3.47)
CCP negative	1.00 (Ref)
CCP low+: >1 to ≤3x ULN	1.71 (0.56-5.21)
CCP high+: >3x ULN	1.66 (0.79-3.52)
p for trend	0.11
RF negative	1.00 (Ref)
RF positive	1.99 (0.97-4.12)
RF negative	1.00 (Ref)
RF low+: >1 to ≤3x ULN	1.19 (0.46-3.11)
RF high+: >3x ULN	**2.47 (1.14-5.37)**
p for trend	**0.01**
CCP-/RF-	1.00 (Ref)
CCP+/RF-	2.15 (0.53-8.71)
CCP-/RF+	3.05 (0.85-10.92)
CCP+/RF+	**2.31 (1.00-5.32)**

Numbers of outcomes in models: any PFT abnormality=100.

*Adjusted for age, sex, education, smoking, body mass index, and RA duration at study baseline.

CCP: cyclic citrullinated peptide antibody; CI; confidence interval; D_{LCO}: Diffusing capacity of the lungs for carbon monoxide; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; OR: odds ratio; PFT: pulmonary function test RA: rheumatoid arthritis; RF: rheumatoid factor; ULN: upper limit of normal

not explained by smoking. Patients with seropositivity may be at risk for obstructive lung diseases, in addition to the previously known association of seropositivity with restrictive lung diseases, such as ILD. Future studies should assess the value of screening for PFT abnormalities in seropositive RA patients, particularly those with high-titer RF+.

Disclosure: S. Huang, None; **X. He**, None; **T. Doyle**, Bristol-Myers Squibb, 2, Genentech, 2; **A. Zaccardelli**, None; **A. Marshall**, None; **H. Friedlander**, None; **R. Blaustein**, None; **E. Smith**, None; **C. Iannaccone**, None; **T. Mahmoud**, None; **M. Weinblatt**, Abbvie, 5, AbbVie, 5, Amgen, 5, BMS, 2, 5, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Canfite, 1, 4, Corrona, 5, Crescendo Bioscience, 2, 5, Eli Lilly and Company, 5, Gilead, 5, Glaxo-Smith Kline, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Lilly, 5, Lily, 5, Lycera, 1, 4, 5, Merck, 5, Novartis, 5, Pfizer, 5, Roche, 5, Samsung, 5, Samsung Bioepis Co., Ltd., 5, Sanofi Regeneron, 2, Sanofi/Regeneron, 2, Sanofi-Regeneron, 2, Scipher, 1, 4, 5, Set Point, 5, SetPoint, 5, Squibb, 5, Vorso, 1; **P. Dellaripa**, Bristol Myers Squibb, 2, Genentech, 2, UpToDate, 7; **N. Shadick**, BMS, 2, Crescendo Biosciences, 2, Mallinckrodt, 2, Sanofi Regeneron, 2, Sanofi/Regeneron, 2; **J. Sparks**, None.

Abstract Number: 2332

Cardiovascular Risk Factors in Rheumatoid Arthritis: Prevalence, Comparison of Risk Calculators and Subclinical Atherosclerosis in Indian Patients

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis(RA) patients have increased cardiovascular(CV) risk with no data on CV risk scores in Indian patients.The primary objective was to study prevalence of traditional CV risk factors in RA. Secondary objectives were to assess performances of various CV risk scores with respect to each other and against subclinical atherosclerosis as measured by carotid intima media thickness(CIMT).

Table1. Demographics, Disease characteristics and prevalence of Traditional risk factors *	
Male:Female	49:285
Age, in years	47.16+12.57
Disease duration, in years	7.25+5.92
Positive anti-CCP (270)#	246 (73.7%)
Positive RF (298)	286 (85.6%)
Erosions (327)	149 (44.6%)
Prevalence of Traditional risk factors	
Smoking ever	23 (6.9%)
Active smoker	16 (4.8%)
Diabetes Type2	40 (12.0%)
Hypertension	71 (21.6%)
Family history of CVD	29 (8.7%)
Obesity(BMI>30)	32(11.7%)
Chronic Kidney Disease	4 (1.2%)
Total Cholesterol	163.21+38.26
LDL	97.61+26.48
Triglyceride	126.61+56.32
HDL	47.105+9.85

*Values expressed as mean± SD for continuous variables and n (percentage) for discrete variables
HDL: High density lipoproteins, LDL: Low density lipoproteins, CVD: Cardiovascular disease

Table2. Comparison between patients with and without subclinical atherosclerosis					
	Without subclinical Atherosclerois	With Atherosclerosis	OR	CI	p
Age	45.08+11.26	59.00+11.96			**<0.001**
Age>50	82 (36.4%)	38 (80.9%)	7.36	3.39-15.93	**<0.001**
Gender	26(11.6%)	15(31.9%)	3.59	1.71-7.50	**0.001**
Duration	7.209_5.835	8.89+7.75			0.101
CCP positive	161(71.6%)	36(76.6%)			0.591
RF positive	192(85.3%)	40(85.1%)			0.999
Erosions	88(39.8%)	28(63.6%)	2.65	1.35-5.17	**0.005**
EAM	10(4.4%)	3(6.4%)			0.476
Traditional risk factors					
Hypertension	43(19.1%)	17(36.2%)			**0.019**
Systolic BP	131.01+19.88	138.36+17.71			**0.020**
Diabetes Mellitus	21(9.3%)	12(25.55%	3.33	1.50-7.37	**0.005**
BMI	28.13+59.93	23.89+4.28			0.629
Waist-Hip Ratio	0.86+0.11	0.86+0.06			0.631
Obesity	26(11.6%)	6(12.8%)			0.805
Smoking	11(4.9%)	8(17.0%)	3.99	1.51-10.55	**0.007**
Family History	19(8.4%)	2(4.3%)			0.547
Lipid Profile					
T.Ch	163.74+37.52	165.63+41.03			0.757
T.Ch>200	35 (15.6%)	9(19.1%)			0.519
LDL	98.88+23.01	101.59+29.38			0.485
LDL>100	85(37.8%)	20(42.6%)			0.622
HDL	47.69+8.86	45.63+9.41			0.154
HDL<40	30(13.3%)	12(25.5%)	2.23	1.04-4.76	**0.045**
TCh/HDL ratio>4	56(24.9%)	17(36.2%)			0.147

EAM: Extraarticular manifestation, BMI:Body Mass Index, TCh:Total Cholesterol, HDL: High density lipoproteins, LDL: Low density lipoproteins

Methods: Patients fulfilling 2010 ACR/EULAR criteria for RA were included. Presence of traditional CV risk factors were recorded. 10-year-CV risks were predicted using Framingham Risk scoring using lipids (FRS-Lipids) and body mass index (FRS- BMI), QRISK-3, SCORE and the algorithm recommended by 2013-ACC/AHA guidelines(ASCVD) in patients who were 40 years or older. CIMT was measured on the far-wall of the common carotid artery at least 5 mm below its end. CIMT value greater than 0.90 mm or presence of plaque was chosen as marker of subclinical atherosclerosis.

Results: Table 1 highlights clinical profile and risk factors in 334 enrolled patients. Friedman's test for global variance of various showed significant difference among various risk predicting algorithms. Post-hoc analysis done with Wilcoxon-signed-rank test showed significant variability between each of them. When subclinical atherosclerosis assessed by CIMT was taken as reference, ASCVD and QRISK-3 showed maximum sensitivity **Fig:1**. Differences in disease characteristics and risk factors between patients with and without subclinical atherosclerosis and are underlined in **Table 2**.

Conclusion: There is considerable variablity between various risk scores and cannot be used indiscriminately in Indian RA patients. ASCVD and QRISK-3 scores had the maximum sensitivity in predicting subclinical atherosclerosis.

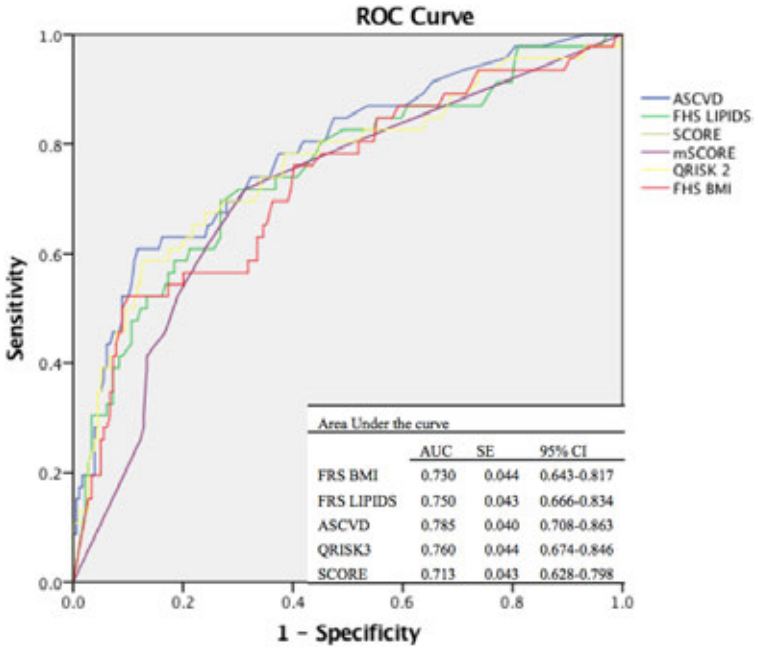

Figure 1. ROC for various risk scores in predicting subclinical atherosclerosis

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Abstract Number: 2333

Risk of Incident Myocardial Infarction Among Disabled Patients with Rheumatoid Arthritis Who Were Beneficiaries of the Social Security Disability Insurance

Iris Navarro-Millan,[1] Mangala Rajan,[1] Geyanne Lui,[1] Lisa Kern,[1] Laura Pinheiro,[1] Sebastian E. Sattui,[2] Lisa Mandl,[3] Fenglong Xie,[4] Jeffrey Curtis,[5] and Monika Safford[1], [1]Weill Cornell Medicine, New York, [2]Hospital for Special Surgery, New York, [3]Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, New York, NY, [4]University of Alabama at Birmingham, Birmingham, [5]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with RA have high risk for myocardial infarction (MI). A meta-analysis showed that the age and sex adjusted pooled relative risk of MI among patients with RA was 1.69, 95% confidence interval (CI) 1.50 - 1.90. There is limited understanding about the prevalence and incidence of MI events among individuals younger than 65 years of age disabled (defined as beneficiaries of the social security disability insurance (SSDI)) with RA.

	Without CVD risk factors	With CVD risk factor	Difference between groups Significance
Number	**16,163 (33%)**	**32,742 (69%)**	p≤0.0001
Age Category, %			
Under 40 years	12.0	3.9	p≤0.0001
51 to 50 years	24.5	15.3	
51 to 60 years	43.5	49.2	
61 to 64 years	20.1	31.6	
Sex, %			p=0.01
Female	79.5	78.5	
Race, %			p≤0.0001
White	78.5	71.2	
Black	11.5	19.6	
Hispanic	5.2	4.8	
Other	4.8	4.4	
CVD Risk Factors, %			
Diabetes	-	36.5	
Hyperlipidemia	-	59.3	
Hypertension	-	78.8	
Obesity	-	20.4	
Baseline CVD, N (%)	**324 (2.0)**	**4,204 (12.8)**	p≤0.0001
Myocardial Infarction, %	0.2	3.0	p≤0.0001
Congestive Heart Failure, %	0.7	6.4	p≤0.0001
Stroke, %	1.2	5.2	p≤0.0001
CVD procedures (CABG, PCI, CEA), %	0.0	1.0	

† CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; CEA = carotid endarterectomy

Table 1: Characteristics of 48,905 Patients with RA <65 Years of Age receiving Social Security Disability Insurance Benefits in 2011, with and without Cardiovascular Disease (CVD) Risk Factors

Among patients with RA < 65 years of age who receive SSDI benefits in 2011, to 1) determine the prevalence of cardiovascular disease (CVD) and CVD risk factors; and 2) among those free of CVD at baseline, to compare the risk of incident MI among those with and without CVD risk factors at baseline, to compare the risk of incident MI among those with and without CVD risk factors at baseline.

	Without CVD Risk Factors	With CVD Risk Factors
N, %	15,839 (36%)	28,538 (64%)
Incident Myocardial Infarctions, N	143	433
Age adjusted incidence of MI (per 1000 person years)	3.42 (2.90 – 4.03)	5.02 (4.52 – 5.58)
Crude Hazard Ratio and 95% Confidence Intervals (Unadjusted)	Ref	1.71 (1.41 – 2.06)
Age and Sex adjusted Hazard Ratio and 95% Confidence Intervals	Ref	1.47 (1.22 – 1.78)

Table 2: Three-Year Incidence of Myocardial Infarction among Patients with Rheumatoid Arthritis <65 Years of Age Receiving Social Security Disability Insurance Benefits and Free of Cardiovascular Disease at Baseline

Methods: We analyzed claims data of the SSDI beneficiaries aged 18-64 years of age with RA, defined as ≥2 ICD-9 CM codes (714.xx) from a rheumatologist > 7 and < 365 days apart, OR 1 ICD-9-CM code from a rheumatologist AND a DMARD in 2011 in a period > 7 and < 365 days. Prevalent CVD was defined by ICD-9-CM code from heart failure, stroke, or CVD procedures (coronary artery bypass grafting, percutaneous coronary intervention, or carotid endartherectomy) in 2011. We used the chronic conditions data warehouse to identify CVD risk factors (ICD-9-CM codes for diabetes, hyperlipidemia, hypertension, obesity) in 2011. We followed subjects without prevalent CVD in 2011, through 2014 to determine incident MI, defined as the first hospitalization for MI (discharge diagnosis ICD-9-CM codes 410.xx). Age adjusted incidence rates were estimated using Poisson models. Age- and sex-adjusted Cox proportional hazard model was used to compare the risk for incident MI between patients with and without CVD factors at baseline.

Results: There were 48,905 patients in the study sample; 78.9% were female, 72.2% were ≤60 years of age, and 69% had at least one CVD risk factor, with hypertension being the most prevalent (52.7%) (Table 1). The prevalence of CVD was 9.3% (N = 4,528). Among the 44,377 without CVD at baseline, 28,538 (64%) had baseline CVD risk factors; 433 MI events occurred among those with CVD risk factors and 143 among those without over 35.9 median months of follow-up (Table 2). The age-adjusted incident rate of MI was 5.02 (95% CI 4.52 – 5.58) per 1000 person-years for those with CVD risk factors and 3.42 (95% CI 2.90 – 4.03) per 1000 person-years for those without CVD risk factors. The age- and sex-adjusted hazard ratio (HR) for incident MI for those with CVD risk factors compared to those without was 1.47 (95% CI 1.22-1.78).

Conclusion: The prevalence of CVD and CVD risk factors was high in this population of disabled individuals younger than 65 years of age with RA. The incident rate for MI was high in the subgroup of patients without CVD risk factors considering that 80% of those patients were 60 year of age or younger (3.42 per 1000 person-year). As expected, patients with CVD risk factors were 47% more likely to experience an MI compare to patients without CVD risk factors.

Disclosure: I. Navarro-Millan, None; **M. Rajan**, None; **G. Lui**, None; **L. Kern**, None; **L. Pinheiro**, None; **S. Sattui**, None; **L. Mandl**, Annals of Internal Medicine, 3, Annals of Internal Medicine- Associate Editor, 3, UpToDate, 7, Wolters Kluwer - Author at UptoDate, 7, Wolters Kluwer - Author at UpToDate, 7, Wolters Kluwer- Author at UpToDate, 7; **F. Xie**, None; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **M. Safford**, Amgen, 2, 9.

Abstract Number: 2334

Is Cardiovascular Risk and Mortality in Rheumatoid Arthritis Compared to Diabetes Mellitus and the General Population Overestimated?

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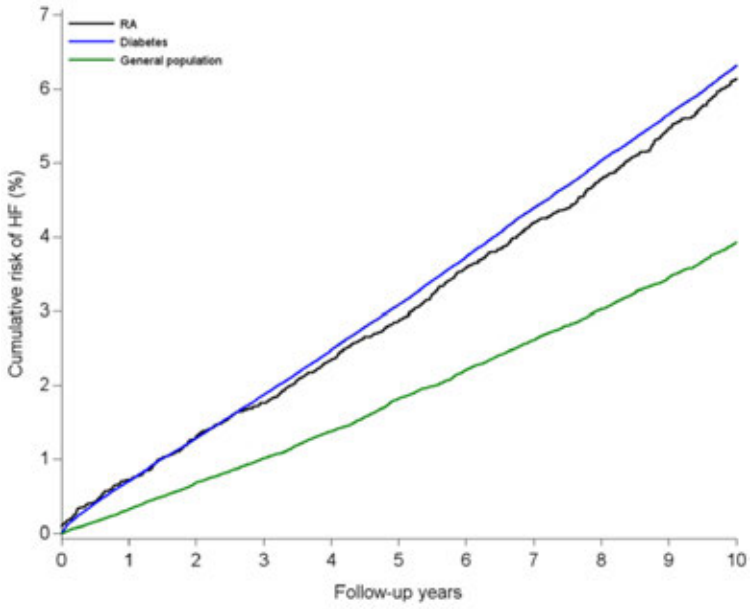

Figure 1. Cumulative risk of heart failure during the 10 year follow-up period.

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To compare the risk of cardiovascular disease (CVD) and mortality in patients with rheumatoid arthritis (RA), diabetes mellitus (DM), and the general population.

Methods: Patients diagnosed with RA were matched 1:5 by age, sex, and year of RA diagnosis with the general population. In the same period, patients with incident DM were included. Outcomes were heart failure (HF), myocardial infarction (MI), coronary revascularization, and death up to 10 years after diagnosis.

Results: We included 15,491 patients with RA, 309,698 patients with DM, and 77,455 persons from the general population. Patients with RA had an increased risk of HF (HR 1.46, 95% CI 1.34-1.59), MI (HR 1.48, 95% CI 1.34-1.63), percutaneous coronary intervention (PCI) (HR 1.37, 95% CI 1.22-1.54), and coronary artery bypass grafting (CABG) (HR 1.20, 95% CI 0.98-1.49) compared to the general population. When comparing RA and DM, RA patients had a lower adjusted risk of HF (HR 0.79, 95% CI 0.73-0.85) and CABG (HR 0.61, 95% CI 0.50-0.74) and similar risk of MI and PCI. The mortality risk among patients with RA and the general population was similar, but lower than in patients with DM (RA vs DM: HR 0.65, 95% CI 0.63-0.68).

Conclusion: This study demonstrates that RA is associated with an increased risk of CVD compared to the general population but without reaching the risk levels observed in patients with DM. Among patients with RA, we observed comparable mortality at 10-year follow-up compared to the general population and significantly lower mortality than patients with DM.

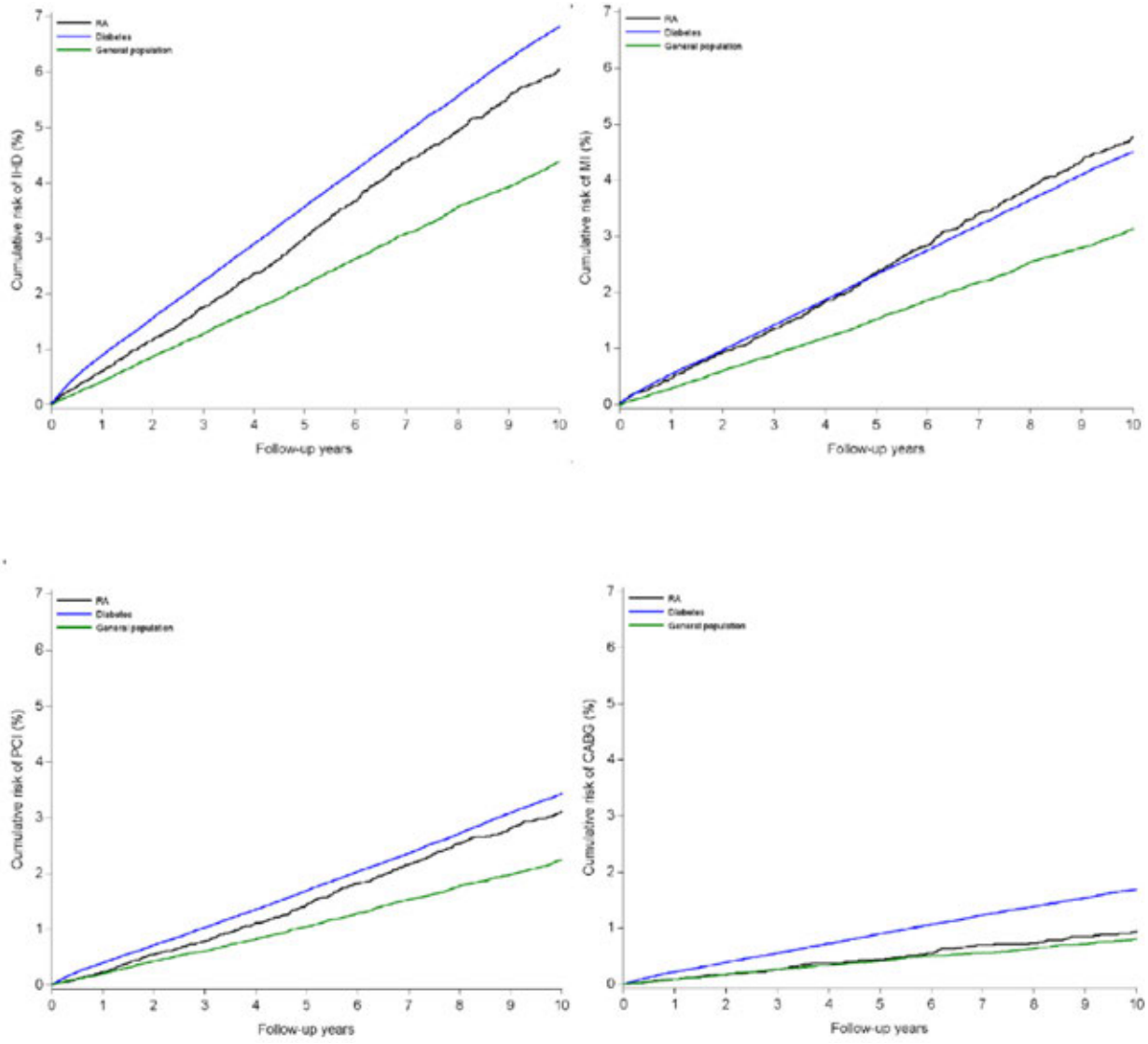

Figure 2. Cumulative risk of ischemic heart disease, myocardial infarction and revascularization during the 10-year follow-up period

Disclosure: B. Løgstrup, None; **T. Ellingsen**, None; **A. Pedersen**, None; **B. Darvalics**, None; **K. Olesen**, None; **H. Bøtker**, None; **M. Mæng**, None.

Abstract Number: 2335

Prediction of Myocardial Fibrosis in Rheumatoid Arthritis Assessed by Cardiac Magnetic Resonance Imaging Using Artificial Neural Networks Models

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiac involvements cause of morbidity and mortality globally in rheumatoid arthritis (RA). Myocardial dysfunction may arise from a number of distinct processes, including myocardial inflammation and myocardial fibrosis, any of which may be active in RA. Global longitudinal strain (GLS), using non-contrast feature tracking cardiac magnetic resonance (FT-CMR), has been reported to be significantly associated with the extent of myocardial fibrosis. Late gadolinium enhancement (LGE) corresponds to histopathologic zones of myocardial fibrosis and necrosis. In the last few years, it has been suggested that artificial neural networks (ANNs) approaches are an established method for analyzing large datasets. ANNs could be a useful tool for prediction in medical scenarios. We aimed to predict myocardial fibrosis in RA assessed by FT-CMR and LGE using ANNs models.

Methods: RA patients and controls with no known heart disease or risk factors were enrolled. The normal threshold was defined based on the statistical±2SD limits on healthy controls in FT-CMR. In this study, a three-layered feed-forward neural network model was structured to detect a myocardial abnormality from GLS and LGE, respectively. Inputs for the network were totally 22 variables including attributes (e.g., Age, Sex, BMI, Duration, RF, SDAI, MMP-3, CRP, ESR, TC, TG, HDL, LDL, sBP/dBP, HbA1c, NTproBNP, MTX, PSL, biologics used) and observed values (e.g., DAS28, ACPA). The network's output was existence or non-existence (1 or 0) of abnormity in each target index. The back-propagation learning algorithm was used to train the ANNs structure. As the hyper parameters of ANNs, the number of neurons (10, 50, 100, 200) in the hidden layer, optimization method (Stochastic Gradient Descent, Adaptive Moment Estimation), initial learning rate (0.001, 0.005, 0.05) in the optimization method and the number of iterations (10, 50, 100, 200, 400) were determined to get the best performance using leave-one-out cross-validation. We calculated accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) to evaluate the performance of the ANNs model.

Results: We evaluated 88 patients with RA (95% women; mean age, 59.5±9. 0 years) and 30 healthy controls (100% women; mean age, 55.7±4.5 years). All 118 subjects underwent FT-CMR and 51 patients underwent LGE. Abnormal GLS values and LGE were seen in 67/88 subjects (76.1%) and 19/51 subjects (37.3%), respectively. We created a mathematical model with an AUC value of 0.73 and 0.71, respectively, able to predict abnormal GLS and LGE. The accuracy, sensitivity, specificity, PPV and NPV for prediction of abnormal GLS values and LGE were 80.7%, 88.1%, 57.1%, 86.8%, 60.0% and 74.5%, 73.7%, 70.6%, 58.3%, 82.8%, respectively.

Conclusion: We applied ANNs to identify a prediction model for myocardial fibrosis in RA assessed by CMR. We could construct a mathematical model with laboratory and clinical items, and treatment, to potentially identify asymptomatic RA patients with myocardial fibrosis. This prediction tool could be used potentially in a clinical practice setting to stratify RA patients according to myocardial fibrosis.

Disclosure: H. Kobayashi, None; **I. Yokoe**, None; **Y. Kobayashi**, Canon Medical Systems, 2; **E. Takaya**, None; **A. Nishiwaki**, None; **K. Sugiyama**, None; **N. Kitamura**, None; **M. Haraoka**, None; **M. Takei**, None.

Abstract Number: 2336

Levels of Proinflammatory Cytokines in Rheumatoid Arthritis Patients with Carotid Plaque: A Case-Control Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with RA have an augmented cardiovascular mortality up to 50% compared to controls. Chronic inflammation of the disease causes endothelial dysfunction and accelerated atherosclerosis. Key molecular pathways in this process are dependent on cytokines like TNF-α, IL-1, IL-6, among others, which are shared with RA. Increased disease activity could contribute to atherosclerosis. Carotid ultrasound (US) has recently been recommended as a screening tool for early detection of subclinical atherosclerosis. Thus, the aim of this study was to compare different cytokines between Mexican-mestizo RA-subjects with/without carotid plaque (CP).

Table 1. Clinical characteristics.

Variable	CP (n= 37)	No CP (n=34)	*P*
Age, years*	59.2 (54.8-66.1)	57.7 (53-61.2)	NS
Female**	35 (94.6)	33 (97.1)	NS
Dyslipidemia**	7 (18.9)	6 (17.6)	NS
T2DM**	10 (27)	7 (20.6)	NS
Hypertension**	12 (32.4)	10 (29.4)	NS
Body Mass Index*	29 (26.5-31.1)	27.9 (24.6-33.2)	NS
Disease duration ***	12.4 ± 9.9	10.6 ± 9	NS
DAS28 CRP*	2.9(1.5-3.9)	2.39 (1.8-3.1)	NS
Methotrexate **	17 (45.9)	22 (64.7)	NS
Prednisone**	27 (73)	24 (70.6)	NS
IL-1 pg/ml*	8.7 (6.7-10.1)	7.9 (6.1-9.3)	NS
TNF-a pg/ml*	76 (61-101)	76 (61-96)	NS
IL-6 pg/ml*	4.4 (4.1-4.9)	4.4 (3.9-4.8)	NS
ICAM ng/ml*	91 (61-118.5)	83.5 (61-217.2)	NS
VCAM ng/ml*	58.1 (42.1-64.8)	54.3 (35.1-65.9)	NS
MMP9 pg/ml*	811 (711-938.5)	821 (724.7-931)	NS
Remission (DAS 28-CRP <2.6) **	12 (33.3)	20 (58.8)	**0.032**

*-variable reported as: median (q25-q75), **-variable reported as: n (%), ***-variable reported as: media ± SD

Table 2. Cytokines levels	
	Median (q25-q75)
IL1, pg/ml	8.1 (6.6-9.6)
TNF-a, pg/ml	76 (61-101)
IL6, pg/ml	4.4 (4.1-4.8)
ICAM, ng/ml	91 (61-141)
VCAM, ng/ml	56.5 (41.3-65.1)
MMP9, pg/ml	811 (721-931)

Methods: An observational cross-sectional trial was designed. Inclusion criteria: age between 40-75 years old, fulfillment of the 2010 ACR/EULAR classification criteria, and detection of a CP during a carotid US. Subjects with a prior diagnosis of cardiovascular disease or a poor US window were excluded. RA subjects were matched to controls (RA patients without CP) by age and cardiovascular (CV) comorbidities. Every subject had a carotid US performed; reviewed by two board-certified radiologists. Cytokines measured were IL-1, IL-6, TNF-α, VCAM-1, ICAM-1 and MMP-9, using an ELISA reader (Glomax E9032). Descriptive analysis was done with frequencies (%), median (q25-q75), and comparisons between groups with Chi square and Mann-Whitney U tests.

Results: 71 subjects were included, 95.8% were females, with a median age of 58 years (54-65). Comparisons between groups are in Table 1 and levels of cytokines in Table 2. Groups were well balanced, with no differences in CV comorbidities ($p > 0.05$). No significant differences among cytokine levels regarding CP were found. Subjects in remission (n=12, 33%) had a lower prevalence of CP ($p < 0.05$, OR: 0.3; 95% CI: 0.1-0.9) and a lower median IL-1 level than those with higher disease activity ($p < 0.05$). No significant differences were found among any other of the compared cytokines.

Conclusion: In our cohort subjects in remission had a lower prevalence of CP. No difference was found between cytokines regarding CP. Subjects with active disease had a higher level of IL-1 than subjects in remission. To our best knowledge, this is the first study to evaluate levels of cytokines in Mexican RA-subjects.

Disclosure: D. Galarza-Delgado, None; **J. Azpiri-Lopez**, None; **I. Colunga-Pedraza**, None; **R. Arvizu-Rivera**, None; **K. Cuellar-Calderon**, None; **G. Garcia-Arellano**, None; **I. Reynosa-Silva**, None; **M. Castro-Gonzalez**, None; **C. Martinez-Flores**, None; **R. Vera-Pineda**, None; **J. Cardenas-De la Garza**, None; **G. Elizondo-Riojas**, None; **C. Guillen-Gutierrez**, None.

Abstract Number: 2337

Treat to Target Is Not Linked to Best Myocardial Strain Indices: Is There Really a Myocardial Dysfunction Directly Associated with Disease Activity?

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The risk of developing heart failure (HF) is twice as high in the RA population. It is hypothesized that, in addition to the atherosclerotic ischemic component and the traditional risk factors, there is a mechanism of cardiotoxicity related to the inflammatory pathways. A few previous studies indicate an association between disease activity and myocardial dysfunction, but they involved elderly population with comorbidities and in use of TNF-α inhibitors. Our main objective is to evaluate the correlation between clinical disease activity index (CDAI) and global longitudinal strain (GLS) — the most sensitive echocardiographic method to detect changes in ventricular contractility — in a RA population without cardiovascular risk factors and using only conventional synthetic DMARDs.

Methods: From June 2016 to January 2019, RA patients were selected to perform transthoracic speckle tracking echocardiography for GLS evaluation. Patients aged 18-60 years and classified according to ACR 2010 criteria were included. Patients with diabetes mellitus, uncontrolled hypertension, smokers, BMI >35, atherosclerotic disease history, and in use of biological medication were excluded. Patients underwent a clinical evaluation in which a single physician measured the CDAI and, within a period of one month, an echocardiographer blinded to the patient's clinical data assessed the GLS. Student's t-test and Spearman correlation were used for statistical evaluation.

Results: Thirty-six patients (91.7% female, with ages ranging from 16 to 56 years) participated in the study. No correlation was found between CDAI and GLS values (Graphic 1). There was no adequate accuracy between values of CDAI≤10 and GLS< -18% and GLS< -20% (values considered normal), according to Table 1. The presence of RF, anti-CCP and the disease duration were also not associated with CDAI values.

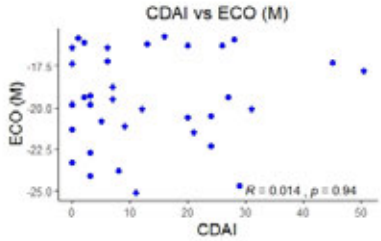
Conclusion: Data from this study (small but with highly selected population) do not corroborate the association of CDAI with myocardial dysfunction and question whether there is a cardiotoxicity factor linked to the disease. Traditional risk factors, subclinical atherosclerotic disease, and cardiotoxic drug effects should be the subject of studies designed to explain the higher prevalence of HF in the RA population.

Table 1 – Acuracy of CDAI≤10 to predict GLS < - 18% and GLS < -20%

GLS	Sensitivity	Specificity	PPV	NPV	Acuracy	p-value
≤-18%	53,8	60,9	43,8	70,0	58,3	0,393
≤-20%	38,1	46,7	50,0	35,0	41,7	0,364

GLS: Global Longitudinal Strain; PPV: Positive Predictive Value; NPV: Negative Predictive Value

GRAPHIC 1: CORRELATION OF CDAI WITH ECOCHARDIOGRAPHY FINDINGS (GLS)



CDAI: Clinical Disease Activity Index

ECO (M): Values of Global Longitudinal Strain

Disclosure: A. Pugliesi, None; **H. Nourani**, None; **J. Matos Souza**, None; **M. Bertolo**, None.

Abstract Number: 2338

Validation of a Claims Algorithm to Identify Interstitial Lung Disease in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is an increasingly important problem for patients with Rheumatoid Arthritis (RA). However, current approaches to ILD case finding are suboptimal or have been evaluated only in limited settings. Our objective was to develop, refine, and validate a claims-based algorithm to identify both prevalent and incident ILD in a cohort of RA patients enrolled in Medicare compared to the gold standard of medical record review.

Methods: We used Medicare administrative claims data 2006-2015 to derive a cohort of RA patients and then identified suspected ILD using variations on several features of the data. These included various ILD diagnosis codes using ICD9/10 coding, evaluation by pulmonologists and rheumatologists, occurrence of chest CT, lung biopsy results, and pulmonary function tests. Suspected ILD cases were evaluated at five participating medical centers: Duke, Medical University of South Carolina, University of Alabama at Birmingham, University of North Carolina, and Vanderbilt. The centers identified patients in their medical systems using either a search tool run against a central data warehouse or repository (e.g. i2b2) or a local ILD registry. Medical record reviewers abstracted the clinical data, including physician notes, CT scan and imaging results, lung pathology reports, and pulmonary Function tests (PFTs), into a case report form which was then adjudicated by two ILD experts (pulmonology and rheumatology). Discordance in adjudication was resolved by consensus. The positive predictive value (PPV), the primary outcome of the study, was calculated for each ILD algorithm for both prevalent and incident ILD and 95% confidence interval (CI) using a binomial distribution.

Results: We identified 264 linkable RA patients with sufficient data to evaluate for ILD. Overall, 115 (44.6%) of suspected cases (based on a highly sensitive case finding approach) were classified as ILD. The most common diagnosis codes identified in this initial search were 515 (Postinflammatory pulmonary fibrosis, 33%), 518.89 (Other disorders of lung, 24%), 714.81 (rheumatoid lung, 9%), 793.19 (Other nonspecific abnormal finding of lung field, 8%), and J84 (Other interstitial pulmonary diseases with fibrosis, 6%). 516 (Other alveolar and parietoalveolar pneumonopathy, 3%). A total of 36.0% of cases were hospitalized (4.9% primary diagnosis code, 31.1% non-primary diagnosis code), and the remainder were outpatient. The best performing algorithm for prevalent ILD had a PPV of 77% (95% CI 67%-85%) and for incident ILD was 74.2% (95% CI 58.9-89.6%).

Conclusion: ILD case finding in RA patients using administrative claims data is feasible and has reasonable accuracy. Both prevalent and incident ILD can be identified.

Disclosure: M. Guthrie, None; **A. Shah**, Beohringer-Ingelheim, 2, Bristol-Myers Squibb, 2, Reata, 2; **L. Lobo**, None; **J. Oates**, None; **C. Clinton**, None; **N. Annapureddy**, None; **F. Xie**, None; **B. England**, None; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5.

Abstract Number: 2339

Exposure to Avian and Fungal Antigens in Patients with Rheumatoid Arthritis-AssociatedInterstitial Lung Disease: Something to Keep in Mind

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis associated interstitial lung disease (RA-ILD) is an extra-articular manifestation with a poor prognosis. In clinical practice, to establish such a diagnosis requires to rule out other causes of ILD.

Usual interstitial pneumonia is the most common high-resolution computed tomography pattern found in RA-ILD and is indistinguishable from that of chronic hypersensitivity pneumonitis, an immune-mediated ILD that can result from the exposure to several widely recognized antigens.[1] To date, it is not known whether the determination of exposure to environmental factors known to cause lung fibrosis, such is the case of avian or fungi antigens, by measuring their antibodies (Ab) plays a role both in diagnosis and further management of patients with RA-ILD.

Our aim was to describe the frequency of significant levels of AA and AF Ab in a cohort of patients with RA-ILD.

Methods: We performed a cross-sectional study including all patients with RA according to the ACR 2010 classification criteria diagnosed with ILD from June 2014 to March 2019 on an ILD multidisciplinary committee of a tertiary referral centre.

Age (Mean ± SD, years)	67.3 ± 11
Sex (female)	26 (74.3%)
RA duration, (median (IQR), years)	9.91 (16.3)
Presence of erosions	24 (68.6%)
Ever-smokers	20 (57.1%)
Antibody status	
ACPA positive	30 (85.7%)
ACPA titres (median (IQR), CU)	873.6 (2020.4)
RF positive	27 (77.1%)
RF titres (median (IQR), IU)	200 (520)
ENA positive	3 (8.6%)
Anti-Ro (SSA)	3
Anti-La (SSB)	1
Type of ILD	
UIP	12 (34.3%)
NSIP	16 (45.7%)
COP	4 (11.4%)
RB-ILD	3 (8.6%)
ILD duration	1.95 (1.3)
Bronchiectasis	25 (71.4%)
Emphysema	14 (40%)
Current treatment	
GC	24 (68.6%)
csDMARD	23 (65.7%)
MTX	14 (40%)
LEF	10 (28.6%)
HCQ	5 (14.3%)
bDMARD	8 (22.9%)
ABA	5 (62.5%)
TCZ	3 (37.5%)
tsDMARD (Tofacitinib)	1 (2.9%)

Table 1. Main demographic and clinical features of included patients expressed as n (%). IQR: Interquartile range; CU: Chemiluminescence Units; IU: International Units; UIP: Usual Interstitial Pneumonia; NSIP: Non-specific Interstitial Pneumonia; COP: Cryptogenic Organising Pneumonia; RB-ILD: Respiratory Bronchiolitis associated ILD; MTX: Methotrexate; LEF: Leflunomide; HCQ: Hydroxychloroquine; ABA: Abatacept; TCZ: Tocilizumab.

All patients were evaluated using a standardized laboratory protocol including: red and white blood cell count, kidney and liver function tests, c-reactive protein, eritrosedimentation rate, rheumatoid factor (RF), antinuclear Ab, extractable nuclear antigens (ENA), ACPA (CCP2), anti-avian (AA) and anti-fungi (AF) Ab.

AA included specific IgG Ab against parakeet and parrot feathers and pigeon droppings and serum proteins. AF included Micropolyspora faeni, Thermoactinomyces vulgaris, Stachybotrys atra, Penicillium sp, Cladosporium herbarum, Aspergillus fumigatus, Candida albicans and Alternaria alternata Ab. Both groups were assessed by ImmunoCAP® IgG Specific (Thermo Fisher Diagnostics). Since there are no validated cut-off levels, we defined significant (positive) levels when above the p90 of the cohort's distribution for the AA or AF Ab with the highest frequency.

Results: 35 patients were included; their main demographic and clinical features are shown in table 1. 3 ENA-positive cases were found; 2 of them had high levels of RF and ACPA titers and the remaining had erosive disease.

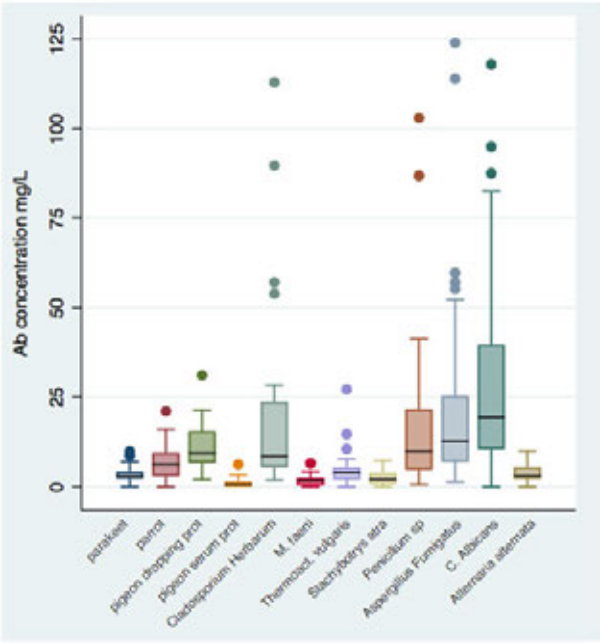

Figure 1. Summary of the distributions of AA and AF antibodies within the cohort M. faeni: Mycropolyspora faeni; Thermoact. vulgaris: Thermoactinomyces vulgaris

Antibodies against C. albicans, A. fumigatus, Penicillium spp, C. herbarum, and pigeon droppings proteins presented the highest levels within the cohort. A summary of the distribution of all Ab is shown in Figure 1.

Overall, 14 (40%) of patients had significant (positive) levels either AA or AF Ab according to our definition. 2 patients had double positivity, 2 had triple and 1 presented quadruple positivity; frequencies of each of the most represent-

Antibodies	n(%)	p90 (mg/L)
Anti-avian		
pigeon dropping proteins	7 (20%)	18
Anti-fungi		
Cladosporium Herbarum	4 (11.4%)	53.9
Penicilium spp	4 (11.4%)	36.1
Aspergillus Fumigatus	4 (11.4%)	57.1
Candida Albicans	4 (11.4%)	82.5
Total positive	14 (40%)	

Table 2. Frequency of patients having significant (positive) levels of antibodies. (Antibodies against parakeet, parrot, pigeon serum proteins, M faeni, St atra, T. vulgaris and A. Alternata antigens were excluded because of the low levels found).

atives Ab are shown in table 2. Of note, 5 out of 14 patients with reported positive Ab levels were not aware of any environmental exposure on anamnesis.

Conclusion: 40% of patients within our cohort presented significant levels of either AA or AF antibodies according to our strict definition. Adding these measurements to the routine work-up of RA-ILD could help the multidisciplinary team's diagnostic decisions. Further research is needed to determine their role in RA-ILD outcomes.

References:

1. Morell F, et al. Lancet Respir Med. 2013;1(9):685-94.

Disclosure: **S. Rodriguez-Garcia**, None; **R. Castellanos-Moreira**, None; **F. Hernández-González**, None; **A. Perez**, None; **J. Francesqui**, None; **S. Cuerpo-Cardeñosa**, None; **V. Ruiz-Esquide**, None; **M. Benegas**, None; **J. Ramírez**, None; **C. Lucena-Pozo**, None; **C. Agustí**, None; **M. Boada**, None; **E. Ruiz**, None; **O. Viñas**, None; **S. Prieto-González**, None; **R. Sanmarti**, None; **G. Espinosa**, None; **M. Pascal**, None; **J. Gomez-Puerta**, None; **M. Sánchez**, None; **J. Sellares**, None.

Abstract Number: 2340

Treatment of Interstitial Lung Disease and Airway Disease Complicated with Rheumatoid Arthritis

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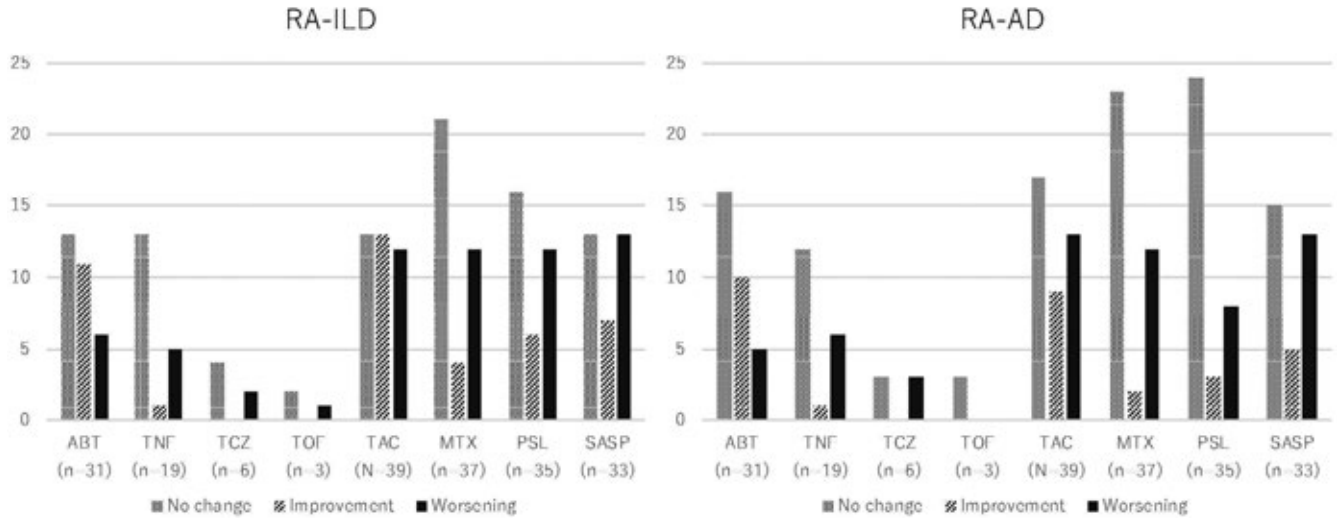
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) complicated with rheumatoid arthritis (RA) is detected in 27 to 67% of patients on high-resolution computed tomography (HRCT), and airway disease (AD) are detected in 39 to 60%. These contribute to an increase in the mortality rate in comparison with RA without respiratory complications. However, the most appropriate treatment for RA-ILD or AD has not been established. In this study, we examined the effectiveness of treatments for these disorders.

Methods: The subjects were consecutive RA patients with ILD and/or AD who were registered in the RA registry in our department between January 2015 and September 2017, and could be followed-up for ≥1 year after the start of intensified treatment. We investigated the clinical data, contents of treatment, imaging findings, and

Figure 1



prognosis after 1 year. HRCT assessment was blindly performed by two pulmonologists specializing in interstitial pneumonia.

Results: The subjects were 95 patients with RA-ILD and/or AD complicated with RA (36 males, 59 females, mean age: 70.0 ± 9.9 years). 87 patients had RA-ILD, 65 had AD, and 57 (60%) had both. 80 patients (84.2%) were positive for RF, and 77 (81%) were positive for ACPA. The mean KL-6 level was 332 U/mL[223-602]. The HRCT pattern was evaluated as UIP in 49 patients (51.6%), NSIP in 27 (28.4%), and others in 11 (11.6%). Concerning treatment, MTX was selected in 37 patients (38%), with a mean dose of 6.9 ± 2.4 mg. PSL was selected in 35 (36%), with a mean dose of 5.6 ± 3.1 mg. TAC was selected in 36 (37%), with a mean dose of 2.1 ± 0.8 mg. IGU, SASP, and BUC were selected in 2 (0.02%), 33 (34%), and 6 (0.06%) patients, respectively. bDMARDs and TOF were used in 61 patients (64%): INF, 3 patients (3%); ETN, 6 (6%); ADA, 5 (5%); GLM, 5 (5%); CTZ, 0 (0%); ABT, 29 (30%); TCZ, 5 (5%); and TOF, 3 (3%). Many patients received ABT. With respect to the prognosis after 1 year, ILD exacerbation on HRCT was correlated with the KL-6 level (p=0.054), but there was no correlation between the exacerbation of AD and KL-6 level (p=0.408). As shown in Figure 1, the improvement ratings of ABT and TAC were higher than that of PSL when investigating the treatment response on HRCT. However, those of TNF and MTX were extremely low.

Conclusion: To treat RA-ILD, biologics were used in 64% of the subjects, suggesting their safety. ABT and TAC may be useful for the treatment of RA-ILD or AD.

Disclosure: T. Shoda, None; **T. Takeuchi**, None; **T. Kotani**, None; **K. Nagai**, None; **K. Hata**, None; **S. Makino**, None; **S. Arawaka**, None.

Abstract Number: 2341

Findings of Pulmonary Abnormalities on High Resolution Computed Tomography in a Cohort of Rheumatoid Arthritis Patients Without Known Lung Disease

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SESSION INFORMATION
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Background/Purpose: Pulmonary manifestations of rheumatoid arthritis (RA) lead to significant morbidity and mortality. Lung manifestations in RA are myriad, however little is known about how to predict those patients at highest risk for development of clinically significant disease.

Methods: In this study we performed a screen for lung disease by high resolution computed tomography (HRCT) scan in a population of patients with RA without known interstitial lung disease. We also collected baseline demographics, clinical information and blood was tested for RA associated antibodies including anti-CCP3 (IgG), CCP3.1 (IgG/IgA), and RF. Chest imaging was reviewed and interpreted by two radiologists with expertise in thoracic radiology who independently reviewed all HRCT scans using a scoring algorithm supplied by the research investigators. For those interpretations which were discriminant between readers, the radiologists discussed the case and came to consensus. We compared demographics (gender, age, duration of RA) and antibody profiles between RA patients with abnormal imaging on HRCT and those who did not have pulmonary disease.

Results: We screened 55 patients from the rheumatology clinic at the University of Colorado, who denied having any lung disease, with HRCT. We found that 31% (n=17) of the patients had findings of pulmonary fibrosis (as defined by abnormal reticulations, evidence of traction bronchiectasis or honeycombing). These 17 patients were determined to have fibrosis in “possible” or “probable” usual interstitial pneumonia (UIP) pattern. We found that those patients with pulmonary fibrosis were older (65.3 vs 54.9 years, p=.007). There was no statistically significant difference in gender, smoking status, duration of RA or antibody profile between those with and without fibrosis. Of the 55 patients scanned, we also found that 62% (n=34) had airways disease as determined by consensus findings of air trapping and bronchial wall thickening without findings of emphysema. In this small cohort, there was no association between presence of airways disease and age, smoking status, duration of RA or antibody positivity.

Conclusion: In this at-risk population for lung disease, we found 31% of RA patients without known lung disease to have findings of pulmonary fibrosis and 62% to have HRCT findings of airways disease. Prospective study of an at risk population for development of lung disease may help inform screening methods.

TABLE 1			
	Fibrosis	No fibrosis	
	n=17, 31%	n=38	
Gender (male)	7, 41%	9, 24%	p=.213
AGE (mean)	65.3	54.9	p=.006
Smoking (ever)	11, 65%	18, 47%	p=.362
Time with RA dx	18.57 years	13.07 years	p=.195
CCP3	16, 94%	31, 82%	p=.411
CCP3.1	16, 94%	33, 87%	p=.654
RF positivity	14, 82%	30, 79%	p=1.0
	Airways dx	No airways dx	
	n=34, 62%	n=21	
Gender (male)	10, 29%	6, 29%	p=1.0
AGE (mean)	60.4	54.6	p=.122
Smoking (ever)	21, 60%	8, 38%	p=.103
CCP3	29, 85%	18, 85%	p=1.0
CCP3.1	31, 91%	18, 85%	p=1.0
RF positivity	28, 82%	16, 76%	p=1.0

Disclosure: **S. Matson**, None; **K. Deane**, Bristol-Myers Squibb, 5, Inova, 9, Janssen, 2, 5, Janssen R&D, 2, Microdrop, 5, Pfizer, 2; **C. Collora**, None; **X. Zheng**, None; **M. Fester**, None; **J. Lee**, None; **M. Demoruelle**, Pfizer, 2.

Abstract Number: 2342

Association of Serum KL-6 Level and Change of Pulmonary Function in Interstitial Lung Disease of Rheumatoid Arthritis - Data from Prospective KOrean Rheumatoid Arthritis Interstitial Lung Disease (KORAIL) Study

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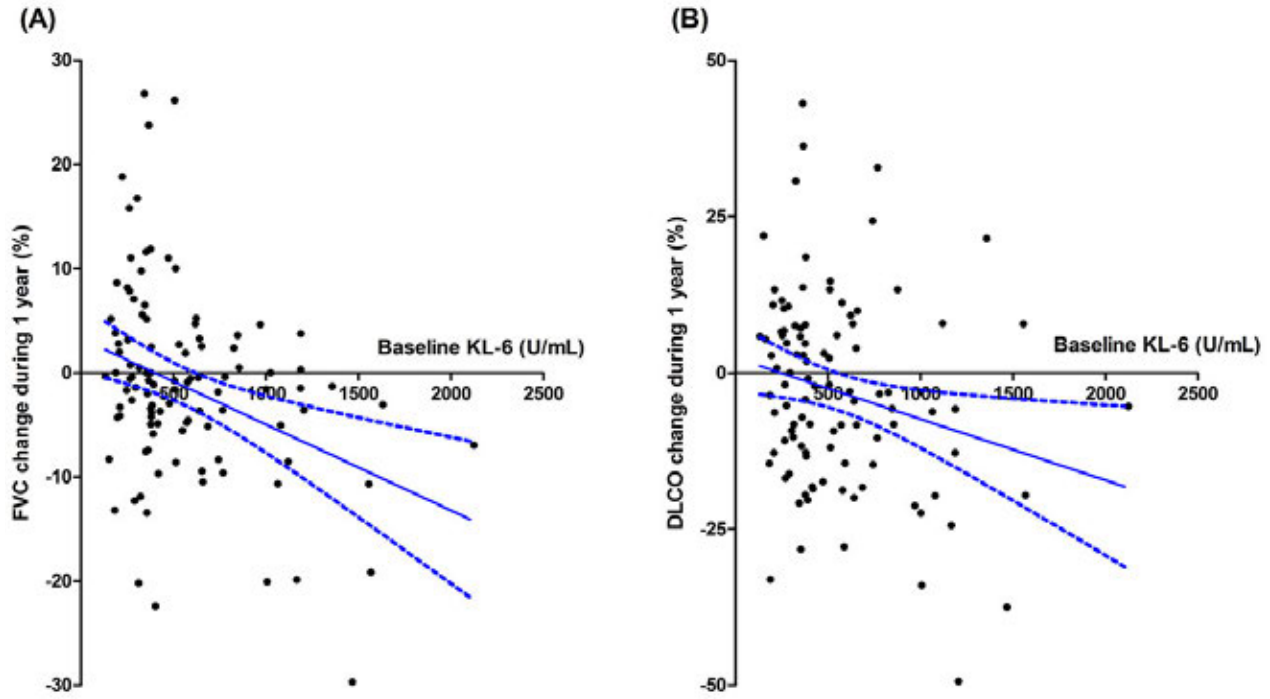
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is the most common lung disease among rheumatoid arthritis (RA) patients. Although the overall mortality rates for RA have decreased in general, ILD is associated with increased morbidity and mortality of RA patients, especially in older age groups. We have launched a multicenter prospective cohort of RA-ILD named as KOrean Rheumatoid Arthritis Interstitial Lung disease (KORAIL) cohort, to explore clinical prognosis using biomarkers and imaging modalities. This is the first disclosure of results originated from KORAIL cohort.

To describe general clinical characteristics of KORAIL cohort. To elucidate the role of serum concentration of Krebs von den Lungen-6 (KL-6), a potential biomarker of ILD, in evaluation of current status and prediction of functional change during first 1 year after enrollment. The association between KL-6 concentration and inflammatory cytokines were also investigated.

Methods: Entering clinical information to e-case report form, chest CT, pulmonary function test, and blood samples were conducted at baseline and followed every year. Serum KL-6 concentration (U/mL) was measured through the Nanopia KL-6 assay latex-enhanced immunoturbidimetric assay method. Multiplex ELISA was used to measure serum concentration of TNF-alpha, IL-6, GM-CSF, and IL-17.

Results: One hundred and sixty eight patients with RA-ILD have been enrolled from six university hospitals in Korea. Till January 2019, 129 patients (76.8%) were followed for 1 year, 71 patients (42.3%) for 2 years, and 21 patients



Higher baseline KL-6 could predict functional deterioration of RA-ILD in next 1 year

(12.5%) for 3 years. RA was diagnosed at 58.7±11.3 (mean±SD, years old), ILD at 63.7±8.6, and enrolled at 66.4±8.0. Baseline KL-6 was significantly associated with baseline DLCO (r=-0.196, p=0.029), 1 year change(%) of FVC (r=-0.319, p=0.001) (figure A) and DLCO (r=-0.191, p=0.048)(figure B). TNF-alpha, IL-6, GM-CSF, and IL-17 had no association with functional deterioration or KL-6.

Conclusion: KL-6 could predict functional deterioration of RA-ILD in next 1 year.

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Abstract Number: 2343

Treatment with Biologic DMARDs Does Not Increase Risk of Severe Pulmonary Events in Patients with Rheumatoid Arthritis and Pre-existing Lung Disease

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary complication is one of the leading causes of mortality in patients with rheumatoid arthritis (RA). Pre-existing lung disease is known as a risk factor for development of severe pulmonary events during treatment with synthetic and biologic disease-modifying anti-rheumatic drugs (DMARDs). However, it remains unknown whether risk of severe pulmonary events is higher in patients treated with biologic DMARDs (bDMARDs) than those without, in the setting of pre-existing lung disease. This study is aimed to clarify this clinical question by using single-center cohort data.

Methods: This study used RA patients registered in a cohort enrolling consecutive patients with RA at Nippon Medical School Hospital, based on the following criteria: satisfaction of 2010 ACR/EULAR classification criteria; pre-existing lung disease, including interstitial lung disease (ILD), chronic obstructive pulmonary disease (COPD), bronchial asthma, airway disease such as bronchiectasisand bronchiolitis, and lung infection such as pulmonary non-tuberculosis mycobacteria (NTM)confirmed by chest CT; and follow-up of at least 52 weeks after chest CT imaging. Severe pulmonary event was defined by newly onset or reactivation pulmonary infection, newly onset or exacerbation of ILD, and drug-induced lung injury that require therapeutic intervention. Baseline characteristics and concomitant treatmentwere compared between patients treated with and without bDMARDs, Then, baseline characteristics and concomitant treatment were matched using the propensity score method. Cumulative rates for severe pulmonary events were compared using Kalan-Meier method, and statistical difference between 2 groups was tested by log-rank test.

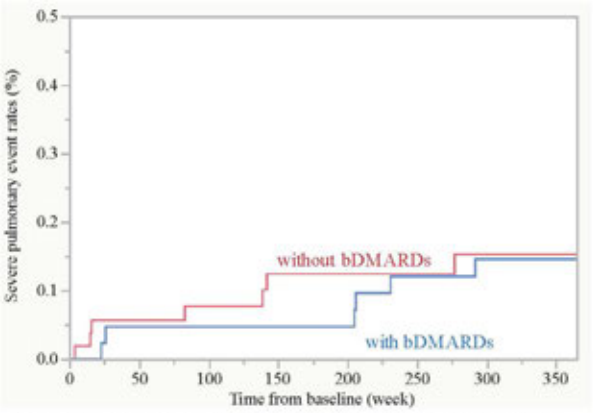

Figure 1A. Severe pulmonary event rates between patients treated with and without bDMARDs in a crude analysis.

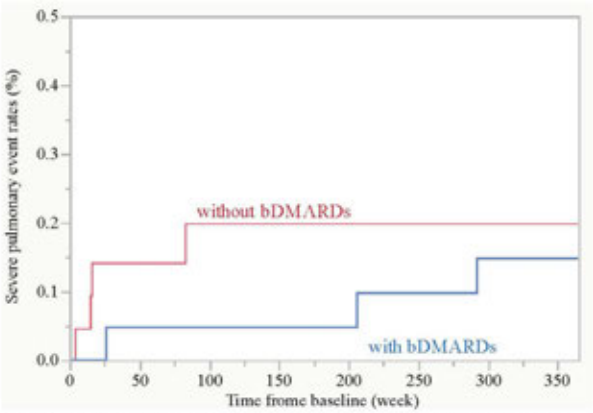

Figure 1B. Severe pulmonary event rates between patients treated with and without bDMARDs by matching baseline characteristics and concomitant treatment using the propensity score method.

Results: This study analyzed 99 patients with RA and pre-existing lung disease. The median age at enrollment was 73 years, and 59% were female. Pre-existing lung diseases included airway disease in 61, ILD in 44, COPD in 22, pulmonary NTM in 4, and bronchial asthma in one.During the follow-up of 52 weeks, 45 patients received 1 or 2 bDMARDs (TNF inhibitors in 15, abatacept in 19, and tocilizumab in 13), while the remaining 54 patients did not. A total of 17 severe pulmonary events occurred in 14 patients (9 pneumonia, 5 worsening of ILD, 2 drug-induced lung injury, and one *Pneumocystis jiroveci*pneumonia). In a crude analysis, there was no difference of cumulative severe pulmonary event rates between patients treated with and without bDMARD (15% versus 15% at 52 weeks, P = 0.81; Figure 1A). Younger age, higher KL-6, and higher anti-CCP antibody titer were significantly associated with use of bDMARDs, but methotrexate and corticosteroids were used similarly between the 2 groups. After propensity score matching by employing age, KL-6, and anti-CCP antibody titer, severe pulmonary event rates were still comparable between patients treated with and without bDMARDs (15% and 20% at 52 weeks, P = 0.54; Figure 1B).

Conclusion: Use of bDMARDs was not associated with increased risk of severe pulmonary events in RA patients with pre-existing lung disease, while this finding should be validated by independent multicenter cohorts.

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Abstract Number: 2344

Efficacy of Mycophenolate Mofetil in the Treatment of Rheumatoid Arthritis Associated Interstitial Lung Disease

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) as an extra-articular manifestation of rheumatoid arthritis (RA) leads to significant morbidity and mortality. As data is limited, this study aims to investigate the efficacy of mycophenolate mofetil (MMF) in the treatment of RA associated ILD.

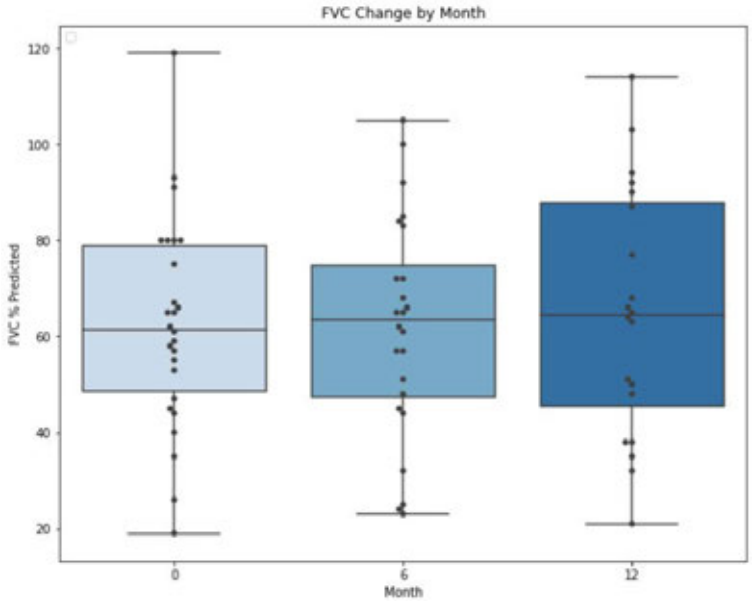
Methods: This retrospective chart review identified patients with a clinical diagnosis of RA and ILD at a single tertiary academic medical center who were treated with MMF for at least 3 months between 1/01/2005 and 12/31/2018. Patients were identified by diagnosis codes, then reviewed to confirm clinical diagnoses and to collect data on concurrent therapies, pulmonary function, infections and hospitalizations.

Results: Twenty six patients were identified; 17 female (65.4%) and 23 Caucasian (88.5%) with a mean age of 57.8 at the time of diagnosis of RA. RF was positive in 20 (76.9%), ACPA in 16 (61.5%) and 10 (38.5%) were seropositive for both, while 3 (11.5%) patients were seronegative. The mean time to diagnosis of ILD after diagnosis of RA was 40.6 months with a range of -50 to 504 months. Seven (26.9%) patients had an ILD diagnosis prior to RA.

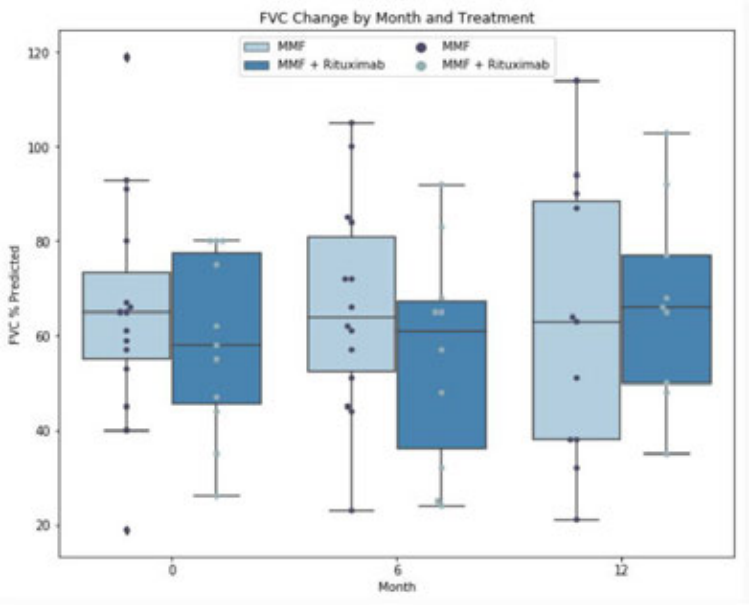
Fourteen (53.8%) patients had usual interstitial pneumonia (UIP), 5 (19.2%) nonspecific interstitial pneumonia (NSIP), 3 (11.5%) organizing pneumonia (OP), and 4 (15.4%) had other forms such as mixed UIP and NSIP. The average duration of MMF therapy was 24.9 months with an average maximum daily dose of 2163.5mg. Eleven (42.3%) patients were concurrently on rituximab (RTX), 1 (3.85%) on methotrexate, 1 (3.85%) on certolizumab, and 1 (3.85%) on sulfasalazine. Fifteen (57.7%) patients were on prednisone ≥10mg daily and 6 (23.1%) were on < 10mg daily for at least one month.

Average FVC for all patients was 62.4 ± 21.9% predicted at the time of initiation of MMF, 61.9% ± 23.0 predicted at 6 months (p=0.95), and 64.8% ± 25.9 predicted at 12 months (p=0.67). In aggregate, 13 (50%) patients on MMF had stable or improved FVC over the 12-month period, of whom 6/13 (46.2%) were on concurrent RTX. Six of 11 (54.5%) patients on combination MMF and RTX had stable or improved FVC over the 12-month period.

There were 26 hospitalizations in 8 (30.8%) patients; 17 (65.4%) for infections, 3 (11.5%) for respiratory failure, and 6 (23.1%) for cardiovascular events. Twenty four (92.3%) hospitalizations were in the combination MMF and RTX treatment group, including all infection related admissions. There were 10 outpatient infections treat-



Boxplot diagram showing the FVC percent predicted for all patients at the time of initiation of mycophenolate mofetil, at 6 months, and at 12 months



Boxplot diagram showing the comparison of the FVC percent predicted for patients on MMF without rituximab, compared to patients on combination therapy with mycophenolate mofetil and rituximab, at the time of initiation of mycophenolate mofetil, at 6 months, and at 12 months.

ed with antimicrobials. There were 8 (30.8%) deaths; 6 were in the MMF and RTX combination group. Two deaths were from infection and ILD, 2 from infection, 2 from cardiac disease, 1 from ILD, and 1 from myasthenia gravis crisis.

Conclusion: In this cohort of 26 RA patients with ILD, treatment with MMF as mono or combination therapy with RTX was associated with a stable or improved FVC in 50% of patients at 12-month. About 55% of patients on combination MMF and RTX showed stability or improvement in FVC. Patients treated with MMF compared to combination MMF and RTX had similar FVC values at the end of the study period, however, the combination therapy had more hospital admissions and infections. Further studies are needed to better understand the efficacy and safety of MMF or combination therapy with RTX in RA associated ILD.

Disclosure: J. Amos, None; **J. Kendall**, None; **R. Moran**, None; **M. Krause**, None; **P. Schmidt**, None; **C. Hall**, None; **M. Hamblin**, None; **M. Maz**, None.

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Abatacept in Rheumatoid Arthritis with Interstitial Lung Disease: A Retrospective Multicenter Study of 263 Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial Lung Disease (ILD) is a severe extraarticular manifestation of rheumatoid arthritis (RA).

Interstitial lung disease (ILD) associated with Rheumatoid Arthritis (RA) has a poor prognosis. Effectives treatments in RA such as anti-TNF have been implicated in the exacerbation of ILD.

Our objective was see the efficacy of Abatacept in ILD associated with RA.

Methods: Retrospective multicenter study of RA patients with ILD treated with ABA atleast for 3 doses. The ILD was diagnosed by HRCT. We have analyzed the following variables: **a)** 1-point change the Modified Medical Research Council (MMRC); **b)** FVC improvement or decline ≥10%; improvement or decrline ≥10% in DLCO **c)** radiological improvement in HRCT scan, **d)** changes in DAS28 score. **e)** prednisone dose. Values were compared with baseline.

Results: We studied 263 patients (150 women /113 men) with ILD associated to RA. The patients were smokers or exsmoker in a 53%. APCC was positive in 88.6%. The follow-up mean was 22.66±19.66 months.

Figure 1	
MMRC, Available data 230	
-Stable	73,4%
-Improvement	20,9%
-Worsening	5,7%
FVC, Available data 162	
-Stable	75,3%
-Improvement	12.3%
-Worsening	12,3%
DLCO, Available data 140	
-Stable	75,7%
-Improvement	15%
-Worsening	9,3%
HRCT, avalaible data 128	
-Stable	57,8%
-Improvement	18,8%
-Worsening	23,4%

The mean age was 64.64 ± 10 years. The median to progression of ILD was 12 [3-41.25] months. The mean DLCO at onset was 65,68±18.33 and the FVC at onset was 85.88±21.77 111 patients were treated in monotherapy.

The most frequent pattern was UIP 41,6% 32,7% NSIP 24,7% “others” thats include mixed patterns BONO or BO.

The Figure1 expresses the evolution of the avalible data.

DAS28 also improved from 4.501±1.486 to 3.107±1.333 and we also appreciate a decrease in the dose of prednisone from the initial mean 7.5 [5-10] to the final mean 5mg [5-7.5]. The global mean of FVC at the end of follow up was 85.3±20.69 the global mean of DLCO at the end of follow up was 65.35±19.88 both similar to the onset mean.

Conclusion: Abatacept could be a relatively safe and effective treatment for patients with interstitial lung involvement associated with rheumatoid arthritis. However, should be verified in prospective and randomized studies.

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Abstract Number: 2346

Interstitial Lung Abnormalities in Rheumatoid Arthritis Patients: Identifying Associated Risk Factors

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Table 1: Baseline characteristics of patients stratified by presence/absence of ILA

	ILA (n=64)	No ILA (n=204)	p-value
Age (years)	**65.6** ± 9.9	**59.5** ± 10.9	**0.001**
Female	46 (**72%**)	175 (**86%**)	**0.023**
Smoking, ever	29 (**45%**)	60/197 (**30%**)	**0.034**
Pack.years	24.6 ± 18.8	27.3 ± 18.1	0.523
Disease duration (years)	11.3 ± 10.5	13.1 ± 10.4	0.237
DAS28-ESR	3.8 ± 1.8	4.2 ± 1.6	0.116
RF positive	45 (87%)	113 (74%)	0.07
RF	216 ± 122	217 ± 193	0.976
Anti-CCP positive	39 (75%)	141 (74%)	0.88
Anti-CCP titer (UI/ml)	334 ± 464	248 ± 317	0.216
Methotrexate use (%)	57 (89%)	194 (95%)	0.08
Any anti-TNF use (%) b	**16 (25%)**	**99 (49%)**	**0.001**
• **Infliximab**	**11 (17%)**	**67 (33%)**	**0.018**
• **Etanercept**	**6 (9%)**	**44 (22%)**	**0.028**
• **Adalimumab**	**5 (8%)**	**45 (22%)**	**0.01**
• **Golimumab**	0 (0%)	6 (2.9%)	0.341
• **Certolizumab**	0 (0%)	7 (3.4%)	0.201
Tocilizumab	2 (3%)	25 (12%)	0.033
Rituximab	10 (16%)	45 (22%)	0.292
Abatacept	8 (13%)	48 (24%)	0.055
Tofacitinib	1 (2%)	5 (2%)	1.00

Data presented as absolute counts (%) or mean ± standard deviation.

Abbreviations: ILA: Interstitial Lung Abnormalities; DAS28: disease activity score-28; ESR: erythrocyte sedimentation rate; RF: rheumatoid factor; CCP: cyclic citrullinated peptide; DMARD: disease modifying anti-rheumatic drugs. **Missing data (ILA / no ILA):** Ever smoking (n=0 / n=7), RF (n=12 / n=52), CCP (n=12 / n=14)

Table 2: Pattern of ILA in RA patients, excluding cases where clinical status could not be determined (n = 3).

Pattern of distribution	ILA (n = 61)
Subpleural	34 (56%)
Centrilobular	8 (13%)
Mixed	9 (15%)
Extensive	10 (16%)

Data presented as absolute counts.

Abbreviations: RA: Rheumatoid arthritis; ILA: Interstitial Lung Abnormalities

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

Background/Purpose: A wide spectrum of interstitial lung abnormalities (ILA) occurs in patients with rheumatoid arthritis (RA). This study characterized ILA in large single-center cohort, including identification of risk factors and parameters that may influence ILA´s progression.

Methods: All clinically-indicated computed tomography (CT) chest scans performed in adult RA patients from 2014-16 were evaluated for the presence of ILA using a sequential reading method. ILA were defined as nondependent changes affecting more than 5% of any lung zone and included nondependent ground-glass or reticular opacities, diffuse centrilobular nodularity, nonemphysematous cysts, honeycombing or traction bronchiectasis. Scans were classified as (a) no ILA, (b) indeterminate (focal alterations with less than 5% involvement of the lung) or (c) ILA; ILA were further subdivided into subpleural, centrilobular, mixed, and extensive distributions.The progression of ILA was determined visually and subsequently quantified by two independent observers blinded to clinical information. Univariate analyses were conducted with Fisher exact test and two-tailed t-tests or Wilcoxon rank-sum tests where appropriate. For multivariate analyses, unadjusted and adjusted logistic regression models were used to assess the strength of the association between RA-ILA and variables of interest. P-values < 0.05 were considered statistically significant.

Results: 293 patients were scored for the presence of ILA. Chest CT were mostly indicated due to respiratory signs and/or symptoms (n = 131), but also not related to pulmonary indications (n = 115), and reasons not identified (n = 44). Twenty -five patients (9%) that presented indeterminate ILA were excluded from the analysis, remaining 268 patients. Sixty-four (22%) presented ILA, predominantly older male smokers, and less likely on biologics/small molecule disease-modifying anti-rheumatic drugs **(table 1)**. The most common pattern of distribution observed was subpleural **(table 2).** Among ILA, 15 (43%) had usual interstitial pneumonia (UIP) or probable UIP on CT, 5 (14%) had

Table 3: Characteristics of subjects with baseline ILA and available sequential CT (n=56) stratified into progressors vs. non-progressors

	Progressor (n = 21)	Non-progressor (n = 35)	p-value
Baseline characteristics			
Age (years)	65 ± 9.4	66 ± 9.9	0.71
Female	17 (81%)	25 (71%)	0.40
Ever Smoking	10 (48%)	14 (40%)	0.56
Pack years	23 [13 – 41]	28 [20 – 40]	0.46
RA duration (years)	6.5 [3 – 21]	7 [2 – 17]	0.51
DAS28-ESR	3.8 ± 1.6	3.9 ± 1.9	0.84
RF positivity	17 (94%)	20 (74%)	0.09
RF titer (UI/ml)	235 ± 132	208 ± 107	0.45
ACPA positivity	12 (70%)	22 (78%)	0.55
ACPA titer (UI/ml)	375 [.210 – 392]	259 [188 – 394]	0.46
Methotrexate use	20 (95%)	29 (83%)	0.19
Biologics/small molecule DMARD use[a]	8 (38%)	11 (31%)	0.59
Anti TNF use [b]	5 (24%)	8(23%)	1.0
Follow up			
Time between baseline and follow-up CT scans (years)	4.9 ± 2	4.1 ± 2.4	0.20
ILA involvement, baseline (extension)	**11% [6 – 24]**	**4% [2.5 – 7.5]**	**0.001**
Death	9 (43%)	8 (23%)	0.31

Data presented as absolute counts (%), mean ± standard deviation, or median [interquartile range].

[a] Infliximab, etanercept, adalimumab, golimumab, certolizumab tocilizumab, rituximab, abatacept, and tofacitinib.

[b] infliximab, etanercept, adalimumab, golimumab, certolizumab

Missing data (Progressor / Non-progressor): RF (n=3 / n=8), ACPA (n=4 / n=7)

Abbreviations: ILA: interstitial lung abnormalities; RA: rheumatoid arthritis; DAS: disease activity score; ERS: erythrocyte sedimentation rate; RF: rheumatoid factor; ACPA: anti-citrullinated protein antibodies; DMARD: disease modifying anti-rheumatic drugs; CT: computed tomography.

nonspecific interstitial pneumonia (NSIP), and 15 (43%) had an unclassifiable pattern. Of the 56 ILA patients with sequential CTs, 38% had evidence of radiologic progression over 4.4 years.

Comparing “progressors group” with “non-progressors group”, the only statistically significant difference among the two groups was a higher median baseline ILA involvement in “progressors”. **(table 3)**

Conclusion: We identified that ILA in RA patients is characterized predominantly by UIP in a subpleural pattern, with an impressive high rate of progression in approximately four years. A lower frequency of biological/small molecules drugs in the non-ILA group is probably explained by a bias of indication due to pulmonary comorbidities. Greater baseline ILA extent, but not RA treatment (even methotrexate and anti TNF), was the most important risk factor for progression. Active surveillance is therefore recommended for these patients.

Disclosure: K. Bonfiglioli, None; **M. Sawamura**, None; **R. Nakagawa**, None; **F. Arimura**, None; **D. Rangel**, None; **C. Bueno**, None; **A. Ribeiro**, None; **C. Carvalho**, None; **E. Bonfa**, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #305068/2014-8), 2, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4 and #2010/10749-0), 2; **R. Kairalla**, None; **L. Kawano-Dourado**, Bristol-Myers-Squibb, 2, 5, Boehringer, 8, Roche, 8.

Abstract Number: 2347

Long-term Survival in Lung Transplantation and Allograft Rejection in Patients with Interstitial Lung Disease Related with Rheumatoid Arthritis: Study from a Single Referral Center

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a leading cause of death in patients with rheumatoid arthritis (RA). In end-stage RA-ILD, lung transplant becomes the only option for these patients. However, there are concerns about worse outcomes and a higher risk of allograft dysfunction in patients with RA after lung transplantation due to the underlying immune dysregulation in this population. The main aim was to assess post-transplant survival in patients with RA-ILD compared with patients with idiopathic pulmonary fibrosis (IPF). Secondary outcomes included rate of acute rejection and chronic rejection.

Methods: Single center study in a referral center for lung transplant of all patients with RA-ILD who underwent lung transplantation from 2008 to 2017 compared with a control group of patients with IPF matched for age, transplant year and basiliximab induction. Cumulative survival rates after lung transplantation were estimated by the Kaplan-Meier method and compared between groups using the log-rank test. Distributions of categorical variables were compared by Pearson Chi2 or Fisher exact test as appropriate.

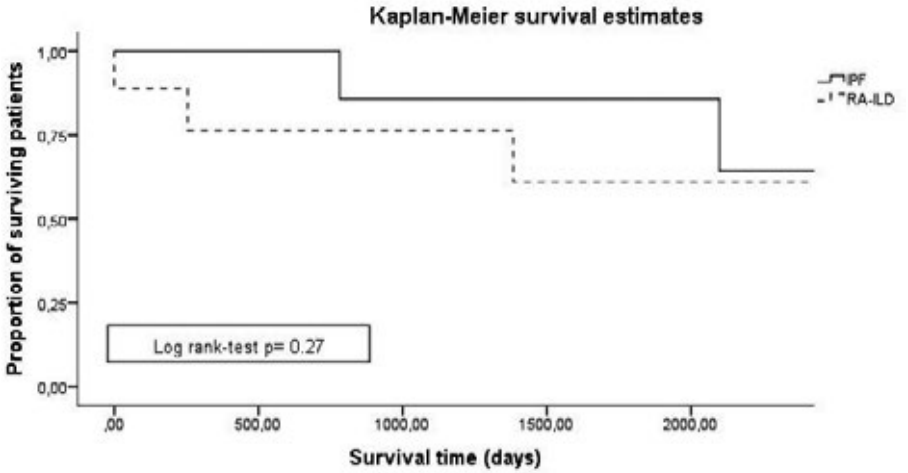
Results: Patients with RA-ILD (n=9) had similar baseline characteristics than IPF patients (n=9) which are shown in the **TABLE**. All patients with RA showed the histological subtype of usual interstitial pneumonia. RA-ILD patients

TABLE

	IPF (n=9)	RA-ILD (n=9)	P
Age *(years)*, mean ± SD	60.9 ± 5.1	58.2 ± 10.2	0.86
Sex *(women)*, *n (%)*	4 (44.4)	6 (66.7)	0.64
Time on waiting list (*days*), median [IQR]	99.0 [14.5-345.0]	90.0 [35.0-161.3]	0.92
Smokers, n (%)	5 (55.6)	6 (66.7)	0.99
Type of transplant (*bilateral*), n (%)	3 (33.3)	4 (44.4)	0.99
Donor CMV + and recipient CMV -, n (%)	2 (22.2)	1 (11.1)	0.45
Basiliximab induction, n (%)	2 (22.2)	2 (22.2)	0.99
Variables at transplant			
FEV 1 (%), median [IQR]	55 [34.0-82.6]	52 [41.8-66.3]	0.97
FVC (%), median [IQR]	53 [36.0-72.3]	57 [44.7-71.8]	0.36
FEV1/FVC, median [IQR]	82 [79.0-84.0]	78 [72.0-96.0]	0.74
DLCO	34 [23.0-40.0]	39 [32.0-64.5]	0.17
KCO	65 [52.0-70.0]	74 [63.0-100.0]	0.09
Serum creatinine (*mg/dL*), mean ± SD	0.79 ± 0.16	0.73 ± 0.28	0.37
Right catheterization, n (%)	4 (44.4)	6 (66.7)	0.64
mPAP (*mm Hg*), mean ± SD	21.0 ± 2.7	30.8 ± 8.9	0.15
PCP (*mm Hg*), mean ± SD	11.7 ± 1.5	13.7 ± 3.6	0.60
Treatment pre-transplant			
Glucocorticoids, n (%)	6 (66.7)	8 (88.9)	0.58
Immunosuppressive drugs, n (%)	2 (22.2)	9 (100.0)	0.002
Allograft dysfunction			
Acute rejection	7 (77.8)	4 (44.4)	0.34
Chronic rejection	1 (11.1)	2 (22.2)	0.45

DLCO: diffusing capacity of lung for carbon monoxide; IFP: idiopathic pulmonary fibrosis; ILD: associated interstitial lung disease; KCO: transfer coefficient of the lung for carbon monoxide; RA-ILD: rheumatoid arthritis-ILD; mPAP: mean pulmonary arterial pressure; PCP: pulmonary capillary pressure.

tended to experience acute graft rejection less commonly than those with IPF (77.8% vs 44.4%; p=0.34). However, a non-statistically significant increased frequency of chronic graft rejection was observed in the group of RA-ILD (11.1% vs 22.2%; p=0.45). Cumulative survival rates at 5 year post-transplant did no differ significantly between RA-ILD and IFP [61.0% vs 85.7% (p=0.27)] **(FIGURE 1)**.



Conclusion: Patients who underwent lung transplantation for RA-ILD in our center showed a trend to lower long-term post-transplant survival than in those with IPF. This could be explained by an increased frequency of chronic graft rejection. However, in selected candidates, RA-ILD should not be considered a contraindication for lung transplantation.

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Abstract Number: 2348

KL-6 Is a Useful Marker to Monitor the Progression of RA-ILD, but Not to Diagnose or Predict the Development of ILD

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
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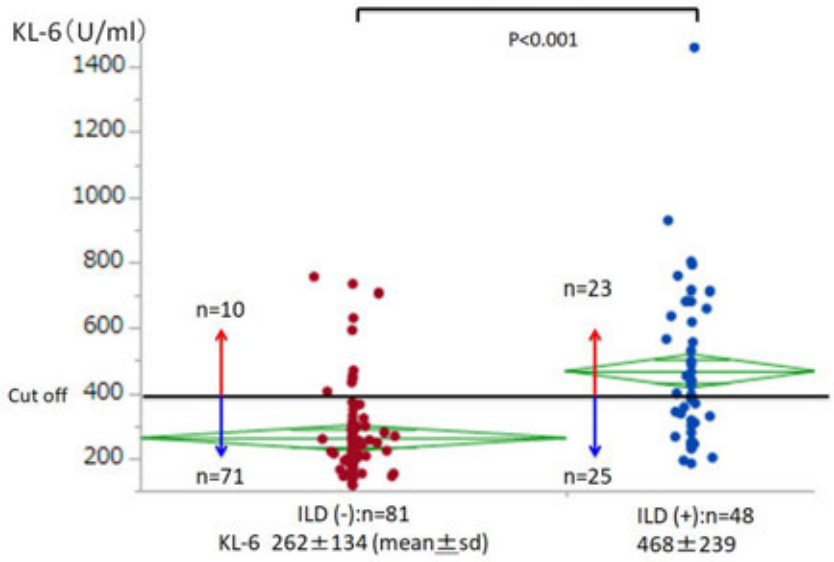
Background/Purpose: Interstitial lung disease (ILD) is a critical comorbidity in RA. To manage RA-ILD, early diagnosis and monitoring disease progression are important. KL-6 is a marker of disease activity of ILD including CTD-ILD such as scleroderma. However, clinical values of KL-6 in the management of RA remain to be elucidated. The purpose of this study is to determine whether KL-6 elevation is useful to diagnose ILD, whether KL-6 elevation predicts newly developing/worsening ILD, and to whether KL-6 increase is associated with developing/worsening ILD.



Serum KL-6 levels in RA patients with/ without ILD

Methods:: A retrospective cohort study. Subjects were consecutive RA patients who started first biologic at Dokkyo Medical University Hospital and received HR-CT examination before and during biologics therapy and serum KL-6 levels were measured before the therapy. Medical records were reviewed retrospectively. Chest radiography was taken before biologics. When KL-6 levels were above 400 U/ml, KL-6 was judged as elevated. CT findings were accepted gold standard for the existence of ILD.

Results: Subjects were 129 patients, M/F; 44/85, mean age; 51.6year old, disease duration; 7.9 years, and RF-positivity; 83%. Chest radiography was taken in 107 cases. A sequential KL-6 examination was carried out in 86 cases. ILD was found in 48 patients (37%). At the entry, KL-6 levels were 468±239 U/ml in ILD group and 262±134 U/ml in non-ILD one (Fig.1). KL-6 elevation was found in 10/81 (11.3%) of non-ILD patients and in 23/48 (48%) of ILD ones.

The sensitivity, specificity, PPV and NPV of KL-6 to detect ILD were 0.47 0.70, 0.70 and 0.73, respectively, while the specificity, specificity, PPV and NPV of chest radiography were 0.6, 0.87, 0.67 and 0.65, respectively.

KL-6 at the entry failed to predict development/worsening of ILD. Newly emerging/ worsening ILD was found in 31/129 (24%) in whole. Newly emerging ILD was found similarly in 3/10 (30%) of patients with KL-6 elevation and 10/71 (14%) of those without elevation in non-ILD group (p=0.20). Worsening ILD was observed in 6/23 (26%) of patients with KL-6 elevation and 11/25 (44%) of those without the elevation in ILD group (p=0.23).

Increasing KL-6 levels during the observation period was associated with development/ worsening of ILD, which were observed in 23/50 (46%) of patients with KL-6 increase and 3/36 (8%) of those without the increase (p=0.0002). Similarly, development of ILD was found in 12/29 (41%) of non-ILD patients with KL-6 increase and 2/23 (9%) of those without the increase (P=0.009), and worsening of ILD was observed in 11/21 (52%) of ILD patients with KL-6 increase and 1/13(8%) of those without the increase (P=0.008).

Conclusion: KL-6 levels were increased in RA with ILD. However, KL-6 elevation was found in non-ILD patients, and there were ILD patients without KL-6 elevation. The ability of KL-6 to detect ILD is low like chest radiography. KL-6 elevation failed to predict development/worsening of ILD. However, the increase in KL-6 level is associated with development/worsening of ILD. Thus, KL-6 is a useful marker to monitor activity of ILD, but not to diagnose and predict it.

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Abstract Number: 2349

Epidemiology, Risk/Prognostic Factors, and Treatment Landscape in Rheumatoid Arthritis-Associated Interstitial Lung Disease: A Systematic Literature Review

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities
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Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is the most common lung manifestation of RA and the 2nd leading cause of death in RA patients.[1,2] The purpose of this literature review was to characterize the epidemiology, risk/prognostic factors, and treatment landscape of rheumatoid arthritis-associated interstitial lung disease (RA-ILD).

Methods: A systematic literature review was conducted by searching MEDLINE, Embase, and Cochrane CENTRAL (inception-Dec 26, 2018) supplemented by conference proceedings from ACR and EULAR, and US and European clinical trial registries (2016 to 2018). Randomized controlled trials (RCTs), non-randomized clinical trials, and observational studies that investigated therapies for adults with RA-ILD and reported efficacy and safety outcomes were

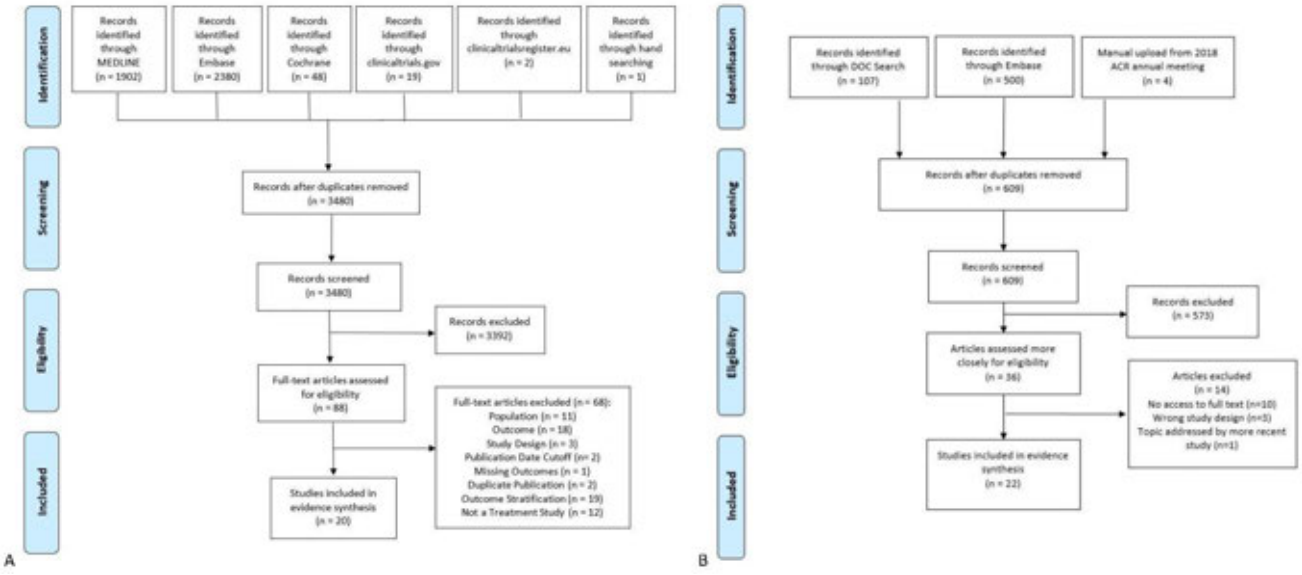

Fig 1AB
Figure: 1A PRISMA diagram for review on treatments; 1B PRISMA diagram for review on epidemiology and risk/prognostic factors

Interventions	Number of Studies	Study Design
Abatacept	4	2 Observational Non-Comparative 2 Retrospective Cohort
Rituximab	3	2 Observational Non-Comparative 1 Retrospective Cohort
Methotrexate	2	1 Case-Control 1 Observational Non-Comparative
Rituximab + Methylprednisolone +/- Conventional Disease-Modifying Antirheumatic Drugs (cDMARDs)[a]	2	2 Observational Non-Comparative
Tocilizumab	2	1 Case-Control 1 Retrospective Cohort
Tumor Necrosis Factor Inhibitors	2	1 Observational Non-Comparative 1 Retrospective Cohort
Abatacept +/- cDMARDs[b]	1	Observational Non-Comparative
Abatacept +/- Immunosuppressor	1	Observational Non-Comparative
Disease-Modifying Antirheumatic Drugs (DMARDs)[c]	1	Observational Non-Comparative
Infliximab + Leflunomide	1	Observational Non-Comparative
Leflunomide	1	Observational Non-Comparative
Methotrexate + Etanercept	1	Observational Non-Comparative
Methotrexate +/- Hydroxychloroquine	1	Prospective Cohort
Mycophenolate Mofetil	1	Observational Non-Comparative
Mycophenolate Mofetil + background Prednisone	1	Observational Non-Comparative
Penicillamine + Prednisone	1	Non-Controlled Clinical Trial
Rituximab + Methylprednisolone	1	Observational Non-Comparative
Sulfasalazine	1	Observational Non-Comparative
Tocilizumab +/- cDMARDs[d]	1	Observational Non-Comparative
Tumor Necrosis Factor Inhibitors + Methotrexate	1	Prospective Cohort

[a] azathioprine, hydroxychloroquine, leflunomide, methotrexate, mycophenolate mofetil, and sulfasalazine

[b] azathioprine, hydroxychloroquine, hydroxychloroquine + leflunomide, leflunomide, leflunomide + cyclosporine, methotrexate, methotrexate + leflunomide, and sulfasalazine

[c] abatacept, adalimumab, azathioprine, etanercept, hydroxychloroquine, infliximab, leflunomide, methotrexate, methotrexate + hydroxychloroquine, mycophenolate mofetil, rituximab, sulfasalazine, and tocilizumab

[d] azathioprine, leflunomide, and methotrexate

Table 1: Breakdown of study count per intervention

included. This was supplemented by a comprehensive search using Doctor Evidence LLC's proprietary search platform (DOC Search) containing MEDLINE, clinicaltrials.gov, WHO-ICTRP, EPAR, Daily Med, and RSS feeds, targeting the most relevant literature on the epidemiology and risk/prognostic factors associated with RA-ILD.

Results: The results of search and screening yielded 42 publications eligible for evidence synthesis; 22 studies reporting on the epidemiology and risk/prognostic factors and 20 studies (1 non-randomized clinical trial and 19 observational studies) on treatments for RA-ILD (Figure 1).

Unadjusted incidence of ILD in RA patients ranged from 1.3/1,000 person-years for interstitial pneumonia-type ILD to 5.0/1,000 person-years for "probable or definite ILD." RA-ILD prevalence ranged widely from 1.8% to 67%. This variation is more likely attributable to the difference in sample sizes, definitions of ILD, and how ILD was diagnosed across the eligible studies. Comorbidities among patients with RA-ILD included ischemic heart disease (13%), congestive heart failure (8.5%), and diabetes (9.9%). Advanced age was the strongest predictor of developing ILD with

pre-existing RA and poorer prognosis once RA-ILD was present. Male gender, RA disease duration, and anti-CCP/CCP2 positivity were also reported as important potential risk factors for ILD. Of the 6 studies that included RA drug treatments in their multivariate models assessing risk factors for ILD among RA patients, only one identified drug use (steroids) as an independent risk factor for developing ILD.

A variety of therapies were used across studies with some studies reporting classes of medication, while others were focused on specific combinations of individual therapies (Table 1). The included studies showed moderate to good effect for all therapies used in RA-ILD for DAS28, dyspnea, diffusing capacity for carbon monoxide, forced vital capacity (FVC), forced expiratory volume (FEV1), FEV1/FVC, and exacerbation of ILD. Few safety outcomes of interest were reported.

Conclusion: This review highlights epidemiology and potential risk factors (male gender, RA duration, and anti-CCP positivity) for ILD development in RA patients. Well-designed RCTs and meta-analyses are warranted to fully assess optimal treatment efficacy and safety of RA-ILD therapies.

1	Raimundo K, Solomon JJ, Olson AL, et al. Rheumatoid Arthritis-Interstitial Lung Disease in the United States: Prevalence, Incidence, and Healthcare Costs and Mortality. *J Rheumatol.* 2018
2	Shaw M, Collins BF, Ho LA, Raghu G. Rheumatoid arthritis-associated lung disease. *European Respiratory Review.* 2015;24(135):1-16.

References

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Abstract Number: 2350

Derivation and Validation of a Biomarker-Based Cardiovascular Risk Prediction Score in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Comorbidities

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Background/Purpose: Rheumatoid arthritis (RA) patients are at elevated risk for cardiovascular (CV) events, but efficient risk stratification based on CV prediction models is not part of routine clinical practice. We constructed and validated a biomarker-based CV risk prediction model and compared it to alternative risk prediction approaches.

Methods: Using Medicare administrative data 2006-2016, we constructed a cohort of RA patients age ≥40 with ≥1 RA diagnosis from a rheumatologist, excluding patients with malignancy, past myocardial infarction (MI) or stroke. Patients were linked to multi-biomarker disease activity (MBDA) test results obtained as part of routine care. The composite CV outcome consisted of MI, stroke, and CV death occurring within 3 years, using validated algorithms.

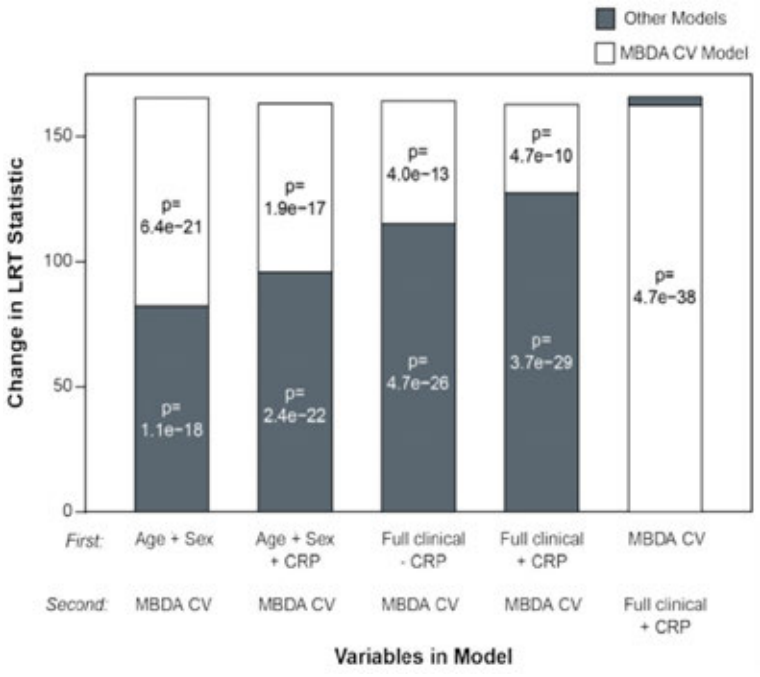

Figure 1: Incremental improvement of MBDA-based RA-CVScore compared to other CV Risk Prediction Models

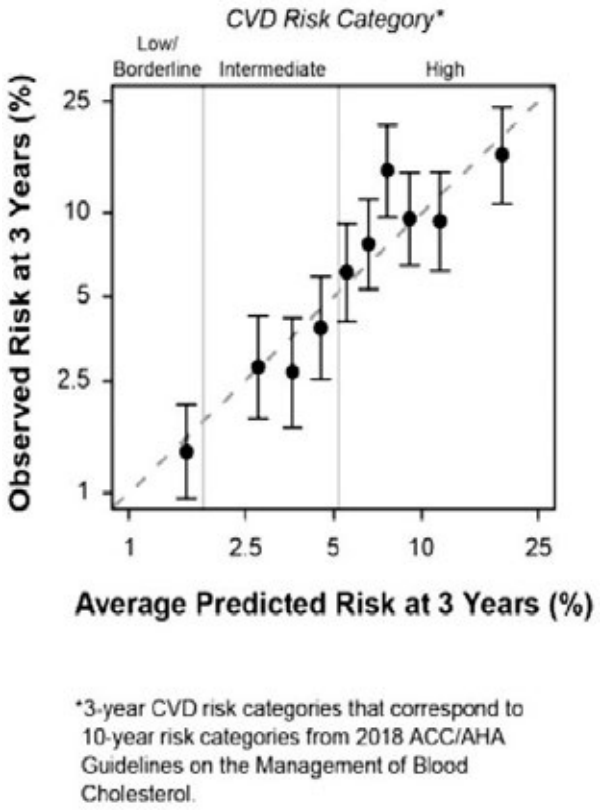

Figure 2: MBDA-Based RA-CVScore Calibration for Composite CV Outcome at 3 years

The cohort was split 2:1 to create a training dataset and an internal validation dataset. Clinical predictors were examined based on subject matter expertise, informed by existing risk prediction scores: age, sex, race, traditional CV risk factors (e.g. diabetes, hypertension, hyperlipidemia, high-risk CV conditions [e.g. ischemic heart disease]), RA-related factors (e.g. glucocorticoid use, methotrexate, number of prior biologics), MBDA score, and its 12 biomarkers, log-transformed. Backward elimination was used to remove predictors with $p \geq 0.05$. The resulting MBDA-based CV risk score was applied to the validation dataset to compare it to four different prediction models (age+sex; age+sex-+CRP; age+sex+diabetes+hypertension+smoking+high risk CV [±CRP]). We evaluated: 1) the incremental improvement in the likelihood ratio (LR) statistic, 2) discrimination (AUROC), and 3) calibration (predicted vs. observed, based on Kaplan-Meier estimates with 95% CI) in CV event-based deciles. Validation followed a pre-specified analysis plan.

Results: 30,751 RA patients were linked to MBDA test results and eligible for analysis. Patient characteristics were mean (SD) age of 68.7 (9.5) years, 23.4% age < 65, 82% women. Comorbidities included diabetes (39%), hypertension (78%), smoking (24%), and history of high-risk CV condition (37%). RA-related features included use of glucocorticoids (58%), methotrexate (60%), TNFi (33%) and other biologics (16%). Mean (SD) MBDA score was 41 (14). The final features included in the MBDA-based CV risk score were age, diabetes, hypertension, smoking, history of high-risk CV conditions, the MBDA score, leptin, TNFRI and MMP-3. Median (IQR) of predicted 3-year CV risk was 3.4% (2.1%, 5.6%). Based on extrapolation to 10-year risk, 19.6% of patients would be considered low/borderline, 52.2% intermediate, and 28.2% high risk per ACC/AHA 2018 guidelines.

Compared to all four simpler CV prediction models, significant improvement in the LR statistic was observed with the addition of the MBDA-based CV risk score (Figure 1). Model accuracy (calibration) was good across deciles (Figure 2). The AUROC was 0.70.

Conclusion: A simple, biomarker-based prediction score incorporating a few clinical risk factors appears to have good accuracy to predict CV risk in RA. Additional validation in independent cohorts will be helpful to verify its performance characteristics.

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Abstract Number: 2351

Withdrawal of Conventional Synthetic Disease-Modifying Antirheumatic Drugs in the Sarilumab Open-Label EXTEND Study: Efficacy and Safety Analysis

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SESSION INFORMATION
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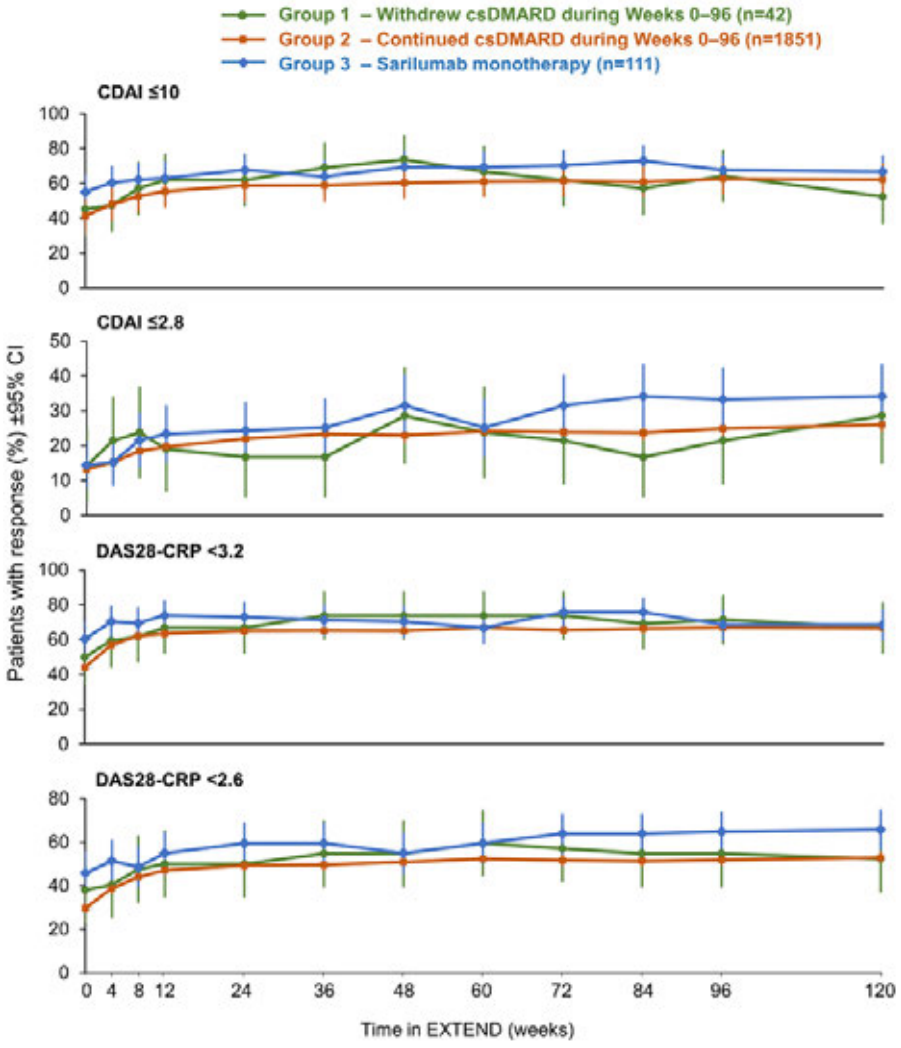
Background/Purpose: The EXTEND open-label extension study (NCT01146652) is collecting data on long-term treatment of RA with sarilumab as monotherapy and in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), predominantly methotrexate. We conducted a post hoc analysis to compare outcomes between patients who received sarilumab monotherapy, sarilumab +csDMARDs, or discontinued csDMARDs during sarilumab treatment.

Methods: Patients enrolled in four trials of sarilumab SC 150 or 200 mg q2w +csDMARDs (MOBILITY, NCT01061736; TARGET, NCT01709578; ASCERTAIN, NCT01768572; and NCT01217814) and a sarilumab monotherapy study (ONE, NCT02121210) were eligible to receive open-label sarilumab SC 200 mg q2w in EXTEND, +csDMARDs if given in the parent trial. In EXTEND, csDMARDs could be stopped at the investigator's discretion (reasons not recorded). Post hoc analyses were conducted on three groups: Group 1 permanently discontinued csDMARDs at any time during Weeks 0–96 of EXTEND and then received sarilumab monotherapy; Group 2 continued csDMARDs; and Group 3 enrolled from the monotherapy study and never received csDMARDs. A subgroup of Group 1, patients who received csDMARDs during Weeks 0–12 and discontinued csDMARDs during Weeks >12–96, was used for sensitivity analysis.

Table. Summary of treatment-emergent AEs			
n (%) [number of events per 100 PYs]	**Group 1 Withdrew csDMARD during Weeks 0–96 (N=42) [PYs=104]**	**Group 2 Continued csDMARD during Weeks 0–96 (N=1851) [PYs=5870]**	**Group 3 Sarilumab monotherapy (N=111) [PYs=230]**
Any AE	41 (97.6) [225]	1626 (87.8) [184]	83 (74.8) [138]
Serious AE	17 (40.5) [17]	475 (25.7) [13]	16 (14.4) [10]
AEs leading to sarilumab discontinuation	15 (35.7) [16]	382 (20.6) [7]	8 (7.2) [3]

Results: There were 42 patients in Group 1, 1851 in Group 2, and 111 in Group 3, with minor differences between groups in demographics and disease characteristics at entry into EXTEND. At 96 weeks, 69%, 80%, and 83% of patients remained on study in Groups 1, 2, and 3, respectively. Similar substantial and durable response rates (Clinical Disease Activity Index [CDAI] ≤2.8 or ≤10, Disease Activity Score (28 joints)-C-reactive protein [DAS28-CRP] < 2.6 or < 3.2) were observed between patients who discontinued csDMARDs, patients who continued csDMARDs, and patients who never received csDMARDs (Figure). Results of the sensitivity analysis subgroup (n=27) were consistent with Group 1. The adverse event (AE) profile was as expected. AE incidence was greater in Group 1 than in Groups 2

Figure. Percentage of patients achieving CDAI ≤10 (low disease activity), CDAI ≤2.8 (remission), DAS28-CRP <3.2 (low disease activity), and DAS28-CRP <2.6 (remission); Last observation carried forward (LOCF) was used to impute missing values and/or for patients who discontinued treatment



and 3 (Table), including hepatic disorders (21, 7, 3 per 100 patient-years [PYs], respectively) and leukopenia (43, 13, 20 per 100 PYs, respectively). Rates of infection and serious infection were lowest in Group 3.

Conclusion: During the 120-week study, patients initially on sarilumab +csDMARDs who subsequently discontinued csDMARDs maintained similar clinical responses to patients who continued sarilumab +csDMARDs or received sarilumab monotherapy throughout. The AE profile was as expected, with no new safety signals.

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Abstract Number: 2352

Real-World Distribution of Anti-Cyclic Citrullinated Peptide Concentrations and Impact on Treatment Patterns of Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Distinct subgroups of RA are being identified by clinical, biochemical, and genomic markers. ACPA positivity is one such biomarker associated with a clinical profile of early rapidly progressing RA. This study aimed to understand the distribution of anti-cyclic citrullinated peptide (anti-CCP2) concentration and its impact on treatment patterns among RA patients in the real-world community practice setting.

Methods: A retrospective cohort study using chart review methodology was used to abstract data of adult RA patients treated in US community rheumatology clinics with biologic disease modifying antirheumatic drug (bDMARD) within 1 year of data collection launch (April 2019). Rheumatologists provided patient-level data from medical records including demographics, biomarkers, treatment sequencing, and clinical outcomes. Patient characteristics and outcomes were summarized descriptively.

Results: The majority (77.6%; n=706) of 910 RA patients meeting eligibility were tested for ACPA at the time of RA diagnosis. Among the 75.9% (n=536) who were ACPA positive (anti-CCP2 >19 AU/mL), the anti-CCP2 quartiles observed were: 20-64 AU/mL, 65-142 AU/mL, 143-246 AU/mL, and 250-19,000 AU/mL. Gender distribution was similar (70%-75% female) across anti-CCP2 quartiles, while median ages were: 45.5, 42.0, 53.0, and 48.0 years, across increasing quartiles. The proportion of patients with rheumatoid factor positivity increased with each anti-CCP2 quartile (79.8%, 90.5%, 91.1%, and 93.1%, respectively). Prior bDMARD use was: 34.6%, 29.5%, 36.7%, and 40.5% in quartiles 1-4, respectively. Among the experienced bDMARD users, higher proportions of patients had ≥2 prior bDMARD use in higher quartiles (25.0%, 19.4%, 34.5%, and 32.1%, respectively). Current bDMARD use was similar across quartiles of anti-CCP2; 25.2% with ACPA positivity were treated with adalimumab, followed by 19.8% etanercept, 17.4% abatacept, 10.4% certolizumab, 10.4% tocilizumab, 6.5% infliximab, 5.4% golimumab, and 4.9% rituximab.

Conclusion: Results of this real-world evidence research demonstrate that while ACPA testing has achieved good adoption in US community rheumatology practice, anti-CCP titers do not appear to be correlated with bDMARD selection. Further research of the prognostic value of ACPA-positivity/titers may further aid in the clinical identification of the most appropriate bDMARD for each patient.

Disclosure: A. Klink, Cardinal Health, 3; **B. Bapat**, Cardinal Health, 3; **J. Kaufman**, Cardinal Health, 3, 4; **F. Lobo**, Bristol-Myers Squibb, 1, 3, Bristol-Myers Squibb Company, 1, 3; **X. Han**, Bristol-Myers Squibb, 3, Bristol-Myers Squibb Company, 3; **L. Ferri**, Bristol-Myers Squibb, 1, 3, 4, Bristol-Myers Squibb Company, 1, 3; **R. Szymialis**, Bristol-Myers Squibb Company, 3; **T. Poretta**, Rutgers University, 2; **B. Feinberg**, Cardinal Health, 3, 4.

Abstract Number: 2353

ACPA Testing and Resultant Treatment Patterns in Patients with Rheumatoid Arthritis: Findings from US Community Rheumatology Practices

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Background/Purpose: Research is redefining RA as a heterogeneous group of diseases distinguished by clinical, biochemical, and genomic markers. ACPA positivity is one such biomarker associated with a clinical profile of early rapidly progressing RA (ERPRA). This study aimed to understand patterns of biomarker testing including ACPA and their impact on treatment patterns in RA patients in the real-world practice setting.

Current bDMARD	ACPA+ (n=536), n (%)	ACPA- (n=170), n (%)
Adalimumab	135 (25.2)	48 (28.2)
Etanercept	106 (19.8)	28 (16.5)
Certolizumab	56 (10.4)	14 (8.2)
Tocilizumab	56 (10.4)	19 (11.2)

Methods: A retrospective cohort study using chart review methodology was used to abstract data of adult RA patients treated in US community rheumatology clinics with bDMARD therapy ≤1 year of data collection launch (April 2019). Rheumatologists provided patient-level data from medical records including demographics, biomarker assessments, treatment sequencing, and clinical outcomes. Patient characteristics and outcomes were summarized descriptively.

Results: There were 910 RA patients meeting eligibility criteria and abstracted between March 2018 and February 2019. Most patients were tested for ACPA status at RA diagnosis (77.6%). Of the ACPA tested patients, 75.9% were ACPA+ (anti-CCP2 concentration >19 AU/mL) and 24.1% were ACPA-. The proportion of patients retested for ACPA status was similar between the 2 cohorts (22.6% ACPA+ vs. 25.9% ACPA-, P=0.67). The majority of RA patients were female (73.7% ACPA+ vs. 75.9% ACPA-, P=0.57), Caucasian (74.3% ACPA+ vs. 80.6% ACPA-, P=0.09), and were covered by commercial health insurance (68.8% ACPA+ vs. 63.5% ACPA-, P=0.20). Although racial distribution was similar among ACPA+ and ACPA- cohorts, ACPA positivity was more prevalent in ACPA tested African Americans compared to ACPA tested Caucasians (87.1% vs. 74.4%, P< 0.01). ACPA+ patients were younger on average compared to ACPA- patients (48 years vs. 52 years, P< 0.01). There were no regional differences by ACPA status. The rate of testing of traditional biomarkers at the time of current bDMARD use: erythrocyte sedimentation rate 92.7%, C-reactive protein 79.1%, RF 98.9%; these rates did not differ by ACPA status (all P >0.05). Higher proportion of ACPA+ patients were RF+ compared to ACPA- patients (90.1% vs. 50.0%, P< 0.01). The treatment with bDMARD had similar distribution regardless of ACPA status as presented in the table.

Conclusion: These retrospective real-world data demonstrate that ACPA testing has attained good adoption among RA patients in US community rheumatology practices. ACPA positivity significantly varies from other biomarkers but does not appear to influence treatment choice. Additional research is needed to affirm published data that ACPA levels may differentiate disease that may be more effectively treated by non-TNF inhibitor bDMARDs.

Disclosure: B. Bapat, Cardinal Health, 3; **A. Klink**, Cardinal Health, 3; **J. Kaufman**, Cardinal Health, 3, 4; **F. Lobo**, Bristol-Myers Squibb, 1, 3, Bristol-Myers Squibb Company, 1, 3; **X. Han**, Bristol-Myers Squibb, 3, Bristol-Myers Squibb Company, 3; **L. Ferri**, Bristol-Myers Squibb, 1, 3, 4, Bristol-Myers Squibb Company, 1, 3; **R. Szymialis**, Bristol-Myers Squibb Company, 3; **T. Poretta**, Rutgers University, 2; **B. Feinberg**, Cardinal Health, 3, 4.

Abstract Number: 2354

Replication of a Prognostic Multivariable Prediction Model for Insufficient Clinical Response to Methotrexate in Early Rheumatoid Arthritis

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Background/Purpose: Methotrexate (MTX) constitutes first-line therapy in rheumatoid arthritis (RA). However, up to 40% of RA patients do not benefit from MTX therapy. To restrain joint damage, prediction of insufficient response to MTX prior to treatment is desirable to initiate alternative treatment options. Previously, we developed a prognostic multivariable prediction model for insufficient clinical response to MTX at 3 months in the "treatment in the Rotterdam early arthritis cohort" (tREACH, ISRCTN26791028). This model was replicated in another Rotterdam cohort (MTX-R), however, information on two predictors: smoking and BMI was absent. The purpose of the current study was to replicate the complete prediction model in an independent, non-Rotterdam early RA cohort (U-Act early), which included data on smoking and BMI.

Methods: Clinical, laboratory and life style parameters were assessed from 91 early RA patients of the MTX treatment arm of the U-Act early cohort (NCT01034137). 92% of the subjects met the 2010 ACR/EULAR classification criteria for RA. Insufficient response was defined as DAS28-ESR >3.2 after 3 months of MTX treatment. The following predictors and the corresponding cut-off values were defined in the prediction model for insufficient response: baseline DAS28 >5.1, baseline HAQ >0.6, baseline erythrocyte-folate < 750 nmol/L, Adenosine triphosphate Binding Cassette transporter (ABC) family B member 1 (ABCB1) rs1045642 genotype, ABCC3 rs4793665 genotype, current smoking and BMI >25kg/m2. Univariable and multivariable logistic regression models were used to assess the associations between the predictors and insufficient response to MTX in the current cohort, which was reported as odds ratio (OR) and 95% confidence intervals (CI). To assess the predictive power of the model, a receiver operating characteristic (ROC) curve was constructed from the predicted probabilities, with its corresponding area under the curve (AUC) and 95% CI. The model in the current study (U-Act early) was considered to be replicated when the 95% CI overlapped with that of the tREACH model (AUC: 0.80, 95% CI: 0.73 – 0.86).

Results: In the U-Act early, the AUC of the complete prediction model was 0.75 (95% CI: 0.64 – 0.85), which resembles the 95% CI of the tREACH (P >0.05). The strongest predictors were baseline DAS28 >5.1 (univariable OR=4.5, 95% CI: 1.7 – 11.6) and baseline HAQ >0.6 (univariate OR=3.0, 95% CI: 1.2 – 7.5), which together constructed a ROC with an AUC of 0.70 (95% CI: 0.59 – 0.80). With the exception of current smoking, all predictors contributed to the improvement of the prediction model in this study. For these predictors the AUC was also 0.75 (95% CI: 0.64 – 0.85).

Conclusion: We successfully replicated our previously published prognostic prediction model of insufficient MTX response constructed of genetic, clinical and life style variables in an independent cohort, where 75% of insufficient responders were correctly classified. A cost-benefit analysis will be decisive on which predictors to use when implementing the model in a clinical setting.

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Abstract Number: 2355

Antirheumatic Therapy Is Associated with Reduced Complement Activation in Rheumatoid Arthritis

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Background/Purpose: Inflammation and immune dysregulation appear to significantly contribute to increased risk of cardiovascular disease (CVD) in rheumatoid arthritis (RA). The complement system is a key component of the innate immune system, and recent research suggests that it might be involved in pathophysiology of CVD in the general population. However, information regarding complement activation in response to treatment and its importance in the development of premature CVD in RA is limited.

We will examine effects of methotrexate (MTX) and tumor necrosis factor inhibitors (anti-TNF) on complement activation using soluble C5b-9 (sC5b-9) levels in RA; and assess associations between sC5b-9 levels and established inflammatory biomarkers.

Methods: From the observational PSARA study, we assessed 64 RA patients starting with MTX monotherapy (n=34) or anti-TNF with MTX co-medication (n=30) due to active disease. The median age was 57 years, median RA duration was 5.5 years, and 73% were women. All patients starting with anti-TNF had previously been unsuccessfully treated with MTX. ELISA was used to measure sC5b-9 complexes in EDTA plasma immediately prepared and stored at minus 80^0C. The patients were examined at baseline and after 6 weeks and 6 months of treatment.

Results: At baseline, the median sC5b-9 level was 1.10 CAU/ml [IQR 0.70], and 57 (89%) patients had sC5b-9 above the upper limit of the estimated reference range (< 0.7). sC5b-9 levels were significantly lower at 6-week (median 0.85 CAU/ml [IQR 0.55]) and 6-month (median 0.80 CAU/ml [IQR 0.58]) visits compared to baseline (p< 0.0005 and p=0.014, respectively). There were no significant differences in sC5b-9 levels between patients treated with MTX monotherapy and those treated with MTX combined with anti-TNF treatment from baseline to 6 weeks (p=0.689) and from baseline to 6 months (p=0.901). The changes in sC5b-9 from baseline to 6 weeks and from baseline to 6 months positively correlated with changes in erythrocyte sedimentation rate (ESR; rs= 0.364, p=0.003 and rs= 0.372; p=0.002, respectively), and C-reactive protein (CRP; rs=0.411; p=0.001 and rs= 0.348; p=0.005, respectively). Similarly, baseline sC5b-9 levels were significantly related to baseline ESR and CRP levels.

Conclusion: Patients with active RA had elevated sC5b-9, indicating increased complement activation. sC5b-9 decreased with antirheumatic treatment during the 6-month treatment period. There were no differences between MTX monotherapy and anti-TNF regimens. Further studies are warranted to determine if the well-known cardioprotective effects of antirheumatic drugs might be partly due to their ameliorating actions on complement activation, and whether the complement system might be a target for therapy in RA.

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Abstract Number: 2356

Antirheumatic Therapy Is Not Associated with Changes in Circulating N-terminal Pro-brain Natriuretic Peptide Levels in Patients with Active Rheumatoid Arthritis

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Background/Purpose: Patients with rheumatoid arthritis (RA) are predisposed to impaired cardiac function and heart failure (HF). While the pathophysiology has not been fully elucidated yet, inflammation is suspected to play an important role. However, the impact of disease-modifying antirheumatic drugs on cardiac dysfunction in RA remains controversial. Although anti-inflammatory drugs might have protective effects, some of them, i.e. tumour necrosis factor inhibitors (anti-TNF), might also negatively influence cardiac function. Serum N-terminal pro-brain natriuretic peptide (s-NT-proBNP) is used as a biomarker of cardiac function, and levels ≤125 ng/L with high probability exclude HF[1].

To examine effects of methotrexate (MTX) and anti-TNF regimens on s-NT-proBNP in patients with active RA, and to assess associations between s-NT-proBNP and endothelial function (EndoF).

Methods: From the observational PSARA study, we examined 64 RA patients starting with MTX monotherapy (n=34) or anti-TNF with MTX co-medication (n=30) due to active disease. All patients starting with anti-TNF regimens had

Table 1 Baseline characteristics

	All patients (n=64)	MTX monotherapy (n=34)	Anti-TNF regimens (n=30)
Age (years)	57 (28-79)	56 (28-79)	58 (39-75)
Women, n (%)	47 (73)	25 (73)	22 (73)
RA duration, years	5.5 (0-30)	3 (0-25)	8 (0-30)
Hypertension, n (%)	17 (26.6)	7 (20.6)	10 (33)
CVD (history of angina, MI, heart surgery, PTA, cerebrovascular disease, thromboembolism, aortic aneurysm, peripheral artery disease), n (%)	17 (26.6)	6 (17.6)	11 (36.7)

Unless indicated otherwise, values are given as mean (range)

been previously unsuccessfully treated with MTX. s-NT-proBNP (ELISA), EndoF (measured by finger plethysmography), and other laboratory and clinical parameters were evaluated at baseline and after 6 weeks and 6 months of treatment.

Results: Median age was 57 years (range 28-79), and 73% were women. 17 (27%) patients had CVD (history of angina, MI, heart surgery, PTA, cerebrovascular disease, thromboembolism, aortic aneurysm, peripheral artery disease). None of the patients had known/symptomatic HF. There were no statistically significant differences between s-NT-proBNP levels at baseline (median 2241 ng/L [IQR 9002]) and after 6 weeks (median 2300 ng/L, [IQR 8960]) and 6 months (median 2358 ng/L [IQR 7772]) of antirheumatic therapy (p=0.992 and p=0.528, respectively). There were no significant differences in the effects of MTX monotherapy and anti-TNF regimens on s-NT-proBNP levels (pbaseline-6weeks=0.779; pbaseline-6months=0.421). At baseline, 57 (89%) patients had s-NT-proBNP >125 ng/L, and 44 (69%) had high s-NT-proBNP levels (s-NT-proBNP >450 ng/L in patients < 50 years old and >900 ng/L in patients ≥50 years old), and these frequencies did not significantly change with antirheumatic treatment. s-NT-proBNP was not related to EndoF.

Conclusion: A large proportion of RA patients without known HF had elevated s-NT-proBNP levels, which might indicate subclinical impairment of cardiac function. s-NT-proBNP levels were not influenced by six-month MTX and/or anti-TNF treatment. Thus, in contrast to some previous studies, our data does not support the notion that anti-inflammatory treatment protects against HF, and that anti-TNF treatment has negative effect on cardiac function in RA. Nevertheless, definitive conclusions cannot be drawn by our study, e.g. due to limitations of s-NT-proBNP as surrogate marker of HF. Cardiac function in terms of s-NT-proBNP levels was not related to EndoF.

Reference:

Ponikowski P et al. *European journal of heart failure*. 2016;18:891-975.

Abstract NT-pro-BNP - Table 1 Baseline characteristics pdf

Disclosure: T. Nguyen, None; **G. Deyab**, None; **M. Fagerland**, None; **S. Agewall**, None; **G. Eilertsen**, None; **M. Feinberg**, None; **K. Mikkelsen**, None; **Ø. Førre**, None; **I. Hollan**, None.

Abstract Number: 2357

Methotrexate Liver Toxicity in a Large Randomized Controlled Trial

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
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Session Time: 9:00AM–11:00AM

Background/Purpose: Liver test abnormalities are known to predict liver pathology in patients using methotrexate (MTX). Monitoring guidelines for MTX suggest frequent assessment of liver tests (AST and ALT). The frequency of liver test abnormalities and liver pathology (liver AEs) in patients using MTX varies substantially in prior studies and there are sparse placebo-controlled data on these issues. We examined liver AEs reported during follow-up in the

Table 1: Risk of Liver Adverse Events Reported Among Patients in CIRT Trial			
	MTX	Placebo	
	N = 2,391	N = 2,395	HR (95% CI)
Any AST or ALT abnormality	937 (39%)	511 (21%)	2.1 (1.9, 2.4)
Mild (>1-2x ULN)	906 (38%)	495 (21%)	2.1 (1.9, 2.4)
Moderate (>2-3x ULN)	152 (6%)	46 (2%)	3.4 (2.4, 4.7)
Severe (>3x ULN)	51 (2%)	21 (1%)	2.5 (1.5, 4.1)
Any liver pathology	14 (0.6%)	9 (0.4%)	1.6 (0.7, 3.6)
Cirrhosis	6 (0.3%)	1 (0.04%)	6.0 (0.7, 50.2)
NASH	8 (0.3%)	8 (0.3%)	1.0 (0.4, 2.7)
HR, hazard ratios calculated in separate Cox regression models. ULN, upper limits of normal. NASH, non-alcoholic steatohepatitis.			

Table 2: Predictors of AST or ALT Abnormalities Among 2,391 Patients Taking MTX in the CIRT Trial	
Baseline variables	HR (95% CI)
Age, per year	0.99 (0.98 – 0.99)
Gender, male	1.07 (0.90 – 1.26)
Diabetes (vs no diabetes)*	0.93 (0.81 – 1.06)
Statin use, yes	1.17 (0.96 – 1.42)
Alcohol, per drink per week	1.17 (1.08 – 1.28)
*Inclusion for CIRT trial required diabetes or metabolic syndrome.	

Cardiovascular Inflammation Reduction Trial (CIRT), a randomized double-blind placebo-controlled trial of MTX for the prevention of cardiovascular disease.

Methods: The current analyses were pre-defined as secondary analyses of the CIRT trial (Ridker et al, NEJM 2019). AST and ALT were collected every 8-10 weeks during CIRT, dosages were adjusted by rheumatologists if liver tests were found to be abnormal, and work-up was recommended for patients with persistently elevated liver tests. Patients were randomized to receive MTX (target dose 15 to 20mg weekly) or placebo. Median trial follow-up was 2.3 years; maximum 5 years. All reports of liver AEs at routine visits or as hospitalized serious AEs were followed up with a request for medical records. These events were adjudicated using a standardized assessment by an internist (DHS) and liver specialist (AR). We examined the frequency in all patients of AST and ALT abnormalities (>upper limits of normal, ULN) and liver pathology, defined as cirrhosis, non-alcoholic steatohepatitis (NASH), and other. AST and ALT abnormalities were also categorized as mild (>1- 2 x ULN), moderate (>2-3 x ULN), or severe (>3 x ULN). The relative rates of these outcomes were estimated using hazard ratios (HR) in adjusted Cox regression. Adjusted Cox regression was also used to examine risk factors for first liver test abnormalities among patients in the MTX arm.

Results: 2,391 patients were randomized to MTX (median dosage of 16mg weekly) and 2,395 to placebo. During follow-up, in the MTX arm, 937 (39%) experienced an AST or ALT abnormality with a rate of abnormal tests (first or recurrent) of 11.5 per 100 tests (95% CI 11.1-11.9). In the placebo arm, 511 (21%) experienced an abnormal test with a rate (first or recurrent abnormality) of 5.1 per 100 tests (95% CI 4.8-5.3). The hazard ratio (HR) for first abnormal liver tests was 2.1 (95% CI 1.9-2.4) in MTX versus placebo. The risk for abnormal liver tests of different severity are shown in **Table 1**. There were 14 (0.6%) patients in the MTX arm and 9 (0.4%) in the placebo arm that were diagnosed with liver pathology during follow-up; the HR for these events was 1.6 (95% CI 0.7-3.6). These events were categorized as cirrhosis (n=6, 0.3% in MTX vs n=1, 0.04% in placebo) and NASH (n=8, 0.3% in MTX vs n = 8, 0.3% in placebo) (see **Table 1**). Predictors of ALT or AST abnormalities in the MTX arm included younger age and more alcohol intake at baseline (see **Table 2**).

Conclusion: Compared to placebo, the risk of abnormal AST or ALT was increased two to three-fold with MTX use; most abnormal values were only mildly elevated. More alcohol intake and younger age were the only clear risk factors for abnormal liver tests among patients randomized to MTX. We found few cases of cirrhosis during follow-up in either arm, but more in the MTX arm.

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Abstract Number: 2358

Short-term Risk of Major Adverse Cardiovascular Events or Venous Thrombo-embolic Events in Patients with Rheumatoid Arthritis Initiating a Janus Kinase Inhibitor: A Meta-analysis of Randomised Controlled Trials

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SESSION INFORMATION
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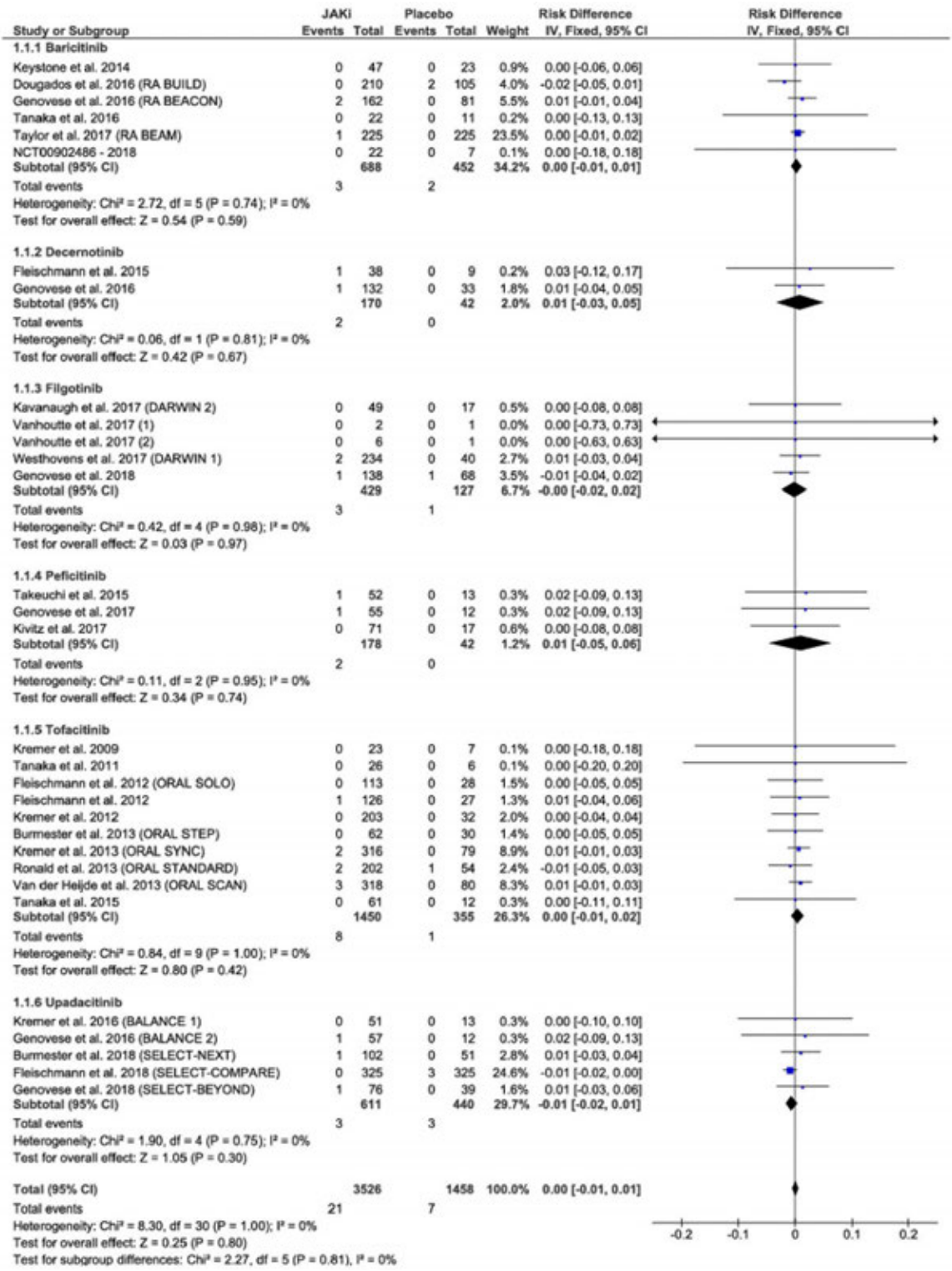
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The objective was to investigate the short-term risk of major adverse cardiovascular events (MACEs) or venous thromboembolic events (VTEs) in patients with rheumatoid arhthritis (RA) initiating a Janus kinase inhibitor (JAKi).

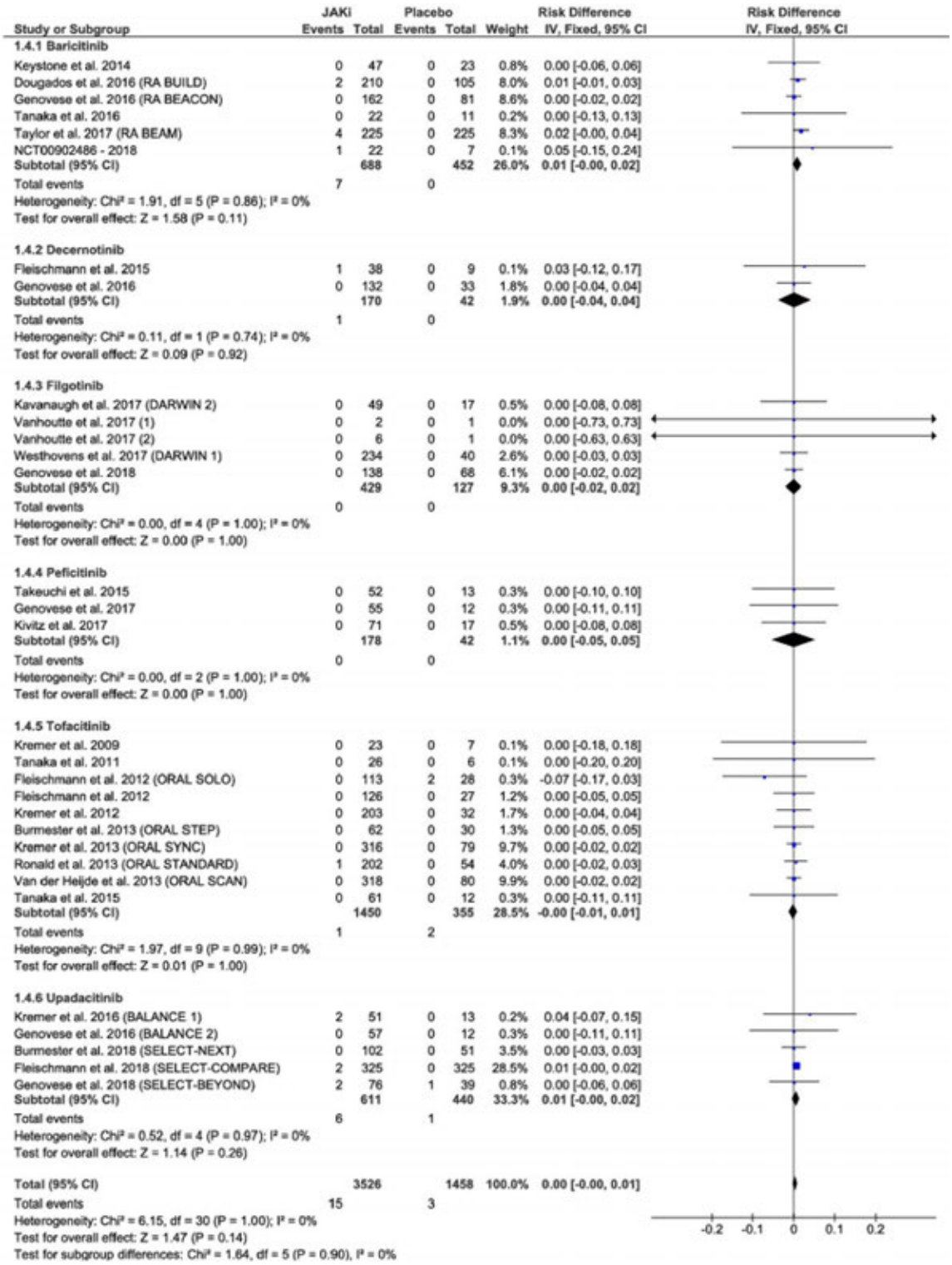
Methods: Screening for the study was carried out using MEDLINE, Cochrane and Embase, from the inception of the database to February 2019. Randomised controlled trials (RCTs) of JAKi for the treatment of rheumatoid arthritis were included. Two investigators independently extracted MACEs or VTEs reported during the placebo-controlled phase. The primary outcome measures were the incidence of MACEs or VTEs.

Results: From 205 references screened, 26 articles were selected, and 3 articles were added by manual searches. Accordingly 30 RCTs were included in the meta-analysis. No statistically significant difference was observed in MACE (Figure 1) or VTE incidences (Figure 2) in patients receiving any of the JAKi compared to the placebo group. A numeric imbalance was observed in the baricitinib group with 7 VTEs (688 P-Y) compared with none in the placebo group (452 P-Y), with 0,01 -0,00 to 0,02 risk difference, which is not statistically significant. A numeric imbalance was also observed in the upadacitinib group with 6 VTEs (611 P-Y) compared to 1 VTE in the placebo group (440 P-Y), with 0,01 -0,00 to 0,02 risk difference, which is not statistically significant neither.

Conclusion: This MA of 30 RCTs did not reveal any statistically significant change in the short-term risk of MACEs or VTEs in patients with RA initiating a JAKi. Data from the long-term extension phases of these RCTs, from studies designed to compare JAKi to bDMARDs with respect to MACEs or VTEs and from the long-term follow-up of patients included in JAKi registries are required to further characterise the risk of MACEs or VTEs in patients with RA treated with JAKi.



Difference in the risk of MACEs in RA patients treated with JAKi compared with the placebo in RCTs.



Difference in the risk of VTEs in RA patients treated with JAKi compared with the placebo in RCTs.

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Abstract Number: 2359

High Body Mass Index Shortens Retention of Tumor Necrosis Factor-α Blocker Treatment in Rheumatoid Arthritis

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SESSION INFORMATION

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Session Title: RA – Treatments Poster III: Safety and Outcomes

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Session Time: 9:00AM–11:00AM

BMI and drug retention

		Episodes	Event (%)	HR	Pv
Total		818	407 (49.8)		
BMI	<24.9	334	152 (45.5)	1.00	.
	25-29.9	261	129 (49.4)	1.21	0.11
	30-34.9	144	70 (48.6)	1.18	0.24
	≥35	79	56 (70.9)	**2.28**	**<0.01**
Drug					
Etanercept		326	154 (47.2)	1.00	.
Infliximab		197	94 (47.7)	1.11	0.42
Adalimumab		215	127 (59.1)	**1.51**	**<0.01**
Golimumab		80	32 (40.0)	1.12	0.56
Etanercept	<24.9	134	56 (41.8)	1.00	.
	25-29.9	104	51 (49.0)	1.27	0.21
	30-34.9	59	27 (45.8)	1.15	0.56
	≥35	29	20 (69.0)	**2.26**	**<0.01**
Infliximab	<24.9	79	34 (43.0)	1.00	.
	25-29.9	58	26 (44.8)	1.66	0.06
	30-34.9	38	19 (50.0)	1.75	0.05
	≥35	22	15 (68.2)	**2.57**	**<0.01**
Adalimumab	<24.9	89	47 (52.8)	1.00	.
	25-29.9	69	43 (62.3)	1.16	0.50
	30-34.9	36	19 (52.8)	1.04	0.87
	≥35	21	18 (85.7)	**2.42**	**<0.01**
Golimumab	<24.9	32	15 (46.9)	1.00	.
	25-29.9	30	9 (30.0)	0.52	0.13
	30-34.9	11	5 (45.5)	0.80	0.66
	≥35	7	3 (42.9)	1.57	0.48
Gender	Male	163	83 (50.9)	1.00	
	Female	655	324 (49.5)	0.95	0.66

Legend: Episode = treatment initiation, Event – drug cessation due to inefficacy, HR-hazard ratio

BMI and drug retention

Background/Purpose: The primary objective was to evaluate the effect of body mass index (BMI) on tumor necrosis factor α (TNF-α) blockers (including etanercept, infliximab, adalimumab and golimumab) retention in patients with RA.

Methods: This prospective cohort study contains data from the Israeli registry of inflammatory diseases, status May 2019. Patients were grouped by BMI: normal (BMI < 24.9 kg/m2), overweight (BMI 25-29.9 kg/m2), obese (BMI 30-34.9 kg/m2) and morbid obese (BMI ≥35 kg/m2). Event-free survival was calculated using Cox regression with a Hazard Ratio and Confidence Interval of 95%. Kaplan-Meier Analysis was used to describe drug survival. Statistical significance was defined as p< 0.05.

Results: The registry included 521 RA patients (80% females) treated with etanercept, infliximab, adalimumab or golimumab. 818 treatment initiations were included in the final analysis, 334 in the normal weight group, 261 in the overweight, 144 in the obese and 79 in the morbid obesity group. 326 treatment episodes were with etanercept, 215 with adalimumab 197 with infliximab, and 80 with golimumab. Negative correlation of elevated BMI with lower drug survival was significant when comparing the morbid obese group to the other patients HR 2.06 (95% CI 1.55-2.73, p< 0.01), indicating a higher rate of treatment switches with BMI >35, the difference was significant in all the drugs, except golimumab that showed insignificant trend. Adalimumab switch rate was higher compared to etanercept with HR =1.51 (95% CI 1.20-1.91, p< 0.01), no other significant differences were noted between the other drugs.

Conclusion: Morbid obese RA patients have lower TNF-α blocker retention compared to normal weight patients.

Disclosure: O. Elkayam, None; **M. Lidar**, None; **T. Reitblat**, None; **D. Zisman**, None; **A. Balbir-Gurman**, Pfizer, 5, 8; **O. Kakakian**, None; **T. Meshiach**, None; **R. Almog**, None; **O. Elalouf**, None.

Abstract Number: 2360

Safety of Biological DMARD in Patients with Interstitial Lung Disease from a Chilean Cohort of Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
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Background/Purpose: Interstitial lung disease (ILD) is a common pulmonary manifestation of rheumatoid arthritis (RA) that may be related to the inflammatory process itself, to infectious complications, and/or to the therapy. Biological disease-modifying antirheumatic drugs (bDMARD) have dramatically improved the outcome of RA, but an increasing number of reports have described the potential lung toxicity of this group of drugs.

Methods: Retrospective cohort study using data from RA patients beneficiaries of the “Ley Ricarte Soto program”, at the Hospital Clínico Universidad de Chile, was conducted to assess ILD prevalence and exacerbations , among users of abatacept (ABA), rituximab (RTX), and anti-TNFα agents. Clinical findings and laboratory data were collected

from medical records. The presence or progression of ILD on HRCT was evaluated by a rheumatologist, a pneumonologist and a radiologists who have expertise in assessing ILD, all part of the Rheumatic Lung Group at our Hospital.

Results: 126 RA patients were included; 85% female, mean (SD) age 55 (13.4) years, mean disease duration 11 (8.7 years). RA was seropositive in 108 patients (85.7%). DAS28 ESR was 6.1 (1.2) previously to initiate bDMARDs. A total of 30 patients (23.8%) had been previously diagnosed with ILD, most common patterns on HRCT were UIP (n=10[33%]) and bronchiolar abnormalities (n=4[13.3%]). Patients with as compared to without ILD at baseline were more frequently males (53 vs 15%, $p < 0.05$), had an older age (62.6 $\pm$ 11.9 vs 55 $\pm$ 13.4, $p < 0.005$), a higher positivity of anti-CCP (73 vs 47.6% $p < 0.005$) and a more frequent history of smoking (43 vs 21%, $p < 0.005$). The patients with a history of ILD were also, significantly more likely to receive ABA (n=24 [82.8] % versus n=35 [36.1%] without ILD; $p < 0.001$) and significantly less likely to receive anti-TNF therapy (n=3 [10.3%] versus n=57 [58.7 %] without ILD; $p < 0.001$). Only 6 patients received RTX, two of them with history of ILD. All patients with RA-associated ILD remained stable at 28 month follow-up. In the group of patients without a history of ILD, only one developed an organizing pneumonia that responded well to corticosteroids and was not related to the biological therapy.

Conclusion: Our data show that, in a real-world setting, there were no significant differences in the risk of complications between patients with or without a baseline history of ILD receiving different biologic agents. In our Cohort, bDMARDs were not associated with new ILD either. These data may be affected by the short follow-up window and the preference for the use of ABA, over anti-TNFα agents, as initial biological therapy in RA-ILD.

Disclosure: S. Saavedra, None; **K. Vergara**, None; **C. Hernandez**, None; **P. Zamorano**, None; **A. Goecke**, Roche, 5, 8, Abbvie, 5, 8, Novartis, 5, 8, Pfizer, 5, 8; **L. Toro**, None; **F. REYES**, None.

Abstract Number: 2361

Early Treatment of Rheumatoid Arthritis with Disease-Modifying Anti-Rheumatic Drugs at < 3 versus 3-6 Months from Onset of Symptoms: Results from a Cohort of Hispanics from Puerto Rico

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: There is no doubt that early treatment of rheumatoid arthritis (RA) with disease-modifying anti-rheumatic drugs (DMARDs) is associated with better long-term outcomes. However, the time frame of early treatment has not been clearly established. Previously, we reported in our cohort of RA patients that those treated with DMARDs within 6 months of disease onset had less physical damage and functional impairment than those treated ≥6 months. Now, we sought to determine if a narrower therapeutic window (< 3 months) would be even more effective.

Methods: A cohort of Hispanics from Puerto Rico with RA (per 1987 American College of Rheumatology classification criteria) was studied. Demographic features, lifestyle behaviors, RA clinical manifestations, disease activity (per Disease Activity Score 28 [DAS-28]), functional status (per Health Assessment Questionnaire [HAQ]), patient's and physician's global assessments (by visual analogue scales), infections, hospitalizations, and RA pharmacotherapy

were determined. Very early treatment (VET) was defined as the initiation of DMARDs (synthetic and/or biological) < 3 months of symptoms attributable to RA, whereas early treatment (EA) was defined as DMARDs treatment ≥3 but < 6 months from RA onset. Study groups were compared using chi-squared, Fisher's exact, Mann Whitney or Student's t tests, as appropriate.

Results: The cohort comprised 394 RA patients, but for this analysis, only those who received VET (n=75) and ET (n=43) were included, for a total of 118 patients. The mean age and disease duration of the study population were 53.7 ± 13.6 and 7.5 ± 7.1 years, respectively. The majority of patients were women (87.3%). Both groups were comparable regarding age, sex, socioeconomic status, disease duration, and health-related behaviors (cigarette smoking, alcohol consumption, and exercise). During the disease course, no significant differences were observed for joint deformities (33.3% vs. 37.2%, p=0.670), requirement of intra-articular joint injections (37.3% vs. 41.9%, p=0.627), joint replacement surgeries (10.7% vs. 4.65%, p=0.259), extra-articular manifestations (38.7% vs. 48.8%, p=0.282), infections (any cause) (46.7% vs. 53.5%, p=0.476), and mean hospitalizations (any cause) (0.1 ± 0.5, p=0.635) between VET and ET groups. Also, at last study visit no differences were seen for mean DAS-28 (3.6 ± 1.3 vs. 3.5 ± 1.5, p=0.534), HAQ (1.0 ± 0.7 vs. 0.8 ± 0.7, p= 0.07), patient's global assessment (43.9 ± 28.9 vs. 38.5 ± 25.7, p=0.376) and physician's global assessment (17.0 ± 18.4 vs. 17.4 ± 19.3, p=0.888) scores. Initial and cumulative treatment with synthetic and biological DMARDs was similar for both groups.

Conclusion: In this group of Puerto Ricans with RA, we found no differences in the clinical outcomes of patients treated with DMARDs < 3 months vs. 3-6 months from onset of RA symptoms. Thus, the therapeutic window of < 6 months seems reasonable for this group of patients. This information is valuable when designing strategies of early intervention for patients with inflammatory arthritis.

Disclosure: M. Arroyo-Ávila, None; **R. Fred-Jiménez**, None; **N. Pérez-Ríos**, None; **N. Rodríguez**, None; **G. Ríos**, None; **L. Vilá**, None.

Abstract Number: 2362

Associations of Disease-Modifying Anti-Rheumatic Drug (DMARD) Adherence with Time to First Biologic and Cycle Time on DMARDs, and Healthcare Utilization/Cost in a New RA Patient Cohort

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SESSION INFORMATION
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Lack of adherence to medications is a well-known problem with chronic conditions, RA included. Nonadherence is associated with decreased quality of life and poorer outcomes. This study explores the effect of adherence to DMARDs on the time to biologic initiation, cycle time on each DMARD, and on healthcare utilization and cost in patients with new-onset RA utilizing a large claims-based database.

Methods: A cohort of adult patients with new-onset RA within Allegheny Health Network Rheumatology was created utilizing our administrative database. Incident RA was defined using a previously validated algorithm: ICD9 code 714 or ICD10 codes M05.XX and M06.XX with no DMARD use for at least 6 months prior, no RA diagnosis visits or biolog-

Variable	Non-adherent (n=42)	Adherent (n=90)	p-value
Age (yrs)	49.8±13	55.2±10	0.011
Gender, Female	26(62%)	56(62%)	0.97
Commercial insurance type ACA exchange Commercial only Medicare co-insured	 2(4.8%) 38(90%) 2(4.8%)	 4(4.4%) 75(83%) 11(12%)	0.42
Income estimate A=1000-14999 B=15000-24999 C=25000-34999 D=35000-49999 E=50000-74999 F=75000-99999 G=100000-124999 H=125000-149999 I=150000-174999 J=175000-199999 K=200000-249999 L=250000+ U=Unknown n=35 and n=79 respectively	 1(2.9%) 2(5.7%) 2(5.7%) 5(14%) 9(26%) 1(2.9%) 4(11%) 5(14%) 2(5.7%) 1(2.9%) 0 1(2.9%) 2(5.7%)	 2(2.5%) 9(11%) 6(7.6%) 4(5.1%) 17(22%) 21(27%) 9(11%) 0 3(3.8%) 0 1(1.3%) 0 7(8.9%)	0.0015
Median adherence until biologic	62.5(39-73)%	100 (94.5-100)%	<0.0001
Time to biologic	287(130-597)	191(91-421)	0.076
Cycle times for DMARD (days) 1st n=42 n=90 2nd n=21 n=42 3rd n=9 n=16 4th n=2 n=6	 115(83-362) 99(34-220) 182(29-425) 214(36-392)	 501(245-881) 314(125-503) 232(87-405) 231(89-614)	<0.0001 0.02 0.9 0.63
Cost of DMARDs until the first biologic (scaled)	4.0(1.7-9.6)	5.90(2.6-13)	0.07
1st DMARD Methotrexate Hydroxychloroquine Leflunomide Sulfasalazine Injectable methotrexate	 20(48%) 10(24%) 5(12%) 5(11.9%) 2(4.8%)	 67(74%) 16(18%) 3(3.3%) 4(4.4%) 0(0%)	0.011
Drug adherence for first DMARD	90.2(60-100)%	93.6(85-99)%	0.20
2nd Medication Sulfasalazine Etanercept Adalimumab Leflunomide Hydroxychloroquine Methotrexate Tocilizumab Abatacept Injectable methotrexate Golimumab	 11(26.1%) 10(24%) 6(14%) 5(12%) 4(9.5%) 4(9.5%) 1(2.4%) 1(2.4%) 0 0	 9(10%) 15(17%) 23(26%) 5(5.6%) 13(14%) 13(14%) 3(3.3%) 1(1.1%) 7(7.7%) 1(1.1%)	0.14
Number of patients with 1st med = DMARD, 2nd med = biologic	21(50%)	48(53%)	0.72
Glucocorticoid dose at last visit, mg (if on steroid, n=15 and n=20, respectively)	5(5-10)	5(5-5)	0.89
Number of other medications at last visit	2(1-5)	3(2-4)	0.059

Table 1: Comparison of non-adherent and adherent groups

ic use for at least 1 year prior, and with continuous enrollment during the study period (01/01/2015-07/31/2018 with a 9 month follow up period to account for adherence until 04/01/2019). Demographics (age/sex), socio-economic status, insurance, medications (non-biologic DMARDs, tofacitinib, biologics, glucocorticoids, other daily oral medications) were recorded. Proportion of days covered (PDC) ≥80% was counted as adherence. Time to biologic initiation

(primary outcome) was defined as number of days from first DMARD prescription until the first biologic prescription. Cycle time on DMARD was defined as number of days on a DMARD before switching to or adding another DMARD. We compared non-adherent vs adherent group characteristics to examine if certain factors correlate with adherence using SAS Enterprise Guide 7.11 HF3.

Results: A total of 132 patients with new-onset RA met our criteria. Ninety patients (68%) were found to be adherent to their non-biologic DMARDs prior to biologic initiation. Our cohort had a mean age of 52 years and 62% female. Patients in the non-adherent group were younger (49 vs 55 years, p-value 0.011) and had lower estimated income (p-value 0.0015). Median time to biologic was longer in the non-adherent group (287 vs 191 days, p-value 0.076). Cycle times on the first and second DMARDs were found to be longer in the adherent vs non-adherent group (501 vs 115 days, p-value < 0.0001, and 314 vs 99 days, p-value 0.02 respectively). Total cost of DMARD medications prior to biologics was higher in the adherent group. The most common first DMARD prescription in both groups was methotrexate, but higher in adherent vs non-adherent (74% vs 48%, respectively, p-value 0.011). In both groups, approximately half of patients were prescribed a biologic as their second medication. Comparison of the groups can be found in Table 1.

Conclusion: Our study found that overall DMARD medication adherence is low and the time to biologic initiation may be longer in the non-adherent patients. Non-adherent patients tended to be younger, have lower household income, and spend less time on each DMARD prior to initiating a biologic. We plan to implement a team-based care approach focusing on medication education and integrating pharmacists and social workers at point of care, especially for those patients with unfavorable social determinants of health.

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Abstract Number: 2363

Influence of the Clinical Characteristics and Different Genetic Polymorphisms Related to MTX, on the Efficacy and Safety in Patients with RA Treated with MTX in Monotherapy

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Rheumatoid arthritis (RA) produces joint destruction, functional deterioration, comorbidity and premature death. The best results are achieved with an early start of a treat-to-target and tight control strategy that allow to quickly and effectively control the inflammatory process. Methotrexate is the *DMARDs* of first choice, but only half of patients (pts) respond satisfactorily in monotherapy and often produces side effects. Studies exploring the contribution of genetic variability to the variability of the efficacy to MTX in RA and its toxicity show highly variable results. The aim was to explore the combined effect of the clinical characteristics related to the patient, the disease and the treatment, and of different genetic polymorphisms linked to the transport and metabolic pathways of MTX, on the therapeutic response of this drug, in terms of efficacy and safety, in a cohort of RA patients treated with MTX in monotherapy.

Table 1.- Bivariate and Multivariate Response / Remission: clinical characteristics

	MTX response		MTX remission	
Characteristics	Bivariate OR [95% CI] (p value)	Multivariate OR [95% CI] (p value)	Bivariate OR [95% CI] (p value)	Multivariate OR [95% CI] (p value)
Sociodemographic				
Age at diagnosis	**1,05 [1,03-1,07] (<0,0001)**	1,04 [0,99-1,06] (0,125)	**1,03 [1,01-1,05] (0,001)**	
Sex woman	0,74 [0,46-1,20] (0,221)	**0,45 [0,20-0,98] (0,044)**	0,71 [0,43-1,18] (0,184)	**0,46 [0,23-0,94] (0,033)**
Current smoker	**0,37 [0,22-0,63] (<0,0001)**	**0,38 [0,17-0,86] (0,021)**	**0,39 [0,21-0,71] (0,002)**	**0,41 [0,19-0,88] (0,022)**
Previous or current drinker	1,36 [086-2,17] (0,188)		1,29 [0,79-2,10] (0,302)	
Of the disease itself				
Symptoms-diagnosis time	1,00 [0,99-1,01] (0,783)		1,00 [0,99-1,01] (0,910)	
RF	0,61 [0,34-1,09] (0,094)		0,88 [0,48-1,59] (0,666)	
ACPA	0,71 [0,43-1,18] (0,185)	1,76 [0,77-4,04] (0,179)	0,70 [0,41-1,17] (0,175)	**2,16 [1,01-4,61] (0,047)**
Bone erosions	**0,26 [0,16-0,42] (<0,0001)**	**0,35 [0,16-0,79] (0,011)**	**0,19 [0,11-0,32] (<0,0001)**	**0,24 [011-0,51] (<0,0001)**
DAS28CPR	**0,08 [0,04-0,14] (<0,0001)**	**0,11 [0,06-0,20] (<0,0001)**	**0,15 [0,09-0,24] (<0,0001)**	**0,19 [0,11-0,34] (<0,0001)**
Extraarticular manifestations	0,59 [0,34-1,01] (0,054)		**0,33 [0,17-0,64] (0,001)**	**0,36 [0,15-0,88] (0,026)**
Positive Mantoux	**0,20 [0,09-0,44] (<0,0001)**	**0,33 [0,11-0,99] (0,047)**	**0,18 [0,06-0,52] (0,001)**	
Of the treatment				
Previous DMARD number	**0,46 [0,31-0,68] (<0,0001)**	0,65 [0,37-1,15] (0,139)	**0,51 [0,33-0,81] (0,004)**	
Symptoms-MTX time	0,99 [0,99-1,00] (0,056)		**0,99 [0,98-1,00] (0,012)**	
Acid folic dose	**0,97 [0,93-0,99] (0,039)**	0,96 [0,91-1,00] (0,063)	0,98 [0,95-1,01] (0,203)	
MTX dose	**0,87 [0,82-0,93] (<0,0001)**		**0,83 [0,78-0,90] (<0,0001)**	**0,90 [0,82-0,99] (0,048)**
Parenteral MTX	1,80 [0,89-3,65] (0,103)		**2,10 [1,05-4,21] (0,036)**	
Prednisone dose	**0,93 [0,90-0,98] (0,004)**	0,95 [0,89-1,02] (0,150)	0,97 [0,92-1,01] (0,131)	
		Pseudo R^2=0,46		Pseudo R^2=0,34

Methods: Case-control study nested in a cohort of patients with RA of the Hospital de Mérida, Spain, (2012-2015), followed-up by protocol in the monographic consultation of RA of the Rheumatology Service and treated with MTX monotherapy (since 1990). Efficacy was defined as a maintained response (low activity) and remission during follow-up, according to DAS28-PCR, and toxicity, as any adverse event related to MTX at any time during treatment. The SNPs *ABCB1*_C3435T, *GGH*_T16C, *FPG*_G2782A, *MTHFR*_C677T, *MTHFR*_A1298C, *AMPD1*_C34T, *ITPA*_C94A and *ADA*_A534G, and variables related to the pts, the disease and the treatment were studied.

Results: A total of 301 pts were included (mean age at diagnosis 50 years, 67% women, mean baseline value of DAS28-PCR of 4.5, baseline deterioration of physical function in 75%, early bone erosions in 55% and extraarticular involvement in 24%), representative of a severe RA. MTX monotherapy failed in half of the pts, generally due to lack of efficacy, and half had adverse events related to MTX, most frequently gastrointestinal, neurological and hepatic, which caused the suspension of MTX in a third of the cases and an 18 % of the total. The probability of MTX response was lower in women, active smokers and patients with more severe disease (higher baseline activity, early erosions and extra-articular manifestations), and independently of the clinical determinants, in homozygotes for the mutated allele (C/C genotype) of the *MTHFR*_A1298C SNP and in the carriers of the CC haplotype of C677T-A1298C of *MTHFR* (28.2%). T/T genotype of MTHFR_677CTc was associated with a higher probability of remission (OR = 4.07). The overall toxicity was more frequent in women and younger pts and C/T genotype of *MTHFR*_C677T. Hepatic toxicity was more frequent with positive Mantoux, G/G genotype of *ADA*_A534G and males, but no fe-

Table 2.- Bivariate and Multivariate Toxicity: clinical characteristics

Characteristics	AE global		AE digestive		AE hepatic		AE hematologic	
	Bivariate OR (p value)	Multivariate OR (p value)	Bivariate OR (p value)	Multivariate OR (p value)	Bivariate OR (p value)	Multivariate OR (p value)	Bivariate OR (p value)	Multivariate OR (p value)
Sociodemographic								
Age at diagnosis	**0,98 (0,012)**	**0,97 (0,001)**	**0,98 (0,015)**	**0,98 (0,039)**	1,00 (0,886)		1,01 (0,531)	
Sex woman	**1,95 (0,007)**	**2,14 (0,004)**	**2,33 (0,005)**	**2,45 (0,004)**	0,69 (0,365)		2,02 (0,285)	3,37 (0,108)
Current smoker	1,04 (0,884)		0,86 (0,601)		1,28 (0,567)		0,37 (0,197)	
Previous or current drinker	0,73 (0,188)		0,63 (0,084)		1,71 (0,186)	1,39 (0,433)	0,53 (0,291)	
Of the disease itself								
Symptoms-diagnosis time	1,00 (0,406)		1,00 (0,865)		1,01 (0,154)		1,00 (0,867)	
RF	0,83 (0,522)		0,82 (0,533)		1,08 (0,882)		3,56 (0,224)	
ACPA	1,03 (0,898)		1,28 (0,403)		0,98 (0,960)		1,57 (0,504)	
Bone erosions	1,33 (0,230)		0,91 (0,719)		1,31 (0,526)		**12,1 (0,017)**	**8,75 (0,045)**
DAS28CPR	**1,38 (0,023)**		1,17 (0,305)		1,55 (0,065)		**1,93 (0,036)**	
Extra-articular manifestations	**1,84 (0,028)**		1,14 (0,658)		2,05 (0,090)		**4,04 (0,009)**	3,01 (0,075)
Chronic disorders number	**1,14 (0,029)**	**1,29 (<0,0001)**	1,07 (0,313)		**1,20 (0,049)**	1,20 (0,062)	**1,8 (<0,0001)**	**1,74 (<0,0001)**
Positive Mantoux	1,71 (0,114)		1,84 (0,077)	**2,15 (0,033)**	**2,97 (0,018)**	**2,65 (0,042)**	0,95 (0,943)	
Of the treatment								
Previous DMARD number	1,30 (0,106)		1,17 (0,332)		1,43 (0,110)		**2,3 (<0,0001)**	
Symptoms-MTX time	1,00 (0,446)		1,00 (0,077)		1,00 (0,355)		1,00 (0,064)	
Acid folic dose D	1,00 (0,976)		1,00 (0,989)		0,94 (0,283)		1,07 (0,354)	
MTX dose	0,72 (0,347)		0,65 (0,300)		0,88 (0,845)		1,85 (0,358)	
Parenteral MTX	1,00 (0,846)		0,99 (0,746)		0,97 (0,408)		0,92 (0,237)	
Prednisone dose	0,99 (0,590)	Pseudo R^2=0,06	0,98 (0,447)	Pseudo R^2=0,05	1,00 (0,964)	Pseudo R^2=0,05	1,08 (0,043)	1,10 (0,066) Pseudo R^2=0,32

Table 3. Summary of the multivariate analysis of polymorphisms: efficacy and safety of MTX

Polymorphism SNP reference	Related way	Expected effect	Previous studies		Cohort of Mérida	
			Toxicity	Eficaccy	Toxicity	Eficaccy
***ABCB1* 3435C>T** rs1045642	MTX efflux	↑ effectiveness ↑ toxicity	Inconclusive	Inconclusive	alelo T (female) ↓ hematologic	Inconclusive
***FPGS* 2572G>A** rs1544105	MTX-PG aggregation	↓ effectiveness ↓ toxicity	Not evaluated	Inconclusive	G/A (male) ↓ digestive	Not related
***GGH* 16T>C** rs1800909	MTX-PG disintegration	↑ effectiveness ↑ toxicity	Not related	Not related	C/C ↑ neurologic	C/C (male) ↓ effectiveness
***MTHFR* 677C>T** rs1801133	Folic acid regeneration and DNA synthesis	↑ homocysteine ↑ effectiveness ↑ toxicity	Related	Not related	T/C ↑ global toxicity	C/C ↑effectiveness (remission)
***MTHFR* 1298A>C** rs1801131	Folate regeneration and DNA synthesis	↑ effectiveness ↑ toxicity	Inconclusive	Not related	C/C (male) ↑ hepatic A/C ↑ alopecia	C/C ↓effectiveness (low activity)
***ITPA* 94C>A** rs1127354	Purine synthesis	↑ adenosine ↑ effectiveness	Not related	↑ effectiveness	Inconclusive	Inconclusive
***AMPD1* 34C>T** rs17602729	Purine synthesis	↑ adenosine ↑ effectiveness	Not related	↑ effectiveness	Inconclusive	Inconclusive
***ADA* 534A>G** rs244076	Purine synthesis	↑ adenosine ↑ effectiveness	Not evaluated	↓ effectiveness	A/G ↓ global and digestive G/G ↑hepatic alelo G ↓ alopecia	Not related
Haplotype *MTHFR* C677T–A1298C	Folate regeneration and DNA synthesis	↑ effectiveness ↑ toxicity			Haplotype C-C (male) ↑ global and hepatic	Haplotypes C-A and C-C ↓effectiveness (LA and Remission)

males, with C/C genotype of MTHFR_A1298C. Some SNPs showed a protective effect for toxicity. Sex behaved as a modifying factor.

Conclusion: Most of the SNPs studied have been associated with some measure of outcome, although the size of the effect is small. Genetic association studies should take into account the sex of patients and other clinical variables. Young patients and women had a worse response. Smoking is the main modifiable risk factor of poor response to MTX in RA.

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Abstract Number: 2364

Multi-center Analyses on 518 Cases with Rheumatoid Arthritis Developing Lymphoproliferative Disorders (RA-LPD): The Prognostic Factors and the Influence of Anti-rheumatic Drugs on LPD Development

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SESSION INFORMATION

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Background/Purpose: Lymphoproliferative disorders (LPD) remains as a major problem to resolve among the patients with rheumatoid arthritis (RA). During few decades, rheumatic therapy has dramatically changed with the ad-

vent of new disease modifying anti-rheumatic drugs (DMARDs). However, it is unclear whether these drugs relate to LPD developing in the patients withRA.

Methods: The current study included 518 RA-LPD patients in a Japanese multi-center collaborative study in order to characterize the current clinicopathological feature of RA-LPD and influence of methotrexate (MTX), tacrolimus (TAC) and biologic agents.

Results: Patient age at RA-LPD diagnosis ranged from 16 to 90 (median 69) years (1:2.43, men:women). Diffuse large B cell lymphoma was most frequent (51.3%), with 225 cases (81.5%) regressing only upon immunosuppressive agent withdrawal. Among these, 63 (27.0%) exhibited regrowth. The 5-year survival rate was 86.9%. Multivariate analysis revealed that sex (male), advanced clinical stage, TAC medication, T cell phenotype, and > 70 years of age upon LPD development constituted unfavorable prognostic factors.Additionally, the current clinicopathological profiles indicated that RA-LPD could be categorized into four groups depending on the use of DMARDs. Naïve, MTX, TAC and Bio (anti-tumor necrosis factor (TNF)). Naïve group consisted of the patients (45 cases) who had not received had MTX, TAC and anti-TNF agents. The positivity of EBER-1 of this group was lower than those of other groups. But it was a poorer prognostic factor. MTX group (461 cases), in which MTX had been administered with or without other DMARDs, showed increase of Hodgkin lymphoma (HL) and pharynx origin and decrease of B cell phenotype, stomach and breast origin. TAC group (78 cases), in which TAC had been used with or without other DMARDs, had a feature of older age, prolonged duration from the time of MTX initial medication to LPD development, the increase of polymorphic-LPD, elevated CRP at the onset of LPD and poorer prognosis. Bio (anti-TNF) group (110 cases), in which biologic agents (anti-TNF) had been given with/without other GMARDs, had a feature of younger age at the onset of LPD, the elongated duration from the time of MTX initial medication to LPD development, increase the frequency of HL, HL-like lesion, EBER-1 positivity, and decrease of Follicular lymphoma.

Conclusion: In conclusion, the current analyses showed the prognostic factors of RA-LPD and the distinctive characteristics in relation to the use of anti-rheumatic drugs.

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Abstract Number: 2365

Risk of Diabetes Treatment Switching or Intensification Associated with Use of Abatacept versus Other Biologic Drugs in Patients with Rheumatoid Arthritis and Diabetes Mellitus

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

Background/Purpose: Rheumatoid arthritis (RA) patients have a high prevalence of cardiovascular comorbidities including diabetes mellitus (DM). Past studies have suggested a potential beneficial effect of abatacept on insulin sensitivity, but the effect of biologic therapy on DM severity in RA patients with DM is generally unknown. The objective of this study was to compare the rates of DM treatment switching or intensification among patients with RA and DM (type 1 or 2), newly initiating abatacept versus other disease-modifying antirheumatic drugs (DMARD).

Methods: We identified RA patients aged ≥18 years with ≥2 RA diagnoses separated by 7-365 days using claims data from Truven MarketScan database (2005-2016). We included new users of abatacept, tumor necrosis factor inhibitors (TNFi) (adalimumab, etanercept, certolizumab, golimumab, and infliximab), rituximab, tocilizumab, and tofacitinib. The date of their 1st drug dispensing was defined as the index date. We required ≥365 days of continuous enrollment prior to the index date, defined as the baseline period. We excluded patients with history of malignancy. Among these RA patients, we identified patients with DM by using ≥1 diagnosis for either type 1 or type 2 DM and ≥1 anti-diabetic drug prescription during baseline. The primary outcome was 'DM treatment switching or intensification' defined as adding or switching to a different oral antidiabetic medication or insulin. We calculated incidence rates (IR) and hazard ratio (HR) of DM treatment switching or intensification in patients initiating abatacept versus other biologic DMARDs or tofacitinib.

Results: We included 10,019 patients with both RA and DM initiating abatacept (mean age 58.5 years, female 78%), TNFi (56.7, 71%), rituximab (58.1, 76%), tocilizumab (57.6, 79%), or tofacitinib (58.0, 77%) (**Table 1**). Cardiovascular comorbidities were prevalent; hypertension was present in up to 74% and hyperlipidemia was present in up to 67% of patients. Baseline insulin use was highest in the rituximab group (44%) and lowest in the tofacitinib group (35%). Over the 7,396 total person-years of follow up, there were 1,643 total DM treatment switching or intensification events (**Table 2**). The crude IR of DM treatment switching or intensification per 1,000 person-years was highest in abatacept initiators (IR 236.7) and lowest in tofacitinib initiators (IR 203.3). After adjusting for 15 baseline covariates, the risk of DM treatment switching or intensification was similar between abatacept and TNFi (HR 0.94, 95% confidence interval [CI] 0.81-1.10), rituximab (HR 0.95, 95% CI 0.78-1.17), and tocilizumab (HR 0.86, 95% CI 0.68-1.07) and lower for tofacitinib (HR 0.78, 95% CI 0.60-1.01).

Conclusion: In patients with both RA and DM, we found no difference in the risk of DM treatment switching or intensification after initiating abatacept versus TNFi, rituximab, and tocilizumab, while the risk appeared to be lower for tofacitinib initiators compared to abatacept.

Table 1. Baseline characteristics of patients with rheumatoid arthritis and diabetes mellitus initiating DMARD therapy

	Abatacept (n=1,785)	TNF inhibitors (n=5,953)	Rituximab (n=888)	Tocilizumab (n=759)	Tofacitinib (n=634)
Mean age (SD), years	58.45 (10.26)	56.71 (10.41)	58.09 (10.75)	57.61 (10.07)	58.03 (9.71)
Female, %	78.0	71.5	75.7	78.9	77.0
Hypertension, %	70.3	67.2	72.4	72.6	73.5
Hyperlipidemia, %	57.3	56.9	58.3	65.2	67.4
Myocardial infarction, %	3.1	2.4	4.5	2.8	3.9
Heart failure, %	10.2	5.9	13.4	8.6	7.4
Renal disease, %	9.4	7.5	12.1	10.8	11.2
Liver disease, %	10.0	9.0	11.2	11.7	11.0
Insulin use, %	39.4	36.4	44.1	42.7	35.0
Methotrexate use, %	55.5	71.0	51.4	53.2	50.6
Hydroxychloroquine use, %	23.0	25.7	22.8	21.5	20.8
Statin use, %	57.2	56.7	54.2	60.9	62.2
ACE inhibitor/ARB* use, %	65.1	65.7	65.7	63.5	68.9
Hemoglobin A1c ordered, %	71.3	75.4	71.6	76.7	75.9
Mean cumulative steroid use (SD), mg	1,600.3 (6,320.2)	1,248.5 (5,280.5)	2,135.0 (4,324.2)	1,928.1 (4,174.8)	1,604.0 (4,694.9)
Mean Charlson comorbidity index (SD)	3.06 (1.26)	2.86 (1.16)	3.25 (1.46)	3.05 (1.27)	3.07 (1.33)

*Angiotensin converting enzyme inhibitor / angiotensin receptor blocker

Table 2. Rates and risk of diabetes treatment switching or intensification in patients with rheumatoid arthritis and diabetes mellitus initiating DMARD therapy

	Patients	Events	Person-years	IR	HR_1 (95% CI)	HR_2 (95% CI)
Abatacept	1,785	295	1,246	236.7	1.0 (ref)	1.0 (ref)
TNF inhibitors	5,953	1,021	4,644	219.8	0.95 (0.83-1.08)	0.94 (0.81-1.10)
Rituximab	888	143	615	232.4	0.97 (0.80-1.19)	0.95 (0.78-1.17)
Tocilizumab	759	106	507	209.0	0.88 (0.71-1.10)	0.86 (0.68-1.07)
Tofacitinib	634	78	384	203.3	0.84 (0.65-1.08)	0.78 (0.60-1.01)

IR per 1,000 person-years

HR_1 Unadjusted model

HR_2 Cox model adjusted for age, sex, index date, renal disease, liver disease, steroid use, number of previous biologic DMARDs, methotrexate use, hydroxychloroquine use, statin use, number of rheumatology visits, number of primary care physician visits, number of endocrinologist visits, number of oral antidiabetic drugs, and number of insulin drugs at baseline

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Abstract Number: 2366

Comparison of Healthcare Resource Utilization (HCRU) and Costs of Type 2 Diabetes Mellitus (T2DM)-Related Complications in TNFi-Experienced Medicare Beneficiaries with Rheumatoid Arthritis (RA) and T2DM Who Switch to Abatacept or Other Targeted Disease-Modifying Anti-Rheumatic Drugs

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with RA experienced an increase in the whole-body insulin sensitivity and a reduction in HbA1c levels from treatment with abatacept, which is a type of targeted DMARD (tDMARD).[1] Abatacept is often used in tumor necrosis factor inhibitor (TNFi)-experienced patients; however, comparative impact of tDMARDs on type 2 diabetes mellitus (T2DM) related outcomes is lacking. This study examined healthcare resource utilization (HCRU) and costs associated with T2DM in TNFi-experienced patients with RA and T2DM who switched to another tDMARD.

Methods: In this retrospective cohort study, 100% Medicare fee-for-service (FFS) claims (Parts A/B/D) were used to identify TNFi-experienced RA patients who initiated abatacept, another TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab) or non-TNFi (anakinra, rituximab, sarilumab, tocilizumab, tofacitinib) from 2010 through 2017. Patients ≥65 years of age were included if they had ≥2 diagnosis of RA, ≥1 diagnoses of T2DM or ≥1 T2DM medications, no recent history of cancer, and were continuously enrolled for 12 months pre-index date or date of tDMARD initiation. Patients were followed from tDMARD initiation until discontinuation of the index treatment, disenrollment, death, or end of study period, whichever occurred first. Patients who switched to abatacept were propensity score (PS) matched to TNFi and non-TNFi users separately on a wide range of confounders. T2DM-related complications for which HCRU and costs were estimated were from the validated Diabetes Severity Complication Index (DCSI)[2] - neuropathy, nephropathy, cerebrovascular, cardiovascular, retinopathy, peripheral vascular disease and metabolic. The HCRU of T2DM-related complications was estimated per 1,000 patients per month using counts of inpatient stay, ER visits and outpatient visits whereas Medicare costs or payments (2019 USD) were estimated as per-patient per month (PPPM).

Results: A total of 1,987 PS-matched pairs of abatacept and TNFi initiators, and 1,697 PS-matched pairs of abatacept and non-TNFi initiators were identified. During follow-up, the rate of hospitalizations with T2DM-related complications per 1,000 patients per month was the lowest in abatacept compared to both TNFi (20.6 vs. 24.2) and other non-TNFi groups (21.6 vs. 22.7). PPPM T2DM-related complication costs were lower in abatacept than in TNFI's and non-TNFI users by $141 and $11 respectively. The major driver of healthcare costs for each group was the utilization of inpatient services. PPPM T2DM-related costs decreased following initiation of the new line of treatment for both abatacept (12%-21%) and non-TNFI (14%) initiators, but it was the opposite for initiators of TNFis (10% increase).

Table. Rates and costs of T2DM-related complications in TNFi-experienced patients

Measures	PS Matched Cohort 1		PS Matched Cohort 2	
	Abatacept (N = 1,987)	TNFi (N = 1,987)	Abatacept (N = 1,697)	Other Non-TNFi (N = 1,697)
Mean Age	73.0	72.9	72.4	72.6
Mean CCI Score	4.4	4.4	4.4	4.5
Mean Duration of Follow-up (days)	377.5	364.3	346.9	334.0
T2DM-related HCRU by setting of care during follow-up, Per 1000 Patients Per Month				
Hospitalizations	20.6*	24.2	21.6	22.7
Cardiovascular	16.8	20.3	18.1	18.8
Cerebrovascular	1.8	2.1	2.0	1.5
Metabolic	0.7	0.4	0.7	0.5
Nephropathy	6.6*	8.9	7.3	8.2
Neuropathy	3.3	2.8	4.0	3.8
Peripheral Vascular Disease	1.8	3.1	2.0	3.2
Retinopathy	0.5	0.7	0.5	0.4
ER Visits	14.6	14.2	14.8	13.7
Hospital Outpatient Visits	115.2	118.2	118.2	113.2
Physician Office Visits	506.0	552.6	525.6	531.9
T2DM-related complication costs, PPPM				
Total Medical	$482*	$623	$504	$515
Inpatient	$254*	$350	$260	$270
ER	$13	$15	$14	$14
Hospital Outpatient	$74	$56	$86	$64
Physician Office	$76	$86	$81	$85
Other Medical (includes costs related to skilled nursing facility, home health and DME, and hospice utilization)	$63*	$116	$62	$81
Follow-up T2DM Medication Costs, PPPM	$64	$67	$71	$75

*P<0.05

T2DM = Type 2 diabetes mellitus, DME = durable medical equipment, PPPM = per-patient per month

Conclusion: These findings suggest that TNFi-experienced Medicare patients with RA and T2DM who switch to abatacept had a reduction in the rate and cost of hospitalizations associated with T2DM-related complications in comparison to patients who switch to other tDMARDs.

References:

1. Ursini F, et al. Medicine (Baltimore). 2015;94(21):e888.

2. Glasheen WP, et al. J Diabetes Complications. 2017;31(6):1007-1013.

Disclosure: V. Patel, Bristol-Myers Squibb, 3; **Z. Pulungan**, Bristol-Myers Squibb, 5; **A. Shah**, Bristol-Myers Squibb, 5; **B. Jones**, Bristol-Myers Squibb, 5; **A. Petrilla**, Bristol-Myers Squibb, 5; **L. Ferri**, Bristol-Myers Squibb, 1, 3, 4, Bristol-Myers Squibb Company, 1, 3; **X. Han**, Bristol-Myers Squibb, 3, Bristol-Myers Squibb Company, 3; **K. Michaud**, FORWARD, The National Databank for Rheumatic Diseases, 3, Pfizer, 2, Pfizer & Rheumatology Research Foundation, 2, Rheumatology Research Foundation, 2, University of Nebraska Medical Center, 3.

Abstract Number: 2367

The Effect of DMARDs on Cardiovascular Outcomes in Rheumatoid Arthritis: A Systematic Literature Review

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
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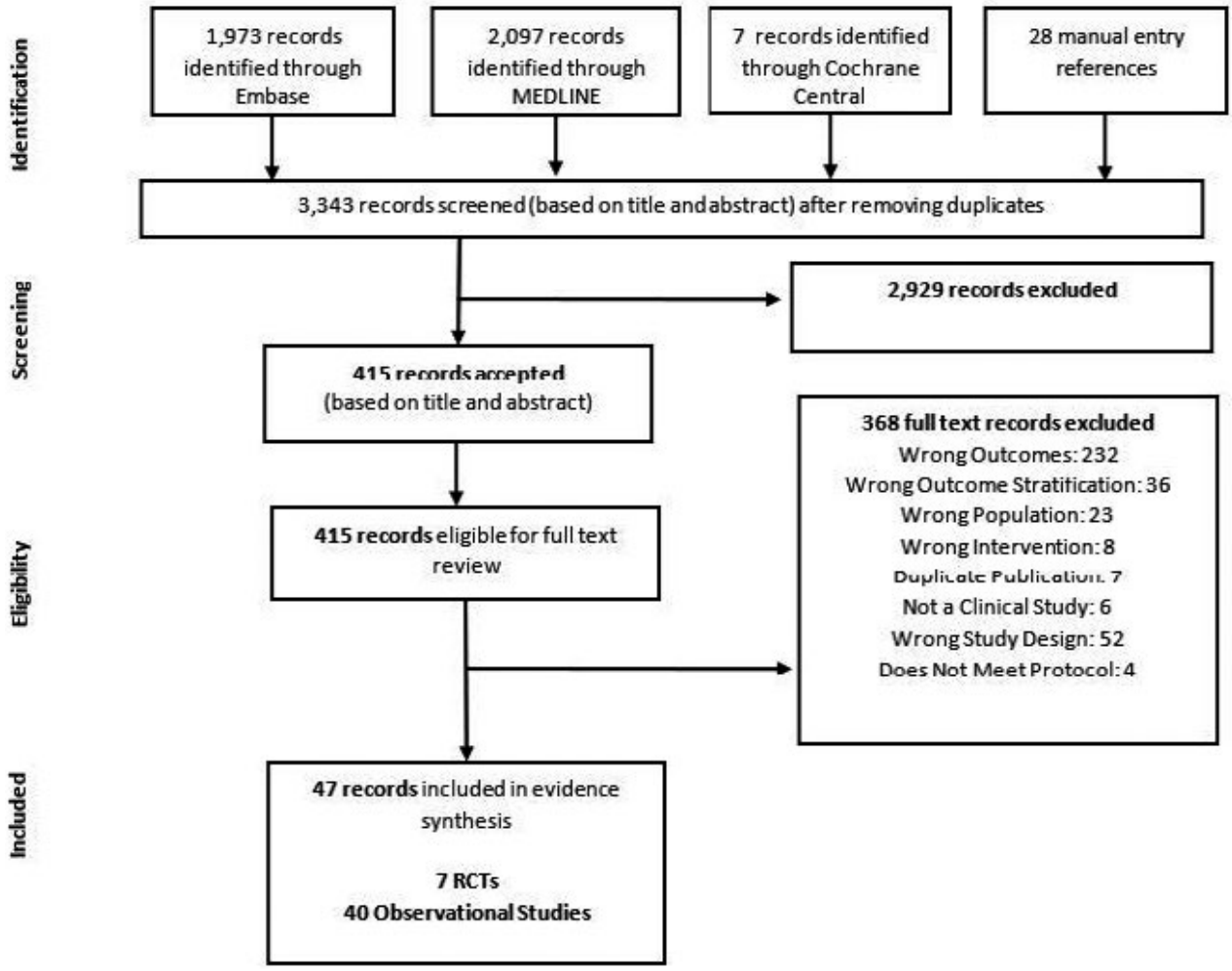
Background/Purpose: Autoantibodies and chronic systemic inflammation experienced in rheumatoid arthritis (RA) increases the risk of cardiovascular disease (CVD). This systematic literature review (SLR) aimed to characterize the available evidence with respect to the effect of DMARDs on cardiovascular outcomes in patients with RA with and without history of CVD.

Methods: A SLR was conducted by searching MEDLINE, Embase, and Cochrane CENTRAL databases (inception to Jan. 2019) supplemented by a search in conference proceedings from ACR and EULAR (2017 to 2019), and US and European clinical trial registries (Jan. 2005 to Jan. 2018). Studies eligible for inclusion were observational studies and randomized controlled trials (RCTs) investigating adult patients with RA treated with biologic and non-biologic DMARDs and reporting cardiovascular events including major adverse cardiac events (MACE), other cardiovascular event composites, myocardial infarction (MI), stroke, and heart failure.

Results: As described in Figure 1, the SLR yielded 47 eligible publications, including 7 RCTs, 6 prospective observational, and 34 retrospective observational studies. Baseline rates of CVD (0%-83%) or history of cardiovascular events (0%-80.1%) varied between studies with six studies entirely excluding patients with cardiovascular comorbidities.

The most commonly reported outcomes were cardiovascular event composites (MACE or other) and MI (Table 1). Incidence rates (per 1000 person-years) for any cardiovascular event composite ranged from 3.1-30.7 for csDMARDs,



DMARDFig1
Figure 1: PRISMA diagram

2.93-35.8 for TNF inhibitors (TNFi) and 3.7-23.8 for non-TNFi. The rate of MI ranged from 2.38-10.4 for csDMARDs, 0.51-9.3 for TNFi and 2-8.43 for non-TNFi. Rates were heterogenous across studies, likely due to differences in cardiovascular characteristics. One study found a five-fold increase in cardiovascular outcomes for patients with a history of CVD, HR 5.302.

Twenty studies reported statistically significant differences between DMARDs for a variety of cardiovascular outcomes (Table 2). Compared to unexposed patients, hydroxychloroquine, TNFi, sulfasalazine, leflunomide, and methotrexate significantly lowered risk of cardiovascular outcomes with HRs ranging from 0.32 (95% CI 0.18-0.56) to 0.89 (0.82-0.98). Head-to-head comparisons of DMARDs found abatacept to significantly lower cardiovascular outcomes compared to TNFi [0.71 (0.55-0.93) to 0.841 (0.75-0.94)]. Another non-TNFi biologic, rituximab, also significantly lowered risk of CV events [0.78 (0.63-0.98)]. TNFi significantly lowered outcome rates compared to non-biologic DMARDs [0.24 (0.06-0.95) to 0.39 (0.19-0.82)] and csDMARDs [0.45 (0.21-0.96) to 0.83 (0.704-0.98)], although a single study found TNFi inferior to MTX for heart failure requiring hospitalization [1.7 (1.07-2.69)].

Study	DMARD	Incidence Rate per 1000 person-years	
		MACE or CV Composite	MI
Gale S. (2017)	TCZ	NR	3.3
Generali E (2017)	ETN	19.6	NR
	TCZ	21.9	NR
Giollo A. (2018)	RTX	10	
Greenberg JD (2010)	MTX	6.73	2.38
	nbDMARD	7.51	2.2
	TNFi	2.93	0.51
Harrold LR (2018)	CTZ	20.8	3.6
	TNFi	20.5	1.2
Herrinton LJ (2018)	MTX	10.1	NR
	MTX + other nbDMARD	10.83	NR
	non-MTX nbDMARD	11.27	NR
	non-TNFi	5.82	NR
	TNFi + MTX	4.79	NR
	TNFi + non-MTX nbDMARD	11.93	NR
	TNFi + MTX + other nbDMARD	6.78	NR
Jacobsson LT (2005)	TNFi	14	NR
	unexposed	35.4	NR
Jin Y (2018) (MarketScan/Medicare)	ABA	13.8/23.8	NR
	TNFi	12.7/35.8	NR
Kang EH (2018)	ABA	23.8	NR
	TNFi	29.7	NR
Kim SC (2017)	TCZ	5.2	NR
	TNFi	5.9	2.7
Kim SC (2018)	ABA	9.6	NR
	TCZ	7	NR
Low AS (2017)	csDMARD	NR	5.6
	TNFi	NR	3.5
Ogdie A (2015)	DMARD	11.1	5.1
	unexposed	13.5	4.5
Sharma TS (2016)	HCQ	3.1	NR
	unexposed	12.8	NR
Solomon DH (2013)	csDMARD	30.7	10.4
	TNFi	23.1	6.7
Wasko MC (2014)	PBO	NR	5.9
	GOL 50-100	NR	1.2
	GOL 100	NR	1.9
Weinblatt ME (2014)	PBO	0	NR
	FST 100	0	NR
	FST 150	8	NR
Xie F (2018) (MarketScan/Medicare)	ABA	8.7/13.7	5.1/7.3
	ADA	5.2/14	2.6/7.2
	ETN	5.5/11.8	2.6/6.4
	IFX	8.2/17.3	3.9/9.3
	RTX	11/16.6	7.2/8.2
	TCZ	5.2/12.9	2.9/7.7
	TNFi	5.8/15	2/6.9
Zhang J (2016)	ABA	13.66	7.36
	ADA	11.02	6.82
	CTZ	9.73	8.02
	ETN	12.09	7.91
	GOL	7.62	5.71
	IFX	14.46	8.78
	RTX	13.36	8.43
	TCZ	8.07	6.23

ABA = abatacept; ADA = adalimumab; bDMARD = biologic DMARD; csDMARD = conventional synthetic DMARD; ETN = etanercept; FST = fostamatinib; GOL = golimumab; HCQ = hydroxychloroquine; IFX = infliximab; MTX = methotrexate; nbDMARD = non-biologic DMARD; RTX = rituximab; SSZ = sulfasalazine; TCZ = tocilizumab; TNFi = tumor necrosis factor inhibitor

DMARDTable1

Table 1: Incidence Rates of MACE or CV Composite and Myocardial Infarction

Conclusion: This review found the rate of cardiovascular outcomes to vary widely across studies. We found DMARDs to consistently lower the rate of cardiovascular events compared to unexposed patients. Although data is still limited, multiple studies reported that non-TNFi significantly lower cardiovascular event rates compared to TNFi.

DMARD	Comparator	Study	Outcome	HR (95% CI)
DMARD vs unexposed patients				
TNFi	unexposed	Jacobsson LT (2005)	CV Hospitalization	0.34 (0.17-0.65)
		Ljung L (2014)	ACS	0.73 (0.6-0.89)
		Naranjo A (2008)	CV Composite	0.64 (0.49-0.83)
			MI	0.42 (0.21-0.81)
SSZ	unexposed	Naranjo A (2008)	CV Composite	0.91 (0.87-0.96)
			MI	0.82 (0.69-0.98)
MTX	unexposed	Naranjo A (2008)	CV Composite	0.85 (0.81-0.89)
			MI	0.82 (0.74-0.91)
			Stroke	0.89 (0.82-0.98)
LefI	unexposed	Naranjo A (2008)	CV Composite	0.59 (0.43-0.79)
HCQ	unexposed	Shapiro M (2018)	MI or Stroke	0.461 (0.274-0.778)
			CV Composite	0.432 (0.243-0.768)
			MI or Stroke	0.433 (0.227-0.827)
		Sharma TS (2016)	CV Disease	0.6 (0.41-0.94)
		Hung YM (2018)	CAD	0.32 (0.18-0.56)
non-TNFi vs TNFi				
ABA	TNFi	Zhang J (2016)	Mortality, Cardiac	0.841 (0.75-0.94)
			MI, Acute	0.7813 (0.63-0.97)
		Jin Y (2018)	CV Composite	0.79 (0.67-0.92)
			MI	0.71 (0.55-0.93)
		Kang EH (2018)	CV Composite	0.81 (0.66-0.99)
			Revascularization	0.74 (0.57-0.97)
			MI	0.77 (0.59-0.998)
TCZ	TNFi	Xie F (2018)	CV Composite	0.7874 (0.63-0.98)
		Kim SC (2017)	CV Composite	0.68 (0.49-0.94)
			Revascularization	0.6 (0.37-0.96)
TNFi vs nbDMARD				
TNFi	nbDMARD	Greenberg JD (2010)	CV Composite	0.39 (0.19-0.82)
			CV Composite, Non-Fatal	0.35 (0.16-0.74)
			MI, Non-Fatal	0.24 (0.06-0.95)
TNFi vs csDMARD				
TNFi	csDMARD	Bili A (2013)	CAD	0.45 (0.21-0.96)
		Solomon DH (2013)	CV Composite	0.71 (0.52-0.97)
		Al-Aly Z (2011)	Cerebrovascular Disease	0.83 (0.704-0.98)
	Non-MTX csDMARD	Low AS (2017)	MI	0.61 (0.41-0.89)
	MTX	Setoguchi S (2008)	HF Hospitalization	1.75 (0.86-3.56)
bDMARD vs bDMARD				
ABA	ETN	Zhang J (2016)	MI, Acute	0.7519 (0.57-0.99)
	IFX		MI, Acute	0.7692 (0.61-0.97)
	RTX		Mortality, Cardiac	0.5692 (0.5-0.65)
TCZ	ABA	Xie F (2018)	MI	0.4149 (0.19-0.89)
	RTX		MI	0.3367 (0.15-0.75)
	IFX		CV Composite	0.6211 (0.47-0.82)
			MI	0.6452 (0.44-0.95)
			Stroke	0.6711 (0.45-0.99)

Data are expressed as hazard ratio and 95% confidence interval. HRs <1 favor the DMARD vs the comparator. ABA = abatacept; ACS = acute coronary syndrome; bDMARD = biologic DMARD; CAD = coronary artery disease; csDMARD = conventional synthetic DMARD; CV = cardiovascular; ETN = etanercept; HCQ = hydroxychloroquine; HF = heart failure; IFX = infliximab; LefI = leflunomide; MI = myocardial infarction; MTX = methotrexate; nbDMARD = non-biologic DMARD; RTX = rituximab; SSZ = sulfasalazine; TCZ = tocilizumab; TNFi = tumor necrosis factor inhibitor

DMARDTable2
Table 2: Significant Differences in Cardiovascular Outcomes

Disclosure: V. Patel, Bristol-Myers Squibb, 3; **L. Ferri**, Bristol-Myers Squibb, 1, 3, 4, Bristol-Myers Squibb Company, 1, 3; **X. Han**, Bristol-Myers Squibb, 3, Bristol-Myers Squibb Company, 3; **L. Mintzer**, Doctor Evidence, 3; **M. Fazeli**, Doctor Evidence, 3.

Abstract Number: 2368

Risk of Diverticulitis and Gastro-Intestinal Perforation in Rheumatoid Arthritis Treated with Tocilizumab Compared to Rituximab and Abatacept: A Prospective Propensity-matched Cohort Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Treatments Poster III: Safety and Outcomes

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Background/Purpose: Several studies have reported an increased risk of gastro-intestinal perforation (GIP) in rheumatoid arthritis (RA) patients treated with tocilizumab (TCZ) compared to conventional synthetic disease modifying anti rheumatic drugs (csDMARDs) or TNF inhibitors (TNFis) (1–3). However, a recent study did not find an increased risk of GIP with TCZ compared to TNFis and even compared to others biologic-DMARDs (bDMARDs), namely rituximab (RTX) and abatacept (ABA) (4). The aim of our study was to compare the risk of diverticulitis and GIP in RA patients treated with TCZ compared to RTX and ABA using a propensity-matched analysis.

	TCZ registry (n=1492)	RTX registry (n=1986)	ABA registry (n=1019)	All patients (n=4501)
Female, % (n)	79.9 (1196)	78.7 (1563)	69.3 (706)	77.0 (3465)
Age, mean+/-SD	56.6+/-13.6	58.0+/-12.7	58.1+/-13.6	57.5+/-13.2
History of DM, % (n)	10.4 (156)	9.9 (196)	11.6 (118)	10.4 (470)
History of neoplasia, % (n)	5.4 (81)	12.4 (238)	5.8 (59)	8.5 (378)
Charlson index, mean+/-SD	3.0+/-1.5	3.2+/-1.8	3.3+/-1.9	3.1+/-1.7
Tobacco exposure, % (n)	21.2 (317)	21.9 (435)	9.8 (100)	18.9 (852)
RA duration, mean+/-SD (months)	152.3+/-120.2	163.4+/-114.7	168.5+/- 114.5	161.0+/-116.6
RF and/or ACPA positive, % (n)	88.0 (1193)	85.6 (1692)	86.9 (831)	87.3 (3716)
Exposure time, mean+/-SD (months)	32.0+/-22.0	38.2+/-32.5	29.0+/-29.5	34.1+/-29.0
Concomitant treatment with csDMARDs, % (n)	59.6 (892)	64.8 (1287)	55.3 (563)	60.9 (2742)
Concomitant treatment with CS, % (n)	68.4 (1024)	77.7 (1544)	74.7 (761)	74.0 (3329)
Daily dose of CS at inclusion, mean+/-SD	10.2+/-7.3	12.1+/-9.9	11.3+/-8.4	11.3+/-8.9
Daily dose of CS during the follow up, mean+/-SD	7.5+/-4.2	6.8+/-4.8	6.4+/-4.5	6.9+/-4.6
DAS28 at inclusion, mean+/-SD	5.1+/-1.3	5.6+/-1.2	5.3+/-1.3	5.3+/-1.3
DAS28 during the follow up, mean+/-SD	3.3+/-1.2	4.3+/-1.1	4.0+/-1.2	3.9+/-1.2

Table 1: Characteristics of patients including in the French registries TCZ=tocilizumab ; RTX=rituximab ; ABA=abatacept ; DM=diabetes mellitus ; RA=rheumatoid arthritis ; RF=rheumatoid factor ; ACPA= anti-citrullinated protein antibodies ; csDMARDs=conventional synthetic disease modifying anti rheumatic drugs ; CS=corticosteroids; SD=standard deviation

Methods: We conducted a study of patients with TNFis refractory RA, prospectively followed in 3 observational French registries evaluating the effectiveness and safety of RTX (Autoimmunity and Rituximab (AIR)), ABA (Orencia and Rheumatoid Arthritis (ORA)), and TCZ (REGistry–RoAcTEmra (REGATE)). Adult patients with RA according to the 1987 ACR criteria, initiating intravenous treatment with RTX, ABA, or TCZ were enrolled from 107 clinical centers between September 2005 and August 2013 (5). Using a propensity score approach, we compared the risk of diverticulitis or GIP during treatment with TCZ vs RTX and ABA. Pearson Chi-squared analysis and multivariable logistic regression were used to evaluate correlation between different risk factors and the onset of diverticulitis or GIP among TCZ, RTX or ABA (the latter 2 pooled). We also retrospectively collected the outcome of these specific adverse events and compared the clinical presentation by treatment.

Results: Forty-one diverticulitis and 19 GIP occurred in 4501 RA patients (patient's characteristics are shown in table 1) (corresponding incidences of 0.027 and 0.012 per 1000 person-years). Based on inverse probability weighting, there was an increased risk of GIP due to diverticulitis (5.66 [2.63-12.18], p< 0.0001) in the TCZ group vs RTX and ABA. There was also an increased risk of diverticulitis and GIP but not GIP due to another etiology. In multivariate analysis, age was associated with an increased risk of diverticulitis (1.03/year [1.01-1.06], p=0.03) in all patients, and history of neoplasia was associated with an increased risk of GIP in patients treated with TCZ (5.04 [1.03-24.65], p=0.04). Compared to RTX and ABA, diverticulitis and GIP during TCZ occurred earlier after the last perfusion (24.5+/-18.4 vs 58.6+/-49.2 days, p=0.01), with usually atypical clinical presentation (slow transit in 30% vs 0, p=0.04) and milder biological inflammatory markers at the time of the event (hemoglobin: 13.9+/-1.8 vs 10.6+/-2.8 g/dL, p=0.01; platelets: 251583+/-85976 vs 371500+/-68066/mm3, p=0.04; and C-reactive protein: 31.2+/- 58.4 vs 88.2+/-89.6 mg/L, p=0.005).

Conclusion: TCZ was associated with an increased risk of diverticulitis, GIP and GIP due to diverticulitis, but not those caused by another etiology, compared to RTX and ABA. Our study confirms an increased risk of GIP in RA patients treated with TCZ and could be explained by an increased risk of diverticulitis with misleading clinical presentation.

Disclosure: C. Rempenault, None; **C. Lukas**, None; **B. Combe**, AbbVie, 5, BMS, 5, 8, Chugai, 5, 8, Eli Lilly, 5, Eli Lilly and Company, 5, 8, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, UCB, 5, USD, 5; **I. Pane**, None; **X. Mariette**, Biogen, 2, Bristol-Myers Squibb, 5, GlaxoSmithKline, 5, Janssen, 5, LFB Pharmaceuticals, 5, OSE Immunotherapeutics, 2, Pfizer, 2, 5, UCB Pharma, 5, 8; **J. Gottenberg**, Abbvie, 8, BMS, 2, 5, Lilly, 5, 8, Pfizer, 2, 5, Roche, 8, Sanofi-Genzyme, 5, 8, UCB, 5, 8; **J. Morel**, None.

Abstract Number: 2369

Treatment Patterns with Disease Modifying Anti-rheumatic Drugs in United States Veterans with Newly Diagnosed Rheumatoid Arthritis, Psoriatic Arthritis, or Ankylosing Spondylitis

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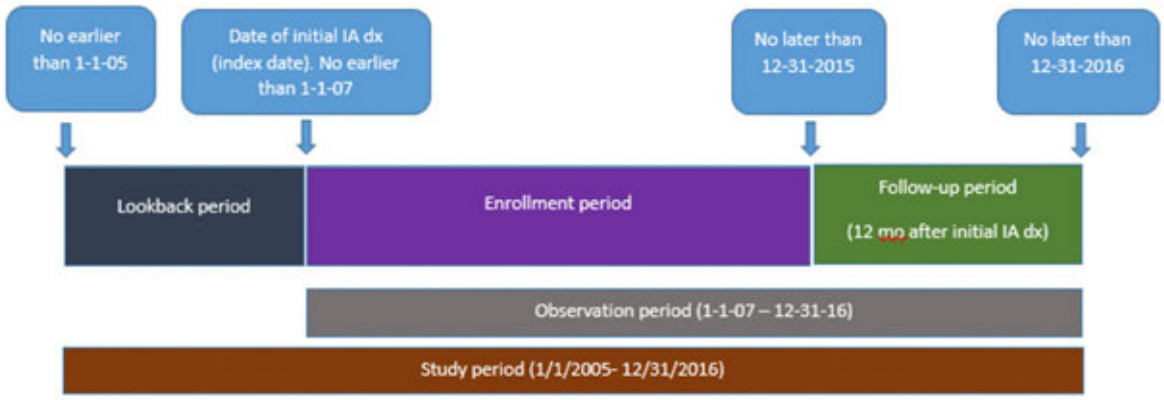
Figure 1. Study intervals



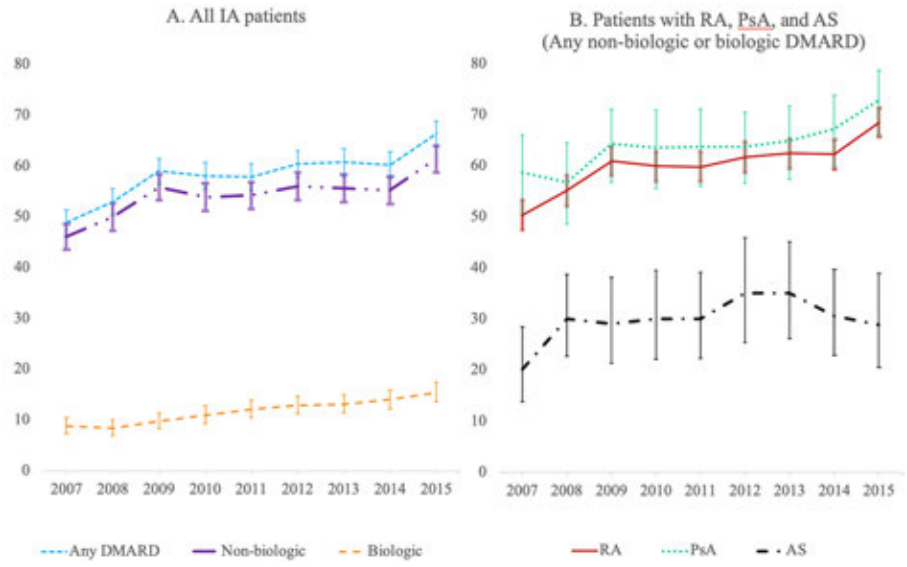
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Delays in treatment for inflammatory arthritis (IA) are associated with unfavorable outcomes, including impaired quality of life, irreversible joint damage, and disability. Our objective of this study was to characterize treatment initiation patterns in Veterans with newly diagnosed rheumatoid arthritis (RA), psoriatic arthritis (PsA) or ankylosing spondylitis (AS).

Table 1. Baseline demographics and characteristics

	All IA (n=12,118)	RA (n= 9,711)	PsA (n=1,472)	AS (n= 935)
	No./Mean (%/SD) [95% CI]	No./Mean (%/SD) [95% CI]	No./Mean (%/SD) [95% CI]	No./Mean (%/SD) [95% CI]
Age	63.7 (13.3) [63.4, 63.9]	65.2 (12.6) [64.9, 65.4]	57.8 (13.1) [57.1, 58.5]	57.6 (16.1) [56.5, 58.6]
Male	11,060 (91.3) [90.8, 91.8]	8798 (90.6) [90.0, 91.2]	1376 (93.5) [92.1, 94.6]	886 (94.8) [93.1, 96.0]
Ethnicity				
Hispanic	618 (5.1) [4.7, 5.5]	487 (5.0) [4.6, 5.5]	93 (6.3) [5.2, 7.7]	38 (4.1) [3.0, 5.5]
Non-Hispanic	10,932 (90.2) [89.7, 90.7]	8746 (90.1) [89.5, 90.6]	1320 (89.7) [88.0, 91.1]	866 (92.6) [90.8, 94.1]
Unknown	568 (4.7) [4.3, 5.1]	478 (4.9) [4.5, 5.4]	59 (4.0) [3.1, 5.1]	31 (3.3) [2.4, 4.7]
Race				
White	9281 (76.6) [75.8, 77.3]	7302 (75.2) [74.3, 76.0]	1247 (84.7) [82.8, 86.5]	732 (78.30 [75.5, 80.8]
Black	1600 (13.2) [12.6, 13.8]	1407 (14.5) [13.8, 15.2]	90 (6.1) [5.0, 7.5]	103 (11.0) [9.2, 13.2]
Other	642 (5.3) [4.9, 5.7]	508 (5.2) [4.8, 5.7]	75 (5.1) [4.1, 6.3]	59 (6.3) [4.9, 8.1]
Unknown	595 (4.9) [4.5, 5.3]	494 (5.1) [4.7, 5.5]	60 (4.1) [3.2, 5.2]	41 (4.4) [3.3, 5.9]
Geographic region at cohort entry				
Southeast	2119 (17.5) [16.8, 18.2]	1701 (17.5) [16.8, 18.3]	222 (15.1) [13.3, 17.0]	196 (20.7) [18.5, 23.7]
North Atlantic	3129 (25.8) [25.1, 26.6]	2546 (26.2) [25.4, 27.1]	406 (27.6) [25.4, 29.9]	177 (18.9) [16.6, 21.6]
Midwest	2862 (23.6) [22.9, 24.4]	2336 (24.1) [23.2, 24.9]	325 (22.1) [20.0, 24.3]	201 (21.5) [19.0, 24.2]
Continental	2123 (17.5) [16.9, 18.2]	1691 (17.4) [16.7, 18.3]	260 (17.7) [15.8, 19.7]	172 (18.4) [16.0, 21.0]
Pacific	1885 (15.6) [14.9, 16.2]	1437 (14.8) [14.1, 15.5]	259 (17.6) [15.7, 19.6]	189 (20.2) [17.8, 22.9]

Figure 2. Percentage of veterans treated with ≥1 DMARD within 12 months after the initial IA diagnosis in A. All Veterans with inflammatory arthritis and B. Veterans with RA, PsA, and AS



Methods: International Classification of Diseases codes and natural language processing were used to identify incident cases of RA, PsA, or AS, between January 1, 2007 and December 31, 2015, in patients enrolled in the Veteran Health Administration. Patterns of treatment initiation and non-treatment with disease modifying anti-rheumatic drugs (DMARDs) were assessed in the 12-month follow-up period after the incident diagnosis (Figure 1). Confidence intervals were used to statistically evaluate differences between comparison groups.

Results: The population consisted of 12,118 IA patients (9,711 RA, 1,472 PsA, 935 AS), with 91.3% males and a mean age of 63.7 (Table 1). The percentage of Veterans treated with ≥1 DMARD during the 12-month follow-up period increased from 48.8% in 2007 to 66.4% in 2015. Amongst Veterans diagnosed with IA in 2015, DMARD treatment was more common for PsA patients (72.9%) and RA patients (68.6%) than AS patients (28.9%). The mean time to the initial DMARD after diagnosis did not change over the observation period (35.5 days for RA, 43.9 days for PsA, 59.5 days for AS). In Veterans diagnosed with IA in 2015, a DMARD was dispensed ≤30 days after diagnosis in 45.8%, 31-90 days in 10.1%, and 91- 365 days for 10.5%; the remaining 33.6% were not treated with a DMARD within the 365-day follow-up period (Figure 2). Rheumatology specialty care was accessed by 87.4% of Veterans treated with a non-biologic DMARD and 92.2% treated with a biologic DMARD, in patients diagnosed in 2015.

Conclusion: DMARD treatment rates during the initial 12 months after diagnosis increased between 2007 and 2015, but non-treatment remained common, particularly in Veterans with AS. Time to treatment after the initial IA diagnosis did not change throughout the study period, and DMARDs were dispensed within 30 days of diagnosis for most Veterans who were treated within the 1-year follow-up period. DMARD treatment was uncommon in patients without rheumatology specialty care.

Disclosure: R. Overbury, None; **S. Pei**, None; **G. Penmetsa**, None; **B. Sauer**, None; **V. Patil**, None; **J. Walker**, None; **J. Clewell**, None; **K. Douglas**, None; **D. Clegg**, None; **G. Cannon**, Amgen, 2; **A. Halwani**, BMS, 2, KHK, 2,

Seattle Genetics, 2, Roche-Genentech, 2, Miragen, 2, Immunedesign, 2, Takeda, 2, Amgen, 2, Pharmacyclics, 2, Abbvie, 2; **J. Walsh**, AbbVie, 2, 5, ABBVIE, NOVARTIS, LILLY, AMGEN, UCB, 5, Amgen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, PFIZER, ABBVIE, 2, UCB, 5.

Abstract Number: 2370

Discontinuation of Disease Modifying Drugs in Patients with Incident Rheumatoid Arthritis

pia Lois,[1] Zulema Rosales Rosado,[1] Judit Font Urgelles,[2] Cristina Vadillo Font,[1] isabel Hernandez Rodriguez,[1] Juan Angel Jover Jover,[1] and lydia Abasolo Alcazar[1], [1]HOSPITAL CLINICO SAN CARLOS, MADRID, Spain, [2]HOSPITAL CLINICO SAN CARLOS, MADRID, Madrid, Spain

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment of Rheumatoid Arthritis (RA) has undergone a big change in the last two decades in strategies, objectives and therapeutic options, especially with the use of the Disease Modifying Drugs (DMARDs), both synthetic and biological. We have little information about the management of these drugs in real life conditions so it is necessary to expand our knowledge about discontinuations and their reasons. Purpose: to describe the discontinuations of DMARDs as well as their causes in patients with incident RA.

Methods: We conducted an observational longitudinal study. Patients: all recent onset RA diagnosed between January 1st 2007 and December 31st 2015 followed in outpatient clinic at Hospital Clínico San Carlos until January 1st 2017, which used any DMARD (synthetic and biologic) during at least 3 months. Primary outcome: discontinuation of the DMARD and cause of discontinuation (adverse event, inefficacy, patient decision, remission, doctor decision, others). Covariables: sociodemographic, clinical and treatment. Incidence rates of discontinuation (IR) per 100 patient-years were estimated using survival techniques with their respective 95% confidence interval [CI].

Results: We included 2388 courses of DMARD treatment in 814 patients (3706.14 patient-years). 77.52% were women with a mean age at diagnosis of 57.53±15.50 years. 72.85% of patients were diagnosed at first visit. From the courses of DMARD, 13.74% were biologicals (72.04% anti-TNF) and 60% were used in monotherapy. 55% of patients were RF positive, 44% ACPA positive and the mean DAS28 was 5.26±1.4. The most commonly prescribed drugs were Methotrexate (MTX) and Antimalarials (AM) among csDMARDs, and Etanercept (ETN) and Adalimumab (ADA) among bDMARDs. There were 1094 DMARDs discontinuations of the 2388 courses (45.81%) in 438 patients with an IR of 29.5[27.8-31.3]. 52% were due to adverse event (IR:15.95), 13.5% to inefficacy (IR: 3.99), 11.6% to doctor decision, 11.2% to patient decision, 5.8% to remission and 5.2% due to other causes. IR was higher in combined therapies, especially in triple therapy (IR: 78.19). It was higher in biologic therapy (IR: 48.8) compared to classical DMARDs. Regarding specific drugs, MTX had the lowest crude incidence (IR: 13.38). All IRs by variables are shown in table 1.

Conclusion: Global discontinuation rate was estimated in 29*patient-years, with 53.8% of treatments discontinued during follow-up. The major cause of suspension was adverse event appearance, followed by inefficacy. It seems that discontinuations are more common in combined therapies (especially in triple therapy) and in therapies including biologic drugs. Methotrexate was the most frequently prescribed drug and also the one with the lowest incidence rate of discontinuations.

	DISCONTINUATIONS			
	Patients/year	N	IR	95%CI
Total	3706,14	1094	29,52	27,82-31,32
By gender				
Female	2976.78	900	30.23	28.32-32.28
Male	729.36	194	26.60	23.11-30.62
By biological DMARD use				
No	3319.50	902	27.17	25.46-29.01
Yes	386.64	192	49.66	43.11-57.20
By type of biological DMARD				
Non biological	3319.50	902	27.17	25.46-29.01
Anti-TNF	295.10	144	48.80	41.44-57.46
Others	91.54	48	52.44	39.52-69.58
By combined therapy				
Monotherapy	2556.41	509	19.91	18.25-21.72
Combined therapy	1149.73	585	50.88	46.92-55.18
By number of DMARDs				
1	2556.41	509	19.91	18.25-21.72
2	957.88	435	45.41	41.34-49.89
≥3	191.85	150	78.19	66.62-91.76
By cause of discontinuation				
Adverse event	3706.14	586	15.95	14.71-17.29
Inefficacy		148	3.99	3.98-4.69
Doctor decision		124	3.35	2.81-3.99
Patient decision		116	3.13	2.61-3.75
Remission		66	1.78	1.40-2.27
Others		54	1.46	1.12-1.90
Synthetical DMARDs				
CQ	684.53	149	21.77	18.54-25.56
HCQ	626.88	108	17.23	14.27-20.80
LEF	482.83	149	30.86	26.28-36.23
MTX	2234.58	299	13.38	11.95-14.99
MTX sc	242.69	58	23.90	18.48-30.91
ORO	136.77	47	34.37	25.82-45.74
SSZ	224.45	72	32.08	25.46-40.41
AZA	37.61	5	13.30	5.53-31.94
Biological DMARDs				
ABA	12.68	11	86.76	48.05-156.66
ADA	123.95	46	37.11	27.80-49.55
CERTO	31.36	25	79.72	53.87-117.98
ETN	101.30	51	50.34	38.26-66.24
GOLI	14.77	10	67.69	36.42-125.80
INF	23.72	12	50.59	28.73-89.08
RTX	62.30	25	40.13	27.12-59.39
TOCI	16.56	12	72.45	41.14-127.57

DISCONTINUATIONS

Disclosure: p. Lois, None; **Z. Rosales Rosado**, None; **J. Font Urgelles**, None; **C. Vadillo Font**, None; **i. Hernandez Rodriguez**, None; **J. Jover Jover**, None; **I. Abasolo Alcazar**, None.

Abstract Number: 2371

Risk of Malignancies Across Biologic Classes in Rheumatoid Arthritis: Analysis of a National Claim Database

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Treatments Poster III: Safety and Outcomes

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Our objectives were to estimate and compare the incidence rate of malignancies associated with the different classes of biologics in RA patients.

Methods: We conducted an historical cohort study within the Frenchour national claim database, named SNIIRAM. Thisthat database prospectively records individual health resource use healthcare data of 86% of the entire French population (65 million inhabitants) since 2007. RA adult patients were identified based on ICD-10 code (M05 or M06) recorded from long-term chronic disease status allowing for full medical reimbursement and/or hospital discharge summaries discharge between 2007-2016. Patients with cancer history before biologic introduction were excluded.

Treatment exposures focused on incident first use of biologics including all anti-TNF, rituximab, abatacept, tocilizumab, ustekinumab, anakinra. To identify incident treatment periods, a one year period prior our period of analysis was analyzed; only patients that did not receive any biologics during this period were included. Patients having previously

Type of malignancies	HR [95% CI] Anti-TNF (ref) vs. other biologics	p-value
All malignancies	0.93 [0.77;1.14]	p=0.499
Solid cancer (excluding non-melanoma skin cancer)	0.92 [0.74;1.14]	p=0. 431
Lymphoma	0.59 [0.26;1.34]	p=0.209
	HR [95% CI] Anti-TNF (ref) vs. Abatacept	p-value
All malignancies	1.21 [0.84;1.73]	p=0. 346
Solid cancer (excluding non-melanoma skin cancer)	1.21 [0.82;1.80]	p=0. 381
Lymphoma	0.95 [0.35;2.53]	p=0. 909
	HR [95% CI] Monoclonal anti-TNF (ref) vs. Etanercept	p-value
All malignancies	1.11 [0.94;1.32]	p=0. 225
Solid cancer (excluding non-melanoma skin cancer)	1.11 [0.92;1.33]	p=0. 293
Lymphoma	1.00 [0.55;1.835]	p=0.992
Other hematologic malignancies	0.83 [0.45;1.52]	p=0. 530

receivedused only csDMARDs during observation period were included. For each individual, the index date was the first prescription of biologic to identify incident treatment periods. In the base case analysis, eExposure definition was considered with a 90-day latency after treatment initiation and a 180-day remanence period after drug discontinuation.

To compare the risk of malignancies between biologics, a propensity score (including age, sexe, year of first occurrence of RA code, date of treatment initiation, number of previous DMARDs, Charlson comorbidity index, diagnosis of tobacco and/or alcohol-associated disorders, number of hospitalisations for RA, cumulative corticosteroid dose) was constructed for each comparison. Hazard Ratios (HRs) for risk of cancer were estimated using Cox proportional hazards model with using propensity score inverse probability of treatment weighting (IPTW)weighting with stabilized weight. Since patients could have been exposed to different biologics, exposure was considered as a time-dependent variables and propensity score was estimated dynamically using pooled logistic regressionreassessed for each new exposure. Sensitivity analyses are ongoing to assess the robustness of our results.

Results: Between 2007 and 2016, 31792 patients (112802 patient-years)- were exposed to biologics. The annual incidence rate of overall malignancies was 0.865 per 100 patients. Malignancies occurred in 712 patients exposed to anti-TNF and 240 patients exposed to another biologic. The overall risk of malignancies and risk of lymphoma did not differ between anti-TNF and other biologics (analysed all together), or abatacept. Within the anti-TNF class, the overall risk of malignancies and risk of lymphoma did not differ between etanercept and monoclonal anti-TNF.

Conclusion: Using a large nationwide healthcare database, representative of the French population, the overall risk of malignancies did not seem to differ across the different classes of biologic. Also, among anti-TNF, etanercept and monoclonal antibodies did not differ regarding the risk of malignancies including the risk of lymphoma.

Comparision of risk of malignancies between biologics in RA patients

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Disclosure: R. Seror, bms, 5, BMS, 5, GSK, 5, gsk, 5, pfizer, 5, PFIZER, 5, ROCHE, 5, roche, 5; **A. Lafourcade**, None; **y. De Rycke**, None; **B. Fautrel**, AbbVie, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Boehringer Ingelheim, 8, Celgene, 5, 8, Eli Lilly and Company, 2, 5, Janssen, 5, 8, Lilly, 8, Medac, 5, 8, MSD, 2, 5, 8, NORDIC Pharma, 5, 8, Novartis, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, Sanofi-Aventis, 5, SOBI, 5, 8, UCB, 5, 8; **X. Mariette**, Biogen, 2, Bristol-Myers Squibb, 5, GlaxoSmithKline, 5, Janssen, 5, LFB Pharmaceuticals, 5, OSE Immunotherapeutics, 2, Pfizer, 2, 5, UCB Pharma, 5, 8; **F. Tubach**, MSD, 5.

Abstract Number: 2372

Post-Approval Comparative Safety Study of Tofacitinib and Biologic DMARDs: Five-Year Results from a US-based Rheumatoid Arthritis Registry

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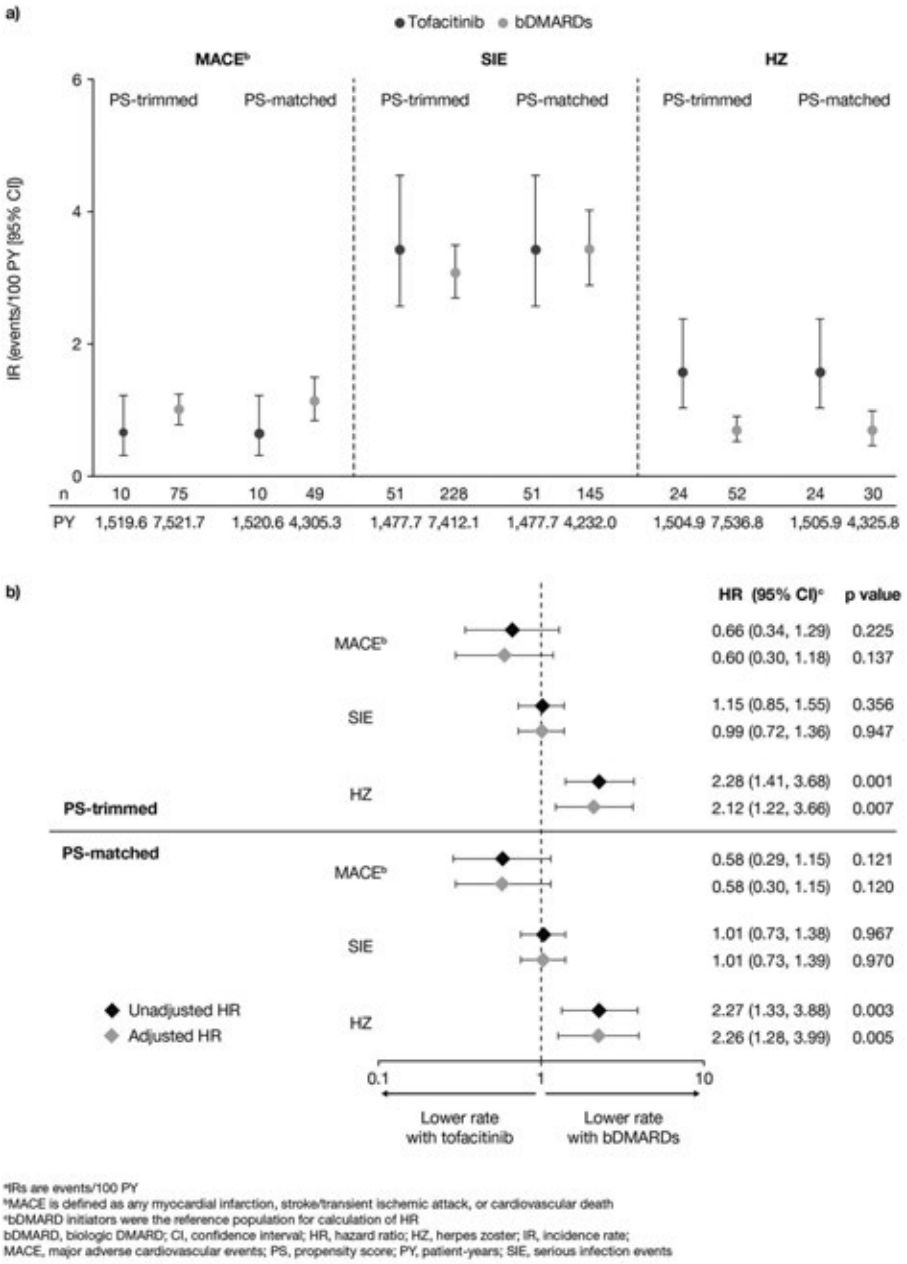
SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Treatments Poster III: Safety and Outcomes

Figure 1. a) Crude IRs[a] for MACE, SIE, and HZ; and b) HR for MACE, SIE, and HZ

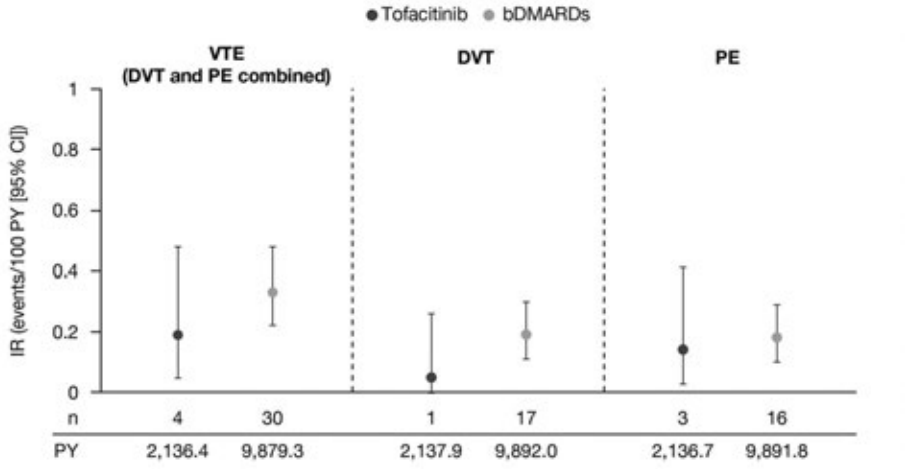


[a]IRs are events/100 PY
[b]MACE is defined as any myocardial infarction, stroke/transient ischemic attack, or cardiovascular death
[c]bDMARD initiators were the reference population for calculation of HR
bDMARD, biologic DMARD; CI, confidence interval; HR, hazard ratio; HZ, herpes zoster; IR, incidence rate; MACE, major adverse cardiovascular events; PS, propensity score; PY, patient-years; SIE, serious infection events

Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Tofacitinib is an oral JAK inhibitor for the treatment of RA. Real-world data (RWD) complement clinical trial data in assessing long-term safety. We evaluated 5-year adverse event (AE) incidence rates (IRs) in new starters of tofacitinib vs biologic (b)DMARDs using cohorts from the US Corrona RA registry.

Figure 2. Age- and gender-standardized IRs[a] for VTE[b]



[a]IRs are events/100 PY
[b]VTE data did not have >80% power to detect a hazard ratio of <2.25 at this data cut, and PS were not calculated; data presented are age- and gender-standardized IRs, estimated using direct standardization (tofacitinib population used as the standard population)
bDMARD, biological DMARD; CI, confidence interval; DVT, deep vein thrombosis; IR, incidence rate; PE, pulmonary embolism; PS, propensity scores; PY, patient-years; VTE, venous thromboembolism

Methods: This prospective, observational 5-year study in the ongoing US Corrona RA registry routinely collected 9 predefined AE categories from participating physicians. Major cardiovascular adverse events (MACE), serious infectious events (SIE), and herpes zoster (HZ) were *a priori* identified as having ≥ 80% power to detect a hazard ratio (HR) of 2.0 (MACE, SIE) or 2.25 (HZ) between patients (pts) starting tofacitinib or bDMARDs between 6 Nov 2012 (US FDA approval) and 30 Jun 2017 (follow-up to 31 Dec 2017). A safety signal for pulmonary embolism and mortality was seen in the tofacitinib 10 mg twice daily arm of an FDA post-marketing study in RA designed to evaluate the long-term risk of MACE and malignancy. Pts in that ongoing, open-label, endpoint-driven study had to be ≥ 50 years of age, have ≥ 1 cardiovascular risk factor, and be on a stable dose of methotrexate to be eligible for enrollment. For MACE, SIE, and HZ analyses, baseline variables with a standardized difference > |0.10| between cohorts, and *a priori*-selected-covariates (gender, age, line of therapy, history of AE of interest) were used to construct propensity scores (PS) to derive PS-trimmed (primary) and PS-matched (sensitivity) populations (ratio: max. 4 bDMARD:1 tofacitinib; caliper=0.05). Pts were followed from start until AE of interest, discontinuation and/or start of new therapy +90 days, death, or end of follow-up, whichever came first. IRs (no. of events/100 pt-years [PY]) were estimated, and multivariable-adjusted Cox regression was used to estimate HRs comparing rates of first events between cohorts.

Results: In total, 1,544 tofacitinib (2,138.2 PY) and 7,083 bDMARD (9,904.9 PY) starters were included. PS-trimming led to 1,117 tofacitinib and 5,542 bDMARD starters. MACE and SIE rates were similar in both cohorts (Figure 1a); adjusted HRs (95% confidence interval) were: MACE 0.60 (0.30, 1.18); SIEs 0.99 (0.72, 1.36; Figure 1b). Compared with bDMARDs, the HZ IR was higher with tofacitinib (Figure 1a) and the HZ HR was significantly increased (adjusted HR 2.12 [1.22, 3.66]; Figure 1b); all HZ events were non-serious with tofacitinib. Similar results were seen in PS-matched populations. Venous thromboembolic event (VTE) IRs were similar in both cohorts (Figure 2).

Conclusion: This is the first comparative analysis of RWD for tofacitinib and bDMARDs to use PS-trimmed and PS-matched analyses to adjust for channeling/prescribing patterns for newly approved therapies. Pts starting tofacitinib or bDMARDs had similar MACE, SIE, and VTE rates. Tofacitinib starters had higher HZ IRs vs bDMARD starters.

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Abstract Number: 2373

Two Decades of Changes in RA Treatment and Disease Outcomes from the United States

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SESSION INFORMATION
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Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: RA causes significant morbidity and mortality. Over the last two decades, several new medications and strategies for treating RA earlier and more aggressively have become available. The objective of this study was to describe changes in RA treatment and the impact on disease outcomes over the last two decades by comparing medication use and patient-reported outcomes in a large, US-wide registry.

Methods: Patients with physician-diagnosed RA in FORWARD, The National Databank for Rheumatic Diseases, were included. Patients observed from 2008–2018 were matched 1:1 at study entry by age, sex and HAQ score to non-overlapping patients observed from 1998–2007. A random observation from each decade group was selected for demographics, disease characteristics, comorbidities, health outcomes and medications using t-test and chi-squared tests as appropriate to describe differences.

Results: We matched 8772 patients in the decade 2008–2018 with 8772 patients from the prior decade. At study entry, the time of the matching (mean [SD] calendar years 2000 [2.8] and 2012 [2.6] for respective decades), average age was 58 years, 83% were female, and mean (SD) HAQ score was 1.1 (0.7). Characterizing these decades with a random observation (Table 1), we observed slightly worse disease activity measures including pain visual analog scale, patient global score, Short Form-36 mental component summary score, quality of life and more comorbidities in the later decade, even when matching for HAQ. For individual HAQ items, better scores were observed in 2008–2018 vs 1998–2007 for items describing the performance of daily activities. There was a higher use of aids (such as canes and wheelchairs) reported in the later decade, resulting in worsened HAQ scores. MTX was the most commonly used conventional synthetic (cs)DMARD over both decades; use of other non-MTX csDMARDs was lower and

Table 1. Patient Demographics and Clinical Characteristics in a Random Matched Observation for Each Decade

Random observations within each decade	1998–2007 (n=8772)	2008–2018 (n=8772)	p value
Variable			
Year	2002.30 (2.92)	2012.81 (2.84)	<0.001
Age, years	59.43 (13.38)	58.90 (13.33)	<0.001
Sex, male, %	17.1	17.1	1.00
Disease duration, years	15.91 (12.22)	15.66 (13.64)	0.202
Married, %	69.9	67.7	0.002
Total income, 10^3 US dollars	45.4 (29.6)	55.5 (36.9)	<0.001
HAQ score (0–3)	1.13 (0.73)	1.13 (0.72)	0.63
Pain VAS (0–10)	4.02 (2.83)	4.24 (2.88)	<0.001
Patient global score VAS (0–10)	3.68 (2.54)	3.84 (2.52)	<0.001
Fatigue score VAS (0–10)	4.61 (3.02)	4.65 (3.05)	0.44
Sleep disturbance VAS (0–10)	3.82 (3.10)	3.90 (3.13)	0.06
SF-36 physical component summary score	36.15 (11.16)	37.06 (11.20)	<0.001
SF-36 mental component summary score	48.78 (11.56)	46.77 (12.09)	<0.001
Comorbidity index (0–9)	1.72 (1.55)	2.01 (1.67)	<0.001
VAS for QOL (0–100)	65.45 (21.25)	63.73 (21.15)	<0.001
HAQ and use of aids (not exhaustive)			
Dress yourself (0–3)	0.59 (0.68)	0.52 (0.65)	<0.001
Climb up five steps (0–3)	0.80 (0.83)	0.65 (0.80)	<0.001
Chores such as vacuuming or yard work (0–3)	1.19 (0.97)	1.08 (0.95)	<0.001
Uses cane, %	17.3	29.4	<0.001
Uses wheelchair, %	4.6	7.1	<0.001
Needs help with dressing and grooming, %	12.8	9.6	<0.001
Medications			
Current csDMARD or bDMARD use, %	78.9	82.1	<0.001
Current csDMARD use, %	72.5	69.4	<0.001
Number of csDMARDs	2.23 (1.65)	1.84 (1.43)	<0.001
Current bDMARD use, %	25.8	44.8	<0.001
Number of bDMARDs	0.44 (0.74)	1.19 (1.35)	<0.001
Current TNFi use, %	25.2	33.3	<0.001
No csDMARD/bDMARD or prednisone use, %	16.2	12.6	<0.001

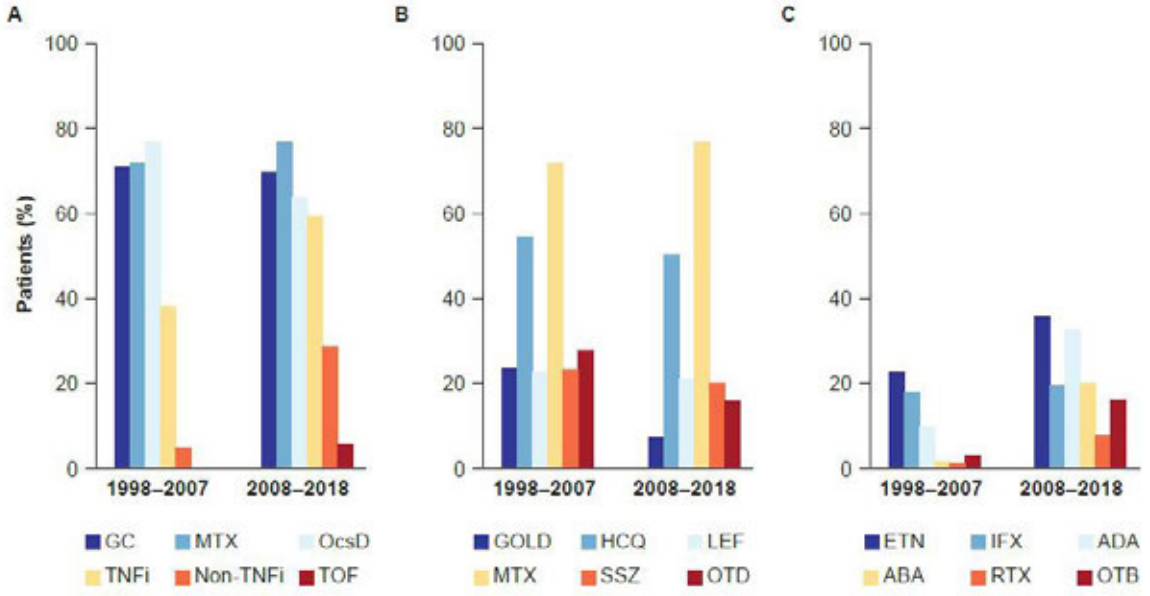
Values are mean (SD) unless indicated otherwise

bDMARD=biologic DMARD; csDMARD=conventional synthetic DMARD; QOL=quality of life; SF-36=Short Form 36; TNFi=TNF inhibitor; VAS=visual analog scale

use of biologic (b)DMARDs was higher in 2008–2018 vs 1998–2007 (Figure 1). Additionally, the use of combined (≥2) csDMARDs was less frequent in 2008–2018 vs 1998–2007, whereas the use of bDMARDs, either as monotherapy or in combination with ≥1 csDMARD, was higher in 2008–2018 vs 1998–2007 (Figure 2).

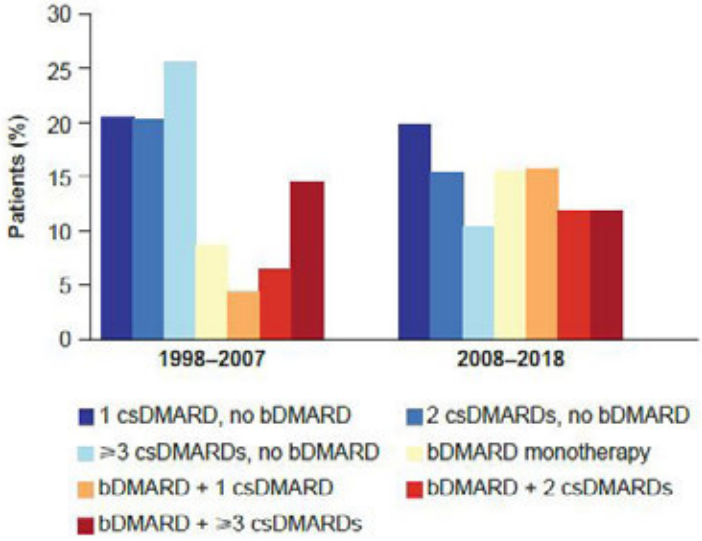
Conclusion: Over the last 20 years, there was a differential pattern of DMARD use between the two time periods (1998–2007 and 2008–2018), with a shift from use of non-MTX csDMARDs toward greater bDMARD use. Although

Figure 1. Comparison of the Proportion of Patients Who Had Ever Used csDMARDs or bDMARDs by Matched Decade (1998–2007 and 2008–2018): (A) Overall, (B) for Individual csDMARDs and (C) for Individual bDMARDs



ABA=abatacept; ADA=adalimumab; bDMARD=biologic DMARD; csDMARD=conventional synthetic DMARD; ETN=etanercept; GC=glucocorticoids; GOLD=injectable gold; HCQ=hydroxychloroquine; IFX=infliximab; LEF=leflunomide; non-TNFi=non-TNF inhibitors; OcsD=other csDMARDs no MTX; OTB=other bDMARDs (anakinra, certolizumab pegol, golimumab and tocilizumab); OTD=other csDMARDs (cyclosporine, doxycycline, azathioprine and cyclophosphamide); RTX=rituximab; SSZ=sulfasalazine; TNFi=TNF inhibitor; TOF=tofacitinib

Figure 2. The Proportion of Patients Using Combined Therapy With csDMARDs and/or bDMARDs at a Random Observation by Matched Decade (1998–2007 and 2008–2018)



bDMARD=biologic DMARD; csDMARD=conventional synthetic DMARD

matching did not allow for differences in functional disability between the two decades, patients in the latter decade had lower scores for performing daily activities and required less assistance from others but had greater use of aids such as a cane or a wheelchair. These results may contribute to a better understanding and management of disease for patients with RA.

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*at the time of the analysis

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Abstract Number: 2374

MRI of the Wrist in Early Rheumatoid Arthritis After 1-year Treat-to-target Strategy

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SESSION INFORMATION
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Session Title: RA – Treatments Poster III: Safety and Outcomes
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Background: There are two types of remission in rheumatoid arthritis. The first, and most commonly applied, is clinical remission. Imaging remission is another aspect to consider given that (a) the correlation between clinical and imaging at presentation is only modest, (b) imaging can show subclinical inflammation not evident clinically and (c) imaging evidence of inflammation can predict structural damage. In this study, we compared clinical and imaging remission in early rheumatoid arthritis (ERA) patients after one year of standard treatment.

Objective: To semi-quantitatively and quantitatively measure the degree of inflammation (synovitis, tenosynovitis, bone marrow oedema) and structural change (erosions, joint space narrowing) on MRI in early RA patients following treat-to-target strategy treatment for one year and to compare this with change in clinical parameters.

Methods: Prospective cross-sectional study of 70 ERA patients underwent treat-to-target strategy treatment for one year. DAS28-ESR remission (DAS28-ESR score < 2.6), 2011 ACR/EULAR definition of remission, SDAI remission (SDAI ≤ 3.3) and Boolean remission was measured before and after treatment. High resolution MRI of the most symptomatic wrist was performed before and after treatment. MRI parameters including RAMRS subscores, synovial volume (synovitis and tenosynovitis), synovial perfusion (max enhancement, enhancement slope) were measured.

Results: 55 (79%) out of 70 ERA patients completed baseline and one-year clinical and MRI assessments. Remission rates for DAS28-ESR, SDAI and Boolean were 60% (33), 44% (24) and 33% (18) respectively. Eight (24%) out of 33 patients with DAS28-ESR remission, showed progression in bone erosion. Four (17%) of 24 patients with SDAI remission showed progression in bone erosion while 1 (5 %) of 18 patients with Boolean remission showed progression in bone erosion. Patients who achieved remission after treatment had a greater reduction in MRI-

evident inflammation as well as bone erosion. At month 12, MRI-evident joint synovitis, tenosynovitis and bone marrow oedema was still frequently seen in ERA patients with clinical remission though patients who achieved Boolean remission had the lowest levels of joint synovitis, bone marrow oedema as well as bone erosion for all patients at one year.

Conclusion: MRI detected inflammation is common even in patients with clinical remission. Patients with Boolean remission had less residual inflammation than DAS28-ESR or SDAI remission patients. Treat to target protocols should ideally target Boolean remission.

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Safety of Baricitinib Under Clinical Settings in Patients with Rheumatoid Arthritis, Using Data from All-Case Post-marketing Surveillance and Spontaneous Reports

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Background/Purpose: Baricitinib (bari), is an oral, selective inhibitor of Janus kinase (JAK) 1/ and JAK 2, is used to treat moderately to severely active RA in adults. The objective of the study was to evaluate Bari's safety under clinical settings in RA patients.

Methods: All-case post-marketing surveillance of Bari (except patients in clinical studies) collects safety and efficacy data for the first 24 weeks starting in September 2017; collection of safety data like serious adverse events (SAEs) continues for 3 years. This interim report summarizes registration data including pretreatment test rates and adverse events (AEs) collected in the surveillance and spontaneous reports.

Results: As of August 2018, 1288 patients had been enrolled. Registration data are as follows: women, 81%; mean age, 64 years old; mean RA duration, 12 years; Steinbrocker stage II, 32%; stage III or IV, 52%; Bari 4 mg, 68%; Bari 2 mg 32%; methotrexate (MTX) use, 57%; corticosteroid use, 51%; pretreatment test for tuberculosis (TB), 93%; HBV, 95%; HCV, 93%; and estimated glomerular filtration rate (eGFR), 96%. Of 299 AEs collected, 53 were SAEs. SAEs reported in 2 or more patients were pneumonia (8), fall (4), osteonecrosis (3), Herpes zoster (2) and interstitial lung disease (2). Pulmonary TB (1), lymph node TB (1) and deep vein thrombosis (1) were also reported as SAEs.

Conclusion: Care is needed to ensure that all pretreatment tests be conducted in all patients; although most patients underwent all tests, some tests were not conducted in some patients. In these preliminary data, consistently with bari's known safety profile, SAEs including infections were reported. Careful monitoring of patients receiving bari is recommended.

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Abstract Number: 2376

Modifiable Factors Associated with Response to Treatment in Early Rheumatoid Arthritis

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SESSION INFORMATION

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Session Title: RA – Treatments Poster III: Safety and Outcomes

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Session Time: 9:00AM–11:00AM

Table 1: Odds of DAS28 Low Disease Activity at 1 year after commencing treatment

Variable	Odds ratio	Lower 95% CI	Upper 95% CI	P-value
Smoking	.	.	.	0.122#
BMI	.	.	.	0.934#
BMI*Smoking History	.	.	.	0.074*
BMI*current smoker	0.805	0.671	0.967	**0.020**
BMI*former smoker	0.916	0.845	0.992	**0.032**
BMI*never smoked	1.004	0.920	1.095	0.934
EPA mean	1.281	1.129	1.454	**<0.0001**
Shared epitope status				
Positive	1.161	0.614	2.196	0.647
Anti CPP status at baseline				
Positive	1.478	0.773	2.823	0.237
Gender				
Female	0.532	0.271	1.045	0.067
Age	0.982	0.962	1.002	0.080

Main effect p-value should be ignored when an interaction term is present

* Global p-value

Background/Purpose: Among the potentially modifiable prognostic factors in RA, there is evidence for associations with smoking history, BMI and dietary fish oil supplementation. An integrated examination of these lifestyle factors as predictors of RA outcomes was undertaken in a single early RA cohort receiving standardised algorithm-directed treat-to-target DMARD therapy.

Methods: Consecutive patients attending the Early Arthritis Clinic at the Royal Adelaide Hospital with recent-onset RA according to the 1987 revised American College of Rheumatology criteria and with disease duration < 12 months were eligible. All patients commenced 'triple therapy' with methotrexate, sulfasalazine and hydroxychloroquine and received advice to take fish oil supplements at anti-inflammatory doses, except for 139 patients within this cohort of 339 who participated in a randomised placebo controlled trial (RCT) of fish oil supplementation. Prognostic variables for DAS28 remission and DAS28 low disease activity (LDA) at the 12 month visit (+/- 6 weeks window was allowed) were identified using multivariable logistic regression models, correcting for potential confounders (age, sex, RF and CCP status and shared epitope). Omega-3 status was assessed as plasma eicosapentaenoic acid (EPA) levels.

Results: Of 311 participants with complete data, 57.6% reached DAS28 LDA and 43.7% were in DAS28 remission at one year. Increase in plasma EPA was associated with an increase in the odds of being in DAS28 LDA (OR=1.28; p< 0.0001) and DAS28 remission (OR=1.22; p< 0.001). There was a statistically significant interaction between smoking status and BMI on DAS28 LDA. Increase in BMI was associated with a decrease in the odds of being in DAS28 LDA in current and former smokers, but had no impact on LDA in patients who had never smoked. There were no statistically significant associations with BMI or smoking history and DAS28 remission. While a 1kg/m2 increase in BMI was associated with a decrease in the odds of having DAS28 low disease activity at 1 year in current and former smokers, it had no impact in patients who had never smoked.

Conclusion: Among all prognostic factors, fish oil supplementation in early RA patients receiving T2T therapy is significantly associated with the greatest increased odds of achieving DAS28 LDA at one year. The effect modification by smoking status on the association of BMI with treatment outcomes in early RA strongly supports counselling for lifestyle modification in patients who have a smoking history, particularly if they are overweight.

Disclosure: Z. Brown, None; **R. Metcalf**, None; **J. Bednarz**, None; **C. Stavrou**, None; **L. Spargo**, None; **M. James**, Melrose Health, 9; **S. Proudman**, Actelion, 2, Boehringer-Ingelheim, 2, 6, Bayer, 2, Corbus, 2, Melrose Health, 9.

Abstract Number: 2377

Methotrexate Discontinuation and Dose Decreases After Therapy with Tocilizumab: Results from the Corrona Rheumatoid Arthritis Registry

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Session Title: RA – Treatments Poster III: Safety and Outcomes

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate (MTX) is frequently prescribed with biologic disease-modifying antirheumatic drugs. Evidence has shown that tocilizumab (TCZ) monotherapy is effective in the treatment of patients with rheumatoid arthritis (RA).[1,2] Similar outcomes have been shown in patients responding to TCZ combination therapy who discontinued MTX or remained on combination therapy.[3] The purpose of this study was to examine MTX discontinuation and dose decreases in patients with RA initiating TCZ and to describe disease activity outcomes in a real-world setting.

Table 1. Change in Disease Activity and PROs* at 6 Months in Patients With RA

	All Patients (N = 444)	Discontinued MTX (n = 72)	Decreased MTX Dose (n = 67)	No Change in MTX Dose (n = 269)	Increased MTX Dose (n = 36)
CDAI	−7.8 (14.3)	−5.5 (13.1)	−7.1 (13.6)	−8.4 (14.7)	−9.8 (15.2)
DAS28	−1.2 (1.7)	−1.0 (1.7)	−1.1 (1.5)	−1.3 (1.6)	−0.9 (2.4)
Tender joint count	−3.2 (7.9)	−1.3 (7.1)	−1.8 (7.5)	−3.8 (8.1)	−4.2 (7.6)
Swollen joint count	−2.6 (5.6)	−2.2 (5.2)	−2.2 (5.1)	−2.7 (5.8)	−3.1 (6.1)
Physician global assessment	−13.1 (23.1)	−13.3 (23.4)	−17.0 (20.7)	−11.8 (23.4)	−16.2 (24.0)
Patient global assessment	−7.6 (25.9)	−6.4 (25.9)	−13.5 (28.5)	−6.4 (25.0)	−7.3 (26.4)
mHAQ	−0.1 (0.4)	−0.1 (0.4)	−0.1 (0.4)	0 (0.4)	−0.2 (0.5)
Patient pain	−7.3 (24.4)	−6.2 (23.7)	−8.2 (24.8)	−7.0 (24.3)	−10.8 (26.2)
Patient fatigue	−6.3 (26.6)	−7.3 (26.5)	−8.6 (30.7)	−5.0 (26.3)	−10.3 (20.2)
Morning stiffness present, n (%)	−29 (7.1)	−6 (9.4)	−5 (8.2)	−17 (6.8)	−1 (3.0)
Morning stiffness time, h	−0.1 (3.7)	−0.7 (2.8)	0 (2.1)	−0.1 (3.8)	0.3 (6.1)

CDAI, Clinical Disease Activity Index; DAS28, Disease Activity Score in 28 joints; mHAQ, modified Health Assessment Questionnaire; MTX, methotrexate; PRO, patient-reported outcome; RA, rheumatoid arthritis.
* Changes in disease activity and PRO measures are presented as mean (SD) unless otherwise indicated.

Methods: TCZ-naïve patients enrolled in the Corrona RA Registry who initiated TCZ and had a 6-month follow-up visit without discontinuation of TCZ were included. Patients were grouped by MTX dose at the time of TCZ initiation (≤ 10 mg, > 10 to ≤ 15 mg, > 15 to ≤ 20 mg, > 20 mg). The primary outcome was the proportion of patients with changes in MTX use at 6 months. Changes in disease activity (Clinical Disease Activity Index [CDAI]) and patient-reported outcomes (PROs) over the follow-up period are described.

Results: Of 444 eligible patients, 82.7% were female, and 83.7% were white, with a mean (SD) disease duration of 11.6 (9.3) years and a baseline CDAI score of 24.0 (15.4). The mean (SD) MTX dose at baseline was 17.7 (5.8) mg. Overall, a total of 139 patients (31.3%) discontinued or decreased MTX at 6 months (overall mean [SD] dose change, –3.0 [7.5] mg); across baseline MTX dose groups, the proportion of patients who discontinued or decreased MTX at 6 months ranged from 28.2% to 38.2%. Improvements in CDAI scores and PROs were observed at 6 months in all baseline MTX dose groups and in patients who discontinued, decreased, maintained, or increased MTX doses at 6 months (**Table 1**). Similar patterns and results were observed at 12 months (not shown).

Conclusion: A considerable proportion of patients initiating TCZ were able to discontinue or decrease the dose of MTX after TCZ initiation. Patients who were able to discontinue or decrease MTX experienced similar improvements in disease activity and functionality. Discontinuing or decreasing MTX may be an effective treatment strategy for patients initiating TCZ combination therapy.

References:

1. Bykerk VP, et al. *Clin Rheumatol.* 2015;34(3):563-571.

2. Jones G, et al. *Ann Rheum Dis.* 2010;69(1):88-96.

3. Kremer J, et al. *Arthritis Rheumatol*. 2018;70(8):1200-1208.

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Disclosure: D. Pappas, AbbVie, 5, Corrona, LLC, 1, 3, Novartis, 5, Roche, 5, Roche Hellas, 5; **T. Blachley**, Corrona, LLC, 3; **S. Zlotnick**, Genentech, 1, 3, Genentech, Inc., 1, 3; **J. Best**, Genentech, Inc., 1, 3; **K. Emeanuru**, Corrona, LLC, 3; **J. Kremer**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 2, 5, Amgen, 5, BMS, 2, 5, Bristol-Myers Squib, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona LLC, 1, 3, Corrona, LLC, 1, 3, Genentech, 5, Genentech, Inc., 5, GSK, 5, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Regeneron, 5, Sanofi, 5.

Abstract Number: 2378

Comparative Analysis of Clinical, Laboratory and Therapeutic Strategies Among Blacks with Rhupus, SLE and RA

Naureen Kabani,[1] Joshy Pathiparampil,[2] Madina Abduraimova,[2] Latoya Freeman-Beman,[2] Sima Terebelo,[1] Abida Hasan,[1] Christon Grant,[1] James Salgado,[1] Manjeet Bhamra,[1] Tracian James-Goulbourne,[1] Khabbab Amin,[1] Yamen Homsi,[3] and Isabel McFarlane[2], [1]SUNY Downstate Medical Center, Brooklyn, [2]SUNY Downstate Medical Center, Brooklyn, NY, [3]NYU Langone Medical Center, Brooklyn, NY

Measurements	Rhupus N=38	RA N=44	SLE N=39	P- Value (NS = Not Significant)
Age	50.9 ± 14.4 (Mean ± SEM)	50.75 ± 14.0	51.69 ± 14.9	NS
Female	94.7%	90.9%	94.9%	NS
Black Race	81.6%	90.7%	89.2%	NS
White Race	18.4%	7%	10.8%	NS
BMI	28.6 ± 7.3	28.64 ± 6.9	27.33 ± 6.6	NS
BMI<20	8.1%	7.3%	11.1%	NS
BMI>30	39.4%	36.6%	25%	NS
At least 1 CVD Risk Factor	71.1%	81.8%	74.4%	NS
3+ CVD Risk Factors	26.3%	13.6%	12.8%	NS
CHF	3.1%	13.6%	5.3%	NS
CAD	15.2%	10.5%	2.6%	NS
DM	18.8%	11.4%	15.4%	NS
HTN	50%	56.8%	51.3%	NS
HLD	18.2%	42.1%	25.6%	NS
CVA/TIA	6.3%	5.4%	12.8%	NS
CVD Outcome	21.2%	15.9%	15.4%	NS
WBC<4k	39.5%	9.1%	21.1%	<0.01
Abs Lymph <1k	36.8%	20.5%	33.3%	NS
Hb	11.3 ± 0.29	11.59 ± 0.26	11.32 ± 0.26	NS
Platelets <100k	2.6%	4.5%	0%	NS
Platelets	268.42 ± 19.84	281.55 ± 14.65	229.66 ± 10.69	NS
ESR > 42	61.1%	57.1%	63.2%	NS
ESR	58.28 ± 5.45	61.99 ± 7.7	59.79 ± 5.1	NS
CRP > 10	44.4%	70.8%	34.4%	0.02
CRP	28.94 ± 8.8	35.67 ± 7.67	41.74 ± 19.94	NS

Table 1 Comparison of the Demographic, Clinical and Laboratory Characteristics of Rhupus, RA, and SLE patients

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rhupus is the overlap of SLE and RA. While a few studies have been conducted among Rhupus patients, no studies have focused on Black population with Rhupus. Our aim was to describe the clinical, laboratory, radiographic and therapeutic profiles of predominantly Black patients with Rhupus and to compare this group with age and sex-matched patients with SLE and with RA.

Methods: Retrospective chart review of SLE and RA overlap patients followed at 2 large urban hospitals. Rhupus patients were identified by ICD codes and compared to age and sex matched cohort of SLE only and RA only groups. Descriptive statistics using SPSS® version 24 were applied to analyze the differences between the three cohorts.

Results: 38 patients met the ACR criteria for both RA and SLE (Rhupus) with 94.7% being women, mean age of 50.9±14.4 (SEM). Blacks represented 81.6% with a BMI of 28.6±7.3Kg/m^2. 50% had hypertension, 71.1% had at least one cardiovascular (CV) risk factor and 26.3% had 3 or more CV risk factors. Mean ESR = 58.28 ± 5.45 and

Measurements	Rhupus N=38	RA N=44	P- Value
Smoking	40%	16.7%	**0.022**
Hyperlipidemia	18.2%	42.1%	**0.03**
CAD	15.2%	10.5%	NS
Hand XR Abnormalities	89.3%	93.8%	NS
Erosions	32.1%	62.5%	0.051
WBC	5.58 ± 0.40	7.95 ± 0.52	**<0.01**
Abs Lymph	1.28 ± 0.11	1.69 ± 0.13	0.054
Antinuclear antibody	100%	40%	**<0.01**
RF positivity	60.6%	90%	**0.021**
Anti-citrullinated protein antibody	58.6%	92.9%	**0.022**
Current Prednisone Use	81.5%	72.5%	*NS*
Current Methotrexate Use	69.2%	52.5%	NS
Current Other DMARD Use	96%	37.1%	**<0.01**
Biologic Use	45%	23.1%	NS
Steroid + DMARD / Bio Use	78.6%	54.5%	**0.039**

Table 2 Comparison of Clinical, Laboratory, Radiographic, and Therapeutic Profiles in patients with Rhupus and RA only patients

Measurements	Rhupus N=38	SLE N=39	P- Value
Smoking	40%	18.4%	**0.042**
Hyperlipidemia	18.2%	25.6	NS
CAD	15.2%	2.6%	0.054
Mucocutaneous Symptoms	56.7%	64.1%	NS
Arthritis	91.4%	56.4%	**<0.01**
Serositis	24.1%	7.7%	0.058
Neurologic	24.1%	15.4%	NS
Lupus Nephritis	16.1%	38.9%	**0.039**
Proteinuria>500mg/g	20%	29.4%	NS
Hand XR Abnormalities	89.3%	30%	**<0.01**
Erosions	32.1%	0%	**0.004**
WBC	5.58 ± 0.40	5.71± 0.41	NS
Antinuclear antibody	100%	100%	NS
dsDNA positivity	78.4%	58.3%	0.065
SSA positivity	66.7%	65.6%	NS
SSB positivity	59.3%	54.5%	NS
Anti-Smith positivity	50%	73.3%	0.067
Anti-RNP positivity	51.9%	80%	**0.02**
RF positivity	60.6%	3.7%	**<0.01**
Anti-citrullinated protein positivity	58.6%	0%	**<0.01**
Current Prednisone Use	81.5%	25.6%	**<0.01**
Current Methotrexate Use	69.2%	2.6%	**<0.01**
Current Other DMARD Use	96%	56.4%	**<0.01**
Current Biologic Use	45%	5.1%	**<0.01**
Steroid + DMARD / Bio Use	78.6%	23.1%	**<0.01**
Cardiolipin Ab	37.5%	8.3%	**0.024**
Lupus AC	9.1%	11.8%	NS
B2GP Ab	9.1%	11.1%	NS

Table 3 Comparison of Clinical, Laboratory, Radiographic, and Therapeutic Profiles of Rhupus and SLE only patients

CRP = 28.94 ± 8.8. There were no significant differences in CV risk factors, CV outcomes and inflammatory markers between the three cohorts. The rate of leukopenia and CRP levels were significantly higher in the Rhupus compared to the SLE and RA groups.

Compared to RA only group there were higher rates of smoking and ANA positivity among Rhupus populations. Leukopenia and positive RF and ACPA rates were frequent among Rhupus patients compared to RA only cohort.

Corticosteroids, MTX, and biologic DMARDs use did not differ between Rhupus and RA cohorts. Rate of utilization of other-than-MTX DMARDs and the combination of steroid with DMARDs was higher among the Rhupus compared to the RA only cohort.

When comparing Rhupus and SLE patients, the rates of mucocutaneous lesions, serositis, neurologic manifestations, and laboratory values including autoantibodies were no different between the groups. Smoking, arthritis, hand XR abnormalities, erosions, seropositive RA were more frequent among the Rhupus vs. SLE patients. However, lupus nephritis and RNP antibodies were less frequent in Rhupus compared to SLE only group. Corticosteroids, MTX, conventional and biologic DMARDs and combination therapy were more frequently used in Rhupus compared to SLE population.

Conclusion: In our predominantly Black population, Rhupus patients had higher rates of smoking and ANA positivity compared to RA patients. It also had lower rate of positivity for RF or ACPA. Rates of smoking, arthritis, erosions, positivity for RF, ACPA and aCL antibodies were higher among Rhupus compared to SLE patients. These results suggest smoking to be a potential risk factor for Rhupus and might play a role in the underlying pathophysiology of this overlap syndrome. Further studies are needed to confirm our findings and elucidate risk factors and predictors of Rhupus to help develop preventive and therapeutic strategies for this important disease entity.

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Abstract Number: 2379

High Initial Methotrexate Dose Is Not Associated with an Increased Risk of Liver Toxicity in Korean Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate (MTX) is the most commonly prescribed disease modifying anti-rheumatic drugs (DMARDs) for the treatment of RA due to its high efficacy and favorable safety profile. However, a higher incidence of MTX toxicity at dose >7.5mg/week has been reported in East Asia, especially in Japan, possibly due to a different genetic background in regard to MTX metabolism. Therefore, it is common to start MTX in a lower dose and to titrate it up slowly to target of 15-20 mg/ week. This approach can be associated with a significant delay in reaching a “therapeutic MTX dose” in RA patients. The aim of this study is to investigate as to whether a certain starting dose of MTX is associated with an increased MTX-toxicity in Korean patients with RA.

Methods: In this retrospective cohort study 2361 MTX-naïve RA patients, in whom MTX was initiated between 2009 and 2018, were included. Patients were divided into a low (≤7.5mg/week), moderate (10-12.5 mg/week) and high (≥15 mg/week) dosing groups. A MTX toxicity is defined as an increase of post-MTX AST or ALT >80 mg/dL. Groups were compared using chi-square and one-way analysis of variance. Factors associated with toxicity on liver were examined using logistic regression analyses. All analyses were performed by using SPSS (IBM SPSS statistics version 25).

Results: The mean age was 54.1 +/- 13.9 year. Women were dominant (79.6%). 31 (1.3%) and 5 (0.2%) patients had hepatitis B and C virus infection, respectively. There was no significant difference in age, sex, underlying liver disease between the three dosing groups. 1756 (74.4%) patients were taking glucocorticoids (prednisolone equivalent 7.7 +/- 4.8 mg/day) and 321 (13.6%) patients were taking leflunomide or sulfasalazine. The mean starting MTX dose was 11.1 +/- 3.0 mg/week. 522 (22.1%) patients, 1162 (49.2%) and 677 (28. 7%) patients started MTX ≤7.5mg/ week, 10-12.5 mg/week and ≥15 mg/week, respectively. All patients received folate supplementation. Liver toxicity was observed in 30 (1.3 %) patients. The rate of liver toxicity did not differ among the groups (1.5% in the low vs. 0.9% in the moderate vs. 1.6% in the high dosing group, P = 0.38). In logistic regression analyses, clinical parameters including age, sex, body mass index and initial MTX dose were not associated with an increased risk of a hepatotoxicity either.

Conclusion: This study demonstrated clearly that the initial MTX dose up to 15 mg /week was not associated with an increased toxicity on liver in Korean patients with RA. Therefore, MTX can be started at 15 mg/week in Korean patients with RA without a safety concern on liver toxicity.

Disclosure: S. Choi, None; **Y. Song**, Astellas Pharma, Inc., 9; **E. Lee**, Seoul National University Hospital, 3; **J. Park**, None.

Abstract Number: 2380

Improving Depression by Joint Surgery in Established Rheumatoid Arthritis; Results from Multicenter Prospective Cohort Study for Evaluation of Joint Surgery on Patient's Reported Outcome

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SESSION INFORMATION

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Session Title: RA – Treatments Poster III: Safety and Outcomes

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Session Time: 9:00AM–11:00AM

Background/Purpose: Total management including reconstructive joint surgery and rehabilitation should be needed for further improvements of physical function for long-standing RA patients. In these days, it is very important to evaluate the effectiveness of joint surgery as well as drug therapy based on patient-reported outcome (PRO) The purpose of this study is to explore the relationship among depression, clinical variables and other PROs including physical function.

Methods: Multicenter prospective observational cohort study was conducted among patients who underwent elective joint surgery for RA from April 2012 to March 2016 (Study registration: UMIN000012649). In this study, we collected data at baseline and at 6 or 12 months after the surgery. These data were as follow; age, sex, disease duration, drug therapies, and disease activity (DAS), TUG, and patient-reported outcome [HAQ-DI, EQ-5D (QOL), pain and BDI-II (depression)]. Correlation between BDI-II and other variables were determined using multiple liner regression analysis.

Results: Totally, 346 patients before elective joint surgery were analyzed cross-sectionally. Mean age, disease duration, pain(VAS), DAS28, HAQ-DI, EQ-5D and BDI-II were 64.2 years, 17.0 years, 36.2 mm, 3.02, 1.11, 0.641 and 13.0, respectively. 52.6% of elective joint surgeries were in upper limbs and 47.4% were in lower limbs. Multiple liner regression analysis showed that HAQ-DI [B:-0.099 (95%CI:-0.117- -0.08) β:-0.48] pain VAS [B:-0.002 (95%CI:-0.002- -0.001) β:-0.26] and BDI-II [B:-0.003 (95%CI:-0.005- -0.002) β:-0.19] were independent factors for EQ-5D. Furthermore, HAQ-DI [B:3.78 (95%CI:2.54- 5.06) β: 0.33] and pain VAS [B: 0.062 (95%CI: 0.023- 0.101) β 0.17] were significant impact on BDI-II. Especially, walking and eating were independent factors for BDI-II in HAQ-DI categories.

We confirmed these BDI-relating factors above in longitudinal analyses, at last observation (6 or 12 months) after joint surgery in lower limbs (n=138). BDI-II was remarkably improved from 12.1 (mean) to 10.5. Change in HAQ-DI had significant impact on that in BDI-II [B:3.183 (95%CI:0.301- 6.065) β:0.229] while that in painVAS did not. The improving in walking was a relevant factor for improving of BDI-II after the surgery [B:2.898(95%CI:0.641- 5.155) β:0.213].

Conclusion: Depression is an important patient-reported outcome for QOL in established RA patients. Improving of physical function with joint surgery in lower limbs caused improving of depression status. Rheumatologists should take the joint surgery into consideration as effective intervention for treatment of established RA patients.

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Abstract Number: 2381

Baseline Characteristics Associated with Sustained SDAI Remission Following Treatment with Abatacept in Combination with MTX Compared with Abatacept Placebo in Combination with MTX in ACPA Positive Patients with Early RA

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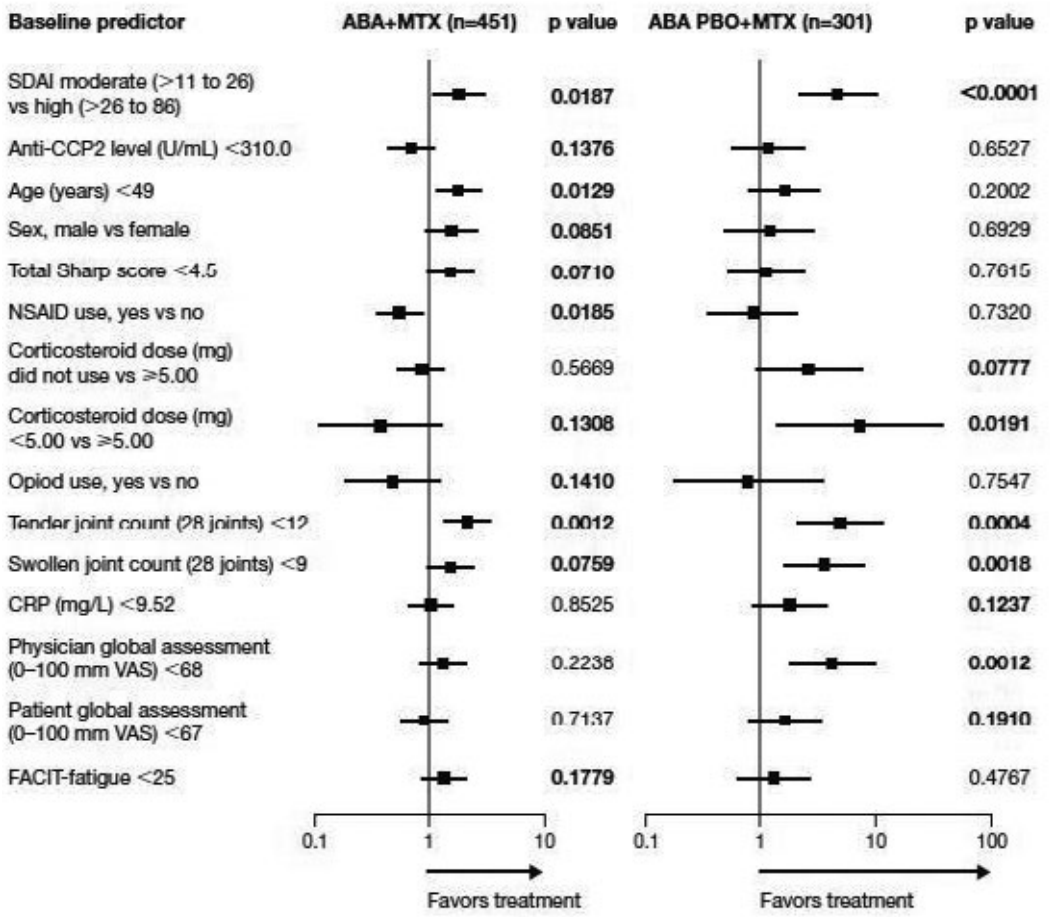
Figure 1. Dichotomized Characteristics Associated With Sustained SDAI Remission in Univariate Analyses*



Sustained SDAI remission: patients in remission at Weeks 40 and 52
Data are odds ratios (95% CI)
*Truncated list from high yield analysis, list includes characteristics used for multivariate analyses
FACIT=Functional Assessment of Chronic Illness Therapy; VAS=visual analog scale

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
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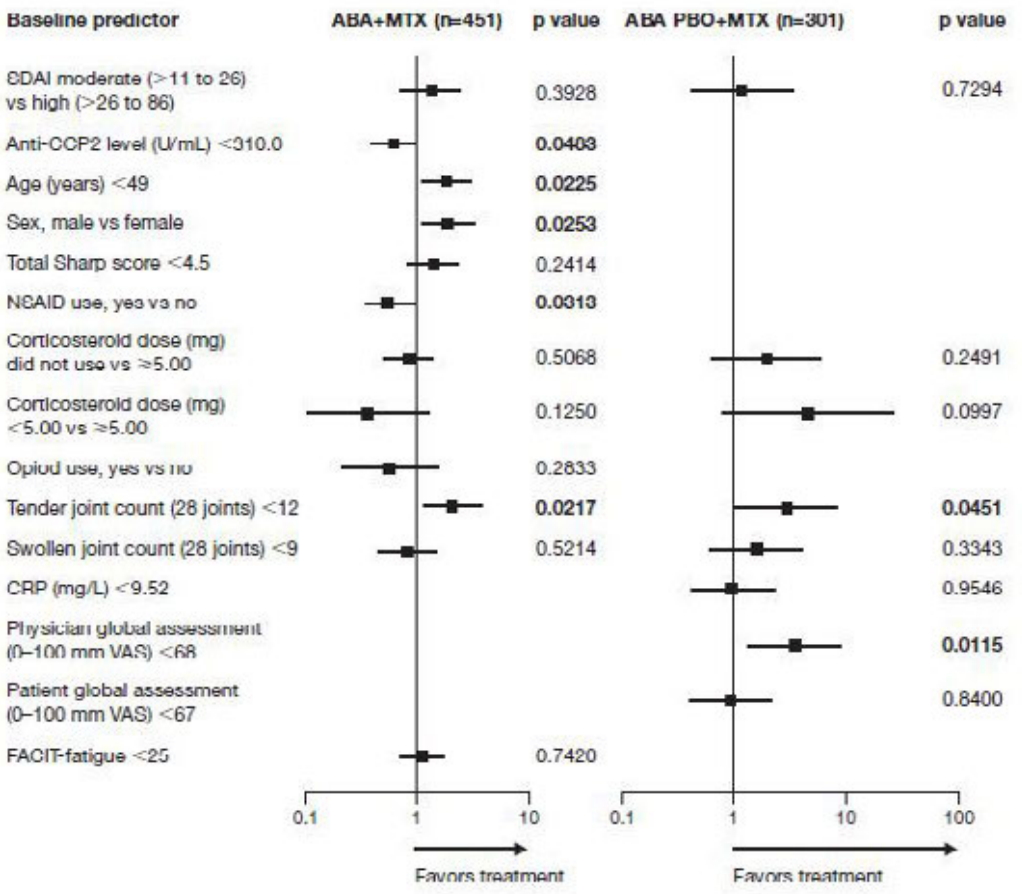
Background/Purpose: The Phase IIIb Assessing Very Early Rheumatoid arthritis Treatment (AVERT)-2 trial (NCT02504268) is evaluating SC abatacept (ABA) + MTX versus ABA placebo (PBO) + MTX in adults with early RA.[1] AVERT-2 was designed to demonstrate that ABA + MTX could achieve higher rates of SDAI remission versus ABA PBO + MTX and to test a clinically meaningful withdrawal strategy. Identifying factors associated with response may help guide treatment decisions, including initial treatment choice and de-escalation of therapy. We investigated baseline characteristics that were associated with sustained SDAI remission (≤3.3 at Weeks 40 and 52), therefore allowing patients to enter the de-escalation period, in AVERT-2.

Methods: For the induction period (IP), patients were randomized 3:2 to SC ABA (125 mg weekly) + MTX or ABA PBO + MTX for 56 weeks. Following the IP, patients entered a 48-week de-escalation period. Key inclusion criteria:

Figure 2. Dichotomized Characteristics Associated With Sustained SDAI Remission in Multivariate Analyses



Sustained SDAI remission: patients in remission at Weeks 40 and 52. As corticosteroid dose (mg) <5.00 vs ≥5.00 had a p value <0.2 in the univariate model, corticosteroid dose (mg) did not use vs ≥5.00 was also included in the multivariate model for completeness, despite having a p value >0.2
Data are odds ratios (95% CI)
FACIT=Functional Assessment of Chronic Illness Therapy; VAS=visual analog scale

age ≥18 years; RA diagnosis ≤6 months (ACR/EULAR 2010 criteria); ACPA+; CRP >3 mg/L or ESR ≥28 mm/h; TJC ≥3 and SJC ≥3; DMARD naive. Logistic models were used to explore potential factors associated with sustained SDAI remission by treatment arm in the cohort 1 analysis population (all randomized patients treated in the IP). Continuous variables were dichotomized based on median values before introduction to the models. A total of 30 baseline characteristics (demographics, disease/clinical endpoints, co-medication use, serum markers, patient-reported outcomes) were tested individually by logistic regression in a univariate analysis, and variables with $p< 0.2$ were entered into a multivariate model.

Results: Overall, 752 patients were randomized and treated in cohort 1 during the IP: 451 with ABA + MTX and 301 with ABA PBO + MTX. Baseline characteristics were similar across treatment arms. A total of 11 and 8 baseline characteristics, respectively, were identified as independently associated with sustained remission with ABA + MTX and ABA PBO + MTX (Fig. 1). Baseline characteristics associated with sustained remission by multivariate analysis (Fig. 2) with ABA + MTX were anti-CCP ≥310 U/mL, age < 49 years, male sex, NSAID naïve and TJC < 12. Baseline characteristics associated with sustained remission by multivariate analysis with ABA PBO + MTX were physician global assessment (PGA) < 68 and TJC < 12 (Fig. 2).

Conclusion: In this population of ACPA+ patients with early RA, several baseline characteristics were found to be associated with sustained SDAI remission in patients treated with abatacept + MTX: anti-CCP2 levels ≥310 U/mL, age < 49 years, TJC < 12, being NSAID naïve and/or being male. In patients treated with abatacept PBO + MTX, having PGA < 68 and/or TJC < 12 were associated with sustained SDAI remission. The identification of baseline characteristics associated with treatment response in patients with very early RA may provide additional insight into which patients may be suitable for de-escalation of therapy.

Reference:

1. Emery P, et al. ACR Annual Meeting 2018: Poster 563.

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Disclosure: P. Emery, AbbVie, 2, 5, 9, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, 9, Gilead, 5, Lilly, 2, 5, 9, MSD, 2, 5, 9, Novartis, 2, 5, 9, Pfizer, 2, 5, 9, Roche, 2, 5, 9, Samsung, 2, 5, 9, Samsung Bioepis Co., Ltd., 2, Sandoz, 2, 5, 9, UCB, 2, 5, 9; **Y. Tanaka**, Abbvie, 8, AbbVie, 5, 8, Asahi-kasei, 2, Asahi-Kasei, 2, Asahi-kasei, BMS, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Ono, Pfizer, Sanofi, Takeda, UCB, 2, Astellas, 8, Astellas Pharma, 9, Astellas Pharma, Inc., 2, 3, 5, 8, 9, Astellas, BMS, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi-Tanabe, Pfizer, Sanofic, UCB, YL Biologics, 8, BMS, 2, 5, 8, Bristol-Myers, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Daiichi-Sankyo, 2, 8, Daiichi-Sankyo, Astellas, Eli Lilly, Chugai, Sanofi, Abbvie, Pfizer, YL Biologics, Bristol-Myers, 8, Eisai, 2, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 8, Genzyme, 5, Glaxo-Smithkline, UCB, Mitsubishi-Tanabe, Novartis, Eisai, Takeda, Janssen, Asahi-kasei, 8, Janssen, 8, Mitsubishi-Tanabe, 2, 8, Mitsubishi-Tanabe, Bristol-Myers, Eisai, Chugai, Takeda, Abbvie, Astellas, Daiichi-Sankyo, Ono, MSD, Taisho-Toyama., 2, Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, 2, Novartis, 8, Ono, 2, Pfizer, 5, 8, Pfizer Inc, 8, Roche, 5, Sanofi, 2, Takeda, 2, 8, Teijin, 8, UCB, 2, YL Biologics, 8; **V. Bykerk**, AbbVie, 5, Amgen, 1, 2, 3, 5, 8, Brainstorm Therapeutics, 1, 2, 3, 5, 8, Bristol-Myers Squibb, 5, Genentech, 5, Gilead, 5, NIH, 2, Pfizer, 1, 2, 3, 5, 8, Regeneron, 5, Regeneron Pharmaceuticals, Inc, 5, Sanofi, 5, Sanofi/Genzyme-Regeneron, 5, Sanofi-Genzyme/Regeneron, 1, 2, 3, 5, 8, Scipher, 1, 2, 3, 5, 8, The Cedar Hill Foundation, 9, UCB, 1, 2, 3, 5, 8, UCB Pharma, 5; **C. Bingham**, Abbvie, 5, AbbVie, 5, BMS, 2, 5, Bristol Meyer Squibb, 2, 5, Bristol Myers-Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Eli/Lilly, 5, Genentech/Roche, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Pfizer Inc, 5, Regeneron/Sanofi, 5, Sanofi/Regeneron, 5; **T. Huizinga**, Abblynx, 2, 5, 8, Abbott, 2, 5, 8, Biotest AG, 2, 5, 8, Boehringer Ingelheim, 2, 5, 8, Boeringher Ingelheim, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Crescendo Bioscience, 2, 5, 8, Eli Lilly, 2, 5, 8, Epirus, 2, 5, 8, Galapagos, 2,

5, 8, Janssen, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Nycomed, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, Sanofi-Aventis, 2, 5, 8, Takeda, 2, 5, 8, UCB, 2, 5, 8, Zydus, 2, 5, 8; **G. Citera**, AbbVie, 5, 8, Abbvie, 2, 5, 8, BMS, 5, BRISTOL MYERS SQUIBB ARGENTINA, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, Gema Biotech, 2, 5, 8, Genzyme, 5, Janssen, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi Genzyme, 5, 8; **K. Huang**, Bristol-Myers Squibb, 1, 3, 4; **S. Connolly**, Bristol-Myers Squibb, 1, 3, 4; **Y. Elbez**, None; **K. Lozenski**, Bristol-Myers Squibb, 3, 4; **R. Fleischmann**, AbbVie, 2, 5, Acea, 2, 5, Akros, 5, Amgen, 2, 5, AstraZeneca, 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, 5, Celltrion, 5, Celtrion, 2, 5, Centrexion, 2, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck-Serono, 2, 5, EMD Serono, 2, EMD-Serano, 2, EMD-Serono, 2, Genentech, 2, 5, Genetech, 2, GlaxoSmithKline, 2, 5, GSK, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Merck, 2, Nektar, 2, Novartis, 2, 5, Pfizer, 2, 5, Pfizer Inc, 2, 5, Regeneron, 2, Resolve, 2, Roche, 2, Samsung, 5, Sandoz, 5, Sanofi Genzyme, 2, Sanofi-Aventis, 2, 5, Sanofi-Aventis, 2, 5, Sanofi-Genzyme, 2, Selecta, 2, Tahio, 5, Taiho, 5, UCB, 2, 5.

Abstract Number: 2382

Relationships Between DAS28 Response and Clinical, Functional and Radiographic Outcomes in Year 2 of the COMET Study of Etanercept in Patients with Rheumatoid Arthritis

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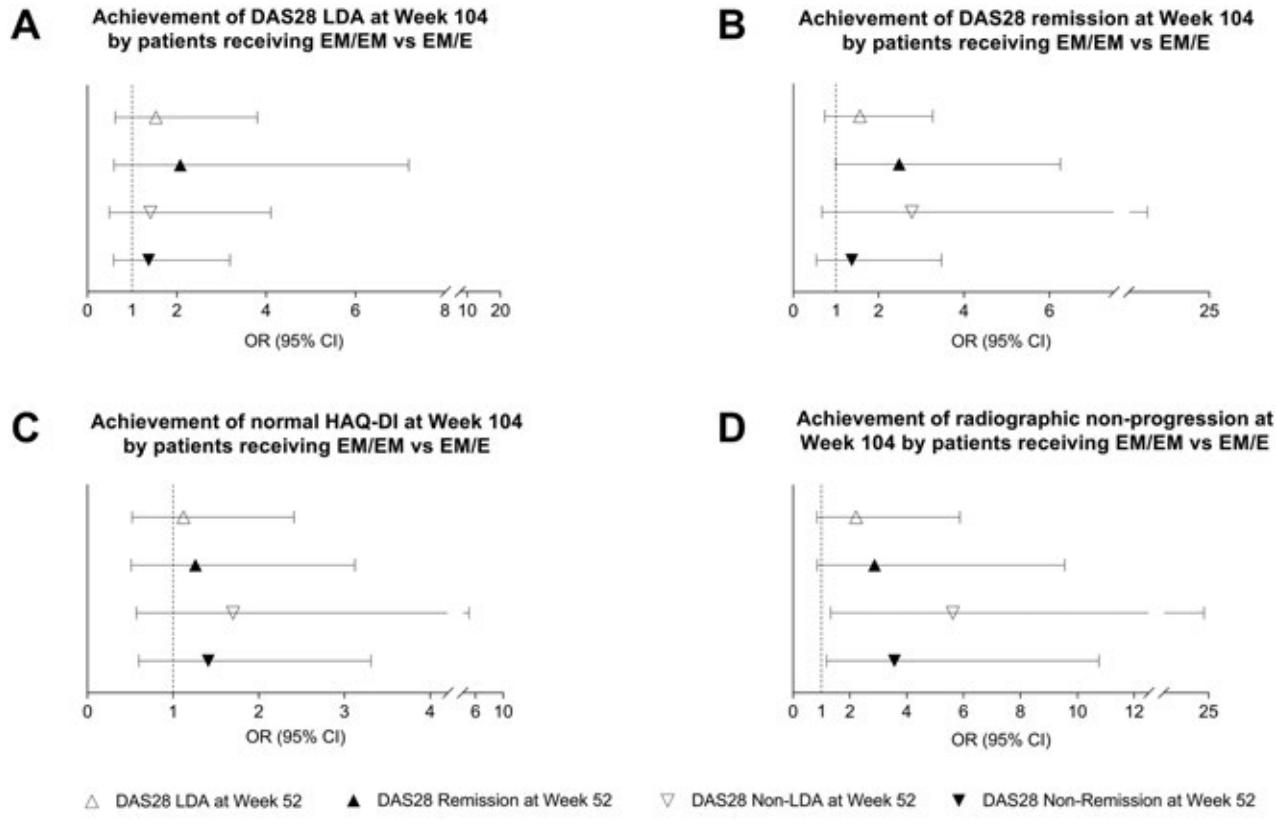
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: For patients with rheumatoid arthritis (RA) who are treated with etanercept (ETN) plus methotrexate (MTX), dosing down of ETN or withdrawal of MTX are options once treat-to-target has been achieved. In the COMET study[1] (NCT00195494), patients with RA received combination therapy (50 mg/week ETN+MTX) for 52 weeks in Period (P) 1, and were then randomized to either continue combination therapy or discontinue MTX and receive ETN monotherapy for a further 52 weeks (P2). The purpose of this analysis was to compare Week 104 clinical, functional, and radiographic outcomes between treatment arms for each patient subgroup, classified by disease activity score in 28 joints (DAS28) response (achievement or not of DAS28 low disease activity [LDA; DAS28 score ≤3.2] or remission [DAS28 score < 2.6]).

Methods: Odds ratios (ORs) comparing the ETN+MTX and ETN P2 treatment arms for each Week 52 DAS28 status were calculated from logistic regression models with treatment, Week 52 DAS28 status, and their interaction as predictors of achieving DAS28 LDA, DAS28 remission, normal Health Assessment Questionnaire-Disability Index (HAQ-DI) score (score ≤0.5), and radiographic non-progression (change from Year 2 baseline in modified Total Sharp Score [mTSS] of ≤0.5) at Week 104.

Results: A total of 208 patients (105 in the ETN+MTX and 103 in the ETN monotherapy P2 treatment arms, respectively) were included in this analysis. The odds of achieving DAS28 LDA, DAS28 remission, or normal HAQ-DI at Week 104 in patients who did or did not achieve a DAS28 response at Week 52 did not generally differ significantly between the treatment groups (Figure, Panels A-C), which could be attributed, at least in part, to lack of power to detect treatment differences due to small sample sizes (36 [ETN+MTX] and 28 [ETN] patients were in the Week 52 LDA



CI, confidence interval; DAS28, disease activity score in 28 joints; E, etanercept; EM, etanercept + methotrexate; HAQ-DI, health assessment questionnaire-disability index; LDA, low disease activity; OR, odds ratio

non-response category while 51 [ETN+MTX] and 40 [ETN] patients were in the remission non-responder category). The only exception was the significantly higher odds of achieving radiographic non-progression in patients treated with ETN+MTX vs ETN monotherapy who did not achieve a DAS28 response at Week 52 (Figure, Panel D). Although the overall lack of significant ORs suggests that there were almost no differences between the two treatment arms, the ETN+MTX treatment arm had ~5-15% higher rates of response compared with ETN monotherapy for the DAS28 and HAQ outcomes (regardless of Week 52 DAS28 subgroup), and for radiographic outcomes for Week 52 DAS28 responders. A ~25% higher rate of response for the ETN+MTX vs the ETN monotherapy treatment arm was seen for radiographic outcomes in the Week 52 DAS28 non-response categories (Table). Week 52 DAS28 status did not modify treatment effect on outcomes, but did increase the ETN treatment effect on radiological efficacy from ~10% for Week 52 DAS28 responders to ~25% for Week 52 DAS28 non-responder.

Conclusion: For patients with RA receiving ETN+MTX who achieved DAS28 LDA or remission after 52 weeks, discontinuation of MTX at Week 52 may result in minimal loss of clinical, functional, and radiological efficacy after an additional 52 weeks of treatment with ETN monotherapy.

Proportion of patients who achieved Week 104 outcomes, stratified by achievement/non-achievement of DAS28 response (LDA/Remission) at Week 52, n/N (%)								
Week 104 outcome	Achieved DAS28 LDA at Week 52 (response)		Did not achieve DAS28 LDA at Week 52 (non-response)		Achieved DAS28 Remission at Week 52 (response)		Did not achieve DAS28 Remission at Week 52 (non-response)	
	EM+EM	EM+E	EM+EM	EM+E	EM+EM	EM+E	EM+EM	EM+E
DAS28 LDA	60/69 (87.0)	61/75 (81.3)	13/36 (36.1)	8/28 (28.6)	50/54 (92.6)	54/63 (85.7)	23/51 (45.1)	15/40 (37.5)
DAS28 Remission	53/69 (76.8)	51/75 (68.0)	9/36 (25.0)	3/28 (10.7)	46/54 (85.2)	44/63 (69.8)	16/51 (31.4)	10/40 (25.0)
Normal HAQ-DI	53/69 (76.8)	56/75 (74.7)	13/36 (36.1)	7/28 (25.0)	44/54 (81.5)	49/63 (77.8)	22/51 (43.1)	14/40 (35.0)
Non-progression in annualized mTSS	56/63 (88.9)	54/69 (78.3)	30/33 (90.9)	16/25 (64.0)	45/49 (91.8)	47/59 (79.7)	41/47 (87.2)	23/35 (65.7)

DAS28 LDA = DAS28 ≤3.2

DAS28 Remission = DAS28 <2.6

Normal HAQ-DI = HAQ ≤ 0.5

Non-progression in annualized mTSS = change from Year 2 baseline mTSS ≤ 0.5

DAS28, disease activity score in 28 joints; E, etanercept; EM, etanercept + methotrexate; HAQ-DI, health assessment questionnaire-disability index; LDA, low disease activity; mTSS, modified Total Sharp Score

Reference:

[1] Emery P, et al. *Lancet* 2008;372:375-82.

Disclosure: **P. Emery**, AbbVie, 2, 5, 9, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, 9, Gilead, 5, Lilly, 2, 5, 9, MSD, 2, 5, 9, Novartis, 2, 5, 9, Pfizer, 2, 5, 9, Roche, 2, 5, 9, Samsung, 2, 5, 9, Samsung Bioepis Co., Ltd., 2, Sandoz, 2, 5, 9, UCB, 2, 5, 9; **F. Breedveld**, None; **R. Pedersen**, Pfizer, 1, 3, 4; **E. Campos**, Pfizer, 3, 4; **A. Szumski**, Pfizer Inc, 1, 3, Syneos Health, 3; **T. Hirose**, Pfizer, 3, 4, Pfizer Inc, 1, 3.

Abstract Number: 2383

Treatment for Rheumatoid Arthritis After Methotrexate-associated Lymphoproliferative Disorder Developed

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Treatments Poster III: Safety and Outcomes

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate-associated lymphoproliferative disorder (MTX-LPD) is important complication in the rheumatoid arthritis (RA) treatment. There were few reports about clinical features of MTX-LPD and RA treatment after MTX-LPD.

Methods: We retrospectively extracted RA patients diagnosed as MTX-LPD in 3 rheumatology centers between March 2019 and January 2008 from medical record.

Results: 39 patients were included. We classified MTX-LPD disease course after withdrawal of MTX in three; not improved group (group A; 8 patients) , completely improved group (group B; 19 patients) , improved once but relapse after few years group (group C; 12 patients).There was significant difference in EBER-ISH positivity between improved after withdrawal of MTX group (group B + group C) and group A (11/17 vs 1/7 p=0.00247). Significant difference was seen in morbidity rate of Sjogren's syndrome (SS) between group B and C (0/19 vs 4/12 p=0.00701). Histopathological examples were obtained 32 patients; 12 of 32 were diagnosed as diffuse large B-cell lymphoma (DLBCL), 8 as Hodgkin's lymphoma(HL), 7 as hyperplasia, 2 as Follicular lymphoma (FL), 1 as peripheral T-cell lymphoma (PTCL), 1 as Angioimmunoblastic T-cell lymphoma (AITL), 1 as Lymphomatoid granulomatosis (LYG). All patients discontinued MTX after diagnosed as MTX-LPD. In improved after withdrawal of MTX group (group B + group C), 25 of 31 patients showed relapse of RA in average 9.61 months after discontinuation of MTX. In group A, all patients received chemotherapy and RA flare was not seen during chemotherapy but three of 8 showed relapse of RA in average 26.5 months. After RA flare following drugs were administered including overlap; Iguratimod(IGU) in 10 cases, Salazosulfapyridine(SSZ) , Abatacept(ABT), and Tacrolimus(TAC) in 8, Bucillamine(BUC) in 6, Mizoribine(MZB) in 5, Tocilizmab(TCZ) in 2, Auranofin(AUR), D penicillamine and Etanercept(ETN) in 1. Recurrence of LPD was seen in 4 cases after additional administration of DMARDs; IGU in 2cases, SSZ and TAC in one.

Conclusion: EBER-ISH positivity was associated with spontaneous improvement of MTX-LPD and absence of SS was associated with completely improvement of MTX-LPD. Relapse of RA after withdrawal of MTX is common and LPD might recur after additional treatment of RA flare, but there was no specific drug to recur LPD.

Disclosure: Y. Yoshioka, None; **S. Nagaoka**, None; **H. Hagiyama**, None.

Abstract Number: 2384

Yoga Improves Fatigue and Mental Health in Rheumatoid Arthritis: Preliminary Results of a Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Treatments Poster III: Safety and Outcomes

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) patients perceive reduced health-related quality of life (HRQOL) through functional disability, pain, increased fatigue and impaired psychological functioning. Previous trials demonstrated that Yoga, a mind-body therapy, can enhance both physical and mental health in various chronic conditions including RA. The primary objective of the study was to explore the efficacy of yoga program in improving HRQOL. Secondary objectives included improvement in fatigue, anxiety, depression and disease activity.

Methods: 43 RA patients (2010 ACR/EULAR criteria), ≥ 18 years, stable on standard pharmacological treatment with disease activity according to DAS28CRP < 5.1 were randomly assigned to 12 weeks yoga intervention (2x/week 90 min; n=22) or arthritis-education control (1x/week 60 min; n=21). Yoga intervention according to „Yoga in daily life system" included asanas, relaxation, pranayama and meditation. Control group had educational lectures on arthritis-related topics delivered by rheumatologist followed by group discussion. Participants completed study evaluations at baseline and post-intervention. Evaluations included The Short Form-36 (SF-36) scores for Physical Component Summary (PCS) and Mental Component Summary (MCS), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Hospital Anxiety and Depression scale (HADS) and Disease Activity Score-28CRP (DAS28CRP) questionnaires. Data were analyzed as differences in post and pre-intervention scores. Between group differences were analyzed using the t-test for independent samples. To assess effects of intervention we used per-protocol analysis. P values < 0.05 were considered statistically significant.

Results: Of the 43 patients included 37 (18 = intervention group, 19 = control group) completed the trial period. Groups did not significantly differ in baseline characteristics (P >0.05 for all analyses). Mean (SD) age was 55 (10.4) years, median (IQR) disease duration 5 (2.5,8) years, 93 % were female. There was no significant difference found between groups for SF-36 MCS (p=0.366), PCS (p=0.511) and DAS28CRP (p=0.724). Yoga group showed statistically significant improvements compared to control in FACIT-F (p=0.013), HADS anxiety (p=0.047) and HADS depression (p=0.004). Results are shown in the Table. No serious adverse events were observed during trial period.

Conclusion: Although Yoga was not associated with change in SF-36 scores and disease activity it led to significant improvement in fatigue, depression and anxiety which are principal contributors to decreased life quality of RA patients. Our findings are limited by small sample sizes and lack of statistical power to obtain significance for some

Table 1. Changes in outcomes from baseline
N= 37

Variables	Baseline mean (SD)	Change from baseline (95%CI) at 12 weeks	95% CI and P-value for difference between groups
FACIT-F (0-52)	Yoga 33.89 (10.77)	4.18 (-0.26, 8.61)	6.66 (1.53, 11.78)
	Control 35.37 (9.3)	-2.17 (-5.58, 1.25)	**P= 0.013**
HADS-A (0-21)	Yoga 7.39 (3.72)	-1.94 (-3.28,-0.6)	-1.83 (-3.64,-0.024)
	Control 6.89 (2.86)	0.056 (-1.39,1.51)	**P= 0.047**
HADS-D (0-21)	Yoga 5.11 (3.03)	-1.06 (-1.92,-0.2)	-1.73 (-2.88,-0.58)
	Control 5.0 (1.82)	0.83 (-0.06,1.72)	**P= 0.004**
SF-36:MCS (0-100)	Yoga 49.49 (11.99)	2.97 (-4.15,10.09)	3.86 (-4.66, 12.33)
	Control 49.71 (8.99)	-1.59 (-7.51, 4.33)	P= 0.366
SF-36:PCS (0-100)	Yoga 52.57 (10.11)	0.44 (-3.13,4.02)	1.61 (-3.31, 6.53)
	Control 48.30 (9.76)	-1.16 (-4.81,2.48)	P= 0.511
DAS28CRP	Yoga 2.32 (0.81)	-0.0024 (-0.42, 0.42)	0.093 (-0.44,0.63)
	Control 2.91 (0.84)	-0.096 (-0.45,0.26)	P=0.724

of presented analyses. Despite limitations, our results suggest that yoga may be of benefit in management of RA patients as supplementary non-pharmacological treatment.

Disclosure: S. Pukšić, None; **J. Mitrović**, None; **M. Čulo**, None; **M. Živković**, None; **B. Orehovec**, None; **D. Bobek**, None; **M. Lucijanić**, None; **J. Morović-Vergles**, None.

Abstract Number: 2385

Efficacy and Safety of Chinese Herbal Medicine Biqi Capsule Combined with Methotrexate in Patients with Rheumatoid Arthritis: A Pilot Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In recent years, the combination therapies of conventional synthetic disease-modifying anti-rheumatic drugs (cDMARDs) with Chinses medicine has prevailed for the treatment of rheumatoid arthritis (RA) in China. The objective of this pilot study was to assess the efficacy and safety of Biqi capsule, a Chinses herbal medicine combined with methotrexate (MTX) against patients with rheumatoid arthritis (RA) comparing with the combination therapy of MTX with Leflunomide (LEF).

Methods: This was a multicenter, open-label, randomized, parallel controlled trial with 24-week course on the treatment of RA. Total of 70 participates with RA were randomly assigned at a ratio of 1:1 to received Biqi capsule at a dose of 1.2g twice daily, or LEF at a dose of 20mg once daily in addition to MTX treatment. The primary outcome was the rate of achievement of 20% improvement in the American College of Rheumatology criteria (ACR 20) at 24 weeks. Secondary outcomes included the ACR50 and ACR70 responses, EULAR response, the side effects of the medications, 28-tender joint count (TJC28), 28-swollen joint count (SJC28), patient's assessment of pain (VAS), patient's and physician's global assessment of disease activity (PaGADA/PhGADA), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor(RF) and health assessment questionnaire (HAQ) score. Efficacy and safety were assessed after 4, 12 and 24 weeks of follow-up.

Results: 59/70 (84.3%) patients completed 24 weeks of the study. In an intention-to-treat analysis (ITT), ACR20 response was attained in 27 (77.1%) of 35 patients with MTX+Biqi treatment and 29 (82.9%) of 35 patients with MTX+LEF treatment at 24 weeks ($p=0.550$). Importantly, fewer adverse events were found in patients treated with Biqi+MTX compared to patients with MTX+LEF ($p< 0.05$).

Conclusion: With a beneficial clinical response and acceptable tolerability, our study suggested that Biqi capsule appeared to be a promising alternative option in combination with MTX in RA treatment.

Disclosure: R. Huang, None; **Q. Huang**, None; **J. Wu**, None; **X. Cai**, None; **X. Chen**, None; **Y. Zhao**, None; **Y. Chu**, None; **J. Zhang**, None; **J. Peng**, None; **Z. Huang**, None; **X. Chen**, None; **Z. Liu**, None; **A. Ou**, None.

Abstract Number: 2386

Consensus Statement and Recommendations on Methotrexate Use in Combined Therapy with Biological or Targeted Synthetic Disease Modifying Drugs in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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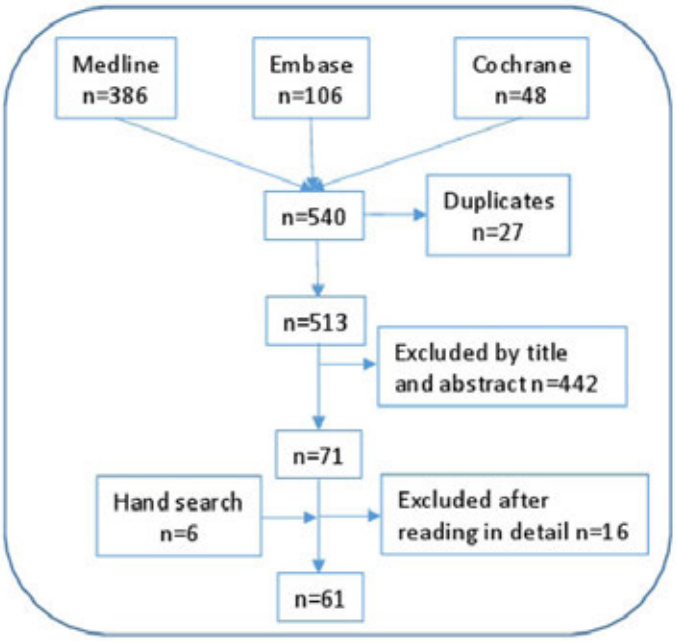
Background/Purpose: Our aim was to develop recommendations for the management of methotrexate (MTX) when considering the combination with biological (b) or targeted synthetic (ts) disease modifying drugs (DMARDs) in rheumatoid arthritis (RA).

Methods: Methodological procedures included nominal discussion group, systematic literature review, and Delphi survey for agreement. A panel of 11 expert rheumatologists, including two coordinators, was selected. The coordinators defined the goals, scope and users of the document and delivered a set of 11 relevant clinical questions regarding the use of MTX in combination with b or tsDMARDs, including the indication, dose, route of administration, dose-adjustments, efficacy and safety. To address them, an extensive systematic literature review was performed. The following PICO queries and inclusion criteria were defined, 1) RA patients (population); 2) on, or considering the start of combined therapy with MTX and b or tsDMARDs (intervention); reporting efficacy and/or safety variables like composite activity indexes, radiographic progression, serious adverse events, etc. (outcomes); 3) searches restricted to systematic literature reviews and meta-analysis, humans, English and Spanish articles. Then, an expert documentalist designed the search strategies (Medline, Embase and the Cochrane Library up to January 2019), using Mesh ant text word terms. Two reviewers selected the articles and collected data, independently. Subsequently, a manual search of the bibliography of the articles that were finally included was performed. Evidence tables were produced. The quality was evaluated with the Oxford Center for Evidence Based Medicine recommendations. Simultaneously, EULAR and ACR abstracts (2017 and 2018) were evaluated, along with national and international consensus and guidelines. This information was used by the coordinators to generate preliminary



Firuge 1. Studies flow-chart.

recommendations. Then, all the experts, in a nominal discussion group, agreed on the proposed objectives, scope and users, and analyzed the results of the review and preliminary recommendations. Recommendations were reformulated as considered, and voted in a Delphi process (yes/no). Agreement was considered if at least 80% of experts voted yes. The level of evidence and grade or recommendation were assigned using the Oxford Centre for Evidence-Based Medicine guidance. The full document was critically appraised by the experts and the project was supervised at all steps by a methodologist.

Results: The systematic literature search retrieved 513 citations of which 61 were finally included. A total of 9 preliminary recommendations were proposed, 2 were not voted and were explained in the main text of the document, 3 new ones were proposed and 10 were finally voted and accepted (depicted in table 1 with their level of evidence, grade of recommendation and grade of agreement). The level of agreement was very high in all of them and was achieved in the first Delphi round.

Conclusion: This document is intended to help clinicians solve usual clinical questions and facilitate decision making when treating RA patients with MTX in combination with bDMARDs or tsDMARDs.

#	RECOMMENDATION	LE	GR	LA
1	In patients with active RA and inadequate response to MTX, this drug should be continued when starting a TNF inhibitor (LE 1a; GR A), ABT (LE 2a; GR B), RTX (LE 1b-2a; GR B)	-	-	100%
2	MTX should not be discontinued in patients with active RA and inadequate response to MTX who start IL-6 inhibitors	1a	A	91%
3	MTX should not be discontinued in patients with active RA and inadequate response to MTX who start JAKs inhibitors	1b	A	91%
4	When starting a combined therapy with MTX and bDMARD in MTX-inadequate responders RA patients, it is recommended to continue with the same MTX doses	1b	A	100%
5	When combining MTX with TNF-inhibitors, the dose of MTX should be at least 10 mg/w	1b	A	100%
6	When starting a combined therapy with MTX and JAKs inhibitors in MTX-inadequate responders RA patients, it is recommended to continue with the same MTX doses	1b	A	100%
7	In RA patients who have achieved and sustained the treatment goal, the panel recommends, as treatment strategy, to give priority to the de-escalation of the bDMARDs, which does not exclude MTX dose adjustments or even MTX withdrawal in some intolerant patients on IL-6 inhibitors	5	D	100%
8	bDMARDs should be combined with MTX as the first csDMARD choice, although other csDMARDs could be considered if MTX intolerance/contraindication	1b	A	100%
9	JAKs inhibitors should be combined with MTX as the first csDMARD choice, although other csDMARDs could be considered if MTX intolerance/contraindication	1b	A	100%
10	Combined therapy of MTX with bDMARDs and tsDMARDs does not imply a different management of the standard of care for routine patient safety monitoring	5	D	100%

Abbreviations: MTX=methotrexate; RA=rheumatoid arthritis; TNF= tumour necrosis factor; ABT=abatacept; RTX=rituximab; mg=milligram; w=week; IL-6=interleukin 6; JAKs=Janus kinases; bDMARD=biológical disease modifying drugs; tsDMARDs=targeted synthetic disease modifying drugs (DMARDs).

Table 1. Recommendations with their level of evidence (LE), grade of recommendation (GR) and grade of agreement (GA).

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Management of Patients with Incident Rheumatoid Arthritis in Rheumatology Clinical Practice

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Treatments Poster III: Safety and Outcomes

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	Global (n=2388)		First course (n=814)		Subsequent courses (n=1574)	
	n	%	n	%	n	%
Combined therapy						
Monotherapy	1431	59.92	755	92.75	676	42.95
Combined	957	40.08	59	7.25	898	57.05
Biological DMARD use						
No	2062	86.35	809	99.39	1253	79.61
Yes	326	13.65	5	0.61	321	20.39
Type of DMARD						
Synthetic	2062	86.35	809	99.39	1253	79.61
Anti-TNF	234	9.80	3	0.37	231	14.68
Other biological DMARD	92	3.85	2	0.25	90	5.72
DMARDs						
CQ	493	20.65	183	22.48	310	19.70
HCQ	488	20.44	137	16.83	351	22.30
LEF	441	18.47	18	2.21	423	26.87
MTX	1257	52.64	472	57.99	785	49.87
MTX sc	206	8.63	17	2.09	189	12.01
Gold	123	5.15	19	2.33	104	6.61
SSZ	202	8.46	22	2.70	180	11.44
AZA	26	1.09	3	0.37	23	1.46
ABA	20	0.84	0	0	20	1.27
ADA	77	3.22	0	0	77	4.89
CERTO	43	1.80	0	0	43	2.73
ETN	85	3.56	2	0.25	83	5.27
GOLI	14	0.59	0	0	14	0.89
INF	15	0.63	1	0.12	14	0.89
RTX	53	2.22	1	0.12	52	3.30
TOCI	19	0.80	1	0.12	18	1.14
DMARD in monotherapy	1431	100	755	100	676	100
CQ	221	15.45	167	22.12	54	7.99
HCQ	179	12.52	106	14.04	73	10.80
LEF	135	9.44	16	2.12	119	17.60
MTX	676	47.27	421	55.76	256	37.87
MTX sc	72	5.03	14	1.85	58	8.58
ORO	23	1.61	6	0.79	17	2.51
SSZ	53	3.71	18	2.38	35	5.18
AZA	12	0.84	3	0.40	9	1.33
ABA	6	0.42	0	0	6	0.89
ADA	11	0.77	0	0	11	1.63
CERTO	9	0.63	0	0	9	1.33
ETN	13	0.91	2	0.26	11	1.63
GOLI	1	0.07	0	0	1	0.15
INF	1	0.07	0	0	1	0.15
RTX	10	0.70	1	0.13	9	1.33
TOCI	8	0.56	1	0.13	7	1.04

Background/Purpose: Treatment of Rheumatoid Arthritis (RA) has changed drastically in the last two decades in strategies and objectives, as well as in therapeutic options, especially with the use of the disease modifying drugs (DMARD), both synthetic and biological. The data on the management of these patients under clinical trial conditions are abundant but it is necessary to expand our knowledge on how to use them in daily clinical practice. Purpose: to describe the clinical management and treatment in a cohort of patients with incident RA on daily clinical practice.

Methods: We conducted an observational longitudinal study. Patients: all recent onset RA diagnosed between January 1st 2007 and December 31st 2015 followed in outpatient clinic at Hospital Clinico San Carlos until January 1st 2017, which used any DMARD (synthetic and biologic) during at least 3 months. Variables: sociodemographic (age and gender), clinical (comorbidities, smoking status, date of diagnosis), quality of life (Rosser index), laboratory test (ESR, Rheumatoid Factor, ACPA), disease activity (HAQ and DAS28), treatments during follow-up (NAIDs, corticoids, DMARD (type, dates of start and discontinuation)) and treatment course (first or subsequent). Descriptive techniques were used of sociodemographic, clinical and treatment characteristics.

Results: We included 2388 courses of DMARD treatment in 814 patients. 77.52% were women with a mean age at diagnosis of 57.53±15.50 years. 63% of them were married and 85% lived with family. 44% had primary studies and 50% were in an active employment situation. The mean time to diagnosis was 8.8±226.3 months with a diagnosis in first visit in 72.9% of patients. 16% of patients were active smokers. The most frequent basal comorbidities were: hypertension (34%), dyslipidemia (30%), diabetes mellitus (13%) and depression (8.7%). The mean quality of life at the beginning of the disease measured by the Rosser index was 0.97 ± 0.04. 55% of patients were Rheumatoid Factor positive, 44% ACPA positive with a high mean DAS28 at the beginning of the disease (5.26±1.4). In table 1 we present all treatments globally and by treatment course. The mean time to the first treatment course was 21 [0-43] days.

Conclusion: Our patients have a poor quality of life at the beginning of the disease and present a severe activity. The management we do is aggressive and early with a diagnosis at first visit in 72.9% of patients. In 25% of patients treatment is prescribed from the moment of diagnosis and at least 50% of our patients are treated before a month from first visit. Most patients start with monotherapy, the frequency of combined treatment increases later on and it is more frequent after the second course of treatment. Methotrexate alone or in combination is the most frequently prescribed treatment. The use of biological DMARD increases throughout the follow-up, the most frequent being Adalimumab. The preferred combinations by our rheumatologists are Methotrexate - Antimalarial, Methotrexate - Leflunomide and Methotrexate - Adalimumab.

Disclosure: i. Hernandez Rodriguez, None; **Z. Rosales Rosado**, None; **p. Lois**, None; **C. Lajas**, None; **J. Font Urgelles**, None; **J. Jover Jover**, None; **I. Abasolo Alcazar**, None.

Abstract Number: 2388

Patient Characteristics Associated with Long Term Glucocorticoid Use in a Commercially Insured Incident RA Cohort

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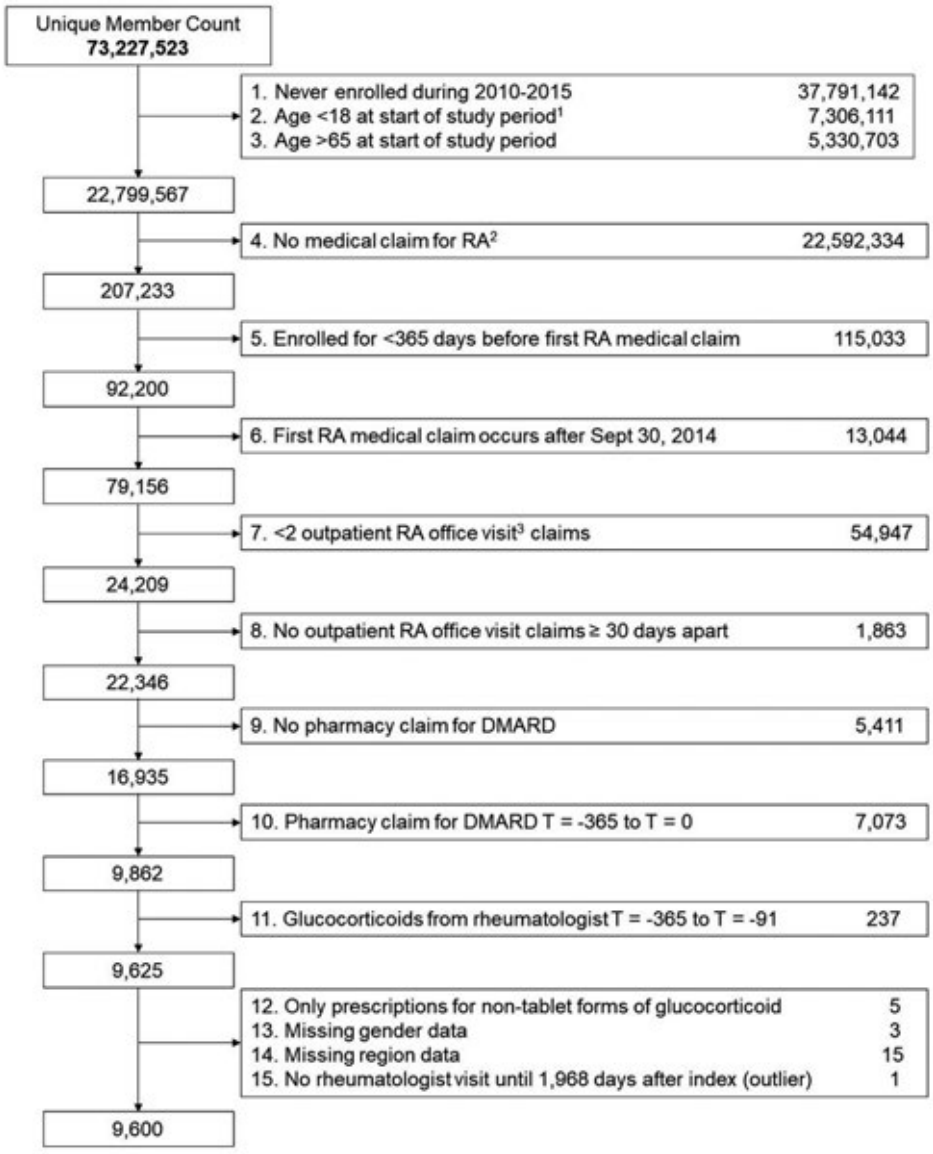

Figure 1: Cohort definition

SESSION INFORMATION

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Background/Purpose: Prior descriptive work revealed high rates of long term (≥3 months) glucocorticoid (GC) utilization in a commercially insured incident RA cohort [1]. We aim to evaluate associations between patient factors and long term GC utilization in this cohort.

	Total (N = 9600)	Filled 90 days GC supply (N = 2933)	Did not fill 90 days GC supply (N = 6667)	P value
Gender, N(%)				
Female	7155 (75%)	1996 (68%)	5159 (77%)	<0.001
Male	2445 (25%)	937 (32%)	1508 (23%)	
Age, mean (SD)	50.3 (10.3)	51.4 (10.0)	49.8 (10.4)	<0.001
18-40, N (%)	1751 (18%)	447 (15%)	1304 (20%)	<0.001
41-50	2535 (26%)	719 (25%)	1816 (27%)	
51-60	3676 (38%)	1190 (41%)	2486 (37%)	
>60	1638 (17%)	577 (20%)	1061 (16%)	
Race, N(%)				
White	6678 (70%)	2090 (71%)	4588 (69%)	0.003
Non-white	2922 (30%)	843 (29%)	2079 (31%)	
Years enrolled, mean (SD)	7.3 (3.6)	7.2 (3.6)	7.3 (3.6)	0.004
Year of RA diagnosis, N(%)				
2010	2276 (24%)	633 (22%)	1643 (25%)	<0.001
2011	2199 (23%)	643 (22%)	1556 (23%)	
2012	2069 (22%)	648 (22%)	1421 (21%)	
2013	1787 (19%)	567 (19%)	1220 (18%)	
2014	1269 (13%)	442 (15%)	827 (12%)	
Count all-cause office visits, median (IQR)	6 (3-10)	7 (4-11)	6 (3-10)	<0.001
Count all prescriptions excluding GC, median (IQR)	7 (3-11)	7 (3-12)	7 (3-11)	0.006
Elixhauser total score, median (IQR)	1 (0-3)	2 (1-3)	1 (0-3)	0.002
0-5, N(%)	9052 (94%)	2730 (93%)	6322 (95%)	0.001
≥6	548 (6%)	203 (7%)	345 (5%)	
Days to first rheumatology visit after RA diagnosis, mean (SD)	87.8 (225.9)	46.5 (139.8)	80.9 (227.4)	<0.001
>3 mos/never, N(%)	3358 (35%)	805 (27%)	2553 (38%)	<0.001
≤3 months	6242 (65%)	2128 (73%)	4114 (62%)	
Count of rheumatologist visits for RA, median (IQR)	3 (0-5)	4 (2-6)	2 (0-5)	<0.001
Time to first DMARD prescription, N(%)				
≤3 months	7254 (76%)	2489 (85%)	4765 (71%)	<0.001
>3 to ≤6 months	746 (7.8%)	224 (8%)	522 (7.8%)	
>6 to ≤12 months	686 (7.2%)	155 (5%)	531 (8.0%)	

table 1 optum modeling abstract

Table 1: Baseline patient characteristics stratified by primary outcome, i.e. filling ≥90 days' supply of glucocorticoid prescriptions within 1 year of RA diagnosis

Methods: Using OptumInsight™ claims data, we identified 9600 adults with ≥2 RA office visits ≥30 days apart between 2010-2014, ≥1 DMARD pharmacy claim, and ≥1 year prior to RA diagnosis with no RA medical claims or DMARD pharmacy claims ("washout") (Fig. 1). We used a Cox proportional hazards regression model to examine

	A. HR (95% CI) ħ90 days filled	B. HR (95% CI) ħ900mg filled
Gender		
Female	Ref	Ref
Male	1.37 (1.261 - 1.478)	1.38 (1.276 - 1.494)
Age		
18-40	0.79 (0.703 - 0.878)	0.81 (0.730 - 0.907)
41-50	0.87 (0.789 - 0.951)	0.86 (0.787 - 0.945)
51-60	Ref	Ref
>60	1.15 (1.044 - 1.276)	1.03 (0.927 - 1.135)
Race		
White	Ref	Ref
Non-white	1.04 (0.962 - 1.131)	0.95 (0.875 - 1.029)
Years enrolled	0.99 (0.976 - 0.996)	0.99 (0.974 - 0.995)
Year of RA diagnosis		
2010	Ref	Ref
2011	1.01 (0.904 - 1.126)	0.95 (0.850 - 1.056)
2012	1.07 (0.957 - 1.192)	1.03 (0.925 - 1.147)
2013	1.00 (0.888 - 1.116)	0.95 (0.844 - 1.057)
2014	1.11 (0.978 - 1.250)	1.07 (0.948 - 1.207)
Count all-cause office visits	1.00 (0.991 - 1.006)	1.00 (0.990 - 1.005)
Count all prescriptions excluding GC	0.99 (0.985 - 1.001)	1.00 (0.992 - 1.008)
Elixhauser total score		
0-5	Ref	Ref
ħ6	1.32 (1.119 - 1.546)	1.25 (1.065 - 1.466)
Time to rheumatology visit		
>3 months/never	Ref	Ref
ħ3 months	1.32 (1.119 - 1.546)	1.25 (1.065 - 1.466)
Time to DMARD prescription		
ħ3 months	Ref	Ref
>3 to ħ6 months	1.08 (0.932 - 1.244)	1.08 (0.938 - 1.247)
>6 to ħ12 months	0.89 (0.748 - 1.060)	1.04 ((0.887 - 1.226)
>12 months/never	0.32 (0.247 - 0.415)	0.38 (0.298 - 0.477)
Count DMARD prescription fills	1.04 (1.032 - 1.045)	1.03 (1.025 - 1.039)
Biologic DMARD filled		
No	Ref	Ref
Yes	1.25 (1.147 - 1.352)	1.31 (1.209 - 1.421)
GC prescription filled prior to index		
No	Ref	Ref
Yes	2.00 (1.855 - 2.164)	2.04 (1.886 - 2.197)

table 2 optum modeling abstract

Table 2: Adjusted hazard ratio (HR) of filling a) ≥90 days' supply of glucocorticoid prescriptions, b) ≥900mg prednisone equivalents' worth of glucocorticoid prescriptions, within 1 year of RA diagnosis

long term GC use, defined as 90 days' GC supply filled within 1 year of first RA claim (study period), adjusted for patient demographics, comorbidity, and overall and RA-related healthcare utilization. We assessed demographics, comorbidity, and overall healthcare utilization over a washout year before first RA claim. We performed a sensitivity

analysis using a dose-based definition, 900mg prednisone equivalent filled during study period (representing 10mg/day for 3 months).

Results: During the study period, 2933 (31%) patients filled 90 days' GC supply, and 3000 (31%) filled 900mg. Baseline patient characteristics are presented in Table 1. Characteristics independently associated with 90 days' GC supply include male sex (adjusted hazard ratio [HR] 1.4, p< 0.001), age >60 years (HR 1.2, p=0.005), having ≥6 Elixhauser comorbidities (HR 1.3, p< 0.001), taking GC prior to RA diagnosis (HR 2.0, p=0.001), use of biologic DMARD (HR 1.3, p< 0.001), and seeing a rheumatologist ≤3 months from RA diagnosis, relative to >3 months (HR 1.3, p=0.006) (Table 2). Age groups 18-40 (HR 0.8, p< 0.001) and 41-50 (HR 0.9, p=0.002) were associated with lower risk of the outcome. Race, year of RA diagnosis, number of pre-diagnosis office visits and prescription fills, and time to first DMARD fill (if ≤12 months) were not significantly associated with the outcome. Findings were similar for the dose-based outcome; association with ≤3 months to rheumatologist was attenuated but significant (HR 1.10, p=0.006) (Table 2).

Conclusion: In this commercially insured incident RA cohort, seeing a rheumatologist within 3 months of diagnosis was independently associated with long term GC utilization, while time to first DMARD (within 12 months) was not. This association, suggested by our prior descriptive work[1], held after controlling for claims-based measures of RA severity like DMARD use, biologic use, and GC use prior to diagnosis. Prior work supports the other factors associated with GC use in this cohort (i.e. male sex, older age, comorbidity)[2]. Further work to evaluate potential associations between rheumatologist access and long term GC utilization is warranted.

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Abstract Number: 2389

Treat to Target by Specific Cytokine Interdiction: Multiple Biomarker Disease Activity Test Deconstructed

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Rheumatologists have been encouraged to achieve low disease activity state when treating rheumatoid arthritis (RA). If it cannot be achieved with initial therapy, experts recommend changing to a different mechanism of action. There is no established means of selecting among the mechanisms of action.

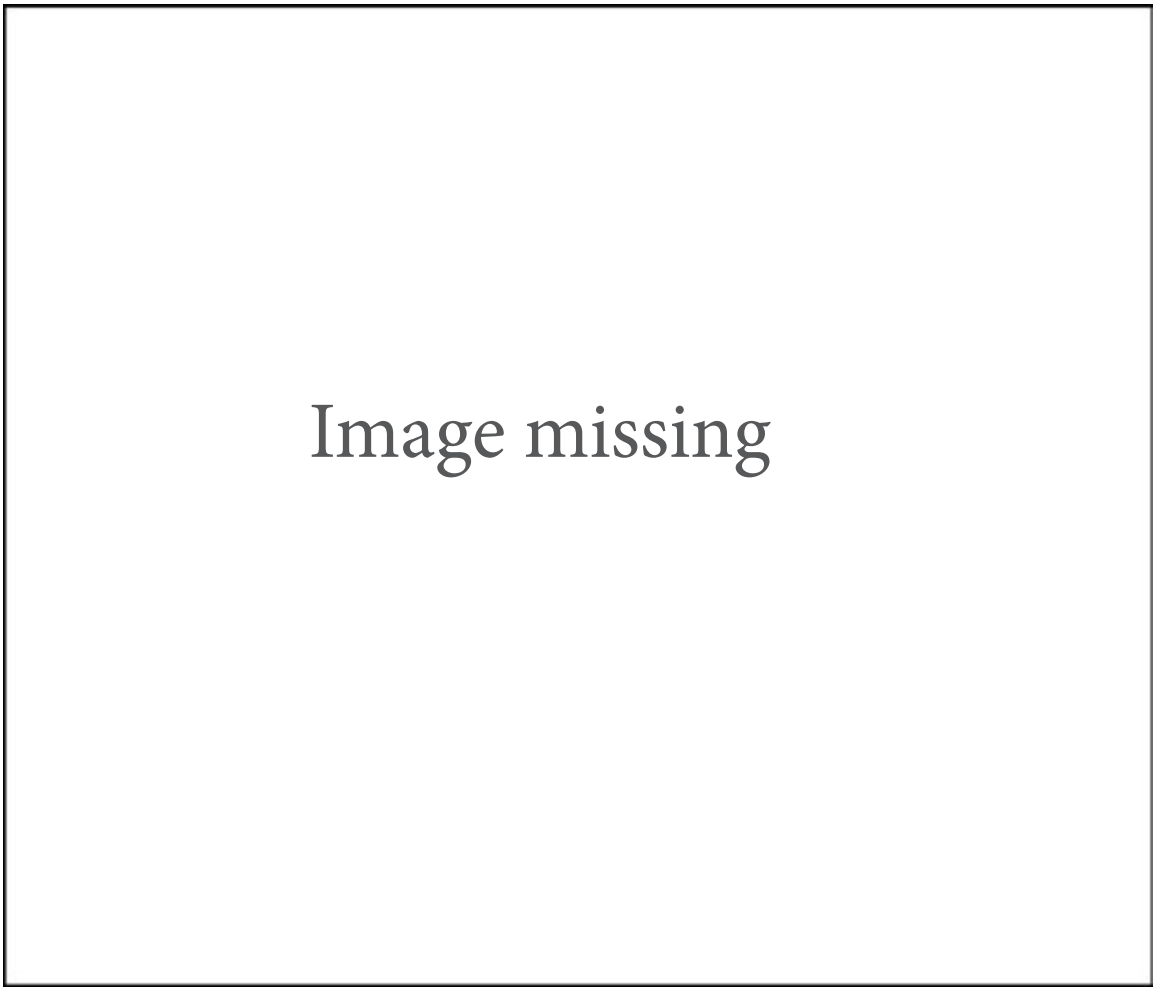
RA is a heterogeneous disease with variations in presentation, extra-articular features, and response to treatment. No single biomarker has been identified to predict response to treatment. Many cytokines have been identified in RA. 12 have become available in one test (MBDA). This study attempted to determine if the patterns of cytokine elevations could be used for treatment selection.

Methods: A literature search was performed, identifying clinical trials on RA which measured responses to the cytokines included in the MBDA: VCAM-1, VEGF-A, IL-G, TNF, MMP-1, MMP-3, YKL-40, Leptin, Resistin, SSA, and CRP. The trials included hydroxychloroquine (HCQ), sulfasalazine (SSZ), methotrexate (MTX), leflunomide (LEF), abatacept (ABA), tocilizumab (TCZ), rituximab (RTX) and tofacitinib (TOFA). A table(Table1) was constructed of cytokines versus treatment. Patients seen in the practice with RA were given the MBDA, and treatment was selected based on

TABLE 1

	HCQ	SSZ	MTX	LEF	TNF	ABA	TCZ	RTX	TOFA
VCAM-1	N	N	N	Y	Y	Y	N	N	N
VEGF-A	N	Y	Y	N	Y	N	Y	N	N
IL-6	Y	Y	Y	Y	N	Y	Y	Y	Y
TNF	N	Y	N	Y	Y	N	N	N	N
MMP-1	N	N	N	Y	Y	N	Y	N	Y
MMP-3	N	Y	Y	Y	Y	Y	Y	N	Y
YKL-40	N	N	N	N	Y	N	Y	N	N
LEPTIN	N	N	N	N	N	Y	N	N	N
RESISTIN	N	N	N	N	Y	N	N	N	N
SSA	Y	Y	Y	Y	Y	N	Y	N	Y
CRP	Y	Y	Y	N	Y	Y	Y	Y	N

Y = published clinical trial data
N = no published clinical trial data



MBDA score distribution using selective cytokine interdiction compared to conventional treat to target strategies

the agents with efficacy on highest number of cytokines elevated or past the 40th percentile reported on the MBDA, excluding EGF (elevated in remission) and leptin, which is affected by body composition, whenever pre-existing conditions, insurance coverage, and patient preference allowed. 263 patients were tested, 2 to 4 times over a 14 month period during routine visits.

Example: 83 year old patient with 6 year history RA: rheumatoid factor 169.6, CCP > 250, Larsen II radiographic changes. Past treatment: prednisone and MTX. MBDA score 09/06/2013: 69 high arthritis activity. VCAM-1 97%, VEGF-A 52%, IL-6 >99%, MMP-1 80%, MMP-3 96%, YKL-40 66%, Resistin 54%, SSA 82%, CRP 98 % percentiles. TOFA prescribed. Post treatment MBDA score 10/14/2016: 31 VCAM-1 67%, IL-6 30%, MMP-1 56%,MMP-3 29%, YLK-40 51%, Resistin 56%, SSA 19%, CRP 43%

Results: The MBDA scores in the physician's practice were graphed against the national average MBDA scores in practices using conventional treat to target strategies (Figure 1). Differences within the distribution of scores, and in the heights of the high, medium, and low MBDA scores can be observed between the two groups

Conclusion: This study is not meant to be a proof of concept achieved though a randomized controlled trial which demonstrated statistical significance. The data from the clinical trials utilized in Table 1 and the practices contain

heterogeneous populations of patients of unknown disease duration and dissimilar prior treatments. This study is observational, without the structure of a clinical trial, generated during routine clinical practice, and could qualify as real world data. Figure 1 may demonstrate an advantage to treatment selection based on the unique cytokine profiles of patient. With the increasing numbers of mechanisms of action, rising costs of treatment, and the shift to value-based care, it may be of value to explore the utility of multiple biomarker arrays in achieving low disease activity states in a directed manner.

Clinical trials that included responses to cytokines contained in the MBDA

Disclosure: L. Graham, None; **L. Graham**, None.

Abstract Number: 2390

Prediction of Disease Relapses by Multi-biomarker Disease Activity Score and Autoantibody Status in RA Patients Tapering DMARD Treatment in Stable Remission

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

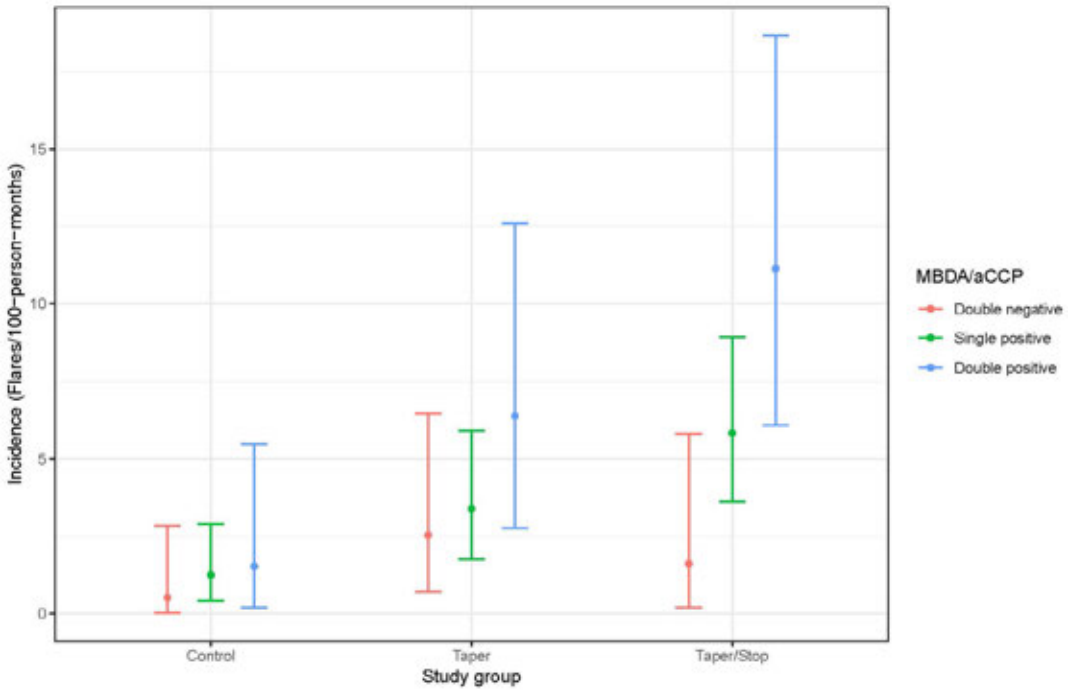
Session Title: RA – Treatments Poster III: Safety and Outcomes

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Achieving remission is the ultimate treatment goal in patients with rheumatoid arthritis (RA). With the development and wider use of highly effective disease modifying anti-rheumatic drugs (DMARD) about half of RA patients reach the disease remission state, raising the question about tapering or stopping anti-rheumatic treatment and appropriate predictors. The purpose was to analyze the effect of multi-biomarker disease activity (MBDA) score and anti-citrullinated protein (ACPA) on relapse rates in RA patients in sustained remission enrolled in the prospective randomized controlled RETRO study.

Methods: MBDA scores and ACPA status were determined in the baseline samples of patients in sustained DAS28-ESR remission fulfilling RETRO inclusion criteria. Patients were unblended and either continued DMARDs (Control),



incidenceplot

tapered dose by 50% (Taper) or stopped DMARDs after tapering (Taper/Stop) for one year according to the RETRO study protocol. MBDA and ACPA status were used as relapse predictors. Relapse was defined as the loss of a DAS28-ESR remission. We calculated incidence of flares and 95% Poisson confidence intervals by baseline ACPA and MBDA status in each study group (double negative, single positive, double positive). We compared the risk of flare in the treatment arms with a Cox regression model and calculated hazard ratios (HR) and 95% confidence interval (CI) for relapses.

Results: Serum samples and follow-up data of 203 patients included in the RETRO trial were analyzed. A flare was observed in 8/59 patients (13.6%) in the Control group, 24/60 (40.0%) patients in the Taper group and 37/68 (54.4%) patients in the Taper/Stop group among the 187 patients that completed their 1-year follow-up. HR (95%CI) for a relapse was 3.43 (1.54-7.66) in the taper group and 5.32 (2.47-11.46) for the control group. HR of flare of a positive MBDA and ACPA was 4.00 (1.72-9.31) compared to a negative MBDA and ACPA. Flare incidence did not differ with baseline MBDA/ACPA status in the control group, whereas in the taper/stop group, number of positive biomarkers could identify three distinct subgroups with a graded incidence of flare (Figure).

Conclusion: Tapering or stopping DMARDs after stable remission was associated with an increased risk of RA flares. Incidence of flares in MBDA/ACPA double-negative patients after tapering and stopping RA treatment was comparable to those that continued treatment within the precision limits of our subgroups.

Disclosure: M. Hagen, None; **K. Tascilar**, None; **M. Reiser**, None; **J. Haschka**, None; **A. Kleyer**, None; **L. Valor**, None; **B. Manger**, None; **G. Schett**, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, 8, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, UCB, 5, BMS, Celgene, GSK, Lilly, Novartis, 2; **J. Rech**, AbbVie, 8, Biogen, 8, BMS, 5, 8, Celgene, 5, 8, Chugai, 5, MSD, 8, Novartis, 5, 8, Roche, 5.

Abstract Number: 2391

Effect of Biologics on the Hemoglobin A1c in a Population of Rheumatoid Arthritis Patients

Ana Goico,[1] **Anoka Martis**,[1] Chistopher Kabir,[1] David Mael,[1] and Shoeb Mohammed[1], [1]Advocate Illinois Masonic Medical Center, Chicago, IL

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor necrosis factor (TNF), a pathogenic inflammatory mediator in Rheumatoid Arthritis (RA), has been shown to play an essential role in the pathophysiology of insulin resistance. Studies have demonstrated the effects of TNF on glucose metabolism, the most important of which is the promising reduction in blood sugar levels. Consequently, TNF inhibitors (TNFi) should have a clinically important impact on glucose control and confer benefits to patients with Type 2 Diabetes Mellitus (DM). More research is needed to fully understand the impact of biologics on glucose control. The objective of this study was to examine the effect of initiating biologic therapy on hemoglobin A1c (HbA1c) among RA patients.

Methods: This retrospective cohort study included adult RA patients who were prescribed one or two disease-modifying antirheumatic drugs, had at least two recorded HbA1c measurements, and were initiated on biologic therapy. RA patients with DM were included if they had an HbA1c $\geq$ 6.5% in the 6 months prior to initiation of biologics. Glucose control was defined as HbA1c $\leq$ 7.0% at their last test result following the initiation of biologics. Medians (interquartile ranges) and numbers (percentages) are reported for descriptive statistics. Stratified by DM diagnosis, change in HbA1c is represented by Kaplan-Meier plots between TNFi and non-TNFi groups and the hazard ratios reported.

Results: Among the 266 RA patients, median age in years was 61 (15) and 48 (18.1%) were males. Biologic therapy distribution was: 93 (35.6%) Adalimumab, 78 (29.9%) Etanercept, 19 (7.3%) Infliximab, and 71 (27.2%) non-TNFi. Sixty-two (60.2%) of non-DM patients and 116 (71.2%) of the DM group were obese, and 23 (14.1%) of DM were on insulin. The median change in HbA1c in the DM group was -0.3 (1.6) and non-DM 0.2 (1.0). Among the DM group, at 1 year, 13% reached glucose control with TNFi and 12% with non-TNFi; no difference was found over the observed time (HR= 0.94; 95% CI = 0.53, 1.67). In the non-DM group, at 1 year, 2% had a final uncontrolled glucose result with TNFi and 3% with non-TNFi; no statistically significant differences in HbA1c was observed over time (HR = 0.65; 95% CI = 0.21, 2.05).

Conclusion: No statistically significant difference in HbA1c levels or glucose control could be determined from initiating biologics in non DMARD-naïve RA patients with or without DM. Further large-scale, prospective studies on the impact of biologic therapy on non-articular outcomes are warranted to assess the need of preferentially starting these medications in the above-mentioned population.

Disclosure: A. Goico, None; **A. Martis**, None; **C. Kabir**, None; **D. Mael**, None; **S. Mohammed**, None.

Abstract Number: 2392

The Effectiveness of anti-IL-6 Therapy to Elderly-onset Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In daily practice, our rheumatologist has experienced different clinical feature of elderly-onset rheumatoid arthritis (EORA) compared with younger-onset RA (YORA). In EORA patients, serological marker of inflammation, like C-reactive protein, tend to be higher than that of YORA. And previous report suggested that significantly higher level of serum interleukin-6 (IL-6) and lower level of serum of tumor necrosis factor -α were detected in EORA compared with YORA patients. Hence, in elderly patients, IL-6 might be more important for the pathogenesis of RA. However, the treatment for EORA remains uncertain. We hypothesize that anti-IL-6 therapy is more effective for EORA patients than YORA patients. The objective this study is to clarify that the efficacy of anti -IL-6 therapy to EORA patients.

Methods: Inclusion criteria were as follows: diagnosis of RA based on 2010 ACR/EULAR classification criteria; the patients treated by anti-IL-6 drugs (tocilizumab or sarilumab); the disease activity could be evaluated at baseline and week 24 from started anti-IL-6 treatments by using disease activity score 28 erythrocyte sedimentation rate (3) (DAS28-ESR (3)). These patients were classified 3 groups according to RA onset age; younger-onset(YO); under 60 years old), middle age onset (MO); 60-69 years old, and elderly-onset (EO); equal or over 70 years old). And we compared the baseline characteristics, disease activity between 3 groups.

Results: We examine 107 RA patients who treated with anti-IL-6 drugs. Sixty-seven patients were YO, 22 were MO, 18 were EO. The rate of female patients was higher in YO compared with EO (92.5% vs 66.7%). Disease duration tends to be longer according to age at disease onset (EO; 11.7 years, MO; 5.5 years, YO; 1.4 years, respectively). And rate of seronegative (rheumatoid factor and anti-cyclic citrullinated peptides antibodies were negative) patients were also higher in EO compared with the other groups. The mean change of DAS28-ESR(3) from baseline to week 24 was significantly greater with EO than MO or YO($p < 0.05$). In analysis of each component of DAS28-ESR (3), tenderness joint count and swollen joint count was tended to decrease in EO. However, only ESR was significantly decreased in EO (< 0.05).

Conclusion: In EORA patients, anit-IL-6 therapy could be more effective than YORA patients. And especially, ESR of EORA patients could be more decreased by anti-IL-6 therapy.

Disclosure: T. Ando, None; **T. Suzuki**, None; **Y. Gotou**, None; **K. Kawahata**, None.

Abstract Number: 2393

Risk of Thromboembolism with Janus Kinase Inhibitors: A Systematic Review and Meta-Analysis of Randomized Placebo Controlled Trials

Jawad Bilal,[1] Irbaz Bin Riaz,[2] Maryam Sadiq,[3] Muhammad Salick,[4] Yahya Nomaan,[5] Nusrum Iqbal,[6] Sandipan Bhattacharjee,[7] Lary Prokop,[8] and C. Kent Kwoh[7], [1]University of Arizona College of Medicine, Tucson, AZ, [2]Mayo Hospital Rochester, Rochester, MN, [3]Nishtar Medical College, University of Health Sciences, Lahore, Albany, NY, [4]Albany Medical Center, Albany, NY, [5]Phoenix Children's Hospital, Phoenix, AZ, [6]St Joseph's Hospital, Tucson AZ, Tucson, AZ, [7]University of Arizona, Tucson, AZ, [8]Mayo Clinic, Rochestor, MN

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Treatments Poster III: Safety and Outcomes

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose:

Importance: The efficacy of Janus kinase (JAK) inhibitors is well established across a range of diseases. However, there is a major concern regarding the potential risk of an increased number of thromboembolic adverse events.

Objective: To assess the risk of thromboembolism in patients treated with JAK inhibitors.

Methods:

Data Sources: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, and Daily, Ovid EMBASE, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus were searched (Inception to May 23, 2019).

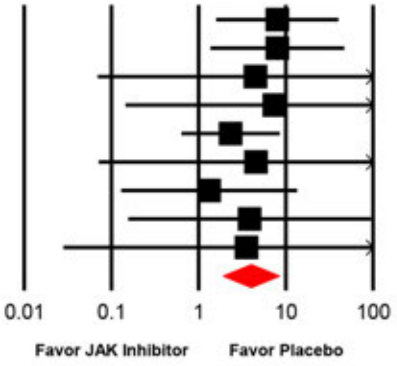
Study Selection: Published randomized, placebo-controlled trials (Phase II and III) that evaluated JAK inhibitor therapies in any disease and had reported safety data.

Data Extraction and Synthesis: This systematic review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Two investigators independently extracted study data, and assessed risk of bias.

Main Outcomes and Measures: The outcome of interest was the number of thromboembolic events in individuals receiving JAK inhibitor therapies compared to placebo. We used the Peto fixed effects model to calculate the pooled odds ratios as this is the appropriate model for rare events.

Results: We included 9 eligible RCTs (9496 patients). Patients receiving JAK inhibitors had higher risk of thromboembolic events OR 4.09 (95% CI 1.91-8.48, P < 0.001, I2=0%;)(figure 1). The results remained consistent with continuity correction OR 3.56 (95% CI 1.74-7.30, P=0.001, I2=0%), and after excluding studies with cancer patients OR 2.98 (95% CI 1.48-6.00, P=0.002, I2=0%). Medications wise analysis showed OR 7.65 (95% CI 2.45-23.88, P=0.002, I2=0%) with bariticinib (3 trials), OR 1.75 (95% CI 0.74-4.13, P=0.19, I2=0%) with ruxolitinib (2 trials), and OR 2.21

Study name	Time point	Statistics for each study				
		Peto odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Taylor	2019	7.990	1.608	39.706	2.541	0.011
Smolen	2019	7.982	1.379	46.205	2.319	0.020
Wallace	2018	4.492	0.071	286.234	0.709	0.478
van der Heijde	2018	7.389	0.147	372.385	1.000	0.317
Hurwitz	2015	2.327	0.643	8.424	1.287	0.198
Genovese	2018	4.543	0.072	285.164	0.717	0.474
Fleischmann	2018	1.322	0.131	13.331	0.237	0.813
Kremer	2016	3.840	0.158	93.606	0.826	0.409
Van Vollenhoven	2012	3.540	0.029	439.382	0.514	0.607
		4.008	1.913	8.398	3.678	0.000



Model		Effect size and 95% interval			Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	9	4.008	1.913	8.398	3.678	0.000	2.977	8	0.936	0.000	0.000	0.715	0.512	0.000
Random	9	4.008	1.913	8.398	3.678	0.000								

request
Table 1

(95% CI 0.40-12.17, P=0.36, I2=0%) with upadacitinib (3 trials). There were 2 trials of tofacitinib and outcome of interest was reported in one trial only which is why drug wise analysis of tofacitinib was not performed.

Limitations: Short follow up duration

Conclusions: Risk of thromboembolism is increased in patients who are treated with JAK inhibitors as compared to placebo. The findings remained consistent even when studies with cancer patients were excluded. In subgroup analyses based on individual medications, only bariticinib showed statistically significant findings of increased thrombosis risk. This analysis provides toxicity estimates for thromboembolic events associated with the use of JAK inhibitors that can inform shared-decision making when patients and clinicians are contemplating the use of JAK inhibitors for various indications.

Disclosure: J. Bilal, None; **I. Riaz**, None; **M. Sadiq**, None; **M. Salick**, None; **Y. Nomaan**, None; **N. Iqbal**, None; **S. Bhattacharjee**, None; **L. Prokop**, None; **C. Kwoh**, Express Scripts, 5, GSK, 5, Kolon Tissue Gene, 5, MerckSerono, 5, Regeneron, 5, Regulus, 5, Taiwan Liposome Company, 5, Thusane, 5.

Abstract Number: 2394

Use and Influence of Biologic/Janus Kinase Monotherapy Among Recently Switched Rheumatoid Arthritis Patients: Results from an Annual National Patient Chart Audit

Lynn Price,[1] Phil Pouliot,[1] and Lauren Schmitt[1], [1]Spherix Global Insights, Exton, PA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: US rheumatologists have long agreed that methotrexate (MTX) is the backbone of rheumatoid arthritis (RA) treatment, and while comfort with biologic/JAK monotherapy is growing, the majority of RA patients remain on a combination regimen, either with MTX or another conventional DMARD. With IL-6 inhibiting biologics and JAKs touted for their efficacy as monotherapy treatment options, this research sought to understand physician's attitudes towards combination therapy and the role monotherapy plays as a driver behind brand choice when switching RA patients from one biologic/JAK to another.

Methods: An independent market analytics firm collaborated with US rheumatologists (n=320) to conduct a retrospective chart review of patients diagnosed with rheumatoid arthritis (RA) (n=1,312), who had switched from one biologic/JAK therapy to another in the prior twelve weeks. Rheumatologists were able to submit up to seven RA patient charts. Data were collected in September 2018 and included clinical and non-clinical patient demographics, as well as physician demographics and attitudinal survey responses. This study was a non-longitudinal trending analysis to 2016 and 2017 audits following the same methodology.

Results: Approximately two-thirds of collaborating US rheumatologists agree with the statements: "MTX is the backbone of RA treatment" and "I prefer to prescribe biologics in combination with MTX whenever possible;" however, three-quarters also agree, "my comfort in using biologics/JAK monotherapy is growing." Indeed, when examining the chart audits of recently switched RA patients, only 35% were on a true monotherapy regimen (no MTX, other conventional DMARDs, or steroids), a figure that has remained stable since 2016. Half of all recently switched, biologic/JAK-treated RA patients were on a combination regimen with MTX, and there were no significant differences in rates of combination MTX use by RA disease severity. The possibility of biologic/JAK monotherapy was significantly more of a driver behind the decision to switch patients to JAK and IL-6 inhibitors than it was for switches to TNF-α inhibitors, abatacept, or rituximab. However, patients recently switched to a TNF were just as likely as those switched to a JAK, and more likely than those switched to an IL-6, to be on a monotherapy regimen.

Conclusion: While US rheumatologists state they are becoming more comfortable with biologic/JAK monotherapy for the treatment of RA, use of biologic/JAK therapy in combination with a conventional DMARD (most commonly MTX), is common practice and has not changed since 2016. The possibility of monotherapy treatment is a factor in the decision to switch patients to JAK and IL-6 inhibitors more commonly than when switching to other biologic classes; however, there are no statistically significant differences in rates of monotherapy by mechanism of action among recently switched RA patients.

Disclosure: L. Price, None; **P. Pouliot**, None; **L. Schmitt**, None.

Abstract Number: 2395

DMARD-naïve Rheumatoid Arthritis (RA) Patients Have Greater RAPID3 Improvement over 6 Months After 1st Visit Than Patients Who Were Treated Previously Treated with DMARDs, Although Baseline RAPID3 Was Similar: The Importance of Early Treatment

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: A study of patients with RA at their first visit to an academic rheumatology site indicated an unexpected observation that 75% of patients had a history of prior treatment with either glucocorticoids or disease modifying antirheumatic drug (DMARD) agents, while only 25% were DMARD-naïve (1). Therefore, we analyzed a hypothesis that DMARD-naïve RA patients would have greater improvement from first visit to 6-month follow-up visit than patients who had prior treatment, according to MDHAQ/RAPID3 (multidimensional health assessment questionnaire/routine assessment of patient index data3) scores.

Methods: The first visit of all RA patients (by ICD codes) to one site that occurred between 5/2011-2/2017 was identified by retrospective chart review. All patients with all diagnoses complete MDHAQ/RAPID3 at all visits. RAPID3 (0-30) is the sum of 3 0-10 scores for physical function, pain visual analog scale (VAS), and patient global assessment VAS; severity categories are ≥12=high, 6.1-12= moderate, 3.1-6= mild, ≤3= remission. Patients who had a complete MDHAQ/RAPID3 at first visit and 6-month follow-up visit were classified into 3 groups on the basis of prior DMARD therapy: 1)"DMARD-naïve" - no glucocorticoid or DMARD; 2) "active DMARD"- had DMARD therapy within previous month; 3)"DMARD-interrupted" - had prior DMARD therapy interrupted for > 1 month. Mean MDHAQ/RAPID3 and individual RAPID3 component scores within each of the 3 groups were compared at first and 6-month follow-up visits for possible change using paired t tests. Differences between the 3 groups in changes over 6 months were compared using analysis of variance (ANOVA).

Results: Demographic data for age, sex, ethnicity, level of formal education, as well as body mass index, did not differ significantly in the 3 RA groups. Median disease duration was 1 year in DMARD-naïve patients, 2 years in active-DMARD, and 5 years in DMARD-interrupted patients (p=0.006). Mean MDHAQ/RAPID3 scores were 15.5 in DMARD-naïve, 14.8 in active-DMARD, and 16.5 in DMARD-interrupted patients, all indicating high severity (≥12) - no clinically or statistically significant differences. At 6-months follow up, MDHAQ/RAPID3 was improved in all RA groups, -5.7 in the DMARD-naïve group vs -2.7 in the active DMARD group vs -3.6 in the DMARD-interrupted group (p=0.05), also reflected in the RAPID3 component scores (Table). The difference in the DMARD-naïve group, but not the other groups, exceeded the minimum clinically important improvement (MCII) criterion of 3.8 for MDHAQ/RAPID3, which was almost met in the DMARD-interrupted group, but not in the active-DMARD group.

Conclusion: Patients with RA improved with treatment from first visit to 6 months later, greatest in DMARD-naïve, less in DMARD-interrupted, and least in the active-DMARD group. The similarity of MDHAQ/RAPID3 scores at baseline of DMARD naïve to those of previously-treated patients suggests that "treat-to-target" appears poorly implemented in routine clinical care. The data appear to reinforce the importance of early treatment for optimal control of RA.

Variable(s)	All RA (n=201)	3 Groups according to treatment				
		DMARD-naïve (n=50)	Active-DMARD (n=100)	DMARD-interrupted (n=51)	p DMARD-naïve RA vs other RA groups	p all 3 groups
RAPID3 (0-30)						
1st visit	15.4	15.5	14.8	16.5	0.89	0.38
6-month	11.8	9.9	12.1	13.0	0.05	0.11
Difference 2 visits	-3.7	-5.7***	-2.7***	-3.6**	0.19	0.05
Physical function (0-10)						
1st visit	3.1	2.9	3.1	3.4	0.36	0.50
6-month	2.5	1.6	2.6	3.0	0.003	0.008
Difference 2 visits	-0.6	-1.2**	-0.5**	-0.4^{NS}	0.007	0.03
Pain (0-10)						
1st visit	6.4	6.7	6.0	6.7	0.27	0.19
6-month	4.9	4.4	4.9	5.3	0.21	0.36
Difference 2 visits	-1.5	-2.3***	-1.1***	-1.4*	0.02	0.07
Patient global assessment (0-10)						
1st visit	5.9	5.9	5.7	6.4	0.99	0.36
6-month	4.4	3.8	4.5	4.7	0.15	0.32
Difference 2 visits	-1.5	-2.1***	-1.2***	-1.7***	0.17	0.26

table -3 RA groups-pdf2

Table. MDHAQ/RAPID scores of new RA patients who were "DMARD-naïve," had "active-DMARD" treatment, or "DMARD-interrupted" treatment, at baseline and 6-month follow-up visits

References:

1 -Chua et al, Arth Rheum, in press

Disclosure: T. Pincus, Helath Services, 7, Medical History Services LLC, 6, 7, 9, Medical history services LLC, 6, 7; **j. Chua**, None; **J. Block**, None; **I. Castrejon**, None.

Abstract Number: 2396

DNA Methylation of the Dual Specificity Phosphatase 22 (DUSP22) Gene Promoter in Plasma and Medication Use in Rheumatoid Arthritis (RA)

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Treatments Poster III: Safety and Outcomes

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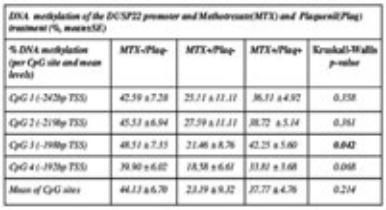
Characteristics or Measures	*RA Population*
Demographics	
No. men	*5*
No. women	*21*
Age, (years ± SE)	*57.76 ± 2.28*
Hispanic	*23*
African American	*3*
Treatment	
MTX	*53.8%*
Plaquenil	*57.7%*
Prednisone	*50.0%*
MTX + Plaquenil	*34.6%*
MTX + Prednisone	*26.9%*
Clinical Characteristics	
% ACPA+	*69.20%*
% RF+	*61.50%*
Disease duration (years)	*11.00 ± 2.71*
CRP	*1.09 ± 0.04*
WBC	*6.96 ± 0.39*
CDAI	*16.12 ± 1.95*
VAS	*4.00 ± 0.61*
NSS	*3.22 ± 0.56*
ID PAIN	*2.52 ± 0.36*
TCNS	*5.08 ± 0.75*
SENS	*20.38 ± 3.91*

ACR Abstract - Table 1



DNA methylation of the DUSP22 promoter and Methotrexate(MTX) and Plaquenil(Plaq) treatment (%, mean±SE)				
% DNA methylation (per CpG site and mean levels)	MTX-/Plaq-	MTX+/Plaq-	MTX+/Plaq+	Kruskall-Wallis p-value
CpG 1 (-242bp TSS)	42.59 ± 7.28	25.11 ± 11.11	36.31 ± 4.92	0.358
CpG 2 (-219bp TSS)	45.53 ± 6.94	27.59 ± 11.11	38.72 ± 5.14	0.361
CpG 3 (-198bp TSS)	48.51 ± 7.35	21.46 ± 8.76	42.25 ± 5.60	**0.042**
CpG 4 (-192bp TSS)	39.90 ± 6.02	18.58 ± 6.61	33.81 ± 3.68	0.068
Mean of CpG sites	44.13 ± 6.70	23.19 ± 9.32	37.77 ± 4.76	0.214

ACR Abstract - Table 2

DNA methylation of the DUSP22 promoter and Methotrexate(MTX) and Prednisone(Pred) treatment (%, mean±SE)				
% DNA methylation (per CpG site and mean levels)	*MTX-/Pred-*	*MTX+/Pred-*	*MTX+/Pred+*	Kruskall-Wallis *p-value*
CpG 1 (-242bp TSS)	*40.86 ±6.00*	*35.52 ± 5.75*	*30.70 ± 7.78*	*0.478*
CpG 2 (-219bp TSS)	*42.74 ±6.15*	*38.03 ± 6.04*	*33.05 ± 7.86*	*0.561*
CpG 3 (-198bp TSS)	*46.02 ±6.39*	*37.38 ± 7.70*	*35.23 ± 7.66*	*0.478*
CpG 4 (-192bp TSS)	*34.06 ± 4.88*	*30.89 ± 5.59*	*28.03 ± 5.03*	*0.771*
Mean of CpG sites	*40.92 ± 5.77*	*35.45 ± 6.19*	*31.75 ± 6.95*	*0.591*

ACR Abstract - Table 3

Background/Purpose: The Dual Specificity Phosphatase 22 (*DUSP22*) gene expression has been shown to be regulated via DNA methylation of its promoter. In addition, aberrant DNA methylation of *DUSP22* in lymphocytes has been observed in RA patients and it has been linked to erosive disease. Global DNA hypomethylation of lymphocyte cell subpopulations from RA patients was reversed after methotrexate (MTX) treatment, suggesting MTX has the ability to alter DNA methylation. However, no study to date has evaluated the effect of RA treatment on *DUSP22* DNA methylation. Here, we investigated whether plasma DNA methylation in the promoter region of *DUSP22* varies by treatment regime in RA and further, we determined *DUSP22* promoter DNA methylation changes after MTX exposure in lymphoblastoid cell lines.

Methods: We recruited 26 patients who satisfied the ACR criteria of RA. DNA was isolated from plasma, bisulfite converted, and pyrosequenced to determine DNA methylation levels in the promoter region of *DUSP22* at four different CpG sites. In addition, lymphoblastoid cell lines of healthy individuals were treated with increasing concentrations (0nM and 50nM) of MTX and DNA methylation of *DUSP22* was determined. Statistical non-parametric testing, Kruskall-Wallis for comparisons across groups and Mann-Whitney for differences between two groups, were conducted.

Results: Of the 26 RA patients included in this study, 20 were under MTX and/or Plaquenil regimens. DNA methylation of the CpG3 (-198bp from transcription start site(TSS)) of *DUSP22* was significantly lower in patients treated with MTX(MTX+) but not with Plaquenil(Plaq-) when compared to those on neither MTX(MTX-) nor Plaquenil(Plaq-) (21.46 ± 8.76% vs. 48.51±7.35%, p=0.034). However, no significant differences were found between the MTX+Plaq- and MTX+Plaq+ groups for this site (21.46 ± 8.76% vs. 42.25±16.40%, p=0.088). No other differences in *DUSP22* DNA methylation were observed for other CpG sites or the mean. In addition, subgroup analysis of MTX and Prednisone versus MTX- use did not yield any statistically significant differences. In *in-vitro* studies, exposure to

50nM MTX increased CpG4 (-192bp from TSS) DNA methylation (0.13±0.48% vs 0.59±0.45%, *p*=0.035) but not of CpG3 (2.25±1.34% vs. 3.09±1.21%, *p*-value=0.133). No other changes in DNA methylation were observed after MTX treatment in cell lines derived from healthy individuals.

Conclusion: Our findings suggest that RA treatment might have an effect on plasma *DUSP22* DNA methylation. These findings also highlight the possibility that different drugs, when used in combination (i.e. Plaquenil and MTX), may interact and affect DNA methylation. *In-vitro* findings mirror previous data in drug naïve patients in which MTX increases DNA methylation, in contrast we found MTX treatment increases plasma *DUSP22* DNA methylation. Our study has a small sample but it is the first one to investigate the effect of several RA drugs on DNA methylation of the *DUSP22* promoter, suggesting mechanisms of action for widely used DMARDs like MTX and Plaquenil. Future studies with larger sample size are needed to confirm our findings, and add to our understanding of the epigenetic effects of RA drugs.

Disclosure: L. Delgado-Cruzata, None; **M. Rodriguez Alvarez**, None; **A. Amarnani**, None; **E. Guzman**, None; **A. Bliese**, None; **B. Albarracin**, None; **C. Cirilli**, None; **S. Hinson**, None.

Abstract Number: 2397

Skin Lesions as a Side Effect of anti-IL6 Therapy: Transcriptome Analysis of Peripheral Blood Shows a Risk of Paradoxical Neutrophil Activation and Exacerbation of Skin Ulcer

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Background/Purpose: Skin lesion as a side effect of Tocilizumab (TCZ) has not been paid much attention. In the drug information sheets, incidence of dermatological adverse reactions was only 1~2%. However, we experienced several RA cases with development of various skin lesions associated with neutrophil activation after TCZ therapy. Although the precise mechanism is still unclear, of particular interest is the decreased neutrophil counts in peripheral blood have been known after initiation of TCZ in clinical trials, which did not affect the rate of serious infections. On the other hand, we also experienced exacerbation of skin ulcer despite the inflammation, such as activity of rheumatoid arthritis, was absolutely under control. In this study, we try to detect the changes in transcriptome of peripheral blood after TCZ treatment.

Methods: As total of 23 RA cases (43.2 person-years) was completely followed in our single hospital from the initiation of TCZ, their medical records were checked to calculate the incidence of dermatological adverse reactions to TCZ from 2014 to 2018. Meanwhile, to explore the normal response to anti-IL6 therapy, peripheral whole blood at just before (pre) and 3 months after (post) TCZ treatment from 10 RA cases without any dermatological problems were subjected to gene expression study. Total RNAs were then extracted with PAXgene miRNA kit. After quantifying the transcripts, differentially expressed genes (DEGs) were selected by paired comparison (post vs. pre), setting

thresholds at 2-fold change up/down and less than P=0.05 in paired T-test. And then, enrichment analysis using gene ontology (GO) terms were performed.

Results: Among 23 patients, 4 cases (9.25/100 person-years) of Skin lesion including neutrophilic dermatosis and leukocytoclastic vasculitis were observed as side effects of TCZ. Although 2 of them required termination of the therapy, others were possible to continue TCZ treatment. We also experienced 2 cases of exacerbation of skin ulcer despite the inflammation was under favorable control. For transcriptome analysis, total of 57571 transcripts were identified and the 52/156 genes of up/down-regulated genes were selected as DEGs from the comparison of post vs. pre treatment of TCZ using paried T-test. Surprisingly, 8 out of the top 10 enriched GO terms in the up-regulated genes were relevant to leukocyte activation such as 'neutrophil chemotaxis'. On the other hand, 6 out of the top 10 enriched GO terms in the down-regulated genes were related to tissue repair, such as "platelet activation" and "wound healing".

Conclusion: As the cytokine network is very complicated and an exquisite balance presented in immune and homeostatic system is strictly maintained, inhibition of a multifunctional cytokine signaling such as IL-6 may cause unexpected adverse reactions. Our findings indicate a potential risk of the development of skin lesions associated with neutrophil activation by anti-IL6 therapy. The mechanism may also help the increased margination of neutrophils in normal situation, and it may be a hint for the secret behind the decreased neutrophil counts after TCZ treatment. Anyway, we will not recommend anti-IL6 therapy for the patients with skin ulcers from our experiences.

Disclosure: Y. Koyama, Ayumi, 8, BMS, 8, Chugai, 8, Asahi-Kasei, 8, Lilly, 8, Tanabe-Mitsubishi, 8; **A. Senoo**, None; **K. Otsuki**, None; **Y. Sato**, None; **M. Yamaguchi**, None; **T. Higuchi**, None.

Abstract Number: 2398

Prevalence of Anxiety and Depression in a Cohort of Patients with Rheumatic Diseases on Biological Infusions

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Background/Purpose: Studies have shown an increased prevalence of psychologic disorders in rheumatic diseases, such as rheumatoid arthritis, systemic lupus erythematosus, and psoriatic arthritis, compared to the general population. Of note, the coexistence of anxiety and depression with rheumatic diseases has been linked to worse outcomes and increased health care utilization. Our aim was to examine the prevalence of anxiety and depression in a cohort of patients with rheumatic diseases on biologic infusions.

Methods: We conducted a retrospective study between 2013 and 2017 at two infusion centers affiliated with the University of Arizona Arthritis Center. We identified patients with rheumatic diseases on biological infusions for the concurrent diagnosis of anxiety and/or depression and examined hospitalizations. Statistical analysis by Fisher's exact test using Baptista-Pike was performed with Prism Software and is represented using the odds ratio with the 95% confidence interval and p-value.

Results: Of the total 548 patients with rheumatologic diagnoses, 77% of the sample was female. The mean age was 63 years. 59.7% had rheumatoid arthritis , 12.9% had osteoporosis, 6% had systemic lupus erythematosus, 5% had psoriatic arthritis, 4% had ankylosing spondylitis, 1.2% had gout, 0.9% had mixed connective tissue disease, 1.2% had juvenile idiopathic arthritis, 1% had anti-neutrophil cytoplasmic antibodies vasculitis, 1.6% had osteoarthritis, 0.3% had Behcet's disease, 0.5% had dermatomyositis, 0.5% had polymyositis, 0.8% had adult-onset still's disease, and 0.3% had giant cell arteritis.

175 patients (31.9%) within the cohort had a diagnosis of anxiety and/or depression. 76 patients (13.8%) had depression, 99 (18%) had anxiety, and 42 (7.6%) had concurrent anxiety and depression. 90/332 (27.1%) with RA, SLE 15/34 (44.1%), osteoporosis 24/71 (33.8%), ankylosing spondylitis 10/29 (34.5%), psoriatic arthritis 7/25 (28%), vasculitis 4/9 (44.4%), others 24/51 (47%) had either depression or anxiety or both.

61/175 (34.9%) of patients with depression and/or anxiety had 1 or more hospitalization compared to 87/373 (23.3%) patients without any psychological diagnosis (**OR 1.76, 95% CI [1.19-2.60],** *P = 0.004*).

Conclusion: The findings of this study show a high prevalence of anxiety and depression in our cohort of patients with rheumatic diseases. Although, patients with one or both of these psychiatric diagnoses had significantly higher rates of hospitalizations but this association needs to be further investigated by regression analysis. Given the high prevalence of anxiety and depression in the rheumatology patient population, an interdisciplinary team approach with rheumatologists, primary care physicians, psychiatrists, and psychologists to manage a patient's mental health may play an important role in improving long-term rheumatic and psychiatric disease outcomes.

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Abstract Number: 2399

Changes in the Initial Usage Pattern of Biologic Disease-modifying Antirheumatic Drugs in Rheumatic Diseases During the past Twelve Years: A Real-world Setting Analysis

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Table 1. Patient characteristics at the start of biological treatment. Pattern of use.

Variable	Period of time				p
	2007-2009	2010-2012	2012-2015	2016-2019	
Number of patients included in this period	1826	967	277	3127	
Sex (women) (%)	1,115 (61.1)	609 (63.0)	152 (54.8)	1,880 (60.1)	0.087
Mean age at the beginning of first biologic (SD)	50.6 (14.1)	51.3 (13.8)	50.9 (15.3)	50.1 (12.9)	0.086
Time of evolution until first biological treatment (SD)	8.6 (9.2)	8.6 (12.5)	7.8 (9.3)	6.5 (7.4)	<0.001
RA	8.7 (9.2)	9.0 (12.8)	8.9 (9.8)	7.0 (7.2)	<0.001
PsA	7.8 (9.2)	6.7 (9.7)	5.5 (6.8)	5.1 (5.9)	<0.001
AS	9.3 (9.3)	9.5 (13.8)	7.6 (9.8)	7.1 (9.1)	<0.001
TNF-inhibitor as first biological treatment (%)	96.6	77.0	81.6	59.8	<0.001
DAS28 at the beginning of biological treatment (only in RA patients)	5.2 (1.6)	4.7 (1.6)	4.1 (2.0)	4.7 (1.4)	<0.001
Comorbidities, n (%)					
Cancer	31 (1.7)	15 (1.6)	3 (1.1)	123 (3.9)	<0.001
Lymphoma	3 (0.2)	1 (0.1)	1 (0.4)	5 (0.2)	0.830
Ischemic cardiopathy	38 (2.1)	18 (1.9)	8 (2.9)	95 (3.0)	0.088
Diabetes	135 (7.4)	63 (6.5)	14 (5.1)	236 (7.7)	0.309
Smoker	315 (17.3)	149 (15.4)	48 (17.3)	686 (21.9)	<0.001
Renal insufficiency	35 (1.99	10 (1.0)	3 (1.1)	46 (1.5)	0.286
Heart failure	19 (1.0)	14 (1.5)	2 (0.7)	33 (1.1)	0.669
Hypercholesterolemia	268 (14.7)	148 (15.3)	48 (17.3)	838 (26.8)	<0.001
COPD	36 (2.0)	24 (2.5)	4 (1.4)	83 (2.7)	0.296
Hypertension	421 (23.1)	209 (21.61)	514 (18.4)	785 (25.1)	0.015
Osteoporosis	207 (11.3)	113 (11.7)	18 (6.5)	319 (10.2)	0.053
Epstein Barr infection	10 (0.6)	1 (0.1)	0 (0.0)	34 (1.1)	0.003
Charlson index, mean (SD)	1.9 (1.2)	1.9 (1.1)	1.9 (1.1)	2.2 (1.5)	<0.001

Background/Purpose: During the past 15 years, advancements in the understanding of the safety and effectiveness, as well as the expanding access and availability of biologic disease-modifying anti-rheumatic drugs (bDMARDs), have likely influenced the pattern of use of such compounds in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS). This analysis is aimed at assesing changes in the baseline characteristics of RA, PsA and AS patients who underwent biological therapy from 2007 to 2019 in a real world setting.

Methods: Data were obtained from BIOBADASER, the Spanish registry of biologics which compiles data from routine clinical practice. Patients diagnosed with RA, PsA and AS who started biological treatment from 2007 to 2019 were included. Sociodemographic and clinical variables, as well as first bDMARD use, were stratified by the starting year period (2007-2009; 2010-2012; 2013-2015; 2016-2019) and then compared using Anova. The therapeutic target chosen by physicians to manage these patients was also analyzed. Parametric values were compared using a general linear model for repeated measures with simple contrast considering the initial value (2007-2009) as the reference.

Results: 6197 patients (3266 RA patients, 1517 PsA and 1414 AS) were included in this analysis (Table 1). Patient age at the beginning of the first biologic was significantly higher during the period 2016-2019 than in 2007-2009 (50.1 vs 50.6). Disease duration until the use of biologics decreased significantly (8.6 vs 6.5). In RA patients, disease activity, as assessed by DAS28 at the start of the biological treatment, was significantly higher during the 2007-2009

period than in the last period analyzed (5.2 vs 4.7). The use of a TNF inhibitor as a first option also changed significantly (96.6% vs 59.8%). Regarding comorbidities, the number of rheumatic patients treated with biologics and who had a history of cancer (1.7% vs 3.9%), hypercholesterolemia (14.7% vs 26.8%), or hypertension (23.1% vs 25.1%) increased significantly. The Charlson index also increased (1.9 vs 2.2).

Conclusion: Our data show that during the last 12 years the usage pattern of biologics in patients with RA, PsA and EA has changed. Nowadays these compounds are used in patients with shorter disease evolution times, with less disease activity and with more comorbidities. The availability of greater pharmacological resources, as well as an increased knowledge of the safety and effectiveness of biologics could explain these findings.

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The Effect of Co-medication with Methotrexate and Other Conventional Synthetic Disease Modifying Anti-rheumatic Drugs on First Tumor Necrosis Inhibitor Drug Survival in Patients with Rheumatoid Arthritis: Results Form a Nationwide Registry

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Background/Purpose: Tumor necrosis factor inhibitors (TNFi) should be used for the treatment of rheumatoid arthritis (RA) in combination with conventional synthetic disease modifying anti-rheumatic drugs (csDMARD), preferably with methotrexate (MTX). However a significant proportion of RA patients receive TNFi in combination with other csDMARD or in monotherapy. We aimed to assess the effect of co-medication with MTX or other csDMARDs on drug survival of the first TNFi in RA.

Methods: All adult patients with RA followed in the Czech national registry ATTRA who started TNFi therapy after January 1st 2012 were considered. Baseline demographic data of patients starting their first TNFi in combination with MTX, with other csDMARD or as a monotherapy were compared. Six-year drug survival was analyzed using Kaplan-Meier method, log rank test was used to compare differences between groups. ATTRA is a centralized prospective computerized registry collecting data on efficacy, safety and quality of life of patients treated with biologic disease modifying anti-rheumatic drugs (bDMARD) in the Czech Republic. TNFi therapy is usually indicated for patients with RA who have failed treatment with at least one csDMARD.

Results: A total of 1841 RA patients initiated first bDMARD treatment during the studied period, with 1724 patients receiving TNFi. 1307 patients (76%) started TNFi therapy in combination with MTX (median dose 15mg weekly),

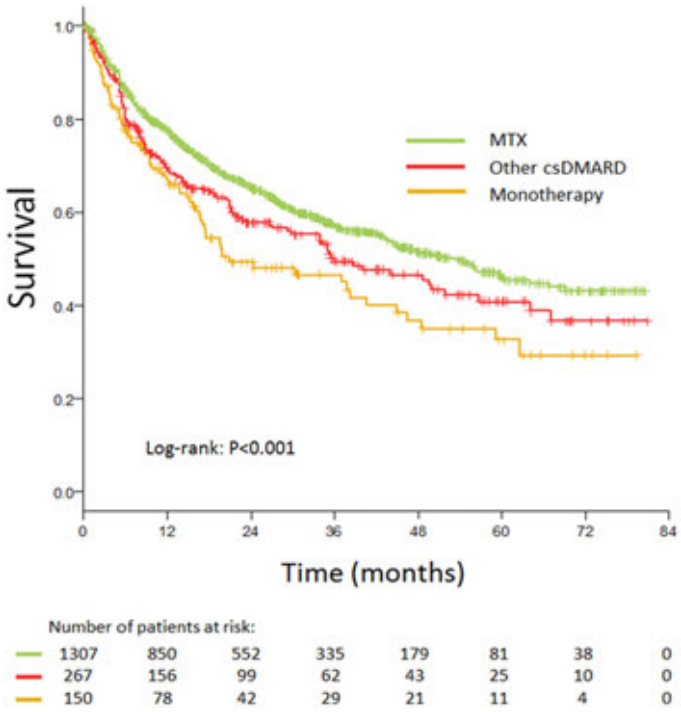

Figure 1: Kaplan–Meier curves of 6-year drug survival of the first TNFi based on co-medication

		MTX (N = 1307)	Other csDMARD (N = 267)	Monotherapy (N = 150)	P-value
Gender (female)	N (%)	993 (76.0%)	216 (80.9%)	114 (76.0%)	0.216
Age (years)	Median (5; 95 perc)	54.0 (29.0; 71.0)	55.0 (33.0; 74.0)	57.0 (33.0; 74.0)	0.007
Disease duration (years)	Median (5; 95 perc)	7.9 (1.4; 27.5)	8.2 (1.5; 27.3)	8.7 (1.0; 26.3)	0.629
Anti-CCP positivity	N (%)	918 (71.6%)	193 (73.7%)	101 (69.2%)	0.618
GC use in the past	N (%)	1157 (88.7%)	233 (87.3%)	132 (88.6%)	0.792
GC use currently	N (%)	923 (70.6%)	186 (69.7%)	90 (60.0%)	0.028
csDMARD use in the past	N (%)	1283 (99.6%)	264 (99.2%)	135 (90.6%)	<0.001
csDMARD number in the past	N (%)				
0		5 (0.4%)	2 (0.8%)	14 (9.4%)	<0.001
1		426 (33.1%)	45 (16.9%)	24 (16.1%)	
2		366 (28.4%)	73 (27.4%)	41 (27.5%)	
3		277 (21.5%)	79 (29.7%)	39 (26.2%)	
4 and more		214 (16.6%)	67 (25.2%)	31 (20.8%)	
CRP (mg/dl)	Median (5; 95 perc)	15.2 (1.4; 68.0)	16.7 (1.4; 75.8)	13.8 (1.4; 78.1)	0.232
Tender joint count (0-28)	Median (5; 95 perc)	13.0 (5.0; 24.0)	12.0 (5.0; 26.0)	13.0 (5.0; 26.0)	0.860
Swollen joint count (0-28)	Median (5; 95 perc)	9.0 (2.0; 18.0)	9.0 (2.0; 19.0)	9.0 (2.0; 20.0)	0.878
DAS28	Median (5; 95 perc)	6.1 (4.9; 7.5)	6.1 (4.6; 7.7)	6.2 (4.7; 7.8)	0.772
HAQ score	Median (5; 95 perc)	1.5 (0.6; 2.5)	1.6 (0.5; 2.5)	1.8 (0.8; 2.5)	0.004

Table 1: Baseline patient characteristics

267 patients (15%) with other csDMARD (most commonly leflunomide) and 150 patients (9%) as monotherapy. The baseline disease activity based on the number of tender/swollen joints, CRP levels and DAS-28 scores was comparable between the three groups. There was a significantly higher number of patients without history of csDMARD therapy prior to TNFi initiation in the monotherapy group (Table 1). Overall TNFi drug survival was significantly better

in patients receiving MTX co-medication (median survival 53 months) compared to those on monotherapy (median survival 21 months). Patients receiving TNFi in combination with other csDMARD had median survival worse than those on methotrexate and better than those on monotherapy (median survival 36 months), albeit the difference was not statistically significant (Figure 1). The most common reason for TNFi discontinuation was loss of efficacy (33%, 37% and 28% for MTX, other csDMARD combination and monotherapy respectively) followed by primary inefficacy (20%, 19% and 27%) and adverse effects (19%, 15% and 23%).

Conclusion: In this registry study of patients with RA, use of MTX co-medication was associated with significantly better first TNFi drug survival compared to monotherapy.

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Abstract Number: 2401

Enhanced Methotrexate Polyglutamation in Japanese as Compared to Caucasian Rheumatoid Arthritis Patients Starting Methotrexate

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SESSION INFORMATION
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Background/Purpose: Methotrexate (MTX) is an anti-folate prodrug activated to MTX polyglutamates (MTXPGs). Japanese Rheumatoid Arthritis (RA) patients are thought to have heightened sensitivity to MTX and guidelines have recommended lower MTX doses in that group of patients as compared to Caucasians. We evaluated the impact of ancestry on the accumulation of MTXPG and the effect of these metabolites on disease control.

Methods: Two cohorts of consented adult RA patients naïve to MTX and scheduled to start oral MTX for their treatment were analyzed. All patients fulfilled the 1987 or 2010 ACR criteria for RA. The first cohort consisted of 48 Caucasians from New York State (73% females, mean age: 56±2 years, mean body mass index [BMI]: 28.6±0.1 kg/m^2). The second cohort consisted of 58 Japanese from the Tokyo metropolitan area (88% females, mean age 57±2 years, BMI=21.9±0.4 kg/m^2). MTX was started at 7.5-8 mg/weekly (with daily folic acid) and escalated every 4 weeks over 4 months, not to exceed 16 mg/week in Japanese RA. Accumulation of MTXPG metabolites was assessed using total red blood cells (RBCs) $MTXPG_{1-5}$ (1 to 5 order of glutamic residue) expressed as nmol/L packed RBCs. MTXPG were measured using liquid chromatography in a central laboratory. Serum transaminases were also collected. All clinicians were blinded to MTXPG levels during clinical assessments. Disease activity was assessed using Disease

	Estimate [SE]	P value
Intercept	-26.4±6.1	<0.001
Age per 10 years	2.9±1.0	0.004
MTX dose per mg weekly	5.4±0.2	<0.001
Per 100 days therapy	10.7±2.4	<0.001
Japanese Ancestry	**16.9±2.7**	**<0.001**

Table: Linear Mixed Effect models of RBC MTXPG1-5 accumulation (Marginal R^2= 0.71; N=467 visits collected in 106 patients)

Activity Score in 28 joints (DAS 28). Group comparisons used Wilcoxon's test. Linear mixed effect with random intercept and fixed slope were used to assess the impact of ancestry on MTXPG accumulation and the effect of these metabolites on disease control.

Results: After 3 months therapy similar MTX dosages were administered in the Japanese and Caucasian cohorts (mean 12±3 [SEM] and 12±2 mg/week, respectively; p=0.65). Japanese ancestry associated with higher RBC MTX-PG1-5 levels (mean 91±28 [SD] nmol/L) as compared to Caucasian ancestry (mean 61±24 nmol/L) (p< 0.01). This heightened RBC MTXPG1-5 accumulation among Japanese remained significant (estimate 16.9±2.7 nmol/L; p< 0.001) after adjusting for MTX dosage, age, duration of MTX therapy (Table) (Marginal R2=71%). Caucasian patients presented with higher DAS28 at baseline (5.1±0.1 points) than Japanese patients (3.5±0.1 points) (p< 0.001). Higher DAS28 at baseline associated with higher disease activity at follow-ups (estimate=0.66±0.04; Marginal R2=0.38). Heightened RBC MTXPG1-5 levels associated with lower DAS28 by univariate analysis (estimate=-1.6±0.1 point per 100 nmol/L; p< 0.001; Marginal R2=0.19) and the impact of the levels on disease control remained significant (estimate=-0.9±1.4 point per 100 nmol/L; p< 0.001) after adjusting for baseline DAS28 and duration of MTX therapy (Marginal R2=0.57). Higher RBC MTXPG1-5 accumulation also associated with elevated serum transaminases (estimate=4.8±0.1 and 10.0±1.9 units per 100 nmol/L MTXPG1-5 for AST and ALT, respectively) (Marginal R2=0.04 each) (p< 0.001).

Conclusion: MTXPG accumulation differs with ancestry. Japanese RA patients present with enhanced MTX polyglutamation as compared to Caucasians.

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Abstract Number: 2402

Which Factors Influence Achievement of Treatment Satisfaction in Rheumatoid Arthritis?

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Parameter	Odds Ratio	95% confidence limits
Satisfied at treatment start	**3.11**	**(2.66; 3.63)**
DAS28 reduction (one unit) after one year	**1.37**	**(1.30; 1.45)**
Reduction (one unit on a scale of 1-10) of pain after one year	**1.28**	**(1.23; 1.32)**
Reduction of sleeping problems (one unit on a scale of 1-10)	1.01	(0.99; 1.04)
Reduction of fatigue (one unit on a scale of 1-10)	1.00	(0.97; 1.03)
Improvement of physical function by 10 percentage points of full capacity	**1.19**	**(1.11; 1.27)**
Prior biologic therapy	**0.81**	**(0.68; 0.97)**
Reduction of glucocorticoid dose (one mg/d)	**1.42**	**(1.10; 1.90)**
Congestive heart failure	1.07	(0.62; 1.84)
Diabetes	0.96	(0.76; 1.22)
Chronic kidney disease	0.94	(0.63; 1.40)
Prior malignancies	1.09	(0.72; 1.64)
Degenerative spine disease	0.93	(0.76; 1.15)
Degenerative joint disease	0.94	(0.78; 1.13)
Osteoporosis	0.85	(0.68; 1.05)
Fibromyalgia	0.70	(0.48; 1.03)
Depression	**0.67**	**(0.52; 0.86)**
Obesity	**0.82**	**(0.70; 0.96)**
Age at disease onset (years)	1.00	(0.995; 1.01)
Men (reference: women)	1.07	(0.88; 1.30)
Seropositivity (RF/ACPA)	1.15	(0.98; 1.35)
Actual smoker (reference: non-smokers)	0.85	(0.71; 1.02)
Former smoker (reference: non-smokers)	0.96	(0.79; 1.18)
Smoking habits unknown (reference: non-smokers)	1.10	(0.78; 1.56)
Biologic therapy (reference: csDMARDs)	1.05	(0.87; 1.25)

Table 1: Results of logistic regression to analyze potential factors influencing satisfaction with drug treatment

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes
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Background/Purpose: The satisfaction of rheumatoid arthritis (RA) patients with their pharmacological therapy is a relevant patient reported outcome which influences treatment adherence and continuation. However, it has not been investigated frequently, and almost never in large studies. The aim of this study was to assess factors exerting a potential influence on the satisfaction with the pharmacological treatment and to quantify the strength of their association.

Methods: The German register RABBIT is a prospective longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one conventional synthetic (cs)DMARD failure. This analysis comprises patients who were enrolled with start of a DMARD between 01/2009 and 10/2018, who were observed for at least 12 months and had been on the therapy prescribed at enrolment for at least six months.

Satisfaction with the applied treatment was measured in four categories from “very satisfied” to “very unsatisfied”. Logistic regression combined with multiple imputation of missing values was performed to calculate odds ratios (ORs) for factors which might have an influence on treatment satisfaction.

Results: At treatment onset, 55% of the 8,677 patients were "very" or "rather" satisfied (in the following: "satisfied"), while the rest was "very" or "rather" unsatisfied (in the following: "unsatisfied") with their therapy. After one year of treatment, 86% of patients were satisfied with their treatment. Satisfaction at baseline, reduction of DAS28-ESR, pain and log glucocorticoid dose as well as the increase of physical function were positively associated with the achievement of treatment satisfaction after one year. Depression, obesity as well as a prior treatment failure of biologic (b) DMARDs were negatively associated with it (see Table 1). A prevalent fibromyalgia tends to have a negative effect as well. Regarding glucocorticoid therapy, being still treated with either 5 to 15 mg/d (OR: 0.69, 95% CI: 0.55; 0.85) or ≥ 15 mg/d glucocorticoids (OR: 0.27, 95% CI: 0.16; 0.44) was negatively associated with the achievement of therapy satisfaction (data not shown).

Conclusion: Reductions in disease activity, pain and glucocorticoid dosage as well as improvement of physical function present a positive association with the achievement of treatment satisfaction, while depression, obesity, and prior treatment failures with bDMARDs present a negative one. Our results show clearly that efforts to taper glucocorticoid doses are positively associated with the improvement of patients' satisfaction.

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Abstract Number: 2403

Adverse Events of Special Interest in Patients with Rheumatoid Arthritis Treated with Peficitinib in Asian Population: Pooled Safety Findings

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SESSION INFORMATION
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Background/Purpose: Peficitinib, a novel oral Janus kinase (JAK) inhibitor, has demonstrated efficacy in studies of Japanese, Korean and Taiwanese patients with RA. This analysis of pooled safety data examines new safety findings and incidence rates for AEs of special interest in studies.

Methods: Safety data from 4 clinical studies of adult patients with active RA defined by 1987 ACR criteria or 2010 ACR/EULAR criteria were pooled. The pooled Phase (Ph) 3 studies included safety data from the Asian Ph 3 study (RAJ3) and Japanese Ph 3 study (RAJ4). The pooled Ph 2/3 studies included Ph 2b study (RAJ1), RAJ3, RAJ4 and extension study (RAJ2 [data cut-off, May 31, 2018]). RAJ1 included RA patients irrespective of RA treatment history including untreated state. RAJ3 included RA patients with inadequate response to conventional DMARDs including MTX. RAJ4 included RA patients who were inadequate responders to MTX. RAJ2 is an open-label extension study of patients completing these 3 studies.

Table 1. Patient demographics for pooled studies

Demographic	Extension study, RAJ2 (N=843)			Total (N=843)	Pooled Phase 2/3 studies (N=1052)
	RAJ1 (n=201)	RAJ3 (n=225)	RAJ4 (n=417)		
Sex, n (%)					
Female	158 (78.6)	164 (72.9)	297 (71.2)	619 (73.4)	778 (74.0)
Age, years					
Mean (SD)	52.7 (11.3)	55.3 (12.7)	57.3 (11.4)	55.7 (11.9)	55.2 (11.8)
<65 (n, %)	168 (83.6)	160 (71.1)	295 (70.7)	623 (73.9)	799 (76.0)
Body weight, kg					
Mean (SD)	57.29 (12.02)	61.18 (12.57)	60.21 (13.34)	59.77 (12.90)	58.10 (12.37)
Region, n (%)					
Japan	201 (100)	188 (83.6)	417 (100)	806 (95.6)	997 (94.8)
Korea	0	19 (8.4)	0	19 (2.3)	31 (2.9)
Taiwan	0	18 (8.0)	0	18 (2.1)	24 (2.3)
Duration of disease, years					
Mean (SD)	7.30 (6.09)	8.71 (7.24)	4.26 (2.97)	6.17 (5.56)	6.36 (5.82)
Concomitant DMARD use, n (%)					
None	201 (100)	29 (12.9)	4 (1.0)	234 (27.8)	296 (28.1)
MTX	0	136 (60.4)	413 (99.0)	549 (65.1)	672 (63.9)
Other DMARD alone	0	60 (26.7)	0	60 (7.1)	84 (8.0)
Concomitant MTX dose (mg/week) n; mean (SD)	–	132; 10.67 (3.44)	405; 9.50 (3.07)	537; 9.79 (3.20)	667; 10.24 (3.05)
Concomitant steroid dose, n (%)					
None	87 (43.3)	130 (57.8)	215 (51.6)	432 (51.2)	498 (47.3)
0–5 mg/day	91 (45.3)	83 (36.9)	167 (40.0)	341 (40.5)	446 (42.4)
>5 mg/day	23 (11.4)	12 (5.3)	35 (8.4)	70 (8.3)	108 (10.3)
Duration of treatment (months)	41.6 (24.6)	17.9 (7.3)	16.2 (8.0)	22.7 (17.4)	26.07 (17.65)
Mean (SD)	51.1	18.4	15.3	18.2	24.7
Median	0.5–70.7	0.9–32.1	0.1–33.1	0.1–70.7	0.07–73.4
Min–Max					
Treatment exposure (patient-years)	707.8	340.2	567.4	1615.3	2336.3

Safety was assessed by monitoring adverse events (AEs) and serious adverse events (SAEs), and summarized using MedDRA Preferred Terms. Two pooled datasets (Ph 3 studies pooled and Ph 2/3 studies pooled) were used for the analyses.

Results: A total of 1052 patients were included in the pooled Ph 2 and 3 studies; of those patients, 843 were enrolled into RAJ2 (**Table 1**). Patient characteristics were similar across all treatment groups. Overall exposure to peficitinib in Ph 2/3 studies was 2336.3 patient-years. Across the 4 studies, there were 3 deaths.

In the pooled Ph 3 studies, there were no deaths. The overall incidence of AEs was similar between the 2 peficitinib groups (**Table 2**): 88.5% in the peficitinib 100 mg/day group, 87.7% in the peficitinib 150 mg/day group, and 89.0%

Table 2. Adverse events in pooled Phase 3 studies

Event	Peficitinib			Etanercept
	100 mg (n=278)	150 mg (n=276)	Combined (n=554)	(n=200)
AEs, n (%)	246 (88.5)	242 (87.7)	488 (88.1)	178 (89.0)
ADRs[1], n (%)	181 (65.1)	186 (67.4)	367 (66.2)	122 (61.0)
Deaths, n (%)	0	0	0	0
SAEs, n (%)	26 (9.4)	21 (7.6)	47 (8.5)	18 (9.0)
Serious ADRs, n (%)	13 (4.7)	11 (4.0)	24 (4.3)	9 (4.5)
≥Grade 3 AEs[2], n (%)	43 (15.5)	51 (18.5)	94 (17.0)	29 (14 5)
Discontinuations, n (%)				
AEs	26 (9.4)	18 (6.5)	44 (7.9)	13 (6.5)
ADRs	14 (5.0)	15 (5.4)	29 (5.2)	11 (5.5)
SAEs	12 (4.3)	6 (2.2)	18 (3.2)	5 (2.5)
Serious ADRs	7 (2.5)	4 (1.4)	11 (2.0)	4 (2.0)
AEs reported by ≥2% of patients in any treatment group (System Organ Class), n (%)				
Infections and infestations	164 (59.0)	163 (59.1)	327 (59.0)	112 (56.0)
Gastrointestinal disorders	80 (28.8)	88 (31.9)	168 (30.3)	43 (21.5)
Laboratory investigations	58 (20.9)	70 (25.4)	128 (23.1)	30 (15.0)
Musculoskeletal and connective tissue disorders	52 (18.7)	45 (16.3)	97 (17.5)	46 (23.0)
Respiratory, thoracic and mediastinal disorders	40 (14.4)	38 (13.8)	78 (14.1)	33 (16.5)
Injury, poisoning and procedural complications	38 (13.7)	27 (9.8)	65 (11.7)	21 (10.5)
Skin and subcutaneous tissue disorders	36 (12.9)	31 (11.2)	67 (12.1)	53 (26.5)
Nervous system disorders	22 (7.9)	37 (13.4)	59 (10.6)	21 (10.5)
Metabolism and nutrition disorders	22 (7.9)	27 (9.8)	49 (8.8)	15 (7.5)
Hepatobiliary disorders	21 (7.6)	27 (9.8)	48 (8.7)	16 (8.0)
General and administration site conditions	19 (6.8)	14 (5.1)	33 (6.0)	40 (20.0)
Vascular disorders	12 (4.3)	19 (6.9)	31 (5.6)	11 (5.5)
Ear and labyrinth disorders	7 (2.5)	9 (3.3)	16 (2.9)	4 (2.0)
Psychiatric disorders	6 (2.2)	4 (1.4)	10 (1.8)	6 (3.0)

[1]Adverse Drug Reactions, defined as AEs considered possibly or probably related to study drug by the investigator

[2]National Cancer Institute grading: grade 3, severe or medically significant; grade 4, life threatening; grade 5, death related to AE

ADR, adverse drug reaction; AE, adverse event; SAE, serious adverse event

in the etanercept (ETN) group. The incidence of SAEs was 9.4%, 7.6%, and 9.0%, respectively. In the peficitinib 100 mg/day group, 9.4% of patients discontinued due to an AE. The most common AE in patients receiving peficitinib was nasopharyngitis, which occurred in 30.5% of patients (31.0% in the ETN group).

Table 3. Adverse events of special interest in pooled studies, overall period. Exposure-adjusted incidence rates (incidence per 100 patient-years, 95% confidence intervals)

	Pooled Phase 3 studies				Pooled Phase 2/3 studies
	Peficitinib			Etanercept	
	100 mg	150 mg	Total		
Serious infection	2.8 (1.3, 5.9)	3.2 (1.6, 6.3)	2.9 (1.9, 4.6)	2.0 (0.8, 5.5)	2.5 (1.9, 3.2)
Herpes zoster-related disease	7.4 (4.7, 11.8)	4.0 (2.1, 7.4)	5.7 (4.2, 7.9)	2.6 (1.1, 6.2)	6.5 (5.5, 7.7)
Malignancies	1.2 (4.0, 3.7)	0	0.6 (0.2, 1.6)	0.5 (0.1, 3.6)	0.9 (0.6, 1.3)
Dyslipidemia	5.8 (3.4, 9.7)	9.8 (6.6, 14.7)	8.5 (6.5, 11.1)	2.6 (1.1, 6.2)	5.6 (4.6, 6.7)
Cardiovascular and cerebrovascular AEs	0.4 (0.1, 2.8)	0.4 (0.1, 2.8)	0.3 (0.1, 1.2)	1.0 (0.3, 4.1)	0.5 (0.3, 0.9)
Gastrointestinal disorder	2.8 (1.4, 5.9)	6.1 (3.7, 10.1)	5.1 (3.6, 7.2)	2.6 (1.1, 6.2)	3.3 (2.7, 4.2)
Anemia	2.0 (0.8, 4.8)	1.6 (0.6, 4.2)	1.7 (0.9, 3.0)	2.6 (1.1, 6.2)	1.1 (0.8, 1.7)
Neutropenia and lymphopenia	8.3 (5.3, 12.9)	5.2 (3.0, 8.9)	6.4 (4.7,8.7)	3.1 (1.4, 6.9)	3.7 (3.0, 4.6)
Hepatic impairment	11.4 (7.8, 16.7)	18.7 (13.9, 25.2)	14.8 (12.1, 18.2)	14.1 (9.6, 20.8)	7.3 (6.2, 8.5)
Renal impairment	3.7 (1.9, 7.0)	1.2 (0.4, 3.7)	2.6 (1.6, 4.2)	2.0 (0.8, 5.5)	1.4 (1.0, 1.9)
Muscle disorder	13.1 (9.2, 18.7)	15.7 (11.4, 21.6)	14.5 (11.8, 17.8)	7.4 (4.4, 12.5)	8.5 (7.3, 9.9)
Interstitial lung disease	0.4 (0.1, 2.8)	0	0.5 (0.1, 1.4)	2.0 (0.8, 5.4)	0.3 (0.1, 0.6)

AEs of special interest were defined as serious infections, tuberculosis, *Pneumocystis jurovecii* pneumonia, herpes zoster-related disease, virus reactivation, malignancies, non-melanoma skin cancer, malignant lymphoma, cardio- and cerebrovascular AEs, dyslipidemia, changes to QT interval, hypertension, gastrointestinal events, anemia, neutro- and lymphopenia, thrombocytopenia, hepatic or renal impairment, muscle disorder, and interstitial lung disease
AE, adverse event

Among AEs of special interest in the pooled Ph 3 studies, the incidence (95% CI) of serious infections was 2.9 (1.9, 4.6) in patients receiving peficitinib and 2.0 (0.8, 5.5) in those receiving ETN (**Table 3**). The incidence of herpes zoster-related disease was greater in peficitinib groups (5.7 [4.2, 7.9]) than in placebo (2.3 [0.6, 9.4]) or ETN groups (2.6 [1.1, 6.2]), and the overall incidence of malignancies (0.6 [0.2, 1.6]) was similar to that in the placebo and ETN groups (1.2 [0.2, 8.3] and 0.5 [0.1, 3.6], respectively).

Conclusion: This analysis provides an overview of safety across peficitinib clinical studies in patients with RA, and shows it is well tolerated with no major specific concerns with longer term administration of peficitinib.

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Abstract Number: 2404

Does Combined Therapy Affects Adherence in Rheumatoid Arthritis?

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SESSION INFORMATION
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Background/Purpose: Treatment adherence in Rheumatoid Arthritis (RA) patients vary from 30 to 80%. It is important to identify the associated factors to a low adherence, so clinicians can make interventions to obtain better therapeutic results. Adherence to treatment has been described to be affected by several factors, such as access to healthcare facilities, education, socioeconomic status, quality of communication between physician and patient, among others. REPAIR® is a software designed with the purpose of improve data collection and medical practice in our outpatient clinic. The aim of this study was to compare the adherence to synthetic Disease-Modifying Antirheumatic Drugs (DMARDs) among RA patients with monotherapy and combined therapy (two medications) in an open population.

Methods: Cross sectional, observational, comparative study. This study was conducted in rheumatology outpatient clinic of University Hospital in Monterrey, México. Consecutive patients with RA were approached during their rou-

Table No. 1

	Monotherapy (n=346)	Combined therapy (n=613)	p
Age (years), median (IQR)	54 (44-63)	53 (43-59)	0.018
Women, n (%)	317 (91.6)	575 (93.8)	0.362
Inadequate adherence to treatment, n (%)	52 (15)	102 (16.6)	0.514
Adequate adherence to treatment, n (%)	294 (85)	511 (83.4)	

Table No.2

	Monotherapy (n=346)	Combined therapy (n=613)
Medication used		
Methotrexate, n (%)	282 (81.5)	264 (43.1)
Leflunomide, n (%)	16 (4.6)	111 (18.1)
Sulfasalazine, n (%)	19 (5.5)	134 (21.9)
Hydroxychloroquine, n (%)	16 (4.6)	42 (6.9)
Chloroquine, n (%)	9 (2.6)	46 (7.5)
DMARDb, n (%)	2 (0.6)	11 (1.8)
Cyclophosphamide, n (%)	0 (0)	1 (0.2)
Mofetil mycophenolate, n (%)	0 (0)	1 (0.2)
Azathioprine, n (%)	0 (0)	2(0.3)
Inadequate Adherence Reasons		
Own Decision, n (%)	10 (20.4)	27 (29)
Economic, n (%)	17 (34.7)	22 (23.7)
Side Effects, n (%)	9 (18.4)	11 (11.8)
Lack of availability, n (%)	5 (10.2)	15 (16.1)
Forgetfulness of dose, n (%)	5 (10.2)	14 (15.1)
Other, n (%)	3 (6.1)	4 (4.3)

tine appointments, march 2018 to december 2018 period, were asked how many days of the last month they forgot or took their DMARDs (self-report). We classified the adherence rate in 2 categories based on the days of the last month they took the indicated medication; adequate: 75%-100% (> 21 days), inadequate < 75% (< 21 days). When adherence was inadequate we ask about the cause. Data was obtained from REPAIR ® (internal electronic patient record). The Kolmogorov-Smirnov test was used to determine normal distribution. Categorical variables are expressed as total number and percentage (%), and numerical variables as median and the 25th-75th percentiles (p25-p75). Chi square and Mann-Whitney U-test were used to compare groups and considered significant if $p< 0.05$. Data was analyzed with SPSS version 24.

Results: A total of 959 patients were included. When comparing adherence to treatment and gender between groups no statistically significant difference was found. The main cause of inadequate adherence in monotherapy group was economic (34.7%) and own decision in combined therapy group (29.1%).

Conclusion: Patients with combined therapy had the same percentage of adherence as patients with monotherapy. These results may indicate that number of drugs prescribed not necessarily affects adherence to treatment in RA patients. The principal causes for an inadequate adherence to treatment were: economic for monotherapy group and own decision for combined therapy group. However, long-term studies are needed to evaluate the persistence of treatment in these groups of patients.

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Abstract Number: 2405

Protein Biomarkers Predicting the Response to IFX+MTX+LEF Treatment in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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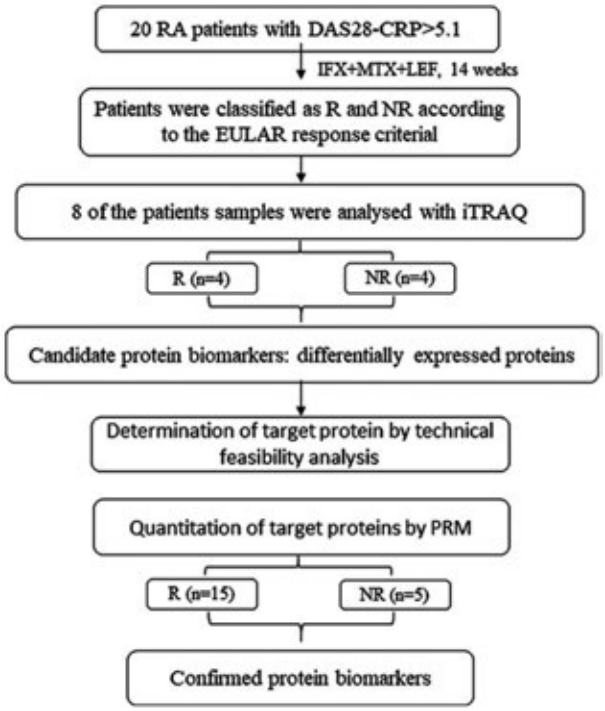
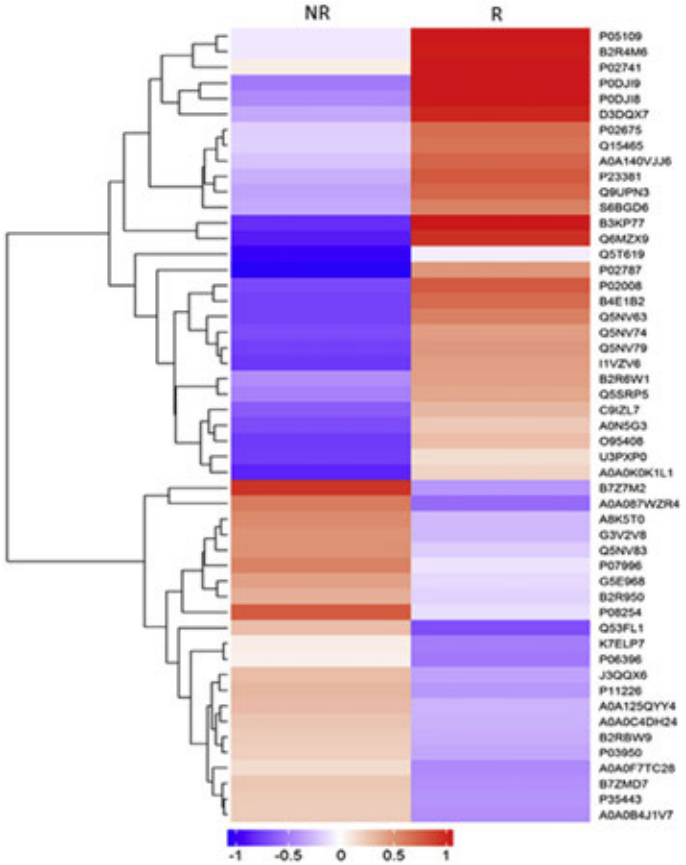
Background/Purpose: Patients with rheumatoid arthritis (RA) usually receive triple therapy with methotrexate (MTX), leflunomide (LEF) and infliximab (IFX), but nearly one-third of them do not respond to triple therapy. This study aimed to identify biomarkers for predicting the efficacy of triple therapy to optimize personalized treatment of RA.

Methods: All 20 enrolled patients met 2010 ACR/EULAR criteria for RA and were classified into good, moderate and non-responders (GR, MR, NR) for triple therapy. The Responders (R) were defined as the sum of GR and MR. Protein profiles of 4 responders and 4 non-responders were investigated via isobaric tags for relative and absolute quantification (iTRAQ), and differentially expressed proteins (DEPs) with high-confidence peptides were validated in 15 responders and 5 non-responders by parallel response monitoring (PRM).

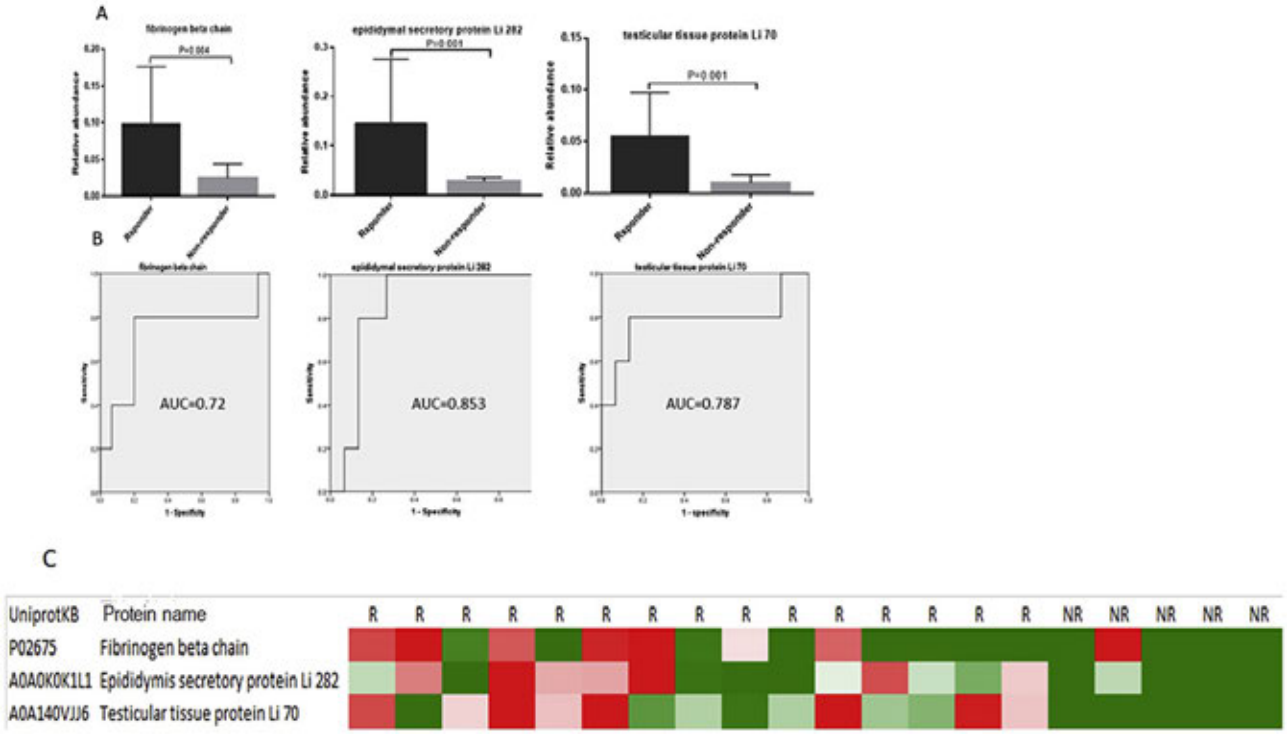
Results: iTRAQ identified 51 DEPs between responders and non-responders ($p < 0.05$, fold change $> \pm 1.2$).The top five up-regulated DEPs were B7Z7M2, A0A087WZR4, Q53FL1, P08254 and G3V2V8, while the top five down-regulated proteins were Q6MZX9, B3KP77, P0DJI9, P0DJI8 and P02787. Targeted mass spectrometry by PRM identified 10 candidate biomarkers, and 3 DEPs including fibrinogen beta chain, epididymal secretory protein Li 282 and testicular tissue protein Li 70 were confirmed as predictive biomarkers.



The workflow of proteomic analysis in this study. The study included candidate biomarkers discovering by iTRAQ and biomarkers confirmation by PRM. R, responders; NR, non-responders; iTRAQ, isobaric tags for relative and absolute quantification; PRM, parallel reaction monitoring



Hierarchical cluster of DEPs between R group and NR group, with folds > ±1.2 and P value <0.05. Rows represent the proteins and columns represent the group of patient. The relative expression level is indicated by the intensity of the color. Red, high expression; Blue, low expression. R, responder; NR, non-responder.



A) Comparison of 3 targeted DEPs. Fibrinogen beta chain, epididymal secretory protein Li 282 and testicular tissue protein Li 70 were up-regulated in R group as compared to NR group with $P < 0.05$. B) ROC curve of 3 targeted DEPs. AUC of the three predictive proteins was 0.720, 0.853 and 0.787, respectively. DEPs, Differentially expressed proteins; R, responder; NR, non-responder; ROC, relative operating characteristic. AUC, Area under the curve. C) Heatmap of 3 targeted DEPs in 15 responders (R) and 5 non-responders (NR). The color indicated the relative expression level. Green: 0.5; white: 1, and red: 2.

Conclusion: This study demonstrated the feasibility of exploring biomarkers by applying iTRAQ and PRM mass spectrometry techniques, and a panel of biomarkers were identified to predict clinical response of IFX+MTX+LEF treatment in active RA patients.

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Abstract Number: 2406

Hepatobiliary Events in >5000 Patients with Inflammatory Arthritis Treated with Biosimilar or Originator Etanercept in Routine Care, Results from the Danish Nationwide DANBIO Registry

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SESSION INFORMATION
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Background/Purpose: Marketing of biosimilar biological drugs may significantly reduce drug costs if comparable safety and efficacy of originator and the biosimilar can be documented. In a phase 3 randomized clinical trial, biosimilar SB4 treatment had a slightly higher occurrence of hepatobiliary adverse events compared with the originator etanercept (ETN) treatment (ref 1) - potentially explained by differences in patients' comorbid diseases and co-medication use (ref 2). In Denmark, biosimilars have high penetration due to a tender-based system with tax-paid biologics. Therefore, in April 2016, Danish patients with inflammatory rheumatic diseases were mandatorily switched from ETN to SB4 (=non-medical switch) (ref 3) and SB4 became the first choice for bio-naïve patients.

We aimed to explore the incidence rates (IRs) of hepatobiliary events during the first 6 months of routine care treatment with either ETN or SB4 among Danish adult patients with inflammatory rheumatic diseases.

Methods: Observational cohort study. Patients initiating treatment with ETN (Jan 2010-April 2016) or SB4 (April 2016-Feb 2018) were identified in the nationwide DANBIO registry. Among SB4 treated patients, the subgroup of non-medical switchers (i.e. had switched from ETN 0-90 days previously) was identified. Furthermore, patients could be either bDMARD-naïve or switchers from previous bDMARD treatment (other than ETN). Incident hospital contacts (hospitalizations or out-patient care) due to hepatobiliary events were identified through linkage to the national patient registry and included diseases of the liver, gallbladder and bile duct system. Age and gender standardized IRs per 100 person-years (PY) during 0-6 months since treatment start were assessed.

Results: A total of 5,738 patients (2,748 ETN/2,990 SB4) were included (Table 1). Among SB4-treated patients, 52% were non-medical switchers. Baseline characteristics were similar for bio-naïve patients who started SB4 or ETN and similarly for patients who had switched from other bDMARD. Non-medical switchers tended to have lower disease activity (Table 1).

During the first 6 months of treatment, 50 hepatobiliary events were identified, of which 23 were hospitalized (Table 2). IRs in all treatment groups were low with wide and overlapping confidence intervals. There was a tendency towards lover IR of hepatobiliary events among SB4 non-medical switchers.

Among the 50 patients with hepatobiliary events, 14 (28%) received concomitant methotrexate. Main events were gall-bladder stones (8 events), elevated transaminases (5 events), liver-cirrhosis (3 events) and pancreatitis (3 events).

Table 1. Baseline characteristics among ETN or SB4 treated patients stratified according to biological treatment history

Table 1	ETN			SB4			
	Bio-naïve (n=1,139)	Switch from other bDMARD (n=1,609)	Overall (n=2,748)	Bio-naïve (n=570)	Non-medical switch from ETN (n=1,540)	Switch from other bDMARD (n=880)	Overall (n=2,990)
Female, %	64.0 %	67.9 %	66.3 %	64.9 %	58.6 %	69.9 %	63.1 %
Age, years	52 (41-62)	53 (42- 62)	53 (41-62)	53 (39-63)	58 (47-68)	55 (43-64)	56 (44-66)
Diagnosis, %							
RA	53.2 %	51.0 %	51.9 %	60.9 %	55.4 %	58.4 %	57.3 %
PsA	27.5 %	20.9 %	23.6 %	15.4 %	22.3 %	14.8 %	18.8 %
AxSpA	19.3 %	28.2 %	24.5 %	23.7 %	22.3 %	26.8 %	23.9 %
Treatment start year, %							
2010 – 2013	92.3 %	77.8 %	83.8 %	0 %	0 %	0 %	0 %
2014 – March 2016	7.7 %	22.2 %	16.2 %	0 %	0 %	0 %	0 %
April 2016 – 2018	0 %	0 %	0 %	100 %	100 %	100 %	100 %
Concomitant MTX, %	49.8 %	45.7 %	47.6 %	42.5 %	48.8 %	43.4 %	46.0 %
Previous bDMARDs, n, %							
0	100 %	0 %	41.5 %	100 %	0 %	0 %	19.1 %
1	0 %	67.9 %	39.7 %	0 %	48.0 %	57.8 %	41.7 %
>1	0 %	32.1 %	18.8 %	0 %	52.0 %	42.2 %	39.2 %
CRP, mg/L	8 (3 – 19)	6 (2 – 16)	6 (2 – 17)	6 (2 – 16)	2.1 (1 – 5)	5 (2 – 14)	3 (1 – 10)
HAQ	1.1 (0.6-1.6)	1.3 (0.8-1.9)	1.3 (0.8-1.8)	1.0 (0.6-1.5)	0.6 (0.1-1.1)	1.1 (0.8-1.8)	0.9 (0.4-1.4)

Numbers are medians (IQR) unless otherwise stated.
Abbreviations: AxSpA: axial spondyloarthritis, CRP: C-reactive protein, ETN: originator etanercept, HAQ: health assessment questionnaire, MTX: methotrexate, PsA: psoriatic arthritis, RA: rheumatoid arthritis, SB4: biosimilar etanercept

Table 2 Crude and age and gender standardized incidence rates of hepatobiliary events per 100 PY 0-6 months after starting treatment with ETN or SB4, stratified by biological treatment history

Table 2		ETN		SB4		
	bDMARD treatment history	Bio-naïve (n=1,139)	Switch from other bDMARD (n=1,609)	Bio-naïve (n=570)	Non-medical switch from ETN (n=1,540)	Switch from other bDMARD (n=880)
	Person years	490.1	647.4	250.6	714.8	370.0
All events*	Number of events, N	10	17	6	6	11
	Crude IR/100 PY (95% CI)	2.04 (0.78, 3.30)	2.63 (1.38, 3.87)	2.39 (0.48, 4.31)	0.84 (0.17, 1.51)	2.97 (1.22, 4.73)
	Adjusted IR[§] (95% CI)	2.08 (0.79, 3.36)	2.58 (1.35, 3.81)	2.41 (0.48, 4.33)	0.84 (0.17, 1.52)	3.02 (1.23, 4.80)
Hospitalized events**	Number of events, N	4	9	4	3	3
	Crude IR/100 PY (95% CI)	0.82 (0.02, 1.62)	1.39 (0.48, 2.30)	1.60 (0.03, 3.16)	0.42 (0.00, 0.89)	0.81 0.00, 1.73)
	Adjusted IR[§] (95% CI)	0.82 (0.02, 1.62)	1.36 (0.47, 2.25)	1.62 (0.03, 3.21)	0.42 (0.00, 0.90)	0.81 (0.00, 1.72)

*Ambulatory care or hospitalized.
** Subgroup of all hepatobiliary events that were hospitalized
[§]Standardized for gender and age (age categories 18-45/46-60/61-95 years)
Abbreviations: IR: incidence rate, PY: person years

Conclusion: In this observational cohort study of >5,000 patients with inflammatory arthritis treated with originator or biosimilar etanercept in routine care, IRs of hepatobiliary events occurring during the first 6 months of treatment showed no apparent differences between the treatment groups.

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Abstract Number: 2407

The Safety Profile of Upadacitinib in Japanese Patients with Rheumatoid Arthritis

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Background/Purpose: Upadacitinib (UPA) is an oral reversible JAK inhibitor engineered for greater selectivity for JAK1 versus JAK2, JAK3, and TYK2, and is currently being assessed for the treatment of RA. Here we report on an integrated, long-term safety analysis of UPA in Japanese patients (pts) with RA from the UPA clinical development program.

Methods: Japanese pts were included from three studies: the Phase 2b/3 SELECT-SUNRISE study[1] (which only enrolled Japanese pts), and the Phase 3 SELECT-EARLY[2] and SELECT-MONOTHERAPY[3] studies (which included subsets of Japanese pts). In SELECT-SUNRISE, pts with an inadequate response (IR) to csDMARDs were randomized to receive UPA 7.5 mg, 15 mg, or 30 mg once daily (QD), or matching placebo (PBO), for 12 weeks in addition to background csDMARDs. In SELECT-EARLY, MTX-naïve pts received monotherapy with UPA 7.5 mg (Japan only), 15 mg, or 30 mg QD, or MTX, for 24 weeks. In SELECT-MONOTHERAPY, MTX-IR pts received monotherapy with UPA 15 mg or 30 mg QD, or continued with MTX monotherapy, for 14 weeks. Each study included the option to continue

Table. Safety profile of UPA in Japanese pts versus the global population

TEAE, events (E/100 PY)[a]	Japanese population			Global population	
	7.5 mg QD (n=121) (PY=171.2)	15 mg QD (n=126) (PY=176.3)	30 mg QD (n=124) (PY=154.7)	UPA 15 mg QD (n=2630) (PY=2655.1)	UPA 30 mg QD (n=1204) (PY=1365.0)
Any AE	645 (376.8)	627 (355.6)	797 (515.2)	7852 (295.7)	5033 (368.7)
Serious AE	28 (16.4)	29 (16.4)	38 (24.6)	399 (15.0)	291 (21.3)
AEs leading to discontinuation of study drug	14 (8.2)	16 (9.1)	24 (15.5)	224 (8.4)	182 (13.3)
Death	0	0	3 (1.9)	11 (0.4)	11 (0.8)
Infection	265 (154.8)	251 (142.4)	279 (180.3)	2487 (93.7)	1581 (115.8)
Serious infection	10 (5.8)	9 (5.1)	16 (10.3)	102 (3.8)	85 (6.2)
Opportunistic infection	2 (1.2)	4 (2.3)	17 (11.0)	17 (0.6)	24 (1.8)
Active/latent tuberculosis	0	1 (0.6)	1 (0.6)	58 (2.2)	21 (1.5)
Herpes zoster	14 (8.2)	25 (14.2)	33 (21.3)	99 (3.7)	96 (7.0)
NMSC	0	0	0	8 (0.3)	15 (1.1)
Malignancy other than NMSC	1 (0.6)	2 (1.1)	3 (1.9)	23 (0.9)	19 (1.4)
Lymphoma	0	0	1 (0.6)	1 (<0.1)	1 (<0.1)
Hepatic disorders	15 (8.8)	24 (13.6)	14 (9.0)	382 (14.4)	173 (12.7)
Gastrointestinal perforation	0	1 (0.6)	2 (1.3)	5 (0.2)	4 (0.3)
Anemia	4 (2.3)	3 (1.7)	13 (8.4)	121 (4.6)	79 (5.8)
Neutropenia	6 (3.5)	3 (1.7)	15 (9.7)	82 (3.1)	93 (6.8)
Lymphopenia	5 (2.9)	6 (3.4)	7 (4.5)	50 (1.9)	42 (3.1)
CPK elevation	8 (4.7)	17 (9.6)	29 (18.7)	163 (6.1)	170 (12.5)
Renal dysfunction	1 (0.6)	1 (0.6)	3 (1.9)	11 (0.4)	14 (1.0)
Adjudicated MACE[b]	1 (0.6)	0	2 (1.3)	17 (0.6)	13 (1.0)
Adjudicated VTE[c]	0	1 (0.6)	1 (0.6)	16 (0.6)	4 (0.3)

BID, twice daily; CPK, creatine phosphokinase MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer PBO, placebo; PY, pt-years; QD, once daily;
TEAE, treatment-emergent adverse event; UPA, upadacitinib
[a]AESIs were identified by a Standardized MedDRA query or Company MedDRA query; TEAEs were defined as any AE with an onset date on or after the first dose of study drug and no more than 30 days after the last dose of study drug if subject discontinued study drug prematurely
[b]Defined as cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke
[c]VTE, venous thromboembolism (pulmonary embolism or deep vein thrombosis)

into a long-term extension. The exposure adjusted event rates (EAERs) of adverse events (AEs) and AEs of special interest (AESI) per 100 pt-years (PY) are reported. Results in Japanese pts were compared with the global population in UPA Phase 3 studies.

Results: Japanese pts (n=371) received UPA 7.5 mg QD (n=121), 15 mg QD (n=126), or 30 mg QD (n=124). Exposure to UPA was 171.2, 176.3, and 154.7 PY in the 7.5 mg, 15 mg, and 30 mg groups, respectively, with mean exposures of 516.8, 511.0, and 455.5 days. The demographic characteristics of pts in all the treatment groups were generally well balanced; the majority of pts were female and aged between 40 and 64 years. Among the Japanese population, EAERs were consistently higher in the 30 mg group compared with the 15 mg and 7.5 mg groups (Table). EAERs in the 15 mg and 7.5 mg groups were comparable. In comparison with the global population, the EAER in the 15 mg

and 30 mg groups was higher in the Japanese population. The EAER of infections (including herpes zoster) was also higher in the Japanese population compared with the global population. The EAERs of AESI (including malignancies, cardiovascular disorders, hepatic disorders, and laboratory abnormalities) were comparable between the Japanese and global populations.

Conclusion: No new safety risks were identified with administration of UPA in Japanese pts. As reported with other JAK inhibitors, herpes zoster occurred at higher rates on UPA in Japanese pts versus the global population. The 7.5 mg and 15 mg doses had lower EAERs of overall AEs, infections and laboratory-related AEs compared to that observed with 30 mg.

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Abstract Number: 2408

A Prospective Analysis of Factors Impacting Medication Decision-Making in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments Poster III: Safety and Outcomes – ARP
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Prior research suggests that medication decision-making in rheumatoid arthritis (RA) patients is affected by disease activity, satisfaction with care, trust in their health care provider, and quality of patient-provider communication.(1-3) Because few studies have used quantitative methodologies to do such, we will describe changes in these key decision-making factors over time.

Methods: We collected data over 6 months (baseline, 1 week, 8 weeks, 16 weeks and 24 weeks) in a sample of 143 RA patient at one University health system. We measured medication adherence with the *Medication Adherence Report Scale-9RA*, a 9-item scale using a 5-point Likert scale (5 = *never* and 1 = *very often;* score range: 9 - 45; Cronbach's α =.77; test-retest reliability = .73).(4-6) Satisfaction with care was measured with the *Client Satisfaction Questionnaire-8,* an 8-item scale using a 4-point Likert-type scale where 4 indicates increased satisfaction (score range 8 – 32; Cronbach's α = .93). A significant correlation with client-reported symptoms supports scale validity.(7) Trust in provider was measured with the *Trust in Physician Scale* (TPS), an 11-item scale using a 5-point Likert scale (1 = *strongly disagree* – 5 *strongly agree;* Cronbach's α = .87).(8) The scale has significant negative correlations with measures of skepticism supporting scale validity.(8) Disease activity was measured with the *Routine Assessment of Patient Index Data 3* (RAPID3) on three domains: physical function, pain, and patient global assessment on a scale of 0 to 10 (range 0 - 30).(9, 10) The RAPID3 has been significantly correlated with other measures of disease activity.(9, 10) We used repeated measure mixed modeling and Friedman's test to describe the factors over time.

Table 1. Repeated measures modeling of key factors over time.

	Potential range	Baseline	1-week	8-weeks	16-weeks	24-weeks	p
Provider communication	20-80	76.58 (0.72)	75.46 (0.84)	73.70 (0.97)	73.69 (1.13)	73.52 (1.28)	**.034**
Trust in provider	0-100	87.43 (1.05)	85.50 (1.22)	82.97 (1.41)	84.13 (1.64)	80.74 (1.86)	**.012**
Satisfaction	8-32	30.13 (0.29)	29.67 (0.35)	29.06 (0.40)	29.25 (0.46)	28.03 (0.53)	**.008**
Medication adherence	9-45	43.18 (0.25)	43.02 (0.30)	43.82 (0.34)	43.81 (0.41)	42.80 (0.46)	.20
Perceived quality of patient communication							
Information verifying	1-7	6.48 (0.05)	6.41 (0.06)	6.40 (0.07)	6.47 (0.08)	6.40 (0.09)	.86
Information seeking	1-7	6.42 (0.07)	6.39 (0.08)	6.28 (0.09)	6.31 (0.11)	6.21 (0.12)	.50
Information giving	1-7	6.49 (0.05)	6.45 (0.06)	6.47 (0.07)	6.51 (0.08)	6.45 (0.09)	.97
Social-emotional	1-7	6.58 (0.06)	6.52 (0.66)	6.42 (0.08)	6.56 (0.09)	6.43 (0.10)	.44

Note: cells contains means and associated standard errors

Table 1. Prospective

Table 2. Disease activity over time.						
	Baseline (*n* = 133)	1 week (*n* = 96)	8 weeks (*n* = 72)	16 weeks (*n* = 53)	24 weeks (*n* = 42)	*P*
Remission	1 (1%)	1 (1%)	1 (1%)	0 (0%)	0 (0%)	.75
Low	2 (1%)	1 (1%)	2 (3%)	0 (0%)	2 (5%)	
Moderate	40 (30%)	30 (30%)	20 (28%)	18 (34%)	10 (24%)	
High	90 (68%)	64 (67%)	49 (68%)	35 (66%)	30 (71%)	

Note: Cells contain frequency and percent.

Table 2. Prospectivedocx

Results: We identified a significant decrease in the patient's perceived quality of provider communication (p=.034), trust in the provider (p=.012) and satisfaction with care over time (p=.008). We did not identify changes over time in medication adherence, any of the four subscales measuring the patient's perception of the quality of their communication with their health care provider, or disease activity overtime (Tables 1 and 2).

Conclusion: Despite stable medication adherence, disease activity did not change significantly over time. Although trust in the provider, satisfaction with care, and quality of provider communication scores were high, these values decreased over time suggesting that providers must make concerted efforts to maintain these key factors during the patient care experience.

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Disclosure: E. Salt, Pfizer, 2, Pfizer and IHI, 2; **A. Wiggins**, Pfizer and IHI, 2; **K. Lohr**, Pfizer and IHI, 2; **M. Rayens**, Pfizer, 2, Pfizer and IHI, 2.

Abstract Number: 2409

24-hour Activity Profiling in People Living with Arthritis: Habits Matter

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Research Methodology Poster – ARP
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Current practices promoting change in physical activity classify individuals as being more or less active. However, across 24-hours people spend time in different types of activities including sleeping. Variations in 24-hour activity may have implications for a person's health and well-being and may influence how a person responds to interventions that promote physical activity. The purpose of this study was twofold. First, we aimed to identify distinct 24-hour activity profiles in people with arthritis. Second, we explored individual characteristics and factors associated with those profiles.

Methods: A secondary analysis of baseline data from two ongoing randomized clinical trials studying the effect of physical activity counselling for people with knee osteoarthritis (OA), rheumatoid arthritis (RA), or systemic lupus erythematosus (SLE). 24-hour activity was measured by a Sensewear Mini worn for seven days. Participants completed an online survey for measures of demographics, occupation, depression (PHQ-9 Depression scale), and habitual sitting and walking behaviors (Self-reported Habit Index: SRHI). Activity profiles were identified using latent class analysis (LCA) to 24-hour activity data from individuals with 4 to 6 days (20+ hours) of wear. Data were stratified by minutes off body, sleeping, resting, sitting, and walking intermittently (< 50 steps / min) or purposefully (> 50 steps / min). Multiple logistic regression with backward elimination were used to identify factors predictive of cluster allocation relative to a reference cluster with the highest sitting reported as an Odds Ratio (95%CI). Predictive variables included age, sex, type of arthritis, depression score, usual occupation and home leisure sitting habit, and outdoor walking habit scores.

Results: In 172 individuals [mean age 58.1 years; 86% female; OA (30%), RA (49%), SLE (21%), mean daily steps 5990 (SD: 3234)] we identified four distinct 24-hour activity profiles relative to the cohort (Figure 1). These included: 1) **Balanced Activity** (n=40) [on average 9.4 hours of sitting, 5.2 hours of walking, 7.4 hours of sleep], 2) **High Sitting** (n=35) [on average 13.2 hours of sitting, 1.9 hours walking, 6.9 hours of sleep], 3) **High Sleeping** (n=45) [on average 10.4 hours sitting, 2.8 hours walking, 8.4 hours of sleep], and 4) **Low Sleeping** (n=52) [on average 12.2 hours of sitting and 3.9 hours of walking, 6.5 hours of sleep] (Table1). Age and self-reported occupational sitting and walking outside habits predicted activity profile; showing that relative to the high sitting cluster, participants in the other clusters were younger (OR: 0.95 to 0.98), had lower occupational sitting (OR: 0.56 to 0.74) and higher walking outside habits (OR: 1.09 to 1.43) (Table2).

Conclusion: Using objectively measured physical activity data, we identified four 24-hour activity profiles. Our findings suggest that some profiles such as individuals with high sitting may be prime targets for future physical activity promotion initiatives, particularly in individuals with strong habitual activity behaviors.

	Balanced Activity	High Sleeping	Low Sleeping	High Sitting
Number (#)	40	45	52	35
Age_Years (mean (SD))	54.9 (12.7)	55.2 (14.2)	60.5 (11.6)	61.8 (15.0)
Sex_Male (%)	12.5	13.3	7.7	22.9
Steps / day (mean (SD))	9378.5 (3085.9)	4229.1 (1422.7)	6706.0 (2618.1)	3317.3 (1738.9)
Arthritis Diagnosis (%)				
Osteoarthritis - Knee	37.5	24.4	28.8	28.6
Rheumatoid Arthritis	47.5	53.3	48.1	48.6
Systemic Lupus Erythematosus	15.0	22.3	23.0	22.9
Usual Occupation (%)				
Full-time employee	27.5	26.7	32.7	25.7
Self-employed	7.5	4.4	0	2.9
Part-time employee	12.5	6.7	17.3	8.6
Household work	25	17.8	13.5	14.3
Retired	20	24.4	19.2	40
Student	2.5	6.7	1.9	0
Volunteer	0	2.2	7.7	0
Other	5	11.1	7.7	8.6
Self-Reported Depression (PHQ-9: 0-27)				
Depression (mean (SD))	6.3 (6.0)	8.5 (5.9)	6.6 (4.9)	6.4 (5.2)
Self-Reported Habit (SRHI:1-7)				
Sitting Habit– Home Leisure (mean (SD))	4.3 (1.5)	4.8 (1.3)	4.7 (1.3)	5.3 (1.0)
Sitting Habit – Usual Occupation (mean (SD))	3.8 (1.8)	4.7 (1.8)	4.6 (1.6)	5.3 (1.4)
Walking Habit – Outside 10+ minutes (mean (SD)	4.5 (1.9)	3.7 (1.8)	4.4 (1.6)	3.6 (1.6)
Time in Activity – Wearable Activity Tracker (min / day)				
Off body (mean (SD))	25.4 (20.2)	29.3 (21.0)	25.0 (17.3)	25.2 (14.2)
Sleep (mean (SD))	445.8 (70.6)	504.3 (59.7)	387.4 (52.3)	415.5 (48.3)
Rest (mean (SD))	90.1 (47.1)	114.7 (63.0)	64.7 (27.0)	95.7 (38.2)
Non-Ambulatory (mean (SD))	563.3 (58.9)	625.0 (70.3)	730.4 (63.7)	790.5 (53.6)
Ambulatory - Intermittent (mean (SD))	266.0 (54.2)	147.1 (35.4)	196.4 (36.1)	94.5 (27.7)
Ambulatory - Purposeful (mean (SD))	49.5 (27.6)	19.7 (12.2)	36.0 (23.2)	18.6 (16.6)

LCA: Latent Class Analyses, PHQ-9: Patient Health Questionaire-9 Depression Scale, SRHI: Self-Reported Habit Index

Table 1: Participant Characteristics x 24-Hour Activity Profile (LCA cluster allocation)

Multivariable Logistic Regression: Backward Selection Method				
Effect	LCA Cluster Comparison	Point Estimate	95% Wald Confidence Limits	
Age (Years)	Balanced Activity	0.947	0.911	0.985
Age (Years)	High Sleeping	0.957	0.922	0.993
Age (Years)	Low Sleeping	0.983	0.948	1.02
Sitting Habit - Usual Occupation (1-7)	Balanced Activity	0.555	0.405	0.762
Sitting Habit - Usual Occupation (1-7)	High Sleeping	0.744	0.55	1.006
Sitting Habit - Usual Occupation (1-7)	Low Sleeping	0.744	0.552	1.003
Walking Habit - Outside 10+ minutes (1-7)	Balanced Activity	1.426	1.062	1.914
Walking Habit - Outside 10+ minutes (1-7)	High Sleeping	1.09	0.829	1.433
Walking Habit - Outside 10+ minutes (1-7)	Low Sleeping	1.366	1.043	1.788
Reference Group: High Sitting (Highest sitting & lowest walking time). Note: Factors excluded from the regression model were sex, type of arthritis, leisure time sitting habit, employment status and depression.				

Table 2: Prediction Factors x Cluster Allocation – Odds Ratio (95%CI)

Figure 1: 24-hour activity profile charts showing hours of time spent in different activities; lying down sleeping or resting (purple), non-ambulatory / sitting (yellow), ambulatory / walking (green) and off body (black). Comparing the cohort as a whole (n=172) to four distinct 24-hour activity profiles.

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Abstract Number: 2410

Using External Data to Estimate Omitted Variables in Observational Data: A Plasmode Simulation Study Investigating the Relationship Between Osteoarthritis and Cardiovascular Diseases to Compare Alternative Approaches in Imputing the Body Mass Index Variable

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Research Methodology Poster – ARP
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: BMI is a well-known confounding factor in the association between osteoarthritis (OA) and cardiovascular diseases (CVD). However, BMI is not usually recorded in administrative databases. When BMI is imputed using the proportion-based imputation (PBI) method, a BMI category is assigned to an individual according to the proportions observed in external data based on a set of pre-defined variables (1). Alternatively, standard Multiple Imputation (MI) methods can also be employed in the same situations. We investigated the OA-CVD relationship as a

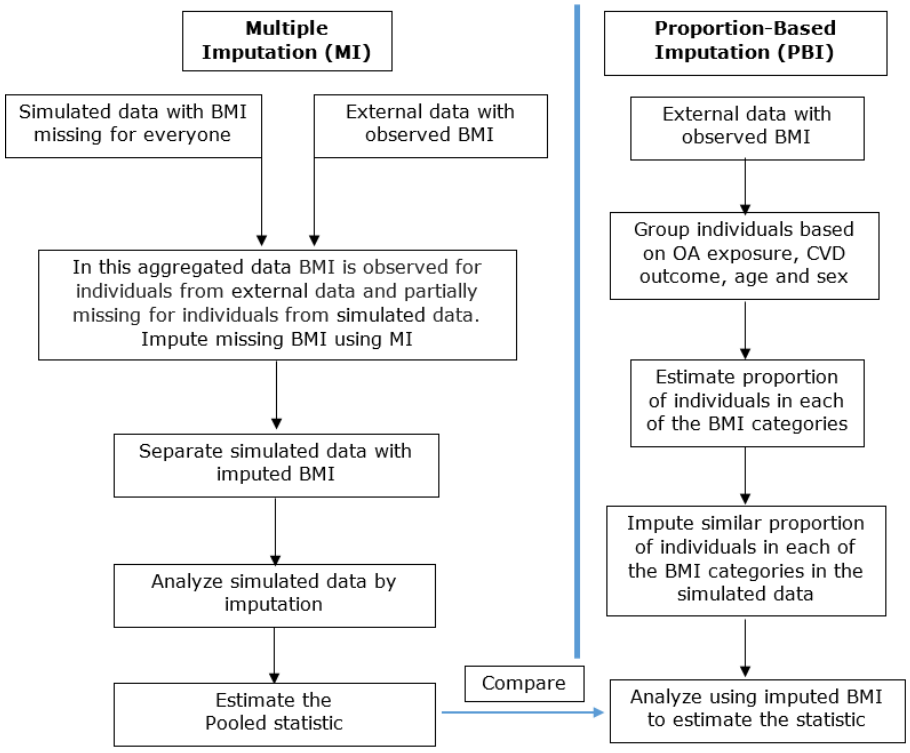

Figure 1: Conceptual framework to compare MI with PBI in imputing BMI variable missing for everyone in a study data using information from external database

Table 1: Description of various datasets used to compare multiple imputation approach with proportion-based imputation method in imputing BMI variable missing for everyone in a database

Dataset	Description	Number of individuals (N)	Comments
Data.1	Study dataset created from CCHS cycle 3.1 (2005)	84,452	All study variables are observed including BMI
Data.2	500 simulated datasets created from study dataset using plasmode simulation	75,000	All study variables are observed including BMI
Data.3	Copies of 500 simulated datasets	75,000	BMI is missing for everyone in the dataset. Other study variables are observed
Data.4	External data (compiled data from CCHS cycles 1.1 and 2.1)	149,810	All study variables are observed including BMI

demonstration to compare MI with PBI (figure 1). We hypothesized that BMI imputed using MI will minimize potential bias in the OA-CVD association compared to BMI categories imputed using PBI.

Methods: In this plasmode simulation study 500 simulated datasets were created using publicly available data from the Canadian Community Health Survey (CCHS) cycle 3.1. BMI was set missing for everyone in the simulated data. This mimics administrative data in which BMI is not recorded and missing for everyone in the database. A large dataset compiled from CCHS cycles 1.1 and 2.1 served as the external data in which BMI was observed for everyone. Table 1 summarizes the databases accessed. BMI missing in copies of simulated data was imputed using MI (with a number of imputations = 5) and PBI accessing observed BMI information in external data. To evaluate the performance of imputation methods, the distribution of the BMI variable and the adjusted odds ratio (aOR) estimated from the multivariable logistic regression model were compared. In this model, CVD outcome was regressed on OA exposure adjusting for age, sex, physical activity index, level of education, household income level, smoking status, diabetes, hypertension and BMI category. After analyzing the imputed datasets, the proportion of individuals in each of the four BMI categories and the ORs were averaged from the 500 simulated datasets. The 95% confidence interval (CI) of the averaged OR was calculated by the percentile method.

Results: Compared to PBI, MI produced proportions of individuals closer to the known proportions across the BMI categories except for the overweight category (Table 2). Considering the known aOR of 1.59 (1.36, 1.82), BMI imput-

Table 2: Comparison of proportion of individuals in each of the four BMI categories after imputing BMI for everyone in the simulated data with the BMI categories originally recorded by Statistics Canada in Canadian Community Health Survey cycle 3.1 (2005) data

BMI category	Data.1	Data.2	Data.3	
			BMI imputed using multiple imputation	BMI imputed using proportion-based imputation
Under weight	2.23	2.26	2.54	2.00
Normal weight	44.84	45.98	41.45	38.35
Over weight	35.12	34.93	38.66	34.77
Obese	17.81	16.83	17.34	24.87

ed using MI introduced less bias in OA-CVD association compared to PBI, the aOR was 1.62 (1.39, 1.86) and 1.66 (1.41, 1.90), respectively.

Conclusion: This is the first study to compare MI with PBI in the context of imputing BMI information that is not recorded at the database level. MI was superior to imputation method based on population-level proportions in imputing BMI missing for everyone in the simulated datasets. The generalizability of these methodological results will become more evident as more similar studies are undertaken in a variety of settings.

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Abstract Number: 2411

Casting a Wide Net: Comparing Strategies for Recruiting 18-35-year-olds with Rheumatic Disease as Study Participants

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Session Date: Tuesday, November 12, 2019
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Young adulthood is a unique life phase that spans 18-35 years, and is characterized by healthcare, educational, vocational and social transitions. Experiences in young adulthood can shape long-term health and socioeconomic outcomes. Yet, young adults with rheumatic conditions are a challenging population to recruit, and as a result are underrepresented in population health research. The objective of this study is to examine and compare recruitment strategies utilized in the construction of a large cohort of young adult participants with rheumatic disease.

Methods: Young adult participants with rheumatic conditions (e.g., juvenile arthritis, systemic lupus erythematosus, rheumatoid arthritis) were recruited as part of a three-year longitudinal study of transitional work experiences in Canada. A multifaceted recruitment strategy was utilized to construct a representative cohort including 1) rheumatology clinics in three provinces; 2) national community-based patient organizations; and 3) a representative panel from a survey research firm. Efforts were taken to recruit participants who varied in terms of disease severity to capture a breadth of experiences. Bivariate analyses (i.e., Chi-Square analysis and analysis of variance) were conducted to examine if participants differed based on sociodemographic (e.g., age, gender and hours worked) and health factors (e.g., pain, fatigue and disease activity) across the three recruitment approaches.

Results: A total of 412 young adult participants (mean age = 29 years ± 4.2) with rheumatic disease were successfully recruited and completed the baseline survey. A majority of participants had rheumatoid arthritis (36%) and juvenile arthritis (20%). Most participants were recruited using the research firm (75%) and community-based organizations (19%). Fewer participants were recruited through clinics (6%). Participants recruited from rheumatology clinics were younger (27 years ± 5.1) when compared to those recruited through community-based organizations (28.5 years ± 4.3) or the research firm (29 years ± 4.0) ($p < .01$). A greater proportion of participants recruited through community-based organizations were female (84%) compared to participants from rheumatology clinics (58%) or the research firm (42%) ($p < .001$). Participants recruited through community-based organizations reported less disease severity (e.g., pain, fatigue, disease activity and depression) and indicated more work hours compared to participants recruited from rheumatology clinics or research firm ($p < .001$).

Conclusion: A multifaceted approach can be effective in recruiting a large cohort of young adults with rheumatic disease. The use of community-based organizations and research firms have the potential to recruit large samples of young adult study participants beyond rheumatology clinics. Participants recruited through different approaches may vary in terms of sociodemographic and health factors and enable researchers to capture a diversity of experiences. The increased inclusion of young adult participants in population health research will offer a better understanding of the impact of rheumatic disease during a critical transitional life phase.

Disclosure: A. Jetha, None; **L. Tucker**, None; **J. Bowring**, None; **C. Backman**, None; **L. Proulx**, None; **V. Kristman**, None; **M. Gignac**, None.

Abstract Number: 2412

Use of Minimal Important Difference (MID) in Randomized Clinical Trials of Pain in Osteoarthritis

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Randomized Clinical Trial	Mean Difference in WOMAC Pain Change by Treatment Group	Proportion of Individuals Attaining Minimal Important Difference (MID)		
	Mean Difference in WOMAC Pain (95% CI)	Risk of MID in Treated (95% CI)	Risk of MID in Control (95% CI)	Risk Difference in MID (95% CI)
Vitamin D vs. Placebo	-1.6 (-7.1, 3.9)	0.31 (0.21, 0.42)	0.42 (0.30, 0.54)	-0.11 (-0.26, 0.05)
Intraarticular Corticosteroid vs. Saline Injection	2.2 (-4.1, 8.5)	0.51 (0.39, 0.64)	0.51 (0.39, 0.64)	0.00 (-0.17, 0.17)
Patellar Knee Brace vs. No Treatment	4.9 (-0.3, 10.3)	0.31 (0.30, 0.32)	0.12 (0.12, 0.13)	0.18 (0.17, 0.19)
Biomechanical Shoe vs. Sham Shoe	13.0 (9.0, 18.0)	0.87 (0.79, 0.92)	0.53 (0.44, 0.63)	0.33 (0.21, 0.44)

Values and 95% CI based on 5000 bootstrap samples.

WOMAC Pain on 0-100 scale, MID used is 12 points. Risk of MID is the proportion of subjects in the group attaining MID and ranges from 0 to 1.

All values adjusted for WOMAC pain at randomization and sex.

Table for Evaluation of MID for RCT of pain in OA v3
Mean Difference, Risk of MID, and Risk Difference Values in RCT

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Research Methodology Poster – ARP
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Minimal important differences (MID), based on within-subject evaluation of attaining an improvement in a continuous outcome such as a pain scale, are important for evaluating the magnitude of treatment effects in randomized clinical trials (RCT) in OA. While designed to assess whether an individual's improvement achieved a meaningful threshold, MID has often been used to gauge the between treatment-group mean difference in change in the outcome. We propose an alternate analysis, where each subject is evaluated for reaching the MID (yes/no) preserving the subject specific meaning of the MID and then the risk of MID is compared between groups, while allowing for adjustment for baseline values. We examine whether this alternative analysis approach provides complementary information to the between group treatment difference in change in pain.

Methods: As our pain measure, we used WOMAC pain on a 0-100 scale. We evaluated mean differences, and risk differences in subject attainment of MID in 4 completed RCT in knee osteoarthritis with treatment effects ranging from negative/null, to moderate, to strong. The difference between the value at randomization and the value at the end of treatment was the change in WOMAC pain. Based on a systematic review, a reduction of 12 (Devji T. *BMJ Open* 2017) was used for the MID. Adjusted between treatment group mean differences in change were estimated by analysis of covariance with the outcome of WOMAC pain at the end, by treatment, adjusting for WOMAC pain at baseline and sex. Adjusted risk differences in subject attainment of MID, by treatment, came from marginalized predicted probabilities generated by logistic regression using attainment of MID as the outcome, with treatment, WOMAC pain at baseline, and sex as predictors. 95% confidence intervals were generated by nonparametric bootstrap methods.

Results: Treatment group mean differences ranged from -1.6 to 13.0, and the risk differences ranged from -0.11 to 0.33 (see table). Only 1 RCT had a mean difference above the MID, yet all studies had substantial percentages of subjects with MID improvement. The direction and significance of the mean difference and risk difference results were usually, but not always, concordant. The risk difference analysis made it clear that the control risk for MID varies across RCT in ways that relate to the trial conditions but not necessarily to the treatment effect.

Conclusion: Rather than use the MID to evaluate between treatment group mean differences, we propose using the proportion of subjects attaining MID as a secondary outcome in an RCT evaluating a continuous measure. This preserves the meaning of the MID for which it was validated and allows identifying important information about the subject response to treatment and control in RCT that is not readily apparent from the mean difference.

Disclosure: L. Michael, None; **M. Parkes**, None; **D. White**, None; **S. Reichebach**, None; **T. McAlindon**, None; **D. Felson**, None.

Abstract Number: 2413

LOU064: A Highly Selective and Potent Covalent Oral BTK Inhibitor with Promising Pharmacodynamic Efficacy on B Cells for Sjoegren's Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Bruton's Tyrosine Kinase (BTK) is a cytoplasmic tyrosine kinase selectively expressed in B cells, macrophages, mast cells and basophils. The essential role of BTK in B cell antigen receptor and Fc receptor signaling is validated by human and mouse genetics, as well as by preclinical pharmacological intervention. BTK inhibition is expected to positively impact autoimmune diseases driven by autoreactive B cells and inflammatory immune-complexes, such as Sjoegren's Syndrome (SjS).

We report preclinical characteristics and selected clinical data of the highly selective BTK inhibitor LOU064 with a potential best in class profile for the therapy of SjS.

Methods: LOU064 was profiled in a series of *in vitro* assays for its effect on BTK dependent signaling, as well as in *in vivo* models for systemic B cell response and inflammation.

LOU064 was assessed in studies with healthy volunteers and asymptomatic atopic subjects. Single doses from 0.5 to 600 mg and multiple doses from 10 to 600 mg/day over 12 days were assessed with regard to safety, pharmacokinetics and pharmacodynamics.

Results: LOU064 potently inhibited *in vitro* BTK activity (IC50 range 0.6 to 1.3 nM) and showed excellent selectivity against 456 other kinases. At the cellular level, LOU064 showed potent inhibition of BTK dependent *in vitro* signaling in human blood B cells (IC50 18.3 nM) and basophils (IC50 66.5 nM), both clinically relevant target cells.

Consistent with covalent target binding, brief systemic LOU064 exposures were sufficient for full and sustained BTK occupancy and PD effects in several animal models. In an *in vivo* model for the inhibition of B cell dependent antibody formation in female rats LOU064 inhibited the IgM antibody response to sheep red blood cells by 96 % at a dose of 3 mg/kg. In the rat collagen induced arthritis model LOU064 induced fast and complete reduction of paw swelling and inhibited histological bone/cartilage erosion and inflammatory infiltrates at a dose of 3 mg/kg. The efficacy of LOU064 was dose proportional and correlated to BTK occupancy.

In healthy volunteer studies, oral LOU064 administration showed rapid absorption, with fast onset of action and sustained blood BTK occupancy starting from 30 mg. The *ex vivo* blood B cell activation marker CD69 was inhibited by 50% or more at doses of 30 mg and higher 24hrs post dose. All doses tested up to 600 mg daily for 12 days were

well tolerated, and no safety stopping criteria were met at any time. No SAEs or AEs leading to study discontinuation or dosing interruption occurred.

Conclusion: LOU064 is a novel covalent BTK inhibitor that showed excellent in vitro selectivity against relevant kinases and very high potency and efficacy in preclinical models of inflammation and B cell function with a very fast onset of action.

In healthy volunteers, LOU064 administration of single and repeated doses up to 600 mg were well tolerated. Short systemic exposure of LOU064 enabled full and sustained BTK occupancy and blood B cell inhibition.

These data make LOU064 a strong candidate for the treatment of chronic diseases driven by B cell autoimmunity and immune-complex mediated macrophage inflammation including SjS.

Disclosure: B. Cenni, Novartis Pharma AG, Switzerland, 1, 3; **P. End**, Novartis Pharma AG, Switzerland, 3; **M. Cabanski**, Novartis Pharma AG, Switzerland, 3; **A. Jakab**, Novartis Pharma AG, Switzerland, 3; **E. Funhoff**, Novartis Pharma AG, Switzerland, 3; **M. Kistowska**, Novartis Pharma AG, Switzerland, 3; **A. Kinhikar**, Novartis Pharma AG, Switzerland, 3; **A. Maiolica**, Novartis Pharma AG, Switzerland, 3; **M. Hirano**, Novartis Pharma, Japan, 3; **B. Nuesslein-Hildesheim**, Novartis Pharma AG, Switzerland, 3; **A. Littlewood-Evans**, Novartis Pharma AG, Switzerland, 3; **D. Angst**, Novartis Pharma AG, Switzerland, 3; **R. Pulz**, Novartis Pharma AG, Switzerland, 3; **M. Kaul**, Novartis Pharma AG, Switzerland, 3.

Abstract Number: 2414

Efficacy and Safety of Abatacept in Patients with Early Active Primary Sjögren's Syndrome – Open-label Extension Phase of a Randomized Controlled Phase III Trial

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

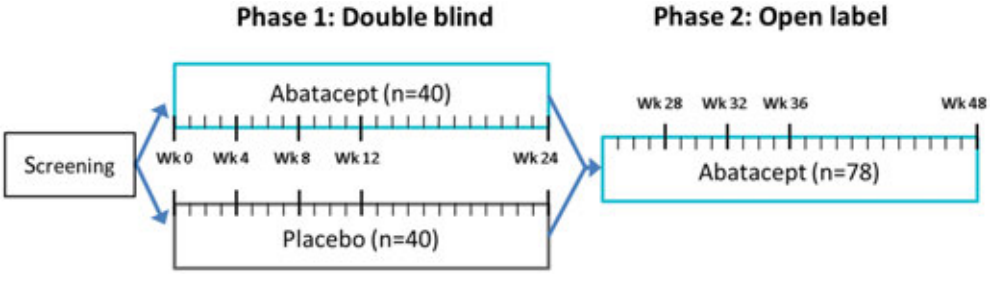

Figure 1: Design of the ASAPIII study.

Table 2: Patient characteristics at baseline and week 24 (start of extension phase)

	Baseline		Week 24	
	Abatacept n=40	Placebo n=40	Abatacept n=40	Placebo n=38*
Age at inclusion, years	48 (15)	49 (16)	NA	NA
Female, n (%)	37 (93)	37 (93)	NA	NA
Years since diagnosis	2 (0-4)	2 (1-4)	NA	NA
Anti-Ro/SSA positive	34 (85)	37 (93)	NA	NA
Previous DMARD use, n (%)	18 (45)	16 (40)	NA	NA
Current corticosteroid use, n (%)	0 (0)	1 (3)	0 (0)	2 (5)
ESSDAI	14.0 (9.0-16.8)	13.0 (8.0-18.0)	8.0 (4.0-14.0)	8.0 (5.0-14.5)
ESSDAI subdomains**, n (%)				
Constitutional	20 (50)	17 (43)	11 (28)	12 (32)
Lymphadenopathy	10 (25)	13 (33)	5 (13)	6 (16)
Glandular	36 (90)	37 (93)	22 (55)	22 (59)
Articular	23 (58)	24 (60)	11 (28)	14 (38)
Cutaneous	11 (28)	7 (18)	6 (15)	6 (16)
Pulmonary	3 (8)	2 (5)	3 (8)	2 (5)
Renal	0 (0)	0 (0)	0 (0)	0 (0)
Muscular	1 (3)	0 (0)	1 (3)	0 (0)
Peripheral nervous system	2 (5)	5 (13)	2 (5)	4 (11)
Central nervous system	0 (0)	0 (0)	0 (0)	0 (0)
Hematological	14 (35)	20 (50)	15 (38)	24 (65)
Biological	32 (80)	31 (78)	30 (75)	27 (73)
ESSPRI	7.0 (5.4-7.7)	7.3 (5.3-8.0)	6.0 (4.4-7.3)	6.7 (4.6-7.9)
EQ-5D-5L	0.71 (0.60-0.80)	0.71 (0.50-0.79)	0.74 (0.57-0.82)	0.75 (0.59-0.81)
UWS (ml/min)	0.05 (0.01-0.12)	0.05 (0.01-0.13)	0.06 (0.01-0.15)	0.04 (0.01-0.10)
SWS (ml/min)	0.16 (0.06-0.33)	0.10 (0.02-0.43)	0.20 (0.08-0.43)	0.10 (0.03-0.29)
OSS***	4.0 (0.5-6.5)	4.5 (2.0-7.0)	3.0 (1.0-6.4)	3.5 (1.3-7.3)
Schirmer*** (mm/5min)	3.5 (0.6-14.0)	2.5 (0.0-8.5)	5.3 (2.1-10.3)	1.0 (0.0-4.0)
IgG (g/L)	17.4 (13.4-26.7)	18.7 (14.8-24.7)	17.0 (12.9-26.0)	19.0 (13.7-25.5)
RF (IU/ml)	32.5 (2.1-71.0)	24.0 (6.8-83.0)	17.5 (1.7-42.0)	29.0 (8.0-90.0)

Values are median (25th percentile-75th percentile) or mean (SD) unless otherwise indicated.
* n=37 for efficacy outcomes of week 24, as efficacy data from one patient was excluded due to use of corticosteroid rescue therapy.
** Number of patients with activity in ESSDAI subdomains (including low, moderate or high activity).
*** Average of left and right eye. NA = Not applicable.

Background/Purpose: Abatacept (CTLA-4-Ig) targets the CD80/CD86:CD28 co-stimulatory pathway required for full T-cell activation and T-cell dependent activation of B-cells. The Abatacept Sjögren Active Patients phase III (ASAPIII) trial assessed the efficacy and safety of treatment with subcutaneous abatacept in patients with early active primary Sjögren's syndrome (pSS). In the double blind phase, no difference was found in the primary endpoint, EULAR Sjögren's syndrome disease activity score (ESSDAI) after 24 weeks, but a higher number of patients receiving abatacept reached the minimal clinically important change in EULAR Sjögren Syndrome Patient Reported Index (ESSPRI). B-cell hyperactivity was decreased by abatacept. The aim of the current analysis is to evaluate efficacy and safety of extended treatment with abatacept after 48 weeks.

Methods: The ASAP-III study is a monocenter, investigator-initiated, double-blind, placebo-controlled trial with an open label extension phase (NCT02067910). ASAP-III included 80 adult patients with biopsy-proven pSS, fulfilling the AECG and ACR/EULAR criteria, with a disease duration of ≤7 years and moderate to high (ESSDAI ≥5).

After receiving weekly subcutaneous injections with abatacept (125 mg) or placebo for 24 weeks, all patients were treated with abatacept for another 24 weeks (figure 1). Concomitant use of other DMARDs including hydroxychloroquine was not permitted, with the exception of a stable dose of prednisone (≤10mg), and rescue therapy with prednisone or cyclophosphamide. At each visit (see figure 1), participants were evaluated by a multidisciplinary team of rheumatologists, ophthalmologists, and oral and maxillofacial surgeons. The primary endpoint was ESSDAI at 24 weeks. Secondary outcomes at 24 and 48 weeks included clinical, patient reported, functional, histological, laboratory, ultrasound, and microbiome parameters, and the occurrence of (serious) adverse events and treatment discontinuation.

Results: Patient characteristics at baseline and in week 24 are shown in table 1. Of 80 included patients, 78 were included in the extension phase. Two patients from the placebo arm were lost to follow up before week 24. Database lock for the extension phase is planned in September 2019. Subsequently, the first analyses of the week 24-48 results will be performed, focusing on ESSDAI, ESSPRI, quality of life (EQ-5D-5L), unstimulated and stimulated whole salivary flow (UWS, SWS), Schirmer's test, Ocular Staining Score (OSS), serological parameters (rheumatoid factor, IgG), and safety parameters.

Conclusion: The ASAP-III trial was designed to assess the clinical efficacy and safety of subcutaneous abatacept in pSS patients with short disease duration and active disease. Results of week 24-48, the open-label extension phase, are available at the ACR 2019 annual meeting.

Disclosure: J. van Nimwegen, Bristol-Myers Squibb, 5, 8; **E. Mossel**, None; **R. Wijnsma**, None; **G. van Zuiden**, Roche, 8; **K. Delli**, None; **A. Stel**, None; **B. van der vegt**, None; **E. Haacke**, None; **L. Olie**, None; **L. Los**, None; **G. Verstappen**, None; **S. Pringle**, None; **F. Spijkervet**, None; **F. Kroese**, Bristol-Myers Squibb, 2, 5, 8, Janssen-Cilag, 8, Roche, 8; **A. Vissink**, None; **S. Arends**, None; **H. Bootsma**, Bristol-Myers Squibb, 2, 5, 8, GlaxoSmithKline, 2, 5, HarmonicSS, 2, MedImmune, 2, 5, Medimmune, 5, Novartis, 5, 8, Roche, 2, 5, UCB, 2, 5, Union Chimique Belge, 5.

Abstract Number: 2415

Evaluation of Pharmacokinetics and Immunogenicity Following Subcutaneous Administration of Abatacept in Primary Sjogren 's Syndrome (pSS) and RA Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Abatacept (ABA) has proven efficacy in autoimmune diseases and is being evaluated in pSS. The purpose of this investigation was to evaluate the pharmacokinetics (PK) and immunogenicity (IM) of subcutaneous (SC) ABA in pSS and RA patients.

Methods: One hundred eighty eight subjects diagnosed with active, moderate to severe pSS who meet the 2016 ACR/EULAR Classification Criteria for pSS and have a ESSDAI disease activity score of at least 5 at screening and are refractory to symptomatic or local therapy (e.g., NSAIDs) were randomized 1:1 to 125 mg SC weekly ABA (95

Table 1. Abatacept Cmin (GM [%CV]) in pSS and RA patients

Disease	Day 15	Day 29	Day 43	Day 57	Day 85	Day 113	Day 141	Day 169
RA	11.2 (44)	15.6 (48)	18.1 (47)	21.7 (47)	20.4 (41)	23.7 (52)		
pSS	15.0 (31.3)	21.4 (36.0)		22.4 (43.0)	27.5 (38.4)	25.5 (42.1)	25.8 (40.8)	24.5 (42.7)

subjects) or placebo (92 subjects) in a double-blind, 24-week, placebo-controlled study (NCT02915159, IM101603) [Ref. 1].

ABA trough (Cmin) samples were collected in all subjects during the treatment window of 365 days and semi-intensive PK samples were collected in a subset of subjects during the first 85 days. Serum ABA concentrations and anti-drug antibodies (ADA) were measured using a validated enzyme immunoassay method and an electrochemiluminescence assay, respectively.

Graphical analyses evaluated the PK profile and Cmin of ABA in pSS and compared to the ACCOMPANY study (IM101173) in RA patients [Ref. 2]. IM101173 was a 4-month open-label Phase 3b study to evaluate the immunogenicity and safety of SC ABA administered 125 mg weekly in the absence of an IV loading dose, when given as monotherapy versus with concomitant MTX, and to assess whether the use of concomitant MTX influenced the development of immunogenicity in RA patients with inadequate response to MTX.

Immunogenicity incidence rates were also summarized in the pSS and RA populations.

Results: Geometric mean (GM) Cmin values in pSS patients of > 15 μg/mL were achieved by Day 15 and remain greater than the threshold of 10 μg/mL that is associated with near maximal efficacy response established in RA patients across all body weights who receive the weekly 125 mg SC dosing (Table 1). ABA GM (%CV) Cmin values at steady state (Day 85) were comparable in pSS (27.5 [38.4%] μg/mL) and RA (20.4 [41%] μg/mL) patients.

During the 168-day blinded period, 1 (1.1%, n=90) subject with pSS had a positive antibody response specific to CTLA4 and possibly Ig relative to baseline while on-treatment. During the 4-month open label period, the overall immunogenicity rate was 4.1% (2/49) in RA subjects.

Conclusion: Subcutaneous administration of ABA 125 mg weekly in pSS achieved consistent target steady state trough concentrations to that observed in RA and shown to be efficacious in RA [Ref 3]. SC abatacept elicited minimal immunogenicity and was associated with no effect on PK or safety in either pSS or RA patients.

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Disclosure: Y. Gandhi, Bristol-Myers Squibb, 1, 3, 4, CSL Behring, 3, 4; **M. Shaikh**, Bristol-Myers Squibb, 3; **B. Vakkalagadda**, Allergan, 3, 4, Bristol-Myers Squibb, 3, 4; **G. Abelian**, Bristol-Myers Squibb, 3; **N. Ray**, Bristol-Myers Squibb, 1, 3; **R. Wong**, Bristol-Myers Squibb, 3, 4; **B. Murthy**, Bristol-Myers Squibb, 1, 3.

Abstract Number: 2416

ALPN-101, a First-in-Class Dual ICOS/CD28 Antagonist, Suppresses Key Effector Mechanisms Associated with Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: ALPN-101 is an Fc fusion protein of a human inducible T cell costimulator ligand (ICOSL) variant immunoglobulin domain (vIgD™) designed to inhibit simultaneously the CD28 and ICOS costimulatory pathways. CD28 and ICOS each play a role in T cell activation and adaptive immunity which can contribute to autoimmune disease when dysregulated. ALPN-101 has previously been shown to have potent immunosuppressive activity in various *in vitro* and *in vivo* models of disease, including acute graft versus host disease, inflammatory arthritis, and multiple sclerosis. We report here *in vitro* assays using PBMC from healthy donors vs. patients to analyze human T cell and B cell activation and suppression of antibodies and inflammatory mediators thought to contribute

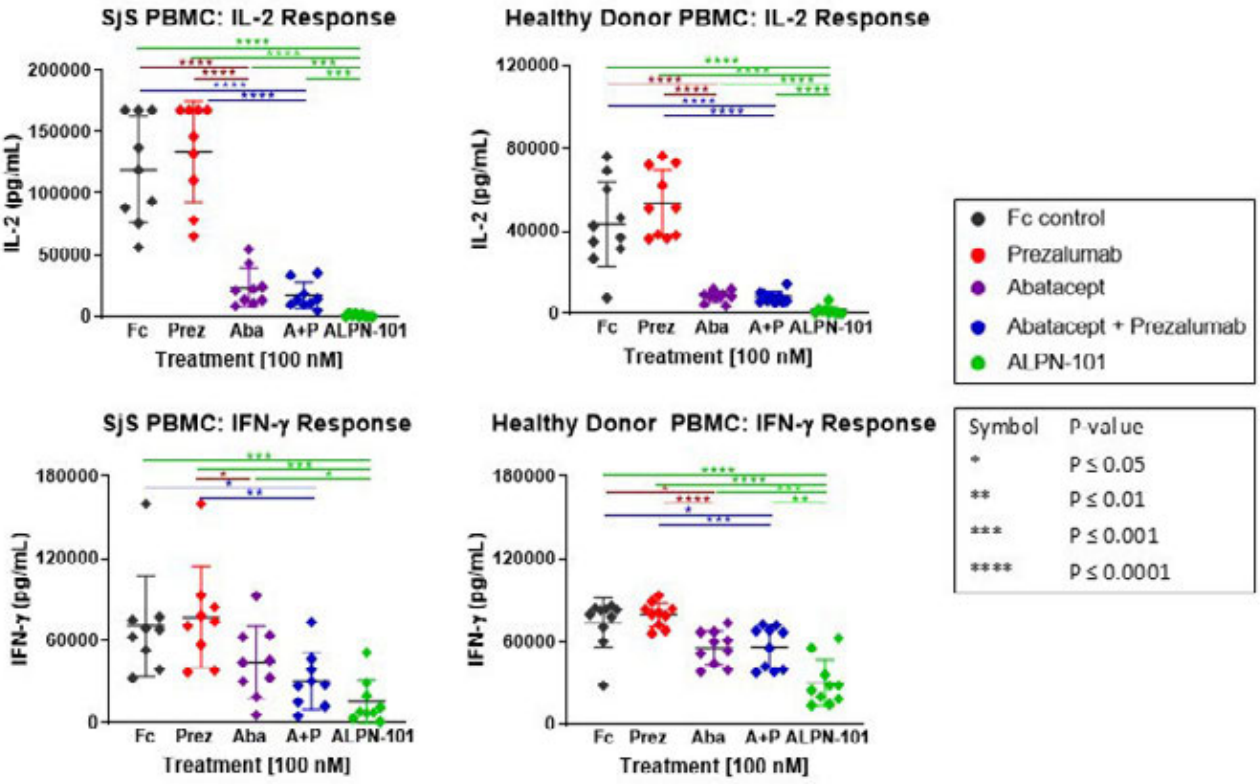

Figure 1: ALPN-101 Potently Inhibits T Cell Activation In Vitro in PBMC from Healthy Donors and Sjogren's Syndrome Patients. In vitro stimulation of healthy donor and Sjogren's syndrome (SjS) patient PBMC with artificial APC [fixed K562 expressing cell surface OKT3 (anti-CD3)/CD80/ CD86/ICOSL)] at a 20:1 ratio. Test articles were added at 100 nM and supernatants were collected and assayed for cytokine concentrations after a 48 hr incubation. ALPN-101 demonstrated statistically significant superiority to prezalumab, abatacept, or a combination of prezalumab+abatacept for the majority of donors and analytes tested.

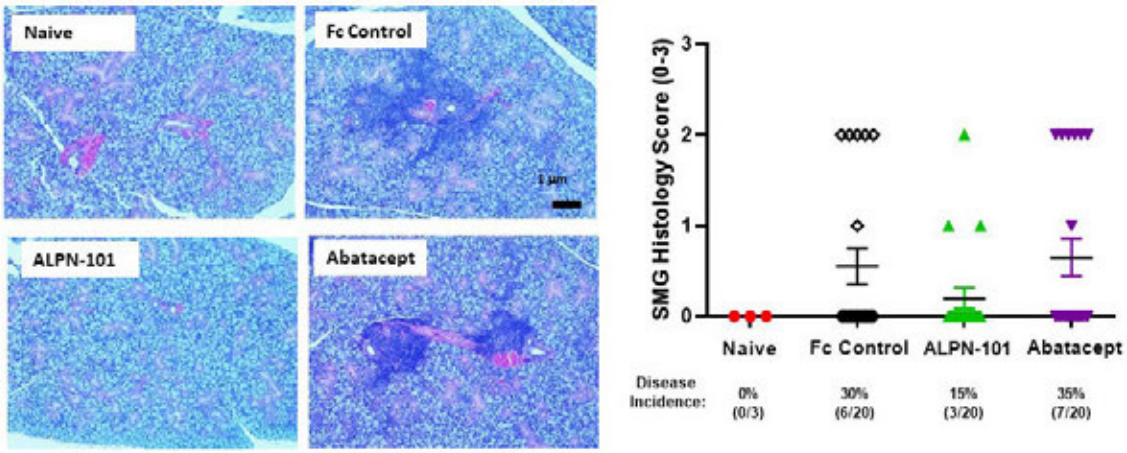

Figure 2: ALPN-101 Inhibits Sialadenitis in the NOD x Anti-PD-L1 Mouse Model of Sjogren's Syndrome. Six-week old female NOD/ShiLtJ mice were treated IP with a blocking anti-mouse PD-L1 antibody (to induce inflammation in the salivary glands, as described in Zhou et al., 2016, Sci. Rep. 6:39105) along with Fc control, abatacept, or ALPN-101 test articles on days 0, 2, 4, and 6. On Day 8, submandibular glands (SMG) were collected, sectioned, and stained with H&E and scored for inflammation on a scale of 0-3.

to the pathogenesis of Sjögren's syndrome (SjS) and other connective tissue diseases. Additionally, the efficacy of ALPN-101 was confirmed *in vivo* in mouse immunization models, and in a mouse model of SjS.

Methods: Primary cell assays were performed with healthy donor and SjS patient PBMC stimulated with K562 cells expressing CD80, CD86, ICOSL, and anti-CD3 (OKT3) to evaluate the potency of ALPN-101 to suppress cytokine production. The activity of dual pathway inhibition by ALPN-101 was compared to the CD28-only inhibitor abatacept (CTLA-4-Fc) and to the ICOS pathway inhibitor prezalumab (AMG-557; anti-ICOSL, Creative Biolabs). ALPN-101 was compared to abatacept *in vivo* in standard mouse immunization models (KLH, sheep RBC), and in a model of SjS involving anti-PD-L1 antibody-mediated acceleration of sialadenitis in NOD mice.

Results: Compared to abatacept, prezalumab, or combination abatacept + prezalumab, ALPN-101 demonstrated superior suppression of pro-inflammatory cytokine (i.e. TNF-α, IFN-γ, IL-1β, IL-2, IL-6, IL-17A, GM-CSF, etc.) release from stimulated healthy or SjS patient PBMCs (Fig. 1). ALPN-101 treatment inhibited antibody production *in vivo* in mouse immunization models, and suppressed proliferation and antibody production in human B cell/T cell co-cultures. In anti-PD-L1-treated NOD mice, ALPN-101 suppressed sialadenitis with activity superior to abatacept (Fig. 2); analyses of SjS-related autoantibodies are underway.

Conclusion: The efficacy of dual CD28/ICOS antagonist ALPN-101 is superior to CD28 or ICOS costimulatory pathway inhibitors, administered individually or in combination, in human *in vitro* and/or mouse *in vivo* translational studies. A Phase 1 clinical trial with ALPN-101 in healthy volunteers is underway, in preparation for future trials in multiple autoimmune diseases.

Disclosure: S. Dillon, Alpine Immune Sciences, 1, 3, 4; **L. Evans**, Alpine Immune Sciences, 1, 3, 4; **K. Lewis**, Alpine Immune Sciences, 1, 3, 4; **S. Bort**, Alpine Immune Sciences, 1, 3, 4; **E. Rickel**, Alpine Immune Sciences, 1, 3, 4; **J. Yang**, Alpine Immune Sciences, 1, 3, 4; **M. Wolfson**, Alpine Immune Sciences, 1, 3, 4; **K. Susmilch**, Alpine Immune Sciences, 1, 3, 4; **S. Mudri**, Alpine Immune Sciences, 1, 3, 4; **S. Levin**, Alpine Immune Sciences, 1, 2, 3, 4; **J. Bhandari**, Alpine Immune Sciences, 1, 3, 4; **F. Ahmed-Qadri**, Alpine Immune Sciences, 3; **M. Rixon**, Alpine Immune Sciences, 1, 3, 4; **J. Hillson**, Alpine Immune Sciences, 1, 3, 4; **S. Peng**, Alpine Immune Sciences, 1, 3, 4, 6; **K. Swiderek**, Alpine Immune Sciences, 1, 3, 4.

Abstract Number: 2417

A Phase 2a Study of MEDI5872 (AMG557), a Fully Human Anti-ICOS Ligand Monoclonal Antibody in Patients with Primary Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The interaction of inducible T cell costimulatory ligand (ICOSL) and the ICOS receptor is key in the pathogenesis of primary Sjögren's syndrome (pSS). MEDI5872 interferes with this pathway by binding to ICOSL. We evaluated the safety and efficacy of MEDI5872 in patients (pts) with pSS.

Methods: We conducted a Phase 2a, randomized, placebo (PBO)-controlled study (NCT02334306) in pts with active pSS (according to American-European Consensus Group criteria for pSS) and active disease defined by EULAR Sjögren's syndrome disease activity index (ESSDAI) ≥6 and markers of B-cell hyperactivity (target enrollment N=42). Pts were randomized (1:1) to MEDI5872 210 mg or PBO subcutaneously (SC) once weekly for 3 weeks, then every 2 weeks for 9 weeks. Beginning on Day 99, all pts received MEDI5872 210 mg for an additional 12 weeks "open-label period" (OLP). The primary endpoint was mean change in ESSDAI score from baseline to Day 99. Secondary endpoints at Day 99 included: proportion of ESSDAI responders (≥3 points decrease in ESSDAI, no discontinuation of investigational product and no use of prohibited medications); changes in ESS patient reported index (ESSPRI) score from baseline; and biomarker endpoints (including changes in plasma cells [PC] and T-follicular helper [Tfh] cells in the peripheral blood [PB] and minor salivary glands [MSG], and changes in MSG biopsy focus score). Duration of response was assessed during the OLP. P-values were not adjusted for multiplicity; P< 0.1 was considered statistically significant.

Results: Baseline characteristics were similar between the MEDI5872 (n=16) and PBO (n=16) arms (enrollment stopped early due to slow recruitment). Mean (SD) ESSDAI score was 11.8 (5.4) and 11.6 (4.5); and mean (SD) ESSPRI score was 6.5 (2.2) and 6.4 (1.8) for MEDI5872 and PBO, respectively. At Day 99 mean (SE) ESSDAI score decreased by 3.8 (0.9) and 2.3 (0.8) with MEDI5872 and PBO, respectively (adjusted mean difference (SE) of –1.4 (1.3), P=0.262). ESSDAI responder criteria were met by 7/16 and 4/16 patients in the MEDI5872 vs. PBO groups, respectively (P=0.458). Two patients in the PBO group had ≥3 points decrease in ESSDAI but were considered non-responders due to drop-out or use of prohibited medication. No other clinical efficacy measurement or PRO showed significant improvement at Day 99. No further improvement was noticed past Day 99 during the OLP.

On MSG biopsies at Day 99, CD4+/ICOS Tfh-like cells decreased from baseline with MEDI5872 and increased from baseline in the PBO group (geometric mean ratio to baseline (SE), MEDI5872 vs. PBO: 0.75 (0.18) vs. 1.76 (0.21), P=0.008). There was no difference in change from baseline in total PC or PD1/ICOS+ Tfh-like cells. No statistically significant differences were observed in PBPC and Tfh cell levels in the blood. IgA, IgG and IgM rheumatoid factor

(RF) levels decreased with MEDI5872 but not with PBO; the difference compared to PBO was statistically significant at Day 99. Adverse event rates were balanced: 11 pts (68.8%) with MEDI5872 vs. 14 pts (87.5%) with PBO experienced ≥1.

Conclusion: In patients with active pSS, despite decreasing the level of RF, MEDI5872 210 mg did not achieve consistent improvement of clinical or other biomarker measures of disease activity.

Disclosure: X. Mariette, None; **M. Bombardieri**, MedImmune, 2, 5, Janssen, 2, 5, Cellgene, 2, GSK, 5, UCB, 5; **I. Alevizos**, Viela Bio, 1, 3, 4; **R. Moate**, AstraZeneca, 1, 3, GlaxoSmithKline, 1; **B. Sullivan**, Amgen, 1, Ultragenyx, 1, 3, 4, BioMarin, 1, 3; **G. Noaiseh**, None; **M. Kvarnström**, None; **W. Rees**, MedImmune, 9, Viela Bio, 3; **L. Wang**, None; **G. Illei**, Viela Bio, 3.

Abstract Number: 2418

Tofacitinib Inhibits Increased Inflammatory Marker Expression in a Human Salivary Cell Line Deficient in Autophagy: A Model of Sjögren's Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's syndrome (SS) is an immune-mediated exocrinopathy, where defects in autophagy could contribute to the pathogenesis. Minor labial salivary glands (MLSG) of primary SS (pSS) patients show increased IL-6 levels, JAK/STAT activation and decreased expression of autophagy markers, such as ATG5 and Beclin-1. Additionally, autophagy activation has been related with a reduced inflammatory response, although this is a controversial topic. Interestingly, activation of the IL-6/JAK/STAT3 pathway inhibits autophagy through increased MCL-1 expression in human small airway epithelial cells[1]. The aim of this study was to determine inflammatory markers expression in autophagy-deficient salivary epithelial cells stimulated with or without IL-6. Finally, inflammatory markers expression relying on JAK/STAT signalling pathway was inhibited using tofacitinib.

Methods: Immortalized human submandibular gland (HSG) cell line were transduced with lentiviral ATG5 shRNA-expressing vector (*shATG5*), and with an empty lentiviral vector used as negative control. The protein levels of ATG5, p62 and LC3B were determined in shATG5 and control cells. The mRNA levels of IL-6, IL-1β, IL-8, MCL-1 and CCL2 were measured by qPCR in control and autophagy deficient HSG cells. Subsequently, 3D-acini were generated from shATG5 and control cells, incubated with 10 ng/mL recombinant IL-6 (with/without tofacitinib) for 24h to measure MCL-1 and IL-6 (both STAT3 target genes) mRNA levels by qPCR.

Results: Increased IL-6, IL-1β and IL-8 mRNA levels was observed in shATG5 cells compared to control cells. Upregulation of these mRNA was observed with IL-6 stimulation and reversed by tofacitinib. Moreover, p62 protein levels increased and LC3B decreased in shATG5 cells, confirming our previous findings in MLSG from pSS patients.

Interestingly, overexpression of mRNA levels of MCL-1, an autophagy inhibitor, was observed with IL-6 stimulation, but reversed in the presence of tofacitinib.

Conclusion: Our findings showed that decreased autophagy increases inflammatory markers expression in HSG cells. Tofacitinib inhibits the inflammatory effect of decreased autophagy, probably through the blocking of IL-6/JAK/STAT3 pathway, having a potential therapeutic effect in SS. More information is needed to establish the contribution of autophagy to SS pathogenesis and its role as a therapeutic target.

References:

1. Cancer Res. 2014 Jul 15; 74(14): 3740–3752.

Fondecyt-Postdoctoral Grant-3170023, Fondecyt-1160015, Fondecyt-Iniciación-11170049.

Disclosure: M. Barrera, None; **S. Aguilera**, None; **P. Carvajal**, None; **I. Castro**, None; **S. González**, None; **C. Molina**, None; **S. Matus**, None; **D. Jara**, None; **M. González**, None.

Abstract Number: 2419

An ex-vivo Assay to Evaluate the Efficacy of Different Treatments for Inhibiting B Lymphocytes Activation by Salivary Gland Epithelial Cells in Sjögren's Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is an auto-immune disorder characterized by a chronic hyperactivation of B lymphocytes. We previously showed that salivary gland epithelial cells (SGECs) could play a role in this B-cell activation (1). We developed a co-culture model of SGECs and B lymphocytes and showed that SGECs from pSS induced a higher survival and activation (when stimulated with Poly(I:C)) of B lymphocytes compared to SGECs from controls. The aims of this study were to identify the factors involved in the activation of B lymphocytes by pSS SGECs and to evaluate the efficacy of different treatments for inhibiting this interaction.

Methods: Patients with pSS according to 2016 EULAR/ACR criteria and controls were studied. Primary cultured SGECs from pSS and from controls were stimulated or not with Poly(I:C) and co-cultured with B lymphocytes sorted from healthy donors blood. Transwell assays were performed. Inhibition experiments with anti-BAFF antibody (belimumab) 10µg/mL, anti-JAK1/3 (tofacitinib) 50nM, anti-APRIL antibody 2µg/mL (kindly provided by P. Schneider) and anti-IL-6 receptor (tocilizumab) 50 µg/mL were performed. Survival and activation (CD38) of B lymphocytes were assessed by flow cytometry

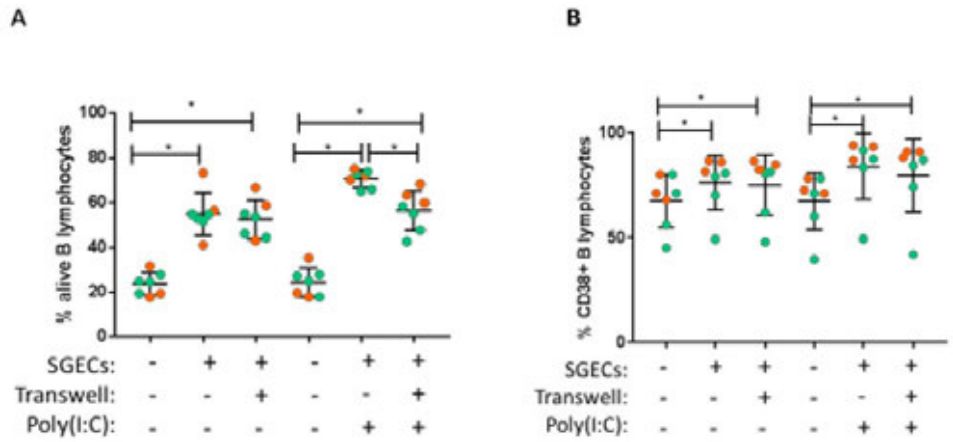

Figure 1: The increases of B lymphocytes viability and activation are mainly due to soluble factors. A: Percentage of alive B lymphocytes at day 5 with and without transwell, in presence or not of Poly(I:C) in co-culutures with SGECs from 3 pSS (in orange) and 4 controls (in green) B: Percentage of CD38+ B lymphocytes at day 5 with and without transwell, in presence or not of Poly(I:C).

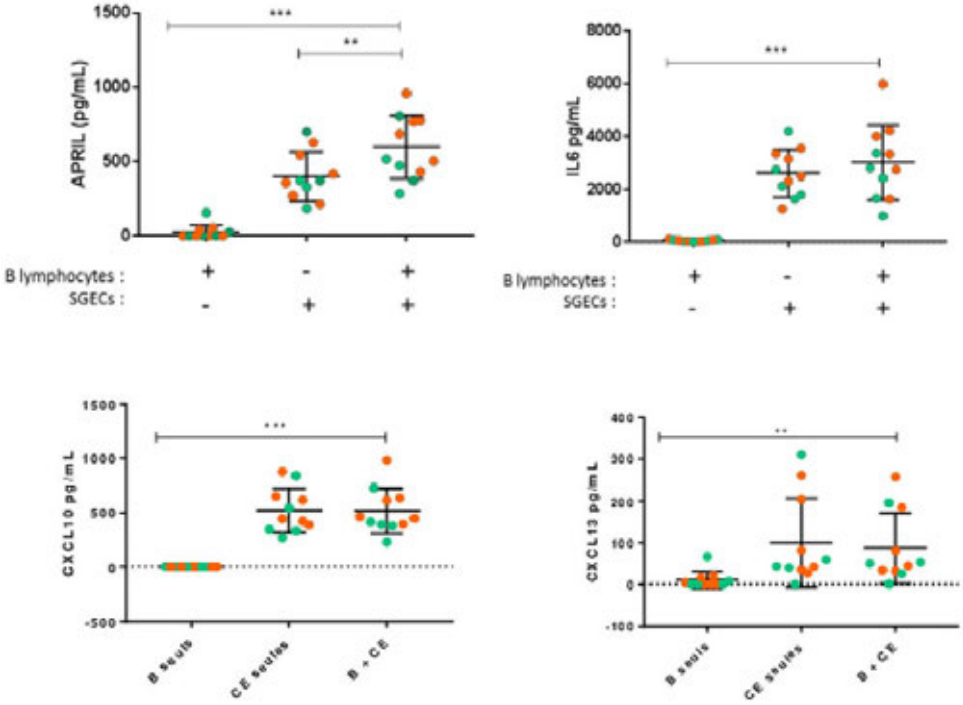

Figure 2: Assessment of soluble factors in the co-cultures supernatants from 6 pSS (in orange) and 5 controls (in green). Dosage of APRIL, IL-6, CXCL10 and CXCL13 in the supernatants of B lymphocytes cultured alone, SGECs cultured alone and B lymphocytes co-cultured with SGEC.

after 5 days of co-culture. Cytokines concentrations were assessed in supernatants (Luminex). Statistical analyses were performed with Prism using Mann-Whitney test (not paired data) and Wilcoxon (paired data) tests.

Results: The induction of B lymphocytes survival and activation was mostly dependent on soluble factors as assessed by transwell assays (Figure 1). Soluble factors were assessed in co-cultures supernatants. BAFF was detectable in co-cultures supernatants only with stimulation with poly(I:C), but adding belimumab to the co-culture did not inhibit the effect of SGECs on B lymphocytes survival and activation, even in the condition stimulated with Poly(I:C). SGECs were able to secrete APRIL and, interestingly, the co-culture of SGECs from pSS with B lymphocytes increased the secretion of APRIL by SGECs compared to SGECs cultured alone (Figure 2). However, inhibition

by an anti-APRIL antibody did not decrease survival of co-cultured B lymphocytes. IL-6 was secreted by SGECs in co-culture supernatants (Figure 2). However, addition of tocilizumab in the co-culture did not inhibit B lymphocytes survival and activation by SGECs. Similar results were obtained with tofacitinib. Lastly, chemokines such as CXCL10 and CXCL13 were also detected in SGECs supernatants (Figure 2).

Conclusion: Several soluble factors secreted by SGECs could play a role in the interactions between SGECs and B lymphocytes. However, targeting one by one the suspected cytokines did not allow identifying a single responsible factor suggesting that a combination of several factors could be required. In the context of the NECESSITY project, further inhibition experiments with the combination of leflunomide and hydroxychloroquine and with inhibitors of specific B-cell mediators as Btk and Pi3K are planned and will be presented at the congress.

Reference:

(1) Rivière E, Pascaud J, Tchitchek N, et al. Crosstalk between salivary gland epithelial cells and B lymphocytes in primary Sjögren's syndrome [abstract]. EULAR 2019

Disclosure: E. Rivière, None; **J. Pascaud**, None; **A. Paoletti**, None; **B. Ly**, None; **G. Nocturne**, None; **X. Mariette**, Biogen, 2, Bristol-Myers Squibb, 5, GlaxoSmithKline, 5, Janssen, 5, LFB Pharmaceuticals, 5, OSE Immunotherapeutics, 2, Pfizer, 2, 5, UCB Pharma, 5, 8.

Abstract Number: 2420

Role of T Follicular Helper Cells and T Peripheral Helper Cells in the Activation of B Cells in Sjögren Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's Syndrome (pSS) is a rare systemic autoimmune disease characterized by a dysregulation of cellular and humoral immunity, leading to a hyper-activation of B cells.

We looked if increase in T follicular helper cells (Tfh) (CD4+PD1+CXCR5+) or T peripheral helper (Tph) cells (CD4+PD1+CXCR5-), as well as cytokines involved in the cross-talk between T and B cells (CXCL-13, soluble CD40L (sCD40L)) could be involved in this B-cell activation.

Methods: We studied two cohorts of patients recruited in the Sjögren reference center of Paris-Sud university (23 controls/29 pSS and 14 controls/18 pSS, respectively). All patients had a diagnosis of pSS according to the ACR/EULAR 2016. Mass cytometry (CYTOF) and flow cytometry were used to quantify circulating cell populations. Cytokines were measured by MULTIPLEX.

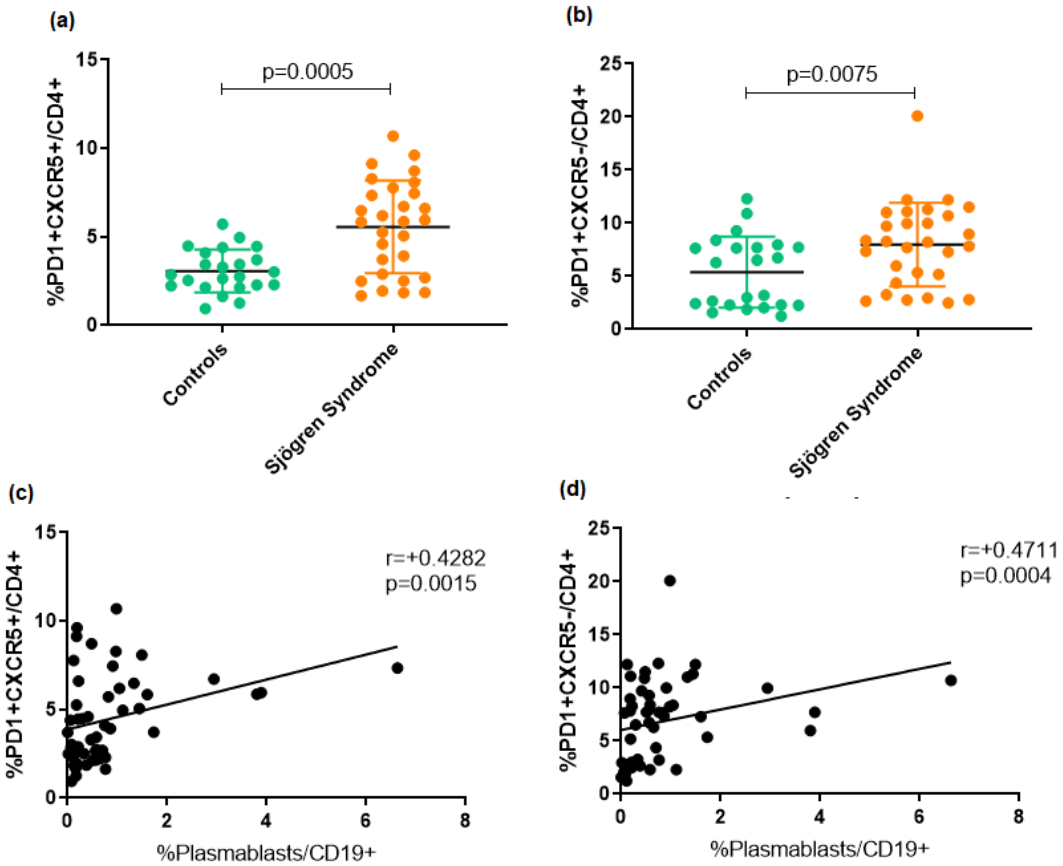

Figure 1: Expansion of circulating Tfh cells (a) and Tph cells (b) in patients with primary Sjögren Syndrome versus healthy controls, assessed by mass cytometry. Correlation between circulating Tfh and plasmablasts (c) and circulating Tph and plasmablasts (d).

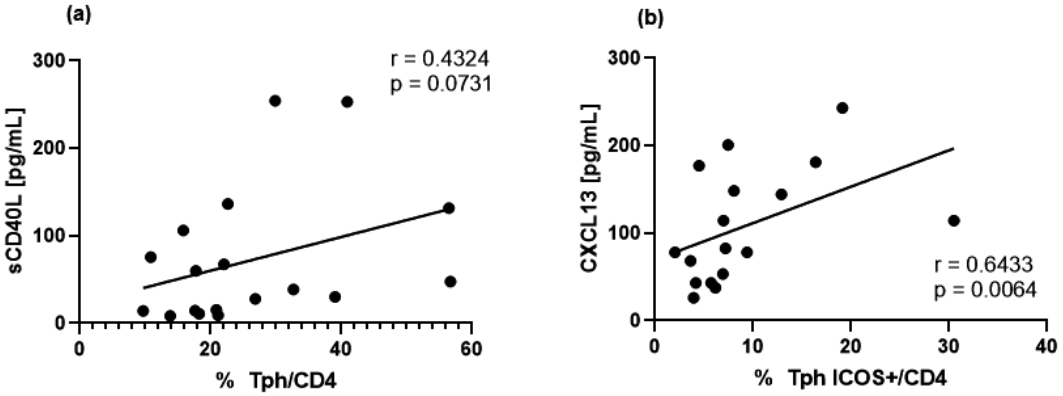

Figure 2: Correlation between plasmatic levels of sCD40L and circulating Tph (a) and between plasmatic levels of CXCL-13 and circulating Tph ICOS+ (b) in patients with primary Sjögren Syndrome.

Results: We showed a peripheral expansion of Tfh (CD4+PD1+CXCR5+) in patients with pSS compared to controls in flow cytometry and mass cytometry (CYTOF): 5.6 +/- 2.6% vs 3.1 +/- 1.2% (p=0.0005) and 10.2 +/- 5.8% vs 6.3 +/- 3.3% (p=0.0349), respectively. Similarly, patients with pSS had higher blood levels of Tph (CD4+PD1+CXCR5-) with both techniques: 8.0 +/- 4.0% vs 5.4 +/- 3.3% (p=0.0075) and 27.3 +/- 13.8% vs 14.9 +/- 9.3% (p=0.0045), respectively. Activated Tph assessed by ICOS expression (CD4+PD1+CXCR5-ICOS+) were also higher in pSS patients: 9.6 +/- 7.1% versus 4.4 +/- 3.3% (p=0.0037).

There was a positive correlation between plasmablasts (CD19+CD27+CD38hi) and Tfh levels (r=+0.43, p=0.0015) and Tph levels (r =+0.47, p=0.0004) in CYTOF.

Patients with pSS also had a trend in favor of a higher level of CXCL13 and soluble CD40L compared to controls: 148.8 +/- 186.2 pg / mL vs 130.5 +/- 207.2 pg / mL (p=0.0846) and 69.9 +/- 70.2 pg / mL mL vs 34.3 +/- 28.2 pg / mL (p=0.0802). There was a positive correlation between Tph and soluble CD40L (r=+0.43, p=0.07) and between activated Tph (CD4+PD1+CXCR5-ICOS+) and CXCL13 (r=+0.64, p< 0.05) in patients with pSS.

Conclusion: Circulating Tfh and Tph T-cell subsets play a role in the hyper-activation of B cells in pSS. Therefore, inhibition of Tfh/Tph function or of cytokines involved in their cross-talk with B cells (CXCL13, CD40L) seems promising therapeutic perspectives in pSS.

Disclosure: A. Dupré, None; **J. Pascaud**, None; **E. Rivière**, None; **M. Mingueneau**, Biogen, 3; **G. Nocturne**, None; **X. Mariette**, Biogen, 2, Bristol-Myers Squibb, 5, GlaxoSmithKline, 5, Janssen, 5, LFB Pharmaceuticals, 5, OSE Immunotherapeutics, 2, Pfizer, 2, 5, UCB Pharma, 5, 8.

Abstract Number: 2421

Circulating CCR7^{lo}PD-1^{hi} Follicular Helper T Cells Indicate Disease Activity and Glandular Inflammation in Patients with Primary Sjögren's Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Since primary Sjögren's syndrome (pSS) is an autoummune disease of B cell hyperactivity and pathologic autoantibody response, follicular helper T (Tfh) cells and follicular regulatory T (Tfr) cells are suggested to be key players in pSS. We examined subsets of Tfh and Tfr cells from the blood in pSS patients, and whether these subsets represent disease activity, glandular inflammation, or autoantibody responses in pSS.

Methods: Circulating Tfh and Tfr cells, along with their specific subsets, were identified from the peripheral blood of 18 pSS patients and 14 age- and sex-matched healthy controls using flow cytometry analysis. Patients with pSS fulfilled the 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for pSS. Serum interleukin (IL)-21 was measured using the enzyme-linked immunosorbent assay. We examined the correlation of blood Tfh and Tfr cells and their subsets with disease activity, blood B-cell subsets, serum autoantibody titers, serum immunoglobulin G (IgG) levels, and serum IL-21 levels in pSS.

Results: Blood Tfr and Tfh cell ratios were increased in pSS patients compared with healthy controls. The CCR7^{lo}PD-1^{hi} subset of circulating Tfh cells was increased in pSS patients with high degree of focal lymphocytic sialadenitis; whereas circulating Tfh cells did not differ between pSS patients and healthy controls. The frequency of CCR7^{lo}PD-1^{hi} Tfh cells was significantly correlated with disease activity scores (Spearman's rho = 0.552, p = 0.018) and differen-

tiated B cells. PD-1 expression on blood Tfh and Tfr cells showed positive correlations with IL-21 in pSS. Increasing trend of blood Tfr cells was observed in primary pSS patients, and blood Tfr cells (particularly Th1 and Th17 subsets) represented hypergammaglobulinemia in pSS.

Conclusion: Circulating $CCR7^{lo}PD\text{-}1^{hi}$ Tfh cells indicated disease activity and glandular inflammation in pSS. Circulating Tfr cells, shifted toward Th1 and Th17 subsets, indicated ongoing IgG production in pSS. Subsets of circulating Tfh or Tfr cells could be biomarkers for disease monitoring and patient stratification in pSS.

Disclosure: J. Kim, None; **J. Lee**, None; **U. Jung**, None; **S. Park**, None; **J. Lee**, None; **S. Kwok**, None; **S. Park**, None.

Abstract Number: 2422

Increased Apoptosis and Compromised Suppressive Capacity of Regulatory T Cells in Primary Sjögren's Syndrome

Min Feng,[1] Xiangcong Zhao,[1] and Jing Luo[1], [1]the second hospital of shanxi medical university, Taiyuan, China (People's Republic)

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the apoptosis and suppressive function of regulatory T cells (Tregs) in primary Sjögren's syndrome (pSS), and the effect of low-dose IL-2 on apoptosis of Tregs.

Methods: Apoptosis of Tregs and effector T (Teff) cells were measured by staining with Annexin V and 7-amino-actinomycin D (7-AAD) in 54 female patients with pSS and 25 aged-matched female healthy controls (HCs) using flow cytometry. The function of Tregs was evaluated by the suppressive capacity to autologous $CD4^{+}CD25^{-}$ responder T (Tresp) cells expansion and was expressed as the proliferation of Tresp cells. The apoptosis degree of 13 pSS after the administration of low-dose IL-2 was also analyzed.

Results: Defect of number (P=0.030) and percentage (P=0.004) of Tregs was observed in pSS. Tregs was more sensitive to apoptosis than Teff cells, and apoptosis degree of Tregs was parallel to disease activity. Functional assay showed a compromised suppression for Tresp proliferation. The administration of low-dose IL-2 reduced the apoptitic rate of Tregs and Teff cells. Furthermore, serum concentrations of interleukin-6 (IL-6), IL-10, IL-17, interferon-γ (IFN-γ) and tumor necrosis factor-α (TNF-α) were positively associated with early apoptotic Tregs and Teff cells, but with late apoptotic Teff cells negatively. In addition, Cystatin C, α1 microglobulin and β2 microglobulin could contribute to the early apoptosis of Tregs (r=0.553, P=0.001; r=0.537, P=0.004; r=0.552, P=0.001) and Teff cells (r=0.534, P=0.001; r=0.560, P=0.002; r=0.401, P=0.019).

Conclusion: Aberrant increased apoptosis and impaired function of Tregs may partially contribute to the immune imbalance, leading to the onset of pSS. And multiple up-regulated cytokines, cystatin C, α1 microglobulin and β2

Table 1. Demographic and serological characteristics of patients and controls

	pSS (n=54)	HCs (n=25)	*P*
Age (years)	59.50 (52.50,65.00)	54.00 (46.50,61.50)	0.115
WBC ($*10^9$/L)	4.97 (3.78,6.45)	4.90 (4.45,6.17)	0.457
RBC ($*10^{12}$/L)	4.13±0.45	4.51±0.26	<0.001
Hb (g/L)	129.00 (116.00,135.25)	137.00 (132.00,141.50)	<0.001
PLT ($*10^9$/L)	179.00 (145.75,237.50)	243.00 (209.50,285.00)	0.003
LYMP ($*10^9$/L)	1.61±0.71	1.71±0.30	0.382
NEUT ($*10^9$/L)	2.73 (1.77,4.16)	2.76 (2.33,3.83)	0.423
ESR (mm/h)	27.00 (15.00,42.50)	7.00 (4.00,8.50)	<0.001
CRP (mg/L)	2.96 (1.92,3.88)	2.00 (1.13,3.20)	0.027
C3 (g/L)	0.85 (0.68,1.00)	-	-
C4 (g/L)	0.19 (0.15,0.22)	-	-
ALT (U/L)	17.35 (11.78,28.10)	14.50 (10.65,17.15)	0.018
AST (U/L)	22.45 (17.35,31.10)	17.00 (14.40,20.60)	0.001
cystatin C (mg/L)	0.80 (0.68,1.02)	-	-
α1 microglobulin (mg/L)	25.27 (20.91,34.56)	-	-
β2 microglobulin (mg/L)	2.74 (1.90,3.63)	-	-
T (cells/μL)	1163.88 (804.33,1556.54)	1185.00 (1046.25,1402.00)	0.480
B (cells/μL)	228.50 (142.02,310.61)	173.59 (135.00,222.00)	0.062
NK (cells/μL)	189.49 (101.41,313.45)	275.65 (179.52,341.53)	0.014
$CD4^+$T (cells/μL)	693.33 (450.33,924.69)	660.00 (559.50,753.08)	0.534
$CD8^+$T (cells/μL)	390.47 (237.24,600.44)	441.00 (324.17,561.43)	0.591
Th1 (cells/μL)	117.70 (66.13,216.03)	121.00 (81.50,143.00)	0.520
Th1 (%)	18.17 (11.45,24.28)	17.11 (11.87,21.09)	0.551
Th2 (cells/μL)	5.33 (3.63,8.48)	7.00 (4.00,12.00)	0.084
Th2 (%)	0.80 (0.60,1.08)	1.23 (0.65,1.86)	0.014
Th17 (cells/μL)	6.34 (4.18,10.69)	6.00 (5.00,7.50)	0.891
Th17 (%)	1.06 (0.70,1.56)	0.88 (0.68,1.25)	0.483
Treg (cells/μL)	31.97±14.31	38.04±9.58	0.030
Treg (%)	4.72±1.69	5.86±1.29	0.004
Th1/Th2	19.99 (15.24,31.12)	14.87 (9.24,24.46)	0.025
Th17/Treg	0.21 (0.15,0.38)	0.17 (0.12,0.26)	0.043
Th1/Treg	4.19 (2.24,6.46)	2.78 (1.97,4.10)	0.071
Th2/Treg	0.18 (0.13,0.25)	0.20 (0.13,0.38)	0.523
B/Treg	6.78±4.96	4.92±1.75	0.016
IL-2 (pg/mL)	3.36 (1.80,6.33)	2.13 (1.59,2.63)	0.002
IL-4 (pg/mL)	3.02 (1.59,8.66)	0.89 (0.67,1.08)	<0.001
IL-6 (pg/mL)	15.11 (5.44,37.70)	1.75 (1.39,2.27)	<0.001
IL-10 (pg/mL)	6.98 (4.19,13.35)	1.17 (0.78,1.39)	<0.001
IL-17 (pg/mL)	27.83 (6.22,65.90)	0.00 (0.00,0.00)	<0.001
IFN-γ (pg/mL)	9.14 (3.96,19.40)	0.53 (0.39,0.86)	<0.001
TNF-α (pg/mL)	5.50 (2.40,13.58)	0.75 (0.50,1.09)	<0.001

Data are reported as mean±SD or median (Q_{25}, Q_{75}), and were analyzed by the independent-samples t test or the Mann-Whitney U test, respectively.

Abbreviation: WBC: white blood cell; RBC: red blood cell; Hb: hemoglobin; PLT: platelet; LYMP: lymphocyte; NEUT: neutrophile granulocyte; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; NK: natural killer; IL-2: interleukin-2; IL-4: interleukin-4; IL-6: interleukin-6; IL-10: interleukin-10; IL-17: interleukin-17; IFN-γ: interferon-γ; TNF-α: tumor necrosis factor-α

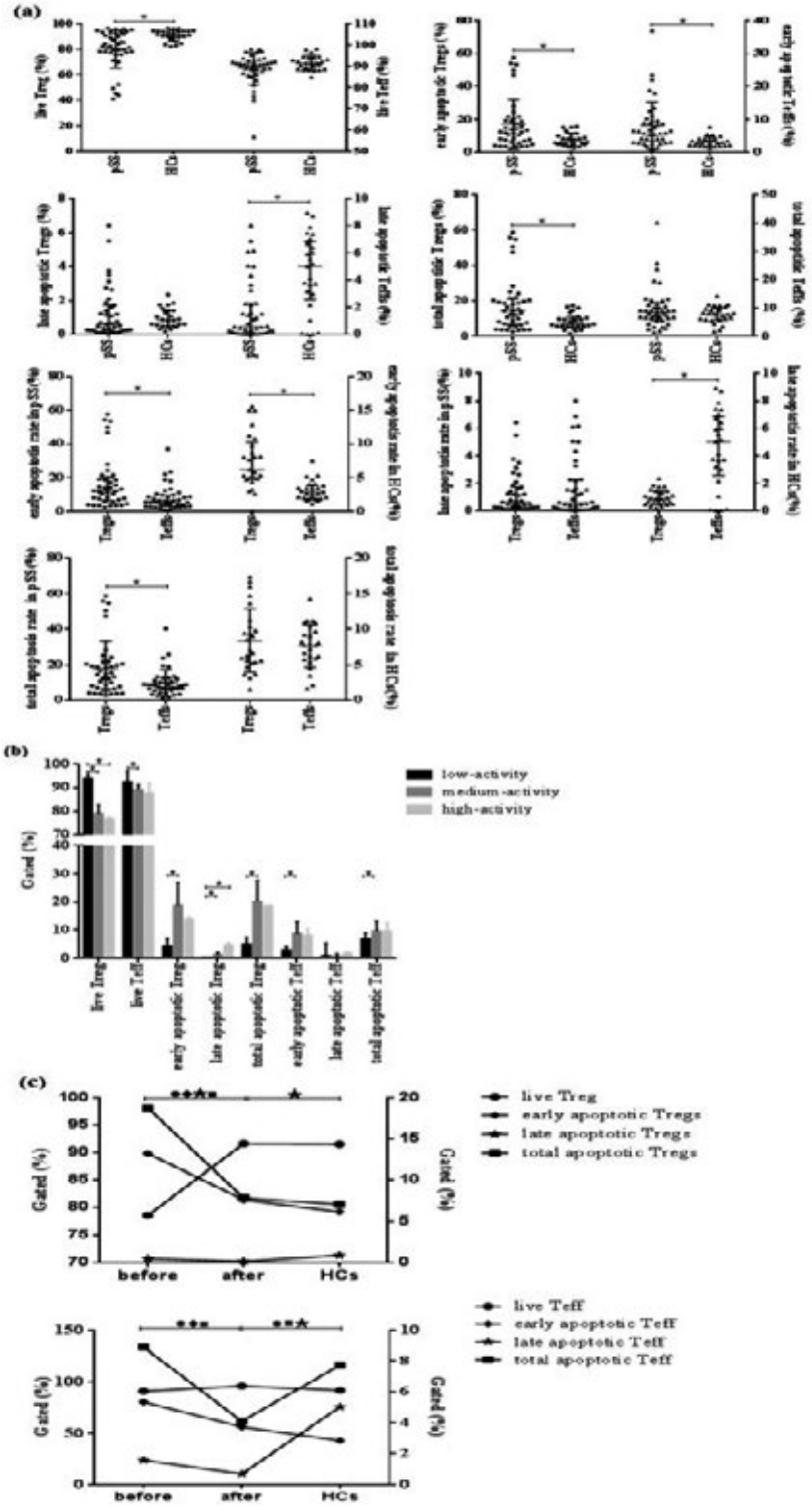

Figure 1: (a) Apoptosis of Tregs and effector T (Teff) cells in pSS and HCs. The left two scatter plots referred to the left Y-axis, and the right two scatter plots referred to the right Y-axis. Comparisons of live, early apoptotic, late apoptotic/necrotic, and total apoptotic Tregs and Teff cells between pSS and HCs. And comparisons of early apoptotic, late apoptotic, and total apoptotic Tregs and Teff cells in pSS and HCs, respectively. (b) Comparisons of rate of live, early apoptosis, late apoptotis, total apoptosis of Treg and Teff cells in low-activity (ESSDAI<5, n=22), medium-activity (5≤ESSDAI≤13, n=29) and high-activity (ESSDAI≥14, n=3) in pSS, respectively. (c) Apoptosis of Tregs and Teff cells in response to low-dose IL-2 administration in pSS was shown. Rate of live cells referred to the left Y-axis, and the proportions of early, late and total apoptotic cells referred to the right Y-axis.

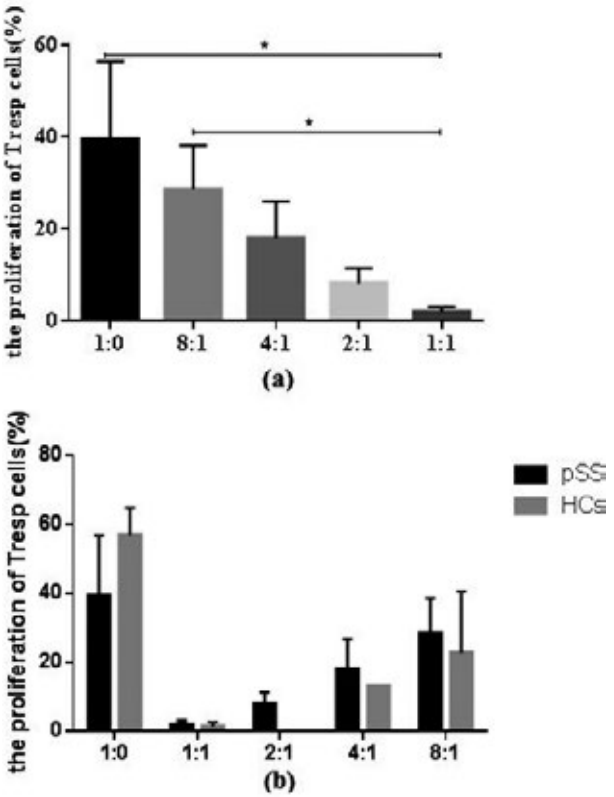

Figure 2. The suppressive function of Tregs for Tresp cells proliferation in different Tresp/Treg ratio (1:0, 1:1, 2:1, 4:1 and 8:1) was examined by flow cytometry. (a) Suppressive capacity of Tregs was in a Tresp/Treg ratio-dependent manner. Data were presented as median (Q25, Q75) and were analyzed by the Independent-samples Kruskal-Wallis test one-way ANOVA. (b) Suppressive capacity of Tregs and the proliferation of Tresp cells themselves were compromised in pSS compared with healthy controls (HCs). Data were presented as median (Q25, Q75) and were compared by Mann-Whitney U-test. *P<0.05.

microglobulin were responsible for the increased sensitivity to apoptosis of Tregs. Low-dose IL-2 could decrease the sensitivity to apoptosis of Tregs and alleviate disease activity.

Disclosure: M. Feng, None; **X. Zhao**, None; **J. Luo**, None.

Abstract Number: 2423

In Primary Sjogren's Syndrome (pSS) IL7 Promotes the Crosstalk Between T Lymphocytes and Salivary Gland Epithelial Cells and Participates to IFN Signature

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: pSS is characterized by lymphocytic infiltration of salivary gland epithelial cells (SGEC). This infiltrate is made of T (TL) and B (BL) lymphocytes. SGEC are now known to be active players of the pathogenesis of the disease. Here we aimed to focus on the crosstalk between SGEC and TL in pSS and on the impact of IL7 on this process given the role of IL7 on TL biology.

Methods: IL-7 serum level was assessed in 372 pSS patients and 73 paired controls. Primary cultures of salivary gland epithelial cells (SGEC) from patients and controls were stimulated by Poly I:C 30 ng/ml, IFN-α 600UI/ml, IFN-γ 5ng/ml and IFN-λ (IL-28) 25ng/ml for 72 hours. IL-7 secretion was tested in culture supernatant (SN) by ELISA and by quantitative RT-PCR. Four-day and eight-day co-cultures (allogenic and then autologous) between LT and SGEC were performed in presence of Poly IC and anti-CD3/anti-CD28 and anti IL7-R (OSE-127, 10 µg/ml) or control isotype. TL survival and activation were assessed by FACS. Last, explants from minor salivary gland biopsies (MSGB) from 9 pSS patients and 3 controls were cultured for 4 days in presence of anti IL7-R (OSE-127, 10 µg/ml) or control isotype. Transcriptomic analysis from the biopsies (explants and cells in the SN) was studied by Nanostring (Immunology panel_v2).

Results: pSS patients had higher serum IL-7 levels than controls: 7.56 ng/ml ± 8.52 (mean ± SD) versus 4.86 ng/ml ± 5.59; p< 0.0001. SGEC stimulation with Poly I:C, IFN-α, -γ and -λ induced IL-7 protein secretion in the supernatant (p=0.002, p=0.004, p=0.007, p=0.004 respectively). IL-7 expression was confirmed by quantitative RT-PCR. Allogenic

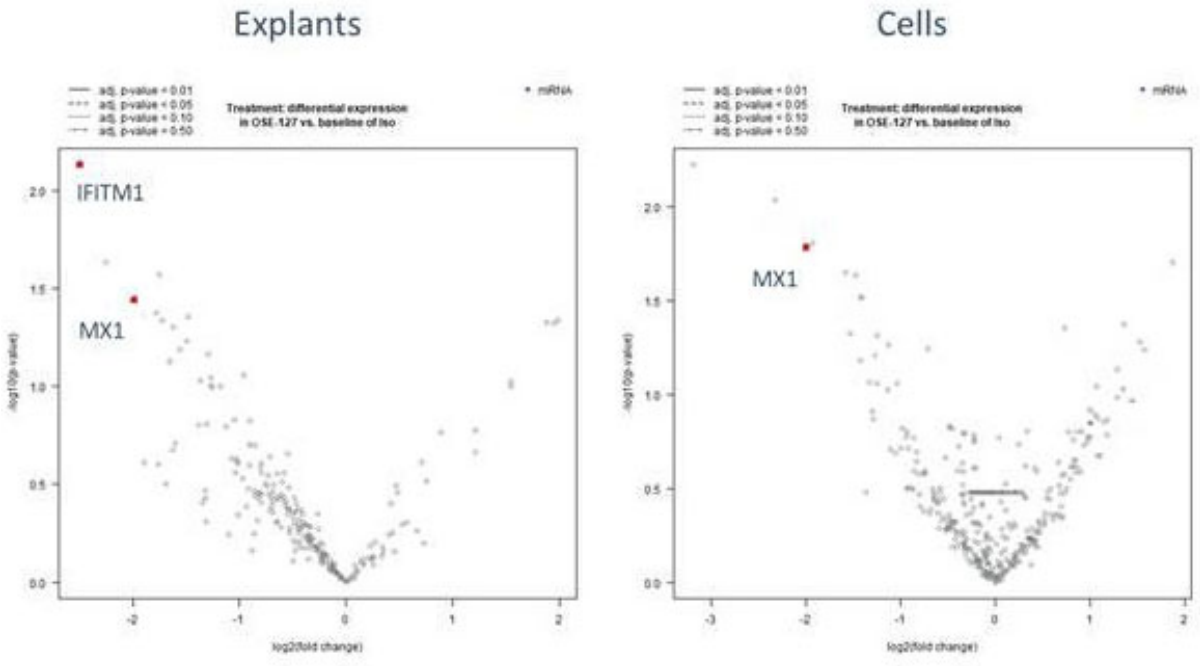

Figure: Volcano plots showing differential expression of the mRNA after exposure to OSE-127

co-culture lead to increased activation of TL as assessed by increased HLA-DR expression and this was partially inhibited by adding OSE-127 in the co-culture. This activation was not observed in autologous co-cultures. Co-cultures of SGECs with either allogenic or autologous TL showed that TL survival was increased by co-culture and this effect was not abolished by inhibiting IL7 signaling with OSE-127. Lastly, analysis of the mRNA signature from MSGB explants from pSS patients revealed that inhibition of IL7 signaling by OSE-127 lead to a decreased of IFN signature as assessed by decreased expression of IFITM1 and Mx-1 both in the explants and in the cells in the SN (Figure).

Conclusion: This study shows that IL7, a key TL cytokine, is increased in pSS and is locally produced by SGEC after PolyI:C and IFNs stimulation. SGEC are likely to have a feeder effect allowing survival of TL but it seems to be independent of IL7. However and interestingly, IL7 signaling may participate to the IFN signature observed in different glandular cellular sub-types in pSS, as demonstrated by decreased IFN signature after IL7-R inhibition both in the explant and in the cellular SN.

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Abstract Number: 2424

RORγt Antagonist Attenuates Experimental Sialadenitis Like Sjögren's Syndrome via Inhibition of CD25 Expression on $CD4^+$ T Cells

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Our previous study demonstrated that T cells specific RORγt transgenic-mice under human CD2 promoter (RORγt-Tg mice) developed severe spontaneous sialadenitis like Sjögren's syndrome (SS) in which RORγt overexpressed $CD4^+$T cells and reduced regulatory T cells (Tregs) contributed to the pathogenesis. The purpose of this study was to clarify the effectiveness and its mechanisms of RORγt antagonist (A213) for sialadenitis like SS in RORγt-Tg mice.

Methods: 1. *In vivo* **experiments**.

6 weeks aged RORγt-Tg mice were administered orally 300 mg/kg of A213 or phosphate buffered saline (PBS) every three days for two weeks. We compared 1) saliva volume, 2) histopathology of salivary glands, 3) proportion of $CD4^+CD25^+$T cells in spleen and cervical lymph nodes (cLNs), 4) percentages of $CD4^+CD25^+Foxp3^+$ and $CD4^+CD25^{+-}$ $Foxp3^-$cells in $CD4^+$T cells of cLNs, and 5) the protein expression levels of CD69 on $CD4^+CD25^+Foxp3^+$ and $CD4^+CD25^{+-}$ $Foxp3^-$cells, between A213 and PBS treated groups.

2. *In vitro* **experiments.**

Splenic $CD4^+$T cells derived from RORγt-Tg mice were cultured with different concentrations of A213 (0, 0.01, 0.1, 1 μM) *in vitro*, and we investigated 1) the expression of CD25 on $CD4^+$T cells, 2) the production of IL-2 from $CD4^+$T cells, and 3) the proportion of IL-$17^+IFN\gamma^-$, IL-$17^-IFN\gamma^+$, and IL-$17^+IFN\gamma^+$ cells in $CD4^+CD25^+$T cells.

Results: 1. *In vivo* **experiments.**

1) A213 significantly recovered the salivary secretion in RORγt-Tg mice compared with PBS (changes in saliva volume at day 14; 1.3±0.3 in PBS group, 3.1±1.4 in A213 group, $P< 0.05$). 2) Infiltration of mononuclear cells in salivary glands was dramatically improved in A213- compared with PBS-treated group. The focus score at day 14 was significantly lower in A213- than in PBS-treated group (2.5±0.6 in PBS-treated group, 0.3±0.3 in A213 treated-group, $P< 0.05$). 3) The proportion of $CD4^+CD25^+$cells in $CD4^+$T cells of spleen was comparable between A213-and PBS-treated group. On the other hand, the proportion of $CD4^+CD25^+$cells in $CD4^+$T cells of cLNs was significantly lower in A213- than PBS- treated group ($P=0.007$). 4) The proportions of both $CD4^+CD25^+Foxp3^+$ and $CD4^+CD25^+Foxp3^-$cells in $CD4^+$T cells of cLNs were significantly decreased in A213- than PBS-treated group ($P< 0.05$). 5) The mean fluorescence intensity (MFI) of CD69 on $CD4^+CD25^+Foxp3^-$cells in cLNs was significantly lower in A213- than PBS-treated group ($P< 0.05$), while no significant difference was detected in CD69 on $CD4^+CD25^+Foxp3^+$cells.

2. *In vitro* **experiments..**

1) A213 (0, 0.01, 0.1, 1 μM) significantly suppressed the expression of CD25 on $CD4^+$T cells derived from RORγt-Tg mice in a dose dependent manner. 2) A high concentration of A213 (1 μM) significantly suppressed the IL-2 production from $CD4^+$T cells derived from RORγt-Tg mice. 3) $IFN\gamma^-$IL-17^+cells were significantly decreased by A213 (0.1, 1 μM), while $IFN\gamma^+$IL-17^- and $IFN\gamma^+$IL-17^+cells were significantly decreased by only a high concentration of A213 (1 μM) in $CD4^+CD25^+$cells ($P< 0.001$).

Conclusion: RORγt antagonist could suppress the sialadenitis like SS via inhibition of $CD4^+CD25^+$cells in cLNs and have potential to be a new promising therapy for SS patients.

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Abstract Number: 2425

The anti-Ro52 Prevalence in the Sjögren's Syndrome Picture: A Single Center Cross Sectional Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren syndrome (SjS) is an autoimmune disorder characterized by inflammation and destruction of exocrine glands. The presence of autoantibodies (AA) against the Ro52/TRIM21, an RNP complex binding to the stem-loop structure of human cytoplasmic RNA, might be relevant in the SjS pathogeny. It has been suggested that distinguishing between antibody reactivity against Ro60 and Ro52/TRIM21 could be helpful in terms of evaluating clinical course, features and even pre-symptomatic stages of the disease. Objective: To evaluate the prevalence of anti-Ro52/TRIM21 antibodies in a cohort of patients diagnosed with primary SjS.

Methods: In this cross-sectional study we evaluated 179 patients with primary SjS according to the ACR classification criteria who had been admitted between December 2008 and December 2018 to our outpatient clinic. All patients had ANA titers higher than 1:320 in at least two positive determinations for any pattern. ANA, anti-Ro52/TRIM21, anti-Ro60, anti-La and rheumatoid factor (RF) were tested by immunoblot (Euroimmun, Lübeck, Germany).

Results: In our cohort the median age at diagnosis was 57 years (range: 20- 85 years) with a clear dominance of females (n=160, 89%). the most frequently reported ANA patterns were speckled (93%), while only few patients had a homogeneous (6%) pattern. 177/179 were positive for anti-Ro52/TRIM21 (98%), 159/179 (88%) for anti-Ro60, 127/179 for anti-La (79%) and 94/179 (52%) showed RF reactivity. 76/179 (42%) patients showed all four reactivities (anti-Ro52/TRIM21, anti-Ro60, anti-La and RF). Out of these 76 patients, 11 (6%) patients exhibited Raynaud's syndrome, 25 (13%) exhibited arthritis/arthralgia, 31 (17%) had hypergammaglobulinemia, 13 (7%) had hypocomplementemia and 26% had elevated free kappa/lambda chains, as typical clinical and laboratory features described in SjS.

Conclusion: Our results showed that anti-Ro52/TRIM21 but not anti-Ro60 is present in virtually all patients with SjS and had the most prevalent antibody reactivity. This finding needs to be considered in the current classification criteria of SjS (2), which include the presence of anti-Ro60, rather than anti-Ro52/TRIM21. Also, including the anti-Ro52/TRIM21 measurement in larger cohorts and longitudinal studies would also help us in improving the knowledge of its pathogenic role and to define of more focused diagnostic/therapeutic strategies.

Disclosure: L. Valor, None; **H. Schenker**, None; **J. Knitza**, None; **M. Hagen**, None; **J. Rech**, AbbVie, 8, Biogen, 8, BMS, 5, 8, Celgene, 5, 8, Chugai, 5, MSD, 8, Novartis, 5, 8, Roche, 5; **G. Schett**, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, 8, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, UCB, 5, BMS, Celgene, GSK, Lilly, Novartis, 2.

Abstract Number: 2426

Distinct Clinical Characteristics of Anti-Ro/SSA Negative Primary Sjögren's Syndrome: Data from a Cohort for Sjögren's Syndrome in Korea

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	Total, n=355	Anti-Ro positive group, n=326	Anti-Ro negative group, n=29	p value
Age (years)	53 (43-60)	53 (43-59)	56 (47-67)	0.111
Gender (female)	351 (98.9)	322 (99.1)	28 (96.6)	0.290
Dry eyes	340 (95.8)	311 (95.4)	29 (100)	0.622
Dry mouth	342 (96.3)	313 (96.0)	29 (100)	0.611
Xerostomia related items				
Unstimulated salivary flow rate <1.5 ml in 15	181/199 (91.0)	159/171 (87.8)	22/28 (78.6)	0.025
Unstimulated salivary flow rate (ml/15min)	0.3 (0.0-1.2)	0.3 (0.0-1.2)	0.3 (0.1-3.2)	0.505
Xerostomia inventory	38 (30-43)	38 (30-43)	40 (28-44)	0.650
Xeroophthalmia related items				
Schirmer I test <5 ml/5 min	264/333 (79.3)	242/307 (78.8)	22/26 (84.6)	0.619
Schirmer I test (ml/5 min)	3 (2-5)	3 (2-5)	3 (2-5)	0.885
Tear break up time (sec)	3 (2-4)	3 (2-4)	3.5 (2-5)	0.353
Meibomian gland dysfunction	171/243 (70.4)	156/221 (70.6)	15/22 (68.2)	>0.999
OSS by SICCA method	4 (1-7)	4 (1-7)	4 (1.8-6.3)	0.964
OSS by van Bijsterveld's method	3 (1-6)	3 (1-6)	4 (1-5)	0.916
OSS by SICCA ≥ 5 (or Bijsterveld ≥ 4)	112/256 (43.8)	100/234 (42.7)	12/22 (54.5)	0.286
Ocular surface disease index	36 (20-54)	38 (20-55)	28 (17-53)	0.234
Minor salivary gland biopsy positvity*	190/213 (89.2)	161/184 (87.5)	29 (100)	0.050
Focus score	3 (2-4)	3 (2-4)	2.5 (1-4)	0.333
VAS for Physician's global assessment	30 (18-45)	30 (19-50)	20 (6-41)	0.008
VAS for Patient's global assessment	62 (47-76)	61 (45-75)	75 (63-84)	0.001
ESSPRI	5 (4-6)	5.3 (4-6.7)	5.3 (4.3-6.7)	0.586
ESSPRI pain	3 (0-5)	3 (0-5)	3 (0.5)	0.764
ESSPRI fatigue	5 (5-7)	5 (5-7)	5 (5-7)	0.378
ESSPRI Dryness	7 (5-8)	7 (5-8)	8 (5-10)	0.048
EuroQol-5 dimensions time tradeoff value	0.85 (0.78-0.91)	0.85 (0.78-0.91)	0.88 (0.75-0.91)	0.985
EuroQol VAS	67 (50-80)	70 (50-80)	65 (50-75)	0.710

Clinical features of 355 enrolled patients with primary Sjogren's syndrome

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate clinical characteristics of patients with primary Sjögren's syndrome (SS) who were negative for anti-Ro/SSA antibody but positive for minor salivary gland biopsy (MSGB) compared to patients who presented positivity for anti-Ro/SSA antibody.

	Total, n=354	Anti-Ro positive group, n=325	Anti-Ro negative group, n=29	P value
ESSDAI total score	3 (1-6)	3 (1-6)	2 (0-5)	0.195
Positivity for each ESSDAI domain				
Constitutional	48 (13.6)	46 (14.2)	2 (6.9)	0.399
Lymphadenopathy	17 (4.8)	17 (5.2)	0 (0)	0.38
Glandular	38 (10.7)	38 (11.7)	0 (0)	0.057
Articular	81 (22.9)	74 (22.8)	7 (24.1)	0.866
Cutaneous	23 (6.5)	22 (6.8)	1 (3.4)	0.708
Pulmonary	34 (9.6)	29 (8.9)	5 (17.2)	0.178
Renal	4 (1.1)	3 (0.9)	1 (3.4)	0.291
Muscular	3 (0.8)	3 (0.9)	0 (0)	>0.999
Peripheral nervous system	14 (4.0)	10 (3.1)	4 (13.8)	0.021
Central nervous system	3 (0.8)	3 (0.9)	0 (0)	>0.999
Hematological	103 (29.1)	100 (30.8)	3 (10.3)	0.019
Biological	191 (54.0)	179 (55.1)	12 (41.4)	0.156
Other extraglandular manifestations				
Raynaud's phenomenom	61 (17.2)	52 (16.0)	9 (31.0)	0.067
Autoimmune thyroid disease	44 (12.4)	42 (12.9)	2 (6.9)	0.556
SSDDI total score	2 (1-3)	2 (1-3)	2 (1-3)	0.970
Positivity for each SSDDI item				
Ocular/salivary damage				
Salivary flow impairment	210 (59.3)	194 (59.7)	16 (55.2)	0.635
Loss of teeth	33 (9.3)	27 (8.3)	6 (20.7)	0.041
Ocular damage				
Tear flow impairment	245 (69.2)	226 (69.5)	19 (65.5)	0.653
Structural abnormalities	209 (59.0)	192 (59.1)	17 (58.6)	0.962
Neurologic damage				
Central nervous system involvement	3 (0.8)	3 (0.9)	0 (0)	>0.999
Peripheral neuropathy	11 (3.1)	9 (2.8)	2 (6.9)	0.225
Pleuropulmonary damage	6 (1.7)	6 (1.8)	0 (0)	>0.999
Renal impairment	5 (1.4)	5 (1.5)	0 (0)	>0.999
Lymphoproliferative disease	0 (0)	0 (0)	0 (0)	

Clinical indices for disease-related systemic activity, extraglandular manifestations and long-term damage

	Total, n=355	Anti-Ro positive group, n=326	Anti-Ro negative group, n=29	P value
White blood cell (x 10^3/mm^3)	4.520 (3.700-5.592)	4.440 (3.600-5.500)	5.155 (4.632-6.147)	0.002
Leukopenia (< 4.00 x 103/mm3)	112/352 (31.8)	110/323 (34.1)	2 (6.9)	0.003
Absolute neutrophil count (x 10^3/mm^3)	2.355 (1.817-3.250)	2.300 (1.760-3.210)	3.120 (2.342-3.475)	0.003
Neutropenia (< 1.50 x 103/mm3)	47/350 (13.4)	46/321 (14.3)	1 (3.4)	0.1
Hemoglobin (g/dl)	12.8 (12.0-13.6)	12.8 (12.0-13.6)	13.4 (12.7-14.0)	0.005
Anemia (< 12 g/dl)	80/352 (22.7)	77 (23.8)	3 (10.3)	0.097
Platelet (x 10^3/mm^3)	221 (188-257)	222 (188-258)	228 (181-273)	0.591
Thrombocytopenia (< 150 x 103/mm3)	24/352 (6.8)	23/323 (7.1)	1 (3.4)	0.707
Anti-nuclear antibody positivity (titer ≥ 320)	204/325 (62.8)	188/297 (63.3)	16/28 (57.1)	0.519
Rheumatoid factor positivity (> 20 IU/ml)	211/320 (65.9)	205/292 (70.2)	6/28 (21.4)	<0.001
Anti-cyclic citrullinated peptides antibody (U/m	1.5 (0.8-4.0)	1.6 (0.9-4.5)	0.8 (0.5-1.3)	0.012
β_2-microglobulin (μg/ml)	1.952 (1.609-2.437)	1.988 (1.656-2.473)	1.538 (1.250-2.205)	0.034
Hypergammaglobulinemia	160/322 (49.7)	158/293 (53.9)	2 (6.9)	<0.001
Immunoglobulin G (mg/dl)	1593 (1355-1983)	1651 (1385-2016)	1288 (1109-1379)	<0.001
Immunoglobulin A (mg/dl)	268 (202-366)	271 (209-377)	202 (154-262)	<0.001
Immunoglobulin M (mg/dl)	115 (85-151)	113 (82-149)	120 (96-173)	0.094
Cryoglobulin	9/299 (3.0)	9/273 (3.3)	0/26 (0)	>0.999
Low C3 (< 76 mg/dl)	55/336 (16.4)	47/308 (15.3)	8/28 (28.6)	0.104
Low C4 (< 12 mg/dl)	17/336 (5.1)	17/308 (5.5)	0/28 (0)	0.379
C3 (mg/dl)	92 (81-102)	91 (81-102)	84 (74-99)	0.079
C4 (mg/dl)	22 (18-26)	22 (18-26)	22 (18-26)	0.956
Anti-La/SSB antibody positivity	186/354 (52.5)	186/325 (57.2)	0 (0)	<0.001
Anti-centromere antibody positivity	38/302 (12.6)	23/274 (8.4)	15/28 (53.6)	<0.001
Anti-topoisomerase antibody positivity	5/282 (1.8)	3/255 (1.2)	2/27 (7.4)	0.074
Anti-ribonucleoprotein antibody positivity	6/207 (2.9)	6/189 (3.2)	0 (0)	>0.999
Anti-Jo-1 antibody positivity	3/295 (1.0)	2/267 (0.7)	1/28 (3.6)	0.259
Anti-DNA antibody positivity	10/315 (3.2)	10/287 (3.5)	0 (0)	0.609

Serological features

Methods: Data of 355 patients from the Korean Initiative of primary Sjögren's Syndrome (KISS), a nationwide prospective cohort for primary SS in Korea, were analyzed. All patients fulfilled 2016 American College of Rheumatology/European League Against Rheumatism (EULAR) classification criteria. Of these patients, 326 were positive for anti-Ro/SSA antibody and 29 were antibody-negative, although they had positive findings in MSGB. Various clinical features including all kinds of tests for evaluating secretory function, disease-related clinical indices and serological values available in the cohort were compared between the two groups.

Results: The anti-Ro/SSA negative group showed less rheumatoid factor positivity ($p < 0.001$), leucopenia ($p = 0.003$), hypergammaglobulinemia ($p < 0.001$), lower serum β_2-microglobulin level ($p = 0.034$), more anti-centromere antibody positivity ($p < 0.001$), higher score in dryness domain of EULAR SS patient reported index ($p = 0.048$) and more positivity for peripheral nervous system domain in EULAR SS disease activity index and loss of teeth in SS disease damage index ($p = 0.021$ and 0.041, respectively) than patients who were positive for anti-Ro/SSA antibody.

Conclusion: Primary SS patients who are negative for anti-Ro/SSA antibody have different clinical characteristics compared to patients who are positive for such antibody in Korea. Therefore, clinicians should consider MSGB in patients with suspicious symptoms who are anti-Ro/SSA negative.

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Abstract Number: 2427

The Positivity for Anti-centromere Antibody Makes Distinct Clinical Features in Primary Sjogren's Syndrome : Data from a Prospective Korean Nation-wide Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

	Total, n=318	Anti-centromere positive SS, n=53	Anti-centromere negative SS, n=265	*p* value
Age (years)	54 (45-60)	56 (48-62)	54 (45-60)	0.042*
Gender (female)	314 (98.7)	53 (100)	261 (98.5)	>0.999
Dry eyes	312 (98.1)	53 (100)	259 (97.7)	0.594
Dry mouth	311 (97.8)	52 (97.7)	259 (97.7)	>0.999
Xerostomia related items				
Unstimulated salivary flow rate < 1.5 ml in 15 min	201/238 (84.5)	36/39 (92.3)	165/199 (82.9)	0.139
Unstimulated salivary flow rate (ml/15min)	0.3 (0.0-1.2)	0.3 (0.1-0.5)	0.3 (0.0-1.2)	0.086
Xerostomia inventory	38 (30-43)	42 (34-46)	37 (30-43)	0.040*
Xeroophthalmia related items				
Schirmer I test <5 ml/5 min	242/298 (81.2)	36/44 (81.8)	206/254 (81.1)	0.911
Schirmer I test (ml/5 min)	3 (2-5)	4 (3-5)	3 (2-5)	0.038*
Tear break up time (sec)	3 (2-4)	4 (2-5)	3 (2-4)	0.028*
Meibomian gland dysfunction	160/228 (70.2)	24/32 (75.0)	136/196 (69.4)	0.520
OSS by SICCA method	4 (1-7)	3 (1-6)	4 (2-7)	0.106
OSS by van Bijsterveld's method	3 (1-6)	3 (1-5)	3 (1-6)	0.603
OSS by SICCA method ≥5 (or Bijsterveld's method ≥4)	105/223 (47.1)	12/32 (37.5)	93/191 (48.7)	0.240
Ocular surface disease index	39 (23-56)	34 (14-54)	40 (23-58)	0.295
Minor salivary gland biopsy positvity*	151/173 (87.3)	35/37 (94.6)	116/136 (85.3)	0.170
Focus score	3 (2-4)	3 (2-4)	4 (2-5)	0.176
VAS for Physician's global assessment	30 (17-45)	33 (10-45)	30 (17-45)	0.770
VAS for Patient's global assessment	65 (48-77)	65 (57-87)	64 (48-77)	0.088
ESSPRI	5.0 (4.0-6.7)	4.7 (4.0-6.0)	5.3 (4.3-6.7)	0.132
ESSPRI pain	3 (0-5)	2 (0-5)	3 (0-5)	0.041*
ESSPRI fatigue	5 (5-7)	5 (5-7)	5 (5-7)	0.363
ESSPRI Dryness	7 (5-8)	7 (5-10)	7 (5-8)	0.319
EuroQol-5 dimensions time tradeoff value	0.85 (0.77-0.91)	0.87 (0.80-0.91)	0.85 (0.77-0.90)	0.311
EuroQol VAS	65 (50-80)	60 (50-75)	65 (50-80)	0.116

Clinical features of 318 enrolled patients with primary Sjogren's syndrome (SS)

	Total, n=317	Anti-centromere positive SS, n=53	Anti-centromere negative SS, n=264	*p* value
Arthralgia/arthritis	143 (45.1)	17 (32.1)	126 (47.7)	0.037*
Raynaud's phenomenon	66 (20.8)	26 (49.1)	40 (15.2)	<0.001*
Lymphadenopathy	43 (13.6)	3 (5.7)	40 (15.2)	0.066
Pulmonary involvement	7 (2.2)	2 (3.8)	5 (1.9)	0.332
ILD	8 (2.5)	2 (3.8)	6 (2.3)	0.625
Cutaneous vasculitis	36 (11.4)	4 (7.5)	32 (12.1)	0.338
Liver involvement	13 (4.1)	7 (13.2)	6 (2.3)	0.002*
Lymphoma	1 (0.3)	0 (0)	1 (0.4)	>0.999
Splenomegaly	1 (0.3)	0 (0)	1 (0.4)	>0.999
Peripheral neuropathy	25 (7.9)	3 (5.7)	22 (8.3)	0.780
Myositis	1 (0.3)	0 (0)	1 (0.4)	>0.999
CNS disease	2 (0.6)	0 (0)	2 (0.8)	>0.999
Autoimmune thyroid disease	41 (12.9)	6 (11.3)	35 (13.3)	0.701
Kidney involement	6 (1.9)	0 (0)	6 (2.3)	0.594

Extraglandular manifestations

	Total, n=315	Anti-centromere positive SS, n=52	Anti-centromere negative SS, n=263	*p* value
White blood cell (x 10^3/mm^3)	4.590 (3.740-5.600)	4.940 (4.155-5.717)	4.520 (3.680-5.570)	0.097
Leukopenia (< 4.00 x 103/mm3)	97 (30.8)	9 (17.3)	88 (33.5)	0.021*
Absolute neutrophil count (x 10^3/mm^3)	2.355 (1.825-3.235)	2.625 (2.105-3.297)	2.315 (1.760-3.222)	0.121
Neutropenia (< 1.50 x 103/mm3)	41 (13.1)	5 (9.6)	36 (13.7)	0.42
Hemoglobin (g/dl)	12.9 (12.0-13.7)	13.2 (12.4-13.7)	12.8 (12.0-13.6)	0.043*
Anemia (< 12 g/dl)	70 (22.2)	7 (13.5)	63 (24.0)	0.096
Platelet (x 10^3/mm^3)	221 (189-256)	205 (186-253)	221 (190-257)	0.325
Thrombocytopenia (< 150 x 103/mm3)	23 (7.3)	3 (5.8)	20 (7.6)	0.778
Anti-nulcear antibody positivity (titer ≥ 32(	197/303 (65.0)	49/51 (96.1)	148/252 (58.7)	<0.001*
Rheumatoid factor positivity (> 20 IU/ml)	197/306 (64.4)	20 (38.5)	177/254 (69.7)	<0.001*
Anti-cyclic citrullinated peptides antibody (	1.4 (0.8-4.0)	1.3 (0.5-2.6)	1.4 (0.9-4.5)	0.053
β_2-microglobulin (μg/ml)	1.952 (1.609-2.437)	2.000 (1.789-2.092)	1.951 (1.615-2.458)	0.794
Hypergammaglobulinemia	145/309 (46.9)	15/51 (29.4)	130/258 (50.4)	0.006*
Immunoglobulin G (mg/dl)	1552 (1337-1948)	1361 (1129-1700)	1611 (1377-1972)	<0.001*
Immunoglobulin A (mg/dl)	265 (195-366)	249 (167-383)	267 (206-366)	0.356
Immunoglobulin M (mg/dl)	118 (86-154)	144 (108-193)	114 (83-149)	<0.001*
Cryoglobulin	5/292 (1.7)	0 (0)	5 (2.0)	>0.999
Low C3 (< 76 mg/dl)	50/310 (16.1)	9 (17.3)	41/258 (15.9)	0.800
Low C4 (< 12 mg/dl)	15/310 (4.8)	2 (3.8)	13/258 (4.8)	>0.999
C3 (mg/dl)	93 (82-102)	88 (80-99)	93 (82-103)	0.244
C4 (mg/dl)	22 (18-26)	21 (18-25)	22 (18-26)	0.336
Anti-Ro/SSA antibody positivity	283/317 (89.3)	32/53 (60.4)	251/264 (95.1)	<0.001*
Anti-La/SSB antibody positivity	161/314 (51.3)	16/50 (32.0)	145/264 (54.9)	0.003*
Anti-topoisomerase antibody positivity	6/294 (2.0)	4/46 (8.7)	2/248 (0.8)	0.006*
Anti-ribonucleoprotein antibody positivity	6/206 (2.9)	2/38 (5.3)	4/168 (2.4)	0.306
Anti-Jo-1 antibody positivity	3/304 (1.0)	0 (0)	3 (1.2)	>0.999
Anti-DNA antibody positivity	10/306 (3.3)	2/46 (4.3)	8/260 (3.1)	0.65

Serological features

Background/Purpose: To clarify clinical features of primary Sjogren's syndrome (SS) patients who show the positivity for anti-centromere antibody in Korea.

Methods: We assessed 318 patients who met 2016 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for primary SS. All patients were selected from the Korean Initiative of Primary Sjogren Syndrome (KISS), a prospective cohort. Among them, 53 patients were positive for anti-centromere antibody, while other 265 patients were not. We compared two groups in various clinical data including demographic features, extraglandular manifestations, clinical indices and laboratory values available from KISS database.

Results: The anti-centromere-positive SS group showed higher median age ($p = 0.042$), xerostomia inventory scores ($p = 0.040$), anti-nuclear antibody and anti-topoisomerase antibody positivity ($p < 0.001$, $p = 0.006$, respectively), more frequent Raynaud's phenomenon and liver involvement ($p < 0.001$, $p = 0.002$, respectively). On the other hand, less frequency of leukopenia ($p = 0.021$), rheumatoid factor and anti-Ro/SSA antibody positivity ($p < 0.001$, both), and hypergammaglobulinemia ($p = 0.006$) were observed in this SS group.

Conclusion: Distinguishing clinical features were discerned in primary SS patients with the positivity for anti-centromere antibody compared to patients without the antibody. This primary SS subset should be investigated further in future studies.

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Abstract Number: 2428

Serum Myositis Specific/associate Autoantibodies Help Identify Early Connective Tissue Diseases Relevant Interstitial Lung Diseases: A Medical Center Experience

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung diseases (ILD), a heterogeneous group of pulmonary disorders, originated from idiopathic causes or secondary to certain etiologies, such as infectious diseases, drugs, or connective tissue diseases (CTD). Common causes of CTD associated ILD (CTD-ILD) include rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc), polymyositis (PM), dermatomyositis (DM), and Sjogren's syndrome (SS). Specific autoantibodies in autoimmune rheumatic diseases (ARD) are clinically useful biomarkers associated with a particular disease and/or clinical manifestations. Myositis-specific autoantibodies (MSAs) and myositis associate autoantibodies (MAAs) have been applied for the diagnosis of PM/DM. MSAs were defined as autoantibodies relatively specific for PM/DM, while MAA could not only be identified in PM/DM but also could be noticed in other autoimmune rheumatic diseases. Some MSAs and MAAs have been detected in patients with ILD and PM/DM simultaneously or idiopathic ILD patients. However, the prevalence of MSAs and MAAs in CTD-ILD is lacking.

Purpose: This study aimed to define the prevalence of MSAs and MAAs in patients with clinical symptoms of ILD in the presence of a particular autoimmune rheumatic disease and to identify the correlation between the presence of MSA/MAAs and ARD specific autoantibodies (autoAb).

MAA				
Antibody	PM100	PM75	Ku	Ro52
Positive rate	3.22%	2.90%	4.35%	33.01%
MSA				
Antibody	oJ	EJ	PL-12	PL-7
Positive rate	0.16%	0.48%	1.45%	1.13%
Antibody	SRP	Jo-1	SAE1	NXP2
Positive rate	2.25%	3.38%	0.64%	1.29%
Antibody	MDA5	TIF1g	Mi-2b	Mi-2a
Positive rate	0.97%	1.45%	3.54%	0.64%

The prevalence of MSA and MAA in patients with CTD-ILD

ILD	ALL(n=58)	Percentage
MSA positivity		
Jo-1	11	18.97%
Mi-2	5	8.62%
SRP	2	3.45%
PL-7	0	0.00%
PL-12	3	5.17%
EJ	1	1.72%
OJ	0	0.00%
MDA5	3	5.17%
MAA positivity		
SSA/Ro-52	42	72.41%
Ku	1	1.72%
PM/Scl75	1	1.72%
PM/Scl100	4	6.90%
Disease positivity		
Polymyositis	12	20.68%
Dermatomyositis	12	20.68%
Sjogren's syndrome	38	65.51%
RA	6	10.34%
SLE	6	10.34%
Systemic sclerosis	1	1.72%

Sjogren's syndrome is the most common cause of CTD-ILD in the cohort.

Methods: 413 subjects who had been diagnosed with at least one of autoimmune rheumatic diseases, including RA, SLE, PM, DM, and SS were included in this prospective study at a single medical center between February 2018 and October 2018. All enrolled patients had experienced clinical evidences of pulmonary diseases and were suspicious of ILD, such as exertional dyspnea or abnormalities on the chest plain film. Serological immunotherapy strips were performed to detect MSA/MAAs. These patients received imaging examinations as well. Correlation analysis was performed among the different collected variables.

Results: The diagnosis of CTD-ILD were confirmed in 58 of 413 patients. The prevalence of MSAs and MAAs were 16.4% and 39.9%, respectively. The most frequently found autoantibody was anti-Ro-52 (33%), followed by anti-Ku (4.35%), anti-Mi-2 (4.1%) , anti-Jo-1 (3.38%), anti-PM/Scl100 (3.22%), anti-PM/Scl75 (2.9%), anti-SRP (2.3%), and anti-PL-12 (1.5%)(Table 1).

To our surprise, SS is the most common disease in these patients with CTD-ILD, followed by PM/DM. MSA/MAAs were identified in patients withRA and SLE relevant ILD (Table 2). Anti-SAE1 and anti-Ku autoAb are positively correlated with anti-RNP autoAb (Phi = 0.323 and 0.246, p = 0.012 and 0.045, respectively). Anti-MDA5 autoAb seems to be possibly associated with anti-La autoAb (p = 0.08)

Conclusion: Our data indicates that MSA/MAAs could be able to detected in CTD-ILD in addition to PM/DM-ILD. The diagnostic criteria of CTD-ILD is unavailable except patients have obvious clinical evidences and imaigings' manifestations. Define how the presence of serum MSA/MAAs are relevant to CTD-ILD could help contribute to early diagnosis and prevent poor prognosis and is warranted in the future.

Disclosure: C. Cheng, None; **W. Ju**, None; **T. Lee**, None; **E. Chao**, None; **H. Chen**, None; **F. Liu**, None; **D. Chang**, None; **C. LU**, None.

Abstract Number: 2429

Zipcode-Binding Protein 1 (ZBP1) Facilitates Ro60 Surface Translocation, Cellular Growth and Autoimmune Sequelae

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite the strong association of maternal anti-Ro60 autoantibodies in the development of SS, Neonatal Lupus (NL) and scLE, understanding causality is challenging given that the intracellular location of the target RNP antigen only becomes accessible to extracellular autoantibodies during cell death. While binding Y RNA is a property of Ro60 in dying cells, Ro60 contributes to events essential to proliferation including the degradation of non-coding RNAs. To define potentially targetable molecular events associated with Ro60 accessibility and their effects on proliferation, we evaluated two candidate chaperone Ro60 binding proteins, ZBP1 (also known as IGF2BP1, which has two RNA recognition domains and plays a role in nuclear export of protein) and PTBP1 (which binds RNA in heterogeneous nuclear complexes).

Methods: Short hairpin (sh)RNA knockdown (KD) of both ZPB1 and PTBP1 was accomplished by using MISSION pLKO.1 derived lentiviral vehicles for targeted shRNA to yield each of the specific depletions in human fetal fibroblasts. Affinity purified anti-Ro60 antibodies (AP60) isolated from the serum of 2 mothers of children with cardiac NL and control IgG isolated from a healthy donor were used to evaluate Ro60 surface translocation in intact and apoptotic cells by flow cytometry. Fibroblast proliferation was determined using 5-ethynyl-2′-deoxyuridine (EdU) incorporation.

Results: KD of targeted transcripts were confirmed by qPCR and western blot. Permeabilized KD and wildtype fibroblasts demonstrated equivalent intracellular expression of Ro60. As expected, flow cytometry with AP60 revealed no surface staining of non-permeabilized wildtype or KD fibroblasts. The next set of experiments addressed binding of AP60 to polyHEMA-apoptotic fibroblasts. Staining with annexin V (a proxy of apoptosis) was uniformly consistent between the wildtype and KD cells. As expected, compared to non-apoptotic fibroblasts, AP60 but not control donor IgG readily bound the surface of wildtype apoptotic fibroblasts, supporting that Ro60 was indeed translocated during apoptosis (MFI of 97 $\pm$ 5 vs 211 $\pm$ 14, respectively; $P < 0.05$; N=3). In contrast, binding of AP60 was significantly attenuated in the ZPB1 KD fibroblasts (81.5 $\pm$ 7; N = 3) vs anti-Ro binding of apoptotic wildtype fibroblasts

(P< 0.05). However, the binding of AP60 was equivalent in the apoptotic PTBP1 KD fibroblasts (MFI of 203 $\pm$ 6, N= 3, P=NS) compared to apoptotic wildtype fibroblasts. With regard to cell proliferation, the percent positive EdU cells of wildtype fetal fibroblasts, ZBP1 KD fibroblasts, and PTBP1 KD fibroblasts were 56%, 2% and 45%, respectively, a result suggesting that the loss of ZBP1 restrains cell cycle progression.

Conclusion: ZBP1 represents a novel and required chaperone for the translocation of Ro60 to the cell surface during apoptosis in addition to contributing to cell proliferation. Given that Ro60 antigen accessibility is essential, not only to the generation of anti-Ro60 responses but also to the formation of surface immune complexes and subsequent tissue injury, ZBP1 may represent a newly targetable candidate to forestall both the initiation and sequelae of auto-immunity.

Disclosure: F. DiDonato, None; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **R. Clancy**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2.

Abstract Number: 2430

Detection and Clinical Significance of Circulating M3 Muscarinic Acetylcholine Receptor Reactive Th17 Cells in Patients with Primary Sjögren's Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's syndrome (SS) is an autoimmune disease which is characterized by lymphocytic infiltration including $CD4^+$ IL-17 producing helper T (Th17) cells to the lacrimal and salivary glands. We previously detected anti-M3 muscarinic acetylcholine receptor (M3R) antibodies and M3R reactive $CD4^+$ IFNγ producing helper T (Th1) cells in patients with SS. Moreover, we clarified that M3R reactive Th1 and Th17 cells had pathogenic roles in the development of auto-immune sialadenitis in SS mice model. The purpose of this study was to identify circulating M3R reactive Th17 cells, those T cell epitopes, and the relationship between these cells and clinical features in patients with primary SS (pSS).

Methods: 1. Peripheral blood mononuclear cells (PBMCs) were isolated from 10 pSS patients and age-gender matched 10 healthy controls (HCs). According to their HLA-DRB1 typing, top 10 ranked 20 mer peptides from the full length of M3R, which were highly predicted to bind to each HLA molecules by using the immune epitope database website, were selected for each case. PBMCs were stimulated with these selected M3R peptides mixture for 40 hours, and M3R reactive IL-17 producing cells were detected by IL-17 enzyme-linked immunospot assay (ELISpot).

2. Clinical features were compared between M3R reactive IL-17 producing cells positive and negative pSS patients.

3. PBMCs from 5 pSS patients positive for M3R reactive IL-17 producing cells, were stimulated with each selected 12-20 mer M3R peptide separately, to identify the dominant M3R peptides responsible for IL-17 secretion.

4. To confirm that detected IL-17 producing cells were Th17 cells, peripheral $CD4^+$ T cells from 3 pSS patients positive for M3R reactive IL-17 producing cells, were co-cultured with dendritic cells (DCs) generated from peripheral $CD14^+$ monocytes in each case, and stimulated with the dominant M3R peptides identified in Methods 3.

Results: 1. 5 of 10 (50%) pSS patients, while none of 10 (0%) HCs, showed significantly increased IL-17 positive spots against selected M3R peptides mixture stimulation compared with non-stimulation in ELISpot. M3R reactive IL-17 producing cells were detected significantly more frequently in pSS than in HCs (p=0.03).

2. 5 pSS patients positive for M3R reactive IL-17 producing cells had significantly higher ESSDAI score than 5 negative pSS patients (8.4±4.8 vs 2.0±0.0, p=0.031).

3. In all 5 pSS patients positive for M3R reactive IL-17 producing cells described in Results 1, IL-17 was produced against M3R AA76-95 stimulation, showing that the sequence might be the dominant M3R peptide responsible for IL-17 secretion.

4. Co-cultured $CD4^+$ T cells with DCs under stimulation with the dominant M3R peptide identified in Results 3, showed significantly increased IL-17 positive spots than non-stimulation, clarifying that M3R reactive Th17 cells were detected.

Conclusion: We detected circulating M3R reactive Th17 cells in pSS patients using ELISpot for the first time. Moreover, T cell epitope of these cells was shown to be M3R AA76-95 in all M3R reactive Th17 cells positive pSS patients. Interestingly, M3R reactive Th17 cells might associate with higher ESSDAI score.

Disclosure: S. Abe, None; **H. Tsuboi**, None; **Y. Ono**, None; **F. Honda**, None; **M. Yagishita**, None; **I. Kurata**, None; **A. Ohyama**, None; **H. Takahashi**, None; **Y. Kondo**, None; **I. Matsumoto**, None; **T. Sumida**, None.

Abstract Number: 2431

Extracellular Vesicles in Primary Sjögren's Syndrome: A Promising Source for Novel Proteomic Biomarkers

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SESSION INFORMATION
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Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is a complex autoimmune disorder characterized by the specific involvement of salivary and lachrymal glands. In the recent past several attempts have been made by using a

proteomic approach to identify valid biomarkers for pSS in whole saliva. Extracellular vesicle (EVs) include exosomes, microvesicles and apoptotic body. Little is known about the potential advantages of EVs proteomics compared to the overall traditional concept of analyzing the proteome of whole saliva nor to what extent their content may reflect the phenotypic state of pSS. In this study, we used a sequential window acquisition of all the theoretical fragment ion spectra (SWATH-MS) approach to monitor the dynamics of saliva EVs sub-proteome of pSS patients compared to healthy controls (HC)

Methods: We included patients with a diagnosis of pSS made according to the AECG 2002 criteria and healthy volunteers as controls. Saliva was collected under standardized conditions. EVs were enriched by sequential ultra-centrifugation steps from saliva samples. Peptide identification and quantitation was performed using a SWATH-MS approach using an assay spectral library for peptide matching. Protein-protein interaction network and pathway analysis were carried out to figure out the most representative biological paths in pSS.

Results: We enrolled 26 pSS patients (AECG 2002 criteria) and 13 healthy subjects. Quantitative data showed a distinct separation between pSS group and HC group, indicating that pSS may influence the phenotype of protein cargoes of salivary EVs. The majority of the differentially expressed proteins were found to be up-regulated in EVs pSS compared to controls. A highly interconnected sub-network of protein involved in several inflammatory processes was generated. Among several inflammatory pathways found in this study, a particular emphasis was given to proteins belonging to IL-12 signaling such as annexin A2, macrophage migration inhibitory factor (MIF), S100A8-A9 and plastin-2 proteins.

Conclusion: Our results highlight the key role of EVs S100 proteins and MIF as putative biomarkers for salivary gland dysfunction in pSS suggesting that the inflammatory phenotype observed in pSS whole saliva is also extended to salivary EVs.

Disclosure: C. Baldini, None; **F. Finamore**, None; **F. Ferro**, None; **S. Rocchiccioli**, None; **M. Mosca**, None; **L. Mattii**, None; **A. Cecchettini**, None.

Abstract Number: 2432

Thymic Stromal Lymphopoietin (TSLP) as a Biomarker of Primary Sjögren's Syndrome (pSS) and Related Lymphoma: Results in Independent Cohorts

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Thymic stromal lymphopoietin (TSLP) has been implicated in primary Sjögren's syndrome (pSS) and related B-cell lymphoproliferation / lymphoma (NHL) by tissue studies on salivary glands (SG). It resulted significantly higher in the serum of pSS patients compared to non-pSS sicca and to healthy subjects, with the highest levels in NHL-pSS. The purpose of this work was to confirm that serum TSLP is elevated in pSS by the study of independent cohorts.

Methods: Serum TSLP levels were measured by ELISA in 91 pSS patients (F=86, 94.5%; mean age 57.2 years, 25-80) from the original cohort (cohort 1) of Udine (UD), Italy. In this study, one additional multicentre cohort (cohort 2) from the Italian SS Study Group (GRISS) was studied, including 125 pSS patients from the Universities of Roma (RO), L'Aquila (L'AQ), Pisa (PI) and Perugia (PG). pSS patients with active NHL (n=12 in cohort 1; n=1 in cohort 2) were excluded from comparative analyses to avoid bias. Secondly, additional serum samples from pSS-related NHL in stable and complete remission, from both cohort 1 and 2, were analysed in a separate subgroup (n = 12). Thirdly, a preliminary evaluation of serum TSLP was performed in pSS patients from a different geographical area (University of Athens, Greece; cohort 3).

Results: Cohort 2 included 125 pSS patients (F=114, 91.2%; mean age 58.1 years, 23-84): 124 benign, 1 with NHL. In this cohort, serum TSLP levels were confirmed to be high (mean 30.26 pg/mL, 0.41-95.21) and comparable to cohort 1 (mean 33.81 pg/mL, 0-140.8; p=ns). No difference was found by the separate analysis of pSS from single Centres between each other (RO n=49, mean 33.21, 1.4-95.21; L'AQ n=34, mean 38.6, 16.31-85.11; PI n=28, mean 20.23, 0.41-56.67; PG n=13, mean 19.39, 1.03-68.38; p=ns), and vs cohort 1 (p=ns). The only patient in cohort 2 with NHL showed serum TSLP of 160.91 pg/mL, comparable to the mean TSLP in the 12 UD pSS with NHL (151.96 pg/mL). Importantly, in pSS-related NHL in stable remission, serum TSLP resulted undetectable (7/13) or detectable at very low levels (6/13) (mean 10.46, 0-38.5), and significantly lower than in benign pSS patients from the two cohorts (n=203, mean 31.48, 0-140.8; p=0.0022). Metachronous samples from one patient, at the stage of NHL activity and then at NHL remission, showed a decrease in TSLP from 128.04 pg/mL to undetectable levels. Finally, TSLP levels were increased also in the Greek cohort (mean 54.9, 26.72-78.95), and significantly higher than the two Italian cohorts (p=0.0085 and p< 0.0001, vs cohort 1 and 2, respectively).

Conclusion: Serum TSLP levels are increased in pSS, as herein confirmed in independent cohorts. TSLP might be important in the disease pathophysiology, and mirrors the course of pSS-related B-cell lymphoproliferation. It may represent a novel important biomarker.

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Abstract Number: 2433

Fatigue in Primary Sjögren's Syndrome as a Manifestation of Heavier Disease Activity of Mucosa-Associated Lymphoid Tissue (MALT)

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SESSION INFORMATION
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Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
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Background/Purpose: Fatigue is one of the most prevalent and impacting symptoms in primary Sjögren's syndrome (pSS), significantly impairing the patient quality of life. To date, even though available measures of fatigue and other patient-reported symptoms (PROs) poorly correlate with pSS disease activity assessed by ESSDAI, therapeutic interventions reducing the burden of pSS disease activity showed utility in improving fatigue in pSS. The purpose of this study was to investigate if fatigue correlates to pSS features reflecting disease activity, by evaluating if a) higher fatigue severity is associated with a heavier involvement of mucosa-associated lymphoid tissue (MALT) in salivary gland (SG) as documented by histopathology or by the clinical presence of SG swelling, and b) if fatigue correlates to other pSS-related somatic symptoms, such as dryness and arthralgias.

Methods: 86 consecutive unselected pSS patients, fulfilling the latest ACR/EULAR pSS classification criteria, reported their degree of fatigue, general dryness, ocular dryness, oral dryness and pain on 10-cm VAS (range 0-100), and completed ESSPRI (range 0-10), PROFAD-SSI-SF (range 0-28) and EQ-5D-scale (0-100) questionnaires. Four subgroups of fatigue severity were studied (1): no fatigue (VAS=0): 12.8% (n=11); low fatigue (VAS=1-24): 25.3% (n=19); moderate fatigue (VAS=25-74): 58.7% (n=44); high fatigue (VAS=75-100): 16% (n=12). As previously reported (1), no significant difference between the four subgroups was observed in age, sex and prevalence of potential contributors to fatigue, such as autoimmune thyroiditis, anemia and fibromyalgia. Frequencies of peculiar pSS manifestations related to a heavier activity of MALT, at any time in the clinical history of patients, such as SG swelling, and a biopsy-proven myoepithelial sialadenitis (MESA) or pSS-related MALT lymphoma, were evaluated for each subgroup. Correlations between VAS fatigue and other PROs were finally performed.

Results: pSS patients with moderate or high fatigue VAS showed significantly higher frequencies of SG swelling ($p=0.0274$), and of MESA or lymphoma histological diagnosis ($p=0.0397$) compared to pSS patients with no or low levels of fatigue. VAS fatigue scores did not correlate with ESSDAI. Patients with higher levels of fatigue showed significant ($p< 0.0001$) higher scores in total ESSPRI, dryness-ESSPRI, pain-ESSPRI, ocular dryness VAS, oral dryness VAS, pain VAS, somatic fatigue domain of PROFAD, arthralgia domain of PROFAD, total SSI and PROFAD-SSI-SF, and reported worst scores in quality of life EQ-5D-scale.

Conclusion: Fatigue severity in pSS appears to mirror the degree of MALT involvement, which is the biological substrate of pSS itself where key pathogenetic events take place. A better definition of the immunobiological basis of pSS fatigue, starting from the study of the MALT, is therefore crucial to identify novel target therapies to treat fatigue, besides symptomatic agents. Since fatigue may also correlate with pSS somatic symptoms, such as dryness and arthralgia, the development of dedicated pSS scoring tools integrating both disease activity, in the MALT perspective, and PROs is definitely worthwhile.

Reference:

(1) Gandolfo S et al, ARD 2018,77(Suppl 2).

Disclosure: S. Gandolfo, None; **M. Binutti**, None; **E. Doriguzzi Breatta**, None; **C. Fabro**, None; **S. De Vita**, None.

Abstract Number: 2434

Risk of Lymphoma and Thyroid Cancer in Primary Sjögren's Syndrome Measured Using the Korean Health Insurance Claims Database

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The development of lymphomas is one of the most serious complications of SjS but the incidence, prevalence and estimated risk of lymphoma in primary SjS vary significantly worldwide. Meanwhile, studies from Taiwan and Spain, the estimated risk of thyroid cancer appears slightly increased in primary SjS compared with previous results. Although primary SjS is a very rare disease and many cases are required to determine the exact risk of malignancy in this condition, most epidemiological studies of primary SjS have been limited to a small number of cases such as case-control studies, leading to low-quality evidence. A large sample size with a significant number of cases is therefore required to analyse the risk of lymphoma and thyroid cancer in primary SjS. The aim of this study was to evaluate the incidence and risk of lymphoma and thyroid cancer in patients with primary Sjögren's syndrome (SjS) employing a large-scale assessment based on the Korean National Health Insurance Service (NHIS) claims database.

Methods: Primary SjS was identified using the Korean NHIS medical claims database between 2007 and 2017. The case definition required more than one visit based on the Sjögren's syndrome diagnostic code and the registration system for rare and incurable diseases. A 3-year washout period was applied in our study to exclude patients who were diagnosed before their information was entered into the national rare and incurable disease database. The presence of a connective tissue disease before the SjS diagnosis and within one year after the SjS diagnosis was ruled out in order to recruit primary SjS only. We included all admissions with a primary diagnosis of lymphoma and thyroid cancer.

Cancer	Sex and age	Observed	Expected	Incidence	95% CI	SIR	95% CI
Lymphoma	Total	12	2.58	0.17	0.09-0.32	4.66	2.69-7.55
	Sex						
	Male	1	0.51	0.14	0.00-1.11	1.97	0.10-9.33
	Female	11	2.07	0.18	0.08-0.34	5.32	2.98-8.81
	Age group, years						
	19-49	2	0.28	0.10	0.01-0.39	7.27	1.29-22.89
	50-69	3	0.94	0.10	0.02-0.32	3.20	0.87-8.28
	≥70	7	1.36	0.41	0.14-1.04	5.13	2.41-9.64
Thyroid cancer	Total	29	23.49	043	0.27-0.68	1.23	0.88-1.68
	Sex						
	Male	0	0.59	0.00	0.00-0.69	0.00	0.00-5.05
	Female	29	22.9	0.48	0.29-0.75	1.27	0.91-1.73
	Age group, years						
	19-49	7	7.68	0.33	0.12-0.81	0.91	0.43-1.71
	50-69	16	12.72	0.55	0.28-1.05	1.26	0.79-1.91
	>70	6	3.09	0.35	0.11-0.94	1.94	0.85-3.83

Incidence and SIR and 95% CI for lymphoma and thyroid cancer in patients with primary Sjogren's syndrome

Results: The primary SjS incidence was 1.88 cases/100,000 inhabitants. Female patients had a higher incidence than male patients, with a female-to-male ratio of 7.65:1. For primary SjS, the standardised incidence ratios for lymphoma and thyroid cancer were 4.66 (95% confidence interval [CI] 2.69–7.55) and 1.23 (95% CI 0.88–1.68), respectively. The lymphoma risk was 4.66-fold higher among the patients with primary SjS than in the general population. Compared with the general population, female patients with primary SjS had a 5.32-fold higher risk of developing lymphoma, while the male patients did not. Patients with primary SjS did not have a higher risk of developing thyroid cancer.

Conclusion: Primary SjS is associated with a higher risk of developing lymphoma. The lymphoma risk appears to have decreased compared with that in previous studies. Our study suggests that the risk of lymphoma or thyroid cancer with SjS is not higher than that reported in previous studies.

Disclosure: J. Ahn, None; **J. Hwang**, None; **G. Seo**, None.

Abstract Number: 2435

Data Driven Prediction Lymphoma Model and 10-year Overall Survival Rates of a Large Harmonized Cohort of Patients with Primary Sjögren's Syndrome Associated Lymphomas

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

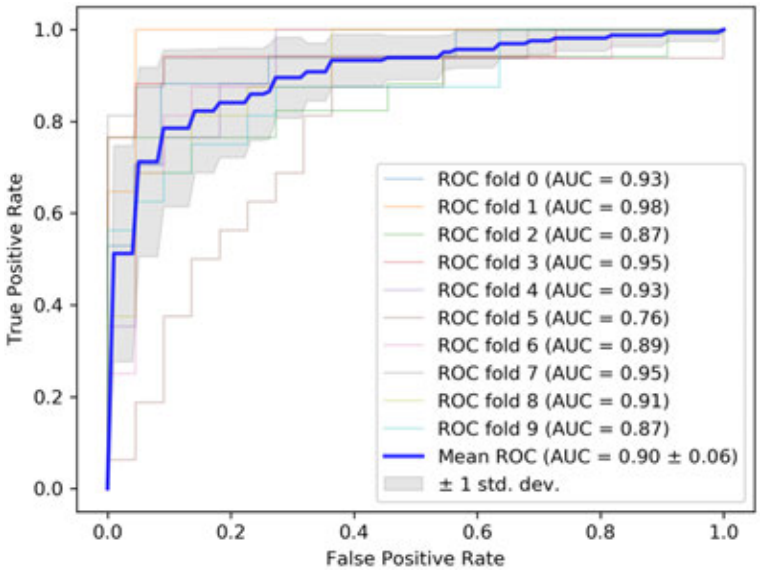
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

Session Type: Poster Session (Tuesday)

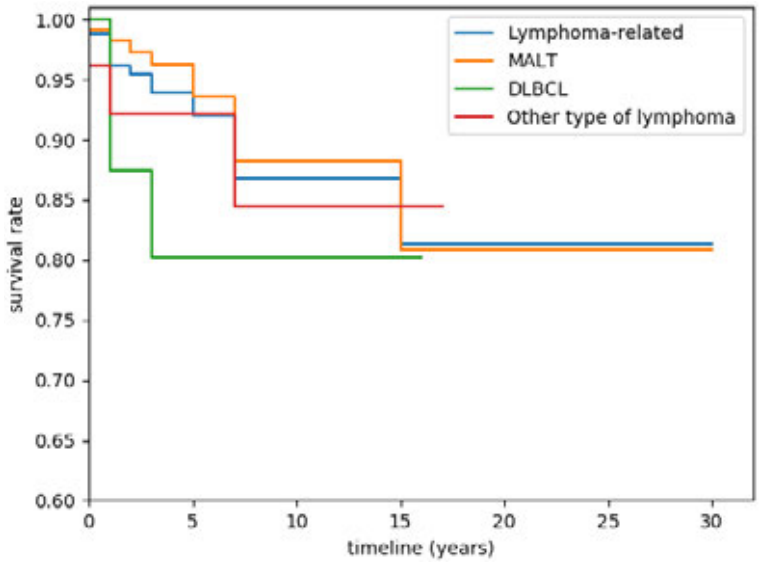
Session Time: 9:00AM–11:00AM

Background/Purpose: Non-Hodgkin's lymphomas (NHLs) may complicate primary Sjögren's syndrome (pSS) with significant impact on morbidity and mortality among patients. A large cohort of SS associated lymphoma patients was constructed from 3 specializing (pSS) centers [Udine, Athens, Piza-(UPA]) aiming to a) identify predictors of lymphoma by applying innovative data driven analysis tools b) estimate outcome and survival curves of SS associated lymphoma patients.

Methods: One hundred and sixty-two patients with SS associated lymphomas who fulfilled the 2016 ACR/EULAR were included in the study. Clinical, histological and laboratory data were collected. For lymphoma prediction, a robust decision-making machine learning algorithm was applied on the harmonized dataset using the Extreme Gradient Boosting (XGBoost) framework. Weak decision tree ensembles were combined through the gradient boosting optimization approach which reduces the prediction errors yielding a high-performance supervised learning model for predicting binary lymphoma outcomes in pSS. Two hundred and seventy-eight SS patients without lymphoma were recruited as controls for the prediction model matched according to age, gender and SS disease suration. A conventional 10-fold cross validation approach was then applied on the harmonized dataset to evaluate the sensitivity, specificity, and accuracy of the robust classifier. Kaplan-Meir survival curves



The ROC curve depicting the performance of the proposed lymphoma prediction model.



Kaplan-Meier curves for overall survival (OS) of SS HNLs patients and SS NHL histologic subgroups

for the total lymphoma population as well as for patients with mucosal associated lymphoid tissue lymphomas (MALTL), diffuse large B cell lymphomas (DLBCL) and other lymphoma types were generated. Lymphoma features were compared between Greek and Italian SS lymphoma patients including gender, age at lymphoma diagnosis, time from SS to lymphoma diagnosis, time from SS onset to lymphoma diagnosis, lymphoma follow up time and histologic lymphoma subtypes.

Results: No differences were found among the main lymphoma features mentioned above between Greek and Italian SS associated lymphoma patients. The median age at lymphoma diagnosis, time from SS diagnosis to lymphoma and lymphoma follow up time of the total population was 58 years old (range: 25-82), 4 years (range: -5, 30) and 6 years (range: 0, 30) respectively. Preliminary data analysis, revealed parotid gland enlargement >2months, neutrophils count at diagnosis, palpable purpura due to cryoglobulinemia, salivary or lachrymal gland enlargement at SS onset and hypergammaglobulinemia as main contributors of the most prominent decision tree pathways, with average area under the curve (AUC) =0.90, sensitivity=0.76, accuracy=0.83, and precision=0.84 (Figure 1). The estimated 10-year overall survival rates (OS) were 87% for the total population, 88,2% for patients with MALTL and 80% for DLBCL group (Figure 2).

Conclusion: To our knowledge, this is the largest pSS associated lymphomacohort. Preliminary harmonized pooling data, after applying novel bioinformatics tools, confirmed classical features as lymphoma predictors, pointing out the dynamic perspective of the proposed lymphoma prediction model. In addition, SS patients with NHLs display a favorable prognosis, especially those with MALTL.

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Abstract Number: 2436

The Salivary Glands as the Key Site of Inflammation and Lymphoproliferation Leading to Lymphoma in Primary Sjögren's Syndrome: Relevance for Dedicated Scoring, Biomarker Development and Lymphoma Prevention

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I

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Background/Purpose: Since the risk of B-cell non-Hodgkin's lymphoma (NHL) evolution is increased in primary Sjögren's syndrome (pSS), its prevention represents a relevant therapeutic end-point. A crucial preliminary step to this end is to determine the key site of inflammation and lymphoproliferation in pSS patients developing NHL.

We investigated the involvement of salivary gland (SG) mucosa-associated lymphoid tissue (MALT) in the development of NHL in pSS, based on: a) the history of major SG swelling (SGSW); b) the presence of geminal centres (GCs) in antedating salivary biopsies; and c) NHL localization itself, in particular salivary or lachrymal. The site of lymphoproliferation may be as relevant as the type of B-cells, given the role of microenvironment in B-cell expansion.

Methods: 165 cases pSS-related NHLs from the UPA Study Group (Udine, Pisa, Athens; 30, 27 and 108 cases respectively) were studied, with matched pSS controls with no lymphoma evolution. The history of SG and lachrymal swelling was evaluated in detail (both at pSS onset and in the follow-up before NHL development, episodical < or >2 months of duration, and chronic) together with the presence of GCs in SG biopsies well before NHL development, the different sites of NHL localization at its onset (salivary, lachrymal, gastric, lung, kidney, breast, skin, bone marrow, lymph nodes, spleen, others), and the NHL histotype.

Results: 165 pSS-related NHLs were studied (149 females: 90.3%; mean age: 56.3 years, range 25-82; mean time to NHL from pSS diagnosis: 5.8 years). Controls were 114, matched for sex, age and disease duration. By stepwise multivariate analyses, association with NHL was found for SGSW lasting > 2 months during follow-up (OR 16.41, 95%CI 5.97-45.08; p< 0.001) and SGSW at onset (OR 3.30, 95%CI 1.28-8.48; p< 0.013). In cases without SGSW at pSS onset, NHL evolution was higher only if SG swelling > 2 months occurred later (OR 114.29, 95%CI 14.05-929.80; p< 0.001). The SGs were then considered as the key site of inflammation and proliferation in pSS-related NHL if: 1) a history of SGSW (as above associated with NHL) was present, and/or 2) GCs were detectable in SG biopsy before NHL, and/or 3) NHL was indeed localized in the SG (n=105) or lachrymal glands (n=6) at its onset. 1 and/or 2 and/or 3 was detected in 85.4% of NHLs (140/165; 80,7% in Italy and 87.8% in Greece). Of note, this occurred more frequently than any lymphoma histotype (MALT NHL being, in any case, the largely most frequent histotype: 74.1%). No differences were noticed between the cohorts.

Conclusion: The SGs proved to be a key and early site of inflammation and lymphoproliferation in pSS-related lymphomagenesis, and the study of pSS-related NHL localization allowed a better understanding of the pathogenetic events implicated. NHL later develops in the SGs themselves or in other sites where MALT is accumulated, highlighting again the role of the local microenvironment. The SG MALT therefore represents a target to develop dedicated activity scoring and novel biomarker tools in pSS. Furthermore, a decrease in the amount and quality of SG MALT is a possible surrogate target for lymphoma prevention therapies in pSS, where long-term studies are poorly feasible.

Disclosure: S. De Vita, None; **S. Gandolfo**, None; **C. Baldini**, None; **M. Isola**, None; **M. Voulgarelis**, None; **A. Goules**, None; **G. De Marchi**, None; **M. Binutti**, None; **S. Zandonella Callegher**, None; **F. Ferro**, None; **C. Battistella**, None; **L. Chatzis**, None; **A. Tzioufas**, None.

Abstract Number: 2437

Autoantibodies from Sjögren's Syndrome Enhance NLRP3 Inflammasome Activation and IL-18 Production in Human Salivary Gland Cell Line A-253

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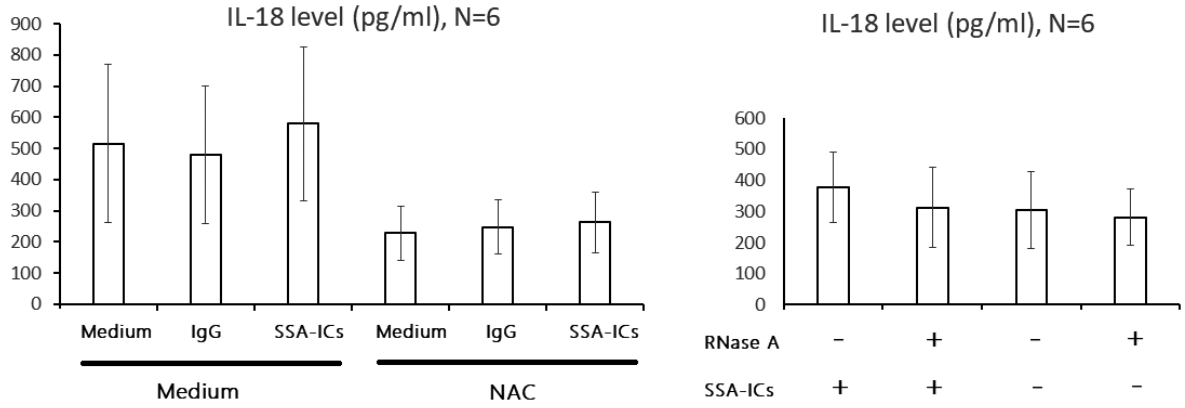
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

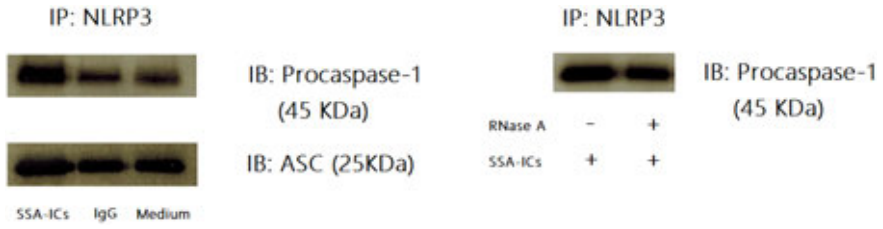
Background/Purpose: Primary Sjögren's syndrome (SS) is a chronic autoimmune epithelitis characterized by the presence of autoantibodies against SS-related antigen A (SSA) and lymphocytic infiltration of exocrine glands. The underlying mechanisms in the initiation and perpetuation of SS remain to be fully elucidated. Recently, the NOD-, LRR- and pyrin domain-containing protein 3 (NLRP3) inflammasome and pro-inflammatory cytokine Interleukin-18 (IL-18) have been implicated in the pathogenesis of SS. IL-18 serum concentrations were significantly higher in anti-SSA+ than in anti-SSA- SS patients and titers of anti-SSA antibodies were closely related with IL-18 protein levels. We hypothesized that immune complexes (ICs) containing anti-SSA antibodies (anti-SSA ICs) would lead to NLRP3 inflammasome activation and eventually to IL-18 production in an experimental model represented by the human salivary gland cell line A-253.

Methods: A-253 cells from human epidermoid carcinoma of the submaxillary gland were cultured. ICs were generated by incubation of cell culture supernatants (which contained released SSA autoantigens) with human anti-SSA antibody (OriGene Technologies, MD, USA), control human IgG and culture medium respectively for 1 hour and were stored at -80°C until used. A-253 cells were subjected to different stimulations for 4 hours. NLRP3, ASC, procaspase1 and IL-18 protein expression were measured by western blot and supernatant IL-18 level by enzyme-linked immunosorbent assay. Anti-SSA antibody and control human IgG were used at a final concentration of 80 ug/ml in all experiments. Results are presented as the mean ± S.D. The Student's t-test was used for comparisons between two groups.

Results: A253 cells spontaneously released IL-18 and supernatant levels of IL-18 were significantly increased after stimulation with anti-SSA ICs, compared with control human IgG (p=0.021). Reactive oxygen species (ROS) scav-



Effect of NAC and RNase A digestion of supernatants on anti-SSA ICs induced IL-18 production in A-253 cells.



Activation of the NLRP3 inflammasome by ICs containing anti-SSA antibodies.

engers, N-acetyl cysteine (NAC, 10mM), significantly decreased the secretion of IL-18 in each group ($p < 0.05$). More importantly, in the presence of NAC (10mM), anti-SSA ICs failed to induce IL-18 production from A-253 cells (p=0.19, compared to medium control). NLRP3 blockade by NAC were confirmed as NAC (25mM) treatment resulted in a marked decrease in the protein expression of the NLRP3 inflammasome and almost completely abolished the production of IL-18 from A-253 cells. Immunoprecipitation of NLRP3 was used to demonstrate that anti-SSA ICs potentiated coprecipitation of ASC and procaspase-1 proteins in A-253 cells. Furthermore, ICs containing anti-SSA antibodies and RNase A-digested cell culture supernatants (RNase A 100 ug/ml, incubation of 2 hours, for the removal of RNA from supernatants) decreased the amount of coprecipitated procaspase-1,secreted less IL-18 (p=0.02 compared to ICs containing no RNase A-digested supernatants) and lost the capacity to induce IL-18 production from A-253 cells (p=0.43, compared to medium control).

Conclusion: This novel study showed that ICs containing anti-SSA antibodies activated NLRP3 inflammasome and induced IL-18 secretion in A-253 cells. Endogenous RNA components of anti-SSA ICs and reactive oxygen species were responsible for this activation.

Disclosure: C. Wu, None; **K. Li**, None; **C. Yu**, None; **S. Hsieh**, None.

Abstract Number: 2438

Autoantibody Mediated Salivary Gland Hypofunction in Sjögren's Syndrome Involves Activation of Innate Immunity and Endothelial Cells

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The presence of autoantibodies reactive against the Ro52/TRIM21 protein is a hallmark of Sjögren's syndrome. We have reported that Ro52-immunized mice develop IgG deposits in their submandibular glands (SMG) and salivary gland dysfunction, which is facilitated by innate immune activation. This study was undertaken to investigate the mechanisms involved in anti-Ro52 mediated salivary gland hypofunction.

Methods: Female NZM2758 mice (12-14 wk old) were injected with alum on days 0 and 10, followed by passive transfer of immune sera from rabbits immunized either with Ro52 or the control protein, Maltose binding protein (MBP). Pilocarpine-induced saliva was measured to evaluate salivary gland function. Gene expression in SMG was analyzed by using the nCounter mouse inflammation panel (Nanostring Technologies Inc). Localization of IgG deposits in the SMG was investigated by immunofluorescence staining for anti-rabbit IgG and neuronal, and endothelial cell markers. Antibody penetration in the brain was studied by fMRI and immunostaining. To investigate the role of innate immunity, serum cytokines levels were measured by BioPlex mouse 23-plex assay in alum injected mice. Effects of cytokines on salivary epithelial cell tight junctions were evaluated by measuring trans-epithelial electrical resistance (TEER) *in vitro*.

Results: NZM2758 mice, pre-treated with alum, and injected with anti-Ro52 rabbit immune sera had significantly lower saliva production than mice receiving anti-MBP sera. The IgG deposits in SMG of anti-Ro52 recipient mice, co-localized with the endothelial cell marker CD31 in small blood vessels and were present in close proximity of the neurons. Compared to anti-MBP treated mice, the SMG from anti-Ro52 recipients showed significantly higher expression of *Ptgs2* that encodes for prostaglandin synthase (p=0.0043). Further, anti-Ro52 recipients showed IgG deposits along the cortical blood vessels in the brain and significant penetration of IgG into the brain parenchyma. IL1α, one of the cytokines induced by alum, induced a drop in TEER indicating disruption of tight junctional complexes.

Conclusion: Our data suggest that in Sjögren's syndrome, antibody deposition on endothelial cells in the vicinity of neurons in salivary glands induces localized inflammation that affects neuronal signaling and saliva production. The pathogenic effects of anti-Ro52 are further enhanced by inflammatory cytokines induced by innate immune activation. In addition, antibody penetration into the brain might contribute to the glandular hypofunction and neurological issues such as brain fog and cognitive dysfunction, a feature often seen in Sjögren's syndrome patients.

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Abstract Number: 2439

Cardiovascular Impact of Hyperuricemia in Patients with Psoriatic Arthritis

Ana B Arevalo,[1] Faris Haddadin,[1] Gustavo Contreras,[1] Shane Murray,[1] Yiming Luo,[1] and Yousaf Ali[1], [1]Mount Sinai St. Luke's - West/ Icahn School of Medicine, New York, NY

Baseline characteristics	PsA without HUC or gout (n=35,150)	PsA with HUC or gout (n=2,165)	p value
Age, mean	60.4 ± 0.2	65.9 ± 0.6	**<0.001**
Female, n (%)	20,500 (58.6)	770 (33.5)	**<0.001**
Race/ethnicity, n (%)			
• White	29,490 (84.2)	1,980 (86.1)	0.316
• Black	925 (2.6)	90 (3.9)	0.112
• Hispanic	1,689 (4.8)	40 (1.7)	**0.002**
• Asian	465 (1.3)	65 (2.8)	**0.024**
• Other	2,581 (7.3)	124 (5.4)	0.211
•			
Dyslipidemia, n (%)	12,630 (36.1)	1,164 (50.6)	**<0.001**
Hypertension, n (%)	17,680 (50.5)	1,140 (49.6)	0.712
Tobacco smoking, n (%)	9,160 (26.2)	725 (31.5)	**0.014**
CKD, n (%)	4,425 (12.6)	665 (28.9)	**<0.001**
Diabetes Mellitus, n (%)	5,595 (15.9)	445 (19.3)	**0.058**
Charlson index, n (%)			
• Index 0	9,820 (28.1)	295 (12.8)	**<0.001**
• Index 1	8,755 (25)	420 (18.3)	**0.001**
• Index 2	6,295 (17.9)	405 (17.6)	0.839
• Index ≥ 3	10,145 (28.9)	1,180 (51.3)	**<0.001**

Table 1 Baseline characteristics
Baseline characteristics of patients with PsA with and without HUC

	PsA without HUC/gout (n=35,150)	PsA with HUC/gout (n=2,165)	Prevalence Odds Ratio	p value
Afib	6.1%	17.8%	POR 1.79, 95% CI 1.31-2.45	**< 0.001**
CAD	19.4%	35.1%	POR 1.21, 95% CI 0.94-1.55	=0.131
HFpEF	3.1%	7.2%	POR 1.56, 95% CI 1.08-2.26	**=0.018**
Adjusted for age, gender, race, CAD, diabetes mellitus, HTN, hyperlipidemia, smoking, chronic kidney disease and Charlson comorbidity index				

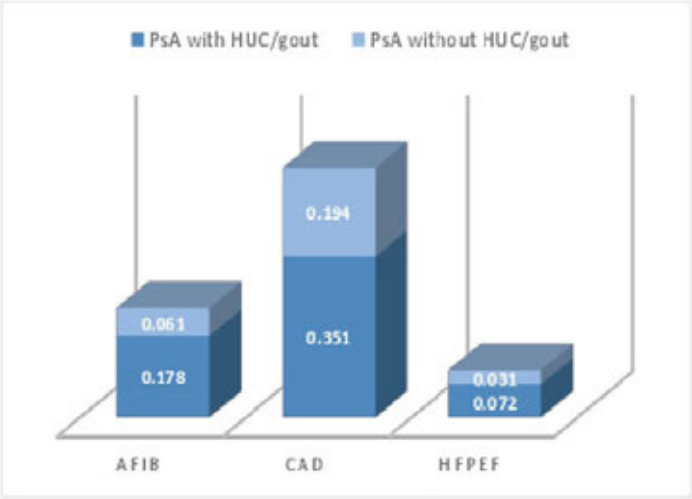

Table 2 Prevalence of Afib, CAD and HFpEF in PsA with and without HUC
Prevalence of Afib, CAD and HFpEF in patients with PsA with and without HUC

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory joint diseases (IJD) such as psoriatic arthritis (PsA) have an increased risk of cardiovascular disease (CVD) since inflammation plays a pivotal role in the pathogenesis of coronary artery disease (CAD), heart failure (HF) and atrial fibrillation (Afib)[1]. Ischemic heart disease and HF are the main causes of the increased and premature mortality among patients with IJD[2].

Additionally, patients with PsA have a prevalence of hyperuricemia (HUC) of 32%, 3 times greater as compared with the general population, which may be related to increased cell turnover as well as the release of pro-inflammatory cytokines and tumor necrosis factor[3].

Prolonged exposure to high levels of uric acid (UA) has been shown to result in oxidative stress causing endothelial dysfunction, ionic channel changes, atrial and ventricular remodeling[4]. There is experimental evidence indicating that uric acid stimulates renin-angiotensin-aldosterone system (RAAS), and it is associated with an increase in cardiac tis-

sue xanthine oxidase activity, all of which induce cardiomyocyte hypertrophy, myocardial oxidative stress, interstitial fibrosis and impaired diastolic relaxation[5].

Methods: This is a retrospective cohort study using the 2016 National Inpatient Sample (NIS) of adults diagnosed with PsA based on ICD-10 codes, to detect the prevalence of cardiovascular (CV) conditions such as CAD, Afib, and HF with preserved ejection fraction (HFpEF) in patients with concomitant HUC or gout versus age matched controls. Chi square was used for point prevalence and multivariate linear regression adjustment was used for age, gender, race, CAD, diabetes mellitus, HTN, hyperlipidemia (HLD), smoking, chronic kidney disease (CKD) and Charlson comorbidity index to obtain prevalence odds ratio (POR). We used STATA-15 for statistical analysis.

Results: We identified 37,315 patients with PsA, of whom 2,165 had concomitant HUC or gout (5.80%). Mean age was 61 years, 57% were females. Our results showed that PsA with concomitant HUC or gout compared to PsA without HUC or gout was associated with a higher rate of Afib (17.8% vs 6.1%, $p < 0.001$), CAD (35.1% vs 19.4%, $p < 0.001$) and HFpEF (7.2% vs 3.1%, $p < 0.001$). Furthermore, patients with PsA and HUC/gout appeared to have more risk of developing Afib (POR 1.79; 95%-CI 1.31-2.45; $p < 0.001$) and HFpEF (POR 1.56; 95%-CI 1.08-2.26; p=0.018), compared to patients with normal uric acid after multivariate-adjustment for risk factors. No statistical difference in CAD was identified between the two groups (POR 1.21; 95%-CI 0.94-1.55; p=0.131) after multivariate linear regression adjustment for confounders.

Conclusion: This study showed that HUC is independently associated with CVD, mainly with Afib and HFpEF in patients with PsA. It remains to be seen if a treat-to-target approach with normalization of UA in patients with PsA will result in improved CV outcomes. We believe that our findings merit further investigation and that this study adds weight to the hypothesis of UA as a potential risk factor for CVD. Prospective studies are needed to establish the role of serum uric acid level as a biomarker or predictor for CVD, including CAD, Afib and HFpEF in patients with PsA.

Disclosure: A. Arevalo, None; **F. Haddadin**, None; **G. Contreras**, None; **S. Murray**, None; **Y. Luo**, None; **Y. Ali**, None.

Abstract Number: 2440

Bone Mineral Density in Psoriatic Arthritis: Results from a Longitudinal Study

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Table 1: Cox proportional regression for patients with BMD testing done (n=214) versus patients without BMD testing (n=1112) adjusted by age at baseline, PsA duration and gender

	Univariate model			Multivariate Full model			Multivariate reduced model		
	HR	95% CI	*p*-value	HR	95% CI	*p*-value	HR	9 5%CI	*p*-value
Age at baseline				1.027	(1.015, 1.039)	<0.001	1.026	(1.014, 1.038)	<0.001
PsA duration				1.006	(0.989, 1.024)	0.48	1.007	(0.991, 1.023)	0.397
Male				1.069	(0.73, 1.567)	0.731	1.123	(0.773, 1.632)	0.542
Total damaged joints	1.003	(0.99, 1.015)	0.654	1.005	(0.993, 1.018)	0.403			
PASI	0.991	(0.967, 1.015)	0.454	0.99	(0.964, 1.017)	0.472			
Menopause	2.101	(1.378, 3.203)	<0.001	1.721	(1.098, 2.699)	0.018	1.802	(1.165, 2.789)	0.008
Malignancy	0.621	(0.341, 1.13)	0.119	0.699	(0.388, 1.258)	0.232			
Biologic use	2.253	(1.691, 3.002)	<0.001	2.024	(1.496, 2.739)	<0.001	2.056	(1.53, 2.764)	<0.001
DMARD use	1.533	(1.16, 2.025)	0.003	1.474	(1.096, 1.982)	0.01	1.41	(1.061, 1.875)	0.018
NSAID use	0.92	(0.694, 1.219)	0.561	0.937	(0.704, 1.248)	0.658			

HR, hazard ratio; CI, confidence interval; BMD, bone mineral density; PsA, psoriatic arthritis; NSAID, nonsteroidal anti-inflammatory drug; DMARD, disease-modifying antirheumatic drug; PASI, psoriasis area and severity index

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Evidence thus far on the effect of psoriatic arthritis (PsA) on bone mineral density (BMD) has been inconsistent. There is also insufficient guidance surrounding BMD testing in PsA patients. The purpose of this study was to determine BMD in the PsA population, factors associated with having BMD testing performed, and the effect of PsA clinical activity on BMD.

Methods: This retrospective cohort study was conducted at the Psoriatic Arthritis Clinic. Patients who had a BMD, irrespective of clinical indication were included. All patients in the cohort fulfilled the 2006 CASPAR criteria. Patients without T-scores reported, those with no visits prior to first BMD and those < 50 years old at the time of BMD were excluded. Descriptive statistics were used to summarize lumbar spine, femoral neck and total hip T-scores. Cox proportional hazard regression was performed on patients with BMDs with visits at the clinic within 2 years of their first BMD to determine covariates that predicted undergoing BMD testing. Subsequently, spearman correlation analysis was used to identify clinical features associated with low bone density. Linear regression analysis was used to model T-scores changes according to different clinical variables.

Results: Of the 214 patients with BMDs, 201 fulfilled inclusion criteria and were included for analysis. Higher age at initial visit (p< 0.001), menopause (p< 0.008), biologic therapy (p< 0.001) and disease-modifying antirheumatic drug (DMARD) use (p< 0.018) were associated with a higher chance of having a BMD when adjusted by age at baseline, PsA disease duration and gender (Table 1). The percentage of patients in the osteopenic and osteoporotic range of BMDs was 45.3% and 12.9% respectively. Mean T-scores at the lumbar spine, femoral neck and total hip were -0.3, -1.1 and -0.45 respectively. Higher body mass index (BMI) was significantly associated with a higher BMD across all measured sites (Table 2). Every unit increased in the Psoriasis Area Severity Index (PASI) was associated with a 0.084 decrease, whereas every unit increased in psoriasis body surface area (BSA) translated to a 0.804 decrease in lumbar spine T-score. For total hip T-scores, every additional damaged joint was associated with a 0.027 decrease in T-score.

Table 2: Spearman correlation analysis between clinical variables and BMD

	Lumbar Spine		Femoral Neck		Total Hip	
	ρ	*p*-value	ρ	*p*-value	ρ	*p*-value
Age	-0.0823	0.2477	-0.29	<0.0001	-0.1652	0.0357
Sex	0.0003	0.9971	-0.082	0.2582	-0.0343	0.6652
Total active joints	0.0379	0.5987	0.0907	0.2147	0.2228	0.0048
Total damaged joints	-0.0115	0.8734	-0.0914	0.2108	-0.1804	0.0229
Acute phase reactants	0.0104	0.8908	0.0334	0.6633	0.1102	0.1869
Biologics	0.0157	0.8256	0.1459	0.0435	0.13	0.0992
Methotrexate use	0.0602	0.3984	0.0427	0.5562	0.0751	0.3425
BSA	-0.0392	0.5874	-0.1141	0.12	-0.0483	0.5478
BMI	0.2266	0.014	0.1929	0.0416	0.4178	<0.0001
Bisphosphonate use	-0.1366	0.0978	-0.1465	0.0809	-0.1402	0.1267
PASI	0.0832	0.3051	0.1487	0.0713	-0.0055	0.9522
Renal disease	0.1361	0.2917	-0.1398	0.2744	-0.1855	0.1456
SF36 physical	-0.1376	0.1213	0.0006	0.9949	-0.0522	0.6024
SF36 mental	0.1204	0.176	0.2602	0.0038	0.1584	0.1118
HAQ	0.0687	0.4234	-0.0573	0.5124	0.0341	0.725
Patient global assessment	0.1004	0.2712	-0.0561	0.5462	0.052	0.5844
PASDAS	0.1816	0.1725	0.0709	0.6003	0.1397	0.3046

ρ=correlation coefficient

BMD, bone mineral density; SF-36, short form health survey; PASDAS, psoriatic arthritis disease activity score; BSA, body surface area; BMI, body mass index, PASI, psoriasis area and severity index; HAQ, health assessment questionnaire

Conclusion: Higher age at initial visit, menopausal status, biologic therapy and DMARD use predicted undergoing BMD testing in our cohort. 45.3% and 12.9% of patients with PsA had osteopenia and osteoporosis respectively, with mean T-scores at the lumbar spine, femoral neck and total hip being -0.3, -1.1 and -0.45 respectively. High BMI was significantly associated with a higher BMD. More research is needed to identify risk factors associated with worsening BMD over time in the PsA population.

Disclosure: T. Kwok, None; **J. Ye**, None; **D. Pereira**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, GSI, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5.

Abstract Number: 2441

Rates of Treated Depression Among Patients with Psoriatic Arthritis Treated with Apremilast, Biologics, DMARDs, and Corticosteroids in the US MarketScan Database

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Depression is common among PsA patients, but rates may differ by PsA treatment. Our study compares rates of treated depression by PsA treatment type in patients with PsA.

Methods: We conducted a population-based cohort study of treated PsA patients in the MarketScan database in 2014-2018. Cohort entry was the date of first prescription for a study drug (apremilast, tumor necrosis factor inhibitor [TNF-i] biologics, interleukin-17 or -12/23 inhibitor [IL-i] biologics, conventional DMARDs, or systemic corticosteroids) after March 21, 2014, the date on which apremilast was approved. Patients with antidepressant treatment before cohort entry were considered prevalent cases and excluded. A patient was considered currently exposed to a study drug from the prescription date through the prescription duration + 30 days. Patients were followed from cohort entry through censor date, defined as the first of the following: index date (date patient became a case), end of record,

Table. IRs for Treated Depression Alone Among PsA Patients Treated With Apremilast, DMARDs, Biologics, and Corticosteroids, and With at Least 1 Year of Recorded History Before the Cohort Entry Date

Exposure at the Index Date	Cases N=643	Person-Years Total=62,380	IR per 1,000 PY (95% CI)
DMARDs only	67	7,276	9.2 (7.1, 11.7)
Apremilast only	18	2,085	8.6 (5.1, 13.6)
TNF-i biologics only	187	19,983	9.4 (8.1, 10.8)
IL-i biologics only	42	3,603	11.7 (8.4, 15.8)
Corticosteroids only	44	3,705	11.9 (8.6, 15.9)
Apremilast + any nonsteroid	6	576	10.4 (3.8, 22.7)
TNF-i with DMARDs	42	4,460	9.4 (6.8, 12.7)
IL-i with DMARDs	7	389	18.0 (7.2, 37.1)
Corticosteroids + any other	92	6,276	14.7 (11.8, 18.0)
Past use*	138	14,027	9.8 (8.3, 11.6)

*Defined as any days after the end of "current use" and before a new study drug prescription.

or end of study period (October 31, 2018). Cases were patients with a first diagnosis of treated depression (without concurrent anxiety), defined as a diagnosis of depression with a prescription for an antidepressant within 30 days, and at least 7 days after cohort entry. We calculated incidence rates (IRs) and 95% confidence intervals (CIs) for each outcome per 1,000 patient-years among patients with at least 1 year of recorded medical history before their cohort entry date. Past use is defined as any days after the end of "current use" and before a new study drug prescription.

Results: The study population included 31,720 patients (median age at cohort entry: 53 years; female: 44%; history of depression: 4.8%). The IRs were similar between treatments with somewhat higher rates of treated depression among patients exposed to corticosteroids alone or in combination with any other study drug and patients exposed to IL-i alone or with DMARDs. Among the 643 treated depression cases, IRs (95% CIs) were as follows: apremilast only, 8.6 (5.1, 13.6); DMARDs only, 9.2 (7.1, 11.7); TNF-i only, 9.4 (8.1, 10.8); IL-i only, 11.7 (8.4, 15.8); and corticosteroids only, 11.9 (8.6, 15.9). The IRs for combination treatments were: TNF-i with DMARDs, 9.4 (6.8, 12.7); past use, 9.8 (8.3, 11.6); apremilast + other non-steroid study drugs, 10.4 (3.8, 22.7); corticosteroid + any other study drug, 14.7 (11.8, 18.0); and IL-i with DMARDs, 18.0 (7.2, 37.1).

Conclusion: Rates of treated depression were similar across PsA treatments, with somewhat higher rates of treated depression among patients exposed to corticosteroids alone or in combination with any other study drug and among patients exposed to IL-i alone or in combination with DMARDs.

Disclosure: C. Vasilakis-Scaramozza, Celgene Corporation, 2; **R. Persson**, Celgene Corporation, 2; **K. Wilcox Hagberg**, Celgene Corporation, 2; **S. Niemcryk**, Celgene Corporation, 3; **M. Peng**, Celgene Corporation, 3; **M. Paris**, Celgene Corporation, 3; **A. Lindholm**, Celgene Corporation, 3; **S. Jick**, Celgene Corporation, 2.

Abstract Number: 2442

The Relationship Between Fatigue and Disease Activity as Determined by Different Indices in Patients with Psoriatic Arthritis (PsA)

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Table 1: Fatigue score according to disease activity levels on DAPSA and DAS28.

	DAPSA			DAS28		
	Number of patients	Fatigue (VAS) Mean (SD)	p	Number of patients	Fatigue (VAS) Mean (SD)	p
Remission	29	2 (1.8)		276	3.9 (2.3)	
Low Disease Activity	256	3.7 (2.3)	<0.05	210	4.8 (2.6)	<0.05
Moderate Disease Activity	365	5.4 (2.5)		476	5.6 (2.6)	
High Disease Activity	214	6.8 (2.5)		94	7.4 (2.1)	

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Fatigue is a substantial problem in patients with psoriatic arthritis (PsA) that needs to be considered in the core set of domains. This study aimed to evaluate the relationship between fatigue and disease activity levels as determined by various scales in patients with PsA.

Methods: A total of 1134 patients (726 females, 408 males) diagnosed with PsA according to the CASPAR criteria were included (Turkish League Against Rheumatism (TLAR) Network multi-center study). Demographic features and clinical conditions of the patients were recorded. The following parameters were assessed: Maastricht Ankylosing Spondylitis Enthesis Score (MASES), Psoriasis Area and Severity Index (PASI), VAS fatigue (0-10 points: 0 - < 2 absent or mild, 2 - < 5 moderate, and 5 - 10 severe fatigue), Hospital Anxiety and Depression Scale (HAD), Fibromyalgia Rapid Screening Tool (FIRST). Disease activity was evaluated using the scores of DAS28, DAPSA, BASDAI, minimal disease activity (MDA), and very low disease activity (VLDA). The Spearman correlation coefficient was used for correlations. The Mann-Whitney U and chi-squared tests were used for between-group comparisons. A P value of less than 0.05 was considered to be statistically significant.

Results: The mean age of the patients was 46.9 (SD:12.1) years, and the median disease duration was four years (range 0-44 years). The mean fatigue score was 4.9 (SD:2.8), being absent or mild, moderate, and severe fatigue in 14.8%, 24.9%, and 60% of the patients, respectively. The mean of women's fatigue VAS was 5.4 (SD:2.7) while the men's fatigue VAS mean was 4.01 (SD:2.7) ($p< 0.05$). Fatigue has good correlation with VAS-pain (rho: 0.595), FIRST (rho: 0.513), anxiety (rho: 0.436), depression (rho: 0.388), MASES (rho: 0.297) and it has poor correlation with PASI (rho: 0.073). DAS28 and DAPSA remission, MDA, and VLDA rates were 24.3%, 2.6%, 13.6%, and 2.3%, respectively. The fatigue score was significantly lower in patients with DAS28 remission, DAPSA remission, MDA and VLDA ($p< 0.05$) and fatigue has a significant correlation with disease activity levels on DAS28 and DAPSA ($p< 0.05$) (Table 1). The DAS28, DAPSA, and BASDAI scores showed significant between-group differences across the three severity groups of fatigue, being the highest disease activity among patients with severe fatigue ($p< 0.05$). Significantly higher FIRST, anxiety and depression scores were noted in patients with DAS28 remission and fatigue compared with patients in remission but no fatigue ($p< 0.05$).

Conclusion: Fatigue is common and associated with disease activity, depression, anxiety, and fibromyalgia in PsA. Patients with remission, according to DAS28, DAPSA, and patients with MDA and VLDA have already mild to moderate fatigue.

Disclosure: M. Duruoz, İbrahim etem, 8, Abdi İbrahim, 8, Abdi Ibrahim, 8, Abvie, 2, 8, AMGEN, 8, AMGEN, Novartis, ILKO, ONKO, İbrahim Ethem, Abdi İbrahim, 8, Ibrahim Ethem, 8, ILKO, 8, Novartis, 8, ONKO, 8; **H. Gezer**, None; **K. Nas**, None; **E. Kilic**, None; **B. Sargin**, None; **S. Acer Kasman**, None; **H. Alkan**, None; **N. Sahin**, None; **G. Cengiz**, None; **N. Cuzdan**, None; **I. Albayrak Gezer**, None; **D. Keskin**, None; **C. Mulkoglu**, None; **H. Resorlu**, None; **Ş. Ataman**, None; **A. Bal**, None; **O. Kucukakkas**, None; **O. Yurdakul**, None; **M. Alkan Melikoglu**, None; **Y. Aydin**, None; **F. Ayhan**, None; **H. Bodur**, None; **M. Calis**, None; **E. Capkin**, None; **G. Devrimsel**, None; **K. Gök**, None; **S. Hizmetli**, None; **A. Kamanli**, None; **Y. Keskin**, None; **H. Kocabas**, None; **O. Kutluk**, None; **N. Sen**, None; **O. Sendur**, None; **I. Tekeoglu**, None; **S. Tolu**, None; **M. Toprak**, None; **T. Tuncer**, None.

Abstract Number: 2443

A Gender-based Analysis of Disease Activity and Its Relationship with Anxiety, Depression, Fatigue, and Fibromyalgia in Psoriatic Arthritis

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Table-1: Clinical and demographic features of women and men in PsA

	Women PsA	Men PsA
Number of patients n (%)	726 (64)	408 (36)
Age mean (SD)	47.4 (12.1)	46 (12.2)
Disease duration, year median (SD)	4 (0-44)	5 (0-42)
Body mass index mean (SD)	29.3(5.5)	27.7 (3.7)
Smoking status n (%)		
Smoker	143 (19.7)	149 (36.5)
Non-smoker	504 (69.4)	148 (36.3)
Ex-smoker	79 (10.9)	111 (27.2)

SD: Standart deviation, PsA: psoriatic arthritis

Table-2: Disease activity level, fatigue, anxiety, depression, FIRST scores of women and men in PsA

Parameter Mean (SD)	Women PsA	Men PsA	P
DAS28	3.5 (1.1)	3.03 (1.2)	*<0.05*
DAPSA	22.7 (15.5)	21.9 (17.8)	*<0.05*
cDAPSA	16.5 (11.8)	12.8 (9.6)	*<0.05*
BASDAI	4.5 (2)	3.9 (1.9)	*<0.05*
Fatigue	5.4 (2.7)	4.01 (2.7)	*<0.05*
Anxiety	7.3 (4.2)	5.5 (3.9)	*<0.05*
Depression	7.1 (4.2)	6.08 (4)	*<0.05*
FIRST score	2.9 (2.1)	1.6 (1.9)	*<0.05*

SD: Standart deviation, PsA: Psoriatic arthritis, DAS28: Disease Activity Score, DAPSA: Disease Activity in Psöriatic Arthritis, cDAPSA: clinical DAPSA, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: This study sought to compare the disease activity and its relationship with anxiety, depression, fatigue, and fibromyalgia of patients with psoriatic arthritis (PsA) between female and male gender in a Turkish population.

Methods: This multi-center Turkish League Against Rheumatism (TLAR) Network study included 1134 patients (726 females, 408 males) diagnosed with PsA according to the CASPAR criteria. Demographic and clinic parameters of the patients were recorded. Disease activity was evaluated using the scores of DAS28, DAPSA, cDAPSA, MDA, VLDA, and BASDAI. Health Assessment Questionnaire (HAQ), SF-36, Hospital Anxiety and Depression Scale (HAD), fatigue VAS (0-10), and Fibromyalgia Rapid Screening Tool (FIRST) were assessed. Disease activity and remission rates were compared in male and female patients, and their relationship with fatigue, anxiety, depression, and fibromyalgia scores was analyzed. The Spearman correlation coefficient was used to assess correlations. Comparisons were made using the Mann-Whitney U and chi-squared tests. $p< 0.05$ was considered significant.

Results: The mean age of the patients was 47.4 years (SD:12.1) for females, 46 years (SD:12.2) for males (Table-1). Disease activity scores of DAS28, DAPSA, cDAPSA, and BASDAI were significantly higher in women than in men ($p< 0.05$) (Table-2), with men having both higher remission and low-activity rates. There was a significant difference in the rate of MDA in favor of men ($p< 0.05$), but not in the rate of VLDA. The frequencies of dactylitis, enthesitis, inflammatory bowel disease, and arthritis were similar in men and women, while men had a higher incidence of spondylitis ($p< 0.05$). Both men and women with MDA had significant improvements in the scores of fatigue, HAQ, FIRST, anxiety and depression as well as in SF-36 subscales as compared with their counterparts without MDA ($p< 0.05$). Overall, although there was no significant between-group difference in age, body mass index, and disease duration, women had significantly higher anxiety, depression, and FIRST scores (fibromyalgia) compared with men ($p< 0.05$) (Table-2). In both men and women, disease activity scores of DAPSA, DAS28, and BASDAI were significantly correlated with the scores of FIRST, anxiety, depression, fatigue, and HAQ ($p< 0.05$).

Conclusion: In patients with PsA, women seem to have lower levels of remission and higher levels of disease activity than men. In both women and men, disease activity scores are significantly correlated with fatigue, functional status, anxiety, depression, fibromyalgia, and quality of life.

Disclosure: M. Duruoz, İbrahim etem, 8, Abdi İbrahim, 8, Abdi Ibrahim, 8, Abvie, 2, 8, AMGEN, 8, AMGEN, Novartis, ILKO, ONKO, İbrahim Ethem, Abdi İbrahim, 8, Ibrahim Ethem, 8, ILKO, 8, Novartis, 8, ONKO, 8; **H. Gezer**, None; **K. Nas**, None; **E. Kilic**, None; **B. Sargin**, None; **S. Acer Kasman**, None; **H. Alkan**, None; **N. Sahin**, None; **G. Cengiz**, None; **N. Cuzdan**, None; **I. Albayrak Gezer**, None; **D. Keskin**, None; **C. Mulkoglu**, None; **H. Resorlu**, None; **Ş. Ataman**, None; **A. Bal**, None; **O. Kucukakkas**, None; **O. Yurdakul**, None; **M. Alkan Melikoglu**, None; **Y. Aydin**, None; **F. Ayhan**, None; **H. Bodur**, None; **M. Calis**, None; **E. Capkin**, None; **G. Devrimsel**, None; **K. Gök**, None; **S. Hizmetli**, None; **A. Kamanli**, None; **Y. Keskin**, None; **H. Kocabas**, None; **O. Kutluk**, None; **N. Sen**, None; **O. Sendur**, None; **I. Tekeoglu**, None; **S. Tolu**, None; **M. Toprak**, None; **T. Tuncer**, None.

Abstract Number: 2444

Real-world Treatment Patterns Among Patients with Psoriatic Arthritis Treated with Biologic Therapies

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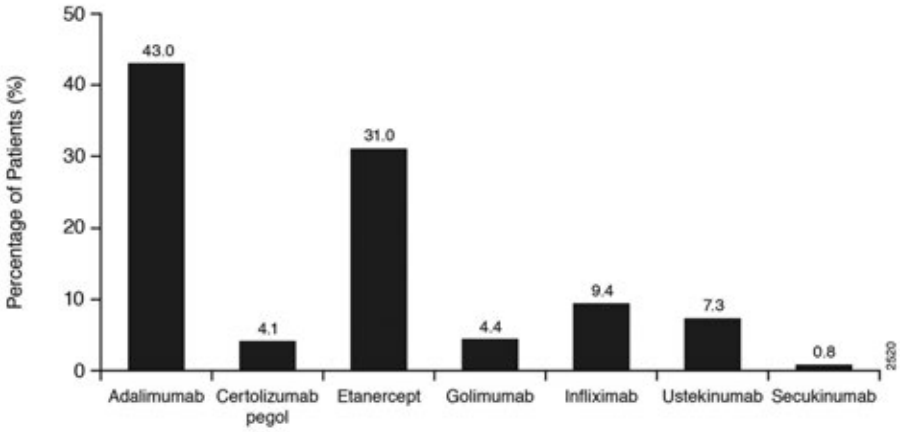
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Though biologic therapies have demonstrated long-term response in randomized clinical trials for psoriatic arthritis (PsA), such patient populations and settings may not reflect the general PsA population

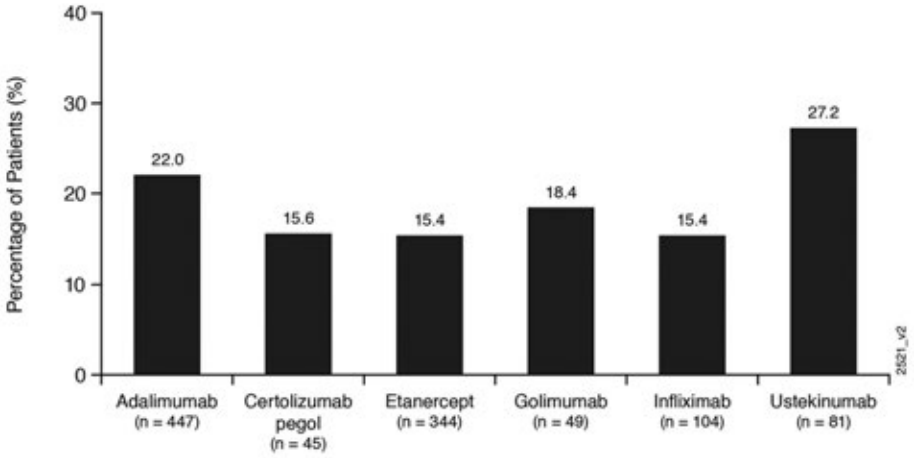
Figure 1. Index Biologic Among Study Patients (N = 1,109)



or real-life practice patterns, e.g., switching or adding therapies for patients with inadequately controlled symptoms. To better understand long-term patterns of biologic use for PsA treatment, this study aimed to describe 2-year adherence, persistence and switching among PsA patients initiated with adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, ustekinumab or secukinumab.

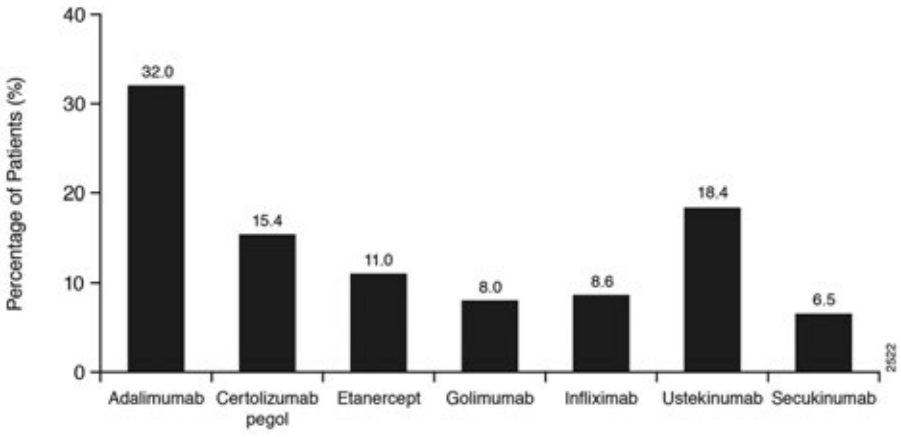
Methods: Adults with ≥ 1 medical or pharmacy claim for the above biologics during 1/1/2013 - 12/31/2016 were selected from Optum's de-identified Clinformatics® Data Mart Database. The date of the first claim was the index date. Patients were required to have ≥ 12 months pre-index and ≥ 24 months post-index continuous enrollment, with ≥2 PsA diagnoses ≥ 30 days apart during the 12-month pre-index through 12-month post-index period, and the first diagnosis occurring on or prior to the index date. Patients were excluded if they had ≥ 2 different biologics on the same day, a medical claim for rheumatoid arthritis, ankylosing spondylitis, other spondyloarthropathies, contraindications, or an index biologic filled during the 12-month pre-index period. Days' supply from medical claims (14.8% of all claims) was imputed based on the most frequently observed days' supply from pharmacy claims (84 days: ustekinumab; 28 or 30 days: other biologics). Baseline characteristics, adjunctive medication, number of patients who discontinued index biologic (ie, had a gap between fills of > 1.5 times the dispensed days' supply(135 days for ustekinumab; 45 days for other biologics), and number of patients who switched to a different biologic were reported by index biologic.

Figure 2. Percentage of Patients Who Persisted with Index Biologic for 24 Months (N = 1,100)



Note: No patients in the secukinumab cohort (n = 9) persisted for 24 months

Figure 3. Subsequent Biologic Among Patients Who Switched Biologic Therapies (N = 337)



Results: Of 1,109 patients included, mean (SD) age was 52.1 (12.8) years and 50.6% were female. The most common index biologics were adalimumab (43%) and etanercept (31%) [Fig 1]. During the 24-month follow-up period, 19.1% of patients persisted on their index biologic; ustekinumab had the highest persistence (27.2%) [Fig 2].The mean (SD) proportion of days covered (PDC) for index biologics was 0.47 (0.31). Of the 897 patients who discontinued their index biologic, 35.2% restarted the same biologic, 37.6% switched to a different biologic, and 33.6% discontinued without restarting or switching. The most common biologics that patients switched to were adalimumab (32%) and ustekinumab (18.4%) [Fig 3]. Of patients (n=864) who persisted with the index biologic for ≥ 90 days, 48.6% received ≥ 1 adjunctive medication during the period from 90 days post index to the end of persistence or 24 months, the most common were corticosteroids (27.7%), opioids (16.7%) and nonsteroidal anti-inflammatory drugs (13.4%).

Conclusion: In this real-world study of biologic PsA therapies, 24-month persistence ranged from 15.4%-27.2%, with ustekinumab having the highest persistence. Of patients who persisted on their index biologic for >90 days, nearly half used adjunctive therapy.

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Abstract Number: 2445

Enthesitis, Dactylitis, and Axial Disease in Psoriatic Arthritis (PsA): Impact on Patient Quality of Life and Work Productivity

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: PsA is a chronic, inflammatory disease characterised by peripheral arthritis, axial disease, dactylitis, enthesitis and skin and nail psoriasis. The impact of skin and joint components of the disease on quality of life and work productivity has been studied (1,2) but the impact of other manifestations has not. This analysis assessed the impact of enthesitis, dactylitis, and axial disease on quality of life and work productivity in PsA patients.

Methods: Cross-sectional study among patients with PsA recruited by rheumatologists and dermatologists in France, Germany, Italy, Spain, UK, and US. Data were collected from Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Physicians recorded (Yes/No) if patients currently presented with enthesitis, dactylitis, inflammatory back pain (IBP), and sacroiliitis (identified by x-ray or MRI). Multiple linear regression

Table 1: Impact of manifestations on PROs: Adjusted* regression coefficient and p-values

Outcome measure (N patients with data available)	Manifestation	Coef.	P value
EQ5D Index (N=771)	Enthesitis	-0.12	0.002
	Dactylitis	-0.07	0.010
	IBP	-0.07	0.001
	Sacroiliitis	-0.06	0.259
EQ5D VAS (N=784)	Enthesitis	-8.86	0.013
	Dactylitis	-4.31	0.123
	IBP	-4.10	0.073
	Sacroiliitis	-10.19	0.043
HAQ DI (N=744)	Enthesitis	0.17	0.096
	Dactylitis	0.17	0.024
	IBP	0.20	0.003
	Sacroiliitis	0.30	0.035
PsAID12 (N=750)	Enthesitis	1.32	0.002
	Dactylitis	1.09	0.003
	IBP	0.47	0.060
	Sacroiliitis	0.59	0.243
WPAI: Productivity (N=485)	Enthesitis	14.40	0.034
	Dactylitis	4.36	0.128
	IBP	4.07	0.185
	Sacroiliitis	-3.86	0.332

* Adjusted for age, gender, number of joints affected, time since diagnosis.

analyses were used to examine the impact of these manifestations on patient reported outcomes (PROs) including EQ5D index, EQ5D VAS, HAQ-DI, PsAID12, and WPAI. Models were adjusted for age, gender, number of joints affected, and time since diagnosis. There was no imputation of missing data.

Results: The sample included 1103 patients: mean age 47.6 [SD 13.2] years, 46% were female, 58% were working full time. Mean number of joints affected by PsA was 3.8 (SD 5.2), and 54.9% were receiving biologic treatment. Enthesitis (present in 6.3% of patients), dactylitis (8.0%) and IBP (12.6%) were associated with worse outcomes overall (Table 1); sacroiliitis (3.9%) was linked to worse physical function and quality of life.

Conclusion: In a multi-national, real-world PsA population, enthesitis, dactylitis, IBP, and sacroiliitis were significantly associated with worse patient quality of life and/or work productivity across a range of PROs independent of the number of joints affected. These manifestations should be considered alongside skin and joint components in order to optimize patient outcomes.

References:

1. Borman P, et al. Clin Rheumatol. 2007;26(3):330–4.

2. de Vlam K, et al. Rheumatol Ther. 2018;5(2):423–36.

Disclosure: J. Walsh, AbbVie, 2, 5, ABBVIE, NOVARTIS, LILLY, AMGEN, UCB, 5, Amgen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, PFIZER, ABBVIE, 2, UCB, 5; **A. Ogdie**, Novartis, 5, 9, Pfizer, 5, 9, Abbvie, 5, Amgen, 5, BMS, 5, Celgene, 5, Corrona, 5, Lilly, 5, Takeda, 5; **K. Michaud**, FORWARD, The National Databank for Rheumatic Diseases, 3, Pfizer, 2, Pfizer & Rheumatology Research Foundation, 2, Rheumatology Research Foundation, 2, University of Nebraska Medical Center, 3; **S. Peterson**, Janssen, 1, 3, BMS, 3; **E.**

Holdsworth, None; **C. Karyekar**, Abbott, 3, BMS, 3, Janssen, 1, 3, Janssen Scientific Affairs, LLC, 3, Novartis, 3; **N. Booth**, Adelphi Real World, 3; **J. Kemp**, None; **S. Chakravarty**, Janssen Research & Development, LLC, 3, Janssen Scientific Affairs, LLC, 1, 3, Johnson & Johnson, 1, 3; **S. Kafka**, Janssen Research & Development, LLC, 3, Janssen Scientific Affairs, LLC, 1, 3; **L. Gossec**, Abbvie, 5, AbbVie, 5, Abbvie, Biogen, BMS, Celgene, Lilly, Novartis, Pfizer, SAnofi-Aventis, UCB, 5, Amgen, 5, Biogen, 5, BMS, 2, 5, Celgene, 5, Celgene Corporation, 2, Janssen, 5, Lilly, 2, 5, MSD, 5, Nordic Pharma, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 5, Sanofi-Aventis, 5, UCB, 5.

Abstract Number: 2446

Gender Differences in Psoriatic Arthritis – Impact on Tumor Necrosis Factor Inhibitors Persistence and Response

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The impact of gender on tumor necrosis factor inhibitors (TNFi) effectiveness has been poorly studied in Psoriatic Arthritis (PsA) patients. The objective of this work was to study gender differences in persistence and response to a first TNFi in PsA patients.

Methods: PsA patients prospectively followed at the Rheumatic Diseases Portuguese Registry (Reuma.pt), treated with a first TNFi, between 2001 and 2017 were included. Drug retention was assessed by Kaplan-Meier survival analysis and Cox models adjusted for the year of starting a TNFi. Response rates measured by European League Against Rheumatism (EULAR) response, Disease Activity Index for Psoriatic Arthritis (DAPSA) remission, Minimal Disease Activity (MDA) and Ankylosing Spondylitis Disease Activity Score (ASDAS) response, applying the LUNDEX method, were compared between genders. Baseline predictors of discontinuation and response were identified (Cox and multivariable multinomial/logistic regression models).

Results: 750 PsA patients were included, mean age 47.6(±11.6) years and 50.3% (n=377) females .PsA females showed significantly different baseline PsA disease characteristics in comparison with males: were older, more of-

ten obese, had a longer delay between diagnosis and the start of the first TNFi, had more severe peripheral disease activity and required more often concomitant corticosteroids and conventional synthetic disease modifying anti-rheumatic drug. The overall TNFi survival rates for females were also significantly lower when compared with those from males. Additionally, PsA females experienced lower rates of response as assessed by good EULAR response, DAPSA remission and MDA at 3 and 6 months, and by ASDAS at 6 months. Female gender was further identified as an independent predictor factor of worse persistence and showed a lower chance of good EULAR response.

Conclusion: PsA female patients from Reuma.pt have distinct PsA features and worse persistence and response to a first TNFi in comparison with males. More successful therapeutic approaches will require considering the impact of gender on TNFi effectiveness.

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Abstract Number: 2447

Characteristics of Psoriasis Patients with Subclinical Signs of Musculoskeletal Involvement Detected by Fluorescence Optical Imaging and Confirmed by MRI-assessment

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriasis (Pso) is one of the most common chronic inflammatory skin diseases in Europe. Psoriatic arthritis (PsA) is closely associated to Pso whereas the skin manifestation appears usually years before PsA-related symptoms emerge. Up to 30% of Pso patients develop PsA, but there is no clear correlation between disease duration of Pso and PsA development. Therefore, biomarkers for its early detection are of major importance. In early PsA, changes in synovial vascularisation combined with increased expression of proangiogenic factors appear first. Therefore, imaging biomarkers for detection of changes in vascularisation can be useful for early detection of joint disease. Fluorescence-optical imaging (FOI) is a new method to detect changes in microvascularisation of the hands.

Methods: Sensitivity of FOI for detection of subclinical signs of inflammation as biomarker for early PsA was observed in a prospective, multicentre study (XCITING) including patients with dermatological confirmed skin psoriasis only. 411 patients were included from dermatology care units across Germany without diagnosis of PsA but potential risk factors for its development (nail psoriasis and/or joint pain or swelling within the last 6 months). Clinical exam-

	Psoriasis only (CE-, US-, FOI-) (n=95)	subclinical PsA with FOI+ only (CE/US -)		PsA confirmed (CE+) (n=143)
		MRI negative (n=70)	MRI positive (n=42)	
Baseline Characteristics				
Age (years, mean)	51,3	52,9	58,8	53,6
Sex (female, %)	52,6	65,7	57,1	51,1
BMI (kg/m^2, mean)	26,9	27	28,1	27,9
CRP (positive, %)	21,1	15,70	16,7	20,9
Concomitant Diseases (%)	53,7	45,7	71,4	58,7
Cardiovascular (ind. hypertension)	24,3	22,9	33,3	29,4
Diabetes Mellitus Type II, Lipid Disorders	6,3	8,6	33,3	11,88
Disease Characteristics				
Age of onset of PsO (years, mean)	27,6	29,9	31,4	31,5
Body Surface Area (%, mean)	8,1	6,8	8,9	9,5
Nail involvement PsO (%)*	54,7	51,4	33,3	55,2
Swollen Joint Count (mean)	0,6	0,1	0,8	3,4
Tender Joint Count (mean)	3,7	4,6	6,7	6,2
Global Disease Activity PsO (mean)	26,6	21,9	24,9	27,9
PsO Plaques at hands (yes, %)	21,1	15,7	35,7	26,6
Treatment for PsO	86,3	81,4	85,7	72,03
Topical steroids (%)	73,7	62,9	64,3	58,1
Topical Vitamin D (%)	40	21,4	30,9	28,7
UV treatment (%)	15,8	8,6	21,4	18,9
Systemic treatment for PsO	6,3	5,7	19,1	7,1
Methotrexat (%)	5,3	5,7	16,7	6,3
Cyclosporine A (%)	2,1	0	2,4	0,7
NSAID treatment (%)	23,2	18,8	40,5	32,9
Selective COX inhibitors (%)	3,2	5,7	4,8	7
Non-selective COX inhibitors (%)	20	12,9	35,7	25,9

*nail involvement was required for inclusion and cannot only be used with limitation within interpretation

ination (CE; swollen (66) and tender (68) joint count, enthesitis, dactylitis assessment) and standardised ultrasound (US) assessment was performed by a qualified rheumatologist to assess musculoskeletal inflammation. FOI was performed additionally. Data was analysed in focus on increased vascularisation of musculoskeletal structures of both hands as inflammatory marker. In cases of discrepant results (positive FOI and negative results for CE and US), MRI was performed to prove the findings.

Results: 83 of the 411 patients of the cohort were negative in all assessments (Pso only). 112 patients showed subclinical signs of musculoskeletal inflammation in the central reading of FOI, whereas CE and US were negative. In 37,5% of those patients, subclinical inflammation was confirmed by MRI assessment. Both groups (MRI pos and MRI neg) were well balanced in age, sex, BMI and CRP. In the MRI pos group, patients had more severe symptoms of Pso/musculoskeletal complains indicated by increased rates for use of topical or systemic treatments (e.g. MTX 16,7 % vs. 5,7% for Pso, Pso plaques at hands 35,7 vs 15,7%) and NSAID (NSAID 40,5% vs 18,8%) and showed an increased incidence for concomitant diseases (71,4% vs 45,7%). Compared to the PsA (n=143) and Pso (n=95) only group, the MRI pos group showed high similarities in age of onset of Pso (mean age 31,4 vs 31,5 years), in TJC (mean of 6,7 vs 6,2), NSAID use (40,5% vs 32,9%) and BSA (mean 8,9 vs 9,5%) to the diagnosed PsA group and in difference to the Pso only and MRI neg group (table 1).

Conclusion: Early detection of development of musculoskeletal symptoms in PsO patients seem to be associated to the severity of skin symptoms and its need for therapeutic intervention. The FOI and MRI pos group had high similarities in several domains with clinically evident active PsA but not to the Pso only group. Moreover, it seems that the use of systemic treatment with e.g. MTX for Pso has no preventive effect on the development of arthritis.

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Abstract Number: 2448

Factors Associated with Discordance Between Patient and Rheumatologist Assessment of Disease Activity in Psoriatic Arthritis Considered in Remission

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Assessment of disease activity in psoriatic arthritis (PsA) requires evaluation of multiple aspects and can be difficult. Perception of disease activity by patient and physician is frequently discordant (1). The aim of our study was to evaluate factors associated with persistence of disease activity evaluated by patients yet considered in remission by their rheumatologist.

Methods: We performed a transversal monocentric study. PsA patients were included if they met the CASPAR criteria and if they were considered in remission by their rheumatologist. Demographic data, characteristics of the disease, treatments were collected. Disease activity was evaluated by several scores: Disease Activity Score (DAS28-CRP), Simple Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Disease Activity in Psoriatic Arthritis (DAPSA), Minimal Disease Activity (MDA), modified Boolean remission criteria for PsA. We collected multiple Patient's Reported Outcomes (PROs): Psoriatic Arthritis Impact of Disease (PsAID), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Health Assessment Questionnaire (HAQ), Dermatology Life Quality Index (DLQI), Beck Depression Inventory (BDI), Fibromyalgia Rapid Screening Tool (FiRST), Pain Catastrophizing Scale (PCS). Discordance was defined by a difference between patient's and rheumatologist's global assessment ≥30/100 on a Visual Analogue Scale (VAS). Univariate and multivariate analyses were performed to evaluate factors associated with the presence of discordance.

Results: 62 PsA patients were included. 40.3 % were women and the mean (SD) age was 55 (14) years (Table 1). 61% patients were in remission (rheumatologist definition) for more than 12 months and 19% for less than 3 months. 50% met MDA, 63% DAS28-CRP < 2,6, 39% SDAI and CDAI remission, 27% DAPSA remission, and 8% Booleans remission criteria. 39% had a discordant disease activity assessment from their rheumatologist. In univariate analysis, factors associated with discordance were a history of depression, an associated fibromyalgia, a history of

	N=62
Age (year), mean (SD)	54.9 (14.4)
Man, n (%)	37 (59.7)
Body Mass Index (kg/m²), mean (SD)	26.6 (4.7)
Disease duration (year), mean (SD)	11 (6.9)
History of clinical enthesitis, n (%)	20 (32.3)
Axial impairment, n (%)	30 (48.4)
Fibromyalgia (ACR criteria), n (%)	6 (9.7)
Rheumatologist disease activity assessment on VAS (0-100), mean (SD)	5.7 (4.2)
Patient disease activity assessment on VAS (0-100), mean (SD)	27.3 (21.2)
Conventional synthetic DMARD, n (%)	13 (21)
Biologic DMARD, n (%)	45 (72.6)
History of corticosteroid use, n (%)	34 (54.8)

Table 1: Demographic characteristics of the 62 PsA patients.

	Discordant group n=24	Concordant group n=38	OR (95%CI)	P
History of depression, n (%)	9 (37.5)	1 (2,6)	22 (2.58-190.84)	<0.001
Fibromyalgia (ACR criteria), n (%)	5 (20.8)	1 (2.6)	9.74 (1.06-89.4)	0.028
At least one enthesitis on the Leeds Enthesitis Index, n (%)	14 (58.3)	34 (89.5)	0.17 (0.04-0.61)	0.006
Treatments				
Previous corticosteroid use, n (%)	8 (33.3%)	26 (68.4%)	0.23 (0.08-0.69)	0.007
Disease activity scores et Patients Reported Outcomes PROs				
DAS28-CRP > median (2.3), n (%)	19 (79.2)	12 (31.6)	8.23 (2.48-27.32)	<0.001
SDAI > median (5.09), n (%)	21 (87.5)	10 (26.3)	19.6 (4.79-80.18)	<0.001
CDAI > median (4.85), n (%)	21 (87.5)	10 (26.3)	19.6 (4.79-80.18)	<0.001
DAPSA > median (7.97), n (%)	22 (91.7)	9 (23.7)	35.4 (6.9-180.8)	<0.001
BDI > median (3), n (%)	14 (58.3)	10 (26.3)	3.92 (1.32-11.62)	0.012
FiRST > median (2), n (%)	17 (70.8)	11 (28.9)	5.95 (1.94-18.37)	0.001
BASDAI > median (2.45), n (%)	19 (79.2)	12 (31.6)	8.23 (2.48-27.32)	<0.001
HAQ> median (0.1), n (%)	16 (66.7)	11 (28.9)	4.91 (1.63-14.76)	0.004
PCS > median (9), n (%)	18 (75)	11 (28.9)	7.36 (2.3-23.5)	<0.001
PsAID > median (2.1), n (%)	18 (75)	13 (34.2)	5.77 (1.84-18.06)	0.002

Table 2: Factors associated with discordance: Univariate analysis

clinical enthesitis and a history of corticosteroid use (Table 2). All disease activity scores and PROs were higher in discordant group and were associated with discordance in univariate analysis. In multivariate analysis, discordance was associated with no previous corticosteroid use (OR 24.5 (95%CI 2.9-203.7), p=0.003), a higher BDI scale (OR

1.4 (95%CI 1.1-1.8) by supplementary point, p=0.017) and a higher DAPSA score (OR 1.5 (95%CI 1.2-2), p< 0.001) by supplementary point.

Conclusion: In this PsA cohort, discordance between patient and rheumatologist is very common. Discordance in assessment of disease activity was associated with no previous corticosteroid use, probably reflecting a less severe disease, presence of depressive symptoms and an increase of DAPSA, reflecting a more active disease.

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Abstract Number: 2449

Assessing Risk of PsA Progression: Results from a Combined Psoriasis-PsA Center Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

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Session Time: 9:00AM–11:00AM

Background/Purpose: About 30% of patients with skin psoriasis (PsO) develop psoriatic arthritis (PsA). The reasons for why only some progress to synovio-enthesial disease from skin involvement remains unknown. Genetic,

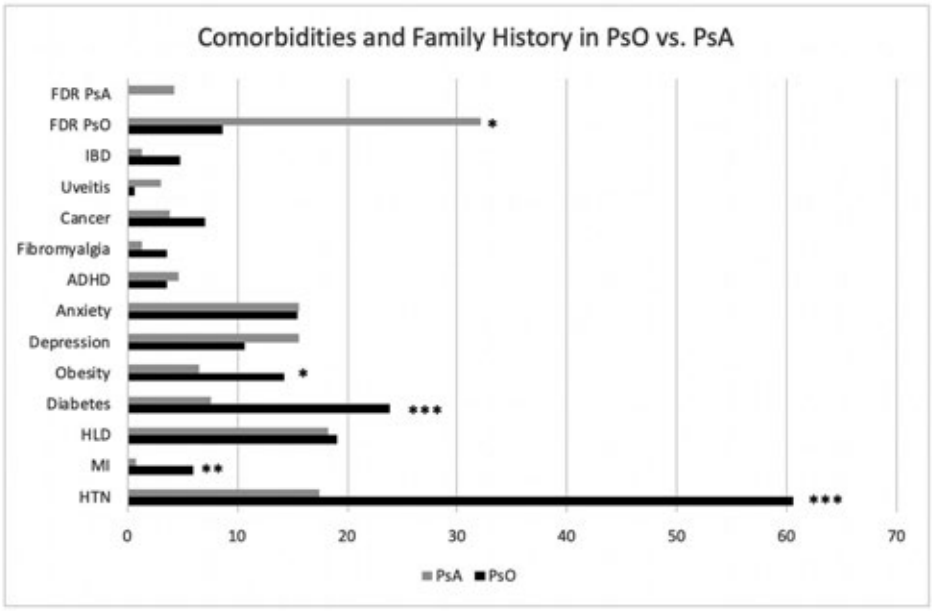

Figure 1. Prevalence of comorbidities and family history of psoriasis in PsO (n=84) and PsA (n=448) populations. *Represents statistical significance as defined by p< .05; **statistical significance as defined by p< .005; *** statistical significance as defined by p <.001.

Psoriasis Involvement	PsO (n=161)	PsA (n=448)	p-value	
Body Surface Area	**5.8**	**3.1**	**.003**	
Type of Psoriasis	PsO n(%)	PsA n(%)	p-value	
Plaque	128 (79.5)	323 (72.1)	.066	
Pustular	2 (1.2)	30 (6.7)	.014	
Guttate	10 (6.2)	24 (5.4)	.838	
Erythrodermic	1 (0.6)	3 (0.7)	.948	
Palmopustular	5 (3.1)	17 (3.8)	.275	
None	0 (0)	2 (0.4)	.999	
Area of involvement	PsO n(%)	PsA n(%)	p-value	Odds ratio (95%CI)
Inverse	33 (20.5)	86 (19.2)	.810	0.92 (.59, 1.44)
Scalp	**50 (31.1)**	**256 (57.1)**	**.000**	2.96 (2.02, 4.34)
Nail pitting	**6 (3.7)**	**124 (27.7)**	**.000**	9.89 (4.26, 22.93)
Nail dystrophy	**14 (8.7)**	**186 (41.5)**	**.000**	7.45 (4.17, 13.31)
Any nail involvement	**14 (8.7)**	**261 (58.3)**	**.000**	14.66 (8.21, 26.16)

Table 1. Psoriasis phenotype in PsO vs PsA population.

environmental and clinical-demographic factors have been implicated, but are yet to be characterized in specialized, combined care centers. We aim to describe clinical phenotypes differentiating patients with PsO from those with PsA at a large, urban tertiary care PsO-PsA clinic.

Methods: Consecutive adult patients meeting CASPAR criteria for PsA (n= 448) or with dermatologist diagnosed skin psoriasis only (n=161) were prospectively recruited at the NYU Psoriatic Arthritis Center and the NYU Psoriasis and Psoriatic Arthritis Clinic. All data was collected utilizing clinical visit notes and additional on-site questionnaires. Type of psoriasis and body surface area (BSA) was determined by dermatologists or rheumatologists specializing in psoriatic disease. Data was analyzed using statistical software SPSS using chi squared test with Yates Continuity Correction for dichotomous/categorical variables and t-test for continuous variables.

Results: Patients with PsO were more likely to be older (52.7 vs. 48.9, p=.032) and have hypertension, obesity, diabetes, and history of myocardial infarction (Figure 1). Patients with PsO had a statistically higher BSA than those with PsA (5.8% vs 3.1%, p=.003). While the type of psoriasis was similar, the site of psoriasis involvement (specifically the scalp and nail) differentiated the populations (Table 1). In PsA compared to PsO, the odds ratio of scalp involvement was 2.96 (95% Confidence Interval [CI] 2.02, 4.34) and that of nail involvement was 14.66 (95% CI 8.21, 26.16). Inverse psoriasis was not different between groups. Additionally, those with PsA were much more likely to have a first degree relative (FDR) with psoriasis compared to those with cutaneous disease alone (31.9% vs. 12.0%, p=.007) (Figure 1).

Conclusion: We report for the first time the comorbidities and psoriasis features of PsA and PsO populations in a large, combined center. We found that scalp involvement and any nail involvement was more prevalent in the PsA as compared to PsO. Only one previous study has identified scalp psoriasis[1] as a possible risk factor for progression, while previous studies looking at nail psoriasis reported much lower odds ratios[1,2]. Patients with PsA also demonstrated a higher number of FDRs with skin psoriasis, reinforcing the notion of strong heritability in PsA. The identification of risk factors for progression is of critical importance to study natural history of psoriatic disease and to inform the adequate design of prevention trials in psoriasis patients who have enriched features associated with future transition to synovio-enthesial disease.

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Abstract Number: 2450

The Paradoxical Effect of Depression on Psoriatic Arthritis Outcomes in a Combined Psoriasis-Psoriatic Arthritis Center

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogenous inflammatory disease affecting skin, joints, and other domains. While psychiatric diseases (i.e., depression and anxiety) are known comorbidities, little is known about their impact on disease severity and patient reported outcomes (PROs). The objective of this study was to characterize the prevalence of psychiatric comorbidities in an academic combined psoriasis-psoriatic arthritis center and determine their impact on PsA clinical and patient derived outcomes.

Methods: Consecutive adult patients meeting CASPAR criteria for PsA (n=436) were prospectively recruited at the NYU Psoriatic Arthritis Center. All data was collected from clinical visits utilizing a standardized EPIC template. Depression was defined by established diagnosis and/or use of anti-depressant medications. Objective measures of disease severity included swollen and tender joint counts (SJC/TJC) and PROs including RAPID3 scores. Data was analyzed using statistical software R.

BASELINE CHARACTERISTICS (n= 436)	
Age	47.5 (range 21-83)
Male	54% (237)
Race/Ethnicity	
White	74.1 % (323)
Black	1.4% (6)
Asian	5.7% (25)
Other/Unknown	19.3% (84)
Hispanic	4.8% (21)
Depression	19.5% (85)
Anxiety	15.6% (68)
ADHD	4.8 % (21)

Table 1. Baseline characteristics of our PsA population.

Outcomes at initial visit*	Depressed Mean	Non-Depressed Mean	p-values
TJC	3.5	2.9	.636
SJC	1.2	1.8	.086
RAPID3	12.7	10.4	**.035**
BSA	1.4	3.03	**.001**
Outcomes at subsequent visits	**Mean Difference** between Depressed and Non-Depressed	p-value	
TJC	0.6	.196	
SJC	-0.5	.134	
RAPID3	2.3	**.004**	
BSA	-1.38	**.015**	
Adjusted TJC**	0.7	.220	
Adjusted SJC**	-0.2	.470	
Adjusted RAPID3**	2.3	**.015**	
Adjusted BSA	-0.96	.293	

Table 2. Outcomes of tender and swollen joint counts and RAPID3 at baseline and over subsequent visits. *Outcomes at the initial visit were analyzed using t-test. Repeated measures were analyzed with Satterthwaite's approximations for the t test within mixed effects linear model with gaussian errors. P-values of equal to or less than .05 were considered significant. ** Adjusted using matching by propensity score that included age, sex, multiple comorbidities, and medication use.

Results: Our cohort was comprised of 436 patients: 54% male, mean age of 47 years, and mostly Caucasians (74.1%). Within our population, 19.5% had depression, 15.6% had anxiety, and 4.8% had ADHD (Table 1). Of those with depression, 71% were on anti-depressive medication. At the initial visit, patients with PsA and depression were more likely to be on medication(s) for PsA (80% vs 65%, p=.01) and had a trend towards higher rates of biologic use (47.5% vs 40.4%, p=.126). Those with depression had a similar TJC to their non-depressed counterparts, but had a trend towards fewer swollen joints and concomitant higher RAPID3 scores (Table 2). When analyzing repeated outcome measures over subsequent visits, individuals with depression were similarly more likely to have a higher TJC, a lower SJC, and a higher RAPID3 score (although only RAPID3 was found to be statistically significant, p=.004). Importantly, these findings persisted when analyzing participants that were matched with propensity scores to adjust for age, sex, comorbidities, and medication use. In addition to joint activity, psoriasis activity measured by body surface area (BSA) was lower in those who were depressed (1.4% vs 3.03%, p=.001) and these differences were maintained over subsequent visits.

Conclusion: Our results expand on prior reports of significantly elevated rates of depression in PsA. Notably, individuals with depression were more likely to be on medication(s) for their PsA, had fewer swollen joints, and a lower BSA but, paradoxically reported higher RAPID3 scores. This discrepancy is likely a manifestation of how depression could affect the way patients experience their PsA despite apparent improvement in skin and joint symptoms. Depression should, therefore, be considered a critical comorbidity when addressing PsA care in routine visits. Further work is needed to understand whether modulation of psychiatric comorbidities can lead to improved PsA outcomes.

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Abstract Number: 2451

Rates of Myocardial Infarction, Stroke, and Revascularization Among Patients with Psoriatic Arthritis Treated with Apremilast, Biologics, DMARDs, and Corticosteroids in the US MarketScan Database

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

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Background/Purpose: Patients with psoriatic arthritis (PsA) are at increased risk for cardiovascular (CV) events, but different treatment options may not have the same rates of CV events (Jamnitski et al. *Ann Rheum Dis.* 2013;72:211-6; Ogdie et al. *Curr Opin Rheumatol.* 2015;27:118-26). This study compared rates of myocardial infarction (MI), stroke, and revascularization by treatment type in patients with PsA.

Methods: We conducted a population-based cohort study of treated PsA patients in the MarketScan database from 2014 to 2016. The cohort entry was the date of the first prescription for a study drug (apremilast [APR] only or in combination with ≥1 other study drugs, anti-TNF-α biologics only, other biologics and DMARDs [OBDs] only, corticosteroids only, OBDs + corticosteroids, and anti-TNF-α biologics with OBDs and/or corticosteroids) after March 21, 2014, the date on which APR was approved. Patients were followed from cohort entry through the censor date, defined as the first of the following: the index date (date patient became a case), end of record, or end of study period (December 31, 2016). MI and stroke cases required 1 inpatient diagnosis plus 2 additional diagnoses on separate days; revascularization required a procedure code for revascularization without MI or stroke, all ≥7 days after cohort entry. A patient was considered currently exposed from the prescription date through the prescription duration + 30 days. We calculated incidence rates (IRs) and 95% CIs for each outcome per 100 patient-years among the entire population and in the subgroup of patients with no history of serious CV disease (CVD).

Results: The study population included 51,971 patients (median age: 52 years; female: 52%; serious CVD history: 4.0%). IRs were low for all outcomes, and between-treatment differences did not reach statistical significance (95% CIs for IRs were overlapping). Among the 187 MI cases, IRs (95% CIs) were as follows: for APR only, 0.10 (0.01, 0.35), or in combination, 0.49 (0.20, 1.02); anti-TNF-α biologics only, 0.13 (0.09, 0.19); anti-TNF-α biologics with OBDs and/or corticosteroids, 0.31 (0.22, 0.43); OBDs only, 0.32 (0.23, 0.44); corticosteroids only, 0.44 (0.27, 0.68); and OBDs + corticosteroids, 0.45 (0.24, 0.76). Among the 79 stroke cases, IRs (95% CIs) were as follows: for corticosteroids only, 0.08 (0.02, 0.22); anti-TNF-α biologics only, 0.09 (0.06, 0.13); for OBDs only, 0.10 (0.05, 0.17); anti-TNF-α biologics with OBDs and/or corticosteroids, 0.12 (0.06, 0.20); APR only, 0.15 (0.03, 0.43), or in combination, 0.14 (0.02, 0.51); and OBDs + corticosteroids, 0.21 (0.08, 0.45). Among the 292 revascularization cases, IRs (95% CIs) were as follows: for APR only, 0.25 (0.08, 0.57), or in combination, 0.42 (0.15, 0.92); anti-TNF-α biologics only, 0.36 (0.29, 0.44); anti-TNF-α biologics with OBDs and/or corticosteroids, 0.37 (0.27, 0.50); OBDs + corticosteroids, 0.38 (0.19, 0.68); OBDs only, 0.48 (0.36, 0.61); and corticosteroids only, 0.49 (0.31, 0.73). Among patients with no serious CVD history, IRs were generally lower but results were not materially different from the main analyses.

Conclusion: Rates of MI, stroke, and revascularization were low for treated PsA patients and were similar across treatments.

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Abstract Number: 2452

The Performance of a Multi-marker Genetic Test to Identify Patients with Psoriatic Arthritis Among Psoriasis Patients

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Background/Purpose: Improved understanding of the complex genetic architecture of PsA along with the reduction in the cost of genetic testing provide an opportunity to assess the application of genetic testing for PsA diagnosis in clinical setting. The study aimed to assess the performance of the multi-SNP genetic test in predicting a clinical diagnosis of PsA by a rheumatologist among psoriasis patients with musculoskeletal symptoms.

Methods: 328 patients with psoriasis and musculoskeletal symptoms that were referred to a rapid access clinic for suspected PsA were enrolled. Patients with a prior diagnosis of PsA were excluded. A rheumatologist evaluated all patients and classified them as "PsA" or "not PsA". All patients who were classified as not PsA at baseline were reassessed 1 year later to determine whether they have developed PsA. We tested 2 outcomes: 1) diagnosis of PsA at baseline; and 2) diagnosis of PsA at baseline or at 1 year. A custom multi-SNP genetic assay was genotyped on a

Table 1 – The association between genetic markers and psoriatic arthritis (selected top markers)

Chrom	SNP	Gene	PsA diagnosis at baseline (N=78)			PsA diagnosis at 1 year (N=95)		
			OR	95% CI	P value	OR	95% CI	P value
1	rs10888503	LCE3A	**1.78**	**1.21, 2.62**	**0.003**	**1.52**	**1.06, 2.17**	**0.02**
6	rs12191877	HLA-C	**0.52**	**0.31, 0.89**	**0.017**	0.63	0.39, 1.01	0.057
6	rs2894207	HLA-C*6	**0.57**	**0.35, 0.93**	**0.025**	**0.62**	**0.39, 0.99**	**0.045**
6	rs13214872	HLA-C	**0.57**	**0.34, 0.96**	**0.035**	0.65	0.41, 1.05	0.078
6	rs12189871	HLA-C	0.55	0.30, 1.01	0.055	0.68	0.40, 1.17	0.169
6	rs4406273	HLA-C	0.57	0.32, 1.02	0.057	0.67	0.40, 1.12	0.122
5	rs146571698	TNIP1	2.03	0.97, 4.24	0.061	**2.07**	**1.02, 4.18**	**0.044**
1	rs4655683	IL-23R	1.42	0.97, 2.08	0.069	**1.52**	**1.06, 2.17**	**0.022**
1	rs2201841	IL-23R	0.72	0.50, 1.05	0.087	0.68	0.48, 0.96	0.054
1	rs12044149	IL-23R	1.34	0.88,2.06	0.167	**1.60**	**1.07, 2.39**	**0.021**

Table 2 – Performance of the genetic assay in predicting PsA								
2A. Prediction of PsA at baseline (N=78)								
Method	**TP**	**TN**	**FP**	**FN**	**Accuracy**	**Sensitivity**	**Specificity**	**AUC**
Logistic Regression	12	242	8	66	0.77	0.15	0.97	0.62
Naïve Bayes	27	203	47	51	0.70	0.35	0.81	0.61
Random Forest	14	237	13	64	0.77	0.18	0.95	0.56
2B. Prediction of PsA at 1 year (N=95)								
Method	**TP**	**TN**	**FP**	**FN**	**Accuracy**	**Sensitivity**	**Specificity**	**AUC**
Logistic Regression	15	218	15	80	0.71	0.15	0.94	0.62
Naïve Bayes	21	203	30	74	0.68	0.22	0.87	0.62
Random Forest	16	204	29	79	0.67	0.17	0.88	0.55
AUC – Area under the receiver operating characteristic curve, FN – False negative, FP-False positive, TN-True negative, TP-true positive								

MassARRAY system (Agena Biosciences). The custom PsA weighted genetic panel included 42 variants in or near 20 genes based on genome-wide significance in PsA studies. We tested the ability of each genetic maker individually to predict PsA using logistic regression models adjusted for age and sex. Machine-learning methods including logistic regression, naïve bayes and random forest were used to identify the optimal prediction model. Age and sex were included in the prediction models.

Results: 78 patients were classified as PsA (PsA-baseline) and the remaining 250 patients as not PsA. After 1 year, 17 additional patients developed PsA resulting in 95 patients with PsA at 1 year (PsA-1 year). The association between the tested SNPs and PsA is shown in Table 1. Five SNPs located at LCE3A (rs10888503), TNIP1 (rs146571698) and IL-23R (rs4655683, rs2201841 and rs12044149) were associated with PsA-baseline or PsA-1 year (all $p< 0.05$). Of the three machine-learning methods used, logistic regression was found to have the best prediction properties (highest AUC). Overall, the performance of prediction models to classify patients as PsA was modest (see Table 2). The AUC, sensitivity and specificity of the models to predict PsA at baseline were: 0.62, 0.15, 0.97, respectively and at 1 year: 0.62, 0.15, 0.94.

Conclusion: Despite the association of several genetic markers with PsA, genetic testing has only a marginal effect on predicting a diagnosis of PsA among patients with psoriasis and musculoskeletal symptoms.

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Abstract Number: 2453

Static and Longitudinal Construct Validity of PROMIS CAT and Profile29 for Assessing Pain Interference, Physical Function and Fatigue in Psoriatic Arthritis

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Background/Purpose: Pain, physical function and fatigue are outcomes reported as having the greatest importance to people with psoriatic arthritis (PsA)[1,2]. We assessed these outcomes in participants in a longitudinal PsA study using Patient Reported Outcomes Measurement Information System (PROMIS) measures, which have not been used before in PsA, concomitantly with measures of PsA-specific disease activity and patient reported outcomes. The objective was to assess construct validity of PROMIS measures in PsA.

PROMIS Instrument T-scores and VAS and HAQ-DI scores	*Visit 1*	*Visit2*	*Change v2-v1*
Mean (SD)	*(n=100)*	*(n=93)*	*(n=93)*
PROMIS29 Pain Interference	55.5 (9.2)	54.8 (9.9)	-0.97 (6.1)
PROMIS-CAT Pain Interference	55.9 (9.4)	55.1 (9.9)	-0.92 (6.8)
Pain VAS (0-100)	36.1 (28.7)	34.5 (28.9)	-2.3 (23.7)
PROMIS29 Physical Function	43.0 (9.4)	44.1 (9.7)	1.0 (4.8)
PROMIS-CAT Physical Function	43.8 (10.3)	45.0 (10.0)	1.1 (4.0)
PROMIS-CAT Mobility	44.2 (9.3)	44.9 (9.3)	0.4 (4.1)
HAQ-DI (0-3)	0.7 (0.8)	0.6 (0.7)	-0.06 (0.3)
PROMIS29 Fatigue	53.8 (10.7)	53.2 (10.7)	-0.9 (7.3)
PROMIS-CAT Fatigue	54.1 (10.7)	53.0 (11.0)	-1.1 (7.2)
Fatigue VAS	41.7 (32.2)	38.0 (30.1)	-5.4 (23.2)

Table 1. Consecutive visit scores and change scores for PROMIS and legacy measures

Spearman correlation coefficients	*Rho (v1)*	*Rho (v2)*	*Rho (v2-v1)*
T-scores		*Pain VAS (0-100mm)*	
PROMIS29 Pain Interference	0.79 (0.69, 0.90)	0.86 (0.80, 0.92)	0.64 (0.49, 0.78)
PROMIS-CAT Pain Interference	0.78 (0.68, 0.88)	0.88 (0.83, 0.93)	0.54 (0.37, 0.72)
T-scores		*HAQ-DI (0-3)*	
PROMIS29 Physical Function	-0.88 (-0.94, -.83)	-0.87 (-0.92, -0.81)	-0.56 (-0.71, -0.40)
PROMIS-CAT Physical Function	-0.87 (-0.92, -0.83)	-0.86 (-0.91, -0.81)	-0.30 (-0.51, -0.08)
PROMIS-CAT Mobility	-0.84 (-0.91, -0.77)	-0.85 (-0.91, -0.79)	-0.33 (-0.51, -0.15)
T-scores		*Fatigue VAS (0-100mm)*	
PROMIS29 Fatigue	0.89 (0.84, 0.94)	0.89 (0.85, 0.94)	0.66 (0.53, 0.80)
PROMIS-CAT Fatigue	0.83 (0.75, 0.91)	0.86 (0.80, 0.93)	0.34 (0.13, 0.54)

Table 2. Spearman correlations (rho) between PROMIS and legacy measure, for point scores at consecutive visits and change scores between the visits

Methods: Participants were followed quarterly in conjunction with rheumatology clinical care visits. Disease activity was assessed using the clinical Disease Activity Score in Psoriatic Arthritis (cDAPSA), Minimal Disease Activity (MDA) state, and their components: 68 tender joint counts, 66 swollen joint counts, Leeds Enthesitis Index (LEI), patient global assessment visual analog scales (VAS) of arthritis/psoriasis and PsA, pain VAS, and Health Assessment Questionnaire Disability Index (HAQ-DI). Pain interference, Physical function/Mobility, and Fatigue PROMIS-Profile29 short forms and computer adaptive test (CAT) were also collected. Spearman correlation coefficients (rho) were computed between PROMIS Pain Interference and Pain Visual Analog Scale (VAS), PROMIS Physical Function/Mobility and HAQ-DI, and PROMIS Fatigue and Fatigue VAS to assess construct validity of point scores (at both visits) and change scores (between the two visits). Approximate 95% confidence intervals for rho were constructed by bootstrapping. We hypothesized moderate to high correlations for point scores (>0.6) and due to measurement error, low to moderate correlations for change scores (>0.2).

Results: One hundred participants had a baseline visit and 93 a second study visit, all met CASPAR PsA classification criteria. Mean age (SD) was 52 (12) years, PsA disease duration 17.7 (13) years, 88% were white and 60% female. At baseline, mean (SD) 68 tender and 66 swollen joint counts were 3.2 (4.9) and 3.1 (3.7), 8% had enthesitis, 3% dactylitis; mean(SD) HAQ-DI was 0.7(0.8), PsAID 3.21 (2.4), pain VAS 36 (28.7)mm, and patient global PsA 37.7 (31.7)mm. MDA state was met by 50% and DAPSA treat-to-target by 55%. Participants were treated with biologicals alone or in DMARD combination (44% TNFi, 5% IL17i, 6% IL12/23i), and 45% with DMARD alone. Visit and change PROMIS scores are shown in Table 1 and were higher/worse than the general population (reference T-score of 50) for Pain interference and Fatigue and lower/worse for Physical Function/Mobility. As hypothesized, correlations between point scores of PROMIS and corresponding instruments were high at both visits (>0.8) and correlation between change scores were low to moderate (>0.3) (Table 2).

Conclusion: PROMIS Profile29 short forms and corresponding PROMIS CAT Pain interference, Physical Function/Mobility and Fatigue have good construct validity for assessing PsA symptoms and life impact in both cross-sectional and longitudinal analyses. PROMIS measures can be used in psoriatic arthritis clinical care and research.

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Abstract Number: 2454

PROMIS Profile29 Differentiates Active Disease from Treat-to-Target State in Psoriatic Arthritis

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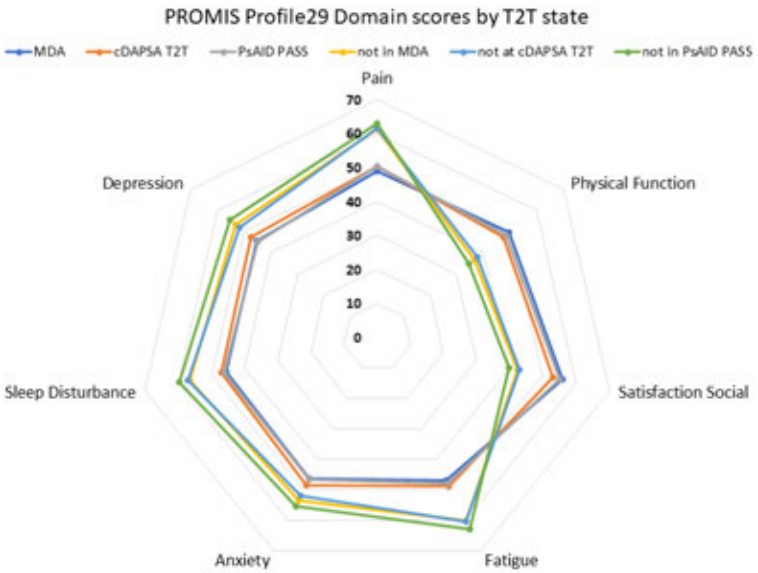

Figure 1. PROMIS Profile29 domain scores at visit1 in Psoriatic Arthritis treat-to-target (T2T) states defined by Minimal Disease Activity (MDA), clinical Disease Activity in Psoriatic Arthritis (cDAPSA) and Psoriatic Arthritis Impact of Disease (PsAID) patient acceptable symptom state (PASS). Mean domain scores in paired T2T states (T2T vs not T2T) are different with statistical significance p<0.001 for MDA; p<0.05 for CDAPSA except for anxiety (p=0.06); and p<0.0001 for PsAID PASS;

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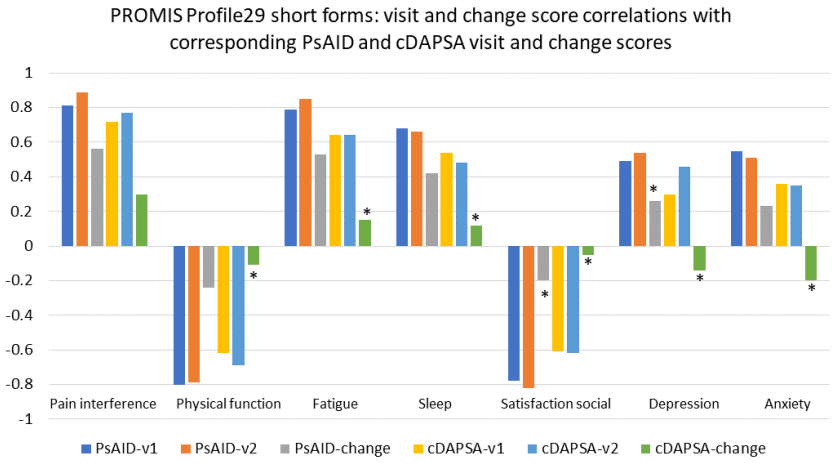

Figure 2. PROMIS Profile29 visit (v1 and v2) and change scores (v2-v1) correlations with corresponding PsAID and cDAPSA visit and change scores (all significant with p<0.05, except if marked with * correlation is not significant)

Background/Purpose: Psoriatic arthritis (PsA) symptoms and quality of life are core domains for PsA assessment[1]. The PROMIS Profile29 measures symptoms and quality of life using a T-score metric referenced to the general population, and has not been used in PsA before. The objective was to assess construct validity of the PROMIS Profile29 in PsA.

Methods: Participants with PsA were followed every 3-6 months in conjunction with rheumatology clinic visits. The PROMIS Profile29 was collected concomitantly with PsA specific measures: clinical Disease Activity Score in Psoriatic Arthritis (cDAPSA), Minimal Disease Activity (MDA), and the Psoriatic Arthritis Impact of Disease (PsAID)[2]. Multiple anchors were used to define treat-to-target (T2T) status: MDA vs not MDA[3], cDAPSA T2T (cDAPSA< 14) vs not[3], and the PsAID patient acceptable symptoms state (PsAID score< 4)[2]. We hypothesized mean PROMIS scores will be worse in patients not at T2T vs T2T, and that correlations with PsAID and cDAPSA will be moderate-high and low-moderate, respectively. We hypothesized lower correlations between change scores versus point scores due to measurement error.

Results: One hundred participants had a baseline visit and 93 a second study visit, all met CASPAR PsA classification criteria. Mean age (SD) was 52 (12) years, PsA disease duration 17.7 (13) years, 88% were white and 60% female. At baseline, mean (SD) tender (out of 68)/swollen (out of 66) joints were 3.2 (4.9)/3.1 (3.7), 8% had enthesitis, 3% dactylitis; mean(SD) HAQ-DI 0.7(0.8), PsAID 3.21 (2.4), pain VAS 36 (28.7)mm, patient global PsA 37.7 (31.7)mm. MDA state was met by 50% and DAPSA treat to target (T2T) by 55%. Treatment included biologicals alone/in DMARD combination in 55% and DMARD alone in 45%. PROMIS Profile29 T-scores (Figure 1) were significantly better across all domains for participants at T2T versus not, using MDA status and PsAID PASS. cDAPSA T2T status grouping yielded similar results, except for PROMIS Anxiety which was not significantly different. Results were consistent at both visits. Spearman correlations with PsAID were very high (>0.8) for PROMIS Profile29 Pain interference, Physical function, Fatigue and Satisfaction with social roles, high (>0.6) for Sleep, and moderate (>0.4) for Depression and Anxiety. Correlations with cDAPSA were high for Pain, Physical function, Fatigue and Satisfaction, moderate with Sleep, and low with Depression and Anxiety. Change score correlations were in the expected direction and lower than point correlations between Profile29 forms and PsAID, except for Depression (not significant). Change score correlations with cDAPSA were low and significant for Pain interference but not the other domains.

Conclusion: PROMIS Profile29 differentiated PsA T2T state from active disease using multiple anchors. Point PROMIS Profile 29 T-scores had moderate-high correlation with PsAID scores; and change scores had low-moderate correlation with PsAID change scores, meeting pre-specified hypotheses. The PROMIS Profile29 can be used to assess clinical status in PsA and it aligns with PsA specific disease activity and life impact measures.

Reference:

1. Orbai A, et al. Ann Rheum Dis 2017; 2.Gossec L, et al. Ann Rheum Dis 2014; 3. Smolen J, et al. Ann Rheum Dis. 2018;

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Abstract Number: 2455

Impact of Enthesitis on Patient Reported Outcomes and Physician Satisfaction with Treatment: Data from a Multinational Patient and Physician Survey

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Background/Purpose: Enthesitis, a characteristic clinical feature of psoriatic arthritis (PsA) [1], is a core outcome for PsA clinical trials. While enthesitis is considered important when treating patients with PsA [2], there is limited evidence to show the impact of enthesitis on patient reported outcomes (PROs) and physician satisfaction with treatment in the real-world. The objective of this analysis is to describe the impact of enthesitis on PROs and physician satisfaction with treatment in a real-world setting.

Methods: Cross-sectional survey of rheumatologists, dermatologists, and their consulting PsA patients in Australia, Canada, EU5, and US, conducted by Adelphi from 2018-2019. Physicians assessed current presence and severity (mild, moderate, or severe) of enthesitis, overall PsA disease severity, symptoms experienced, and their satisfaction with disease control the current treatment provides (5-point Likert scale: very satisfied to very dissatisfied). Patient self-reported data included current level of pain (1-10 scale), EQ-5D, Psoriatic Arthritis Impact of Disease (*PsAID12*), Health Assessment Questionnaire Disability Index (HAQ-DI) and Work Productivity and Activity Impairment Index

	Overall (N=3157)	With enthesitis (N=205)	Without enthesitis (N=2952)	P-value
Physician-rated disease severity, % (n)				<0.0001
Mild	74.9 (2634)	47.8 (98)	76.8 (2266)	
Moderate	22.2 (702)	40.0 (82)	21.0 (620)	
Severe	2.9 (91)	12.2 (25)	2.2 (66)	
Extraarticular manifestations present, % (n)				
Nail deformities	16.0 (506)	33.2 (68)	14.8 (438)	<0.0001
Dactylitis	7.5 (238)	31.7 (65)	5.9 (173)	<0.0001
Uveitis	0.8 (25)	1.0 (2)	0.8 (23)	0.6754
Inflammatory bowel disease	1.5 (46)	2.0 (4)	1.4 (42)	0.5386
Sacroiliitis	3.8 (121)	10.7 (22)	3.4 (99)	<0.0001
Inflammatory back pain	9.7 (305)	18.5 (38)	9.0 (267)	<0.0001
Number of joints affected by PsA, mean (n)	3.18 (3157)	6.13 (205)	2.98 (2952)	<0.0001

Table 1: Physician reported clinical characteristics

	Overall	With enthesitis	Without enthesitis	P-value
EQ-5D utility, mean (n)	0.81 (1399)	0.67 (91)	0.81 (1308)	<0.0001
HAQ-DI, mean (n)	0.50 (1349)	0.89 (88)	0.47 (1261)	<0.0001
WPAI				
% overall work impairment	22.64 (643)	34.75 (30)	22.05 (613)	0.0010
% work time missed (n)	5.25 (657)	5.00 (31)	5.26 (626)	0.9333
% impairment while working (n)	19.59 (723)	34.29 (35)	18.84 (688)	<0.0001
% activity impairment (n)	26.75 (1386)	40.77 (91)	25.76 (1295)	<0.0001
Pain, mean [1-10 scale]	3.01 (1382)	4.27 (90)	2.92 (1292)	<0.0001
PsAID12, mean (n)	2.48 (1157)	4.29 (69)	2.36 (1088)	<0.0001

Table 2: Patient reported outcomes

(WPAI-SHP). Bivariate descriptive analyses were conducted to describe features and outcomes in patients with and without enthesitis.

Results: Rheumatologists (454) and dermatologists (238) provided information related to enthesitis for 3157 PsA patients with 653 patient self-completed questionnaires. Mean (SD) age was 49.2 (13.3) years, mean (SD) body mass index 26.9 (6.5), 45.9% were female and 57.4% were in full-time employment. Enthesitis was present in 6.5% (205) of PsA patients surveyed. Patients with current enthesitis had worse overall disease severity compared to patients without enthesitis (12.2% vs. 2.2% severe) [Table 1]. Patients with enthesitis had more extraarticular manifestations, including nail deformities, dactylitis, sacroiliitis and inflammatory back pain than patients without enthesitis [Table 1]. Enthesitis was associated with more pain, worse quality of life (QoL), more disability, and a greater impact on work [Table 2]. Patients with enthesitis had increase NSAID and opioid pain medication use, but similar biologic use (with enthesitis 58.5% vs. without enthesitis 58.5%, p=1.0000). Physicians were significantly less satisfied with the control the current treatment provided in patients with enthesitis vs without enthesitis (57.6% vs 84.3% satisfied, p< 0.0001).

Conclusion: PsA patients with enthesitis had more severe disease and experienced worse QoL than patients without enthesitis but were not more likely to receive advanced therapies. Physicians were significantly more dissatisfied with treatment for patients with enthesitis than those without.

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Abstract Number: 2456

Validity of Patient-reported Cardiovascular Events in a Large Longitudinal Cohort of Patients with Psoriatic Arthritis and Psoriasis

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Table 1. Performance of rheumatologist-assessed cardiovascular event ascertainment

Cardiovascular Outcome	Number of events	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Any cardiovascular event	402	87.2	99.1	90.6	98.8
Angina	99	82.1	83.3	75.3	88.2
MI	88	88.2	90.6	84.8	92.8
Revascularization	101	48.0	99.0	98.0	66.5
CHF	48	56.4	94.5	71.0	90.2
CVA	42	81.8	94.7	75.0	96.4
TIA	24	33.3	98.3	70.0	92.6
CHF, congestive heart failure; CVA, cerebrovascular accident; MI, myocardial infarction; NPV, negative predictive value; PPV, positive predictive value; TIA, transient ischemic attack					

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Background/Purpose: Valuable information on cardiovascular disease outcomes can be obtained from large cohort studies. Such studies often rely on self-reported events, which are best validated with linkage to administrative data or review of electronic medical records. Given the increased risk of cardiovascular disease in patients with inflammatory rheumatic diseases, we aimed to assess the validity of patient-reported and physician-recorded cardiovascular events in a large cohort of patients with psoriatic disease.

Methods: Patients enrolled in a prospective cohort study from 1978 to 2018 were included in the analysis. Participants are assessed by a rheumatologist at 6-12 month intervals according to a standardized protocol that includes information about co-morbidities. Typically, patients report their co-morbidities which are recorded by the physician. The information is stored in a computerized database. We searched the database for records of cardiovascular events recorded during the follow-up period. Cardiovascular outcomes included angina, myocardial infarction (MI), revascularization procedures, congestive heart failure (CHF), cerebrovascular accident (CVA) and transient ischemic attack (TIA). The accuracy of the outcomes was verified by linkage to hospital discharge databases and review of medical records, which was considered as the gold standard ascertainment method. The validity of cardiovascular events by rheumatologists was assessed by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV).

Results: 2,171 patients with psoriatic disease (1498 with psoriatic arthritis, 673 with psoriasis only) were followed in the cohort from 1978 to 2018. The mean duration of follow-up for patients with psoriatic arthritis and psoriasis only was 10.2 years and 4.1 years, respectively. During this period, 204 (9.4%) patients reported 402 events (Table 1). Sixty-three events from the lost-to-follow up period were excluded. Overall the accuracy of patient-reported cardiovascular events was good to excellent. The sensitivity, specificity, PPV, NPV for any cardiovascular event was 87%, 99%, 91%, 99%, respectively. A similar pattern of results was observed for angina, MI and CVA. Identification of TIA showed poor sensitivity (33%), followed by revascularization (48%) and CHF (56%). NPV of all outcomes were excellent, with the exception of revascularization.

Conclusion: Ascertainment of self-reported cardiovascular events by rheumatologists is fairly accurate for identifying incident occurrences of cardiovascular events. Additional methods, such as record linkage and chart review, could be used to identify events not captured by conventional methods.

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Increased Prevalence of Systemic Lupus Erythematosus Co-morbidity in Patients with Psoriatic Arthritis: A Population-Based Case-Controlled Study

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Background/Purpose: Patients with psoriasis and psoriatic arthritis (PsA) can develop a variety of comorbidities which may influence the therapeutic regimen and affect treatment results. Previous studies show a high incidence of coexistence of psoriasis and systemic lupus erythematosus (SLE). Unlike psoriasis, the coexistence of PsA and SLE has been reported only in case reports.

Objective: To assess the prevalence of SLE in a PsA patient cohort and to compare it to the general population using the database of a large health care provider.

Methods: A retrospective database study consisting of a PsA cohort matched for age and sex with randomly selected control patients was conducted on patient data from 2002-2017, including demographics, clinical and laboratory manifestations of SLE and dispensed medications including SLE-inducing drugs. Statistical analysis was conducted using Student's t-test or Chi square test, as appropriate. In the PsA group, incidence density sampling procedure (SAS v9.4) was performed matching PsA patients without co-existing SLE as controls to each case of PsA with co-existing SLE by age and follow-up time which was defined as date of SLE diagnosis. Univariable and multivariable conditional logistic regression analysis were used to assess the influence of drugs, age at PsA diagnosis, PsA duration on development of SLE. All tests were 2-sided; p values of < 0.05 were considered statistically significant.

Results: The PsA study group consisted of 4836 subjects, median age of 56+/-15, 2603 (53.8%) of whom were female. The control group consisted of 24180 subjects matched for age and sex. Eighteen patients (0.37%) in the PsA study group and 39 patients (0.16%) in the control group where diagnosed with SLE (p=0.002). SLE patients without co-existing PsA had higher anti-double stranded DNA positivity (92.3% vs 66.7%, p=0.022) and positive

anti-cardiolipin antibodies (46.2% vs 16.7%, p=0.041). No other significant differences were observed between the two groups in terms of SLE clinical and laboratory manifestations. PsA patients with concomitant SLE compared to PsA patients without SLE were more often female (100% vs 53.7%, p< 0.0001), had more osteoporosis (38.9% vs 12.8%, p=0.005) and were more likely to be treated with beta blockers (27.8% vs 9.8% p=0.027). Usage of drugs with known potential to induce SLE prior to diagnosis of SLE was higher in the PsA than in the control group (11 out of 18 patients), but there was no difference in SLE manifestations between the groups. Univariable and multivariable conditional logistic regression analysis showed that older age at PsA diagnosis (p=0.001, p=0.008, respectively), shorter PsA duration (p= 0.06, p=0.03) and statin treatment (p=0.01, p=0.012) were associated with SLE in PsA patients.

Conclusion: A 2.3 fold increase in the prevalence of SLE in PsA patients relative to control group was found in our study population. Risk factors for SLE development included older age at PsA diagnosis, shorter PsA duration, and statin treatment. The positive correlates between SLE and PsA may point to common underlying pathogenetic pathways and may affect treatment choices and medication development.

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Abstract Number: 2458

Predictors of Structural Progression in Psoriatic Arthritis: Clinical versus Systemic Inflammation

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Background/Purpose: Psoriatic arthritis (PsA) belongs to the group of the spondylarthropathies. It is associated with psoriasis and typically seronegative for autoantibodies. PsA disease activity can be measured using the Disease Activity in Psoriatic Arthritis (DAPSA) score which is based on both clinical (e.g., swollen joint count, SJC) and systemic (e.g., C-reactive protein, CRP) markers of inflammation. However, the impact of clinical and systemic inflammation on structural progression is unclear. In this analysis, our aim was to determine the contribution of clinical and systemic inflammation to structural progression of patients with PsA.

Methods: In a secondary data analysis, we analyzed patient data from the IMPACT 2 trial of infliximab (INF) vs. placebo (PLC) in patients with established PsA (disease duration in years: INF: 7.5±7.8, PLC: 8.4±7.2). Concomitant methotrexate treatment was allowed but not mandatory in both treatment arms. We obtained modified Sharp-van-der-Heijde scores from X-rays performed at baseline and after one year to compute radiographic progression. We further extracted levels of SJC and CRP and calculated time-averaged SJC (taSJC) and CRP (taCRP) values to reflect the clinical and systemic inflammation, respectively. In a multivariable binary logistic regression model, we assessed the impact of taSJC, taCRP, and their interaction, on structural progression. Next, we divided patients into different subgroups depending on their taSJC and taCRP levels into active (+) or inactive (-). We tested whether radiographic progression was different in taSJC+ vs. taSJC- and taCRP+ vs. taCRP- using the Mann-Whitney-U-test.

Results: We analyzed available data of 151 patients (76 PLC, 75 INF). Patients in the INF arm showed no radiographic progression (-1.16±3.96), while patients in the PLC arm showed little progression (0.74±2.98). We therefore focused on the 76 PLC patients. Despite the small overall progression, taSJC, taCRP, and their interaction were associated with radiographic progression (OR for taSJC: 1.24, CI 95 %: 1.04-1.47, p=0.016; OR for taCRP: 6.08, CI 95%: 1.12-33.03, p=0.036; interaction term: p=0.097). Radiographic progression was higher in taSJC+ patients compared to taSJC- patients (1.05±3.21 and 0.56±2.30, respectively; p=0.016), as well as numerically higher without statistical significance in taCRP+ vs. taCRP- patients (1.14±3.23 and 0.05±2.37, respectively; p=0.532). Also, despite the limited power of subgroup analyses, there was evidence that SJC activity plays a role in CRP- patients (p=0.076), whereas CRP activity seems to be of less importance SJC- patients (p=0.643).

Conclusion: In patients with PsA, both clinical and systemic inflammation have impact on structural progression; in patients without systemic inflammation, clinical joint activity may still be considered as a risk factor for progression.

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Abstract Number: 2459

Effect of Obesity and Surgical Weight Loss on Joint Surgery Hospitalizations in Psoriatic Arthritis: Data from National Inpatient Sample

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Background/Purpose: Obesity is associated with higher disease activity and poor treatment response in patients with psoriatic arthritis (PsA). However, there is limited data as to how weight loss strategies affect outcomes in PsA. The aim of our study was to compare joint surgery hospitalizations (as a surrogate marker of significant radiographic damage and progression) among (1) obese and non-obese PsA patients; (2) obese PsA patients without and with a history of bariatric procedure and subsequent weight loss.

Methods: National Inpatient Sample (2001-2014) was used to identify patients ≥ 18 years with PsA using ICD-9 code 696.0. To increase the specificity, we excluded patients with RA (ICD-9 code 714.0) and AS (ICD-9 code 720.0) (Figure 1). For each patient with PsA, a matched control of the same age (± 1 year), sex, race/ethnicity and NIS stratum (based on hospital's census region or division, ownership/control, location/teaching, and bed size) was randomly selected. We compared hospitalizations for joint surgeries among obese and non-obese PsA patients. Joint surgeries related to trauma/fracture were excluded. Secondly, we performed univariate and multivariate regression to compare joint surgery hospitalizations among PsA patients with a history of bariatric procedure vs. those without bariatric procedure. For this analysis, hospitalizations prior to 2006 were excluded as the ICD-9 code for history of

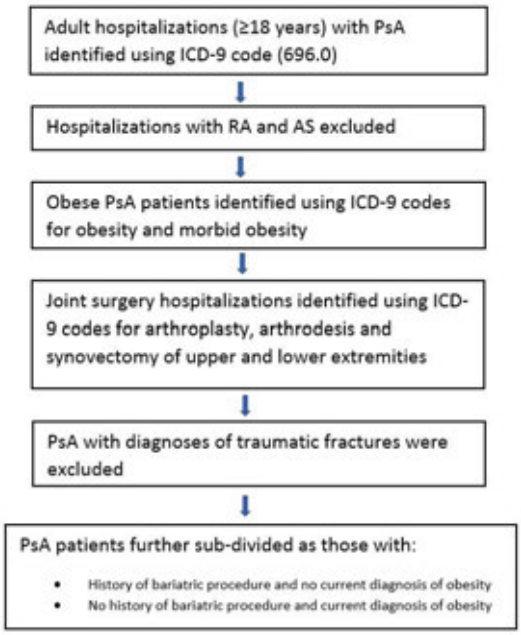

Figure 1. Flow chart showing the selection of PsA patients with joint surgery hospitalizations

bariatric procedure (V45.86) did not exist. Patients with current hospitalization for bariatric surgery were excluded to avoid confounding in the time gap between surgery and weight loss. Patients with a diagnosis of obesity were excluded from the group with a history of bariatric procedure in order to identify post-bypass patients who were no longer obese.

Results: In 2001-2014, there were 266,096 PsA hospitalizations. Among them, 44,055 (16.6 %) PsA patients had obesity or morbid obesity compared to 11.6% in the general population ($p < 0.001$). The overall hospitalization for joint surgeries in PsA was 7.42%. The rates of joint surgeries were significantly different among obese versus non-

	Overall PsA	PsA with obesity	PsA with no obesity	P value
Hospitalizations for joint surgery (%) (arthroplasty, arthrodesis or synovectomy)	7.42	9.55	7	<0.001
Female (%)	7.85	9.61	7.43	<0.001
Mean age for joint surgery hospitalizations (years)	61.61±10.59	59.68 ± 9.42	62.13± 10.83	<0.001

Table 1- Hospitalizations for joint surgery in obese and non-obese psoriatic arthritis patients (2001-2014)

	Univariate analysis	Multivariate analysis ***
History of bariatric surgery and no current obesity (ref: no history of bariatric surgery and current obesity diagnosis)	0.77 (0.51 – 1.18), p=0.24	0.84 (0.54 – 1.27), p =0.4

Table 2- Univariate and multivariate regression analyses of risk of joint surgery hospitalizations in patients with psoriatic arthritis treated with bariatric surgery (2006-2014) *** Multivariate analysis adjusted for age, gender, insurance status, hypertension, diabetes mellitus, dyslipidemia, current smoking status, hospitalization year and NIS stratum

obese PsA hospitalizations (9.55 % vs 7.0%, p< 0.001) (Table 1). Mean age of joint surgery was 59.68 ± 9.42 years vs. 62.13± 10.83 years (p< 0.001) in obese PsA compared to non-obese PsA patients (Table 1). In the years 2006-2014, a total of 1,640 (0.91%) PsA hospitalizations had a history of bariatric surgery with no current diagnosis of obesity. There was no significant difference in overall joint surgery hospitalizations among these surgically treated formerly obese patients compared to currently obese PsA patients with no history of bariatric surgery (OR 0.83, 95% CI 0.54 – 1.27, p=0.4)(Table 2).

Conclusion: Our study showed obese PsA patients had higher hospitalizations for joint surgeries compared to non-obese patients. However, no difference was noted in joint surgery hospitalizations among PsA patients without and with a history of bariatric procedure and not currently obese. While few studies have shown improvement in disease activity after weight loss, the benefit of weight loss might be more in early PsA. Further longitudinal studies should explore the short and long-term effect of weight loss on PsA disease outcomes.

Disclosure: R. Dhital, None; **D. Poudel**, None; **A. Donato**, None; **O. Oladunjoye**, None; **P. Karmacharya**, None.

Abstract Number: 2460

Frailty in Ankylosing Spondylitis, Psoriatic Arthritis, and Rheumatoid Arthritis: Data from a National Claims Database

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Table 1. Characteristics of patients with AS/PsA and RA

Characteristic	AS/PsA (n=6485)	RA (N =50744)	p-value
Age, n (%)			<0.0001
<30 years	116 (1.8)	647 (1.3)	
31-40 years	652 (10.1)	2689 (5.3)	
41-50 years	1654 (25.5)	8499 (16.8)	
51-60 years	2826 (43.6)	24677 (48.6)	
61-64 years	1237 (19.1)	14232 (28.1)	
Female, n (%)	3250 (50.1)	39804 (78.4)	<0.0001
Race/ethnicity, n (%)			<0.0001
Black or African American	361 (5.6)	8152 (16.1)	
White	533 (8.2)	5742 (11.3)	
Other	5292 (81.6)	34713 (68.4)	
Hispanic	299 (4.6)	2137 (4.2)	
Charlson-Deyo score			<0.0001
1	4950 (76.3)	26613 (52.5)	
2	925 (14.3)	14498 (28.6)	
3-4	495 (7.6)	7780 (15.3)	
≥5	115 (1.8)	1853 (3.7)	

Table 2. Prevalence of frailty components in patients with AS/PsA and RA

Frailty component	AS/PsA (n=6485)	RA (n=50744)	p-value
Frail (≥2 components), n (%)	50 (0.77)	590 (1.16)	0.005
Gait abnormality, n (%)	113 (1.74)	1181 (2.33)	0.003
Malnutrition, n (%)	158 (2.44)	1339 (2.64)	0.34
Failure to thrive, n (%)	4 (0.06)	74 (0.15)	0.08
Cachexia, n (%)	5 (0.08)	68 (0.13)	0.23
Debility, n (%)	30 (0.46)	372 (0.73)	0.01
Difficulty walking, n (%)	49 (0.76)	561 (1.11)	0.01
History of fall, n (%)	33 (0.51)	347 (0.68)	0.10
Muscle wasting, n (%)	9 (0.14)	96 (0.19)	0.38
Muscle weakness, n (%)	65 (1.00)	554 (1.09)	0.50
Decubitus ulcer, n (%)	34 (0.52)	432 (0.85)	0.006
Senility, n (%)	0 (0)	6 (0.01)	0.38
Durable medical equipment use, n (%)	2 (0.03)	11 (0.02)	0.60

Background/Purpose: Frailty, a state of decreased homeostatic reserve, is associated with increased disability and mortality, independent of age. Frailty has been evaluated in large datasets using validated algorithms in the elderly. Although frailty has been investigated in several rheumatic diseases, including RA, to our knowledge, frailty has not been investigated in AS and PsA, which often affect younger patients. In this study, we evaluated the prevalence of frailty among patients < 65 years old with AS and PsA compared to RA in a national claims database.

Methods: We performed a cross sectional study of Centers for Medicare and Medicaid Services (CMS) Medicare beneficiaries (Part A and B) from 2014 who were < 65 years old. Patients with an ICD-9-CM code for AS, PsA, or RA on 2 occasions ≥7 days apart within a year or 1 ICD-9-CM code and ≥1 DMARD prescription (from Part D) were included. Patients with SLE, IBD, cancer, human immunodeficiency virus, end stage renal disease, skin psoriasis, or organ transplantation were excluded. Sociodemographic characteristics, Charlson-Deyo score (CDS), and previously published frailty components [1] were compared between those with AS/PsA and RA. Frailty was defined as presence of ≥2 components [1] (Table 2). Logistic regression was used to determine the odds of being frail in AS/PsA and RA, adjusting for age, gender, race/ethnicity, and CDS.

Results: 6485 AS/PsA and 50744 RA beneficiaries were identified. AS/PsA patients were more often white (81.6% v. 68.4%, p< .0001), male (49.9% v. 21.6%, p< .0001), and younger (37.4% v. 23.3% ≤ 50 years old, p< .0001) as compared to those with RA (Table 1). Enrollees with AS/PsA had lower CDS than those with RA (p< .0001). Fewer patients with AS/PsA were frail (0.77%) compared to those with RA (1.16%) (p=.005) (Table 2). Several frailty components, including gait abnormality (p=.003), debility (p=.01), difficulty walking (p=.01), and decubitus ulcer (p=.006), were less common in those with AS/PsA. After adjustment for confounders, odds of frailty did not differ significantly between AS/PsA (OR 0.89, 95% CI 0.66-1.20) and RA.

Conclusion: The prevalence of frailty in AS/PsA was lower than that in RA; however, odds of frailty were similar in both groups after adjustment for confounders. The prevalence of frailty in RA was lower than in prior cohorts of young RA patients [2-3], possibly suggesting that this frailty definition may underestimate frailty prevalence. Data analysis is ongoing to compare these findings with models using other validated frailty algorithms. It will be important to have accurate frailty estimates to leverage the information in large administrative datasets to optimize patient outcomes.

1. Joynt et al. 2017

2. Haider at al. 2018

3. Cleutjens et al. 2018

Disclosure: S. Lieber, None; **M. Rajan**, None; **S. Sattui**, None; **G. Lui**, None; **S. Schwartzman**, AbbVie, 5, 8, Genentech, 8, Janssen, 5, 8, Lilly, 5, 8, Novartis, 5, 8, Pfizer, 4, 8, Regeneron, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Gilead, 4, 5, Medtronic, 4, Crescendo, 5, Dermtech, 5, Myriad, 5, Samsung, 5, National Psoriasis Foundation, 6, Amgen, 4, Boston scientific, 4; **L. Mandl**, Annals of Internal Medicine, 3, Annals of Internal Medicine- Associate Editor, 3, UpToDate, 7, Wolters Kluwer - Author at UptoDate, 7, Wolters Kluwer - Author at UpToDate, 7, Wolters Kluwer- Author at UpToDate, 7; **I. Navarro-Millan**, None.

Abstract Number: 2461

Clinical Presentation and Treatment of Oligoarticular Psoriatic Arthritis in Canada: High Frequency of Smaller Joint Involvement

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

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Background/Purpose: Oligoarticular disease in patients with psoriatic arthritis (PsA) is often underdiagnosed and undertreated. The goal of this study is to understand and identify current practices and unmet needs in the treatment of patients with oligoarticular PsA in Canada.

Methods: Twenty-one rheumatologists took part in a 25-minute online survey, conducted in English and French, between December 2018 and January 2019 from multiple locations across Canada. The participating rheumatologists were required to have diagnosed at least 1 patient with PsA currently presenting with 1 to 4 active joints. In addition, the participants were required to review charts of patients with oligoarticular PsA who were at least 18 years of age and had never been treated with apremilast, tofacitinib, or biologics.

Results: Data from the clinical practices of the participating rheumatologists over the 4 weeks before the survey indicated that >50% of patients with PsA presented with oligoarticular disease. A review of 97 charts of patients with

Figure 1. Presentation of Active Joints in Patients With Oligoarticular PsA (N=97)

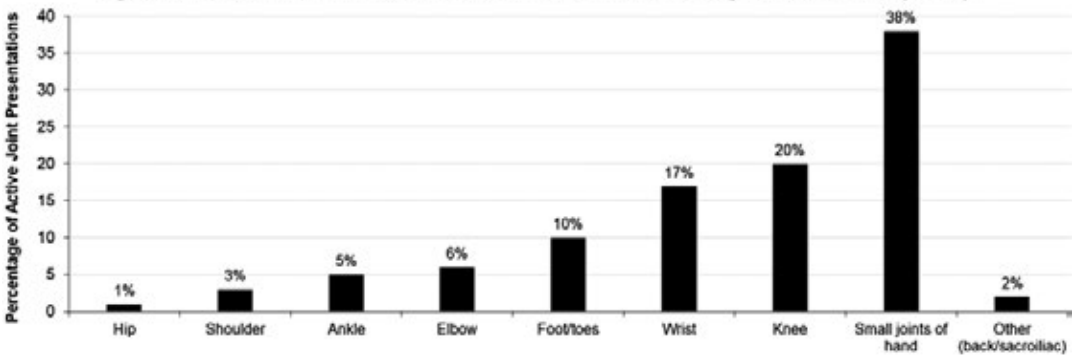
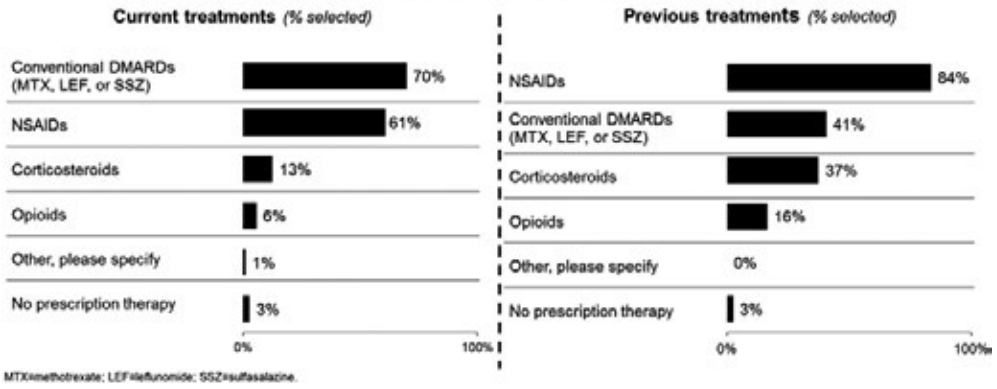


Figure 2. Current and Previous Treatments for the Management of PsA



oligoarticular PsA revealed that most (66%) were of working age (25-64 years), had a mean disease diagnosis of 5 years, and presented with 3 active joints on average, the majority of which were swollen. The most frequently mentioned presentation of active joints in patients with oligoarticular PsA was small joints of the hand (38%), knee (20%), and wrist (17%) (**Figure 1**). Patients presented with other manifestations of the disease, particularly skin disease (79%), nail disease (35%), dactylitis (32%), and enthesitis (29%). With respect to treatment, 70% of patients were currently being treated with conventional DMARDs; despite this, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and opioids continued to be utilized (**Figure 2**). Only 29% of physicians reported being extremely satisfied with their patients' current therapy in terms of overall disease management and were least satisfied with the management of their patients' enthesitis (only 14% extremely satisfied). Participating rheumatologists indicated a preference for switching therapies in 79% of the patients; however, 57% of the participants cited not doing so because of patient hesitation.

Conclusion: Patients with oligoarticular PsA present with manifestations across all disease domains. Despite commonly held beliefs that oligoarthritis predominantly affects large joints, our data suggest that smaller joints, including those of the hand and wrist, are important manifestations of the condition. Patients are not adequately controlled by conventional DMARDs, and physician satisfaction with current therapies remains low.

Disclosure: A. Cividino, AbbVie, BMS, Celgene Corporation, Pfizer, 2, 5; **D. Nicholson**, Celgene Corporation, 3; **S. Guindi**, Celgene Corporation, 3; **J. Jelley**, Celgene Corporation, 3; **A. Gaudreau**, Celgene Corporation, 3; **D. Gladman**, AbbVie, 2, 5, AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Gilead, 5, GlaxoSmithKline, 5, 8, Janssen, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5.

Abstract Number: 2462

Use of Complementary and Alternative Medicine (CAM) in a Psoriatic Arthritis Cohort

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SESSION INFORMATION

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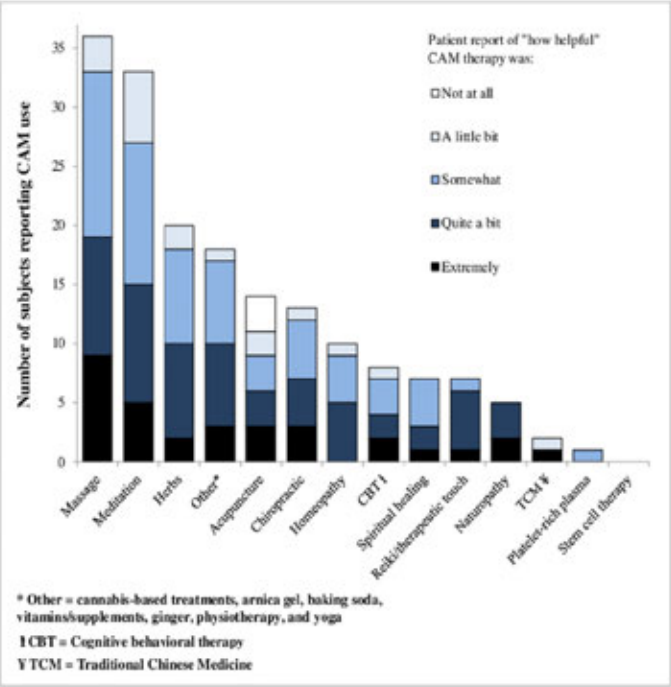
Session Time: 9:00AM–11:00AM

Figure 1. Frequency of CAM use (N=68).

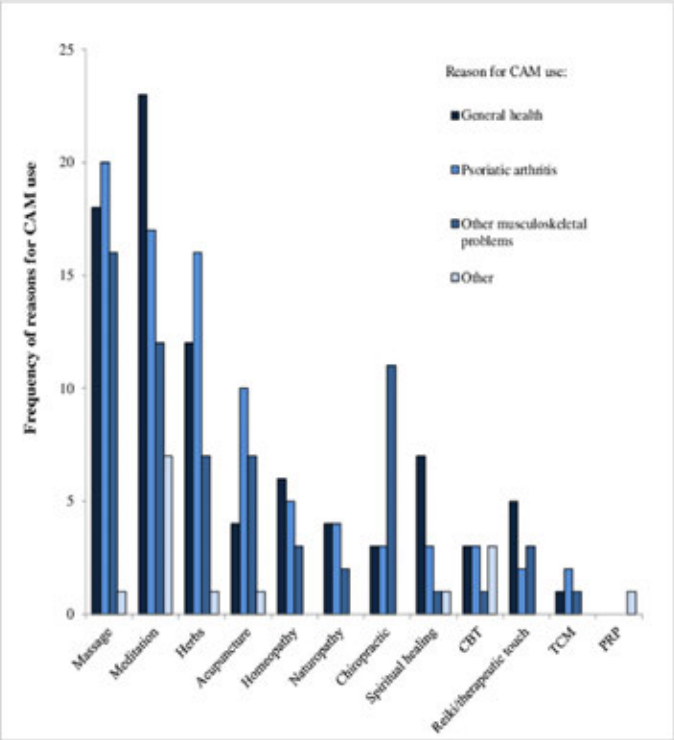


Background/Purpose: Approximately one third of people in the United States use complementary and alternative medicines. While there is published data on the use of CAM in the general population and some disease states, use in patients with psoriatic arthritis (PsA) has not been explored in detail. In this study we evaluated CAM use in an institutional cohort of validated PsA patients.

Methods: PsA patients seen at a single center between January 1, 2013 and December 31, 2017 were identified using ICD-9 and ICD-10 codes. Of those patients identified, patients who met CASPAR classification criteria were enrolled, and current biologic therapies and targeted synthetics were abstracted from chart review. All patients with available email addresses were surveyed regarding their use of CAM in the last 12 months, reason for CAM use, and helpfulness of CAM use. Patients were asked about specific commonly used complementary and alternative medicine treatments, based on literature review. A Wilcoxon rank-sum test was used to compare median age between CAM and non-CAM users. Pearson's chi-squared tests were used for sex and race, and a Fisher's exact test was used to compare biologic and/or targeted synthetic medication use among CAM and non-CAM users.

Results: 328 subjects were sent the questionnaire, and the response rate was 39.3% (129/328). 53% had used CAM in the last 12 months (Figure 1). CAM users were younger: 58 years vs. 63 years (p-value: 0.057), and more likely to be female: 64.7% vs 37.7% (p-value: 0.002). There was no association between race and CAM use (p-value: 0.74). The most popular CAMs used were massage, meditation, and herbs. Reasons for use of CAMs: 34.0% for PsA, 34.4% for general health, 25.6% for other musculoskeletal problems, and 6.0% for other reasons (Figure 2). 26.5% of patients reported using CAM not listed in the questionnaire. These included: cannabis-based treatments, arnica gel, baking soda, vitamins/supplements, ginger, physiotherapy, and yoga.

Figure 2. Patient-reported reason for CAM use.*



* For each CAM, subjects had the option of indicating multiple reasons for use.

Table 1. Biologic and/or targeted synthetic use among CAM and non-CAM users.

	CAM users (n=68) N (%)	Non-CAM users (n=61) N (%)
Biologics	**35 (51.5)**	**35 (57.4)**
Adalimumab	12 (17.6)	11 (18.0)
Etanercept	4 (5.9)	7 (11.5)
Secukinumab	10 (14.7)	10 (16.4)
Infliximab	1 (1.5)	5 (8.2)
Ustekinumab	1 (1.5)	2 (3.3)
Certolizumab	2 (2.9)	0 (0.0)
Golimumab	1 (1.5)	2 (3.3)
Ixekizumab	2 (2.9)	1 (1.6)
Rituximab	2 (2.9)	0 (0.0)
Guselkumab	0 (0.0)	1 (1.6)
Targeted Synthetics	**3 (4.4)**	**8 (13.1)**
Apremilast	2 (2.9)	8 (13.1)
Tofacitinib	1 (1.5)	0 (0.0)
Overall	**38 (55.9)**	**43 (70.5)**

Overall, 18.4% found CAM use to be extremely helpful; 33.9% quite a bit helpful; 35.6% somewhat helpful; 10.3% a little bit helpful; 1.7% not at all helpful. Although not statistically significant, CAM users were less likely to be on biologics and/or targeted synthetic medications than were non-CAM users (55.9% vs. 70.5%; p-value: 0.26) (Table 1).

Conclusion: CAM use is common in a validated PsA cohort, with more than half of respondents reporting use of at least one type of CAM in the last 12 months. CAM use is more common among those not on biologics/targeted synthetics. Further studies are needed to determine whether CAMs are being used in lieu of standard medications used to treat PsA and if CAM use impacts adherence to traditional therapy.

Disclosure: J. Roberts IV, None; **L. Mandl**, Annals of Internal Medicine, 3, Annals of Internal Medicine- Associate Editor, 3, UpToDate, 7, Wolters Kluwer - Author at UptoDate, 7, Wolters Kluwer - Author at UpToDate, 7, Wolters Kluwer- Author at UpToDate, 7; **Z. Abutalib**, None; **S. Schwartzman**, AbbVie, 5, 8, Genentech, 8, Janssen, 5, 8, Lilly, 5, 8, Novartis, 5, 8, Pfizer, 4, 8, Regeneron, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Gilead, 4, 5, Medtronic, 4, Crescendo, 5, Dermtech, 5, Myriad, 5, Samsung, 5, National Psoriasis Foundation, 6, Amgen, 4, Boston scientific, 4.

Abstract Number: 2463

Body Composition and Fat Distribution in Patients with Psoriasis or Psoriatic Arthritis

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
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Background/Purpose: Obesity is a leading comorbidity in both psoriasis (Pso) and psoriatic arthritis (PsA) and is associated with common metabolic complications and increased cardiovascular (CV) risk. Obesity is also a risk factor for the onset of these diseases. Body composition and fat distribution have been rarely evaluated in Pso and PsA. In this study, we aimed to characterize the fat mass distribution in patients with Pso or PsA compared to a control group, with a special emphasis on the android/visceral region.

Methods: case-control study (NCT02849795). Patients with Pso (plaque psoriasis) or PsA (CASPAR criteria) were evaluated. Each patient was paired to a control subject, recruited in the same outpatient population, and matched for sex, age and body mass index (BMI) category. Clinical assessment included BMI, anthropometric measurements (waist circumference, waist /hip ratio), disease activity (PASI for Pso, CPDAI for PsA) and the SCORE CV risk score. Laboratory parameters of inflammation (ESR, CRP, IL-6), lipid parameters (total cholesterol, LDL and HDL cholesterol, triglycerides), metabolic parameters (glycemia, insulin, HOMA), serum adipokines (total and high molecular weight [HMW] adiponectin, leptin, resistin and retinol binding protein 4 [RBP4]) were measured. Body composition (lean mass, fat mass) and fat distribution (android/gynoid regions and visceral fat) were evaluated (DEXA, Lunar GE, CoreScan). Our primary criteria was the fat mass in the android/visceral region. Comparisons between patients and controls were performed with paired t tests, between all groups with ANCOVA (adjusted for age, sex, and BMI category) and Tukey post-hoc tests. Pearson correlations between CV risk and fat mass were calculated within groups.

	PsA	Controls	Pso	Controls
N	52	52	52	52
Age (years)	52.5 ± 11.7	52.8 ± 11.1	50.5 ± 12.8	50.7 ± 12.9
M/F	25/27	25/27	38/14	36/16
BMI (kg/m^2)	27.42 ± 5.9	27.69 ± 6.4	28.42 ± 5.8	28.22 ± 6.1
BMI categories:	%		%	
< 18.5	0	0	1.9	3.8
18.5- 24.99	34.6	36.5	25	23.1
25- 29.99	44.2	34.6	40.4	38.5
>29.99	21.2	28.8	32.7	34.6
Waist circumference (cm)	91.67 ± 14	94.12 ± 12.9	99.52 ± 17.4 *	98.16 ± 16.2
Waist/hip ratio	0.90 ± 0.10	0.91 ± 0.09	0.95 ± 0.09	0.95 ± 0.12
Disease duration (years)	9.1 ± 6.7		18.1 ± 13.8	
PASI	2.43 ± 4.1		8.43 ± 4.9	
CPDAI	7.42 ± 3.34			
SCORE	1.39 ± 1.89		1.53 ± 1.53	
ESR (mm/h)	19.84 ± 16.6 ***	6.96 ± 5.8	10.75 ± 8.8 ***	6.4 ± 6.5
CRP (mg/L)	10.6 ± 11.8 ***	3.98 ± 4.8	5.96 ± 9.0	4.7 ± 5.5
IL-6 pg/ml)	10.05 ± 15.1 ***	3.02 ± 3.0	3.63 ± 3.1	2.98 ± 2.4
Insulin (pmol/L)	57.48 ± 39.6 *	42.53 ± 26.4	68.22 ± 45.4 ***	42.8 ± 22.8
HOMA	1.79 ± 1.2	1.43 ± 0.9	2.37 ± 2.0 ***	1.47 ± 0.9
Leptin (pg/mL)	26.6 ± 30.2 *	19.38 ± 19.1	21.28 ± 23.4	17.25 ± 20.4

Table 1 ADIPSO

Table 1: clinical characteristics, laboratory parameters, serum adipokines, metabolic parameters and body composition measurements of patients with Pso and PsA and their respective control subjects (Quantitative variables are presented as mean ± standard deviation; Pso: psoriasis; PsA: psoriatic arthritis; * p <0.05; **p <0.01; ***p<0.005).

Results: 52 patients with Pso and 52 patients with PsA and their respective paired-control were evaluated (Table 1). Total fat mass was increased in Pso but not in PsA. Android fat and visceral fat were found higher in Pso ($p< 0.05$) while the fat mass measurements did not differ between the patients with PsA and their controls. Waist circumference was higher in patients with Pso compared to their controls. Leptin, leptin/fat mass ratio, and total adiponectin were

elevated in PsA while only the HMW/total adiponectin ratio was decreased in Pso. Insulin levels and HOMA were increased in both Pso and PsA groups. Finally, RBP4 was higher in both Pso and PsA patients compared to their respective controls. In patients with Pso, android and visceral fat were correlated with SCORE (r=0.3, p=0.02 and r= 0.6, p < 0.0001 respectively). In ANCOVA analysis, visceral fat was higher in Pso patients (p=0.0029), with a trend toward higher android fat (p=0.055), compared to PsA patients.

Conclusion: visceral fat is increased in patients with Pso but not in PsA. In parallel, both groups showed an elevation of circulating RBP4. Patients with Pso and PsA were also characterized by metabolic disturbances as showed by the increase in HOMA, and specific adipokine changes. In the Pso group, visceral fat is associated with CV risk evaluated by SCORE. Weight control and reduction of fat mass, especially visceral fat mass, may thus be an important concern in patients with Pso and appears less relevant in PsA.

Disclosure: E. Toussirot, None; **F. Aubin**, None; **m. Desmarets**, None; **D. WENDLING**, None; **b. Augé**, None; **j. Gillard**, None; **o. messica**, None; **X. Guillot**, None; **c. Laheurte**, None; **e. monnet**, None; **g. dumoulin**, None.

Abstract Number: 2464

Multidisciplinary Unit of Psoriatic Arthritis: Clinical Results

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SESSION INFORMATION

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Background/Purpose: The multidisciplinary unit of psoriatic arthritis (PsA) are attractive to improve the early diagnosis and optimize the management of complex patients with PsA. There are published data about different models, activity data and patient satisfaction in this kind os unit. To evaluate its effectiveness, we also need to know the clinical results of patients with PsA who visit them.

The objective of this study is to evaluate the control of the cutaneous and articular activity of the patients with psoriatic arthritis in our multidisciplinary unit.

Methods: We reviewed 199 medical records and included 132 patients with peripheral, mixed or axial PsA, treated with DMARDs or biological therapy (TB), followed up for at least 6 months in our unit. Epidemiological, clinical and skin and joint activity data are collected, evaluating DAPSA, PASI, BSA, PGA and percentage of patients that reach MDA (minimal disease activity). The data is analyzed using SPSSv23.

Results: 132 patients, 65.2% males, with a mean age (SD) of 54.98 (13.99) years, and a time of evolution of 110.37 months (SD 89.77). Diagnosis: 65.9% peripheral PsA, 30.3% mixed and 3.8% pure axial involvement. 68.2% had one comorbidity and 27.3% two or more. 56.8% had a family history of psoriasis and 19.7% of PsA. The presentation of

	DAPSA	PASI	BSA
Nº of patients	121	122	123
Mean	5,6419	3,020	3,721
Median	3,5300	2,000	2,000
Standard Deviation	6,76648	2,9095	3,9312
Minimum	0,06	0,0	0,0
Maximum	54,50	13,00	18,00

Cutaneous and joint activity

			Minimal Disease Activity		Total
			No	Yes	
Remission	(DAPSA < 4) No	Nº of patients %	39 68.4%	18 31.6%	57 100.00%
	(DAPSA < 4) Yes	Nº of patients %	5 7.8%	59 92.2%	64 100.00%
Total		Nº of patients %	44 36.4%	77 63.6%	121 100.00%

Outcome measures

psoriasis was predominantly in plaques (81.8%) and 8.3% in folds. 36.4% had previous enthesitis, 39.4% previous dactylitis. 68.2% had received one DMARD, 37.1% two or more. 22% had received previous biological therapy and 10.6% had received at least two biological drugs. Current treatment: 57 patients (43.1%) received BT and 75 patients received DMARD (only 2.3% receive two DMARDs). BT: 30.3% anti-TNF, 6.1% Ustekinumab, 3.8% Secukinumab and 3.8% Apremilast. Time of current treatment in months: mean 59.79 (SD 58.87). Cutaneous and joint activity: median of DAPSA 3.53 (0.06-54.50), PASI 2 (0-13) and BSA 2 (0-18). PGA from very mild to mild 83.6%, mild PASI 79% and mild BSA 52%. DAPSA of low activity 90.1% and DAPSA of remission (< 4) 59.2%. 62.4% of the patients reached MDA criteria.

Conclusion: We consider that the clinical results of the patients visited in our multidisciplinary clinic are in general, good or very good, even in the subgroup of more complex patients. It would be necessary to carry out an additional cost study to assess its efficiency.

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Abstract Number: 2465

Reliability and Validity of the Self-Administered Comorbidity Questionnaire in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The Self-Administered Comorbidity Questionnaire (SCQ) is a self-report questionnaire. It assesses 13 common medical conditions and the impact of comorbidities on functional status (1). The aim of this study is to investigate the validity and reliability of the Turkish version of the SCQ in Psoriatic Arthritis (PsA).

	Rho	P value
Convergent validity		
The effect of comorbid diseases on QoL (VAS)	**0.723**	<0.005
Patient global assessment of general health (VAS)	**0.512**	<0.005
HAQ	**0.486**	<0.005
PsAQoL	**0.519**	<0.005
SF-36		
Physical functioning	**-0.611**	<0.005
Physical role	**-0.396**	0.001
Bodily pain	**-0.336**	0.006
General health	**-0.618**	<0.005
Vitality	**-0.423**	<0.005
Mental health	-0.199	0.111
Emotional role	-0.195	0.119
Social functioning	**-0.329**	0.008
Divergent validity		
Age	**0.463**	<0.005
Disease duration	0.164	0.192
Body mass index	**0.276**	0.026

Table 1. Construct validity of SCQ (Correlation coefficient with other parameters)

Methods: Patients with PsA, according to Classification Criteria for Psoriatic Arthritis (CASPAR), were included in the study. Data about age, sex, body mass index (BMI), disease duration (month) were noted. Psoriatic Arthritis Quality of Life (PsAQoL) scale and Short Form 36 (SF-36) were used to assess the quality of life. The Health Assessment Questionnaire (HAQ) was used to evaluate the physical disability. The effects of comorbid diseases on quality of life (QoL) and Patient Global Assessment of General Health (PGA) were assessed on the Visual Analogue Scale (VAS). The English version of SCQ was the original scale used for translation and adaptation. Translation, back translation, and cross-cultural adaptation of the SCQ into Turkish were done according to the standard procedure. The reliability of SCQ was determined by internal consistency (Cronbach's alpha coefficient). Face validity and construct validity (convergent and divergent validities) were evaluated. For the face validity, the final Turkish version of SCQ was tested by 15 patients to determine if they could understand the items. The correlations of the SCQ with the HAQ, SF-36, PsAQoL, the VAS scores of the effect of comorbid diseases on QoL and PGA were assessed for convergent validity. The relation of the SCQ with age, BMI, and disease duration were assessed for divergent validity. The construct validity of the SCQ scale was determined by Spearman's correlation coefficient. The descriptive analysis was done for demographic data. $P< 0.05$ accepted as significant.

Results: The mean age of 65 patients (46 female, 19 male) with PsA was 46.20 (SD: 13.05) years. The median (min-max) duration of disease was 24 (1-384) months. The mean BMI of patients was 29.06 (SD: 5.92). The Cronbach's alpha coefficient of the SCQ for internal consistency was 0.755. The SCQ score had moderate and significant positive correlations with HAQ, PsAQoL, the VAS scores of the effect of comorbidity on QoL and PGA ($p< 0.05$). The significant negative correlations were detected with physical function, physical role limitation, bodily pain, general health, vitality and social function subgroups of the SF-36 ($p< 0.05$). The SCQ score had positive correlations with age and BMI ($p< 0.05$). There was no correlation between SCQ score and duration of disease (rho: 0.164, p: 192). The correlations of SCQ with the clinical variables that show convergent and divergent validities were given in Table 1.

Conclusion: The Turkish version of the SCQ is a valid and reliable instrument in PsA. The SCQ is a simple, accurate and not time-consuming self-report instrument to assess comorbidities in patients with PsA.

Reference::

1. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. Arthritis Rheum. 2003; 49(2):156-63.

Disclosure: D. Erdem, None; **H. Gezer**, None; **S. Acer Kasman**, None; **M. Duruoz**, İbrahim etem, 8, Abdi İbrahim, 8, Abdi Ibrahim, 8, Abvie, 2, 8, AMGEN, 8, AMGEN, Novartis, ILKO, ONKO, İbrahim Ethem, Abdi İbrahim, 8, Ibrahim Ethem, 8, ILKO, 8, Novartis, 8, ONKO, 8.

Abstract Number: 2466

Evolution of Health-Related Quality of Life in Psoriatic Arthritis Patients

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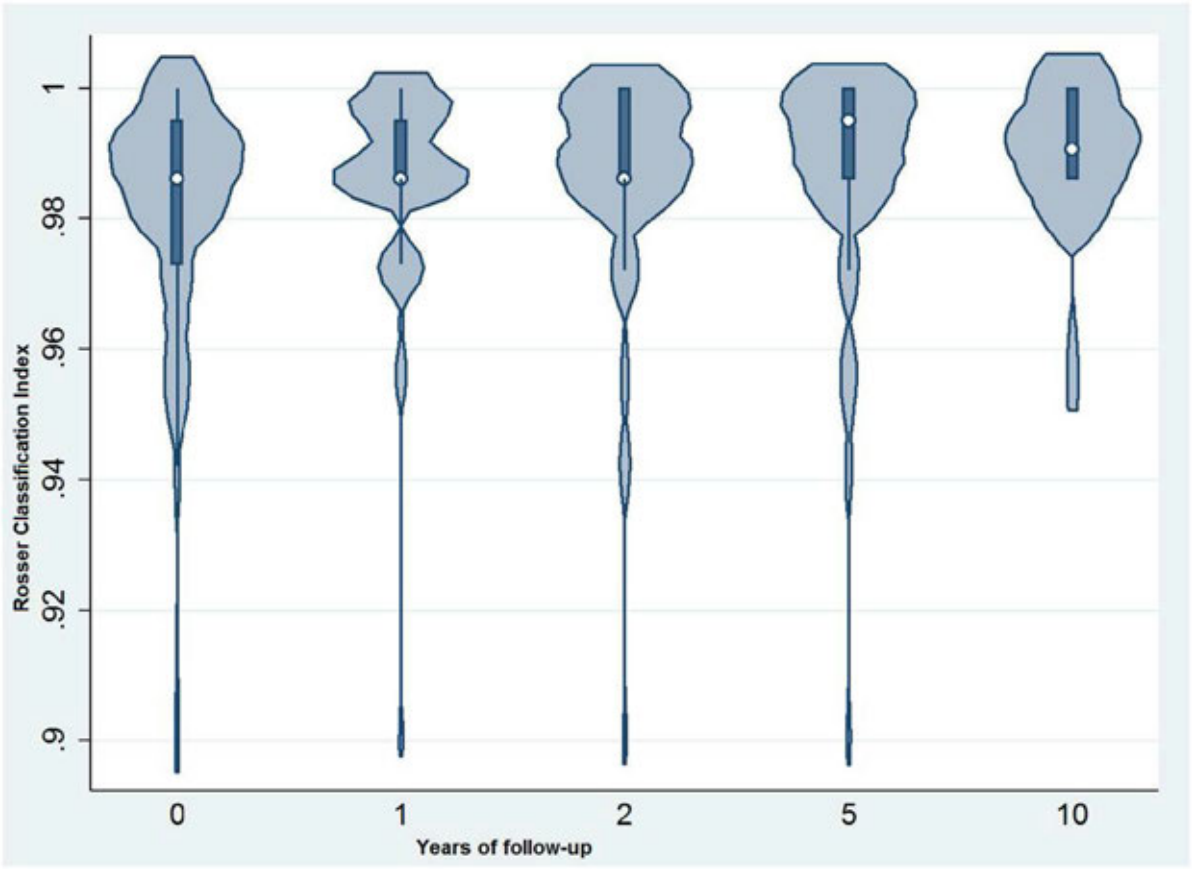
SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features



Graph 1. Rosser classification index throughout the follow-up.

Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is consider a multifaceted disease, with patients reporting lower health-related quality of life (HRQoL). Data of burden of disease is substantial and there exists a need for properly designed studies to learn more about the evolution of HRQoL in this condition. **Purpose:** To analyze the evolution on HRQoL in patients with PsA and to evaluate factors that may influence this evolution.

Methods: Retrospective longitudinal observational study including incident patients diagnosed with PsA from 2007 to 2016, and followed-up until loss of follow-up or December 2017; with at least two registered visits; PsA diagnosis according to The CASPAR criteria (ClASsification criteria for Psoriatic ARthritis) and symptoms onset after 16 years old. Patients were from the rheumatology outpatient clinic of Hospital Clínico San Carlos, Madrid, Spain. Clinical information was collected from a departmental electronic health record, including demographic, clinical, treatment, and HRQoL related variables (measured with the Rosser Classification Index), reported numerically on a scale between 0 and 1, as a result of the combination of two different categories disability and distress; The influence of these variables in repeated measures of HRQoL were analysed using bivariate and multivariate generalized estimating equations (GEE) models nested by patient. Those variables with a p-value < 0.20 (plus age, sex, follow-up time, and calendar year) were introduced in the multivariate analysis. Bonferroni p-value threshold adjustment was carried out.

Results: We included 248 patients, with a median follow-up of 4.3±3.3 years. 57.6% were male, with a median age at the onset of symptoms and diagnosis of 48 and 49 years, respectively. 88% of patients had a personal history of Psoriasis. Regarding clinical manifestations during the follow-up, 86%, 33%, 35%, and 30% of the patients presented with peripheral arthritis, inflammatory low back pain, enthesitis and dactylitis, respectively. In addition, they received treatment with nonsteroidal antiinflammatory medications (NSAIDs), oral glucocorticoids and disease-modifying antirheumatic drugs (DMARDs) 74%, 59% and 86%, respectively. 22% received biological agents. The Rosser mean value (SD) at the first visit was 0.98 (0.02), with a slight improvement after the first 2 years and worsening after 5 years of follow-up (Graph 1). Regarding to the variables independently associated with HRQoL during follow-up, obesity (p=0.018), osteoporosis (p=1.3e-03), osteoporotic fractures (p=5.7e-12) and chronic obstructive pulmonary disease (p=6.7e-06) were associated with a poorer HRQoL. Conversely, treatment with methotrexate (p=8.2e-05), and the use of bisphosphonates (p=4.9e-04) were associated with better HRQoL. Interestingly the presence of enthesitis was also associated to worse HRQoL, although not significantly after p-value adjustment.

Conclusion: We observed that the presence of certain comorbidities were independently associated with a worse HRQoL. In addition, regarding different treatments, the use of methotrexate and the concomitant use of treatment with bisphosphonates were independently associated with a better HRQoL.

Disclosure: D. Freites Nuñez, None; **L. León**, None; **P. Lois**, None; **A. Madrid García**, None; **J. Font Urgelles**, None; **C. Vadillo Font**, None; **I. Abasolo Alcazar**, None; **J. Jover Jover**, None; **B. Fernández Gutiérrez**, None; **L. Rodríguez-Rodríguez**, None.

Abstract Number: 2467

Pain and Anxiety Are Independent Factors Associated to Sleep Impairment in Psoriatic Arthritis: A Multicentric Study in 14 Countries

Penelope Palominos,[1] Laura Coates,[2] Charles Kohem,[3] Ana-Maria Orbai,[4] Josef Smolen,[5] Maarten de Wit,[6] Uta Kiltz,[7] Ying-Ying Leung,[8] Juan Cañete,[9] Rossana Scrivo,[10] Andra Balanescu,[11] Emmanuelle Dernis,[12] Sandra Talli,[13] Martin SOUBRIER,[14] Sibel Zehra Aydin,[15] Inna Gaydukova,[16] Umut Kalyoncu,[17] and Laure Gossec[18], [1]Serviço de Reumatologia, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul,, Porto Alegra, Brazil, [2]University of Oxford, Oxford, United Kingdom, [3]Serviço de Reumatologia, Hospital de Clinicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil, [4]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, Maryland, Baltimore Maryland, [5]Medical University of Vienna, Vienna, Austria, [6]Department of Medical Humanities, Amsterdam Public Health (APH), Amsterdam University Medical Centre, Amsterdam, Netherlands, [7]Rheumazentrum Ruhrgebiet/Ruhr University Bochum, Herne, Germany, Herne, Germany, [8]Department of Rheumatology and Immunology, Singapore General Hospital,, Singapore, Singapore, [9]Department of Rheumatology, Hospital Clínic, Barcelona, Barcelona, Spain, [10]Rheumatology Unit, Department of Internal Medicine and Medical Specialties, Sapienza Università di Roma,, Rome, Italy, [11]Sf Maria Hospital, University of Medicine and Pharmacy Carol Davila, Bucharest, Romania, [12]Rheumatology Department, Le Mans Central Hospital, Le Mans, France, [13]Rheumatology Department, East-Tallinn Central Hospital, Tallinn, Estonia, [14]CHU Gabriel Montpied, Clermont Ferrand, Auvergne, France, [15]University of Ottawa Faculty of Medicine, Rheumatology,Ottawa Hospital Research Institute, 1967 Riverside Drive, Ottawa, ON, K1H 7W9, CANADA, Ottawa, Canada, [16]North-western State medical university, St Petersburg, Russia, [17]Hacettepe University Department of Rheumatology, Ankara, Turkey, [18]Sorbonne Université and Hôpital Pitié-Salpêtrière, Paris, France

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Table 1: Poisson regression model to evaluate independent factors associated to sleep impairment (patient self-evaluation of sleep in PSAID12 ≥ 4)

Variable	Prevalence ratio	95%CI	P value
Gender			
Male	1.00		
Female	1.04	0.94-1.16	0.723
Age in years	1.00	0.99-1.00	0.879
Education in years	1.01	0.99-1.02	0.566
DAPSA components*			
Pain	1.06	1.03-1.09	**<0.001**
TJC	1.00	0.99-1.01	0.464
SJC	1.01	1.00-1.01	0.107
CRP	1.00	0.99-1.01	0.300
Current medication			
bDMARD	1.01	0.91-1.02	0.843
corticosteroid	0.96	0.81-1.13	0.601
Obesity (body mass index 30)	1.06	0.94-1.19	0.338
Leeds enthesitis score	1.02	0.97-1.06	0.491
Anxiety PSAID- 12	1.05	1.02-1.08	**0.003**
Depression PSAID-12	1.01	0.98-1.04	0.721
Self evaluation of psoriasis	1.01	0.99-1.03	0.508
HAQ			
Mild (from 0 to ≤1)	1.00		
Moderate (from >1 to 2)	1.05	0.91-1.21	0.532
Severe (from >2 to 3)	1.22	0.98-1.52	0.072
Symptoms caused by other disease **	1.01	0.99-1.03	0.168

CI, confidence interval; DAPSA, disease activity in psoriatic arthritis; TJC, tender joint count, SJC, swollen joint count; CRP, C reactive protein; bDMARD, biologic disease modifying antirheumatic drug; Psoriatic Arthritis Impact of Disease Questionnaire-version with 12 questions; HAQ, Health Assessment Questionnaire.

* Patient global evaluation had to be excluded from the model due to multicollinearity effect

** Physician opinion, in a 0-10 numerical rating scale, that the cause of the patient's current symptoms is other disease and NOT psoriatic arthritis (such as osteoarthritis, fibromyalgia, comorbidities, etc)

Background/Purpose: Sleep quality is diminished in patients with psoriatic arthritis (PsA) and close to 40% of PsA patients consider sleep impairment a priority domain.This work analyzed determinants of impaired sleep in patients with PsA.

Methods: This was a cross-sectional analysis of an observational study (ReFlap, NCT03119805), which included adult patients with definite PsA with ≥ 2 years disease duration from 14 countries (ref 1). Sleep was assessed using the patient self-reported evaluation of sleep on a 0-10 numerical scale, included in the Psoriatic Arthritis Impact of Disease questionnaire (PSAID-12) (ref 2). A score ≥ 4 was considered as sleep impairment. Demographic and clinical variables associated to sleep impairment were assessed through univariate analysis; prevalence ratios (PR)[95% CI] were reported. Variables independently associated to sleep impairment in the univariate analysis (with p-value < 0.05) were entered in the Poisson regression model.

Results: A total of 396 patients were analyzed: mean age 51.9 ± 12.6, 51% (N= 202) were females, 59.7% were receiving biologic therapy (N= 221), 53.3% (N=201) of participants had 1-5% of body surface area (BSA) affected by psoriasis, 74% (N=293) had mild disability (defined as a score ≤1 in the Health Assessment Questionnaire-HAQ); 23.7% (N=94) were in remission and 36.9% (N=146) in low disease activity according to the Disease Activity in Psoriatic Arthritis (DAPSA) score. Median (25th-75th) patient's self-evaluation of sleep difficulties was 2 (0-6), 39.9% (N=158) were considered as having sleep impairment. In the univariate analysis, factors independently associated to sleep impairment were: moderate (HAQ >1 to 2) and severe (HAQ >2 to 3) disability (PR: 1.55 [1.39-1.72] and 2.07 [1.97-2.18] respectively, p< 0.001), glucocorticoid use (PR: 1.52 [1.16-1.99], p=0.003), obesity (PR: 1.50 [1.06-2.11], p=0.021), psoriasis affecting >20% of BSA (PR: 1.12 [1.08-1.17], p< 0.001), moderate and high disease activity by DAPSA (PR: 7.01 [3.54-13.8] and 8.71 [4.46-17.9] respectively, p< 0.001) and self-reported levels of anxiety, depres-

sion and fatigue (PR: 1.22 [1.18-1.28], 1.16 [1.14-1.21] and 1.28 [1.23-1.33] respectively, p< 0.001). Poisson regression model showed only self-reported levels of anxiety (PR: 1.05 [1.02-1.08], p=0.003) and the pain component of DAPSA (PR: 1.06 [1.01-1.09], p< 0.001) contributing to sleep impairment (Table 1).

Conclusion: Sleep impairment was frequent in this population of PsA patients; pain and anxiety were independently associated to sleep impairment.

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Abstract Number: 2468

JAK-STAT Signaling System in Pannus Formation of Psoriatic Arthritis: A Therapeutic Target

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) involves inflammation of the joint synovium where synovial cells (FLS) are the target for T cell activated cytokines for pannus formation. The T cell secreted cytokines (IL-17A, IL-22 and TNF-α) signal through the JAK family of tyrosine kinases. Activated JAKs recruit and activate STATs, which in turn drive gene transcription. IL-17A, IL-22 and TNF-α play leading roles in PsA but their regulatory role on JAK-STAT signaling for pannus formation remains largely unknown. Here we have addressed (A) whether these key regulatory cytokines induce phosphorylation of STAT3 and thus regulates (i) FLS proliferation and (ii) IL-6, IL-8 and MMP3

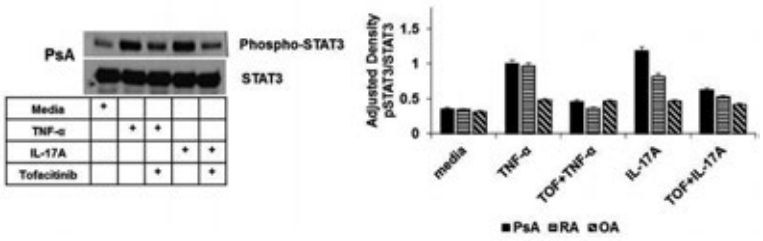

Fig 1. IL-17A and TNF-α activate JAK-STAT signaling pathway. STAT3 is a transcription factor that plays a significant role in the pathogenesis of PsA. IL-17A and TNF-α induced phosphorylation of STAT3 by a fold change of 2 compared to the untreated PsA FLS (p<.01). PsA FLS pre-treated with tofacitinib (TOF) inhibited IL-17A and TNF-α induced phosphorylation of STAT3 (p<.01). Similar results were also seen in RA FLS.

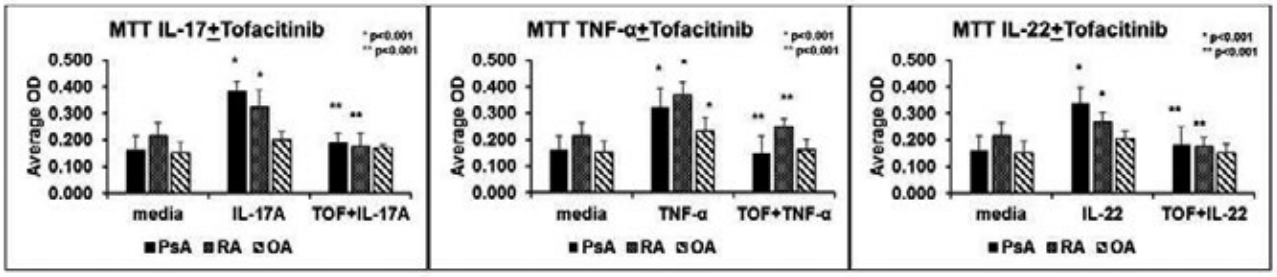

Fig 2 - Anti-Proliferative effect of pan-JAK inhibitor (Tofacitinib) on IL-17, TNF-α and IL-22 induced PsA FLS and RA FLS proliferation. * Compared with the media (<.001); ** Compared with IL-17A vs IL-17A+ Tofacitinib (<.001); ** Compared with TNF-α vs TNF-α + Tofacitinib (<.001); ** Compared with IL-22 vs IL-22+ Tofacitinib (<.001).

production by FLS. (B) Can a JAK-STAT inhibitor (Tofacitinib) inhibit this process and thus brakes pannus formation induced by TNF-α, IL-17 and IL-22.

Methods: FLS were isolated from synovial tissue biopsies of PsA, RA and OA (n=5, for each). They were cultured in presence or absence of tofacitinib (50nM) with TNF-α (20ng/mL), IL-17A (100ng/mL) or IL-22 (100ng/mL); supernatants were collected on the day 5. ELISAs were performed for IL-6, IL-8 and MMP-3 with ELISA kits (PeproTech). MTT assay was done for proliferation. Immunoblot studies of FLS lysates were done to identify for STAT3/ phospho-STAT3.

Results: 1. We observed that IL-17/IL-22/TNF-α induced phosphorylation of STAT3 by 2 fold change relative to the untreated PsA FLS. PsA FLS pre-treated with tofacitinib showed decreased levels of phospho-STAT3 compared to the FLS cells not treated with tofacitinib (p< 0.01) (Fig 1). 2. We observed IL-17, TNF-α and IL-22 induced significant proliferation of PsA and RA FLS compared to the media (p< 0.001); and cells that were pre-treated with tofacitinib had significantly lower proliferation (p< 0.001) (Fig 2). 3. PsA and RA FLS stimulated with IL-17A, TNF-α or IL-22 produced significantly more IL-6 IL-8 and MMP-3 compared to media (p< 0.001) and that could be significantly reduced when these FLS were pre-treated with tofacitinib (p< 0.001).

Conclusion: The two critical events of inflammatory/proliferative process for pannus formation are: (i) FLS proliferation; (ii) IL-6, IL-8 and MMP-3 production by FLS. Here we observed: (i) IL-17A, TNF-α and IL-22 the most critical cytokines for the disease process of PsA regulate these biological functions of FLS by activating JAK-STAT kinase system (ii) Further tofacitinib a pan jAK inhibitor effectively blocked these effects. These observations support a critical role for JAK-STAT signaling pathways in PsA and provide mechanisms of actions of tofacitinib for its efficacy.

Disclosure: S. Raychaudhuri, AbbVie, 2, Amgen, 5, Janssen, 2, 5, Lilly, 5, Novartis, 2, 5, Pfizer, 2, 5, Pfizer Inc, 2, Sun Pharma, 2; **S. Raychaudhuri**, Sun Pharmaceutical Industries Limited, 2.

Abstract Number: 2469

Diversity of Poly-Functional T Cells in Psoriatic Arthritis and Rheumatoid Arthritis and Its Therapeutic Significance

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
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Session Time: 9:00AM–11:00AM

Background/Purpose:: Importance to specific T cell subpopulations has been attributed for specific diseases such as Th17 cells in psoriatic disease, Th1 cells in TB and Th2 response for intracellular parasite infections. However, there are evidences that immune response is not a watertight condition for a specific T cell sub population. As a clinician, we notice this diversity too; a patient of psoriatic arthritis (PsA) may respond to an anti-TNF agent whereas anti-IL-17A may not work; a patient may respond to anti-IL-23 but fails anti-IL-17A or anti-TNF agents. Considering this background here we have addressed poly-functionality of the activated effector memory T cells as well the difference of poly functionality in T cells between individual autoimmune disease such as in PsA and rheumatoid arthritis (RA).

Methods: Peripheral blood (PBMC) synovial fluid (SFMC) mononuclear cells were collected from untreated PsA and RA (n=15/each) patients with active disease. Magnetically sorted $CD3^+$ T cells were isolated from PBMCs and SFMCs; were activated (10^6 cells/ml) with anti-human CD3/CD28 cocktail and cultured in RPMI medium for 5 days (Fig 1). Hi-D FACS studies were performed to: (i) identify activated memory cells (CD3+CD4+CD45RO+) T cells (ii) identify the percentage of following Th1/Th17 cytokine profile: IL-17A, IL-22, TNFα, IFNy. The percentages of each cell population and the mean fluorescence intensity (MFI) were analyzed using Flow Jo software.

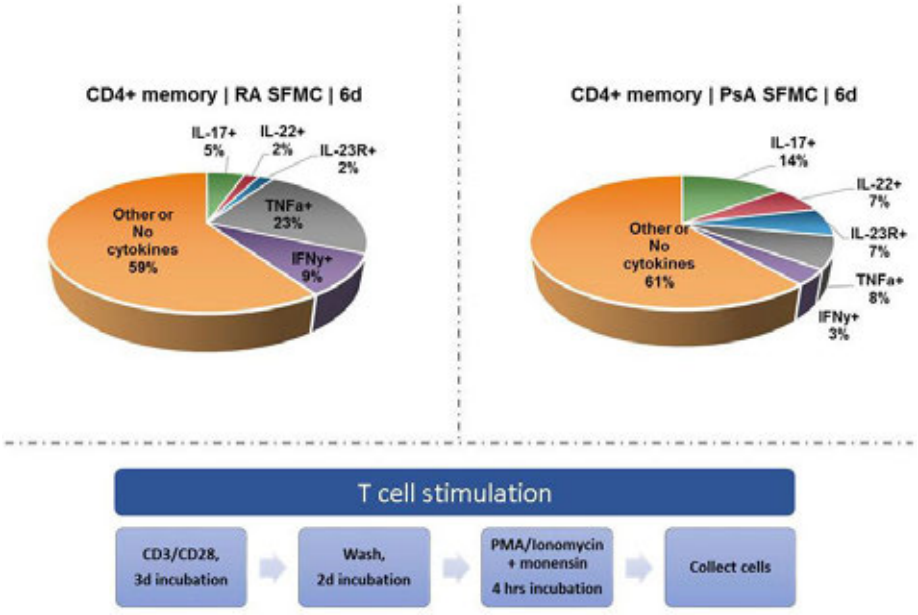

Figure 1. Poly-Functional synovial fluid mononuclear (SFMC) T cells and its variance in psoriatic arthritis (PsA) and rheumatoid arthritis (RA).

Results: We noticed a marked polyfunctionality in PBMC/SFMC T cells both in PsA and RA. SFMC T-cells exhibited greater cytokine polyfunctionality, compared with matched blood. In PsA SFMCs the number of IL-17A (7.5+0.4%), IL-22(6.4+0.3%) and IL-23R (6.5+0.%) secreting cells were significantly higher than the PsA PBMCs (3.8+0.3%, 1.1+0.5%, 1.2+0.7%, respectively; p< 0.001). Whereas % of TNFα T cells in PsA PBMCs (20.7+0.66) was higher than PsA SFMCs (8.16+0.11, p< 0.001); IFNy expressing cells in PBMCs and SFMCs were similar. RA SFMCs had significantly higher numbers of IL-17A (4.9+0.2%), IL-22 (2.5+0.1%), IL-23R (2.1+0.4%) and IFNy (24.3+0.2%) compared to RA PBMCs (1.8+0.%%, 0.8+0.2%, 1.0+0.5%, and 14.7+0.%% respectively, p< 0.001). RA PBMCs had higher numbers of TNFα secreting cells than RA SFMCs (15.8+0.5% vs 7.9+0.2%; p< 0.001).

Conclusion: Consistent to our and other reports we noticed activated CD4 memory T cells were the major source for these cytokines. Compared to RA (Fig 1), in PsA SFMCs significantly higher levels of IL-17A, IL-22 and IL-23R were noticed. In RA SFMCs the levels of TNFα and IFNγ were significantly higher- a trend towards a Th1 pattern. The study supports the common view that in PsA the T cells are more skewed towards Th17 cells. Probably that explains better efficacy for anti-IL-17A targeted therapy in PsA compared to RA. More intriguing result is that in both in PsA and RA the pathological T cells in the SF were vastly polyfunctional. It is expected the kinetics of the polyfunctionality and thus their cytokine profile would vary at different time point of the disease and this could be one possible explanation for variations for responsiveness or failure to a specific anti-cytokine therapy.

Disclosure: S. Raychaudhuri, AbbVie, 2, Amgen, 5, Janssen, 2, 5, Lilly, 5, Novartis, 2, 5, Pfizer, 2, 5, Pfizer Inc, 2, Sun Pharma, 2; **S. Raychaudhuri**, Sun Pharmaceutical Industries Limited, 2.

Abstract Number: 2470

Relationship Between Serum Calprotectin Level and Presence of Subclinical Atherosclerosis and Arterial Stiffness in Patient with Psoriatic Arthritis

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Background/Purpose:: Calprotectin is a member of S100 leukocyte. Serum calprotectin is a sensitive biomarker of disease activity in patients with psoriatic arthritis (PsA). While various CV risk score only shown modest correlation with augmented CV risk in patient with PsA, whether calprotectin could play an addition role remains uncertain. Therefore, the aim of this study is to elucidate the association between serum calprotectin and subclinical atherosclerosis and arterial stiffness in patient with PsA

Methods: Seventy-eight PsA patient (age: 53±11 years, 47(54%) male) without CV event was recruited into this cross-sectional study. High resolution carotid ultrasound was performed to assess the presence of carotid plaque and intima-media thickness (IMT). Arterial stiffness was measured by branchial-ankle pulse wave velocity (PWV) and augmentation index (AIx). Serum calprotectin level was measured by QUANTA Lite Calprotectin Extended Range ELISA kit from (INOVA Diagnostics, San Diego, CA, USA).

Multivariate analysis for factors associated with presence of carotid plaque.

	OR	95% CI	*p*
Disease duration (years)	1.10	1.02 to 1.19	0.018
Ln Calprotectin	3.25	1.22 to 8.69	0.019

*Factors included in the multivariate analysis: age, gender, disease duration, swollen joint count, hyperlipidemia, Framingham 10-year CVD risk >10%, current use of statins, and calprotectin level

Table 1 - Multivariate analysis for factors associated with presence of carotid plaque

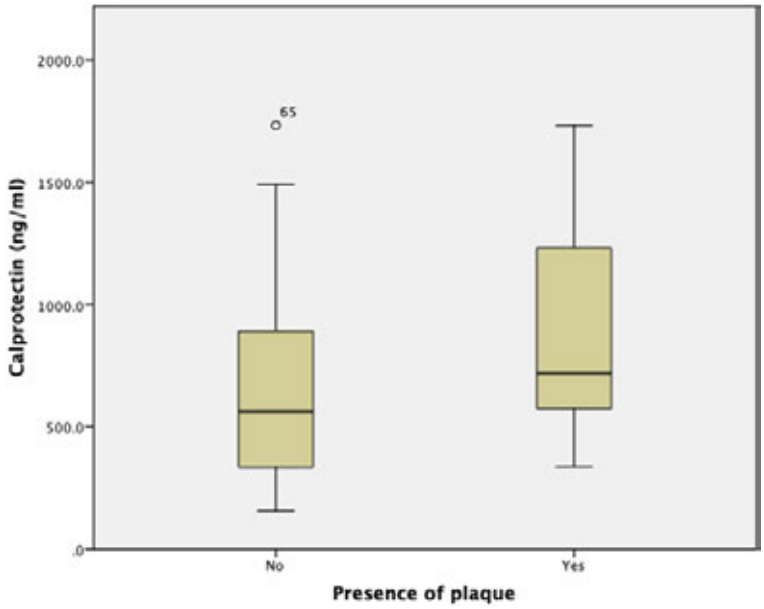

Figure 1 - Calprotectin level in subjects with or without carotid plaque

Results: 29/78 (38%) of patient had carotid plaque (CP+). Subjects in the CP+ group were older, had higher inflammatory burden in terms of higher number of swollen joint and longer disease duration. The prevalence of statins use was also higher in the CP+ group. Serum calprotectin level were significantly higher in the CP+ group (CP- group: 639.2 ±378.2 ng/ml,vs CP+ group: 911.8ng/ml ±429.4, p=0.005) (Figure 1). Using multivariate logistic regression analysis, higher level of ln calprotectin was an independent explanatory variable associated with the presence of carotid plaque (OR: 3.25, 95%CI: 1.22 to 8.69, p=0.019) after adjusting for baseline covariates. There was also significant correlation between calprotectin level and C-Reactive Protein (CRP) (r=0.237, p=0.037), mean IMT (r=0.301, p=0.021) and maximum IMT (r=0.265, p=0.043). However, no significant association were observed between calprotectin level and PWV or AIx.

Conclusion: Increased calprotectin level were associated with presence of plaque and increased IMT. Serum calprotectin may be a novel biomarker for assessing CV risk in patient with PsA.

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Abstract Number: 2471

Regional Difference in Disease Burden Among Patients with Psoriatic Arthritis: A Multi-Center Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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Background/Purpose: Psoriatic arthritis (PsA) has been defined as an inflammatory arthritis associated with psoriasis. The disease activity can be evaluated using many scales in patients with PsA. There is a great temperature difference between geographic region in Turkey. For example,the average annual air temperature in Erzurum (one of the Eastern Anatolian cities) is 5.7° C whereas in Antalya (one of the Mediterranean region cities) average temperature is 18.7° C. Furthermore, altitude of Eastern Anatolian cities is higher than Mediterranean cities.

The aim of this study was to assess whether there are regional differences in disease burden in patients with PsA.

Methods: Patients with PsA over the age of 18 who met the CASPAR classification criteria were enrolled consequently in this multicenter cross-sectional observational study. Turkish League Against Rheumatism (TLAR)- Network was formed with the participation of 25 different centers. Patients were grouped for 7 geographic regions (Marmara, Aegean, Mediterranean, Central Anatolia, Black Sea, Eastern Anatolia and southeastern Anatolia) in Turkey. Clinical and laboratory data were recorded. PsQoL; HAQ; BASFI, VAS-fatigue, VAS-pain, patient and physician GA; DAPSA,

	Marmara (n:407)	Central Anatolia (n:370)	Aegean (n:138)	Mediterranean (n:60)	Black Sea (n:59)	Eastern Anatolia (n:60)	Southeastern Anatolia (n:36)	p	Whole PsA (n:1130)
Age, year	46.12±12.05	47.94±12.04	49.01±12.99	50.42±11.47	47.58±10.35	40.03±13.19	43.33±11.18	**<0.0001**	46.96±12.25
Male (%)	146(35.9)	135(36.5)	51(37)	12(20)	26(44.1)	24(40.0)	13(36.1)	**0.042**	407(36)
BMI, kg/m2	29.16±4.90	28.69±5.09	28.91±5.80	29.79±5.45	28.71±3.99	26.33±3.57	27.87±4.63	**0.002**	28.79±5.04
Symptom durations, year	8.85±8.11	9.03±9.04	12.25±11.65	11.18±8.20	10.98±7.95	8.07±6.40	5.25±5.47	**<0.0001**	9.40±8.88
Diagnostic delay, year	2.97±4.45	2.61±4.54	3.94±5.94	2.24±3.63	3.20±3.88	2.93±4.01	2.33±3.15	0.096	2.92±4.58
VAS-pain (0-10)	4.54±2.72	4.79±2.61	4.42±2.51	4.32±2.23	4.58±2.09	4.73±2.56	7.33±2.11	**<0.0001**	4.69±2.62
PtGA	4.46±2.76	4.66±2.53	4.14±2.22	4.02±1.83	4.97±2.17	4.65±2.46	5.39±2.11	**0.041**	4.53±2.53
PhGA	3.66±2.29	4.11±2.22	3.91±2.08	3.48±1.93	3.83±1.85	4.38±2.35	5.17±2.18	**<0.0001**	3.92±2.22
VAS-fatigue	5.06±2.92	5.25±2.77	4.68±2.73	4.37±2.12	3.54±3.00	5.00±3.02	5.19±3.08	**0.001**	4.96±2.85
TJC	4.80±8.66	6.32±8.86	3.77±7.16	6.81±7.51	4.29±5.10	8.90±10.33	10.37±11.95	**<0.0001**	5.67±8.70
SJC	1.54±3.69	1.36±2.96	0.84±1.65	1.85±5.03	0.53±1.46	2.13±2.04	1.86±2.16	**0.028**	1.40±3.17
DAPSA	15.64±12.50	18.18±13.04	14.43±10.38	18.00±14.06	16.00±7.82	20.43±13.69	24.54±15.39	**<0.0001**	17.05±12.65
DAS28	3.32±1.21	3.35±1.26	3.42±1.09	3.41±1.27	3.23±0.94	3.82±1.23	4.24±1.32	**<0.0001**	3.40±1.22
BASDAI	4.32±2.47	3.91±2.41	3.12±1.85	3.44±1.65	3.37±1.30	3.63±2.05	5.03±2.11	**<0.0001**	3.93±2.31
BASFI	2.81±2.42	2.28±2.29	2.18±2.35	3.30±2.05	2.00±1.19	3.37±2.94	3.02±2.40	**<0.0001**	2.60±2.38
PASI	2.92±5.02	3.29±5.46	3.23±4.05	1.28±1.63	1.28±1.44	3.59±3.05	4.84±5.62	**0.001**	3.00±4.79
PsAQoL	7.52±6.33	7.28±6.44	5.61±6.26	6.88±7.01	5.22±4.64	4.22±4.85	6.75±6.12	**<0.0001**	6.85±6.30
HAQ	0.42±0.47	0.43±0.47	0.35±0.45	0.65±0.58	0.34±0.31	0.45±0.42	0.54±0.38	**0.001**	0.43±0.47

Table 1 Comparison of crude disease activity, quality of life and disability measures between 7 geographic regions of Turkey in patients with PsA (mean ± SD)

DAS28, BASDAI, and PASI scores were assessed. Statistical analysis was performed using the SPSS v22 package program. One-way ANOVA test were used to compare 7 geographic regions. Regression analysis was used to calculate adjusted disease measures. $p<0.05$ was considered statistically significant.

Results: A total 1130 patients (36% male, 64% female) with PsA included in this study. The mean age was 46.96 ± 12.25 years. The mean symptom duration was 9.40 ± 8.88 years. Crude results related to disease activity, quality of life and disability were summarized in table 1. Statistically significant differences observed for age, sex and BMI between groups. Thus, adjusted values of disease activity, quality of life and disability were calculated (table 2). Eastern Anatolian patients were youngest whereas Mediterranean patient were oldest (40.03 ± 13.19 vs 50.42 ± 11.47, $p< 0.0001$). Diagnostic delay time similar between groups (p:0.096). Crude VAS-pain, fatigue, PtGA, PhGA were significantly different between groups whereas this difference disappeared when adjustment for age, sex and BMI were made in table 2. Disease activity score were highest in Mediterranean region and lowest in eastern Anatolia region according to adjusted DAPSA (17.72 ± 1.75 vs 16.35 ± 1.62, $p< 0.0001$), DAS28 (3.53 ± 0.29 vs 3.25 ± 0.28 $p< 0.0001$) and BASDAI (4.12 ± 0.48 vs 3.80 ± 0.49, p:0.080). Adjusted BASFI (2.83 ± 0.52 vs 2.28 ± 0.51, $p< 0.0001$), PsAQoL (7.54 ± 1.48 vs 6.07 ± 1.44, $p< 0.0001$) and HAQ (0.48 ± 0.11 vs 0.36 ± 0.13, $p< 0.0001$) score were highest in Mediterranean region and lowest in Eastern Anatolia region. Additionally, PASI score lowest in Mediterranean region and highest in Eastern Anatolia region.

	Marmara (n:407)	Central Anatolia (n:370)	Aegean (n:138)	Mediterranean (n:60)	Black Sea (n:59)	Eastern Anatolia (n:60)	Southeastern Anatolia (n:36)	p	Whole PsA (n:1130)
VAS-pain (0-10)	4.71±0.47	4.68±0.48	4.68±0.50	4.85±0.39	4.61±0.50	4.65±0.46	4.69±0.47	0.160	4.69±0.47
PtGA	4.54±0.41	4.51±0.42	4.52±0.45	4.66±0.35	4.46±0.43	4.48±0.40	4.53±0.41	0.140	4.53±0.42
PhGA	3.93±0.25	3.91±0.25	3.92±0.27	4.01±0.21	3.88±0.26	3.88±0.24	3.91±0.25	0.088	3.92±0.25
VAS-fatigue	4.98±0.74	4.94±0.74	4.96±0.77	5.22±0.62	4.84±0.76	4.82±0.70	4.93±0.74	0.068	4.96±0.74
TJC	5.74±1.50	5.64±1.49	5.77±1.62	6.18±1.37	5.51±1.35	5.00±1.17	5.43±1.41	**0.001**	5.67±1.49
SJC	1.41±0.15	1.39±0.16	1.38±0.18	1.40±0.14	1.39±0.15	1.45±0.17	1.44±0.14	**0.015**	1.40±0.16
DAPSA	17.14±2.00	16.98±1.96	17.18±2.13	17.72±1.75	16.84±1.90	16.35±1.62	16.67±1.76	**0.007**	17.05±1.97
DAS28	3.41±0.33	3.40±0.33	3.43±0.33	3.53±0.29	3.36±0.30	3.25±0.28	3.34±0.32	**<0.0001**	3.40±0.33
BASDAI	3.95±0.56	3.92±0.56	3.92±0.60	4.12±0.48	3.87±0.56	3.80±0.49	3.89±0.54	0.080	3.93±0.56
BASFI	2.59±0.58	2.63±0.57	2.67±0.60	2.83±0.52	2.50±0.45	2.28±0.51	2.44±0.55	**<0.0001**	2.60±0.57
PASI	3.04±0.55	2.96±0.53	2.92±0.53	2.79±0.52	3.02±0.49	3.25±0.57	3.14±0.51	**<0.0001**	3.00±0.54
PsAQoL	6.88±1.71	6.86±1.68	6.96±1.76	7.54±1.48	6.68±1.44	6.07±1.44	6.55±1.62	**<0.0001**	6.85±1.68
HAQ	0.42±0.13	0.43±0.12	0.44±0.12	0.48±0.11	0.42±0.11	0.36±0.13	0.40±0.12	**<0.0001**	0.43±0.13

Table 2 Comparison of adjusted disease activity, quality of life and disability measures between 7 geographic regions of Turkey in patients with PsA [mean ± SD)(adjustment for age, sex and BMI)

Conclusion: This is the first study reporting that geographic region differences may affect disease activity as well as patient characteristic in patients with PsA. Regional weather conditions such as temperature, humidity and altitude may explain the regional differences in disease activities and other clinical characteristics.

Disclosure: E. Kilic, None; **G. Kilic**, None; **K. Nas**, None; **B. Sargin**, None; **S. Acer Kasman**, None; **H. Alkan**, None; **N. Sahin**, None; **G. Cengiz**, None; **N. Cuzdan**, None; **I. Albayrak Gezer**, None; **D. Keskin**, None; **C. Mulkoglu**, None; **H. Resorlu**, None; **I. Sunar**, None; **A. Bal**, None; **M. Duruoz**, İbrahim etem, 8, Abdi İbrahim, 8, Abdi Ibrahim, 8, Abvie, 2, 8, AMGEN, 8, AMGEN, Novartis, ILKO, ONKO, İbrahim Ethem, Abdi İbrahim, 8, Ibrahim Ethem, 8, ILKO, 8, Novartis, 8, ONKO, 8; **O. Kucukakkas**, None; **O. Yurdakul**, None; **M. Alkan Melikoglu**, None; **Y. Aydin**, None; **F. Ayhan**, None; **H. Bodur**, None; **M. Calis**, None; **E. Capkin**, None; **G. Devrimsel**, None; **K. Gök**, None; **S. Hizmetli**, None; **A. Kamanli**, None; **Y. Keskin**, None; **H. Kocabas**, None; **O. Kutluk**, None; **N. Sen**, None; **O. Sendur**, None; **I. Tekeoglu**, None; **S. Tolu**, None; **M. Toprak**, None; **T. Tuncer**, None.

Abstract Number: 2472

The Role of Ultrasound for the Assessment of Psoriatic Arthritis Patients with Fibromyalgia – Interim Analysis

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Background/Purpose: Psoriatic arthritis is a chronic inflammatory disease. More than 20% of patients with PsA patients suffer from fibromyalgia, a chronic pain syndrome characterized by widespread pain and tender points. PsA patients with concomitant fibromyalgia have high scores of disease activity, irrespective of underlying inflammatory process. Thus, assessment of clinical disease activity in those patients is challenging. Ultrasound (US) is a common imaging modality for disease activity evaluation. Hence, the aim of the current study is to examine whether US can be used as an objective tool for assessment of disease activity in PsA patients with fibromyalgia.

Methods: The study population included consecutive PsA patients that were recruited prospectively. All the patients fulfilled the CASPAR criteria. The assessment of the patients included complete medical history and physical examination, including assessment of 68 joints, enthesitis (Leeds and SPARCC) and fibromyalgia tender points. All the patients were assessed by the widespread pain index (WPI) and symptom severity score (SSS) for fibromyalgia. Patients were classified with fibromyalgia if they fulfilled the 1990 or 2010 classification criteria for fibromyalgia. All the patients underwent a detailed US evaluation including 40 joints, 40 tenosynovitis and 14 points of entheses (according to the MASES index plus bilateral lateral epicondyles). The score of the US was based on the summation of semi-quantitative score (0-3) for joints and tendons plus enthesitis score based on the MASEI score. Both clinical and sonographic evaluation occurred in the same day and the sonographer was blinded to the clinical data.

Results: Eighty-six patients completed the study. Overall, 3440 joints, 3440 tendons and 1204 entheses were scanned by the US. Thirty-three patients (38%) classified with both PsA and fibromyalgia were compared to 53 (62%) PsA patients without fibromyalgia. The demographic data were overall similar in PsA patients with and without fibromyalgia (Table 1). Patients with PsA and fibromyalgia had significantly increased scores for almost all the clinical measures, including not being in MDA (97% vs 56.6%, $p< 0.001$), CPDAI (11.5 vs. 7.3, $p< 0.001$) and DAPSA (33.6 vs. 15.5, $p< 0.001$). The total US score were similar between patients with and without fibromyalgia. Furthermore, the subcategories of US synovitis, tenosynovitis and enthesitis were comparable in both groups (Table 2).

Characteristics	PsA without Fibromyalgia N=53	PsA with Fibromyalgia N=33	P-Value
Age, mean (± s.d)	55.8 (12)	52.3 (14.4)	0.24
Gender, Female, n (%)	29 (54.7)	21 (63.6)	0.55
BMI, mean (± s.d)	27.9 (5)	28.1 (4.4)	0.9
Smoking, n (%)	32 (62.7)	16 (48.5)	0.32
Worker, n (%)	40 (75.5)	13 (40.6)	0.02
Education, Academic, n (%)	45 (84.9)	20 (60.6)	0.04
PSO duration, mean (± s.d)	21.5 (15.4)	17.7 (15.4)	0.27
PsA duration, mean (± s.d)	11.8 (13.4)	10.4 (10.6)	0.61
TJC, mean (± s.d)	6.1 (6.1)	15.8 (12.1)	<0.001
SJC, mean (± s.d)	0.89 (1.96)	0.9 (2.1)	0.9
Leeds Enthesitis, mean (± s.d)	0.8 (1.27)	2.4 (1.75)	<0.001
SPARCC, mean (± s.d)	1.7 (2.13)	5.7 (4.25)	<0.001
PASI, mean (± s.d)	2.1 (4.28)	0.8 (1.84)	0.11
GPhA	1.61 (1.72)	3.6 (2.57)	<0.001
CRP mg/l, mean (± s.d)	6 (8.6)	10.4 (9.6)	0.03
ESR, mm/h, mean (± s.d)	17.6 (10.6)	29.7 (15.8)	0.01
MDA, n (%)	30 (56.6)	32 (97)	<0.001
CPDAI, mean (± s.d)	7.3 (3.7)	11.5 (1.1)	<0.001
DAPSA, mean (± s.d)	15.5 (11.2)	33.6 (13.9)	<0.001
WPI	2.2 (2.8)	10.2 (4.2)	<0.001
SSS	2.9 (2.5)	8.2 (2.3)	<0.001
Tender points, mean (± s.d)	1.6 (3.2)	9 (5.7)	<0.001
Treatment			
sDMARDs, n (%)	25 (47.2)	16 (48.5)	1
Otezla, n (%)	1 (1.9)	2 (6.1)	0.67
Biologics, n (%)	31 (58.5)	15 (45.5)	0.4

Table 1 Demographic and clinical data
Demographic and cinical characteristics

	PsA without Fibromyalgia N=53	PsA with Fibromyalgia N=33	P-Value
Total US Score, mean (± s.d)	29.2 (18.8)	26 (23.8)	0.5
Synovitis score, mean (± s.d)	11.9 (12)	11.1 (16.2)	0.8
Tenosynovitis score, mean (± s.d)	2.6 (3.4)	2.6 (3.7)	0.9
Enthesitis score, mean (± s.d)	14.4 (9.1)	12.1 (8.9)	0.3

Table 2. Sonographic comparison between PsA with to without fibromyalgia
Table 2. Sonographic comparison between PsA with and without fibromyalgia

Conclusion: While patients with PsA and fibromyalgia had increased scores of clinical measures of disease activity compared to those without fibromyalgia, US scores were similar between the groups. Hence, US can be used as a discriminative tool for objective assessment of disease activity in patients with PsA and concomitant fibromyalgia.

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Abstract Number: 2473

Implementing the Psoriatic Arthritis Disease Activity Score (PASDAS) in Routine Clinical Practice: (im)possible?

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous disease, with involvement of at least five health domains: peripheral joint disease, enthesitis, dactylitis, axial involvement, and skin and nail psoriasis. Because of the heterogeneity of the disease, assessment of disease activity is challenging. One of the many single or composite outcome measures that has been developed is the Psoriatic Arthritis Disease Activity Score (PASDAS). The PASDAS is a comprehensive measure that takes arthritis (66/68 joint score), dactylitis, enthesitis, CRP, physician disease activity VAS score and patient-reported outcomes into account. Furthermore, it is a continuous outcome measure in contrast to the Minimal Disease Activity criteria (MDA), facilitating the longitudinal follow-up of disease activity. The PASDAS also has better parametric distribution and discriminative capacity compared to other outcome measures such as the Disease Activity for PSoriatic Arthritis score (DAPSA). However, feasibility of PASDAS use in routine clinical care has been questioned due to its complexity. It requires a CRP and filled-out SF36 form at time of assessment, does not include a formal skin assessment, is difficult to calculate and is time consuming for both patient and physician. Here we describe our efforts to mitigate these drawbacks and to implement routine measurement of the PASDAS for all 1200 PsA patients in our clinical practice.

Methods: The implementation consisted of the following stages: 1) assessment of patients' acceptability of measurement burden; 2) implementation of mathematical calculations of the PASDAS in our electronic health record; 3) PASDAS and skin assessment training of rheumatology nurses and rheumatologists; and 4) (logistic) adjustments to the outpatient visit.

Results: Our patient partners preferred comprehensive clinical assessment of skin and joints above a limited assessment, although the former would be more time consuming. For this reason, and to comply with international guidelines, we decided to also add assessment of skin disease, by using the Body Surface Area (BSA) and Physician Global Assessment score (PGA). Furthermore, research demonstrated that for the PASDAS calculation the physical component score (PCS) of the SF36 could be substituted by the SF12-PCS. As the SF12 is more concise, minimizing patient burden, we chose to implement the SF12 instead of the SF36. To enable hassle free calculation of the PASDAS, the scoring formulas including mannequins for joint, enthesitis and dactylitis scoring, and the SF12v1 together with the skin scores (BSA and PGA) were implemented in our electronic health record. Lastly, we set-up a three phase consultation that consists of laboratory tests and consultation with a rheumatology nurse who performs the physical measurements before each visit with the physician.

Conclusion: Standardized and routine measurement of the PASDAS and skin involvement at each outpatient visit of all our PsA patients before consultation with the treating rheumatologist was successfully implemented, underscoring the feasibility of this approach. In addition to improving clinical care, routine outcome measurements can be used for a variety of clinical studies.

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Abstract Number: 2474

Impact of Multidomain Disease Presentations on Overall Disease Burden Among Patients with Psoriatic Arthritis: Results from the Corrona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry

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SESSION INFORMATION

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Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory disease with heterogeneous presentations that may involve peripheral arthritis, axial disease, enthesitis, dactylitis, and psoriatic skin and nail disease, either alone or in combination. Prior studies have characterized patients affected in one domain; however, there is limited evidence in understanding the differential impact of multidomain vs single-domain presentations on the overall disease burden in PsA. We aim to compare disease characteristics, quality of life, and work productivity at enrollment among patients with PsA who have multidomain vs single-domain presentations in the Corrona PsA/SpA Registry.

Methods: This study included adult patients with PsA enrolled in the Corrona PsA/SpA Registry between March 2013 and August 2018. Patients were evaluated for the presence of 6 disease domains at enrollment: enthesitis (SPARCC enthesitis count > 0), dactylitis (dactylitis count > 0), peripheral arthritis (PA; tender and/or swollen joint count > 0), nail psoriasis (global nail psoriasis VAS > 0), axial disease (physician-reported presence of spinal involvement, based on clinical judgment and/or radiographs or MRI showing sacroiliitis), and skin disease (BSA > 0%), and were further classified as having multidomain or single-domain disease presentations. Separate multivariable linear regression models evaluated the association of the presence of multidomain presentations with selected PsA disease characteristics, quality of life, and work productivity measures relative to single-domain presentations. Models were adjusted for age, sex, race, BMI, disease duration, and current and prior biologic, conventional synthetic disease-modifying antirheumatic drug, and prednisone use.

Results: Of 2315 patients with PsA enrolled in the Corrona PsA/SpA Registry who had ≥ 1 disease domain presentation, 1698 patients (73.3%) were classified as having multidomain disease presentations and 617 (26.7%) as single-domain presentations. The most common single-domain and multidomain presentations, respectively, were skin disease (12.7%) and PA + skin disease (11.7%). At enrollment, patients with multidomain presentations had higher BMI; shorter disease duration; were more likely to have fibromyalgia, depression, and anxiety; and were more likely

Table 1. Demographics, Treatment Profiles, Disease Activity, Quality of Life, and Work Productivity at Enrollment for Patients With Multidomain vs Single-Domain PsA Disease Presentations

Characteristic*	Multidomain (N = 1698)	Single Domain† (N = 617)	*P* Value‡
Age, years	53.5 (13.2) [1678]	54.5 (12.9) [607]	0.20
Female, n/m (%)	907/1689 (53.7)	314/610 (51.5)	0.35
Race, n (%)	n = 1655	n = 596	0.04
White	1548 (93.5)	572 (96.0)	
Black	9 (0.5)	4 (0.7)	
Other	98 (5.9)	20 (3.4)	
BMI, kg/m^2	32.0 (7.4) [1658]	31.3 (7.6) [600]	< 0.01
Symptom duration, years	11.3 (10.7) [1651]	11.0 (9.7) [594]	0.51
Disease duration, years	7.7 (8.8) [1662]	8.5 (8.1) [598]	< 0.01
Select comorbidities, n (%)			
Psoriasis	1537 (90.5)	520 (84.3)	< 0.01
Nail psoriasis	602 (35.5)	81 (13.1)	< 0.01
Depression	280 (16.5)	57 (9.2)	< 0.01
Fibromyalgia	114 (6.7)	23 (3.7)	< 0.01
Anxiety	65 (3.8)	12 (1.9)	0.03
History of biologic use, n (%)	561 (33.0)	151 (24.5)	< 0.01
History of csDMARD use, n (%)	478 (28.2)	151 (24.5)	0.08
History of prednisone use, n (%)	230 (13.5)	83 (13.5)	0.95
Current biologic use, n (%)	980 (57.7)	378 (61.3)	0.13
Current csDMARD use, n (%)	859 (50.6)	339 (54.9)	0.06
Current prednisone use, n (%)	122 (7.2)	42 (6.8)	0.75
Physician global assessment (VAS 0-100)	24.3 (21.4) [1686]	10.9 (15.0) [612]	< 0.01
Physician global assessment of psoriasis (VAS 0-100)	28.0 (22.6) [1661]	12.9 (15.0) [594]	< 0.01
Patient pain (VAS 0-100)	44.8 (29.2) [1590]	28.6 (26.9) [580]	< 0.01
Patient-reported fatigue (VAS 0-100)	45.9 (29.2) [1676]	33.8 (28.4) [602]	< 0.01
Patient global assessment (VAS 0-100)	43.1 (28.4) [1669]	36.8 (31.5) [605]	< 0.01
HAQ-DI (0-3)	0.8 (0.7) [1600]	0.5 (0.6) [586]	< 0.01
EQ-5D (0-1)	0.7 (0.2) [1592]	0.8 (0.2) [579]	< 0.01
EQ VAS (0-100)	67.4 (21.5) [1667]	75.5 (19.8) [606]	< 0.01
WPAI domains			
Current employment, n/m (%)	987/1646 (60.0)	381/595 (64.0)	0.08
% Work time missed	6.2 (17.5) [842]	2.7 (11.3) [323]	< 0.01
% Impairment while working	22.9 (24.4) [887]	12.4 (18.9) [344]	< 0.01
% Overall work impairment	26.2 (26.8) [798]	13.0 (19.5) [306]	< 0.01
% Activity impairment	34.7 (29.9) [1530]	19.1 (24.3) [549]	< 0.01

BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; EQ-5D, EuroQol-5 Dimensions; EQ VAS, EuroQol visual analogue scale; HAQ-DI, Health Assessment Questionnaire Disability Index; PsA, psoriatic arthritis; WPAI, Work Productivity and Activity Impairment questionnaire; VAS, visual analog scale.
* All values were calculated based on available data and are presented as "mean (SD) [n]" unless otherwise stated.
† Single-domain disease presentations for PsA overall (N = 617) included skin disease (53.8%), peripheral arthritis (29.0%), nail psoriasis (10.9%), axial disease (3.4%), enthesitis (1.8%), and dactylitis (1.1%).
‡ *t*-test or Wilcoxon rank-sum test for continuous variables and χ^2 or Fisher's exact test for categorical variables.

to have prior biologic use vs those with single-domain presentations (**Table 1**). In adjusted analyses, the presence of multidomain presentations was associated with significantly worse patient and physician global assessment of disease, pain, fatigue, HAQ-DI and EQ-5D scores, and work productivity and activity at enrollment (**Table 2**).

Table 2. Multidomain vs Single-Domain Impact on Outcomes—Multivariable Regression Coefficients Estimating the Association of Presence of Multidomain Presentations With Selected PsA Disease Activity, Quality of Life, and Work Productivity and Activity Measures Relative to Single-Domain Presentations in Patients With PsA

Outcomes*	β Coefficient (95% CI)	*P* Value
Physician global assessment	12.16 (10.30, 14.01)	< 0.001
Physician global assessment of psoriasis	14.03 (12.03, 16.04)	< 0.001
Patient pain	14.02 (11.26, 16.78)	< 0.001
Patient-reported fatigue	10.09 (7.38, 12.81)	< 0.001
Patient global assessment	5.65 (2.81, 8.49)	< 0.001
HAQ-DI	0.26 (0.20, 0.32)	< 0.001
EQ-5D	−0.07 (−0.09, −0.06)	< 0.001
% Work time missed	2.71 (0.57, 4.84)	0.013
% Impairment while working	8.63 (5.72, 11.55)	< 0.001
% Overall work impairment	11.02 (7.69, 14.36)	< 0.001
% Activity impairment	13.47 (10.65, 16.29)	< 0.001

BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; EQ-5D, EuroQol 5-Dimensions; HAQ-DI, Health Assessment Questionnaire Disability Index; PsA, psoriatic arthritis.
* Single-domain disease is the reference group. Adjusted for age, sex, race, BMI, disease duration, and current and prior biologic, csDMARD, and prednisone use.

Conclusion: In this US real-world cohort, nearly three-quarters of patients with PsA had multidomain disease presentations, which were associated with worse disease activity, quality of life, and work productivity measures compared with single-domain disease presentations. Assessing all PsA domains is critical for developing a comprehensive management plan and reducing the impact of PsA on patients' lives.

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Abstract Number: 2475

Prevalence of Disease Domain Presentations Among Patients with Psoriatic Arthritis: Results from the Corrona Psoriatic Arthritis/ Spondyloarthritis (PsA/SpA) Registry

Alexis Ogdie,[1] Peter Hur,[2] Mei Liu,[3] Sabrina Rebello,[3] Robert McLean,[3] Blessing Dube,[3] Meghan Glynn,[4] and Philip Mease[5], [1]Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [3]Corrona, LLC, Waltham, MA, [4]Corrona, LLC, Waltham, [5]Swedish Medical Center/Providence St Joseph Health, and University of Washington, Seattle, WA

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

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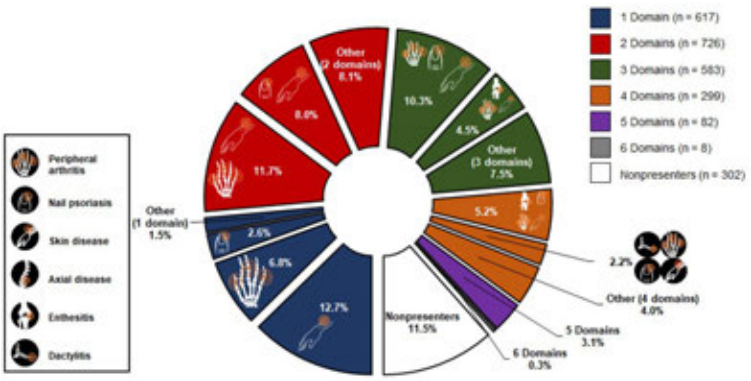
Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous, chronic inflammatory disease of the skin and musculoskeletal system. Six key domains of PsA have been identified to help guide treatment: peripheral arthritis, axial disease, enthesitis, dactylitis, nail psoriasis, and skin disease.[1] Understanding the epidemiology of these different disease presentations is important for the management and treatment of PsA, yet there is limited evidence available. We aim to describe the prevalence of disease domain presentations among patients with PsA at enrollment in the Corrona PsA/SpA Registry.

Methods: This study included adult patients with PsA enrolled in the Corrona PsA/SpA Registry between March 2013 and August 2018. Patients were evaluated for the presence of 6 disease domains at enrollment: enthesitis (Spondyloarthritis Research Consortium of Canada enthesitis count > 0), dactylitis (dactylitis count > 0), peripheral arthritis (PA; tender and/or swollen joint count > 0), nail psoriasis (global nail psoriasis visual analog scale > 0), axial disease (physician-reported presence of spinal involvement, based on clinical judgment and/or radiographs or MRI showing sacroiliitis), and skin disease (BSA > 0%). The most common mutually exclusive disease presentations were summarized among all patients with PsA and those who initiated biologics using frequency counts and percentages.

Results: Of 2617 patients with PsA enrolled in the Corrona PsA/SpA Registry, 1698 patients (64.9%) had multidomain disease presentations, 617 (23.6%) had single-domain presentations, and 302 (11.5%) had no presentations. Overall, 1814 (69.3%) patients presented with skin disease, 1523 (58.2%) with PA, 1042 (39.8%) with nail psoriasis, 539 (20.6%) with enthesitis, 319 (12.2%) with axial disease, and 235 (9.0%) with dactylitis at enrollment. Among all patients with PsA, the most common disease presentations were skin disease (12.7%), PA + skin disease (11.7%), and PA + nail psoriasis + skin disease (10.3%) (**Figure 1**). A total of 354 patients initiated biologics at enrollment. Of these, 289 patients (81.6%) had multidomain disease presentations, 45 (12.7%) had single-domain presentations, and 20 (5.6%) had no presentations; 273 patients (77.1%) presented with PA, 267 (75.4%) with skin disease, 159 (44.9%) with nail psoriasis, 115 (32.5%) with enthesitis, 70 (19.8%) with dactylitis, and 64 (18.1%) with axial disease at enrollment. The most common disease presentations were PA + nail psoriasis + skin disease (11.6%), PA + skin disease (11.3%), enthesitis + PA + nail psoriasis + skin disease (8.8%), and enthesitis + PA + skin disease (5.9%) (**Figure 2**).

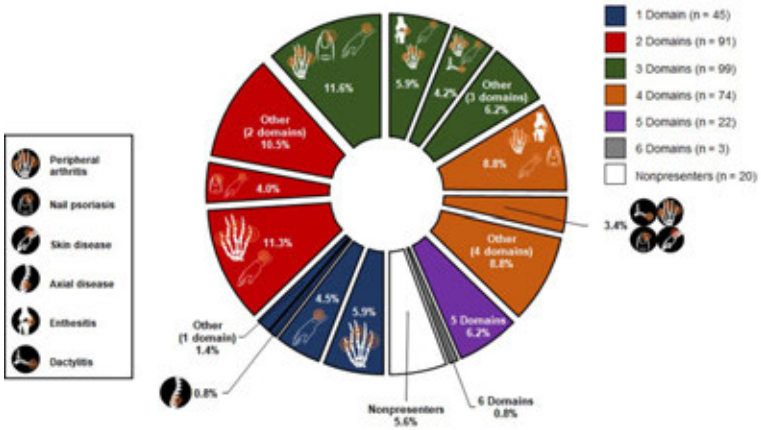
Conclusion: The majority of patients with PsA presented with multiple disease domains. Biologic initiators generally had a higher prevalence of all disease features. These results may increase the physician awareness of the heteroge-

Figure 1. Most Common PsA Domain Presentations by Number of Domains Affected Among All Patients With PsA (N = 2617)



PsA, psoriatic arthritis.
* Other (2-4 domains) presentations include all other combinations of ≥ 2 domains not shown in the figure.
† Other (1 domain) presentations include axial disease, enthesitis, and dactylitis.

Figure 2. Most Common PsA Domain Presentations by Number of Domains Affected Among Biologic Initiators (n = 354)



PsA, psoriatic arthritis.
* Other (2-4 domains) presentations include all other combinations of ≥ 2 domains not shown in the figure.
† Other (1 domain) presentations include axial disease, enthesitis, and dactylitis.

neity of disease presentations among patients with PsA, which can be important for the development of an effective management plan.

References:

1. Coates LC, et al. *Arthritis Rheumatol.* 2016;68(5):1060-71.

Disclosure: A. Ogdie, AbbVie, 5, 8, Amgen, 2, 5, 8, BMS, 5, Celgene, 5, 8, Corrona, LLC, 5, Lilly, 5, National Psoriasis Foundation, 2, NIH/NIAMS, 2, Novartis, 2, 5, 7, Pfizer, 2, 5, Rheumatology Research Foundation, 2, Takeda, 5; **P. Hur**, Novartis, 3, Novartis Pharmaceuticals Corporation, 3, Novartis Pharmaceuticals Corporations, 3; **M. Liu**, Corro-

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Abstract Number: 2476

Side Effects of Methotrexate and TNFi: Differences in Tolerability Among Patients with PsA and RA

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate (MTX) is generally well tolerated in rheumatoid arthritis (RA) but little is known about the tolerability of MTX in psoriatic arthritis (PsA). One recent study has identified shorter MTX persistence among patients with PsA compared to RA in the US,[1] while another study in Europe found similar persistence on MTX in RA and PsA.[2] In addition, tolerability to MTX may be lower than tumor necrosis factor inhibitors (TNFi) in both PsA and RA. We hypothesized that shorter MTX persistence in patients with PsA is due to lower tolerability relative to RA patients.

Objective: To examine the relative reporting of side effects to MTX and TNFi among patients with PsA compared to RA within one year of drug initiation.

Methods: Retrospective cohort study conducted using data from the Forward, The National Databank for Rheumatic Diseases, from 2000 through 2018. Patients enroll in the registry and complete questionnaires every 6 months. Patients with RA and PsA were included in this study if they had at least one questionnaire completed prior to initiating a target drug (MTX or a TNFi) and at least one questionnaire within 12 months after initiation (new user design). The

Table 1. Baseline characteristic of new initiators of MTX and TNFi. Forward Databank

	MTX Initiators[a]		TNFi Initiators[b]	
	RA	PSA	RA	PsA
	N (SD)	N (SD)	N (SD)	N (SD)
N	2047	54	3793	107
Age (mean, SD)	59.76 (12.6)	52.13 (11.9)	59.85 (12.1)	55.01 (11.3)
Female (N, %)	1677 (83%)	41 (77%)	3,093 (82 %)	73 (68%)
Duration (mean, SD)	14.55 (11.1)	12.71 (10.8)	14.89 (10.9)	12.36 (9.3)
Some College (N, %)	1168 (59.5)	34 (69.4)	2,184 (59.9)	65 (63.7)
BMI (mean, SD)	28.07 (6.8)	32.12 (8.53)	28.3 (6.9)	31.31 (8.15)
Obese (N, %)	628 (33%)	30 (56%)	1,202 (33%)	50 (48%)
Comorbidity Count (mean, SD)	1.5 (1.75)	1.61 (1.86)	1.4 (1.58)	1.54 (1.53)
Symptoms Reported (mean, SD)	8.64 (6.39)	10.65 (7.61)	8.11 (6.02)	8.84 (6.33)
Depression (N, %)	367 (19%)	18 (33%)	587 (16%)	26 (24%)
Fibromyalgia[c] (N, %)	65 (3%)	6 (11%)	95 (3%)	8 (7%)

Notes: [ab] The MTX and TNFi initiator groups for RA and PsA include both the mono and combo therapy initiators (e.g., the MTX initiator groups include MTX mono initiators and TNFi users who added MTX). [c] Physician-diagnosed fibromyalgia.

primary outcome of interest was the rate of reported side effects to the target drug. The prevalence of side effects over 1 year was reported among patients with RA and PsA, and stratified by use of MTX monotherapy, TNFi monotherapy, or MTX-TNFi combination therapy (starting either MTX or TNFi and adding second to regimen). In the primary analysis, patients could enter the TNFi cohort more than once if more than one drug was initiated. In a sensitivity analysis, we only allowed patients to enter the cohort for first TNFi.

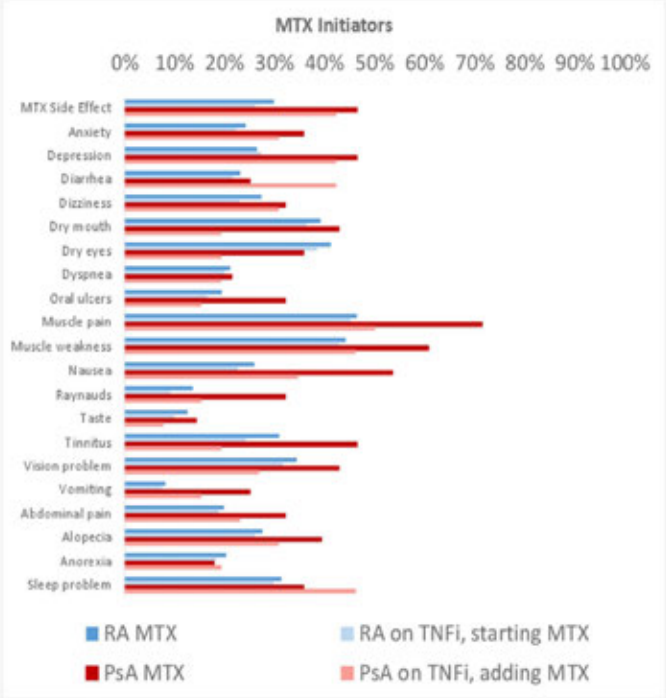

Figure 1. Patient-reported side effects among new initiators of MTX.

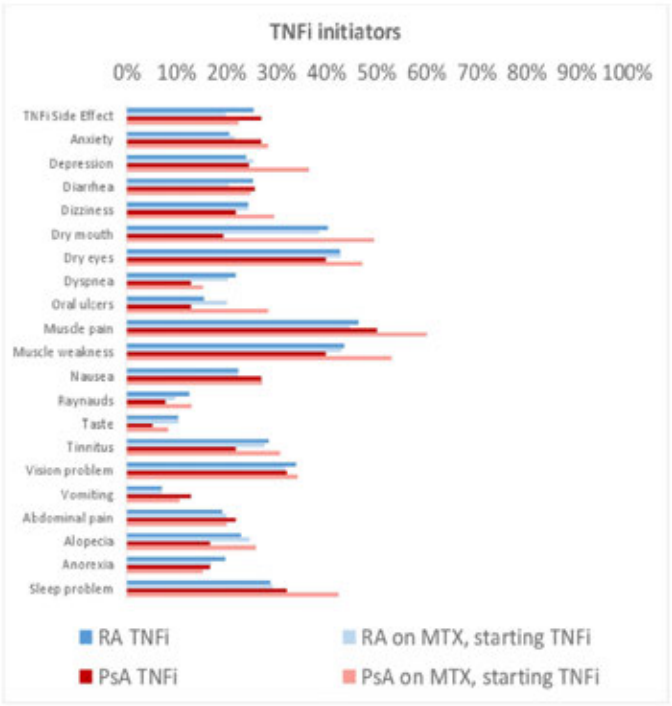

Figure 2. Patient-reported side effects among new initiators of TNFi.

Results: Use of MTX or TNFi was reported among 11,571 patients with RA and 598 patients with PsA. Of these, 2,047 RA and 54 PsA patients were new initiators of MTX, and 3,793 RA and 107 PsA patients were new initiators of a TNFi. Baseline characteristics are shown in Table 1. Among initiators of MTX, 26-30% of RA patients compared to 42-46% of PsA patients reported a side effect in the first year (Figure 1). Among initiators of TNFi, 20-25% of RA and 22-27% of PsA patients reported a side effect in the first year (Figure 2). PsA patients initiating MTX were more likely to report nausea, vomiting, abdominal pain, anxiety, depression, tinnitus, and alopecia compared to RA patients initiating MTX or PsA patients initiating a TNFi.

Conclusion: Patients with PsA, in general, reported more symptoms than patients with RA. In particular, patients with PsA patients reported more side effects to MTX compared to patients with RA or patients with PsA initiating a TNFi.

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1. George, M.D., Baker, J.F. and Ogdie, A., Discontinuation of Methotrexate or TNF Inhibitors in Patients with Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis [abstract]. Arthritis Rheumatol 2018; (Vol. 70, suppl 10).

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Abstract Number: 2477

Burden of Disease at Treatment Initiation Among Biologic-Naïve Patients with Oligoarticular versus Polyarticular Psoriatic Arthritis in the Corrona Psoriatic Arthritis/Spondyloarthritis Registry

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Oligoarticular PsA accounts for ≈50% of PsA worldwide, but only a paucity of data describes disease burden among these patients. The Corrona PsA/SpA Registry, a prospective, US-based, observational cohort study, collects real-world data on PsA patient characteristics and treatment, including oligoarthritis. This analysis characterized patient demographics, clinical characteristics, and patient-reported outcomes (PROs) at treatment initiation in the Corrona PsA/SpA Registry in biologic-naïve patients with oligoarticular (≤4 swollen and ≤4 tender joints) vs polyarticular (>4 swollen or >4 tender joints) PsA.

Methods: Biologic-naïve patients ≥18 years of age diagnosed with PsA and enrolled in the registry who initiated apremilast, biologics, and/or csDMARDs for PsA from March 2013–December 2018 were included. Patient demographics, disease activity, treatment history, comorbidities, and PRO data were analyzed at treatment initiation; comparisons between oligoarticular and polyarticular PsA patients were performed using *t*-tests or Wilcoxon rank-sum tests for continuous variables and chi-square tests or Fisher's exact tests for categorical variables.

Results: 330 biologic-naïve PsA patients initiating apremilast, biologics, and/or csDMARDs were included (oligoarthritis: n=149; polyarthritis: n=181). Demographics and clinical characteristics were mostly similar for patients with oligoarthritis and polyarthritis, including mean age (51.6 vs 54.3 years; *P*=0.068), proportion of females (51.0% vs 59.7%; *P*=0.117), mean disease duration (3.0 vs 3.1 years; *P*=0.789), and prior use of csDMARDs (13.4% vs 21.0%; *P*=0.072). Comorbidity history was similar between the 2 groups, but the proportion of patients with fibromyalgia was higher in the polyarthritis group (2.0% vs 8.8%; *P*=0.008; Table 1). Patients with oligoarthritis had lower disease activity at treatment initiation vs those with polyarthritis based on SJC (0-66) and TJC (0-68), nail psoriasis VAS score, cDAPSA score, presence of enthesitis, SPARCC enthesitis score, presence of dactylitis, and dactylitis count. More patients with oligoarthritis were classified with minimal disease activity vs patients with polyarthritis (Table 2). Mean Pain VAS (42.6 vs 59.8), Fatigue VAS (41.9 vs 55.3), Patient's Global Assessment of Disease Activity VAS (38.6 vs 47.7), and HAQ-DI (0.7 vs 1.0) scores were significantly lower and the proportion of patients with HAQ-

Table 1. History of Comorbid Conditions Among Biologic-Naïve Patients With Oligoarticular vs. Polyarticular PsA*,§

History of Comorbidity, n (%)	Oligoarthritis n=149	Polyarthritis n=181	*P* Value
Cancer (any except NMSC)	15 (10.1)	19 (10.5)	0.898
Cardiovascular disease	17 (11.4)	23 (12.7)	0.719
Depression	20 (13.4)	36 (19.9)	0.119
Diabetes mellitus	20 (13.4)	33 (18.2)	0.236
Fibromyalgia	3 (2.0)	16 (8.8)	0.008
Hyperlipidemia	26 (17.4)	38 (21.0)	0.418
Hypertension	48 (32.2)	74 (40.9)	0.104
Metabolic syndrome	19 (12.8)	33 (18.2)	0.174
Nail psoriasis	65 (43.6)	97 (53.6)	0.071
Psoriasis	121 (81.2)	150 (82.9)	0.694

*Oligoarticular PsA (≤4 swollen and ≤4 tender joints) vs. polyarticular PsA (>4 swollen or >4 tender joints). §Includes patients initiated on apremilast, biologics and/or csDMARDs. NMSC=non-melanoma skin cancer.

Table 2. Disease Characteristics of Biologic-Naïve Patients With Oligoarticular vs. Polyarticular PsA*,§

Disease Characteristic	Oligoarthritis n=149	Polyarthritis n=181	*P* Value
Swollen joint count (0-66), mean (SD)	1.3 (1.5)	6.2 (5.3)	<0.001
Tender joint count (0-68), mean (SD)	1.6 (1.5)	13.9 (12.7)	<0.001
Nail psoriasis VAS, mean (SD)	11.4 (23.6)	15.7 (24.6)	0.037
cDAPSA score, mean (SD)	10.9 (5.6)	31.1 (15.8)	<0.001
High (>27) cDAPSA, n (%)	0 (0.0)	91 (52.0)	<0.001
Presence of enthesitis, n (%)	37 (24.8)	84 (46.4)	<0.001
SPARCC enthesitis score, mean (SD)	2.1 (1.3)	4.4 (3.4)	<0.001
Presence of dactylitis, n (%)	25 (16.8)	54 (29.8)	0.006
Dactylitis count, mean (SD)	1.9 (1.6)	2.4 (1.7)	0.060
Minimal disease activity, n (%)	40 (29.6)	6 (3.6)	<0.001

*Oligoarticular PsA (≤4 swollen and ≤4 tender joints) vs. polyarticular PsA (>4 swollen or >4 tender joints). §Includes patients initiated on apremilast, biologics and/or csDMARDs. SPARCC=Spondyloarthritis Research Consortium of Canada.

DI score < 0.5 was significantly greater for patients with oligoarthritis vs polyarthritis (39.7% vs 20.1%) (all $P \leq 0.001$). Presence of inflammatory back pain (8.7% vs 10.5%; $P=0.588$) and mean psoriasis-involved body surface area (8.0% vs 6.8%; $P=0.276$) were similar in the 2 groups.

Conclusion: This Corrona PsA/SpA Registry analysis showed similar overall disease and comorbidity burden in biologic-naïve patients with oligoarthritis and polyarthritis. However, patients with oligoarthritis vs polyarthritis had lower scores on disease activity and PRO measures at treatment initiation.

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Brsitol Myers Squibb,Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, Amgen, 2, 5, 6, 8, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, and UCB, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 2, 5, Boerhinger Ingelheim, 5, Bristol Myers Squibb, 2, 5, 8, Bristol Myers Squibb Co., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8, Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8.

Abstract Number: 2478

Enthesitis Frequency and Treatment Patterns in Patients with Psoriatic Arthritis in Europe and Japan

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesitis, a symptom commonly associated with psoriatic arthritis (PsA), negatively affects quality of life. Although enthesitis is routinely reported in randomized clinical trials of new therapies for PsA, it has not been well characterized in real-world patient populations. The aim of this study is to determine the frequency and severity of enthesitis and describe treatment patterns in PsA patients with enthesitis in Europe and Japan.

Methods: Data were analysed from the Adelphi PsA Disease Specific Programme, a cross-sectional survey of 344 rheumatologists (and orthopedic surgeons and internists in Japan), 171 dermatologists and their consulting patients in France, Germany, Italy, Spain, UK (5EU) and Japan from 03/2018 to 11/2018. Participating physicians completed patient record forms capturing clinical and treatment information based on medical record data. Patients with a physician-confirmed diagnosis of PsA who were ≥18 years old and not participating in a clinical trial were eligible for inclusion. The proportion of patients with enthesitis was assessed overall and by country at several times during the PsA disease course. For patients currently experiencing enthesitis, data describing enthesitis severity and PsA-related treatments were collected.

Table 1. Frequency of Enthesitis in 5EU and Japan at Various Times in the PsA Disease Course

Region	N	Ever had enthesitis n (%)	Currently have enthesitis n (%)	Enthesitis at PsA diagnosis n (%)	Enthesitis at most recent treatment initiation n (%)
Overall	1945	522 (26.8)	233 (12.0)	406 (22.0)[a]	456 (23.8)[a]
5EU	1675	426 (25.4)	177 (10.6)	322 (20.3)[a]	368 (22.3)[a]
France	277	74 (26.7)	28 (10.1)	47 (18.4)[a]	59 (21.9)[a]
Germany	360	56 (15.6)	26 (7.2)	40 (11.5)[a]	49 (13.7)[a]
Italy	360	105 (29.2)	44 (12.2)	80 (23.7)[a]	87 (24.9)[a]
Spain	369	113 (30.6)	49 (13.3)	98 (27.6)[a]	100 (27.5)[a]
UK	309	78 (25.2)	30 (9.7)	57 (19.5)[a]	73 (23.8)[a]
Japan	270	96 (35.6)	56 (20.7)	84 (32.3)[a]	88 (32.6)

[a]Percentages calculated on non-missing values; missing values were <8%. 5EU, France, Germany, Italy, Spain, and UK; UK, United Kingdom.

Table 2. Treatments Used in Patients with PsA and Current Enthesitis

Treatments	Overall, N=233		5EU, N=177	
	Current Use n (%)	Ever Used n (%)	Current Use n (%)	Ever Used n (%)
NSAIDs	75 (32.2)	168 (72.1)	48 (27.1)	127 (71.8)
Corticosteroids	32 (13.7)	94 (40.3)	24 (13.6)	83 (46.9)
csDMARDs	110 (47.2)	167 (71.7)	96 (54.2)	145 (81.9)
tsDMARDs	28 (12.0)	34 (14.6)	14 (7.9)	19 (10.7)
bDMARDs	136 (58.4)	140 (60.1)	110 (62.2)	114 (64.4)

5EU, France, Germany, Italy, Spain, and United Kingdom; bDMARDs, biologic DMARDs; csDMARDs, conventional synthetic DMARDs; NSAIDs, nonsteroidal anti-inflammatory drugs; tsDMARDs, targeted synthetic DMARDs.

Results: 1945 patients with PsA were included. Mean age was 48.9 (SD 13.6) years, 54.2% were male, and mean time since diagnosis was 59.3 (SD 5.9) months (n=1595). Overall, 26.8% of patients ever had enthesitis, 12.0% of patients currently had enthesitis, 22.0% had enthesitis at the time of PsA diagnosis, and 23.8% had enthesitis at their most recent PsA-related treatment initiation (Table 1). At each time point assessed, the proportion of patients with enthesitis was greatest in Japan and lowest in Germany. Of patients with current enthesitis, 28.8% of cases were moderate or severe compared with 70.0% of cases at diagnosis and 61.8% of cases at initiation of patients' most recent PsA-related treatment regimen. The most frequently used medications among patient with current enthesitis were biologic DMARDs (58.4%), conventional synthetic DMARDs (47.2%), and NSAIDs (32.2%) (Table 2).

Conclusion: Enthesitis is a common disease manifestation in real-world PsA patients in Europe and Japan. The majority of patients with current enthesitis were treated with advanced therapies; physicians rated patients' enthesitis as moderate or severe in 28.8% of those who continued to have enthesitis despite treatment, suggesting an unmet need and target for future PsA therapies.

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Abstract Number: 2479

Unmet Treatment Needs in Patients with Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite significant advances in the treatment of psoriatic arthritis (PsA), disease control and remission remain a challenge. Research characterizing residual disease burden with current therapies and identifying unmet treatment needs across clinical, patient-focused, and economic domains has been limited. The aim of this

		Data Source	
		Randomized, controlled trials	Observational studies
DAS28	% achieving remission (≤2.6)	No Data	6 mo: 50.0%[1]; 12 mo: 48.8%–71.0%[1, 2]
	Mean change	12 mo: (-1.2)–(-2.4)[3-5]	6 mo: (-1.1)–(-2.3)[6-11]; 12 mo: (-1.1)–(-2.2)[7, 9]
MDA	% achieving MDA*	6 mo: 35.9%–52.0%[10-12] 12 mo: 23.6%–40.0%[11, 13]	6 mo: 35.5%–49.1%[1, 7, 14]; 12 mo: 36.8%–64.0%[1, 2, 7, 14, 15]
HAQ-DI	Mean change	6 mo: (-0.3)–(-0.4)[16]; 12 mo: (-0.4)–(-0.6)[3-5]	6 mo: (-0.1)–(-0.5)[6, 7]; 12 mo: (-0.1)–(-0.6)[7, 17]
	% improvement	6 mo: 41.2%[18]; 12 mo: 41.9%–60.5%[5, 18]	6 mo: 10.9%–41.8%[6, 7]; 12 mo: 7.8%–51.2%[7, 17]
	% achieving ≥0.3-unit improvement	6 mo: 45.6%[18]; 12 mo: 48.7%–55.5%[3, 18]	No Data
Pain (VAS 0–100)	Mean change	6 mo: -22.3[18]; 12 mo: (-12.9)–(-24.0)[18, 19]	6 mo: (-9.9)–(-33.2)[7, 8]; 12 mo: (-12.8)–(-31.5)[7, 17]
Fatigue (FACIT-F score)	Mean change	6 mo: 1.6–6.5[18, 20]; 12 mo: 3.7–8.5[18, 21-23]	6 mo: 4.4[24] 12 mo: 5.6[24]
Enthesitis	% achieving resolution	6 mo: 31.0%–61.4%[16, 25-27]; 12 mo: 26.1%–69.8%[4, 5]	6 mo: 53.8%[28]
SF-36	Mean change in MCS score**	6 mo: 2.5–5.5[16, 18, 25, 29, 30]; 12 mo: 2.4–4.8[3, 16, 18]	12 mo: -0.1[17]
	Mean change in PCS score**	6 mo: 3.9–9.5[16, 18, 25, 27, 29, 30] 12 mo: 6.3–10.2[3, 4, 16, 18, 29]	12 mo: 7.3[17]

*MDA is assessed as five of the seven following criteria: ≤1 tender joint count, ≤1 swollen joint count, PASI≤1 or body surface area ≤3%, patient pain VAS≤15, patient global assessment of disease activity VAS≤20, HAQ-DI≤0.5, tender entheseal points≤1

**SF-36 summary scores (PCS-36 and MCS-36) range from 0 to 100, with higher scores representing better self-reported health

DAS=Disease Activity Score; FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI=Health Assessment Questionnaire Disability Index; MCS=Mental Component Summary; MDA=Minimal Disease Activity; mo=Months; PCS=Physical Component Summary; PsA=Psoriatic Arthritis; SF-36=36-Item Short Form Health Survey; VAS=Visual Analog Scale

Table 1. Clinical and patient-reported outcomes 6- and 12-months post-advanced therapy initiation among patients with PsA

review is to establish unmet needs in PsA patients with respect to the clinical, patient-reported and economic outcomes associated with current treatments.

Methods: A review of the literature from January 2008 to May 2019 was conducted. EMBASE and MEDLINE databases were searched to identify full-text, English-language articles and rheumatology conference abstracts evaluating the clinical, patient-reported, and economic outcomes associated with currently available advanced therapies (biologic disease-modifying anti-rheumatic drugs [DMARDs] and targeted synthetic DMARDs) and conventional synthetic DMARDs (csDMARDs) for adults with PsA. Randomized-controlled trials (RCTs), non-interventional observational studies, and economic models evaluating the impact of treatment on at least one outcome from the above categories were eligible for inclusion.

Results: Among 1,026 records initially screened, 100 articles were selected for inclusion. Of these, 52, 74, and 20 studies reported on the impact of treatment on at least one clinical, patient-reported, and economic outcome, respectively. Across studies, treatment with advanced therapies resulted in greater clinical efficacy and effectiveness, improvements in patient-reported outcomes, and higher 12-month persistence rates compared with csDMARD treatment. Advanced therapies were generally found to be cost-effective. Long-term outcomes over four or more years

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were investigated in 15 studies, revealing improvements in clinical outcomes consistent with shorter-term studies. Clinical and patient-reported outcome data at six and 12 months post-treatment initiation among patients treated with advanced therapies are summarized in Table 1. The proportion of patients achieving minimal disease activity at 12 months post-treatment initiation ranged from 23.6%–64.0%. The impact of advanced therapies on pain and physical functioning varied considerably across RCTs and observational studies. Though commonly assessed in RCTs, little real-world data are available for fatigue, enthesitis, and quality of life in PsA patients initiating advanced therapies.

Conclusion: While more effective than csDMARDs, a substantial proportion of PsA patients still fail to achieve complete disease control or remission with advanced therapies. There remains a need for new treatment options to further improve treatment outcomes in this patient population.

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Abstract Number: 2480

Opioid Use Surrounding Diagnosis of Inflammatory Arthritis

Anna Sheahan,[1] Victor Sloan,[1] Jeffrey Stark,[2] and Robert Suruki[1], [1]UCB Pharma, Raleigh, NC, [2]UCB Pharma, Smyrna, GA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Although treatment of inflammatory arthritis (IA) has improved, opioid use among patients remains common. A study from Finland showed increases in opioid use leading up to a diagnosis of IA, then a decrease after diagnosis, and that opioid use in axial spondyloarthritis was higher than in other IAs.[1] In a study of patients with AS, 44% of patients were using opioids, and 26% of these patients were using only opioids.[2] The timing of opioid use surrounding IA diagnosis in the USA is not known. The objective of this study was to describe opioid use in the year preceding and following diagnosis of AS, RA, and PsA.

Methods: This retrospective observational study analyzed USA commercial claims data (IBM® MarketScan®) from patients with an International Classification of Diseases (ICD) 9/10 code for AS, RA, or PsA (index date) between 2010–2017. Three controls, matched on year, age, sex, region, and insurance plan type, were selected for each disease case. Opioid pharmacy claims were examined in a 12-month baseline (BL) and 12-month follow-up (FU) period after index date with further division into 3-month periods. Chronic opioid use was defined as ≥90 cumulative days' supply in a 12-month period and was assessed separately in BL and FU. Long-term use was defined as ≥1 opioid claim in ≥3 of 4 quarters in FU. Prevalence ratios for long-term opioid use in the disease vs matched control cohorts were calculated for FU.

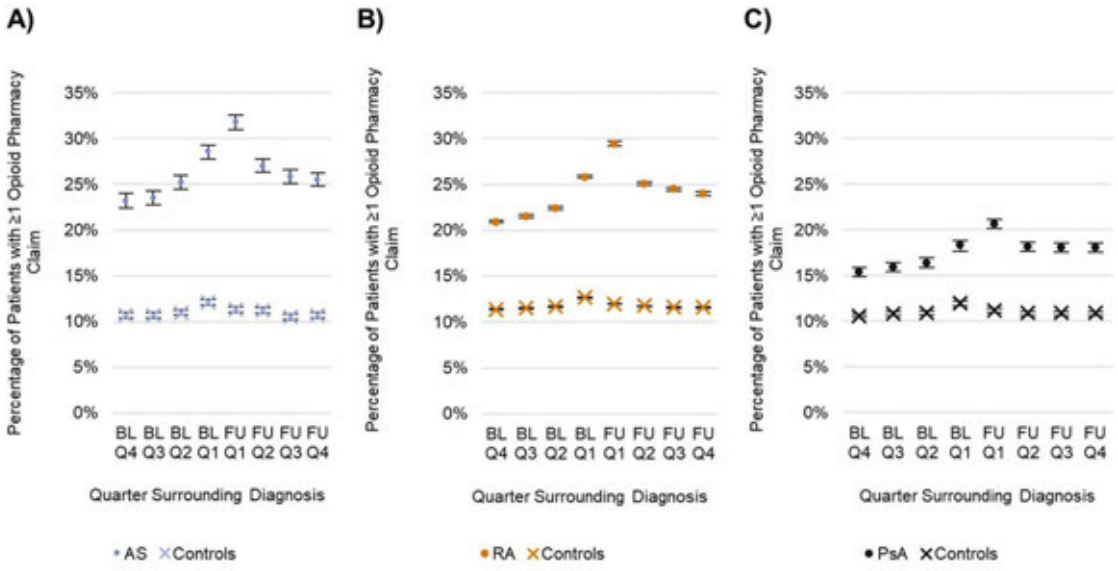
Results: The study included 12,377 AS, 215,286 RA, and 20,679 PsA patients (**Table**). In all 3 cohorts, prevalence of opioid exposure was highest in the quarter following (inclusive of) diagnosis, and prevalence of use was higher in all disease vs matched control cohorts for each quarter (**Figure 1**). Compared to matched controls, prevalence of chronic opioid use was higher in disease cohorts in BL and FU (**Table**), and prevalence of long-term use in FU was also higher (**Figure 2**).

Table 1: Characteristics of the AS, RA, and PsA cohorts and their matched controls

	Ankylosing spondylitis (AS)		Rheumatoid arthritis (RA)		Psoriatic arthritis (PsA)	
	AS cohort (n=12,377)	Matched controls (n=37,131)	RA cohort (n=215,286)	Matched controls (n=645,858)	PsA cohort (n=20,679)	Matched controls (n=62,037)
Age, mean years (SD)	51.1 (15.0)	51.1 (15.0)	55.3 (14.6)	55.3 (14.6)	51.5 (12.9)	51.5 (12.9)
Females (%)	48.5	48.5	71.5	71.5	52.5	52.5
Chronic opioid use in baseline (%)	16.6	5.0	13.5	5.5	8.7	4.9
Chronic opioid use in follow-up (%)	19.2	5.2	16.2	5.7	10.5	5.1

SD: standard deviation.

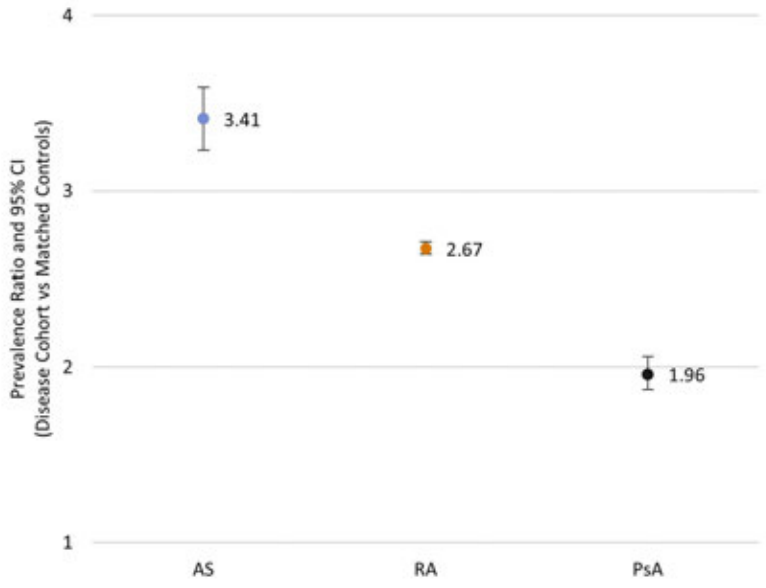
Figure 1: The percentage (and 95% confidence intervals) of patients with ≥1 opioid claim in the 4 quarters of BL preceding diagnosis and the 4 quarters of FU after diagnosis (inclusive) among A) AS patients and matched controls, B) RA patients and matched controls, and C) PsA patients and matched controls



BL: baseline; FU: follow-up; Q: quarter.

Conclusion: Opioid use is common among patients with IA in both the year preceding and the year following diagnosis, peaking at the time of diagnosis. For all IAs, prevalence of opioid claims and long-term opioid use were higher than in matched controls. Although patterns in these data are similar to those seen in Finland, the overall prevalence of any opioid use (in cases and controls) was higher in the USA. The prevalence of long-term opioid use was highest in AS patients compared to matched controls and highest among the 3 IAs, similar to the finding in Finland. The prev-

Figure 2: Prevalence ratios and 95% CIs for long-term opioid use in the 12 months following diagnosis (inclusive of the diagnosis date) among patients with AS, RA, or PsA compared to matched controls



CI: confidence interval

alence of opioid use in IA suggests the presence of uncontrolled pain in the period surrounding diagnosis. Given the ineffectiveness of opioids to address the underlying cause of IA, more comprehensive or appropriate treatments such as DMARDs and/or biologics to address the underlying disease should be considered, in accordance with relevant guidelines.

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Disclosure: A. Sheahan, UCB Pharma, 1, 3; **V. Sloan**, UCB Pharma, 1, 3, Rutgers-Robert Wood Johnson Medical School, 6; **J. Stark**, UCB Pharma, 1, 3; **R. Suruki**, UCB Pharma, 1, 3.

Abstract Number: 2481

Uveitis in 320 Patients with Psoriatic Arthritis. Epidemiology, Clinical Features and Biological Treatment: Study from a Single University Center

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

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Session Time: 9:00AM–11:00AM

	Uveitis (n=10)	Non uveítis (n= 310)
Baseline general features		
Age, years (mean±SD)	42.2 ± 16.8	46.4 ± 11.9
Sex, n (m/w) (%)	4/6 (40/60)	134/176 (43.2/56.8)
HLAB27, positive %	60	11.8
Disease Characteristics		
Axial arthritis, %	40.0	37.0
Peripheral arthritis, %	80.0	72.9
Hip affection, %	30.0	20.0
Enthesitis, %	60.0	40.5
Dactylitis, %	20.0	29.5
Scores		
BASDAI (mean ± SD)	3.3±2.08	2.4±1.9
BASFI (mean ± SD)	2.7±1.9	1.6±1

Table.

Background/Purpose: Uveitis is an extra articular manifestation of psoriatic arthritis (PsA). Uveitis may be more chronic Biological therapy, especially monoclonal TNF inhibitors, are useful to prevent and to treat refractory non-infectious uveitis. However, other biologics had been related to paradoxical uveitis. Our aim was to assess **a)** the epidemiological and clinical features of uveitis associated to PsA and **b)** its relationship with biological treatment used in PsA.

Methods: Observational study of unselected consecutive patients studied in a single reference University Hospital with**: a)** diagnosis of PsA by CASPAR criteria and **b)** diagnosis of uveitis by ophthalmologist exploration. Demographics features, clinical findings, complementary tests and treatment were recorded.

Results: We studied 320 (182 women/138 men) patients with PsA; mean age at PsA diagnosis of 41.7±15.79 years and with a delay of diagnosis from the onset of symptoms of 2.6±2.01 years.

Ten patients (4 men/6 women) out of 320 patients (prevalence 3.13%) with a mean age of 42.2 ± 16.8 years were diagnosed of uveitis after a mean follow-up of 10±7.9 years. In all cases, the uveitis had an anterior pattern. Only 1 (10%) of them had a bilateral affection, acute onset in 10 patients (100%), and 4 of them (40%) had a recurrent pattern. The diagnosis of uveitis preceded the one of PsA in 5 (50%) patients in 1.6±0.87 years. In those with a previous diagnosis of PsA, it was done 13.3±10.4 years before the uveitis onset. Only 1 patient (10%) with recurrent unilateral uveitis presented vitritis. In 10 patients the mean number of anterior chamber cells was 2±0.4. Comparison of baseline characteristics and clinical features between patients who developed uveitis and those who did not is shown in **table.**

Only 2 patients (20%) with uveitis received biological therapy. The first one developed its first episode of uveitis after 29 months with etanercept. After the episode, a switch to adalimumab was done, without any other episode of uveitis after 22 months of treatment. The second one was a patient with multiple episodes of recurrent uveitis, who developed new flares with adalimumab, certolizumab and golimumab.

Conclusion: Most of the uveitis had an anterior and unilateral pattern. The onset of uveitis in patients with PsA can either precede or go after the diagnosis of the PsA. HLA B27+ was more frequent in patients with uveitis. Biological therapy did not achieve good answer in patients with recurrent uveitis.

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Abstract Number: 2482

Differences and Similarities According to Gender in Patients with Psoriatic Arthritis Initiating Biological Therapy

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	Male n=55 (51 %)	Female n= 54 (49 %)	p-value
Age (years)	55.8 (12.2)	58.3 (16.7)	0.2
Disease duration (years)	17.3 (7.3)	18.1 (10.9)	0.6
BMI	27.7 (3.8)	26.7 (5.9)	0.3
Smokers & ex smokers	19 (34.5%)	19 (35.2 %)	1.0
HLA B27	8/28 (28.6 %)	3/20 (15.0 %)	0.3
RF	2/47 (4.3%)	4/48 (8.3%)	0.4
Axial and/or Oligoarticular manifestations	37 (67.3%)	20 (37.2 %)	**0.01**
Poliarticular manifestations	18 (32.0%)	34 (63.1 %)	**0.02**
bASDAS	3.1 (1.0)	3.3 (1.0)	0.5
bDAPSA	21.3 (11.8)	29.4 (15.5)	0.08
bESR	19.8 (19.2)	31.6 (19.7)	0.2
bCRP mg/L	11.9 (16.16)	9.6 (10.7)	0.1
Baseline PGA	45.1 (20.8)	50.4 (20.8)	0.4
Baseline MTX	27 (49.1 %)	38 (70.4 %)	**0.02**
Baseline SSZ	10 (18.2 %)	8 (14.8 %)	0.6
Baseline PRD	14 (25.5%)	20 (37.1 %)	0.2
Infliximab	15 (27.3 %)	12 (22.2 %)	0.9
Adalimumab	6 (10.9 %)	15 (27.8 %)	0.2
Etanercept	24 (43.6 %)	22 (40.7 %)	0.8
Golimumab	6 (10.9 %)	2 (3.7 %)	0.4
Secukinumab	4 (7.3 %)	3 (5.6 %)	0.9

Table 1. Gender-stratified characteristics at the visit starting the biological therapy. Results are shown as mean (standard deviation) or absolute number (percentage).

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
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Background/Purpose: Growing evidence has pointed gender as a key variable influencing clinical response to biological drugs in psoriatic arthritis(PsA). Although the reasons remain unclear, it has been hypothesized that different clinical presentations could contribute to this gender-related contrast in treatment effectiveness.

Objective: to analyse the disease profile in male and female patients with PsA starting biological treatment.

Methods: Data from an observational prospective cohort including all patients with PsA initiating biological therapy from 2002-2018 in a university hospital was conducted. Demographic information, laboratory tests, disease presentation (axial presentation, including oligoarticular affection, and poliarticular presentation), disease activity indexes (ASDAS and DAPSA for axial and peripheral-only presentations, respectively) and concomitant treatment were collected before starting biological drug. Patients were stratified by gender to compare the characteristics of the populations. Chi-squared for categorical and t-student tests for continuous variables were used to analyse the differences between groups.

Results: Out of 109 included patients, 55 (51%) were males and 54 (49%) females. Baseline gender-stratified characteristics are shown in Table 1. Including the whole population of the study, mean age at diagnosis was 57 ± 14.6 years, mean PsA duration was 17.7 ± 9.2 years, and mean Body Mass Index (BMI) was 27.2 ± 4.9. Axial or oligoarticular presentation was shown in 57 patients (52%), whereas 52 patients (48%) had poliarticular manifestations. Mean

baseline ASDAS was 3.2 ± 1.0 and mean baseline DAPSA was 25.4 ± 13.6. Biological therapies initiated included etanercept in 42% of the cases, infliximab in 25%, adalimumab in 19%, golimumab in 7% and secukinumab in 6%. No significant differences were observed between genders for most of the characteristics including: age at starting biologic, disease duration, BMI, smoking habit, positive HLA B27 and rheumatoid factor, baseline activity, baseline ESR, baseline CRP, baseline sulfasalazine (SSZ), baseline prednisone (PRD), baseline patient global assessment and biological drug use. However, there was differences between gender in some other characteristics. While males had higher axial presentation of the disease (p=0.01), females had higher poliarticular disease (p=0.02) and used methotrexate more frequently (p=0.02). These differences in methotrexate use might be explained by the predominance of peripheral presentation in female patients.

Conclusion: In clinical practice, biological therapy (TNFi and IL-17i) is prescribed in a similar frequency in male and female patients with PsA. Nevertheless, the predominant articular manifestation behind the prescription of the biological therapy is different among genders: while men have predominant axial disease, women have predominant peripheral manifestations. These differences in clinical presentation in both genders may contribute to differences in therapeutic management, such as increased use of methotrexate in women with PsA who initiate biological therapy.

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Abstract Number: 2483

Comparison Between Composite Activity Indices to Assess Clinical Response to Biological Therapy in Patients with Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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Background/Purpose: Assessment of the disease in psoriatic arthritis (PsA) remains a clinical challenge. Hence, there is no agreement on which index best correlates with the actual disease state of patients.

Objective: to assess the performance of and agreement between composite activity indices of common use in clinical practice (DAPSA and DAS66) and the physician global assessment (PhGA) to evaluate disease activity in PsA patients under biological therapy.

Methods: Patients with peripheral-only PsA initiating a first biological therapy (TNFi and IL-17i) between 2002 and 2018 in a university hospital were included. Demographic information, laboratory tests, concomitant treatments, PhGA and disease activity indexes (DAPSA and DAS66) were collected at baseline and 6 months (6 m) after starting biological treatment. At 6 m, the patients were classified in the following disease activity status: remission (DAPSA PhGA was also determined at 6 months, and it was assorted by consensus of 3 expert rheumatologists in remis-

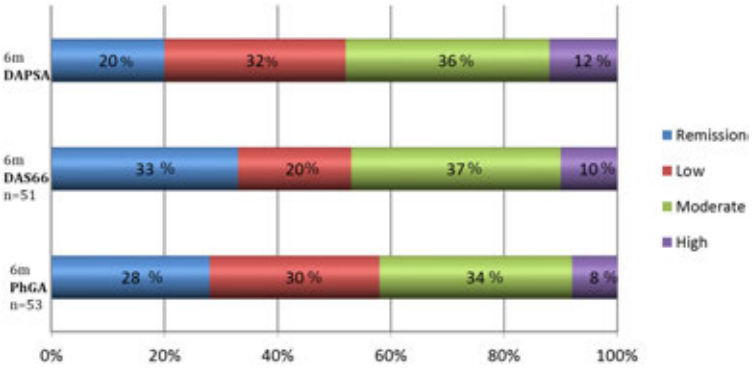

Figure 1. Clinical response after 6 months of biological therapy, shown as percentage of the total in each group.

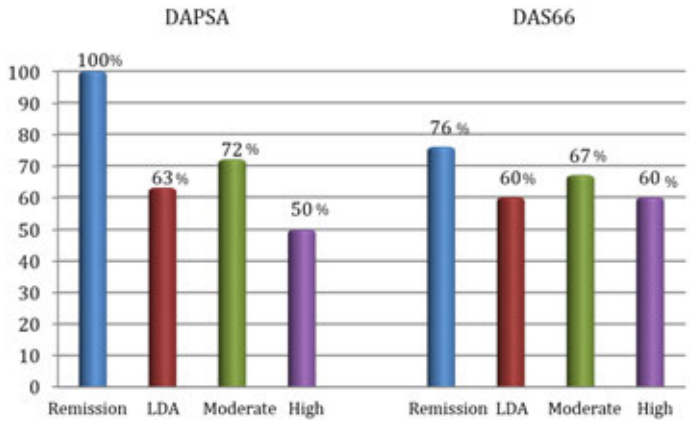

Figure 2. Agreement for disease activity status between disease activity indexes and PhGA.

sion (PhGA ≤ 10), LDA (PhGA >10-≤30), moderate activity (PhGA >30≤-60) and high activity (PhGA >60). The number (%) of patients achieving the different disease activity status by each of the different indexes at 6m and the agreement between PhGA scores and disease activity indices were determined.

Results: Out of 54 included patients, 20 (37%) were males, 37 (68%) were non-smokers, 34 (63%) had a BMI ≥25, with mean (SD) baseline disease activity indices of DAS 66: 4.8 (1.2) and DAPSA: 26 (14.9). Biological therapies initiated included etanercept in 37% of the cases, infliximab in 32%, adalimumab in 20%, golimumab in 4% and secukinumab in 7%. Clinical response at 6m according to different indexes and PhGA is depicted in Figure 1. More than half of the patients achieved at least LDA disease activity after 6 months of biological treatment, regardless of the index used. Thus, physician-perceived remission or LDA was frequent (58%). DAPSA index was the most stringent in terms of classifying patients in remission. Moderate to strong positive correlation was observed between DAS 66 and PhGA (Spearman $r = 0.729$, $p < 0.001$) and a strong correlation was observed between DAPSA and PhGA (Spearman $r = 0.852$, $p < 0.001$). The relative agreement between disease activity indexes and PhGA at 6 m for different disease activity states are shown in Figure 2. DAPSA classified better the patients in remission according to the PhGA.

Conclusion: In clinical practice, 50 % of the patients with PsA achieve at least a low activity state of the disease at 6 m after receiving a first biological therapy, and this is replicated by different indices. DAPSA based remission/LDA performed better than DAS66 to detect PhGA-defined remission or LDA.

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Abstract Number: 2484

Gender Influence on Treatment Effectiveness in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Gender has been lately suggested as influential in the response to treatment with biological drugs in spondyloarthritis. However, data about the association between gender and treatment response in axial PsA (axPsA) or peripheral PsA (pPsA) are scarce.

Objective: to analyze the association between gender and clinical response to biological therapy in patients with axPsA and pPsA.

Methods: An observational cohort study was conducted, prospectively collecting data from 108 patients treated with biological therapy (93% TNFi and 7% IL-17i) from 2002-2018. Patients were divided into two groups according to their clinical predominant manifestation: axPsA or pPsA. Disease activity indexes (ASDAS and BASDAI for axPsA and DAPSA and DAS28 for PsA) were collected before starting drug and 6 months later (baseline and 6m visit, respectively). Low disease activity (LDA) was defined as ASDAS < 2.1 or BASDAI < 4 (axPsA) and DAPSA ≤14 or DAS28 ≤ 3.2 (pPsA). Clinical improvement was defined as an improvement ≥ 1.1 points in ASDAS (dASDAS) or 50% in BASDAI (BASDAI50) for axPsA, and an improvement of 50 % in DAPSA (DAPSA50) or dDAS28 ≥ 1.2.

First, the frequency of male- and females - patients achieving LDA and clinical improvement at 6m were compared using Fisher test, separately for axPsA and pPsA. Second, the association between gender and each of the clinical outcomes was analyzed using logistic regression models adjusted for confounders (age, disease duration, previous biologics, smoking habit, body mass index (BMI), baseline DMARDs and baseline disease activity).

axPsA (n= 55)				pPsA (n= 54)			
	Males (n= 35)	Females (n= 20)	p-value		Males (n= 20)	Females (n=34)	p-value
LDA				LDA			
ASDAS <2.1	25 (74 %)	7 (37 %)	0.02	DAPSA ≤14	14 (74 %)	12 (39 %)	0.02
BASDAI < 4	24 (72 %)	5 (26 %)	0.02	DAS28 ≤ 3.2	13 (68 %)	6 (31%)	0.09
Clinical Improvement				Clinical Improvement			
dASDAS ≥ 1.1	20 (59 %)	7 (37 %)	0.15	DAPSA50	10 (53 %)	11 (36 %)	0.25
BASDAI50	16 (48 %)	3 (16 %)	0.04	dDAS28 ≥ 1.2	11 (57 %)	8 (42 %)	0.15

Table 1. Response rates after 6 months of biological therapy, stratified for PsA subtype and gender.

Results: Out of 108 included patients, 55 (51%) had predominant axPsA and 54 (49%) pPsA.

In the group of axPsA, 35 (64%) were males, 33 (60%) were nonsmokers, 33 (60%) had a BMI ≥25, with mean (SD) baseline disease activity of ASDAS: 3.3 (1.0) and BASDAI: 5.4 (2.0). The frequency of patients achieving clinical response was higher in males than females (Table 1). After adjusting for confounders, male gender was significantly associated with higher probability of achieving LDA (ASDAS OR=4.4; p=0.03 and BASDAI OR=6.0; p=0.01), and clinical improvement (dASDAS: OR=4.8; p=0.04 and BASDAI50: OR=5.19; p=0.03).

In the group of pPsA, 20 (37%) were males, 37 (68%) were nonsmokers, 34 (63%) had a BMI ≥25, with mean (SD) baseline disease activity indexes of DAPSA: 26 (14.9) and DAS 28: 4.8 (1.2). The frequency of patients achieving LDA was higher in males than females (74% vs 39%; p=0.02, respectively). After adjusting for cofounders, male gender was independently associated with higher probability of achieving LDA by DAPSA (OR=4.0; p=0.03) and DAS28 (OR= 2.1; p=0.3). Finally, an association between male gender and clinical improvement was also observed but this was statistically significant only when using dDAS28 as the outcome: OR=2.9; p=0.1 for DAPSA50 and OR=5.8; p=0.02 dDAS28.

Conclusion: Male gender is associated with a higher rate of response to biological treatment (TNFi and IL-17i) in axPsA and pPsA. This association is robust despite using the new recommended disease activity indices and cut-off points for clinical practice. Further investigations of these gender-related differences are important for a better management of PsA and for the development of new therapies.

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Abstract Number: 2485

Red Cell Distribution Width Positively Correlates with Atherosclerotic Cardiovascular Disease Risk Score in Psoriatic Arthritis and Decreases with BDMARD Therapy

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Red blood cell distribution width (RDW) is a parameter that measures variation in red blood cell size and volume. It is elevated when there is variation in red cell size (anisocytosis). RDW has been found to be a predictor of cardiovascular disease (CVD), but is not commonly incorporated in current risk evaluation instruments. Research has linked an elevated RDW to disease activity in psoriasis, but limited data is available on the relationship between these parameters and psoriatic arthritis.

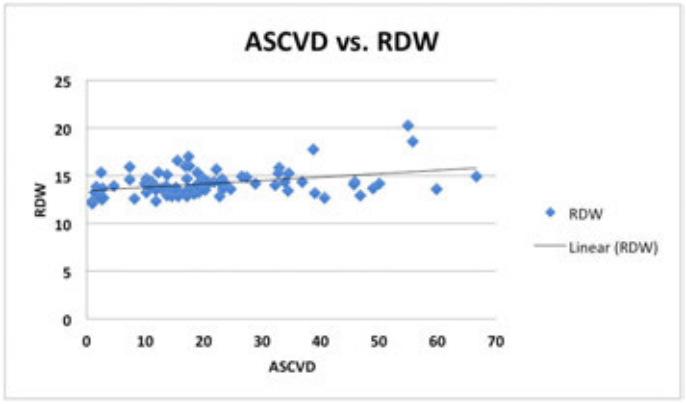

Figure 1 depicts the positive linear correlation between ASCVD score and RDW (r =.35, p-value = 0.001).

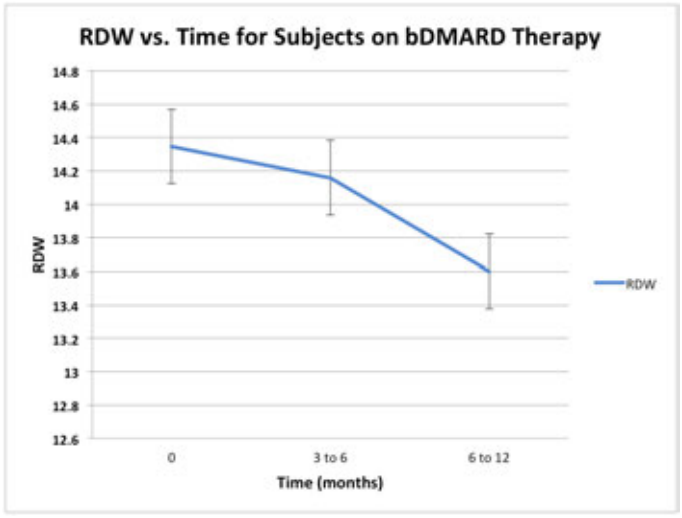

Figure 2 depicts the relationship between RDW over time for patients on bDMARD therapy alone. A trend towards a decline in RDW from 0 to 12 months was observed (p = 0.11).

Methods: We performed a retrospective chart review study examining the relationship between RDW, MPV, hemoglobin, absolute lymphocyte count (ALC), and atherosclerotic cardiovascular disease (ASCVD) 10 year risk score (incorporating age, hypertension status, diabetes mellitus (DM) status, lipid profile, and smoking status) in a cohort of patients with psoriatic arthritis, taking into account their HLA-B27 status, race, and treatment history.

Results: RDW was positively correlated with ASCVD score, and RDW was found to decrease over 12 months for all patients started on bDMARD therapy. As expected, we found positive correlations between ASCVD score, hemoglobin A1c, and age, and negative correlations between ASCVD score, hemoglobin, and albumin. Patients started on NSAID therapy had a statistically significant increase in RDW between time 0 and 6 months (p = 0.03), but this was not maintained at twelve months. Patients on csDMARD therapy did not experience a statistically significant change in RDW at 6 or 12 months, while patients on bDMARD and bDMARD + csDMARD therapy experienced a statistically significant decline in RDW from 0 to 6 months (p = 0.046) and from 0 to 12 months (p = 0.040). When patients on

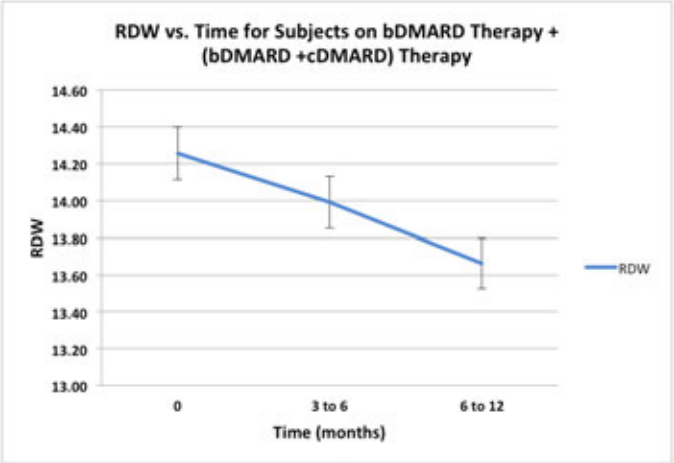

Figure 3 shows the relationship between RDW over time for patients on both bDMARD therapy and bDMARD and cDMARD therapy. A statistically significant decline in RDW from 0 to 6 months (p = 0.046) and from 0 to 12 months (p = 0.040) was observed.

bDMARD therapy were analyzed alone, a trend towards a decline in RDW from 0 to 12 months was also observed (p = 0.11).

Conclusion: This data shows that not only is there is a positive correlation between RDW and traditional cardiovascular risk factors, as represented by ASCVD score, in patients with psoriatic arthritis, but also that bDMARD therapy appears to be associated with decreasing RDW in these patients over time, the latter consistent with RDW in part reflecting disease activity. Whether RDW adds to cardiovascular risk assessment beyond traditional cardiovascular risk factor analysis is yet to be determined. Data here suggest it may be a viable candidate since it appears to reflect both disease activity and traditional risk factors. More investigation related to bDMARD therapy and other non-conventional parameters of disease activity in psoriatic arthritis as they relate to CVD is warranted. This could have powerful clinical implications, as having other approaches of monitoring disease activity (aside from ESR and CRP) would be beneficial for patients.

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Abstract Number: 2486

Evaluation of Clinical and Functional Parameters by Joint Involvement and Remission in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Disease activity of psoriatic arthritis (PsA) is affected by many parameters including joint, spinal and skin involvement, enthesitis, dactylitis and pain. According to disease activity indices such as DAPSA, DAS28 and MDA, some patients may not be in remission even though they do not have joint involvement and arthritis.

The aim of this study was to assess the clinical parameters that affect remission in patients with PsA

Methods: This study involved patients with PsA consistent with CASPAR criteria from Turkish League Against Rheumatism (TLAR) Network multi-centre study. The demographic and clinical parameters of patients (pain VAS, patient global VAS, doctor global VAS, tender and swollen joint) were recorded. Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), Psoriasis Area and Severity Index (PASI), fatigue with the VAS (0-10), Hospital Anxiety and Depression Scale (HAD), Fibromyalgia Rapid Screening Tool (FIRST), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Health Assesment Questionnaire (HAQ) were evaluated. DAS28, DAPSA and minimally disease activity (MDA) were used to asses the disease activity and remission. The patients were classified into two groups, according to their remission status and swollen joint count. (group 1 are in remission and no swollen joint; group 2 patients are not in remission and no swollen joint). The Spearman correlation coefficient was used to evaluate the correlations between variables. The Mann-Whitney-U test and Chi-squared test were used for comparison between the groups. $P< 0.05$ was considered statistically significant. The SPSS22.0 statistic package was used for statistical analysis.

Results: Of 1134 patients diagnosed with PsA, 720 patients (471 female (%65.4), 249 male (%34.6) were found to have peripheral involvement. The mean age was 47,6 years (SD:12.03). The median disease duration was 6.47 years (min:0, max:44). DAPSA, DAS28 and MDA scores were obtained in 561, 687 and 553 patients (Table 1). The two groups were similar in terms of age, gender, educational status, disease duration ($P >0.05$). Group 1 and 2 differed significantly in terms of VAS pain, VAS global pain, VAS doctor global, tender joint count, fatigue, anxiety, depression, FIRST score, PASI, BASDAI, enthesitis and HAQ score ($p< 0.05$) (Table-2)

	DAS28	DAPSA	MDA
Swollen joint 0 and remission n (%)	108 (15)	10 (1.4)	62 (8.6)
Group-1			
Swollen joint 0 and not remission n (%)	242 (33.6)	269 (37.4)	220 (30.6)
Group-2			
Swollen joint ≥1 and not remission n (%)	305 (42.5)	279 (38.8)	258 (35.8)
Swollen joint ≥1 and remission n (%)	32 (4.4)	3 (0.4)	13 (1.8)

Table-1: Patients according to DAPSA remission, DAS28 remission and MDA DAS28 DAPSA MDA

	DAPSA remission			MDA		
Parameters mean (SD)	Group-1	Group-2	*P*	Group-1	Group-2	*P*
Pain VAS	3.4 (2.06)	5.1(2.2)	*<0.05*	2.1 (1.7)	5.2 (2)	*<0.05*
Patient Global VAS	3.08 (1.7)	5.06 (2.2)	*<0.05*	2.14 (1.7)	5.02 (1.9)	*<0.05*
Physicians Global VAS	2.6 (1.4)	4.3 (1.8)	*<0.05*	1.9 (1.3)	4.2 (1.7)	*<0.05*
Tender joint	2.5 (1.9)	8.7 (10)	*<0.05*	1.2 (0.5)	9.4 (10.5)	*<0.05*
Fatigue	3.7 (2.3)	5.5 (2.5)	*<0.05*	2.8 (2.2)	5.4 (2.4)	*<0.05*
Anxiety	5.6 (4)	7.1 (4.2)	*<0.05*	5.4 (4.1)	7.2 (4)	*<0.05*
Depression	5.5 (3.9)	7.1 (4)	*<0.05*	5 (4)	7.3 (4)	*<0.05*
FIRST	1.7 (1.9)	2.82 (2.1)	*<0.05*	1.2 (1.8)	2.9 (2.1)	*<0.05*
PASI	2.4 (4.1)	2.8 (5)	*<0.05*	1.7 (4)	3.2 (5)	*<0.05*
BASDAI	3 (1.4)	4.4 (1.9)	*<0.05*	2.5 (1.3)	4.3 (1.8)	*<0.05*
HAQ	0.1 (0.2)	0.47 (0.4)	*<0.05*	0.11 (0.1)	0.46 (0.4)	*<0.05*
BMI	27.8 (4.5)	29.7 (5)	*<0.05*	28.7 (4.7)	29.5 (4.8)	*>0.05*
Enthesitis median (min-max)	1 (0-13)	2 (0-13)	*<0.05*	0 (0-13)	2 (0-13)	*<0.05*

Table-2: Comparison of the groups according to DAPSA remission and MDA

Conclusion: PSA may not be in remission even though joint involvement has been controlled. In these patients fatigue, pain, anxiety, depression, fibromyalgia, functional disorders, skin lesions, enthesitis, tender joint and spinal involvement more often than the patients in remission and no active joint involvement. In the evaluation of the disease activity, it is necessary to make evaluations by using composite scales.

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Abstract Number: 2487

Identification of Circulating MicroRNA Signatures in Patients with Psoriasis and Psoriatic Arthritis to Develop Novel Strategies for Early Diagnosis of a Bone and Joint Involvement

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: MicroRNAs (miRNAs) are small non-coding RNAs which are regulating physiologic and pathological processes. In numerous diseases specific miRNA signatures have been identified and can potentially serve as biomarkers. In psoriatic arthritis (PsA) no specific biomarker is available so far. As previously shown, inflammation of peripheral joints in patients with psoriasis can be identified using MRI technique despite no clinical evidence for psoriatic arthritis. Therefore, specific biomarkers to capture these patients at an early time point is of clinical interest. The aim of this pilot study was to identify specific circulating miRNA signatures in patients with psoriasis and psoriatic arthritis and to investigate potential biomarkers for inflammatory involvement of joints.

Methods: 16 patients with (PsA) fulfilling CASPAR criteria and 16 patients with psoriasis (PsO) without any current or past clinical symptom of arthritis or enthesitis received high field MRI of the hand, demographic and clinical data including disease duration, activity scoring as well as demographic data were collected. MRI scans were scored according to PsAMRIS method. 187 miRNAs were quantified in serum of PsA and PsO patients and 16 age- and sex-matched controls (CO) using RT-qPCR (TAmiRNA Vienna).

Results: PsA patients, PsO patients and CO had a comparable age (median (IQR), years, 48.5 (13.0) vs 53.0 (10.0) vs 48.0 (15.0), p=0.547). In all 3 cohorts 50% were females. BMI was higher, but not significantly above the upper normal range in PsA and PsO patients compared to CO(p=0.177). The median (IQR) disease duration of PsA patients was 2.5 (10) years. Duration of skin disease was 14.0 (31) years in PsA patients vs. 12.0 (14) years in PsO patients. 60% of PsO patients reported unspecific arthralgias without clinical signs of arthritis. In PsA Minimal Disease Activity (MDA) was present in 46.7% of patients. Psoriasis Area and Severity Index (PASI) was 0 (0.1) in PsA vs. 1.7 (5.3) in PsO patients. In MRI osteitis was found in 18.8% of PsA patients vs. 12.5% of PsO patients. Synovitis was present in 37.5% of PsA patients and in 43.8% of PsO patients. 1 patient of each group showed periarticular inflammation and tenosynovitis was only detected in PsA patients (25%). In the first analysis significant differences in miRNA profiles of patients with PsA, PsO and controls have been revealed. We were able to identify 51 miRNAs in the PsO and 64 miRNAs in the PsA group significantly down or upregulated (BH-adjusted $p < 0.05$) compared to healthy CO. Between

these signatures, an overlap of 33 miRNAs, which were significantly changed in PsA and PsO compared to CO was detected (adjusted p< 0.05), while 18 (PsO) and 31 (PsA) miRNAs were specific to each group.

Conclusion: The results of miRNA analysis in this pilot study in patients with psoriasis and psoriatic arthritis suggest that serum microRNA levels are not identical between PsO and PsA compared to CO, and that miRNAs could serve as biomarkers to detect a joint involvement in psoriasis in the future.

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Abstract Number: 2488

MDA *Versus* DAPSA: Applicability in a Real World

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a progressive, chronic, and potentially irreversible inflammatory disorder. Systematic clinical follow-up of PsA patients is necessary to maintain and adjusting the proposed therapy. There are two different disease activity composite index suggested by Treat To Target (1). MDA (2) defines a state of illness and includes joint involvement, skin, enthesis and quality of life questionnaire, while DAPSA (3) stratifies disease activity in remission, low, moderate or high disease activity, and does not evaluate skin, enthesitis neither quality of life. Thus, our work aims to establish if these indexes are comparable and evaluates the feasibility of applying each one of them in the clinical practice of our outpatients.

Methods: Methodology: We used data of 124 outpatients of Clinicals Hospital of Federal University of Pernambuco (HC-UFPE), Brazil, between October 2016 and December 2018, who met the criteria of CASPAR (4) and aged ≥18 years. The study was approved by the local medical research ethics committee (CAAE 08028119.7.0000.8807). MDA was defined as having at least five of the seven items that compose it (painful joints ≤1, swollen joints ≤1, LEI ≤1, PASI ≤1, patient global visual analogue scale (VASptGlobal) ≤20mm, patient pain (VASptPain) ≤15mm and HAQ ≤0.5. DAPSA is calculated with the number of painful + swollen joints + VASptGlobal (0-10 cm) + VASptPain (0-10 cm) + PCR mg/dL and low disease activity or remission (DAPSA-LDA/REM) if ≤14. Average disease burden of patients in MDA and DAPSA-LDA/REM was compared. The agreement between the tested definitions was established using 2×2 tables and calculation of a *kappa*.

Results: Of the total population (124 patients), MDA was performed in 107 (86.3%), of which 40 (37.4%) reached MDA (minimum 5/7); and DAPSA could be done in 77 (62.1%) patients, of which 48 (62.3%) were in DAPSA LDA/REM. There was a moderate agreement between DAPSA LDA/REM and MDA (*kappa*=0.544) (95%IC: 0.371 to 0.717) as shown in table 1. All patients in MDA, except 2, were with DAPSA LDA/REM, however, some who achieve DAPSA

	DAPSA REM/LDA	DAPSA MDA/HDA	*kappa*
MDA	33	2	0.544
NOT-MDA	16	26	

table DAPSA REM

TABLE 1. Number of patients according disease status DAPSA LDA/REM (Low/Remission) or DAPSA MDA/HAD (Moderate/High), and achieving or not MDA

LDA / REM did not reach the MDA. Of the 14 patients in DAPSA LDA/REM, but not in MDA, did not fill at least 1/7 of the domains, as 6 for the (HAQ), 4 (PASI/BSA), 2 (joint pain and edema), and 2 (enthesitis). In addition, of the 48 patients who reached DAPSA LDA/REM, 6 (12.5%) patients had at least one enthesitis. With regard to the achievement of the disease activity composite indexes, it was not possible to perform the DAPSA in 47 (37.9%) patients, since 34 (27.4%) patients had no CRP result needed to perform calculation and the other 12 had chronic pain secondary to fibromyalgia. In the other hand, was not possible to perform the MDA in 17 (13.7%) because there was no record in the last consultation of the updated BSA/PASI skin or HAQ, or by associating fibromyalgia.

Conclusion: Because they have moderate agreement, both can be used in clinical practice. Though, we believe that MDA could be the more feasible in following-up our patients, noting that the difficulty of performing CRP was the main limitation for DAPSA. Besides, enthesitis was present in 12.5% even when in LDA/REM

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Abstract Number: 2489

Differences in Clinical Characteristics, Quality of Life, Disability, and Work Productivity in Psoriatic Arthritis Patients by Gender: Findings from a Cross-sectional Survey in the US and Europe

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

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Background/Purpose: Psoriatic arthritis (PsA) prevalence is equal in men and women, though gender may play a role in driving mechanisms of PsA leading to differences in manifestations of clinical disease (1). This analysis assessed key differences in clinical characteristics, disability, quality of life, and work productivity by gender in real-world practice.

Methods: Cross-sectional survey of rheumatologists and dermatologists and their patients in France, Germany, Italy, Spain, UK, and US. Data were collected from Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Data were analyzed by gender. Demographic characteristics, treatment use, and clinical characteristics (Tender Joint Count [TJC], Swollen Joint Count [SJC], Body Surface Area [BSA] psoriasis) were

Table 1: Demographic and clinical characteristics in women and men [mean (SD) or n (%)]

	Women	Men	P value
n (%)	1047 (46.1)	1223 (53.9)	-
Age, years	48.3 (13.7)	48.8 (12.8)	0.42
Working full time*, n (%)	206 (49.4)	350 (68.6)	<0.01
Charlson Comorbidity Index score	1.10 (0.51)	1.15 (0.58)	<0.01
Time from first symptoms to diagnosis, years	1.48 (3.53)	1.14 (2.48)	0.76
PsA duration, years	4.87 (6.15)	4.95 (5.79)	0.42
Currently receiving biologic treatment, n (%)	557 (53.2)	674 (55.1)	0.38
BSA psoriasis involvement, mean %	5.5 (8.4)	5.5 (8.1)	0.87
Swollen Joint Count	3.2 (7.0)	3.5 (6.9)	0.39
Tender Joint Count	4.1 (5.2)	4.5 (8.0)	0.03
Enthesitis, n (%)	59 (5.6)	72 (5.9)	0.86
Dactylitis, n (%)	79 (7.5)	75 (6.1)	0.21

*Outside the home

Table 2: Quality of life, disability, and work productivity in women and men [mean (SD)]

	Women	Men	P value
EQ5D utility score	0.80 (0.18)	0.82 (0.17)	0.02
HAQ-DI score	0.56 (0.60)	0.41 (0.52)	<0.01
PsAID12 score	2.66 (2.07)	2.27 (1.98)	<0.01
WPAI percentage of activity impairment	27.9 (22.0)	24.6 (22.4)	<0.01
WPAI percentage of work time missed	4.0 (14.0)	5.8 (19.2)	0.62

reported by physicians, while quality of life (EQ5D and PsAID12), disability (HAQ-DI), and work productivity (WPAI) were reported by patients. Men and women were compared using parametric tests and non-parametric tests where appropriate.

Results: Data were collected for 2270 patients (595 US, 1675 Europe). Demographic characteristics, time from first symptoms to diagnosis, biologic treatment, and clinical characteristics were comparable between women and men (Table 1). More women reported worse quality of life, disability, and work activity impairment than men (Table 2).

Conclusion: In women and men with similar PsA disease activity and treatment rates, women experienced worse quality of life, greater disability, and greater work impairment, despite a lower burden of comorbidities.

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Disclosure: L. Gossec, Abbvie, 5, AbbVie, 5, Abbvie, Biogen, BMS, Celgene, Lilly, Novartis, Pfizer, SAnofi-Aventis, UCB, 5, Amgen, 5, Biogen, 5, BMS, 2, 5, Celgene, 5, Celgene Corporation, 2, Janssen, 5, Lilly, 2, 5, MSD, 5, Nordic Pharma, 5, Novartis, 5, Pfizer, 2, 5, Sanofi, 5, Sanofi-Aventis, 5, UCB, 5; **J. Walsh**, AbbVie, 2, 5, ABBVIE, NOVARTIS, LILLY, AMGEN, UCB, 5, Amgen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, PFIZER, ABBVIE, 2, UCB, 5; **K. Michaud**, FORWARD, The National Databank for Rheumatic Diseases, 3, Pfizer, 2, Pfizer & Rheumatology Research Foundation, 2, Rheumatology Research Foundation, 2, University of Nebraska

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Abstract Number: 2490

The Cutaneous Microbiome of Psoriatic Disease Is Influenced by Disease Susceptibility *HLA* Alleles but Not Clinical Phenotype

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SESSION INFORMATION

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Background/Purpose: Psoriasis is an inflammatory skin disease. Psoriatic arthritis (PsA) is an inflammatory arthritis that affects 30% of psoriasis patients. The heterogeneity of psoriatic disease (PsD- psoriasis and PsA) is partly explained by genetic heterogeneity: human leukocyte antigen (*HLA)-C*06* is the strongest genetic risk factor for psoriasis without arthritis (PsC), while *HLA-B*27* and other *HLA-B* alleles are more strongly associated with PsA. Yet, PsD pathogenesis is not fully understood, inspiring an interest in the role of an important environmental factor: the microbiome. We aimed to characterize the cutaneous microbiome of psoriatic plaques and compare its diversity between PsC and PsA patients and between the major PsD-associated *HLA* alleles.

Methods: Skin swabs were obtained from a psoriatic lesion on the extensor aspect of the elbow or knee, and from unaffected skin on the contralateral joint in PsC patients (psoriasis diagnosed by a dermatologist, evaluated by a rheumatologist to exclude PsA) and PsA patients satisfying CASPAR criteria. Control samples were taken from matched sites in healthy subjects. PsA patients were evaluated by a rheumatologist using a standard protocol to determine the number of affected joints, peripheral and/or axial joint involvement. Subsequently, microbial DNA was isolated from the swab samples, and high-throughput 16S ribosomal DNA sequencing was utilized to characterize the cutaneous microbiota. Molecular HLA Class I typing was done from DNA obtained from peripheral blood, and subjects were classified as being *HLA-C*06* positive, *HLA-B*27* positive or *HLA-C*06* and *-B*27* negative (termed double negative). All study subjects were Caucasian. Dada2 pipeline was used in the bioinformatic analysis to infer unique amplicon sequences from raw reads and remove chimeric sequences. QIIME v.1.9.1 was used to assign taxonomy with reference to an internally-designed 16S database, and to compute alpha-diversity. Biostatistical analysis was performed in R.

Results: We recruited 34 healthy controls (59% male), 55 PsC patients (47% male), and 136 PsA patients (63% male). 38 PsC and 90 PsA patients were included in this analysis after excluding subjects with recent use of topical

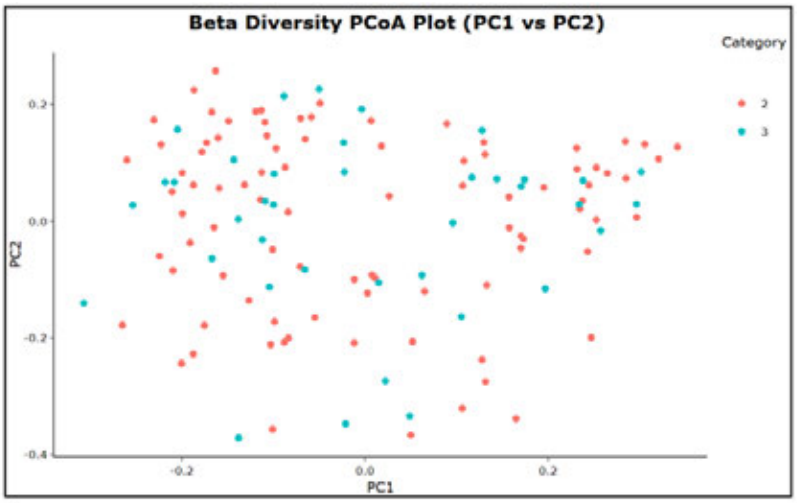

Figure 1: PsC vs PsA lesions demonstrate no distinct clustering of PsA (pink) and PsC (blue) on a beta-diversity principal coordinate analysis plot

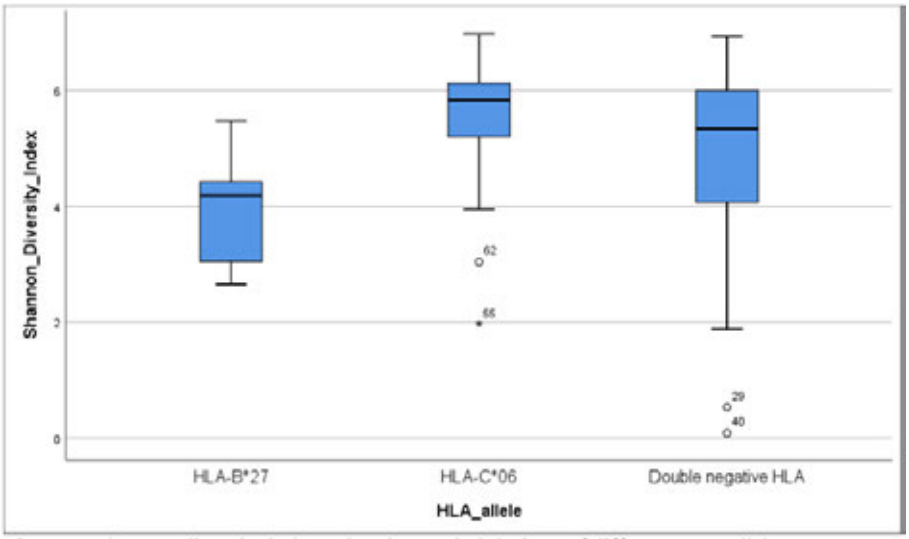

Figure 2: Shannon diversity index values in psoriatic lesions of different HLA alleles

ointments (≤7 days), antibiotics (≤3 months), and other related treatments. Linear model demonstrated that alpha diversity was significantly higher in lesional compared to unaffected samples in all PsD patients, as measured by Shannon diversity index (p=0.0106). However, there was no significant difference in lesional diversity between PsA and PsC patients (p=0.2244) (Figure 1). Interestingly, while there was no significant difference in alpha diversity between lesional swabs from *HLA-B*27*-positive compared to double negative patients (p=0.1401), it was shown to be significantly higher in lesional swabs from *HLA-C*06*-positive patients compared with both *HLA-B*27*-positive patients (p=0.0066) and double negative patients (p=0.0331) (Figure 2) by analysis of variance with Tukey's correction for multiple comparisons.

Conclusion: The cutaneous lesional microbial diversity of patients with psoriatic disease may be influenced by the *HLA-C*06* but not *–B*27* alleles.

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Abstract Number: 2491

Predictors of DAPSA28 Remission at 6 Months in Bio-Naive Patients with Psoriatic Arthritis Starting a TNF Inhibitor in Clinical Practice– Results from the EuroSpA Collaboration

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Table 1. Baseline characteristics

	Patients with assessment of DAPSA28 at follow-up (n= 7,975)		Patients without assessment of DAPSA28 at follow-up (n= 8,255)	
	No. of patients with available data, n	Median (IQR) or percentage	No. of patients with available data, n	Median (IQR) or percentage
Age, years	7,975	49 (40 - 57)	8,255	49 (40 - 57)
Male	7,975	48.6 %	8,255	49.0 %
Concomitant csDMARD	7,284	36.6 %	6,860	44.4 %
Time since diagnosis, years	3,848	4 (1 - 8)	5,314	4 (1 - 9)
Current smoking	6,767	16.2 %	5,945	16.8 %
Treatment	7,975		8,255	
Infliximab		21.1 %		19.6 %
Etanercept		33.5 %		36.2 %
Adalimumab		29.5 %		32.9 %
Certolizumab		4.4 %		2.3 %
Golimumab		11.6 %		9.0 %
Year of treatment	7,975		8,255	
Start 2015-2017		26.0 %		25.2 %
Start 2012-2014		27.8 %		22.3 %
Start 2009-2011		22.1 %		25.7 %
Start before 2009		24.1 %		26.8 %
CRP, mg/L	7,011	7 (2.9 - 17)	5,776	5 (1.2 - 13)
28SJC	6,911	3 (0 - 6)	5,131	2 (0 – 6)
28TJC	6,915	5 (2 - 10)	5,115	4 (1 - 9)
DAS28, units	5,850	4.38 (3.5 - 5.16)	3,600	4.2 (3.3 - 5.01)
DAPSA28, units	6,378	27.2 (17.6 - 39.7)	3,431	23.9 (15.4 - 35.9)
VAS Global, mm	7,015	64 (46 - 79)	5,381	60 (41 - 79)
VAS Fatigue, mm	3,419	65 (40 - 80)	1,809	63 (40 - 79)
HAQ, mm	6,618	0.88 (0.5 - 1.38)	4,382	0.88 (0.5 - 1.38)
VAS Pain, mm	6,957	62 (41 - 75)	4,659	60 (40 - 75.5)
Physician Global, mm	4,067	40 (24 - 60)	3,743	42 (26 - 60)

Data are as observed, median (IQR) or percentage; csDMARD: conventional synthetic Disease Modifying Anti Rheumatic Drug; DAS28Disease Activity in 28 joints; DAPSA28: Disease Activity in Psoriatic Arthritis in 28 joints; SJC28:28 Swollen Joint Count; 28TJC: 28 Tender Joint Count; VAS: visual analogue scale; HAQ: Health Assessment Questionnaire.

Background/Purpose: Tumor necrosis factor inhibitors (TNFi) have contributed to improved prognosis in patients with psoriatic arthritis (PsA). However, many patients treated with TNFi fail to achieve a treatment target of remission. Hence, the aims of this study were to identify predictors of 6-month Disease Activity in Psoriatic Arthritis in 28 joints (DAPSA28)(1) remission (DAPSA28≤4) in bio-naive PsA patients starting TNFi in clinical practice and investigate the performance of the derived prediction model.

Methods: Pooled data from PsA patients in 13 European registries participating in the EuroSpA Research Collaboration were analyzed(2). Patients with a 6-month follow-up visit (time window 3-9 months) with data allowing for calculation of DAPSA28, were included. The study cohort was divided into a derivation and validation cohort (50% of patients from each registry in each sub-cohort). Logistic regression analyses were applied to identify conventional

Table 2. Multivariate models for prediction of DAPSA28 remission at 6 months by variables assessed at baseline in the derivation cohort

	Initial model			Final model		
	Odds ratio	95 % CI	p-value	Odds ratio	95 % CI	p-value
Intercept	4.453	(2.802, 7.077)	<0.0001	4.545	(2.878, 7.177)	<0.0001
Smoking status (Past)	0.776	(0.638, 0.943)	0.0108	0.775	(0.637, 0.942)	0.0102
Smoking status (Current)	0.779	(0.605, 1.004)	0.0535	0.781	(0.606, 1.005)	0.0547
Year of treatment (Start 2012-2014)	1.082	(0.873, 1.343)	0.4722	1.096	(0.884, 1.359)	0.4026
Year of treatment (Start 2009-2011)	0.859	(0.676, 1.092)	0.2149	0.882	(0.694, 1.121)	0.3035
Year of treatment (Start before 2009)	0.643	(0.495, 0.835)	0.0009	0.674	(0.522, 0.871)	0.0026
CRP, mg/L (10-30)	1.402	(1.140, 1.724)	0.0013	1.442	(1.174, 1.770)	0.0005
CRP, mg/L (>30)	1.375	(1.045, 1.809)	0.0229	1.449	(1.104, 1.901)	0.0074
28SJC, per joint increase	1.017	(0.990, 1.044)	0.2179			
28TJC, per joint increase	0.936	(0.915, 0.958)	<0.0001	0.945	(0.926, 0.964)	<0.0001
VAS Global, per mm increase	0.991	(0.985, 0.997)	0.0020	0.991	(0.986, 0.996)	0.0002
VAS Fatigue, per mm increase	0.990	(0.984, 0.995)	0.0001	0.988	(0.983, 0.994)	<0.0001
HAQ, per unit increase	0.664	(0.542, 0.814)	<0.0001	0.658	(0.537, 0.807)	<0.0001
VAS Pain, per mm increase	0.997	(0.991, 1.003)	0.3331			
Physician Global, per mm increase	1.004	(0.999, 1.010)	0.1469			

Reference: never smoking, start of treatment 2015-2017, C-Reactive Protein (CRP)<=10.
DAPSA28: Disease Activity in Psoriatic Arthritis in 28 joints; 28SJC: 28 Swollen joint Count; 28TJC: 28 Tender Joint Count; VAS Global; Visual Analogue Scale Patient Global, VAS Fatigue; Visual Analogue Scale Fatigue; HAQ: Health Assessment Questionnaire; VAS Pain: Visual Analogue Scale Pain.

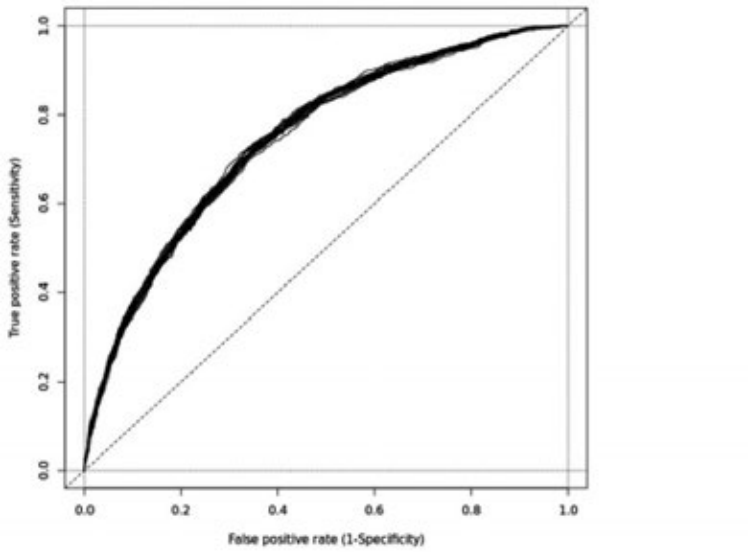

Figure 1: Receiver Operating Curves in the validation cohort (20 imputed datasets).

clinical variables (marked with bold in Table 1) associated with DAPSA28≤4 at 6 months in the derivation cohort. Missing covariate data were imputed with Multiple Imputation with Chained Equations. Variables with a p-value < 0.25 in univariate analyses were included in the initial multivariable model. A priori it was decided to adjust for age, gender and country. Purposeful selection guided removal of variables from the multivariable model. Model fit was tested in the validation cohort by area under the Receiver Operating Curve (ROC) and misclassification error.

Results: Of the 16,230 PsA patients in the EuroSpA database 7,975 patients initiating 1st TNFi had a registered follow-up visit with registered variables for DAPSA28 calculation and were included in the study. The study cohort had slightly higher baseline disease activity than the patients without DAPSA28 assessment at follow-up (Table 1). At 6 months, 1,956 (24.5%) patients were in DAPSA28 remission. Based on univariate analyses, all tested variables except concomitant csDMARD and time since diagnosis were included in the initial multivariate model. The final multivariate model identified that current or past smoking, treatment start prior to 2009, normal CRP, high 28TJC, high global, fatigue and HAQ scores decreased the probability of DAPSA28 remission at 6 months (Table 2). The regression coefficients of the model were used to derive a prediction index for each patient in the validation cohort, determining their predicted probability of DAPSA28 remission at 6 months. The ability of the model to correctly predict DAPSA28 remission using different cut-offs for predicted probability are shown with the ROC (Figure 1). The fit was deemed reasonable (median area under the curve 0.75, misclassification error 0.22).

Conclusion: A prediction model based on conventional clinical variables correctly predicted DAPSA28 remission status at 6 months in 3 out of 4 patients in a validation cohort. Future studies should investigate the potential of improving the model by addition of imaging and soluble biomarkers.

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Abstract Number: 2492

Efficacy and Safety of Disease-Modifying Drugs in Psoriatic Arthritis (PsA): A Systematic Literature Review

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Drug target	Drug name (No. of Trials)	Population	Primary Endpoint met (n/N)
Biological DMARDs			
TNFi	Golimumab (1)	csDMARD/NSAID-IR	yes (1/1)
	Etanercept (1) [1]	MTX + DMARD naive	yes (1/1)
	Adalimumab biosimilar (CT-P13) (1)	csDMARD-IR	yes (non-inferiority; 1/1)
	CHS-0214 (1) [1]	csDMARD-IR	yes (non-inferiority; 1/1)
IL17	Ixekizumab (2)	csDMARD-IR / TNFi-IR	yes (2/2)
	Secukinumab (3)	NSAID-IR / mixed csDMARD/TNFi-IR	yes (3/3)
TNF/IL17A	ABT-122 (1)	csDMARD/TNFi-IR	yes (1/1)
IL12/23	Ustekinumab (1) [2]	Patients with active enthesitis	yes (1/1)
IL23-19p	Risankizumab (1) [1]	NSAID/csDMARD/TNFi-IR	yes (1/1)
	Guselkumab (1)	csDMARD/TNFi-IR	yes (1/1)
IL6	Clazakizumab (1)	NSAID/csDMARD-IR	yes (1/1)
CD80/86	Abatacept (1)	csDMARD/TNFi-IR	yes (1/1)
Targeted synthetic DMARDs			
PDE-4	Apremilast (4)	csDMARD-IR / TNFi-IR / csDMARD naive	yes (4/4)
JAK 1/2/3	Tofacitinib (2)	csDMARD-IR / TNFi-IR	yes (2/2)
JAK 1	Filgotinib (1)	csDMARD-IR	yes (1/1)
csDMARD: conventional synthetic disease modifying anti-rheumatic drug; IR: insufficient responders			
[1] Conference abstract			
[2] open-label trial (Ustekinumab vs. TNFi)			

Table 1. Drugs investigated in PsA randomised controlled trials, 2015-2018.

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: There is now an increasing range of drug options in PsA. To inform the update of the EULAR PsA management recommendations (Ref 1), we performed a systematic literature review assessing the efficacy and safety of pharmacological agents in PsA.

Methods: Original articles published since the last EULAR literature review (2015) until 2018 in English were searched in Medline, Embase and Cochrane Library, as well as ACR/EULAR abstracts (2015-2018). For efficacy, randomised controlled trials (RCTs) investigating pharmacological interventions, defined as biological (b)DMARDs, targeted synthetic (ts)/conventional synthetic (cs)DMARDs were analysed. The main efficacy outcomes were ACR response criteria, PASI75, enthesitis, physical function and radiographic progression. For safety, also cohorts and case-control studies were analysed with a focus on adverse events, infections, cancer and cardio-vascular events.

Results: Of 6380 articles (efficacy: 2191, safety: 4189), 76 (68 original articles and 8 abstracts) were analysed. The drugs most investigated over the timeframe of this search were TNFi (5 trials) and IL17i (5 trials) (Table 1). Other drugs with mechanisms not previously published on in this indication were especially IL23-p19 inhibitors and JAK inhibitors (Table 1).

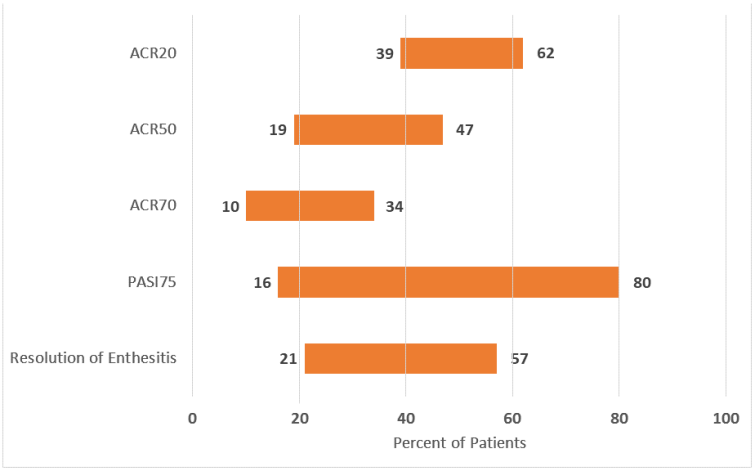

Figure 1. Chart showing range of efficacy across trials, in the active treatment arms, at the primary timepoint on different outcomes in PsA randomised controlled trials published 2015-2018.

All trials of original drugs, except one open-label study comparing Ustekinumab to TNFi, were placebo-compared trials and met their primary endpoint, ACR20 (Table 1). Figure 1 indicates the variety of responses across disease manifestations. Biosimilar comparison with bio-originator showed non-inferiority.

Safety was evaluated in 32 articles. One article, investigating patients in the ARTIS and DANBIO registries did not show an increased risk of cancer with TNFi compared to TNFi naïve PsA patients and the general population. There was an increased risk of Candida infections and inflammatory bowel disease with IL17 inhibiting agents. Two longitudinal cohorts showed an elevated risk for major adverse cardiac events in PsA. One longitudinal cohort study showed no association of cardiovascular events with any treatment.

Conclusion: New drugs targeting IL17A, IL23-p19, JAK, CD80/86, TNF/IL17A and IL6 demonstrated efficacy for the treatment of PsA with varying responses across different disease domains. Efficacy of TNFi agents and other bDMARDs was confirmed. Investigated biosimilars were non-inferior to their reference products. No new major safety signals were identified, though long-term studies and more registry data are needed. This literature review informed the EULAR updated recommendations for management of PsA.

Reference:

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Abstract Number: 2493

IL-6 and TNF-α Influence on Clinical Manifestations, Activity and Comorbidity in Psoriatic Arthritis Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The activation of the Th-1 and Th-17 lymphocytes response seems to be one of the causes associated with PsA onset. During this process cytokines like TNF-α and Il-6 play an important role in chronic inflammatory response. However, their role in clinical manifestations and comorbidity is less known.

Purpose: To relate the IL-6 and TNF-α serum levels with clinical spectrum, presence of dactylitis, enthesitis, disease activity and comorbidity in a group of patients with PsA.

Methods: A Cross-sectional study with 194 PsA patients (diagnosed by the CASPAR criteria). IL-6 and TNF-α serum levels were determined by ELISA. The clinical variables measured were: clinical spectrum (peripheral, axial or mixed), presence of dactylitis, enthesitis, psoriasis (measured by PASI score) and HLA-B27. Disease activity was measured with the minimal disease activity criteria (MDA). In regards to comorbidity, we measured cardiovascular risk markers such as waist-to-hip ratio (WHR), Apolipoprotein A, Apolipoprotein B, Lipoprotein A, Insulin, Insulin resistance and microalbuminuria; hepatic steatosis was measured by ultrasound and fatigue by FACIT-F questionnaire.

Results: Of the 194 patients, 107 were men (55.2%) and 87 (44.8%) female. The mean of age was 53.33 years (SD: 10.86). 14.9% were receiving biological therapy. Eighteen patients had an exclusive axial affectation, 72 mixed and 104 peripheral only. 17.5% were HLA-B27 positive and 52.1% had a MDA. Regarding IL-6, we found no correlation

	Mean IL6 (SD)	P
Biological therapy (yes/no)	5,97(5,20)/ 5,68(4,24)	0,87
Dactylitis (yes/no)	7,35(4,63)/5,26(4,66)	0,24
MDA (yes/no)	5,15(4,65)/6,34(4,53)	0,38
Axial/mixed/peripheral	4,33(3,24)/ 6,87(5,31)/5,20(4,89)	0,34
HLA-B27 (+/-)	2,84(1,70)/6,29(4,76)	0,001
Axial+Mixed+HLA-B27(-)/Axial+Mixed+HLA-B27(+)	7,54(5,02)/2,91(1,89)	0,01
Hepatic steatosis (yes/no)	6,07(4,79)/3,82(2,87)	0,17

Table 1

	Mean TNF-α (SD)	p
Biological therapy (yes/no)	180,68(176,20)/12,57(10,12)	0,001
Dactylitis (yes/no)	24,75(18,75)/57,48(37,95)	0,29
MDA (yes/no)	74,86(62,66)/18,93(9,20)	0,009
Axial/mixed/ peripheral	50,70(37,32)/63,12(97,98)/28,86(18,79)	0,19
HLA-B27 (+/-)	72,68(67,24)/45,58(41,42)	0,23
Axial+Mixed+HLA-B27(-)/Axial+Mixed+HLA-B27(+)	46,02(40,83)/38,61(3,27)	0,70

Table 2

with the number of entheses affected, SJC, PASI, ESR, WHR, Apolipoprotein A, Apolipoprotein B, Lipoprotein A, Insulin, Insulin resistance, microalbuminuria, nor FACIT-F. We found a positive correlation between IL6 levels and CRP (R=0.41, p< 0.0001). The rest of the results are shown in Table1.

Regarding TNF-α, we found no correlation with number of entheses affected, SJC, PASI, ESR, CRP, WHR, Apolipoprotein A, Apolipoprotein B, Lipoprotein A, insulin, insulin resistance, microalbuminuria nor FACIT-F. The rest of the results are shown in Table2.

Due to the close correlation between the use of biologicals and TNF-α serum levels, we analyzed them between TNF-i and Ustekinumab/Secukinumab (242.18 SD: 207.71 vs. 32 SD: 27.32, p < 0.007). In the analysis excluding patients treated with biologicals, we only found a positive correlation with microalbuminuria (R:0.72, p< 0.001), even when excluding patients with a history of hypertension or diabetes (R: 0.37, p< 0.004). We found no correlation between IL-6 and TNF-α levels (R:-0.01, p< 0.85).

Conclusion: Excluding CRP, we found no correlation between IL-6 levels and clinical disease activity or comorbidity. In our results HLA-B27 influenced IL-6 levels, but it is unknown the pathogenesis on which this relationship is based, however findings that correlate IL-6 polymorphisms with HLA-B27 may indicate that the relationship obtained is not casual. On the other hand, blockade of TNF-α causes higher TNF-α serum levels. TNF-α was associated with subclinical kidney damage in PsA patients with or without diabetes. Even though this cytokine is known to be involved in kidney damage this correlation has not been documented in non-diabetic PsA patients.

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Abstract Number: 2494

Comparison of Comorbidity in Spondyloarthritis: Influence on Inflammatory Activity in Patients with Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous disease that is included in the group of spondyloarthritis. Although PsA has its own clinical characteristics, it has a relatively specific comorbidity in relation to the rest of the entities that make up the group. The most frequent comorbidities in PsA are emotional disorders (anxiety and depression) and obesity. Its presence implies a deterioration in the quality of life, an increase in mortality and constitutes a factor to be taken into account in the selection of treatment. However, the influence of these comorbidities on the activity of the disease is less known.

Purpose: To compare the presence of psycho-affective disorders and factors associated with obesity in patients with spondylitis and PsA. Relate them to the activity of the disease in patients with PsA.

Methods: Prospective longitudinal study that included 100 patients with ankylosing spondylitis (AE) and 160 patients with PsA who attended the outpatient clinics of a tertiary hospital. Patients with PsA who had at least four assessments of the activity in one year, measured by the minimum disease activity (MDA), were included in the study. We compared those patients who met MDA criteria in the four visits compared to the rest of the patients. The tendency to anxiety and depression was evaluated using the Hospital Anxiety and Depression Scale (HADS) questionnaire. Regarding cardiovascular comorbidity, the waist / hip ratio and the analytical variables were measured: apolipoprotein A, apolipoprotein B, A lipoprotein, C peptide, insulin, insulin resistance (HOMA) and leptin. CRP, ESR and IL-6 were also measured. The age, the disease duration and the treatment used were collected basally. Due to the circadian

	AE	PsA	P	Multivariate
Age	52,09(11,89)	55,27(12,04)	0,01	NS
Disease duration (years)	13,44(8,83)	15,37(6,8)	0,3	
Gender (M/F)	66/34	93/67	0,03	NS
bDMARD(%)	24	21,25	0,7	
Waist/hip ratio	0,91(0,09)	0,90(0,1)	0,5	
Leptin(ηg/ml)	11,5(9,1)	18,72(14,7)	0,002	0,04(OR: 1,03)(IC:1,001-1,007)
C peptide	2,19(0,92)	2,62(1,18)	0,1	
HOMA	2,56(2,52)	3,09(2,17)	0,01	NS
ApoA(mg/dL)	152,78(23,7)	159,83(26,44)	0,03	NS
ApoB(mg/dL)	95,99(26,95)	99,05(26,9)	0,1	
A Lipoprotein	47,56(16,32)	44,99(20,32)	0,4	
HAD Anxiety	6,36(4,32)	7,1(4,21)	0,4	
HAD Anxiety>8(%)	38	38,2	0,9	
HAD Depression	4,47(3,74)	5,05(3,85)	0,3	
HAD Depression>8(%)	23	24	0,9	
ESR	15,4(12,5)	19,15(15,53)	0,3	
CRP	0,55(1,01)	2,03(2,12)	0,4	
IL6	5,00(4,31)	6,76(5,13)	0,2	

Table 1

	MDA (90)	NO MDA (70)	P	Multivariate
Age	54,45(12,93)	55,76(11,51)	0,4	
Disease duration (years)	16,45(10,01)	14,95(9,81)	0,5	
Gender (M/F)	58/32	35/35	0,06	
bDMARD(%)	26,6	14,92	0,08	
Waist/hip ratio	0,91(0,1)	0,92(0,8)	0,6	
Leptin (ηg/ml)	15,30(12,47)	22,95(18,62)	0,01	0,04(OR: 1,02)(IC:1,001-1,043)
C peptide	2,24(0,86)	2,70(1,25)	0,1	
HOMA	1,55(0,76)	3,12(2,61)	0,4	
ApoA(mg/dL)	157,17(22,3)	165,49(29,94)	0,06	
ApoB(mg/dL)	102, 23(25,60)	97,05(23,7)	0,2	
A Lipoprotein	37,43(17,69)	42,84(20,34	0,1	
HAD Anxiety	5,8(3,96)	8,02(4,09)	0,02	NS
HAD Depression	3,54(3,25)	6,22(4,64)	0,017	NS
ESR	15,5(9,7)	18,23(11)	0,3	
CRP	1,25(3,34)	2,28(4,75)	0,4	
IL6	4,18(5,69)	5,88(7,79)	0,2	

Table 2

variation of these determinations, all were collected at the same time. Patients with diabetes mellitus, dyslipidemia in treatment or thyroid disease due to the influence on the parameters associated with cardiovascular comorbidity were excluded.

Results: The significant differences between the patients with ankylosing spondylitis and Aps are shown in Table 1. When comparing the patients with PsA that reached a MDA compared to the rest, the following significant differences were found Table 2. Among the variables that make up the MDA concept, only the number of swollen joints (r: 0.22, $p < 0.009$) and HAQ (r: 0.20, $p < 0.01$) were correlated with the concentration of leptin . There was no correlation between leptin levels and those of PCR, VSG or IL-6.

Conclusion: In our study, patients with PsA presented a higher concentration of several markers of vascular risk (insulin resistance, apoprotein A and leptin) compared to patients diagnosed with spondylitis. In the PsA, leptin influenced to a greater extent than the emotional factors (anxiety and depression) to reach a prolonged MDA. Leptin correlated with the number of swollen joints but not with acute phase reactants (ESR and CRP) or IL-6. These results could confirm that leptin would promote a low-grade inflammation not detected by the levels of ESR, CRP or IL-6.

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Abstract Number: 2495

Oligoarticular Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Table 1: Patient Characteristics based on active joint involvement		
Number of patients	192	215
Males [N (%)]	112 (58.3)	126 (58.6%)
Age at Psoriasis (yrs)	29.1	31.4
Age at PsA (yrs)	42.5	43.6
Duration of PsA (yrs)	0.37	0.42
BMI	28.5	30.6
PASI	4.1	5.1
Actively inflamed Joints	1.8	13.8
Dactylitis	14.6%	36.3%
Enthesitis	15.6%	29.3%
Axial disease	10.4%	18.1%
UE SJ	41%	87%
UE LJ	19%	54%
LE SJ	21%	76%
Large joints lower	20%	49%
Highest medication		
NSAIDs	34.4%	29.3%
DMARDs	12.5%	18.6%
Biologics	5.7%	3.7%
BMI-body mass index; PASI-psoriasis area severity index; actively inflamed joints-tender and/or swollen joints; UE-upper extremity; SJ-small joints; LJ- large joints; LE-lower extremity; NSAIDs-non steroidal anti-inflammatory drugs; DMARDs-disease modifying anti-rheumatic drugs		

Table 2: Weibull regression model for actively inflamed joint progression adjusted for age at diagnosis of PsA and sex

Covariate	Univariate analysis		Multivariate analysis			
			Full Model		Reduced Model	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
PASI	1.00 ((0.96,1.05)	0.88	1.01 (0.97, 1.06)	0.61		
APC	1.12 (0.66, 1.90)	0.67	1.03 (0.59, 1.78)	0.93		
DMARDs	1.35 (0.73, 2.51)	0.34	1.41 (0.72, 2.75)	0.32		
Biologics	1.05 (0.46, 2.39)	0.90	1.44 (0.60, 3.44)	0.41		
UE SJ	1.97 (1.11, 3.49)	0.02	2.21 (1.23, 3.96)	0.008	1.97 (1.11, 3.49)	0.02
UE LJ	1.63 (0.82, 3.21)	0.16	1.59 (0.79, 3.18)	0.19		
LE-SJ	0.96 (0.46, 2.00)	0.92	1.08 (0.52, 2.27)	0.83		
LE-LJ	1.47 (0.79, 2.75)	0.22	1.53 (0.80, 2.94)	0.20		
mSS	1.02 (0.98, 1.06)	0.28	1.01 (0.97, 1.06)	0.49		
Axial disease	0.62 (0.26, 1.46)	0.28	0.55 (0.23, 1.30)	0.17		
Age at Dx			1.00 (0.98, 1.03)	0.78	1.01 (0.99, 1.03)	0.45
Sex M vs F			0.89 (0.51, 1.55)	0.68	0.89 (0.52, 1.53)	0.68

PASI-Psoriasis Area Severity Index; APC-acute phase reactant; DMARDs-disease modifying anti-rheumatic drugs; UE- upper extremity; LE- lower extremity; SJ-small joints; LJ-large joints; Dx-diagnosis; mSS-modified Steinbrocker score

Background/Purpose: Oligoarthritis, defined as ≤4 affected joints, was recognized as a pattern of psoriatic arthritis (PsA) by Moll and Wright. In some jurisdictions, patients with oligoarticular disease are not able to receive biologic therapy. It remains unclear whether patients with oligoarticular disease differ from those with polyarticular disease and what predicts progression from oligoarticular to polyarticular disease.

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whether patients with oligoarticular disease differ from those with polyarticular disease and what predicts progression from oligoarticular to polyarticular disease.

Methods: Patients followed at the PsA clinic within 1 year of diagnosis were included. Patients were followed according to a standard protocol at 6-12 month intervals. All information was tracked in a computerized database. Oligoarthritis was defined in two ways. First, based on the presence of ≤ 4 inflamed joints, and second based on ≤ 4 involved joints (including both inflammation and damage). Descriptive statistics are provided for patients presenting with oligoarthritis and polyarthritis at baseline. Multivariate Weibull regression models for handling interval- and right-censored data were developed with the outcome being progression to polyarticular disease. All models are adjusted for age at diagnosis of PsA and gender.

Results: 407 inception patients who had at least two visits were included. Of those 192 presented with oligoarthritis and 215 with polyarthritis. Demographic features were similar in the two groups. As expected, polyarticular involvement was associated with a higher number of actively inflamed joints. The distribution of joints involved was similar in the two group, with small joints of the hands and feet being most commonly involved (Table 1).

Of the 192 patients who presented with oligoarthritis 75 remained oligoarticular and 117 evolved into polyarticular. The only predictor for progressing to polyarthritis was the presence of small hand joint involvement. (Table 2). When we considered oligoarthritis definition based on inflamed and/or damaged joints the predictors for progression included small joints upper extremity as well as use of DMARDs.

Conclusion: Oligoarticular disease is similar to polyarticular disease. Most patients present with upper extremity small joint involvement. The majority of patients who present with oligoarticular disease progress to polyarticular involvement. Patients with oligoarticular disease should be treated aggressively to prevent polyarticular involvement.

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Abstract Number: 2496

Serum Metabolomic Analysis of Psoriatic Arthritis Using Solid Phase Microextraction – Liquid Chromatography – High-Resolution Mass Spectrometry Identifies Putative Disease Activity Markers

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
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Session Time: 9:00AM–11:00AM

Background/Purpose: Disease activity in psoriatic arthritis (PsA) is often difficult to assess but drives treatment decisions, joint damage and long-term outcomes. We aimed to identify serum markers for PsA disease activity using metabolomics.

Figure 1a: PCA (PC1:25.4%, PC2:16.5%) plot of healthy controls and patients with PsA. Data obtained from positive mode acquisition. 1b: OPLS-DA (Comp1: 12.3%, Comp 2: 18.2%) plot of mild vs severe PsA patients. The model was found to have a goodness of fit of $R^2y = 0.73$ and predictability of $Q^2=0.44$. Although this predictability falls below the acceptable 0.5, validation via permutation revealed a significant model $p < 0.05$ for both model quality parameters.

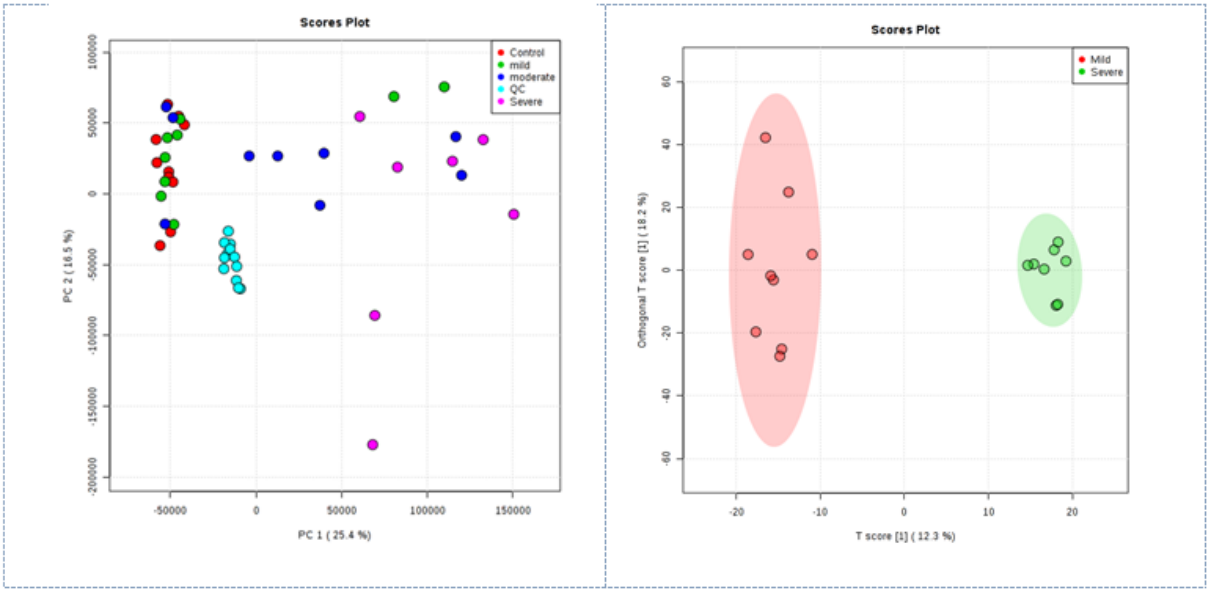

Table 1. Tentatively annotated features showing statistically significant differences across varying Degrees of psoriatic arthritis activity for negative mode data

Feature No.	Tentative ID	m/z	Retention time (s)	Adduct	P value	Q value
4448	2-Hydroxydecanedioic acid 3-Hydroxysebacic acid cis-4-Hydroxycyclohexylacetic acid	217.1077	707	$[M-H]^-$ $[M+CH3COO]^-$	0.001554	0.02996
3752	p-Coumaroylagmatine Undecanedioic acid	275.1501	729	$[M-H]^-$ $[M+CH3COO]^-$	0.000846	0.02996
1139	3-Hydroxydodecanedioic acid	281.1162	840	$[M+Cl]^-$	0.001861	0.02996
3689	Dodecanedioic acid	289.1659	761	$[M+CH3COO]^-$	0.002212	0.02996
216	S-aminomethyldihydrolipoamide	295.1163	802	$[M+CH3COO]^-$	0.000925	0.02996
2254	1,11-Undecanedicarboxylic acid	303.1818	804	$[M+CH3COO]^-$	0.006367	0.04040
2412	Phenylbutyrylglutamine	327.1118	782	$[M+Cl]^-$	0.001907	0.02996
2240	Arginyl-Lysine	337.1744	738	$[M+Cl]^-$	0.00136	0.02996
2522	6-Keto-PGF1a	429.2488	1134	$[M+CH3COO]^-$	0.001482	0.02996
2256	N1-(alpha-D-ribosyl)-5,6-dimethyl-benzimidazole L-phenylalanyl-l-hydroxyproline Prolyl-Tyrosine	313.0959	735	$[M+Cl]^-$ $[M+Cl]^-$ $[M+Cl]^-$	0.001482	0.02996

Methods: Serum samples were obtained from a cohort of carefully phenotyped patients with PsA satisfying CASPAR criteria (n=30, 15 males, mean age 48 years, disease duration 11 years) and healthy controls (n=10, mean age 43 years). Based on the number of actively inflamed (swollen or tender joints) patients were grouped as mild (< 4 actively inflamed and 0 swollen joints; n = 10), moderate (4-5 actively inflamed and < 3 swollen joints; n = 10) and severe (>5 actively inflamed and >3 swollen joints; n = 10). Serum samples were processed using thin film microextraction using an established protocol. For metabolite identification high performance liquid chromatography with high-resolution mass spectrometric detection was performed using a ThermoScientific Q-Exactive mass spectrometer. MS/MS validation was performed via parallel reaction monitoring. The MS/MS spectrum obtained was compared to the fragmentation patterns of metabolites in the m/z cloud of MS finder databases. Human metabolome database was used for annotation of extracted peak using XCMS online and METLIN. Statistical analysis was performed using Metabo-

Table 2. Tentatively annotated features showing statistically significant differences between healthy controls and severe psoriatic arthritis patients for positive mode data

Feature No.	Tentative ID	m/z	Adduct	Retention time (min)	P value	Q value
57	S-aminomethyldihydrolipoamide	237.1090	$[M+H]^+$	13.25	0.00008	0.018
130	hydroxycapric acid	189.1485	$[M+H]^+$	14.84	0.0002	0.02
304	Glutamyl-tyrosine	310.1159	$[M+H]^+$	14.01	0.00057	0.043
365	1-methyladenosine isoleucyl glutamate	282.1197 282.1186	$[M+H]^+$ $[M+Na]^+$	12.17	0.0007	0.026
531/1302	Adenosine or deoxyguanosine isobutyryl carnitine S-aminomethyldihydrolipoamide	285.1306 254.1363 254.1355	$[M+NH4]^+$ $[M+Na]^+$ $[M+NH4]^+$	11.05	0.001	0.03
549	Gamma-glutamyltyrosine	311.1238	$[M+H]^+$	13.45	0.001	0.03
715	Arginyl-glycine	254.1224	$[M+Na]^+$	13.33	0.002	0.04

analyst 4.0. For univariate analysis, a Kruskal Wallis with a false discovery rate (FDR) adjusted p-value of 0.05 was applied. For multivariate analysis, Principal Component Analysis (PCA), Partial Least Square – Discriminant Analysis (PLS-DA) and Orthogonal Projection to Latent Structures – Discriminant Analysis (OPLS-DA) were performed.

Results: PCA (figure 1a) revealed clear distinction between mild, moderate and severe PsA, but no difference between healthy controls and mild PsA. OPLS-DA (figure 1b) demonstrated a cross-validated significant separation between mild and severe PsA. Multivariate and univariate analysis yielded 10 statistically significant features across the three PsA groups, tentatively identified using xMSAnnotator for negative mode data (Table 1) while 7 statistically significant features were found to differentiate controls from patients with severe PsA and were tentatively identified using XCMS online for positive mode data (Table 2). Some of these tentatively identified compounds were found to be associated with the serine and threonine metabolism pathways and most if not all compounds presented a relative increase in concentration proportional to disease severity.

Conclusion: Untargeted metabolomics of serum via solid phase microextraction has the potential to identify markers for PsA disease activity.

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Abstract Number: 2497

Description and Prevalence of Spondyloarthritis in Unselected Patients with Psoriasis, Acute Anterior Uveitis, and Inflammatory Bowel Disease Presenting with Undiagnosed Back Pain

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

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Session Time: 9:00AM–11:00AM

N=246 unless otherwise stated	Psoriasis	AAU	IBD
Total number (%)	46 (18.7%)	73 (29.7%)	127 (51.6%)
Age, mean (SD) years	36.7 (6.0)	34.0 (5.8)	34.0 (7.3)
Males, N (%)	24 (52.2%)	41 (56.2%)	64 (50.4%)
Symptom Duration, mean (SD) years	7.7 (7.7)	8.7 (6.7)	6.3 (5.9)
B27+, N (%)	10 (21.7%)	51 (69.9%)	28 (22.0%)
Inflammatory back pain >5/10, N (%)	34 (73.9%)	51 (69.9%)	68 (53.5%)
Family history of SpA, N (%)	15 (32.6%)	15 (20.5%)	20 (15.7%)
Enthesitis, N (%)	15 (32.6%)	13 (17.8%)	39 (30.7%)
Peripheral arthritis, N (%)	13 (28.3%)	2 (2.7%)	5 (3.9%)
Dactylitis, N (%)	4 (8.7%)	2 (2.7%)	3 (2.4%)
Radiographic sacroiliitis, %	3 (6.5%)	17 (23.3%)	13 (10.2%)
Meets mNY classification criteria	2 (4.3%)	13 (17.8%)	9 (7.1%)
MRI indicative of axSpA, %, N=146	6 (18.2%)	20 (43.5%)	10 (14.9%)
MRI positive by ASAS definition, %, N=146	4 (12.1%)	11 (23.9%)	7 (10.4%)
Axial SpA rheumatologist diagnosis, %	21 (45.7%)	45 (61.6%)	51 (40.2%)
Axial SpA diagnosis, confidence ≥7/10, %	14 (30.4%)	37 (50.7%)	43 (33.9)%
Meets ASAS classification criteria, %	12 (26.1%)	52 (71.2%)	35 (27.6%)
Meets ASAS imaging arm criteria, %	6 (13.0%)	23 (31.5%)	17 (13.4%)
Meets ASAS clinical arm criteria, %	9 (19.6%)	48 (65.8%)	25 (19.7%)

Table 1

Demographics	axSpA YES (n=117, 47.6%)	Not axSpA (n=129, 52.4%)	P value
Male, N (%)	72 (61.5%)	57 (44.2%)	0.006
Mean (SD) age, years	33.7 (6.7)	35.2 (6.7)	ns
Mean (SD) symptom duration, years	7.6 (6.3)	7.0 (6.8)	ns
Inflammatory Back Pain (Global), N(%)	102 (87.2%)	72 (55.8%)	<0.00001
Inflammatory Back Pain (ASAS), N(%)	93 (79.5%)	69 (53.5%)	0.00002
Inflammatory Back Pain (Berlin), N(%)	95 (81.2%)	65 (50.4%)	<0.00001
Respond to NSAID within 48 hrs, N(%)	58 (49.6%)	59 (45.7%)	ns
Family history of SpA, N (%)	22 (18.8%)	28 (21.7%)	ns
Enthesitis, N(%)	29 (24.8%)	38 (29.5%)	ns
Enthesitis of the heel, N(%)	10 (8.5%)	18 (14.0%)	ns
Swollen joints N(%)	10 (8.5%)	10 (7.8%)	ns
Dactylitis, N(%)	4 (3.4%)	5 (3.9%)	ns
Lateral lumbar flexion <10cm, N(%)	17 (14.5%)	6 (4.7%)	0.008
Chest expansion <4cm, N(%)	15 (12.8%)	15 (11.6%)	ns
B27 positive, N(%)	61 (52.1%)	28 (21.7%)	<0.00001
Elevated CRP (> 6.0mg/L), N(%)	43 (36.8%)	32 (24.8%)	0.042
Radiographic sacroiliitis, N(%)	30 (25.6%)	2 (1.6%)	<0.00001
Unilateral grade 2 sacroiliitis, N(%)	46 (39.3%)	5 (3.9%)	<0.00001
MRI indicative of axSpA, N(%)	34/67(50.7%)	2/79 (2.5%)	<0.00001

Table 2

Background/Purpose: There is limited prospective data as to the frequency of axial spondyloarthritis (axSpA) in unselected patients referred to rheumatologists with undiagnosed back pain who have presented with acute anterior uveitis (AAU), psoriasis, or colitis to their respective specialists. It is also unclear which clinical features discriminate between axSpA and non-specific causes of back pain that might inform the development of a screening strategy to expedite referral of patients to rheumatologists. Our aims were: 1. To determine the prevalence of axSpA in unselected patients referred with undiagnosed back pain presenting with AAU, psoriasis, or colitis. 2. To determine which clinical characteristics define patients with axSpA.

Methods: The multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at facilitating early detection of axial SpA. First and last patients were recruited on February 2013 and March 2018, respectively. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, AAU, or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA and MRI evaluation is ordered per rheumatologist decision. Differences in clinical characteristics between those who were diagnosed as axSpA or non-specific back pain were analyzed using chi-squared and t-tests.

Results: A total of 246 patients were recruited, 47.6% were diagnosed with axSpA, and these included 68.5% of B27 positive patients. Symptom duration was 7-8 years and the majority had back pain severity >5 on a 0-10 scale (Table 1). Diagnosis of axSpA was established in 45.7%, 61.6%, and 40.2% of patients, while ASAS classification criteria were met by 26.1%, 71.2%, and 27.6% of patients with psoriasis, AAU, and IBD, respectively. Inflammatory back pain, male gender, lateral lumbar flexion, CRP, B27 positivity, and positive imaging discriminated axSpA from other causes of back pain (Table 2) and these remained significant in multivariate analysis adjusted for age, gender, and symptom duration.

Conclusion: Substantial diagnostic delay was evident in this prospective cohort of patients presenting with extra-articular manifestations despite a substantial burden of back pain. Referral to a rheumatologist should constitute standard of care, especially if B27 positive and presenting with psoriasis or AAU.

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Abstract Number: 2498

Incidence and Predictors of Heart Failure in Patients with Psoriatic Disease – a Cohort Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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Background/Purpose: Data about heart failure (HF) in patients with psoriatic disease (PsD) are sparse. The aims of the study were to: 1) determine the incidence and predictors for HF in patients with PsD and 2) describe their electrocardiographic (ECG) and echocardiographic (TTE) findings.

Methods: A cohort analysis was conducted on patients followed prospectively from 1978 to 2018 in the psoriatic disease program. Participants were assessed according to a standard protocol that included demographics, medications, measures of disease activity and comorbidities. The primary outcome was the first incident event of HF. HF events were further classified into ischemic and non-ischemic HF. Potential HF events were identified by searching the cohort database and linkage with provincial hospitalization and mortality databases. Patients with HF prior to study entry were excluded. The association between cardiovascular risk factors, measures of disease activity and occurrence of HF events was assessed using Cox proportional hazard models with time varying co-variates. Review of medical records identified ECG and TTE findings in patients with HF.

Table 1: Predictors for congestive heart failure events – Multivariate Cox proportional hazards model with age as time scale (n=1991, 64 events)

	All CHF (N=64)*		Ischemic CHF (N=38)‡		Non-ischemic CHF (N=26)‡‡	
Variable	**HR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**
Sex: Male	0.95 (0.55, 1.62)	0.84	1.27 (0.61, 2.67)	0.52	0.61 (0.27, 1.36)	0.23
Smoking:						
Current vs. Never	1.40 (0.58, 3.49)	0.44	2.61 (0.75, 9.11)	0.13		
Past vs. Never	0.89 (0.48, 1.67)	0.72	1.25 (0.51, 3.06)	0.63		
Race: Caucasian	0.90 (0.36, 2.24)	0.82				
Diabetes	1.73 (0.61, 4.90)	0.30	1.61 (0.74, 3.49)	0.23	1.63 (0.86, 3.09)	0.13
Hypertension	1.68 (0.72, 3.89)	0.22	1.34 (0.54, 3.32)	0.53	1.58 (0.68, 3.71)	0.29
Systolic						
Diastolic						
BMI	1.02 (0.97, 1.08)	0.42	0.98 (0.90, 1.07)	0.64	1.06 (0.99, 1.14)	0.08
Cholesterol	0.94 (0.73, 1.22)	0.67	1.03 (0.81, 1.31)	0.81		
Triglycerides	1.08 (0.79, 1.46)	0.60	1.20 (0.84, 1.70)	0.30		
Ischemic Heart Disease	**5.52 (2.97, 10.17)**	**<0.0001**	**19.29 (7.84, 47.94)**	**<0.0001**		
Tender joint count	**1.46 (1.12, 1.90)**	**0.006**	1.41 (0.94, 2.13)	0.10	**1.57 (1.11, 2.23)**	**0.01**
AM-Tender joint count	**1.51 (1.07, 2.14)**	**0.02**	1.25 (0.73, 2.11)	0.42	**1.83 (1.22, 2.75)**	**0.004**
Swollen joint count	1.62 (0.92, 2.83)	0.09	1.53 (0.73, 3.22)	0.27	**2.39 (1.02, 5.58)**	**0.047**
AM-Swollen joint count	**1.82 (1.03, 3.25)**	**0.04**	1.36 (0.52, 3.49)	0.53	**3.56 (1.79, 7.10)**	**0.0003**
PASI	1.14 (0.75, 1.75)	0.53	0.76 (0.36, 1.64)	0.50	1.57 (0.95, 2.61)	0.08
AM-PASI	1.35 (0.85, 2.14)	0.19	1.28 (0.64, 2.56)	0.48	1.61 (0.90, 2.89)	0.11
Damaged joint count	1.11 (0.93, 1.32)	0.22	1.08 (0.87, 1.36)	0.44	**1.29 (1.01, 1.65)**	**0.04**
ESR	**1.19 (1.05, 1.34)**	**0.006**	1.10 (0.91, 1.32)	0.29	**1.26 (1.08, 1.47)**	**0.002**
AM-ESR	**1.26 (1.06, 1.49)**	**0.009**	**1.27 (1.02, 1.58)**	**0.03**	**1.26 (1.02, 1.57)**	**0.04**
CRP	1.12 (0.97, 1.30)	0.13	1.09 (0.84, 1.42)	0.49	1.12 (0.87, 1.44)	0.36
AM-CRP	**1.27 (1.03, 1.55)**	**0.02**	**1.33 (1.03, 1.73)**	**0.03**	1.25 (0.91, 1.72)	0.15
HAQ	**1.95 (1.31, 2.92)**	**0.001**	**2.22 (1.31, 3.78)**	**0.003**	1.93 (0.95, 3.93)	0.07
Pain score	1.12 (0.98, 1.29)	0.09	1.10 (0.94, 1.28)	0.23	**1.22 (1.00, 1.49)**	**0.047**
PGA arthritis	1.12 (0.98, 1.26)	0.10	1.08 (0.95, 1.23)	0.22	1.19 (0.99, 1.43)	0.06
MDA state	**0.40 (0.17, 0.96)**	**0.04**	**0.40 (0.17, 0.96)**	**0.04**	0.29 (0.08, 1.03)	0.055
AM %of time in MDA state	0.46 (0.16, 1.36)	0.16	0.38 (0.11, 1.30)	0.12	0.37 (0.09, 1.56)	0.18

Results: A total of 1994 patients with PsD with 22,437 patient years were analyzed. During the follow-up period, 64 new HF events occurred (38 ischemic, 26 non-ischemic). The cumulative prevalence of HF by the age of 70 and 80 years was 1.4% and 3.7%, respectively. The incidence rate of first HF event during the study period was 2.85 per 1000 patient years. Of the 41 cases with available medical records, there were 19 cases of ischemic HF and 22 cases of non-ischemic HF (arrhythmias, cardiomyopathy and valvular dysfunction). In all events, the most common ECG findings were atrial fibrillation (22%), bundle branch blocks (29%) and pathological Q waves (33%). In all HF events, TTE revealed 37% reduced ejection fraction, 29% preserved ejection fraction, wall motion abnormalities (61%), left ventricular hypertrophy (41%) and valvular abnormalities (32%).

On multivariate analysis (Table 1), the following variables were independent predictors for all HF events: ischemic heart disease ($p< 0.001$), adjusted mean (AM)-tender joint count (TJC), AM-swollen joint count, AM-ESR, and HAQ (all $p< 0.05$). The strength of association of disease activity measures was higher when the analysis was restricted to non-ischemic HF as the outcome, with pain score, AM-TJC, AM-SJC, ESR and damaged joint count as independent predictors (all $p< 0.05$). The strongest predictor of ischemic HF was prior ischemic heart disease and additional independent predictors included: AM-ESR and HAQ ($p< 0.05$). Being in a minimal disease activity state was protective for all HF and ischemic HF ($p< 0.05$).

Conclusion: Increased risk of HF in PsD is associated with a combination of traditional cardiovascular risk factors and disease activity, particularly in patients with non-ischemic HF. The effect of inflammation on HF may be partially independent of atherosclerotic disease.

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Abstract Number: 2499

Predicting Risk of Developing Psoriatic Arthritis (PsA) in Siblings of Patients with Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Delay in diagnosis of psoriatic arthritis (PsA) has been shown to contribute to poor radiographic and functional outcome and less successful response to treatment (Haroon et al 2015). Disease interception models are now being proposed to identify siblings at risk of psoriasis (PsC) and PsA among PsA probands, to facilitate earlier management strategies. We set out to determine genetic variants that are likely to be associated with the risk of developing PsC and PsA among siblings of PsA patients.

Methods: A total of 195 probands were identified from well-established PsA cohorts. Family history and clinical assessment of siblings was systematically evaluated, and DNA of siblings was also collected. SNP genotyping was performed using 42 PsA-weighted SNPs on the probands and siblings. 308 siblings were collected (179 unaffected siblings and 129 affected of which 71 had psoriasis without PsA (PsC), and 56 had PsA). For analysis the concordance of genes from probands to sibling pairs (PsA -PsC , PsA-PsA and PsA-PsC or PsA) were compared with PsA-unaffected sibling pair. Probandwise concordance rates were determined using the formula 2C/(2C+D), in which C is the number of concordant pairs and D is the number of discordant pairs. The concordance difference between two groups were calculated using fisher exact test with an odds ratio (OR) > 1 indicating that the concordance rate in affected siblings was greater than unaffected sibling.

Table 1

PsA or PsC Siblings					
Gene	SNP	P-value	OR	95%. CI lower	95%. CI upper
PTPN22	rs2476601	0.0005	0.28	0.113	0.633
LCE3A	rs10888503	0.021	1.78	1.069	2.983
IL12B	rs2082412	0.016	1.98	1.111	3.600
HLA-C	rs12191877	0.0002	2.88	1.574	5.443
HLA-C*0602	rs2894207	0.009	2.05	1.174	3.661
PsA Siblings					
PTPN22	rs2476601	0.005	0.26	0.093	0.695
LCE3A	rs10888503	0.001	3.10	1.505	6.766
HLA-B*3906	rs2844603	0.023	0.48	0.238	0.944
HLA-C	rs12191877	0.029	2.33	1.079	5.394
PsC siblings					
PTPN22	rs2476601	0.008	0.30	0.108	0.795
HLA-C	rs12191877	0.0006	3.55	1.592	8.779
HLA-C*0602	rs2894207	0.039	2.09	1.029	4.445

Results: The mean age of the PsA probands at assessment was 48.1 yrs (±14.6) (age of onset of PsC 26.4 (±12.1) and PsA 34.4 (±10.9) yrs). The mean age of PsC siblings at assessment was 53.1 yrs (±14.3) (age onset of PsC at 27.5 (±15.7). The PsA siblings at assessment was 55.2 yrs (±13.4), with age of onset of PsC at 29.4 (±14.9) and PsA 36.1 (±12.9) yrs. Finally, the mean age of assessment of unaffected sibling was 50.2 yrs (±13.2). A differential concordance rate was noted for three genes with PsC, 4 genes with PsA, six genes for PsC or PsA, compared to the unaffected sibling (Table). In addition, when the concordance of PsA siblings were compared to PsC siblings, LCE3A was more likely (OR 2.6, p=0.015) in PsA and HLA-B*3906 was less likely (OR 0.43, p=0.038) to be shared in PsA .

Conclusion: There is greater concordance of known susceptibility genes among PsA siblings and PsC siblings of PsA probands. The genotype of the PsA probands along with the siblings is helpful in determining siblings at risk and should be considered as a potential biomarker for risk prediction.

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Abstract Number: 2500

Current Smoking Status Increases the Risk of Axial Psoriatic Arthritis: An Explanation to Smoking Paradox

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SESSION INFORMATION

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Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Smoking has been shown to be associated with an increased risk of psoriatic arthritis (PsA) in the general population, but there are controversies among patients with psoriasis. We hypothesize that smoking is a risk factor for axial PsA specifically, similar to axial spondyloarthritis, more than the other PsA phenotypes.

Axial Disease present vs absent			
	Multivariate analysis n=1528		
Variables	OR	95%CI for OR	P
Age	0.98	0.98-0.99	**0.001**
Gender (male vs female)	1.49	1.17-1.89	**0.001**
Smoking			**0.029**
Current vs never	1.42	1.07-1.88	**0.014**
Ex-smoker vs never	0.97	0.71-1.31	0.859
Nail involvement, ever (presence vs absence)	1.43	1.14-1.80	**0.002**
Polyarthritis, ever (presence vs absence)	0.71	0.56-0.89	**0.003**
DIP involvement, ever (presence vs absence)	0.56	0.40-0.80	**0.001**

CI: Confidence Interval, DIP: Distal Interphalangeal, OR: Odds Ratio.

Table 1. Multivariate analysis on factors associated with axial psoriatic arthritis

Methods: *PsArt-ID (Psoriatic Arthritis- International Database)*] is a multicenter, international database, investigating the disease characteristics in real life. From that registry, 1535 PsA patients with smoking data were included for this analysis. Smoking status was categorized as never, current smoker or ex-smoker. Axial PsA was based on the clinicians' judgement, requiring clinical features but not mandating any imaging. In addition grading of sacroiliitis was done by a central reader, whenever available. The effect of smoking, as well as other potential predictor factors on axial PsA and radiographic sacroiliitis, was assessed using a logistic regression analysis.

Results: Axial PsA was more common across current smokers compared to ex and non-smokers (38.9% vs 27.2% vs 26.8%, respectively; p< 0.001). Multivariate analysis to predict axial PsA showed that younger age [Odds ratio (OR)=0.98, 95% Confidence Interval (CI)= 0.97-0.99, p=0.014], male gender (OR=1.49, 95% CI=1.17-1.89, p=0.001), current smoking status (OR=1.42, 95% CI=1.07-1.88, p=0.014) and presence of nail disease (OR=1.43, 95% CI=1.14-1.80, p=0.002) were significant predictors for axPsA whereas polyarticular (OR=0.71, 95% CI=0.56-0.89, p=0.003) and distal joint involvement (OR=0.56, 95% CI=0.40-0.80 p=0.001) were protective (Table 1). Current smoking status was also found a significant predictor for radiographic sacroiliitis (OR=13.6, 95% CI= 2.87-64.6, p=0.001) (Table 2).

Conclusion: Current smoking is a significant risk factor for both axial PsA and radiographic sacroiliitis in patients with PsA, and not the peripheral phenotypes.

Radiographic sacroiliitis present vs absent			
	Multivariate analysis n=125		
Variables	OR	95%CI for OR	P
Gender (Male vs Female)	0.74	0.27-2.0	0.573
PsA duration	1.09	0.98-1.21	0.089
Smoking			**0.004**
Current vs never	13.6	2.87-64.6	**0.001**
Ex-smoker vs never	1.71	0.46-6.34	0.422
BMI	0.88	0.78-0.99	0.034
Polyarthritis (Presence vs absence)	0.79	0.27-2.25	0.662
DIP involvement (Presence vs absence)	0.36	0.59-2.22	0.273
Peripheral Joint Deformity (Presence vs absence)	0.21	0.06-0.71	**0.012**
Morning stiffness	0.99	0.98-1.01	0.753
HAQ	3.15	1.23-8.0	**0.017**
CRP (>10 mg/L vs ≤10 mg/L)	3.56	1.09-11.5	**0.035**

BMI: Body Mass Index, CRP: C - reactive protein, CI: Confidence Interval, DIP: Distal Interphalangeal, HAQ: Healthy Assessment Questionnaire, OR: Odds Ratio, PsA: Psoriatic Arthritis.

Table 2. Multivariate analysis on factors associated with radiographic sacroiliitis

Disclosure: D. Solmaz, None; **U. Kalyoncu**, UCB, 5; **I. Tinazzi**, None; **S. Bakirci**, None; **O. Bayindir**, None; **A. Dogru**, None; **E. Dalkılıç**, None; **G. Kimyon**, None; **C. Ozisler**, None; **G. Cetin**, None; **L. Kilic**, None; **A. Omma**, None; **M. Can**, None; **S. Yılmaz**, None; **A. Erden**, None; **S. Aydin**, None.

Abstract Number: 2501

The Association Between Metabolic Syndrome and Radiographic Damage in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic Arthritis (PsA) is associated with a higher prevalence of metabolic syndrome (MetS). MetS itself is also associated with a state of chronic, low-grade inflammation. With the hypothesis that MetS

Table 1: Demographic and disease features of patients with psoriatic arthritis included in the study

Variable	Non-MetS (N=319)	MetS (N=319)	*P* Value
Caucasian, n (%)	286 (90%)	283 (89%)	0.70
Sex, n (%)			0.20
. FEMALE	147 (46%)	131 (41%)	
. MALE	172 (54%)	188 (59%)	
Age at assessment	56.2 (14.1)	64.2 (11.2)	<.001
Age at diagnosis of Psoriasis	26.2 (13.4)	32.0 (15.4)	<.001
Age at diagnosis of PsA	33.4 (12.9)	42.0 (12.9)	<.001
Ever Smoker (+), n (%)	133 (42%)	174 (55%)	<.001
Comorbidities			
Diabetes Mellitus type 2 or its treatment, n (%)	4 (1%)	81 (25%)	<.001
Cardiovascular Disease, n (%)	14 (4%)	27 (8%)	0.036
Waist circumference (cm)	93.5 (13.8)	106.5 (13.7)	<.001
BMI	27.4 (5.1)	31.8 (6.2)	<.001
Clinical Features			
Inflammatory back pain (+), n (%)	42 (13%)	39 (12%)	0.72
Mech. Back pain (+), n (%)	37 (12%)	109 (34%)	<.001
BSA with psoriasis, median (min, max)	0.0 (0.0, 45.0)	1.0 (0.0, 80.0)	<.001
No of actively inflamed joints (Swollen or Tender), median (min, max)	1.0 (0.0, 47.0)	0.0 (0.0, 50.0)	<.001
No. of swollen joints, median (min, max)	0.0 (0.0, 21.0)	0.0 (0.0, 29.0)	<.001
No. of damaged joints, median (min, max)	0.0 (0.0, 47.0)	0.0 (0.0, 50.0)	0.004
Dactylitis ever, n (%)	164 (51%)	165 (52%)	0.94
Enthesitis ever, n (%)	125 (39%)	204 (64%)	<.001
Radiographic Features			
Syndesmophytes (+) (Cervical, thoracic or Lumbar), n (%)	58 (18%)	42 (13%)	0.08

Table 2 – Logistic regression for outcome Metabolic Syndrome (Yes vs No) adjusted for PsA duration, sex, and biologics treatment.

Variable	Univariate				Multivariate Reduced model			
	OR	95% CL		p-value	OR	95% CL		p-value
Biologics treatment					1.114	0.672	1.846	0.6767
PsA duration					1	0.98	1.02	0.982
Sex (Male)					1.46	0.878	2.426	0.1445
Actively inflamed joint count	1.028	0.983	1.075	0.2215				
Swollen joint count	1.008	0.921	1.103	0.8701				
Tender joint count	1.035	0.984	1.089	0.1815				
Syndesmophytes	1.849	0.916	3.731	0.0863				
No. of joints with radiographic damage	1.012	0.99	1.034	0.303				
Sacroiliitis- New York criteria	1.019	0.639	1.627	0.9356				
Plantar and/or Achilles calcaneal spurs	2.568	1.645	4.009	<.0001	1.935	1.179	3.176	0.009
Plantar and/or Achilles calcaneal erosion	0.843	0.344	2.067	0.7091				
DISH	6.044	2.309	15.82	0.0002	3.557	1.279	9.89	0.015
CDD	2.708	1.737	4.224	<.0001	1.716	1.002	2.941	0.0493
DDD	3.864	2.426	6.156	<.0001	2.705	1.556	4.705	0.0004
Atlanto-axial subluxation	0.808	0.176	3.712	0.7843				
HAQ	2.303	1.498	3.54	0.0001				
SF36 PCS	0.952	0.934	0.971		0.953	0.933	0.973	<.0001
SF36 MCS	0.987	0.968	1.008	0.2213				
Pain score	1.138	1.052	1.232	0.0013				
Patient Global assessment	1.176	1.081	1.279	0.0002				

is associated with radiographic damage in patients with PsA, we aimed to determine the association between MetS and axial as well as peripheral radiographic abnormalities in PsA.

Methods: Data on clinical (including MetS) and radiographic features were obtained from a large PsA cohort. Patients were classified as having MetS at the last clinic visit if they satisfied the harmonized definition of MetS by Albert KG et al (1). Demographic, clinical and radiographic data were compared between groups using t-test, Wilcoxon test or chi square test as appropriate. Regression methods were used to adjust for differences in age, sex or PsA duration and treatment, as appropriate. We used multivariable logistic regression to identify features independently associated with MetS in PsA patients.

Results: 319 PsA patients with MetS were compared to 319 patients without MetS (Table 1). Patients with MetS were older at assessment, and had an older age at onset of psoriasis and PsA. As expected, they had a higher waist circumference, BMI, diabetes and cardiovascular comorbidities. Patients with MetS were also more likely to be treated with conventional DMARDs and biologics indicating more severe disease. Patients with MetS were more likely to have calcaneal spurs, DISH, cervical and lumbar degenerative disc disease, after accounting for sex, PsA duration and biologic therapy. There were no differences in the presence of sacroiliitis (NY criteria) or radiographic damage to peripheral joints. Patients with MetS also reported a higher HAQ, pain score and global disease activity score. Multivariate regression analyses identified calcaneal spurs, DISH, cervical and lumbar degenerative disc disease as features independently associated with MetS in patients with PsA.

Conclusion: PsA patients with MetS present at an older age, have higher prevalence of comorbidities and more severe disease when treatment and patient reported outcomes are considered. MetS is not associated with radiographic severity of PsA but is associated with osteoarthritic and metabolic changes in the spine and enthuses.

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Abstract Number: 2502

Normalization of Inflammatory Gene Expression and Cellular Markers by Abatacept in the Skin Lesions of Psoriatic Arthritis Patients: A Biopsy Substudy of a Phase III Study

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SESSION INFORMATION
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Background/Purpose: Abatacept (ABA), a selective T-cell co-stimulation modulator, has been shown to improve disease activity in patients with psoriatic arthritis (PsA), but its effect on psoriatic inflammation at a molecular level has not been determined.

Methods: 40 patients received ABA and 38 received PBO in this substudy of a 24 week, Phase 3, randomized, double blind, placebo (PBO) controlled, multicenter study, followed by a 28 week open-label period in subjects with active PsA based on the Classification Criteria for Psoriatic Arthritis (CASPAR). 3mm punch skin biopsies were taken of lesional and non-lesional skin at Day 1 and of lesional skin at 24 weeks. Gene expression analysis was conducted using Affymetrix HGU133 2.0+ arrays. Differentially expressed genes (DEG) were evaluated with a cut-off of fold change >2.0 and FDR < 0.05. Results were validated with RT-PCR. To summarize per-patient differences across pathways, we also used gene set variation analysis (GSVA).

Results: Globally, gene expression of lesional skin (LS) in the ABA treatment group at week 24 more closely resembled non-lesional (NL) skin than did the placebo group at week 24. Comparing LS at week 24 to baseline NL skin, the placebo group had 38% more DEG (more transcriptionally abnormal). The ABA treated group had 48% fewer DEG (less transcriptionally abnormal). Improvement analysis showed significant normalization in curated gene sets representative of active psoriasis. Both the “PsA skin vs normal skin” gene set and the “PsA synovium vs normal synovium” gene set showed greater improvement in the ABA treated group than the placebo treated group. The improvement in many gene sets appeared to be amplified (50-90% improvement) for patients who achieved an ACR20, PASI75, and KRT16-75 responses vs those who did not regardless of treatment. Several cellular markers of epidermal growth and differentiation were reduced in both drug and PBO treated groups. This was significant in the ABA treated group for K16 and Ki67. There was a significantly greater % reduction in thickness, KRT16, Ki67, CD3 and CD11c in the ABA treated ACR20 and KRT16-75 responders group than in the ABA treatment group as a whole. In the ABA group, but not in PBO group, mRNA expression of IL22, IL17F, KRT16, CXCL1, CXCL8, IL1B, IL26, CCL18, iCOS, and CTLA4 was significantly decreased at Week 24 compared to Day 1 ($p < 0.05$). Changes in IL17A and IL23p19 mRNA in the skin were correlated with joint tenderness in all patients.

Conclusion: Abatacept modulates a wide range of inflammatory molecules in psoriasis skin lesions. At a molecular level, patients treated with ABA showed a reversion toward more transcriptionally normal gene patterns and markers of epidermal growth and differentiation. While the primary purpose of this study was to look at the effect of ABA on psoriatic inflammation, this was also an opportunity to evaluate any associations between the ACR20 components

and changes in the skin at a molecular level over time. IL17A and IL23p19 in the skin were correlated with joint tenderness. Cytokines produced in the skin might affect joints via diffusion through the blood.

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Abstract Number: 2503

Achilles Tendon Enthesitis and Disease Burden in Psoriatic Arthritis and Axial Spondyloarthritis: Baseline Results from a Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesitis is a common feature of Spondyloarthritis (SpA)[1]. Enthesitis at the Achilles tendon is an important manifestation with impact on function which is often refractory to standard NSAID/corticosteroid treatment[1,2]. ACHILLES is a double blind, placebo-controlled, multicenter Phase 3 trial designed to investigate the efficacy of secukinumab on enthesitis by clinical as well as imaging assessments in patients (pts) with active psoriatic arthritis (PsA) and axial SpA (axSpA). Here we report the impact of enthesitis on the burden of disease based on the ACHILLES pts characteristics.

Methods: Pts (≥18 years) with active PsA [CASPAR criteria and ≥1 TJC and SJC] or axSpA [ASAS axSpA criteria and total BASDAI ≥ 4], and MRI-positive heel enthesitis (according to the investigator`s judgement) refractory to standard treatment were enrolled in the trial. Enrolment was completed in October 2018. Pts were randomized to receive subcutaneous secukinumab 150 or 300 mg or placebo at baseline (BL), Weeks (Wk) 1, 2, 3, and 4, followed by once every 4 wks. Starting at Wk 24, all pts received secukinumab 150 or 300 mg. The primary endpoint of ACHILLES is the proportion of pts achieving resolution of Achilles tendon enthesitis with secukinumab vs placebo at Wk 24. BL clinical characteristics were analyzed after the last pt was randomized. Summary statistics are presented separately for PsA and axSpA indications, irrespective of treatment arm in order to preserve the blinding of the trial. In addition, the BL characteristics of PsA pts, representing 62.7% of the total ACHILLES population, were compared to PsA pts without enthesitis from the FUTURE studies.

Results: Of the 304 pts screened, 204 (128 PsA and 76 axSpA) pts completed the screening phase and were randomized. BL and disease characteristics of enrolled pts are shown in **Table 1**. PsA pts presented with a higher weight/BMI compared to axSpA pts at BL. Time since diagnosis was shorter for axSpA pts while duration of enthesitis was comparable for both indications. Physician's (PhGA) and patient's global assessment (PtGA) of disease activity scores (0-100 VAS) in the PsA pts were 57.2 and 62.3, respectively, and 66.8 and 71.8, respectively, in the axSpA pts,

Table 1: Baseline characteristics of patients in the ACHILLES trial

Variables mean (SD) unless otherwise specified	**PsA N = 128**	**axSpA N = 76**
Age (years)	49.4 (11.1)	45.1 (10.9)
Male, n (%)	54 (42.2)	37 (48.7)
BMI (kg/m^2)	30.1 (6.1)	28.1 (6.4)
Time since diagnosis (months)	63.9 (77.8)	52.9 (70.1)
Duration of Enthesitis (months)	34.0 (57.2)	34.1 (63.1)
Number of LEI counts present	2.6 (1.6)	2.4 (1.6)
Tender joint total score (78 joints)	14.9 (14.8)	-
Swollen joint total score (76 joints)	6.8 (8.1)	-
hsCRP (mg/L)	9.7 (20.3)	11.0 (13.7)
Heel pain (NRS, 0-10)	5.8 (2.3)	7.1 (1.6)
Physician's global assessment of heel enthesiopathy activity (VAS, 0-100)	60.0 (18.6)	68.1 (15.9)
Patient's global assessment of heel enthesiopathy activity (VAS, 0-100)	62.8 (23.9)	71.5 (15.6)
Physician's global assessment of disease activity (VAS, 0-100)	57.2 (20.0)	66.8 (15.8)
Patient's global assessment of disease activity (VAS, 0-100)	62.3 (21.9)	71.8 (15.5)
Patient's assessment of PsA pain intensity (VAS, 0-100)	60.8 (21.4)	-

N, number of patients randomized
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; hsCRP, high-sensitivity C-reactive protein; LEI, Leeds Enthesitis Index; NRS, numerical rating scale; VAS, visual analogue scale

Table 2: Baseline demographics and disease characteristics of ACHILLES PsA patients compared to pooled FUTURE 2 and 3 patients without enthesitis		
Variables Values are mean (SD) unless otherwise specified	**Pooled FUTURE pts without enthesitis N = 246**	**ACHILLES PsA pts N = 128**
Age (years)	48.4 (12.9)	49.4 (11.1)
BMI (kg/m^2)	28.8 (5.1)	30.1 (6.1)
Male, n (%)	142 (57.7)	54 (42.2)
Tender joint total score (78 joints)	15.2 (11.5)	14.9 (14.8)
Swollen joint total score (76 joints)	9.3 (7.5)	6.8 (8.1)
Number of LEI counts present	0	2.6 (1.6)
Physician's global assessment of disease activity (VAS, 0-100)	51.5 (17.7)	57.2 (20.0)
Patient's global assessment of disease activity (VAS, 0-100)	56.4 (20.6)	62.3 (21.9)
Patient's assessment of PsA pain intensity (VAS, 0-100)	53.1 (21.9)	60.8 (21.4)

indicating a high disease burden. Interestingly, while patient's global assessment of heel enthesiopathy activity and PtGA were comparable in both indications, the physician's global assessment for enthesitis was rated higher than the PhGA. Comparison with BL data from pooled FUTURE 2 and 3 trials show that pts without enthesitis reported lower PsA pain and PhGA/PtGA scores at BL, although with a higher SJC but comparable clinical characteristics in terms of age and weight (**Table 2**).

Conclusion: In SpA patients suffering from enthesitis, axSpA pts present with a higher burden of disease compared to PsA pts. PsA pts report higher disease burden when compared to pts without enthesitis, suggesting that enthesitis may be an important factor contributing to the burden of disease in PsA.

References:

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Disclosure: F. Behrens, Abbvie, 2, 5, 8, Biotest, 5, 8, BMS, 5, 8, Boehringer, 5, 8, Celgene, 5, 8, Chugai, 2, 5, 8, Galapagos, 5, 8, Genzyme, 5, 8, Janssen, 2, 4, 5, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 5, 8, Sanofi-Genzyme, 5, 8, UCB, 5, 8; **P. Sewerin**, AbbVie, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Celgene, 2, 5, 8, Chugai, 2, 5, 8, Hexal, 5, 8, Janssen-Cilag, 2, 5, 8, Lilly, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, Sanofi-Genzyme, 5, 8, Swedish Orphan Biovitrum, 5, 8, UCB, 2, 5, 8; **E. de Miguel**, AbbVie, 2, 5, 8, BMS, 8, BMS, MSD, UCB, Roche, 8, MSD, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 8, UCB, 8; **Y. Patel**, None; **A. Batalov**, AbbVie, Roche, MSD, Novartis, Pfizer, UCB, 5; **E. Dokoupilova**, None; **C. Kleinmond**, Novartis, 5; **E. Pournara**, Novartis, 3; **A. Shekhawat**, Novartis, 3; **C. Jentzsch**, Novartis, 3, Novartis Pharma GmbH, 3; **A. Wiedon**, Novartis, 3; **X. Baraliakos**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, BMS, 2, 5, 8, 9, Bristol-Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, 9, Chugai, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Lilly, 2, 8, 9, Merck, 2, 5, 8, MSD, 2, 5, 8, 9, Novartis, 2, 5, 8, 9, Novatis, 2, 5, 8, Pfizer, 2, 5, 8, 9, UCB, 2, 5, 8, 9, UCB Pharma, 2, 5, 8, Werfen, 2, 5, 8.

Abstract Number: 2504

Differential Expression of Human Endogenous Retroviruses in Psoriatic Disease

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Human endogenous retroviruses (HERV) are the stably inherited remnants of ancient retroviruses that infected the ancestral germline. A growing body of research has associated the differential expression and regulation of HERVs with a number of diseases, including systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). HERVs are thought to contribute to the pathogenesis of autoimmune diseases by modulating the expression of host immune-related genes, molecular mimicry, or cross reactivity of host proteins with HERV encoded products. We aimed to compare the expression of 4 HERVs previously associated with autoimmune disorders (HERV-K, HERV-K10, HERV-W, and HERV-H) in whole blood, CD3+ T cells, and CD14+ monocytes of patients with cutaneous psoriasis without arthritis (PsC), psoriatic arthritis (PsA), and healthy controls.

Methods: PsC, PsA patients satisfying the CASPAR criteria, and healthy controls were recruited for the study. RNA was extracted from whole blood collected in Tempus tubes and HERV expression was measured by quantitative real time PCR (qRT-PCR) or droplet digital (dd)PCR with normalization to *GAPDH*. HERV expression in whole blood RNA from 40 PsA patients was compared to 40 age and sex matched PsC patients and 40 age and sex matched healthy controls. Subsequently, HERV expression in 55 PsC patients who progressed to develop PsA (converters) was compared to 55 age and sex matched PsC patients who did not develop PsA over the same duration of follow-up (non-converters). Finally, HERV expression in RNA isolated from CD3+ T cells and CD14+ monocytes from 19 PsA patients was compared to 13 PsC and 8 healthy controls. Expression differences between groups were determined by one-way ANOVA, Kruskal-Wallis and Mann-Whitney tests where appropriate.

Results: In whole blood, HERV-K was significantly differentially expressed between 40 PsA and 40 PsC patients (fold change [FC]=1.57, p=0.008). HERV-K was also significantly differentially expressed in baseline samples from 55 converters compared to 55 non-converters (FC=1.93, p=0.03). No other HERV genes were differentially expressed between these groups in whole blood. Significant expression differences were more evident in purified cells (Table 1).

Conclusion: In whole blood, expression of HERV-K differentiates PsA and PsC patients, and its expression is significantly elevated in PsC patients prior to the development of PsA. HERV expression differences between the groups are also evident in purified T cells and monocytes. These data suggest a role for HERVs in the pathogenesis of psoriatic disease and their potential use as prognostic markers of arthritis in patients with psoriasis.

Table 1. Differential expression of HERVs in purified T cells and monocytes.

	PsA vs. PsC		PsA vs. Controls		PsC vs. Controls	
	CD3+ T cells FC, p value	CD14+ Monocytes FC, p value	CD3+ T cells FC, p value	CD14+ Monocytes FC, p value	CD3+ T cells FC, p value	CD14+ Monocytes FC, p value
HERV-K	0.43, p=0.02	0.30, p<0.01	ns	0.17, p<0.01	2.18, p=0.02	ns
HERV-K10	2.94, p=0.02	ns	6.87, p<0.01	2.60, p=0.04	ns	ns
HERV-H	ns	ns	3.19, p<0.01	0.36, p=0.02	2.67, p=0.01	0.27, p<0.01
HERV-W	1.27, p=0.04	ns	4.12, p<0.01	ns	3.24, p=0.01	0.47, p=0.04

Ns, not significant.

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Abstract Number: 2505

Can Biologics "Prevent" the Development of Psoriatic Arthritis in Psoriasis Patients? Data from a Large University Hospital Cohort in Argentina

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Background/Purpose: As psoriasis (Pso) commonly precedes psoriatic arthritis (PsA), an important unanswered question is whether treatment of Pso might influence the development of PsA in patients with psoriasis.

The objective of this study was to analyze the incidence of PsA in a large cohort of patients with PsO according to different treatments, with the hypothesis that treatment with biologics might prevent the development of PsA.

Methods: Patients with PsO without PsA followed at a University Hospital were included in this retrospective cohort study. Data was obtained from the Hospital Electronic Medical Record (EMR). Patients were classified according to their treatment in topics group (topic and phototherapy), conventional DMARDs (cDMARDs) group (Methotrexate (MTX) and cyclosporine (Cyc)), and biologic DMARDs group (bDMARDs) (TNFi, IL17i, and IL12-23i). Patients contributed time since beginning of the corresponding treatment until diagnosis of PsA, lost of follow up, end of treatment or end of study. Incident cases of PsA were attributed to one treatment if developed during the administration of that treatment and up to 6 months after its discontinuation if no other treatment was started. Incident cases that developed more than one year after discontinuation of treatment were disregarded (3 cases). Incidence rate was calculated for the whole population and for each one of the treatment groups and compared with chi2test, and rate ratios were calculated as well. A multivariable logistic model for the development of PsA was analyzed by treatment groups, adjusting by other variables.

Results: 797 patients, contributed a total of 10017 patient/years. Patient's characteristics are shown in table 1. 599 (75%) patients were treated only with topics or phototherapy, 106 (13%) with cDMARDs (81% MTX and 19% Cyc) and 92 (11.5%) with biologics (TNFi: 64: etanercept: 44, adalimumab:23, infliximab:6 ; IL17i: 43: 14 Ixekizumab, 29 Secukinumab; IL12-23i: (Ustekinumab) 16; some patients received more than one biologic). During follow-up 72 patients developed PsA (68 under topics; 3 under cDMARDs (2 MTX and 1 Cyc) and 1 under biologics (1 Secukinumab): Global incidence rate: 7.2 per 1000 patient/years (table 1). Although numerically the incidence of PsA in PsO patients treated with biologics was lower, the difference was not statistically significant. In Cox regression analysis, after adjusting by sex, age, and BMI, treatment with biologics was significantly associated with a reduced risk of developing PsA: Hazard ratio (95% CI): 0.1 (0.013 – 0.7); p= 0.021.

	Topics, n= 599	cDMARDs, n=106	bDMARDs, n=92	Total group, n=797
Mean age at PsO diagnosis (SD)	43.6 (20.6)	46.2 (20.7)	35.1 (18.9)	42.9 (20.6)
Female, n (%)	314 (52)	53 (50)	36 (39)	403 (50.5)
Plaque PsO, n/N (%)	514/578 (89)	93/103 (90)	85/90 (94)	692/771 (90)
BMI, n; Mean (SD)	498; 27.6 (5.4)	80; 28.5 (5.6)	91; 30 (7)	659; 28 (5.7)
N Developed PsA (%)	68 (8.5)	3 (0.38)	1 (0.13)	72 (9)
Follow up (patient/years)	9153	316	548	10017
Incidence rate/1000 Patient/ years (95% CI)	7.4 (5.8-9.4)	9.5 (1.9-27.5)	1.81 (0.04-10)	7.2 (5.6-9)
Median years between PsO and PsA (IQR)	10 (2-21)	Patient 1: 23 Patient 2: 11.7 Patient 3: 24.7	Patient (1): 9.6	10.5 (2-20.8)

Conclusion: Treatment with biologics in patients with PsO seemed to reduce the risk of PsA and preventing its development in this retrospective single center cohort.

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Abstract Number: 2506

The 'Severity of Nail Psoriasis Score' (SNAPS) Is Feasible, Reliable and Demonstrates Construct Validity Against the mNAPSI in an Observational Cohort of Patients with Psoriatic Arthritis

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Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Background: Longitudinal assessment of psoriatic nail dystrophy and its response to treatment is limited outside of research settings due to the complexity of existing scoring tools. The 'Severity of Nail Psoriasis Score' (SNAPS; previously known as the Bath Nail Score) is a simple tool developed for use in the observational setting. It assesses for the presence of 4 features of fingernail psoriasis (pitting, onycholysis, hyperkeratosis, and severe nail deformity; score 0-40). We aimed to validate this tool in an observational cohort of patients with Psoriatic Arthritis (PsA).

Methods: Consenting consecutive patients enrolled in the Bath PsA longitudinal cohort underwent photography of their fingernails. Clinical assessments included 66/68 tender and swollen joint count, Psoriasis Area and Severity Index, Leeds Enthesitis Index, Leeds Dactylitis Index, and Physician Nail Visual Acuity Scale (PhNVAS). Participants completed the Health Assessment Questionnaire-Disability Index and a Patient Nail VAS (PtNVAS). Dorsal view photographs of each fingernail were acquired using a tripod-mounted DSLR camera with macro lens. An angled mirror was positioned distally to capture the presence of hyperkeratosis. Scoring was conducted by two assessors (WT and AA) using the modified Nail Psoriasis Severity Index (mNAPSI; range 0-130) and SNAPS tools (Table 1). Timed scoring was conducted in a third of patients to assess the feasibility of both tools. Five patients were scored by both assessors at two time points to assess for inter-rater and test-retest reliability using interclass correlation coefficients (ICCs) for absolute agreement of single measures. The correlation between outcome variables was assessed using Pearson's correlation (r) and Spearman's rho where appropriate.

Results: Nineteen consecutive patients with and 2 consecutive patients without nail involvement were included. Mean (SD) age was 55 (11.2) years and 42.9% were female. Mean (SD) mNAPSI and SNAPS scores were 24 (17.2) and 14 (8.8). Median (IQR) PhNVAS and PtNVAS were 20 (13.0-37.0) and 18 (9.5-29.3). A total of 210 nails were assessed. Nail disease was present in 90.5% of patients using either score, and in 79% of nails using SNAPS and 82.4% of nails using mNAPSI. The main nail feature contributing to this discrepancy was splinters. Mean time to score the nails per patient using the SNAPS and mNAPSI was 59 (13.0) and 136 (27.8) seconds respectively. The inter-rater and test-retest reliability of the SNAPS was 0.92-0.94 ($p< 0.001$) and 0.93-0.96 ($p< 0.005$). The inter-rater and test-retest reliability of the mNAPSI was 0.71-0.78 ($p< 0.03$) and 0.95-0.97 ($p=0.002$). There was a strong correlation between the SNAPS and mNAPSI ($r=0.95$, $p< 0.001$) (Figure 1), and a moderate correlation between the SNAPS and PhNVAS ($r=0.77$, $p< 0.001$) and PtNVAS ($r=0.63$, $p=0.002$), and the mNAPSI and PhNVAS ($r=0.84$, $p< 0.001$) and PtNVAS ($r=0.64$, $p=0.002$). The SNAPS scores did not demonstrate significant floor or ceiling effects (Figure 2).

Nail Scores *	Pitting	Onycholysis and Oil Drop Dyschromia	Crumbling	Severe nail deformity ᵃ	Leukonychia	Splinter Haemorrhages	Hyperkeratosis	Lunula Red spots
mNAPSI (0-13)	0-3	0-3	0-3		0-1	0-1	0-1	0-1
SNAPS (0-4)	0-1	0-1		0-1			0-1	

*Per nail

ᵃ Psoriatic nail dystrophy affecting both sides of the nail, i.e. across the longitudinal midline

Table 1. Nail Psoriasis Scoring Systems

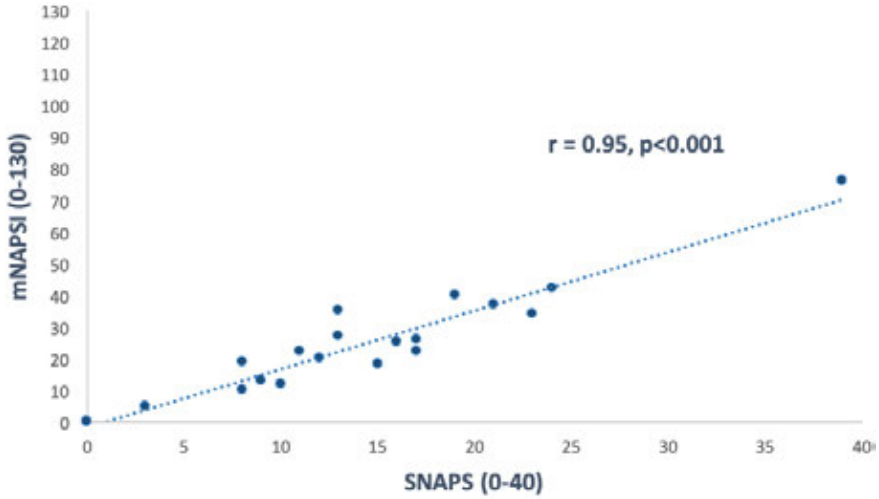

Figure 1. Correlation between the mNAPSI and SNAPS

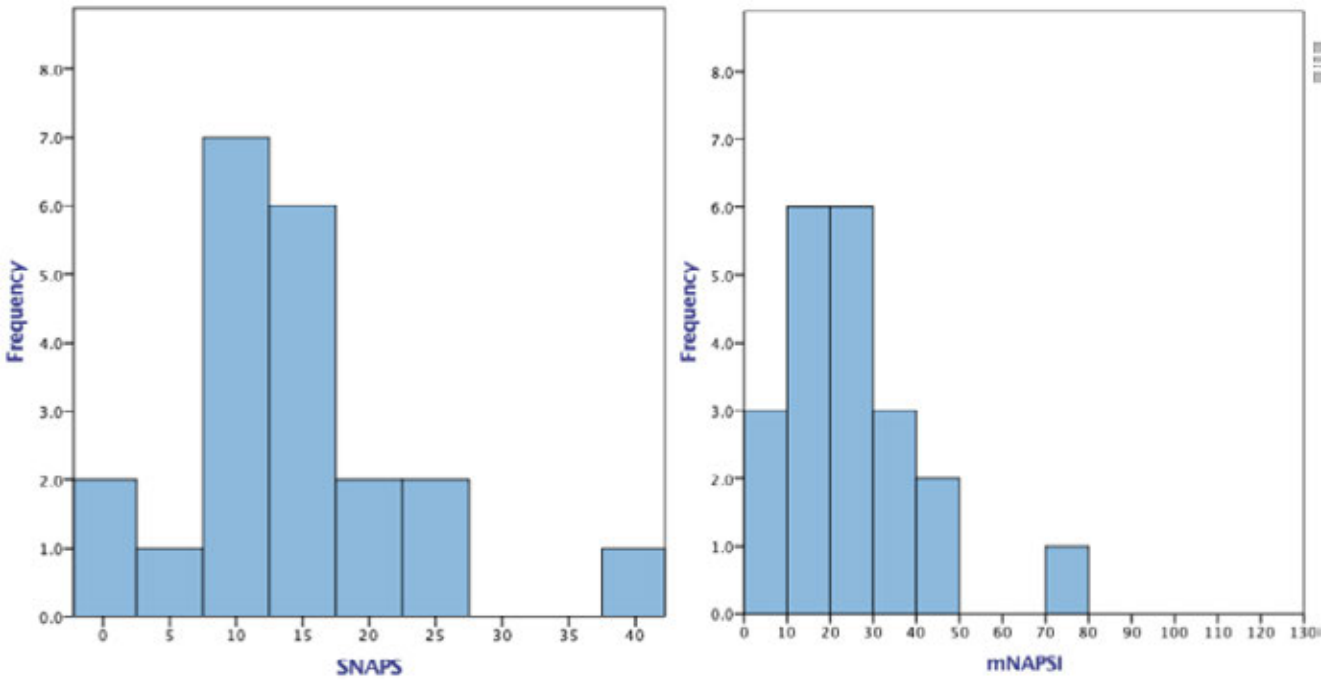

Figure 2. Histograms of Nail Scores

Conclusion: SNAPS is feasible, reliable and demonstrates construct validity against mNAPSI for assessing psoriatic nail dystrophy. Follow-up data is needed to assess longitudinal validity.

Disclosure: A. Antony, None; **D. Hart**, None; **C. Cavill**, AbbVie, 2, Celgene Ltd, 2, Novartis, 2, 8; **E. Korendowych**, None; **N. McHugh**, None; **C. Lovell**, None; **W. Tillett**, None.

Abstract Number: 2507

The Impact of Psoriasis Severity on Outcomes Among Psoriatic Arthritis Patients Receiving Adalimumab

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous, chronic, immune mediated disease associated with psoriasis (PsO), with varying skin severity which can range from mild to severe involvement. It is not well understood how skin severity can impact treatment outcomes.

Here we evaluate the impact of PsO severity on clinical, functional, and structural outcomes among PsA pts treated with adalimumab (ADA) or placebo (PBO).

Methods: Pts with baseline PASI and BSA available from ADEPT, a phase 3, randomized, double-blind, PBO-controlled trial of ADA 40 mg every other week, were included in this post hoc analysis.2 Pts were sub-grouped based on baseline PsO severity (severe PsO: PASI ≥12 OR BSA ≥10%; mild-to-moderate PsO: PASI < 12 AND BSA < 10%), relative to overall study population. Clinical outcomes at wk 24 were assessed by attainment of minimal disease activity (MDA), remission and low disease activity (LDA) by disease activity index for psoriatic arthritis (DAPSA), and PASI50/75/90; function and structural progression were assessed by the % of pts experiencing HAQ-DI normative values (≤0.25) and improvement from baseline ≥0.22 (MCID), and the % of pts having change from baseline in mTSS ≤0 and ≤0.5 in the modified total Sharp score (mTSS) respectively. A logistic model with treatment group baseline PASI/BSA and PASI/BSA by treatment interaction was fit for each outcome variable. P-values for interaction term and baseline BSA/PASI were calculated. Non-responder imputation was used for missing clinical and functional endpoints. 75th percentiles were imputed for missing radiographic data. Treatment-emergent adverse events (TEAEs) were monitored throughout.

Results: Of the 163 pts enrolled in the study with baseline PASI and BSA, only 23% (n=37;ADA: 17; PBO: 20) were classified as having severe PsO and had similar characteristics to those with mild-to-moderate PsO, except for numerically higher physician's global assessment, dactylitis, and enthesitis scores. Following 24 wks of treatment, 41% of ADA-treated pts achieved MDA and 45% achieved DAPSA LDA or better, a finding consistent irrespective of baseline PsO severity (**Table**). 72% of ADA-treated pts with baseline PsO did not exhibit any structural progression by mTSS (≤0) through 24 wks as compared to 55% receiving PBO. Logistic regression analyses confirmed limited role that PsO severity played across examined outcomes. DAPSA remission was more likely at wk 24 among pts with higher baseline PASI scores, and this effect was less apparent with ADA treatment. TEAEs appeared comparable between ADA and PBO groups; fewer infectious AEs occurred in the ADA severe PsO group vs the mild-to-moderate PsO group.

Table. Clinical, Functional, and Structural Outcomes Through 24 Weeks Among Adalimumab- and Placebo-treated Patients Having Severe[a] or Mild-to-Moderate[b] Psoriasis at Baseline Relative to the Overall Study Population.

	ADA 40 mg eow				PBO eow			
n (%)	Severe Ps (N=17)	Mild-to-Moderate Ps (N=66)	Mild-to-Severe Ps (N=83)	Total study population (N=151)	Severe Ps (N=20)	Mild-to-Moderate Ps (N=60)	Mild-to-Severe Ps (N=80)	Total study population (N=162)
MDA	5 (29)	29 (44)	34 (41)	53 (35)	3 (15)	6 (10)	9 (11)	11 (7)
VLDA	3 (18)	10 (15)	13 (16)	13 (9)	0	1 (2)	1 (1)	1 (1)
DAPSA ≤4	4 (24)	19 (29)	23 (28)	33 (22)	1 (5)	1 (2)	2 (3)	4 (2)
DAPSA >4, ≤14	4 (24)	10 (15)	14 (17)	33 (22)	3 (15)	5 (8)	8 (10)	14 (9)
HAQ-DI ≤0.25	6 (35)	29 (44)	35 (42)	70 (46)	4 (20)	12 (20)	16 (20)	33 (20)
ΔHAQ-DI ≥0.22	12 (75)	43 (80)	55 (79)	99 (79)	5 (31)	16 (38)	21 (36)	52 (42)
PASI50[d]	14 (82)	42 (64)	56 (68)	N/A	3 (15)	8 (13)	11 (14)	N/A
PASI75[d]	8 (47)	35 (53)	43 (52)	N/A	1 (5)	3 (5)	4 (5)	N/A
PASI90[d]	7 (41)	24 (36)	31 (37)	N/A	1 (5)	2 (3)	3 (4)	N/A

All analyses are non-responder imputation, unless otherwise noted.
[a]Severe psoriasis defined as psoriasis activity and severity index (PASI) ≥12 OR body surface area (BSA) ≥10%; [b]mild-to-moderate psoriasis defined as PASI <12 AND BSA <10%; [c]imputation using ranks of total Sharp score and 75th percentile; [d]PASI responses were only collected for patients with mild-to-severe psoriasis at baseline; ADA: adalimumab; eow: every other week; PBO: placebo; Ps:psoriasis; MDA:minimal disease activity; DAPSA:disease activity index for psoriatic arthritis; HAQ-DI: health assessment questionnaire disability index; ΔHAQ-DI:change from baseline in HAQ-DI; ΔmTSS:change from baseline in modified total Sharp score.

Conclusion: Prevalence of severe PsO in this population of PsA pts was consistent with previous observations.[3] Treatment with ADA was associated with better PsA outcomes as compared to PBO irrespective of the degree of PsO severity at baseline.

References: 1. Singh, et al. Arthritis Rheumatol, 2018;71:2-29. 2. Mease, et al. Arthritis Rheumatol, 2005;52:3279-89. 3. Alinaghi, et.al. J. Am. Acad. Der, 2019;80(1):251-265.e219.

Disclosure: J. Merola, AbbVie, 2, 5, 8, Aclaris, 2, 5, Almirall, 2, 5, Amgen, 5, Biogen, 2, 5, Biogen Idec, 2, 5, Biogen IDEC, 5, Brigham and Women's Hospital, Harvard, 3, Burrage Capital Management Boston Advisory Board, 6, Celgene, 2, 5, Dermavant, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 5, GlaxoSmithKline, 5, GSK, 2, 5, Incyte, 2, 5, Janssen, 2, 5, Leo Pharma, 2, 5, Lilly, 5, Merck, 5, Merck Research Laboratories, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Regeneron, 5, Samumed, 2, 5, Sanofi, 5, Sanofi Regeneron, 2, 5, Science 37, 5, Sun Pharma, 2, 5, UCB, 2, 5; **L. Coates**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, AbbVie, Amgen, BMS, Celgene Corporation, Eli Lilly, Galapagos, Janssen, MSD, Novartis, Pfizer, Prothena, Sun Pharma, UCB, 5, Abbvie, Amgen, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB, 5, Abbvie, Amgen, Lilly, Novartis, Pfizer, UCB, 8, AbbVie, Celgene Corporation, Eli Lilly, Janssen, Novartis, UCB, 8, AbbVie, Celgene Corporation, Eli Lilly, Novartis, Pfizer, 2, AbbVie, Celgene Corporation, Novartis, Pfizer, 2, Abbvie, Celgene, Novartis, Pfizer, Lilly, 2, Amgen, 5, 8, Biogen, 8, Bristol-Myers Squibb, 5, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, Gilead, 5, Janssen, 2, 5, 8, Janssen Research & Development, LLC, Lilly, 2, 5, 8, MSD, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 8, Prothena, 5, Sun Pharma, 5, UCB, 5, 8, UCB Pharma, 5; **E. Lesser**, AbbVie, 1, 3, 4; **W. Valdecantos**, AbbVie, 3, 4; **Y. Song**, AbbVie, 3, 4, Abbvie, 1, 4; **P. Mease**, Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, Roche, UCB, 2, 5, Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB, 8, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Abbvie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer and UCB., 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB, 2,

Abbvie, Amgen, Brsitol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Brsitol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Brsitol Myers Squibb,Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, Amgen, 2, 5, 6, 8, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, and UCB, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 2, 5, Boerhinger Ingelheim, 5, Bristol Myers Squibb, 2, 5, 8, Bristol Myers Squibb Co., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8, Genentech, 2, 5, 6, 8, Gilead, 2, 5, 8, Janssen, 2, 5, 6, 8, Janssen Inc, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 6, 8, Merck, 2, 5, 8, Novartis, 2, 5, 6, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 6, Sun, 2, 5, SUN, 2, 5, Sun Pharma, 2, 5, Sun Pharmaceutical Industries, 2, 5, Sun Pharmaceutical Industries, Inc., 2, 5, 8, UCB, 2, 5, 6, 8, UCB Pharma, 2, 5, 8.

Abstract Number: 2508

Large Joint and Lower Extremity Involvement Has Higher Impact on Disease Outcomes in Oligoarticular PsA

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Joints with different sizes (e.g. small and large joints) and anatomical locations (upper and lower extremities) can be affected in psoriatic arthritis (PsA). Our aim was to explore the effect of these different joint patterns on patient reported outcomes (PROs) in a patient population presenting with mono-oligoarthritis.

Methods: PsArt-ID (Psoriatic Arthritis- International Database) is a multicentre registry aiming to understand the disease characteristics of PsA in real life. From that registry, 387/1670 patients who had oligo-monoarthritis in cross sectional assessment were included. Mono-oligoarthritis was defined as having 1-4 joints that were tender and swollen in the same assessment. The joints were categorized according to their size (small and large) and location (upper and lower extremity). Patients who had combination of these joints were excluded. PROs (health assessment

Table 1. Disease outcomes and C-reactive protein levels based on the joint size

	1-2 Joints		p	3-4 Joints		p
	Small joints*	Large joints**		Small joints*	Large joints**	
HAQ (0-3), mean (SD)	0.72 (0.66)	0.70 (0.65)	0.749	0.95 (0.72)	1.1 (1.01)	0.986
Pain (0-100), mean (SD)	41.71 (22.54)	46.17 (26.37)	0.307	51.14 (24.16)	72.50 (16.87)	**0.007**
Patient Global Assessment (0-100), mean (SD)	34.84 (25.81)	35.77 (29.58)	0.901	38.93 (27.71)	60.00 (25.29)	**0.016**
Physician Global Assessment (0-100), mean (SD)	27.32 (20.62)	26.90 (24.05)	0.504	34.88 (24.79)	56.36 (25.30)	**0.010**
Fatigue (0-100)	36.26 (26.23)	36.46 (29.82)	0.895	40.64 (29.24)	60.91 (25.86)	**0.038**
Morning stiffness, (min), mean (SD)	30.08 (29.56)	35.83 (42.41)	0.937	52.43 (64.73)	72.73 (50.76)	0.068
CRP (mg/dl), mean (SD)	7.52 (12.11)	15.31 (25.56)	**0.005**	14.03 (18.23)	28.24 (38.05)	0.080

*" Small joints" are used to refer the distal interphalangeal joints, proximal interphalangeal joints, metacarpophalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists.

**" Large joints" are used to define shoulders, elbows, hips, knees, and ankles.

HAQ= Health Assessment Questionnaire, CRP = C-reactive protein, SD= Standard deviation

questionnaire, pain score, patient global assessment (PGA), fatigue, morning stiffness), physician global assessment, C-reactive protein (CRP) were compared based on the joint patterns**.** Analysis was made by categorizing according to joint counts (1-2 joints and 3-4 joints).

Results: The mean age (SD) was 46.9 (14.24) with a mean (SD) PsA duration of 3.93 (6.03) years. For joint counts, 194 (50.1%) patients had 1, 108 (27.9%) had 2, 46 (11,9 %) had 3 and 39 (10.1%) patients had 4 joints involved. Within patients with 1-2 involved joints, size of the joints only had an impact on CRP values with large joints having higher CRP (p=0.005) (Table 1), similar to joints of the lower extremity (p= 0.004) (Table 2). None of the PROs were significant based on the size or the location, if 1-2 joints were inflamed. Within patients with 3-4 involved joints, PGA, pain, fatigue and physician global assessment were higher in patients with large joint involvement. Similarly, PGA, pain and physician global assessment was higher in patients with lower extremity involvement as well as higher CRP values.

Table 2. Disease outcomes and C-reactive protein levels based on the joint location

	1-2 Joints		p	3-4 Joints		p
	Upper extremity	Lower extremity		Upper extremity	Lower extremity	
HAQ (0-3), mean (SD)	0.77 (0.67)	0.66 (0.64)	0.131	0.97 (0.72)	0.95 (0.88)	0.649
Pain (0-100), mean (SD)	43.60 (23.63)	44.16 (25.52)	0.995	49.92 (24.87)	67.35 (18.03)	**0.009**
Patient Global Assessment (0-100), mean (SD)	35.86 (26.32)	34.79 (29.11)	0.638	38.20 (28.34)	54.44 (24.30)	**0.019**
Physician Global Assessment (0-100), mean (SD)	27.90 (20.40)	26.35 (24.16)	0.218	34.40 (24.99)	49.72 (25.63)	**0.025**
Fatigue (0-100)	37.31 (26.26)	35.47 (29.73)	0.444	40.25 (29.54)	54.44 (27.27)	0.076
Morning stiffness, (min), mean (SD)	30.32 (30.59)	35.47 (41.49)	0.849	52.87 (67.42)	63.33 (46.11)	0.094
CRP (mg/dl), mean (SD)	7.34 (12.01)	15.28 (25.33	**0.004**	13.33 (18.59)	25.34 (30.50)	**0.012**

HAQ= Health Assessment Questionnaire, CRP = C-reactive protein, SD= Standard deviation

Conclusion: For PsA patients with 3-4 joints involved, lower extremity and larger joints are associated with poorer outcomes with worse PROs, physician global assessment and higher CRP. The size and anatomical location of the joints are less important for patients with 1-2 joints in terms of the outcomes.

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Abstract Number: 2509

Psoriasis Impact on Patient-Reported Outcomes in Psoriatic Arthritis in a Real-World Setting: Results from the APOPSIS Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic progressive inflammatory arthropathy associated with psoriasis (PsO). PsA places a considerable burden, adversely affecting health-related quality of life (HRQoL).

So far, all studies evaluating effectiveness and outcomes of PsA management have focused on arthritis while the impact on the skin component has served as a secondary endpoint. Hence, there is a knowledge gap on how both components interact with each other and impact patient-perceived dermatology-specific HRQoL.

This study evaluates the patient-perceived burden of skin disease in a PsA cohort.

Methods: This was a multicenter, single-country, cross-sectional observational study primarily aiming to evaluate the importance of skin disease to Greek PsA patients adjusting for arthritis activity, in a routine clinical practice setting. Patients were classified into three groups according to their arthritis activity, which was defined using the DAS28 cut-off points: DAS28-CRP≤ 3.2 (low); DAS28-CRP >3.2 to ≤5.1 (moderate); and DAS28-CRP >5.1 (high). Within each arthritis group, patients were further sub-divided based on PsO severity, defined by the Body Surface Area (BSA) affected by PsO using a cutoff of 3% (Figure 1). PsO-dependent HRQoL was measured with the Dermatology Life Quality Index (DLQI). The primary endpoint was the mean difference in DLQI score between patients with BSA< 3% (mild PsO) versus patients with BSA ≥ 3% (moderate-to-severe PsO) within each of the defined PsA activity groups. A two-way factorial Analysis of Variance (ANOVA) was used to evaluate the difference of DLQI measurements between PsO severity levels in each PsA activity group.

Results: Overall, 222 patients with purely peripheral or predominantly peripheral joint involvement were enrolled. All patients were Caucasian with a mean (SD) age of 53.7 (13.4) years. The median BSA was 3.0% (IQR: 1.0-5.0), and the median DAS28-CRP score was 3.7 (IQR: 3.1-5.2). Psoriatic plaques affected high impact sites, i.e. hands, feet, face, neck, scalp, genitals/groin, and intertriginous areas in 74.3% (165/222) of patients (Table1). With regard to the primary endpoint, results showed that the interaction between PsO severity and PsA activity overall was not statistically significant (p=0.672). However, a statistically significant main effect of PsO severity on DLQI was identified (p< 0.001) showing that the mean DLQI difference between PsO levels is the same in each of the PsA activity groups. The

Figure 1. Patient groups in APOPSIS study

	BSA < 3%	BSA ≥3%
DAS28-CRP > 5.1	PsA: high activity PsO: mild	PsA: high activity PsO: moderate to severe
<3.2 DAS28-CRP ≤ 5,1	PsA: moderate activity PsO: mild	PsA: moderate activity PsO: moderate to severe
DAS28-CRP≤3,2	PsA: low activity PsO: mild	PsA: low activity PsO: moderate to severe

TABLE 1. Patients' demographics & disease characteristics

		DAS28-CRP≤3.2		<3.2 DAS28-CRP ≤ 5,1		DAS28-CRP>5.1	
	Overall (N=222)	BSA< 3% (N=37)	BSA≥3% (N=37)	BSA< 3% (N=37)	BSA≥3% (N=37)	BSA< 3% (N=37)	BSA≥3% (N=37)
Female	119 (53.6%)	13 (35.1%)	25 (67.6%)	20 (54.1%)	14 (37.8%)	25 (67.6%)	22 (59.5%)
Age (yrs), mean(SD)	53.7(13.4)	54.4(12.2)	47.9(12.1)	52.8(13.5)	49.8(13.7)	60.4(11.3)	56.814.2()
Weight(kg), mean(SD)	82.7(17.7)	84.2(17.3)	75.7(15.7)	81.7(19.4)	92.6(20.0)	79.6(15.6)	82.7(13.9)
BMI (kg/m²), mean(SD)	29.0(5.1)	29.2(5.1)	26.9(3.7)	28.5(5.2)	30.7(6.3)	28.5(4.7)	29.9(4.8)
Obese (BMI≥30 kg/m²)	79(35.6%)	12(32.4%)	8(21.6%)	12(32.4%)	17(45.9%)	13(35.1%)	17(45.9%)
Current smokers	72(32.4%)	9(24.3%)	17(45.9%)	17(45.9%)	9(24.3%)	10(27.0%)	10(27.0%)
Duration of disease(yrs), Psoriasis Psoriatic arthritis	15.1(7.3-23.1) 6.3(2.1-11.6)	18.0(8.1-24.5) 8.0(3.1-11.7)	16.2 (6.2-23.1) 4.7(2.1-11.2)	10.1(6.0-22.0) 3.3(1.7-10.1)	13.9(7.1-20.1) 4.9(1.9-9.5)	13.2(7.1-28.0) 8.2(2.4-11.6)	17.8(10.1-22.9) 9.35(3.1-16.7)
BSA (%)	3.0(1.0-5.0)	1.0(1.0-2.0)	5.0(4.0-8.0)	2.0(1.0-2.0)	5.0(4.0-8.0)	2.0(1.0-2.0)	7.0(4.0-10.0)
Psoriatic plaques affecting crucial and/or visible body areas*	165 (74.3%)	19(51.4%)	28(75.7%)	25 (67.6%)	32 (86.5%)	27 (73.0%)	34 (91.9%)
CRP (mg/L)	3.2(1.1-6.9)	1.4(0.9-3.2)	3.0(1.0-5.0)	3.0(1.0-4.0)	3.0(1.3-7.3)	6.8(3.5-11.8)	6.4(3.5-13.0)
Joint counts (28) Swollen Tender	4.0(1.0-8.0) 6.0(3.0-11.0)	2.0(1.0-3.0) 2.0(2.0-4.0)	1.0(0.0-2.0) 2.0(1.0-3.0)	4.0(1.0-5.0) 5.0(3.0-6.0)	4.0(1.0-7.0) 6.0(3.0-8.0)	10.0(7.0-14.0) 12.0(10.0-15.0)	8.0(6.0-10.0) 12.0(9.0-16.0
Joint counts (66/68) Swollen Tender	N=172 6.0(2.0-10.0) 7.0(4.0-14.0)	N=29 2.0(1.0-4.0) 4.0(2.0-5.0)	N=23 1.0(1.0-2.0) 3.0(2.0-6.0)	N=29 5.0(4.0-8.0) 6.0(6.0-8.0)	N=33 6.0(3.0-9.0) 6.0(5.0-10.0)	N=30 13.5(9.0-18.0) 14.5(12.0-20.0)	N=28 10.5(7.5-15.5) 15.5(12.0-19.0)
DAS28-CRP	3.7(3.1-5.2)	2.9(2.8-3.0)	2.9(2.7-3.1)	3.6(3.4-3.9)	4.0(3.6-4.5)	5.3(5.2-5.5)	5.4(5.2-5.6)
Clinical pattern of PsA at enrollment Pure peripheral Predominant peripheral with coexistent axial disease	132(59.5%) 90(40.5%)	23(62.2%) 14(37.8%)	23(62.2%) 14(37.8%)	18 (48.6%) 19(51.4%)	23(62.2%) 14(37.8%)	25(67.6%) 12(32.4%)	20(54.1%) 17(45.9%)
Dactilitis at enrollment present	36(16.2%)	1(2.7%)	1(2.7%)	8(21.6%)	6(16.2%)	11(29.7%)	9(24.3%)
Enthesitis at enrollment present	79(35.6%)	7(18.9%)	7(18.9%)	15 (40.5%)	12 (32.4%)	20 (54.1%)	18 (48.6%)
Nail psoriasis at enrollment present	99 (44.6%)	13 (35.1%)	14 (37.8%)	15 (40.5%)	21 (56.8%)	14 (37.8%)	22 (59.5%)
Number of nails affected	N=97 6.0 (3.0-9.0)	N=13 3.0 (2.0-6.0)	N=14 4.5 (3.0-10.0)	N=15 4.0(4.0-6.0)	N=20 6.0(3.0-11.5)	N=14 7.0(4.0-10.0)	N=21 6.0(4.0-10.0)
Extraarticular manifestations present	97(43.7%)	10 (27.0%)	7(18.9%)	17(45.9%)	18 (48.6%)	28 (75.7%)	17(45.9%)

two-way factorial ANOVA mean difference in DLQI total scores between patients with 'moderate-to-severe' and patients with 'mild' PsO was estimated to be 4.7 (95% CI: 3.1-6.3; p< 0.001) across all three PsA activity levels (Table2). Moreover, patients with PsO plaques at high impact sites reported DLQI scores 2.4 points (95% CI: 0.4-4.3; p=0.019) higher than those for patients without plaques at such sites.

Table 2. Estimated total DLQI scores at enrollment per PsO severity level within each PsA activity level of the two-way factorial ANOVA with the main effect of PsO severity levels adjusted for PsA activity levels

Patient-rated total DLQI score estimates of patient-rated total DLQI score at enrollment per PsO severity level within each PsA activity level of the two-way factorial ANOVA with the main effect of PsO severity levels adjusted for PsA activity levels; Number of observations used: N=222

	DLQI score			
			95% CI	
PsO severity level &PsA activity level	Sample means	Estimates	Lower limit	Upper limit
BSA<3% & DAS28-CRP≤3.2	2.3	2.0	0.4	3.6
BSA≥3% & DAS28-CRP≤3.2	6.5	6.7	5.1	8.3
BSA<3% & 3.2<DAS28-CRP≤5.1	4.8	5.3	3.7	6.9
BSA≥3% & 3.2<DAS28-CRP≤5.1	10.5	9.9	8.3	11.5
BSA<3% &DAS28-CRP>5.1	5.5	5.3	3.7	6.9
BSA≥3% & DAS28-CRP>5.1	9.7	9.9	8.3	11.5

Conclusion: This study provides novel real-world evidence demonstrating that PsO severity negatively impacts the dermatology-specific HRQoL independent of the PsA disease activity. In addition, PsO localization at high impact sites (excluding nails) adversely affects dermatology-specific HRQoL.

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Abstract Number: 2510

Validation of the Modified Stokes Ankylosing Spondylitis Spinal Score (mSASSS) as a Tool to Assess Axial PsA

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial joint involvement commonly links psoriatic arthritis (PsA) to spondyloarthritis with widely variable prevalence (25-70%). Patients with axial PsA (AxPsA) are older than patients with ankylosing spondylitis (AS) and identifying radiographic changes related to the spondylitis may be more challenging leading to disagreement among readers. Currently, there is no universally accepted method to score AxPsA. In AS, the mSASSS system is the most widely used tool to assess the severity of spondylitis and define progression. Based on previous studies in AxPsA, the mSASSS had the highest sensitivity, specificity, and odd ratios of determining disease progression. We

aimed to assess the reliability of the mSASSS scoring system between two rheumatologists and various confounders using the PsA Scoring Module for Axial Radiograph Toronto (SMART) tool developed by Biagioni et al.

Methods: A retrospective study was conducted in which radiographs from 2015-2018 in our Psoriatic Arthritis Clinic database were retrieved by an assessor (DIP) via convenience sampling and scored with the SMART tool by two rheumatologists (SET, AW). According to the SMART tool, patients are scored for the presence of osteophytes, degenerative disc disease, osteopenia, and diffuse proliferative skeletal hyperostosis (DISH). We then removed patients who had DISH recorded in our database. Discordant radiographs were adjudicated by a third independent reader (DDG, N = 11). The intra-rater reliability was reported in Intraclass Correlation Coefficient (ICC) with the balanced one-fold random model in all patients as scored by two readers (N = 119), and after adjudication and removing the DISH patients (N = 109).

Results: Patients (N = 119) with well-established PsA with and without axial disease were included. The mean age was 58.19 ± 14.15 years, the mean age at PsA diagnosis was 36.74 ± 12.59 years. 17 patients had inflammatory back pain and 34 had mechanical back pain. The intra-rater ICC between readers of the total mSASSS, cervical mSASSS, and lumbar mSASSS were 0.25, 0.23, and 0.20 respectively. With DISH exclusion, the ICC were 0.89, 0.93, and 0.40 respectively.

Conclusion: Initial results demonstrated poor agreement between readers in the presence of DISH and other confounders. With removal of radiographs with DISH and adjudication of discordant readings, the total mSASSS demonstrated moderate intra-reader reliability. Therefore, the presence of DISH leads to misinterpretation of mSASSS scores and should be considered when reading radiographs in AxPsA.

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Abstract Number: 2511

What Influences Patients' Opinion of Remission and Low Disease Activity in Psoriatic Arthritis? Principal Component Analysis of an International Study

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Variable	REMISSION			LDA		
	Exp (B)	Lower 95% CI	Upper 95% CI	Exp (B)	Lower 95% CI	Upper 95% CI
Groll comorbidity Index	1.216	0.958	1.543	1.286	1.032	1.603
Psoriasis body surface area (BSA)	0.541	0.335	0.875			
Patient pain score	0.776	0.636	0.948	0.780	0.655	0.929
PsAID total score	0.731	0.571	0.935	0.746	0.610	0.911
Physician global of arthritis				0.821	0.717	0.939
Physician score of symptoms due to joint damage	1.113	0.999	1.240	1.110	0.987	1.249

Table 1. Multivariate analysis of factors associated with patients' opinion of remission and LDA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In psoriatic arthritis (PsA), the objective of treatment is remission or low disease activity (LDA), but there is little research into patients' perception of remission. The aim of this analysis was to identify which factors associate with patient-defined remission.

Methods: This is an analysis of ReFlap (NCT03119805), a cross-sectional international study of consecutive adult patients with PsA > 2 years of disease duration. Remission was defined by a positive response to the question "At this time, is your psoriatic arthritis in remission, if this means: you feel your disease is as good as gone?"; LDA by the question "At this time, are you in low disease activity, if this means: your disease is in low activity but it's not as good as gone?".

Potential variables that may associate with the opinion of remission/LDA were analysed using stepwise multivariable logistic regression. Variables were demographic (age, gender, disease duration, Groll comorbidity index), disease-related (joint counts, psoriasis body surface area (BSA), enthesitis, CRP), patient-reported outcomes (pain, PsAID, HAQ) and physician opinion of cause of symptoms (physician score for symptoms due to PsA, to joint damage or to other disease all scored 0-10). Due to high levels of correlation between variables, principal component analysis (PCA) was used to explore clustered components associated with remission/LDA. PCA was used to extract factors with orthogonal rotation. Factors with an eigenvalue of ≥1 were included.

Results: Among 466 recruited cases, 31 did not meet inclusion criteria and 11 had missing data leaving 424 for analysis. A total of 94 (22.2%) patients self-classified as remission and 285 (67.2%) as low disease activity or remission.

MEN			WOMEN		
Factor	Components	Variance	Factor	Components	Variance
1	Disease impact (pain, PsAID, HAQ) Arthritis (TJC/SJC)	27.5	1	Disease impact (pain, PsAID, HAQ)	22.2
2	Age/Chronicity (age, comorbidities and damage/other diseases causing symptoms)	17.2	2	MSK disease (TJC/SJC, enthesitis)	19.1
3	Psoriasis and enthesitis	10.6	3	Chronicity (age and comorbidities) with controlled psoriasis	11.6
4	TJC in shorter duration disease	9.99	4	Joint damage (disease duration and damage)	9.27
5	CRP	7.99	5	CRP and psoriasis	9.13
			6	Other diseases causing symptoms	9.11

Table 2. Principal component analysis of factors associated with patients' opinion of remission

When exploring factors associated with patients' opinion of remission in multivariate analysis, pain, psoriasis BSA, PsAID total score, NRS of physician score of symptoms related to joint damage and Groll comorbidity index were identified as independent predictors. For LDA, results were similar except for the addition of physician global and loss of psoriasis as significant predictors (table 1).

As PCA cannot include binary variables, PCA was performed separately by gender. For remission, variance explained by the key factors was 74% for men and 80% for women. Key factors (table 2) for remission were, for both genders, disease impact (PsAID, pain, HAQ). Other factors identified included MSK disease activity, chronicity/joint damage, psoriasis BSA, enthesitis and CRP. For women, physician's opinion of symptoms related to other disease was a separate factor. For LDA, similar factors were identified but the percentage variance explained was lower (64-68%).

Conclusion: When considering the patients' opinion of remission, a number of factors contribute to this perception dominated by disease impact measured by pain, PsAID and HAQ. In addition, disease activity in all domains, chronicity/age, comorbidities and other conditions contribute to a robust model highlighting how multifaceted "remission" can be for individuals.

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Abstract Number: 2512

A Qualitative Study of Clinicians' Perspectives on Barriers to Implementation of Treat to Target in Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: European League Against Rheumatism Treatment recommendations support implementing a treat-to-target (T2T) approach in psoriatic arthritis (PsA) based on the findings of the TICOPA trial. However, a UK survey estimated that ~90% of clinicians do not follow this. This study explored clinicians' views on implementing T2T in PsA.

Methods: Individual interviews and a focus group with clinicians, audio-recorded and analysed using thematic analysis. Datasets were compared and integrated for analysis.

Results: Eight rheumatologists and two healthcare professionals (5-26 years' experience) participated in telephone interviews (25-35 minutes). One consultant delivered PsA-specific clinics. Seven rheumatologists and two trainees (3-22 years' experience) participated in a focus group (102 minutes). Three clinicians delivered PsA-specific clinics. There were four main themes:

Individual motivation to change clinical practice: "We have set up weekly psoriatic arthritis clinics at our hospital and it took almost 2 ½ years." Typically, individual clinicians with a specialist interest developed care pathways for PsA patients. They sought external information, training and support to champion T2T in their local service.

A lack of consensus on what to measure: "There has to be a strong argument to get me to do any other type of assessment because PsARC is quicker and we've been trained appropriately." Views varied on the assessments

needed to inform disease management. A strong justification would be needed for measures that could increase appointment time and patient burden.

What is achievable with limited resources: "If it's a mixed clinic it isn't really that feasible"

Lack of nursing support and registrar training in skin/joint scores were barriers to T2T. Challenges were amplified when PsA patients attended general rheumatology clinics and there were no dedicated database systems to support data collection.

Mandatory versus voluntary pressures to change: "Actually knowing somebody's watching you… with an audit makes a hell of a difference to how you run your service." Changes in practice were more likely when mandated by service providers and linked to tariffs/funding. Sharing local guidelines and protocols could facilitate T2T implementation.

Conclusion: A driver of T2T implementation was clinicians with a specialist interest in PsA who set up dedicated clinics. Barriers included a lack of consensus about targets, and practical challenges (clinical time, collecting outcomes, insufficient training and database requirements). T2T implementation in PsA requires an integrated approach to address support and resource needs of individual clinicians, teams, local IT systems, and service providers.

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Abstract Number: 2513

Relationships Between Psoriatic Arthritis Disease Activity Score and Patient-Reported Outcomes in Patients with Psoriatic Arthritis: Post Hoc Analysis of Two Phase 3 Studies

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a complex heterogeneous disease associated with multiple domains. Psoriatic Arthritis Disease Activity Score (PASDAS) is a composite disease activity measure for PsA, developed to assess improvements in multiple clinical outcomes in response to treatment using a single instrument.[1] The

objective of this post hoc analysis was to evaluate associations between PASDAS and a set of patient-reported outcomes (PROs).

Methods: All available data from two Phase 3 studies in patients with PsA (OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439])[2,3] were analyzed. PASDAS (score range 0–10) is based on the following measures: Patient's Global Assessment of PsA Visual Analog Scale (VAS); Physician's Global Assessment of PsA VAS; tender and swollen joint counts; Leeds Enthesitis count; tender dactylitis count; Short-Form 36 Health Survey Physical Component Summary (SF-36 PCS); and C-reactive protein. PASDAS cut-offs for low and high disease activity are 3.2 and 5.4, respectively.[4] A set of PROs was analyzed (Table 1). A repeated measures regression model was used to evaluate the relationship between PASDAS and PROs. A sensitivity analysis to assess the linearity assumption was performed.

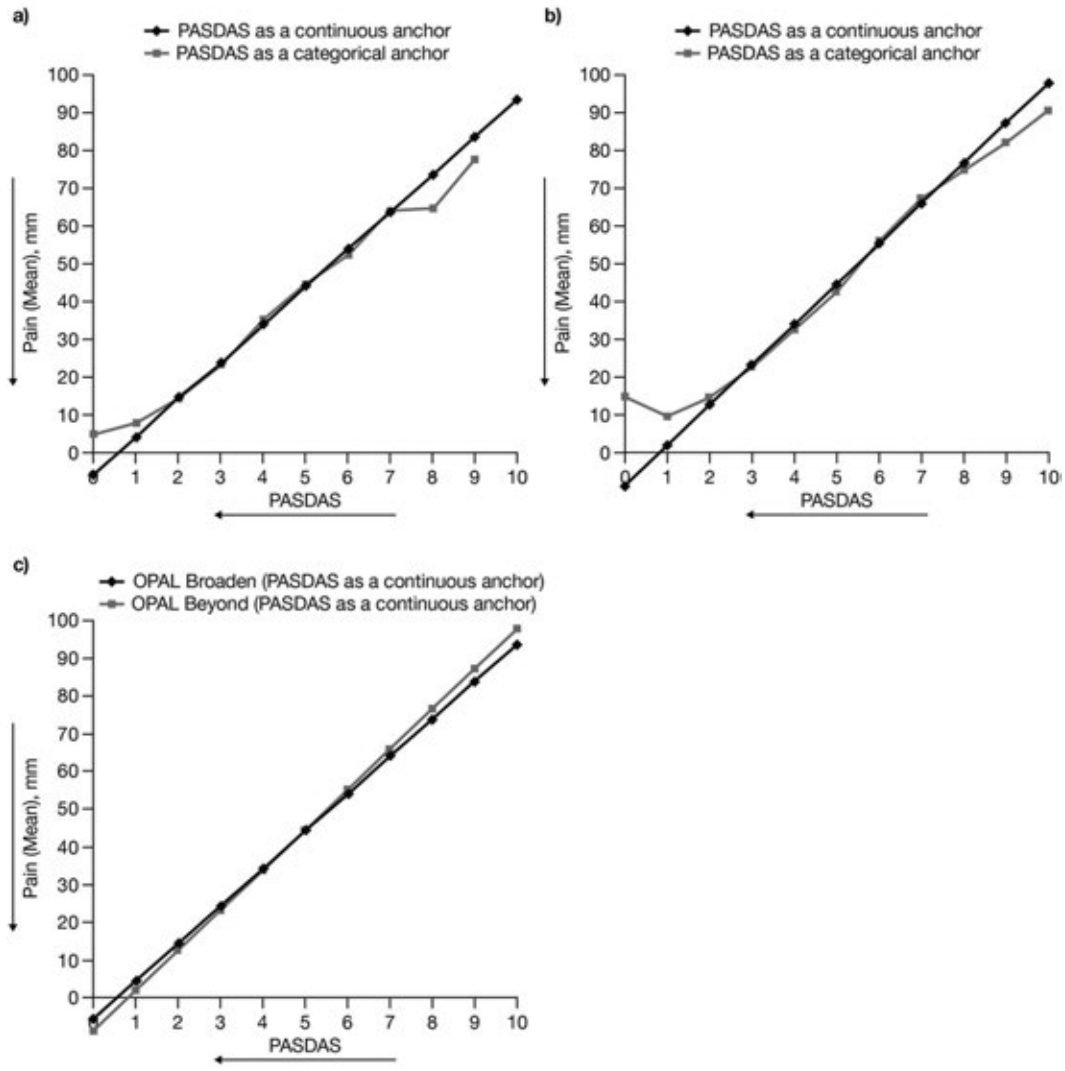
Results: An approximately linear relationship was observed between PASDAS and PROs, which was consistent across all PROs and both studies. For example, in OPAL Broaden, a 1-point difference in PASDAS was associated with a mean (95% CI) difference in Patient's Assessment of Arthritis Pain VAS (Pain) score of 9.9 mm (9.4, 10.4) (OPAL Beyond: 10.7 mm [10.1, 11.2]). Mean Pain scores (95% CI) corresponding to PASDAS low and high disease activity cut-offs, respectively, were 26.3 mm (25.0, 27.5) and 48.0 mm (46.7, 49.4) in OPAL Broaden (OPAL Beyond: 25.4 mm [23.7, 27.1] and 48.8 mm [47.4, 50.3], respectively) (Figure 1). In OPAL Broaden, a 1-point difference in PASDAS was associated with a mean (95% CI) difference in Patient's Global Joint and Skin assessment (PGJS)-VAS score of 12.0 mm (11.6, 12.4) (OPAL Beyond: 12.6 mm [12.1, 13.1]). Mean (95% CI) PGJS scores corresponding to PASDAS low and high disease activity cut-offs, respectively, were 28.2 mm (27.1, 29.3) and 54.7 mm (53.6, 55.8) in OPAL Broaden (OPAL Beyond: 27.8 mm [26.3, 29.2] and 55.4 mm [54.1, 56.7], respectively).

Conclusion: The approximately linear association observed here provides insight into the relationship between PASDAS and examined PROs, some of which were components of PASDAS, while others were independent outcomes. Results were similar in both studies, suggesting that findings are consistent across different populations.

Table 1. Patient Reported Outcomes included in analysis

Patient Reported Outcome	Description
Pain	Patient's Assessment of Arthritis Pain Visual Analog Scale
SF-36v2 Physical Component Summary Physical Functioning Domain	36-Item Short-Form Health Survey, Version 2
HAQ-DI	Health Assessment Questionnaire-Disability Index
FACIT-F Total Score Experience Domain Impact Domain	Functional Assessment of Chronic Illness Therapy-Fatigue
PGJS-VAS	Patient's Global Joint and Skin assessment - Visual Analog Scale
PGJS-VAS-Arthritis	Patient's Global Joint and Skin Assessment - Visual Analog Scale - Arthritis Question
PGJS-VAS-PsO	Patient's Global Joint and Skin Assessment - Visual Analog Scale - Psoriasis Question
EQ-5D Visual Analog Scale Utility Index	EuroQol Five Dimension 3 Level

Figure 1. Estimated relationships between Pain and PASDAS in a) OPAL Broaden, b) OPAL Beyond, and c) OPAL Broaden vs OPAL Beyond



Pain: 0 (no pain) – 100 (most severe pain)
Arrows on the figure indicate the direction of improvement
Pain, Patient's Assessment of Arthritis Pain Visual Analog Scale; PASDAS, Psoriatic Arthritis Disease Activity Score

1. Helliwell PS et al. Ann Rheum Dis 2013;72:986–91.
2. Gladman D et al. N Engl J Med 2017;377:1525–36.
3. Mease P et al. N Engl J Med 2017;377:1537–50.
4. Helliwell PS et al. J Rheumatol 2014;41:1212–17.

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Lilly, 2, 5, 8, MSD, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 8, Prothena, 5, Sun Pharma, 5, UCB, 5, 8, UCB Pharma, 5; **A. Bushmakin**, Pfizer Inc, 1, 3; **O. FitzGerald**, AbbVie, 2, 8, Abbvie, 2, 8, BMS, 2, 5, Bristol Myers Squibb Co., 2, 5, Celgene, 5, Celgene Corp., 5, Janssen, 5, 8, Janssen Inc, 5, 8, Lilly, 2, 5, Novartis, 2, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, 8; **D. Gladman**, AbbVie, 2, 5, AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Gilead, 5, GlaxoSmithKline, 5, 8, Janssen, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **L. Fallon**, Pfizer Inc, 1, 3; **J. Cappelleri**, Pfizer Inc, 1, 3, Pfizer Inc., 1, 3; **M. Hsu**, Pfizer Inc, 1, 3; **P. Helliwell**, AbbVie, 2, 8, Amgen, 8, Celgen, 8, Celgene, 8, Galapagos, 8, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, Pfizer, 8, Pfizer Inc, 8, UCB, 8.

Abstract Number: 2514

Relationships Between Minimal Disease Activity and Patient-Reported Outcomes in Patients with Psoriatic Arthritis: Post Hoc Analysis of Two Phase 3 Studies

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

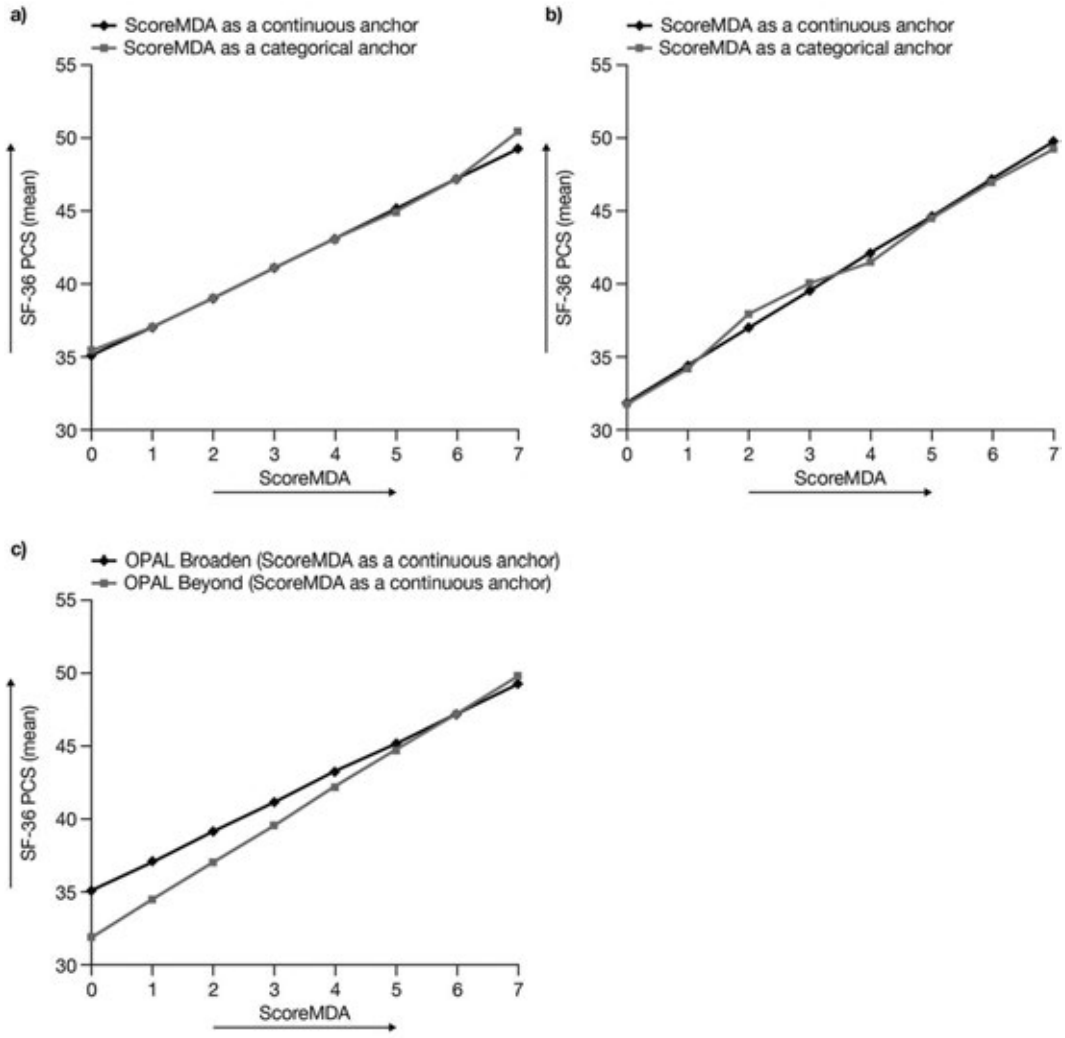
Background/Purpose: PsA is associated with multiple disease domains, requiring the use of different clinical measures and patient-reported outcomes (PROs) to assess improvements in disease activity following treatment. However, the relationship between clinical measures and PROs is not well understood. The objective of this post hoc analysis was to evaluate associations between Minimal Disease Activity (MDA) and a set of PROs.

Methods: All available data from two Phase 3 studies in patients with PsA (OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439])[1,2] were analyzed. MDA in PsA, as a binary outcome, is defined as meeting ≥ 5/7 of the following criteria: tender joint count ≤ 1; swollen joint count ≤ 1; Psoriasis Activity and Severity Index ≤

Table 1. Patient Reported Outcomes included in analysis

Patient Reported Outcome	Description
SF-36v2 Physical Component Summary Physical Functioning Domain	36-Item Short-Form Health Survey, Version 2 acute
FACIT-F Total Score Experience Domain Impact Domain	Functional Assessment of Chronic Illness Therapy-Fatigue
PGJS-VAS	Patient's Global Joint and Skin assessment - Visual Analog Scale
PGJS-VAS-PsO	Patient's Global Joint and Skin Assessment-Visual Analog Scale - Psoriasis Question
EQ-5D Visual Analog Scale Utility Index	EuroQol Five Dimension 3 Level

Figure 1. Estimated relationships between SF-36 Physical Component Summary and ScoreMDA in a) OPAL Broaden, b) OPAL Beyond, and c) OPAL Broaden vs OPAL Beyond



SF-36 PCS: norm-based scores were used (a score of 50 representing the mean for the general population [Ware JE et al. Quality Metric 2000]), with higher scores indicating less impairment; ScoreMDA: continuous MDA with values from 0–7 (0–4, no MDA; 5–7, MDA) Arrows on the figure indicate the direction of improvement
MDA, Minimal Disease Activity; SF-36 PCS, 36-Item Short-Form Health Survey Physical Component Summary

1 or body surface area ≤ 3%; patient global disease activity Visual Analog Scale (VAS) ≤ 20; Patient's Assessment of Arthritis Pain VAS (Pain) ≤ 15; HAQ-Disability Index (DI) score ≤ 0.5; and tender entheseal points ≤ 1. For the purpose of this analysis, an alternative MDA outcome is proposed (ScoreMDA) by considering every criterion as an individual item (ie 1 if true and 0 if false, to give a score range of 0–7; scores ≥ 5 indicate the patient had MDA). A set of PROs was analyzed (Table 1). A repeated measures regression model was used to evaluate the relationship between ScoreMDA and PROs. A sensitivity analysis to assess the linearity assumption was performed using ScoreMDA as a categorical anchor (represented by integer values 0–7).

Results: Results indicated a linear relationship between ScoreMDA and PROs, which was similar across all PROs and in both Phase 3 studies. For example, in OPAL Broaden, a 1-point difference in ScoreMDA was associated with a mean (95% CI) difference in SF-36 Physical Component Summary (PCS) score of 2.0 points (1.9, 2.2) (OPAL Beyond: 2.5 points [2.3, 2.7]) (Figure 1). These results indicate that improvements in any one MDA criterion is associated with an improvement in SF-36 PCS score approaching clinical relevance (clinically important difference [CID] for SF-36

PCS is 3 points) and improvements in any two criteria in MDA is associated with an improvement in SF-36 PCS score that exceeds the CID. Results were closely aligned when ScoreMDA was used as a categorical or a continuous anchor, thus supporting a linear relationship between ScoreMDA and the PROs.

Conclusion: There was a robust linear relationship between ScoreMDA and selected PROs. Results were similar across studies, suggesting that they may be generalizable to different populations. This method provides insight into the relationships between clinical measures and PROs in PsA, which could aid their interpretation and facilitate the assessment of disease activity.

1. Gladman D et al. N Engl J Med 2017;377:1525–36.
2. Mease P et al. N Engl J Med 2017;377:1537–50.

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Abstract Number: 2515

Disease Activity Influences Cardiovascular Risk Reclassification Based on Carotid Ultrasound in Patients with Psoriatic Artrhitis

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Table 1. SCORE risk category re-classification after carotid sonography

		SCORE Risk Category after Carotid Ultrasound Assessment					
		Low	Moderate	High	Very high	% patients being	p*
Initial SCORE risk category							
Controls							
Low	139	120	0	0	19	13,7%	
Moderate	28	0	10	0	18	64,3%	
High	12	0	0	2	10	83,3%	
Very High	0	0	0	0	0	-	
	179	120	10	2	47	26,3%	
Psoriatic arthritis patients							
Low	101	71	0	0	30	29,7%	**0.002**
Moderate	78	0	24	0	54	69,2%	0.54
High	19	0	0	7	12	63,2%	0.42
Very High	8	0	0	0	8	-	
	206	71	24	7	104	50,5%	**0.000**

SCORE. Systematic Coronary Risk Evaluation

*p values refers to the comparition between patients and controls for each SCORE category and for total both populations

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical Poster III: Psoriatic Arthritis, Clinical Features

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: ***Objectives*****.** The addition of carotid ultrasound CU into composite cardiovascular risk (CVR) scores has been found useful in the identification of high CVR in patients with inflammatory arthritis. We aim to evaluated if the performance of CU in the CVR stratification of patients with psoriatic arthritis (PsA) would identify patients in the very-high SCORE risk category and if this reclassification could be explained through features related to disease activity.

Methods: A cross-sectional study including a set of 206 patients fulfilling CASPAR criteria for PsA and 179 controls was performed. The following data were assessed: lipid profile; Systematic Coronary Risk Evaluation SCORE risk stratification; disease activity indexes through Disease Activity in Psoriatic Arthritis -DAPSA-, Bath Ankylosing Spondylitis Disease Activity -BASDAI-, Bath Ankylosing Spondylitis Functional Index -BASFI., skin disease activity measurements by Psoriasis Area Severity Index -PASI-, Body Surface Area -BSA-, and Nail Psoriasis Severity Index -NAPSI- scores; and the presence of carotid plaques and carotid intima media thickness (cIMT) trough ultrasound. A multivariable regression analysis, adjusting for classic cardiovascular risk factors, was performed in order to evaluate if risk reclassification following (CU) could be explained by features related to the disease and independently of traditional CVR factors.

Results: 49% patients with PsA had carotid plaques compared to 26% in controls (p=0.000). Similarly, cIMT was found to be higher in patients in comparison with controls (0.606 ± 0.116 *vs.* 0.679 ± 0.165, p=0.000). 51% of the patients were reclassified into a very-high SCORE risk category after carotid ultrasound compared to controls (26%, p=0.000). Principally, patients in the low SCORE category risk were significantly more reclassified (14% vs. 30%, p=0.002). Age (p=0.000), hypertension (p=0.000), obesity (p0.011), the use of statins (p=0.000), disease duration (p=0.000), and DAPSA score (p=0.049) were the variables that positive and univariately were associated with reclassification in PsA patients. Interestingly, PsA patients being reclassified disclosed lower total cholesterol (197 ± 36 vs. 179 ± 40 mg/dl, p=0.001) and LDL cholesterol serum levels (116 ± 35 vs. 106 ± 34 mg/dl, p=0.032) compared to controls. When the association of disease relation data with reclassification was assessed through multivariable regression, DAPSA score was associated with a higher probability of being reclassified (beta coef. 1.09 [95%CI 1.01-1.18]), p=0.035) after adjusting for age and traditional (CVR) factors. This relation was also found using DAPSA score. In this sense, a moderate or high activity category disclosed an odds ratio of 13.09 (95%CI 1.44-1118.76), p=0.022, compared to those patients in the low activity

Conclusion: Patients with PsA are more frequently reclassified into the very-high SCORE risk category after carotid ultrasound performance compared to controls. This reclassification can be independently explained by the activity produced by the disease

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Abstract Number: 2516

Development of a Biomarker Panel for Prediction of Disease Flares in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

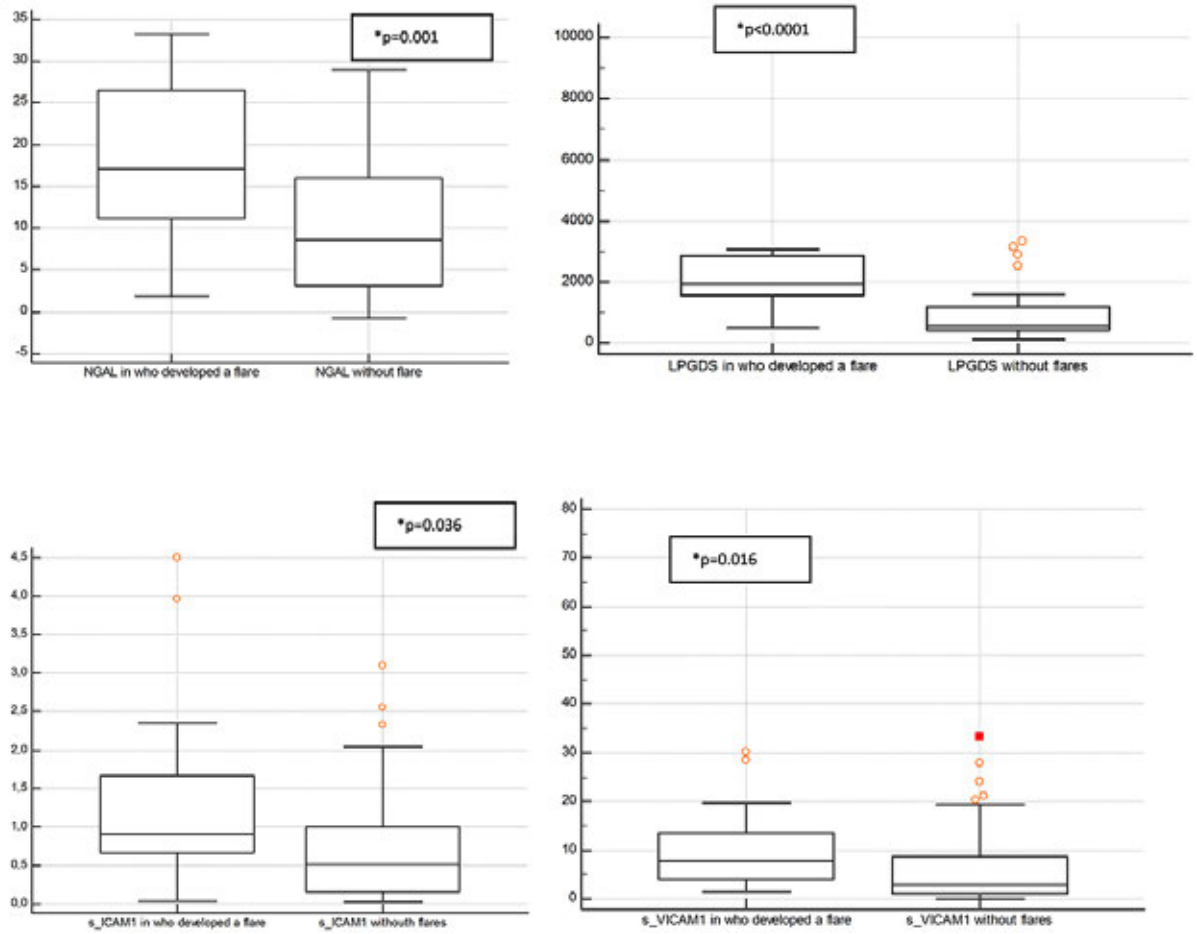
Session Title: SLE – Clinical Poster III: Treatment

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Fig 1

Comparison of urinary biomarkers levels between SLE patients who develop a flare after 12 weeks of urine collection and patients without flares.



Background/Purpose: Systemic Lupus Erythematosus (SLE) is an autoimmune disease with a relapsing-remitting course. Uncontrolled lupus flares might lead to organ damage. The routinely performed biomarkers (antidsDNA Ab and serum complement) have a limited predictive value for the prediction of flares. Recent evidence suggests that novel urinary biomarkers, namely vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1), monocyte chemoattractant protein 1 (MCP-1), Urinary Neutrophil Gelatinase Associated Lipocalcin (NGAL) and Lipocalin-type Prostaglandin D-Synthetase (L-PGDS) are able to discriminate between SLE patients with ongoing renal activity and those without nephritis (1-3).

Objective. To assess the ability of novel urinary biomarkers in predicting flares in comparison to the conventional biomarkers and to derive a biomarker panel which may improve diagnostic accuracy.

Methods: Urine samples were collected from patients prospectively followed at our clinic who fulfilled ≥4 of the ACR 1997 revised criteria for the classification of SLE (4) and who were in stable disease at baseline visit (no new features of lupus disease activity compared with the previous assessment). Flares were identified by SELENA flare index (SFI) after 3 and 6 months of urine collection (5). Urinary biomarkers levels were measured in the second void urinary sample by ELISA assay. Data were compared by the unpaired student's t test or the Mann–Whitney U test as appropriate. Receiver operating characteristic (ROC) analysis was used to calculate the area under the curve (AUC) with associated 95% confidence interval (CI) to find the best cut-off values. Multiple regression was used to build models identifying independent predictors of disease flares.

Results: Urine specimen was collected from 71 patients, including 68 females and 3 males with a mean age of 44.4 years(±11.2) and a median SLEDAI2K of 2 (IQR 0-4). During 6 months-follow-up, 18 (25%) out of the 71 patients experienced a single disease flare. Among them, 8 episodes had renal involvement. Urinary L-PGDS, NGAL, ICAM-1 and VCAM-1 levels were significantly increased 12 weeks before a disease flare ($p< 0.05$; Figure1). Urinary MCP-1 levels were no significantly increased. Based on ROC analysis, urinary NGAL (AUC: 0.75) and L-PGDS (AUC: 0.82) outperformed conventional biomarkers (Table1). At univariate analysis(Table2), NGAL, L-PGDS, ICAM-1,VCAM-1, hypocomplementemia, anti dsDNA antibodies were predictors of lupus flares, while age at inclusion was protective. At multivariate analysis, antidsDNA antibodies and L-PGDS were independent predictors of lupus flares with OR=11.8 and 24.5, respectively. A combination of novel and conventional biomarkers demonstrated an excellent ability for accurately identifying a flare. (AUC >0.9; Table2)

Conclusion: This study has demonstrated the ability of a novel biomarker panel in predicting a lupus flare in its incipient phase. Further studies are needed to determine its clinical utility in everyday practice.

Table 1. Area under the curve (AUC), cut off values, sensitivity and specificity for novel and standard biomarkers for disease flares.

Variables	AUC	95% CI	Cut off values	sensitivity	specificity	VPP	VPN	p value
C3	0.71	0.59 - 0.81	100 mg/dl	88%	50%	38%	92%	0.001
Anti dsDNA antibodies	0.74	0,63-0,84	10 UI	66%	84%	60%	88%	0.002
L-PGDS	0.82	0.70 - 0.90	1500 ng/ml	78%	85%	67%	91%	<0.0001
NGAL	0.75	0.63- 0.85	10.95 ng/ml	83%	62%	46%	91%	0.0001
ICAM1	0.66	0.53-0,77	0.59 ng/ml	76%	59%	38%	88%	0.046
VCAM1	0.72	0,59-0,82	6 ng/ml	71%	73%	46%	88%	0.001
MCP1	0.61	0.49-0.73	213.41 ng/ml	82%	41%	32%	87%	>0.05

Table 2. Factors predicting lupus flares during follow-up in univariate analysis and effect on the area under the receiver operating characteristic curve of adding biomarkers to the regression model

Variables	OR	95% CI	p value
hypocomplementemia	3,2	1,03-9,88	0.043
Anti dsDNA antibodies	7,45	2,28-24,37	0.0009
L-PGDS	17,57	4,39-70,31	0.0001
NGAL	8,3	2,11-32,80	0.002
ICAM1	4,64	1,32-16,23	0.016
VCAM1	6,34	1,88-21,29	0.002
MCP1	3,01	0,76-11,82	>0.05
Age at inclusion	0,92	0,87-0,98	0.014
Disease duration	0,96	0,92-1,01	>0.05
SDI at inclusion	0,70	0,34-1,45	>0.05
glomerulonephritis (ever)	2,24	0,73-6,85	>0.05

Biomarker combinations included in the binary logistic regression models	AUC
L-PGDS+ NGAL	0,86
L-PGDS+ NGAL+ ICAM1	0,92
L-PGDS+ NGAL+ ICAM1+VCAM1	0,93
L-PGDS+ NGAL+ ICAM1+VCAM1+ Anti dsDNA antibodies	0,94
L-PGDS+ NGAL+ ICAM1+VCAM1+ Anti dsDNA antibodies+C3	0,95

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5.Petri M. et al. NEJM 2005

Disclosure: S. Fasano, None; **L. Pierro**, None; **A. Borgia**, None; **M. Coscia**, None; **R. Formica**, None; **a. Riccardi**, None; **F. Ciccia**, None.

Abstract Number: 2517

Hydroxychloroquine Is a Modifiable Predictor of Durable LLDAS

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The Lupus Low Disease Activity State (LLDAS), a potential treat to target goal in systemic lupus erythematosus (SLE), has been found to correlate with reduced damage accrual in SLE. In particular, SLE patients, in LLDAS for more than half of the observation time, have a lower risk of new damage. We identified predictors of being in LLDAS over 50% of the observation time.

Methods: This analysis was based on cohort data from its inception until May, 2019. A total of 2363 SLE patients, diagnosed according to the SLICC or ACR classification criteria and with at least two clinical visits, were included. We applied the definition of LLDAS and determined whether LLDAS was satisfied at each visit for each patient. Then, each observation for each patient was defined based on the status at the following visits throughout the whole follow

	LLDAS < 50% n=1165	LLDAS≥50% n=1198	OR (95% CI)	p-value
Sex, Female				0.9746
Female	1074 (49.3%)	1104 (50.7%)	Ref	
Male	91 (49.2%)	94 (50.8%)	1.01 (0.75-1.36)	
Ethnicity				<.0001
Black	615 (64.8%)	334 (35.2%)	0.33 (0.27-0.39)	
White	460 (37.5%)	766 (62.5%)	Ref	
Other	90 (47.9%)	98 (52.1%)	0.65 (0.48-0.89)	
Age at diagnosis, years	27.8 (20.9-36.3)	32.2 (24.8-42.8)	1.03 (1.02-1.04)	<.0001
Education				<.0001
Below High-School	172 (61.0%)	110 (39.0%)	Ref	
High School	294 (52.6%)	265 (47.4%)	1.41 (1.05-1.88)	
Some College	315 (48.9%)	329 (51.1%)	1.64 (1.23-2.17)	
College Graduate	384 (43.7%)	494 (56.3%)	2.01 (1.53-2.64)	
History of smoking	426 (49.8%)	430 (50.2%)	0.96 (0.82-1.14)	0.6726
Duration of SLE	11.1 (5.4-18.9)	12.9 (6.6-20.2)	1.01 (1.005, 1.02)	0.0007
Mean Prednisone Dose	8.8 (4.1-14.0)	0.29 (0-3.7)	0.76 (0.74-0.77)	<.001
Hydroxychloroquine use				
Percentage of time	88% (12%-100%)	96% (57-100%)	1.86 (1.51-2.29)	<.0001
Immunosuppressant use				
Percentage of time	41% (0%-90%)	0% (0%-27%)	0.20 (1.16-0.25)	<.0001
Ever Low C3	802 (60.9%)	514 (39.1%)	0.34 (0.29-0.4)	<.0001
Ever Low C4	698 (61.6%)	435 (38.4%)	0.38 (0.32-0.45)	<.0001
Ever Anti SM positivity	326 (65.7%)	170 (34.3%)	0.42 (0.34-0.51)	<.0001
Ever Anti RNP positivity	439 (63.9%)	248 (36.1%)	0.42 (0.35-0.50)	<.0001
Ever Anti-dsDNA positivity	837 (56.6%)	641 (43.4%)	0.45 (0.38-0.53)	<.0001
Antiphospholipid antibodies				
Anti-Cardiolipin	527 (47.4%)	584 (52.6%)	1.13 (0.96-1.33)	0.1410
Lupus anti-coagulant (RVVT)	301 (49.1%)	312 (50.9%)	0.99 (0.82-1.19)	0.8743

*Continous variables were presented as median (IQR).

Table 1. Patients demographics and laboratory characteristics, grouped according to percentage of time in LLDAS

	LLDAS < 50% n=1165	LLDAS≥50% n=1198	OR (95% CI)	p-value
Ever Cutaneous activity	1102 (49.2%)	1140 (50.8%)	1.09 (0.75-1.57)	0.6541
Malar Rash	587 (51.3%)	557 (48.7%)	0.86 (0.73-1.01)	0.0609
Discoid	281 (60.3%)	185 (39.7%)	0.57 (0.47-0.70)	<.0001
Photosensitivity	586 (48.1%)	633 (51.9%)	1.11 (0.94-1.30)	0.2253
Mucosal Ulcer	581 (46.8%)	661 (53.2%)	1.24 (1.05-1.45)	0.0105
Alopecia	733 (54.9%)	603 (45.1%)	0.59 (0.50-0.70)	<.0001
Raynaud's	609 (50.2%)	603 (49.8%)	0.92 (0.78-1.08)	0.3127
Subacute Cutaneous Lupus	70 (56.5%)	54 (43.6%)	0.74 (0.51-1.06)	0.0988
Bullous	9 (50.0%)	9 (50.0%)	0.96 (0.38-2.44)	0.9388
Vasculitis	214 (63.3%)	124 (36.7%)	0.51 (0.40-0.65)	<.0001
Livedoid Rash	251 (41.2%)	358 (58.8%)	1.55 (1.28-1.86)	<.0001
Leg ulcers	40 (69.0%)	18 (31.0%)	0.43 (0.24-0.75)	0.0031
Panniculitis	31 (56.4%)	24 (43.6%)	0.75 (0.43-1.28)	0.2849
Ever Musculoskeletal activity	891 (51.5%)	840 (48.5%)	0.71 (0.59-0.86)	0.0003
Arthritis	871 (51.4%)	824 (48.6%)	0.74 (0.62-0.89)	0.001
Myositis	117 (63.2%)	68 (36.8%)	0.54 (0.39-0.73)	<.0001
Ever Renal activity	795 (60.4%)	522 (39.6%)	0.36 (0.3-0.42)	<.0001
Proteinuria	700 (65.1%)	375 (34.9%)	0.30 (0.25-0.36)	<.0001
Nephrotic Syndrome	323 (73.9%)	114 (26.1%)	0.27 (0.21-0.34)	<.0001
Hematuria	441 (65.8%)	229 (34.2%)	0.38 (0.32-0.46)	<.0001
Renal Insufficiency	435 (62.6%)	260 (37.4%)	0.46 (0.39-0.56)	<.0001
Renal Failure	136 (72.7%)	51 (27.3%)	0.33 (0.24-0.47)	<.0001
Ever Hematological activity	481 (59.2%)	332 (40.8%)	0.47 (0.39-0.56)	<.0001
Coombs	264 (63.5%)	152 (36.5%)	0.44 (0.35-0.55)	<.0001
Hemolytic Anemia	149 (62.9%)	88 (37.1%)	0.53 (0.40-0.70)	<.0001
Thrombocytopenia	278 (57.6%)	205 42.4%)	0.66 (0.54-0.8)	<.0001
Ever Serositis activity	677 (58.6%)	478 (41.4%)	0.48 (0.41-0.56)	<.0001
Damage accrual during follow up				<.0001
SDI≤1	724 (46.2%)	844 (53.8%)	Ref	
SDI>1	432 (55.5%)	347 (44.5%)	0.69 (0.58-0.82)	

Table 2. Clinical manifestations of patients, grouped according to percentage of time in LLDAS

up. Follow up visits that occurred after a gap of more than 12 months (+/- 1 month) between clinic visits were excluded. Percentage of time in LLDAS was calculated. Durable LLDAS was defined as being in LLDAS for over 50% of the observation time. Patients were then classified into groups based on whether they had durable LLDAS or not. We analyzed the predictors of durable LLDAS from the stepwise selection procedure in logistic regression.

Results: Ninety-two percent of the patients were female, 40.2% African-American, and 51.9% Caucasian. 50% of the patients were diagnosed with SLE under the age of 30 years, 25% were between the age of 30 and 40, 14.5% were between 40 and 50, and 10.5% were diagnosed at age of 50 and over. 1198 (50.6%) patients overall, including 35.2% of African-Americans, achieved durable LLDAS. Patients with durable LLDAS, were significantly older at diagnosis, more educated, had longer disease duration, and were less likely to be African-American (Table 1,2). In the multivariable model, African-American ethnicity, ever having low C3, subacute cutaneous lupus erythematosus, alopecia, renal insufficiency, anti-RNP positivity, % of time with immunosuppressant use, and mean prednisone dose remained negative predictors, while age at diagnosis, disease duration, hemolytic anemia and higher % of time with hydroxychloroquine use remained positive predictors of durable LLDAS (Table 3).

Conclusion: A higher percentage of time with hydroxychloroquine use is a modifiable predictor of durable LLDAS, even after adjustment for clinical, demographic and other treatment variables. Only one third of African-American patients achieved durable LLDAS. Hydroxychloroquine use (and demonstration of adherence) remains essential in both clinical practice and in randomized clinical trials.

Table 3. Predictors for Durable LLDAS		
	OR (95% CI)	**p-value**
Ethnicity		
Caucasian	Ref	
African American	0.43 (0.33-0.55)	<.0001
Other	1.09 (0.71-1.67)	0.6823
Age at diagnosis (per year difference)	1.02 (1.01-1.03)	0.0003
SLE duration (per year difference)	1.03 (1.02-1.05)	<.0001
% of time with hydroxychloroquine use (per % difference)	1.37 (1.01-1.84)	0.0432
Low Complement 3		
Ever	0.59 (0.46-0.74)	<.0001
Never	Ref	
Anti-RNP positivity		
Ever	0.70 (0.59-0.94)	0.0069
Never	Ref	
Subacute cutaneous lupus erythematosus		
Ever	0.46 (0.28-0.74)	0.0014
Never	Ref	
Alopecia		
Ever	0.74 (0.59-0.94)	0.0147
Never	Ref	
Renal Insufficiency		
Ever	0.75 (0.58-0.98)	0.0344
Never	Ref	
Hemolytic anemia		
Ever	1.74 (1.18-2.59)	0.0057
Never	Ref	
% of time with Immunosuppressant use (per % difference)	0.46 (0.34-0.62)	<.0001
Mean prednisone dose (per unit difference)	0.78 (0.75-0.80)	<.0001
Other covariates in the final multivariable model included; years of education, ever low C4, anti-Sm, anti-DNA, damage accrual over the follow up period, discoid, mouth ulcers, vasculitis, panniculitis, leg ulcers, livedo, arthritis, myositis, proteinuria, nephrotic syndrome, hematuria, renal failure, coombs positivity, thrombocytopenia, serositis.		

Disclosure: H. Babaoglu, None; **J. Li**, None; **D. Goldman**, None; **L. Magder**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 2518

Time to Lupus Low Disease Activity State: Role of African-American Ethnicity

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	Median time to LLDAS	Univariate		Multivariable	
		HR (95% CI)	p value	HR (95% CI)	p value
Ethnicity					
Non-African-American	0.95	Ref		Ref	
African-American	1.5	0.63(0.55-0.73)	<0.001	0.61(0.52-0.70	<0.001
Duration of SLE*					
<1 year	1	Ref		Ref	
1-5 years	1.2	0.75(0.62-0.89	0.001	0.8(0.67-0.96	0.016
>5 years	1.4	0.72(0.62-0.85	<0.001	0.79(0.66-0.94	0.007
Prednisone dose*					
≤10 mg	0.6	Ref		Ref	
>10 mg	1.4	0.56(0.48-0.64)	<0.001	0.57(0.49-0.66)	<0.001
Hydroxychloroquine use*					
No	1.3	Ref			
Yes	1	1.23(1.07-1.41)	0.004		
Hypocomplementemia*					
No	0.9	Ref		Ref	
Yes	1.5	0.66(0.57-0.76)	<0.001	0.68(0.59-0.79	<0.001
anti-dsDNA positivity*					
No	1.1	Ref			
Yes	1.3	0.85(0.73-0.98)	0.026		
PGA*					
≤1	1	Ref			
>1	1.3	0.78(0.68-0.90	<0.001		
SLICC/ACR Damage Index Score*					
≤1	1	Ref		Ref	
>1	1.4	0.79(0.67-0.92)	0.003	0.84(0.71-0.99)	0.041
SELENA-SLEDAI*					
≤4	1	Ref			
>4	1.4	0.81(0.70-0.92)	0.002		
Cutaneous activity*					
Absent	1.2	Ref		Ref	
Present	0.9	1.23(1.06-1.44)	0.007	1.19(1.01-1.39)	0.035
Renal activity*					
Absent	1	Ref		Ref	
Present	1.6	0.70(0.59-0.82)	<0.001	0.72(0.61-0.85)	<0.001
Lupus Anticoagulant					
Never	1.1	Ref			
Ever	1.3	0.85(0.72-0.99)	0.042		

Median time to LLDAS was presented as years. There was no significant association between time to LLDAS and baseline age, sex, history of smoking, immunosuppressant use, musculoskeletal activity, hematological activity, serositis, and anticardiolipin antibody positivity. SELENA-SLEDAI and PGA were not included in the final multivariable model due to their collinearity with cutaneous and renal activity.
LLDAS=lupus low disease activity state, SLE=Systemic Lupus Erythematosus, C3=Complement 3, C4=Complement 4, Anti-dsDNA=anti double stranded DNA, PGA=Physician Global Assessment, SLICC/ACR= Systemic Lupus International Collaborating Clinics/ American College of Rheumatology, SELENA-SLEDAI= the Safety of Estrogens in Lupus Erythematosus National Assessment version of the SLE disease activity index, and *= baseline.

Table 1. Predictors of time to LLDAS

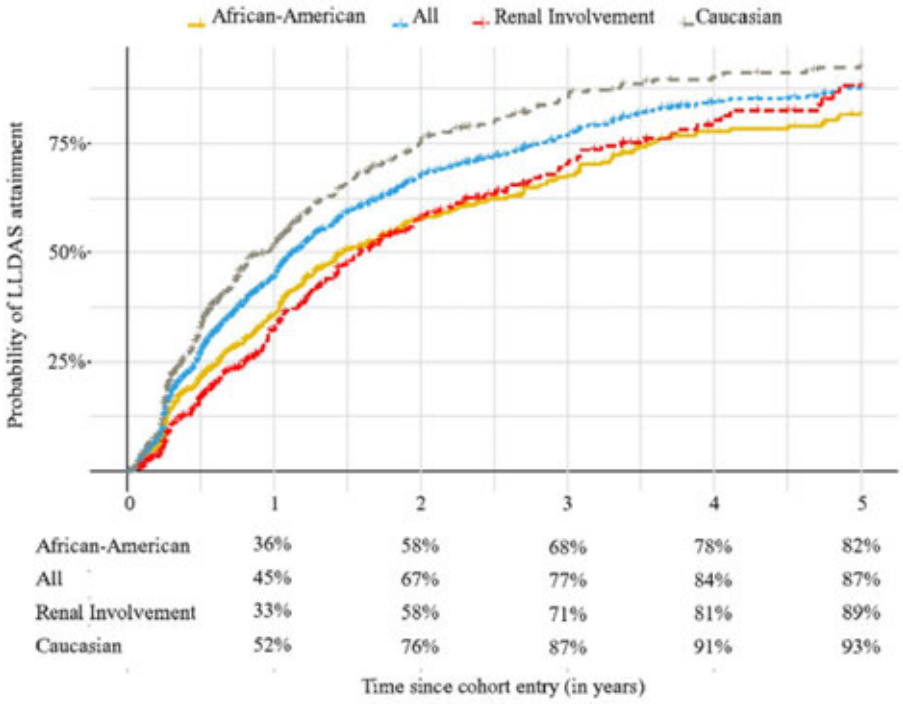

Figure 1. Probability of LLDAS attainment according to patients ethnicity and renal involvement at the stated time points

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus Low Disease Activity State (LLDAS) is a potential treat to target goal in systemic lupus erythematosus (SLE). It is well established that SLE patients who were in LLDAS for more than half of the observation period have a lower risk of new damage. The presentation and course of SLE is affected by ethnicity. African-American SLE patients are known to experience more severe SLE and, more chronic disease activity pattern. LLDAS in African-Americans has not been fully elucidated. In this study, we determined the time to LLDAS and predictors of time to LLDAS in a cohort with both Caucasian and African-American representation.

Methods: This analysis was based on cohort data from its inception until January, 2019. A total of 2,512 SLE patients, diagnosed according to the SLICC or ACR classification criteria, were included. We applied LLDAS (1), which was defined as a SELENA-SLEDAI score of ≤4 with no scores for the renal, central nervous system, cardiopulmonary, vasculitis, fever, no hemolytic anemia or gastrointestinal activity, no increase in any SELENA-SLEDAI component since the previous visit, a PGA of ≤1, and a prednisone dose of ≤7.5 mg/day. Immunosuppressant and hydroxychloroquine treatment were allowed for LLDAS. Patients were grouped according to LLDAS status at cohort entry. Those who did not satisfy LLDAS at cohort entry were analyzed prospectively. The Kaplan Meier approach was used to estimate the distribution of time to LLDAS and probability of patients achieving LLDAS after cohort entry, censoring patients who had a gap of 7 or more months in their follow-up time or who dropped out of the study before attaining LLDAS. Cox regression was used to identify patient characteristics that were associated with time to LLDAS.

Results: 1086 (43.2%) patients were in LLDAS at the first cohort visit. The probability of LLDAS attainment within one year was 52% for Caucasians, and 36% for African-Americans. Among those with renal involvement, the

estimated probability of achieving LLDAS within one year was 33% (Figure 1). The median time to LLDAS was 1.1 years. In multivariable models, African-American ethnicity, baseline prednisone >10 mg daily, baseline hypocomplementemia, baseline damage, and baseline renal activity remained significant predictors of longer time to attain LLDAS, while disease duration < 1 year and cutaneous activity were associated with earlier attainment (Table 1).

Conclusion: We demonstrated the achievability of LLDAS in both African-Americans and Caucasian patients, supporting the validity of LLDAS in multiple ethnicities. The time to LLDAS was longer in African-American SLE. Characteristics of African-American SLE such as renal activity and hypocomplementemia were also independent predictors of slower attainment of LLDAS. These findings point to the need to include African-American SLE patients in both clinical and pharmaceutical research, as we cannot generalize from studies from Europe and Asia.

Disclosure: H. Babaoglu, None; **J. Li**, None; **D. Goldman**, None; **L. Magder**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 2519

Cenerimod, a Potent, Selective and Orally Active Sphingosine 1-phosphate Receptor 1 Modulator, Reduced Blood Antibody-secreting Cells in Patients with SLE

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is an autoimmune disease driven by autoreactive T and B lymphocytes. Lymphocytes infiltrate self-antigen expressing tissues, in which tertiary lymphoid structures are often observed, suggesting local generation of autoreactive effector cells. Autoreactive B lymphocytes produce autoantibodies leading to deposition of autoantibody immune complexes in tissues. The pathological process is amplified by secretion of inflammatory molecules. Reported here is the *in-vitro* and clinical characterization of cenerimod, a potent, selective, and orally active sphingosine 1-phosphate receptor 1 ($S1P_1$) receptor modulator **(1).**

Methods: All patients with SLE were classified according to ACR criteria. Primary lymphocytes from patients with SLE and healthy subjects were isolated from blood and characterized for $S1P_1$ receptor surface expression and cenerimod-induced $S1P_1$ receptor internalization by flow cytometry. In a phase 2 clinical trial in patients with SLE (NCT02472795) **(2)**, blood T and B lymphocyte populations were enumerated by flow cytometry before and after 12-weeks of treatment with different doses of cenerimod. Unbiased analysis of flow cytometry data was employed to identify novel cenerimod-responsive lymphocyte populations. Inflammatory biomarkers were measured by ELISA in plasma samples.

Results: Surface expression of $S1P_1$ receptor was demonstrated on primary blood lymphocytes both in healthy subjects and patients with SLE *in-vitro*. $S1P_1$ receptor expression levels were ~3-fold higher on B cells compared to T cells. Cenerimod was potent and efficacious at $S1P_1$ receptor internalization in T and B lymphocyte populations with an EC_{50} of ~15 nM in both healthy subjects and patients with SLE. In a cenerimod phase 2 clinical trial in patients with SLE, a dose-dependent reduction of blood T and B lymphocyte populations was evident, with a reduction of CD4+ T cells (up to 95%) and CD19+ B cells (up to 90%). Unbiased analysis discovered an ~85% cenerimod-induced reduction of blood antibody-secreting cells (CD45+/CD19+/CD27+/IgD-/CD20-/CD38++), which were demonstrated to be increased two-fold in patients with SLE compared to healthy subjects.

In the phase 2 clinical trial in patients with SLE, cenerimod reduced plasma IFN-a levels compared to placebo. IFN-a was shown to correlate with inflammatory molecules elevated in patients with SLE.

Conclusion: These data demonstrated for the first time $S1P_1$ receptor surface expression on blood T and B lymphocytes in patients with SLE, in which cenerimod was potent and efficacious in reducing $S1P_1$ receptor surface expression. In the phase 2 clinical trial in patients with SLE, cenerimod dose-dependently reduced blood T and B lymphocyte populations. Blood antibody-secreting cells, potentially involved in SLE pathogenesis, were increased in patients with SLE and reduced by cenerimod treatment in the phase 2 clinical trial.

The results warrant further investigation of the clinical efficacy of cenerimod and the impact on SLE biomarkers in the currently recruiting phase 2b clinical trial (NCT03742037).

Disclosure: D. Strasser, Idorsia Pharmaceuticals Ltd, 1, 3, 4; **V. Sippel**, Idorsia Pharmaceuticals Ltd, 1, 3, 4; **U. Grieder**, Idorsia Pharmaceuticals Ltd, 1, 3, 4; **A. Kieninger-Graefitsch**, None; **G. Pierlot**, Idorsia Pharmaceuticals Ltd, 1, 3; **H. Farine**, Idorsia Pharmaceuticals Ltd, 1, 3, 4; **P. Kulig**, Idorsia Pharmaceuticals Ltd, 1, 3, 4; **G. Bourquin**, Idorsia Pharmaceuticals Ltd, 1, 3, 4; **M. Keller**, Idorsia Pharmaceuticals Ltd, 1, 3, 4; **P. Groenen**, Idorsia Pharmaceuticals Ltd, 1, 3, 4, Basel Area Swiss, 9; **M. Trendelenburg**, Idorsia Pharmaceuticals Ltd, 2, Novartis Institute of Biomedical Research, 2, F. Hoffmann-La Roche Ltd, 2, Swiss National Science Foundation 310030_172956, 2; **M. Murphy**, Idorsia Pharmaceuticals Ltd, 1, 3, 4.

Abstract Number: 2520

Treatment of SLE Patients with the Immunoproteasome Inhibitor KZR-616: Results from the First 3 Cohorts of an Open-Label Phase 1b Dose Escalation Trial

Richard Furie,[1] Darrin Bomba,[2] Maria Dall'Era,[3] Amber Khan,[4] Miguel Soneira,[4] Janet Anderl,[2] Jinhai Wang,[2] Christopher Kirk,[2] and Niti Goel[5], [1]Northwell Health, Great Neck, NY, [2]Kezar Life Sciences, SOUTH SAN FRANCISCO, CA, [3]University of California, San Francisco, San Francisco, CA, [4]Accurate Clinical Research, Houston, TX, [5]Kezar Life Sciences, Duke University School of Medicine, South San Francisco, CA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

n (%, # of AEs)	Cohort 1 45 mg N=8	Cohort 2 60 mg N=5	Cohort 2a 30→60 mg N=11	All KZR-616 N=24
TEAEs	8 (100.0, 44)	5 (100.0, 58)	7 (63.6, 47)	20 (83.3, 149)
Serious TEAEs	0 (0, 0)	1 (20.0, 1)	1 (9.0, 1)	2 (8.3, 2)
Serious infectious TEAEs	0 (0, 0)	0 (0, 0)	1 (9.0, 1)	1 (4.2, 1)
Non-serious infectious TEAEs	1 (12.5, 1)	0 (0, 0)	2 (18.2, 2)	3 (12.5, 3)
Any injection site reaction (ISR) TEAEs	6 (75.0, 35)	4 (80.0, 19)	4 (36.4, 24)	14 (58.3, 78)
Any non-ISR TEAE	5 (62.5, 9)	5 (100.0, 39)	5 (45.5, 23)	15 (62.5, 71)
Any non-ISR TEAE in ≥2 pts				
Nausea	2 (25.0, 2)	4 (80.0, 6)	3 (27.3, 4)	9 (37.5, 12)
Vomiting	1 (12.5, 1)	5 (100.0, 7)	2 (18.2, 3)	8 (33.3, 11)
Headache	1 (12.5, 1)	2 (40.0, 13)	1 (9.1, 1)	4 (16.7, 15)
Dizziness	1 (12.5, 1)	2 (40.0, 2)	0 (0, 0)	3 (12.5, 3)
Pyrexia	0 (0, 0)	2 (40.0, 2)	1 (9.1, 4)	3 (12.5, 6)
Chills	0 (0, 0)	1 (20.0, 1)	1 (9.1, 2)	2 (8.3, 3)

Table 1. Treatment Emergent Adverse Events (TEAEs), Safety Population

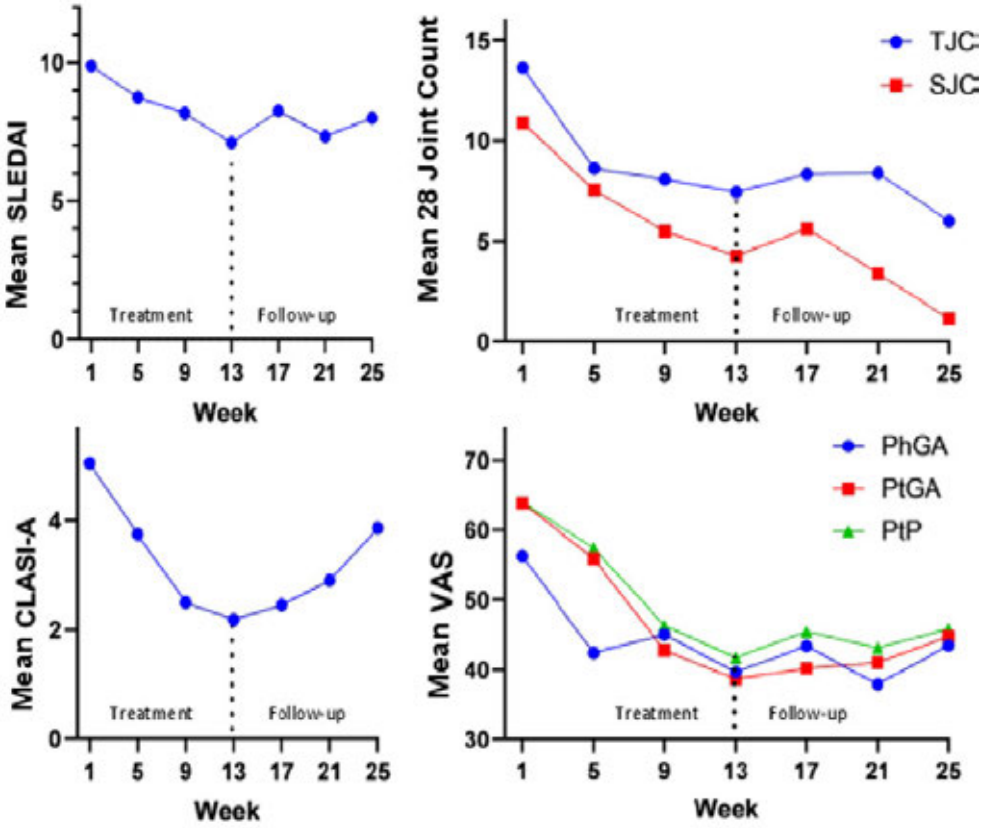

Figure 1. Efficacy Assessments in Evaluable Patients (N=16).

Background/Purpose: Nonspecific proteasome inhibitors, eg, bortezomib (BTZ), target both the constitutive and immuno- proteasome and are approved for the treatment of multiple myeloma. While BTZ has been used to treat refractory SLE and LN, it is associated with adverse events (AEs) that limit its use. KZR-616, a first-in-class selective immunoproteasome inhibitor, is highly active in murine SLE (Muchamuel et al. ARD 2018. 77:A685). In healthy vol-

unteers (HV), KZR-616 subcutaneously (SC) at 30 and 45 mg weekly (QW) was shown to be safe, be well tolerated, and achieve target levels of immunoproteasome inhibition (Lickliter et al. ARD 2018. 77:A1413). We report here the preliminary safety and efficacy of KZR-616 in the Phase (Ph) 1b portion of the MISSION Study KZR-616-002 in active SLE patients (pts) (NCT03393013).

Methods: This open-label multicenter dose escalation trial enrolled SLE pts with SLEDAI ≥4 despite stable background immunosuppressants, antimalarials, and/or corticosteroids (≤20 mg prednisone equivalent). The pts received KZR-616 at 45 mg (Cohort 1), 60 mg (Cohort 2), or 30 mg stepped up to 60 mg (Cohort 2a) SC QW through Week 13 (W13) with 12 weeks of follow up. Enrollment in Cohort 2a continued until ≥6 pts had ≥4 weeks of dosing with 60 mg. Safety data included AEs, vitals, ECGs, and laboratory tests. Pharmacokinetics (PK) and pharmacodynamics (PD) were assessed at baseline (BL) and W5. Efficacy measures included the SLEDAI, Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), 28 tender (T) and swollen (S) joint counts (JC), Physician (Ph) and Patient (Pt) Global Assessments (GA), and Patient Pain (PtP) in evaluable pts (receive ≥1 month of KZR-616; non-evaluable pts were replaced). No corrections were made for missing data.

Results: Twenty-four pts were enrolled as of 6 May 2019 (Table 1): 91.7% were female; BL median SLEDAI was 10.0. All pts received ≥1 dose of KZR-616. In each cohort, 3 pts discontinued early: 3 due to withdrawn consent in Cohort 1; 1 due to AE and 2 due to withdrawn consent in Cohort 2; 1 due to loss to follow-up and 2 due to AEs in Cohort 2a. The majority of AEs were mild (85.8%) to moderate (12.8%) with no signs of peripheral neuropathy or clinically significant hematologic AEs. One pt in Cohort 2 had a serious AE (SAE) of thrombotic microangiopathy and withdrew from the study. In Cohort 2a, there was 1 SAE of localized herpes zoster; the pt resumed and completed dosing after SAE resolution. All pts in Cohort 2 vomited within ~8-24 hours (h) of their first dose (typically resolving within 24 h); 2 of the 5 pts completed the study at either 45 or 60 mg. Cohort 2a pts (30 to 60 mg step up) tolerated 60 mg without significant vomiting. The PK and PD at 45 and 60 mg were similar to that measured for the same doses in HV. Figure 1 shows mean evaluable pt efficacy data. Of 11 pts reaching W13 to date, 3 of 6 with low BL complement levels had resolution; 5 (45.5%) had a SLEDAI improvement of ≥4 points from BL.

Conclusion: KZR-616 at 45 mg SC QW or with step up dosing to 60 mg appears safe and well tolerated and showed evidence of improvement in disease activity at W13 in active SLE pts on stable background therapy. The Ph 2 doses in the first randomized placebo-controlled trial with KZR-616 in active LN pts on mycophenolate and prednisone are 30 and 45 mg.

Disclosure: R. Furie, Biogen, 5, GlaxoSmithKline, 2, 5, UCB Pharma, 2, 5; **D. Bomba**, Kezar Life Sciences, 3, 4; **M. Dall'Era**, Biogen,, 5, Genentech, 5, Janssen Pharmaceuticals, 5, Kezar Life Sciences, 2, Pfizer, 5; **A. Khan**, Kezar Life Sciences, 2; **M. Soneira**, Kezar Life Sciences, 2; **J. Anderl**, Kezar Life Sciences, 3, 4; **J. Wang**, Kezar Life Sciences, 3, 4; **C. Kirk**, Kezar Life Sciences, 3, 4, 6; **N. Goel**, Kezar Life Sciences, 3, 4, 6.

Abstract Number: 2521

Rituximab Treatment Is Not Associated with Increased Risk of Infection or Mortality in Refractory SLE Patients: Results from the British Isles Lupus Assessment Group Biologics Registry (BILAG-BR)

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: SLE – Clinical Poster III: Treatment

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

	Deceased (n=28)	Alive (n=687)	(Ranksum Analysis) P-Value
Gender (M: F %) (n= 708)	7:21 (25% M, 75% F)	63:617 (9.26% M, 90.74% F)	0.01
Median Age at Diagnosis in years (IQR) (n = 713)	51.5(42.5-66.5)	39(30-49)	0.00
Median Disease Duration in years (IQR) (n=647)	13(11-19)	10(6-16)	0.03
Median Cumulative Rituximab dose in mg (IQR) (n=567)	2000 (2000-4000)	2000 (2000-4000)	0.53
Ethnicity (Caucasian: Non-Caucasian) (n =491)	17:5 (77.27% Caucasian, 24% Non-Caucasian)	291:178 (62.05% Caucasian, 37.95% Caucasian)	0.27
Median Last Oral Steroid Dose in mg (IQR) (n = 715)	10(5-14)	7(5-10)	0.17
Median Last SLEDAI score (IQR) (n=659)	2(2-6)	4(1-8)	0.74
Median Last SDI score (IQR) (n= 636)	2(0-3)	0(0-2)	0.01
Ever had Renal BILAG (A or B) (n = 677)	7/28 (25%)	94/649 (14.48%)	0.08
Baseline Hypogammaglobulinaemia (IgG < 6) (n=714)	4/28 (14.29%)	26/686 (3.79%)	0.01
Hypertension (n=715)	11/28 (39.29%)	159/687 (25.36%)	0.00
Ischaemic Heart Disease (n=715)	4/28 (14.29%)	11/687 (1.6%)	0.00
Diabetes Mellitus (n=715)	7/28 (25%)	15/687 (2.2%)	0.00
Asthma (n=715)	4/28 (14.29%)	48/687 (6.99%)	0.15
COPD (n=715)	1/28 (3.57%)	15/687 (2.18%)	0.63
Malignancy (n=715)	4/28 (14.29%)	26/687 (3.78%)	0.01
Median Number of Co-morbidities (IQR) (n=715)	2(0.5-4)	0 (0-2)	0.00

Table 1. Demographic data in RTX-treated patients by who died during follow-up

	RTX-treated patients who had serious infection within 9 months (n=56)	RTX-treated patients who didn't have serious infection within 9 months (n =659)	(Ranksum Analysis) P-value
Gender (n =708)	50:6 (F=89.29%, M= 10.71%)	588:64 (F= 90.18%, M =9.82%)	0.82
Median Age in Years (IQR) (n =713)	43 (33.5-53)	40 (30-50)	0.19
Median Disease duration In Years (IQR) (n = 647)	10 (6-14)	11 (6-17)	0.30
Baseline Median Oral Steroid Dosing in mg (IQR) (n = 713)	15 (7.5-30)	10 (5-20)	0.01
Baseline Renal Disease (BILAG A or B) (n =651)	8/50 (16.00%)	64/601 (10.65%)	0.24
Baseline Neurological Disease (BILAG A or B) (n = 651)	7/50 (14.00%)	73/601 (12.15%)	0.70
Baseline Haematological Disease (BILAG A OR B) (n = 651)	4/50 (8.00%)	31/601 (5.16%)	0.39
Baseline Musculoskeletal Disease (BILAG A OR B) (n = 651)	16/50 (32.00%)	237/601 (39.43%)	0.30
Baseline Median SLEDAI Score (IQR) (n= 648)	8 (4-14)	8 (4-12)	0.69
Baseline Median SDI Score (IQR)(n = 617)	1 (0-2)	0 (0-1)	0.07
Baseline Hypogammaglobulinaemia: IgG < 6 (n= 714)	5/55 (9.09%)	25/659 (3.79%)	0.06

Table 2. Demographic data in RTX-treated patients who suffered serious infection during follow-up.

Background/Purpose: Mortality in Systemic Lupus Erythematosus (SLE) is increased compared to the general population. We sought to investigate mortality rates and associated factors in a cohort of refractory SLE patients treated with Rituximab (RTX).

Methods: Patients recruited to a national biologics registry (first or repeat cycle of RTX-treated and standard of care-SOC) groups were included. Demographics, concurrent medication use, disease activity (BILAG 2004/SLEDAI-2K) and damage scores (SLICC/ACR-Damage Index -SDI) were recorded. Information regarding mortality and infection was collected from study centres and the national death registry. Serious infection events (SIEs) were defined as any infection resulting in treatment with intravenous antibiotics, hospitalization, disability or death. An infection occurring with 9 months of treatment was classified as associated with RTX. Logistic regression analysis was performed using Stata (v14).

Results: 830 patients were included (715 RTX and 115 SOC-treated) with 2693 person years of follow-up. 33 deaths were reported and there was no difference in mortality between RTX and SOC groups – 28 (3.9%) RTX-treated patients died vs 5 SOC (4.3%) (1.2 deaths vs 1.5 deaths/100 pt yrs follow up). Median cumulative RTX dose did not differ between deceased and alive groups.

The primary cause of death was identifiable in 24 RTX-treated patients and included infection (n=11, 45.83%), ischaemic heart disease (n=5, 20.83%) and malignancy (n=4, 16.67%). Factors associated with mortality in the RTX group included male sex, disease duration, older age at diagnosis, hypogammaglobulinaemia and higher SDI. There was also an excess of traditional cardiovascular risk factors including hypertension and diabetes in the deceased group (Table 1).

125 SIEs occurred in 56 patients (7.8%) and 18 SIEs occurred in 7 patients (6.1%) in the RTX and SOC groups respectively during 9 months follow-up. SIE rates did not differ between groups (5.29 in RTX vs 5.46 in SOC /100 pt. yrs. follow up). The commonest SIEs in the RTX group were respiratory (n= 35, 28%). Patients who suffered SIEs within the RTX group had significantly higher baseline steroid dosing (15mg vs 10mg, p= 0.01) and demonstrated a trend to older age at recruitment, renal involvement, hypogammaglobulinaemia and higher SDI (Table 2).

Logistic regression analysis of the RTX group identified previous myocardial infarction (OR= 12.33, 95% CI 1.57-97.48), hypogammaglobulinaemia (OR= 4.25, 95% CI 1.06-16.91), diabetes (OR= 4.30, 95% CI =1.55-11.86), malignancy (OR= 3.64, 95% CI 1.51-8.81), respiratory disease (OR 2.61, 95% CI 1.15-5.90), total previous immunosuppressant use (OR 1.27, 95% CI = 1.02-1.58), SDI (OR 1.26, 95% CI 1.05-1.51) and baseline steroid use (OR 1.02, 95% CI 1.00-1.05) as significant predictors of SIEs within 9 months of treatment.

Conclusion: Despite having refractory disease, RTX-treated patients did not exhibit increased mortality or SIE rates compared to patients receiving SOC. Mortality was instead associated with co-morbidities as well as some SLE severity markers. Monitoring higher risk individuals more closely and proactive management of these risk factors may further improve outcomes in this refractory population.

Disclosure: S. McDonald, None; **E. McCarthy**, None; **A. Aksoy**, None; **B. Parker**, Abbvie, 5, Astra Zeneca, 5, Astra Zenica, 5, Bristol-Myers Squibb, 5, Celltrion, 5, GlaxoSmithKline, 2, 5, GSK, 2, 5, Pfizer, 5, Sanofi Genzyme, 2, UCB, 5, UCB Pharma, 5; **I. Bruce**, Astra Zenica, 5, AstraZeneca, 5, Eli Lilly, 5, 8, Genzyme Sanofi, 2, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, 8, ILTOO, 5, Iltoo, 5, MedImmune, 5, 8, Medimmune, 5, Merck Serono, 5, 8, Merk Serono, 5, Roche, 5, 8, Sanofi Genzyme, 2, UCB, 2, 5, 8, UCB Pharma, 5, 8.

Abstract Number: 2522

Frequency and Early Prediction of Hydroxychloroquine Induced Retinopathy in SLE

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In 2016, the American Academy of Ophthalmology (AAO) published recommendations designed to reduce hydroxychloroquine induced retinopathy via early detection and reduction of hydroxychloroquine dosing from 6.5 mg/kg to less than 5 mg/kg. We prospectively determined the frequency and the predictive role of blood levels of hydroxychloroquine to identify those at greater future risk of retinopathy. Blood hydroxychloroquine levels are preferred over plasma levels, as they more accurately reflect exposure over the last month.

Methods: 382 SLE patients were examined by ophthalmologists with retina specialization, with a fundus examination and one or more of the newer retinal screening tests: Spectral-Domain Optical Coherence Tomography (OCT); Multifocal Electroretinogram (mfERG); Microperimetry (MP1); and Fundus Autofluorescence (FAF). Hydroxychloroquine blood levels were tested at every visit and quantified by liquid chromatography-tandem mass spectrometry.

Results: Twenty-three patients had confirmed hydroxychloroquine toxicity for an overall retinopathy frequency of 4.3%. The frequency of retinopathy was: 1% in the first 5 years, 1.8% from 6 to 10 years, 3.3% from 11 to 15 years, 11.5% from 16 to 20 years, and 8.0% after 21 years of use (Table 1). Higher hydroxychloroquine blood levels (both mean and maximum) predicted later hydroxychloroquine retinopathy (Table 2).

Conclusion: The frequency of retinopathy in our prospective study was much less than in the retrospective Kaiser Permanente study. Hydroxychloroquine blood levels in the upper tertile predicted retinopathy. Mean hydroxychloroquine levels likely better predict risk than the maximum level. Hydroxychloroquine blood levels would allow clinicians to either decrease the dose or increase monitoring in those with blood levels in the highest tertile. Currently, however, availability of hydroxychloroquine blood levels has been limited.

Duration of use (years)	Total	N	Percent	P-value	P-value for Trend
5 or less	103	1	0.97%	0.0006	0.0002
6 to 10	109	2	1.83%		
11 to 15	91	3	3.30%		
16 to 20	96	11	11.46%		
21 or more	75	6	8.00%		

Table 1. Frequency of Hydroxychloroquine Retinopathy by Duration of Use

	No Toxicity n (%)	Toxicity n (%)	P-value	P-value for Trend
HCQ Maximum Tertiles (ng/mL)			0.0340	0.0143
0 – 1182	161 (98.8%)	2 (1.2%)		
1183 – 1752	157 (95.2%)	8 (4.8%)		
1753 – 6281	153 (93.3%)	11 (6.7%)		
HCQ Mean Tertiles (ng/mL)			0.0124	0.0027
0 – 741	162 (98.8%)	2 (1.2%)		
741.5 – 1176.5	158 (96.3%)	6 (3.7%)		
1177 – 3513	151 (92.1%)	13 (7.9%)		

Table 2. Hydroxychloroquine Toxicity in Each Hydroxychloroquine Blood Level Tertile

Disclosure: J. Li, None; **D. Goldman**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 2523

Contemporary Prescription Opioid Use and Predictors Among Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: SLE is a complex illness that can be associated with chronic pain. In recent years, an international opioid epidemic has become a major public health concern and is attributed, in part, to prescription opioids. We assessed contemporary patterns of opioid prescribing among patients with SLE in a general population context and examined potential associations with prescription opioid use.

Methods: Using a United Kingdom general population database, we conducted a cohort study of adult SLE patients, identified by Read codes. The exposures of interest were opioid prescriptions between January 1, 2007 and December 31, 2016. We classified opioids as weak, including tramadol and codeine, and strong, including hydrocodone, morphine, fentanyl, oxycodone, hydromorphone, and methadone. We examined the proportion of patients receiving prescriptions for weak and strong opioids and performed logistic regression to assess whether prescription use of these medications varied by age, sex, duration of SLE, other medication use for SLE, comorbid conditions, lifestyle exposures, and socioeconomic status. We adjusted for age and sex.

Results: Of 10,784 SLE patients, (86% female, mean age 51.2 years), 32% were prescribed weak opioids and 10% were prescribed strong opioids during the study period. 21% and 7% received multiple prescriptions for weak and strong opioids, respectively. Concomitant diagnoses of fibromyalgia and OA each increased the odds of receiving prescription opioids (adjusted odds ratios [aOR] for strong opioids: 2.37 [96% CI 1.84-3.06] and 1.22 [95% CI 1.03-1.44] for fibromyalgia and OA, respectively) (**Table 1**). SLE patients who were also taking NSAIDs, DMARDs, or glucocorticoids each had increased odds of receiving prescription opioids. Current smokers were also more likely to be prescribed prescription opioids. There was a trend towards higher odds of prescription opioid use with increasing deprivation score, a measure of socioeconomic status; the aOR was 1.33 (95% CI 1.03-1.71) for weak opioid use among the highest deprivation quintile.

Conclusion: In this general population-based cohort study, nearly one-third of SLE patients were prescribed weak opioids and 10% were prescribed strong opioids. Prescription opioid use is higher among patients who are also taking NSAIDs, glucocorticoids, and DMARDs, among those with lower socioeconomic status, and in those with concomitant fibromyalgia or OA. These findings indicate the use of these potentially dangerous medications among a substantial portion of SLE patients. Future studies should assess the impact of opioid usage on mortality and other important outcomes among patients with SLE.

Table 1. Associations with Prescription Opioid Usage Among Patients with SLE

Characteristics	New weak opioid prescription			New strong opioid prescription		
	N (%)	Crude OR (95% CI)	Adjusted* OR (95% CI)	N (%)	Crude OR (95% CI)	Adjusted* OR (95% CI)
Sex						
Female	3,010 (34)	1.00 (Ref)	1.00 (Ref)	934 (11)	1.00 (Ref)	1.00 (Ref)
Male	488 (25)	0.66 (0.59-0.74)	0.69 (0.61-0.77)	166 (9)	0.80 (0.68-0.95)	0.78 (0.67-0.94)
Age						
< 30 Years	183 (19)	1.00 (Ref)	1.00 (Ref)	44 (5)	1.00 (Ref)	1.00 (Ref)
30-39 Years	478 (29)	1.70 (1.40-2.07)	1.74 (1.43-2.11)	113 (7)	1.51 (1.06-2.16)	1.60 (1.11-2.29)
40-49 Years	759 (33)	2.10 (1.75-2.52)	2.19 (1.82-2.65)	194 (8)	1.92 (1.37-2.69)	2.05 (1.46-2.89)
>50 Years	2,078 (35)	2.31 (1.95-2.74)	2.27 (1.91-2.70)	749 (13)	3.03 (2.21-4.13)	2.94 (2.14-4.03)
Duration of SLE						
<5 years	1,641 (31)	1.00 (Ref)	1.00 (Ref)	504 (10)	1.00 (Ref)	1.00 (Ref)
>5 years	1,857 (34)	1.14 (1.05-1.23)	1.23 (1.12-1.35)	596 (11)	1.16 (1.02-1.31)	1.35 (1.17-1.55)
Other Medication Use						
DMARD non-user	2,059 (29)	1.00 (Ref)	1.00 (Ref)	648 (9)	1.00 (Ref)	1.00 (Ref)
DMARD user	1,439 (39)	1.59 (1.46-1.73)	1.55 (1.41-1.69)	452 (12)	1.41 (1.24-1.60)	1.48 (1.29-1.69)
NSAIDs non-user	1,076 (27)	1.00 (Ref)	1.00 (Ref)	679 (9)	1.00 (Ref)	1.00 (Ref)
NSAIDs user	1,422 (46)	2.32 (2.12-2.53)	2.15 (1.97-2.36)	421 (14)	1.63 (1.44-1.86)	1.57 (1.37-1.80)
Glucocorticoid non-user	2,386 (29)	1.00 (Ref)	1.00 (Ref)	646 (1)	1.00 (Ref)	1.00 (Ref)
Glucocorticoid user	1,112 (41)	1.69 (1.55-1.85)	1.46 (1.33-1.61)	454 (17)	2.35 (2.06-2.67)	1.92 (1.68-2.21)
Alcohol use						
Non-user	975 (37)	1.00 (Ref)	1.00 (Ref)	364 (14)	1.00 (Ref)	1.00 (Ref)
Current user	2,119 (32)	0.81 (0.74-0.89)	0.89 (0.81-0.99)	614 (9)	0.64 (0.56-0.74)	0.74 (0.64-0.85)
Smoking Status						
Non-user	2,463 (32)	1.00 (Ref)	1.00 (Ref)	736 (9)	1.00 (Ref)	1.00 (Ref)
Current user	990 (36)	1.20 (1.09-1.32)	1.32 (1.20-1.47)	347 (13)	1.38 (1.20-1.59)	1.70 (1.46-1.98)
Fibromyalgia						
No	3,272 (32)	1.00 (Ref)	1.00 (Ref)	1,010 (10)	1.00 (Ref)	1.00 (Ref)
Yes	226 (56)	2.81 (2.29-3.43)	2.50 (1.96-2.96)	90 (22)	2.87 (2.11-3.43)	2.37 (1.84-3.06)
Osteoarthritis						
No	2,770 (30)	1.00 (Ref)	1.00 (Ref)	843 (9)	1.00 (Ref)	1.00 (Ref)
Yes	728 (45)	1.92 (1.72-2.14)	1.63 (1.45-1.84)	257 (16)	1.89 (1.62-2.19)	1.22 (1.03-1.44)
Deprivation Score						
0	140 (28)	1.00 (Ref)	1.00 (Ref)	36 (7)	1.00 (Ref)	1.00 (Ref)
1	676 (30)	1.14 (0.91-1.43)	1.06 (0.84-1.34)	209 (9)	1.29 (0.88-1.89)	1.11 (0.75-1.64)
2	569 (31)	1.21 (0.96-1.52)	1.13 (0.89-1.44)	190 (11)	1.50 (1.02-2.21)	1.32 (0.89-1.96)
3	615 (33)	1.29 (1.03-1.63)	1.20 (0.95-1.53)	190 (10)	1.49 (1.02-2.19)	1.31 (0.88-1.94)
4	510 (36)	1.48 (1.17-1.87)	1.36 (1.07-1.74)	153 (11)	1.43 (0.97-2.12)	1.21 (0.81-1.82)
5	376 (35)	1.43 (1.12-1.83)	1.33 (1.03-1.71)	123 (12)	1.66 (1.11-2.47)	1.42 (0.94-2.14)

*Adjusted for age and sex

Deprivation Score, measure of socioeconomic status, based on Townsend Deprivation Index. A score of 5 represents the most deprived and 0 represents the least deprived.

NSAIDs, non-steroidal anti-inflammatory drugs; DMARDs, disease modifying anti-rheumatic drugs

Table 1. Characteristics of SLE patients enrolled in this study *1 Two patients received multiple immunosuppressants. *2 Four patients received antiplatelet agent and anticoagulant agent. *3 Anti-dsDNA positive means anti ds-DNA titer increases over 12 IU/ml. *4 Low complement means any of C3, C4 and CH50 decreases to less 68mg/dl, less 12mg/dl, less 30U/ml.

Disclosure: A. Jorge, None; **N. Lu**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5.

Abstract Number: 2524

24-Month Outcomes Associated with Belimumab in Black/African-American Patients with Systemic Lupus Erythematosus in a Clinical Practice Setting in the United States

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SESSION INFORMATION
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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by diverse clinical manifestations and organ damage accrual. Black/African-American (B/AA) race is associated with higher SLE prevalence, disease activity, organ damage, and mortality than in Caucasian patients Although the efficacy and safety of belimumab (BEL) has been evaluated in adult patients of B/AA race with active SLE in a randomized clinical trial (EMBRACE; NCT01632241), real-world BEL effectiveness data in B/AA patients is limited. We report clinical outcomes in B/AA patients with SLE treated with BEL in a US clinical practice setting.

Methods: OBSErve US (evaluation **O**f use of **B**elimumab in clinical practice **SE**ttings in the US; GSK Study 117295) was an observational cohort study that randomly recruited non-academic rheumatologists from a national physician database. Data were collected on randomly selected adult patients with SLE who had received ≥8 BEL infusions as part of standard care. Patient demographics, disease characteristics, clinical outcomes, healthcare resource utilization, and oral corticosteroid (OCS) use were extracted from medical charts for 6 months prior to index date (1st BEL infusion), and then prospectively every 6 months up to Month 24. The primary outcome was physician-assessed overall clinical response relative to the previous 6-month time point. *Post hoc* analysis was performed (GSK Study 208439) on the B/AA subpopulation who completed the 24-month study period.

Results: OBSErve US enrolled 501 patients; 123 (24.5%) were B/AA and 69/123 (56.1%) B/AA patients continued to receive BEL at Month 24. Baseline (BL) characteristics of the Month 24 completers included: female 88.4%, mean age (standard deviation [SD]) 41.6 (12.5) years; severe SLE at BEL initiation (34.8%), and key clinical diagnoses: lupus nephritis (27.5%) and hypertension (26.1%). At Month 24, 33/69 (47.8%) B/AA patients had ≥50% improvement in physician-assessed overall clinical response between index and the previous 6 months, with further improvements observed in each subsequent 6-month period (**Figure 1**). By Month 24, 52/69 (75.4%) B/AA patients had mild SLE (severe SLE: 2.9%, **Figure 2**). Of the 69 B/AA patients with BL moderate/severe disease, 36/69 (52.2%) had consistent mild SLE at Month 6, 12, 18, and 24. At BEL initiation, 57/69 (82.6%) B/AA patients received OCS (mean [SD] dose: 19.7 [12.8] mg/day); and at Month 24, 40.4% had discontinued OCS with a mean (SD) OCS dose of 3.1 (3.2) mg/day.

Figure 1. Clinical responses in B/AA patients at Month 24 (n=69), according to physicians' impression of overall change in SLE manifestations relative to previous time point

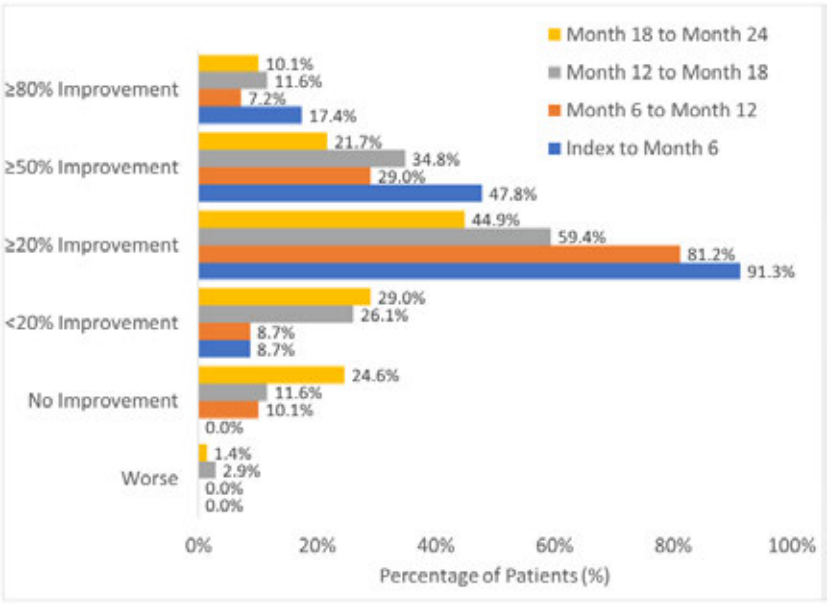
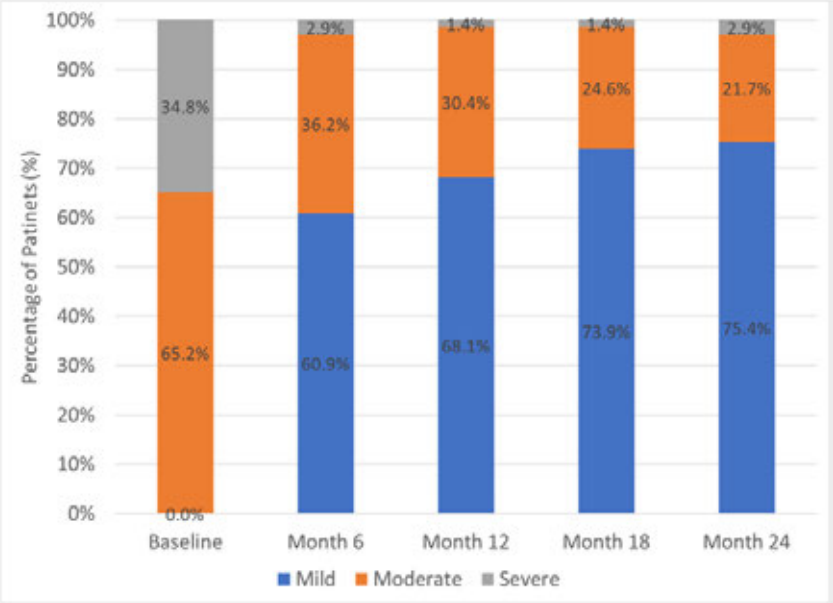


Figure 2. Disease severity according to physician assessment in B/AA patients at Month 24 (n=69 at each time point)



Conclusion: OBSErve US results from the B/AA SLE subpopulation who received BEL over 24 months in a clinical practice setting suggested substantial improvements in clinical outcomes (eg, reduced disease activity, severity, OCS utilization). While results may be limited with regards to sample size, subjective assessments, and analysis-by-responder bias, they demonstrated the effectiveness and durability of BEL in B/AA patients with SLE over 24 months. Results might inform decision-making when considering BEL for the treatment of B/AA patients with SLE, particularly in the context of published BEL efficacy and data from clinical trials.

Study Funding: GSK.

Disclosure: C. Collins, Exagen, 2, 5; **G. Kerr**, N/A (Received in the past for asymptomatic hyperuricemia and ultrasound study), 2, Novartis, 2; **J. Von Feldt**, GlaxoSmithKline, 1, 3; **B. Rubin**, GlaxoSmithKline, 1, 3; **A. Katz**, GlaxoSmithKline, 1, 3; **V. Castellano**, GlaxoSmithKline, 1, 3; **J. Chung**, GlaxoSmithKline, 1, 3; **C. Bell**, GlaxoSmithKline, 1, 3, 4.

Abstract Number: 2525

Within-Trial Cost Analysis of Flares from a Phase 3 Clinical Trial Evaluating Subcutaneous Belimumab for the Treatment of Systemic Lupus Erythematosus

Tasneem Lokhandwala,[1] Binglin Yue,[1] Anna Coutinho,[1] and **Christopher Bell** [2], [1]Xcenda AmerisourceBergen, Palm Harbour, FL, [2]GSK, Research Triangle Park, NC

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is a chronic autoimmune disease characterized by diverse clinical manifestations and flares associated with organ damage, resulting in substantial short-term management costs. Results from the BLISS-SC trial demonstrated that subcutaneous (SC) belimumab plus standard of care (SoC) compared with placebo plus SoC was associated with significant reductions in flares.[1] This study evaluated whether reductions in flares were associated with lower healthcare costs when comparing belimumab and placebo in the United States (US).

Methods: This retrospective, observational, *post hoc* economic analysis (GSK study 207134) from the US payer perspective used data from BLISS-SC, a 52-week, Phase 3, randomized trial (NCT01484496), comparing weekly belimumab 200 mg SC plus SoC and placebo plus SoC in adults with active SLE. The primary endpoint was the cost of treating severe flares; the secondary endpoint was the cost of treating flares of any severity. The time horizon was 52 weeks. Unit cost per flare (2017 US$) was calculated from an analysis using an algorithm to identify flares in US claims data.[2] An event-based costing methodology was subsequently applied to flare events observed in BLISS-SC, allowing for a comparison of costs associated with treating flares in the belimumab group versus placebo. Generalized linear models with negative binominal distribution were used to predict adjusted rates of severe and mild/moder-

Figure 1. Adjusted costs associated with treating SLE flares

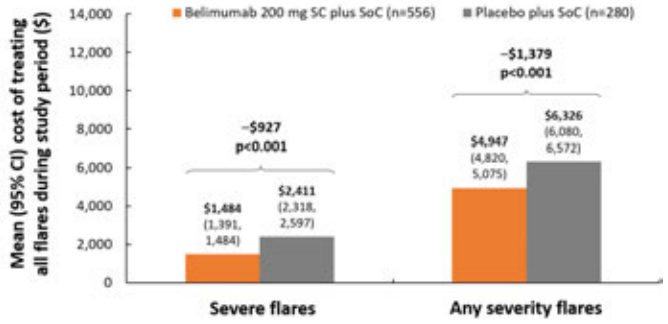
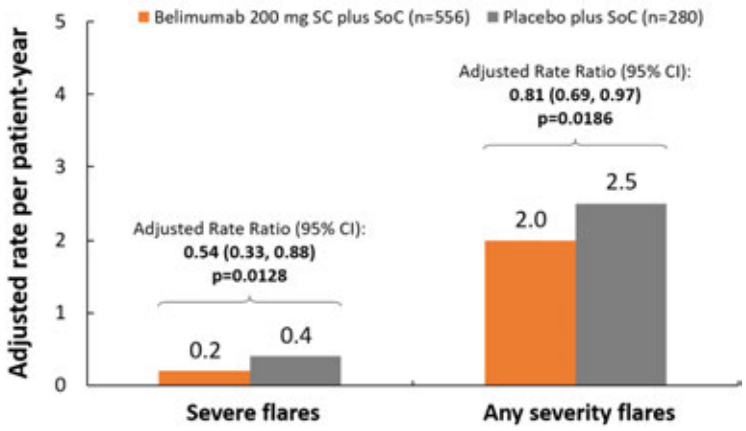


Figure 2. Adjusted rates of SLE flares per patient-year by severity



ate flares per patient. Adjusted rates of flares per patient were then multiplied by the flare unit cost (from claims data) to obtain adjusted costs associated with treatment of severe and mild/moderate flares. The mean (95% confidence interval [CI]) adjusted costs of any severity flares were computed by adding the estimated costs of severe and mild/moderate flares per patient.

Results: 836 patients from the intent-to-treat BLISS-SC population were included (belimumab plus SoC, n=556; placebo plus SoC, n=280); mean (standard deviation, SD) age was 38.6 (12.3) years; 94.4% were female. The mean (SD) unit cost was $9,273 ($38,800) per severe flare and $2,303 ($7,821) per mild/moderate flare. Mean adjusted predicted costs associated with treating flares during follow-up were significantly lower in the belimumab plus SoC group than in the placebo plus SoC group (severe flares, $927 lower, p< 0.001; flares of any severity, $1,379 lower, p< 0.001) (**Figure 1**). The adjusted rate of severe flares per patient-year was lower in the belimumab plus SoC versus the placebo plus SoC group (**Figure 2**).

Conclusion: This *post hoc* analysis of BLISS-SC data showed significantly lower costs of treating flares in patients with SLE treated with SC belimumab plus SoC compared with placebo plus SoC. Although the study is representative of a select clinical trial population and may differ from real-world patients with SLE, these results may help inform decision makers considering the introduction of SC belimumab to their healthcare system.

Study funding: GSK. Medical writing support: Gosia Carless, PhD, Fishawack Indicia Ltd, UK (funded by GSK).

[1]Stohl W, *et al. Arthritis Rheum.* 2017;69(5):1016–27
[2]Garris C, *et al. J Med Econ.* 2013;16(5):667–77

Adjusted cost estimates were obtained by multiplying the unit cost of flares by the adjusted rate of flares. The adjusted rate of flares was obtained using a generalized linear model with negative binominal distribution. Treatment arm (belimumab versus placebo) was used to predict the flare rate; other covariates included baseline complement levels (low C3 and/or low C4 versus no low C3 or C4), race (African-American versus other), and baseline Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index score (≤9 versus ≥10). Patient follow-up time as log10 (patient-years) was used as an offset variable in the model.

Disclosure: T. Lokhandwala, Xcenda, 3; **B. Yue**, AmerisourceBergen, 1, Xcenda, 3; **A. Coutinho**, AmerisourceBergen, 1, Xcenda, 3; **C. Bell**, GlaxoSmithKline, 1, 3, 4.

Abstract Number: 2526

Antimalarial Agents Improve Physical Functioning in Patients with Systemic Lupus Erythematosus

Ioannis Parodis,[1] Sofia Soukka,[1] Alvaro Gomez,[1] Yvonne Enman,[1] Petter Johansson,[1] Sharzad Emamikia,[1] and Katerina Chatzidionysiou[1], [1]Division of Rheumatology, Department of Medicine, Karolinska Institutet, Stockholm, Sweden

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) suffer an impaired health-related quality of life (HRQoL), and the majority of them experience fatigue as a major problem. Traditionally, treatment of SLE has been symptomatic, and antimalarial agents (AMA) are considered a cornerstone of SLE treatment. In previous literature, results regarding the effect of antimalarial agents on HRQoL have been conflicting. In this study, we aimed at investigating the potential influence of AMA on SLE patients' self-perception of HRQoL aspects.

Methods: We utilised pooled baseline data from the BLISS-52 and BLISS-76 clinical trials of belimumab (n=1684). Access to data was granted by GlaxoSmithKline. The patients' HRQoL and fatigue were self-reported using the Medical Outcomes Study (MOS) short form 36 (SF-36) health survey, the functional assessment of chronic illness therapy (FACIT)-Fatigue scale and the three-level ^{EuroQol}-5 Dimension (EQ-5D) questionnaire. Minimal clinically important difference (MCID) was set to ≥5.0 points for SF-36 subscales, ≥2.5 points for SF-36 component summary scores, and ≥4 points for FACIT-Fatigue scores. High disease activity was defined as a SELENA-SLEDAI score ≥10. Organ damage was assessed using the SLICC/ACR Damage Index (SDI). The non-parametric Mann-Whitney *U* test was used for comparisons between AMA users and non-users. Linear regression models were next used in order to adjust for possible confounding factors; these included age, sex, ethnic origin, SLE disease activity, SLE duration, organ damage, corticosteroid use and use of other immunosuppressive agents.

Results: Results are presented as mean values ± standard devation. Patients receiving AMA (n=1098) performed better than patients who did not receive AMA (n=586) with regard to SF-36 physical component summary (PCS) scores (39.6 ± 9.5 versus 38.1 ± 9.9; P=0.001), physical functioning (61.1 ± 24.9 versus 55.0 ± 26.5; P< 0.001), role physical (53.2 ± 26.9 versus 50.3 ± 27.7; P=0.036), bodily pain (49.5 ± 23.8 versus 47.1 ± 25.3; P=0.016), FACIT-Fatigue scores (30.5 ± 11.8 versus 29.3 ± 11.9; P=0.046), EQ-5D scores (0.75 ± 0.18 versus 0.72 ± 0.19; P=0.004) and EQ-5D visual analogue scale (VAS) scores (64.6 ± 19.4 versus 61.7 ± 18.6; P=0.001). The difference in SF-36 physical functioning was the greatest among the SF-36 parameters, exceeding the corresponding MCID (≥5.0 points). The association between AMA use and better physical functioning was still significant after adjustment for confounding factors (standardised coefficient, β =0.08; P=0.001). In this analysis, Asian patients performed better in physical functioning (β =0.07; P=0.004) while African/African American patients performed worse (β =-0.07; P=0.003). High disease activity (β =-0.09; P< 0.001) and organ damage (β =-0.12; P< 0.001) were also independent factors of worse physical functioning, whereas corticosteroid use independently improved the outcome (β =0.06; P=0.022).

Conclusion: In the SLE populations of the BLISS-52 and BLISS-76 clinical trials, AMA use was associated with favourable HRQoL in terms of physical functioning independently of other factors.

Disclosure: I. Parodis, None; **S. Soukka**, None; **A. Gomez**, None; **Y. Enman**, None; **P. Johansson**, None; **S. Emamikia**, None; **K. Chatzidionysiou**, None.

Abstract Number: 2527

Cytokine and Autoantibody Profiles During Treatment with Belimumab in Patients with Systemic Lupus Erythematosus

Ioannis Parodis,[1] Emil Åkerström,[1] Christopher Sjöwall,[2] Azita Sohrabian,[3] Andreas Jönsen,[4] Alvaro Gomez,[1] Martina Frodlund,[2] Agneta Zickert,[1] Anders Bengtsson,[4] Johan Rönnelid,[3] and Iva Gunnarsson[1], [1]Division of Rheumatology, Department of Medicine, Karolinska Institutet, Stockholm, Sweden, [2]Department of Clinical and Experimental Medicine, Rheumatology/Division of Neuro and Inflammation Sciences, Linköping University, Linköping, Sweden, [3]Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden, [4]Lund University, Lund, Sweden

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: SLE – Clinical Poster III: Treatment

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The anti-BAFF monoclonal belimumab is approved for the treatment of systemic lupus erythematosus (SLE) since 2011. Effects of belimumab on anti-double stranded (ds)DNA levels, as well as serum levels of B cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL), both belonging to the tumour necrosis factor (TNF) ligand superfamily, have been demonstrated in previous studies. We investigated whether belimumab treatment impacts levels of other cytokines of interest in SLE (i.e. IFN-α2, IL-6, IL-10 and IL-17A), autoantibodies (i.e.anti-dsDNA, anti-TRIM21, anti-SSA (Ro60), anti-SSB, anti-Sm, anti-SmRNP, anti-U1-RNP, anti-histone, anti-ribosomal P, anti-PCNA antibodies), and circulating immune complexes (ICs).

Methods: Longitudinally collected serum samples for up to 24 months of treatment from 78 belimumab-treated patients with SLE from the Karolinska, Skåne and Linköping University hospitals were analysed. Serum cytokine levels were measured using Luminex xMAP technology (Milliplex Map kit HCYTOMAG-60K-04; EMD Millipore Corp., Billerica, USA). Nuclear antigen autoantibody specificities were determined by addressable laser bead immunoassay (ALBIA) using the Connective profile MX117 FIDIS kit (Theradiag, Paris, France). Circulating C1q-binding ICs were measured using enzyme-linked immunosorbent assay (ELISA) (Quanta Lite, Inova, San Diego, USA). P values < 0.05 derived from paired Wilcoxon signed rank tests between baseline and follow-up time points were considered statistically significant.

Results: In patients with detectable cytokine levels at baseline, serum levels of IFN-α2 were lower at month 6 (median: 8.9; IQR: 1.5–54.9 pg/mL) compared with baseline (median: 28.4; IQR: 20.9–100.3 pg/mL; P=0.043). Levels of IL-6 showed decreases from baseline (median: 7.1; IQR: 2.9–16.1 pg/mL) to month 6 (median: 0.5; IQR: 0.5–6.3 pg/mL; P=0.018) and throughout the 24-month follow-up. Levels of IL-10 (baseline median: 12.6; IQR: 2.8–29.7 pg/mL) showed more rapid decreases as soon as from month 3 (median: 1.8; IQR: 0.6–9.1 pg/mL; P=0.003) and remained significantly lower than baseline levels over the 24-month follow-up. Only one patient had detectable levels of IL-17A at baseline. In patients with positive autoantibody levels at baseline (>40 international or arbitrary U/mL), levels of anti-dsDNA (P< 0.001), anti-Sm (P=0.002), anti-SmRNP (P=0.028), anti-U1-RNP (P< 0.001) and anti-ribosomal P (P=0.012) antibodies decreased as soon as from month 3 and remained significantly lower than baseline levels over the study period. Anti-histone antibody levels showed decreases at month 3 (P=0.008) and month 6 (P=0.003) from treatment initiation, but were not significantly changed compared to baseline at later time points. In patients with

baseline circulating ICs 10.8 mg Eq/mL or higher (reference value), IC levels showed decreases at month 3 (P=0.028), month 6 (P=0.009) and month 12 (P=0.021), but not at month 24 (P=0.345).

Conclusion: In our cohort, belimumab treatment lowered IFN-α2, IL-6, IL-10 and circulating IC levels, as well as levels of multiple autoantibodies against nuclear components.

Disclosure: I. Parodis, None; **E. Åkerström**, None; **C. Sjöwall**, None; **A. Sohrabian**, None; **A. Jönsen**, None; **A. Gomez**, None; **M. Frodlund**, None; **A. Zickert**, None; **A. Bengtsson**, None; **J. Rönnelid**, None; **I. Gunnarsson**, None.

Abstract Number: 2528

Effect of Additional Administration of HCQ on Pro-inflammatory Cytokine Expression, Especially in Lupus Nephritis

Risa Wakiya,[1] Kiyo Ueeda,[2] Hiromi Shimada,[2] Shusaku Nakashima,[1] Mai Mahmoud Fahmy Mansour,[1] Mikiya Kato,[1] Taichi Miyagi,[1] Tomohiro Kameda,[1] and Hiroaki Dobashi[2], [1]Kagawa University, Kagawa, [2]Kagawa University, Kagawa, Japan

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine(HCQ) is recommended for all patients with SLE in EULAR recommendation 2019, however, there are not enough data about the effect of additional HCQ treatment on the expression of pro-inflammatory cytokines, which plays an important role in SLE pathogenesis. The aim of this study is to clarify the effect of additional HCQ treatment on pro-inflammatory cytokines in SLE patients with low disease activity(LDA).

Methods: All patients with LDA enrolled in this study started HCQ treatment and had been receiving oral HCQ continuously for at least 3 months without using other immunosuppressive treatments or glucocorticoids. LDA was defined as SELENA-SLEDAI score of 8 or less with no activity in major organ systems and current prednisolone or equivalent dose of 10mg per day or less and well-tolerated maintenance doses of immunosuppressant. Serum levels of IFN-α, MRP8, MRP14, TNF-α, IL-2, IL-6, IL-8, VEGF-A, MCP-1, MIP-1α, IL-1β, IL-1ra, and G-CSF were measured at the time of HCQ administration and 3 months later using ELISA (CircuLex ELISA Kit, MBL)(Human IFN-alpha ELISA Kit, R&D) or a multiplex immunoassay (Luminex Assay, R&D). Data was analyzed using JMP® 13 software (SAS Institute Inc., Cary, NC, USA).

Results: 42 patients were enrolled in this study (M:F; 4:38, average age; 41.3±13.3; Table 1). 19 cases were in sustained remission of lupus nephritis(LN) patients. Serum levels of MRP8, MRP14 and IL-1ra at baseline were significantly higher in patients with a history of LN compared with those without LN (p=0.012, p=0.0043 and p=0.0092, respectively). Serum levels of MRP8, MRP14, TNF-α, IL-6, VEGF-A, IL-1ra, and IL-2 decreased significantly 3 months after additional HCQ treatment. The expressions of IFN-α didn't decrease significantly in 9 cases that could be detected.

Serum levels of IL-8 and MIP-1a decreased 3 months after additional HCQ treatment, but the difference was not statistically significant (p=0.211, p=0.109). However, serum levels of IL-8 same as VEGF-A significantly decreased in patients with a history of LN (with LN: IL-8, p=0.0026; VEGF-A, p=0.048; without LN: IL-8, p=0.370; VEGF-A, p=0.284).

Characteristics	n=42
Female, no(%)	38(90)
Age, years, mean ± SD	41.4 ± 13.3
Disease duration, years, mean ± SD	14.8 ± 11.8
Complication	
APS	7 (17)
Past involvement	
Skin involvement	37 (88)
Renal involvement	19 (45)
Duration of CR free, years	6.0 ± 5.2
NPSLE	2 (5)
Concomitant immunosuppressive treatments	
Prednisone	
No.(%)	32 (86)
Median Dosage, mg/day (range)	5.0 (1-10)
Other immunosuppressant*1	24 (57)
Tacrolimus	13 (31)
Mycophenolate mofetil	7 (16)
Cyclosporine A	2 (5)
Mizoribine	1 (2)
Methotrexate	1 (2)
Azathioprine	2 (5)
Anti-thrombotic therapy	
Anti-thrombotic therapy*2	23 (55)
Antiplatelet agent	16 (38)
Anticoagulant agent	11 (26)
Positive rate of autoantibody	
Anti-Sm	8 (19)
Anti-RNP	20 (48)
Anti-SS-A	20 (48)
Anti-SS-B	9 (21)
Lupus anticoagulant	9 (21)
Anti-cardiolipin	16 (38)
Anti-β2GPI	3 (7)
Disease activity	
SELENA-SLEDAI score	3.7 ± 2.0
CLASI activity score	3.1 ± 3.1 (n=27)
CLASI damage score	0.5 ± 1.3 (n=27)
anti-dsDNA positive, no(%) *3	15 (36)
anti-dsDNA (IU/mL)	15.7 ± 18.2
C3 (mg/dL)	80.9 ± 23.7
C4 (mg/dL)	16.0 ± 7.9
CH50 (U/mL)	35.2 ± 8.7
low complement, no(%) *4	22 (52)
White Blood Cell (/μL)	4960.5 ± 1630.6
Lymphocytes (/μL)	1208.0 ± 673.9
Platelet ($\times 10^4$/μL)	21.5 ± 7.3

Table 1. Characteristics of SLE patients enrolled in this study *1 Two patients received multiple immunosuppressants. *2 Four patients received antiplatelet agent and anticoagulant agent. *3 Anti-dsDNA positive means anti ds-DNA titer increases over 12 IU/ml. *4 Low complement means any of C3, C4 and CH50 decreases to less 68mg/dl, less 12mg/dl, less 30U/ml.

In addition, the magnitude of the changes in serum IL-8 levels in patients with a history of LN was significantly higher than in those without a history of LN (p=0.0039; Figure 1). The changes of IL-8 levels were correlated with those of serum MRP8 (r=0.32, p=0.049, Figure2).

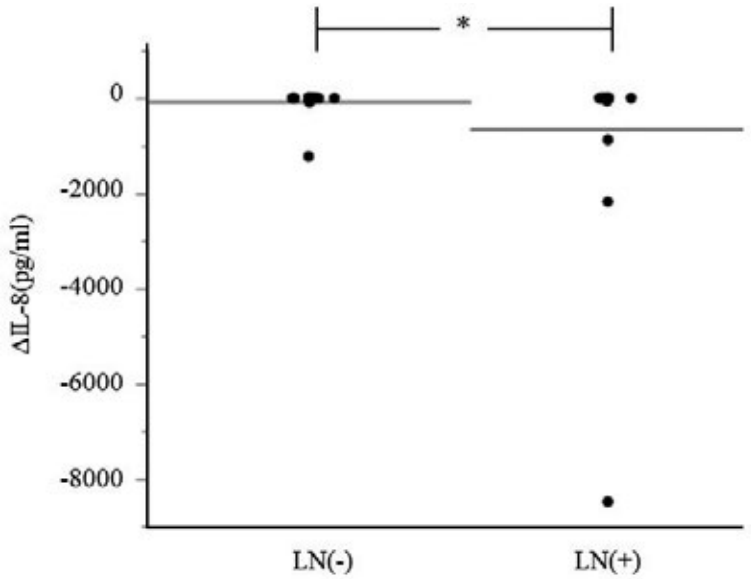


Figure 1. The magnitude of changes in serum IL-8 levels in patients with a history of LN were significantly higher than in patients without a history of LN. For statistical analyses * p<0.05, NS: Not significant, P value: Steel-Dwass test

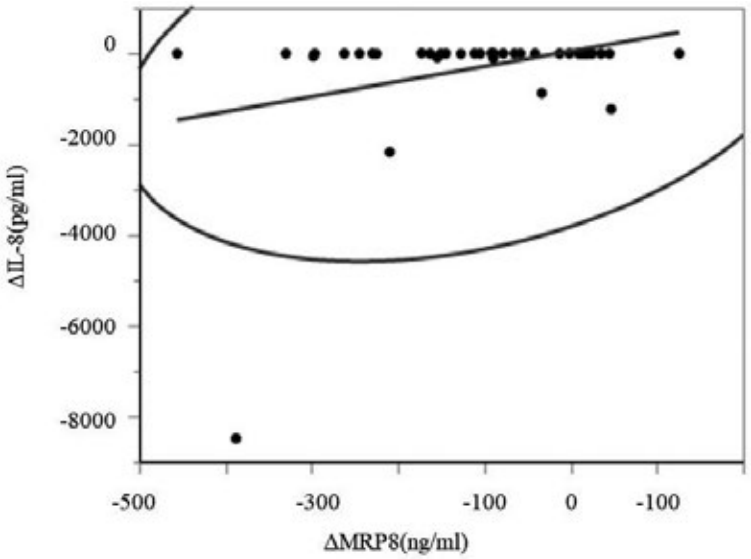


Figure 2. Correlation between the changes of IL-8 and those of MRP8 (r=0.32 p<0.05).

Conclusion: Additional HCQ treatment could decrease the several pro-inflammatory cytokines expression in SLE patients with LDA, especially in LN. Additionally, our data indicates that the effect of additional HCQ treatment could reduce the IL-8 expression in remission LN subjects significantly, which is reported to be associated with improvement of LN prognosis. HCQ use should be considered to be prescribed for all SLE patients as described in EULAR recommendation 2019.

Disclosure: R. Wakiya, None; **K. Ueeda**, None; **H. Shimada**, None; **S. Nakashima**, None; **M. Mahmoud Fahmy Mansour**, None; **M. Kato**, None; **T. Miyagi**, None; **T. Kameda**, None; **H. Dobashi**, None.

Abstract Number: 2529

Safety of Chloroquine and Hydroxychloroquine During Pregnancy: A Systematic Review and Meta-Analysis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

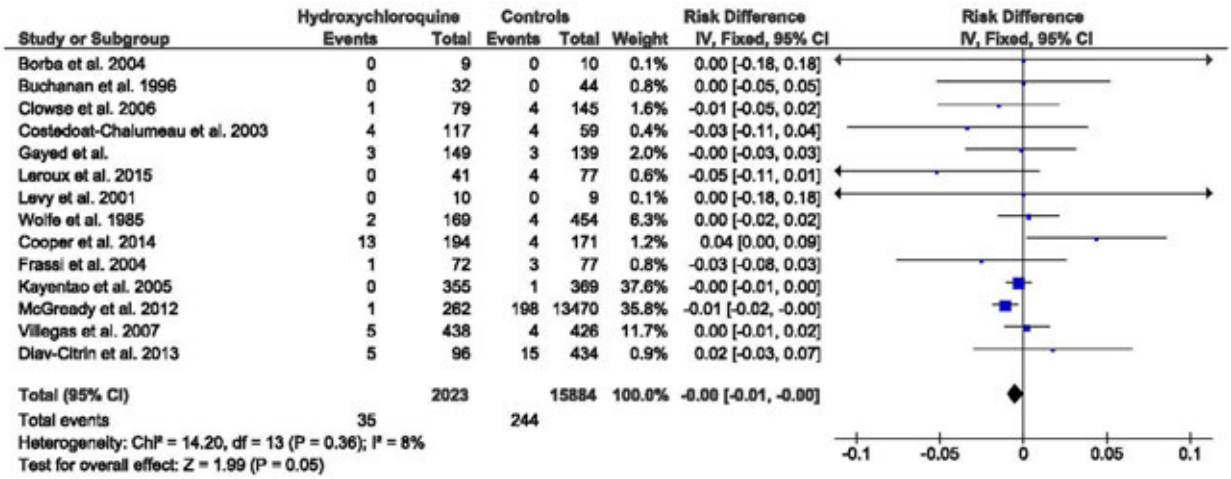
Session Title: SLE – Clinical Poster III: Treatment

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Chloroquine (CQ) and Hydroxychloroquine (HCQ) have been used for years during pregnancy for multiple indications (malaria prevention, autoimmune disorders, etc.…). Recently, some countries face restrictions to prescribe these drugs during pregnancy, due to report of ocular toxicity in animal models and potential genotoxicity. Change of the summary of product characteristics could significantly impact the adherence to this essential treatment for pregnancy in CQ/HCQ treated patients. The aim of this study was to perform a systematic review and a meta-analysis of fetal malformation rate under CQ and HCQ (all indications) during pregnancy. In the subgroup of patients suffering from an autoimmune disease, we performed an analysis of CQ and HCQ efficacy on maternal and pregnancy outcomes.

Methods: We systematically searched literature from inception to February 2 2019 (via Pubmed, Embase and abstracts from ACR and EULAR congresses) for studies that compare fetal malformation rate and pregnancy outcomes of CQ/HCQ versus placebo. Two independent reviewers carried out the review. A meta-analysis was performed, using the inverse variance approach, to estimate risk differences for malformation rate with its 95% confidence interval. Maternal and pregnancy outcomes will be analyzed with global odds-ratios and their 95% confidence interval.



Study or Subgroup	Hydroxychloroquine Events	Total	Controls Events	Total	Weight	Risk Difference IV, Fixed, 95% CI
Borba et al. 2004	0	9	0	10	0.1%	0.00 [-0.18, 0.18]
Buchanan et al. 1996	0	32	0	44	0.8%	0.00 [-0.05, 0.05]
Clowse et al. 2006	1	79	4	145	1.6%	-0.01 [-0.05, 0.02]
Costedoat-Chalumeau et al. 2003	4	117	4	59	0.4%	-0.03 [-0.11, 0.04]
Gayed et al.	3	149	3	139	2.0%	-0.00 [-0.03, 0.03]
Leroux et al. 2015	0	41	4	77	0.6%	-0.05 [-0.11, 0.01]
Levy et al. 2001	0	10	0	9	0.1%	0.00 [-0.18, 0.18]
Wolfe et al. 1985	2	169	4	454	6.3%	0.00 [-0.02, 0.02]
Cooper et al. 2014	13	194	4	171	1.2%	0.04 [0.00, 0.09]
Frassi et al. 2004	1	72	3	77	0.8%	-0.03 [-0.08, 0.03]
Kayentao et al. 2005	0	355	1	369	37.6%	-0.00 [-0.01, 0.00]
McGready et al. 2012	1	262	198	13470	35.8%	-0.01 [-0.02, -0.00]
Villegas et al. 2007	5	438	4	426	11.7%	0.00 [-0.01, 0.02]
Diav-Citrin et al. 2013	5	96	15	434	0.9%	0.02 [-0.03, 0.07]
Total (95% CI)		2023		15884	100.0%	-0.00 [-0.01, -0.00]
Total events	35		244			

Heterogeneity: Chi² = 14.20, df = 13 (P = 0.36); I² = 8%

Test for overall effect: Z = 1.99 (P = 0.05)

Heterogeneity was tested with Cochran's Q-test and I^2 value, and a random effect model was performed if needed. Revman software was used, considering a p-value threshold of 5%.

Results: From 2801 articles, the literature search revealed 90 articles and abstracts of potential interest, and further examination resulted in 14 studies fulfilling required criteria, with 12 cohort studies (7 prospective and 5 retrospective), and 2 randomized controlled trials. The selected articles include a total of 2023 exposed children of mothers treated by CQ/HCQ for an autoimmune disease (lupus, Sharp syndrome, Sjogren…) or malaria indication (treatment or prevention), compared to 15884 children in the control group.

The meta-analysis did not highlight any increase of malformation rate between the two groups (DR=0,00 $[-0.01, 0.00]_{95\%}$; p=0.05, I^2=8%).

In the secondary analysis on the maternofetal outcomes within studies on autoimmune diseases, the analyses did not reveal any difference between the two groups for occurrence of disease flare (OR=0.89 $[0.21, 3.77]_{95\%}$; p=0.88; I^2=79%), pre-eclampsia (OR=1.14 $[0.59, 2.23]_{95\%}$; p=0.69; I^2=5%), prematurity (OR=1.17 $[0.46, 2.97]_{95\%}$; p=0.75; I^2=81%), foetal growth restriction (OR=0.54 $[0.10, 2.82]_{95\%}$; p=0.46; I^2=89%), or congenital auriculo-ventricular block (OR=0.61 $[0.17, 2.1]_{95\%}$; p=0.43; I^2=0%). Conversely, the systematic literature reviews identified several cohort studies confirming the importance of HCQ in preventing lupus flares.

Conclusion: In our study, prenatal exposure to CQ or HCQ was not associated with any congenital abnormalities. HCQ should be continued in pregnancy for maintenance of remission or treatment of a disease flare.

Disclosure: T. Naveau, None; **O. Lichau**, None; **T. Barnetche**, None; **T. Schaeverbeke**, BMS, 5, Janssen, 5, Lilly, 5, Nordic Pharma, 5, Novartis, 5, Pfizer, 5, Roche Chugai, 5, Sanofi, 5; **E. Lazaro**, None; **M. Truchetet**, None; **C. Richez**, astrazeneca, 5, 8, BMS, 5, 8, Glenmark, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8.

Abstract Number: 2530

Safety, Pharmacokinetics, and Pharmacodynamics of a Lyophilized Drug Product of KZR-616, a Selective Inhibitor of the Immunoproteasome

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: KZR-616, a first-in-class selective inhibitor of the immunoproteasome, is being evaluated for the treatment of multiple autoimmune diseases, including LN and PM/DM. At 30 and 45 mg subcutaneously (SC) weekly (QW), KZR-616 is well tolerated and achieves target levels of immunoproteasome inhibition in healthy volunteers (HV) (Lickliter et al. ACR 2017). Initial doses of 60 mg or higher were associated with an adverse drug reaction including self-limited vomiting in both HV and SLE patients (pts) (Furie et al. EULAR 2019). Preliminary evidence from SLE pts suggests intrasubject dose escalation ('step-up dosing') may allow use of higher doses of KZR-616. Here we

n (%, # of TEAEs)	Cohort 1a 30→45→60 →75 mg N=7	Cohort 1b 30→60 mg N=9	Cohort 1c 30→75 mg N=6	All KZR-616 N=22	PBO N=7
TEAEs	7 (100.0, 52)	8 (88.9, 35)	6 (100.0, 37)	21 (95.5, 124)	5 (71.4, 13)
Study discontinuation due to TEAEs	2 (28.6, NA)	0 (0, 0)	1 (16.7, NA)	3 (13.6, NA)	1 (14.3, NA)
Serious TEAEs	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Non-serious Infectious TEAEs	0 (0, 0)	0 (0, 0)	1 (16.7, 1)	1 (4.5, 1)	0 (0, 0)
Any ISR TEAEs	7 (100.0, 22)	7 (77.8, 20)	5 (83.3, 10)	19 (86.4, 52)	4 (57.1, 8)
Any non-ISR TEAE	7 (100.0, 28)	6 (66.7, 15)	6 (100.0, 16)	19 (86.4, 59)	2 (28.6, 5)
Any non-ISR TEAE in ≥3 HV					
Headache	3 (42.9, 5)	3 (33.3, 3)	3 (50.0, 3)	9 (40.9, 11)	1 (14.3, 1)
Nausea	4 (57.1, 5)	2 (22.2, 2)	3 (50.0, 4)	9 (40.9, 11)	0 (0, 0)
Anemia/iron deficiency anemia	1 (14.3, 1)	0 (0, 0)	0 (0, 0)	1 (4.5, 1)	2 (28.6, 2)

Table 1. Treatment Emergent Adverse Events (TEAEs), Safety Population

Dose (mg)	Formulation	N	AUC (hr*ng/ml)	C_{max} (ng/ml)
30	Frozen[b]	12	201 (40.1)	75.1 (27.9)
	Lyophile[b]	19	195 (36.2)	75.5 (24.5)
45	Frozen[c]	12	397 (62.2)	155 (60.5)
	Lyophile[c]	6	307 (52.4)	90.1 (32.3)
60	Frozen[b]	12	411 (85.8)	160 (61.1)
	Lyophile[d]	11	431 (121)	140 (52.2)

Table 2. Mean (± SD) Exposure following SC administration of KZR-616 in healthy volunteers. (a) Combined cohort data; (b) Day 1; (c) Day 8; (d) Days 8 and 15

Dose (mg)	Formulation	N	% Inhibition
30	Frozen[b]	24	85.5 (0.9)
	Lyophile[b]	7	84.7 (1.2)
45	Frozen[b]	6	90.2 (0.7)
	Lyophile[c]	6	91.1 (1.1)
60	Frozen[b]	12	91.9 (0.5)
	Lyophile[d]	5	90.9 (1.1)
75	Lyophile[e]	2	92.0 (0.8)

Table 3. Mean (SEM) inhibition of immunoproteasome enzymatic activity following SC administration of KZR-616 in healthy volunteers. (a) Combined cohort data; (b) Day 1; (c) Day 8; (d) Day 15; (e) Day 22

report the preliminary results of a single-center, randomized, placebo (PBO)-controlled study evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) of a new lyophilized formulation of KZR-616 administered SC using step-up dosing (ACTRN12618002060224).

Methods: Female HV were enrolled because autoimmune diseases, eg, SLE, predominantly affect females who also have an apparent increased adverse drug reaction risk. There were 3 multiple ascending dose (MAD) SC cohorts (Table 1) and 3 single ascending dose intravenous (IV) cohorts at 15, 30, and 45 mg. Randomization of KZR-616:PBO

was 6:2 per cohort; HV who discontinued early could be replaced. Safety was assessed via adverse event (AE) monitoring, physical examinations, vital signs, electrocardiograms, and laboratory tests, with analyses both by cohort and by dose. Placebo data were pooled. Pharmacokinetics were measured by liquid chromatography tandem-mass spectrometry, and PD (immunoproteasome inhibition) was measured using enzymatic activity and active site binding (ProCISE) assays in peripheral blood mononuclear cells (PBMCs). Plasma cytokines/chemokines were measured by electrochemiluminescent detection (Meso Scale Diagnostics).

Results: Preliminary results from the SC cohorts are presented. There were 29 HV enrolled, 22 of whom received ≥1 dose of KZR-616. Average age was 22.6 years (PBO) and 27.9 years (KZR-616). In the SC cohorts, 95.5% of KZR-616 treated and 57.7% of PBO-treated HV experienced AEs (Table 1). All AEs were mild to moderate. The most common AEs were injection site reactions (ISRs), headache, and nausea, which were generally transient. The AE frequency or severity did not seem to increase with dose increase. There was one isolated Grade 3 laboratory value on KZR-616-treated: neutropenia in Cohort 1b at Day 4. The PK at 30, 45, and 60 mg were similar to data reported in the previous HV study (Table 2). Based on comparisons to the IV cohorts' PK, KZR-616 administered SC was 100% bioavailable. Inhibition of immunoproteasome enzymatic activity was also similar with SC administration of the new drug product as compared to previously reported data (Table 3).

Conclusion: No apparent dose limiting toxicities were observed in the MAD SC subjects at doses up to 75 mg when an initial dose of 30 mg was administered. The PK and PD in this study support the utilization of this lyophilized formulation of KZR-616 and administration of doses SC up to 75 mg in patients with rheumatic diseases.

Disclosure: B. Snyder, None; **D. Bomba**, Kezar Life Sciences, 3, 4; **K. Harvey**, Kezar Life Sciences, 5; **J. Anderl**, Kezar Life Sciences, 3, 4; **C. Kirk**, Kezar Life Sciences, 3, 4, 6; **J. Wang**, Kezar Life Sciences, 3, 4; **R. Fan**, Kezar Life Sciences, 3, 4; **N. Goel**, Kezar Life Sciences, 3, 4, 6.

Abstract Number: 2531

Low Vitamin D Is Associated with Miscarriage and Preterm Birth in SLE with a U-shaped Relationship

Michelle Petri,[1] and Jessica Li[1], [1]Johns Hopkins University School of Medicine, Baltimore, MD

First vitamin D Level (ng/mL)	Miscarriage		Preterm birth (<37 weeks)		Weeks of gestation (excl. miscarriage/ terminations)	
	OR (95% CI)	p-value	OR (95% CI)	p-value	Mean estimate (95% CI)	p-value
<20	4.32 (1.23 ,15.19)	0.0227	2.53 (1.14 ,5.64)	0.0232	-1.2 (-2.24 ,-0.16)	0.0239
20-30	4.75 (1.3 ,17.38)	0.0188	1.93 (0.87 ,4.28)	0.1045	-0.84 (-1.77 ,0.08)	0.0736
30-40	2.84 (0.78 ,10.37)	0.1132	1.81 (0.83 ,3.96)	0.1365	-0.87 (-1.8 ,0.06)	0.0664
40-50	Ref group		Ref group		Ref group	
50-60	4.66 (1.09 ,20.04)	0.0385	2.07 (0.65 ,6.58)	0.2161	-0.22 (-1.36 ,0.91)	0.6998
60+	4.62 (0.91 ,23.42)	0.0646	1.85 (0.43 ,7.93)	0.4090	-0.57 (-2.26 ,1.13)	0.5125

Table 1. Association between 25(OH) vitamin D levels and pregnancy outcomes adjusted for lupus anticoagulant

First vitamin D Level (ng/mL)	Miscarriage		Preterm birth (<37 weeks)		Weeks of gestation (excl. miscarriage/ terminations)	
	OR (95% CI)	p-value	OR (95% CI)	p-value	Mean estimate (95% CI)	p-value
<20	2.79 (0.46 ,16.82)	0.2629	4.74 (1.14 ,19.69)	0.032	-2.54 (-5.27 ,0.2)	0.0688
20-30	1.39 (0.26 ,7.51)	0.7009	1.12 (0.39 ,3.2)	0.8338	-0.19 (-1.58 ,1.2)	0.7874
30-40	1.84 (0.34 ,9.98)	0.4819	0.78 (0.29 ,2.08)	0.6152	0.5 (-0.7 ,1.7)	0.4120
40-50	1.00 (Ref Group)		1.00 (Ref Group)		0.00 (Ref Group)	
50-60	0.67 (0.23 ,1.97)	0.4704	1.01 (0.24 ,4.16)	0.9903	0.29 (-1.47 ,2.06)	0.7459
60+	7.47 (1.14 ,48.82)	0.0357	0.57 (0.05 ,7.21)	0.6662	0.94 (-0.8 ,2.67)	0.2902

Table 2. Association of 25(OH) vitamin D levels and pregnancy outcomes in those pregnancies in which level was measured in the first or second trimester (adjusted for lupus anticoagulant)

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In the general population, low vitamin D has been associated with adverse pregnancy outcomes including preterm birth, pre-eclampsia and small for gestational age. In the general pregnancy population, replacement of vitamin D has been proven to reduce adverse pregnancy outcomes. We examined whether low vitamin D was also associated with adverse pregnancy outcomes in a large lupus pregnancy cohort.

Methods: A total of 268 patients (431 pregnancies) had blood levels of 25 hydroxy vitamin D (25(OH) vitamin D) measured as part of cohort follow-up. Pregnancies were followed with outcomes characterized as miscarriage or preterm birth < 37 weeks. A GEE model was used to estimate odds ratios (OR) and significance.

Results: There were 365 (84.7%) live births, 51 (11.8%) miscarriages, and 15 (3.5%) terminations. 34.7% of patients were African-American, 54.9% were Caucasian, and 10.4% were of other ethnicities. Compared to the reference vitamin D group of 40-50 ng/mL, patients with a first vitamin D below 30 ng/mL during cohort follow up had significantly higher odds of miscarriage (Table 1), but a U-shaped curve was found, with higher risk at high 25(OH) vitamin D levels, as well. The result did not change after adjustment for lupus anticoagulant. Similarly, patients with first vitamin D below 20 ng/mL had significantly higher odds of preterm birth. There were 180 pregnancies (122 patients) in which 25(OH) vitamin D had been measured in the first or second trimester. In those, there remained a significant association of preterm birth with 25(OH) vitamin D levels < 20 ng/mL (Table 2). The OR for miscarriage (2.79), although high, did not reach statistical significance in this smaller sample.

Conclusion: We found a U-shaped relationship, with miscarriage and preterm birth more common at both LOW and at HIGH levels of 25(OH) vitamin D (with the reference group at 40-50 ng/mL). The association at low vitamin D levels

mirrors what has been found in non-SLE pregnancies. The increase at high levels, though, cannot be explained, and has not been identified in the general pregnancy population. Although calcium supplements and prenatal vitamins are commonly prescribed in all pregnancies, particular monitoring of 25(OH) vitamin D levels (and replacement in those who are low) is not routine in SLE pregnancy management. Our data show, though, that there is a potential "therapeutic window", such that over-replacement must be avoided.

Disclosure: M. Petri, Eli Lilly and Company, 5, Exagen, 2, 5; **J. Li**, None.

Abstract Number: 2532

Effect of Treatment on Antiphospholipid Antibodies in SLE

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Unlike primary antiphospholipid syndrome patients, most SLE patients with antiphospholipid antibodies are on one or more treatments for their SLE that might affect levels of their antiphospholipid antibodies. We examined the effect of prednisone and hydroxychloroquine on antiphospholipid antibodies in an SLE longitudinal cohort.

Definition of Antiphospholipid	Number of informative strata	Current Prednisone Dose	Odds ratio of having APL on visits by Prednisone exposure	P-value[1]
aCL IgG>20	211	No Prednisone	1.0 (Ref)	
		Some but less than 10mg/d	0.61 (0.46, 0.80)	0.0004
		10+mg/day	0.39 (0.28, 0.54)	<0.0001
aCL IgG>40	84	No Prednisone	1.0 (Ref)	
		Some but less than 10mg/d	0.55 (0.33, 0.91)	0.020
		10+mg/day	0.52 (0.29, 0.93)	0.027
aCL IgM>20	242	No Prednisone	1.0 (Ref)	
		Some but less than 10mg/d	1.02 (0.77, 1.36)	0.88
		10+mg/day	0.80 (0.58, 1.10)	0.17
aCL IgM>40	110	No Prednisone	1.0 (Ref)	
		Some but less than 10mg/d	1.14 (0.72, 1.81)	0.57
		10+mg/day	0.84 (0.50, 1.42)	0.52
aCL IgA>20	80	No Prednisone	1.0 (Ref)	
		Some but less than 10mg/d	0.69 (0.40, 1.19)	0.18
		10+mg/day	0.56 (0.29, 1.09)	0.088
aCL IgA>40	32	No Prednisone	1.0 (Ref)	
		Some but less than 10mg/d	1.20 (0.44, 3.24)	0.73
		10+mg/day	2.01 (0.67, 6.08)	0.21
dRVVT>45	372	No Prednisone	1.0 (Ref)	
		Some but less than 10mg/d	1.08 (0.88, 1.34)	0.45
		10+mg/day	1.01 (0.80, 1.27)	0.93
Any of the above	549	No Prednisone	1.0 (Ref)	
		Some but less than 10mg/d	0.92 (0.77, 1.09)	0.34
		10+mg/day	0.82 (0.67, 0.99)	0.048

Table 1. Odds ratio of having an antiphospholipid antibody on visits with various levels of prednisone compared to visits without prednisone

Definition of aPL	Number of informative strata [1]	Odds ratio of having the APL on visits with HCQ compared to visits without HCQ	P-value
aCL IgG>20	149	0.56 (0.43, 0.72)	<0.0001
aCL IgG>40	56	0.35 (0.22, 0.55)	<0.0001
aCL IgM>20	169	0.51 (0.39, 0.67)	0.0002
aCL IgM>40	80	0.56 (0.36, 0.87)	0.010
aCL IgA>20	56	1.08 (0.62, 1.87)	0.80
aCL IgA>40	25	2.28 (0.99, 5.26)	0.053
dRVVT>45	268	0.71 (0.58, 0.86)	0.0007
Any of the above	377	0.64 (0.55, 0.75)	<0.0001

[1] In each cell, individuals are informative if they have at least one visit with antiphospholipid positivity, at least one visit without antiphospholipid antibody, at least one visit with when treated with HCQ, and at least one visit when not treated with HCQ.

Table 2. Odds ratio of having antiphospholipid antibodies on visits with hydroxychloroquine compared to visits without hydroxychloroquine

Methods: 943 SLE patients, who were tested for each anticardiolipin isotype (aCL IgG, IgM and IgA; INOVA) and lupus anticoagulant (dRVVT with further confirmatory testing) for at least 10 quarterly clinic visits, were included. We compared visits positive for antiphospholipid antibodies to visits negative for antiphospholipid antibodies, with respect to treatment, using conditional logistic regression and conditioning on the patient.

Results: The effect of prednisone on anticardiolipin and dRVVT > 45 (with further confirmatory testing) is shown in Table 1. The effect of hydroxychloroquine is shown in Table 2.

Conclusion: Prednisone does not reduce IgM or IgA isotypes of anticardiolipin, or lupus anticoagulant. These results explain why prednisone does not reduce thrombosis in SLE. Hydroxychloroquine, on the other hand, significantly reduces all antiphospholipid types except for the IgA isotype of anticardiolipin. This may explain why IgA isotypes are more common in SLE. It may also explain why hydroxychloroquine leads to only a 50% reduction in thrombosis, as IgA isotypes do confer some risk of thrombosis.

Disclosure: M. Petri, Eli Lilly and Company, 5, Exagen, 2, 5; **L. Magder**, None; **D. Goldman**, None.

Abstract Number: 2533

Hydroxychloroquine Increases Low C3 in SLE

Michelle Petri,[1] and Jessica Li[1], [1]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine is considered an immunomodulatory that does not affect serology. Hydroxychloroquine (HCQ) was recently introduced into Japan. In SLE patients who started hydroxychloroquine, there was improvement in hypocomplementemia (Y Ikeda, H Tamaki, M Okada. Abstract, Lupus 2019 Meeting, San Francisco, CA, April 6, 2019). We asked whether this was true in United States patients as well.

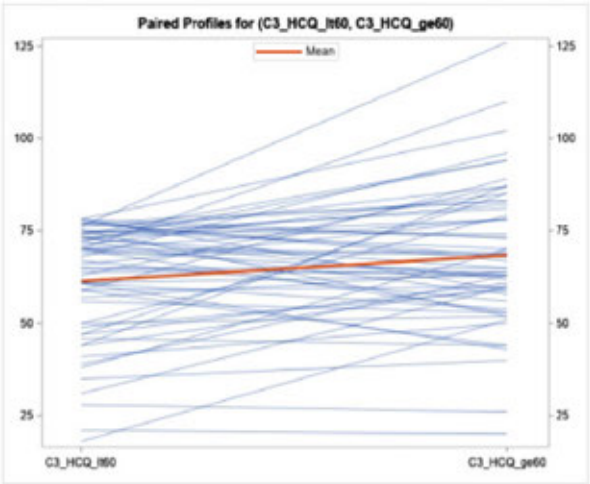

Figure 1. Improvement in C3 levels with HCQ

	Unadjusted		Adjusted[1]		Adjusted[2]	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
HCQ blood level (per 100 unit increase)	0.27 (0.07, 0.47)	0.0081	0.26 (0.06, 0.46)	0.0101	0.26 (0.06, 0.46)	0.0100
Prednisone (per unit increase)			0.03 (-0.07, 0.13)	0.5307	0.02 (-0.08, 0.12)	0.6823
BMI (per unit increase)					0.21 (0.01, 0.42)	0.0397
[1]adjusted for prednisone [2]adjusted for prednisone and BMI						

Table 2. Within Patient Analysis: Patient had at Least One Visit with HCQ Negative and Low C3

Methods: A paired analysis of visits where HCQ level was 0 and a visit where it was higher was done. HCQ blood levels were quantified by liquid chromatography-tandem mass spectrometry. The visit with HCQ level of 0 must also have had low C3 (C3 < 79). There were 59 paired visits with HCQ blood level of 0 at first visit. We took the first visit in which the HCQ blood level was 0. We also did a "within patient" analysis of all visits in a patient who had at least one visit with a HCQ blood level of 0, using a linear mixed effects model.

Results: Figure 1 shows the C3 levels in ng/mL for the paired visits. The average difference in C3 level between the visit with HCQ less than 60 ng/mL (negative) and the visit with HCQ >=60 ng/mL (positive) is 7.08 (p = 0.0022). Table 2 shows the "within patient" analysis of ALL visits, with a p-value of 0.008. HCQ blood level remained significant after adjusting for prednisone, or prednisone and body mass index (BMI).

Conclusion: HCQ increases low C3, confirming the Japanese finding. This may explain multiple benefits of HCQ such as prevention of renal lupus and prevention of thrombosis, in which low C3 is an important risk factor. It also may affect SLEDAI improvement in clinical trials, if SLE patients become more compliant with hydroxychloroquine.

Disclosure: M. Petri, Eli Lilly and Company, 5, Exagen, 2, 5; **J. Li**, None.

Abstract Number: 2534

Vitamin D Reduces Cardiovascular Risk Factors in SLE

Michelle Petri,[1] Jessica Li,[1] and Daniel Goldman[2], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Vitamin D has effects on the cardiovascular system, including decreased renin-angiotensin, decreased insulin resistance, increased vascular relaxation and decreased vascular smooth muscle cell proliferation, that suggest it should have benefits for cardiovascular risk factors. It already has a role in the control of SLE disease activity, as it in particular reduces the urine protein/cr ratio. We explored this in a longitudinal SLE cohort.

Methods: This analysis included 1,503 patients, contributing 21,216 visits with 25(OH) vitamin D levels from May 2009 to March 2019. They were observed from 1 to 48 visits with a median of 12 visits per patient. 134 patients (9%) had 1 visit, 300 (20%) had 2-5 visits, 234 (16%) had 6-10 visits, and 835 (56%) had 11 or more visits in this analysis. 92% of the patients were female, 50% Caucasian, and 41% African American. At the first visit when

Range of mean Vitamin D level	Unadjusted		Adjusted (1)		Adjusted (2)	
	Slope (95% CI)	p-value	Slope (95% CI)	p-value	Slope (95% CI)	p-value
0 to 50 ng/mL	-4.9 (-6.6, -3.1)	<0.0001	-5.9 (-7.7, -4.0)	<0.0001	-5.0 (-7.0, -3.1)	<0.0001
50+ ng/mL	3.9 (-1.0, 8.7)	0.1163	3.6 (-1.2, 8.4)	0.1379	3.2 (-1.4, 7.9)	0.1754

(1) adjusted for age, age-squared, sex, ethnicity

(2) adjusted for age, age-squared, sex, ethnicity, mean body mass index, mean prednisone dose, proportion of time on statins, and proportion of time on hydroxychloroquine

Table 1. Estimated difference in person-specific mean cholesterol per 10 ng/mL difference in person-specific mean vitamin D (model allowing slope to differ before and after 50 ng/mL)

Range of mean Vitamin D level	Unadjusted		Adjusted (1)		Adjusted (2)	
	Slope (95% CI)	p-value	Slope (95% CI)	p-value	Slope (95% CI)	p-value
0 to 40 ng/mL	-3.7 (-4.7, -2.7)	<0.0001	-4.2 (-5.1, -3.2)	<0.0001	-3.2 (-4.1, -2.3)	<0.0001
40+ ng/mL	0.4 (-0.7, 1.5)	0.4770	-0.25 (-1.3, 0.8)	0.6242	0.4 (-0.5, 1.3)	0.4393

(1) adjusted for age, age-squared, sex, ethnicity

(2) adjusted for age, age-squared, sex, ethnicity, mean body mass index, mean prednisone dose, proportion of time on anti-hypertensive, and proportion of time on hydroxychloroquine

Table 2. Estimated difference in person-specific mean systolic blood pressure per 10 ng/mL difference in person-specific mean vitamin D (model allowing slope to differ before and after 40 ng/mL)

	Unadjusted		Adjusted (1)		Adjusted (2)	
	Slope (95% CI)	p-value	Slope (95% CI)	p-value	Slope (95% CI)	p-value
Vitamin D level (Per 10 ng/mL difference)	-0.8 (-1.5, -0.03)	0.0422	-1.8 (-2.6, -1.1)	<0.0001	-1.0 (-1.7, -0.3)	0.0050

(1) adjusted for age, age-squared, sex, race

(2) adjusted for age, age-squared, sex, race, mean body mass index, mean prednisone dose, and proportion of time on hydroxychloroquine

Table 3. Estimated difference in person-specific mean glucose per 10 ng/mL difference in person-specific mean vitamin D

25(OH) vitamin D level was measured, mean age was 42.9 (SD=13.6) years. 20% were under the age of 30, 36% were between the age of 30 and 44, 33% between 45 and 59, and 12% were 60 or older. 77% had their first vitamin D level below 40 ng/mL and 26.5% had their first vitamin D level below 20 ng/mL. Longitudinal regression models between 25(OH) vitamin D levels and cholesterol levels, systolic blood pressure and glucose levels were constructed.

Results: We performed "between" person analyses: whether patients with higher levels of 25(OH) vitamin D had lower levels of the cardiovascular risk factors; serum cholesterol (Table 1), systolic blood pressure (Table 2) and glucose (Table 3). The reduction in serum cholesterol and systolic blood pressure was best fit by a two slope model, with the break point at 50 ng/mL and 40 ng/mL of 25(OH) vitamin D, respectively. Below the break point, the reduction was markedly greater. In a separate analysis, we demonstrated similar benefits in patients over time ("within patient"), with reduced cardiovascular risk factors at visits in which 25(OH) vitamin D levels were higher.

Conclusion: Higher 25(OH) vitamin D levels resulted in significantly lower total cholesterol, lower systolic blood pressure and lower glucose. No additional benefit was achieved above 50 ng/mL (for cholesterol) or 40 ng/mL (for systolic blood pressure). A similar break point of 40 ng/mL was found for the benefit of vitamin D supplementation on SLE disease activity. This "breakpoint" means that the target 25(OH) vitamin D is at a safe level, without risk of toxicity. Given the role of vitamin D in vascular repair and endothelial function, and its anti-inflammatory activity in blocking NF-kappa beta and reducing production of pro-inflammatory cytokines, replacement of vitamin D in SLE patients who are deficient or insufficient should be recommended, both for disease activity and also for long-term cardiovascular benefit.

Disclosure: M. Petri, Eli Lilly and Company, 5, Exagen, 2, 5; **J. Li**, None; **D. Goldman**, None.

Abstract Number: 2535

Identifying Subgroups of SLE Patients with Differential Responses to a BLyS Inhibitor: Application of a Machine Learning Algorithm to Clinical Trial Data

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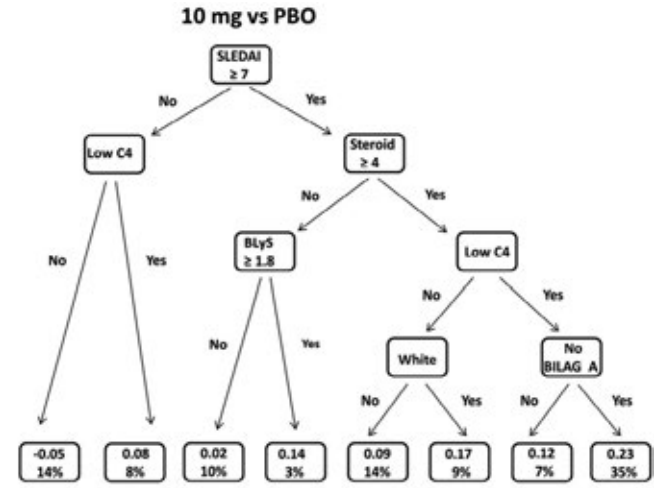
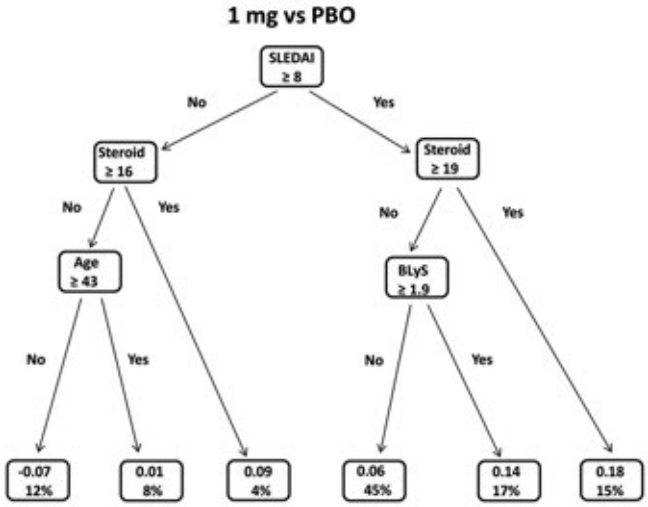


Top number in terminal node: Expected difference in response rates (Belimumab – SoC)
Bottom number: % of subjects in that subgroup



SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Given the heterogeneity of systemic lupus erythematosus (SLE), the effect of any intervention is expected to vary. The ability to identify those most and least likely to benefit from a treatment would improve the interpretability of trial outcomes and advance medical care. Conventional subgroup analyses suffer from low power, can encompass only a few variables at a time, and require *a priori* specification of cut-points for continuous variables. We explored the utility of a machine learning-based algorithm for discovering in a SLE trial the subgroups in which adding experimental therapy to standard of care considerably enhances or diminishes response compared to placebo (PBO).

Methods: A two-step "virtual twin" (VT) method was applied to combined data from the BLISS-52 (N=865) and BLISS-76 (N=819) trials. A random forest algorithm was first used to estimate for each patient, given baseline char-

acteristics, the probabilities of SRI-4 response to belimumab and PBO. A regression tree was then constructed to partition the study population into distinct subgroups and identify those in which the estimated difference in these response probabilities is much greater or smaller than the treatment effect in the overall population. Two separate VT analyses were conducted of the 10 mg/kg and 1 mg/kg belimumab doses compared to PBO. Cross-validation was used to assess the method's performance.

Results: In the combined BLISS trials, response rates to the primary endpoint (SRI-4) were 51% in those receiving 10 mg/kg belimumab, 46% (1 mg/kg), and 39% (PBO). VT analysis of 10 mg/kg vs. PBO found a 23% belimumab response advantage over PBO in patients with *SLEDAI ≥ 7 & steroid dose ≥ 4 mg/d & low C4 & no BILAG A at baseline*, vs 12% in the total population. In contrast, the estimated response difference in those entering with *SLEDAI < 7 & normal C4* was 5% lower on 10 mg/kg than PBO. In analysis of 1 mg/kg vs. PBO, two subgroups showed enhanced belimumab effect: *SLEDAI ≥ 8 & steroid dose ≥ 19 mg/d* and *SLEDAI ≥ 8 & steroid dose < 19 mg/d & BLyS ≥ 1.9 ng/mL*; average estimated between-treatment response differences were 18% and 14%, respectively, compared to 7% in the overall population. But in patients with *SLEDAI < 8 & steroid dose < 16 mg/d & age < 43*, the 1 mg/kg belimumab response rate was estimated to be 7% lower. Cross-validation indicated the accuracy of the VT method to identify subgroups exceeded 70%.

Conclusion: Enhanced belimumab response was associated with low C4 and higher disease activity, steroid dose, and BLyS levels, as in prior studies. However, the VT method identified alternative cutpoints for continuous variables and additional features predicting non-response. SLEDAI ≥ 7 or 8 was most predictive of response to treatment. Thus, lower response difference is identified in patients who are potentially too ill (BILAG A severity) or not ill enough (minimal disease criteria) to benefit from adding belimumab. The 1 mg/kg belimumab effect was enhanced only in those on high baseline steroid doses. The VT and other machine learning techniques are promising for subgroup discovery in SLE trials as more sophisticated biomarkers, especially potent but less common indicators, become available.

Disclosure: M. Kim, Celgene, 5; **K. Pradhan**, None; **P. Izmirly**, Glaxosmithkline, 5, GSK, 5; **K. Kalunian**, GSK, 5; **L. Hanrahan**, None; **J. Merrill**, Xencor, 2.

Abstract Number: 2536

Distribution and Predictors of Whole Blood Hydroxychloroquine Levels in Clinical Rheumatology Practices in the United States

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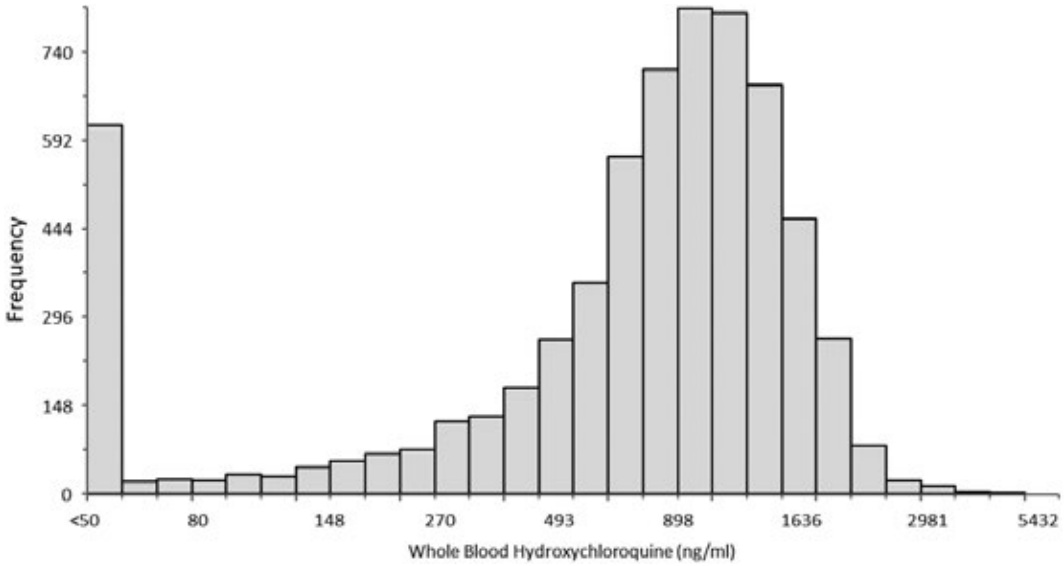
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Therapeutic drug monitoring of whole blood Hydroxychloroquine (HCQ) can help identify patients at risk of flares due to underexposure (e.g. severe non-adherence, < 200 ng/ml) or alternatively those with heightened risk of retinal toxicity due to overexposure (e.g. HCQ >1733 ng/ml) (Petri M et al. Arthritis Rheumatol.



2018). Our purpose was to report and evaluate factors associated with HCQ exposure in a large population of patients with rheumatic diseases.

Methods: The cohort of patients evaluated for this analysis originated from clinical rheumatology practices in the United States. Physicians (n=526) submitted specimens collected from patients under HCQ to reference clinical laboratory accredited by the College of American Pathologists. Levels were measured using venous blood collected in EDTA containing tubes or capillary blood collected on volumetric absorptive microsamplers. Recommendation was made to collect specimens after 6 months therapy (steady state). HCQ was measured using liquid chromatography coupled with tandem mass spectrometry and reported to clinicians within 5 days of specimen receipt. For each patient, mean HCQ blood level was calculated. Statistical analysis consisted of logistic regression analysis. Longitudinal changes were analyzed using linear mixed effect models.

Results: A total of 10523 specimens were collected from 6559 patients (mean [SD] age =52±15 years, 90% females). Average [SD] whole blood HCQ blood levels were 959±653 ng/ml (n=10523) and comparable between venous blood (946±6542 ng/ml, n=9391) and capillary blood (1063±654 ng/ml, n=1132). The distribution of mean HCQ levels per patient is highlighted in the Figure. The proportion of patients presenting with low HCQ blood levels (< 200 ng/ml) was 13.9% (912/6559), and these low levels associated with age (OR=0.71 CI95%:0.66-0.76 per 10 years) (p< 0.001), HCQ dose (OR=0.66 CI95%: 0.53-0.81 per 200 mg) (p< 0.001) and gender (OR=0.67 CI95%: 0.48-0.93 for females) (p< 0.001). HCQ levels greater than 500 ng/ml (indicative of compliance) were achieved in 74% patients (4901/6559) and 11% patients (716/6559) presented with potential overexposure to HCQ (>1733 ng/ml). Total non-adherence (HCQ< 50 ng/ml) in the presence of reported HCQ dose ≥200mg daily on test requisitions was 4.8% (223/4601 patients). In 4127 specimens collected from 2527 patients with HCQ dosing available (median 400 mg/daily), linear mixed effect models revealed that HCQ levels associated with HCQ dosage (estimate= 228±18 ng/ml per 200 mg HCQ, p< 0.001), patient age (93±7 ng/ml per 10-year, p< 0.001) and female gender (141±40 ng/ml, p< 0.001). This effect of age and gender on HCQ exposure was also significant in the subset of patients (n=2048, 3505 measurements) presenting with mean HCQ levels greater than 500 ng/ml and thus likely compliant to therapy (age: 65±7 ng/ml; gender: 123±41 ng/ml) (p< 0.001) after adjusting for HCQ dosing (206±20 ng/ml, p< 0.001).

Conclusion: Whole blood HCQ levels are significantly associated with gender, age, and HCQ dosing and remain essential in assessing adherence. As whole blood accurately reflects HCQ exposure (rather than plasma level), whole blood HCQ levels will have a future role in identifying overexposure as well.

Disclosure: T. Dervieux, Exagen, 1, 3, 4, 6; **K. Brady**, Exagen, 3; **D. Thomas**, None; **J. Conklin**, Exagen, 3; **E. Fung**, None; **C. Ibarra**, Exagen, 1, 3, 4; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 2537

Influential Factors in Promoting Treat-to-Target for Systemic Lupus Erythematosus via Empowering Patients: A Cohort Study from China by Smart System of Disease Management (SSDM)

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Treating to target is routine in rheumatoid arthritis, but no comparable standard has been defined for SLE. In 2015, the definition of Lupus Low Disease Activity State (LLDAS) was generated by Asia-Pacific

Baseline\Last follow-up	Number	%	SLEDAI≤4	%	SLEDAI≥5	%
SLEDAI≤4	737	53.17%	571	77.48%	166	22.52%
SLEDAI≥5	649	46.83%	362	55.78%	287	44.22%
Total	1386	100%	933	67.32%	453	32.68%

Table 1. The T2T results at baseline and in final follow up.

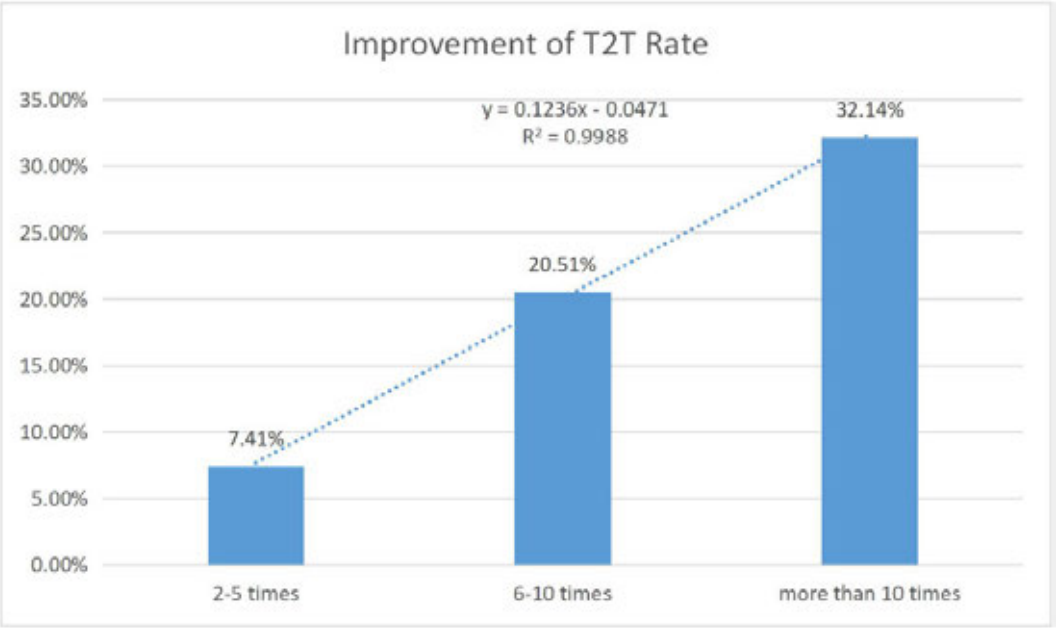

Figure 1. The improvement of T2T rate(y) was positively correlated with times of self-assessment for SLEDAI-2K(x) independently. The regression equation as "y = 0.1236x - 0.0471 R2 = 0.9988", p<0.01.

Lupus Collaboration, and the preliminary validation demonstrated its attainment to be associated with improved outcomes in SLE. A SLEDAI-2K score lower than 4 is the main criteria for LLDAS. SSDM is an interactive mobile disease management application, including application systems for both the doctors and patients. The patients can perform self-assessment, including SLEDAI-2K, 36-item short-form health survey (SF-36), and medical records entry (including medication and laboratory test results) through the mobile application. The data is synchronized to the SSDM of authorized rheumatologists and stored in cloud database. Based on the patients' data, rheumatologists will provide medical advices to the patients.

The objective of this study is to evaluate the patterns of T2T and related influential factors among SLE patients after applying SSDM in real world.

Methods: Patients were trained to master SSDM by rheumatologists or nurses in clinics. The first assessment for SLEDAI-2K was performed as the baseline. Patients were required to perform repeated assessments after leaving the clinics.

Results: From July 2015 to May 2019, 24,531 SLE patients enrolled in SSDM and mean age is 34.39±13.21(14-80) years old. And median disease duration is 3.29 years. The most commonly used drugs are hydroxychloroquine, glucocorticoids, leflunomide, mycophenolate mofetil, cyclophosphamide, methotrexate and cyclosporine A. Among them 1,386 SLE patients from 191 hospitals across China were followed up for more than 12 months through SSDM, and the results were summarized in Table 1.

The ratio of T2T achievers was 53.17% (737/1,386) at the baseline and improved significantly to 67.32% (933/1,386) after a 12-month follow-up, p< 0.01. Among T2T achievers at baseline, 77.48% (571/737) maintained T2T, and 22.52% (166/737) relapsed. Of patients who didn't achieve T2T at baseline, 55.78% (362/649) of the patients achieve T2T after 12-month follow-up.

The impact of the times of self-assessment for SLEDAI-2K on T2T has been analyzed. The more frequent of the self-assessments being conducted by patients, the higher improvement of T2T rate will be. We performed linear regression analysis of variables in statistics and parameter estimation by least square method. The improvement of T2T rate(y) was positively correlated with times of self-assessment for SLEDAI-2K(x) independently. The regression equation as "y = 0.1236x - 0.0471 R2 = 0.9988", $p < 0.01$. (Figure 1)

Conclusion: After proactive disease management via SSDM for more than 12 months, the rate of T2T in SLE patients increased significantly. Patients with SLEDAI-2K≤4 score at baseline had a significantly higher retention rate of disease activity. The patients who performed more self-assessments through SSDM had lower probability of relapse and higher rate of T2T maintaining and achievement. SSDM is a valuable tool for long term SLE follow-up through empowering patients.

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Abstract Number: 2538

Importance of Serum Phosphatidylserine-Specific Phospholipase A_1 (PS-PLA_1) as a Novel Disease Activity Biomarker of Systemic Lupus Erythematous

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Phosphatidylserine-specific phospholipase A_1 (PS-PLA_1) is a secreted lipase that is proposed to be a producing enzyme for lysophosphatidylserine (LysoPS), which is an emerging lipid mediator with a number of immunomodulative effects. The aim of the present study was to assess the utility of serum levels of PS-PLA_1 in systemic lupus erythematosus (SLE).

Methods: Serum PS-PLA_1 was measured by enzyme-linked immunosorbent assay in 146 patients with SLE (including 43 untreated patients), 80 disease controls (35 active rheumatoid arthritis [RA], 23 Sjögren's syndrome [SS], and 22 systemic sclerosis [SSc]), and 237 healthy controls.

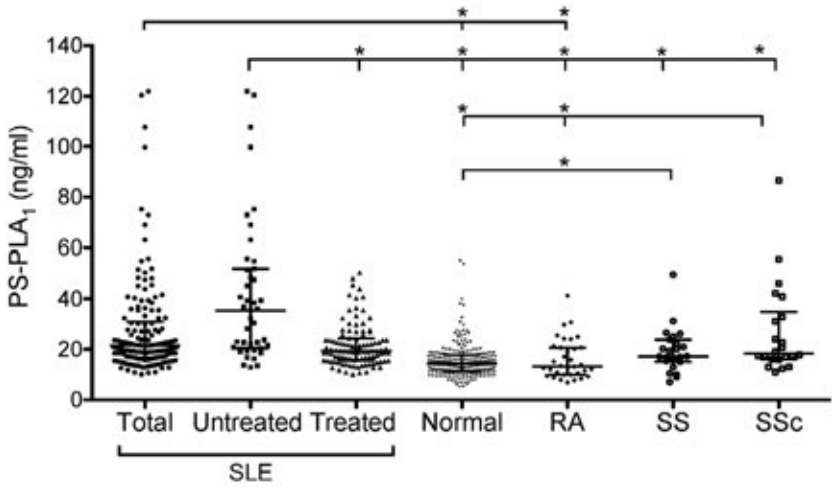

Figure 1. Distribution of the serum levels of phosphatidylserine phospholipase A1 (PS-PLA1) in patients with systemic lupus erythematosus (SLE), healthy controls (normal), and patients with rheumatoid arthritis (RA), systemic sclerosis (SSc), or Sjögren's syndrome (SS).

Results: Serum PS-PLA_1 was significantly higher in SLE patients than in healthy controls and RA patients. Although serum PS-PLA_1 was significantly elevated in SSc and SS patients compared with healthy controls, serum PS-PLA_1 was significantly higher in untreated SLE patients than in treated SLE patients and disease control patients. Receiver operating characteristic analysis revealed that a cut-off value of 17.9 ng/mL distinguished untreated SLE from disease control, with sensitivity and specificity of 88.4% and 57.0%, respectively. Serum PS-PLA_1 was significantly correlated with SLE Disease Activity Index (SLEDAI) and IgG with a correlation coefficient of 0.56 and 0.31, respectively, and inversely correlated with white blood cell counts, lymphocyte counts, total complement hemolytic activity (CH50), complement C3, and C4 with a correlation coefficient of -0.32, -0.26, -0.42, -0.39, and -0.18, respectively, in SLE patients overall. Stepwise multiple regression analysis identified SLEDAI, CH50, and IgG as significant parameters. In SLEDAI-based disease activity groups, serum PS-PLA_1 was significantly higher in SLE patients with high disease activity than in those with low disease activity. Serum PS-PLA_1 decreased significantly in parallel with SLEDAI in 25 SLE patients whose paired serum samples were available pre- and post-treatment.

Conclusion: Serum PS-PLA_1 was associated with disease activity of SLE, suggesting that serum PS-PLA_1 may be useful as a biomarker for monitoring disease activity of SLE.

Disclosure: T. Sawada, None; **M. Kurano**, None; **H. Shirai**, None; **Y. Iwasaki**, None; **K. Tahara**, None; **H. Hayashi**, None; **K. Igarashi**, None; **K. Fujio**, None; **J. Aoki**, None; **Y. Yatomi**, None.

Abstract Number: 2539

Patient Perception of Benefit and Risks Associated with Hydroxychloroquine Use in Systemic Lupus Erythematosus (SLE)

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is recommended in all patients with systemic lupus erythematosus (SLE). Studies suggest that a significant proportion of subjects are non-adherent to daily HCQ, leading to poor disease control, increasing morbidity and mortality. One of the main barriers to adherence is reported to be patients' fear of side effects most notably retinopathy. The objectives of this study were to assess SLE patients' (1) perception of the risk vs. benefit associated with the use of HCQ, (2) awareness of the risk factors of HCQ-induced retinopathy.

Methods: We administered an internet-based survey to SLE patients registered in the Lupus Alliance of Upstate New York (LAUNY) email listserv over 3 months. The survey included demographic information, such as age, gender, ethnicity, and education level, and their perception of the risks and benefits of HCQ therapy. Participation was voluntary, anonymous, and restricted to adults 18 years or older.

Results: A total of 94 subjects completed the survey. The mean age of responders was 48.4 ± 13.1 years; 98% (N=92) were women, 80% (N=75) Caucasian and 10% (N=9) African American. Fifty percent (N=47) had a bachelor's degree or higher education. The mean duration of SLE was 14 years with upper and lower quartiles of 21 and 5 years. Ninety five percent of patients (N=89) were either current or past users of HCQ (66 current use, 23 past use). Among them, 97% (N=86) of patients reported regular visits to eye doctors and 82% (N=73) had a baseline eye exam with HCQ initiation. The mean duration of HCQ use was 10 years with 15 years and 3 years of upper and lower quartiles. Twenty three percent of patients (N=22) with HCQ exposure were unaware of the potential ocular toxicity associated with HCQ use. More than 60% (N=57) reported that they will continue HCQ in view of its beneficial effects, despite potential risk of eye related-side effects. A significant proportion (37%, N=34) of patients were concerned about ocular toxicity associated with HCQ and expressed their desire to stop or discuss discontinuation of HCQ with their physician. Up to 60% of patients were not aware of predictors of retinal toxicity associated with HCQ.

Conclusion: Almost all of our patients on HCQ reported having regular eye check-ups for retinal toxicity. Many patients were concerned about potential retinal toxicity with HCQ use and were considering stopping the medication. In addition, a substantial number of patients were not aware of HCQ associated retinopathy. Our study identified a need for patient education regarding risks, benefits of HCQ therapy and awareness about potential predictors of HCQ retinal toxicity. Furthermore, educating healthcare providers to address HCQ toxicity on an ongoing basis will lead to better medication compliance and disease outcomes.

Disclosure: S. Kwon, None; **J. Farrell**, None; **S. Hasni**, None; **S. Banerjee**, None.

Abstract Number: 2540

Impact of IL34, IFN-α and IFN-λ1 on Disease Activity of SLE Patients in Egypt

Yasmin Hussein,[1] and Yousra Sadeq[1], [1]Mansoura University Hospital, Mansoura, Egypt

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is a systemic inflammatory and autoimmune disease. IL-34 plays pivotal roles in the proliferation and differentiation of mononuclear phagocyte cells, osteoclastogenesis and inflammation. IFN-α play an important role in SLE pathogenesis and proportion of patients displays increased serum IFN-α and IFN-λ1. Interestingly, the gene signatures of IFN-λ1 and IFN-α overlap. Our objective was to assess IL34, IFN-λ1 and IFN-α in SLE with relationship to clinical, laboratory parameters, treatment response and disease progression. We hypothesized a subgroup of patient with a concordance of high level of these cytokines that could have a different disease behavior.

Methods: 82 newly diagnosed SLE Egyptian patients. History, examination and laboratory investigation with assessment of disease activity. Pretreatment assessment of IL34, IFN-α and IFN-λ1 level by ILIZA. Patients started treatment (antimalarial ±Steroid ±immunosuppressive drugs) with response evaluation after six months.

Results: 14 male (17.1%) and 68 female (82.9%), age mean±SD (48.6±8.2). Mean±SD of IL34, INFα and INF-λ1were 175.9±125.9 pg/mL, 109.3±32.5 pg/mL and 227.9±144.8 pg/mL respectively. 21 patients (25.6%) had lupus nephritis, 32 patients (39%) with SLAM >6 and 22 patients (26.8%) with SLEDAI >6. IL34 was positively correlated with anti-dsDNA (P= 0.002) but inversely correlated with C3 level (P = 0.009). IL34 was highly presented with lupus nephritis (P 0.005), SLAM >6 (P 0.03), SLEDAI >6 (P 0.007) and poor responder to treatment (P 0.02). IFNα was inversely correlated with C3 (P 0.001). IFNα was highly presented with lupus nephritis (P 0.02) and poor responders (P 0.01) however no relation with SLAM >6 nor SLEDAI >6. INF-λ1 was positively correlated with anti-dsDNA (P= 0.02) but inversely correlated with C3 (P = 0.01). INF-λ1 was highly presented with lupus nephritis (P 0.001), with SLAM >6 (P 0.04), with SLEDAI >6 (P 0.02). Accumulation of ≥3 clinical features during follow up was associated with high IL34 (P 0.001), high IFNα (P 0.001) and high INF-λ1 (P 0.001). We assigned high levels (i.e., ≥ 75% or third quartile)

	$IL34^{high}$, $IFN\alpha^{high}$ and $IFN\text{-}\lambda^{high}$	All others	p
Patients with Lupus Nephritis (21)	10 (47.6%)	11 (52.4%)	0.001
Patients without Lupus Nephritis (61)	7 (11.5%)	54 (88.5%)	
Patients with SLAM>6 (32)	11 (34.4%)	21 (65.6%)	0.02
Patients with SLAM≤6 (50)	6 (12%)	44 (88%)	
Patients with SLEDAI>6 (22)	8 (36.4%)	14 (63.6%)	0.03
Patients with SLEDAI≤6 (60)	9 (15%)	51 (85%)	
Patients with poor response (27)	10 (37%)	17 (63%)	0.01
Patients with good response (55)	7 (12.7%)	48 (87.3%)	

of each cytokine. Triple high (IL34high, IFNα high and IFN-λ1 high) found in 17 patients (20.7%) and were positively correlated with anti-dsDNA (P= 0.001) but inversely correlated with C3 (P = 0.001). Triple cytokines level was highly presented with lupus nephritis (P 0.001), SLAM >6 (P 0.02), SLEDAI >6 (P 0.03) and poor response to treatment (P 0.01) indicating these patients have aggressive disease. 28 patients developed (3 – 8) accumulated clinical features during the disease course, out of them 15 patients (53.5%) have high level of the triple cytokines indicating a poor prognosis of these subgroup.

Conclusion: High pretreatment serum IL-34 or IFN-λ1 has a prognostic significance in SLE patients. Patients with high IL-34 or IFNα or IFN-λ1 had more kidney affection and poor response to treatment. Triple cytokines elevation significantly associated with lupus disease activity, more kidney affection and poor response to treatment so, this aggressive phenotype of patients may be in need for combination of targets or a multicytokines targeted therapy.

Disclosure: Y. Hussein, None; **Y. Sadeq**, None.

Abstract Number: 2541

Pharmacokinetics of Hydroxychloroquine in Systemic Lupus Erythematosus Patients with Renal Impairment

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: A low glomerular filtration rate (GFR: < 60 mL/min/1.73 m^2) is an established risk of hydroxychloroquine (HCQ) retinopathy and is presumably related to higher HCQ concentrations. However, the pharmacokinetics of HCQ in impaired renal function are not known. Herein, we evaluated the pharmacokinetics of HCQ in systemic lupus erythematosus (SLE) patients with renal insufficiency using single-dose and population pharmacokinetic analysis.

Methods: The present study was conducted in both the in-patient and out-patient settings at three hospitals and enrolled 20 SLE patients with various degrees of renal impairment. An HCQ dose of 300 mg/d (one 200 mg tablet and 100 mg of crushed HCQ) based on 6.5 mg/IBW was administered. Nine whole blood samples were collected from inpatients, and fewer samples were collected from outpatients from the pre-dose period up to 72 hours post-dose for single-dose pharmacokinetic analysis, and four to six blood samples after at least 16 weeks starting HCQ were collected from outpatients for population pharmacokinetics. The HCQ concentrations were measured using a validated LC/MS/MS. The pharmacokinetic parameters were estimated by the two-compartment model. The area under the blood concentration-time curve (AUC) was analyzed using moment analysis if five or more samples were collected for single-dose pharmacokinetic analysis. Population pharmacokinetics were analyzed by computer using a non-linear mixed-effects model.

	eGFR (ml/min/1.73 m^2)		
	-44	45-59	60-
N	5	8	6
No. of blood samples	45	70	70
Age	56.8 (6.8)	50.5 (13.8)	37.5 (8.6)
Cr (mg/dl)	1.45 (0.25)	0.92 (0.09)	0.66 (0.06)
eGFR (ml/min)	34.8 (5.6)	51.6 (3.9)	81.8 (11.9)
BMI	21.6 (6.0)	21.7 (2.0)	21.3 (5.0)
Dose/IBW (mg/kg)	5.6 (0.5)	6.1 (0.4)	5.6 (0.3)
Dose/ABW (mg/kg)	5.7 (1.5)	5.6 (0.5)	5.5 (0.9)

Numbers represent the mean (SD).

Table 1. Patient demographics

	eGFR (ml/min)		
	-44	45-59	60-
C1max (μg/ml)	0.26 (0.09)	0.33 (0.21)	0.31 (0.12)
Tmax (h)	3.8 (0.45)	2.6 (1.1)	3.2 (1.3)
AUC (μg/mL·hr)	10.9 (3.2) *1	10.7 (2.3) *2	7.6 (2.6) *3
Css (μg/ml)	0.98 (0.29)	1.03 (0.36)	0.76 (0.20)
CL/F （L/h)	11.5 (4.0)	12.2 (7.6)	16.2 (6.8)
T1/2 (h)	16.9 (14.2)	20.6 (19.9)	10.8 (7.8)

Numbers represent the mean (SD).

*1: n=2, *2: n=4, *3: n=5

Table 2. Pharmacokinetic parameters

Results: One patient was excluded from analysis due to malabsorption syndrome. Six patients with GFR >60 mL/min/1.73 m^2, eight patients with GFR 45-59 mL/min/1.73 m^2, and five patients with GFR 15-44 mL/min/1.73 m^2 were included. The patient background is shown in Table 1. The dosage based on actual body weight and body habitus was similar between groups. The pharmacokinetic parameters are summarized in Table 2. In total, 185 HCQ concentration measurements were obtained from 19 patients.

There was a trend towards increased AUC, decreased renal elimination, and prolonged elimination half-life in patients with moderately impaired renal function. In population pharmacokinetics, HCQ clearance tended to be influenced by renal function.

Conclusion: Adjusting the HCQ dosage may be warranted in patients with moderately impaired renal function.

Disclosure: N. Yokogawa, None; **M. Hashiguchi**, None; **Y. Nagai**, None; **K. Shimada**, None; **S. Sugii**, None; **M. Oshima**, None; **K. Setoguchi**, None; **M. Shimizu**, None.

Abstract Number: 2542

An Updated Meta-Analysis of the Efficacy and Safety of Mycophenolate Mofetil in the Induction Treatment of Chinese Patients with Lupus Nephritis

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SESSION INFORMATION
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Background/Purpose: Achieving clinical remission while reducing toxicity are primary objectives in the treatment of lupus nephritis (LN). Mycophenolate mofetil (MMF) has demonstrated efficacy benefits with good tolerance as the induction therapy in LN patients of Hispanic or mixed race. However, a comprehensive view is lacking in its usage among Chinese patients with LN. We conducted this meta-analysis based on most updated studies to review the efficacy and safety of MMF induction therapy in Chinese patients with LN.

Table 1. Basic clinical data for the 18 studies included

Reference	Sample size (T/C)	Age (years)*	Treatment regimen in MMF group	Treatment regimen in CYC group	Treatment duration (months)	Major outcome measures	Pathologic type of LN
Chan et al. 2005	33/31	T: 38.1 (10.2) C: 41.8 (8.9)	MMF: 2 g/day x 6 mos; mt with rd Pred: initially 0.8 mg/kg/day, then rd	CYC: oral 2.5 mg/kg/day x 6 mos; mt with AZA Pred: initially 0.8 mg/kg/day, then rd	24	CR, PR, TR, relapse	IV
Feng et al. 2014	30/30	T: 29.9 (1.8) C: 35.4 (2.1)	MMF: 2 g/day x 6 mos Pred: initially 0.5 mg/kg/day, then rd	CYC: IV drip 0.5 g every 2 wks x 6 mos Pred: initially 0.5 mg/kg/day, then rd	6	CR, PR, TR,	III/IV/V
Hu et al. 2002	23/23	T: 28.0 (8.8) C: 29.5 (10.2)	MMF: initially 1.0–1.5 g/day, then 0.5–1.0 g/day 3–6 mos later Pred: initially 10–30 mg/day, then rd to 10–15 mg/day	CYC: IV drip 0.75–1.00 g/m²/mo x 6, mt at ¼ dose for 1 yr MP: 0.5–1.0 g/day, then Pred 0.8 mg/kg/day, then rd	6	%UP ↓ by ⩾50%	IV
Wang et al. 2007	9/11	T: 32.2 (12.0) C: 30.8 (12.7)	MMF: 1.5–2.0 g/day x 6 mos MP: 0.5 g/day x 3 days; Pred: initially 0.6–0.8 mg/kg/day, then rd	CYC: IV drip 0.75–1.0 g/m² per mo x 6 mos MP: 0.5 g/day x 3 days; Pred: initially 0.6–0.8 mg/kg/day, then rd	6	CR, PR, TR	IV
Li et al. 2012	20/20	T: 26.5 (range 16–62) C: 33.0 (range 17–64)	MMF: 1.5–2.0 g/day x 6 mos Pred: initially 0.8–1.0 mg/kg/day, then rd	CYC: IV drip 0.5–0.75 g/m² per mo x 6 mos Pred: initially 0.8–1.0 mg/kg/day, then rd	6	CR, PR, TR	III/IV/V
He et al. 2010	30/30	NA	MMF: 1.5–2.0 g/day x 6 mos	CYC: IV drip 0.75 g/m² per mo x 6–9 mos	6	CR, PR, TR	III/IV/V

Table 2. Relative risks of adverse events with MMF versus cyclophosphamide induction therapy

Adverse event	No. of studies	MMF (n/N)	CYC (n/N)	RR (95% CI)	p value
Infection	11	47/296	87/287	0.52 (0.38, 0.71)	< 0.0001
Amenorrhoea	9	8/225	45/214	0.21 (0.11, 0.39)	< 0.0001
Leucopenia	11	10/262	26/256	0.44 (0.23, 0.83)	0.01
Alopecia	6	1/159	25/157	0.12 (0.04, 0.37)	0.0002
Gastrointestinal symptoms	11	27/282	59/279	0.48 (0.32, 0.71)	0.0002
Liver damage	6	4/109	12/114	0.44 (0.18, 1.12)	0.08

CI, confidence interval; CYC, cyclophosphamide; MMF, mycophenolate mofetil; RR, relative risk.

Methods: Relevant clinical trials were identified by searching PubMed, EMBASE, Cochrane Collaboration, Medline, National Guideline Clearinghouse, Best Evidence, China National Knowledge Infrastructure, Wangfang, SinoMed, China Science and Technology Journal Database, and WHO ICTRP (in February 2019). The search strategies consisted of (mycophenolate mofetil AND (cyclophosphamide OR azathioprine)) AND (lupus nephritis OR lupus glomerulonephritis OR proliferative glomerulonephritis OR membranous glomerulonephritis OR systemic lupus erythematosus) in English and in Chinese. Retrieved studies were assessed independently by two reviewers. Meta-analysis was conducted using RevMan5.3 software. This review was registered on PROSPERO (CRD42018086209).

Results: Eighteen randomized controlled trials (5 English and 13 Chinese articles; totalling 927 patients) were included in the analysis (Table 1). Complete remission (CR) and total remission (TR, CR + partial remission) were reported in 14 RCTs. MMF showed an efficacy advantage in terms of CR (44.7% vs 32.9%; relative risk [RR] 1.34; 95% confidence interval [CI]: 1.13, 1.58; p=0.0007) and TR (84.3% vs 70.9%; RR 1.16; 95% CI: 1.02, 1.33; p=0.03) compared to CYC (Figure 1). MMF was associated with lower risks of infection (RR 0.52; 95% CI: 0.38, 0.71; p< 0.0001), amenorrhea (RR 0.21; 95% CI: 0.11, 0.39; p< 0.00001), leukopenia (RR 0.44; 95% CI: 0.23, 0.83; p=0.01), alopecia (RR 0.12; 95% CI: 0.04, 0.37; p=0.0002), and gastrointestinal symptoms (RR 0.48; 95% CI: 0.32, 0.71; p=0.0002) than CYC (Table 2). Relapse rate seemed to be comparable between MMF and AZA groups (RR 1.16; 95% CI: 0.59, 2.28; p=0.68).

Conclusion: This meta-analysis of Chinese LN patient revealed that MMF is more effective than CYC in achieving CR and TR, and it is associated with lower incidences of infections, amenorrhea, leukopenia, alopecia, and gastrointestinal symptoms.

Disclosure: M. Zhou, None; **Y. yang**, Shanghai Roche Pharmaceuticals Ltd, 3, Shanghai Roche Pharmaceuticals Ltd, 3; **X. Han**, Shanghai Roche Pharmaceuticals Ltd, 3; **X. Yu**, Shanghai Roche Pharmaceuticals Ltd, 3; **H. zhang**, None.

Abstract Number: 2543

Meta-Analysis Examining the Clinical Significance of Monitoring of Hydroxychloroquine Levels in SLE

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Despite the pivotal role hydroxychloroquine (HCQ) plays in treating SLE, less than 50% of patients take HCQ as prescribed. Nonadherence versus lack of effect to HCQ are difficult to distinguish, underscoring the importance of measuring HCQ blood levels to assess adherence. Despite this, information and consensus on the clinical impact of incorporating routine testing of HCQ blood levels is lacking. Therefore, we systematically reviewed publications examining the correlation between 1) HCQ levels and adherence, and 2) HCQ levels and SLEDAI scores, in SLE patients. *We hypothesized that low HCQ levels would correlate with nonadherence and higher SLEDAI scores*.

Figure 1. Forest Plot of correlation of measured HCQ blood levels with assessed adherence

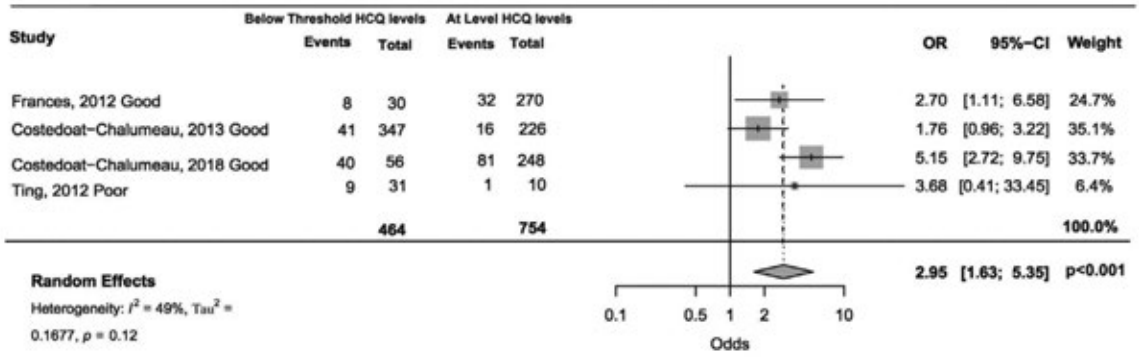
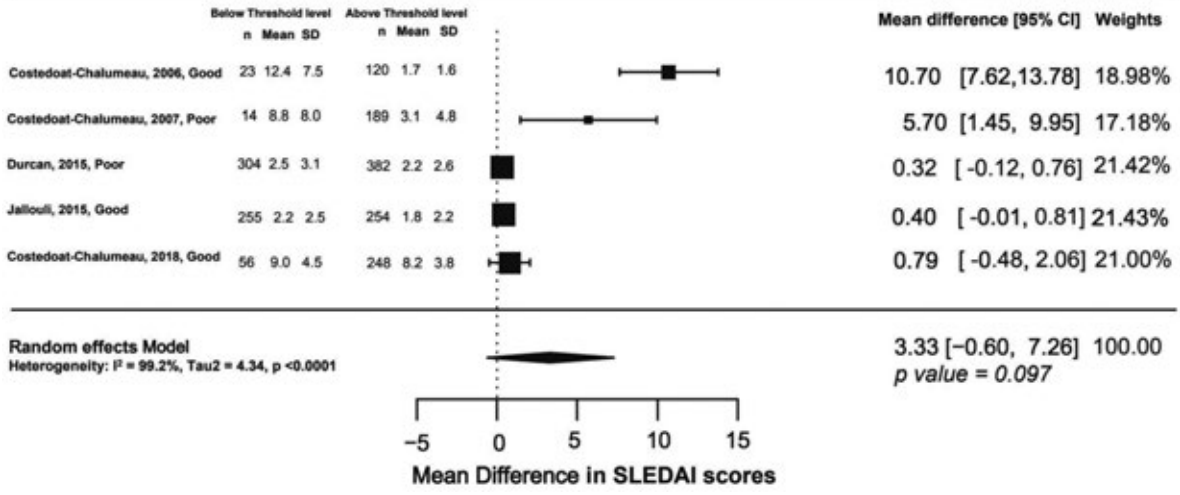


Figure 2. Forest Plot of correlation of measured HCQ levels with SLEDAI scores



Methods: A comprehensive search was performed using MeSH heading and keywords in Medline, Embase, CINHL and Web of Science databases. We selected observational and interventional studies that measured HCQ levels and assessed adherence and/or SLEDAI scores in adults with SLE. Newcastle Ottawa Scale and Cochrane Collaboration Risk Assessment tools were used to rate the quality of observational and intervention studies, respectively. We used Forest plots to compare pooled estimates (95% CI) of correlations between HCQ levels and patient or physician reported nonadherence and SLEDAI scores. Heterogeneity was assessed using I^2.

Results: From 306 manually reviewed abstracts, four studies analyzing correlation between HCQ levels and adherence, and five studies examining the correlation between SLEDAI and HCQ blood levels, met inclusion criteria. The odds of nonadherence measured by physician or reported by the patient was 3 times higher in patients with below threshold HCQ blood levels, compared to those with higher HCQ blood levels (OR 2.95, 95% CI 1.63, 5.35, $p < 0.001$, I2 49%) (Figure 1). The mean SLEDAI score was 3.33 points higher in groups with HCQ levels below threshold levels, but this trend was not statistically significant (δ3.33, 95% CI -0.60, 7.26, p=0.097, I2 99%) (Figure 2). Risk of bias assessment revealed three poor quality studies which were excluded in sensitivity analysis; results remained unchanged. Limitations of our analysis include study heterogeneity and lack of consensus on optimal blood HCQ levels.

Conclusion: We found a good correlation between HCQ levels and non-adherence. While patients with low HCQ levels had higher SLEDAI scores, the p-value for this finding was not statistically significant. Future studies should clarify optimal blood HCQ levels to control lupus, and then investigate the value of measuring blood HCQ levels in clinical care.

Disclosure: S. Garg, None; **R. Unnithan**, None; **K. Hansen**, None; **N. Costedoat-Chalumeau**, None; **C. Bartels**, Pfizer, 2, Pfizer Independent Grants for Learning and Change, 2.

Abstract Number: 2544

Results of the Open-label, Non-randomized 52-Week Study to Evaluate Treatment Holidays and Rebound Phenomenon After Treatment with Belimumab in Patients with SLE

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SESSION INFORMATION
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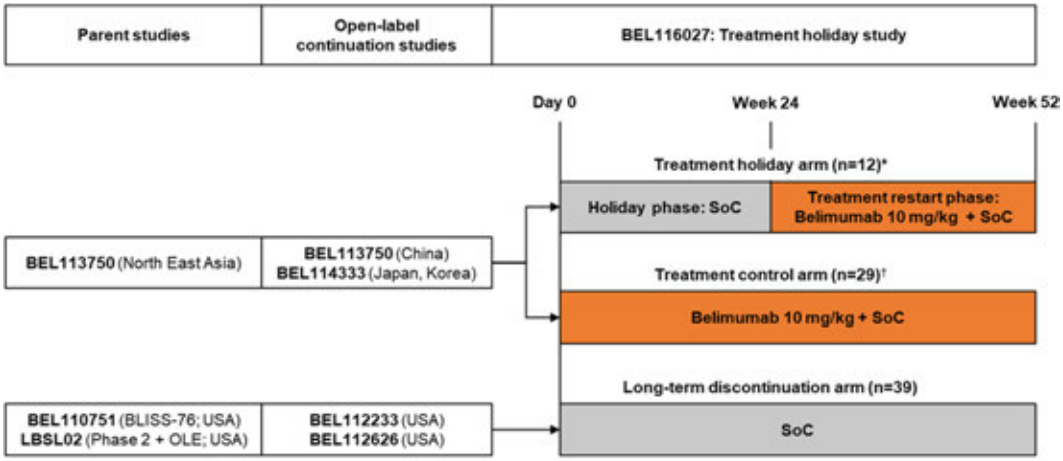
Background/Purpose: Belimumab is approved as add-on therapy in active, autoantibody-positive SLE. Safety and efficacy up to 13 years has been reported in adults, but potential for rebound upon temporary discontinuation of belimumab has not been investigated. This study (BEL116027; NCT02119156) assessed the impact of temporary withdrawal of intravenous (IV) belimumab.

Methods: In this 52-week open-label study, adults with SLE who received belimumab 10 mg/kg IV for ≥6 months in open-label studies were recruited to three arms: treatment holiday (TH; 24-week belimumab withdrawal, reintroduction for 28 weeks); continuous belimumab (treatment control; TC), and long-term discontinuation (LTD) (**Figure**).



*†Key selection criteria for treatment holiday and treatment control ONLY: Low disease activity, defined by SELENA-SLEDAI score ≤3 after a minimum of 6 months of belimumab, C3 and C4 complement levels ≥ lower limit of normal, no mild-moderate or severe flare during screening, receiving stable SLE SoC with no new immunosuppressive/ immunomodulatory agent, anti-malarial, or NSAID (for >1 week) and prednisone (or equivalent) ≤20 mg/day within the 30 day screening period; SELENA-SLEDAI, Safety of Estrogens in Lupus National Assessment-Systemic Lupus Erythematosus Disease Activity Index; SoC, standard of care; NSAID, nonsteroidal anti-inflammatory drug; OLE, open-label extension

Figure. Study Design

Endpoint	TH		TC	LTD
	Holiday phase 24 weeks (n=12)	Restart phase 28 weeks (n=11)	52 weeks (n=29)	52 weeks (n=39)
Number of patients with a SFI flare, n (%)	4 (33)	2 (18)	9 (31)	28 (72)
Number of SFI flares	5	2	17	74
Rate of SFI flares/patient-years	1.0	0.3	0.6	2.1
Baseline SELENA-SLEDAI score in parent study, mean (SD)	7.9 (4.19)	NA	9.2 (3.06)	10.2 (3.15)
Rebound (SELENA-SLEDAI exceeding parent study baseline, anytime up to Week 24), n	0	NA	2	2

ITT, intent-to-treat; NA, not applicable; SD, standard deviation; SFI, SELENA-SLEDAI flare index.

Table 1. Efficacy endpoints (ITT)

The primary endpoint was time to first SLE flare (SFI). Secondary endpoints included flare rates and evidence of rebound (SELENA-SLEDAI [SS] exceeding parent study baseline score, anytime post baseline to Week 24). Anti-drug antibodies (ADAs) and changes in immunoglobulins and B Cells were measured. Safety was monitored.

Due to slow enrollment the study was amended to reduce sample size; all analyses are descriptive.

Results: The ITT comprised 80 patients (TH: n=12, TC: n=29; LTD: n=39). The majority were female (88.8%), ≤45 years of age (71.3%), and had SS >3 at baseline in the parent study (97.5%). Day 0 disease activity, race and geographic distribution differed for LTD vs TC/TH. A higher proportion of LTD patients (8/39; 20.5%) had flares during screening for this study vs TH (1/12; 8.3%) or TC arms (0/29; 0%). Also, 41.0% of LTD patients were recruited from the US and 23.1% were White; TC and TH arms were recruited from China, Korea and Japan (100% Asian).

The majority in the holiday phase did not flare and flare rate during this time (1.0) was comparable to TC (0.6) (**Table 1**). Flare rate was highest in LTD (2.1). There were 9 severe and 4 renal flares in LTD and none in TH/TC.

n (%)	TH		TC	LTD
	Holiday phase (n=12)	Restart phase (n=11)	52 weeks (n=29)	52 weeks (n=39)
At least 1 AE	7 (58)	10 (91)	21 (72)	37 (95)
At least 1 SAE	0	1 (9)	2 (7)	6 (15)

Table 2. Summary of AEs (52-week study period)

No TH patients rebounded; two TC and two LTD patients rebounded (**Table 1**).

Adverse event (AE) and serious AE (SAE) rates were higher in LTD vs TC (**Table 2**). There were no withdrawals due to AEs and no SAEs in the holiday phase.

No ADAs were detected. In all arms, median levels of anti-dsDNA remained suppressed and complement C3/C4 levels remained above baseline over 52 weeks. At Day 0, median immunoglobulin levels were below baseline relative to the parent study and remained decreased throughout for all arms. B Cell levels remained depleted in TC throughout; in TH and LTD, CD19, CD20, and naïve B Cell counts started to recover after 16 weeks off-treatment but rapidly decreased to minimal levels following restart (TH). No Grade 3/4 laboratory abnormalities were noted in the TH arm. A small proportion of patients in the TC and LTD arms had Grade 3/4 laboratory abnormalities.

Conclusion: Temporary (24-week) discontinuation of belimumab in patients with low disease activity did not appear to increase risk of SLE flares or rebound. Across 52 weeks, no ADAs were identified in any arm and the belimumab safety profile was consistent with previous reports. Small sample size and differences in Day 0 characteristics between LTD and TC arms limit the ability to draw inferences.

Study funding: GSK. Medical writing support: C Brazaitis, PhD, Fishawack Indicia Ltd, UK (funded by GSK).

Disclosure: S. Bae, None; **R. Dimelow**, GlaxoSmithKline, 1, 3; **B. Ji**, GlaxoSmithKline, 1, 3, 4; **R. Kurrasch**, GlaxoSmithKline, 1, 3; **S. Muzaffar**, GlaxoSmithKline, 1, 3; **R. Punwaney**, GlaxoSmithKline, 1, 3; **D. Roth**, GlaxoSmithKline, 1, 3, 4; **P. Stober**, GlaxoSmithKline, 1, 3; **Y. Song**, Astellas Pharma, Inc., 9; **W. Xie**, GlaxoSmithKline, 1, 3; **F. Zhang**, GlaxoSmithKline, 9.

Abstract Number: 2545

Belatacept in Systemic Lupus Erythematosus (SLE) Kidney Transplant Patients

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SESSION INFORMATION
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Session Type: Poster Session (Tuesday)
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Background/Purpose: Lupus nephritis (LN) ultimately requires renal replacement therapy (RRT) in 10-30% of LN patients. Thirty percent of these patients receive a kidney transplant. Belatacept is a second-generation, selective, T-cell co-stimulator blocker (inhibits CTLA-4) used as an alternative to calcineurin inhibitors (CNI) for maintenance regimens after kidney transplants. The pathogenic relevance of CTLA-4 inhibition and the favorable cardiovascular

Table 1: Characteristics of the 7 patients on belatacept.

ID	Age at SLE dx	Race	LN class	Time to KT (yrs)	Type KT	Induction	Reason for Bela Conversion	Immunosuppressive Régimen before Bela Conversion
A	16	Black	IV, VI	13	DDKT	Thymo	Non-adherence	TAC, MMF
B	30	Asian		2	LRKT	Thymo	Mod IFTA & Arteriosclerosis	TAC, MPA, PRED
C	18	White	IV, V	23	DDKT	Thymo	Cortical necrosis	CYC, MMF, PRED
D	19	Black	V	9	LUKT	Thymo	CNI side effects	TAC, MPA, PRED
E	22	Asian		5	LRKT	Thymo	CNI side effects	TAC, MMF, PRED
F	18	Black	V	17	DDKT	Alemtuzumab	CNI side effects	TAC, MMF, PRED
G	25	White (Hispanic)	III, IV	23	DDKT	Basiliximab	TMA on biopsy	TAC, MPA, PRED

Pt #: patient number; dx: diagnosis; y: years; DDKT: deceased donor KT; LRKT: living related KT; LURT: living unrelated KT; Thymo: thymoglobulin; TAC: tacrolimus; MMF: mycophenolate mofetil; PRED: prednisone; MPA: mycophenolic acid; CYC: cyclosporine;

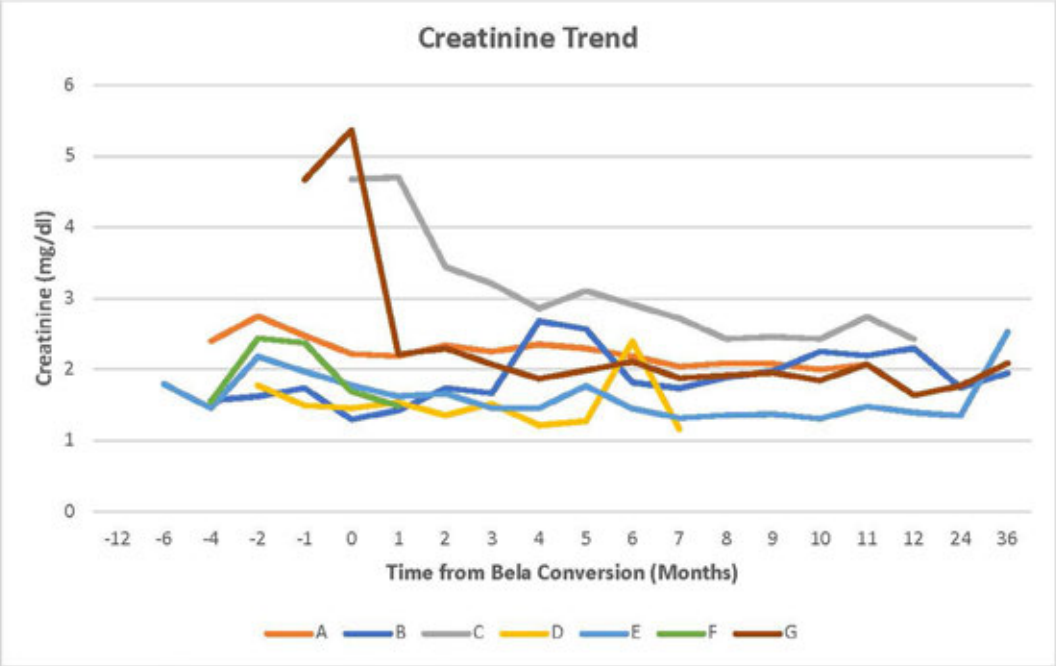

Figure 1: Trends in creatinine before and after belatacept conversion.

profile of belatacept make it an attractive therapeutic option in SLE. Additionally, intravenous administration of belatacept ensures therapeutic adherence.

Methods: This retrospective, single-center study evaluates the outcomes of LN kidney transplant recipients treated with belatacept from 2006 – 2018 at the Columbia University Lupus and Renal Transplant Cohorts. The treatment regimen consisted of 5mg/kg belatacept every 2 weeks for a total of 10 weeks (5 doses total), followed by monthly dosing. CNI weaning among the belatacept group was not standardized. Immunosuppressive regimen, kidney allograft function, and SLE activity were examined.The current study was initiated to evaluate the effect of belatacept on graft function and extrarenal SLE.

Results: Forty-eight patients with LN had undergone a kidney transplant between 2006 and 2018 with a mean follow-uptime of 72.2 ± 74.6 months. Belatacept was started in seven patients on CNI regimens (TAC n=6, cyclosporine n=1) at 15.5 ± 17.1 months following kidney transplantation. All patients were female with a mean age at SLE diagnosis of 21.1 ± 4.9 years. Five patients had undergone RRT prior to kidney transplantation (4 hemodialysis, 1 peritoneal

dialysis) for 38.7 ± 37.8 months. The mean interval between SLE diagnosis and KT was 13.1 ± 8.3 years. At the time of belatacept initiation, all patients were also treated with prednisone (7.1 ± 2.7 mg/day). Six were additionally treated with mycophenolate (1123 ± 625 mg/day), and one was additionally treated with azathioprine (25mg/day). CNIs were continued in five of seven patients at six months after belatacept. Two patients were on hydroxychloroquine, 2 took it only prior to KT. In five patients, creatinine levels stabilized six months after belatacept, one returned to hemodialysis due to CNI-toxicity and pyelonephritis and one is relisted for a kidney transplant due to ACR and cortical necrosis(Fig. 1). No allograft failure due to recurrent LN was noted in any of the patients. Five patients are currently followed for extrarenal lupus, and no extrarenal manifestations are documented in the other two patients. Data on SLE disease activity pre- and post- belatacept were available and scored in three of five patients using the SLEDAI-2KG which accounts for clinical and laboratory manifestations, as well as steroid use (Fig. 2). Mean ds-DNA pre and post belatacept was 133 ± 178 UI/mL and 58 ± 72 UI/mL, mean C3 89 ± 31mg/dL pre and 91 ± 21 mg/dL post, and mean C4 35 ± 15 mg/dL and 38 ± 7 mg/dL, respectively.

Conclusion: Belatacept in LN kidney transplant recipients may decrease extrarenal manifestations, attenuate CNI toxicity and stabilize allograft function, providing a better alternative to CNI regimens. Furthermore, these data suggest that belatacept may be a therapeutic option in SLE.

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Abstract Number: 2546

Clinician's Simple Opinion of SLE Disease Progress: Used in a Clinical Trial

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Measuring improvement or worsening is problematic in lupus trials. The British Isles Lupus Assessment Group (BILAG) index often fails to capture sustained decrease in disease activity when the change levels off. The SLE Disease Activity Index (SLEDAI) is inflexible if improvement does not meet a low threshold definition. False positive or negative flares create additional problems. "Mild/moderate" worsening on the SLEDAI Flare Index (SFI) can be due to insignificant changes. According to an older BILAG flare definition (>/= 2 new B or 1 new A), which is still commonly used, a false flare occurs if previously improving disease stabilizes, while true worsening is frequently missed when organ scores remain unchanged. A newer BILAG flare definition addresses most of these issues, but fails to account for > 1 feature flaring in a single organ or to allow a moderately severe flare in only 1 organ to rate more than "mild." Given the pitfalls of glossary-based measures, we sought the advice of the clinician in determining changes in disease severity.

Methods: A simple algorithm for clinician's global impression of change (CGIC) was tested during a phase 2 trial of the B Cell modulator, Xmab5871. investigators were asked to rate disease progress at each visit as "no change or

TABLE 1: Disease Change in SLE Disease Activity Indices: Correlation to CGIC

(All p values: </= 0.0000002)

	Change in SLEDAI	Change in PGA	CGIC
Change in BILAG	0.423	0.664	0.684
Change in SLEDAI		0.353	0.412
Change in PGA			0.745

Spearman Rank Order Correlation (both improvements and worsening were assessed)

TABLE 2: Percent of 102 SLE Patients Reaching Day 225 (end of treatment period) Without Worsening

Flare Definition	All Patients %	Xmab5871 %	PBO %	p value (chi sq)
OLD BILAG	21.5	21.5	21.5	NS
NEW BILAG	24.5	25	23.5	NS
SFI	22.5	25	19.6	NS
CGIC	33.3	43	23.5	0.059

a n=12 nondiabetic healthy subjects. Data represent mean ± standard error of mean. Abbreviation: RCI, repository corticotropin injection.

insignificant change" (NC) "significant partial improvement" (PI), "major or complete improvement" (MI), "significant moderate worsening" (MW), or "severe worsening" (SW). Discrepancies between the CGIC and other instruments were brought to the investigators' attention, but it was emphasized that the clinician's opinion could conflict with the technical scoring. Results were collected in an online database along with the BILAG, SLEDAI, PGA and SFI results.

Results: Of 104 randomized patients, data from 102 were available from 2-11 visits. The results of the trial have been reported elsewhere; briefly, the primary endpoint, maintenance of improvement, was met by 42% of XmAb5871-treated patients vs 28.6% of the placebo (PBO) group (p=0.18) and time to flare was longer in the XmAb5871 group (p=0.025). Using the CGIC, clinicians rated 445 visits as NC, 148 PI, 64 MI, 84 MW and 8 SW. CGIC was tested as a gold standard for the comparison of other measures of change that are used in SLE trials. Results of this study are summarized in Tables 1 and 2.

Conclusion: Clinician's opinion, recorded using CGIC, is better reflected by changes of BILAG and PGA than it is by the SLEDAI, which offers fewer gradations of scoring. More patients were free of flare using the CGIC compared to other instruments. In the double-blind trial of Xmab5871 the increased CGIC threshold for defining worsening disease impacted results for patients receiving active treatment more than PBO, suggesting the utility of CGIC as a gold standard for clinical significance.

Disclosure: A. Askanase, Xencor, 2; **A. Saxena**, Xencor, 2; **A. Thanou**, Neovacs, 5; **C. Arriens**, AstraZeneca, 5, BMS, 2, 5, Exagen, 2, GSK, 2, 5; **D. Zack**, Xencor, Inc., 3; **J. Merrill**, Xencor, 2.

Abstract Number: 2547

Safety Results of 50% Enrollment from a Multicenter, Randomized, Double-blind, Placebo-controlled Study to Assess the Efficacy and Safety of Repository Corticotropin Injection in Patients with Systemic Lupus Erythematosus Despite Moderate-dose Corticosteroid Use

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
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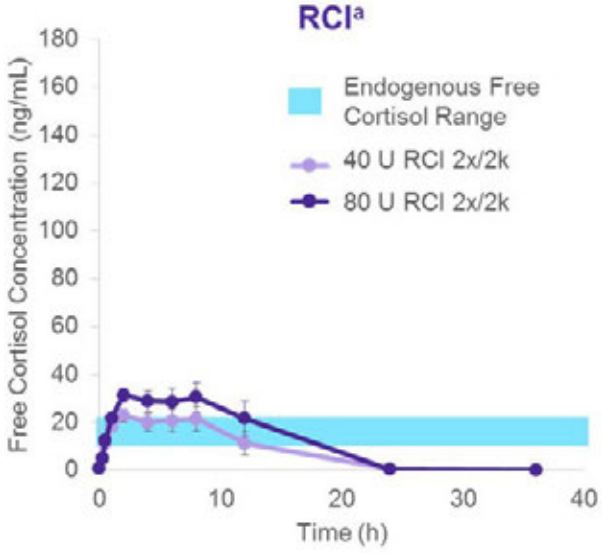
Background/Purpose: Repository corticotropin injection (RCI) is a naturally sourced complex mixture of adrenocorticotropic hormone ($ACTH_{1-39}$) analogues and other pituitary peptides that stimulates endogenous corticosteroid (CS) production and is an agonist for all 5 melanocortin receptors. RCI is approved by the US FDA for the treatment of acute exacerbations or as maintenance therapy in patients with systemic lupus erythematosus (SLE). In a pilot study,[1] RCI improved disease activity (vs placebo) and was well tolerated in patients with SLE. In a separate study, RCI increased endogenous cortisol levels to a similar extent as < 10 mg ofexogenous prednisone (**Figure 1**; data on file). The current trial was designed to assess the efficacy and safety of RCI in patients with persistently active SLE despite use of moderate-dose CSs (ClinicalTrials.gov ID: NCT02953821). This abstract describes the safety data from 50% of the expected enrolled subjects from the blinded and ongoing trial.

Methods: Patients enrolled in this multicenter, double-blind, randomized, placebo-controlled, 24-week trial are required to have SLE (≥4 of 11 ACR 1997 criteria) and active disease (moderate to severe rash and/or arthritis) despite stable doses of CSs ≥4 weeks before screening. Treatments are 1 mL RCI (80 U) or placebo subcutaneously every other day for 4 weeks, followed by twice per week for 20 weeks. Randomization is stratified by study site location (US



a n=12 nondiabetic healthy subjects. Data represent mean ± standard error of mean. Abbreviation: RCI, repository corticotropin injection.

Characteristic	Patients, n=80
Age, mean (SD), y	41.5 (13.5)
Female, no. (%)	74 (92.5)
Race, no. (%)	
White	33 (41.3)
Black or African American	11 (13.8)
American Indian/Alaska Native	14 (17.5)
Other	13 (16.3)
Ethnicity, n (%)	
Hispanic/Latino	53 (66.3)
Not Hispanic/Latino	23 (28.8)
Weight, mean (SD), kg	75.1 (20.0)
SLEDAI-2K total score, mean (SD)	9.7 (2.8)
BILAG total score	18.9 (5.6)
PGA, mean (SD), mm	62.3 (12.0)
Prednisone/equivalent daily dosage, mean (SD), mg	11.2 (5.3)
Prednisone/equivalent dosage, no. (%)	
≤20 mg/d	75 (93.8)
>20 mg/d	5 (6.3)
Antimalarials, no. (%)	52 (65.0)
Immunosuppressants, no. (%)	48 (60.0)
Complement C3, mean (SD), mg/dL[b]	118.9 (34.1)
Complement C4, mean (SD), mg/dL[b]	22.1 (10.1)
Anti-ds DNA antibody, mean (SD), IU/mL[b]	25.9 (65.0)

a Maximum, 100 mm. b n=79. Abbreviations: anti-ds, anti–double stranded; BILAG, British Isles Lupus Assessment Group; mITT, modified intent-to-treat; PGA, Physician's Global Assessment; SD, standard deviation; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index-2000.

System Organ Class Preferred Term	Patients, n=80 No. (%)
Any TEAE of special interest	5 (6.3)*
Infections and infestations	2 (2.5)
Pneumonia	1 (1.3)
Pyelonephritis	1 (1.3)
Metabolism and nutrition disorders	2 (2.5)
Hyperglycemia	2 (2.5)
Vascular disorders	2 (2.5)
Hypertension	2 (2.5)

*One patient had 2 TEAEs. Abbreviation: TEAE, treatment-emergent adverse event.

or outside of US) and prednisone or equivalent dose (≤20, >20 mg/d). Patients remain on stable doses of CSs through week 16, with tapering encouraged between weeks 16 and 24. The primary efficacy end point is the proportion of SLE Responder Index-4 (SRI-4) responders at week 16. Secondary and exploratory end points include measures of disease activity, prednisone dose, and serum biomarkers (ie, complements, autoantibodies, and inflammatory and bone turnover markers). Target enrollment is 270 patients; 162 are expected to be randomly assigned at ~60 global sites. Safety assessments include treatment-emergent AEs (TEAEs), physical examination, and vital signs and are summarized with descriptive statistics only.

Results: The 80 patients in this evaluation represent ~50% of the patients expected to be randomly assigned in the study. Data from these patients were blinded. Demographics and baseline characteristics show a racially diverse population (**Table 1**). A total 53 (66.3%) patients reported a TEAE, with the most common being headache (8.8%) and insomnia (6.3%). TEAEs of special interest are shown in **Table 2**. The reported serious AEs (pneumonia, hypertension) were deemed related to treatment and expected. No Suspected Unexpected Serious Adverse Reactions or deaths were reported.

Conclusion: In a study of RCI in patients with active SLE despite moderate-dose CS, blinded 50% enrollment data show disease characteristics consistent with those expected for patients with moderate/severe SLE. The safety profile suggests that RCI is well tolerated, consistent with a modest increase in cortisol production. The complete dataset will provide valuable information on the role of RCI in refractory SLE.

1 Furie R, et al. *Lupus Sci Med*. 2016;3(1):e000180.

Disclosure: A. Askanase, None; **D. Munirathinam**, Mallinckrodt Pharmaceuticals, ARD, LLC, 3; **E. Zhao**, Mallinckrodt Pharmaceuticals, ARD, LLC, 3; **J. Zhu**, Mallinckrodt Pharmaceuticals, ARD, LLC, 3; **E. Connolly-Strong**, Mallinckrodt Pharmaceuticals, ARD, LLC, 3; **R. Furie**, Biogen, 5, GlaxoSmithKline, 2, 5, UCB Pharma, 2, 5.

Abstract Number: 2548

Abatacept Failed to Demonstrate Efficacy in an SLE Trial with Low Placebo Response Rates, Although Global Assessments Indicated Less Flare Severity

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SESSION INFORMATION
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Abatacept (ABA) is a fusion protein of the extracellular domain of CTLA4 and human IgG1-Fc, constructed to inhibit B/T cell co-stimulation. Previous studies of ABA in lupus failed to show benefit, but improvement in arthritis was suggested. Those studies included significant background medications and steroid rescue. The current 6-month randomized, double-blind, placebo (PBO)-controlled study of ABA in patients with SLE arthritis withdrew background medications to facilitate assessments.

Methods: Patients were entered with moderate to severe arthritis (BILAG A or B with ≥3 swollen and ≥3 tender joints). All SLE treatment except low dose prednisone was withdrawn and patients were randomized 1:1 to weekly sc ABA or PBO. DepoMedrol injections (≤320mg total) were allowed, if needed, until Month 2. At Month 3, additional steroids, immune suppressants or open-label ABA were allowed, but designated non-response. The primary endpoint was the BILAG-based Combined Lupus Assessment (BICLA) response at Month 6. The SELENA-SLEDAI PGA (SSPGA) and the LFA-Rapid Evaluation of Activity in Lupus (LFA-REAL) were used as exploratory endpoints. The SSPGA is a single visual analogue scale (VAS) assessing overall lupus activity, and the LFA-REAL derives a total VAS score by summing individual symptoms (1).

Results: 66 randomized patients received at least one dose of the study drug. Placebo response rates were lower than most SLE trials, but no primary or secondary endpoints were met (Table). The safety profile of ABA was consistent with its known effects. Additionally, a flare analysis was performed.

	ABA (n=31)	PBO (n=35)	p value
BICLA	8(26%)	8(23%)	>0.999
SRI4	9(29%)	8(23%)	0.587
SLEDAI 4 point improvement	9(29%)	8(23%)	0.587
SLEDAI arthritis improvement	9(29%)	8(23%)	0.587
BILAG A/B MSK improvement	9(29%)	8(23%)	0.587
SLEDAI 2	8(26%)	7(20%)	0.769
LLDAS	6(19%)	8(23%)	0.772

Table. Primary and secondary efficacy assessments at Month 6.

By Month 6, 13 (42%) patients on ABA vs. 15 (45%) PBO had a moderate/severe flare and 22 (71%) patients on ABA vs. 22 (67%) PBO experienced flare or treatment failure (dropout or added medications) (Log-Rank test, p=0.941 and p=0.539, respectively). Using the modified SELENA-SLEDAI Flare Index (mSSFI) (2) or BILAG flare index, global flare severity did not differ between groups, even after adjusting for rescue steroids, SLEDAI at screening and SLEDAI at visit prior to flare. Similarly, BILAG musculoskeletal (MSK) flares did not differ between groups.

Using the SSPGA and LFA-REAL, flare severity was greater in the PBO group vs. the ABA group. Adjusting for LFA-REAL MSK score at visit prior to flare and flare severity by BILAG MSK, increase in LFA-REAL MSK at flare visits was 8.7±1.5 for PBO and 3.0±1.5 for ABA (p=0.07). Adjusting for SSPGA at visit prior to flare and flare severity by mSSFI, increase in SSPGA at flare visits was 10.4±1.6 for PBO and 4.8±1.7 for the ABA group (p=0.017). The score difference for LFA-REAL was 15.5±2.7 for PBO vs. 5.1±2.8 for ABA-treated patients (p=0.008).

Conclusion: This protocol lowered PBO response rates to ≤23% by mandating withdrawal of background treatments. ABA did not demonstrate improvement in controlling disease activity. SSPGA and LFA-REAL scores suggested a decrease in flare severity in the ABA-treated patients.

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2. Thanou A, Chakravarty E, James JA, Merrill JT. Rheumatology (Oxford) 2014;53(12):2175-81.

Disclosure: A. Thanou, Neovacs SA, 5, BMS, 2, GSK, 2; **C. Arriens**, AstraZeneca, 5, BMS, 2, 5, Exagen, 2, GSK, 2, 5; **T. Aberle**, None; **H. Miller**, None; **L. Mitchell**, None; **S. Kamp**, None; **A. Askanase**, Xencor, 2; **S. Stavrakis**, Neovacs SA, 5, BMS, 2, GSK, 2; **J. James**, Abbvie, 5, Janssen, 5, Progentec, 2, Progentec Diagnostics, Inc., 2, Xencor, 2, Xencor, Inc., 2; **J. Merrill**, Abbvie, 5, Amgen, 5, Astellas, 5, AstraZeneca, 5, BMS, 2, 5, Celgene, 5, EMD Serono, 5, GSK, 2, 5, Idorsia, 5, ILTOO, 5, Immupharma, 5, Incyte, 5, Janssen, 5, Lilly, 5, Remegen, 5, Servier, 5, Xencor, Inc., 2.

Abstract Number: 2549

Population Pharmacokinetics of Atacicept in Systemic Lupus Erythematosus (SLE) – an Analysis of Three Clinical Trials

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Atacicept targets the B-cell stimulating factors BLyS and APRIL and has been shown to reduce SLE disease activity. The aim of the analysis was to describe the pharmacokinetic (PK) profile of total (i.e. bound and unbound) atacicept after subcutaneous (sc) administration in healthy volunteers (HV) and SLE patients using a semi-mechanistic population PK model and to identify covariates explaining PK variability.

Methods: A total of 540 subjects, 37 from a Phase I study in Caucasian and Japanese HV where single 25, 75 or 150 mg sc doses of atacicept were administered, 298 from a Phase II study in SLE (NCT00624338) where 75 or 150 mg sc doses were administered weekly (QW) for 52 weeks (bi-weekly for the first 4 weeks of treatment), and 205 from

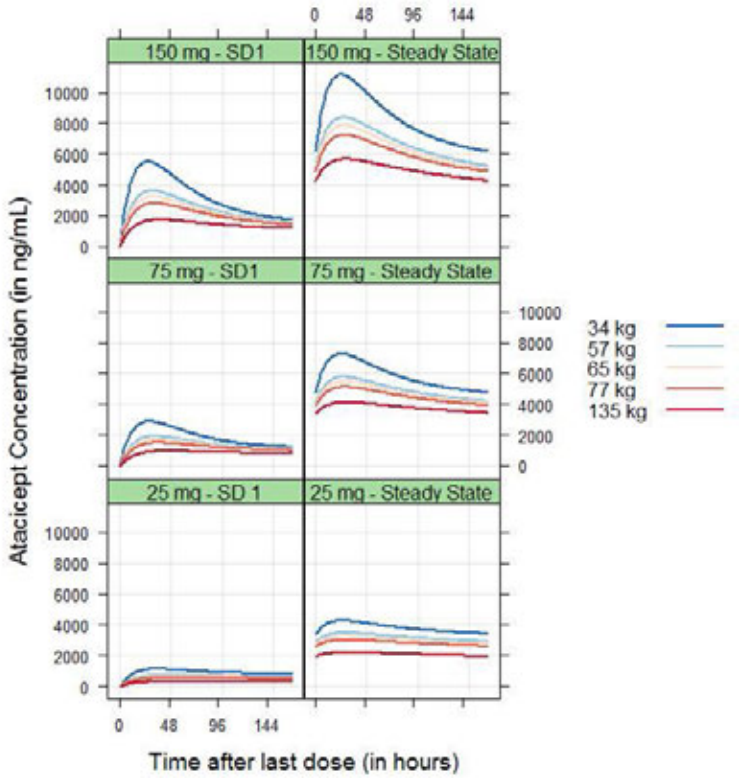

Figure 1. Simulated Typical Subject PK Profiles of total Atacicept for a Range (min, quartiles, max) of Baseline Weights – First Dose and Steady State – QW Dosing

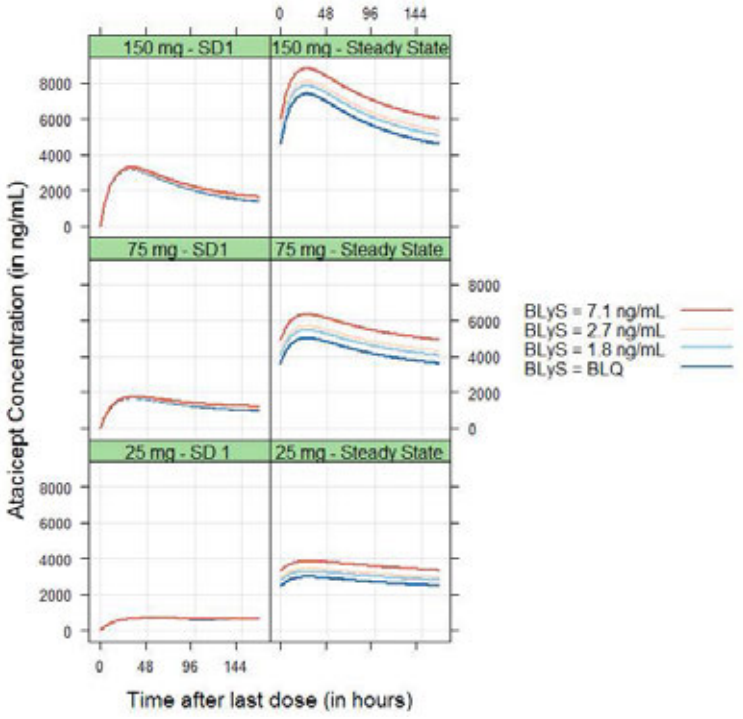

Figure 2. Simulated Typical Subject PK Profiles of total Atacicept for a Range of Baseline BLyS concentrations: BLQ (minimum and 1st quartile), 1.8 (median), 2.7 (3rd quartile) and 7.1 (97.5th percentile, as the maximum was a clear outlier) – First Dose and Steady State – QW Dosing

a second Phase II study in SLE (NCT01972568) with QW sc dosing of 75 or 150 mg for 24 weeks, contributed 3640 measurements of total atacicept in serum. Modeling was performed with the NONMEM software. A Quasi-Steady-State (QSS) approximation [1] of the target-mediated drug disposition (TMDD) [2] model was used to describe drug concentrations. Covariates tested in the model were weight, age, creatinine clearance, serum BLyS and APRIL (all at baseline), gender, race, dose and SLE vs HV population. Model-based exposure metrics (e.g. area under the concentration curve, AUC) were derived. Covariate effects were evaluated via simulations.

Results: A two-compartment QSS TMDD binding model with first-order absorption described total atacicept concentrations of the three trials, adequately capturing the central tendency and variability in the data. The model provided precise (relative standard errors < 20%) estimates of all parameters, including binding (K_{ss}=19.9 ng/mL), target turnover (R_{max}=715 ng/mL; K_{deg}=0.00362 h^{-1}), and drug-target complex elimination (K_{int}=0.000618 h^{-1}) parameters. The typical estimates of apparent linear clearances and volumes of distribution of the drug were: CL/F=0.324 L/h, Vc/F=36.3 L, Q/F=0.149 L/h and Vp/F=38.5 L. Residual variability was moderate, slightly higher in SLE patients (CV=25%) than in HV (CV=19%).

Drug CL/F and central volume Vc/F increased with body weight following allometric relationships (exponents of 0.75 and 1.00, respectively), while baseline target concentration (R_{max}) increased with baseline BLyS concentration (as R_{max} ~$(BLyS/2.56)^{0.176}$); however, resulting differences in exposure were small (Figure 1 and 2). No significant differences in PK between HV and SLE patients or racial groups were detected.

Conclusion: The developed population PK model allowed the description of the complete atacicept concentration time profile in SLE patients, a first step in the identification of exposure-response relationships for pharmacodynamic/clinical/safety endpoints that informed on Phase III study design.

References:

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[2] Mager DE, Jusko WJ. General pharmacokinetic model for drugs exhibiting target-mediated drug disposition. J Pharmacokinet Pharmacodyn, 2001; 28:507-532.

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Abstract Number: 2550

Impact of Pathogenic and Protective Environmental Exposures on Autoimmune Disease—The Microbiome Effects on Lupus (MEL) Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic and often severe multi-organ autoimmune disease characterized by the production of autoantibodies and heterogeneous clinical manifestations. African Americans (AA) and young women are disproportionately affected by SLE, and AAs develop SLE at a younger age with a higher prevalence of kidney involvement (lupus nephritis, LN) compared to other racial/ethnic groups.

Little is known about the etiology of SLE. Genetic inheritance alone is insufficient for developing SLE, suggesting environmental triggers play a role in disease expression. Gut microbiota play a key role in setting the systemic immune tone and influences regulatory and inflammatory immunologic responses. Our study investigates gut microbiome characteristics that may lead to development, progression, and severity of disease in SLE. We hypothesize that gut microbial variation exists at the structural level between patients with SLE (either with or without LN), and healthy controls. Furthermore, we suspect higher microbiome diversity is protective against autoimmunity and a higher proportion of “pro-inflammatory” microbes is a risk factor for SLE and LN.

Methods: We characterized the microbial composition of fecal DNA from samples obtained from AA patients with SLE and from non-SLE AA controls. All participants provided informed consent for research participation and SLE/LN vs control status was confirmed during in-person interview, examination, lab evaluation, and record review. We performed genomic assessment of gut microbial communities using whole genome shotgun sequencing. Gut microbiota was quantified using a sequence-based profiling method. These metagenomes were analyzed against known microbial genome databases (NCBI-NR). Genus abundance profiles were constructed to evaluate microbial species distribution.

Results: 58 samples have been collected (28 SLE/LN and 30 controls) to date. Of these, 44 samples have been sequenced (27 patients and 17 unrelated controls) with the remaining pending at this time. Using metagenomic phylogenetic analysis, 371 species were identified. Principal coordinate analysis between female patients and female controls revealed no significant difference in organism abundance (p-value= 0.5914). In patients with lupus nephritis (n=9) compared to lupus patients without renal disease and controls (n=35), there was no significant difference in abundance at the phylum level (p-value= 0.3681).

Conclusion: Our preliminary studies show that among AA females with SLE and lupus nephritis, gut microbiome composition appears similar to that of unrelated controls. Other similar studies have shown significant differences in microbiome composition between SLE patients and controls, however patients included in our studies had low SLEDAI scores, indicating low disease activity at time of sample collection. We plan to perform multivariate modeling to determine if environmental factors (age, medications, diet, smoking, occupational exposures) in addition to SLE disease status affect microbial composition.

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Abstract Number: 2551

Validity and Reliability of Patient Reported Outcomes Measurement Information System (PROMIS) Computerized Adaptive Tests (CAT) in a Canadian Cohort of Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
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Background/Purpose: Patient-reported outcome measures are invaluable tools in clinical practice and are central in providing patient-centered care. There has been minimal research on the use of the Patient Reported Outcomes Measurement Information System (PROMIS) computerized adaptive test (CAT) in adults with systemic lupus erythematous (SLE). The present study aims to examine the construct validity and test-retest reliability of the PROMIS CAT in a Canadian cohort of patients with adult SLE.

Methods: All consecutive adult (≥18 years) patients with SLE visiting a Canadian Lupus Clinic between July-September 2018 were approached to participate. Patients completed PROMIS CAT during their clinical visit assessing 14 domains of health: physical function, mobility, pain behaviour, pain interference, ability to participate in social roles, satisfaction with social roles and activities, fatigue, sleep disturbance, sleep-related impairment, applied cognition-abilities, applied cognition-general concerns, anger, anxiety, and depression. C**onstruct validity** (using Spearman correlation, r) of PROMIS CAT scales was evaluated against commonly-used legacy instruments: SF-36, LupusQoL, the Perceived Deficits Questionnaire (PDQ-20), Beck Depression Scale - 2nd edition (BDI-II), Beck Anxiety Inventory (BAI), the Assessment of Chronic Illness Therapy Fatigue Scale (FACIT), and the Epworth Sleepiness

Table 1. PROMIS domains scores

Domain	Mean ± SD
Physical function	43.6 ± 9.2
Mobility	44.7 ± 9.6
Pain behaviour	53.7 ± 10.8
Pain Interference	55.2 ± 10.7
Ability to participate in social roles	48.2 ± 9.8
Satisfaction with social roles & activities	48.7 ± 11.4
Fatigue	57.3 ± 10.5
Sleep disturbance	55.4 ± 10.2
Sleep related impairment	56.0 ± 10.7
Anger	51.3 ± 9.8
Anxiety	55.6 ± 8.9
Depression	52.3 ± 9.8
Applied cognition-abilities	46.7 ± 9.3
Applied cognition-general concerns	46.4 ± 8.8

Domains highlighted in grey fell out of +/- 0.5 SD of population mean

Table 2. Test-retest reliability (Intraclass Correlation Coefficient (ICC [2;1]), n= 81

Domain	ICC (2, 1) and 95% CI
Physical function	0.90 (0.83, 0.94)
Mobility	0.91 (0.85, 0.95)
Pain behaviour	0.73 (0.50, 0.90)
Pain Interference	0.78 (0.63, 0.92)
Ability to participate in social roles	0.85 (0.75, 0.93)
Satisfaction with social roles & activities	0.70 (0.44, 0.88)
Fatigue	0.79 (0.65, 0.88)
Sleep disturbance	0.69 (0.49, 0.83)
Sleep related impairment	0.76 (0.64, 0.87)
Anger	0.71 (0.52, 0.85)
Anxiety	0.70 (0.51, 0.84)
Depression	0.82 (0.76, 0.90)
Applied cognition-abilities	0.64 (0.50, 0.78)
Applied cognition-general concerns	0.83 (0.72, 0.93)

Scale. **Test-retest reliability** (intraclass correlation coefficient (ICC [2;1]) was evaluated using baseline data and PROMIS CAT scores 7-10 days after baseline.

Results: 182 patients (91.2% females) with a mean age of 49.0± 14.1 years and mean disease duration of 18.5 ±12.2 years were enrolled. **Table 1** demonstrates the PROMIS sample mean with the population mean of 50±10 as reference. Half of domains' scores appeared to be within + /- 0.5 Standard Deviation (SD) of the population mean while Physical function and Mobility fell below 0.5 SD and Pain Interference, Fatigue, Sleep disturbance, Sleep related impairment, and Anxiety fell above 0.5 SD. Moderate-high correlations (r= 0.59-0.87) between PROMIS scores and relevant legacy instruments were demonstrated confirming a priori hypotheses regarding construct validity of the PROMIS CAT scales [e.g. r=0.85 for SF-36 Physical Functioning and PROMIS Physical Functioning; r=0.82 for FACIT-F and PROMIS Fatigue]. In 81 patients, good test-retest agreement was found for the majority of domains [ICC (2;1) range 0.64-0.93] (**table 2**). The lowest ICCs [2;1] were identified for applied cognitive abilities (ICC 0.64, 95% CI:0.50-0.78) and sleep disturbance (ICC 0.69, 95% CI:0.49-0.83).

Conclusion: This is the first study to examine the construct validity and the reliability of PROMIS CAT in a Canadian adult SLE cohort. Compared to legacy instruments (such as SF-36), PROMIS CAT has moderate-high correlation confirming its **construct validity** and good-excellent **reliability**. Considering the increasing use of the PROMIS across different health diagnoses, the PROMIS may be a promising non-diagnostic instrument to enhance SLE research and clinical practice.

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Abstract Number: 2552

Design and Development of an Online Intervention for Lupus Self-Management Based on the Transtheoretical Model of Change

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Background/Purpose: The Lupus Foundation of America is in Year 4 of a 6-year cooperative agreement with the Centers for Disease Control and Prevention to develop an online lupus self-management program based on the Transtheoretical Model of Change (the "stage model"). The program, *Strategies to Embrace Living with Lupus Fearlessly* (SELF), is a web-based intervention designed to help users adopt 4 key lupus self-management behaviors: 1) managing symptoms, 2) managing stress, 3) managing medications, and 4) working with a health care team. These behaviors were identified and operationally defined in year 3 of the cooperative agreement. We summarize the program design, as well as feedback from early users and engagement experts.

Methods: The intervention consists of 4 complementary components: 1) user assessments, 2) a web portal with stage-matched activities and information, 3) outbound text messages and emails to facilitate change and user engagement, and 4) a reporting tool to measure program utilization and outcomes.

The intake process consists of 4 modules, each focused on one of the 4 key behaviors. The modules provide feedback tailored to user responses to questions. After intake, users select a behavior to focus on, and a customized web portal becomes available. The portal includes stage-matched activities, a symptom tracker, a journal, information on the 4 key lupus self-management behaviors, and links to the Foundation's National Resource Center on Lupus, Health Educators, and LupusConnect™ messaging boards for peer support. Participants can sign up for emails or texts with stage-matched tips and links to the portal activities.

Every two weeks, the program delivers a mini assessment to track changes in self-efficacy, and asks users to select the behavior they would like to focus on next. Every 90 days, the program administers a comprehensive assessment and a printable report summarizing data on lupus symptoms, self-management behaviors, and stage of change that can be shared with a provider.

5 individuals with lupus with diverse demographic characteristics recruited by the Lupus Foundation of America served as early program testers. Engagement experts also reviewed the program design and structure.

Results: Feedback from early users and engagement experts was largely positive and used to refine the online program. Program development will be finalized by the Fall of 2019, at which time pilot testing will begin.

Conclusion: The SELF program is designed to provide a cohesive, tailored experience to help individuals with lupus manage their condition. This is the first program of its kind to deliver information and activities tailored to stage of change for four key behaviors for lupus self-management.

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Abstract Number: 2553

Prescription Opioid Use and Osteoporotic Fractures in Systemic Lupus Erythematosus: The Michigan Lupus Epidemiology & Surveillance (MILES) Cohort

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Background/Purpose: We recently reported prescription opioid use in nearly one-third of systemic lupus erythematosus (SLE) patients in our population-based cohort. Data suggest that opioids may be associated with falls and decreased bone mineral density (postulated via impaired osteoblast activity and indirectly via hypothalamic-pituitary-adrenal axis dysfunction and hypogonadism), both of which increase fracture risk. Osteoporosis rates are elevated in SLE due to factors including use of glucocorticoids and gonadotoxic therapies (that can result in primary ovarian insufficiency). This analysis examines the association between opioid use and osteoporotic fractures in SLE.

Methods: The study included SLE patients from the population-based MILES Cohort. Sociodemographic, clinical and prescription data were obtained by structured interviews. Osteoporotic fracture history was ascertained from the validated Lupus Damage Index Questionnaire (LDIQ). Locally weighted scatterplot smoothing (Lowess) curve was fit to visualize the relationship between opioid duration and osteoporotic fracture, and determine the appropriate functional form for modelling. Multivariable logistic regression was then used to model the relationship between opioid usage and osteoporotic fracture, controlling for other variables specified *a priori* as relevant: age, sex, race, ethnicity, smoking history (daily cigarette smoking for ≥6 months), body mass index, SLE duration, high steroid exposure history (≥10 mg oral steroids for ≥1 month) and for females, cessation of menses prior to age 40 years, not due to surgery (indicator of primary ovarian insufficiency).

Results: Among the 458 SLE participants in this study, average age was 53.4 years (SD 12.3), 427 (93.2%) were female, and race was primarily self-reported as black (205; 44.8%) or white (233; 50.9%). Current prescription opioid use was reported by 141 participants (30.8%). History of osteoporotic fracture was reported in 16/141 participants with current prescription opioid use (11.4%) vs 17/317 not using opioids (5.4%); p=0.022. From multivariable regression, current opioid use (binary variable) was not associated with fractures; however, duration of opioid use was sig-

nificantly associated. Lowess curve indicated a piecewise linear relationship with an inflection at 15 years: for those with opioid use ≤15 years (n=120), odds of fracture were 16% more likely per year increase [OR 1.16 (95% CI 1.06, 1.26), p< 0.001], after adjusting for the covariates. Results were similar when restricting to females. Data were sparse beyond 15 years of opioid use (n=11) thus statistically unstable.

Conclusion: Duration of opioid use was associated with osteoporotic fracture in SLE patients. The odds of fracture increased by 16% for each year of use within 15 years of opioid initiation. Although a temporal association cannot be established from this study, and mitigating factors such as inactivity secondary to pain may be involved, our data suggest that chronic opioid therapy is an indicator for osteoporosis screening in the SLE. The potential for adverse effects on bone health further provides impetus for alternative pain management strategies.

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Abstract Number: 2554

Do All Patients Who Achieve Lupus Low Disease Activity State Have Similar Outcomes?

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Background/Purpose: Lupus Low Disease Activity State (LLDAS) has been associated with favourable outcomes in systemic lupus erythematosus (SLE). However, the complexity of its defining criteria (SLEDAI-2K≤4, no major organ involvement, no new clinical manifestation, no increase in Physician' s Global Assessment, daily prednisone dose≤7.5mg/day and stable doses of antimalarials, immunosuppressives and biologics) allows for considerable heterogeneity among these patients. The aim of the present study was to describe the major LLDAS phenotypes in inception patients first achieving LLDAS with emphasis on the likelihood of flare.

Methods: Inception patients from the Lupus Clinic (enrolled within 18 months since diagnosis) who achieved LLDAS for two consecutive visits from January 2000 to December 2016 were included. All patients were followed for at least two years and divided into major phenotypes as follows: glucocorticosteroid use (or not), clinical SLEDAI-2K≤2 on antimalarials only (or not) and serologically active clinically quiescent (SACQ) disease (or not). The likelihood of disease flare (any deviation from LLDAS) was assessed over the next 2 and then 5 years. SAS 9.4 was used for statistics; p< 0.05 was considered significant.

Results: Four hundred twenty one patients achieved LLDAS for two consecutive visits; 357 had at least two years and 295 had at least five years of follow-up. At two years, 149/357 (41.7%) patients flared after 1.1 years on average

Likelihood of lupus flare in the different subgroups of the patients who achieved LLDAS				
	At 2 years (n=357)		At 5 years (n=295)	
	Flares (n, %)	*p*	Flares (n, %)	*p*
No glucocorticosteroids	54/154 (35.1%)	0.026	79/127 (62.2%)	0.013
Treatment with glucocorticosteroids	95/203 (46.8%)		127/168 (75.6%)	
Clinical SLEDAI-2K≤2 on AM only	40/129 (30%)	0.002	64/107 (59.8%)	0.0047
Clinical SLEDAI-2K>2 on AM or glucocorticosteroids or immunosuppressives	109/228 (47.8%)		142/188 (75.5%)	
SACQ* only	69/149 (46.3%)	0.138	89/124 (71.8%)	0.536
Non-SACQ**	80/208 (38.5%)		117/171 (68.4%)	
*SACQ: serologically active clinically quiescent disease (LLDAS where the only SLEDAI-2K component is serology) ** LLDAS where SLEDAI-2K components must include clinical manifestations AM: antimalarials Flares were defined as any deviation from the LLDAS				

whereas at five years 206/295 (69.8%) patients flared after 1.9 years on average. The differences in the likelihood of flares are shown in the table.

Conclusion: Within the LLDAS population, patients who achieved a clinical SLEDAI-2K≤2 on antimalarials only as well as the patients who were not treated with glucocorticosteroids developed significantly less flares over 2 and 5 years. These findings suggest that the use of glucocorticosteroids or immunosuppressives and the nature of the clinical manifestations impact the ability of LLDAS to predict flares over the next 2 and 5 years.

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Abstract Number: 2555

Antimalarial-Induced Cardiomyopathy: Outcome in 10 Patients

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Outcomes of structural, functional, conduction and biochemical abnormalities in AMIC		
Outcome	**At AMIC diagnosis**	**At last visit**
Death	N/A	1/10 (three months after diagnosis due to refractory heart failure)
Left ventricular hypertrophy (by echocardiogram)	Mild: 6 Moderate-to-severe: 4	Mild: 7 Moderate-to-severe: 3
Septal hypertrophy (by echocardiogram)	Mild (12-14mm): 7 Moderate-to-severe (≥15mm): 3	Mild (12-14mm): 8 Moderate-to-severe (≥15mm): 2
Left atrium	Mildly dilated or normal: 4 Moderate-to-severely dilated: 6	Mildly dilated or normal: 8 Moderate-to-severely dilated: 2
Systolic dysfunction (EF≤ 45%)	One patient	Full recovery
Diastolic dysfunction	Grade 1-2: 7 Grade 3: 3	Grade 1-2: 8 Grade 3-4: 2
Severe arrhythmias (requiring hospitalization)	One patient with permanent pacemaker due to complete AVB	One patient developed complete AVB and received a permanent pacemaker 18 months after drug withdrawal Two patients developed paroxysmal atrial fibrillation (12 months after drug withdrawal) and were managed with ablation
Troponin I	Abnormal in all patients	Serum levels reduced significantly in 7/10, unchanged in 2/10, increased in one patient Still abnormal in 8/10 at last visit
BNP	Abnormal in all patients	Reduced in 6/10 patients, still abnormal in 6/10 Normalized in 4/10

Background/Purpose: Antimalarial-induced cardiomyopathy (AMIC) is a hypertrophic cardiomyopathy with conduction system disorders, cardiac biomarker abnormalities and a short-term mortality of 45%. Data on the reversibility of the disease are sparse. The aim of this study is to assess the evolution of AMIC in the long term in patients with systemic lupus erythematosus (SLE).

Methods: Ten patients with SLE who developed AMIC were analyzed (mean age at diagnosis 63±8.7 years, mean disease duration 32.8±12.7 years, mean antimalarial treatment duration 22.4±9.4 years). Diagnosis was confirmed by myocardial biopsy in three patients (extensive cardiomyocyte vacuolation, intracytoplasmic myelinoid and curvilinear bodies) and considered probable in another seven cases based on a combination of abnormal cardiac biomarkers (high sensitivity troponin I and brain natriuretic peptide, BNP), hypertrophic cardiomyopathy (based on cardiac magnetic resonance, CMR) and the exclusion of other causes (coronary artery disease, uncontrolled hypertension). Other types of idiopathic hypertrophic cardiomyopathy and/or Anderson-Fabry cardiomyopathy were excluded by genetic testing.

Results: Mean follow-up after AMIC diagnosis was 23.7±10.7 months; antimalarials were discontinued in all patients, while diuretics were commenced or intensified in three. The evolution of structural, functional and conduction system abnormalities as well as the cardiac biomarkers are shown in the table.

All four patients with severe arrhythmias had a right bundle branch block and two of them had bifascicular block for years before the arrhythmia. The median reduction of troponin I (7/10 patients) was 29.7% at one year, 53.1% at two years and 74.1% at three years (compared to baseline). The median reduction of BNP (6/10 patients) was 49% at one year, 81.3% at two years and 68.8% at three years (compared to baseline).

Conclusion: Recovery of the structural (left ventricular and septal hypertrophy, left atrium enlargement), functional (systolic and diastolic dysfunction) and biochemical variables (troponin I, BNP) occurs in most patients with AMIC but this is slow and often incomplete even after two years. Conduction abnormalities may still develop many months after drug withdrawal.

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Abstract Number: 2556

Histologic Findings from Paired Renal Biopsies and Clinical Outcomes: Results from a Single Site in the Phase III Study of Abatacept in Patients with Proliferative LN

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Table 1. Baseline Demographics, Disease Characteristics, Duration of Therapy and Mean Time Between Bx

	Abatacept	Placebo
Age, years, mean	29.6	33.5
UPCR, baseline/at Year 1, mean (g/g)	4.12/0.56	4.18/1.53
Duration of therapy, days, mean	795	750
Time between first Bx and first study treatment, days, mean	92	102
Time between Bx, months, mean	39	32
First Bx, AI/CI, mean	5.4/3.4	4.8/3.8
Second Bx, AI/CI, mean	0.8/4.4	2.9/3.6

AI=activity index; Bx=biopsy; CI=chronicity index; UPCR=urine protein to creatinine ratio

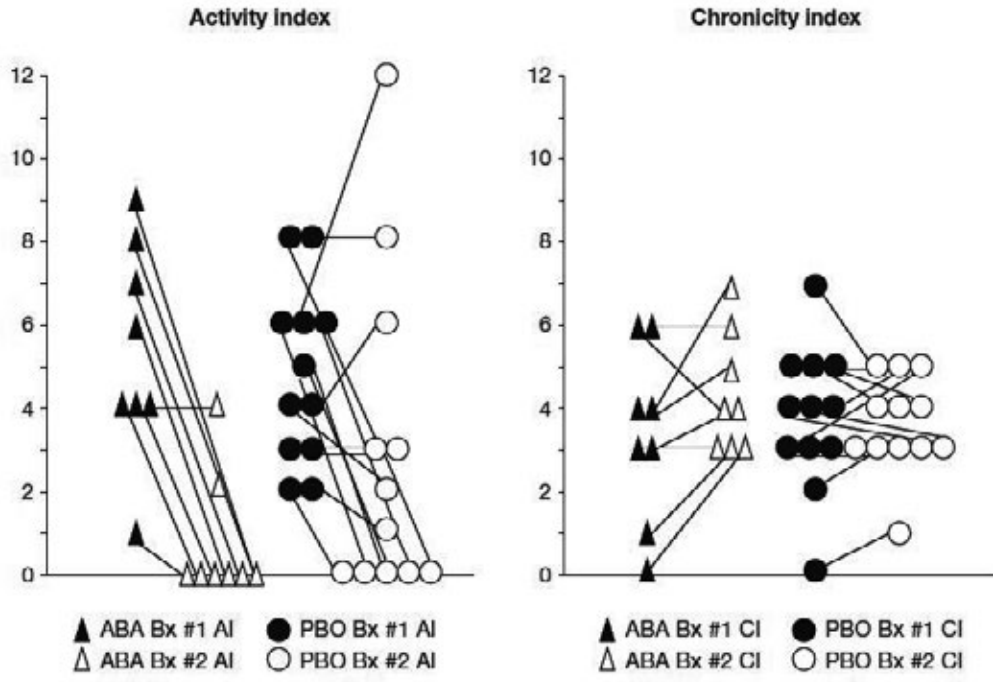
Table 2. Classification of LN Using International Society of Nephrology/Renal Pathology Society 2003 Classification

ABA, ID	Bx #1	Bx #2	PBO, ID	Bx #1	Bx #2
1-CR	IV (A/C)	III (C)	**1-NR**	IV (A/C)	IV (A/C)
2-NR	IV (A/C) +V	IV (A/C) +V	**2-NR**	IV (A/C)	III (A/C)
3-CR	IV(A/C) +V	III (C) + V	**3-CR**	III (A/C) +V	IV (C)
4-CR	IV (A/C)	III (C)	**4-NR**	III (A/C)	III (A/C)
5-CR	III (A/C)	III (C)	**5-NR**	IV (A/C)	IV (A/C)
6-CR	IV (A/C)	IV (C)	**6-NR**	III (A/C) +V	III (A/C) +V
7-CR	IV (A/C)	III (C)	**7-CR**	III (A/C)	III (C)
8-NR	IV (A/C)	IV (A/C)	**8-CR**	IV (A/C) +V	III (C)
			9-CR	III (A/C)	III (A/C)
			10-NR	III (A/C)	IV (A/C)
			11-CR	III (A)	III (C)
			12-CR	III (A/C)	III (C)

ABA=abatacept; Bx=biopsy; CR=complete responder; NR=non-complete responder; PBO=placebo

Background/Purpose: Current therapeutic management of active Class III or IV proliferative LN relies on the use of maintenance therapy following induction. The optimal method for determining the length of maintenance therapy remains a challenge. Most clinicians use a combination of clinical parameters and length of treatment. Unfortunately, there can be a disassociation between clinical parameters and renal biopsies, the gold standard for assessing dis-

Figure. National Institutes of Health Activity and Chronicity Indices



ABA=abatacept; AI=activity index; Bx=biopsy; CI=chronicity index; PBO=placebo

ease activity.[1] Here we present the findings of repeat renal biopsies and a *post hoc* analysis of their correlation with clinical outcomes from a single site in ALLURE (NCT01714817), a randomized, double-blind Phase III study comparing abatacept (ABA) with placebo (PBO) on background MMF and CS in patients with active Class III or IV LN.

Methods: We evaluated 20 patients from a single site who underwent repeat kidney biopsy (Bx) as part of standard practice. The first Bx was for diagnostic purpose and the second Bx was performed after study discontinuation for clinical decision making. Bx were processed using standard techniques and read, classified using International Society of Nephrology/Renal Pathology Society 2003 Classification and scored using the National Institute of Health activity and chronicity indices (AI/CI) by a single pathologist, blinded to clinical data.[2] Renal pathology findings were correlated with clinical outcomes collected during study participation.

Results: 20/25 patients randomized at the site had paired pre- and post-treatment Bx to be analyzed (ABA n=8; PBO n=12). Demographics and disease characteristics at baseline, duration of therapy and mean time between Bx were comparable (Table 1). 4 patients discontinued treatment, all due to lack of efficacy (ABA n=1; PBO n=3). Most patients achieved a urine protein to creatinine ratio (UPCR) ≤0.5 at least once during therapy (ABA 6/8; PBO 8/12) but mean UPCR at Year 1 was lower in the ABA arm (ABA 0.56; PBO 1.53). While the groups had comparable AI and CI scores at baseline, the ABA group had a lower mean score at the 2nd Bx (0.8 vs PBO 2.9; Table 1). 6/8 of the ABA group had an AI of 0 on repeat Bx vs 5/12 in PBO group (Fig. 1). 2 PBO patients had UPCR ≤0.5 but had some activity on 2nd Bx; 2 ABA patients without activity on 2nd Bx had UPCR >0.5 (0.6 and 0.8). After an average of >2 years of treatment, most responders were classified as III (C) on a repeat Bx (Table 2). Overall safety was comparable in both groups; 2 ABA patients had serious infections (pneumonia and gastroenteritis) that did not lead to discontinuation.

Conclusion: Repeat kidney Bx in patients with active LN after prolonged therapy can reveal discrepancies between clinical and histological responses. Most patients treated with abatacept showed lack of activity even with mild, residual proteinuria. Better methodologies are needed to detect renal activity and improve clinical decision making in patients with LN.

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2. Austin HA 3rd, et al. *Am J Med* 1983;**75**:382–91.

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Abstract Number: 2557

Proton Pump Inhibitor Induced Subacute Cutaneous Lupus Erythematosus: Clinical Characteristics and Outcomes – Case Control Study

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Background/Purpose: Drug induced subacute cutaneous lupus erythematosus has rarely been described. There is a growing literature reporting the association between proton pump inhibitor (PPI) use and subacute cutaneous lupus erythematosus (SCLE).

To compare the clinical characteristics of a cohort of patients with proton pump inhibitor induced subacute cutaneous lupus erythematosus, their clinical course and treatment with a control group of primary subacute cutaneous lupus erythematosus patients not exposed to proton pump inhibitors.

Methods: A matched case-control study in a tertiary referral setting at the Louise Coote Lupus Unit. There were 50 SCLE patients (25 patients with PPI induced SCLE and 25 patients with Primary SCLE). Clinical details recorded included underlying systemic lupus erythematosus (SLE) and SCLE, extent of cutaneous involvement, time to pres-

	PPI Group n= 25	Control Group n= 25	P value
Mean age ±SD, y, (range)	56 ± 13.3 (24,74)	46 ±13.6 (24,72)	
Gender, n (%)			
Male	3 (12%)	2 (8%)	
Female	22 (88%)	23 (92%)	
Previous Systemic Lupus Erythematosus	19 (76%)	25 (100%)	
Immunological Profile, n (%)			
+ANA	22 (88 %)	21 (84 %)	
+Anti dsDNA	12 (48 %)	9 (36 %)	
+Anti Sm	7 (28 %)	7 (28 %)	
+Anti Ro 60	19 (76 %)	15 (65 %)	
+Anti Ro 52	6 (66%)	6 (42 %)	
Eosinophils	Normal	Normal	
Extent of rash, n (%)			
Face	11 (44 %)	11 (44 %)	
Trunk	24 (96 %)	19 (76%)	
Upper limbs	20 (80 %)	21 (84%)	
Lower limbs	19 (76%)	0 (0%)	< 0.0001

Table 1. Clinical and immunological details

entation, type of proton pump inhibitor and dosage, histological characteristics, immunological profiles, treatment and time to resolution.

Results: There were 25 patients in the PPI group and 25 patients in the Primary SCLE group. There was no significant gender difference, the mean age at diagnosis was 56.3 years for PPI group and 46 years for Primary SCLE group. Nineteen patients (76%) had underlying SLE in the PPI group. In this subgroup, only one patient had SCLE as part of their initial SLE presentation. Lower limb skin lesions were significantly more prevalent in the PPI group ($p< 0.0001$). No significant immunological profile difference was observed between the two groups in terms of anti-double stand DNA, anti Ro-60 antibody and Anti-Sm antibodies. The prevalence of anti Ro-52 antibodies was slightly higher in PPI group 66% compared with 42% in Primary SCLE group. Peripheral blood eosinophils were normal in all patients in the PPI group, supporting the hypothesis of drug induced SCLE rather than a true allergic reaction. Twelve patients underwent a skin biopsy in the PPI group and 11 patients had histology in keeping with SCLE. The median time to presentation was 12 months (range 3 weeks - 12 years) and median resolution period was 1 month (range 1 week- 5 months). Proton pump inhibitor was stopped in 23 patients while 2 patients could not stop it for another clinical indications. Ten patients (40%) received concurrent oral corticosteroid.

Conclusion: Proton pump inhibitor induced SCLE is more common in older patients and may be associated with anti-Ro 52 antibodies. Lower limb involvement is a pointer to PPI induced SCLE. Clinical resolution of the rash may take few days up to a few months. This is likely a class effect with all proton pump inhibitors.

Disclosure: A. Alrashid, None; **Y. Poh**, None; **D. D'Cruz**, AstraZeneca, Bristol-Myers Squibb, 2, 5, Eli Lilly, Eli Lily, 2, 5, GlaxoSmithKline, 2, 5, Human Genome Sciences, 5, Idorsia, Merck Serono, 2, 5, Pfizer, Roche, 5, TEVA, 2, 5; **S. Sangle**, None; **D. McGibbon**, None; **E. Benton**, None; **E. Higgins**, None.

Abstract Number: 2558

Profiling of Gene Expression, Immune Cell Subtypes, and Circulating Protein Biomarkers in Systemic Lupus Erythematosus Patients Treated with the Selective Immunoproteasome Inhibitor, KZR-616

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: KZR-616 is a selective inhibitor of the immunoproteasome, the form of proteasome found predominantly in immune cells. In nonclinical studies, KZR-616 blocks acute production of inflammatory cytokines, modulates T- and B-cell activation/differentiation *in vitro*, and is efficacious in murine SLE models[1]. Recently, we presented initial safety and efficacy data from the first 2 cohorts of an open-label study of KZR-616 in SLE patients (pts) [2]. Here we describe their baseline (BL) profile and post-treatment changes in transcriptomic and phenotypic analyses of circulating immune cells and plasma biomarker levels.

Methods: Pts (N=13) received KZR-616 subcutaneously at 45 or 60 mg weekly for 13 weeks with follow-up through Week (W) 25. Disease assessments were performed at BL and W5, 9, 13, 17, 21, and 25. Biomarker samples were

collected at BL and W5, 17, and 25 (~50% of pts had samples for all timepoints). Comparisons at BL were made to samples from 2 separate healthy volunteer (HV) studies. Proteasome activity was measured by enzymatic and active site binding assays[3]. RNA sequencing was performed using Illumina TruSeq® with whole blood collected in PAXgene® RNA tubes and isolated peripheral blood mononuclear cells (PBMCs). Expression of immune gene modules[4] was compared within and across pts. Cryopreserved PBMCs were analyzed by flow cytometry to profile immune cell subtypes. Plasma cytokines/proteins were quantified by electrochemiluminescent assays (Meso Scale Diagnostics) and colorimetric ELISAs.

Results: At BL, immunoproteasome enzymatic activity and subunit composition in SLE pts were not significantly different from that of HV. Whole blood gene expression, noted with treatment as early as W5, revealed a reduction in gene modules enriched for plasma cell, T-cell activation, inflammation, neutrophil, and IFNα response genes. Within individual pts, there was substantial heterogeneity in gene expression with the most marked changes in pts with greater clinical improvement. Consistent with the gene expression analyses, by flow cytometry, we detected reductions in double-negative B cells, class-switched memory B cells, plasmablasts, monocytes, and activated T cells in the 4 of 5 pts with available samples. Post-treatment, several SLE-related cytokines (eg, IL-6, BAFF, MIP-3β) were reduced in some pts and 3 chemokines (RANTES, MIP-3α, and MCP-4) were reduced in most pts (>3 of 6)

Conclusion: KZR-616 treatment was correlated with changes in gene expression, immune cell subtypes, and circulating protein biomarkers in SLE pts. Consistent with nonclinical data, we demonstrated a reduction in inflammatory activity across T, B, and innate immune effector cells at transcriptomic, cellular, and protein levels, supporting a broad mechanism of action for this first-in-class agent. Analyses of additional cohorts are underway to further elucidate these initial findings and may inform future study patient stratification based on molecular or cellular diagnostic criteria.

References:

1. Muchamuel et al. ACR 2017; 69 (suppl 10).
2. Furie et al. EULAR 2019. Abstract #FR0196
3. Lickliter et al. ACR. 2017; 69 (suppl 10).
4. Chaussabel et. al., Immunity. 2008 29(1):150

Disclosure: R. Fan, Kezar Life Sciences, 3, 4; **J. Anderl**, Kezar Life Sciences, 3, 4; **B. Tuch**, Kezar Life Sciences, 3; **D. Bomba**, Kezar Life Sciences, 3, 4; **N. Goel**, Kezar Life Sciences, 3, 4, 6; **C. Kirk**, Kezar Life Sciences, 3, 4, 6.

Abstract Number: 2559

A Phase 2, Open-label Extension Study to Evaluate Long-term Safety of Anifrolumab in Adults with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Anifrolumab is a fully human, IgG1κ monoclonal antibody that binds to the type I IFN receptor and inhibits activity of all type I IFNs.[1] In the MUSE phase 2b randomized controlled trial (Study 1013, NCT01438489), anifrolumab demonstrated an acceptable safety profile and efficacy on a range of clinical endpoints in patients with moderate to severe SLE. An open-label extension (OLE) of Study 1013 (Study 1145, NCT01753193) evaluated long-term safety and tolerability of anifrolumab.

Methods: Study 1145 was a 3-year, multinational OLE in adults with moderate to severe SLE (per ACR classification criteria, assessed in Study 1013) who completed randomized treatment with anifrolumab 1000 or 300 mg or placebo in Study 1013 to Day 337 with follow-up to Day 422. All patients in Study 1145 initially received IV anifrolumab 1000 mg every 4 weeks (Q4W). After data from Study 1013 showed the 300-mg dose had a better benefit/risk profile, the dosage in Study 1145 was amended to 300 mg Q4W. Patients received anifrolumab Q4W over 156 weeks with 85 days of follow-up. The primary objective was to evaluate long-term safety/tolerability. Efficacy, pharmacodynamics, and health-related quality of life (HRQoL) were exploratory objectives. Safety was assessed at every visit; SLEDAI-2K and SLICC Damage Index were measured every 3 and 6 months, respectively.

Results: Of 305 randomized patients in Study 1013, 218 (71.5%) at 59 sites participated in Study 1145; 66/218 (30.3%) received placebo in Study 1013. Of 218 patients in Study 1145, 139 (63.8%) completed 3 years of treatment. The most common reason for treatment discontinuation was patient withdrawal (31/218, 14.2%). Treatment was discontinued due to adverse events (AEs) for 15/218 patients (6.9%). During Year 1, 152/218 patients (69.7%) had ≥1 AE (**Table**). Over the full study period, the rate of serious AEs was 8.56 per 100 patient-years (PY); the most common

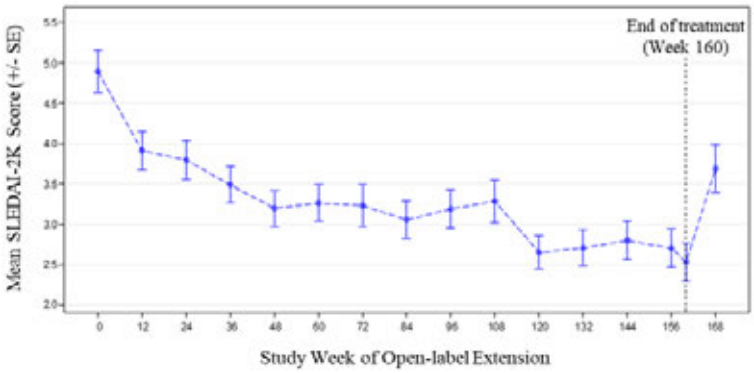

Figure 1. Mean SLEDAI-2K score during open-label treatment with anifrolumab

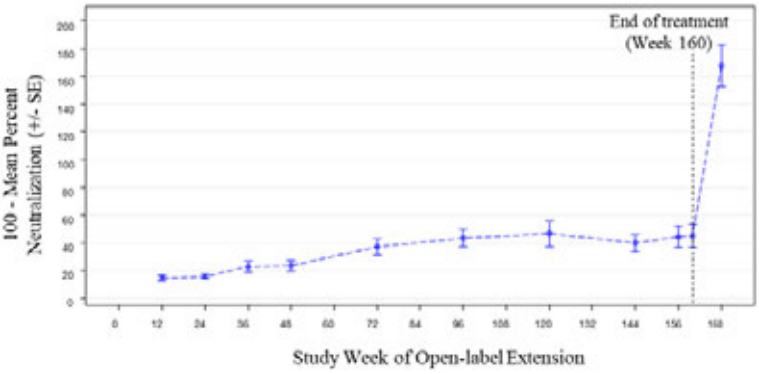

Figure 2. Neutralization of type I IFN gene signature during open-label treatment with anifrolumab in patients with high IFN gene signature expression at baseline

AE category by preferred term (MedDRA version 21.0)	Anifrolumab (N=218)
	AEs during first year of Study 1145
Any AE, n (%)	152 (69.7)
AEs in ≥5% of patients, n (%)	
Nasopharyngitis	24 (11.0)
Bronchitis	21 (9.6)
Headache	14 (6.4)
Upper respiratory tract infection	14 (6.4)
Total PY exposure	572.21
	Serious AEs during entire Study 1145[a]
Any serious AE, n (%)	49 (8.56)
Serious AEs in ≥2 patients, n (exposure-adjusted rate per 100 PY)	
Systemic lupus erythematosus	4 (0.70)
Pneumonia	4 (0.70)
Bronchitis	2 (0.35)
Chikungunya virus infection	2 (0.35)
Dysfunctional uterine bleeding	2 (0.35)
Femur fracture	2 (0.35)
Gastroenteritis	2 (0.35)
Nephrotic syndrome	2 (0.35)
Osteonecrosis	2 (0.35)
Pleural effusion	2 (0.35)
Post procedural infection	2 (0.35)
Spinal column stenosis	2 (0.35)
Urinary tract infection	2 (0.35)
AEs of special interest, n (exposure-adjusted rate per 100 PY)	**AEs of special interest during entire Study 1145[a]**
Patients with ≥1 AE of special interest	24 (4.19)
Herpes zoster infection	11 (1.92)
Infusion-related reaction, hypersensitivity, anaphylaxis	7 (1.22)
Drug hypersensitivity	1 (0.17)
Hypersensitivity	2 (0.35)
Infusion-related reaction	4 (0.70)
Nausea (infusion-related)	1 (0.17)
Latent tuberculosis	5 (0.87)
Vasculitis	2 (0.35)

AE=adverse event; PY=patient years.
[a]Events occurred from the date of the first dose of Study 1145 anifrolumab until the last dose date plus 85 days.

Table. Percentages of patients with AEs during anifrolumab treatment in the first year of Study 1145 and exposure-adjusted rates of serious AEs and AEs of special interest per 100 PY throughout Study 1145

serious AEs were SLE flares and pneumonia (each 0.70 per 100 PY). The most common AE of special interest was herpes zoster (1.92 per 100 PY). There was 1 death due to pneumonia. Two of 218 patients were anti-drug antibody positive at any time during treatment (both persistently positive). Sustained improvement of the SLEDAI-2K was observed through the end of treatment (mean change –2.1 [SD=3.5] from baseline to Week 160; **Figure 1**). Short Form 36 Health Survey physical and mental component scores showed similar patterns of sustained improvement. SLICC Damage Index generally remained stable over time (mean change 0.1 [SD=0.6] from baseline to Week 168). Neutralization of type I IFN gene signature (IFNGS) expression was rapid and sustained in patients with high baseline IFNGS (**Figure 2**). C3, C4, and anti-dsDNA showed numeric trends toward sustained improvement.

Conclusion: Long-term anifrolumab treatment for up to 3 years was generally safe and well tolerated. The safety profile was consistent with the 52-week Study 1013. Disease activity, HRQoL, and SLE-related serology showed sustained improvement.

Writing assistance by Maria Prada, PhD (JK Associates Inc., Fishawack Group of Companies).

Reference: 1. Riggs JM, et al. *Lupus Sci Med.* 2018;5:e000261.

Disclosure: W. Chatham, AstraZeneca, 2; **R. Furie**, AstraZeneca/MedImmune, 2, 5, AstraZeneca/Medimmune, 2, 3; **A. Saxena**, None; **P. Brohawn**, AstraZeneca, 1, 2, 3, 4; **E. Schwetje**, AstraZeneca, 1, 3, 4; **G. Abreu**, AstraZeneca, 3; **R. Tummala**, AstraZeneca, 3.

Abstract Number: 2560

Factors Associated with Hydroxychloroquine Use in Systemic Lupus Erythematosus Patients with End Stage Renal Disease

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) use in SLE has been associated with a lower risk of end-organ damage, SLE flares, and thrombosis[1,2]. However the benefits of HCQ among SLE with end stage renal disease (ESRD) are less clear[3]. Despite HCQ benefits, fewer than 30% of SLE continue HCQ after ESRD onset[3]. On the other hand, there is an increased risk of HCQ toxicity among SLE-ESRD[4]. It has not been studied what factors are associated with HCQ use after ESRD. Understanding these factors may inform future studies assessing the safety and efficacy of HCQ in SLE-ESRD and address the "confounding by-indication" bias (i.e. different treatments are intentionally chosen for patients with different prognoses) when analyzing retrospective data regarding HCQ use in SLE patients with ESRD. Therefore, the objective of this study was to determine the factors associated with HCQ use among SLE patients with ESRD.

Methods: We performed a retrospective chart review of SLE patients with ESRD at a single tertiary care center between 2010-2017. All included patients met ACR and/or SLICC criteria for SLE and had at least one visit with rheumatology, nephrology, dermatology or primary care, before and after the development of ESRD. SLE-related symptoms, serologic markers of disease activity, and rheumatology visits were identified, both pre- and post-ESRD onset. Transplanted patients were excluded at the time of their first renal transplant.

Results: A total of 69 patients were included, 58 had pre-ESRD data. Of these patients, 33/58 (57%) were taking HCQ prior to ESRD onset. Following the diagnosis of ESRD, 40/69 (58%) were prescribed HCQ within six months after ESRD onset. Of these, six discontinued HCQ by the last documented visit, and one patient initiated HCQ six months after ESRD onset (prescribed by a rheumatologist). At the last documented visit, 35/69 patients (51%) had an active HCQ prescription. Patients taking HCQ were younger, more likely to be followed by a rheumatologist, had a higher frequency of documented arthritis, higher frequency of corticosteroid use and immunosuppressive medication use (Table 1). A history of oral ulcers, cytopenias, and elevated levels of dsDNA at any point (either pre or post-ESRD onset) was not significantly associated with HCQ use at the last visit.

Conclusion: HCQ is more likely to be continued among patients with signs of persistently active SLE. HCQ was more likely to be prescribed by a rheumatologist and was associated with the presence of arthritis. None of the se-

Table 1: Factors associated with HCQ use at the last visit post ESRD*			
	HCQ+ last ESRD visit N=35	HCQ- last ESRD visit N=34	p-value
Age at ESRD onset, median (IQR)	33 (26, 46)	46 (29, 53)	**0.05**
Time from ESRD onset to the last visit, months, median (IQR)	40 (21, 72)	59 (11, 99)	0.3
Women, n(%)	29 (83)	28 (82)	0.95
Renal transplantation, n(%)	13 (37)	11 (32)	0.68
Arthritis, n(%)	7 (20)	0	**0.01**
Rash, n(%)	2 (6)	1 (3)	0.61
Oral ulcers, n(%)	1 (3)	0	0.33
Alopecia, n(%)	1 (3)	2 (6)	0.52
Serositis, n(%)	2 (6)	3 (10)	0.59
Cytopenia, n(%)	27 (82)	26 (79)	0.75
Low complement, n(%)	16 (50)	19 (58)	0.54
Elevated dsDNA, n(%)	12 (39)	10 (31)	0.54
Corticosteroid use, n(%)	31 (89)	23 (72)	**0.08**
Immunosuppressive use, n(%)	25 (71)	14 (42)	**0.02**
Rheum visit post ESRD at least once, n(%)	29 (85)	20 (59)	**0.02**
History of anti-phospholipid syndrome, ever, n(%)	4 (12)	4 (13)	0.96
History of deep vein thrombosis, ever, n(%)	2 (6)	1 (3)	0.50
*Symptoms and medications recorded as "ever" after ESRD onset			

Table 1. Factors associated with HCQ use at the last visit post ESRD Factors associated with HCQ use at the last visit post ESRD

rology markers of disease activity were associated with HCQ prescription. Limited systemic evaluation and/or documentation by the different providers may have resulted in under-recognition and under-reporting of some of the SLE symptoms. However, these findings reflect the "real-world" experience with HCQ use after ESRD in a large tertiary care center.

Disclosure: M. Salgado Guerrero, None; **A. Londono Jimenez**, None; **C. Dobrowolsky**, None; **S. Wang**, None; **W. Mowrey**, None; **A. Broder**, None.

Abstract Number: 2561

Deep Remission During Induction Therapy for Lupus Nephritis Prevents Damage Accrual and Associates with the Baseline Proportions of Peripheral Treg, CD8$^+$ T Cells, and NKT-like Cells

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: SLE – Clinical Poster III: Treatment

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

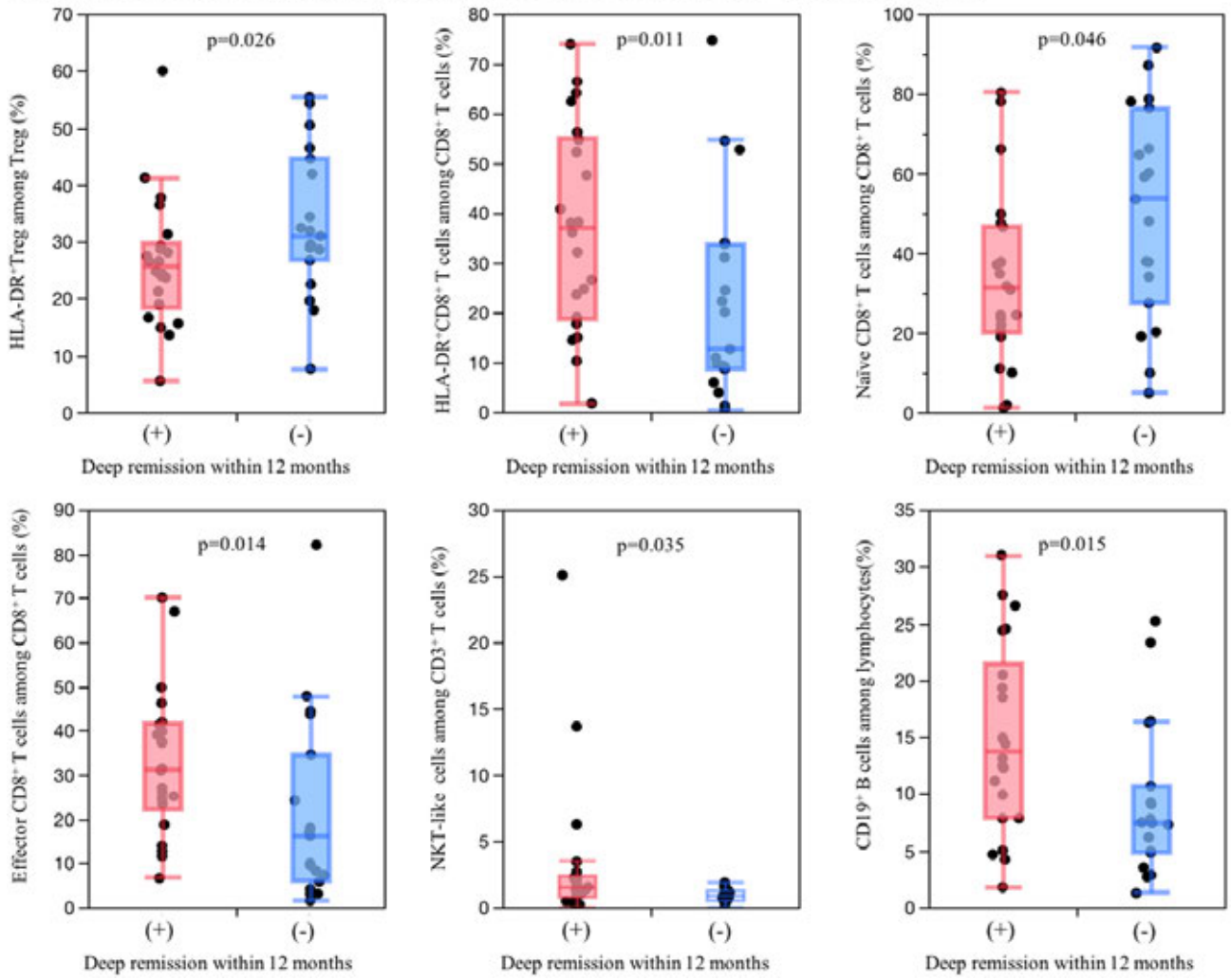
Background/Purpose: chievement of renal remission has been the target of the induction therapy in patients with active lupus nephritis (LN). Deep remission (DR) defined as the reduction of urine protein Cr ratio (UPCR) to 0.15 g/gCr was reported to reduce renal flare. However, the utility and associated factors of DR are not clearly evaluated enough. We herein evaluated the characteristics of the patients with DR.

Table.1 Clinical characteristics associated with achievement of deep remission within 12 months after starting induction therapy.

Clinical characteristics	Deep remission (+) N=22	Deep remission (-) N=19	P-value
At baseline			
Age, years	37.5 ± 13.6	44.7 ± 11.9	0.054
Female, n(%)	20 (90.9)	15 (79.0)	0.280
Disease duration, months	57.9 ± 69.1	109.7 ± 103.2	0.077
Classification of renal pathology	III/IV:13, III/IV+V:2, V:1, N/A:5	III/IV:8, III/IV+V:6, V:2, N/A:3	0.322
Mucocutaneus, n(%)	11 (50)	7 (36.8)	0.397
Musculoskeletal, n(%)	**10 (45.5)**	**0 (0)**	**<0.001**
Anti-Sm antibodies, n(%)	9 (40.9)	9 (47.4)	0.565
Anti-dsDNA antibodies, n(%)	209.4 ± 179.6	85.7 ± 122.3	0.061
eGFR, ml/min/1.73m^2	82.1 ± 31.5	72.4 ± 27.6	0.367
UPCR, g/gCr	1.88 ± 2.43	2.42 ± 1.68	0.056
SLEDAI	**22.0 ± 9.56**	**15.8 ± 6.34**	**0.033**
Initial dose of prednisolone, mg/kg/day	0.95 ± 0.17	0.83 ± 0.30	0.464
Intravenous cyclophosphamide/ mycophenolate mofetil	8 (40) / 12 (60)	8 (61.5) / 5 (38.5)	0.226
At final visits			
ASLICC damage index ≥1, n(%)	**1 (4.6)**	**6 (31.6)**	**0.022**
UPCR, g/gCr	**0.11 ± 0.25**	**0.53 ± 0.56**	**<0.001**
eGFR, ml/min/1.73m^2	82.8 ± 22.8	71.7 ± 26.6	0.300

Cut-off for significance was p-value <0.05. Wilcoxon's test and Pearson's test were used for numerical and categorical analysis, respectively.

Figure 1. The significantly different proportions of peripheral immune cells between the patients achieving deep remission during 12 months after induction therapy and those without. Cut-off for significance was p-value <0.05 (Wilcoxon's test).



Methods: We enrolled the patients with active LN who started induction therapy from February 2015 to February 2018 in our hospital and were followed for more than 12 months. We prospectively assessed the achievement of complete renal response (CR), defined as stabilization (within 25%) in serum Cr with reduction of UPCR to 0.5 g/gCr, and DR. Standardized peripheral immunophenotyping by flowcytometry was analyzed with whole blood samples from all patients before starting induction therapy. Finally, we assessed a renal flare and the progression of damage accrual with SLICC-damage index (SDI) and the associations with achievement of DR.

Results: Forty-one patients were enrolled. Mean initial dose of prednisolone was 0.89 ± 0.24 mg/kg/day with 39.0% of intravenous cyclophosphamide, 41.5% of mycophenolate mofetil, and 17.1% of tacrolimus. Mean observational period was 31.3 ± 11.3 months. CR was achieved in 31 (75.6%) patients within 6 months and 33 (80.5%) within 12 months after starting induction therapy. DR was achieved in 15 (36.6%) and 22 (53.7%) within 6 and 12 months, respectively. Five (12.2%) patients had renal proteinuric flare, and no patient achieving DR had experienced it during observational periods. Increase in SDI was observed in 17.1% of patients. Especially, DR within 12 months was significantly associated with no progression of SDI (p=0.022). In addition, UPCR at final visit was significantly lower

in patients with DR ($p< 0.001$). Patients with DR within 12 months had a higher titer of SLEDAI score ($p=0.033$) and higher prevalence of co-existing musculoskeletal manifestation ($p< 0.001$) at baseline. The proportions of HLA-DR$^+$ Treg ($CD3^+CD4^+CD25^+CD127^{low}$) and naïve $CD8^+$ T cells ($CD3^+CD8^+CD45RA^+CCR7^+$) were lower and the proportions of $CD19^+$ B cells, HLA-DR$^+$ $CD8^+$ T cells, effector $CD8^+$ T cells ($CD3^+CD8^+CD45RA^+CCR7^-$), and NKT-like cells ($CD3^+CD19^-CD56^+\gamma\delta TCR^-$) were significantly higher in patients with DR than those without.

Conclusion: Achievement of DR within 12 months after induction therapy was associated with reduction in damage accrual in patients with active LN, which indicated DR can be a selected target of the treatment. Higher disease activity score and the proportions of peripheral Treg, $CD8^+$ T cells, and NKT-like cells at baseline might be surrogate markers for achievement of DR.

Disclosure: J. Kikuchi, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **H. Hanaoka**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **S. Saito**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **T. Oshige**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **K. Hiramoto**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **Y. Kaneko**, Mitsubishi Tanabe Pharma Corporation Sohyaku, 2; **N. Seki**, Mitsubishi Tanabe Pharma Corporation, 3; **H. Tsujimoto**, Mitsubishi Tanabe Pharma Corporation, 3; **T. Takeuchi**, Mitsubishi Tanabe Pharma Co., 2, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8.

Abstract Number: 2562

Glucocorticosteroid Usage and Major Organ Damage in Patients with Systemic Lupus Erythematosus - Meta-analyses of Observational Studies Published Between 1979 and 2018

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SESSION INFORMATION

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Session Title: SLE – Clinical Poster III: Treatment

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The impact of glucocorticoid (GC) use on major organ damage in SLE patients has not been formally studied by amalgamating the relevant data published in the literature over the past 40 years. We aimed to study the association between GC use and the occurrence of major organ damage in SLE patients by performing meta-analyses of observational studies published between 1970 and December 2018.

Methods: Literature search on PubMed (from 1966 to December 2018) for prevalence and longitudinal studies which reported GC exposure (proportion of GC users in the cohort [%GC use] and/or GC use in defined doses) and the occurrence (prevalence/incidence) of major organ damage in SLE patients using the keywords “cataract”, “cerebrovascular” (CVA), “stroke”, “cardiovascular” (CVS), “angina”, “myocardial infarction” (MI), “coronary artery bypass”, “osteoporosis”, “avascular necrosis” (AVN) and “osteonecrosis” in respective combinations with “lupus” was conducted. Studies with sample size < 50 and observation duration < 12 months were excluded. The logit of the proportion of patients with disease damage was modelled as a random effect in the meta-analysis, which was employed to study the association between the proportion of patients with organ damage and variables of GC use (mean daily [mg/day] and cumulative [gm] prednisone [PDN] doses and %GC use). A 2-stage estimation of the random-effects logistic

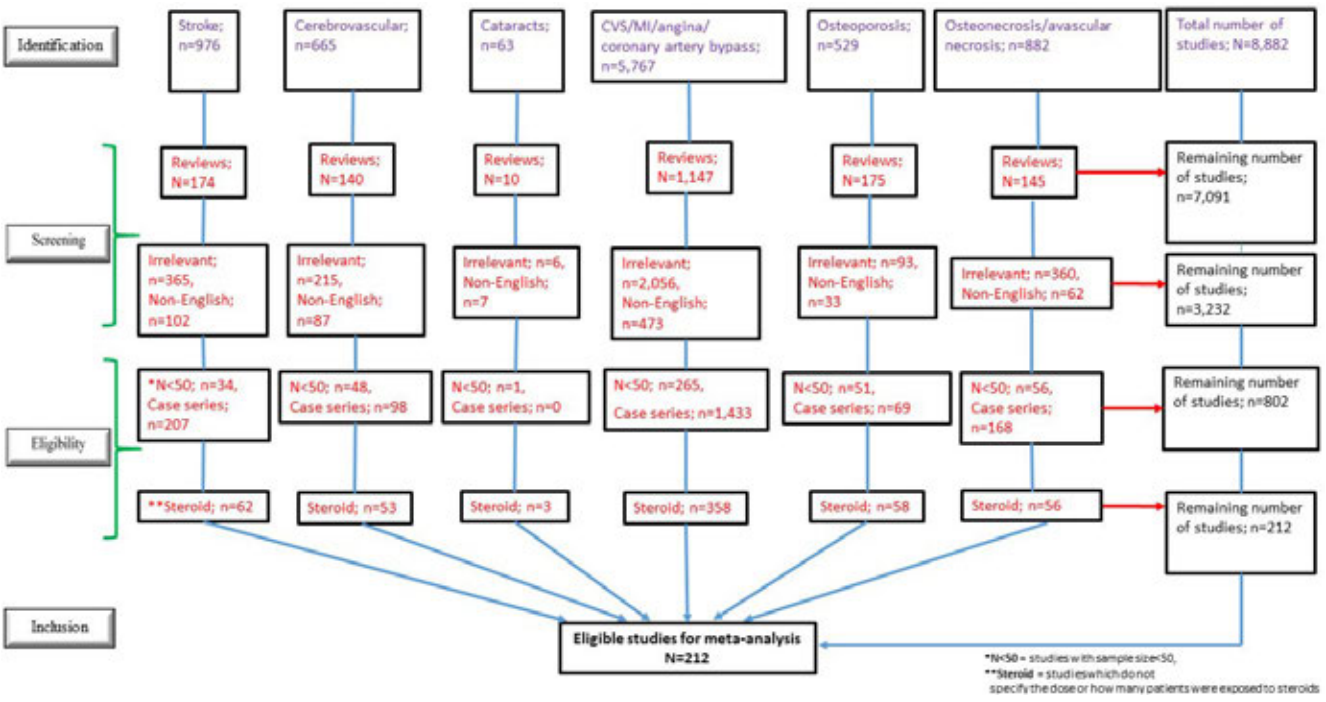

Figure 1. Result of literature search

regression models was used with restricted maximum likelihood estimation. Univariate associations between organ damage and moderators were examined for statistical significance, and variables related to GC use were adjusted for SLE disease duration in multivariate models if their univariate P values were < 0.2.

Results: Out of 8,882 publications screened, 212 articles involving 205,619 SLE patients were eligible for the meta-analyses (Figure 1), of which 97 were prevalence and 115 were longitudinal studies. Univariate analyses of prevalence studies revealed that mean daily PDN dose (odds ratio [OR]=1.10, p=0.007) and lower proportion of female in the cohort (OR=0.002, p=0.002) were associated with the prevalence of overall CVS events. Mean daily PDN dose (OR=1.52, p< 0.001) and %GC use (OR=2,255.2, p< 0.001) were associated with the prevalence of AVN. A significant association between cumulative PDN dose and prevalence of CVA was found after multivariate adjustment for SLE disease duration (OR=1.07, p=0.017). In longitudinal studies, a significant association was identified between cumulative PDN dose and incidence of cataracts after adjustment for SLE disease duration (OR=1.04, p=0.013). While the incidence of MI in SLE patients has dropped over the past 40 years (OR=0.94, p=0.002), it was associated with % GC use after adjustment for SLE disease duration (OR=8.18, p=0.012). Interestingly, significant univariate associations were found between antimalarial use and lower prevalence of MI (OR=0.05, p=0.002) and lower incidence of CVA (OR=0.20, p=0.032).

Conclusion: Independent of SLE disease duration, cumulative PDN dose was associated with higher prevalence of CVA and incidence of cataracts, and higher incidence of MI was associated with overall GC use.

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Abstract Number: 2563

PK/PD, Safety and Exploratory Efficacy of Subcutaneous Anifrolumab in SLE: A Phase-II Study in Interferon Type I High Patients with Active Skin Disease

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
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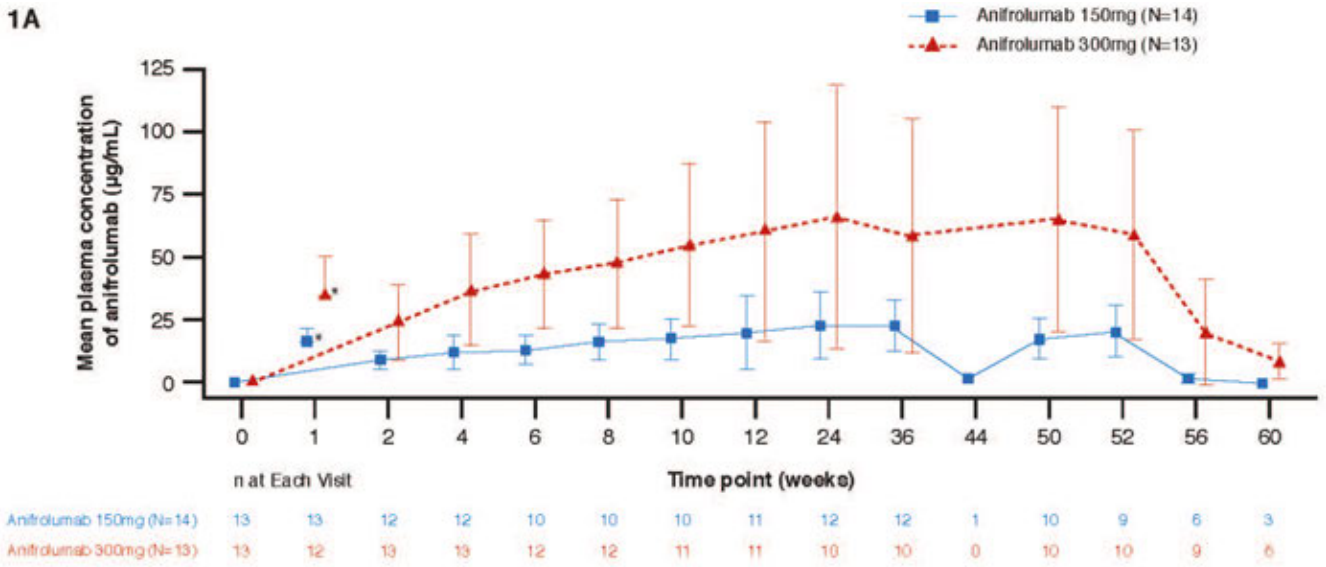
Session Time: 9:00AM–11:00AM

Background/Purpose: Anifrolumab, a fully human anti–IFN Type I receptor mAb, is under investigation for the treatment of SLE at a dose of 300 mg intravenously (IV) once every 4 weeks (Q4W), as added to Standard of Care (SOC) therapy. As subcutaneous (SC) administration may offer a greater treatment convenience and accessibility for patients, we evaluated the PK, PD, safety, tolerability, and efficacy of SC anifrolumab, when added to SOC in adults with Type I IFN test-high SLE and active skin disease.

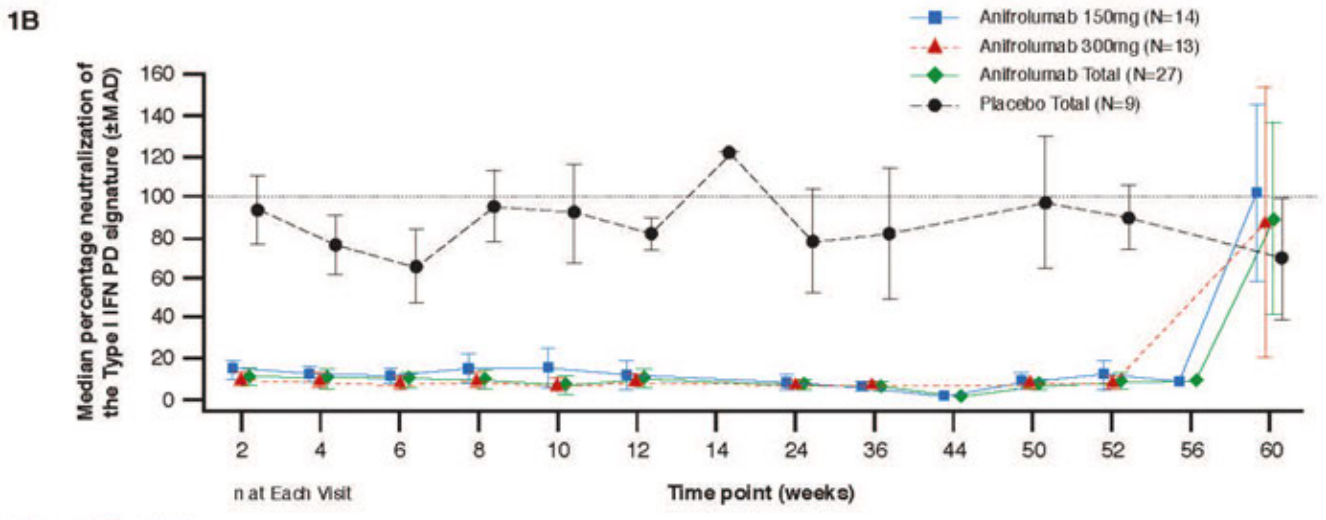
Methods: Patients (all fulfilling 1997 ACR SLE criteria) were randomized to the following, added to SOC, for up to 52 weeks (followed by an 8-week follow-up period): anifrolumab 150 mg, anifrolumab 300 mg or corresponding placebo, all SC Q2W (NCT02962960). Primary endpoints: PK (concentration of anifrolumab) and PD (Type I IFN gene suppression) at Week 12. Secondary endpoints: safety, tolerability and immunogenicity of anifrolumab over 52 weeks. Exploratory endpoint: efficacy of SC anifrolumab on active SLE skin disease using change from baseline in Cutaneous Lupus erythematosus disease Area and Severity Index (CLASI) activity score.

Results: Patients (anifrolumab 150 mg [n=14], 300 mg [n=13], placebo [n=9]), were Caucasian (77.8%) or Asian (22.2%); mean age 44.9 years; 89% female; 94% ANA positive; and 64% anti-dsDNA positive. Low C3 or C4 was observed in 53% and 36% of patients, respectively. Baseline mean CLASI and mean total SLEDAI-2K scores were 15.5 and 9.6, respectively. The baseline mean OCS dose differed between treatment groups: 8.2 mg/day prednisone or equivalent for combined anifrolumab groups and 10.3 mg/day for placebo group. The majority (75%) were on stable anti-malarial therapy.

Anifrolumab exhibited nonlinear PK where trough concentration increases were more than dose-proportional (Figure 1A). At Week 12, the median percentage neutralization of the Type I IFN PD signature was 88.0%, 90.7% and 18.5% in the anifrolumab 150 mg, 300 mg, and placebo groups, respectively; suppression was sustained over the 52-week treatment period (Figure 1B). At Week 12, a ≥75% neutralization of the Type I IFN PD signature was observed in 66.7%, 76.9%, and 11.1% of patients in the anifrolumab 150 mg, 300 mg and placebo groups, respectively. Over 52 weeks, 85.2% (combined anifrolumab) and 77.8% (placebo) of patients experienced ≥1 AE (Table 1). Ten SAEs were reported in 6 patients, all in anifrolumab groups (Table 1). The most commonly reported AEs across all treatment groups were upper respiratory tract infection, nasopharyngitis, bronchitis and headache. Anifrolumab exhibited low immunogenicity, with ADA detected post-baseline in only 2 patients and in low titers. No injection site reactions were reported. Greater reductions in CLASI activity score were observed at Week 52 in the anifrolumab 150 mg and 300 mg groups, vs. placebo (–10.2 and –13.2, vs. –6.3, respectively) (Figure 2).

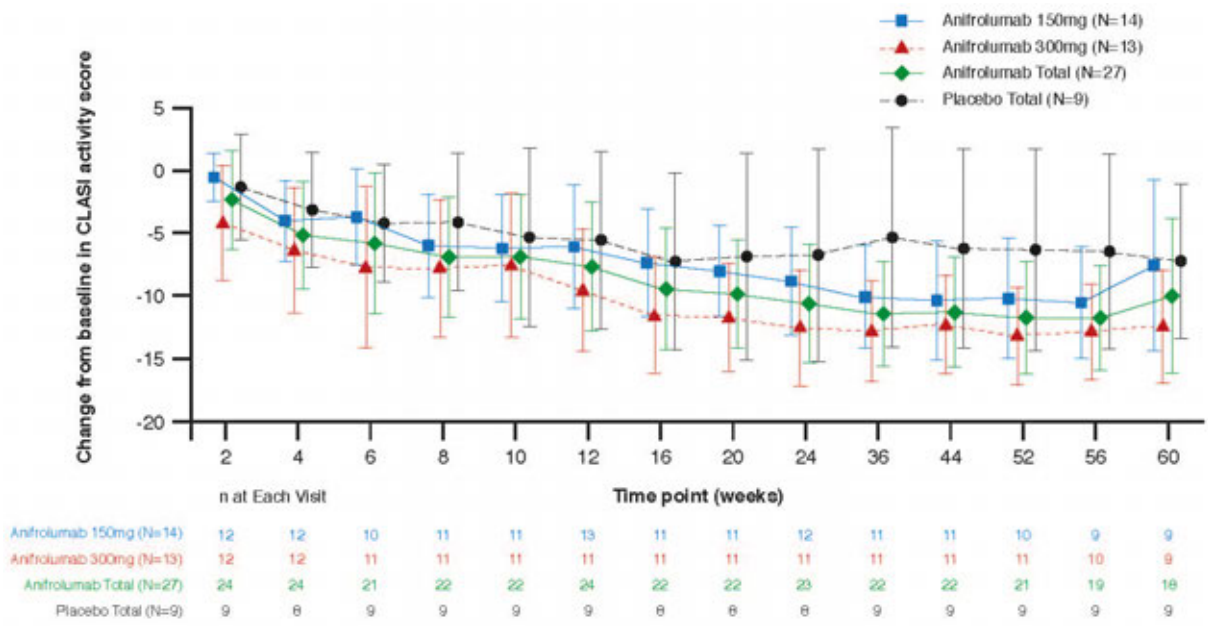


*Mean plasma concentration of anifrolumab was measured post-dose at Week 1. All other measurements were pre-dose.
N Number of patients in treatment group. n Number of patients at each visit. Number of patients with readings above the LLOQ was equal to n at each visit.
Serum concentrations below LLOQ prior to the first quantifiable concentration are set to a value of LLOQ/2.
Early discontinuation visits are mapped to the visit windows they were collected in.
LLOQ, lower limit of quantification.



N number of patients in treatment group. n number of patients at each visit.
The precision bars are ± MAD.
Median percentage neutralization represents the IFN21 PD signature score at post-dose time points relative to baseline values normalized to 100%.
MAD, median absolute deviation; IFN, interferon; % TM, percent target modulation.

Figure 1. A) Mean plasma concentration of anifrolumab versus time (Linear scale; PK analysis set); B) Median percent suppression of Type I IFN over time (PD analysis set)



N Number of patients in treatment group. n Number of patients at each visit.
The precision bars are ± SD.
CLASI, Cutaneous Lupus erythematosus disease Area and Severity Index; SD, standard deviation.

Figure 2. Mean change in CLASI Activity Score over time by treatment group (Full analysis set)

Conclusion: The observed PK/PD profile of SC anifrolumab was consistent with previous studies using IV administration. In addition, SC anifrolumab showed low immunogenicity and an acceptable safety and tolerability profile, similar to previous, larger IV studies in SLE. These findings support further development of SC anifrolumab as a treatment for SLE.

AE category	Anifrolumab 150 mg (N=14)		Anifrolumab 300 mg (N=13)		Anifrolumab total (N=27)		Placebo total (N=9)	
	Exposure (11.6 years)[a]		Exposure (10.4 years)[a]		Exposure (22.0 years)[a]		Exposure (9.0 years)[a]	
	Patients n (%)[b]	Event rate (per 10 pt-yrs)	Patients n (%)[b]	Event rate (per 100 pt-yrs)	Patients n (%)[b]	Event rate (per 100 pt-yrs)	Patients, n (%)[b]	Event rate (per 100 pt-yrs)
Any AE	12 (85.7)	103.5	11 (84.6)	105.3	23 (85.2)	104.4	7 (77.8)	78.0
Any acute AE	8 (57.1)	69.0	3 (23.1)	28.7	11 (40.7)	49.9	2 (22.2)	22.3
Any AE with outcome of death	0	0	0	0	0	0	0	0
Any SAE (including events with outcome of death)	4 (28.6)	34.5	2 (15.4)	19.1	6 (22.2)[c]	27.2	0	0
Any AE leading to discontinuation of IP	2 (14.3)	17.3	3 (23.1)	28.7	5 (18.5)	22.7	0	0
Any AE related to IP	8 (57.1)	69.0	4 (30.8)	38.3	12 (44.4)	54.5	3 (33.3)	33.4
Any AE of severe intensity	2 (14.3)	17.3	1 (7.7)	9.6	3 (11.1)	13.6	0	0
Any AESI	5 (35.7)	43.1	1 (7.7)	9.6	6 (22.2)	27.2	1 (11.1)	11.1
Any AESI of non-opportunistic serious infections	0	0	0	0	0	0	0	0
Any AESI of opportunistic infections	0	0	0	0	0	0	0	0
Any AESI of anaphylaxis	0	0	0	0	0	0	0	0
Any AESI of malignancy	0	0	0	0	0	0	0	0
Any AESI of herpes zoster	3 (21.4)	25.9	0	0	3 (11.1)	13.6	1 (11.1)	11.1

[a]Exposure on treatment, only used to calculate on-treatment event rates. [b]Patients with multiple events in the same category are counted only once in that category. Patients with events in more than one category are counted once in each of those categories. [c]Five SAEs experienced by one patient each (herpes zoster infection, otitis media acute infection, transient ischaemic attack, mouth ulceration, lupus nephritis); one SAE experienced by two patients (systemic lupus erythematosus).

AE, adverse event; AESI, adverse event of special interest; IP, investigational product; SAE, serious adverse event

Table 1. Adverse events and event rates by study period (Full analysis set)

Disclosure: I. Bruce, Astra Zenica, 5, AstraZeneca, 5, Eli Lilly, 5, 8, Genzyme Sanofi, 2, GlaxoSmithKline, 2, 5, 8, GSK, 2, 5, 8, ILTOO, 5, Iltoo, 5, MedImmune, 5, 8, Medimmune, 5, Merck Serono, 5, 8, Merk Serono, 5, Roche, 5, 8, Sanofi Genzyme, 2, UCB, 2, 5, 8, UCB Pharma, 5, 8; **A. Nami**, None; **E. Schwetje**, AstraZeneca, 1, 3, 4; **M. Pierson**, AstraZeneca, 1, 3, 4; **Y. Chia**, MedImmune/AstraZeneca, 3; **D. Kuruvilla**, AstraZeneca, 1, 3; **G. Abreu**, AstraZeneca, 3; **R. Tummala**, AstraZeneca, 3; **C. Lindholm**, AstraZeneca, 3.

Abstract Number: 2564

Adherence to Hydroxychloroquine Influences the Incidence of Organ Damage During Follow-up in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Hydroxychloroquine (HCQ) is a cornerstone drug in patients with systemic lupus erythematosus (SLE), decreasing the risk of flares and comorbidities and improving survival. This study investigated the effects of HCQ adherence on clinical manifestations, disease activity, and organ damage in Korean patients with SLE.

Methods: Data on 299 SLE patients were obtained from the Korean Lupus Network registry. Demographic variables, clinical manifestations, laboratory findings, PGA, and SLEDAI-2000 and SLICC damage index scores were recorded at the time of enrollment and repeated annually for 4 consecutive years. Patients were divided into two groups according to the level of HCQ adherence. Adherence was defined by the medication possession ratio and dichotomized as ≤ 80% vs. > 80%. Univariate and multivariate analyses were performed to assess the impact of adherence to HCQ on clinical outcomes.

Results: Of the 299 patients, 31 (10.4%) showed poor drug adherence during the follow-up period. Patients with poor HCQ adherence were older (P=0.011), less insured (P=0.024), experienced lower employment (P=0.033), and had a higher rate of comorbidities such as hypertension (P=0.048) and depression (P< 0.001). The non-adherent group had higher mean and changed SLICC damage index scores than the adherent group across all 4 years. In the multivariate analysis, HCQ non-adherence was significantly associated with older age (OR, 1.043; 95% CI, 1.006–1.081; P=0.021), depression (OR, 11.98; 95% CI, 1.099–130.6; P=0.042), and an annual increase in the SLICC damage index score (OR, 2.275; 95% CI, 1.369–3.779; P=0.002).

Conclusion: HCQ adherence might be influenced by age and depressive mood. Additionally, the poor adherence to HCQ in SLE patients was correlated with higher cumulative organ damage. Therefore, patients with SLE should be educated to take HCQ appropriately to improve their clinical outcome in clinical practice.

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Abstract Number: 2565

Pharmacokinetics and Exposure-response of Intravenous Belimumab in Children with Systemic Lupus Erythematosus

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Background/Purpose: Belimumab is approved in adults with active SLE and for childhood-onset SLE (cSLE). PLUTO, a Phase 2, placebo-controlled, double-blind trial (114055; NCT01649765), was the first study of belimumab in cSLE. Efficacy, safety, and pharmacokinetics (PK) of intravenous (IV) belimumab 10 mg/kg, plus standard therapy were evaluated. Pediatric and adult belimumab exposures were compared.

Methods: Patients with cSLE, 5–17 years of age, who were randomized to belimumab 10 mg/kg IV every 4 weeks, and for whom ≥1 PK sample was obtained, were included. Patients were required to have active SLE according to ACR classification criteria. A linear 2-compartment population PK model with first-order elimination described the pharmacokinetics of the population. An exploratory *post hoc* exposure-response analysis assessed the impact of between-patient exposure variability on clinical response (SLE Responder Index 4 [SRI4]) at Week 52, and the occurrence of a serious adverse event (SAE) at any time during the study.

Results: Data for 53 belimumab-treated patients were analyzed. Following three biweekly loading doses on Days 0, 14, and 28, belimumab pre-infusion (C_{min}) and post-infusion (C_{max}) concentrations reached steady-state levels over 8 weeks of treatment and were maintained over the 52-week treatment period for all cohorts. Week 24 C_{max} and Week 52 C_{min} values were consistent across cohorts, with a trend towards slightly higher exposure in the older versus younger age group (**Table**). The population PK model estimated a clearance of 158 mL/day, a steady-state volume of distribution of 3.5 L, a terminal half-life of 16.3 days, and a distribution half-life of 0.8 days in the overall population. Body size dependence was defined by the fat-free mass, a pharmacokinetically relevant covariate of clearance, and volume of distribution. Baseline white blood cell count on the central volume of distribution, and baseline IgG, proteinuria, and estimated glomerular filtration rate on central clearance, were also relevant covariates, although their relative influence on PK was smaller. After accounting for body size, age had no statistically significant effect on clearance. Individual and median steady-state pediatric PK profiles were similar to adult profiles[1] (**Figure**). At Week 52, SRI responders (n=28) had similar exposures to non-responders (n=25); median (interquartile range [IQR]) concentrations were 116 [96–140] µg/mL and 109 [88–134] µg/mL, respectively) and variability in exposures of both groups overlapped. Patients who experienced a SAE (n=9) had similar exposures to those who did not (n=44) (median [IQR] 128 [108–161] µg/mL and 110 [86–136] µg/mL, respectively).

Conclusion: Exposure estimates for belimumab 10 mg/kg IV in the pediatric population were consistent with adult exposures. No clinically meaningful correlations between exposure parameters and efficacy or safety were iden-

	Cohorts 1 and 3 (12–17 years of age) (n=43)	Cohort 2 (5–11 years of age) (n=10)
Week 24 C_{max}*, µg/mL, geometric mean (95% CI)	334.4 (289.8, 385.9)	288.8 (234.1, 356.1)
n	37	9
Week 52 C_{min}, µg/mL, geometric mean (95% CI)	59.7 (46.4, 76.8)	45.0 (27.5, 73.4)
n	33	9

*Measured at 5 mins or 2 h (Cohorts 1 and 2) or within 0–4 h (Cohort 3) post infusion
CI, confidence interval

Table. Belimumab concentrations at Weeks 24 and 52

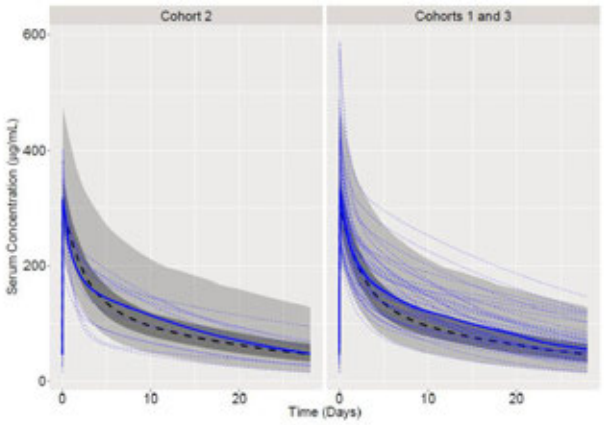

Figure. Comparison of simulated steady-state pediatric PK profiles (by age group) with adult PK profiles from three Phase 3 trials of belimumab IV (1)

tified, confirming that the belimumab 10 mg/kg IV dose used in adults is appropriate for pediatric patients with cSLE.

Study funding: GSK. Medical writing support: Liam Campbell, PhD, Fishawack Indicia Ltd, UK (funded by GSK).

Reference: : [1]Struemper H, *et al. J Clin Pharmacol* 2013; 53(7): 711–20

Disclosure: R. Dimelow, GlaxoSmithKline, 1, 3; **B. Ji**, GlaxoSmithKline, 1, 3, 4; **H. Struemper**, GlaxoSmithKline, 1, 3.

Abstract Number: 2566

Polypharmacy and Potentially Inappropriate Medication Use in Young versus Older Adults with SLE

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Polypharmacy, typically defined as ≥ 5 medications (meds), is a strong risk factor for adverse clinical outcomes, including delirium, falls, hospitalization, and death, especially in older adults. Previously, we presented novel data on the prevalence and risk factors for polypharmacy and potentially inappropriate medications (PIMs), such as benzodiazepines and other sedative-hypnotics (BZD/Z-drugs), in older adults with SLE. In this study we evaluate and compare polypharmacy and PIM use in all adults with SLE. Specific aims: 1. Compare prevalence of polypharmacy [a) ≥5 and b) ≥10 meds] and PIM use [a) opioids, b) BZD/Z-drugs] between age groups (< 40 vs. ≥65,

< 40 vs. ≥40, and < 65 vs. ≥65 years). 2. Assess any association between polypharmacy, PIM use, and their potential risk factors, including age, sex, SLE duration, and rural residence.

Methods: Population: Adults aged ≥18 years meeting ACR/SLICC SLE criteria and seen in our rheumatology clinic < 2 years ago. For age < 50 years, every 3rd patient included. Patients lacking data in the Manitoba Drug Program Information Network (DPIN) were excluded. Procedures: All demographic and clinical variables were determined using data from electronic medical records. For unadjusted bi-variate analyses, we chose alpha of 5%. Multivariable logistic regression models were constructed with inclusion of explanatory variables based on a priori clinical reasoning rather than stepwise selection.

Results: 271 patients included: 92% female, 13% < 3y SLE duration, 40% rural, 68% on ≥5 and 31% on ≥10 meds, 28% on BZD/Z-drugs, and 24% on opioids (Table 1). Prevalence of polypharmacy (≥5 meds) rose with age group (< 40 vs. 40-64 vs. ≥65 years), and was higher in women, rural residents, and SLE duration ≥3 years. Observations on ≥10 meds were similar except that sex difference was reversed (with fewer men). Prevalence of BZD/Z-drugs increased with age, whereas opioid use peaked in 40-64 year-olds. Prevalence of BZD/Z-drugs was higher in women, but opioid use higher in men. Rural residents had higher prevalence of PIMs compared to urban dwellers. The proportion of patients on BZD/Z-drugs was increased with SLE duration ≥3 years. However, the null hypotheses that these inter-group differences are due to chance were not rejected based on our alpha (i.e. $p > 0.05$). In multivariable models, polypharmacy was associated with older age (OR 2.27, 95% CI 1.16-6.31 for ≥40 vs. < 40 years for ≥5 meds). Opioids and BZD/Z-drugs were associated with polypharmacy (any definition) [OR 7.90 (95% CI 3.02-20.67) and 6.05 (2.63-13.96), respectively, for ≥5 meds].

Conclusion: This is the first study to investigate the prevalence and potential risk factors of polypharmacy and PIMs in SLE patients, including young adults. According to this study, polypharmacy and PIM use are highly prevalent in SLE, and the prevalence of polypharmacy and BZD/Z-drugs appears to increase with age. Moreover, PIM use is strongly associated with polypharmacy, independent of other patient characteristics.

Our future goals are to include all eligible clinic patients in these analyses and to evaluate impact of polypharmacy and PIM use on SLE clinical outcomes.

			Age-group		
Variable	**All patients**	**<40**	**40 - 64**	**65+**	**p-value**
N (%)	(N = 271)	(N = 36)	(N = 158)	(N = 77)	
Females	250 (92.3)	34 (94.4)	145 (91.8)	71 (92.2)	0.949
SLE duration < 3y	34 (12.6)	9 (25.0)	14 (8.9)	11 (14.3)	0.030
Rural residence	108 (39.9)	20 (55.6)	58 (36.7)	30 (39.0)	0.110
Polypharmacy					
≥ 5 Medications	185 (68.3)	19 (52.8)	109 (69.0)	57 (74.0)	0.076
≥ 10 Medications	84 (31.0)	8 (22.2)	50 (31.7)	26 (33.8)	0.455
PIM use					
BZD/Z-drugs	75 (27.7)	5 (13.9)	46 (29.1)	24 (31.2)	0.122
Opioids	66 (24.4)	7 (19.4)	43 (27.2)	16 (20.8)	0.454

Table 1. Descriptive Statistics

Disclosure: D. Seguin, None; **C. Peschken**, Astra Zeneca, 2, Celgene, 2, Janssen, 2; **C. Dolovich**, None; **R. Grymonpre**, None; **P. St. John**, None; **A. Tisseverasinghe**, None.

Abstract Number: 2567

Prospective Evaluation of American Academy of Ophthalmology Low Dose Hydroxychloroquine Recommendation in Stable Lupus Nephritis with High-Risk Retinopathy: Lipid Profile and Flare Rates

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: SLE – Clinical Poster III: Treatment

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is the most well established therapy for SLE, as it provides several beneficial properties, such as favorable effects on lipid profile, reduced cardiovascular (CV) risk and reduction in flares. However, one of the main concerns about HCQ use is retinopathy. In this regard, the American Academy

	Before AAO dose reduction	After AAO dose reduction	p
Total cholesterol (mg/dL)	165 (90-343)	163 (111-264)	0.471
> 200 mg/dL	9 (17)	10 (19)	0.800
HDL (mg/dL)	55 (23-95)	50 (16-102)	0.240
< 40 mg/dL	9 (17)	10 (19)	0.800
LDL (mg/dL)	88 (14-224)	89 (40-158)	0.992
> 130 mg/dL	4 (7)	8 (15)	0.359
Triglyceride (mg/dL)	101 (38-386)	98 (39-537)	0.886
> 150 mg/dL	13 (24)	10 (19)	0.637
Glycemia (mg/dL)	83 (69-133)	85 (65-321)	0.841
> 126 (mg/dL)	1 (2)	1 (2)	1.000
Insulin therapy	1 (2)	1 (2)	1.000
Oral antidiabetic drugs	2 (3)	2 (3)	1.000
Lipid-lowering drugs	9 (16)	10 (17)	0.802

Results are expressed in median (minimum-maximum) and n (%).

Table 1. Lipoprotein and glycemia levels, and frequencies of lipoprotein high cardiovascular risk in 53 patients with lupus nephritis before (retrospective evaluation) versus after hydroxychloroquine American Academy of Ophthalmology (AAO) dose reduction (end of prospective analysis)

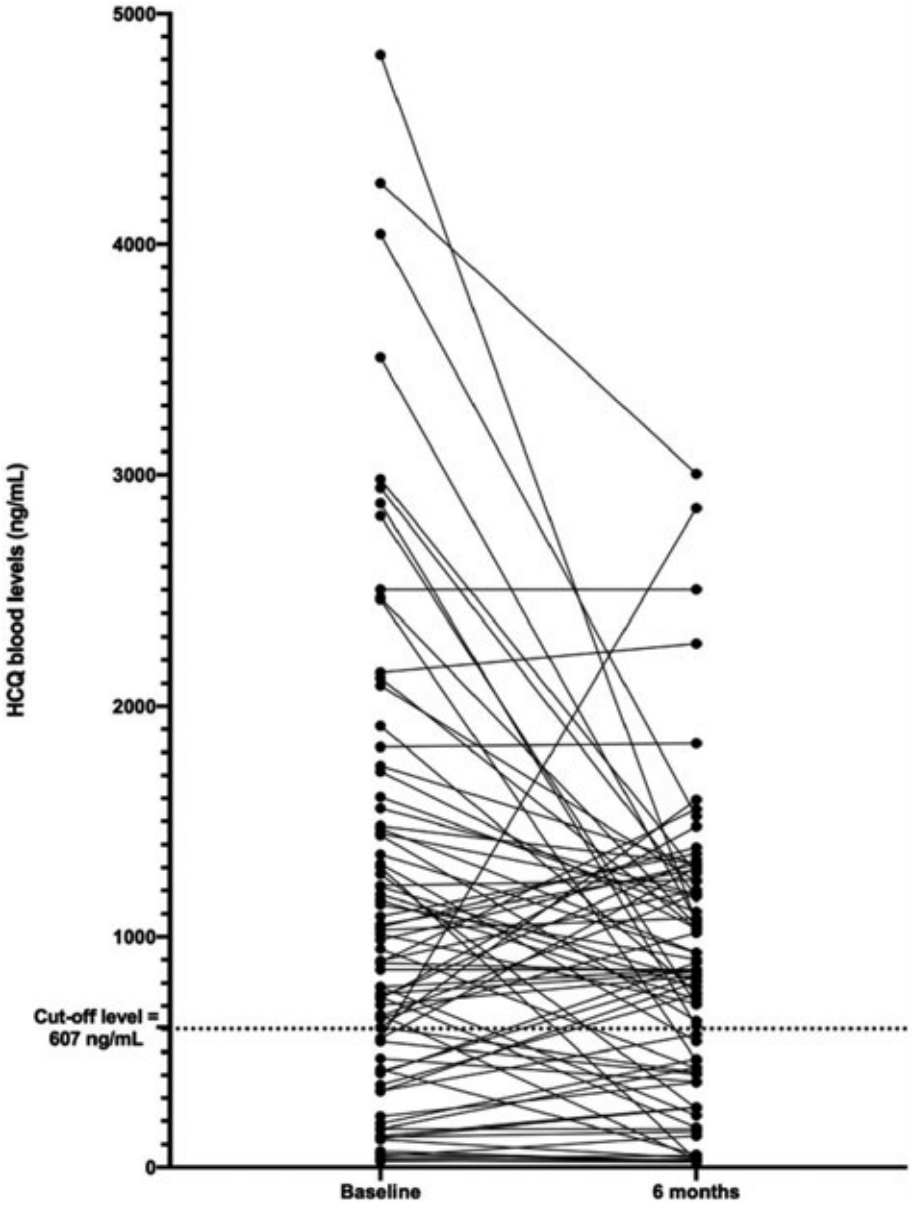

Figure 1. Prospective evaluation of hydroxychloroquine blood levels at baseline and after 6 months in lupus nephritis patients. The dotted line indicates blood HCQ cut-off level for disease flare.

of Ophthalmology (AAO) recently recommended the maximum daily dose of 5.0 mg/kg of real weight but this recommendation is only focused on retinal safety and there are no data evaluating if reduced doses would sustain the beneficial effects of this drug with regard to lipid profile and flare rates. Therefore, the aim of this study was to prospectively assess lipid profile and flare rate in high-risk retinopathy stable LN patients using low dose HCQ AAO recommendation.

Methods: Eighty-two stable LN patients (6-months before entry), ≥5 years of HCQ were evaluated at entry and after 6-months (6M). None of them had retinopathy (spectral-domain optical coherence tomography). HCQ blood levels were determined by liquid chromatography-mass spectrometry. Fasting lipoproteins/blood glucose levels were determined et entry and 6M. Flare was defined as increase in SLEDAI-2K≥3 and/or change in therapy. We also evaluated retrospectively lipid profile, high CV risk and flare rates before HCQ dose reduction according to AAO and compared to the same patients at the end of prospective analysis.

Results: Total/LDL/HDL cholesterol and triglyceride levels remained stable throughout the study (p >0.05) and no significant differences were observed in frequencies of high CV risk levels (p >0.05). Nine of 82 LN patients (10.97%) had flare during the 6-months follow-up. HCQ blood levels were significantly lower in patients with compared to those without flare [220.4(32.1-1471.7) vs. 986.6(26.1-4265.0)ng/mL, p=0.015]. Comparisons of other baseline characteristics demonstrated similar demographic data, disease parameters and concomitant treatment of LN patients with and without flare. An HCQ blood level cut-off of 607ng/ml was a predictor of 6-months flare [OR=5.67, 95%CI 1.34-24.03; sensitivity 78%, specificity 71%, p=0.002). Of note, retrospective analysis revealed comparable lipoprotein and glycemia levels as well as, frequencies of high CV risk and flare rates (9% vs. 10%, p=0.751) before and after AAO dose reduction (Table 1). HCQ blood levels were classified in low (< 607 ng/mL) or adequate (≥607 ng/mL) according to the cut-off level. At 6M evaluation, blood HCQ levels remained within the same range in 67 patients (82%), whereas it turned from low to adequate in six and from adequate to low in nine patients (McNemar's test, p= 0.606) (Figure 1).

Conclusion: We provide novel evidence that AAO HCQ low dose recommendation in stable LN patients with high-risk retinopathy is not associated with a deleterious effect on lipid profile or increased flare rates. This finding supports the notion that this new regimen retains the beneficial effect of HCQ with the advantage of a lower long-term cumulative dose and toxicity.

Disclosure: T. Pedrosa, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2017/14352-7), 2; **S. Pasoto**, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2; **E. Yuki**, None; **N. Aikawa**, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2; **E. Borba**, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #306879/2018-2), 2; **J. Ferreira Filho**, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2017/11516-9), 2; **P. Carricondo**, None; **C. Zanetti**, None; **P. Conde**, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2017/11854-1), 2; **N. Fontoura**, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2017/11644-7), 2; **P. Romano**, None; **V. Carvalho**, None; **C. Silva**, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #303422/2015-7), 2; **E. Bonfa**, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #305068/2014-8), 2, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4 and #2010/10749-0), 2.

Abstract Number: 2568

Iguratimod Is an Alternative Option for Refractory Lupus Nephritis: A Preliminary Observational Study

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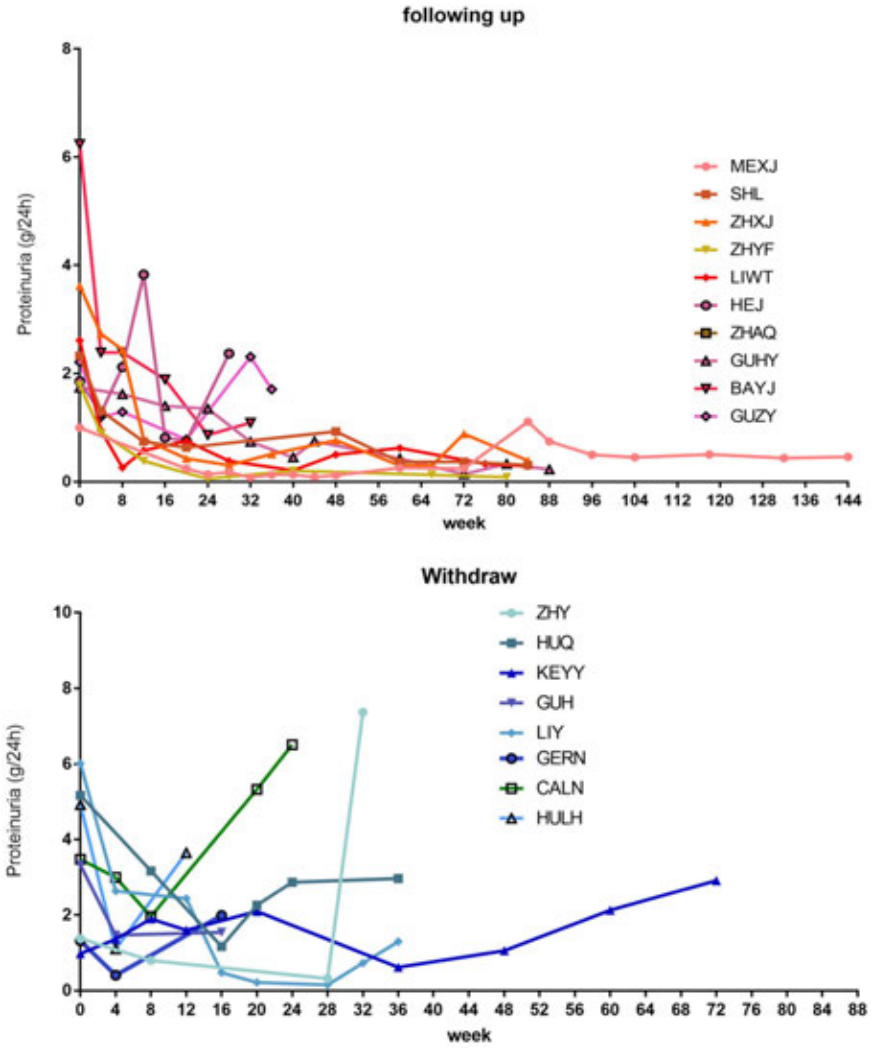
SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: SLE – Clinical Poster III: Treatment

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM



The 24h total proteinuria of each patient.

Background/Purpose: Despite significant advances in the management of patients with lupus nephritis (LN), a significant proportion of patients either do not respond to first-line immunosuppressive drugs, or relapse after initial remission. Iguratimod is a novel disease modifying anti-rheumatic drug that has been approved for treating rheumatoid arthritis in East Asia and has shown benefits in lupus animal model in our previous research. The aim of this study was to make a preliminary observation on the efficacy and safety of iguratimod in treating refractory LN patients.

Methods: We have enrolled adult refractory LN patients since 2015, who were eligible if they experienced at least two times of failure or relapse before enrollment. Failure was defined as no response to one certain immunosuppressive drug for at least six months. After enrollment, we simply switched their previous immunosuppressant to iguratimod (25 mg twice per day) and keeping all other medications. Complete/partial remission (PR/CR) at Week 24 was used as the primary outcome. An extended follow-up would continue once the patient achieved remission.

Results: A total of 20 refractory LN patients had been enrolled (18 female and 2 male patients) since 2015. At enrollment, the median proteinuria was 2.59g/24h (interquartile range, IQR: 1.52-4.92g/24h). None of them had observable

extra-renal symptoms. All of them had biopsy-proven LN (class III/IV/V) and two patients agreed repeated biopsy before switching to iguratimod. The median prednisone dosage was 10mg/d (IQR: 0-10mg/d). One withdrew the consents. Of the remaining 19 patients, the renal response rate was 84.2% at week 24. The median response duration (MRD) was 12 weeks and the IQR was 10-18 weeks. In follow-up of the 16 remitted patients, 25% (4/16) patients had renal relapse (median relapse duration: 32 weeks) and 4 patients exited the study for other reasons (one had extra-renal flare, one had severe adverse event, one lost of follow-up another was for incompliance). For the remaining 9 patients who were still in follow-up, the median follow-up was 84 weeks (IQR: 42-118 weeks), with 4 having CR and 5 PR.

Conclusion: Out study provided preliminary but promising clinical evidence for iguratimod in treating refractory LN patients. A large randomized clinical trial is needed to establish its safety and efficacy for refractory LN.

Disclosure: Q. Yan, None; **C. Bao**, None; **Y. Kang**, None; **Q. Fu**, None; **R. Wang**, None.

Abstract Number: 2569

Guidelines on Prescribing and Monitoring Antimalarials in Rheumatic Diseases: A Systematic Review

Gemma Cramarossa,[1] Janet Pope,[2] and Matthew Turk[3], [1]Schulich School of Medicine & Dentistry, University of Western Ontario, London, ON, Canada, [2]Western University, London, ON, Canada, [3]University of Western Ontario, London, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The purpose of this systematic review was to identify existing guidelines for antimalarial prescribing and monitoring in rheumatic diseases, specifically for hydroxychloroquine, and how these guidelines compare between organizations and have evolved over time.

Both Databases:
Hydroxychloroquine OR (Hydroxychlorochin OR Hydroxychloroquine OR Oxychlorochin OR Oxychloroquine OR Plaquenil).mp
AND
Retinal diseases OR (Retinopath* OR maculopathy* OR retinal toxicit* OR macular toxicit*).mp
AND

Embase:
Practice guideline/ OR Gold Standard/ OR Consensus/ OR Consensus development/ OR Professional standard/ OR Algorithm/ OR (best practice* OR guideline* OR current practice* OR care standard* OR gold standard* OR recommendation* OR expert consensus OR expert panel OR consensus development OR professional standard* OR algorithm* OR critical path*).mp

Medline:
Guideline.pt. OR Guidelines as Topic/ OR Practice Guideline.pt. OR Practice Guidelines as Topic/ OR Standard of care/ OR Quality Indicators, Health Care/ OR Consensus/ OR Consensus Development Conference, NIH.pt. OR Consensus Development Conference.pt. OR Consensus Development Conferences, NIH as Topic/ OR Consensus Development Conferences as Topic/ OR Algorithms/ OR (best practice* OR guideline* OR current practice* OR care standard* OR gold standard* OR recommendation* OR expert consensus OR expert panel OR consensus development OR professional standard* OR algorithm* OR critical path*).mp

Figure 1. Embase and Medline Search Strategies. .mp: Multiple Posting; *: Truncation Symbol; /: Subject Heading; .pt: Publication Type

Guidelines/ Recommendations	Maximum HCQ and CQ doses	Frequency of Screening	Method of Screening
American Academy of Ophthalmology (2002)	HCQ: <6.5 mg/kg/day CQ: <3 mg/kg/day	• Baseline ophthalmology exam • Screening q2-4 years, annually after 5 years • Annual screening in patients with risk factors	• Visual acuity • Dilated cornea and retina exam • Amsler grid or Humphrey 10-2 VF • Optional: colour testing, fundus photography, mfERG
American Academy of Ophthalmology (2011)	HCQ: ≤400 mg/day or 6.5 mg/kg/day using ideal body weight (IBW) if short stature CQ: ≤250 mg/day or 3 mg/kg/day using IBW if short stature	• Baseline ophthalmology exam • Annual exam after 5 years • Annual screening in patients with risk factors	• Dilated retinal exam • VF with white 10-2 automated threshold testing • If available, one objective test: SD-OCT, mfERG or FAF
American Academy of Ophthalmology (2016)	**HCQ: ≤5.0 mg/kg/day using real weight CQ: ≤2.3 mg/kg/day using real weight**	**• Baseline ophthalmology exam • Annual exam after 5 years • Annual screening in patients with risk factors**	**• Fundus evaluation of macula • 10-2 automated VF • SD-OCT • Optional: mfERG and FAF**
Royal College of Ophthalmologists (1998)	HCQ: ≤6.5 mg/kg/day using lean body weight	• Baseline and annual assessment of vision during rheumatology clinic visit • Optometry and/or ophthalmology referral if concerns, with further visits at their discretion	• Visual acuity using a reading chart in rheumatology clinic • Colour vision • VF using red pin and red Amsler grid • Cornea and retina exam
Royal College of Ophthalmologists (2009)	HCQ: ≤6.5 mg/kg/day using lean body weight	• Baseline and annual assessment of vision during rheumatology clinic visit • No systematic screening program recommended • Optometry and/or ophthalmology referral if concerns, with further visits at their discretion	• Visual acuity using a reading chart in rheumatology clinic • Colour vision • Central VF using Amsler Chart or Humphrey 10-2 protocol • Cornea and retina exam • Consider retinal photography, SD-OCT, FAF, and other imaging
Royal College of Ophthalmologists (2018)	**HCQ: <5 mg/kg/day using absolute body weight**	**• Baseline ophthalmology exam • Annual screening from initiation of CQ or if on HCQ with risk factors • Annual exam after 5 years of HCQ**	**• 10-2 Humphrey VF testing using white stimulus • Pupillary dilation exam • Both SD-OCT and FAF if available • If abnormalities on FAF with normal 10-2 VF test results, 30-2 visual field testing is warranted • mfERG if VF deficits and no other imaging abnormality**

Table 1. International Ophthalmology Guidelines on Antimalarial Use. HCQ: Hydroxychloroquine; CQ: Chloroquine; VF: Visual Fields; SD-OCT: Spectral-Domain Optical Coherence Tomography; mfERG: Multifocal Electroretinography; FAF: Fundus Autofluorescence

Recommendations	Maximum HCQ dose	Frequency of Screening	Method of Screening
American College of Rheumatology (2016)	≤5 mg/kg/day using real body weight	• Baseline ophthalmology exam • Annual screening in patients with risk factors • Annual screening after 5 years if no risk factors	• Dilated retina exam • Humphrey 10-2 automated VF test • If available, mfERG, SD-OCT, or FAF also recommended
CRA Consensus Conference (1998)	≤6.5 mg/kg/day using ideal body weight or real body weight, whichever is less	• Baseline ophthalmology exam • Follow-up every 12-18 months, more frequently if risk factors	• Fundoscopic examination of macula • Central 10-degree VF testing using manual or automated methods • Visual acuity • Colour vision • Slit lamp dilated pupil examination

Table 2. Recommendations from Rheumatology Associations. HCQ: Hydroxychloroquine; VF: Visual Fields; SD-OCT: Spectral-Domain Optical Coherence Tomography; mfERG: Multifocal Electroretinography; FAF: Fundus Autofluorescence

Methods: A literature search was conducted using Embase and Medline to identify guidelines published from 1946 to September 2018. MeSH terms were employed for the search strategy with alternative spelling and related words entered as keywords and separated by 'OR' to broaden results (Figure 1). The Embase and Medline strategies both contained the same sub-searches for antimalarials and retinal disease, however they differed in the use of MeSH terms pertaining to guidelines. In addition to reviewing all English search results, references of all articles were reviewed to retrieve additional guidelines.

Results: A total of 243 results were reviewed, after accounting for duplicates, to obtain 11 recommendations. The American Academy of Ophthalmology, Royal College of Ophthalmologists and Canadian editorials summarize ophthalmology recommendations. (Table 1) Rheumatology sources include American College of Rheumatology and Canadian Rheumatology Association statements. (Table 2) American and British guidelines changed from suggesting hydroxychloroquine doses ≤6.5 mg/kg/day to ≤5 mg/kg/day more recently. American guidelines recommended baseline visual field testing and annual screening after five years. Visual field testing evolved from using Amsler grids to current recommendations of 10-2 automated visual fields and spectral-domain optical coherence tomography (SD-OCT). The 2012 Canadian recommendations suggested initial field testing every two years, with SD-OCT after 10 years. Older British guidelines advocated for baseline and annual assessment with Amsler grids during rheumatology clinic visits. The 2018 British guidelines support baseline and annual screening after five years with 10-2 visual fields, SD-OCT and fundus autofluorescence.

Conclusion: The newest recommendations suggest a hydroxychloroquine dose of ≤5 mg/kg/day. Retinal toxicity is irreversible; and the risk increases over time on antimalarial therapy. Annual screening after five years of treatment with automated visual fields and SD-OCT seems to be warranted to detect early changes and discontinue therapy if necessary. It is uncertain whether the magnitude of retinal toxicity is increasing due to early detection with more sensitive tests or if newer recommendations are based on best evidence.

Disclosure: G. Cramarossa, None; **J. Pope**, AbbVie, 5, Abbvie, 5, Actelion, 5, Actellion, 5, Amgen, 2, 5, AstraZeneca, 2, Astra-Zeneca, 2, Bayer, 2, 5, BMS, 2, 5, Eicos Sciences, 5, Eli Lilly & Company, 5, Eli Lilly and Company, 5, EMERALD, 5, Emerald, 5, Genzyme, 5, Janssen, 5, Lilly, 5, Merck, 2, 5, Novartis, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 5, Sanofi, 5, Seattle Genetics, 2, UCB, 2, 5, 8; **M. Turk**, None.

Abstract Number: 2570

Urinary Cellular Profile as a Biomarker for Proliferative Lupus Nephritis

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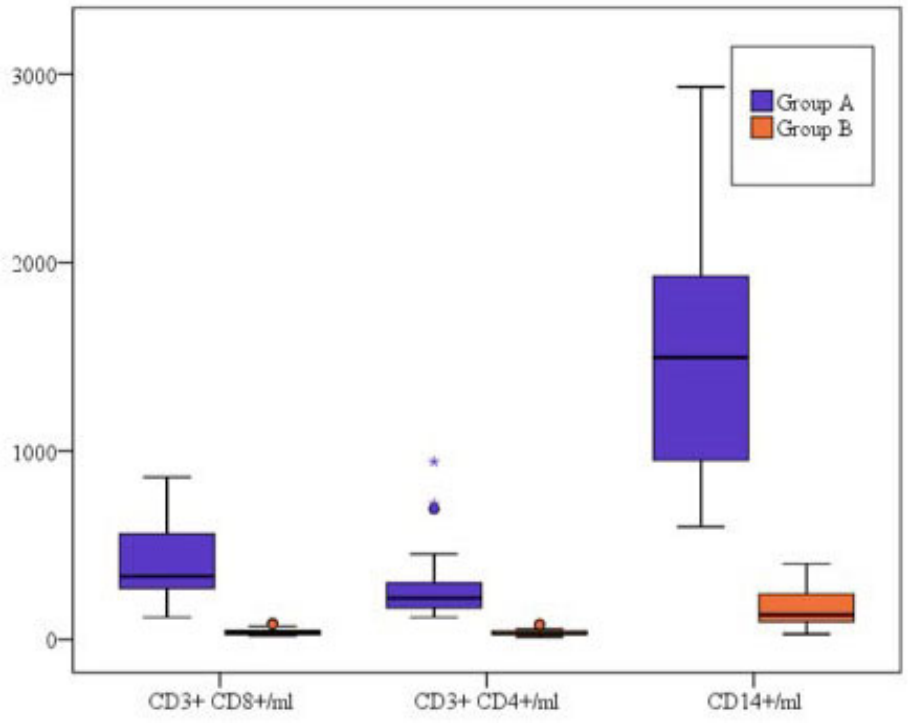
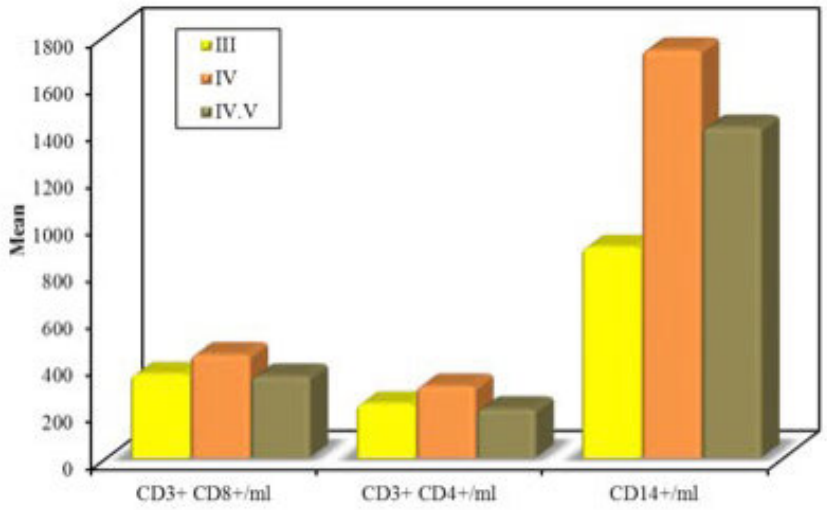
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Proliferative lupus nephritis (LN) is one of the most common and serious manifestations of SLE and is a major cause of morbidity. A search for the ideal biomarker for LN is still underway, one that can be used for early detection, and correlate with the class & activity of LN. Urine is normally devoid of leucocytes, however, it has been observed that macrophages and T-lymphocytes are routinely present in the urine of LN patients and those with other proliferative renal diseases.This provided the idea for their potential use as biomarkers for proliferative LN. The objective is to study the urinary CD4+, CD8+ T Lymphocytes, and CD14+ monocytes in patients with proliferative lupus nephritis, and explore their use as a biomarker for LN.

Methods: Our subjects included 30 patients with biopsy-proven proliferative LN (Group A) and 30 SLE patients without clinical or lab evidence of LN as controls (Group B). Laboratory investigations included serum creatinine, urine analysis, protein: creatinine ratio, anti-ds DNA Ab, C3 and C4. For the flow cytometric analysis, 100 ml of freshly voided urine in a sterile container were obtained from patients and controls. All samples were processed within 2-4 hours of collection to ensure viability of the cells. Urine mononuclear cell count was done using a hemocytometer. The urine



Comparison between the two groups according to CD3+ CD8+/ml, CD3+ CD4+/ml and CD14+/ml



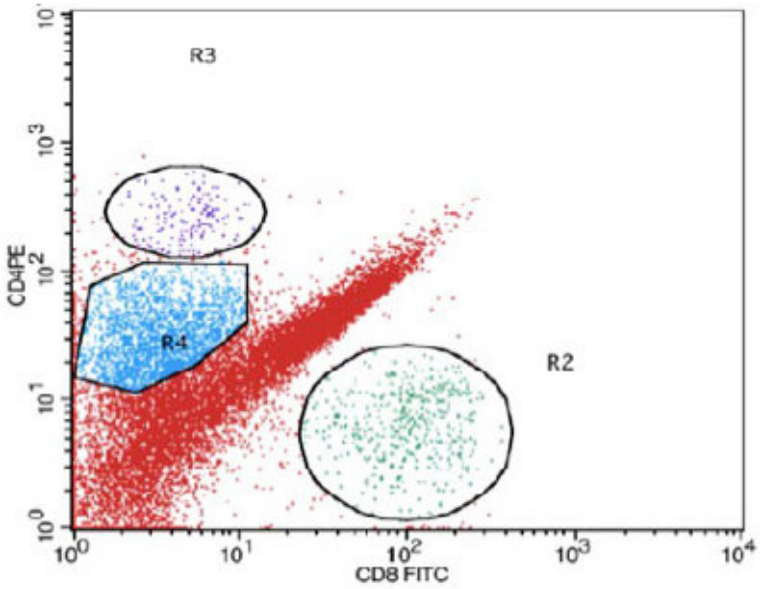
Comparison between the different classes of LN according to CD3+ CD8+/ml, CD3+ CD4+/ml and CD14+/ml.

samples were centrifuged then washed twice by phosphate-buffered saline/bovine serum albumin (PBS/BSA) & re-suspended in about 300 µls PBS. The cells were stained with anti CD8- FITC, anti CD4- PE, anti CD14-PERCP and anti- CD3-APC monoclonal antibodies. The flow cytometric analysis was done using Becton Dickinson, FACS Calibur multi-parameter flow cytometer equipped with BD CellQuest Pro software for data analysis.

Results: CD14 + cells were the most abundant cells in the urine of LN patients. The mean numbers of urinary CD8+, CD4+ and CD14+ cells/ml were significantly higher in patients with LN (405.6 ± 200.0, 281.1 ± 195.3, and 1554.7 ± 606.8 respectively) than in those without (39.30 ± 17.56, 34.33 ± 16.41, and 161.17 ± 90.91 respectively). AUC for ROC = 1.0 for all 3 markers with CD8+ >85 cells/ml, CD4+ >80 cells/ml, and CD14+ >400cells/ml being observed exclusively in LN.

The cell counts correlated significantly with the protein: creatinine ratio, but not with other markers of disease activity.

The CD4: CD8 ratio was significantly lower in LN patients (0.69 ± 0.21) than in those without (0.91 ± 0.31).



A dot plot of flow cytometric analysis of urinary T cells and monocytes in a patient with lupus nephritis showing increased both CD4+ and CD8+ T cells and macrophages (dim CD4 expression and CD14 positive (not shown))

Urinary CD14+ cells seem to occur in much higher counts in Class IV (1736.7 ± 522.0) than Class III LN (898.5 ± 17.68) p=0.084.

Conclusion: Urinary CD8+, CD4+, and CD14+ cells are highly sensitive and specific markers for detecting proliferative LN. A low CD4: CD8 ratio provides a further clue. The cell counts correlate with proteinuria. CD14 cell counts may be a potential biomarker to differentiate between the different classes of proliferative LN.

Disclosure: A. El Gerby, None; **A. Abdelati**, None; **H. Donia**, None; **N. Eshak**, None.

Abstract Number: 2571

Early Improvement in SLEDAI-2K Responder Index-50 Predicts SRI-4 Response in a Randomized Placebo-Controlled Trial of Ustekinumab (UST) in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: While traditional Systemic Lupus Erythematosus (SLE) Disease Activity Index 2000 (SLEDAI-2K) scoring assesses complete SLE response for individual disease manifestations, the SLEDAI-2K Responder Index-50 (S2K RI-50) evaluates responses using partial improvement (≥50%) in each of the 9 organ systems of SLEDAI-2K. Ustekinumab (UST), a monoclonal antibody that targets the shared p40 subunit of the cytokines IL-12 & IL-23, is being investigated in patients with active SLE. We have previously shown in a Phase 2 placebo (PBO)-controlled trial of UST in SLE[1] that not only SLEDAI-2K and the SLE Responder Index 4 (SRI-4), but also S2K RI-50 can discriminate a treatment effect of UST vs PBO at week 24.[2,3] Here, we aimed to ascertain whether a minimal threshold of partial improvement in S2K RI-50 could be used as an early predictor of SRI-4 response.

Methods: This phase 2, PBO-controlled study enrolled adults with seropositive, active disease (SLEDAI score ≥6 with ≥1 BILAG A &/or ≥2 BILAG B scores) despite standard therapy. Patients (n=102) were randomized (3:2) to receive UST IV ~6 mg/kg or PBO at week 0, followed by SC injections of UST 90mg or PBO q8w beginning at week8, both added to standard of care. We calculated S2K RI-50 response through week 24 in all patients, including 60 patients receiving UST and 42 patients receiving PBO, using increasing cut-offs of S2K RI-50 reductions from baseline. To help determining a minimal cut-off that discriminated a treatment effect reflecting partial improvement, nominal p values are reported for this post hoc analysis. Logistic regression models were used to evaluate the relationship between reduction in S2K RI-50 at week 12 or week 16 and SRI-4 response at week 24, followed by correlation of binary response data between the two instruments.

Results: A 2-point reduction from baseline (improvement) in S2K RI-50 appeared to be the lowest threshold of response to demonstrate a treatment difference in the proportion of responders at week 24 with UST (93.5%) vs PBO (79.3%) (Δ14.2%, p=0.03). The relationship between 2-point improvement in S2K RI-50 at week 12 or week 16 and SRI-4 response at week 24 is presented in the total study population and by treatment group (Table). In the total population, 78/102 (76.6%) patients at week 12 and 74/102 (72.5%) patients at week 16 had at least a 2-point im-

Treatment Group	Visit	Correlation	Odds Ratio[a] [95% CI]	Predictive p-value[a]
Total Population	Week 12	0.62	7.6 [2.4-24.3]	0.0007
UST	Week 12	0.49	4.4 [1.1-16.9]	0.0311
PBO	Week 12	NE[b]	NE[b]	NE[b]
Total Population	Week 16	0.76	15.4 [4.2-55.8]	<0.0001
UST	Week 16	0.74	13.5 [2.6-69.8]	0.0020
PBO	Week 16	0.74	15.0 [1.7-130.7]	0.0142

[a] Predictive p-values and odds ratios are based upon logistic regression models. Predictive p-values are nominal and represent measures of the likeliness of association between a 2-point response in S2K RI-50 at week 12/16 and SRI-4 response at week 24 in the model.
[b] Not estimable (NE) due to no values present in one cell in the 2x2 table.
UST = Ustekinumab, PBO = Placebo

provement in S2K RI-50. Of those, 47/78 (60.3%, r=0.62) at week 12 and 48/74 (64.9%, r=0.76) at week 16 achieved an SRI-4 response at week 24. Odds ratios for the association between SRI-4 response at week 24 and 2-point or greater improvement in S2K RI-50 were 7.6 (CI 2.4-24.3, p=0.0007) at week 12 and 15.4 (CI 4.2-55.8, p< 0.0001) at week 16. Similar analyses performed by treatment group demonstrated that these relationships were consistent in the UST and PBO groups (Table).

Conclusion: S2K RI-50 captures partial improvement of ≥50% in SLE disease activity and could be a useful outcome in clinical trials to predict early clinical response. These findings will be confirmed in an ongoing Phase 3 study.

References:

1. van Vollenhoven et al. Lancet. 2018:392:1330.
2. Touma Z et al. EULAR June 2018, Amsterdam, NL.
3. Touma Z et al. APLAR. April 2019, Brisbane, Australia.

Disclosure: Z. Touma, Janssen Research & Development, LLC, 2, Janssen Scientific Affairs, LLC, 2; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, GSI, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5; **S. Rose**, Janssen Research & Development, LLC, 3; **K. Fei**, Janssen Research & Development, LLC, 3; **Y. Gregan**, Janssen Research & Development, LLC, 3; **R. Gordon**, Janssen Research & Development, LLC, 3; **K. Lo**, Janssen Research & Development, LLC, 3; **M. Urowitz**, Janssen Research & Development, LLC, 2, UCB Pharma, 9.

Abstract Number: 2572

Efficacy Analysis of Patients with Systemic Lupus Erythematosus Treated with Belimumab or Placebo Plus Standard Therapy in Phase 3 Trials by Baseline Levels of BLyS mRNA and Type 1 Interferon Inducible Gene Signature Status

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Belimumab (BEL) is a B-lymphocyte stimulator (BLyS) inhibitor approved as an add-on to standard of care (SoC) for patients with autoantibody-positive SLE with active disease. This meta-analysis was performed to investigate the efficacy of BEL vs placebo (PBO) plus SoC when participants were stratified by whole blood BLyS mRNA levels and by type 1 interferon-inducible gene signature (IFN-1) status at study baseline.

Methods: This study (GSK study 208651) is a *post hoc* analysis of two Phase 3 trials (BLISS-76 [BEL110751] and -52 [BEL110752]) in which patients received intravenous BEL 10 mg/kg plus SoC or PBO plus SoC. The population for the analysis included all randomized patients with an mRNA sample that passed quality control who received at least one dose of BEL or PBO. Co-primary endpoints were SLE Responder Index (SRI)-4 response within each subgroup and the correlation between baseline BLyS mRNA and IFN-1 levels overall. For binary endpoints, a logistic regression model was used to estimate the odds of SRI response for BEL vs PBO within BLyS mRNA subgroups (high/medium/low tertiles according to quantitative PCR mRNA delta cycle threshold), IFN-1 (high/low) subgroups (according to the median mRNA level of IFI27, IFI44, IFI44L, and RSAD2, defined with reference to samples from 25 healthy volunteers and the trough in bimodal distribution) and overall. To assess SRI-4 response, patients were required to have a Safety of Estrogens in Lupus Erythematosus National Assessment-SLE Disease Activity Index score ≥4 at baseline. The

Table 1. SRI-4 response at Week 52 of treatment by BLyS mRNA subgroup

	BLyS mRNA low		BLyS mRNA medium		BLyS mRNA high	
	PBO (n=85)	BEL (n=95)	PBO (n=102)	BEL (n=79)	PBO (n=84)	BEL (n=100)
Response, n (%)	38 (44.7)	48 (50.5)	35 (34.3)	42 (53.2)	34 (40.5)	48 (48.0)
Odds ratio (95% CI) BEL vs PBO†	1.10 (0.58, 2.07)		2.17 (1.16, 4.04)		1.62 (0.87, 3.01)	
p-value†	0.7785		**0.0153**		0.1255	

†Covariates include treatment group, study, baseline SELENA-SLEDAI score (≤9 vs ≥10), baseline proteinuria (<2 g/24 hours vs ≥2 g/24 hour equivalent) and race (African descent or indigenous American descent vs other) BLyS, B-lymphocyte stimulator; BEL, belimumab; CI, confidence interval; PBO, placebo; SELENA-SLEDAI; Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index; SRI-4, Systemic Lupus Erythematosus Responder Index

Table 2. SRI-4 response at Week 52 of treatment by IFN-1 subgroup

	IFN-1 low		IFN-1 high	
	PBO (n=43)	BEL (n=46)	PBO (n=228)	BEL (n=228)
Response, n (%)	18 (41.9)	21 (45.7)	89 (39.0)	117 (51.3)
Odds Ratio (95% CI) BEL vs PBO†	1.36 (0.55, 3.34)		1.58 (1.08, 2.31)	
p-value†	0.5002		**0.0186**	

†Covariates include treatment group, study, baseline SELENA-SLEDAI score (≤9 vs ≥10), baseline proteinuria (<2 g/24 hour vs ≥2 g/24 hour equivalent) and race (African descent or indigenous American descent vs other) BEL, belimumab; CI, confidence interval; IFN-1, type 1 interferon-inducible gene signature; PBO, placebo; SELENA-SLEDAI; Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index; SRI-4, Systemic Lupus Erythematosus Responder Index

correlation between BLyS gene expression and IFN-1 was analyzed by Spearman's rank correlation coefficient and further by Chi Square test to compare subgroups.

Results: This analysis was based on N=281 (BEL) and N=273 (PBO). Baseline demographics were similar across the BLyS and IFN subgroups. There were more SRI-4 responders at Week 52 for BEL vs PBO in all three BLyS mRNA subgroups but the odds ratio (OR) only achieved statistical significance for the BLyS medium subgroup (**Table 1**). Baseline BLyS gene expression and IFN-1 were significantly correlated (Spearman's rank correlation coefficient 0.7799; 95% CI: 0.7451, 0.8106; p< 0.0001). The percentage of responders at Week 52 was greater for BEL vs PBO for both the low and high IFN-1 subgroups and the OR achieved statistical significance in the high IFN subgroup (**Table 2**).

Conclusion: This study demonstrated a tendency toward better response to BEL as add-on therapy vs SoC alone in patients who had higher baseline BLyS mRNA and IFN-1. However, this was an exploratory analysis, the sample size was opportunistic, with the consequence that the BLyS and IFN-1 subgroups were not explicitly powered to detect a difference in response rates. More studies are necessary to understand whether these biomarkers should be used as treatment decision tools.

Study funding: GSK. Medical writing support: Jennie McLean, PhD, Fishawack Indicia Ltd, UK (funded by GSK).

†Covariates include treatment group, study, baseline SELENA-SLEDAI score (≤9 vs ≥10), baseline proteinuria (<2 g/24 hours vs ≥2 g/24 hour equivalent) and race (African descent or indigenous American descent vs other) BLyS, B-lymphocyte stimulator; BEL, belimumab; CI, confidence interval; PBO, placebo; SELENA-SLEDAI; Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index; SRI-4, Systemic Lupus Erythematosus Responder Index

†Covariates include treatment group, study, baseline SELENA-SLEDAI score (≤9 vs ≥10), baseline proteinuria (<2 g/24 hour vs ≥2 g/24 hour equivalent) and race (African descent or indigenous American descent vs other) BEL, belimumab; CI, confidence interval; IFN-1, type 1 interferon-inducible gene signature; PBO, placebo; SELENA-SLEDAI; Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index; SRI-4, Systemic Lupus Erythematosus Responder Index

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Disclosure: A. Jones-Leone, GlaxoSmithKline, 1, 3; **S. Flint**, GlaxoSmithKline, 1, 3; **R. Levy**, GlaxoSmithKline, 1, 3, 4; **D. Roth**, GlaxoSmithKline, 1, 3, 4; **R. Henderson**, GlaxoSmithKline, 1, 3; **C. Wilkinson**, GlaxoSmithKline, 1, 5; **B. Ji**, GlaxoSmithKline, 1, 3, 4; **D. Bass**, GlaxoSmithKline, 1, 3, 4.

Abstract Number: 2573

Hydroxychloroquine Levels in Patients with Systemic Lupus Erythematosus: Comparison of Whole Blood and Serum Levels

Benoit Blanchet,[1] Jallouli Moez,[2] Marie Allard,[3] Veronique le guern,[4] Jean-Charles Piette,[5] Noémie Jourde-Chiche,[6] and **Nathalie Costedoat-Chalumeau** [7], [1]Cochin, Paris, France, [2]sfax, SFAX, Tunisia, [3]Hôpital Bichat Claude-Bernard, Paris, France, [4]APHP, paris, France, [5]Hôpital Pitié-Salpêtrière, Paris, France, [6]APHM, Marseille, Marseille, France, [7]Cochin University Hospital, Paris, France

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) levels can be measured in whole blood as well as in serum but both methods have never been compared. Cut offs for non-adherence (200 ng/mL or lower) have been established in whole blood.

The aims of this study were to compare the interest of whole blood versus serum levels for drug monitoring of HCQ, and since it would be very interesting to retrospectively assess severe non-adherence in clinical trials or in large cohort of patients in which only serum samples are usually available, to evaluate if HCQ serum level cut off could be determined to identify non-adherent patients.

Methods: The HCQ and desethylchloroquine (DCQ) levels were measured in serum and whole blood from 573 systemic lupus erythematosus (SLE) patients. The risk factors for active SLE (SLEDAI score >4) were identified using multiple logistic regression. HCQ serum level was also measured in 68 additional non-adherent patients (whole blood HCQ level < 200 ng/mL).

Results: The mean HCQ and DCQ levels were 916 ± 449 and 116 ± 55 ng/mL in whole blood, respectively; and 469 ± 223 and 63 ± 31 ng/mL in serum, respectively. The mean ratio of serum /whole blood level for HCQ was 0.53 ± 0.15.

A strong positive correlation was found between serum and whole blood levels of HCQ (rho=0.837 [CI95% 0.810-0.860], p< 0.0001), and DCQ (rho=0.771 [CI95% 0.736-0.802], p< 0.0001). In the multivariate analysis, only corticosteroids (p=0.044), immunosuppressant (p=0.027), HCQ whole blood level (p=0.023) and hemoglobin (p=0.009) were identified as an independent risk factor of active SLE but serum HCQ level was not.

Given that the mean ratio of serum/whole blood level for HCQ was 0.53, we extrapolated that serum HCQ level cut offs of 106 and 53 ng/mL would correspond to the previously used cut-off of 200 and 100 ng/mL of HCQ in whole blood. The positive and negative predictive values of serum HCQ < 106 ng/ml to detect non-adherence (defined by blood HCQ < 200 ng/ml) were 86.8% and 85.7%, respectively.

All serum HCQ levels of patients exhibiting whole blood HCQ below the detectable levels (< 50 ng/mL) were also below the detectable levels for serum (37.5 ng/mL).

Conclusion: These data suggest that whole blood is better than serum when assessing pharmacokinetic/pharmacodynamic relationship of HCQ. When whole blood is not available, our results support the use of HCQ serum level to assess non-adherence with a cut off of 106 ng/mL corresponding to 200 ng/ml in whole blood.

Disclosure: B. Blanchet, None; **J. Moez**, None; **M. Allard**, None; **v. le guern**, None; **J. Piette**, None; **N. Jourde-Chiche**, None; **N. Costedoat-Chalumeau**, None.

Abstract Number: 2574

Safety, Tolerability, Pharmacokinetic and Pharmacodynamic Effect of BIIB059, a Monoclonal Antibody Targeting BDCA2 Following Administration of Subcutaneous Single Doses in Japanese Healthy Volunters

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, when ligated inhibits the production of inflammatory mediators and Type I Interferon (INF), a major player in Systemic and Cutaneous Lupus Erythemtosus's (SLE and CLE) pathogenesis. Targeting BDCA2 with BIIB059, a high affinity humanized IgG1 mAb, represents an attractive therapeutic strategy. BIIB059 was previously tested in a Phase 1 study in non-Japanese healthy volunteers (HV) (NCT02106897)* and is currently in phase 2 development for the treatment of SLE and Cutaneous Lupus Erythematosus (CLE) (NCT02847598) .

Methods: A total of 32 HV from Japanese descend matched for body weight (NCT02106897), were enrolled into 4 cohorts to receive a single subcutaneous (SC) injection of 20-, 50-, 150- or 450 mg of BIIB059 or placebo (6 BIIB059: 2 Placebo). Blood samples were obtained to characterize PK and PD profiles and establish PK-PD relationships for BIIB059. Safety and tolerability data were monitored and reviewed.

Results: BIIB059 was generally well tolerated; no SAEs were observed. Adverse events were reported by 9 (37.5%) and 0 (0.0%) subjects in the BIIB059- and placebo-treated groups, respectively. Overall, 33.3% and 4.2% subjects reported AEs that were mild or moderate in severity, respectively. Three subjects (12.5%) experienced AEs considered related to study drug and mild in severity. All AEs resolved without treatment. There were no clinically significant findings on laboratory measures or in physical examination. Following single SC BIIB059 administration, Cmax and AUC(0-inf) increased with doses. Mean t1/2 ranged from 10 to 27 days. A PK and PD comparison between non-japanese and japanese HV is being conducted and results will be presented here. Eleven subjects (45.8%) treated with BIIB059 tested positive for anti-BIIB059 antibodies at ≥ 1 postdose timepoint (ADA). There was no apparent relationship between incidence of ADA and dose, no apparent effect on drug exposure and no association with clinically relevant observations. Following BIIB059 administration, BDCA2 expression on pDCs sharply decreased with levels returning towards baseline in a dose-dependent manner as serum concentrations of BIIB059 decreased.

Conclusion

- BIIB059 was generally well tolerated.
- BIIB059 exposure increased with dose.
- Preliminary results suggest no apparent PK/PD and safety differences between body weight matched Japanese and Non-Japanese healthy subjects at all doses after single BIIB059 administration.
- BDCA2 expression on pDCs decreased rapidly and sharply and returned to baseline levels in a dose-dependent manner.

Disclosure: C. Musselli, Biogen, 1, 3, 4; **F. Gaudreault**, Biogen, 1, 3, 4; **N. Himanshu**, Biogen, 1, 3, 4; **H. Carroll**, Biogen, 1, 3, 4; **A. Sharma**, Biogen, 1, 3, 4; **X. Huang**, Biogen, 1, 3, 4; **N. Franchimont**, Biogen, 1, 3.

Abstract Number: 2575

Electronic Monitoring of Medication Adherence in Young Adults with Childhood-Onset Systemic Lupus Erythematosus over 12 Weeks

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Table 1. Baseline demographical, disease, and barriers characteristics of subjects

Characteristic	Control (n=11)
Demographics	
Age, mean, (SD) in yrs.	20.5 (1.6)
Gender (female), %	100
Race, No, (%)	
White	4 (36)
Black	6 (55)
Asian	-
Multiple	1 (9)
Insurance type, %	
Public	45
Private	55
cSLE	
Disease duration, yrs., (SD)	4 (3)
SLEDAI‡, mean, (range)	5 (2-10)
SLICC¥, mean, (range)	0.5 (1-2)
Physician global, mean (range)	1 (0-3.5)
Nephritis, No. (%)	5 (45)
PROMIS fatigue, mean (SD)	57±2.9
PROMIS pain intensity, mean (SD)	3.6±2.3
No of Pills†, mean (SD)	7 (3.5)
Presence of comorbidity (%)	11 (100)
Hypertension, No. (%)	3 (27)
Depression, No. (%)	3 (27)
Obesity, No. (%)	7 (66)
Barriers¶, No (%)	
Forgetting	11 (100)
Taste	9 (81)
Side effects	
Current	8 (73)
Future	6 (55)
Fertility concerns	7 (64)
Treatment upsetting	6 (55)
Inconvenient	6 (55)
Cost	5 (45)

†Includes both lupus and non-lupus medications being taken by subjects.
‡SLEDAI 2K score from clinic visit preceding start of study.
¥SLICC Damage Index obtained from annual calculated score within 12 months of study initiation.
¶Includes barriers with fewer than 3 respondents such as difficulty swallowing pills, running out of medication, refusing to take treatment, believing treatment to be unnecessary, desire to keep treatment private from others, lack of perceived treatment benefit, treatment getting in the way, and hard instructions.

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Table 2. Descriptive Statistics for Electronic Measurements of Adherence for Time Points 1, 2, and 3

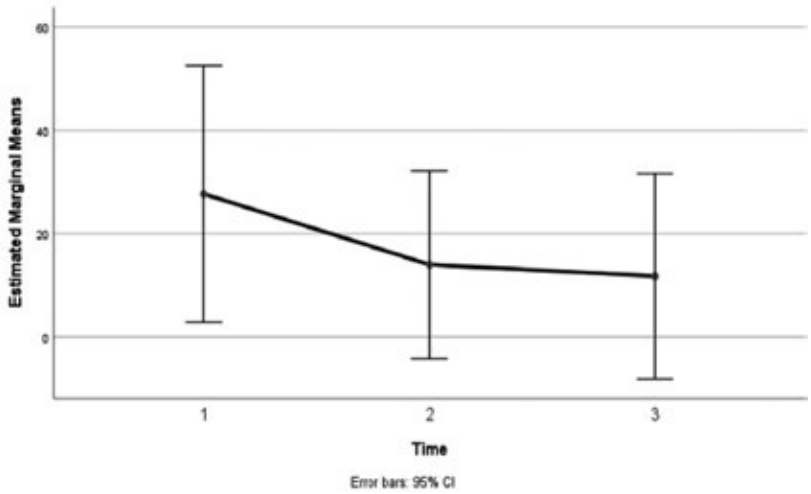
	N	Mean	Std. Deviation
Time Point 1 (1st month)	9	27.67	32.296
Time Point 2 (2nd month)	9	14.00	23.617
Time Point 3 (3rd month)	9	11.78	25.820

Background/Purpose: Young adults with childhood-onset lupus (cSLE) are 20 times more likely to die compared to healthy age- and gender-matched counterparts. Their clinical course is more severe than adult-onset lupus, with a 2-3 times increased mortality rate. Poor adherence (i.e. the extent to which an individual's behavior matches treatment regimens) to therapeutic regimens is a major contributor to negative health outcomes - increased morbidity, mortality, healthcare utilization, and costs. Reliably measuring adherence is critical in targeting this significant problem. However, non-invasive estimates of adherence vary based on measurement method (e.g., self-report, refill data). There is, therefore, a need for objective and reliable methods of measuring adherence to all daily medications. The objective of this study is to examine the feasibility, acceptability, and efficacy of using an electronic pillbox to measure adherence in young adults with cSLE.

Methods: Eleven young adults with cSLE (mean age 20.5±1.6; 36% Caucasian; 55% Black; 1% mixed race) were followed prospectively over 12 weeks. Subjects were recruited during routine pediatric rheumatology clinic visits and met ACR criteria for SLE. All subjects received SimpleMed+ (Viaca, Tel Aviv, Israel) pillboxes that track adherence, for multiple medications and up to four daily doses, using cellular technology. Self-report of adherence using the Medication Adherence Self-Report Inventory (MASRI) was implemented. Additional questionnaires and chart review data were collected. Descriptive analysis and a one-way repeated measures ANOVA were performed.

Results: Demographic and disease characteristics are summarized in Table 1. Forgetting, after taste, current medication side effects, and fertility concerns were top barriers to medication adherence (see Table 1). Eighty-one per-

Figure 1: Estimated Marginal Means of Adherence over 3 Time Points - 1st, 2nd, and 3rd months respectively



cent of participants (9/11) completed the study and found the pillbox acceptable and easy to use. Reasons for not completing the study were forgetting to refill and/or charging the pillbox. The means and standard deviations of a one-way repeated measure ANOVA (conducted for mean electronic measurements of adherence at 3 time points - 1st, 2nd, and 3rd months) are presented in Table 2. There was no significant effect for time, Wilks' Lambda = .52, F (2, 7) = 3.24, p = 0.10, multivariate partial η^2 = .48. Although mean self-reported adherence increased from 70.5% to 80% from baseline to study completion, electronically measured adherence decreased over time (Figure 1).

Conclusion: Measuring adherence to multiple medications is feasible with electronic pillboxes. Results from this study suggest that poor medication adherence will not improve without intervention. Consistent with prior studies, our study indicates that self-report of adherence may overestimate true medication adherence. Despite the small sample size, our study show that electronic pillboxes may be a reliable non-invasive method of measuring adherence to *all* medications taken by patients with cSLE. Establishing a reliable method of measuring adherence to multiple medications is an essential tool for the advancement of adherence research and the ultimate resolution of this significant public health issue.

Disclosure: O. Harry, None; **T. Ting**, None; **J. Huggins**, None.

Abstract Number: 2576

Clinical Evidence Supporting Therapeutic Potential of Activating the Immune Checkpoint Receptor BTLA in SLE

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SESSION INFORMATION
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Immune checkpoint inhibitors have demonstrated durable benefit in some cancer patients. However, checkpoint inhibitors are also associated with new onset autoimmune adverse events. The link between checkpoints and autoimmune disease suggests that activating immune checkpoint receptors might be useful in treating autoimmune diseases like SLE. As the role of B cells and T cells are implicated in SLE, we became interested in modulating BTLA (B- and T-lymphocyte attenuator) as potential therapeutic target for SLE. The endogenous ligand for BTLA is HVEM (Herpes virus entry mediator), and BTLA attenuates lymphocytes by recruiting phosphatases SHP-1 and SHP-2 to the B cell receptor and T cell receptor signaling complexes, respectively. The current study examined the BTLA/HVEM signaling pathway in two large phase 3 trials in SLE to determine if there was a therapeutic rationale for activating BTLA in SLE.

Methods: Whole blood gene expression data from 1760 SLE patients was obtained from the phase 3 ILLUMINATE-1 and ILLUMINATE-2 studies in patients with SLE and active disease activity defined as SLEDAI-2K $\geq$ 6 (NCT01205438, NCT01196091). Control samples were obtained from healthy donors. Blood was collected in Tempus tubes at baseline, week 16, and week 52. RNA was analyzed using Affymetrix Human Transcriptome Array 2.0.

Results: High levels of BTLA mRNA were observed on B cells, CD4+ T cells, CD8+ T cells and plasmacytoid dendritic cells. HVEM mRNA levels were lower in SLE patients compared to healthy controls, while BTLA levels were similar between SLE and control. Low levels of HVEM mRNA were associated with increased disease activity at baseline, including proportion of patients with SLEDAI ≥ 10, and frequency of patients with anti-dsDNA antibodies, low complement (C3 and C4), and elevated interferon gene signature.

Conclusion: The analysis confirmed that BTLA is present on key immune cells linked to the pathogenesis of SLE. The reduced levels of HVEM in SLE patients compared to control suggests that ligand deficiency in the BTLA system may play a role in SLE. Importantly, low HVEM was associated with increased disease activity across multiple disease characteristics, including measures of high disease activity, serology and gene expression. These data provide clinical rationale for evaluating a BTLA agonist in SLE. A phase 1 trial with a BTLA agonist antibody in healthy volunteers is in progress.

Disclosure: M. Linnik, Eli Lilly and Company, 1, 3, 4; **A. Godzik**, Eli Lilly and Company, 2; **L. Jaroszewski**, Eli Lilly and Company, 2; **C. Ware**, Eli Lilly and Company, 2; **A. Vendel**, Eli Lilly and Company, 1, 3, 4.

Abstract Number: 2577

SLE Disease Activity May Be Associated with Choroidal Thickness

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is an autoimmune disease with widespread organ involvement. High disease activity has previously been associated with higher risk of organ damage and mortality. However, it is often difficult to resolve which clinical symptoms reflect SLE disease activity, leading to potential over or under treatment. Inflammation of the choroid (the outer vascular layer of the eye) may reflect inflammation of the kidney in lupus, since both have similar vascular designs, contain fenestrated capillaries, are composed of a3-5 type IV collagen, and are organized in lobules. In addition, clinical choroidopathy has been observed in patients with SLE high disease activity, especially renal or CNS involvement. In a recent publication, choroid thickening (CT) was reported in a cohort of SLE patients compared to non-SLE controls, but disease activity was not described. In the present study, we investigated whether CT is associated with extra-renal SLE flare, extra-renal disease activity, or renal disease in complete remission. We hypothesize that CT is associated with SLE disease activity.

Methods: This is a retrospective case-control study of SLE patients meeting either American College of Rheumatology (ACR) or Systemic Lupus International Collaborating Clinics criteria who were followed at Washington University School of Medicine Rheumatology, Nephrology, or Ophthalmology clinics. Data was derived from 21 patients with SLE, 14 of whom had biopsy-proven lupus nephritis (LN). The nephritis of all LN patients was in complete clinical remission as defined by the ACR. Disease activity was assessed using the S2K RI-50 instrument, with scores > 4 defined as active. Major flare was defined by Fortin criteria. CT was measured at three locations through the fovea using optical coherence tomography, a noninvasive imaging modality used by ophthalmologists to follow retinal disease. After exporting images into Adobe Photoshop, CT was measured independently by 2 investigators. Intra-rater and

inter-rater reliabilities were 0.982 and 0.96, respectively. Comparisons were made with Student's t-test for parametric and Mann-Whitney U for nonparametric data.

Results: Compared to control subjects with inactive SLE and no history of LN, the CT of subjects with active SLE was marginally thicker (348 µm [IQR 308-425] vs 264 [IQR 228-343], p = 0.061 at 500 µm nasal to the fovea, n = 4 vs 14 eyes, respectively). However, the CT of subjects who met criteria for extra-renal flare (293±87µm vs 270±74µm, p = 0.286 at 500 µm nasal to the fovea, 310±89µm vs 284±74 µm, p = 0.229 at the fovea, and 301±84µm vs 274±68µm, p = 0.163 at 500 µm temporal to the fovea, n = 21 vs 41 eyes) or inactive LN were not different from controls (272±79 µm vs 268±69 µm, p = 0.862 at 500 µm nasal to the fovea, 281±78 µm vs 288±70 µm at the fovea, and 271±64µm vs 272±72µm at 500 µm temporal to the fovea, n = 23 vs 20 eyes).

Conclusion: CT may be associated with some manifestations of active SLE (S2K RI-50 > 4)**.** CT was not associated with extra-renal flare or LN in remission. Study conclusions are limited by the retrospective observational design and small sample size. The study supports the need for additional research examining CT - SLE disease activity relationships.

Disclosure: I. Lee, None; **B. Marshall**, None; **P. Ranganathan**, None; **S. Eisen**, None; **R. Rajagopal**, None; **A. Kim**, Exagen Diagnostics, Inc., 5, 8, Exagen Diagnotics, Inc., 5, 8, GlaxoSmithKline, 2, 5, 8, Kypha, Inc, 2, Kypha, Inc., 2; **T. Li**, None.

Abstract Number: 2578

Effect of Omega-3 Fatty Acids on Systemic Lupus Erythematosus Disease Activity: A Systematic Review and Meta-Analysis

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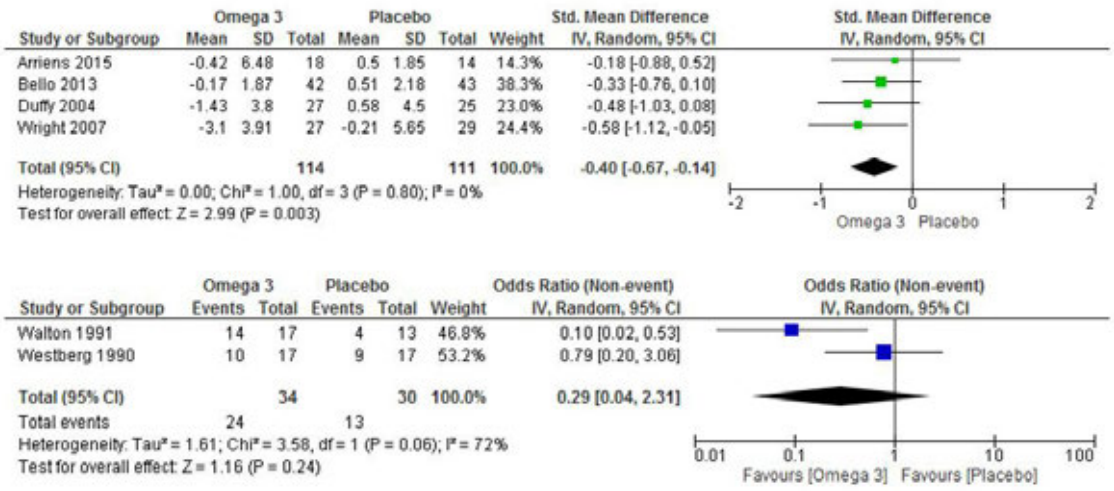
SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: SLE – Clinical Poster III: Treatment

Session Type: Poster Session (Tuesday)



Forest plot of the effects of Omega 3 fatty acids vs. placebo in trials. Upper panel continuous outcomes. Lower panel dichotomous outcomes.

Session Time: 9:00AM–11:00AM

Background/Purpose: Omega-3 fatty acids may have anti-inflammatory properties. In animal models of systemic lupus erythematosus (SLE) Omega-3 fatty acids decrease autoantibody levels, reduce inflammatory markers and prolong the lifespan of lupus-prone mice. However clinical studies in patients with SLE have been small, with wide confidence intervals and conflicting findings. Thus, we aimed to perform a systematic review and meta-analysis to determine a more accurate and precise estimate effect of omega-3 fatty acids on SLE disease activity in adults.

Methods: Following an *a priori* established protocol, a comprehensive search in any language of several databases designed by two expert librarians was conducted from database's inception to January 11th, 2019. Studies that were randomized controlled trials (RCT) of adults with SLE comparing omega 3 fatty acids supplementation to placebo or standard of care and reported SLE disease activity were included. Abstracts and full text reviews were evaluated independently and in duplicate by two investigators.

To combine outcomes, we standardized the disease activity scales (SLEDAI and SLAM) into standardized mean differences (SMD). Since small sample sizes can lead to biased overestimation of the SMD, we used Hedges' (adjusted) *g* methods. For continuous outcomes we calculated the SMD and 95% confidence interval (95CI), we used the inverse variance approach random-effects model. Dichotomous outcomes were reported as odds ratio (OR) and 95CI. Heterogeneity was calculated with the I^2 statistic. Results were presented in standardized mean response for SLE disease activity and 95CI. To improve clinical interpretability, the pooled data was scaled back to the SLEDAI by multiplying SMD by standard deviation of the studies that utilized SLEDAI.

Results: Six studies were included in the meta-analysis. The studies were published between 1990 and 2015. All the included studies were RCTs. The treatment group sizes ranged from 8-43 patients (median 20). In total 180 patients were in the comparison groups and 183 in the treatment groups. Half of the studies utilized the usual dose 3 grams or less of Omega 3 fatty acids while the rest used up to 20 grams. The trial follow-up time ranged from 22 – 52 weeks. The mean age of the patients was 43.2 years and 80% or more were female.

Four RCTs with 225 participants had continuous outcomes, 2 used SLEDAI and 2 used SLAM to measure SLE disease activity. As shown in the figure, the SMD of the included trials ranged from -0.18 (95CI, -0.88, 0.52) to -0.58 (95CI, -1.12,-0.05). The pooled SMD was -0.4 (95CI, -0.67, -0.14). We transformed the SMD to units of the SLEDAI scale. Compared to placebo, Omega 3 fatty acids reduced disease activity by 1.4 (95CI, -2.9, -1) SLEDAI points. The statistical heterogeneity was low with an I^2 of zero.

Two RCTs with dichotomous variables were included in the analysis. 64 patients were part of these studies. The pooled odds ratio was 0.29 (95CI, 0.04, 2.31). The statistical heterogeneity was high with an I^2 of 72%.

Conclusion: This meta-analysis evaluated the efficacy of Omega-3 fatty acids for the treatment of SLE. Our results suggest that Omega-3 fatty acids are a potential therapy that can be added to the immunosuppressive treatments used for SLE.

Forest plot of the effects of Omega 3 fatty acids vs. placebo in trials. Upper panel continuous outcomes. Lower panel dichotomous outcomes.

Disclosure: A. Duarte Garcia, None; **E. Myasoedova**, Pfizer, 2; **P. Karmacharya**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **K. Warrington**, Eli Lilly, 2, GlaxoSmithKline, 2, roche, 2, 8, Roche, 2, 5, 8, Sanofi, 5, sanofi, 5.

Abstract Number: 2579

A Quality Improvement Project in Determining If Cardiac Enzymes Play a Role in Surveillance of Possible Hydroxychloroquine Induced Cardiotoxicity

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is a commonly used medication in our field of work with retinal toxicity being a known possible long-term side effect of the medication. Studies and case reports have described a role of HCQ in cardiotoxicity although, the relation is not completely clear [Drug Saf. 2018 Oct;41(10):919-931]. The gold standard of diagnosis would be an endomyocardial biopsy however, it is impractical to have the biopsy done on anyone suspected of having HCQ induced cardiomyopathy [J Rheumatol. 2019 Apr;46(4):391-396]. Our goal is to evaluate if cardiac injury markers as predictors of HCQ-induced cardiotoxicity.

Methods: This quality improvement project retrospectively analyzed medical record of patients taking HCQ with a diagnosis of an arrhythmia, cardiomyopathy, or heart failure at SUNY Upstate Medical University in Syracuse, New York. Established causes of heart disease, such as hypertension or congenital malformations were excluded. Patients

Table 1. Sensitivity of Two cardiac injury tests in patients taking Hydroxychloroquine before and after a cardiac diagnosis. NT – Not tested

	Start HCQ before a cardiac Dx		Start HCQ after a cardiac Dx	
TEST	Troponin	BNP	Troponin	BNP
Arrhythmia+ Test +	20	26	9	12
Arrhythmia+ Test -	40	25	12	4
Arrhythmia+ NT	49	58	45	50
Sensitivity (%)	33.3	50.1	43	75
p-value		0.06		0.0506
Cardiomyopathy+ Test +	20	21	7	14
Cardiomyopathy+ Test -	19	18	14	4
Cardiomyopathy+ NT	9	9	7	10
Sensitivity (%)	51.2	53.8	33	78
p - value		0.8206		0.0055
Heart Failure+ Test+	58	81	34	42
Heart Failure+ Test-	42	11	23	11
Heart Failure+ NT	73	81	36	40
Sensitivity (%)	58	88	60	79
p-value		<0.0001		0.0263
Total Number of Patients Tested	330	330	187	187

were distinguished as to whether they had the cardiac diagnosis before or after the starting HCQ. Cardiac injury markers, CK, CKMB, troponin, BNP, were evaluated in each subject. Statistical analyses of categorical variables were performed with chi-square test using GraphPad software.

Results: 8220 patients were identified to be on HCQ between 2013 and 2019. 854/8220 (10.4%) had a cardiac diagnosis, such as arrhythmia, cardiomyopathy, or heart failure. 517/854 had a cardiac diagnosis not attributed to a known cause such as hypertension or congenital malformations. Of 517 cases, heart disease was recorded in 187 patients before and 330 patients after initiation of HCQ treatment. Among laboratory tests examined, BNP testing was found to be most sensitive to detect heart disease in both groups. In patients who were diagnosed with heart disease after having started HCQ, BNP was 88% sensitive for detection of heart failure ($p < 0.0001$ over other tests). BNP was also most sensitive to detect cardiomyopathy or heart failure in patients subsequently started on HCQ.

Conclusion: Cardiotoxicity is a newly recognized possible side effect of HCQ therapy. While clinicians are aware of surveillance for possible retinal and guidelines have been established, there are no guidelines for cardiotoxicity monitoring. This study indicates that BNP may be a sensitive test for detecting heart disease in patients taking HCQ either before or after initiation of therapy. These results advocate for including BNP for safety monitoring of patients treated with HCQ.

Disclosure: E. Liu, None; **A. Perl**, None.

Abstract Number: 2580

Pharmacotherapies Targeting Type 2 SLE Symptoms

Raeann Whitney,[1] Amanda Eudy,[1] Megan Clowse,[1] Lisa Criscione-Schreiber,[1] Jayanth Doss,[1] David Pisetsky,[2] Kai Sun,[1] Rebecca Sadun,[1] and Jennifer Rogers[1], [1]Duke University, Durham, [2]Duke University, Durham VAMC, Durham

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: We propose categorizing lupus activity to better align with patient experience: Type 1 SLE activity includes classic symptoms such as arthritis and nephritis; Type 2 includes widespread pain, fatigue, depression, sleep disturbance, and perceived cognitive dysfunction. We previously found that only 53% of our patients with active Type 2 SLE received direct treatment for these symptoms, which is currently extrapolated from fibromyalgia treatment. We aimed to evaluate prescription of pharmacotherapies for Type 2 SLE symptoms one year after implementing the Type 1 and 2 categorization system.

Methods: This was a cross-sectional study of SLE patients (SLICC 2012 criteria) in a university lupus clinic from May 2018-March 2019. All patients completed Patient Health Questionnaire-9 (PHQ-9) and 2016 ACR Fibromyalgia criteria questionnaires. Active Type 2 SLE was defined as having a fibromyalgia severity score (FSS) > 10. We defined Type 2 medications as antidepressants (serotonin and norepinephrine reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressant **(**TCAs), mirtazapine, bupropion), muscle relaxers (cyclobenzaprine, tizanidine, baclofen, metaxalone), gabapentinoids (gabapentin, pregabalin), topiramate, zolpidem, trazodone, tramadol, anxiolytics, stimulants, and DHEA. Relationships between clinical variables and medications in different groups were analyzed using t-tests and Fisher's exact test.

	n=158
Age	42.6 (13.3)
Sex, female	151 (96%)
Race	
White	55 (35%)
Black	91 (58%)
Other	12 (8%)
Hispanic	9 (6%)
History of LN	83 (53%)
Length of SLE diagnosis, years	14.7 (8.4)

All outcomes are reported as mean (SD) or n (%)
n=150 for Length of SLE diagnosis

Table 1. Patient Demographics

	Patients with Type 2 Activity n=54	Patients without Type 2 Activity n=104	Total n=158	p-value
Any Type 2 Med	38 (70%)	42 (40%)	80 (51%)	0.0004
Antidepressants				
SNRI	17 (31%)	6 (6%)	23 (15%)	<0.0001
SSRI	6 (11%)	10 (10%)	16 (10%)	0.8
TCA	3 (6%)	7 (7%)	10 (6%)	1.0
Bupropion	2 (4%)	8 (8%)	10 (6%)	0.5
Mirtazapine	1 (2%)	1 (1%)	2 (1%)	1.0
Antiepileptics				
Gabapentin or pregabalin	20 (37%)	14 (13%)	34 (22%)	0.001
Topamax	1 (2%)	0 (0%)	1 (0.6%)	0.3
Anxiolytics				
Benzodiazepines	5 (9%)	1 (1%)	6 (4%)	0.02
Buspirone	1 (2%)	0 (0%)	1 (0.6%)	0.3
Muscle relaxer	11 (20%)	6 (6%)	17 (11%)	0.01
Pain Medications				
NSAIDs	17 (31%)	28 (27%)	45 (28%)	0.6
Other opioids	13 (24%)	10 (10%)	23 (15%)	0.02
Tramadol	5 (9%)	6 (6%)	11 (7%)	0.5
Sedating medications				
Trazodone	8 (15%)	4 (4%)	12 (8%)	0.02
Sedating anti-histamine	4 (7%)	1 (1%)	5 (3%)	0.05
Zolpidem	3 (6%)	3 (3%)	6 (4%)	0.4
Stimulant	2 (4%)	2 (2%)	4 (3%)	0.6
Supplements				
Vitamin D	19 (35%)	40 (38%)	59 (37%)	0.7
Vitamin B12	8 (15%)	13 (13%)	21 (13%)	0.8
DHEA	0 (0%)	1 (1%)	1 (0.6%)	1.0

All outcomes are reported as mean (SD) or n (%)
SNRI - Serotonin and norepinephrine reuptake inhibitors
SSRI - Selective serotonin reuptake inhibitor
TCA - Tricyclic antidepressant

Table 2. Comparing medication use in patients with and without Type 2 SLE activity

Results: Single-visit data from 158 patients were included (Table 1). There was a clear difference in prescribing patterns based on the presence or absence of Type 2 SLE: 70% of patients with active Type 2 SLE took at least one Type 2 medication compared to 40% of those without (Table 2). Medications differentially prescribed to patients with Type 2 activity included SNRIs (prescribed in 31% with Type 2 activity vs 6% without, $p < 0.0001$; primarily duloxetine),

	Active Type 2 SLE		
	No Corticosteroids n=34	Current Corticosteroids n=20	p-value
Fibromyalgia Scores			
Fibromyalgia Severity Score (FSS)	15.5 (4.4)	15.8 (4.8)	0.9
Symptom Severity Score (SSS)	8.1 (2.1)	8.2 (2.0)	0.9
ACR Fibromyalgia Criteria (Moderate or Severe)			
Cognitive dysfunction	15 (47%)	8 (40%)	0.8
Fatigue	29 (91%)	18 (95%)	1.0
Waking unrefreshed	29 (91%)	17 (89%)	1.0
Depression			
Criteria met for depression by PHQ9	5 (19%)	6 (40%)	0.3
PHQ9 Score	9.7 (3.8)	10.1 (4.4)	0.8
Physician assessment of Type 2 severity (0-3)	1.4 (0.8)	1.5 (0.8)	0.7

All outcomes are reported as mean (SD) or n (%)

Table 3 There is no difference in symptom scores among patients with Active Type 2 SLE currently taking and not taking corticosteroids

gabapentinoids (37% vs 13%, p = 0.001; primarily gabapentin), muscle relaxers (20% vs 6%, p = 0.01; primarily cyclobenzaprine), opioids (24% vs 10%, p = 0.02), trazodone (15% vs 4%, p = 0.02), and benzodiazepines (9% vs 1%, p = 0.02). There was no difference in prescriptions for SSRIs, NSAIDs, Vitamins D, or B12. Steroid use was higher in patients with active Type 1 symptoms (51% vs 33%) and average dose was higher (13 mg vs 7 mg). Among patients with active Type 2 SLE, there was no difference in Type 2 symptom severity between those who were taking corticosteroids and those who were not (Table 3).

Conclusion: After instituting formal assessments for Type 2 SLE activity, prescription of medications to address these symptoms has increased from 53% to 70%, aligning treatment patterns with patient symptomatology. Patients with active Type 2 SLE are differentially prescribed SNRIs, gabapentinoids, and muscle relaxers. Corticosteroids are more often prescribed to address active Type 1 rather than Type 2 activity and are not associated with Type 2 symptom severity. Together, these findings highlight the need for longitudinal studies to evaluate therapeutic efficacy of these medications and identify optimal pharmacologic and non-pharmacologic interventions for Type 2 SLE.

Disclosure: R. Whitney, None; **A. Eudy**, GSK, 2; **M. Clowse**, GSK, 2, UCB, 5; **L. Criscione-Schreiber**, None; **J. Doss**, None; **D. Pisetsky**, None; **K. Sun**, None; **R. Sadun**, None; **J. Rogers**, None.

Abstract Number: 2581

Clinical Impact of Decreasing Hydroxychloroquine Dose According to the 2016 American Academy of Ophthalmology Guidelines in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is one of the main drugs used for the treatment of systemic lupus erythematosus (SLE). Nonetheless, HCQ-induced retinal toxicity remains a major concern. To reduce the risk of HCQ-induced retinopathy, in 2016 the American Academy of Ophthalmology recommended a maximum daily HCQ dose of ≤5.0 mg/kg real weight. However, it is uncertain if this recommended dose would have an impact on the clinical course and outcome of SLE patients. Thus, we compared outcome measures in a cohort of SLE patients before and after adjusting HCQ dose to ≤5mg/kg/day.

Methods: Sixty Hispanics from Puerto Rico with SLE (per 1997 revised American College of Rheumatology [ACR] criteria) treated with HCQ who were changed to HCQ ≤5.0 mg/kg/day were studied. Visits were ascertained every 6 months for 2 years prior to HCQ dose adjustment (baseline visit) and up to 2 years afterwards. Disease activity (per Systemic Lupus Disease Activity Index [SLEDAI]), SLE exacerbations, emergency room visits, hospitalizations, damage accrual (per Systemic Lupus International Collaborating Clinics/ACR Damage Index [SDI]), prednisone (or equivalent) exposure, prednisone (or equivalent) mean dose, and immunosuppressive drugs exposure were determined before and after HCQ dose change. Statistical analyses were performed using Exact McNemar's test and Wilcoxon signed-rank test, as appropriate.

Results: At baseline visit, the mean age was 44.0 ± 14.9 years. All patients were women. The mean disease duration and HCQ treatment duration were 13.8 ± 9.1 and 12.5 ± 15.1 years, respectively. The mean daily HCQ doses before and after adjustment were 395 ± 28 mg and 256 ± 50 mg, respectively. All patients had at least 1 year of follow-up, 41 (68.3%) had 1.5 years of follow-up, and 39 (65.0%) had 2 years of follow-up after dose adjustment. Before HCQ dose adjustment, patients had more mean hospitalizations (any cause) (0.08 ± 0.20 vs. 0.02 ± 0.07, p=0.031) and mean hospitalizations attributed to SLE (0.04 ± 0.16 vs. 0.00, p=0.045) when compared to visits after HCQ dose reduction. No significant differences (p >0.05) were observed for mean SLEDAI scores (2.2 ± 2.9 vs. 2.1 ± 2.9), lupus exacerbations (0.18 ± 0.25 vs. 0.16 ± 0.25), emergency room visits (any cause) (0.06 ± 0.22 vs. 0.17 ± 0.78), emergency room visits attributed to SLE (0.02 ± 0.78 vs. 0.01 ± 0.06), and mean daily prednisone dose (7.9 ± 17.3 mg vs. 5.2 ± 5.8 mg) before and after HCQ dose adjustment. Likewise, no differences were observed for exposure to corticosteroids, mycophenolate mofetil, azathioprine, cyclophosphamide, tacrolimus, rituximab or methotrexate. Patients did not accrue more damage from baseline visit to last study visit (mean SDI score: 0.9 ± 1.4 vs. 1.0 ± 1.4, p=0.190), and no deaths occurred.

Conclusion: This study suggests that adjustment of daily HCQ dose to ≤5.0 mg/kg real weight does not have a significant impact in the short- and mid-term outcomes of SLE patients. Nevertheless, a larger number of patients and longer follow-up are necessary to reach further conclusions.

Disclosure: N. Medina-Cintrón, None; **I. Vázquez-Otero**, None; **M. Arroyo-Ávila**, None; **L. González-Sepúlveda**, None; **L. Vilá**, None.

Abstract Number: 2582

Incidence of Antimalarials-Induced Retinopathy in Inflammatory Rheumatic Diseases, Using OCT and Visual Field Test : A Systematic Review and Meta-analysis

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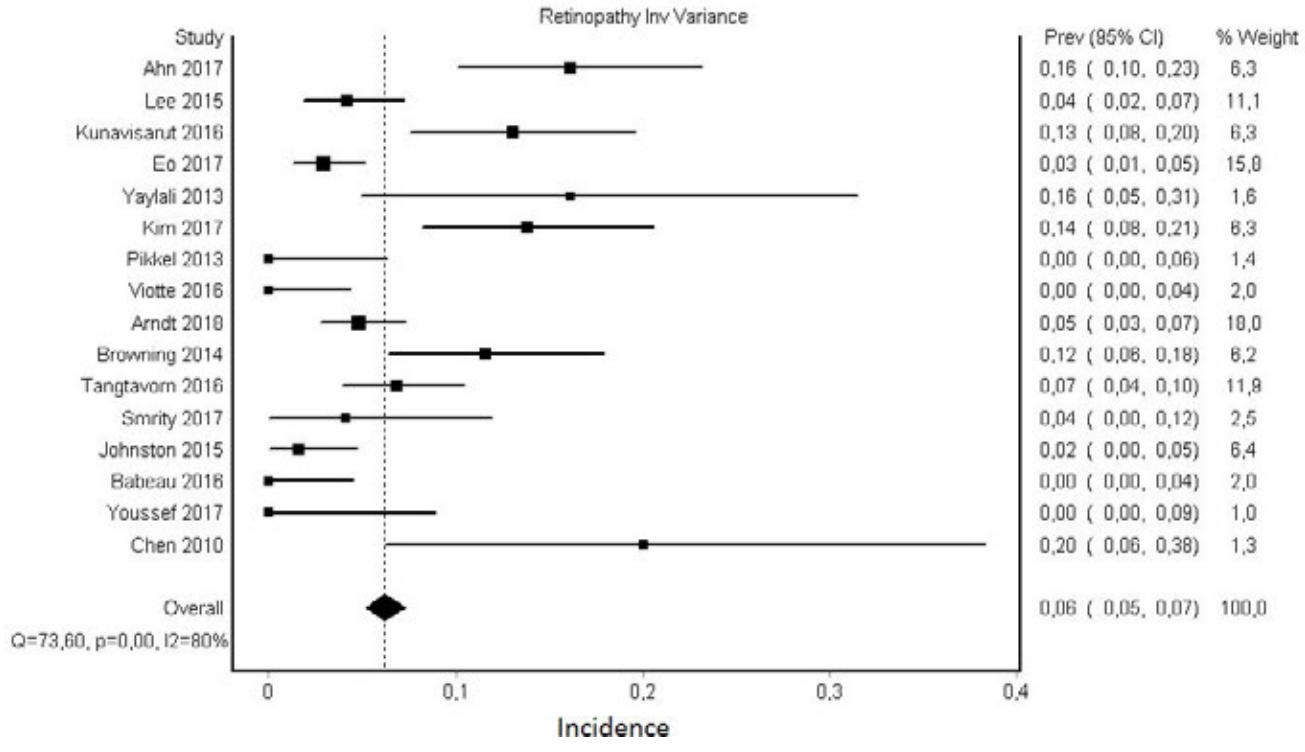
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Antimalarials (AM) are frequently used as first-line therapy in mild inflammatory diseases, because of a good benefit/risk ratio. Their most severe side effect is retinopathy, which can potentially lead to blindness, but remains reversible if detected early, provided the treatment is stopped. This complication has been described early [1], but its incidence remains uncertain. A recent update of the American Association of Ophtalmology (AAO) recommendations on screening for chloroquine and hydroxychloroquine retinopathy, suggests to screen patients under AM treatment, with a frequency depending on risk factors, and with the systematic and minimal use of Optical Coherence Tomography (OCT) and Visual Field (VF) test, completed by others tests if required [2]. We aimed at estimating the exact incidence of AM-induced retinopathy, based on available published literature about this issue, with particular reference to detection performed with OCT and VF test.

Methods: A systematic literature search was conducted in Pubmed, Cochrane and Embase databases until April 6th 2018, completed by a manual search in references from the resulting selected articles. We first selected all publications about the incidence of retinopathy linked to AM in patients treated for inflammatory diseases and included them in the systematic literature search. Among them, and in order to minimize heterogeneity of results, we focused on those which had used at least OCT and VF test, as recommended by the AAO, to perform a meta-analysis. Analysis was conducted using MetaXL for Microsoft Excel, applying the Inverse of Variance method.

Results: Among the 3890 articles of potential interest, we selected 91 articles appropriately addressing the topic and included them in the systematic literature search. They were dated between 1964 and 2018, with variable population sizes (10 to 3580 patients). Patients were treated with hydroxychloroquine, chloroquine or both for an inflammatory disease (usually lupus or rheumatoid arthritis). Mean treatment duration ranged from 1 to 14,1 years. Most of them



were retrospectively designed, and diagnostic method were variate. For the aforementioned meta-analysis, we used data from 16 articles published between 2010 and 2018, in which every patient had at least OCT and VF Test. We found a pooled estimate of prevalence of 6.05% (IC 95% [5.18 – 7.31]), with a heterogeneity coefficient of 80 %.

Conclusion: We found a pooled prevalence of approximately 6% of retinopathy linked to AM when OCT and VF test are used. However diagnostic criteria are not consensually well-defined, leading to heterogeneous data.

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Abstract Number: 2583

Prevalence and Risk Factors of Herpes Zoster Reactivation in Patients with Biopsy Proven Lupus Nephritis Undergoing Immunosuppressive Therapies

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To study the prevalence of Herpes Zoster (HZ) reactivation in patients with biopsy confirmed lupus nephritis (LN) undergoing immunosuppressive therapies.

Methods: Patients who had biopsy confirmed active LN (2003-2018) were retrospectively reviewed for the occurrence of HZ infection. The following data were collected: age, sex, SLE disease activity scores, maximum daily dose and total duration of high-dose prednisolone and other immunosuppressive drugs in the induction period, maintenance therapies, laboratory parameters at baseline and 6 months post-therapy that included lupus serology, albumin, globulin, IgG/A/M levels, white cell counts, histological classes of LN and renal response. The incidence of HZ reactivation at 2 years of LN treatment and on follow-up was calculated. Risk factors for HZ reactivation were studied by logistic regression.

Results: 251 patients with 311 episodes of active LN were studied (92% women; age 34.2±14.2 years). Histological LN classes were: III/IV±V(69%), I/II/V/VI(31%). Induction regimens were: moderate/high dose prednisolone in combination with cyclophosphamide (17%), azathioprine (11%), mycophenolate mofetil (MMF) (42%), tacrolimus (25%). Renal response at 6m was: complete response (CR) (59%), partial response (PR) (27%) and non-response (NR) (15%).

Within 2 years of therapies, 55(18%) episodes of LN were complicated by HZ infection (incidence: 8.84/100 patient-year). The median time for HZ reactivation since LN therapy was 11 months. 28 patients had HZ infection beyond 2 years (overall prevalence: 3.24/100 patient-years). The distribution of HZ lesions was: head and neck (15%), lower limbs (27%), trunk (55%) and upper limbs (4%). 75% of the episodes were treated by oral acyclovir. Secondary bacterial infection or significant neuralgia occurred in 18% of the episodes. Disseminated disease or mortality was not reported. Patients with HZ reactivation were more likely to have first-time renal disease (76% vs 58%; p=0.02) and a shorter SLE duration at LN (31.4±50 vs 62.7±72 months; p=0.02). A trend of higher SLEDAI, higher anti-dsDNA, lower C3/albumin but more refractory disease was observed in HZ-infected patients. Histological LN classes, neutrophil/lymphocyte counts and immunoglobulin levels at baseline and 6 months post-therapy were not significantly different between HZ-infected and control patients. HZ-infected patients had been treated with a significantly higher dose of prednisolone (0.72±0.40 vs 0.63±0.24 mg/kg/day) at induction. Higher doses of other immunosuppressive drugs had also been used in patients with HZ reactivation but the difference was not statistically significant. Logistic regression revealed first-time LN (OR 2.25[1.08-4.71]; p=0.003), peak MMF dose (OR 1.24[1.10-3.07]; p=0.02) and cumulative CYC dose (OR 1.14[1.01-1.28]; p=0.04) during induction therapy were significantly associated with HZ at 2 years.

Conclusion: HZ reactivation is fairly common in LN patients undergoing immunosuppressive therapies but unpredictable from clinical parameters. Minimization of immunosuppression and HZ vaccination may help reduce the risk of HZ infection.

Disclosure: C. Mok, None; **K. Chan**, None; **S. Tse**, None; **L. Ho**, None.

Abstract Number: 2584

Management of Cutaneous Manifestations of Lupus Erythematosus: A Systematic Review

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical Poster III: Treatment
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Background/Purpose: Cutaneous lupus erythematosus (CLE), occurring with or without systemic lupus erythematosus (SLE), is a group of inflammatory skin diseases that can be very debilitating, causing significant psychological distress, and in some cases scarring. We sought to comprehensively present the evidence for different treatment modalities in patients with cutaneous manifestations of lupus erythematosus (LE).

Methods: Medline, Embase, Scopus and Cochrane CENTRAL were searched electronically from 1990 to March 2019, using keywords related to cutaneous lupus and synonyms and treatment. Articles retrieved were screened for relevance, including reference lists of retrieved reviews. We included clinical trials, observational studies or case series with 5 or more patients focussing on treatment of CLE, with or without SLE.

Results: The search identified 6637 studies, of which 104 were included. Each study commonly included a heterogenous mixture of CLE subtypes, with or without SLE. The 104 included studies investigated 11 different categories of treatment in 6811 patients. Treatments included topical calcineurin inhibitors (CNIs) (13 studies), sun protection (5

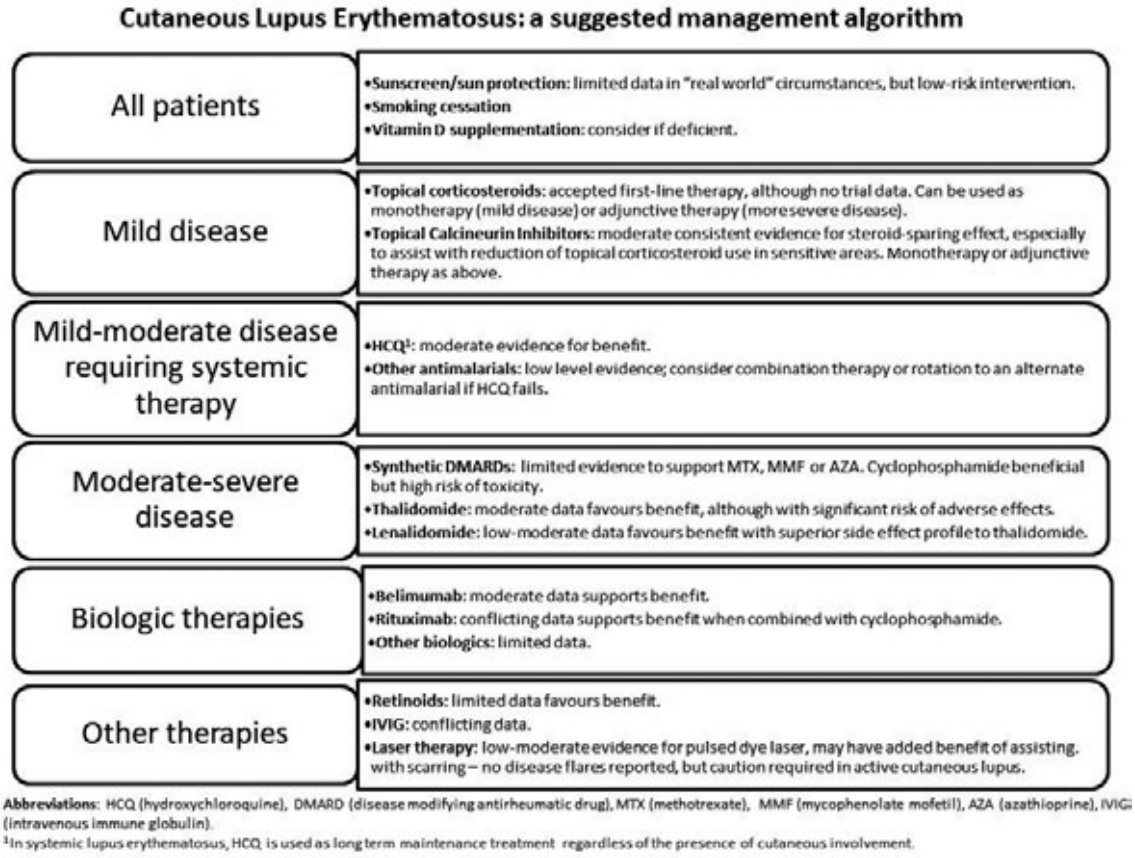

Figure 1. a suggested management algorithm for cutaneous lupus erythematosus

studies), R-salbutamol cream (2 studies), antimalarials (23 studies), synthetic disease modifying anti-rheumatic drugs (DMARDs)(10 studies), retinoids (2 studies), thalidomide/lenalidomide (22 studies), biologic therapies (12 studies), intravenous immune globulin (3 studies), laser (6 studies) and other therapies (6 studies). A suggested management algorithm based on these data, determined by disease severity, is summarised in Figure 1. General measures to be considered include smoking cessation, sun protection measures and optimisation of vitamin D levels. Moderate evidence exists for benefit with topical CNIs, particularly as a steroid sparing agent in areas at high risk of steroid complications (e.g. facial skin). There is moderate evidence for hydroxychloroquine, which is first-line in SLE patients, limited evidence to support other synthetic DMARDs, and moderate evidence supporting thalidomide but with significant risk of toxicity. Of biologic therapies, there are moderate data to support belimumab. Limited evidence exists for other therapies.

Conclusion: Many management options are available for CLE, including topical, systemic and biologic therapies, with a variable balance of efficacy and toxicity. There is a paucity of high-quality clinical trial data. Further trials are required to better understand optimal management of CLE, particularly in specific subgroups.

Disclosure: J. Fairley, None; **S. Oon**, None; **A. Saracino**, None; **M. Nikpour**, Actelion, 2, Arthritis Australia, 2, Australian Rheumatology Association, 2, Bayer, 2, BMS, 2, GSK, 2, Pfizer, 2, Roche, 2, Scleroderma Victoria and Australia, 2, St Vincent's Hospital Melbourne Research Endowment Fund, 2.

Abstract Number: 2585

A Comparison of Risk of Ovarian Failure Following Intravenous Cyclophosphamide Therapy in Juvenile versus Adult Systemic Lupus Erythematosus

Shefali sharma,[1] Hemanth Chinthala,[2] Siddharth Jain,[2] Arghya Chattopadhyay,[2] Pooja Bahl,[2] Varun Dhir,[3] Naresh Sachdeva,[2] and Surjit Singh[4], [1]Dr., Chandigarh, Chandigarh, India, [2]Post Graduate Institute of Medical Education and Research, chandigarh, Chandigarh, India, [3]Post Graduate Institute of Medical Education and Research, Chandigarh, India, [4]Allergy Immunology Unit, Department pf Pediatrics, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India

SESSION INFORMATION

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Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Premature ovarian failure is a dreaded complication of cyclophosphamide (CYC). It is related to age of initiation of therapy and the cumulative dose. This study was done to evaluate and compare the prevalence of ovarian failure in adult SLE(aSLE) and juvenile SLE(jSLE) post CYC .

Table 1

Hormone (normal range)	Group	Mean level (±SD)	Range	Number of patient's withnormal serum levels (%)
LH (2.4-12.6 mIU/ml)	jSLE (n=14)	3.75 ± 3.86	0.10 – 11.67	8 (57.1%)
	aSLE(n=14)	15.38 ± 26.35	1.38 – 103.00	9 (64.3%)
FSH (3.5-12.5 mIU/ml)	jSLE (n=14)	3.64 ± 1.89	0.75 – 6.85	7 (50%)
	aSLE (n=14)	14.29 ± 37.10	1.41 – 143.00	9 (64.3%)
E2 (12.5 – 166 pg/ml)	jSLE (n=14)	54.08 ± 55.40	5.00 – 179.40	9 (64.3%)
	aSLE (n=14)	117.32 ± 92.18	10.41 – 355.90	10 (71.4%)
AMH (ng/ml)	j SLE (n=14)	2.954 ± 1.57	0.979 – 6.705	14 (100%)
	aSLE (n=14)	2.30 ± 2.91	0.010 – 9.868	13 (92.9%)
Inhibin B	j SLE (n=14)	89.81 ± 122.91	33.33 – 442.03	12 (85.7%)
	aSLE (n=14)	47.47 ± 8.84	35.40 – 66.90	14 (100%)

Ovarian volume	Number	Mean ovarian volume cm^3	Range
jSLE *	11	4.85 ± 3.43	2.09 – 10.99
aSLE**	11	10.10 ± 5.60	2.87 – 18.84
Follicular count	**Number**	**Mean total follicular count**	**Range**
jSLE	7	9.28 ± 4.53	3 – 18
aSLE	8	7.25 ± 3.28	5 – 13

*cSLE ovarian volume was calculated in 11 patients out of 14 patients and three patients had small or streaky ovaries. **aSLE ovarian volume was calculated in 11 patients out of 14 patients and two patients had polycystic ovaries and in one patient ovaries were not visible.

Methods: jSLE and aSLE patients post CYC therapy were enrolled. Their medical records were reviewed and cumulative dose and duration of CYC therapy noted. A detailed menstrual history was sought and serum levels of FSH, LH, E2, AMH, Inhibin and ultrasonography for ovarian volume and follicular count was done between 3-5 days of menstrual cycle.

Results: Twenty eight (14 jSLE, 14 aSLE) patients were included. The mean age was 14.79 ± 4.7 years and 29.07 ± 5.7 years respectively. Mean cumulative dose of CYC was 3996.4 ± 1800 mg in jSLE , and 5235.7 ± 2563.6 mg in aSLE

Among 14 jSLE patients, 12 had not attained menarche when CYC was administered, and all of them subsequently attained menarche (Mean age = 14.78 ± 2.33 years). Two patients in the jSLE group developed menstrual abnormalities: 1 had transient amenorrhea which recovered in 3 monthsof stopping CYC, the other developed persistent oligomenorrhea, although with normal AMH. Among 14 aSLE patients, 11 developed menstrual abnormalities after initiating CYC which recovered to normal in 8 patients. Three patients continued to have oligomenorrhea . Serum levels of FSH, LH, E2, AMH, Inhibin and ultrasound for ovarian volume and follicular count have been summarized in Table 1&2.

Conclusion: There was no delay in attainment of menarche in jSLE patients who received CYC before menarche. None of the patients developed overt ovarian failure in either jSLE or aSL, although persistence of oligomenorrhea was noted in a few patients.

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Abstract Number: 2586

Clinical Characteristics and Survival in Systemic Sclerosis-mixed Connective Tissue Disease and Systemic Sclerosis-overlap Syndrome

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

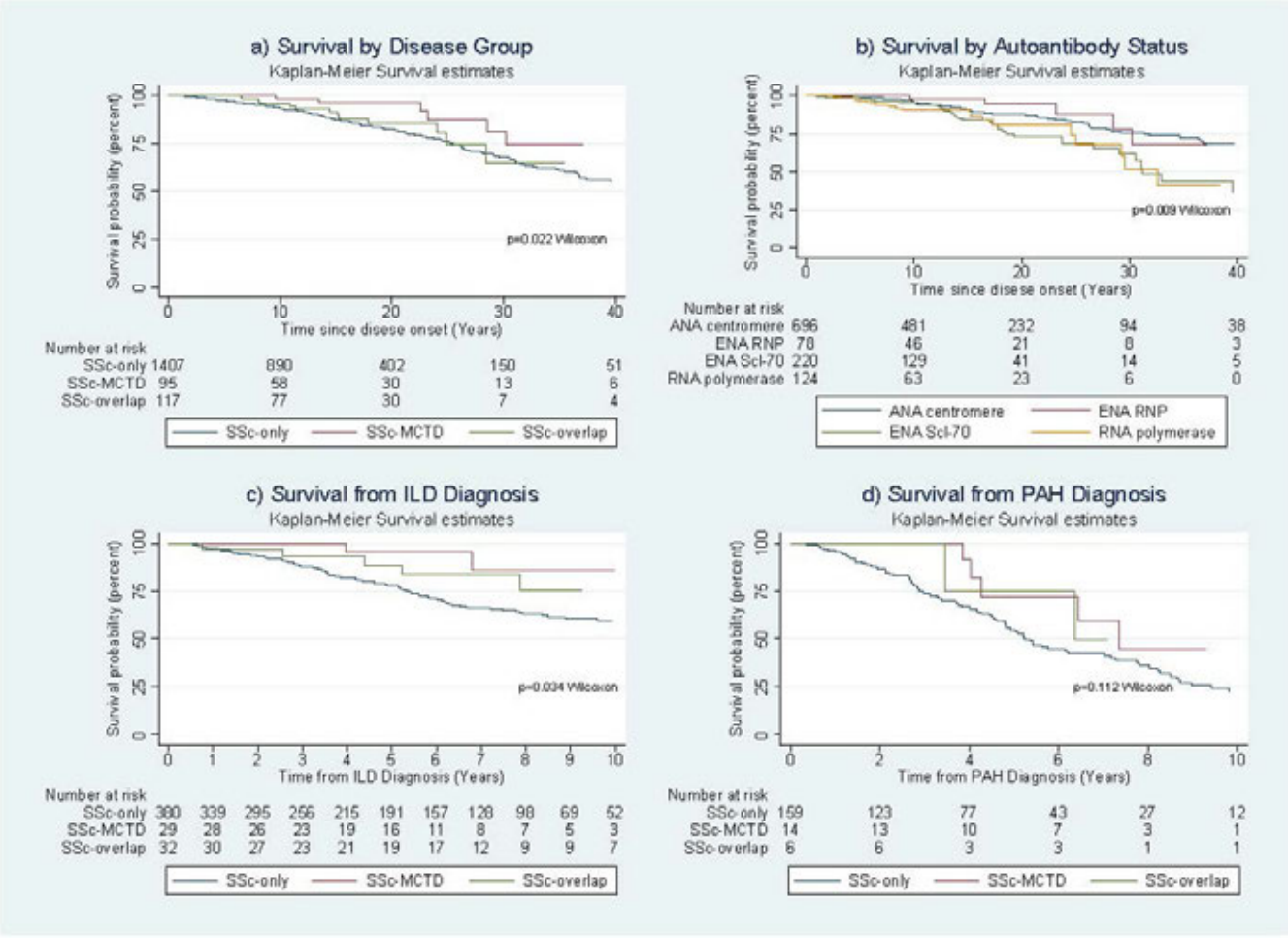

Figure 1. a) Survival by disease group; b) survival by antibody status; c) survival from diagnosis of ILD according to disease group; d) survival from diagnosis of PAH by disease group.

Background/Purpose: Mixed connective tissue disease (MCTD) is defined by presence of anti-RNP antibody together with 3 or more of swollen hands, synovitis, myositis, Raynaud phenomenon or acrosclerosis. Patients who fulfil diagnosis of SSc and have features of other connective tissue diseases are often classified as SSc-overlap. Our study aims to describe the clinical characteristics and outcomes of SSc-MCTD and SSc-overlap.

Methods: We included patients from the Australian Scleroderma Cohort Study (ASCS) who met ACR/EULAR diagnostic criteria for SSc. Three mutually exclusive groups were created: SSc-MCTD, SSc-overlap and SSc-only group (remaining patients). Univariate comparison of clinical features among groups was performed by ANOVA or chi-square. Survival analysis was performed using Kaplan-Meier curves, Wilcoxon test and Cox regression.

Results: Of 1728 patients, 102 (5.9%) had SSc-MCTD and 125 (7.2%) SSc-overlap. Those with MCTD-SSc were more commonly Asian (18.4% vs 9.3% in SSc-overlap and 3.6% in SSc-only, $p< 0.0001$). Those with SSc-MCTD or SSc-overlap were more likely to have limited SSc (81-84% vs. 73.1% for SSc-only). Both SSc-MCTD and SSc-overlap groups were more likely than SSc-only to have numerous positive autoantibodies such as anti-Ro, anti-Jo-1 and anti-Sm. SSc-MCTD and SSc-overlap had similar frequency of interstitial lung disease (ILD), while those with SSc-MCTD had higher frequency of pulmonary arterial hypertension (PAH) (13.7% vs 4.8% in SSc-overlap and 11% in SSc-only, $p=0.0589$). Synovitis and myositis were equally common in SSc-overlap and SSc-MCTD groups. SSc-MCTD or SSc-overlap conferred a higher likelihood of exposure to immunosuppression including prednisolone, synthetic and biologic DMARDs, than SSc-only . Overall survival was better in SSc-MCTD than SSc-overlap or SSc-only (Figure 1 a). However, scleroderma-specific antibodies were also survival prognostic markers, with ANA-centromere or anti-RNP conferring better survival than anti-Scl-70 or anti-RNA polymerase 3 (Figure 1 b). SSc-MCTD and SSc-overlap had lower all-cause mortality following diagnosis of ILD (Figure 1 c) and PAH than patients with SSc-only (Figure 1 d).

Conclusion: This study reveals significant clinical and survival differences between patients with SSc-MCTD, SSc-overlap and SSc-only. Importantly, despite higher frequency of PAH in SSc-MCTD, survival is better in SSc-MCTD and SSc-overlap than in SSc-only patients.

Disclosure: J. Fairley, None; **D. Hansen**, None; **S. Proudman**, Actelion, 2, Boehringer-Ingelheim, 2, 6, Bayer, 2, Corbus, 2, Melrose Health, 9; **J. Sahhar**, None; **G. Ngian**, None; **J. Walker**, None; **G. Strickland**, None; **M. Wilson**, None; **K. Morrisroe**, None; **N. Ferdowski**, None; **G. Major**, None; **J. Roddy**, None; **W. Stevens**, Bayer, 2, BI, 2, Arena, 2, Actelion, 2, Corbus, 2; **M. Nikpour**, Actelion, 2, Arthritis Australia, 2, Australian Rheumatology Association, 2, Bayer, 2, BMS, 2, GSK, 2, Pfizer, 2, Roche, 2, Scleroderma Victoria and Australia, 2, St Vincent's Hospital Melbourne Research Endowment Fund, 2.

Abstract Number: 2587

Prognostic Role of Measurement of Renal Resistive Index in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Spectrum of vascular involvement in systemic sclerosis (SSc) is diverse like Raynaud's phenomenon, digital ulcers, pulmonary hypertension and renal disease. Recognition of markers of subclinical disease is an area of active interest in SSc. This study was undertaken to assess the correlation of renal resistive index (RRI) with both renal and systemic vasculopathic manifestations.

Methods: In this single-centre prospective study, RRI was calculated for consecutive SSc patients classified as per the ACR/EULAR 2013 criteria. Elevated RRI (>0.7) was correlated with renal function (eGFR and proteinuria). RRI was compared with other systemic vasculopathic manifestations like digital ulcers, digital infarcts and pulmonary hypertension.

Results: Seventy three patients (mean age= 41.79 ±10.92) were included. Mean RRI in the right and left renal artery was 0.65 ±0.082 and 0.66±0.075 respectively. Sixteen out of 73 patients (21.9%) had increased RRI (>0.7). A negative correlation was noted between elevated RRI and eGFR (r= -0.958 p=0.026). Patients with significant proteinuria was also higher in the group with elevated RRI (r= 1), although not statistically significant (p=0.164). Similarly, digital ulcers and infarcts/pitting were numerically higher in the group with raised RRI, although statistical significance was not reached (p=0.09 and 0.28 respectively). No correlation of RRI with pulmonary arterial hypertension was identified (r=0.009, p=0.948).

Conclusion: Measurement of RRI holds promise as a tool for assessment of subclinical renal vasculopathy and systemic vasculopathy, and needs to be addressed in larger systematically designed studies with longer follow-up.

Disclosure: s. sharma, None; **A. Chattopadhyay**, None; **s. Jain**, None; **V. Dhir**, None; **m. Prakash**, None; **m. Rathi**, None.

Abstract Number: 2588

Myositis-specific and -associated Antibodies in Systemic Sclerosis: Prevalence and Clinical Associations

Amélie Leurs,[1] Sylvain Dubucquoi,[1] François Machuron,[1] Maité Balden,[1] Florence Renaud,[1] Stéphanie Rogeau,[1] Benjamin Lopez,[2] Marc LAMBERT,[3] Sandrine Morell-Dubois,[4] Hélène Maillard,[4] Hélène Behal,[1] Eric Hachulla,[5] David Launay,[1] and **Vincent Sobanski** [1], [1]CHU Lille, Lille, France, [2]Institute of Immunology, CHU Lille, University of Lille, Lille, France, [3]Lille University Hospital, Lille, France, [4]Department of Internal Medicine and Clinical Immunology, CHU Lille, University of Lille, Lille, France, [5]Dept. of Internal Medicine and Clinical Immunology, Hôpital Claude Huriez, University of Lille, Lille, France, Lille, France

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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Background/Purpose: In systemic sclerosis (SSc) and idiopathic inflammatory myopathies (IIM), auto-antibodies are used in daily practice as potent biomarkers of clinical phenotypes. This study aimed at estimating the prevalence of myositis-specific (MSA) and myositis-associated (MAA) autoantibodies in SSc, and studying their clinical associations.

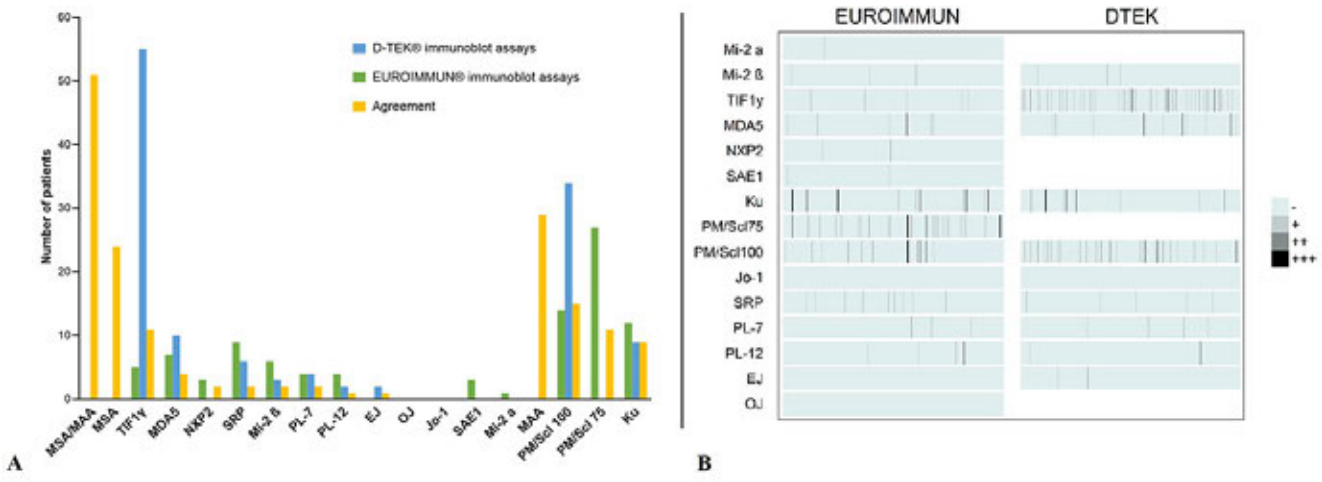

Figure 1. Distribution of patients with positive MSA and MAA in this cross-sectional study of 300 SSc patients. (A) Prevalence of MSA and MAA with EUROLINE, D-TEK immunoblot assays and after agreement. (B) Heatmap of the MSA and MAA immunoblot assay reactivities among patients. EJ: anti-glycyltRNA synthetase; Jo-1: anti-histidyl-tRNA synthetase; Ku: anti-DNA-dependent protein kinase; MAA, myositis associated antibodies; MDA5: anti-melanoma differentiation-associated gene 5; Mi-2: Anti-nuclear helicase/ATPase; MSA, myositis specific antibodies; OJ: anti-isoleucyl-tRNA synthetase; PM/Scl: anti-polymyositis scleroderma antigen; NXP2: anti-nuclear matrix protein 2; PL-7: anti-threonyl-tRNA synthetase; PL-12: anti-alanyl-tRNA synthetase; SRP: anti-signal recognition particle; TIF1γ: anti-transcriptional intermediary factor 1 gamma

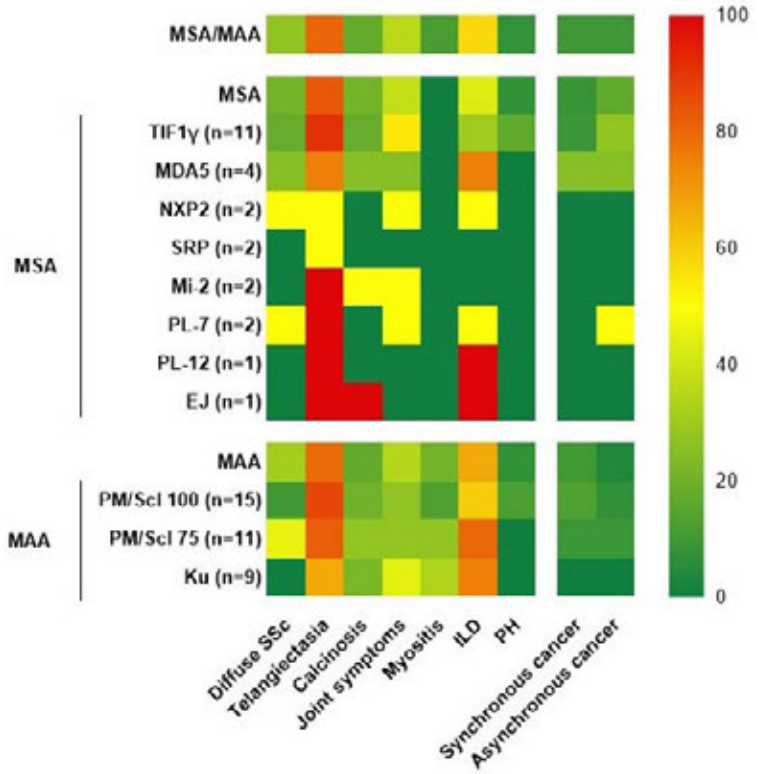

Figure 2. Main characteristics of MSA and MAA positive patients in in this cross-sectional study of 300 SSc patients. EJ: anti-glycyltRNA synthetase; ILD, interstitial lung disease; Jo-1: anti-histidyl-tRNA synthetase; Ku: anti-DNA-dependent protein kinase; MAA, myositis associated antibodies; MDA5: anti-melanoma differentiation-associated gene 5; Mi-2 β: Anti-nuclear helicase/ATPase Béta; MSA, myositis specific antibodies; OJ: anti-isoleucyl-tRNA synthetase; PH, pulmonary hypertension; PM/Scl: anti-polymyositis scleroderma antigen; NXP2: anti-nuclear matrix protein 2; PL-7: anti-threonyl-tRNA synthetase; PL-12: anti-alanyl-tRNA synthetase; SRP: anti-signal recognition particle; TIF1γ: anti-transcriptional intermediary factor 1 gamma.

Methods: We realized a cross-sectional, observational, single-center study. The sera of 300 consecutive patients were tested with myositis antibodies Euroimmun® and D-tek® immunoblot assays to estimate prevalence of MSA and MAA and study their clinical associations.

Results: Prevalence of MSA/MAA, MSA and MAA were 17%, 8.0% and 9.7%, respectively. Anti-PM/Scl 100 were found in 5.0% (95% confidence interval 2.8; 8.1); anti-PM/Scl 75 and anti-TIF1γ in 3.7% (1.8; 6.5); anti-Ku 3.0% (1.4; 5.6); anti-MDA5 in 1.3% (0.4; 3.4); anti-Mi-2β, anti-NXP2, anti-PL7 and anti-SRP in 0.7% (0.08; 2.4); anti-EJ and anti-PL-12 in 0.3% (0.01; 1.8) of patients. No reactivity against SAE1, Jo-1 or OJ was observed (**Figure 1**). Anti-PM/Scl 75 antibodies were associated with interstitial lung disease (80% vs 42%, p = 0.022) and myositis (27% vs 3%, p = 0.005); anti-PM/SCL 100 antibodies were associated with abdominal discomfort (38% vs 8%, p = 0.029); anti-Ku antibodies were associated with myositis (33% vs 3%, p = 0.003). There was a trend towards an association between anti-TIF1γ and cancer (27% vs 8%, p = 0.060) (**Figure 2**).

Conclusion: In this cross-sectional study of 300 SSc patients, the prevalence of MSA/MAA, MSA and MAA were 17%, 8.0% and 9.7%, respectively. MAA positivity was associated with ILD and myositis, but this study did not highlight any clinical associations with MSA positivity.

Disclosure: A. Leurs, None; **S. Dubucquoi**, None; **F. Machuron**, None; **M. Balden**, None; **F. Renaud**, None; **S. Rogeau**, None; **B. Lopez**, None; **M. LAMBERT**, None; **S. Morell-Dubois**, None; **H. Maillard**, None; **H. Behal**, None; **E. Hachulla**, Actelion, 2, 5, Bayer, 2, 5, Chugai Pharma France, 8, GSK, 2, 5, Pfizer, 2, 5, Roche SAS, 5; **D. Launay**, Actelion, 8, GSK, 8, Octapharma, 8, Pfizer, 8, Shire, 8; **V. Sobanski**, Actelion, 8, Grifols, 8, GSK, 8, octapharma, 8, Pfizer, 8, shire, 8.

Abstract Number: 2589

Searching the Calcinosis Signature: A Case Control Study Analyzing Limited Systemic Sclerosis Female Patients with and Without Calcinosis, Paired by Disease Duration, Age and Body Mass Index

Marilia Sampaio-Barros,[1] Lorena Castelo-Branco,[1] Liliam Takayama,[1] Marco Pontes-Filho,[1] Percival Degrava Sampaio-Barros,[2] and **Rosa Pereira** [3], [1]University of Sao Paulo, Sao Paulo, Brazil, [2]Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, BR, Brazil, Sao Paulo, Brazil, [3]Faculdade de Medicina da Universidade de Sao Paulo, São Paulo, Sao Paulo, Brazil

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
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Background/Purpose: Calcinosis usually represents a late manifestation of limited systemic sclerosis (lSSc), inducing chronic calcifications that lead to significant impairment in the quality of life. As an effective treatment for calcinosis in SSc is an unmet need in clinical practice, the identification of risk factors associated with its presence is rather important for the development of therapeutic strategies.

The aim of this study was to compare and analyze clinical aspects and laboratory parameters, including bone metabolism, in female lSSc patients with and without calcinosis, paired by disease duration, age and body mass index (BMI).

Methods: Thirty-six female lSSc patients with calcinosis were compared to 36 female lSSc patients without calcinosis, matched by disease duration, age and BMI. Modified Rodnan skin score (mRSS) was used to determine

the extension of the skin involvement. Organ involvement, autoantibodies, bone mineral density (BMD) by DXA and laboratory parameters were analyzed. The past and current treatment modalities were also questioned. Statistical significance was considered if $p< 0.05$.

Results: Esophageal hypomotility, digital ulcers and interstitial lung disease were the most frequent clinical manifestations of lSSc patients, present in similar frequency in both groups. In univariate analysis, calcinosis was significantly associated with acroosteolysis (69% vs. 22%, $p< 0.001$), higher modified mRSS (4.28±4.66 vs 1.17±2.50, $p< 0.001$), higher 25OH vitamin D (24.46±8.15 vs. 20.80±6.60ng/ml, $p=0.040$) and phosphorus serum levels (3.81±0.41 vs. 3.43±0.45mg/dl; $p< 0.001$). Antinuclear antibodies (ANA) was positive in 89% in both groups. Anticentromere antibody was frequent (44% and 31%), while positive anti-Scl70 was rare in both groups. Regarding treatment, current use of glucocorticoid was lower in patients with calcinosis compared to patients without calcinosis (8% vs. 28%; $p=0.032$). Osteoporosis was more frequent in the group with calcinosis (31% vs.17%), although not statistically significant. Multivariate analysis confirmed and quantified the risk for calcinosis: acroosteolysis (OR=12.04; 95% CI:2.73-53.04; $p=0.001$), mRSS (OR=1.37; 95% CI:1.11-1.69; $p=0.003$), phosphorus serum levels (OR=5.07; 95% CI:1.06-24.23; $p=0.042$), and lower glucocorticoid use (OR=0.07; 95% CI:0.007-0.66; $p=0.021$).

Conclusion: This study showed that lSSc patients with calcinosis present a distinct clinic and biochemical profile, characterized by acroosteolysis, higher mRSS score, higher serum levels of phosphorus and lower glucocorticoid use, when compared to a matched group without calcinosis, paired by disease duration, age, and BMI.

Disclosure: M. Sampaio-Barros, None; **L. Castelo-Branco**, None; **L. Takayama**, None; **M. Pontes-Filho**, None; **P. Sampaio-Barros**, None; **R. Pereira**, None.

Abstract Number: 2590

Computer Vision Applied to Dual Energy Computed Tomography Images for Precise Calcinosis Cutis Quantification in Patients with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Calcinosis cutis, found in both systemic sclerosis (SSc) and juvenile dermatomyositis patients, can be extensive and debilitating. Potential treatments have been identified, but a standardized and validated method for precise and accurate whole-body calcinosis cutis burden quantification is necessary to allow for valid clinical trials. Dual energy computed tomography (DECT) can differentiate between calcinosis cutis and healthy bone, but a radiologist must manually quantify the irregularly shaped lesions, which is time-consuming and costly. Computer vision, including convolutional neural network (CNN) algorithms, has been increasingly applied to solve problems in clinical medicine with success. The aim of this study is to optimize a CNN algorithm to facilitate quantification of calcinosis cutis disease burden.

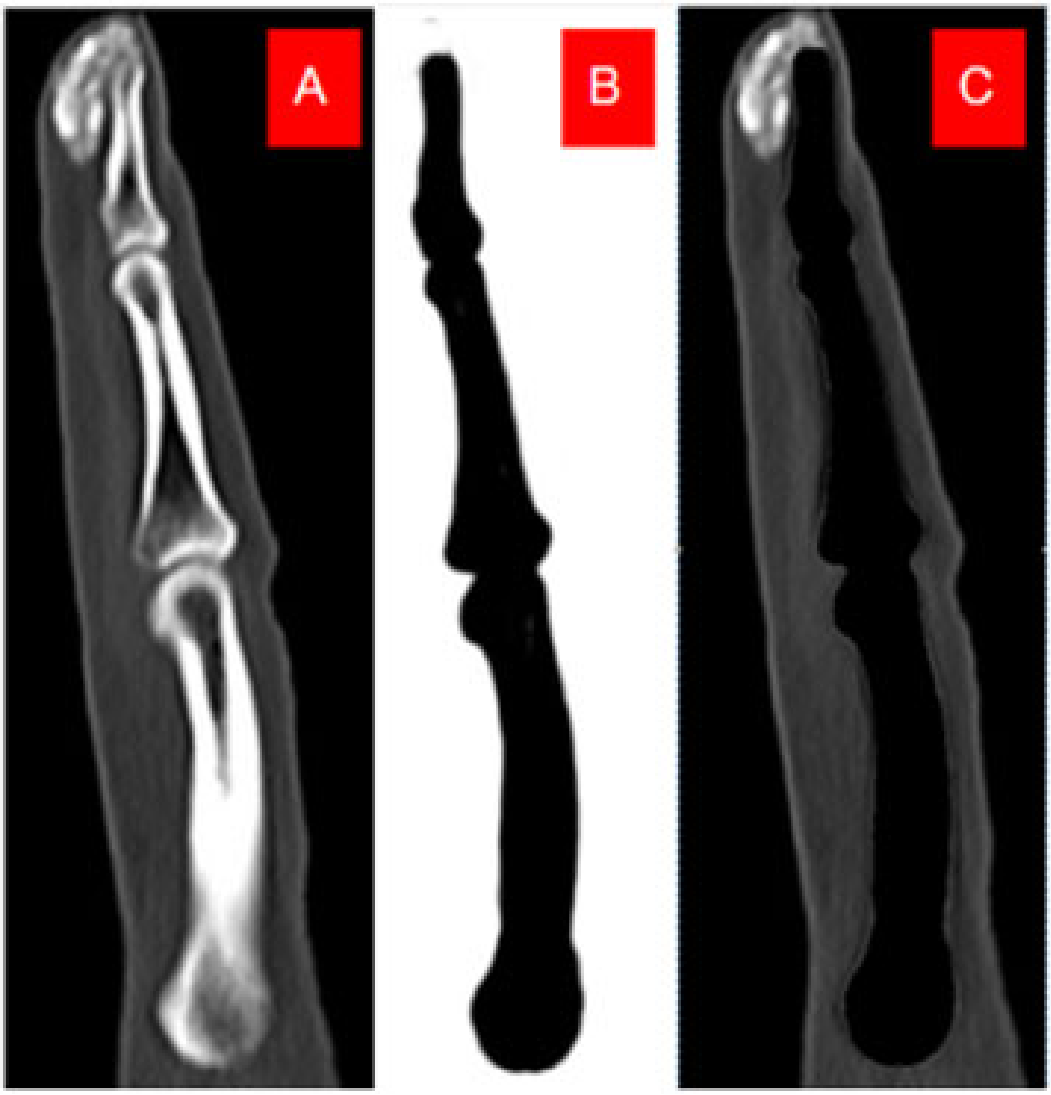
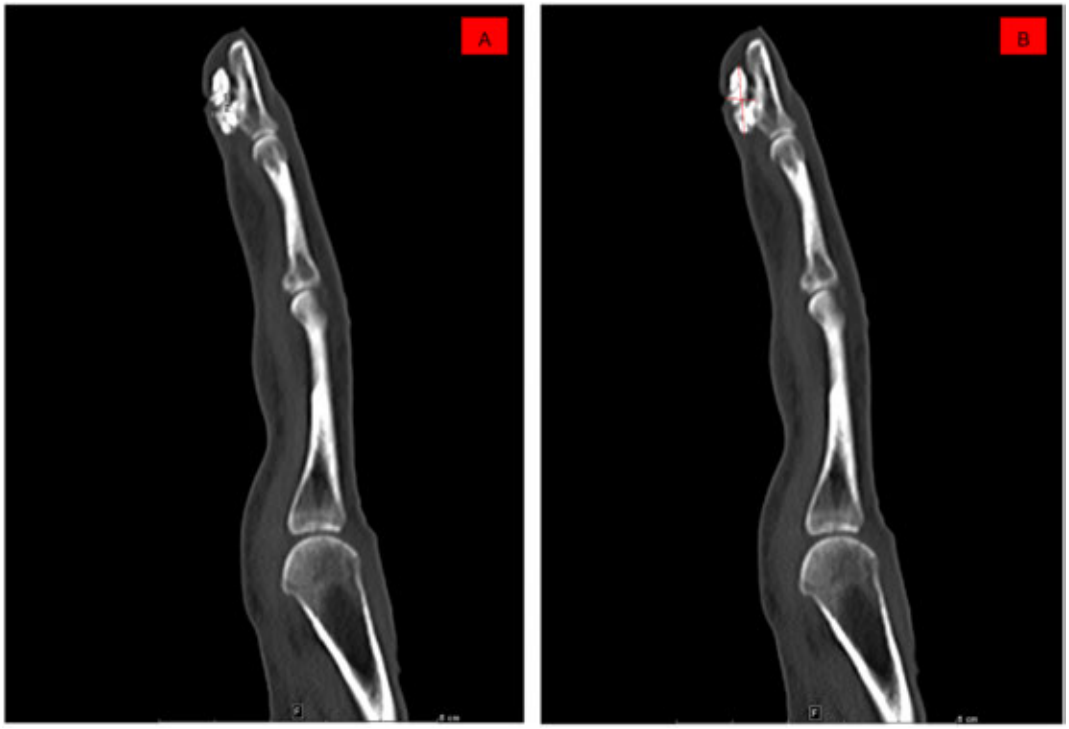


Image 1A. Representative 2D DECT hand image from a patient with SSc Image 1B: Segmented healthy finger bone Image 1C: Highlighted calcinosis cutis lesion, identified by subtracting normal finger bone from the overall image, emphasizing the area of dystrophic calcium

Methods: De-identified 2-dimensional (2-D) DECT images from patients with SSc, with clinically apparent calcinosis cutis, were obtained. An expert musculoskeletal radiologist manually segmented the three forefinger phalanges to serve as the gold standard comparison. Computer scientists then trained and tested the CNN algorithm for finger bone segmentation. After reliable finger bone segmentation was achieved, the area of a calcinosis cutis lesion was measured and compared to measurements performed by a radiologist to test the utility of the CNN approach.

Results: Thirty 2D DECT hand images from patients with SSc were used to identify the most appropriate CNN algorithm for finger bone segmentation (Image 1A, representative image). The U-net CNN algorithm demonstrated superior performance. 500 epochs were necessary to adequately segment healthy finger bones from adjacent dystrophic calcifications (Image 1B). Calcinosis cutis lesions were then identified by subtracting normal finger bones from the image to permit the computer to “see” the dystrophic calcium lesions (Image 1C). When measured by a radiologist, the length x width of the lesion was used to calculate the 2-D area, assuming a relatively smooth lesion contour (Image 2A), whereas the CNN-calculated 2-D area utilized pixel intensities (Image 2B).



A demonstrates a radiologist-measured calcinosis cutis lesion, using the length x width of the lesion and assuming a relatively smooth contour, while B demonstrates the same lesion measured by the CNN algorithm, utilizing pixel intensities.

Conclusion: To our knowledge, the present study is the first to apply computer vision to the challenge of calcinosis cutis quantification. We demonstrate that CNN algorithms applied to DECT hand images of SSc patients can be used to differentiate calcinosis cutis lesions from adjacent healthy bone. When compared to the gold standard of radiologist review, CNN algorithms take into account lesion irregularity, which may allow for more precise measurements.

Disclosure: A. Chandrasekaran, None; **I. Omar**, None; **Z. Fu**, None; **S. Ren**, None; **M. Hinchcliff**, None.

Abstract Number: 2591

Hospitalization Among Incident Cases of Systemic Sclerosis: Results from a Population-based Cohort (1980-2016)

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is an autoimmune disorder associated with multi-organ dysfunction, requiring long-term and multi-disciplinary care. Few studies have estimated the healthcare resource usage of patients with SSc. The purpose of this study was to compare hospitalization among incident cases of SSc vs age- and sex-matched comparators.

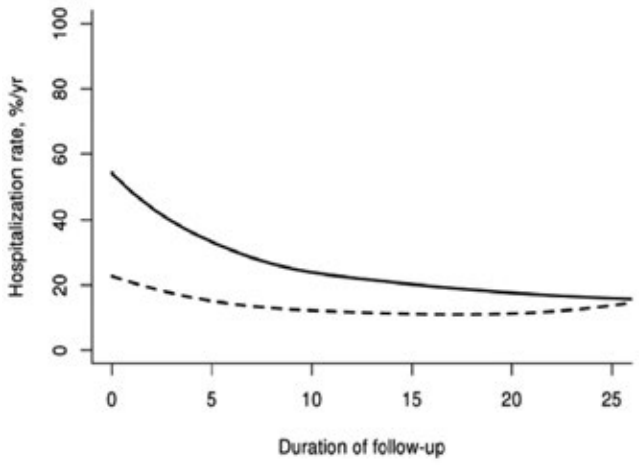
Methods: A retrospective, population-based cohort of physician-diagnosed patients with SSc in a geographically well-defined area from Jan 1, 1980 to Dec 31, 2016 was identified and utilized for this study. A 2:1 cohort of age- and sex-matched non-SSc subjects from the same population was randomly selected for comparison. Patients who died or emigrated from the area prior to 1987 were excluded. Patients were followed until death, migration from the geographic area or Sep 30, 2018. All hospitalizations in the geographic area from Jan 1, 1987 to Sep 30, 2018 were obtained. Primary discharge diagnosis information was available for hospitalizations in 1995 to present. Readmission was defined as occurring within 30 days of a discharge. Rates of hospitalization of cases and comparators were analyzed using person-year methods and rate ratios. Length of stay was analyzed using generalized linear models adjusted for age, sex and calendar year, with random intercepts to account for multiple hospitalizations per patient.

Results: The cohort included 76 incident SSc cases and 155 non-SSc comparators (mean age of 56 ± 16 years at diagnosis/index, both 91% female). Mean length of follow-up was 11.5 (SD 8.5) years for SSc subjects and 13.3 (SD 8.6) years for comparators. Rates of hospitalization among cases and comparators were 31.9 and 17.9 per 100 person-years, respectively (rate ratio [RR]:1.78; 95% confidence interval (CI):1.52-2.08)(Table). By sex, men (RR:4.33;

Table. Hospitalization rates in patients with and without SSc overall and by sex

Group	Cohort	Number of hospitalizations	Person-years of follow-up	Rate per 100py	Rate Ratio (95% CI)
Overall	SSc	278	872.4	31.9	1.78 (1.52, 2.08)
	Non-SSc	369	2062.7	17.9	
Women	SSc	239	813.4	29.4	1.63 (1.38, 1.92)
	Non-SSc	349	1929.9	18.1	
Men	SSc	39	59.1	66.0	4.33 (2.58, 7.60)
	Non-SSc	20	132.8	15.1	

Figure. Age- and sex- adjusted hospitalization rates among SSc patients (solid line) and non-SSc comparators (dashed line) according to disease duration



95%CI:2.58-7.60) and women (RR:1.63; 95%CI:1.38-1.92) with SSc had substantially higher hospitalization rates than comparators.

Hospitalization rates were higher in SSc compared with non-SSc subjects during the first 5 years after SSc diagnosis (RR: 2.16; 95%CI:1.70-2.74). This difference decreased over time and was no longer significant for ≥15 years after SSc incidence/index (Figure). Patients age 65+ were more frequently hospitalized than younger subjects in both SSc and comparator groups, and the difference in hospitalization rates between groups was largest in those age < 50 years (RR: 2.54: 95% CI: 1.73-3.75).

SSc subjects were more frequently hospitalized for infections and diseases involving circulatory, digestive, and respiratory systems than comparators, with ratios ranging from 1.96 to 3.90. Lengths of stay (median (IQR) 4 (2-6) vs 3(2-6); p=0.52) and readmission rates (25% vs 23%; p=0.51) were similar among cases and comparators.

Conclusion: A higher frequency of hospitalization occurred among patients with SSc compared to non-SSc subjects, indicating high inpatient care needs in this population. Hospitalization rates were highest among SSc subjects during the first 5 years of SSc diagnosis. Hospitalization rates approached those of non-SSc comparators over time after diagnosis, possibly due to confounding by age and other comorbidities.

Disclosure: C. Coffey, None; **A. Sandhu**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **S. Achenbach**, None; **E. Matteson**, Boehringer Ingelheim, 5, Pfizer, 2, Sun Pharmaceuticals, 2; **T. Osborn**, None; **K. Warrington**, Eli Lilly, 2, GlaxoSmith-Kline, 2, roche, 2, 8, Roche, 2, 5, 8, Sanofi, 5, sanofi, 5; **A. Makol**, None.

Abstract Number: 2592

Longitudinal Changes in Health-related Quality of Life in Systemic Sclerosis Treated with Autologous Hematopoietic Stem Cell Transplant Compared to Standard of Care

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In severe, early progressive systemic sclerosis (SSc), autologous hematopoietic stem cell transplantation (AHSCT) allows significant improvements in overall and event free survival. The objectives of this study were to quantify the magnitude, domains and duration of improvement in HRQoL in SSc subjects treated with AHSCT compared to standard of care in the setting of routine clinical care.

Methods: We compared SSc patients treated with AHSCT to SSc patients who fulfilled ASTIS eligibility criteria for AHSCT but who were treated with standard of care. Outcomes of interest were the Health Assessment Questionnaire

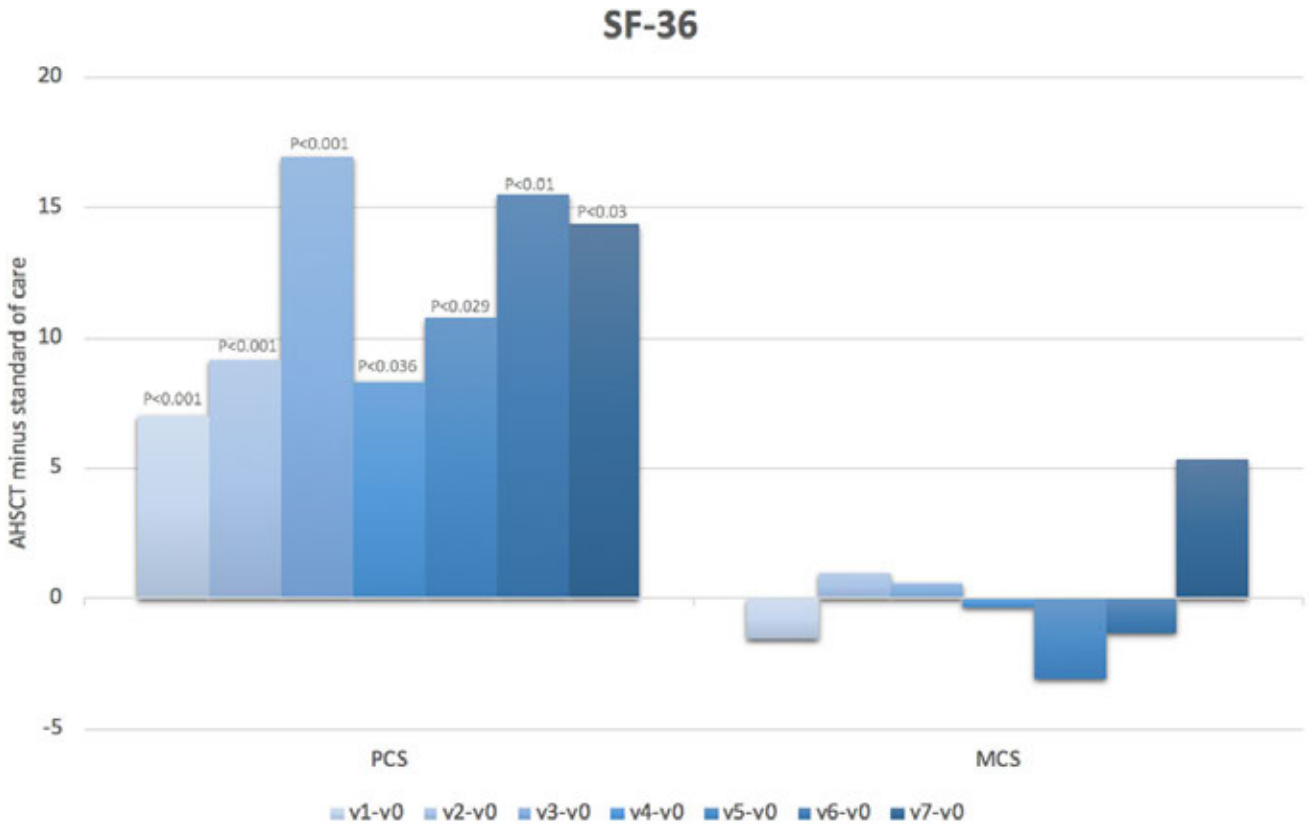

Figure 1. SF-36 Physical and Mental Component Summary Scores. X axis shows differences in scores between follow up study visits and baseline. Y axis shows the differences in scores between subjects treated with AHSCT versus those treated with standard of care.

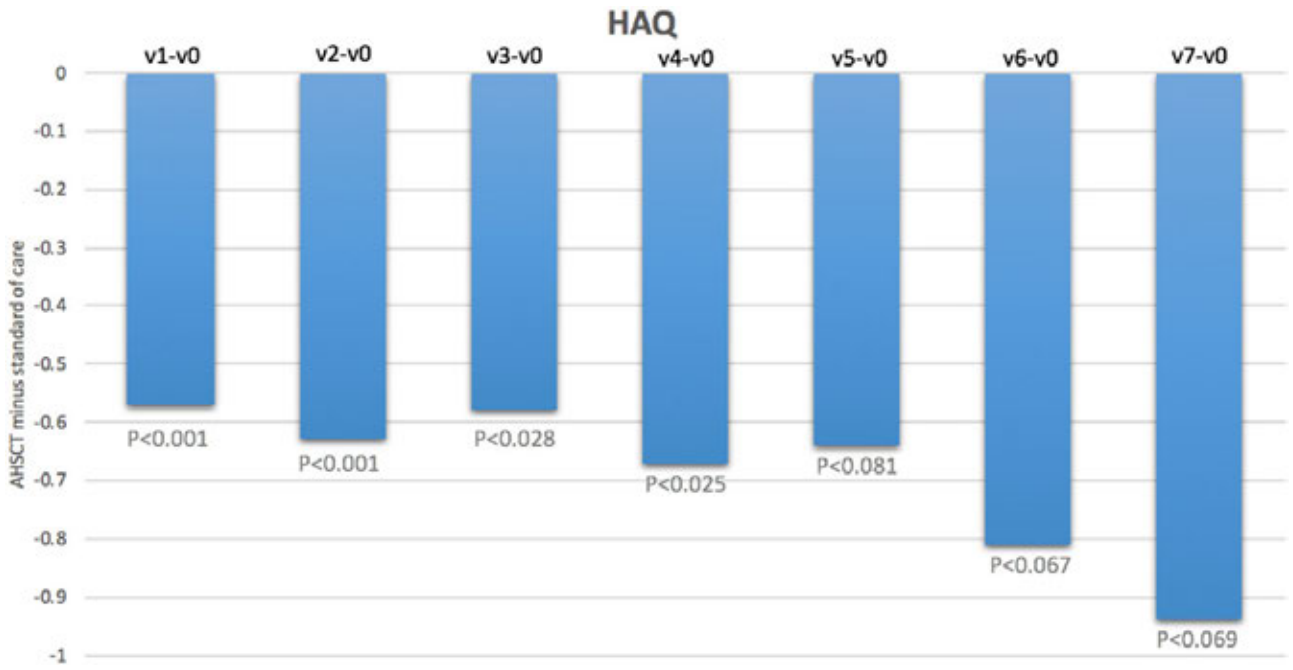

Figure 2. Health Assessment Questionnaire (HAQ) scores. X axis shows differences in scores between follow up study visits and baseline. Y axis shows the differences in scores between subjects treated with AHSCT versus those treated with standard of care.

(HAQ) and its disease-specific visual analogue scales (VAS), and the Short Form Health Survey-36 (SF-36) Physical Component Summary (PCS) and Mental Component Summary (MCS) scores. Differences in HAQ, VAS and SF-36 scores were compared using linear models, adjusting for baseline scores and inverse probability of treatment weights

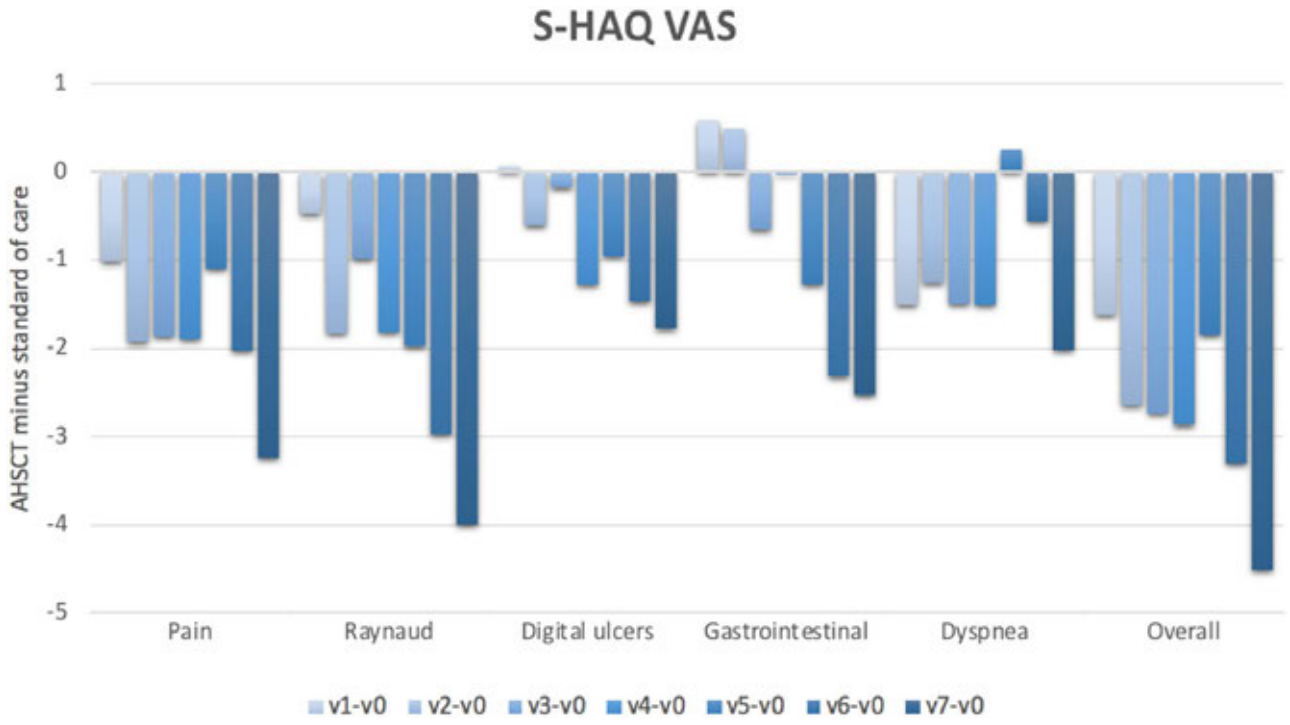

Figure 3. Scleroderma-Health Assessment Questionnaire Visual Analogue Scales (S-HAQ VAS). X axis shows differences in scores between follow up study visits and baseline. Y axis shows the differences in scores between subjects treated with AHSCT versus those treated with standard of care.

(iptw), calculated as 1/propensity score (ps) for the AHSCT subjects and 1/(1-ps) for the standard of care subjects. Propensity scores were estimated using logistic regression including the following covariates: female, age, disease duration, and other variables with a p-value < 0.10 in univariate comparisons. In addition, to account for the potential informative censoring between baseline and follow-up visits, the inverse probability of censoring weights (ipcw) was estimated by logistic regression, using the same covariates as in the propensity score model. The outcome model was a marginal linear model including only AHSCT, weighted by the product of the iptw and ipcw.

Results: We included 41 subjects who underwent AHSCT (66% female, mean age 44.7 years, mean disease duration 2.6 years, mean modified Rodnan skin score (mRss) 25, interstitial lung disease (ILD) present in 93%, FVC %predicted 79% and DLCO %predicted 55%) and 69 subjects treated with standard of care (78% female, mean age 53.9 years, mean disease duration 1.5 years, mean mRss 27, ILD 47%, FVC %predicted 84% and DLCO %predicted 64%). Baseline HAQ scores were 1.4$\pm$0.7 in both groups. Baseline SF-36 PCS and MCS scores were 33.4 and 30.1, and 41.8 and 46.2, respectively, in the AHSCT and standard of care subjects. At baseline, the most severely affected VAS scale was that of general health. On a scale of 0-10, the mean was 4.9 in the AHSCT subjects and 5.1 in the standard of care subjects. In marginal linear weighted models, HAQ, VAS and SF-36 PCS scores were significantly better in subjects treated with AHSCT compared to standard of care, and the differences largely surpassed minimal clinically important differences (Figures 1-3). These differences also increased over time. However, there were no differences in SF-36 MCS scores in subjects treated with AHSCT compared to standard of care.

Conclusion: AHSCT was associated with marked improvement in physical HRQoL compared to standard of care, and the improvement was sustained and increased over time. This adds considerable complementary data to traditional biomedical outcome measures to support the role of AHSCT in severe SSc. Further research will be needed to understand why there is no difference in mental HRQoL after AHSCT compared to standard of care.

Disclosure: N. Maltez, None; **M. Puyade**, None; **P. Lansiaux**, None; **M. Wang**, None; **M. Baron**, None; **I. Colmegna**, None; **D. Farge**, None; **M. Hudson**, None.

Abstract Number: 2593

Cyclophosphamide for the Treatment of Skin Fibrosis in Systemic Sclerosis: A Systematic Review

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a chronic disease characterized by multi-organ involvement. Excess collagen deposition and fibrosis is thought to result from a complex interplay between vasculopathy and inflammation. Skin fibrosis, and its extent, is a cardinal feature of SSc, and permits its classification in diffuse and limited subsets. Evidence for the pharmacologic management of skin involvement is limited and there is a need for further clinical guidance. Cyclophosphamide is an alkylating agent with potent immunomodulating effects, commonly used in rheumatic diseases. The objective of this systematic review was to assess the efficacy of Cyclophosphamide in the treatment of skin fibrosis in patients with SSc.

Methods: Embase, MEDLINE and Cochrane Central Register of Controlled Trials were searched for all randomized control trials (RCTs), quasi-randomized studies, case-control studies, controlled before-after studies, prospective and retrospective cohort studies, case series and cross-sectional studies on February 7, 2019. Case reports were excluded. The Health Canada registry, clinicaltrials.gov, the ISRCTN registry, and the World Health Organization (WHO) international clinical trials registry were searched for grey literature. Studies pertaining to patients with a diagnosis of SSc were included with no limitation on specific classification criteria. The main intervention of interest was Cyclophosphamide with no limitation of regimens or route of administration. Comparators were other standard disease modifying agents or placebo. The outcome of interest was extent of skin fibrosis defined by the modified Rodnan skin score (mRss). Two review authors completed independent and duplicate abstract and full text screening. Data extraction and quality appraisal were completed independently by two review authors. Meta-analysis was performed for the primary outcome (mRSS) through random-effects models.

Results: Thirty-one studies conducted between 1994 and 2018 were included: 11 RCTs, 13 case series, 4 retrospective cohort studies and 3 prospective cohort studies. The majority of the 11 RCTs showed some concerns in regards to risk of bias. After 12 months of treatment with Cyclophosphamide, mean mRSS decreased 6.30 points (95% CI, 4.95 to 7.64). The effect remained significant when pooling both 6- and 12-month outcomes – mRSS decreased 4.11 points (95% CI, 0.97, 7.25). Heterogeneity of comparators, use of steroids, and outcome endpoints did not allow for subgroup analyses to be completed as planned.

Conclusion: Statistically and clinically significant improvements in mRSS with administration of Cyclophosphamide were demonstrated in patients with SSc. The effect was greater at 12 months of follow-up. The lack of consistent standard of care for the treatment of skin fibrosis in SSc was highlighted by the variability in the type and duration of comparator treatments used in clinical trials. Although the use of Cyclophosphamide for skin fibrosis in SSc is justified by these results, there is a need for more consistent recommendations regarding treatment regimens, and longer clinical follow-up to better understand the role of immunosuppression as a treatment for this disease manifestation.

Disclosure: M. Hudson, None; **N. Maltez**, None; **C. Ivory**, None; **M. Demery-Varin**, None.

Abstract Number: 2594

Associations Between Antibodies to the Angiotensin II Type 1 Receptor and Endothelian-1 Type a Receptor and the Incidence of Vascular Complications in Early Diffuse Systemic Sclerosis

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Table 1: Baseline Characteristics in Early Diffuse SSc Patients

	Overall cohort	ETAR negative N=38	ETAR positive N=18	p-value	AT1R negative N=39	AT1R positive N=17	p-value
Median age (years)							
At diagnosis	53 (STD 14)						
At first visit	53 (STD 15)	55	50	0.22	55	50	0.23
Female	64%	27	9	0.15	26	10	0.76
Caucasian	91%	36	15	0.31	36	15	0.63
Median disease duration at first visit (years)	0.76 (IQR 0.52, 1.32)	0.78 (0.57, 1.26)	0.81 (0.42, 1.49)	0.9	0.79 (0.56, 1.31)	0.64 (0.42, 1.38)	0.36
Active smoker at first visit	13%	5	2	1.00	5	2	1.00
Complications of SSc at first visit							
fibrosis	39%	10	6	0.49	11	5	0.72
ILD	41%	13	7	1.00	14	6	1.00
Renal crisis	4%	2	0	1.00	2	0	1.00
Digital pitting	27%	9	6	0.52	10	5	0.75
Digital ulceration	5%	2	1	1.00	2	1	1.00
Digital gangrene	32%	17	1	0.32	16	1	0.30
PAH	0%	0	0	--	0	0	--
PH	4%	2	0	1.00	2	0	1.00
Scl70 Positive	21%	4	7	0.04	7	4	0.44
Vascular severity score at first visit				0.32			0.45
Absent	21%	8	4		8	4	
Mild	50%	21	7		21	7	
Moderate	23%	7	6		8	5	
Severe	4%	2	0		2	0	
End stage	2%	0	1		0	1	
Comorbidities							
Diabetes	7%	4	0	0.29	4	0	0.30
Hypertension	21%	8	4	1.00	9	3	0.73
Hyperlipidemia	25%	11	3	0.51	11	3	0.51
CAD	7%	2	2	0.59	3	1	1.00

Table 2. Incidence of Vascular Complications Stratified by Autoantibody Status in Diffuse SSc						
	ETAR negative N=38	ETAR positive N=18	p-value	AT1R negative N=39	AT1R positive N=17	p-value
Renal crisis	4	1	0.65	4	1	1.00
Digital pitting	3	2	0.65	2	3	0.14
Digital ulceration	8	3	1.00	8	3	1.00
Digital gangrene	0	2	0.10	1	1	0.5
PAH	2	1	1.00	3	0	0.54
PH	2	2	0.60	3	1	1.00

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Recently, the hypothesis that autoantibodies to the angiotensin II type 1 (AT1R) and endothelian-1 type A (ETAR) receptors are driving the vascular injury and fibrosis in systemic sclerosis (SSc) has gained support from both clinical and basic science research. Cross sectional studies show levels of AT1R and ETAR are associated with increased risk of pulmonary arterial hypertension (PAH), scleroderma renal crisis (SRC) and digital ulcers (DU). Exposure to immunoglobulins from patients with AT1R and ETAR antibodies directly inhibits angiotensin converting enzyme-2 activity and both antibodies induce fibrotic and vasoconstrictive cellular signaling. We hypothesized that the presence of AT1R and ETAR would be associated with the development of vascular complications in an observational cohort of very early diffuse SSc patients followed from their first SSc Center visit.

Methods: Patients with early stage diffuse cutaneous SSc (< 2 years of disease) who were consented to a prospective, observational cohort study at their first visit between 1/1/2009 and 5/15/2014 were included. Patients were followed for at least 5 years with vascular complications noted at each visit, specifically digital pitting, digital ulceration, digital gangrene, SRCand PAH. SSc-associated antibodies were run by immunoprecipitation and immunodiffusion. ELISA assays of AT1R and ETAR (Cell Trend GmbH) were performed on serum samples obtained at the time of first visit. SAS 9.4 (Cary, NC) was used for statistical analysis.

Results: 56 patients were seen over a period of 5 to 10 years with a median of 7 follow-up visits (IQR 2, 11.5). Baseline characteristics are in Table 1. There was no difference in rates of vascular complications at baseline in those positive for ETAR and AT1R antibodies (Table 1). There was no difference in incidence of vascular complications, although digital gangrene approached statistical significance in ETAR positive patients (Table 2). There was a significantly higher frequency of ETAR antibodies in Scl-70 positive patients which is consistent with prior studies.

Conclusion: To our knowledge, this is the first study to use a inception cohort of early diffuse SSc to evaluate for an association between AT1R and ETAR antibody positivity and incident vascular complications. The lack of association between presence of AT1R or ETAR antibodies and either early or new development of vascular complications in early diffuse SSc does not support the hypothesis that the vascular injury that characterize SSc is due to functional AT1R

or ETAR antibodies nor support utilizing these autoantibodies as prognostic markers for the development vascular complications.

Disclosure: K. Downer, None; **R. Domsic**, Boehringer Ingelheim, 5, Boehringer-Ingelheim, 5, Eicos, 5, EICOS Sciences Inc, 5; **C. Bentlejewski**, None; **A. Zeevi**, None; **L. Zhu**, None.

Abstract Number: 2595

Asymptomatic Scleroderma Antibody Positivity and Progression to Systemic Sclerosis

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Background/Purpose: Systemic sclerosis is an autoimmune disease characterized by inflammation, vasculopathy and fibrosis of the skin, vasculature and internal organs along with disease specific autoantibody formation. Patients are subtyped as limited or diffuse scleroderma based on extent of skin involvement and autoantibody profile. Recent retrospective studies have shown that autoantibodies may precede a clinical diagnosis of scleroderma by several years. However, some individuals with scleroderma specific autoantibodies and no symptoms never progress to a clinical diagnosis of scleroderma. The purpose of this study is to investigate the characteristics of asymptomatic scleroderma antibody positive (ASAP) individuals in a longitudinal biorepository.

Methods: All subjects gave written informed consent for longitudinal collection of their data. Data is collected on demographics, baseline disease phenotype, baseline disease activity scores including modified Rodnan skin score (mRSS), scleroderma health assessment questionnaire disability index (HAQ-DI), gastrointestinal score, physician global assessment and Medsger severity score. Data were analyzed using GraphPad Prism (version 7.0).

Results: At the time of data-lock, there were 90 patients with data available for analysis. At the baseline visit, 41 fulfilled ACR criteria for limited scleroderma, 19 met criteria for diffuse scleroderma, and 30 patients were in the ASAP group. There were no statistically significant differences in age, gender or race in the limited, diffuse of ASAP patients. Patients with limited scleroderma were more commonly centromere antibody positive (p 0.0031). As expected, baseline mRSS was significantly higher in the diffuse scleroderma subset. Over a mean follow up of 1.27 years, patients in the ASAP group demonstrated no significant change in mRSS indicating lack of progression of disease.

Conclusion: The current study investigated a cohort of asymptomatic scleroderma antibody positive individuals enrolled in the STOP scleroderma biorepository who do not exhibit diagnostic criteria for scleroderma at baseline and did not demonstrate progression to clinically diagnosable scleroderma. This cohort of patients with autoantibody positivity but no progression of disease is of interest to investigate molecular biomarkers of non-progression in patients with scleroderma specific antibody positivity.

Disclosure: D. Jones, None; **M. Mangini**, None; **S. Wearing**, None; **V. Shanmugam**, AbbVie, 2.

Abstract Number: 2596

The Contribution of Left Heart Disease in Patients with Systemic Sclerosis-associated Pulmonary Hypertension Having Normal Pulmonary Artery Wedge Pressure

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic sclerosis (SSc) complicates variety of cardiopulmonary diseases which can result in pulmonary hypertension (PH). The types of PH are usually classified by the result of right heart catheterization (RHC) based on values of mean pulmonary arterial pressure (mPAP), pulmonary artery wedge pressure (PAWP), and pulmonary vascular resistance (PVR): Group 1 as mPAP >20mmHg, PAWP ≤15mmHg, and PVR ≥3WU; Group 2 as mPAP >20mmHg, PAWP >15mmHg, and PVR < 3WU. However, by this classification, patients with PH having normal PAWP (≤15mmHg) and normal PVR (< 3 WU) are categorized as neither Group 1 PH nor Group 2 PH and have a possible contribution of left heart disease (LHD). We therefore examined whether LHD is contributing among SSc-PH patients with such RHC results.

Methods: We retrospectively investigated 43 patients with SSc who were diagnosed as PH by RHC from 2006 through 2018 at our University hospital. Nice classification updated in 2018 was used in the diagnosis and classification of PH. To identify lesions responsible for PH, inspections with cardiac echocardiography, cardiac MRI, and myocardial scintigraphy were conducted.

Results: The mean age of the enrolled 43 patients was 66 (11) year-old, 88% of them were female. Twenty-one percent of the patients had diffuse cutaneous SSc. Mean follow-up periods were 56 (33) months. Of the 43, 17 (40%) of the patients had severe interstitial lung disease with % forced vital capacity ≤70% (Group 3). Among the rest of 26 patients, 5 (19%) had PAWP >15mmHg (Group 2). Of the remaining 21 patients, only 10 patients (48%) had PVR ≥3 WU and was classified as Group 1 and another 11 had PAWP ≤15mmHg and PVR < 3WU. Among them, 9 patients (82%) showed less than 7 of diastolic pressure gradient obtained from RHC, indicating the presence of postcapillary PH. Among them, 6 patients (55%) had an elevation of E/e' and/or left atrial volume index (LAVI), suggesting left diastolic dysfunction by cardiac echocardiography. Myocardial damage was detected by cardiac MRI [n = 6 (55%)] or myocardial scintigraphy [n = 6 (55%)]. Based on the results, 5 patients were diagnosed as precapillary PH and another 5 as postcapillary PH in addition to 5 with PAWP >15mmHg [in total, 10 / 43 (23%) with SSc-PH had LHD-associated PH]. The diagnosis was undetermined in one patient who had mixed characteristics of pre- and postcapillary PH. Pulmonary vasodilators were introduced in 5 patients who were clinically diagnosed as precapillary PH while diuretics and/or antihypertensive drugs were introduced in another 4 diagnosed as postcapillary PH. One patient died from PAH during the mean follow-up.

Conclusion: Since significant number of patients may have LHD, particularly diastolic dysfunction-associated PH even among SSc patients with normal PAWP as well as those with PAWP >15mmHg, careful diagnosis and therapeutic intervention with pulmonary vasodilator are required in this patient population. Longitudinal follow up will be needed to study the impact of the LHD on the survival.

Disclosure: Y. Yamasaki, None; **K. Suzuki**, None; **K. Sakurai**, None; **Y. Asari**, None; **H. Yamada**, None; **K. Kawahata**, None.

Abstract Number: 2597

Prevalence and Clinical Associations of Degos Lesions in Systemic Sclerosis

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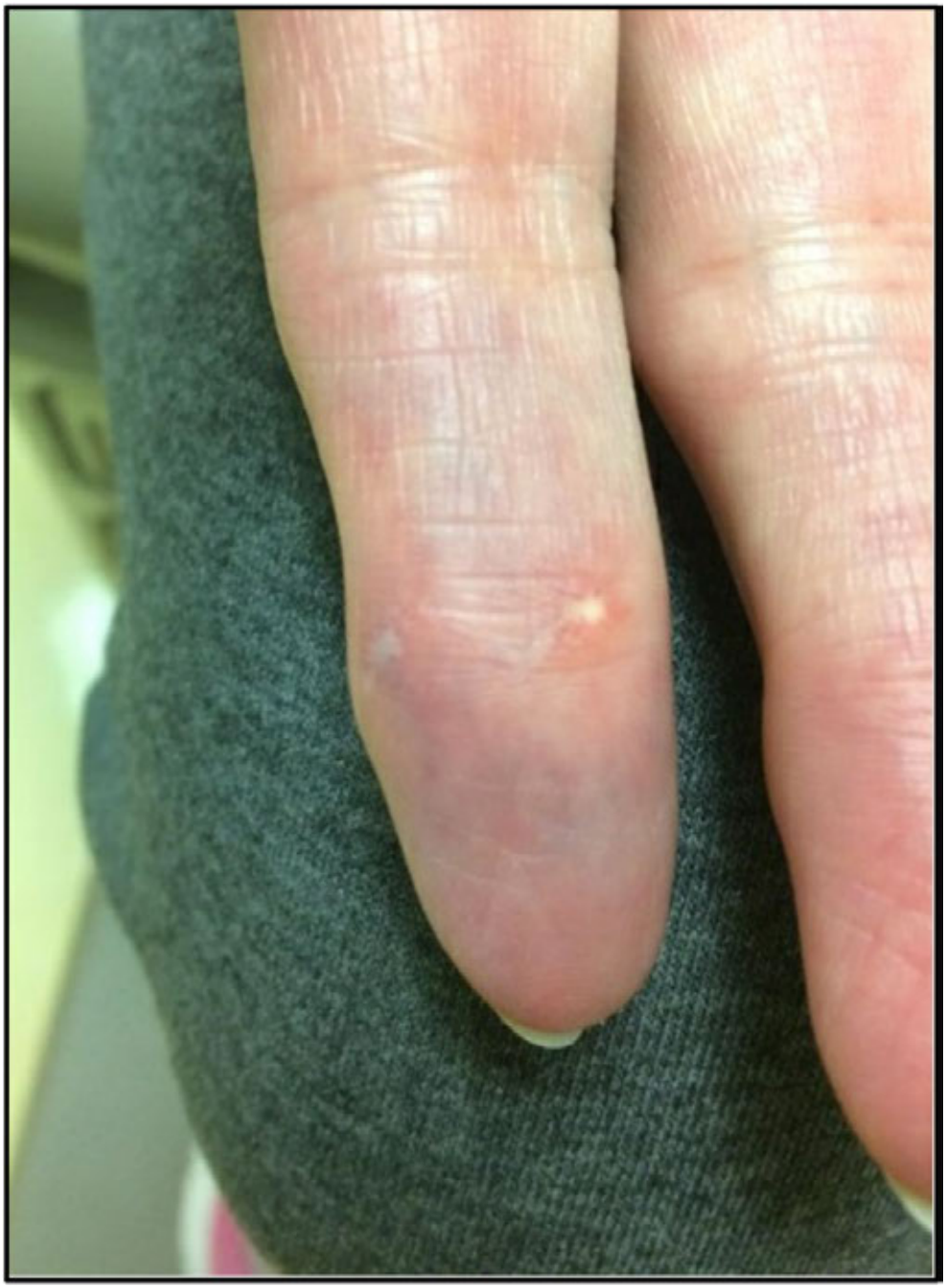

Figure 1. Right index finger of a patient with SSc showing two Degos lesions, which are characterized by erythematous telangiectatic rims with porcelain-white atrophic centers

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session (Tuesday)

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Table 1. Characteristics of patients with and without Degos lesions

	With Degos n (%)	Without Degos n (%)	*p-value*
Total	21	483	
Gender			1
Male	2 (9.5)	57 (11.8)	
Female	19 (90.5)	426 (88.2)	
Race			0.325
White/Caucasian	18 (85.7)	279 (57.8)	
African American	0 (0)	23 (4.8)	
Asian	1 (4.8)	67 (13.9)	
Pacific Islander	0 (0)	2 (0.4)	
Other or mixed	2 (9.5)	83 (17.2)	
Unknown	0 (0)	24 (5.0)	
Missing	0 (0)	5 (1.0)	
SSc subtype			**0.056**
Limited[a]	8 (38.1)	284 (58.9)	
Diffuse	13 (61.9)	177 (36.7)	
Missing	0 (0)	22 (4.6)	
ANA			0.657
Positive	19 (4.0)	393 (83.6)	
Negative	2 (0.4)	56 (11.9)	
Missing	0 (0)	34 (2.28)	
Anti Centromere			0.625
Positive	8 (1.9)	151 (35.4)	
Negative	9 (2.1)	259 (60.7)	
Missing	4 (19.1)	73 (15.1)	
Anti Scl-70			0.153
Positive	7 (33.3)	91 (18.8)	
Negative	11 (52.4)	341 (70.6)	
Missing	3 (14.3)	51 (10.6)	
Anti RNA pol III			0.718
Positive	3 (14.3)	54 (11.2)	
Negative	8 (38.1)	156 (32.3)	
Missing	10 (47.6)	273 (56.5)	
Anti PM-SCl			0.158
Positive	2 (9.5)	15 (3.1)	
Negative	9 (42.9)	179 (37.1)	
Missing	10 (47.6)	289 (59.8)	
Anti U1-RNP			0.557
Positive	2 (9.5)	42 (8.7)	
Negative	16 (76.2)	319 (66.1)	
Missing	3 (14.3)	122 (25.3)	
Telangiectasia			**0.055**
Present	19 (90.5)	320 (66.3)	
Absent	2 (9.5)	159 (32.9)	
Missing	0 (0)	4 (0.8)	
Digital ulcer			0.458
Present	10 (47.6)	175 (36.2)	
Absent	11 (52.4)	304 (62.9)	

Table 2. Clinical characteristics associated with GAVE

	OR (95% CI)	*p-value*
Univariate logistic regression		
SSc subtype Diffuse vs. Limited[a]	1.63 (0.70 - 3.79)	0.257
ANA positivity	0.32 (0.12 - 0.87)	**0.025**
Anti RNA pol III positivity	6.81 (2.24 - 20.72)	**0.001**
Degos lesions	3.57 (0.96 - 13.27)	**0.057**
Digital ulcers	1.83 (0.79 - 4.25)	0.161
Acro-osteolysis	0.78 (0.22 - 2.84)	0.708
Pitting scar	1.81 (0.66 - 4.98)	0.248
Nailfold capillary changes	1.04 (0.38 - 2.90)	0.935
Calcinosis	1.33 (0.53 - 3.32)	0.547
Digital ischemic loss	1.07 (0.30 - 3.83)	0.913
SRC	5.76 (1.73 - 19.18)	**0.004**
PAH	0.91 (0.30 - 2.77)	0.874
Multivariable logistic regression		
RNA pol III	7.01 (2.78 - 21.56)	**0.001**
Degos lesions	3.68 (0.91 - 14.95)	**0.069**

[a]Includes patients with sine sclerosis
Abbreviations: ANA=anti-nuclear antibody; GAVE=gastric antral vascular ectasia; PAH=pulmonary arterial hypertension; SRC=scleroderma renal crisis; SSc=systemic sclerosis

Background/Purpose: Degos disease, also known as malignant atrophic papulosis (MAP), is a rare small-vessel vasculopathy that has characteristic cutaneous manifestations consisting of erythematous telangiectatic rims with porcelain-white atrophic centers with variable gastrointestinal vasculopathy that can be fatal (Figure 1). Studies suggest that endothelial dysfunction and immune dysregulation may play a role in subsequent intimal proliferation and occlusive vasculopathy in cutaneous Degos lesions. Lesions that mimic the cutaneous findings in Degos disease have been described in other rheumatic diseases, although their significance is unclear. We sought to evaluate the prevalence and clinical associations of Degos lesions in patients with systemic sclerosis (SSc).

Methods: This was a retrospective cohort study of 504 patients with SSc, who were seen at a tertiary referral center between 1998 and 2018. All patients fulfilled 2013 ACR/EULAR classification criteria for SSc. Demographics, autoantibodies, and cutaneous and internal organ manifestations of patients with and without Degos lesions were compared using chi-squared tests for categorical variables, accounting for missing data. Logistic regression analyses were performed to evaluate whether Degos lesions were predictive of any internal organ complications.

Results: Of 504 SSc patients, 21 (4.2%) had Degos lesions. In 19 (90.5%), Degos lesions were found on the hands, notably the fingers. Two patients had Degos lesions involving the lower extremities. Degos lesions were significantly associated with acro-osteolysis, calcinosis, and digital ischemic loss (Table 1). There was a trend towards statistically significant associations with diffuse SSc subtype and telangiectasias. We further assessed whether Degos lesions were predictive of any internal organ complications. We found a trend, both in univariate and multivariate logistic regression analyses, towards an association with GAVE (Table 2).

Conclusion: Degos lesions are present in 4.2% of our SSc cohort. Degos lesions are associated with other cutaneous manifestations of SSc including acro-osteolysis, calcinosis, and digital ischemia, supporting an underlying ischemic and vasculopathic etiology. Our findings suggest that Degos lesions may be associated with the presence of GAVE.

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Abstract Number: 2598

Different Treatment Backgrounds Do Not Influence Aminaphtone Efficacy in Primary and Secondary Raynaud's Phenomenon

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Aminaphtone treatment improves clinical symptoms of Raynaud's phenomenon (RP) and increases peripheral blood perfusion (BP) in patients with either primary or secondary RP (1-2).The aim of this study was to assess possible interferences of different treatment backgrounds on RP related clinical symptoms as well as on skin BP in patients treated with aminaphtone, during a six-month follow-up.

Methods: Forty-six patients with active RP were enrolled during routine clinical assessment (11 primary RP, mean age 49±19 SD years, mean RP duration 6±3 years; and 35 secondary RP to systemic sclerosis (SSc), mean age 61±17 years, mean RP duration 11±9 years). Aminaphtone was orally administered 75 mg twice daily in addition to current standard treatments, and all patients were on a stable drug regimen since at least two months, which remained unmodified during the follow-up. All patients were taking aspirin. Six groups of treatment backgrounds were identified: 1) hydroxychloroquine (2 patients); 2) methotrexate (3 patients); 3) colchicine (5 patients); 4) cyclosporine A (6 patients); 5) mycophenolate (6 patients); 6) proton-pomp inhibitors (12 patients); 7) no further treatments (12 patients). Raynaud's condition score (RCS) and both frequency and duration of Raynaud's attacks were assessed at the same time. Blood perfusion was measured by Laser Speckle Contrast Analysis (LASCA) (3) at the level of fingertip, periungual areas, dorsum and palm of hands, and face at baseline (T0), after one (T1), four (T4), twelve (T12) and twentyfour (T24) weeks of treatment. Statistical analysis was performed by non-parametric tests.

Results: During aminaphtone treatment, a progressive statistically significant increase of blood perfusion, as well as an improvement of RP clinical symptoms (decrease of RCS, frequency and duration of RP attacks/day), were observed in all above reported seven groups of RP patients with different treatments backgrounds from T0 to T12 in all skin areas ($p< 0.01$). There were no statistically significant difference between the seven groups of patients concerning skin BP at different times ($p=0.60$). The results were similar in both primary and secondary (to SSc) RP patients ($p=0.40$). Aminaphtone administration had to be stopped in 2 patients due to headache, and one patient was lost during follow-up.

Conclusion: This study demonstrates that the increase of skin blood perfusion and the improvement of RP clinical symptoms are not influenced by different treatment backgrounds in RP patients treated with aminaphtone.

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Disclosure: A. Sulli, None; **F. Goegan**, None; **E. Gotelli**, None; **M. Patane'**, None; **C. Pizzorni**, None; **S. Paolino**, None; **E. Alessandri**, None; **B. Ruaro**, None.

Abstract Number: 2599

Body Composition and Nailfold Videocapillaroscopy Patterns in a Cohort of Systemic Sclerosis Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a chronic autoimmune disease, characterized by microvascular damage and progressive fibrosis. Among clinical complications, abnormal body composition and sarcopenia have been reported in SSc patients (1,2). Nailfold videocapillaroscopy (NVC) is a safe diagnostic tool to assess microvascular progressive damage and may predict severe organ involvement in SSc (3).

The aim of this study was to evaluate body composition in SSc patients and assess possible differences between patients with specific NVC patterns of microangiopathy.

Methods: 42 patients (6 men and 32 women) fulfilling ACR 2013 criteria for SSc underwent NVC (Videocap, DS MediGroup, Milan) to assess their NVC patterns ("Early", "Active" and "Late" pattern) (4) and dual-energy X-ray absorptiometry scan (DXA) (Lunar Prodigy) to evaluate body composition. In particular we analyzed: total mass, total lean mass, total fat mass, bone mineral content (BMC), and bone mineral density (BMD) in seven body areas (head, upper limbs, lower limbs, trunk, spine, ribs, pelvis). Sarcopenia was diagnosed in patients with reduced skeletal

muscle index (RSMI) below 5.45 Kg/m^2 for females and 7.25 Kg/m^2 for males (5). Statistical analysis was performed by non parametric tests.

Results: The mean age of patients was 65±10 years, mean disease duration 18.5 ±7.2 years, mean Rodnan skin score (mRSS) 11.2±9.3, and mean RSMI 6.3±1.1 g/cm^2. All the patients showed a NVC "scleroderma pattern": in particular 15 patients showed the "Late" pattern, 15 patients the "Active" pattern and 8 patients the "Early" NVC pattern. The "Late" NVC pattern group comparing to "Early/Active" group showed significantly lower total mass (57280±8107 *vs* 67025±10456 gr, p=0.01), lean mass (34259±3266 *vs* 40532±7659 gr, p=0.04), RSMI (5.8±0.91 *vs* 6.5±1.0 g/cm^2, p=0.02), BMC (1769±332 *vs* 2075±501 gr, p=0.04), trunk BMD (0.71±0.11 *vs* 0.88±0.13 g/cm^2,p=0.05) and spine BMD (0.90±0.17 *vs* 1.05±0.15 g/cm^2, p=0.008). No statically significant difference between the two group was observed regarding total fat mass, total body BMD and BMD at upper limbs, lower limbs, head, ribs and pelvis. Interestingly, 25% of SSc patients were found affected by sarcopenia, and the most of sarcopenic patients showed the "Late" NVC pattern (65%). Comparing age, disease duration, mRSS between sarcopenic and non sarcopenic patients there was no difference between the groups, but sarcopenic patients presented a statistically significant lower BMI (p=0.02).

Conclusion: This study demonstrates in SSc patients a relationship between a more severe microvascular damage ("Late" SSc pattern) and the body composition, characterized by lower weight, lower total lean mass, lower bone mineral content and sarcopenia, without any significant variation in total fat mass. These clinical conditions seem not to be associated with severity of skin involvement and/or disease duration.

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Disclosure: T. Veronica, None; **S. Paolino**, None; **A. Sulli**, None; **E. Gotelli**, None; **A. Casabella**, None; **F. Cattelan**, None; **S. Carlotta**, None; **C. Pizzorni**, None; **E. Alessandri**, None; **M. Cutolo**, Boehringer, Actelion, Celgene, Bristol-Mayer Squibb, 2.

Abstract Number: 2600

'If You Don't Use It, You Lose It': Rehabilitation of Finger Dexterity and Ability to Perform Activities of Daily Living in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Hand involvement due to increased skin thickness and skin collagen content is one of the first manifestations of systemic sclerosis (SSc) leading to a reduced joint mobility, flexion contractures and an reduced ability to perform activities of daily living (ADL) (Young et al., 2016). However, successful execution of ADLs

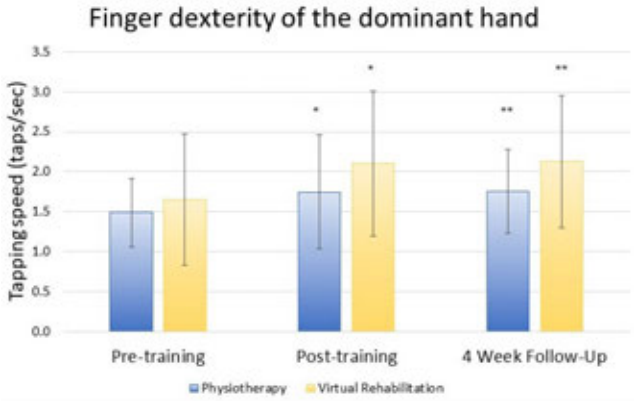

Figure 1. Finger dexterity of Digits 2-4 assessed in a keyboard tapping exercise. Tapping speed over 15 seconds was calculated. *Significant improvement in tapping speed between the pre- and post-training was maintained for 4 weeks after exercise completion (**) significant improvement between pre-training and after 4 weeks wash-out period (4 Week Follow Up).

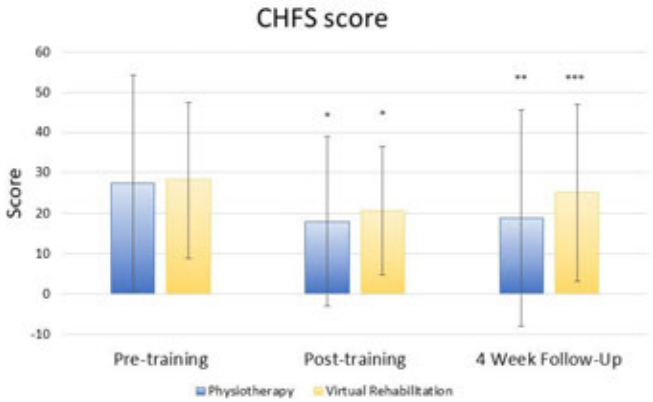

Figure 2. Cochin Hand Function scale (CHFS) score was significantly reduced after exercises (*significant change in CHFS between pre-training and post-training test). In the Physiotherapy group, this was maintained after the four week wash out period (** significant reduced CHFS score between pre-training and 4 Week Follow up). The virtual rehabilitation group showed a loss in hand function after the four week follow up resulting in a non-significant difference between pre-training and 4 week follow up test, but a significant increase between post-training and 4 week follow up (***).

not only relies on hand mobility, but also finger dexterity (Perez-Marmol et al., 2017). The activation of small muscles to synchronise hand and finger movement during ADLs is under neural control and reduced use of muscles leads to inefficient recruitment of motor units, and therefore reduced motor skills. Recommended hand exercises for SSc (Young et al., 2016) train range of motion, but less so dexterity. Virtual rehabilitation programmes have shown beneficial effects on both range and motor control (Levin et al., 2015). The aim of this study was to compare the effect of physiotherapy and virtual rehabilitation on finger dexterity and ability to perform ADLs.

Methods: Twenty SSc patients were recruited from a rheumatology clinic (mean age: 54.8yrs± 23.1yrs; female: n=19, male = 1) and randomly split into two groups (each n= 9, drop out: n =2) performing 90min of hand exercises per week for four weeks. One group followed a novel virtual rehabilitation programme, involving playing a computer game using hand movements. The second group completed a physiotherapy exercise regime. Prior to, immediately after and four weeks after completion of the exercises patients filled in the Cochin Hand Function Scale (CHFS). A finger dexterity test on a customised keyboard was completed using digits 2-4 and the average tapping speed over 15 seconds was calculated. A two-way mixed design ANOVA for the CHFS and finger dexterity test was conducted in SPSS and the change in CHFS and dexterity were correlated using bivariate two-tailed Pearson correlation.

Results: Both interventions showed significant improvements in ability to perform ADLs (Figure 1) ($p = 0.03$) and finger dexterity (Figure 2) ($p = 0.02$) when comparing pre-training and post-training tests. Whilst finger dexterity was maintained over the 4-week wash out period (post-training to 4-Week follow up), the ability to perform ADLs was not sustained in the virtual rehabilitation group ($p = 0.05$). No intervention programme showed a significantly better improvement than the other group on either outcome measure ($p = 0.401$). Change in CHFS and finger dexterity between test sessions was not correlated ($r = -0.09$, $p= 0.72$). This pattern was identical in the non-dominant hand, showing there is no effect of hand dominance.

Conclusion: Exercise improved both functional and neural aspects of hand function. The improvement in finger dexterity suggests that patients not only suffer a structural limitation but also a loss in fine motor skills. Finger dexterity could therefore form an important new outcome measure to assess the key clinical issue of reduced hand function in SSc. Further hand function rehabilitation in SSc should integrate a component to address dexterity in addition to mobility. The loss of neural control over finger motion in SSc should be assessed further assessed in future research.

Disclosure: E. Eusterwiemann, None; **M. Anderson**, None; **M. Robinson**, None; **G. Barton**, None.

Abstract Number: 2601

Trabecular Bone Score and Malnutrition in a Cohort of Systemic Sclerosis Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
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Background/Purpose: Systemic sclerosis (SSc) is a connective tissue disease characterized by microvascular damage, immune system activation and progressive fibrosis of the skin and internal organs. Gastrointestinal (GI) involvement induce malnutrition due to gastroesophageal symptoms GI dismotility and malabsorption that are related to fibrosis of bowel wall and bacterial overgrowth[1]. Therefore the disease is associated with secondary osteoporosis with a few studies evaluating the bone microarchitecture.

The aims of the staid is to evaluate a relationship between malnutrition and bone microarchitecture detected by trabecular bone score (TBS) in SSc patients

Methods: 38 patients (6 male and 32 female) fulfilling ACR 2013 criteria for SSc underwent dual-energy X-ray absorptiometry scan (DXA) to detect quantitative lumbar spine bone mineral density and TBS. DXA also assess body composition with a software that provides the physician quantitative parameters, including free fat mass index (FFMI), that identifies the patient with malnutrition (values< 15 kg/m2 in women and 17 kg/m2 in men), according to the

ESPEN criteria. Body mass index was calculated for all SSc patients and every patient completed a diary reporting GI symptoms possibly related to intestinal disbiosis. Fasting blood samples were obtained in order to analyse some biochemical parameters of malnutrition (total proteins, albumin, total cholesterol and blood lymphocyte count)2 Continue variables were summarized as mean and standard deviation or median and inter quartile range, discrete variables were summarized with count and percentage. Correlation was tested with Pearson or Spearman method. T-test was used to compare TBS between dichotomic groups. Uni and multivariate linear regression models were used as well the Multiple R-squared variation was applied.

Results: The mean age of patients was 64.2±11.3 years with mean disease duration 19.2±7.6 years. 36.8% of patients was found malnourished. The univariate analysis showed that only higher age of patients correlated to lower TBS ($p< 0.001$). The R2 of multivariate linear regression showed that about 45% of the TBS variations (TBSv) can be explained by the variation of the following variables (age, disease duration, lymphocyte count). Age explains about 25% of the TBSv. Older patients had lower TBS, with 0.05 points of TBS loss every decade ($p=0.001$). The presence of symptom possibly related to intestinal disbiosis, added to the model, might explains about 12% more of TBSv. Patients with symptom related to bacterial overgrowth had lower TBS respect to patients without (-0.08 $p=0.002$). Disease duration, added to the model, further explains about 4% more of TBSv and suggest a trend between highest disease duration and higher TBS ($p=0.103$). Lymphocyte count added to the model also seems to explain about 4% more of TBSv, in fact lowest number appear to have interference on TBS ($p=0.020$)

Conclusion: This study shows that a more severe microarchitectural bone defect correlates with gastrointestinal involvement in term of symptom related to intestinal disbiosis and with selected blood biochemical markers of malnutrition

1. Caimmi et al Clin Rheum 2017.37:987-997 2.Omran et al Clin_Geriatr_Med 2002.18:719-36

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Abstract Number: 2602

Changes in Fecal Microbiota Composition After Fecal Microbiota Transplantation in Systemic Sclerosis

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SESSION INFORMATION
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Background/Purpose: In the double-blind, placebo-controlled 16-week pilot including 10 systemic sclerosis (SSc) patients with upper and lower gastrointestinal (GI) symptoms we found that fecal microbiota transplantation (FMT) with commercially-available anaerobic cultivated human intestinal microbiota (ACHIM) reduced lower GI symptoms. Here, we aimed to determine relative abundance of gut microbiota at baseline and changes after FMT.

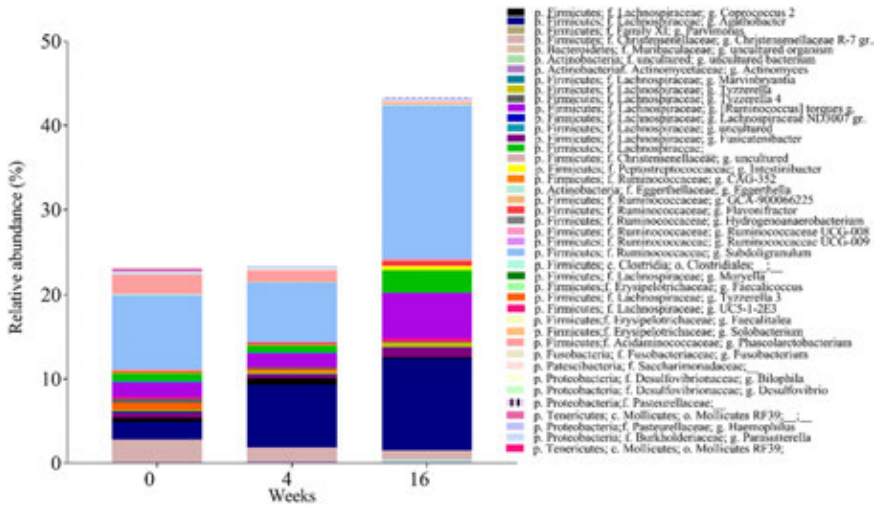

Figure 1. Relative abundance of unsorted (total) bacteria. Only bacteria with change (p<0.1) in relative abundance of unsorted bacteria from week 0-4 or week 0-16 are shown.

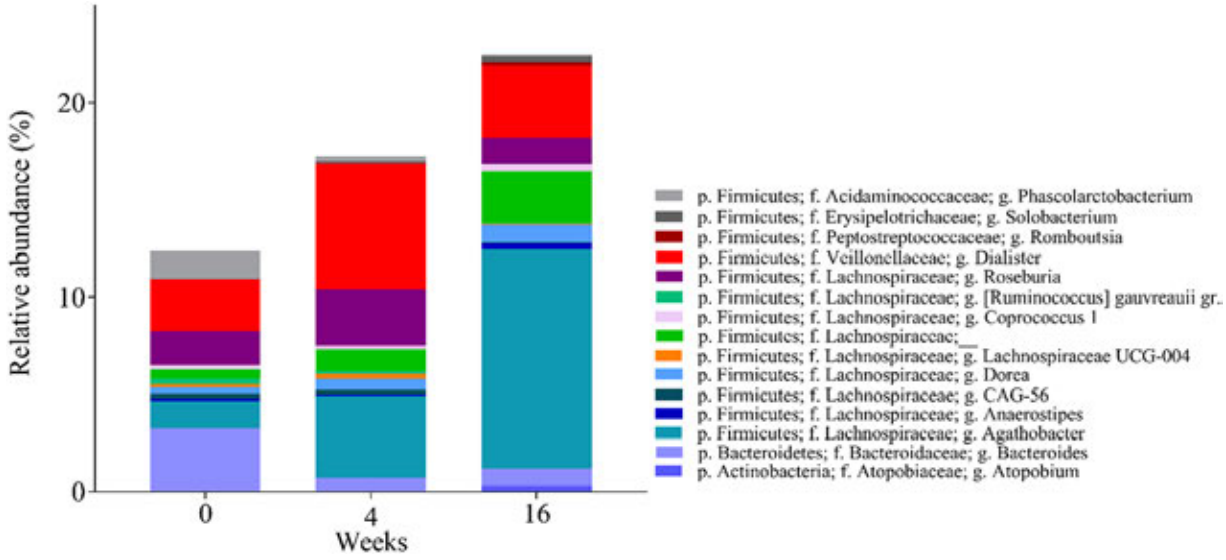

Figure 2A. Relative abundance of IgA coated bacteria. Only bacteria with changes (p<0.1) in relative abundance of IgA coating from week 0-4 or week 0-16 are shown.

Methods: Gastroduodenoscopy transfer of ACHIM or placebo was performed at weeks 0 and 2; fecal material was collected at week 0, 4 and 16. Relative abundance of total, immunoglobulin (Ig) A- and IgM-coated fecal bacteria was measured by 16s rRNA sequencing at week 0, 4 and 16. Relative abundance and taxonomic profiles were computed, alpha diversity and beta diversity were determined. Linear mixed models analysis were used to estimate changes in the microbiota composition and in IgA and IgM coating patterns over the entire follow-up period (i.e. baseline, 4 weeks, and 16 weeks).

Results: At baseline (week 0), there were no significant differences in fecal bacteria composition between the FMT (n=5) and placebo (n=4) groups, as measured by alpha and beta diversity. At week 16, but not at week 4, we identified differences in fecal bacteria composition between the FMT and placebo groups by the beta diversity ($p< 0.02$). The relative abundances of several genera changed at weeks 4 and 16 in the FMT group (Figure 1). The relative abundance of three bacterial families (Ruminococcaceae, Lachnospiraceae and Eggerthellaceae), which are dominant

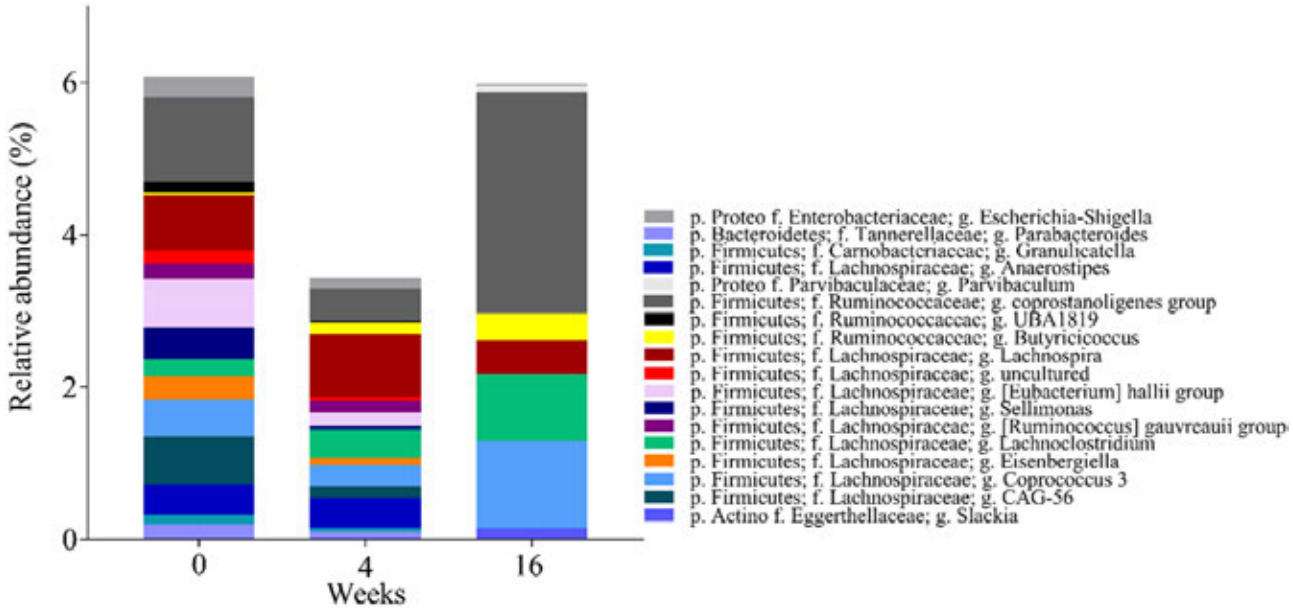

Figure 2B. Relative abundance of IgM coated bacteria. Only bacteria with change ($p<0.1$) in relative abundance of IgM coating from week 0-4 or week 0-16 are shown.

in ACHIM, increased post-intervention, consistent with engraftment after FMT. To assess if FMT triggered adaptive immunity in patients with SSc, we sorted and sequenced IgA and IgM coated bacteria from fecal samples and compared relative coating amongst FMT and placebo. Relative abundance of IgA-coated and IgM-coated bacteria fluctuated more after FMT, than after placebo (Figure 2 A and B). Some of the bacteria that were found to change their IgM coating pattern after FMT, like the genera Parabacteroides, Anaerostipes and Escherichia-Shigella, were present in the in vitro cultured fecal microbiota. Some of the bacteria which have previously been associated with other autoimmune diseases or pro-inflammatory status (Coprococcus, Roseburia, Dialister and Anaerostipes) were altered in their IgA coating patterns after FMT.

Conclusion: These observations support the notion of dynamic and ongoing immune responses to gut bacteria, and indicate that acquisition of a different gut microbiota induce immunological changes, as reflected by alterations in the pattern and/or extent of IgA and IgM coating. As mentioned above ACHIM reduced lower GI symptoms in patients with SSc. A possible link between the present observation and improved intestinal functions with ACHIM will be further studied in an upcoming investigation.

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Abstract Number: 2603

Course of Progressive Lung Fibrosis in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD) in the EUSTAR Database

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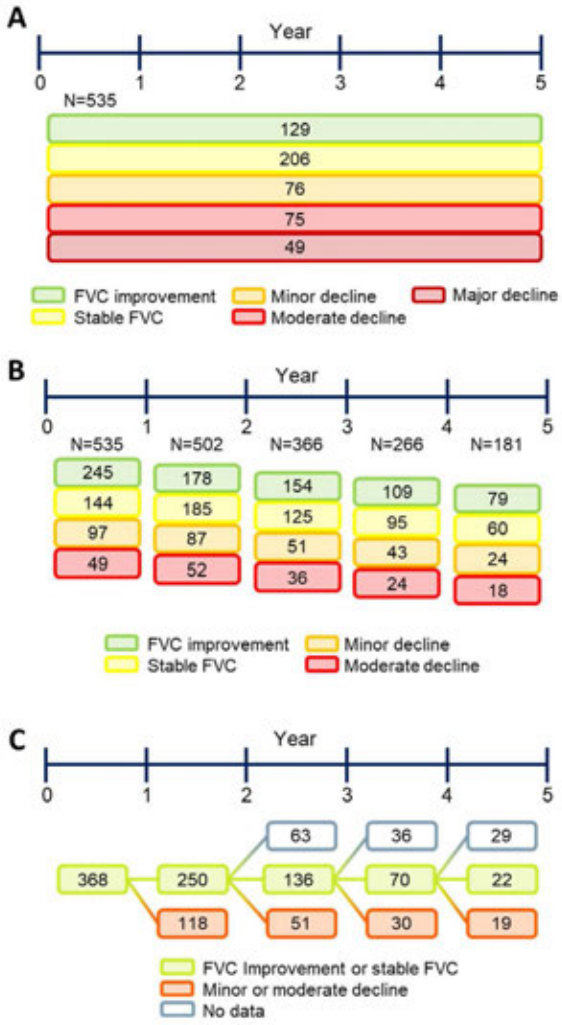
Background/Purpose: The course of systemic sclerosis-associated interstitial lung disease (SSc-ILD) is heterogeneous; some patients may experience rapid decline in lung function, while others have relatively stable disease. Large patient registries, such as The European Scleroderma Trials and Research (EUSTAR) database, can assist in mapping the trajectory of SSc-ILD and identifying patients at risk of progression.

Methods: Patients with SSc-ILD by high-resolution computed tomography, according to American College of Rheumatology/European League Against Rheumatism criteria, who were registered in the EUSTAR database with lung function measurements at baseline and after 12±3 months, and known disease duration, were eligible. Patients had to have ≥3 serial annual forced vital capacity (FVC) measurements available. The overall FVC course was assessed using absolute changes in FVC (% predicted) from baseline to last available FVC measurement. Patients were divided into five subgroups: improved FVC (FVC increase of ≥5%); stable FVC (FVC decline or increase of < 5%); minor FVC decline (FVC decline of 5–10%); moderate FVC decline (FVC decline of >10–20%); and major FVC decline (FVC decline of >20%). Absolute FVC changes (% predicted) in individual patients in each 12-month interval during the 5-year follow-up period were then determined and defined as follows: FVC improvement (FVC increase of ≥5%); stable FVC (FVC decline or increase of < 5%); minor decline (FVC decline of 5–10%) and moderate decline (FVC decline of >10%). Candidate predictors of FVC decline were selected based on published reports and expert opinion and tested using linear mixed-effect regression analysis.

Results: Of 826 eligible patients with SSc-ILD, 535 (65%) had ≥3 serial annual FVC measurements available. Overall FVC course among these patients is shown in Figure 1A: over the mean 5-year follow-up period, 335 (63%) patients showed overall improved or stable FVC, while 200 (37%) patients experienced overall mild, moderate or major FVC decline. Among patients whose overall FVC course was improved or stable, 157 (47%) experienced one or more 12-month intervals in which their FVC declined by ≥5% (Table 1). In total during the observation period, 357 patients (67%) experienced one or more 12-month intervals with an FVC decline of ≥5% (Table 1; Figure 1B). 80% of patients who experienced a 12-month interval of FVC decline did not experience further decline in the following 12-month period. Male sex, gastroesophageal reflux disease, skin score, disease duration, age, diffusion capacity of the lungs for carbon monoxide, New York Heart Association class and erythrocyte sedimentation rate were baseline risk factors for FVC decline over a mean of 5 years (Table 2).



FVC, forced vital capacity; SSc-ILD, systemic sclerosis-associated interstitial lung disease

FVC course among patients with SSc-ILD in the EUSTAR database (number of patients per category): A. Overall FVC change during mean 5-year follow-up period; B. FVC changes during 12-month follow-up intervals; C. Subsequent FVC course during 12-month intervals among patients with improved or stable FVC during the first year of follow-up

Overall FVC change from baseline	12-month intervals					
	No FVC decline (n=178)	One with FVC decline (n=220)		Two or more with FVC decline (n=137)		
		Minor decline (n=113)	Moderate decline (n=107)	Only minor declines (n=65)	One moderate and ≥1 minor decline (n=25)	Only moderate declines (n=47)
Improved (n=129)	79 (44)	22 (20)	21 (20)	1 (2)	3 (12)	3 (6)
Stable (n=206)	99 (56)	59 (53)	29 (27)	13 (20)	1 (4)	5 (11)
Minor decline (n=76)		28 (25)	17 (16)	25 (39)	1 (4)	5 (11)
Moderate decline (n=75)		2 (2)	29 (27)	23 (35)	10 (40)	11 (23)
Major decline (n=49)		2 (2)	11 (10)	3 (5)	10 (40)	23 (49)

FVC, forced vital capacity; SSc-ILD, systemic sclerosis-associated interstitial lung disease

Changes in FVC% predicted (n [%]) during 12-month follow-up intervals among patients with SSc-ILD in the EUSTAR database

	Multivariable		
Predictor variable	Coefficient	95% CI	*P* value
Time	0.80	0.22 to 1.39	0.007
Time×mRSS	−0.06	−0.10 to −0.02	0.002
Time×Sex	−1.30	−2.10 to −0.49	0.002
Time×GERD	−0.72	−1.34 to 0.10	0.024
Age	0.47	0.37 to 0.57	<0.001
DL_{CO} (% predicted)	0.45	0.37 to 0.52	<0.001
NYHA class	−4.76	−6.59 to −2.92	<0.001
ESR	−0.09	−0.15 to −0.03	0.005

The model included a random intercept and slope. Time, sex, age, NYHA class, DL_{CO}, CRP, ESR, mRSS, SSc subtype, ATA, ACA and ARA, disease duration, synovitis and muscle weakness were fixed effects. ACA, anticentromere antibody; ARA, anti-RNA polymerase III antibody; ATA, anti-topoisomerase I antibody; CI, confidence interval; CRP, C-reactive protein; DL_{CO}, diffusion capacity of the lungs for carbon monoxide; ESR, erythrocyte sedimentation rate; FVC, forced vital capacity; GERD, gastroesophageal reflux disease; mRSS, modified Rodnan skin score; NYHA, New York Heart Association; SSc, systemic sclerosis; SSc-ILD, systemic sclerosis-associated interstitial lung disease.

Risk factors for FVC% change over the 5-year observation period in multivariable mixed-effect regression analysis in patients with SSc-ILD

Conclusion: These results support close monitoring of patients with SSc-ILD, as most patients experienced at least one 12-month interval with FVC decline during their 5-year follow-up period. Moreover, intervals of FVC decline were seen in some patients who appeared stable overall. Importantly, the risk factors for FVC decline identified herein could help identify patients at risk of disease progression.

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Bio Science, 5, Target BioScience, 5, UCB, 2, 5, 9, UCB in the area of potential treatments of scleroderma and its complications, 2, 5.

Abstract Number: 2604

Pain Chronification and the Important Role of Non-disease Specific Symptoms in Patients with Systemic Sclerosis

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Background/Purpose: Pain is a frequent, yet inadequately explored challenge in patients with systemic sclerosis (SSc). The aim of this study was to conduct an extensive pain assessment, examining pain chronification and its association with disease manifestation.

Methods: Consecutive SSc patients attending their annual assessment in the Department of Rheumatology, Zurich, Switzerland were included into the study. SSc specific features were addressed as defined by European Scleroderma Trial and Research Group (EUSTAR). We conducted a detailed pain analysis including pain intensity, localization, treatment, pain chronification grade according to the Mainz Pain Staging System (MPSS), general well-being using the Marburg questionnaire on habitual health findings (MFHW), as well as symptoms of anxiety and depression using the Hospital Anxiety and Depression Scale (HADS).

Results: One hundred forty seven SSc patients completed a pain questionnaire, 118/147 (80.3%) reported pain and were included for further assessment. The median pain intensity during the last 4 weeks was 4/10 on a numeric rating scale (NRS). The most frequent major pain localizations were hand and lower back. The number of patients with low back pain as main pain was significantly higher in patients with very early SSc than in patients with advanced and established disease stages ($p = 0.01$). Those patients also showed the highest amount of pathological HADS scores for depression as well as for anxiety with 25% each and more pathological scores in the MFHW. Regarding pain chronification, 34.8% of all patients were in stage I according to the Mainz Pain Staging System, 45.2% in stage II and 20.0% in stage III. There was no significant correlation with chronification grade and disease severity, but higher chronification grades were significantly more frequent in patients with low back pain ($p = 0.024$). Advanced chronification was also significantly associated with pathological scores in the HADS ($p < 0.0001$) and was linked with decreased well-being. Therefore, patients with primarily back pain showed more pathological HADS scores than those with primarily hand pain. Patients with higher chronification grades also showed more pain related effects like higher use of analgesics and poorer subjective therapy effects. Furthermore, we found that most patients did not receive adequate pain therapy; only 4.4% of all examined patients reported seeing a pain specialist.

Conclusion: Contrary to our expectations, pain severity and chronification were not associated with more severe disease manifestation in systemic sclerosis. This study showed that low back pain, being associated with advanced

pain chronification and increasing psychological problems, represents an important problem in patients with systemic sclerosis, especially in early stages of the disease. Therefore, our study implies that also non-disease specific symptoms such as low back pain need to be considered in SSc patients and it underlines the importance of preventing pain chronification in order to enhance quality of life for these patients.

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Abstract Number: 2605

Men and Black Persons Die at Younger Ages from Systemic Sclerosis: A Nationwide Population-based Study

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Background/Purpose: Systemic sclerosis (SSc) is more common in women than men, but men tend to have a faster disease progression than women. However, conflicting results with regards to sex differences in SSc mortality have been reported. A few studies found standardized mortality ratios for SSc to be similar between men and women, whereas others found SSc standardized mortality ratios to be higher in men than women. We conducted a population-based study comprising of all recorded SSc deaths across the US to determine: a) the median age at SSc death by sex and race, b) odds ratios for the risk of SSc deaths by sex and race in different age groups, c) trends in the proportions of total SSc deaths by sex and race at different age groups over 5 decades, and d) SSc age-standardized mortality rate (ASMR) and case-fatality rate by sex and race.

Methods: We constructed histograms that depict the absolute number of SSc deaths for each age separately by sex and race. We then assessed the cumulative percent death at each age and determined the median age at death for each demographic group. We then calculated the percent of total SSc deaths by sex/race at different age groups every 10 yrs from 1970. We performed Chi-square test with Yates correction and quantified the odds ratio (OR) with 95% CI. Finally, we calculated ASMRs, and case-fatality rates (i.e., mortality rate in SSc population = SSc mortality rate / SSc prevalence) by sex and race.

Results: SSc was recorded as the cause of death in 5,061 women and 1,222 men in the US during 2011-2015. Deceased SSc persons were 4,426 white and 956 black. The median age at SSc death was 63 yrs in men vs. 68 yrs in

women, and 57 yrs for black persons vs. 70 yrs for white persons during 2011-2015. Higher proportions of men than women (54.5% vs. 40.2%), and of black than white persons (72.5% vs. 34.0%) died of SSc before 65 yrs of age. The risk of SSc death before 65 yrs of age was significantly higher in men than in women (OR 1.8, 95% CI 1.6-2.0, p< 0.0001) and in black than in white persons (OR 5.1, 95% CI 4.4-6.0, p< 0.0001). We then assessed trends in the proportion of SSc deaths by sex and race over 5 decades. The proportions of male and female SSc deaths were similar in all age groups in 1970, but significantly higher proportions of male SSc deaths relative to female SSc deaths were noted in the younger age groups at later timepoints (1990 and later in 45-64 and 2015 in ≤44 age groups). Compared to white persons, black persons had higher percentages of total SSc deaths in younger age groups (≤44 and 45-64) throughout the study period. Black persons also had significantly higher ASMRs than white persons. Women had 3-4-fold higher ASMRs than men, e.g., SSc-ASMR was 4.9 (95% CI 4.6-5.2) in women and 1.4 (95% CI 1.2-1.5) in men in 2015. However, this difference was obviated when mortality rates were corrected tor the differences in SSc prevalence between women and men, e.g., case-fatality rates for SSc were 3.0 in women and 2.1 in men in 2015.

Conclusion: Men and black persons died of SSc at younger ages than did women and white persons, respectively. Understanding the mechanisms of these disparities and identifying potentially modifiable risk factors might inform targeted research and public health programs to promote health equity in all SSc subpopulations.

Disclosure: R. Singh, None; **D. Singh**, None; **E. Yen**, None.

Abstract Number: 2606

Evolution of Systemic Sclerosis-Related Interstitial Lung Disease After Autologous Hematopoietic Stem Cell Transplantation

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Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Three trials demonstrated the overall superiority of autologous hematopoietic stem cell transplantation (HSCT) compared to pulsed cyclophosphamide (CYC) in SSc. An improvement in forced vital capacity (FVC) has also been described, but whether this indicates a reduction in extension of ILD has not been extensively evaluated. The main purpose of our study is to evaluate the efficacy of HSCT in inducing reduction of ILD extension assessed through high-resolution computed tomography (HRCT) in SSc patients. The secondary aims are to compare the evolution of fibrosis score after HSCT and after CYC, to evaluate how FVC changes associate with HRCT modifications, and which patients are most likely to show ILD reduction.

Methods: All SSc patients fulfilling the 2013 ACR classification criteria for SSc and treated with either HSCT or pulse CYC between 2004 and 2018 were selected. Patients with evidence of ILD at HRCT and high-quality images before and after treatment (6-18 months) available, were included. Two experienced researchers, blinded for clinical data and treatment, scored HRCTs independently and retrospectively using the “Goh score”. Discrepancies above 10% were discussed to reach consensus. Changes in mean total Goh score, and mean total scores for ground glass and reticular pattern are described. A cut-off of 5% was used to define improvement/progression. PFTs close to the HRCT

Table 1: Baseline characteristics			
	HSCT	**CYC**	**P-value**
Demographic	n=22	n=31	
Females, n (%)	12 (54)	24 (77)	ns
Age (years), mean (SD)	45.8 (10)	51 (12.8)	ns
Disease duration (years), median (IQR)	2.1 (1.2-4.7)	1.8 (0.7-4.4)	ns
Disease subset			
DcSSc, n (%)	20 (91)	19 (61)	0.016
Autoantibodies			
ATA, n (%)	15 (68)	17 (55)	ns
HRCT scores *			
Ground glass score, mean % (SD)	18.5 (14.2)	21.7 (12.5)	ns
Reticular pattern score, mean % (SD)	12.6 (11)	14.4 (9.1)	ns
Total Goh score, mean % (SD)	24.5 (15.9)	25 (13)	ns
Pulmonary function tests			
FVC, mean (SD), % predicted	79.1 (18)	80.3 (16.5)	ns
FEV1, mean (SD), % predicted	77.9 (16.5)	82.6 (15.7)	ns
DLCO-SB, mean (SD), % predicted	55.4 (19.5)	53.3 (11.6)	ns

*** Of note: at the moment of writing this abstract, the results are preliminary: all HRCTs have been scored by at least 1 reader, and 45% have been scored by 2.**

Legend. HSCT: hematopoietic stem cell transplantation; CYC: cyclophosphamide; SD: standard deviation; dcSSc: diffuse cutaneous systemic sclerosis; ATA: anti-topoisomerase I antibodies; HRCT: high-resolution computed tomography; FVC: forced vital capacity; FEV1: forced expiratory volume in 1 second; DLCO-SB: single-breath diffusing lung capacity for carbon monoxide.

time points were compared to calculate differences between pre- and post-treatment values. Regression analysis was used to study the association of relative changes in FVC and single-breath diffusing lung capacity for carbon monoxide (DLCO-SB), with change in mean total Goh score, and to study which patients are most likely to improve.

Results: Of note: at the moment of writing this abstract, the results are preliminary: all HRCTs have been scored by at least 1 reader, and 45% have been scored by 2. Thus, the reported data consist of the mean score of 2 readers in 45% of patients, and the score of 1 reader in 55%. We included 22 patients treated with HSCT and 31 with monthly CYC (Table 1). In patients treated with HSCT, mean Goh score decreased by 5.1±10.4%, which was mainly determined by a decrease in ground glass score (p= < 0.001 in linear regression). Overall, 7 HSCT patients improved (32%)

Table 2: Comparison between pre- and post-treatment			
	HSCT	**CYC**	**P-value**
HRCT, time before treatment (months), mean (SD)	4.8 (3.1)	1.6 (1.5)	<0.001
HRCT, time after treatment (months), mean (SD)	12.2 (2.3)	10.9 (3.3)	ns
HRCT scores *			
Ground glass score difference, mean (SD), absolute %	-6.2 (9.8)	-2.2 (9.8)	ns
Reticular pattern score difference, mean (SD), absolute %	-0.4 (2.6)	-0.1 (4.1)	ns
Total Goh score difference, mean (SD), absolute %	-5.1 (10.4)	-2 (9.8)	ns
Improvement, n (%)	7 (32)	6 (19)	ns
Stability, n (%)	14 (64)	21 (68)	ns
Progression, n (%)	1 (4)	4 (13)	ns

*** Of note: at the moment of writing this abstract, the results are preliminary: all HRCTs have been scored by at least 1 reader, and 45% have been scored by 2.**

Legend. HSCT: hematopoietic stem cell transplantation; CYC: cyclophosphamide; SD: standard deviation; HRCT: high-resolution computed tomography; FVC: forced vital capacity; FEV1: forced expiratory volume in 1 second; DLCO-SB: single-breath diffusing lung capacity for carbon monoxide; Improvement: absolute decrease in Goh score >5%; Stability: absolute change in Goh score <5%; Progression: absolute increase in Goh score >5%

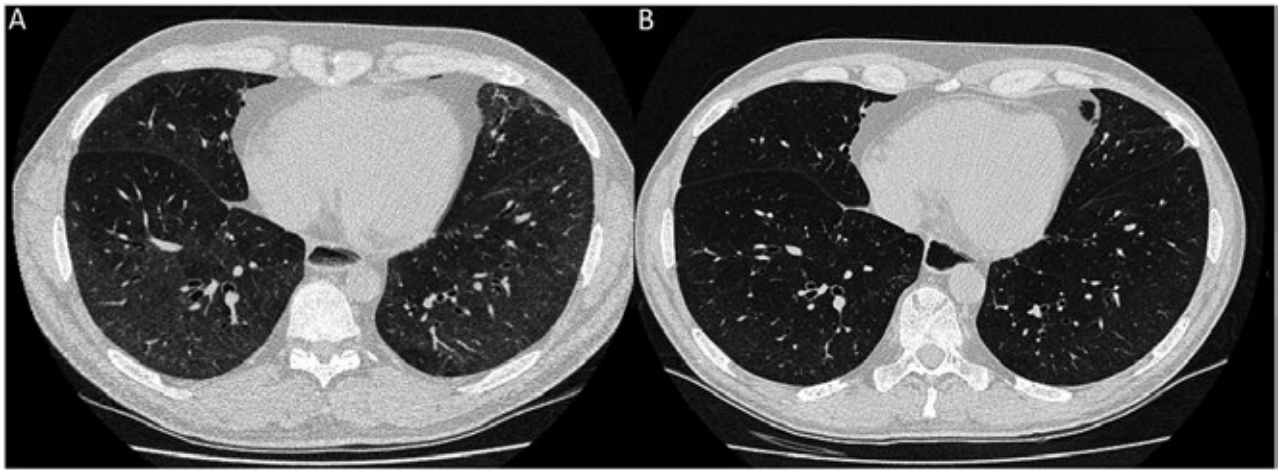

Figure 1. Axial plane HRCT scan above the level of the diaphragm showing marked reduction of ILD extension in a 45-year old man treated with HSCT. Fig. A: 4 months before HSCT; Fig. B: 13 months after HSCT.

(Figure 1), 14 remained stable (64%), and 1 progressed (4%) (Table2). In the CYC group, mean Goh score decreased by 2±9.8%. Six patients improved (19%), 21 remained stable (68%), and 4 progressed (13%) (all p= >0.05) (Table 2). For all patients, changes in FVC (p= < 0.001), and DLCO-SB (p= 0.018) were associated with change in mean total Goh score. In univariate analysis, patients with improvement did not differ with respect to age or disease duration but had higher total Goh score, higher ground glass score, and a trend for lower DLCO-SB at baseline.

Conclusion: HSCT resulted in reduction of ILD in 32% of SSc patients during the first year after treatment, which is mainly explained by a reduction of ground glass opacity. Changes in HRCT findings are significantly associated with changes in PFTs. In this small population, improvement/stable disease was numerically more frequent after HSCT compared to CYC, but no statistically significant difference was found.

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Abstract Number: 2607

Ultrasound Detection of Calcinosis and Correlation with Ulnar Artery Occlusion in Patients with Systemic Sclerosis

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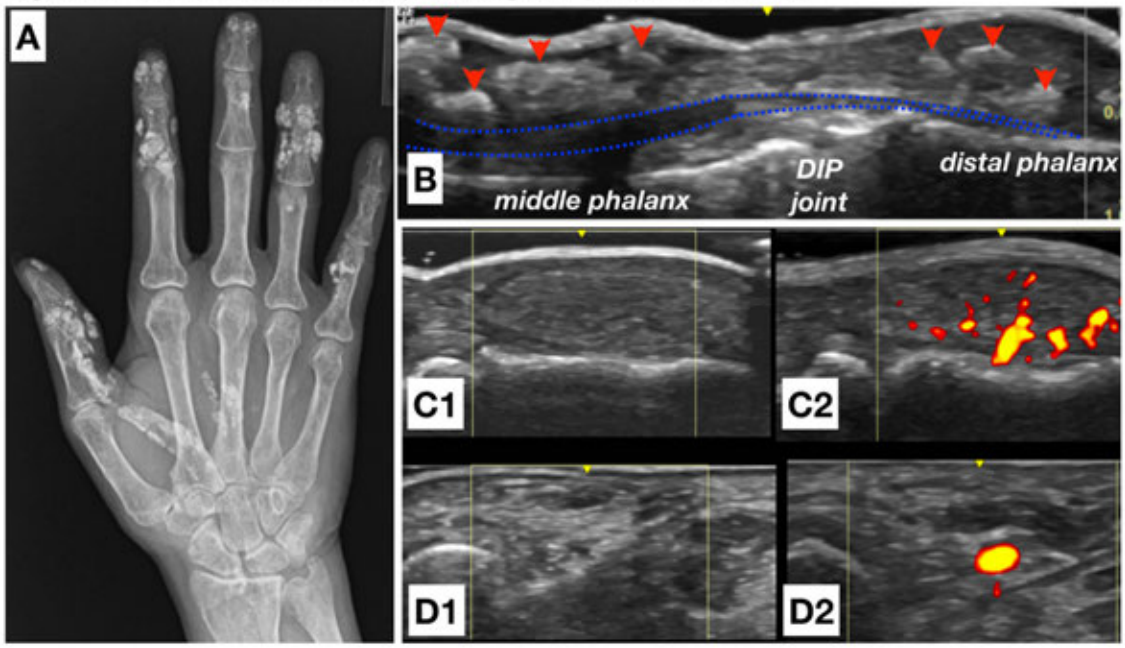
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is a progressive fibrotic and vascular disease affecting multiple organs. Calcinosis cutis in SSc is characterized by calcium deposition in the skin and subcutaneous tissues and can lead to significant morbidity. While the pathophysiology of calcinosis in SSc is poorly understood, vascular ischemia is thought to play a role. Ultrasound (US) is well suited to vascular and soft tissue interrogation and may be helpful to detect, monitor, and study calcinosis in SSc. We sought to evaluate the ability of US to detect calcinosis in the hands and wrists of SSc patients versus X-ray identified calcinosis and to evaluate the relationship between ultrasound markers of pathologic perfusion and the presence of calcinosis.

Methods: Patients meeting 2013 ACR/EULAR classification criteria for SSc were prospectively evaluated for calcinosis in the hands and wrists by both X-ray and US. US was performed by submerging the hands and wrists in a water bath for evaluation of all surfaces. The presence or absence of calcinosis was recorded for each of 44 zones (22 left and 22 right) based on our previously published methods, and the sensitivity and specificity for calcinosis detection by US versus X-ray was determined. We also obtained bilateral US vascular measurements of ulnar artery occlusion (UAO) and finger pulp blood flow (FPBF) in the 3rd and 4th digits. For each hand, associations between markers of pathologic blood flow (UAO, FPBF, and a composite severity score of UAO and FPBF) and the presence of calcinosis were assessed using generalized estimating equations.

Results: 43 SSc patients (19 diffuse and 24 limited) were enrolled and 17 (39.5%) were found to have X-ray evidence of calcinosis in at least 1 hand (10 bilateral, 7 unilateral). US identified 13 patients with calcinosis (9 bilateral, 4 unilateral). Of the 748 zones evaluated, X-rays identified 72 zones (9.6%) with calcinosis while US showed 76 (10.2%). The sensitivity and specificity for US detection of calcinosis versus X-ray was 61% and 95% by zone, 78% and 98% by hand, and 76% and 100% by patient, respectively. UAO was seen in 13/43 (30%) and 12/43 (28%) of left and right hands, respectively, and FPBF was absent in 1 or both digits of the left and right hands in 21 (49%) and 19 (44%), respectively. We found a strong association between UAO and X-ray identified calcinosis (OR 8.08, 95% CI 2.45-

Figure 1. Ultrasound and X-ray findings in systemic sclerosis



Systemic sclerosis patients with (A) X-ray findings of calcinosis, (B) ultrasound identified calcinosis [red arrowheads] in the longitudinal palmar aspect of the 2nd finger [blue outline = flexor tendon], (C1-C2) absent and normal FPBF respectively, and (D1-D2) UAO and no UAO, respectively. UAO = ulnar artery occlusion, FPBF = finger pulp blood flow, DIP = distal interphalangeal

Table 1. Sensitivity and specificity of ultrasonography for X-ray identified calcinosis

	Sensitivity	Specificity	TP	FP	TN	FN
By Zone	61%	95%	44	32	644	28
By Hand	78%	98%	21	1	58	6
By Patient	76%	100%	13	0	26	4

TP = true positive, FP = false positive, TN = true negative, FN = false negative

Table 2. US and X-ray features and associations between US markers of pathologic blood flow and calcinosis

	Imaging Features	
	Left Hand n =43	Right Hand n =43
UAO, n (%)	13 (30)	12 (28)
FPBF absent*, n (%)	21 (49)	19 (44)
Calcinosis by US, n (%)	11 (26)	11 (26)
Calcinosis by X-ray, n (%)	15 (35)	12 (28)
	Associations with Calcinosis	
	OR (95% CI)	***p***
UAO	8.08 (2.45, 26.60)	0.001
FPBF	2.66 (0.83, 8.52)	0.10
FPBF + UAO severity score	3.23 (0.96, 10.92)	0.06

US = ultrasound, OR = odds ratio by generalized estimating equations. UAO = ulnar artery occlusion, FPBF = finger pulp blood flow. *FPBF absent if one or both measurements per hand were absent.

26.60, p< 0.001). Both FPBF (OR 2.66, 95% CI 0.83-8.52, p=0.099) and the composite severity score (OR 3.23, 95% CI 0.96-10.92, p=0.059) failed to show a significant association with calcinosis.

Conclusion: In a cohort of SSc patients we developed a new method for ultrasound detection and quantification of calcinosis and found it to be sensitive, and highly specific versus X-ray. We also found a strong relationship between UAO, a marker of decreased peripheral perfusion, and X-ray identified calcinosis. This is the first study to evaluate the performance of ultrasound in the detection of calcinosis and provides further support for an association between vascular disease in SSc and the pathogenesis of calcinosis.

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Abstract Number: 2608

Subsets in Systemic Sclerosis-ILD: Working Towards Consensus-Based Definitions

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

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Background/Purpose: Systemic sclerosis associated interstitial lung disease (SSc-ILD) is heterogeneous, with varying degrees of severity and risk of disease progression. No consensus-based definitions of disease severity, progression, or risk of progression exist. The purpose of this study was to use expert classification of real-world cases of SSc-ILD to derive definitions of SSc-ILD subsets that can be incorporated into clinical practice and trials.

Methods: All patients included in this study met American College of Rheumatology Criteria for Systemic Sclerosis (N=80).

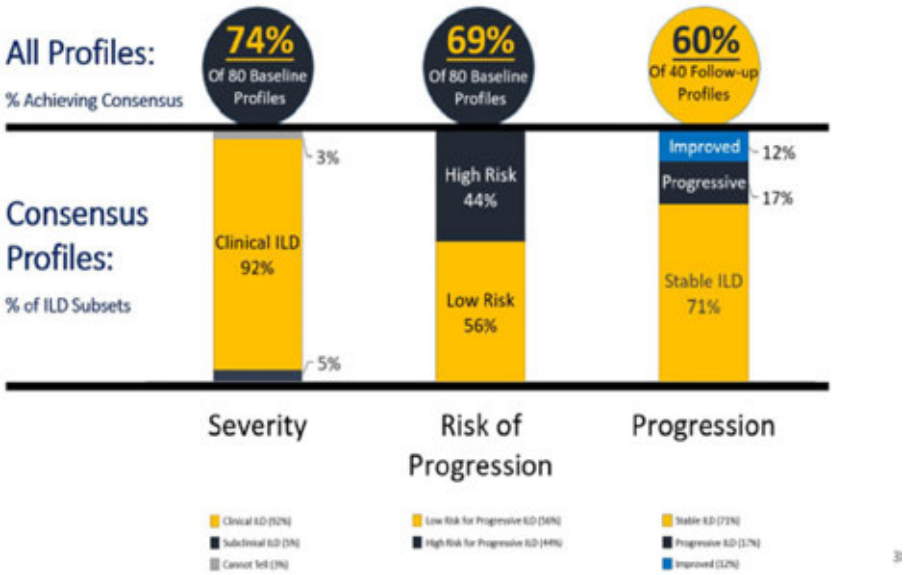

Figure. Percent Profiles Achieving Consensus and Distribution of Consensus Profiles by ILD Subset

	SEVERITY: Clinical vs. Subclinical	RISK OF PROGRESSION: Low vs. High Risk	PROGRESSION: Stable vs. Progression
	Ranking*	Ranking*	Ranking*
Demographics & Disease Features			
Race	10 (least cited)	9 (tied with SGRQ)	--
Duration of SSc	8	1 (most cited)	--
Type of SSc	7	5	--
Antibody Status	9	4	--
Assessments of Disease Severity			
FVC%	1 (most cited)	2	1 (most cited)
DLCO%	4	7	5
Total lung involvement on HRCT	2	3	2
Total lung fibrosis of HRCT	5	6	3
Dyspnea Index	3	8	4
St George Respiratory Questionnaire	6	9 (tied with Race)	6 (least cited)

*Determined by number of times this was chosen as the most influential reason for Experts' choice; ranked from most frequently cited (1) to least frequently cited (10).
– These features were not assessed for Progression.

Table. The Most Influential Factors Used in Classification by Dimension

Patient profiles were developed from participants in the Scleroderma Lung Study-II and ILD patients seen at a Scleroderma Center. Experts in rheumatology, pulmonary medicine, radiology, and members of the OMERACT CTD-ILD Working Group [1] provided key domains to be included in profiles. These included information on demographics, disease features (limited vs. diffuse SSc, ANA status, antibody status), pulmonary function testing, patient-reported assessments, and quantitative analysis of lung involvement on high resolution computerized tomography of the chest (HRCT) for baseline profiles; and for those with follow-up data, how these measures change over time.

Eighty-three ILD experts were surveyed for classification of 80 baseline and 40 follow-up profiles. Baseline profiles were classified based on: 1- Severity (clinical vs. subclinical) and 2- Risk of Progression (low vs. high); follow-up profiles were classified on 3- Progression over time (stable vs. progressive vs. improved). Each profile was rated by a minimum of 4 experts; consensus on a classification was achieved with 75% concordance. For each profile, experts provided input on the top features that helped in making their classification decision.

Results: Fifty percent (N=42) of invited experts, from 10 countries, completed the survey.

Along the dimensions of severity, risk of progression, and progression, a majority of profiles achieved consensus ratings (Figure). Of those profiles achieving consensus, the majority were classified as “clinical ILD”, “low risk”, and “stable”. Table provides a ranking of the most influential features used in classification on these dimensions.

Conclusion: These data represent the first step in creating operational definitions for ILD subsets. This expert-derived classification advances the characterization of a subset of severity (clinical ILD), subsets of risk of progression (low and high risk), and a subset of progression (stable ILD).

Features used to classify profiles on severity and progression overlapped (forced vital capacity, whole lung involvement on HRCT, dyspnea ratings), whereas the risk of progression was influenced by disease duration, type of SSc, and SSc autoantibodies in addition to the measures endorsed for severity and progression.

The next steps are to reach operational definitions for those ILD subsets not yet reaching consensus (subclinical ILD, progressive ILD, improved ILD).

References:

1. Khanna, D. *et al. J. Rheumatol.* **42**, 2168–2171 (2015)

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Abstract Number: 2609

Anti-angiogenic VEGF-A_{165}b Is Associated with Systemic Sclerosis Peripheral Vasculopathy

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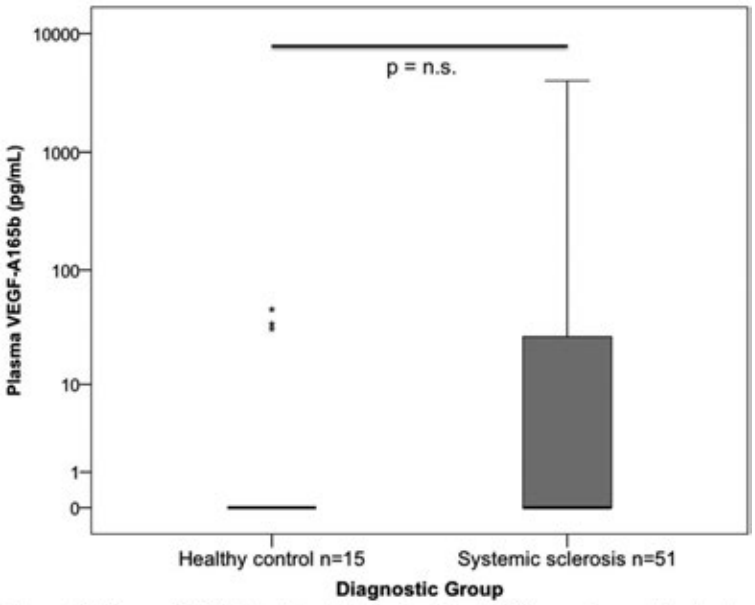

Figure 1. Plasma VEGF-A_{165}b levels. No significant difference in median levels was noted between SSc and controls (Mann-Whitney U) due to high number of undetectable VEGF-A_{165}b in both groups. Plasma VEGF-A_{165}b was detectable in 31% of SSc (max. >4000pg.mL) versus 20% of controls (max. 46pg/mL).

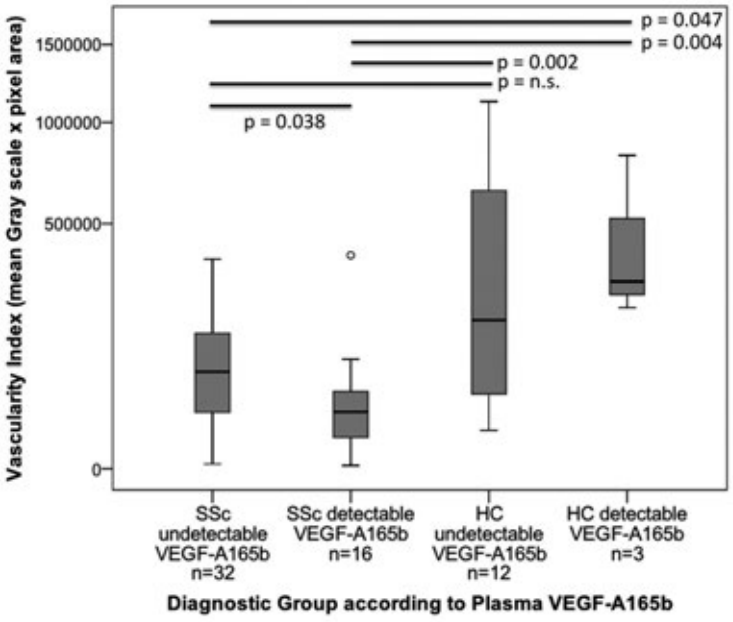

Figure 2. Vascularity Index on HFUS is reduced in SSc. Vascularity index is reduced in SSc compared to controls with a further significant reduction in the presence of detectable VEGF-A_{165}b. Statistical comparisons by Kruskal-Wallis.

Background/Purpose: The anti-angiogenic isoform of Vascular Endothelial Growth Factor-A (VEGF-A_{165}b) has been implicated in Systemic sclerosis (SSc) vasculopathy. High frequency ultrasound (HFUS) is a novel approach to assessing digital perfusion. We report on the relationship between plasma VEGF-A_{165}b and peripheral microvascular perfusion using HFUS in SSc.

Methods: Fifty-one patients fulfilling 2013 ACR/EULAR criteria for SSc and fifteen healthy controls (HC) underwent HFUS Doppler assessment of microvascular flow at the distal middle finger, from which a Vascularity Index was cal-

culated. Plasma VEGF-A_{165}b levels were assessed using ELISA. Ongoing administration of vasodilator and disease modifying therapies were permitted.

Results: Plasma VEGF-A_{165}b was detectable in 16/51 (31%) of SSc with a peak level of >4000pg/mL (Figure 1). In contrast, only 3/15 (20%) healthy controls had plasma VEGF-A_{165}b greater than the lower limit of detection by ELISA, with a maximum plasma level of 46pg/mL. Median levels were not significantly different between groups. When VEGF-A_{165}b was detectable, it was associated with significantly reduced Vascularity Index in SSc (Figure 2). In contrast, HC showed no difference in the Vascularity Index irrespective of VEGF-A_{165}b. Additionally, the Vascularity Index correlated with VEGF-A_{165}b in SSc (Spearman's ρ = -0.289, p=0.039) but not HC. The Vascularity Index was reduced in SSc even in those with undetectable VEGF-A_{165}b compared to HC (both with detectable (p=0.047) and undetectable (non-significant) VEGF-A_{165}b).

Conclusion: Increased levels of VEGF-A_{165}b are associated with reduced digital vascularity in SSc. Low levels of VEGF-A_{165}b are sometimes detected in HC but are not associated with reduced digital perfusion. Peripheral vascular compromise in SSc is evident even in the absence of detectable VEGF-A_{165}b. Further longitudinal studies are needed to investigate the role of VEGF-A_{165}b in determining microvascular flow and the impact of disease duration and intervention on VEGF-A_{165}b and digital perfusion over time.

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Relationship Between Parenchymal and Vascular Features in Systemic Sclerosis-Interstitial Lung Disease: Results from Quantitative Analysis of Chest Computed Tomography

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Background/Purpose: Interstitial lung disease (ILD) and pulmonary arterial hypertension negatively impact on Systemic sclerosis (SSc) prognosis. Chest computed tomography (CT) is the gold standard in assessing ILD and helps in evaluating associated vascular involvement. However, CT scans qualitative analysis is limited by low reproducibility and time constraints. Recently developed quantitative techniques may overcome these limitations. We aimed at

Table 1. Correlation between quantitative parenchymal and vascular data

		TV_cm3	AV_cm3	VV_cm3	TV%	AV%	VV%
normal%	Pearson R	-,270	-,340*	-,142	-,540**	-,564**	-,470**
	p value	,080	,026	,365	<0,001	<0,001	,001
GG%	Pearson R	,230	,305*	,099	,516**	,543**	,441**
	p value	,137	,047	,527	<0,001	<0,001	,003
RET%	Pearson R	,161	,202	,087	,398**	,406**	,357*
	p value	,302	,194	,580	,008	,007	,019
HC%	Pearson R	-,056	-,081	-,014	,096	,066	,127
	p value	,723	,606	,927	,539	,673	,416

evaluating parenchymal and vascular features in SSc-ILD by using quantitative analysis (QA) of CT scans and test correlation with clinical-functional data.

Methods: We analyzed chest CT scans in SSc patients performed with spirometric gating at TLC. A computational platform for texture analysis of ILD patterns (CALIPER), through Imbio LTA Launchpad, quantified the extent of normal pattern (NP%), ground glass opacities (GG%), reticulation (RET%), and honeycombing (HC%) [1]. An automated vessels segmentation was performed using a software program developed by the Ludwig Boltzmann Institute for Lung Vascular Research [2], calculating total, arterial, and venous vascular volumes (TV, AV, VV), and relative volumes (TV%, AV%, VV%). Clinical, lung functional and diffusion data, as well as disability indexes were also collected.

Results: 44 patients/CT scans were eligible (89% female, 42% diffuse, 7% PAH) for both software analysis. CALIPER showed GG% as the most frequent radiological pattern (median 2.7%, 0.2-7.6 IQR), with positive correlation with mRSS (r=0.363, p=0.016) and increasing NYHA class (r=0.306, p=0.037), while negative correlation with FVC (r=-0.371, p=0.009) and TLC (r=-0.356, p=0.024). Similarly, RET% showed positive correlation with mRSS (r=0.491, p=0.001) and negative correlation with desaturation on 6 minutes walking test (r=-0.433, p=0.017). On the vascular analysis, TV% had positive correlation with increasing NYHA class (r=0.319, p=0.048), difficulty increase in walking domains of HAQ-DI (r=0.607, p=0.002) and Dlco/AV (r=0.414, p=0.007), while negative correlation with FVC (r=-0.449, p=0.003) and TLC (r=-0.496, p=0.003), with similar significant correlations replicated for AV%. When testing parenchymal with vascular data (Table 1), higher GG% and RET% correlated with higher vascular relative volumes. In addition, GG% correlated with AV. Conversely, increasing NP% was associated to a decrease in AV and in all vascular relative volumes.

Conclusion: This is the first study that shows a direct link between ILD and increase in lung vascular volume in SSc patients. Different hypothesis could be postulated, such as a reduction in pulmonary volume due to fibrosis, an increase in absolute vascular volumes as a phenomenon of neo-angiogenesis secondary to fibrosis, or a paraphysiological mechanism of redistribution of blood flow in lung areas less involved by ILD. Further studies on lung vessel quantification and distribution are ongoing.

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Mesenchymal Stem Cells in Scleroderma: A Systematic Review

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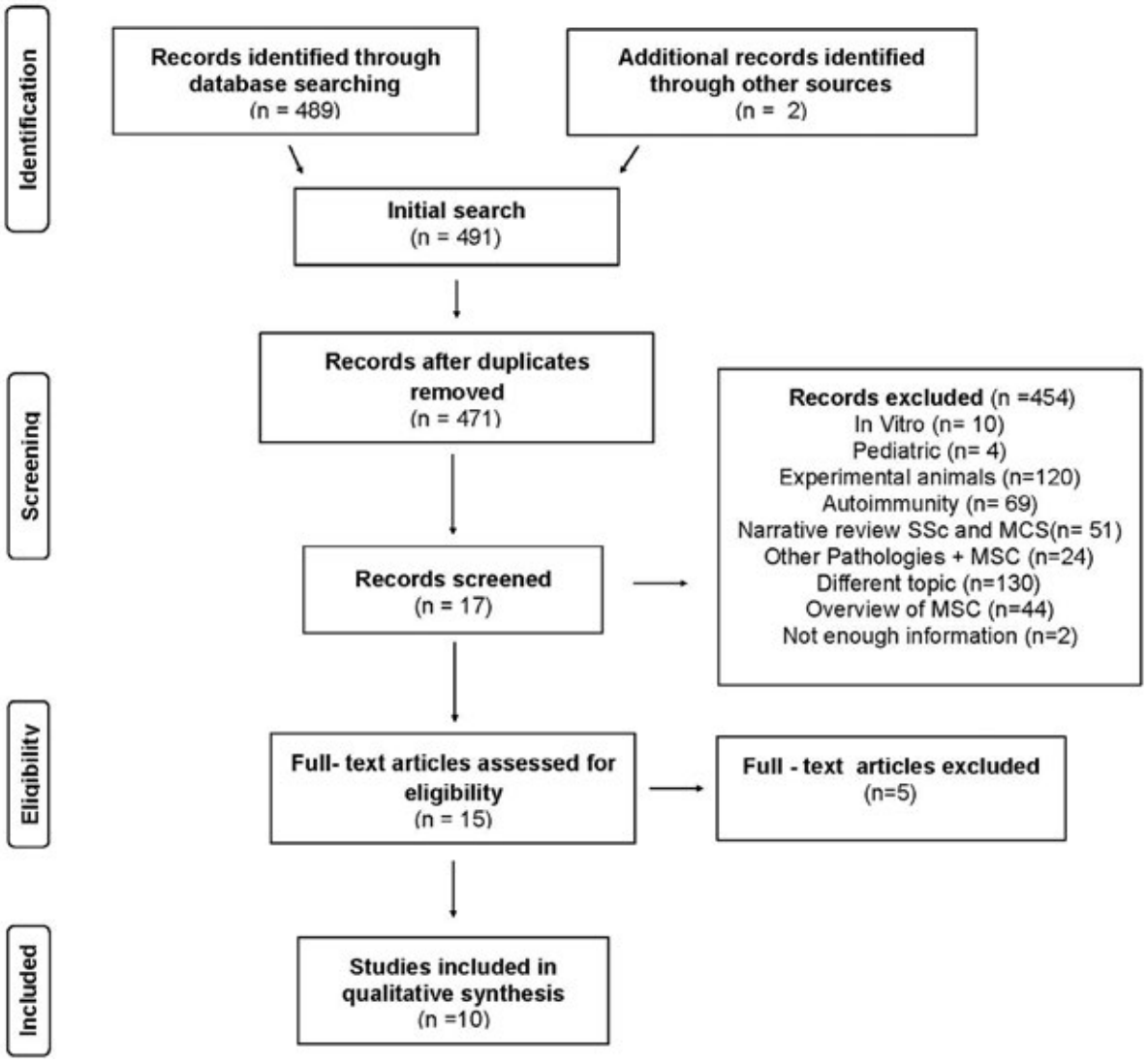

Figure1. PRISMA flowchart

Table 1. Articles included

Reference/ Study design	Population	Intervention	Comparator	Outcome
Serena Guiducci, et al. 2010. / CR	A woman, aged 34 years, with SSc who developed acute gangrene of the upper and lower limbs.	Autologous : bone marrow. 3 IV infusions. First of 0, 9x10^6/ Kg. Second and third of 0,8x10^6/Kg	None	1. **Areas of necrotic skin** were reduced after the first MSC infusion. 2. After the third infusion, angiography showed revascularization of the patient's extremities
Chakr, R. et al. 2013./ **CR**	A 36-year-old. Diffuse SSc (severe scleroderma, Rodnan score 47/51). Skin ulcers and extensive lung fibrosis refractory	Two infusions 2x106/ Kg/infusion. Allogeneic unrelated MSC	None	3 weeks: **death** (shock and respiratory failure)
Kamata, Y. et al 2007. / **CR**	Four SSc patients (49 to 72 yearsold), Longstanding intractable DU and finger necrosis with severe pain	Autologous bone marrow MNCs: 0.5 ml were implanted IM at 20 different sites in palms and/or soles. Peripheral blood MNCs were implanted on the opposite side to compare the difference in effectiveness.	MNCs from bone marrow Vs MNCs from peripheral blood.	1. **Pain:** improved remarkably up to 1 month after implantation of bone marrow or peripheral MNCs to the same extent. 2. **Transcutaneous oxygen pressure and thermogram:** No significant differences were found. 3. **Intra-arterial digital subtraction angiography:** Bone marrow MNCs increased blood flow of the hand Vs peripheral MNCs did not.
Christopeit, M. et al 2008. / **CR**	A 41-year-old female SSc. Painful ulcerations at acral.	MSC from an allogeneic haploidentical-related donor IV of106 MSCs per kg (6 107 MSCs total).	None	Subjective improvement in her condition. (Stiffnes and warming). **Painful ulcerations:** significant decrease in the patient's painful ulcerations (Three months after) **Vascular ultrasound** Marked improvement in the blood circulation of hands and fingers (6 months after) **Rodnan skin score :** reduced from 25 to 11

Table 1. Main characteristics of included studies.

Background/Purpose: Scleroderma (systemic scleroderma or systemic sclerosis, SSc), is a highly heterogeneous autoimmune disease of unknown etiology, with a high rate of therapeutic failure and a progression of the disease. Although recently it has been noted a decrease in mortality It is still high, therefore SSc treatment is considered a therapeutic challenge. The immunomodulatory capacity of the mesenchymal stem cells (MSC), has increased the at-

tention of the scientific community, considering them an alternative therapy that could potentially exceed the efficacy of available therapeutic options; we consider to evaluate through a systematic literature review (SLR), the efficacy, and safety of MSC in patients with SSc.

Methods: A SLR was conducted by two independent researchers (following PRISMA guidelines) in Medline/OVID, Lilacs, Embase and Cochrane/OVID databases (up until February 2019, no language restriction). All clinical study types were considered: Patients over 18 years of age, with SSc who received treatment with MSC (all clinical outcomes). Exclusion criteria: Animal Models, Bone marrow stromal cell transplant, Autologous hematopoietic stem cell transplant, Narrative reviews, Letters to the editor. The specified MeSH terms and keywords were used on the search strategy. Rayyan® Microsoft Excel® and review Manager ® 5.2 software were used for the different steps of the SLR. Data extraction (using a predesigned data extraction form) and quality assessment was also undertaken independently by two reviewers with disagreements resolved by discussion or by a third reviewer. Joanna Briggs Institute quality appraisal checklist was used to appraise the quality of studies. The Oxford Centre classifications for levels of evidence were used.

Results: Once the search was done on electronic bases and the grey literature, it was identified a total of 491 items. Duplicate articles were resolved, obtaining 471. 17 articles were screened by title and abstract, of which 15 articles were chosen and by full text 10 were included (6 case report, 3 Case series, and 1 pilot study). Figure1

The total population corresponds to 62 patients (age range 18 – 75 years old), most of them refractory to conventional treatment. The different interventions and clinical outcomes are shown in Table 1. Overall appraisal through Joana Briggs checkout was inclusion decision. The level of evidence for the majority of studies was 4.

Conclusion: The reported data are too scarce to come to a clear assessment of the benefit/risk on the use of MSC in SSC. Further well-designed, standardized research studies are required assuming the potential challenges of SSc treatment and the great promise of MSC intervention based on its immunomodulatory functions.

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Abstract Number: 2612

Minocycline for Refractory Calcinosis in Systemic Sclerosis: A Single-Centre Observational Cohort Study

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Background/Purpose: Calcinosis represents a major challenge for patients with systemic sclerosis (SSc) for which there is no standard therapy. Minocycline has been proposed for treatment of refractory calcinosis in SSc (1,2). We assessed the possible benefit and adverse events (AE) of minocycline in cohort of SSc patients with calcinosis.

Methods: We reviewed patients with SSc, attending a large tertiary referral centre, that were treated with minocycline for severe calcinosis. Data collected included: gender, scleroderma subtype, autoantibodies, dose and regime of administration of the minocycline, response to the treatment, AE, tolerability and proton pump inhibitors (PPI) use, if any, at the time of the treatment with minocycline. Treatment response was recorded either as subjective clinical improvement of the symptoms associated with calcinosis, or lack of response.

Results: We identified 78 SSc patients treated with minocycline and this cohort reflects the spectrum of refractory calcinosis in SSc with typical ANA association (Table 1). Disease duration in the majority of the cases was longer than 10 years. The prescribed oral dose ranged from 50-200 mg daily and was administered in the majority of the cases for 6-12 weeks in repeated courses. Autoantibody status included typical SSc reactivity with 35.8% anti-centromere antibody (ACA), 15.3% Pm-SCL, 14.1% anti-topoisomerase I, 11.5% anti-RNA polymerase antibody (ARA) (Table 1). 34/78 patients (43.6%) reported clinical improvement in calcinosis related symptoms. Response was similar between different autoantibody groups with exception of patients with ARA, in which clinical improvement was reported in 88.9% of the cases ($p< 0.005$). 25.6% reported minor AE: skin pigmentation after 10 years of use (1 case), gastro-intestinal intolerance (3 patients), elevated liver transaminases (1 case), and unspecified poor tolerance (9 patients). AE were more frequent in the group that did not report benefit (2 vs18). No additional serological abnormalities or autoimmune diseases was observed during treatment period. Different types of PPI were prescribed in 65% of the cohort and this was evenly distributed in the 2 outcome groups.

Conclusion: Within the largest reported series of SSc calcinosis treated with minocycline, our results suggest clinical improvement in almost half of the patients treated with acceptable tolerability. We observed that ACA and late-stage ARA positive patients both had troublesome calcinosis but ARA positive were more likely to respond than other sub-groups. This observation suggests that calcinosis pattern may differ amongst autoantibody defined groups, perhaps reflecting distinct pathogenic mechanisms. Overall, minocycline may be helpful in the management of calcinosis in patients with SSc. A future prospective trial, stratified by SSc autoantibodies, is required to confirm these findings.

Table 1: Clinical features of SSc cohort with calcinosis

			Clinical improvement		No response	
			n	%	n	%
Total		78	34	43.6	44	56.4
Gender						
	Female	75	32	42.7	43	57.3
	Male	3	2	66.7	1	33.3
Subtype						
	Limited	57 (73.1%)	23	40.4	34	59.6
	Diffuse	21 (26.9%)	11	52.4	10	47.6
Antibodies						
	Anti-centromere	28 (35.8%)	12	42.9	16	57.1
	Anti-topoisomerase I	11 (14.1%)	4	36.4	7	63.6
	Anti-Pm-SCL	12 (15.3%)	3	25.0	9	75.0
	ANA positive	9 (11.5%)	3	33.3	6	66.7
	Anti-RNA polymerase	9 (11.5%)	8	88.9*	1	11.1
	Anti-U3 RNP	1 (1.2%)	1	100.0	0	0.0
	Anti-nRNP	2 (2.5%)	1	50.0	1	50.0
	ANA negative	3 (3.8%)	1	33.3	2	66.7
	Anti-Ro	1 (1.2%)	0	0.0	1	100.0
	Unknown	2 (2.5%)	1	50.0	1	50.0

*$p<0.005$.

References:

1) Roberson et al, Ann Rheum Dis. 2003;62:267-269. 2) Balin et al, Arch Dermatol. 2012;148:455-62

Disclosure: C. Fonseca, None; **V. Ong**, None; **C. Denton**, Actelion, 5, Actelion Pharmaceuticals, 5, Actelion, GlaxoSmithKline, Bayer, Sanofi, Inventiva, Boehringer Ingelheim, Roche, Bristol Myers Squibb, CSL Behring, UCB, Leadiant Biosciences, 5, Bayer, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Bristol-Myers Squibb, 5, Corbus Pharmaceuticals, 5, CSL Behring, 2, 5, GlaxoSmithKline, 2, 5, Inventiva, 2, 5, Leadiant Biosciences, 2, 5, Inventiva, 5, Pfizer, 5, Roche, 5, Sanofi, 5, UCB, 5.

Abstract Number: 2613

Hsp90 as a Potential Biomarker of Lung and Skin Involvement in Patients with Systemic Sclerosis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Our previous study demonstrated that Hsp90 is overexpressed in the skin of patients with systemic sclerosis (SSc), in cultured SSc fibroblasts and preclinical models of SSc in a TGF-β dependent manner. We showed that Hsp90 is a new regulator of canonical TGF-β signaling and its inhibition prevents the stimulatory effects of TGF-β on collagen synthesis and dermal fibrosis[1]. The aim of this study was to evaluate plasma Hsp90 of SSc patients and characterize its potential association with skin changes and SSc-related features.

Methods: A total of 92 patients (79 females; mean age 52.7; disease duration 6.0 years; diffuse cutaneous (dc)SSc / limited cutaneous (lc)SSc = 38/54) and 92 age- and sex- matched healthy individuals were included. Plasma Hsp90 levels were measured by ELISA (eBioscience, Vienna, Austria). Data are presented as median.

Results: Plasma Hsp90 levels were increased in SSc patients compared to healthy controls [12.5 (9.6–17.9) vs. 9.8 (7.7–12.4) ng/mL, p=0.0001]. Hsp90 levels in all patients positively correlated with CRP (r=0.271, p=0.015). Furthermore, Hsp90 concentrations were negatively associated with functional parameters of ILD: FVC (r=-0.291, p=0.013), FEV1 (r=-0.248, p=0.036), DLCO (r=-0.290, p=0.012) and SpO_2 (r=-0.317, p=0.038). When adjusted for CRP, these correlations still remained significant in multivariate analysis. Higher Hsp90 concentrations were associated with presence of synovitis [17.6 (15.4 – 24.0) vs. 12.2 (9.3 – 17.3), p=0.039]. In addition, only in patients with dcSSc, Hsp90 levels positively correlated with the mRSS (r=0.437, p=0.006). In a prospective analysis of patients with progressive SSc-ILD treated with 6 (n=21 patients) or 12 (n=14 patients) monthly i.v. pulses of cyclophosphamide (CPA, 10 mg/kg) we did not observe any significant differences between the baseline sample (month 0) and blood drawn after 1,

6 and 12 months. However, baseline Hsp90 was able to predict long-term response after one year of CPA treatment ($DLCO_{m12-m0}$; r=-0.494, p=0.037). Moreover, change in Hsp90 after one month of CPA treatment ($Hsp90_{m1-m0}$) was able to predict the short-term inflammatory response (CRP_{m3-m0}, r=-0.495, p=0.019; ESR_{m3-m0}, r=-0.496, p=0.031). Concentrations of extracellular Hsp90 were not significantly affected by other main clinical parameters of SSc.

Conclusion: We demonstrated higher plasma levels of Hsp90 in SSc patients compared to healthy controls. Concentrations of extracellular Hsp90 increase with higher inflammatory activity, with deteriorated lung functions in ILD and also with the extent and severity of the skin involvement in patients with diffuse cutaneous SSc. These data further highlight the role of Hsp90 as a significant regulator of fibroblast activation and tissue fibrosis in SSc. In addition, Hsp90 could become a predictor of treatment response.

References: [1]Tomcik M et al., Ann Rheum Dis.2014;73(6):1215-22.

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Abstract Number: 2614

Association of Body Composition in Scleroderma Patients with Disease Activity, Serum Levels of Inflammatory Cytokines and Parameters of Nutrition and Lipid Metabolism

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Table 1: Body composition in SSc and HC.

Correlated parameters	SSc (n=59)	HC (n=59)	p-value
BMI (Body Mass Index) (kg/m^2)	22.4±4.3	27.4±8.3	<0.001
BF% (Body Fat %) (iDXA)	32.6±8.2	38.0±7.6	<0.001
BF% (Body Fat %) (BIA)	24.3±7.9	31.3±7.6	<0.001
VF (Visceral Fat) (kg)	0.5±0.5	1.0±0.8	0.001
LBM (Lean Body Mass) (kg, iDXA)	47.8±7.0	51.9±8.4	0.005
LBM (Lean Body Mass) (kg, BIA)	40.9±6.8	45.4±7.3	0.005
ECM/BCM (Extracellular Mass/Body Cell Mass ratio)	1.28±0.4	1.03±0.1	<0.001
BMD (Bone Mineral Density) (g/cm^2)	1.0±0.1	1.2±0.1	<0.001
HAP (Human Activity Profile)	64.1±17.2	84.7±6.6	<0.001

Table 2: Correlation of body composition parameters and clinical features of SSc: disease activity, skin score, quality of life, fatigue and physical ability.		
Correlated parameters	**r**	**p-value**
ECM/BCM:ESSG (European Scleroderma Study Group Activity Score)	0.273	0.044
BF% (iDXA):ESSG (European Scleroderma Study Group Activity Score)	-0.324	0.014
ECM/BCM:mRSS (Modified Rodnan Skin Score)	0.371	0.005
ECM/BCM:CRP (C-reactive Protein)	0.292	0.028
ECM/BCM:ESR (Erythrocyte Sedimentation Rate)	0.302	0.023
ECM/BCM:HAQ (Health Assessment Questionnaire)	0.438	0.001
ECM/BCM:SHAQ (Scleroderma Health Assessment Questionnaire)	0.268	0.044
ECM/BCM:FSS (Fatigue Severity Scale)	0.366	0.004
ECM/BCM:HAP (Human Activity Profile)	-0.644	<0.001
BMD:HAP (Human Activity Profile)	0.28	0.032

Table 3: Correlation of body composition parameters and serum levels of inflammatory cytokines/chemokines (pg/mL).		
Correlated parameters	**r**	**p-value**
LBM (Lean Body Mass) (kg, iDXA; BIA):IL-1b	0.347; 0.289	0.009; 0.034
LBM (Lean Body Mass) (kg, iDXA; BIA):IL-6	0.275; 0.280	0.035; 0.035
LBM (Lean Body Mass) (kg, iDXA; BIA):IL-17	0.387; 0.388	0.002; 0.003
LBM (Lean Body Mass) (kg, iDXA; BIA):EOTAXIN	0.267; 0.299	0.041; 0.024
LBM (Lean Body Mass) (kg, iDXA; BIA):TNF	0.284; 0.267	0.031; 0.047
BMR (Basal Metabolic Rate) (kcal):IL-b1; IL-6; IL-17; EOTAXIN; TNF	0.339; 0.282; 0.383; 0.258; 0.288	0.011; 0.03; 0.003; 0.048; 0.028
TBW (Total Body Water) (%):IL-1b; IL-6; IL-5; IL-8; EOTAXIN	0.441; 0.314; 0.361; 0.367; 0.338	<0.001; 0.017; 0.009; 0.005; 0.01
TNF:VF (Visceral Fat) (kg); FFM (Fat Free Tissue) (kg); A/G (Android/Gynoid ratio); BMD (Bone Mineral Density) (g/cm^2)	0.299; 0.287; 0.369; 0.262	0.023; 0.029; 0.004; 0.047
Table 4: Correlation of body composition parameters and serum parameters of nutrition.		
Correlated parameters	**r**	**p-value**
LBM (kg; iDXA):prealbumin (g/dL); total protein (g/dL)	0272; -0.31	0.037; 0,017
LBM (kg; BIA): C-peptide (ng/mL)	0.306	0.019
FFM (Fat Free Mass) (kg; iDXA):prealbumin (g/dL); total protein (g/dL)	0.033; -0.306	0.033; 0.019
FM (Fat Mass) (kg; BIA):insulin (µU/mL)	0.152	0.036
BF% (Body Fat):albumin (g/dL)	0.281	0.272
VF (Visceral Fat) (kg; iDXA); A/G (Android/Gynoid ratio):total protein (g/dL)	-0.271; -0.318	0.038; 0.014
ECM/BCM (Extraellular mass/ Body cell mass):prealbumin	-0.349	0.007
BMR (Basal Metabolic Rate) (kcal; iDXA):prealbumin (g/dL); total protein (g/dL) BMR (Basal Metabolic Rate) (kcal; BIA):prealbumin (g/dL)	0.278; -0.307 0.316	0.033; 0.018 0.016
Table 5: Correlation of body composition parameters and serum parameters of lipid metabolism.		
Correlated parameters	**r**	**p-value**
BMD (Bone Mineral Density) (g/cm^2): AI (atherogenic Index); HDL (High-density Lipoprotein, mmol/L); apoA (Apolipoprotein A; g/L)	0.289; -0.372; -0.355	0.027; 0.004; 0.006
LBM (kg, iDXA); FFM (Fat Free Mass) (kg, iDXA): triglycerides (mmol/L)	-0.371; -0.305	0.004; 0.019
VF (Visceral Fat) (kg, iDXA); A/G (Android/Gynoid ratio):triglycerides (mmol/L)	-0.321; -0.319	0.013; 0.014
BMR (Basal Metabolic Rate) (kcal; iDXA):triglycerides (mmol/L)	-0.302	0.020

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibrosis of the skin and visceral organs, especially digestive tract, and musculoskeletal involvement in systemic sclerosis (SSc) can have a negative impact on body composition, physical activity and nutritional status. The aim was to assess body composition and physical activity of SSc patients and healthy controls (HC) and the association with selected inflammatory cytokines and laboratory markers of nutritional status in SSc.

Methods: 59 patients with SSc (50 females; mean age 52.5; disease duration 6.7 years; lcSSc:34/dcSSc:25) and 59 age-/sex-matched HC (50 females, mean age 52.5) without rheumatic or tumour diseases were included. SSc patients fulfilled ACR/EULAR 2013 criteria. We assessed body composition (densitometry: iDXA Lunar, bioelectric impedance: BIA-2000-M), physical activity (Human Activity Profile, HAP questionnaire), disease activity (ESSG activity index), serum levels of 27 cytokines/chemokines (commercial multiplex ELISA kit, Bio-Rad Laboratories) and serum levels of chosen parameters of nutrition and lipidogram. Data are presented as mean±SD.

Results: Compared to HC, patients with SSc had significantly lower body mass index (BMI), body fat % (BF%) and visceral fat weight (VF), and also significantly decreased lean body mass (LBM), and bone mineral density (BMD). Compared to HC, patients with SSc had increased extracellular mass/body cell mass (ECM/BCM) ratio, reflecting deteriorated nutritional status and worse muscle predispositions for physical activity (Table 1). Increased ECM/BCM in SSc positively correlated with disease activity (ESSG), skin score (mRSS) and inflammation (CRP, ESR), and was associated with worse quality of life (HAQ, SHAQ), fatigue (FSS), and decreased physical activity (HAP). ESSG negatively correlated with BF%. HAP positively correlated with BMD (Table 2). Serum levels of several inflammatory cytokines/chemokines (Table 3) and markers of nutrition and lipid metabolism were associated with alterations of body composition (Table 4 and 5).

Conclusion: Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our SSc patients, which are associated with the disease activity and physical activity, and could reflect their nutritional status, and gastrointestinal and musculoskeletal involvement. Serum levels of certain inflammatory cytokines/chemokines and markers of nutrition and lipid metabolism were associated with alterations of body composition in SSc patients.

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Abstract Number: 2615

Cumulative Incidence, Survival and Predictors of Pulmonary Arterial Hypertension in Disease Subsets of Systemic Sclerosis: PAH Is Not Increased in Limited vs Diffuse Patients by Adjusted Competing Risk Analysis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary arterial hypertension (PAH) is a life-threatening complication of systemic sclerosis (SSc), thought to be more commonly found among the limited cutaneous (lcSSc) compared to diffuse (dcSSc) disease subtype. Since lcSSc is associated with better prognosis, it is unclear whether a higher occurrence of PAH in lcSSc is a reflection of survival bias, especially when longer disease duration and older age increase the risk of PAH. We assessed survival and incidence of PAH, after accounting for death as competing event, in a large multi-center cohort of SSc patients, and explored predictors of PAH development and survival.

Methods: The study consisted of 1689 SSc patients from Canadian Scleroderma Research Group registry, followed for up to 14 years. To compare cumulative incidence between disease subsets, a competing risk analysis (Fine-Gray model with death as competing event) unadjusted and adjusted for sex, age and SSc-related autoantibodies was performed (SAS 9.4). Survival was analyzed by Kaplan-Meier with Log-Rank (Mantel Cox) test; Cox proportional hazards analysis with demographic, clinical, and laboratory characteristics as predictor variables was used to develop prediction models for PH (SPSS 25.0).

Results: Out of 1431 patients (43% dcSSc, 57% lcSSc, mean age at SSc diagnosis 48±13, follow up 3.5±2.9 yrs., range 1-14 yrs.) with sufficient data for PAH, 157 patients had PAH either confirmed by RHC or post mortem. Regardless of SSc subtype, patients with PAH had more severe disease (by HAQ-DI and patient's global assessment of health) and higher mortality (74% vs 11%, p< 0.0001), compared to those without PAH (Table 1). The lcSSc patients with PAH were older at SSc diagnosis and had a longer disease duration from Raynaud's phenomenon (RP), compared to lcSSc without PAH. The dcSSc patients with PAH had more severe peripheral vascular (SHAQ RP and finger ulcers) and gastrointestinal (SHAQ intestinal problems) vs dcSSc without PAH. 47% of patients with PAH died: 45 lcSSc and 29 dcSSc. Male gender and anti-Scl70 were associated with earlier development of PAH from both SSc diagnosis (p< 0.0001 and p=0.002, respectively) and first non-RP symptom (p< 0.0001 and p=0.001, respectively).To

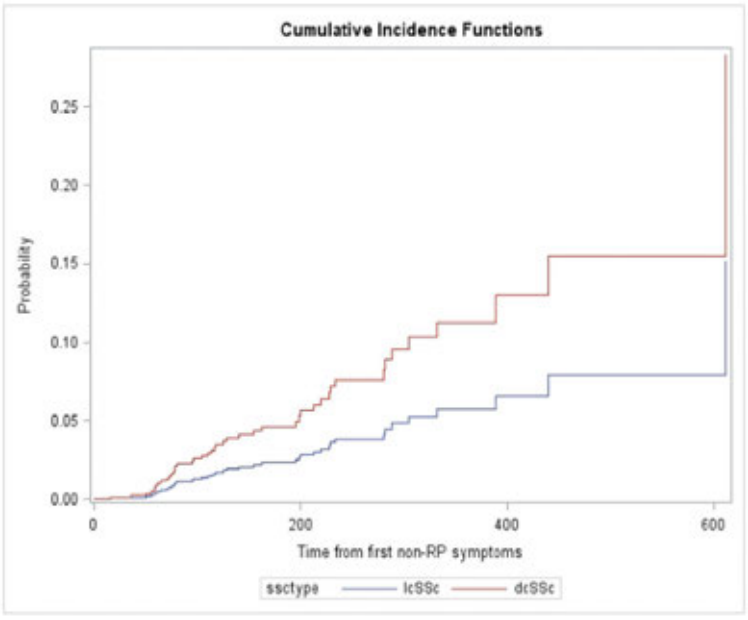

Table 1. Baseline Demographics by Trajectory Groups for SSc-ILD

	SSc, n=1431		dcSSc, n=609		lcSSc, n=816	
	PAH"+" n=157	PAH"-" n=1268	PAH"+" n=62	PAH"-" n=547	PAH"+" n=95	PAH"-" n=721
Female, n (%)	135(86)	1106(87)	45(73)	445(81)	90(95)	661(92)
Age, mean +/- SD yrs	60.6±10.2***	56.8±12.5	56.3±9.4	55.5±12.5	63.4±9.8***	57.9±12.3
Age at diagnosis, mean +/- SD yrs	51.7±13.5**	47.8±13.3	47.6±13.2	46.6±13.2	54.3±13.1***	48.8±13.2
Disease duration from first non-RP symptom, mean +/- SD, mo	12.7±10.5	12.1±9.6	10.9±9.9	11.4±8.9	13.9±10.8	12.6±10.0
Disease duration from RP, mean +/- SD, mo	16.5±12.5**	12.8±11.9	11.9±10.4	10.1±11.2	18.8±12.8**	14.1±12.0
Death, n(%)	74(47)***	139(11)	29(47)***	74(14)	45(47)***	65(9)
Interstitial changes in lungs by HRCT, n(%)	29(88)	80(91)	9(69)	45(88)	20(100)	35(95)
Severity: mild/moderate, %	20/80*	43/58	33/67	47/53	14/86	37/63
HAQ-DI, mean +/- SD	1.1±0.7***	0.8±0.7	1.3±0.7**	0.9±0.8	0.8±0.7***	0.6±0.7
Health status assessed by patients, VAS 0-10	4.7±2.6***	3.4±2.5	5.2±2.5***	3.6±2.5	4.3±2.6***	3.3±2.5
SHAQ Pain	4.0±2.9*	3.4±2.8	4.4±2.9	3.7±2.8	3.7±2.9	3.2±2.8
SHAQ RP	3.3±2.9	2.9±2.9	4.2±2.7*	3.1±2.9	2.8±3.0	2.9±2.9
SHAQ Finger ulcers	2.3±3.2*	1.7±2.8	3.1±3.5*	2.1±3.0	1.7±2.8	1.4±2.6
SHAQ Intestinal problems	2.4±3.0*	1.8±2.8	3.1±3.5*	2.0±2.7	2.0±2.6	1.7±2.5
SHAQ Breathing problems	4.8±2.9***	1.7±2.4	5.2±2.8***	1.9±2.5	4.6±3.0***	1.6±2.3
SHAQ Disease overall	4.7±2.6**	3.3±2.6	5.5±2.6***	3.6±2.5	4.2±2.5***	3.1±2.6

*-p<0.05, **-p<0.001, ***- p<0.0001; NRP - non-Raynaud's phenomenon

Table 1. Characteristics of patients with and without PAH in the entire SSc cohort, as well as separately in dcSSc and lcSSc sub-groups.

		Hazard ratio (95% CIs)	P values
Crude Model	DcSSc vs lcSSc	2.03 (1.13, 3.66)	0.0186
Adjusted model	DcSSc vs lcSSc	1.82 (0.93, 3.57)	0.0818
	Female vs male	0.98 (0.42, 2.32)	0.9660
	Age	1.00 (0.99, 1.02)	0.7041
	Antibodies		
	ACA vs negative	0.95 (0.46, 1.96)	0.8991
	ATA vs negative	1.93 (0.84, 4.42)	0.1198
	Anti-RNAP vs negative	1.24 (0.45, 3.43)	0.6841

Table 2. Sub-distribution Hazard ratio of PAH by Fine-Gray model accounting for death as competing event

avoid left-censoring problem, 113 pts with PAH diagnosed at or before baseline registry visit were excluded from the cumulative incidence and survival analyses. Cumulative incidence of PAH from the onset of first non-RP symptom was higher in dcSSc than in lcSSc after accounting for death as competing event in unadjusted, but not adjusted competing risk analysis (see Table 2 and Figure). Survival (mean±SE) from PAH onset was similar in lcSSc and dcSSc (44±8 mo vs 38±7 mo, p=0.59).

Conclusion: Cumulative incidence of PAH from the onset of first non-Raynaud's phenomenon symptom was not higher in lcSSc, after accounting for death as competing event and adjusting for age, sex and antibody status. Males and a-Scl-70-positive patients developed PAH earlier.

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Abstract Number: 2616

Forced Vital Capacity Trajectories for Systemic Sclerosis-associated Interstitial Lung Disease—Analysis from the University of Michigan Scleroderma Cohort

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial Lung Disease (ILD) is the leading cause of morbidity and mortality in systemic sclerosis (SSc) patients. Forced Vital Capacity (FVC, recorded as % predicted) is a valid outcome measure to assess lung function in patients with ILD. Our objective was to determine whether varying trajectories of FVC in patients with SSc-ILD were associated with different phenotypes of disease.

Methods: Patient data was collected from the electronic medical records of SSc patients seen in the senior author's clinic. SSc patients who completed Chest Computed Tomography (CTs), to evaluate presence of ILD, and had at least 3 FVC measurements that were at least 3 months apart were included in the analysis. A latent class growth analysis model, PROC TRAJ, was used to identify heterogeneous groups among SSc-ILD patients according to their FVC trajectories over time.T-test and Chi-square test were used to compare baseline characteristics among the identified subpopulations.

Results: Out of 484 SSc patients in our cohort, 293 had evidence of ILD on a chest CT of which 86% of which were high resolution CTs (HRCTS). Of the 293 patients with ILD,188 also had at least 3 FVC measurements performed at least 3 months apart. The median (IQR) for follow-up was 42 (25) months and estimated change in FVC among all patients was --2.87% in 100 months. We identified 5 subpopulations with distinct trajectories of FVC% in SSc-ILD patients (group mean trajectories as shown in Figure 1). Groups 1-3 had abnormal baseline FVC% (mean < 80%) whereas Groups 4 and 5 had normal mean baseline FVC% (Table 1). The majority of our cohort fell into Group 2 (27%), Group 3 (22%), or Group

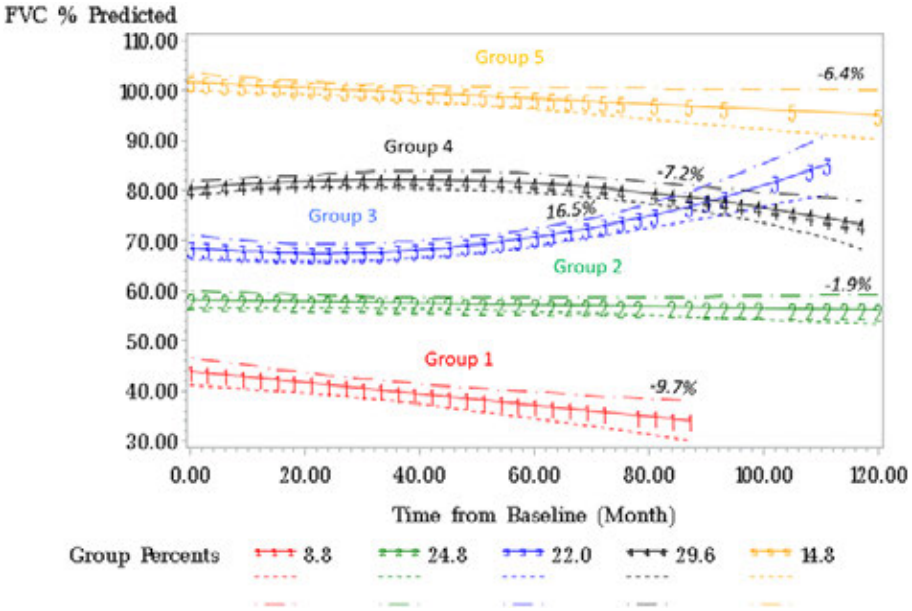

Figure 1. Trajectory Groups for SSc-ILD

Variables		Overall n = 188	Group 1 n = 16	Group 2 n = 50	Group 3 n = 38	Group 4 n = 56	Group 5 n = 28	P-Value
Age in years, Mean (SD)		52.3 (12.2)	47.4 (16.7)	49.7 (12.1)	55.6 (11.3)	53.2 (12.0)	53.2 (9.7)	0.087
Female Sex, n (%)		144 (76.6%)	8 (50.0%)	39 (78.0%)	27 (71.1%)	49 (87.5%)	21 (75.0%)	0.029*
Race, n (%)	White, n (%)	146 (78.1%)	7 (46.7%)	34 (68.0%)	30 (79.0%)	48 (85.7%)	27 (96.4%)	0.002*
	Black, n (%)	9 (15.5%)	7 (46.7%)	13 (26.0%)	5 (13.2%)	4 (7.1%)	0 (0.0%)	
Disease Duration at diagnosis of ILD, median (range)		2.0 (0, 42.9)	1.5 (0, 28.2)	2.4 (0, 13.3)	1.0 (0, 15.4)	2.4 (0.1, 42.9)	2.0 (0.3, 11.5)	0.642
Deceased, n (%)		17 (9.0%)	3 (18.8%)	3 (6.0%)	5 (13.2%)	5 (8.9%)	1 (3.6)	0.369
SSc Classification, n (%)	Diffuse	102 (54%)	8 (50%)	32 (64%)	23 (61%)	24 (43%)	15 (54%)	0.3974
	Limited	65 (35%)	8 (50%)	13 (26%)	10 (26%)	22 (39%)	12 (43%)	
ILD CT Pattern, n (%)	NSIP Pattern	160 (85%)	9 (56%)	36 (72%)	33 (87%)	54 (96%)	28 (100%)	<.0001*
	UIP Pattern	24 (13%)	7 (44%)	12 (24%)	3 (8%)	2 (4%)	0 (0%)	
PFT, % Predicted, Mean	FVC %	72.0 %	41.7%	58.9%	68.9%	81.0%	99.3%	<.0001*
	DLCO %	57.9%	32.7%	45.6%	52.3%	64.8%	80.2%	<.0001*
Autoantibodies	Anti-Centromere	17 (11%)	1 (8%)	3 (7%)	3 (12%)	6 (13%)	4 (17%)	0.7830
	Anti-topoisimerase-1	54 (32%)	4 (27%)	17 (39%)	12 (38%)	15 (29%)	6 (22%)	0.5641

Table 1. Baseline Demographics by Trajectory Groups for SSc-ILD

4 (30%). Group 1 had the lowest estimated FVC% at baseline and greatest decline in estimated FVC%, younger age, higher prevalence of males and African-Americans, and had higher deaths compared to the other groups; the median disease duration was similar in the 5 groups (Table 1) at baseline. Significant differences were found in the patterns of ILD on chest CTs, with Usual Interstitial Pneumonitis (UIP) being more prevalent in low FVC Groups (1 and 2).

Conclusion: Our results suggest 5 distinct groups of patients with SSc-ILD with respect to change in FVC over time. Ongoing work will quantify degree of ILD on chest CTs and the impact of immunosuppressive therapy on long term outcomes in this cohort.

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Abstract Number: 2617

Responsiveness to Change of the Modified Rodnan Skin Score in a Phase I/II Double-Blind Randomized Placebo-Controlled Trial

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Modified Rodnan skin score (mRSS) is used as primary and secondary outcome measure in different trials of diffuse cutaneous systemic sclerosis (dcSSc) [1]. As part of a Phase I/II trial assessing the safety of tofacitinib 5 mg twice a day versus placebo in dcSSc (clinicaltrials.gov NCT03274076[2]), we assessed the performance of 3 different methods of scoring the modified Rodnan skin score (mRSS)[1].

Methods: A 6-month, double-blind, randomized placebo-controlled trial was conducted in dcSSc with disease duration of ≤ 60 months (defined as first non–Raynaud phenomenon) and mRSS ≥ 10 and ≤ 45 units. Efficacy end point included the change in the mRSS at 6 months. Each anatomical area was scored as Global Average score where the examiner takes average of the area; Maximum score where an examiner scores the area according to the most severe local involvement; and the Representative area where the examiner assigns a score that is most representative of the area. Responsiveness to change was evaluated using the effect size (ES) and standardized response mean (SRM). Both indices are ratios of observed change to a measure of variance (also known as signal to noise). For two indices, the numerator is the mean change from the baseline to Month 6 for mRSS and the denominators are the standard deviation at baseline (ES) and the standard deviation of change (SRM). Cohen's rule-of-thumb for interpreting responsiveness to change was applied to determine the magnitude of change where 0.20-0.49 represents a small change, 0.50-0.79 a medium change, and 0.80 or greater a large change.

Table 1: Responsiveness to change in the mRSS using different scoring methods

mRSS	Baseline Mean (SD)	Change at 24 weeks	Effect Size (Mean Δ/SD at baseline)	SRM (Mean Δ/SD of change)
Global Average Score	23.3 (8.4)	-4.9 (6.7)	-0.58	-0.73
Representative Score	23.5 (8.3)	-5.1 (6.3)	-0.61	-0.81
Maximum Score	27.0 (8.8)	-5.8 (6.9)	-0.66	-0.84

Results: 15 participants were randomized (2:1; 10 to TOFA and 5 to PLA) and formed the mITT group; 10 (100%) and 4 (80%) completed the 6-month treatment period in TOFA and PLA groups, respectively. The mean baseline scores were similar in the Global Average and Representative groups and higher in the Maximum group (Table 1). Using the ES, the magnitude of responsiveness was similar in all 3 groups (Medium change). Using the SRM, the magnitude of change was numerically greater in the Representative and Maximum groups (Large change) vs. Global Average (Medium change).

Conclusion: In a small trial of 15 participants, all 3 methods to score the mRSS yielded similar magnitude of responsiveness to change. The mRSS was conducted by experienced researchers in this trial and these results should be validated in a larger trial with multiple centers.

1. Khanna D, et al. JSRD 2017
2. Khanna D, et al Submitted American College of Rheumatology 2019

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Disclosure: E. Bush, None; **V. Nagaraja**, None; **R. Lafyatis**, BioDiscovery- Forbius, 5, Formation Biologics, 5, FBM Therapeutics, 5; **D. Khanna**, Acceleron, 5, 8, Acceleron Pharma, 5, Actelion, 5, 8, Actelion Pharmaceuticals, 5, Astra Zeneca, 5, Bayer, 2, 5, 8, Behring, 5, Blade, 5, Blade Therapeutics, 5, 8, Blade therapeutics, 5, BMS, 2, 5, 8, Boehringer Ingelham, 5, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 5, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Celegene, 5, Celgene, 5, 8, ChemomAB, 5, ChemomAb, 5, CiviBioPharma, Inc., 3, Corbus, 5, Corobus, 5, Corpus, 5, CSL Behring, 5, 8, Curizon, 5, Curzion, 5, Cytori, 5, 8, Eicos, 4, Eicos Sciences, 4, Eicos Sciences, Inc, 4, Eicos Sciences, Inc/ CiviBioPharma, Inc, 1, 4, Eicos Sciences, Inc/ CiviBioPharma, Inc., 1, Eicos, Inc, 4, Eicos, Inc., 5, 8, Eicos, INC., 4, Galapagos, 5, Genentech, 5, Genentech/Roche, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 2, 5, Mitsubishi Tanabe Pharma, 5, Mitsubishi Tanabe Pharma Dev America, 5, Mitsubishi Tanabe Pharma Development America, 5, Mitsubishi Tanabi, 5, NIH K24 and R01, 2, NIH / NIAMS K24 AR-063120, 2, NIH/NIAMS R01& K24, 2, Pfizer, 2, 5, Sanofi, 5, Sanofi Aventis, 5, Sanofi-Aventis, 5, 8, Sanofi-Aventis/Genzyme, 5, UCB, 5, UCB Pharma, 5.

Abstract Number: 2618

Anti-RNPC-3 Antibodies Are Associated with Nuclear Speckled Immunofluorescence Pattern and Enriched in Triple Negative Systemic Sclerosis Patients

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-nuclear antibodies (ANA) are present in approximately 90% of sera from systemic sclerosis (SSc) patients and play an important diagnostic and prognostic role in SSc. Besides anti-Scl-70 (topo I), anti-centromere and anti-RNA Polymerase III which are included in the SSc classification criteria, several other antibodies can be found, some of which clearly associate with defined disease phenotypes. Anti-U11/12 Ribonucleoprotein (RNP) antibodies have been reported in a small portion of SSc patients especially with pulmonary fibrosis. RNPC-3, also known as U11/U12 small nuclear ribonucleoprotein, is a 65 KDa protein that has been reported as an autoantibody target and to be associated with a nuclear speckled indirect immunofluorescence (IIF) pattern on HEp-2 cells. Recently we described a novel linear B-Cell epitope that was used for the development of an autoantibody assay to detect a subpopulation of anti-RNPC-3 antibodies. Our aim in this study was to determine the prevalence of anti-RNPC-3 antibodies in a cohort of well characterized SSc patients and to assess clinical associations.

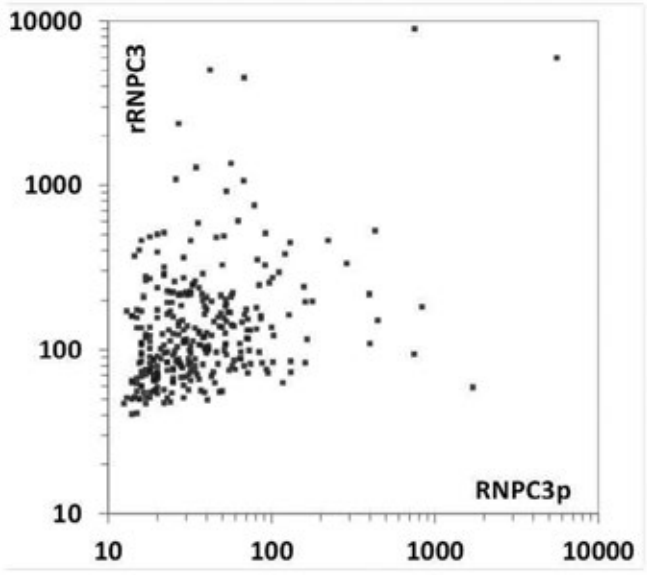

Figure 1
Comparison of rRNPC-3 and RNCP-3p

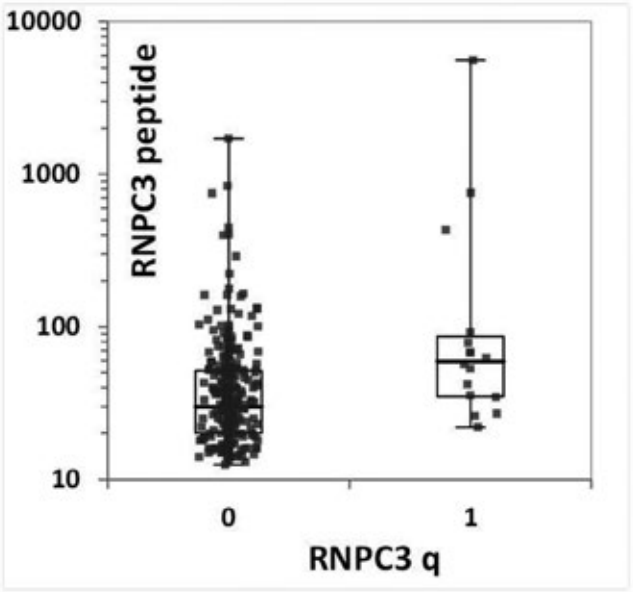

Figure 2
Association of antibodies to recombinant RNPC-3 and the novel linear B-cell epitope.

Table Clinical characteristics of anti-RNPC-3 positive and negative patients (rRNPC-3=recombinant RNPC-3; RNPC-3p=RNPC-3 peptide)

	RNPC-3p (+) (n=15)	# of missing	RNPC-3p (-) (n=284)	# of missing	*P* values	rRNPC3 (+) (n=15)	# of missing	rRNPC-3 protein (-) (n=284)	# of missing	*P* values
ILD, n (%)										
Baseline	5 (33.3%)	0	75 (27.3%)	9	0.567	7 (46.7%)	0	73 (26.6%)	9	0.133
Last f/u	4 (44.4%)	6	62 (33.7%)	100	0.495	6 (50.0%)	3	60 (33.2%)	103	0.345
FVC, mean ± sd										
Baseline	90.1 ± 21.6	0	93.5 ± 19.5	28	0.515	88.5 ± 14.3	0	93.6 ± 19.8	28	0.329
Last f/u	74.6 ± 22.4	8	90.9 ± 21.3	155	0.059	82.2 ± 16.5	5	90.7 ± 21.8	158	0.210
DLCO, mean ± sd										
Baseline	65.7 ± 20.5	1	67.7 ± 19.0	45	0.607	65.1 ± 18.4	2	67.7 ± 19.2	44	0.624
Last f/u	57.0 ± 20.1	8	63.6 ± 21.3	160	0.459	64.0 ± 19.1	5	63.2 ± 21.5	163	0.966
GI 14 at baseline, mean ± sd	3.0 ± 3.0	0	4.4 ± 3.1	26	0.069	4.4 ± 3.1	1	4.4 ± 3.1	25	0.895
Medsger for GI at baseline, mean ± sd	1.6 ± 0.8	0	2.0 ± 0.7	4	0.068	1.7 ± 0.7	0	1.9 ± 0.8	4	0.211
Medsger for GI ≥ 2 at baseline, n (%)	12 (80.0%)	0	254 (90.7%)	4	0.173	13 (86.7%)	0	253 (90.4%)	4	0.648
SIBO at baseline, n (%)	0	0	36 (12.8%)	2	0.230	0	0	36 (12.8%)	2	0.230
Total parenteral nutrition at baseline, n (%)	0	1	7 (2.5%)	4	1.000	0	0	7 (2.5%)	5	1.000
Esophageal dilatation at baseline, n (%)	0	0	31 (11.2%)	7	0.382	3 (20.0%)	0	28 (10.1%)	7	0.205
Cancer at all visit, n (%)	0	0	36 (12.7%)	0	0.230	2 (13.3%)	0	34 (12.0%)	0	0.699

Methods: A total of 299 SSc patient samples from a large research cohort enriched for samples with a nuclear speckled IIF pattern were tested using a novel particle-based multi-analyte technology (PMAT) for antibodies to recombinant RNPC-3 (rRNPC-3) and the newly described RNPC-3 derived peptide (RNPC-3p). Immunoadsorption experiments by liquid phase inhibition was carried out to estimate the contribution of antibodies to the novel B-cell epitope compared with the whole anti-RNPC-3 antibody response. Clinical and serological associations were ascertained.

Results: The levels of antibodies to rRNPC-3 and RNPC-3p correlated moderately (See Figure, Spearman=0.32, p=0.0001; chi-squared p=0.0002). As expected, levels of anti-RNPC-3p antibodies were higher in patients positive for the recombinant antigen (p=0.0013). Both rRNPC-3 and RNPC-3p were associated with a speckled pattern. Immunoadsorption showed significant inhibition using the RNPC-3 derived peptide, but not with a control peptide. Prevalence and levels of anti-RNPC-3 antibodies were higher in anti-Scl-70, anti-Cenp, and/or anti-RNA Pol III triple negative patients [10/106 (9.4%) *vs.* 6/193 (3.1%), p=0.03; and median titers 122.0 vs. 107.5, p=0.08]. Patients positive for anti-RNPC-3 antibodies tended to have more interstitial lung disease, especially when considering follow-up. None of the clinical associations reached statistical significance most likely due to limited sample size and prevalence of anti-RNPC-3 antibodies.

Conclusion: Our study confirms the association of anti-RNPC-3 antibodies with the nuclear speckled IIF pattern and their increased prevalence in SSc triple negative patients (anti-Scl-70, anti-centromere, and anti RNA-Pol III antibodies). The previously identified RNPC-3 peptide represents a significant target of anti-RNPC-3 antibodies, but does not capture the entire reactivity indicating the presence of additional epitopes. Further studies are needed to verify the clinical utility of the assays.

Disclosure: M. Mahler, Inova Diagnostics, 3; **F. Roup**, Inova Diagnostics, 3; **C. Bentow**, Inova Diagnostics, 3; **M. Hudson**, None; **M. Baron**, None; **M. Choi**, None; **M. Fritzler**, Alexion Canada, 7, BioRad, 5, Dr. Fooke Laboratorien GmbH, 5, Euroimmun GmbH, 5, 7, ImmunoConcepts, 7, Inova Diagnostics, 5, 7, 8, Inova Diagnostics Inc. San diego, CA, 5, Inova Dx, Mikrogen GmbH, 5, Werfen International, 5.

Abstract Number: 2619

Rituximab for Eosinophilic Granulomatosis with Polyangiitis: A Systematic Review of Observational Studies

Giovanni Pomponio,[1] Vincenzo Menditto,[2] Giulia Rossetti,[3] Alessia Angeletti,[3] Diletta Olivari,[3] and Armando Gabrielli[3],
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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: More than 40 studies containing data about adults affected by EGPA treated with Rituximab (RTX) have been published in the last decade. Nevertheless, due to observational design and low methodological quality, its efficacy and safety is still unclear. We conducted a systematic review of the available clinical studies in order to examine the case for undertaking a randomized trial by providing an explicit evaluation of the weaknesses of available research and to provide findings useful to inform the design of a future trial.

Methods: MEDLINE, SCOPUS, Web of Science and Cochrane Central Register were searched up to end of January 2019 without language restriction. Reference lists of pertinent studies were analyzed through manual search to identify additional relevant studies. Missing information or data were required by email to corresponding authors. Articles and conference abstracts including at least one patient affected by EGPA, treated with RTX and assessing

clinical outcomes were included and analyzed by four independent investigators and data extracted in a structured form. Following data were collected: patients' characteristics (age, sex), sample size, diagnostic criteria used, baseline and final (at latest follow-up) vasculitis activity score, disease extension (organ involvement) and refractoriness, Rituximab schedule of administration, co-treatments, median follow-up (months), complete and partial remission rate (according to given definitions) and other secondary outcomes: steroid reduction (PDN≤7.5 mg/die), relapses, serious adverse events, infections, neoplasms and deaths.

Results: A total of 1973 studies were identified, 43 of which met inclusion criteria (see figure 1), accounting for 395 EGPA patients treated with Rituximab. All of the studies were case reports, case series or retrospective cohort studies. Analysis of retrieved data is shown in table 1 and table 2. Overall, 46,1% and 17,2% patients achieved complete and partial remission respectively. A number of counfonding factors affecting the probability to reach remission has been identified and discussed. In particular, the use of standardized criteria for diagnosis and remission definition, the 'ad hoc' outcome selection, and the number of enrolled patients strongly influence the likelihood of response. In particular, case reports tend to overestimate efficacy of the treatment due to publication bias.

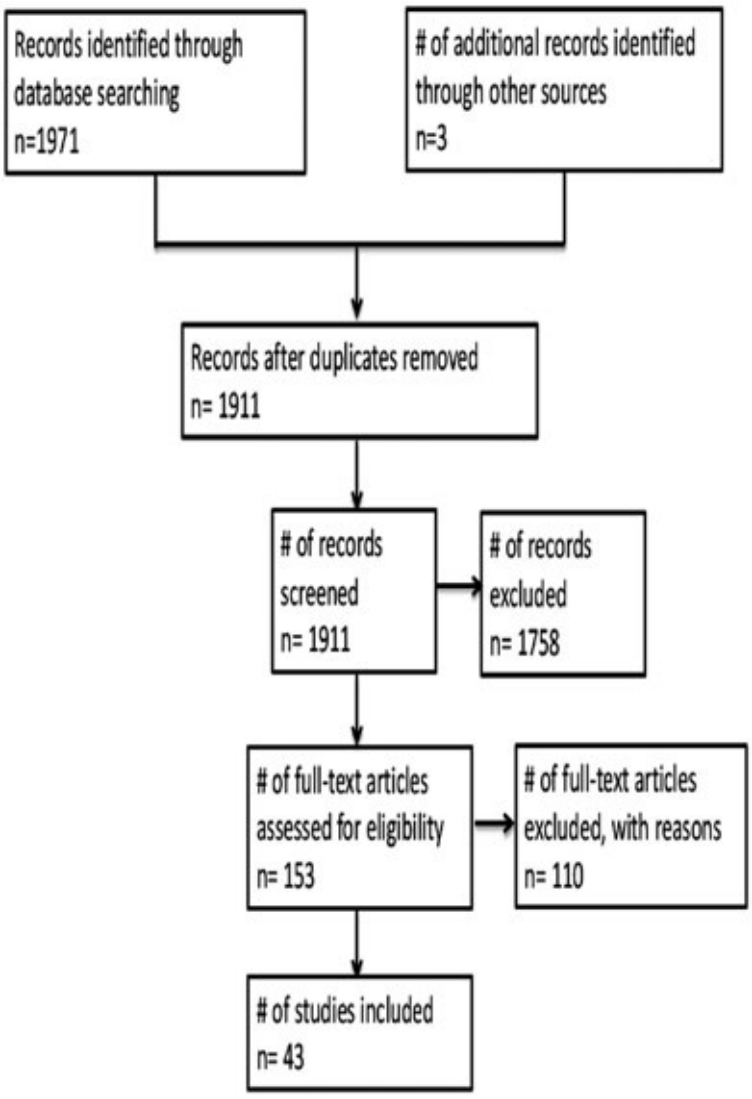

Figure 1: search algorithm

	Number of evaluable patients	Results
Gender, female, n (%)	249	125 (50,2)
Age in years, media (range)	41	46,35 (16-72)
EGPA diagnosis with ACR criteria, n (%)	144	54 (37,5)
ANCA positive type, n (%) p-ANCA c-ANCA ANCA positive (not specified)	265	135 (50,9) 79 (29,8) 21 (7,9) 35 (13.2)
Baseline BVAS, media (range)	143	7,98 (4-32)
BVAS at the end of follow-up, media (range)	67	3,95 (0-9)
RTX treatment, n (%) as 1st line ≥2nd line	300	 92 (30,7) 208 (69,3)
RTX regimen, n (%) 1000 mg x2 375 mg/m²/wk x4 375 mg/m²/wk x3 500 mg/m²/wk x4 500 mg/m²/wk x2 800 mg/m²/wk x2	149	 101 (67,8) 39 (26,2) 1 (0,7) 4 (2,7) 3 (2) 1 (0,7)

Table 1. Characteristics of population and treatment regimens. EGPA: Eosinophilic Granulomatosis with PolyAngiitis; ANCA: Aanti-Neutrophil Cytoplasmatic Antibodies; BVAS: Birmingham Vasculitis Activity Score; RTX: Rituximab

	Number of evaluable patients	Results
Complete remission, n (%) defined as BVAS=0, n (%)	395	182 (46,1) 107 (27,1)
Partial remission, n (%) defined as reduction of BVAS≥50%, n (%)	395	68 (17,2) 37 (9,4)
Steroid reduction ≤7,5 mg/die, n (%)	130	97 (74,6)
Relapse, n (%)	293	89 (30,4)
Death, n (%)	395	2 (0,5)
SAEs/infection/neoplasia, n (%)	280/306/250	26 (9,3) /61 (19,9)/15 (0,06)
Duration of follow-up in month, media (range)	388	38,98 (3-119)

Table 2. Main results from the 43 included studies. BVAS: Birmingham Vasculitis Activity Score; SAEs: Serous Adverse Events

Conclusion: Rituximab might be an effective therapeutic alternative in severe refractory EGPA. However, despite high number (considering the low prevalence of the disease) of RTX treated EGPA patients described in available literature, the high risk of positive effect overestimation which tipically affects case reports and low quality observational studies, as well as flaws in outcome selection, definition and measurement hinder the possibility to achieve reliable conclusions about efficacy and safety of this therapeutic approach. Results from this systematic review could be hopefully used to better design future clinical trials to clarify this relevant topic.

Disclosure: G. Pomponio, None; **V. Menditto**, None; **G. Rossetti**, None; **A. Angeletti**, None; **D. Olivari**, None; **A. Gabrielli**, None.

Abstract Number: 2620

Effects of Tofacitinib Suppressed Pulmonary Vascular Remodeling of Allergic Vasculitis in a Murine Model

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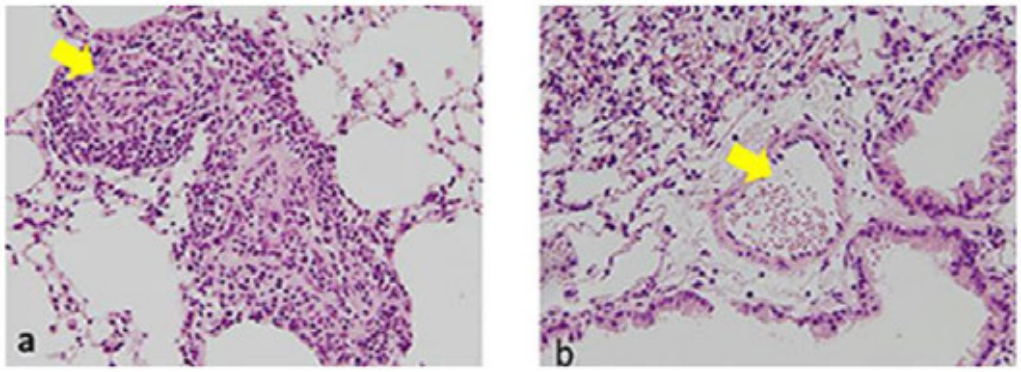
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: We reported allergic granulomatous vasculitis with eosinophil infiltration in an asthma model of C57BL/6 sensitized with ovalbumin (OVA). TGF-btea and IL-6 are thought to play an important role in fibroblasts proliferation and is critical to vascular remodeling in vasculitis. Tofacitinib inhibits vascular endothelial cells proliferation and canalization.

To elucidate the role of tofacitinib in vascular remodeling of allergic granulomatous vasculitis, we examined the effects of tofacitinib on the vasculitis of the murine model.

Methods: C57BL/6 mice (6-8 weeks) were sensitized with ovalbumin (OVA) and alum. The positive controls (n=9) were exposed to aerosolized OVA daily for 7 days. The other group of mice (tofacitinib treated mice(n=9)) were administered with tofacitinib (100mg/kg intraperitoneal administration) in parallel with daily exposure to aerosolized OVA for 7 days. On 7th day, bronchoalveolar lavage (BALF) was performed and the lungs were excised for pathological analysis. Cytokines in BALF were measured.

Results: The total cell number and the number of Eosinophils in BALF on the 7th day were decreased significantly in the tofacitinib-treated mice compared with those of the control-positive mice. The blood eosinophil counts in the



a. Positive control: Totally occluded pulmonary artery by intraluminal myofibroblasts in the OVA-sensitized mice with exposure to OVA in 7th day. (HE staining) b. Tofacitinib: Intraluminal myofibroblast accumulation was not observed in the OVA-sensitized mice with exposure to OVA and treated with tofacitinib in 7th day. (HE staining).

positive control increased after OVA inhalation. The blood eosinophil counts in the tofacitinib treated mice were lower on the than those in the positive control.

The concentrations of IL-4, IL-5, IL-6 and TGF-beta in BAL fluids reduced significantly in the tofacitinib treated group. The pathological scores reduced significantly in the tofacitinib treated group compared to the positive control group. Intra luminal infiltration and proliferation of Ki67 positive myofibroblasts, IL-6 positive cell and α-SMA positive cells in pulmonary arteries were reduced dramatically in the tofacitinib treated group compared to the positive control group.

Conclusion: Tofacitinib suppressed pulmonary vascular remodeling in a murine model of allergic vasculitis with eosinophil infiltration. Tofacitinib is a hopeful therapeutic drug for Eosinophilic granulomatosis with polyangiitis.

Disclosure: Y. Oikawa, None; **K. Yamauchi**, None; **M. Maemondo**, None.

Abstract Number: 2621

Association Between Outcome Renal, Clinical Variables and Findings of Renal Biopsy in Patients with ANCA Vasculitis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated Poster I
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Session Time: 9:00AM–11:00AM

Background/Purpose: In associated ANCA vasculitis (AAV), rapidly progressive glomerulonephritis (GN) is one of the most serious complications. In 40% of cases they progress to chronic kidney disease (CKD), others to hemodialysis (HD) or death. According to the classification of the European AAV group (EUVAS), the histopathological findings of the biopsy can predict the outcome renal with better results in the focal class, followed by the mixed and sclerotic class. **Our objective is to evaluate the association between outcome renal and histopathological findings of patients with AAV**

Methods: Cohort study, retrospective patients with AAV (ACR 1990 / Chapell Hill 2012) and rapidly progressive GN of three centers of high complexity in the Autonomous City of Buenos Aires between January 2012 - December 2018. Demographic, clinical, analytical variables were recorded and follow-up for one year, at diagnosis. The immunoserology patterns (ANCA and PR3 / MPO), Five Factor Score (FFS), BVASv3 (0-63) and VDI (0-64) per year are evaluated. Renal biopsies (optical microscopy and immunofluorescence) were reviewed. The **glomerular lesions** were classified according to EUVAS and its association with CKD, HD and death was evaluated

Table 1.

Clinical Variable	Basal mean n=33	Year mean n=33
Basal creatinine (Crb)	3 mg / dL (SD +/- 2.8 IC95% 1.8-4.1)	2.18 mg/dL(SD +/- 2.6 IC95% 1.14-3.2)
eGFR	32.5 ml /min/ 1.73m2 (SD +/- 26 IC95% 22-43)	43 ml / min / 1.73m2 (SD +/- 30 IC 95% 31-55)
Proteinuria 24 hs	1,88 g/L(SD +/-1,17 IC95% 1,48-2,28)	

Results: 33 patients were included, 57.6% males. Mean age 51 (SD +/- 16 IC 95% 45-58). GPA 65%, and MPA 33%. ANCAc n: 20, PR3 52%. ANCAp n: 13, MPO 30%. Histopathology: Glomerular lesions: **Focal** 18%, **Crescentic** 27% **Sclerotic** 12% and **Mixed** 43%. **Grade 1**: 24%, **grade 2**: 27% and **grade 3**: 49%. Fibrinoid necrosis in 61%. **Global Interstitial Commitment** (tubilitis, tubular atrophy, fibrosis and inflammatory infiltrate) 97%; **grade 0**: 12%, **grade 1**: 58%, **grade 2**: 30%. **cell infiltrate** in 85% monomorphonuclear 73%, polymorphonuclear 6%. **Vascular damage** (subintimal sclerosis) 79%: **mild** 46%, **moderate** in 36% and **severe** 11%. The patients presented severe clinical compromise with a median BVASv3 15 (RIC 7-48). FFS: I: 24%; II: 42%; III: 18%; IV: 6%. PCR 23 (RIC 1-321) and VDI at year 3 (RIC 2-5), the baseline clinical variables and at one year are summarized in Table 1.

HD requirement at the start of 36%, achieving independence of HD (HDI) per year by 30%, the variables associated with HDI were Crb and eGFR p = 0.014 and p = 0.012 respectively and focal class with p = 0.032. The CKD was 33%, with the mixed class being the most associated p = 0.017. Relapse in 30% associated with the type of glomerular lesion with p = 0.006. Death 4 (activity and infection). The association between tubulointerstitial involvement and CKD and HDI was not significant.

Conclusion: Crb and the glomerular filtration rate were the best predictors of CKD and HDI. The mixed class was associated with CKD. We found an association between the focal class and the HDI. Relapses are associated with the type of glomerular pattern. The percentage of progression to CKD was low and high rate of HDI. There was no association between tubulointerstitial involvement and progression to CKD.

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Abstract Number: 2622

A Single Center Retrospective Analysis of Efficacy and Safety Between Low-Dose versus High-Dose Rituximab as Remission Induction Therapy with ANCA-Associated Vasculitis

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Background/Purpose: Rituximab therapy for ANCA-associated vasculitis (AAV) patients was covered by insurance from 2013 in Japan. Administration of four once-weekly doses of 375 mg/m2 rituximab (RTX) has been indicated for ANCA-associated vasculitis (AAV) as remission induction therapy. However, randomized controlled trial for Japanese AAV patients have never been conducted, although Japanese AAV patients are characterized by the predominance of elderly patients with microscopic polyangiitis (MPA). To compare the efficacy and safety between low-dose versus high-dose RTX therapy as remission induction therapy in Japanese patients with AAV.

Methods: A single center retrospective analysis of 34 consecutive AAV patients with RTX therapy was performed from 2013 to 2019. 25 patients were treated with low-dose RTX infusions, while 9 patients with high-dose RTX infusions. The primary endpoints were complete remission (CR) rate, defined as Birmingham Vasculitis Activity Score (BVAS)=0 and prednisone < 7.5 mg/day, survival rate and severe adverse effects at 6 months. Fisher's exact test were used for categorical data and Mann-Whitney U test for continuous data to compare background data. Roglank test was used to complete remission rate, compere survival rate and severe adverse effects at 6 months.

Results: The frequency of elder (79 vs 71, P=0.045), female (64% vs 21%, P=0.07) patients were significantly high in low-dose group and the duration of hospitalization (22 days vs 38 days, P=0.339) was shorter in low-dose group, whereas the frequency of smoking (36% vs 89%, P=0.017) was significantly higher in high-dose group and the ANCA titer (93.9 vs 176.0, P=0.081) and PSL dose (30mg/day vs 40mg/day, P=0.062) was higher in high-dose group.

Compared with low-dose group with high-dose group, there was no significant difference with complete remission rate (58% vs 50%, P=0.485), survival rate (87.6% vs 88.9%, P=0.87) and probability of remaining free of severe adverse effects (61.5% vs 88.9%, P=0.176).

	Low dose(n=25)	High dose(n=9)	P=
Age, median	79 (57-85)	71 (64-82)	0.045
Sex, male (%)	9 (36%)	8 (89%)	0.017
Diagnosis, MPA(%)	21 (84%)	8 (89%)	1
BVAS	12 (6-32)	14 (8-35)	0.813
Severity (EUVAS)			
Severe (%)	11 (44%)	4 (44%)	1
Generalized (%)	14 (56%)	5 (56%)	
Smoking history (%)	9 (36%)	8 (89%)	0.017
Duration of hospitalization, days	22 (2-119)	38 (14-91)	0.339
Interstitial pneumonia (%)	13 (55.6%)	5 (52%)	1
RPGN (%)	23 (92%)	9 (100%)	1
Hemodialysis induced (%)	4 (16%)	0 (0%)	0.56
Creatinine, mg/dL	2.74 (0.54-7.84)	2.70 (1.10-7.60)	0.759
ANCA titer, IU/mL	93.9 (1.0-300)	176.0 (75.6-300)	0.081
PSL dose, mg/day	30 (5-60)	40 (9-60)	0.062
mPSL pulse (%)	15 (60%)	6 (67%)	1
Other ISAs (%)	9 (36%)	5 (56%)	0.435

Backgrounds

	Low dose	High dose	P=
Complete remission rate (%)	58%	50%	0.485
Survival rate (%)	87.6%	88.9%	0.87
Probability of remaining free of severe adverse effects (%)	61.5%	88.9%	0.176

Results

Conclusion: Our retrospective analysis indicated that cumulative CR rates and 6 month-survival rates did not significantly differ between low-dose versus high-dose RTX as remission induction therapy in Japanese AAV patients, mostly elderly MPA female patients, although there was no significant difference in severe adverse effects such as opportunistic infections between them.

Disclosure: K. Hirose, None; **M. Hirata**, None; **A. Ueno**, None; **M. Yamamura**, None.

Abstract Number: 2623

Abnormality of Percentages and Absolute Numbers of CD4$^+$ Memory and Regulatory T Subset Cells in ANCA-associated Vasculitis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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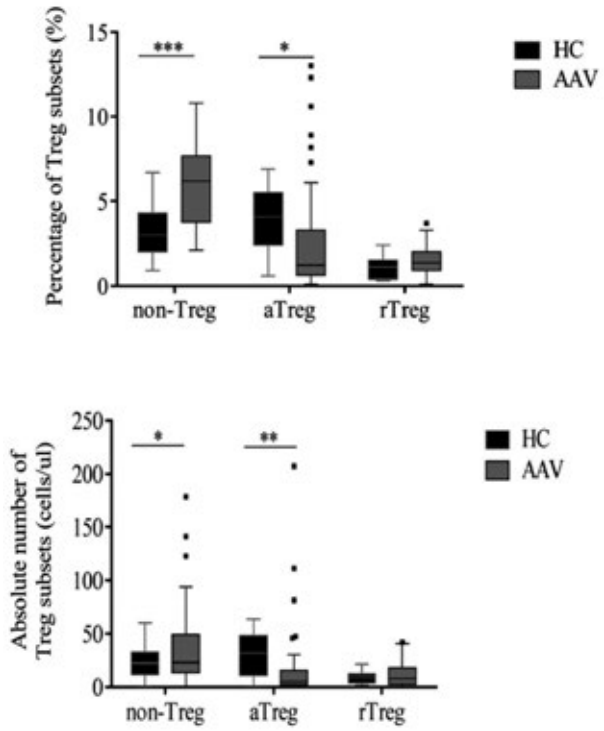
Background/Purpose: CD4+ T cell subsets control immune system in check and prevent autoimmunity by keeping a balance among them. However, their levels of blood in ANCA-associated vasculitis (AAV), especially absolute numbers, are still remains unclear. We therefore analyzed the percentages and absolute numbers of CD4+ T cell subsets as well as their diagnostic values in patients with AAV.CD4+ T cell subsets control immune system in check and prevent autoimmunity by keeping a balance among them. However, their levels of blood in ANCA-associated vasculitis (AAV), especially absolute numbers, are still remains unclear. We therefore analyzed the percentages and absolute numbers of CD4+ T cell subsets as well as their diagnostic values in patients with AAV.CD4+ T cell subsets control immune system in check and prevent autoimmunity by keeping a balance among them. However, their levels of blood in ANCA-associated vasculitis (AAV), especially absolute numbers, are still remains unclear. We therefore analyzed the percentages and absolute numbers of CD4+ T cell subsets as well as their diagnostic values in patients with AAV. CD4+ T cell subsets control immune system in check and prevent autoimmunity by keeping a balance among them. However, their levels of blood in ANCA-associated vasculitis (AAV), especially absolute numbers, are still remains unclear. We therefore analyzed the percentages and absolute numbers of CD4+ T cell subsets as well as their diagnostic values in patients with AAV.

Figure 1



Methods: AAV patients (n = 54) and healthy controls (HCs) (n = 19) were enrolled. Of them, 38 patients were renal vasculitis. Proportions and absolute numbers of $CD4^+$T cell subsets were determined by flow cytometry. The diagnostic value for Treg subsets was evaluated by the areas under the receiver operating characteristic curves (AUC). Correlations of clinical indicators with the $CD4^+$ T subsets were systematically analyzed.

Results: Percentages of activated Treg cells (aTreg, p=0.044) in AAV patients were decreased, but those of effector memory T-cell subpopulation (TEM) (p< 0.001) and Treg cells (p=0.001) were increased. Similar results were observed when we compared absolute numbers of the above corresponding cells in AAV patients and HCs, except TEM. Furthermore, the percentage of aTreg (p=0.043) was decreased while that of Th17 cells (p=0.027) was increased in renal vasculitis patients. A significant correlation was observed between the ratio of Th17 to Treg subset and creatinine or BUN in renal vasculitis patient. Interestingly, the AUC of the aTreg improved significantly the diagnostic potential of AAV. In addition, we found that cytokine IL-2 and IL-4 exhibited a downward while IL-6, IL-10, TNF-α, IFN-γ and IL-17A trend upward in AAV patients.

Conclusion: We identified decrease in aTreg cells and increase in $T_{EM,}$ which associated with the ANCA-related immune response. Correcting the above-mentioned T cell abnormality will potentially be powerful therapeutic tools for AAV.

Disclosure: Y. Wang, None; **X. Zhao**, None; **C. Gao**, None; **J. Luo**, None.

Abstract Number: 2624

Comparison Between Long-Term and Conventional Rituximab-Maintenance Treatments: Results of a Placebo-Controlled Randomized Trial

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SESSION INFORMATION

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Background/Purpose: MAINRITSAN-trial results[1] demonstrated rituximab superiority (500 mg on days 0 and 14, then at months 6, 12 and 18) to azathioprine to maintain remission of ANCA-associated vasculitides (AAVs). In that trial, at month 28, 5% of rituximab-treated patients had experienced a major relapse but, at month 60 of follow-up, major relapse-free survival was 49.4%.[2]

The MAINRITSAN3 trial (NCT02433522) aimed to evaluate the efficacy of long-term rituximab administration to prevent AAV relapses in patients in remission after a first phase of rituximab-maintenance therapy.

Methods: To be included, patients had to have been enrolled in the MAINRITSAN2 trial[3] (randomized–controlled trial comparing 2 rituximab-infusion strategies for patients with newly diagnosed or relapsing granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) in complete remission after induction therapy: tailored-arm patients received a 500-mg rituximab infusion at randomization, with rituximab reinfusion only when CD19+ B lymphocytes or ANCA had reappeared or ANCA titer rose markedly; controls received a fixed 500-mg rituximab infusion on days 0 and 14 postrandomization, then at months 6, 12 and 18) and be in complete remission at the end of MAINRITSAN2 at month 28. At that time, patients were enrolled in MAINRITSAN3 and re-randomized to receive 4 more rituximab infusions, at inclusion and months 34, 40 and 46, or a placebo. Premedication for all patients comprised acetaminophen (1000 mg), methylprednisolone (100 mg) and dexchlorpheniramine (5 mg).

The primary endpoint was relapse-free survival at 56 months. Relapse was defined as new or reappearing symptom(s) or worsening disease with BVAS >0 and was evaluated by an independent Adjudication Committee.

Results: Between March 2015 and April 2016, 97 patients were enrolled in MAINRITSAN3 in 45 centers in France: 50 to receive rituximab and 47 placebo-group controls. Their mean age was 63.9 years, 35.1% were women, 68 (70.1%) had GPA and 29 (29.9%) had MPA, and 50% were ANCA-positive at enrollment. Comparing rituximab vs placebo groups, respectively: relapse-free survival rates were 96% [95% confidence interval (CI), 90.7–100%] vs 74.3% [62.8–88%], hazard ratio: 7.5 [1.67–33.6%] (p=0.008); major relapse-free survival rates were 100% [100–100%] vs 87.1% [78–97.3%] (p=0.009). Twelve (24%) rituximab recipients vs 14 (29.8%) controls had at least 1 severe adverse event (SAE) (p=0.65). No patient died. Six (12%) rituximab recipients had 9 infectious SAEs (septic shock or urinary, 2 each; Lyme disease, acute cholangitis, neutropenia, bronchitis or pneumonia, 1 each) vs 4 (8.5%) controls with 6 (4 pneumonia, 1 flu or 1 *Pneumocystis jiroveci* infection in a patient receiving methotrexate and glucocorticoids postrelapse after study discontinuation).

Conclusion: Long-term rituximab maintenance achieved significantly lower AAV relapse rates. SAEs were not more frequent in rituximab recipients.

1) Guillevin L *et al*. N Engl J Med 2014;371:1771–80
2) Terrier B *et al.* Ann Rheum Dis 2018;77:1150–6
3) Charles P *et al.* Ann Rheum Dis 2018;77:1143–9

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Abstract Number: 2625

Predictors of Advanced Chronic Kidney Disease in Patients with ANCA Vasculitis and Renal Involvement

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Background/Purpose: The aim of this study was to evaluate the predictors of advanced chronic kidney disease (ACKD) in patients with Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis and renal involvement.

Methods: Observational retrospective study. We included all patients with biopsy-proven ANCA glomerulonephritis (GN) diagnosed between 2001 and 2016, with at least one year of follow-up. Data was recorded at diagnosis, end of induction treatment, after one year of treatment, and at the end of follow-up. We analyzed serum creatinine, estimated glomerular filtration rate (eGFR), proteinuria, hematuria, renal histopathology and autoantibodies, as well as received treatments, requirement of dialysis, and renal or extra-renal relapses. Renal biopsies were reviewed and classified in accordance to the 2010 histopathologic classification of ANCA-associated GN. Univariate analysis were performed to identify factors associated with long-term ACKD (eGFR < 30 ml/min, stages 4 or 5 of KDIGO classification). The diagnostic accuracy for ACKD of each predictor variable were compared using areas under the curve (AUC) of ROC (receiver operating characteristic) curves.

Results: Sixty patients with ANCA GN were included: 17 Granulomatosis with polyangiitis (GPA), 14 Microscopic polyangiitis (MPA), 5 Eosinophilic granulomatosis with polyangiitis (EGPA), and 24 Renal-limited vasculitis (RLV). Forty-six patients were women (76.7%), with a mean age of 67.8 years (SD 13.1) at diagnosis. Median follow-up time was 4.2 years (IQR 2.2-6.8). The most frequently found histopathologic class was the focal class (20 patients, 33.3%), followed by mixed (17 patients, 28.3%), crescentic (16 patients, 26.7%), and sclerotic class (7 patients, 11.7%). Regarding treatment, 53 patients (88.3%) received cyclophosphamide, 42 (70%) IV pulse steroid therapy, 11 (18.3%) plasmapheresis and 10 (16.7%) transient dialysis. Seventeen patients (28.8%) needed to be re-biopsied during follow-up, and renal relapse was confirmed on 14 (26.4%) of them. Additionally, 11 patients (19.6%) had an extra-renal relapse. Four patients (6.7%) remained on permanent dialysis. At the end of follow-up, 12 patients (20.7%, 95% CI 11.9-33.4%) had an eGFR < 30 ml/min (Table 1). The univariate analysis showed a statistically significant association of ACKD with the sclerotic class biopsy (OR 7.17, 95% CI 1.34-38.31, p 0.02), and serum creatinine at diagnosis (OR 1.24, 95% CI 1.02-1.52, p 0.03), end of induction (OR 15.4, 95% CI 2.41-98.28, p 0.004), and after

	n=60
Age (years), mean±SD	67.8 ± 13.1
Female gender (%)	46 (76.7)
Follow-up time (years), median (IQR)	4.2 (2.2-6.8)
Classification of Vasculitis, n (%)	
GPA	17 (28.3)
MPA	14 (23.3)
EGPA	5 (8.3)
RLV	24 (40)
ANCA by IIF, n (%)	
Positive	55 (93.2)
c-ANCA	18 (30.5)
p-ANCA	37 (62.7)
Negative	4 (6.8)
Histopathologic class, n (%)	
Focal class	20 (33.3)
Crescentic class	16 (26.7)
Mixed class	17 (28.3)
Sclerotic class	7 (11.7)
Induction treatment, n (%)	
Cyclophosphamide	53 (88.3)
IV Pulse steroid therapy	42 (70)
Plasmapheresis	11 (18.3)
ACEIs-ARBs, n (%)	40 (66.7)
Renal rebiopsy, n (%)	17 (28.8)
Renal relapse, n (%)	14 (26.4)
Extra-renal relapse, n (%)	11 (19.6)
Transient dialysis, n (%)	10 (16.7)
Permanent dialysis, n (%)	4 (6.7)
ACKD (eGFR < 30ml/min), n (%)	12 (20.7%, IC 95% 11.9-33.4%)

Table 1. Baseline characteristics and clinical evolution of patients.

	OR (CI 95%)	p
Age at diagnosis (years)	1.06 (0.99-1.13)	**0.06**
Male gender	1.20 (0.27-5.28)	0.81
Baseline creatinine (mg/dl)	**1.24 (1.02-1.52)**	**0.03**
Baseline eGFR (ml/min)	**0.92 (0.85-0.99)**	**0.02**
Baseline hematuria	0.45 (0.09-2.15)	0.32
Baseline hemoglobinuria	1.07 (0.11-10.59)	0.95
Baseline proteinuria	1.52 (0.89-2.61)	**0.12**
Baseline BVAS	1.02 (0.91-1.16)	0.69
Extra-renal involvement at diagnosis	0.46 (0.12-1.74)	0.25
IV Pulse steroid therapy	1.45 (0.34-6.16)	0.61
Plasmapheresis	2.78 (0.66-11.82)	**0.16**
Cyclophosphamide	1.65 (0.18-15.19)	0.66
Hypertension	2.11 (0.50-8.84)	0.31
Diabetes	3.50 (0.66-18.43)	**0.14**
Sclerotic class biopsy	**7.17 (1.34-38.31)**	**0.02**
Crescentic class biopsy	0.21 (0.02-1.77)	**0.15**
6-month creatinine	**15.40 (2.41-98.28)**	**0.004**
6-month eGFR	**0.84 (0.74-0.94)**	**0.004**
6-month persistent hematuria	1.48 (0.24-8.91)	0.67
6-month hemoglobinuria	0.59 (0.11-3.31)	0.55
6-month proteinuria	2.31 (0.68-7.77)	**0.18**
6-month ANCA positivity	4.48 (0.88-22.71)	**0.07**
12-month creatinine	**19.25 (2.75-134.92)**	**0.003**
12-month eGFR	**0.86 (0.78-0.95)**	**0.003**
12-month persistent hematuria	4.62 (0.56-37.91)	**0.15**
12-month hemoglobinuria	3.00 (0.43-21.01)	0.27
12-month proteinuria	42.42 (0.55-3290.8)	**0.09**
12-month ANCA positivity	1.43 (0.23-9.01)	0.70
ACEIs - ARBs	0.45 (0.11-1.81)	0.26

Table 2. Univariate analysis to identify factors associated with long-term ACKD (eGFR <30 ml/min) at the end of follow-up.

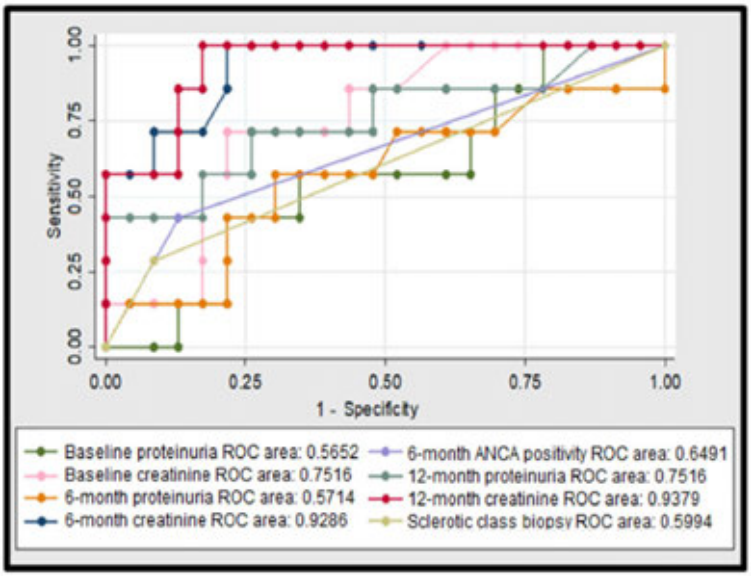

Figure 1. ROC curves to determine ACKD at the end of follow-up.

12 months (OR 19.25, CI 95% 2.75-134.92, p 0.003). We found no significant association of ACKD with proteinuria, hematuria, ANCA positivity at different times nor any other of the analyzed variables (Table 2). The best diagnostic accuracy in ROC curves was shown by serum creatinine at the end of induction (AUC 0.93, 95% CI 0.83-1.00) and at 12 months (AUC 0.94, 95% CI 0.85-1.00) (Figure 1).

Conclusion: In this cohort of patients with ANCA vasculitis and renal involvement, serum creatinine at the end of induction and after 12 months of treatment were the best predictors of ACKD (eGFR < 30ml/min) at the end of follow-up.

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Abstract Number: 2626

Cell-free Mitochondrial DNA Levels in Granulomatosis with Polyangiitis

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SESSION INFORMATION
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Background/Purpose: Circulating cell-free mitochondrial DNA (mtDNA) is released during non-apoptotic processes such as NETosis. Increased levels of mtDNA are associated with autophagic dysfunction and inflammasome activation. In critically ill patients mtDNA levels correlate with mortality. In Granulomatosis with Polyangiitis (GPA) there is evidence that innate immune system activation is involved in pathogenesis and propagation of disease. The role of autophagic dysfunction and subsequent effects on the inflammasome as it relates to mtDNA has yet to be robustly investigated in GPA. The aim of this study was determine whether increased circulating mtDNA levels correlate with disease activity in GPA.

Methods: Plasma samples and clinical data from the Wegener's Granulomatosis Etanercept Trial were utilized. Cell-free mtDNA levels were measured in banked plasma by applying a SYBR Green-qPCR assay using a PRISM 7300 sequence detection system (Applied Biosciences). All mtDNA level data were log-transformed. Samples were categorized based on disease activity and severity. The primary aim was to determine if mtDNA levels correlated with disease activity as defined by BVAS/WG. Samples were classified as pre-flare, flare, or remission, with flare further subcategorized into severe or non-severe

Results: 100 of the 180 participants in WGET had available plasma at 2 or more visits, and were data from these patients and sample were used for this analysis. No significant differences in patient demographics were observed between those with and without plasma. There was no difference in mtDNA copy number across visit types (pre-flare, flare, and remission). While mtDNA level was not a significant predictor of disease activity in univariate models, there was trend within severe flare: an increase in mtDNA level was indicative of increased odds of severe flare (Odds Ratio = 1.32; (0.78 – 2.22) In paired analysis (n=40), mean mtDNA level was significantly higher during a severe flare

(N=100)	Odds Ratio (95% CI)
Disease activity	
Severe flare	1.320 (0.78 – 2.22)
Non-Severe flare	0.972 (0.61 – 1.56)
Severe persistent	2.78 (0.22 – 35.66)
Non-Severe persistent	0.893 (0.29 – 2.76)
Remission	0.846 (0.56 – 1.28)

Table 1. Univariate logistic models: mtDNA and disease activity

(N=9)	Pre-Severe Flare	Severe Flare	p-value
Mean ± SD	7.23 ± 1.15	7.76 ± 1.32	0.185
Pre indicates 3 months before flare.			
(N=12)	**Pre-Severe Flare**	**Post-Severe Flare**	**p-value**
Mean ± SD	7.25 ± 1.07	7.83 ± 1.00	0.052
Pre/Post indicates 3 months before or after referenced flare.			
(N=40)	**Severe Flare**	**Remission**	**p-value**
Mean ± SD	7.75 ± 1.47	7.36 ± 1.17	0.038

Table 2. Paired t-tests: Log-transformed mtDNA levels across visit type

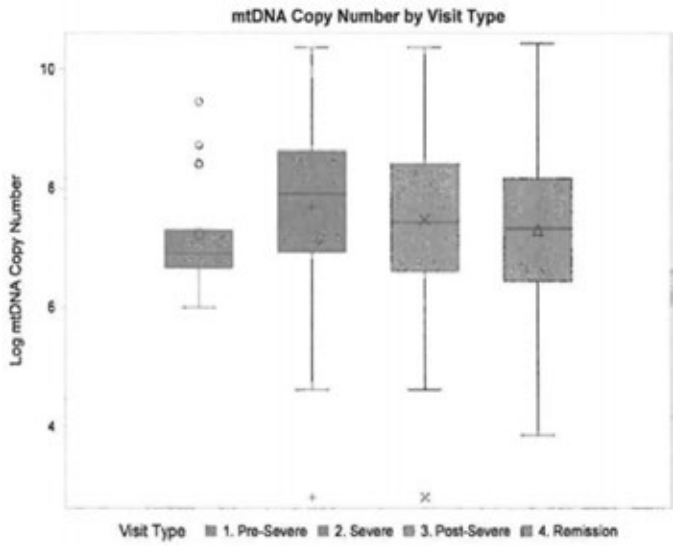

Figure 1. Distribution of mtDNA copy number by visit type

as compared to remission (M=7.75 ± 1.47, M=7.36 ± 1.17, respectively; p=.038). In a subset of the paired analysis (n=13), restricted to pre- and post-severe flare observations, mean mtDNA level was significantly higher 3 months following the flare as compared to pre-flare in relation to an index severe flare (7.83 ± 1.00 vs 7.25 ± 1.07, p=.052). Mean mtDNA between pre-severe flare and severe flare (n=9) was not significantly different (7.23 ± 1.15 vs 7.76 ± 1.32, p=.185).

Conclusion: This exploratory study suggests that mtDNA levels may be elevated in states of high disease activity among patients with GPA. However, firm conclusions are limited by small sample size. These findings suggest a role for deregulated autophagy in GPA. Finally, mtDNA level, a non-invasive and rapidly performed test, may potentially serve as a useful biomarker for disease activity in GPA, although additional examination in a larger cohort of patients is warranted to determine its utility and sensitivity.

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Abstract Number: 2627

Association of Work Productivity Assessed by Absenteeism and Presenteeism with Disease Activity, Damage and Health-related Quality of Life in Patients with ANCA-associated Vasculitis

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SESSION INFORMATION
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Background/Purpose: Chronic inflammatory diseases such as antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) substantially affects patients' daily lives, including their ability to work. Although the management of AAV has improved, many patients still have to take sick leave or even stop working because of their diseases (i.e., absenteeism). Even for those remaining in paid work, patients may experience problems due to AAV resulting in productivity loss while at work (i.e., presenteeism). However, little has been reported on absenteeism and presenteeism in patients with AAV. We aimed to investigate the absenteeism and presenteeism in patients with AAV and associated factors.

Methods: Patients with AAV were defined and classified according to the European Medicines Agency algorithm. Patients were approached during their outpatient appointments in the three different university hospitals from November 2017 through February 2018. Some of the hospitalized patients were also eligible. Patients were asked to complete the Work Productivity and Activity Impairment–General Health (WPAI-GH) questionnaire, the 5-level EuroQoL 5-Dimensions Questionnaire (EQ-5D-5L), which is the generic measures of health-related quality of life (HRQoL), and other related demographic questionnaires. An EQ-5D-5L health state was converted to a single summary index by applying the formula and ranges from 0 to 1; 0 meaning death and 1 complete health. Physicians, who were blind-

ed to the WPAI-GH and EQ-5D-5L results, completed the the Birmingham Vasculitis Activity Score (BVAS) and the Vasculitis Damage Index (VDI) simultaneously and record other medical information.

Results: A total of 92 patients with AAV (microscopic polyangiitis 42, granulomatosis with polyangiitis 24, eosinophilic granulomatosis with polyangiitis 22, renal limited AAV 3, and unclassified AAV 1) participated. In the study population, the mean age was 65.4, 60 were women, the mean disease duration was 5.5 years, the mean prednisolone dosage was 7.5 mg/day, the mean BVAS was 3.6, and the mean VDI was 1.6. The mean EQ-5D-5L index value was 0.755 and significantly lower than the value of the age- and sex-matched national norms ($p < 0.01$). A total of 25 (27%) patients worked for pay and significantly younger than those who did not work ($p < 0.01$). Of the 25 patients working for pay, 11 reported missing work due to their health problem, accounting for 17% of their working time (absenteeism) on average, and 32% of their work was impaired due to their health problem (presenteeism) on average. WPAI absenteeism was weakly to moderately correlated with the and BVAS and EQ-5D-5L scores ($r = 0.24$ and -0.61, respectively), whereas not with the VDI scores ($r = 0.08$). WPAI presenteeism was weakly to moderately correlated with the BVAS, VDI, and EQ-5D-5L scores ($r = 0.39$, 0.38, and -0.58, respectively). Patients with lower HRQoL status (low/high EQ-5D-5L scores by median) had significantly higher absenteeism (28%/17%, $p = 0.01$), and presenteeism (48%/32%, $p = 0.002$) than those with higher HRQoL status.

Conclusion: Work productivity assessed by absenteeism and presenteeism are associated with disease activity, damage, and HRQoL in patients with AAV.

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Abstract Number: 2628

Mortality Predictors in ANCA-associated Vasculitis: Experience of a Brazilian Monocentric Cohort of a Rheumatology Center

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

Background/Purpose: Mortality of patients with ANCA-associated vasculitis (AAV) is higher than the general population. There are few papers in the literature regarding the factors associated with this unfavorable outcome, most of them in the eastern population or from nephrology centers. To date, there is no study with this approach in Latin-American patients, a miscegenated population.

Our objective was to identify clinical and laboratory features associated with increased mortality in Latin-American patients with AAV.

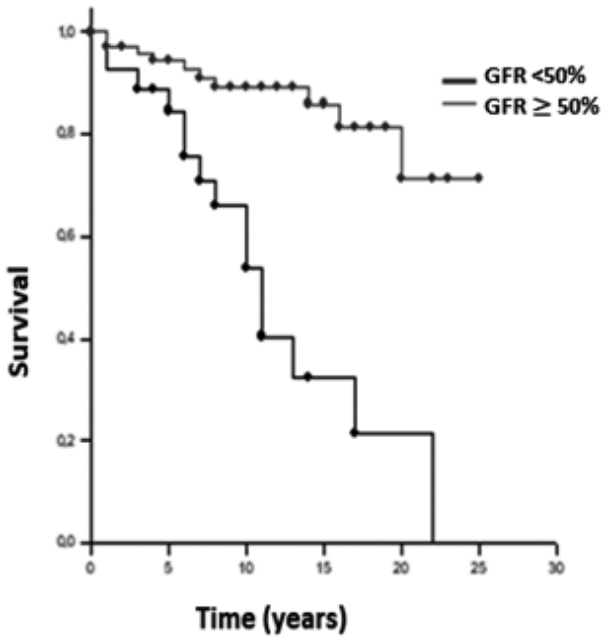

Figure. Survival Analysis of the patients based on their GFR.

Methods: All the patients fulfilling the Chapel Hill Criteria (2012) and ACR criteria (1990) for AAV followed between 2000 and 2018 in our Rheumatology Vasculitis Outpatient Clinics were selected. Data were obtained from an ongoing electronic database protocol that was carried out for all patients at 1- to 6-month intervals. Patients were divided in two groups - dead or alive in 2018. Information about the death was obtained from medical records, family members and death certificates. Variables analyzed were age at the onset of the vasculitis, ANCA frequency, Birmingham Vasculitis Activity Score (BVAS), Vasculitis Damage Index (VDI) and laboratory parameters in the most recent attendance or in the last attendance before death. Comparisons were made by non-paired t-tests or Mann-Whitney tests for continuous variables and Fisher's exact test for categorical variables. Logistic regression was used to analyze association between death (dependent variable) and variables with significance in the univariate analyses. A log-Rank survival analysis was performed. Statistical significance was set at $p < 0.05$.

Results: 128 patients were included; 101 had GPA, 21 had EGPA and 6 had MPA. In 2018, 78 were alive, 25 had died and 25 had lost contact. The main cause of death was infection (64%). The vasculitis was considered a contributing factor in 40% of the deaths. The patients who died were older at diagnosis (40.9 vs. 51.2 years, p=0.007) and had higher activity and damage index (BVAS 3 vs. 8, p =0.001; VDI 3.5 vs. 6.9, p< 0.001). Laboratorial features related with mortality were creatinine (1.24 vs. 3.5 mg/dL, p < 0.001), hemoglobin (13.3 vs. 10.7 g/dL, p< 0.001), ESR (19.7 vs. 38.6 mm/1sthour, p=0.038) and CRP (5.4 vs. 68.9 mg/L, p< 0.001). The dose of prednisone taken in the last attendance was higher in the dead-group (9.8 vs. 18.9 mg/day, p=0.018). No difference was observed regarding the presence of ANCA or the immunosuppressive treatment. Logistic regression showed that VDI (OR 1.35, p=0.03), creatinine (OR 1.31, p=0.01) and CRP (OR 1.04, p=0.04) were independent factors related to mortality. The VDI items statistically different between the groups were: EGFR < 50%, proteinuria >0.5 g/24h, end stage renal disease, chronic breathlessness, significant muscular atrophy/weakness, malignancy, visual impairment and oral ulcers. Survival was importantly decreased among patients with GFR < 50% (p < 0.001) (figure).

Conclusion: This is the first study analyzing outcomes of Latin-Americans patients with AAV. Damage index, renal impairment and high CRP were independent factors associated with mortality. Survival rates were significantly decreased among patients with lower GFR.

Disclosure: M. Dagostin, None; **S. Nunes**, None; **S. Shinjo**, None; **R. Pereira**, None.

Abstract Number: 2629

Urinary Inflammatory Cell Analysis Reflects the Renal Histopathology in Anti-neutrophil Cytoplasmic Antibody-associated Vasculitis

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SESSION INFORMATION

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Session Title: Vasculitis – ANCA-Associated Poster I

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The anti-neutrophil cytoplasmic autoantibody (ANCA)- associated vasculitides (AAVs) include microscopic polyangiitis (MPA), granulomatosis with polyangitis (GPA), and eosinophilic granulomatosis with polyangitis (EGPA). These small-vessel vasculitides are characterized by necrotizing inflammation of the vessel wall, particularly affecting small arteries, arterioles, and capillaries in systemic organs, and the kidney is one of the organs most frequently involved. Although kidney biopsy is necessary for deciding the therapeutic protocol, it is invasive and sometimes difficult to perform in patients who are in poor general condition. We have already reported that T cells and macrophages appear in the urine of patients with glomerulonephritis, accompanied by active cellular infiltration such as cellular crescent formation and diffuse interstitial cell infiltration, but not in the urine of patients with glomerulonephritis without the active inflammatory lesions. In this study, we examined the utility of urinary inflammatory cell analysis for assessment of kidney histopathology in AAVs.

Methods: This was a cross-sectional, retrospective chart study. Thirty-six AAV patients who had been referred to Niigata University Hospital between 2002 and 2018, and had undergone percutaneous kidney biopsy and urinary inflammatory cell analysis, participated. Thirty-two patients had MPA, and 4 had GPA. The kidney biopsy findings were classified according to Berden's classification (a method for categorizing glomerular lesions into four classes) and Neumann's classification (a method for evaluating glomerular, tubulo-interstitial, and vascular lesions on the basis of activity indices and chronicity indices). Flow-cytometric analysis of urinary inflammatory cells was performed for each subject. The numbers of urinary T cells or macrophages were determined by multiplying the number of viable cells in the gated mononuclear cell region in each sample by the percentage of urinary CD3-positive or CD14-positive cells in the population, respectively. The correlations between the results of the two methods and the numbers of urinary inflammatory cells were examined using Kruskal-Wallis test and Spearmann's rank correlation coefficient. Differences at $p < 0.05$ were considered to be statistically significant.

Results: In Berden's classification, the numbers of urinary inflammatory cells showed a non-significant tendency to be increased in the crescentic category. Meanwhile, in Neumann's classification, activity indices showed significant positive correlations with the numbers of urinary CD3-positive cells ($r = 0.541$, $p = < 0.001$), CD14-positive cells ($r = 0.354$, $p = 0.034$), and total inflammatory cells ($r = 0.449$, $p = 0.006$).

Conclusion: The numbers of urinary inflammatory cells reflect kidney histopathology in terms of active lesions, suggesting the usefulness of urinary inflammatory cell analysis for assessment of kidney biopsy findings in patients with AAVs.

Disclosure: Y. Wada, None; **M. Sudo**, None; **T. Kuroda**, None; **M. Nakano**, None; **I. Narita**, None.

Abstract Number: 2630

A Dutch Consensus Statement on the Diagnosis and Treatment of ANCA Associated Vasculitis

Ebru Dirikgil,[1] Peter Verhoeven,[2] Sander Tas,[3] Abraham Rutgers,[4] Hein Bernelot Moens,[5] Jacob van Laar,[6] Willem Jan Bos,[7] and Onno Teng[1], [1]LUMC, Leiden, Netherlands, [2]The Dutch Vasculitis Foundation, Silvolde, Netherlands, [3]Amsterdam Rheumatology & immunology Center, Amsterdam UMC/University of Amsterdam, Amsterdam, Netherlands, [4]University Medical Center Groningen, Groningen, Netherlands, [5]Ziekenhuisgroep Twente, Almelo, Netherlands, [6]UMC Utrecht, Department of Rheumatology & Clinical Immunology, Utrecht, The Netherlands, Utrecht, Netherlands, [7]St. Antoniusziekenhuis, Nieuwegein, Netherlands

SESSION INFORMATION

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Background/Purpose: Several guidelines have been published on the diagnosis and treatment of anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitis (AAV). These guidelines provide an evidence-based approach to support clinical-decision making and adequate implementation is needed to improve care. As part of an implementation strategy, national consensus meetings in the Netherlands were initiated in order to establish consensus on broad aspects of the diagnosis and treatment of AAV based upon the recently published guidelines, relevant to daily clinical practice.

Methods: A national, multidisciplinary working group of physicians (nephrologists, rheumatologists, immunologists, pulmonologist, pathologist) with expertise on AAV addressed the broad spectrum of diagnosing, treating and organisation of care for AAV patients. Consensus was established using a Delphi-based method in a national conference in conjunction with a nationally distributed online consensus survey. This survey was distilled from the current published international guidelines. Cut-off for consensus was 70% (dis-)agreement.

Results: Ninety-eight professionals were involved in the Delphi procedure to assess consensus on 52 statements regarding diagnosis, treatment and organisation of care for AAV patients. From 52 statements, consensus was achieved for 39 statements (75%). Consensus was achieved on aspects of AAV disease definition, nomenclature, distinct disease states through follow-up, treatment algorithm and organisation of care for AAV. No consensus was achieved on the necessity of histopathological evidence, regular blood testing for ANCAs and standard BVAS, VDI and PROMs assessment.

Conclusion: This study describes the results of a national consensus statement on diagnosing and treatment of AAV patients as part of an implementation strategy in the Netherlands of (inter-)national guideline-derived recommendations. Future studies should evaluate whether the consensus statement has facilitated local implementation, reduced clinical practice variation and, ultimately, improved care for AAV patients in the Netherlands.

Disclosure: E. Dirikgil, None; **P. Verhoeven**, None; **S. Tas**, None; **A. Rutgers**, None; **H. Bernelot Moens**, None; **J. van Laar**, Roche, 2, 8, Arthrogen, 5, Thermofisher, 2, BMS, 8, MSD, 2, Eli Lilly, 8, Gesynta, 5, Leadiant, 5, Arxx Tx, 5, Astra Zeneca, 2, Sanofi, 8; **W. Bos**, None; **O. Teng**, None.

Abstract Number: 2631

Increased Risk of Acute Coronary Artery Disease and Ischemic Stroke in Patients with Eosinophilic Granulomatosis with Polyangiitis

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Background/Purpose: Current treatment approaches have greatly improved the survival of eosinophilic granulomatosis with Polyangiitis (EGPA) patients, however both morbidity andmortality are still significant mainly due to cardiovascular complications.Premature and accelerated atherosclerosis has emerged as an important facet of ANCA associated vasculitis (AAV) cardiovascular risk but, eosinophil infiltration could also be responsible of endomyocardial damage and direct vascular injury in EGPA. Several studies showed a higher frequency of cardiovascular disease in patients with AAV or granulomatosis with polyangiitis but data on cardiovascular disease risk in EGPA patients are scarce. The aim of our study was to assess acute coronary artery disease and ischemic stroke, incidence and predictors, in eosinophilic granulomatosis with Polyangiitis(EGPA).

Methods: We conducted a retrospective cohort study of all EGPA, diagnosed between 1982 and 2018, who met Chapel Hill Consensus Conference classification criteriaafter thorough medical chart review. Major cardiovascular eventwas defined as acute coronary artery disease or ischemic stroke. We calculated the comparative morbidity/mortality figure (CMF)and we used Cox proportional hazards regression models to assess the risk of acute coronary artery disease, ischemic stroke associated with EGPA, after adjusting for covariates.

Results: We identified 67 subjects, only 55 met the inclusion criteria, 29 (55%) were men, with a mean follow-up of 8.1 ±7.7 years since EGPA diagnosis.

Acute coronary artery disease occurred in 9 patients, and ischemic stroke occurred in 2 patients (incidence rates of 21.1 per 1,000 person-years and 4.3 per 1,000 person-years, respectively). Using direct standardization, acute coronary artery diseaseincidence was seven times higher than in the general population (CMF 7.20; 95% CI 6.46 – 14.72) and, ischemic stroke incidence was tree times higher than in the general population (CMF 3.74; 95% CI 3.40 – 13.09). Age over 58 years and purpura were independently associated with coronary artery disease occurrence (adjusted HR 13.3; 95% CI 1.6 – 107.9, and adjusted HR 4.1; 95% CI 1.0 – 16.1, respectively). We did not identify factors significantly associated with ischemicstroke occurrence. In our cohort, none of the classic cardiovascular risk factors were associated with an increased risk of acute coronary artery disease or ischemic strokeoccurrence. Using direct standardization, the age-adjusted overall mortality rate was 8.9 per 1000 person-years and was not different than the general population.

Conclusion: EGPA have a significantly increased risk of acute coronary artery disease and ischemic stroke. Monitoring for these complications and attempts strict management of cardiovascular risk factors are warranted in this population as part of the long-term management of this condition.

Disclosure: M. Mourguet, None; **D. Chauveau**, None; **S. Faguer**, None; **J. Ruidavets**, None; **Y. Béjot**, None; **G. Prevot**, None; **O. Lairez**, None; **D. Ribes**, None; **A. Huart**, None; **L. Alric**, None; **L. Astudillo**, None; **L. Sailler**, None; **G. Pugnet**, None.

Abstract Number: 2632

Changing Trends in the Management of ANCA-associated Vasculitis at an Academic Medical Center

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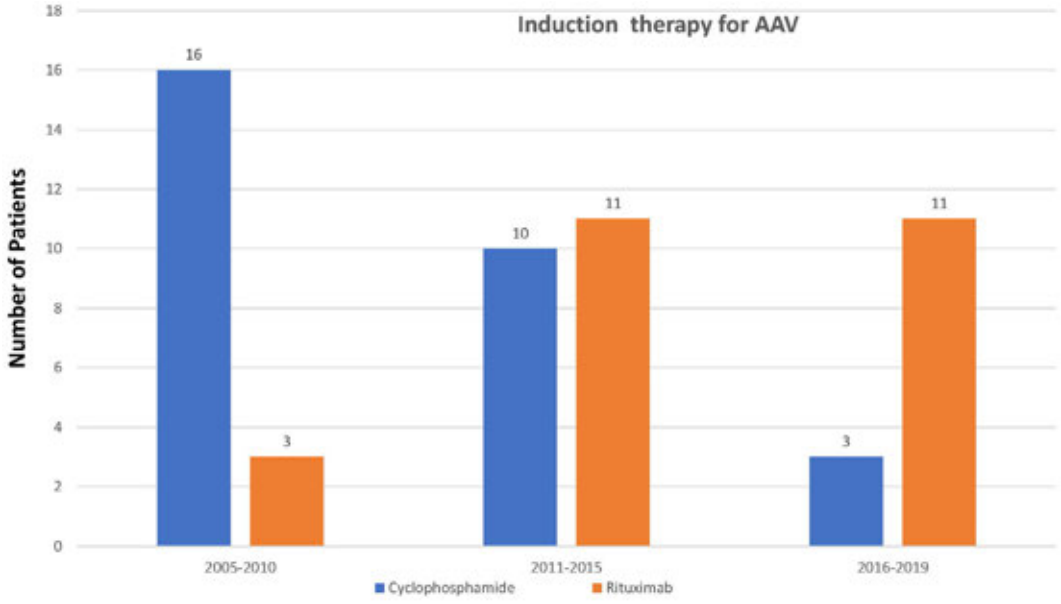
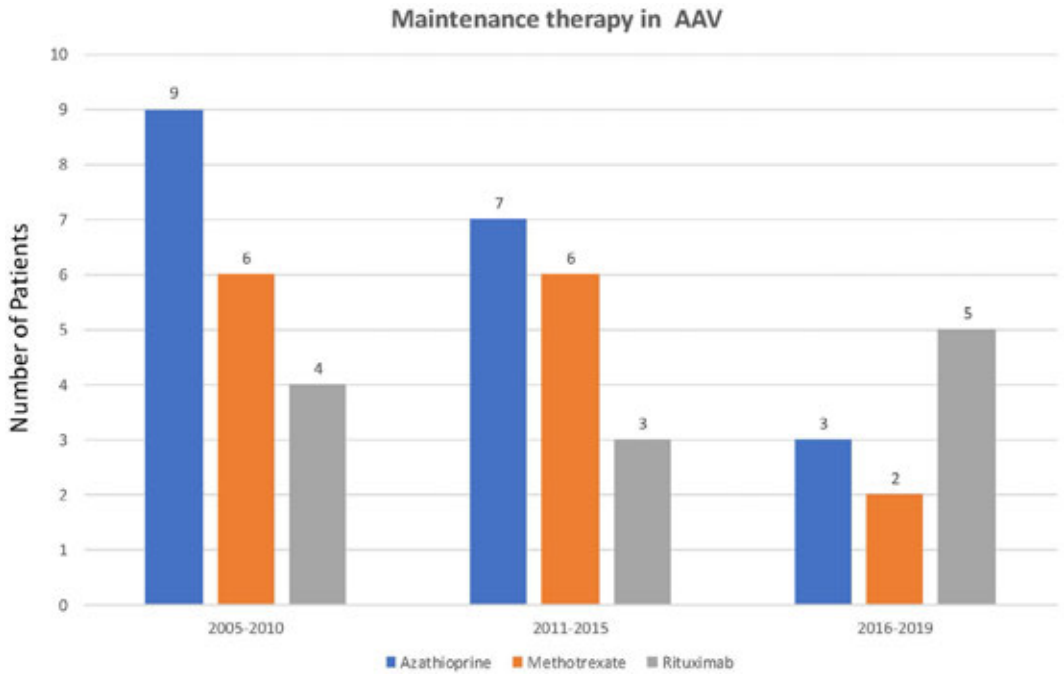
Session Time: 9:00AM–11:00AM

Background/Purpose: For years, cyclophosphamide (CYC) has been the primary treatment for severe anca-associated vasculitides (AAV) and has significantly improved disease related mortality. In addition, maintenance therapy, traditionally with methotrexate (MTX) or azathioprine (AZA), is imperative in preventing relapse. Since the approval of rituximab (RTX) for potential induction and maintenance therapy of AAV, it is unclear how substantially rheumatologists have responded and altered their treatment approach. we evaluated changes in treatment and disease outcomes of AAV at a large medical center.

Methods: IRB approval was obtained for medical record review of patients with diagnoses of AAV at an academic medical center. Consecutive patients seen between 2005 and 2019 were evaluated for diagnosis year, demographics,





disease characteristics, induction and maintenance therapies, and remission and relapse. Patients who had sufficient disease severity to receive either CYC or RTX induction were included. Three time periods were evaluated based on diagnosis year, 2005-2010, 2011-2015, and 2016-2019 and data analyzed using chi-squared for differences in medication use and disease outcomes between time periods and medication regimens.

Results: Fifty-four patients (mean age 58±18 years, 74% female, 28 PR3 positive, 20 MPO positive and 6 both PR3/MPO) who received either RTX or CYC for remission induction were included in the final analysis. The use of RTX for induction increased significantly (p=0.001) during each study time period, from 19%, 53%, and 73%, respectively (Figure 1). However, RTX use for maintenance therapy did increase, but not significantly, from 21% to 50% (p=0.081) (Figure 2). There was no significant difference in the rate of remission following induction therapy during each study time period (63%, 66%, and 75%, respectively, p=0.191). Similarly, the relapse rate was not different during these three time periods (52%, 50%, and 36%, respectively, p=0.167).

At 6 months, 64% (35/54) patients achieved remission at 6 months. There was no significant difference in the achievement of remission between CYC (18/29) and RTX (17/25) (p=0.467). During long term follow-up, 46% (24/54) of patients relapsed. The risk of relapse was significantly lower in the RTX induction group 28% (7/25) compared to CYC group 58%(17/29) (p=0.018). Interestingly, rates of relapse on maintenance therapy were significantly (p=0.042) lower with RTX (36%) and AZA (36%) versus MTX (71%).

Conclusion: Following the approval of RTX for treatment of AAV, its use has significantly increased for induction therapy, however, not for maintenance therapy. This may be due to the lack of clear guidelines and data for optimal maintenance regimens. There were no differences in disease remission at 6 months in CYC vs RTX groups, however, relapses appeared to be fewer in those induced with RTX. Interestingly, the risk of relapse was higher in MTX maintenance group compared to AZA or RTX. These results are promising, suggesting that real world outcomes are mir-

roring what was seen in larger clinical trials. However, it suggests the need for more studies and guidelines regarding optimal management strategies for maintenance therapy in AAV.

Disclosure: S. Afroz, None; **N. Shakoor**, None.

Abstract Number: 2633

Efficacy of Remission Induction Regimens in Elderly Patients with ANCA-Associated Glomerulonephritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Induction regimens using either cyclophosphamide (CYC) or rituximab (RTX) have been shown to have similar efficacy and similar rates of adverse events in randomized trials of patients with a mean age of 54 yrs. Little is known about outcomes among older patients with ANCA-associated glomerulonephritis (ANCA GN) receiving such therapies. This study aimed to compare these outcomes in elderly ANCA GN on the basis of induction therapy regimen (CYC vs RTX).

Methods: Patients, ages 60 and above, diagnosed with ANCA GN clinically and histologically from 2004 to 2018 were retrospectively identified. Baseline characteristics and outcomes across several clinical parameters were recorded and compared between groups using t-test, Mann-Whitney-U test and Fisher's exact test for significance as appropriate.

Results: Among a cohort of 64 patients with ANCA GN with a mean (SD) age of 75 ($\pm$7) years at diagnosis, patients treated with CYC (n = 27) compared to those treated with RTX (n = 37) had a higher peak serum creatinine at baseline (4.7 mg/dl vs. 2.5 mg/dl, p = 0.0005), higher hemodialysis dependence pre-renal biopsy (35% versus 2%, p = 0.01), and higher use of plasmapheresis (33% vs. 4%, p = 0.02). The mean GFR at 12 months was higher in rituximab patients (40 vs. 32, p=0.05). There were no statistically significant differences between the two groups in prednisone dose at 6 months (7 mg/day vs. 6 mg/day, p = 0.14) or at 12 months (4 mg/day vs. 3mg/day, p = 0.11), disease remission (100% vs. 97%, p = 1.0), combined outcome of end stage renal disease and/or death at 12 months (7% vs. 3%, p = 0.57), or disease relapse (22% vs. 13%, p = 0.61) (Table 1). Patients treated with CYC had a higher number of patients with bone marrow suppression (30% vs. 5%, p = 0.01) and developed an infection requiring hospitalization at 12 M of follow-up compared to RTX treated group (56% versus 16%, p = 0.001). Additionally, after adjustment for age, GFR and prednisone dose at 6 months, CYC use was associated with higher infection risk [aOR 6.22, 95% CI (1.70-22.80)] (Table 2).

Conclusion: CYC and RTX appear to be effective in remission induction in elderly patients with ANCA GN. Use of CYC was associated with a higher risk of bone marrow suppression and infections requiring hospitalization compared to RTX. More information is needed on the comparative safety of induction therapy strategies in elderly ANCA GN patients.

	Cyclophosphamide treated group (>3,000mg of CYC), *n=27*	Rituximab treated group (RTX and <3,000mg of CYC), *n=37*	p-value
Prednisone dose at 6 months, *mean (SD) (mg)*	7.4 (5.4)	5.8 (5.2)	0.143
Prednisone dose at 12 months, *mean (SD)* (mg)	3.9 (2.5)	3.0 (2.3)	0.113
Remission achieved, *n* (%)	27 (100)	36 (97.3)	1
ESRD or death at 1 year, *n* (%)	2 (7.4)	1 (2.7)	0.568
GFR at 12 months, *mean (SD)*	32 (17)	40 (16)	0.055
Relpase, *n* (%)	6 (22.2)	5 (13.5)	0.609
Infection requiring antibiotic use, *n* (%)	15 (55.6)	6 (16.22)	0.001
Bone marrow suppression, *n* (%)	8 (29.6)	2 (5.41)	0.013

Table 1. Clinical outcomes table for patients treated with cyclophosphamide and rituximab

Infection Requiring Hospitalization	Odds Ratio	Std. Err.	P>|z|	[95% Conf. Interval]
Age	1.80	1.099185	0.333	0.54 - 6.0
Pred at 6 M	1.00	.0551608	0.973	0.90 – 1.12
Baseline GFR	1.00	.0214642	0.880	0.95 - 1.04
CYC vs. RTX	6.22	4.122285	0.006	1.69 -22.80
Cons	0.16	.1418301	0.040	0.03 – 0.92

Table 2. Logistic regression table for infection requiring hospitalization, adjusting for age, GFR, and Prednisone dose at 6M

Disclosure: A. Hopkins, None; **S. Chu**, None; **P. Seo**, None; **E. Gapud**, None; **B. Antiochos**, None; **S. Eid**, None; **J. Liebowitz**, None; **D. Geetha**, Consultant to ChemoCentryx and Genentech.

Abstract Number: 2634

ANCA Response upon Rituximab or Cyclophosphamide in ANCA-associated Vasculitis Patients

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent studies have demonstrated that in patients with anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) with successful remission-induction (RI) after cyclophosphamide (CYC), maintenance treatment with ANCA-guided rituximab (RTX) improved relapse free survival (RFS). However, current recommended RI treatment is RTX, CYC or a combination of both. As yet it is unclear how these different RI therapies affect ANCA levels. Therefore, this study aimed to investigate the potential of RTX, CYC, or RTX+CYC to achieve an ANCA-negative status and its effect on RFS to further improve the insight on ANCA-guided treatment in AAV patients.

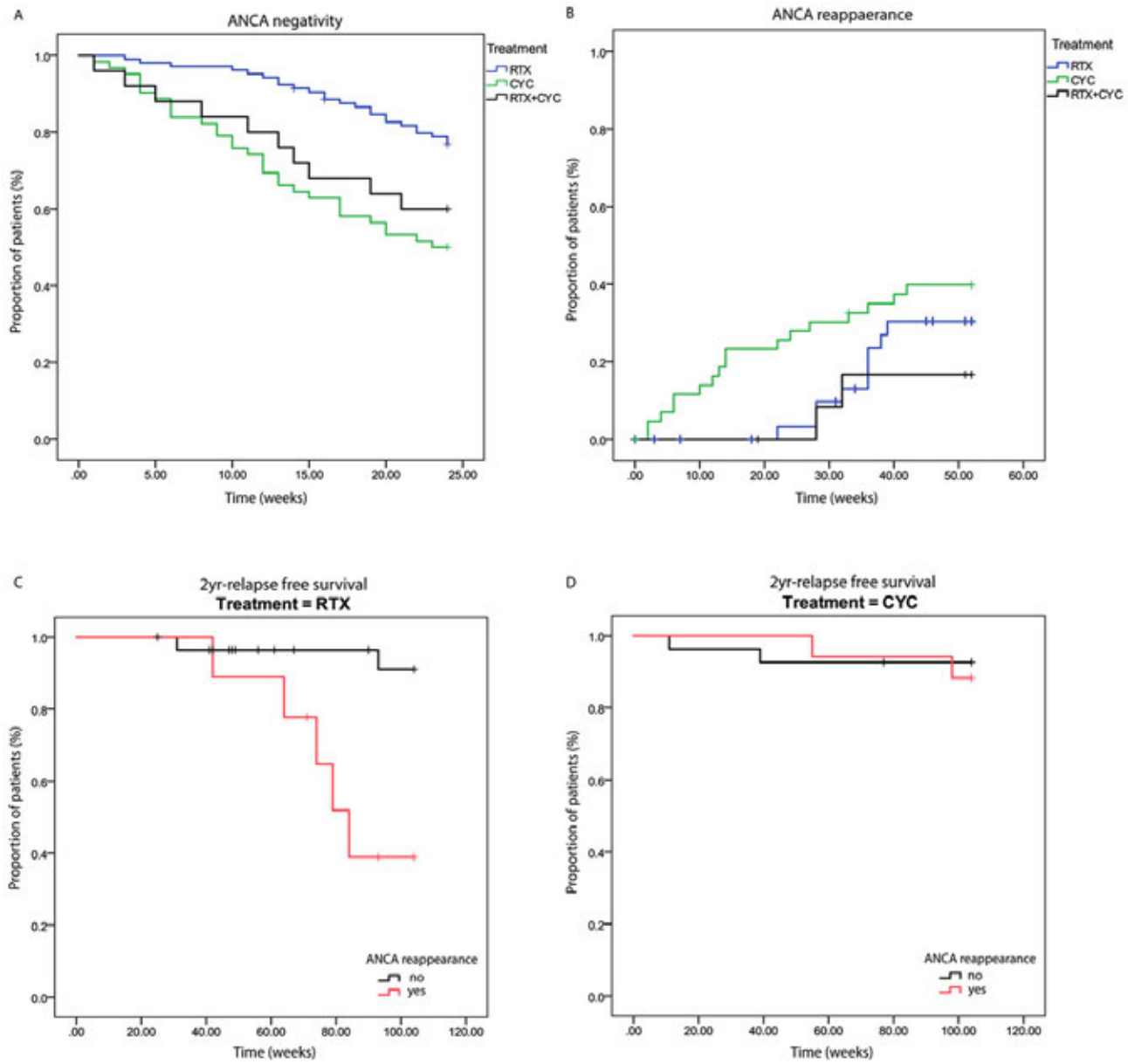

Figure 1. ANCA responses are assessed in ANCA-associated vasculitis patients after different remission-induction regimens. A) The achievement of ANCA negativity within 6 months after remission induction (RI)-therapy with Rituximab (blue line), Cyclophosphamide (green line) or a combination of Rituximab plus Cyclophosphamide (black line). B) ANCA reappearance within one year after achievement of ANCA negativity was investigated for the different RI regimens. C) 2-year major relapse free survival in C) RTX-treated patients and D) CYC-treated patients with (red line) or without ANCA reappearance (black line).

Methods: This retrospective single centre study involved 129 ANCA-positive AAV patients treated with 200 remission-induction regimens, including RTX (n=109), CYC (n=66), or RTX+CYC (n=25) between 1990 – 2018 with a mean follow-up (FU) of 328 weeks. ANCA serum levels and major RFS were assessed.

Results: Within 6 months, 23% of RTX-treated, 50% of CYC-treated and 40% of RTX+CYC-treated AAV patients achieved an ANCA-negative status (p=0.0001) (Figure 1A). Time to ANCA negativity was significantly shorter after CYC+/- RTX (mean±SD: 11±6 weeks) as compared to RTX (16±6 weeks; p=0.02). ANCA reappearance within 1 year after achieving ANCA negativity, occurred in 9 out of 38 (24%) RTX-treated, 17 out of 44 (39%) CYC-treated and 2

out of 14 (14%) RTX+CYC-treated patients (p=0.17), which happened significantly faster in CYC-treated patients at an average of 18 weeks as compared to RTX+/- CYC at an average of 30 weeks (p=0.003) (Figure 1B). Both 1yr and 2yr major RFS was significantly less for RTX-treated (86% and 68%) as compared to CYC-treated (97% and 91%) and RTX+CYC-treated patients (100%, 91%) (p=0.02, p=0.005). Overall, patients that reached an ANCA-negative status had a better 2yr-RFS. ANCA reappearance associated with major relapses in RTX-treated group (56% vs 7%; p=0.002) (Figure 1C) but not in CYC-treated group (12% vs 7%; p=0.68) (Figure 1D).

Conclusion: This study demonstrates that an ANCA-negative status was achieved more frequently and quicker with CYC +/- RTX as compared to RTX and associated with a better 2yr-RFS. ANCA reappearance was associated with relapses in RTX-treated patients but not in CYC-treated patients. Thus, monitoring ANCAs to guide tailored maintenance treatment is most relevant in RTX-treated AAV patients.

Disclosure: L. van Dam, None; **E. Dirikgil**, None; **E. Bredewold**, None; **A. Ray**, None; **T. Rabelink**, None; **C. van Kooten**, None; **O. Teng**, None.

Abstract Number: 2635

Accuracy of Self-Reported Diagnosis of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To determine the reliability of self-reported diagnosis of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis: granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA) from a large, international, internet-based cohort.

Methods: The web-based registry includes data provided by patients (or caregivers) with different forms of primary vasculitis collected through standardized forms including type of vasculitis, disease manifestations, and information regarding how diagnosis was made. This analysis included 150 randomly-selected patients with GPA (out of 484) with complete data and all patients with MPA and EGPA. Primary outcome was percentage of patients who met the 1990 American College of Rheumatology (ACR) classification criteria and/or 2012 Chapel Hill Consensus Conference (CHCC) definitions for vasculitis. ACR criteria for GPA were modified to include ANCA positivity.

Results: The study cohort included 150 patients (70% female) with GPA, 164 patients (81% female) with MPA and 116 patients (66% female) with EGPA.

GPA: Clinical manifestations included sinus/nasal (84%), pulmonary (63%, alveolar hemorrhage in 34%) and renal involvement (57%). ANCA was reported as positive in 123 of 134 patients (92%) who knew their ANCA status. 70% patients reported having at least one biopsy and 61% patients reported diagnosis by a biopsy. Overall, 96% patients

met either the modified ACR criteria or the CHCC definition. 93% patients met both the modified ACR criteria and CHCC definition.

MPA: Clinical manifestations included pulmonary (62%, alveolar hemorrhage in 36%), renal involvement (84%), and neurologic (65%). ANCA was reported as positive in 147 of 153 patients (96%) who knew their ANCA status. Biopsies were performed in 131 patients (80%) with 77% patients reporting diagnosis by biopsy. 95% patients met the CHCC definition.

EGPA: Clinical manifestations included asthma (95%), nasal/sinus (94%), peripheral nerve involvement (88%), non-asthma pulmonary disease (74%). ANCA was reported as positive in 33 of 79 patients (42%) who knew their ANCA status. Peripheral eosinophilia was reported in 108 of 112 patients (96%). 100 patients (86%) met ≥ 4 ACR criteria and 75 (65%) met the CHCC definition. All patients who met CHCC definitions also met ACR criteria.

Conclusion: Patient self-report of a diagnosis of ANCA-associated vasculitis is reliable with 86-96% of patients fulfilling the ACR criteria or CHCC definitions for their disease. Additional confirmation of the findings using medical records is currently underway. These results strongly support the validity of utilizing online, patient-generated data for clinical and epidemiological research in ANCA-associated vasculitis.

Disclosure: T. Kermani, None; **J. Springer**, InflaRx, 9; **A. Sreih**, Bristol-Meyers Squibb, 3, Bristol-Myers Squibb, 3; **D. Shaw**, None; **K. Young**, None; **C. Burroughs**, None; **P. Merkel**, Abbvie, 5, AbbVie, 5, AstraZeneca, 2, 5, AstraZeneca,, 2, 5, Biogen, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, Celegene, 2, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Genentech/Roche, 2, 5, Genetech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Kypha, 2, TerumoBCT, 2, UpToDate, 7.

Abstract Number: 2636

Cluster Analysis for Classification of Japanese Antineutrophil Cytoplasmic Antibody-associated Vasculitis: Subgroup Analysis of Nationwide Cohort Studies

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The predominance of myeloperoxidase-antineutrophil cytoplasmic antibody (ANCA) and interstitial lung disease (ILD) have beenreported as characteristics of Japanese patients with ANCA-associated vasculitis (AAV) recently. A previous report using cluster analysis showed that the importance of ANCA type and renal involvement in Western countries. Because of the considerable differences in demographic and clinical characteristics, other relevant clusters may be identified in Japanese patients.

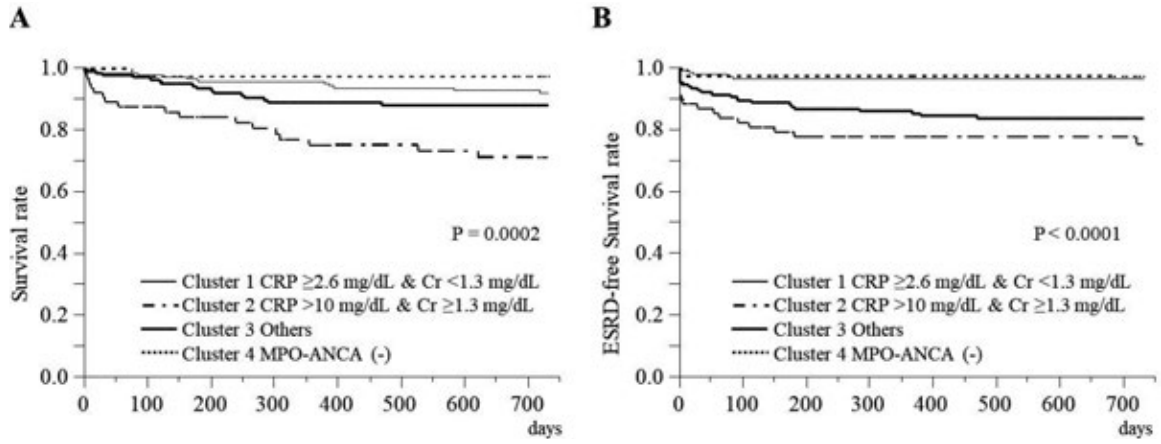

Figure. Overall survival and ESRD-free survival rates according to clusters of Model 2 (A) Overall survival rates and (B) ESRD-free survival rates. Analysis performed using a log-rank test. ESRD, end-stage renal disease; Cr, creatinine; CRP, C-reactive protein; MPO-ANCA, myeloperoxidase-antineutrophil cytoplasmic antibody.

Methods: Using the dataset of two nationwide cohort studies for AAV, we performed multiple correspondence and cluster analysis. Model 1 included ANCA type, items of Birmingham Vasculitis Activity Score (BVAS), and ILD, and Model 2 included serum creatinine and C-reactive protein (CRP) levels additionally. Clustering was performed for finding homogeneous clusters, and clinical characteristics and clinical outcomes were compared among determined clusters. Multivariable regression analysis was conducted to explore factors related to CRP levels among BVAS items and ILD.

Results: After excluding patients with eosinophilic granulomatosis with polyangiitis or missing of proteinase 3 (PR3)-ANCA test, 427 patients were enrolled. Seven and four clusters were determined in Model 1 and Model 2, respectively. In seven clusters of Model 1, ANCA negative (n=8) and PR3-ANCA positive (n=41) group emerged as distinct two clusters. Other myeloperoxidase-ANCA positive five clusters were characterized by ear, nose and throat (n=47), cutaneous (n=36), renal symptoms (n=256), the absence of renal symptoms (n=33), and others (n=6). Four clusters of Model 2 were characterized either by MPO-ANCA negativity (n=42, cluster 4), high CRP (>10mg/dL) and increase of creatinine (creatinine ≥1.3 mg/dL) levels (n=71, cluster 2), increase of CRP (≥2.6 mg/dL) without increase of creatinine (< 1.3 mg/dL) levels (n=157, cluster 1), and others (n=157, cluster 3). Overall survival, renal survival, and relapse rates were significantly different across the four clusters of Model 2 (log-rank test; P=0.0002, P< 0.0001 and P=0.0051, respectively, **Figure**). Multivariable regression analysis revealed that fever (β coefficient [95% confidence interval], 2.1 [1.5–2.6]), myalgia (2.5 [2.0–3.1]), massive hemoptysis/alveolar hemorrhage (1.3 [0.43–2.2]) and mononeuritis multiplex (1.2 [0.47–2.0]) were independently associated with CRP level.

Conclusion: Cluster analysis indicated the association of the distinct clinical and laboratory characteristics with outcomes in Japanese patients with AAV. Prognostic values of improvements in CRP and serum creatinine levels by treatments should be evaluated in future research.

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Abstract Number: 2637

Urine Complement Ba Levels During Flares of Renal Disease in Patients with ANCA-Associated Vasculitis

Salem Almaani,[1] Christopher Toy,[2] Anna Levesque,[2] Lynn Fussner,[1] Alexa Meara,[1] Lianbo Yu,[1] David Cuthbertson,[3] Simon Carette,[4] Nader A. Khalidi,[5] Curry L. Koening,[6] Carol Langford,[7] Carol A. McAlear,[8] Larry Moreland,[9] Christian Pagnoux,[10] Philip Seo,[11] Antoine Sreih,[12] Steven Ytterberg,[13] Paul Monach,[14] Peter Merkel,[12] Brad Rovin,[1] and Dan Birmingham[15], [1]The Ohio State University Medical Center, Columbus, OH, [2]Ohio State University, Columbus, OH, [3]University of South Florida, Tampa, FL, [4]Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, Canada, [5]McMaster University, Hamilton, ON, Canada, [6]University of Utah Hospital, Salt Lake City, UT, [7]Cleveland Clinic, Cleveland, OH, [8]University of Pennsylvania - VCRC Project Manager, Philadelphia, PA, [9]University of Pittsburgh, PITTSBURGH, PA, [10]Mount Sinai Hospital and University Health Network, Toronto, ON, Canada, [11]Johns Hopkins Medicine, Baltimore, MD, [12]University of Pennsylvania, Philadelphia, PA, [13]Mayo Clinic College of Medicine, Rochester, MN, [14]Brigham and Women's Hospital, Boston, MA, [15]The Ohio State University Medical Center, Columbus

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – ANCA-Associated Poster I

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: The alternative complement pathway has been implicated in the pathogenesis of ANCA-associated vasculitis (AAV). Change in markers of complement activation within patients have not been reported. This study measured levels of urinary complement fragment Ba (uBa) longitudinally in patients with AAV.

Methods: Urine levels of uBa were measured by ELISA (corrected to urine creatinine) in 3-4 serial samples in 60 patients with AAV: 20 who developed a flare with renal disease (ReF), 20 who developed a non-ReF (NReF), and 20 in long term remission (LTR). Because timing of pre-flare to flare visits differed from patient to patient, these values were averaged for each patient (pre-ReF or pre-NReF), normalized by natural log-transformation, and compared to flare by paired t test. Differences between ReF and NReF levels were assessed by unpaired t test. Differences between pre-ReF, pre-NReF, and average LTR levels were assessed by ANOVA.

Results: The median age of participants was 59 years, 53% were male, 93% were White, and 93% were ANCA positive. There were no differences in uBa levels between pre-ReF, pre-NReF, and LTR (P=0.360) (Figure). Despite overlap,

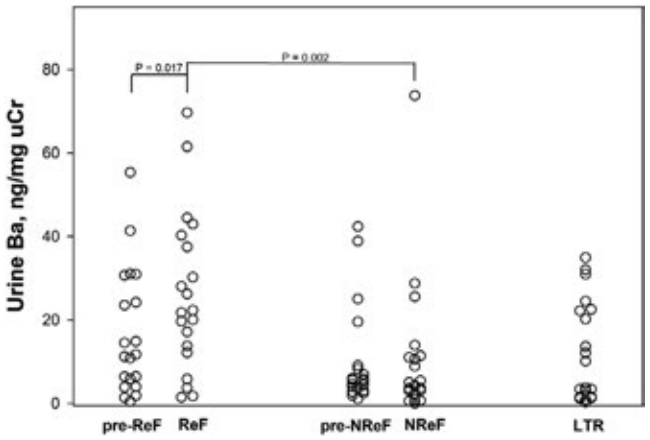

Figure 1. Urine Ba levels in patients with ANCA-Associated vasculitis. Pre-ReF: mean level before renal flare. ReF: level at renal flare. Pre-NReF: mean level before non-renal flare. NReF: level at non-renal flare. LTR: mean level with long-term remission.

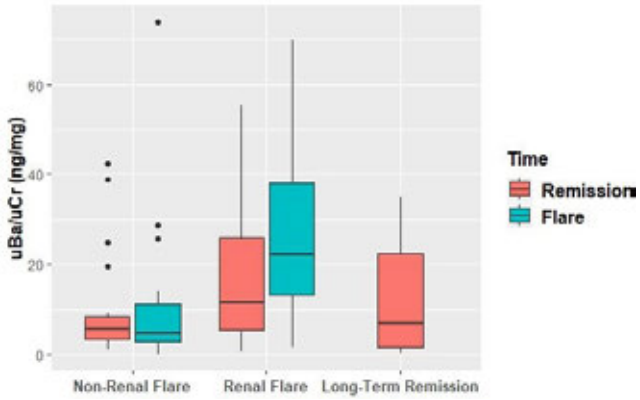

Figure 2. Figure 1: Urine Ba levels in patients with ANCA-Associated vasculitis. Pre-ReF: mean level before renal flare. ReF: level at renal flare. p-value Renal Flare (remission vs. flare 0.017). p-value Flare (Renal flare vs Non-renal flare=0.002)

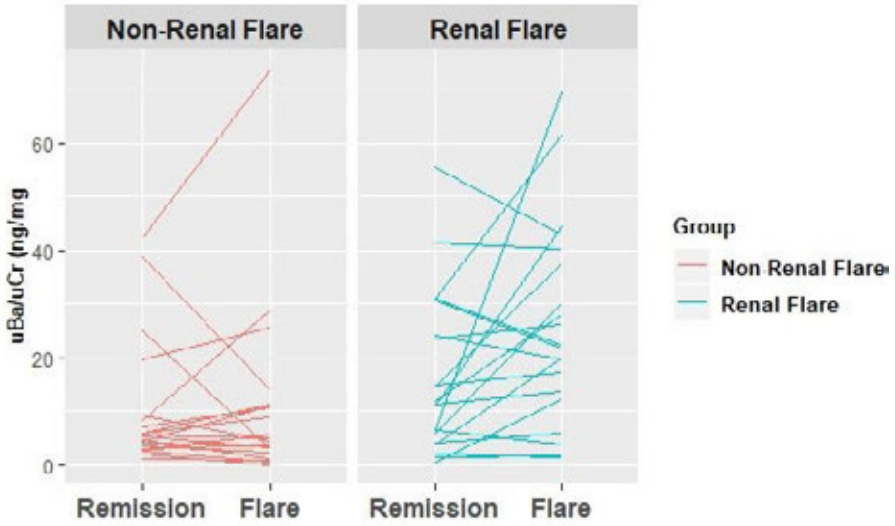

Figure 3: Change in urine Ba levels in individual patients before and at flare.

overall uBa levels were higher in ReF compared to pre-ReF (P=0.017), and to NReF (P = 0.002). Levels of uBa levels did not change from pre-NReF to NReF (P=0.232).

Conclusion: Increased uBa levels suggests that alternative complement pathway activation contributes to the pathogenesis of ReF in AAV. However, many patients experiencing ReF do not show high uBa levels. Thus, uBa may identify a subset of patients with ReF who might benefit from complement-targeted therapies. Other factors defining this subset remain to be determined.

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ChemoCentryx, 2, 5, CSL Behring, 5, Genentech/Roche, 2, 5, Genetech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Kypha, 2, TerumoBCT, 2, UpToDate, 7; **B. Rovin**, Genentech, Inc., 9, Admirx, 5, Alexion, 5, Aurinia, 5, Biogen, 5, Biomarin, 5, Bristol Myers Squibb, 5, Callidates, 5, ChemoCentryx, 2, 5, Chugai Pharmaceuticals, 5, EMD Serono, 2, 5, Genentech, 5, Janssen, 5, Lupus Foundation of America, 5, Mallinckrodt, 5, MedImmune, 5, Morphosys, 5, Novartis, 5, Omeros, 3, Pfizer, 5, Ra Pharmaceuticals, 5, Retrophin, 2, 5, Rigel, 2, 5, Takeda, 5, AstraZeneca, 2, Hoffman-La Roche, 2, Human Genome Sciences Inc., a GSK Company, 2, NIH/NIDDK, 2, RILITE Foundation, 2; **D. Birmingham**, None.

Abstract Number: 2638

The Cumulative Burden of Damage for Patients with Eosinophilic Granulomatosis with Polyangiitis

Irena Doubelt,[1] David Cuthbertson,[2] Gunnar Tomasson,[3] Simon Carette,[1] Nader A. Khalidi,[4] Curry L. Koening,[5] Carol Langford,[6] Carol A. McAlear,[7] Larry W. Moreland,[8] Paul Monach,[9] Philip Seo,[10] Ulrich Specks,[11] Antoine Sreih,[12] Kalen Young,[13] Steven Ytterberg,[11] Peter A. Merkel,[14] Christian Pagnoux,[1] and VCRC Vasculitis Clinical Research Consortium[15], [1]Mount Sinai Hospital and University Health Network, Toronto, ON, Canada, [2]University of South Florida, Tampa, FL, [3]Faculty of Medicine, University of Iceland and Landpitali University Hospital, Reykjavik, Iceland, [4]McMaster University, Hamilton, ON, Canada, [5]University of Utah Hospital, Salt Lake City, UT, [6]Cleveland Clinic, Cleveland, OH, [7]University of Pennsylvania - VCRC Project Manager, Philadelphia, PA, [8]University of Pittsburgh, Pittsburgh, PA, [9]Brigham and Women's Hospital, Boston, MA, [10]Johns Hopkins Medicine, Baltimore, MD, [11]Mayo Clinic College of Medicine, Rochester, MN, [12]University of Pennsylvania, Philadelphia, PA, [13]Vasculitis Foundation, Kansas City, MO, [14]Univeristy of Pennsylvania, Philadelphia, PA, [15]University of Pennsylvania, Division of Rheumatology, philadelphia

SESSION INFORMATION
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Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is characterized by asthma and other manifestations of vasculitis, some of which can be life-threatening, cause major organ damage, or become chronic. Data on damage in EGPA is limited, mainly due to the rarity of the disease. This study aimed at describing damage in patients with EGPA enrolled in the Vasculitis Clinical Research Consortium(VCRC).

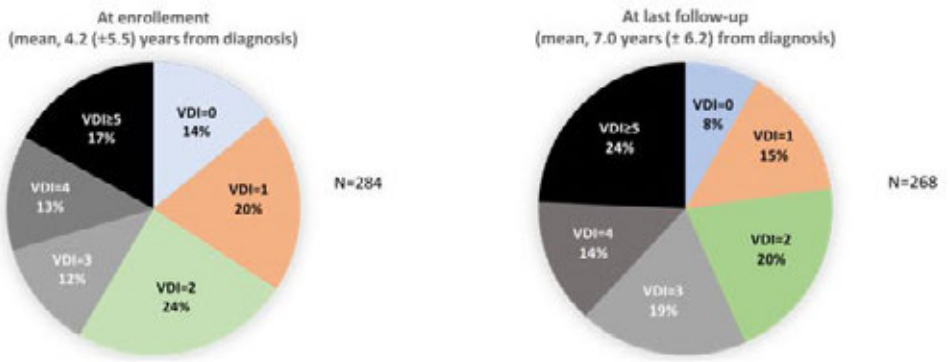

Figure 1. Distribution of vasculitis damage index (VDI) scores for patients with eosinophilic granulomatosis with polyangiitis in the Vasculitis Clinical Research Consortium at enrollment, and last follow-up (for the patients with a follow-up post-diagnosis >1 year).

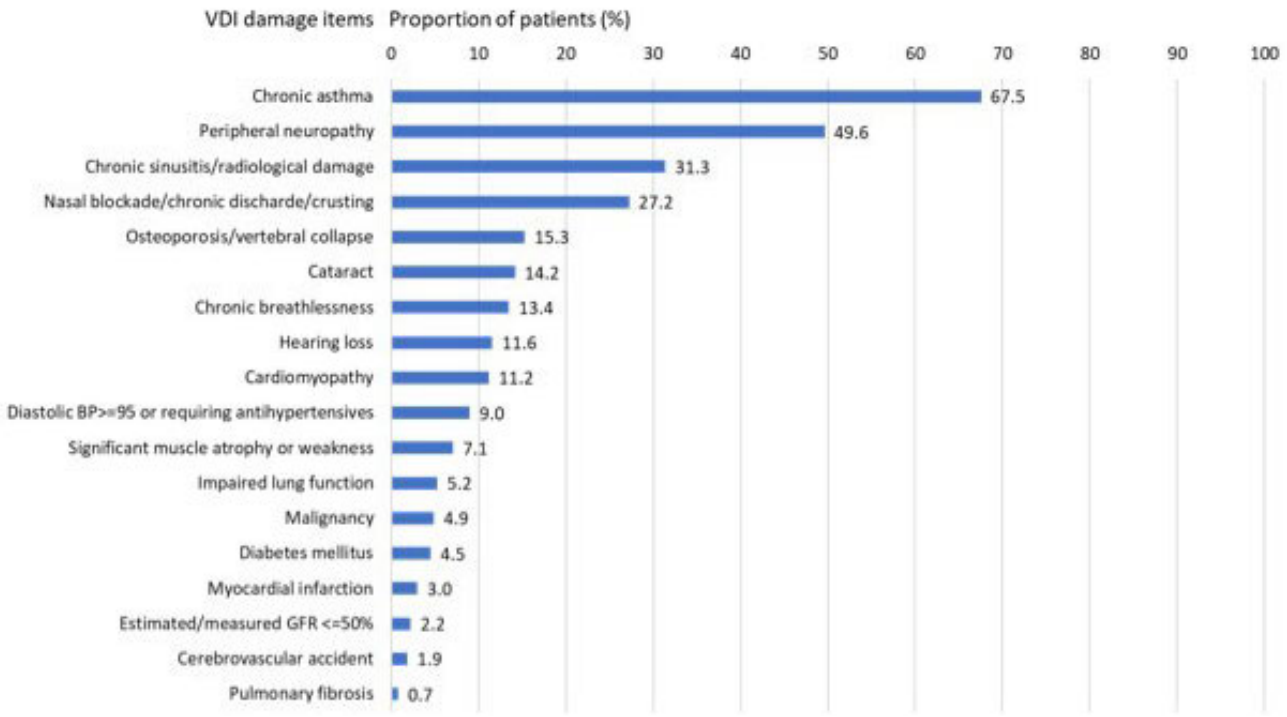

Figure 2. Main items of damage at last follow-up for patients with eosinophilic granulomatosis with polyangiitis in the Vasculitis Clinical Research Consortium. 268 patients with >1 year of follow-up post-diagnosis (mean, 7.0 ± 6.2 years).

Methods: Retrospective analysis of damage in patients with EGPA participating in the VCRC Longitudinal Study (LS) or One-Time DNA (OT) studies from 2003-2019. Patients were ≥18 years of age at enrollment and fulfilled the modified American College of Rheumatology 1990 criteria. Data elements included demographics, ANCA status, use of cyclophosphamide (CYC), cumulative duration of glucocorticoid (GC) use, relapses, all items of the Vascular Damage Index (VDI). VDI is a validated, cumulative damage score, which includes 64 items, grouped by organ or system and each scoring 1 point (range, 0-64; by design, VDI is 0 at diagnosis). VDI scores and items were analyzed at enrollment (for all patients with a diagnosis made >3 months prior to enrollment, and at the farthest visit from diagnosis for patients with a follow-up >1-year post-diagnosis. For the last VDI score, associations of age, sex, CYC use, duration of GC use, and relapses with accrual of damage were explored.

Results: The cohort included 354 patients, of which 336 had a follow-up post-diagnosis >3 months. Mean age at diagnosis for the latter was 50.0 (SD ±14.1) years; 197 (58.6%) were female. Of those tested for ANCA, 132 (42.7%) were positive. A total of 112 (41.9%) LS patients received CYC at some point during their disease; mean duration of GC use was 13.7 (±20.7) months. With a mean follow-up from diagnosis for all 336 patients of 7.2 (±6.1) years, 173 (51.4%) had at least one relapse. VDI at enrollment (for the 284 patients enrolled >3 months' post-diagnosis; mean 4.2 (±5.5) years from diagnosis), and last follow-up visit for patients with >1 year of follow-up post-diagnosis (n=268) were 2.61 (±2.17) and 3.19 (± 2.24), respectively. VDI score distributions and items for the latter are showed in Figures 1 and 2. Univariate analysis of data from the 128 LS patients with a follow-up post-diagnosis >1 year identified male sex, older age, longer duration of GC use, and having relapsed as significantly associated with higher VDI at last visit. Multivariate Poisson regression analysis retained only male sex (mean VDI of 3.80 ±0.31 in male vs. 3.0 ±0.23 in female patients; $P< 0.01$) and longer duration of GC use (increase of the VDI by 0.5% for each additional month of GC use; $P< 0.01$) as being associated with a higher last VDI.

Conclusion: Patients with EGPA accumulate substantial permanent damage from the disease and treatment, even several years after diagnosis. Strategies to attain sustained, long-term limitation of damage should be important as-

pects of the management of patients with EGPA. Identification of more effective and safer treatments for EGPA are needed, especially to limit the use of GC.

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Abstract Number: 2639

Comparison of Patient Self-reported Data to Physician-driven Cohorts in Patients with Eosinophilic Granulomatosis with Polyangiitis

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SESSION INFORMATION

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Background/Purpose: Aligning perspectives of patients and physicians in the diagnosis and management of diseases is imperative, particularly in rare, chronic diseases such as vasculitis. We sought to compare patient-reported vs. physician-reported clinical manifestations, treatments, and outcomes in patients with eosinophilic granulomatosis with polyangiitis (EGPA).

Methods: Retrospective, comparative analysis of patients ≥18 years old with EGPA from Canada or the United States, from two separate databases: 1) Vasculitis Patient-Powered Research Network (VPPRN), a self-enrolled, secure patient portal with patient-entered data updated quarterly from 2013-2019, and 2) Vasculitis Clinical Research Consortium (VCRC) Longitudinal (LS) or the One-Time DNA (OT) studies, a combined physician-entered database (2003-2019). A few patients are in both databases, which are not presently linked due to protected health information policies. For validation of the diagnosis, patients in the VPPRN were excluded if they indicated that the diagnosis was not made by doctor and/or if they never used systemic glucocorticoids. Patients in the VCRC fulfilled the modified American College of Rheumatology 1990 criteria. Studied parameters included demographics, clinical manifestations, ANCA status, treatments received since diagnosis, and relapses.

Characteristic	VPPRN n=195	VCRC n=354	P-value
Female, n (%)	135 (69.2)	209 (59.0)	0.02
Age at diagnosis, years ±SD	47.3 ±14.3	50.0 ±14.2	0.04
Positive test for ANCA, n (%)	64/131 (48.8)	123/316 (38.9)	0.07
Manifestations (ever), n (%)			
Asthma	177/184 (96.2)*	329 (92.9)	0.13
Alveolar hemorrhage	24/168 (14.3)	21 (5.9)	<0.01
Lung disease	128/174 (73.6)	295 (83.3)	0.01
Sinus-nasal	165/181 (91.2)	292 (82.5)	0.01
Fever	82/148 (55.4)	62 (17.5)	<0.01
Weight loss	95/171 (55.6)	106 (29.9)	<0.01
Arthralgia	116/173 (67.0)	140 (39.6)	<0.01
Skin	125/177 (70.6)	106 (29.9)	<0.01
Cardiac	44/153 (28.8)	75 (21.2)	0.08
Renal disease	39/174(22.4)	36 (10.2)	<0.01
Neuropathy	155/177 (87.6)	214 (60.5)	<0.01
Eye disease	42/161 (26.1)	31 (8.8)	<0.01
Gastrointestinal	10/165 (6.1)	22 (6.2)	0.95
Thrombosis	24/171 (14.0)	24 (6.8)	0.01
Follow-up, years ±SD			
From diagnosis	8.0 ±6.8	7.0 ±6.2	0.08
From enrollment	2.2 ±1.1	3.6 ±3.5	<0.01
Relapses, n (%)			
Ever, since diagnosis	N/A	175 (49.4)	
After enrollment	63 (32.3)	99 (35.7)†	0.33
Ever received, n (%)			
Systemic glucocorticoids	195 (100)	354 (100)†	1.0
Cyclophosphamide	79 (40.5)	115 (41.5)†	0.07
Mepolizumab	20 (10.3)	25 (9.0)†	0.25
Rituximab	47 (24.1)	29 (10.5)†	<0.01

VPPRN: Vasculitis Patient-Powered Research Network.
VCRC: Vasculitis Clinical Research Consortium.
ANCA: antineutrophil cytoplasmic antibody; SD: standard deviation.
* *For the VPPRN patients, denominator is number of patients who responded Yes/No (response of "I don't know" excluded)*
† *Data available only for the 277 patients in the VCRC*

Table 1. Main characteristics of patients with eosinophilic granulomatosis with polyangiitis from the Vasculitis Patient-Powered Research Network and the Vasculitis Clinical Research Consortium

Results: 208 patients self-registered with a diagnosis of EGPA in the VPPRN (195 had a validated diagnosis) and 354 patients were enrolled in the VCRC. 135 (69.2%) of the 195 VPPRN patients were female; 176 (92.1%) were white, 4 (2%) Asian, and 1 (0.5%) Black or African American. Mean age at first disease symptoms and diagnosis were 41.9 (SD ±14.9) years and 47.3 (±14.3) years, respectively. Method of diagnosis reported by patients was based on symptoms (91.3%), laboratory testing (80.5%), biopsy results (50.3%), and imaging (50.3%). At enrollment, 80 (41%) reported that the EGPA was active. **Table 1** shows the main characteristics and outcomes of the VPPRN patients compared to those from the VCRC. Patients in the VPPRN were predominantly female, slightly younger at diagnosis than in the VCRC cohort, and reported more frequent disease manifestations in almost all organ systems, but less lung disease, and similar frequencies of asthma, cardiac and gastrointestinal manifestations. With a mean follow-up of 2.2 (±1.1) years post-enrollment, 63 (32.3%) of the VPPRN patients reported at least 1 relapse post-enrollment, which was comparable to the VCRC patients.

Conclusion: This analysis comparing patient vs. physician data in EGPA showed some differences with patients generally reporting more manifestations of disease. These differences suggest that patient self-reported data can provide additional useful information. How to best combine patient-reported and physician-reported data for research studies in vasculitis warrants additional study.

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Abstract Number: 2640

Performance of Berden's Classification and ANCA Renal Risk Score for the Prediction of End-Stage Renal Disease in ANCA-associated Vasculitis

Onay Gercik,[1] Emre Bilgin,[2] Dilek Solmaz,[1] Fulya Cakalagaoglu,[3] Arzu Saglam,[4] Ozge Aybi,[5] Riza Kardas,[5] Zeki Soypacaci,[6] Gokhan Kabadayi,[7] Tolga Yildirim,[8] İdil Kurut Aysin,[9] Omer Karadag,[10] and Servet Akar[11], [1]Izmir Katip Celebi University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, İzmir, Turkey, [2]Hacettepe University Vasculitis Centre, Ankara, Turkey, Ankara, Turkey, [3]Izmir Katip Celebi University, Faculty of Medicine, Department of Pathology, Izmir, Turkey, [4]Hacettepe University, Faculty of Medicine, Department of Pathology, Ankara, Turkey, [5]Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Ankara, Turkey, [6]Izmir Katip Celebi University Faculty of Medicine, Department of Internal Medicine, Division of Nephrology, Izmir, Turkey, [7]Izmir Katip Celebi University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, İzmir, Turkey, [8]Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Nephrology, Ankara, Turkey, [9]Izmir Katip Celebi University Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, İzmir, Turkey, [10]Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey, [11]Izmir Katip Celebi University, Faculty of Medicine, Division of Rheumatology, İzmir, Turkey

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Background/Purpose: Renal involvement in ANCA-associated vasculitides (AAVs) is an important factor for morbidity and mortality. Berden's histopathologic classification for ANCA-associated glomerulonephritis has been proven to be helpful for predicting the renal outcome. Recently, the ANCA renal risk score, a new scoring system which needs to be validated, has been proposed to predict end-stage renal disease (ESRD) in AAV patients. In this study, we aimed a) to assess prognostic factors for renal survival in our AAV patients with renal involvement, b) to evaluate the performances of the Berden's histopathological classification and ANCA-renal risk score, for predicting ESRD.

Methods: Patients with AAV who were categorized according to the 2012 Chapel Hill consensus nomenclature were included in this study. Patients with only renal involvement clinically and diagnosed by renal biopsy were classified as renal-limited vasculitis (RLV). Renal biopsies were reviewed according to the Berden's histopathological classification, and the percentages of normal glomeruli, tubular atrophy and interstitial fibrosis were determined in order to calculate ANCA renal risk score. The clinical data and laboratory parameters were collected retrospectively. Renal survival was defined as the time between diagnosis and the development of ESRD. Factors predictive of renal survival were evaluated by Kaplan-Meier method and the Cox proportional hazard model.

	GPA (n=90)	MPA (n=39)	EGPA (n=8)	RLV (n=30)	AAV Total (n=167)
Male sex, n (%)	55 (61)	21 (54)	4 (50)	15 (50)	95 (57)
Age at diagnosis, mean (SD) (years)	51.10 ∓ 15.16	59.15 ∓ 13.14	52.0 ∓ 17.06	54.13 ∓ 16.46	53.60 ∓ 15.27
ANCA					
Positive, n (%)	82 (95)	26 (67)	7 (88)	26 (87)	141 (87)
Negative, n (%)	4 (4)	13 (13)	1 (13)	4 (13)	22 (13)
ANCA subtype					
p/MPO-ANCA	18 (22)	22 (85)	5 (71)	20 (77)	65 (46)
c/PR3-ANCA	64 (78)	4 (15)	2 (29)	6 (23)	76 (54)
Organ/system Involvements (n) (%)					
Lung	70 (81)	30 (77)	8 (100)	0 (0)	108 (66)
ENT (ear-nose-throat)	61 (71)	2 (5)	4 (50)	0 (0)	67 (41)
Eye	20 (24)	1 (3)	1 (13)	0 (0)	22 (14)
Cardiac	4 (5)	3 (8)	1 (13)	0 (0)	8 (5)
GI	8 (9)	5 (13)	0 (0)	0 (0)	13 (8)
CNS	4 (5)	0 (0)	0 (0)	0 (0)	4 (2)
MNM	9 (11)	3 (8)	3 (38)	0 (0)	15 (9)
FFS (n=145); (n) (%)					
0	10 (14)	2 (5)	4 (50)	1 (4)	17 (12)
1	25 (34)	2 (5)	3 (38)	2 (7)	32 (22)
2	26 (36)	24 (65)	1 (13)	18 (67)	69 (48)
3	12 (16)	7 (19)	0 (0)	6 (22)	25 (17)
4	0 (0)	2 (5)	0 (0)	0 (0)	2 (1)
Maximum Creatinine level at diagnosis (mg/dl) (median, IQR)	3.50 (5.75)	4.81 (4.88)	1.24 (0.80)	4.66 (4.17)	3.74 (5.32)
ESRD development (n) (%)	27 (32)	8 (24)	0 (0)	17 (60.7)	52 (34)
Hemodialysis at diagnosis (n) (%)	31 (38)	22 (56)	0 (0)	19 (68)	72 (46)
Plasmapheresis at diagnosis (n) (%)	22 (27)	20 (51)	1 (13)	13 (48)	56 (36)
BVAS at diagnosis, mean (SD) (n=62)	23.85 ∓ 7.32	18.33 ∓ 7.66	22.43 ∓ 5.94	11.0 ∓ 2.64	21.44 ∓ 7.93
Overall mortality (n) (%)	20 (23)	13 (33)	0 (0)	10 (33)	43 (26)
First-year mortality (n) (%)	10 (12)	8 (22)	0 (0)	3 (10)	21 (13)
Berden's histopathological classification	45	33	1	27	106
Sclerotic (n) (%)	5 (11)	2 (6)	0 (0)	7 (26)	14 (13)
Crescentic (n) (%)	20 (44)	10 (30)	0 (0)	11 (41)	41 (39)
Mixed (n) (%)	13 (29)	13 (39)	0 (0)	7 (26)	33 (31)
Focal (n) (%)	7 (16)	8 (24)	1 (100)	2 (7.4)	18 (17)
ANCA Renal Risk Score					
Low (total 0)	6 (16)	4 (13)	1 (100)	2 (8)	13 (14)
Medium (2-7)	23 (62)	24 (80)	0 (0)	12 (46)	59 (63)
High (8-11)	8 (22)	2 (7)	0 (0)	12 (46)	22 (23)

*ANCA: Anti-Neutrophil Cytoplasmic Antibody; AAV: ANCA-Associated Vasculitis; GPA: Granulomatosis with PolyAngiitis; MPA: Microscopic PolyAngiitis; EGPA: Eosinophilic Granulomatosis with PolyAngiitis; RLV: Renal Limited Vasculitis; GFR: Glomerular Filtration Rate, MPO: Myeloperoxidase; PR3: Proteinase3; c-ANCA: Cytoplasmic-ANCA; p-ANCA: Perinuclear-ANCA; GI: Gastrointestinal; CNS: Central Nervous System; MNM: MonoNeuritis Multiplex; FFS: Five Factor Score; IQR: Inter Quantile Range ; ESRD: End-Stage Renal Disease; BVAS: Birmingham Vasculitis Activity Score: SD: Standard Deviation

Table 1. Demographic, clinical characteristics, histopathological classes and ANCA-renal risk scores of ANCA-associated vasculitis patients with renal involvement

Results: 167 AAV patients with renal involvement were included in the study. ESRD had developed in 52 (34%) patients and renal survival was median 31 (0-240) months. According to the histopathological classification ESRD had developed in %79 patients in the sclerotic group, % 51 patients in the crescentic group, %32 patients in the mixed group and %18 patients in focal group (p=0.003). According to the ANCA renal risk score, ESRD had developed in %8 patients in the

Parameters	Model 1			Model 2			Model 3		
	HR	**CI 95%**	**p**	**HR**	**CI 95%**	**p**	**HR**	**CI 95%**	**p**
Age at diagnosis	1.01	0.98-1.03	0.39	0.98	0.96-1.01	0.41	1.01	0.99-1.04	0.18
AAV subgroups			0.36			0.21			0.06
GPA vs MPA	2.10	0.87-5.08	0.09	2.72	1.07-6.92	0.03	4.07	1.45-11.39	0.007
EGPA vs MPA	0	0-N/A	0.98	0.02	0-N/A	0.99	0	0-N/A	0.98
RLV vs MPA	2.22	0.86-5.75	0.09	2.20	0.80-6.05	0.12	2.92	0.99-8.60	0.05
Histopathological classification	-	-	**0.04**	-	-	0.08	-	-	-
Focal vs sclerotic	0.20	0.05-0.75	0.01	0.31	0.07-1.27	0.10	-	-	-
Mixed vs sclerotic	0.32	0.11-0.87	0.02	0.25	0.08-0.76	0.01	-	-	-
Crescentic vs sclerotic	0.57	0.23-1.41	0.22	0.53	0.21-1.29	0.16	-	-	-
GFR at diagnosis	-	-	-	0.90	0.86-0.95	**<0.001**	-	-	-
ANCA renal risk score	-	-	-	-	-	-	-	-	**0.04**
Moderate vs low	-	-	-	-	-	-	5.62	0.74-42.35	0.09
High vs low	-	-	-	-	-	-	10.48	1.32-82.88	0.02

*ANCA: Anti-Neutrophil Cytoplasmic Antibody; AAV: ANCA-Associated Vasculitis; GPA: Granulomatosis with PolyAngiitis; MPA: Microscopic PolyAngiitis; EGPA: Eosinophilic Granulomatosis with PolyAngiitis; RLV: Renal Limited Vasculitis; GFR: Glomerular Filtration Rate, HR: Hazard Ratio; CI: Confidence Interval

Table 2. Multivariate analysis models which predict renal survival in ANCA-associated vasculitis

low-risk group, %42 patients in the medium-risk group and %67 patients in the high-risk group (p=0.005). In univariate analysis the age at diagnosis (HR 1.02, 95 % CI 1.00-1.04, p=0.045), AAV subgroups (p=0.01) (Figure), histopathological classification (p=0.009), ANCA renal risk score (p=0.01), maximum creatinine level at diagnosis (HR 1.14, 95 % CI 1.09-1.19, p< 0.001), glomerular filtration rate (GFR) (HR 0.92, 95 % CI 0.89-0.95, p< 0.001), hemodialysis (HR 4.81, 95 % CI 2.53-9.17, p< 0.001) and plasmapheresis at diagnosis (HR 2.36, 95 % CI 1.32-4.22, p=0.004) were the factors associated with renal survival. In multivariate analysis, histopathological classification predicted mortality in model 1, but when GFR at diagnosis is included in the model (model 2), the model lost its significance. However, the ANCA renal risk score was found to be an independent prognostic risk factor for renal survival (model 3, table 2).

Conclusion: According to our results, the ANCA renal risk score may be more advantageous in predicting ESRD development compared to Berden's histopathological classification, and this may be due to the inclusion of glomerular filtration in scoring.

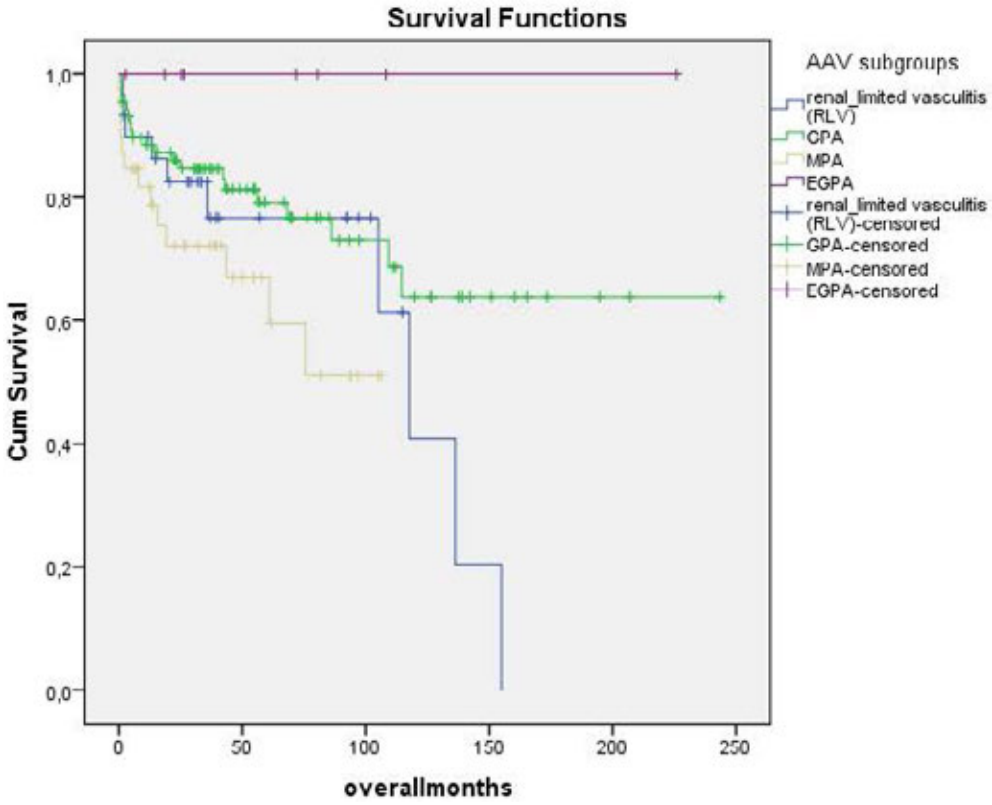

Figure. The results of the Kaplan-Meier analysis. Renal survival was significantly associated with AAV subgroups patients with ANCA-associated vasculitis with renal involvement

Disclosure: O. Gercik, None; **E. Bilgin**, None; **D. Solmaz**, None; **F. Cakalagaoglu**, None; **A. Saglam**, None; **O. Aybi**, None; **R. Kardas**, None; **Z. Soypacaci**, None; **G. Kabadayi**, None; **T. Yildirim**, None; **İ. Kurut Aysin**, None; **O. Karadag**, None; **S. Akar**, Abbvie, 2, 5, Amgen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 8, Roche, 2, 5, UCB, 2, 5.

Abstract Number: 2641

Clinical Characteristics of a Cohort of Patients with a Self-Reported Diagnosis of Granulomatosis with Polyangiitis or Microscopic Polyangiitis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Table 1: Clinical manifestations in a patient-reported cohort of granulomatosis with polyangiitis and microscopic polyangiitis

Clinical Manifestation	GPA*	MPA*
Fever >38℃	331/557 (59%)	64/139 (46%)
Rashes	401/698 (57%)	
Joint involvement	549/688 (80%)	106/154 (69%)
Any ENT manifestation		
Nasal/sinus symptoms	612/704 (87%)	89/146 (61%)
Hearing loss	322/666 (48%)	22/144 (15%)
Tracheal involvement	183/610 (30%)	13/133 (10%)
Any Pulmonary involvement	518/719 (72%)	95/153 (62%)
Alveolar hemorrhage	282/700 (40%)	58/161 (36%)
Any Renal involvement	408/707 (58%)	137/163 (84%)
Dialysis	73/721 (10%)	18/163 (11%)
Renal transplant	10/730 (1%)	7/163 (4%)
Pulmonary-renal syndrome	184/723 (25%)	47/164 (29%)
Peripheral nerve involvement	411/654 (63%)	95/147 (65%)
Gastrointestinal involvement	14/683 (2%)	4/147 (3%)
Venous Thromboembolism	96/701 (14%)	21/154 (14%)
Pericardial involvement	49/609 (8%)	6/132 (5%)
Positive ANCA	652/692 (94%)	147/153 (96%)
* Denominator is number of patients who responded Yes/No (response of "I don't know" excluded)		

Background/Purpose: To provide a feasible and sustainable platform for conducting patient-centered research in vasculitis, a prospective, international, internet-based registry of patients with vasculitis has been established. The aim of this study is to describe the self-reported clinical features of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) from this registry.

Methods: Patients (or caregivers) with different forms of vasculitis can join the web-based registry. All information is self-reported through standardized forms, including type of vasculitis, symptoms at disease onset and later in the disease course, and information regarding how diagnosis was made. For each manifestation, patients can respond with "Yes", "No", or "I don't know". Only patients with GPA or MPA were included in this analysis. Other analyses demonstrated that in this cohort the accuracy of the self-reported diagnosis of GPA or MPA is > 90%.

Results: The study cohort included 762 patients (68% female) with GPA and 164 patients (81% female) with MPA.

GPA Cohort: 98% of patients reported a physician-confirmed diagnosis. Commonly reported means of diagnosis were combinations of laboratory testing (74%), symptoms (70%), biopsy (62%), and imaging (38%). 562 patients (74%) reported having at least one biopsy, including skin (70 patients), kidney (283 patients), lung (192 patients), nasal/sinus (146 patients), nerve (10 patients), other (36 patients). ANCA was reported in 652/692 (94%) patients who knew their ANCA status. Clinical manifestations at entry into the cohort are summarized in Table 1.

MPA Cohort: 99% of patients reported a physician-confirmed diagnosis. Commonly reported means of diagnosis were combinations of laboratory testing (79%), symptoms (67%), biopsy (77%), and imaging (42%). 131 patients (80%) reported having at least one biopsy, including kidney (103 patients), lung (20 patients), skin (15 patients), nerve (6 patients), and nasal (4 patients). ANCA was reported as positive in 147/153 (96%) patients who knew their ANCA status. Clinical manifestations at entry into the cohort are summarized in Table 1.

Conclusion: In this large cohort patients with a self-reported diagnosis of GPA or MPA, disease manifestations were consistent with each type of ANCA-associated vasculitis. As expected, sinus manifestations were more frequently reported in GPA cohort while renal manifestations were more frequent in the MPA cohort. Given the rarity of these and other vasculitides, conducting some types of research through online registries may provide an efficient alternative to in-person, center-of-excellence clinical trials.

Disclosure: J. Springer, InflaRx, 9; **T. Kermani**, None; **A. Sreih**, Bristol-Meyers Squibb, 3, Bristol-Myers Squibb, 3; **D. Shaw**, None; **K. Young**, None; **C. Burroughs**, None; **P. Merkel**, Abbvie, 5, AbbVie, 5, AstraZeneca, 2, 5, AstraZeneca,, 2, 5, Biogen, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, Celegene, 2, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Genentech/Roche, 2, 5, Genetech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Kypha, 2, TerumoBCT, 2, UpToDate, 7.

Abstract Number: 2642

ANCA Testing: Final Diagnoses in Cases with Positive Immunofluorescence and Negative ELISA

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: With the widespread availability of anti-neutrophil cytoplasmic antibody (ANCA) testing, interpreting positive results has become increasingly challenging. In addition to ANCA Associated Vasculitis (AAV), the spectrum of diseases associated with ANCAs has broadened to include a wide range of other inflammatory and infectious diseases including Inflammatory bowel disease, systemic lupus erythematosus, rheumatoid arthritis and drug-induced vasculitis, calling into question the diagnostic implications of ANCA positivity in a hospital setting. Immunofluorescence (IF) on ethanol-fixed neutrophils is used to detect ANCA, which can be divided into three patterns; cytoplasmic ANCA (c-ANCA), perinuclear ANCA (p-ANCA) and atypical ANCA (a-ANCA). Enzyme-linked immunosorbent assay (ELISA) is used in diagnostic laboratories to detect ANCA to specific antigens. The most common antigens used in ELISA testing are myeloperoxidase (MPO) and proteinase-3 (PR3).

Discrepancies may exist between IF and ELISA ANCA testing. We studied cases with positive ANCA IF testing but negative ELISA for both MPO and PR3, looking for their final diagnoses.

Methods: ANCA tests performed between 2000-2018 were identified using the medical center laboratory data system. Of those, all cases with negative MPO and PR3 testing were collected. Medical records of those cases were retrieved to look for their clinical features and final diagnoses.

Table 1: Final diagnoses of patients with positive Immunofluorescence Anti-neutrophil cytoplasmic antibodies (ANCA) and negative Enzyme-linked immunosorbent assay (ELISA) tests:

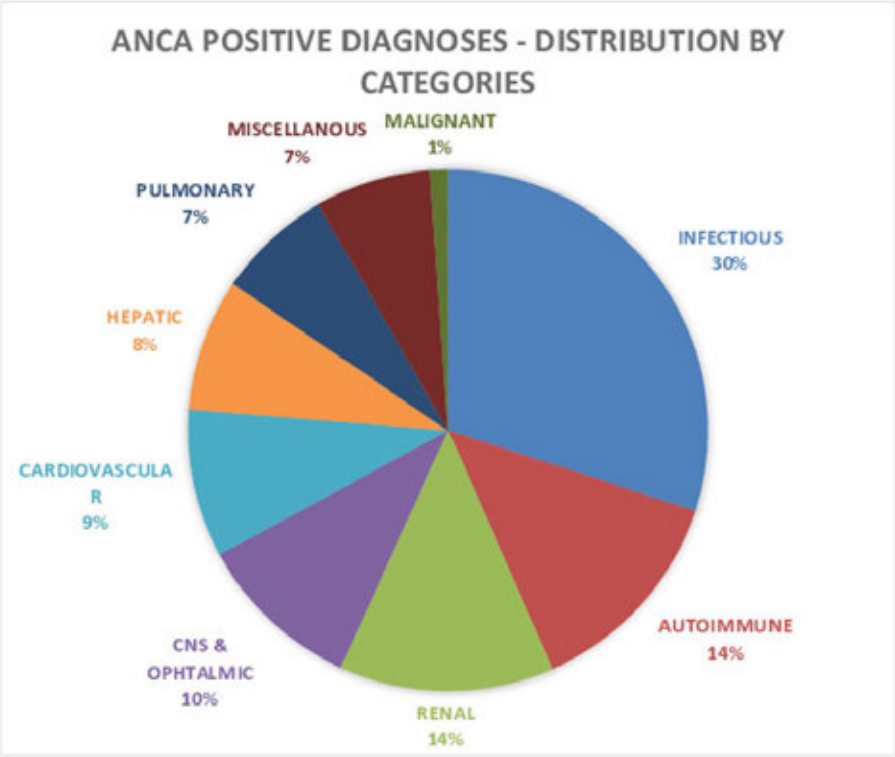
	Diagnosis	Atypical ANCA 62 Cases	P ANCA 22 Cases	C ANCA 9 Cases
AUTOIMMUNE	Hemolytic Anemia	2		
	SLE/ITP	2	1	
	Pancreatitis	1		
	Takayasu/Vasculitis	1	1	
	Ulcerative Colitis	1		
	Microscopic polyangiitis/ GPA		2	
	Autoimmune hepatitis	1		
	ALPS			1
	RPGN/Anti GBM	1	1	
	Drug-related positive ANA		1	
INFECTION	Bacterial infections	16	6	5
	Viral infections	1	1	1
HEPATIC	cirrhosis	3	4	
RENAL	Acute tubular necrosis/Rhabdomyolysis	1	1	1
	Post obstructive uropathy	1		
	Hyponatremia	1		
	Interstitial nephritis	1	1	
	Acute / Chronic kidney injury	3		1
CARDIOVASCULAR	Pericarditis	2		1
	Pulmonary edema	6		
PULMONARY	Restrictive/ Interstitial	2	1	
	Pleuritis	2		
	PE	1		
	COP	1		
CNS & OPHTHALMIC	Uveitis/ Papillitis	2	1	
	Retinal artery occlusion	1		
	NPH/Frontal Lobe syndrome	2		
	CVA	3		
	Neuropathy	1		
MALIGNANT	Ovarian cancer	1		
MISCELLANOUS	Myelodysplasia/myelofibrosis	1		1
	Splenic Infarction	1		
	FUO	1	1	
	Ruptured breast implants		1	

(A few patients carried more than one final diagnosis)

Abbreviations:

ALPS - Autoimmune Lymphoproliferative Syndrome, ANA- Antinuclear antibodies , CDT - Clostridium Difficile Toxin, COP – Cryptogenic Organizing Pneumania, CVA – Cerebrovascular Accident,, FUO – Fever of Unknown origin, GBM – Glomerular Basement Membrane, GPA – Granulomatosis polyangitis, HTN – Hypertension, ITP - Immune throbocytopenia, NPH – Normal Pressure Hydrocephalous, PE- Pulmonary emboli, RPGN - Rapidly progressive Glomerulonephritis, SLE- Systemic lupus Erythematosus, UTI – Urinary tract infection.

Results: 9189 ANCA tests were ordered between the years 2000-2018 of which 549 (5.9% were positive by at least one method. 114 (1.2%) cases showed discrepancy, 93 (0.01%) were ANCA IF-positive ELISA-negative. 62 were a-ANCA positive, 22 were p-ANCA positive and 9 were c-ANCA positive. Only 2 case were diagnosed with AAV, both had p-ANCA. All other patients had a broad spectrum of diagnoses, including autoimmune, infectious, and other conditions involving the renal, hepatic, cardiovascular, and central nervous systems (Table 1, Figure 1).



Conclusion: Diagnosis of AAV is highly unlikely in cases with ANCA IF-positive ELISA-negative.

Disclosure: G. Breuer, None; **B. Fteiha**, None; **A. Benaya**, None; **M. Abu Sneineh**, None; **G. Nesher**, None.

Abstract Number: 2643

Comparative Study of Renal Transplantation Due to Rapidly Progressive Glomerulonephritis (RPGN): Study of 42 Patients from a Single Tertiary Centre

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Rapidly Progressive Glomerulonephritis (RPGN) is characterized clinically by a rapid and severe decline in kidney function. Thus, this entity may lead to an end stage renal disease, with kidney transplantation. RPGN is classificated in three groups: a) Type I or associated to anti-glomerular basement membrane antibodies (RPGN-GBMa), b) Type II or associated to immunocomplexes (RGPN-immunocomplexes), and c) Type III or pauci-immune (RPGN-pauci-immune). Besides, RPGN can be primary, without extra-renal involvement (RPGN-

TABLE 1. Evolution of creatinine and proteinuria levels after renal transplant in RPGN types

	1 Month				6 Months				1 Year				3 Years				5 Years			
Serum Creatinine mg/dL	RPGN-type I	RPGN-type III	RPGN-type IIII	Total	RPGN-type I	RPGN-type II	RPGN-type III	Total	RPGN-type I	RPGN-type II	RPGN-type III	Total	RPGN-type I	RPGN-type III	RPGN-type III	Total	RPGN-type I	RPGN-type II	RPGN-type III	Total
N	11	2	26	39	10	2	22	34	10	2	22	34	11	2	20	33	8	2	18	28
Mean±SD	1.78±0.8	3.85±.4.03	1.64±0.67	2.08±1.52	1.59±0.73	1.45±0.77	1.99±1.31	1.79±0.95	1.55±0.62	1.50±0.70	1.77±1.10	1.73±0.92	1.64±0.74	1.70±0.69	1.85±1.34	1.69±0.83	1.55±0.86	1.60±0.84	1.72±0.82	1.77±1.13
Proteinuria mg/24 h	RPGN-type I	RPGN-type III	RPGN-type IIII	Total	RPGN-type I	RPGN-type II	RPGN-type III	Total	RPGN-type I	RPGN-type II	RPGN-type III	Total	RPGN-type I	RPGN-type III	RPGN-type III	Total	RPGN-type I	RPGN-type II	RPGN-type III	Total
N	9	2	23	34	10	1	19	30	10	ND	19	29	11	2	17	30	8	2	16	26
Mean±SD	470.00±566.85	400.00±565.68	408.22±446.00	512.71±966.64	911.87±832.20*	797.00±556.29*	362.98±325.38*	475.53±561.34*	1656.10±1206.68	ND	262.54±272.35	398.38±696.81	510.79±832.90	272.57±291.20	340.65±344.17	382.41±527.44	238.23±311.19	443.88±300.87	279.26±111.45	473.17±883.08

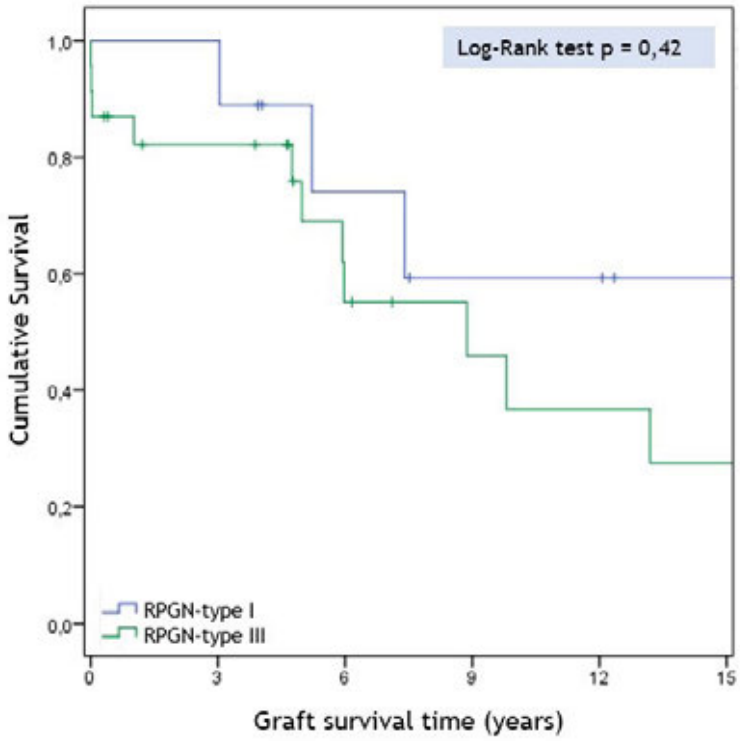
*p<0.05

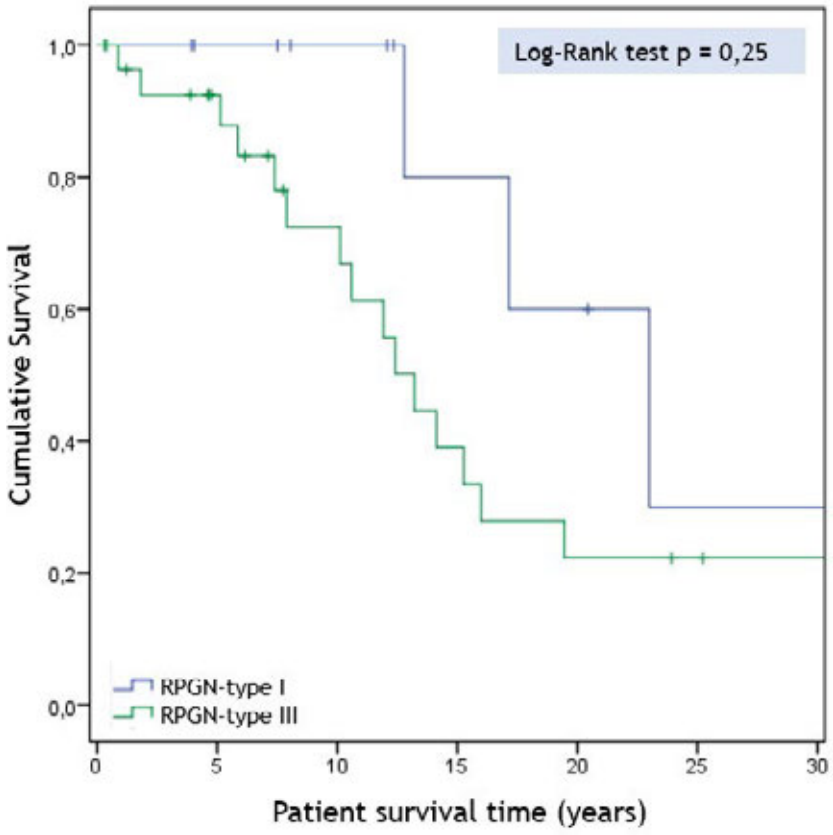
renal-limited), or secondary to systemic autoimmune disorders (RPGN-SAD), infectious diseases or drugs. Kidney transplantation in RPGN-SAD may be associated to a worse outcome.

In a series of 42 patients with first transplantation due to RPGN our aim was to assess **a**) clinical features of the three types of RPGN, **b)** comparison of post-transplant survival and graft survival between these three types.

Methods: We study three groups of patients according to renal biopsy: **a)** RPGN-GBMa (n = 11), **b)** RPGN-immunocomplexes (n = 2) and c) RPGN-pauci-immune (n=29).

All these patients were transplanted in a single reference University Hospital. The main outcome variables were a) graft survival up to 15 years and patient survival up to 30 years and b) evolution of renal function (serum creatinine





and proteinuria) in the first 5 years of follow-up. Cumulative survival rates after transplantation were estimated by the Kaplan-Meier method and compared between groups using the log-rank test. Kruskal-Wallis test was used to compare quantitative variables and chi^2/Fisher's exact test for qualitative variables.

Results: We included a total of 42 patients with renal transplant due to RPGN, with a mean age at diagnosis of 44.87±17.01 years (48.53±17.45 at the time of the transplant). No significant differences at baseline were observed between the three RPGN groups regarding sex, age and cardiovascular risk factors. Renal biopsy had been performed in the 42 patients with RPGN: type I or RPGN-GBMa (n=11, 26.2%), type II or RPGN-immunocomplexes (n=2, 4.8%) and type III or RPGN-pauci-immune (n=29, 69.0%).

It was also reported the presence or absence of systemic autoimmune disorders (31% RPGN-SAD and 69% RPGN-renal-limited). According to the presentation and the clinical characteristics of the patients, another classification has been established: a) type I (18.2% (2) Goodpasture-syndrome), b) type II (100% renal-limited), c) type III (13.8% (4) granulomatosis with polyangiitis and 20.70% (6) microscopic polyangiitis. The evolution of serum creatinine and the proteinuria after the transplant is shown in **TABLE 1**. There were no significant differences between the three groups in the serum creatinine values during at 1st, 6th, 12th, 36th and 60th months post-transplant. Neither differences were found in terms of graft and patient survival between the 3 groups **(Figures 1 and 2).**

Conclusion: Our study shows similar graft and patient survival as well as renal outcome in renal transplant due to the three types of RPGN. Therefore, renal transplantation could be the best option for patients with end stage renal disease due to RPGN regardless of systemic manifestations.

Disclosure: L. Sanchez-Bilbao, None; **M. De Cos-Gomez**, None; **I. Gonzalez-Mazon**, None; **B. Atienza-Mateo**, None; **J. Martín-Varillas**, None; **M. Calderón-Goercke**, None; **D. PRIETO- PENA**, None; **J. Ruiz-San Millan**, None; **M. Gonzalez-Gay**, Abbvie, 2, 5, 8, Celgene, 5, 8, Janssen, 2, MSD, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, Sanofi, 5, 8, Sobi, 5, 8; **R. Blanco**, None.

Abstract Number: 2644

Ultrasound to Monitor Treatment Response in Large Vessel Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: On ultrasound (US) examinations, large vessel vasculitis (LVV) has been reported to be present in up to 55% of Giant cell arteritis (GCA) patients. No consensus exists on how to evaluate treatment response in LVV. US yields a high sensitivity and specificity on GCA diagnostics . The aim of this study was to examine if the US of the large supraaortic arteries could be used to monitor treatment response in patients with LVV-GCA.

Methods: We included retrospectively patients who were diagnosed with new-onset LVV-GCA (positive US of the supraaortic vessel(s) and typical clinical manifestations) after they had been referred to the Department of Rheumatology, Martina Hansens Hospital in Bærum, Norway between September 2017 and April 2019. The intima-media complex (IMC) thickness of the supraaortic arteries (carotid, subclavian, axillary proximal and distal) was measured at diagnosis (and within 3 days after the initiation of prednisolone) and after one month. C-reactive protein (CRP) and prednisolone dose were also registered. Appropriate statistical tests were applied and p values < 0.05 were considered as significant.

Results: Twenty patients (14 females, 6 males) were included in this study, with a mean age of 67 years. The mean starting dose of prednisolone was 46 mg and one month later, prednisolone dose was reduced by 16 mg (95% CI 9-22, p< 0.005). The mean CRP at disease onset was 80 mg/dl and one month later it was reduced by 77 mg/dl (95%

Artery	Mean difference (onset-1 month later)	95% Confidence Interval	P values
Left axillary proximal	0,16	0,01-0,31	0,03
Left axillary distal	0,45	0,2 -0,69	<0,05
Right axillary proximal	0,22	0,04-0,40	0,02
Right axillary distal	0,41	0,12-0,70	0,01
Right carotid	0,33	-0,04-0,71	0,06
Left carotid	0,36	0,00-0,71	0,05
Right subclavian	0,22	0,08-0,36	<0,05
Left subclavian	0,41	0,11-0,70	0,01

Table 1. Mean differences of the IMC thickness in the supraaortic vessels

CI 40-115, p=0.001). After one month, and except for the right carotid artery, a significant reduction of IMC thickness in all supraaortic vessels was observed (table 1).

Conclusion: The US of the supraaortic arteries may be a useful tool to monitor treatment response in LVV-GCA. Thus, the US of the large vessels has the potential to be used for the assessment of disease activity in LVV-GCA patients. These promising results have to be confirmed in larger cohorts of patients.

Disclosure: A. Bull Haaversen, None; **V. Holt**, None; **S. Nabizadeh**, None; **A. Slagsvold**, None; **A. Diamantopoulos**, None.

Abstract Number: 2645

The Anteromedial Ultrasound Examination of the Large Supraaortic Vessels Identifies Higher Rates of Large Vessel Involvement Than Previous Reported in Patients with Giant Cell Arteritis

Anne Bull Haaversen,[1] and Andreas P Diamantopoulos[2], [1]Martina Hansens Hospital, Sandvika, Norway, [2]Martina Hansens Hospital, SANDVIKA, Oslo, Norway

SESSION INFORMATION
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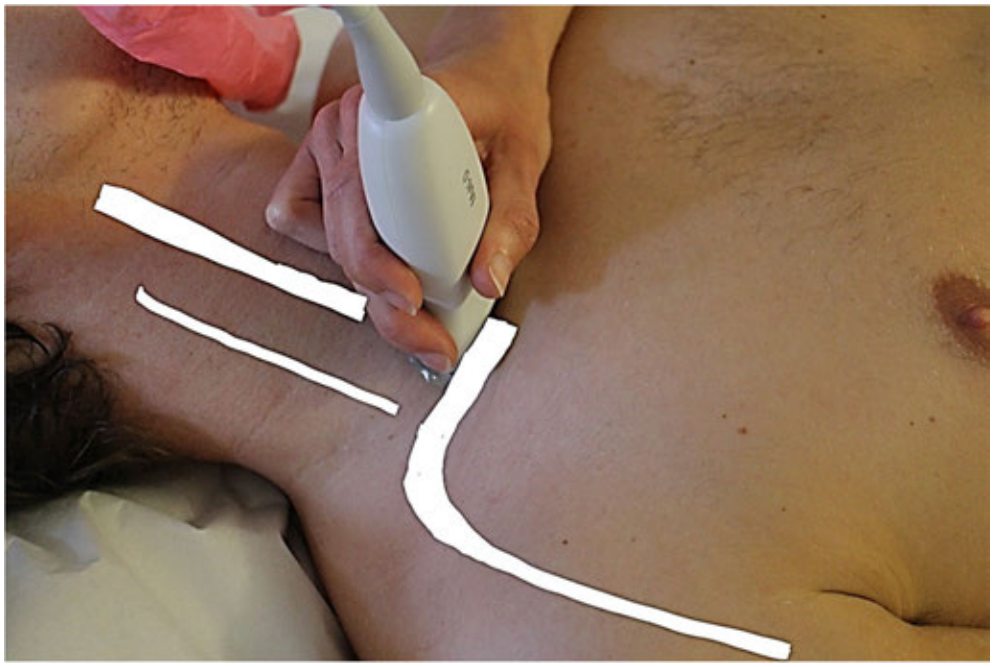
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) affects both the cranial and large vessels. Ultrasonographic studies have reported that the incidence of large vessel vasculitis (LVV) in patients with GCA varies from 30% to 55%. The aim of this study was to investigate the rate of LVV in patients with GCA by using the new anteromedial approach to examine the large supraaortic vessels in addition to the cranial arteries.

Methods: Patients with new-onset GCA referred to the Department of Rheumatology, Martina Hansens Hospital in Bærum, Norway between September 2017 and April 2019 were included. The diagnosis was based on typical clinical manifestations and ultrasound findings. All the patients were scanned by ultrasound using the anteromedial approach for the supraaortic vessels (carotid, vertebral, subclavian, axillary proximally and distally), in addition to the examination of the cranial vessels (temporal, facial). The anteromedial approach consists of a continuous ultrasound evaluation of the large supraaortic vessels with the patient in a supine position (figure 1). The examination was performed with a General Electric S8 ultrasound machine with a 9-12 Mhz linear probe for the large vessels and an 18 Mhz hockey stick probe for the cranial arteries. The age, gender, CRP and the distribution of vasculitis in the vessels were recorded. The cut-off for vasculitis of the large vessels was set at 1 mm (homogeneous, hypoechoic or isoechoic thickness of the intima-media complex).

Results: Forty-one patients, 30 (73%) females, and 11 (27%) males were diagnosed with GCA during the recruitment period. The mean age was 71 years (95% CI (67-74)). Mean CRP was 79.6 mg/dl (95% CI (63-96)). Of the 41 GCA patients, 10 patients (24 %) had cranial GCA only, 12 patients (30 %) had LVV only and 19 patients (46 %) had both cranial and LVV GCA. The temporal arteries were the most frequently inflamed in 56 % of the patients, followed by the facial artery(left 29% and right 24%). The large supraaortic vessels mostly inflamed were the right proximal and left distal axillary (41 %), the left proximal axillary (37%) and the subclavian (left 34% and right 32%) (tables 1 and 2).



The anteromedial ultrasound examination of the large supraaortic vessels.

Cranial arteries	% of all GCA patients (number of pts)
Left temporal	56 *(23)*
Right temporal	56 *(23)*
Left facial	30 *(12)*
Right Facial	24 *(10)*

Table 1. Distribution of the inflammation in the cranial arteries

Supraaortic Arteries	% of all GCA patients (number of pts)
Left carotid	27 *(11)*
Right carotid	10 *(4)*
Left vertebral	25 *(10)*
Right vertebral	17 *(7)*
Left subclavian	34 *(14)*
Right subclavian	32 *(13)*
Left axillary proximal	37 *(15)*
Right axillary proximal	41 *(17)*
Left axillary distal	41 *(17)*
Right axillary distal	32 *(13)*

Table 2. Distribution of the inflammation in the supraaortic arteries

Conclusion: The anteromedial ultrasound examination revealed inflammation of the large supraaortic vessels in 76 % of the GCA patients. This indicates that the involvement of supraaortic arteries is more common in GCA than previously reported. Possible explanations may include the visualization of all the supraaortic arteries and both the upper and lower arterial wall when using the anteromedial ultrasound scanning.

Disclosure: A. Bull Haaversen, None; **A. Diamantopoulos**, None.

Abstract Number: 2646

Survival of Large Vessel Giant Cell Arteritis in Northern Italy During a 26-year Period : No Correlation with Demographical, Clinical, Laboratory and Imaging Data

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the relationship between demographical, clinical, laboratory and imaging data and survival in patients with large vessel giant cell arteritis (LVGCA) in a defined area of Northern Italy.

Methods: All patients with incident LVGCA diagnosed between 1 January 2005 and 31 December 2016 and living in the Reggio Emilia area, were identified by capture and re-capture checking of computerized discharge diagnosis codes (ICD10) and using outpatients databases from rheumatology, internal medicine, surgery, pathology, imaging departments of Reggio Emilia Hospital as well as by examining the Reggio Emilia district database for rare diseases. To be included in the study, patients must satisfy the following 2 criteria: age at disease onset ≥50 years; evidence of large-vessel vasculitis (LVV) by clinical criteria, angiography, MRA, CTA, PET/CT and/or ultrasonography. Demographic, clinical, laboratory and imaging data collected at first visit and during follow-up (FU) were retrived from patients records. For each case, we identified one control from the same geographic area matched for age and gender. Mortality rates and specific causes of death were reported and compared between cases and controls. Demographical, clinical laboratory and imaging data entered in a Cox proportional regression analysis (CPRA) along with total corticosteroid (CS) cumulative dose, first 6 and 12 months cumulative CS dose, number of flares, and disease remission during the FU period.

Results: There were 93 incident cases of LVGCA (71% women, mean ± SD age at diagnosis 72 ± 9 years, mean duration of FU 65 + 38 months) with complete clinical, laboratory and survival data during the 12-year study period. During the FU period, 16 (17%) patients died (mean survival time from disease onset 16 + 12 months). At univariate analysis (UVA) factors significantly linked to survival ($p< 0.05$) were the presence of hypertrigliceridemia (HTG) and the involvement of brachio-cephalic artery (BCA). All the variables with a value of $p< 0.20$ at UVA (HTG, BCA, hypertension, concomitant PMR, cumulative CS dose at 6 and 12 months and aortic involvement) entered in a CPRA but none of them maintained statistical significance. Survival of LVGCA patients was not different from controls (logrank=0.004, p=0.947). The most frequent causes of death were cardiovascular diseases, cancer, and respiratory diseases. No significant differences in causes of death were observed comparing the patients with control population.

Conclusion: In an incident cohort of LVGCA we have not found any correlation between baseline and follow up clinical, demographical, laboratory and imaging data with survival.

Patients with LVCGA have no difference of survival time and causes of death with the control population.

Disclosure: L. Boiardi, None; **M. Catanoso**, None; **G. Restuccia**, None; **F. Muratore**, None; **P. Macchioni**, None; **C. Salvarani**, None.

Abstract Number: 2647

Flares and Long-term Remission in Large-vessel Giant Cell Arteritis in Northern Italy: Characteristics and Predictors in a Long-term Follow-up Study

Carlo Salvarani,[1] Luigi Boiardi,[2] Alberto Cavazza,[3] Massimiliano Casali,[4] Lucia Spaggiari,[5] Luca Cimino,[6] Raffaella Aldigeri,[7] Francesco Muratore,[8] Giovanna Restuccia,[8] Nicolò Pipitone,[5] and Pierluigi Macchioni[5], [1]Azienda USL-IRCCS di Reggio Emilia, REGGIO EMILIA, Emilia-Romagna, Italy, [2]Division of Rheumatology, Azienda Unita' Sanitaria Locale IRCCS di Reggio Emilia, Reggio Emilia, Italy, [3]Pathology Unit, Azienda Unita' Sanitaria Locale IRCCS di Reggio Emilia, Reggio Emilia, Italy, [4]Azienda USL-IRCCS di Reggio Emilia, REGGIO EMILIA, Italy, [5]Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, [6]Ophthalmology Unit, Azienda Unita' Sanitaria Locale IRCCS di Reggio Emilia, Reggio Emilia, Italy, [7]Università degli Studi di Parma, Parma, [8]Division of Rheumatology, Azienda Unita' Sanitaria Locale IRCCS di Reggio Emilia, Reggio Emilia, Italy

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the frequency, timing, and characteristics of flares and to evaluate the frequency of long-term remission after glucocorticoids (GCs) suspension in an Italian cohort of patients with large-vessel (LV) giant cell arteritis (GCA) and to identify factors that may predict the occurrence of flares and long-term remission.

Methods: We evaluated 75 patients with LV GCA diagnosed and followed up at the Rheumatology Unit of Reggio Emilia Hospital (Italy) for whom information was available from the time of diagnosis until at least 2 years of follow-up. In all patients the diagnosis of LV GCA was confirmed by imaging. Flares were defined as reappearance of signs/symptoms or worsening in vascular imaging requiring treatment adjustment. Long-term remission was defined as complete clinical remission without elevation of inflammatory markers for at least one year after the GC withdrawal.

Results: 34 patients (45.3%) experienced one or more flares. Twenty (38.5%) of the 52 total flares were experienced during the first year after diagnosis. The majority of relapses occurred with doses of prednisone < 10 mg/day (80.7%), while only 3.8% for doses > 25 mg/day. Polymyalgia rheumatica (PMR) (34.6%) and worsening of LV imaging (34.6%) were the most frequently observed flaring manifestations. Cumulative prednisone dose during the first year and total cumulative prednisone dose were significantly higher in flaring patients compared to those without flares ($p = 0.006$ and $p = 0.0001$, respectively). The total duration of prednisone treatment was longer in flaring patients ($p = 0.0001$).

Patients with disease flares had at diagnosis more frequently fever > 38°C ($p = 0.04$) and less frequently jaw claudication ($p = 0.02$) compared to those without flares. In the multivariate model fever > 38 °C (HR 2.94, 95%CI:1.25-6.91, $p = 0.01$), PMR (HR 3.59, 95%CI: 1.61-8.03, $p= 0.002$), visual manifestations (HR 3.24, 95%CI: 1.09-9.67, $p = 0.035$)

were significantly associated with an increased risk of flares, while jaw claudication (HR 0.11, 95%CI: 0.02-0.48, p = 0.004) with a reduced risk.

33 patients (44%) experienced long-term remission. PMR and disease flares were less frequently observed in patients with long-term remission compared to those without (p = 0.002 and p < 0.0001, respectively). The initial prednisone dosage was higher in patients with long-term remission (p = 0.03), while the total cumulative prednisone dose and the duration of prednisone treatment were significantly lower (p = 0.02 and p = 0.003, respectively). In the multivariate model the duration of prednisone treatment was significantly negatively associated with long-term remission (HR 0.97, 95%CI: 0.96-0.98, p < 0.0001).

Conclusion: In our cohort of patients with LV GCA a flaring course and long-term remission were observed in around half of the patients.

Disclosure: C. Salvarani, None; **L. Boiardi**, None; **A. Cavazza**, None; **M. Casali**, None; **L. Spaggiari**, None; **L. Cimino**, None; **R. Aldigeri**, None; **F. Muratore**, None; **G. Restuccia**, None; **N. Pipitone**, None; **P. Macchioni**, None.

Abstract Number: 2648

Association Between Specimen Length and Number of Sections and Diagnostic Yield of Temporal Artery Biopsy: A Retrospective, Single Center Experience over a 21 Years' Period

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the association between specimen length and number of sections and the diagnostic yield of temporal artery biopsy (TAB) for giant cell arteritis (GCA).

Methods: A pathologist with expertise in vasculitis and blinded to clinical data and final diagnosis reviewed all TABs performed for suspected GCA at our hospital between January 1991 and December 2012. The biopsies were routinely fixed in formalin and completely embedded in paraffin. Sections of 4 microns thickness were cut from paraffin blocks and stained with hematoxylin-eosin. TABs were classified into three categories: inadequate, when the biopsy did not sample the muscular artery; negative when the temporal artery was devoid of inflammation and positive when the temporal artery showed inflammation, arbitrarily defined as at least 1 aggregate of at least 15 inflammatory cells. The blocks of all the inadequate and negative biopsies were recut, and at least three further slides at deeper levels were stained with hematoxylin-eosin in order to avoid missing skip inflammatory lesions.

Results: 694 TABs were performed in the study period and were reviewed. 32 (4.6%) were classified as inadequate and were excluded from the analysis. Of the remaining 662 TABs [71% female; mean (SD) age, 73.2 (8.8) years], mean

(SD) post fixation length was 6.63 (4.42) mm, and median number of sections evaluated was 3 (range 1-33). 382 (58%) TABs were classified as negative and 280 (42%) as positive. Compared with negative TAB, patients with positive TAB were older [mean age (SD) 74 (7.5) years vs 72 (9.6), p=0.009] and there was a trend for female predominance (75% vs 68%, p=0.077). Post fixation length of the specimens was significantly lower in negative compared with positive TAB [mean (SD) 6.37 (4.26) mm vs 6.99 (4.61) respectively, p=0.026]. Piecewise logistic regression identified 5 mm as the TAB length change point for diagnostic sensitivity. Compared with TAB length of < 5 mm, age- and sex-adjusted odds ratio for positive TAB in samples ≥5 mm long were 1.536 (95% confidence interval, 1.108 to 2.130).

The median (IQR) number of sections evaluated were 2 (1-3) for positive TAB and 4 (2-5) for negative TAB, p< 0.0001. In 26/280 (9.3%) positive TABs, the first section was negative, and the inflammation was detected only in deeper sections (the positive section was the second in 14 TABs, the third in 9 and the fourth in 3). In all 26 cases, inflammation detected in deeper section was not transmural, but limited to adventitial or periadventitial small vessels.

Conclusion: Our data confirm that a post fixation TAB length of at least 5 mm should be sufficient to make a histological diagnosis of inflamed temporal artery. According to our data, in order to avoid missing skip inflammatory lesions, at least 3 further sections at deeper levels should be cut and evaluated in all negative TABs.

Disclosure: F. Muratore, None; **L. Boiardi**, None; **A. Cavazza**, None; **G. Tiengo**, None; **R. Aldigeri**, None; **L. Cimino**, None; **C. Salvarani**, None.

Abstract Number: 2649

Comparison of Biopsy Proven Giant Cell Arteritis in North America and South Europe: A Population-Based Study

Francesco Muratore,[1] Cynthia Crowson,[2] Luigi Boiardi,[3] Ambra Pinelli,[4] Matthew Koster,[5] Giovanna Restuccia,[1] Tanaz Kermani,[6] Eric Matteson,[7] Carlo Salvarani,[8] and Kenneth Warrington[5], [1]Division of Rheumatology, Azienda Unita' Sanitaria Locale IRCCS di Reggio Emilia, Reggio Emilia, Italy, [2]Mayo Clinic Rochester, Rochester, [3]Division of Rheumatology, Azienda Unita' Sanitaria Locale IRCCS di Reggio Emilia, Reggio Emilia, Italy, [4]Division of Rheumatology, University of Modena and Reggio Emilia, Reggio Emilia, Italy, [5]Mayo Clinic Rochester, Rochester, MN, [6]University of California Los Angeles, Los Angeles, CA, [7]Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA, Rochester, [8]Division of Rheumatology, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
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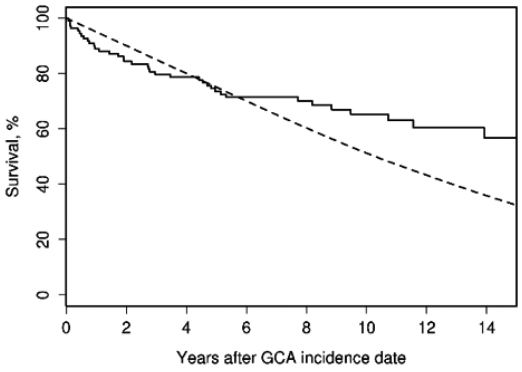
Background/Purpose: To compare clinical characteristics, treatment, long-term follow-up and prognosis of two population-based cohorts of patients with biopsy-proven giant cell arteritis (GCA) from North America (American cohort) and South Europe (European cohort).

Methods: All patients residing in these two geographic regions with a new diagnosis of biopsy-proven GCA in 1986-2007 were retrospectively identified. Patients were followed from GCA diagnosis to death, migration or September 2011. Comparisons were performed using Chi-square and rank sum tests, Kaplan-Meier methods and Cox models. To account for differences in general population survival between the 2 geographic regions, survival in each GCA cohort was compared to expected rates obtained from age-, sex- and calendar year-specific lifetable rates for the general population of its region.

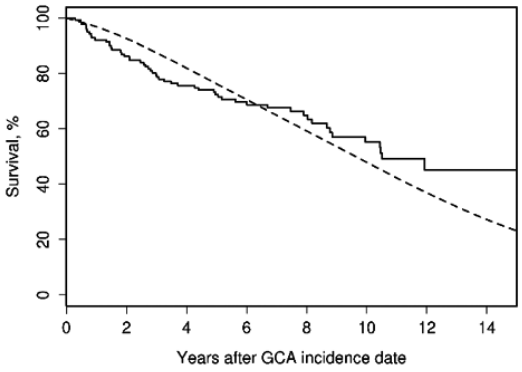
Figure 1A. Survival of North American residents with GCA compared to expected rates from North America lifetables



SMR (95% CI) 0.69 (0.49, 0.95), log-rank p-value = 0.024

(observed: solid line; expected dashed line)

Figure 1B. Survival of South Europe residents with GCA compared to expected rates from South Europe lifetables



SMR (95% CI) 0.66 (0.50, 0.87), log-rank p-value = 0.001

(observed: solid line; expected dashed line)

Results: The study included 110 patients in the American and 144 in the European cohort. Compared with the American cohort, patients from the European cohort were younger (mean±SD age 74.6±7.4 years vs 77.8±7.6, p=0.002), had longer duration of symptoms prior to diagnosis (median [IQR] 1.4 [1.0, 2.7] months vs 0.7 [0.2, 1.3], p< 0.001) and were more likely to have cranial symptoms (93% vs 86%, p=0.048), partial or complete unilateral or bilateral permanent vision loss (21% vs 6%, p=0.001), systemic symptoms (67% vs 46%, p=0.001) and polymyalgia rheumatica at or before GCA diagnosis (47% vs 26%, p< 0.001). ESR and CRP were higher (mean 88±29 mm/h vs 73±77, p< 0.001 and mean 89.0±60.2 mg/L vs 35.2±43.4, p< 0.001 respectively) and hemoglobin lower (mean 11.2±1.4 g/dl vs 11.8±1.4, p=0.004) in European than in the American cohort. Patients from the American cohort received a higher initial prednisone dose (mean 53.6±15.3 mg/day vs 49.5±12.8, p=0.001). There were no differences in relapse rates, cumulative glucocorticoid (GC) dosages at 1, 2 and 5 years, and time to first GC discontinuation.

Overall survival curves showed a better survival of patients with GCA from both study cohorts compared to expected rates obtained from age-, sex- and calendar year-specific lifetable rates for the general population of the respective regions (Figure 1A-B). As shown by survival curves, the mortality of patients with GCA was similar to the general population in the first 6 years from GCA diagnosis (SMR [95% CI] 1.07 [0.72, 1.53], log-rank p-value = 0.71 for the American cohort, and 0.91 [0.65, 1.24], log-rank p-value = 0.55 for the European cohort), but became significantly lower in both study cohorts after 6 years from GCA diagnosis (SMR [95% CI] 0.27 [0.11, 0.57], log-rank p-value < 0.001 for the American cohort, and 0.36 [0.19, 0.61], log-rank p-value < 0.001 for the European cohort). The most common cause of death was heart diseases in both the study cohorts, followed by cancer, pulmonary diseases, infection and stroke.

Conclusion: The clinical features at onset of GCA differ between patients from South Europe and North America. Geographical, genetic and/or environmental factors may contribute to the differences observed in this study. Improvement in survival for the GCA cohorts is a novel finding that will require further validation.

Disclosure: F. Muratore, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **L. Boiardi**, None; **A. Pinelli**, None; **M. Koster**, None; **G. Restuccia**, None; **T. Kermani**, None; **E. Matteson**, Boehringer Ingelheim, 5, Pfizer, 2, Sun Pharmaceuticals, 2; **C. Salvarani**, None; **K. Warrington**, Eli Lilly, 2, GlaxoSmithKline, 2, roche, 2, 8, Roche, 2, 5, 8, Sanofi, 5, sanofi, 5.

Abstract Number: 2650

Predictors of Relapse in Giant Cell Arteritis: Data from an International Collaboration

Laure Delaval,[1] Raphael Porcher,[2] Kenneth Warrington,[3] Francesco Muratore,[4] Cynthia Crowson,[5] Daniel Blockmans,[6] Christian Agard,[7] Alexis Régent,[8] Maxime Samson,[9] Loic Guillevin,[8] Carlo Salvarani,[10] and **Benjamin Terrier** [8],
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SESSION INFORMATION
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Background/Purpose: Roughly half of giant-cell arteritis (GCA) patients taking only glucocorticoids (GCs) relapse. The relapse rate seems to reflect, in part, the duration of GC intake, more than the initial dose at induction. However, the GCA-relapse rate varied widely in observational studies and randomized–controlled trials. We aimed to identify factors predictive of GCA relapse based on data from patients enrolled in 3 international GCA cohorts.

Methods: This international study included patients ≥50 years old and fulfilling ACR criteria for GCA from three cohorts : Northern Europe (n=351), US (n=285) and Southern Europe (n=142) cohorts. The primary endpoint was the time from diagnosis to first relapse or death. Relapse-free survival was estimated with the Kaplan–Meier product-limit method. Cox proportional hazards models were stratified by cohort. Missing data were handled through multiple imputation by chained equations. Internal validation of the model was carried out using 200 bootstrap resamples, on which the entire model building strategy was repeated. Model performance was evaluated both by the concordance (c) statistic, as a measure of discrimination, and the calibration curve. The final model was presented with hazard ratios (HR) obtained after shrinkage by the calibration slope and their 95% confidence intervals (95% CI).

Results: This study included 778 patients (24% men; median age 71 [IQR 61–78] years). Median follow-up was 51 [IQR 24–102] months. During 36 months of follow-up, 382 patients relapsed; relapse-free survival at 36 months was 45.3% (95% CI 41.6–49.2), with marked differences among the cohorts. French and Reggio Emilia cohorts had better relapse-free survival rates than the Mayo Clinic cohort.

To adjust for optimism induced by the model-selection procedure, regression coefficients where shrunk by multiplying them by the calibration slope, which was 0.714, indicating a reasonable level of overfitting in the original model. The final model (corrected for over-optimism) comprised headaches (HR 1.18, 95% CI 1.00–1.39; P=0.052), limb claudication (HR 1.34, 95% CI 0.95–1.89; P=0.091), aortitis (HR 1.20, 95% CI 0.97–1.48; P=0.096) and CRP levels (after logarithmic transformation) (HR 1.11, 95% CI 1.02–1.22; P=0.014). The model was well calibrated, but with relatively limited discriminative ability. Using the pooled coefficients for each imputed dataset yielded a corrected c-statistic of 0.562 (95% CI 0.525–0.598).

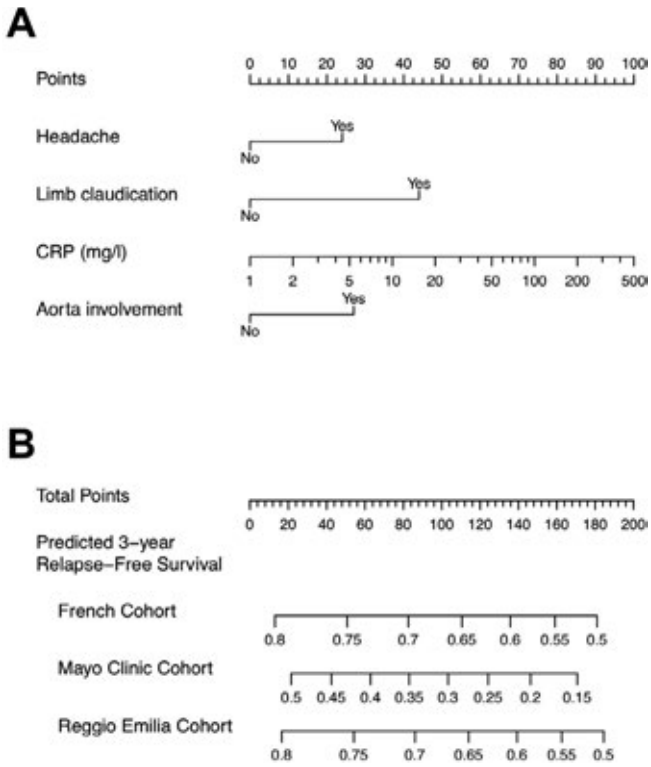

Figure 1. Nomogram allowing the calculation of the predicted 3-year relapse free survival.

We set up a nomogram allowing the calculation of the predicted 3-year relapse free survival. Points (ranging from 0 to a maximum of 100) is attributed for each of the four previous items (Figure A). Total score (ranging from 0 to 200) is used to predict the 3-year relapse free survival in each cohort (Figure B).

Conclusion: The risk of GCA relapse varies among observational cohorts. A model comprising the headaches, limb claudication, aortitis and CRP levels was well calibrated, and could help identify patients at high-risk of relapse. However, this model had relatively limited discriminative ability, possibly due to unmeasured variables that might explain the observed heterogeneity among cohorts.

Disclosure: L. Delaval, None; **R. Porcher**, None; **K. Warrington**, Eli Lilly, 2, GlaxoSmithKline, 2, roche, 2, 8, Roche, 2, 5, 8, Sanofi, 5, sanofi, 5; **F. Muratore**, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **D. Blockmans**, None; **C. Agard**, None; **A. Régent**, None; **M. Samson**, None; **L. Guillevin**, None; **C. Salvarani**, None; **B. Terrier**, Grifols, 8, GSK, 8, LFB, 8, Roche, 8.

Abstract Number: 2651

Are There Phenotypic Overlaps Between Giant Cell Arteritis Subgroups?

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

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Background/Purpose: In parallel to the improvements in imaging, increasing data is accumulated regarding phenotypes of primary vasculitides. Giant cell arteritis (GCA) is a large vessel vasculitis encompassing cranial and extracranial arterial involvements and as well as polymyalgia rheumatica (PMR). Clinical manifestations and treatment responses may be different in the course of GCA. In this survey, we purpose to investigate the phenotypic overlap between the different vascular GCA subtypes and PMR.

Methods: We retrospectively analyzed the 55 GCA patients of the Hacettepe University Vasculitis Center (HUVAC). All clinical, laboratory, imaging and histopathological features were analyzed. The revised 2016 ACR and ACR 1990 GCA classification criteria were applied to patients diagnosed GCA according to the multidisciplinary expert group. Patients were grouped according to cranial, extracranial and PMR symptoms. Cranial GCA group comprised new headache, clinical temporal artery abnormality, visual disturbance, and jaw claudication; extracranial GCA group, limb claudication, bruits and Raynaud's phenomenon; Polymyalgic+GCA group, bilateral shoulder/hip pain, morning stiffness and peripheral arthritis(1). Some patients had characteristics of more than one group, so the key phenotypic features of GCA were evaluated in 87 cases. Two patients were not included in any group because they did not have any symptoms according to this classification. Subgroup comparisons were done in terms of clinical features.

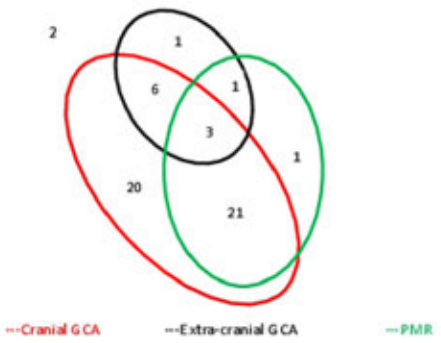
Results: A total of 55 GCA patients (Female/Male: 40/15) with a mean age and mean age of diagnosis patients were 73.0±9.7 and 67.7±9.2 years, respectively. Of the 43 patients (%78) met ACR 1990 classification criteria and 44 patients (%80) the revised 2016 ACR in our cohort. Temporal artery Doppler ultrasonography was applied to 36 patients and 10 (28%) of them were compatible with GCA and temporal artery biopsy was compatible in 26/36 (72%) of the patients. According to this classification 50 patients had cranial, 11 patients extracranial and 26 patients polymyagic symptoms. Of the 21 patients had characteristics features of both cranial and PMR group, 6 patients both cranial and extracranial group, and 3 patients all 3 groups. In comparison with extracranial GCA (9%) and polymyagic+GCA group (3%), cranial GCA group (40%) tends to occur more isolated. The phenotypic overlap between these groups

Table. Clinical symptoms and signs in giant cell arteritis groups

Symptoms and signs	Cranial GCA n=50, (%)	Extracranial GCA n=11, (%)	Polymyagic-GCA n=26, (%)
Headache	43 (86)	7 (64)	20 (77)
Arterial swelling/tenderness	23 (49)	3 (30)	9 (36)
Jaw claudication	23 (46)	6 (55)	13 (50)
Visual symptoms/complications	21 (42)	2 (18)	8 (31)
Fever, weight loss	17 (34)	5 (46)	7 (27)
High ESR and/or CRP	35 (70)	8 (73)	19 (73)
Limb claudication	3 (6)	**4 (36)***	1 (4)
Arterial bruits	2 (4)	**4 (36)****	2 (8)
Raynaud's phenomenon	3 (6)	**3 (27)*****	0
Polymyalgic symptoms	19 (38)	7 (63)	17 (66)
Morning stiffness	11 (22)	3 (27)	10 (39)
Peripheral arthritis	12 (24)	2 (18)	11 (42)

GCA; Giant cell arteritis, PMR; polymyalgia rheumatica, ESR; erythrocyte sedimentation rate, CRP; *C-reactive protein*.
p values; * 0.019, ** 0.018, *** 0.028

Figure. The phenotypic overlap between **Giant cell arteritis subgroups**



was also illustrated in the Figure. The most common clinical signs and symptoms observed in GCA groups were shown in Table. Limb claudication (p=0.019), arterial bruits (p=0.018) and Raynaud's phenomenon (p=0.028) were significantly higher in extracranial GCA group than other 2 groups.

Conclusion: Most of the phenotypic features were similar among GCA groups except for limb claudication, arterial bruits and Raynaud's phenomenon in extracranial GCA group. Although there was a relationship between all groups, the cranial GCA group may exist with less clinical features.

References: 1. Dejaco C, et al. Rheumatology (Oxford). 2017

Disclosure: B. Armagan, None; **A. Yildirim**, None; **A. Sarı**, None; **B. Farisoğulları**, None; **E. Bilgin**, None; **L. Kilic**, None; **U. Kalyoncu**, UCB, 5; **Ş. Apras Bilgen**, None; **O. Karadag**, None.

Abstract Number: 2652

Comparison Between Transmural and Isolated Periadventitial And/or Adventitial Inflammation at Temporal Artery Biopsy: A Single Center Cohort of Biopsy-Positive GCA with Long Term Follow-up

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Temporal artery biopsy (TAB) showing transmural inflammation is considered the gold standard for the diagnosis of giant cell arteritis (GCA). In some cases, inflammation is confined to the periadventitial small vessels and/or to the adventitia. The aim of the present study was to compare treatment and long-term outcomes of

patients with transmural inflammation with those of patients with periadventitial and/or adventitial inflammation in a single center cohort of patients with biopsy-positive GCA with long term follow-up.

Methods: All TABs performed for suspected GCA between 1986 and 2013 were reviewed by a single pathologist. Based on the localization of the inflammation, inflamed TABs were classified into 2 categories: transmural inflammation (TMI), with external elastic lamina disruption and extension of the inflammation to the media; periadventitial and/or adventitial inflammation (PA/AI), with inflammation limited to small periadventitial vessels devoid of muscular coat and/or to the adventitia without extension to the media. All medical records of these patients were retrospectively reviewed from the date of TAB to 31 December 2018 or death. Only patients with a follow-up duration of at least 18 months after GCA diagnosis were included.

Results: In the study period, 274 TMI and 80 PA/AI were identified. Baseline clinical manifestations and laboratory findings of the two study cohorts have been already reported (1). Large vessel involvement was found in 6/22 (27%) patients with PA/AI and 32/81 (40%) patients with TMI, p=0.292. 118 patients with TMI and 35 with PA/AI had a follow-up duration longer than 18 months and were included for the outcomes analysis. Median (IQR) follow-up duration was 79.5 months (52, 114) for patients with TMI and 67 months (34, 124) for those with PA/AI, p=0.125. Compared to patients with TMI, those with PA/AI received a significant lower initial prednisone dose (mean (SD) 35.8 mg (22.0) vs 46.8 (15.0), p< 0.0001), reached sooner a prednisone dose < 10 mg/day (median 20 weeks vs 26, p=0.004) and < 5 mg/day (median 32 weeks vs 44, p=0.005), had a lower cumulative prednisone dose at 1 year (mean (SD) 5.8 gr (3.8) vs 7.2 (2.3), p=0.005) and at the end of the follow-up period (mean (SD) 10.0 gr (9.0) vs 12.9 (9.6), p=0.015), and showed a trend for an earlier first relapse (median 52 weeks vs 63, p=0.052). There were no differences in the frequencies of relapse (43% of patients with TMI vs 46% of those with PA/AI, p=0.794) and long term remission (53% of patients with TMI vs 49% of those with PA/AI, p=0.616), time to first GC discontinuation (median 72 weeks in patients with TMI vs 62 weeks in those with PA/AI, p=0.080) and treatment duration (median 33.5 months in patients with TMI vs 26 months in those with PA/AI, p=0.159).

Conclusion: Our study demonstrates for the first time that patients with GCA with isolated periadventitial and/or adventitial inflammation and those with the classic transmural pattern have similar frequency of large vessel involvement and similar disease course. These data confirm that TAB showing inflammation confined to the periadventitial small vessels and/or the adventitia could be considered part of the histopathologic spectrum of GCA.

1. Am J Surg Pathol. 2014;38:1360-70:

Disclosure: E. Galli, None; **F. Muratore**, None; **L. Boiardi**, None; **A. Cavazza**, None; **G. Restuccia**, None; **L. Cimino**, None; **C. Salvarani**, None.

Abstract Number: 2653

Adventitial Fibroblast, an Important Actor in Giant Cell Arteritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Giant cell arteritis (GCA) is a systemic vasculitis affecting large vessels. The diagnosis is based on temporal artery biopsy (TAB) which shows an arterial infiltration accompanied by a destruction of the internal elastic layer of the media and a hyperplasia of the intima by proliferation of myofibroblasts. The origin of these myofibroblasts is controversial. Evidences suggest the activation of adventitial fibroblasts into myofibroblasts and their migration into the intima. The objective of this study was to determine whether adventitial fibroblasts migrate to the intima and thereby contribute to intimal hyperplasia during CGA.

Methods: Immunohistochemistry: Arterial sections from TAB of patients with GCA (n=24) and control subjects (n=24) were analyzed. Immunohistochemical analysis were performed using antibodies directed against fibroblasts (CD90, vimentin), myofibroblasts (alpha smooth muscle actin {ASMA}), vascular smooth muscle cells (desmin {VSMC}), prolyl-4-hydroxylase (collagen secretion activity {P4H}) and myosin (contraction activity). Stainings were quantified using ODPviewer® (Kamax Innovative System). Co-expression of CD90 with different stainings (ASMA, myosin and P4H) was also performed.

Culture cells: TABs were dissected to separate the adventitia from the other two layers (media and intima). Each fragment was seeded separately. Cells were identified by immunocytochemistry. Functional assays were performed using culture cells obtained from GCA patients' TABs (n=8) and controls (n=7): proliferation (bromodeoxyuridine incorporation test), migration (scratch test) and invasion (boyden chamber). Several conditions were used: i) DMEM-Glutamax alone, ii) addition of 10% fetal bovine serum (FBS), iii) addition of platelet-derived growth factor (PDGF) to 40 ng/mL, iv) supernatants of cells.

Results: CD90 and vimentin (fibroblasts) were significantly higher in GCA than controls in adventitia and intima. ASMA (myofibroblasts) was significantly higher in the 3 tunics of patients with GCA. Expression of desmin (VSMC) was only present in the media for both groups. The adventitial and intimal CD90+ cells co-expressed ASMA, P4H and myosin more importantly during GCA.

Cultured cells from adventitia expressed CD90 and did not express desmin. These adventitial cells had an increased in vitro proliferation ability during GCA compared to controls in the presence of FCS, PDGF and fibroblast supernatants of control or GCA patients. Migration and invasion rates of these cells were also significantly increased during GCA in the presence of FCS or PDGF.

Conclusion: Vascular remodeling during GCA would start in the adventitial layer with a key role of fibroblasts. Adventitial fibroblasts could be activated into myofibroblasts and acquire proliferative and migratory abilities. They would participate in the intimal hyperplasia. Finally, the activating signal of adventitial fibroblasts into myofibroblasts is not yet known during GCA and requires further studies.

Disclosure: S. Parreau, None; **N. Vedrenne**, None; **A. Régent**, None; **L. Richard**, None; **P. Sindou**, None; **L. Mouthon**, None; **A. Fauchais**, None; **M. Jauberteau**, None; **K. Ly**, None.

Abstract Number: 2654

Comparison of Aortitis and Non-Inflammatory Thoracic Aortic Aneurysms Undergoing Open Surgical Repair

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Table 1. Patient and Aneurysm Characteristics

Characteristic	Aortitis (n=43)	Control (n=219)	P-value
Demographics			
Age at time of surgery	70 (10)	63 (13)	<0.01
Female	65%	31%	<0.01
Comorbidities			
Coronary artery disease	21%	44%	0.01
Hypertension	88%	71%	0.02
Hyperlipidemia	60%	57%	0.64
Diabetes Mellitus	16%	9%	0.20
Smoking history			
Never	42%	48%	0.58
Former	42%	38%	0.55
Current	16%	15%	0.66
Pre-operative imaging findings			
Wall thickening of repaired aorta	3 (7%)	0 (0%)	<0.01
Wall thickening of other unrepaired vasculature	5 (12%)	1 (1%)	< 0.01
Stenosis or occlusion of repaired aorta	1 (2%)	1 (1%)	0.30
Stenosis or occlusion of other unrepaired vasculature	11 (26%)	29 (13%)	0.04
Calcification or atheroma of repaired aorta	16 (38%)	62 (29%)	0.22
Calcification or atheroma of other unrepaired vasculature	22 (51%)	92 (42%)	0.24
Thrombus	2 (5%)	6 (3%)	0.62
Largest diameter of aneurysm, mm	60.0 (10)	50.0 (10)	0.04

Values expressed as mean (standard deviation) or percentage

Table 2. Factors Independently Associated with Aortitis in Multivariate Analysis

Factor	Unadjusted Odds Ratio (95% CI)	P-value	Adjusted Odds Ratio (95% CI)	P-value
Age at time of surgery	1.06 (1.03 to 1.10)	< 0.01	1.08 (1.03 to 1.13)	< 0.01
Female	4.11 (2.08 to 812)	< 0.01	2.36 (1.01 to 5.51)	0.04
Absence of CAD	2.92 (1.32 to 6.45)	< 0.01	6.92 (2.14 to 22.34)	0.04
Hypertension	3.13 (1.17 to 8.35)	0.02	2.98 (0.94 to 9.48)	0.06
Diameter of aneurysm, per mm	1.60 (1.03 to 2.48)	0.03	1.74 (1.02 to 2.98)	0.04
Any aortic or arterial wall thickening on imaging	24.94 (2.91 to 213.94)	< 0.01	56.93 (4.31 to 752.33)	< 0.01

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Aortitis is challenging to diagnose and is often detected on surgical pathology. A subset of these patients could benefit from early medical therapy as a way to prevent progression of disease or improve surgical outcomes. This study compared pathology-diagnosed aortitis to non-inflammatory aortic aneurysms with respect to pre-operative patient characteristics, laboratory, and imaging data.

Methods: This is a single center matched case-control study. Cases had biopsy-proven aortitis following open thoracic aortic aneurysm repair in the University of Pennsylvania Health System between 2007 and 2017, without evidence of infection or prior known diagnosis or symptoms of rheumatologic disease. Approximately five controls were matched to each case by year of surgical repair and lacked significant inflammation on pathology. Preoperative patient data, such as demographics, comorbidities, laboratory testing and vessel imaging were collected. These were compared between the two groups using conditional logistic regression to evaluate associations between exposures and outcomes. Backward stepwise logistical regression was used to determine factors independently associated with aortitis.

Results: The prevalence of newly-diagnosed aortitis was 4% (total 1,373 aortic surgical specimens reviewed). For the analysis, 262 patients were included: 43 patients with aortitis and 219 matched controls. The ascending aorta was the most common site of surgical repair (95% in both groups). Patients with aortitis were more likely than controls to have granulomatous inflammation (35% vs 0%), giant cells (86% vs 0%), and adventitial inflammation (70% vs 0%). Compared to matched controls, patients with aortitis were older at the time of surgery, more likely to be female, and less likely to have a history of coronary artery disease (CAD). Multivariable analysis revealed that aortitis is independently associated with an older age at the time of surgery (OR 1.08 [95% CI 1.03,1.13], p< 0.01), female gender (OR 2.36 [95% CI 1.01,5.51], p=0.04), absence of CAD (OR 6.92 [95% CI 2.14,22.34] p=0.04), larger diameter of aneurysm (OR 1.74 [95% CI 1.02,2.98], p=0.04), and presence of arterial wall thickening on imaging (OR 56.93 [95%CI 4.31,752.33] p< 0.01).

Conclusion: Among patients who underwent open surgical repair of a thoracic aortic aneurysm, elderly females without a prior history of CAD, those with larger aneurysms at the time of surgery or evidence of vessel wall thickening on imaging were more likely to have underlying aortitis. Patients with these risk factors may benefit from further preoperative screening and assistance in peri-operative management by a rheumatologist.

Disclosure: L. Quimson, None; **A. Mayer**, None; **S. Capponi**, None; **B. Rea**, None; **R. Rhee**, None.

Abstract Number: 2655

Large Vessel Vasculitis: Diagnosis Is Very Frequent with Ultrasound Examination and Shows Responsiveness to Treatment

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

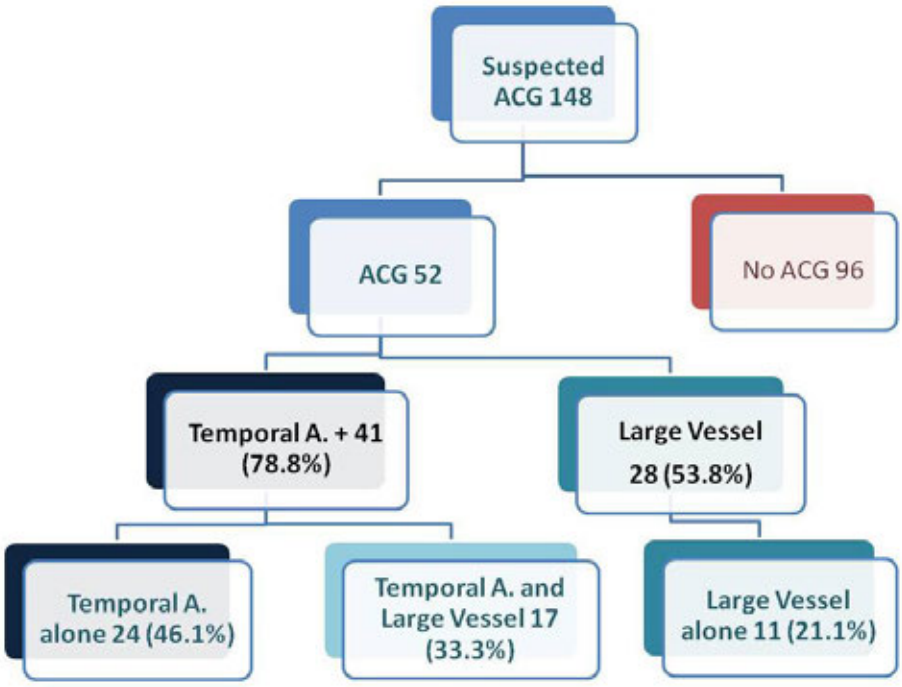

Figure 1: Patterns of GCA

Background/Purpose: Giant cell arteritis (GCA) is the most common systemic vasculitis in the elderly. In the EULAR recommendations of 2018 for the use of imaging in GCA, color Doppler ultrasound (CDUS) is recognized as the first diagnostic tool to be performed in centers with experience and OMERACT 2018 definitions and reliability of elemental ultrasound lesion of GCA have been published. Today the CDUS of TA is well known and used in clinical practice but the involvement of large vessel vasculitis (LVV) remains underdiagnosed by ultrasound and most of the diagnoses are performed by MRI or PET. In other way, TA halo sign responsiveness to the treatment and apparition in relapses is well know, but the information about this finding is sparse and even in the GiACTA study MRI lack of response in many patients was present. The objective of the present study was to know the frequency, pattern and sensitivity to change of CDUS to detect elemental lesions characteristics of cranial and LVV in patients with GCA diagnosis.

Methods: Observational descriptive study of 148 consecutive patients sent to our fast track clinic with suspicion of GCA. Every patient had a clinical history and a CDUS examination of TA and large vessel (LV) including axilary, subclavian, vertebral and carotid arteries. The OMERACT definitions of halo sign with an hypoechoic wall thickness ≥ 0.34 mm for TA pathology was used for GCA ultrasound diagnosis and for axilary, subclavian and carotids arteries and homogeneous hypoechoic thickness ≥ 1mm of the arterial wall were applied, in vertebral arteries we used a clear halo sign. Atherosclerosis lesions were evaluated to detect this disease as a possible false positive halo sign. The medical records of these patients were reviewed and demographic, physical examination, clinical and laboratory data were collected. The clinical diagnosis based on the evolution of the patient over at least one year was established as the definitive diagnosis.

Results: Of the 148 cases explored 52 had GCA, 34 women, mean age 77.2±7,9 years. The patterns of GCA were: 41 (78.8%) had cranial involvement of TA, with 24 patients with only temporal artery pathology in CDUS and 17 with a mixed patter of TA and LVV. In other way, 28 patients had LVV (53.8%) (17 with TA affectation and 11 with isolated LVV). This means that in our cohort we can see three patterns of GCA affectation: 1) a cranial pattern (affectation of TA) in the 46.1% of cases; 2) a mixed pattern of cranial and LVV affected the 33.3% of the patients and 3) an isolated LVV pattern in the 21.1% of the patients. Mean age of patients with LVV was younger that patients with cranial vasculitis 74 vs. 79 years, with a mean age of mixed pattern of 77 years. In the follow-up we can see as 9 patients with LVV

reduce the thickening of the arterial wall below the 1mm cut-off point showing sensitivity to change with the treatment and open the possibility to use ultrasound to measure activity or relapses in GCA LVV.

Conclusion: Ultrasound is an useful tool for the screening GCA including LVV. LVV is very common in our patients (53.8% of GCA cases) and 21.1 % presented only a LVV pattern. LV arteries should be included in the ultrasound examination of GCA suspicions. Ultrasound is sensitive to change in LVV.

Disclosure: E. de Miguel, AbbVie, 2, 5, 8, BMS, 8, BMS, MSD, UCB, Roche, 8, MSD, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 8, UCB, 8; **I. Monjo**, BMS, 2; **E. Fernández**, None; **D. Peiteado**, None; **C. Plasencia**, None; **A. Balsa**, BMS, 2, Roche Pharma, 2.

Abstract Number: 2656

The Veterans Health Administration (VHA) National Database Cohort: Incident Ophthalmic Complications in Giant Cell Arteritis (GCA) Patients with a Negative Temporal Artery Biopsy

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Time: 9:00AM–11:00AM

Background/Purpose: This study aimed to identify the incidence of ophthalmic complication of giant cell arteritis (GCA) among subjects with negative temporal artery biopsy (TAB) and to determine if duration of prednisone exposure prior to GCA diagnosis was associated with the development of ophthalmic complication in TAB-negative subjects.

Methods: The Veterans Health Administration (VHA) national database was queried for subjects between 1999-2017 with 1) ICD-9 or -10 diagnosis code for GCA 2) procedure code for TAB and 3) ICD-9 or -10 diagnosis code for blindness, anterior or posterior ischemic optic neuropathy (AION; PION), or branch or central retinal artery occlusion (BRAO; CRAO) accrued up to 1 year after GCA diagnosis date. TAB result (positive or negative) was reviewed manually and recorded. Prescription data regarding prednisone dosage, dispense date relative to GCA diagnosis and date that TAB was performed were collected. Logistic regression models were run using Stata 11.2.

Results: 11,820 subjects in the database had an ICD-9 or -10 diagnosis code for GCA; incident accrual of an ICD-9 or ICD-10 code for ophthalmic complication within 1 year following GCA diagnosis date was 4.5% (n=528) of the total GCA cohort. 25% (n=2,929) of the total GCA cohort had TAB performed in the VHA system; incident ICD-9 or -10 code for ophthalmic complication was significantly higher in subjects who underwent TAB (6.6%; $p< 0.001$; Table 1) and significantly higher in those with positive TAB (9.7%; $p< 0.05$; Table 1). Age, TAB laterality, and TAB length did not affect the outcome variable of incident ophthalmic complication after GCA diagnosis. Compared to a reference group of prednisone initiation 0-14 days prior to GCA diagnosis, the likelihood of accruing an ICD-9 or -10 code for ophthalmic complication within 1 year after GCA diagnosis was increased with delayed prednisone dispense dates relative to GCA diagnosis and reached statistical significance when prednisone initiation occurred 14-28 days after GCA diagnosis (OR 2.3, CI 1.01-5.34; Table 2).

Table 1. Incident accrual of ICD-9 or -10 diagnosis code of blindness, ischemic optic neuropathy, or retinal artery occlusion within 1 year after GCA diagnosis code. Percentages pertain to corresponding category (TAB performed or not; TAB result positive or negative).		
	Incident ophthalmic complication	
Was TAB performed? Total n=11,820	**No**	**Yes**
No	8,541 (96.3%)	332 (3.7%)
Yes	2,751 (93.4%)	196 (6.6%)
	p<0.001	
Was TAB positive? Total n = 2,929	**No**	**Yes**
No	2,465 (93.8%)	164 (6.2%)
Yes	271 (90.3%)	29 (9.7%)
	p<0.05	

Table 2. Logistic regression of prednisone exposure relative to GCA diagnosis on incident ophthalmic complication within 1 year of GCA diagnosis among subjects with negative TAB. Total subjects with negative TAB n=2,629; total observations 1,734. Prednisone exposure as a categorical variable is producing the reported odds ratio when compared to the reference category (0-14 days before GCA diagnosis).			
Prednisone dispensed relative to GCA diagnosis ICD-9/-10 code date	N (total n=1,734)	**Odds Ratio** (OR)	**p-value** (95% CI)
>42 days after	8 (0.5%)	--	--
28-42 days after	4 (0.2%)	--	--
14-28 days after	51 (2.9%)	2.3	p=0.046 (1.01-5.34)
0-14 days after	468 (26.8%)	1.1	p=0.524 (0.75-1.74)
0-14 days before	1,203 (68.9%)	*Reference*	--

Conclusion: In the Veterans Health Administration national database, incident ophthalmic complication within a year following GCA diagnosis occurred in 6.2% of subjects with negative TAB per pathology report despite prednisone exposure. Among subjects with negative TAB, the odds of developing an ophthalmic complication increased the later prednisone was initiated; this association reached significance in subjects who initiated prednisone 14-28 days after GCA diagnosis.

Disclosure: S. Chung, None; **M. Morcos**, None; **S. Pollock**, None; **B. Ng**, None.

Abstract Number: 2657

The Association Between Bisphosphonates and Giant Cell Arteritis: A Retrospective Cohort Study

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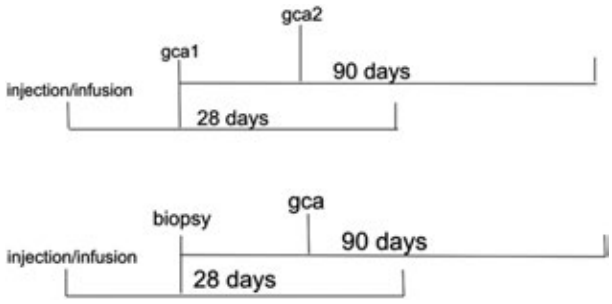

GCA diagnosis algorithm

Study Cohort	Zoledronic acid	Ibandronate
Total claims with infusion/injection	699,886	89,991
Total claims with infusion/injection covered by Medicare Part A and Part B	677,901	87,643
Claims diagnosed with GCA after infusion/injection	5,477	2,198
Claims diagnosed with at least one GCA within 28 days after infusion/injection	790	276
Claims diagnosed with at least two GCA within 90 days after infusion/injection	544	206
Total claims of biopsy covered by Medicare Part A and Part B	23,858	23,858
Claims of biopsy after infusion/injection	50	6
Claims with at least one biopsy 28 days and diagnosed with GCA within 90 days	17	1
Final cohort	**546**	**206**

Patient selection from the Medicare 2008-2014 20% random sample

	Zoledronic acid infusion		Ibandronate injection	
	Total claims	claims with GCA (%)	Total claims	claims with GCA (%)
Overall	677,901	546 (0.08%)	87,643	206 (0.24%)
Age group				
<65 years old	56,414	11 (0.02%)	4,134	8 (0.2%)
65-75 years old	217,163	166 (0.08%)	15,113	45 (0.3%)
75-85 years old	268,531	267 (0.1%)	36,200	107 (0.3%)
> 85 years old	135,793	102 (0.08%)	32,196	46 (0.14%)
Gender				
Male	225,668	71 (0.03%)	5,627	11 (0.2%)
Female	452,233	475 (0.11%)	82,016	195 (0.24%)
Race				
White	598,106	511 (0.09%)	82,260	206 (0.25%)
Black	51,778	13 (0.03%)	1,833	0
Asian	7,533	6 (0.08%)	1,332	0
Hispanic	8,100	9 (0.11%)	991	0
Other race	12,384	7 (0.06%)	1,227	0
Census region				
Northeast	120,392	118 (0.1%)	16,196	36 (0.22%)
Midwest	166,425	146 (0.09%)	20,925	50 (0.24%)
South	273,563	172 (0.06%)	32,747	63 (0.19%)
West	116,262	109 (0.09%)	17,281	57 (0.33%)
Missng	1,259	1 (0.08%)	494	0

GCA Prevalence by Age, Gender and Race

SESSION INFORMATION
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Background/Purpose: Bisphosphonates have been used to treat disorders of bone metabolism for several years. A common adverse reaction associated with their use constitutes a transient acute-phase response mediated by increased pro-inflammatory cytokine release. This can affect up to 40% of patients and is characterized by fever, joint

swelling, and orbit inflammation. GCA is a condition characterized by granulomatous inflammation involving medium-to-large sized arteries. Pro-inflammatory cytokines are known to play a significant role in its pathogenesis. A case report linking the development of GCA with bisphosphonate use was recently published. We sought to describe the prevalence of GCA after bisphosphonate administration to further explore this possible relationship.

Methods: We used the 20% Medicare random sample data (including Part A and Part B) from between 2008 and 2014 to identify elderly patients who received either zoledronate or ibandronate infusions and subsequently developed GCA. We used two ways to identify such patients. In the first method we included patients who had the diagnosis of GCA claimed within 28 days of the infusion and again within 90 days of the initial diagnosis. In the second method we included patients who had a temporal artery biopsy performed within 28 days of the infusion and subsequently had a GCA diagnosis claimed within 90 days of their biopsy being performed. ICD-9-CM diagnosis codes were used to define diagnosis claims and Healthcare Common Procedure Coding System (HCPCS) code was used to identify the biopsy claim.

Results: We identified 677,901 claims for zoledronate and 87,643 for ibandronate out of which 546 and 206 respectively met our criteria for a diagnosis of GCA. Hence, the prevalence of GCA was 0.08% and 0.24% after zoledronate and ibandronate administration respectively. The prevalence of GCA was highest in the 75-85 years old age group with 0.1% for zoledronate and 0.3% acid for ibandronate. We found the prevalence to be higher in females compared to males for zoledronate (0.11% vs 0.03%) as well as for ibandronate (0.24% vs 0.2%). Racially, Hispanics compared to other races had the highest prevalence after zoledronate administration (0.11%), while Caucasians had the highest prevalence for ibandronate (0.25%). Looking at the regional level the highest prevalence was in the northeast for zoledronate (0.1%) and west for ibandronate (0.33%).

Conclusion: Clinicians should be cognizant that there could be an association between bisphosphonate therapy and the subsequent development of autoimmune reactions including GCA. This association may not follow the trend of preference for the Caucasian and Midwest populations as previously described. Further studies are needed to better elucidate this relationship and describe if differences exist in the incidence of GCA after treatment with different bisphosphonate therapies.

Disclosure: S. Mahmood, None; **Y. Ji**, None; **Y. Peng**, None; **Z. Abou Zahr**, None.

Abstract Number: 2658

Giant Cell Arteritis Diagnostic Workup Among Medicare Beneficiaries

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Table 1. Procedures, Lab Tests, and Concurrent Diagnoses Among Beneficiaries with Suspected Incident GCA[a]

	Provider Specialty from the first GCA claim													
	Primary Care[b] (n=3,709)		Ophthalmology (n=1,759)		Neurology (n=1,086)		Rheumatologist (n=421)		Surgeon[c] (n=523)		Other (n=1,125)		All (n=9,159)[d]	
Procedures														
TAB														
90 days prior	3.4	(2.9, 4.1)[f]	5.1	(4.2, 6.3)	0.9	(0.5, 1.7)	4.8	(3.1, 7.3)	46.5	(42.2, 50.8)	5.2	(4.1, 6.7)	19.8	(19.0, 20.6)
90 days after[e]	16.2	(15.1, 17.4)	9.0	(7.8, 10.5)	5.7	(4.5, 7.3)	19.5	(16.0, 23.5)	17.0	(14.0, 20.5)	13.2	(11.3, 15.3)		
TA ultrasound														
90 days prior	0.2	(0.1, 0.5)	0.2	(0, 0.5)	1.3	(0.8, 2.2)	0.2	(0, 1.5)	0.4	(0, 1.5)	0.5	(0.2, 1.2)	1.2	(1.0, 1.4)
90 days after	0.5	(0.3, 0.8)	0.1	(0, 0.4)	3.0	(2.2, 4.3)	0.2	(0, 1.5)	0.8	(0.2, 2.0)	0.4	(0.2, 1.1)		
Imaging														
90 days prior	4.4	(3.8, 5.1)	2.3	(1.7, 3.1)	6.8	(5.5, 8.5)	5.5	(3.6, 8.1)	7.5	(5.5, 10.1)	5.3	(4.2, 6.8)	10.0	(9.4, 10.6)
90 days after	5.1	(4.4, 5.8)	4.9	(4.0, 6.0)	8.1	(6.6, 9.9)	5.2	(3.4, 7.8)	3.3	(2.0, 5.2)	4.6	(3.5, 6.0)		
Lab Tests														
CRP														
90 days prior	11.1	(10.2, 12.2)	20.7	(18.9, 22.7)	18.2	(16.1, 20.6)	23.3	(19.5, 27.6)	12.6	(10.0, 15.8)	8.7	(7.2, 10.5)	19.4	(18.6, 20.3)
90 days after	5.7	(5.0, 6.5)	4.3	(3.5, 5.4)	2.7	(1.9, 3.8)	6.2	(4.2, 8.9)	7.1	(5.2, 9.6)	6.0	(4.7, 7.5)		
ESR														
90 days prior	21.5	(20.3, 22.9)	21.9	(20.0, 23.9)	31.6	(28.9, 34.4)	22.3	(18.6, 26.6)	23.3	(19.9, 27.1)	14.6	(12.6, 16.8)	27.6	(26.6, 28.5)
90 days after	6.3	(5.5, 7.1)	5.0	(4.0, 6.1)	3.1	(2.2, 4.4)	4.5	(2.9, 7.0)	7.3	(5.3, 9.8)	6.7	(5.3, 8.3)		
PMR Suspected/Diagnosis														
365 days prior	7.9	(7.1, 8.8)	2.1	(1.5, 2.9)	2.2	(1.5, 3.3)	24.0	(20.2, 28.3)	10.3	(8.0, 13.2)	6.1	(4.9, 7.7)	11.6	(11.0, 12.3)
365 days after	5.9	(5.2, 6.7)	2.4	(1.8, 3.3)	1.3	(0.8, 2.2)	8.8	(6.4, 11.9)	9.2	(7.0, 12.0)	4.8	(3.7, 6.2)		
Beneficiaries with TAB[g]	(n= 629)		(n=181)		(n=68)		(n=84)		(n=93)		(n=154)		(n=1,301)	
Any GCA claim within 30 days following TAB	50.0	(45.9, 53.7)	45.9	(38.8, 53.1)	35.2	(25.0, 47.2)	57.1	(46.5, 67.2)	32.3	(23.6, 42.3)	37.7	(30.4, 45.5)	46.3	(43.6, 49.0)

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GCA, giant cell arthritis; PMR, polymyalgia rheumatic; TAB, temporary artery biopsy; TA, temporary artery
a Suspected incident GCA defined as GCA claim following at least one year of continuous enrollment with no GCA claims
b Primary Care includes Internal Medicine, Family Medicine, Geriatric Medicine, General Practice, Physician Assistant, Nurse Practitioner, Hospitalist
c Surgeon includes general surgery or vascular surgery
d 536 missing data for healthcare provider specialty
e Only among those beneficiaries who did not have the procedure/test/diagnosis in the prior period (if the procedure/test/diagnosis is on the same date as the first GCA claim, it is considered prior)
f Percent, and Agresti and Coull 95% confidence intervals
g Among beneficiaries with a GCA claim before the TAB; provider specialty categorized from the first GCA claim

Background/Purpose: Giant cell arteritis (GCA) has traditionally been diagnosed by a combination of symptoms, clinical findings, laboratory results, and temporal artery biopsy. More recently, imaging studies have proven to be useful for the diagnosis. The purpose of our study was to describe the diagnostic workup for GCA in clinical practice among Medicare beneficiaries in the United States.

Methods: We conducted a cohort study of Medicare beneficiaries enrolled between 2011 and 2016, using a 5% representative sample. Beneficiaries with incident suspected GCA were identified by requiring at least one year of continuous enrollment in Part A and B prior to the first GCA-related claim, and the specialty of the provider who filed the claim was determined by the referring physician NPI number. We estimated the proportion of beneficiaries with procedures 90 days before or after the initial GCA claim, including temporal artery biopsy (TAB), temporal artery (TA) ultrasound (US), other imaging including MRA, CTA, and PET/CT of different vascular territories, and laboratory tests including CRP and ESR. Diagnosis of polymyalgia rheumatica (PMR) the year before or after the initial GCA claim was also ascertained. Agresti and Coull 95% confidence intervals were calculated for the proportions.

Results: Incident suspected GCA was identified in 9,159 beneficiaries; 71.6% women, 88.1% white, 7.7% African American, with mean age 77.0 (SD: 9.2). Initial GCA-related claims were filed by primary care providers (43.0%), ophthalmologists (20.4%), neurologists (12.6%), surgeons (6.1%), rheumatologists (4.9%), and other types of providers (13.0%); provider specialty from the initial claim was not available for 536 beneficiaries. Among beneficiaries with incident suspected GCA, 19.8% (95%CI: 19.0, 20.6) underwent TAB, 1.2% (95%CI: 1.0, 1.4) had US of the TA, and 10.0% (95%C: 9.4, 10.6) underwent other imaging within 90 days before or after the initial claim. Laboratory tests included CRP (19.4%; 95%CI: 18.6, 20.3) and ESR (27.6%; 95%CI: 26.6, 28.5). PMR was suspected or diagnosed in the year before or after the initial GCA claim for 11.6% (95%CI: 11.0, 12.3), though notably higher for patients seen by rheumatologists (32.8%; 95%CI: 28.5, 37.4). Among beneficiaries who underwent TAB, 46.3% (95CI: 43.6, 49.0) had

a GCA diagnosis claim during the 30 days following the TAB, potentially reflecting the biopsy result; among patients seen by rheumatologists, 57.1% (95%CI: 46.5, 67.2) had a GCA diagnosis claim within 30 days after the TAB. Details by provider specialty are shown in Table 1.

Conclusion: Medicare beneficiaries with suspected GCA did not commonly undergo TAB, imaging studies, and laboratory tests for ESR and CRP between 2012 and 2016, suggesting that clinical criteria were primarily used during diagnostic workup. GCA claims were most often first filed by primary care physicians and uncommonly first filed by rheumatologists. Our results suggest that guidelines for diagnosis of GCA in the United States are warranted. Development of Fast-Track Clinics for GCA to assure rapid access to a multidisciplinary team lead by rheumatologists are also highly recommended.

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Abstract Number: 2659

Giant-Cell Arteritis Associated with Myeloproliferative Neoplasms: A Retrospective Case–Control Study

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Background/Purpose: Giant-cell arteritis (GCA) is a large-vessel vasculitis affecting patients >50 years, whose origin remains widely unelucidated. Recent studies demonstrated that myeloid disease-related somatic mutations were frequent in healthy aged patients, defining the concept of clonal hematopoiesis. Those mutations, especially *JAK2*^{V617F}, which occur even more frequently in patients with atherosclerosis, are suspected of inducing monocyte/macrophage inflammatory responses through IL-1β and IL-6 secretion. Because GCA pathogenesis involves myeloid cells and inflammatory cytokines, and JAK/STAT was shown to be a major inflammatory pathway, we aimed to analyze characteristics of GCA patients with associated myeloproliferative neoplasms (MPNs).

Methods: We conducted a nationwide multicenter retrospective study, including 17 patients with MPN-associated GCA (cases) and 50 GCA patients without MPN (controls), matched for age and sex. All patients satisfied the American College of Rheumatology criteria. Clinical characteristics, laboratory parameters and outcomes were analyzed and compared between groups.

Results: The most frequent MPNs associated with GCA were essential thrombocytosis (n=11), primary myelofibrosis (n=2), polycythemia vera (n=2) and chronic myelomonocytic leukemia (n=1). One case had an isolated *JAK2*^{V617F} mutation without myeloproliferation.*JAK2*^{V617F} mutation was found in 88% of cases with a median [IQR] various allele frequency of 14.5% [4.6–47.2]. Seven cases were diagnosed with MPN before GCA (median 18 [4–44] months), 1 simultaneously, and 9 after (median 12 [5–54] months). MPN–GCA cases, compared to controls, respectively, had less frequent constitutional symptoms (35% vs. 76%; p=0.003), less frequent cephalic symptoms (70% vs. 96%; p=0.003) and scalp hyperesthesia (23% vs. 56%; p=0.003), but more frequent monocular blindness (18% vs. 2%; p=0.04). GPA–MPN case's platelet counts were significantly higher (491 [346–654] vs. 376 [299–475] $\times 10^9$/L; p=0.03); however, their temporal artery biopsy-positivity rates were comparable (p=0.91).

First-line therapy mostly relied on oral prednisone and aspirin for cases and controls, and did not differ between groups. No patient received JAK inhibitors during follow-up. Relapse-free survival was comparable for the 2 groups. Immunosuppressants were used as glucocorticoids-sparing agents for 12% in each group, with methotrexate being the most frequently prescribed. Mortality was higher for GCA–MPN cases (29 vs. 2%; p=0.003) with shorter overall survival (log-rank test, p=0.008), compared to GCA controls.

Conclusion: Essential thrombocytosis is the most frequent MPN associated with GCA. A high platelet count at GCA diagnosis should lead to a search for JAK2*V617F* mutation. Compared to controls, GCA patients with MPN seem to have a poorer prognosis with a low overall survival, probably due to the MPN or associated comorbidities.

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Abstract Number: 2660

Rationalizing the Use of MRI of the Scalp Arteries in the Diagnosis of Giant Cell Arteritis Through Multivariable Predictive Modelling

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SESSION INFORMATION
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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
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Background/Purpose: It has been historically difficult to develop effective diagnostic strategies and criteria in giant cell arteritis (GCA). While temporal artery biopsy was previously thought of as a diagnostic standard, there has been increasing recognition of so-called 'biopsy negative' GCA. As such, the disease has become increasingly challenging

	No GCA n=194	GCA n=130	Odds ratio	95% Lower CI	95% Upper CI
Age*	66.7 ± 11.3	73.4 ± 9.7	1.06	1.04	1.09
Sex (female)	139 (71.6)	88 (67.7)	0.83	0.51	1.34
Headache	168 (87.5)	111 (85.4)	0.83	0.44	1.6
Scalp Tenderness	84 (43.8)	60 (46.2)	1.1	0.7	1.72
Temporal Artery Tenderness	65 (33.5)	50 (38.8)	1.26	0.79	2
Jaw claudication	37 (19.2)	46 (35.4)	2.29	1.38	3.81
Vision Loss	18 (9.4)	32 (24.6)	3.16	1.68	5.91
Other vision changes	86 (45.3)	61 (47.7)	1.1	0.7	1.73
Constitutional Symptoms	43 (22.6)	37 (29.1)	1.41	0.84	2.35
Weight Loss	15 (7.8)	18 (13.8)	1.9	0.92	3.92
CRP**	4.7 (1.5-12.8)	19.8 (5.5-50.7)	1.02	1.01	1.03
ESR**	20 (8-45)	42 (21-70)	1.02	1.01	1.03
Abnormal MRISA	16 (8.4)	77 (64.7)	19.82	10.5	37.41
Temporal Artery Biopsy (positive/total)	0/105	44/113			

descriptive features of the study population and univariate analysis. ** denotes median and interquartile range.

	β coefficient	Standard Error	p	Odds Ratio	95% CI
Intercept	-6.082	1.180	<0.001		
Age	0.044	0.014	0.001	1.05	1.02 – 1.07
Headache	0.723	0.439	0.010	2.06	0.87 – 4.87
TA tenderness	0.626	0.303	0.039	1.87	1.03 – 3.38
Jaw Claudication	0.640	0.322	0.047	1.90	1.01 – 3.57
No PMR	0.542	0.317	0.088	1.72	0.92 – 3.20
Vision Loss	1.068	0.431	0.013	2.91	1.25 – 6.78
Log(CRP)	1.026	0.221	<0.001	2.79	1.81 – 4.30

Table 2. The multivariable predictive model for the clinical diagnosis of GCA. Receiver-Operator Characteristic = 0.774.

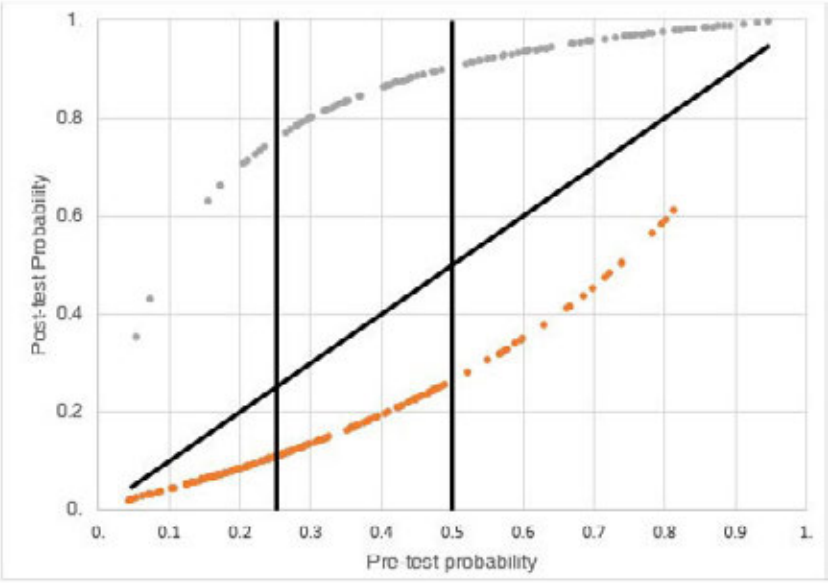

Figure 1. MRISA pre/post-test diagnostic curve. Orange points denote the post-test probability of disease in those who had a negative MRISA using the generated predictive model; grey points for those who had a positive MRISA. The two vertical lines indicate cases that would be included/excluded with calculated probabilities of disease of 0.25 and 0.5 respectively.

to accurately investigate and diagnose. MRI of the scalp arteries (MRISA) has been demonstrated to be more sensitive than temporal artery biopsy, but it's utility in the diagnosis of 'clinical GCA' is thus far unknown.

Methods: This analysis considered a retrospective cohort of 324 patients who had been previously referred to a rheumatologist for evaluation of possible GCA. The clinical information of 171 of these patients was made available from a previous clinical trial; the remaining 153 were consented for participation in a prospective GCA diagnostic database. A clinical diagnosis, regardless of agreement with American College of Rheumatology (ACR) criteria or biopsy, was used as the gold standard. Data concerning clinical features, inflammatory markers, imaging, and biopsy results were extracted for analysis. Best subset forward selection was used to create a multivariable logistic regression model to predict the diagnosis of GCA. Using this model, disease probabilities were calculated and the positive/negative predictive value (PPV/NPV) of MRISA in the diagnosis of clinical GCA was determined.

Results: As seen in table 1, univariate analysis demonstrated that those diagnosed with clinical GCA were older, more likely to have jaw claudication or vision loss, and had higher ESR and/or CRP than those without the diagnosis. An abnormal MRISA was strongly associated with the diagnosis of GCA (OR 19.82, 95% CI 10.5-37.41). Multivariable logistic regression demonstrated that increasing age, the presence of headache, temporal artery tenderness, jaw claudication, vision loss, log(CRP), and the lack of symptoms of PMR were all predictive of the diagnosis of GCA with an area under the receiver-operator curve of 0.774, 95% CI 0.719 - 0.829 (table 2). When a calculated probability of 25% or greater was considered a positive diagnosis, the model was 91.1% sensitive and 46.2% specific for the diagnosis of GCA; at 50% or greater it was 48.2% and 85.4% respectively. This compared to 54.6% and 66.0% using the 1990 ACR criteria. MRISA was found to have 64.7% sensitivity and 91.5% specificity for the clinical diagnosis of GCA. For those determined to be disease negative using the 25% cut-off, a negative MRISA was found to have an 93.5% NPV to rule out GCA; the 50% cut-off was found to have 80.9% NPV (see figure 1).

Conclusion: Multivariable logistic regression was able to fairly model the clinical diagnosis of GCA. MRISA was found to be less sensitive and more specific than previously reported in other studies in the diagnosis of biopsy positive GCA patients; this likely reflects that within this cohort the diagnosis was contaminated by MRISA being used to direct the diagnosis. Regardless, given the high NPV in those of low to medium pre-test probability of GCA, MRISA can assist in ruling out the diagnosis of GCA and avoid temporal artery biopsy.

Disclosure: M. Junek, None; **A. Hu**, None; **K. Beattie**, None; **K. Legault**, None; **S. Garner**, None; **R. Rebello**, None; **N. Khalidi**, None.

Abstract Number: 2661

A Ten-Year Retrospective Review of Temporal Artery Biopsy Lengths in Alberta

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SESSION INFORMATION

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Background/Purpose: Temporal arteritis or giant cell arteritis (GCA) is a large vessel vasculitis that involves extracranial arteries. The historical gold standard for diagnosis is a temporal artery biopsy (TAB) which has potential for false negativity. Current guidelines recommend biopsy lengths of at least one cm with no suggestion of an upper limit. The purpose of this study is to review all biopsy lengths performed in the province of Alberta, Canada to identify an ideal biopsy length as well as other predictors of a positive diagnosis of GCA.

Methods: A retrospective chart review was performed on patients who had undergone a TAB procedure in 22 sites between January 1st, 2008 to January 1st, 2018.Data extracted included patient's age sex, levels of inflammatory markers (ESR and CRP), side of biopsy, post-fixation length and final pathological diagnoses. Predictors of positive pathology were modelled using logistic regression. Stata 14.1 (StataCorp) was used for data analysis.

Results: A total of 1203 biopsies were identified over the decade. Median age was 73 (quartile range [QR], 64–80) years, with 806 (67%) female patients. A total of 235 (20%) biopsies were diagnosed as GCA, with median biopsy length of 1.3 cm (QR, 0.9–1.8 cm). Biopsy lengths between sites ranged between 0.8 cm (QR, 0.6–1.1 cm) to 2.2 cm (QR, 1.5–3.3 cm). Univariate analysis noted increased age (odds ratio [OR] 1.04 per year, 95% CI, 1.02–1.05; $p < 0.001$), ESR (OR 1.01 per unit, 95% CI, 1.01–1.02; $p < 0.001$), CRP (OR 1.01 per unit, 95% CI, 1.01–1.01; $p < 0.001$) and biopsy lengths (OR 1.25 per cm, 95% CI, 1.06–1.46; $p = 0.007$) were associated with positive GCA diagnosis. In multivariate analysis, only age (OR 1.04 per year, 95% CI, 1.02–1.05; $p < 0.001$) and CRP (OR 1.01 per unit, 95% CI, 1.00-1.01; $p < 0.001$) remained statistically significant predictors of a positive GCA diagnosis. We noted an increasing odds ratio for a positive biopsy with increasing length of biopsy up until 2.00–2.49 cm (OR 2.79 per cm 95% CI, 1.10 – 7.09).

Conclusion: This study indicates the optimal upper end of temporal artery biopsy length is between 2.00-2.49 cm. We note the highest OR of a positive biopsy is associated with biopsies of this length, with longer biopsies not providing additional diagnostic yield to justify risks. Our study also shows that age, ESR, CRP and TAB length were significant independent predictors of pathological diagnosis.

Disclosure: R. Chu, None; **C. Foster**, None; **M. Ali**, None; **T. Chaba**, None; **J. Soo**, None; **A. Clifford**, None; **J. Cohen Tervaert**, None; **E. Yacyshyn**, None.

Abstract Number: 2662

Temporal Artery Biopsy Lengths in Alberta: Which Surgical Subspecialty Achieves Optimal Biopsy Lengths?

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SESSION INFORMATION

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Background/Purpose: Temporal arteritis or giant cell arteritis (GCA) is a large vessel vasculitis that involves extracranial arteries. Diagnosis requires a combination of clinical manifestations including symptoms of (scalp tenderness, claudication, visual disturbances), in the context of elevated inflammatory markers, in patients > 50 years of age. The gold standard of diagnosis continues to be a temporal artery biopsy. There is varying evidence regarding an ideal

biopsy length, although current guidelines recommend at least 1 cm, with some evidence suggesting longer biopsies being ideal. The purpose of our study is to investigate whether biopsies performed in the province of Alberta, Canada are meeting guideline recommendations and whether different surgical subspecialties affect results of biopsies.

Methods: A retrospective chart review was performed on patients who had undergone a TAB procedure in 22 sites between January 1st, 2008 to January 1st, 2018. Data extracted included location of biopsy, post-fixation length, final pathological diagnoses and surgical subspecialty of individual performing biopsy. Predictors of positive pathology were modelled using logistic regression. Stata 14.1 (StataCorp) was used for data analysis.

Results: A total of 1203 biopsies were identified over the decade. Of these biopsies, we were able to identify the surgical specialist who performed the biopsy of 1003 biopsies. General surgery performed 428 (70 positive [16.36%]) positive biopsies with median length of 1 cm (QR, 0.7 – 1.5), Ophthalmology performed 393 (100 positive [25.45%]) biopsies with median length of 1.6 cm (QR, 1.2 – 2.1), Plastic Surgery performed 162 (28 positive [17.28%]) biopsies with median length of 1.2 cm (QR, 0.8 – 1.7), Otolaryngology performed nine (one positive [11.11%]) biopsies with median length of 1.3 cm (QR, 0.3 – 1.5), Vascular Surgery performed eight (one positive [12.50%]) biopsies with median length of 3 cm (QR, 1.85 – 3.35), Family Medicine surgical assistants performed two (zero positive [0%]) biopsies with median length of 0.825 cm (QR, 0.65 – 1) and Neurosurgery performed one biopsy at 0.8 cm, which was negative for GCA. Univariate analysis noted ophthalmology as the only surgical subspecialty that was associated with positive GCA diagnosis with OR 1.74, 95% CI, 1.24 – 2.46; p = 0.001. We found that of the 22 sites who performed at least 31 biopsies, median lengths ranged between 0.8 cm to 2.2 cm.

Conclusion: This analysis evaluated the various surgical specialties who complete temporal artery biopsies. The surgical specialty with the highest yield of positive temporal artery biopsies was Ophthalmology, who perform the longest biopsies amongst surgical subspecialties and has the highest positive yield for a GCA diagnosis. Our study also indicates there are institutions in the province of Alberta who consistently do not meet the one cm biopsy length recommendations. This baseline data will inform further practice management for optimal biopsy lengths.

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Abstract Number: 2663

Maintained Benefit in Health-Related Quality of Life of Patients with Giant Cell Arteritis Treated with Tocilizumab Plus Prednisone Tapering: Results from the Open-Label, Long-Term Extension of a Phase 3 Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

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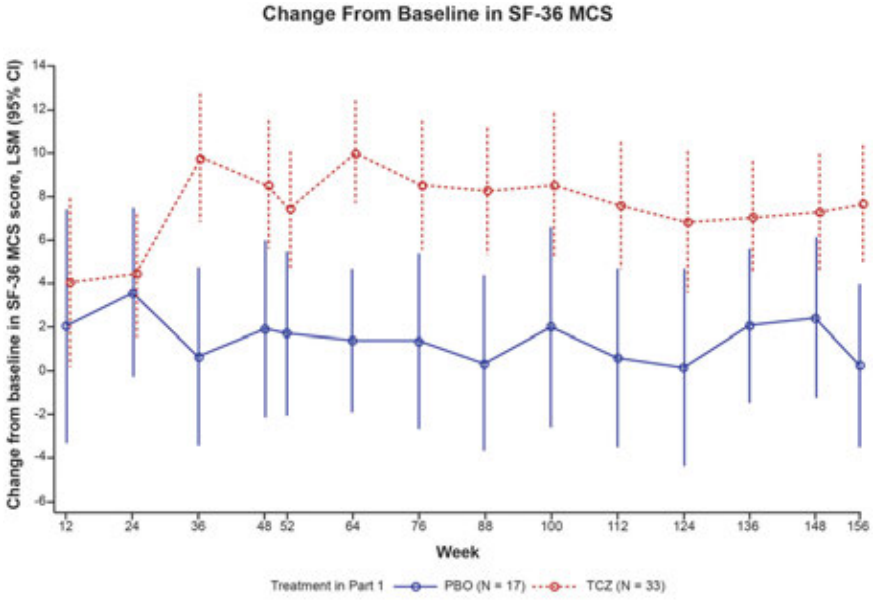
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with giant cell arteritis (GCA) treated with tocilizumab (TCZ) plus prednisone tapering achieved higher rates of sustained glucocorticoid (GC)-free remission and had lower cumulative GC doses than patients treated with prednisone tapering alone in part 1 of the 52-week, double-blind GiACTA trial.[1] During therapy, patients who received weekly TCZ reported improvement in the 36-item Short-Form Health Survey (SF-36) Mental Component Summary (MCS) and Physical Component Summary scores and FACIT-Fatigue scores that were statistically significant and clinically meaningful compared with patients who received prednisone alone.[2] The objective of this analysis was to analyze whether such benefit in SF-36 MCS was maintained in patients originally assigned to receive TCZ in comparison with those originally assigned to receive placebo (PBO) plus a 26- or 52-week prednisone taper (PBO group) among patients who achieved clinical remission at week 52 and maintained treatment-free clinical remission in the 2-year, long-term extension of GiACTA.

Methods: At the end of part 1 of GiACTA, patients entered open-label part 2, in which GCA therapy (including initiation/termination of open-label TCZ and/or GCs) was given at the investigator's discretion according to disease status. The change from baseline in SF-36 MCS score was compared for combined original TCZ (n = 33) and PBO (n = 17) patients who achieved clinical remission at week 52 and maintained treatment-free (no TCZ or GCs) clinical remission in part 2 using a repeated-measures model. The minimal clinically important difference (MCID) for SF-36 MCS is >2.5.[3]

Results: During treatment, SF-36 MCS scores in all 50 patients who maintained treatment-free clinical remission in part 2 had diverged between the TCZ and PBO groups as early as 36 weeks after baseline, with greater improvements evident in the TCZ group (Figure 1). The difference in least squares mean (LSM) change between TCZ and PBO was statistically significant at week 52 (p = 0.016) and maintained at weeks 100 (p = 0.023) and 156 (p = 0.0019). The LSM difference (95% CI) between TCZ and PBO at weeks 52, 100, and 156 was 5.6 (1.1-10.2), 6.5 (0.9-12.1), and 7.4 (2.9-11.9), respectively, exceeding the MCID.



Patients who achieved clinical remission at week 52 and maintained clinical remission while remaining free from GCA treatment (TCZ or GCs) are included. LSM; Least squares mean. MCS, mental component summary; PBO, placebo; SF-36; Short-Form 36. TCZ, tocilizumab.

Conclusion: Among patients who maintained treatment-free clinical remission during part 2 of GiACTA, those originally assigned to receive TCZ plus a prednisone taper during part 1 maintained statistically significant and clinically meaningful improvements in SF-36 MCS up to week 156 compared with those originally assigned to receive PBO plus a prednisone taper in part 1. This was true even though neither of the patient groups received TCZ or GC treatment after they achieved clinical remission at week 52.

References:

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3. Lubeck DP. *Pharmacoeconomics* 2004;22:27-38.

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Abstract Number: 2664

Color Doppler Ultrasound for the Diagnosis of Giant Cell Arteritis in Montreal: A Canadian Single Center Experience

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
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Background/Purpose: Giant Cell Arteritis (GCA) remains challenging to diagnose as false negative temporal artery biopsy (TAB) can occur. Color doppler ultrasonography (CDUS) of the temporal, axillary and carotid arteries is useful when GCA is suspected. A wide range of sensitivities and specificities of CDUS are reported, with better results when performed by a trained sonographer using high resolution equipment. The new GCA probability score (GCAPS) is intended to risk-stratify patients with suspected GCA into those with high probability versus low probability of GCA.

This study aimed to 1) compare CDUS results against TAB with final diagnosis of the specialist as the reference standard; 2) determine how GCAPS performs in relation to the final diagnosis.

Methods: A retrospective chart review was performed for all patients with suspected GCA who had a CDUS from July 2017 to May 2019, at Hopital du Sacre-Coeur de Montreal (University of Montreal). All exams were performed by the same ultrasonographer with the Zonare Z One Ultra Ultrasound System™ using a linear array probe (L14-5Mhz). Data collected included patient characteristics, clinical presentation, physical examination, bloodwork, initial clinical suspicion of GCA (low or moderate/high) and CDUS results of the temporal, carotid and axillary arteries. TAB results and final diagnosis as determined by the treating physician were documented. GCAPS was retrospectively calculated if all the required items were available.

Results: A total of 56 patients had a CDUS examination during the specified time period; amongst them, 31 patients had a TAB. GCA was the final diagnosis in 20 patients, as determined by the treating specialist. Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were 95.0%, 100%, 100%, 97.3% for CDUS; and 81.3%, 100%, 100%, 83.3% for TAB, respectively. There were no false positive CDUS in patients without GCA. Only 1 patient with GCA had a negative CDUS while the TAB was positive. A false negative TAB was observed in 3 patients with GCA, all of which had a positive CDUS. In those 3 patients with negative TAB and positive CDUS, one had extra-cranial large-vessel vasculitis on PET/CT, the second had abnormal temporal arteries on physical examination (tenderness and pulselessness) and the third had classic cranial symptoms of GCA with thrombocytosis and elevated inflammatory markers. False negative rate of CDUS was 5% as opposed to 18.7% for TAB.

GCAPS score of < 9.5 points was found in 1 patient with GCA and 21 patients without GCA. At a cut-off value of 9.5 points, Se, Sp, PPV and NPV for the GCAPS were 95.0%, 65.6%, 69.3% and 95.5% respectively. In our cohort, GCA was the final diagnosis for all patients with a GCAPS ≥ 13 points.

Conclusion: CDUS of the temporal, carotid and axillary arteries showed a high Se and Sp and helped to identify TAB negative patients with GCA. We validated that the GCAPS is a useful clinical tool in our patient population; a score < 9.5 points makes the diagnosis of GCA unlikely.

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Abstract Number: 2665

Clinical Outcomes of Patients with Giant Cell Arteritis and Polymyalgia Rheumatica Symptoms Treated with Tocilizumab in Routine Clinical Practice

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

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Session Time: 9:00AM–11:00AM

Table 1. Patient Characteristics at GCA Diagnosis and Treatment Received

	With PMR Symptoms (n = 32)	Without PMR Symptoms (n = 28)
Age, mean (SD)	67.0 (9.3)	71.8 (9.1)
Female, n (%)	23 (71.9)	20 (71.4)
White, n (%)	27 (84.4)	26 (92.9)
Clinical manifestations at disease onset, n (%)		
Localized headache	28 (87.5)	19 (67.9)
Scalp tenderness	15 (46.9)	11 (39.3)
Jaw claudication	16 (50.0)	15 (53.6)
Amaurosis fugax	5 (15.6)	6 (21.4)
Blurry vision	9 (28.1)	9 (32.1)
Permanent vision loss	2 (6.3)	6 (21.4)
Diplopia	1 (3.1)	1 (3.6)
Weight loss	6 (18.8)	14 (50.0)
PMR symptom(s) only, n (%)	2 (6.3)	0
ESR (mm/hr), mean (SD)	67.9 (36.5)	78.3 (29.4)
CRP (mg/L), mean (SD)	63.1 (59.7)	92.4 (84.9)
Positive TA biopsy, n (%)*	13/27 (48.1)	13/24 (54.2)
Disease duration before TCZ initiation, median (IQR), years	0.7 (0.2-1.9)	0.6 (0.2-1.4)
Duration of TCZ treatment (years), median (IQR)	0.6 (0.3-1.3)	0.5 (0.2-1.5)

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PMR, polymyalgia rheumatica; TA, temporal artery; TCZ, tocilizumab.
* Of patients with TA biopsies performed.

Table 2. Clinical Outcomes Before and After TCZ Initiation

	With PMR at Diagnosis (n = 32)		Without PMR at Diagnosis (n = 28)	
	Before TCZ Initiation	After TCZ Initiation	Before TCZ Initiation	After TCZ Initiation
Patients with ≥ 1 flare, n (%)	24 (75.0)	11 (34.3)	19 (67.9)	7 (25.0)
With PMR symptom(s)*	21 (65.6)	8 (25.0)	4 (14.3)	2 (7.1)
Without PMR symptom(s)*	3 (9.4)	3 (9.4)	15 (53.6)	5 (17.9)
No. of flares	60	23	42	14
With PMR symptom(s), n (%)*	50 (83.3)	18 (78.3)	7 (16.7)	3 (21.4)
Without PMR symptom(s), n (%)*	10 (16.7)	5 (21.7)	35 (83.3)	11 (78.6)
Annual flare rate (95% CI)†	1.34 (0.84 to 2.13)	0.54 (0.28 to 1.05)	1.59 (0.78 to 3.23)	0.71 (0.29 to 1.74)
Time to flare (years), median (IQR)	0.3 (0.2-0.7)	2.1 (0.6-2.6)	0.5 (0.3-0.8)	2.6 (0.9-2.6)

GC, glucocorticoids; GCA, giant cell arteritis; IQR, interquartile range; PMR, polymyalgia rheumatica; TCZ, tocilizumab.
* Symptoms are after GCA diagnosis.
† Rates are estimated from a Poisson regression model with treatment, age, smoking history and new and relapsing GCA as covariates and random patient effect.

Background/Purpose: Approximately 50% of patients with giant cell arteritis (GCA) also have polymyalgia rheumatica (PMR) symptoms.[1] The purpose of this study was to determine whether the presence of PMR symptoms upon GCA diagnosis impacts GCA clinical outcomes and to evaluate the effectiveness of tocilizumab (TCZ) for controlling PMR symptoms in patients with GCA.

Methods: This was a retrospective analysis of patients with GCA treated with TCZ at a single center (2010-2018). Disease flares, defined as re-appearance of clinical manifestations (eg, cranial or PMR signs or symptoms), were assessed among patients with or without PMR at the time of GCA diagnosis. PMR symptoms during disease flares were assessed before and after TCZ initiation.

Results: A total of 60 patients with GCA (71.7% female; mean age, 69.3 years) were followed for a mean (SD) of 2.3 (2.2) years. At diagnosis, 32 had PMR symptoms (2 patients with PMR symptoms only). **Table 1** shows baseline patient characteristics. Among patients with PMR at diagnosis, 75% (n = 24) had a total of 60 flares before TCZ initiation and 34.3% (n = 11) had a total of 23 flares after TCZ initiation (**Table 2**). Among 28 patients without PMR at diagnosis, 67.9% (n = 19) had a total of 42 flares before TCZ initiation and 25% (n = 7) had a total of 14 flares after TCZ initiation (**Table 2**). TCZ was associated with a significant reduction in the annual flare rate both in patients with PMR symptoms ($P = 0.003$) and without PMR symptoms ($P = 0.03$) at diagnosis (**Table 2**). Median time to flare was significantly longer after initiation of TCZ in patients with PMR symptoms (hazard ratio [HR] [95% CI]: 0.18 [0.06 to 0.53]; $P = 0.002$) and without PMR symptoms (HR [95% CI]: 0.21 [0.05 to 0.87]; $P = 0.032$) at diagnosis. Before TCZ initiation, PMR symptoms were observed in 55.9% of flares (57/102) occurring in 43 patients (71.1%). After TCZ initiation, PMR symptoms were observed in 56.8% of flares (21/37) occurring in 18 patients (30%).

Conclusion: TCZ improved clinical outcomes in patients with GCA regardless of the presence or absence of PMR symptoms at diagnosis. These real-world findings suggest that TCZ is also effective in patients with GCA who have symptoms of PMR.

Reference:

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Abstract Number: 2666

Development and Outcome of Aortic Complications During Tocilizumab (TCZ) Treatment of GCA and Histopathologic Evidence of Residual Inflammation

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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Background/Purpose: GCA may affect the aorta and lead to dissections and aortic aneurysms. TCZ treatment may control aortic inflammation as demonstrated by CRP normalization and imaging data. However, limited data is available on the histopathological findings obtained from patients who undergo surgery because of aortic complications during TCZ.

Methods: We performed a retrospective case series of 5 patients with GCA treated with TCZ, who presented in our clinic between 2011 and 2019. Three patients underwent surgery and aortic specimen underwent histopathologic examination

Results: We report on 5 female patients with a mean age of 69 $\pm$ 18 yrs, diagnosed with GCA involving the aorta. 3 patients presented with aneurysms at the time of diagnosis, 1 patient with aortic aneurysm and another patient with dissection developed these complications during TCZ therapy. An enlargement of pre-existing aneurysms was observed in 2 patients after stopping TCZ (after a time interval of 10 weeks and 4 months, respectively). Both patients were not eligible for surgical intervention and died during F/up. 3 patients (2 with aortic aneurysm, 1 with dissection) underwent surgery after having been on TCZ on 7 weeks, 9 months, and 4 years. Imaging before surgery showed remission on MRI and PET-CT, respectively. At the time of surgery, all 3 patients had a normal CRP. Histopathological evaluation of the aortic wall showed persistent lymphoplasmacellular infiltrates (predominantly $CD3^{+}CD4^{+}$ T cells in patient 1) and, in addition, giant cells in pat 2 and 3.

Conclusion: Aortic aneurysms and dissections may occur in patients with aortic involvement during treatment with TCZ, suggesting that regular imaging is necessary in this patient population. Residual inflammation might present an additional risk factor for aortic complications.

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Efficacy and Safety of Tocilizumab in Giant Cell Arteritis: A Monocentric Real-life Experience

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SESSION INFORMATION
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Background/Purpose: Tocilizumab (TCZ) has recently been shown to be effective and safe for the treatment of patients with giant cell arteritis (GCA). Here we describe our real-life experience with TCZ in a large cohort of GCA patients from a single Italian Centre.

Methods: GCA patients, diagnosed according to the 1990 ACR criteria, followed-up at our Large Vessel Vasculitis Clinic and treated with TCZ were included. We retrospectively evaluated demographic features, disease characteris-

Table 1.

Patient	Age/Sex	TAB (performed/ diagnostic)	Imaging	PMR	Cranial	Extra-Cranial	GIACTA inclusion criteria	GIACTA exclusion criteria	Disease length before TCZ (months)	GC side effects / contra-indications	GC dependence
1	79/M	+/+	MRA	-	+	-	+	-	9	+	+
2	70/F	+/+	PET	+	+	+	-	-	5	-	+
3	68/M	-/-	-	-	+	-	+	-	23	-	+
4	68/F	-/-	-	+	+	-	-	-	3	-	+
5	80/F	+/+	-	-	+	-	+	-	6	+	+
6	76/F	-/-	-	+	+	-	-	-	3	+	+
7	56/F	-/-	PET MRA	+	-	+	+	-	3	-	+
8	67/F	-/-	-	-	+	-	-	+	84	-	+
9	87/F	-/-	-	-	+	-	-	-	5	-	+
10	77/M	-/-	-	-	+	+	+	-	2	-	+
11	76/F	-/-	PET	-	+	+	+	-	30	-	+
12	52/M	-/-	-	-	+	-	-	-	24	-	+
13	57/F	-/-	-	+	+	-	-	-	0	+	-
14	79/F	+/+	-	-	+	-	-	-	4	+	+
15	81/F	+/+	-	+	+	-	-	+	56	-	+
16	72/F	-/-	-	-	+	-	-	+	15	+	+
17	81/F	+/+	-	+	+	-	+	-	14	-	+
18	58/F	-/-	PET	-	+	+	-	-	7	-	+
19	75/F	+/+	PET	+	+	+	-	+	18	-	+
20	91/M	-/-	-	-	+	-	+	-	3	-	+
21	55/F	-/-	PET	-	+	+	-	+	28	+	+
22	79/F	+/+	-	+	+	-	+	-	71	+	+
23	70/F	-/-	PET	-	-	+	-	-	22	+	+
24	66/F	+/+	PET MRA	+	-	+	-	+	6	+	+
25	65/F	-/-	-	+	+	-	-	+	9	-	+
26	60/F	-/-	PET	-	+	+	+	-	29	+	+
27	62/F	-/-	-	-	+	-	-	-	6	+	+
28	79/F	+/-	PET	-	+	+	+	-	12	-	+
29	70/F	-/-	PET	-	+	-	+	+	8	-	+
30	51/M	-/-	MRA	+	+	+	-	+	108	-	+
31	52/F	+/-	PET MRA	+	-	+	-	-	132	-	+
32	71/F	-/-	-	+	+	+	-	-	3	-	+
33	77/F	-/-	PET	+	+	+	+	+	21	-	+
34	62/F	+/-	-	+	+	+	-	+	12	-	+
TOTAL		12/9		16	30	16	13	23		12	33

tics, reasons for TCZ introduction and discontinuation, concomitant therapies and response to treatment. For each patient we also evaluated potential eligibility for GiACTA trial. For statistical comparisons non-parametric tests were used.

Results: 34 patients (28 women, mean age 71.3±10 years) were included. Table 1 summarizes GCA clinical features, tools for GCA diagnosis (imaging and/or biopsy), and reasons for TCZ introduction. Mean disease duration before TCZ introduction was 23±31.3 months. Only 11 patients met both GiACTA inclusion and exclusion criteria at TCZ introduction. 26 patients were followed up for 3 months, 22 for 6 months and 15 for 12 months. Mean prednisone (PDN) dose at TCZ introduction was 23.23±13.84 mg. Mean PDN dose was 8.41±7.10 mg ($p < 0.001$) at month 3, 4.95±5.63 mg ($p = 0.02$) at month 6, and 2.66±2.7 mg ($p = 0.05$) at month 12. PDN was stopped in 9 patients (2 at

month 3, 5 at month 6, 2 at month 12) due to optimal disease control with TCZ alone. At TCZ introduction 4 patients were already on methotrexate (MTX). MTX was subsequently stopped in 2 patients (1 at month 3, 1 at month 6) due to disease control. TCZ was temporarily held off in 2 patients due to zoster reactivation and in 2 patients due to mild bacterial infections, and definitively stopped after 2 months (when PDN dose was still high) in 2 patients due to severe bacterial infections. No patient experienced severe neutropenia or liver enzymes elevation. In no case TCZ was judged inefficient.

Conclusion: Our data confirm TCZ is highly effective in GCA treatment and has a significant steroid-sparing effect. In our real-life retrospective study TCZ was also shown to be a safe option in patients with relapsing or refractory GCA.

Disclosure: E. Baldissera, Sobi, 8, Sanofi, 5, Roche, 8, Pfizer, 8, Novartis, 8, Abbvie, 8, Alfa-sigma, 8; **A. Tomelleri**, None; **C. Campochiaro**, GSK, 8, GSK, SOBI, Pfizer, 5, 8, Pfizer, 8, SOBI, 5; **S. Sartorelli**, None; **L. Dagna**, Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI., 5, 8.

Abstract Number: 2668

Pharmacokinetics and Pharmacodynamics of Tocilizumab in Combination with Prednisone Tapering in Patients with Giant Cell Arteritis: 3-Year Results from a Randomized Controlled Phase 3 Trial

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Tocilizumab (TCZ) administered subcutaneously weekly or every 2 weeks with a 26-week prednisone taper (TCZ-QW or TCZ-Q2W) was superior to placebo given with a 26-week or 52-week prednisone taper for the achievement of sustained glucocorticoid (GC)-free remission in patients with giant cell arteritis (GCA) in part 1 of the double-blind phase 3 GiACTA trial.[1] Part 2 was a 2-year, open-label, long-term extension in which TCZ could

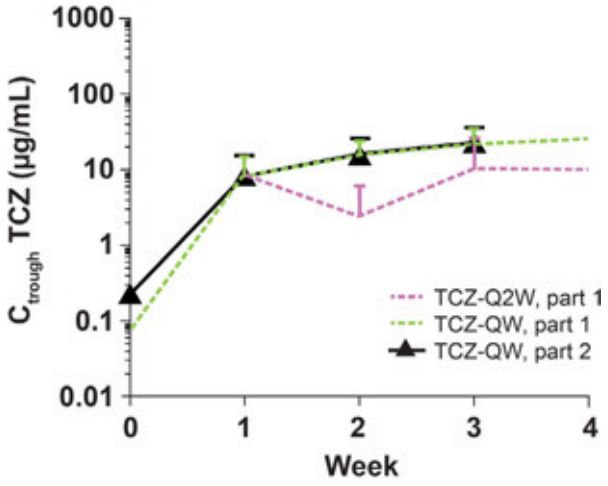

Table. PK and PD parameters at the end of part 2					
	According to treatment[a]		According to GCA flare		
	TCZ-QW only group N=89	Part 1 TCZ-QW[b] N=100	Did not experience flare at any time N=110	Experienced flare while receiving TCZ N=17	Experienced flare while not receiving TCZ N=88
TCZ C_{trough}, µg/mL	70.4 (36.7) n=45	67.9 (34.4) n=72	-	-	-
sIL-6R, ng/mL	678.8 n=45	600.5 n=73	153.8 (273.0) n=95	577.5 (241.4) n=17	240.6 (280.7) n=88
IL-6, pg/mL	58.6 n=45	66.0 n=69	17.9 (43.8) n=89	66.5 (35.7) n=17	36.3 (73.8) n=88
CRP, mg/dL	0.72 n=46	2.08 n=49	3.2 (3.6) n=101	4.5 (15.3) n=17	15.4 (24.4) n=88
ESR, mm/h	5.0 n=47	4.41 n=74	16.6 (12.8) n=99	7.7 (16.0) n=17	29.5 (27.7) n=88

[a]Data from the TCZ-Q2W only group were excluded due to limited data (n=6)
[b]Data from originally assigned treatment group at the end of part 1.
Data are presented as mean or mean (SD).

be stopped or started as needed to achieve disease control. In this analysis, the impact of TCZ dosing interruption was assessed on pharmacokinetic (PK) and pharmacodynamic (PD) end points.

Methods: PK was assessed as predose serum TCZ concentrations (C_{trough}), and serum PD biomarkers measured were interleukin-6 (IL-6), soluble IL-6 receptor (sIL-6R), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). To assess the impact of TCZ on PK/PD during initial drug exposure and at steady state, data were assessed in patients receiving their first 4 doses in part 2 after a dosing interruption of ≥4 weeks (TCZ-break group) and in patients who had received TCZ QW ≥12 weeks (TCZ-QW group). The 4-week dose interruption was included to allow drug levels to fall to negligible levels in patients treated with TCZ in part 1, thereby allowing data from patients who received placebo or TCZ in part 1 to be pooled for part 2 analyses. The 12-week dosing period in part 2 was based on the time to reach steady state after TCZ-QW dosing as determined in part 1. Data from part 1 were used for comparison. PD parameters from patients who experienced flare in part 2 were also examined to determine the prognostic value of biomarkers, regardless of treatment assignment.

Results: Among 250 patients who received treatment in part 1 (TCZ-QW, n = 100; TCZ-Q2W, n = 49; PBO+26, n = 50; PBO+52, n = 51), 215 entered part 2. Seventy patients had a ≥4-week dosing interruption, received the first 4 consecutive TCZ-QW doses in part 2, and were included in the TCZ-break group. During the first 4 weeks of dosing, TCZ C_{trough} levels were comparable in the TCZ-break group and the part 1 TCZ-QW group (Figure). In part 2, TCZ C_{trough} and PD biomarkers after the first initial 4 doses and at steady state were comparable to the values at the end of part 1 (Table). Patients who experienced flare while on TCZ had low levels of CRP and ESR. Patients who experienced flare while not receiving TCZ had higher levels of CRP and ESR compared to those who experienced flare on TCZ, where flares occurred despite low levels of these inflammatory markers.

Conclusion: Restarting TCZ-QW treatment after dose interruption resulted in exposure and PD biomarker profiles similar to those observed with double-blind TCZ-QW treatment, suggesting there were no negative effects for patients with GCA who stopped and restarted TCZ. Low levels of CRP and ESR confirm that despite adequate control by TCZ, these biomarkers are not the sole indicators of flare in GCA patients receiving TCZ, but, in the absence of TCZ, they could serve as indicators of risk for flare.

Reference:

1. Stone JH et al. *N Engl J Med* 2017;377:317-328.

Disclosure: N. Malallieu, Roche, 1, 3; **M. Bao**, Genentech, 1, 3, Genentech, Inc., 3, Roche, 4; **J. Stone**, Genentech, 2, 5, Roche, 2, 5, Xencor, 2, 5.

Abstract Number: 2669

Survival Trends in Giant Cell Arteritis: A Population-based Cohort Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate survival trends in patients with giant cell arteritis (GCA) diagnosed over a 60-year period.

Methods: We assembled a population-based incidence cohort of patients with GCA diagnosed between 1950 and 2009 based on American College of Rheumatology 1990 GCA classification criteria. Patients aged ≥ 50 years with elevation of erythrocyte sedimentation rate or C-reactive protein and radiographic evidence of large vessel vasculitis attributed to GCA were also included. Patients were followed until death, last contact, or December 31, 2018. Survival trends were analyzed by grouping patients according to year of GCA diagnosis into the following categories: Group A (years of diagnosis (1950-1979), Group B (1980-1989), Group C (1990-1999) and Group D (2000-2009). Mortality rates were estimated using the Kaplan-Meier method and were compared with expected mortality rates for persons of the same age, sex, and calendar year estimated using Minnesota population life tables.

Results: The study population included 245 incident cases of GCA; 194 (79%) women and 51 (21%) men, with mean age (±SD) 76.2 ± 8.3 years and median follow-up 10.6 years. Based on comparison to Minnesota lifetables, there

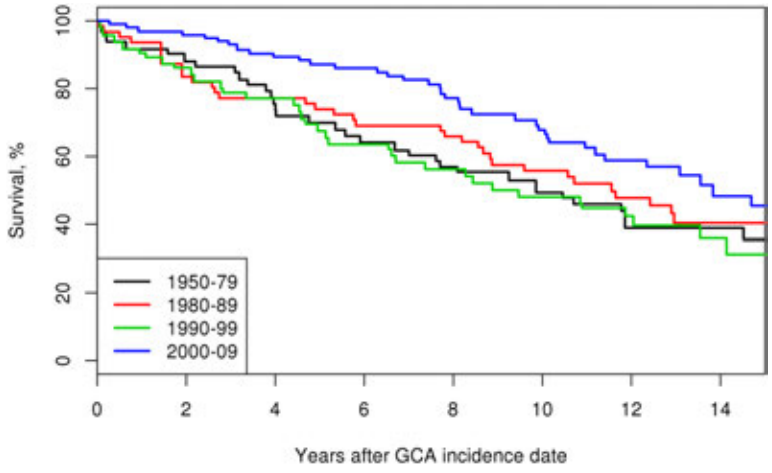


Figure 1. Age and sex adjusted comparison of survival of Olmsted County residents with incident GCA by time period.

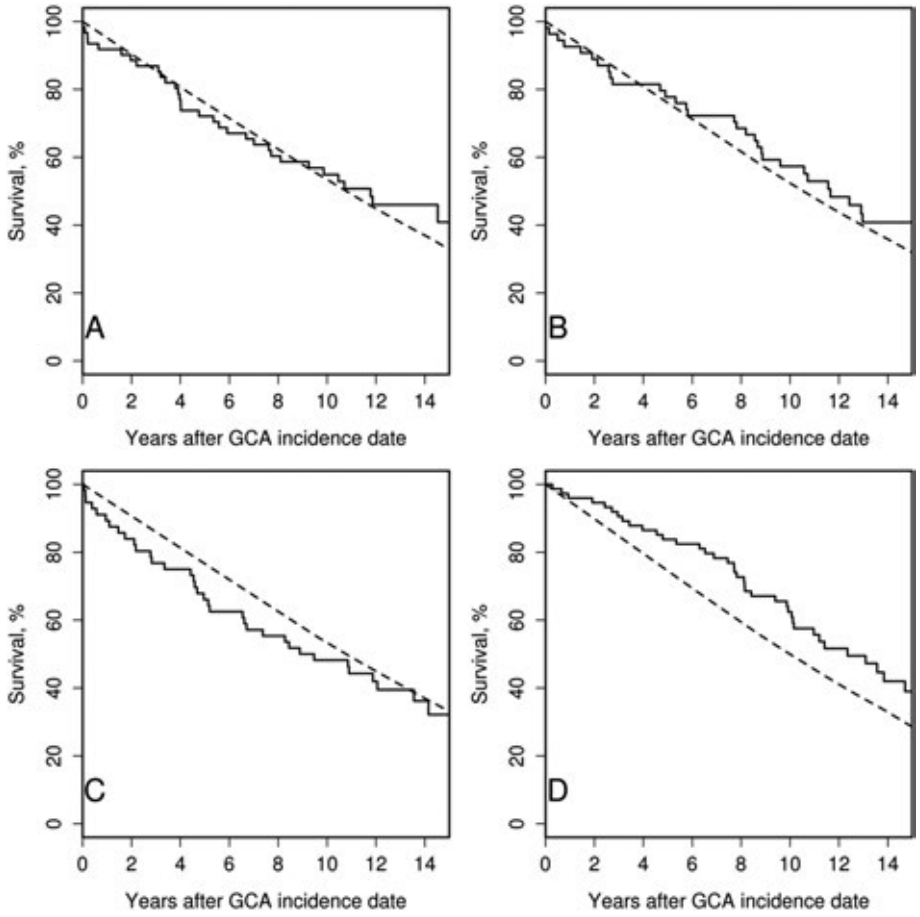


Figure 2. Survival of Olmsted county residents with incident GCA in 1950-2009 compared to expected rates from Minnesota lifetables (observed: solid line; expected dashed line) by time period (A: 1950-79, B: 1980-89, C: 1990-99, D: 2000-09).

was no overall difference in survival when comparing the GCA cohort to the general population. The 2, 5 and 10 year survival rates (95% CI) were 89% (86, 93), 76% (70, 81) and 56% (50, 63) respectively with a standardized mortality ratio of 0.99 (0.86, 1.14). The standardized mortality ratios for Groups A, B, C and D were 0.83 (0.57, 1.17) p=0.30; 0.92 (0.63, 1.3) p=0.63; 1.21 (0.85, 1.69) p=0.25 and 0.70 (0.50, 0.95) p=0.02, respectively.

Conclusion: In this population based-cohort of patients with GCA diagnosed over a 60-year period, the survival of patients diagnosed in recent years was significantly better than that of the general population. The explanation for this novel finding is unclear, but likely to be multifactorial. Improved treatment of co-morbidities, mitigation of glucocorticoid toxicity such as osteoporosis, and improved management of aortic complications may be contributing to improved survival in GCA.

Disclosure: T. Garvey, None; **C. Crowson**, Crescendo Bioscience, 5, Crescendo BioScience Inc., 5, Crescendo Bioscience Inc., 5, Crescendo Biosciences inc., 5, Pfizer, 2; **M. Koster**, None; **E. Matteson**, Boehringer Ingelheim, 5, Pfizer, 2, Sun Pharmaceuticals, 2; **K. Warrington**, Eli Lilly, 2, GlaxoSmithKline, 2, roche, 2, 8, Roche, 2, 5, 8, Sanofi, 5, sanofi, 5.

Abstract Number: 2670

Giant Cell Arteritis with Intracranial Vasculitis: A Case Series

Catalina Sanchez-Alvarez,[1] Alexander Hawkins,[1] Matthew Koster,[2] Vance T. Lehman,[3] Cynthia Crowson,[1] and Kenneth Warrington[2], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic Rochester, Rochester, MN, [3]Mayo Clinic, Rochester

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

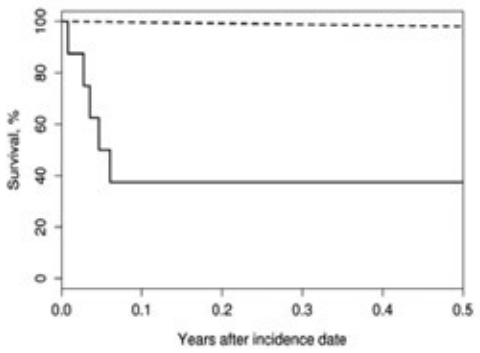
Background/Purpose: Giant cell arteritis (GCA) is a large vessel vasculitis that primarily affects the aorta and its branches. Extracranial branches of the carotid artery are frequently affected; however, intracranial involvement in GCA is rare.

To determine the clinical features and outcome of patients with intracranial giant cell arteritis (IC-GCA).

Methods: A retrospective medical record review was performed to identify all patients with IC-GCA from 1/1996 through 5/2018. Demographic, clinical, laboratory, radiographic, and treatment data at baseline and subsequent follow-up visits were collected. Data was summarized using descriptive statistics

Results: The study cohort included 9 patients with IC-GCA (78% male, mean [±SD] age 72.1 [±7.9] years). 8 of 9 patients had positive temporal artery biopsies. One patient with negative biopsy had evidence of large-vessel GCA on thoracic CT angiography. The mean time from onset of GCA to intracranial involvement was 17 months (±38). All patients had neurologic symptoms, 33% (n:3) had a stroke and 22% (n:2) had a transient ischemic attack. IC-GCA was diagnosed by cranial imaging in 8 patients and by autopsy in one. Cranial imaging modalities used included magnetic resonance angiography (n=8), CT angiography (n=2) and cerebral angiography (n=2). Intracranial vasculitis most commonly affected the internal carotid artery 78% (N=7) followed by the, vertebral artery 56% (n=5), posterior cerebral artery 56% (n=5), middle cerebral artery 44% (n=4), anterior cerebral artery 33% (n=3) and posterior inferior cerebral artery 11% (n=1). Stenosis was present in 89%, occlusion in 33%, dilatation in 11%, and wall thickening in 11%. All patients received glucocorticoids. For treatment of intracranial disease additional agents included: cyclophosphamide (67%), Tocilizumab (22 %). Despite treatment, outcomes for patients with IC-GCA were poor. Five of nine patients died during a mean length of follow-up of 2.4 months. Comparing IC-GCA patient survival to the

Image 1. Survival of 9 patients with intracranial GCA compared to expected rates from US population lifetables (observed: solid line; expected dashed line)



expected rates from the U.S. population (Figure 1), the standardized mortality ratio (95% CI) for IC-GCA was 179.7 (58.3, 419.4); p< 0.001.

Conclusion: Although rare, IC-GCA is associated with significant morbidity and mortality. It occurs predominantly in men, presenting with ischemic cerebrovascular events. Current treatment strategies appear to be of limited efficacy for IC-GCA.

Disclosure: C. Sanchez-Alvarez, None; **A. Hawkins**, None; **M. Koster**, None; **V. Lehman**, None; **C. Crowson**, None; **K. Warrington**, Eli Lilly, 2, GlaxoSmithKline, 2, roche, 2, 8, Roche, 2, 5, 8, Sanofi, 5, sanofi, 5.

Abstract Number: 2671

PET/CT Vascular Findings at Baseline and Six Months in Patients with Newly Diagnosed Giant Cell Arteritis

Anthony Sammel,[1] Edward Hsiao,[1] Geoff Schembri,[1] Elizabeth Bailey,[1] Katherine Nguyen,[1] Janice Brewer,[1] Beatrice Janssen,[1] Leslie Schrieber,[1] Peter Youssef,[2] Clare Fraser,[3] and Rodger Laurent[1], [1]Royal North Shore Hospital, Sydney, Australia, [2]Royal Prince Alfred Hospital, Sydney, Australia, [3]Save Sight Institute, Sydney, Australia

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
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Session Time: 9:00AM–11:00AM

Background/Purpose: PET/CT is a useful modality to diagnose GCA but there is limited knowledge as to how inflammatory vascular findings evolve on follow-up scans. This cohort study aimed to determine the change and clinical significance in vascular wall tracer (FDG) uptake in GCA patients from diagnosis to six-months.

Methods: This study included a subset of patients from the previously reported Giant Cell Arteritis and PET Scan (GAPS) cohort (Sammel et al. Arthritis Rheumatol. 2019). Patients were newly suspected of having GCA and were prospectively enrolled if they had either 1) mural or periadventitial small vessel inflammation on temporal artery biopsy or 2) unequivocal large vessel vasculitis on baseline CT angiogram. Only patients with a clinical diagnosis of

	Vascular territory	Baseline	6 months	p value
Visual Grade	All vessels	0.81	0.32	<0.01
	Cranial arteries	0.73	0.26	0.01
	Supra-aortic large arteries	1.29	0.41	<0.01
	Thoracic aorta	0.71	0.27	<0.01
SUV_{max}/SUV_{LA}	All vessels	1.26	1.18	0.16
	Vertebral arteries	1.24	1.01	0.03
	Supra-aortic large arteries	1.22	1.14	0.25
	Thoracic aorta	1.38	1.37	0.90

Notes:
P value was calculated using the two-tailed paired samples t-test
SUV was not reported for the temporal, maxillary or occipital arteries to avoid the potential for partial volume errors
Supra-aortic large arteries included subclavian, axillary, carotid and brachiocephalic arteries
Cranial arteries included temporal, maxillary, occipital and vertebral arteries
Visual grade and SUV_{max}/SUV_{LA} definitions are provided in the abstract text

Table 1. Mean visual and standard uptake value (SUV) vascular scores on baseline and six month PET/CT

GCA were included in the final analysis. PET/CT from the vertex to diaphragm was performed at baseline and at six-months. A single PET-experienced physician, blinded to clinical, biopsy and study inclusion details, reported the grade of vascular FDG uptake for 18 artery segments (0 = none, 1 = minimal/equivocal, 2 = moderate, 3 = very marked). The maximum standard uptake value (SUV) for each vessel was compared to the mean SUV in the left atrium to give an SUV_{max}/SUV_{LA} ratio. Patients and clinicians were unaware of the six-month PET vascular findings and were followed for 12-months.

Results: 24/64 GAPS patients met inclusion criteria, of whom 15 consented to six-month PET/CT and had a clinical diagnosis of GCA. From baseline to six-months, the mean vascular uptake grade per patient decreased from 0.81 to 0.32 (Table 1) with significant reductions in all vascular territories ($p < = 0.01$). The average SUV_{max}/SUV_{LA} per patient decreased non-significantly from 1.26 to 1.18 ($p = 0.16$). Over this period the mean CRP fell from 70 to 9 mg/L and ESR fell from 59 to 15 mm/hr. 5/15 (33%) patients had persistent grade 2 (moderate) uptake in at least one artery on the six-month scan. Compared with their counterparts, these 5 patients had a non-significantly higher mean CRP (12 vs 8 mg/L), ESR (16 vs 15 mm/hr) and were taking a lower mean dose of prednisone (8 vs 12 mg). 3 were taking concomitant methotrexate and one an IL-6 inhibitor. None of these 5 patients experienced a clinical flare from 6-12 months but 60% had flares in the preceding six-months.

Conclusion: PET/CT vascular scores decreased in the first six-months following diagnosis of GCA. One-third of patients had significant ongoing vascular uptake at six-months but this did not predict future clinical flare.

Disclosure: A. Sammel, None; **E. Hsiao**, None; **G. Schembri**, None; **E. Bailey**, None; **K. Nguyen**, None; **J. Brewer**, None; **B. Janssen**, None; **L. Schrieber**, None; **P. Youssef**, None; **C. Fraser**, None; **R. Laurent**, None.

Abstract Number: 2672

Ultrasonography in the Diagnosis of Giant Cell Arteritis

ROK JESE,[1] Ziga Rotar,[1] Matija Tomšič,[2] and **Alojzija Hocevar** [3], [1]UMC LJUBLJANA, DPT. OF RHEUMATOLOGY, LJUBLJANA, Slovenia, [2]Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia, LJUBLJANA, Slovenia, [3]Department of Rheumatology, University Medical Center Ljubljana, Slovenia, LJUBLJANA, Slovenia

Table 1. Involvement of cranial and aortic arch arteries in GCA assessed by CDS

Arteries	No (%) of positive CDS	Halo (No) bi/uni lateral	IMT (cm)* inflamed artery	noniflamed artery
Temporal	167 (78.8)	133 / 34	0.069 (0.060-0.080)	0.024 (0.020-0.028)
Facial	103 (48.6)	59 / 44	0.070 (0.059-0.088)	0.028 (0.023-0.034)
Occipital	63 (29.7)	39 / 24	0.069 (0.055-0.079)	0.023 (0.023-0.028)
Thyroid	25 (11.8)	18 / 7	0.066 (0.060-0.082)	NOT REGULARLY DETERMINED
Carotid	26 (12.3)	22 / 4	0.145 (0.110-0.164)	0.081 (0.067-0.090)
Vertebral	19 (9.0)	12 / 7	0.129 (0.100-0.152)	0.046 (0.040-0.054)
Subclavian	53 (25.0)	48 / 5	0.165 (0.134-0.190)	0.070 (0.060-0.079)
Axillary	48 (22.6)	41 / 7	0.160 (0.130-0.200)	0.060 (0.051-0.062)
Any artery	208 (98.1)			

Legend: IMT intima-media thickness; * median (IQR), IQR interquartile range

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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Imaging has been recently recognized as a tool equivalent to the temporal artery biopsy in diagnosing giant cell arteritis (GCA). Amongst a variety of imaging modalities, color Doppler Ultrasonography (CDS) is the most convenient. We aimed to evaluate the frequency of cranial- and aortic arch-artery involvement in GCA using CDS.

Methods: We performed CDS examination of cranial and aortic arch arteries in new, clinically diagnosed GCA patients between October 2013 and April 2019, using a Philips IU22 with 5–17.5 MHz linear probe or Philips Epiq 7 with 5–18.5 MHz linear probe. Temporal, facial, occipital, thyroid, carotid, vertebral, subclavian, and axillary arteries were examined bilaterally. A halo with positive compression sign was considered a positive finding. Additionally, the thickness of intima-media complex was measured. .

Results: During the 67-month period 212 newly diagnosed GCA patients (63.2% females, median (IQR) age 75.4 (67.2-80.8) years) underwent vascular CDS evaluation. CDS was performed prior to glucocorticoid initiation in 201 patients (94.8%), and delayed by a median (IQR) of 1 (1-3) days (range 1-6 days) for the rest.

The CDS was positive in 208 (98.1%) patients in at least one of the examined arteries. Temporal arteries, involved in 167 (78.8%) patients, were the most commonly affected vessels. Extracranial large vessel involvement (LVV) was found in 70 (33.0%) patients (30 patients had isolated LVV, and 40 concomitant temporal artery involvement). Among the 142 patients without LVV, 11(5.2% of the studied cohort) had involvement of cranial arteries other than temporal arteries (we found facial, occipital and thyroid artery involvement in 9, 3 and 2 patients, respectively). Table 1 shows the frequency of individual vessel involvement and the intima-media thickness of inflamed and non-inflamed arteries.

Conclusion: CDS of eight preselected cranial and aortic arch arteries provides a high diagnostic yield in GCA.

Disclosure: R. JESE, None; **Z. Rotar**, AbbVie, 9, Amgen, 5, 8, Eli-Lilly, 9, MSD, 5, Novartis, 9, Pfizer, 9, Sanofi, 5; **M. Tomšič**, None; **A. Hocevar**, None.

Abstract Number: 2673

Presentation and Management of Giant Cell Arteritis in a Real-World Setting (Artemis Study)

Alfred Mahr,[1] Eric Hachulla,[2] Hubert de Boysson,[3] Nassim Guerroui,[4] Emmanuel Héron,[5] Stéphane Vinzio,[6] Jonathan Broner,[7] François-Xavier Lapebie,[8] Martin Michaud,[9] Laurent Sailler,[8] Thierry Zenone,[10] Mohamed Djerad,[11] Mathieu Jouvray,[12] Emilie Shipley,[13] Nathalie Tieulie,[14] Isabelle Idier,[15] Marc Paccalin,[16] and Valérie Devauchelle Pensec[17], [1]Hospital Saint-Louis, University Paris Diderot, Paris, France, [2]Dept. of Internal Medicine and Clinical Immunology, Hôpital Claude Huriez, University of Lille, Lille, France, Lille, France, [3]University Hospital of Caen, Caen, France, [4]European Hospital of Marseille, Marseille, France, [5]Quinze-Vingt Hospital, Paris, France, [6]GHM Grenoble, Grenoble, France, [7]University Hospital of Nîmes, Nîmes, France, [8]University Hospital of Toulouse, Toulouse, France, [9]Joseph Ducuing Hospital, Toulouse, France, [10]Hospital of Valence, Valence, France, [11]Hospital of Nevers, Nevers, France, [12]Hospital of Arras, Arras, France, [13]Hospital of Dax, Dax, France, [14]University Hospital of Nice, Nice, France, [15]Chugai Pharma France, Paris La Défense, France, [16]University Hospital of Poitiers, Poitiers, France, [17]University Hospital of Brest, Brest, France

SESSION INFORMATION
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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
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Session Time: 9:00AM–11:00AM

Background/Purpose: We have few real-world data on the natural history and care of patients with giant cell arteritis (GCA). The objective of this observational study (ARTEMIS) was to describe the characteristics and care of patients with GCA in real-life settings in France.

Methods: This cross-sectional, non-interventional, multicentre, single-visit survey was conducted among hospital-based physicians specialized in internal medicine or rheumatology. Investigators enrolled consecutive patients ≥50 years old who consulted for GCA and were under treatment. Information on patient characteristics and diagnostic journey, diagnostic methods and specific GCA treatments were collected on an electronic case report form. Newly-diagnosed GCA was defined as diagnosis-to-visit interval < 6 weeks. Descriptive statistics were used for quantitative and qualitative data.

Results: Over the 3-month inclusion period (August–November 2018), 306 patients were recruited (females: 67%, mean age: 74.0±7.9 years) by 69 investigators (internists: 85%, rheumatologists: 15%) and 53 hospital departments; 13% had newly-diagnosed GCA and overall mean follow-up was 21.0±26.4 months. The original referral of patients to specialized centres was from general practitioners (56%), ophthalmologists (10%), neurologists (7%), emergency physicians (5.6%), internists (4%) and rheumatologists (5%). The most common medical histories were hypertension (46%), psychiatric disorders (10%), dyslipidemia (12%), diabetes (9%) and osteoporosis (6%). Initial GCA presentations included cranial symptoms (89% of patients), constitutional symptoms (74%), polymyalgia rheumatica (48%), and other extra-cranial manifestations (35%). Temporal artery biopsy, high-resolution temporal artery Doppler, 18FDG-PET and aortic angio-CT were performed for 85%, 31%, 26% and 30% of patients, respectively, and contributed to the GCA diagnosis for 67%, 53%, 70% and 37%. All patients received glucocorticoids (GCs) and GC therapy was ongoing for 89%. The mean total cumulative oral GC dose, assessed for 87 patients, was 5179±4987 mg. In all, 87 (28%) patients also received ≥1 adjunctive medication, mainly methotrexate (58 patients [19%]) and/or tocilizumab (47 patients [15%]). Overall, 40% of patients had ≥1 relapse (mean number of relapses: 1.7±1.0) after a mean time to a first relapse of 13.3±12.8 months. Thirty-seven percent had ≥1 comorbidity related to or aggravated by GCs, most frequently diabetes (12%), hypertension (10%), osteopenia/osteoporosis/osteoporotic fractures (7%), insomnia (3%) and infections (3%).

Conclusion: This observational, cross-sectional study of a large number of recently diagnosed patients provides insight into current medical practices for GCA in France. Despite extensive use of large-vessel imaging, the proportion of patients with a diagnosis of non-cranial GCA is low (11%). The substantial proportion of patients with relapsing disease results in high cumulative doses of GCs. Methotrexate and tocilizumab were the most commonly prescribed adjunct medications.

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Abstract Number: 2674

Clinical Symptoms and Associated Vascular Imaging Findings in Takayasu's Arteritis Compared to Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Takayasu's arteritis (TAK) and giant cell arteritis (GCA) are the two major forms of large vessel vasculitis. The study objectives were to compare clinical symptoms of the head, neck, and upper extremities between TAK and GCA in association with vascular activity on ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) and arterial damage by magnetic resonance angiography (MRA).

Methods: Patients with TAK and GCA were recruited into a prospective observational cohort. Clinical and imaging assessments were performed within a 24-hour period, blinded to each other. Abnormal PET activity was defined as arterial FDG uptake > liver by visual assessment. Vascular damage was defined as stenosis, occlusion, or aneurysm in specific angiographic territories by MRA. Clinical features present on the day of imaging assessment (carotidynia; posterior neck pain; vertigo; lightheadedness, frontotemporal or posterior headache; arm claudication), were compared to corresponding imaging angiographic abnormalities by MRA and PET in TAK and GCA separately. Presence of clinical features at any point during disease, were studied in association with the number of damaged neck arteries (carotid and vertebral arteries). The association between clinical symptoms and imaging features was assessed by generalized mixed model regression, adjusting for repeated study visits. The association between historical symptoms and number of affected neck arteries was assessed by ordinal regression.

Results: 111 participants (TAK=56; GCA=55) contributed data from 270 study visits. Patients with TAK were more likely to report carotidynia than patients with GCA [12 (21%) vs 0 (0%), p< 0.01]. Clinical features and imaging findings are detailed in the Table. Carotidynia was associated with abnormal activity on FDG-PET (Sensitivity 27%, Specificity 96%, p< 0.01) and less strongly associated with damage on MRA (Sensitivity 11%, Specificity 95%, p=0.02) in TAK. Posterior neck pain was more common in patients with GCA than TAK [10 (18%) vs 4 (7%), p=0.09]. Posterior neck pain was associated with vertebral artery PET activity in GCA (p=0.03). Vertigo was associated with vertebral artery damage in TAK (p< 0.01), whereas lightheadedness was associated with carotid artery damage in GCA (p< 0.01). Posterior headache was associated with vertebral PET activity in GCA (p=0.04). Frontotemporal headache was not associated with carotid PET activity or damage in either disease. Arm claudication was associated with subclavian damage in both TAK and GCA (p< 0.01 and p=0.02 respectively). Patients with increased burden of damaged neck arteries were more likely to experience lightheadedness (p=0.03), positional lightheadedness (p< 0.01), posterior neck pain (p=0.02) or a major CNS event (p< 0.01) at some point during the disease.

Table. Association of Clinical features with Imaging Findings In TAK and GCA

Symptom	Arterial Territory	LVV	Image	TN	TP	FN	FP	P value	Sensitivity	Specificity
Carotidynia	Carotid	TAK	PET	166	10	27	7	<0.01	27% (14-44%)	96% (92-98%)
			MRA	90	12	95	5	0.02	11% (6-19%)	95% (88-98%)
		GCA	PET	No patients with GCA had carotidynia						
			MRA							
Posterior Neck pain	Vertebral	TAK	PET	208	0	1	3	1	0% (0-97%)	98% (96-100%)
			MRA	159	0	42	3	1	0% (0-8%)	98% (95-100%)
		GCA	PET	244	3	22	1	0.03	12% (3-31%)	100% (98-100%)
			MRA	229	0	25	4	1	0% (0-14%)	98% (96-100%)
Vertigo	Vertebral	TAK	PET	209	0	1	2	1	0% (0-97%)	99% (97-100%)
			MRA	161	1	41	1	<0.01	2% (0-13%)	99% (97-100%)
		GCA	PET	231	0	25	14	1	0% (0-14%)	94% (91-97%)
			MRA	222	3	21	11	0.7	12% (3-32%)	95% (92-98%)
Lightheadedness	Carotid	TAK	PET	156	4	33	16	0.96	11% (3-25%)	91% (85-95%)
			MRA	92	13	94	3	0.08	12% (7-20%)	97% (91-99%)
		GCA	PET	166	2	99	2	0.95	2% (0-7%)	99% (96-100%)
			MRA	175	1	82	3	<0.01	1% (0-6%)	98% (95-100%)
Posterior Headache	Vertebral	TAK	PET	206	0	1	4	0.98	0% (0-97%)	98% (95-99%)
			MRA	159	1	40	3	0.97	2% (0-13%)	98% (95-100%)
		GCA	PET	238	3	21	4	0.04	12% (3-32%)	98% (96-99%)
			MRA	229	3	22	4	0.11	12% (2-31%)	98% (96-99%)
Frontotemporal Headache	Carotid	TAK	PET	165	4	33	8	0.84	11% (3-25%)	95% (91-98%)
			MRA	92	7	99	3	0.23	7% (3-13%)	97% (91-99%)
		GCA	PET	149	7	63	18	0.92	10% (4-19%)	89% (83-93%)
			MRA	163	11	73	13	0.53	13% (7-22%)	93% (88-96%)
Arm claudication	Subclavian	TAK	PET	142	8	19	42	0.03	29% (14-50%)	77% (70-83%)
			MRA	89	42	60	9	<0.01	41% (31-51%)	91% (83-96%)
		GCA	PET	129	25	81	32	0.57	23% (16-33%)	80% (73-86%)
			MRA	126	49	75	10	0.02	40% (31-49%)	93% (87-96%)

TN = True Negative; TP = True Positive; FN = False Negative; FP = False Positive

Conclusion: The distribution of clinical symptoms and association with vascular imaging abnormalities differs between TAK and GCA. In both diseases, vascular symptoms have low sensitivity and high specificity for imaging abnormalities. These findings may help clinicians predict likely associated PET and MRA findings based on the presence of a specific symptom in patients with TAK and GCA.

Disclosure: D. Michailidou, None; **J. Rosenblum**, None; **C. Rimland**, None; **J. Marko**, None; **M. Ahlman**, None; **P. Grayson**, None.

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Risk of Potential Glucocorticoid-Related Adverse Events in Patients with Giant Cell Arteritis: Results from a US-based Electronic Health Records Database

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Oral glucocorticoids (OGC) have been the mainstay of treatment for giant cell arteritis (GCA). However, OGCs are associated with several adverse events (AEs). The purpose of this study was to estimate the risk of potential OGC-related AEs in patients with GCA.

Methods: This retrospective, observational cohort study utilized the 2008-2017 IBM Explorys Electronic Health Records database which includes laboratory values. Inclusion criteria included age ≥ 50 years with ≥ 2 GCA diagnoses ≥ 7 days apart, 1 OGC prescription within 6 months of the first GCA diagnosis (index date = date of first OGC prescription) followed by a second OGC prescription, no other autoimmune disease requiring high-dose OGCs, no exposure to anti-tumor necrosis factor or anti–interleukin-6 therapies, ≥ 1 C-reactive protein (CRP)/erythrocyte sedimentation

Table 1. Adverse Events During the 12-Month Post-Index Period, Stratified by OGC Daily Dose

	Dose Q1 ≥ 1.00 to ≤ 13.75 mg N = 184	Dose Q2 > 13.75 to ≤ 25.00 mg N = 184	Dose Q3 > 25.00 to ≤ 40.00 mg N = 198	Dose Q4 > 40 mg N = 161
Patients without type 2 diabetes and without HbA1c ≥ 7.5 in the pre-index period, n	120	136	130	110
With type 2 diabetes diagnosis or HbA1c ≥ 7.5 in the post-index period, n (%)	9 (7.5)	16 (11.8)	16 (12.3)	27 (24.5)
Maximum HbA1c value across HbA1c lab results during post-index, mean (SD)	7.75 (2.46)	8.30 (2.86)	8.25 (2.42)	8.61 (3.09)
Patients with diabetes diagnosis in the pre-index period but without HbA1c ≥ 7.5 in the pre-index period, n	31	18	40	15
With worsening diabetes with HbA1c ≥ 7.5 in the post-index period, n (%)	10 (32.3)	6 (33.3)	20 (50.0)	4 (26.7)
Patients without blood glucose level ≥ 200mg/dL in the pre-index period, n	173	169	179	147
With blood glucose level ≥ 200mg/dL in the post-index period, n (%)	13 (7.5)	15 (8.9)	24 (13.4)	22 (15.0)
Adverse events in the post-index period, n (%)				
Serious infection requiring hospitalization for infection and/or IV antibiotics	31 (16.8)	39 (21.2)	44 (22.2)	40 (24.8)
Serious infection requiring IV antibiotics	29 (15.8)	33 (17.9)	42 (21.2)	35 (21.7)
Serious infection requiring hospitalization for infection	6 (3.3)	12 (6.5)	12 (6.1)	8 (5.0)
Cataracts	22 (12.0)	27 (14.7)	34 (17.2)	35 (21.7)
Gastrointestinal bleeding or ulcer	11 (6.0)	11 (6.0)	13 (6.6)	19 (11.8)
Patients with BMI in pre- and post-index, n	171	162	181	141
Increase in BMI by 5, n (%)	7 (4.1)	5 (3.1)	9 (5.0)	9 (6.4)

BMI, body mass index; HbA1c, hemoglobin A1c; IV, intravenous; Q, quartile.

rate (ESR) laboratory test and 12 months of data available pre- and post-index. Potential AEs assessed during the 12 months post-index were descriptively summarized across cohorts of patients based on quartiles (Q) of mean daily dose of OGCs measured over 6 months post-index among this patient sample (Q1: ≥ 1.00 to ≤ 13.75 mg; Q2: > 13.75 to ≤ 25.00 mg; Q3: > 25.00 to ≤ 40.00 mg; Q4: > 40.00 mg). Potential AEs included type 2 diabetes (T2D) diagnosis, hemoglobin A1c (HbA1c), blood glucose level, serious infections, cataracts, gastrointestinal bleeding or ulcer and increases in body mass index (BMI). Actual OGC use by patient could not be confirmed and is a limitation of this study.

Results: Mean age of the 785 eligible patients was 76 years (SD 9); 70% were female. Mean Deyo Charlson Comorbidity Index score at baseline was 1.57 (SD 2.01). The most common baseline comorbid conditions were cerebrovascular disease, diabetes, chronic pulmonary disease, and renal disease. Mean daily OGC dose was 28.9 mg during the first 6 months post-index. Mean (SD) CRP and ESR during the 12-month follow-up was 5.1 (13.6) and 26.5 (20.7), respectively. The proportion of patients with newly diagnosed T2D or with HbA1c ≥ 7.5 during the 12-month follow-up ranged from 7.5% to 24.5% from OGC daily dose Q1 to Q4 cohorts. The proportion of patients with glucose ≥ 200 mg/dL ranged from 7.5% to 15.0% from Q1 to Q4. Serious infections ranged from 16.8% to 24.8% from Q1 to Q4 and cataract ranged from 12.0% to 21.7% from Q1 to Q4. The proportions of patients with gastrointestinal bleed/ulcer ranged from 6.0% in Q1 to 11.8% in Q4. An increase in BMI of 5 ranged from 4.1% to 6.4% from Q1 to Q4.

Conclusion: In patients with GCA, potential OGC-related AEs increased with increased daily OGC dose. This highlights the need for effective therapies for GCA that reduce the exposure and potential risk of OGCs.

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Disclosure: J. Best, Genentech, 1, 3, Genentech, Inc., 1, 3; **A. Kong**, IBM Watson Health, 3; **O. Tran**, IBM Watson Health, 3; **M. Michalska**, Genentech, Inc., 3.

Abstract Number: 2676

Cardiovascular Treatment and the Incidence of Giant Cell Arteritis (GCA) – a Population-Based Case-Control Study

Aladdin Mohammad,[1] Pavlos Stamatis,[1] and Aleksandra Turkiewicz[2], [1]Lund University, Lund, Skane Lan, Sweden, [2]Lund University, Lund, Sweden

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The aetiology of giant cell arteritis (GCA) is largely unknown. We aimed to evaluate ACE-inhibitors (ACE-i), angiotensin II receptor blockers (ARBs), beta-blocking agents, calcium antagonists, diuretics or other cardiovascular drugs as risk factors for incident GCA.

Methods: We included 574 biopsy-proven GCA cases diagnosed between Jan 1st2006 and Oct 31st2015 in the Skåne region, Sweden and 5740 controls matched on age, sex and residential area. Using the Swedish Prescribed Drug Register containing all prescribed and dispensed drugs, we identified the GCA cases and controls who had at least one dispensation of the following groups of drugs: ACE-i or ARBs (ATC-code C09), beta-blocking agents (C07), calcium antagonists (C08), diuretics (C03), statins (C10AA) or cardiac therapy (C01) between Jul 1st2005 and the index date (i.e. the date of GCA diagnosis for both cases and their matched controls). To study *incident* drug use,

Table 1. Descriptive data.

	Controls, n=5740	GCA, n=574
Age in index year (years), mean (SD)	71 (8)	73 (8)
Sex, male, n (%)	427 (30)	83 (30)
Income, in 100 SEK, mean (SD)	1.78 (2.95)	1.65 (1.4)
Education, up to 9 years, n (%)	477 (35)	100 (36)
Education, 10-12 years, n (%)	527 (38)	117 (42)
Education, 13-14 years, n (%)	146 (11)	22 (8)
Education ,15+ years, n (%)	226 (16)	38 (14)
If married or registered partner, n (%)	1109 (79)	213 (77)
Any diagnosis from group I, n (%)	688 (49)	172 (61)
Myocardial infarction (I25), n (%)	42 (3)	15 (5)
Hypertension (I10), n (%)	303 (22)	89 (32)
Angina pectoris (I20), n (%)	41 (3)	17 (6)
Thrombo-embolic diseases (I80-I82, I74), n (%)	80 (6)	19 (7)
Diabetes mellitus (E10-E14), n (%)	112 (8)	21 (7)

Table 2. Percentage of persons having dispensed the drugs of interest at least once before the index date (the date of GCA diagnosis for cases and the same date for their matched controls).

	Control	GCA
ACE-inhibitors and ARBs	37	34
Beta-blocking	39	36
Calcium antagonists	25	22
Diuretics	41	34
Statins	36	30
Cardiac therapy	20	17

	Whole cohort, adjusted for cardiovascular diagnosis		Subgroup with cardiovascular diagnosis		Subgroup on cardiovascular treatment	
	All, n=6314	Incident users, n=1690	All, n=3768	Incident users, n=860	All, n=4661	Incident users, n=723
ACE-inhibitors and ARBs	0.84 [0.69,1.01]	1.02 [0.70,1.48]	0.86 [0.71,1.03]	1.01 [0.55,1.89]	0.92 [0.74,1.13]	1.08 [0.64,1.84]
Beta-blockers	0.81 [0.67,0.98]	1.02 [0.70,1.49]	0.84 [0.69,1.01]	0.89 [0.49,1.61]	0.91 [0.74,1.13]	1.05 [0.62,1.78]
Calcium antagonists	0.84 [0.68,1.04]	1.03 [0.64,1.65]	0.85 [0.69,1.05]	0.86 [0.42,1.78]	0.90 [0.72,1.13]	1.03 [0.56,1.87]
Diuretics	0.74 [0.61,0.90]	0.91 [0.63,1.32]	0.75 [0.62,0.91]	0.65 [0.35,1.19]	0.75 [0.60,0.93]	1.11 [0.65,1.88]
Statins	0.72 [0.60,0.88]	0.64 [0.42,0.98]	0.74 [0.61,0.90]	0.55 [0.28,1.10]	0.79 [0.63,0.97]	0.68 [0.39,1.20]
Cardiac therapy	0.76 [0.60,0.97]	1.02 [0.61,1.71]	0.79 [0.63,1.00]	1.58 [0.72,3.45]	0.80 [0.63,1.02]	1.09 [0.57,2.09]

Table 3. Odds ratios [95% CI] for association between drug exposure and incident GCA. The estimates are from a conditional logistic regression (matching factors: age, sex residential area) adjusted for marital status, education and income.

we performed a second analysis, were all persons that dispensed the any of the drugs listed above at least once between July 1st2005 and Jun 30th2006 were excluded. We used conditional logistic regression adjusted for income, education, and marital status and if being diagnosed with cardiovascular diseases (ICD-10 code from group I). The data on cardiovascular diagnoses were retrieved from Skåne Healthcare Register covering the whole population of the region (including primary care) between the year 1998 and the data of the first dispensation of a cardiovascular drug. A separate regression model was fitted for each drug group of interest. To take into account bias by indication we performed two subgroup analyses, one only among those with a cardiovascular disease, second among those on any cardiovascular drug (ATC code C).

Results: The included persons were on average (SD) 75 (8) years old and 29% were male, 70% were diagnosed with a cardiovascular disease (47% with hypertension, Table 1). Of the GCA cases 71% had at least one dispensation

of any cardiovascular drug before the index date, compared to 74% among controls (Table 2). Among the persons that dispensed at least one drug of interest, 75% had at least one dispensation of a drug from another group (53% among incident users). The odds ratios for the association between drug exposure and GCA were close to 1 for most drugs. The only drug consistently associated with lower odds of GCA were statins with 12% to 40% lower risk of GCA (Table 3).

Conclusion: After taking into account confounding and bias-by-indication, we found that of the evaluated cardiovascular drugs only statins may be associated with lower risk of incident biopsy-proven GCA.

Disclosure: A. Mohammad, None; **P. Stamatis**, None; **A. Turkiewicz**, None.

Abstract Number: 2677

Healthcare Resources Utilization in Giant Cell Arteritis – a Population-Based Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
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Background/Purpose: To study the healthcare resource utilization (HRU) in patients with giant cell arteritis (GCA) compared with the background population in southern Sweden.

Methods: The study includes patients diagnosed with biopsy-proven GCA between 2001 and 2011 and their randomly selected age-, sex- and residency area matched reference persons (1:10). Data on all healthcare consultations and admissions were extracted from a regional administrative database, the Skåne Healthcare Register, which records data on all healthcare consultations and hospitalizations using the ICD-10 codes. Frequencies of HRU were analysed as numbers and rates of primary healthcare visits, hospital visits and hospitalizations. HRU was assessed from three years prior to index date (i.e. the date of GCA diagnosis for both GCA and their respective matched ref-

Table 1. Incidence rate ratio (95% confidence interval) of different study outcomes (healthcare visits and admission to hospitals) for GCA patients vs. reference subjects.

	Mean no. of visits/hospitalizations during 5-year after index date (95% CI)		Incidence rate ratio (95% CI)
	GCA	References	GCA/References
Any healthcare visit	64.0 (60.6, 67.5)	47.0 (46.1, 47.9)	1.36 (1.29, 1.44)
Primary care physician visit	12.6 (11.9, 13.3)	10.5 (10.3, 10.7)	1.20 (1.13, 1.27)
Primary care non-physician visit	21.0 (18.9, 23.2)	14.9 (14.4, 15.4)	1.41 (1.28, 1.56)
Specialist care physician visit	17.9 (16.9, 18.8)	12.2 (11.8, 12.5)	1.47 (1.39, 1.56)
Specialist care non-physician visit	8.5 (7.5, 9.6)	5.8 (5.5, 6.1)	1.47 (1.29, 1.67)
Hospital admission	2.4 (2.1, 2.6)	1.9 (1.8, 2.0)	1.23 (1.11, 1.36)
Hospital inpatient days	17.1 (15.1, 19.2)	12.2 (11.5, 12.8)	1.40 (1.23, 1.60)

All models were adjusted for sex, age, year of diagnosis, and outcome level over 3-year before index date.

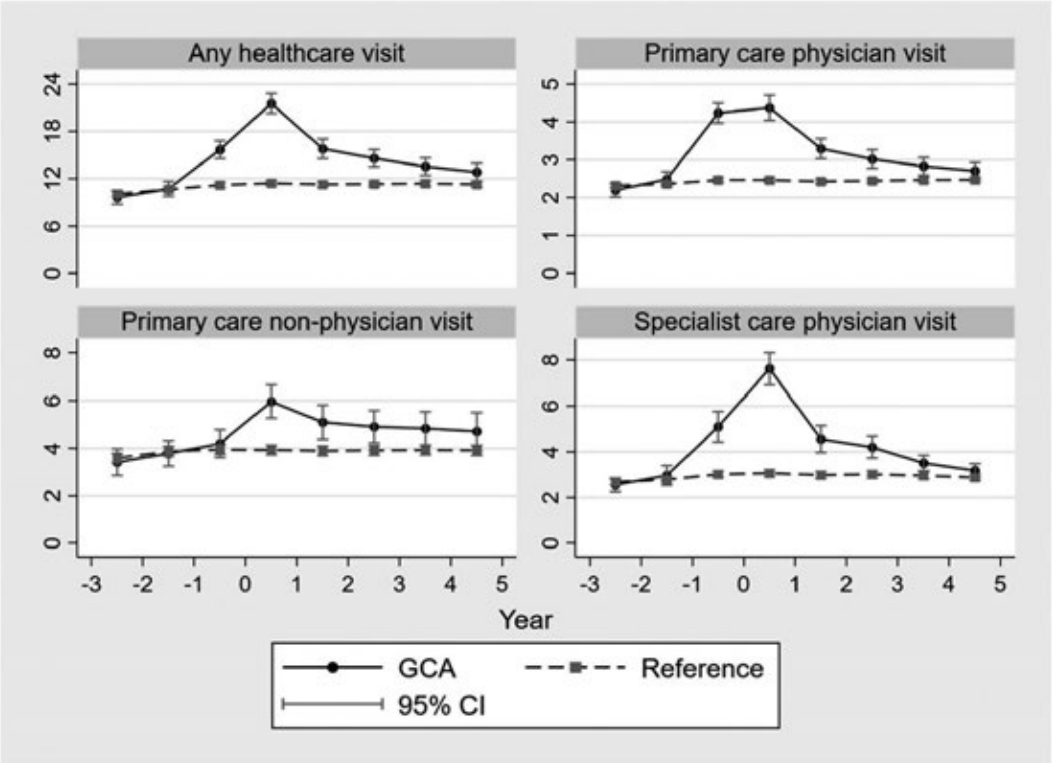

Figure 1. The mean numbers of visits to different level of healthcare providers three years before and five years after date of diagnosis of giant cell arteritis (GCA) or index date for reference subjects.

erence subjects) to five years after. The HRU (i.e. the number of healthcare visits) during 5 years after the index date was analysed using zero-inflated negative binomial regressions assuming the same propensity to use healthcare for both GCA and references and adjusted for sex, age, year of diagnosis, and HRU over 3-year before index date.

Results: The matched cohort included a total of 7,282 subjects (GCA patients, n = 662; references,

n =6,620) with mean (SD) age 75.3 (8.3) years, and 73.4% women. Over 5 years after index date, HRU was higher in patients with GCA compared to reference subjects with incidence rate ratios of 1.36 (95% CI 1.29-1.44) for all visits, 1.21 (1.14-1.28) for primary healthcare physician visits and 1.47 (1.39-1.56) for specialist care physician visits (Table 1). Hospital admissions were more frequent among GCA patients with rate ratios of 1.23 (1.11-1.36) for admissions and 1.41 (1.24-1.60) for inpatient days. Notably, the HRU started to diverge from the year before the index date up to four years after (Figure 1). When stratifying consultations or hospitalization by diagnoses, consultations rates were higher in GCA patients than in reference subjects for the following diagnoses: infections, cardiovascular diseases, respiratory diseases, musculoskeletal, nervous disorders and ear and eye diseases. However, endocrine diagnoses were lower prior to the onset of GCA compared to the period preceding the index date in reference subjects.

Conclusion: In this population-based study, patients with GCA had higher rates of HRU compared to the reference population. The increase in HRU was evident one year before diagnosis and continued over four years after. The systemic inflammatory burden and the adverse effects of treatment may account for the increase in the HRU after GCA diagnosis.

Disclosure: A. Mohammad, None; **A. Turkiewicz**, None; **P. Stamatis**, None; **C. Turesson**, None; **M. Englund**, None; **A. Kiadaliri**, None.

Abstract Number: 2678

Response to Tocilizumab in Patients with Giant Cell Arteritis, According to Ischemic vs Systemic Symptoms

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

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Background/Purpose: In Giant Cell Arteritis (GCA) two dominant cytokine clusters have been linked to disease activity, IL-6 – IL-17 axis (Th17) and IL-12 – IFN γ axis (Th1). The first one related to systemic symptoms and the second

TABLE

	Basal	Month 1 n=132	Month 3 n=122	Month 6 n=99	Month 12 n=71
SYSTEMIC MANIFESTATIONS					
Fever, n (%)	9 (6.7)	0	1 (0.8)	1 (1.0)	1 (1.4)
Constitutional syndrome, n (%)	31 (23.1)	12 (9.1)	6 (4.9)	2 (2.0)	2 (2.8)
PMR, n (%)	73 (54.5)	18 (13.6)	14 (11.5)	4 (4.0)	0
ISCHEMIC MANIFESTATIONS					
Visual involvement, n (%)	28 (20.9)	14 (10.6)	9 (7.4)	5 (5.1)	4 (5.6)
Headache, n (%)	70 (52.2)	14 (10.6)	7 (5.7)	6 (6.1)	2 (2.8)
Jaw claudication, n (%)	14 (10.4)	0	0	1 (1.0)	1 (1.4)
ACUTE PHASE REACTANTS					
ESR, mm/1st hour, mean (SD)	33 [14.5-61] ** (129)	6 [2-12] ** (102)	4 [2-7.5] ** (116)	4 [2-8] ** (93)	4 [2-8] ** (71)
CRP, mg/dL mean (SD)	1.7 [0.4-3.2] ** (131)	0.1 [0-0.5] ** (98)	0.1 [0-0.4] ** (110)	0.1 [0.-0.2] ** (92)	0.1 [0-0.2] ** (67)

**p<0.001

route responsible for ischemic symptoms. Tocilizumab (TCZ) performs its effect mainly by inhibiting Th17 axis and terminally Th1 route.

Our aim was to evaluate the effect of TCZ on ischemic and systemic symptoms throughout the follow-up.

Methods: Retrospective, multicenter study of 134 patients diagnosed of GCA on treatment with TCZ. We evaluate the efficacy of TCZ by improving ischemic (visual involvement, headache, jaw claudication) and systemic symptoms (fever, constitutional syndrome, polymyalgia rheumatica (PMR)).

Results: We evaluated 134 patients (101 w/33 m) and its main symptoms at TCZ onset, **TABLE**. 73 (54.5%) patients presented PMR followed by headache in 70 (52.2%) cases, constitutional syndrome in 31 (23.1%) and visual involvement in 28 (20.9%) patients. After one month of treatment there was an important clinical improvement, persisting in 13,6% of patients PMR, 10.6% headache and 10.6% visual involvement. Throughout the follow-up, the improvement of ischemic symptoms was slower. At month 12, in 5.6% (4) of patients persisted with visual impairment, and 2.8% (2) patients presented headache and constitutional syndrome. However, the analytical improvement was statistically significant from the first month and sustained during follow-up.

Conclusion: According to the results of our study, we can conclude that in clinical practice, ischemic symptoms take longer to improve than systemic symptoms; being visual affectation the most frequent symptom after 12 months of follow-up.

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Tocilizumab in Giant Cell Arteritis: Route of Administration: Intravenous or Subcutaneous

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SESSION INFORMATION

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Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

TABLE 1

	TCZ IV (n=104)	TCZ SC (n=30)	p
BASAL FEATURES AT TCZ ONSET			
GENERAL FEATURES			
Age, years, mean± SD	73.4 ± 8.2	71.9 ± 10.6	0.501
Sex, female/male n (%)	77/27	24/6	0.504
Time from GCA diagnosis to TCZ onset (months), median [IQR]	14.5 [5-35]	11.5 [5-25.5]	0.447
AORTITIS AND ANOTHER LVV involvement, n (%)	49 (47.1)	9 (30)	0.096
ACUTE PHASE REACTANTS			
ESR, mm/1st hour, mean (SD)	41.8 ± 31.2	35.9 ± 31.7	0.301
CRP, mg/dL mean (SD)	3.3 ± 5.8	2.1 ± 3.1	0.191
Hemoglobin, g/dL, mean (SD)	12.1 ± 1.4	12.7 ± 1.6	0.145
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose, mg/d mean (SD)	16.9 ± 13.2	13.6 ± 11.2	0.457

TABLE 2

	TCZ IV (n=104)	TCZ SC (n=30)	p
EFFICACY AND SAFETY AFTER TCZ			
Prolonged remission n (%)			
Month 6	45 (56.3)	13 (65)	0.712
Month 12	35 (61.4)	11 (91.7)	**0.043**
Month 24	21 (63.6)	6 (85.7)	0.257
Relapses n (%)			
Month 1	2 (2.0)	2 (6.9)	0.184
Month 3	3 (3.1)	4 (15.4)	**0.017**
Month 6	5 (6.3)	0	0.251
Month 12	9 (15.8)	0	0.140
Month 24	7 (21.2)	0	0.180
Corticosteroids sparing effects, median [IQR]			
Month 1	16.9 [7.5-23.8]	13.6 [7.5-15]	0.257
Month 3	10.6 [5-12.5]	9.2 [5-10.6]	0.359
Month 6	6.9 [2.5-7.6]	3.8 [1-5]	**0.032**
Month 12	3.7 [0-5]	1.7 [0-4.4]	0.085
Month 24	2.4 [0-5]	0 [0-0]	**0.021**
Side effects, n (%)			
Relevant adverse events	29 (27.9)	3 (10)	**0.043**
Serious infections	14 (13.5)	2 (6.6)	0.544

Background/Purpose: Recently, based on the GiACTA trial results, weekly subcutaneous Tocilizumab (TCZ) has been approved for the treatment of Giant Cell Arteritis (GCA). It has showed to be effective and safety.

Our aim was to compare the efficacy of TCZ according the route of administration.

Methods: Multicenter study of 134 GCA patients in treatment with TCZ. It was performed a comparative study between 2 groups according the route of administration of TCZ, intravenous (IV) or subcutaneous (SC).

Results: We study 134 patients divided in 2 groups: a) IV TCZ, 104 cases and, b) SC TCZ, 30 cases, with a mean age 73.4±8.2 years vs 71.9±10.6 years, respectively (p=0.501). Disease duration, clinical manifestations and acute phase reactants at TCZ onset were similar in both groups with non-statistical difference. 91.7% patients who received SC TCZ achieved prolonged remission after 12 months of treatment (p=0.043). And the glucocorticoid sparing effect of TCZ was greater in the same group, reaching a statistical difference at 3 and 24 months (p=0.017 and p=0.021). Patients under IV TCZ treatment suffered more adverse event during follow up (p=0.043). **TABLE 1** and **2** summarizes the comparative study.

Conclusion: Patients in treatment with SC TCZ, reached prolonged remission after 12 months of treatment and were able to discontinue prednisone dose after 24 months of follow up. The incidence of adverse events was more frequent in the IV TCZ group, without difference in relation to infections.

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Optimization of Tocilizumab Therapy in Giant Cell Arteritis: A Multicenter Real Life Study of 134 Patients

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

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Background/Purpose: Tocilizumab (TCZ) is the only biological agent approved in Giant Cell Arteritis (GCA). There is general agreement on the initial and the standard maintenance dose of TCZ. However, information on duration and optimization of TCZ in GCA is scarce.

TABLE 1

	OPTIMIZED-TCZ GROUP (n=43)	NON-OPTIMIZED TCZ GROUP (n=91)	p
BASAL FEATURES AT TCZ ONSET			
GENERAL FEATURES			
Age, years, mean± SD	68.9 ± 8.7	71.4 ± 8.5	0.125
Sex, female/male n (%)	32/10	68/24	0.779
Time from GCA diagnosis to TCZ onset (months), median [IQR]	19.5 [7.75-45]	10.5 [4 – 25]	0.047
SYSTEMIC MANIFESTATIONS			
Fever, n (%)	1 (2.4%)	8 (8.7%)	0.176
Constitutional syndrome, n (%)	11 (26.2%)	19 (20.7%)	0.476
PMR, n (%)	18 (42.9%)	56 (60.9%)	0.052
ISCHEMIC MANIFESTATIONS			
Visual involvement, n (%)	5 (11.9%)	23 (25%)	0.084
Headache, n (%)	26 (61.9%)	42 (45.7%)	0.081
Jaw claudication, n (%)	1 (2.4%)	11 (12%)	0.072
ACUTE PHASE REACTANTS			
ESR, mm/1st hour, mean (SD)	40 ± 32.9	41.2 ± 31.1	0.874
CRP, mg/Dl mean (SD)	2.4 ± 3.9	3.8 ± 7	0.220
Hemoglobin, g/Dl, mean (SD)	12.3 ± 1.3	12.3 ± 1.5	0.838
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose, mg/d mean (SD)	15.1 ± 11.1	25 ± 17.4	0.001
ROUTE OF TCZ ADMINISTRATION			
IV / SC, n (%)	30 (71.4) / 12 (28.6)	76 (82.6) / 16 (17.4)	0.140
THERAPY			
Monotherapy/Combined treatment, n (%)	23 (54.8) / 19 (45.2)	62 (67.4) / 30 (32.6)	0.159

TABLE 2

Pre-optimized dose	Optimized doses	Optimized patients (n)
162 mg/SC/week	162 mg/SC/10 days	7
	162 mg/SC/2 week	9
8 mg/kg/4 week IV	4 mg/kg/4 week	11
	4 mg/kg/8 week	1
	6 mg/kg/4 week	6
	6 mg/kg/5 week	1
	6 mg/kg/6 week	2
	7 mg/kg/4 week	2
	8 mg/kg/4 week	2
	8 mg/kg/6 week	1

Our aim was to assess efficacy and safety of TCZ therapy optimization in an unselected wide series of GCA in clinical practice.

Methods: Multicenter study on 134 patients with GCA who received TCZ therapy due to inefficacy or adverse events of previous therapy. Once complete remission was reached and based on a shared decision between the patient and the physician TCZ was optimized in some cases. Complete remission was defined as normalization of clinical an analytical (CRP and ESR) findings. Optimization was done by decreasing the dose and/or prolonging the TCZ dosing interval progressively. We performed a comparison between optimized and non-optimized patients.

Results: We evaluated 134 GCA patients treated with TCZ (101 women/33 men); mean age 73.0±8.8 years. TCZ was administered IV to 106 (79.1%) patients and SC to 28 (20.9%). The initial dose was 8 mg/kg/IV/4 weeks or 162 mg/SC/week, respectively. TCZ was optimized in 42 (31.3%) patients. No demographic, clinical manifestations or laboratory data differences had been found at TCZ onset between both groups **(TABLE1).** After a median [25-75th] follow up of 12 [6-15.5] months, and in a complete remission for 6 [3-12] months; the first TCZ optimization was performed in the optimized group. The median prednisone dose at first TCZ optimization was 2.5 [0-5] mg/day. TCZ IV was optimized from 8 to 4 mg/kg/4 weeks in 11 of 106 (10.4%) and from 162 mg/SC/week to 162 mg/SC/2 weeks in 9 of 28 (32.1%) cases. In **TABLE 2** data of the optimized doses. Five (11.9%) of the 42 optimized cases relapsed. In 4 of these cases, the relapses were treated increasing TCZ up to the pre-optimization dose, and in 1 case the route of administration of TCZ was change (4 mg/kg/4week to 162 mg/SC/week). In 8 of 42 optimized patients (19%), it was possible to withdraw TCZ after complete remission for 30 [16.25-45.75] months. Regarding adverse events, severe infections were less frequent in the optimized group (14.3% vs 11%) with non-statistical significance.

Conclusion: Once remission is reached in GCA patients under TCZ treatment, optimization of TCZ may be performed. Based on our experience it could be performed by reducing the dose with IV TCZ or by prolonging dosing interval with SC TCZ. It seems to be effective and safe.

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Abstract Number: 2681

Tocilizumab in Giant Cell Arteritis: The Safest and Most Effective Initial Dose of Prednisone

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Tocilizumab (TCZ) has been approved for the treatment of Giant Cell Arteritis (GCA). It showed to be effective to induce remission, prevent relapses and decrease the cumulative prednisone dose. However, the glucocorticoids are the mainstay in the acute treatment of GCA.

Our aim was to compare the efficacy and safety of the initial dose of prednisone at the onset of TCZ treatment.

Methods: Retrospective, multicenter study on 134 patients with GCA in treatment with TCZ. We compared two subgroups of patients according to the initial dose of prednisone at TCZ onset. Clinical efficacy, analytical improvement and safety was studied.

Results: We studied 134 patients (101 w/33 m) and made a comparative study between 2 groups: a) TCZ and ≤ 15 mg of prednisone; 68 (50.7%) cases, and b) TCZ and > 15 mg of prednisone, 66 (49,3%) patients. It is summarized

TABLE 1

	PREDNISONE ≤ 15 mg (n=68)	PREDNISONE > 15 mg (n=66)	p
ACUTE PHASE REACTANTS			
ESR, mm/1st hour, mean (SD)	38.6 ± 30.5	34.5 ± 32.2	0.500
CRP, mg/dL mean (SD)	3.3 ± 6.8	2.6 ± 3.2	0.603
Hemoglobin, g/dL, mean (SD)	11.5 ± 0.64	13.2 ± 1.5	0.104
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose, mg/d mean (SD)	9.8 ± 3.7	34.8 ± 14.3	**<0.001**
EFFICACY AND SAFETY AFTER TCZ			
Prolonged remission n (%)			
Month 6	37 (69.8)	21 (44.7)	**0.018**
Month 12	27 (73)	19 (59.4)	0.232
Month 24	19 (82.6)	8 (47.1)	0.018
Relapses n (%)			
Month 1	3 (4.5)	1 (1.6)	0.620
Month3	3 (4.9)	4 (6.6)	1.000
Month 6	2 (3.8)	3 (6.4)	0.664
Month 12	3 (8.1)	6 (18.8)	0.285
Month 24	2 (8.7)	5 (29.4)	0.113
SIDE EFFECTS, n (%)			
Relevant adverse events	8 (11.8)	24 (36.4)	**0.001**
Serious infections	3 (4.4)	13 (19.7)	**0.006**

TABLE 2

	PREDNISONE ≤ 15 mg (n=68)	PREDNISONE > 15 mg (n=66)
SERIOUS INFECTIONS, n (%)		
Cytomegalovirus (bilateral pneumonia)	-	1 (1.5)
Endocarditis	-	1 (1.5)
Facial Herpes Zoster Infection	-	2 (3.0)
Bacterial Infective Bursitis	-	1 (1.5)
Severe Infectious Cellulitis	-	1 (1.5)
Infectious Meningitis	-	1 (1.5)
Infected ulcer	-	1 (1.5)
Infected Necrotizing ulcer	-	1 (1.5)
Pneumonia	2 (2.9)	1 (1.5)
Recurrent urinary infection and sepsis		2 (3.0)
Urinary sepsis	1 (1.5)	1 (1.5)
Anal abscess		1 (1.5)

in TABLE 1. It was no statistical significance according to age, sex and evolution time of disease. In the group receiving > 15 mg of prednisone, the patients presented more visual involvement ($p< 0.001$) at TCZ onset. In terms of prolonged remission and relapses no significant difference was seen between both groups. The risk of presenting adverse effects (11.8% vs 36.4%) and severe infections (4.4% vs 19.7%) was related with the prednisone dose, being more frequent in the group with > 15 mg of prednisone ($p=0.001$ and $p=0.006$, respectively). In TABLE 2 summarizes the infections of our patients.

Conclusion: According with our results, we can conclude that TCZ is equally effective; in terms of prolonged remission and relapses, with doses ≤ 15 mg of prednisone at treatment onset. Being the most important data, the higher risk to develop adverse effects, as well as infections with higher doses of prednisone.

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Efficacy of Tocilizumab in Giant Cell Arteritis, Independent of the Time of Disease Evolution

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SESSION INFORMATION

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TABLE 1

	GCA ≤ 6 MESES (n=44)	GCA > 6 MESES (n=90)	p
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose, mg/d mean (SD)	31.3 ± 16.5	17.7 ± 14.2	**<0.001**
EFFICACY AND SAFETY AFTER TCZ			
Prolonged remission n (%)			
Month 6	16 (57.1)	42 (58.3)	0.272
Month 12	11 (64.7)	35 (67.3)	0.843
Month 24	6 (66.7)	21 (67.7)	0.952
Relapses n (%)			
Month 1	2 (4.9)	2 (2.3)	0.593
Month 3	4 (10.8)	3 (3.5)	0.197
Month 6	1 (3.6)	4 (5.6)	1.000
Month 12	2 (11.8)	7 (13.5)	0.857
Month 24	1 (11.1)	6 (19.4)	0.567
CORTICOSTEROIDS SPARING EFFECTS, median [IQR]			
Month 1	18.8 [10-30]	10 [5-15]	**<0.001**
Month 3	12.5 [7.5-20]	7.5 [5-10]	**<0.001**
Month 6	5 [4.4-10.6]	5 [2.5-7.5]	0.202
Month 12	5 [0-5]	2.5 [0-5]	0.335
Month 24	0 [0-4.4]	0 [0-5]	0.724
SIDE EFFECTS, n (%)			
Relevant adverse events	14 (31.8)	18 (24)	0.132
Serious infections	6 (13.6)	10 (11.1)	0.672

Table 1. Time evolution

Background/Purpose: Tocilizumab (TCZ) has proved to be effective in the management of Giant Cell Arteritis (GCA). Based on results of the GiACTA trial, it has been approved by the FDA and the European Commission for GCA treatment. Nevertheless, almost half of the GiACTA trial patients presented a short time evolution disease.

Our aim was to evaluate the efficacy of TCZ according the time of disease evolution.

Methods: Retrospective, multicenter study of 134 patients with GCA in treatment with TCZ. A comparative study between two groups according to the time from disease diagnosis and TCZ onset was performed.

Results: Our study included 134 GCA patients. TABLE 1 summarizes a comparative study between: a) ≤ 6 months of disease evolution, and b) > 6 months of disease evolution. Non-significant difference in baseline characteristics was found. In terms of visual involvement, we observed more patients affected in the first group (≤ 6 months) (p=0.30). Analyzing clinical improvement non-significant difference was seen during follow-up. At TCZ onset, in the group of ≤ 6 months of evolution, the prednisone dose was higher with a mean dose of 31.3±16.5 mg/d vs 17.7±14.2 mg/d (p< 0.001), however, a similar reduction of corticosteroids was achieved in both groups after 6 months of follow-up. The incidence of adverse events and severe infections was similar in both groups (p=0.132 and p=672 respectively).

Conclusion: In this retrospective analysis, our results support the previously reported efficacy and safety profile of TCZ. We can conclude that TCZ can be used in GCA independently the time of disease evolution.

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Visual and Quantitative Assessment of Cranial Arteries on FDG-PET/CT Can Reliably Diagnose Cranial Giant Cell Arteritis

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Background/Purpose: Assessing cranial artery inflammation plays an important role in the diagnosis of cranial giant cell arteritis (GCA). Although an established tool for assessing large vessel vasculitis, fluorine-18-deoxyglucose (FDG) positron emission tomography (PET)/CT imaging is not recommended for detecting cranial artery inflammation. Assessing FDG uptake in the cranial arteries may increase the diagnostic value of FDG-PET/CT for GCA and may provide more detailed information regarding involved arteries and extent of the disease. It may thus provide a viable alternative for Duplex ultrasonography (US) and temporal artery biopsy (TAB) as a first line investigation in GCA.

This study aimed to evaluate the diagnostic accuracy of FDG-PET/CT for the detection of cranial artery inflammation in GCA.

Methods: This retrospective case control study included glucocorticoid-naive TAB positive GCA patients who underwent FDG-PET/CT as part of the diagnostic work-up. Controls were age- and sex-matched melanoma patients in remission with FDG-PET/CT after 6 months follow-up.

To attain high quality PET images on the Siemens Biograph 64 PET/CT, optimal PET image acquisition and reconstruction parameters were determined and applied to all images. Visual assessment by an experienced nuclear medicine physician was based on uptake intensity compared to surrounding tissue on a 0-2 scale (Figure 1). Additionally, FDG uptake in the cranial arteries was quantified by measuring the maximum standardized uptake value (SUVmax) in the target arteries. The temporal arteries (TA), maxillary arteries (MA), vertebral arteries (VA), and occipital arteries (OA) were assessed bilaterally.

Student t and chi-squared tests were used for evaluation of the visual assessment. Receiver operating characteristics (ROC) analysis was performed for evaluation of the quantitative assessment. Cohen's kappa was used to assess agreement of the visual and quantitative assessments.

Results: A total of 24 GCA patients and 24 controls were included. The mean age for both groups was 71 years (SD: 8) and 12/24 were women. Large vessel involvement was seen on PET in 15/24 patients. Duplex US of the temporal artery was performed in 15/24 patients, of which 9 were positive. Median ESR and CRP were 73 ($CI_{95\%}$: 53; 104) mm/h and 73 ($CI_{95\%}$: 37; 110) mg/L, respectively.

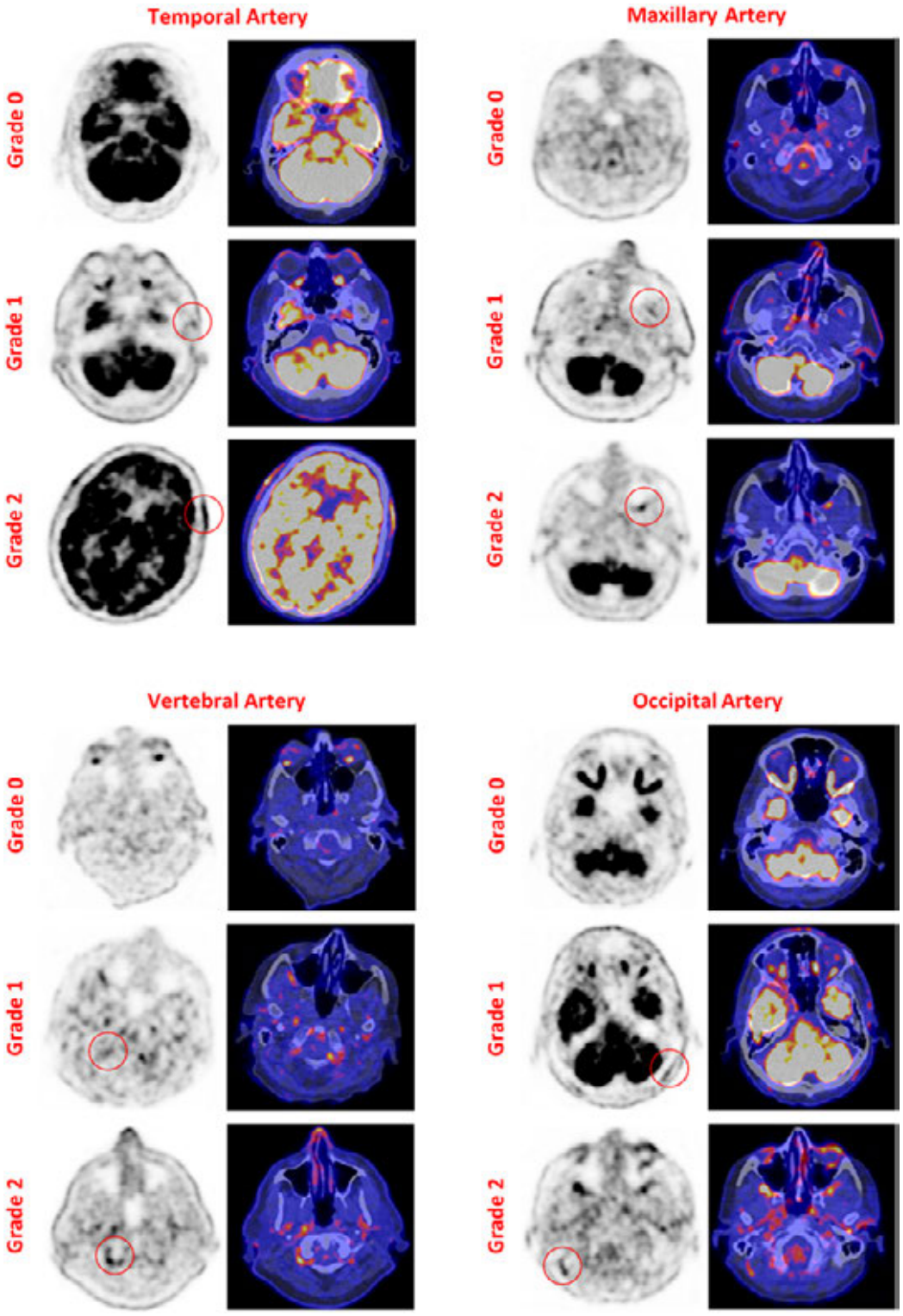

Figure 1. Visual assessment of cranial artery inflammation on FDG-PET/CT. Temporal Artery (TA), Maxillary Artery (MA), Vertebral Artery (VA), and Occipital Artery (OA) were visually scored from 0-2. Scoring definition: 0: no uptake above surrounding tissue; 1: uptake just above surrounding tissue; 2: uptake significantly above surrounding tissue. The red circle denotes the visually determined area of increased uptake.

Visual assessment revealed a sensitivity of 83% ($CI_{95\%}$: 64; 93) and a specificity of 75% ($CI_{95\%}$: 55; 88) for GCA denoted by a score of ≥1 (uptake higher than background). Receiver-operating characteristic (ROC) analysis of the quantitative assessment revealed an AUC of 0.88 ($CI_{95\%}$=0.77-0.99) resulting in a sensitivity of 79% ($CI_{95\%}$: 60; 91) and

Type of Assessment	Cranial Artery	Assessment Conclusion	GCA	Control	Sensitivity ($CI_{95\%}$)	Specificity ($CI_{95\%}$)
Visual Assessment Positive: score=1 Negative: score=0	TA/MA/VA/OA	Positive	20	6	83% (64;93)	75% (55;88)
		Negative	4	18		
	TA	Positive	18	2	75% (55;88)	92% (74;99)
		Negative	6	22		
	MA	Positive	12	1	50% (31;69)	96% (80;100)
		Negative	12	21		
	VA	Positive	10	0	41% (24;61)	100% (86;100)
		Negative	14	24		
	OA	Positive	7	2	29% (15;49)	92% (74;99)
		Negative	17	22		
Quantitative Assessment Positive: SUVmax=5.00 Negative: SUVmax<5.00	TA/MA/VA/OA	Positive	19	2	79% (60;91)	92% (74;99)
		Negative	5	22		
	TA	Positive	19	2	46% (28;65)	100% (86;100)
		Negative	5	22		
	MA	Positive	11	0	29% (15;49)	100% (86;100)
		Negative	13	24		
	VA	Positive	17	1	71% (51;85)	96% (80;100)
		Negative	7	23		
	OA	Positive	3	1	13% (4;31)	96% (80;100)
		Negative	21	23		

Table 1. Cross tabulation of the results of the visual and the quantitative assessments of FDG uptake in the cranial arteries. Visual scoring definition: 0: no uptake above surrounding tissue; 1: uptake just above surrounding tissue; 2: uptake significantly above surrounding tissue. TA, temporal artery; MA, maxillary artery; VA, vertebral artery; OA, occipital artery; SUVmax, maximum standardized uptake value; CI95%, 95% confidence interval.

a specificity of 92% ($CI_{95\%}$: 74; 99) for a SUVmax threshold value of 5.00 (Table 1). The agreement between the two assessment methods was 77% (kappa 0.55).

Conclusion: Using optimal scan data reconstruction, visual and quantitative FDG-PET/CT assessment methods can reliably diagnose GCA based on cranial artery inflammation. Extending the use of FDG-PET/CT to the cranial arteries may improve the diagnostic accuracy for GCA. Moderate agreement between visual and quantitative assessment methods suggests that diagnostic accuracy may be improved when combining both methods.

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Real-world Comparative Study of Methotrexate vs Tocilizumab in Patients with Giant Cell Arteritis with Large Vessel Involvement

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Background/Purpose: Giant cell arteritis (GCA) is the most common large vasculitis in elderly patients. According to previous studies, 50% of patients with GCA in whom PET/CT was performed showed large vessel involvement (LV-GCA). In these patients there is a higher risk of vascular complications. Thus, an early and adequate therapy is needed. Glucorcorticoids (GC) remain to be the cornerstone of GCA. However, relapses are common when the prednisone dose is tapered. Thus, additional therapies are required. In this regard, methotrexate (MTX) is commonly used. However, its efficacy is modest and, in some patients, biological therapy is required. Tocilizumab (TCZ) has demonstrated to be effective.

Our aim was to compare clinical evolution, normalization of acute phase reactants and normalization of vascular ^{18}F-FDG uptake assessed by PET/CT in patients with GCA treated with MTX vs TCZ in clinical practice.

Methods: Comparative multicentric study of 23 patients with GCA treated with MTX compared with 36 patients with refractory GCA to MTX treated with TCZ who had a baseline and follow-up PET/CT scan. We assessed clinical improvement (no improvement/partial/complete), normalization of acute phase reactants (CRP ≤ 0.5mg/dL and/or ESR ≤ 20 mm/1st hour) and reduction of ^{18}F-FDG uptake in PET/CT (no reduction/partial/complete normalization). Images were evaluated qualitatively by experienced nuclear medicine physicians. Prednisone tapering was also assessed.

TABLE 1

	MTX (n=23)	**TCZ (n=36)**	**P**
Demographic data			
Age, *mean ± SD*	65.6 ± 7.9	67.9 ± 14.4	0.50
Sex (women), *n (%)*	20 (87.0)	27 (77.1)	0.50
Evolution time before treatment (months), *median [IQR]*	6.7 ± 2.4	12.2 ± 4.6	< 0.01
Clinical manifestations, n (%)			
Polymyalgia rheumatica	13 (56.5)	25 (69.4)	0.31
Constitutional syndrome	5 (21.7)	10 (27.8)	0.60
Fever	1 (4.3)	3 (8.3)	0.99
Headache	6 (26.1)	11 (30.6)	0.71
Jaw claudication	1 (4.3)	2 (5.6)	0.99
Laboratory markers			
ESR (mm/1st hour), *mean ± SD*	50.8 ± 25.8	43.4 ± 31.4	0.34
CRP (mg/dL), *mean ± SD*	2.5 ± 2.1	7.4 ± 2.3	0.06
Hb (g/dL), *mean ± SD*	11.7 ± 1.1	12.1 ± 1.2	0.21
Extension of FDG vascular uptake in PET/CT, n (%)			
1 affected area	6 (26.2)	7 (19.4)	0.55
2 affected areas	7 (30.4)	12 (33.4)	0.82
3 affected areas	7 (30.4)	10 (27.8)	0.83
>4 affected areas	3 (13.0)	7 (19.4)	0.52
Previous treatment			
Prednisone dose (mg/day), *mean ± SD*	14.5 ± 8.5	21.3 ± 7.5	0.19

TABLE 2

	MTX (n=23)	TCZ (n=36)	P
Complete clinical improvement, *n/N (%)*			
- 6 months	9/23 (39.1)	28/35 (80.0)	0.002
- 12 months	8/18 (44.4)	24/27 (88.9)	0.003
- 18 months	7/11 (63.6)	21/22 (95.4)	0.03
- 24 months	7/9 (77.8)	17/18 (94.4)	0.25
Normalization of ESR and/or CRP, *n/N (%)*			
- 6 months	6/23 (26.1)	30/35 (85.7)	< 0.01
- 12 months	10/21 (47.6)	25/27 (92.6)	< 0.01
- 18 months	10/11 (90.9)	23/23 (100.0)	0.32
- 24 months	9/9 (100.0)	19/19 (100.0)	0.99
Normalization of ^{18}F-FDG PET/CT, *n/N (%)*			
- 6 months	0/11 (0.0)	0/8 (0.0)	0.99
- 12 months	0/14 (0.0)	3/13 (23.0)	0.10
- 18 months	0/5 (0.0)	3/11 (27.3)	0.51
- 24 months	1/7 (14.3)	1/4 (25.0)	0.99
Dose of Prednisone (mg/day), *median [IQR]*			
- 6 months	7.5 [5.0-15.0]	5.0 [0.3-5.0]	< 0.01
- 12 months	5.0 [5.0-10.0]	0.0 [0.0-5.0]	< 0.01
- 18 months	5.0 [3.0-6.0]	0.0 [0.0-3.3]	0.03
- 24 months	2.5 [0.0-3.0]	0.0 [0.0-0.0]	0.07

Statistical analysis was performed with SPSS. Student´s t test or Mann-Whitney U test was used to compare continuous variables, and Chi-squared test or Fisher´s exact test for categorical variables as appropriate.

Results: We included 23 patients with GCA treated with MTX (20 women/3 men); mean age 65.6 ± 7.9 years; and 36 patients treated with TCZ (27 women/9 men); mean age 67.5 ± 8.3 years. Baseline characteristics were similar in both groups (**TABLE 1**). All patients with MTX received doses ranging between 20 and 25 mg/week as subcutaneous injections. Most of patients with TCZ received treatment as intravenous infusions (80.6%) and almost half of them (52.7%) received combined therapy with MTX. Clinical, analytical, ^{18}F-FDG vascular uptake evolution and prednisone tapering is shown in the **TABLE 2**. After one year of treatment, the percentage of patients who experienced complete clinical improvement (88.9% vs 44.4%; p=0.003) and normalization of acute phase reactants (92.6% vs 47.6%; p=0.001) was higher in patients who received TCZ. No differences were found between patients who received TCZ monotherapy and those who received combined therapy. In regard with reduction of ^{18}F-FDG vascular uptake, complete normalization was only achieved in 25% of patients who received TCZ and 14.3% of those who received MTX at 24 months. A higher cumulative incidence of infections was found in patients who received TCZ (7.4 vs 4.3 infections/100 patients/year).

Conclusion: Patients with GCA who received TCZ experienced a more rapid and effective clinical and analytical improvement than patients who received MTX. Besides, prednisone tapering was quicker in patients with TCZ. However, complete normalization of vascular ^{18}F-FDG uptake was only observed in around 20% of patients in both groups.

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Banzo, None; **M. González-Gay**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Celgene, 5, 8, Eli Lilly, 2, 5, EliLilly, 2, 5, Jansen, 2, Janssen, 2, MSD, 2, 5, 8, Novartis, 2, 5, Pfizer, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, Sobi, 5, 8; **R. Blanco**, None.

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Factors Contributing to Capturing Positive Findings on Temporal Artery Biopsy: An Australian Experience from Two Rheumatology Referral Centers

Victor Yang,[1] Benjamin Sutu,[2] Christopher McMaster,[3] Claire Owen,[1] Alexander Strathmore,[4] Gene-Siew Ngian,[2] Shereen Oon,[4] Jessica Leung,[1] Ian Wicks,[5] Russell Buchanan,[1] and **David Liew** [1], [1]Austin Health, Heidelberg, Victoria, Australia, [2]Melbourne Health, Parkville, Victoria, Australia, [3]Austin Health, Melbourne, Victoria, Australia, [4]Melbourne Health, Melbourne, Victoria, Australia, [5]Melbourne Health, Parkville, Australia

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Temporal artery biopsy (TAB) is widely recognised as the diagnostic gold standard for GCA, despite having a poor sensitivity due to the presence of 'skip' lesions. There is however a lack of consensus guiding TAB practice, particularly in relation to optimal length, need for bilateral specimens and number of segments examined. This study investigated the impact of factors such as total biopsied length, laterality, segment number, and referral center on histopathological outcomes in an Australian setting.

Methods: Reports for all available biopsy specimens labelled "temporal artery" were extracted from the pathology service records of two rheumatology referral centers with adjacent geographic catchments. Each histopathology report was manually reviewed to establish length of biopsied artery, laterality and number of segments, along with

	Negative (n=455)	Positive (n=122)	Overall (n=577)
Age (years)			
Mean (SD)	72 (± 11)	75 (± 8.9)	73 (± 10)
Sex			
Female	310 (68 %)	88 (72 %)	398 (69 %)
Male	145 (32 %)	34 (28 %)	179 (31 %)
Maximum Biopsy Length (cm)			
Mean (SD)	1.8 (± 0.86)	2.0 (± 1.1)	1.9 (± 0.92)
Total Biopsy Length (cm)			
Mean (SD)	2.4 (± 1.6)	2.8 (± 2.1)	2.5 (± 1.7)
Mean Biopsy Length (cm)			
Mean (SD)	1.7 (± 0.78)	1.9 (± 0.97)	1.7 (± 0.83)
Laterality			
Bilateral	130 (29 %)	39 (32 %)	169 (29 %)
Unilateral	325 (71 %)	83 (68 %)	408 (71 %)

Table 1. Patient characteristics by biopsy result.

	Overall positive finding	Intimal hyperplasia	Giant cells	Adventitial inflammation
Total Biopsy Length (cm)	1.25 (1.06 – 1.47)	1.18 (0.98 – 1.40)	1.21 (1.00 – 1.46)	1.07 (0.87 – 1.31)
Unilateral (vs bilateral)	1.56 (0.82 – 3.07)	1.12 (0.56 – 2.30)	1.28 (0.61 – 2.77)	0.82 (0.38 – 1.82)
Age (years)	1.02 (1.00 – 1.05)	1.02 (1.00 – 1.04)	1.03 (1.00 – 1.05)	1.00 (0.98 – 1.03)
Male (vs female)	0.83 (0.52 – 1.29)	0.63 (0.37 – 1.05)	0.59 (0.32 – 0.92)	0.75 (0.41 – 1.31)
Center 2 (vs center 1)	0.54 (0.34 – 0.84)	0.41 (0.24 – 0.68)	0.55 (0.32 – 0.92)	0.46 (0.25 – 0.82)

Table 2. Associations with positive TAB on multivariable logistic regression.

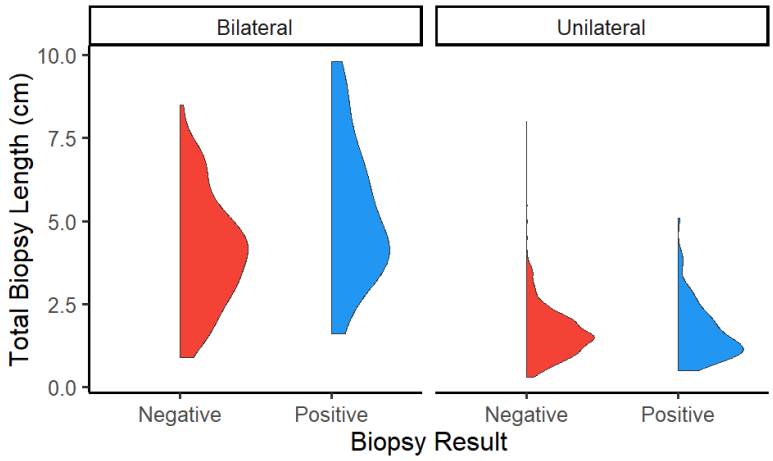

Figure 1. The effect of total biopsy length on result, stratified by laterality.

patient demographics such as age, sex, and referral center. Key histopathological findings including intimal hyperplasia, disruption of the internal elastic lamina, presence of giant cells and adventitial inflammation were recorded. Multivariable logistic regression with site-varying intercept was performed.

Results: TAB reports from a total of 577 patients were captured, with results available from the two centers from 1999-2019 and 2010-2019 respectively. The mean age in this group was 73, and 69% were female (Table 1). A bilateral TAB was performed in 29%, and the mean total biopsy length was 2.5cm. Of these patients, 122 had positive biopsies (21%), with intimal hyperplasia reported in 100 (17%), giant cells in 83 (14%) and adventitial findings in 68 (12%). Positive biopsy weakly correlated with increased total length of biopsy in centimetres (OR 1.25 [1.06-1.47]) (Figure 1) and increased age in years (OR 1.02 [1.00-1.05]) but not laterality or sex (Table 2). There was a substantial difference between the two centers, which was incompletely accounted for once corrected for total biopsy length and calendar year of biopsy, suggesting either unmeasured differences in patient demographics or a difference in clinical practice. This change was preserved across analysis of different histopathological subtypes.

Conclusion: Total biopsy length was weakly associated with a positive TAB result, but differences in results between referral centers independent of biopsy length suggest other selection factors may be important in determining TAB yield. Examination of differences in results between a greater number of referral centers would assist in determining the extent of this variability.

Disclosure: V. Yang, None; **B. Sutu**, None; **C. McMaster**, None; **C. Owen**, None; **A. Strathmore**, None; **G. Ngian**, None; **S. Oon**, None; **J. Leung**, None; **I. Wicks**, None; **R. Buchanan**, None; **D. Liew**, None.

Abstract Number: 2686

Real Life Data over 4 Years from a Fast Track GCA Pathway in Coventry

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: University Hospital Coventry and Warwickshire NHS Trust (UHCW) established its one stop Fast Track Pathway (FTP) for Giant Cell Arteritis (GCA) in 2013. It sought to address previously unmet needs by offering patients a same day clinical review, ultrasound Doppler, diagnosis, and treatment initiation for patients with GCA. It aims to prevent GCA related complications like vision loss by treating affected patients promptly whilst avoiding exposing unaffected patients to corticosteroids. Patients are normally reviewed on the same day and have an USS doppler performed in the vascular lab if indicated and then a decision is made about treatment. This abstract details the results of this pathway for the period of 2014 to 2017.

Methods: The clinical records of all patients with suspected GCA seen on the UHCW GCA Fast Track Pathway between, and including, January 2014 and December 2017 were reviewed. Patients were identified from ultrasonography lists as all patients attending the fast track pathway are required to undergo an ultrasound Doppler of their temporal arteries. A predetermined piloted proforma was used to collect data regarding patient demographics, clinical features, investigation results, steroid use, and final diagnosis. All patients who had been referred with suspected GCA were included and missing data was sought from electronic and paper records.

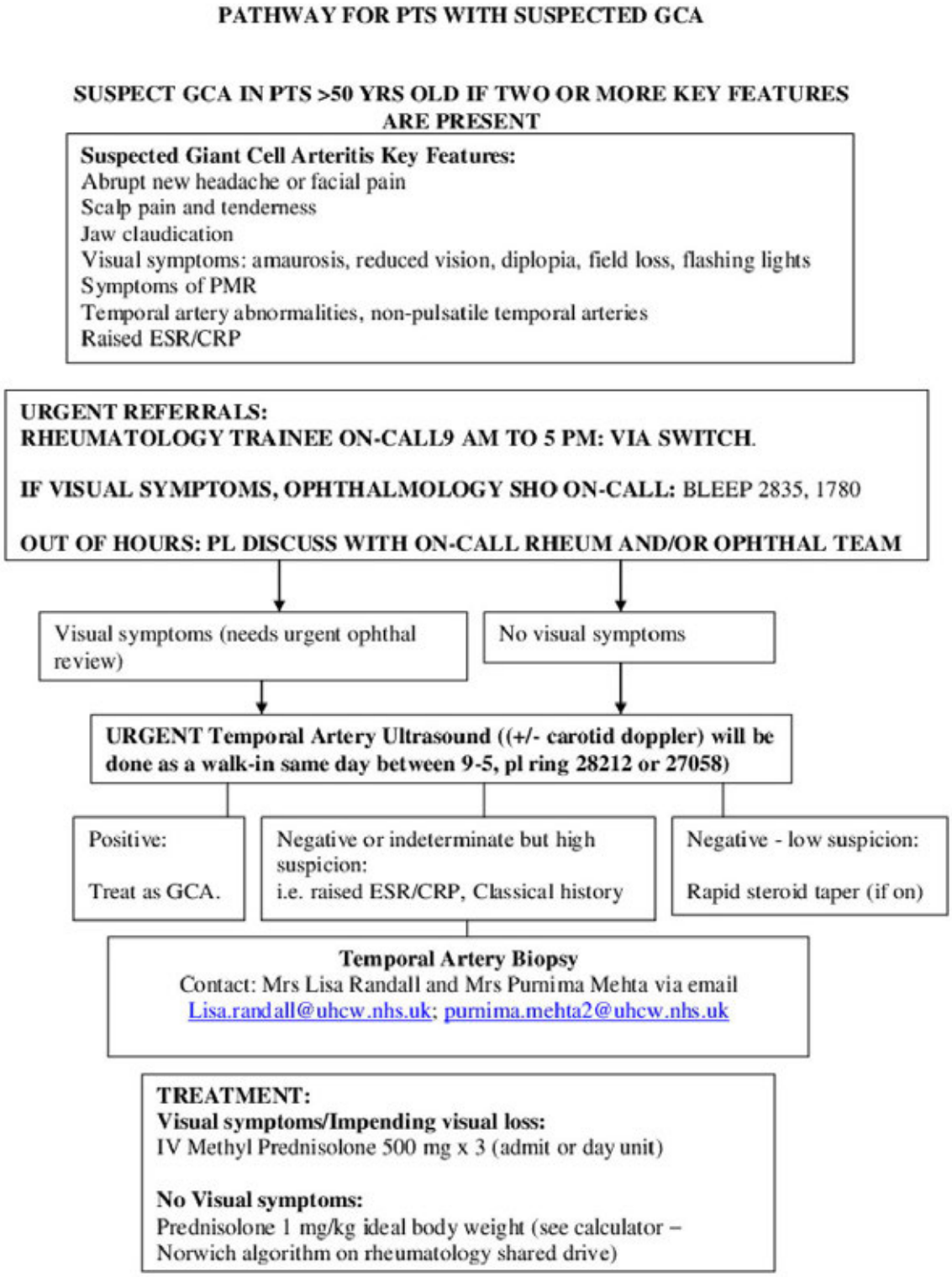
Descriptive analysis was performed on the data using Microsoft Excel. Ethical approval was granted by the UHCW Research and Development Department.

Results: Total of 652 patients were assessed on the GCA pathway between 1st January 2014 and 31st December 2017 (both inclusive). The numbers have progressively increased each year (98/154/123/277). Demographic details revealed that 435 patients were female (~66%). Ages ranged between 52 and 95 years; median age was 70 years. Of these, 143 patients were diagnosed with GCA; 509 patients did not have GCA. Headache was the commonest presenting symptom (~74%), with visual symptoms also being common (~45%).

We evaluated the utilty of our vascular doppler service compared to clinical diagnosis (see table below).

We also evaluated the utility of temporal artery biopsies which are only being performed within our pathway when the diagnosis is uncertain after the initial evaluation. This showed Sensitivity 36.73%; Specificity 100.00%; Positive predictive value 100.00%; Negative predictive value 62.20%.

A very high proportion of patients (~57%) did not need to start steroids at all on the basis of this pathway.



Coventry GCA pathway algorithm

Conclusion:

1. This is the largest series of suspected GCA patients in the world looking at real life performance of vascular doppler and temporal artery biopsy.

2. The UHCW GCA FTP was effective in reducing the proportion of unaffected patients who were exposed to corticosteroids and reduced the duration of exposure for those that did receive them, thereby minimising the risk of harm with unnecessary treatment.

3. Performance of Vascular doppler was at least comparable to previous studies and is an integral part of this pathway allowing clinicians to reassure patients with low clinical probability of GCA and negative USS to be discharged without any steroid exposure.

Disclosure: S. Dubey, None; **J. Pinnell**, None; **C. Tiivas**, None; **K. Chaudhuri**, None; **P. Mehta**, None.

Abstract Number: 2687

Clinicopathologic Associations in a Large International Cohort of Patients with Giant Cell Arteritis

Michael Putman,[1] K Bates Gribbons,[2] Anthea Craven,[3] Cristina Ponte,[4] Joanna Robson,[5] Ravi Suppiah,[6] Richard Watts,[7] Raashid Luqmani,[3] Peter Merkel,[8] Amy Archer,[9] and Peter C. Grayson[10], [1]Northwestern University, Chicago, [2]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [3]University of Oxford, Oxford, United Kingdom, [4]Department of Rheumatology, Hospital de Santa Maria, Lisbon, Portugal, [5]Faculty of Health and Applied Sciences, University of the West of England, Bristol, United Kingdom, [6]Department of Rheumatology, Auckland District Health Board, Auckland, New Zealand, [7]Norwich Medical School, University of East Anglia, Norwich, United Kingdom, [8]University of Pennsylvania, Pennsylvania, [9]Northwestern, Chicago, [10]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) of the National Institutes of Health, Bethesda, MD, Bethesda, MD

Table 1: Common Pathologic Findings of Temporal Artery Biopsies and their Associations with Demographic Characteristics and Clinical Manifestations at Presentation in Giant Cell Arteritis

Predictors		Giant cells		Fragmentation of internal elastic lamina		Intimal thickening		Mononuclear leukocytes	
		OR	CI	OR	CI	OR	CI	OR	CI
Age	<68	*Referent*		*Referent*		*Referent*		*Referent*	
	68-74	2.12	1.31-3.42*	0.85	0.51-1.42	1.02	0.60-1.74	0.86	0.51-1.43
	75-79	1.83	1.08-3.08*	1.56	0.92-2.66	1.48	0.85-2.59	1.26	0.73-2.17
	>79	2.35	1.45-3.79*	2.38	1.47-3.86*	1.96	1.19-3.24*	1.03	0.63-1.70
Sex	Male	*Referent*		*Referent*		*Referent*		*Referent*	
	Female	1.21	0.84-1.73	1.22	0.84-1.77	1.01	0.68-1.48	0.88	0.60-1.29
Headache	No	*Referent*		*Referent*		*Referent*		*Referent*	
	Yes	0.98	0.61-1.56	1.16	0.71-1.90	1.00	0.60-1.65	0.76	0.47-1.24
Jaw Claudication	No	*Referent*		*Referent*		*Referent*		*Referent*	
	Yes	1.26	0.89-1.80	1.13	0.78-1.62	1.17	0.82-1.71	1.14	0.78-1.66
Scalp Tenderness	No	*Referent*		*Referent*		*Referent*		*Referent*	
	Yes	0.80	0.55-1.17	1.10	0.75-1.61	1.23	0.83-1.83	0.94	0.63-1.40
Abnormal Temporal Artery on Physical Exam	No	*Referent*		*Referent*		*Referent*		*Referent*	
	Yes	1.06	0.75-1.52	1.32	0.92-1.89	1.38	0.95-2.02	2.01	1.38-2.94*
Abnormal Serum C-Reactive Protein Level	No	*Referent*		*Referent*		*Referent*		*Referent*	
	Yes	1.11	0.58-2.13	0.57	0.29-1.10	1.21	0.59-2.46	1.32	0.65-2.69
Number of Days from Symptom Onset to Vasculitis Diagnosis	<30 Days	*Referent*		*Referent*		*Referent*		*Referent*	
	30-90 Days	1.23	0.80-1.89	1.20	0.77-1.87	1.00	`0.63-1.57	1.16	0.73-1.82
	>90 Days	1.15	0.73-1.80	0.79	0.50-1.26	0.93	0.58-1.50	0.97	0.60-1.55
Vision Loss	Yes	*Referent*		*Referent*		*Referent*		*Referent*	
	No	0.90	0.59-1.35	1.23	0.74-1.72	1.17	0.76-1.80	0.98	0.63-1.51

Data from four logistic regressions with pathologic findings as dependent variables and demographic characteristics, clinical variables, and outcomes included as covariates

* $p < 0.05$

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: In addition to aiding in diagnosis, histopathologic findings from temporal artery biopsy (TAB) specimens in giant cell arteritis (GCA) may be valuable for their associations with clinical features of the disease. The study objective was to compare specific histopathologic findings on TAB with biopsy interpretation, demographic, clinical, and imaging features at diagnosis.

Methods: Patients who had a diagnosis of GCA confirmed by expert review were selected from an international, multicenter observational cohort. Associations between demographic, clinical, radiographic, and histopathologic features were identified using bivariate testing and multivariate regression modeling.

Results: Six hundred forty-seven patients with GCA who underwent TAB were included. Pathology interpretations included definite vasculitis (69%), normal temporal artery biopsy (13%), consistent with vasculitis but not definite (9%), or non-diagnostic (8%). For 467 biopsies, specific findings were detailed, including the presence of giant cells (63%), fragmentation of the internal elastic lamina (50%), intimal thickening (39%), predominantly mononuclear leukocytes (39%), vascular thrombosis (6%), granuloma (5%), and perivascular inflammation without vessel wall involvement (1%). In a model that included the common TAB findings (>10% prevalence), a pathology interpretation of definite vasculitis was independently associated with giant cells (OR 123.4, CI 47.1-323.5), predominantly mononuclear leukocytes (OR 11.8, CI 6.0-23.0), and fragmentation of the internal elastic lamina (OR 4.5, CI 2.4-8.3). Out of 207 patients who had a temporal artery ultrasound, 166 patients had a halo sign, which was significantly associated with the presence of giant cells (88% vs. 76% without, p=0.04) and intimal thickening (90% vs. 78% without, p = 0.04). Out of 70 patients who underwent PET scanning, no pathologic findings on TAB were associated with PET abnormalities. Temporal artery abnormalities on exam were associated mononuclear leukocytes (OR 2.01, CI 1.38-2.94). Older age was associated with the presence of giant cells, fragmentation of the internal elastic lamina, and intimal thickening (see Table 1). No pathologic findings were associated with vision loss at presentation.

Conclusion: Pathologic findings of temporal artery biopsies in GCA are associated with diagnostic interpretations but not with clinical manifestations of vasculitis. Associations between pathologic findings and imaging abnormalities should be investigated further.

Disclosure: M. Putman, None; **K. Gribbons**, None; **A. Craven**, None; **C. Ponte**, None; **J. Robson**, None; **R. Suppiah**, None; **R. Watts**, None; **R. Luqmani**, Roche, 8, Roche, Vifor, InflaRx, 2; **P. Merkel**, None; **A. Archer**, None; **P. Grayson**, None.

Abstract Number: 2688

Comparisons of Strategies for Diagnostic Assessment in Giant Cell Arteritis: Results from an International Observational Cohort

K Bates Gribbons,[1] Cristina Ponte,[2] Anthea Craven,[3] Joanna Robson,[4] Ravi Suppiah,[5] Raashid Luqmani,[3] Richard Watts,[6] Peter Merkel,[7] and Peter C. Grayson[8], [1]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [2]Department of Rheumatology, Hospital de Santa Maria, Lisbon, Portugal, [3]University of Oxford, Oxford, United Kingdom, [4]Faculty of Health and Applied Sciences, University of the West of England, Bristol, United Kingdom, [5]Department of Rheumatology, Auckland District Health Board, Auckland, New Zealand, [6]Norwich Medical School, University of East Anglia, Norwich, United Kingdom, [7]University of Pennsylvania, Philadelphia, PA, [8]National Institute of Arthritis and Musculoskeletal and Skin Diseases [NIAMS] of the National Institutes of Health, Bethesda, MD, Bethesda, MD

Table 1. Demographic and clinical associations of patients with giant cell arteritis receiving a temporal artery biopsy

	Odds ratios (95% CI)	P-value
Age (per year)	1.02 (1.00-1.04)	0.04
Sex - male	1.34 (1.16-1.51)	0.002
Large-vessel involvement by imaging	0.47 (0.29-0.64)	<0.001
Temporal artery abnormality on exam	1.28 (1.11-1.46)	0.004
Sudden ongoing visual loss	1.49 (0.67-1.22)	0.01
Jaw claudication	1.11 (1.18-1.81)	0.27

CI: Confidence interval

Table 2. Diagnostic assessment in association with temporal artery biopsy results in giant cell arteritis

	TA-US	LV-Imaging	TA-US and LV-imaging	No other assessment
Positive TAB (n = 446)	36 (8.1)	103 (23.1)	116 (26.0)	191 (42.8)
Negative TAB (n = 258)	24 (9.3)	70 (27.1)	51 (19.8)	113 (43.8)
No TAB (n = 237)	10 (4.2)	103 (43.5)	91 (38.4)	33 (13.9)

SESSION INFORMATION
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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Diagnostic assessment in giant cell arteritis (GCA) is rapidly changing as large-vessel (LV) involvement becomes increasingly recognized and non-invasive vascular imaging techniques become more available. The purpose of this study was to assess how clinicians around the world use diagnostic assessment strategies to assess arterial involvement in GCA.

Methods: Patients were included from a large, international cohort with standardized data collection from 2011-2017. Study centers were located in Asia, Australia/New Zealand, Europe, and North America. All patients had a confirmed diagnosis of GCA. Diagnostic assessments were performed at the discretion of the submitting physician. LV-imaging included angiography, ultrasonography, or PET imaging of the extra-cranial arteries. Temporal artery assessment included temporal artery biopsy (TAB) or ultrasonography (TA-US). Nominal logistic regression was used to study the associations between the decision to obtain a TAB and demographic data, ischemic cranial symptoms, and large-vessel involvement (aorta and its primary branches).

Results: 941 patients with GCA from 72 centers were included in the analysis, 783 (83%) patients were Europe, 111 (12%) patients from North America, and 47 (5%) patients from other regions. Overall, 704 patients (75%) had a TAB, 446 TABs (66%) were considered diagnostic for GCA. 328 (35%) patients had a TA-US, 258 (79%) patients had a halo sign and most came from European centers (n=321, 98%). 534 patients (57%) had LV-imaging, 40% (n=216) showed LV involvement. 431 patients (45%) had both LV-imaging and temporal artery-assessment. Only 33 patients (4%) did not have any diagnostic testing performed beyond clinical assessment. Male patients were significantly more likely to undergo a TAB than female patients, independent of cranial ischemic symptoms, age at diagnosis, temporal-artery abnormality on physician exam, or presence of LV involvement (Table 1). There was no sex preference in the rate

of TA-US (Male: 37% vs Female: 34%, p=0.38) or LV-imaging (Male: 58% vs Female: 56%, p=0.70). Patients who received a TAB were older (mean age 73 years vs 71 years, p< 0.01) and patients who received LV-imaging were younger (mean age 72 years vs 74 years, p< 0.01). Most patients had multiple forms of diagnostic assessment (Table 2). Regardless of TAB results, approximately 60% of patients had vascular imaging studies performed in addition to biopsy. Vascular imaging was performed in 86% of patients who did not have a TAB and confirmed disease in 70% of these patients. TA-US was rarely used alone as a form of assessment. 69% (n=227) of patients with a TA-US also underwent TAB. Only 1% of patients had TA-US without another form of assessment compared to the 11% and 32% of patients that had only LV-imaging and TAB.

Conclusion: Vascular imaging is increasingly incorporated into the diagnostic assessment of GCA. The majority of patients with GCA underwent multiple forms of diagnostic testing, including TAB and vascular imaging studies. Demographic factors, clinical features, and regional differences in clinical practice influence diagnostic assessment strategies in GCA.

Disclosure: K. Gribbons, None; **C. Ponte**, None; **A. Craven**, None; **J. Robson**, None; **R. Suppiah**, None; **R. Luqmani**, Roche, 8, Roche, Vifor, InflaRx, 2; **R. Watts**, None; **P. Merkel**, AbbVie, 5, AstraZeneca, 2, 5, Biogen, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Genentech/Roche, 2, 5, Genetech/Roche, 2, 5, Genzyme/Sanofi, 5, GlaxoSmithKline, 2, 5, InflaRx, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Kypha, 2, TerumoBCT, 2, UpToDate, 7; **P. Grayson**, None.

Abstract Number: 2689

GM-CSF Pathway Signature Identified in Temporal Artery Biopsies of Patients with Giant Cell Arteritis

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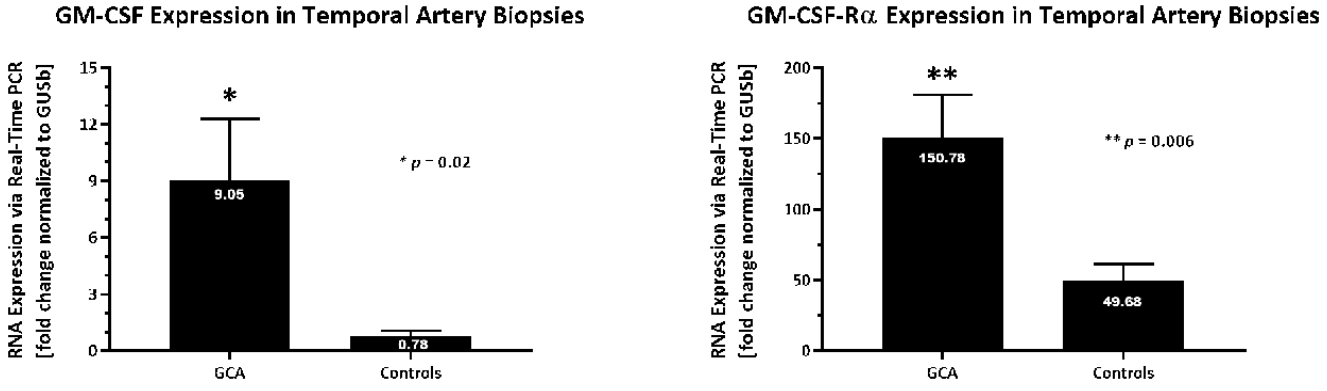
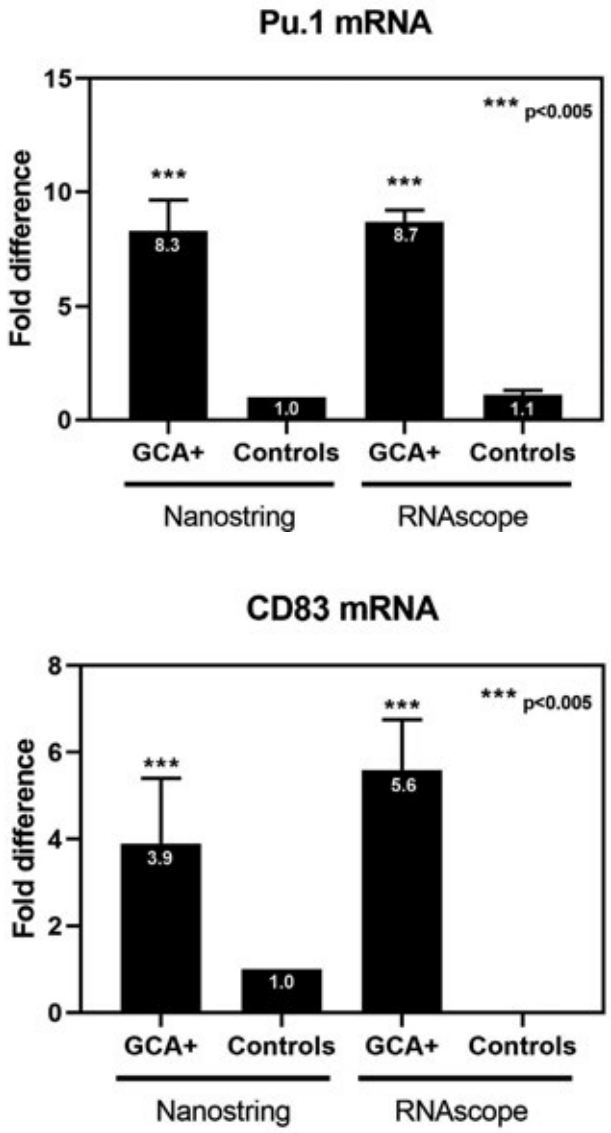


GM-CSF and GM-CSFRalpha Expression in Temporal Artery Biopsies



Background/Purpose: Giant Cell Arteritis (GCA) is a type of large vessel vasculitis that can cause blindness and aortic aneurysms. A significant unmet medical need remains in GCA, as current treatment options are limited and relapse increases corticosteroid (CS) exposure and toxicity.

The primary role of macrophages/dendritic cells (DCs) and T_H1/T_H17 lymphocytes in GCA pathogenesis has been highlighted previously. Granulocyte-macrophage colony stimulating factor (GM-CSF) may contribute to GCA pathogenesis by stimulating giant cell formation. GM-CSF produced by $CD4^+$ T helper T_H1 and T_H17 cells can stimulate conventional DCs and promote differentiation of monocyte-derived DCs. Notably GM-CSF RNA has been reported in GCA lesions and in peripheral blood mononuclear cells of symptomatic patients.

We hypothesized elevation of the GM-CSF pathway signature in GCA vessels versus controls.

Methods: Two independent sources of temporal artery biopsies were utilized. First, GCA (n=17) and control (symptomatic patients suspected for GCA, but with a normal temporary artery biopsy; n=5) biopsies were analyzed for 15 mRNA transcripts representing T_H1, T_H17, and GM-CSF signaling (RNAscope; RS) and for mRNA transcripts

representing the autoimmune panel (Nanostring; NS). Semi-quantitative scoring was performed on RS images and fold-change of representative T_H1, T_H17 and GM-CSF related mRNA transcripts were calculated via NS nCounter analysis. Additional GCA and control biopsies were obtained and analyzed by qPCR for a subset of transcripts (n=10 each) and by confocal microscopy for GM-CSF and GM-CSF-Rα protein (n=2 each). *Ex vivo* cultures of GCA+ arteries were treated with placebo or mavrilimumab for 5 days and assayed for gene expression by qPCR.

Results: Upregulation of the GM-CSF signaling pathway molecular signature was confirmed by 4 independent analyses.

GM-CSF-associated and T_H1-associated genes were upregulated in GCA biopsies versus control (GMCSF: 3-4x RS; GM-CSF-Rα: 6.7x NS, 6x RS; and CD83: 3.9x NS, 6x RS; TNFα: 2x NS, 3x RS; IFNγ: 2x RS; IL-1β: 6x RS). T_H17 associated genes were not elevated, potentially due to concomitant CS treatment.

Upregulation of both GM-CSF (12x) and GM-CSF-Rα (3x) mRNA was confirmed in a separate cohort of biopsies from GCA pts vs. controls by qPCR (Figure). GM-CSF protein was detected in the luminal endothelium, neovessels and inflammatory cells of GCA patients. In normal temporal arteries GM-CSF protein was not detected.

Pu.1, a transcription factor downstream of GM-CSF signaling, was increased 8x in GCA vs. controls (RS, NS) (Figure)

Treatment of ex vivo cultures of GCA arteries with Mavrilimumab (anti-GM-CSF-Rα) reduced expression patterns of known pathogenic cell-types and cytokines (CD3ε, CD83, HLA-DRA Pu.1, and TNFα).

Conclusion: GM-CSF and T_H1 pathway signatures were demonstrated in GCA patient temporal arteries by independent analytical techniques. Active GM-CSF signaling in diseased tissue is evidenced by increased expression of Pu.1 in the vessel wall. Treatment with mavrilimumab reduced inflammatory cell markers and pathogenic cytokines. These data implicate the GM-CSF pathway in GCA pathophysiology and increase confidence in rationale for targeting GM-CSF in GCA.

Disclosure: M. Cid, Roche, 9; **R. Gandhi**, Kiniksa Pharmaceuticals Corp., 3; **M. Corbera-Bellalta**, None; **N. Terrades-Garcia**, None; **S. Muralidharan**, Kiniksa Pharmaceuticals Corp., 3; **J. Paolini**, Kiniksa Pharmaceuticals, 3.

Abstract Number: 2690

Fast Track Clinic (FTC) for Giant Cell Arteritis (GCA) – the United States Experience

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

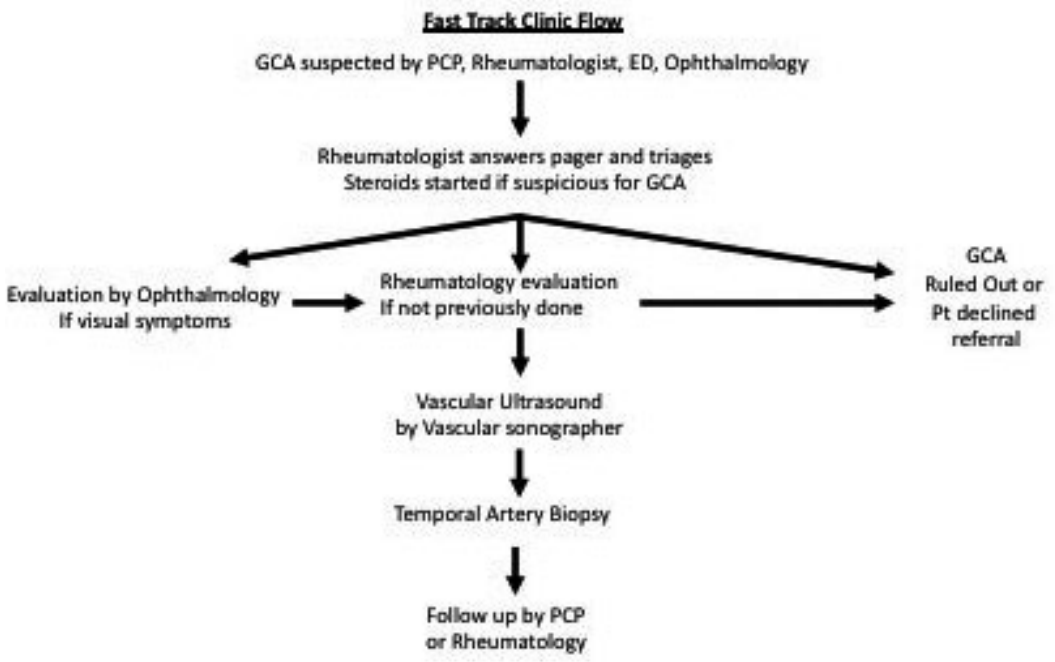

Figure 1. Fast Track Clinic Flow Chart

Background/Purpose: Giant cell arteritis (GCA) is the most common form of vasculitis in adults and if untreated, may result in visual impairment. Although the gold standard for diagnosis is the temporal artery biopsy (TAB), it does not detect extracranial large vessel vasculitis. New guidelines recommend early imaging, including ultrasound. Fast Track clinics (FTC) in Europe have reduced the time to rheumatology evaluation, with ultrasound replacing TAB for diagnosis in selected cases. Four rheumatologists and two vascular sonographers were trained to detect GCA by ultrasound and an FTC was established for early diagnosis and treatment of GCA. This retrospective study reports patients suspected of having GCA who went through the FTC vs those who received standard care (SC).

Methods: We obtained IRB approval and performed a retrospective review of patients seen through the FTC versus SC from November 2017 through May 2019. FTC inclusion criteria were patients over the age of 50 suspected of GCA who had both ultrasound and TAB. SC included patients over 50 years old suspected of GCA who received TAB. A FTC rheumatologist answered calls to a dedicated pager at a major academic center. Steroids were started immediately if diagnosis of GCA was likely; patients were seen by a rheumatologist within 48 hours and at the rheumatology clinic visit, patients were referred to vascular ultrasound and for TAB (Figure 1). Vascular ultrasound was performed by trained sonographers on a Philips Epiq 7 and interpreted by a vascular surgeon (Figure 2).

Results: There were 31 patients who fulfilled FTC criteria (Table 1). There were 7 positive biopsies and 13 positive ultrasounds. In FTC patients, the median time from referral to rheumatology evaluation was 1 day, time to ultrasound was 1 day and time to TAB was 7 days. There were16 patients in the SC group and the median time to rheumatology evaluation was 3.5 days; initial presentation to TAB was 10 days. Ultrasounds were positive in 8 FTC patients who had negative biopsies, including 4 with halo sign of the temporal artery and 4 with extracranial large vessel vasculitis (LVV).

	FTC n=31	Standard care n=16	p-values[a]
Baseline demographics			
Age, years	72 (8.5)	75 (13)	
Female gender	22/31 (73%)	11/16 (69%)	
White race	28/31 (90%)	13/16 (81%)	
Clinical characteristics of GCA			
ESR, mm/h	52.5 (47)	48.0 (36)	
CRP, mg/L	34.4 (76)	35.5 (51)	
Met ACR criteria for GCA	20/28 (71%)	10 (63%)	
Clinical outcomes			
Time from FTC referral to ultrasound, days	1 (1)		
Time from initial presentation to TAB, days	7 (3)	10.0 (9)	0.41
Time from FTC referral to TAB, days	6 (5)		
Time from FTC activation (FTC) or Rheum referral (SC) to rheumatology evaluation[b]	1 (1) 19 patients	3.5 (3) 4 patients	
Positive TAB	7/31 (22%)	3/16 (19%)	1.0
Positive ultrasound	13/31 (42%)		
Clinically treated as GCA	17/27 (63%)	6/15 (40%)	0.8
Visual loss	1/24 (4%)	1/16 (6.3%)	1.0
Death	2/31 (6.5%)	1/16 (6.2%)	1.0
Ultrasound Data			
	Positive Ultrasound	Negative Ultrasound	
Positive Biopsy	5	2	
Negative Biopsy	8	16	

Both FTC and standard care patients were evaluated in the rheumatology clinic during the period from 11/2017-5/2019.
Median (IQR) reported for continuous variables.
[a]Assessed using Fisher's exact test for categorical variables and the Mann-Whitney-U test for continuous variables.
[b]In patients who had not had rheumatology assessment when FTC was activated
Abbreviations: FTC, fast track clinic; GCA, giant cell arteritis; IQR, interquartile range; TAB, temporal artery biopsy

Table 1. Comparison of baseline characteristics and outcomes of FTC and patients receiving standard care (SC) for suspected GCA.

Conclusion: FTCs are new in the United States and may operate differently from European FTCs with some sonographers performing vascular ultrasound rather than rheumatologists. Although FTC and SC groups were not significantly different in time to TAB, vascular ultrasound detected 8 cases of vasculitis in patients with negative TAB. The high rate of positive ultrasounds is likely due to the short turnaround to ultrasound facilitated by FTC as well as detection of extracranial GCA. FTC may improve the rate of GCA and LVV diagnosis and should be considered at major academic centers.

	Right	Left
Halo sign	Yes/No	Yes/No
Common Temporal	Yes/No	Yes/No
Frontal Temporal Proximal	Yes/No	Yes/No
Frontal Temporal Distal	Yes/No	Yes/No
Parietal	Yes/No	Yes/No
Facial	Yes/No	Yes/No
Occipital	Yes/No	Yes/No
Intimal Media Thickness		
Common Carotid (cut-off 1.50 mm)	_ mm	_ mm
Internal Carotid (cut-off 1.50 mm)	_ mm	_ mm
Subclavian (cut-off 1.50 mm)	_ mm	_ mm
Axillary (cut-off 1.00 mm)	_ mm	_ mm

Figure 2. Vascular Ultrasound Protocol

Disclosure: I. Sacksen, None; **E. Jernberg**, None; **S. Pollock**, None; **J. Liew**, None; **S. Chung**, None; **R. Zierler**, None; **A. Bays**, None.

Abstract Number: 2691

Treatment Patterns, Disease Burden and Outcomes in Patients with Giant Cell Arteritis and Polymyalgia Rheumatica

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Table 1. Outcomes at 2 Years Post-Index Date

Total patients	GCA Only (n = 81)	PMR Only (n = 779)	GCA and PMR (n = 97)	Total (N = 957)	*P* Value
Achieved remission, n (%)	26 (32.1)	248 (31.8)	26 (26.8)	300 (31.3)	0.7921
Persistent remission, n (%)	14 (17.3)	176 (22.6)	17 (17.5)	207 (21.6)	0.5139
Time to remission, days*					
Mean (SD)	224.3 (171.7)	226.5 (198.6)	208.4 (186.6)	224.7 (194.9)	0.0361
Median (range)	213 (0-577)	203.5 (0-635)	157 (0-619)	202.5 (0-635)	

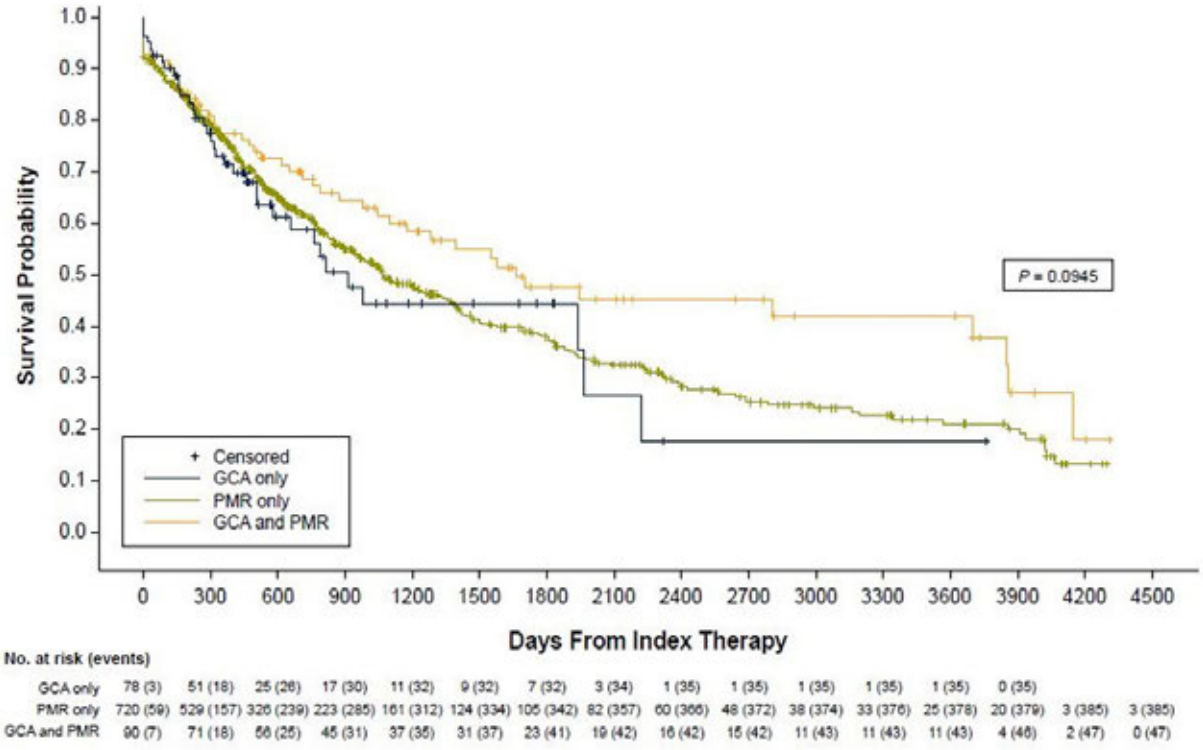
* Among patients who achieved remission.
GCA, giant cell arteritis; PMR, polymyalgia rheumatica.

Table 2. Prednisone Dose at 2 Years Post-Index Date

	GCA Only (n = 26)	PMR Only (n = 341)	GCA and PMR (n = 60)	Total (N = 427)	*P* Value
Prednisone dose, mg/day*					
Mean (SD)	9.5 (10.6)	8.8 (9.2)	12.6 (15.9)	9.4 (10.5)	0.0819
Median (range)	5 (0-40)	5 (0-66)	7.5 (0-80)	5 (0-80)	

* Among patients who had prednisone dose information available at 2 years.
GCA, giant cell arteritis; PMR, polymyalgia rheumatica.

Figure 1. Time to Remission Following Initiation of Glucocorticoids



GCA, giant cell arteritis; PMR, polymyalgia rheumatica.

Background/Purpose: For patients with giant cell arteritis (GCA) and/or polymyalgia rheumatica (PMR), glucocorticoids are the mainstay of treatment. However, due to the chronic nature of these diseases, patients may require continued glucocorticoid treatment to achieve treatment targets or prevent disease relapse, over time resulting in high cumulative doses and associated adverse events. The purpose of this study was to assess patterns of glucocorticoid use and outcomes in patients with GCA, PMR or both.

Methods: This retrospective cohort study used electronic medical records from a single US community-based rheumatology clinic utilizing the JointMan rheumatology software application. Patients age ≥ 50 years with a diagnosis of

either GCA or PMR and ≥ 1 entry for glucocorticoid following the diagnosis were included and followed until lost to follow-up or the end of the study period (30 Nov 2017). The index date was defined as the date of first glucocorticoid prescription received at or after the earliest GCA or PMR diagnosis date. Outcomes at 2 years included the proportion of patients achieving remission (defined as not receiving steroids for ≥ 6 months), time to remission, persistence of remission (defined as not receiving steroids for ≥ 6 months and still not receiving steroids at 2 years) and prednisone dose at follow-up, and were compared between patients with GCA only, PMR only or both GCA and PMR. *P* values are reported using F-test (ANOVA) for continuous variables and Chi-squared test for categorical variables.

Results: We identified 81 patients with GCA only, 779 with PMR only and 97 with GCA and PMR. Mean (SD) age was 70.0 (9.1) years; 64.2% were women. Mean (SD) daily prednisone dose at the index date was 46.7 (30.9) mg for patients with GCA only, 20.1 (14.2) for PMR only and 29.0 (23.4) for patients with both GCA and PMR. Two years after the index date, 32% of patients with GCA only, 32% with PMR only and 27% with GCA and PMR had achieved remission; 17%, 23% and 18% were in persistent remission, respectively (**Table 1**), with no significant differences between groups. Among patients who achieved remission, overall median time to first remission was 202.5 (0-635) days and was shorter for patients with both GCA and PMR (157 [0-619] days) vs GCA (213 [0-577] days) or PMR (203.5 [0-635] days) only. Kaplan-Meier estimates of time to remission for each group are shown (**Figure 1**)**.** Most patients required a daily prednisone dose at 2 years, with similar doses observed between groups (**Table 2**).

Conclusion: Patients with either GCA and/or PMR are exposed to significant doses of prednisone. In this study, fewer than one-third of patients with GCA and/or PMR achieved remission; the majority of patients continued to require prednisone therapy for at least 2 years after its initiation. These data highlight the need for the use of more efficacious and steroid-sparing therapies in patients with GCA and/or PMR.

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Disclosure: G. Craig, Arthritis NW, PLLC, 4, Discus Analytics, 4, Premera Blue Cross, 5, Bristol-Myers Squibb, 8, Eli Lilly and Company, 8, Genentech, Inc., 8, Celgene, 8, AbbVie, 8, Novartis, 8, Sandoz, 8; **K. Knapp**, Discus Analytics, LLC, 3; **B. Salim**, Axio Research, LLC, 3; **S. Mohan**, Genentech, Inc., 3; **M. Michalska**, Genentech, Inc., 3.

Abstract Number: 2692

Coronary Artery Disease in a Population-Based Cohort of Biopsy-Proven Giant Cell Arteritis in Southern Sweden

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster III: Giant Cell Arteritis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study was to estimate the incidence rate and prevalence of coronary artery diseases (CAD) in patients with temporal artery positive giant cell arteritis (TAB+GCA) from a defined population in southern Sweden, and to describe characteristics of CAD in this sample.

	Patients with GCA without CAD	Patients with GCA with CAD
Number (%)	1076 (89.5)	126 (10.5)
Female sex (%)	795 (73.9)	69 (54.8)
Mean age at diagnosis of GCA; years (SD)	75.2 (7.9)	75.2 (8.4)
Mean age at diagnosis of CAD; years (SD)	N/A	76.8 (9.2)
Percutaneous coronary intervention (%)	N/A	38 (30.2)
Coronary artery bypass grafting (%)	N/A	14 (11.1)
Dead during follow-up (%)	445 (41.3)	54 (42.9)
Mean age at death; years (SD)	85.2 (7.1)	84.6 (7.2)

GCA: giant cell arteritis, CAD: coronary artery disease, SD: standard deviation, N/A: not applicable

Table 1. Characteristics of patients with giant cell arteritis with and without coronary artery disease in a population-based cohort from southern Sweden.

Methods: The study cohort consisted of 1202 patients (71.9% women) diagnosed with TAB+GCA between 1997 and 2016. Patients were identified from the database of the Department of Pathology which covers all the hospitals in the Skåne region of Sweden. The cohort was linked to the registry for acute coronary care (SWEDEHEART) which provides nationwide coverage since 1995. All the GCA patients with symptoms suggesting acute coronary syndrome who had been admitted to a coronary care unit (CCU) were identified. CAD was defined as an admission to a CCU for ST-Elevation Myocardial Infarction (STEMI), Non-ST-Elevation Myocardial Infarction (NSTEMI), stable angina, or unstable angina. For incidence rate analyses, the person-years of follow-up was calculated from GCA diagnosis until first CAD, death or December 31, 2016, whichever came first.

Results: 126 of 1202 GCA patients had suffered at least one acute coronary event (Table 1) yielding the cumulative incidence of 10.5% (95% CI 8.7-12.3). Of the 126 patients with CAD, 44 (34.9%) were diagnosed with CAD before their GCA diagnosis, 11 (8.7%) both before and after their diagnosis, and 71 (56.3%) solely after their GCA diagnosis. The total number of CCU admissions of all the 126 GCA CAD+ patients was 209: 101 admissions (48.3%) for NSTEMI, 55 (26.3%) for stable angina, 29 (13.9%) for STEMI, and 24 (11.5%) for unstable angina. Eighty-two GCA patients (61% women) developed CAD after their diagnosis of GCA. During a total follow-up time of 8047 person-years, the incidence rate of CAD in patients with TAB+GCA was 1.0 per 100 person-years (95% CI 0.8-1.2) for all patients, 0.8 (95% CI 0.6-1.1) for women and 1.6 (95% CI 1.1-2.2) for men, p=0.02. Fifteen GCA patients suffered from a CAD event in 1156 person-years during the first year after the GCA diagnosis, resulting in an incidence rate of 1.3 per 100 person-years (95% CI 0.6-2.0). 703/1202 (58.5%) GCA patients were alive on December 31, 2016, of which 72 patients had at least one previous CAD event yielding a prevalence of CAD in GCA of 10.2%.

Conclusion: The incidence of CAD in GCA is comparable to what has been previously found in the Swedish background population. The incidence rate is higher among men compared to women. Coronary artery disease affects every tenth patient with TAB+GCA in this cohort. Further studies are needed to explore the impact of CAD on clinical outcomes in patients with GCA.

Disclosure: P. Stamatis, None; **M. Mohammad**, None; **P. Merkel**, AbbVie, 5, AstraZeneca, 2, 5, Biogen, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Genentech/Roche, 2, 5, Genetech/Roche, 2, 5, Genzyme/Sanofi, 5, GlaxoSmithKline, 2, 5, InflaRx, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Kypha, 2, TerumoBCT, 2, UpToDate, 7; **M. Englund**, None; **C. Turesson**, None; **D. Erlinge**, None; **A. Mohammad**, None.

Abstract Number: 2693

Increasing Use of Biologics over Time in the First Year After Diagnosis of Systemic JIA Among Patients Enrolled in the Childhood Arthritis & Rheumatology Research Alliance (CARRA) Registry

Ginger Janow,[1] Timothy Beukelman,[2] Yukiko Kimura,[3] Rayfel Schneider,[4] Shalini Mohan,[5] Gail Rodich,[6] and Mary Beth Son[7], [1]Joseph M. Sanzari Children's Hospital at Hackensack University Medical Center, NJ, [2]University of Alabama Birmingham, Birmingham, AL, [3]Joseph M Sanzari Children's Hospital, Hackensack University Medical Center, Cincinnati, OH, [4]Hospital for Sick Children, Toronto, ON, Canada, [5]Genentech, Inc., South San Francisco, CA, [6]Genentech, San Francisco, [7]Boston Children's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

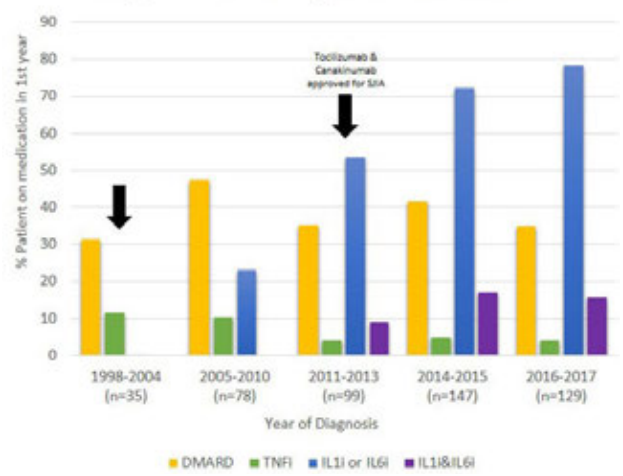
Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Prior to the development of anti-cytokine therapies, treatment for systemic juvenile idiopathic arthritis (SJIA) included high dose glucocorticoids and non-biologic disease modifying anti-rheumatic drugs (DMARDs) with suboptimal outcomes. Recent studies of SJIA patients treated with biologics, including IL-1 inhibitors (IL-1i) and IL-6 inhibitors (IL-6i), demonstrated excellent clinical responses, with steroid-sparing benefits and improved short-term outcomes. Our aim was to assess temporal trends in non-biologic DMARD and biologic medication use in the first year after diagnosis of SJIA using data from the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry.

Methods: Medication use during the first year after diagnosis of SJIA was assessed for all patients enrolled in the CARRA Registry through 2017. Medication information is collected retrospectively for all patients at the time of enrollment in the Registry and prospectively after enrollment. Patients with missing diagnosis date or month of medication start date were excluded. Patients were grouped by year of diagnosis based on medication availability at the time and numbers of patients available for assessment: (1)1998-2004: little biologic use; (2) 2005-2010: mostly anakinra use; (3) 2011-2013: post-FDA approval of tocilizumab and canakinumab; (4) 2014-2015; and (5) 2016-2017. Medi-

Figure 1: Trends in Medication Use During 1st Year of Diagnosis Over Time



cations were grouped by mechanism of action, and temporal trends in medication class usage were assessed using frequencies.

Results: A total of 488 patients were included in the analysis: 35 patients in the 1998-2004 cohort, 78 from 2005-2010, 99 from 2011-2013, 147 from 2014-2015, and 129 from 2016-2017 (Figure 1). Non-biologic DMARD use fluctuated between 31% and 47% over the study period. Use of IL-1i or IL-6i consistently increased over time to >75% by 2017. In recent years, approximately 15% of patients received both IL-1i and IL-6i, and TNF inhibitor (TNFi) use decreased to < 5% in the first year.

Conclusion: Our analysis shows a dramatic increase over time in use of IL-1i and IL-6i in the first year of treatment for SJIA patients, with over 75% of patients now receiving these treatments. Use of non-biologic DMARDs was stable over the study period, indicating a change in the standard of care. Use of both IL-1i and IL-6i by a significant minority of patients suggests variability of clinical response in individual patients.

Disclosure: G. Janow, None; **T. Beukelman**, CARRA, 6, UCB, 5; **Y. Kimura**, Novartis, 5, Sobi, 5; **R. Schneider**, Novimmune, 5, Sobi, 5, Novartis, 5; **S. Mohan**, Genentech, Inc., 3; **G. Rodich**, Genentech, 3; **M. Son**, None.

Abstract Number: 2694

Inpatient Treatment Variation in New-Onset Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The effectiveness of IL-1 and IL-6 inhibitors as first-line therapy in patients with new-onset systemic JIA has led to the concept of a "window of opportunity" in systemic JIA in which early initiation of biologic therapy improves outcomes. Despite this, provider surveys indicate there is significant variation in treatment with biologic therapy at diagnosis. We leveraged encounter data from the Pediatric Health Information System (PHIS) to describe treatment patterns in a large inpatient multi-site cohort of new-onset systemic JIA patients.

Methods: Using the PHIS de-identified data from inpatient encounters across 45 tertiary care children's hospitals across the United States, we identified the index admission for children age ≤ 18 years with a discharge ICD-10 code for systemic JIA (M08.2*) between October 1, 2015 and June 1, 2018. Index admission was defined as the first admission during the inclusion period with the diagnosis code of M08.2* excluding patients with a prior admission with this code or an ICD-9 code for systemic JIA (714.30) in ≥ 1 year prior. Patients were excluded if 1) there was no administration of a conventional or biologic disease-modifying drug, glucocorticoids (GCs), or Nonsteroidal Anti-inflammatory Drugs (NSAIDs), 2) biologic or GC exposure occurred on the day of admission or hospital day 2, or 3) the primary discharge diagnosis was infection. Mixed-effects logistic regression was used to determine patient and hospital level predictors of treatment with admission hospital included as a random effect to account for clustering. Variation in treatment over time was analyzed using an extension of the Wilcoxon rank-sum test for trends.

Admit age, median (IQR)	6.0 (3.0, 12.0)
Female sex, n (%)	71 (51%)
Race	
White	91 (66%)
Black	21 (15%)
Asian	7 (5%)
Other	19 (14%)
Hospital Region	
Northeast	53 (38%)
Southeast	22 (16%)
Southwest	19 (14%)
Midwest	18 (13%)
West	26 (19%)
Length of stay in days, median (IQR)	6.0 (4.0, 9.0)
ICU level of care	11 (8%)
Medicaid insurance	63 (46%)
Macrophage activation syndrome*	17 (12%)
Treatment	
IL-1 inhibitor#	56 (41%)
IL-6 inhibitor#	7 (5%)
Glucocorticoids	70 (51%)
Methotrexate	6 (4%)
Scheduled NSAIDs	122 (88%)
Readmission within 90 days	12 (9%)

*Based on discharge ICD-10 CM code. Diagnosis of MAS may have occurred at any point during hospitalization.
Not mutually exclusive. 1 patient received both IL-1 and IL-6 inhibition during hospitalization.

Table 1. Baseline characteristics (n = 138)

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Patient level factors		
Age	1.01 (0.94-1.09)	-------
Female gender	1.67 (0.76-3.65)	1.65 (0.76-3.59)
Race		
White	[Reference group]	[Reference group]
Black	0.77 (0.25-2.42)	0.52 (0.17-1.63)
Asian	1.29 (0.21-8.16)	1.24 (0.17-8.94)
Other	0.89 (0.26-2.97)	0.64 (0.19-2.18)
Medicaid insurance	0.91 (0.41-2.03)	-------
Hospital level factors		
Systemic JIA case volume during study period*	1.22 (1.04-1.44)	1.28 (1.04-1.58)
Hospital inpatient admissions per year		
Low (< 15,000)	[Reference group]	[Reference group]
Medium (15,000-20,000)	3.66 (0.97-13.85)	2.17 (0.58-8.17)
High (>20,000)	4.31 (1.25-14.86)	1.69 (0.40-7.08)
Pediatric Rheumatology fellowship	1.38 (0.51-3.74)	-------
Region		
Northeast	[Reference group]	[Reference group]
Southeast	2.49 (0.57-10.89)	3.74 (0.95-14.76)
Southwest	2.76 (0.58-13.08)	4.72 (1.15-19.43)
Midwest	0.92 (0.17-4.86)	1.13 (0.27-4.74)
West	1.70 (0.41-7.03)	2.84 (0.72-11.24)

*Systemic JIA case volume treated as a continuous variable in regression model.

Table 2. Unadjusted and adjusted odds ratios for biologic exposure according to patient and hospital level factors.

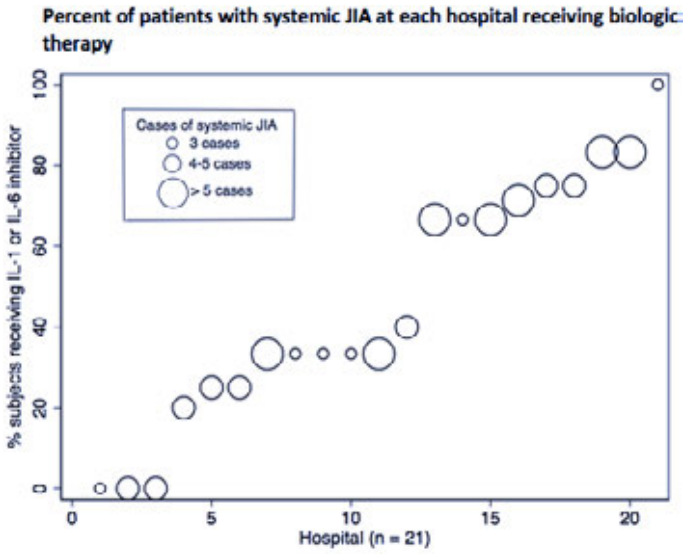

Figure 1. Variation in biologic treatment of children with new-onset systemic JIA across hospitals. Percent of children with systemic JIA at each hospital who received biologic therapy (IL-1 or IL-6 inhibitor). Only hospitals with at least 3 cases of systemic JIA are included.

Results: A total of 138 children with new-onset systemic JIA were admitted across 45 children's hospitals, of which 46% received biologic therapy (89% IL1i, 11% IL6i) and 51% received GCs. Demographics and clinical characteristics are presented in Table 1. The average length of stay was 6 days (IQR 4-9) and all-cause 90-day readmission rate was 9%. After adjustment for patient and hospital level factors, site systemic JIA volume was a positive predictor of biologic exposure (OR 1.28, [1.04-1.58]) (Table 2). Predictors of GC exposure included low hospital volume (OR 30.40, [5.40-171.03]), West region (OR 11.91, [1.89-74.92]), and on-site pediatric rheumatology fellowship (OR 4.45, [1.13-17.55]). Biologic exposure increased over time (p = 0.03), while GC exposure remained unchanged (p = 0.85). The median proportion of patients with GC and biologic exposure within sites was 0.67 (IQR 0.2-1) and 0.33 (IQR 0-0.67), respectively. Variability in the unadjusted use of biologics across hospitals is shown in Figure 1.

Conclusion: Treatment of children with new-onset systemic JIA varies considerably between tertiary care children's hospitals in the United States. Patients admitted to sites with a higher number of systemic JIA cases were more likely to be exposed to biologics, whereas GC exposure was more likely at lower volume hospitals. GC use has remained unchanged over time despite increasing biologic use. Further study is needed to determine the impact of early biologic use on hospital outcomes and contributors to low biologic use and high GC use at certain si tes.

Disclosure: R. Peterson, None; **R. Xiao**, None; **H. Katcoff**, None; **B. Fisher**, None; **P. Weiss**, None.

Abstract Number: 2695

Early Treatment with Anakinra in Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
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Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) accounts for 10-20% of all patients with JIA. sJIA should be considered as a polygenic autoinflammatory disease. Interleukin 1 (IL-1) has been shown to be a major mediator of the inflammatory cascade that underlies sJIA. Treatment with anakinra has been reported to be effective in a sizable portion of patients with sJIA.

Objective: To assess clinical response rate and disease course in sJIA patients treated with anakinra. To evaluated whether the response to anakinra was related to baseline variables

Methods: We reviewed 57 (28 F) consecutive patients with sJIA treated with anakinra for at least 6 months in our institution. We analyzed the effect of anakinra on fever, rash, number of active joints, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cells count, platelets count and ferritin levels. Clinically inactive disease (CID) was defined according to Wallace criteria. Clinical and laboratory data were obtained using a standard data collection form.

Results: The median age at the disease onset was 5.6 (IQR 2.7-10.0) years. The median time from onset to received anakinra was 1.9 (IQR 0.7-9.5) months. At baseline 53/57 (92.9%) of patients had fever and median number of active joints was 2 (IQR 1-4). After 6 months of treatment 40 patients (70.2%) met criteria for inactive disease. Among 57 patients 17 (30.3%) received anakinra in monotherapy and 40 (70.2%) received anakinra with glucocorticoids. There were no statistically significant differences between the two groups for demographic, clinical and laboratory features. 13/17 (76.4%) patients treated with anakinra alone and 27/40 (67.5%) patients treated with anakinra and glucocorticoids met criteria for CID off glucocorticoids at 6 months (p=0.75). Among the 57 patients, 30 (52.6%) received anakinra within 2 months from disease onset. There were no statistically significant differences for demographic, clinical and laboratory features among patients who started anakinra in the first 2 months from disease onset compared to those that started anakinra after 2 months. At 6 months after beginning of anakinra treatment, 28/30 patients (93.3%) who started anakinra within 2 months from disease onset and 12/27 (44.4%) who started anakinra after 2 months from disease onset reached clinical inactive disease off glucocorticoids (p=0.0001). Patients who started anakinra after the first 2 months from disease onset have a significantly higher risk of non-response (OR=8.06, 95% CI: 2.03-32.0).

Conclusion: According with several observations, anakinra is effective in a significant proportion of patients with sJIA. A possible approach to introduce IL-1 inhibitor, with or without concomitant glucocorticoids, early in the disease course taking advantage of a “window of opportunity” has been suggested. Our observation confirms that earlier treatment with anakinra is associated with a better short-term outcome. Moreover, our results show that beginning of treatment after two months of disease is correlated with a high risk of non-response.

Disclosure: M. Pardeo, None; **C. Bracaglia**, None; **A. Tulone**, None; **A. Insalaco**, None; **G. Marucci**, None; **R. Nicolai**, None; **V. Messia**, None; **E. Sacco**, None; **F. De Benedetti**, AbbVie, 2, BMS, 2, Novartis, 2, Novartis, Novimmune, Hoffmann- La Roche, SOBI, AbbVie, Pfizer, 2, Novimmune, 2, Pfizer, 2, Roche, 2, Sanofi, 2, Sobi, 2, Swedish Orphan Biovitrum, 2, UCB, 2.

Abstract Number: 2696

Long-Term Efficacy and Safety of Canakinumab in Children with Systemic Juvenile Idiopathic Arthritis

Ekaterina Alexeeva,[1] Rina Denisova,[2] Tatyana Dvoryakovskaya,[2] Ksenia Isaeva,[2] Ivan Kriulin,[2] Alina Alshevskaya,[3] and Andrey Moskalev[3], [1]National Medical Research Center of Children`s Health, Moscow, Russia, [2]NMRCCH, Moscow, Russia, [3]Biostatistics and Clinical Trials Center, Novosibirsk, Russia

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
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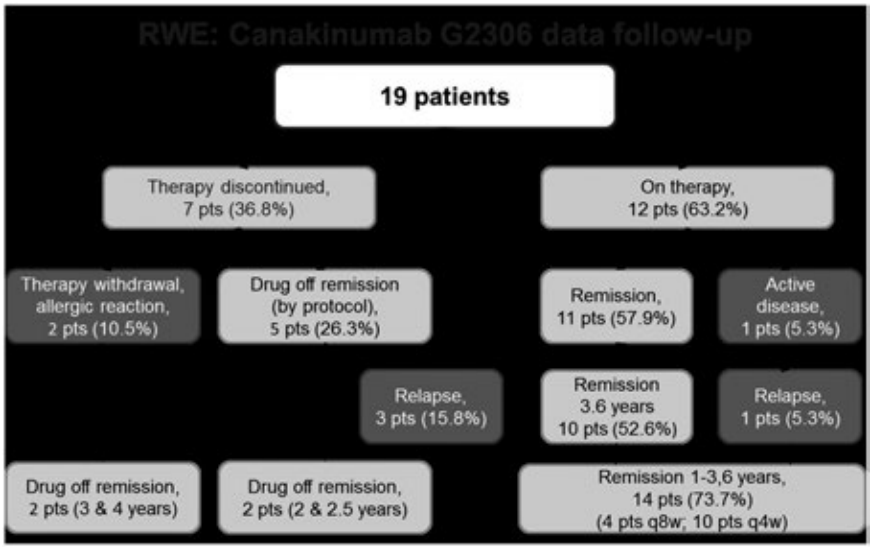
Background/Purpose: Canakinumab (CAN) is an efficacious option for treatment of systemic juvenile idiopathic arthritis (sJIA). However, it is still disputable whether long-term therapy is efficacious and drug-free remission can be achieved. This study aimed to analyze the efficacy and safety of long-term CAN treatment in children.

Methods: Nineteen patients aged 2.3–15.6 years who had started CAN therapy under CACZ885G2306 clinical trial were enrolled in this study. The patients' median age at treatment initiation was 9.6 (IQR 6.4–11.1) years; age at sJIA onset was 3.2 (1.9–5.1) years; and sJIA duration was 4.4 (1.2–7.0) years. Before the initiation of CAN therapy, two (10.5%) patients were biologic-naïve; 12 (63.2%) patients had received one prior biologic agent; and 5 (26.3%) patients had received at least two prior biologic agents. All patients had been earlier treated with NSAIDs; 16 (84.2%) patients had been receiving glucocorticoids; 15 (78.9%), methotrexate; 10 (52.6%), cyclosporine A; and one (5.3%) patient, sulfasalazine. Response to therapy was assessed using the ACRPedi 30/50/70/90 criteria and the C. Wallace criteria for clinical remission. Safety was assessed at each visit

Results: At treatment initiation, disease activity was high in all patients. Depending on the criteria used for evaluation, JIA activity was as follows: 14.7 (12.2–25.3) for JADAS-71; 41 (36.5-69) for physician's global assessment VAS; 54 (45-79.5) for patient's global assessment VAS; and 0.5 (0.1-0.8) for the CHAQ disability index. After 12-month treatment, 14 (73.7%) patients attained inactive disease according to the C. Wallace's criteria. JADAS-71 decreased



Study scheme

by 14.5 (11-25.4) points (p< 0.001 compared to baseline). Fourteen (73.7%) patients achieved an ACR100 response. The median treatment duration was 42.6 (39.5-72.5) months; total treatment duration was 79.2 patient-years. Figure shows the treatment outcomes and the reasons for therapy discontinuation.

One of 11 patients remaining in therapy developed a relapse accompanied by a MAS episode that required elevation of the GC dose. CAN therapy was continued, and the patient achieved remission again. Fourteen (73.7%) of 19 patients receiving CAN therapy achieved remission lasting 1–3.6 years; the interval of CAN administration was increased to 8 weeks in four patients.

Four (21.1%) patients achieved drug-free remission and had no relapses over the follow-up period of 2-4 years.

During the follow-up period, serious adverse events (SAE) were reported in two (6.1%) patients (severe allergic reaction – 1 and enteritis – 1). Five (10.2%) patients had AEs (allergy – 1; hepatotoxicity – 2; exacerbation of herpes infection –1; and neutropenia – 1).

Conclusion: Long-term CAN therapy proved to be efficacious and safe; patients remain in remission after medication discontinuation.

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Abstract Number: 2697

Risk Score of Macrophage Activation Syndrome in Patients with Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION
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Background/Purpose: Macrophage Activation Syndrome (MAS) is a severe, life-threatening, complication of rheumatic diseases in childhood, particularly of systemic Juvenile Idiopathic Arthritis (sJIA), occurring in approximately 25% of the patients with sJIA. The mortality rate of MAS is still significantly high. A score that identify sJIA patients who are at high risk to develop MAS would be useful in clinical practice. There are no parameters available to identify from onset sJIA patients with high risk to develop MAS in their disease course.

Table 1. Laboratory parameters and cut-off used to create the MAS risk score in sJIA patients

Laboratory parameters	Cut-off	Rate
Ferritin (ng/ml)	>900	1
AST (UI/L)	>35	1
LDH (UI/l)	>550	1
gammaGT (UI/L)	>30	2
Triglycerides (mg/dl)	>150	2

Table 2. Sensitivity and Specificity of the best Risk core

Sensitivity (Se)	0.950	CI95% 0.842-0.988
Specificity (Sp)	0.848	CI95% 0.718-0.928
Positive predictive value (PPV)	0.792	CI95% 0.654-0.887
Negative predictive value (NPV)	0.966	CI95% 0.864-0.995

Table 3. Sensitivity and Specificity of the MAS risk score in the validation cohort

Sensitivity (Se)	0.833	CI95% 0.691-0.921
Specificity (Sp)	0.724	CI95% 0.572-0.840
Positive predictive value (PPV)	0.652	CI95% 0.499-0.781
Negative predictive value (NPV)	0.875	CI95% 0.739-0.949

Methods: We evaluated whether routine laboratory parameters at disease onset may predict the development of MAS in patients with active sJIA and we defined a risk score of MAS for sJIA patients using these parameters. Laboratory parameters of disease activity and severity (WBC, N, PLT, Hb, ferritin, AST, ALT, gGT, LDH, TGL, fibrinogen, D-dimer and CRP), were retrospectively evaluated in 85 sJIA patients referred to our Division of Rheumatology from 1998 to 2018 with at least one year of follow-up. Laboratory parameters were evaluated during active sJIA, without MAS, at time of hospitalization (T1) and immediately before treatment for sJIA was started (T2). Patients were divided in two groups: group 1 (sJIA patients without history of MAS), group 2 (sJIA patients with at least one MAS episode during disease course). To calculate a MAS risk score, laboratory parameters, collected at T2, with a statistically significant difference between the two groups of patients were selected.

Results: Thirty-two patients, that fulfilled the 2016 classification criteria for MAS [1] at time of sampling, were excluded from the analysis. Therefore, we analysed laboratory parameters of 53 patients with sJIA, 33 of whom without history of MAS (group 1) and 20 who developed at least one episode of MAS during disease course (group 2). Levels of ferritin, AST, LDH, gGT and TGL, collected at T2, were statistically significant higher in patients with a history of MAS compared to those without a history of MAS. For each of these parameters an arbitrary cut-off was defined. In order to define the final score an arbitrary rate was attributed to each parameter (Table1). Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were calculated to define the best scoring system. The scoring system with the best sensitivity was chosen (Table 2). A MAS risk score >3 identified 19 out of 20 sJIA patients with a history of MAS and 5 out of 33 sJIA patients without history of MAS. In order to validate the MAS risk score on a different population, we applied the score on 47 patients from other Paediatric Rheumatologic centres, 29 without history of MAS and 18 with at least one episode of MAS. Sensitivity and specificity of the score are reported in table 3.

Conclusion: In conclusion we developed a MAS risk score based on routine laboratory parameters, available worldwide, that can help clinicians to identify these patients early in the disease course. The initial validation analysis is promising but we need to validate the score on a larger population.

Reference:

1. Ravelli A et al. Ann Rheum Dis. 2016 Mar;75(3):481-9.

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Pfizer, 2, 5, 8, Roche, 2, 5, 8; **N. Čekada**, None; **M. Jelusic**, None; **O. Vougiouka**, None; **M. Kostik**, None; **A. Gagro**, None; **C. Kessel**, None; **F. Minoia**, None; **F. De Benedetti**, AbbVie, 2, BMS, 2, Novartis, 2, Novartis, Novimmune, Hoffmann- La Roche, SOBI, AbbVie, Pfizer, 2, Novimmune, 2, Pfizer, 2, Roche, 2, Sanofi, 2, Sobi, 2, Swedish Orphan Biovitrum, 2, UCB, 2; **C. Bracaglia**, None.

Abstract Number: 2698

Reasons for Initiation of Canakinumab of Patients with Systemic Juvenile Idiopathic Arthritis: A Retrospective Medical Chart Review from the United States

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SESSION INFORMATION
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Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
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Background/Purpose: Systemic juvenile idiopathic arthritis **(**SJIA) is a rare autoinflammatory disease characterized by fever and arthritis, often accompanied by rash. Canakinumab (CAN) was approved in the United States (US) in 2013 for SJIA treatment. However, prescribing patterns among physicians who have initiated CAN in real world settings are not well understood. This study aimed to assess the physician reason(s) for initiating CAN and characterize the clinical and treatment profiles of SJIA patients (pts) in US clinical practice.

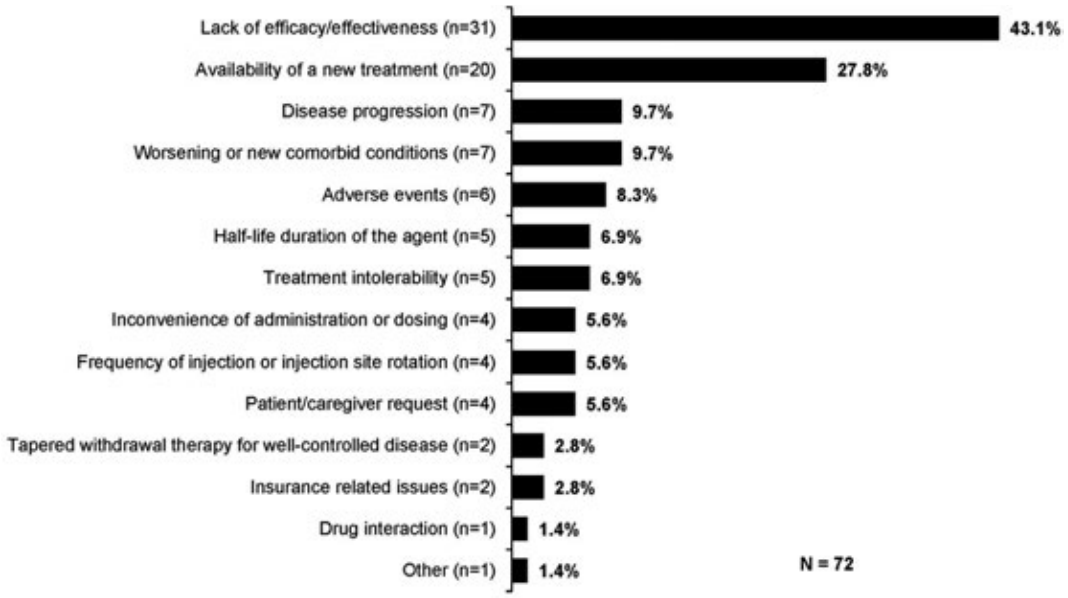

Figure 1. Reasons by SJIA patients for discontinuation of long-term treatments prior to canakinumab initiation

Figure 2. Reasons by SJIA patients for the initiation of canakinumab treatment

Methods: Online medical charts were reviewed retrospectively to collect data from US rheumatologists/ dermatologists/ allergists / immunologists on pts (pediatrics [Ped; < 18 yrs] and adults [Adt; ≥18 yrs]) diagnosed with SJIA who were initiated on CAN therapy by the responding physician between 2016 and 2018. Online case report forms were used to collect information on pt demographics, disease characteristics at CAN initiation, pre-CAN treatment history, and CAN prescribing patterns. Reasons for discontinuation of previous treatment and initiation of CAN were also collected.

Results: Medical charts were reviewed by 43 physicians who had specialty in rheumatology (22; Adt 82%, Ped 18%), dermatology (12; Adt 75%, Ped 25%), immunology (5; Adt 40%, Ped 60%), and allergy (4; Adt 100%). Of the 72 pts, 57% were female and 61% were Ped. The mean age at CAN initiation was 19.4 yrs (Adt, 33.5 yrs; Ped, 10.4 yrs). At CAN initiation, 71% of pts were with and 29% were without active systemic features. Median age at SJIA diagnosis was 11 yrs (IQR: 6.5-16). The key methods of diagnosis were assessment of clinical symptoms and complications (92%), exclusion/rule-out diagnosis (e.g., infection, neoplasms; 75%), and age of onset (67%). The main diagnoses which were ruled out included fever of unknown origin (76%), other JIA subtype (43%), and other PFS (39%). The severity of SJIA was mild (11%), moderate (75%), or severe (14%). The most common symptoms at CAN initiation were fever (72%), fatigue/malaise (58%), skin rashes (47%), and arthritis (46%). A large part of pts at CAN initiation had 1-4 joints with active inflammation (69%) and 1-4 joints with limited range of motion (63%). Nearly all pts (90%) received other long-term treatments in the last line of therapy prior to CAN, including biologics (e.g., 28% etanercept, 19% anakinra, 17% adalimumab, and 11% tocilizumab), methotrexate (9%), and NSAIDs (8%). The main reasons for discontinuation of treatment prior to CAN initiation were lack of efficacy/effectiveness (43%) and availability of a new treatment (28%; Fig. 1). Decision to initiate CAN was decided most often by both physician and pt/caregiver (72%), followed by physician only (26%), and then by the pt/caregiver only (1%). The prime reasons for CAN initiation included efficacy/effectiveness (78%), lack of response to previous treatment (46%) and convenience of administration or dosing (26%; Fig. 2).

Conclusion: Findings from this study provide insight into physicians' characteristics in clinical practice as well as the reasons for CAN initiation in SJIA pts. The efficacy/effectiveness of CAN, lack of response to previous treatment and convenience of CAN administration or dosing were the most common reasons.

Disclosure: P. Hur, Novartis, 3, Novartis Pharmaceuticals Corporation, 3, Novartis Pharmaceuticals Corporations, 3; **R. Ionescu-Ittu**, Analysis Group, Inc., 3, Novartis Pharmaceuticals Corporation, 5, Novartis Pharmaceuticals Corporations, 5; **A. Manceur**, Analysis Group, Inc., 3, Novartis Pharmaceuticals Corporation, 5, Novartis Pharmaceuticals Corporations, 5; **K. Lomax**, Novartis Pharmaceuticals Corporation, 3, Novartis Pharmaceuticals Corporations, 3; **J. Cammarota**, Analysis Group, Inc., 3, Novartis Pharmaceuticals Corporation, 5, Novartis Pharmaceuticals Corporations, 5; **J. Xie**, Analysis Group, Inc., 3, Novartis Pharmaceuticals Corporation, 5, Novartis Pharmaceuticals Corporations, 5; **N. Sanghera**, Novartis Pharmaceuticals Corporation, 3, Novartis Pharmaceuticals Corporations, 3; **A. Grom**, AB2 Bio Ltd, 2, 5, AB2Bio, 2, 5, Children's Hospital Medical Center, 3, Novartis, 2, 5, Novartis Pharmaceuticals Corporation, 2, 5, Novartis Pharmaceuticals Corporations, 5, NovImmune, 2, 5, Novimmune, 2, 5.

Abstract Number: 2699

Systemic Therapy in Children with Juvenile Idiopathic Arthritis-Associated Uveitis Immediately Following Failure of Methotrexate, Adalimumab and Infliximab

Najima Mwase,[1] Theresa Hennard,[2] Joseph McDonald,[3] Amy Cassedy,[4] Onengiya Harry,[3] and **Sheila Angeles-Han** [5], [1]Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Division of Rheumatology, Cincinnati Children's Hospital and Medical Center, Cincinnati, OH, [3]Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, [4]Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, [5]Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cinicinnati

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile idiopathic arthritis-associated uveitis (JIA-U) is the most common extra-articular manifestation of JIA, leading to ocular complications and blindness when not adequately treated. First line treatment includes topical glucocorticoids followed by methotrexate (MTX). While monoclonal TNF-α inhibitors (TNFi) such as adalimumab (ADA) and infliximab (IFX) are widely accepted as treatment escalation for refractory uveitis or initial therapy in complicated disease, evidence is lacking on the selection of the next optimal agent if MTX and traditional TNFi are ineffective. Our objective is to describe use of immunosuppressive agents for refractory JIA-U immediately following MTX and traditional TNFi treatment failure.

Methods: We retrospectively reviewed medical records for 48 JIA-U children enrolled in a prospective JIA/uveitis study conducted at a tertiary pediatric center since February 2017. All children were treated with systemic immunosuppressive therapy for either 1) uveitis only or 2) uveitis and arthritis. Treatment failure was defined as the escalation of treatment to another biologic indicated for uveitis. Treatment discontinuation was defined as the provider's decision to either 1) permanently discontinue medication or 2) not re-initiate use of medication following patient nonadherence. Traditional TNFi refers to the use of ADA or IFX either concurrently with or following the discontinuation of MTX.

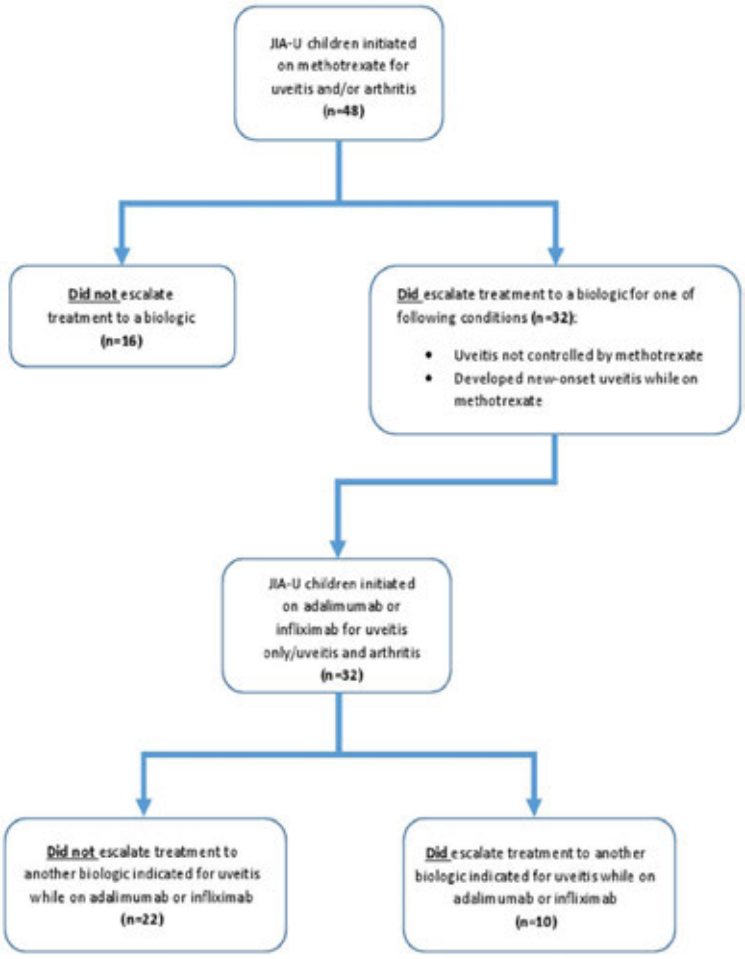

Figure 1: Use of Systemic Immunosuppression in Children with JIA-U

Children were first stratified into 2 groups by treatment response to MTX monotherapy. Those who failed MTX monotherapy and started traditional TNFi were further stratified into 2 groups based on the addition of a third biologic (Figure 1). Additional information (i.e. treatment indication, duration of treatment and reason for discontinuation) were collected for all qualifying systemic medications.

Results: Of the 48 JIA-U children, 16 remained on MTX monotherapy (26%), 22 escalated treatment to traditional TNFi only (46%) and 10 escalated treatment to a third biologic beyond traditional TNFi (21%).

Of the 22 children treated with traditional TNFi only, 18 began on ADA (82%) and 11 began on IFX (50%). Overall, 7 were treated with both ADA and IFX (32%) (Table 1).

Of the 10 children treated with a third biologic beyond traditional TNFi, 5 began on tocilizumab (50%), 3 golimumab (30%) and 2 abatacept (20%). Prior treatment included ADA (60%) or ADA and IFX (40%). Treatment discontinuation occurred only on abatacept (2/2) due to disease activity (Table 2).

Conclusion: 21% of children with JIA-U in our cohort needed treatment beyond MTX and traditional TNFi. Studies report that 50-60% of children with uveitis will fail MTX. Tocilizumab was most commonly used in children requiring treatment beyond traditional TNFi. Both tocilizumab and golimumab were able to control uveitis, suggesting they

Table 1: Characteristics of Children with Juvenile Idiopathic Arthritis Associated Uveitis on Biologic Therapy, N (%) Unless Otherwise Indicated		
	Traditional TNFi (adalimumab and/or infliximab only) (n=22)	Biologics initiated after traditional TNFi failure (abatacept, golimumab, tocilizumab) (n=10)
Demographics		
Age at enrollment, mean (SD)	9.7 (4.7)	12.9 (5.1)
Race		
White	19 (86.4)	9 (90.0)
Black or African American	2 (9.1)	0 (0.0)
Asian	0 (0.0)	1 (10.0)
American Indian/Alaska Native	1 (4.5)	0 (0.0)
Female	17 (77.3)	10 (100.0)
Non-Hispanic or Latino	19 (86.4)	10 (100.0)
JIA Characteristics		
Age at diagnosis, mean (SD)	4.1 (3.4)	2.6 (1.2)
Duration of disease, years, mean (SD)	7.2 (4.7)	11.6 (5.6)
JIA subtype		
Oligoarticular, persistent	6 (27.3)	1 (10.0)
Oligoarticular, extended	5 (22.7)	3 (30.0)
Polyarticular RF (-)	6 (27.3)	4 (40.0)
Enthesitis related arthritis	1 (4.5)	0 (0.0)
Psoriatic arthritis	4 (18.2)	2 (20.0)
ANA positive	18 (81.8)	8 (80.0)
Uveitis Characteristics		
Age at diagnosis, mean (SD)	4.7 (2.5)	3.6 (1.6)
Duration of disease, years, mean (SD)	6.5 (4.8)	10.7 (5.7)
Disease laterality and location		
Bilateral	15 (68.2)	10 (100.0)
Anterior location[1]	21 (95.5)	9 (90.0)
Ocular complications, ever		
Amblyopia	1 (4.5)	1 (10.0)
Band keratopathy	0 (0.0)	1 (10.0)
Cataracts	5 (22.7)	5 (50.0)
Glaucoma/ocular hypertension	8 (36.4)	8 (80.0)
Synechiae	6 (27.3)	6 (60.0)
Systemic treatment for uveitis, ever		
Adalimumab	18 (81.8)	10 (100.0)
Weekly dosing	3 (13.6)	3 (30.0)
Infliximab	11(50.0)	4 (40.0)
Dose ≥10mg/kg every 4 weeks	5 (22.7)	2 (20.0)
Use of both adalimumab and infliximab	7 (31.8)	4 (40.0)
Abatacept		2 (20.0)
Golimumab		3 (30.0)
Tocilizumab		6 (60.0)
[1]Uveitis location unknown for 3 patients (1 from traditional TNFi, 2 from biologics initiated after TNFi failure)		

both are potential treatment options for uveitis. Because evidence is lacking on the long term efficacy of these biologics in treating JIA-U, further research should include factors associated with treatment response (i.e. dosing, disease characteristics) to optimize treatment for refractory uveitis.

Table 2: Systemic Treatment Initiated Immediately After Failure of Adalimumab and/or Infliximab, N (%) Unless Otherwise Indicated			
	Abatacept (n=2)	Golimumab (n=3)	Tocilizumab (n=5)
Indication			
Uveitis and arthritis	2 (100.0)	3 (100.0)	5 (100.0)
Duration of treatment, years, mean (SD)	3.8 (0.6)	2.1 (1.4)	1.5 (1.1)
Previous use of adalimumab and/or infliximab	2 (100.0)	3 (100.0)	5 (100.0)
Adalimumab only	1 (50.0)	2 (66.7)	3 (60.0)
Adalimumab and infliximab	1 (50.0)	1 (33.3)	2 (40.0)
Discontinued systemic treatment (abatacept, golimumab or tocilizumab)	2 (100.0)	0 (0.0)	0 (0.0)
Reason for discontinuation of systemic treatment (abatacept, golimumab or tocilizumab)			
Loss of efficacy (uveitis and arthritis)	1 (50.0)	0 (0.0)	0 (0.0)
Quiescent disease (uveitis and arthritis)	1 (50.0)	0 (0.0)	0 (0.0)
Transitioned to another biologic for treatment (abatacept, golimumab or tocilizumab)	1 (50.0)	0 (0.0)	0 (0.0)

Disclosure: N. Mwase, None; **T. Hennard**, None; **J. McDonald**, None; **A. Cassedy**, None; **O. Harry**, None; **S. Angeles-Han**, None.

Abstract Number: 2700

Adalimumab Alone Is Superior to Adalimumab Plus Methotrexate in Juvenile Idiopathic Arthritis Associated Uveitis: Data from the ORCHIDEA Registry

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

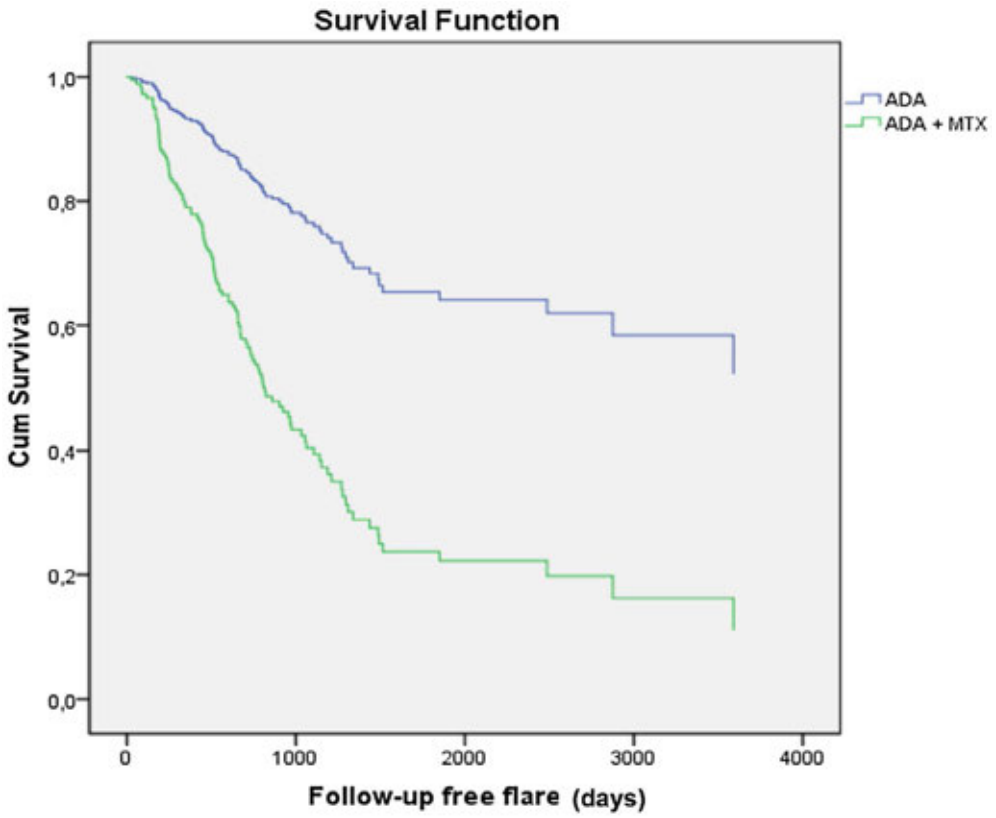
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: To compare the efficacy and safety of Adalimumab alone (ADA) *versus* ADA in combination with Methotrexate (ADA-MTX) in an open-label, retrospective, comparative, multicentre cohort study of Juvenile Idiopathic Arthritis Uveitis (JIA-U).

Methods: Patients with JIA-U treated with ADA were managed by astandardized protocol and data were entered in the ORCHIDEA registry. At baseline, all patients wererefractory to standard immunosuppressive MTX treatment. Data



recordedevery 3 months were uveitis course, number/type of ocular flares and complications, drug-relatedadverse events (AE), and treatment switch or withdrawal. The primary outcome was to assess the time to the first uveitis relapse on ADA treatment, once persistent inactive disease has been achieved. Inactive uveitis was defined as rare or < 1 cell per field at standard slit-lamp examination for at least 3 months. The choice of keeping MTX at 15mg/mq2 with ADA was an opinion-based decision shared between treating ophthalmologist and rheumatologist, at the time of the anti-TNFa start. Data of patients treated for ≥1 year were analyzed.

Results: Up to December 2018, 201 patients (40 Males, median age 4 yrs, range 1-17) with ≥12 months follow-up were enrolled 170 were in the ADA-MTX group, 31 in ADA group. Median age at uveitis onset resulted lower in ADA-MTX group (4 yrs, range 1-17) than ADA (5 yrs, 1-17, Mann-Whitney U test, p< 0.05). No statistical differences between the two groups with regard to age at arthritis onset, number of relapses previous anti TNF treatment, uveitis duration at anti TNF starting and presence of eye complications at base-line have been detected. The overall median time of follow-up without uveitis flares in remission was 24 months (range 1–154). ADA-MTX group showed a shorter relapse-free interval as compared with the ADA group (22 months, range 1-154 vs34 months, range 10-102, Mann-Whitney U test, p= 0.004). Stratifying the two groups by the presence of eye complications at base-line, no significant difference has been noted in 144 JIA-U children without complications. In 57 complicated JIA-U (48 ADA-MTX; 9 ADA), time on remission on treatment resulted shorter in ADA-MTX as compared to ADA (29.2 +24.9 months vs 53.2 +24.5 months, Mann-Whitney U test, p=0.006). Cox regression analysis, at mean of the above-reported covariates, showed a higher probability of maintaining remission on ADA treatment compared to ADA +MTX administration (Mantel-Cox chi-square =19.6, p < 0.001; Figure). The number of pts who experienced drug-related adverse events was not different between the groups: ADA-MTX 44/170 (25.9%) vs ADA 5/31 (16.1%), p: n.s.

Conclusion: JIA-U treating physicians commonly use ADA in combination with MTX. However, according these retrospective data from the ORCHIDEA registry, this approach, even if safe, seems not to provide significant benefits in controlling JIA-U activity over time.

Disclosure: G. Simonini, None; **F. Vittadello**, None; **F. Tirelli**, None; **M. Zannin**, None; **E. Del Giudice**, None; **C. Bracaglia**, None; **S. Pastore**, None; **M. Alessio**, None; **A. Ravelli**, Angelini, AbbVie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reckitt Benkiser, and Roche, 2, 5, 8; **F. La Torre**, None; **R. Gallizzi**, None; **I. Maccora**, None; **F. Zulian**, None.

Abstract Number: 2701

Frequency of Juvenile Idiopathic Arthritis (JIA) Subgroups and JIA-associated Uveitis Among JIA Patients Admitted to Referral Pediatric Rheumatology Clinics In TurkEy: A Retrospective Study, JUPITER

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is a chronic childhood arthritis with onset before age of 16 and has a significant degree of morbidity that negatively affects quality of life. Uveitis, which is defined as the inflammation of the iris, ciliary body and choroid, is the most common cause of morbidity of JIA. This study was planned to collect data from a Turkish cohort to provide the initial national prevalence data of patients with JIA. The objective of this study was to determine the frequency of JIA subtypes in Turkey. We also aimed to assess the frequency and characteristics of eye involvement in JIA.

Methods: This national, non-interventional, multicenter, observational study was conducted in a retrospective manner in four study centers which were main referral pediatric rheumatology clinics across Turkey. Data on patient demography, medical history, JIA disease characteristics, laboratory data, cases of JIA-associated uveitis, JIA treatment history and data on other comorbidities were collected from a cohort of 500 patients.

Results: Oligoarthritis (n=194, 38.8%) was the most common JIA disease characteristic in this study cohort. The frequency of the subgroups was as follows: Enthesitis-Related Arthritis (ERA) in 23.2% (n=116), polyarthritis in 15.6% (n=78), systemic arthritis in 12.2% (n=61), psoriatic arthritis in 5.2% (n=26), idiopathic arthritis in 2.8% (n=14) and

polyarthritis (RF+) in 2.2% (n=11) of patients were identified. The most frequently prescribed treatment for JIA was methotrexate (n=384, 76.8%). A total of 85 comorbidities were reported, and the most frequently reported comorbidity was Familial Mediterranean Fever (FMF) (n=63, 12.6%).

The number of patients with JIA-associated uveitis diagnosis was 34 (6.8%), and the mean duration of uveitis was 3.2 (±2.3) years. The mean duration between the initial JIA diagnosis and diagnosis of uveitis was 1.8 (±1.9) years. Among 34 patients with uveitis, 45 eye involvements were identified; left eye, right eye and both eyes were affected in 5, 8 and 16 patients, respectively. Five patients (14.7%) had uveitis-related complications that required surgical intervention.

Conclusion: The main difference from the European Caucasian population is the lower frequency of oligoarticular JIA and higher frequency of ERA in Turkish JIA patients. Uveitis was also somewhat lower than expected. Geographic and ethnic factors, that may affect these differences, need further investigation.

Disclosure: S. Sahin, AbbVie, 2; **C. Acari**, AbbVie, 2; **H. Sonmez**, AbbVie, 2; **F. Kilic**, AbbVie, 2; **E. Sag**, AbbVie, 2; **H. Adiguzel Dundar**, AbbVie, 2; **A. Adrovic**, AbbVie, 2; **S. Demir**, AbbVie, 2; **K. Barut**, AbbVie, 2; **Y. Bilginer**, AbbVie, 2; **B. Sozeri**, AbbVie, 2, 5, 8, Celltrion, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8; **E. Unsal**, AbbVie, 2, 8, Novartis, 2, 8, Roche, 2, 8, Kocak Pharma, 2, 8; **S. Ozen**, Enzyvant, 8; **O. Kasapcopur**, AbbVie, 2.

Abstract Number: 2702

Patients' and Parents' Perception of Disease and Its Impact on Life in Juvenile Idiopathic Arthritis: Results from Multinational Virtual Focus Groups by the OMERACT JIA Working Group

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose:: The OMERACT Juvenile Idiopathic Arthritis Core Set Working Group formed in 2015 as an international initiative to revise the existing Core Set with relevant patient and caregiver input. In efforts to develop an updated, patient-centered Core Outcome, multinational virtual focus groups (VFGs) were conducted to identify main patient-valued themes regarding the impact of Juvenile Idiopathic Arthritis (JIA), with special emphasis on patient and

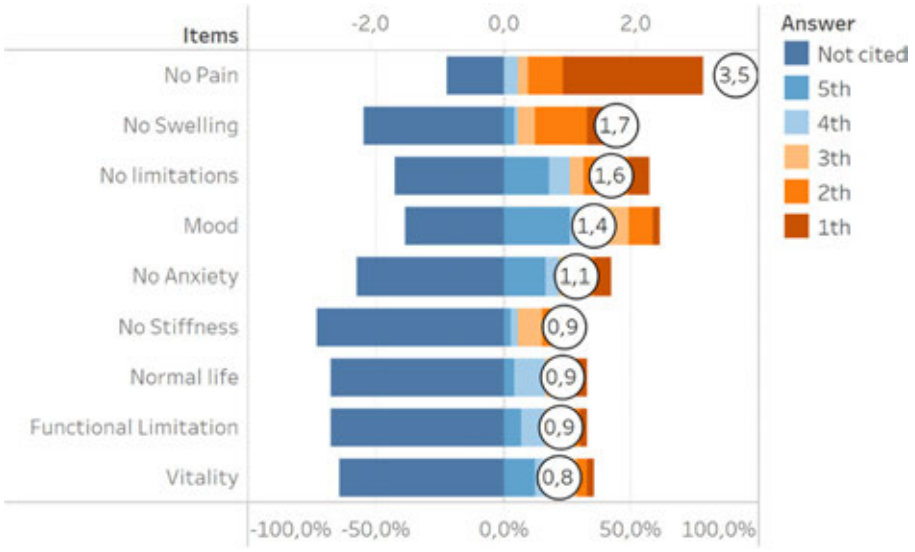
parental perception of disease activity states, and to examine the validity of the identified domains across different populations.

Methods:: Two sets of paired VFGs were conducted with JIA patients (adolescents and young adults) and parents (split by ages of their children) in two clinics, in the US and in Italy respectively. 86 subjects were included. Caregivers were split by ages of their children (under and over 15 years old in the US sample; under and over 10 years old in the Italian sample). Patients were split in adolescents (15-17 years old in the US sample, 15-18 years old in the Italian sample) and young adults (18-24 years old in the US sample, 19-25 years old in the Italian sample). A 3-day facilitated online board was held per group, focusing on the impact of JIA on physical, mental and social health, and the perceived differences between active and inactive JIA. Qualitative analysis of transcripts was first conducted independently in the two centers and compared. Transcripts were further analyzed using text network analysis, that allows studying the interactions between domains and the impact of specific items, as measured by centrality indexes.

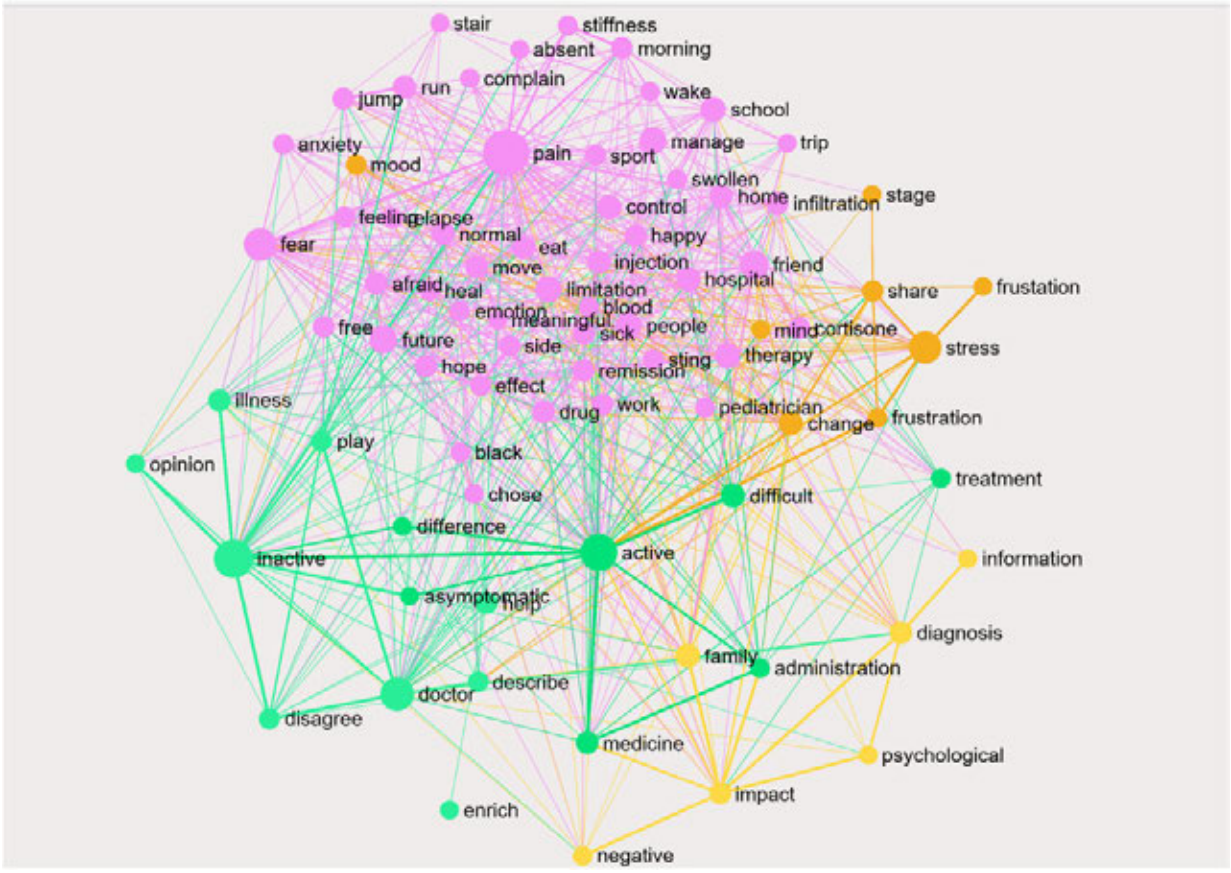
Results: Key domains and group-specific themes were identified, with cross-cultural and age-specific differences between groups, as described in the table. Psychosocial impact and limitations in daily activities emerged as main domains in both samples. Among the main cross-cultural differences, fear of relapses and burden of medications were indicated as concerns by Italian patients and caregivers, while impact on children's activities and family life were more relevant in US groups. Participants were asked to identify and rank their five top priority features defining inactive disease. Absence of pain, swelling and activity restrictions received top-ranking, mood improvement and reduction of disease-related anxiety were ranked as most important, with no significant differences between the two populations (graph 1). Fatigue was cited among relevant themes only by US subjects. Network analysis of transcripts (graph 2) confirmed pain as the single item with the highest degree, closeness and between centrality, indicating high relevance, together with psychosocial distress and activity restriction.

Themes	Italian Groups				US Groups			
	Teens (15-18 y.) N. = 11	Young Adults (19-25 y.) N. = 10	Parents of younger patients (< 10 y.) N. = 10	Parents of older patients (> 10 y.) N. = 10	Teens (15-17 y.) N. = 11	Young Adults (18-24 y.) N. = 13	Parents of younger patients (< 15 y.) N. = 10	Parents of older patients (> 15 y.) N. = 10
Frequent	-Limitations in daily activities -Fear of hospitalization , therapy -Relationship with peers -Fear of Relapses	-Limitations in daily activities -Fear of Relapses -Relationship with peers -Fear of hospitalization , therapy	-Psychosocial impact -Burden of medications -Limitation in daily activities - Fear of Relapses	-Psychosocial impact - Fear of Relapses - Demands on family -Limitations in daily activities -Impact on future abilities	-Relationship with peers -Limitations in daily activities	-Limitations in daily activities -Impact on career trajectory	-Psychosocial impact -Functional limitations, symptoms -Demands on caregivers	-Demands on family -Limitations in daily activities
Less Frequent	Individual costs	-Loss of ability to work -Individual costs		Burden of medications	Loss of ability to work		-Fear of death	Intangible costs
Group-specific		Loss of ability to work	Burden of medications	Side effects (steroids)	Impact on sports	Impact on career goals	-Poor understanding of illness -Guilt about late diagnosis	- Advocacy at school -Concerns about siblings 'well being

Table. Key domains and group-specific themes with cross-cultural and age-specific differences between groups.



Graph 1. «Top Five» remission features, ranked from 1th (most important) to 5th (less important). Percentages of participants assigning each rank are shown for the domains. The average ranking score for each domain is indicated in the circles.



Graph 2. Network graph of trascripts shows the structure of connection between domains, with main macrodomains highlighted in different colors, based on word co-occurrence. The node dimension expresses the between-centrality for each word.

Conclusion: VFGs revealed pain, participation restriction and emotional function as main patient-relevant domains. Differences in the two populations include the role of relapses, treatments and secondary demands in the impact of disease. These results served as inputs for the development of the updated OMERACT JIA Core Domain Set.

Further analysis and cross-cultural validation are planned to inform the development of patient-centered outcomes measures.

Disclosure: A. Alongi, None; **S. Calandra**, None; **S. Thornhill**, None; **J. Stinson**, None; **J. Horonjeff**, None; **D. Horton**, None; **A. Consolaro**, Abbvie, 2, Pfizer, 2; **E. Morgan**, None.

Abstract Number: 2703

The Childhood Arthritis and Rheumatology Research Alliance Start Time Optimization of Biologic Therapy in Polyarticular JIA Study: Patient Characteristics, Patient Reported Outcomes and Consensus Treatment Plan Choices

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Table 1. Baseline Patient Characteristics

	Total Cohort (n=401)	Step up (n=257)	Early Combination (n=100)	Biologic First (n=44)	P value
Female N (%)	295 (74)	192 (75)	75 (75)	22 (67)	0.285
White N (%)	292 (72.8)	156 (72)	53 (63)	28 (64)	0.327
Age in yrs - mean (range)	10 (1-18)	10 (1-18)	11 (1-18)	11 (1-18)	
JIA Category N (%)					0.001
Extended Oligoarticular	15 (4)	13 (5)	0	2 (5)	
Polyarticular (RF-)	244 (61)	172 (67)	54 (54)	18 (41)	
Polyarticular (RF+)	77 (19)	41 (16)	28 (28)	8 (18)	
Psoriatic	23 (6)	12 (5)	5 (5)	6 (14)	
Enthesitis-related	32 (8)	14 (5)	10 (10)	8 (18)	
Undifferentiated	10 (3)	5 (2)	3 (3)	2 (5)	
Number of Active Joints - mean (range)	13 (5-50)	12 (5-49)	16 (5-50)	11 (5-41)	<0.001
Physician Global Assessment of Disease Activity (cJADAS-10) - mean (range)	5.5 (0-10)	5.1 (0-10)	6.4 (1-10)	6.1 (1-10)	<0.001
Juvenile Arthritis Disease Activity Score - mean (range)	18 (6-29)	17 (7-29)	20 (6-29)	19 (10-29)	<0.001
CHAQ Score - mean (range)	0.9 (0-3)	0.8 (0-3)	1.1 (0-3)	1.2 (0-3)	0.001
Oral steroids prescribed at baseline - N (%)	85 (25)	57 (26)	23 (27)	5 (15)	

Table 2: PROMIS® Baseline Pain Interference and Mobility Scores

	Total	Step Up	Early Combination	Biologic First
Pain Interference				
N	237	149	56	32
Mean (SD)	55.2 (8.8)	56.3 (8.4)	56.3 (8.4)	55.8 (9.4)
Mobility				
N	259	167	60	32
Mean (SD)	37.6 (10.0)	38.5 (10.5)	35.3 (8.8)	37.6 (9.5)

Table 1. Relationship between JADAS-27 (dependent variable) and demographic and clinical characteristics of JIA patients.

Table 3: cJADAS-10 scores and disease activity categories over time

	Baseline	3 mo	6 mo	9 mo	12 mo
N	360	280	282	226	217
Mean (SD)	18.1 (4.6)	10.2 (6.7)	7.0 (6.0)	5.4 (5.8)	4.6 (5.3)
Range (0-30)	6-29	0-27	0-25	0-28	0-26
Disease activity categories					
Inactive (≤ 1) N (%)	0 (0)	28 (10.0)	52 (18.4)	70 (31.0)	79 (36.4)
Low (1-2.5)	0 (0)	17 (6.1)	31 (11.0)	28 (12.4)	25 (11.5)
Moderate (2.5-8.5)	7 (2)	84 (30.0)	106 (37.6)	77 (34.1)	68 (31.3)
High (>8.5)	353 (98)	151 (53.9)	93 (33.0)	51 (22.6)	45 (20.7)

Background/Purpose: There continues to be uncertainty regarding when to start biologic medications for polyarticular juvenile idiopathic arthritis (P-JIA). The Childhood Arthritis and Rheumatology Research Alliance (CARRA) developed consensus treatment plans (CTPs) that reflect the most commonly-used strategies for starting biologic treatment in untreated P-JIA patients. The CARRA STOP-JIA study compares the effectiveness of the CARRA CTPs in achieving clinical inactive disease (CID) at 12 months using a prospective, observational study design. Enrollment was completed in August 2018.

Methods: Untreated P-JIA patients with ≥ 5 active joints were enrolled into the CARRA Registry. One of the CARRA P-JIA CTPs was chosen by the physician and patient/family to follow without randomization or blinding: 1) Step-Up (begin with non-biologic DMARD and add biologic after 3 months if needed); 2) Early Combination (begin both DMARD and biologic at baseline); and 3) Biologic First (biologic monotherapy). Providers prescribed glucocorticoids per their usual practice. Patient Reported Outcomes (PROs) included the CHAQ, Patient/Parent Global Assessment, PROMIS® Pain Interference and Mobility measures.

Results: Four hundred and one patients were enrolled at 44 sites in the US and Canada between 11/2015 and 8/2018. Table 1 shows the baseline data. The most commonly chosen CTPs were Step-Up (n=257; 64%) and Early Combination (n=100; 25%). At baseline, 343 (86%) of patients were started on a non-biologic DMARD (methotrexate). 147 (37%) were started on a biologic DMARD, most commonly etanercept (n=103, 26%) and adalimumab (49, 13%). To date, 320 patients have completed 12-months follow up. 278 patients completed at least one PRO measure at baseline. Table 2 shows mean PROMIS® Pain Interference and Mobiity scores for each treatment group. Table 3 shows the clinical Juvenile Arthritis Disease Activity Scores based on 10 joints (cJADAS-10) and the percentage of participants in each disease activity score category (inactive, low, moderate and high) over time.

Conclusion: STOP-JIA has successfully completed enrollment. Patients enrolled into all CTP choices; however, the Step-Up CTP was most common. There are differences between the treatment groups at baseline, including in

PROMIS® measures, which will require statistical adjustment to reduce bias. Overall, disease activity reduced across all treatment groups over time. Once all patients have completed 12-month follow-up, analyses comparing the effectiveness of the different CTP strategies will be performed.

Disclosure: S. Ringold, Childhood Arthritis & Rheumatology Research Alliance, 2, 6; **G. Tomlinson**, None; **P. Weiss**, Childhood Arthritis and Rheumatology Research Alliance, 6, Lily, 5; **L. Schanberg**, CARRA, 9, Childhood Arthritis and Rheumatology Research Alliance, 2, Sanofi, 5, 9, SOBI, 5, UCB, 5; **M. Riordan**, Childhood Arthritis and Rheumatology Research Alliance, 2; **A. Dennos**, Childhood Arthritis and Rheumatology Research Alliance, 3; **V. Del Gaizo**, Childhood Arthritis and Rheumatology Research Alliance, 3; **K. Murphy**, None; **B. Feldman**, Pfizer, 5, BMS, 5, Abbvie, 5, OPTUM, 5, AGILITY, 5; **Y. Kimura**, Novartis, 5, Sobi, 5.

Abstract Number: 2704

Injection Fear in Juvenile Idiopathic Arthritis Patients Using Injectable Medications

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
Session Type: Poster Session (Tuesday)
Session Time:9:00AM–11:00AM

Background/Purpose: Injectable medications are frequently used to treat Juvenile Idiopathic Arthritis (JIA). Fear of pain and needle fear have been identified as barriers to injectable medication adherence. High levels of injection fear have correlated with worse disease outcomes in other chronic diseases such as type 1 diabetes. The purpose of this study was to evaluate the prevalence of injection fear in a population of JIA patients using injectable medicines.

Methods: Inclusion criteria included a diagnosis of Juvenile Idiopathic Arthritis based on ILAR criteria and treatment with an injectable JIA medication. Patients and parents completed questionnaires on injection fear, medication adherence, anxiety, depression, and arthritis disease activity. Data about JIA disease characteristics and details about the patient's injectable medicine were also collected. Injection fear was measured using the injection section of the Diabetes Fear of Injecting and Self-Testing Questionnaire (D-FISQ). Patients age 10-22 completed the self-report D-FISQ, and parents completed the D-FISQ as proxy reporters for patients ages 5-17. The D-FISQ is a 15-item survey about emotions and physical symptoms at time of an injection. Each item has 4 possible answer choices with a corresponding numerical score (almost never 0, sometimes 1, often 2, almost all the time 3). The D-FISQ score is the sum of all items with scores ranging 0 to 45. Previous work has defined a D-FISQ score ≥6 to indicate injection fear with higher scores indicating greater levels of injection fear. The prevalence of injection fear was determined by calculating the number of patients with D-FISQ score ≥6 divided by the total number of patients surveyed. A similar calculation was made for D-FISQ scores obtained by parent report.

Results: Seventy-three JIA patients ages 5-22 and 58 parents from a pediatric rheumatology clinic were enrolled. The patients were 71% female and 63% white. The age range of the enrolled patients was 6-22 with mean age 14.77 (SD 3.98). JIA patient D-FISQ scores ranged from 0 to 41 with median of 11 (IQR 17). Parents proxy report on D-FISQ showed similar scores to patient report with range 0-43 and median 10 (IQR 21.75). The patient report D-FISQ classified 47 patients as having injection fear with a prevalence of injection fear in this cohort as 64.38% by patient

report. Parent proxy D-FISQ identified 37 patients with injection fear with injection fear prevalence of 63.79% by parent report.

Conclusion: This study found that approximately 64% of patients with JIA using injectable medications have injection fear. The prevalence of injection fear in JIA patients as determined by the D-FISQ is higher than previously reported rates of injection fear in pediatric patients with type 1 diabetes (23% in one study, 37% in another). The high rate of injection fear in JIA patients highlights the importance of future research to better understand the association between injection fear and outcome measurements.

Disclosure: K. Collins, None; **A. Wren**, None; **T. Lee**, None.

Abstract Number: 2705

Profiling Behavioral and Psychological Symptoms in Children with Spondyloarthritis and Polyarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Mental health disorders are thought to be common in patients with rheumatic disease, but studies examining behavioral issues in patients with juvenile idiopathic arthritis (JIA) have shown mixed results. This may be because JIA comprises a heterogeneous group of diseases and few studies examine psychopathology in different subtypes and disease activity states. This study aims to evaluate emotional and behavioral symptoms in children with juvenile spondyloarthritis (SpA) and polyarticular arthritis (PolyA) as compared to a national normative population using the Child Behavior Checklist (CBCL), and the relationship between CBCL scores and disease activity.

Methods: In this cross-sectional study, patients with JIA aged between 6 and 17 years were recruited at follow-up visits from our Pediatric Rheumatology clinic from April 2018 to April 2019. Patients meeting the ILAR criteria of enthesitis-related arthritis, undifferentiated arthritis or psoriatic arthritis and those with IBD-related arthritis or reactive arthritis were classified as SpA, while PolyA included those meeting the ILAR criteria for polyarticular JIA or extended oligoarticular JIA. Patients with active IBD and severe psoriasis (involvement of BSA >10%) were excluded. After enrollment, parents filled out the CBCL for their children while both providers and parents contributed to the Juvenile Arthritis Disease Activity Score (JADAS) using the clinical JADAS10. We abstracted demographic and clinical data from the charts and presented the findings for the two arthritis groups. Primary outcome measures were CBCL total competence, internalizing, externalizing and total problem raw scores. We compared the outcomes from each group to the national CBCL normative data. As exploratory analyses, we also looked at OCD problem scores, self-harm, and individual internalizing and externalizing syndrome scores which were identified apriori. To investigate the relationship between CBCL scores and disease activity, we ran a generalized linear regression model for all arthritis patients with JADAS as the main predictor to control for age, sex and medical co-morbidities.

Results: Our study includes 111 patients (53 with SpA and 58 with PolyA) and 1753 healthy controls. Median age at enrollment is 13-14 years. Most of our patients were on arthritis medications at the time of completing CBCL (table 1).

	Spondyloarthritis (n=53)	Polyarthritis (n=58)
Demographic characteristics		
Age at CBCL (years)	14.0 +/- 3.0	13.0 +/- 6.0
Age at diagnosis (years)	11.5 +/- 4.1	6.6 +/- 6.9
Duration of illness since diagnosis (years)	1.8 (3.6)	6.6 (7.9)
Sex		
Male	26 (49.1)	14 (24.1)
Female	27 (50.9)	44 (75.9)
Race/ethnicity[a]		
Non-Hispanic white	21 (39.6)	26 (44.8)
Non-Hispanic black	1 (1.9)	0
Non-Hispanic Asian	6 (11.3)	3 (5.2)
Hispanic	11 (20.8)	17 (29.3)
Other	9 (17.0)	6 (10.3)
Unknown	5 (9.4)	6 (10.3)
Clinical characteristics		
Taking rheumatologic medication[b]	**44 (83.0)**	**54 (93.1)**
NSAID alone	**8 (15.0)**	**7 (12.1)**
DMARD +/- NSAID	**8 (15.1)**	**8 (13.8)**
Biological agents alone +/- NSAID	**22 (41.5)**	**22 (37.9)**
Combination of DMARD and biological agents	**6 (11.3)**	**17 (29.3)**
Medical co-morbidities[c]	32 (60.4)	25 (43.1)
HLA-B27		
Positive	18 (34.0)	1 (1.7)
Negative	23 (43.4)	16 (27.6)
Not done	12 (22.6)	41 (70.7)
JADAS	3.9 +/- 5.7	2.6 +/- 6.1
Physician global assessment	0.5 +/- 1.8	0.5 +/- 1.8
Parent global assessment	1.5 +/- 3.2	1.6 +/- 2.4
Active joint counts	0 +/- 1.0	0 +/- 3.0
Active disease (cJADAS10>1)	41 (77.4)	44 (75.9)
Active disease (cJADAS10>2)	33 (62.3)	33 (56.9)

Data are presented as n (%) for categorical variables, and median +/- interquartile range for continuous variables.

[a]Self-reported race and ethnicity

[b]Rheumatologic medication includes NSAID, methotrexate, TNF inhibitor, sulfasalazine, tociliuzimab, abatacept, leflunomide, oral steroids, janus kinase (JAK) inhibitors, and mycophenolate mofetil.

[c]Medical co-morbidites are defined as any current medical diseases through chart reviews and CBCL questionnaires, excluding psychiatric and developmental disorders.

Table 1. Demographic and clinical characteristics of patients with spondyloarthritis or polyarthritis

When compared to healthy controls, patients with SpA or PolyA had worse total competence and internalizing scores (mainly driven by somatic complaints) but better externalizing scores. Self-harm was almost four times more likely in patients with PolyA than healthy controls (table 2). Higher JADAS was associated with worse total competence scores, worse internalizing scores (mainly driven by anxiety/depression) and higher total problem scores (table 3). Most of these differences reached statistical significance ($p< 0.01$).

	Spondyloarthritis (n=53)		Polyarthritis (n=58)	
	Adjusted difference (with reference to healthy controls)[a]	P value	Adjusted difference (with reference to healthy controls)[a]	P value
Total competence	-1.5 (0.6)	0.018	-1.6 (0.6)	0.006*
Internalizing problems	1.5 (0.7)	0.047	1.9 (0.7)	0.007*
Anxious/depressed	-0.1 (0.4)	0.916	0.6 (0.4)	0.144
Withdrawn/depressed	0.4 (0.3)	0.206	0.2 (0.3)	0.439
Somatic complaints	1.2 (0.3)	<0.001*	1.2 (0.2)	<0.001*
Externalizing problems	-2.7 (0.9)	0.004*	-1.9 (0.9)	0.033
Rule-breaking behavior	-1.1 (0.4)	0.004*	-1.1 (0.4)	0.002*
Aggressive behavior	-1.6 (0.6)	0.012*	-0.8 (0.6)	0.189
Total problems	-3.3 (2.5)	0.191	-0.3 (2.4)	0.906
OCD problems	-0.1 (0.2)	0.684	0.1 (0.2)	0.075
Self-harm[b]	0.8 (0.1-5.9)[b]	0.817	3.6 (1.3-9.6)[b]	0.011*

Scores in bold are primary outcome measures. Raw scores are used to account for the full-range variation.
*Statistically significant p values with the level of significance set at 0.013 which is 0.05 divided by 4.
[a]age and sex adjusted
[b]Logistic regression model for a binary outcome derived from two CBCL problem question 18 (deliberately harms self or attempts suicide) and question 91 (talks about killing self); result is presented as odds ratio (95% confidence interval).

Table 2. Age and sex adjusted differences in CBCL raw scores between patients with spondyloarthritis or polyarthritis and healthy controls.

	Spondyloarthritis (n=53)		**Polyarthritis (n=58)**	
	Adjusted difference by each point increase in JADAS (SE)[a]	P value	Adjusted difference by each point increase in JADAS (SE)[a]	P value
Total competence	-0.4 (0.1)	0.009*	-0.3 (0.1)	<0.001*
Internalizing problems	0.5 (0.2)	0.007*	0.3 (0.2)	0.088
Anxious/depressed	0.3 (0.1)	0.004*	0.1 (0.1)	0.482
Withdrawn/depressed	0.1 (0.1)	0.179	0.1 (0.1)	0.045
Somatic complaints	0.1 (0.1)	0.167	0.1 (0.1)	0.038
Externalizing problems	0.1 (0.1)	0.710	0.1 (0.1)	0.766
Rule-breaking behavior	-0.1 (0.1)	0.836	0.1 (0.1)	0.094
Aggressive behavior	0.1 (0.1)	0.528	-0.1 (0.1)	0.743
Total problems	1.0 (0.4)	0.023	0.6 (0.5)	0.218
OCD problems	0.1 (0.1)	0.218	0.1 (0.1)	0.521

Scores in bold are primary outcome measures. Raw scores are used to account for the full-range variation.
*Statistically significant p values with the level of significance set at 0.013 which is 0.05 divided by 4.
[a]Adjusted for JADAS, age, sex and medical comorbdities.

Table 3. Adjusted differences in CBCL raw scores, by cJADAS10, in patients with spondyloarthritis or polyarthritis

Conclusion: Our study shows patients with arthritis and more active disease have worse total competence scores and internalizing scores reported by parents, suggesting functional deterioration in activities, school and socialization and more internalized emotional disturbances.

Disclosure: A. McHugh, None; **A. Chan**, None; **C. Herrera**, None; **M. Thienemann**, None; **J. Frankovich**, None.

Abstract Number: 2706

Association of Body Mass Index with Juvenile Idiopathic Arthritis Disease Activity: A Portuguese and Brazilian Collaborative Analysis with Data from Reuma.pt Registry

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

Session Type: Poster Session (Tuesday)

Session Time:9:00AM–11:00AM

Background/Purpose: In adults with Rheumatoid Arthritis, obesity has been associated with higher disease activity. However, in Juvenile Idiopathic Arthritis (JIA), the influence of body mass index (BMI) on disease activity is uncertain and a previous study has failed to find any association. We aim to clarify the relationship between BMI and JIA disease activity.

Methods: An international, multicenter, observational analysis was conducted. JIA patients (according to ILAR criteria) aged ≤ 18 years, registered at Rheumatic Diseases Portuguese Register (Reuma.pt) in Portugal and Brazil were included. Anonymized data of the first registered visit was analyzed. Age- and sex-specific BMI percentiles (P) were calculated based on WHO growth standard charts and categorized into underweight (P< 3), normal weight (3≤P≤85), overweight (85< P≤97) and obesity (P >97). Disease activity was assessed by Juvenile Arthritis Disease Activity Score (JADAS-27). Univariate linear regression was used to examine the association of BMI categories with JADAS-27. Two multivariate regression models were performed: a) adjusting for gender, ethnicity, country, disease duration and JIA category (model 1); b) adjusting for those covariates plus use of oral glucocorticoids (GC) and DMARDs (model 2).

Results: 275 patients included, mean age 10.2±4.6 years, mean disease duration 6.1±4.9 years; 62% female. Thirty-two percent were persistent oligoarticular, 8% extended oligoarticular, 26% RF- polyarticular, 7% RF+ polyarticular, 6% systemic, 15% enthesitis-related arthritis, 5% psoriatic arthritis and 1% undifferentiated arthritis. The prevalence

Table 1. Relationship between JADAS-27 (dependent variable) and demographic and clinical characteristics of JIA patients.

	Univariate analysis			Multivariate analysis					
				Model 1 (R^2 = 0.235)			Model 2 (R^2 = 0.303)		
	B	95% CI	*p*-value	B	95% CI	*p*-value	B	95% CI	*p*-value
Age, years	-0.281	[-0.501 – (-0.061]	**0.013**		-			-	
Disease duration, years	-0.360	[-0.580 -(-0.141)]	**0.001**	-0.363	[-0.564-(-0.161)]	**<0.001**			
Gender (female)	0.081	[-2.059 – 2.222]	0.940						
Country (Portugal)	-5.403	[-8.575- (-2.230)]	**0.001**						
Ethnicity									
White european*									
White non-european	-3.652	[-9.789 – 2.485]	0.242						
Black	6.985	[0.848 – 13.123]	**0.026**	5.298	[0.286 - 10.476]	**0.046**			
Biracial	-4.244	[-11.303 – 2.815]	0.238						
Romani	1.223	[-10.907 – 13.353]	0.843						
Asiatic	-0.727	[-10.651- 9.197]	0.885						
JIA category									
Persistent oligoarthritis*									
Extending oligoarthritis	-1.241	[-5.083-2.602]	0.525						
RF-positive polyarthritis	6.203	[3.626-8.780]	**<0.001**	7.076	[3.223 – 10.928]	**<0.001**	5.287	[0.707 – 9.866]	**0.024**
RF-negative polyarthritis	8.763	[4.681-12.845]	**<0.001**	4.901	[2.602 – 7.201]	**<0.001**	3.653	[1.039 – 6.267]	**0.006**
Systemic-onset	3.020	[-1.493 – 7.533]	0.189						
Enthesitis-related arthritis	2.205	[-0.882 – 5.292]	0.161						
Psoriatic arthritis	2.936	[-1.715 – 7.586]	0.215						
Undifferentiated arthritis	9.000	[-2.614 – 20.614]	0.128						
BMI									
Underweight*									
Normal weight	-9.865	[-13.838 – (-5.892)]	**<0.001**	-9.429	[-13.338-(-5.519)]	**<0.001**	-9.430	[-13.753 – (-5.107)]	**<0.001**
Overweight	-10.596	[-15.156 – (-6.036)]	**<0.001**	-9.309	[-13.818-(-4.800)]	**<0.001**	-9.295	[-14.482 – (-4.108)]	**0.001**
Obesity	-7.510	[-12.378 – (-2.642)]	**0.003**	-7.310	[-12.124-(-2.496)]	**0.003**	-9.120	[-14.445 – (-3.795)]	**0.001**
Oral GC use	4.151	[0.755 – 7.547]	**0.017**				4.984	[1.820 – 8.147]	**0.002**
cDMARD use	-3.399	[-5.885-(-0.783)]	**0.011**					-	
bDMARD use	-2.707	[-6.153-0.739]	0.123					-	
Any DMARD use	-4.912	[-7.489-(-2.335)]	**<0.001**				-5.542	[-7.939 - (-3.145)]	**<0.001**

*Reference group

Model 1: adjusting for gender, country, ethnicity, disease duration and JIA category.
Model 2: adjusting for those covariates plus use of GC and DMARDs.

of underweight, normal weight, overweight and obesity was 6.9%, 67.3%, 15.3% and 10.5%, respectively. In the univariate linear regression, underweight was significantly associated with higher JADAS-27, compared to normal weight (p< 0.001), overweight (p< 0.001) and obesity (p=0.003). Younger age (p=0.013), shorter disease duration (p=0.001), black race (p=0.026), living in Brazil (p=0.001), RF- polyarthritis (p< 0.001), RF+ polyarthritis (p< 0.001), the absence of DMARD therapy (, p< 0.001) and the use of GC (p=0.017) were also associated with higher JADAS-27 (table 1). In the model 1 of multivariate analysis, the same variables, except the country, remained significantly associated with higher disease activity. When GC and DMARD therapies were added to the model (model 2), the association of normal weight (p< 0.001), overweight (p< 0.001) and obesity (p=0.003) with lower disease activity persisted significant, compared to underweight patients, as well as those under DMARD therapy (p< 0.001). RF- (p=0.006) and RF+ polyarthritis (p=0.024) and the use of oral GC (p=0.002) were associated with higher disease activity.

Conclusion: There seems to be an independent association between underweight and higher disease activity in JIA patients, suggesting that active disease can impair child's weight gain. Longitudinal analysis are needed to confirm these findings and understand the underlying mechanisms of this association.

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Abstract Number: 2707

Improvement in Patient-Reported Outcomes in Patients Aged 2–5 Years with Polyarticular-Course JIA Treated with Subcutaneous Abatacept: 2-Year Results from a Phase III International Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Efficacy of SC abatacept in patients with polyarticular-course JIA (pJIA) was shown in a 2-year, open-label, Phase III international study (NCT01844518).[1] Pediatric patient-reported outcomes (PROs) were improved with IV and SC abatacept in patients aged 6–17 years.[2,3] Here we report the effect of SC abatacept on PROs (Activity Limitation Questionnaire [ALQ], Childhood HAQ-Disability Index [CHAQ-DI], Pain Assessment and Parent Global Assessment of Overall Patient Well-being [PaGA]) in the 2–5-year-old patients with active pJIA over 2 years.

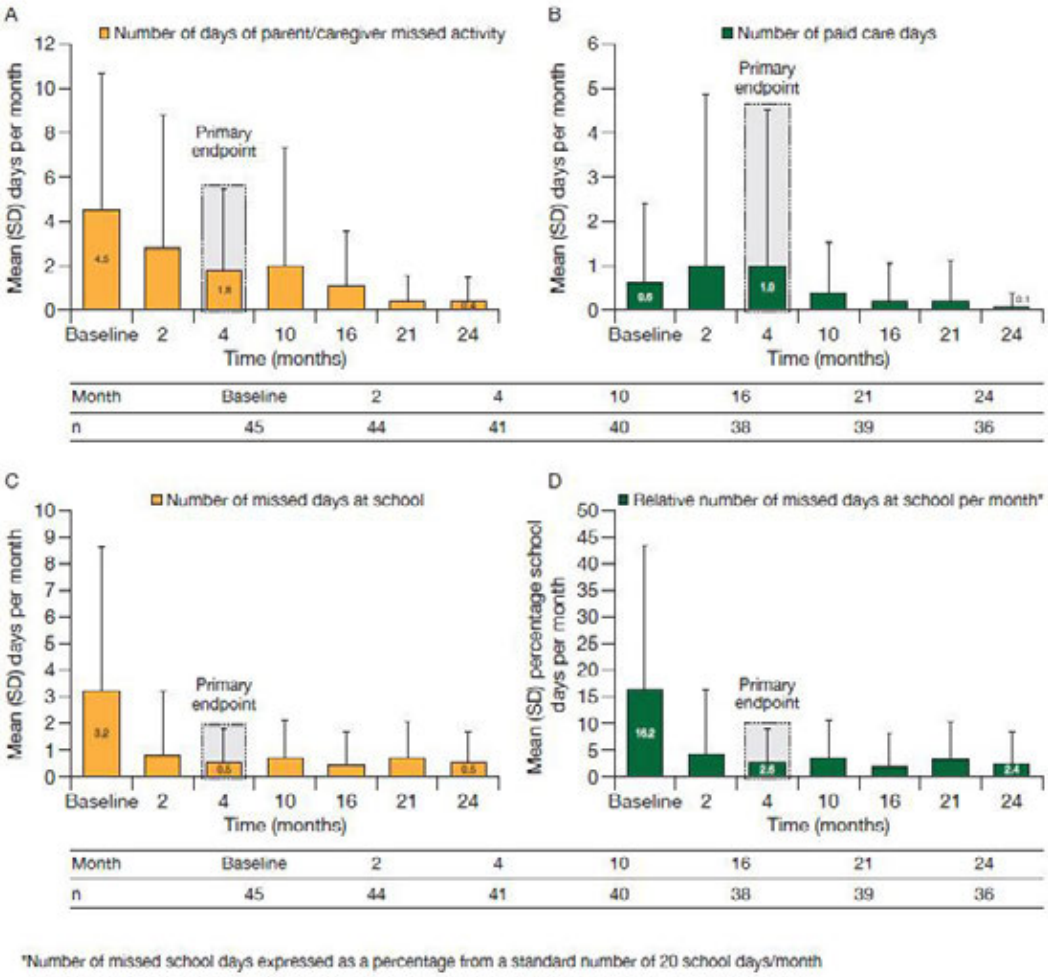
Methods: Patients with pJIA were grouped into two age cohorts (2–5 and 6–17 years) and received weight-tiered SC abatacept (10 to < 25 kg [50 mg], 25 to < 50 kg [87.5 mg], ≥50 kg [125 mg]) weekly for 4 months. JIA-ACR30 criteria

Table. CHAQ-DI, Pain and PaGA Scores Over Time in the 2–5-Year Cohort

	Baseline (n=46)	Month 2 (n=46)	Month 4 (n=42)	Month 16 (n=40)	Month 24 (n=37)
CHAQ-DI	1.1 (0.66)	0.8 (0.69)	0.6 (0.64)	0.5 (0.53)	0.4 (0.49)
Pain (mm VAS)	39.6 (27.02)	22.2 (22.91)	17.8 (22.21)	14.1 (17.62)	7.5 (10.33)
PaGA (mm VAS)	38.6 (23.94)	22.1 (20.48)	15.2 (17.22)	11.8 (15.90)	8.3 (12.72)

Data are mean (SD). For CHAQ-DI (scale 0–3), pain (0–100 mm VAS) and PaGA (0–100 mm VAS), higher scores indicate greater dysfunction and pain, and lower well-being, respectively
CHAQ-DI=Childhood HAQ-Disability Index; PaGa=Parent Global Assessment of Overall Patient Well-being; VAS=visual analog scale

Figure. Change Over Time in Activities of Daily Living Limitation: (A) Days of Parental/Caregiver Missed Activity; (B) Paid Care Days; (C) Missed School Days [Absolute Values]; (D) Missed School/Nursery Days [Relative Values]) in 2–5-Year-Old Patients



*Number of missed school days expressed as a percentage from a standard number of 20 school days/month

responders at Month 4 could receive SC abatacept for another 20 months.[1] For the 2–5-year cohort reported here, ALQ (mean [SD] number of days of parental/caregiver missed activity, paid care and missed school [absolute values per month and percentage of days missed per month relative to an assumed average of 20 school days/month]), CHAQ-DI (0–3 scale across 8 domains of disability component), pain (0–100 mm visual analog scale [VAS]) and PaGA (0–100 mm VAS) were evaluated.

Results: Baseline characteristics of the 46 patients with pJIA from the 2–5-year cohort included median (min, max) age of 4.0 (2.0, 5.0) years and median (interquartile range) number of active joints of 7.0 (6.0, 12.0). At baseline, 80.4% of patients received MTX (median dose: 13.3 mg/m^2/week) and 21.7% of patients had prior biologic failure. CHAQ-DI, pain and PaGA improved from baseline to Month 24 (Table). Most ALQ components improved from baseline to Month 4 (primary endpoint); these improvements were largely maintained over time to Month 24 (Figure). Relative percentage of days missed from school decreased from 16.2% (baseline) to 2.4% (Month 24, Figure D).

Conclusion: In this analysis of patients with pJIA aged 2–5 years, SC abatacept demonstrated a beneficial effect on PROs including improvement in well-being (PaGA) and reductions in disability (CHAQ-DI), pain and activity limitation (ALQ) over 24 months.

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Abstract Number: 2708

Effect of Immunogenicity on Efficacy and Safety of Subcutaneous or Intravenous Abatacept in Pediatric Patients with Polyarticular-Course JIA: Findings from Two Phase III Trials

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Table 1. Prevalence of ADAs in Pts Aged 2–5 and 6–17 Yrs With pJIA Treated With SC ABA

Period	Anti-CTLA-4	Anti-IgG1	Total
2–5-yr-old cohort			
Overall, on treatment	2/46 (4.3)	3/46 (6.5)	5/46 (10.9)
Overall, follow-up visits*	2/8 (25.0)	1/8 (12.5)	3/8 (37.5)
Overall	4/46 (8.7)	3/46 (6.5)	7/46 (15.2)
6–17 yr old cohort			
Overall, on treatment	1/172 (0.6)	3/172 (1.7)	4/172 (2.3)
Overall, follow up visits*	4/44 (9.1)	2/44 (4.5)	6/44 (13.6)
Overall	5/172 (2.9)	3/172 (1.7)	8/172 (4.7)

Data are n/m (%); m indicates total number of patients with evaluable data

*Visits on Months 1, 3 and 6 after the last ABA dose

ABA=abatacept; ADA=anti-drug antibody; CTLA-4=cytotoxic T lymphocyte-associated antigen-4; pJIA=polyarticular-course JIA; pt=patient; yr=year

Table 2. Prevalence of ADAs in Pts Aged 6–17 Yrs With pJIA Treated With IV ABA

Period and treatment	Anti-CTLA4	Anti-IgG1	Total
Period A			
ABA	4/188 (2.1)	0/162	4/188 (2.1)
Period B			
ABA	7/55 (12.7)	0/49	7/55 (12.7)
PBO	22/54 (40.7)	0/46	22/54 (40.7)
Period C			
Overall, on treatment	12/148 (8.1)	8/139 (5.8)	19/148 (12.8)
Overall, follow-up visits	6/115 (5.2)	6/104 (5.8)	12/115 (10.4)
Overall	16/150 (10.7)	11/141 (7.8)	26/150 (17.3)

Data are n/m (%), m indicates total number of patients with evaluable data

ABA=abatacept; ADA=anti-drug antibody; CTLA-4=cytotoxic T lymphocyte-associated antigen-4; PBO=placebo; pJIA=polyarticular-course JIA; pt=patient; yr=year

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients (pts) with polyarticular-course JIA (pJIA) may develop anti-drug antibodies (ADAs) in response to biologics.[1] Presence of ADAs has been associated with treatment (tmt) failure and hypersensitivity in pts with pJIA.[1] Abatacept (ABA), a fully human co-stimulation modulator, consists of the extracellular domain of cytotoxic T lymphocyte–associated antigen-4 (CTLA-4) linked to Fc portion of IgG1. Here we evaluate immunogenicity (IMG) of SC and IV ABA, and effect of IMG on efficacy, pharmacokinetics (PK) and safety in an open-label (OL), Phase III study of SC ABA (NCT01844518) and in a double-blind, Phase III study of IV ABA (NCT00095173).

Methods: Study design and eligibility criteria for both studies were reported previously.2,3 In the SC study, pts with pJIA and prior DMARD failure were stratified by age cohort (2–5 and 6–17 years [yrs]) to receive weight-tiered SC ABA (10 to < 25 kg [50 mg], 25 to < 50 kg [87.5 mg], ≥50 kg [125 mg]) weekly for 4 months. JIA-ACR30 responders at Month 4 could receive SC ABA for another 20 months.2 ADAs were detected by electrochemiluminescence. In the IV study, pts with pJIA and prior DMARD failure received OL IV ABA (10 mg/kg body weight) for 4 months (Period A); JIA-ACR30 criteria responders at Month 4 were randomized 1:1 to receive IV ABA (10 mg/kg) or placebo (PBO) for 6 months or until flare (Period B). Pts could receive OL ABA in a 5-yr follow-up (Period C).3 ADAs were detected by ELISA.

Results: In the SC study, ADA rate was low in both cohorts (Table 1). In the 2–5-yr cohort, of 3 ADA positive (+) CTLA-4-specific pts, 2 had neutralizing antibodies detected (ADA-NAb+); no 6–17-yr-old pts (of 3 ADA+ CTLA-4-specific) were ADA-NAb+ over 24 months. ADA positivity on tmt did not impact JIA-ACR30 response. ABA steady-state serum trough concentration was similar between ADA+ and ADA negative pts (data not shown). Pts treated with ABA+MTX, but not with ABA alone, developed ADAs in the 2–5- (7/36 [19.4%]) and 6–17-yr (8/135 [5.9%]) cohorts.

In the IV study, ADAs were infrequent for pts who remained on ABA versus those on PBO (Table 2). Of 6 ADA+ pts with ADA-NAb assessments, 3 were ADA-NAb+ in Period C. In Period B, of 7 ABA-treated pts with flare and 47 ABA-treated pts without flare, respectively, 0 and 7 (14.9%) were ADA+ CTLA-4-specific; in the PBO arm, 7/26 (26.9%) and 15/28 (53.6%) pts with and without flare, respectively, were ADA+ CTLA-4-specific. In Period A, 2/140 (1.4%) ABA+MTX-treated pts and 2/49 (4.1%) pts treated with ABA alone developed ADAs. Pts treated with ABA+MTX, but not pts treated with ABA alone, developed ADAs during Period B (7/45 [15.6%]).

No new safety signals, including those suggestive of hypersensitivity were reported in ADA+ pts in either study.

Conclusion: IMG of SC and IV abatacept was low and did not have any impact on the efficacy, PK and safety of abatacept. Contrary to previous reports for other biologics,[1] in this study, MTX did not lower the incidence of ADAs when co-dosed with abatacept.

References:

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3. Ruperto N, et al. *Lancet* 2008;**372**:383–91.

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Abstract Number: 2709

Secukinumab Is a Promising Treatment for Patients with Juvenile Enthesitis Related Arthritis Nonresponsive to Anti-TNF Treatment According the Juvenile Spondyloarthritis Disease Activity Index

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Secukinumab (SEC) is licensed to treat adults with spondyloarthritis and psoriatic arthritis. It is not licensed for juvenile patients yet. As biologic agents up till now only etanercept and adalimumab are licensed for enthJIA. Not all enthJIA patient reaching remission with an anti-TNF therapy. We review our patients, who did not reach remission under anti-TNF and were switched to SEC.

Methods: We conducted a retrospective monocentric chart review of patients with enthJIA, who were ever treated with SEC with enthJIA, at least for 3 months till 15thof March 2019. We used the JADAS10 and the Juvenile Spondyloarthritis Disease Activity Index (jspADA) [1]to evaluate response.

Results: 17 patients with enthJIA were treated till 15thof March 2019. 77 % were female. The mean age of the patients at the start of the treatment was 19.5 years. The mean disease duration was 6.3 years. The patients received in average 1.9 different anti-TNF´s before switching to SEC. The JADAS-10 was 8.3 and the jspADA 2.4 at the time initiation of SEC. SEC was applied according the adult dosing schedule, the mean weight of the patients was 65 kg. The mean dose at week 0 was 185 mg/dose, at 12 months 270 mg/dose (n=15) and at 24 months 280mg/dose (n=9). Mean follow up of the patients under SEC was18months. JADAS 10 dropped from 8.35 at timepoint 0 to 5.8 at 3 months (n=17); 5.1 at 6 months (n=16), 5.5 at 12 months (n=15) and to 6.5 at 24 months (n=9) . jspADA, a more sensitive outcome parameter for enthJIA dropped from 2.41 at timepoint 0 to 1.6 at 3 months (n=17); 1.7 at 6 months (n=16), 1.2 at 12 months (n=15)and to 1.3 at 24 months (n=9) . In two patients SEC after 24 months was switched to tofacitinib, because of nonresponse. There was no SAE observed.

Conclusion: In our anti-TNF nonresponder patients SEC showed quite good effectiveness regarding the improvement in jspADA and less in JADAS 10, which is less specific for enthJIA. The 150 mg dose seems to be not sufficient in anti-TNF nonresponder patients, in most of the patients the dose had to be increased to 300 mg /dose per application.

Reference:

1. Weiss, P.F., et al., *Development and retrospective validation of the juvenile spondyloarthritis disease activity index* .Arthritis Care Res (Hoboken), 2014. **66**(12): p. 1775-82.

Disclosure: I. Foeldvari, Beyer, 5, BMS, 5, Glaxo, 5, Inventa, 5, Novartis, 5; **J. Baer**, None.

Abstract Number: 2710

Sarilumab, a Human Monoclonal Antibody to the Interleukin-6 Receptor, in Polyarticular-course Juvenile Idiopathic Arthritis: A 12-week, Multinational, Open-label, Dose-finding Study

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SESSION INFORMATION

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Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Sarilumab blocks interleukin-6 (IL-6) from binding to membrane and soluble IL-6 receptor-α. Sarilumab is approved for adults with rheumatoid arthritis (RA) and is being investigated in a Phase 2 trial (NCT02776735) in 2–17-year-old patients (pts) with polyarticular-course juvenile idiopathic arthritis (pcJIA), comprising rheumatoid-factor (RF)-positive and RF-negative polyarticular and extended oligoarticular JIA. This study aimed to evaluate pharmacokinetics (PK), pharmacodynamics (PD), safety, and efficacy of 3 subcutaneous (SC) sarilumab doses in pcJIA.

Figure: Mean (CV%) individual sarilumab exposure, following first SC dose, and after repeated SC administration at Weeks 10–12 or Weeks 11–12, in patients with pcJIA

pcJIA treatment		First SC administration			Repeated SC administration (Weeks 10–12 or Weeks 11–12)		
Patient weight group	Sarilumab dose	N	C_{trough} mg/L (CV%)	$AUC_{0-\tau}$ day mg/L (CV%)	N	C_{trough} mg/L (CV%)	$AUC_{0-\tau}$ day mg/L (CV%)
10–<30 kg (Group B)	2.5 mg/kg q2w	6	0.54 (48)	63 (30)	5	1.83 (101)	118 (37)
	4.0 mg/kg q2w	7	3.77 (43)	167 (26)	7	11.90 (41)	310 (26)
	2.5 mg/kg qw	9	5.22 (39)	45 (36)	5	25.10 (29)	203 (25)
30–60 kg (Group A)	2.0 mg/kg q2w	7	0.63 (63)	53 (46)	5	1.99 (86)	114 (18)
	3.0 mg/kg q2w	7	1.84 (69)	123 (24)	6	8.46 (68)	269 (34)
	2.0 mg/kg qw	6	8.07 (32)	61 (22)	6	30.40 (28)	250 (24)

AUC, area under the serum concentration versus time curve, calculated using trapezoidal method during a dose interval; C_{trough}, serum concentration observed before treatment administration during repeated dosing; CV, coefficient of variance; N, number of patients; pcJIA, polyarticular-course juvenile idiopathic arthritis; qw, every week; q2w, every 2 weeks; SC, subcutaneous.

Dose interval ($_\tau$) was 2 weeks for q2w, or 1 week for qw regimen.

Methods: A 12-week dose-finding study was performed to identify an appropriate sarilumab dose for use in the pcJIA population. Pts were divided by body weight into 2 groups: A (30–60 kg) and B (10–< 30 kg), and received sequential ascending doses of sarilumab, Dose 1 (Group A/B): 2.0/2.5 mg/kg q2w; Dose 2 (Group A/B): 3/4 mg/kg q2w; and Dose 3 (Group A/B): 2.0/2.5 mg/kg qw. pcJIA doses were targeted to achieve similar exposure to adult RA doses (150 mg q2w, 200 mg q2w, and 150 mg qw). Primary outcome was PK; secondary outcomes were safety, PD, and efficacy of sarilumab.

Results: 42 pts enrolled (20/22 in Groups A/B); mean age was 13.0/5.2 years. At baseline, mean pcJIA duration, number of active joints, and JADAS27-CRP were 4.6/1.7 years, 17.2/11.0, and 22.2/19.1, in Groups A/B, respectively. As in adult pts, sarilumab exhibited nonlinear PK with target-mediated drug disposition (TMDD). Following repeated SC administrations, exposure increased in a greater than dose-proportional manner and accumulated 1.9–4.5-fold over 12 weeks. Sarilumab exposure was similar in both weight groups for each dose (Figure), and comparable to corresponding adult doses. Treatment-emergent adverse events (AEs) were reported in 36/42 (85.7%) pts (comparable across dose and weight groups); infections (28/42, 66.7%) were the most frequently reported AE. 12 grade 3/4 neutropenias were identified, mostly in Dose 3 (n=6) and in Group B (n=8). None was associated with infection; all resolved in a few days. Overall, 4 pts discontinued due to neutropenia and 1 due to alanine aminotransferase increase. There were no serious AEs, no cases of GI perforation, and no deaths. By Week 12, as observed while on-treatment: all pts attained JIA ACR30; 50%, 62%, and 100% of pts attained JIA ACR70 with Doses 1, 2, and 3, respectively; JADAS27-CRP mean % changes from baseline in Doses 1, 2, and 3 were –74.6%, –73.1%, and –87.9%, respectively.

Conclusion: Sarilumab exhibited nonlinear PK with TMDD. Doses tested in pcJIA yielded similar exposure in both weight groups and were comparable to equivalent doses in adults with RA. All dose regimens proved effective for decreasing disease activity. Safety profile was consistent with class effects; higher incidences of neutropenia were observed with Dose 3, and in pts weighing 10–< 30 kg.

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Abstract Number: 2711

Utilization of Biologic Treatments in Oligoarticular and Polyarticular Juvenile Idiopathic Arthritis

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SESSION INFORMATION

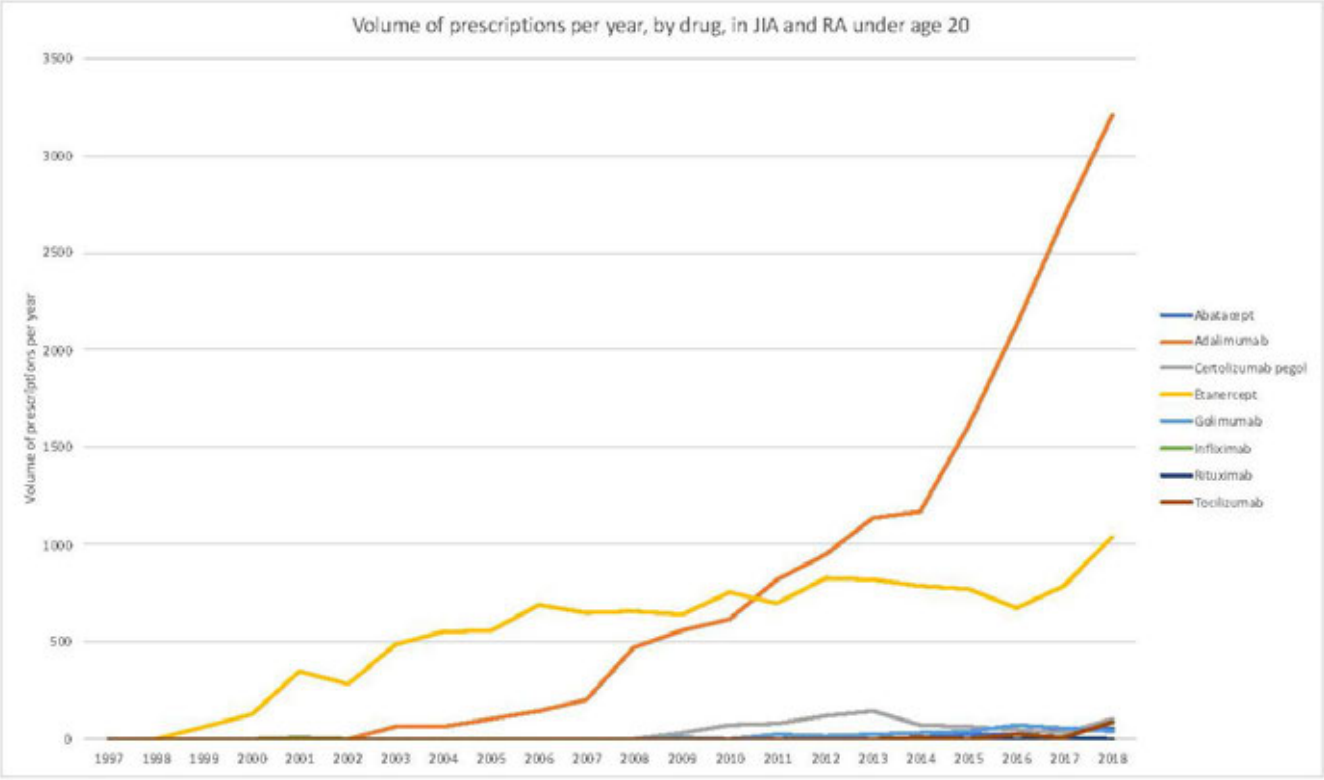
Session Date: Tuesday, November 12, 2019

Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: In recent years, juvenile idiopathic arthritis (JIA) treatment options have expanded to include biologics such as tumor necrosis factor inhibitors (TNF_i) and non-TNF inhibitors (non-TNF_i). While several studies have characterized utilization of these drugs in adults, few have done so in pediatric and adolescent settings. In this study, we aimed to characterize the trends in biologic utilization among patients with oligoarticular and polyarticular arthritis in the United States.



Volume of prescriptions by year, by drug in JIA and RA under the age of 20

Methods: We performed a retrospective cohort analysis using a large US commercial insurance database to identify patients with a diagnosis of JIA between January 1, 1997 and October 19, 2018. To identify cases of oligoarticular and polyarticular JIA, we included diagnosis codes for JIA (ICD-9 714.3; ICD-10 M08) or rheumatoid arthritis (ICD-9 714.x; ICD-10 M06) under age 20. We identified biologic therapies claims by biologic generic names that included: TNF_i drugs: etanercept, adalimumab, infliximab, golimumab and certolizumab pegol and non-TNF_i drugs: tocilizumab, abatacept and rituximab. Prescription patterns (initiation, switches, and persistence) were described overall, and by drug.

Results: A total of 29,537 unique biologic prescriptions were identified, with prescription volume increasingly steadily over the years examined. Approximately three-fifths (59%) of prescriptions were for females, and the median age of biologic recipients was 16 years (interquartile range 13-18 years). Etanercept accounted for approximately 41% of total prescriptions and increased relatively steadily between 1998 and 2018, whereas adalimumab accounted for more than half (54%) of total prescriptions and increased gradually between 2002 and 2007, moderately between 2007 and 2014 and sharply between 2014 and 2018. Certolizumab pegol, while not approved for use in JIA in the US, comprised approximately 3% of all biologic prescriptions, while other biologics accounted for less than 1% of total volume observed.

Conclusion: To our knowledge, this study is one of the first to examine long-term trends in the biologic treatment of oligoarticular and polyarticular JIA in the US. During the examination period the market was dominated by etanercept and adalimumab with a trend toward a sharp increase of adalimumab use starting in 2014.Further analyses will examine patient-level factors associated with biologic initiation, adherence and persistence in children and adolescents with JIA, as well as the effect that utilization management strategies, clinician and patient preferences may have on the patterns observed.

Disclosure: D. Basodan, None; **K. Andersen**, National Heart, Lung and Blood Institute (NHLBI) Pharmacoepidemiology T32 Training Program (T32HL139426-01)., 2, National Heart, Lung and Blood Institute Pharmacoepidemiology T32 Training Program (T32HL139426-01)., 2; **X. Li**, None; **J. Curtis**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **G. Alexander**, Chair of FDA's Peripheral and Central Nervous System Advisory Committee, 9, Monument Analytics, a health care consultancy whose clients include the life sciences industry as well as plaintiffs in opioid litigation, 4, 5, OptumRx's National P&T Committee, 6, Serves as a paid advisor to IQVIA, 5, This arrangement has been reviewed and approved by Johns Hopkins University in accordance with its conflict of interest policies..

Abstract Number: 2712

Patterns of Etanercept Use in the Childhood Arthritis and Rheumatology Research Alliance Juvenile Idiopathic Arthritis Registry

Natalie Shiff,[1] Aimee Lougee,[2] Roland Matsouaka,[2] David Collier,[3] Yukiko Kimura,[4] Dax Rumsey,[5] Jennifer Schenfeld,[6] Scott Stryker,[3] Marinka Twilt,[7] and Timothy Beukelman[8], [1]University of Florida, Gainesville, FL, [2]Duke University, Durham, NC, [3]Amgen Inc., Thousand Oaks, CA, [4]Joseph M Sanzari Children's Hospital, Hackensack University Medical Center, Cincinnati, OH, [5]University of Alberta, Edmonton, AB, Canada, [6]Amgen, Inc, Thousand Oaks, CA, [7]University of Calgary, Calgary, AB, Canada, [8]University of Alabama Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose:: Etanercept (ETN) is an anti-tumor necrosis factor (anti-TNF) therapy that is FDA approved for the treatment of polyarticular juvenile idiopathic arthritis (JIA). This study describes the use of ETN in JIA patients enrolled in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) JIA Registry.

Methods: The CARRA Registry is a convenience cohort of children that includes patients with JIA. Retrospective data is collected at enrolment and prospective observational data is collected twice a year, as well as when a JIA medication is initiated. Data were collected from June 30, 2015 to June 30, 2018 from 60 U.S. and 3 Canadian clinical

Table 1. Characteristics of patients at start of ETN who had a clinical visit within 30 days, by JIA category*

Characteristic	All patients	PersistOligo¶	ExtOligo§	Poly RF+©	Poly RF-β	ERAδ	Psoriaticπ	SJIA⌘	Undiffθ
Number of patients	465	53	52	64	192	57	33	3	11
Female, n (%)	328 (70.5%)	35 (66.0%)	45 (86.5%)	53 (82.8%)	139 (72.4%)	26 (45.6%)	25 (75.8%)	2 (66.7%)	3 (27.3%)
Age at diagnosis, n	444	51	46	64	181	56	33	3	10
Median years (25th, 75th)	10.0 (5.0, 14.0)	5.0 (2.0, 10.0)	6.0 (3.0, 9.0)	13.0 (10.0, 15.0)	10.0 (5.0, 13.0)	11.0 (9.0, 14.0)	9.0 (2.0, 14.0)	6.0 (3.0, 17.0)	14.0 (11.0, 15.0)
Time from diagnosis to start of ETN, n	444	51	46	64	181	56	33	3	10
Median months (25th, 75th)	4.2 (1.2, 15.0)	14.4 (5.5, 48.0)	9.8 (3.0, 39.4)	2.5 (0.3, 8.3)	3.4 (1.1, 9.8)	4.6 (1.3, 19.4)	3.8 (0.8, 6.5)	4.1 (1.0, 88.3)	2.3 (0.9, 9.8)
Clinical features at time of ETN initiation:									
Active Enthesitis, %	67 (14.4%)	2 (3.8%)	4 (7.7%)	4 (6.3%)	15 (7.8%)	32 (56.1%)	8 (24.2%)	0	2 (18.2%)
Clinically active sacroiliitis, %	33 (7.1%)	0	1 (1.9%)	1 (1.6%)	4 (2.1%)	21 (36.8%)	4 (12.1%)	0	2 (18.2%)
Active joint count, n	457	52	51	64	190	53	33	3	11
Median (25th, 75th)	5.0 (2.0, 11.0)	1.5 (1.0, 2.0)	3.0 (1.0, 5.0)	7.5 (5.0, 16.5)	6.0 (3.0, 14.0)	3.0 (1.0, 9.0)	5.0 (2.0, 8.0)	2.0 (1.0, 20.0)	4.0 (3.0, 12.0)
CHAQ, n	369	45	43	47	149	47	26	2	10
Median (25-, 75-)	0.6 (0.1, 1.1)	0.1 (0.0, 0.6)	0.4 (0.0, 0.9)	1.1 (0.4, 1.5)	0.6 (0.1, 1.3)	0.5 (0.3, 0.9)	0.6 (0.3, 1.1)	0.5 (0.1, 0.9)	0.7 (0.3, 1.0)
cJADAS10, n	365	45	38	49	156	44	23	1	9
Median (25th, 75th)	13.0 (8.0, 18.0)	7.0 (4.5, 11.0)	10.0 (7.0, 12.5)	18.5 (12.0, 22.0)	15.0 (9.3, 20.0)	11.5 (7.8, 16.0)	13.0 (8.0, 17.0)	11.5 (11.5, 11.5)	11.0 (7.5, 14.0)
Physician Global, n	430	51	46	58	180	54	29	2	10
Median (25th, 75th)	4.0 (2.0, 5.0)	3.0 (2.0, 4.0)	3.0 (2.0, 4.0)	5.0 (3.0, 7.5)	4.0 (2.8, 6.0)	3.0 (2.0, 5.0)	4.0 (2.0, 5.0)	5.0 (3.5, 6.5)	3.0 (2.0, 5.0)
Patient Global, n	384	46	42	50	160	48	26	2	10
Median (25th, 75th)	4.0 (2.0, 6.0)	2.5 (0.0, 5.0)	3.0 (1.0, 5.0)	5.0 (3.0, 7.0)	4.0 (2.0, 6.0)	4.0 (2.0, 6.0)	3.0 (2.0, 6.0)	6.5 (6.0, 7.0)	2.0 (1.0, 5.0)
Pain VAS, n	306	42	32	37	122	42	21	2	8
Median (25th, 75th)	4.0 (2.0, 6.0)	2.5 (0.0, 6.0)	3.0 (1.5, 6.0)	5.0 (3.0, 7.0)	4.0 (2.0, 6.0)	5.0 (3.0, 7.0)	4.0 (1.0, 5.0)	5.5 (4.0, 7.0)	5.0 (3.0, 6.0)

*JIA category is defined as the ILAR category at ETN initiation (prior to or up to 30 days after or closest visit to initiation);¶PersistOligo=persistent oligoarticular JIA; §ExtOligo=extended oligoarticular JIA; ©Poly RF+=polyarticular rheumatoid factor positive JIA; βPoly RF-=polyarticular rheumatoid factor negative JIA; δERA=enthesitis related arthritis; πPsoriatic=psoriatic JIA; ⌘SJIA=systemic JIA; θUndiff=undifferentiated JIA

Table 2. Patterns of methotrexate (MTX) use at start of etanercept (ETN) therapy*

Characteristic	Combination therapy: MTX started concurrently with ETN (N = 258)	Step up therapy: MTX started >1 mo. prior to ETN and continued >1 mo. after ETN (N = 892)	MTX to ETN switchers: MTX started >1 mo. prior to ETN and disc. within 1 mo. prior to or after ETN (N = 172)	MTX added after ETN: MTX started >1 mo. after ETN (N = 144)	ETN only: no observed MTX use (N = 215)
JIA category**					
Oligoarthritis, %	34 (9.3%)	184 (50.3%)	66 (18.0%)	29 (7.9%)	53 (14.5%)
Persistent, %	13 (8.1%)	76 (47.2%)	24 (14.9%)	12 (7.5%)	36 (22.4%)
Extended, %	15 (8.3%)	101 (56.1%)	37 (20.6%)	15 (8.3%)	12 (6.7%)
Unknown, %	6 (20.0%)	11 (36.7%)	6 (20.0%)	2 (6.7%)	5 (16.7%)
Polyarthritis (RF -), %	113 (15.4%)	437 (59.4%)	67 (9.1%)	57 (7.7%)	62 (8.4%)
Polyarthritis (RF +), %	49 (23.6%)	109 (52.4%)	10 (4.8%)	23 (11.1%)	17 (8.2%)
Psoriatic arthritis, %	29 (21.6%)	59 (44.0%)	9 (6.7%)	12 (9.0%)	25 (18.7%)
Enthesitis related arthritis, %	23 (14.1%)	65 (39.9%)	11 (6.7%)	13 (8.0%)	51 (31.3%)
Systemic arthritis, %	4 (10.0%)	23 (57.5%)	3 (7.5%)	9 (22.5%)	1 (2.5%)
Undifferentiated arthritis, %	6 (17.6%)	15 (44.1%)	6 (17.6%)	1 (2.9%)	6 (17.6%)

*in patients with at least 1 study visit ≥6 months after starting ETN

sites were included in this analysis. JIA patients treated with ETN were included if the month and year of initiation were available. Concomitant methotrexate use was described for patients who had >1 follow-up visit ≥ 6 months after beginning treatment with ETN. Descriptive statistics including means, standard deviations, medians, and interquartile ranges for continuous variables, and proportions for categorical variables were calculated as appropriate.

Results: At the time of data extraction, there were 5641 patients with JIA in the registry, and 2032 patients met inclusion criteria (74% female, median age of diagnosis 6.0 years [25th and 75th percentiles 2.0, 11.0]). Reported JIA ILAR categories were: 22.5% oligoarticular, 42.6% polyarticular RF negative (RF- pJIA), 11.9% polyarticular RF positive (RF+ pJIA), 8.1% psoriatic, 10.2% enthesitis related arthritis (ERA), 2.6% systemic, and 2.0% undifferentiated. There were 465 participants with a study visit within 30 days of starting ETN (Table 1). Within this group, ETN was started ≤3 months after diagnosis by 38% and >3 months after diagnosis by 57% (5% missing), while 62% started a non-biologic DMARD prior to ETN, primarily MTX. By ILAR category, RF+pJIA had the highest active joint count and clinical Juvenile Arthritis Disease Activity Score limited to 10 joints (cJADAS10), followed by RF-pJIA (Table 1). Fifty three percent of RF- pJIA, 44% of RF+ pJIA and 58% of ERA with a study visit within 30 days of ETN initiation started ETN >3 months after diagnosis. Table 2 shows the pattern of MTX use in individuals with at least one visit 6 months after starting ETN (n=1681). In all categories of JIA, the most common treatment approach was adding ETN after initiating MTX (step up strategy).

Conclusion: This study describes contemporary patterns of ETN use in the CARRA Registry, a North American convenience cohort that includes a large population of JIA patients. Most JIA patients started ETN >3 months after diagnosi

Disclosure: N. Shiff, CARRA, 9; **A. Lougee**, None; **R. Matsouaka**, None; **D. Collier**, Amgen Inc., 1, 3, 4, Amgen, Inc, 1, 3; **Y. Kimura**, Novartis, 5, Sobi, 5; **D. Rumsey**, None; **J. Schenfeld**, Amgen, Inc, 3, 4; **S. Stryker**, Amgen Inc., 3, 4, Amgen, Inc, 3, 4; **M. Twilt**, None; **T. Beukelman**, CARRA, 6, UCB, 5.

Abstract Number: 2713

Juvenile Spondyloarthritis in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry: High Biologic Use, Low Prevalence of HLA-B27, and Equal Sex Representation in Those with Sacroiliitis

Dax Rumsey,[1] Aimee Lougee,[2] Roland Matsouaka,[2] David Collier,[3] Laura Schanberg,[4] Jennifer Schenfeld,[5] Natalie Shiff,[6] Matthew Stoll,[7] Scott Stryker,[3] Pamela F. Weiss,[8] and Timothy Beukelman[9], [1]University of Alberta, Edmonton, AB, Canada, [2]Duke University, Durham, NC, [3]Amgen Inc., Thousand Oaks, CA, [4]Duke University Medical Center, Durham, NC, [5]Amgen, Inc, Thousand Oaks, CA, [6]University of Florida, Gainesville, FL, [7]University of Alabama at Birmingham, Birmingham, AL, [8]Children's Hospital of Philadelphia, Philadelphia, PA, [9]University of Alabama Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

Session Type: Poster Session (Tuesday)

Session Time:9:00AM–11:00AM

Background/Purpose:: Herein we describe characteristics of children with juvenile spondyloarthritis (JSpA, i.e. enthesitis-related arthritis [ERA] or juvenile psoriatic arthritis [JPsA]) enrolled in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry, which was established in 2015.

Methods:: All children with physician-diagnosed ERA or JPsA enrolled in the CARRA Registry between June 2015 and June 2018 were identified. Demographics, clinical characteristics, and treatments of children with ERA and JPsA were described and contrasted. Additionally, children with JSpA and sacroiliitis were compared to those without sacroiliitis. Finally, in the group with sacroiliitis, the first visit with clinically active sacroiliitis was compared to the first visit without clinically active sacroiliitis. 'Clinical sacroiliitis' was at the discretion of the treating physician and sacroiliitis by imaging was diagnosed by MRI, X-ray, and/or CT.

Results:: Nine hundred two children with JSpA – 522 (58%) with ERA and 380 (42%) with JPsA - were identified. Children with ERA were older at diagnosis (10.8 versus 8.2 years) and more likely to be male (56% versus 38%). Pol-

Table 1: Characteristics of Children with Enthesitis Related Arthritis (ERA) or Psoriatic Arthritis (PsA) by JIA Category at the Most Recently Occurring Visit

Characteristic	Overall (N = 902)	ERA (N = 522)	PsA (N = 380)
Mean Age at Diagnosis (years)	9.7 (SD 4.2)	10.8 (SD 3.4)	8.2 (SD 4.6)
Female, %	467 (52%)	231 (44%)	236 (62%)
Reported Race – White, %*	731 (81%)	417 (80%)	314 (83%)
Polyarticular Involvement, Ever	563 (62%)	293 (56%)	270 (71%)
Sacroiliitis, Ever	252 (28%)	208 (40%)	44 (12%)
Enthesitis, Ever	476 (53%)	407 (78%)	69 (18%)
HLA B27 Present**	222 (24%)	197 (38%)	25 (7%)
At least 1 Biologic Taken	622 (69%)	377 (72%)	245 (64%)

*Approximately 8% responded with either 'multiple races', 'other', or 'prefer not to answer'.

**HLA-B27 status unknown in 0% of the ERA patients and in 47% of the PsA patients.

Table 2: Characteristics of Children with Enthesitis Related Arthritis (ERA) or Psoriatic Arthritis (PsA) by Sacroiliitis Category (Ever Reported by Clinical Exam or Imaging)

Characteristic	Sacroiliitis Ever Reported (N = 252; 28%)	Sacroiliitis Never Reported** (N = 619; 69%)
Female, %	137 (54%)	312 (50%)
HLA B27 Present*	86 (34%)	132 (21%)
At least 1 biologic taken	203 (81%)	403 (65%)

*HLA-B27 status unknown in 5% of those with sacroiliitis ever reported and in 25% of those with sacroiliitis never reported.

**Sacroiliitis status was unknown for 31 (3%) of patients

Table 3: Characteristics of Children with Ever Reported Sacroiliitis at First Visit with Clinically Active Sacroiliitis Versus First Visit without Clinically Active Sacroiliitis

Characteristic	1st Visit with Clinically Active Sacroiliitis (N = 163)	1st Visit with No Clinically Active Sacroiliitis (N = 163)	p-value
Mean PGA	2.9 (SD 2.2); N = 154	1.8 (SD 1.9); N = 150	<0.001
Mean Parent/Patient Global	3.5 (SD 2.5); N = 132	2.9 (SD 2.5); N = 122	0.023
Mean Active Joint Count	3.5 (SD 5.1); N = 160	1.5 (SD 2.9); N = 162	<0.001
Mean cJADAS 10	9.3 (SD 6.2); N = 126	5.8 (SD 5.0); N = 115	<0.001
Mean Physical Function Mobility	31.3 (SD 8.0); N = 46	29.8 (SD 4.0); N = 41	0.95
Mean CHAQ	0.5 (SD 0.6); N = 138	0.4 (SD 0.5); N = 116	0.09
Mean Pain Intensity	4.0 (2.5); N = 111	3.6 (SD 2.5); N = 94	0.37
Mean Pain Interference	62.3 (SD 6.2); N = 88	61.5 (SD 6.6); N = 77	0.42

yarticular involvement (ever) was reported in 56% of children with ERA and 71% of those with JPsA. Sacroiliitis (ever, by imaging and/or clinical exam) was reported in 40% of those with ERA versus 12% of those with JPsA. Enthesitis was reported in 78% of children with ERA and 18% of those with JPsA. HLA-B27 was positive in 24% of those with ERA and 7% of those with JPsA (see Table 1 for comment on missing data). At least one biologic was taken by 72% of those with ERA and 64% of those with JPsA (Table 1), mostly TNF inhibitors.

Twenty-eight percent of the children with JSpA had sacroiliitis (by imaging and/or clinical diagnosis). Of the children with JSpA who had sacroiliitis, 54% were female, while 50% of those without sacroiliitis were female. Of those with sacroiliitis, 34% were positive for HLA-B27 versus 21% of the children without sacroiliitis (see Table 2 for comment on missing data). Of those with sacroiliitis, 81% took at least one biologic during follow-up versus 65% of those without sacroiliitis (Table 2).

In those with sacroiliitis, the first visit with active sacroiliitis was compared to the first visit without sacroiliitis. At the active visit, the physician global assessment, parent/patient global, active joint count, and cJADAS 10 were all significantly worse. However, there was no significant difference between visits in the physical function, CHAQ, or pain measures (Table 3).

Conclusion: In the CARRA Registry, there are currently over 900 children with physician-diagnosed JSpA. There are clear phenotypic differences between the children with ERA versus those with PsA. There was high biologic use, especially TNF inhibitors, in this population. It was particularly high in those with sacroiliitis. Further, there was equal sex representation in those with sacroiliitis.

Disclosure: D. Rumsey, Childhood Arthritis and Rheumatology Research Alliance (CARRA), 9; **A. Lougee**, None; **R. Matsouaka**, None; **D. Collier**, Amgen Inc., 1, 3, 4, Amgen, Inc, 1, 3; **L. Schanberg**, CARRA, 9, Childhood Arthritis and Rheumatology Research Alliance, 2, Sanofi, 5, 9, SOBI, 5, UCB, 5; **J. Schenfeld**, Amgen, Inc, 3, 4; **N. Shiff**, CARRA, 9; **M. Stoll**, None; **S. Stryker**, Amgen Inc., 3, 4, Amgen, Inc, 3, 4; **P. Weiss**, None; **T. Beukelman**, CARRA, 6, UCB, 5.

Abstract Number: 2714

Investigation of Inactive Disease Activity States Among JIA Patients in the CARRA Registry

Melissa Mannion,[1] Fenglong Xie,[2] and Timothy Beukelman[3], [1]University of Alabama at Birmingham, Alabama, [2]University of Alabama at Birmingham, Birmingham, [3]University of Alabama Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Inactive disease is the stated goal of treatment in juvenile idiopathic arthritis (JIA) and is typically measured by a composite score that combines several different factors including provider and parent or patient assessments. Various definitions of inactive disease may identify different JIA populations because each score utilizes different components. We compared and contrasted the JIA patients who met various definitions for inactive disease.

Methods: We used the Childhood Arthritis & Rheumatology Research Alliance (CARRA) Registry of clinical data from >65 pediatric rheumatology clinics in the United States and Canada. Individuals with JIA with at least 12 months of observable time after enrollment and completion of the 1 year follow up visit were included. Individuals were excluded if they had incomplete inactive disease measures at the 1-year visit. Demographic and disease characteristics were reported at baseline and the 1-year visit to allow for at least 1 year of disease duration. The frequency and proportion of outcomes for all patients at 1-year follow up were reported regardless of disease duration. The Pearson correlation coefficient was calculated between physician global, patient global, active joint count, and pain at 1-year for all patients.

Results: There were 2164 JIA patients enrolled in the CARRA Registry with completion of 1-year follow up visit (Table 1). Of these 2164 individuals, 70% were treated with a conventional disease modifying anti-rheumatic drug (DMARD) between enrollment and 1-year follow up and 66% were treated with a biologic DMARD. Among all 2164 individuals at the 1-year visit, 1453 (67%) had no active joints, 1068 (49%) had a physician global of 0, 1012 (47%) had a patient global of 0, 998 (46%) met the American College of Rheumatology preliminary criteria for clinical inactive disease (ACR CID), and 964 (45%) had a clinical Juvenile Arthritis Disease Activity Score 10 (cJADAS10) < 1 (Figure 1). There was moderate correlation between physician global and active joint count ($R=0.62$, $p< 0.001$), patient global and pain score ($R=0.48$, $p< 0.001$), physician global and patient global ($R=0.45$, $p< 0.001$), patient global and active joint count ($R=0.32$, $p< 0.001$), and a weak correlation between physician global and pain score ($R=0.24$, $p< 0.001$).

Conclusion: In a multicenter cohort of JIA patients in North America, a large proportion of patients had inactive disease by single or composite measures after 1 year of observation in the Registry. There was significant overlap between patients who met ACR CID criteria and cJADAS10 $\leq$ 1 which may indicate acceptable use of either composite measure for disease management in the clinical setting. Additional studies are needed to evaluate the reasons

Characteristic	N (%) or median (IQR) at baseline	N (%) or median (IQR) at 1 year
Female	1571 (73%)	
Race:		
White	1785 (83%)	
Black	105 (5%)	
Asian	93 (4%)	
Hispanic	202 (9%)	
other	30 (1%)	
Age (years)	12 (8, 15)	
ILAR category:		
Systemic	208 (10%)	
Oligo	557 (26%)	
RF+ poly	178 (8%)	
RF- poly	847 (39%)	
ERA	187 (9%)	
Psoriatic	148 (7%)	
undifferentiated	39 (2%)	
Active joint count	1 (0, 4)	0 (0, 1)
Limited joint count	1 (0, 3)	0 (0, 1)
CHAQ	0.13 (0, 0.63)	0 (0, 0.38)
pain	0 (0, 2)	0 (0, 0)
Physician global	1.5 (0, 3.5)	0.5 (0, 2)
Patient global	1 (0, 4)	1 (0, 3)
cJADAS10	5 (1, 11)	2 (0, 6)
IQR – interquartile range; ILAR – International League of Associations for Rheumatology; Oligo – oligoarticular; RF – rheumatoid factor; poly – polyarticular; ERA – enthesitis related arthritis; CHAQ – Childhood Health Assessment Questionaire; cJADAS10 – clinical Juvenile Arthritis Disease Activity Score 10		

Table 1. Demographic and disease activity characteristics of JIA patients at enrollment and 1-year follow up, n= 2164

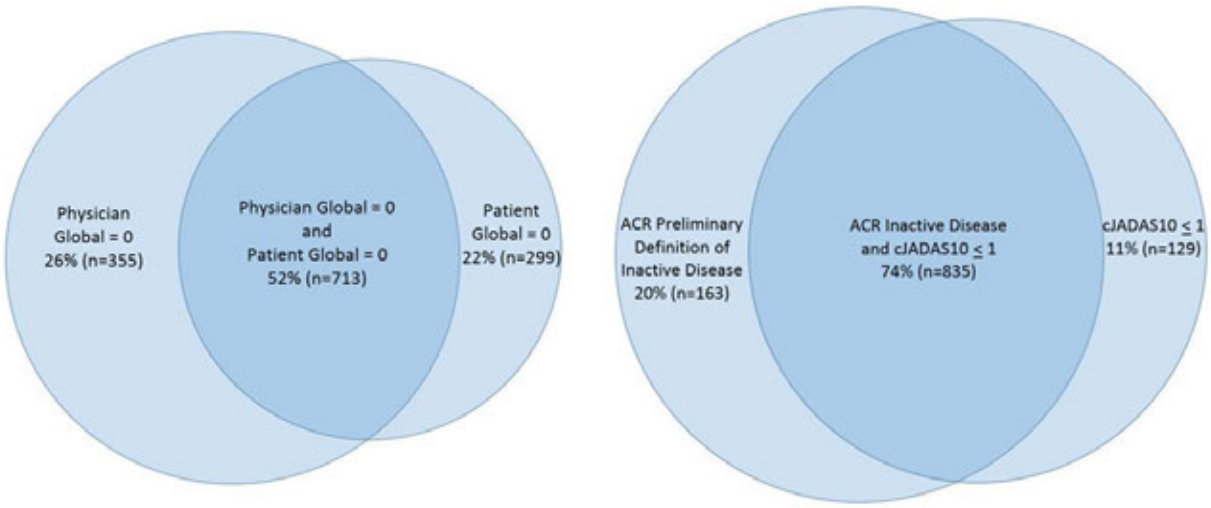


Figure 1. Frequency and overlap of simple and composite inactive disease criteria at 1-year follow up visit for patients who met at least 1 criterion

for discordance in inactive disease measures and to identify the clinical outcomes following achievement of inactive disease by different composite measures.

This study was performed with the support of the CARRA Registry Investigators.

Disclosure: M. Mannion, None; **F. Xie**, None; **T. Beukelman**, CARRA, 6, UCB, 5.

Abstract Number: 2715

Incidence of Juvenile Idiopathic Arthritis in the United Kingdom: Estimates from a National Primary Care Dataset

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common childhood onset inflammatory arthritis. The last estimates of incidence of this disease in the United Kingdom are from nearly 30 years ago, prior to international classification consensus and the emergence of paediatric and adolescent rheumatology as a specialty. The aim of this study was to estimate incidence of JIA from primary care records in the UK since 2000.

Methods: The study used data from the Clinical Practice Research Datalink (CPRD) Gold, a database of UK primary care records considered broadly representative of the UK as a whole in terms of age, gender and ethnicity. A predefined list of JIA Read codes were used to identify incident cases annually from 2000-2018. Incidence rates with 95% confidence intervals (CI) were calculated. The denominator was the population of CPRD < 16 years old on the 31st December each year. Age and gender stratified rates were calculated. Direct standardisation was used to estimate the UK IR using the Office for National Statistics mid-2017 population data (latest available). Incidence rates in 5-year groupings were calculated 2000-2015 to identify any change over time.

Results: There were 1927 incident cases of JIA from 2000-2018, from a total population of 23,328,676 children < 16 years old in CPRD. This gave a total incident rate (IR) (95% confidence interval (CI)) of 8.26 (7.90-8.64) per 100,000 population. There was a slight female preponderance, with IR (95% CI) 9.83 (9.27-10.43) per 100,000 in females, compared to 6.78 (6.33-7.27) per 100,000 in males. Age adjusted direct standardisation to the UK population estimated a total IR of 9.66 per 100,000 person years. Incident rates by age group are shown in table 1. There appeared to be a slightly lower incidence in middle childhood compared to early childhood and adolescents, as well as infancy where lower rates may be due to difficulties in recognising the disease. IRs over time did not appear to change (figure 1).

Conclusion: This is the first study to provide contemporary UK estimates of the incidence of JIA for nearly 30 years. We have shown JIA is more common in girls compared to boys, and is slightly more common in early childhood and

Age *(years)*	Denominator	Cases	IR (95% CI) *Per 100,000*
0-2	1739417	113	6.5 (5.40-7.81)
>2-6	5763003	534	9.27 (8.51 – 10.08)
>6-12	9464988	693	7.32 (6.80-7.90)
12-15	6361268	587	9.22 (8.51-10.01)

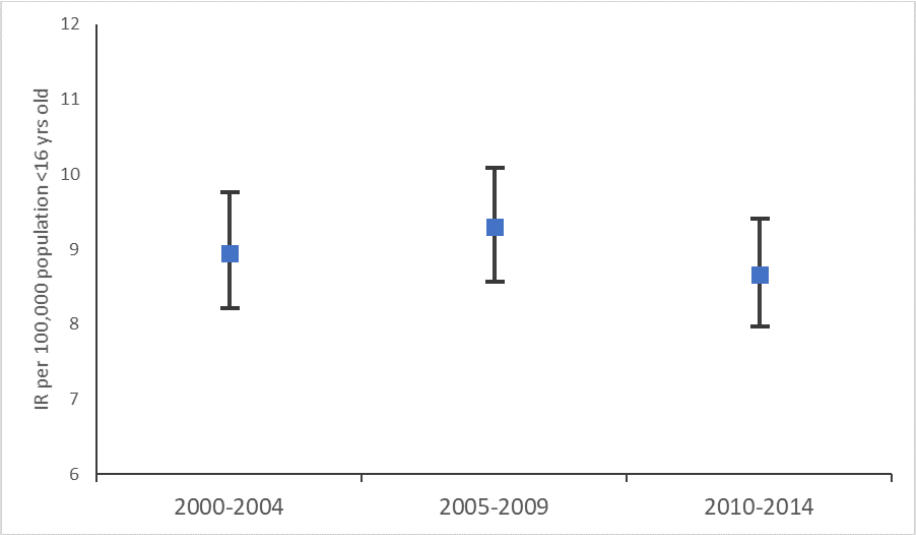

Figure 1. Incidence rates over time

adolescence compared to other age groups. Incidence appears to have been stable over a fifteen-year period. These data provide important information for patients, their families and healthcare providers; in addition, they are vital for appropriate resource planning and service provision in paediatric and adolescent rheumatology.

Disclosure: R. Costello, None; **J. McDonagh**, None; **W. Dixon**, None; **K. Hyrich**, AbbVie, 2, 8, BMS, 2, Pfizer, 2, UCB, 2; **J. Humphreys**, None.

Abstract Number: 2716

Long Term Outcomes of Childhood Onset Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

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Background/Purpose: Childhood onset rheumatoid arthritis (CORA) describes patients with juvenile idiopathic arthritis (JIA) who are rheumatoid factor (RF) or anti-cyclic citrullinated antibody (ACPA) positive. Phenotypically, CORA parallels adult rheumatoid arthritis (RA). Weighted genetic variant testing suggests CORA is more similar to RA than

other JIA subtypes. However, data describing outcomes of this population is limited. Here we describe long-term outcomes of a cohort of CORA patients from our single-center, academic, pediatric rheumatology practice.

Methods: The Intermountain States Database of Childhood Rheumatic Diseases (ISDCRD) is a longitudinal cohort study started at the University of Utah in 1997 which currently includes >700 patients with JIA. Clinical data collected includes date of diagnosis, pre-diagnosis symptom duration, ILAR subtype, and initial clinical presentation (joint count and laboratory studies). CORA subjects were identified in the ISDCRD. A detailed chart review was completed to describe the treatment course and outcomes from diagnosis until current date. Descriptive statistics were used. Study approval was obtained from our Institutional Review Board.

Results: The current cohort includes 51 patients enrolled between 1997 and 2018. Of these, 27 (52.9%) subjects remain in an IRB accessible electronic medical record (EMR). Subject demographic and disease characteristics are summarized in Table 1. 21 subjects were female (77.8%). 25 were White (92.6%). 4 (14.8%) identified as Hispanic. Median number of joints at diagnosis was 13 (range 1 - 44). Median age at diagnosis was 11.8 years (range 2.0-15.9). Median age at time of follow up was 24.6 years (range 10.3 to 35.2). 25 subjects (92.6%) were > 18 years old at the time of most recent follow up. 18 (66.7%) were confirmed polyarticular (≥ 5 active joints) at diagnosis. Of the 4 who were oligoarticular (≤ 4 active joints) at diagnosis, 3 of these extended to polyarticular disease. 15 have known erosive disease (57.7%). 20 (74.1%) were confirmed RF+ (2 positive values ≥ 3 months apart). 7 (25.9%) were confirmed ACPA+ (2 positive values ≥ 3 months apart) . 25 (92.6%) were ever RF+. 22 (81.5%) were ever ACPA+. 1 (3.7%) and 2 (7.4%) were never tested for RF or ACPA respectively. The current treatment of this cohort is described in Figure 1. 21 subjects (77.8%) currently require biologic therapy. 14 (51.9%) failed prior biologic therapies due to intolerance or insufficient response. 2 demonstrated no clinical disease or erosions on last follow up despite minimal treatment (hydroxychloroquine or non-steroidal medication); both were RF+ and ACPA+. Comorbidities included anxiety and depression (n = 4, 14.8%), interstitial lung disease (ILD) (n = 1, 3.7%), and joint surgery (n = 4, 14.8%).

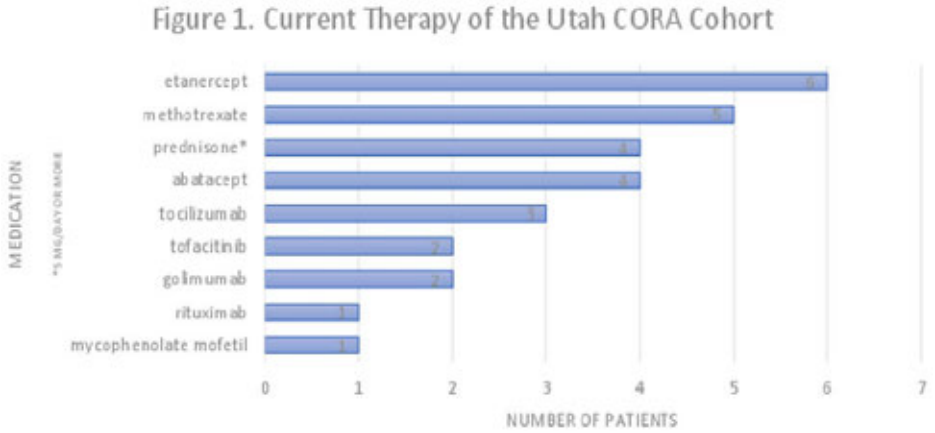
Table 1. Patient characteristics of the Utah CORA cohort

Sex	Race and Ethnicity ±				Age at Onset, median (range)	Current Age, median (range)	Joint Count at Onset, median (range)	Extended Disease	Evidence of Erosion*	Total
	Black	White	Hispanic	South Asian						
Male	0	5	1	0	12.5 (11.8-15.7)	22.6 (19.9-24.6)	10.0 (1-22)	1/1	2	6
Female	0	21	3	1	10.9 (2.0-15.9)	25.6 (10.3-35.2)	15.0 (1-44)	2/3	14	21

± not mutually exclusive
*radiographs, radiograph report, clinic note, problem list

n = 27

Table 1. Incidence rates by age group



Conclusion: This is one of the first studies to describe the long-term outcomes of a cohort of CORA patients. Phenotypically, CORA appears similar to adult RA (e.g. polyarticular presentation, high frequency of erosions, extra-articular disease, need for biologic therapy). In order to better understand the adult-outcomes of CORA we plan to expand this cohort to include data on patients not accessible through EMR review.

Disclosure: R. Overbury, None; **A. Hersh**, None; **C. Inman**, None; **S. Stern**, None; **K. James**, None; **J. Bohnsack**, AbbVie, 2, Bristol-Myers Squibb, 2, Janssen, 2, Pfizer, 2, Roche, 2.

Abstract Number: 2717

Long-term Outcome of Juvenile-onset Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
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Session Time: 9:00AM–11:00AM

Background/Purpose: There is no consensus in the literature with regard to the features and long-term prognosis of psoriatic arthritis (PsA) starting in childhood (jPsA). We aimed to describe the outcome of patients with jPsA in comparison to adult-onset (aPsA).

Methods: A large cohort of PsA patients with known diagnosis date and follow-up were divided into two groups according to the age at PsA diagnosis: jPsA- diagnosis ≤16 years of age and aPsA >16 years of age. The two groups were compared regarding demographics, family history, disease manifestations (number of tender (TJ) and swollen (SJ) joints, enthesitis, dactylitis, the presence of inflammatory back pain, skin involvement (PASI score), comorbidities, functional class (FC), patient and physician assessments of diseases activity at baseline and after 5, 10, 15, 20, and 25 years of follow-up. Patients' contribution to the time interval follow-up groups depended on their follow-up period in the database. Adjusted mean scores were calculated for all disease manifestations during each follow-up period. Chi square test, Student's t-test or Mann-Whitney test were used, as appropriate to compare between the two groups. Comparisons of comorbidities between the two age groups included first time diagnosis during follow up, cumulative morbidity and the influence of disease duration. Generalized estimating equations procedure of repeated measurements were performed to assess the effect of age on study variables. Relative risk ratios and 95% confidence intervals were calculated from the models. The results were considered statistically significant for 2-sided p value< 0.05.

Results: The jPsA group included 78 patients, 41% males, age at diagnosis 11.48±4.97 years, age at baseline 33.53±14.92 years, contributing 612 patient visits. The aPsA group consisted of 2182 patients, 54.2% males (p=0.02),

age at diagnosis 40.29±13.15 years, age at baseline 47.47±13.28 years, contributing 19784 patient visits. Arthritis preceded psoriasis in 21(26.9%) individuals in the jPSA group compare to 123 (5.6%) in the aPsA group (p< 0.0001). After ≥25 years of disease, the following adjusted mean scores were reported in the jPsA group: TJ= 3.86±6.04, SJ= 1.18±3.05, enthesitis 0.21±0.64, dactylitis 0.2±1.22, inflammatory back pain in 20.8%. The majority (62.5%) were in FC I, 32.5% in FC II, and 5% in FC III. No statistically significant differences were noted between jPsA and aPsA groups in TJ, SJ, enthesitis and dactylitis counts, PASI score, inflammatory back pain, or FC nor in the patient and physician assessments of disease activity. There were no statistically significant differences in the prevalence of malignancy, hyperlipidemia, diabetes mellitus and myocardial infarction between the two groups although the jPsA group was much younger. Hypertension was more common in the aPsA (47.2% versus 20.6%, p=0.003) whereas depression was more common in the jPsA group (20.6% versus 8.7%, p=0.03).

Conclusion: The overall prognosis of jPsA ≥25 years following diagnosis is good and resembles that of aPsA group. However, patients with jPsA developed joint symptoms earlier compared to skin disease, and accrue comorbidities at a younger age.

Disclosure: D. Zisman, Pfizer, 5, 8; **T. Gazitt**, None; **A. Haddad**, None; **I. Lavi**, None; **S. Barac**, None; **V. Chandran**, None; **J. Dutz**, None; **L. Eder**, Abbvie, 2, 5, 8, Celgene, 5, Janssen, 5, Lily, 2, 5, Novartis, 2, 5, Pfizer, 2, 8, UCB, 2; **J. Elder**, None; **R. Hayday**, None; **P. Rahman**, AbbVie, 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, and Novartis, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, and UCB, 5, AbbVie, Eli Lilly, Pfizer, Novartis , UCB, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 2, 5, 8, Janssen Inc., 2, 5, 8, Janssen, Novartis, 2, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **C. Ritchlin**, AbbVie, 2, 5, 9, Amgen, 2, 5, BMS, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Lilly, 5, Novartis, 5, Pfizer, 2, Pfizer Inc, 5, UCB, 2, 5; **S. Rohekar**, None; **C. Rosen**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, GSI, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5.

Abstract Number: 2718

A Retrospective Study Comparing Refractoriness to Biologic Disease Modifying Anti-Rheumatic Drugs in Adults with Juvenile Idiopathic Arthritis as Compared to Those with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
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Session Time: 9:00AM–11:00AM

Background/Purpose:: The use of biologic DMARDs (bDMARDs) has vastly changed the treatment of autoimmune arthritis, both Rheumatoid Arthritis (RA) and polyarticular and oligoarticular Juvenile Idiopathic Arthritis (JIA). At this time 5 bDMARDs are approved by the FDA for JIA, however, many patients fail these medications, due to adverse effects or inefficacy. Studies looking at retention rate for these medications have found varying reasons for discontinuation of first line treatments between adults and children, however attention has not been paid to those patients who fail multiple rounds of bDMARDs, and have come to be considered refractory. As childhood-onset rheumatic disease is often more severe than adult-onset, we hypothesize that JIA patients will have an increased rate of refractoriness when compared to RA patients. This study aims to characterize and compare refractory patients with JIA and RA.

Methods:: This is a retrospective chart review of adult patients diagnosed with polyarticular or oligoarticular JIA as children and adult-onset RA seen in the Los Angeles County + University Southern California Medical Center (LAC+USC) and Keck University Hospital from January 2010 to December 2017. All JIA patients were diagnosed and treated by pediatric rheumatologists as children and all RA patients were diagnosed based on the 1987 ACR classification criteria. Patients were deemed refractory if they failed ≥ 3 DMARDs, one of which is a bDMARD. Refractory patients were included in the study as cases and controls were selected from non-refractory patients. Descriptive statistics were reported for demographic and clinic data. Logistic regression models were used to evaluate the association between arthritis type (JIA vs. RA) and refractoriness while controlling for disease duration.

Results:: A total of 100 patients were reviewed, 53 adults with polyarticular or oligoarticular JIA and 47 RA patients. Ninety-three percent were women and 76% were Hispanic. The JIA group was younger (mean age 27.7 years, SD of 10.3) than the RA group (mean age 55.9 years, SD of 11.8). However, average disease durations were comparable (mean of 15.5 years in the JIA group, 14.3 in the RA group). There was no difference in number of refractory cases between JIA and RA patients, 50.9% and 53.2%, respectively. Comparison of the refractory cases and their controls, however, showed an increase in disease duration (mean 17.8 years vs. 11.8 years) as well as a higher prevalence of sero-positivity for both RF and anti-CCP status (82.70% and 78.57% as compared with 58.33% and 66.67%) and erosive disease (55.77% as opposed to 20.83%).

Conclusion: This study failed to find an association between adult JIA patients and refractory disease when compared with RA patients. Although JIA patients are equally refractory to DMARDs when adjusted for disease duration, this still presents a formidable problem when it comes to the future of these patients, as they likely have at least double the number of years with disease ahead of them when compared to RA patients. Future studies evaluating the continued bDMARD use in young, refractory patients are necessary to better understand how best to treat these patients.

Disclosure: K. Taba, None; **E. Ortiz**, None.

Abstract Number: 2719

Predictors of Health Care Transition Practices Among North American Pediatric Rheumatology Providers

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
Session Type: Poster Session (Tuesday)
Session Time: 9:00AM–11:00AM

Background/Purpose: The transition from pediatric to adult-oriented health care represents a vulnerable period for young adults with chronic rheumatic diseases. In spite of this, a 2010 study of Childhood Arthritis and Rheumatology Research Alliance (CARRA) rheumatologists showed that less than 10% were familiar with existing transition guidelines. Since then, new health care transition guidelines and an ACR transition toolkit have been disseminated. We resurveyed CARRA members to assess the impact of new guidelines and tools on transition practices and explored predictors of transition practices.

Methods: An online survey on health care transition was emailed to CARRA providers in April 2018. Pediatric rheumatology physicians and fellows in the United States (U.S.) or Canada were included in analysis. Univariate comparisons and multivariate linear and logistic regression were performed to identify factors that predict age of transfer and transition practices, including self-assessed performance on Got Transition's Current Assessment of Health Care Transition Activities (CAHCTA), which measures the level of health care transition support provided by a practice, with scores ranging from 6 (basic) to 24 (comprehensive).

Results: The response rate was 212/396 (54%), of which 192 responses were analyzed: 147 pediatric rheumatologists, 8 dual-boarded adult/pediatric rheumatologists, and 37 fellows, inclusive of 180 U.S. and 12 Canadian providers (from 4 academic institutions). Table 1 shows unadjusted, univariate statistics alongside multivariate modeling for transfer age and CAHCTA score. In multivariate analysis, providers who transfer patients prior to age 21 are more likely to practice in Canada (OR=16.6, 95% CI: 3.0-92.4) and to have been in practice for 5-15 years (OR=2.7, 95% CI: 1.3-5.6). Whereas 92% of Canadian providers routinely ask parents leave the room for at least part of the visit before patients reach the age of 18, only 41% of U.S. respondents do so (p=0.001). Similarly, 56% of private practice pediatric rheumatologists use an adult model of care, compared to only 20% in other practice settings (p=0.03). Finally, Canadian pediatric rheumatologists have a significantly higher mean CAHCTA score (15.0 v 10.3; p< 0.0001), whereas providers believing pediatric staff lack skills in transition support have lower scores (8.7 vs 11.0; p=.003).

Table 1. Univariate and Multivariate Modeling of Transition Outcomes

Transfer of Care Before Age 21		
	Univariate	**Multivariate***
	OR (95% CI)	*OR (95% CI)*
Canada vs. United States	9.2 (1.9, 43.4)	16.5 (2.9, 93.8)
Adult and Pediatric vs. Pediatric Provider	0.5 (0.1, 4.9)	–
Private Practice vs. Other Practice Setting	1.9 (0.4, 10.0)	–
Duration in Practice		
5-15 years vs <5 years	3.1 (1.4, 6.6)	2.7 (1.3, 5.9)
>15 years vs <5 years	0.8 (0.3, 2.1)	0.5 (0.2, 1.3)
Size of Pediatric Rheumatology Practice		
Solo vs. Large Practice (≥7 providers)	0.6 (0.2, 1.9)	–
Small (2-3 provider) vs. Large (≥7 providers)	0.6 (0.3, 1.6)	–
Medium (4-6 providers) vs. Large (≥7 providers)	0.4 (0.2, 0.9)	–
View "staff lack of transition skills" as Major Barrier	0.6 (0.2, 1.5)	–
CAHCTA Score		
	Univariate	**Multivariate***
	B (95% CI)	*B (95% CI)*
Canada vs. United States	4.6 (2.6, 6.5)	3.9 (2.0, 5.9)
Adult and Pediatric vs. Pediatric Provider	0.9 (-1.8, 3.6)	–
Private Practice vs. Other Practice Setting	-2.3 (-4.7, 0.1)	–
Duration in Practice		
5-15 years vs <5 years	1.3 (-0.4, 3.0)	–
>15 years vs <5 years	2.3 (0.5, 4.1)	–
Size of Pediatric Rheumatology Practice		
Solo vs. Large Practice (≥7 providers)	-2.8 (-4.9, -0.7)	-2.1 (-4.0, -0.2)
Small (2-3 provider) vs. Large (≥7 providers)	-1.5 (-3.2, 0.1)	-1.4 (-2.9, 0.1)
Medium (4-6 providers) vs. Large (≥7 providers)	-0.3 (-1.6, 1.1)	-0.4 (-1.7, 0.8)
View "staff lack of transition skills" as Major Barrier	-2.5 (-4.1, -0.9)	-2.0 (-3.4, -0.5)

Conclusion: This survey highlights clinic staff training in transitional care skills as a potential avenue to enhance health care transition support in pediatric rheumatology. In addition, this survey underscores ways in which transition support services are more established in Canada, given stricter mandates to transfer patients at age 18 and the subsequent development of national strategies to support young adults. Canadian CARRA members' experiences with transitional support services will contribute to CARRA's new Transition Learning Collaborative, developed to facilitate dissemination and implementation of transition programs and services in a way that addresses the heterogeneous landscape of health care transition.

Disclosure: R. Sadun, None; **A. Eudy**, GSK, 2; **P. Chiraseveenuprapund**, Novartis, 5, Pfizer, 2, Sobi, 2; **C. Edens**, None; **A. Hersh**, None; **K. Johnson**, None; **E. Lawson**, None.

Abstract Number: 2720

Implementation of an Evidence-based Transition Clinic in a Pediatric Rheumatology Academic Institution

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SESSION INFORMATION

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Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis

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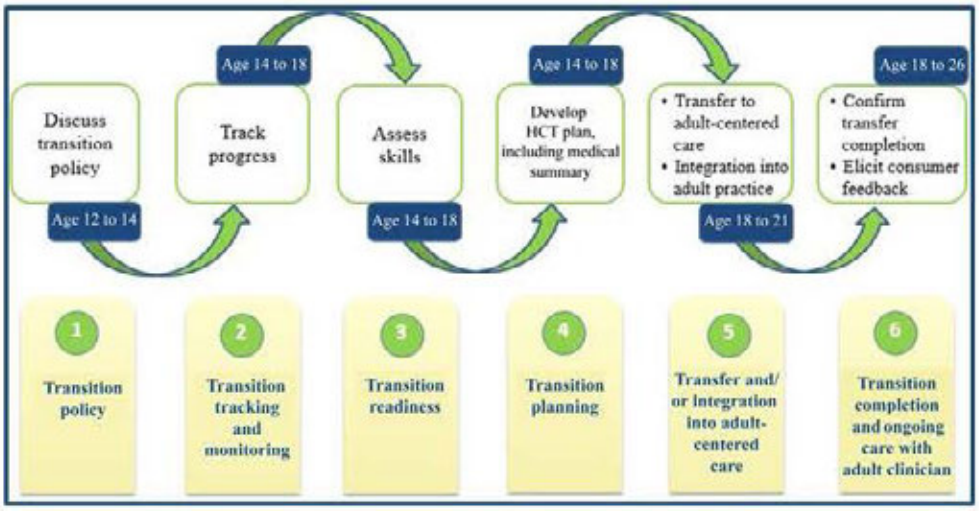
Background/Purpose: Transition from pediatric to adult rheumatology care is more likely to be successful if a transition program is in place. Previously successful interventions to improve transition outcomes have included integrating an adult subspecialist in the pediatric clinic setting. We hypothesize that we will improve transition outcomes by implementing a transition clinic which includes an adult rheumatologist providing care within a pediatric rheumatology clinic.

Methods: We initiated a weekly transition clinic in November 2018 called ACCORD (Adult Center for Childhood Onset Rheumatic Disease). This clinic is staffed by 1 adult rheumatologist (board certified in internal medicine and pediatrics), 1 pediatric nurse, a research coordinator, and a social worker. Patients can be seen if they are ≥ 16 years old with known rheumatic disease or suspicion for rheumatic disease. All patients receive education and monitoring of transition readiness. We provide transition readiness education in 5 discrete modules (Fig 1); education materials

Figure 1. Five modules for transition readiness education

Module 1	*12-14 yo*	Transition Policy	Introductory Information			
Module 2	*14-18 yo*	Transition Readiness Assessment	Medical Plan			
Module 3	*14-18 yo*	Medication List	Medical Summary			
Module 4	*18-21 yo*	"10 Things to Know" about Adult Care				
Module 5	*18-26 yo*	Medical Summary	Medical Plan	Medication List	Transition Readiness	Transfer Letter

Figure 2. "Six Core Elements" (Patience H. White et al. Pediatrics 2018)



are adapted from Got Transition $_{Tm}$ (Fig 2). All patients complete patient reported outcome measures (PRO's). We maximize continuity of care in several ways: our adult rheumatologist meets pediatric patients who anticipate transfer to the transition clinic, she manages all transition clinic visits, and if possible, she migrates care to our institution's associated adult rheumatology clinic. Demographics, PRO's, transition readiness measures, and clinical outcomes are collected in a prospective longitudinal registry. IRB approval was obtained for this study.

Results: In 7 months, 65 patients visited the transition clinic (Table 1). 70.8% were new patients. Of these, we diagnosed 34.8% with a new rheumatic disease (rheumatoid arthritis (RA), mixed connective tissue disease, antiphospholipid syndrome, Raynaud phenomenon, spondyloarthritis (SpA), enteropathic arthritis, gout, Ehlers-Danlos syndrome, and linear morphea). 29.2% were transfers for known rheumatic disease of childhood onset (juvenile idiopathic arthritis (JIA), systemic lupus erythematosus, SpA, and Sjogren's syndrome). Nine (13.8%) have scheduled upcoming visits with the adult rheumatologist in our affiliated adult rheumatology clinic. Four (6.2%) have completed

Table 1. Demographics of transition clinic*

	Sex		Mean Age (years)		Race or Ethnicity					
	Male n (%)	*Female n (%)*	*Male / Female*		*White n (%)*	*Black n (%)*	*Hispanic n (%)*	*Pacific Islander n (%)*	*Native American n (%)*	*Total*
Transition of care	4 (6.2)	15 (23.1)	19.8	19.9	14 (21.5)	1 (1.5)	3 (4.6)	0	1 (1.5)	19
New with diagnosis	2 (3.1)	14 (21.5)	16.5	16.9	13 (20)	0	2 (3.1)	1 (1.5)	0	16
New without diagnosis	5 (7.7)	25 (38.5)	16.6	16.6	26 (40)	2 (3.1)	2 (3.1)	0	0	30
Total	11 (16.9)	54 (83.1)	17.7	17.6	53 (81.5)	3 (4.6)	7 (10.8)	1 (1.5)	1 (1.5)	65

* All percentages are of the entire cohort (n = 65)

durable transfer to our adult rheumatology clinic (defined as one or more scheduled and completed appointments). One (1.5%) patient has successfully transitioned to an outside adult rheumatologist.

Conclusion: We have successfully initiated an evidence-based transition clinic in a pediatric rheumatology academic institution that integrates the care of an adult rheumatologist. The transition clinic has diagnosed 16 new rheumatologic diagnoses in adolescence, eliminating the future need for transition to an adult provider. We have established 19 patients with our adult rheumatologist in the transition clinic, alongside our pediatric rheumatology clinic. We have transferred 9 patients to an adult rheumatology clinic, 8 to our associated adult rheumatology clinic, and 4 have completed a durable transition to date. Future research of this registry will analyze this cohort and the impact of this intervention on clinical outcomes and PRO's.

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Abstract Number: 2721

Subjective and Objective Dyscognition in Adolescents with Juvenile Fibromyalgia Syndrome

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SESSION INFORMATION
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Background/Purpose: Dyscognition, including loss of mental clarity and problems with attention and memory, often affects adolescents with juvenile fibromyalgia syndrome (JFMS). Our understanding of this neuropsychological symptom, however, is limited. It is unclear whether adolescents with JFMS experiencing subjective (or self-reported symptoms of) dyscognition have objectively measurable neurocognitive deficits. We aimed to determine 1) the prevalence of subjective and objective dyscognition and 2) the association between subjective and objective dyscognition among adolescents with JFMS.

Methods: We conducted a pilot, prospective cohort study of children ages 12-17 years diagnosed with JFMS according to 2010 ACR criteria for fibromyalgia syndrome seen in a pediatric rheumatology pain clinic from July 2017-February 2019. Exclusion criteria included non-English speaking patients, use of stimulant medication, or a condition precluding completion of assessments. Subjects completed both patient-reported outcomes (PROs) and neurocognitive testing. Subjects with poor effort based on the Memory Validity Profile (MVP) or Medical Symptoms Validity Test (MSVT) were excluded from objective dyscognition analyses. Subjective dyscognition was defined as a Pediatric Quality of Life Inventory (PedsQL) Cognitive Functioning Scale score ≤50 or self-reported Behavior Rating Inventory of Executive Function (BRIEF-2) global executive composite (GEC) score ≥ 70. Objective dyscognition was defined as impairment of more than two standard deviations in any of the domains in the neurocognitive battery. We assessed the association of clinical signs and symptoms with the presence of subjective dyscognition using Fisher-Exact test or Wilcoxon-rank test. The association between subjective and objective dyscognition was analyzed via Fisher-Exact test.

Table.1 Demographics, Clinical Characteristics and Patient-reported Outcome Measures (PROs) among Adolescents with Juvenile Fibromyalgia Syndrome

	All Subjects (n=19)	(+) Subjective Dyscognition (n=12)	(-) Subjective Dyscognition (n=7)	p-value
Demographics				
Age (median, IQR)	15 (12.0 – 16.0)	14.5 (12.0 – 16.0)	15 (12.0 – 17.0)	0.85
Female, n (%)	15 (79%)	8 (67%)	7 (100%)	0.25
White, n (%)	19 (74%)	9 (75%)	5 (71%)	0.60
Non-Hispanic, n (%)	22 (89%)	11 (92%)	6 (86%)	0.49
Clinical Characteristics, median, IQR				
Pain Duration (months)	12 (7.0 – 36.0)	15 (08.0 – 36.0)	10 (05.0 – 60.0)	0.33
Pain Visual Analog Scale (VAS) (0-100)	61 (53.0 – 69.0)	62.5 (58.0 – 72.5)	52 (16.0 – 66.0)	0.42
Widespread Pain Index (WPI) (0-19)	11 (8.0 – 12.5)	11 (07.0 – 12.5)	12 (09.0 – 13.0)	0.53
Symptom Severity Score (SSS) (0-12)	7 (6.5 – 8.5)	7 (07.0 – 09.0)	6 (05.0 - 07.0)	0.06
Patient-reported Outcome Measures (PROs), median (IQR)				
Functional Disability Inventory (FDI) (0-60)	24 (15.5 – 31.0)	27.5 (21.5 – 35.5)	16 (11.0 – 26.0)	0.22
PROMIS Global Health 7 (PGH-7)	37.2 (31.6 – 40.4)	35.6 (30.8 – 38.8)	42.1 (38.8 – 45.7)	0.01*
14-item Resilience Scale (14-98)	72.0 (61.0 – 78.0)	64 (51.5 – 70.5)	79 (75.0 – 86.0)	0.01*
CDI-2 (Depression)	59.0 (52.0 – 70.5)	67 (59.5 – 76.0)	51 (47.0 – 56.0)	<0.01*
MASC-2 (Anxiety)	64.0 (51.5 – 71.5)	70 (64.5 – 83.0)	52 (45.0 – 55.0)	<0.01*
PedsQL Total Multidimensional Fatigue Scale (MFS) (0-100)	39.0 (33.0 – 56.5)	34.5 (30.5 – 38.5)	60 (56.0 – 63.0)	<0.001*
MFS General Fatigue	33.0 (25.0 – 48.0)	27 (21.0 – 37.5)	50 (42.0 – 63.0)	0.01*
MFS Sleep	46.0 (37.5 – 54.0)	42 (27.0 – 50.0)	58 (50.0 – 63.0)	0.01*
MFS Cognitive	42.0 (33.0 – 67.0)	35.5 (25.0 – 42.0)	71 (63.0 – 75.0)	<0.001*
BRIEF-2 Global Executive Composite (GEC) T Score	53.0 (50.5 – 65.0)	62.5 (57.0 – 72.5)	50 (44.0 – 53.0)	<0.01*

*Significant p-values suggesting statistical significance. For subjective dyscognition, 8 subjects were positive on the PedsQL (Pediatric Quality of Life Inventory) Cognitive Functioning Scale only and 4 subjects were positive on the BRIEF-2 (Behavior Rating Inventory of Executive Function-2) Global Executive Composite (GEC) and PedsQL Cognitive Functioning Scale. IQR= interquartile range. PROMIS = Patient Reported Outcome Measurement Information System. CDI-2 = The Children's Depression Inventory, 2nd Edition. MASC-2 = The Multidimensional Anxiety Scale for Children, 2nd Edition. PedsQL MFS = The Pediatric Quality of Life Inventory Multidimensional Fatigue Scale.

Table 2. Objective Dyscognition Based on Subjective Symptoms among Adolescents with Juvenile Fibromyalgia Syndrome

Neurocognitive Battery Test (Objective Measure), n (%)	(+) Subjective Dyscognition (n=11)	(-) Subjective Dyscognition (n=7)	p-value
Any impairment	6 (54.5)	2 (28.6)	0.22
General intellect (WASI-II)	0 (0)	0 (0)	---
Memory (ChAMP, WISC-V, WAIS-IV)	0 (0)	0 (0)	--
Attention (CPT-3)	3 (27.3)	1 (14.3)	0.38
Executive Function (D-KEFS)	3 (27.3)	0 (0)	0.20
Complex Psychomotor Speed (Grooved Pegboard Test)	3 (27.3)	2 (28.6)	0.40

One subject was excluded due to poor effort. WASI-II = The Wechsler Abbreviated Scale of Intelligence). ChAMP = Children and Adolescent Memory Profile. WAIS-IV (Wechsler Adult Intelligence Scale, 4th Edition) and WISC-V (Wechsler Intelligence Scale for Children, 5th Edition) Digit Span subtests test auditory working memory ability. CPT-3 = The Conners Continuous Performance Test, 3rd Edition. D-KEFS = Delis-Kaplan Executive Function System.

Results: Nineteen subjects met criteria and completed the study. Most subjects were female (79%), non-Hispanic (89%) and Caucasian (74%) (Table 1). Median age at enrollment was 15 years (IQR: 12.0-16.0). Sixty-three percent

(n=12) of subjects reported subjective dyscognition and 44% (8/18) had objective dyscognition in ≥ 1 domain. Subjective dyscognition was associated with greater symptoms of anxiety, depression, lower resilience, lower health-related quality of life, greater fatigue, and poorer sleep (all $p < 0.05$; Table 1). The neurocognitive battery domains most commonly impaired included complex psychomotor speed (28%), attention (22%) and executive function (17%) (Table 2). The presence of subjective dyscognition was not significantly associated with objective dyscognition (all $p > 0.05$).

Conclusion: Sixty-three percent and 44% of adolescents with JFMS had subjective or objective dyscognition, respectively. Subjective dyscognition was not associated with objective dyscognition. This discrepancy may be due to the exacerbation of subjective dyscognition by co-morbid depression, anxiety and/or fatigue. As this study is ongoing, we anticipate that analyzation of additional data will help explain this discrepancy and also guide evidence-based recommendations for neuropsychological testing for JFMS.

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Abstract Number: 2722

The down Syndrome Arthropathy Cohort in the New Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry: Clinical Characteristics, Treatment and Outcomes

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SESSION INFORMATION
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Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis
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Background/Purpose: Down syndrome arthropathy (DA) is under-recognized with a 19-month average delay in diagnosis (1). The majority present with polyarticular, rheumatoid factor (RF) and anti-nuclear antibody (ANA) negative disease. The current therapies for juvenile idiopathic arthritis (JIA) appear to be poorly tolerated, more toxic and less effective in patients with DA (1). The objective of this study was to characterize clinical manifestations and therapeutic preferences in DA, using the new Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry.

Methods: The new CARRA Registry began prospectively collecting data on children with JIA in the United States and Canada in July 2015. Down syndrome (DS) is documented in the CARRA Registry as a coexisting condition. Within the new CARRA Registry, between the dates of July 2015 and March 2019, patients with JIA and DS were identified and an observational cohort analysis was performed. Collected data included demographics, disease characteristics, laboratory results, and treatment exposure.

Results: Thirty-six patients with DA were identified in the total population of 7337 JIA patients (0.005%) in the Registry with a mean follow-up period of 4.5 years (SD 3.2). The mean age at onset of musculoskeletal symptoms was 7.1 years (SD 3.9) and the mean months to JIA diagnosis was 11.5 months (SD 21.6). At diagnosis, 64% had a polyarticular RF negative presentation, 39% reported morning stiffness with an average of 4 active (SD 7; range 0 - 27) and 4 limited joints (SD 6; range 0-23), and a mean physician global of disease activity of 2.7 (SD 2.6; range 0

Table 1. Therapy throughout course of Down syndrome Arthropathy

Treatment	Patient (n/total)	Response* (n/total)
Oral Steroid	10/36,	1/10
Intra-articular Steroid	15/36	1/15
DMARDs	28/36	
Methotrexate	28/28	5/28
Leflunomide	1/28	0/1
Azathioprine	1/28	0/1
Biologics	27/36	
Etanercept	19/27	7/19
Adalimumab	14/27	8/14
Abatacept	6/27	1/6
Tocilizumab	5/27	2/5
Infliximab	1/27	1/1
Anakinra	1/27	0/1
Canakinumab	1/27	0/1

*Defined as tolerating and not requiring an increase in therapy

Table 2. Outcomes throughout course of Down syndrome Arthropathy

Outcome	At Diagnosis Mean (SD)	At Last Visit Mean (SD)	p - value
Active joints	4.4 (7.0)	2.9 (5.6)	**0.03**
Limited joints	4.3 (6.3)	3.3 (5.5)	0.59
Physician global*	2.7 (2.6)	1.2 (1.4)	**0.01**
Patient global**	4.0 (3.2)	2.3 (2.5)	0.12
CHAQ†	1.2 (0.8)	1.1 (0.7)	0.34

*Physician global assessment of disease activity, 0-10 Likert scale, 0 = inactive disease
**Patient global assessment of disease burden, 0-10 Likert scale, 0 = no disease burden
†Childhood health assessment questionnaire, 0-3, 0 = good physical function

- 9). At diagnosis, 22% had elevated inflammatory markers (CRP, ESR), while 33% and 17% were positive for ANA and HLA-B27, respectively. Over half the patients (64%) were started on a disease modifying antirheumatic drug (DMARD) at diagnosis with 36% simultaneously starting a biologic. Over the course of disease, 78% used a DMARD (100% used methotrexate [MTX] at some point) and 75% used a biologic (mostly etanercept [70%]). Of those exposed to DMARD therapy, fifteen patients (54%) had at least one change of their DMARD (most due to MTX adverse effect [46%]), however, at the last recorded visit, 42% were on methotrexate. Fifteen patients (55%) had at least one change in biologic therapy due to inadequate response to therapy (Table 1). Between the first and last visit significant ($p < 0.05$) improvements were seen for active joint count and physician global of disease activity (Table 2).

Conclusion: In a large multicenter observational registry of JIA patients in North America, patients with Down syndrome arthropathy continue to have an approximate year-long delay in diagnosis from symptom onset. Treatments included corticosteroids (oral and intra-articular), DMARDs and biologic therapies throughout the course of the disease. Although there was a statistically significant improvement in active joint count and physician global assessment, there was no significant difference in limited joints, CHAQ, or patient global assessment with treatment. Optimal therapy remains unclear and current barriers are DMARD intolerance and anti-TNF effectiveness. More research is needed to determine optimal therapeutic approach.

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Abstract Number: 2723

Alagille Syndrome and Chronic Arthritis: An International Case Series

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Background/Purpose: Alagille syndrome is a complex multisystem disease characterized by chronic cholestasis due to a paucity of intrahepatic bile ducts, congenital heart disease and ocular embryotoxon. Skeletal involvement consists mainly of vertebral anomalies and osteoporosis. The association of Alagille syndrome and inflammatory arthritis is exceptional and to date only 4 cases have been described. Our purpose is to collect and describe a cases series of children affected by Alagille syndrome who developed an inflammatory arthritis.

Methods: This was a retrospective analysis of clinical charts from 6 centres in Italy, USA and France, including the Hospital where Dr. Alagille worked and described the syndrome.

Results: We collected 9 cases of Alagille syndrome associated with chronic arthritis, 5 females and 4 males, median age 11 years (range 4-18) at last follow up. All patients had neonatal cholestasis; 9/9 cardiac involvement; 8/9 characteristic facies; 8/9 ocular abnormality; 6/9 kidney disease; 3/9 osteoporosis and 2 butterfly vertebrae. Median age at arthritis onset was 6.2 years (range 2-10); the median number of active joints at onset was 3 (range 1-8). The most common site of arthritis was the knee (8/9) followed by ankle (6/9), elbow (4/9), wrist (3/9), small joints of hands or feet (3/9), cervical spine (2/9), temporomandibular (2/9), shoulder (1/9) and hip (1/9). Two patients also had uveitis, one of which with other signs typical of sarcoidosis. Three patients had skin manifestations. Two patients had ANA positivity (³1:160) and 8/9 high inflammatory markers. Synovial fluid examination, performed in 3 patients, revealed mild to moderate leucocytosis (200-15.000 WBC/mm^3). Five patients received at least one intraarticular injection of corticosteroids, 7/9 received an anti-TNF, 2/9 ustekinumab, and one patient received consecutively methotrexate, anakinra, abatacept and tocilizumab. Two patients underwent liver transplantation with arthritis resolution in one and partial remission in the other one. One patient died before transplantation; 4 patients still had active arthritis despite treatment, 2 had a mild improvement of arthritis with biologic therapies.

Conclusion: In our series the frequency of chronic arthritis among patients affected by Alagille syndrome (9/150 patients followed in the same centers) was 50 times higher than the expected frequency in the general population (1/1000). All patients had arthritis resistant to conventional treatments and only the patient who underwent liver transplantation reached clinical remission. The etiology of chronic arthritis in Alagille syndrome is not known. The two genes associated with Alagille syndrome, JAG1 and NOTCH2, have a role in regulation of angiogenesis and T cells

function, possibly explaining the occurrence of joint inflammation. While the chronic course, the elevated inflammatory markers, the leucocytosis in synovial fluid and the age at onset < 16 years could be suggestive of juvenile idiopathic arthritis, the high incidence among patients with Alagille syndrome, the resistance to common treatments and the resolution with liver transplantation may suggest a role of the underlying disease in the pathogenesis of arthritis.

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Abstract Number: 2724

Farber Disease (Acid Ceramidase Deficiency): The First Natural History Study of This Rare Disease Involving Symptoms Which Can Mimic JIA

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Background/Purpose: The cardinal clinical symptoms of Farber disease (arthritis/contractures, subcutaneous granulomatous nodules, dysphonia) may be misdiagnosed as JIA. Mutations in the *ASAH1* gene and the resulting deficiency of the lysosomal enzyme acid ceramidase leads to accumulation of the pro-inflammatory sphingolipid ceramide, causing a broad spectrum of disease severity and presentation of symptoms, which may delay diagnosis or lead to misdiagnosis. This study represents the first comprehensive, systematic collection of retrospective and prospective clinical data on the natural history of Farber disease.

Methods: The Observational and Cross-Sectional Cohort Study of the Natural History and Phenotypic Spectrum of Farber Disease (NCT03233841) is collecting retrospective and prospective data, including demographics, clinical presentation, phenotype, and diagnostic history, of patients diagnosed with Farber disease who have or have not undergone hematopoietic stem cell transplantation (HSCT). This data, along with specific prospective clinical evaluations in living patients, will be communicated.

Results: Since November 2017, 43 patients (26 living, 17 deceased) have been enrolled in the study. To date, patients have been enrolled at 15 centers in 9 countries. In patients whose data was available for analysis, the average age of the living patients is 9 years (range 1 to 28 years), and the average time from onset of first symptoms to diagnosis is 2 years (range < 1 to 12 years). Of the non-HSCT patients, 32% were treated with a biologic. Childhood Health

Assessment Questionnaire Disability Index Scores (CHAQ DI) ranged from 1.25 to 3 across the non-HSCT population (n=14), including those patients treated with DMARDs and/or biologics.

Conclusion: Among patients representing the broad phenotypic spectrum of Farber disease, from rapidly progressive (severe) to slowly progressive (attenuated), the data confirms that patients can be misdiagnosed as having JIA, and that there is a high disease-related burden as demonstrated by the CHAQ DI scores, which symptomatic treatment with biologics does not resolve. Demographic information and numbers of patients enrolled indicate that Farber disease is likely not as rare as previously thought.

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Abstract Number: 2725

Clinical Factors Distinguishing Between Pediatric Tumors with Arthritis at Onset and JIA: Preliminary Analysis of the ONCOREUM Study

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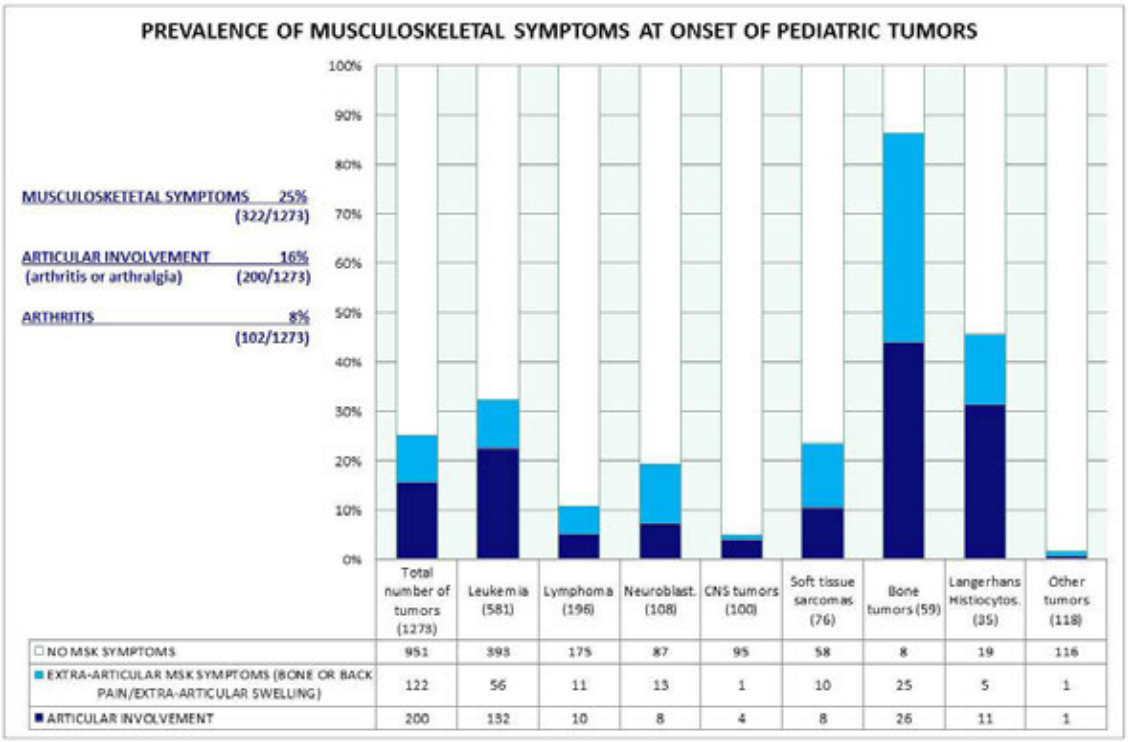
Session Time: 9:00AM–11:00AM

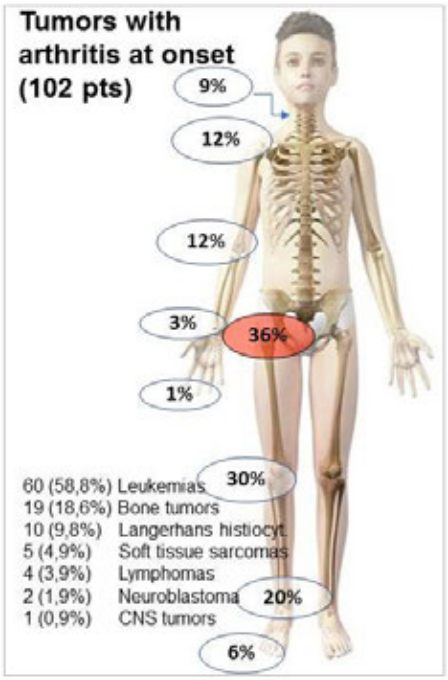
Background/Purpose: Musculoskeletal (MSK) symptoms are a common presenting complaint in pediatric primary care (estimated prevalence 25-50%) and may be the initial manifestation of cancer in rare cases. An articular involvement has been observed in about 20% of onset leukemias, with pictures that can mimic juvenile idiopathic arthritis (JIA) leading to inappropriate steroid or immunosuppressive therapy and diagnostic delay. The primary objective of this study is to assess the prevalence and features of MSK symptoms at the onset of pediatric tumors. The secondary objective is to identify predictors of malignancy comparing tumors with MSK symptoms at onset and new cases of JIA diagnosed in the same period

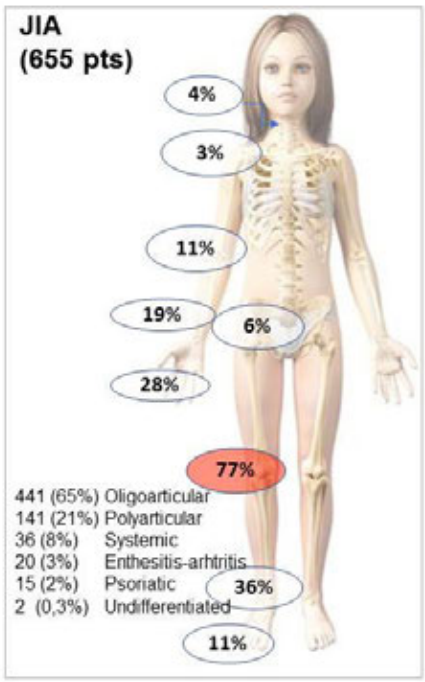
Methods:: The ONCOREUM is a multicenter, observational, cross-sectional study conducted between 2015 and 2018 by 25 Centers of the Italian Association of Pediatric Hematology and Oncology (AIEOP) and 22 Rheumatological Centers of the Italian Society of Pediatrics (SIP). A web based data collection within the AIEOP platform managed by CINECA was performed after local ethics committees approval and written informed consent. We analyzed clinical and laboratory data of patients (pts) < 16 years of age with new diagnosis of tumors or JIA. The data were compare dusing χ^2 for categorical variables and t-test, Welch's test, or Mann-Whitney U test for continuous variables. Statistical analysis was performed by the open source statistical software R.

Results: We considered eligible 1928 pts: 655 of them were affected by JIA and 1273 by tumor. MSK symptoms at onset were found in 25% of cases of tumors, articular involvement (arthritis and/or arthralgia) in 16% and arthritis in 8% (Fig. 1). An initial rheumatological diagnosis was suspected in 9% (29/322) of tumors with MSK symptoms and in 17% (17/102) of tumors with arthritis at onset. The highest frequency of initial rheumatic suspicion was found in neuroblastoma (5/21), Langerhans histiocytosis (3/16) and leukemia (17/188). The most frequent misdiagnosis were hip synovitis, JIA and reactive arthritis. In this preliminary analysis, we compared the clinical features of pts with tumors and arthritis at onset (102) and pts with JIA (655). We found a difference in the frequency of involvement of specific joints: hip and shoulder were significantly associated with tumors; knee, ankle, wrist and small joints of the hands with JIA (Fig 2). We also found that: monoarthritis, arthralgia, bone pain, back pain, disproportionate pain, night pain, refusal to walk, systemic symptoms and male sex were significantly associated with tumors, while poliarthritis (> 4 joints), joint swelling and morning stiffness with JIA (Tab.1)



PATIENTS WITH ARTHRITIS: DISTRIBUTION OF ARTICULAR INVOLVEMENT





Tumors > JIA	
Hip	(p <0,0001)
Shoulder	(p <0,0001)
JIA > Tumors	
Knee	(p <0,0001)
Wrist	(p <0,0001)
Small joints of the hands	(p <0,0001)
Ankle	(p 0,001)

PATIENTS WITH ARTHRITIS: COMPARISON OF CLINICAL FEATURES BETWEEN TUMORS AND JIA

Associated with tumor / Associated with JIA	Tumors (102 pz) (%)	JIA (655 pz) (%)	p
Male sex	54 %	28 %	<0.0001
Age (average)	6 y	6 y	0.629
Duration of symptoms (median)	31,5 d	71 d	<0.0001
Number of joints (average)	1,7 (1-9)	3,3 (1-20)	<0.0001
Monoarthritis	65%	37%	<0.0001
- hip	21%	1%	<0.0001
- knee	16%	29%	0.005
- ankle	8%	4%	0.064
- cervical spine	7%	1%	<0.0001
- elbow	7%	1%	<0.0001
- shoulder	6%	0	<0.0001
- wrist	1%	1%	0.668
2-4 involved joints	29 %	39 %	0.057
> 4 involved joints	6 %	24 %	<0.0001
Swelling	28 %	95 %	<0.0001
Joint pain	98 %	83 %	<0.0001
Limitation of motion	94 %	88 %	0.077
Bone pain	33 %	1 %	<0.0001
Back pain	14 %	7 %	0,011
Disproportionated pain	19 %	1 %	<0.0001
Night pain	9 %	3 %	0.003
Limp	52 %	51 %	0.878
Refusal to walk	31 %	12 %	<0,0001
Morning stiffness	5 %	42 %	<0.0001
Systemic symptoms	65 %	14 %	<0.0001

Conclusion: MSK symptoms at onset of pediatric tumors were observed in 25% of pts, with joint involvement in more than half of cases. Comparing pts with tumors and arthritis with JIA, we found that some clinical feature are useful in differential diagnosis. It is important to carefully evaluate involvement of specific joint at onset (hip and shoulder), monoarticular involvement, specific characteristic of pain, sex and presence of systemic symptoms since these factors have been shown to be significantly associated with oncologic diagnosis.

Disclosure: A. Civino, None; **G. Alighieri**, None; **R. Rondelli**, None; **S. Magni-Manzoni**, None; **M. Romano**, None; **G. Filocamo**, None; **F. Santarelli**, None; **F. Ricci**, None; **A. Olivieri**, None; **S. Pastore**, None; **P. Barone**, None; **R. Gallizzi**, None; **A. Miniaci**, None; **M. Marsili**, None; **R. Podda**, None; **B. Lattanzi**, None; **M. Maggio**, None; **R. Consolini**, None; **F. La Torre**, None; **M. Pelagatti**, None; **F. Soscia**, None; **A. De Fanti**, None; **D. Rigante**, None; **E. Prete**, None; **G. Stabile**, None; **A. Roncadori**, None; **L. Lepore**, None; **V. Conter**, None; **A. Pession**, None; **A. Ravelli**, None.

Abstract Number: 2726

Baseline Characteristics and Quality of Life Metrics in Non-Infectious Uveitis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Pediatric Rheumatology – ePoster III: Systemic JIA, Fever, & Vasculitis – ARP

Session Type: Poster Session (Tuesday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Uveitis is a heterogenous group of ocular inflammatory diseases. Underlying disease and treatment can lead to poor quality of life (QOL), depression, and increased health care costs. Our aim is to evaluate overall QOL, vision related QOL, anxiety and depression in a cohort of children with non-infectious uveitis at the Cincinnati Children's Hospital Medical Center.

Methods: Patients and parents completed questionnaires within two weeks of the ophthalmic evaluation which included: Pediatric Quality of Life Inventory (PedsQL) for overall QOL, Effects of Youngsters' Eyesight on Quality of Life (EYE-Q) for uveitis-specific QOL and function, and the Revised Children's Anxiety and Depression Scale (RCADS) for anxiety and depression. PedsQL scores range from 0-100 and EYE-Q ranges 0-2. Higher scores indicate better overall and vision related QOL. RCADS score of >65 indicates clinically meaningful anxiety or depression. We compared children's questionnaire scores using medians and interquartile range by diagnosis, gender, race, use of topical drops, use of systemic medications, presence of ocular complications, and uveitis activity using Wilcoxon rank sum tests (SAS software).

Results: Forty-eight patients were included: 28 JIA-associated uveitis (JIA-U) and 20 non-JIA-U (Other U). Children with JIA-U were primarily female (82% vs. 50%, p = 0.012), white (89% vs 75%, p = 0.012), younger at uveitis diagnosis (6 vs 10 p< 0.001), have a longer mean duration of disease (5.7 vs 2.6 years, p=0.008), and had anterior uveitis (100% vs 70%, p=0.003). (Table 1). The most common ocular complications were ocular hypertension (46%), cataract (35 %), and posterior synechiae (33%) formation. Topical medications were commonly used at last follow up (~60%), with more JIA-U patients requiring systemic immunosuppressive therapy (79% vs 55%, p=0.082). Parent and patients with JIA-U and Other U reported similar median scores on the EYE-Q, PedsQL and RCADS (Table 2). No differences were observed in QOL metrics based on topical or systemic medication use, ocular complications or uveitis activity. Although females had worse RCADS scores for both the parent (female 43.0 vs male 36.7, p< 0.05) and patient (female 33.6 vs male 30.1, p< 0.05) questionnaires, this was not clinically relevant. There was a trend towards worse uveitis related QOL in non-white patients and those with Other-U.

Table 1. Characteristics of Children with Juvenile Idiopathic Arthritis and Uveitis			
N (%), unless indicated	JIA-U[b] (n = 28)	Other U[c] (n = 20)	JIA-U vs. Other Uveitis T-Score or χ^2 (p-value)
Characteristics			
Demographics			
Age, Mean (SD)[d]	11.8 (4.0)	13.1 (4.0)	-1.04 (0.305)
Patient is Male	5 (17.9)	10 (52.6)	6.30 (0.012)
Patient was White	25 (89.3)	15 (79.0)	1.71 (0.250)*
Specific Racial Categories			
White	25 (89.3)	15 (79.0)	
African American	1 (3.6)	4 (21.1)	
American Indian/Alaskan Native	1 (3.4)	0 (0.0)	
Asian	2 (7.1)	0 (0.0)	
Multi-racial	1 (3.6)	1 (5.3)	
Unknown/Declined	0 (0.0)	1 (5.3)	
Ethnicity, Hispanic	2 (7.4)	1 (5.3)	0.084 (1.000)*
Uveitis Characteristics			
Has Active Uveitis	9 (32.1)	6 (31.6)	0.01 (0.968)
Age at Diagnosis, Mean (SD)	6.0 (3.8)	10.7 (3.2)	-4.40 (<0.001)
Duration of Disease, years, Mean (SD)	5.7 (4.7)	2.6 (2.6)	2.80 (0.008)
Bilateral Disease	20 (71.4)	14 (70.0)	0.40 (0.817)
Anterior Chamber Cells >0.5+	2 (7.4)	2 (10.0)	0.10 (1.000)*
Visual Acuity 20/50 or worse	0 (0.0)	1 (9.1)	1.42 (0.423)*
Location			
Anterior	28 (100.0)	14 (70.0)	9.60 (0.003)*
Intermediate	1 (3.6)	4 (20.0)	3.37 (0.146)*
Posterior	0 (0.0)	1 (5.0)	1.43 (0.417)*
Panuveitis	0 (0.0)	3 (15.0)	4.48 (0.066)*
Has Any Type of Ocular Complication	16 (57.1)	16 (80.0)	2.74 (0.128)*
Ocular Complications, ever (List all that apply)			
Glaucoma or Glaucoma Suspect	3 (10.7)	4 (20.0)	0.81 (0.369)
Cataracts	10 (35.7)	7 (35.0)	0.003 (0.960)
Synechiae	9 (32.1)	7 (35.0)	0.04 (0.836)
Band Keratopathy	1 (3.6)	3 (15.0)	1.99 (0.294)*
Amblyopia	2 (7.1)	1 (5.0)	0.09 (1.000)*
Ocular Hypertension	12 (42.9)	10 (50.0)	0.24 (0.724)
Cystoid Macular Edema	0 (0.0)	1 (5.0)	1.43 (0.417)*
Other[e]	0 (0.0)	4 (20.0)	6.11 (0.025)*
Is Using Topical Drops	18 (64.3)	14 (70.0)	0.17 (0.679)
Is On Systemic Medication	22 (78.6)	11 (55.0)	3.02 (0.082)
Treatment, at time of visit (List all that apply)			
Steroid drops	17 (60.7)	13 (65.0)	0.09 (0.762)

Table 2. Patient Reported Outcome Measures in Children with Juvenile Idiopathic Arthritis Associated Uveitis and Other Uveitis											
	Parent - Report					Patient - Report					
	EYE-Q Parent, median (IQR)			RCADS Total, median (IQR)	PedsQL Total, median (IQR)	EYE-Q Child, median (IQR)			RCADS Total, median (IQR)	PedsQL Total, median (IQR)
	EYE-Q Total	Visual Function	Uveitis-related QOL			EYE-Q Total	Visual Function	Uveitis-related QOL		
Group										
JIA-U	1.9 (1.79 - 1.96)*	1.94 (1.81 - 2)	1.75 (1.63 - 1.88)*	41.44 (36.83 - 49.19)	89.67 (72.83 - 94.57)	1.91 (1.75 - 1.96)	1.9 (1.81 - 2)	1.88 (1.75 - 2)	32.5 (29.84 - 35.51)	89.67 (74.46 - 95.65)
Other Uveitis	1.8 (1.71 - 1.87)*	1.88 (1.81 - 1.94)	1.63 (1.5 - 1.75)*	41.59 (35.81 - 46.43)	85.87 (77.17 - 94.57)	1.81 (1.5 - 1.92)	1.88 (1.56 - 1.94)	1.73 (1.5 - 2)	32.24 (30 - 35.05)	89.13 (79.35 - 94.57)
Topical Drops										
No Topical Drops	1.83 (1.79 - 1.96)	1.94 (1.88 - 2)	1.73 (1.5 - 2)	39.41 (36.57 - 42.52)	88.04 (81.52 - 94.57)	1.83 (1.75 - 1.95)	1.93 (1.8 - 1.94)	1.75 (1.57 - 2)	32.07 (29.83 - 34.53)	89.67 (81.52 - 94.02)
Using Topical Drops	1.83 (1.75 - 1.92)	1.94 (1.75 - 2)	1.75 (1.57 - 1.86)	42.33 (36.87 - 47.96)	85.87 (72.83 - 95.65)	1.84 (1.63 - 1.96)	1.84 (1.56 - 2)	1.88 (1.63 - 2)	32.92 (30 - 35.91)	89.13 (72.83 - 95.65)
Systematic Medications										
No Systemic Medications	1.8 (1.78 - 1.91)	1.9 (1.88 - 2)	1.69 (1.5 - 1.75)	41.94 (37.38 - 49.14)	84.78 (76.09 - 94.57)	1.81 (1.75 - 1.95)	1.88 (1.69 - 1.94)	1.71 (1.5 - 2)	33.54 (31.01 - 36.76)	89.67 (80.44 - 97.83)
On Systemic Medications	1.87 (1.75 - 1.96)	1.94 (1.75 - 2)	1.75 (1.57 - 1.88)	40.95 (36.57 - 45.49)	89.67 (72.83 - 94.57)	1.89 (1.67 - 1.96)	1.9 (1.69 - 2)	1.88 (1.75 - 2)	31.65 (29.84 - 34.53)	89.13 (75 - 94.57)
Ocular Complications										
No OC Complications	1.82 (1.78 - 1.96)	1.94 (1.88 - 2)	1.71 (1.5 - 2)	41.44 (37.1 - 49.14)	83.7 (76.09 - 93.48)	1.83 (1.75 - 1.95)	1.88 (1.81 - 1.94)	1.75 (1.57 - 2)	32.5 (29.83 - 35.11)	89.13 (83.7 - 94.02)

Conclusion: We report on the clinical characteristics, QOL and functioning of children with uveitis. Our results suggest there may be differences in QOL and function related to sex, race, and uveitis diagnosis. Larger and more diverse cohorts with varied uveitis, visual impairment and disease activity are needed to better understand the impact of uveitis and treatment on a child and family's QOL and function.

Disclosure: J. Shantha, None; **A. Cassedy**, None; **J. McDonald**, None; **T. Hennard**, None; **N. Mwase**, None; **S. Yeh**, None; **S. Angeles-Han**, None.

Abstract Number: 2727

Mitochondrial Contribution to Juvenile Dermatomyositis Pathogenesis

Bhargavi Duvvuri,[1] Lauren Pachman,[2] Richard Moore,[1] Gabrielle Morgan,[2] Marisa Klein-Gitelman,[2] Megan L. Curran,[3] **Stephen Doty**,[4] and Christian Lood[1], [1]University of Washington, Seattle, [2]Northwestern University, Chicago, [3]University of Colorado, Aurora, CO, [4]Hospital for Special Surgery, New York

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Plenary III
Session Type: Plenary Session III
Session Time: 11:00AM–12:30PM

Background/Purpose: Though mainly found intracellularly, we recently observed mitochondrial extrusion upon cell death, contributing to inflammation and organ damage in lupus-prone mice. Of note, mitochondria are immunogenic, promoting development of anti-mitochondrial antibodies (AMAs). Mitochondrial remnants, including DNA, are observed in the circulation of many systemic diseases, including lupus, and thought to partake in the disease pathogenesis. However, the role of mitochondrial extrusion in children with juvenile dermatomyositis (JDM) has not been addressed. The aim of this study was to investigate markers of mitochondrial extrusion, including mtDNA and AMAs, in JDM children to determine their clinical utility.

Methods: AMAs, as well as cell-free mtDNA levels were analyzed in healthy children (HC, n=22), pediatric lupus (n=10), polymyositis (n=7), JDM patients (n=61), and RNP+ myositis (12), by a state-of-the-art flow cytometry technique as well as an in-house qPCR assay. Mitochondrial markers were associated with disease activity score (DAS), calcinosis, as well as autoantibody profiles. Muscle biopsies were analyzed using electron microscopy.

Results: Electron microscopy imaging demonstrated profound mitochondrial abnormalities in JDM muscle, including intramitochondrial calcification associated with degenerate muscle fibers and mitochondrial extrusion. As compared to healthy controls, JDM patients had increased levels of cell-free mtDNA ($p=0.02$) but not genomic DNA ($p=0.09$) in peripheral blood, especially in children with calcinosis ($p=0.002$). As determined by Western blot, JDM patients had autoantibodies reacting towards mitochondrial antigens of 60 kDa, similar to what was seen in jSLE. By flow cytometry, 40% of JDM patients were found to be positive for AMAs ($p< 0.001$). Consistent with the immunogenic nature of mitochondria, AMA levels correlated with presence of antigen, e.g. mtDNA, in peripheral blood ($r=0.28$, $p< 0.05$), as well as with immune complex (IC) levels ($r=0.56$, $p< 0.0001$) and complement C4 consumption ($r=-0.59$, $p=0.01$). Upon activation with mitochondrial ICs, neutrophils induced IL-8 production ($p< 0.01$) as well as underwent formation of neutrophil extracellular traps (NETs, $p< 0.05$), clearly demonstrating the inflammatory potential of mitochondrial ICs. AMA positivity was associated with calcinosis (OR=6.1, $p=0.006$). Of importance, AMA became elevated prior to the clinical diagnosis of calcinosis (OR=11.1, $p< 0.05$), with a sensitivity and specificity of 80% and 73.5%, respectively, to identify calcinosis-prone individuals within the group of children with JDM, suggesting a prognostic potential of AMA in JDM calcinosis development.

Conclusion: JDM patients have obvious mitochondrial abnormalities in tissue and periphery. Our novel findings of mitochondrial antibodies in JDM, preceding clinical diagnosis of calcinosis, support i) mitochondrial extrusion as a potential therapeutic targetable pathway, and ii) the use of AMAs as prognostic markers, allowing for early, preventive treatment, reducing development of disabling calcinosis in those children.

Disclosure: B. Duvvuri, None; **L. Pachman**, Reveragen, 2, SBIR grant Eric P. Hofffman, PhD RevaraGen, unrelated.,, 9; **R. Moore**, None; **G. Morgan**, None; **M. Klein-Gitelman**, None; **M. Curran**, None; **S. Doty**, None; **C. Lood**, None.

Abstract Number: 2728

Efficacy and Safety of Upadacitinib in a Randomized, Double-Blind, Placebo-Controlled, Multicenter Phase 2/3 Clinical Study of Patients with Active Ankylosing Spondylitis

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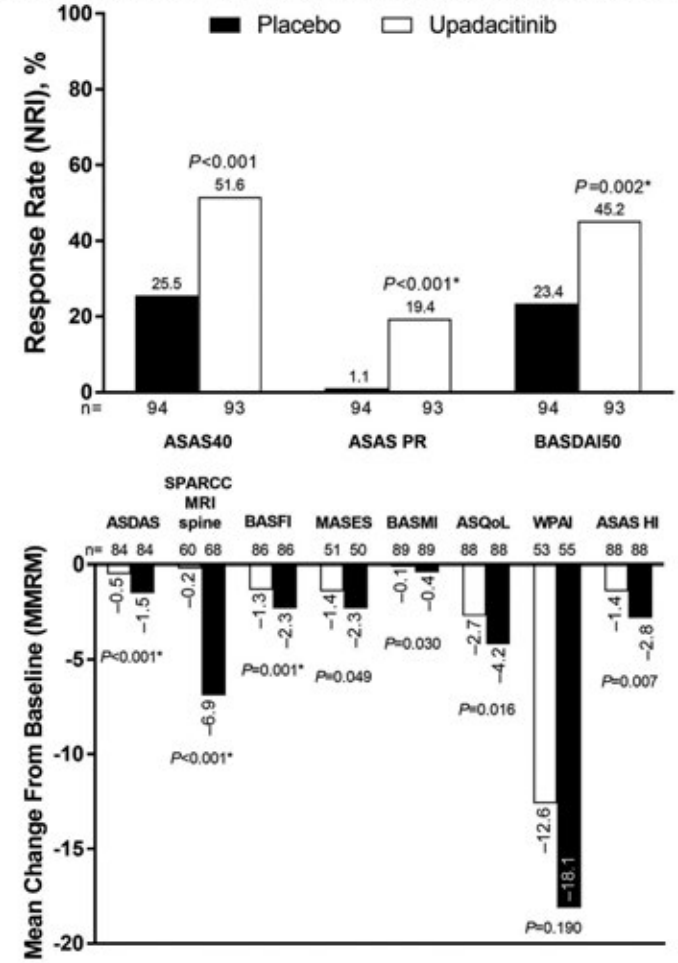
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Plenary III
Session Type: Plenary Session III
Session Time: 11:00AM–12:30PM

Background/Purpose: Patients (pts) with ankylosing spondylitis (AS) who have an inadequate response/contraindication to NSAIDs have limited treatment options other than biologics. The Janus kinase (JAK) pathway is a potential therapeutic target in AS. This study assessed the efficacy and safety of upadacitinib (UPA), a selective JAK1 inhibitor, in pts with active AS.

Methods: In this double-blind, placebo (PBO)-controlled, phase 2/3 study (NCT03178487; SELECT-AXIS 1) pts with AS were randomized 1:1 to UPA 15 mg or matching placebo. Enrolled pts (≥18 y) met modified New York Criteria for AS based on central reading of radiographs, had a BASDAI ≥4 and pt assessment of total back pain ≥4 (numeric rating scale, 0–10) at screening and baseline (BL), were biologic DMARD naive, and had inadequate response to ≥2 NSAIDs or intolerance to/contraindication for NSAIDs. The primary efficacy endpoint was Assessment of SpondyloArthritis international Society (ASAS) 40 response at wk 14. Multiplicity-adjusted key secondary endpoints included change from BL to wk 14 (Δ) in Ankylosing Spondylitis Disease Activity Scores (ASDAS), Δ Spondyloarthritis Research Consortium of Canada (SPARCC) MRI spine, BASDAI50 at wk 14, Δ AS quality of life (QoL), ASAS partial remission (PR) at wk 14, Δ BASFI, Δ BASMI, Δ Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), Δ Work Productivity and Activity Impairment (WPAI), and Δ ASAS health index (HI). Adverse events (AEs) were monitored throughout the study.

Results: All randomized pts (N=187) received assigned treatment (PBO, n=94; UPA, n=93); 95.7% of pts completed the study through wk 14 (PBO, 90/94; UPA, 89/93). Most pts were male (70.6%) and HLA-B27 positive (76.5%). Mean symptom duration was 14.4 y, and mean age was 45.4 y; BL disease characteristics were balanced between arms. Significantly more pts treated with UPA vs PBO achieved the primary endpoint of ASAS 40 response at wk 14 (51.6% vs 25.5%; $P< 0.001$; **Figure**). Accounting for multiplicity-adjustment, the following endpoints were statistically significant for UPA vs PBO at week 14: Δ ASDAS, Δ SPARCC MRI spine, BASDAI50, ASAS PR, and Δ BASFI (**Figure**). Other ranked secondary endpoints, except WPAI, were significant based on nominal P values (**Figure**). The proportions of pts with AEs leading to discontinuation (2.2% vs 3.2%), serious AEs (1.1% vs 1.1%), and infections (20.4% and 27.7%) were similar for UPA and PBO groups, respectively. No serious infections, herpes zoster, malignancy, venous thromboembolic events, or deaths were reported.

Figure. Primary (ASAS 40) and Multiplicity-adjusted Key Secondary Endpoints at Week 14



ASAS40, Assessment of SpondyloArthritis international Society 40% response; ASQoL, Ankylosing Spondylitis Quality of Life score; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI 50, 50% improvement from baseline in BASDAI; HI, Health Index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; NRI, non-responder imputation; MMRM, mixed model for repeated measures; PR, partial remission; SPARCC, Spondyloarthritis Research Consortium of Canada; WPAI, Work Productivity and Activity Impairment.
*Significant in multiplicity-adjusted analysis. Nominal P values are shown.
MASES assessment includes patients with baseline enthesitis; WPAI assessment includes patients currently employed; SPARCC MRI assessment population as pre-specified.

Conclusion: UPA 15 mg QD was significantly more efficacious than PBO at wk 14 in pts with active AS for improvement in signs and symptoms, function, and imaging. The proportion of patients with AEs was similar in the UPA and PBO arms, and no new safety findings were observed compared with previous UPA studies in other diseases.

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Abstract Number: 2729

Ixekizumab in Non-Radiographic Axial Spondyloarthritis: Primary Results from a Phase 3 Trial

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Plenary III
Session Type: Plenary Session III
Session Time: 11:00AM–12:30PM

Background/Purpose: Ixekizumab (IXE), a high affinity IL-17A monoclonal antibody, previously showed efficacy in AS/radiographic-axSpA[1,2]. COAST-X (NCT02757352) is a phase 3 study that assessed efficacy and safety of IXE in patients (pts) with active nr-axSpA and objective signs of inflammation.

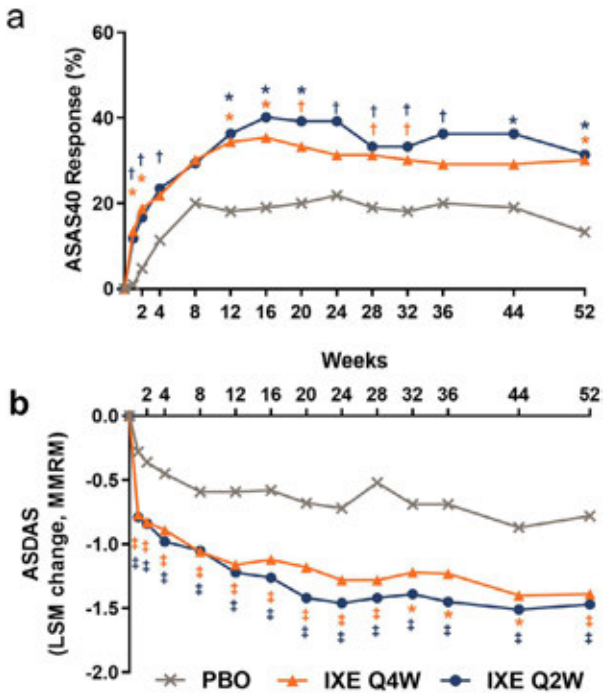

Figure. Key efficacy outcomes over 52 weeks. (a) ASAS40 responses and (b) ASDAS LSM change from baseline over 52 weeks are shown for PBO, IXE Q4W, and IXE Q2W. For ASAS40, a logistic regression model was used for comparisons between placebo and IXE treatment arms; missing data and switch to open-label IXE Q2 were considered as nonresponse. For ASDAS comparisons were made by mixed model of repeated measures (MMRM). ‡p<0.001, *p<0.01; †p<0.05. ASAS, Assessment of SpondyloArthritis international Society; ASDAS, Ankylosing Spondylitis Disease Activity Scores; IXE, ixekizumab; LSM, least squares mean; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks.

Table 1. Demographics and baseline characteristics

	PBO N=105	IXE Q4W N=96	IXE Q2W N=102
Age (years), mean (SD)	39.9 (12.4)	40.9 (14.5)	40.0 (12.0)
Female, n (%)	61 (58.1)	46 (47.9)	53 (52.0)
Geographic region, n (%)			
North and South America	33 (31.4)	32 (33.3)	37 (36.3)
Asia	15 (14.3)	12 (12.5)	11 (10.8)
Europe	57 (54.3)	52 (54.2)	54 (52.9)
Symptom duration (years), mean (SD)	10.1 (8.3)	11.3 (10.7)	10.6 (10.1)
Years with axSpA diagnosis, mean (SD)	3.1 (4.5)	4.2 (5.5)	3.4 (4.6)
Positive for HLA-B27, n (%)	77 (74.0)	71 (74.7)	73 (72.3)
BASDAI score, mean (SD)	7.2 (1.5)	7.0 (1.5)	7.3 (1.3)
ASDAS score, mean (SD)	3.8 (0.9)	3.8 (0.8)	3.9 (0.8)
BASFI score, mean (SD)	6.7 (2.0)	6.4 (2.1)	6.5 (1.8)
CRP (mg/L), mean (SD)	14.3 (24.4)	12.4 (18.0)	12.1 (17.8)
SI joint SPARCC score, mean (SD)	6.2 (9.1)	5.3 (8.3)	7.5 (10.8)
MRI/hsCRP stratification, n (%)[a,b]			
MRI+/hsCRP+	38 (36.2)	30 (31.3)	39 (38.2)
MRI+/hsCRP-	40 (38.1)	36 (37.5)	34 (33.3)
MRI-/hsCRP+	26 (24.8)	30 (31.3)	28 (27.5)
Concomitant medication, n (%)			
NSAIDs	96 (91.4)	81 (84.4)	95 (93.1)
Methotrexate	17 (16.2)	17 (17.7)	15 (14.7)
Sulfasalazine	21 (20.0)	23 (24.0)	27 (26.5)
Corticosteroid	14 (13.3)	8 (8.3)	20 (19.6)

[a]Randomization stratified by country and screening MRI/hsCRP status (positive MRI and elevated hsCRP, positive MRI and non-elevated hsCRP, negative MRI and elevated hsCRP). [b]Elevated hsCRP defined as >5.00 mg/L. Percentages were calculated based on the number of patients with nonmissing values. axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C-reactive protein; HLA, human leukocyte antigen; hsCRP, high-sensitivity C-reactive protein; IXE, ixekizumab; MRI, magnetic resonance imaging; NSAIDs, nonsteroidal anti-inflammatory drugs; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; SD, standard deviation; SI, sacroiliac; SpA, spondyloarthritis; SPARCC, Spondyloarthritis Research Consortium of Canada.

Table 2: Primary and secondary efficacy outcomes at Week 16 and Week 52 and safety at Week 52

	Week 16			Week 52		
	Placebo N=105	IXE Q4W N=96	IXE Q2W N=102	Placebo N=105	IXE Q4W N=96	IXE Q2W N=102
Primary & secondary outcomes						
ASAS40 response						
ITT population, n (%)[a,b]	20 (19.0)	34* (35.4)	41* (40.2)	14 (13.3)	29* (30.2)	32* (31.4)
Escaped patients, n/N (%)[c]	4 / 62 (6.5)	12 / 40 (30.0)	9 / 42 (21.4)	21 / 56 (37.5)	15 / 37 (40.5)	15 / 36 (41.7)
ASDAS LDA (<2.1), n (%)[a,b]	13 (12.4)	26* (27.7)	33‡ (32.4)	9 (8.6)	28‡ (29.8)	28‡ (27.5)
Change from baseline, LS mean (SE)						
ASDAS[b,d]	-0.58 (0.10)	-1.12‡ (0.10)	-1.26‡ (0.10)	-0.78 (0.14)	-1.39‡ (0.12)	-1.47‡ (0.12)
BASDAI[b,d]	-1.51 (0.22)	-2.18† (0.22)	-2.52* (0.22)	-1.76 (0.31)	-2.89* (0.27)	-3.04* (0.27)
BASFI[d]	-1.34 (0.23)	-2.01† (0.23)	-2.28* (0.23)	-1.57 (0.33)	-2.63† (0.29)	-2.75* (0.29)
SF-36 PCS[b,d]	5.21 (0.80)	8.06† (0.81)	7.96† (0.80)	4.72 (1.25)	8.92† (1.08)	9.33* (1.08)
SI Joint SPARCC Score[b,e]	-0.31 (0.54)	-3.38‡ (0.55)	-4.52‡ (0.53)	-1.92 (0.87)	-4.40† (0.73)	-6.16‡ (0.71)
Safety outcomes						
TEAEs, n (%)	51 (49.0)	52 (54.2)	65 (63.7)	60 (57.7)	63 (65.6)	79 (77.5)
SAEs, n (%)	1 (1.0)	0	1 (1.0)	1 (1.0)	2 (2.1)	1 (1.0)
Discontinuations due to AEs, n (%)	2 (1.9)	0	1 (1.0)	2 (1.9)	1 (1.0)	1 (1.0)

‡p<0.001, *p<0.01; †p<0.05. [a]Logistic regression analysis with nonresponder imputation for missing data. [b]A primary or major secondary endpoint. Comparisons between each of the ixekizumab treatment arms and placebo for primary and major secondary endpoints were all statistically significant as calculated using a graphical multiplicity testing method. [c]Percentages based on observed cases and initial randomized treatment. [d]Mixed effects model of repeated measures analysis. [e]Analysis of covariance of observed cases. AEs, adverse events; ASAS, Assessment of SpondyloArthritis international Society; CRP, C-reactive protein; HLA, human leukocyte antigen; ITT, intent to treat; IXE, ixekizumab; LDA, low disease activity; LSmean, least squares mean; MRI, magnetic resonance imaging; Q2W, every 2 weeks; Q4W, every 4 weeks; SAEs, serious adverse events; SE, standard error; SF-36 PCS, Medical Outcomes Questionnaire Short Form-36 Principal Component Summary; SI, sacroiliac; SPARCC, Spondyloarthritis Research Consortium of Canada; SpA, spondyloarthritis; TEAEs, treatment-emergent adverse events.

Methods: COAST-X was a 52-wk, randomized, double-blind, PBO-controlled study enrolling adults with an established diagnosis of axSpA who met ASAS classification (but not modified New York) criteria, had BASDAI ≥4, back pain ≥4, inflammation [sacroiliitis on MRI or elevated CRP >5 mg/L], and inadequate response or intolerance to NSAIDs. All images were centrally read. After stratification by country and screening MRI/CRP status, pts were randomized 1:1:1 to 80 mg IXE every 4 wks (Q4W), 80 mg IXE every 2 wks (Q2W), or PBO. Changes to conventional back-

ground medication (NSAIDs, csDMARDs, analgesics, and low dose corticosteroids) as well as escape to open label (OL) IXE Q2W were allowed at investigator discretion after Wk 16. Subsequent escape to OL TNF-inhibitor treatment was permitted after ≥8 wks of OL IXE Q2W. Primary endpoints were ASAS40 at Wks 16 and 52. Patients missing data or switched to OL IXE Q2W were imputed as non-responder. A logistic regression model with nonresponder imputation was used for categorical data. A mixed effects model of repeated measures was used for continuous variables. Analysis of covariance was used for sacroiliac joint (SIJ) MRI SPARCC scores.

Results: Table 1 shows baseline characteristics; 303 subjects were randomized: PBO (N=105), IXE Q4W (N=96), IXE Q2W (N=102). Significantly more pts achieved ASAS40 at Wk 16: IXE Q2W (40%), IXE Q4W (35%) vs PBO (19%, $p< 0.01$) and at Wk 52: IXE Q2W (31%), IXE Q4W (30%) vs PBO (13%, $p< 0.01$) (Fig. & Table 2). Compared to PBO, pts on either IXE regimen had significantly greater changes from baseline at Wk 16 and Wk 52 for disease activity, functional status, and SIJ SPARCC scores (Fig. & Table 2). Statistically significant improvements for both IXE regimens vs PBO were first observed at Wk 1 for ASAS40. A notable proportion of pts who escaped to OL IXE Q2W had ASAS40 response at the time of escape (16.7%, 25%, and 6.5% on IXE Q2W, IXEQ4W, and PBO, respectively), and ASA40 rates increased further on open label IXE Q2 (Table 2). The frequency of serious adverse events and adverse events that led to treatment discontinuation was low and similar across all arms (Table 2). No new safety signal was identified.

Conclusion: The primary endpoint of ASAS40 and all major secondary endpoints for IXE Q4W and Q2W were met at Wk 16 and Wk 52 with no unexpected safety findings. IXE added to conventional background medication was superior to conventional background medication and PBO for improving signs, symptoms, and inflammation on MRI in pts with nr-axSpA.

References:

1. Deodhar, et al. (2018). *Arthritis Rheumatol.* 71(4):599-611.
2. van der Heijde, et al. (2018). *Lancet*. 392(10163):2441-51.

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5, 9, Novartis, 2, 5, 9, Pfizer, 2, 9, Spondylitis Association of America, 6, Spondyloarthritis Research and Treatment Network (SPARTAN), 6, UCB, 2, 5, 9, UCB Pharma, 2, 9; **T. Kim**, None; **W. Maksymowych**, Eli Lilly and Company, 2, 5, 8, AbbVie, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8, Celgene, 5, Boehringer Ingelheim, 5, Galapagos, 5, CaRE Arthritis, 6; **M. Østergaard**, AbbVie, 2, 8, 9, Abbvie, 2, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, UCB, 5, 8, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, 5, 8, Abbvie, Celgene, Centocor, Merck, and Novartis, 2, Abbvie, Celgene, Centocor, Merck, Novartis, 2, BMS, 2, 5, 8, 9, Boehringer Ingelheim, 5, 8, Boehringer-Ingelheim, 2, 8, Boehringer-ingelheim, 9, Celgene, 2, 5, 8, Centocor, 2, Eli Lilly, 5, 8, 9, Eli Lilly and Company, 5, 8, Eli-Lilly, 2, 8, Hospira, 2, 5, 8, Janssen, 2, 5, 8, 9, Merck, 2, 5, 8, 9, Novartis, 2, 5, 8, Novo, 2, 5, 8, Novo Nordisk, 5, 8, Orion, 2, 5, 8, Pfizer, 2, 5, 8, 9, Regeneron, 2, 5, 8, Roche, 2, 5, 8, roche, 9, Sandoz, 2, 8, Sanofi, 2, 8, UCB, 2, 5, 8; **D. Poddubnyy**, Abbvie, 2, 5, 8, AbbVie, 2, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 2, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8; **H. Marzo-Ortega**, AbbVie, 5, 8, AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, 5, Abbvie, Celgene, Janssen, Lilly, Novartis, Pfizer, Ucb, 5, 8, AbbVie, Celgene, Janssen, Lilly, Novartis,Pfizer and UCB, 8, Celgene, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 2, 5, 8, Janssen and Novartis, 2, Janssen, Novartis, 2, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **L. Bessette**, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, Amgen, BMS, Janssen, Roche, UCB Pharma, AbbVie Inc, Pfizer, Merck, Celgene, Sanofi, Eli Lilly, and Novartis., 2, 5, 8, BMS, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Bristol-Myers-Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, UCB Pharma, 2, 5; **T. Tomita**, AbbVie, 5, 8, Astellas, 5, 8, BMS, 5, 8, Eisai, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Mitsubishi Tanabe, 5, 8, Novartis, 5, 8, Takeda, 5, 8, Pfizer, 5, 8; **G. Gallo**, Eli Lilly, 1, 3, 4, Eli Lilly and Company, 1, 3, 4; **D. Adams**, David Adams, 3, 4, Eli Lilly and Company, 1, 3; **A. Leung**, None; **F. Zhao**, Eli Lilly, 1, 3, 4, Eli Lilly and Company, 1, 3, 4; **M. Hojnik**, Eli Lilly and Company, 3, 4; **H. Carlier**, Eli Lilly and Company, 1, 3, 4; **J. Sieper**, AbbVie, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Novartis, 5, 8.

Abstract Number: 2730

Efficacy and Safety of Romosozumab vs Placebo Among Patients with Mild-to-Moderate Chronic Kidney Disease

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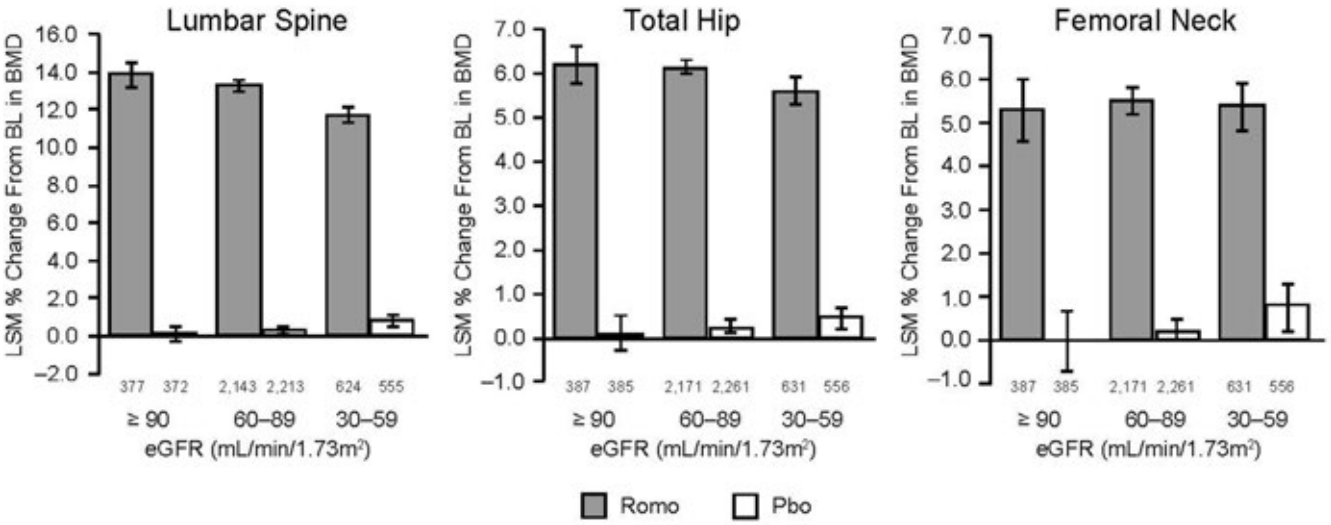
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Plenary III
Session Type: Plenary Session III
Session Time: 11:00AM–12:30PM

Background/Purpose: Osteoporosis and renal insufficiency are coexisting disease states in a substantial proportion of postmenopausal women. Since bisphosphonates are generally contraindicated in patients with estimated GFR (eGFR) < 35 mL/min, it is important to evaluate other osteoporosis treatments in this setting. This post hoc anal-

Figure. LSM (95% CI) % Change in BMD From Baseline to Month 12



Change in BMD from baseline for the eGFR 15–29 mL/min/1.73m^2 subgroup is not reported since there were only 7 pts in the pbo group for each of the measured sites and only 7, 8, and 8 pts in the romo group for LS, TH, and FN, respectively. Number of pts are shown below each bar. Error bars represent 95% CIs.
Abbreviations: BL, baseline; LSM, least squares mean.

ysis of the FRAME study assessed the efficacy and safety of romosozumab (Romo) vs placebo (Pbo) among patients with different levels of renal function.

Methods: FRAME enrolled 7,180 postmenopausal women with T-scores –2.5 to –3.5 at the total hip (TH) or femoral neck (FN). In the Pbo-controlled double-blind treatment phase, patients received Romo 210 mg or Pbo monthly for 12 months. Patients were grouped by baseline eGFR (mL/min/1.73m^2) normalized to body surface area, calculated using the MDRD study equation. Renal function was categorized as normal renal function (eGFR ≥ 90) or mild (eGFR 60–89 [chronic kidney disease (CKD) stage 2]), moderate (eGFR 30–59 [CKD stage 3]), or severe (eGFR 15–29 [CKD stage 4]) renal insufficiency. The least squares mean % change from baseline in bone mineral density (BMD) at the lumbar spine (LS), TH, and FN; incidence of new vertebral fractures and adverse events; and CKD progression were assessed for each eGFR category at month 12.

Results: At baseline, most patients (88%) had mild or moderate renal insufficiency; 0.3% had severe renal insufficiency. In the overall patient population, the least squares mean % change (95% CI) from baseline in BMD (Romo vs Pbo) was 13.1% (12.8–13.3) vs 0.4% (0.2–0.5) for LS, 6.0% (5.9–6.2) vs 0.3% (0.1–0.4) for TH, and 5.5% (5.2–5.7) vs 0.3% (0.1–0.5) for FN. Changes in BMD were similar irrespective of baseline eGFR (Figure). Incidence of new vertebral fractures (Romo/Pbo) in patients with normal renal function, CKD 2, or CKD 3 was 0.5%/3.0%, 0.4%/1.5%, and 0.6%/2.1%, respectively. The overall incidence of adverse events and serious adverse events, and the incidence of positively adjudicated cardiovascular events were similar between treatment groups for all eGFR categories. One patient (CKD 2 at baseline) in the Romo group had grade 2 hypocalcemia. Mild-to-moderate calcium decrease occurred in 4 patients in the Pbo group and 13 patients in the Romo group. Most patients (approximately 80% in each group) had no changes from baseline eGFR category at the end of the 12-month period.

Conclusion: Romo increased BMD across eGFR subgroups vs Pbo, and the reduction in new vertebral fractures was not notably affected by eGFR level. Safety was also generally comparable among eGFR subgroups.

Disclosure: P. Miller, Amgen, 2, 5, Radius Pharma, 2, 5, Alexion, 5; **A. Chines**, Amgen, 1, 3, Amgen Inc., 1, 3; **B. Albergaria**, Amgen, 2, 8, Merck & Co, 2, Novartis, 2, 8, Organon, 2, Radius, 2, Roche, 2, 8, Sanofi-Aventis, 2, 8, UCB, 2, 8, Eli Lilly, 8, Merck Sharp & Dohme, 8, Servier, 8; **E. Gielen**, UCB, 5, Takeda, 8; **B. Langdahl**, Amgen, 2, 5, 8, Novo Nordisk, 2, Eli Lilly, 5, 8, UCB, 5, 8; **A. Miyauchi**, None; **M. Vanderkelen**, UCB Pharma, 1, 3; **C. Milmont**, Amgen, 1, 3; **J. Maddox**, Amgen, 1, 3; **J. Adachi**, Abbvie, 2, Amgen, 2, 5, 8, Amgen Inc., 2, 5, 8, Eli Lilly, 5, Lilly, 5, Pfizer, 2, UCB, 2.

Abstract Number: 2731

Decomposition Analysis of Spending and Price Trends for Biologic Anti-Rheumatic Drugs in Medicare and Medicaid

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Plenary III
Session Type: Plenary Session III
Session Time: 11:00AM–12:30PM

Background/Purpose: Billions of public dollars are spent each year on biologic disease-modifying anti-rheumatic drugs (bDMARDs), but the drivers of bDMARD spending and per-patient cost increases are unclear. We characterized changes in total spending and unit-prices for bDMARDs in Medicare and Medicaid and quantified the major sources of spending increases for public programs and beneficiaries.

Methods: Data Source and Measures: We accessed Medicare Parts B & D and Medicaid drug spending data for years 2012-2016. These contained aggregated prescription claims for all beneficiaries enrolled in Medicare Parts B (fee-for-service) or Part D (stand-alone or Medicare Advantage plans) or Medicaid. All bDMARDs with FDA approval for ≥ 1 rheumatic disease through Dec. 2014 were included. For each bDMARD and calendar-year we extracted total annual spending, and number of recipients, claims, and doses dispensed, and calculated drug unit-price (average cost/dose).

Statistical Analysis: We calculated five-year changes in total spending and unit-prices for each bDMARD and in-aggregate, after adjusting for general inflation to 2016 dollars. We then performed standard decomposition analyses to isolate the contributions of four sources of spending growth (drug prices, uptake [number of recipients], treatment intensity [mean # of doses per-claim], and annual # of claims per-recipient) for each bDMARD. We conducted our analysis including statutory Medicaid rebates (as these decrease public spending), and both excluding and including Medicare rebates (as these are paid by manufacturers to Pharmacy Benefit Managers and Part D plans). We used time-varying rebates reported by the Congressional Budget Office.

Table: Spending and Uptake for Biologic DMARDs Covered under Medicare Parts D and B (drugs ranked by 2016 spending)

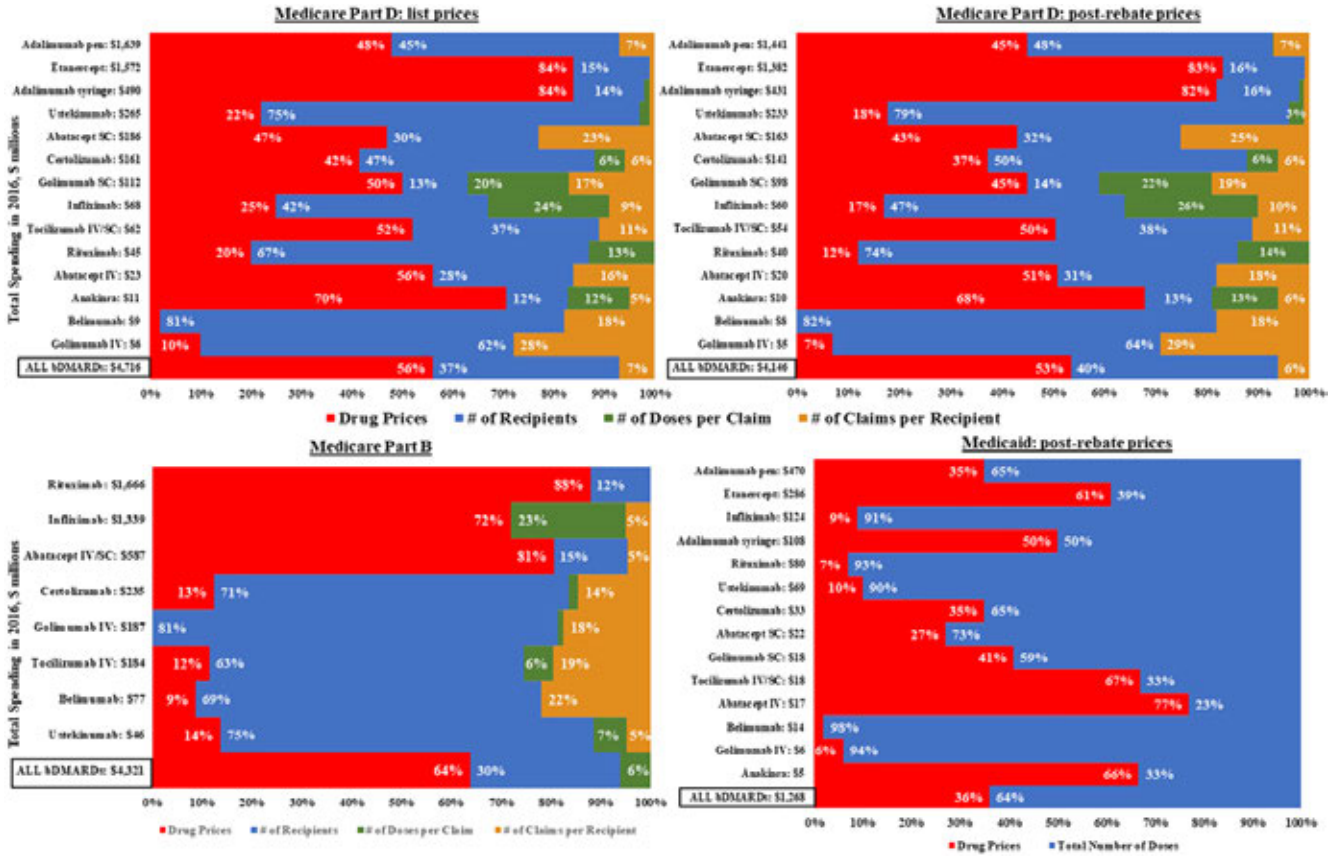
MEDICARE PART D							
Biologic DMARD	Total Spending in 2016[a]	# of Recipients in 2016	Change from 2012				
			Total Spending	Total Spending, Rebate-Adjusted[c]	# of Recipients	Drug Prices	Drug Prices, Rebate-Adjusted[c]
Adalimumab SC (injector pen)	$1,638,715,583	48,164	261%	237%	80%	84%	72%
Etanercept SC	$1,572,038,339	47,795	107%	93%	11%	88%	75%
Adalimumab SC (pre-filled syringe)	$490,135,622	15,477	107%	93%	11%	84%	72%
Ustekinumab SC	$264,877,321	6,616	401%	367%	249%	37%	28%
Abatacept SC[b]	$185,560,929	6,916	72%	66%	19%	31%	26%
Certolizumab SC	$160,787,675	5,903	172%	154%	61%	51%	41%
Golimumab SC	$111,914,458	3,549	124%	109%	11%	49%	39%
Infliximab IV	$68,074,955	2,407	110%	96%	37%	20%	12%
Tocilizumab (IV or SC)[b]	$61,489,157	3,499	142%	134%	60%	100%	93%
Rituximab IV	$45,242,671	1,756	94%	81%	65%	16%	8%
Abatacept IV	$22,475,179	1,162	99%	85%	24%	54%	44%
Anakinra SC	$10,858,651	388	142%	126%	11%	87%	74%
Belimumab IV	$8,612,441	388	385%	352%	304%	3%	-4%
Golimumab IV[b]	$5,836,741	292	149%	141%	70%	17%	13%
ALL	$4,715,757,411	-	176%	158%	-	52%	42%

MEDICARE PART B					
Biologic DMARD	Total Spending in 2016[d]	# of Recipients in 2016	Change from 2012		
			Total Spending	# of Recipients	Drug Prices
Rituximab IV	$1,665,667,928	69,941	11%	2%	18%
Infliximab IV	$1,338,726,191	58,397	27%	-2%	20%
Abatacept (IV or SC)	$586,532,893	22,879	104%	11%	79%
Certolizumab SC[b]	$235,364,173	11,953	93%	60%	8%
Golimumab IV[b]	$186,707,915	10,521	195%	144%	0%
Tocilizumab IV	$184,202,071	11,167	102%	56%	8%
Belimumab IV	$76,797,133	2,922	124%	84%	8%
Ustekinumab SC	$46,408,889	1,752	379%	235%	21%
ALL	$4,320,542,877	-	45%	-	20%

Results: From 2012-2016, annual spending on the 11 included bDMARDs by US public programs and beneficiaries nearly doubled (from $5.3 to $10.3 billion); drug prices increased by a mean of 52% in Part D and just 20% in Part B (**Table**). Controlling for general inflation, unit-price increases alone accounted for 56% ($1.7 billion) of the five-year, $3.0 billion spending increase within Part D (**Figure**); increased uptake accounted for 37% ($1.1 billion). After accounting for time-varying rebates, price hikes were still responsible for 53% ($1.4 billion) of the Part D spending increase. Adalimumab and etanercept, two of the oldest bDMARDs, were prescribed to the largest numbers of Part D beneficiaries and had the biggest unit-price increases: 84% and 88%, respectively. Medicaid spending and price trends were similar to Part D (**Figure**).

Majority of spending growth for the oldest Part B drugs (rituximab, abatacept, and infliximab) was from price increases (72-88%), while for the five newer drugs (golimumab, ustekinumab, tocilizumab, certolizumab, and belimumab), number of recipients was the main driver (63-81% of spending growth).

Conclusion: Post-market drug-price changes alone accounted for the majority of recent bDMARD spending growth, and manufacturers' rebates had little impact on these findings. Beyond rebates, policy interventions that target price increases, particularly under Part D plans, may help mitigate public-payer drug spending and out-of-pocket costs for the elderly and disabled beneficiaries who rely on bDMARDs.



Component proportion of Biologic DMARD spending increases from 2012 to 2016, by public program (drugs ranked by 2016 spending, $ millions)

Disclosure: N. McCormick, None; **Z. Wallace**, National Institute of Arthritis, Musculoskeletal, and Skin Diseases, 2, Rheumatology Research Foundation, 2; **C. Sacks**, None; **J. Hsu**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5.

Abstract Number: 2732

The Relationship Between Gout and Cardiovascular Disease Outcomes: A Health Data Linkage Study of 1 Million New Zealanders Using Population-level Cardiovascular Risk Prediction Equations

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Plenary III

Session Type: Plenary Session III

Session Time: 11:00AM–12:30PM

Background/Purpose: Some studies have reported that gout is an independent risk factor for cardiovascular events. Furthermore, urate-lowering therapy such as allopurinol may be associated with reduced risk of cardiovascular disease (CVD). Recently, population-level cardiovascular risk prediction equations for health planning have been developed and validated using linked health data in New Zealand (Mehta, Int J Epidemiol. 2018). We examined the association of gout with population-level estimated CVD risk and CVD outcomes using linked national health data.

Methods: National registries of medicines dispensing data, hospitalisation, and death were linked to the Auckland/Northland regional repository of laboratory results from January 1, 2012 to December 31, 2016. There were 65.6% (n=968,986) of the resulting health contact population who had no prior CVD in 2012 and formed the cohort for this study. Sex-specific baseline 5-year CVD risk (of cardiovascular death, non-fatal myocardial infarction, stroke, or other vascular event) was derived using the published population-level CVD risk scores. A validated national health data definition of gout was used to define those with gout: discharge diagnosis of gout (ICD-9 274, ICD-10 M10) from a public hospital admission or having been dispensed gout specific medications (Winnard, Rheumatology 2012). Data were limited to patients aged ≥20 years with a primary residence in the Auckland/Northland region for the last 3 years.

Results: Of the 968 986 people included in the study, 32 805 (3.4%) had gout. The population-level estimated 5-year CVD risk and rates of CVD events (fatal and non-fatal) were higher in both women and men with gout (**Table**). After adjustment for age, gender, ethnicity, deprivation quintile and population-level estimated 5 year CVD risk, gout was independently associated with an increased odds of fatal (adjusted OR 1.37, 95% CI: 1.27-1.48) and non-fatal CVD events (adjusted OR 1.41, 95% CI: 1.35-1.47). Compared with people without gout, there was no statistically significant difference in adjusted odds ratio for those with gout dispensed allopurinol compared with those not dispensed allopurinol (for fatal CVD events, adjusted OR 1.38, 95% CI: 1.27-1.50 vs. 1.33, 95% CI: 1.14-1.55; for non-fatal CVD events, adjusted OR 1.41, 95% CI: 1.34-1.47 vs. 1.42, 95% CI: 1.31-1.54). There was also no statistically significant difference in adjusted odds ratio for those with serum urate above 6mg/dL or below 6mg/dL (for fatal CVD events, adjusted OR 1.38, 95% CI: 1.23-1.54 vs. 1.33, 95% CI: 1.13-1.55; for non-

	Gout		Non-Gout	
	Women	**Men**	**Women**	**Men**
Participants	6971 (21.2)	25834 (78.8)	527060 (56.6)	404737 (43.4)
Allopurinol dispensing [a]	4991 (71.6)	20569 (79.6)	-	-
Serum urate level monitoring [b]	4798 (68.8)	18127 (70.2)	-	-
Population-level CVD risk score				
< 5%	3362 (48.2)	12957 (50.2)	466414 (88.5)	318420 (78.7)
5-10%	1586 (22.8)	5963 (23.1)	34348 (6.5)	47634 (11.8)
10-15%	821 (11.8)	3004 (11.6)	11608 (2.2)	18552 (4.6)
15-20%	474 (6.8)	1466 (5.7)	6263 (1.2)	8020 (2.0)
> 20%	728 (10.4)	2444 (9.5)	8427 (1.6)	12111 (3.0)
Outcomes				
CVD deaths	540 (7.7)	1271 (4.9)	10075 (1.9)	8349 (2.1)
Non-fatal CVD events	930 (13.3)	2398 (9.3)	13144 (2.5)	13962 (3.4)

[a] dispensed at least once in the last 5 years, [b] tested at least once in the last 3 years

fatal CVD events, adjusted OR 1.50, 95% CI: 1.42-1.59 vs. 1.35, 95% CI: 1.24-1.47), when compared to people without gout.

Conclusion: Gout is associated with an increased estimated risk of CVD events calculated from population-level cardiovascular risk equations. Even after adjustment for estimated 5 year CVD risk and additional weighting of risk factors within it, gout independently increased the odds for fatal and non-fatal events. This effect was not ameliorated by allopurinol use or serum urate lowering to treatment target.

Disclosure: K. Cai, Arthritis Australia, 2; **B. Wu**, None; **S. Mehta**, Health Research Council, 2; **N. Dalbeth**, Abbvie, 5, 8, 9, Amgen, 2, AMGEN, 2, AstraZeneca, 2, 5, 8, 9, Dyve, 5, 8, 9, Dyve BioSciences, 5, Hengrui, 5, 8, 9, Horiaon, 5, 8, Horizon, 5, 8, 9, Janssen, 5, 8, 9, Kowa, 5, 8, 9, Pfizer, 5, 8, 9; **R. Jackson**, None; **P. Katrina**, Heart Foundation, 2.

Abstract Number: 2733

Inhibition of Neutrophil Elastase Reduces Autoantibody Levels and Renal Inflammation in Murine Lupus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Edmond L. Dubois, MD Memorial Lecture: SLE – Basic Science
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Dysregulated neutrophil extracellular trap (**NET**) release has been proposed as a source of autoantigens in lupus. Furthermore, it has recently been shown that the onset of lupus nephritis is predicted by a "neutrophil signature" in lupus blood. Neutrophil elastase (**NE**) is a serine protease uniquely expressed by neutrophils, which is known to activate matrix metalloproteinases, inflammatory cytokines, and degrade extracellular matrix components. NE is also required for many forms of NETosis, and has been reported to circulate at high levels in lupus patients. Inhibition of NE has proven effective in models of cardiopulmonary disease and inflammatory arthritis. Previously, we demonstrated the efficacy of a single NE inhibitor in mitigating organ damage (proteinuria, cardiac fibrosis) in lupus-prone NZW x BXSB F1 mice. However, we have not previously characterized how specific immune-cell populations or autoantibody responses might be modulated by NE inhibition.

Methods: Lupus-prone MRL-*lpr* female mice were treated with two different selective NE inhibitors: GW311616A (**GW**, 2.2 mg/kg by oral gavage three times per week) or Alvelestat (**ALV**, 10 mg/kg by oral gavage three times per week) from 8 to 16 weeks of age. We measured NETosis efficiency and autoantibody levels using standard ELISAs. Spleens, lymph nodes (mandibular, axillary, and inguinal), and kidneys were harvested and immune-cell profiling was performed with flow cytometry.

Results: Both GW- and the ALV-treated mice demonstrated reduced levels of autoantibodies against double-stranded DNA (both groups demonstrating ~50% reduction) and beta-2 glycoprotein I (~30% reduction). Peripheral blood analysis revealed a significant reduction in the number of circulating neutrophils in inhibitor-treated mice (~20% reduction), but no difference in the number of cell-free NETs. Intriguingly, elastase inhibition resulted in a marked re-

duction in CD45+ cells infiltrating kidneys (approximate 3-fold reduction for both inhibitor groups). Regarding specific leukocyte populations, there was a 5-fold or greater reduction in renal-infiltrating CD19+ B cells, CD4+ T cells, and CD8+ T cells. Analysis of lymph nodes demonstrated reduced expansion of activated CD4+ and CD8+ T cells (30% reduction) with NE inhibition, which was accompanied by reduced numbers of CD44+ CD62L+ central-memory T cells. Furthermore, there was a 2-fold reduction in the percentage of germinal-center B cells, and a corresponding increase in immature B cells. Experiments are underway to precisely define kidney histology and immune-complex deposition in NE inhibitor-treated mice as compared with vehicle-treated controls.

Conclusion: Treatment of MRL-*lpr* mice with two distinct orally-bioavailable NE inhibitors (GW311616A or Alvelestat) led to the reduction in autoantibody levels, decreased immune-cell infiltration into kidneys, and altered immune-cell profiles in lymph nodes. These data provide further evidence that NE is a valid therapeutic target in lupus, and perhaps especially as a strategy for preventing lupus nephritis.

Disclosure: G. Sule, None; **K. Gilley**, None; **A. Fernandes**, None; **S. Yalavarthi**, None; **J. Knight**, None.

Abstract Number: 2734

Signaling Lymphocytic Activation Molecule Family (SLAMF) Receptors Deregulation Is Implicated in the Altered Function of NK Cells in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Edmond L. Dubois, MD Memorial Lecture: SLE – Basic Science
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

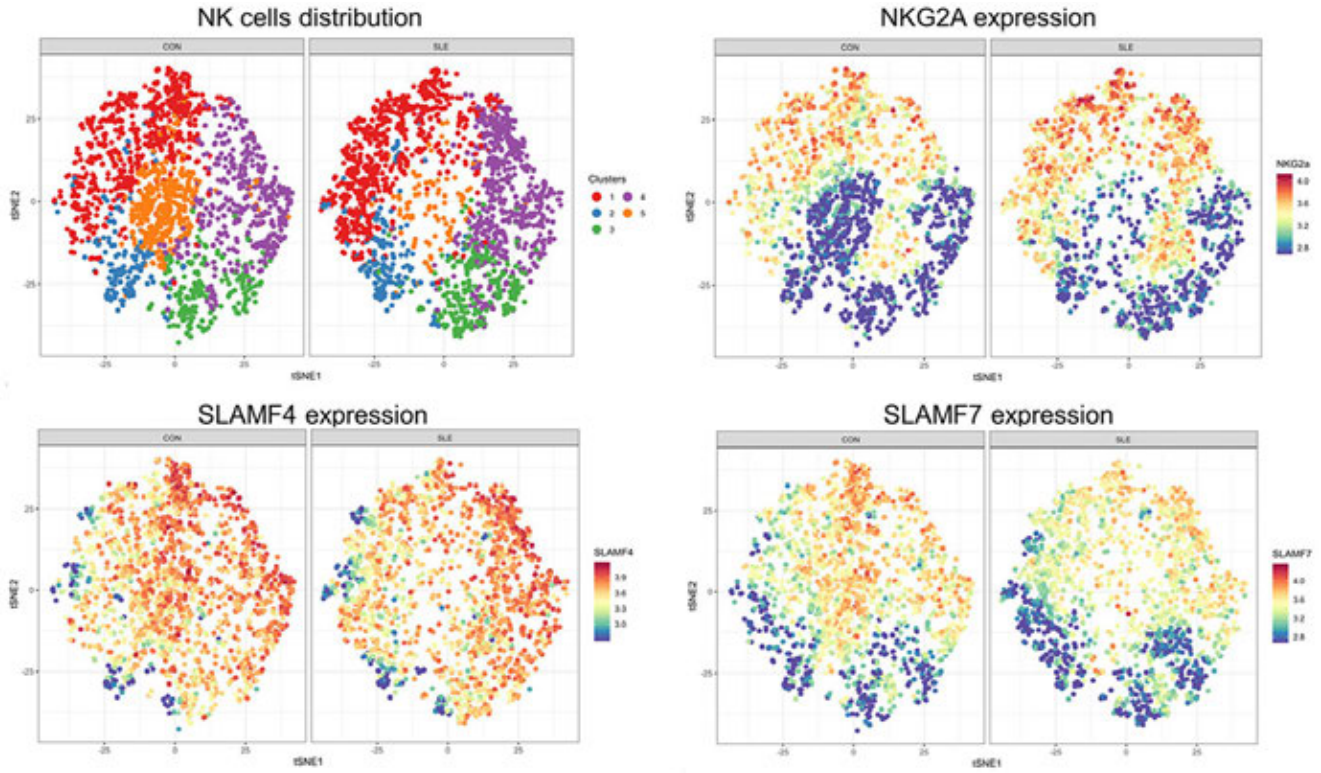
Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystemic autoimmune disease characterized by quantitative and qualitative deficiencies of immune cells. Natural killer (NK) cells are innate lymphoid cells that play an important role in the interaction between innate and adaptive immune systems and contribute to the elimination of infected, damaged and tumor cells. Altered NK function is one of the features that characterizes human SLE and lupus prone mice. Despite recent progress into the understanding of NK cells in SLE, the cellular and molecular mechanisms involved in their dysfunction remain elusive. In this context, we carried out an exhaustive analysis of SLE NK cells.

Methods: Cryopreserved peripheral blood mononuclear cells (PBMC) from 24 SLE patients and gender-, age- and ethnicity matched controls were examined by mass cytometry (CyTOF). A panel of 40 markers comprising the conventional inhibitory and activator molecules was designed to characterize NK cells. Cytolytic enzyme expression, cytokine production and degranulation were examined by flow cytometry. Different type of stimulations were used in the above experiments to activate NK cells: cytokines mix, monoclonal antibodies, phorbol 12-myristate-13-acetate/ionomycin and/or K562 and P815 tumor cells.

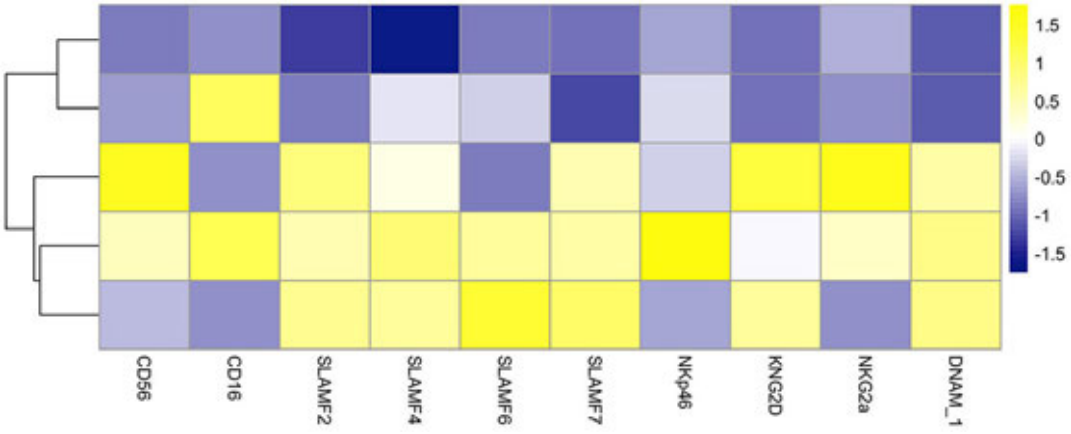
Results: As previously described, our results confirmed a significant decrease in the number and frequency of NK cells in the peripheral blood of SLE patients compared to controls. SLE NK cells exhibited altered functional properties. We observed that cytokine production, cell degranulation and cytotoxic lysis of target tumor cells were reduced. Bioinformatic analysis of mass cytometry data permitted to detect subtle alterations in the expression of phenotypic markers in SLE NK cells discerning them from control NK cells.

This comprehensive analysis emphasized that SLE NK cells display an aberrant expression of receptors belonging to the Signaling Lymphocytic Activation Molecules Family (SLAMF), a group of 8 cell surface receptors, involved in the regulation of immune cells activation. This dysregulation concerns mainly SLAMF1 and SLAMF7, which are respectively positively and negatively regulated on the surface of activated SLE NK cells compared to healthy controls. Further examination of SLAMF1 and SLAMF7 with confocal microscopy show that their distribution is altered on SLE NK cell surface.

Conclusion: Our data confirmed that NK cells isolated from the peripheral blood of SLE patients are dysfunctional, as cytokine production, degranulation and cytotoxic response are compromised. This comprehensive analysis of NK cell surface markers was designed to identify an immune signature characterizing SLE NK cells and permit to demonstrate that SLAMF receptors dysregulation plays a major role in the impairment of SLE NK cells.



t-Distributed Stochastic Neighbor Embedding (t-SNE) plot showing NK cells clustering in controls (CON) and SLE (top left). Examples of colour scale showing the expression of NK surface molecules NKG2A (top right), SLAMF4 (bottom left), SLAMF7 (bottom right).



Heatmap showing NK cells clustering. Surface markers selection is restricted to those that differentiate SLE patients from controls.

Disclosure: M. Humbel, None; **F. Bellanger**, None; **C. Fenwick**, None; **A. Horisberger**, None; **C. Ribi**, None; **D. Comte**, None.

Abstract Number: 2735

Response Gene to Complement -32 Exerts Proinflammatory and Profibrotic Effects in Immune Complex Gediated Glomerulonephritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Edmond L. Dubois, MD Memorial Lecture: SLE – Basic Science
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Response Gene to Complement (RGC)-32 is a cell cycle regulator widely expressed in normal tissues, multiple tumors and a variety of cell lines. RGC-32 is induced by TGF-β in fibroblasts, astrocytes and human renal proximal tubular cells and mediates TGF-β dependent profibrotic pathways. In immune cells, RGC-32 is upregulated preferentially in murine and human Th17 cells and promotes their differentiation in vitro and in vivo. Increased expression of IL-17 in kidneys of SLE patients and lupus prone mice is critical for the development of lupus nephritis (LN). We have previously shown that RGC-32 expression is increased in T cells from SLE patients and in tubules and glomerular infiltrating cells in kidney biopsies of patients with LN. To directly assess whether RGC-32 plays a local role in LN downstream of antibody production, we used the nephrotoxic nephritis (NTN) model of immune complex mediated glomerulonephritis to compare parameters of disease severity in RGC-32 deficient and sufficient mice.

Methods: NTN was induced in WT and RGC-32-/- mice by immunization with sheep IgG in Complete Freund's Adjuvant followed by injection of sheep nephrotoxic serum. Proteinuria, blood urea nitrogen and kidney histopathology were determined to assess kidney function and damage. Single cell suspension of kidneys and spleens were analyzed by flow cytometry. Circulating levels and kidney deposition of mouse anti-sheep IgG were quantitated by

ELISA and IF, respectively. Splenic B and T cell responses were characterized by flow cytometry. mRNA expression of IL-17A, CXCL1, CXCL5, collagen I, III, IV and FN was determined by RT-PCR.

Results: RGC-32 mRNA was significantly upregulated in the renal cortex and kidney infiltrating cells of WT mice with NTN compared to controls. RGC-32 KO mice displayed attenuated renal damage as shown by decreased proteinuria and glomerular scores and a trend for decreased blood urea nitrogen. RGC-32 deficiency did not interfere with the induction of NTN as mouse anti-sheep IgG titers, percentage of splenic germinal center B cells, plasma cells, effector $CD4^+$ T cells, Tregs, IL-17A and IFN-g secreting cells did not differ between RGC-32 KO and WT mice. Furthermore, kidney deposition of autologous antibodies and C3 were comparable between the two groups. IL-17 mRNA expression in renal cortex and the proportion of $CD4^+$ $IL17A^+$ cells isolated from kidneys on day 7 after NTN induction were significantly upregulated in WT but not RGC-32 KO mice. RGC-32 KO mice displayed decreased frequency of infiltrating PMN and downregulation of CXCL1 and CXCL5, suggesting a decrease in IL-17 dependent neutrophil recruitement. Collagen I, III , IV and Fibronectin (FN) were significantly lower in RGC-32 KO mice by RT- PCR, while trichrome and FN staining showed decreased interstitial, glomerular and periglomerular fibrosis.

Conclusion: These results suggest that RGC-32 contributes to the pathogenesis of immune complex mediated GN by promoting proinflammatory and profibrotic pathways. These data support further efforts to examine the mechanisms by which RGC-32 modulates these pathways and suggest that RGC-32 is a potential novel therapeutic target in the treatment of LN.

Disclosure: V. Nguyen, None; **A. Tatomir**, None; **H. Rus**, None; **C. Drachenberg**, None; **J. Papdimitriou**, None; **T. Badea**, None; **I. Luzina**, None; **V. Rus**, None.

Abstract Number: 2736

Mucosal-associated Invariant T Cells Can Be Therapeutically Targeted in Lupus

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SESSION INFORMATION
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Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Mucosal-associated invariant T (MAIT) cells are innate T cells that are restricted by the non-polymorphic MHC-related molecule-1 (MR1) and express a semi-invariant TCRα chain: Vα7.2-Jα33 in humans and Vα19-Jα33 in mice. Previously, we reported that the activated status of MAIT cells correlated with disease activity in patients with systemic lupus erythematosus (SLE), and MAIT cells were accumulated in the kidneys from patients with lupus nephritis. Because MAIT cell deficiency reduced autoantibody production and the disease severity in FcγRIIb$^{-/-}$*Yaa* mice, a spontaneous animal model of lupus, we investigated mechanisms by which MAIT cells enhanced autoimmune response and investigated whether MAIT cells could be therapeutically targeted in lupus.

Methods: FcγRIIb$^{-/-}$*Yaa* mice were crossed to MR1-deficient mice lacking MAIT cells, and the levels of serum anti-dsDNA antibody and urinary albumin were measured. The severity of nephritis was assessed histologically. T and B cell subsets in the spleen and kidneys at 2 months of age were analyzed by using flow cytometry. To evaluate whether inhibition of MAIT cell activation suppress the disease course of lupus, FcγRIIb$^{-/-}$ *Yaa* mice were treated with isobutyryl 6-formyl pterin (i6-FP), a suppressive MR1 ligand, orally three times weekly for 4 weeks starting at 4 weeks of age. B cells from FcγRIIb$^{-/-}$*Yaa* mice were stimulated with lipopolysaccharide in the presence of MAIT cells and autoantibody production was assessed by ELISA.

Results: Activated MAIT cells were infiltrated into the kidneys of FcγRIIb$^{-/-}$*Yaa* mice. Reduced autoantibody production and disease severity by MR1 deficiency was associated with reduced germinal center and T cell responses in FcγRIIb$^{-/-}$*Yaa* mice. The suppression of MAIT cell activation by i6-FP administration decreased serum anti-dsDNA antibody levels and the deposition of IgG and C3 in the glomeruli. i6-FP administration also reduced germinal center responses and activated T cell infiltration into kidneys in FcγRIIb$^{-/-}$*Yaa* mice. MAIT cells directly enhanced autoantibody production by B cells *in vitro*, and this was markedly reduced by blocking CD40L-CD40 or the MR1-TCR pathway.

Conclusion: MAIT cells exacerbated the disease severity of lupus by enhancing autoantibody production and tissue inflammation in FcγRIIb$^{-/-}$ *Yaa* mice. MAIT cells enhanced autoantibody production by B cells dependent on the CD40-CD40L and TCR pathways. Together with our previous findings in patients with SLE, MAIT cells may contribute to lupus pathology and serve as potential novel therapeutic target for autoimmune diseases such as SLE.

Disclosure: G. Murayama, None; **A. Chiba**, None; **T. Mizuno**, None; **A. Nomura**, None; **T. Kuga**, None; **H. Amano**, None; **K. Yamaji**, ASAHI KASEI PHARMA, 2, Astellas pharma, 2, 8, bristol myers, 8, Chugai Pharma, 2, Janssen Pharma, 8, Mitsubishi-Tanabe Pharma, 2, 8, Sanofi Pharma, 8, Takeda Pharma, 2; **N. Tamura**, AbbVie GK, 8, AbbVie pharma, 8, ASAHI KASEI MEDICAL, 2, ASAHI KASEI PHARMA, 2, astellas pharma, 2, 8, Astellas Pharma Inc., 2, 8, AYUMI PHARMA, 2, AYUMI Pharmaceutical Corporation, 2, bristol myers, 8, Bristol-Myers Squibb, 8, Chugai Pharmaceutical Co. Ltd., 2, Chugai Pharma, 2, Eisai Co., Ltd., 2, Eisai Pharama, 2, Janssen Pharma, 8, Janssen Pharmaceutical K.K., 8, Mitsubishi Tanabe Pharma Corporation, 2, 8, Mitsubishi-Tanabe Pharma, 2, 8, Sanofi K.K., 8, Sanofi Pharma, 8, Takeda Pharma, 2, Takeda Pharmaceutical Company Ltd., 2; **S. Miyake**, Bristol myers squibb, 2, Bristol-Myers Squibb, 2, Pfizer, 2, Pfizer Japan Inc., 2, Taiho pharmaceutical, 8, TAIHO PHARMACEUTICAL CO., LTD., 8.

Abstract Number: 2737

HIF-1α and miR-210 Differential and Lineage-specific Expression in Systemic Lupus Erythematosus

Barry Garchow,[1] and Marianthi Kiriakidou[1], [1]Thomas Jefferson University, Philadelphia, PA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Edmond L. Dubois, MD Memorial Lecture: SLE – Basic Science
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Hypoxia inducible factor 1 is a key transcription factor that regulates the cellular response to oxygen stress. In the adaptive immune system, HIF-1α is mainly expressed by CD4$^+$ T cells in response to TCR ligation and enhanced by exposure to inflammatory cytokines. Transcriptional activation of HIF-responsive genes influence T cell differentiation and function. MicroRNAs are a class of endogenous non-coding RNAs that exert a regulatory influence on almost every aspect of cellular biology. Aberrant expression of many miRNAs have been shown to correlate with poor clinical outcome across a wide spectrum of diseases. MiR-210 is a hypoxia-responsive miRNA transcriptionally regu-

lated by HIF-1α. HIF-1α is also a direct miR-210 target suggesting an important role for miR-210 in regulation of T cell response. Abnormal T cell function is increasingly recognized as a major contributing factor in SLE immunopathology however, the expression and function of HIF-1α and miR-210 in SLE remains largely unexplored.

Methods: Lymphocyte subsets were purified from lupus-prone *Sle123* mice with mild or severe disease and from age-matched WT controls and assayed for miR-210 expression by real-time RT-PCR. Peripheral lymphocytes were purified from human SLE patients and healthy subjects and assayed for HIF-1α, miR-210, RORγt and IL-17 expression by real-time RT-PCR. Mean, error and significance values were determined using an unpaired Student's t test assuming equal variance. *p* values < 0.05 were considered significant. All animal procedures were conducted under an approved IACUC protocol. Human peripheral blood samples were collected with prior written informed consent under an approved IRB protocol.

Results: $CD4^+$, $CD8^+$ and $CD19^+$ lymphocyte subsets were purified from *Sle123* mice with mild or severe disease and assayed for miR-210 expression by real-time PCR. MiR-210 expression was similar across subsets from mice with mild disease compared to age/sex-matched wild-type controls. MiR-210 was 352-fold up-regulated in the $CD4^+$ T cell subset from mice with advanced disease and 2.3-fold and 2.5-fold up-regulated in the $CD8^+$ and $CD19^+$ lineages respectively. $p< 0.001$ ($CD4^+$ and $CD8^+$) and < 0.01 ($CD19^+$), n = 3. We purified peripheral blood mononuclear cells (PBMC) from lupus patients with active disease and quantified HIF-1α and miR-210 expression levels by qRT-PCR. We measured 5.3 HIF-1α and 43.4-fold miR-210 differential-expression in human SLE PBMCs compared to healthy controls ($p < 0.001$ (miR-210) and < 0.05 (HIF-1α), n = 4. RORγt and IL-17 expression associate with HIF-1α and miR-210 activity. We purified peripheral lymphocytes from human lupus patients with active disease and healthy controls and assayed for RORγt and IL-17 expression by qRT-PCR. We measured 4.6-fold RORγ*t* differential-expression and 3.2-fold differential-expression of its transcriptional target IL-17. $p< 0.001$ (RORγt) and < 0.05 (IL-17), n = 4.

Conclusion: Our results suggest that HIF-1α may play an important and previously unrecognized role in the pathobiology of SLE. HIF-1α and HIF-1a regulated pathways may represent a novel and productive direction for future etiological studies in lupus.

Disclosure: B. Garchow, None; **M. Kiriakidou**, None.

Abstract Number: 2738

Differential Methylation of Peripheral Blood Adaptive Immune Cells in Individuals at High Risk for RA and with Early RA Compared with Controls Identifies Pathways Important in Transition to Arthritis

Rizi Ai,[1] David Boyle,[2] Deepa Hammaker,[3] Kevin Deane,[4] V. Michael Holers,[5] Andre Matti,[6] William Robinson,[7] Jane Buckner,[8] Navin Rao,[9] Frédéric Baribaud,[10] George Vratsanos,[11] Sunil Nagpal,[9] Wei Wang,[2] and Gary Firestein[3], [1]University of California San Diego, San Diego, [2]University of California, San Diego, San Diego, CA, [3]University of California, San Diego, San Diego, [4]University of Colorado Denver, Division of Rheumatology, Aurora, CO, USA, Aurora, CO, [5]University of Colorado Denver, Division of Rheumatology, Aurora, CO, USA, Denver, [6]UCSD, La Jolla, CA, [7]Stanford University, Stanford, CA, [8]Benaroya Research Institute, Seattle, WA, [9]Janssen R&D, Spring House, PA, [10]Janssen Research & Development, LLC, Spring House, PA, [11]JNJ, Raritan, NJ

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

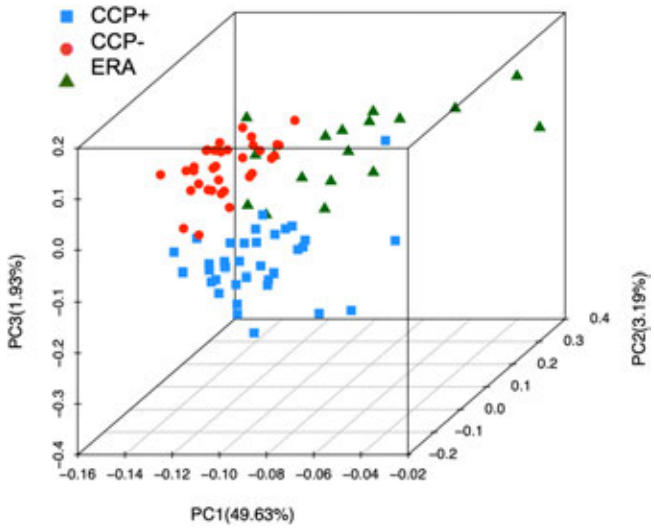

Figure 1. PCA shows the separation of CCP+, CCP- and ERA patients in memory T cells based on DMLs in confirmatory cohort.

Background/Purpose: The "Targeting Immune Responses for Prevention of RA" (TIP-RA) collaboration studies individuals at high risk for developing RA because of serum anti-citrullinated protein antibody positivity in absence of arthritis, and is focused on defining how they transition from at-risk to classifiable disease. One potential mechanism is through alterations in epigenetics patterns in adaptive immune cells. Previous studies showed that DNA methylation patterns of early RA (ERA) synoviocytes differ from long-standing RA, suggesting that abnormal methylation occurs early in synovium and evolves over time. To extend these observations, we performed a cross-sectional analysis in TIP-RA of DNA methylation signatures in peripheral blood cells in ERA, at-risk anti-CCP3+ individuals and demographically matched CCP- controls.

Methods: Genomic DNA was isolated from two independent cohorts of CCP- (cohorts 1 and 2, respectively: B cell: n = 17/34; memory T cell: n = 21/34; and naïve T cell: n = 21/33), CCP3+ (B cell: n = 18/37; memory T cell: n = 20/36; and naïve T cell: n = 20/35), and CCP3+ ERA (B cell: n = 4/18; memory T cell: n = 5/18; and naïve T cell: n = 5/18) after separating PBMCs using antibodies and magnetic beads. Methylation was measured by Illumina Infinium MethylationEPIC chip. Differentially methylated loci (DMLs) were identified using Welch's *t*-test and mapped to gene promoter regions to define DM genes (DMGs). Principal component analysis (PCA) was used to represent relationship among groups. Pathway analysis was applied by Reactome.

Results: For the initial cohort, 1494, 1097 and 1330 DMLs were identified among CCP+, CCP- and ERA in B cells, memory T cells and naïve T cells, respectively. For the confirmatory cohort, 523, 793 and 548 DMLs were found in corresponding cell populations. The DML overlap between the 2 cohorts was highly significant (p= 2.48E-77). The DMLs were combined for both groups and corresponded to 411, 412, and 351 DMGs in B cells, memory T cells and naïve T cells. Of these, we found 246, 198 and 195 DMGs between CCP3+ and ERA in each peripheral blood cell population, respectively. PCA showed separation of CCP+, CCP- and ERA in each of the three blood cell types by DMLs (Fig. 1). DMGs were mapped to biological pathways to identify DM pathways. Although most were not significant, there were several highly significant differences comparing CCP+, ERA and CCP- in memory T cells involving pathways, including "Interferon gamma signaling" (*FDR* 7.48E-14), "PD-1 signaling" (*FDR* 8.71E-10), "Translocation of ZAP-70 to Immunological synapse" (*FDR* 4.75E-10), and "Phosphorylation of CD3 and TCR zeta chains" (*FDR* 8.71E-10).

Conclusion: We identified reproducible methylation signatures of CCP-, CCP+, and ERA in peripheral blood B cells, memory T cells and naïve T cells in initial and confirmatory cohorts. The methylome of ERA also demonstrated a distinctive pattern from CCP+, indicating that progression to RA is accompanied by epigenetic remodeling, especially in

T cell signaling and interferon responses. These signatures identify critical pathways in CCP positivity and classifiable RA and could provide the basis of novel interventions to prevent disease.

Figure 1. PCA shows the separation of CCP+, CCP- and ERA patients in memory T cells based on DMLs in confirmatory cohort.

Disclosure: **R. Ai**, None; **D. Boyle**, Janssen, 2; **D. Hammaker**, None; **K. Deane**, Bristol-Myers Squibb, 5, Inova, 9, Janssen, 2, 5, Janssen R&D, 2, Microdrop, 5, Pfizer, 2; **V. Holers**, AdMIRx, 1, 2, 4, 5, 6, Alexion, 7, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 5, Janssen R&D, 2, 5, Pfizer, 2; **A. Matti**, None; **W. Robinson**, None; **J. Buckner**, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Janssen, 2, Novo Nordisk, 2, Pfizer, 2; **N. Rao**, Janssen Research & Development, 3, Johnson & Johnson, 1, 3, 4; **F. Baribaud**, Janssen Research & Development, LLC, 3; **G. Vratsanos**, Janssen Research & Development, 1, 3; **S. Nagpal**, Janssen Research & Development, 3, Janssen Research, Johnson&Johnson, 1, 3, 4, Johnson & Johnson, 1, 4; **W. Wang**, None; **G. Firestein**, Abbvie, 2, Janssen, 2.

Abstract Number: 2739

Skin Disease Activity and Autoantibody Phenotype Are Major Determinants of Blood Interferon Signatures in Dermatomyositis

Mika Tabata,[1] Kavita Sarin,[2] Karen Page,[3] Christine Huard,[3] Shanrong Zhao,[3] Donald Bennett,[3] Jillian Johnson,[3] Kristen Johnson,[3] and David Fiorentino[2], [1]Stanford University School of Medicine, Stanford, CA, [2]Department of Dermatology, Stanford University School of Medicine, Redwood City, CA, [3]Pfizer, Boston

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Genetics, Genomics & Proteomics

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

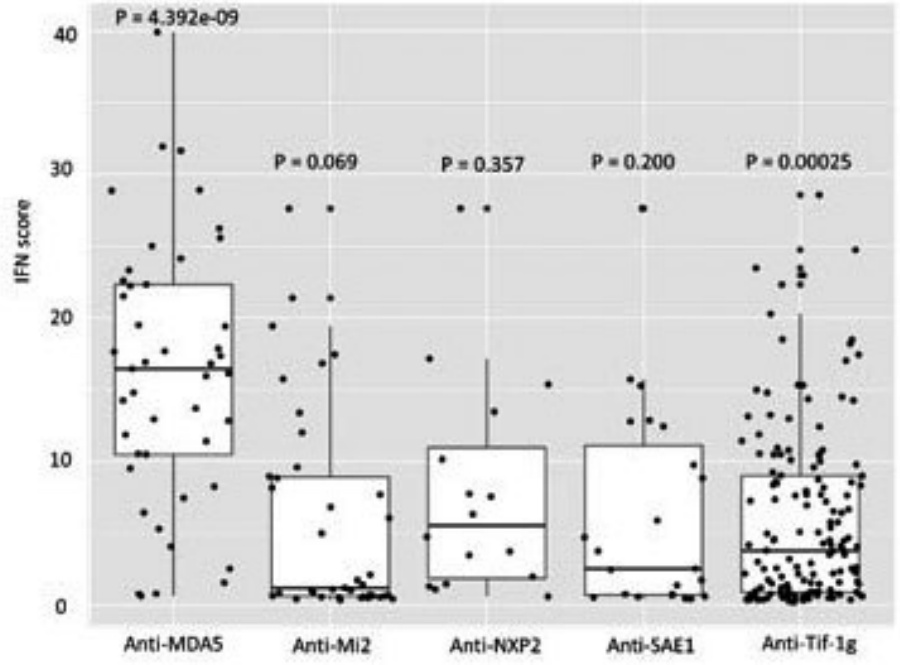

Figure 1. IFN scores by antibody subtype

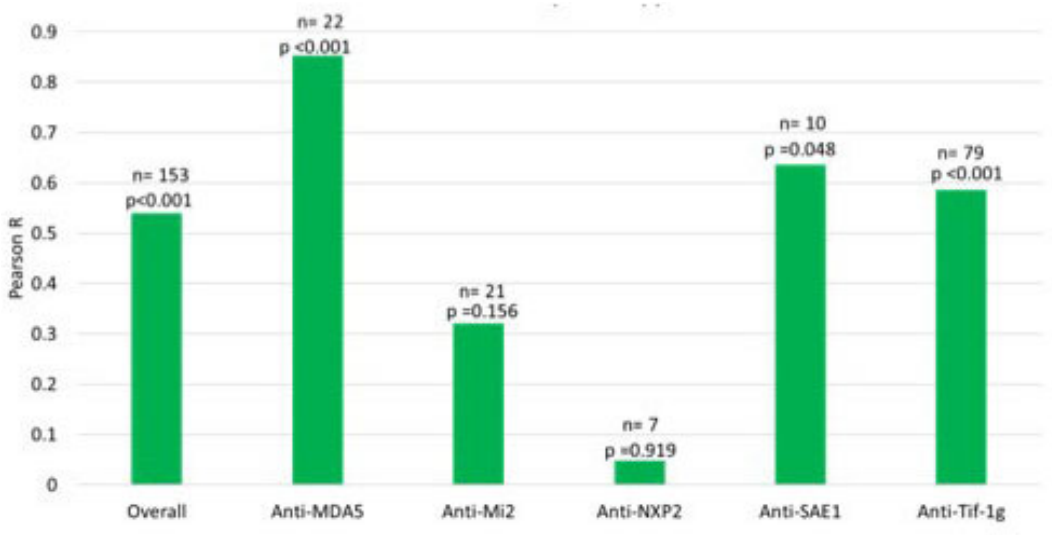

Figure 2. Correlations of longitudinal IFN score with CDASI across antibody subtype

Background/Purpose: Interferon (IFN) signaling is upregulated in dermatomyositis (DM) and thought to play a role in pathogenesis. An IFN gene signature in peripheral blood of DM patients correlates with skin disease and may predict disease activity. However, studies have not analyzed how IFN signaling differs across DM subtypes or how it is influenced by multiple organ system involvement. Autoantibodies in DM distinguish subsets of disease with unique clinical features and outcomes. We hypothesized that strength and clinical utility of the DM blood IFN signature depends on autoantibody subtype and other clinical factors. Utilizing a clinically phenotyped DM cohort, we sought to understand the utility of blood IFN gene signature as markers of skin disease severity across patients differing in autoantibody subtype, muscle disease, interstitial lung disease (ILD), and cancer status.

Methods: Stranded RNA sequencing was performed on 377 whole blood samples derived from 205 DM patients seen at the Stanford Outpatient Clinic. The least absolute shrinkage and selection operator (LASSO) method for linear regression selected optimal gene signatures and errors were calculated in an independent dataset. An IFN score was calculated by averaging the healthy-normalized FPKM values for a selection of genes. Skin disease activity was quantitated using the Cutaneous Dermatomyositis Activity and Severity Index activity score (CDASI-a). Linear regression and Pearson correlation analyzed the association between longitudinal CDASI-a and IFN scores, adjusted and stratified across antibody subtype, ILD, cancer, and muscle disease status.

Results: We found that the blood IFN score is significantly elevated in the anti-MDA5 subtype compared to other subtypes (average 16.12, $p < 0.001$) [Figure 1]. Change in CDASI-a correlates most strongly with change in IFN score in the anti-MDA5 ($R=0.85$, $p< 0.001$) subtype, followed by anti-Tif-1g ($R=0.59$, $p< 0.001$) and anti-SAE1 ($R=0.64$, $p =0.048$) [Figure 2]. Conversely, the correlation is weak in anti-Mi2 and anti-NXP2 subtypes. These patterns persist after adjustment for ILD, muscle disease, cancer, and medications. The correlation is stronger when baseline IFN score is greater than 1.5 ($R =0.59$, $p < 0.001$). The correlation between IFN score and CDASI-a score is weaker in patients with active muscle disease and stronger in patients with active lung disease but is unaffected by cancer status.

Conclusion: Using a large prospective dataset of DM patients, we demonstrate that IFN-driven gene expression as an activity measure in DM is related to specific autoantibody subtypes. This relationship is also impacted by clinical factors such as ILD and muscle disease status. These results suggest that careful attention to antibody status and clinical factors could help inform interpretation of IFN biomarker data in future clinical trials in DM.

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Abstract Number: 2740

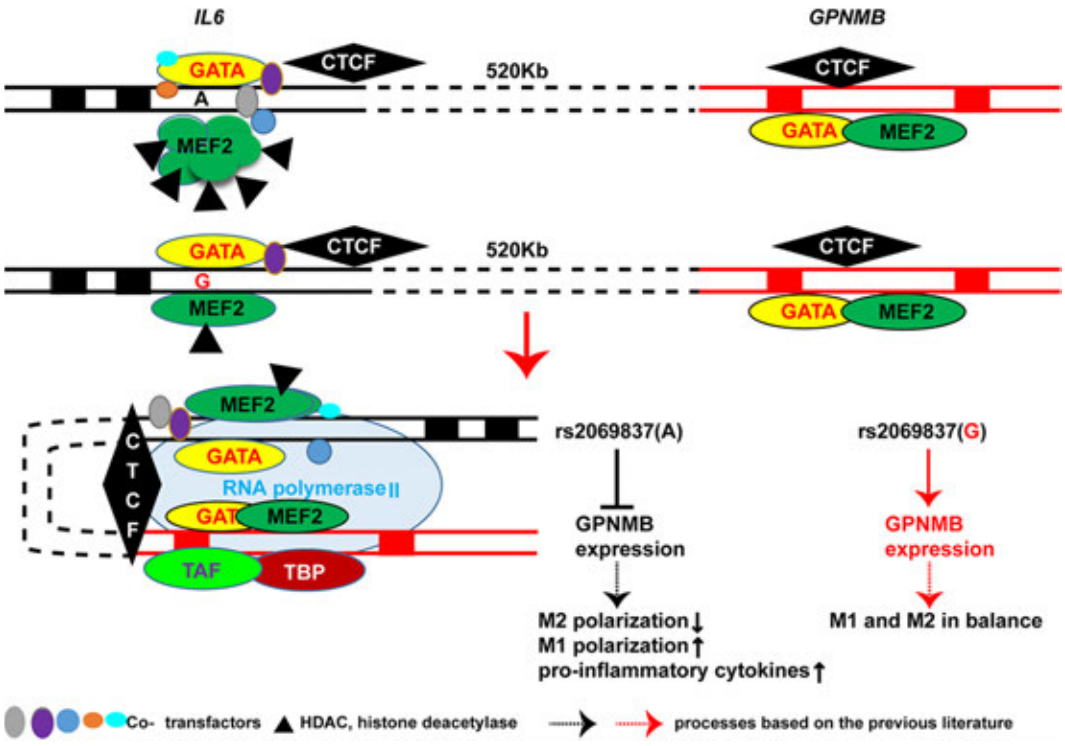
Takayasu Arteritis Associated Risk Locus in IL6 Represses the Anti-inflammatory Gene GPNMB Through Chromatin Looping and Recruiting MEF2-HDAC Complex

Xiufang Kong,[1] and **Amr Sawalha** [2], [1]University of Michigan & Fudan University, Ann Arbor, MI[2]University of Pittsburgh & University of Michigan, Pittsburgh, PA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Previous work has revealed a genetic association between Takayasu arteritis and a non-coding genetic variant in an enhancer region within *IL6* (rs2069837 A/G). The risk allele in this variant (allele A) has a protective effect against chronic viral infection and cancer. The goal of this study was the characterize the functional consequences of this disease-associated risk locus.

Methods: A combination of experimental and bioinformatics tools were used to mechanistically understand the effects of the disease-associated genetic locus in *IL6*. These included electrophoretic mobility shift assay (EMSA), DNA



A proposed model for the regulatory mechanism of rs2069837 on the expression of GPNMB. The Takayasu arteritis risk allele A at this SNP preferentially recruits MEF2 and thereby HDAC proteins compared to the G allele resulting in a repressive effect by weakening the enhancer function of this locus. CTCF binding downstream of this SNP mediates the interaction between this locus to the regulatory locus in GPNMB, where a CTCF binding site also exists. The differential binding of MEF2-HADAC complex between A and G results in differential expression of GPNMB, with inhibited expression in the presence of risk allele A. Inhibiting GPNMB suppresses M2 macrophage polarization and enhances of M1 polarization and overexpression of pro-inflammatory cytokines.

affinity precipitation assays followed by mass spectrometry and western blotting, luciferase reporter assays, and chromosome conformation capture (3C) to identify chromatin looping in the *IL6* locus. Both cell lines and peripheral blood primary monocyte-derived macrophages were used.

Results: We identified the monocyte/macrophage anti-inflammatory gene *GPNMB*, ~520kb from *IL6*, as a target gene regulated by rs2069837. We revealed preferential recruitment of myocyte enhancer factor 2-histone deacetylase (MEF2-HDAC) repressive complex to the Takayasu arteritis risk allele. Further, we demonstrated suppression of GPNMB expression in monocyte-derived macrophages from healthy individuals with the AA compared to AG genotype, which was reversed by histone deacetylase inhibition. Our data show that the risk allele in rs2069837 represses the expression of GPNMB by recruiting MEF2-HDAC complex, enabled through a long-range intra-chromatin looping. Suppression of this anti-inflammatory gene might mediate increased susceptibility in Takayasu arteritis and enhance protective immune responses in chronic infection and cancer.

Conclusion: Takayasu arteritis disease risk locus in *IL6* might increase disease susceptibility by suppression of the anti-inflammatory gene *GPNMB*, which is located about 520kb away, through chromatin looping and recruitment of MEF2-HDAC epigenetic repressive complex. Our data highlight long-range chromatin interactions in functional genomic and epigenomic studies in autoimmunity.

Disclosure: X. Kong, None; **A. Sawalha**, None.

Abstract Number: 2741

Integration of Single Cells from Inflammatory Disease Tissues Reveals Common and Unique Pathogenic Cell States

Fan Zhang,[1] Joseph Mears,[1] ilya Korsunsky,[1] Kevin Wei,[2] Anna Helena Jonsson,[2] Deepak Rao,[1] Edy Kim,[3] Laura Donlin,[4] Jill Buyon,[5] Michelle Petri,[6] Chaim Putterman,[7] Thomas Tuschl,[8] Nir Hacohen,[9] Betty Diamond,[10] Michael Brenner,[11] and Soumya Raychaudhuri[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [3]Brigham and Women's Hospital, Boton, MA, [4]Hospital For Special Surgery, New York, NY, [5]New York University School of Medicine, New York, NY, [6]Johns Hopkins University School of Medicine, Baltimore, MD, [7]Albert Einstein College of Medicine, New York, NY, [8]Rockefeller Research Laboratories, New York, [9]Broad Institute, Cambridge, [10]Feinstein Institutes for Medical Research, Manhasset, [11]Brigham and Women's Hospital:, Boston

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Different autoimmune diseases can co-exist in an individual and share similar genetic associations, autoimmune signaling pathways, and clinical manifestations. However, autoimmune diseases present varied cellular heterogeneities and may be distinguished by their primary target organs or tissues. The immune mechanisms that are shared between similar autoimmune diseases remain poorly understood due to limited access to affected human tissues and computational scalability. Recently, high resolution single-cell RNA-seq profiles have provided the opportunity for study of the contribution of diverse cell populations to disease pathogenesis. This advance has enabled unbiased comparison of disease across affected tissues with the goal of understanding autoimmune similarities.

Methods: We have analyzed and integrated ~80,000 cells from 176 donors from publicly available single-cell RNA-seq datasets generated from rheumatoid arthritis (RA) and osteoarthritis (OA) synovium[1], pulmonary fibrosis and healthy lung, systemic lupus erythematosus (SLE) and healthy kidney and skin[2,3], inflammatory bowel disease (IBD)

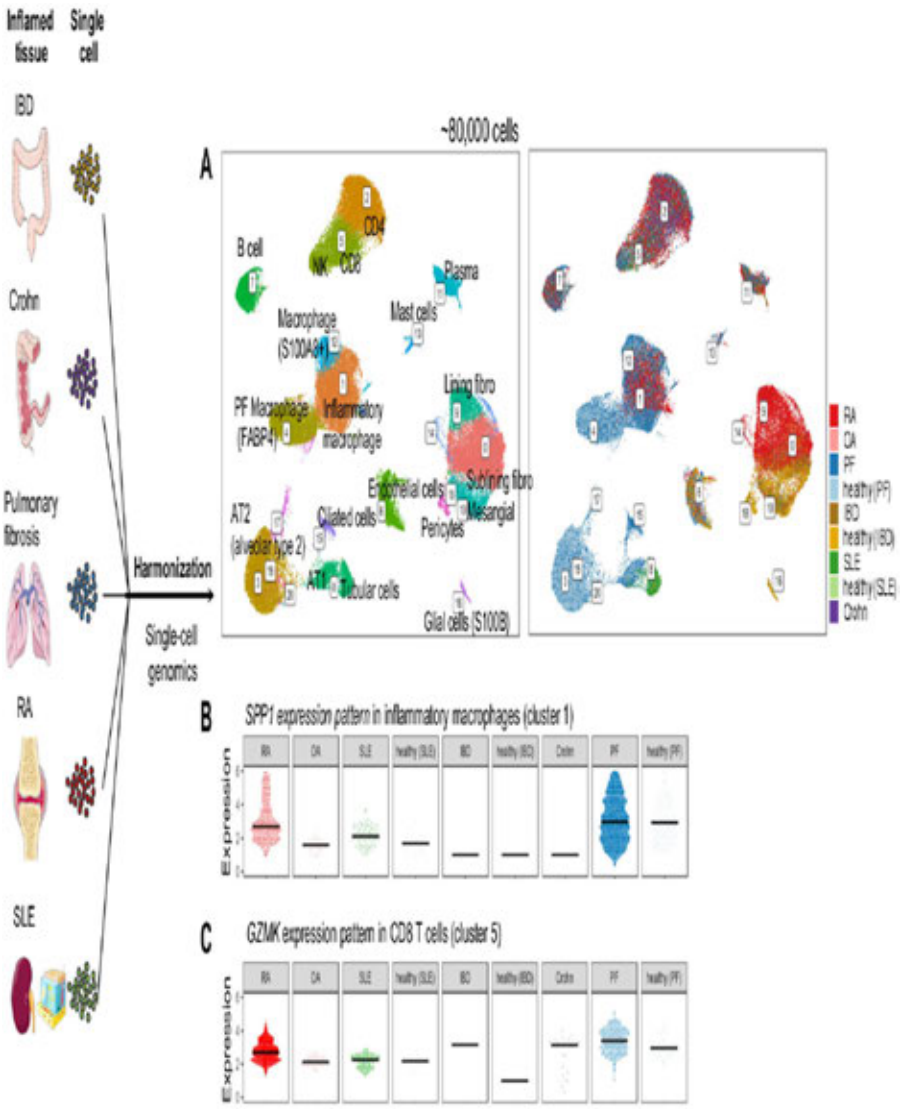

Figure 1. Integration of ~80,000 cells from 176 donors reveal common and unique cell populations from RA and OA synovium, pulmonary fibrosis and healthy lung, SLE and healthy kidney and skin, IBD and healthy colon, and Crohn. **A**. Shared and unique cell states across multiple tissues. **B**. SPP1 expression pattern for each disease and tissue source in inflammatory macrophages. **C**. GZMK expression pattern for each disease and tissue source in CD8 T cells.

and healthy colon, and Crohn intestinal mucosal biopsies. We use a robust integrative strategy[4] to cluster and project all the cells into two dimensional-space by correcting technical batch effect across tissue, donor, and single-cell platform (10X Genomics, Celseq2, Dropseq, Fluidigm, and Smartseq).

Results: We identify 21 diverse cell type populations across multiple tissue sources (Figure 1A). In the myeloid cell population, we observed four distinct subsets including *VSIG4*+ M2-like macrophages, *S100A8*+ macrophages, *SPP1*+ *MMP9*+ inflammatory macrophages, and dendritic cells (DC). The *SPP1*+ *MMP9*+ inflammatory macrophage population with high expression of matrix metalloproteinases genes is co-localized between macrophages in RA synovium, SLE kidney, and alveolar from pulmonary fibrosis lung, and is absent in healthy lung tissue (Figure 1B). For CD8 T cells and nature killer cells, we identified a shared transcriptional gradient of granzyme-expressing cytotoxic effectors between RA synovium, SLE kidney, and fibrotic lung. Interestingly, the *GzmK*+ CD8 T cell population is absent in the healthy lung (Figure 1C). The patterns of cytotoxic effector states may suggest similarities between the

primary sites of inflamed RA and inflamed fibrotic lung, including potential common active pathways. In the stromal cell compartment, we observed distinct populations across different diseases and tissues, including fibroblasts, pericytes, mesangial, and tubular cells.

Conclusion: We demonstrate that integrative analyses between disease tissues by single-cell transcriptomics is capable to discovering shared and unique disease-specific gene expression modules and cell states, and may help predict potential therapeutic targets for inflammatory and fibrotic diseases.

Reference:

1. Zhang, F. *et al*. *Nat Immunol* (2019)
2. Der, E., *et al*. *Nat Immunol* (2019)
3. Arazi, A., *et al*. *Nat Immunol*, In press
4. Korsunsky, I., *et al*. *bioRxiv* (2018)

Disclosure: F. Zhang, None; **J. Mears**, None; **i. Korsunsky**, None; **K. Wei**, None; **A. Jonsson**, Amgen, 2; **D. Rao**, Janssen, 5, Merck, 2, Pfizer, 5; **E. Kim**, None; **L. Donlin**, Karius Inc, 9, Karius, Inc, 2, Stryker, 5; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5; **C. Putterman**, Equillium, 5, Equillium, Inc, 2, 5, Exagen, 2; **T. Tuschl**, None; **N. Hacohen**, Neon Therapeutics, 1, 8; **B. Diamond**, GSK, 5, Jansen, 5, Lilly, 5; **M. Brenner**, None; **S. Raychaudhuri**, None.

Abstract Number: 2742

Toward a Liquid Biopsy for Lupus Nephritis: Urine Proteomic Analysis of SLE Identifies Inflammatory and Macrophage Signatures

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Genetics, Genomics & Proteomics
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Lupus nephritis (LN) complicates up to 60% of patients with systemic lupus erythematosus (SLE) and carries a high morbidity and mortality. The definitive diagnosis is based on kidney biopsy. This is invasive and not always readily available, thus delaying treatment. Sometimes multiple biopsies are required over the course of the disease. Importantly, while renal pathology is accurate at describing the morphology of renal disease, the underlying biology and molecular pathways are not thoroughly assessed. Urine proteomics is a non-invasive strategy that may provide insights regarding ongoing renal disease.

Methods: One thousand proteins were quantified (RayBiotech Kiloplex assay) on a total of 112 longitudinal urine samples from 32 SLE patients with active LN and 7 healthy controls (HC) enrolled in the Accelerating Medicines Partnership (AMP). All patients underwent treatment as directed by their own physicians. Differentially excreted proteins at baseline (SLE vs HC, proliferative vs membranous LN, responders vs non responders) were identified using a linear

Figure 1. Differentially excreted urine proteins in lupus nephritis.

model with moderated t statistic. Response to treatment was defined based on proteinuria at 1 year as "complete" (< 0.5g/24h) or "partial" (50% reduction but >0.5/24h). In the longitudinal analysis, a mixed model was employed to identify markers associated with proteinuria. Pathway enrichment analysis was performed using the genes coding for the differentially excreted analytes using Ingenuity Pathway Analysis (IPA) and other publicly available pathway libraries.

Results: There were 186 proteins increased in SLE patients (Fig. 1). The most enriched pathway was TNFa ($p < 0.001$). We found 74 differentially excreted proteins comparing proliferative and pure membranous LN. CD4, MCP-1, MIP-1a, RANTES, IL-16, and IL-7, markers involved in CD4 T cell and monocyte biology, were enriched in proliferative disease. A few targets were exclusively identified in either class (i.e. CD4 in proliferative nephritis). We used a longitudinal model to identify specific urine proteins associated with worse proteinuria as a marker of severity. Proteinu-

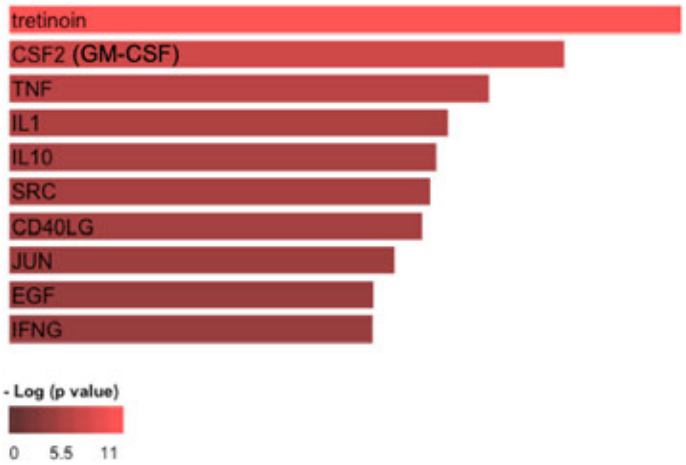

Figure 2. Top canonical pathways associated with proteinuria.

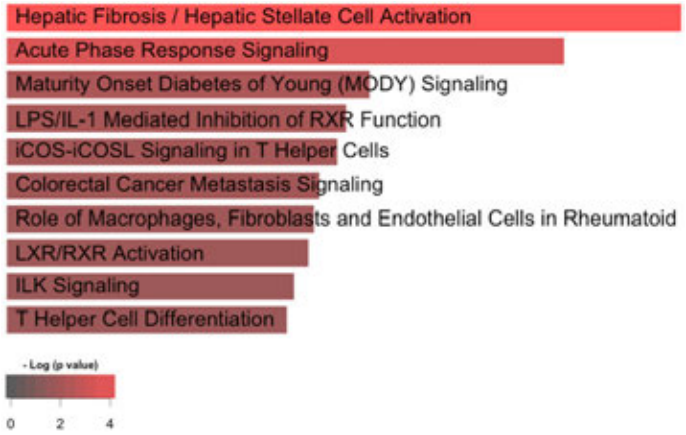

Figure 3. Top upstream regulators: responders vs non-responders.

ria was associated with 105 markers (FDR < 0.05), the strongest association being CD163 (p = 10-9), a phagocyte marker. IPA implicated several pathways involving fibrosis, acute phase response, LPS/IL1, RXR, ICOS signaling and macrophage/fibroblasts (Fig. 2). Next, we identified 27 differentially excreted proteins in non-responders. IPA revealed that tretinoin, GM-CSF, TNF, and IL1 were among the top upstream regulators (Fig. 3).

Conclusion: There is an inflammatory signature in the urine of patients with LN implicating monocyte and TNFa pathways. These signatures are associated with proliferative disease, worse proteinuria, and non-response to treatment. Of note, TNFa is involved in LN and has therapeutic potential. In phase 1 of AMP, monocytes were the main urine cell type identified by singe cell RNA sequencing in patients with LN. These results suggest that urine proteomics might identify and infer active pathological mechanisms in LN, paving the way for a more personalized approach to treatment. Further work in Phase 2 of AMP is being pursued to validate and extend these findings.

Disclosure: A. Fava, None; **Y. Zhang**, None; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **H. Belmont**, None; **P. Izmirly**, Glaxosmithkline, 5, GSK, 5; **C. Mohan**, Equillium, 5, Equillium, Inc, 5; **T. Zhang**, None; **T. Accelerating Medicines Partnership**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 2743

Characterizing the Epigenomic Landscape of Psoriasis Patients Destined to Develop Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Time: 2:30PM–4:00PM

Background/Purpose: Approximately 30% of psoriasis patients develop psoriatic arthritis (PsA), an inflammatory musculoskeletal disease, usually after psoriasis onset. A large proportion of individuals with PsA remain undiagnosed. An understanding of how the epigenome changes during the transition to PsA could yield predictive biomarkers and facilitate PsA diagnosis. We hypothesized that DNA methylation changes occur early in PsA pathogenesis, prior to overt clinical symptoms, and can be used as biomarkers for disease prediction. The specific aim was to characterize the epigenomic landscape of psoriasis patients who later developed PsA (converters) and compare it to psoriasis patients who did not develop PsA (non-converters).

Methods: We performedan epigenome-wide comparison of DNA methylation in baseline whole blood samples from psoriasis converters (n=58) and non-converters (n=59) from a longitudinal cohort. Post-conversion samples taken at the time of PsA diagnosis were available on 23 of the converters. Patients were matched for age, sex, psoriasis duration, and duration of follow-up. No patients were taking biologic agents. DNA was bisulfite converted was analyzed on Human MethylationEPIC BeadChips using the Bioconductor package ChAMP. Cell type heterogeneity was corrected using RefbaseEWAS. Differentially methylated probes (DMPs) and regions (DMRs) were identified using limma and DMRcate. The FEM package was used to infer differentially methylated gene modules (subnetworks) within a protein-protein interaction (PPI) network.

Results: Converter baseline samples were collected a median of 4.2 (interquartile range 1.9-6.3) years prior to the onset of PsA, while non-converters samples were collected a median of 4.3 (1.2-7.3) years prior to the most recent clinic visit. Between converters and non-converters, there were 129 DMPs and 15 DMRs containing at least 4 significant CpGs (FDR< 0.05). DMRs were identified in FBXO27 (fold change [FC]=0.06, FDR=2.2x10-24), a ubiquitin ligase involved in lysosomal degradation, RCAN1 (FC=0.05, FDR=4.2x10-12), a protein involved in bone homeostasis, and PMAIP1 (FC=0.04, FDR=6.0x10-12), which encodes the NOXA protein involved in mediating apoptosis of activated B cells. Differentially methylated promoters mapped to PPI subnetworks involved in canonical toll-like receptor/NFKB signaling (MYD88, TICAM1, TLR6, TOLLIP), alternative NF-KB signaling (MYD88, TICAM1, TNFRSF13C, TNFSF13B), and MAPK signaling (p38, MEF2D, DUSP10, PTPN7, STK39, MKNK2). Between non-converters and post-conversion samples, 25 DMPs and 3 DMRs in genes such as SERPINF1 (FC=-0.04, FDR=1.13x10-18) was found. Significant PPI subnetworks included notch signaling (APH1A, MAML3, NOTCH4, PSEN1) and ephrin signaling (EFNA1, EFNA2, EPHA7, EPHA2).

Conclusion: Changes in individual CpGs, DMRs, and inflammatory pathways were detected in baseline samples of psoriasis converters compared to non-converters and between non-converters and post-conversion samples. These preliminary data support our hypothesis that DNA methylation changes occur early in PsA pathogenesis and can potentially serve as prognostic biomarkers of future onset of arthritis in psoriasis patients.

Disclosure: R. Pollock, None; **R. Machhar**, None; **V. Chandran**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, BMS, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 5, Galapagos NV, 5, Gilead, 5, GSI, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5.

Abstract Number: 2744

Altered Expression of CD52 Facilitates Adhesion of Circulating CD14$^+$ Monocytes in Systemic Sclerosis

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Background/Purpose: Infiltration of inflammatory cells, including monocytes, into the organs is a major process leading to fibrosis, remodelling and organ dysfunction in systemic sclerosis (SSc). Adhesion is a key process for cell infiltration. However, its pathomechanisms in SSc remain elusive.

CD52 protein is highly expressed on CD4$^+$ T-cells and plays an important role in the modulation of T-cell receptor signalling. Nevertheless, the function of this protein on monocytes is not completely understood.

We aimed to investigate the process of monocyte adhesion in SSc with a special focus on the influence of CD52 expression.

Methods: Biopsies from the heart, lungs and skin of SSc patients (n=11, 7, 7, respectively) and healthy controls (HC) (n=10, 7, 9, respectively) were analysed by immunohistochemistry for the presence of CD14$^+$ cells. RNAseq of CD14$^+$ blood monocytes of lcSSc (n=5, age=54.4±6.7), dcSSc patients (n=5, age=51.8±7.2) and age- and sex-matched HC (n=5, age=50.8±9.7) was performed. Differentially expressed genes were computed using DeSEQ2 algorithm. Gene ontology and pathway analysis were performed using Metacore software and ShinyApp. Expression of adhesion molecules was confirmed by flow cytometry (HC n=16, SSc n =76). Adhesion of CD14$^+$ monocytes to ICAM1 and TNFα-stimulated endothelial cells was checked using the 96-well plate adhesion assay (HC n=12, SSc n=40). CD52 regulation in CD14$^+$ monocytes from HC (n=4) was analysed on mRNA level upon stimulation with LPS, IFNγ, IL-4 and IL-13. Adhesion under the physiological shear flow of THP-1 cell lines with overexpression and silencing of CD52 was investigated (n=4).

Results: Immunohistochemistry confirmed higher infiltration of CD14+ cells in the heart ($p< 0.01$), lung ($p< 0.05$) and skin ($p< 0.001$) of SSc patients. 1440 differentially expressed genes were detected between dcSSc vs HC and 225 between lcSSc and HC ($p\leq0.01$; log2 ratio≥0.5). Pathway analysis revealed significant alterations in adhesion and chemotaxis pathways. Flow cytometry confirmed upregulation of adhesion molecules CD11b ($p< 0.01$) and CD18 ($p< 0.05$). In contrast, expression of CD52 was downregulated in SSc patients ($p< 0.05$). SSc CD14$^+$ monocytes exhibited

increased adhesion both to ICAM1-coated plates ($p< 0.01$) and to TNFα-stimulated endothelial cells ($p< 0.05$). CD52 mRNA was increased in a dose-dependent manner after IL-4 and IL-13 stimulation and decreased after LPS and IFNγ stimulation ($p< 0.05$). Overexpression of CD52 in THP-1 monocytes decreased adhesion to TNFα-stimulated endothelial cells ($p< 0.01$) under the shear flow conditions. Accordingly, silencing of CD52 increased adhesion of THP-1 monocytes ($p< 0.01$).

Conclusion: Here we pointed to an increased adhesion of peripheral blood $CD14^+$ monocytes to ICAM1 and endothelial cells in SSc. Our results suggest the primary activation of monocytes in peripheral blood, which may translate into higher organ infiltration in SSc patients. Finally yet importantly, we characterised a novel function of the CD52 molecule on monocytes and its possible contribution during the course of the disease.

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Abstract Number: 2745

Iguratimod Treated Scleroderma with Interrupted Egr1/TGF-β Loop

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SESSION INFORMATION
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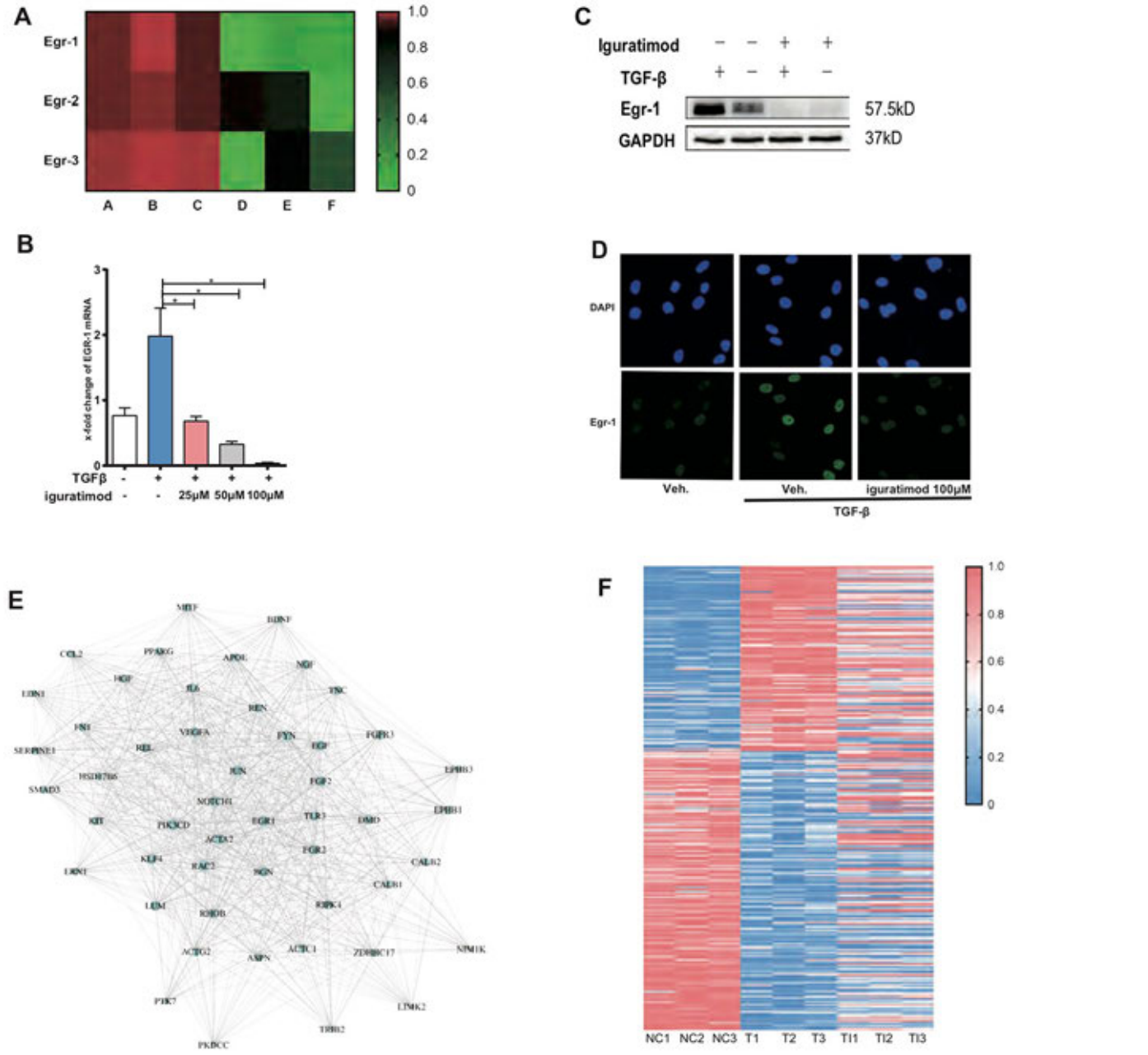
Background/Purpose: Iguratimod is a novel disease modifying anti-rheumatic drug that has been approved for treating rheumatoid arthritis in East Asia. Transcription factor early growth response 1 (*Egr1*) is one the most down-regulated genes in with iguratimod treatment. Egr1 forms a positive feedback loop with TGFβ and is overexpressed in lesional skin from systemic sclerosis (SSc) patients. This study is aim to investigate the anti-fibrotic effect of iguratimod in scleroderma models and patient skin grafts.

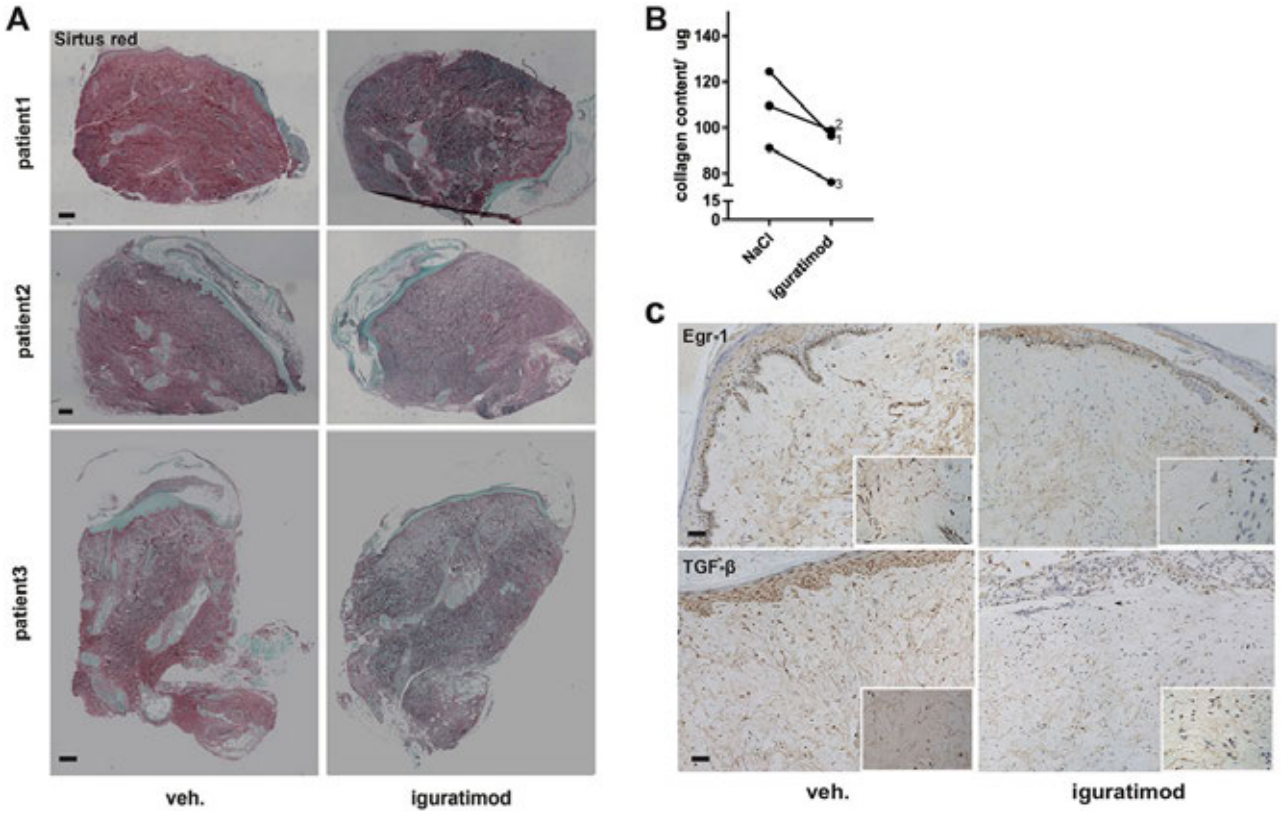
Methods: We used iguratimod to treat TGFβ-stimulated human skin fibroblast, bleomycin induced mice, tight skin 1 (TSK-1) mice and SSc skin grafts. The bleomycin model contained pre-establish fibrosis and late onset treatment. The skin grafts came from three SSc patients and was planted into irradiated nude mice.

Results: Iguratimod strongly inhibited *egr1* expression in human skin fibroblast, with moderate down-regulation of Egr2/3. Iguratimod neutralized effects of TGFβ on 232/327 Egr1 inducible genes according to transcriptome sequencing. Further protein interaction analysis showed that Egr1 was one of the hub genes of iguratimod working network. Collagen production and α-SMA production were decreased by iguratimod. Knocking down Egr1 using siRNA



Iguratimod inhibited Egr1 expression in primary human dermal fibroblast. Human fibroblast were stimulated by TGF-β and treated with 0.1% DMSO (T) or 100μM iguratimod (TI). (A) Iguratimod treatment suppressed multiple egr genes, particularly egr1. RNA was isolated and sequenced to Illumina Hiseq. Each line represents an independent experiment. (B) Iguratimod inhibited egr1 mRNA expression in dose dependent manner. N = 3 per group. *P<0.05, **P<0.01, ANOVA. (C, D) Iguratimod significantly reduced egr-1 protein synthesis at 100μM. (E) Analysis of 327 Egr1 response gene expression (genes with FDR < 0.05; fold change ≥ 1.5 in NC vs T comparison). Iguratimod could largely neutralize the effects of TGF-β on Egr-1 response genes. (F) Gene interaction analysis on the top 50 regulated genes between T and IGT groups using STRINGS data base. Egr1 was in the center of the network.

could mimic these effects. Both oral and topical iguratimod could treat dermal thickening and collagen deposition in bleomycin induced skin fibrosis. α-SMA (+) myofibroblast counts, as well as Egr1 (+) and TGFβ (+) fibroblast counts were significantly reduced by iguratimod. Similarly, topical iguratimod ameliorated dermal fibrosis in TSK-1 mice. Of note, 5-week iguratimod local injection remarkably reduced collagen content in skin grafts from three SSc patients, with simultaneous inhibited Egr1 and TGFβ staining.



Iguratimod treated fibrosis of skin grafts from systemic sclerosis (SSc) patients with interrupted Egr1/TGF-β loop. Lesional skin tissue from each SSc patient were transplanted subcutaneously into two irradiated nude mice. The grafts were injected with 0.1mg/ml iguratimod or vehicle every day for 5 weeks. (A) Sirius red staining for each graft. The red parts represent collagen and green parts represent total protein. (B) The collagen content of each skin tissue was quantified by eluting the dye and colorimetric assay. (C and D) Representative images of Egr1 and TGFβ staining.

Conclusion: We found the potential of iguratimod to treat SSc, which was characterized as the interruption of Egr1/TGFβ loop. Further clinical investigations for its safety and efficacy is warranted.

Disclosure: Q. Yan, None; **L. Shen**, None; **X. Chen**, None; **L. Lu**, None.

Abstract Number: 2746

Dimethyl Fumarate Ameliorates the GATA6 Deficiency-Induced Pulmonary Hypertension by Normalizing Oxidative and ER Stress

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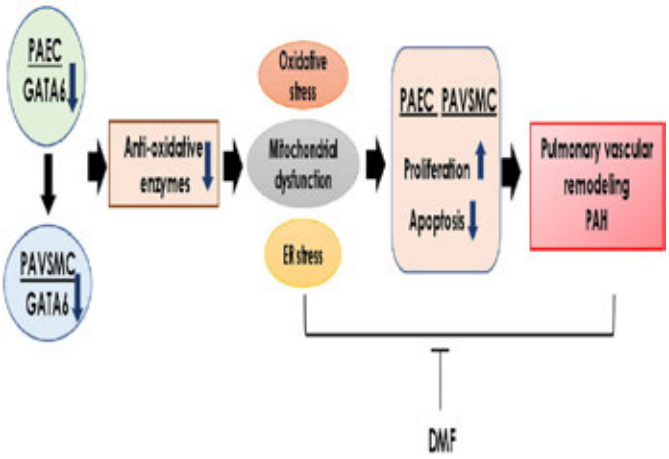
SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorder – Basic Science

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM



Background/Purpose: Pulmonary arterial hypertension (PAH) is a leading cause of death in patients with limited form of systemic sclerosis (SSc). We have previously reported that GATA6 is downregulated in pulmonary vasculature in SSc-PAH and IPAH patients and that endothelial cell deficiency of GATA6 is sufficient to promote PAH development in mice (Ghatnekar et al, 2013). The goal of this study was to gain further insights into the mechanism of deficient GATA6-induced PAH and to evaluate the therapeutic potential of dimethyl fumarate **(**DMF) in preclinical models of PAH.

Methods: In vitro experiments used early-passage distal pulmonary artery endothelial cells (PAEC) and smooth muscle cells (PAVSMC) from PAH and non-diseased lung. GATA6 was depleted in control human PAEC and PAVSMC by transfecting with siRNA GATA6 or restored by transduction with human GATA6 expressing adenovirus. Enzymatic activities of superoxide dismutase 2 (SOD2), glutathione peroxidase 1 (GPX1) and catalase was determined using commercially available kits. Cellular and mitochondrial ROS production was examined using CellROX and MitoSOX probes, respectively. In vivo experiments used mice with endothelial-specific Gata6 deficiency (Gata6 CKO). DMF or vehicle control were administered daily for 3 weeks via i.p. injection.

Results: Transcriptome analysis of human PAEC transfected with GATA6 siRNA revealed downregulation of multiple genes involved in the antioxidant stress response, including SOD2, catalase, and GPX family members. ChIP analysis indicated that GATA6 is a direct transcriptional regulator for SOD2 and GPX1. Human PAEC with siRNA-induced GATA6 depletion showed marked increase in both cellular and mitochondrial ROS production in parallel with the up-regulation of the ER stress genes. Reduced levels of GATA6 were also present in PAEC and PAVSMC obtained from patients with PAH and were associated with increased cell growth. Adenoviral delivery of GATA6 in human PAH PAEC and PAVSMC reduced their growth and induced PAVSMC apoptosis. Importantly, GATA6 and SOD2 were downregulated in control PAVSMC treated with conditioned media obtained from GATA6 siRNA treated PAEC. Increased oxidative and ER stress were also recapitulated in Gata6 CKO mice. Treatment with DMF normalized pulmonary pressure and partially reversed right heart hypertrophy in Gata6 CKO mice. DMF also normalized expression of antioxidant enzymes, including SOD2 and GPX and reversed the oxidative and ER stress in the lungs of Gata6 CKO mice. DMF also restored eNOS expression levels previously shown to be downregulated in these mice.

Conclusion: Deficiency of GATA6 is a shared pathological feature between PAEC and PAVSMC in human SSc-PAH and experimental PAH. GATA6 acts as a direct positive regulator of SOD2 and other antioxidant enzymes, providing protection from oxidative stress and supporting pulmonary vascular homeostasis. GATA6 controls PAEC-PAVSMC communication and endothelial GATA6 deficiency results in GATA6 loss and consequent proliferation of PAVSMC, exacerbating pulmonary vascular remodeling and PAH. Beneficial effects of DMF on the key pathways contributing to PAH, supports its testing in PAH treatment in patients.

Disclosure: A. Ichihara, None; **T. Toyama**, None; **T. Kudryashova**, None; **Y. Shen**, None; **D. Goncharov**, None; **E. Goncharova**, None; **M. Trojanowska**, None.

Abstract Number: 2747

Identification of Naturally Presented Peptides of the Autoantigen Topoisomerase-I Reveals a Common Pathogenic Mechanism in Patients with Systemic Sclerosis

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SESSION INFORMATION

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Session Time: 2:30PM–4:00PM

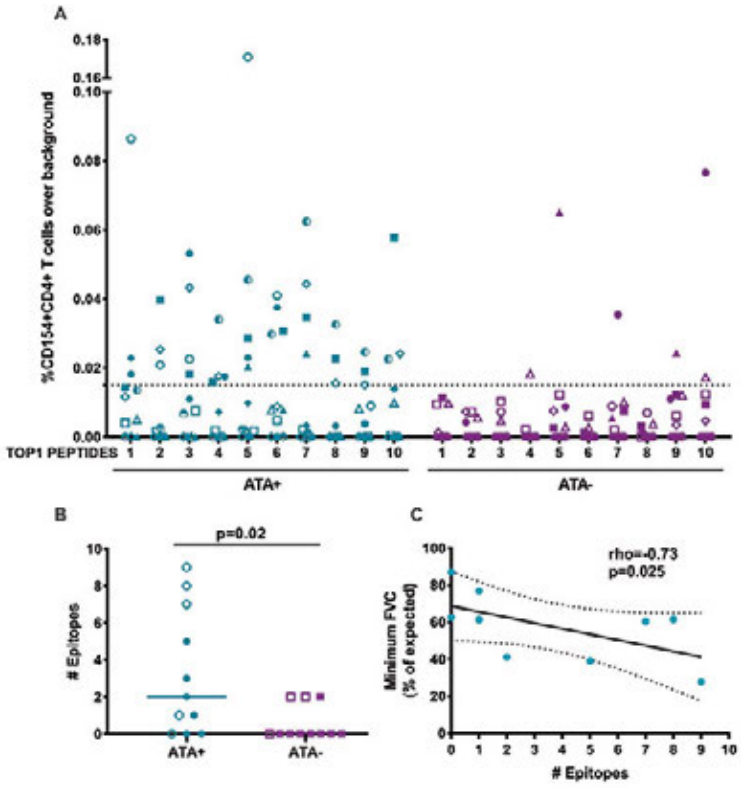

Figure 1. Distribution and clinical significance of CD4+ T cell responses to naturally presented TOP1 epitopes in SSc. (A) %CD154+CD4+ T cell responses over background observed with media alone for 11 ATA-positive and 11 ATA-negative SSc patients for each of the 10 naturally processed TOP1 peptides identified using NAPA are shown. The dotted line represents the cutoff for positivity that was defined as >95th percentile of the T cell responses observed in ATA-negative patients (95th percentile=0.015%). Each colored symbol represents a unique patient. (B) The number of peptides eliciting a response in ATA-positive (n=11) and ATA-negative (n=11) SSc patients is shown (Mann-Whitney, p=0.02). Open symbols represent patients that possess at least one ATA-associated HLA-DRB1 allele. (C) The minimum FVC (% of expected) was plotted against the number of TOP1 epitopes eliciting a T cell response in ATA-positive SSc patients with clinically documented ILD (n=9). The correlation between minimum FVC and the number of stimulatory TOP1 epitopes was analyzed using a Spearman's rho test. A p-value <0.05 was considered significant throughout.

Background/Purpose: Autoimmune responses to DNA topoisomerase-I (TOP1) are found in a subset of patients with scleroderma at high risk for interstitial lung disease (ILD) and mortality. Anti-TOP1 antibodies (ATA) are associated with specific *HLA-DRB1* alleles, and the frequency of HLA-DR-restricted TOP1-specific CD4+ T cells is associated with the presence, severity, and progression of ILD. Although this strongly implicates the presentation of TOP1 peptides by HLA-DR in scleroderma pathogenesis, the processing and presentation of TOP1 has not been studied.

Methods: We developed a novel natural antigen processing assay (NAPA) which relies on the sensitivity and specificity of the cellular MHC class II antigen processing machinery. Monocyte-derived dendritic cells were generated from six SSc patients with anti-Topo-I antibodies (ATA) and pulsed with Topo-I protein. HLA-DR:peptide complexes were isolated by immunoprecipitation and eluted peptides were analyzed by mass spectrometry. We then examined the ability of these naturally presented putative epitopes to induce CD4+ T cell activation, as measured by upregulation of the early activation marker CD154 in PBMCs from ATA-positive (n=11) and ATA-negative (n=11) SSc patients.

Results: Using NAPA, we found that presentation of TOP1 epitopes was restricted to only 10 hot spots within TOP1, across patients with different HLA-DR variants. Further analysis revealed shared peptide-binding motifs within the HLA-DRβ chains of ATA-positive patients and a subset of TOP1 epitopes with distinct sets of anchor residues capable of binding to multiple different HLA-DR variants. The naturally presented TOP1 peptides elicited robust CD4+ T cell responses in ATA-positive patients, and the number of epitopes recognized correlated with the severity of lung fibrosis (Figure 1).

Conclusion: This study suggests a mechanism in which autoimmunity to TOP1 in scleroderma is driven by the presentation of a communal set of TOP1 peptides in patients with diverse *HLA-DRB1* alleles.

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Abstract Number: 2748

Cracking a Novel Profibrotic Molecular Mechanism: lncRNA H19X and DDIT4L Crosstalk

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SESSION INFORMATION
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Background/Purpose: Long noncoding RNAs (lncRNAs) are an emerging class of noncoding transcripts involved in the regulation of gene expression in health and disease. LncRNAs function via different mechanisms either acting cis, regulating the expression of nearby genes, or in trans, modulating the expression of distant genes. We have

identified a novel TGFβ regulated lncRNA, H19X, which was strongly and consistently upregulated in a wide variety of fibrotic disorders. Moreover, we were able to demonstrate that H19X is a key driver of myofibroblast formation and extracellular matrix (ECM) overproduction. Here we aimed to define the mode of action of H19X and to assess H19X functions that may drive myofibroblast differentiation and ECM production.

Methods: The function of H19X was investigated in SSc dermal fibroblasts (n=5) by knocking down H19X with locked nucleic acid oligonucleotides (LNA GapmeRs) followed by TGF-β stimulation and microarray analysis with Illumina HT-12 arrays. In situ hybridization for H19X was performed using Stellaris FISH probes. Genomic regions of interaction with H19X were identified by Chromatin Isolation by RNA Purification (ChIRP) using biotinylated probes tiling the transcript, RNA pull-down and sequencing. Chromatin remodeling was investigated by Assay for Transposase-Accessible Chromatin using sequencing (ATAC-seq). DNA damage-inducible transcript 4-like protein (DDIT4L) function was tested using siRNA in parallel to H19X downregualtion.

Results: As analyzed by microarray, none of the 16 genes belonging to the same genomic region (1 Mb) as H19X locus was affected by its downregulation, indicating that in-cis regulation is not a major mechanism of H19X activity. Cellular localization can give a first indication about lncRNA trans function: FISH staining of SSc fibroblasts stimulated with TGF-β revealed tightly localized nuclear foci in TGF-β treated cells. Moreover, increased numbers of positive nuclei were also recorded after TGF-β stimulation. H19X nuclear localization was confirmed by cell fractionation, where H19X expression was peaking in the nucleus of cells after 6h of treatment with TGF-β.

Next, we identified 58 genomic regions that directly interact with H19X using ChIRP. In order to establish the effect of H19X physical presence at these sites, the expression of the genes with the closest transcription start site was analyzed in the microarray data set. Among these genes, DDIT4L displayed the strongest induction following H19X knockdown. Furthermore, we cloud identify chromatin rearrangements caused by H19X knockdown in close proximity with its interaction site with DDIT4L locus using ATAC-seq. Interestingly, DDIT4L expression was consistently repressed by TGFβ stimulation at mRNA and protein level. Additionally, DDIT4L knockdown was able to restore COL1A1 expression that was reduced by H19X downregulation but only in presence of TGFβ. These data indicate that H19X mediates its effects unabeling DDIT4L transcription which, in turn, is a novel repressor of TGFβ pathway activity.

Conclusion: Our data uncover a novel mechanism for the TGFβ regulated profibrotic effects of H19X including direct effects on chromatin organization associated with fibrotic pathways.

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Abstract Number: 2749

Long Non-coding RNA HOTAIR Induces Myofibroblast Activation in Systemic Sclerosis Through EZH2 Dependent De-repression of NOTCH Signalling Pathway Activation

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Systemic Sclerosis & Related Disorder – Basic Science

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Fibroblasts explanted from affected tissues in Systemic Sclerosis (SSc), conserve their pro-fibrotic phenotype characterised by increased secretion of collagens and other extracellular matrix proteins and comprise a large proportion of a-Smooth Muscle Actin (a-SMA) positive myofibroblasts. Long non-coding RNAs (lncRNAs) within the HOX loci have been described as master epigenetic regulators within the connective tissue. Specifically, HOTAIR has been shown to drive the specific phenotype of the hands and feet which are also the first body regions affected by SSc. Here we aimed to unravel the mechanisms responsible for the epigenetically stable activation of SSc fibroblasts

Methods: Full thickness skin biopsies were surgically obtained from the forearms oftwelve adult patients with SSc of recent onset. Fibroblasts were isolated and cultured in monolayers and protein and RNA extracted from the fibroblast cultures. Laser capture was performed to isolate cells expressing or not a-SMA as a marker of myofibroblast differentiation. HOTAIR was expressed in healthy dermal fibroblasts by lentiviral induction employing a vector containing the specific sequence. Gamma secretase inhibitors RO4929097 and DAPT were employed to block Notch signalling in SSc fibroblasts. EZH2 was blocked in SSc fibroblasts with the specific inhibitor GSK126.

Results: HOTAIR expression was increased in SSc patients' skin (100 fold) and in SSc explanted fibroblasts (5 fold). These results were highly significant ($p< 0.001$ for both). Further, laser captured a-SMA expressing myofibroblasts expressed in average 2.5 fold greater HOTAIR RNA levels compared to a -SMA negative cells from the same donors ($P< 0.05$). In vitro, we demonstrated that lentiviral induced stable overexpression of HOTAIR in healthy dermal fibroblasts led to their profibrotic activation, including significantly increased expression of Col1A1 and a-SMA both at mRNA and protein levels (2.8 and 1.8 fold respectively, $p< 0.05$). We further showed that HOTAIR-induced profibrotic activation was due to EZH2 dependent spread of H3k27me3 methylation marker, as demonstrated by complete inhibition by treatment with GSK126. Additionally, we showed that EZH2 led to profibrotic activation by decreasing the expression of miRNA 34a. The reduced miRNA 34a levels in turn led to NOTCH increased expression and signalling pathway activation. Consistent with these findings, treatment of the HOTAIR expressing cells with two different types of gamma secretase inhibitors known to block NOTCH activation, normalised a-SMA expression and suppressed collagen production by 50%. Importantly, treatment with the EZH2 inhibitor GSK126 suppressed collagen production in the HOTAIR expressing cells and SSc fibroblasts by 30% and 50% respectively ($p< 0.05$) and normalised a-SMA levels in both cell lines to control levels ($p< 0.05$).

Conclusion: Here we show that the epigenetically stable activation of SSc dermal fibroblasts is due to HOTAIR led EZH2 dependent de-repression of NOTCH signalling. The results of these studies identify a new venue to modulate fibroblasts biology which could inform clinical research to resolve chronic fibrosis and re-establish tissue homeostasis in SSc.

Disclosure: C. Wasson, None; **G. Abignano**, None; **R. Ross**, None; **H. Hermes**, None; **S. Jimenez**, None; **F. Del Galdo**, AstraZeneca, 5, 8, GSK, 5, 8, Boehringer-Ingelheim, 5, 8, Actelion, 5, 8, Capella Biosciences, 2, 5, Chemomab, 2, 5.

Abstract Number: 2750

Development and Preliminary Validation of a Novel Lung Ultrasound Interpretation Criteria for the Detection of Interstitial Lung Disease in Patients with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Imaging of Rheumatic Diseases II
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Interstitial lung disease (ILD) is a frequent complication of systemic sclerosis (SSc), and screening, characterization, and monitoring of disease activity are important for therapeutic decision-making and prognostication. High resolution computed tomography (HRCT) is the gold standard for ILD diagnosis. More recently, lung ultrasonography (LUS) has been proposed as a potential alternative imaging modality for ILD detection. In this study, we develop and test a novel LUS interpretation criteria for detecting SSc-ILD.

Methods: Patients with prevalent SSc and prior or planned HRCT within 3 months were prospectively enrolled and assessed by LUS. We included 14 lung positions and used a novel acquisition technique, collecting several seconds of real-time images rather than still images with the probe oriented in a sagittal rather than transverse orientation. This technique affords better visualization and tracking of pleural lesions with respiration. Prior studies identified B-line quantification, pleural irregularity, and pleural thickness as features sensitive for SSc-ILD. Although B-line quantification has been extensively studied, it is a less specific and artifactually based finding and highly dependent on ultrasound technique and machine settings. Given the high resolution of current US machines, granular appearing pleural thickening and pleural irregularity (defects in the pleural surface) were easy to visualize and highly reproducible (Figure 1). Using a combination of these features, we developed LUS interpretation criteria for SSc-ILD detection (Figure 2). These interpretation criteria were used to evaluate LUS examinations of our SSc cohort and were read by

Figure 1. Interstitial lung disease findings on lung ultrasound

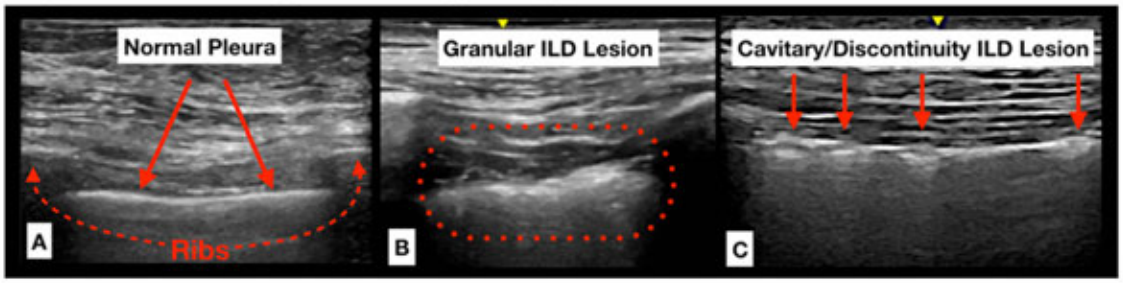

Figure 2. Ultrasound interpretation criteria for interstitial lung disease

Lung zones are considered positive if both criteria I and II are met:

I. Lesions must be characterized by *either*:
- A) Discontinuities or cavitations in the linear pleural surface (hypoechoic centers and hyperechoic rims)
- B) A hyperechoic, granular appearance

II. Lesions must demonstrate *all three (3)* of the following conditions:
- A) Be identified as 1 or more distinct lesions > 2 mm in width OR as confluent lesions involving the entire pleural surface
- B) Demonstrate pseudo-thickening: any degree of increased hyperechoic transmission deep to lesions compared to normal pleura
- C) Track with lung movement

1 or more positive lung zones indicates a positive study for interstitial lung disease.

Table 1. Detection of SSc-ILD via LUS versus HRCT using LUS interpretation criteria

	Reader 1 (ultrasonographer)		Reader 2 (non-ultrasonographer)
Patients, n		**20**	
Lung zones examined, n		278	
SSc-ILD per HRCT, n (%)		9 (45)	
LUS – ILD detection per patient			
Read as positive, n (%)	11 (55)		11 (55)
Read as negative, n (%)	9 (45)		9 (45)
Sensitivity vs HRCT	100%		100%
Specificity vs HRCT	84.6%		84.6%
Kappa		1.00	
LUS – ILD detection per lung zones			
Read as positive, n (%)	65 (23)		59 (21)
Read as negative, n (%)	213 (77)		219 (79)
Concordance		93.8%	
Kappa		0.82	

HRCT = high resolution computed tomography, LUS = lung ultrasound, ILD = interstitial lung disease, SSc-ILD = systemic sclerosis associated interstitial lung disease.

two independent readers (1 ultrasonographer and 1 non-ultrasonographer) who were blinded to HRCT results and ILD diagnosis. The sensitivity and specificity for SSc-ILD detection was assessed and agreement was measured with Cohen's Kappa statistic.

Results: We evaluated 20 SSc patients by LUS examination (278 lung zones) and HRCT. HRCT confirmed ILD in 9 patients (45%). LUS was read as positive for SSc-ILD in 11 patients (55%) with a sensitivity of 100% and specificity of 84.6% versus HRCT with perfect agreement between the two readers (κ= 1). Analysis by individual lung zones found excellent agreement between readers with 93.8% concordance and κ = 0.82 (Table 1).

Conclusion: We developed a novel ultrasound technique and interpretation criteria that are highly sensitive and specific for ILD detection in an SSc cohort. Our interpretation criteria are feasible and reliable, affording perfect agreement between ultrasonographer and non-ultrasonographer readers for SSc-ILD detection. Moving forward we hope to validate these criteria in a larger cohort of patients with SSc, dermatomyositis and polymyositis.

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Abstract Number: 2751

Very Low Prevalence of Ultrasound Determined Tendon Abnormalities in Healthy Subjects Throughout the Age Range: An Outcome Measures in Rheumatology (OMERACT) Ultrasound Minimal Disease Study

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	HS 18-39 y	HS 40-59 y	HS ≥60 y	RA ≤ 12	RA > 12	5 groups p value	RA ≤12 vs >12 p value
n	408	311	180	30	114		
Age, y (IQR)	29 (25-33)	49 (44-55)	68 (62-72)	58 (52-69)	53 (42-65)	<0.001	0.03
Female (%)	270 (66)	270 (83)	114 (62)	20 (67)	86 (75)	<0.001	0.2
DAS 28 CRP (IQR)	-	-	-	5.4 (4.2-6.1)	4.8 (4.1-5.7)	-	0.1
Tender joint* (IQR)	0	0	0	18 (10-23)	17 (11-29)	<0.001	0.9
Swollen joint* (IQR)	0	0	0	8 (3-18)	6 (3-9)	<0.001	0.1
DF 1-5 TSH grade ≥1 (%)	8 (0.2)	9 (0.3)	2 (0.1)	54 (18)	125 (11)	<0.001	0.06
DF 1-5 PD grade ≥1 (%)	3 (0.05)	2 (0.06)	0	49 (16)	85 (8)	<0.001	0.02
ECU TSH grade ≥1 (%)	1 (0.1)	11 (1.8)	5 (1.4)	13 (22)	52 (23)	<0.001	0.8
ECU PD grade ≥1 (%)	0	0	0	12 (20)	50 (22)	<0.001	0.7

*RA patients had 66/68 joint count

Demographics and summary tendon data for healthy subjects by age groups, and RA patients by early and late presentation

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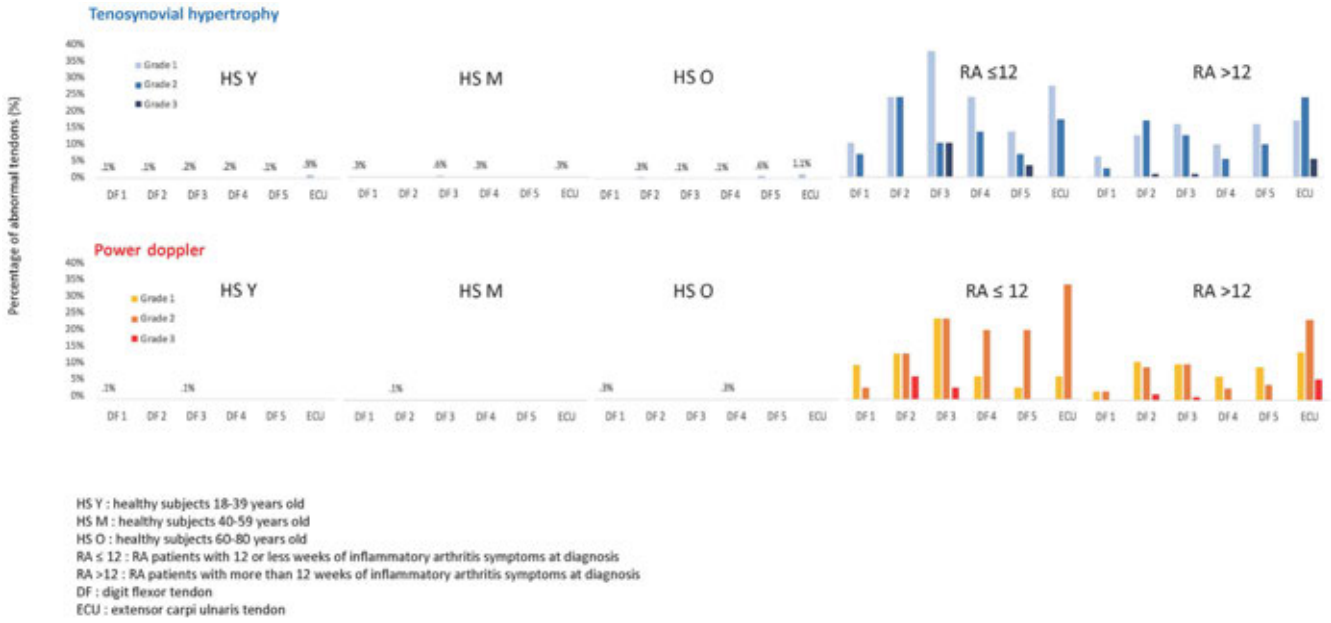
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Imaging of Rheumatic Diseases II
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Tenosynovitis (TS) is a common, often clinically undetectable finding in Rheumatoid Arthritis (RA). Recent data showed TS on ultrasound (US) has a role in predicting outcome in early disease and flare in clinical remission. However data is limited on US measured TS in healthy subjects (HS), none specifically encompassing the older age range when RA commonly presents. This OMERACT study aimed to determine prevalence of US measured tendon abnormalities in HS throughout the age range.

Methods: Adult healthy subjects without: joint pain (VAS < 10/100), hand osteoarthritis (ACR criteria), or inflammatory arthritis were recruited in 23 international centres from Aug 2017-Dec 2018. MCP, PIP and wrist joints were



Percentage of abnormal digit flexor and extensor carpi ulnaris tendons by age group of healthy subjects, and early or late presenters in RA patients

clinically examined. Bilateral digit flexor (DF) 1-5 and extensor carpi ulnaris (ECU) tendons were scanned for tenosynovial hypertrophy (TSH) and power Doppler (PD) signal and graded (OMERACT US scoring system). A comparison cohort of DMARD-naive patients with RA (ACR-EULAR 2010 and/or 1987 criteria) at presentation was taken from the Birmingham Early Arthritis (BEACON) inception cohort, who underwent identical tendon US assessment. They were grouped into ≤12 and > 12 weeks from symptom onset. Abnormal ultrasound findings were dichotomised in to grade 0 (absent) or grade 1-3 (present) for statistical analysis (Fisher's exact test).

Results: Data from 899 HS and 144 RA patients were included. Prevalence of TSH and particularly PD abnormalities in HS was very low in all age groups, and was all grade 1 except in one individual ECU tendon. ECU TSH grade≥1 was more common than DF grade≥1 in the older HS groups, and less common in the 18-39 age group (p=0.011). TSH and PD of grade ≥1 were common in RA patients (p ≤0.001), with DF PD abnormalities more common in early disease (p=0.02).

Conclusion: Very low prevalence of TSH or PD abnormalities in tendons of healthy subjects even in old age suggests ultrasound determined tenosynovitis will be a robust tool in clinical management of RA.

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Abstract Number: 2752

Successfull Evaluation of a Predefined Set of Anatomic Sites in the Pelvis of Patients with Polymyalgia Rheumatica Showing Extracapsular Inflammation as Visualized by Contrast Enhanced Magnetic Resonance Imaging

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Imaging of Rheumatic Diseases II
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: The diagnosis of polymyalgia rheumatica (PMR) is based on a thorough clinical evaluation of the patient - including exclusion of other diseases, since there is no decisive diagnostic test. A characteristic pattern of extracapsular inflammation in the pelvis of patients with PMR as assessed by contrast enhanced magnetic reso-

nance imaging (MRI) has been recently described (1). We evaluated the performance of a predefined set of anatomic sites in the pelvis of patients with PMR vs. controls.

Methods: A total of 120 pelvic MRI scans of patients who had presented to our tertiary center with pelvic girdle pain in the last 3 years, including 40 patients with an expert rheumatologist diagnosis of PMR and 80 controls with other reasons of pelvic pain was evaluated by 3 radiologists blinded to clinical diagnosis and patient demographics. The experts scored the presence or absence of contrast enhancement at 19 predefined tendinous and capsular pelvic structures. Different patterns of involvement were compared and statistically evaluated by ROC analysis. Kappa statistics were applied to calculate inter- and intrareader agreement.

Results: Mostly bilateral peritendinitis and capsulitis including uncommon sites such as the proximal origins of the muscles rectus femoris and adductor longus were found almost exclusively and, thus, typically in PMR patients: the difference in the mean number of sites showing contrast enhancement was significantly different with 13.4±2.7 for PMR vs 4.0±2.3 for controls. A cut-off of ≥10 inflamed sites discriminated very well between the groups resulting in a sensitivity and specificity of 95.8% and 97.1%, respectively. Just concentrating on the most frequently involved anatomic sites bilateral inflammation of proximal M. rectus femoris or adductor longus tendons together with at least 3 other bilaterally inflamed sites performed even better with a sensitivity and specificity of 100% and 97.5%, respectively.

Conclusion: This study strongly confirms that the previously described pattern of extracapsular pelvic inflammation as assessed by contrast enhanced MRI is very typical for patients with PMR. In addition, the high sensitivity and specificity of the set of anatomic sites evaluated suggest their definite potential for use as a confirmatory diagnostic test.

1. Fruth M et al, Clin Exp Rheumatol. 2018

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Abstract Number: 2753

Major Salivary Gland Ultrasound: Pilot Study of Findings and Feasibility in Childhood-Onset Systemic Lupus Erythematosus (cSLE)

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SESSION INFORMATION
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Session Title: Imaging of Rheumatic Diseases II
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Ultrasonography is becoming an increasingly useful tool in evaluating patients in pediatric rheumatology. It is predominantly used for musculoskeletal assessments, however, major salivary gland ultrasound (SGUS) is being used in adults for assessment of primary and secondary Sjögren's syndrome. Very few studies have been done examining salivary gland ultrasound in children and they have been confined to primary Sjögren's syndrome. Examining children with rheumatic diseases who may be at risk for Sjögren's syndrome such as childhood onset systemic lupus erythematosus (cSLE) may reveal early changes allowing for targeted intervention. Our primary objective is to determine acceptability and feasibility of SGUS in a pediatric rheumatology clinic. A secondary objective is to evaluate differences in ultrasound findings between cSLE Ro/La+ patients vs. cSLE Ro/La- patients.

Methods: Patients completed questionnaires rating symptoms of dryness, fatigue, pain, and reported any history of difficulty swallowing or episodic cheek swelling. Each patient underwent major SGUS of bilateral parotid glands (in two views) and bilateral submandibular glands (single view). Patients were asked to provide feedback on exam acceptability. Utilizing a previously published scoring system each major salivary gland image was scored by a blinded reviewer using a scale of 0-3 with a score of 0 representing a normal homogenous gland and a score of 3 representing diffuse gland heterogeneity. Scores of 2 or 3 were considered abnormal. The highest score was used as the overall ultrasound score for each patient. We used two sample independent t-tests or Fisher's exact tests to compare disease factors and ultrasound scores between cSLE patients Ro/La+ vs. cSLE patients Ro/La-. A second analysis was

Table 1: Demographic and Disease Characteristics Stratified by Ro/La Antibody Status

	Ro/La+ (n=10)	Ro/La- (n=10)	p-value
Age, years, Mean	18.7	18.3	0.65
Female	90%	90%	1.00
Caucasian	60%	40%	0.65
Black/African American	30%	60%	0.37
Asian	10%	0%	1.00
Disease Duration, years, Mean	5.3	4.9	0.57
SLEDAI[a], Mean	3.8	5.2	0.52
IgG[b], Mean	1927	1530	0.31
Dryness Score[c]	3	2.3	0.57
Fatigue Score[c]	2.8	3.3	0.69
Pain Score[c]	1.4	1.9	0.60
Needs water to swallow	20%	30%	1.00
Episodic cheek swelling	30%	0%	0.21
Abnormal U/S Score[d]	20%	20%	1.00

[a]SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, most recent value; [b]IgG level at disease diagnosis; [c]Dryness, Fatigue, and Pain scores on a scale of 0-10 with 10 being the worst score; [d]Abnormal U/S score is a score of 2 or 3 based on a 0-3 scale as defined by Theander & Mandl. Arthritis Care & Research, 2014

Table 2: Demographic and Disease Characteristics Stratified by U/S Score

	Normal U/S (n=16)	Abnormal U/S (n=4)	p-value
Age, years, Mean	18.6	18.3	0.12
Female	94%	75%	0.37
Caucasian	63%	0%	0.09
Black/African American	31%	100%	**0.03***
Asian	6%	0%	1.00
Disease Duration, years, Mean	4.8	5.2	0.81
SLEDAI[a], Mean	5.1	2.5	0.40
IgG[b], Mean	1530	2518	**0.03***
Dryness Score[c]	3	1	0.18
Fatigue Score[c]	3.3	2	0.40
Pain Score[c]	1.9	0.5	0.22
Needs water to swallow	25%	25%	1.00
Episodic cheek swelling	23%	0%	1.00
Anti Ro/La+[d]	50%	50%	1.00

[a]SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, most recent value; [b]IgG level at disease diagnosis; [c]Dryness, Fatigue, and Pain scores on a scale of 0-10 with 10 being the worst score; [d]Any history of anti-Ro and/or La positivity

Table 1. Summary of WOMAC OA Pain Score Change from Baseline through Day 94 - mITT Set

performed to compare differences between cSLE patients with abnormal ultrasound score vs. cSLE patients with normal scores.

Results: Twenty cSLE patients were recruited, 90% were female, 50% were Caucasian. The average disease duration among all patients was 5 years. All twenty patients deemed the ultrasound examination acceptable. Average time to complete the ultrasound examination protocol was 4.5 minutes. No negative effects on clinic flow were reported. Age, gender, race, disease duration, SLEDAI, IgG level at diagnosis, dryness, fatigue, pain, and abnormal ultrasound scores did not differ between Anti-Ro/La+ cSLE patients compared to Anti-Ro/La- cSLE patients (Table 1). The data were also analyzed comparing patients with normal vs. abnormal SGUS scores. IgG level at diagnosis and Black race were significantly associated with abnormal SGUS scores (Table 2).

Conclusion: This is one of the first studies to assess major SGUS in a cohort of patients with cSLE. We demonstrate acceptability and feasibility of this ultrasound protocol performed by rheumatologists in a pediatric rheumatology clinic. Although the sample size was small we found SGUS abnormalities in 20% of patients. IgG level at diagnosis and Black race may predict risk for SGUS abnormalities. Larger cohort studies would be helpful to determine risk factors for SGUS abnormalities in children; ultimately leading to earlier diagnosis and treatment interventions.

Disclosure: J. McDonald, None; **P. Vega-Fernandez**, None; **T. Ting**, None.

Abstract Number: 2754

AxSpA Patients with Symptom Onset < 30 Years Have More Structural Lesions on MRI of the Sacroiliac Joints When Fulfilling the Modified New York Criteria

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Imaging of Rheumatic Diseases II
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: The modified New York criteria (mNY) combine clinical symptoms with radiographic sacroiliitis on conventional pelvic radiographs (X-SI) classifying radiographic axial SpA patients (r-axSpA). AxSpA is known to typically start in the third era of life but there is a diagnostic delay of ±7 years. As the mNY criteria classify the most typical and severe expression of axSpA it is suggested that the mNY criteria are less useful in younger patients. Purpose of the study is to explore the diagnostic utility of the mNY criteria in newly diagnosed axSpA patients with a symptom onset < 30 years. In addition, describe the extent of lesions on MRI of the sacroiliac joints (MRI-SI) in mNY positive (mNY+) patients with a symptom onset < 30 years.

Methods: This study involved newly diagnosed axSpA patients, age ≥18 years, from a Belgian (Be-Giant) cohort. Patients underwent diagnostic tests involving clinical examination, lab tests, and imaging assessment containing an X-SI and an MRI-SI. mNY criteria was assessed on X-SI. MRI-SI reads contained the assessment of inflammatory lesions according to the Spondyloarthritis Research Consortium of Canada (SPARCC) scoring method and erosions, fatty lesions (FL), sclerosis, ankylosis using an adapted method of the SPARCC. Also, the ASAS definition of a positive MRI-SI was evaluated. T1-weighted and STIR images were viewed simultaneously. X-SI and MRI-SI were evaluated independently by 3 trained readers who were also blinded for clinical features. Imaging scores (X-SI grading according to the mNY criteria and mNY fulfillment, and MRI-SI lesion scores) were calculated as 2 out of 3 reader scores.

Results: In the 173 patients with available X-SI, the average age at symptom onset was 27.4 years old. In 114/173 (65.9%) patients, the symptom onset was below 30 years. Of those, 11 (9.6%) patients fulfilled the mNY criteria. Seven of the 11 (63.6%) patients that were mNY+ were male, which was slightly lower than in the mNY- patients (n=55; 53.4%). The presence of HLA-B27 was comparable between mNY+ and mNY- patients; 8 (72.7%) patients and 82 (79.6%) patients, respectively. Average X-SI grading in mNY+ patients was 4.7±1.3 (on a scale from 0-8) and in mNY negative (mNY-) patients (n=103) the average X-SI grading was 1.1±1.1.When looking at the MRI-SI assessment, 8/11 mNY+ patients (72.7%) and 60/103 mNY- patients (58.3%) had a positive MRI-SI (ASAS definition). The table shows

Table: Average MRI-SI lesion scores in axSpA patients with a symptom onset of <30 years fulfilling and not fulfilling the modified New York criteria.

MRI lesions	mNY+ (n=11)	mNY- (n=103)	P-value
Inflammatory lesions (SPARCC score)*	8.9 (±6.0)	7.3 (±7.2)	0.341
Erosions*	7.6 (±4.4)	3.5 (±4.2)	0.003
Fatty lesions*	6.6 (±8.3)	1.8 (±4. 6)	0.005
Sclerosis*	1.1 (±2.0)	0.9 (±2.6)	0.237
(Partial) Ankylosis*	7.6 (±11.5)	0.8 (±3.2)	0.030

* mean (±SD)

the mean scores for MRI-SI lesions. In erosions, fatty lesions and ankylosis, either partial or complete ankylosis, there was a statistically significant difference ($p< 0.05$) between mNY+ and mNY- patients.

Conclusion: Patients with newly diagnosed axSpA and a symptom onset before 30 years infrequently fulfill the mNY criteria. A statistically significant difference in the presence of MRI-SI structural lesions was reported between mNY+ and mNY- patients. AxSpA patients with an early symptom onset have more erosions, fatty lesions and ankylosis on MRI when fulfilling the mNY criteria.

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Abstract Number: 2755

Assessing the Sensitivity to Change of the OMERACT Ultrasound Structural Gout Lesions During Urate-Lowering Therapy

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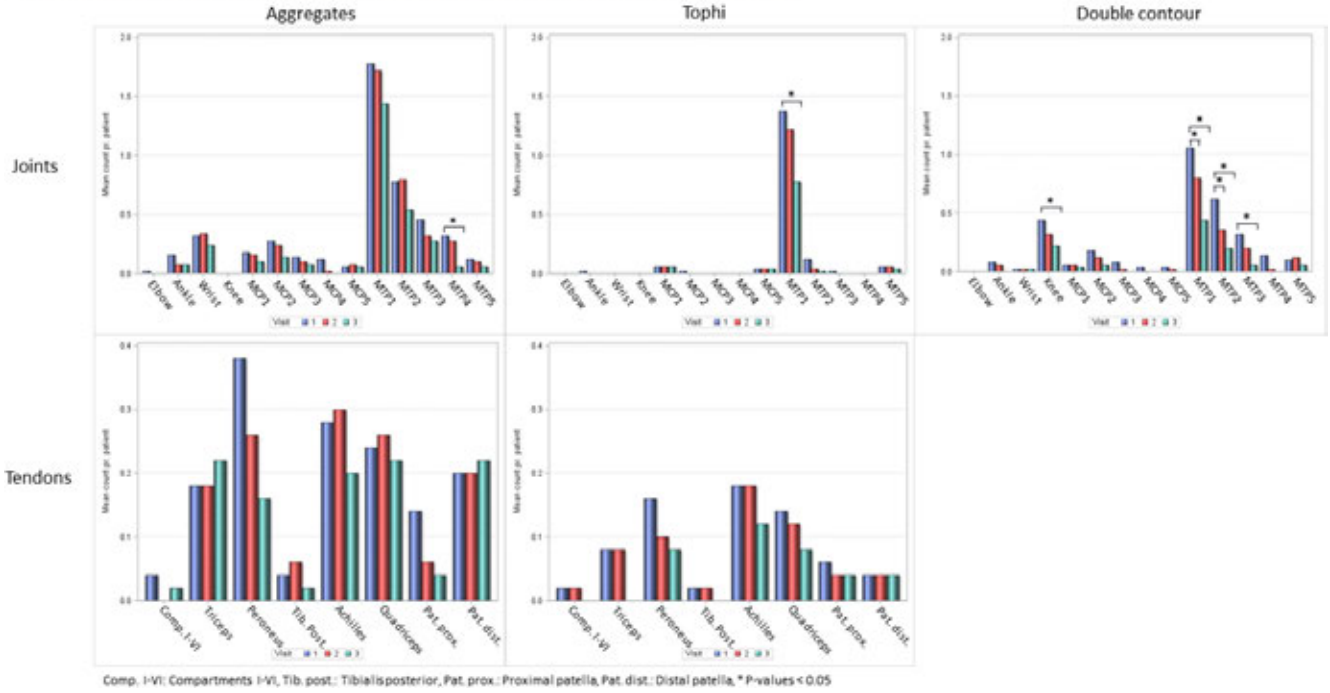
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Imaging of Rheumatic Diseases II
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: To evaluate the sensitivity to change of ultrasound (US) structural gout lesions, as defined by the OMERACT US group, in gout patients during urate lowering therapy.

Methods: US examination (28 joints, 26 tendons) was performed in patients with microscopically verified gout, who initiated or increased urate lowering therapy. Joints and tendons were evaluated by US for the OMERACT structural gout lesions (double contour sign (DC), tophus, aggregates and erosions), scored binarily (0/1). Synovial changes were graded by grey scale (GS) and color Doppler (CD), both scored semiquantitatively (0-3), where a score ≥ 1 was considered pathological. A sum score was calculated for each lesion for each patient. Numbers of gout attacks within the last 4 and 12 weeks and Patient Reported Outcomes (PROs) regarding pain (visual analogue scale (VAS)) and physical function (HAQ) were obtained, as were CRP, p-urate and clinical joint examination. All examinations were repeated after 3 and 6 months. Changes in patient's sum scores and lesion scores at different locations (joints and tendons) were evaluated using Wilcoxon-Pratt signed-rank test. Furthermore, changes in lesion scores between groups that did/did not achieve the treatment target (p-urate < 0.36 mmol/L) were compared using Mann Whitney U test and Chi square test.

Table 1: Course of ultrasound, biochemical and clinical variables during 6 months follow up.													
		Baseline (n=50)			3 months' follow up (n=46)			6 months' follow up (n=41)			Δ 0-3 months	Δ 3-6 months	Δ 0-6 months
	Variable (possible range)	Mean	Median (range)	Quartile range	Mean	Median (range)	Quartile range	Mean	Median (range)	Quartile range	p-value	p-value	p-value
Laboratory / clinical parameters	P-urate (mmol/L)	0.49	0.48 (0.32-0.78)	[0.42 ; 0.56]	0.36	0.35 (0.24-0.55)	[0.30 ; 0.39]	0.33	0.31 (0.22-0.51)	[0.29 ; 0.34]	<0.001	0.014	<0.001
	CRP (mg/L)	15.2	5.2 (0.3-120)	[0.9 ; 22]	5.5	2.5 (0.3-53)	[0.7 ; 6.6]	4.75	2.3 (0.3-43)	[0.7 ; 3.0]	0.053	0.854	0.001
	Swollen joints (0-60)	1.96	1 (0-14)	[0 ; 2]	1.30	0 (0-14)	[0 ; 1]	0.71	0 (0-6)	[0 ; 1]	0.032	0.210	<0.001
	Tender joints (0-60)	2.74	2 (0-18)	[1 ; 4]	1.54	0 (0-12)	[0 ; 2]	0.83	0 (0-5)	[0 ; 1]	0.006	0.091	<0.001
PROs	Patient VAS (0-100)	37.3	33 (0-95)	[15 ; 55]	18.6	9 (0-85)	[0 ; 40]	10.6	5 (0-60)	[0 ; 15]	<0.001	0.003	<0.001
	HAQ (0-3)	0.27	0 (0-2)	[0 ; 0.375]	0.19	0 (0-1.625)	[0 ; 0.125]	0.12	0 (0-1.75)	[0 ; 0]	0.464	0.344	0.129
	No. of joint attacks (12 weeks)	2.36	2 (0-8)	[1 ; 3]	0.74	0 (0-6)	[0 ; 1]	0.49	0 (0-3)	[0 ; 1]	<0.001	0.340	<0.001
	No. of joint attacks (4 weeks)	1.16	1 (0-4)	[1 ; 1]	0.35	0 (0-2)	[0 ; 1]	0.29	0 (0-3)	[0 ; 0]	<0.001	0.640	<0.001
Ultrasound findings	Double contour (0-28)	3.16	3 (0-9)	[1 ; 4]	2.33	2 (0-8)	[1 ; 3]	1.34	1 (0-7)	[0 ; 2]	<0.001	<0.001	<0.001
	Tophi (0-54)	2.68	2 (0-11)	[1 ; 4]	2.43	2 (0-8)	[1 ; 3]	1.83	1 (0-8)	[1 ; 3]	0.002	<0.001	<0.001
	Aggregates (0-54)	6.14	5 (0-20)	[3; 9]	6.02	6 (0-15)	[4 ; 8]	5.02	5 (0-12)	[2 ; 7]	0.597	0.002	<0.001
	Erosions (0-28)	1.98	2 (0-6)	[1 ; 3]	2.17	2 (0-6)	[1 ; 3]	2.02	2 (0-5)	[1 ; 3]	0.289	0.432	0.967
	Synovial hypertrophy (0-132)	9.30	9 (2-21)	[5 ; 12]	8.41	7 (1-21)	[5 ; 11]	7.80	6 (2-21)	[4 ; 10]	0.063	0.378	0.031
	Synovial Doppler (0-132)	3.44	3 (0-10)	[2 ; 5]	1.89	2 (0-7)	[0 ; 3]	2.24	2 (0-8)	[0 ; 4]	<0.001	0.096	0.003

Figure 1: Development in ultrasound structural lesions in joints/tendons during 6 months' follow up



Comp. I-VI: Compartments I-VI, Tib. post.: Tibialis posterior, Pat. prox.: Proximal patella, Pat. dist.: Distal patella, * P-values < 0.05

Results: 50 patients (48 males, 2 females), mean age of 68.9 years (range 30-88) were included. US showed a statistically significant decrease in DC and tophus sum scores from both 0-3 and 3-6 months (table 1). The aggregate sum score only showed a statistically significant decrease from 3-6 months, whereas the erosion sum score was almost unchanged in the follow-up period. GS and CD synovitis sum scores both showed statistically significant decreases at 6 months' follow up, and for CD also from 0-3 months (table 1).

Structural lesions were most commonly found in metatarsophalangeal 1-4 and knee joints, which were also the locations with the most pronounced changes in scores (figure 1).

Tender and swollen joint counts, PROs and number of joint attacks declined statistically significantly from 0-3 months, except for the HAQ, which only declined numerically. P-urate levels decreased statistically significantly from both 0-3 months and 3-6 months (table 1).

No statistically significant differences in US sum score changes during follow up were observed between groups that did/did not obtain the treatment goal.

Conclusion: Of the four US structural gout lesions, DC and tophus showed sensitivity to change after only 3 months of urate lowering therapy, using a binary score, whereas aggregates only showed a change after 6 months follow-up.

This study indicates that US assessment of the OMERACT structural gout lesions, particularly DC and tophus, seems to be a useful tool for monitoring improvement over time. Future studies should investigate whether more sensitive monitoring may be obtained by using a semiquantitative scoring system.

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Abstract Number: 2756

Subcutaneous Tanezumab versus NSAID for the Treatment of Osteoarthritis: Joint Safety Events in a Randomized, Double-Blind, Active-Controlled, 80-Week, Phase-3 Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical II: Novel Therapies
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Tanezumab, a monoclonal antibody inhibiting nerve growth factor (NGF), is under investigation for the treatment of chronic pain conditions. In prior osteoarthritis (OA) studies, intravenous tanezumab was effective and generally well tolerated, and the risk of increased joint damage required further assessment. This study was conducted to evaluate the efficacy and safety of subcutaneous (SC) tanezumab vs NSAID in patients (pts) with OA; findings on the long-term risk of joint safety events are presented here.

Methods: Eligible pts had OA of the hip or knee based on ACR criteria with x-ray confirmation; baseline (BL) WOMAC Pain and Physical Function scores of ≥5 (11-pt numeric rating scale [0-10]); BL Patient's Global Assessment of OA (PGA-OA) of "fair," "poor," or "very poor"; history of inadequate pain relief with acetaminophen; inadequate pain relief with/intolerance to tramadol or an opioid; or unwillingness to take an opioid. Pts were on a stable dose of oral NSAID before study entry and during screening. Pts were randomized to tanezumab (2.5 mg or 5 mg SC q 8 wk) or NSAID (naproxen 500 mg, celecoxib 100 mg, or diclofenac ER 75 mg orally bid) for 56 wk. Radiographic/magnetic resonance imaging was performed at screening, wk 24 and 56 (treatment period), and wk 80 (safety period). Pts meeting pre-specified criteria for increased severe or persistent joint pain had additional follow-up imaging. All images were evaluated by central reader; joint safety events and total joint replacements (TJR) were adjudicated by blinded committee. Observation time-adjusted rates/1,000 pt-y of adjudicated rapidly progressive OA type 1 or 2 (RPOA1 or 2), primary osteonecrosis, subchondral insufficiency fracture (SIF), and pathologic fracture over 80 wk were analyzed (combined as primary composite joint safety endpoint and individually), as was the TJR rate.

Results: A total of 2,996 pts were randomized, received ≥1 dose of study drug, and were analyzed for joint safety events. During 80 wk of observation, the time-adjusted rate/1,000 pt-y for the primary composite joint safety endpoint was higher with tanezumab 2.5 mg (37.4 [p=0.002]) and tanezumab 5 mg (71.5 [p< 0.001]) than NSAID (14.8) (Table). The majority of joint safety events adjudicated as RPOA were RPOA1 (89 of 107 [83.2%]). Rates of RPOA1 were higher with tanezumab 2.5 mg (28.4 [p=0.005]) and tanezumab 5 mg (49.1 [p< 0.001]) than NSAID (10.9), as were rates of RPOA2 (2.9 [p=0.321] and 13.9 [p=0.001] vs 1.0, respectively). In the tanezumab 2.5 and 5 mg groups, SIF rates were 5.8 (p=0.539) and 6.9 (p=0.364) vs 3.9 in the NSAID group. Primary osteonecrosis occurred in 1 pt in the tanezumab 5-mg group; no pathological fractures were observed. TJR rates were also higher with tanezumab 2.5 mg (51.8 [p=0.003]) and 5 mg (79.7 [p< 0.001]) than NSAID (25.7). Of 159 pts with TJR, 28 (17.6%) had an adjudicated joint safety outcome; in these 28 pts, the event was RPOA1 in 42.9%; RPOA2, 39.3%; primary osteonecrosis, 3.6%; and SIF, 14.3%.

Joint safety outcome	NSAID (n=996)	Tanezumab 2.5 mg (n=1,002)	Tanezumab 5 mg (n=998)
Adjudicated for joint safety*, no. of pts (%)	49 (4.9)	115 (11.5)	171 (17.1)
Adjudicated as normal progression of OA, no. of pts (%)	27 (2.7)	66 (6.6)	79 (7.9)
Primary composite joint safety endpoint, no. of pts (%) [95% CI]	15 (1.5) [0.8, 2.5]	38 (3.8) [2.7, 5.2]	71 (7.1) [5.6, 8.9]
Observation time, pt-y	1,011	1,017	993
Observation time-adjusted rate/1,000 pt-y [95% CI]	14.8 [8.9, 24.6]	37.4 [27.2, 51.3]	71.5 [56.7, 90.2]
Rate difference vs NSAID [95% CI]		22.5 [8.5, 36.6]	56.7 [38.4, 74.9]
p-value		0.002	<0.001
RPOA1 and RPOA2 combined, no. of pts (%) [95% CI]	12 (1.2) [0.6, 2.1]	32 (3.2) [2.2, 4.5]	63 (6.3) [4.9, 8.0]
Observation time, pt-y	1,012	1,018	995
Observation time-adjusted rate/ 1,000 pt-y [95% CI]	11.9 [6.7, 20.9]	31.4 [22.2, 44.4]	63.3 [49.5, 81.1]
Rate difference vs NSAID [95% CI]		19.6 [6.8, 32.4]	51.5 [34.5, 68.5]
p-value		0.003	<0.001
RPOA1†, no. of pts (%) [95% CI]	11 (1.1) [0.6, 2.0]	29 (2.9) [1.9, 4.1]	49 (4.9) [3.7, 6.4]
Observation time, pt-y	1,012	1,020	998
Observation time-adjusted rate/ 1,000 pt-y [95% CI]	10.9 [6.0, 19.6]	28.4 [19.8, 40.9]	49.1 [37.1, 65.0]
Rate difference vs NSAID [95% CI]		17.6 [5.4, 29.8]	38.2 [23.1, 53.4]
p-value		0.005	<0.001
RPOA2‡, no. of pts (%) [95% CI]	1 (0.1) [0, 0.6]	3 (0.3) [0.1, 0.9]	14 (1.4) [0.8, 2.3]
Observation time, pt-y	1,016	1,027	1,010
Observation time-adjusted rate/ 1,000 pt-y [95% CI]	1.0 [0.1, 7.0]	2.9 [0.9, 9.1]	13.9 [8.2, 23.4]
Rate difference vs NSAID [95% CI]		1.9 [-1.9, 5.8]	12.9 [5.4, 20.4]
p-value		0.321	0.001
TJR, no. of pts (%) [95% CI]	26 (2.6) [1.7, 3.8]	53 (5.3) [4.0, 6.9]	80 (8.0) [6.4, 9.9]
Observation time, pt-y	1,013	1,022	1,004
Observation time-adjusted rate/ 1,000 pt-y [95% CI]	25.7 [17.5, 37.7]	51.8 [39.6, 67.9]	79.7 [64.0, 99.2]
Rate difference vs NSAID [95% CI]		26.2 [9.1, 43.3]	54.0 [33.9, 74.0]
p-value		0.003	<0.001

Statistical method: Poisson model for rate difference.
*Adjudicated joint safety events included possible/probable joint safety events identified by a central reader, TJRs, and investigator-reported adverse events of RPOA, SIF, primary osteonecrosis, or pathological fracture. Dossiers including reports from clinical exams/consultations, available study data and imaging, and narrative of clinical events were provided to a blinded committee for review and adjudication. This adjudication committee of external experts provided the final classification of joint safety events and TJR. †Defined as significant loss of joint space width ≥2 mm (predicated on optimal joint positioning) within approx. 1 year, without gross structural failure. ‡Defined as abnormal bone loss or destruction, including limited or total collapse of ≥1 subchondral surface, that is not normally present in conventional end-stage OA.
CI, confidence interval; NSAID, non-steroidal anti-inflammatory drug; OA, osteoarthritis; pts, patients; pt-y, patient-years; RPOA, rapidly progressive osteoarthritis; SIF, subchondral insufficiency fracture; TJR, total joint replacement

Table. Summary of adjudicated joint safety events and TJR with tanezumab compared with NSAID in pts with OA over 80 wk of observation (56-wk treatment and 24-wk safety period).

Conclusion: In this study, adjudicated joint safety endpoints, particularly RPOA1, and TJR were significantly more common with tanezumab than NSAID. Additional research is ongoing to explore potential reasons for this imbalance and dose-response relationships.

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Abstract Number: 2757

Clinical Effectiveness of Ultrasound-guided Intra-articular Corticosteroid and Local Anaesthetic Injections for Hip Osteoarthritis: A Randomised Controlled Trial (HIT)

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SESSION INFORMATION
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Session Time: 2:30PM–4:00PM

Background/Purpose: Evidence of the effectiveness of intra-articular corticosteroid injection for hip osteoarthritis (OA) is limited and conflicting. The HIT trial compared the clinical effectiveness of an ultrasound-guided intra-articular hip injection (USGI) of 40mg triamcinolone acetonide and 4ml 1% lidocaine hydrochloride combined with best current treatment (BCT) with (i) BCT alone (primary objective) and (ii) an USGI of 5ml 1% lidocaine only combined with BCT (EudraCT: 2014–003412-37).

Methods: This was a pragmatic, three-arm, single-blind, randomised controlled trial in adults with painful hip OA recruited from community musculoskeletal services and primary care. Participants were randomised equally to one of three treatment groups: (1) BCT alone, (2) BCT plus USGI of triamcinolone and lidocaine, or (3) BCT plus USGI of lido-

caine only. Outcomes were collected postally at 2 weeks, 2, 4 and 6 months. The primary outcome was self-reported current hip pain intensity (0-10 numeric rating scale (NRS)) over 6 months (repeated measures analysis). Secondary outcomes included pain, stiffness and physical function (Western Ontario and McMaster University Arthritis Index, WOMAC), patient's global impression of change, and pain self-efficacy. 204 participants were required to detect a minimum difference of 1 point in mean pain NRS score between arms (1) and (2) with 80% power (5% two-tailed significance level, 15% loss to follow-up). Analysis was by intention-to-treat.

Results: 199 participants were recruited (43% male, mean age 63 years), 67 to arms (1) and 66 each to arms (2) and (3). Primary outcome completion rates were 95% at 2 weeks, 94% at 2 months, 90% at 4 months, and 89% at 6 months.

Greater mean improvement in hip pain intensity (0-10 NRS) over 6 months was seen with BCT plus USGI of triamcinolone/lidocaine compared with BCT alone: 1: -1.43 (95%CI -0.72, -2.15). Greater mean improvement in pain intensity was seen at 2 weeks (-3.17; -2.28, -4.06) and 2 months (-1.81; -0.92, -2.71), but not at 4 (-0.86; -1.78, 0.05) or 6 months (0.12; -0.80, 1.04). Participants treated with BCT plus USGI of triamcinolone/lidocaine compared with BCT alone had greater mean improvement in function (WOMAC-F -5.47; (-9.41, -1.53)) and pain self-efficacy (5.87; 2.30, 9.45) over 6 months. More participants reported being completely recovered/much better at 2 months with BCT plus USGI triamcinolone/lidocaine than with BCT alone (45.4% v 6.9% RR=6.7; 2.5, 17.9). There was no statistically significant difference over 6 months between BCT plus USGI of triamcinolone/lidocaine compared with BCT plus USGI of lidocaine only for hip pain intensity (-0.52; -1.21, 0.18) or function (-3.60; 7.40, 0.21). There was one treatment-related serious adverse event: a participant with no signs of infection at randomisation died from endocarditis four months after USGI of triamcinolone/lidocaine.

Conclusion: USGI of triamcinolone and lidocaine combined with BCT leads to greater improvements in pain and function over 6 months in adults with hip OA than BCT alone. However, there was no significant difference between the groups receiving USGI of triamcinolone and lidocaine and USGI of lidocaine only raising the possibility of a placebo effect.

Disclosure: Z. Paskins, None; **K. Bromley**, None; **M. Lewis**, None; **G. Hughes**, None; **E. Hughes**, None; **A. Cherrington**, None; **A. Hall**, None; **M. Holden**, None; **R. Oppong**, None; **K. Stevenson**, None; **A. Menon**, None; **P. Roberts**, None; **G. Peat**, None; **C. Jinks**, None; **N. Foster**, None; **C. Mallen**, None; **E. Roddy**, None.

Abstract Number: 2758

Nortriptyline in Knee Arthritis (Nortika): A Randomised Controlled Double Blind Trial of Nortriptyline for Pain in Knee Osteoarthritis

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SESSION INFORMATION
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Session Time: 2:30PM–4:00PM

Background/Purpose: Osteoarthritis (OA) is the most common joint disease and is a major cause of pain and disability There is currently no cure for OA and management is focused on relief of pain and maintenance of function

Tricyclic antidepressants (TCAs) have long been used in other chronic pain conditions, but their analgesic effect in OA has not previously been evaluated. To investigate the analgesic effectiveness of nortriptyline in people with OA of the knee.

Methods: We undertook a two-arm parallel-group 1:1 double blind randomised placebo-controlled trial. Participants were recruited from orthopaedic outpatient clinics, primary care, and by public advertising. 205 adults with knee OA as defined by the American College of Rheumatology clinical criteria for the classification of idiopathic OA of the knee, and with pain rated as ≥20 points on the 50 point Western Ontario and McMaster University (WOMAC) pain sub-scale, were randomised to receive either nortriptyline (n=103) or placebo (n=102) in addition to their usual analgesia for 14 weeks. Treatment was divided into a dose-adjustment phase (weeks 0 to 7) and a steady-dose phase (weeks 8 to 14). Participants were instructed to commence taking one capsule (25mg of nortriptyline or placebo) daily for two weeks at which time they were contacted by a research nurse by telephone who advised participants to increase (or decrease) their dose by one capsule per day according to the participant's level of knee pain and adverse effects. Further dose adjustments occurred at four, six and eight weeks, up to a maximum dose of four capsules daily (100 mg nortriptyline daily in the treatment group). Primary outcome was knee pain at 14 weeks measured using the WOMAC pain sub-scale. Secondary outcomes included function, stiffness, non-steroidal anti-inflammatory (NSAID), opioid and/or paracetamol use, participant global assessment, and adverse effects at 14 weeks.

Results: The baseline adjusted mean WOMAC pain subscale score at week 14 was 6.15 points lower (95% CI -0.26 to 12.6, $p = 0.060$) in the nortriptyline vs. the placebo arm. Differences in secondary outcomes generally favoured the nortriptyline arm, but were small and unlikely to be clinically relevant. For example the number needed to treat to achieve one responder was 10 (95% CI = 4.2 to Inf, $p = 0.14$). Dry mouth (87% vs. 51%, $p < 0.001$), constipation (69% vs. 30%, $p < 0.001$), and sweating (31% vs. 21%, $p = 0.033$) were all more commonly reported by participants taking nortriptyline.

Conclusion: This study suggests nortriptyline provides a clinically insignificant reduction in pain in people with knee OA. Adverse effect profile was as expected.

Trial registration: Australian New Zealand Clinical Trials Registry: ACTRN12614000683639.

Disclosure: B. Hudson, None; **L. Toop**, None; **J. Williman**, None; **G. Hooper**, None; **D. Mangin**, None; **J. Alchin**, None; **B. Thompson**, None; **L. Stamp**, None.

Abstract Number: 2759

Stopping NSAIDs for Arthritis Pain (SNAP): A Randomized Withdrawal Trial Comparing NSAIDs to Cognitive Behavioral Therapy

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SESSION INFORMATION
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Background/Purpose: NSAIDs are associated with uncertain long-term benefits and significant toxicity in patients with knee osteoarthritis (OA). Our objective was to evaluate if discontinuing NSAIDs and engaging in a telephone-based cognitive behavioral therapy (CBT) program is non-inferior to continuing NSAIDs.

Methods: Patients in 4 medical centers, taking NSAIDs for knee OA pain on most days of the week for at least 3 months, were randomized to meloxicam or placebo for 4 weeks (blinded Phase 1). Those on meloxicam continued this medication for 10 weeks while those on placebo participated in a 10-week telephone-based CBT program (unblinded Phase 2). The primary outcome was the WOMAC pain score (LIKERT version) at 4-weeks. The minimum clinically important difference (MCID) is 2.1; the non-inferiority margin was set at 1. Secondary outcomes included time-averaged area under the curve (AUC) pain score at 4-weeks as well as AUC pain, WOMAC pain and disability scores, and global impression of change at end of Phase 2. Data were analyzed using linear regression models adjusted for baseline pain and site. We also estimated the incremental cost effectiveness ratio (ICER) of CBT compared to meloxicam at one year.

Results: 364 participants were randomized: 180 to placebo followed by CBT and 184 to meloxicam. Baseline demographic and clinical characteristics were well-balanced (Table 1). The overall mean pain at baseline was 5.6 (SD= 3.8). At 4 weeks, the raw mean pain score increased to 7.77 (SD= 4.01) in the placebo group and 6.75 (SD= 3.81) in the meloxicam group. After adjusting for baseline pain and site, the mean pain difference between placebo and meloxicam at 4 weeks was 1.35 (95% CI= 0.61 to 2.09, non-inferiority test p-value= 0.82). At week 14, the adjusted mean pain difference between placebo and meloxicam was 1.19 (95% CI= 0.39 to 1.99), non-inferiority p-value= 0.68). Mean pain scores over time (smoothed estimates) are illustrated in the Figure. There was no evidence of a difference in the global impression of change (p= 0.15) or lower extremity disability (p= 0.45) between the two groups at the end of Phase 2. Except for dyspepsia, which was more common in the meloxicam group (7.6% vs 0.6%), there were no significant differences in adverse events across groups. The ICER for CBT compared to continued meloxicam was $22,126.92 per quality-adjusted life year (QALY) gained. One-way sensitivity analyses of all input parameters across their plausible ranges showed that CBT remained cost-effective (ICERs < $100,000/QALY gained) compared to meloxicam.

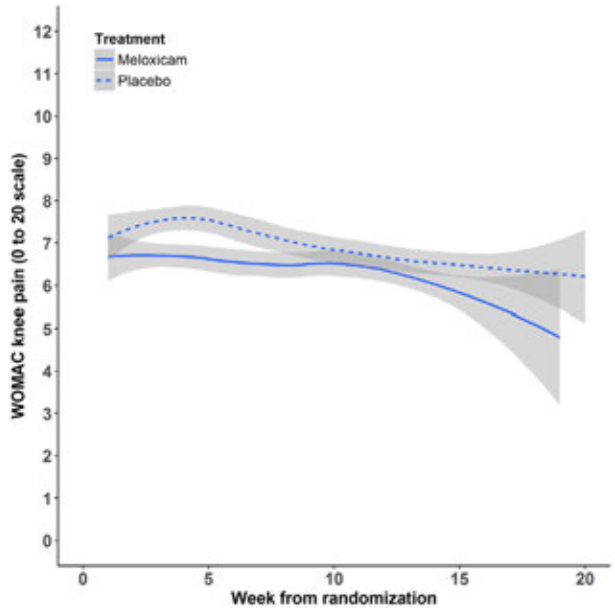
Table 1. Participant Characteristics at Baseline

Characteristic	Placebo (n=180)	Meloxicam (n=184)	Overall (n=364)
Mean age, mean (SD)	58.2 (11.8)	58.5 (10.0)	58.4 (10.9)
Male, n (%)	161 (89.4)	154 (84.2)	315 (86.8)
Non-Hispanic White	120 (66.7)	112 (60.9)	232 (63.7)
4-year college degree or higher, n (%)	65 (36.1)	56 (30.4)	121 (33.2)
Full time employee/student, n (%)	73 (40.6)	73 (39.7)	146 (40.1)
Excellent/very good health status, n (%)	49 (27.2)	62 (33.7)	111 (30.5)
BMI, mean (SD)	33.9 (7.1)	33.4 (7.2)	33.7 (7.2)
Psychiatric comorbidity, n (%)	88 (49.2)	96 (52.2)	184 (50.7)
WOMAC pain (0 to 20), mean (SD)	5.4 (3.8)	5.9 (3.9)	5.6 (3.8)
WOMAC disability (0 to 68), mean (SD)	17.5 (12.1)	17.9 (11.9)	17.7 (12.0)

Table 2. Primary and Secondary Analysis Results

Outcome	Placebo		Meloxicam		Adjusted Difference Placebo vs. Meloxicam	
Primary Analysis	**N**	**LS Mean (SE)**	**N**	**LS Mean (SE)**	**Mean (95% CI)**	**p-value**
WOMAC knee pain at week 4	152	8.08 (0.3)	169	6.73 (0.28)	1.35 (0.61, 2.09)	0.82[1]
Secondary Analyses	**N**	**LS Mean (SE)**	**N**	**LS Mean (SE)**	**Mean (95% CI)**	**p-value**
WOMAC knee pain at week 14 (0 to 20)	140	7.08 (0.32)	146	5.89 (0.32)	1.19 (0.39, 1.99)	0.68[1]
WOMAC knee pain in final week[3] (0 to 20)	176	6.64 (0.27)	179	6.05 (0.27)	0.58 (-0.10, 1.27)	0.12[1]
WOMAC knee pain AUC weeks 1 to 4 (0 to 20)	167	7.73 (0.23)	173	6.65 (0.23)	1.07 (0.49, 1.65)	0.0003[2]
WOMAC knee pain AUC over all weeks (0 to 20)	175	7.48 (0.21)	179	6.43 (0.21)	1.06 (0.53, 1.58)	<0.0001[2]
Global impression of change (1=Much better, 5=Much worse)	160	2.15 (0.08)	176	2.30 (0.08)	-0.15 (-0.36, 0.05)	0.15[2]
WOMAC disability in final week (0 to 68)	160	19.69 (0.93)	176	18.81 (0.88)	0.88 (-1.41, 3.17)	0.45[2]

1. Non-inferiority (1-sided); alpha=.025
2. Difference (2-sided); alpha=.05
3. Last observation carried forward



Conclusion: Among patients with knee OA, we could not conclude that placebo and placebo followed by CBT is non-inferior to meloxicam within a non-inferiority margin of 1. However, the pain score differences between the two groups was small (less than the MCID of 2.1) and there was no difference in participants' global impression of change or function at 14 weeks. Telephone-based CBT is cost effective compared to meloxicam.

Disclosure: L. Fraenkel, None; **E. Buta**, None; **J. Goulet**, None; **M. Brennan**, None; **A. Heapy**, None; **L. Suter**, None.

Abstract Number: 2760

A Phase 2 Double-Blind Clinical Trial to Examine the Comparative Effects on Osteoarthritic Knee Pain of CGS-200-1 (1% Capsaicin Topical Liquid), CGS-200-5 (5% Capsaicin Topical Liquid), and CGS-200-0 (Vehicle, No Capsaicin)

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Table 1

Summary of WOMAC OA Pain Score Change from Baseline through Day 94 - mITT Set

Day	LSM Difference	Between Group Difference	95% CI[a]	p-value[a]
35	CGS-200-1 – CGS-200-0	-32.6	(-84.2, 19.0)	0.2137
64		-5.0	(-53.4, 43.3)	0.8366
94		-33.1	(-85.9, 19.7)	0.2171
35	CGS-200-5 – CGS-200-0	-61.0	(-112.3, -9.8)	0.0200
64		-94.7	(-142.4, -47.1)	0.0001
94		-67.0	(-120.0, -15.8)	0.0111

Abbreviations: LSM, Least-squares means; SD, standard deviation.

Notes: Only the assessment from "study knee" was included in the analysis.
Treatment success represents a reduction of at least 50% in WOMAC OA pain score from baseline. Subjects with missing data were considered a treatment failure for that visit.

Table 2

Summary of WOMAC OA Pain Score Change from Baseline through Day 94 Using AUC- mITT Set

Pain Score		CGS-200-0	CGS-200-1	CGS-200-5
Day 35 Mean SD		 -2385.1 2557.78	 -4060.4 3253.83	 -5289.0 3308.18
Day 64 Mean SD		 -4914.1 5270.18	 -7065.8 5835.81	 -10067.1 6094.49
Day 94 Mean SD		 -7246.8 7861.64	 -9770.9 8426.98	 -14677.7 9108.35q
LSM Difference	**Day**	**Between Group Difference**	**95% CI[a]**	**p-value[a]**
CGS-200-1 – CGS-200-0	35	-1675.3	(-3048.5, -302.1)	0.0172
	64	-2151.7	(-4745.4, 443.0)	0.1032
	94	-2524.1	(-6381.0, 1332.8)	0.1974
CGS-200-5 – CGS-200-0	35	-2903.8	(-4268.4, -1539.2)	< 0.0001
	64	-5153.0	(-7714.6, -2591.4)	0.0001
	94	-7430.9	(-11236.7, -3625.2)	0.0002

Abbreviations: LSM, Least-squares means; SD, standard deviation.

Notes: Only the assessment from "study knee" was included in the analysis.
Treatment success represents a reduction of at least 50% in WOMAC OA pain score from baseline. Subjects with missing data were considered a treatment failure for that visit.
[a]ANCOVA model for comparison of change from baseline with treatment as a fixed effect and baseline value as a covariate

SESSION INFORMATION

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Table 3

Summary of Durability of Clinical Response - mITT Set

Clinical Response Status	CGS-200-0 (N = 40)	CGS-200-1 (N = 40)	CGS-200-5 (N = 41)	Trend Test p-value[a]
Day 5				
Responder	7 (17.5%)	11 (27.5%)	19(46.3%)	
Non-responder	33 (82.5%)	29 (72.5%)	22(53.7%)	
Day 19				
Responder	7 (17.5%)	14 (35.0%)	21(51.2%)	
Non-responder	33 (82.5%)	26 (65.0%)	20(48.8%)	
Day 35				
Responder	11 (27.5%)	15 (37.5%)	19 (46.3%)	
Non-responder	29 (72.5%)	25 (62.5%)	22 (53.7%)	
Day 64				
Responder	9 (22.5%)	5 (12.5%)	23 (56.1%)	
Non-responder	31 (77.5%)	35 (87.5%)	18 (43.9%)	
Day 94				
Responder	10 (25.0%)	10 (25.0%)	18(43.9%)	
Non-responder	30 (75.0%)	30 (75.0%)	23(56.1%)	
Durable Clinical Response up to Day 35	6 (15.0%)	9 (22.5%)	15(36.6%)	0.0288
Durable Clinical Response up to Day 64	6 (15.0%)	4 (10.0%)	14(34.1%)	0.0365
Durable Clinical Response up to Day 94	5 (12.5%)	4 (10.0%)	12(29.3%)	0.0566
Comparison	**Day**	**Difference in Proportions (%)**	**95% CI[b]**	**p-value**
CGS-200-1 – CGS-200-0	35	7.5	(-15.5, 29.9)	0.5679
	64	-5.0	(-27.6, 18.0)	0.7370
	94	-2.5	(-25.2, 20.4)	1.0000
CGS-200-5 – CGS-200-0	35	21.6	(0.5, 42.4)	0.0415
	64	19.1	(-2.0, 40.1)	0.0703
	94	16.8	(-4.5, 37.8)	0.1004
CGS-200-5 – CGS-200-1	35	14.1	(-7.0, 35.6)	0.2246
	64	24.1	(3.0, 44.7)	0.0148
	94	19.3	(-2.0, 40.1)	0.0488

Notes: Only the assessment from "study knee" was included in the analysis.
Responder represents a reduction of at least 50% in WOMAC OA pain score from baseline. Subjects with missing data were considered a non-responder for that visit.
Percentages are based on the total number of mITT subjects in each treatment group (N).
Durable clinical response analysis is performed based on Section 6.3 in the SAP.

[a] Trend Test p-value was calculated using the Cochran-Armitage trend test.

[b] The 95% Confidence Interval (CI) of the difference in proportions and p-value are calculated using exact method.

Background/Purpose: There is considerable unmet medical need for an osteoarthritic knee pain (OAKP) treatment that does not require regular daily use, does not carry gastrointestinal risk (e.g., NSAIDs), liver risk (e.g., acetaminophen) or addiction risk (e.g., opiates), and can safely provide long-lasting pain relief after a brief course of treatment. The Sponsor has clinically shown that topical OTC-strength 0.25% (w/w) capsaicin is well tolerated and provides OAKP relief. The Sponsor has now produced in the same vehicle (CGS-200) high potency, 5% (w/w) capsaicin (CGS-200-5) and 1% (w/w) capsaicin (CGS-200-1) topical products to evaluate as treatments for the relief of OAKP using the WOMAC subscales for pain, stiffness and function as well as total WOMAC score.

Methods: This was a multi-center, randomized (1:1:1), double-blind, parallel group, vehicle-controlled trial comparing topical CGS-200-1 or CGS-200-5 versus CGS-200-0 in 122 randomized subjects who had OA of at least one knee according to 1986 ACR criteria and a WOMAC pain score of ≥ 250. Subjects continued ongoing non-prohibited analgesic medication(s) (e.g., oral NSAIDs) at study entry with the expectation that the daily dose was to be maintained throughout the study if possible. Treatment was applied for 1 hour to both knees on 4 consecutive days (Study Days 1-4) by the subject under clinic supervision and then washed off. Clinical efficacy and safety assessments were made on Study Days 5, 19, 35 (the primary endpoint was Day 35 change in WOMAC pain score from baseline), 64, and 94. The modified intent to treat (mITT) subset of subjects was used for all efficacy analyses.

Results: CGS-200-5, but not CGS-200-1, met the primary Day 35 OAKP WOMAC pain efficacy endpoint compared to vehicle ($p = 0.020$, mITT population) and post-hoc analysis showed statistical separation from CGS-200-0 (Vehicle) on Days 64 ($p = 0.0001$) and 94 ($p = 0.0111$) **(Table 1)**. Post-hoc analysis showed a statistical difference in WOMAC OA total scores between both treatment groups and Vehicle at Days 35, 64 and 94 **(Table 2)**. The proportion of subjects with a durable clinical response (WOMAC pain reductions ≥ 50% on all study day visits minus one) was higher in the CGS-200-5 group at all visits **(Table 3)**. A slightly larger percentage of CGS-200-5 patients reported ≥ 1 TEAEs (all were mild or moderate in severity) compared to the CGS-200-0 or CGS-200-1 arms, with little difference between groups in the types of TEAEs. Application site pain (mostly mild to moderate) was observed in all treatment groups, with a higher proportion of subjects in the CGS-200-5 group experiencing pain than the CGS-200-5 group. The mean tolerability AUCs in both active treatment groups decreased with each consecutive dosing day.

Conclusion: CGS-200-5 was well-tolerated and efficacious following application to both knees for 60 minutes on 4 consecutive days. Due to the significant efficacy and good safety and tolerability observed in this study, further clinical development of CGS-200-5 is warranted.

Disclosure: M. Billard, Vizuri Health Sciences, LLC, 3, 4; **J. Todhunter**, Vizuri Health Sciences, LLC, 3, 4; **M. Fleming**, Vizuri Health Sciences, LLC, 3, 4; **T. Warneke**, Vizuri Health Sciences, LLC, 3, 4; **Y. Qiu**, None; **N. Ly**, None; **W. Aronstein**, None; **W. Moore**, Vizuri Health Sciences, LLC, 1, 3, 4, 6.

Abstract Number: 2761

Cartilage Thickness Modification with Sprifermin in Knee Osteoarthritis Patients Translates into Symptomatic Improvement over Placebo in Patients at Risk of Further Structural and Symptomatic Progression: Post-Hoc Analysis of a Phase II Trial

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	Sprifermin 100 µg q6mo (N=33) vs PBO (N=34)		
	Observed mean difference [95% CI]	**Adjusted mean difference [95% CI]**	**Trend test* (nominal p value)**
Y1	-5.81 [-15.96, 4.35]	-3.65 [-15.73, 8.43]	>0.05
Y2	-10.45 [-22.76, 1.85]	-5.82 [-18.87, 7.23]	>0.05
Y3	-14.51 [-26.16, -2.85]	-8.75 [-22.42, 4.92]	**<0.05**

*Across 4 sprifermin groups and PBO using the adjusted values

Table 1. Observed and adjusted mean difference [95% CI] in WOMAC pain scores for sprifermin vs PBO in the "at risk" subgroup

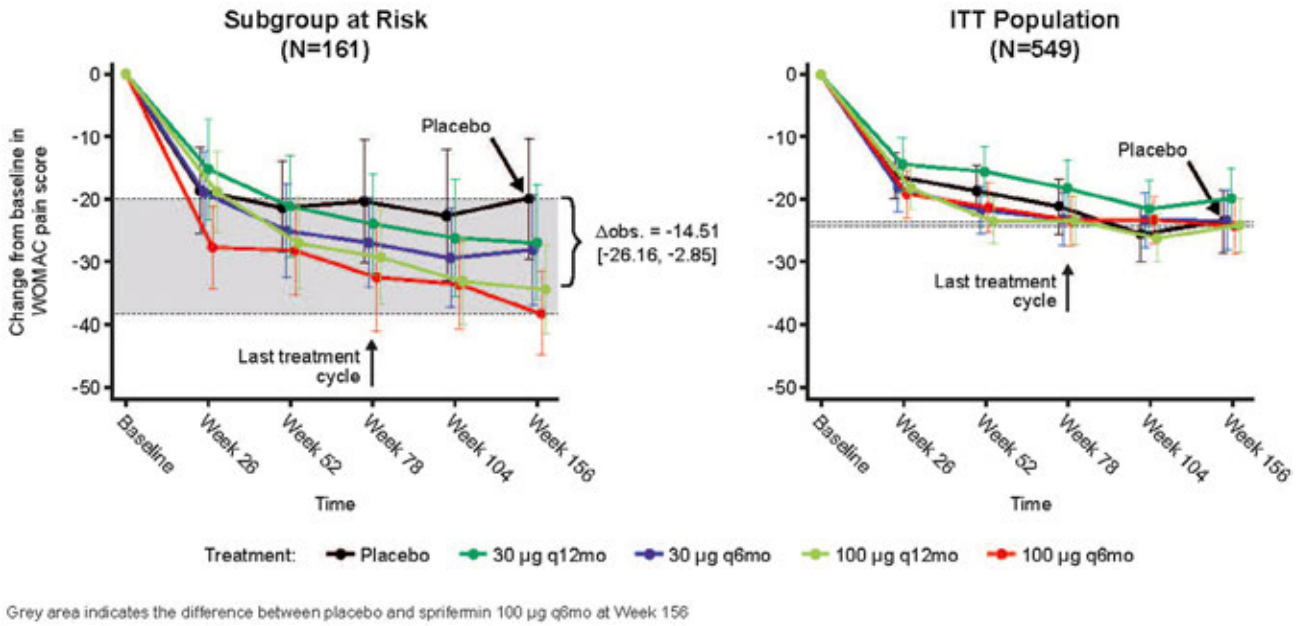

Figure 1. Mean change [95% CI] in WOMAC pain scores in the 'at risk' subgroup and the overall ITT population over 3 years

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Osteoarthritis – Clinical II: Novel Therapies
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Results from the 5-year Phase II FORWARD study showed significant dose-dependent modification of total femorotibial joint (TFTJ) cartilage thickness change with sprifermin at 2 and 3 years, by quantitative MRI. Total WOMAC scores improved by ~50% in all treatment groups, including placebo (PBO). Selection of a patient (pt) subgroup with higher pain scores and lower joint space width (JSW) at baseline (BL), to identify pts who are at higher risk of further structural and symptomatic progression, may facilitate better WOMAC discrimination.

We undertook a post-hoc analysis to evaluate cartilage thickness changes and symptomatic outcomes in an 'at risk' subgroup (BL medial or lateral minimum [m]JSW 1.5–3.5 mm and BL WOMAC pain score of 40–90 on a scale of 0-100).

Methods: Pts in FORWARD were randomized 1:1:1:1:1 to: sprifermin 100 µg every 6 months (q6mo); 100 µg q12mo; 30 µg q6mo; 30 µg q12mo; and PBO. The treatment period was 2 years, with an extended follow up of 3 years. Post-hoc analysis was conducted in the 'at risk' subgroup.

Changes over time are presented using descriptive statistics and CIs. Treatment benefits were estimated using a repeated measures model, controlling for BL, treatment, time, pooled country and treatment by time interaction. Linear dose-effect trend tests were performed exploratively at each timepoint. Confidence intervals (CIs) for treatment benefit were adjusted for multiplicity of treatments using Dunnett adjustment.

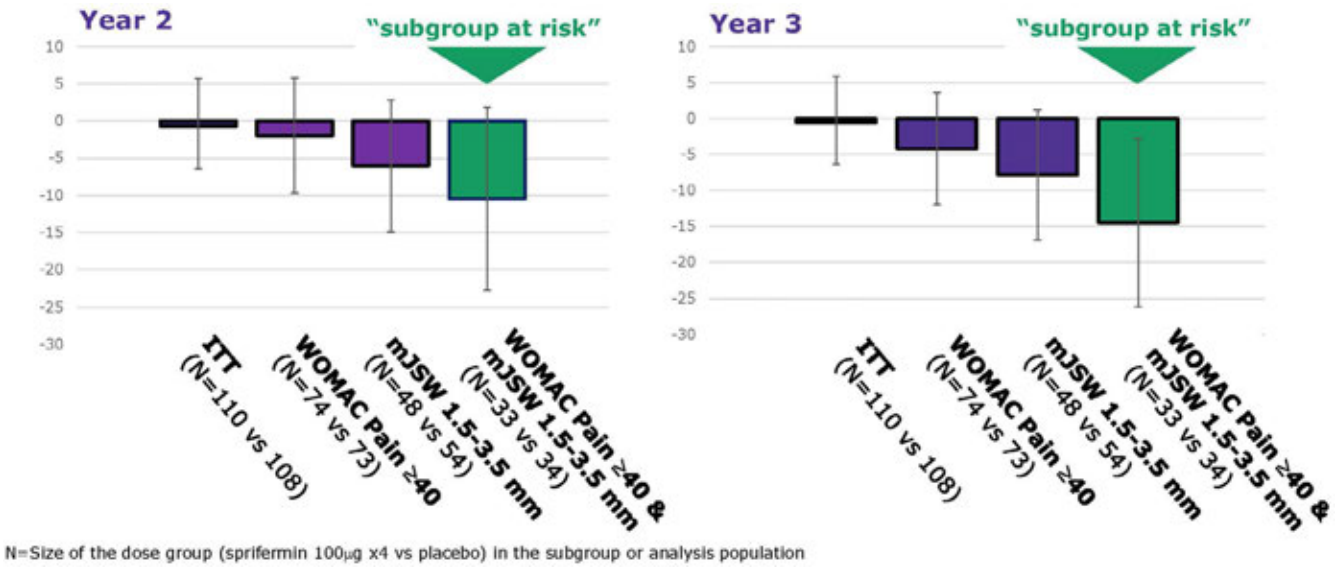

Figure 2. Observed mean differences [95% CI] in WOMAC pain scores for sprifermin 100 µg q6mo vs PBO across different risk subgroups at 2 and 3 years

Results: 161/549 (29%) pts met criteria for the 'at risk' subgroup. In this subgroup, BL characteristics were quite balanced between treatment arms. Pts in the PBO arm had more cartilage loss at 2 and 3 years vs the modified intent-to-treat (mITT) PBO arm (mean change from BL in mm [SD]: Year 2 -0.05 [0.10] vs -0.02 [0.07]; Year 3 -0.07 [0.09] vs -0.05 [0.07]), but TFTJ net cartilage modification with sprifermin 100 µg q6mo vs PBO was similar (adjusted mean difference from PBO [95% CI] in the 'at risk' subgroup vs the mITT group: Year 2 0.06 [0.01, 0.11] vs 0.05 [0.02, 0.08]; Year 3 0.05 [-0.01, 0.12] vs 0.05 [0.02, 0.09]). At Year 3 (18 mos after last injection), the mean difference [95% CI] in WOMAC pain score for sprifermin 100 µg q6mo vs PBO in the 'at risk' subgroup was -8.75 [-22.42, 4.92] vs 0.97 [-6.22, 8.16] for the intent-to-treat (ITT) population (Fig 1). The exploratory dose-effect trend test using the adjusted values had a nominal p-value of < 0.05 (Table 1). Having both medial or lateral mJSW 1.5–3.5 mm AND pain score ≥40 at BL led to greater differentiation in WOMAC pain scores for sprifermin 100 µg q6mo vs PBO than having either BL characteristic alone (Fig 2).

Conclusion: Despite substantial structural and symptomatic progression in the 'at risk' subgroup, structural improvement with sprifermin was maintained, and WOMAC score improvements vs PBO increased over time and were significant at Year 3. This supports further investigation of sprifermin as a potential disease-modifying osteoarthritis drug in a targeted population where structural improvement may translate into symptomatic benefit vs PBO within a reasonable timeframe.

Disclosure: H. Guehring, Merck KGaA, Darmstadt, Germany, 3; **J. Kraines**, EMD Serono Research and Development Institute, Inc., 3, EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), 3; **F. Moreau**, EMD Serono Research and Development Institute, Inc., 3, EMD Serono Research and Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), 3; **B. Daelken**, Merck KGaA, Darmstadt, Germany, 3; **C. Ladel**, Merck KGaA, Darmstadt, Germany, 3; **W. Wirth**, Chrondrometrics GmbH, 1, 3; **P. Conaghan**, Abbvie, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, 8, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Eli Lilly, 8, EMD, 5, EMD Serono, 5, EMD Serono Research and Development Institute, Inc., 5, 8, Flexion, 5, 8, Flexion Therapeutics, 5, 8, Galapagos, 5, 8, Glaxo Smith Kline, 5, GlaxoSmithKline, 5, 8, Lilly, 8, Medivir, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Samumed, 5, 8, Serono, 5, Stryker, 5, 8; **F. Eckstein**, Chrondrometrics GmbH, 1, 3, Merck KGaA, Darmstadt, Germany, 5, Samumed LLC, 5, Galapagos, 5, Abbvie, 5, Bioclinica, 5, Kolon TissueGene, 5, Novartis, 5, Servier, 5, Roche, 5; **M. Hochberg**, Bioiberica SA, 5, Bone Therapeutics, 5, BriOri Biotech, 4, Bristol Myers Squibb, 5, Eli Lilly, 5, Elsevier, 7, EMD Serono, 5, EMD Serono Research and Development Institute, Inc., 5, Galapagos, 5, Galapagos, IQVIA and Hoffman LaRoche, 9, IBSA Biotechniq SA, 5, Novartis Pharma AG, 5, Pfizer, 5, Pfizer Inc, 5, Plexxikon, 5, Regenosine, Samumed LLC, Symic Bio Inc., Theralogix LLC, TissueGene Inc., TLC Biopharmaceuticals, Inc., and Zynerba, 5, Rheumcon, Inc, 3, Samumed LLC, 5, Theralogix LLC, 4, 5, TissueGene Inc, 5, UpToDateTM, 7.

Abstract Number: 2762

The Preparation and Recovery Experience from Total Knee Replacement of Patients with Osteoarthritis: A Qualitative Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes II: Patient Preferences, Beliefs, & Experiences

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Up to 30% of patients may have persistent pain post-total knee arthroplasty (TKA). One possible approach to improve these outcomes is to optimize muscle strength, physical condition, and mental preparation before surgery. Our purpose was to elicit patients' experiences with TKA with the goal of understanding the utility and logistics of implementing a *pre*-habilitation program delivered by peer coaches (i.e. a patient who has already undergone a TKA and has been trained to provide personalized pre-TKA support).

Methods: Qualitative study guided by Social Cognitive Theory (SCT). SCT posits that direct personal agency (*self-efficacy*), proxy agency *(peer or social support); sociocultural factors*, and *outcome expectations* influence *goals* and *outcomes.* Patients were > 65 years old from Hospital for Special Surgery and have had primary TKA with good clinical outcome, defined as a Knee Injury and Osteoarthritis Outcome Score (KOOS) score >65 one year post-operatively. We asked patients about their challenges before and after TKA, potential barriers to accessing a pre-habilitation program and perspectives on what it might be like working with a peer coach to encourage regular exercise prior TKA. We analyzed the data thematically using *a priori* coding that corresponded to SCT constructs.

Results: We conducted four focus groups and two individual interviews (N = 31). Mean age was 75 years (6.85 SD); age range 65-89 years of age. Forty-eight percent had previously had a primary TKA on their contralateral knee. Overall, 61% (N = 19) were women and 90% (N= 28) were white. Table 1 shows the major themes that emerged, grouped by SCT constructs supported patient quotes. Patients with high outcome expectations who were undergoing their contralateral primary TKA learned from their first experience and reported feeling motivated to engage in physical activity before their contralateral TKA (*Theme 1*). Patients expressed that they did not know what type of exercises were good for them once they decided to have a TKA (*Theme 2*). Patients, for whom this was their first TKA, stated that connecting with another patient who already had a TKA was important in their decision making to choose TKA, also in how to prepare for TKA (*Theme 3*). These participants articulated they had gained knowledge from the experience of having a previous primary TKA, and were able to identify factors they felt were important to have a good outcome after TKA (*Theme 4*). They expressed that working with a peer coach would be beneficial for both preparation and recovery from TKA (*Theme 5*).

Conclusion: Preparation and expectations for TKA were influenced by patients' own prior experience with TKA and the experience of other patients who already had TKA. Patients expressed that their own experiences with TKA made them more informed, self-efficacious, and physically active to prepare for their contralateral primary TKA. These data suggest that a formal peer-to-peer intervention that prepares patients for their first TKA by interacting with an experienced post-TKA patient about the mental and physical preparation to undergo TKA was of interest to patients and could help improve TKA outcomes.

Table 1: Themes that Emerged from Focus Groups and Interviews with Patients who had Primary Total Knee Arthroplasty (TKA) with the Corresponding Social Cognitive Theory Construct and Patients' Quotes

Themes	Social Cognitive Theory Construct	Patients' Quotes
1) Expectations from TKA on the basis of previous experience with TKA	Outcome expectation	*Because the second [knee] was much easier than the first, and I think that is because I had gone through it once, and I kind of knew what to expect.* *When I was going to physical therapy after the first surgery, I definitely used to say to the PT, "I want to deal with my other leg too." I wanted to be strong when I have this [going into the surgery for the other knee]. So I learned from surgery one. What I wanted to do for surgery two.* *When I came to the second knee, I knew all about it. I had been doing the exercise before there was pain [in the other knee].*
2) Limited knowledge on how to prepare for TKA	Socio-cultural Factors (Limited resources or knowledge about exercises)	*My surgeon did not say anything about any exercise pre-surgery...* *I was swimming of all things. The thing I wish I would had done before the knee replacement was more strength training. I mean, I was foolish not to do a lot more lower body strength training.* *I think that if I got the doctor's orders to exercise before (TKA), that I would do it.*
3) Advice from other patients about preparation and recovery from TKA.	Peer/Social support Self-efficacy	*I know somebody who had knee surgery, and he told me he had it done and it was pretty good. So I said, "Okay, I'll try it." Just the fact that this person had it done and was okay, that was good enough for me.* *I talked to somebody who had knee surgery and they said, "I made a mistake." he said, "I want to tell you about it so you don't do it. When you were told about the exercises to do in recovery", he said, "follow those absolutely to the letter. If you do, you will be okay. I had to go back in and have my surgery redone."*
4) Advice to other patients about preparation and recovery from TKA.	Self-efficacy Outcome expectation	*Prepare yourself mentally, physically for that event (TKA).* *When I do get a word in edgewise of people who are going to be doing knee replacement surgery, my biggest thing is just do strength exercises. You do not need cardio; you need strength exercises.* *Get yourself; get your legs as strong as you can before you do it (TKA) because it's not going to be fun afterwards.* *As far as afterwards, I think you really have to follow the physical therapy. If you go to physical therapy two, three times a week, you still have to, on your own, on the other days, keep doing the exercises.*
5) Perceptions of working with a peer coach	Peer support	*I would think that a peer coach would have more time to spend (with you) than a doctor.* *I think it's an excellent idea (having a peer coach) because it's one thing if you have a lot of friends and you're sitting across the bridge table, let's say I'm going to have surgery. It's an imposition to ask friends to help you out with this. That I think somebody who has had some kind of training and it's more or less of a professional relationship, I think it's a much better idea.*

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Abstract Number: 2763

What Disease Do You Have? – Assessment and Predictors of Accurate Illness Naming in Rheumatology

Jacob Meindertsma,[1] Kara Harrison,[1] Nicholas Lucchesi,[1] and Adam Carlson[1], [1]University of Virginia, Charlottesville, VA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Patient Outcomes, Preferences, & Attitudes II: Patient Preferences, Beliefs, & Experiences
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Shared decision making remains central to the effective treatment of many rheumatologic conditions and is most appropriate when the patient and physician agree on which disease is being treated. Several studies in the oncology literature have shown that patients frequently do not understand their cancer diagnosis, including what stage of cancer or whether their cancer is in remission. Few studies to date have investigated whether patients with rheumatic disease have an accurate understanding of the diagnoses for which they are receiving treatment. In this study, we sought to assess the concordance between physician and patient reported diagnoses and factors associated with this concordance.

Methods: Over a four-week period in 2019, established patients presenting for a follow up visit in the University of Virginia Rheumatology Clinic were asked to complete a brief questionnaire. This questionnaire included self-reported diagnoses, an assessment of current disease activity, and demographic information. Patient reported diagnoses were compared with the diagnoses recorded by their rheumatologist in the electronic medical record. Allowing for misspellings and multiple answers, patients were considered concordant as long as one diagnosis was correctly identified. Eight patient characteristics including demographic and disease-specific variables were then compared between the concordant and discordant groups using chi-squared testing or Fisher's exact test as appropriate.

Results: A total of 170 patients completed the questionnaire. Forty-two of 170 patients wrote responses that did not match their rheumatologist's documented diagnosis (75.3% concordant, 24.7% discordant). Statistically significant predictors of discordance were non-white race ($p = 0.02$), non-English first language ($p = 0.008$), an annual household income below $50,000 ($p = 0.007$), and fewer years of completed education ($p < 0.001$). Predictors that did not associate with concordance were age, sex, disease length, and the type of disease (e.g. connective tissue disease, arthritis, vasculitis, etc.). Binary logistic regression modeling indicated that postgraduate education was the best predictor of concordance with an adjusted odds ratio of 3.4 ($p = 0.002$). Interestingly, patients who incorrectly named their diagnosis had a significantly higher score on a self-reported 100mm visual analog scale of global disease activity with an average of 34mm in the concordant group vs. 56mm in the discordant group ($p < 0.001$).

Conclusion: One quarter of surveyed patients inaccurately named their documented rheumatologic diagnosis. Poor agreement between patient and physician reported diagnoses spanned all types of rheumatic disease and was best predicted by lower levels of education. Poor agreement on diagnoses was also associated with higher patient reported global disease activity. This study reinforces the importance of addressing poor disease understanding in order to improve shared decision making between patients and their rheumatologists.

Disclosure: J. Meindertsma, None; **K. Harrison**, None; **N. Lucchesi**, None; **A. Carlson**, None.

Abstract Number: 2764

Medication Necessity and Concerns Beliefs Are Distinct, Interactive Predictors of Treatment Adherence in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes II: Patient Preferences, Beliefs, & Experiences

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Medication adherence is instrumental for the successful management of rheumatoid arthritis (RA) to a goal of remission. Awareness of medication necessity and concerns regarding its use influence adherence and respectively foster or undermine the achievement of treatment goals. We here explored the unique and interactive roles of patient beliefs about the necessity of RA medications and concerns about them in predicting adherence to prescribed treatments.

Methods: We evaluated 316 patients with established RA from a single center. Beliefs about the necessity of RA medications and concerns regarding their use were evaluated with the Beliefs about Medicines Questionnaire-Specific (BMQ) Necessity and Concerns scales (range 5-25). Self-reported rheumatoid arthritis treatment adherence was assessed using the Simplified Medication Adherence Questionnaire (SMAQ, range 0-6). Multivariable linear regression evaluated the effects of necessity, concerns and their interactions with adherence. A latent profile analysis (LPA) subsequently classified patients in groups according to patterns of necessity and concerns; adherence scores were then compared across latent groups using analysis of covariance (ANCOVA).

Results: Full adherence (SMAQ score 6/6) was reported by 101 (32%) patients. Necessity and concerns had independent and opposing contributions to adherence (β=0.21 and β=-0.28 respectively, both $p< 0.001$, figure 1a) even after adjustments for age, gender and disease duration. An interaction between necessity and concerns with adherence was also observed (p=0.009); post-hoc simple-slope tests indicated that necessity predicted adherence in the context of

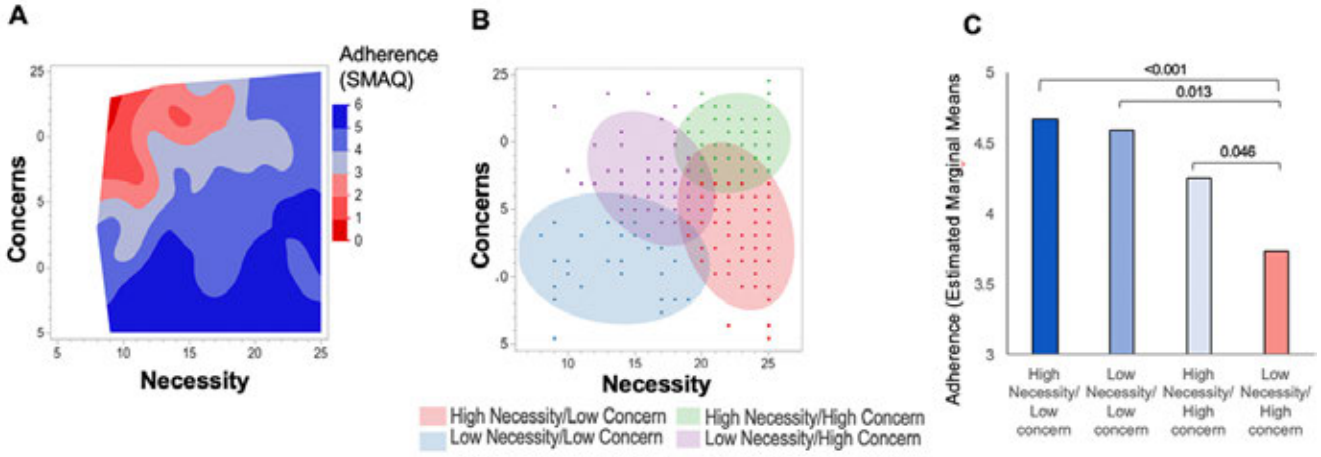

Figure 1: Effect of interaction between Necessity and Concerns on RA medication adherence.

increasing concerns. The Johnson-Neyman technique revealed that while concerns were significantly associated with adherence across the entire range of necessity scores,necessity was significantly related to adherence only at high BMQ Concerns scores (³13).LPA revealed four latent patient groups (figure 1b): Low necessity/ Low concerns (indifferent, n=33), Low necessity/ High concerns (skeptical, n=70), High necessity/ High concerns (ambivalent, n=92) and High necessity/ Low concerns (accepting, n=121). Adherence varied across groups even after adjusting for between-group differences (p=0.002, Figure 1c); adherence was highest in the accepting group and lowest in the skeptical group.

Conclusion: The relationship between necessity and concern beliefs regarding RA medications significantly influences adherence behavior and may further direct physicians to effectively tailor their education efforts in diverse patient groups. A message aimed at reducing concerns might be more effective in the ambivalent group, whereas emphasizing medication necessity may be more fruitful in the skeptical group.

Disclosure: G. Karpouzas, Bristol Meyer Squibb, 8, bristol Meyer Squibb, 8, Bristol-Meyer-Squibb, 8, Pfizer, 2, 9, pfizer, 2, Sanofi, 5, 8; **E. Hernandez**, None; **L. Ruiz**, None; **V. Strand**, Abbvie, 5, AbbVie, 5, Amgen, 5, Amgen, Abbvie, Bayer, BMS, Boehringer Ingelheim, Celltrion, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, UCB, 5, AstraZeneca, 5, AURA, 8, Bayer, 5, BMS, 5, Boehringer Ingelheim, 5, Celgene, 5, Celltrion, 5, Cleveland Clinic, 8, CORRONA, 5, Crescendo, 5, Crescendo Bioscience, 5, Eli Lilly, 5, EMD Serono, 5, Genentech, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Inmedix, 5, Janssen, 5, Kezar, 5, Lilly, 5, Merck, 5, NACCME, 8, Novartis, 5, Pfizer, 5, Purdue, 8, RA Forum, 8, RAN, 8, Regeneron, 5, Roche, 5, Samsung, 5, Sandoz, 5, Sanofi, 5, Servier, 5, Setpoint, 5, SLRA, 8, UCB, 5, Up to Date, 7, Washington University, 8, WIR, 8, WRA, 8; **S. Ormseth**, None.

Abstract Number: 2765

Assessing the Impact of Digital Health Coaching on Quality Adjusted Life Years, Symptom Severity and Disease Activity in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Rheumatoid arthritis (RA) is the most common autoimmune inflammatory arthritis in adults. RA has a significant negative impact on the ability to perform daily activities, including work and household tasks as well as health-related quality of life. Improving patients' quality of life by reducing symptoms and reducing functional limitations are some of the goals of RA treatment. This prospective study (n=314) examines the impact of a digital health coaching intervention on an RA population measured by quality-adjusted life years (QALY) as well as symptom severity and disease activity. One QALY equates to one year spent in perfect health and the PROs measure individual aspects of overall RA health.

Methods: RA patients (n=314) were recruited from sources such as the ACR RISE registry, clinical referral, consented, and enrolled in a 12-week digital health coaching behavior modification program with data collection at baseline and upon completion in the program. Information about mental and physical health was collected through Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health-10. Using a formula developed by Revicki et al.1 and patient responses to the PROMIS Global-10 assessment, a calculation on the number of added

QALYs was made for patients receiving the intervention. In addition to PROMIS, the CASE Adherence Index was used to measure medication adherence and patients reported the number of flares they experienced the previous month before and after the intervention.

Results: Results indicate significant improvements in average PROMIS Mental Health score (pre = 42.2 vs post = 48.3, p< 0.001) and PROMIS Physical Health Score (pre = 37.4 vs post = 41.5, p< 0.001) for RA patients with a result of 1.8 QALY. In addition, the average number of flares dropped by 50% (pre = 6.6 vs post = 3.3) and medication adherence improved by 11% (pre = 69% vs post = 80%).

Conclusion: The results of the study indicate that digital health coaching improves healthy behaviors, overall quality of life and decrease RA symptoms. Future studies should examine the impact of coaching in various segments of RA patients such as underserved, those with multiple comorbidities and those newly diagnosed versus patients living with RA for multiple years.

Disclosure: M. Allsion, None; **M. McMorris**, None; **D. Patel**, None; **B. Burton**, None.

Abstract Number: 2766

Patient Preferences for Attributes of Treatments for Chronic Pain Associated with Osteoarthritis Pain and Chronic Low Back Pain That Differentiate Nerve-Growth Factor Inhibitors, Nonsteroidal Anti-inflammatory Drugs, and Opioids in the United States: A Discrete-Choice Experiment

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Type: ACR Abstract Session
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Background/Purpose: Monoclonal antibodies that inhibit nerve growth factor (NGF-abs) may offer an alternative to current nonsteroidal anti-inflammatory drug (NSAID) and opioid treatments for osteoarthritis (OA) pain and chronic low back pain (CLBP). NGF-abs differ from these treatments in several ways, including mode of administration, duration of effect, efficacy, and safety. NGF-abs also avoid some adverse effects (AEs) associated with opioids and NSAIDs—risk of physical dependence and cardiovascular risks, respectively. However, they may be associated with the risk of rapidly progressive OA (RPOA) and other AEs not seen with opioids or NSAIDs. Our objective was to quantify patients' preferences for attributes of treatments for chronic moderate-to-severe musculoskeletal pain associated with OA and CLBP that both differentiate NGF inhibitors, NSAIDs, and opioids and are relevant to patients.

Methods: We used a discrete-choice experiment (DCE) to elicit preferences for attributes of OA and CLBP pharmaceutical treatments. The survey was completed by 602 United States residents with a self-reported physician diagnosis of hip or knee OA only, CLBP only, or comorbid OA and CLBP (OA/CLBP) diagnosed at least 3 months ago. Respondents had self-assessed moderate-to-severe pain in the hip, knee, and/or lower back, defined as a

rating of 5 or greater on average in the past week on an 11-point numeric rating scale ranging from 0 (no pain) to 10 (worst possible pain). Respondents had to have taken or tried (a) 3 or more classes of pain treatment in the past 2 years, or (b) 2 prior classes of treatment if NSAIDs were contraindicated or if the patient refused to take opioids, or (c) 1 prior class of treatment if both NSAIDs were contraindicated and opioids were refused. In the DCE, respondents chose between two hypothetical treatments in a series of questions. Each hypothetical treatment was defined by six attributes: pain and symptom control, risk of RPOA, risk of heart attack, risk of physical dependence, mode and

Table 1. Attributes and Levels Included in the Discrete-Choice Experiment

Attribute	Attribute Label	Attribute Levels	
Pain and symptom control (patient global assessment)	**Symptom control:** Symptom control while you are taking the medicine	Very good (no symptoms; no limitations on normal activities)	
		Good (mild symptoms; no limitations no normal activities)	
		Fair (moderate symptoms; limitations on some normal activities)	
		Poor (severe symptoms; unable to carry out most normal activities)	
Incremental treatment-related risk of rapidly progressive osteoarthritis (RPOA)	**Additional risk of severe joint problems:** Additional risk each year of having joint problems that are severe enough that you would need a total joint replacement while you are taking the medicine or within 6 months of stopping the medicine	No additional risk (0%)	
		5 people out of 1,000 (0.5%)	
		40 people out of 1,000 (4%)	
Incremental treatment-related risk of heart attack	**Additional risk of heart attack:** Additional risk each year of having a heart attack while you are taking the medicine	No additional risk (0%)	
		2 people out of 1,000 (0.2%)	
		5 people out of 1,000 (0.5%)	
Treatment-related risk of physical dependency	**Risk of physical dependency:** Risk each year of becoming physically dependent on the medicine	No risk (0%)	
		50 people out of 1,000 (5%)	
		250 people out of 1,000 (25%)	
Mode and frequency of administration	**How you take the medicine**	Oral pills 2 or more times a day	
		Oral pills once a day	
		Injection every 4 weeks (about once a month)	
		Injection every 8 weeks (about once every two months)	
Variable created for scope test (not visible to respondents)[a]		Narrow range	Wide range
Personal (out-of-pocket) monthly cost	**Cost:** Personal cost of the medicine to you every month	$0 every month	$30 every month
		$55 every month	$75 every month
		$85 every month	$110 every month

[a] To implement a scope test, respondents were assigned to one of the 2 cost-value ranges in the DCE questions—a narrow or wide range of cost values. This table shows the levels for cost in both the narrow and wide ranges that were include in the DCE questions.

frequency of administration, and cost (Table 1). A random parameters logit model was used to estimate preferences and conditional relative attribute importance.

Results: Patients with OA pain only (n = 201), CLBP only (n = 202), and comorbid OA/CLBP (n = 199) completed the survey. Mean (SD) age was 63.7 (10.8) years. Mean (SD) current pain ratings for OA and CLBP were 6.4 (1.6) and 6.6 (1.4), respectively (Table 2). The relative importance of non-cost treatment attributes (mean [SE]) in descending order, rescaled so that the most important attribute was 10, was: improvement in pain and symptoms (10.00 [1.04]), risk of

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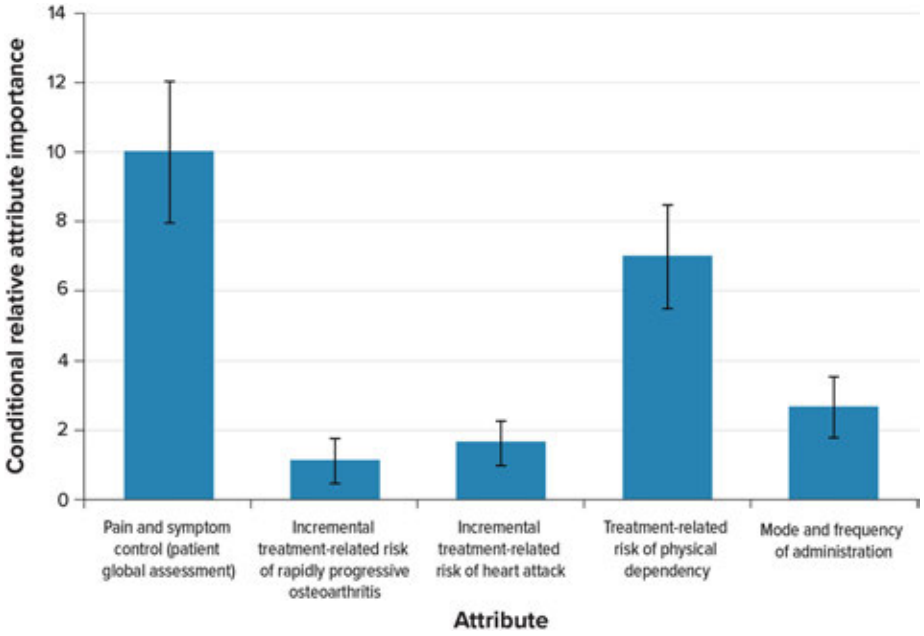
Table 2. Characteristics of Respondents

Respondent Characteristic		OA Only (n = 201)	CLBP Only (n = 202)	OA/CLBP (n = 199)	Full Sample (N = 602)
Gender	Male	70 (34.8%)	110 (54.5%)	66 (33.2%)	246 (40.9%)
	Female	131 (65.2%)	92 (45.5%)	133 (66.8%)	356 (59.1%)
Age	Mean (SD)	65.7 (8.7)	60.1 (12.8)	65.2 (9.5)	63.7 (10.8)
	Median	66	63	66	66
	Min, max	21, 87	21, 83	25, 90	21, 90
Marital status	Married/living as married	122 (60.7%)	143 (70.8%)	126 (63.3%)	391 (65.0%)
	Other	79 (39.3%)	59 (29.2%)	73 (36.8%)	211 (35.0%)
Race/ethnicity[a]	White	189 (94.0%)	188 (93.1%)	189 (95.0%)	566 (94.0%)
	Hispanic or Latino	6 (3.0%)	4 (2.0%)	2 (1.0%)	12 (2.0%)
	Black or African American	5 (2.5%)	7 (3.5%)	10 (5.0%)	22 (3.7%)
	Native American or American Indian	6 (3.0%)	4 (2.0%)	2 (1.0%)	12 (2.0%)
	Asian/Pacific Islander	3 (1.5%)	5 (2.5%)	1 (0.5%)	9 (1.5%)
	Other	2 (1.0%)	1 (0.5%)	0	3 (0.5%)
Education	High school equivalent or less	30 (14.9%)	28 (13.9%)	32 (16.1%)	90 (15.0%)
	More than high school	171 (85.1%)	174 (86.1%)	167 (83.9%)	512 (85.0%)
Employment	Employed full-time	25 (12.4%)	56 (27.7%)	31 (15.6%)	112 (18.6%)
	Not Employed full-time	176 (87.6%)	146 (72.3%)	168 (84.4%)	490 (81.4%)
Time since OA diagnosis	n	201	—	199	400
	Less than 1 year	15 (7.5%)	—	32 (16.1%)	47 (11.8%)
	At least 1 year ago, but less than 2 years	20 (10.0%)	—	30 (15.1%)	50 (12.5%)
	At least 2 years ago	166 (82.6%)	—	137 (68.8%)	303 (75.8%)
Time since CLBP diagnosis	n	—	202	199	401
	Less than 1 year	—	20 (9.9%)	28 (14.1%)	48 (12.0%)
	At least 1 year ago, but less than 2 years	—	28 (13.9%)	25 (12.6%)	53 (13.2%)
	At least 2 years ago	—	154 (76.2%)	146 (73.4%)	300 (74.8%)
OA Pain level	n	201	—	199	400
	Mean pain level (SD)	6.6 (1.2)	—	6.1 (1.8)	6.4 (1.6)
	Median pain level	7	—	7	7
CLBP Pain level	n	—	202	199	401
	Mean pain level (SD)	—	6.6 (1.2)	6.6 (1.6)	6.6 (1.4)
	Median pain level	—	6	7	7

CLBP = chronic low back pain; max = maximum; min = minimum; OA = osteoarthritis; SD = standard deviation.
[a] Respondents could provide multiple responses to these questions. Therefore, the totals may exceed the total number of respondents.



physical dependence (6.99 [0.74]), mode and frequency of administration (2.66 [0.43]), treatment-related risk of heart attack (1.64 [0.31]), and treatment-related risk of RPOA (1.10 [0.32]) (Figure 1).

Conclusion: Respondents were willing to accept substantial treatment-related risks to improve pain and symptoms of OA and CLBP and avoid the risk of physical dependence. Having effective alternatives to opioids is important to patients. In patients for whom NSAIDs are contraindicated, providing an effective treatment other than opioids or NSAIDs may be particularly important.

Disclosure: D. Turk, AcelRx, 5, Eli Lilly, 5, GlaxoSmithKline/Novartis, 5, Pfizer, 5; **M. Boeri**, RTI Health Solutions, 3; **L. Abraham**, Pfizer, LTD, 3; **B. Hauber**, RTI Health Solutions, 3; **J. Atkinson**, Pfizer, LTD, 3; **A. Bushmakin**, Pfizer Inc, 1, 3; **J. Cappelleri**, Pfizer Inc, 1, 3, Pfizer Inc., 1, 3; **L. Russo**, Pfizer, Inc., 3; **L. Viktrup**, Eli Lilly and Company, 1, 3, 4; **D. Walsh**, GlaxoSmithKline, 5, Pfizer Ltd, 5, 8, Sherwood Forest Hospitals NHS Foundation Trust (non-personal pecuniary), 2.

Abstract Number: 2767

Importance of Discussing RA Treatment Goals: Patients Report Providers Seldom Discuss Treatment Goals and Outcomes Improve When Goals Are Discussed

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Patient Outcomes, Preferences, & Attitudes II: Patient Preferences, Beliefs, & Experiences

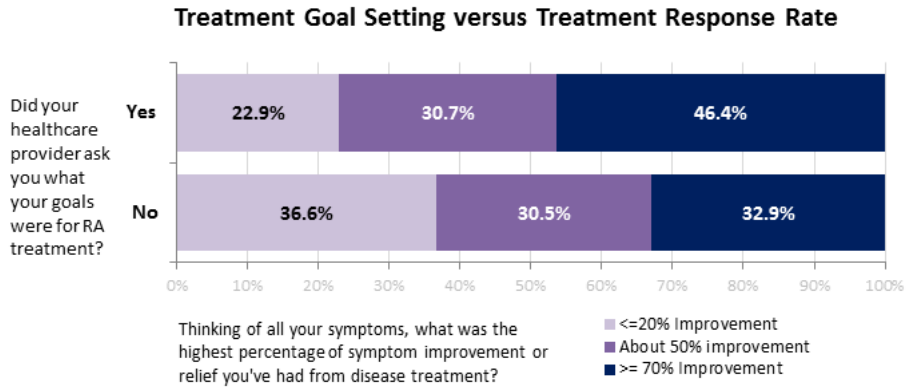
Session Type: ACR Abstract Session

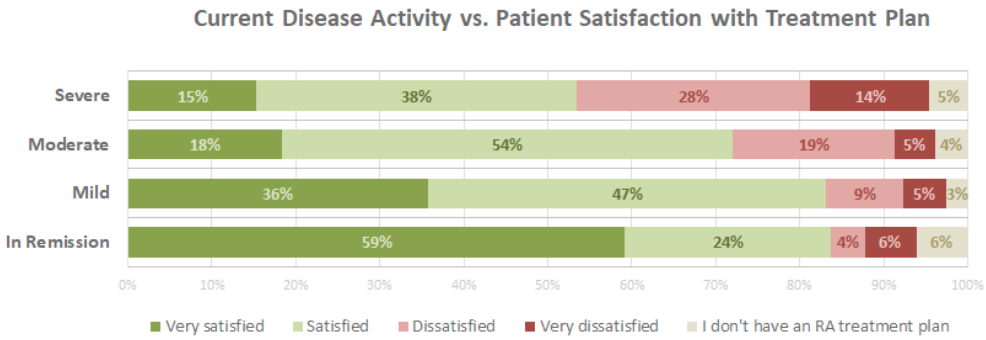
Session Time: 2:30PM–4:00PM

Table 1. Responses by whether provider asked about treatment goals

	No (N=571)	Yes (N=336)	p value
How satisfied are you with your rheumatoid arthritis (RA) treatment plan with your healthcare provider?			<0.001
Dissatisfied	140 (25%)	23 (7%)	
I don't have an RA treatment plan	30 (5%)	5 (1%)	
Satisfied	276 (48%)	157 (47%)	
Very dissatisfied	41 (7%)	20 (6%)	
Very satisfied	84 (15%)	131 (39%)	
How would you describe your current RA disease activity?			0.188
In Remission	25 (4%)	24 (7%)	
Mild	118 (21%)	78 (23%)	
Moderate	311 (54%)	175 (52%)	
Severe	117 (20%)	59 (18%)	
Which of the following best describes the pattern of your RA disease symptoms?			<0.001
I have constant symptoms that don't change	91 (16%)	46 (14%)	
I have constant symptoms that get worse over time	173 (30%)	96 (29%)	
I have no disease symptoms (remission)	8 (1%)	13 (4%)	
Symptoms come and go, and get worse over time	185 (32%)	80 (24%)	
Symptoms come and go, but don't get worse over time	114 (20%)	101 (30%)	
Improvement			<0.001
Less than 20% improvement	101 (18%)	28 (8%)	
About 20% improvement	108 (19%)	49 (15%)	
About 50% improvement	174 (30%)	103 (31%)	
About 70% improvement	113 (20%)	84 (25%)	
>=90% improvement	75 (13%)	72 (21%)	
How would you describe your state of health?			0.015
Fair	237 (42%)	118 (35%)	
Good	169 (30%)	135 (40%)	
Poor	98 (17%)	44 (13%)	
Very good	31 (5%)	22 (7%)	
Very poor	35 (6%)	17 (5%)	

Background/Purpose: Treat-to-target is a guiding principle in the management of rheumatoid arthritis (RA), and randomized clinical trials demonstrate its value in improving outcomes. However, implementation remains infrequent and standardized methods for establishing individual treatment targets remain problematic and lack input from patients. Building on a collaboration between a non-profit organization and an academic rheumatology center, we





aimed to gain greater understanding of patient treatment goals and preferences and examine how these may relate to treatment satisfaction or success.

Methods: A 28-item anonymous, web-based questionnaire developed and pilot-tested by the study team was presented over 7 days in 2019 on a secure survey system preventing multiple entries. Eligible participants were U.S. residents age ≥18 years with a self-reported diagnosis of RA by a medical professional. Participants were recruited through email, social media, and the web. Participants were asked closed- and open-ended questions about sociodemographics, their RA disease activity (DA), diagnosis and DMARD history, improvement from RA treatment, and the nature of RA treatment goals or plans created with their provider. Analyses included descriptive statistics with chi-square and rank sum tests for comparisons.

Results: The questionnaire was completed by 907 self-reported RA patients (90% women, 10% men), with a mean (SD) age of 58 years and a mean of 11.1 (10.1) years since diagnosis. According to self-reports, 5% were in remission, 22% reported mild DA, 54% moderate DA, and 19% severe DA. The majority (571; 63%) of patients were not asked by a provider about goals for their RA treatment. Of these, 32% were dissatisfied or very dissatisfied with their RA treatment plan, compared with only 13% of those who were asked about treatment goals.

Patients not asked about RA treatment goals had DA improvement levels resembling those of the whole study population. However, those whose providers discussed goals with them were more likely to have more DA improvement. Of those who said they discussed goals, fewer had DA improvement levels of ≤20% (no, 23%; yes, 37%); and more had DA improvement levels ≥90% (no, 13%; yes 21%).

Those who did not discuss treatment goals with their provider were less likely to achieve remission than those who did not (4% and 7% respectively). Those discussing treatment goals were less likely to have severe DA (no, 21%; yes, 18%). When asked whether they were likely to use materials to help set treatment goals with providers, 79% were likely or very likely to use them. Patients with higher levels of DA improvement were as likely to prefer treatment goal setting materials as those with lower levels of improvement.

Conclusion: This web-based survey showed that most RA patients are not asked about their treatment goals by their providers. However, a majority of RA patients favor tools to help patients set treatment goals together with providers. Of those who are not asked to set goals, 75% report having moderate to severe DA. Further research should seek a broader understanding of patient preferences for treatment goals and how they relate to successful management of RA.

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Abstract Number: 2768

Changes in B Cell Profile as a Marker of Clinical Remission to TNF Inhibitors in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Treatments IV: Novel Therapy & Predicting Response
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: According to the EULAR recommendations, the therapeutic objective in patients with rheumatoid arthritis (RA) should be remission. Biological therapies, as TNF inhibitors (TNFi), have allowed to increase remission rates although these are still limited (20-47%). There is still unknown if peripheral blood mononuclear cells (PBMC) play a role as predictors of response in patients with RA and if they can be modified with treatment. This study aims to analyse the change of peripheral blood mononuclear cells (PBMC) profile after 6 months (m) of treatment with TNFi in order to find baseline cellular markers of response.

Methods: This was a prospective bi-center pilot study including 98 RA patients. PBMC were isolated from patients at baseline and after 6m of treatment with TNFi, and analysed by flow-cytometry. Clinical activity at baseline and after 6m was assessed by DAS28. Clinical remission (DAS28≤2.6) at 6m was considered as optimal response. The association between clinical remission (REM) and the percentage of change (Δ, 6m-0m) within each PBMC subset was analysed through univariable and multivariate logistic regression model. All the analyses were adjusted by sex, ACPA, rheumatoid factor, baseline-CRP and baseline-DAS28.

Characteristics	Total patients (n=98)	DAS28>2.6 (n=60; 61%)	DAS28≤2.6 (n=38; 39%)	p-value
Age (years)	53±13	54±14	52±12	0.5
Female	83 (85)	54 (90)	29 (76)	0.1
Disease duration (years)	8 (4-12)	8 (4-12)	7 (4-11)	0.9
RF positive	76 (78)	42 (71)	34 (89)	<0.05
ACPA positive	82 (84)	46 (78)	36 (95)	<0.05
Smoking habit *(n=82)*				0.2
no	38 (46)	26 (53)	12 (36)	
smoker	44 (54)	23 (47)	21 (63)	
Body mass index (kg/m2)	24.8 (22.9-29.7)	25.4 (23.1-29.6)	24.7 (22.0-30.2)	0.3
DAS28	4.9±1.1	5.3±1.0	4.3±0.9	<0.001
CRP (mg/L)	5.7 (2.1-12.1)	6.4 (2.5-18.3)	3.0 (0.7-9.6)	<0.01
Previous TNFi treatment	12 (12)	7 (12)	5 (13)	1.0
TNFi type				0.1
Monoclonal antibodies	53 (54)	37 (62)	16 (42)	
Etanercept	45 (46)	23 (38)	22 (58)	
TNFi monotherapy	3 (3)	1 (2)	2 (5)	1.0
Concomitant csDMARDs	95 (97)	59 (98)	36 (95)	1.0
MTX [±OD]	74 (76)	48 (79)	26 (68)	1.0
Only OD	21 (21)	11 (19)	10 (27)	0.2
Prednisone	57 (59)	36 (60)	21 (55)	0.8

Table 1. Baseline characteristics of patients included in the study. The table shows mean±SD, median (IQR) or absolute number (percentage) for all patients included (n=98). RF, rheumatoid factor; ACPA, anti-citrullinated protein antibodies; DAS28, Disease Activity Score-28; CRP, C reactive protein; TNFi, Tumour Necrosis Factor inhibitor; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; MTX, methotrexate; OD, other conventional synthetic disease-modifying anti-rheumatic drugs than methotrexate (leflunomide, sulphasalazine, hydroxychloroquine). The differences between DAS28 groups were analysed considering p-value<0.05 as statistically significant result.

Results: Demographic characteristics before starting TNFi therapy are shown in table 1. After 6m of TNFi treatment, 39% patients achieved clinical remission by DAS28. Univariable analyses (odds ratio; 95% CI; p-value) was performed to investigate the association between REM and the baseline variables (table 1). A significant association was found for positivity of rheumatoid factor (OR: 3.44; 95% CI: 1.06-11.19; p: 0.04), presence of ACPA (OR: 5.09; 95% CI: 1.08-24.00; p: 0.04), lower CRP (OR: 0.95; 95% CI: 0.91-0.99; p: 0.03) and lower baseline DAS28 (OR: 0.33; 95% CI: 0.19-0.54; p< 0.0001). In the multivariate analysis, only lower baseline DAS28 (OR: 0.32; 95% CI: 0.18-0.56; p< 0.0001) remained independently associated with REM after 6m of treatment. Decreased percentage of B cells (ΔCD19+) was found after 6m of TNFi treatment in patients in REM, while no-REM patients did not show differences with the baseline (OR: 0.77; 95% CI: 0.61-0.97; p: 0.027). This effect was essentially owing to a reduction of naïve B cells (OR: 0.80; 95% IC: 0.68-0.95; p: 0.009) (figure 1). No significant association was found between the other PBMC subsets (monocytes, NK cells, CD4+ T cells and CD8+ T cells) and REM.

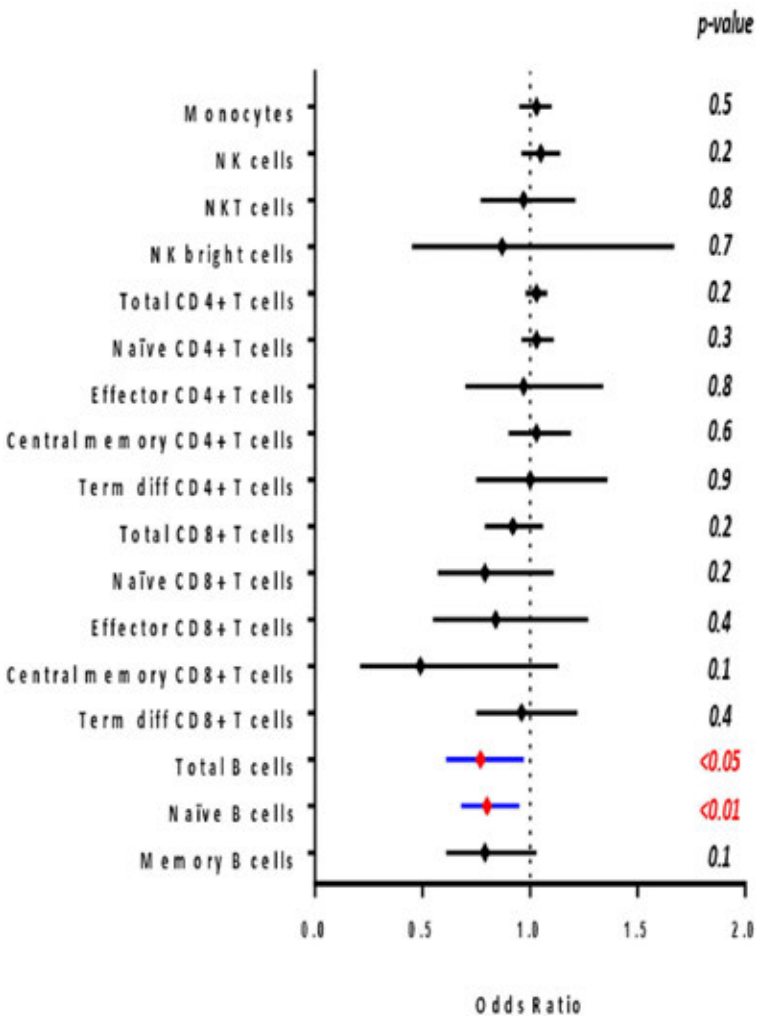

Figure 1. Association between the percentage of change (ΔPBMC, 6m-0m) within each PBMC subset and the clinical remission. Univariate logistic regression analysis was performed for each PBMC subset. The analyses were adjusted by sex, ACPA, rheumatoid factor, baseline-CRP and baseline-DAS28. The percentage of changes (Δ, 6m-0m) in total B cells and in naïve B cells were independently associated with the clinical response. No association was found in other PBMC subsets.

Conclusion: Our results suggest that B cells, specially naïve B cells, are the main PBMC subset involved in patients who respond to TNFi. This cell population was modified by the TNFi therapy only in responder patients. Therefore, we suggest that B cell may be useful as a marker of response to TNFi in RA patients.

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Abstract Number: 2769

The Pre-Treatment Gut Microbiome Predicts Early Response to Methotrexate in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Treatments IV: Novel Therapy & Predicting Response

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Early treatment initiation in rheumatoid arthritis (RA) is fundamental to avoid chronic joint destruction and disability. Despite remarkable advances in RA therapeutics, oral methotrexate (MTX) remains the anchor drug and mainstay of treatment worldwide. However, MTX bioavailability has a wide inter-individual variability and >50% of patients with moderate or severe RA show no or suboptimal improvement in their symptoms in response to MTX. The reasons for these disparities in treatment response remain unclear. Prior studies have shown that the biotransformation of MTX is altered in germ-free and microbiome-depleted mice, prompting us to hypothesize that inter-individual differences in the human gut microbiome could impact drug bioavailability and thus clinical efficacy. We sought to determine differences in the microbiome of drug-naïve, new onset RA (NORA) patients that could predict response to MTX therapy.

Methods: We enrolled 27 drug-naïve, NORA patients priori to MTX initiation (test cohort), and classified them as either MTX-responders (MTX-R; 39% of the cohort) or non-responders (MTX-NR; 61%) based on a stringent definition of clinical response (delta improvement of DAS28 >1.8 by month 4). We performed 16S rRNA gene and Shotgun Metagenomic sequencing on the baseline gut microbiomes of these NORA patients and confirmed the results in an independent validation cohort (n=31). NMR and LC-MS were performed in ex vivo incubations to measure the capacity of each NORA microbiome to metabolize MTX.

Results: Our analysis revealed significant associations between the abundance of gut bacterial taxa and future MTX response. Patients that responded to therapy had significantly lower microbial diversity ($p< 0.05$). A significant difference in overall gut microbial community structure was also observed between groups (Bray-Curtis distance; PERMANOVA < 0.05). At the class level, we observed statistically higher abundance of Clostridia and lower abundance of Bacteroidia in MTX-NR ($p< 0.05$; $q< 0.2$). Furthermore, the baseline metagenome separated most MTX-R from MTX-NR (PCoA; PERMANOVA $p< 0.05$). We identified 8 microbial modules and 23 pathways, whose abundance significantly differed between groups ($p< 0.05$, $q< 0.2$), including genes related with purine and MTX metabolism, indicating a major difference in metabolic and biosynthetic potential between the microbiome of MTX-R and MTX-NR patients. Machine learning techniques were applied to this metagenomic data, resulting in a robust model based on bacterial gene abundance that accurately predicted response to MTX in an independent cohort. Finally, MTX available levels remaining after *ex vivo* incubation with distal gut samples from pre-treatment RA patients significantly correlated with the magnitude of future clinical response, suggesting a direct effect of the gut microbiome on MTX bioavailability and response to therapy.

Conclusion: Together, these results provide the first step towards predicting response to oral MTX in NORA patients and support the utility of the gut microbiome as a prognostic tool and perhaps even as a target for manipulation in the treatment of rheumatic and autoimmune disease.

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Abstract Number: 2770

Towards the Lowest Efficacious Dose (ToLEDo): Results of a Multicenter Non-Inferiority Randomized Open-Label Controlled Trial Assessing Tocilizumab or Abatacept Injection Spacing in Rheumatoid Arthritis Patients in Remission

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	Abatacept	Tocilizumab	Whole population
Step 0	20.0%	35.1%	31.2%
Step 1-3	50.0%	50.9%	50.6%
Step 4	30.0%	14.0%	18.2%

Table 1. description of Spacing arm at the end of the follow-up

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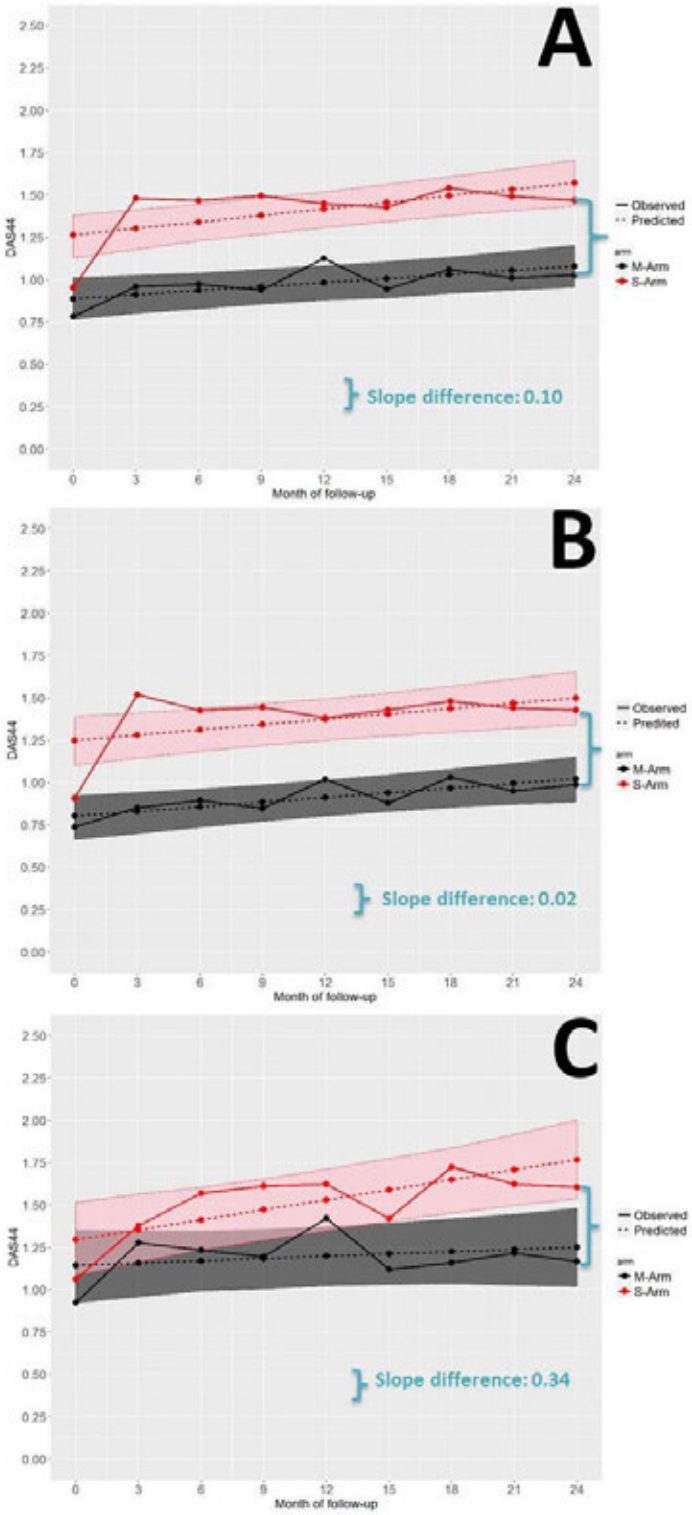

Figure 1. evolution of DAS44 in overall (A), TCZ (B) and ABA populations (C), and between Maintenance arm (black) and Spacing arm (red)

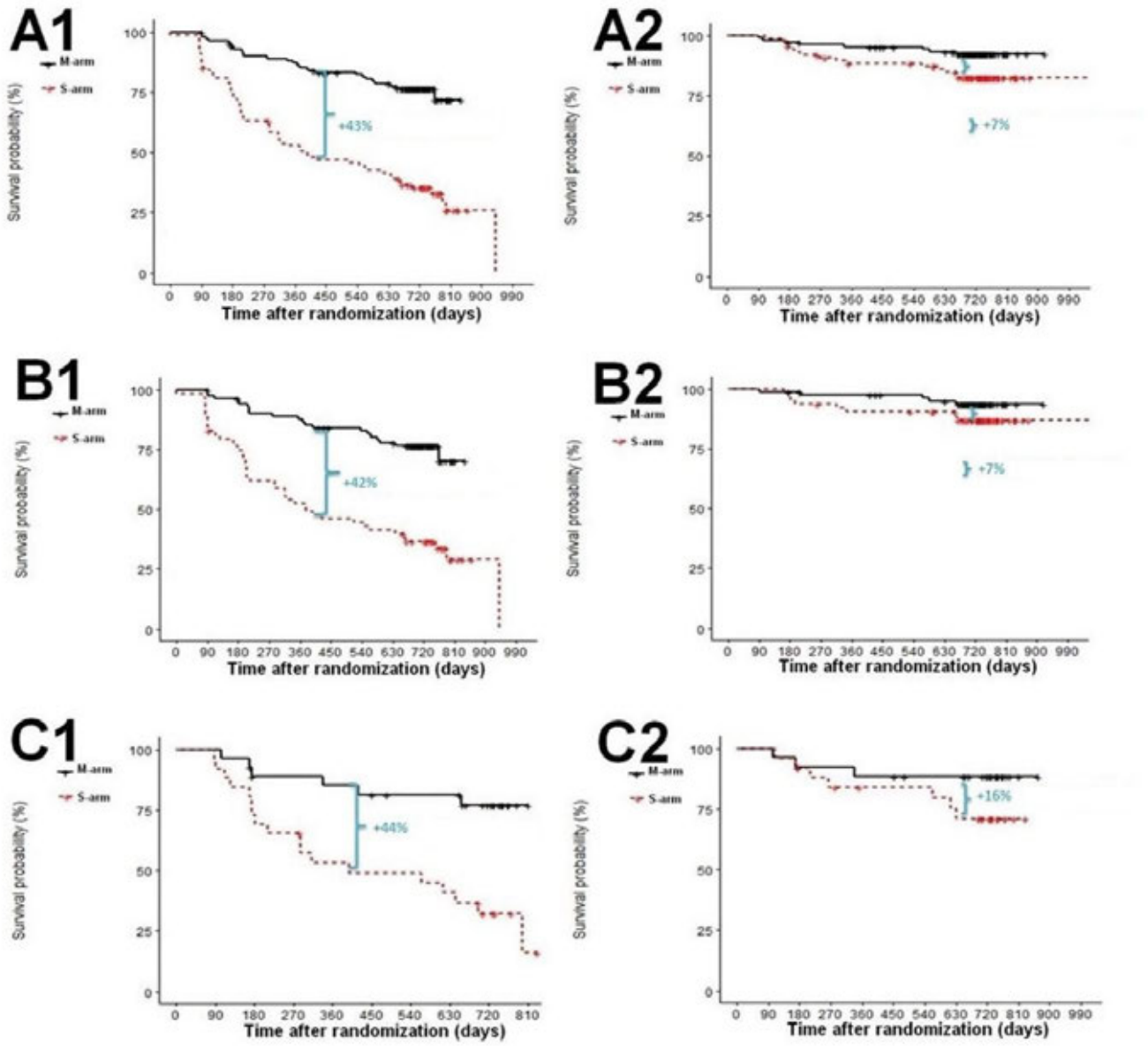

Figure 2. relapse-free (1) and major relapse-free (2) survival in overall (A), TCZ (B) and ABA populations (C), and between Maintenance arm (black) and Spacing arm (red)

Background/Purpose: Biologic Disease Modifying Anti-Rheumatic Drugs (bDMARD) tapering is proposed by clinical practice guidelines in rheumatoid arthritis (RA) patients in sustained remission. However, no randomized control trial (RCT) has been implemented to date to answer the question of tapering tocilizumab (TCZ) or abatacept (ABA).

The ToLEDo (Towards the Lowest Efficacious Dose) trial aimed to assess the impact on disease activity of progressive spacing of TCZ or ABA injections in RA patients in sustained remission compared to their maintenance at full dose.

Methods: ToLEDo is a multicenter open-label non-inferiority (NI) RCT conducted in RA patients fulfilling ACR-EULAR 2010 criteria. Patients had to be 1) treated with ABA or TCZ for ≥ 1 year (monotherapy or in combination with csDMARD, corticosteroid allowed at a dose ≤ 5 mg / day), 2) in DAS28ESR remission (DAS28ESR < 2.6) for ≥ 6 months and 3) with no X-ray damage progression in the year before inclusion. They were randomized into 2 arms: TCZ or ABA maintenance at full dose or DAS28-driven progressive injection spacing arm, in which bDMARD IV or SC injections were progressively spaced out every 3 months according to a predetermined 4-step algorithm up to bDMARD

discontinuation at step 4. Spacing was reversed to the previous step in case of flare. The primary outcome was the evolution of disease activity according to DAS44 during the 2-year follow-up, analyzed in a linear mixed-effect model. Secondary outcomes were flare and major flare rates (respectively defined as DAS28 > 3.2, and DAS28 >3.2 not recovered at the following visit despite bDMARD escalation at previous step) were also compared between the 2 arms. Analyses were done per protocol (PP) according to a NI hypothesis (NI margin at 0.25 for DAS44 and 0.07 for flare rates).

Results: Overall, 233 patients were randomized but 229 were treated and 199 were considered for PP analysis (89 in Spacing arm and 110 in Maintenance arm). 146 (73.4 %) patients were treated with TCZ and 53 (26.6%) with ABA. At the end of the follow-up in the Spacing arm, 18.2% of patients discontinued their bDMARD (step 4), 50.6% had tapered them (step 1 to 3) and 31.2% needed to go back to initial step (step 0) (Table 1). In terms of DAS44, the slope difference was 0.10 [95% CI: -0.10, 0.31] in the whole population, 0.34 [95% CI: -0.07, 0.74] for ABA subgroup and 0.02 [95% CI: -0.22, 0.26] for TCZ subgroup. The upper limit of the 1-sided 95% CI of slope difference exceeded 0.25, failing to demonstrate NI in the whole population and in the ABA subgroup (0.28 and 0.68 respectively), but NI was demonstrated in the TCZ subgroup (0.22, p=0.03) (Figure 1). Flares (Figure 2) were more frequent in the Spacing arm: +0.43 [95% CI: 0.30, 0.55], +0.44 [95% CI: 0.20, 0.68] and +0.42 [95% CI: 0.27, 0.57] in the whole population, ABA and TCZ subgroups respectively. Major flares were more frequent in the Spacing arm: +0.07 [95% CI: -0.01, 0.14], +0.16 [95% CI: -0.05, 0.37] and +0.07 [95%CI: -0.03, 0.16] in the whole population, ABA and TCZ subgroups respectively, compared with Maintenance arm.

Conclusion: The ToLEDo trial failed to demonstrate the NI of the proposed ABA or TCZ tapering strategy in comparison to maintenance at full dose. Thus, it is not in favor of tapering ABA and TCZ according to this scheme.

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Abstract Number: 2771

A Phase I, Randomized, Double-blind, Placebo-controlled, Single Center, Single-dose Escalation to Investigate the Safety, Tolerability, and Pharmacodynamics of Subcutaneously Administered DEN-181 in Adult Patients with ACPA+ Rheumatoid Arthritis on Stable Methotrexate

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SESSION INFORMATION

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Background/Purpose: Antigen-specific immunological tolerance strategies leverage the natural process of antigen presentation by dendritic cells (DCs) to regulate pathogenic T cells and B cells. We developed a nanoparticulate liposome formulation that encapsulates autoantigenic peptide and NF-kB inhibitor, 1,25 dihydroxycholecalciferol (calcitriol), to target DCs. In mouse models of autoimmune arthritis, multiple doses of liposomes promote disease suppression as well as stable regulation of effector-memory T cells with an increase in the proportion of naive T cells in an antigen-specific manner. We carried out a dose-ranging double-blind placebo-controlled phase I clinical trial of a single dose of liposomes encapsulating 40mg/ml collagen $II_{259-273}$ (CII) peptide + 400ng/ml calcitriol (DEN-181). The primary objective was assessment of safety and tolerability, and the secondary objectives were assessment of peripheral blood (PB) total and CII-specific naïve, effector and regulatory T cells, clinical response, and calcitriol levels after DEN-181 treatment.

Methods: Vehicle or 3 different dose levels of DEN-181 were administered via single s.c. injection to 17 anti-citrullinated peptide antibody (ACPA)+ HLA-DRB1*0401 or *0101+ RA patients on methotrexate. CII-specific and total CD4+ T cells were evaluated 0, 7 and 28 days post-treatment by flow cytometry using haplotype-specific tetramers. Plasma calcitriol was measured using an ultra-sensitive assay, hourly for 4h post-dose.

Results: Seventeen enrolled patients with a mean age of 50 (range 20-64), methotrexate dose 17.1 (5-25) mg/week, disease duration 4.9 (0.5-18) years, and DAS28CRP 2.66 (1.36-4.65) received vehicle or 3 different dose levels of DEN-181 (6x placebo, 4x 0.3ml, 3x 1ml and 4x 3ml). DEN-181 was generally well tolerated. One treated (1ml) and 1 control patient had AST >1.5x normal. Disease flares requiring steroids occurred in 1 control and 1 treated (3 ml) patient Plasma calcitriol levels were greater than placebo in the 3 ml but not in the 1 or 0.3 ml cohort.. Pre-treatment, CII-specific CD45RO+ memory T cells were identified in PB (range 30-66%). Relative to baseline, the % naïve CII-specific T cells increased and DAS28CRP decreased 7 days after a dose of 0.3ml, while the 3ml dose had the opposite effect (p=0.02 naïve, p=0.06 DAS). Changes in CII-specific naïve T cells differed between dose cohorts over time (p=0.04). After 7 days, reduced DAS28CRP of DEN-181-treated patients was associated with decreases in %CII-specific PD1+ T cells, CII-specific TCR expression, and ACPA IgG/IgA titre.

Conclusion: DEN-181 immunotherapy was safe and modulated antigen-specific T cells in RA patients of appropriate HLA type, where the pharmacodynamic effect of the 0.3ml dose suggests a skew toward immunological tolerance.

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Abstract Number: 2772

Clinical and Biological Changes in Rheumatoid Arthritis Patients Exposed to an Anti-inflammatory Diet

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Background/Purpose: RA patients often inquire about dietary interventions to improve disease control, as they perceive quick changes in pain and/or swelling after consumption of certain foods. Of particular interest is the influence of diet on modifying circulating pro/anti-inflammatory oxylipins and how this relationship affects pain/inflammation. Here, we determine the effect of a 2-week anti-inflammatory diet on clinical and biological outcomes in RA patients.

Methods: Patients with a diagnosis of RA and at least 3 tender and 3 swollen joints in physical exam and no change on medication in previous 2-3 months, who declined escalation therapy, were offered a 2-week anti-inflammatory diet and recruited in our study. This diet comprises of ingredients that increase omega-3/6 ratio, anti-inflammatory species such as turmeric, anti-oxidants, and prebiotics and probiotics. It also eliminates pro-inflammatory ingredients such as lactose, gluten and red meat. In their first visit (day -14), we established their clinical and biological baseline. In their second visit (at day 0) we collected clinical parameters. Patients were given instruction of how to follow the diet and were asked to follow a daily diet log. In their third visit (at day 14), we evaluated study feasibility outcomes, diet adherence and clinical parameters. We also collected blood in all three visits. Trend in clinical changes were examined between day -14 and 0, and between 0 and 14 in a subgroup of these patients (n=10). Serum oxylipins were determined by mass spectrometry before and after diet. Data processing and statistical analysis were performed in SPSS.

Results: In an ongoing clinical trial, 22 RA patients were recruited from 35 screened patients, and 17 of them (100% seropositive RA women, age average: 55, standard deviation (SD): 5) went through the complete trial. A diet index score (up to 200) showed a good diet adherence (-41.3 (70.9) vs 117.1 (52.1), $p< 0.001$, for before and after diet trial respectively). As shown in table 1, several clinical outcomes including evaluation of the number of tender (TJC) and swollen joints (SJC), Health Assessment Questionnaire (HAQ), and assessments of pain, fatigue, global disease severity by patients and by physicians, and composite measures of peripheral arthritis such as Disease Assessment Score (DAS)28-CRP and Clinical Disease Activity Index (CDAI) were significantly lower after the 2-week

Table 1 **RA clinical outcomes after diet (n=10).**

	Day -14 (visit 1)	Day 0 (visit 2)	Day +14 (visit 3)	p
DAS28 (mean ± SD)	4.42 ± 0.99	4.58 ± 0.97	3.3 ± 1.5	0.006
CDAI (mean ±sd)	22.4 ± 7.7	23.3 ± 8.3	11.6 ± 9.2	0.07
HAQ (mean ± SD)	0.83 ± 0.72	0.8 ± 0.68	0.57 ± 0.63	0.001
VAS Pt global (mean ± SD)	3.9 ± 2.4	3.2 ± 2.25	2.1 ± 2.2	0.003
VAS MD global (mean ±sd)	5 ± 1.33	5.3 ± 1.77	2.3 ± 1.94	<0.001
Number of tender joints MD (mean ± SD)	8.3 ± 3.3	8.6 ± 4	4.4 ± 4	0.017
Number of swollen joints MD (mean ± SD)	5.3 ± 1.6	6.2 ± 1.7	3.1 ± 2.3	0.002
Number of tender joints Pt (mean ± SD)	7.4 ± 4.3	5.8 ± 3.9	3.7 ± 3	0.007
Number of swollen joint Pt (mean ± SD)	5.3 ± 3.7	4.5 ± 3.3	2.3 ± 2.4	0.019
Pain level Pt (mean ± SD)	3.8 ± 1.87	3.7 ± 1.94	2.1 ± 1.8	0.005
Fatigue level Pt (mean ± SD)	4.5 ± 2.9	3.2 ± 2.7	1.7 ± 1.77	0.018
Stiffness (minutes) (mean ± SD)	32.5 ± 32.7	32.8 ± 39.2	23.5 ± 24.9	0.29
Stress level Pt (mean ± SD)	2.1 ± 1.66	1.8 ± 1.47	1.2 ± 1.13	0.011

anti-inflammatory diet (table 1). DAS28-CRP after the 2-weeks of anti-inflammatory diet also correlated with the diet index score at visit 3 (p=0.02). Of interest, several pro and anti-inflammatory linoleic acid-derived oxylipins including 13-HODE, 9,10 diHOME and 9,10 EpOME significantly changed after the diet and correlated with index score at visit 3 (p=0.02).

Conclusion: Modulating diet has the possibility to complement medication and improve quality of life for RA patients. Here we showed that RA patients are motivated and followed the diet with good adherence. Diet index scores after the trial correlated with clinical scores and changes in pro- and anti-inflammatory oxylipins suggesting that these mediators could play a role in the clinical effect of this diet in RA patients.

DAS28: Disease activity score on 28 joints; CDAI: clinical disease activity index; HAQ: health assessment questionnaire; VAS Pt global: patient's visual analogue scale for global disease VAS MD global: MD's visual analogue scale for global disease; Pt: patient. Statistical analysis conducted using Repeated Measures Analysis of Variance.

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Individually Tailored Predictions of Flare Probability for Rheumatoid Arthritis Patients on Biologic DMARDs Based on Machine Learning Stacking Meta-Classifier

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SESSION INFORMATION

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Background/Purpose: Tapering or stopping conventional and biologic DMARDs in patients with rheumatoid arthritis (RA) in stable remission may be feasible in a subset of patients [1]. However, the prediction of the patients' individual flare risk remains challenging. Hence, reliable models based on machine learning algorithms could be helpful tools for flare prediction [2]. Therefore, the purpose of this study was to investigate the feasibility of building a predictive model for estimating the individual flare probability in RA patients tapering biologic DMARDs using (1) a small cohort of patients, (2) high quality data and (3) a combination of different machine learning models.

Methods: Longitudinal clinical data of RA patients on biologic DMARDs from the phase-3, multicentre, randomised, open, prospective, controlled, parallel-group RETRO study (EudraCT number 2009-015740-42) was used. In order to exploit the flexibility obtained by combining different machine learning models a stacking meta-classifier is used [3]. At first, four models are trained: log. regression, random forest, k-NN and naïve Bayes which output the flare probability at each patient visit. These probabilities are the input features for the stacking logistic regression meta-classifier. The final prediction performance expressed as the AUROC is estimated using the nested cross-validation [4]. The importance of single predictors was estimated using the permutation importance approach [5].

Results: Data of 41 RETRO study patients with 135 follow-ups were used. The measured AUROC of the model was 0.802 (95%CI 0.717 – 0.887, Figure 1). A steadily growing model performance was observed with the increasing size of the available data (Figure 2). Of the ten most important variables for the machine learning model, the dose percentage change of bDMARD, clinical disease activity (DAS28-ESR), disease duration and inflammatory markers such as ESR or CRP reached the highest significance (Figure 3).

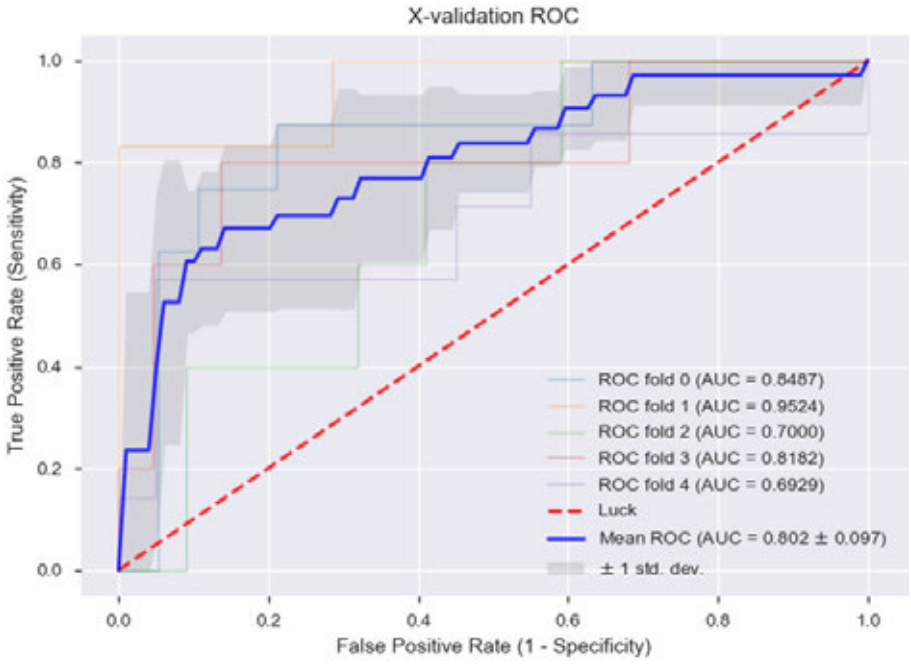

Figure 1. AUROC curve for the predictive machine learning model

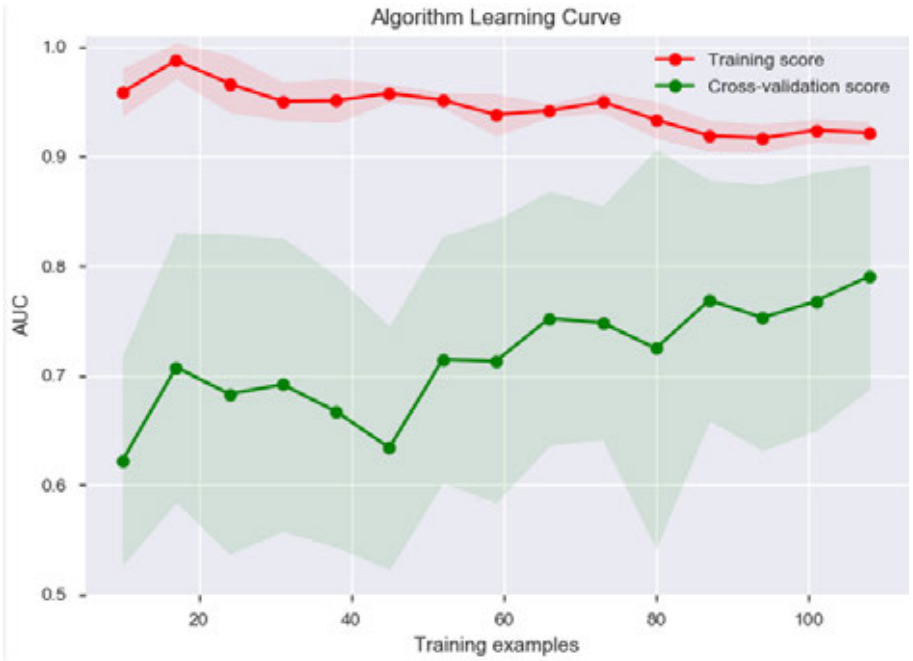

Figure 2. Learning curve of the stacking meta-classifier

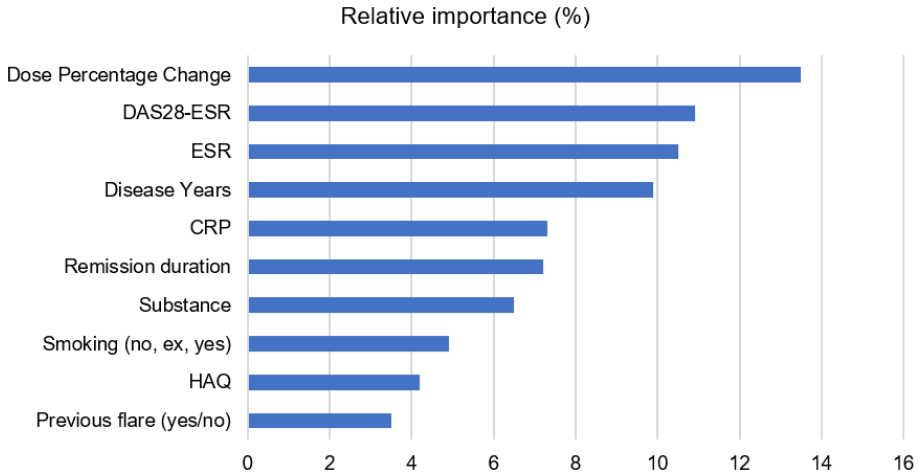

Figure 3. Relative importance of clinical and demographic variables for the machine learning model Dose Percentage Change: change in the percentage of full standard dose from its last value recorded within last 24 weeks; DAS28: Disease Activity Score 28; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; HAQ: Health Assessment Questionnaire

Conclusion: It is possible to train a good predictive model for RA flare probability with small data of high quality using a flexible combination of different classifiers. These results confirm the feasibility of guided tapering based on machine learning models and show that such models could be a reliable flair risk assessment tool for physicians in the future.

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Disclosure: A. Vodencarevic, Siemens Healthcare GmbH, 1, 3, 4; **D. Simon**, None; **F. Hartmann**, None; **M. Reiser**, None; **A. Hueber**, None; **K. Tascilar**, None; **A. Kleyer**, None; **M. Zimmermann-Rittereiser**, Siemens Healthcare GmbH, 1, 3, 4; **G. Schett**, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, 8, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, UCB, 5, BMS, Celgene, GSK, Lilly, Novartis, 2.

Abstract Number: 2774

Cluster-based Spondyloarthritis Phenotypes Defined at Baseline Are Predictive of Different Severity Outcomes at 5-Year in the DESIR Cohort

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical V: Axial Spondyloarthritis Clinical Studies

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Session Time: 2:30PM–4:00PM

Background/Purpose: The course of axial spondyloarthritis (SpA) is heterogeneous and remains to be better defined. DESIR is a longitudinal French cohort of early undifferentiated axial SpA, allowing to define different disease courses. We recently performed a cluster analysis, based on baseline characteristics and identified 2 SpA clusters: one, characterized by an isolated axial disorder (A for axial), the other by additional high prevalence of peripheral manifestations (B for both) (Costantino et al. Arthritis Rheumatol, 2016). These two clusters may be linked to different levels of disease severity. The aim of the present study was to assess whether cluster-based SpA phenotypes identified at baseline are stable over time and might predict different severity disease outcomes at follow-up.

Methods: We analysed longitudinal data from the 535 patients fulfilling the ASAS classification criteria (either axial or peripheral criteria) and who completed all follow-up visits until year 5 (months 6, 12, 18, 24, 36, 48 and 60) out of the 679 patients in the DESIR cohort used to define clusters at baseline. We performed a linear mixed-effect analysis for quantitative variables and a generalized linear mixed-effect analysis for qualitative variables with cluster and follow-up visits as fixed effects and subjects as random effect. *P*-values were obtained by likelihood ratio tests of the full model with cluster against the model without cluster as fixed effects. To determine a way to predict a definite cluster in a given patient at baseline, a classification and regression tree (CART) analysis was performed. A 10-fold cross validation was used to estimate misclassification rates.

Results: Over the time, both clusters continued to show significant differences with respect to prevalence of peripheral involvement, higher disease activity, worse patient-reported outcome, higher frequency of conventional DMARDs and TNF inhibitor use in cluster B, and higher prevalence of radiographic and MRI sacroiliitis at 2 and 5 years in cluster A (Table 1). CART analysis (Figure 1) shows that probability to maintain the same cluster over time is very high if a given patient belongs to a definite cluster-phenotype (A or B), with sensitivity of 98%, specificity of 87% and positive likelihood ratio of 7.62 at baseline (Table 2).

Variable (range)	Beta (Cluster B vs A)	95% CI	P-value
Disease activity			
- BASDAI (0-100)	6.89	3.80 – 9.98	1.5×10^{-5}
- ASDAS-CRP	0.18	0.06 – 0.31	4.7×10^{-3}
Functional outcome / Quality of life			
- BASFI (0-100)	6.37	3.09 – 9.65	1.5×10^{-4}
- HAQ - AS (0-3)	0.19	0.11 – 0.27	2.1×10^{-6}
- BASG (0 – 10)	0.75	0.26 – 1.24	3.0×10^{-3}
- ASQOL (0-18)	1.75	0.93 – 2.56	3.2×10^{-5}
Clinical manifestations			
- Tender joint count (0-53)	2.51	1.80 – 3.22	1.0×10^{-11}
- Swollen joint count (0-53)	0.08	0.01 – 0.14	0.01
- MASES enthesitis score	1.06	0.64 – 1.49	9.5×10^{-7}
- Psoriasis	-0.06	-0.9 – 0.78	NS
- IBD	0.06	-0.78 – 0.90	NS
- Uveitis	0.24	-0.52 – 1.01	NS
Acute phase reactants			
- CRP (mg/l)	0.09	-1.06 – 1.23	NS
- ESR (mm)	-0.46	-2.10 – 1.18	NS
Treatment			
- ASAS NSAID score (last 6 months)	3.37	-2.04 – 8.78	NS
- ASAS NSAID score (last week)	4.27	-1.20 – 9.75	NS
- Analgesics use (at the time of the visit)	0.80	0.28 – 1.31	1.9×10^{-4}
- Conventional DMARD (at the time of the visit)	2.16	1.14 – 3.17	1.2×10^{-13}
- Corticosteroids use (at the time of the visit)	0.44	-0.09 – 0.98	NS
- TNF blocker (at the time of the visit)	1.70	0.60 – 2.81	1.0×10^{-6}
Imaging			
- Total MSASSS	0.37	-0.19 – 0.94	NS
- Radiographic sacroiliitis (NY criteria)	-1.04	-2.18 – 0.1	0.001
- MRI SPARC spine score	-0.78	-1.71 – 0.16	NS
- MRI SPARC sacroiliac score	-2.22	-3.45 – -1	4.8×10^{-4}
- MRI sacroiliitis (ASAS criteria)	-1.35	-2.13 – -0.56	5.3×10^{-5}

Table 1. Results of the linear mixed effect and generalized linear mixed-effect analysis.

	Actual class		
Predicted class	Cluster A	Cluster B	Actual total
Cluster A	258	35	293
Cluster B	5	237	242
Predicted total	263	272	535
Accuracy = 93% ; Sensitivity = 98% ; Specificity = 87% ; LR+ 7.62			

Table 2. Performance of the decision tree for cluster determination

Conclusion: Cluster-based SpA phenotypes identify different severity outcomes at 5 years. We develop a decision tree for cluster determination, which shows accurate classification performance. This algorithm is easy to use (only three clinical parameters) and could help to identify patients at risk of poor outcome in early axial SpA.

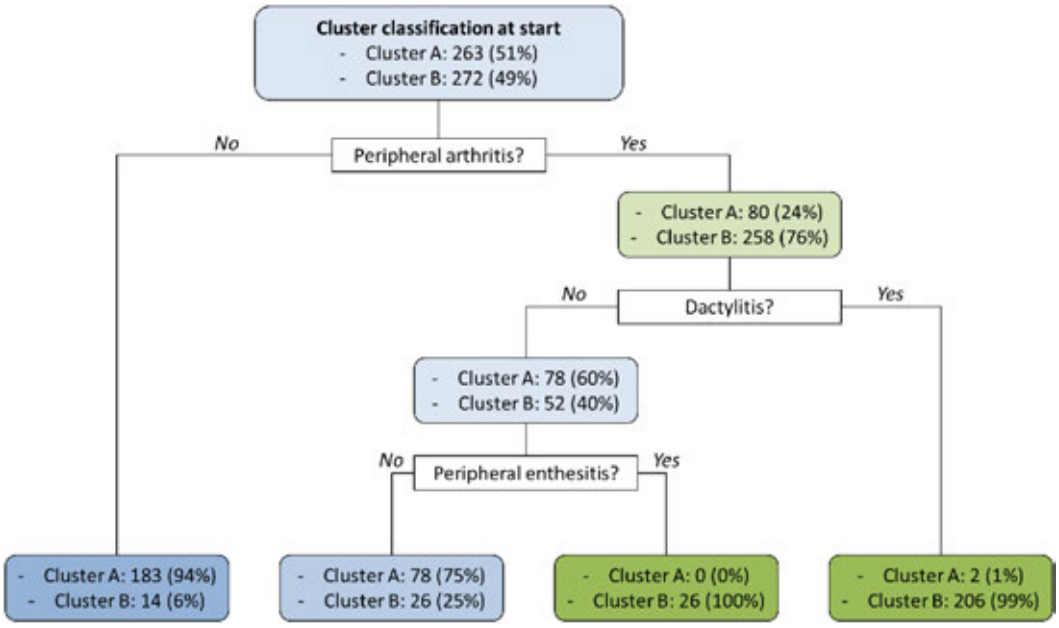

Figure 1. Decision tree for cluster (number of patients in each cluster following by percentages are given in each case

Disclosure: F. Costantino, None; **P. Aegerter**, None; **A. Moltó**, None; **G. Schett**, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, 8, AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, UCB, 5, BMS, Celgene, GSK, Lilly, Novartis, 2; **M. Breban**, None; **M. D'Agostino**, None.

Abstract Number: 2775

Pregnancy Rates and Outcomes in Early Axial Spondyloarthritis: Analysis of the DESIR Cohort

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SESSION INFORMATION
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Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Only scarce data is available on regarding pregnancy rates and pregnancy outcomes in early axial spondyloarthritis (axSpA). The objectives of this study were to estimate the probability of achieving a clinical pregnancy and presenting an unfavorable pregnancy outcome, and determined their associated factors, in this population.

Methods: Observational prospective French cohort (DESIR) with 6y of follow-up, including 381 of TNF-naïve women with early axSpA. Study visits were scheduled every 6 months in the first two years and then yearly up to 6 years. Data on pregnancy were collected retrospectively (before cohort inclusion) and prospectively (since inclusion) up to

6y of follow-up. Baseline characteristics of nulligravidae and uni/multigravidae patients were compared. The probability of achieving at least one pregnancy over time was estimated (Kaplan Meier). Associated factors were estimated by Frailty Shared Models and mixed models taking into account the correlation between several pregnancies from the same women. The probability to present an unfavorable pregnancy outcome over time (i.e a miscarriage or pre-term delivery or an elective termination of pregnancy) was estimated only during the prospective period (Kaplan Meier). Associated factors to an unfavorable pregnancy outcome were estimated by multivariable Frailty shared Models and mixted models.

Results: Of the 381 women included in the analysis, 289 (75.9%) and 92 (24.1%) women were respectively multigravidae and nulligravidae at the end of the 6y follow-up. Multigravidae women were significantly older (36.7±8.2 vs 27.8 ± 7.2, p< 0.01), less educated (56.9% vs 72.5% university studies, p=0.01), and had higher BASDAI (4.9±1.9 vs 4.4±2.0, p=0.04), and higher BASFI (3.5±2.4 vs 2.8±2.2, p=0.008) scores at baseline. The probability to have at least one pregnancy throughout life was 61.8% [55.1-67.5]. The mean age of the first pregnancy was 27.3 years old. One hundred and twenty-four pregnancies occurred during follow-up. Lack of TNFi use in the 6 months preceding the pregnancy outcome (HR=2.0 [95%CI 1.1-3.3], p=0.01) and a CRP≥ 6mg/L (HR=1.7 [95%CI 1.2-2.5], p=0.01) were found to be associated with pregnancy over follow-up.

Among the 80 pregnancies occurring after inclusion with data available on the outcome, 60 (75%) presented a full-term delivery while 12 (15%) presented an unfavorable pregnancy outcome (6 (7.5%) and 6(7.5%) had a miscarriage or a pre-term delivery, respectively), 2(2.5%) had an elective abortion, and 6(7.5%) were pregnancies still ongoing at the end of follow-up. The probability to present an unfavorable outcome was 16.7% [0.1-0.2]. Only NSAID use (HR=2.5 [95%CI 1.1-5.0], p=0.02) within 6 months of delivery were associated with an unfavorable outcome.

Conclusion: More than 70% patients had at least one pregnancy. A favorable pregnancy outcome (i.e.full-term delivery) was observed in 75% of patients, which is comparable to the general population data. Patients who achieved a pregnancy were more likely to have stopped their TNFi 6 months prior to the pregnancy outcome, and increased their CRP at the previous visit. NSAID use within 6 months of delivery was independently associated with an unfavorable pregnancy outcome.

Disclosure: M. Pons, None; **N. Costedoat-Chalumeau**, None; **K. Briot**, None; **P. Goupille**, AbbVie, 5, Amgen, 5, Biogaran, 5, BMS, 5, Celgene, 5, Eli Lilly, 5, Hospira, 5, Janssen-Cilag, 5, MSD, 5, Pfizer, 5, Sanofi-Genzyme, 5, UCB, 5; **C. Roux**, None; **M. Dougados**, AbbVie, 2, 5, 8, Amgen, 5, Biogen, 5, BMS, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, Merck, 2, 5, Merck Inc, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8; **A. Moltó**, None.

Abstract Number: 2776

5-years Treatment Effect of TNF Alpha Inhibitor in Early Axial Spondyloarthritis and Associated Factors: An Inverse Probability Weighting Analysis of the DESIR Cohort

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SESSION INFORMATION
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Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Only scarce date is available on the long term treatment effect in a real-life setting (i.e. effectiveness) of TNFi in early axial SpA forms and its predisposing associated factors; furthermore, unbiased evaluation of treatment effect in non-randomized clinical trials is challenging, and new methods have been developed to overcome prescription bias.

The objectives of the study were a) to estimate the probability to initiate a TNFi over 5 years of follow-up in real life setting using novel statistical methods to overcome prescription bias; b) to determine the long term effectiveness of first TNFi and its predisposing factors.

Methods: Observational prospective French cohort (DESIR) with 5 years of follow-up, including 708 TNFi-naïve patients with early axial spondyloarthritis. Study visits were scheduled every 6 months in the first two years of follow-up then yearly up to 5 years. Treatment (TNFi or other) was at the discretion of the treating rheumatologist's. The probability to initiate a TNFi was estimated by the Kaplan Meier Method, assuming non informative dropouts. Effectiveness of the first TNFi was defined as the probability to reach an ASAS40 response in both groups (TNFi vs. any other treatment) after at least 10 months of exposure. To evaluate treatment effect and overcome prescription bias repeatedly occurring over time, we have applied an iterative method based on inverse propensity score (PS) weighting using a marginal structural model, that allows the integration of the repeated weights derived from the propensity score at each visit (i.e. the probability to receive the treatment at each visit). The structural model used for this analysis was a PS-weighted cox regression, to estimate the probability to present an ASAS40 response after at least 10 months of treatment. Factors predicting first TNFi effectiveness, were explored by Cox (univariate and then multivariate) regression models.

Results: Of the 708 patients included in the analysis, 258 patients initiated a first TNFi during the first five years of follow-up. The probability to initiate a TNFi treatment was 41.3% [95%CI 37.2-45.1]. Among the 258 patients who received a first TNFi, 163 (63.2%) were exposed for at least 10months. On the original data, ASAS40 response was observed in 50/163 (30.7%) vs.58/450 (12.9%) patients from the TNFi and usual care groups, respectively. The likelihood of an ASAS40 response was greater in the TNFi exposed group (HR= 3.3[95%CI 2.9-3.8], p< 0.001). Male gender (HR=1.5[95%CI 1.1-2.1]), HLAB27+ (HR= 1.4[95%CI 1.1-2.0]) and the presence of at least one objective sign of inflammation (MRI or CRP) or structural damage (radiographic sacroiliitis) (HR = 1.7[95%CI 1.2-2.4]) were jointly predictive of an improved outcome.

Conclusion: Our study, applying novel statistical techniques to overcome prescription bias, confirms the 5-year effectiveness of TNF alpha inhibitors (TNFi) in patients with early axial spondyloarthritis (axSpA), and we confirm that male gender, with HLAB27 positive and the presence of at least one objective sign of inflammation or structural damage are more frequently associated with such effectiveness.

Disclosure: M. Pons, None; **S. Chevret**, None; **K. Briot**, None; **M. D'Agostino**, None; **C. Roux**, None; **M. Dougados**, AbbVie, 2, 5, 8, Amgen, 5, Biogen, 5, BMS, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, Merck, 2, 5, Merck Inc, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8; **A. Moltó**, None.

Abstract Number: 2777

What Is Axial Spondyloarthritis? A Latent Class and Transition Analysis in the SPACE and DESIR Cohorts

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical V: Axial Spondyloarthritis Clinical Studies

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Session Time: 2:30PM–4:00PM

Background/Purpose: Axial spondyloarthritis (axSpA) is a disease with a rather heterogeneous presentation that may be difficult to diagnose. Classification criteria, such as the ASAS criteria, developed and validated against the gold-standard 'expert diagnosis', exist, but may suffer from circularity because features deemed important by experts may have got a too prominent, and therefore biased, role. If classification criteria are used inappropriately to confirm a diagnosis, overdiagnosis may be an unwarranted consequence. We aimed to gain an unbiased insight into the concept of axSpA, by circumventing expert opinion and investigating its 'latent constructs': We examined the SpA-features' mutual statistical coherence, established the unbiased 'Gestalt' of SpA, and evaluated how the ASAS axSpA criteria capture these 'latent constructs'.

Methods: Two independent cohorts of patients (pts) with early onset chronic back pain (SPACE cohort) and inflammatory back pain (IBP) (DESIR cohort) were included. Latent class analysis (LCA) (different than a cluster analysis) was used to estimate the latent (i.e. unobserved) 'Gestalt' of axSpA by modelling the covariance of the observed SpA features (without 'a priori' assumptions on their 'weights'). The selected best LCA model splits axSpA into a number of (clinically meaningful) classes with best data fit. Each class was labelled by us and named according to most prominent features. The latent axSpA classes were then used as 'gold-standard' against which the ASAS axSpA, pSpA (ignoring IBP) and both (SpA criteria) were tested. Finally, 5-year follow-up data from DESIR were used to perform a latent transition analysis (LTA) in order to examine if patients change classes over 5-year time.

Results: In total, data of 465 (SPACE) and 576 (DESIR) pts were analyzed. SPACE yielded 4 latent classes (Table 1). The 'Axial' class characterized by highest likelihood on abnormal imaging and HLA-B27-positivity; the 'IBP+Peripheral' class had 100% likelihood of IBP in association with peripheral signs. The 'At risk' class is anchored on a positive family history and HLA-B27 positivity in association with IBP; and the 'No SpA' class had very low likelihoods for all SpA-features. The analysis in DESIR (without 'no-SpA' pts) yielded identical latent classes ('Axial':19%; 'IBP+Peripheral':27% and 'At risk':55%) (Table 2). The ASAS axSpA criteria, tested in SPACE ('No SpA' absent in DESIR), captured 67% of patients in the 'Axial' and 'IBP+Peripheral' classes ('latent gold-standard'), but sensitivity was better (87%) if axSpA and pSpA criteria were combined. Of note, the axSpA criteria captured only 4% of the pts from the 'No SpA' class. The LTA suggests that transition between classes over time was unlikely. 'Axial' and 'IBP+Peripheral' patients did not switch and only 11% of 'At risk' pts had switched to 'IBP+Peripheral' after 5 years.

Table 1. Latent class analysis model in SPACE (N=465)

	'Axial' (P*=15.9%)	'IBP+Peripheral' (P*=20.0%)	'At risk' (P*=24.3%)	'No SpA' (P*=39.7%)
	Estimated probability (95% CI)	Estimated probability (95% CI)	Estimated probability (95% CI)	Estimated probability (95% CI)
Inflammation on MRI-SIJ (ASAS)	***0.74 (0.52; 0.88)***	0.04 (0.01; 0.14)	0.00 (0.00; 1.00)	0.03 (0.01; 0.08)
Radiographic sacroiliitis (mNY)	**0.32 (0.19; 0.49)**	0.09 (0.04; 0.20)	0.01 (0.00; 0.32)	0.03 (0.01; 0.08)
Elevated CRP (≥ 6 mg/dL)	**0.49 (0.32; 0.65)**	0.22 (0.13; 0.34)	0.21 (0.13; 0.32)	0.20 (0.15; 0.28)
BME on MRI-Spine (≥ 5 lesions)	**0.25 (0.14; 0.42)**	0.02 (0.00; 0.18)	0.00 (0.00; 1.00)	0.00 (0.00; 0.11)
≥ 1 syndesmophyte on X-spine	0.03 (0.01; 0.11)	0.06 (0.03; 0.14)	0.00 (0.00; 1.00)	0.04 (0.02; 0.08)
Good response to NSAIDs (ever)	*0.59 (0.41; 0.75)*	***0.85 (0.72; 0.93)***	0.25 (0.14; 0.42)	0.20 (0.14; 0.29)
Peripheral arthritis (ever)	0.17 (0.09; 0.30)	**0.44 (0.30; 0.58)**	0.04 (0.01; 0.15)	0.10 (0.06; 0.17)
Dactylitis (ever)	0.02 (0.00; 0.17)	**0.18 (0.11; 0.29)**	0.00 (0.00; 1.00)	0.03 (0.01; 0.07)
Heel enthesitis (ever)	0.10 (0.04; 0.25)	***0.66 (0.50; 0.79)***	0.13 (0.06; 0.24)	0.04 (0.01; 0.11)
HLA-B27	***0.84 (0.67; 0.93)***	0.33 (0.23; 0.46)	*0.69 (0.24; 0.94)*	0.00 (0.00; 1.00)
Family history of SpA	0.38 (0.24; 0.54)	0.50 (0.38; 0.62)	***0.71 (0.56; 0.82)***	0.21 (0.10; 0.38)
Psoriasis (ever)	0.10 (0.04; 0.22)	**0.31 (0.21; 0.43)**	0.02 (0.00; 0.23)	0.08 (0.05; 0.14)
Uveitis (ever)	**0.13 (0.06; 0.24)**	0.07 (0.03; 0.17)	0.12 (0.06; 0.22)	0.02 (0.00; 0.11)
IBD (ever)	0.03 (0.01; 0.16)	**0.15 (0.08; 0.25)**	0.00 (0.00; 1.00)	0.10 (0.06; 0.17)
Inflammatory back pain	*0.68 (0.55; 0.79)*	***1.00 (0.00; 1.00)***	*0.66 (0.53; 0.76)*	0.49 (0.39; 0.59)

* Probability of the latent class. Values are the conditional probability (95% confidence interval) for each SpA feature positivity within each latent class (range: 0-1). Values in **bold** highlight dominant features between latent classes. Values in *italic* highlight dominant features (probability >50%) within each class. BME, bone marrow edema; IBD, Inflammatory bowel disease.

Table 2. Latent class analysis model in DESIR (N=576)

	'Axial' (P*=18.8%)	'IBP+Peripheral' (P*=26.7%)	'At risk' (P*=54.5%)
	Estimated probability (95% CI)	Estimated probability (95% CI)	Estimated probability (95% CI)
Inflammation on MRI-SIJ (ASAS)	***0.83 (0.69; 0.92)***	0.22 (0.15; 0.30)	0.09 (0.06; 0.16)
Radiographic sacroiliitis (mNY)	***0.58 (0.45; 0.70)***	0.06 (0.02; 0.13)	0.02 (0.01; 0.08)
Elevated CRP (≥ 6 mg/dL)	***0.56 (0.44; 0.67)***	0.41 (0.32; 0.51)	0.14 (0.10; 0.20)
BME on MRI-Spine (≥ 5 lesions)	**0.20 (0.13; 0.30)**	0.00 (0.00; 1.00)	0.01 (0.00; 0.03)
≥ 1 syndesmophyte on X-spine	**0.11 (0.06; 0.20)**	0.05 (0.02; 0.11)	0.06 (0.04; 0.10)
Good response to NSAIDs (ever)	***0.97 (0.90; 0.99)***	*0.84 (0.76; 0.90)*	*0.82 (0.77; 0.86)*
Peripheral arthritis (ever)	0.09 (0.04; 0.20)	***0.73 (0.49; 0.88)***	0.00 (0.00; 1.00)
Dactylitis (ever)	0.03 (0.01; 0.15)	**0.46 (0.36; 0.55)**	0.01 (0.00; 0.31)
Heel enthesitis (ever)	0.26 (0.18; 0.37)	***0.60 (0.51; 0.69)***	0.45 (0.39; 0.51)
HLA-B27	***0.90 (0.79; 0.96)***	*0.52 (0.43; 0.61)*	*0.53 (0.47; 0.59)*
Family history of SpA	**0.48 (0.37; 0.58)**	0.44 (0.36; 0.53)	0.41 (0.36; 0.48)
Psoriasis (ever)	0.09 (0.04; 0.18)	**0.29 (0.22; 0.38)**	0.14 (0.10; 0.19)
Uveitis (ever)	0.08 (0.04; 0.18)	**0.12 (0.07; 0.20)**	0.08 (0.05; 0.12)
IBD (ever)	0.02 (0.00; 0.10)	0.05 (0.02; 0.11)	0.05 (0.03; 0.08)

* Probability of the latent class. Values are the conditional probability (95% confidence interval) for each SpA feature positivity within each latent class (range: 0-1). Values in **bold** highlight dominant features between latent classes. Values in *italic* highlight dominant features (probability >50%) within each class. BME, bone marrow edema; IBD, Inflammatory bowel disease.

Conclusion: The 'Gestalt' of axial spondyloarthritis comprises three distinguishable clinical entities ('pure axial SpA', 'axial SpA with peripheral signs, and 'axial SpA at risk'). Patients keep their clinical entity over 5 years and transition is very rare. The 'Axial' and 'IBP+Peripheral' entities are best captured by combining the ASAS axSpA and pSpA criteria.

Disclosure: A. Sepriano, None; **S. Ramiro**, AbbVie, 5, 8, Eli Lilly, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **P. Hoonhout**, None; **A. Moltó**, None; **A. Saraux**, None; **M. Dougados**, AbbVie, 2, 5, 8, Amgen, 5, Biogen, 5, BMS, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, Merck, 2, 5, Merck Inc, 2, 5, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 2, 5, Roche, 2, 5, 8, UCB, 2, 5, 8; **R. Landewé**, Abbott, 2, 5, 8, Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8.

Abstract Number: 2778

Alcohol Consumption as a Predictor of the Progression of Spinal Structural Damage in Axial Spondyloarthritis: Data from the Catholic Axial Spondyloarthritis COhort (CASCO)

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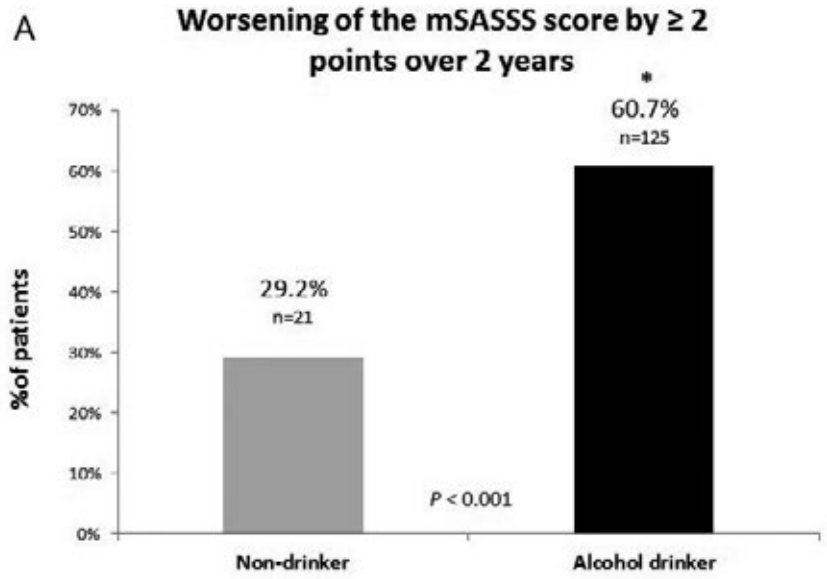
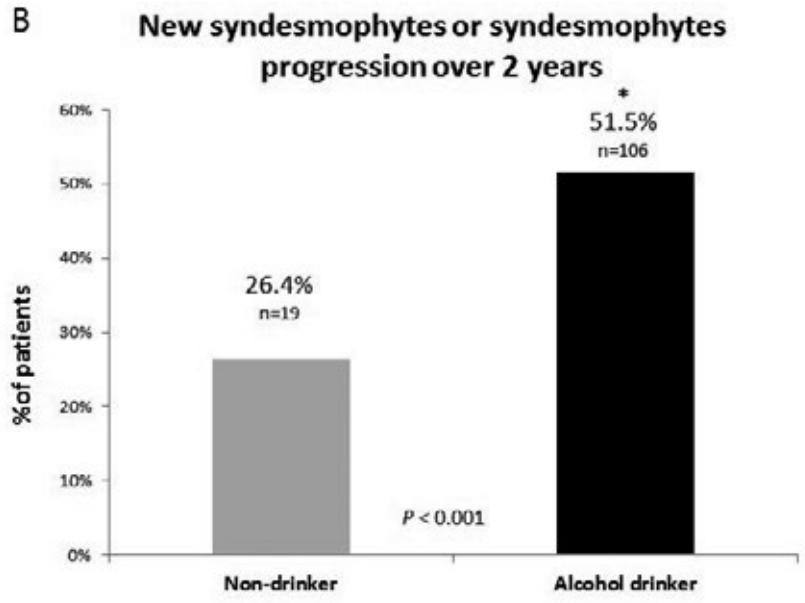
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical V: Axial Spondyloarthritis Clinical Studies
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: The purpose of the present study was to demonstrate the predicting factors of spinal structural damage in axial spondyloarthritis (axSpA) in a prospective cohort study.

Methods: AxSpA patients were enrolled from a single tertiary hospital in a prospective cohort. Baseline data were collected, and 2 year follow-up radiographic data were collected. We analyzed the progression of spinal structural damage in 278 axSpA patients and grouped them into alcohol drinkers and non-drinkers. Baseline and follow up characteristics were compared between the two groups. Univariable and multivariable logistic regression analysis were performed to reveal predictors of spinal structural damage.





Results: Change of modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) and syndesmophyte count over the 2 year period were more prominent in the alcohol drinker group than in the non-drinker group (2.7 ± 3.6 vs 1.5 ± 2.8, P=0.007, 0.9 ± 1.3 vs 0.4 ± 1.2, P=0.003). The alcohol drinker group showed more frequent significant mSASSS changes (≥2 units for 2 years follow up) and new syndesmophyte/progression of pre-existing syndesmophyte than the non-drinker group (60.7% vs 29.2%, P< 0.001, 51.5% vs 26.4%, P< 0.001, respectively). On univariable and multivariable regression analysis, drinking alcohol showed a significant relationship with the progression of spinal structural damage for both mSASSS and syndesmophyte progression.

Conclusion: The present study showed that alcohol consumption could predict progression of spinal structural damage in axSpA. This is meaningful because drinking alcohol is a modifiable behavior and education on alcohol consumption could aid in attenuating spinal structural damage in axSpA.

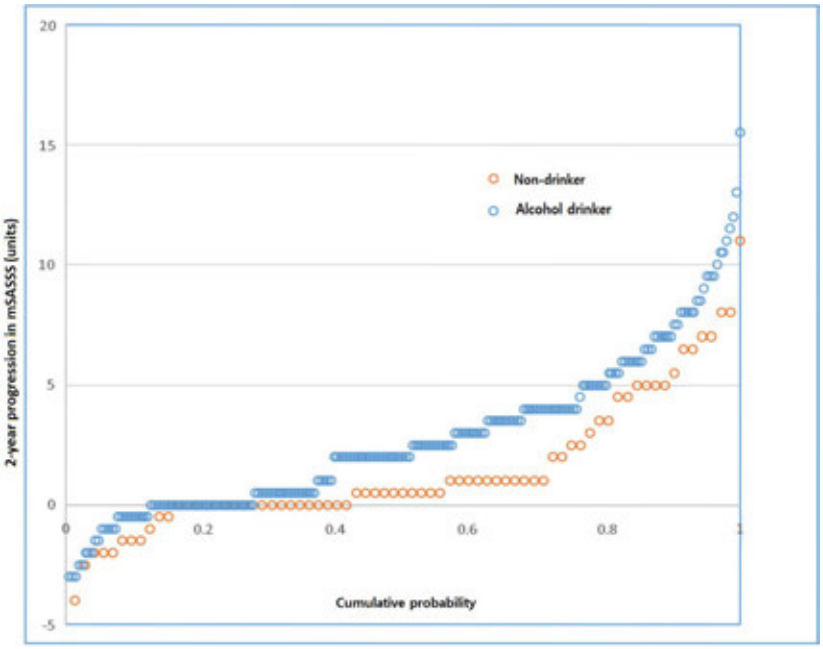


Table 2. Univariable and multivariable regression analysis of predicting worsening 2 unit or more of mSASSS over 2 years

	Univariable			Model 1*			Model 2†		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Age	1.039	1.016, 1.062	**0.001**	1.030	1.005, 1.057	**0.021**	1.030	1.004, 1.057	**0.021**
Male	1.580	0.900, 2.774	0.111						
Obesity (BMI≥25kg/m^2)	1.074	0.653, 1.764	0.779						
Alcohol drinker	3.748	2.098, 6.694	**<0.001**	4.529	2.361, 8.688	**<0.001**	4.439	2.305, 8.551	**<0.001**
Current smoker	1.317	0.772, 2.248	0.312				1.048	0.575, 1.909	0.879
Uveitis history	1.870	1.155, 3.029	**0.011**	2.130	1.220, 3.719	**0.008**	2.100	1.200, 3.674	**0.009**
Elevated BASDAI (≥4)	1.218	0.713, 2.081	0.471						
Very high ASDAS-CRP (>3.5)	3.232	0.870, 12.015	0.080	2.311	0.579, 9.234	0.236	2.343	0.580, 9.461	0.232
Positive HLA-B27	0.843	0.304, 2.335	0.743						
Mean grade of sacroiliitis	1.554	1.230, 1.963	**<0.001**	1.355	1.048, 1.751	**0.020**	1.357	1.045, 1.763	**0.022**
Pre-existing syndesmophyte	2.268	1.380, 3.729	**<0.001**						

ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; OR, odd ratio

* All variable yielding *P* value under 0.1 in univariable logistic regression analysis was included in model 1, and multivariable logistic regression analysis was performed by backward stepwise manner.

† Multivariable logistic regression analysis was performed by adding smoking status to the variables included in model 1.

Disclosure: H. Min, None; **S. Kwok**, None; **S. Lee**, None.

Abstract Number: 2779

Higher Disease Activity Is Associated with More Spinal Radiographic Progression in Patients with Axial Spondyloarthritis Independently of Prior Exposure to TNF Inhibitors

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical V: Axial Spondyloarthritis Clinical Studies

Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: The association between disease activity and spinal radiographic progression in radiographic axial spondyloarthritis (r-axSpA) has been previously shown in a cohort of patients (pts) not being treated with TNF inhibitors (TNFi).[1] We aimed to test the possible association between disease activity and spinal radiographic progression in r-axSpA in a real-life cohort, also including patients treated with TNFi.

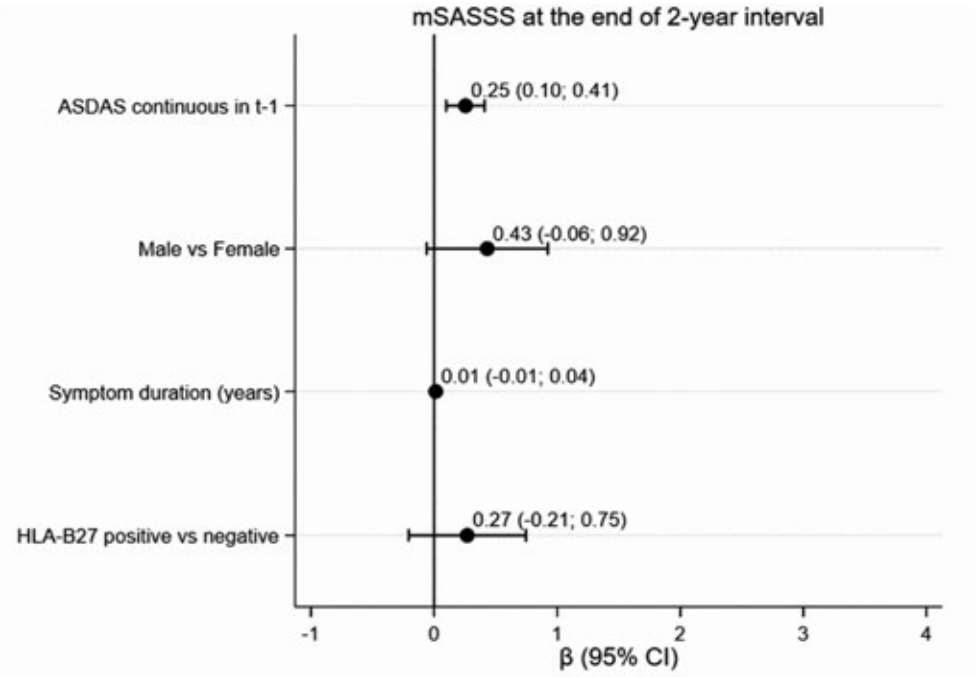

Figure. Longitudinal effect of ASDAS at the start of the interval on mSASSS 2 years later in a multilevel, multivariable linear GEE model with autoregression [N=313; model also adjusted for mSASSS at t-1 ('autoregressor'), Number of TNFi before baseline (continuous) and TNFi at t-1 (yes vs no)].

Methods: Pts with axial spondyloarthritis (axSpA) fulfilling the modified New York criteria (mNY) were included in this prospective, observational cohort (ALBERTA FORCAST). Clinical and imaging data were collected at baseline and every 2 years up to 10 years of follow-up. Radiographs of the spine were independently scored by 2 central readers and one adjudicator (if disagreement), with known chronological order but blinded to clinical data, using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). To be included, pts had to have ≥ one 2-year interval with data on mSASSS from ≥1 reader available as well as complete data on ASDAS and TNFi exposure at the start of the interval. The association between ASDAS at the start of the interval (t) and mSASSS 2 years later (t+1) was tested in two types of longitudinal GEE models: i. multilevel (2 readers) model with the individual reader scores as outcome (2-level models); ii. Using as outcome averaged scores between readers (1-level models). Both type of models were adjusted for mSASSS at t (autoregression) and for a set of potential confounders defined a priori on clinical grounds (Figure).

Results: In total, 314 pts (442 intervals) were included [74% males, mean symptom duration 17.8 (SD 11.7) years, 83% HLA-B27 positive and 7% previously treated with ≥1 TNFi]. At baseline the mean ASDAS was 2.7 (1.3) and the mean mSASSS 13.8 (18.9). During follow-up 213 (68%) pts received treatment with TNFi in ≥1 visit. Overall, the average 2-year progression was 1.33 (2.68) mSASSS-units per 2-year interval. In the 2-level multivariable model, 1 ASDAS-unit increase at t was associated with an increase of 0.25 mSASSS-units at t+1 [β (95% CI): 0.25 (95%CI 0.10; 0.41)] (Figure). Results were similar using the averaged mSASSS as the outcome [β (95% CI): 0.25 (0.08; 0.43)].

Conclusion: These data indicate that a higher ASDAS is associated with higher spinal radiographic progression in pts with r-axSpA and this is independent of prior treatment with TNFi.

Disclosure: A. Sepriano, None; **S. Ramiro**, AbbVie, 5, 8, Eli Lilly, 5, 8, Lilly, 5, 8, MSD, 2, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sanofi, 5, 8; **S. Wichuk**, None; **P. Chiowchanwisawakit**, None; **T. MacCosham**, None; **J. Paschke**, None; **D. van der Heijde**, AbbVie, 5, AbbVie, Amgen, Astellas, AstraZeneca, BMS, 5, Amgen, 5, Astellas, 5, 9, Astellas Pharma, 5, AstraZeneca, 5, BMS, 5, Boehringer Ingelheim, 5, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Daiichi, 5, 9, Daiichi Sankyo, 5, Director of Imaging Rheumatology, 6, Director of Imaging Rheumatology bv, 9, Eli Lilly, 5, Eli Lilly and Company, 5, Eli-Lilly, 5, Galapagos, 5, Gilead, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, GSK, 5, 8, Imaging Rheumatology bv, 9, Imaging Rheumatology BV, 9, Imaging Rheumatology bv., 9, Janssen, 5, 8, Janssen Pharmaceutica, 5, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Pfizer Inc, 5, Regeneron, 5, 8, Rheumatology bv, 4, 9, Roche, 5, 8, Sanofi, 5, 8, Takeda, 5, 8, Takeda Pharmaceutical Company, 5, UCB, 5, 8, UCB Pharma, 5; **R. Landewé**, Abbott, 2, 5, 8, Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 8, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, AbbVie, 5, Abbvie, 5, 8, AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering- Plough, UCB, Wyeth, 5, Ablynx, 5, Amgen, 2, 5, 8, AstraZeneca, 5, BMS, 5, 8, Bristol Myers Squibb, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Centocor, 2, 5, 8, Director of Rheumatology Consultancy BV, which is a registered company under Dutch law, 6, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Eli-Lilly, 5, 8, Galapagos, 5, 8, Gilead, 5, 8, GlaxoSmithKline, 5, Glaxo-Smith-Kline, 5, 8, Janssen, 5, 8, Merck, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Rheumatology bv, 4, Rheumatology Consultancy BV, 9, Roche, 2, 5, 8, Schering-Plough, 2, 5, 8, UCB, 5, 8, UCB Pharma, 2, 5, 8, Wyeth, 2, 5, 8; **W. Maksymowych**, Abbvie, 2, 5, 8, Boehringer, 5, 8, Celgene, 5, 8, Galapagos, 5, 8, Lilly, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 5, 8.

Abstract Number: 2780

Identification of SLE Subgroups at Risk for Poor Outcomes After Hydroxychloroquine Taper or Discontinuation

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical V: Emerging Knowledge of Current Treatments
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: The risks and benefits of long-term hydroxychloroquine (HCQ) use in systemic lupus erythematosus (SLE), versus tapering or stopping, remain uncertain. We aimed to identify predictors of a poor outcome once HCQ is tapered or discontinued in SLE.

Methods: We studied a clinical cohort of adult patients meeting ACR classification criteria for SLE. From January 2002 and December 2018, we identified the first visit with HCQ exposure for each patient. We then determined those tapering (sub-cohort 1) or discontinuing (sub-cohort 2) HCQ at a follow-up visit. This follow-up visit represented time zero for the remaining analyses. The primary outcome was time to the first of the following events: a) increase of ≥4 points in the SLE Disease Activity Index (SLEDAI-2K); b) hospitalization for SLE; and/or c) augmented SLE therapy (i.e. an increase in HCQ, or a new start/increase in corticosteroids or immunosuppressants). Cox regression was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) to determine if baseline characteristics (age at SLE diagnosis, sex, education and race/ethnicity) were associated with our outcome.

Results: We identified 228 patients tapering HCQ (sub-cohort 1) and 188 stopping HCQ (sub-cohort 2). Most patients were female (90%) and white (70%), and the mean±SD age at SLE diagnosis was 32±13 years. The mean±SD follow-up time from our time zero was 6.7±4.4 years in sub-cohort 1 and 5.6±4.7 in sub-cohort 2. Within the first year of observation, 167 (73%) patients who tapered HCQ and 133 (71%) patients who discontinued HCQ had at least one poor outcome. The most common poor outcome was need for therapy augmentation (70% after tapering and 64% after stopping HCQ), followed by SLEDAI-2K increase ≥4 (37% after tapering and 32% after stopping HCQ) and hospitalization for SLE (7% after tapering and 8% after stopping HCQ). Patients with higher age at SLE diagnosis and those with SLEDAI-2K ≥4 and/or requiring prednisone/mycophenolate at baseline were more likely to experience poor outcomes after HCQ discontinuation (Table 1). Patients with renal damage were more likely to have an increase in disease activity after tapering HCQ (adjusted HR: 2.02; 95%CI: 1.13, 3.62).

Conclusion: Though some SLE patients do well after tapering or discontinuing HQN, others have poor outcomes including SLE-related hospitalization. Our results suggest caution in tapering or discontinuation of HCQ in some groups of SLE patients, such as those with renal damage, unstable disease activity, or requiring prednisone/mycophenolate. The identification of these predictors is an important approach to promote personalized medicine.

Disclosure: C. Almeida-Brasil, None; **E. Vinet**, None; **C. Pineau**, None; **S. Bernatsky**, None.

Abstract Number: 2781

Risk of Cardiovascular Disease Associated with the Use of Glucocorticoids in Patients with Incident Systemic Lupus Erytematosus: A Population-based Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical V: Emerging Knowledge of Current Treatments
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) have an increased risk for cardiovascular disease (CVD). SLE itself predisposes patients to accelerated atherosclerosis. In addition, the risk of CVD may be due to effects of drugs used to treat SLE, particularly glucocorticoid (GC). However, population-based studies assessing the risk of CVD associated with the use of GC with proper adjustment of time-varying confounders that might be also acting as intermediary variables in patients with newly diagnosed SLE are limited. We aim to address this question and the idea that recency of GC use may impact the effect.

Methods: Our data included all outpatient and inpatient visits, demographic data, cancer registry and vital statistics from Jan 1990 to Mar 2015 and all dispensed medication from Sept 1995 to Mar 2015 in the province of British Columbia, Canada. Using a previously validated SLE case definition, we assembled an incident cohort of all SLE patients who received health care between January 01 1997 and March 31 2015 with no exposure to GC before SLE onset. CVD events (myocardial infarction (MI) or stroke) were identified using both hospitalization and vital statistics data. Individuals were followed until they experienced a CVD outcome, died, left BC, or follow-up ended, whichever occurred first. We used the marginal structure Cox model to estimate the impact of the GC initiation on the risk of CVD, adjusting for both baseline and time-dependent covariates (including health resource utilization and relevant medications (listed in table1)) that were updated every three months during follow-up. We defined GC exposure in four more ways: current use (yes/no), current dose (mg/day), cumulative dose (grams), cumulative duration (months). All were used as time-dependent variables. To permit the effect of a GC use in the past 180 days to vary by its recency, we created weighted versions of the cumulative dose and duration (i.e., straight-line, concave, convex, and half-normal weighting function). Cox proportional hazard models were used to estimate the risk of CVD of these GC exposure measures.

Results: We identified 2,653 incident SLE patients with no GC use history at baseline (mean age 47, 86% females). During follow-up, 1,720 (65%) received GC. GC users spend an average 15% of their follow-up time on GC with a median dose of 5 mg/day and a median duration per GC course of 29 days. During follow-up, we identified 108 CVD events (MI 69; stroke 45). Using marginal structure model, the hazard ratio (HR) after GC initiation was 1.82 (95%CI; 1.18-2.81) adjusted for baseline and time-dependent variables. Current GC use and current daily dose were associated with significantly increased risk of CVD (HR; 1.76 (95%CI; 1.06-2.94) and 1.14 (95%CI; 1.03-1.26)) (Table 2). Concave function for both cumulative dose and cumulative duration of use were selected as the best weighting function with the smallest AIC. Both of them were statistically significant (HR: 1.59 (95% CI; 1.23-2.05) and 1.21 (95% CI; 1.04-1.41)).

Characteristics	All SLE patients N=2653	Exposed to GC N=1720	Never exposed to GC N=933
Women, number (%)	2285 (86.13%)	1483 (86.22%)	802 (85.96%)
Mean age (sd)	47.00 (14.02)	46.93 (14.34)	47.11 (13.42)
Health Resource Utilization, mean (sd)			
Number of outpatient visits	10.04 (9.85)	10.04 (9.88)	10.04 (9.79)
Number of hospitalization	0.22 (0.66)	0.23 (0.71)	0.19 (0.56)
Number of rheumatologist visits	0.15 (0.74)	0.14 (0.73)	0.17 (0.76)
Medication Use, number (%)			
Cardiovascular drug use	228 (8.59%)	156 (9.07%)	72 (7.72%)
Angiotensin converting enzyme inhibitors	126 (4.75%)	85 (4.94%)	41 (4.39%)
Beta Blockers	155 (5.84%)	109 (6.34%)	46 (4.93%)
Alpha Blockers	8 (0.30%)	5 (0.29%)	3 (0.32%)
Calcium channel blockers	24 (0.90%)	16 (0.93%)	8 (0.86%)
Angiotensin receptor blocker	67 (2.53%)	43 (2.50%)	24 (2.57%)
Cardiac glycosides	6 (0.23%)	4 (0.23%)	2 (0.21%)
Diuretics	175 (6.60%)	125 (7.27%)	50 (5.36)
Antiarrhythmic agents	4 (0.15%)	2 (0.12%)	2 (0.21%)
Anticoagulants	32 (1.21%)	15 (0.87)	17 (1.82)
Nitrates	34 (1.28%)	24 (1.40%)	10 (1.07%)
Diabetes drugs	65 (2.45%)	46 (2.67%)	19 (2.04%)
Oral contraceptives	238 (8.97%)	147 (8.55%)	91 (9.75%)
Fibrates	11 (0.41%)	9 (0.52%)	2 (0.21%)
Statins	133 (5.01%)	80 (4.65%)	53 (5.68%)
Nsaids	603 (22.73%)	410 (23.84%)	193 (20.69%)
Cox2	114 (4.30%)	68 (3.95%)	46 (4.93%)
DMARDs	154 (5.80%)	92 (5.35%)	62 (6.65%)
Comorbidities			
Charlson index, mean (sd)	0.25 (0.68)	0.26 (0.71)	0.24 (0.63)
COPD related, number (%)	184 (6.94%)	130 (7.56%)	54 (5.79%)

Table1. Baseline characteristics of the incident SLE cohort

Model	GC exposure (unit)	Univariate HR (95% CI)	Multivariate HR (95% CI)
1	Current use (yes/no)	1.92 (1.16-3.17)	1.76 (1.06-2.94)
2	Current mean daily dose (5mg)	1.15 (1.04-1.27)	1.14 (1.03-1.26)
3	Total past cumulative dose (1g) concave function	1.65 (1.29-2.12)	1.59 (1.23-2.05)
4	Total cumulative duration of use (month) concave function	1.25 (1.08-1.45)	1.21 (1.04-1.41)

Table2. Unadjusted and adjusted cox regression models assessing the effects of the different GC exposure measures on the risk of CVD

Conclusion: We found that the initiation of GC use is associated an 82% increased risk of CVD during follow-up. Higher risk of CVD is also associated with current GC use, higher current and cumulative GC dose and longer duration of GC use.

Disclosure: L. Li, None; **H. Xie**, None; **E. Sayre**, None; **J. Avina-Zubieta**, None.

Abstract Number: 2782

Comparative Risks of Cardiovascular Disease Among SLE Patients Receiving Immunosuppressive Medications

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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Session Type: ACR Abstract Session

Session Time: 2:30PM–4:00PM

Table 1. Baseline characteristics of propensity-score matched Medicaid SLE patients (2000-2010), newly using MMF vs CYC and MMF vs AZA[a]

	MMF vs. CYC propensity score-matched cohort		MMF vs. AZA propensity score-matched cohort	
	MMF (n = 674)	CYC (n = 674)	MMF (n = 1,350)	AZA (n = 1,350)
Age, mean (SD)	35.9 (12.1)	35.7 (12.2)	34.8 (11.6)	34.5 (11.5)
Women, n (%)	612 (90.8)	607 (90.1)	1,234 (91.4)	1,245 (92.2)
Race/ethnicity, n (%)				
White	156 (23.2)	166 (24.6)	354 (26.2)	342 (25.3)
Black	338 (50.2)	321 (47.6)	611 (45.3)	631 (46.7)
Residing in South, n (%)	319 (47.3)	300 (44.5)	454 (33.6)	466 (34.5)
Comorbidities, n (%)				
Diabetes mellitus	116 (17.2)	107 (15.9)	147 (10.9)	146 (10.8)
Chronic kidney disease	19 (2.8)	19 (2.8)	19 (1.4)	22 (1.6)
Hyperlipidemia	71 (10.5)	53 (7.9)	99 (7.3)	88 (6.5)
Hypertension	296 (43.9)	325 (48.2)	418 (31.0)	420 (31.1)
Lupus nephritis[b]	368 (54.6)	363 (53.9)	410 (30.4)	427 (31.6)
Obesity	33 (4.9)	29 (4.3)	39 (2.9)	42 (3.1)
Smoking	49 (7.3)	55 (8.2)	71 (5.3)	70 (5.2)
Medications, n (%)				
Hydroxychloroquine	203 (30.1)	229 (34.0)	720 (54.0)	735 (54.4)
Cyclophosphamide	0	674 (100.0)	61 (4.5)	55 (4.1)
Azathioprine	73 (10.8)	70 (10.4)	0	1,350 (100.0)
60-d corticosteroid dose > 15mg/d[c]	198 (29.4)	257 (38.1)	319 (23.6)	392 (29.0)
NSAIDs	173 (25.7)	177 (26.3)	378 (28.9)	379 (28.1)

[a] Assessed during the 6-mo prior to and including the index date. Chi-square tests, Fisher's exact tests, Wilcoxon rank sum tests, Mann-Whitney U tests, and t-tests were used to compare groups (mycophenolate mofetil [MMF] vs. cyclophosphamide [CYC] and MMF vs. azathioprine [AZA]), p-values for all comparisons were greater than 0.05, with the exception of corticosteroid dose.

[b] Defined as ≥ 1 International Classification of Diseases, Ninth Revision code for glomerulonephritis, proteinuria, or renal failure on or after diagnosis of systemic lupus erythematosus (SLE).

[c] Determined during the 60 days prior to and including the index date, based on prednisone-equivalent doses.

Table 2. Intent-to-treat and as-treated analyses for MMF versus CYC for rates and risks of first CVD event[a]

	MMF (n=674)				CYC (n=674)			
	No. of cases	Total person-years	Incidence rate per 100 person-years (95% CI)	HR_{SD} (95% CI)	No. of cases	Total person-years	Incidence rate per 100 person-years (95% CI)	HR_{SD} (95% CI)
As-treated	22	524.6	4.19 (2.76-6.37)	0.68 (0.37, 1.22)	22	232.5	9.46 (6.23-14.4)	Reference
Intent-to-treat								
6 months	18	314.1	5.73 (3.61-9.10)	0.80 (0.43, 1.48)	23	315.0	7.30 (4.85-11.0)	Reference
12 months	29	588.2	4.93 (3.43-7.09)	0.75 (0.46, 1.21)	40	583.1	6.86 (5.03-9.35)	Reference

[a]Competing risk models adjusting for the competing risk of death, cumulative corticosteroid dose in the 60 days prior to and including the index date, hypertension, and hyperlipidemia. Corticosteroid dose was categorized as a mean daily dose of 0-5mg, >5-15 mg, and >15 mg. MMF = mycophenolate mofetil; CYC = cyclophosphamide; CVD = cardiovascular disease; 95% CI = 95% confidence interval; HR_{SD} = subdistribution hazard ratio.
[b]CVD events a composite of acute myocardial infarction, cerebrovascular accident, heart failure, percutaneous coronary intervention, or coronary artery bypass graft, determined by primary or secondary hospital discharge diagnosis for CVD event

Background/Purpose: Human studies examining cardiovascular disease (CVD) risk associated with immunosuppressants (IS) have been limited, but mycophenolate mofetil (MMF) was shown to suppress vascular smooth muscle and endothelial cell proliferation in murine models. In a large SLE Medicaid cohort, we compared CVD event risks among those initiating MMF vs. cyclophosphamide (CYC), used interchangeably for lupus nephritis and severe SLE manifestations, and MMF vs. azathioprine (AZA), used interchangeably longer-term for lupus nephritis or moderately active SLE.

Methods: Within the Medicaid Analytic eXtract (2000-2010; 29 most populated US states), we identified adults ages 18–65 years, with ≥2 International Classification of Diseases, Ninth Revision (ICD-9) SLE codes (710.0) ≥30 days apart. Among them, we identified those filling a new prescription for MMF, AZA, or CYC with continuous Medicaid enrollment ≥6 months prior to first prescription (index date). The CVD event outcome included hospitalized acute myocardial infarction, cerebrovascular accident, heart failure, percutaneous coronary intervention, or coronary artery bypass graft by validated administrative algorithms. Based on sociodemographic, comorbidity, and medication use variables during the baseline (pre-index date), we calculated propensity scores for MMF vs. CYC and MMF vs. AZA. After 1:1 propensity score matching, we estimated incidence rates for first CVD events after drug initiation. Fine-Gray regression models estimated subdistribution hazard ratios (HR_{SD}) for incident CVD events and 95% confidence intervals (95% CIs), accounting for the competing risk of death, additionally adjusting for cumulative corticosteroid dose, hypertension, and hyperlipidemia. Intent-to-treat (ITT) analyses followed subjects from index date for 6 or 12 months, censoring at first CVD event, Medicaid disenrollment or 12/31/2010. As-treated analyses additionally censored at > 60 day gaps in index medication.

Results: We studied 674 propensity-score matched pairs of MMF vs. CYC initiators and 1,350 pairs of MMF vs. AZA initiators. Baseline characteristics were balanced in the matched treatment groups (**Table 1**). In those with more severe SLE, the point estimate HR_{SD} for first CVD event for MMF vs. CYC (ref.) was < 1, although not statistically signifi-

Table 3. Intent-to-treat and as-treated analyses for MMF versus AZA for rates and risks of first CVD event[a]

	MMF (n=1,350)				AZA (n=1,350)			
	No. of cases	Total person-years	Incidence rate per 100 person-years (95% CI)	HR_{SD} (95% CI)	No. of cases	Total person-years	Incidence rate per 100 person-years (95% CI)	HR_{SD} (95% CI)
As-treated	29	1,051.3	2.76 (1.92-3.97)	0.76 (0.47, 1.25)	35	875.1	4.00 (2.87, 5.57)	Reference
Intent-to-treat								
6 months	18	634.9	2.84 (1.79-4.50)	0.63 (0.35, 1.14)	29	627.4	4.62 (3.21-6.65)	Reference
12 months	31	1,177.4	2.63 (1.85-3.74)	**0.58 (0.37, 0.91)**	54	1,169.2	4.62 (3.54-6.03)	Reference

[a]Competing risk models adjusting for the competing risk of death, cumulative corticosteroid dose in the 60 days prior to and including the index date, hypertension, and hyperlipidemia. Corticosteroid dose was categorized as a mean daily dose of 0-5mg, >5-15 mg, and >15 mg. MMF = mycophenolate mofetil; AZA = azathioprine; CVD = cardiovascular disease; 95% CI = 95% confidence interval; HR_{SD} = subdistribution hazard ratio.
[b]CVD events a composite of acute myocardial infarction, cerebrovascular accident, heart failure, percutaneous coronary intervention, or coronary artery bypass graft, determined by primary or secondary hospital discharge diagnosis for CVD event

cant: HR_{SD} 0.68 (95% CI 0.37, 1.22) in the as-treated analysis, and HR_{SD} 0.75 (95% CI 0.46, 1.21) in the 12-month ITT analysis (**Table 2**). In those with more moderate SLE, MMF was associated with a reduced risk of CVD vs. AZA (ref). This was non-significant in the as-treated analysis (HR_{SD}: 0.76 [95% CI 0.47, 1.25]), but significant in the 12-month ITT analysis: (**HR_{SD} 0.58 [95% CI 0.37, 0.91]**, **Table 3**).

Conclusion: In a rigorous head-to-head propensity score matched analysis of SLE Medicaid patients in a large longitudinal study, CVD event risks appeared to be reduced among those taking MMF vs. CYC or AZA, although only significantly lower for MMF vs. AZA in the 12 month ITT analysis. These comparisons adjusted for multiple factors, including corticosteroid use and lupus nephritis. We are obtaining longer Medicaid follow-up data to pursue this interesting finding.

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Abstract Number: 2783

Hydroxychloroquine Blood Levels and Risk of Thrombotic Events in Systemic Lupus Erythematous

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

	Mean HCQ blood level (mean ± SD)		
	With thrombosis	Without thrombosis	p-value
Any thrombosis	679.6 ± 470.7	860.5 ± 573.2	0.0393
Any venous thrombosis			
With superficial	673.4 ± 480.2	873.6 ± 574.6	0.0616
Without superficial	629.4 ± 491.3	872.4 ± 573.8	0.0249
Any arterial thrombosis	761.1 ± 551.8	853.7 ± 578.4	0.3720
Stroke	747.3 ± 599.2	856.3 ± 573.7	0.3457

Table 1. Prospective Analysis of Risk of Thrombosis and Mean Hydroxychloroquine Blood Levels

	Mean HCQ dose in mg/kg (mean ± SD)		
	With thrombosis	Without thrombosis	p-value*
Any thrombosis	4.60 ± 1.45	4.84 ± 1.34	0.0392
Any venous thrombosis			
With superficial	4.49 ± 1.48	4.84 ± 1.34	0.0081
Without superficial	4.45 ± 1.47	4.84 ± 1.35	0.0048
Any arterial thrombosis	4.73 ± 1.39	4.77 ± 1.37	0.7361
Stroke	4.75 ± 1.41	4.78 ± 1.37	0.8660

Table 2. Cross-Sectional Analysis of Risk of Thrombosis and Mean Prescribed Hydroxychloroquine Dose

Background/Purpose: The antimalarial drug hydroxychloroquine (HCQ) has a primary role in the treatment of systemic lupus erythematous (SLE). Beyond its pleiotropic immunomodulatory effects on TLR and type I interferon signaling, HCQ use has been found to be protective for thrombosis in SLE. Optimal dosing of HCQ in SLE is unknown. The longitudinal measurement of HCQ blood levels may provide an opportunity to individualize weight-based dosing strategies and reduce risk of toxicity. We examined the association of HCQ blood levels with thrombotic events in a longitudinal SLE cohort.

Methods: Patients with no HCQ level measured prior to the thrombosis were excluded. 812 SLE patients were included: 93% female, 43% African-American, 46% Caucasian. HCQ blood levels were quantified by liquid chromatography-tandem mass spectrometry. Mean HCQ blood levels (± SD) over all cohort visits prior to occurrence of thrombosis were calculated for each patient. Thromboses were defined as venous (DVT/PE or other venous) or arterial thrombosis (stroke, myocardial infarction, digital gangrene or other arterial).

Results: Thrombosis had occurred during prospective follow up in 44 patients (5.4%), venous in 3.0% and arterial in 2.5%. Lupus anticoagulant was strongly associated with a history of any thrombosis (OR 3.25, P< 0.0001), venous thrombosis (OR 3.53, P< 0.0001), and arterial thrombosis (OR 3.08, P< 0.0001). A prospective analysis (Table 1) shows that for any thrombosis and for venous thrombosis, the HCQ blood level was significantly lower. Higher prescribed doses of HCQ (as opposed to HCQ blood levels) were also associated with decreased odds of any thrombosis and also of venous thrombosis (Table 2) in a separate cross-sectional analysis (OR 0.88, P=0.04 and OR 0.83, P=0.009, respectively for each 1 mg/kg increase in prescribed HCQ).

Conclusion: HCQ blood levels are inversely associated with risk of any thrombosis and of venous thrombosis in patients with SLE in a prospective analysis. Reduction of HCQ dosing, as suggested by the American Academy of Ophthalmologists, could reduce or eliminate the benefit of hydroxychloroquine to prevent thrombosis.

Disclosure: M. Konig, None; **J. Li**, None; **M. Petri**, Eli Lilly and Company, 5, Exagen, 2, 5.

Abstract Number: 2784

Alterations in Inflammatory, TNF-Superfamily, and IFN-Associated Chemokines Precede Clinical Changes in SLEDAI After Methylprednisolone Treatment of SLE Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Clinical V: Emerging Knowledge of Current Treatments
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Background/Purpose: SLE is typified by a wide spectrum of clinical manifestations and immune dysregulation. Corticosteroids are almost universally effective, but marked by unacceptable side effects. An understanding of steroid efficacy signals may provide clues for safer, more targeted treatments.

Table 1. MP Induced Decrease in Select Immune Mediator Levels

SLE-associated Autoantibody Specificities (Serum)	Soluble Mediators (Plasma)		
	Inflammation	TNF Superfamily	IFN-associated Chemokines
dsDNA	IL-6	TNF-α**	MCP-1/CCL2***
chromatin	IL-2Rα***	TNFRI*	MIP-1α/CCL3
Ro/SSA	SCF****	TNFRII**	MIP-1β/CCL4
La/SSB	IL-10**	Fas*	MIG/CXCL9
Sm	TGF-β (Total)	BLyS****	IP-10/CXCL10***
SmRNP	*p≤0.05' **p<0.01; ***p<0.001; ****p<0.0001		
RNP	Significant decrease after MP (23±5 days post-Rx)		

Figure 1. Changes in hSLEDAI, BLyS*, and AutoAbs Post-Flare**

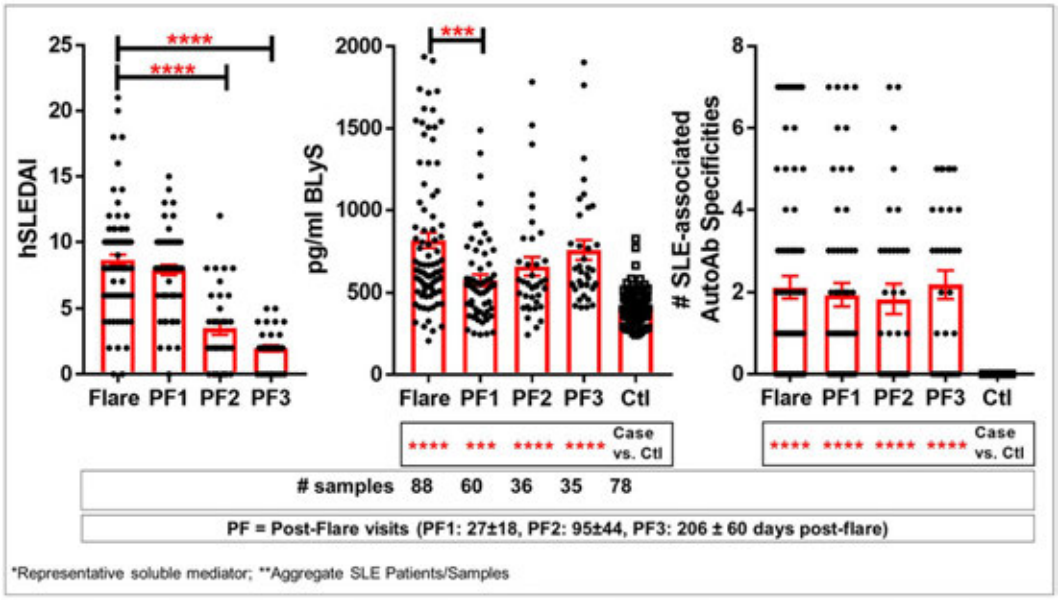
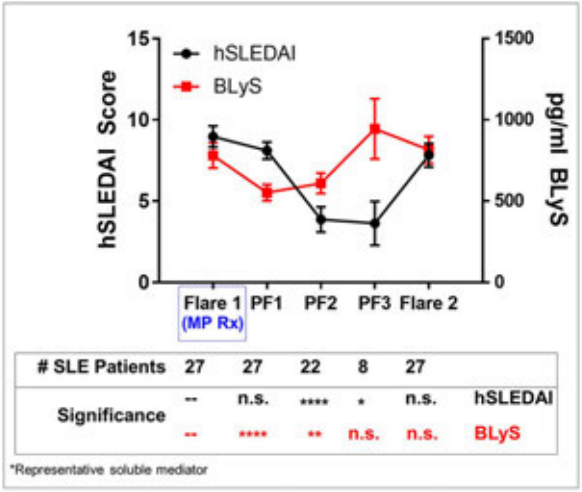


Figure 2. BLyS* Levels Increase Prior to New Flare



Methods: This study capitalized on entry samples from the Phase 2 **XmAb®5871** study to define which immune effectors are sensitive to methylprednisolone (MP). Plasma immune mediators and serum autoantibodies (AutoAbs) were evaluated by xMAP assay in 103 active SLE pts (≥ 4 ACR criteria) assessed pre- and post-MP Rx vs. race/sex/age-matched controls (n=78). Fifty-two patients were randomized to continue the study on placebo, and were serially followed for 191 ± 75 days for changes in clinical disease activity (by hybrid SLEDAI [hSLEDAI]). Biomarkers (**Table 1**) were measured in an average of 5 serially collected plasma samples (range 3-6, average of 45 days between sample visits). The advantage of this *BOLD* trial design was the control of MP Rx by intramuscular injection and required withdrawal of background immunosuppressants other than HCQ and ≤ 10 mg prednisone/equivalent/day.

Results: MP resulted in decreased levels of a number of immune mediators (all $p \leq 0.02$, **Table 1**) that were readily detected in SLE plasma and higher in cases vs. ctls ($p < 0.0001$); BLyS and Stem Cell Factor (SCF) levels were most affected ($p < 0.0001$). This occurred prior to or in conjunction with decreased hSLEDAI scores ($p = 0.0001$), decreased arthritis ($p = 0.0471$), and decreased serologic ($p = 0.0003$) features (**Figure 1**). Of 52 placebo pts with serial samples, 49 exhibited clinical disease flare at one or more visits, primarily due to increased arthritis and mucocutaneous features. When we evaluated samples at time of clinical disease flare and up to three post-flare samples thereafter in aggregate (**Figure 1**), we noted that specific immune mediators, including TNF-α, TNFRII, SCF, IL-2Rα, MCP-1, IP-10, and BLyS transiently decreased (all $p \leq 0.03$) in the first post-flare sample (PF1).These same mediators then increased again to clinical flare levels in PF2 and PF3 samples, preceding clinical evidence of new disease flares (**Figure 2**). Within the 145 ± 75 days between flares, there was little to no effect on number or type of SLE-associated AutoAbs (**Figure 1**).

Conclusion: Changes in a distinct subset of immune mediators are sensitive to MP Rx and were observed before or with hSLEDAI improvement. Subsequent resurgence of BLyS, TNF-α, TNFRII, SCF, IL-2Rα, MCP-1, and IP-10 preceded new clinical disease flares. This study underscores the probable utility of these markers for early intervention before clinical disease flares.

Disclosure: M. Munroe, Progentec Diagnostics, Inc., 2; **C. Guthridge**, None; **S. Kleckner**, None; **L. Tran**, None; **J. Guthridge**, DxTerity, 2; **D. Zack**, Xencor, Inc., 3; **J. James**, Abbvie, 5, Janssen, 5, Progentec, 2, Progentec Diagnostics, Inc., 2, Xencor, 2, Xencor, Inc., 2; **J. Merrill**, Abbvie, 5, Amgen, 5, Astellas, 5, AstraZeneca, 5, BMS, 2, 5, Celgene, 5, EMD Serono, 5, GSK, 2, 5, Idorsia, 5, ILTOO, 5, Immupharma, 5, Incyte, 5, Janssen, 5, Lilly, 5, Remegen, 5, Servier, 5, Xencor, Inc., 2.

Abstract Number: 2785

Cancer Risk in a Large Inception SLE Cohort: Effects of Age, Smoking, and Medications

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SESSION INFORMATION

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Background/Purpose: Many studies of cancer risk in SLE are limited by small sample size or use of administrative data, which rely on billing code diagnoses instead of clinical data. No studies to date focused on incident SLE. We studied cancer risk in the largest-ever cohort of clinically confirmed incident SLE patients.

Methods: Patients meeting ACR criteria for new-onset SLE (within 15 months of diagnosis) were enrolled into the SLICC Inception Cohort, across 32 centres. Patients are followed yearly using a standard protocol, with detailed data collection including SLE Disease Activity Index-2000 (SLEDAI-2K) and damage, and drugs in the past year. New cancer diagnoses are recorded by the examining physician at the annual study visit, and confirmed with chart review including pathology reports.

Multivariate proportional hazard regression was performed, using baseline variables for demographics (age at SLE onset, sex, race/ethnicity), and time-dependent variables for drugs (corticosteroids, anti-malarial drugs, immunosup-

Baseline characteristics	No Cancer (N=1608)	Cancer (N=60)
N (%) Female	1435 (89.2)	45 (75.0)
N (%) white race/ethnicity	783 (48.7)	41 (68.3)
Average age (years) at SLE diagnosis (SD)	34.2 (13.1)	44.7 (14.2)
SLE duration (months) at enrollment (SD)	5.6 (4.2)	5.5 (3.8)
Smoking ever	537 (33.4)	28 (46.7)
Steroids ever	1204 (74.9)	43 (71.7)
Cyclophosphamide ever	139 (8.6)	3 (5.0)
Azathioprine ever	458 (28.5)	16 (26.7)
Methotrexate ever	188 (11.7)	8 (13.3)
Mycophenolate ever	245 (15.2)	6 (10.0)
Antimalarial ever	1267 (78.8)	46 (76.7)
NSAID ever	319 (19.8)	11 (18.3)
Aspirin ever	306 (19.0)	13 (21.7)
Biologic ever	39 (2.4)	0 (0.0)
Positive anti-dsDNA ever	537 (33.4)	12 (20.0)

Table 1. SLE patients who later developed cancer and those remaining cancer-free

pressive drugs), smoking, and SLEDAI-2K. As well as cancer over-all, we evaluated risk factors for the most common cancer types.

All type of cancers	Unadjusted HR (95% CI)	Fully adjusted HR (95% CI)[a]	Partially adjusted HR (95% CI)[b]
Age at SLE Diagnosis	**1.06 (1.02, 1.1)**	**1.06 (1.01, 1.1)**	**1.06 (1.02, 1.1)**
Female Sex	**0.36 (0.2, 0.64)**	**0.48 (0.26, 0.9)**	**0.48 (0.26, 0.87)**
White Race/Ethnicity	2.37 (1.38, 4.09)	1.49 (0.82, 2.70)	1.51 (0.85, 2.68)
Top quartile SLEDAI at entry	1.68 (1.01, 2.80)	0.53 (0.23, 1.21)	0.56 (0.25, 1.26)
Smoking ever	0.40 (0.18, 0.89)	1.16 (0.68, 1.98)	1.15 (0.68, 1.94)
Steroids ever	0.71 (0.39, 1.30)	0.92 (0.47, 1.81)	1.04 (0.56, 1.95)
Cyclophosphamide ever	0.79 (0.36, 1.74)	1.19 (0.50, 2.82)	1.16 (0.51, 2.61)
Azathioprine ever	0.77 (0.45, 1.31)	1.02 (0.57, 1.84)	1.07 (0.61, 1.86)
Methotrexate ever	1.42 (0.78, 2.59)	1.62 (0.87, 3.04)	1.50 (0.82, 2.74)
Mycophenolate ever	0.78 (0.42, 1.45)	1.08 (0.55, 2.15)	1.07 (0.56, 2.05)
Antimalarial use ever	0.66 (0.34, 1.28)	0.67 (0.34, 1.32)	0.68 (0.35, 1.33)
Breast cancer	**Unadjusted HR (95% CI)**	**Fully adjusted HR (95% CI)[a]**	**Partially adjusted HR (95% CI)[b]**
Age at SLE Diagnosis	**1.06 (1.02, 1.1)**	**1.06 (1.01, 1.1)**	**1.06 (1.02, 1.10)**
Race/Ethnicity	1.14 (0.37, 3.54)	0.72 (0.20, 2.59)	0.73 (0.22, 2.35)
Top quartile SLE	0.29 (0.04, 2.29)	0.37 (0.04, 3.20)	0.39 (0.05, 3.10)
Smoking ever	1.01 (0.30, 3.36)	0.82 (0.24, 2.83)	0.82 (0.24, 2.84)
Steroids ever	0.65 (0.18, 2.43)	0.76 (0.17, 3.42)	0.94 (0.23, 3.78)
Cyclophosphamide ever	0.84 (0.33, 2.13)	3.29 (0.56, 19.5)	2.08 (0.44, 9.76)
Azathioprine ever	0.53 (0.14, 1.98)	0.60 (0.14, 2.54)	0.77 (0.20, 2.98)
Methotrexate ever	2.13 (0.64, 7.09)	2.66 (0.77, 9.25)	2.13 (0.64, 7.10)
Mycophenolate ever	0.55 (0.12, 2.52)	0.59 (0.11, 3.32)	0.80 (0.17, 3.82)
Antimalarial use ever	**0.25 (0.07, 0.84)**	**0.20 (0.06, 0.70)**	**0.24 (0.07, 0.81)**
Non-melanoma Cancer	**Unadjusted HR (95% CI)**	**Fully adjusted HR (95% CI)[a]**	**Partially adjusted HR (95% CI)[b]**
Age at SLE Diagnosis	**1.07 (1.03, 1.12)**	**1.06 (1.01, 1.11)**	**1.06 (1.01, 1.10)**
Sex	0.43 (0.09, 2.06)	0.96 (0.18, 5.19)	0.71 (0.14, 3.56)
Race/Ethnicity	8.94 (1.12, 71.5)	7.18 (0.75, 68.68)	5.18 (0.61, 43.8)
Smoking ever	2.23 (0.6, 8.33)	1.38 (0.34, 5.52)	1.26 (0.33, 4.84)
Steroids ever	0.80 (0.17, 3.85)	0.62 (0.09, 4.06)	1.51 (0.30, 7.53)
Cyclophosphamide ever	**4.69 (1.26, 17.5)**	**12.3 (2.37, 64.0)**	**9.29 (2.39, 36.0)**
Azathioprine ever	0.81 (0.20, 3.23)	0.81 (0.17, 3.96)	1.36 (0.32, 5.67)
Methotrexate ever	2.44 (0.61, 9.85)	3.55 (0.81, 15.54)	2.27 (0.56, 9.26)
Mycophenolate ever	1.67 (0.40, 6.95)	1.46 (0.29, 7.37)	2.68 (0.63, 11.43)
Antimalarial >5 years	0.15 (0.01, 1.49)	0.11 (0.01, 1.29)	0.13 (0.01, 1.37)
Biologic ever	1.59 (0.19, 13.2)	0.79 (0.08, 8.03)	2.13 (0.25, 18.2)

[a] All variables were considered in the model

[b] Adjusted for age at SLE diagnosis, sex, and race/ethnicity.

Table 2. Hazard Ratio for cancer in SLE (univariate, full model and partials models)

Results: Of 1848 new-onset SLE patients enrolled between 1999-2011, 1668 had at least one follow-up; these were the sample for the current analysis. End date was the first of death, last visit, or end of study interval for this analysis (Aug. 2015). Baseline demographics are shown in Table 1.

Over 14,215 years (mean 8.5 years) there were 60 cancers (incidence 4. 2 events per 1,000 patient-years). This included 12 breast cancers, 9 non-melanoma skin, 7 lung, 6 hematological, 5 melanoma, 5 prostate, 3 cervical, 3 renal, 2 gastric, 2 head and neck, 2 thyroid, and one each rectal, sarcoma, thymoma, and uterine. Almost half of the cancer cases (including all of the lung cancers) were associated with baseline smoking, versus only one-third of those patients who did not develop cancer. Univariate analyses of all cancer types suggested a higher risk of cancer among patients of white race/ethnicity and among those with the highest quartile of disease activity at cohort entry.

However, the multivariate proportional hazard regression indicated that among SLE patients, the over-all cancer risk was related primarily to male sex and older age at SLE diagnosis. In those analyses, the effect of race/ethnicity was not clearly evident, and the point estimate for highest quartile of disease activity actually reversed to suggest a non-significant trend towards lower cancer risk.

In the multivariate analyses specifically for breast cancer, age at SLE diagnoses remained a risk factor, and anti-malarials were associated with a decreased risk. This effect of anti-malarials was not clearly seen for any other cancer type. For non-melanoma skin cancer, both age at SLE diagnosis and cyclophosphamide were strongly linked with risk.

Conclusion: This is the first large, multicentre cohort study to clearly show how different cancer types in SLE are associated with specific risk factors. Additional follow-up may allow additional determination of the possible effects of disease activity and drugs on cancer subtypes.

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Abstract Number: 2786

Renal Histopathological Classifications Predict the Renal Outcomes of Plasma Exchange-Treated ANCA-Associated Vasculitides with Renal Failure

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated II
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: ANCA-associated vasculitides (AAVs) are the most frequent cause of rapidly progressive glomerulonephritis (RPGN), for which the major prognostic issue is the risk of developing end-stage renal disease (ESRD) or dying. The large, multicenter, prospective PEXIVAS trial, including patients with severe AAVs, i.e. lung hemorrhage and/or renal failure (estimated glomerular filtration rate (eGFR) < 50 ml/min/1.73 m2),showed that plasma exchanges (PLEX) did not lower the ESRD or death risk for AAV patients, but the prognostic impact of renal histology on the renal outcome and response to PLEX was not assessed.We aimed to evaluate whether histopathological findings could predict the renal outcome of PLEX-treated AAV patients.

Methods: This retrospective, multicenter study included patients with microscopic polyangiitis, granulomatosis with polyangiitis or renal-limited vasculitis, fulfilling ACR criteria or Chapel Hill Consensus Conference definitions. All patients had a renal biopsy and were treated with PLEX. Two histopathological classifications were evaluated from renal biopsy reports: Berden's, distinguishing 4 categories (focal, crescentic, mixed and sclerotic), using the percentages of different glomeruli lesions; and Brix's, discerning 3 risk groups (low, medium or high), using the percentages of normal glomeruli, tubular atrophy and interstitial fibrosis, and baseline eGFR. The primary endpoint was dialysis independence and survival at month (M) 12. Secondary endpoints were eGFR >30 ml/min/1.73 m^2at M12, and delta eGFR >15 ml/min/1.73 $m^2$from baseline to M12.

Results: We included 163 patients from 19 centers: 99 (61%) men; 92 (56%) MPO-ANCA+, 65 (40%) PR3-ANCA+; mean±SD baseline serum creatinine 555±274 µmol/L, 62 (38%) with alveolar hemorrhage; 139 (85%) given cyclophosphamide and 30 (18%) received rituximab; 74 (45%) required dialysis at baseline. Mean number of PLEX was 7.0±2.3.

Berden categories were focal (19%), crescentic (39%), mixed (20%) and sclerotic (21%). Brix risk groups were low (11%), medium (48%) and high (41%). Both Berden and Brix histopathological classifications on baseline renal biopsies were associated with the primary endpoint, i.e. dialysis independence and survival at M12 (χ2 24.9; P< 0.0001,

and χ2 11.7; P=0.003, respectively).In contrast, baseline serum creatinine levels did not differ betweenfavorable and poor-prognosis groups (respectively:526±252 µmol/L vs. 597±300 µmol/L; P=0.11). Secondary endpoints were also associated with Berden and Brix classifications, respectively: achievement of eGFR >30 ml/min/1.73 m2at M12 (χ2 14.0; P=0.003, and χ2 17.3; P=0.0002); andimproved renal function with delta eGFR >15 ml/min/1.73 m2from baseline to M12 (χ2 18.1; P=0.0004, and χ2 17.7; P=0.0001).

Conclusion: In a cohort of AAV patients treated with PLEX for RPGN, our findings suggest that renal biopsy classification at diagnosis strongly predicted renal outcome at M12. AAV patients with RPGN should undergo renal biopsy to help physicians identify who among them would benefit the most from PLEX.

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Predictors of Renal Involvement in ANCA-Associated Vasculitis

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SESSION INFORMATION
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Background/Purpose: Renal involvement in the context of anti-neutrophil cytoplasm antibody (ANCA)-associated vasculitis (AAV) is associated with significant morbidity and higher mortality rates. This study examined predictive factors associated of renal involvement in AAV within a large, international cross-sectional cohort.

Methods: Univariate and multivariate analyses were performed to identify risk factors associated with renal disease, which was defined as i) an increase of serum-creatinine > 30%; ii) a fall in creatinine-clearance < 25%; or iii) haematuria attributable to active vasculitis.

Results: Of the 1230 patients eligible, 723 patients (58.8%) presented with renal involvement. The majority of patients with microscopic polyangiitis (82.2%) and granulomatosis with polyangiitis (58.6%) had renal involvement, while 26.4% with eosinophilic granulomatosis with polyangiitis presented with renalvasculitis. The following clinical factors were more common among patients with renal disease that among patients without renal disease. Older age (57.9 versus 53.9 years, p=0.001), fever (39.8% versus 23.7%, p< 0.001), fatigue (68.0% versus 50.1%, p=0.005), weight loss (43.4% versus 26.2%, p=0.001), polyarthritis (19.4% versus 15.0%, p=0.036), petechiae/purpura (18.0% versus 12.0%, p=0.022), pulmonary haemorrhage (24.8% versus 7.1%, p=0.014), gastrointestinal symptoms (25.9% versus 15.8%, p=0.002), serum albumin below 30 g/L (36.6% versus 11.6%, p< 0.001), higher CRP

Table 1. Disease manifestations and their association with renal involvement in cases with ANCA-associated vasculitis. Multivariate analysis was performed when variables were significantly associated with renal involvement in univariate analysis. Abbreviations used: OR: odds ratio, CI: confidence interval, ENT: ear, nose and throat, PAH: pulmonary alveolar haemorrhage.

	Renal involvement (+)	Renal involvement (-)	Univariate analysis p-value	OR (95% CI)	Multivariate analysis p-value
Multisystemic disease	460/723 (63.6%)	276/507 (54.4%)	0.001	1.16 (0.91-1.49)	0.234
General manifestations	628/723 (86.9%)	363/507 (71.6%)	<0.001	1.21 (0.79-1.83)	0.379
Fever	288/723 (39.8%)	120/507 (23.7%)	<0.001	1.97 (1.35-2.88)	<0.001
Fatigue	492/723 (68.0%)	254/507 (50.1%)	<0.001	1.55 (1.14-2.10)	0.005
Fever above 38°C (100.4F)	255/723 (35.3%)	126/507 (24.9%)	<0.001	1.16 (0.78-1.72)	0.458
Weight loss	314/723 (43.4%)	133/507 (26.2%)	<0.001	1.62 (1.23-2.12)	0.001
Musculoskeletal manifestations	447/723 (61.8%)	254/507 (50.1%)	<0.001	1.26 (0.81-1.97)	0.306
Polyarthritis	140/723 (19.4%)	76/507 (15.0%)	0.048	1.39 (1.02-1.89)	0.036
Arthralgia (joint pain)	355/723 (49.1%)	194/507 (38.3%)	<0.001	1.14 (0.76-1.71)	0.529
Myalgia (muscle pain) or muscle cramps	188/723 (26.0%)	105/507 (20.7%)	0.035	1.12 (0.80-1.57)	0.506
Cutaneous manifestations	269/723 (37.2%)	170/507 (33.5%)	0.204		
Petechiae or purpura	130/723 (18.0%)	61/507 (12.0%)	0.005	1.47 (1.06-2.05)	0.022
Gangrene	11/723 (1.5%)	8/507 (1.6%)	1.000		
Ulcer	25/723 (3.5%)	23/507 (4.5%)	0.371		
Eye manifestations	212/723 (29.3%)	122/507 (24.1%)	0.044	1.09 (0.75-1.59)	0.650
Red eye(s)	122/723 (16.9%)	52/507 (10.3%)	0.0017	1.52 (0.91-2.52)	0.107
Proptosis /Exophthalmos	5/723 (0.7%)	19/507 (3.7%)	<0.001	0.18 (0.06-0.50)	0.001
Conjunctivitis	44/723 (6.1%)	12/507 (2.4%)	0.002	1.74 (0.84-3.60)	0.135
Scleritis or episcleritis (inflammation of the sclera)	64/723 (8.9%)	29/507 (5.7%)	0.048	1.19 (0.68-2.08)	0.549
ENT manifestations	302/723 (41.8%)	267/507 (52.7%)	<0.001	0.95 (0.70-1.29)	0.741
Saddle nose deformity (nasal bridge collapse)	10/723 (1.4%)	30/507 (5.9%)	<0.001	0.38 (0.17-0.83)	0.015
Sensorineural hearing loss	44/723 (6.1%)	45/507 (8.9%)	0.073		
Nasal polyps	35/723 (4.8%)	82/507 (16.2%)	<0.001	0.31 (0.20-0.47)	<0.001
Nasal septal defect / perforation	16/723 (2.2%)	51/507 (10.1%)	<0.001	0.27 (0.15-0.50)	<0.001
Respiratory manifestations	512/723 (70.8%)	322/507 (63.5%)	0.008	1.12 (0.41-3.11)	0.823
Upper airway disease	283/722 (39.1%)	280/507 (55.2%)	<0.001	0.89 (0.54-1.46)	0.636
Respiratory distress /pulmonary fibrosis/asthma	164/341 (48.1%)	136/146 (93.2%)	<0.001	0.08 (0.04-0.19)	<0.001
Haemoptysis, PAH	179/723 (24.8%)	36/507 (7.1%)	<0.001	5.23 (1.39-19.63)	0.014
Wheeze or evidence of obstructive airway disease	59/723 (8.2%)	116/507 (22.9%)	<0.001	0.29 (0.16-0.52)	<0.001
Respiratory compromise requiring oxygen	78/723 (10.8%)	32/507 (6.3%)	0.008	1.51 (0.73-3.11)	0.268
Respiratory failure requiring intubation	25/723 (3.5%)	5/507 (1.0%)	0.007	2.90 (0.58-7.59)	0.261
Cardiovascular manifestations	105/723 (14.5%)	94/507 (18.5%)	0.070		
Cardiomyopathy	12/723 (1.7%)	23/507 (4.5%)	0.003	0.30 (0.08-1.08)	0.065
Arrhythmia	15/723 (2.1%)	18/507 (3.6%)	0.151		
Gastrointestinal manifestations	187/723 (25.9%)	80/507 (15.8%)	<0.001	2.19 (1.34-3.58)	0.002
Bloody diarrhea	21/723 (2.9%)	8/507 (1.6%)	0.181		
Peritonism (rigid abdomen with rebound tenderness)	2/723 (0.3%)	1/507 (0.2%)	1.000		
Neurologic manifestations	266/723 (36.8%)	216/507 (42.6%)	0.044	0.95 (0.70-1.29)	0.728
Neuropathy	149/723 (20.6%)	139/507 (27.4%)	0.006	0.71 (0.50-1.01)	0.059
Photophobia	17/723 (2.4%)	5/507 (1.0%)	0.083		
Occipital or cervical seizure	23/723 (3.2%)	5/507 (1.0%)	0.011		
Mononeuritis multiplex	57/723 (7.9%)	70/507 (13.8%)	0.001		
Motor neuropathy (not due to radiculopathy)	73/723 (10.1%)	63/507 (12.4%)	0.230		
Sensory neuropathy (not due to radiculopathy)	125/723 (17.3%)	104/507 (20.5%)	0.158		

(105.86 ± 96.56 versus 54.25 ± 61.60, p=0.038), low C3 at baseline (7.6% versus 2.9%, p=0.015), ANCA positivity (p< 0.001), myeloperoxidase-ANCA (43.9% versus 29.6%, p< 0.001) and proteinase 3-ANCA (48.4% versus 40.5%, p=0.020).Patients with proptosis/exophthalmos (0.7% versus 3.7%, p=0.001), saddle nose deformity (1.4% versus 5.9%, p=0.015), nasal polyps (4.8% versus 16.2%) and nasal septal defect/perforation (2.2% versus 10.1%) (p< 0.001 each), respiratory distress/pulmonary fibrosis/asthma (48.1% versus 93.2%, p< 0.001) or wheeze/obstructive

	Renal involvement (+)	Renal involvement (-)	Univariate analysis p-value	OR (95% CI)	Multivariate analysis p-value
Demographics					
Age (years)	57.90 ± 16.38	53.89 ± 15.61	**<0.001**	1.013 (1.006-1.021)	**0.001**
Renal parameters					
Maximum creatinine (µmol/L)	2.76 ± 2.69	0.92 ± 0.43	**<0.001**	1.073 (0.533-2.161)	0.844
Rise in serum creatine by > 30% or fall in creatine clearance by > 25%	353/676 (52.2%)	20/486 (4.1%)	**<0.001**	16.807(10.247-27.566)	**<0.001**
Albumin below 30 g/L	248/678 (36.6%)	54/465 (11.6%)	**<0.001**	2.421 (1.642-3.569)	**<0.001**
Protein on urine dipstick	575/709 (81.1%)	84/495 (17.0%)	**<0.001**	11.683 (7.194-18.971)	**<0.001**
Blood on urine dipstick	690/710 (97.2%)	0/494 (0.0%)	**<0.001**	-	-
Leucocytes or nitrites on urine dipstick	238/674 (35.3%)	34/491 (6.9%)	**<0.001**	2.285 (1.241-4.209)	**0.008**
Red blood cell casts in urine	208/570 (36.5%)	0/395 (0.0%)	**<0.001**	6.357 (4.208-9.604)	**<0.001**
24 hour urine protein > 1g/d	212/494 (42.9%)	20/289 (6.9%)	**<0.001**	3.287 (1.601-6.746)	**0.001**
Markers of inflammation, Immunologic Parameters, and Autoantibodies					
Maximum ESR (mm/hr)	73.29 ± 35.06	49.14 ± 34.10	**<0.001**	1.651 (0.831-3.277)	0.152
Maximum CRP (mg/L)	105.86 ± 96.56	54.25 ± 61.60	**<0.001**	2.058 (1.042-4.063)	**0.038**
Peripheral blood eosinophilia (>500/µl)	65/723(9.0%)	147/507 (29.0%)	**<0.001**	0.764 (0.380-1.536)	0.450
Cryoglobulins	15/190 (7.9%)	8/101 (7.9%)	**1.000**	-	-
Monoclonal immunoglobulin	4/723 (0.6%)	0/507 (0.0%)	**0.148**	-	-
Low C3	34/446 (7.6%)	6/210 (2.9%)	**0.022**	3.864 (1.295-11.532)	**0.015**
Low C4	26/446 (5.8%)	7/211 (3.3%)	**0.186**	-	-
Autoantibodies					
cANCA (IF)	326/620 (52.6%)	153/412 (37.1%)	**<0.001**	3.999 (2.424-6.598)	**<0.001**
pANCA (IF)	246/611 (40.3%)	125/404 (30.9%)	**0.003**	4.107 (2.489-6.775)	**<0.001**
PR3 ANCA (ELISA)	331/684 (48.4%)	186/459 (40.5%)	**0.009**	3.399 (1.216-9.500)	**0.020**
MPO ANCA (ELISA)	300/683 (43.9%)	134/453 (29.6%)	**<0.001**	7.970 (2.737-23.204)	**<0.001**
Other ANCA	14/262 (5.3%)	11/175 (6.3%)	**0.680**		
Anti GBM AB	10/353 (2.8%)	0/74 (0.0%)	**0.222**	-	-
RF	200/450 (44.4%)	89/285 (31.2%)	**<0.001**	1.401 (0.596-3.293)	**0.439**
ACPA	8/196 (4.1%)	10/118 (8.5%)	**0.133**	-	-
ANA	141/613 (23.0%)	68/383 (17.8%)	**0.055**	-	-
dsDNA AB	8/396 (2.0%)	6/199 (3.0%)	**0.567**	-	-
Anti-Scl-70 (topoisomerase I)	5/304 (1.6%)	0/189 (0.0%)	**0.162**	-	-
Lupus anticoagulant	15/110 (13.6%)	3/70 (4.3%)	**0.045**	2.880 (0.532-15.603)	**0.220**
Anti-cardiolipin IgG	12/164 (7.3%)	4/109 (3.7%)	**0.294**	-	-
Anti-cardiolipin IgM	6/141 (4.3%)	5/100 (5.0%)	**0.766**	-	-
Anti ß2-glycoprotein 1	6/109 (5.5%)	3/66 (4.5%)	**1.000**	-	-

Table 2. Laboratory parameters associated with renal involvement. Significant associations in univariate analysis were either confirmed or rejected by multivariate analysis. Abbreviations used: OR: odds ratio, CI: confidence interval, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, ANCA: anti-neutrophil cytoplasm antibody, c-ANCA: cytoplasmic ANCA, p-ANCA: perinuclear ANCA, PR3: proteinase 3, MPO: myeloperoxidase, ELISA: enzyme-linked immunosorbent assay, GBM: glomerular basement membrane, RF: rheumatoid factor, ACPA: anti-cyclic citrullinated peptide antibody, ANA: anti-nuclear antibody, dsDNA AB: double-stranded DNA antibody.

airway disease (8.2% versus 22.9%, p< 0.001) had a lower likelihood of developing renal involvement. (see Table 1 and Table 2).

Conclusion: In this large international study, we identified clinical factors associated with renal involvement in AAV, including concomitant pulmonary alveolar haemorrhage, low C3, and elevated C-reactive protein. Further large studies arenecessary to confirm our findings.

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Abstract Number: 2788

Longitudinal Changes in the Nasal Microbiome and Disease Activity in Patients with Granulomatosis with Polyangiitis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Vasculitis – ANCA-Associated II
Session Type: ACR Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Microbial organisms have been theorized to contribute to disease activity in granulomatosis with polyangiitis (GPA) but little is known about what changes occur in commensal microbes in association with disease relapse. This longitudinal study examined compositional changes in the nasal microbiome and its association with disease activity in patients with GPA. We hypothesized that the overgrowth of pathogenic bacteria in the nasal cavity is associated with local and systemic disease activity (or flare).

Methods: Nasal bacterial composition was examined using 16S rRNA gene sequencing of DNA obtained from nasal swabs of 19 patients with GPA who were followed longitudinally (approximately every 3 months) for a total of 78 visits. Nine patients had at least 1 visit with a flare visit and 10 patients remained in remission during follow-up. Disease activity was determined by BVAS/WG. The main variables of interest were the relative abundance of the 5 most abundant taxa (or bacterial genera) as well as ratios between these taxa (to understand potential interactions between bacteria). As opposed to genus-level comparisons, species-level assignment was predicted based on the 16S gene (R package *Unassigner*) since bacterial interactions and effects can be specific to a particular species. Linear mixed effects models evaluated the association between bacteria and disease activity, accounting for repeated measures within an individual. Models adjusted for use of antibiotic and immunosuppressive medications, and sinus irrigation.

Results: Among the 19 patients enrolled, 10 patients never relapsed while 9 patients had 12 flares during follow-up. Of the 12 flare visits, 8 had clinically-identifiable sinonasal involvement and only 1 flare visit was a patient receiving full-dose trimethoprim-sulfamethoxazole. *Corynebacterium*, *Propionibacterium*, *Staphylococcus*, *Alloiococcus*, and *Streptococcus* were the most abundant bacterial genera in the samples. A higher ratio of the bacterial genera *Staphylococcus* to *Corynebacterium* occurred at the visit prior to flare, even after adjusting for medications and sinus irrigation ($P < 0.01$; **Figure 1**). Higher resolution species-level examination found *Corynebacterium tuberculostearicum* was associated with disease activity while other nasal commensals, such as *Propionibacterium acnes* and *Staphylococcus epidermidis*, decreased during flare ($P = 0.04$; **Figure 2**).

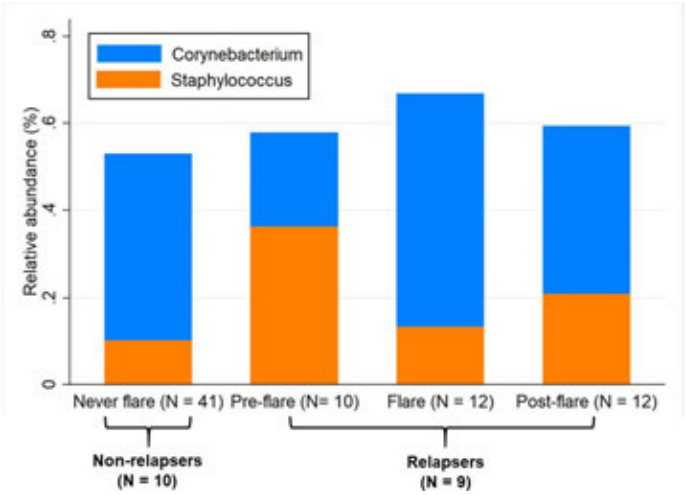

Figure 1. Genus-level analysis demonstrates an increase in Staphylococcus to Corynebacterium ratio that occurs prior to development of flare in granulomatosis with polyangiitis. Stacked bar plots show the median relative abundance of bacterial genera Staphylococcus and Corynebacterium in 2 groups: patients who never flare ("Non-relapsers"; N = 10) and those who develop a flare ("Relapsers"; N = 9). The Relapsers are further separated by visit to show longitudinal changes over time. A significant increase in the Staphylococcus to Corynebacterium ratio occurs prior to the development of a flare (adjusted $P < 0.01$). Patients who do not flare have a consistently lower ratio of Staphylococcus to Corynebacterium.

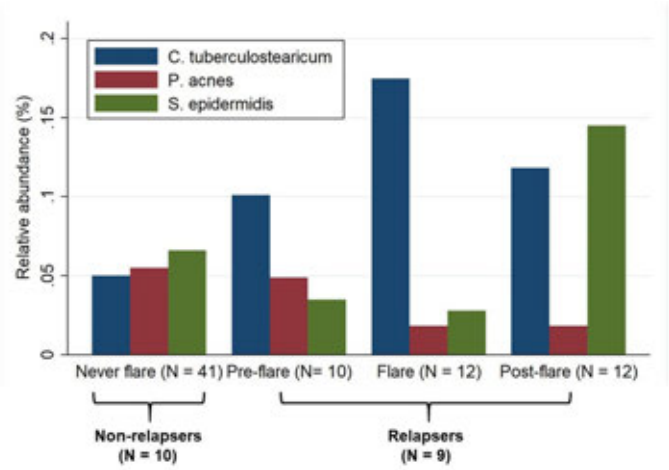

Figure 2. Predicted species-level assignments suggest increase in abundance of species Corynebacterium tuberculostearicum is associated with flare in granulomatosis with polyangiitis. Evaluation of most probable bacterial species (based on 16S gene sequences) identify an increase in the abundance of C. tuberculostearicum during flare while other nasal commensals, such as Propionibacterium acnes and Staphylococcus epidermidis, decrease during flare ($P = 0.04$).

Conclusion: In patients with GPA, significant changes occur in the nasal microbial composition over time in association with vasculitis disease activity. A higher ratio of *Staphylococcus* to *Corynebacterium* prior to development of flare suggests bacterial interactions may be an important risk factor for flare, possibly mediated through the outgrowth of *C. tuberculostearicum*. Notably, prior studies have shown that *C. tuberculostearicum* has pathogenic potential to cause sinusitis in murine models. These findings support the long-standing theory that overgrowth of pathogenic bacteria are potentially implicated in the disease process of GPA.

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Abstract Number: 2789

Neutrophil Extracellular Traps Induce Tissue-Invasive Macrophages in Granulomatosis with Polyangiitis Dominated by Ear, Nose and Throat Manifestations

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SESSION INFORMATION
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Session Type: ACR Abstract Session
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Background/Purpose: Granulomatosis with polyangiitis (GPA) is a small vessel vasculitis characterized by acute and chronic tissue destruction in the nose, sinuses, lungs and kidneys. In a subset of patients, tissue inflammation predominantly occurs in the ear, nose, throat and eye (ENT-dominated) manifesting with tissue-invasive and space-consuming lesions, such as saddlenose, septal perforation, orbital and ear bony wall destruction, and epiglottitis. ENT-dominated GPA is often chronic-relapsing and associated with autoantibodies against PR-3. A critical element in the pathogenesis of GPA is the production of neutrophil extracellar traps (NETs) from dying neutrophils. Whether NET-related pathology is different in distinct subsets of GPA patients is unknown. We have compared NET-induced inflammatory responses in patients with systemic GPA versus ENT-dominated GPA.

Methods: Patients with renal versus ENT-dominated GPA (rGPA; ENT-GPA) were recruited from a database that prospectively follows vasculitis patients. Patients with disease duration of >5 years and matched for immunosuppressive therapy were enrolled. Neutrophils and monocytes from rGPA, ENT-GPA and age-gender matched healthy donors were isolated from peripheral blood. NETosis was induced in isolated neutrophils and quantified with SYTOX green (ThermoFisher) and analyzed by flow cytometry. Isolated NETS were cocultured with monocyte-derived macrophages and the induction of pro-inflammatory mediators was examined by RT-PCR and flow cytometry. Tissue invasiveness of monocytes/macrophages was measured in a 3D matrix system.

Results: Neutrophils from patients with ENT-GPA had more intense NETosis with higher frequencies of netting neutrophils ($P < 0.01$) and more NETs released ($P < 0.01$). Purified NETs functioned as potent activators of monocytes and macrophages and induced a pro-inflammatory phenotype. Netting neutrophils from ENT-GPA were more efficient in upregulating pro-inflammatory cytokines in monocytes/macrophages ($P < 0.01$) when compared to neutrophils isolated from rGPA or age-matched controls. Measurements of matrix-invasive capacity of monocytes and macrophages exposed to control and patient-derived NETs revealed that ENT-GPA-derived NETs were able to induce monocytes and macrophages that were highly efficient in tissue invasion.

Conclusion: Neutrophils from patients with specified GPA disease patterns differ in NET formation. Highly efficient NETosis is associated with predominance of ENT manifestations. NETs are recognized by monocytes and macrophages and act as pro-inflammatory triggers. NETs derived from ENT-GPA patients are strong inducers of a tissue-destructive and invasive phenotype, reminiscent of the clinical manifestations in ENT-dominated GPA.

Disclosure: M. Akiyama, None; **N. Ibrahim**, None; **M. Zeisbrich**, None; **P. Hwang**, None; **J. Goronzy**, None; **C. Weyand**, Kiniska Pharmaceuticals, 2.

Abstract Number: 2790

Platelet Mediates Neutrophil Extracellular Traps Formation via TLR Signaling in ANCA-associated Vasculitis

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SESSION INFORMATION
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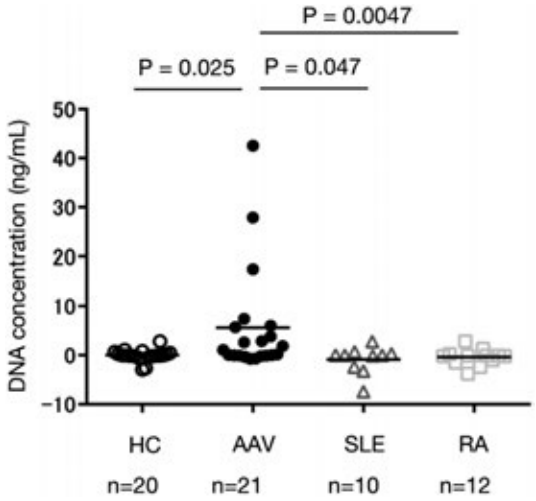
Background/Purpose: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is an autoimmune disease that affects small- to medium-sized blood vessels and causes vascular inflammation and multiple organ damage. The pathogenesis of AAV is still unclear. However, neutrophil extracellular traps (NETs) is thought to be one of important triggers of vascular endothelial dysfunction in the disease process of AAV, and it is recently reported that platelets stimulated via toll-like receptor (TLR) pathways can induce NETs formation. Thus, platelets may be alternative key players in AAV pathogenesis. In this study, we investigated the role of platelets and involvement of TLR signaling in the process of NETs formation in patients with AAV.

Methods: Twenty-one patients with AAV (granulomatosis with polyangiitis [GPA]: n=12, microscopic polyangiitis [MPA]: n=9) who visited Keio University Hospital between August 2017 and October 2018 were consecutively enrolled. Ten SLE, 12 RA, and 20 healthy controls (HCs) were included as controls. All AAV patients fulfilled the 2012 Revised International Chapel Hill Consensus Conference Nomenclature. Expression of platelet-associated TLRs were examined using flow cytometry. Clinical information was obtained from patients' record and association with expression of TLR was also examined. In order to examine functional involvement of platelets in NETs formation, platelets from AAV patients or HCs were co-cultured with peripheral neutrophils. In some experiments, platelets were stimulated with TLR agonist in advance. NETs formation visualized by Picogreen was detected and quantified using confocal fluorescent microscopy.

Results: As shown in the figure, platelets from AAV patients increased NETs formation compared with those from RA ($p=0.0047$), SLE ($p=0.047$) or HC ($p=0.025$). Flow cytometric analysis revealed that the expression of TLR9 ($p=0.0011$) but not other TLRs, such as TLR2 ($p=0.71$) and TLR4 ($p=0.93$), in platelets was elevated in platelets from AAV patients compared with HCs. In particular, the proportion of $TLR9^{+}$platelets was elevated in patients with pulmonary involvement compared with those without ($p=0.012$), and was correlated with patients' serum Krebs Von Den Lungen-6 level ($r^2=0.31$, $p=0.049$). Interestingly, we found that TLR9 agonist (CpG oligodeoxynucleotides)-stimulated platelets from AAV patients induced NETs formation compared with control oligodeoxynucleotides-stimulated platelets.

Conclusion: These results suggest that platelets play a key role in NETs formation in the pathogenesis of AAV and TLR9 signaling is involved in this process.



Summary of DNA concentration from neutrophils induced by exposure to platelets from HC (n=20) and patients with AAV (n=21), SLE (n=10) and RA (n=12).

Disclosure: K. Matsumoto, None; **H. Yasuoka**, None; **K. Suzuki**, AbbVie, 2, Bristol-Myers Squibb, 2, Chugai, 2, Daiichi-Sankyo, 2, Eisai, 2, Fuji Film, 2, Kissei, 2, Mitsubishi Tanabe, 2, Ono, 2, Pfizer, 2, Takeda Pharmaceutical, 2; **T. Takeuchi**, Mitsubishi Tanabe Pharma Co., 2, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8.

Abstract Number: 2791

Treatment Response Criteria for Anti-neutrophil Cytoplasmic Antibodies (ANCA)-vasculitis: Results of a Scoping Review

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SESSION INFORMATION
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Session Title: Vasculitis – ANCA-Associated II
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Session Time: 2:30PM–4:00PM

Background/Purpose: A comprehensive assessment of outcome measures to assess response to treatment in ANCA-associated vasculitis (AAV) is necessary to implement.

Methods: We performed a scoping review of available randomized controlled trials (RCTs) to assess the tools previously used as outcome measures in clinical trials of AAV. Medline, Embase, Cochrane Central and ClinicalTrials.gov were searched from inception until November 26, 2018 to identify RCTs enrolling patients with granulomatosis with polyangiitis (GPA) and/or microscopic polyangiitis (MPA). This study is part of an ongoing international project to develop response criteria for AAV.

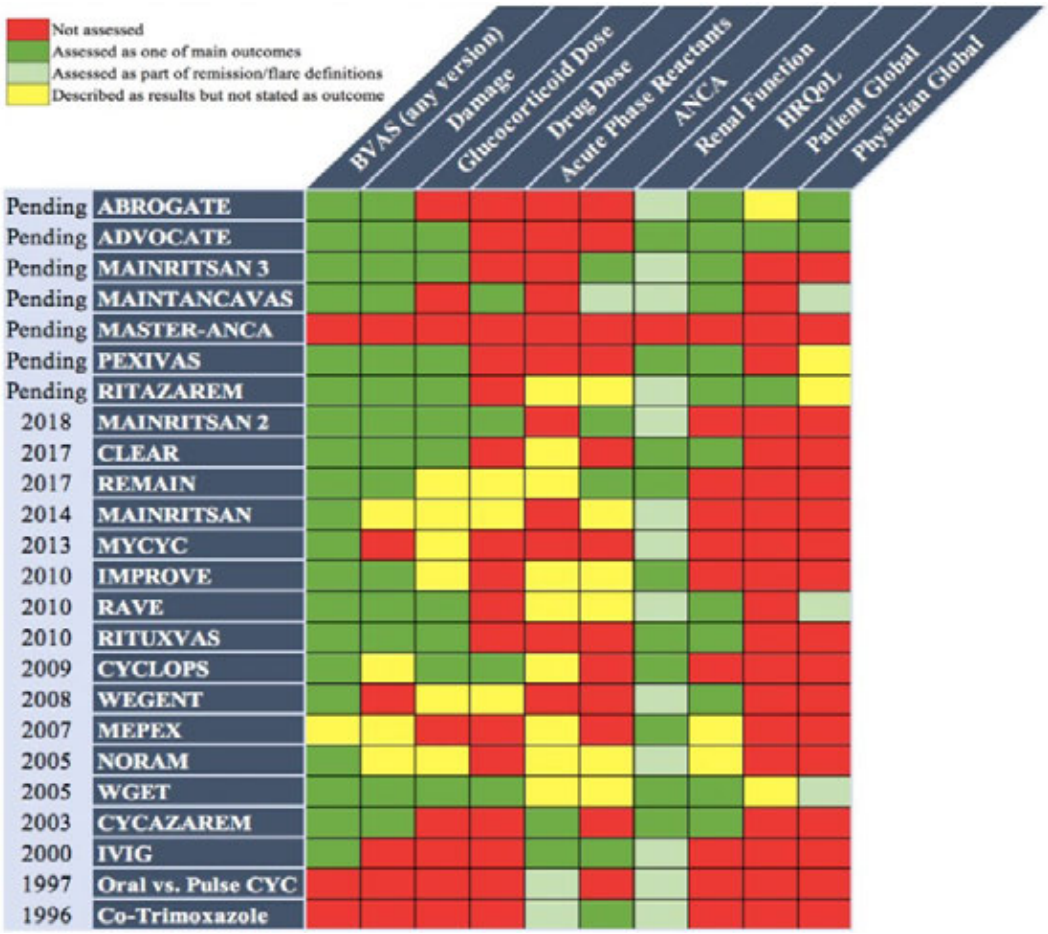

Figure 1. Overview of outcomes assessed in randomized controlled trials of ANCA-associated vasculitis

Results: Various versions of the Birmingham Vasculitis Activity Score (BVAS) were the most widely used instrument for assessing disease activity in AAV. BVAS was almost always used as a dichotomous variable (0 or > 0) providing distinction between remission and active disease. Among 24 eligible RCTs (Figure 1) reduction and/or achievement of BVAS=0 represented a main study outcome (stated as primary or secondary endpoint) in 20/24 (83%) RCTs; 6 of these trials used the BVAS/WG. Damage, mainly assessed by the Vasculitis Damage Index (VDI), was an outcome for 14/24 (58%) RCTs. Physician global assessment and patient-reported outcomes (PROs) were assessed in 7 (29%) and 14 (58%) RCTs, respectively. Assessment of renal function (part of BVAS) was a major outcome or specifically included in definitions of remission/relapse in 23/24 (96%) RCTs. Timing for outcome measure assessment differed significantly among RCTs, with baseline, 6 months (15/20 RCTs), and 12 months (14/20) after enrollment in the study being the most common time points for collecting BVAS and VDI. However, assessment of response occurred as early as 1-4 weeks after enrollment, with 6/24 (25%) RCTs assessing disease activity at 6 weeks and 13/24 (54%) at 3 months.

Conclusion: Review of outcome measures used in RCTs of AAV demonstrates the recurrent use of certain specific tools to assess disease state, although with heterogeneity in the definitions for remission/relapse, and timing of assessment. Intermediate states of disease activity of importance to patients and investigators are currently poorly defined or evaluated. Furthermore, other important outcomes in AAV, including PROs, damage measures, and global assessments are often not included as primary or confirmatory secondary outcomes in RCTs in AAV. Data-driven composite measures integrating a combination of these measures and accounting for different levels of responsiveness to therapy may result in increased power to detect clinically meaningful differences in efficacy of future treatments.

Disclosure: S. Monti, None; **K. Quinn**, None; **R. Christensen**, AbbVie, 2, Amgen, 2, Axellus A/S, 2, Biogen, 2, BMS, 2, cambridge weight plan, 2, Celgene, 2, Eli Lilly, 2, Hospira, 2, MSD, 2, Norpharma, 2, Novartis, 2, Oak Foundation (OCAY-13-309), 2, Orkla Health, 2, Pfizer, 2, Research Unit for Musculoskeletal Function and Physiotherapy, Institute of Sports science and Clinical biomechanics, University of Southern Denmark, 9, Roche, 2, Sobi, 2, Takeda, 2; **A. Mahr**, Celgene, 8, Chugai Pharma France, 8, Roche, 8, Roche, Chugai, 8; **C. Pagnoux**, ChemoCentryx, 5, Chemocentryx, 5, Genetech/Roche, 5, Genzyme/Sanofi, 5, GlaxoSmithKline, 5, Hoffman-La Roche, 2, 5, 8, Hoffman-LaRoche, 2, 5, 8, Sanofi, 5; **C. Langford**, Bristol-Myers Squibb, 2, GlaxoSmithKline,, 2, ChemoCentryx, 2, Genentech, 2, Bristol-Myers Squibb, 5, 9, Abbvie, 9, AstraZeneca, 9; **D. Jayne**, Astra Zeneca, 5, Boehringer-Ingelheim, 5, Celgene, 5, ChemoCentryx, 2, 5, GSK, 2, 5, Infla-Rx, 5, InflaRx GmbH, 5, Insmed, 5, Roche Genetech, 2, Sanofi Genzyme, 2, Takeda, 5; **P. Merkel**, Abbvie, 5, AbbVie, 5, AstraZeneca, 2, 5, AstraZeneca,, 2, 5, Biogen, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, Celegene, 2, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Genentech/Roche, 2, 5, Genetech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Kypha, 2, TerumoBCT, 2, UpToDate, 7; **G. Tomasson**, None.

Abstract Number: 2792

The Need for Personalized, Non-Pharmacological Intervention Programmes in Autoimmune Connective Tissue Disorders: Results of a EULAR-Funded Scoping Review with a Nested, Descriptive Meta-Analysis

Valentin Ritschl,[1] Ricardo Ferreira,[2] Rúben Fernandes,[2] Eduardo Santos,[2] Essi Juutila,[3] Erika Mosor,[1] Kim Fligelstone,[4] Helena Gaspar,[5] Linda Schraven,[6] Judy Ammerlaan,[7] Georg Stummvoll,[8] Maria João Salvador,[2] Janet Poole,[9] Cornelia van den Ende,[10] Carina Boström,[11] and Tanja Stamm[1], [1]Medical University of Vienna, Vienna, Austria, [2]Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal, [3]Metropolia University of Applied Sciences, Helsinki, Finland, [4]Federation of European Scleroderma Associations, Tournai, Belgium, [5]Portuguese League Against Rheumatic Diseases, Portugal, Portugal, [6]Federation of European Scleroderma Associations, Sweden, Sweden, [7]University Medical Centre, Utrecht, Netherlands, [8]Klinikum Malcherhof Baden, Baden, Austria, [9]University of New Mexico, Albuquerque, NM, [10]Sint Maartenskliniek Nijmegen, Nijmegen, Netherlands, [11]Karolinska Institutet, Stockholm, Sweden

SESSION INFORMATION

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Session Title: Clinical Aspects & Outcomes Research

Session Type: ARP Abstract Session

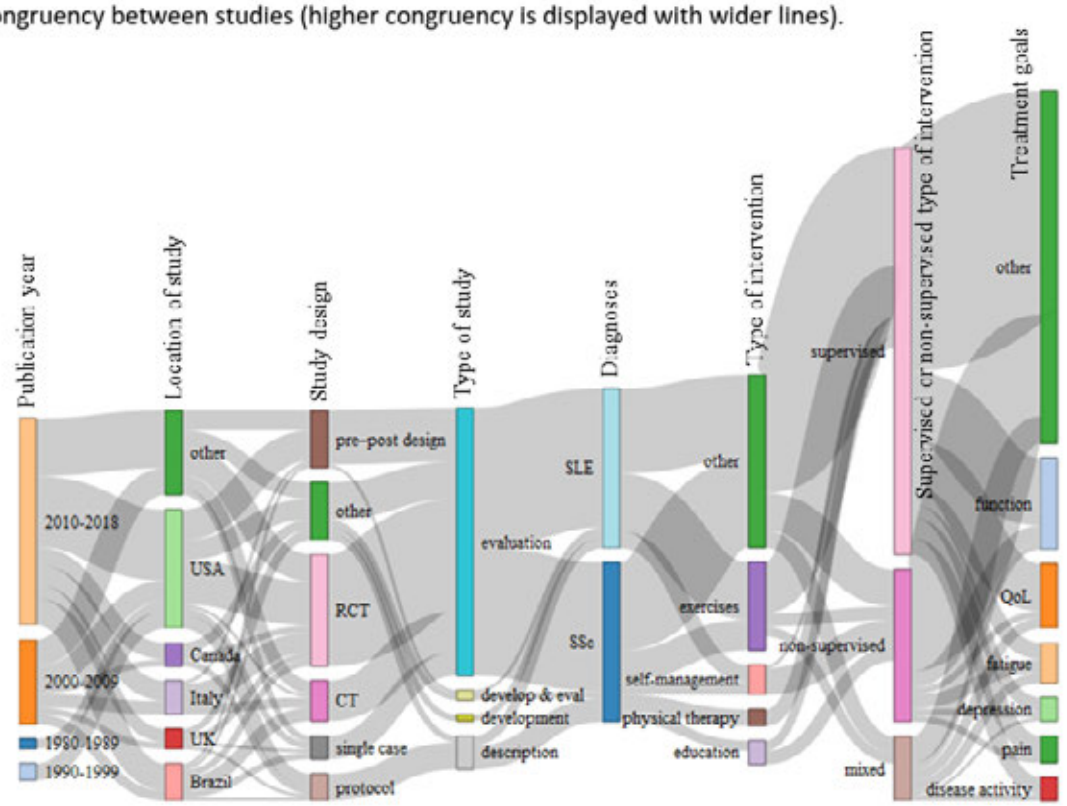
Session Time: 2:30PM–4:00PM

Background/Purpose: Autoimmune Connective Tissue Disorders (CTDs), including Mixed Connective Tissue Disorders (MCTD), systemic sclerosis (SSc) and systemic lupus erythematous (SLE) can lead to Raynaud phenomenon, involvement of internal organs, pain in joints, skin abnormalities and muscle weakness. Consequently, people with CTDs experience limitations in activities of daily life and restrictions in participation. Programmes promoting patient education, self-management, physical activity, and healthy life style, provided by health professionals are therefore essential to these patients. However, there is a substantial gap of knowledge about the content which should be included in non-pharmacological intervention programmes.

The purpose of this study was to identify, map and appraise the content of existent face-to-face, digital and/or distance-learning non-pharmacological intervention programmes for patients with MCTD, SSc and/or SLE to inform a EULAR funded project with the overall aim to develop a new distance learning programme realizable with digital technologies.

Methods: A scoping literature review with a nested descriptive meta-analysis was performed in MEDLINE [Pubmed], EMBASE [OVID], CINAHL [EBSCO], PsycINFO [ProQUEST], the Cochrane Database of Systematic Reviews, OT-

Figure 1. Sankey diagram. This diagram illustrates the relationships between the different study characteristics. The width of the grey connections lines between the bars are reflecting a higher congruency between studies (higher congruency is displayed with wider lines).



Seeker, PEDro, and SciELO in September 2018. Furthermore, an international task-force identified additional grey literature and ongoing research projects. Eligibility checks of the articles based on pre-defined in- and exclusion criteria and data extractions were done independently by two researchers. The interventions contained in these programmes were extracted using the "Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide". A Sankey diagram and descriptive statistics were used to illustrate the relationships between the interventions and other characteristics of the studies. The protocol was pre-published on ResearchGate.

Results: Of 6667 identified records, 94 papers were eligible. Sixty-one studies (65%) were conducted between 2000 and 2018, mainly in the USA (35 [37%]), Brazil (11 [12%]) and Italy (10 [11%]). Thirty-three studies (35%) were randomised controlled trials, 17 (18%) were one-group pre-post-test designs and 12 (16%) clinical trials without randomisation (Figure 1). Overall, 4274 patients participated; 2955 had SLE [69%] and 1319 had SSc [31%], thus no studies with MCTD where found. The main content of the intervention programmes included exercises (22 [23%]), self-management (9 [10%]) and education (7 [7%]), with treatment goals focusing mainly on physical function (27 [29%]), quality of life (19 [20%]) and fatigue (12 [16%]). The interventions (67 [72%]) included or were based on an initial face-to-face component.

Conclusion: There was a variety of programmes content and interventions due to different consequences regarding activity limitations and participation restrictions in autoimmune CTDs. This highlights the need for personalized, multicomponent, non-pharmacological interventions.

Disclosure: V. Ritschl, None; **R. Ferreira**, None; **R. Fernandes**, None; **E. Santos**, None; **E. Juutila**, None; **E. Mosor**, None; **K. Fligelstone**, None; **H. Gaspar**, None; **L. Schraven**, None; **J. Ammerlaan**, None; **G. Stummvoll**, None; **M. Salvador**, None; **J. Poole**, None; **C. van den Ende**, None; **C. Boström**, None; **T. Stamm**, Janssen, 8, MSD, 8, Novartis, 8, Roche, 2, 8.

Abstract Number: 2793

Methotrexate Intolerance: A Qualitative Descriptive Study of the Adult Rheumatoid Arthritis Patients' Perspectives

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Session Type: ARP Abstract Session
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Background/Purpose: An estimated 11% to 33% of persons taking methotrexate for rheumatoid arthritis (RA) are reported to be at least moderately intolerant to this medication. The published literature has largely measured methotrexate intolerance using a scale composed of four domains: abdominal pain, nausea, vomiting and behavioral symptoms. These symptoms largely ignore the definition of "intolerance" or the "unwillingness or refusal to tolerate or respect opinions or beliefs contrary to one's own". As such, the patients' perspective is not captured. The purpose of this study is to use qualitative methodologies to describe methotrexate intolerance from the adult patient with RA's perspective.

Methods: We conducted semi-structured audio-recorded individual interviews with 14 adult English-speaking patients who have a rheumatology health-care provider confirmed diagnosis of RA, and who had been prescribed, were taking, or had ever taken oral or subcutaneous methotrexate. We identified 489 labels for common words or phrases or codes during line-by-line coding which were categorized using constant comparative analysis and then collapsed into three central themes.

Results: Findings from the conducted interviews suggest that methotrexate intolerance is a construct conceptualized from three themes: *Beliefs about the Risk of Methotrexate, Beliefs about the Benefits of Methotrexate, and Beliefs about the Threat of RA*. The complex beliefs about methotrexate involved both perceived risks and benefits which resulted from knowledge obtained from sources with varying perceived value such as the Internet, others with RA, or their health care provider. The experiences of trusted peers with RA and the relationship with their health care provider were influential in the decision to tolerate methotrexate. The amount of information and timing in which to participants' sought information varied.

Participants also described beliefs about the threat of RA which often resulted from personal experiences with pain and difficulty functioning or observing the experiences of other with RA. Patients often reported the desire to avoid "being crippled" or requiring the use of assistive devices including a wheel chair. The belief in the perceived benefit of methotrexate, which was often improved functioning in activities of daily living, and threat of the RA hindering this functioning often was a stimulus to tolerate perceived risks or to take methotrexate despite known risks (e.g., hair loss and nausea).

Conclusion: Findings from this study suggest that intolerance to methotrexate involves a complex belief system where patients with RA weigh beliefs about risks and benefits of methotrexate alongside beliefs about the threat of RA.

Disclosure: E. Salt, Pfizer, 2, Pfizer and IHI, 2; **M. Rayens**, Pfizer, 2, Pfizer and IHI, 2; **L. Crofford**, None; **J. Studts**, Pfizer, 2.

Abstract Number: 2794

Predictors of Incident and Worsening Lumbar Spine Degeneration: The Johnston County Osteoarthritis Project

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Clinical Aspects & Outcomes Research
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Our aim was to determine whether demographics, clinical characteristics or appendicular joint osteoarthritis predict the incidence and worsening of lumbar spine disc space narrowing (DSN), facet joint OA (FOA), osteophytes (OST), and spondylolisthesis.

Methods: These analyses used baseline (2006-2010) and follow-up (2013-2015) data from the Johnston County OA Project. Paired (baseline and follow-up) lumbar spine radiographs were graded for OST and DSN (0-3), spondylolisthesis (0-5) and FOA (present or absent). Incidence was defined as the absence of a specific radiographic feature at baseline and the presence of that feature at follow-up. Worsening was defined as ≥ 1-unit increase from baseline to follow-up for a given radiographic feature. Demographic characteristics of age, race (African American vs. white), and sex, clinical characteristics of the history of low back symptoms, comorbidities (diabetes, high blood pressure and ever smoking), and back injury were determined by self-report. Body mass index (BMI) variables of weight and height were measured at the research clinic visit with obesity defined as BMI≥30 kg/m^2. Appendicular OA was defined as a Kellgren-Lawrence grade ≥2 at the knee or hip or a grade ≥2 in a minimum of one distal interphalangeal (IP) joint and 2 other joints (IP or carpometacarpal) at the hand. Weibull models, which account for interval censoring, were used to estimate adjusted (simultaneously for all predictors) hazards ratios (aHR) and 95% confidence intervals (CI) and whether the effects differed in those with and without low back symptoms.

Results: Paired lumbar spine radiograph scores were available for 819 participants. Baseline characteristics were mean age 66.1 (SD 7.5), mean BMI 31.5 (6.1) kg/m^2; 67.9% were women, 31.8% were African American, and 39.6% had radiographic knee OA, 35.5% hip OA, 32.0% hand OA, and 34.8% had low back symptoms. The incidence of OST, FOA, DSN and spondylolisthesis was 59.0%, 11.1%, 38.1% and 9.1%, respectively. Worsening of OST, DSN, and spondylolisthesis occurred in 33.8%, 23.9% and 7.8%, respectively.

AAs were less likely to develop FOA with symptoms and DSN with symptoms. Women were more likely to develop spondylolisthesis. (Table 1a) Obesity was a predictor of incidence for all lumbar spine features. Smokers were less likely to develop DSN and FOA with symptoms. Participants with diabetes were less likely to develop DSN with symptoms and without. (Table 1b) Presence of Knee OA predicted incident: vertebral OST with symptoms, DSN with symptoms, FOA and FOA with symptoms. (Table 1c)

	Osteophytes*	Osteophytes with Sx *	Disc Space Narrowing*	Disc Space Narrowing with Sx *	Facet joint OA **	Facet Joint OA with Sx**	Spondylolisthesis**	Spondylolisthesis with Sx **
A. Demographic								
Women versus Men	2.31 (0.89-6.04)	1.16 (0.78-1.73)	1.33 (0.79-2.23)	1.19 (0.78-1.81)	0.50 (0.14-1.75)	1.47 (0.92-2.35)	**2.16 (1.07-4.34)**	1.40 (0.72-2.72)
African American versus White	1.19 (0.60-2.37)	0.59 (0.39-0.89)	0.69 (0.41-1.17)	**0.52 (0.39-0.82)**	0.96 (0.29-3.23)	**0.49 (0.30-0.82)**	1.20 (0.66-2.18)	0.68 (0.36-1.29)
Age 55-65 versus Age<55	0.41 (0.11-1.58)	1.03 (0.39-2.71)	1.05 (0.34-3.23)	1.15 (0.39-3.35)	0.69 (0.03-14.9)	0.93 (0.27-3.18)	0.67 (0.19-2.41)	0.85 (0.19-3.85)
Age 65+ versus Age<55	0.38 (0.09-1.55)	0.79 (0.29-2.16)	1.24 (0.37-4.10)	0.94 (0.31-2.84)	1.09 (0.05-26.1)	0.80 (0.23-2.80)	0.96 (0.26-3.59)	0.90 (0.19-4.19)
B. Clinical Characteristics								
BMI ≥30 versus BMI <30	0.63 (0.31-1.27)	**1.50 (1.04-2.16)**	**1.80 (1.09-2.98)**	**1.68 (1.11-2.87)**	**4.99 (1.46-17.10)**	**1.88 (1.22-2.88)**	**1.87 (1.02-3.43)**	**2.41 (1.30-4.49)**
Back Injury Yes versus No	0.57 (0.07-4.59)	1.00 (0.24-4.25)	0.56 (0.07-4.43)	1.51 (0.45-5.04)	NR	1.23 (0.16-9.56)	1.82 (0.24-14.0)	2.37 (0.30-18.4)
Ever Smoker Yes versus No	0.87 (0.49-1.56)	0.75 (0.52-1.08)	**0.61 (0.38-0.98)**	0.66 (0.45-0.97)	0.82 (0.20-3.35)	**0.62 (0.40-0.95)**	0.79 (0.46-1.38)	0.71 (0.40-1.27)
Diabetes Yes versus No	0.51 (0.17-1.57)	0.70 (0.42-1.16)	**0.54 (0.30-0.97)**	**0.56 (0.33-0.94)**	0.82 (0.20-3.35)	0.83 (0.46-1.50)	0.69 (0.34-1.39)	0.55 (0.25-1.20)
High Blood Pressure Yes versus No	0.80 (0.42-1.50)	1.34 (0.93-1.93)	0.76 (0.48-1.21)	1.38 (0.94-2.02)	1.04 (0.35-3.11)	1.39 (0.91-2.13)	0.79 (0.46-1.38)	1.71 (0.92-3.17)
C. Appendicular Joint OA								
Knee OA K-L ≥2 versus <2	1.28 (0.62-2.65)	**1.49 (1.05-2.12)**	0.92 (0.54-1.57)	**1.63 (1.12-2.95)**	**4.18 (1.44-12.2)**	**1.54 (1.02-2.33)**	0.88 (0.50-1.53)	1.35 (0.78-2.36)
Hip OA K-L ≥2 versus <2	0.61 (0.34-1.10)	1.01 (0.71-1.45)	0.80 (0.48-1.34)	0.90 (0.62-1.32)	0.41 (0.13-1.27)	1.13 (0.75-1.70)	1.28 (0.74-2.22)	1.27 (0.73-2.21)
Hand OA K-L ≥2 versus <2	1.02 (0.56-1.84)	1.14 (0.78-1.66)	1.16 (0.68-1.97)	1.27 (0.86-1.87)	0.58 (0.16-2.09)	1.09 (0.70-1.69)	1.20 (0.66-2.19)	1.13 (0.63-2.04)

Sx=low back symptoms; OA=osteoarthritis; BMI= body mass index; K-L=Kellgren Lawrence
* Adjusted simultaneously for all predictors in this table and presence of facet joint OA
** Adjusted simultaneously for all predictors in this table and the presence of disc space narrowing and OST
NR= not reported due to small sample size

Table 1. Predictors of Incidence for Lumbar Spine Degeneration

Women were more likely to develop worsening of DSN. AAs were less likely to develop worsening of OST and DSN with symptoms. (Table 2a) Obesity was a predictor of worsening for all lumbar spine features. Diabetes was a predictor of osteophyte worsening. (Table 2b) Appendicular joint OA did not predict worsening of spine OA features. (Table 2c)

	Osteophytes*	Osteophytes with Sx*	Disc Space Narrowing*	Disc Space Narrowing with Sx*	Spondylolisthesis**	Spondylolisthesis with Sx**
A. Demographic						
Women versus Men	0.85 (0.63-1.13)	1.04 (0.74-1.46)	**1.46 (1.02-2.08)**	1.36 (0.92-2.03)	1.93 (0.96-3.87)	1.39 (0.72-2.70)
African American versus White	1.04 (0.77-1.40)	**0.68 (0.48-0.97)**	0.79 (0.55-1.13)	**0.53 (0.35-0.80)**	1.19 (0.66-2.13)	0.68 (0.36-1.31)
Age 55-65 versus Age<55	0.84 (0.41-1.74)	1.65 (0.65-4.19)	1.40 (0.55-3.60)	1.13 (0.39-3.23)	0.67 (0.19-2.40)	0.82 (0.18-3.71)
Age 65+ versus Age<55	0.89 (0.43-1.88)	1.35 (0.52-3.50)	1.29 (0.49-3.38)	0.90 (0.31-2.63)	0.90 (0.24-3.33)	0.83 (0.18-3.88)
B. Clinical Characteristics						
BMI ≥30 versus BMI <30	**0.75 (0.57-0.99)**	**1.37 (1.00-1.89)**	**1.51 (1.09-2.09)**	**1.56 (1.10-2.23)**	1.77 (0.97-3.22)	**2.32 (1.25-4.29)**
Back Injury Yes versus No	0.58 (0.18-1.83)	1.42 (0.51-3.94)	0.61 (0.15-2.49)	1.75 (0.63-4.85)	1.41 (0.19-10.6)	2.03 (0.27-15.5)
Ever Smoker Yes versus No	1.00 (0.76-1.30)	0.78 (0.57-1.05)	1.08 (0.79-1.47)	0.75 (0.53-1.06)	0.77 (0.44-1.35)	0.72 (0.40-1.28)
Diabetes Yes versus No	**1.38 (1.00-1.92)**	0.92 (0.63-1.35)	0.85 (0.56-1.28)	0.74 (0.47-1.16)	0.81 (0.40-1.62)	0.55 (0.25-1.21)
High Blood Pressure Yes versus No	0.88 (0.67-1.16)	1.25 (0.91-1.71)	0.88 (0.64-1.20)	1.32 (0.92-1.89)	1.15 (0.64-2.04)	1.66 (0.90-3.06)
C. Appendicular Joint OA						
Knee OA K-L ≥2 versus <2	0.97 (0.74-1.28)	1.28 (0.95-1.73)	0.84 (0.61-1.16)	1.36 (0.97-1.90)	0.83 (0.48-1.45)	1.39 (0.80-2.42)
Hip OA K-L ≥2 versus <2	0.91 (0.69-1.19)	1.03 (0.76-1.40)	0.72 (0.52-1.00)	0.85 (0.60-1.21)	1.11 (0.64-1.91)	1.18 (0.68-2.05)
Hand OA K-L ≥2 versus <2	0.98 (0.73-1.32)	1.04 (0.75-1.45)	1.06 (0.75-1.48)	1.41 (0.99-2.02)	1.05 (0.58-1.90)	1.14 (0.64-2.05)

Sx=low back symptoms; OA=osteoarthritis; BMI= body mass index

*Adjusted simultaneously for all predictors in this table and facet joint OA

**Adjusted simultaneously for all predictors in this table and disc space narrowing and OST

Table 2. Predictors of Worsening for Lumbar Spine Degeneration

Conclusion: Obesity consistently predicted incidence and worsening of lumbar spine radiographic features with and without low back symptoms. Notable variation in other predictors for incidence and worsening suggest that the etiological process of degeneration may differ for some radiographic features.

Disclosure: A. Goode, None; **R. Cleveland**, None; **D. Hu**, None; **S. George**, None; **V. Byers Kraus**, None; **T. Schwartz**, None; **R. Gracely**, None; **L. DeFrate**, None; **J. Jordan**, None; **Y. Golightly**, None.

Abstract Number: 2795

Patterns of Ambulatory Health Care Utilization and Medication Adherence Among Transition-Age Youth with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Clinical Aspects & Outcomes Research
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Youth with child-onset systemic lupus erythematosus (SLE) transitioning from pediatric to adult health care systems may be at higher risk for poor outcomes than children or older adults with SLE. We leveraged US private insurance claims to describe patterns of ambulatory subspecialty care in transition-age youth with SLE, and to compare health care use and medication adherence before and after transfer to adult care. We hypothesized that ambulatory follow-up care and medication adherence decrease during the transfer period with a concurrent increase in acute care use.

Figure 1. Ambulatory rheumatology and nephrology subspecialty care utilization patterns

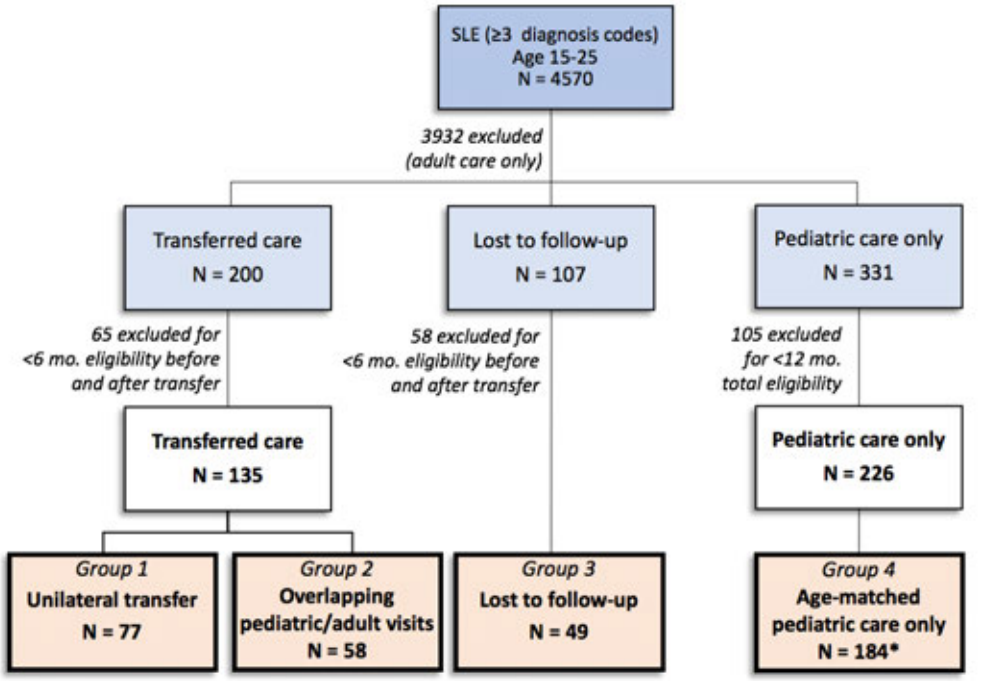

Figure 1. Flowchart demonstrating application of selection criteria and categorization of ambulatory rheumatology/nephrology visits into patterns of pediatric and adult care use. *Represents 107 unique patients sampled with replacement and age-matched to youth in groups 1-3

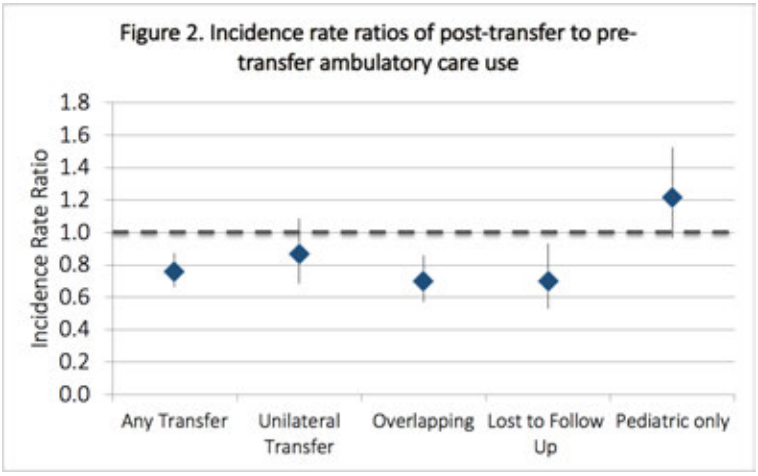

Figure 2. Incidence rate ratios comparing rates of ambulatory care visits before and after the index (transfer) date were estimated using negative binomial regression models for each pattern of subspecialty care, clustered by subject.

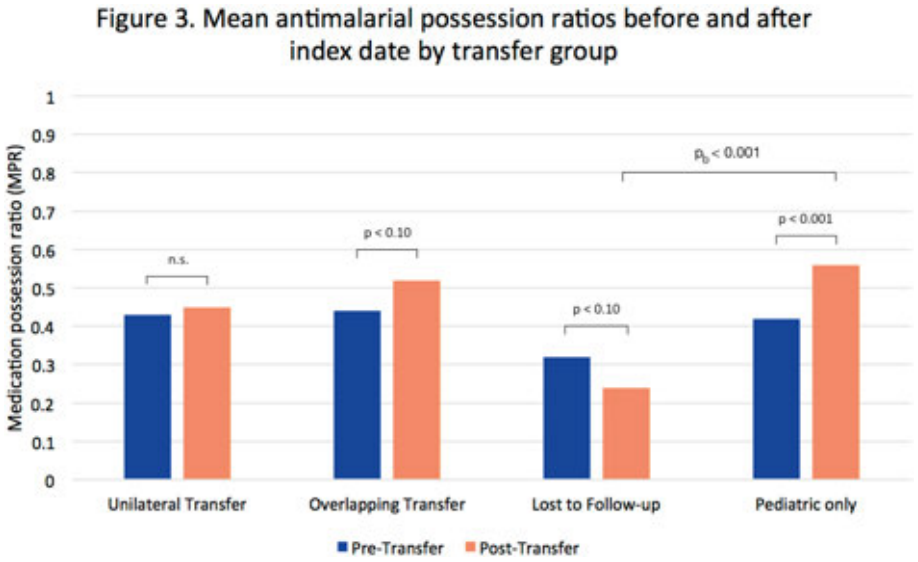

Figure 3. Average medication possession ratios (MPR) one year before and after transfer were compared within groups using paired t-tests. Between-group differences were tested using two-sample t-tests, of which statistically significant differences are also shown (pb).

Methods: Using Clinformatics DataMart® (OptumInsight, Eden Prairie, MN) de-identified US claims data (2000-2016), we categorized youth ages 15-25 yrs with SLE by pattern of rheumatology/nephrology ambulatory care into those that 1) transferred unilaterally to adult care within 1 yr of the last pediatric visit, 2) had overlapping pediatric and adult visits before remaining in adult care 3) were lost to follow-up (> 1 yr between last pediatric and first adult visit or end of enrollment), or 4) remained in pediatric care (Fig 1). The transfer index date was defined as the last pediatric visit for groups 1-3. Pediatric-only youth were age-matched to the other groups. We used negative binomial regression to compare pre- and post-transfer health care utilization rates within groups. We used paired t-tests to compare pre-/post- antimalarial medication possession ratios (MPR) in prevalent users, and compared MPRs between youth in groups 1-3 and their pediatric-only matches.

Results: A total of 184 youth with SLE met inclusion criteria for transfer out of pediatric rheumatology/nephrology care, of which 77 (42%) transferred unilaterally to adult care within a year, 58 (32%) had overlapping pediatric/adult care over a median of 12 months (IQR 4 – 27) before the last pediatric visit, and 49 (27%) were lost to follow-up. Of the 226 youth remaining in pediatric care, 107 were age-matched to each transfer group. Unilateral transfers were older

than the lost to follow-up group (mean age 19.4 vs. 18.5, p 0.02) and more likely to live in the Northeast (p 0.04). Rates of ambulatory visits decreased after transfer among those with overlapping care and loss to follow-up, but remained unchanged among unilateral transfers (Fig 2). Rates of acute care utilization decreased across all groups (IRRs 0.14-0.30, p< 0.01). Average pre-transfer antimalarial MPRs ranged from 0.3-0.5 (Fig 3). Post-transfer MPRs were lower in the lost to follow-up group compared to age-matched peers remaining in pediatric care (mean 0.2 vs. 0.6, p< 0.01).

Conclusion: Among transition-age youth with SLE who have continuous private insurance coverage, acute care utilization does not increase during transfer to adult care. However, a substantial proportion of youth fail to see an adult provider within 12 months of the last pediatric visit. These youth have decreased rates of ambulatory care use and medication adherence compared to the pre-transfer period, and may be at highest risk for inadequate follow-up and poor outcomes. Additional data is needed to determine whether transfer patterns are associated with longitudinal health outcomes.

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Disclosure: J. Chang, None; **A. Knight**, None; **E. Lawson**, None.

Abstract Number: 2796

The Association Between Omega-3 Supplementation and Disease Activity in a Rheumatoid Arthritis (RA) Observational Cohort

Adel Andemeskel,[1] Vivi Feathers,[1] Christine Iannaccone,[1] Jing Cui,[1] and Nancy Shadick[1], [1]Brigham Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Clinical Aspects & Outcomes Research
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Omega-3 supplementation is one of a few complementary and alternative medicine (CAM) therapies that has shown promise in improving RA symptoms through small, randomized control trials. However, there is little research looking at the association of disease activity of RA patients and omega-3 supplementation. This study aims to identify the association between disease activity of RA patients who do and do not take omega-3 in an observational longitudinal cohort.

Methods: Data from a longitudinal RA registry was used for this study. Information concerning use of herbal medications, including omega-3 supplementation, was collected semi-annually. Subjects ever reporting use of fish oil, flaxseed, docosahexanoic acid (DHA), eicosapantaenoic acid (EPA), and alpha linolenic acid (ALA) at least once were identified as an omega-3 user. First, we compared demographic and clinical characteristics between omega-3 users and omega-3 non-users at the date of first supplementation for users and date of cohort enrollment for non-users. Then, a generalized linear mixed model (GLMM) analyzed associations between subjects' omega-3 supplementation and the outcomes, Disease Activity Score (DAS28-CRP3), painful joint count, and swollen joint count one year later. The lagged model (Fig. 1) controlled for repeated measures and adjusted the outcomes for age, gender, education, seropositivity, steroid, NSAID, biologic and methotrexate use.

Results: Overall 1,557 subjects had a mean age of 56 years (± 14), with a median disease duration of 12 (8, 20) years. Subjects were 92% white, 82% female, and 57% had a college degree or higher. Of all participants, 640 indicated

Figure 1: Lagged GLMM Analysis between Omega-3 Supplementation and Disease Outcomes

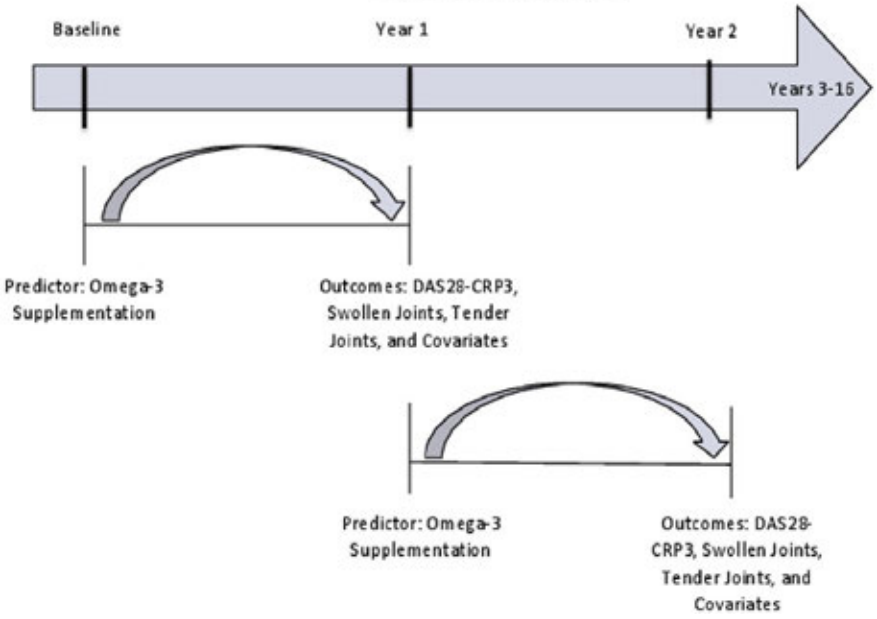

Table 1: Baseline characteristic comparisons between omega-3 users vs non-omega-3 users involving 1,557 RA subjects in an observational cohort

Baseline Characteristics	Omega-3 (n=640)	No Omega-3 (n=917)	p-value
Age (years), mean (SD)	57.1 (13.1)	57.1 (15.0)	0.96
Female, n (%)	541 (85%)	733 (80%)	0.02*
White, n (%)	586 (92%)	839 (92%)	0.84
Education, n (%)			0.001*
High school degree	223 (35%)	386 (42%)	
College degree	214 (34%)	273 (30%)	
Graduate degree	186 (29%)	218 (24%)	
Disease duration (years), median (IQR)	11.4 (8, 18)	12.8 (8, 20)	0.25
DAS28-CRP3, median (IQR)	3.5 (3.4, 4.7)	3.6 (3.4, 4.9)	0.24
Seropositive, n (%)	424 (69%)	576 (68%)	0.65
* indicates significant p-value			

that they had taken an omega-3 supplement at least once. The average duration of omega-3 supplementation was 33 months. Omega-3 users were more likely to be female (p=0.02) with a higher education level (p=0.001) (Table 1). The lagged GLMM showed that omega-3 users were more likely to have a significantly lower DAS28-CRP3 (p< 0.0001), painful joint count (p=0.001), and swollen joint count (p=0.0009) 1 year later after adjustment for seropositivity, demographic and medication variables. (Table 2).

Conclusion: The data suggest that independent of clinical, demographic and medication variables, patients from an observational cohort who take omega-3 supplementation are more likely to have lower DAS28-CRP3 scores, less

Table 2: Lagged GLMM Analysis - Association between prior omega-3 use (lagged 1 year) and disease activity variables involving 1,557 RA subjects in an observational cohort

Primary Predictor	Outcomes		
	DAS28-CRP3 β-Estimate (p-value)	Painful Joint Count β-Estimate (p-value)	Swollen Joint Count β-Estimate (p-value)
Omega-3	-0.159 (p<0.0001)	-0.136 (p=0.001)	-0.123 (p=0.0009)
Co-variates			
Age	0.009 (p<0.0001)	0.005 (p=0.0008)	0.008 (p<0.0001)
Gender	0.095 (p=0.03)	0.210 (p<0.0001)	0.115 (p=0.006)
Education	-0.210 (p<0.0001)	-0.231 (p<0.0001)	-0.137 (p<0.0001)
Seropositive	0.363 (p<0.0001)	0.314 (p<0.0001)	0.386 (p<0.0001)
Corticosteroid Use	0.561 (p<0.0001)	0.491 (p<0.0001)	0.548 (p<0.0001)
NSAID Use	0.316 (p<0.0001)	0.305 (p<0.0001)	0.293 (p<0.0001)
Biologic Use†	-0.117 (p=0.0003)	-0.092 (p=0.01)	-0.005 (p=0.87)
Methotrexate Use	-0.183 (p<0.0001)	-0.208 (p<0.0001)	-0.079 (p=0.01)

† Biologics including abatacept, etanercept, adalimumab, anakinra, infliximab, rituximab, certolizumab, and tocilizumab

painful joints, and less swollen joints. These findings suggest the need for further study of omega-3 supplementation with particular attention to dosage and duration of use as an adjunct to conventional medicine for RA.

Disclosure: A. Andemeskel, None; **V. Feathers**, None; **C. Iannaccone**, None; **J. Cui**, None; **N. Shadick**, BMS, 2, Crescendo Biosciences, 2, Mallinckrodt, 2, Sanofi Regeneron, 2, Sanofi/Regeneron, 2.

Abstract Number: 2797

Exploring Possible Predictors of Physical Activity in Knee Replacement Patients

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Clinical Aspects & Outcomes Research
Session Type: ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Following total knee replacement (TKR), patients do not achieve recommended physical activity for overall health. The implications of physical inactivity on individuals and the healthcare system are substantial and well documented, yet why these patients do not achieve recommended levels are not well understood. The concept of physical literacy - if people have the knowledge, competence and confidence to undertake physical activities effectively to reach optimum levels of performance - has not been explored in an adult population. Given the

grave health implications associated with physical inactivity, this study aimed to examine physical activity levels and potential factors, including physical literacy, that may influence activity levels in this population.

Methods: This study used a prospective observational design and included people having primary TKR for osteoarthritis.The primary outcome was change in physical activity as measured by the Rapid Assessment of Physical Activity survey tool. To examine predictors of physical activity levels, we evaluated the following: age, sex, BMI, comorbidity count, Patient Health Questionnaire Depression Scale, Pain Disability Index, P-4 pain intensity measure, Arthritis Self-Efficacy Scale, and Adult Physical Literacy Assessment.The physical literacy measure evaluates the domains of environment, self-efficacy, and relative rankings of literacies. We hypothesized differences in the amount of physical activity relating positively or negatively to the predictive factors. Standard definitions described categorical variables. Continuous variables were categorized according to the results of Shapiro Wilks and Kolmogrov tests. We compared changes in outcome measure scores using percentage or mean change. The statistical significance of changes was assessed using McNemar's test or a paired *t* test. Lastly, predictors of physical activity at 12 months were assessed using regression models as determined by assessments of normality and verification of assumptions.

Results: The sample included 104 patients; male (31%) and female (72%) with ages ranging from 52-87 years. Physical activity levels were different between T1 and T2 in some participants. There was a significant change in aerobic activities with a small effect size. There was no significant change in strength and flexibility. Age, sex, comorbid illness and depression did not predict aerobic change. However, changes in self-reported measures of physical activity (p=0.02) and depression (p=0.001) were significant from Time 1 to Time 2. Physical literacy scores were not predictive of physical activity scores. However, those who reported lower physical literacy scores also reported lower physical activity scores and those with higher physical literacy reported higher physical activity scores.

Conclusion: As in other studies, individuals who are active prior to surgery resume activity and those who are not active prior to surgery do not increase their activity after surgery. Physical literacy introduces a novel concept that seems to be related to activity level. Future studies should further evaluate this concept as it may be a target for enabling people to be physically active.

Disclosure: B. Tanenbaum, None; **A. Davis**, None; **D. Kennedy**, None; **J. Bhatti**, None.

Abstract Number: 2798

Trajectories of Opioid Filling Patterns After Total Knee Replacement

Chandrasekar Gopalakrishnan,[1] Jessica Franklin,[2] Yinzhu Jin,[3] Daniel Solomon,[4] Jeffrey Katz,[5] Yvonne Lee,[6] Patricia Franklin,[6] Joyce Lii,[2] Rishi Desai,[7] and **Seoyoung C. Kim** [3], [1]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [2]Brigham and Women's Hospital, Harvard Medical School, Boston, [3]Brigham and Women's Hospital and Harvard Medical School, Boston, [4]Brigham and Women´s Hospital, Div. of Rheumatology, Immunology and Allergy, Boston, MA, [5]Brigham and Women's Hospital/Harvard Medical School, Boston, [6]Northwestern University Feinberg School of Medicine, Chicago, [7]Brigham and Women's hospital, Boston

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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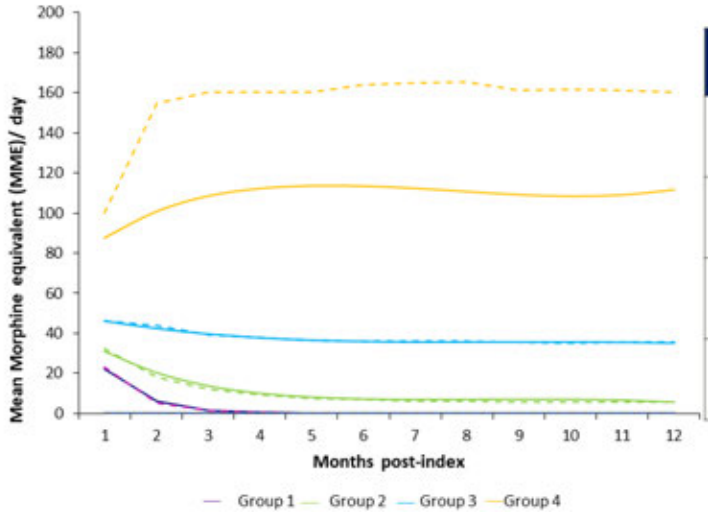
Session Type: ACR/ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Patients undergoing total knee replacement (TKR) are at increased risk of persistent opioid use and opioid dependence. Group-based trajectory models can identify clusters of patients with clinically distinct,

dynamic patterns of medication use over time. Evaluating the characteristics of patients prior to TKR within these empirically identified trajectories of prescription opioid use may be useful in identifying high-risk subgroups.

Methods: Using Medicare Parts A, B and D claims (2010-2014), we identified patients aged ≥65 years who underwent a TKR. All patients were required to be continuously enrolled in Medicare for ≥360 days prior to TKR. To determine opioid filling patterns after TKR, patients were followed up to 360 days from the day of TKR. We modeled 12 monthly indicators of filling as both a continuous (Mean morphine equivalents (MME)/day) variable for Model 1 and a binary (Yes/No for any opioid fill) response variable for Model 2 using censored normal and logistic group-based trajectory models, respectively. Model fit was assessed using a combination of the Bayesian Information Criterion (BIC), predicted probability of group membership and number of patients assigned to each trajectory group. Baseline

Figure 1 - Observed and predicted patterns of opioid use (MME/day) in each trajectory group for Model 1



Group	N	Average MME/day, mg Mean (SD)	Total opioid days covered in 360 day follow-up
4	2,175	149.8 (89.8)	220.3 (119.3)
3	8,057	42.4 (16.3)	214.8 (103.8)
2	37,691	18.9 (10.5)	100.4 (69.8)
1	135,450	20.1 (12.1)	18.9 (14.6)

Table 1 – Baseline patient characteristics by trajectory groups from Model 1

Patient Characteristic	Group 1 (Lowest)	Group 2	Group 3	Group 4 (Highest)	Standardized differences (Group 4 vs Group 1)
N	***135,450***	***37,691***	***8,057***	***2,175***	
Age (Mean, SD), years	73.2(5.4)	72.4(5.1)	71.3(4.8)	70.7(4.6)	-0.50
Female (n, %)	82467(60.9)	26026(69.1)	5510(68.4)	1467(67.4)	0.14
Combined Comorbidity index (Mean, SD)	0.7(1.8)	1.1(2.1)	1.4(2.3)	1.8(2.5)	0.50
Frailty Score (Mean, SD)	0.16 (0.04)	0.17 (0.04)	0.19 (0.05)	0.21 (0.06)	0.98
Frailty categories					
Mild (n, %)	33808(25.0)	5543(14.7)	619(7.7)	100(4.6)	-0.60
Moderate (n, %)	52594(38.8)	12520(33.2)	1996(24.8)	314(14.4)	-0.57
Severe (n, %)	49048 (36.2)	19628(52.1)	5442(67.5)	1761(81.0)	1.02
Cancer (n, %)	26572(19.6)	6547(17.4)	1331(16.5)	370(17)	-0.07
Any Opioid use in prior year (n, %)	62831(46.4)	30863(81.9)	7754(96.2)	2138(98.3)	1.42
Tobacco use (n, %)	14900(11)	5335(14.2)	1730(21.5)	562(25.8)	0.39
Alcohol abuse (n, %)	902(0.7)	343(0.9)	131(1.6)	47(2.2)	0.13
Anxiety (n, %)	10846(8)	4872(12.9)	1694(21)	570(26.2)	0.50
Falls (n, %)	4577(3.4)	1885(5)	674(8.4)	237(10.9)	0.29
Back Pain (n, %)	54001(39.9)	20368(54)	5623(69.8)	1816(83.5)	1.00
Depression (n, %)	14181(10.5)	6465(17.2)	2164(26.9)	825(37.9)	0.68
Diabetes (n, %)	36901(27.2)	12522(33.2)	2843(35.3)	719(33.1)	0.13
Drug Abuse (n, %)	84(0.1)	78(0.2)	93(1.2)	48(2.2)	0.20
ER Visit (n, %)	26504(19.6)	10139(26.9)	2836(35.2)	884(40.6)	0.47
Number of Drugs (Mean, SD)	9(5)	12(5.8)	14.5(6.5)	16.4(7.1)	1.21
Number of Office Visits (Mean, SD)	11.3(6.7)	13.3(7.7)	15.5(9)	18.8(10.3)	0.13

patient characteristics (assessed in the 360 days prior to TKR) were then tabulated by trajectory group for the final model.

Results: We identified 183,373 patients who underwent TKR during the study period. We selected the 4-group trajectory model as having the best fit for both continuous and binary indicators of filling. Observed and predicted patterns of opioid use in each of the 4 trajectory groups identified by Model 1 are summarized in **Figure 1.** 78% (n=1,686) of patients assigned to Group 4 (highest opioid use group) from Model 1 were also assigned to Group 4 in Model 2 though the average MME/day in Group 4 was higher (149.8 mg vs. 43.0) in Model 1 compared to Model 2. Hence, Model 1 provided more clinically-meaningful discrimination between patients' opioid use, and we used trajectory membership based on Model 1 to describe baseline patient characteristics **(Table 1)**. Differences were noted in the baseline characteristics of patients assigned to group 4 compared to those assigned to Group 1 (lowest opioid use). Patients in Group 4 were more likely to be younger, female, have opioid use in the year prior to TKR, and had a greater burden of comorbidities (such as depression, anxiety disorders, back pain), more likely to have used tobacco, alcohol and used more healthcare services in general (number of ER visits, physician office visits and medications used). Patients in Group 4 were also more likely to be frail as assessed by the claims-based frailty index.

Conclusion: Group-based trajectory models identified a subgroup of patients with high opioid use and whose baseline characteristics prior to TKR were substantially different than those in other groups. Future work could further determine the predictors of persistently high-dose opioid users after TKR and associated adverse events.

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Abstract Number: 2799

Does Early Anterior Cruciate Ligament Reconstruction Prevent Further Meniscal Damage? Secondary Analysis of a Randomized Controlled Trial

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SESSION INFORMATION
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Background/Purpose: It has been suggested that recurrent instability episodes in a non-reconstructed anterior cruciate ligament (ACL) injured knee increase the risk for an incident meniscal tear. However, the evidence comes from observational studies with high risk on selection bias. Our objective was to determine development of meniscal damage over 5 years after ACL injury using data from the only randomized controlled trial in the field, comparing rehabilitation plus early ACL reconstruction ("early ACLR") vs rehabilitation with optional delayed ACL reconstruction ("optional delayed ACLR").

Methods: We used longitudinal knee MRIs including 121 young adults (ISRCTN 84752559; ethics approval LU 535-01). One musculoskeletal radiologist read baseline and 5-year follow-up images using the Anterior Cruciate Ligament Osteoarthritis Score (ACLOAS). We defined development of meniscal damage both dichotomously and as sum score representing severity (based on the sum of reclassified ACLOAS meniscus grades). Using a full analyzis set as randomized, we studied the development of meniscal damage (yes/no) with logistic regression, and severity with zero-inflated Poisson regression. Analyses were performed both on knee and on compartment level, and adjusted for age, sex, and baseline meniscal damage.

Results: In early ACLR, 60 of 62 participants remained (2 missing baseline MRIs). In optional delayed ACLR, 55 of 59 subjects had longitudinal MRIs. After 5 years we found a relative risk for development of meniscal damage on knee level of 1.3 (95% confidence interval [95%CI]=0.9-1.9) in optional delayed ACLR vs early ACLR (Table 1). For medial and lateral meniscal damage, respectively, the relative risks were 2.1 (95%CI=1.1-3.9) and 1.0 (95%CI=0.6-1.5). The mean severity score was 1.5 higher (more severe damage) on knee level in optional delayed ACLR vs early ACLR (95%CI=1.1-1.9) among those with meniscal damage at 5 years. For medial and lateral meniscal damage, respectively, the corresponding scores were 1.7 (95%CI=1.2-2.5) and 1.0 (95%CI=0.8-1.4) (Figure 1).

Conclusion: A strategy of early ACLR may reduce development of medial meniscal damage following ACL injury. For the lateral meniscus, ACLR seems neither to be protective nor to increase the risk of damage.

Table 1 - Results of the logistic regression analysis for development of meniscal damage and the zero inflated Poisson regression analysis for meniscal severity scores at 5 years compared to baseline for the optional delayed ACL reconstruction arm compared to the early ACL reconstruction arm

	Development of meniscal damage		Meniscal damage severity score
	Risk ratio (95%CI)	Risk difference (%) (95%CI)	Ratio of means (95%CI)
Knee level			
Unadjusted	1.17 (0.81 – 1.71)	7.7 (-10.5 – 26.0)	1.25 (0.92 – 1.72)
Adjusted	1.32 (0.92 – 1.88)*	13.3 (-3.8 – 30.4)*	1.46 (1.13 – 1.87)†
Medial meniscus			
Unadjusted	2.08 (1.11 – 3.92)	19.9 (3.7 – 36.0)	1.73 (1.07 – 2.79)
Adjusted	2.10 (1.14 – 3.86)*	20.1 (4.5 – 35.7)*	1.71 (1.18 – 2.47)†
Lateral meniscus			
Unadjusted	0.60 (0.33 – 1.09)	-14.9 (-31.2 – 1.5)	0.88 (0.62 – 1.24)
Adjusted	0.97 (0.63 – 1.52)*	0.0 (-13.9 – 12.4)*	1.06 (0.80 – 1.40)†

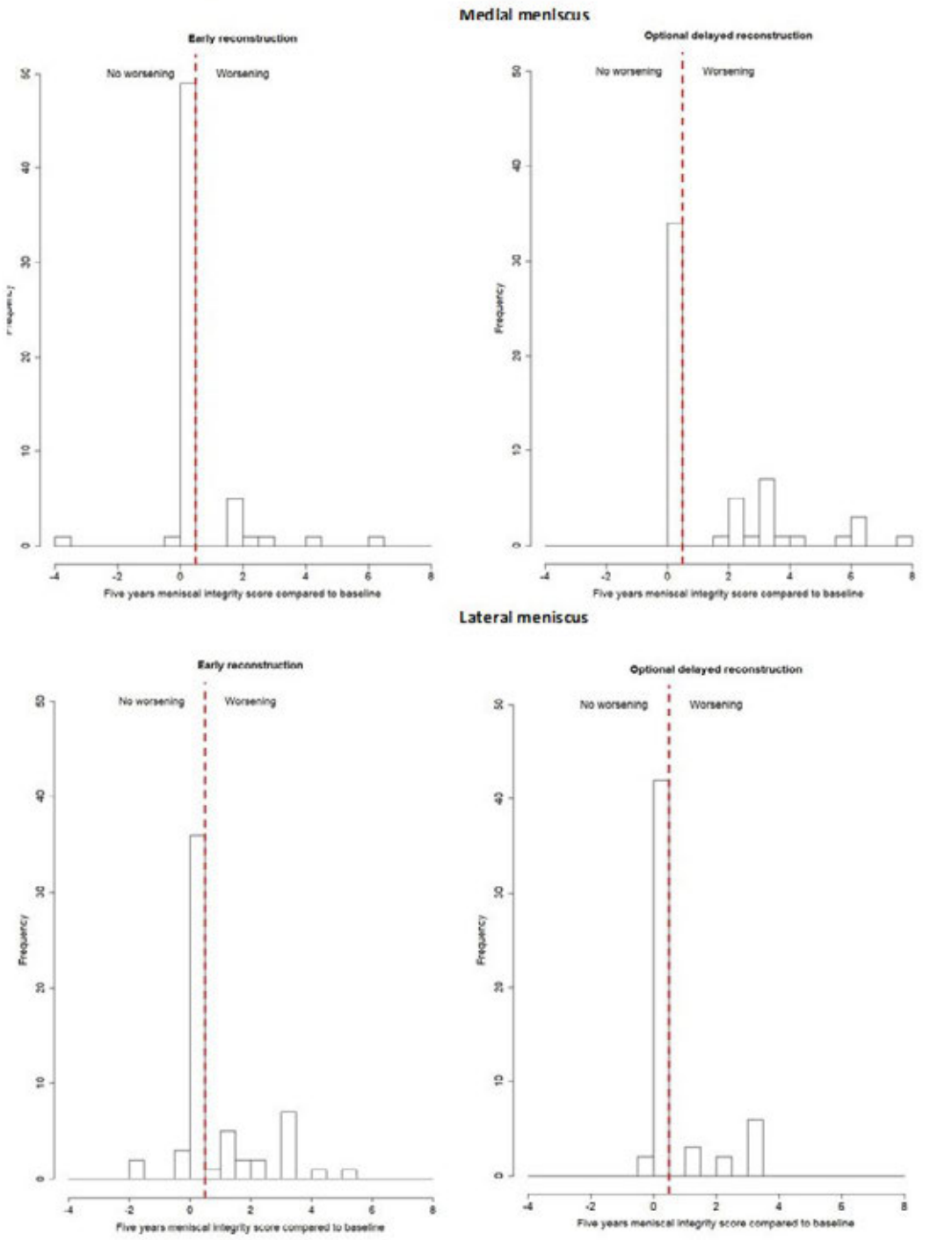
CI=confidence interval, Ratio of means = concerns the subjects that had a positive probability of a non-zero score

N=60 for early arm due to one missing baseline MRI reading and one lost to follow up, and N=55 for optional delayed arm due to four missing five year MRI readings

* Adjusted for age, gender, and baseline meniscal damage

† Adjusted for age, gender, and baseline meniscal damage severity score

Figure 1 - Change in meniscal damage score from the baseline to the 5-year follow-up examination for medial and lateral meniscus in the rehabilitation plus early ACL reconstruction arm and the rehabilitation plus optional delayed ACL reconstruction arm



Disclosure: B. Snoeker, None; **F. Roemer**, BICL, 1, Boston Imaging Core Lab, 1, 6, Shareholder BICL,LLC, 1; **A. Turkiewicz**, None; **S. Lohmander**, Pfizer, 8, Roche, 5, GSK, 5, Johnson & Johnson, 5, Galapagos, 5, Regeneron, 5; **R. Frobell**, None; **M. Englund**, None.

Abstract Number: 2800

Five Year Structural Changes in Patients with Meniscal Tear and Osteoarthritis from an RCT of Arthroscopic Partial Meniscectomy vs. Physical Therapy

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Orthopedics, Low Back Pain & Rehabilitation
Session Type: ACR/ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Meniscal tear is an independent risk factor of structural progression in OA; Arthroscopic partial meniscectomy (APM) is also associated with progression, though it is unclear if APM confers additional risk beyond that of the underlying meniscal tear. The goal of this study was to evaluate changes in knee MRI findings over 60 months in patients with meniscal tear and OA treated with either APM (and postop physical therapy (PT)) or with PT alone as a part of a multicenter RCT.

Methods: We used data from an RCT of APM and PT vs. PT alone (denoted in this abstract as APM vs. PT) for patients ≥ 45 years old with knee pain, meniscal tear on MRI, and OA changes on radiograph or MRI. Patients were excluded from this analysis if they were randomized to but did not receive APM, crossed over to APM > 6 months from randomization, or if they had no MRIs. We performed as-treated analysis: subjects who crossed over from PT to APM within 6 months from randomization were analyzed in the APM group.

Baseline (BL), 18-month (18m), and 60-month (60m) MRIs were read using the MRI OA Knee Score (MOAKS), which assesses damage in several joint features including osteophyte, cartilage surface area, and cartilage thickness. Each feature was scored ordinally from 0 - 3, (higher is worse) in each of 14 subregions (SR) for cartilage and 12 for osteophytes. We summed the scores from all SRs within the osteophyte, cartilage surface area and cartilage thickness domains. We used a linear mixed effects model to assess the relationship between the APM and PT groups and the changes in damage scores within each domain for two time intervals: BL-18m and 18m-60m.

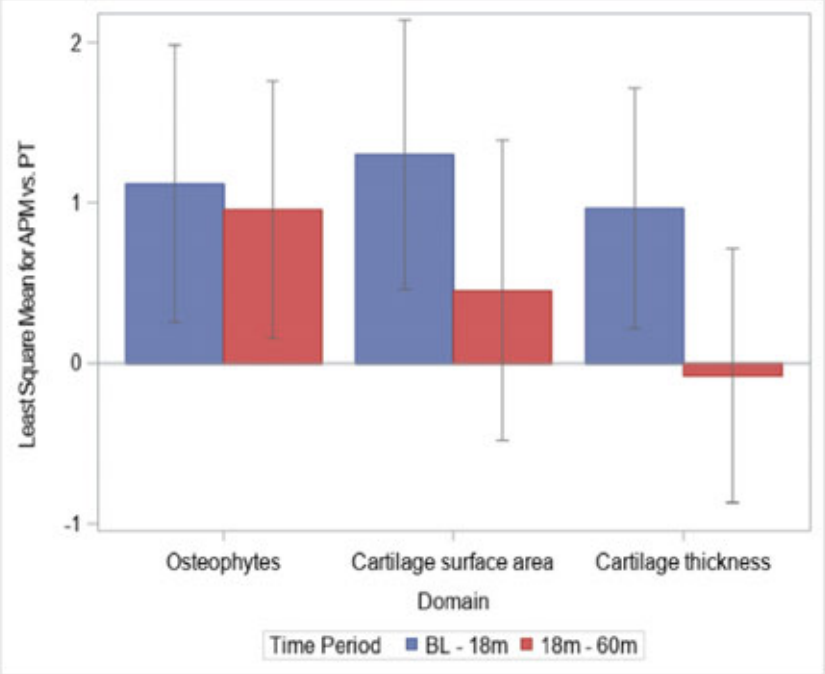
Results: Of 351 randomized subjects, we excluded 10 randomized to but not undergoing APM, 14 randomized to PT who crossed over after 6m and 32 with no MRI. The analytic cohort included 295 subjects with mean age 58 (SD 7) years and mean baseline KOOS pain (0-100, 100 worst) 47 (SD 16). 193 (65%) received APM and 102 (35%) received PT. The groups were balanced on BL demographic and clinical characteristics. 285 (97%) subjects had MRI at BL 221 (75%) at 18m and 165 (56%) at 60m.

Descriptive statistics on change in both time periods are presented in the Table. Both treatment groups worsened in all domains for both time periods, with more worsening over BL – 18m than 18m – 60m. The Figure displays the difference in change in score for each domain for APM vs. PT, from the mixed effects model. Worsening in osteophyte score was significantly greater in the APM group vs. the PT group for both time periods. Change in both cartilage surface area and cartilage thickness scores were significantly different between the groups for the BL – 18m period, but not the 18m – 60m period.

Table 1. Change over Time in Each Domain Score, Overall by Treatment Group

Domain	Overall n Mean (SD)	APM Group n Mean (SD)	PT Group n Mean (SD)
Osteophytes			
BL – 18m	212 3.3 (3.4)	141 3.8 (3.5)	71 2.5 (3.0)
18m – 60m	148 2.2 (2.8)	94 2.6 (3.1)	54 1.5 (2.0)
Cartilage Surface Area			
BL – 18m	210 2.7 (3.1)	139 3.0 (3.2)	71 1.9 (2.9)
18m – 60m	148 1.1 (3.0)	93 1.3 (3.3)	55 0.8 (2.5)
Cartilage Thickness			
BL – 18m	210 1.6 (2.2)	139 1.8 (2.4)	71 1.1 (1.8)
18m – 60m	148 1.4 (2.2)	93 1.4 (1.9)	55 1.5 (2.6)

Figure. Least Square Mean (95% CI) from Mixed Effects Model of Change for APM vs. PT in Score by Domain and Time Period. Positive values indicate that the APM group had more change, and negative values indicate that the PT group had more change. If the 95% confidence interval excludes 0 then the difference is statistically significant.



Conclusion: In subjects with underlying meniscal tear, APM was associated with greater worsening in cartilage surface area, cartilage thickness, and osteophytes over 18m post randomization, and greater worsening in osteophytes, but not in cartilage scores, in the subsequent 42 months. Future work will consider missing not at random imputation for subjects undergoing TKR, examine outcomes from an intention to treat perspective, and determine the magnitude of change in structure that is associated with clinically meaningful changes in symptoms.

Disclosure: S. Shrestha, Roche/Genentech, 2; **J. Katz**, Flexion, 2, Flexion Therapeutics, 2, Samumed, 2; **E. Losina**, Flexion, 2, Flexion Therapeutics, 2, Pfizer, 2, Pfizer Inc, 2, Regeneron, 5, Regeneron Pharmaceuticals, 5, Roche/Genentech, 2, Samumed, 2, TissueGene, 2, Velocity, 5, Velocity Pharaceutical Development, 5, Velocity Pharmaceutical Development, 5; **J. Collins**, Boston Imaging Core Lab, 5, Boston Imaging Core Labs, 2, Genentech, 2, Roche/Genentech, 2.

Abstract Number: 2801

Optimal Threshold of Walking Speed Predictive of Mortality Risk over 9 Years in Knee Osteoarthritis: Data from Osteoarthritis Initiative

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SESSION INFORMATION
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Background/Purpose: Knee osteoarthritis (OA) is associated with mortality, and walking difficulty is known to mediate this relationship. However, little is known about what specific aspects of walking difficulty increase mortality risk. We investigated the relationship of walking speed, as a measure of walking difficulty, to mortality and studied what thresholds that best discriminate risk of mortality in people with knee OA. Since knee OA frequently occurs in mid-life, we additionally investigated if walking speed is a relevant predictor of mortality and studied the thresholds that best discriminate the mortality risk in younger adults (aged < 65 years) with knee OA.

Methods: We used data from the Osteoarthritis Initiative (OAI). Walking speed was measured via the 20-meter (m) walk test. We quantified time to mortality over 9 years, i.e., until the 108-month OAI visit. To examine the association of walking speed with mortality over 9 years, we calculated hazard ratios (HR) and 95% confidence intervals (CI) from the Cox regression model adjusted for potential confounders. To identify an optimal threshold of walking speed predictive of mortality risk, we used the Maximal Likelihood Ratio Chi-square Approach. This approach selects the threshold that is most concordant with mortality risk over the observed follow-up times, a metric similar to maximizing Youden index when using a receiver operating curve method. Specifically, we ran adjusted Cox regression models for different thresholds of the walking speed iteratively. We then identified the optimal threshold from the model that yielded the maximal chi-square value (Table). We repeated these analyses separately for younger adults with knee OA.

Results: Of 4775 participants who completed the 20-m walk at baseline (age [mean (± sd)] 61.1 ± 9.2 years, BMI 28.6 ± 4.8 kg/m^2, 59% female), 6.5% (312/4755) died over 9 years. For younger adults, 3.0% (88/2966) died. Walking 0.1 meters/second (m/s) slower during the 20-m walk was associated with 16% [Adjusted HR 1.16, 95% CI (1.09, 1.23)] and 14% [Adjusted HR 1.14, 95% CI (1.02, 1.28)] higher risk of mortality over 9 years in the overall analytic sample and younger adults, respectively. Walking slower than 1.2 m/s was found to be an optimal threshold to best discriminate those with and without mortality for both the entire cohort, and among younger adults (Table).

Conclusion: Walking speed, an objective measure of walking difficulty is associated with mortality in knee OA. Specifically, walking slower than 1.2 m/s during a 20-m walk test may identify the risk of mortality in people with OA.

Table: Maximal Likelihood Ratio Chi-Square Approach^ to identify the optimal threshold of walking speed that predicted the risk of mortality in A) overall sample and B) younger adults with or at risk of knee OA

Walking speed thresholds	# deaths/total people		*Adjusted HR (95% CI)	**Likelihood Ratio Chi-Square
	Walk < threshold	Walk ≥threshold		
A) Overall sample (N=4775)				
1.4 m/s	246/3089 (8%)	66/1686 (3.9)	1.48 (1.11, 1.99)	278.82
1.3 m/s	200/2185 (9.2%)	112/2590 (4.3%)	1.62 (1.26, 2.09)	285.81
1.2 m/s†	**146/1355 (10.8%)**	**166/3420 (4.9%)**	**1.81 (1.41, 2.31)**	**293.20†**
1.1 m/s	88/686 (12.8%)	224/4089 (5.5%)	1.97 (1.49, 2.60)	292.85
1.0 m/s	48/317 (15.1%)	264/4458 (5.9%)	2.02 (1.44, 2.83)	286.25
0.9 m/s	20/118 (16.9%)	292/4657 (6.3%)	2.43 (1.49, 3.98)	281.57
B) ***Younger adults (N=2966)				
1.4 m/s	63/1734 (3.6%)	25/1232 (2.0%)	1.54 (0.93, 2.54)	36.34
1.3 m/s	48/1171 (4.1%)	40/1795 (2.2%)	1.64 (1.03, 2.61)	37.70
1.2 m/s†	**33/678 (4.9%)**	**55/2288 (2.4%)**	**1.92 (1.19, 3.11)**	**40.06†**
1.1 m/s	19/334 (5.7%)	69/2632 (2.6%)	1.89 (1.06, 3.37)	37.86
1.0 m/s	7/147 (4.8%)	81/2819 (2.9%)	1.13 (0.47, 2.72)	33.42
0.9 m/s	5/61 (8.2%)	83/2905 (2.9%)	2.30 (0.78, 6.74)	35.24

*Adjusted for baseline age, BMI, sex, race, education, comorbidities, the presence of depression (≤ vs. >16), and symptomatic knee OA (yes or no), defined as presence of Kellgren–Lawrence grade ≥ 2 on x-ray in one or both knees, and pain, aching, or stiffness on most days of a month during the previous year

**Likelihood Ratio Chi-Square values are obtained from adjusted Cox regression models

***Younger adults are participants with or at risk of knee OA who are aged less than 65 years old

^Approach states that higher chi-square values represent greater concordance between the threshold and mortality.

† Model that yielded maximum chi-square value

These same thresholds also apply to younger adults with knee OA. Thus, walking speed may be a simple indicator of health in adults with knee OA. Health care professionals may use walking speed to assess expected health and tailor goals of care for knee OA population.

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Abstract Number: 2802

High Intensity Interval Training for Knee Osteoarthritis: A Pilot Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Orthopedics, Low Back Pain & Rehabilitation

Session Type: ACR/ARP Abstract Session

Session Time: 2:30PM–4:00PM

Background/Purpose: Physical activity reduces pain and increases physical function in people with knee osteoarthritis (OA), but few achieve recommended levels of physical activity because of pain or functional limitations. High-intensity interval training (HIIT) is a time-efficient exercise strategy with minimal joint impact that requires reduced frequency and duration of exercise compared to traditional long duration low-to-moderate intensity exercise. The

purpose of this study was to determine short-term changes in outcomes among patients with symptomatic knee OA participating in a HIIT intervention.

Methods: Twenty-nine participants with symptomatic knee OA enrolled in a single-arm 12-week HIIT intervention. Participants had a mean BMI of 32 kg/m^2 (2/3 were obese) and a mean age of 63 (range 44-75 years); 2/3 were women and 62% were White, 24% were Black, and 7% were Hispanic. All training was performed under one-on-one supervision from trained research personnel, 2 times per week for 12 weeks. Participants chose the mode of exercise (e.g., walking, cycling). Each training session consisted of a 3-5 minute warm-up and 10 repetitions of 1-minute bouts at individualized training intensity (based on the participant's peak oxygen consumption [VO_2peak test]) with 1-minute rest periods. Baseline, 6-week, and 12-week measures included: performance-based physical function (40 meter fast-paced walk test, 30-second chair-stand test, a stair-climb test, Timed Up and Go Test), WOMAC total and subscale scores, balance measures (single leg stance, side-by-side, semi-tandem, tandem), isometric knee extensor and flexor strength, cardiorespiratory fitness (VO_2peak, time to exhaustion, maximum heart rate), and body composition determined from dual energy x-ray absorptiometery (lean body mass, fat mass, visceral fat, leg lean mass, % fat). Separate linear mixed models were fit for each outcome. Fixed effects were time, age, sex, and baseline BMI, and random effects were baseline values (intercepts); correlation among visits was modeled as unstructured. Mean change between baseline, 6-week, and 12-week assessments was estimated for each outcome.

Results: At 6 weeks, statistically significant improvements were noted for all four physical function measures, isometric knee extensor strength, VO_2peak, and time to exhaustion (Table). At 12 weeks, these changes continued to

	Visit effect		
Outcome (each a separate model)	*6 week change from baseline*	*12 week change from baseline*	*6 to 12 week change*
Physical Function			
20 m fast-paced walk test (seconds)	**-0.79 (-1.24, -0.34)**	**-1.13 (-1.61, -0.64)**	-0.33 (-0.81, 0.15)
30 s chair-stand test (no.)	**1.6 (0.9, 2.3)**	**2.6 (1.8, 3.4)**	**1.0 (0.2, 1.8)**
Stair-climb test (seconds)	**-0.98 (-1.65, -0.30)**	**-1.42 (-2.13, -0.71)**	-0.44 (-1.16, 0.27)
Timed Up and Go test (seconds)	**-0.49 (-0.83, -0.15)**	**-0.58 (-0.95, -0.22)**	-0.10 (-0.44, 0.24)
Knee OA Symptomatic Burden			
WOMAC pain subscale (0-20)	-0.6 (-1.7, 0.4)	**-1.7 (-2.8, -0.6)**	-1.1 (-2.2, 0.1)
WOMAC stiffness subscale (0-8)	-0.4 (-0.9, 0.0)	**-1.2 (-1.7, -0.7)**	**-0.8 (-1.3, -0.2)**
WOMAC function subscale (0-68)	-2.9 (-5.9, 0.1)	**-6.3 (-9.6, -3.1)**	**-3.4 (-6.7, -0.2)**
WOMAC total score (0-96)	-4.0 (-8.1, 0.0)	**-9.7 (-13.6, -4.9)**	**-5.7 (-9.6, -0.8)**
Balance			
Single leg stand (seconds) — max=30s	2.78 (-0.17, 5.73)	**3.41 (0.26, 6.56)**	0.63 (-2.55, 3.80)
Muscle Strength: Isometric Strength			
Flexor			
Right knee, maximum (kg)	-1.85 (-5.72, 2.02)	3.34 (-0.74, 7.41)	**5.18 (1.10, 9.27)**
Left knee, maximum (kg)	1.39 (-3.85, 6.64)	-0.84 (-6.36, 4.69)	-2.23 (-7.78, 3.32)
Extensor			
Right knee, maximum (kg)	**9.36 (1.58, 17.14)**	**9.99 (1.80, 18.18)**	0.63 (-7.61, 8.86)
Left knee, maximum (kg)	**9.24 (0.25, 18.23)**	**9.86 (0.40, 19.33)**	0.62 (-8.89, 10.14)
Cardiorespiratory Fitness			
Peak oxygen consumption, VO_2peak (L/min)	**0.18 (0.08, 0.28)**	**0.14 (0.03, 0.24)**	-0.04 (-0.15, 0.07)
Time to exhaustion (minutes)	**0.89 (0.48, 1.29)**	**1.07 (0.63, 1.50)**	0.18 (-0.26, 0.62)
Maximum heart rate (beats/min)	1.5 (-1.3, 4.2)	**4.5 (1.5, 7.5)**	**3.0 (0.1, 6.0)**
Body Composition			
Lean body mass (kg)	0.22 (-0.19, 0.63)	-0.12 (-0.56, 0.31)	-0.35 (-0.78, 0.09)
Fat mass (kg)	-0.46 (-1.23, 0.30)	-0.28 (-1.10, 0.54)	0.19 (-0.63, 1.01)
Visceral fat (kg)	-0.14 (-0.33, 0.05)	-0.19 (-0.40, 0.02)	-0.05 (-0.26, 0.15)
Right leg, lean mass (kg)	0.12 (-0.04, 0.28)	0.11 (-0.06, 0.28)	-0.01 (-0.18, 0.16)
Left leg, lean mass (kg)	0.18 (-0.03, 0.40)	0.23 (-0.00, 0.46)	0.05 (-0.18, 0.28)
% Fat	0.08 (-0.44, 0.60)	0.11 (-0.44, 0.66)	0.03 (-0.53, 0.58)

Significant effects at a 0.05 level shown in bold.
*Linear mixed models adjusted for fixed effects of time, age, sex, and baseline BMI and random intercepts. Where appropriate ($p<0.1$) quadratic effects of age and BMI were included. Models used restricted maximum likelihood method and unstructured covariance matrix for correlations over time and missing data were assumed to be missing at random.

Table. Adjusted* estimates and 95% confidence intervals (95% CI) of change in assessment measure outcome over time using models for each outcome.

increase, and additional statistically significant improvements were observed for the WOMAC, single leg stand, and maximum heart rate (Table). Changes in isometric knee flexor strength and body composition were not statistically significant, although the changes in visceral fat and left leg lean mass at 12 weeks were clinically meaningful.

Conclusion: A 12-week supervised HIIT program improved WOMAC scores, physical function, balance, isometric knee extensor strength, and cardiorespiratory fitness, with most changes occurring as early as 6 weeks.

Disclosure: Y. Golightly, None; **C. Alvarez**, None; **M. Blue**, None; **K. Allen**, None; **A. Nelson**, Flexion Therapeutics, 5, Health Press Ltd, 7, MedScape, 8; **A. Smith-Ryan**, None.

Abstract Number: 2803

Efficacy of a 3-Month Wearable-enabled Physical Activity Counselling Program for People with Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Orthopedics, Low Back Pain & Rehabilitation
Session Type: ACR/ARP Abstract Session
Session Time: 2:30PM–4:00PM

Background/Purpose: Current guidelines emphasize an active lifestyle in the management of knee osteoarthritis (OA), but up to 90% of OA patients are inactive. We previously demonstrated that an 8-week physical therapist (PT)-led counselling intervention, with the use of a consumer-grade wearable device, improved step count and quality of life in people with knee OA, compared to a control [1]. In the current study, we aimed to assess the efficacy of this intervention for improving activity participation and disease status in people with knee OA after the counselling component was withdrawn.

Methods: Eligible participants had a self-reported knee OA diagnosis, or symptoms of knee OA based on a validated questionnaire. After baseline assessment (T0) and randomization, the *Intervention Group (IG)* received standardized education, a Fitbit, access to FitViz (a personalized Fitbit compatible app), and 4 biweekly phone calls by a PT to counsel activity goals over an 8-week period. Participant then continued to use the Fitbit and FitViz app independently up to week 12. The *Control Group (CG)* received a monthly e-newsletter from the research team. Participants were assessed again at the end of 12 weeks (T1). The primary outcome was time in daily moderate/vigorous physical activity at ≥3 METS and in bouts of ≥10 mins (**3+ MVPA**) measured with a SenseWear® monitor. Secondary outcomes were: 1) daily step count, 2) MVPA at ≥4 METS and in bouts of ≥10 mins (4+ MVPA, reflects purposeful activities), 3) time in sedentary activity in bouts of >20 mins, 4) Knee Injury & OA Outcome Score (KOOS); 5) Partners in Health Scale (PIHS; measured self-management capacity). We used Analysis of Covariance (ANCOVA) to assess the effect of the intervention on the outcomes at T1 after adjusting for T0. The robust regression procedure (SAS *proc robustreg*) was used to limit the impact of outliers.

Table 1: Results of outcome measures

	Intervention Group (n = 26)		Control Group (n = 25)	
	T0	T1	T0	T1
Mean 3+ MVPA time [mins]	31.0 (37.3)	37.7 (30.5)	71.3 (99.8)	49.4 (63.6)
Mean daily steps	6294.0 (3418.0)	7133.3 (3603.3)	7030.1 (3921.6)	6232.7 (3086.1)
Mean sedentary time [mins]	567.5 (183.1)	531.4 (173.5)	551.1 (234.9)	558.3 (224.9)
Mean 4+ MVPA time [mins]	11.1 (19.5)	13.3 (20.0)	42.1 (80.2)	23.1 (37.1)
KOOS (0-100; higher = better)				
Symptoms	68.5 (10.7)	69.3 (12.7)	65.7 (12.3)	66.9 (14.9)
Pain	72.6 (13.5)	73.1 (15.3)	65.1 (13.7)	65.9 (15.6)
ADL	75.5 (14.7)	75.0 (13.1)	72.2 (15.8)	70.3 (16.9)
Sports & recreation	47.9 (23.7)	47.1 (22.4)	46.8 (25.4)	52.2 (22.7)
Qol	44.0 (16.0)	48.7 (17.5)	47.5 (16.0)	46.9 (13.6)
Partners in Health Scale	6.4 (0.9)	6.4 (1.0)	6.5 (1.0)	6.8 (0.8)

Results: We enrolled 51 participants (*IG*: n=26, 88.5% women; *CG*: n=25, 76.0% women). Both groups were similar in age [*IG:* 65.0 (8.3) years; *CG*: 64.8 (SD 9.0)] and body mass index [*IG*: 29.8 (SD 9.0); *CG*: 28.9 (SD 6.2)]. **Table 1** summarizes the results. The *CG* accumulated significantly more 3+/4+ MVPA time at baseline. The adjusted mean difference in 3+ MVPA at T1 was 13.1 mins (95% CI: 1.6, 24.5, p=0.03). The secondary physical activity outcomes improved, although not statistically significant - step count: 1,106.5 (95% CI: -19.9, 2,232.9, p=0.05); 4+ MVPA: 1.6 mins (95% CI: -3.0, 6.1, p=0.50); sedentary time: -29.5 mins (95% CI: -75.8, 16.7, p=0.21). We found similar results in the KOOS and PIHS.

Conclusion: Our findings showed that the wearable-enabled intervention improved physical activity in people with knee OA 4 weeks after the counselling component ended. Further research will be required to examine the effectiveness of this intervention for promoting long-term physical activity and improving health outcomes.

[1] Li et al. *JMIR* 2018; 20(4):e159.

Disclosure: H. Xie, None; **L. Li**, None; **N. Lu**, None; **D. Gromala**, None; **C. Shaw**, None; **C. Backman**, None; **J. Tam**, None; **N. Gregory**, None; **J. Avina-Zubieta**, None; **A. Hoens**, None; **A. Townsend**, None; **L. Feehan**, None.

Abstract Number: 2804

Neutrophil Passage Through the Megakaryocyte Cytoplasm via Emperipolesis Modulates Neutrophil Migration

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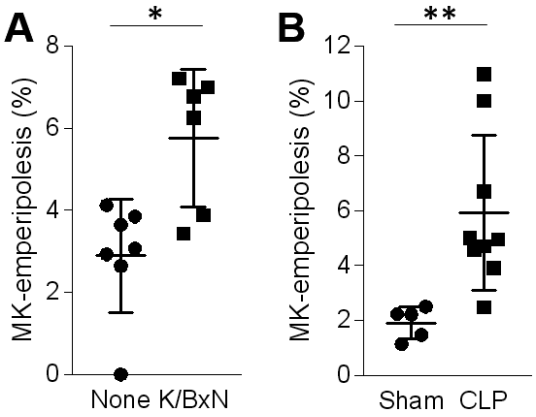
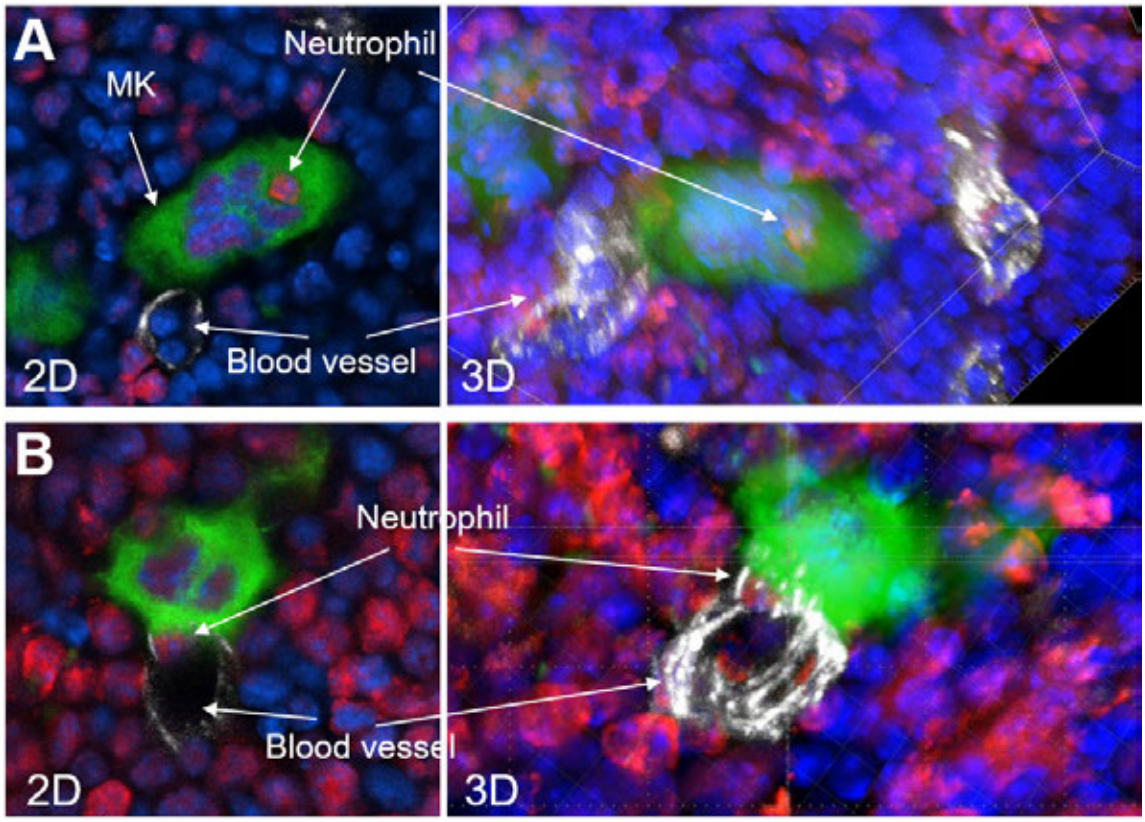
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Innate Immunity
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

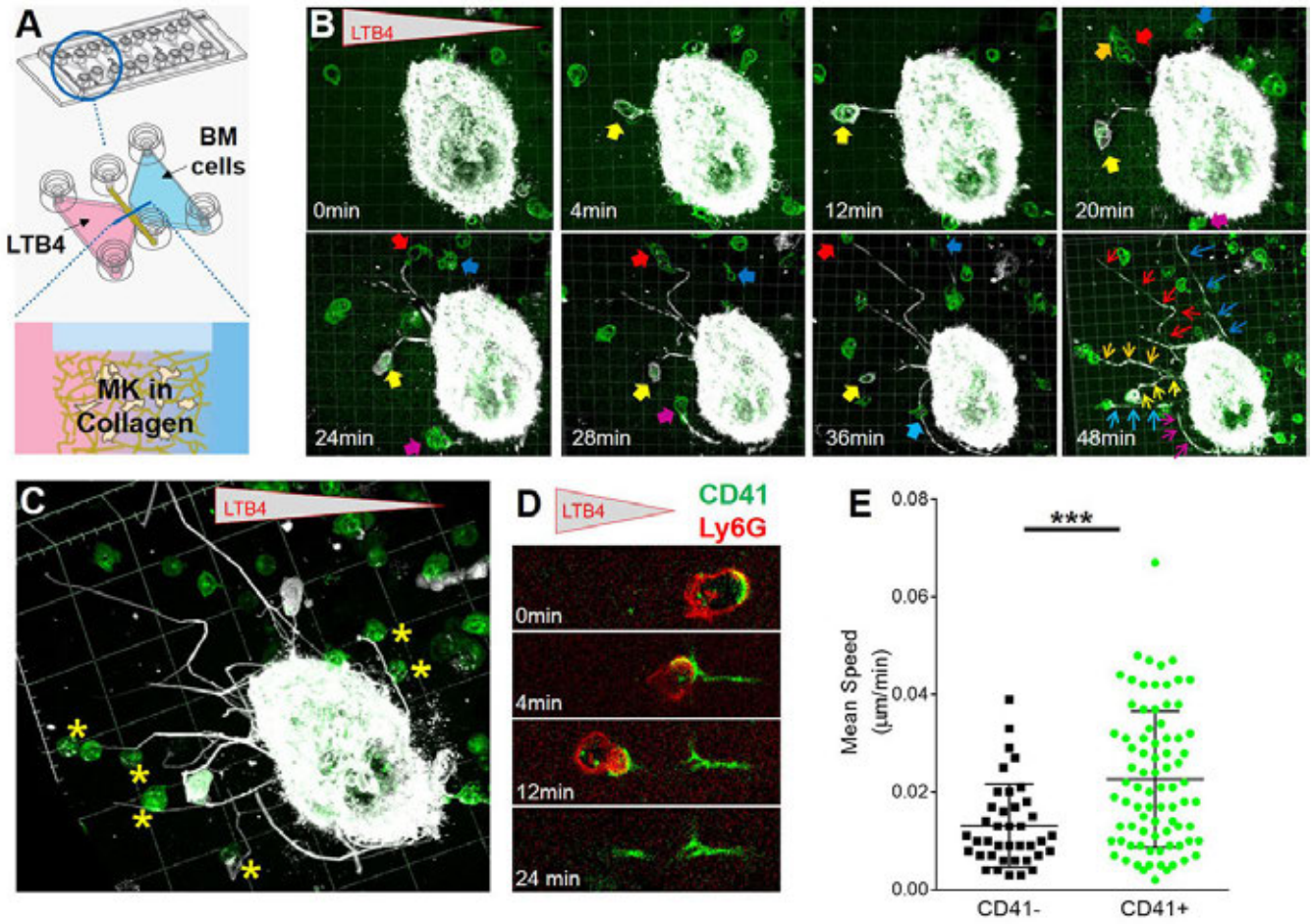
Background/Purpose: Emperipolesis (EP) is a little-understood phenomenon referring to the presence neutrophils within megakaryocytes (MKs). We developed methods to study EP *in vitro* and *in vivo*, finding that EP is a highly regulated cell-in-cell interaction, requires cytoskeleton rearrangement by neutrophils and MKs, and results in the re-



Percent of MK containing neutrophil (A) 8 days after arthritis induction and (B) 4 days after cecal ligation and puncture (CLP) surgery.



Whole bone marrow stained for CD41 (MK, green) Ly6G (neutrophil, red), CD31/CD144 (bone marrow sinusoids, white) and Hoescht (DNA, blue). (A) MK attached on a sinusoid and containing PMN. (B) Neutrophil in a vascular gap, at the interface between circulation and MK in the bone marrow compartment.



(A) µslide chemotaxis chamber (B) Neutrophils (Ly6G, green) migrating through a MK (CD41, white). Each colored arrow follows a neutrophil over time. The passage inside MK is confirmed by analyzing each Z-stacks for each time point (not shown). The image at 48 min shows trails left by neutrophils (colored arrows) (C) 3D reconstitution in high resolution of the MK in (B). Asterisks show neutrophils attached on trails. (D) Trails left by neutrophils are Ly6G negative and CD41 positive, demonstrating a MK origin. (E) Average speed of neutrophils positive for the MK marker CD41 (green circles) or CD41 negative (black squares). Representative of 3 experiments.

ciprocal exchange of cell membrane and proteins between both lineages (Cunin P *et al. eLife 2019;8:e44031*). At the end of EP, neutrophils exit MK cytoplasm alive and intact, but the consequences for neutrophil function are unknown

Methods: We assessed the frequency of EP in healthy mice, in the K/BxN mouse model of inflammatory arthritis and in the cecal ligation and puncture model. A model of EP was developed through incubation of MKs together with neutrophils and characterized using confocal imaging and electron microscopy. The biology of EP was interrogated *in vitro* by time-lapse microscopy on µ-slide chemotaxis chambers, and *in vivo* using whole-mount immunofluorescence of bone marrow. The role of EP on neutrophil migration was investigated *in vitro* using transwell assay and *in vivo* through engraftment of labelled neutrophils co-cultured or not with MKs back into mice subjected to inflammation

Results: Histological sections of bone marrow revealed that EP is increased 2-3 fold in inflammatory arthritis and after cecal ligation and puncture, a model of polymicrobial sepsis (Figure 1). Whole-mount immunostaining in bone marrow showed that EP is restricted to MKs in contact with vascular sinusoids, and neutrophils can be observed in the space between MKs and blood vessels, suggesting egress directly into blood (Figure 2). *In vitro*, we observed that neutrophils enter MKs through a membrane-lined vacuole, termed “emperisome”. We routinely noted the appearance of MK-derived exosomes in the emperisome, and the uptake of MK exosomes by internalized neutrophils. Migration

assay on μ-slide chemotaxis chambers revealed that neutrophils enter and exit MKs following a chemotactic gradient, using a "trans-MK" route (Figure 3A-B). After their passage into MK, neutrophils deposit MK material behind them during their migration, forming a "trail"-like structure made of MK proteins involved in immune cell attachment, and these neutrophils exhibit a clear migratory advantage (Figure 3B-E and not shown). In transwell assay, we observed that neutrophils previously co-cultured with MKs migrate more efficiently toward an LTB_4 gradient. Neutrophil migration is not modulated after culture with MK supernatant or PFA-fixed MKs, excluding an effect from MK-derived microparticles, cytokines, or surface proteins and suggesting a role for EP. *In vivo*, neutrophils previously incubated with MKs migrated more efficiently into the peritoneal cavity during LPS- or IL-1β-induced peritonitis

Conclusion: EP is dramatically increased during inflammation and mediates transfer of membranes and MK-exosome contents to internalized neutrophils. 3-D bone marrow microscopy and migration assays suggest that neutrophils can exit from MKs directly into the circulation, resulting in enhanced migratory capacity. Additional consequences of EP for neutrophil biology remain to be defined

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Disclosure: P. Cunin, None; **A. Wactor**, None; **L. Guo**, None; **A. Weyrich**, None; **É. Boilard**, None; **P. Nigrovic**, None.

Abstract Number: 2805

Natural Killer Cells Gene Expression Can Differentiate Rheumatoid Arthritis Patients from Healthy Controls

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Innate Immunity
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Rheumatoid arthritis (RA) is the most prevalent autoimmune diseases (1-3% of the world's population). RA is a prototypic inflammatory disease, being characterized by an altered state of homeostasis, in which immunological stimulation and unwanted inflammation prevail (Pincus, Brooks et al. 1994). The molecular triggers for the development of RA in healthy subjects are still not clearly defined. Identification of RA specific transcriptional signature can shed the light on the molecular pathogenesis of RA. Such signature facilitates the selection of biomarkers that can be used for early detection of RA and prediction of effectiveness of RA treatment. Most of the current transcriptome analyses in RA had focused on whole peripheral blood mononuclear cells (PBMCs). Few studies have indicated that natural killer (NK) cells may play either a pathogenic or a protective role in RA (Shegarfi, Naddafi et al. 2012, Yap, Tee et al. 2018). Hence, in this study we aimed at exploring NK cell markers that could possibly be used to aid in evaluating the differences among healthy controls and RA patients.

Methods: Publicly available transcriptome dataset (GSE93777) of sorted immune cells from RA patients and healthy volunteers were reanalyzed using in house pipeline for normalization and filtration of the raw probes' expression. Gene Set Enrichment analysis was used to identify genes that are differentially expressed (DEG) between different immune cells as compared to NK cells. Next, DEG between NK cells of RA patients and healthy controls were selected. Both lists of identified DEG were validated in peripheral blood collected from healthy controls and RA patients. Whole blood samples were collected from the recruited 11 RA patients (satisfying the 2010 ACR/EULAR classification

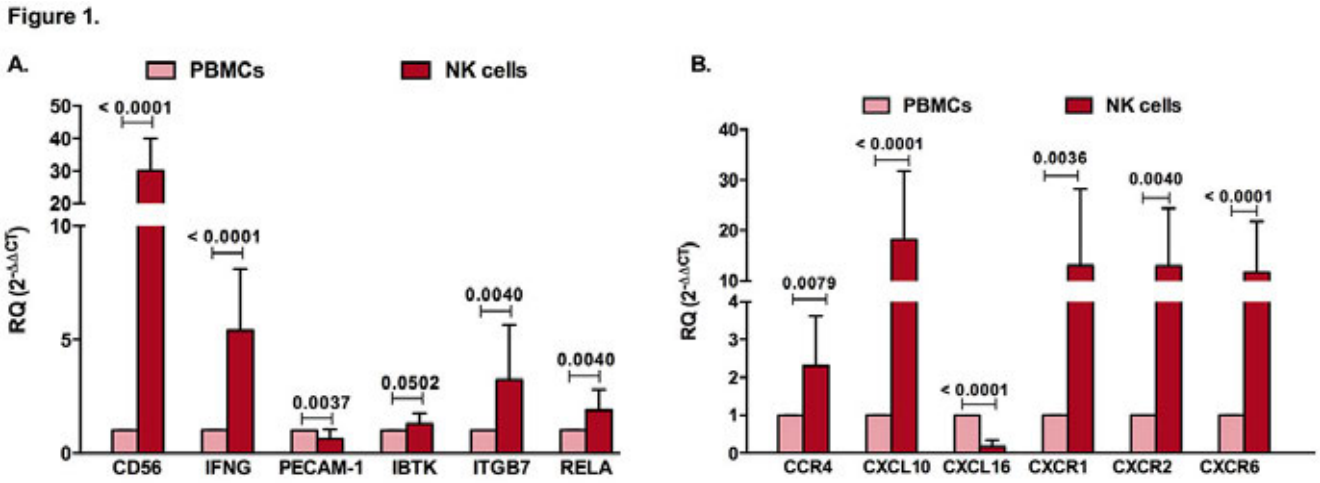

Figure 1. Differentially expressed genes (A) and chemokine ligands/receptors (B) between PBMCs and NK cells.

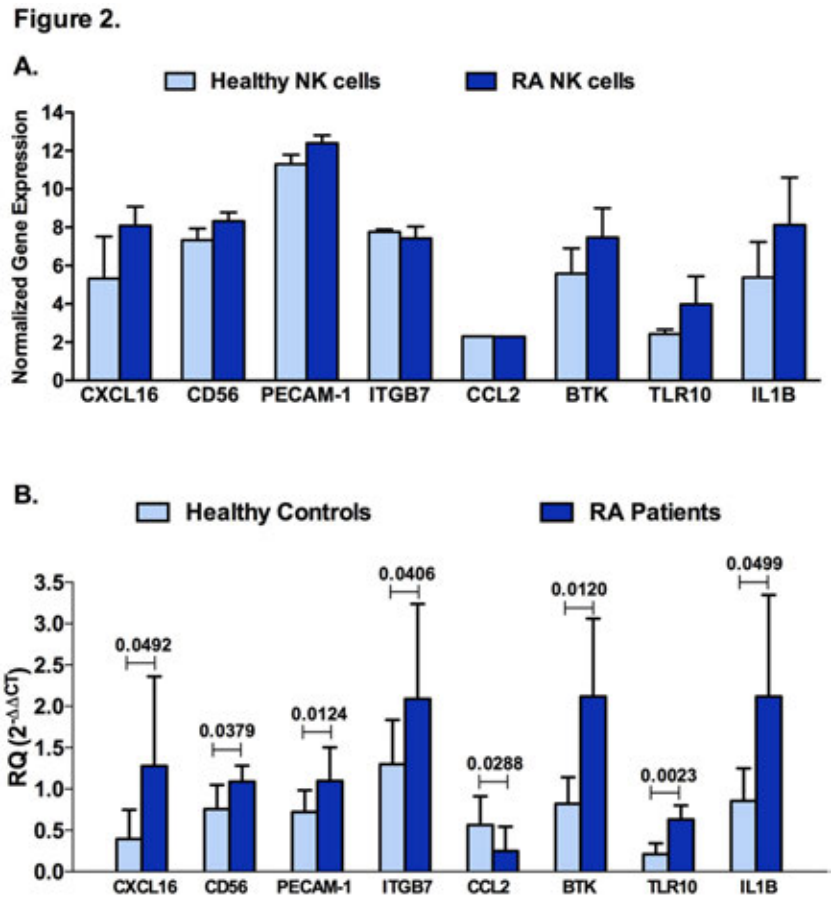

Figure 2. (A) In silico Gene Set Enrichment Analysis identified DEG between NK cells of RA patients and healthy controls. (B) Ex-vivo validation showed that NK cells from recruited RA patients showed differential expression of the predicted genes compared to healthy individuals.

criteria for RA) and 10 healthy controls (with no diagnosis of autoimmune diseases). Then, PBMCs were separated by Ficoll density gradient method, while NK cells were isolated using RosetteSep negative selection method. RNA was extracted and gene expression was assessed using qRT-PCR. Statistical analysis was done using Mann-Whitney test. Binary regression test was used to predict the probabilities of being a case based on the values of the selected genes.

Results: Similar to CD56, a known marker for NK cells, and interferon gamma (IFN-γ), a prototype cytokine secreted by these cells, PECAM-1, IBTK, ITGB7, and RELA were expressed in NK cells (Figure 1A). Furthermore, chemokine ligands and receptors (CCR4, CXCL10, CXCL16, CXCR1, CXCR2, CXCR6) were specifically expressed by NK cells in comparison to PBMCs (Figure 1B). Additionally, as predicted by bioinformatics (Figure 2A), CXCL16, CD56, PECAM-1, ITGB7, BTK, TLR10, and IL-1β were significantly upregulated in NK cells of RA patients when compared to healthy controls, whereas CCL2 was downregulated (Figure 2B). In this study, we applied a logistic regression model using some of the identified NK genes expression (RELA, BTK, IL-1β, CKLF, PECAM-1, TLR10, IL1RN, IFN-γ) where it showed a good prediction power as predictors for RA.

Conclusion: Gene expression of these molecules; namely CXCL16, CD56, PECAM-1, ITGB7, BTK, TLR10 and IL-1β, in NK cells might be used as promising biomarkers for RA disease.

Disclosure: N. Elemam, None; **M. Hachim**, None; **S. Hannawi**, None; **A. Maghazachi**, None.

Abstract Number: 2806

Single Cell RNA-sequencing Reveals Distinct Macrophage Subsets in the Joint with Differing Ontogenies During Steady-state and Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Innate Immunity
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Macrophages in the synovial lining of the joint are critical players in the pathogenesis of rheumatoid arthritis (RA). However, their heterogeneity remains poorly characterized.

Methods: Using single cell RNA-sequencing (scRNA-seq), we uncovered 4 distinct subsets of mouse synovial macrophages during steady state distinguishable by expressions of CX3CR1 and MHCII.

Results: MHCII- subsets preferentially expressed markers associated with tissue-residency, including Sepp1 and C1qc, whereas MHCII+ subsets expressed monocyte-associated markers such as Ccr2 and Cd74, Ly6c2, a key maker of classical monocytes, was expressed only in CX3CR1+MHCII+ subset. Fate mapping experiments confirmed the differing ontogenies of synovial macrophage subsets. During inflammatory conditions (serum transfer induced arthritis), we observed the expansion of CX3CR1+MHCII+ subset and increased expression of monocyte-associated genes in all macrophages, which coincides with the recruitment of circulating monocytes. These subsets are recapitulated in scRNA-seq data from synovial biopsies of RA patients.

Conclusion: Our results support a dynamic role for synovial macrophages in inflammation.

Disclosure: A. Montgomery, None; **S. Chen**, None; **P. Homan**, None; **G. Gadhvi**, None; **D. Winter**, None; **H. Perlman**, None.

Abstract Number: 2807

Activation of the STING Pathway Is a Shared Feature of Salivary Gland and Lung Inflammation in Sjogren's Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Innate Immunity
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Sjögren's syndrome is a chronic autoimmune disorder characterized by an increased type 1 interferon gene signature. The engagement of stimulator of interferon genes (STING) is a critical pathway involved in the production of type I IFNs. The gain of function mutations in *TMEM173*, encoding STING, results in a severe vasculopathy affecting the skin and lungs. We have previously reported that systemic activation of the STING pathway in mice, using a STING agonist DMXAA, causes an Sjögren's syndrome-like disease characterized by sialoadenitis and salivary gland dysfunction. Considering that lungs are affected in 9-20% of Sjögren's syndrome patients, this study was undertaken to investigate lung involvement in DMXAA treated mice.

Methods: Female C57BL/6 mice (8-10 wks. old) were injected with DMXAA ((20mg/kg body wt) either once (day 0) or twice (days 0 and 21). Serum IFN-α and IFN-β levels were measured by a multiplex bead-based assay. Proinflammatory cytokine gene expression in lungs was analyzed by real-time PCR and by using the Nanostring mouse inflammation panel. The innate lymphoid cell populations and lymphatic endothelial cells in lungs were studied by flow cytometry. H&E stained lung sections were used to evaluate the presence of inflammatory foci in the lungs. The role of STING expression in hematopoietic cells on lung inflammation, was investigated in bone marrow chimeras of WT into STING$^{-/-}$ mice and vice versa.

Results: DMXAA treatment induced a rapid, but transient spike in circulating type I IFN levels, which returned to baseline in 24h. At 4h post-treatment, there was a significant increase in the expression of *IL-6*, *TNF-α*, *IFNβ*, *Mx1,* and *IFNγ*, in the lungs. This was followed by an increase in type 1 innate lymphoid cells on day 8. Histopathologic analysis showed the presence of peri-bronchial inflammatory infiltrates on day 35, which persisted until day 57. The lung inflammation was associated with an increased expression of multiple proinflammatory genes, including *Ccl20*, *Cxcl10*, *Cxcl9*, and *Il17α*. Also, there was an increased frequency of lymphatic endothelial cells, suggestive of lymphangiogenesis. Although STING expression was seen in bronchial epithelium and alveolar cells, bone marrow chimeras between STING$^{-/-}$ and wild type mice suggest that STING expression in bone marrow derived cells was critical for lung inflammation.

Conclusion: Our data suggest that systemic activation of STING is a common pathway involved in the induction of salivary gland and lung inflammation in Sjögren's syndrome. In addition, activation of innate immunity in bone marrow-derived cells is critical for initiating lymphocytic infiltration in organs targeted in Sjögren's syndrome.

Disclosure: J. Papinska, None; **G. Gmyrek**, None; **U. Deshmukh**, None; **H. Bagavant**, None.

Abstract Number: 2808

Linking Toll-Like Receptor Signaling and Type I Interferons to Inflammation and Fibrosis in a Macrophage/Fibroblast Model of Congenital Heart Block

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Innate Immunity
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Since one of the strongest associations with antibodies (abs) to SSA/Ro (Ro60) is the development of congenital heart block (CHB), this model provides an exceptional opportunity to define novel insights that link maternal abs with an inflammatory cellular response which eventuates in fibrotic replacement of the AV node. We recently compiled risk genes based on an agnostic transcriptomic survey of macrophages isolated from hearts of fetuses dying with CHB and healthy aged matched fetuses electively terminated, noting that IFN related genes (IRGs), including IFN induced Protein with Tetratricopeptide Repeats 1(IFIT1) and Sialic Acid Binding Ig Like Lectin 1 (SIGLEC1), are highly upregulated in the CHB hearts. Accordingly, this study addressed the hypothesis that IRGs contribute to CHB pathogenesis.

Methods: hY3 RNA, a noncoding ssRNA and TLR7/8 agonist, was used as a proxy of the Ro60 immune complex. Human derivatives included healthy peripheral blood macrophages and fibroblasts isolated from a healthy human fetal heart. Neutralizing IFNα and IFNβ abs were used to assess the contribution of the respective cytokines to the model. Macrophage readouts included the expression of IFIT1 and SIGLEC1 transcripts (qPCR, units, fold change based on 2-ΔΔCT, relative expression of transcript normalized to GAPDH) and myofibroblast phenotype (EdU imaging and SMAc by IF, respectively).

Results: As expected, exposure of macrophages to IFNα resulted in a significant upregulation of IFIT1 and SIGLEC1 compared to untreated macrophages (70±25 vs 1, and 17±9, vs 1, respectively with both N=3, P< 0.05). Similarly, exposure to IFNβ also resulted in the upregulation of these transcripts (254±237 vs 1, p=0.03, and 21±14 vs 1, respectively with both N=4, p< 0.03). The expression of these transcripts by IFNα- and IFNβ-treated macrophages was completely attenuated by co-treatment using respective Type I IFN-specific neutralizing antibodies. In parallel, transfection of human macrophages with hY3 also resulted in upregulation of IFIT1 (112±30 vs 1, p=0.02, N=3) and SIGLEC (13±7 vs 1, N=3). To confirm TLR7/8 dependency of IRGs, the addition of TLR7/8 antagonist IRS661 to our in vitro model resulted in a significant decrease of IFIT1 expression to 14% (14±10, n=6) and SIGLEC1 to 54% (7±5, n=7, both P=0.03). Co-treatment with neutralizing antibody against IFNα reduced the expression of IFIT1 to 9% (10±9, n=3) and SIGLEC1 to 35% (5±3, n=3). Co-treatment with neutralizing antibody against IFNβ also reduced the expression of IFIT1 to 24% (24±6, n=2) and SIGLEC1 to 59% (3±5, n=3). For a survey of direct effects of type I IFN, IFNα and IFNβ were shown sharing the capacity to stimulate fibroblast proliferation (EdU, % positive) yielding a result of untreated (16%), IFNα (40%), and IFNβ (48%). In addition, exposure of human fibroblasts to IFNα as well as IFNβ induced expression of the myofibroblast marker, SMAc (IF) versus no expression by the untreated fibroblasts.

Conclusion: These results suggest that type I IFN contributes to the inflammatory and profibrosing milieu associated with the development of CHB. Feed forward expression of IFN related genes in response to TLR signaling may provide new targets towards the prevention of disease.

Disclosure: M. Chang, None; **R. Clancy**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2.

Abstract Number: 2809

Single-Cell RNA Sequencing of Murine Neutrophils Identifies a Transcriptional Continuum ("Neutrotime") Across Biological Compartments

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Neutrophils are key first responders of innate immunity, participating in both defense and inflammatory disease. Phenotypic heterogeneity is recognized but the existence of *bone fide* subsets remains unknown. We applied single-cell transcriptomics to define the relationships among individual neutrophils in heathy mice.

Methods: We profiled neutrophils from bone marrow, peripheral blood and spleen from 6-8 week male C57Bl/6 mice. Ly6g+ neutrophils were sorted for single-cell RNA sequencing using the 10X platform. We applied a multinomial model to the raw unique molecular identifier (UMI) counts to assign cells to one of 265 known cell populations and thereby ensure restriction of the analysis to neutrophils. Following exclusion of low-quality cells and transcripts expressed in fewer than 10 cells, 12,011 cells and 2,709 highly-expressed transcripts were retained for downstream analysis. We compared methods for dimensionality reduction, including PCA/tSNE and diffusion maps, to optimally reflect gene expression patterns.

Results: An average of 1,439 UMI and 482 genes were detected per cell. Linear dimensionality reduction could identify clusters of neutrophils, but underlying patterns were in fact best captured through diffusion maps, a nonlinear method. Using diffusion pseudotime analysis, we reconstructed a continuum of neutrophil maturation that defined a sequential gene expression program. The genes anchoring the two poles of this "neutrotime" spectrum were *Ly6g*, *Camp*, *Ltf*, *Lcn2* in less mature cells and *Il1b*, *Ccl6*, *Csf3r* in more differentiated cells. Cells all along the neutrotime continuum were found in all profiled organs, but regional transcriptomic differences were also observed. For example, *Il1b* was highly expressed in blood and spleen but weakly in bone marrow. Conversely, *Ly6g* transcript abundance was highest in bone marrow and to a lesser extent in spleen, but only weakly detectable in blood. Interestingly, we identified a small cluster of cells defined by high expression of interferon response genes including *Ifit1*, *Ifit3*, *Isg15*, *Ifitm3*. This interferon-responding population was present in all profiled organs but less common in bone marrow than in blood and spleen, suggesting a more mature neutrophil population with a function yet to be defined.

Conclusion: Neutrophils have traditionally been characterized by nuclear morphology, cell density, and surface markers. Here we expanded this perspective via unbiased single-cell approach transcriptomics, demonstrating technical feasibility despite low transcript density. We identify a single developmental continuum shared by neutrophils across biological compartments, termed here 'neutrotime', that appears to represent much but potentially not all of their phenotypic heterogeneity. Our data define the baseline gene expression landscape of murine neutrophils and will facilitate further transcriptomic and functional investigations, as well as rational gene perturbations, potentially highlighting opportunities for therapeutic exploitation of the diversity within this important immune population.

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Abstract Number: 2810

Does Loss-of-function Variants in *SAT1* Cause X-linked Pediatric Lupus?

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SESSION INFORMATION
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Session Title: SLE – Etiology & Pathogenesis I: Signaling Pathways
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Background/Purpose: Mendelian inheritances of highly penetrant single gene variants have been reported as monogenic forms of SLE. To explore novel risk variants, we carried out whole-exome sequencing to identify underlying monogenic causes in two multiplex families that each contains unaffected parents and two sons with pediatric-onset SLE, and assessed candidate rare variants for Mendelian inheritance and functional consequences.

Methods: Whole-exome sequencing, variant calling and annotation were conducted using Illumina Hiseq2000, the Genome Analysis Toolkit GATK and ANNOVAR, respectively. Variants in the gene of interest were confirmed by Sanger sequencing. Functions of candidate variants were tested using Minigene assay for differential splicing, and CRISPR/Cas9 mediated knock-in (KI) mice for the frameshift variant.

Results: In each family, we identified a putative loss-of-function variant in the *SAT1* gene that co-segregated with lupus in an X-linked recessive pattern. This variant is extremely rare in the population (absent in > 200,000 individuals), and is not in previously known SLE-associated genes. In one family, a *SAT1* frameshift mutation, which is expected to trigger nonsense-mediated mRNA decay, was transmitted from the mother to the two sons affected with SLE, but not to the unaffected son. Using CRISPR/Cas9, we have 5 founders of frameshift mutation KI mice and are establishing a colony for lupus-like phenotype studies. In the other family, we found a missense variant on exon 2 that was predicted to be deleterious by altering transcript splicing. Using the Minigene assay, we confirmed that the mutant construct

resulted in aberrantly spliced transcripts, including ~30% intron 2 containing, ~20% exon 2 skipping and 50% normal transcripts, in transiently transfected 293T or HeLa cell lines. We further extended Sanger sequencing of *SAT1* in 566 SLE patients enriched in multiplex male lupus and pediatric patients, found 4 common variants and 12 additional rare variants, but none had robust evidence for functions based on HaploReg v4.1 and Regulome database.

Conclusion: We identified two rare *SAT1* loss-of-function variants on the X chromosome that segregate with SLE phenotype in two families that each contained two sons with pediatric-onset SLE. The exon 2 variant disrupted the splice donor site, and the frameshift variant created a premature stop codon. *SAT1* encodes spermidine/spermine-N^1-acetyltransferase, a rate-limiting enzyme that regulates polyamine catabolism. The low or absent function of *SAT1* might perturb polyamine catabolism, predisposing to SLE, especially in boys.

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Abstract Number: 2811

The IRE1α Pathway Mediates Neutrophil Stress and NETosis in Lupus

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SESSION INFORMATION
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Background/Purpose: Immune complex (**IC**)-activated neutrophils appear to amplify inflammation in lupus through the release of neutrophil extracellular traps (**NETosis**). There is presently no consensus as to how to most effectively inhibit NETosis in patients. Recent studies have implicated the inositol-requiring enzyme 1 alpha (**IRE1α**) pathway (a mediator of the endoplasmic reticulum stress response) as a perpetuator of inflammation in infections, sepsis, and inflammatory disorders such as rheumatoid arthritis. However, the IRE1α pathway has been little studied in relation to neutrophil function or lupus pathogenesis.

Methods: Total IgG was isolated from lupus patients and bound to ribonucleoprotein to generate lupus ICs, which were used to stimulate neutrophils. IRE1α activity was measured by quantifying splicing of X-box binding protein 1 (**XBP1**) gene transcripts (spliced transcripts encode active XBP1 protein, recognized as a major facilitator of the IRE1α pathway). We tested the impact of specific inhibition of neutrophil IRE1α on reactive oxygen species (**ROS**) production, caspase activation, mitochondrial function, and NETosis. Finally, we assessed the therapeutic efficacy of inhibition of the IRE1α-XBP1 pathway in the toll-like receptor 7 (**TLR7**)-agonist mouse model of lupus.

Results: *In vitro*, control neutrophils stimulated with lupus ICs demonstrated increased IRE1α pathway activity as measured by the ratio of spliced XBP1 transcripts to total XBP1 transcripts. Inhibition of IRE1α's ribonuclease activity with the specific inhibitor 4μ8C alleviated lupus IC-triggered NETosis, as well as "spontaneous" NETosis of patient neutrophils. Treatment of neutrophils with lupus ICs resulted in cytosolic ROS formation (mean 2-fold increase) and caspase 2 activation (mean 6-fold increase), both of which were significantly reversed by 4μ8C. Mitochondrial dysfunction was also appreciated in IC-stimulated neutrophils (mean 8-fold increase in mitochondrial ROS), and could be

neutralized by either traditional ROS scavengers or treatment with 4μ8C. Finally, we induced a lupus-like phenotype in mice by treating BALB/c mice with the TLR7-agonist R848 (topical application, 10 mg/kg three times weekly) over six weeks. R848 treatment resulted in activation of the neutrophil IRE1α-XBP1 pathway (mean 1.5-fold increase in XBP1 splicing). Administration of 4μ8C (10 mg/kg, three times weekly over the duration of R848 treatment) not only reduced IRE1α pathway activation in neutrophils, but also significantly reduced mitochondrial ROS levels. Furthermore, R848 treatment resulted in an elevation of plasma NET remnants (mean 2-fold increase), which returned to baseline levels with 4μ8C treatment.

Conclusion: These data are the first to identify a role for IRE1α-XBP1 in the activated state of lupus neutrophils, with this pathway apparently upstream of mitochondrial dysfunction and ROS generation. Inhibition of IRE1α reduced mitochondrial ROS formation in peripheral blood neutrophils of lupus mice, and normalized plasma NET levels of the same mice. Inhibition of the IRE1α pathway appears to be a potential strategy for neutralizing NETosis in lupus.

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Abstract Number: 2812

A New Role for Selectins in Systemic Lupus Erythematosus

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SESSION INFORMATION
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Background/Purpose: In systemic lupus erythematosus (SLE), blood platelets have an activated phenotype, and express high levels of CD40L and P-selectin. Our group demonstrated that SLE patients' platelets increase type I interferon production by plasmacytoid dendritic cells through CD40-CD40L interaction [1]. Recently, we found that T regulatory cells (Tregs) expressed high levels of P-selectin glycoprotein ligand-1 (PSGL-1), suggesting potential Tregs/platelet interactions.

Methods: Flow cytometry was used for analysis of surface and intracellular molecules expressed on blood cells of active (aSLE, SLEDAI ≥ 6, n= 13), inactive (iSLE, SLEDAI < 6, n = 20) SLE patients and healthy donors (HD, n = 17). To assess Tregs immunosuppressive functions, we conducted co-culture experiments of Tregs ($CD25^{high}$ $CD127^{low}$ $CD4^{+}$) and CFSE-labelled T effector (Teff; $CD25^{-}CD127^{high}CD4^{+}$) purified from HD. Cells were cultured at a 1:1 ratio with anti-CD3/CD28 activation +/- platelet or recombinant selectin for 6 days. At the end, Teff proliferation was evaluated using cytometry.

Results: Patients with aSLE had significantly more platelet/Tregs aggregates defined as $CD61^{+}$ Tregs (figure 1a), than patients with iSLE and HD (figure 1b-c). Conversely, levels of platelet/Teff aggregates were similar in the 3 groups suggesting a specific interaction. To understand the impact of platelet/Tregs interaction, we conducted Teff/Treg

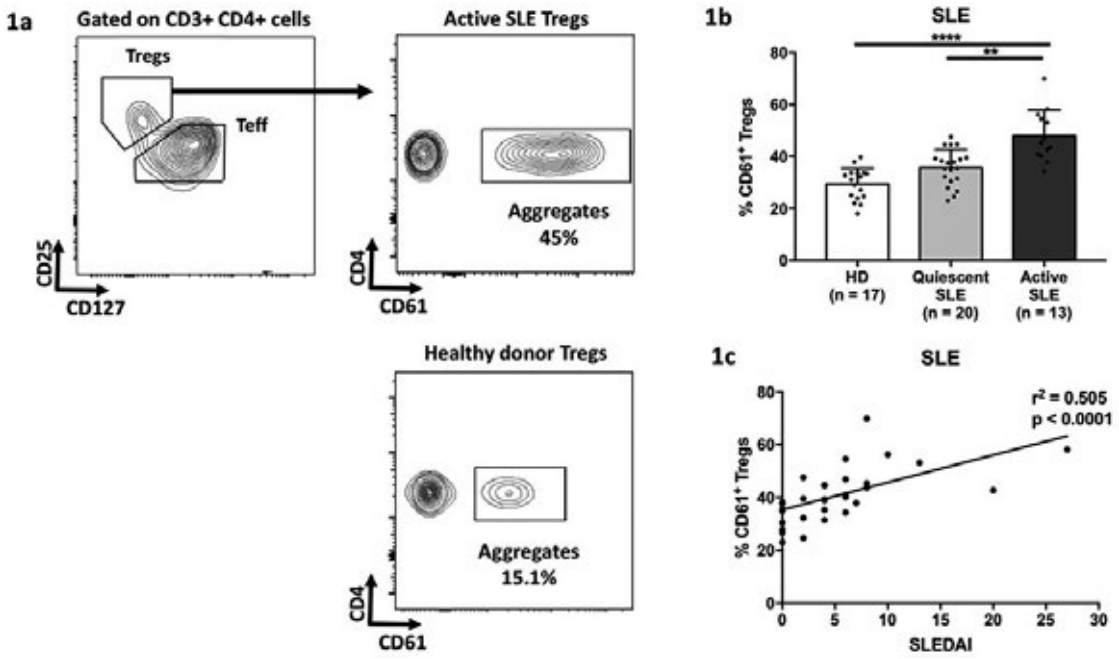

Figure 1. Platelet/Tregs interactions are increased in active SLE. Fresh whole blood samples from healthy donors or patients with SLE were stained for the study of Tregs/platelet interaction. (a) Gating strategy to assess Platelet/Tregs circulating aggregates. (b) Percentage of Platelet/Tregs aggregate in healthy donors or patient with SLE. Quiescent SLE (SLEDAI < 6), Active SLE (SLEDAI ≥ 6).**, $p < 0.01$; ****, $p < 0.0001$. (c) Correlation between the percentage of platelet/Tregs aggregates and SLE disease activity as assessed by the SLEDAI.

co-cultures. Platelets addition to the co-culture inhibited Tregs immunosuppressive functions in a dose-dependent manner. Addition of an anti-PSGL-1 antibody rescued Tregs functions. Lastly, replacing platelets with (P-, E- or L-) selectin could recapitulate these *in vitro* results.

Mechanistically, P-selectin binding on Tregs induced Syk phosphorylation, which induced a strong intracytosolic calcium release. No similar signals were found with P-selectin binding on Teff. In co-culture assays, Syk inhibition rescued immunosuppressive functions from Tregs exposed to P-selectin.

A transcriptomic analysis of P-selectin-exposed Tregs identified a significant downregulation of the TGF-beta axis. We subsequently confirmed *in vitro*, by qPCR and cytometry, that P-selectin induced a downregulation of TGF-beta and its chaperone molecule GARP at the RNA and protein levels.

To assess the relevance of selectins in human SLE, we measured levels of soluble selectins (using ELISA) and selectin+ microparticles (by cytometry). Patients with aSLE had increased level of both soluble and microparticular selectins compared to HD and iSLE ($p < 0.01$ for all comparisons). Microparticular and soluble selectins levels correlated with the SLEDAI ($r^2 = 0.278$, $p < 0.001$ and $r^2 = 0.116$, $p < 0.001$, respectively).

Conclusion: The selectin/PSGL-1 axis represents a new pathway responsible for Tregs dysfunction in SLE through downregulation of the TGF-beta axis. Blocking P-selectin (in development for sickle cell disease [2]) might be an innovative treatment option. To evaluate this strategy, we are currently treating DNASE1L3-KO SLE mouse model with an anti-P selectin monoclonal antibody.

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Abstract Number: 2813

Pentameric, but Not Monomeric C-reactive Protein, Limits the SnRNP-immune Complex Triggered Type I Interferon Response: Implications for Lupus Pathogenesis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune systemic disease affecting multiple organs and which is characterized by autoantibodies directed against nuclear constituents. Common autoantibody targets include double-stranded (ds) DNA and small nuclear ribonucleoproteins (snRNPs; *i.e.* U1-snRNP). Uptake of immune complexes (ICs) by plasmacytoid dendritic cells (pDCs) can activate endosomal toll-like receptors (TLRs) such as TLR-7 and TLR-9 if nucleic acids are present in the ICs. Such activation is dependent on IC internalization by Fcγ receptor type IIa (FcγRIIa), and results in production of type I interferons (IFNs), a hallmark of SLE and a target for therapeutic interventions. The acute phase protein C-reactive protein (CRP) binds FcγRs, as well as some nuclear proteins, including snRNPs. Pentameric (native) CRP has previously been suggested to inhibit the production of type I IFNs in peripheral mononuclear cells (PBMCs) in response to ICs formed by autoantibodies against snRNP, an effect which was further investigated herein.

Methods: PBMCs or magnetically (MACS) purified pDCs were retrieved from whole blood of healthy volunteers. Type I IFN gene transcription and production was stimulated by addition of snRNP containing ICs +/- pentameric CRP (pCRP) or monomeric CRP (mCRP) in different sequential order. IC formation was achieved through simultaneous addition of snRNP and bulk IgG, retrieved from an SLE patient with high levels of snRNP autoantibodies, directly to the cells. Type I IFNs and inflammatory cytokines were investigated using quantitative PCR, ELISA and cytometric bead array, and cells responsible for production of the type I IFNs were characterized using flow cytometry. For statistics, a two-tailed t-test was performed.

Results: pCRP had an inhibitory effect on the IFN gene expression in PBMCs after incubation with ICs, p=0.044 for IFNα4 and p=0.047 for IFNβ at the 4h time-point compared to IC only. pCRP also showed a dose-dependent inhibitory effect on the type I IFN production in the cells. The monomeric form of CRP showed modest or no effect on IFN levels; p=0.82 for IFNα4 and p=0.58 for IFNβ at the 4h time-point, compared to IC only. A pre-incubation of the cells with pCRP increased the inhibitory effects compared to simultaneous addition of pCRP and ICs, suggesting that initial binding to the cells is a critical step for inhibition. Flow cytometry suggested that pDCs are the main producer of the type I IFNs. In addition, pCRP seems to have a more general inhibitory effect on type I IFNs, as seen in the reduction of IFN production in response to the TLR-9 ligand CpG.

Conclusion: pCRP has a distinct inhibitory effect on type I IFNs, which is largely not seen for the dissociated form of CRP (mCRP). The more general inhibitory effects shown by pCRP highlights its immune regulatory function in pathologies characterized by high production of type I IFNs. The identity of the initial receptors responsible for pCRP mediated effects, as well as of the involved signaling pathways, will be further investigated.

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Abstract Number: 2814

Methionine Commits Immunometabolism and Epigenetic Regulation of BACH2 Loci in B Cells, Resulting in Biases Toward Plasmablast Differentiation in the Pathogenesis of SLE

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Background/Purpose: Amino acids play an important role in various metabolic processes. However, the role of amino acid metabolism in the regulation of human B cell function remains elusive. To determine the role of essential amino acids in human B cell differentiation and relevance to the pathogenesis of SLE.

Methods: In the in vitro arm of the study, purified $CD19^+$B cells from healthy donors were cultured withTLR7/9 ligand (LOX or CpG),IFN-α and B cell receptor (BCR) cross-linking, in the presence or absence of amino acids. We determined 1) the types of amino acids that are important for PB differentiation, 2) the amino acid transporters that are important for PB differentiation, 3) the main signaling pathway(s) involved in the presence of amino acids, 4) the transcriptional factors used in the presence of amino acids. In the clinical arm of the study, peripheral blood mononuclear cells (PBMCs) were obtained from 24 patients with RA, 35 patients with SLE, and 21 age-matched healthy controls, and subjected to flow cytometric analysis to determine the expression of amino acids-related markers.

Results: 1) Stimulation with the combination of BCR, IFN-α and TLR7/9 ligand induced PB differentiation accompanied by uptake of amino acids. PB differentiation was abrogated in the absence of essential amino acid methionine, and to a lesser extent leucine, but not in non-essential amino acid cystine. 2) LAT1 and CD98 are known amino acid transporters. The process of plasmablast differentiation encompassed a trade-off balance between upregulation of CD98 and downregulation of LAT1. 3) BCR and mTORC1 signals were susceptible to methionine, while mTORC1 signals were susceptible to leucine. In the presence of methionine, activation of Syk and mTORC1 signals synergistically induced methyltransferase EZH2 expression. EZH2 induced H3K27me3 at BACH2 loci and suppressed BACH2 expression, leading to induction of BLIMP1, XBP1 expression, and plasmablast differentiation. 4)Assessment of the expression of amino acid transporters CD98, LAT1 and EZH2 in B cells in RA and SLE patients showed overexpression of CD98 and EZH2, but not LAT1, in SLE, compared with RA and control. In SLE patients, EZH2 expression

level correlated with that of CD98 in B cells. EZH2 expression also correlated with disease activity scores, such as of SLEDAI and BILAG and anti-dsDNA antibodies in patients with SLE.

Conclusion: The results indicate that methionine activates signaling by controlling immunological metabolism in B cells and plays an important role in differentiation of B cells to plasmablasts through epigenome modification through the induction of EZH2, suggesting that methionine is closely related to the pathogenesis of SLE.

Disclosure: M. Zhang, None; **S. Iwata**, None; **M. Hajime**, None; **N. Ohkubo**, None; **Y. Todoroki**, None; **H. Miyata**, None; **J. Fan**, None; **S. Nakayamada**, Bristol Myers, Sanofi, Abbvie, Eisai, Eli Lilly, Chugai, Pfizer, 8; **K. Yamagata**, None; **Y. Tanaka**, Abbvie, 8, AbbVie, 5, 8, Asahi-kasei, 2, Asahi-Kasei, 2, Asahi-kasei, BMS, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Ono, Pfizer, Sanofi, Takeda, UCB, 2, Astellas, 8, Astellas Pharma, 9, Astellas Pharma, Inc., 2, 3, 5, 8, 9, Astellas, BMS, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi-Tanabe, Pfizer, Sanofic, UCB, YL Biologics, 8, BMS, 2, 5, 8, Bristol-Myers, 2, 8, Bristol-Myers Squibb, 2, 8, Chugai, 2, 8, Daiichi-Sankyo, 2, 8, Daiichi-Sankyo, Astellas, Eli Lilly, Chugai, Sanofi, Abbvie, Pfizer, YL Biologics, Bristol-Myers, 8, Eisai, 2, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 8, Genzyme, 5, Glaxo-Smithkline, UCB, Mitsubishi-Tanabe, Novartis, Eisai, Takeda, Janssen, Asahi-kasei, 8, Janssen, 8, Mitsubishi-Tanabe, 2, 8, Mitsubishi-Tanabe, Bristol-Myers, Eisai, Chugai, Takeda, Abbvie, Astellas, Daiichi-Sankyo, Ono, MSD, Taisho-Toyama., 2, Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, 2, Novartis, 8, Ono, 2, Pfizer, 5, 8, Pfizer Inc, 8, Roche, 5, Sanofi, 2, Takeda, 2, 8, Teijin, 8, UCB, 2, YL Biologics, 8.

Abstract Number: 2815

Lower IL-4R in IgD$^+$ Naïve B Cells Is a Pre-disposing Factor for Development of T-bet$^+$ DN2 B Cells in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: SLE – Etiology & Pathogenesis I: Signaling Pathways
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Studies to date have primarily focused on stimulators that are overexpressed and activate B cells in SLE subjects. Factors that can maintain B cells in a resting state and may be under-expressed in SLE are largely unknown. We utilized a combined single-cell B cell transcriptome and high dimensional flow cytometry analysis approach for a coordinated understanding of factors that are both over- and under-expressed in B-cell developmental checkpoints in SLE.

Methods: The expression of IL-4R and interferon beta (IFNβ) in subsets of B cells was analyzed using high dimensional flow cytometry analysis (n=47 patients who met the ACR classification criteria for SLE). Total B cells from 3 autoantibody (anti-DNA, anti-Sm, and anti-histone)$^+$ African American (AA) SLE patients, 1 autoAb(–) Europeran American (EA) SLE patient and 1 AA healthy control were purified using the StemCell Human B cell isolation kit. A high-throughput scRNA-seq was carried out using a droplet-based 10x Chromium approach. The effects of IL-4 on

IFNβ-induced IRF7 as well as on IFNɣ + a defined stimulatory media (DSM)(anti-Ig+BAFF+IL-21+TLR7+IL-2)-induced double negative 2 (DN2: $CD21^{-}CD27^{-}IgD^{-}CD11c^{+}T\text{-}bet^{+}$) B cells were analyzed using an *in vitro* culture approach.

Results: At the protein level, within naïve ($IgD^{+}CD27^{-}$) B cells, higher expression of IFNβ and lower expression of IL-4R correlated with the percent of activated naïve $CD21^{lo}IgD^{+}$ and $CD21^{lo}IgD^{-}$ DN B cells. There was higher percent of $IFN\beta^{+}IL\text{-}4R^{lo}$ naïve B cells in AA compared to EA SLE patients. However, in EA, but not AA, patients, higher percent of $IFN\beta^{+}IL\text{-}4R^{lo}$ naïve B cells was found in anti-Sm^{+} and renal disease^{+} patients. scRNA-seq analysis shows that the molecular signature of B cells from autoAb(+) patients is type I IFN stimulated genes (ISGs), including *IRF7*, *ISG15*, *ISG20*, *MX1*, and *STAT1*. The molecular signature of B cells from autoAb(-) patients is *IL4R*, *BACH2*, *S1PR1*, and *FCER2.* The high *ISG* and low *IL4R* was evident during the early transitional stage 1 B cells and persisted in pre-switched *IGHD*+ B cells. Stimulation of B cells with DSM+IFNɣ promoted DN2 development whereas addition of IL-4 inhibited DN2 and preserved B cells at the resting naïve stage ($IgD^{+}CD11c^{-}T\text{-}bet^{-}$). IL-4 also inhibited IFNβ-induced IRF7.

Conclusion: Down-regulation of IL-4R in naïve B cells is a major dysregulation in SLE since it may predispose SLE B cells to both type I IFN and type II IFN stimulation. Further, lower IL-4R together with upregulation of endogenous IFNβ in naïve B cells was an important signature for activated naïve B cells. Such signature was associated with development of DN2 B cells and, in EA patients, development of anti-Sm autoantibody. Modulation of IL-4R signaling may be developed into a novel therapy for SLE.

Disclosure: J. Mountz, VA Merit Review grant (I01BX004049), 2, Lupus Research Alliance Distinguished Innovator Award, 2, NIH R01-AI-071110, R01 AI134023, P30-AR-048311, 2; **M. Gao**, None; **Q. Wu**, None; **P. Yang**, None; **A. Essman**, None; **O. Ojo**, None; **S. Liu**, None; **J. Chen**, None; **I. Sanz**, None; **W. Chatham**, None; **H. Hsu**, Lupus Research Alliance Novel Research Award, 2.

Abstract Number: 2816

An Expanded Granzyme K^{+} CD8 T Cell Population Induces Inflammatory Responses in Rheumatoid Arthritis Synovium

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: CD8 T cells represent nearly half of T cells in inflamed synovium from patients with rheumatoid arthritis (RA). Research to date has focused on CD4 T cells, yet we have found that synovial CD8 T cells express IFNgat a higher frequency and TNF at a similar frequency compared to CD4 T cells. Recent single-cell transcriptomic analysis of RA synovial tissue has suggested that CD8 T cells form sub-populations characterized by expression of secreted proteases granzyme K (GzmK) and granzyme B (GzmB).

Methods: We have assembled a single-cell RNA-seq data set of approximately 20,000 CD8 T cells by integrating new and publicly available data from synovial tissue (N=22) and fluid (N=1) from patients with RA and from blood (N=3) from healthy controls. RA patients met the 2010 ACR criteria for RA. Additional data were collected by flow

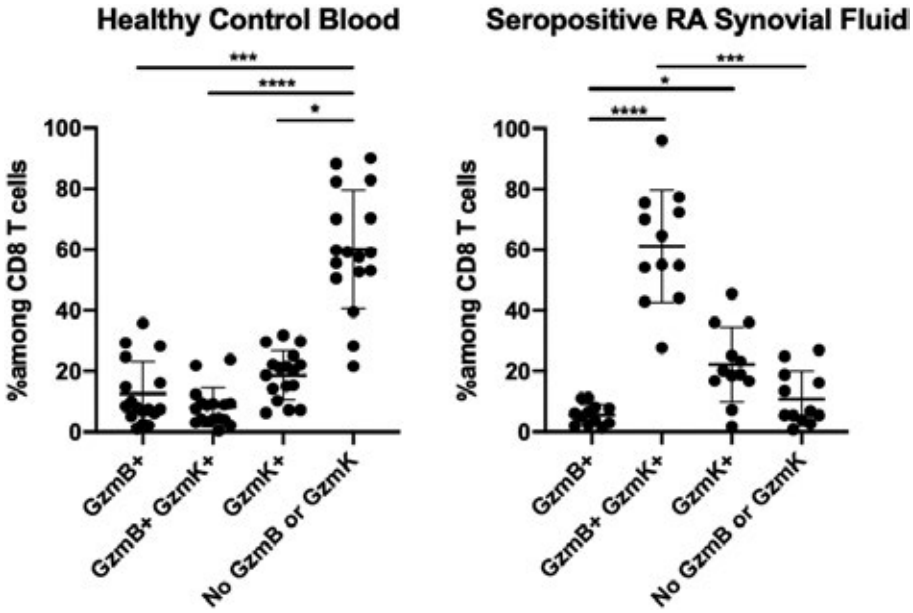

Figure 1. Frequencies of GzmK vs GzmB expression in blood from healthy controls and synovial fluid from patients with seropositive RA. Statistical comparison by Friedman test. * p<0.05 , *** p<0.001, **** p<0.0001.

cytometry or low-input RNA-seq from synovial tissue, synovial fluid, and blood from patients with clinical diagnoses of rheumatoid arthritis or healthy controls. In *in vitro* cultures, human synovial fibroblast cells were treated with recombinant granzyme K. Cytokine production was measured by ELISA, and reactive oxygen species were measured by a H_2DCFDA fluorescence assay.

Results: At both the mRNA and protein levels, the vast majority of CD8 T cells in synovial tissue and fluid from patients with seropositive RA express GzmK, either alone or together with GzmB, a marked enrichment compared to blood (Figure 1). Very few synovial CD8 T cells express GzmB alone, which is the pattern seen in late differentiated cytotoxic T lymphocytes (CTLs). Unlike GzmB, GzmK does not activate apoptotic caspases. Instead, we find that GzmK has pro-inflammatory effects on synovial fibroblasts, inducing them to produce IL-6, CCL2, and reactive oxygen species (ROS), all of which are upregulated in inflamed synovium. GzmK$^+$ CD8 T cells in blood express high frequencies of chemokine receptors CCR2, CCR5, and CXCR3, while CD8 T cells expressing GzmB alone express CX3CR1, suggesting that GzmK$^+$ CD8 T cells and CTLs are recruited to sites of inflammation through different pathways. Interestingly, preliminary analysis of a large,integrated single-cell RNA-seq dataset of CD8 T cells from synovial tissue, synovial fluid, and blood shows selective expression of genes encoding Nur77, Ki67, and activation markers in distinct CD8 subsets, suggesting that some CD8 T cell subsets receive T-cell receptor (TCR)-mediated signals whereas others are activated through TCR-independent mechanisms.

Conclusion: The vast majority of CD8 T cells in RA synovial tissue and fluid express GzmK and express a phenotype and transcriptome distinct from typical GzmB$^+$ CTLs. GzmK$^+$ CD8 T cells appear to traffic to sites of inflammation using different chemokine receptors than CTLs. GzmK induces synovial fibroblasts to produce pro-inflammatory effector molecules including IL-6, CCL2, and ROS. Preliminary analysis of a large single-cell RNA-seq data set suggests differential TCR-mediated and cytokine-mediate activation of CD8 T cell subsets in inflamed joints. Together, these findings form the basis of a new model of CD8 T cell migration and function in RA and potentially other rheumatologic diseases.

Disclosure: A. Jonsson, Amgen, 2; **F. Zhang**, None; **G. Watts**, None; **K. Wei**, None; **D. Rao**, Janssen, 5, Merck, 2, Pfizer, 5; **S. Raychaudhuri**, None; **M. Brenner**, None.

Abstract Number: 2817

Lysosomal Placement of the Energy Sensors AMPK and mTORC1 Controls Tissue Inflammation in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: CD4 T cells from patients with rheumatoid arthritis (RA) are metabolically reprogrammed, diverting glucose away from glycolysis towards the production of biosynthetic precursors. Several of the pro-inflammatory effector functions of such CD4 T cells are metabolically controlled; including T cell longevity, differentiation into Th1 and Th17 cells and the formation of tissue-invasive membrane ruffles.

Methods: T cells from seropositive RA patients with active disease and age-matched healthy controls were examined. Intra- and extracellular metabolites were quantified, and energy sensing was assessed by pAMPK and pS6K1 analysis. Lysosomal localization of mTORC1 and AMPK was examined by confocal microscopy and immunoblotting. T cell differentiation into pro-inflammatory effector cells was determined through lineage-determining transcription factors and intracellular cytokines. Tissue inflammation in human synovium was evaluated in NSG chimeric mice engrafted with human synovium and reconstituted with human T cells.

Results: In response to T cell receptor triggering, RA T cells hyperproliferated while intracellular ATP concentrations were significantly lower than in control T cells. Despite a high AMP/ATP ratio, RA T cells failed to activate the energy senor AMPK, but mTORC1 activation was sustained. AMPK activation occurs on the lysosomal surface where the kinase colocalizes with mTORC1 to enable cross-regulation of both energy sensors. Immunoblotting and imaging analysis revealed a lack of lysosomal AMPK in RA T cells, while mTORC1 was maintained on the outer lysosomal membrane. Lysosomal anchoring requires AMPK lipidation through posttranslational myristoylation. RA T cells were deficient in N-myristoyltransferase 1 (NMT1), the enzyme which catalyzes the transfer of myristate from CoA to AMPK. Restoring NMT1 expression rescued the lysosomal recruitment of AMPK, secured the activation of the kinase, inhibited the unopposed activation of mTORC1 and prevented the differentiation of T cells into cytokine producing, pro-inflammatory effector cells in vitro and in vivo. We devised multiple therapeutic interventions to overcome the lack of lysosomal AMPK and tested their tissue-protective effects in the human synovium-NSG chimeras; including forced overexpression of NMT1 in RA T cells; treatment with A769662, an AMPK activator that acts independently of the lysosome, and injection of the mTORC1 inhibitor Rapamycin. All interventions were equally potent in suppressing synovitis.

Conclusion: Pro-inflammatory effector functions of T cells are highly dependent on the subcellular localization and cross-regulation of the energy sensors AMPK and mTORC1. Deficiency of protein myristoylation due to loss-of-function of NMT1 deviates AMPK away from the lysosomal surface, prevents its proper activation and enables unopposed mTORC1 activity. Protein trafficking and subcellular localization of the energy sensors AMPK and mTOC1 may be druggable by novel therapeutic strategies.

Disclosure: Z. Wen, None; **K. Jin**, None; **Y. Li**, None; **B. Wu**, None; **J. Goronzy**, None; **C. Weyand**, Kiniska Pharmaceuticals, 2.

Abstract Number: 2818

Differences in the Phenotypic Landscape and Antigen Specificity of CD4+ T Cells Are Present in CCP+ Subjects Before the Onset of Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: The "Targeting Immune Responses for Prevention of RA" (TIP-RA) collaboration studies individuals at high risk for developing rheumatoid arthritis (RA) because of serum anti-citrullinated protein antibody (ACPA) positivity in absence of arthritis at baseline, and is focused on defining how they transition from at-risk to classifiable disease. One potential mechanism is the expansion of antigen specific T cells that recognize self-antigens and acquisition of disease associated T cell phenotypes. ACPA emerge years prior to clinically apparent disease and subsequently increase in their titer and breadth of specificity. However, few studies have characterized T cells during this transition. Therefore, individuals enrolled in the TIP-RA cohort were analyzed by multi-parameter flow cytometry to identify features associated with progression to RA.

Methods: HLA class II tetramer staining and flow cytometry were performed on peripheral blood samples from a baseline visit from CCP3- controls (n=34), CCP3+ at-risk (n=26), CCP3+ positive individuals who transitioned in the near-term to RA (called "RA converters", n=4), and seropositive early-RA (n=21). Our staining panel allowed us to assess the frequencies of T cells specific for citrullinated alpha-enolase, aggrecan, cartilage intermediate layer protein, fibrinogen and vimentin. We then applied both supervised phenotyping and a cluster-based computational approach to compare the phenotypic landscape and specificity of CD4+ T cells in each cohort.

Results: In comparison with controls, we observed higher frequencies of T cells that recognize citrullinated epitopes in CCP3+ at-risk subjects ($p< 0.05$), suggesting that these T cells expand prior to disease onset. Supervised phenotypic analysis revealed an increase in CCR4+ CD4+ T cells in CCP3+ at risk subjects ($p< 0.001$) and a corresponding decrease in CXCR3+ CD4+ T cells that was most pronounced in RA converters and seropositive early-RA ($p< 0.05$). Cluster-based phenotypic analysis revealed a landscape of ten distinct immunophenotypes present within all subjects. Among these, a CCR4 immunotype was progressively enriched in ACPA+ at risk subjects, RA converters, and seropositive early-RA ($p=0.007$). Correspondingly, a CXCR3/CCR4/CCR6 immunotype was progressively depleted in ACPA+ at risk subjects, RA converters, and seropositive early-RA ($p=0.05$). Each of these ten immunotypes was shown to contain tetramer positive T cells that recognize citrullinated epitopes. However, the predominant immunotype varied for different antigens and unique phenotypic patterns were observed for different subject groups.

Conclusion: Our data suggest a progressive change in T cell phenotypes during disease development and subsequent transition to classified RA. Disease associated changes in the antigen specificity and phenotype of CD4+ T cells are present in CCP3+ at-risk subjects before the onset of symptoms and development of classified RA. This

finding suggests that there is a continuum of immunologic changes that drive disease evolution and that exploring emerging antigen specificities and immunophenotypes will aid our understanding of risk and shape approaches for intervention.

Disclosure: V. Muir, None; **C. Rims**, None; **K. Deane**, Bristol-Myers Squibb, 5, Inova, 9, Janssen, 2, 5, Janssen R&D, 2, Microdrop, 5, Pfizer, 2; **J. Carlin**, None; **S. Posso**, Janssen, 2; **S. Nagpal**, Janssen Research & Development, 3, Janssen Research, Johnson&Johnson, 1, 3, 4, Johnson & Johnson, 1, 4; **N. Rao**, Janssen Research & Development, 3, Johnson & Johnson, 1, 3, 4; **F. Baribaud**, Janssen Research & Development, LLC, 3; **G. Vratsanos**, Janssen Research & Development, 1, 3; **W. Robinson**, None; **G. Firestein**, Abbvie, 2, Janssen, 2; **V. Holers**, AdMIRx, 1, 2, 4, 5, 6, Alexion, 7, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 5, Janssen R&D, 2, 5, Pfizer, 2; **P. Linsley**, None; **E. James**, Pfizer, 2, Janssen, 2; **J. Buckner**, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Janssen, 2, Novo Nordisk, 2, Pfizer, 2.

Abstract Number: 2819

The Transcription Factor MAF Controls the Ability of T Peripheral Helper (Tph) Cells to Help B Cells

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Pathologic T cell-B cell interactions are hallmark features of many autoimmune diseases. PD-1hi CXCR5- T peripheral helper (Tph) cells are B cell-helper T cells that are highly expanded in the joints of seropositive RA patients and in the circulation of SLE patients. Like T follicular helper (Tfh) cells, Tph cells produce IL-21 and stimulate B cell differentiation into plasmablasts *in vitro*. B cell helper-function is often considered dependent on the transcription factor Bcl6, a master regulator of Tfh-cells. However, Tph cells do not express high levels of Bcl6, which suggests that transcription factors other than Bcl6 may control IL-21 production and B cell-helper function in human CD4+ T cells. Here we evaluated the role of the transcription factor MAF in controlling T cell help to B cells.

Methods: MAF expression in human CD4+ T cell subsets was determined by RNA-seq and flow cytometry. To evaluate the role of MAF, we disrupted the gene encoding MAF by nucleofection of a CRISRP/Cas9 ribonucleoprotein (RNP) complex in primary $CD4^+$ T cells and in sorted Tph cells. Expression of IL-21 and other cytokines was determined by RT-PCR and ELISA. B cell-helper function of CRISPR-treated T cells was evaluated by co-culturing sorted T cell subsets from SLE or control donors with memory B cells plus SEB. Plasmablast formation was determined by flow cytometry.

Results: RNA-seq analyses of CD4+ T cell subsets revealed high expression of *MAF*, but not *BCL6*, in both Tph cells and Tfh cells sorted from blood of RA and SLE patients (Fig. 1A). After 2 days of CD3/CD28 stimulation, Tph cells and Tfh cells expressed >2-fold higher levels of MAF protein than did naive or $PD\text{-}1^{neg}$ memory CD4+ T cells. High expression of MAF in both Tph cells and Tfh cells, two subsets that produce IL-21, suggested a possible connection between MAF and IL-21. To test this, we deleted MAF in primary human CD4+ T cells by nucleofection of a MAF-targeting CRISPR/Cas9 RNP. This method abrogated MAF protein expression in >80% of T cells. Compared to a control CRISPR targeting CD8, MAF deletion reduced mRNA expression of *IL21* and *IL10* in 4 independent donors and inhibited secretion of IL-21 protein (Fig. 1B). Using Tph cells sorted from blood of SLE patients, we confirmed that

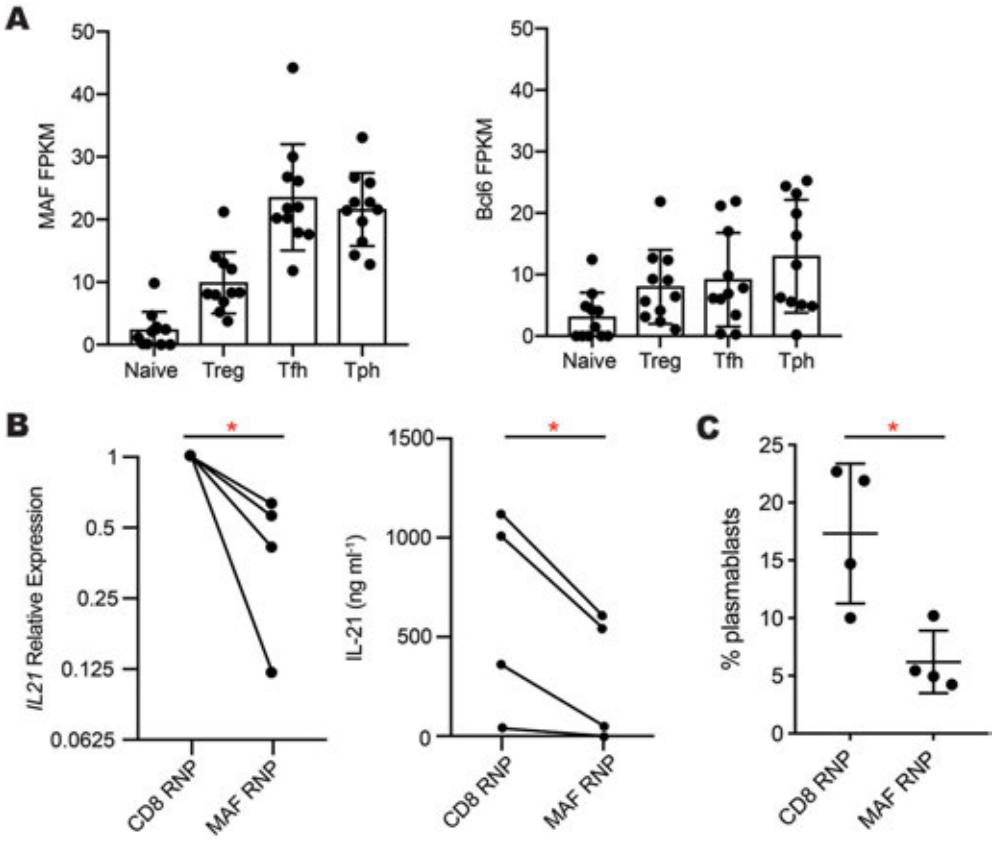

Figure 1. The role of MAF in human Tph cell function. A) MAF and Bcl6 expression in RNA-seq data of T cell subsets sorted from blood of RA (n=5) and SLE (n=6) patients. B) Reduced IL-21 mRNA expression (left) and protein secretion (right) by primary human CD4+ T cells after CRISPR-deletion of MAF (n=4 donors). C) Plasmablast generation in co-cultures of Tph cells treated with MAF- or CD8-targeting complexes co-cultured with allogeneic memory B cells. *p<0.05 by paired t-test.

Tph cells stimulate differentiation of memory B cells into plasmablasts in an IL-21-dependent manner, as neutralization of IL-21, but not IL-10, inhibited plasmablast formation by ~50%. To evaluate the effect of MAF on B cell-helper function, we deleted MAF by CRISPR in sorted human Tph cells from SLE patients or controls and then co-cultured these cells with memory B cells. Deletion of MAF reduced the ability of Tph cells to induce B cell differentiation into plasmablasts by over 50% compared Tph cells treated with a control RNP (Fig. 1C).

Conclusion: High expression of MAF is a common feature of both Tph cells and Tfh cells, two T cell populations that produce high levels of IL-21. Loss of MAF inhibits IL-21 expression in primary human CD4+ T cells and abrogates the ability of Tph cells to help B cells. MAF may regulate key components of T cell help to B cells in autoimmune conditions.

Disclosure: A. Bocharnikov, None; **V. Wacleche**, None; **Y. Cao**, None; **D. Rao**, Janssen, 5, Merck, 2, Pfizer, 5.

Abstract Number: 2820

Calcium/ Calmodulin - Dependent Protein Kinase IV Associates with Phosphofructokinase to Promote Glycolysis and Limit IL-2 Production

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Systemic lupus erythematosus (SLE) is disease characterized by an imbalance between pro-inflammatory (such as Th1 and Th17) and regulatory cells (Tregs). Th1 and Th17 T cells preferentially rely on glucose as opposed to Treg that utilize fatty acids as an energy source. Treatment of lupus-prone mice with 2DG, a glycolysis inhibitor, reduced disease activity by normalizing T cell metabolism. Our previous work showed that calcium/calmodulin-dependent protein kinase IV (CaMK4) is overexpressed in SLE CD4 T cells reprogramming T cells towards a proinflammatory phenotype. Based on mass spectrometry data, we hypothesized that CaMK4 affects SLE T cell phenotype by regulating the expression of phosphofructokinase (PFKP), a key regulatory enzyme of glycolysis.

Methods: CD4+ cells were isolated from healthy donors (HD), patients with SLE (SLEDAI 0-26) or mice (control, Camk4-/-, MRL-lpr). RNA-sequencing was performed by BGI; CUFFDIFF2 was used for analysis. PFKP was detected by RT-PCR and Western blotting. Glycolysis was measured by ECAR on Seahorse XFp analyzer. Proteins bound to CaMK4 were detected by mass-spectrometry after performing a pull-down assay with Flag-tagged human CaMK4 overexpressed in HEK293T cells.

Results: To address whether CaMK4 is involved in glycolysis we measured ECAR in CD3/CD28-ionomycin stimulated CaMK4-deficient and -sufficient CD4+ cells. Cells lacking CaMK4 had significantly decreased glycolysis ($n=4$; $p< 0.05$) suggesting that CaMK4 promotes glycolysis. To elucidate the mechanistic link between CaMK4 and metabolic reprogramming we performed a pull-down assay followed by mass-spectrometry that identified PFKP as a binding partner. Next, we examined whether the CaMK4-PFKP interaction is important in T cell differentiation. Naïve CD4 cells were cultured under Th1 or Treg-polarizing conditions. We observed 4.8-fold decrease of PFKP mRNA expression in wild type Tregs which was further reduced by 58% in Tregs lacking CaMK4. Moreover, the differentiation potential toward Tregs and IL-2 production was by 18% greater in CD4 T cells lacking CaMK4. This was in contrast to wild type CD4 T cells in which PFKP was overexpressed. We analyzed PFKP expression in CD4 T cells obtained from patients with SLE and found a statistically significant upregulation (vs. HD; $n=14$; $p< 0.01$). PFKP mRNA expression was higher in patients with active disease as measured by SLEDAI ($p=0.003$) even after adjusting for age or sex and degree of immunosuppression ($p=0.01$). PFKP upregulation in T cells obtained from SLE patients, compared to HD, was confirmed at the protein level as well ($p< 0.05$). Similarly, PFKP protein was significantly upregulated in MRL.lpr CD4 T cells compared to cells from control mice ($n=8$; $p< 0.05$).

Conclusion: We have generated evidence that CaMK4 interacts with PFKP to promote glycolysis and limit regulatory potential of Tregs by suppressing their differentiation and IL-2 production. In addition, we found that PFKP is significantly overexpressed in CD4 T cells from patients with SLE and lupus-prone mice. Our data identify PFKP as a novel therapeutic target to restore Treg functional homeostasis.

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Abstract Number: 2821

Clonal Expansion of a Specific Subset of Cytotoxic CD4+T Cells and Tissue Apoptosis in Patients with IgG4-related Disease

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: In IgG4-related disease (IgG4-RD), both activated B cells and CD4+ cytotoxic T lymphocytes (CD4+CTLs) expand clonally, accumulate in tissues, likely recognize distinct epitopes on the same protein antigens, and thus, work together to contribute to fibrosis. We have previously reported that CD4+CTLs synthesize IL-1β and TGF-β in disease tissues, indicating that they are reactivated at lesional sites by antigen presenting cells, possibly activated B cells. However, the effector subset of CD4+CTLs and the mechanism by which they contribute to fibrosis has not yet been determined.

Methods: We used multi-color flow cytometry to identify subsets of CD4+CTLs. CD4+CTL subsets were quantified in the blood of 48 IgG4-RD subjects at the time of active disease and correlated with clinical parameters. Twenty age-matched healthy donors and 19 non-fibrotic sarcoidosis patients were used as controls. We then examined the TCR clonal frequencies and transcriptional profiles comparing CD4+CTL subsets using Next Generation Sequencing. Finally, we used multi-color immunofluorescence to determine tissue infiltration by effector CD4+CTLs and explore the possibility that apoptosis contributes to fibrosis in IgG4-RD.

Results: Compared to other subsets, the $CD28^{Low}CD57^{Hi}$ subset of CD4+CTLs accumulated to the greatest degree in the blood of IgG4-RD patients with the most severe clinical phenotype. The $CD28^{Low}CD57^{Hi}$ subset of CD4+CTLs demonstrated marked clonal-expansion and had a transcriptional profile suggesting that these cells are poised for survival, metabolically active and activated through TCR engagement. In contrast, the $CD28^{Hi}CD57^{Low}$ subset of CD4+CTLs accounted for most CD4+CTLs in the blood of healthy individuals, were reduced in the blood of IgG4-RD patients and enriched for a regulatory transcriptional phenotype with FoxP3 upregulation. These subsets expressed differing chemokine receptors suggesting different tissue honing capacity. In the diseased tissues, CD4+CTLs and B cells make cell-cell contact suggesting that B cells either present antigens to CD4+CTLs or secrete activating cytokines. Additionally, we demonstrated increased activated caspase-3 in disease tissues, particularly, in cells of mesenchymal origin.

Conclusion: The $CD28^{Low}CD57^{Hi}$ subset of CD4+CTLs is clonally-expanded in IgG4-RD and correlates with disease severity. This subset is metabolically active, TCR-activated and infiltrates diseased tissues, suggesting an effector phenotype. The physical contact of B cells and CD4+CTLs in IgG4-RD tissues, along with the observed increase in caspase activation, suggests a possible mechanism of fibrosis in IgG4-RD such that CD4+CTLs, activated by antigen-presenting B cells, may cause apoptotic death of vimentin positive stromal cells. The ensuing cytokine se-

cretion by activated CD4+CTLs and B cells might contribute to an over-exuberant tissue healing process, resulting in fibrosis. (Supported by NIH U19 AI 110495 and UM1 AI144295)

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Abstract Number: 2822

Depression and Subsequent Risk for Incident Seronegative Rheumatoid Arthritis Among Women

Jeffrey Sparks,[1] Susan Malspeis,[1] Jill Hahn,[2] Andrea Roberts,[2] Laura Kubzansky,[2] and Karen Costenbader[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Harvard School of Public Health, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
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Session Time: 4:30PM–6:00PM

Background/Purpose: Depression is associated with elevated systemic inflammation and risk of several chronic diseases including lupus, psoriasis, and inflammatory bowel disease. However, the association between depression and subsequent risk for developing RA is less clear. Therefore, we hypothesized that depression may increase RA risk. Since depression may develop in the period prior to clinical RA diagnosis, we decreased the potential for reverse causation by including a time separation between the assessment of depression and RA risk window.

Methods: We performed a prospective cohort study investigating depression and incident RA. We pooled data from the Nurses' Health Study (NHS, 1992-2014) and NHSII (1993-2015). As in previous studies, depression was defined using a composite definition: report of clinician diagnosis, regular antidepressant use, or Mental Health Inventory-5 score < 60. Women reported RA diagnosis and 2 rheumatologists performed medical record review to confirm diagnosis using objective criteria and identify the date of diagnosis and serologic phenotype (seropositive: RF+ or CCP+). All incident RA cases met 1987 ACR or 2010 ACR/EULAR criteria. Measures of depression and covariates including smoking, body mass index, dietary quality, physical activity, and menopausal factors were obtained using biennial questionnaires. Cox regression estimated HRs and 95%CIs for RA (overall and by serologic phenotype) according to depression status, adjusted for potential confounders. All analyses included a lag that separated depression status and the window for RA risk by at least 4 years to lower the possibility that depressive symptoms preceding RA diagnosis explained the results.

Results: We analyzed n=194,700 women; mean age at baseline of 46.8 (SD 11.5) years and 24% of women had depression. A total of 834 incident RA cases (64% seropositive) occurred during 2,994,244 person-years of follow-up. In the age-adjusted analysis, women with depression had HR for all RA of 1.41 (95%CI 1.22-1.64, **Table**). After adjusting for covariates, the HR for all RA was attenuated, but still showed a modest but significant association (multivariable HR 1.28, 95%CI 1.28, 95%CI 1.10-1.49). After adjustment for covariates, depression was not statistically associated with seropositive RA (multivariable HR 1.10, 95%CI 0.91-1.32). However, depression was strongly associated with risk for incident seronegative RA (multivariable HR 1.70, 95%CI 1.32-2.19), independent of potential confounders including smoking, dietary intake, body mass index, physical activity, and menopause.

	No Depression HR (95%CI)	Depression* HR (95%CI)
Outcome: All RA		
Case/person-years	535/2,143,731	299/850,513
Age-adjusted	1.00 (Ref)	**1.41 (1.22-1.64)**
Multivariable**	1.00 (Ref)	**1.28 (1.10-1.49)**
Outcome: Seropositive RA		
Case/person-years	355/2,141,798	182/849,534
Age-adjusted	1.00 (Ref)	**1.22 (1.01-1.47)**
Multivariable**	1.00 (Ref)	1.10 (0.91-1.32)
Outcome: Seronegative RA		
Case/person-years	180/2,139,980	117/848,863
Age-adjusted	1.00 (Ref)	**1.86 (1.45-2.37)**
Multivariable**	1.00 (Ref)	**1.70 (1.32-2.19)**

*Depression was defined as a composite of self-reported clinician-diagnosed depression, Mental Health Inventory (MHI)-5 score <60, or regular antidepressant use.
**Adjusted for age, questionnaire cycle, cohort (NHS, NHSII), median household income (quartiles), US region (West, Midwest, Mid-Atlantic, Southeast, New England), smoking pack-years (never, >0 to 10, >10 to 20, >20 pack-years), body mass index (<25.0, 25.0 to <30.0, ≥30.0 kg/m^2), cumulative average sedentary activity (<3, ≥3 MET-hrs/week), cumulative average Alternative Healthy Index score (quartiles), parity/breastfeeding duration (nulliparous, parous/none to <1, parous/1-11, parous/≥12 months), menopausal status/postmenopausal hormone use (premenopausal, postmenopausal/never use, postmenopausal/ever use, perimenopause), physical examination in previous 2 years (yes, no)

Table. Hazard ratios for incident rheumatoid arthritis according to presence or absence of depression* among women in the Nurses' Health Studies (n=194,700), lagged by two questionnaire cycles (at least 4 years between depression and rheumatoid arthritis diagnosis assessments).

Conclusion: In this large prospective study, depression was associated with increased risk for incident RA, using stringent methods for RA case identification. The association of depressive symptoms with seronegative RA was not explained by measured lifestyle factors. We accounted for potential reverse causation of early RA symptoms leading to depression. Future studies are needed to replicate these findings and to elucidate potential mechanisms linking depression and seronegative RA, such as systemic inflammation or aberrant pain sensitivity.

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Abstract Number: 2823

Progression to Inflammatory Arthritis After Screening Autoantibody Positive in a Non-Clinical Setting

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health III: RA
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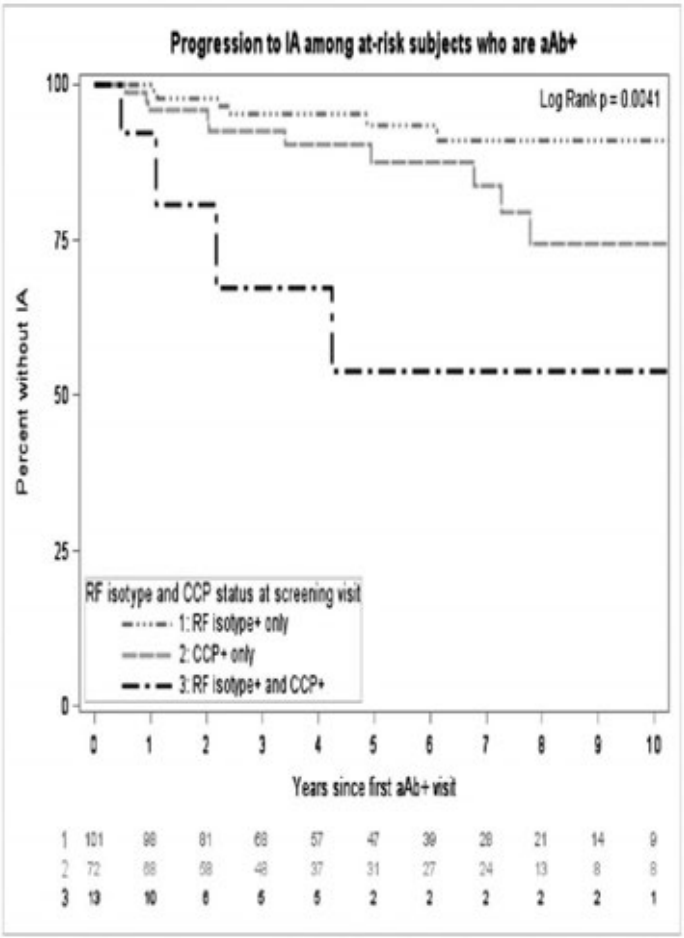

Table. Factors associated with developing IA after screening aAb positive

aAb status at first positive (screening) visit	HR (95% CI)*	p-value	Percentage who develop IA after screening aAb+
Any aAb+ (definition of cohort)	-	-	11.8%
RF+ isotype only	Referent		6.9%
CCP+ only	2.14 (0.82,5.59)	0.12	15.3%
CCP+ and RF+ isotype	5.38 (1.54,18.74)	0.01	30.8%
CCP+ > 2x cutoff versus all others	3.55 (1.49,8.41)	0.004	27.3%
CCP+ > 3x cutoff versus all others	3.04 (1.22,7.57)	0.02	28.6%
RF+ isotype >2x cutoff versus all	1.83 (0.73,4.62)	0.20	14.6%
RF+ isotype >3x cutoff versus all	2.28 (0.80,6.49)	0.12	15.2%

*HR represents the increased hazard of developing IA/RA. Models are adjusted for ever smoker status and education level (which were significant covariates in the models).
CCP+ = positive for either CCP2 or CCP3.1
RF+ isotype = positive for either IgM or IgA

Background/Purpose: Rheumatoid arthritis (RA)-related autoantibodies are typically elevated prior to the onset of seropositive RA. Screening for autoantibody (aAb) positive individuals is a means to assemble a cohort at high risk for future RA for epidemiologic, mechanistic and interventional studies. However, little is known about the stability of RA-related aAbs over time, and the likelihood of developing inflammatory arthritis (IA) in individuals without RA who screen aAb positive in a non-clinical setting.

Methods: The Studies of the Etiologies of RA (SERA) prospectively follows subjects who are RA-free but are at increased risk for future RA because they are a first-degree relative of an RA proband (n=1780), or come from a cohort enriched for HLA-DR4 alleles (n=629). We screened for serum aAbs to CCP (CCP2 and/or CCP3.1), and RF IgA

and IgM isotypes. Positivity was based on cut-offs as defined by manufacturer's recommendations. Overall, 15% (368/2409) tested positive for at least one aAb during screening. To evaluate outcomes of aAb+ subjects identified via screening, the cohort was limited to the 193 subjects that had at least one follow-up visit after their aAb+ visit. Seven subjects that were determined to have IA at screening were removed from the prospective analysis of aAb persistence and progression to IA, for a cohort of 186 aAb+ subjects (mean age: 47.7, SD 15.1). For the IA risk analyses, we explored combinations of aAb and high titer aAb, as defined by 2-times (2x) and 3-times (3x) the cutoff at the screening visit.

Results: Of the 186 screened aAb+ subjects, 61.1% tested aAb+ again on their next visit. During a median follow-up of 4.2 years (IQR: 2.2-7.3), 22/186 subjects (11.8%) developed IA, which was defined as having at least 1 joint with synovitis on exam, and of those subjects 16 were eventually classified as RA by 2010 ACR/EULAR criteria. Risk of developing IA differed significantly by aAb+ status at screening (Figure). Adjusting for ever smoking status and education, subjects that screened positive for both CCP and RF isotypes had over a 5-fold increased risk of developing IA than those positive for RF isotypes alone (Table). Those with CCP+ at >2x the cutoff were at 3.5-fold increased risk of IA compared to those CCP+ using the normal cutoff.

Conclusion: These findings support the utility of screening for RA risk in a non-clinical setting, and provides information regarding the likelihood of both retesting positive and future IA/RA. Specifically, in individuals who screen aAb+, ~60% will re-test positive, and either the presence at screening of both CCP and RF isotypes using the normal cut-offs, or the presence of CCP at > 2x cutoff predicts who will develop IA, while a CCP 3x cutoff does not improve prediction.

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Abstract Number: 2824

Antibiotic Use and the Development of Rheumatoid Arthritis (RA) and Risk of RA Flares: Case-Control and Self-Controlled Case Series Studies in Two National Electronic Patient Databases (SIDIAP and CPRD)

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SESSION INFORMATION
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Background/Purpose: The microbiome and specific bacterial triggers have been hypothesised to be involved in the pathogenesis of Rheumatoid Arthritis (RA) and RA flares. Antibiotic usage can mediate changes in the microbiome,

and act as a surrogate for infection with potentially pathogenic bacteria. We aimed to determine the association of antibiotic usage and RA/RA flare diagnosis.

Methods: Analyses were performed using the Catalan SIDIAP, and UK CPRD, national electronic primary care databases. Within SIDIAP, patients with an initial diagnosis of RA and 5 age, gender and practice matched patients were selected. Missing data (present for BMI, smoking and alcohol drinking) was imputed using multiple imputation with chained equations. Within CPRD, RA diagnosed patients with ≥1 RA flare recorded were included.

We performed a case-control study using SIDIAP and a self-controlled case series (SCCS) study using the UK CPRD.

Antibiotics grouped by the WHO ATC classification were the study exposures. Outcomes of interest were initial RA diagnosis in SIDIAP and RA flare in CPRD.

Multivariate conditional logistic regression was performed using SIDIAP data to determine associations with specific antibiotic group use, controlling for age, BMI, gender, smoking status, alcohol consumption socioeconomic status, medical co-morbidities, primary care attendance and other antibiotic group use. Conditional fixed-effects Poisson regression models were used to determine incidence rate ratios of RA flares in relation to antibiotic usage within CPRD.

Results: 13,920 RA patients and 69,535 controls from the SIDIAP database were identified. Use of beta-lactams or quinolones in the 2 years prior to diagnosis were associated with RA (OR 1.23, 1.16-1.29; OR 1.32, 1.26-1.38 respectively; p< 0.0001). Only beta-lactams showed a consistent dose-response gradient (Q1 OR 1.19, 1.10-1.29; Q2 OR 1.22, 1.12-1.34; Q3 OR 1.31, 1.20-1.42; Q4 OR 1.42, 1.31-1.54; p< 0.0001) and association with recency of use (current: OR 1.82, 1.61-2.06; recent: OR 1.54, 1.36-1.74; and previous use: OR 1.20, 1.14-1.26, p< 0.0001). In parallel, 1,192 RA patients were identified from the CPRD (from 31,992 patients), with ≥1 flare/s recorded. Sulphonamide and trimethoprim use was associated with an increased risk of RA flare at 29-90 days (IRR 1.71, CI 1.12–2.59, p=0.012); 91-183 days (IRR 1.57, CI 1.06–2.33, p=0.025); and 184-365 days (IRR 1.44, CI 1.03–2.02, p=0.033) after antibiotic treatment commencement. No other antibiotic groups were associated with RA or RA flare risk.

Conclusion: Usage of broad-spectrum beta-lactam antibiotics was associated with index RA diagnosis in the Catalan population in a dose and time-dependent manner. Usage of sulphonamide and trimethoprim antibiotics appeared associated with a 70% increased risk of RA flare at 1-3 months, which remained significant up to 12 months after treatment. We hypothesise that antibiotic use is a surrogate of a pathogenic bacterial infection in index RA and that the delayed onset of RA flares after specific antibiotics is mediated through the gut or urinary microbiomes. Further epidemiological and mechanistic research is also needed to determine whether acute infections are associated with RA.

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Abstract Number: 2825

Provider Variability in Glucocorticoid Prescribing for Patients with Rheumatoid Arthritis and Impact on Chronic Glucocorticoid Use

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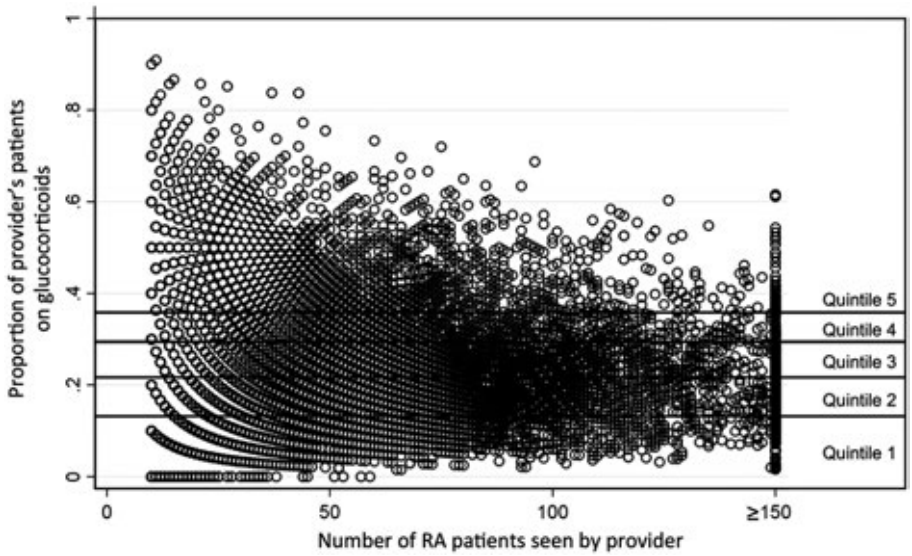

Figure 1. Variability in rheumatologist glucocorticoid prescribing for rheumatoid arthritis. Each circle represents a rheumatologist, with rheumatologists contributing a separate observation for each year they have seen at least 10 RA patients. The proportion of the rheumatologist's patients receiving at least 30 days of oral glucocorticoids within 90 days of the first DMARD prescription of each year is shown.

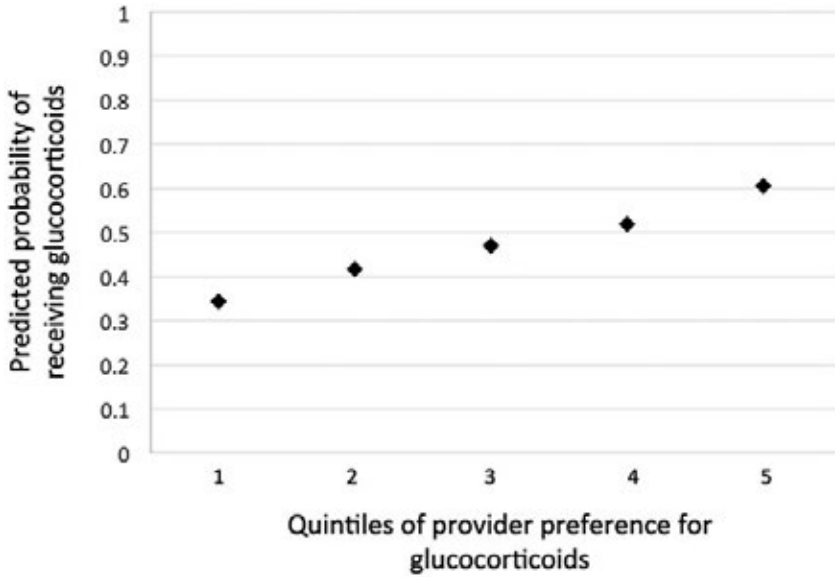

Figure 2. Predicted probability of a patient with RA on stable DMARD treatment receiving oral glucocorticoids 3-6 months after starting their DMARD course, calculated from a logistic regression model including their rheumatologist's preference for glucocorticoids in quintiles (see Figure 1) and covariates including demographics, comorbidities, and healthcare utilization measures (error bars obscured by markers, all $p < 0.001$).

SESSION INFORMATION

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Session Title: Epidemiology & Public Health III: RA

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Background/Purpose: Glucocorticoids are recommended as short-term bridging therapy in patients with rheumatoid arthritis (RA), but as many as 30-40% of patients remain on glucocorticoids chronically. We aimed to measure the variability in the prescribing of glucocorticoids among rheumatologists and determine whether seeing a provider

with a greater preference for glucocorticoids was independently associated with glucocorticoid use among patients on stable DMARD treatment.

Methods: Two cohorts were created using Medicare claims data 2006-2015. First, to measure provider variability, we identified patients with 2 diagnoses of RA within a given year who received methotrexate or a biologic. Patients could contribute to each year in which they fulfilled criteria. Among rheumatologists seeing at least 10 patients with RA in a given year, we defined the "provider preference" for glucocorticoids as the proportion of the provider's patients receiving ≥30 days of oral glucocorticoids within 90 days of the first DMARD treatment of that year. Each year was evaluated separately to allow for changing practices over time. We then identified a separate cohort of patients with 2 diagnoses of RA who initiated methotrexate or a biologic and remained on stable DMARD therapy without biologic additions or changes for ≥6 months. We used logistic regression to determine if provider preference for glucocorticoids (measured in the larger cohort using all other patients seen by the same provider in the same year) was independently associated with a patient receiving glucocorticoids 3-6 months after the start of the DMARD course, adjusting for patient demographics, comorbidities, and healthcare utilization.

Results: We identified 1,272,644 patient-year episodes among 385,597 unique patients. Among providers seeing ≥10 patients in a given year (28,936 provider-year combinations among 6,875 providers), the proportion of a physician's patients receiving ≥30 days of glucocorticoids was highly variable even among providers with a large patient volume (Figure 1) [median 24.3%, IQR 16.7% to 33.3%]. We identified a separate cohort of 192,614 RA patients on stable DMARD treatment for at least 6 months (47% receiving biologics) for whom we could identify the treating rheumatologist and assign a provider preference for glucocorticoids (calculated among all other patients seen by the same rheumatologist that year in the larger cohort). Provider preference for glucocorticoids was highly associated with receiving glucocorticoids 3-6 months after beginning the current DMARD course, with predicted probability ranging from 34.4% (95% CI 33.9-34.8) for patients seen by providers in the lowest quintile to 60.6% (95% CI 60.1-61.1) for those seen by providers in the highest quintile (Figure 2, all $p < 0.001$; first stage regression R^2 0.055, F 1597).

Conclusion: Glucocorticoids prescribing practices for RA vary widely between rheumatologists. **P**rovider preference for the use of glucocorticoids can help predict whether a patient remains on glucocorticoids during treatment. These data support the use of provider preference as an instrumental variable for epidemiologic studies evaluating glucocorticoid risk.

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Abstract Number: 2826

Risk of Serious Infections in Tofacitinib versus Other Biologic Drug Initiators in Patients with Rheumatoid Arthritis: A Multi-database Cohort Study

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SESSION INFORMATION
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Session Time: 4:30PM–6:00PM

Background/Purpose: It is well-known that biologic or targeted synthetic DMARDs increase the risk of serious infections (SIs), but few studies have directly compared the risk of SI across these DMARDs in a real-world setting. We aimed to compare incidence rate (IR) of serious bacterial, viral or opportunistic infection in rheumatoid arthritis (RA) patients initiating tofacitinib (TOF) (common exposure) versus other biologic DMARDs: abatacept (ABA), adalimumab (ADA), certolizumab (CER), etanercept (ETA), golimumab (GOL), infliximab (INF) or tocilizumab (TCZ).

Methods: We analyzed data from 3 U.S. healthcare claims databases: Medicare (2012-2015), Optum (2012-09/2017) and MarketScan (2012-2017). RA patients aged≥18 years who initiated TOF or other biologic DMARD without any prior use of biologics or JAK inhibitors were identified. We excluded patients with recent infection, malignancy or rituximab use. The primary outcome was a composite endpoint of incident SI that included bacterial, viral or opportunistic infection based on the inpatient principal diagnosis code. Secondary outcomes were specific subtypes of SIs. We adjusted for >70 potential confounders including demographics, prior DMARD and antibiotic use, comorbidities, other medications, and healthcare utilization factors in each database through propensity score (PS)-based

Table 1. Risk of incidence serious infection associated with initiating tofacitinib versus other biologics: a propensity score–based inverse probability treatment weighting (IPTW) as-treated analysis

	Exposure	Reference						
	Tofacitinib (n=5,394)	Abatacept (n= 14,075)	Adalimumab (n= 33,651)	Certolizumab (n= 7,797)	Etanercept (n= 34,394)	Golimumab (n= 6,315)	Infliximab (n= 16,891)	Tocilizumab (n= 4,513)
Outcome	**Hazard Ratio (95%CI)**							
Primary								
Serious infection	-	1.20 (1.09-1.31)	1.09 (0.98-1.22)	1.04 (0.87-1.25)	1.27 (1.14-1.42)	1.35 (1.29-1.40)	0.89 (0.62-1.29)	1.46 (1.31-1.63)
Secondary								
Serious bacterial infection	-	1.15 (1.09-1.21)	0.92 (0.66-1.29)	1.16 (1.10-1.23)	1.14 (1.04-1.26)	1.21 (1.06-1.39)	0.91 (0.62-1.33)	0.88 (0.54-1.41)
Pyelonephritis/UTI	-	1.41 (1.26-1.59)	1.39 (1.26-1.52)	0.95 (0.47-1.93)	1.33 (1.12-1.57)	2.61 (1.98-3.43)	2.17 (1.85-2.56)	1.28 (0.84-1.97)
Skin/soft tissue infection	-	2.55 (1.99-3.26)	1.74 (0.97-3.14)	0.86 (0.29-2.51)	2.34 (1.89-2.89)	1.37 (0.81-2.34)	2.05 (1.86-2.26)	0.89 (0.30-2.67)
Pneumonia/Upper resp. tract infection	-	1.47 (1.18-1.84)	1.22 (1.08-1.37)	1.11 (0.89-1.39)	1.43 (1.11-1.84)	1.32 (1.12-1.55)	0.87 (0.53-1.43)	1.24 (1.12-1.38)
Septicemia/bacteremia	-	1.09 (0.87-1.38)	0.96 (0.62-1.48)	1.31 (1.28-1.35)	1.08 (0.86-1.37)	1.18 (0.96-1.45)	0.85 (0.48-1.49)	1.34 (1.32-1.37)
Herpes zoster-specific*	-	1.90 (1.07-3.40)	1.45 (0.46-4.60)	2.94 (0.48-2.07)	1.64 (0.70-3.40)	0.63 (0.09-4.66)	1.36 (0.31-5.96)	2.33 (1.45-3.73)
Herpes zoster-broad**	-	1.38 (1.15-1.65)	1.53 (1.14-2.06)	1.39 (1.15-1.68)	1.48 (1.12-1.96)	1.29 (1.09-1.52)	1.18 (1.02-1.37)	1.29 (1.22-1.36)
	Incidence Rate per 100 person-years (95%CI)							
Primary								
Serious infection	3.56 (2.98-4.21)	3.44 (3.11-3.79)	2.77(2.58-2.98)	4.40 (3.86-5.00)	2.27 (2.10-2.45)	3.41 (2.87-4.02)	5.79 (5.33-6.27)	3.57 (2.95-4.29)
Secondary								
Serious bacterial infection	2.34 (1.88-2.89)	2.60 (2.31-2.91)	2.12 (1.95-2.30)	2.99 (2.54-3.48)	1.85 (1.70-2.02)	2.41 (1.96-2.94)	3.94 (3.56-4.34)	3.66 (3.03-4.38)
Pyelonephritis/UTI	0.37 (0.20-0.62)	0.42 (0.31-0.56)	0.30 (0.24-0.37)	0.64 (0.45-0.89)	0.27 (0.22-0.34)	0.43 (0.26-0.68)	0.54 (0.41-0.70)	0.49 (0.28-0.80)
Skin/soft tissue infection	0.34 (0.18-0.59)	0.10 (0.05-0.18)	0.17 (0.13-0.23)	0.35 (0.21-0.54)	0.13 (0.09-0.17)	0.26 (0.13-0.47)	0.18 (0.11-0.28)	0.37 (0.19-0.64)
Pneumonia/Upper resp. tract infection	1.06 (0.76-1.44)	1.05 (0.87-1.25)	0.76 (0.66-0.87)	1.44 (1.13-1.80)	0.62 (0.54-0.72)	1.06 (0.77-1.43)	2.05 (1.79-2.34)	1.13 (0.80-1.56)
Septicemia/bacteremia	1.19 (0.87-1.59)	1.46 (1.25-1.70)	1.19 (1.06-1.33)	1.41 (1.12-1.77)	0.97 (0.86-1.09)	1.25 (0.93-1.64)	2.23 (1.95-2.54)	1.33 (0.96-1.79)
Herpes zoster-specific*	0.21 (0.09-0.42)	0.12 (0.07-0.20)	0.10 (0.07-0.15)	0.04 (0.00-0.13)	0.08 (0.05-0.12)	0.12 (0.04-0.28)	0.16 (0.09-0.26)	0.06 (0.01-0.22)
Herpes zoster-broad**	4.37 (3.72-5.10)	2.79 (2.49-3.11)	2.27 (2.10-2.46)	2.62 (2.20-3.09)	2.23 (2.07-2.41)	2.72 (2.24-3.28)	3.32 (2.96-3.69)	2.46 (1.95-3.07)

Notes: 1. For the primary as-treated analysis, follow-up time started the day after cohort entry and ended on treatment discontinuation (60-day gap and grace period), outcome occurrence, disenrollment, death, or the end of dataset.
2. Hazard ratios for tuberculosis and viral hepatitis (secondary outcomes) are not reported since no events occurred for these endpoints in either tofacitinib or other biologic groups.
3. Hazard ratios (HR) from the 3 PS-weighted cohorts were combined by an inverse variance-weighted, fixed-effects model.

*Required 1 inpatient code at principal diagnosis position with antiviral use within 7 days of the diagnosis claim.
**Required 1inpatient or outpatient at any diagnosis position without requirement of antiviral use.

inverse probability treatment weighting. For the as-treated analysis, follow-up time started the day after cohort entry until the earliest of: treatment discontinuation, switching to any biologic other than index therapy, nursing home admission, death, disenrollment, or the end of study period. For each drug-comparison, weighted Cox proportional hazards models estimated the HRs and 95% CIs. The estimates from 3 databases were combined using an inverse variance-weighted, fixed-effects meta-analysis.

Results: A total of 123,960 biologic initiators were identified across 3 databases, of which 5,531 (4.5%) were TOF initiators. Mean age was 72 years in Medicare, 54 in Optum and 52 in MarketScan. During the 180-day baseline period, 64-71% patients used methotrexate and 68-73% used corticosteroids. After PS-weighting, all covariates were well balanced. The median follow-up time (days) in the as-treated analysis ranged from 164 (Optum) to 182 (MarketScan). A total of 2,958 SI events occurred. In the TOF group, the crude IR for SIs per 100 person-years ranged from 2.80 (MarketScan) to 7.89 (Medicare). Adjusted HRs showed higher risk of composite SIs in TOF compared to ABA (HR 1.20, 95% CI 1.09-1.31), ETA (1.27, 1.14-1.42), GOL (1.35, 1.29-1.40) and TCZ (1.46, 1.31-1.63), but similar risk compared to ADA, CER and INF. Serious bacterial infection risk was higher in TOF than ABA, CER, ETA and GOL. Secondary analyses showed consistent findings (**Table 1**).

Conclusion: This large multi-database cohort study of RA patients found a higher risk for the composite endpoint of SIs requiring hospitalization after initiating TOF versus ABA, ETA, GOL and TCZ as their first biologic or targeted synthetic DMARD therapy. The risk of serious bacterial infection, pneumonia, herpes zoster, and skin and soft tissue infections was also higher in TOF initiators versus several other biologics.

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Abstract Number: 2827

Weight Fluctuation and Risk of Cardiovascular Events in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Epidemiology & Public Health III: RA
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Fluctuations in weight (weight cycling) occur in rheumatoid arthritis (RA) in association with severe disease features and comorbidity. In the general population, weight fluctuation has been linked to the development of metabolic and cardiovascular disease. Accurate prediction of cardiovascular events is an important challenge in patients with RA. We aimed to determine if fluctuations in weight can help to predict cardiovascular events this population.

Methods: We studied patients with RA from the Corrona registry enrolled from October 2001 to March 2018 with least three recorded visits. The exposure was the time-varying percent change in weight from the prior visit (standardized to a per-year rate of change). Weight change was categorized as loss of ≥10%, loss of 5-10%, stable weight, gain of 5-10%, and gain of ≥10% based on prior definitions of important weight change. We also categorized pa-

	Percent Change in Weight (Visit 1- Visit 2)					
	≤ -10%	> -10% - ≤ -5%	>-5% - <5%	≥5% - < 10%	≥10%	P-value
	N=3139	N=3317	N=16791	N=3961	N=3972	
Age	58.2(13.9)	59.3(13.1)	58.6(13)	57.4(13.3)	56.8(13.7)	<0.0001
Female, N(%)	2498(79.6)	2513(75.8)	12722(75.8)	3087(77.9)	3105(78.2)	<0.0001
Disease Duration	9(9.8)	9.5(10.2)	9.2(9.7)	8.7(9.7)	8.2(9.4)	<0.0001
Visit 1 BMI	30.5(7.7)	29.6(6.9)	29.3(6.9)	29.1(7)	28.4(6.8)	<0.0001
mHAQ	0.4(0.5)	0.4(0.4)	0.3(0.4)	0.3(0.4)	0.4(0.5)	<0.0001
CDAI	13(12.7)	11.7(11.9)	11.1(11.3)	11.8(11.6)	13.1(12.2)	<0.0001
Disabled, N(%)	472(15)	380(11.5)	1907(11.4)	449(11.3)	537(13.5)	<0.0001
CV Disease N(%)	297(9.5)	324(9.8)	1433(8.5)	363(9.2)	372(9.4)	0.0793
Hyperlipidemia, N(%)	662(21.1)	751(22.6)	3630(21.6)	837(21.1)	811(20.4)	0.1944
Hypertension, N(%)	1039(33.1)	1083(32.6)	5280(31.4)	1197(30.2)	1191(30)	0.0118
Hx Diabetes, N(%)	301(9.6)	280(8.4)	1342(8)	338(8.5)	352(8.9)	0.0314
Statin use, N(%)	621(19.8)	664(20)	3361(20)	776(19.6)	758(19.1)	0.7396
TNF use, N(%)	1223(39)	1296(39.1)	6662(39.7)	1622(40.9)	1601(40.3)	0.3582
MTX use, N(%)	1967(62.7)	2082(62.8)	10423(62.1)	2497(63)	2575(64.8)	0.0302
Prednisone Use N(%)	784(25)	742(22.4)	3611(21.5)	914(23.1)	1126(28.3)	<0.0001
Any Drinking, N(%)	1209(38.5)	1361(41)	7363(43.9)	1795(45.3)	1638(41.2)	<0.0001
Any Exercise, N(%)	2065(65.8)	2175(65.6)	11174(66.5)	2590(65.4)	2507(63.1)	0.0017
Smoking						
Never, N(%)	1697(54.1)	1758(53)	9544(56.8)	2249(56.8)	2155(54.3)	<0.0001
Former, N(%)	899(28.6)	1010(30.4)	4826(28.7)	1131(28.6)	1145(28.8)	
Current, N(%)	543(17.3)	549(16.6)	2421(14.4)	581(14.7)	672(16.9)	

Table 1. Characteristics of study participants at visit 2 among patients categorized by weight change from visit 1.

	Hazard Ratio for CV Events (*(2,277 events; 135,395 P-Ys)*		
	All Participants	***Underweight/Normal***	***Overweight/Obese***
Time-Varying	***aHR (95% CI)***	***aHR (95% CI)***	***aHR (95% CI)***
Lost >=10%	1.18 (1.03, 1.36)*	1.34 (1.08, 1.66)**	1.10 (0.92, 1.31)
Lost 5-10%	1.03 (0.90, 1.18)	1.18 (0.94, 1.48)	0.97 (0.82, 1.14)
No change	1 (reference)	1 (reference)	1 (reference)
Gained 5-10%	1.22 (1.08, 1.39)**	1.07 (0,82, 1.41)	1.26 (1.09, 1.45)**
Gained >=10%	1.20 (1.04, 1.38)*	1.74 (1.41, 2.24)***	1.04 (0.88, 1.45)
Adjusted for age, sex, race, calendar year, disease duration, hx of diabetes, hypertension, hyperlipidemia and CV disease at baseline; and statin use smoking, alcohol, reported exercise, methotrexate use, prednisone use, TNFi use, disease activity, HAQ and work disability as time varying covariates			

Table 2: Sequential Cox proportional hazard models evaluating the risk of weight change from the prior visit adjusting for demographics, CV risk factors, disease characteristics, and disability.

tients by quintile of variability in weight in all prior observation periods as previously described (operationalized as the average absolute difference of weight change over all prior intervals). Incident cardiovascular events were identified and adjudicated in a subset. Sequential Cox proportional hazard models explored independent associations between weight change and variability in weight and the risk of CV events before and after adjusting for baseline characteristics and CV risk factors, RA disease features, and disability as time-varying covariates. We tested for interaction to determine if associations between weight change and CV events were modified by current body mass index (BMI).

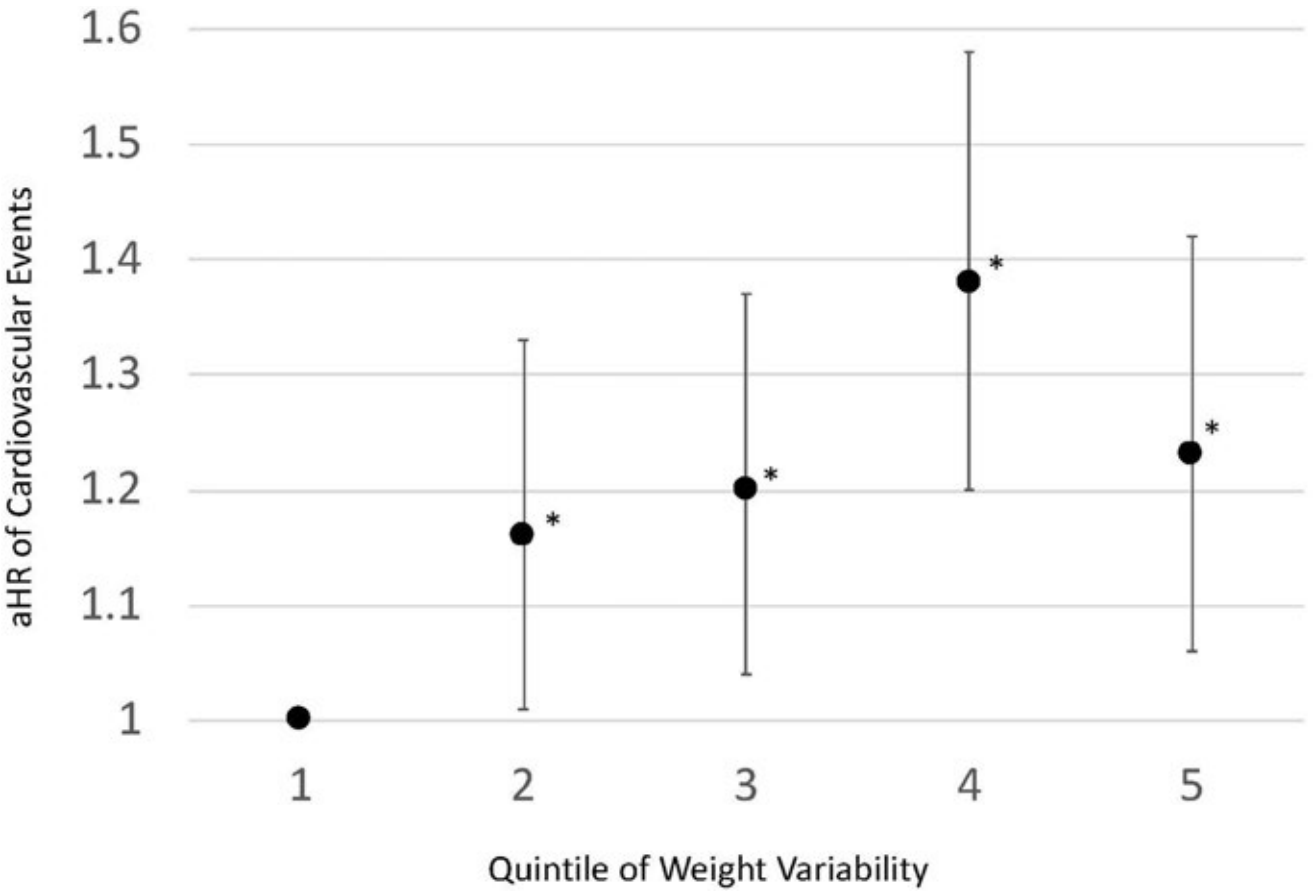

Figure. Hazard Ratio for cardiovascular events for higher variability in BMI over prior observations compared to the lowest variability between observations.

Results: Among 31,381 participants, there were 2,277 events in 135,395 person-years. It was common for participants to lose (10% of observations) or gain (13%) at a rate of 10% per year between observations. Both weight loss and weight gain were associated with greater disease activity, disability, smoking, and use of corticosteroids (Table 1). In models adjusting for demographics, BMI, and calendar year, a greater risk of CV events was observed in those that experienced 10% weight loss [HR: 1.34 (1.17, 1.53) p< 0.001] or 10% weight gain [HR: 1.31 (1.14, 1.51) p< 0.001]. In adjusted models, these associations were slightly attenuated (Table 2). There were significant interactions with current BMI suggesting that the risk of weight loss or gain was greatest in non-overweight participants (BMI < 25 kg/m2). Patients with greater variability in weight over prior observation periods were at higher risk of CV events compared to those with the most stable weight over time, independent of their current BMI (Figure).

Conclusion: Fluctuations in weight (both weight gain and weight loss) predict a greater risk of cardiovascular events in RA over time. The association is observed primarily among non-overweight patients and is independent of traditional risk factors. These findings suggest that weight fluctuation may be a marker of metabolic disturbances that may help in risk prediction in this group. Further study is necessary to determine if fluctuations in weight have direct adverse cardiometabolic consequences by promoting cardiometabolic disease.

Disclosure: J. Baker, Bristol-Myers Squib, 5, Burns-White LLC, 5, Myriad RBM, 2; **G. Reed**, Corrona LLC, 1, 5, Corrona Research Foundation, 3, Corrona, LLC, 1, 3; **J. Kremer**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 2, 5, Amgen, 5, BMS, 2, 5, Bristol-Myers Squib, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona LLC, 1, 3, Corrona, LLC, 1, 3, Genentech, 5, Genentech, Inc., 5, GSK, 5, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Regeneron, 5, Sanofi, 5.

Abstract Number: 2828

Implementing the BP Connect Systems-Based Blood Pressure Follow-Up Protocol with Community Rheumatology Clinic Teams

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Measures of Healthcare Quality II: Quality Improvement in Rheumatology – Still Getting Better

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

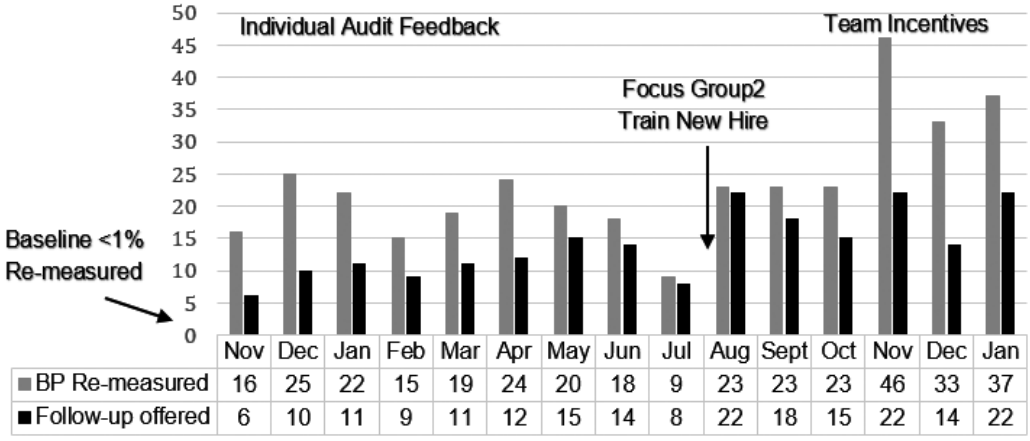
Background/Purpose: Despite recognition that rheumatoid arthritis (RA) accelerates cardiovascular disease (CVD) and hypertension impacts 50% of RA patients, up to 50% lack blood pressure (BP) control, overlooking *the* most modifiable CVD risk factor. Rheumatology clinics record BP routinely but do not routinely manage it. As we previously reported, only 10% of RA clinic notes with high BP included follow-up recommendations. We subsequently reported that our adapted evidence-based BP Connect staff protocol doubled the odds of timely follow-up of high BPs and reduced population level BPs across three academic rheumatology clinics (Bartels et al. *AC&R* 2019). Preparing for wider dissemination, we sought to replicate our findings in a community rheumatology clinic setting.

Table 1. Monthly Staff Performance of BP Connect Based on Electronic Health Record Data

	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Total
Total Visits	194	331	382	232	415	511	520	482	419	507	425	433	458	419	422	6150
Visits w/ high BP (≥140/90)[1]	19 10%	41 12%	42 11%	21 9%	54 13%	62 12%	68 13%	60 12%	56 13%	52 10%	49 12%	54 12%	74 16%	60 14%	55 13%	767 12%
BP Re-measured[2]	16 84%	25 61%	22 52%	15 71%	19 35%	24 39%	20 29%	18 30%	9 16%	23 44%	23 47%	23 43%	46 62%	33 55%	37 84%	353 46%
Confirmed High BP	10	17	19	13	15	18	17	14	7	19	20	21	31	20	22	263
Follow-up offered [3]	6 60%	10 59%	11 58%	9 69%	11 73%	12 67%	15 88%	14 100%	8 100%	22 100%	18 90%	15 71%	22 71%	14 70%	22 74%	209 79%
Follow up accepted [4,a]	5 50%	5 29%	7 37%	3 23%	3 20%	6 33%	8 47%	4 29%	4 57%	12 63%	7 35%	11 52%	14 45%	11 55%	9 41%	109 41%

Percentages based on [1] total visits, [2] visits with high BP, and [3, 4] visits with high 2nd BP logged. [a] Accepted or already scheduled.
Baseline <1% on BP Re-measured and Follow-up offered.

Figure 1. Monthly Staff Performance of Key Target Behaviors of BP Connect



Methods: We prospectively examined the feasibility and impact of our staff-based BP Connect protocol at a community rheumatology clinic using pre-post design. Pre-and post-protocol rates of primary care BP follow-up referrals were the primary outcome of electronic health record (EHR) data analysis. We first analyzed workflows through a focus group with clinic staff nurses, medical assistants, and schedulers to tailor protocols for the new clinic. Next, a one hour training was provided on rheumatologic CVD risk and BP, BP measurement skills review, protocol talking points, and EHR navigation. Two EHR alerts and monthly staff audit feedback supported implementation. Mid-implementation focus groups and questionnaires evaluated staff feasibility and acceptability.

Results: Overall, compared to < 1% baseline remeasurement of high BPs in the rheumatology clinic, we reached two monthly peaks of 84%, and overall in 353 of 767 (46%) patients, high BP was re-measured post-implementation. Among 263 rheumatology patients with confirmed high BP re-measurement, 209 (79%) were offered follow-up for high BP, and among those, 109 (41%) accepted primary care follow-up (Table 1). After initial gains, a mid-implementation decline corresponded to clinic staff turnover and reduced staff-to-visit ratios. Increases in the last months occurred following focus group problem-solving, new hire training, and the introduction of modest team incentives based on clinic-level goals for staff performance (Fig 1).

Mixed methods findings included staff focus group and questionnaire responses. Rheumatology staff's baseline usual practices followed three steps: (1) identifying high BP, (2) variable follow-up within the clinic, and (3) occasional follow-up across settings (i.e., primary care). Post-implementation, staff were satisfied with protocol support for these steps. Among six pre- and four post-implementation respondents, self-efficacy and confidence in perceived ability to do something to improve BP care increased from 3.8 to 4.5 on a 5-point Likert scale.

Conclusion: Replicating the implementation of the BP Connect systems-based staff protocol in a community rheumatology clinic improved primary care follow-up referrals for high BP. Findings highlight a scalable strategy to improve BP follow-up and rheumatology population health and new findings regarding the potential role of team-based incentives.

Disclosure: E. Ramly, None; **D. White**, None; **A. Perez**, None; **C. Bartels**, Pfizer, 2, Pfizer Independent Grants for Learning and Change, 2.

Abstract Number: 2829

Improving SLE Care by Enhancing Medication Adherence Using a Tailored Clinic Intervention: HCQ-Crosswalk

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Measures of Healthcare Quality II: Quality Improvement in Rheumatology – Still Getting Better
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Up to 83% of patients with SLE are nonadherent to hydroxychloroquine (HCQ) which results in a 36% higher risk of renal failure, and 8-fold higher risk of premature death. Therefore, clinicians must address HCQ nonadherence. Our recent meta-analysis reported three times higher odds of low HCQ blood levels in SLE patients who self-report HCQ nonadherence. Results suggest that when asked, most patients accurately report HCQ adherence. Despite this, one study reported that patients were *never* asked about medication nonadherence during 200 recorded

Table 1. Crosswalk to Adherence Strategies by Leading Barrier	
Barrier Category	**Crosswalk Strategy Options**
(S) System *Inability to get refills*	Arrange transport services, use auto-refills, involve family members
(M) Motivation *Med side effects*	Conduct motivational interview, strategies to manage adverse effects, alternative anti-malarial options, involve family
(U) Understanding *Outcome concerns*	Use teach back, simple language, visual aids, involve caregivers and family
(M & U) Motivation & Understanding *Other side effects & concerns*	Discuss expected outcomes, use teach back, simple language and treatment recommendations, visual aids, involve family, conduct motivational interview
(R) Recall *Forgetfulness*	Consolidate doses, use pillboxes or phone reminders, involve family members
(F) Financial *Inability to afford HCQ*	Change to low cost alternatives, alt. manufacturers, offer coupons, patient assistance referral

Figure 1. Reported Key Adherence Barriers by Category

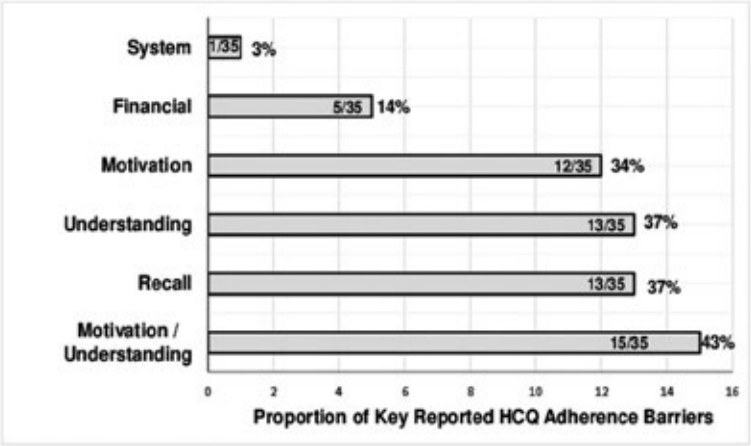

Table 2. Feasibility of Administering HCQ-Crosswalk during SLE visits (n=113 visits)	
Demographics	Mean age 45 (19-78) 92% female; 83% white
Non-adherence (<80%)	33%
Intervention completion	93%
Barriers addressed	86%*
Time to assess & address nonadherence	2.6±1.0 (1-5) mins
Intervention completed by non-MD	40%

**14% had an absolute contraindication to HCQ*

rheumatology visits at 4 centers. Barriers to addressing nonadherence include limited time and expertise in using lengthy gold-standard self-report tools (14+ items). Therefore, we aimed to develop a tool to assess nonadherence, categorize specific adherence barriers, and guide clinicians to prepare an adherence plan with individual SLE patients.

Methods: We implemented a 26-week single center study to test the feasibility of administering our adapted seven-item HCQ Adherence Tailoring Crosswalk (HCQ-Crosswalk) intervention in all consecutive SLE visits (n =113). The intervention was based on key domains of two gold-standard adherence tools (MASRI & BMQ). The first item, a visual-analogue adherence scale, was completed by SLE patients. Those who reported nonadherence (adherence < 80%) on the first item were prompted to complete the next six questions to identify their key adherence barrier(s). Upon identifying 1-2 key adherence barrier categories, clinicians were directed to the crosswalk to adherence strategies (Table 1) which were discussed with patients to tailor an individual adherence plan. To assess the tool's feasibility, we calculated the percentage of visits completing the intervention, the mean time spent, the percentage of barriers addressed, and proportion completed by a non-MD (e.g. pharmacy student).

Results: Nonadherence was identified at 33% of 113 consecutive visits among 65 SLE patients. Nonadherence rates were comparable to published rates using a gold-standard tool (33% vs 51%, *p 0.08*). The HCQ-Crosswalk intervention was completed in 93% of visits. Patients reported Motivation & Understanding as the key barrier (43%), which included the fear of side effects and lack of knowledge on long-term benefits of HCQ (Figure 1). Other commonly reported barriers included forgetfulness (Recall) and inability to afford medications (Financial). Using this intervention, we addressed 86% of barriers within 2.6±1 mins and 40% of the discussions were completed by a non-MD (Table 2).

Conclusion: The HCQ-Crosswalk is a feasible intervention to assess and address nonadherence in under 3 minutes. Future work will aim to validate HCQ-Crosswalk intervention versus gold-standard tools and to examine its role in improving HCQ adherence in SLE.

Disclosure: S. Garg, None; **B. Chewning**, None; **K. Hansen**, None; **B. Martin**, None; **C. Bartels**, Pfizer, 2, Pfizer Independent Grants for Learning and Change, 2.

Abstract Number: 2830

Treatment Delays Associated with Prior Authorization for Infusible Medications: A Cohort Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Measures of Healthcare Quality II: Quality Improvement in Rheumatology – Still Getting Better
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Prior authorizations (PA) are commonly required by health payers as cost-containment strategies for expensive medications, including infused biologics. In rheumatology, these medications are frequently prescribed to treat rare conditions that can be organ- or life-threatening and for which few or no medications have regulatory approval because of their relative scarcity. Infused medications often have neither generic substitutes nor oral or subcutaneous formulations and inevitably require advanced planning to administer. There are scarce data about the effect of PA requirements for infused medications on patient-oriented outcomes.

	Overall N (%)	No PA Required N (%)	PA Required N (%)
N	225 (100)	65 (29)	160 (71)
Female	149 (66)	41 (63)	108 (68)
Race			
White	188 (84)	54 (83)	134 (84)
Black	11 (5)	3 (5)	8 (5)
Asian	10 (4)	3 (5)	7 (4)
Other	13 (6)	3 (5)	10 (6)
Unknown	3 (1)	2 (3)	1 (1)
Ethnicity			
Non-Hispanic	213 (95)	62 (95)	151 (94)
Hispanic	12 (5)	3 (5)	9 (6)
Age [Mean, SD]	53 [15]	62 [16]	50 [13]
Disease or Disease Category			
Inflammatory Arthritis	71 (32)	27 (42)	44 (28)
Vasculitis	52 (23)	16 (25)	37 (23)
IgG4-Related Disease	38 (17)	9 (14)	29 (18)
Connective Tissue Disorder	23 (10)	3 (5)	20 (13)
Myositis/Interstitial Lung Disease	20 (9)	5 (8)	15 (9)
Other	21 (9)	5 (8)	15 (9)
Designated Rare Disease*	119 (53)	33 (51)	86 (54)
Condition with No FDA-Approved Medication	89 (40)	22 (34)	67 (42)
Private Insurance	160 (71)	28 (43)	132 (83)
Medication			
Rituximab	157 (70)	49 (75)	108 (68)
Infliximab	39 (17)	10 (15)	29 (18)
Tocilizumab	21 (9)	6 (9)	15 (9)
Zoledronic Acid	7 (3)	0 (0)	7 (4)
Intravenous Immunoglobulin	1 (<1)	0 (0)	1 (1)
New Request	131 (51)	30 (46)	101 (63)
Outcomes Following Infusion Order			
PA – Approval	127 (56)	0 (0)	127 (79)
PA – Denial	33 (15)	0 (0)	33 (21)
No Authorization Required	65 (29)	65 (100)	0 (0)

*Examples include systemic vasculitis, interstitial lung disease related to connective tissue disease, IgG4-related disease, inflammatory myopathy, and autoinflammatory disorders

Baseline Cohort Demographics

Methods: We included subjects for whom an infusible medication was prescribed in our academic rheumatology practice for a rheumatologic condition. The exposures of interest were a PA requirement and the PA outcome (approved vs. denied). The primary outcome was the difference in days from medication request to infusion. Secondary outcomes included time to PA approval, the proportion of denied PAs, and glucocorticoid exposure among those approved and denied following PA request.

Results: Of the 225 subjects (Table 1), 160 (71%) required a PA. Of the PA-requiring cases, the conditions most often being treated were inflammatory arthritis (44, 28%) and vasculitis (37, 23%). In 67 (42%) cases requiring a PA, the condition had no FDA-approved medication. The PA request was initially denied in 33 (21%) subjects, 21 (64%) of whom had conditions with no FDA-approved medications (Table 2); twenty-seven (82%) of these denials were eventually approved. Thus, 96% of all PAs were ultimately approved. PAs were associated with a greater median number of days to infusion compared to cases in which no authorization was required (31 days [15, 60] vs 27 days [13, 41], p=0.045; Table 3). Compared to those in whom no PA was required, subjects in whom a PA request was initially denied had substantially longer time to approval (22 days [15, 41] vs 0 days [0, 0]), P< 0.001) and infusion (50 days [31, 76] vs 27 days [13, 41], P< 0.001). PA denials were associated with a 3.8-fold greater median prednisone-equivalent

	PA Denied N (%)
Number of Denials	33 (100)
Disease or Disease Category	
IgG4-Related Disease	10 (33)
Connective Tissue Disease	9 (27)
Inflammatory Arthritis	5 (15)
Vasculitis	3 (9)
Myositis/Interstitial Lung Disease	2 (6)
Other	4 (12)
Designated Rare Disease	20 (61)
Medication Requested	
Rituximab	23 (70)
Infliximab	4 (12)
Tocilizumab	4 (12)
Intravenous Immunoglobulin	1 (3)
Zoledronic acid	1 (3)
Reason for Request*	
Prednisone-sparing	13 (39)
Currently on or had tried oral DMARD**	16 (48)
Organ-threatening disease	10 (30)
Subcutaneous formulation not ideal for patient	3 (9)
Prior response to requested treatment	6 (18)
Reason for Denial	
Off-Label Use	27 (82)
Condition has no FDA-approved medication	21 (78)
Systemic Lupus Erythematosus	5 (19)
Diagnostic uncertainty	1 (4)
Preferred drug not tried†	5 (16)
Safety concern	1 (3)
Response to Denial‡	
Physician peer-to-peer	27 (82)
Additional laboratory testing	1 (3)
Treatment postponed	1 (3)
Use preferred drug	5 (15)
Ultimately Approved	27 (82)

*Multiple reasons possible for one patient, totals greater than 100%;

†Psoriatic Arthritis, Rheumatoid Arthritis, Uveitis;

**Disease-Modifying Anti-Rheumatic Drug (DMARD);

‡One subject had a failed peer-to-peer and tried preferred drug

Characteristics of Denied Prior Authorizations

glucocorticoid exposure in the 3 months following the request than when a PA was not required (605mg [0, 1575] vs 160mg [0, 675], P=0.01).

Conclusion: PA requirements for infusible medications are associated with delays in treatment. There is a striking three-week delay to approval and one-month delay to treatment among those whose PAs are initially denied. PA denials are further associated with excess glucocorticoid exposure. Thus, PAs constitute a barrier to the introduction of effective treatment in an expeditious manner. Because the great majority of PA requests are ultimately approved, the value of PA requirements and their impact on patient safety should be re-evaluated.

	Overall	No PA Required	PA Required		
			All	Approved	Denied
N	225 (100%)	65 (29%)	160 (71%)	127 (79%)	33 (21%)
Days between PA request* and insurance response (Median, IQR)†	1 (0, 7)	0 (0, 0)	**5 (1, 9)**	**4 (0, 9)**	**8 (5, 13)**
Days between PA request and insurance approval	1 (0, 9)	0 (0, 0)	**6 (1, 15)**	**4 (0, 9)**	**22 (15, 41)**
Days between PA request and infusion	29 (15, 53)	27 (13, 41)	**31 (15, 60)**	27 (13, 56)	**50 (31, 76)**
90 Day Glucocorticoid (mg) Exposure‡	360 (0, 900)	160 (0, 675)	364 (0, 1089)	280 (0, 1035)	**605 (0, 1575)**

Bold font indicates P<0.05 when comparing category vs. no authorization required;
*PA request refers to either date of PA request or, for patients who did not require a PA, the date that that determination was made;
†Across all subgroups, the median (IQR) time between physician order and PA request processing was 1 (0, 3) days;
‡ Prednisone-equivalent glucocorticoid exposure

Patient-Oriented Outcomes Following Prior Authorization (PA) Request Submission According to Prior Authorization Requirement

Disclosure: Z. Wallace, National Institute of Arthritis, Musculoskeletal, and Skin Diseases, 2, Rheumatology Research Foundation, 2; **T. Harkness**, None; **X. Fu**, None; **J. Stone**, Genentech, 2, 5, Roche, 2, 5, Xencor, 2, 5; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5; **R. Walensky**, None.

Abstract Number: 2831

Cracks in Your Referral Process? Find Your Sustainable Solution Here

Sheetal Vora,[1] Amanda Moyer,[2] Lynn Kalhagen,[2] Anna Sherrod,[2] Thomas Griffin,[2] Kristen Corcoran,[2] Sarah Mabus,[2] and Talia Buitrago[2], [1]Atrium Health, Charolotte, [2]Atrium Health, Charlotte

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Measures of Healthcare Quality II: Quality Improvement in Rheumatology – Still Getting Better
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Early diagnosis for rheumatic conditions is crucial for children to achieve the best functional outcomes. Access to care is difficult due to the volume of referrals and paucity of pediatric rheumatologists. This compelling need to expediently triage dire and complex rheumatology referrals has been painfully demonstrated in our clinic. When this project was initiated there was a 3-month backlog to see a new referral. During this time, several patients were assigned delayed appointment dates due to our lack of a triage process. Improving the referral process so the appropriate patient is seen quickly is important for early diagnosis and earlier treatment, which improves quality of care for children with chronic debilitating rheumatic conditions. We intended to increase from 35% to 85% our rate of appointments scheduled within 30 business days for referred pediatric patients who require ongoing rheumatologic care by December 30, 2018. Our process measures were 0 to 90% increase in use of referral tool by primary care providers and 0 to 90% increase in appropriate use of triage tool by our clinic staff. Our balancing measures were no show rates and patient volume.

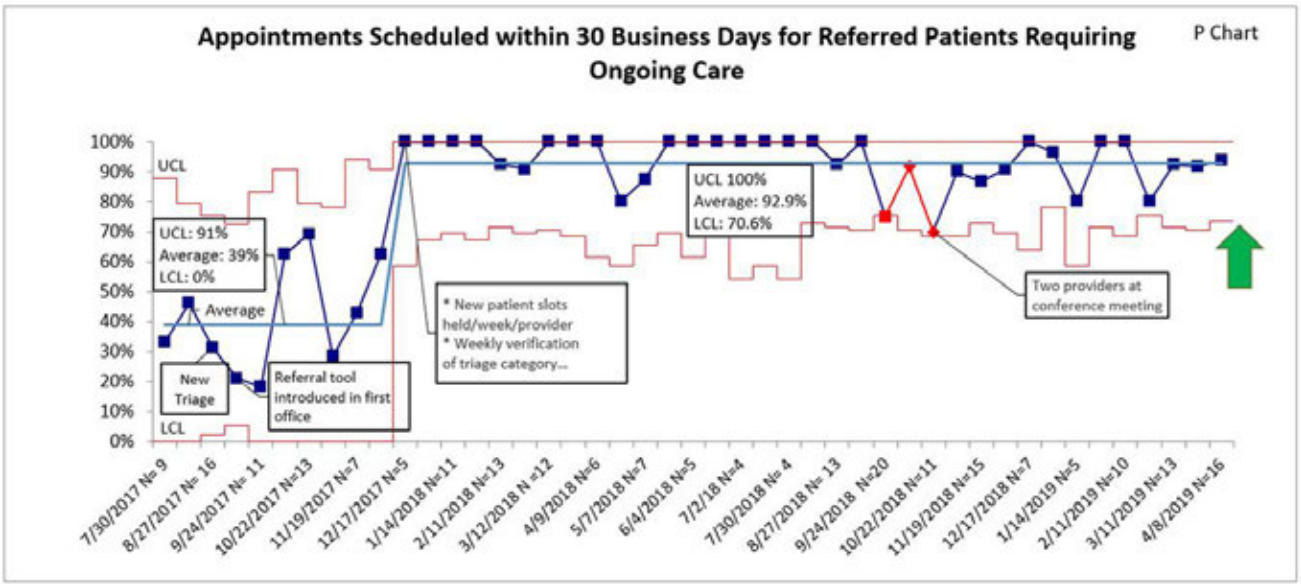

Figure 1. Appointments Scheduled within 30 Business Days for Referred Patients Requiring Ongoing Care Figure 2. Business Days Between Referral Date and Consult Figure 3.

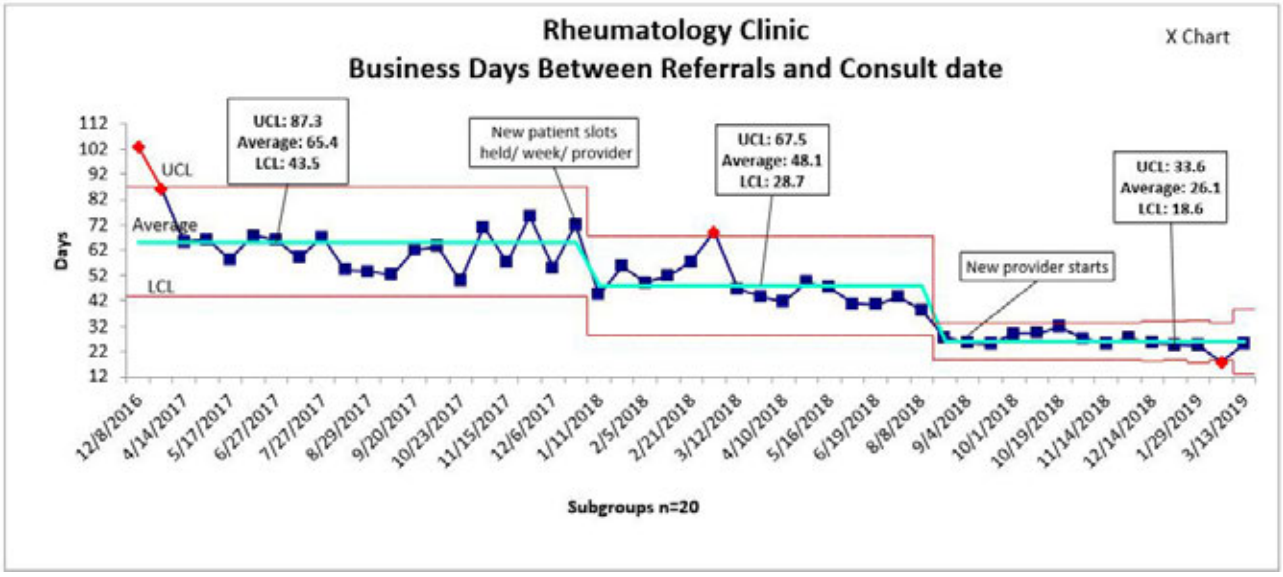

Figure 2. Business Days Between Referral Date and Consult

Methods: The improvement methodology used for this project was the Model for Improvement with rapid Plan, Do, Study, Act cycles. We defined current state by collecting baseline data, completing a root cause analysis, and surveying staff and patients to identify the most common and impactful barriers of lack of a standardized referral and triage process, lack of available appointments for higher acuity patients, and limitations in staff and families' ability to make contact.

We used a Key Driver Diagram to define leading factors and guide change ideas, and an aim statement and data management plan to guide the work and data collection. Our measures were evaluated using run charts and later moved into a Statistical Process Control Chart.

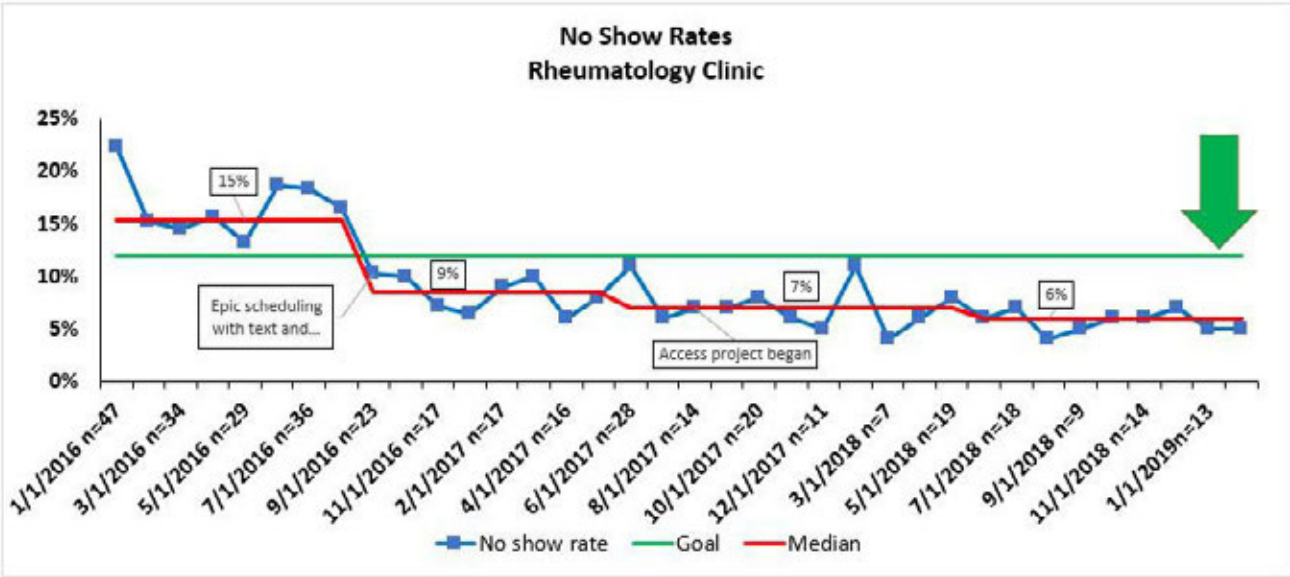

Figure 3. No Show Rates

Results: We have sustained our average performance for our target population at 92% since December 2017 (Figure 1). This represents an 8% improvement over our initial goal of 85% and a 135% improvement over baseline.

Additionally, we reduced time from referral received to the patient being seen by a provider for the overall clinic population from an average of 65.4 business days to 26.1 (Figure 2). Our no-show rate was reduced from 15% to 6% (Figure 3) and our total volume of patients increased by an average of 30 per month. This ultimately yielded a return on investment of greater than $300k in sixteen months.

Conclusion: Improvement science offers a methodology to strategically address inefficiencies and communication barriers, ensuring improved quality and safety, and better patient experience. By investing time in creative problem-solving, streamlining, and clear communication, and by facilitating staff empowerment and ownership, this project achieved remarkable gains in patient access and care delivery. Most importantly, we ensured longevity for this crucial improvement, thus promising significant long-term benefits. This result is a process that can be transferred to other settings, and holds great value given the universal challenges of supply/demand.

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Abstract Number: 2832

Using a Learning Collaborative to Develop an RA Disease Activity Communication Tool to Promote Shared Decision-Making in Treat to Target

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TREATMENT PROGRESS WORKSHEET

Name _____ DoB _____ Visit date _____

Completed by patient

What's on my mind today:

The following activities bring me joy:

My treatment goals:

Use this tool to think about your treatment goals, and get the most out of your conversation with your clinician.

I manage pain and stress by:

Some conversation-starters for your visit with your clinician:

I would like to talk about…

This is important to me because…

It may help you to know…

I hope this conversation leads to…

I'm nervous this conversation will lead to…

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Measures of Healthcare Quality II: Quality Improvement in Rheumatology – Still Getting Better

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: A treat to target (T2T) approach in managing RA can improve patient outcomes. A key component to T2T is establishing personalized treatment targets through shared decision-making (SDM) with patients, which can be difficult to implement in practice. We established a learning collaborative to develop a patient communication tool to help promote SDM and T2T in RA.

Methods: The RISE Learning Collaborative (RISE-LC) was established in March 2019 to share and coordinate quality improvement (QI) efforts in adult rheumatology practices across multiple centers. The structure of the RISE-LC is based on the Institute for Healthcare Improvement's Breakthrough Series[1], where Collaborative faculty and participants work together to improve performance on agreed upon quality measures. Participants completed a survey ranking quality measures of interest, then attended in an in-person meeting with Collaborative faculty to develop goals for RISE-LC, including 1) improving physician-patient communication about disease activity (DA) and patient-reported outcomes (PRO) and 2) formally soliciting patient goals and incorporating them into a personalized treatment target through SDM. We used a human-centered design process to develop components of a DA communication tool, based on a series of patient and physician focus groups. The RISE-LC participants implemented the tool through Plan-Do-Study-Act (PDSA) cycles, and iterative changes were made based on participants' input.

Results: We recruited a total of 9 sites from 8 states, mostly representing academic centers (7/9). At baseline, all sites had a workflow in place for measuring RA DA, although performance was variable (range 30% to 90%). Participants agreed on a group QI project to solicit patient goals and improve SDM to support T2T. The first iteration of tool development was based on findings from patient focus groups that revealed that patients prefer a graphic display for DA[2]. Participants performed initial PDSA cycles to pilot use of the tool in their practices. Subsequent iterations of the tool incorporated the open-ended question "What's on your mind today?" (used in one faculty's [PB's] health system) and RA-specific questions based on an Arthritis Conversation Tool developed by one faculty expert (JLB) (Fig 1). A second PDSA cycle of the revised tool demonstrated feasibility and patient acceptance (3/9 sites).

Conclusion: The RISE-LC is a continuous, systematic model for sharing in QI efforts across rheumatology clinics. Through broad participant input, human-centered design, and iterative tests of change, an innovative patient communication tool was developed. Future work will examine the impact of the tool on improving documentation of DA, treatment goals, and patient satisfaction and engagement.

[1] The Breakthrough Series: IHI's Collaborative Model for Achieving Breakthrough Improvement. IHI Innovation Series white paper. Boston: Institute for Healthcare Improvement; 2003. (Available on www.IHI.org)

[2] Ragouzeos D, Gandrup J, Berrean B, et al. "Am I OK?" using human centered design to empower rheumatoid arthritis patients through patient reported outcomes. Patient Educ Couns. 2019; 102(3):503-510

Disclosure: L. Liu, None; **S. Choden**, None; **J. Barton**, None; **P. Bajaj**, None; **C. Bartels**, Pfizer, 2, Pfizer Independent Grants for Learning and Change, 2; **M. Danila**, Pfizer, 2, Sanofi Regeneron, 5; **E. Wahl**, None; **K. Reiter**, None; **J. Zell**, None; **C. Downey, MD**, None; **E. Weinstein**, None; **G. Schmajuk**, None; **J. Yazdany**, Astra Zeneca, 5, Pfizer, 2.

Abstract Number: 2833

Shared Decision Making in Routine Clinical Practice: An Assessment of Audio-recorded Consultations with Rheumatoid Arthritis Patients

Elke Mathijssen,[1] Johanna Vriezekolk,[2] and Bart van den Bemt[2], [1]Sint Maartenskliniek, Ubbergen, Netherlands, [2]Sint Maartenskliniek, Nijmegen, Netherlands

Table 1. Characteristics of the clinician, patient, and consultation

Clinician (N = 22)	
Rheumatology center, N (%)	
Reade	7 (31.8)
Sint Maartenskliniek	15 (68.2)
Sex, N (%)	
Male	16 (72.7)
Female	6 (27.3)
Age in years, mean (SD)	48 (8.3)
Profession, N (%)	
Rheumatologist	20 (90.9)
Physician assistant	2 (9.1)
Work experience in years, mean (SD)	15.7 (9.1)
Patient (N = 168)	
Rheumatology center, N (%)	
Reade	47 (28)
Sint Maartenskliniek	121 (72)
Sex, N (%)	
Male	52 (31)
Female	116 (69)
Age in years, mean (SD)	61.2 (11.4)
Educational level, N (%)	
Low	38 (23.2)
Medium	71 (43.3)
High	55 (33.5)
Disease duration in years, median (IQR)	9 (4-16.5)
Presence of comorbidities, N (%)	
No	39 (23.2)
Yes	129 (76.8)
Number of conventional DMARDs in use, N (%)	
1	136 (81)
2	26 (15.5)
3	6 (3.6)
Biologic DMARDs in use, N (%)	
No	116 (69.1)
Yes	52 (31)
Glucocorticoids in use, N (%)	
No	134 (79.8)
Yes	34 (20.2)

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Measures of Healthcare Quality II: Quality Improvement in Rheumatology – Still Getting Better

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: International guidelines for rheumatoid arthritis (RA) treatment emphasize that all treatment decisions should be made through a shared decision making (SDM) process between clinicians and patients (1,2). Observations of routine clinical practice are needed to obtain insight into the actual implementation of SDM. The aim of this study was to assess the level of SDM in RA treatment from an observer perspective and the association with characteristics of the clinician, patient, and consultation.

Methods: Audio-recordings of 168 unique consultations with RA patients were available. The level of SDM was assessed by scoring the audio-recorded consultations with the 5-item observation-based OPTION scale (3). The OPTION scores ranged from 0 to 100 with higher scores indicating higher levels of SDM. Descriptive statistics were computed. First, associations with characteristics of the clinician (age, sex), patient (age, sex, educational level, disease duration, comorbidities, medication beliefs, health status), and consultation (length, type of treatment decision) were assessed using univariate regression analyses. Thereafter, variables with a p-value < 0.2 were included in a multilevel model with random intercepts. Statistical significance was set at $P < 0.05$.

Results: Characteristics of the clinician, patient, and consultation are shown in table 1. The mean OPTION score was 28.3 ± 15.1. The multilevel model included 4 variables, namely the clinician's age, patient's age, consultation length, and type of treatment decision. The level of SDM was significantly associated with the consultation length (B=0.63, P=0.01), decision for stopping and/or starting medication (B=14.3, P=0.00), decision for adjusting doses (B=8.38, P=0.00), and decision for administering single dose glucocorticoids (B=15.03, P=0.00). No other significant associations were found.

Conclusion: A higher level of SDM is associated with a longer consultation length and the type of treatment decision. Overall, the level of SDM in RA treatment leaves room for improvement. However, an observer's assessment of the efforts of clinicians to involve patients in decision making may not be congruent with clinicians' and patients' perspectives of SDM.

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(2) Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol 2016;68:1-26.

(3) Elwyn G, Tsulukidze M, Edwards A, et al. Using a 'talk' model of shared decision making to propose an observation-based measure: Observer OPTION 5 Item. Patient Educ Couns 2013;93:265-71.

Disclosure: E. Mathijssen, None; **J. Vriezekolk**, None; **B. van den Bemt**, AbbVie, 2, 5, 8, Biogen, 8, BMS, 2, Novartis, 5, Pfizer, 2, 5, Sandoz, 8, UCB, 2, 5, 8.

Abstract Number: 2834

Assessing the Risk of Gout with Sodium Glucose Co-Transporter-2 Inhibitors: A Population-Based Cohort Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Metabolic & Crystal Arthropathies II: Genetics & Physiology

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Hyperuricemia is common in patients with type 2 diabetes mellitus and is associated with an increased risk of gout. Sodium-glucose cotransporter 2 (SGLT2) inhibitors, the newest class of medications for adults with diabetes mellitus, promote glycosuria and also lower serum uric acid levels through urinary excretion. The objective of our study was to assess the risk of gout among adults prescribed an SGLT2 inhibitor versus a glucagon-like peptide-1 receptor (GLP1) agonist.

Methods: We conducted a population-based new-user cohort study from March 2013 to December 2017 using claims data from a US nationwide commercial insurance database (IBM MarketScan). Patients with type 2 diabetes mellitus newly prescribed an SGLT2 inhibitor were 1:1 propensity score-matched to patients newly prescribed a GLP1 agonist. Patients were excluded if they had a history of gout or had received gout-specific treatment previously. The primary outcome was new diagnosis of gout based on an inpatient diagnosis of gout or the combination of an outpatient diagnosis and use of a gout-related medication within 14 days thereafter. The rate of heart failure hospitalization (positive control based on the known effect of SGLT2 inhibitor on reducing heart failure) and cellulitis (negative control) were also assessed. Cox proportional hazards regression was used to estimate hazard ratios (HR) of the primary outcome and 95% confidence intervals (CI).

Results: We identified 295,907 adults with type 2 diabetes mellitus who were newly prescribed an SGLT2 inhibitor or a GLP1 agonist. After 1:1 propensity score matching, we identified 111,419 pairs of patients prescribed an SGLT2 inhibitor or GLP1 agonist. The mean age was 54 years, 52% were female, and 26% were prescribed insulin at base-

Table 1. Baseline characteristics before and after matching

	After matching		
	SGLT2i	GLP1	SD
	N = 111419	N = 111419	
Female sex	57,953 (52.0%)	57,580 (51.7%)	0.007
Mean age (sdev)	54.2 (9.9)	54.2 (10.1)	0.002
Diabetic retinopathy	5,067 (4.5%)	5,066 (4.5%)	0
Diabetic neuropathy	12,939 (11.6%)	12,904 (11.6%)	0.001
Diabetic nephropathy	5,796 (5.2%)	5,853 (5.3%)	0.002
Cerebral vascular disease	1,341 (1.2%)	1,367 (1.2%)	0.002
Coronary artery disease	10,388 (9.3%)	10,416 (9.3%)	0.001
Hypertension	75,811 (68.0%)	75,893 (68.1%)	0.002
Dyslipidemia	74,726 (67.1%)	74,828 (67.2%)	0.002
Chronic kidney disease	3,552 (3.2%)	3,701 (3.3%)	0.008
Metformin	71,198 (63.9%)	70,638 (63.4%)	0.01
Insulin	28,638 (25.7%)	28,774 (25.8%)	0.003
Diuretic	19,320 (17.3%)	19,448 (17.5%)	0.003
Oral steroids	11,324 (10.2%)	11,310 (10.2%)	0
Anti-inflammatory drugs	21,487 (19.3%)	21,544 (19.3%)	0.001

Legend: GLP1 - glucagon like peptide-1 analogue, SGLT2i - sodium glucose co-transporter 2 inhibitor, sdev = standard deviation, SD = standardized difference, values below 0.1 indicate adequate balance. Anti-inflammatory drugs include NSAIDS and COXIBs.

Table 2. Rate of gout after use of SGLT2 inhibitor versus GLP1

	SGLT2i	GLP1
	N = 111,419	N = 111,419
Number of person-years	91,231	79,200
Number of events	448	640
Rate per 1,000 person-years	4.91	8.08
Hazard ratio (95% CI)	0.61 (0.54, 0.69)	Ref.
Legend: GLP1 - glucagon like peptide-1 analogue, SGLT2i - sodium glucose co-transporter 2 inhibitor.		

line (Table 1). The incidence rate of gout was lower for patients prescribed an SGLT2 inhibitor (4.9 events per 1,000 person-years) compared to those prescribed a GLP1-agonist (8.1 events per 1,000 person-years), with a HR of 0.61 (95%CI 0.54-0.69) over a median follow-up of 177 days. As anticipated, SGLT2 inhibitor initiators had a lower rate of heart failure (HR 0.63, 95%CI 0.51-0.78) and a similar rate of cellulitis (HR 1.05, 95%CI 1.00-1.11) compared to patients prescribed a GLP1 agonist.

Conclusion: Adults with type 2 diabetes prescribed an SGLT2 inhibitor had a lower rate of gout compared to those prescribed a GLP1 agonist. SGLT2 inhibitors may reduce the risk of developing gout among adults with type 2 diabetes mellitus, though future studies are necessary to confirm this observation.

Disclosure: M. Fralick, None; **S. Chen**, None; **E. Patorno**, Dr. Patorno reports grants from the National Institute on Aging, GlaxoSmithKline, and Boehringer Ingelheim outside the submitted work., 2; **S. Kim**, AbbVie, 2, AstraZeneca, 2, Bristol-Myers Squibb, 2, Merck, 2, Pfizer, 2, research grants to Brigham and Women's Hospital from Pfizer, AbbVie, Bristol-Myers Squibb, and Roche for unrelated topics, 2, Roche, 2, Roche/Genentech, 2.

Abstract Number: 2835

A Burden of Missense Genetic Variants in Urate Secretory Genes Is Associated with Inadequate Response to Allopurinol in People with Gout

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Metabolic & Crystal Arthropathies II: Genetics & Physiology
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Current understanding of why the urate lowering effect of allopurinol varies among individuals with gout is limited. The rs2231142 (Q141K) variant of *ABCG2* is associated with inadequate response to allopurinol. The goal of this research was to identify variations in genes grouped by function and how they affect allopurinol response.

Methods: The exomes of 77 people with gout recruited in New Zealand were sequenced. Gout was defined by American Rheumatism Association classification criteria. Thirty-six participants had a good response to allopurinol, defined as serum urate < 360μmol/L (6mg/dL) with allopurinol dose ≤300mg/day. Forty-one participants had an inadequate

Table 1.- Total counts of variants (1 or 2 copies of a variant in an individual was given a score of 1) clustered by function, in good and inadequate responders to allopurinol

Functional cluster	Good responders n (rate)	Inadequate responders n (rate)	Ratio inadequate/good responder	p value
Number of participants	36	41		
Secretory transporter (including Q141K)	**48 (1.33)**	**105 (2.56)**	**1.92**	**1.37×10^{-4}**
Secretory transporter (excluding Q141K)	**38 (0.78)**	**71 (1.73)**	**1.64**	**1.28×10^{-2}**
Reuptake transporter	**32 (0.89)**	**41 (1.00)**	**1.13**	**0.62**
Allopurinol to oxypurinol metabolism	**56 (1.56)**	**53 (1.29)**	**0.83**	**0.33**

Secretory transporter genes: *ABCC4, ABCC5, ABCG2, SLC17A1, SLC17A3, SLC22A6, SLC22A8*

response, defined as serum urate ≥360μmol/L with allopurinol dose >300mg/day. Participants with a plasma oxypurinol level < 20μmol/l were excluded due to potential non-adherence to allopurinol treatment. Variants (missense and nonsense) were grouped by the function of candidate causal genes– secretory urate transporters (*ABCC4, ABCC5, ABCG2, SLC17A1, SLC17A3, SLC22A6, SLC22A8*), reuptake urate transporters (*SLC22A12, SLC2A9, SLC22A11*) and genes involved in conversion of allopurinol to oxypurinol (*AOX1, MOCOS, XDH*). The rate of variants within a functional group was compared between good and inadequate responder subsets by Poisson approximation.

Results: A higher rate of variants in secretory urate transporter genes was observed in inadequate responders (105 variants in 41 participants) compared with good responders (48 variants in 36 participants, $p=1.37 \times 10^{-4}$, Table 1). This difference remained significant when the *ABCG2* Q141K variant was excluded from analysis (71 variants in 41 inadequate responders versus 38 variants in 36 good responders, p=0.013). No difference was observed in the rate of variants in urate reuptake transporter genes (41 variants in 41 inadequate responders versus 32 variants in 36 good responders, p=0.62) or allopurinol to oxypurinol metabolism (53 variants in 41 inadequate responders versus 56 variants in 36 good responders, p=0.33).

Conclusion: A burden of variants in secretory transporters of urate is associated with inadequate response to allopurinol. There was no evidence that genetic variants relating to reuptake-transport and allopurinol to oxypurinol conversion were associated with inadequate response.

Disclosure: N. Fanning, None; **R. Topless**, None; **C. Frampton**, None; **M. Cadzow**, None; **M. Wallace**, None; **N. Dalbeth**, Abbvie, 5, 8, 9, Amgen, 2, AMGEN, 2, AstraZeneca, 2, 5, 8, 9, Dyve, 5, 8, 9, Dyve BioSciences, 5, Hengrui, 5, 8, 9, Horiaon, 5, 8, Horizon, 5, 8, 9, Janssen, 5, 8, 9, Kowa, 5, 8, 9, Pfizer, 5, 8, 9; **T. Merriman**, Ardea Biosciences, 2, 5, AstraZeneca, 2, 5, Ironwood Pharmaceuticals, 2; **L. Stamp**, None.

Abstract Number: 2836

Do Serum Urate-associated Genetic Variants Differentially Contribute to Gout Risk According to Body Mass Index? Analysis of the UK Biobank

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SESSION INFORMATION

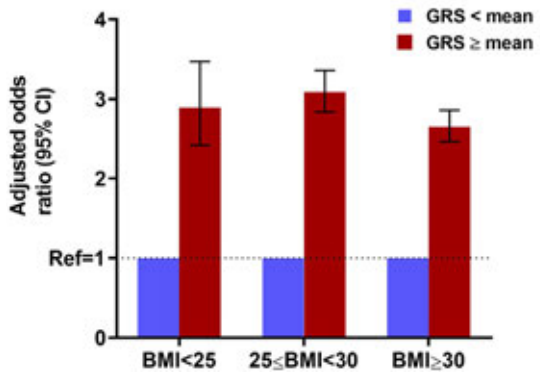
Session Date: Tuesday, November 12, 2019

Session Title: Metabolic & Crystal Arthropathies II: Genetics & Physiology

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Figure: Association between genetic risk score (GRS) and gout for each body mass index (BMI) category. Data were adjusted by age, sex, diuretic use, renal failure, diabetes mellitus, hypertension, hypercholesterolemia, alcohol intake and smoking. Adjusted odds ratio (95% CI) are shown.



Background/Purpose: Both serum urate-associated genetic variants and body mass index (BMI) are associated with gout risk. The aim of this study was to systematically examine whether serum urate-associated genetic variants differ in their influence on gout risk according to BMI, and to test for interactions between these genetic variants and BMI.

Methods: This research was conducted using the UK Biobank Resource. Participants of European ethnicity, aged 40-69 years, and with genome-wide genotypes were included. Gout was defined using a validated definition (self-report of gout or urate-lowering therapy use). Medication use and co-morbidity data were collected via self-report. Participants were divided into three BMI groups (BMI < 25 kg/m^2 [low/normal], 25 kg/m^2 ≤ BMI < 30 kg/m^2 [overweight], and BMI ≥ 30 kg/m^2 [obese]). The 30 serum urate-associated SNPs reported by Kottgen et al. (Nature Genetics 2013) in the large (>140,000 European participants) Global Urate Genetics Consortium GWAS were tested for their association with gout according to BMI group. A weighted genetic risk score (GRS) for gout risk was calculated to model the cumulative effects for the 30 variants. Gene-BMI interactions for gout association were tested using a genetic risk score (GRS) and individual SNPs by logistic regression, adjusting for age, sex, diuretic use, renal failure, diabetes mellitus, hypertension, hypercholesterolemia, alcohol intake and smoking.

Results: Data were available for 358,728 individuals, including 7,311 gout cases (2.0%). Gout was present in 634 (0.5%) individuals in the low/normal BMI group, 3100 (2.0%) in the overweight BMI group, and 3577 (4.3%) in the obese BMI group. Mean GRS was higher in those with gout compared to those without gout in the low/normal BMI group (mean [SD] 1.82 [0.29] vs 1.65 [0.27], P = 2.45×10^{-60}), overweight BMI group (mean [SD] 1.83 [0.27] vs 1.65 [0.27], P < 1×10^{-300}), and obese BMI group (mean [SD] 1.80 [0.27] vs 1.64 [0.27], P = 6.43×10^{-261}). Compared with a lower GRS (< mean), a higher GRS (≥ mean) was positively associated with gout in all BMI groups (Figure). A GRS-BMI interaction was observed, due to a mildly attenuated effect of a higher GRS on gout risk in the obese BMI group compared to the overweight BMI group (interaction P = 0.046). There was no GRS-BMI interaction for comparisons between the low/normal and overweight BMI groups, nor between the low/normal and obese BMI groups. No individual SNP-BMI interactions for gout were observed.

Conclusion: In individuals of European ancestry, the association of genetic factors is mildly attenuated in individuals with obesity compared to overweight. However, even for those with obesity, genetic variants have a strong effect on gout risk.

Disclosure: V. Tai, None; **R. Narang**, None; **G. Gamble**, None; **L. Stamp**, None; **T. Merriman**, Ardea Biosciences, 2, 5, AstraZeneca, 2, 5, Ironwood Pharmaceuticals, 2; **N. Dalbeth**, Abbvie, 5, 8, 9, Amgen, 2, AMGEN, 2, AstraZeneca, 2, 5, 8, 9, Dyve, 5, 8, 9, Dyve BioSciences, 5, Hengrui, 5, 8, 9, Horiaon, 5, 8, Horizon, 5, 8, 9, Janssen, 5, 8, 9, Kowa, 5, 8, 9, Pfizer, 5, 8, 9.

Abstract Number: 2837

Asymptomatic Monosodium Urate Crystal Deposition Associates with Increased Expression of Pro-Inflammatory Genes

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Metabolic & Crystal Arthropathies II: Genetics & Physiology

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Session Time: 4:30PM–6:00PM

Background/Purpose: Persistent hyperuricaemia is a prerequisite for gout. However, only 10% of people with hyperuricaemia develop symptomatic gout, whereas 25-35% have asymptomatic monosodium urate (MSU) crystal deposits. Whether these asymptomatic deposits are truly inert, or exert a sub-clinical pro-inflammatory effect is unknown. Since the immune response in gout is mediated primarily by the NLRP3 inflammasome, we hypothesized that the presence of MSU crystals in people with hyperuricaemia but no previous gout flares will initiate changes in the expression of inflammasome-associated genes.

Methods: Individuals recruited into the study were screened for serum urate (SU) levels and presence of MSU crystals within joints by ultrasonography. They were divided into 3 groups: (a) normal SU (< 360μmol/L) without MSU deposits; (b) high SU (>360μmol/L) without MSU deposits; and (c) high SU with MSU deposits. Peripheral blood was collected in PAXgene blood RNA tubes and total RNA was extracted according to the manufacturer's protocol. Quan-

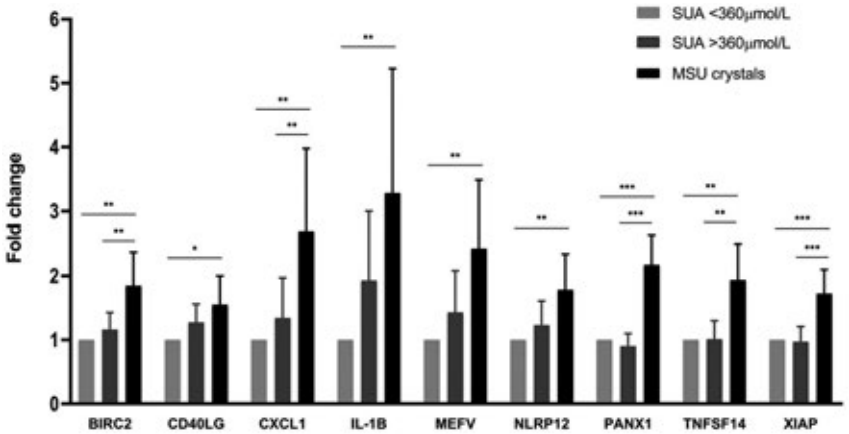

Figure 1. Significant fold changes relative to the normouricaemic group. Relative mRNA levels were evaluated by quantitative RT-PCR. The expression was normalised to RPLP0 gene and compared among groups using the Kruskal-Wallis H test. FDR 5% was used to correct for multiple testing. Note there was not a significant difference between normal SU and high SU without crystal deposits in all genes. *p=0.01, **p=0.001, ***p<0.0001.

titative RT-PCR was used to analyse the expression of 86 inflammasome and toll-like receptors (TLRs)-associated genes using a customised QIAGEN RT^2 Profiler Array. Data were normalised to RPLP0, and the $2^{-\Delta\Delta CT}$ method was used to calculate fold changes. Differences in relative expression among groups were evaluated using the Kruskal-Wallis H test. P values were corrected for multiple testing using a false discovery rate of 5%. Genes were clustered into four groups, specifically NLRP3 inflammasome-assembly mechanisms, TLRs, NLRP3 inflammasome-effector mechanisms, and inflammasome down-regulators, to evaluate their variation across normouricaemia, hyperuricaemia, and hyperuricaemia with MSU crystal deposits. The models were evaluated using linear regression.

Results: After RNA extraction and cDNA synthesis, 92 samples passed the quality control parameters and underwent the expression profiling. There were 31 participants in the normouricaemic group, 44 in the hyperuricaemia only group, and 17 in the hyperuricaemia with MSU crystal deposit group. Out of 86 genes, 13 showed a significant difference among groups (adjusted p value < 0.05). However, only BIRC2, CD40LG, CXCL1, IL-1β, MEFV, NLRP12, PANX1, TNFSF14 and XIAP had a large upregulation (fold change >1.5) in at least one of the high SU groups, compared to the normal SU group (Figure 1). IL-1β had the largest fold changes in both high SU without MSU crystals and high SU with MSU crystals (1.9 and 3.3 respectively). Moreover, from the four gene-groups, the TLRs gene cluster showed the highest R^2 (0.458), followed by the NLRP3 inflammasome-effector mechanism (R^2=0.371), the R^2 for inflammasome-assembly mechanisms and inflammasome negative regulators were 0.244 and 0.233 respectively.

Conclusion: The differences in the expression of immune-associated genes observed in this study suggest that initial MSU crystal deposition within joints, although asymptomatic, initiates the activation of pro-inflammatory mechanisms. These results only reflect systemic responses on gene-expression, and cytokine assay is underway. Further studies are needed to validate these results in synovial fluid samples.

Disclosure: G. Sandoval-Plata, None; **K. Morgan**, None; **T. Guetta-Baranes**, None; **A. Valdes**, None; **M. Doherty**, None; **A. Abhishek**, AstraZeneca, 2, Ironwood Pharmaceuticals, 2.

Abstract Number: 2838

The First Phase 2a Proof-of-Concept Study of a Selective NLRP3 Inflammasome Inhibitor, Dapansutrile™ (OLT1177™), in Acute Gout

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SESSION INFORMATION

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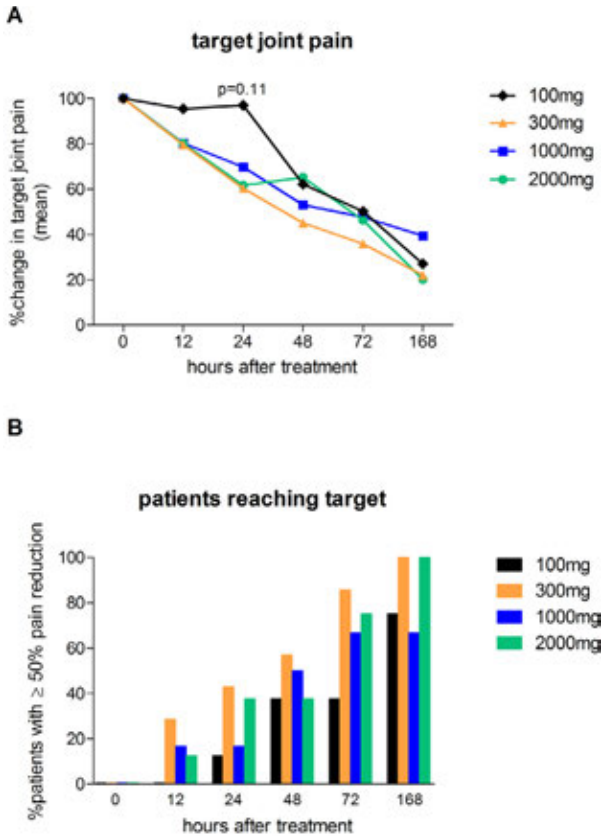
Session Title: Metabolic & Crystal Arthropathies II: Genetics & Physiology

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Acute gout is a severe debilitating type of arthritis that is treated in the acute phase with potent anti-inflammatory drugs. To date, prednisolone, colchicine and/or non-steroidal anti-inflammatory drugs are the standard of care despite serious side effects of chronic use, especially in the elderly population. In addition, interleukin (IL)-1 biologics (e.g., canakinumab/rilonacept/anakinra) have proven efficacy in RCTs, however, these biologics have not been broadly adopted due to barriers such as the requirement of parenteral administration, cost and risk of



A: Percent change in pain scores up to 1 week of Dapansutrile treatment; Patients scored target joint pain scored on a 0-100mm VAS scale. Data presented as mean of the percent change in target joint pain (baseline was set at 100%). p=0.11 for Mann-Whitney test between cohorts of 100mg and 2000mg at t=24h. B: % patients who reached the primary outcome target of ≥50% pain reduction during the first week of Dapansutrile treatment.

infection. Therefore, there is an unmet need for a safe, oral, cost effective IL-1 inhibitor targeting the NLRP3 inflammasome pathway.

Dapansutrile™ (OLT1177™) was shown to inhibit the NLRP3 inflammasome and inhibit joint inflammation in murine models of acute arthritis. Dapansutrile's™ Phase 1 dose escalation clinical trial demonstrated safety at doses up to 1000 mg/day for 8 days.

Methods: A Phase 2a, dose ranging, proof-of-concept trial was conducted to demonstrate safety/tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and the clinical effectiveness of Dapansutrile™ in treating the clinical signs and symptoms of acute gout over an 8-day treatment period. Four cohorts of 8 patients per cohort were included at doses of 100mg, 300mg, 1000mg or 2000mg daily (of which 29 were analyzed per protocol). Clinical effect was targeted to be greater than 50% pain reduction from baseline at approximately 72 hours after the first dose. VAS pain, general disability and walking disability scores were measured by daily diary and blood sampling was conducted on study days 0 (baseline), 3, 7 and 14 to assess PK and PD (including hsCRP, SAA and plasma cytokine levels). Safety was measured over the duration of the study with clinic visits on study days 0 (baseline), 3, 7, 14 and a follow-up telephonic visit on day 35.

Results: The ≥50% target joint pain reduction on a 0-100mm VAS scale at day 3 was met in the 300, 1000 and 2000mg Dapansutrile™ cohorts; contrary the 100mg dose appeared inadequate. Investigator-assessed joint tenderness and swelling at day 3 showed a dose-dependent response. Treatment responses at day 7 were similar for all cohorts. As markers for systemic inflammation, hsCRP and SAA demonstrated a dose-dependent reduction in

cohorts taking 2000mg, 1000mg and 300mg daily, but demonstrate no reduction in the cohort taking 100mg daily. Oral intake of Dapansutrile™ resulted in adequate plasma concentrations for NLRP3 inflammasome inhibition, there were no metabolic, physiological or haematological changes and all doses were well tolerated.

Conclusion: Dapansutrile™ was shown to have a significant positive clinical anti-inflammatory effect and clean safety profile in the treatment of monoarticular gout attacks. The oral NLRP3 inhibitor showed a broad therapeutic range dosed at a daily 300-1000-2000mg and holds promise for further clinical development in acute gout.

Disclosure: T. Jansen, AbbVie, Celgene Corporation, 5, Grunenthal, Sobi, 8, Olatec, Grunenthal, 2; **V. Kluck**, None; **M. Janssen**, None; **A. Comarniceanu**, None; **M. Efdé**, None; **C. Scribner**, Olatec Therapeutics LLC, 3; **D. Skouras**, Olatec Therapeutics LLC; **C. Dinarello**, Olatec Therapeutics LLC; **L. Joosten**, Olatec Therapeutics LLC.

Abstract Number: 2839

Association of a Gout Polygenic Risk Score with Disease Severity Phenotypes Amongst Caucasian Gout Patients in Three Independent Cohorts

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SESSION INFORMATION
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Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: This study aimed to determine whether a polygenic risk score (PRS) based on gout-associated genetic variants is associated with gout disease severity phenotypes such as age at onset, presence of tophi and flare frequency.

Methods: A genome wide association study (GWAS) for gout was performed on all genotyped SNPs (single nucleotide polymorphisms) in approximately 500,000 individuals from the UK Biobank cohort. All genome-wide significant SNPs ($P < 5 \times 10^{-8}$; total 129) were extracted and manually grouped into loci if they were within 500 kb of eachother.

This resulted in a total of 12 loci, from which the most significant SNP of each locus was selected for analysis. Three cohorts of gout patients were involved in this analysis: the New Zealand Gout Study Caucasian cohort (NZ Gout; 782 males, 164 females), the Ardea cohort (1121 males, 57 females) and the EuroGout cohort (1114 males, 143 females). A PRS was calculated for each individual based on their genotypes at the 12 SNPs of interest and weighted by the effect size (odds ratio) of each SNP as determined by GWAS. The PRS was modelled against each of the three phenotypes of interest using linear and logistic models, adjusted by age at collection, sex and BMI (for all three cohorts) and the top 10 principle components (for the NZ Gout cohort). The adjusted models were meta-analysed.

Results: The PRS was distributed similarly for all three cohorts and ranged from 4.73 to 28.49. It showed a highly significant positive association with gout status in the NZ Gout study cohort (OR = 1.21 (95%-CI: 1.16 to 1.26), P = < 2E-16; performed using matched non-gout controls from the NZ population). Meta-analysis of the three cohorts identified a statistically significant negative association between the PRS and the age at onset phenotype with each PRS unit increase associated with a 0.43 year decrease in age at onset (95%-CI: -0.61 to -0.25, P < 0.0001). Presence of tophi was also found to be statistically significantly associated with increasing PRS in the three cohorts (OR = 1.059 (95%-CI: 1.03 to 1.09), P < 0.0001). However, when adjusting for disease duration, the strength of the association was reduced (OR = 1.031 (95%CI: 1.00 to 1.062), P = 0.046). The flare frequency phenotype did not show significant association with the PRS in any cohort, or under meta-analysis (Beta = 0.022 (95%-CI: -0.063 to 0.107), P = 0.61).

Conclusion: A polygenic risk score may be useful for predicting the severity of gout for severity phenotypes that are non-confounded, such as age at onset. Earlier age at onset results in a longer disease duration, which in turn may be causally associated with increased risk of tophi, and those with tophi may experience significantly more gout flares per year. As the PRS can aid in prediction of age of onset, it may be possible to effectively predict and manage those that are more likely to experience severe gout. As GWAS become larger, more gout associated loci will likely be identified, thus enabling improvement of the current PRS and likely improving prediction for severe gout phenotypes.

Disclosure: N. Sumpter, None; **T. Merriman**, Ardea Biosciences, 2, 5, AstraZeneca, 2, 5, Ironwood Pharmaceuticals, 2; **R. Reynolds**, None; **A. Abhishek**, None; **M. Andrés**, None; **N. Dalbeth**, Abbvie, 5, 8, 9, Amgen, 2, AMGEN, 2, AstraZeneca, 2, 5, 8, 9, Dyve, 5, 8, 9, Dyve BioSciences, 5, Hengrui, 5, 8, 9, Horiaon, 5, 8, Horizon, 5, 8, 9, Janssen, 5, 8, 9, Kowa, 5, 8, 9, Pfizer, 5, 8, 9; **M. Doherty**, None; **L. Jacobsson**, None; **M. Janssen**, None; **T. Jansen**, AbbVie, Celgene Corporation, 5, Grunenthal, Sobi, 8, Olatec, Grunenthal, 2; **L. Joosten**, Olatec Therapeutics LLC; **M. Kapetanovic**, Abbvie, 5, Pfizer, 2; **F. Lioté**, None; **H. Matsuo**, None; **G. McCarthy**, None; **F. Perez-Ruiz**, None; **P. Riches**, None; **P. Richette**, Janssen, 8; **E. Roddy**, None; **B. Stiburkova**, None; **A. So**, None; **L. Stamp**, None; **A. Tausche**, None; **R. Torres-Jimenez**, None; **T. Uhlig**, None.

Abstract Number: 2840

Reliability, Validity and Responsiveness of PROMIS PF-20 in Patients with Inflammatory Myopathy

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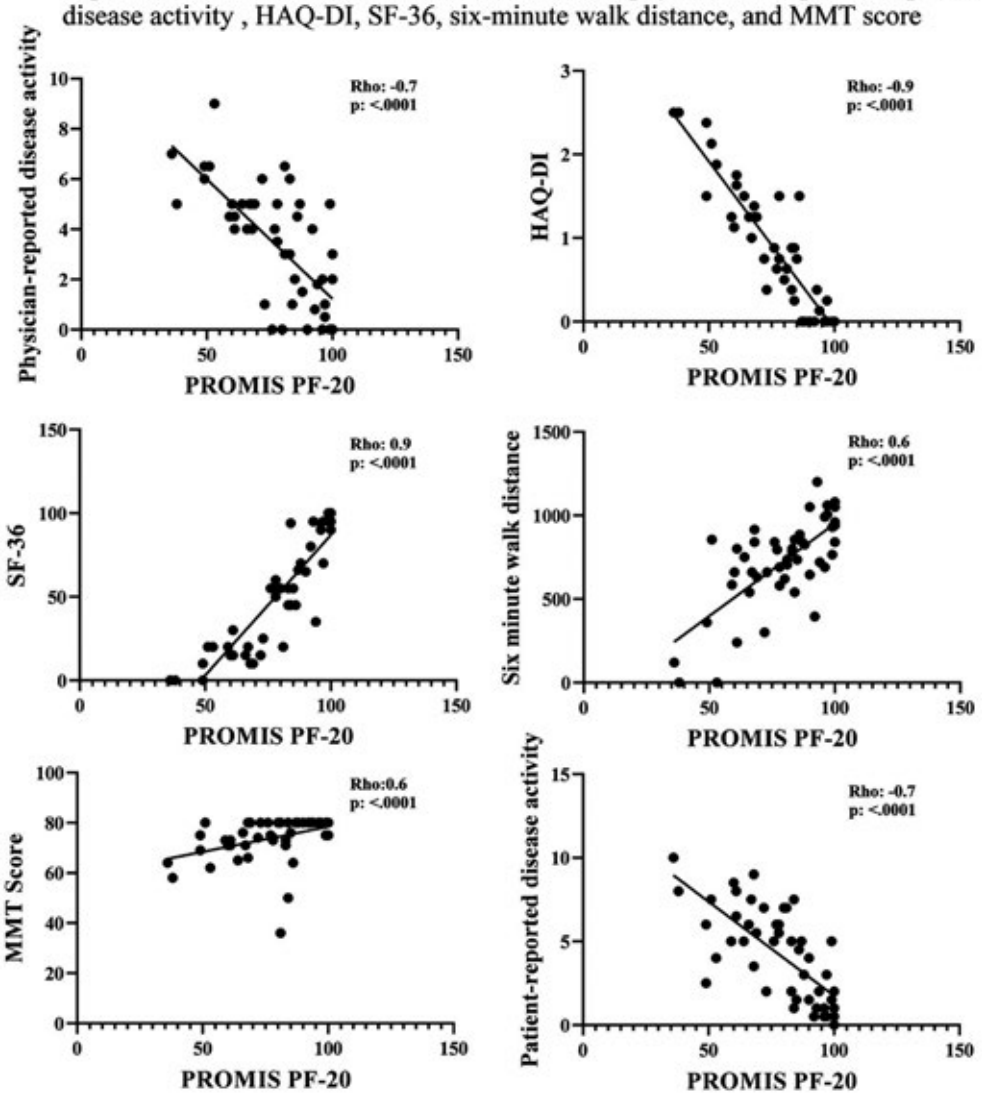
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Muscle Biology, Myositis & Myopathies II
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Figure. Correlations between PROMIS PF-20 and physician- and patient-reported disease activity , HAQ-DI, SF-36, six-minute walk distance, and MMT score



Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a group of rare, debilitating systemic diseases characterized by proximal muscle weakness, which limit activities of daily living and lower health-related quality of life. Patient's assessment of physical functional status is a core outcome measure in IIM contributing to treatment decisions and the FDA has strongly endorsed development and validation of patient-reported outcomes as critical measures in rheumatic diseases. Patient Reported Outcomes Measurement Information System (PROMIS) is a validated, patient-reported outcome measure developed by the NIH, but it has not been studied in adult IIM. Currently, the most commonly used PRO in IIM is Health Assessment Questionnaire (HAQ-DI), which has several limitations. PROMIS-physical function-20 (PF-20) offers several superior features over HAQ related to clarity of questions, improved items, computer adaptive options and allowing comparison across different disease states. In this study, we investigated reliability, validity and responsiveness of PROMIS PF-20 in patients with IIM compared to HAQ-DI by employing a longitudinal prospective study design.

Methods: Patients with IIM [dermatomyositis (DM), polymyositis (PM), necrotizing myopathy (NM) or anti-synthetase syndrome] completed PROMIS PF-20 as well as 6 myositis core set measures [manual muscle testing (MMT), physician global disease activity (MD-GDA), patient global disease activity (PT-GDA), extra-muscular global disease activity (EM-GDA), HAQ-DI and creatine kinase (CK)], SF-36 and 3 functional measures [six-minute walk (6MWD), timed

Table. Correlations of HAQ-DI and PROMIS with other outcome measures

Outcome measures	HAQ-DI		PROMIS	
	Rho	p value	Rho	p value
Cutaneous disease activity	0.02	0.8	-0.007	0.9
Pulmonary disease activity	-0.03	0.8	-0.05	0.7
Extramuscular global disease activity	0.26	0.06	-0.34	0.01
Muscle disease activity	0.75	<0.0001	-0.67	<0.0001
Physician-reported disease activity	0.70	<0.0001	-0.68	<0.0001
MMT score	-0.70	<0.0001	0.57	<0.0001
Patient-reported disease activity	0.67	<0.0001	-0.74	<0.0001
SF-36	-0.84	<0.0001	0.91	<0.0001
Sit-to-stand	-0.50	0.0003	0.47	0.0006
Timed-up and go	0.12	0.4	-0.23	0.1
Six-minute walk distance	-0.53	<0.0001	0.64	<0.0001
Creatine kinase level	0.08	0.6	-0.09	0.5
Total improvement score (6 mo)	-0.59	<0.0001	0.76	<0.0001

HAQ-DI: Health assessment questionnaire-disability index, MMT: Manual muscle testing, SF-36: Short-form 36

Table 2. n = number, GI = gastrointestinal, FMS = fibromyalgia syndrome, CK = creatine kinase, AST = aspartate aminotransferase, MMT8 = manual muscle testing 8, HAQ = health assessment questionnaire, VAS= visual analogue scale, PGA = patient global activity scale, MDGA = physician global activity, IGA = investigators global assessment of skin involvement, SSI = symptom severity index, WPI = widespread pain index.

up-and-go (TUG) and sit-to-stand tests (STS)] at baseline, 3 and 6 months. PROMIS PF-20 consists of 20 items. Each item is scored on a 5-point rating scale, with higher scores indicating better functioning (0-100). HAQ-DI consists of 20 items. Each item is scored on a 4-point scale with higher scores indicating worse functioning (0-3). Physician-reported change and total improvement score (TIS) using 2016 ACR/EULAR myositis response criteria were obtained at each visit as measures of change.

Results: Fifty patients [mean age, 53.6 (±14.6); 60% females] were studied; 11 PM, 28 DM, 7 NM and 4 with anti-synthetase syndrome. PROMIS PF-20 showed strong test-retest reliability when repeated in 1 month in stable patients (Rho:0.9, p< .0001). PROMIS PF-20 at baseline correlated strongly with MD-GDA, PT-GDA, MMT, HAQ-DI, SF-36, and 6MWD and moderately with STS and weakly with EM-GDA (Figure). There was no correlation with cutaneous and pulmonary disease activity, TUG, and CK levels. Longitudinal change in PROMIS PF-20 strongly correlated with TIS (Rho:-0.8, p< .0001) at 6 months and showed significant differences between physician-reported change demonstrating excellent responsiveness (p< .0001). HAQ and PROMIS-20 showed similar correlations with other outcome measures, however changes in PROMIS-20 over 6 months had stronger correlations with TIS which may indicate better responsiveness (Table).

Conclusion: PROMIS PF-20 demonstrates good test-retest reliability, construct validity and responsiveness in a large cohort of patients with IIM and could replace the HAQ-DI as a core-set measure in myositis.

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Abstract Number: 2841

A Double-Blind, Placebo-Controlled, Phase 2 Trial of a Novel Toll-Like Receptor 7/8/9 Antagonist (IMO-8400) in Dermatomyositis

Yoo Jung Kim,[1] Elena Schiopu,[2] Katalin Dankó,[3] Tahseen Mozaffar,[4] Srinivas Chunduru,[5] Kirstin Lees,[6] Namita Goyal,[4] David Fiorentino,[7] and Kavita Sarin[7], [1]Stanford University School of Medicine, Redwood City, CA, [2]Department of Rheumatology, University of Michigan, Ann Arbor, [3]Department of Clinical Immunology, Medical Faculty, University of Debrecen, Debrecen, Hungary, [4]Department of Neurology, University of California Irvine, Irvine, CA, [5]Idera Pharmaceuticals, Inc., Cambridge, MA, [6]Idera Pharmaceuticals, Inc., Cambridge, [7]Department of Dermatology, Stanford University School of Medicine, Redwood City, CA

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Muscle Biology, Myositis & Myopathies II
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Dermatomyositis (DM) is a rare inflammatory disease of skin and muscle associated with characteristic skin findings, muscle weakness, interstitial lung disease, pruritus, and malignancies. Increased interferon (IFN) signaling is a prominent feature of DM, but the mechanisms leading to IFN production in DM are not understood. As toll-like receptor (TLR) 7/8/9 activation can lead to type I IFN production, TLR7/8/9 antagonism may provide therapeutic benefit in DM.

Methods: A double-blind, randomized, placebo-controlled, 24-week trial of IMO-8400 (a novel investigational oligonucleotide TLR7/8/9 antagonist [Idera Pharmaceuticals, Inc.]) was conducted with 30 eligible participants with definite or probable DM based on the criteria of Bohan and Peter. Participants were randomized to treatment with IMO-8400 0.6 mg/kg, IMO-8400 1.8 mg/kg, or placebo. The primary endpoint was the change in the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score after 24 weeks of treatment. Exploratory analysis included type I IFN signaling as measured by a 10-gene expression score and patient-reported 5-D Itch Scale, a validated inventory for pruritus. Blood and skin samples were obtained at baseline and end of treatment to measure changes in type I IFN signaling.

Results: CDASI activity scores decreased in all trial arms by the end-of-trial visit, per repeated measures mixed model analysis: -9.3 in 0.6 mg/kg, -8.8 in 1.8 mg/kg, and -7.3 in placebo. We observed no change in skin and blood type I IFN signature scores or CDASI activity scores across treatment arms. We found an association between CDASI and skin IFN signature scores ($\beta = 12.9$, $P = 0.0002$), a moderate association between 5-D Itch Scale and skin IFN signature scores ($Rho = 0.65$, $P < 0.0001$), a lack of association between 5-D Itch Scale and blood IFN signature scores ($Rho = 0.22$, $P = 0.24$), and a positive correlated trend that did not reach significance between CDASI and 5-D Itch Scale scores. 5 patients experienced treatment-emergent adverse effects prompting discontinuation: 3 in low-dose (abdominal discomfort/flu, anxiety, urticaria), 1 in high-dose (thrombocytopenia), and 1 in placebo (muscle weakness).

Conclusion: IMO-8400 did not reach clinical efficacy in reducing cutaneous DM disease activity nor in decreasing the type I IFN signature in skin or blood, suggesting that TLR7/8/9 signaling may not play a causal role in IFN dysregulation in DM. Furthermore, our exploratory findings suggest that skin type I IFN signature scores provide a stronger indication of DM skin disease activity than blood type I IFN signature scores and that skin type I IFN signaling may be a pathway to target in improving pruritus symptoms in DM patients.

Disclosure: Y. Kim, None; **E. Schiopu**, None; **K. Dankó**, None; **T. Mozaffar**, aTyr, 2, 5, 9, Alnylam, 5, Alexion, 2, 5, 8, 9, Amicus, 2, 5, 9, Argenx, 2, 5, 9, Audentes, 5, 9, Sanofi-Genzyme, 2, 5, 8, 9, Sarepta, 5, Spark Therapeutics, 2, 5, 9, MT-Pharma, 5, 9, Ultragenyx, 5, 9, CSL Behring, 8, Grifols, 2, 8, Bristol-Myers-Squib, 2, Idera, 2, Ionis, 2, Momenta, 2, Ra Pharmaceuticals, 2, UCB Pharmaceuticals, 2, Valerion, 2; **S. Chunduru**, Idera Pharmaceuticals, 3, 4, 9; **K. Lees**, Idera Pharmaceuticals, 3; **N. Goyal**, None; **D. Fiorentino**, Janssen, 5, Pfizer, 2, 5, UCB Pharmaceuticals, 5; **K. Sarin**, None.

Abstract Number: 2842

Paraoxonase 1 Activity Is Abnormal in Patients with Idiopathic Inflammatory Myopathies and Associates with Poor Disease Control

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Muscle Biology, Myositis & Myopathies II

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Table 1. IIM compared to healthy controls

	IIM (N=169)	Controls (N=112)
Age, years, mean(SD)	50(15)	47(16)
Sex, Female (%)	129 (75)	100 (76)
Race, White (%)	129 (75)	63 (53)
Lipid panel, mg/dl, mean (SD)		
Total cholesterol	209(50)	199(43)
LDL-C	121(43)	115(35)
HDL-C	59(21)	62(19)
Triglyceride	165(116)*	114(66)
Body mass index, kg/m^2	28(6)	27(7)
Erythrocyte Sedimentation Rate, mm/hr	30(26)*	14(11)
hsCRP, mg/L	6.3(10.0)*	3.8(10.0)
PON1 activity, mmol/min/ml, mean (SD)	221.3(63.6)*	366.3(89.0)
IIM disease characteristics		
IIM type		
Dermatomyositis (%)	123(73)	
Polymyositis (%)	46(27)	
Disease duration, years	4.3(7.3)	
ILD, yes n(%)	59(35)	
Ab subtype, n(%)#		
Antisynthetase ab	21(12)	
MDA5 ab	9(5)	
SRP, HMGCR ab	13(9)	
P155/140	18(11)	
Mi2	6(4)	
MJ/NXP2	8(5)	
Other MSA/MAA	15(9)	
Non MSA/MAA ab	11(7)	
No ab	11(7)	
Physician global activity VAS (0-100)	40(19)	
CPK., U/L	619(1545)	

*p<0.05 on chi-square test for categorical variables and Wilcoxon rank-sum test for continuous variables. ESR, erythrocyte sedimentation rate; hsCRP, high sensitivity C-Reactive Protein, CPK, creatine phosphokinase

Ab testing available in 112 subjects

Table 2. Univariate regression analysis of PON1 activity in IIM patients

Variable	IIM (N=169)	Category assessed (vs Referent group)	Regression coefficient (95%CI)	P
Age, yrs	50.5(40.3-61.4)		-0.41(-0.67, -0.16)	**0.002**
Sex, n(%) females	129(75)	Females	6.98(-1.61, 5.57)	0.11
Race, n(%) white	129(75)	White	3.34(-5.54, 12.22)	0.46
IIM type, n(%) DM	125(73)	DM	-1.45 (-9.92, 7.02)	0.73
Disease duration, yrs¶	1.21(0.24-5.23)	<1.21	0.07(-0.44, 0.59)	0.77
Ab subgroups, n§				
Antisynthetase ab	21(12)	Positive	-14.22(-25.45, -3.0)	**0.01**
MDA5 ab	9(5)	Positive	-9.88(-26.61, 6.85)	0.24
SRP or HMGCR ab	13(9)	Positive	-3.80(-17.05, 9.45)	0.57
P155/140	18(11)	Positive	4.93(-8.12, 17.98)	0.45
No ab	11(7)	No ab	1.35(-15.45, 18.14)	0.87
Other antibodies	ref		0	
Physician global Disease activity VAS, 0-10 cm	42(24-51)	>42	-2.96(-4.87, -1.05)	**0.003**
CPK, every 100 U/L	107(62-349)	>107	-0.36(-0.01, -0.1)	**0.006**
ESR, mm/hr	23(10-44)		-0.13(-0.27, 0.01)	0.07
hsCRP, mg/L	2(0.8-7.1)		-0.28(-0.65,0.09)	0.13
Medications, n(%)				
Methotrexate	44(25)	Using	1.32(-7.18, 9.83)	0.76
TNF inhibitor	5(3)	Using	2.41(-19.93, 24.74)	0.83
Leflunomide	4(2)	Using	5.99(-18.83, 30.84)	0.66
Azathioprine	24(15)	Using	1.82(-9.08, 12.73)	0.74
Mycophenolate	43(25)	Using	-0.66(-9.36, 8.04)	0.88
Rituximab	13(8)	Using	1.67(-12.49, 15.83)	0.82
Cyclophosphamide	9(5)	Using	0.43(-16.31, 17.17)	0.96
Prednisone	123(72)	Using	2.51(-5.71, 10.73)	0.55
Prednisone dose (mg/day)	10(0-25)	>10	1.30(-6.30, 8.89)	0.73
Statin	19(11)		-5.28(-17.48, 6.93)	0.39
Lipid panel, mg/dl				
Total cholesterol	203(174-239)		0.13(0.06-0.21)	**0.001**
LDL-C	118(94-148)		0.08(-0.011-0.172)	0.09
HDL-C	55(44-69)		0.21(0.03-0.38)	**0.02**
Triglyceride	133(92-193)		0.023(-0.01-0.06)	0.18
CV risk factors				
HTN, n(%)	45(26)		-0.25(-8.92-8.41)	0.95
Diabetes, n(%)	23(13)		-5.19(-16.37-6.00)	0.36
Family history‡	7(4)		7.25(-11.21-5.72)	0.44

Median (IQR) unless specified # avail in 161; ¶ avail in 171; ‡ avail in 168; § avail in 112

Background/Purpose: Inflammation and damage to the vascular endothelium are implicated in the pathogenesis of idiopathic inflammatory myopathies (IIM), particularly dermatomyositis. Paraoxonase 1 (PON1) is a high density lipoprotein (HDL)- associated enzyme, which normally protects the vascular endothelium from damage due to oxidized phospholipids, which accumulate under conditions of oxidative stress. The current work evaluates PON1 activity in IIM patients compared to healthy controls.

Table 3. Multivariate model for PON1 activity

Variables	Model 1 (Total population) (N=281)		Model 2 (IIM only) (N=169)		Model 3 (IIM only) (N=169)	
	β (95% CI)	P	β (95% CI)	P	β (95% CI)	P
IIM diagnosis (vs HC)	**-51.43(-60.93, -41.93)**	**<0.001**	-		-	
Physician global disease activity VAS (0-100mm)	-		**-0.25(-0.44,-0.05)**	**0.01**	-	
CPK (100 U/L)	-		-		**-0.27(-0.51,-0.03)**	**0.03**
Age, years	-0.22 (-0.47, 0.03)	0.08	**-0.51(-0.76,-0.26)**	**<0.001**	**-0.49 (-0.75, -0.24)**	**<0.001**
Gender, Female (vs Male)	**10.87 (2.33, 19.43)**	**0.01**	4.21(-3.92,12.33)	0.31	7.27(-1.30, 15.83)	0.09
Race, White	6.18 (-2.61, 14.97)	0.17	-1.26(-9.56, 7.05)	0.77	-2.78 (-11.58, 6.01)	0.53
ESR (mm/hr)	-0.09 (-0.27, 0.08)	0.27	-		-	
hsCRP (mg/L)	-0.25 (-0.69, 0.19)	0.27	-		-	
Triglyceride (mg/dL)	0.03 (-0.00, 0.07)	0.07	-		-	
HDL-C (mg/dL)	-		**0.20 (0.03, 0.37)**	**0.02**	**0.23 (0.06, 0.40)**	**0.01**
Antisynthetase ab, yes	-		-10.04 (-21.09, 1.01)	0.07	-10.31 (-21.52, 0.89)	0.07

Model 1 including IIM and HC (N=281), Model 2 including IIM only (N=169) with disease activity measured as VAS, Model 3 including IIM only with disease activity measured as CPK.
For Model 2, although Total cholesterol and HDL were both significant in univariate analysis, only HDL was included in the model as the two lipid variables were significantly correlated.

Methods: In a cross sectional analysis of 169 patients with IIM and 112 healthy controls we measured plasma PON1 activity using the arylesterase assay (Clin Chim Acta. 402(1-2):67-74, 2009). Lipoprotein cholesterol levels, inflammatory markers, and myositis autoantibodies(ab) were assessed by standard assays, and myositis disease activity was assessed using physician global 100 mm visual analogue scales (VAS) and CPK levels.

Results: Patients with IIM had significantly lower PON1 activity compared to healthy controls (Table 1). Univariate analysis of PON1 activity in IIM patients showed associations of lower PON1 activity with higher disease activity measured by VAS and CPK, as well as with the presence of antisynthetase antibodies (Table 2). PON1 activity remained strongly associated with IIM diagnosis and myositis disease activity measures after multivariate adjustment for demographic factors (age, gender, race) and factors that were significantly different in univariate analysis (Table 3).

Conclusion: In a large cross sectional cohort of IIM patients, plasma PON1 activity was significantly lower than healthy controls of similar demographics, and was associated with myositis disease activity. Low PON1 activity has been previously associated with increased vascular risk and may warrant further investigation for its role in perpetuation of vascular damage in IIM patients.

Disclosure: S. Bae, None; **I. Golub**, None; **J. Wang**, None; **A. Shahbazian**, None; **S. Reddy**, None; **C. Charles-Schoeman**, Abbvie, 2, AbbVie, 2, Amgen, 5, BMS, 2, Bristol Myers Squibb, 2, Gilead, 5, Octapharma, 2, 5, Pfizer, 2, 5, Regeneron, 5, Regeneron/Sanofi, 5, Sanofi, 5.

Abstract Number: 2843

Safety and Efficacy of Lenabasum at Week 68 in an Open-Label Extension of a Phase 2 Study of Lenabasum in Refractory Skin-Predominant Dermatomyositis (DM) Subjects

Victoria Werth,[1] David Pearson,[2] Joyce Okawa,[2] Rui Feng,[3] Josef Concha,[2] Basil Patel,[2] Emily Hejazi,[2] Scott Constantine,[4] Nancy Dgetluck,[4] and Barbara White[4], [1]Corporal Michael J. Crescenz VAMC, Philadelphia, PA, USA and Department of Dermatology, University of Pennsylvania, Philadelphia, PA, USA, Philadelphia, PA, [2]Philadelphia Veteran Affairs Medical Center, University of Pennsylvania, Philadelphia, PA, [3]University of Pennsylvania, Philadelphia, [4]Corbus Pharmaceuticals, Norwood, MA

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Muscle Biology, Myositis & Myopathies II

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Lenabasum is a rationally-designed preferential cannabinoid receptor type 2 agonist that activates resolution of innate immune responses to reduce tissue inflammation and fibrotic processes. Lenabasum had acceptable safety and tolerability and improved efficacy outcomes in the initial 16-week double-blinded, randomized, placebo-controlled Part A of Phase 2 trial JBT101-DM-001 (NCT02466243) in classic or amyopathic dermatomyositis (DM) subjects with refractory skin disease and minimal or no active muscle involvement at the time of enrollment.

Methods: To provide long-term safety and efficacy data in DM subjects in study JBT101-DM-001, subjects who completed Part A were eligible to receive oral lenabasum 20 mg BID in an open-label extension (OLE) of that study that assessed safety and efficacy at 4 weeks, then every 8 weeks.

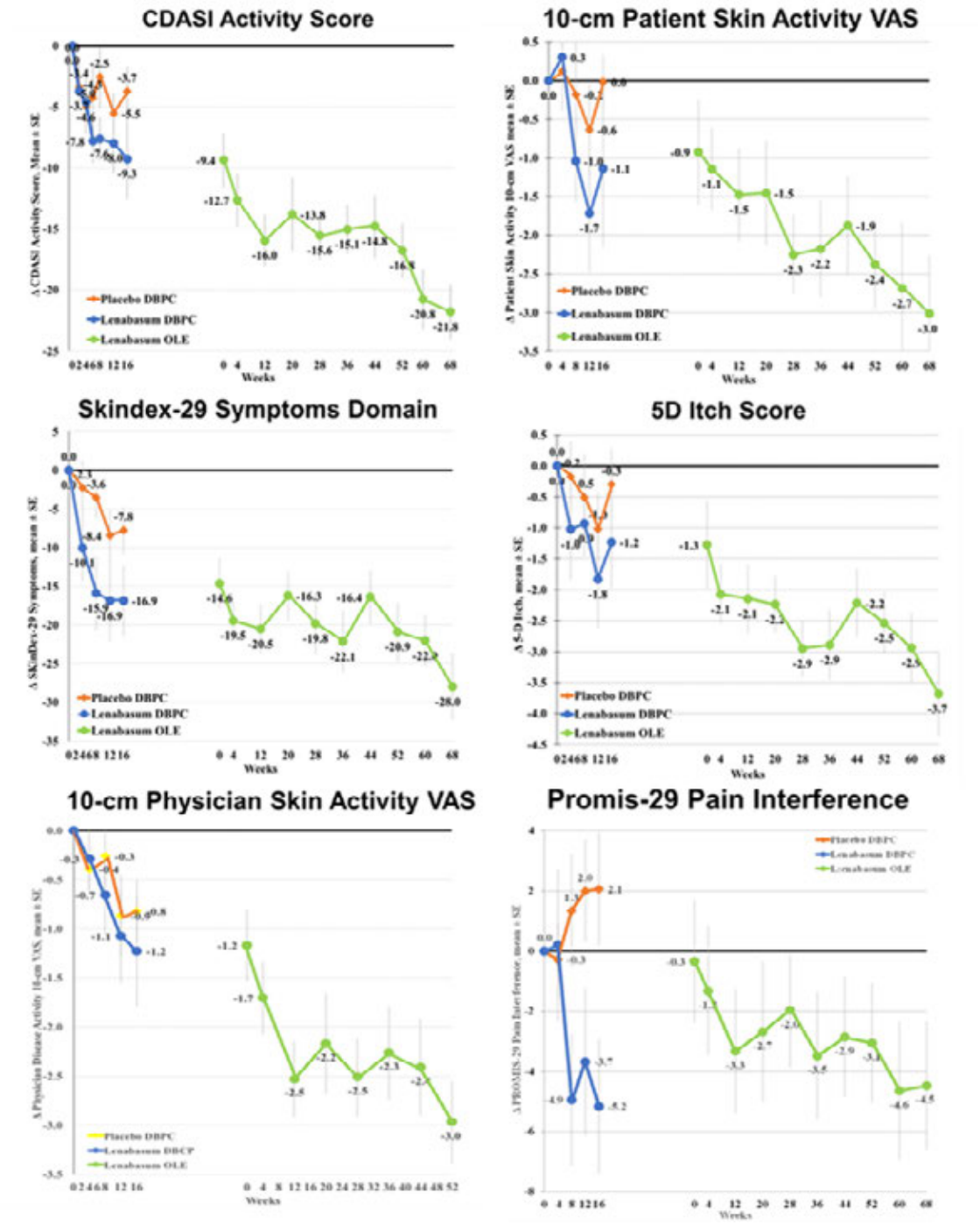
Results: 20/22 (91%) eligible subjects received lenabasum in the OLE. Seventeen (85%) subjects were on stable baseline immunosuppressive drugs. At the time of data cut-off, 18 (90%) subjects who enrolled in the OLE had entered the second year of the OLE, and all 18 had completed Week 68.

Twenty/20 (100%) of subjects experienced at least 1 AE, with 65 total AEs occurring among the subjects during the OLE to date. The majority of AEs were mild (n = 16, 80%), and only 1 subject had an AE probably or definitely-related to lenabasum (mild fatigue). Only 1 subject had a severe AE (fatigue) and that AE was considered unrelated to lenabasum. AEs occurring in 3 (15%) subjects were dermatomyositis worsening (2 mild, 1 moderate), dizziness (all mild), fatigue (2 mild, 1 severe), nasopharyngitis (all mild). AEs occurring in 2 (10%) subjects were headache, herpes zoster, nausea, sinusitis, upper respiratory tract infection, and urinary tract infection – all were mild except 1 AE of sinusitis was moderate. No serious AEs have been reported in this study to date.

Improvement was seen in multiple physician- and patient-reported efficacy outcomes; selected outcomes are presented in Figure 1. Mean (SE) changes from study start at Week 68 in the OLE were: CDASI activity score = -21.8 (2.26), Patient Skin Activity VAS = -3.0 (0.75); Skindex-29 Symptoms Domain = -28.0 (SD); 5D Itch Score = -3.7 (SD); Physician Overall Disease VAS = -3.0 (SD); and Promis-29 Pain Interference = -4.5 (SD). Improvements were seen in other patient- and physician-reported efficacy outcomes. During the OLE, 2 subjects reduced mycophenolate, 2 were switched from methotrexate to mycophenolate, 1 started methotrexate, and 1 had a burst and taper of steroids.

Conclusion: To date, lenabasum treatment has been safe and well tolerated in the Phase 2 study JBT101-DM-001, with no serious AEs or study discontinuations related to lenabasum. The CDASI activity score and multiple other physician and patient-reported outcomes improved, although limitations of attributing efficacy to lenabasum in the

Figure 1. Change from Baseline in Selected Efficacy Outcomes in OLE of Phase 2 Trial JBT101-DM-001



setting of open-label dosing is acknowledged. These data support further testing of lenabasum for the treatment of DM, and a Phase 3 study of lenabasum in DM has started.

Disclosure: V. Werth, Biogen, 2, 5, Corbus Pharmaceuticals, 2, 9, University of Pennsylvania, 9; **D. Pearson**, None; **J. Okawa**, None; **R. Feng**, None; **J. Concha**, None; **B. Patel**, None; **E. Hejazi**, None; **S. Constantine**, Corbus Pharmaceuticals, 1, 3, 4; **N. Dgetluck**, Corbus Pharmaceuticals, 3, 4; **B. White**, Corbus Pharmaceuticals, 1, 3, 4, 6.

Abstract Number: 2844

Predictive Factors for Mortality in Anti-melanoma-associated Gene 5 Antibody-associated Interstitial Lung Disease

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SESSION INFORMATION
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Background/Purpose: Anti-melanoma differentiation-associated gene 5 (MDA5) antibody is useful to predict mortality in patients with myositis–associated interstitial lung disease (ILD) because of high prevalence of rapidly progressive ILD, which is often refractory to conventional immunosuppressive treatment. In Japan, an intensive combination therapy consisting of corticosteroids (CS), calcineurin inhibitor, and intravenous cyclophosphamide, named the triple combo therapy, is widely used in patients with anti-MDA5-associated ILD anecdotally without evidence. A number of reports have shown that a group of anti-MDA5-associated ILD patients poorly respond to triple combo therapy. The aim of this study is to identify baseline characteristics that predict a poor response to triple combo therapy in patients with anti-MDA5-associated ILD, using a multicenter retrospective/prospective cohort JAMI, involving 497 incident cases of adult myositis-ILD.

Methods: We selected 212 patients with anti-MDA5 from the JAMI database. First, baseline characteristics and treatment regimens were compared between survivors and non-survivors to identify factors associated with mortality using univariate analysis. We then conducted a multivariate logistic regression analysis to identify independent risk factors for mortality with stepwise selection method, in which explanatory variables were selected using backward deletion ($P \geq 0.15$) and forward inclusion ($P < 0.1$). A stratification tree model was constructed based on the combination of risk factors. Finally, we compared survival rates between patients treated with initial triple combo therapy and those without, by selecting patients randomly using JMP®13 software (SAS Institute Inc., Cary, NC, USA) by matching the baseline risk stratification and additional treatment regimen such as CS pulse therapy. Cumulative survival rates were compared using log-rank test.

Results: Mean age at disease onset was 55, 136 (64%) were female, and median disease duration at entry was 2 months. 73 patients died due to respiratory insufficiency at median of one month after treatment introduction. In-

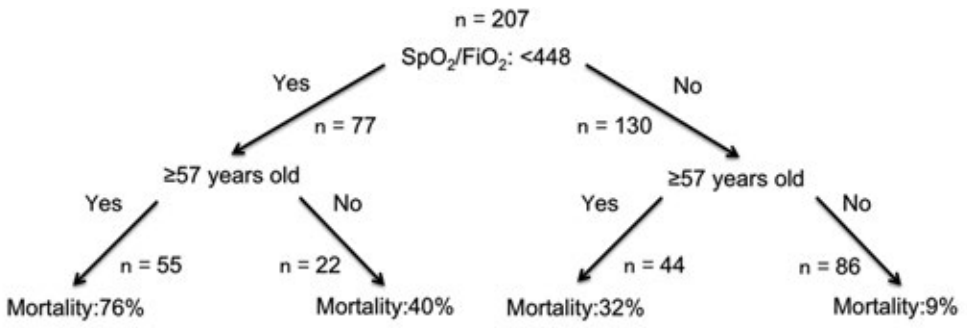

Figure 1. Stratification tree model for mortality in patients with anti-MDA5 antibody-associated ILD

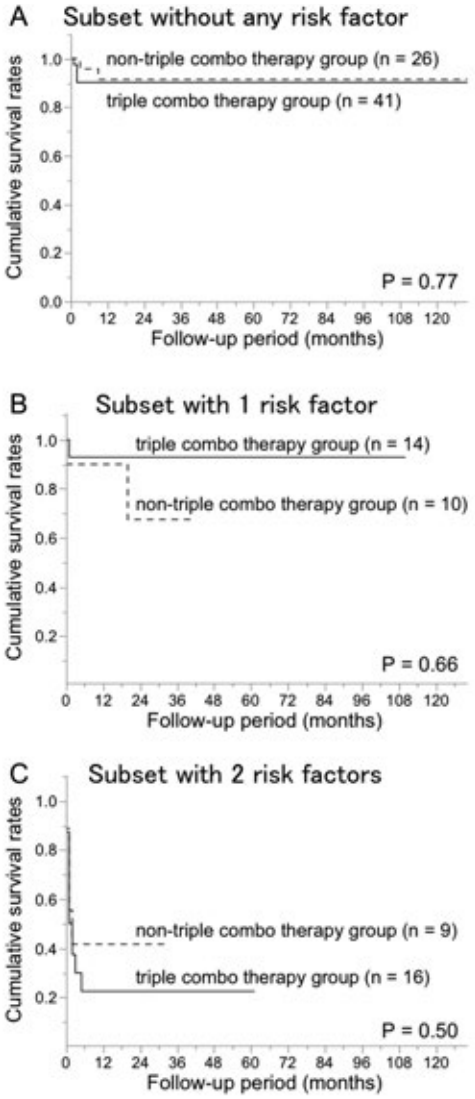

Figure 2. Comparison of overall survival rates between triple combo therapy group and non-triple combo therapy group in each subset stratified by risk factors

dependent risk factors for mortality were older age (odds ratio [OR] 1.07, 95% confidence interval [CI] 1.04-1.12, P < 0.0001), and lower SpO_2/FiO_2 ratio (OR 0.98, 95%CI 0.96-0.99, P < 0.0001). Cut-off values that best discriminate survivors and non-survivors identified using ROC curve analysis included age of 57 years and SpO_2/FiO_2 ratio of 450. We successfully generated a stratification tree model for mortality (Figure 1). Patients older than 57 years with SpO_2/FiO_2 ratio < 450 at diagnosis had the worst outcome with mortality rate of 76%. Cumulative survival rates were comparable between patients treated with initial triple combo therapy and those without even after matching the baseline risk stratification and additional treatment regimen (Figure 2).

Conclusion: Age and SpO_2/FiO_2 ratio at diagnosis are independent predictors for mortality in patients with anti-MDA5-associated ILD. We failed to demonstrate superiority of triple combo therapy over conventional therapy even adjusting baseline risk factors, suggesting urgent need of other therapeutic regimen for this devastating condition.

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Abstract Number: 2845

Pain Patterns in Idiopathic Inflammatory Myopathy (IIM): Associations with Disease Activity Measures (Muscle Enzymes, Manual Muscle Testing 8), Patient-Reported Quality of Life (HAQ) and Pain Scales (Widespread Pain Index (WPI), Symptom Severity Index (SSI) and Visual Analogue Scale)

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	DM	ASS	OM	PM	INMN	IBM
N (%)	28 (55%)	9 (17.6%)	7 (13.7%)	5 (9.8%)	1 (2%)	1 (2%)
Females (%)	21 (75%)	6 (66.7%)	5 (71.4%)	5 (100%)	0	0
W/B/H	25/2/1	7/2/0	4/1/2	5/0/0	1/0/0	1/0/0
Age (years)/SD	51.4/14.9	54.7/6.7	57.1/16.4	58.6/9.3	53	69
Disease Duration (months)/SD	103.4/88.6	142.5/88	123.4/80.2	130.4/66.1	7	65
ANA: Neg/S/N/H	12/13/1/0	8/0/1/0	0/6/0/1	3/0/1/0	1/0/0/0	1/0/0/0
MAA: Negative SSA 52 Kd NXP2 TIFF 1 γ	 16 8 2 2	 0 5 1 Jo-1 1 EJ	 2 3 1 U1-RNP 1	 4 1	 1	 1
GI (%)	8 (28.6%0	4 (44.4%)	6 (85.7%)	2 (40%)	1(100%)	0
ILD (%)	4 (14.3%)	1 (20%)	3 (43%0	1 (20%)	0	0
FMS (%)	6 (21.4%)	2 (22.2%)	2 (28.6%)	3 (60%)	1 (100%)	0
CK (mean/SD)	500.1	111.2/74	347.5	304/198	5312	253
Aldolase (mean/SD)	9.35	4.1/1.1	7.4/5	9.4/8.5	75	5
AST (mean/SD)	48.1	30.7/21.5	36/12.8	40/18	246	47
MMT8 (mean/SD)	143.2/13.9	147.9/11.3	140.1/12	138/24	123	148
HAQ (mean/SD)	1.05/.9	0.875	0.78	1.92/0.68	1.62	0.675
Pain VAS (mean/SD)	2.5	3.05	3.2/2.5	6.7/2.2	7.5	0
PGA (mean/SD)	3.1/3.1	4.22/3.7	2.3/2.2	6/2.1	9.0	0
MDGA (mean/SD)	3.18/3.17	3.1/2.5	2.4/0.9	3.8/3.5	9.0	2
IGA (mean/SD)	1.9/1	0.67	0.86/0.37	0.4	0	0
SSI (mean/SD)	4.43/2.3	5.11	5.29/3	6.4/3.7	8	1
WPI (mean/SD)	4.04	4.78	4.57	6.4/2.6	13	0

Table 1. N = number, DM= dermatomyositis, ASS = anti-synthetase syndrome, PM = polymyositis, INMN = necrotizing myositis, IBM = inclusion body myositis, W/B/H = white/black/Hispanic, SD = standard deviation, ANA = anti-nuclear antibody, Neg/S/N/H = negative/speckled/nucleolar/homogeneous, MAA = myositis associated antibodies, GI = gastrointestinal, ILD = interstitial lung disease, FMS = fibromyalgia syndrome, CK = creatine kinase, AST = aspartate aminotransferase, MMT8 = manual muscle testing 8, HAQ = health assessment questionnaire, VAS= visual analogue scale, PGA = patient global activity scale, MDGA = physician global activity, IGA = investigators global assessment of skin involvement, SSI = symptom severity index, WPI = widespread pain index.

	Has FMS (n=14) Mean (SD)	No FMS (n=37) Mean (SD)
Age (yrs)	**47.3 (11.9)**	**56.6 (13.1)**
Disease Duration (mths)	102 (106.5)	117.2 (75.8)
CK	1124.6 (2198.8)	237.9 (219)
Aldolase	19.6 (29.5)	5.3 (2.1)
AST	**77.8 (80.7)**	**34.7 (18.7)**
HAQ	**1.77 (0.68)**	**0.81 (.84)**
MMT8	**137 (13.8)**	**145.1 (14.1)**
Pain VAS	**5.75 (2.67)**	**2.17 (2.4)**
PGA	**5.78 (2.99)**	**2.75 (2.95)**
GI	**0.71 (0.47)**	**0.30 (0.46)**
WPI	**9.29 (3.67)**	**2.78 (3.11)**
SSI	**8.07 (1.49)**	**3.65 (1.81)**
MDGA	4.5 (3.48)	2.73 (2.54)

Bold: p<.05

Table 2. n = number, GI = gastrointestinal, FMS = fibromyalgia syndrome, CK = creatine kinase, AST = aspartate aminotransferase, MMT8 = manual muscle testing 8, HAQ = health assessment questionnaire, VAS= visual analogue scale, PGA = patient global activity scale, MDGA = physician global activity, IGA = investigators global assessment of skin involvement, SSI = symptom severity index, WPI = widespread pain index.

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Muscle Biology, Myositis & Myopathies II
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: IIMs associate with significant lifelong disability due to progressive loss of muscle function and lack of curative interventions; little is known about the relative contribution of different pain patterns in IIMs. Although not commonly associated with inflammatory myositis, myalgia is a sine qua non component of central pain states and is frequently perceived by patients as a sign of “inflammation”. Our objective is to evaluate the prevalence of central pain in different types of IIM (dermatomyositis (DM), polymyositis (PM), immune-mediated necrotizing myositis (IMNM), overlap myositis (OM), anti-synthetase syndrome (ASS) and inclusion body myositis (IBM)) and how it relates to objective disease activity measures and patient-reported quality of life measures.

Methods: In a single Myositis Center we collected demographic and clinical information in a cross-sectional manner in 51 consecutive IIM patients (2018-present): age, gender, race, type of IIM, disease duration (from diagnosis to clinic visit), anti-nuclear antibody pattern and titer, myositis specific antibodies, presence/absence of gastrointestinal (GI) and pulmonary (interstitial lung disease, ILD) comorbidities, serum muscle enzymes (creatine kinase (CK), aldolase and aspartate aminotransferase (AST)) and manual muscle testing 8 (MMT8). In addition, each patient completed the Health Assessment Questionnaire-Disability Index (HAQ-DI), which includes the pain visual analogue scale (pain VAS), the patient global activity scale (PGA) and the 2010 American College of Rheumatology self-reported Fibromyalgia (FMS) diagnostic criteria, including the symptom severity index (SSI) and widespread pain index (WPI) (Fig. 1). A single assessor (ES) performed the physician global activity (MDGA) and the investigators global assessment of skin involvement (IGA: 0=no involvement, 1= minimal-, 2= mild-, 3= moderate- and 4= severe skin erythema). Descriptive statistics and comparisons on demographic and disease variables between those with or without fibromyalgia using non-parametric statistics (Wilcoxon Mann-Whitney) are presented.

UMHS: Department of Rheumatology: Patient Questionnaire

1. For each symptom listed below, use the following scale to indicate the severity of the symptom **during the past 7 days.**

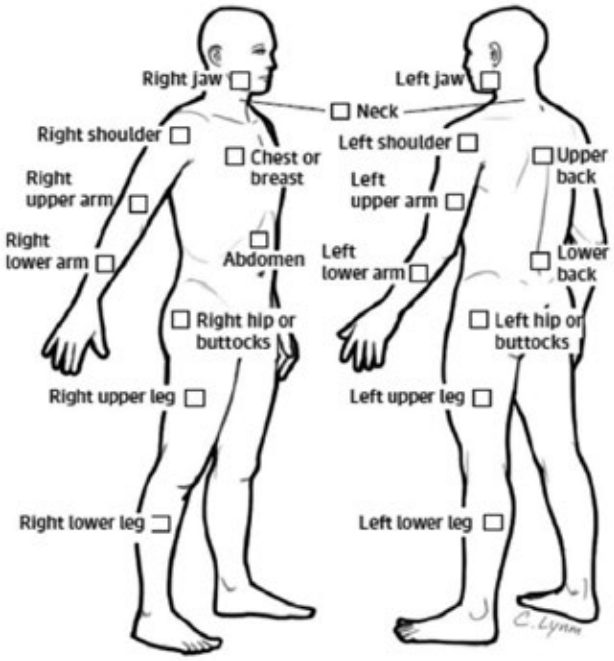
	No Problem	Mild (Mild/Intermittent)	Moderate (Considerable /often present)	Severe (Continuous/life disturbing)
Fatigue	☐	☐	☐	☐
Trouble thinking or remembering	☐	☐	☐	☐
Waking up tired (unrefreshed)	☐	☐	☐	☐

2. Indicate which of the following symptoms you have had over the past **7 days** by (circling) the symptom:

Bladder spasms	Easy bruising	Insomnia	Numbness/tingling
Blurred vision	Fatigue	Irritable bowel syndrome	Oral ulcers
Chest pain	Fever	Itching	Pain in upper abdomen
Constipation	Frequent urination	Loss of appetite	Pain/cramps in abdomen
Depression	Hair loss	Loss/Change in taste	Painful urination
Diarrhea	Headache	Muscle pain	Rash
Dizziness	Hearing problem	Muscle weakness	Raynaud phenomenon
Dry eyes	Heart burn	Nausea	Hives
Dry mouth	Seizure	Shortness of breath	Sun sensitivity
Vomiting	Wheezing	Ringing in ears	Thinking/memory problem
Nervousness			

3. Have the symptoms in 1-2 been present at a similar level for at least **3 months**? **Yes** ☐ **No** ☐

4. On the image below, **CHECK ALL** areas of your body where you have had pain or tenderness which has **persisted or recurred** for **the last 3 months or longer**.



5. If you have had **NO PAIN** please check this box: ☐

6. If you marked pain, do you have a disorder that would otherwise explain the pain? If so what disorder?

Yes ☐ ---------- (list the disorder)

No ☐

Adapted from Clauw DJ. Fibromyalgia: A Clinical Review. JAMA. 2014;311(15):1547-1555. doi:10.1001/jama.2014.3266

Results: Mean age/SD at the time of analysis was 54/13.3yrs, and the mean/SD disease duration from diagnosis was 113/84 months; most of our cohort had DM (54.9%) and AAS (17.6%), were female (72.5%), white (84.3%), 30 (58/8%) had GI involvement and 17 (33.3%) had ILD. Differences among different IIMs are presented in Table 1. Twelve (23.5%) of the 51 IIM patients met the classification criteria for central pain syndrome (FMS-ness) and the parallels between the groups with and without FMS are presented in Table 2.

Conclusion: A large proportion of patients with IIM met classification criteria for FMS, and when compared to patients without FMS, they were almost a decade younger, weaker, had significantly higher AST (but not aldolase or CK), were more likely to have PM or INMN, and had significantly lower levels of function (ΔHAQ almost 1.0). Myalgia is not specific or included in the IIM diagnostic criteria, but it could interfere with rehabilitative exercise. Careful phenotyping of pain patterns in IIMs could help functionality by customizing treatment approaches.

Disclosure: E. Schiopu, None; **S. Farshad**, None; **N. Abdulaziz**, None; **S. Anderson**, None; **A. Impens**, None.

Abstract Number: 2846

Outcomes over the First 5 Years of Follow up in a Very Early Rheumatoid Arthritis (RA) Cohort Recruited over 20 Years: Most of the Improvement Occurred Before the 2011 Implementation of Treat-to-Target (T2T)

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes IV: Outcomes
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: To analyze the evolution over 20 years of disease activity, treatments and radiographic progression over the first 5 years of follow up of patients with incident RA.

Methods: Since July 1998, the Early Undifferentiated PolyArthritis (EUPA) cohort recruited consecutive adults with recent-onset immune-mediated synovitis affecting at least 3 joints. From the start, patients were treated aiming at 0 swollen joint. Outcomes over 5 years were compared in patients fulfilling RA criteria according to date of inclusion (Period 1: 1998-2004; Period 2: 2005-2010; Period 3: 2011-2018). Disease activity was measured according to DAS28-CRP and SDAI; remission was also studied according to ACR/EULAR criteria. Use of conventional DMARD treatments was defined as none, simple, double and triple; mean MTX dose and biologic DMARD use were also compared across periods. Erosive damage was scored according to Sharp/van der Heijde; erosive status was defined as ≥5 Erosion units. False discovery rate correction was used to adjust p-values for multiple comparisons.

Results: 753 patients were included: 247, 263 and 243 in Periods 1, 2 and 3, respectively. Over the 5 years of follow up, DAS-28 scores significantly decreased and the number of patients reaching DAS-28 remission increased between Periods 1 and 2 (RR(95%CI)= 1.14 (1.03-1.26), p=0.04) and Periods 1 and 3 (RR=1.13 (1.01-1.27), p=0.055), but not between Periods 2 and 3. SDAI remission was not significantly different between Periods; however, SDAI remission was reached earlier during Period 3. Nonetheless, ACR/EULAR remission was reached earlier and was significantly more frequent in Period 3 than in Periods 1 and 2 (RR=1.43 (1.14-1.79), p=0.005; RR=1.36 (1.10-1.68), p=0.006 respectively), but not between Periods 2 and 1. There were no significant differences in mean HAQ scores nor Patient Evaluation of disease activity between Periods. The use of combination DMARDs increased between Periods at each follow up visit, reaching a peak of 25.7% receiving triple therapy at 18 months during Period 3 (versus 5.6% and 12.4% during Periods 1 and 2). Mean MTX dosage increased significantly from Period 1 to Period 2

		Follow-up (Months)					Period Comparisons	Adjusted p-value
		0	18	30	42	60		
DAS28-CRP	1998-2004	5.5 (4.3-6.3)	2.5 (1.9-3.5)	2.4 (1.8-3.2)	2.4 (1.8-3.2)	2.2 (1.7-3.1)	2 vs. 1	**0.0015**
Med. (IQR)	2005-2010	5.1 (4.1-6.1)	2.5 (1.9-3.4)	2.1 (1.7-3.0)	2.1 (1.6-2.8)	1.9 (1.5-2.6)	3 vs. 1	**0.0003**
	2011-2018	5.0 (4.1-6.1)	2.0 (1.5-3.1)	2.1 (1.5-2.7)	1.7 (1.3-2.4)	1.9 (1.4-2.6)	3 vs. 2	0.1081
DAS28-CRP	1998-2004	5 (2)	119 (52)	131 (59.3)	117 (56)	120 (59.4)	2 vs. 1	**0.0387**
remission	2005-2010	9 (3.5)	128 (55.9)	136 (66)	139 (69.5)	129 (75.4)	3 vs. 1	0.0546
n (%)	2011-2018	7 (3.3)	109 (65.3)	104 (71.7)	88 (77.9)	50 (75.8)	3 vs. 2	0.8796
SDAI	1998-2004	33.0 (21.5-48.0)	6.6 (2.8-13.4)	4.8 (2.5-10.4)	5.7 (2.1-10.6)	5.1 (1.7-9.7)	2 vs. 1	0.0620
Med. (IQR)	2005-2010	30.3 (20.8-44.1)	6.5 (3.2-12.5)	5.1 (2.1-9.6)	4.4 (1.5-8.8)	3.9 (1.4-7.8)	3 vs. 1	0.0620
	2011-2018	29.4 (20.6-43.8)	4.4 (1.4-10.4)	4.5 (1.8-9.3)	2.8 (1.1-6.8)	3.8 (0.9-6.6)	3 vs. 2	0.7082
SDAI	1998-2004	0 (0)	64 (27.9)	84 (38)	70 (33.5)	78 (38.6)	2 vs. 1	0.6538
remission	2005-2010	0 (0)	60 (26.1)	79 (38.3)	84 (42)	75 (43.6)	3 vs. 1	0.3755
n (%)	2011-2018	0 (0)	69 (41.6)	62 (42.8)	61 (54)	29 (44.6)	3 vs. 2	0.3755
ACR/EULAR	1998-2004	0 (0)	45 (19.5)	54 (24.2)	47 (22.3)	54 (26.6)	2 vs. 1	0.6859
remission	2005-2010	2 (0.8)	37 (15.8)	48 (22.6)	61 (29.9)	58 (31.5)	3 vs. 1	**0.0051**
n (%)	2011-2018	0 (0)	67 (36.2)	52 (32.1)	54 (43.2)	35 (44.9)	3 vs. 2	**0.0059**
HAQ	1998-2004	0.8 (0.4-1.4)	0.3 (0-0.6)	0.1 (0-0.5)	0.1 (0-0.6)	0.3 (0-0.5)	2 vs. 1	0.3222
Med. (IQR)	2005-2010	0.8 (0.4-1.4)	0.3 (0-0.6)	0.1 (0-0.5)	0.1 (0-0.6)	0.1 (0-0.6)	3 vs. 1	0.1440
	2011-2018	0.8 (0.4-1.3)	0.1 (0-0.5)	0.1 (0-0.5)	0.1 (0-0.5)	0.1 (0-0.5)	3 vs. 2	0.3222
Patient global	1998-2004	59 (36-80)	21 (5-48)	19 (5-39)	22 (3-48)	20 (3-45)	2 vs. 1	0.3877
assessment	2005-2010	56.5 (38-78.5)	30.5 (11-51)	20 (5-45)	19 (5-47)	16.5 (5-37)	3 vs. 1	0.3877
n (%)	2011-2018	49 (27-72)	19 (5-41)	21 (5-48)	12 (3-35)	12 (4-34)	3 vs. 2	0.2094
Erosion score	1998-2004	1 (0-3)	3.5 (1-8)	5 (2-10)	5 (1-12)	6 (1-13)	2 vs. 1	**0.0165**
Med. (IQR)	2005-2010	1 (0-3)	2 (0-5)	3 (0-5)	3 (0-6)	2 (0-6)	3 vs. 1	**0.0003**
	2011-2018	0.5 (0-2)	1 (0-4)	1 (0-4)	2 (0-5)	2 (1-5)	3 vs. 2	**0.0276**
Erosions ≥5	1998-2004	44 (18.2)	95 (41.7)	119 (53.4)	109 (52.9)	116 (57.4)	2 vs. 1	**0.0002**
n (%)	2005-2010	46 (18.5)	68 (29.4)	67 (31.6)	74 (36.3)	62 (32.8)	3 vs. 1	**0.0002**
	2011-2018	19 (10.7)	29 (19.9)	29 (19.7)	30 (27.3)	22 (32.4)	3 vs. 2	**0.0069**
DMARD use	1998-2004	60 (24.3)	214 (92.6)	192 (86.9)	172 (81.5)	167 (82.3)	2 vs. 1	**0.0081**
n (%)	2005-2010	77 (29.3)	228 (97.9)	203 (95.8)	189 (92.6)	168 (91.3)	3 vs. 1	0.4071
	2011-2018	62 (25.5)	182 (99.5)	153 (96.2)	117 (92.9)	76 (97.4)	3 vs. 2	**0.0173**
MTX use	1998-2004	32 (13)	166 (71.9)	155 (70.1)	146 (69.2)	138 (68)	2 vs. 1	**0.0003**
n (%)	2005-2010	54 (20.5)	219 (94)	187 (88.2)	170 (83.3)	148 (80.4)	3 vs. 1	**0.0435**
	2011-2018	45 (18.5)	175 (95.6)	131 (82.4)	97 (77)	64 (82.1)	3 vs. 2	**0.0048**
MTX use	1998-2004	10 (7.5-12.5)	14.9 (12.5-17.8)	16.6 (12.5-21)	16 (12.5-22.5)	17.7 (12.3-22.5)	2 vs. 1	**0.0002**
Dosage	2005-2010	15 (12.5-18.2)	20.7 (17.9-23.6)	22.5 (19.7-25)	22.6 (18.3-25)	20 (16.6-25)	3 vs. 1	**0.0002**
Med. (IQR)	2011-2018	19 (15-20)	21.7 (19.8-24)	24.1 (20-25)	20 (15.8-25)	20 (15-25)	3 vs. 2	**0.0010**
Prednisone use	1998-2004	61 (24.7)	128 (55.4)	69 (31.2)	40 (19)	38 (18.7)	2 vs. 1	0.7793
n (%)	2005-2010	91 (34.6)	146 (62.7)	47 (22.2)	30 (14.7)	25 (13.6)	3 vs. 1	0.7793
	2011-2018	89 (36.6)	118 (64.5)	19 (11.9)	11 (8.7)	6 (7.7)	3 vs. 2	0.7793
Biologics use	1998-2004	0 (0)	8 (3.5)	14 (6.3)	16 (7.6)	14 (6.9)	2 vs. 1	**0.0003**
n (%)	2005-2010	2 (0.8)	38 (16.3)	47 (22.2)	44 (21.6)	42 (22.8)	3 vs. 1	**0.0224**
	2011-2018	0 (0)	19 (10.4)	27 (17)	24 (19)	16 (20.5)	3 vs. 2	**0.0224**
Triple Therapy	1998-2004	0 (0)	13 (5.6)	16 (7.2)	18 (8.5)	17 (8.4)	2 vs. 1	**0.0015**
n (%)	2005-2010	0 (0)	29 (12.4)	39 (18.4)	39 (19.1)	29 (15.8)	3 vs. 1	**0.0003**
	2011-2018	2 (0.8)	47 (25.7)	33 (20.8)	18 (14.3)	10 (12.8)	3 vs. 2	0.4653

Table
Outcome comparisons during 5 years of follow up in 753 RA patients recruited over 3 successive Periods: 1998-2004; 2005-2010; 2011-2018

to Period 3. The use of biologic DMARDs markedly increased between Periods 1 and 2 (RR=3.27 (1.92-5.57), p< 0.001), but significantly decreased from Period 2 to 3 (RR=0.62 (0.41-0.93), p=0.02). The use of corticosteroids did not differ significantly between Periods. Erosive damage decreased significantly over each Period (Periods 2 versus

1: RR= 0.65 (0.53-0.81), p=0.002; Periods 3 versus 1: RR=0.42 (0.31-0.56), p=0.002; Periods 3 versus 2: RR=0.64 (0.46-0.88), p=0.007).

Conclusion: In this cohort of recent onset (mean 3.8 months) RA recruited over 20 years, we observed during the 2005-2011 Period, relative to 1998-2004, a marked improvement in control of disease activity and in erosive damage concomitant with use of higher doses of MTX, more combination DMARDs and more biologic DMARDs. The major changes observed after the 2011 launch of Treat-to-Target initiative, were faster control of disease activity and faster attainment of deep levels of remission, resulting in improved radiographic outcomes despite less frequent use of biologic DMARDs.

Disclosure: N. Carrier, None; **S. Roux**, None; **A. Masetto**, None; **A. deBrum Fernandes**, None; **P. Liang**, None; **M. Maoui**, Bristol-Myers Squibb Canada, 3; **G. Boire**, Bristol-Myers Squibb Canada, 2, 5.

Abstract Number: 2847

Testing Different Thresholds for Patient Global Assessment in Defining ACR-EULAR Boolean Remission Criteria for RA

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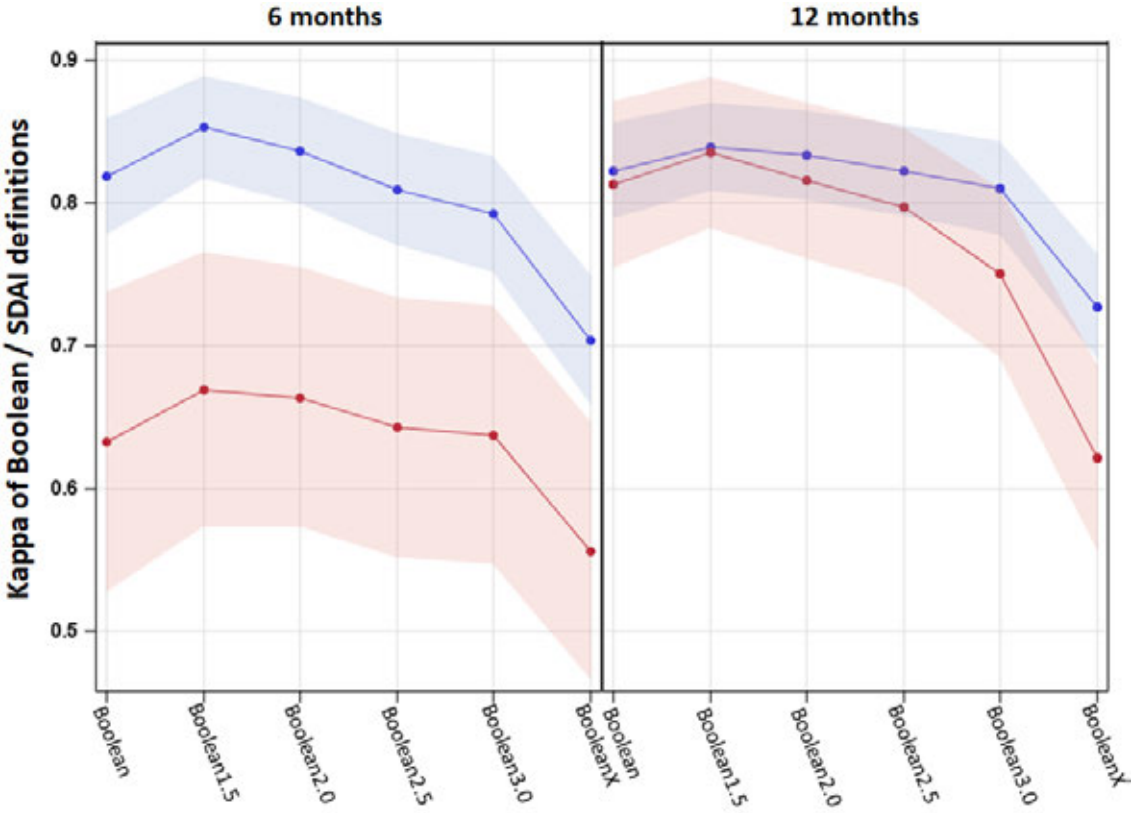

Figure: Kappa with confidence intervals between Boolean remission categories and SDAI remission, separately for early RA (blue line) and established RA (red line) at 6 month and 1 year.

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes IV: Outcomes
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: The patient global assessment (PGA) is a core set variable to assess RA disease activity. It is strongly linked to patient-reported pain and is a limiting factor for reaching when the ACR/EULAR Boolean remission definition is used, where PGA may not be greater than 1 on a 0-10 scale. Here we assessed different PGA criteria.

Methods: We used data from six RCTs testing the efficacy of TNF inhibitors vs MTX. Included were 3 trials of early RA: ASPIRE (infliximab), Go Before (golimumab), PREMIER (adalimumab); and 3 of established RA: ATTRACT (infliximab), DE019 (adalimumab) and Go Forward (golimumab). We increased the threshold for the 0-10 score for PGA gradually by 0.5 (Boolean1.5) up to 3 (Boolean3.0), and also omitted the criterion completely (BooleanX, i.e. requiring only CRP, SJC, TJC≤1). We assessed frequencies of remission by these definitions at 6 and 12 months and evaluated agreement with the Index based (SDAI) definition of remission (which does not include an inherent cut-off for PGA). Further the impact on functional and radiographic outcomes after 1 year were explored based on achievement of each of these remission definitions at 6 months. Using recursive partitioning (CART) we attempted to determine a PGA cut-off that optimized agreement with SDAI remission.

Results: Data from 2600 trial patients, 1680 with early RA (mean disease duration: 1.5±2.96years) and 920 with established RA (mean disease duration: 9.7±8.44 years) were included. The proportion of patients achieving Boolean remission increased with higher thresholds for PGA from 12.4% to 19.7% in early RA and 5.9% to 12.3% in established RA at 6 month and 19.9% to 30.1% and 11.4% to 22.5% respectively at 1 year. Best agreement with SDAI remission occurred at a PGA cut-off of 1.5 and 2.0, while agreement decreased with PGA thresholds of ≥ 2.5 (**Figure**). Compared with Boolean (using 1.0), at Boolean2.0 the number of persons who were in remission per SDAI criteria increased from 74% to 85% of all SDAI remitters at 6 months. In early RA patients evaluating data at 6 months CART analyses showed that optimal agreement with SDAI remission occurred at a PGA threshold between 1.4 and 1.7cm.

Changing PGA thresholds at 6 months did not affect radiographic outcome with scores similar across different thresholds (mean ΔsmTSS for Boolean, 1.5, 2.0, 2.5, 3.0 and BooleanX were: 0.35±5.4, 0.38±5.14, 0.41±5.1, 0.37±4.9, 0.34±4.9 and 0.27±4.7). However, for both early and late RA, the lower the PGA threshold, the lower the HAQ score. The proportion attaining HAQ≤0.5 was 90.2%, 87.9%, 85.2%, 81.1%, 80.7% and 73.1% for Boolean, 1.5, 2.0, 2.5, 3.0 and BooleanX respectively. Omitting PGA was associated with much worse functional outcomes.

Conclusion: Increasing the PGA cut-off to 1.5cm would provide highest consistency between Boolean with the Index based remission; the integer cut-off of 2.0cm performed similarly and would also allow the use of numerical rating scales. This new cut-off discounts the excessive stringency of the current PGA cut-off in the remission context, while maintaining similar functional and radiographic long-term outcomes.

Disclosure: P. Studenic, None; **D. Felson**, None; **M. de Wit**, Abbvie, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen-Cilag, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8; **F. Alasti**, None; **T. Stamm**, Janssen, 8, MSD, 8, Novartis, 8, Roche, 2, 8; **J. Smolen**, AbbVie, 2, 5, 8, Abbvie, 2, 5, Amgen, 5, 8, AstraZeneca, 2, 5, 8, Astra-Zeneca, 5, Astro, 5, 8, BMS, 5, Celgene, 5, 8, Celltrion, 5, Celtrion, 5, 8, Chugai, 5, Eli Lilly and Company, 2, 5, Gilead, 5, GlaxoSmithKline, 5, 8, ILTOO, 5, 8, ILTOO Janssen, 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Medimmune, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, Novartis- Sandoz, 5, Novartis-Sandoz, 2, 5, 8, Pfizer, 2, 5, 8, Pfizer Inc, 5, Roche, 2, 5, Roche;, 2, 5, 8, Samsung, 5, 8, Sanofi, 5, 8, Sanofi-Aventis, 5, UCB, 5, 8; **D. Aletaha**, AbbVie, 2, 5, 8, AbbVie, Janssen, Lilly, Novartis, Pfizer, and Roche, 5, AbbVie, Merck Sharp and Dohme, and Roche., 2, Amgen, 5, 8, Bristol-Myers Squibb, 8, Bristol-Myers Squibb,

Celgene, Merck Sharp and Dohme, and UCB, 8, Celgene, 5, 8, Janssen, 5, Lilly, 5, 8, Medac, 5, 8, Merck, 5, 8, Merck Sharp and Dohme, 2, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, Sandoz, 5, 8, Sanofi/Genzyme, 5, 8, UCB, 8.

Abstract Number: 2848

Semiquantitative Assessment of Synovial Inflammation on US-Guided Synovial Membrane Biopsy Is Contingent to Disease Phase, Autoimmune Profile and Treatment Response in Rheumatoid Arthritis: Large Single Center Experience (SYNGem Cohort)

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes IV: Outcomes
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Ultrasound (US)-guided minimally-invasive Synovial Tissue (ST) biopsy is a well tolerated procedure for basic and translational studies on chronic inflammatory joint diseases as Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and Spondyloarthritis (SpA). The aim of the study was to evaluate the utility of histopathologic criteria to differentiate US-guided ST biopsies in daily clinical care in relation to diagnosis, disease characteristics, US parameters and treatment response in a large single center ST biopsy Unit.

Methods: 1064 patients [545 RA, 167 PsA, 75 SpA, 199 Undifferentiated Peripheral Inflammatory Arthritis (UPIA), 18 crystal arthritis, 26 connective tissue diseases and 34 osteoarthritis (OA) respectively] who underwent US-guided ST biopsy were enrolled. US parameters (Synovial Hyperthrophy and Power Doppler signal respectively) were recorded for each biopsied joint. RA, PsA and SpA patients were stratified based on disease activity phase (naive to DMARDs, DMARDs resistant and in sustained remission, respectively). Clinical, demographic and immunological characteristics were recorded for each patient. All ST FFPE specimens were routinely processed and stained with H&E and classified by a pathologist, blinded to clinical characteristics, using the Krenn score to assess the degree of ST inflammation[1]. Moreover, the presence/absence of lymphocytes, plasmacells, granulocytes and oedema was assessed for each ST. All naive to treatment RA were treated according to the T2T scheme and followed for at least 12 months and DAS remission rate was recorded.

Results: In the cohort, the distribution of synovitis score was significantly different among patients with inflammatory chronic diseases (RA, PsA, SpA and UPIA respectively) compared to OA (ANOVA Test $p< 0.001$). Moreover, Krenn score directly correlated with synovial hyperthrophy ($R=0.36;p< 0.001$) and Power Doppler signal ($R=0.40;p< 0.001$) of the biopsied joint. Considering the RA cohort, naive RA showed a higher Krenn score compared to resistant RA ($p< 0.001$) and RA in sustained clinical and US remission ($p< 0.001$), directly correlating with DAS28 ($R=0.51;p< 0.001$). Moreover, ACPA and RF positivity was related to the Krenn score and to ST plasmacells presence at RA onset ($p< 0.05$ and $p< 0.001$, respectively) but not at the time of DMARDs-failure or sustained remission achievement ($p >0.05$ for both). Stratifying naive RA based on disease duration at ST biopsy, naive RA with symptoms duration >1 year, showed higher Krenn score compared to those with symptoms duration < 3 months ($p< 0.001$). Finally, logistic

regression analysis revealed that, in naive RA, Krenn score ≥4.5 at baseline is an independent factor of no DAS remission achievement within 12 months [OR(95%CI):0.37(0.20-0.67)p< 0.001].

Conclusion: Krenn score is a reliable tool for the semi-quantitative assessment of ST inflammation on US-guided ST biopsies being differentially distributed among various chronic inflammatory joint diseases and contingent to disease phase, autoimmune profile and therapeutic response in RA.

References: [1]Krenn V, et al. Histopathology 2006

Disclosure: S. Alivernini, None; **B. Tolusso**, None; **M. Gessi**, None; **M. Gigante**, None; **L. Petricca**, None; **C. Di Mario**, None; **S. Perniola**, None; **A. Fedele**, None; **G. Peluso**, None; **L. Bui**, None; **A. Capacci**, None; **F. Federico**, None; **G. Ferraccioli**, None; **E. Gremese**, AbbVie, 5, 8, Abbvie, 5, 8, BMS, 5, 8, Bristol-Myers Squibb, 5, 8, Celgene, 5, 8, Jannsen, 5, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sandoz, 5, 8, UCB, 5, 8.

Abstract Number: 2849

Radiographic Progression During a 10-Year Follow-Up : Results from the French Cohort ESPOIR

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes IV: Outcomes
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: In early arthritis, identification of patients at risk of developing joint damage is an important issue. In rheumatoid arthritis (RA), the rate of progression is highest during the first 2 years and most of the damage occurs within the first 5 years.

The aim of this study was to describe the patterns of radiographic progression during a 10-year follow-up in the French cohort ESPOIR.

Methods: In this national multicenter cohort, 813 adult patients with suspected or confirmed early RA were included between December 2002 and March 2005, and followed up during 10 years. Radiographs were obtained and modified Sharp scores (vSHS) were determined by a blinded reader. The primary outcome was radiographic progression (RP) at 10 years, defined as a significant increase of vSHS (smallest detectable difference ⩾11). Secondary outcomes were rapid radiographic progression (RRP), defined as >5-point annual increase in vSHS, and non-progression (NP), defined as < 1-point increase in vSHS at the end of the follow-up. Quantitative variables were described by mean ± SD and qualitative variables by number and percentage. The patient groups were compared using Fisher exact test for qualitative variables and Mann-Whitney test for quantitative variables. P values ≤ 0.05 were considered statistically significant.

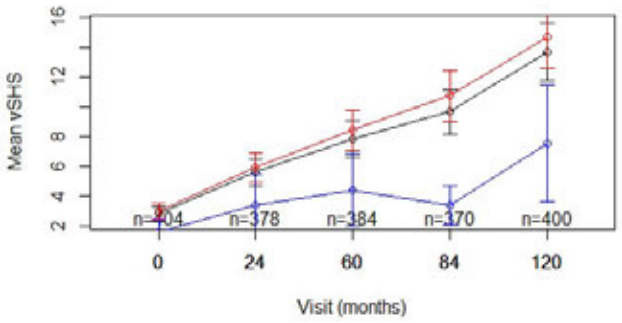

Figure 1. mean radiographic progression during the 10-year follow-up (black: overall population; red: patients fulfilling ACR-EULAR 2010 criteria at baseline; blue: patients not fulfilling ACR-EULAR 2010 criteria at baseline)

Results: Overall, 400 patients (49.2%) had complete data at the end of the follow-up; among them, 343 patients fulfilled ACR-EULAR 2010 criteria at baseline. Radiographs scoring was available for M0, M24, M60, M84 and M120.

The mean progression was of 10.9 (SD=17.9) during the 10-year follow-up, and was significantly higher in patients fulfilling ACR-EULAR 2010 criteria compared with those who weren't (11.9 (SD=18.5) and 5.9 (SD=12.4) respectively, p=0.002). Progression was more important during the 5 first years (Figure 1). The mean progression on erosion score was of 4.0 (SD=8.4) and the mean progression on joint space narrowing score was of 6.9 (SD=10.7).

At the end of the follow-up, 93 patients (23.3%) experienced RP, 16 of whom (4.0%) experienced RRP, 227 patients (56.7%) progressed below the smallest detectable change, and 80 patients (20.0%) did not progress, 8 of whom (2.0%) had an improvement in their vSHS. There was a significant difference in terms of RP between patients fulfilling or not ACR-EULAR 2010 criteria (N=86 (21.6%) and N=7 (10.8%) respectively, p=0.03), but there was no difference for RRP (N=15 (3.8%) and N=1 (1.5%) respectively, p=0.49) and NP (N=63 (15.8%) and N=13 (20%) respectively, p=0.10).

Conclusion: Overall, about 20% of the patients experienced RP at the end of the 10-year follow-up, with significantly more progressors among patients fulfilling ACR-EULAR 2010 criteria. Predictors of RP are currently investigated.

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Abstract Number: 2850

Exploring Heterogeneity in Rheumatoid Arthritis: Outcomes up to 4 Years of Follow-Up in Patient Clusters Identified by Data-driven Analysis of the BRASS Registry

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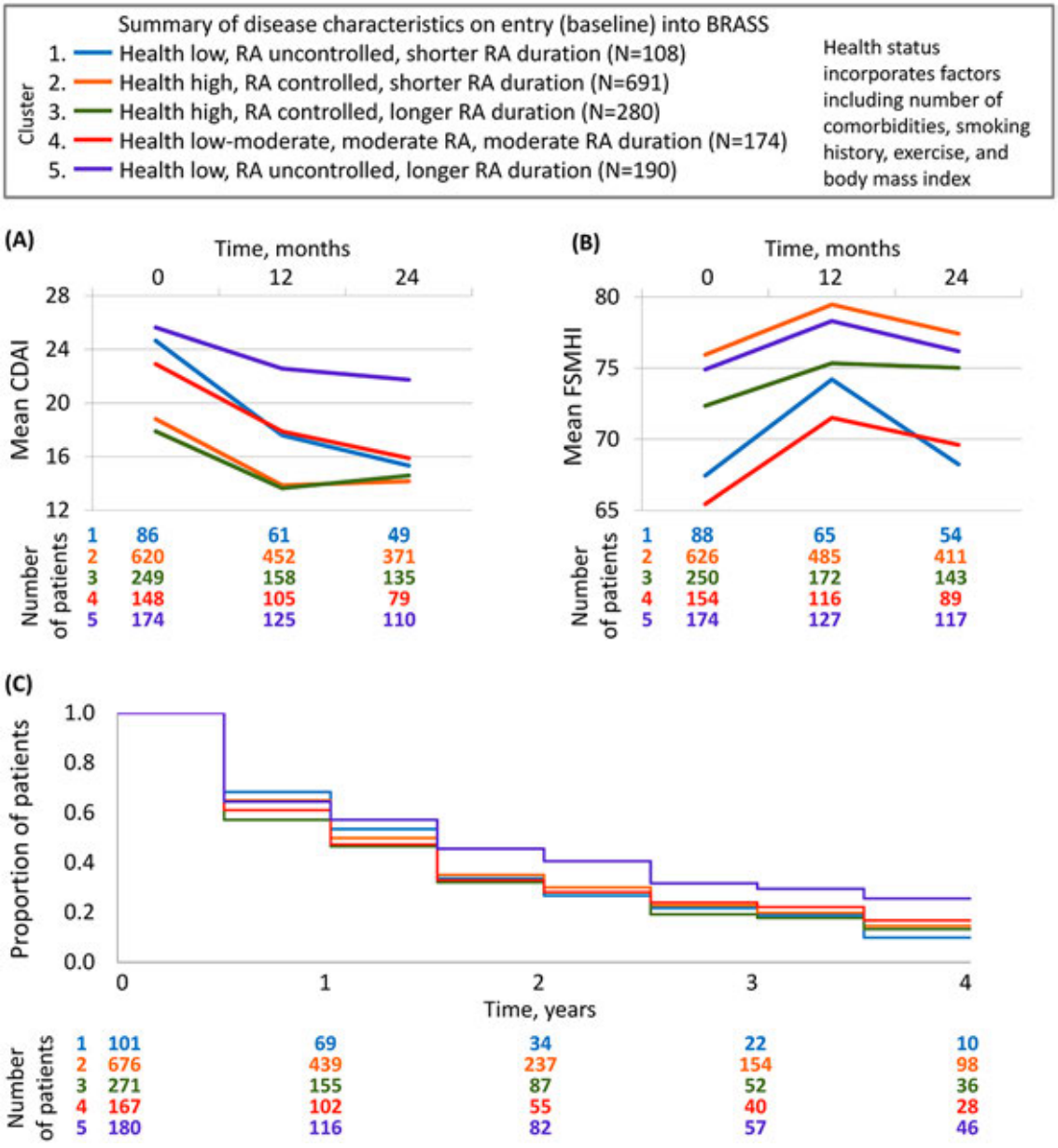
Figure. (A) mean Clinical Disease Activity Index (CDAI), (B) mean Functional Status Mental Health Index (FSMHI), (C) time to first change in baseline conventional synthetic or biological disease-modifying antirheumatic drug in five objectively identified patient cluster phenotypes



SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes IV: Outcomes

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Patients with rheumatoid arthritis (RA) may share characteristics that relate to their future outcomes. We investigated clinical outcomes over a 4-year follow-up period in objectively identified RA patient clusters derived empirically via a data-driven approach using the BRASS registry.

Methods: Patient clusters were identified by principal components (PC) and cluster analysis of demographic, socio-economic, health and disease characteristics using patient data collected at entry (baseline) into the BRASS registry. Patients in BRASS are followed in the clinic at least annually and are sent questionnaires at 6-month intervals. Mean score of clinical measures were observed at 12- and 24-months of follow-up including Clinical Disease Activity Index (CDAI), Disease Activity Score 28-joint count C-reactive protein (DAS28-CRP), BRASS self-administered Rheumatoid Arthritis Disease Activity Index (RADAI), swollen and tender joint count (SJC and TJC), Multidimensional Health Assessment Questionnaire (MDHAQ), and Functional Status Mental Health Index (FSMHI). Time to first infection and to first RA medication change over 4 years were analysed via Kaplan-Meier curves.

Results: PC analysis of variables among 1443 patients recorded at entry into BRASS identified 41 PCs that capture the fundamental characteristics involved in RA. These PCs informed the identification of 5 novel patient clusters. Cluster 1 patients ("health low, RA uncontrolled, shorter RA duration") exhibited the greatest reduction in TJC. Cluster 2 patients ("health high, RA controlled, shorter RA duration") remained free of infection longer than other clusters. Cluster 3 patients ("health high, RA controlled, longer RA duration") sustained the lowest mean SJC throughout follow-up. Cluster 4 patients ("health low–moderate, moderate RA, moderate RA duration") exhibited the greatest improvement in mental health (FSMHI; Figure). Cluster 5 patients ("health low, RA uncontrolled, longer RA duration") exhibited the highest CDAI scores (Figure) and the highest persistence of therapies at baseline without change.

Conclusion: Five patient clusters identified by data-driven PC analysis of the BRASS registry exhibited distinct patterns of clinical outcomes and management over 4 years. The clinical outcomes data suggest the clusters represent clinically meaningful profiles of RA and illustrate the potential of data-driven patient profiling as a tool to support personalized medicine in RA. Validation in an independent dataset is ongoing.

Disclosure: J. Curtis, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Lilly, Janssen, Myriad, Pfizer, Regeneron, Roche, and UCB, 2, 5, Amgen, 2, 5, Amgen Inc., 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, Genentech, 2, 5, Janseen, 5, Janssen, 2, 5, Janssen Research & Development, LLC, 2, Lilly, 2, 5, Myriad, 2, 5, Patient Centered Outcomes Research Insitute (PCORI), 2, Pfizer, 2, 5, Radius Health, Inc., 9, Regeneron, 2, 5, Roche, 2, 3, 5, Roche/Genentech, 5, UCB, 2, 5; **M. Weinblatt**, Abbvie, 5, AbbVie, 5, Amgen, 5, BMS, 2, 5, Bristol Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Canfite, 1, 4, Corrona, 5, Crescendo Bioscience, 2, 5, Eli Lilly and Company, 5, Gilead, 5, Glaxo-Smith Kline, 5, GlaxoSmithKline, 5, GSK, 5, Horizon, 5, Lilly, 5, Lily, 5, Lycera, 1, 4, 5, Merck, 5, Novartis, 5, Pfizer, 5, Roche, 5, Samsung, 5, Samsung Bioepis Co., Ltd., 5, Sanofi Regeneron, 2, Sanofi/Regeneron, 2, Sanofi-Regeneron, 2, Scipher, 1, 4, 5, Set Point, 5, SetPoint, 5, Squibb, 5, Vorso, 1; **K. Saag**, Abbvie, 5, AbbVie, 5, Amgen, 2, 5, Ampel, 2, Bayer, 5, Gilead, 5, Horizon, 2, 5, Ironwood/AstraZeneca, 2, 5, Kowa, 5, kowa, 5, Mereo, 2, Radius, 5, Radius Health, 2, 5, Roche/Genentech, 5, SOBI, 2, 5, Sobi, 2, 5, Takeda, 2, 5, Teijin, 5, Tejin, 5; **V. Bykerk**, AbbVie, 5, Amgen, 1, 2, 3, 5, 8, Brainstorm Therapeutics, 1, 2, 3, 5, 8, Bristol-Myers Squibb, 5, Genentech, 5, Gilead, 5, NIH, 2, Pfizer, 1, 2, 3, 5, 8, Regeneron, 5, Regeneron Pharmaceuticals, Inc, 5, Sanofi, 5, Sanofi/Genzyme-Regeneron, 5, Sanofi-Genzyme/Regeneron, 1, 2, 3, 5, 8, Scipher, 1, 2, 3, 5, 8, The Cedar Hill Foundation, 9, UCB, 1, 2, 3, 5, 8, UCB Pharma, 5; **C. Charles-Schoeman**, Abbvie, 2, AbbVie, 2, Amgen, 5, BMS, 2, Bristol Myers Squibb, 2, Gilead, 5, Octapharma, 2, 5, Pfizer, 2, 5, Regeneron, 5, Regeneron/Sanofi, 5, Sanofi, 5; **S. Fiore**, Sanofi, 1, 3; **G. St John**, Regeneron, 1, 3, 4, Regeneron Pharmaceuticals, Inc, 1, 3; **T. Kimura**, Regeneron, 1, 3, Regeneron Pharmaceuticals, Inc, 1, 3; **S. Zheng**, Sanofi, 3, 5; **C. Bingham**, Abbvie, 5, AbbVie, 5, BMS, 2, 5, Bristol Meyer Squibb, 2, 5, Bristol Myers-Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Eli/Lilly, 5, Genentech/Roche, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Pfizer Inc, 5, Regeneron/Sanofi, 5, Sanofi/Regeneron, 5; **G. Wright**, AbbVie, 5, 8, Abbvie, 5, 8, Amgen, 5, 8, Autoimmune, 5, 8, BMS, 5, 8, Exagen, 5, 8, Lilly, 5, 8, Myriad, 5, 8, Myriad Autoimmune, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Regeneron, 5, 8, Sanofi Genzyme, 5, 8, UCB, 5, 8; **M. Bergman**, Abbvie, 5, 8, AbbVie, 5, 8, AbbVie, BMS, Celgene Corporation, Genentech, Janssen, Merck, Novartis, Pfizer, Sanofi, 5, AbbVie, Celgene Corporation, Novartis, Pfizer, Sanofi, 8, Amgen, 5, 8, BMS, 5, 8, Celgene, 5, 8, Genentech, 5, Genentech/Roche, 5, 8, Genentech-Roche, 5, Gilead, 5, GlaxoSmithKline, 8, GSK, 8, Horizon, 5, Janssen, 5, 8, JNJ (parent of Janssen), 1, JNJ stock, 1, Johnson

& Johnson, 1, 4, Johnson and Johnson, 1, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Sandoz, 5, Sanofi, 5, 8, Sanofi/Regeneron, 5, 8, Sanofi-Regeneron, 5, 8; **K. Nola**, Coherus, 8, Gilead, 1, 5, Johnson & Johnson, 1, Proctor & Gamble, 1, Regeneron, 5, Sanofi Genzyme, 5; **D. Furst**, Actelion, 2, 5, Actelion Pharmaceuticals, 2, 5, Amgen, 2, 5, BMS, 2, 5, CME, 5, 8, Corbus, 2, 5, Galapagos, 2, 5, Galapogos Novartis, 5, GlaxoSmithKline, 2, GSK, 2, 5, NIH, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche/Genentech, 2, 5, Sanofi, 2, 5; **N. Shadick**, BMS, 2, Crescendo Biosciences, 2, Mallinckrodt, 2, Sanofi Regeneron, 2, Sanofi/Regeneron, 2.

Abstract Number: 2851

Limiting Factors of Reaching ACR/EULAR Boolean Remission in Early RA Patients Treated According to Current Recommendations

Nina Sundlisater,[1] Anna-Birgitte Aga,[2] Ulf Sundin,[3] Hilde Hammer,[1] Till Uhlig,[4] Tore Kvien,[4] Espen Haavardsholm,[4] and Siri Lillegraven[5], [1]Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Norway, [2]Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Oslo, Norway, [3]Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Norway. University of Oslo, Oslo, Norway, Oslo, Oslo, Norway, [4]Diakonhjemmet Hospital, Dept. of Rheumatology / University of Oslo, Faculty of Medicine, Oslo, Norway, [5]Diakonhjemmet Hospital, Dept. of Rheumatology, Oslo, Norway

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes IV: Outcomes
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: Abrogation of inflammation is important to prevent irreversible joint damage and maximize health-related quality of life in early RA patients. The ACR/EULAR Boolean remission criteria have the most stringent remission definition.(1) It has been reported that patient global assessment (PGA) is the variable most commonly scored above the cut-off in patients who almost fulfill the ACR/EULAR Boolean remission criteria.(2) Our objective was to assess which components of the ACR/EULAR Boolean criteria that most often limit attainment of remission in modernly treated early RA, and quantify the extent of subclinical inflammation in these patients.

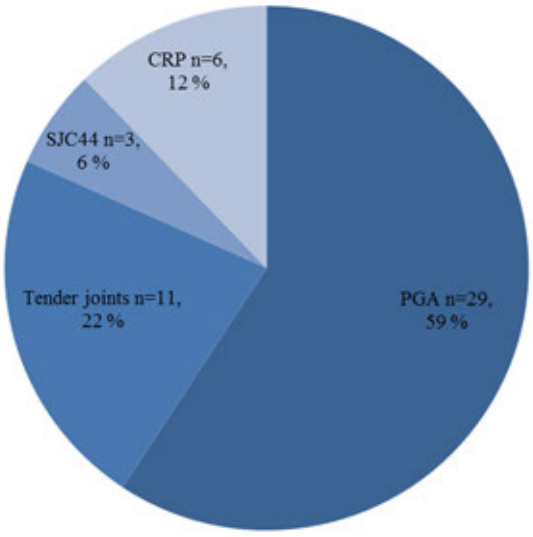
Methods: DMARD-naïve early RA patients included in the treat-to-target ARCTIC trial were followed by a strict tight control regime aiming for DAS remission and no swollen joints, with an additional target of ultrasound remission in half of the patients.(3) Examination of all patients included 44SJC, Ritchie articular index (RAI), laboratory tests, patient reported outcomes included physical function (PROMIS), ultrasound (US) of 32 joints and magnetic resonance imaging (MRI) of the dominant hand and wrist (scored according to RAMRIS). Patients with complete clinical data at the 2-year follow-up visit were included in the current analyses. We assessed the proportion of patients fulfilling ACR/EULAR Boolean remission (based on 44 joints) and the proportion of patients fulfilling three out of four remission criteria, and in such cases, which were the limiting factors. We compared physical function and imaging inflammation (assessed by US power Doppler score, US grey scale score, MRI synovitis and bone marrow edema) in patients reaching complete ACR/EULAR Boolean remission to patients not reaching ACR/EULAR Boolean remission due to the most often limiting factors. Chi2 test and Wilcoxon rank sum test were used for the comparisons.

Results: Of the 203 patients included, 62% were females, mean (SD) age was 52 (13) years, and 81% were ACPA positive. ACR/EULAR Boolean remission was achieved by 112 of 203 patients after 24 months (55%), while 49 (24%) fulfilled three of the four remission criteria. Among these 49 patients, the major limiting factor for not reaching remission was PGA (n=29, 59%), with tender joints as the second most common limiting factor (n=11, 22%) (Figure). In patients not achieving remission due to PGA, the median [IQR] PGA value was 3.1 [2, 4.4]. Subclinical inflammation measured by ultrasound and MRI was not significantly different for patients in ACR/EULAR Boolean remission

Table: Characteristic of patients in ACR/EULAR Boolean remission (N=112) and patients with SJC44≤1 & CRP≤1 (N=61) after two years of treat-to-target. Variables are median [IQR] unless otherwise stated. P-values <0.05 in bold.

	ACR/EULAR Boolean remission	SJC44≤1 + CRP≤1 + PGA >1 and/or tender joints >1	P-value for difference
Age	53.6 [41.1, 63.4]	53.3 [43, 61.2]	0.77
Female, n (%)	65 (58.0)	44 (72.1)	0.07
ACPA, n (%)	88 (78.6)	53 (86.9)	0.18
RF, n (%)	74 (66.1)	43 (70.5)	0.55
PROMIS physical function t-score	62.5 [50.0, 62.5]	45.3 [40.2, 50.0]	**<0.001**
Fatigue VAS (0-100)	3.5 [1.0, 12.0]	34.0 [17.0, 50.0]	**<0.001**
Physician's global (0-10)	0.2 [0.1, 0.8]	0.8 [0.4, 1.2]	**<0.001**
Ultrasound power Doppler score (0-96)	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.75
Ultrasound Grey Scale score (0-96)	3.0 [1.0, 5.5]	3.0 [0.0, 6.0]	0.69
MRI RAMRIS synovitis (0-39)	5.4 [3.7, 7.1]	5.0 [3.8, 6.2]	0.68
MRI RAMRIS bone marrow edema (0-105)	1.0 [0.0, 3.2]	1.8 [0.0, 3.2]	0.21

Figure: The proportion of patients with failure to fulfill the ACR/EULAR Boolean remission criteria due to one of the four components; tender joint count >1 or SJC44 >1 or CRP>1 mg/dl or PGA>1. N=49.



compared to patients not fulfilling these criteria due to PGA and /or tender joints (Table), but the latter reported more subjective symptoms such as fatigue and impaired physical function.

Conclusion: PGA and tender joints are the variables most often limiting patients from achieving ACR/EULAR Boolean remission, also in a treat-to-target setting with high remission rates. The level of subclinical inflammation is not elevated in these patients compared to patients in ACR/EULAR Boolean remission. Further research is still needed to assess which clinical remission criterion is best suited to guide treatment.

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Abstract Number: 2852

Shared and Differing Risk Factors for PsA, Psoriasis, AS, and RA: A Series of Case-control Studies

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical VI: Psoriatic Arthritis Clinical Studies
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: While a handful of clinical risk factors for the development of inflammatory diseases have been identified, to date, no studies have compared risk factors across multiple inflammatory diseases. The objective of this study was to compare the strength of association of selected potential risk factors for the development of psoriasis, PsA, RA, and AS.

Methods: We performed a series of case-control studies in The Health Improvement Network, a general practitioner database in the United Kingdom. Data between 1994-2015 were included. We identified patients with at least one code for PsA, RA, AS, or psoriasis using validated code lists and matched them to up to ten controls from the general population without these diseases based on age (within 2.5 years), sex, practice and year of diagnosis (controls were required to be in the practice on the diagnosis date and were assigned the same 'diagnosis date'). We began with an extensive code list of over 100 potential risk factors including common comorbidities, infections, trauma, and a limited number of medications (e.g., statins). Potential risk factors were assessed from the time of enrollment into a THIN practice until the end of the observation period, end of enrollment, or death. Hypothesized risk factors with a

Table 1. Demographics

		PsA Cases	PsA Controls	AS Cases	AS Controls	PsO Cases	PsO Controls	RA Cases	RA Controls
N		7,594	75,930	3,253	32,530	111,375	1,113,345	28,341	283,226
Age	Median	48.3	48.2	40.7	40.8	43.1	43.1	59.9	59.9
	IQR	(38.1 - 58.6)	(38.0 - 58.6)	(31.7 - 54.3)	(31.6 - 54.2)	(28.3 - 59.7)	(28.2 - 59.)6	(48.0 - 71.1)	(48.0 - 71.0)
Sex	Female	3,883 (51.1%)	38,830 (51.1%)	979 (30.1%)	9,790 (30.1%)	58,155 (52.2%)	581,356 (52.2%)	19,342 (68.2%)	193,342 (68.3%)
BMI	Mean (SD)	29.2 (6.4)*	27.9 (6.0)	27.0 (5.6)*	27.6 (5.7)	27.6 (6.3)*	27.3 (6.1)	27.5 (6.2)	27.5 (6.0)
Follow up (Years)	Median	7.2*	7.7	6.4*	6.9	6.7*	7.2	6.4*	6.9

Matched on age, sex, practice and calendar year of diagnosis; * p-value<0.001

Table 2. Univariable Odds Ratios in Match Case-Control Studies				
Risk Factor	PsA OR (95%CI)	AS OR (95%CI)	PsO OR (95%CI)	RA OR (95%CI)
BMI 25-30 (vs <25)	1.21 (1.13, 1.30)**	0.90 (0.82, 1.00)	1.06 (1.04, 1.08)**	0.94 (0.91, 0.97)**
BMI >=30 (vs <25)	1.59 (1.49, 1.70)**	0.77 (0.69, 0.86)**	1.15 (1.13, 1.17)**	0.97 (0.94, 1.01)
Current Smoker (v Nonsmoker)	0.99 (0.92, 1.06)	1.25 (1.15, 1.37)**	1.53 (1.50, 1.55)**	1.43 (1.38, 1.48)**
Past smoker (v Nonsmoker)	1.47 (1.40, 1.55)**	1.08 (0.99, 1.18)	1.46 (1.44, 1.48)**	1.39 (1.35, 1.42)**
Current alcohol (v Nondrinker)	1.34 (1.20, 1.50)**	1.08 (0.92, 1.26)	1.28 (1.25, 1.32)**	0.99 (0.94, 1.04)
Past alcohol (v Nondrinker)	1.75 (1.55, 1.98)**	1.40 (1.17, 1.68)**	1.32 (1.28, 1.36)**	1.34 (1.26, 1.41)**
Substance Abuse	0.66 (0.49, 0.89)*	0.77 (0.51, 1.15)	1.00 (0.94, 1.07)	0.91 (0.76, 1.09)
Trauma	1.13 (1.07, 1.20)**	1.02 (0.94, 1.12)	1.01 (1.00, 1.03)	0.97 (0.94, 1.00)
Trauma to foot	1.25 (1.12, 1.40)**	0.92 (0.75, 1.12)	1.04 (1.00, 1.07)	1.11 (1.04, 1.19)**
Trauma to hand	1.24 (1.09, 1.41)**	1.05 (0.86, 1.28)	1.09 (1.05, 1.13)**	1.28 (1.18, 1.37)**
Trauma to joint	1.40 (1.29, 1.51)**	1.19 (1.05, 1.34)**	1.07 (1.05, 1.10)**	1.28 (1.23, 1.34)**
Trauma to skin	1.13 (1.03, 1.25)*	0.96 (0.82, 1.12)	1.11 (1.08, 1.14)**	0.99 (0.94, 1.04)
Fracture	0.91 (0.84, 0.99)	0.94 (0.82, 1.07)	0.85 (0.84, 0.87)**	0.73 (0.70, 0.77)**
Osteoporosis	1.05 (0.86, 1.27)	2.73 (1.99, 3.74)**	0.76 (0.72, 0.81)**	1.15 (1.08, 1.23)**
Menopause	1.15 (1.01, 1.32)*	0.92 (0.64, 1.33)	1.08 (1.03, 1.13)**	1.24 (1.16, 1.33)**
Hysterectomy	1.68 (1.45, 1.94)**	1.39 (0.97, 2.00)	1.34 (1.27, 1.41)**	1.53 (1.42, 1.64)**
Thyroid disease	1.38 (1.23, 1.55)**	0.98 (0.76, 1.26)	1.08 (1.04, 1.12)**	1.39 (1.32, 1.46)**
Acne	1.08 (0.95, 1.23)	1.27 (1.07, 1.51)**	0.96 (0.93, 0.98)*	0.98 (0.90, 1.06)
Anemia	1.12 (1.00, 1.25)	1.64 (1.37, 1.96)**	0.70 (0.67, 0.72)**	1.21 (1.15, 1.27)**
Gout	2.36 (2.11, 2.64)**	0.74 (0.56, 0.97)	0.93 (0.89, 0.97)*	1.38 (1.30, 1.48)**
Diabetes	0.85 (0.78, 0.92)**	0.67 (0.57, 0.78)**	0.71 (0.69, 0.73)**	0.72 (0.69, 0.75)**
Hyperlipidemia	0.90 (0.82, 0.99)	0.72 (0.61, 0.87)**	0.87 (0.84, 0.89)**	0.78 (0.75, 0.82)**
Statin use	0.63 (0.59, 0.67)**	0.53 (0.47, 0.60)**	0.61 (0.60, 0.62)**	0.51 (0.49, 0.52)**
Hypertension	0.99 (0.92, 1.05)	0.88 (0.79, 0.99)	0.91 (0.90, 0.93)**	0.87 (0.85, 0.90)**
Myocardial infarction	0.90 (0.71, 1.13)	1.13 (0.80, 1.58)	0.89 (0.84, 0.95)**	0.83 (0.75, 0.92)**
Urethritis	1.22 (0.78, 1.89)	1.25 (0.60, 2.61)	1.00 (0.87, 1.13)	1.06 (0.85, 1.32)
Uveitis	3.56 (2.78, 4.56)**	45.00 (35.29, 57.39)**	1.29 (1.16, 1.43)**	1.83 (1.57, 2.13)**
IBD	1.05 (0.81, 1.37)	5.99 (4.84, 7.42)**	1.11 (1.03, 1.19)*	1.66 (1.48, 1.85)**
Diarrhea	1.14 (1.06, 1.23)**	1.15 (1.01, 1.30)*	0.93 (0.91, 0.95)**	0.92 (0.88, 0.96)**
GI infection	1.23 (1.10, 1.38)**	1.37 (1.15, 1.63)**	1.05 (1.02, 1.08)**	1.09 (1.02, 1.16)*
GU infection	1.32 (1.16, 1.51)**	1.19 (0.94, 1.51)	1.22 (1.18, 1.27)**	1.08 (1.00, 1.16)
Pharyngitis	1.46 (1.35, 1.58)**	1.25 (1.11, 1.41)**	1.30 (1.28, 1.32)**	1.33 (1.27, 1.40)**
Skin Infection	1.44 (1.37, 1.53)**	0.89 (0.80, 0.99)	1.15 (1.14, 1.17)**	0.95 (0.92, 0.98)**
Any liver disease	1.02 (0.80, 1.29)	1.07 (0.72, 1.59)	0.74 (0.69, 0.81)**	0.75 (0.65, 0.87)**
Depression	1.29 (1.21, 1.37)**	1.11 (1.00, 1.23)	1.05 (1.03, 1.07)**	1.14 (1.10, 1.17)**
Back Pain	1.17 (1.11, 1.24)**	606.83 (386.41, 952)**	0.90 (0.88, 0.91)**	1.01 (0.98, 1.04)
In this analysis, we only included risk factors with a prevalence of 1% in the control population. Highlighted in yellow are those with an effect size >1.15 or <0.75 and significant association with p value<0.01. P values <0.001 have two asterisks and <0.02 have one asterisk.				

prevalence of ≥1% were included in the final models and tables. Univariable logistic regression was used to screen risk factors for association with the disease of interest. Multiple testing was accounted for by setting a p-value of 0.02 as the level of statistical significance. Finally, a multivariable logistic regression model was constructed for each disease using the significant risk factors, stratified by sex.

Results: Demographics of the patient population are shown in Table 1. 7,594 incident PsA cases, 3, 253 incident AS cases, 111,375 incident psoriasis cases, and 28,341 incident RA cases were identified and matched to 75,930, 32,530, 1,113,345, and 282,226 controls respectively. Median age at diagnosis was 48.3 (IQR 38-59), 40.7 (31-54), 43.1 (31-54), and 59.9 (48-71) respectively. Sex was balanced in psoriasis and PsA but more female in RA (68%) and more male in AS (70%). Mean follow up time ranged from 6.4-7.2 years and was slightly longer among controls. In univariable analyses (Table 2), previously identified risk factors in PsA were replicated including obesity, uveitis, and trauma. Smoking was identified as a risk factor in RA as previously described. There were some similar risk factors

across all 4 diseases including a positive association between pharyngitis, IBD and uveitis (strongest for AS and PsA) and a similarly strong protective effect of statins. Skin infections were associated with PsA and psoriasis, skin trauma with psoriasis and joint trauma with PsA. Diarrheal infections were associated with PsA and AS. Most risk factors maintained statistical significance in the multivariable models though final models differed slightly by sex.

Conclusion: This set of parallel case-control studies identifies differences between PsA, psoriasis, AS and RA that supports the previous theories of pathophysiologic triggers related to these diseases but also demonstrates some commonalities between diseases.

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Abstract Number: 2853

The Pattern of Musculoskeletal Complaints in Patients with Suspected Psoriatic Arthritis and Their Correlation with Physical Examination and Ultrasound

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Table 1 – Musculoskeletal symptoms and patient reported outcomes by disease status

Variable	All (N=203)	Not PsA (N=137)	Possible PsA (N=48)	PsA (N=18)	P value PsA vs. Possible/Not PsA
Prolonged MSK pain (>2 years)	111 (56.1%)	73 (54.9%)	27 (57.5%)	11 (61.1%)	P=0.80
Duration of joint pain (years)	3.5 (8.5)	3.6 (9)	3 (1.5)	3.6 (8.2)	P=0.80
Duration of back pain (years)	6.9 (14.6)	6.1 (14.7)	8.6 (12.4)	12.5 (11)	P=0.31
Presence of morning stiffness	152 (77.2%)	102 (77.2%)	36 (76.6%)	14 (77.8%)	P=1
Duration joint stiffness>1 hour	32 (15.7%)	19 (13.9%)	8 (16.7%)	5 (27.8%)	P=0.17
Duration back stiffness >1 hour	35 (17.2%)	25 (18.3%)	8 (16.7%)	2 (11.1%)	P=0.74
Peripheral joint pain	183 (90.2%)	121 (88.3%)	45 (93.8%)	17 (94.4%)	P=1
Heel pain	76 (37.4%)	46 (33.6%)	24 (50%)	6 (33.3%)	P=0.80
Axial pain	168 (82.8%)	114 (83.2%)	41 (85.4%)	13 (72.2%)	P=0.21
Back stiffness	114 (56.2%)	71 (51.8%)	4 (70.8%)	9 (50%)	P=0.62
Inflammatory back pain	54 (26.6%)	31 (22.6%)	19 (39.6%)	4 (22.2%)	P=0.79
PSAID score	**2.5 (4.3)**	**2.2 (3.6)**	**2.6 (5)**	**5.3 (3.2)**	**P=0.004**
FACIT Fatigue scale	**38 (16)**	**40 (14)**	**38 (17)**	**30 (9.5)**	**P=0.02**
SF-36 (PCS)	43.5 (16.5)	43 (17.8)	45.4 (12.5)	46.3 (15)	P=0.77
SF-36 (MCS)	**46.7 (18)**	**47.9 (17)**	**45.1 (20.4)**	**40.7 (13.3)**	**P=0.02**
DLQI	**4 (8)**	**4 (7.5)**	**6 (11)**	**9.5 (14)**	**P=0.002**
Pain score (0-10)	3 (4)	3 (4)	4 (3)	5.5 (4)	P=0.16
HAQ	**0.25 (0.63)**	**0.13 (0.63)**	**0.25 (0.62)**	**0.50 (0.50)**	**P=0.06**

DLQI- dermatology life quality index; FACIT - Functional Assessment of Chronic Illness Therapy; HAQ – health assessment questionnaire; MSK-musculoskeletal; PsA – psoriatic arthritis; PSAID – Psoriatic arthritis impact of diseases; SF-short form;

SESSION INFORMATION
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Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Table 2 – Comparison of patient characteristics by ultrasound inflammation (at least 1 joint or entheseal site with positive Doppler)

Variable	Ultrasound inflammation negative (N=83)	Ultrasound inflammation positive (N=120)	P value
Age (years)	**45 (14)**	**54.8 (13)**	**<0.0001**
Sex: Female	25 (30.1%)	45 (37.5%)	0.28
Prolonged musculoskeletal pain (>2 year)	43 (52.4%)	68 (58.6%)	0.39
Use of non-biologic medications for psoriasis	4 (4.8%)	3 (2.5%)	0.37
Use of biologic medications	9 (10.8%)	13 (10.8%)	0.99
Severe psoriasis (PASI>10)	15 (18.1%)	20 (16.7%)	0.79
Duration of joint pain	6.5 (8.3)	6.9 (8.3)	0.75
Duration of back pain	10.2 (10.9)	10.9 (10.5)	0.73
Morning stiffness	**43 (51.8%)**	**81 (67.5%)**	**0.02**
Duration morning stiffness>1 hour	12 (14.5%)	20 (16.7%)	0.67
Duration back stiff >1 hour	15 (18.1%)	20 (16.7%)	0.79
Peripheral joint pain	74 (89.2%)	109 (90.8%)	0.69
Heel pain	35 (42.2%)	41 (34.2%)	0.25
Axial pain	69 (83.1%)	99 (82.5%)	0.91
Back stiffness	41 (49.4%)	73 (60.8%)	0.11
Inflammatory back pain	24 (28.9%)	30 (25%)	0.53
BMI (kg/m^2)	29.6 (7.1)	29 (6.1)	0.55
Nail psoriasis	30 (36.6%)	49 (40.8%)	0.54
Pitting	21 (25.6%)	31 (26.1%)	0.94
Onycholysis	9 (11%)	25 (21%)	0.06
PASI score	**3 (3.1)**	**4.4 (6.4)**	**0.04**
Tender joint count	**1.9 (2.5)**	**3.3 (4.1)**	**0.003**
Swollen joint count	**0.3 (0.8)**	**1.3 (2.3)**	**<0.0001**
Clinical Enthesitis count	1.5 (2.4)	1.6 (2.2)	0.83
Fibromyalgia	1 (1.2%)	3 (2.5%)	0.52
CRP (mg/dL)	3.8 (4.3)	4 (8.6)	0.85
ESR (mm/hr)	13.4 (9.4)	12.9 (9.4)	0.70
PSAID score	3.5 (3.3)	3.4 (2.7)	0.83
FACIT fatigue score	35.4 (11.3)	35.6 (11.2)	0.91
SF-36 (PCS)	44.6 (10.5)	42.9 (9.9)	0.28
SF-36 (MCS)	43.2 (10.9)	44.4 (10.8)	0.47
DLQI	6.6 (6.3)	6.7 (6.5)	0.87
Pain score (0-10)	3.5 (2.3)	4.2 (2.5)	0.32
HAQ	**0.3 (0.4)**	**0.4 (0.4)**	**0.02**

BMI- body mass index; CRP- C-reactive protein; DLQI- dermatology life quality index; ESR- erythrocyte sedimentation rate; FACIT - Functional Assessment of Chronic Illness Therapy; HAQ – health assessment questionnaire; PASI-psoriasis arear and severity index; PSAID – Psoriatic arthritis impact of diseases; SF-short form

Table 3 – Agreement between methods of joint/enthesis assessment (50 tender or swollen joints on physical examination, the presence of positive Doppler on ultrasound)

Method 1	Method2	Kappa (95% CI)	% positive agreement	% of negative agreement	PABAK
Rheumatologist	Physiotherapist	0.28 (0.21, 0.35)	0.31	0.97	0.87
Rheumatologist	Ultrasound	0.11 (0.05, 0.17)	0.18	0.92	0.71
Rheumatologist	Patient	0.12 (0.09, 0.15)	0.16	0.91	0.68
Physiotherapist	Patient	0.18 (0.15, 0.22)	0.26	0.90	0.65
Physiotherapist	Ultrasound	0.08 (0.03, 0.12)	0.21	0.84	0.46
Patient	Ultrasound	0.08 (0.04, 0.12)	0.21	0.81	0.39

PABAK - Prevalence Adjusted and Bias Adjusted Kappa

Background/Purpose: There is limited information about the constellation of musculoskeletal symptoms experienced by patients with early psoriatic arthritis (PsA). This study aims to describe the pattern of musculoskeletal symptoms and their correlation with clinical and sonographic findings among psoriasis patients with suspected PsA.

Methods: The study evaluated patients with psoriasis and musculoskeletal complaints who did not have a prior diagnosis of PsA. These patients were evaluated in a rapid access clinic that included a central triage system using the following modalities: 1) screening questionnaires that included homunculus where patients marked the location of the affected joints, 2) assessment by an advanced practice physiotherapist, 3) musculoskeletal ultrasound (MSK-US) of joints and entheses. In addition, patients completed questionnaires about the nature and duration of their musculoskeletal symptoms, physical function and quality of life. All patients were then assessed by a rheumatologist who classified each patient to: “PsA”, “Not PsA”, or “Possibly PsA”. Agreement between modalities was assessed using Kappa statistics.

Results: 203 patients with psoriasis and musculoskeletal symptoms were enrolled in the study. 18 (8.8%) and 48 (23.6%) were classified as “PsA and “possible PsA”, respectively. There was no difference between the two groups in the presence, distribution and duration of musculoskeletal pain (Table 1). Patients with PsA had higher intensity of musculoskeletal and skin-related symptoms (DLQI) and worse scores in domains such as physical function (HAQ), quality of life (PSAID) and fatigue (FACIT). Patients who were classified as “PsA” were more likely to use systemic medications for psoriasis (< 0.05), have severe psoriasis (p=0.02) and nail lesions (p=0.02) and have synovitis/enthesitis by MSK-US (p=0.01). Patients with positive MSK-US inflammation were older (p< 0.001), reported more joint stiffness (p=0.02) and physical dysfunction (by HAQ, p=0.02, Table 2), irrespective of the clinical diagnosis. Analysis of agreement between modalities revealed the strongest agreement between the rheumatologist and physiotherapist (k=0.28, Table 3). The lowest levels of agreement were found between ultrasound and patient (k=0.08) and physiotherapist and ultrasound (k=0.08).

Conclusion: The intensity, rather than the type, duration or distribution of musculoskeletal symptoms, is associated with psoriatic arthritis among patients with psoriasis. The correlation between musculoskeletal symptoms, patient reported outcomes and sonographic findings is poor in patients with suspected PsA. MSK-US provides additional information to the clinical assessment and aid in diagnosing PsA patients at earlier stages.

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Abstract Number: 2854

Delay Between the Onset of Psoriasis and Arthritis in PsA Patients from the PsART International Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical VI: Psoriatic Arthritis Clinical Studies

Session Type: ACR Abstract Session

Session Time: 4:30PM–6:00PM

Background/Purpose: Psoriatic arthritis is a heterogenous disorder not only with respect to patterns and components of musculoskeletal involvement but also with respect to types of skin involvement and the timing of joint and skin disease. The interrelationships between characteristics of skin psoriasis, arthritis and the timing of arthritis are not well studied; we therefore sought to explore these in a large international cohort.

Methods: PsART-international is a web-based registry of PsA patients under routine care in Turkey, Italy and Canada including detailed disease history about type and onset of skin and joint disease. We extracted data on demographic characteristics, family history of psoriatic disease (regardless of skin or arthritis) , types of skin psoriasis, site of skin psoriasis onset, and components of psoriatic arthritis ever observed. For descriptive purposes we tabulated patient characteristics in three groups; arthritis-first, psoriasis-first and synchronous, the latter indicating the onset of skin and joint disease within 12 months. The primary analysis outcome was the absolute time elapsed in months after skin disease to arthritis (negative values indicating arthritis onset before psoriasis). We constructed a linear regression model for this primary outcome using demographic, skin disease and arthritis characteristics to explore the associations.

Table-1 Patient characteristics

		Arthrtitis first	Psoriasis first	Synchronous	Overall
N		71	1251	309	1631
Education years, mean (SD)		9.8 (4.8)	9.4 (4.8)	10 (4.7)	9.5 (4.8)
Age at PsA, mean(SD)		40.8 (13)	42.2 (13.5)	40.2 (13.7)	41.8 (13.5)
Age at Pso, mean(SD)		46.3 (12.3)	29.4 (14.8)	40.1 (13.7)	32.2 (15.4)
Delay, mean(SD)		-67.4 (60.9)	155.6 (125.8)	1.8 (3.9)	116.7 (132)
PsA duration, mean(SD		11.4 (8.7)	4.6 (6.4)	6.5 (7.9)	5.3 (7)
BMI		29.3 (5.1)	28.1 (5.2)	28.6 (5.5)	28.2 (5.2)
Male gender		30 (42.3)	473 (37.8)	103 (33.3)	606 (37.2)
Smoking status	Current	15 (21.1)	256 (20.5)	60 (19.4)	331 (20.3)
	Ex-smoker	17 (23.9)	239 (19.1)	65 (21)	321 (19.7)
	Never	36 (50.7)	671 (53.6)	160 (51.8)	867 (53.2)
PsA Involvement,N(%)	DIP involvement	9 (12.7)	176 (14.1)	55 (17.8)	240 (14.7)
	Dactylitis	17 (23.9)	292 (23.3)	59 (19.1)	368 (22.6)
	Polyarthritis	24 (33.8)	618 (49.4)	147 (47.6)	789 (48.4)
	Oligoarthritis	32 (45.1)	384 (30.7)	91 (29.4)	507 (31.1)
	Monoarthritis	0 (0)	41 (3.3)	9 (2.9)	50 (3.1)
	Arthritis mutilans	0 (0)	3 (0.2)	1 (0.3)	4 (0.2)
	Axial involvement	27 (38)	360 (28.8)	86 (27.8)	473 (29)
Skin involvement,N(%)	Pustular type,N(%)	13 (18.3)	149 (11.9)	51 (16.5)	213 (13.1)
	Plaque type,N(%)	45 (63.4)	735 (58.8)	163 (52.8)	943 (57.8)
	Flexural type, N(%)	2 (2.8)	24 (1.9)	9 (2.9)	35 (2.1)
	Inverse psoriasis, N(%)	4 (5.6)	19 (1.5)	3 (1)	26 (1.6)
	Erythrodermic psoriasis	3 (4.2)	71 (5.7)	17 (5.5)	91 (5.6)
	Nail involvement,N(%)	34 (47.9)	616 (49.2)	124 (40.1)	774 (47.5)
Initial lesion,N(%)	Scalp	25 (35.2)	604 (48.3)	123 (39.8)	752 (46.1)
	Torso	9 (12.7)	235 (18.8)	48 (15.5)	292 (17.9)
	Extremity	46 (64.8)	736 (58.8)	178 (57.6)	960 (58.9)
	Genital	9 (12.7)	77 (6.2)	15 (4.9)	101 (6.2)

Table-2 Regression analysis for the delay between onset of psoriasis and arthritis.

Term	Estimate	P	Conf. limits	
			5%	95%
(Intercept)	65.3	<0.001	40.7	89.9
Female	8.8	0.229	-5.6	23.3
Nail involvement	27.3	<0.001	13.2	41.4
Skin psoriasis type				
Erythrodermic	15.5	0.313	-14.6	45.5
Flexural	-11.3	0.682	-65.3	42.8
Inverse	-18.9	0.542	-79.8	41.9
Plaque	20.0	0.012	4.3	35.7
Pustular	-28.7	0.009	-50.4	-7.1
Initial skin involvement				
Scalp	12.4	0.122	-3.3	28.1
Torso	5.4	0.550	-12.4	23.2
Extremity	11.9	0.168	-5.0	28.7
Genital	-6.3	0.678	-36.3	23.6
Family history	24.7	0.001	9.9	39.4
DIP involvement	-4.3	0.671	-24.0	15.5
Dactylitis	11.2	0.180	-5.2	27.6

Results: We included 1631 patients; 71 had arthritis first, 309 had synchronous onset and 1251 had psoriasis first. Data shows that the age of psoriasis onset and not that of arthritis determined whether arthritis or psoriasis would be the first to appear (Table-1). Results of the regression analysis shows that the model intercept, delay of arthritis after psoriasis when other independent variables are set to their baseline values, is 65 months, pustular psoriasis is associated with onset of arthritis circa 2 years earlier than the intercept interval whereas nail involvement, plaque psoriasis or family history of psoriasis are associated with an increased delay from psoriasis to arthritis, by approximately 2 years-each (Table-2). Adding all types of articular involvement into the model did not cause a material change in the point estimates however reduced the precision of terms for skin psoriasis type (data not shown).

Conclusion: The age of psoriasis determines whether arthritis or psoriasis starts first in PsA patients. Pustular psoriasis is associated with a shorter time interval after psoriasis to arthritis while nail involvement, plaque psoriasis and psoriatic family history are associated with a longer interval.

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Abstract Number: 2855

Clinically Relevant Patient Clusters Identified by Machine Learning Tools in a Large Database from the Secukinumab Psoriatic Arthritis Clinical Development Program

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

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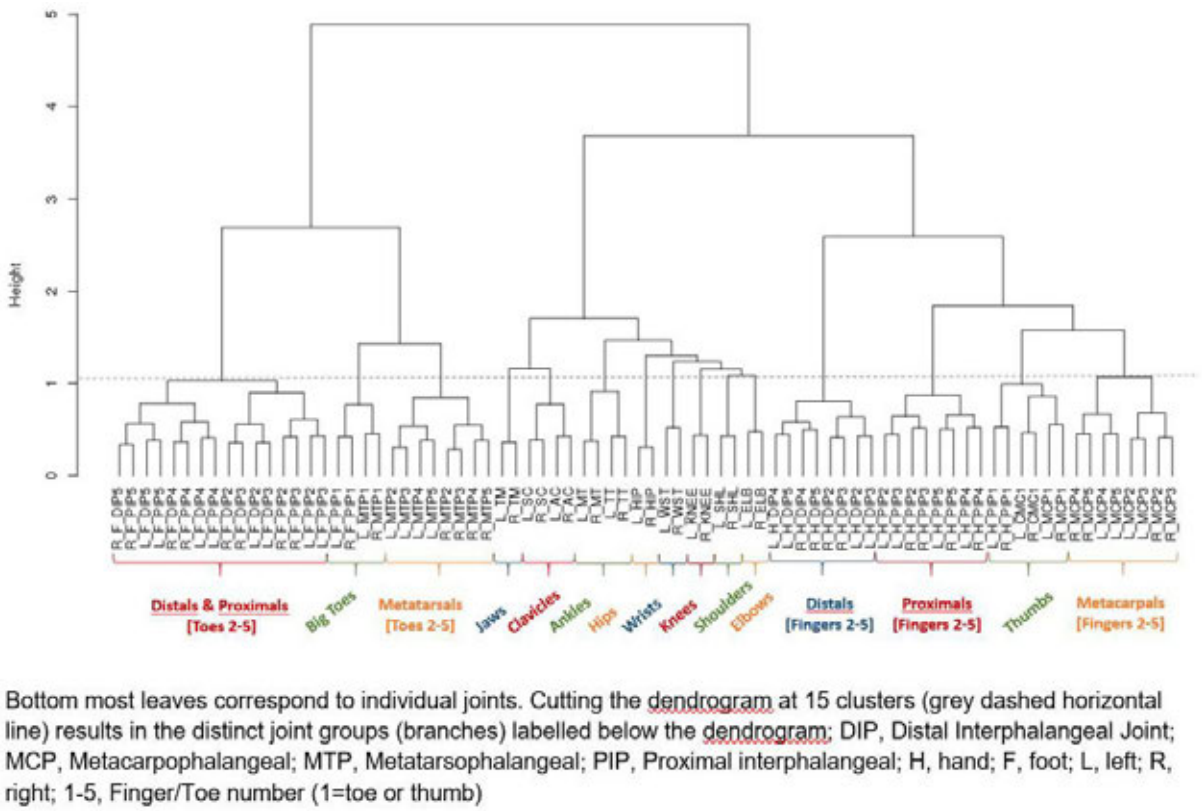
Session Time: 4:30PM–6:00PM

Background/Purpose: Identifying clinically relevant patient phenotypes amidst the variability and heterogeneity of the clinical manifestations of psoriatic arthritis (PsA) is currently challenging. Using machine-learning (ML) techniques could be the first critical step towards better understanding of disease pathotypes, and support progression towards precision medicine.[1] Clusters of PsA patients based on presence/absence of disease domains were identified using ML from the secukinumab FUTURE trials program.

Methods: Hierarchical clustering was performed on the composite using "1-correlation" as the dissimilarity metric and Ward's agglomeration method for pairwise grouping; a dendrogram was used to visualize and assess the resulting groupings. Pairwise correlations were explored in various clinical domains of PsA including dactylitis, NAPSI,



Bottom most leaves correspond to individual joints. Cutting the dendrogram at 15 clusters (grey dashed horizontal line) results in the distinct joint groups (branches) labelled below the dendrogram; DIP, Distal Interphalangeal Joint; MCP, Metacarpophalangeal; MTP, Metatarsophalangeal; PIP, Proximal interphalangeal; H, hand; F, foot; L, left; R, right; 1-5, Finger/Toe number (1=toe or thumb)

Figure 1. Dendrogram of Hierarchical Clustering of 78 Joints

PASI, enthesitis, swollen or tender joints, spondylitis, and CRP measurements from >2,700 patients across five phase 3 studies with ≈425,000 data entries at baseline and were visualized using heatmaps. Mixture (of Bernoullis) Model was applied to obtain the clusters across all domains. The model assumes that two patients share a cluster only if they have similar probability of presence of symptom across all clinical domains.

Results: The hierarchical clustering algorithm grouped the 78 individual joints into distinct and natural clusters. At higher level of the dendrogram, the algorithm grouped separately all foot, larger (jaws, clavicles, ankles, hips, wrists, knees, shoulders, elbows), and hand joints. An example for hierarchical clustering of 78 joints is shown in **Figure 1.** Cutting the dendrogram at 15 clusters separated all the joints into distinct groups; hand joints (distal and proximal phalanges, metacarpals and thumbs), and foot joints (distal and proximal phalanges, metatarsals and big toes). Associations of the joint clusters with other disease manifestations such as skin and nail involvement revealed distinct patient clusters, enabling to investigate differences in disease pathogenesis and treatment outcomes. For example, in one of the clusters with patients having high polyarticular burden (high number of affected joints), there was a high probability of nail involvement and psoriasis. These clusters were further refined when response to treatment over time was added in the model.

Conclusion: Machine learning methodology confirmed a natural grouping of joints in patients with psoriatic arthritis based on baseline swelling and tenderness and revealed complex correlation patterns. Additional cluster analyses including psoriatic arthritis disease manifestations and response to treatment revealed distinct patient clusters with potential clinical implications.

Reference: 1. Grys BT et al., *J Cell Biol.* 2017; 216(1): 65-71.

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Abstract Number: 2856

Drug Retention of Biological DMARDs Targeting IL-12/IL-23 or IL-17 versus TNF Inhibitors, After a First Line TNF Inhibitor, in Patients with Psoriatic Arthritis – an Analysis in the Swiss SCQM Register

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical VI: Psoriatic Arthritis Clinical Studies

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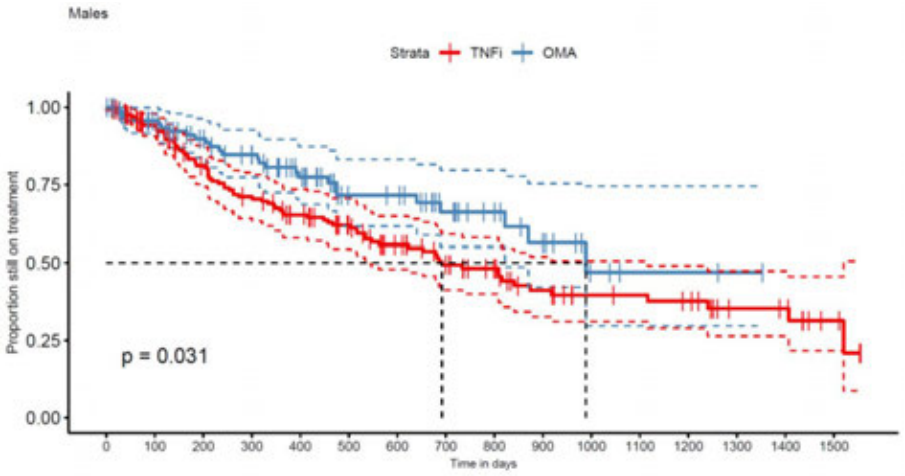
Session Time: 4:30PM–6:00PM

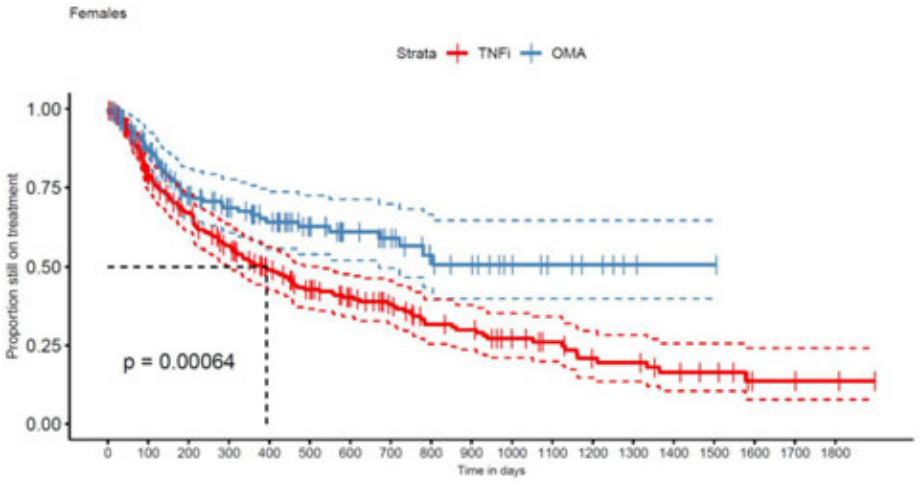
Background/Purpose: Tumor necrosis factor inhibitors (TNFi) were the first approved biological disease modifying antirheumatic drugs (bDMARDs) for psoriatic arthritis (PsA). IL-12/23 and IL-17-specific antibodies provide another mode of action (OMA) than TNFi and were more recently approved for PsA. In 2018, ACR recommended TNFi as a first-line treatment option for PsA. Here, we aimed to compare these two bDMARD classes for PsA in a real world setting.

We hypothesized that response to a bDMARD rather depends on the disease-related activation of a target than the pharmacological profile of different inhibitors for the same target. Consequently, we postulated better drug persistence of OMA bDMARDs than another TNFi bDMARD after having stopped a TNFi either for lack of efficacy or tolerability reasons.

Methods: We analyzed all available bDMARD treatment courses (TC) of PsA patients in the Swiss register for Clinical Quality Management in Rheumatology (SCQM), after date of launch of the first OMA bDMARD in 2014 and after use of a first TNFi. We estimated drug retention by using Kaplan-Meier plots and equality of survival using Log-Rank tests. After multiple imputation of missing covariates, we included line of bDMARD treatment with two levels, 2nd



Kaplan-Meyer plot for drug retention in male



Kaplan-Meyer plot for drug retention in female

versus 3rd or later line of therapy, smoking, age, BMI and disease activity score (DAS28-CRP) baseline covariates together with the bDMARD treatment category into adjusted models

Results: A total of 663 TC from 449 patients met our inclusion criteria, with 422 TNFi TCs and 241 OMA bDMARD TCs. An IL-12/IL-23 inhibitor was used in 97 and an IL-17i specific compound in 144 OMA bDMARD TCs. At baseline, median DAS28-CRP was 2.7 [1.9; 3.9] in the TNFi group and 3.2 (2.5; 4.0) in the OMA bDMARD group (p=0.02). Furthermore, TNFi were more frequently used as a second line treatment (n=191, 45%) than OMA bDMARDs (n=53, 22%). TNFi TCs (n=397, 94%) were more frequently observed in OMA bDMARD naïve patients, but OMA bDMARD TCs were more frequent after another previous OMA bDMARD TC (n= 198, 82%, p< 0.0001). Other covariates such as sex (399 women and 264 men, p = 0.87), smoking status (n=90, p=0.30), median age (51 [42; 59] years, p = 0.25) and BMI at baseline (28 [24; 31.5] kg/m2, p = 0.57), were similarly distributed between the two treatment groups. In the crude analyses, the estimate of median drug retention time was 516 days for TNFi as compared to 989 days for the OMA bDMARD group (p < 0.0001). OMA bDMARDs had a longer drug retention both in men (p=0.031, Fig 1) and women (p< 0.001, Fig 2). In multivariable-adjusted analyses in 208 TNFi and 111 OMA bDMARD TCs, OMA bDMARDs were on average late discontinued than TNFi (HR=0.49 [0.33, 0.72], p< 0.001), but second line indication (HR=1.44 [1.02, 2.03]) and male sex (HR= 1.52 [1.07, 2.15] were associated with better drug retention rates.

Conclusion: After use of a first TNFi, OMA bDMARDs displayed better drug retention in PsA than another TNFi. As OMA bDMARD were more often used in less favorable later line indication, they appear according to this analysis as the preferential choice among the alternative bDMARD treatment options in TNFi experienced patients.

Disclosure: B. Moeller, AbbVie, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Merck, 2, 8, Novartis, 2, 8, Pfizer, 2, 8, UCB, 2, 9; **E. Papagiannoulis**, None; **L. Christ**, None; **A. Ciurea**, AbbVie, 5, Celgene, 5, Eli Lilly, 5, Janssen-Cilag, 5, MSD, 5, Novartis, 5, Pfizer, 5, UCB, 5; **T. Hugle**, None; **R. Mueller**, None; **M. Nissen**, Abbvie, Celgene, Lilly, MSD, Novartis, Pfizer, 5, 8; **A. Scherer**, None; **G. Scholz**, None; **P. Villiger**, Novartis, 2; **N. Yawalkar**, None.

Abstract Number: 2857

Decision Tree Analysis to Identify Inflammatory Arthritis Patient Subgroups with Different Levels of Treatment Persistence with First-Line Subcutaneous TNF-alpha Inhibitors

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SESSION INFORMATION
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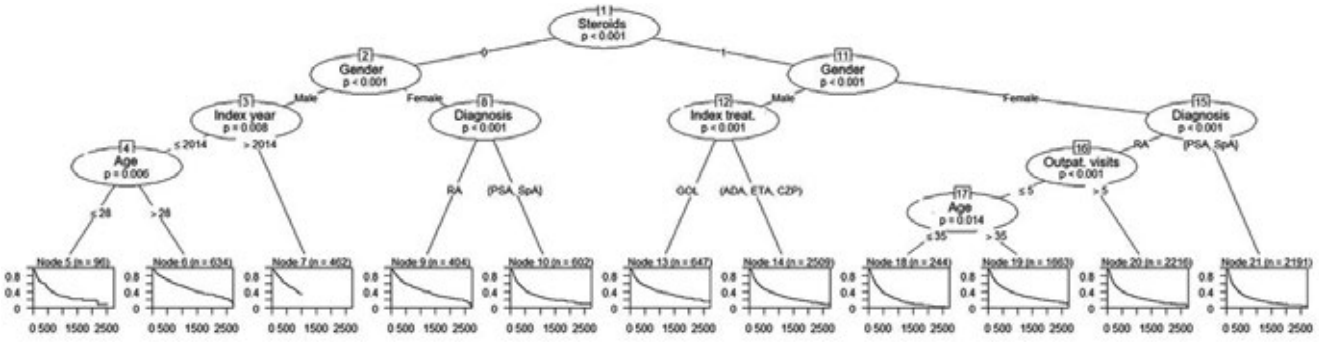
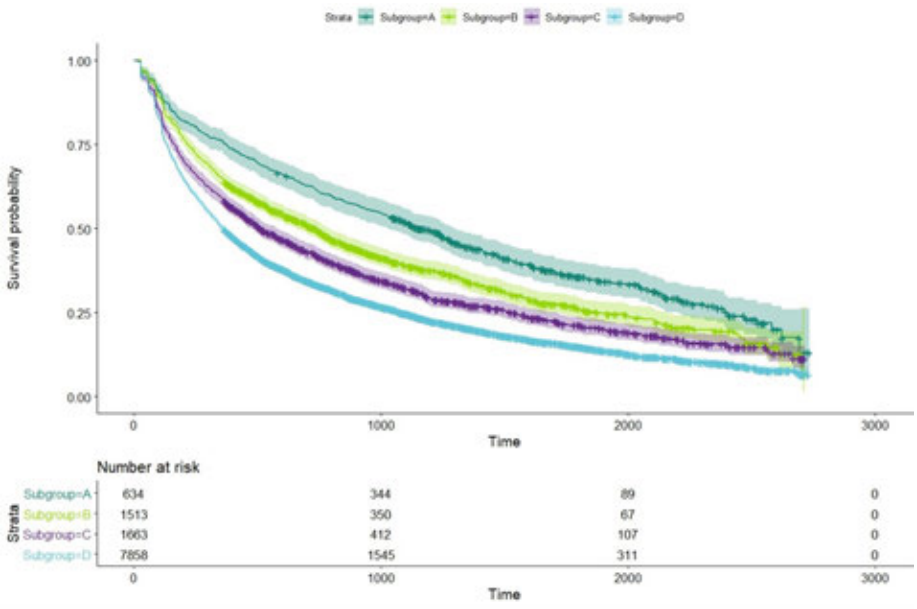
Session Type: ACR Abstract Session
Session Time: 4:30PM–6:00PM

Background/Purpose: The advent of biologic medications, such as subcutaneous TNF-alpha inhibitors (SC-TNFi), has transformed the management of inflammatory arthritis (IA) during the last decades. However, a significant proportion of patients with IA fail to respond, lose response, or experience adverse events while being treated with a biologic, and may therefore be required to discontinue or switch treatment. The aim of this study was to identify IA patient subgroups with different levels of treatment persistence through decision tree analysis using recursive partitioning methods.

Methods: Using data from Swedish Health Data Registers, adult, biologic treatment-naïve patients initiating treatment for IA with any available SC-TNFi (adalimumab, etanercept, certolizumab, and golimumab) between May 1, 2010 and October 31, 2016 were included. Treatment persistence was derived based on information from filled prescriptions (e.g. dispensing date, pack information, and defined daily dose) and a grace period of 60 days. A number of covariates were derived from data collected in the year prior to treatment initiation, including Charlson Comorbidity Index and its components, number of visits and inpatient stays in specialized care, and treatment initiation year, and



Decision tree for drug persistence in IA patients. GOL=golimumab, ADA=adalimumab, ETA=etanercept, CZP=certolizumab pegol, RA=rheumatoid arthritis, PsA=psoriatic arthritis, SpA=spondyloarthritis



Drug persistence for combination of terminal nodes into groups. Group A=node 6, group B=nodes 7, 13 and 9, group C=node 19, group D=nodes 14, 5, 10, 20, 18 and 21. Patient characteristics by node are presented in Figure 1.

filled prescriptions for systemic corticosteroids, DMARDs and/or NSAIDs. In addition, age at treatment initiation, sex, IA diagnosis [spondyloarthritis (SpA) / psoriatic arthritis (PsA) / rheumatoid arthritis (RA)], index biologic treatment were included as covariates in the analysis. The decision tree was created through recursive partitioning, and the analysis was performed with the cTree method (in R statistical software), which uses a conditional inference framework. Differences between terminal nodes were examined using log-rank tests.

Results: A total of 11,668 patients were included in the study. The decision tree analysis resulted in 11 terminal nodes (Figure 1). The highest persistence was found in male patients, aged over 28 years who did not use systemic corticosteroids in the year prior to SC-TNFi initiation, and who initiated treatment prior to 2015. The lowest persistence was found in females with a diagnosis of SpA or PsA using systemic corticosteroids in the year prior to treatment initiation. Four groups of patients were found to have significant differences in drug persistence when the terminal node subgroups were compared. Median survival by group ranged between 1 year and 3.2 years (Figure 2). Golimumab was the only therapy that has a positive predictive effect on persistence.

Conclusion: This study uses a conditional inference method for decision tree analysis to identify patient subgroups with different levels of treatment persistence. The results may serve as a basis for further research needed to understand the reasons for treatment discontinuation in subgroups with low drug persistence. In addition, the results from this analysis may aid physicians in anticipating treatment persistence and monitor certain subgroups of patients more closely who are more likely to discontinue treatment.

Disclosure: E. Hernlund, Merck & Co., Inc., 9; **J. Klint**, Merck & Co., Inc., 9; **A. Svedbom**, Merck & Co., Inc., 9; **J. Dalén**, Merck & Co., Inc., 9; **C. Black**, Merck & Co., Inc., 1, 4; **A. Puenpatom**, Merck & Co., Inc., 1, 4.

Abstract Number: 2858

The Role of Bradykinin Receptor B1 and Its New Ligand Soluble CD13 in Rheumatoid Arthritis and Inflammatory Arthritis Mouse Model

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
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Session Type: ACR Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is an inflammatory disorder characterized by synovial hyperplasia, inflammatory cell infiltration and pannus formation. We have shown that soluble CD13 (sCD13) induces angiogenesis, monocyte and lymphocyte chemotaxis and arthritis through G protein-coupled receptors (GPCRs). However, the receptor for sCD13 is not yet defined.

Methods: A GPCR screening assay for potential receptors for sCD13 identified bradykinin receptor B1 (B1R). Binding of sCD13 and B1R was studied by immunoprecipitation and immunoblotting of lysates of FLS that had been treated with a chemical cross-linker, BS3. Immunofluorescence was performed to verify the physical binding of sCD13 to B1R on cell membranes. The expression of B1R on RA synovium and fibroblast-like synoviocytes (FLS) was tested using immunofluorescence and flow cytometry, respectively. We also tested the inducibility of B1R on RA FLS by quantitative PCR and Western blotting. Western blotting was performed to test the role of B1R in sCD13 induced phosphorylation of signaling molecules in RA FLS, including use of the B1R antagonist, R715. Monocyte (MN) chemotaxis assays using a modified Boyden chamber were done to examine the effect of B1R antagonism on sCD13 induced MN migration. We also performed RA synovial tissue organ culture with a B1R antagonist, SSR240612 (SSR), and cytokines in the culture media were measured by ELISA. In vivo, B1R antagonists including R715 and SSR, or vehicle were injected intraperitoneally in C57Bl/6 mice daily for 9 days during induction of K/BxN serum-transfer arthritis, and ankle circumference was measured every day.

Results: B1R was found to be a potential receptor for sCD13 by GPCR screening. Following cross-linking of sCD13 to FLS, biochemical analysis showed a band that was identified by both anti-B1R and anti-CD13 at an apparent molecular mass consistent with the sum of the masses of sCD13 and B1R. Blockage of RA FLS with recombinant human CD13 decreased the binding of anti-B1R antibody to B1R on the FLS surface, confirming the binding of sCD13 to the same receptor. B1R was present in RA synovium and was highly expressed by RA FLS. Both TNF-α and IL-1β upregulated the expression of B1R in RA FLS, indicating B1R is inducible in inflammation. Blocking B1R with R715 reduced sCD13 induced phosphorylation of signaling molecules such as Erk1/2, and Akt in RA FLS. We also found that R715 inhibited sCD13 induced MN migration ($p< 0.01$). Synovial tissue organ culture showed that blocking B1R with SSR reduced the secretion of Monocyte Chemoattractant Protein-1 by RA synovium compared to non-treated ($p< 0.05$). In vivo, R715 or SSR suppressed the development of K/BxN serum-transfer arthritis as shown by significantly reduced ankle swelling compared to vehicle, starting from the 6th day ($p< 0.05$).

Conclusion: B1R is highly expressed in RA synovium and RA FLS and is inducible in inflammation. B1R is a receptor for sCD13 and mediates CD13 induced chemotaxis and signal transduction. The potent arthritogenic properties of sCD13 indicate that B1R could be an important pro-inflammatory receptor in both RA and an inflammatory arthritis mouse model, and also a compelling novel therapeutic target.

Disclosure: C. Lu, None; **P. Campbell**, None; **J. Hervoso**, None; **S. Rasmussen**, None; **W. Fu**, None; **J. Ruth**, None; **D. Fox**, None; **M. Amin**, None.

Abstract Number: 2859

Citrulline Reactive B Cells Are Present in the Lungs of Early Untreated RA

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SESSION INFORMATION

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Background/Purpose: Structural changes, increased tissue citrullination, signs of local inflammation and anti-citrullinated protein autoantibodies (ACPA) are present in the pulmonary compartment of early untreated seropositive rheumatoid arthritis (RA). These findings provide evidence of a potential role for the lungs in generation and initiation of RA-associated autoimmunity. Here we aimed to investigate the presence of citrulline-reactive B cells in the lung compartment of early untreated RA patients by single-cell cloning of monoclonal antibodies (mAbs) from lung-derived B cells.

Methods: Bronchoalveolar lavage (BAL) fluid cells were obtained from ACPA positive individuals with arthralgia (n=2) and early untreated ACPA positive RA patients (n=5) at the time of diagnosis.The demographics of the individuals included in the study are shown in Table 1.CD19+ B cells were single cell sorted by flow cytometry. Immunoglobulin heavy and light chain variable regions were PCR amplified, sequenced, and analyzed by V-Quest and IgBLAST towards the IMGT database to annotate variable gene usage. Sequences having high somatic hypermutations (SHM) and Fab N-glycosylation sites were selected to be cloned and expressed as humanIgG1 recombinant mAbs. Citrulline reactivity was determined by CCP2 assay and in-house ELISA against citrullinated and native peptides from vimentin, a-enolase, fibrinogen and filaggrin. Polyreactivity was determined by reactivity against double stranded DNA, bacterial lipopolysaccharides (LPS) and insulin.

Results: Significant numbers of B cells could be retrieved from the BAL. CD19+ B cells [n=6144, median(range): 960 (288-1248)] were single sorted from 5 early RA as well as 2 risk-individuals. PCR amplification and subsequent BCR sequencing from 2 of the early RA patients (n=1536 CD19+ B cells) yielded 192 and 213 paired heavy and light chain sequences. 44 monoclonal antibodies (22 from each patient) were selected for expression based on high number of SHM and predicted Fab N-linked glycosylation. Notably, four of the mAbs (9%; 2 antibodies from each patient) were determined to be ACPAs by CCP2 ELISA. The 4 ACPAs had varying ACPA fine-specificity against citrullinated a-enolase, filaggrin, vimentin and fibrinogen peptides (figure 1) without any native peptide binding (figure 1). All the 4 monoclonal ACPAs were negative in polyreactivity test. Sequence analysis of the heavy chain variable region revealed unique V gene usage of the ACPAs arising from different patients, V4-39 or V3-49.

	Early RA	Risk RA
No. of Subjects	5	2
Age	43 (28-77)	67 (65-67)
Male : Female	1:4	2:0
Non : Ex : Current Smoker	4:1:0	0:0:2
Cells obtained ($X 10^6$)	14.8 (13.0-22.5)	70.2 (66.6-73.8)

Table 1: Demographics of the individuals

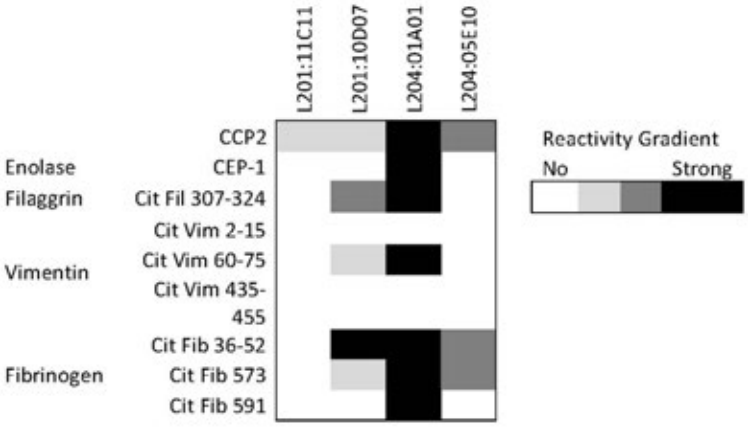

Figure 1. Heatmap showing reactivity of the 4 ACPA against various citrullinated antigens.

Conclusion: We demonstrate for the first time that citrulline-reactive B cells are present in the lung compartment of early untreated RA. This provides a strong link between the lung and the adaptive autoreactive response in RA, and support the hypothesis of the lung as one of the key sites of initiation and propagation of disease in RA.

Disclosure: V. Joshua, None; **M. Loberg-Haarhaus**, None; **H. Wähämaa**, None; **A. Hensvold**, None; **K. Amara**, None; **L. Israelsson**, None; **R. Stålesen**, None; **M. Sköld**, None; **J. Grunewald**, None; **C. Grönwall**, None; **V. Malmström**, None; **A. Catrina**, None.

Abstract Number: 2860

Perturbation of the Human Gut Microbiome by Methotrexate Contributes to the Resolution of Inflammation and Autoimmune Disease

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Background/Purpose: The trillions of microorganisms (microbiota) found within the human gut play a critical role in shaping the immune system, yet these complex microbial communities are also highly sensitive to numerous environmental factors. While much of the focus to date has been on dietary intake, emerging data has begun to suggest that the use of pharmaceutical drugs, even those that are not considered to be antibiotics, can alter the human gut microbiota with unknown consequences for treatment outcomes. Here, we examine the effect of methotrexate (MTX), which is first-line therapy for rheumatoid arthritis (RA), on microbiota composition and physiology as well as downstream consequences on the host's immune system.

Methods: To examine the effect of MTX on human gut microbiota composition *in vivo*, gnotobiotic mice were colonized with microbiota from either healthy or RA patient donors and treated with oral MTX at varying doses. We performed high-throughput sequencing of the 16S rRNA gene to examine changes in taxonomic composition. We looked at the effects of varying the route of administration or co-administration with folic acid. To determine the direct effects of MTX on bacterial growth, we treated monocultures of 42 different human gut isolates with MTX and monitored growth using optical density. To identify MTX-induced transcriptional changes, we performed RNA-Seq on 4 isolates treated with MTX. To determine the effects of MTX on bacterial taxonomy *in vivo*, fecal samples from RA patients (100% fulfilling ACR criteria) starting MTX were profiled longitudinally using 16S sequencing. To determine if MTX-induced shifts reduce the inflammatory potential of the RA microbiome, microbiota from RA patient donors either before or after MTX initiation were transplanted into germ-free mice. These mice were challenged with an inflammatory trigger with dextran-sodium sulfate (DSS), and immune profiling was done to assess inflammation.

Results: MTX altered community composition *in vivo* in humanized mice, leading to reduced Bacteroidetes and increased Firmicutes. Varying the route of drug administration or co-administration with folic acid produced similar, reproducible shifts. MTX directly altered growth of many human gut isolates. At the phylum level, Bacteroidetes tended to be more sensitive than Firmicutes, recapitulating the trends observed in gnotobiotic mice *in vivo*. RNA-Seq revealed that MTX alters transcriptional pathways involved in purine and pyrimidine metabolism. Furthermore, longitudinal analyses of the *in vivo* gut microbiotas of RA patients showed that MTX-induced shifts in bacterial relative abundance are associated with improved drug response. Transplant experiments revealed that mice harboring MTX-altered microbiota exhibited a reduced Th17 and Th1 response to DSS compared to mice harboring pre-treatment microbiota, suggesting that MTX alters the inflammatory potential of the RA patient microbiome.

Conclusion: Together, these results suggest that the mechanism-of-action of non-antibiotic drugs may be due in part to off-target effects on the gut microbiota, while providing a critical first step towards explaining long-standing differences in drug response between patients.

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Abstract Number: 2861

Lung-Related Factors Are Associated with Transitions from Systemic Anti-CCP Antibody Positivity to Classified RA

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Background/Purpose: Systemic autoimmunity associated with RA precedes the onset of inflammatory arthritis (IA) by several years. In particular, the presence of systemic anti-cyclic citrullinated peptide (CCP) antibody is a strong predictor of developing classified RA in the future. However, the mechanisms involved in the transition from systemic anti-CCP to IA classifiable as RA are unknown. Our group has previously identified the local generation of anti-CCP and rheumatoid factor (RF) antibodies in the sputum of subjects at-risk for RA, including those with serum anti-CCP positivity. It has also been demonstrated that a portion of serum anti-CCP+ individuals have chronic lung disease preceding joint disease in RA. Herein, we aimed to determine the relationship between lung-related factors and the transition from systemic autoimmunity to classified RA.

Methods: In 49 subjects who were serum anti-CCP-IgG+ without IA, we collected baseline induced sputum using hypertonic saline. Baseline serum and sputum supernatant were tested by ELISA for CCP-IgG (CCP3, Inova), RF-IgM (Inova) and RF-IgA (Inova). Sputum antibody positivity was defined as a level above the 95th percentile in values determined from a separate cohort of 80 serum anti-CCP negative controls without IA. All subjects were followed longitudinally up to 3 years. Incident RA was determined by 2010 ACR/EULAR classification criteria. Chi-square and Wilcoxon rank-sum testing was used to compare factors associated with incident RA.

Results: Eight (16%) of 49 subjects developed classified RA during follow-up (median time to RA 14 months). Factors associated with developing RA are listed in the Table. Similar to previous data, we found that higher serum anti-CCP-IgG level (p=0.05) and serum RF positivity (p< 0.01) were associated with developing RA. In addition, we also found multiple lung-related factors associated with developing classified RA, including a self-reported history of any chronic lung disease (OR=7.6, 95% CI 1.2-48.4), sputum positivity for anti-CCP-IgG or 2 RF isotypes (RF-IgA and RF-IgM) (OR=12.0, 95% CI 2.2-66.3) and a trend toward an association with current smoking (OR=13.3, 95% CI 1.0-170.6). Of note, both current smokers who developed classified RA had sputum autoantibody positivity. When considering these lung factors in aggregate, incident RA was 15 times more likely in subjects with sputum RA-related antibodies or chronic lung disease (OR=14.6, 95% CI 14.4-87.7).

Table. Baseline clinical features, serologic biomarkers and sputum biomarkers associated with developing classified RA in serum anti-CCP-IgG positive individuals			
	Developed RA (N=8)	Did not develop RA (N=41)	p-value
Clinical Features			
Age, in years	57 (47-65)	60 (45-68)	0.72
Women	7 (88)	26 (63)	0.25
Ever smoker	4 (50)	13 (32)	0.42
Current smoker	2 (25)*	1 (2)*	0.07
Smoking pack-years	1 (0-5)	0 (0-1)	0.33
Chronic lung disease**	3 (38)	3 (7)	**0.05**
Study follow-up, in months	14 (10-17)	22 (12-35)	0.10
Serologic Biomarkers			
≥ 1 shared epitope allele	5 (63)	20 (49)	0.70
Serum anti-CCP-IgG level, in ELISA units***	150 (34-239)	40 (27-72)	**0.05**
Serum RF-IgA+ and RF-IgM+	4 (50)	1 (2)	**<0.01**
Sputum Biomarkers			
Sputum anti-CCP-IgG+	3 (38)	5 (12)	0.11
Sputum RF-IgM+	3 (38)	2 (5)	**0.03**
Sputum RF-IgA+	4 (50)	9 (22)	0.18
Sputum RF-IgM and RF-IgA+	3 (38)	0 (0)	**<0.01**
Sputum anti-CCP-IgG+ or Sputum RF-IgM and RF-IgA+	5 (63)	5 (12)	**<0.01**
Chronic lung disease or Sputum anti-CCP-IgG+ or Sputum RF-IgM and RF-IgA+	6 (75)	7 (17)	**<0.01**

All values are median (IQR) or N (%)

* The 2 current smokers who developed RA were sputum anti-CCP+ or RF-IgM+ and RF-IgA+. The 1 current smoker that did not develop RA was sputum anti-CCP and RF negative.

**The presence of chronic lung disease was based on questionnaire and self-report. In the group that developed RA, 2 reported asthma and 1 reported interstitial lung disease. In the group that did not develop RA, 2 reported asthma and 1 reported bronchiectasis.

*** Anti-CCP-IgG was measured using CCP3 (IgG, Inova) ELISA which has a positive cut-off level set by the manufacturer at ≥20 units.

Conclusion: In a cohort of serum anti-CCP+ subjects, we found that lung-related factors at baseline, including sputum anti-CCP, sputum RF isotypes and a history of chronic lung disease, were associated with developing classified RA within a short duration of follow-up (< 3 years). These data support that biological pathways in the lung may be important in transitions from systemic autoimmunity to arthritis in RA. Based on our findings, it will be particularly important to understand whether the generation of anti-CCP and RF in the lung is a mediating factor that links smoking and RA. In addition, 2 of 8 subjects who developed RA did not have sputum autoantibodies or chronic lung disease, which could suggest other mucosal site involvement in their transitions to RA.

Disclosure: A. Visser, None; **M. Feser**, None; **C. Fleischer**, None; **L. Lenis-Charry**, None; **J. August**, None; **E. Bemis**, None; **J. Norris**, BMS, 5, Celgene, 5, Janssen R&D, 2, Pfizer, 2; **V. Holers**, AdMIRx, 1, 2, 4, 5, 6, Alexion, 7, BMS, 5, Bristol-Myers Squibb, 5, Celgene, 5, Janssen R&D, 2, 5, Pfizer, 2; **K. Deane**, Bristol-Myers Squibb, 5, Inova, 9, Janssen, 2, 5, Janssen R&D, 2, Microdrop, 5, Pfizer, 2; **M. Demoruelle**, Pfizer, 2.

Abstract Number: 2862

Hypoxia Resistant Pathogenic B Cells Accumulate in the RA Synovial Tissue in a CXCR3 Dependent Manner

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SESSION INFORMATION
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Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease of unknown and complex aetiology with severe detrimental effects for the patient's quality of life. While autoantibodies have been used extensively for the diagnosis of RA, no clear mechanism of action towards disease pathogenesis and progression has been identified. Importantly, both seropositive and seronegative RA patients experience significant improvement in disease severity following B cell depletion. Therefore, we hypothesized that B cells have a central, autoantibody independent, role in RA.

Methods: Synovial tissue biopsies from RA patients with paired blood/synovial fluid, were obtained through key-hole arthroscopy followed flow cytometric analysis of B cell subpopulations and chemokine receptor expression in the periphery and synovial tissue. Multiparametric SPICE analysis for the chemokine receptor expression (CXCR5, CXCR3, CCR7, CCR6. CCR4) of synovial tissue invading B cells was performed followed by B cell invasion assays. Functional characterization of RA sorted B cells, cultured *in vitro* in a hypoxia chamber simulating the unique environment of the inflamed joint. Characterization of B cell Glut1 expression and pSTAT3 was achieved by flow cytometric analysis and Western blot analysis. Glucose uptake inhibition by 2DG.

Results: There is a significant accumulation of $CD27^+$ and double negative ($CD27^-IgD^-$) memory B cells in the synovial tissue and synovial fluid of RA patients irrespective of ACPA status. SPICE analysis of peripheral blood B cells for a panel of chemokine receptors revealed a definitive bias towards a specific disease dependent chemokine receptor expression pattern, present from arthralgia-early in disease subjects. Tissue invading B cells showed a clear preference for the expression of CXCR3. Blockade of CXCR3 in invasion assays performed *in vitro* resulted in reduced B cell invasion in response to RA patient synovial tissue conditioned media. Importantly returning RA patient B cells following rituximab mediated B cell depletion express high levels of CXCR3. By simulating the unique hypoxic conditions of the inflamed joint, we observed significant alteration in B cell activation with RA B cells showing increased pro-inflammatory cytokine production and Glut1 expression. B cell Glut1 expression correlates with pSTAT3, while blockade of glucose uptake by 2DG abolishes RA B cell pro-inflammatory cytokine production under normoxic or hypoxic conditions.

Conclusion: The accumulation of pro-inflammatory B cell subpopulations in the synovium of RA patients, is CXCR3 mediated and offers an opportunity for early therapeutic intervention. Once in the hypoxic environment of the inflamed RA joint, B cells show altered activation, pro-inflammatory cytokine production and metabolism that could prove important for understanding the role of B cells in disease pathogenesis of RA.

Disclosure: A. Floudas, None; **C. Low**, None; **M. Biniecka**, None; **K. Murray**, None; **R. Mullan**, None; **D. Veale**, Health Beacon, 1; **U. Fearon**, None.

Abstract Number: 2863

Increased Expression of Extracellular Matrix Proteins in Human Fibroblast Synoviocytes and Lung Epithelial Cells Following Malondialdehyde-Acetaldehyde Adduct (MAA)/Citrullinated Protein Stimulation

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SESSION INFORMATION

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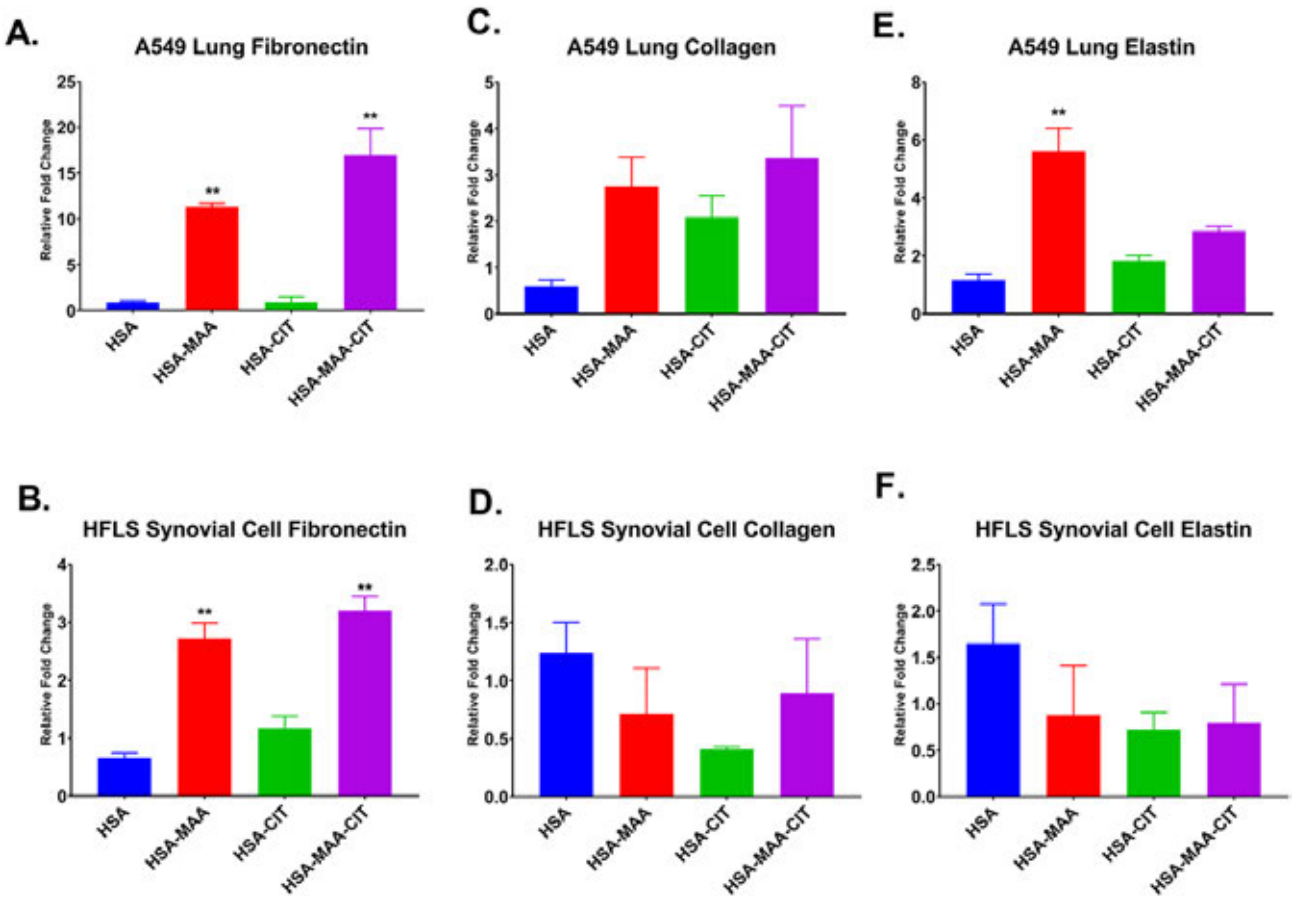

Figure 1. Increase in Extracellular Matrix Proteins in Lung and Synovial Cells. (A). Increased expression of fibronectin message in A549 cells. Significantly increased in HSA-MAA ($p<0.001$) and HSA-MAA-CIT ($p<0.001$) compared to HSA or HSA-CIT antigen stimulation. (B) Increased expression of fibronectin message in HFLS-RA cells. Significantly increased in HSA-MAA ($p<0.001$) and HSA-MAA-CIT ($p<0.001$) compared to HSA or HSA-CIT antigen stimulation. (C) No significant differences seen for Collagen expression in either A549 cells or (D) HFLS-RA cells. (E) Elastin expression was significantly increased ($p<0.001$) in only HSA-MAA stimulated A549 cells compared to all other treatments. (F) No significant increase in elastin was observed in the HFLS-RA cells. (N=6)

Background/Purpose: Recently we have shown that both malondialdehyde-acetaldehyde adducts (MAA) and citrullinated proteins (CIT) are co-localized in joint and lung tissues of patients with rheumatoid arthritis (RA). Therefore, to investigate the possibility that these post-translational modifications pose a synergistic pathogenic role in RA, human synovial fibroblasts and lung epithelial cells were exposed to MAA, CIT or the combination of MAA-CIT and the expression of extracellular matrix proteins (ECMP) were determined.

Methods: Human fibroblast-like synovial cells (HFLS) and lung epithelial cells (A549) were grown to confluency in 24-well plates. Following serum starvation, the cells were incubated with 25 μg/ml of human serum albumin (HSA), HSA-MAA, HSA-CIT, or HSA-MAA-CIT for 4 hours (n=5 each group). RNA was extracted from the cells and subjected to RT-PCR for expression of select ECMPs including fibronectin, collagen, and elastin.

Results: Stimulation with either HSA-MAA or HSA-MAA-CIT significantly increased fibronectin expression (mRNA) compared to stimulation with HSA or HSA-CIT in both the HFLS (Panel A) and A549 (Panel B) cell lines (Figure 1). Stimulation with HSA-MAA, HSA-CIT, and HSA-MAA-CIT did not significantly alter collagen expression in either cell line ($p > 0.05$; Panels C and D), although collagen expression was quantitatively increased with HSA-MAA, HSA-CIT, and HSA-MAA-CIT stimulation (vs. HSA alone) in the A549 lung cell line (Panel D). HSA-MAA stimulation significantly ($p < 0.001$) increased elastin expression in the A549 lung cell line as compared to all other groups (Panel E). Stimulation with HSA-MAA, HSA-CIT, and HSA-MAA-CIT (vs. HSA) did not significantly alter elastin expression in the HFLS cell line (Panel F).

Conclusion: Proteins that are MAA modified or MAA modified and citrullinated induce fibronectin expression in both lung epithelial cells as well as synovial fibroblasts. This effect appears to be particularly striking in lung epithelial cells where dually modified protein induced a ~15-fold increase in fibronectin exposure. While the impact of these protein modifications on collagen and elastin expression were more variable, these data suggests MAA and/or CIT modifications may expert relevant pathogenic (pro-fibrotic effects) in RA that could be both protein and site-dependent.

Disclosure: M. O'Dell, None; **L. Duryee**, None; **L. Klassen**, None; **J. O'Dell**, None; **B. England**, None; **M. Duryee**, None; **G. Thiele**, None; **T. Mikuls**, BMS, 2, Horizon, 2.

Abstract Number: 2864

Efficacy and Safety of Intravenous Belimumab in Children with Systemic Lupus Erythematosus: An Across-Trial Comparison with the Adult Belimumab Studies

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SESSION INFORMATION
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Background/Purpose: Belimumab (BEL) is the first treatment approved for children with systemic lupus erythematosus (SLE) from 5 years of age and older.[1] This approval was based on the PLUTO trial (NCT01649765), which was designed to assess the safety and efficacy of BEL in children with SLE.[2] Additional evidence to support the consistency of effect of BEL in children included an across-trial comparison of efficacy and safety in adult SLE with

	PLUTO (Pediatric)		BLISS-52 (Adult)		BLISS-76 (Adult)	
	PBO N=40	BEL 10 mg/kg IV N=53	PBO N=287	BEL 10 mg/kg IV N=290	PBO N=275	BEL 10 mg/kg IV N=273
SRI4 Wk 52 Response, n (%)	17 (43.6)	28 (52.8)	125 (43.6)	167 (57.6)	93 (33.8)	118 (43.2)
Difference BEL vs PBO (%) OR (95% CI)	9.24 1.49 (0.64, 3.46)		14.03 1.83 (1.30, 2.59)		9.41 1.52 (1.07, 2.15)	
SRI6 Wk 52 Response, n (%)	13 (34.2)	21 (41.2)	81 (28.2)	127 (43.8)	52 (18.9)	84 (30.8)
Difference BEL vs PBO (%) OR (95% CI)	6.97 1.35 (0.56, 3.22)		15.6 2.20 (1.51, 3.20)		11.9 2.00 (1.33, 3.01)	
Time to first severe flare over 52 wks HR (95% CI)	0.38 (0.18, 0.82)		0.57 (0.39, 0.85)		0.72 (0.50, 1.05)	

AIA, African or indigenous American descent; HR, hazard ratio; SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index.
Note: Results of the BEL 1-mg/kg arms are not included from the adult studies as this is not a commercially approved dose. For BLISS-52 and BLISS-76, OR (95% CI) was calculated using a logistic regression for the comparison between BEL and PBO with covariates (baseline SELENA-SLEDAI score (≤9 vs ≥10), baseline proteinuria level (<2 g/24 hour vs ≥2 g/24 hour equivalent) and race (AIA vs Other). A Cox proportional hazards model was used for the comparison between BEL and PBO adjusting for baseline stratification factors. For PLUTO, OR (95% CI) was calculated using a logistic regression model for the comparison between BEL and PBO with covariates (treatment group, baseline age (5–11 vs 12–17), and baseline SELENA-SLEDAI score (≤12 vs ≥13). A Cox proportional hazards model was used for the comparison between BEL and PBO adjusting for baseline age (5–11 vs 12–17) and baseline SELENA-SLEDAI score (≤12 vs ≥13).

Table 1. Efficacy endpoints: PLUTO, BLISS-52, BLISS-76 (ITT population)

	Number (%) patients				
	PLUTO (Pediatric)		BLISS-52/BLISS-76/LBSL02 (Pooled adult)		
Patients with ≥1:	PBO N=40	BEL 10 mg/kg IV N=53	PBO N=675	BEL 10 mg/kg IV N=674	BEL (All doses) N=1458
AE	33 (82.5)	42 (79.2)	623 (92.3)	625 (92.7)	1354 (92.9)
Treatment-related AE	15 (37.5)	19 (35.8)	282 (41.8)	268 (39.8)	586 (40.2)
Serious AE	14 (35.0)	9 (17.0)	103 (15.3)	113 (16.8)	248 (17.0)
Death	1 (2.5)	0	3 (0.4)	6 (0.9)	11 (0.8)

Note: The category "All doses" includes the 1-mg/kg, 4-mg/kg, and the 10-mg/kg dose of belimumab.

Table 2. Adverse event summary: PLUTO, pooled adult trials (BLISS-52, BLISS-76, LBSL02)

the BLISS-52 (NCT00424476), BLISS-76 (NCT00410384), and LBS02 (safety only; NCT00071487) trials. Results are presented below.

Methods: The trials enrolled patients aged 5–17 years (PLUTO) and ≥18 years (BLISS-52 and BLISS-76) with a diagnosis of SLE, and active disease and seropositivity at screening. Patients were randomized to BEL 10 mg/kg given intravenously (IV) or placebo (PBO), plus standard of care (SoC) in PLUTO; and BEL 1 mg/kg or 10 mg/kg IV or PBO, plus SoC, in the BLISS trials. The primary endpoint across these trials was the SLE Responder Index 4 (SRI4) at Week (Wk) 52. Additional endpoints included SRI6 at Wk 52 (*post hoc* endpoint in the BLISS trials) and time to first severe

flare over 52 wks. An across-trial comparison (intent-to-treat [ITT]) of PLUTO, BLISS-52, and BLISS-76 summarizes the treatment effect of BEL IV plus SoC versus PBO plus SoC on SRI4 and SRI6 at Wk 52, reported as odds ratio (OR; 95% confidence interval [CI]), and time to first severe flare, reported as a reverse hazard ratio (95% CI). Safety analyses included adverse events (AEs), serious AEs (SAEs), and AEs of special interest (AESI) for PLUTO and pooled data from BLISS-52, BLISS-76 and LBSL02. The results of both the efficacy and safety across-trial comparisons are descriptive only.

Results: SRI4 and SRI6 responses at Wk 52 consistently favored BEL IV plus SoC. Reduction in the risk of severe flare was seen with BEL IV plus SoC versus PBO plus SoC in the PLUTO, BLISS-52, and BLISS-76 trials (**Table 1**). The incidences of patients experiencing ≥1 AE and ≥1 SAE in the PLUTO trial and the pooled safety data from the adult studies were similar (**Table 2**). With respect to AESI, there was no difference between treatment groups across the pediatric and adult studies in malignant neoplasms and post-infusion systemic reactions. The rate of all infection AESI was higher in PLUTO (PBO 7.5% and BEL 13.2%) compared with the adult studies (PBO 5.5%, BEL 10 mg/kg 4.7%), with an observed increase in herpes zoster events but no clinically meaningful differences in serious infections in PLUTO compared with the adult studies. There was no imbalance between treatment groups in depression/suicide/self-injury AESI in PLUTO, and the incidence was lower in the BEL group in PLUTO (1.9%) compared with that in the adult studies (BEL 10 mg/kg 8.8%).

Conclusion: The efficacy and safety of BEL IV plus SoC in children with SLE are consistent with those in the adult BEL study populations and support a favorable benefit/risk profile in ages 5 and older.

Study funded/conducted by GSK.

References:

1) Benlysta prescribing information https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/125370s064,761043s007lbl.pdf [Accessed May 2019].
2) Brunner HI, et al. *Arthritis Rheumatol*. 2018;70(59):3224–5, Abst. 2867

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Abstract Number: 2865

Application of Bayesian Statistics to Support Approval of Intravenous Belimumab in Children with Systemic Lupus Erythematosus in the United States

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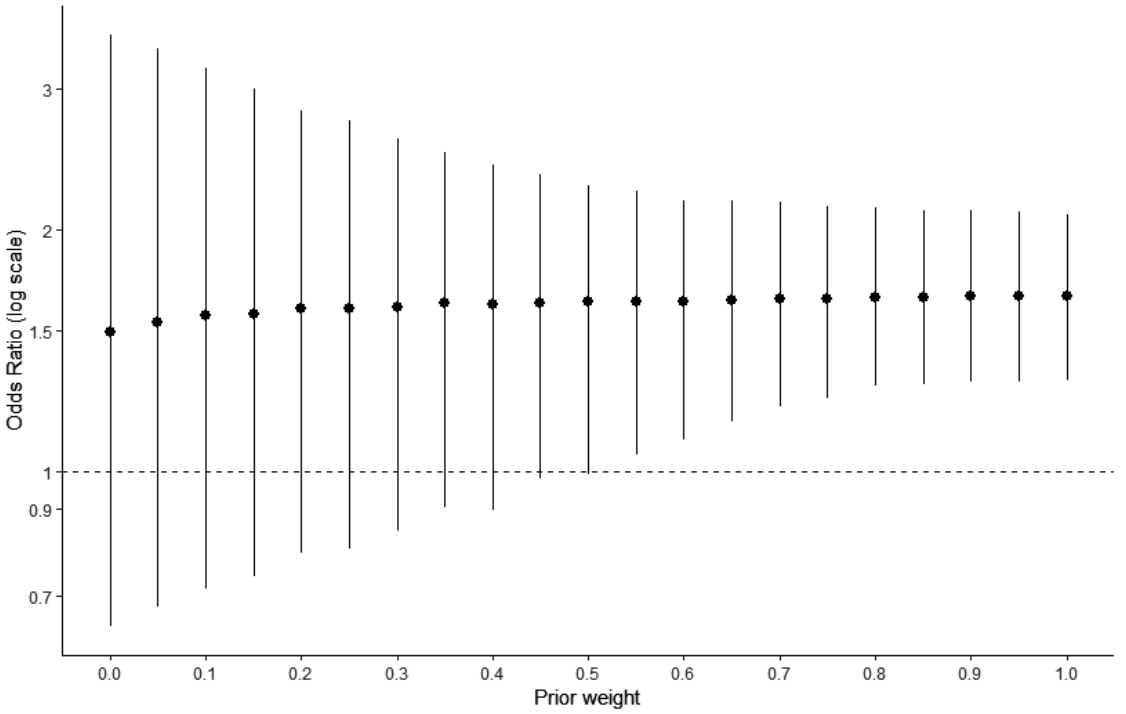
SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: Pediatric Rheumatology – Clinical III: Juvenile SLE & Dermatomyositis
Session Type: ACR Abstract Session
Session Time: 9:00AM–10:30AM

Figure 1. Posterior Distribution of the Odds Ratio of SRI Response across Different Weight Value



Background/Purpose: In April 2019, FDA approved the first treatment, intravenous (IV) belimumab (BEL), specifically for children 5 to 17 years of age with active, seropositive SLE receiving standard care (SOC). The approval was supported by a single post-marketing required randomized, controlled trial (NCT01649765) that evaluated the efficacy, safety and pharmacokinetics (PK) of 10 mg/kg IV BEL vs placebo in 93 pediatric patients. Due to the rarity of childhood onset SLE limiting enrollment, by design, the study was not adequately powered to make formal statistical inferences on its own. Determination of efficacy was therefore based on PK and efficacy results from the study, as well as extrapolation of the established efficacy of IV BEL from the two phase 3 adult studies. To provide more reliable efficacy estimates in this context, FDA also employed a novel post-hoc Bayesian analysis which borrowed information from the phase 3 adult IV studies, under a reasonable assumption about the similarity between the adults and pediatric subjects.

Methods: A Bayesian logistic regression model was used to analyze the treatment effect in SLE Responder Index (SRI) response in pediatric patients, which adjusted covariates for treatment group, baseline SELENA SLEDAI score (< 13 vs. ≥ 13), and age group (5-11 vs. 12-17 years of age). A prior for the treatment effect in the pediatric population was constructed using a weighted combination of a skeptical prior and the treatment effect estimate distribution in adults, where the weight represented the degree of belief in the similarity of the pediatric and treatment effects estimated using two phase 3 adult studies.

Results: The key baseline disease characteristics and PK were similar between the pediatric and adult IV study populations. A plot of the point estimates and 95% credible intervals for varying weights is shown in Figure 1. A prior weight of 55% or larger provided 95% credible intervals that excluded an odds ratio of one, corresponding to a 97.5% posterior probability of efficacy (positive estimate of treatment effect) which is analogous to a rejection of the null hypothesis with a one-sided type I error of 0.025. These results were further supported by the secondary efficacy endpoints and safety, described in the FDA-approved belimumab labeling.

Conclusion: We applied a Bayesian approach to support approval of IV BEL, the first treatment for children with SLE in the United States. Given the similarity between the adult and pediatric populations and studies, a weight of at least 55% weight on the relevance of the adult information to the pediatric population is reasonable, ensuring that there is at least 97.5% posterior probability that belimumab 10 mg/kg has a positive treatment effect in pediatric subjects. The results of this unique analysis supported a conclusion that the treatment effect of IV BEL in the pediatric population favored BEL 10 mg/kg as compared to placebo under reasonable assumption. This innovative approach, especially if pre-specified, may help expedite clinical development in pediatric rheumatic diseases, and address some of the challenges with conducting trials in the setting of these rare conditions.

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Abstract Number: 2866

Factors Associated with Cardiac Dysfunction in a Longitudinal Follow-Up of Neonatal Lupus

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SESSION INFORMATION
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Background/Purpose: Cardiac manifestations of neonatal lupus (NL) have been associated with significant morbidity and mortality, however there has been minimal information on long-term outcomes of affected individuals. This study was initiated to evaluate the presence of and risk factors associated with cardiac dysfunction in NL after birth in multiple age groups to improve counseling, further understand pathogenesis and provide potential preventative strategies.

Methods: Echocardiogram reports throughout life were evaluated in 239 individuals with cardiac-NL: 143 from ages 0-1 years, 176 from >1-17 years, and 64 >17 years. Cardiac dysfunction was defined as one or more of the following 1) qualitatively decreased left ventricular function on echocardiogram, 2) concurrent use of cardiac medications 3) heart transplant. Aortic dilation was defined as root or ascending aorta z-score >2.0. Multivariable logistic regression analyses were performed to evaluate associations of cardiac dysfunction at each age group with demographic, fetal and postnatal factors.

Results: Cardiac dysfunction was identified in 22.4% of children at ages 0-1, 14.8% ages >1-17 and 28.1% ages >17. In multivariable analysis of the age 0-1 group, female sex (OR 0.41, p=0.046), older age at the time of echo (OR 0.14, p=0.067) and higher in utero nadir ventricular heart rate (OR 0.95, p=0.077) were protective, while greater length of time paced (OR 10.82, p=0.035) was associated with increased odds of cardiac dysfunction. In the age >1-17 group, black race (OR 10.28, p=0.021), length of time paced (OR 1.31, p=0.039), in utero extranodal disease (OR 3.11, p=0.061) and a severity score representing overall fetal disease weighted by mortality risk factors (OR 1.17, p=0.048) associated with cardiac dysfunction. In those >17, a greater length of time paced (OR 1.29, p=0.018) and

the severity score (OR 1.42, p=0.037) were associated with dysfunction. In 106 children with echos at ages 0-1 and >1-17, 43.8% (95% CI: 19.8, 70.1%) of those with dysfunction at 0-1 were also affected at >1-17, while all others reverted to normal. Of those without dysfunction at ages 0-1, 8.9% (CI: 3.3, 16.8%) developed new dysfunction at >1-17 years. Among the 34 with echos at ages >1-17 and >17, 6.5% (CI: 0.8, 21.4%) with normal function at >1-17 developed dysfunction in adulthood. Aortic dilation was present in 13.5% at ages 0-1, 15.0% at >1-17, and 9.4% at >17. Of the 15 (14.3%; CI: 8.2, 22.5%) of 105 children with dilation at age 0-1, 9 (60.0%; CI: 32.2, 83.7%) still had dilation at >1-17, while the other 6 reverted to normal. Among the 90 cases without dilation at age 0-1, 8 (8.9%; CI: 3.9, 16.8%) developed dilation at >1-17 years. For the 34 children with echos at both >1-17 and >17, none had aortic dilation at age 1-17, with one (2.9%; CI: 0.1, 15.3%) developing dilation after 17.

Conclusion: Risk factors in early fetal life can influence cardiac morbidity into the adult years. Cardiac dysfunction in the first year normalizes by later childhood in the majority of cases, possibly due to the short-term effects of cardiac pacing or resolution of inflammation with the clearance of maternal autoantibodies. New onset dysfunction and aortic dilation, albeit rare, can occur de novo after the first year of life.

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Abstract Number: 2867

Nocturnal Blood Pressure Dipping as a Marker of Endothelial and Cardiac Function in Pediatric-onset Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: Pediatric Rheumatology – Clinical III: Juvenile SLE & Dermatomyositis
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Background/Purpose: There is a need for clinically useful measures of cardiovascular (CV) risk in pediatric-onset SLE (pSLE). Nocturnal blood pressure (BP) non-dipping (loss of the physiologic nocturnal decline in BP) is a reversible

Table 1. Blood Pressure Categories by ABPM

	All (N = 18)	Nocturnal HTN	<10% Nocturnal Dip
	n (%)	n	n
Normal	10 (55%)	1	5
White coat hypertension	6 (33%)	0	3
Masked hypertension	1 (6%)	1	0
Unclassified*	1 (6%)	0	1
Totals		2 (11%)	9 (50%)

Blood pressure categories based on updated definitions from the 2017 AAP guidelines:
Nocturnal Hypertension: SBP/DBP load ≥ 50% by ABPM
White coat hypertension: Clinic BP ≥ 95th%ile but mean S24-hr BP/DBP < 95th%ile and SBP/DBP load < 25% by ABPM
Masked hypertension: normal clinic BP but mean 24-hr SBP/DBP > 95th%ile and SBP/DBP load ≥ 25% by ABPM
*Unclassified: elevated clinic BP (> 90th but < 95th%ile) with normal ABPM

Table 2. Factors Associated with Attenuated Nocturnal Blood Pressure Dipping

	Total (N = 18)*	Normal Dipping (N = 9)	Non-Dipping (N = 9)
Demographic Characteristics			
Age in years, mean (±SD)	16.3 (±2.8)	17.1 (±2.2)	15.6 (±3.2)
Disease duration, yrs (±SD)	2.9 (±2.1)	3.6 (±2.3)	2.3 (±1.8)
Female sex, n (%)	15 (83)	7 (78)	8 (89)
Race			
White/Caucasian	6 (33)	4 (44)	2 (22)
Black/African American	7 (39)	2 (22)	5 (56)
Asian	3 (17)	2 (22)	1 (11)
Other race	2 (11)	1 (11)	1 (11)
Hispanic ethnicity	3 (17)	1 (11)	2 (22)
Highest household education			
Did not complete high school	2 (11)	2 (22)	0 (0)
High school/general education degree	9 (50)	4 (44)	5 (63)
Bachelor's degree or more	6 (33)	3 (33)	3 (33)
Household income			
< $25K	5 (28)	1 (12)	4 (44)
$25K or more	12 (67)	7 (88)	5 (56)
Traditional Cardiovascular Risk Factors			
Physical activity score,¶ mean (±SD)	1.8 (±0.8)	1.8 (±0.6)	1.9 (±0.9)
BMI %ile for age-sex, mean (±SD)	68 (±28)	56 (±30)	81 (±20)
History of physician diagnosis of hypertension	3 (17)	1 (11)	2 (22)
Fasting lipids, mean mg/dL (±SD)			
Low-density lipoprotein	89 (±24)	91 (±23)	88 (±26)
High-density lipoprotein	52 (±10)	44 (±5)	59 (±8)
Triglycerides	84 (±36)	87 (±46)	81 (±30)
Family history early CVD, n (%)	4 (22)	2 (22)	2 (22)
Disease Characteristics			
Most recent SLEDAI-2K†, median [IQR]	2 [0-2]	2 [0-2]	2 [0-2]
Time-averaged SLEDAI	4 [3-6]	4 [3-5]	5 [3-9]
Antiphospholipid antibodies (persistent), n (%)	6 (33)	4 (44)	2 (22)
Nephritis	4 (22)	1 (11)	3 (33)
Neuropsychiatric manifestation	1 (1)	0 (0)	1 (11)
Current oral glucocorticoid use	6 (33)	1 (11)	5 (56)
Months on oral glucocorticoids, median [IQR]	8 [2-20]	8 [2-30]	11 [4-19]
ACEi/ARB current use, n (%)	3 (17)	1 (11)	2 (22)

* Only 18/20 subjects completed ABPM wear to determine dipping vs non-dipping

¶ Validated physical activity questionnaire (PAQ); normative means in children and adolescents are 3.4 (±0.68) and 2.3 (±0.63), respectively

† SLE Disease Activity Index 2000; cumulative time-averaged scores calculated using the summation of (average scores over each time interval x length of time between measurements), over total duration

marker of CV risk and potential treatment target that can be reproducibly measured by ambulatory blood pressure monitoring (ABPM). We assessed the frequency of non-dipping BP in pSLE and evaluated its association with vascular and cardiac function.

Table 3. Association between ABPM findings with vascular and cardiac stiffness and function

		% SBP Dip		% DBP Dip		SBP load		DBP load	
Measure	Description	r*	p	r*	p	ρ†	p	ρ†	p
PWV Z-score	*Arterial stiffness*	0.3	0.29	-0.1	0.76	0.4	0.06	0.1	0.73
Aix	*Central BP*	0.3	0.30	0.3	0.31	0.6	0.01	0.7	<0.01
Aix @HR75	*Central BP*	0.2	0.40	0.2	0.35	0.7	0.00	0.6	0.01
$IVRT_c$	*Cardiac stiffness*	-0.6	0.16	-0.9	0.01	0.0	0.97	0.1	0.82
LV circ. strain§	*Cardiac deformation*	-0.5	0.02	-0.4	0.09	0.0	0.90	0.2	0.41
lnRHI†	*Endothelial function*	0.19	0.49	0.5	0.04	-0.3	0.19	-0.4	0.14

*Pearson's correlation coefficients (*r*) estimating the relationship between percent nocturnal BP dipping and measures of arterial stiffness and cardiac function, at a significance level alpha of 0.10.
† Spearman rank correlations (*ρ*) were used to assess associations with BP load (% of total BP readings >95th%ile).
SBP = systolic blood pressure; DBP = diastolic blood pressure; PWV = pulse wave velocity (m/s); Aix = augmentation index (%); Aix@HR75 = augmentation index normalized to heart rate of 75 bpm; IVRTc = isovolumetric relaxation time (seconds) corrected for age
§ Left ventricular global peak circumferential strain; more negative strain values represent greater circumferential wall shortening during contraction.
† Digital reactive hyperemia index measured by EndoPAT; higher values correspond to better vasodilatory function of the endothelium

Methods: Twenty subjects 9-21 years of age with prevalent pSLE underwent comprehensive vascular testing, including 24-hour ABPM, peripheral endothelial function (EndoPAT), pulse wave velocity (PWV) for arterial stiffness, pulse wave analysis (PWA) for central BP, carotid ultrasound for intima-media thickness (cIMT), echocardiography for left ventricular (LV) strain and diastolic function, and fasting lipids. Additional clinical data was abstracted from charts, including longitudinal disease activity (SLEDAI-2K) scores. The primary outcome was prevalence of non-dipping (< 10% nocturnal decline in mean SBP or DBP). Secondary outcomes included prevalence of nocturnal and masked hypertension, defined by BP load (% of readings >95th%ile). We used descriptive statistics to assess patient characteristics in dippers and non-dippers. We used Pearson or Spearman rank correlation tests to evaluate relationships between SBP/DBP dipping, BP load and vascular measures.

Results: The majority of subjects had inactive disease at the time of assessment (median SLEDAI 2 [interquartile range 0-2]), with a mean disease duration of 2.9 years (±2.1). 18/20 ABPM studies were evaluable. Agreement between hypertension category by manual office BP and 24-hour ambulatory mean SBP/DBP was poor (kappa 0.08). The prevalence of non-dipping and nocturnal hypertension was 50% and 11%, respectively, which occurred even in the absence of white coat or masked hypertension (Table 1). Compared to subjects with normal dipping, non-dippers were more often from low-income households and still using glucocorticoids. They also tended to have higher body mass index and time-averaged cumulative disease activity (Table 2). Reduced SBP/DBP dipping correlated with poorer endothelial function, decreased myocardial shortening (less negative strain) and increased LV stiffness (prolonged isovolumetric relaxation) (Table 3). In contrast, higher BP load was strongly correlated with increased arterial stiffness and central BP, but not with endothelial or cardiac function.

Conclusion: In a racially diverse group of children and adolescents with pSLE with low disease activity, there is a high prevalence of nocturnal BP non-dipping even in the absence of systemic hypertension. BP load relates to arterial stiffness, whereas nocturnal BP dipping relates to subclinical LV strain and endothelial function, and therefore ABPM abnormalities may represent two distinct mechanisms of early CV disease in pSLE. There is a potential role for routine ABPM in cardiovascular risk stratification of youth with pSLE.

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Abstract Number: 2868

Baseline Clinical and Serological Findings in Pediatric-Onset Discoid Lupus Erythematosus: Analysis of a Multicenter Retrospective Cohort Study

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: Pediatric Rheumatology – Clinical III: Juvenile SLE & Dermatomyositis

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Background/Purpose: DLE is a rare, disfiguring disorder in children. Small retrospective studies suggest 20-25% of patients progress to SLE. Progression risk factors are poorly understood, but DLE has been associated with delay in SLE diagnosis and reduced access to care. This multicenter retrospective cohort study aimed to describe baseline characteristics and clinical phenotypes of pediatric DLE patients at diagnosis.

Methods: Medical records at eighteen sites were reviewed for pediatric dermatology and rheumatology patients with DLE. For inclusion, patients required clinical and/or histopathologic findings consistent with DLE. Baseline data were collected at the first documented visit including sociodemographic data, ACR/SLICC SLE criteria (i.e. DLE+SLE), date of DLE onset/diagnosis, DLE distribution, family history, comorbidities, and treatment. Outcome variables included

Table 1. Baseline data for patients with DLE at diagnosis

	DLE n, (%)	DLE + SLE n, (%)	Total n, (%)	p-value
Female sex	185 (67)	133 (81)	318 (72)	**0.003**
Race/Ethnicity				
Asian	17 (16)	23 (14)	40 (9)	**0.006**
Black	88 (32)	65 (39)	153 (35)	0.1
Hispanic	69 (25)	27 (16)	96 (22)	**0.03**
White	67 (20)	20 (12)	87 (20)	**0.002**
Not Reported	38 (14)	29 (18)	67 (15)	
DLE distribution				
Localized	222 (81)	97 (59)	319 (73)	**<0.001**
Generalized	47 (17)	63 (38)	110 (25)	
Any family history of SLE	39 (14)	37 (22)	76 (17)	**0.03**

Bolded values represent statistically significant differences between patients with DLE vs DLE + SLE diagnosed at the baseline visit.

Table 2. Baseline clinical and laboratory characteristics based on ACR classification criteria for patients with DLE at diagnosis

ACR classification criteria	DLE n, (%)	DLE + SLE n, (%)	Total	p-value
Malar rash	12 (4)	75 (46)	87 (20)	**<0.001**
Photosensitivity	31 (11)	63 (38)	94 (21)	**<0.001**
Oral/nasal ulceration	10 (4)	63 (38)	73 (17)	**<0.001**
Non-erosive arthritis	7 (3)	77 (47)	84 (19)	**<0.001**
Pleuritis	0 (0)	9 (6)	9 (2)	**<0.001**
Pericarditis	0 (0)	10 (6)	10 (6)	**<0.001**
Seizures	0 (0)	7 (4)	7 (4)	**<0.001**
Psychosis	0 (0)	8 (5)	8 (2)	**<0.001**
Persistent proteinuria	7 (5)	48 (34)	55 (20)	**<0.001**
Cellular casts	2 (1)	28 (17)	30 (7)	**<0.001**
Hemolytic anemia	1 (0.4)	13 (8)	14 (3)	**<0.001**
Leukopenia	17 (8)	77 (49)	94 (26)	**<0.001**
Lymphopenia	9 (4)	82 (55)	91 (24)	**<0.001**
Thrombocytopenia	3 (1)	33 (21)	36 (10)	**<0.001**

Bolded values represent statistically significant differences between patients with DLE vs DLE + SLE diagnosed at the baseline visit.

Table 3. Baseline serologies for patients with DLE at diagnosis				
Auto-antibodies	DLE n, (%)	DLE+SLE n, (%)	Total	p-value
ANA				
1:40 or negative	126 (46)	8 (5)	134 (31)	**<0.001**
1:80	24 (9)	8 (5)	32 (7)	
1:160	27 (10)	17 (10)	44 (10)	
1:320	15 (6)	14 (9)	29 (7)	
1:640	12 (4)	36 (22)	48 (11)	
1:1280 or higher	11 (4)	55 (33)	66 (15)	
Positive, no titer	21 (8)	25 (15)	46 (11)	
Not done	38 (14)	2 (1)	40 (9)	
Anti-B2 glycoprotein	5 (11)	12 (13)	17 (12)	0.71
Anti-Cardiolipin	6 (8)	64 (44)	70 (31)	**<0.001**
Anti-dsDNA	21 (11)	104 (65)	125 (36)	**<0.001**
Anti-La/SSB	13 (7)	41 (27)	54 (16)	**<0.001**
Anti-Ro/SSA	43 (23)	72 (47)	115 (34)	**<0.001**
Anti-Smith	10 (7)	100 (67)	110 (38)	**<0.001**
Anti-U1RNP	15 (12)	94 (65)	109 (40)	**<0.001**
Lupus Anticoagulant	4 (6)	31 (28)	35 (20)	**<0.001**

Bolded values represent statistically significant differences between patients with DLE vs DLE + SLE diagnosed at the baseline visit.

ACR (primary outcome) /SLICC SLE criteria. Rates of progression from skin-limited DLE (DLE) to SLE (DLE+SLE) were evaluated. Analysis included descriptive statistics, chi-square and Wilcoxon tests.

Results: Out of >1,000 patients reviewed, 441 met inclusion criteria. The cohort was predominantly female (72%) and racially/ethnically diverse (Table 1). A minority presented at baseline with SLE based on ACR and SLICC criteria, respectively (n=165, 37%; n=183, 42%). DLE+SLE patients were older (median 13.7y vs 10.2y) with shorter time from DLE onset to diagnosis (median 2 mo vs 7 mo), compared to DLE patients ($p< 0.001$). DLE patients presented with low incidence of renal involvement, serositis, seizures or psychosis ($p< 0.001$, Table 2). DLE+SLE patients had more positive serologies and higher-titer ANAs ($p< 0.001$, Table 3), although 5% were ANA negative. Among 231 DLE patients with³1 follow up visit, median follow-up was 2.7 y (range 0-13.9y) with 747 total subject-years. Progression to SLE occurred in 20% and 25% of patients based on ACR and SLICC criteria, respectively.

Conclusion: To date, this is the largest investigation of pediatric DLE. Patients with DLE + SLE were most likely to present in adolescence with abnormal serologies and end-organ disease. Progression of DLE to SLE occurred at rates consistent with previous literature. All patients with DLE require SLE surveillance at diagnosis and regular follow-up, particularly during adolescence. Limitations include the retrospective study design with potential for misclassification, and analysis restricted to the baseline visit. Further analysis of follow up visits will evaluate for baseline risk factors and biomarkers of evolving SLE, as well as timing of progression, identifying DLE patients at highest risk for systemic disease.

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Abstract Number: 2869

Access to Care and Diagnostic Delays in Juvenile Dermatomyositis

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: Pediatric Rheumatology – Clinical III: Juvenile SLE & Dermatomyositis
Session Type: ACR Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: Factors associated with diagnostic delay in Juvenile Dermatomyositis (JDM) are not known. We hypothesized that limited access to pediatric rheumatologists can lead to delay in the diagnosis of JDM and worse outcomes. We investigated demographic factors, including access to care, associated with diagnostic delays and clinical outcomes of subjects with JDM in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Legacy Registry.

Methods: This was a cross-sectional study of JDM subjects enrolled in the CARRA Legacy Registry from 2010-2015. We used two measures of access to care: distance to care, calculated as miles by driving from subject zip code to treating rheumatology center using the R package "gmapsdistance", and state density of pediatric rheumatologists calculated as child population divided by number of pediatric rheumatologists. An ordered generalized additive model (GAM) was used to determine the association these two predictors, included as smoothed terms, and diagnostic delay adjusting for age, sex, income, and race. Delay was categorized as early (< 30 days), typical (1-3 mos), moderate (3-12 mos) and severe (>12 mos). The association between access to care and patient outcomes, including physician and parent global scores, childhood HAQ, and ACR functional class, was also assessed.

Results: A total of 464 JDM subjects were included in the analysis. The median time to diagnosis was 3.1 months (IQR 1.4-7.0). Moderate to severe diagnostic delay was found in nearly 52% of subjects. The median distance to care was 37.5 miles (IQR 17.0-90.3). The median density of children per pediatric rheumatologist was approximately 250,000 (IQR 147,000-399,000). In an ordered GAM, there was a modest association between greater delay in states with more children per pediatric rheumatologist (AIC decrease of 1.4, p = 0.060, Fig 1), a trend that was observed up to 500,000 children per rheumatologist, after which the confidence intervals widened due to few observations in very underserved states. Younger age at JDM onset was associated with diagnostic delay (OR 0.94 per year increase, p = 0.01), while having a household income >$150,000 compared to < $25,000 was protective (OR 0.47, p = 0.04). Non-black minority race compared to white race was also protective against delay (OR 0.43, p = 0.01). There was a modest trend toward having more functional limitation as measured by current ACR class of 2 or greater with increasing distance to care (AIC decrease of 0.9, p = 0.08, Fig 2).

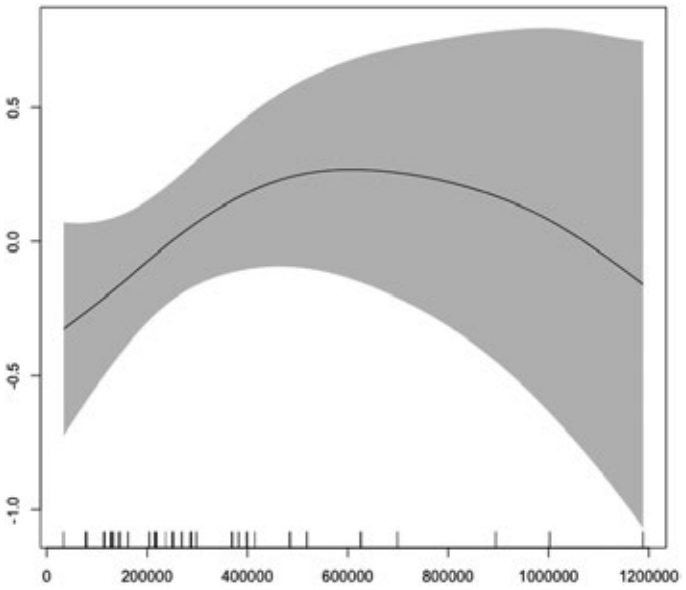

Figure 1. Log odds of increasing by one or more delay categories as number of children per rheumatologist increases. There are very few states with fewer pediatric rheumatologists than 1 per 500,000 children.

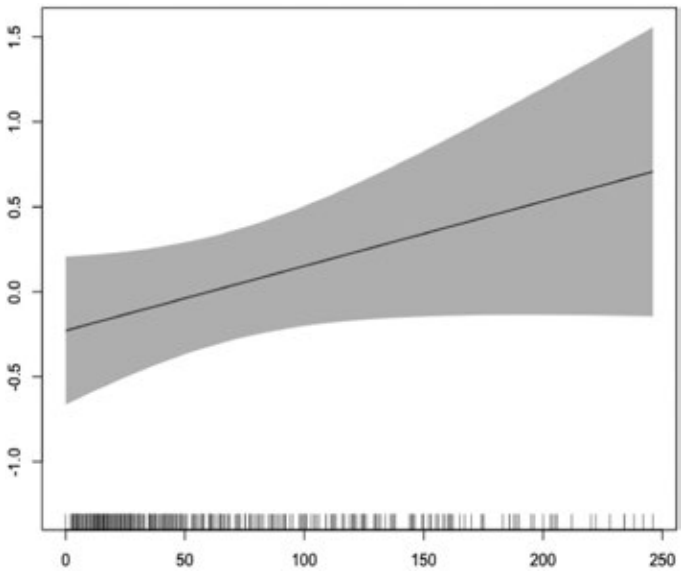

Figure 2. Log odds of increasing by one or more delay categories as distance from treating rheumatology center increases.

Conclusion: In the CARRA Legacy Registry, we found moderate to severe diagnostic delays in the majority of subjects with JDM. Our data suggests that access to care, measured as density of rheumatologist by state, is an important factor associated with delay in care but also highlights other contributing demographic factors, including younger age at disease onset and poverty. We also found a trend towards more functional limitation in patients with increasing distance to care. In addition to increasing the pediatric rheumatology workforce, efforts to increase awareness of rare conditions like JDM among general practitioners and subspecialists may help shorten referral time to pediatric rheumatologists and improve outcome in patients with JDM.

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Abstract Number: 2870

Persistence of B Cell-rich Synovitis Following Conventional Synthetic Disease Modifying Anti-Rheumatic Drug Treatment in Early Rheumatoid Arthritis Is Associated with Radiographic Progression Independently of Clinical Response

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes V: Treatment

Session Type: ACR Abstract Session

Session Time: 9:00AM–10:30AM

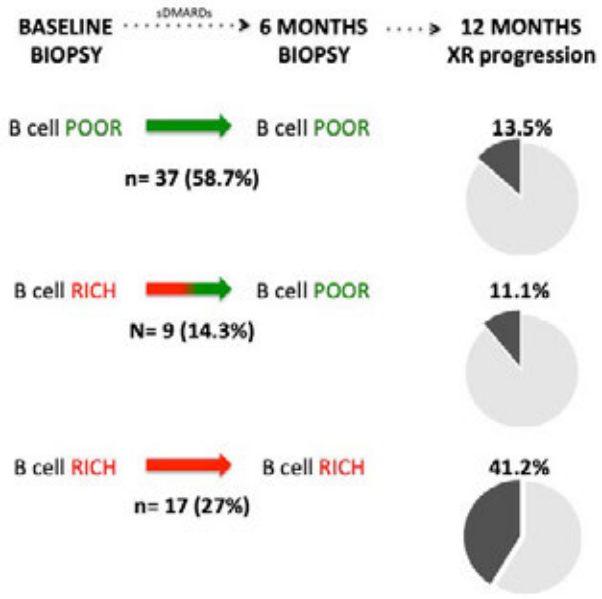
Background/Purpose: Synovial B cell aggregates in patients with early Rheumatoid Arthritis (RA) have been associated with disease severity and radiographic progression. Here, we analysed the presence of B cells and their association with clinical outcomes in matched synovial biopsies pre- and post- treatment with conventional synthetic Disease Modifying anti-Rheumatic Drug (scDMARDs).

Methods: DMARD-naïve patients with early (< 12 months) RA (n=164) fulfilling the 2010 ACR/EULAR criteria were recruited as part of the Pathobiology of Early Arthritis Cohort at Barts Health NHS Trust. Patients underwent ultrasound-guided synovial biopsy at baseline (n=164) and 6 months after standard treatment with synthetic DMARDs (n=104). Sequentially-cut sections were stained by HE for semi-quantitative (SQ) assessment of synovitis and by IHC for SQ

Table 1

		Baseline biopsy n=143#			6 months biopsy n=104#		
		B cell poor 93 (65%)	B cell rich 50 (35%)	p	B cell poor 82 (78.%)	B cell rich 22 (21.2%)	P
DAS28 mean (SD)		5.6 (1.38)	6.1 (1.2)	0.005	3.7 (1.9)	4.1 (1.2)	ns
TJ mean (SD)		11.3 (7.3)	13 (7.7)	ns	6.4 (8.1)	6.2 (7.6)	ns
SJ mean (SD)		7.1 (5.4)	8.8 (5.7)	0.048	2.6 (3.2)	4 (4.9)	ns
VAS GH, mean (SD)		60.6 (28.6)	64.8 (25.2)	ns	37.4 (33.2)	40.3 (32.2)	ns
ESR mean (SD)		34.6 (28.9)	49.5 (28.9)	0.001	19.1 (17.7)	24.9 (18.7)	ns
CRP mean (SD)		17.5 (32.7)	21.5 (24.2)	0.012	4.9 (10.3)	7.5 (13.2)	ns
ACPA %		59.8%	78.4%	0.024	61%%	90.9%	0.008
RF+ %		62%	80.4%	0.023	61%%	81.8%	ns
csDMARDs 6m %	0	22.6%	14%	na	12.2%	0%	ns
	1	7.5%	8%		9.8%	9.1%	
	2	66.7%	68%		68.3%	81.8%	
	3	3.2%	10%		9.8%	9.1%	
Steroids 6m %		30.1%	40%	na	36.6%	45.5%	ns
Synovitis score mean (SD)		3 (1)	6 (1)	<0.0001	2 (1)	6 (2)	<0.0001
Delta DAS28 6m mean (SD)		2.1 (1.9)	2.3 (1.6)	ns	2.1 (1.8)	2.1 (1.6)	ns
EULAR good or moderate responders 6m, %		76.9%	83.7%	ns	77.3%	81.8%	ns
Radiographic progression 12m, %		10.4%	29%	0.03	11.3%	36.8%	0.01

excluding patients with ungraded synovial biopsy samples;



assessment of CD20+ B cells (0-4) and classification into B cell-rich (≥2) or poor (< 2). X rays at baseline and 12 months underwent scoring for erosions and joint space narrowing, with radiographic progression defined as an increase in total score ≥ 1.

Results: At baseline, patients classified as B cell-rich (35%) had significantly higher disease activity, inflammatory markers, autoantibody positivity and synovitis score when compared to B cell-poor (Table 1). There were no differences between B cell-rich and poor patients in terms of drug exposure and EULAR clinical response at 12 months. However, patients with B cell-rich synovitis had a significantly higher rate of radiographic progression at 12 months. At the 6 months repeated synovial biopsy, 21.2% of the patients had B cell-rich synovitis, which still associated with ACPA positivity and higher synovitis score but not with other clinical features, including the use of csDMARDs and clinical response at 12 months. However, patients with a B cell-rich synovitis at 6 months showed significantly higher rates of radiographic progression at 12 months. Upon assessing the change of B cell infiltrates between 0 and 6 months, patients with a reduction in synovial B cell score (from B cell rich to poor) had a lower rate of radiographic progression compared to patients with persistent B cell-rich infiltrate (Figure 1).

Conclusion: We here confirm that B cell-rich synovitis in early RA patients is associated with disease severity and radiographic progression, particularly when the B cell-rich synovial infiltrate persist after 6 months treatment with csDMARDs, independently of the clinical response. This suggests that the presence of B cell-rich synovitis represents an important prognostic factor in RA.

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Abstract Number: 2871

Advances in Treatment of Rheumatoid Arthritis: ACPA-positive Patients Benefited More Than ACPA-negative Patients; 25 Year Results of a Longitudinal Cohort Study

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes V: Treatment
Session Type: ACR Abstract Session
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Background/Purpose: The last 25 years, treatment of rheumatoid arthritis (RA) has changed considerably. Although clinically relevant joint damage has become infrequent, it is less established to what extent other long-term outcomes have improved. Moreover, anti-citrullinated anti-bodies (ACPA)-positive and ACPA-negative disease subsets were discovered and it is unknown they have benefited equally from these improvements. Therefore our aim was to investigate the influence of improved treatment strategies on disease activity (DAS), sustained drug-free remission (SDFR) and functional disability, and if this differed for ACPA-positive and ACPA-negative RA-patients.

Methods: In the Leiden early arthritis cohort, consecutive patients with RA (1987 criteria) were included between 1993-2016. Patients were treated in routine care; initial and subsequent treatment changed over time; divided in 5 inclusion periods: 1993-1996 delayed mild disease modifying anti-rheumatic drug (DMARD) initiation; 1997-2000 early

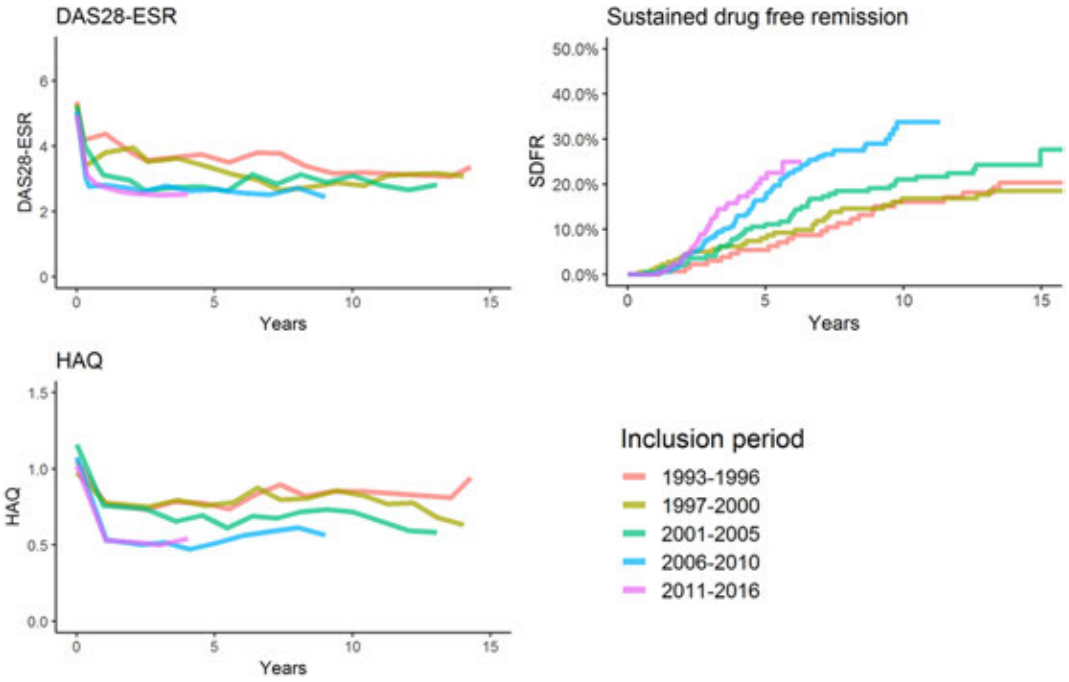

Figure 1. Outcomes over time stratified per inclusion period Legend: For DAS28-ESR and HAQ mean values of imputed data from visits that were attended are shown; When <15% of patients attended the visit, lines were truncated.

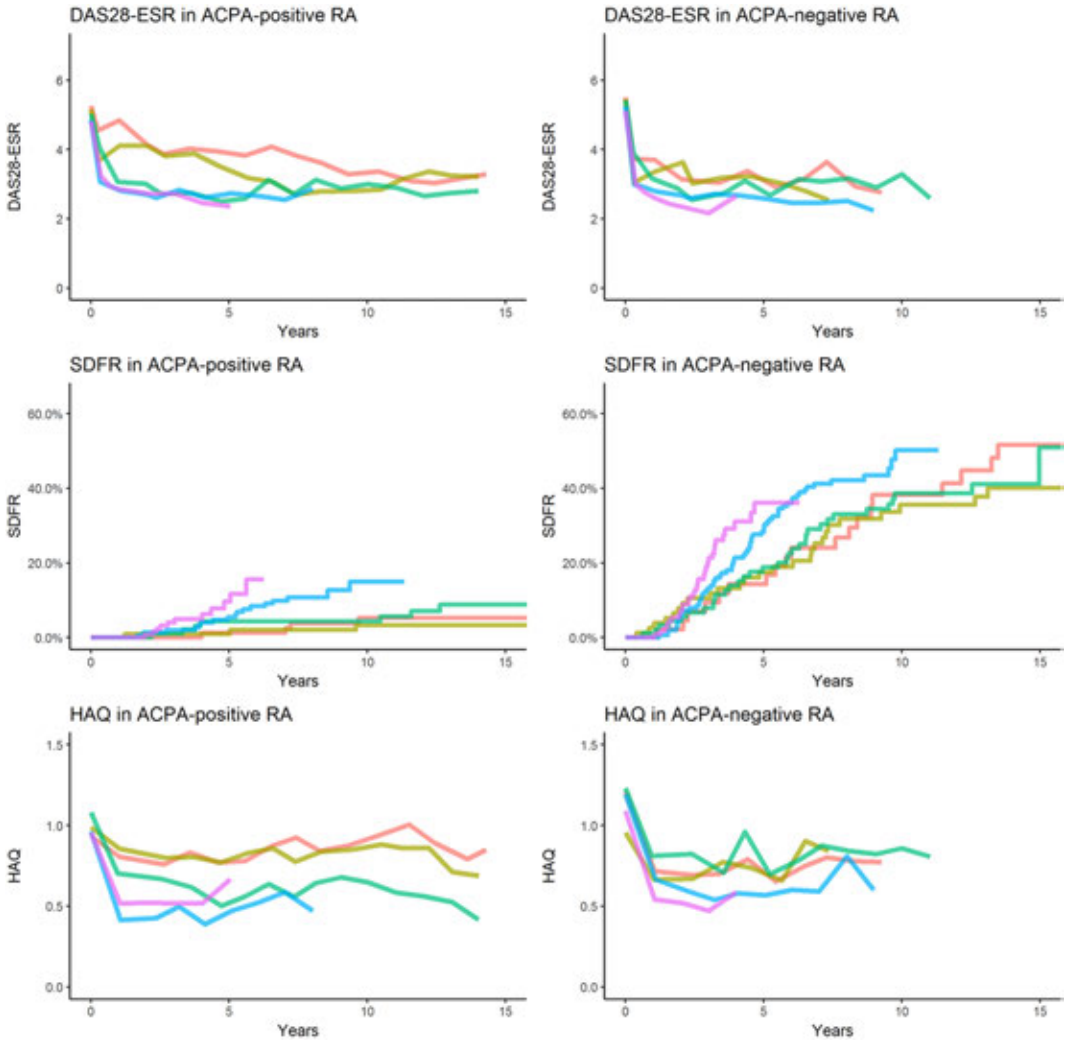

Figure 2. Outcomes over time stratified per inclusion period and ACPA-status Legend: Inclusion periods: Red: 1993-1996; Yellow: 1997-2000, Green 2001-2005, Blue 2006-2010, Purple 2011-2016. RA: Rheumatoid Arthritis; SDFR: Sustained drug-free remission. For DAS28-ESR and HAQ mean values of imputed data from visits that were attended are shown; When <15% of patients attended the visit, lines were truncated.

mild DMARDs; 2001-2005 early methotrexate; 2006-2010 early methotrexate followed by treat-to-target treatment adjustments; 2011-2016 idem plus additional efforts for very early referral.

SDFR was defined as persistent absence of synovitis after DMARD-cessation and was determined during all follow-up. Disease activity was measured yearly by the DAS28-ESR and functional disability by health assessment questionnaires (HAQ) and analysed with linear mixed models; time to SDFR with Cox regression. Analyses were stratified for ACPA (IgG anti-CCP2).

Results: In total 1291 RA-patients were included (168, 185, 210, 338 and 390 in the respective inclusion periods); baseline age, gender and ACPA-status were similar. All outcomes improved significantly over time (Figure 1) and this differed between ACPA-positive and ACPA-negative patients (Figure 2). In the reference period (1993-1996), ACPA-positive RA had worse outcomes than ACPA-negative RA in DAS (Difference of 0.81 points (0.48;1.13)), SDFR (HR 0.07 (0.02;0.21)) and HAQ over time (Difference of 0.15 points (-0.02;0.32)). Compared to the reference period, DAS improved gradually and significantly in ACPA-positive RA whereas the improvement was significantly less in ACPA-negative RA. SDFR-rates increased significantly in ACPA-positive RA, whereas there was no significant improvement in ACPA-negative RA. Functional disability over time improved more in ACPA-positive RA (improvement of -0.18

points in 2001-2005, -0.35 in 2006-2010 and -0.29 in 2011-2016) than in ACPA-negative RA (improvement of -0.19 in 2011-2016). In the most recent inclusion cohort (2011-2016), HAQ was similar in ACPA-positive and ACPA-negative RA. SDFR rates had become more similar although they remained higher in ACPA-negative RA.

Conclusion: ACPA-positive RA, traditionally the most severe RA-subset, benefited most from the improvements in treatment strategies, whereas ACPA-negative RA benefited little; This further demonstrates that these are indeed separate disease subsets that deserve equal attention.

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Abstract Number: 2872

Risk of 30-day Readmission and Adverse Events After Primary Hip or Knee Arthroplasty: A Comparison of Patients with Rheumatoid Arthritis versus Osteoarthritis Using the Nationwide Readmission Database

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes V: Treatment
Session Type: ACR Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: To assess the risk of 30-day readmission, mortality, and adverse events among adults with Rheumatoid Arthritis as compared to Osteoarthritis after primary hip or knee arthroplasty.

Methods: We identified index hospitalizations with a principal procedure of primary HA or KA using a nationally representative U.S. sample, the Nationwide Readmission Database (2010-2013). Excluded were persons aged < 18 years or who did not survive the index hospitalization. The principal procedure and diagnoses were identified using

Table of Abbreviations	
RA	Rheumaoid Arthritis
OA	Osteoarthritis
HA	Total or Partial Hip Arthroplasty
KA	Total Knee Arthroplasty
CAD	Coronary Artery Disease
VHD	Valvular Heart Disease
CHF	Congestive Heart Failure
CKD	Chronic Kidney Disease
PVD	Peripheral Vascular Disease
AKI	Acute Kidney Injury
COPD	Chronic Obstructive Pulmonary Disease
OR	Odds Ratio
CI	Confidence Interval

ICD-9 codes. Using survey logistic regression, we calculated the unadjusted and adjusted risk of 30-day readmission, all-cause mortality, and composite adverse events which included infections, cardiovascular events, venous thromboembolic events, mechanical complications, and AKI, after adjusting for age, sex, and major comorbidities.

Results: There were 1,977,214 index hospitalizations of which 10,802 were in persons with RA and 1,966,413 in persons with OA. Persons with RA were older (66.9 vs. 65.6; P< 0.01), more likely to be women (80.7% vs. 59.5%; P< 0.01), and to have existing comorbid conditions of CAD (10.0% vs. 8.0%;P< 0.01), chronic CHF (2.4% vs. 0.6%;P< 0.01), CKD (6.6% vs. 3.8%; P< 0.01), cancer (1.6% vs. 0.9%; P< 0.01), PVD (3.1% vs. 1.4%; P< 0.01), and COPD (20.8% vs. 14.0%; P< 0.01). There were 68,897 (3.5%) 30-day readmissions. The readmission rate was higher among persons with RA compared to OA (7.1% vs. 3.5%; P< 0.001). Stratified readmission rates for RA versus OA were (9.3% vs. 3.4%; P< 0.001) and (4.2% vs. 3.5%; P=0.18) in HA and KA, respectively. The adjusted OR for readmission was 2.06 [95% CI: 1.75,2.42], all-cause mortality 9.87 [95% CI:5.02,19.41], and composite event 2.29 [95% CI:1.81,2.89]. In analyses stratified by procedure type, the adjusted OR post-HA for readmission was 2.35 [95% CI: 1.94,2.83], all-cause mortality 6.16 [95% CI:2.96,12.82], and composite event 2.32 [95% CI:1.79,2.99] while post-KA the risk of readmission was 1.36 [95% CI: 1.02,1.80], all-cause mortality 13.81 [95% CI:3.35,56.90], and 1.78 for composite event [95% CI:1.14,2.78]. The overall adjusted risk for mechanical complications [OR:4.38; 95% CI:2.56,7.47], all-type infections [OR:2.23; 95% CI:1.71,2.92], and AKI [OR:3.78; 95% CI:1.41,10.13] was higher in RA while the risk for CVD [OR:1.73; 95% CI:0.77,3.87], DVT/PE [OR:0.95; 95% CI:0.45,2.02], or surgical site infections [OR:1.51; 95% CI:0.98,2.31] did not differ relative to OA. In stratified analyses, the risk for AKI and all-type infections was higher among persons RA in both procedure types while the risk for mechanical complications was only significant in HA [OR:1.99; 95% CI:1.14,3.47].

Conclusion: After primary joint arthroplasty, the 30-day rehospitalization, all-cause mortality, and composite events were more likely among persons with RA relative to OA, even after accounting for demographics and major comorbidities. All-type infections and acute kidney injury were more likely among person with RA after both hip and knee arthroplasty, while mechanical complication was significantly higher in persons with RA as compared to OA only after hip arthroplasty.

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Abstract Number: 2873

Antimicrobial Use Is High in Patients with Rheumatoid Arthritis, and Further Increases with First-Line TNFi Therapy – Nationwide Results from Iceland

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: RA – Diagnosis, Manifestations, & Outcomes V: Treatment

Session Type: ACR Abstract Session

Session Time: 9:00AM–10:30AM

Table 1

Antibiotic use as mean number of prescriptions (NP) and defined daily dose (DDD), per individual, two years before and after TNFi therapy.

	NP		DDD	
	RA *n = 366*	**Control** *n = 1830*	**RA** *n = 366*	**Control** *n = 1830*
Antibacterial *before TNFi*	2.6 ± 3.3	1.5 ± 2.4	33.4 ± 70.9	17.3 ± 34.9
after TNFi	3.2 ± 3.6**	1.5 ± 2.4	34.7 ± 58.7	17.4 ± 39.2
Antifungal *before TNFi*	0.16 ± 0.7	0.06 ± 0.5	0.43 ± 2.9	0.13 ± 1.2
after TNFi	0.25 ± 1 *	0.08 ± 0.4	0.78 ± 4.6*	0.23 ± 1.9
Antivirals *before TNFi*	0.05 ± 0.47	0.06 ± 0.45	0.36 ± 3.4	0.3 ± 3.3
after TNFi	0.15 ± 0.73**	0.06 ± 0.64	0.77 ± 4*	0.33 ± 3.6

*p<0.05; **p<0.001 by Wilcoxon-squared test

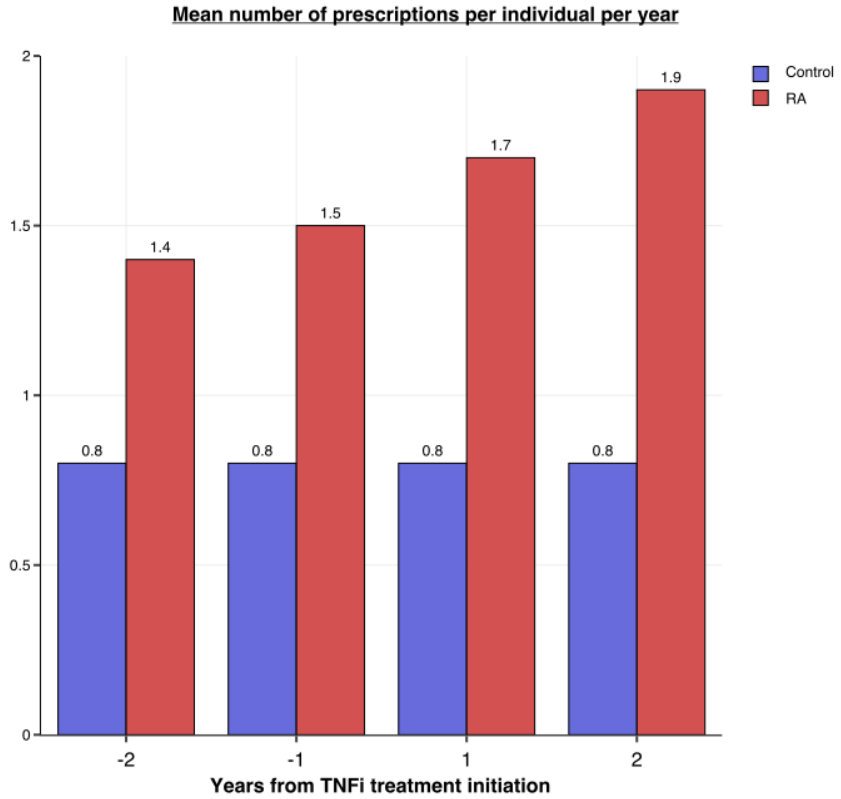

Figure 1. Antimicrobial use as mean yearly number of prescription per individual in relation to initiation of TNFi therapy (baseline). Patients with RA (red) received significantly higher number of prescriptions compared to controls (blue). Antimicrobial usage in patient with RA increased through the two-year period following TNFi therapy.

Background/Purpose: Severe infections, frequently resulting in hospitalization, are a well-known adverse effects of tumor necrosis factor inhibitors (TNFi). However, studies regarding outpatient treated infections are needed.

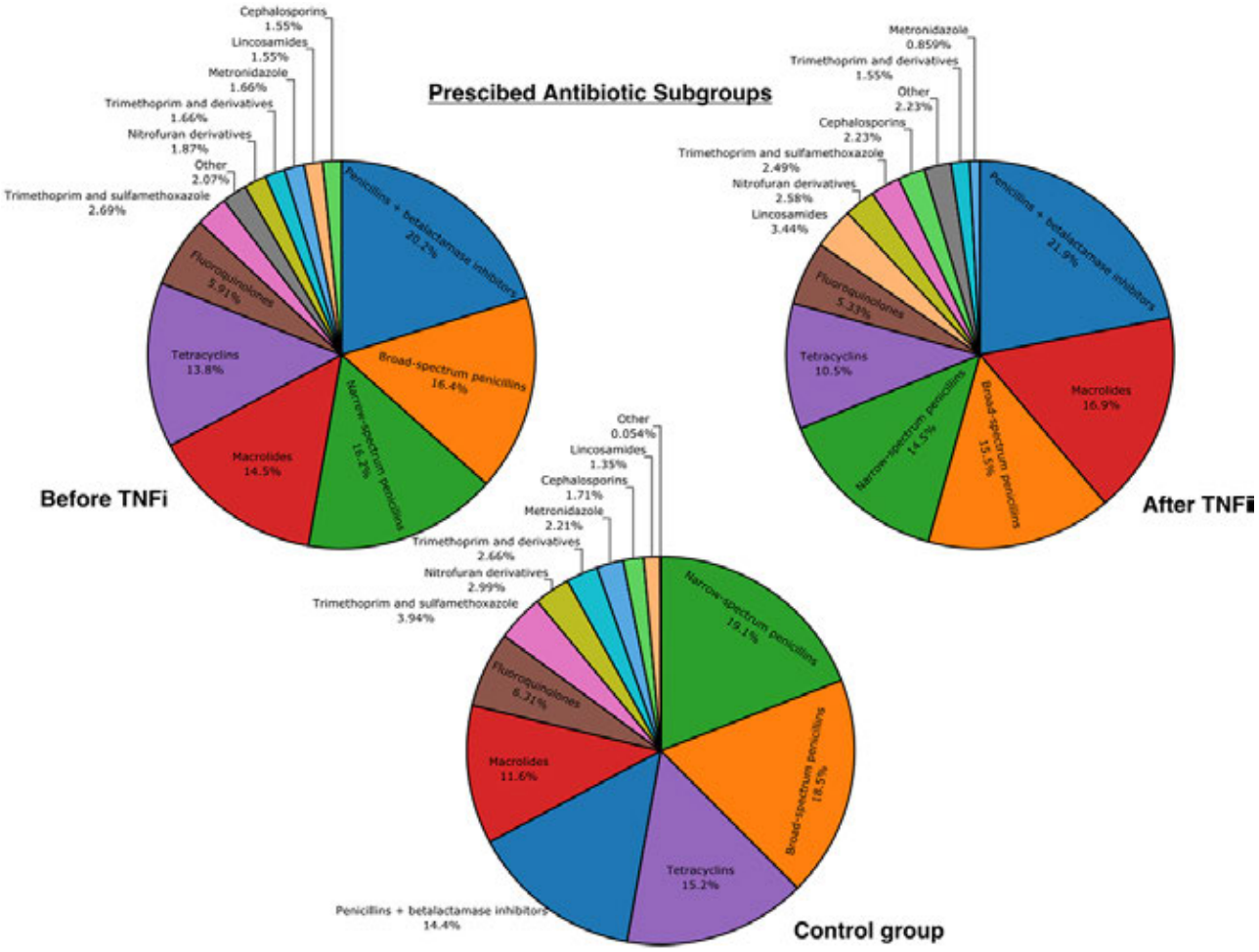

Figure 2. Pie chart of prescribed antibiotic subgroups as defined by the Anatomical Therapeutic Chemical (ATC) classification system. Prescription patterns are similar before (upper left) and after (upper right) initiation of TNFi therapy. Below is the pie chart for the control group.

Our objective was to investigate the use of antimicrobials (antibiotics, antifungals and antivirals; excluding antimycobacterials) in patients with rheumatoid arthritis (RA) and the effect of initiation of TNFi in biologic-naïve patients.

Methods: Over 98% of patients with inflammatory arthritides who are treated with biologic DMARDs in Iceland are registered in ICEBIO, a nationwide registry. On February 1st 2016, ICEBIO contained information on 1058 individuals. Information about all biologic-naïve patients with RA was extracted and each patient matched on age, sex and calendar time to five randomly selected individuals. All filled antimicrobial prescriptions in the two years before and after initiation of first TNFi were extracted from the Icelandic Medicine Database (IMD), a registry that includes over 95% of all filled prescriptions in Iceland. Antimicrobial use was quantified using the number of filled prescriptions (NP) and defined daily dose (DDD). NP and DDD are shown as individual means per two years before and after TNFi therapy.

Results: We extracted information on 366 patients with RA and 1833 controls. Patients with RA received nearly twice the number of antimicrobial prescriptions compared to controls before TNFi therapy (2.9 vs 1.6 NP; $p< 0.001$, figure 1). After initiation of TNFi the mean NP for RA patients increased (2.9 to 3.6; $p< 0.001$) and further increased over a two-year period (figure 1); antibiotics 2.6 to 3.2 ($p< 0.001$), antivirals 0.06 to 0.15 ($p< 0.001$) and antifungals 0.16 to 0.25 ($p< 0.05$) (table 1). Conversely, DDD of antibiotics was stable (33.4 to 34.7; $p >0.1$). However, DDD for both antivirals and antifungals increased ($p< 0.05$). After TNFi initiation, antifungal usage increased predominantly in women (0.4 to 0.84 DDD; $p< 0.05$) and antivirals in men (0.00 to 0.82 DDD; $p< 0.05$). No correlation was found between NP

and age, BMI or baseline DAS28-CRP. However, a minor positive correlation (r 0.2) was between NP and HAQ score at beginning of TNFi therapy. Patients with HAQ score higher than 2.0 received significantly higher NP after TNFi therapy (3.1 vs 5.7 NP; p< 0.001). No difference was found between smokers and non-smokers (3.1 vs 3.8; p=0.38). Interestingly, mean DDD per prescription decreased after initiation of TNFi (14.5 to 10.2 DDD, p< 0.001). Physicians selection of antibiotics did not appear to change after TNFi treatment (figure 2).

Conclusion: Patients with RA use significantly more antimicrobials two years antedating TNFi treatment compared to controls. TNFi treatment further increases antimicrobial use in patients with RA and usage increased throughout the two-year period. This contrasts the literature regarding hospital admissions due to infections, where admissions frequency peaks the first year after TNFi treatment, but then decreases with TNFi treatment duration[1]. High HAQ score at the start of TNFi treatment was related to increased antimicrobial usage following TNFi therapy.

Reference:

1) Askling J., et al., *Ann Rheum Dis*, 2007;*66*;1339–44.

Disclosure: A. Bjornsson, None; **O. Palsson**, None; **M. Kristjansson**, None; **P. Gunnarsson**, None; **G. Grondal**, None; **B. Gudbjornsson**, Actavis, 8, Amgen, 8, Novartis, 8, Pfizer, 8; **T. Love**, Celgene, 5.

Abstract Number: 2874

Comparison of Malignancy and Mortality Rates Between Tofacitinib and Biologic DMARDs in Clinical Practice: Five-Year Results from a US-Based Rheumatoid Arthritis Registry

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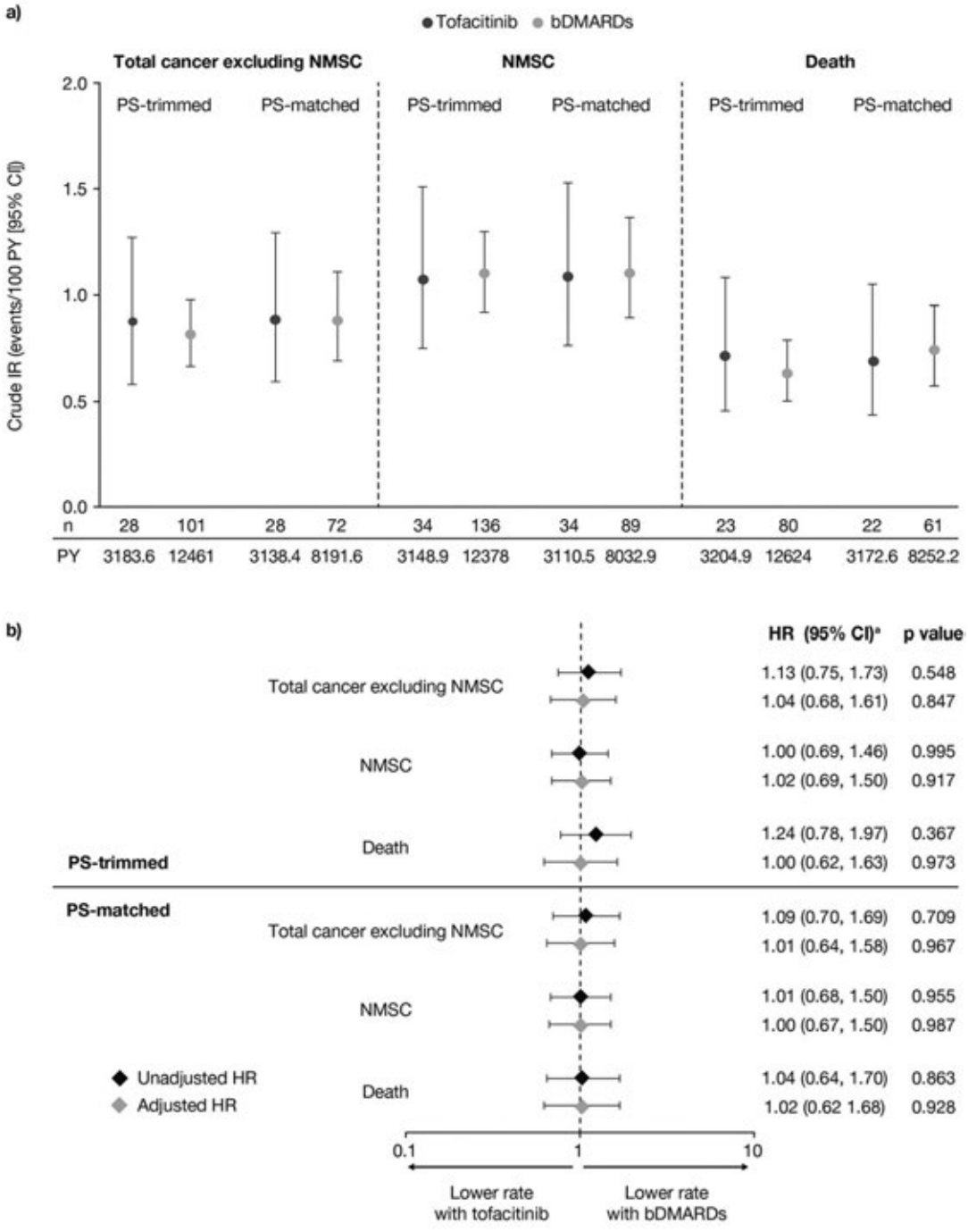
SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: RA – Diagnosis, Manifestations, & Outcomes V: Treatment
Session Type: ACR Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: Real-world evidence (RWE) is key to understanding post-approval long-term safety of medications. Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. A prospective observational 5-year study, embedded within the US Corrona RA registry, was initiated to evaluate the safety of tofacitinib after US Food and Drug Administration approval on Nov 6, 2012. The objective of this analysis was to compare 5-year incidence rates (IRs) of malignancy and mortality in patients (pts) initiating tofacitinib vs biologic (b)DMARDs using US Corrona RA registry cohorts.

Methods: This prospective, observational 5-year study derived from the ongoing US Corrona RA registry routinely collects structured safety data on serious adverse events (AEs) and AEs of interest from investigators. IRs (no. of events/100 pt-years [PY]) of total cancer (excluding non-melanoma skin cancer [NMSC]), NMSC, and death were compared using propensity score (PS) methods to adjust for non-random treatment assignment among RA pts who newly initiated tofacitinib (US approved dose 5 mg twice daily) or a bDMARD regardless of dose/schedule between Nov 6, 2012 and July 31, 2018 (follow-up through Jan 31, 2019). Sufficient malignancy and mortality events occurred

Figure 1. a) Crude IRs (events/100 patient-years) for total cancer excluding NMSC, NMSC, and death, and b) HRs for total cancer excluding NMSC, NMSC, and death



[a]bDMARD initiators were the reference population for calculation of HR
bDMARD; biologic disease-modifying antirheumatic drug; CI, confidence interval; HR, hazard ratio; IR, incidence rate; NMSC, non-melanoma skin cancer; PS, propensity score; PY, patient-years

to provide 80% power to detect a hazard ratio (HR) of 2.0. Baseline variables with standardized difference > | 0.10 | between cohorts and *a priori* selected covariates (gender, age, line of therapy, history of AE of interest) were used to derive PS-trimmed (primary analysis) and PS-matched populations (ratio: max. 4 bDMARD:1 tofacitinib; caliper=0.05). Analyses used a 'once exposed, always exposed' approach following patients from therapy initiation until an AE of interest, loss to follow-up, or end of data collection period, whichever came first; follow-up continued if a patient discontinued or switched therapy. Multivariable-adjusted Cox regression was used to estimate HRs of first events between cohorts.

Results: In total, 1999 tofacitinib (4505.62 PY) and 6354 bDMARD (16670.84 PY) initiators were included. Following PS trimming, analyses for total cancer excluding NMSC, NMSC, and death, respectively, included 1420/1419/1419 tofacitinib initiators, and 4820/4820/4821 bDMARD initiators. Of tofacitinib and bDMARD initiators, respectively, 88% and 59% had prior bDMARD use. IRs of all three outcomes were similar in both cohorts; the adjusted HR (95% confidence interval [CI]) was 1.04 (0.68, 1.61) for total cancer excluding NMSC, 1.02 (0.69, 1.50) for NMSC, and 1.0 (0.62, 1.63) for death (Figure 1). Similar results were observed in PS-matched populations.

Conclusion: To our knowledge, this is the first comparative RWE for tofacitinib and bDMARDs to use PS-trimmed/matched analyses to adjust for channeling/prescribing patterns. RA pts initiating tofacitinib or bDMARDs had similar rates of total cancer excluding NMSC, NMSC, and death.

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Disclosure: J. Kremer, AbbVie, 2, 5, Amgen, 5, Bristol-Myers Squibb, 2, 5, Corrona, 1, Genentech, 2, 5, Gilead, 5, Lilly, 2, 5, Novartis, 2, Pfizer, 2, 5, Regeneron, 5, Sanofi, 5; **C. Bingham**, Abbvie, 5, AbbVie, 5, BMS, 2, 5, Bristol Meyer Squibb, 2, 5, Bristol Myers-Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Eli/Lilly, 5, Genentech/Roche, 5, Janssen, 5, Janssen Research & Development, LLC, 2, Pfizer Inc, 5, Regeneron/Sanofi, 5, Sanofi/Regeneron, 5; **L. Cappelli**, Bristol Meyer Squibb, 2, Bristol-Myers Squibb, 2, Regeneron/Sanofi, 5, Regeneron/Sanofi Genzyme, 5; **J. Greenberg**, Corrona, LLC, 1, 3; **A. Madsen**, Pfizer Inc, 1, 3; **J. Geier**, Pfizer Inc, 1, 3; **J. Rivas**, Pfizer Inc, 1, 3; **A. Onofrei**, Corrona, LLC, 3; **C. Barr**, Corrona, LLC, 1, 3; **D. Pappas**, AbbVie, 5, Corrona, LLC, 1, 3, Novartis, 5, Roche, 5, Roche Hellas, 5; **H. Litman**, Corrona, LLC, 3; **K. Dandreo**, Corrona, LLC, 3; **A. Shapiro**, Pfizer Inc, 1, 3; **C. Connell**, Pfizer Inc, 1, 3; **A. Kavanaugh**, Abbott, 2, Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, 2, Amgen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 2, Janssen, 2, Janssen Research & Development, LLC, 2, Novartis, 2, 5, Pfizer, 2, Pfizer Inc, 2, Roche, 2, UCB Pharma, 2.

Abstract Number: 2875

Effects of Filgotinib on Anemia, Thrombocytopenia and Leukopenia: Results from a Phase 3 Study in Patients with Active Rheumatoid Arthritis and Prior Inadequate Response or Intolerance to Biological DMARDs

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

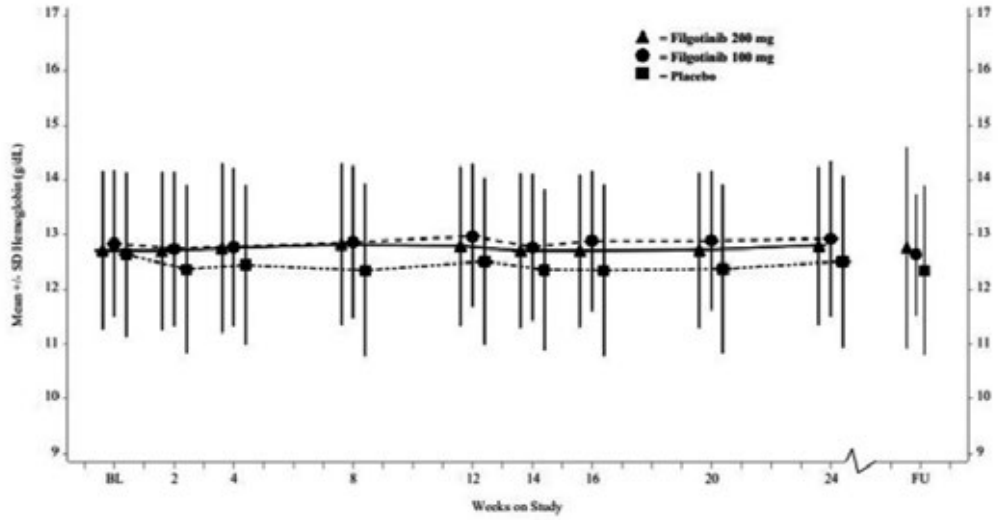
Session Title: RA – Diagnosis, Manifestations, & Outcomes V: Treatment

Session Type: ACR Abstract Session

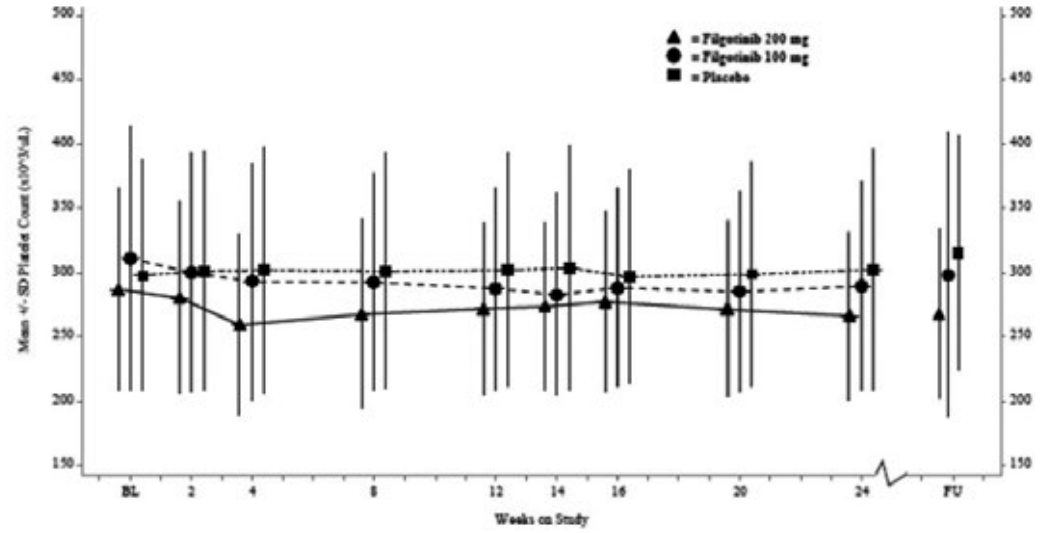
Session Time: 9:00AM–10:30AM

Figure. Mean (±SD) hemoglobin, platelet, lymphocyte and neutrophil count by study visit

A.



B.



Background/Purpose: Anemia, thrombocytopenia and leukopenia in RA patients treated with non-Janus Kinase 1 (JAK1) selective inhibitors may be due to inhibition of hematopoietic growth factors signaling through JAK2. Therefore, we investigated the extent of anemia, thrombocytopenia and leukopenia in patients with active RA with a prior inadequate response/intolerance to biological DMARD (bDMARD) treated with filgotinib (FIL), a novel and selective JAK1 inhibitor, during a Phase 3, 24-week trial (FINCH-2; NCT02873936).

Methods: In the randomized, double-blind, placebo-controlled Phase 3 FINCH-2 trial, patients were randomized 1:1:1 to receive oral FIL 200 mg, 100 mg, or placebo (PBO) once daily for 24 weeks in addition to conventional synthetic DMARDs. We assessed shifts from baseline at 12 and 24 weeks in hemoglobin, platelets, neutrophils and lymphocytes in FINCH-2 patients, assessed by baseline values as normal, mild-moderate and severe for these variables.

Table: Shift from baseline in hemoglobin, platelet, neutrophil and lymphocyte category at Weeks 12 and 24

Hemoglobin							
Baseline level	**Normal***			**Mild-Moderate†**			**Severe**
Treatment arm	**PBO N=101**	**FIL 100 mg N=117**	**FIL 200 mg N=101**	**PBO N=47**	**FIL 100 mg N=36**	**FIL 200 mg N=46**	**n/a**
Week 12, n/N# (%)							
Normal*	83/129 (64.3)	99/138 (71.7)	84/136 (61.8)	2/129 (1.6)	13/138 (9.4)	14/136 (10.3)	-
Mild‡	6/129 (4.7)	6/138 (4.3)	7/136 (5.1)	34/129 (26.4)	19/138 (13.8)	29/136 (21.3)	-
Moderate§	0	0	0	3/129 (2.3)	1/138 (0.7)	2/136 (1.5)	-
Severe‖	0	0	0	1/129 (0.8)	0	0	-
Missing	12	12	10	7	3	1	-
Week 24, n/N# (%)							
Normal*	54/92 (58.7)	82/116 (70.7)	73/122 (59.8)	7/92 (7.6)	11/116 (9.5)	16/122 (13.1)	-
Mild‡	9/92 (9.8)	7/116 (6.0)	10/122 (8.2)	18/92 (19.6)	13/116 (11.2)	21/122 (17.2)	-
Moderate§	0	0	0	4/92 (4.3)	2/116 (1.7)	2/122 (1.6)	-
Severe‖	0	0	0	0	1/116 (0.9)	0	-
Missing	38	28	18	18	9	7	-
Platelet							
Baseline level	**Normal***			**Mild-Moderate†**			**Severe**
Treatment arm	**PBO N=146**	**FIL 100 mg N=152**	**FIL 200 mg N=145**	**PBO N=1**	**FIL 100 mg N=1**	**FIL 200 mg N=2**	**n/a**
Week 12, n/N# (%)							
Normal*	125/128 (97.7)	138/138 (100)	134/136 (98.5)	1/128 (0.8)	0	2/136 (1.5)	-
Mild‡	2/128 (1.6)	0	0	0	0	0	-
Moderate§	0	0	0	0	0	0	-
Severe‖	0	0	0	0	0	0	-
Missing	19	14	11	0	1	0	-
Week 24, n/N# (%)							
Normal*	90/91 (98.9)	114/114 (100)	118/121 (97.5)	1/91 (1.1)	0	2/121 (1.7)	-
Mild‡	0	0	1/121 (0.8)	0	0	0	-
Moderate§	0	0	0	0	0	0	-
Severe‖	0	0	0	0	0	0	-
Missing	56	38	26	0	1	0	-
Neutrophil							
Baseline level	**Normal***			**Mild-Moderate†**			**Severe**

Results: A total of 448 patients were enrolled and treated, FIL 200 mg, n = 147; FIL 100 mg, n = 153; PBO, n = 148. Overall, hemoglobin levels, platelet, lymphocyte and neutrophil counts remained consistent throughout the study (Figure). At baseline, 129 (28.8%), 4 (0.9%), 10 (2.2%) and 26 (5.8%) patients had mild-moderate low levels of hemoglobin, platelet, neutrophil and lymphocyte, respectively, and 5 (1.1%) had severely low levels of lymphocytes. Of the patients with mild-moderate hemoglobin levels at baseline, 13.1% with FIL 200 mg, 9.5% with FIL 100 mg, and

7.6% with PBO achieved normal hemoglobin at Week 24, respectively (Table). Of those with normal baseline hemoglobin levels, only 6.0–9.8% had mild low levels at Week 24. All patients with baseline mild-moderate low platelets and neutrophils had normal levels at Week 24, except for one patient with mild neutropenia receiving FIL 100 mg. Of the patients with normal platelet and neutrophil levels at baseline, >94% maintained these at Week 24 in all treatment groups. By Week 24, 3.2%, -5.2% and 2.2% of patients treated with FIL 200 mg, FIL 100 mg and PBO, respectively in the mild-moderate subgroup and 1.7% in the severe subgroup treated with FIL 100 mg had normal lymphocyte counts.

Conclusion: In this FINCH-2 subgroup analysis, most patients with normal hemoglobin, platelet, lymphocyte and neutrophil levels at baseline maintained them over 24 weeks of FIL treatment. Of the patients with mild-moderately low hemoglobin at baseline, >9% shifted towards hemoglobin normalization. Similar patterns of improvement from baseline were observed for platelet, lymphocyte and neutrophil counts. These results suggest that FIL does not increase the incidence of anemia, thrombocytopenia or leukopenia in patients who entered the study with active RA despite prior biologic therapies.

Disclosure: M. Genovese, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 9, Astellas, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck Serono, 2, 5, Galapagos, 2, 5, Galapagos NV, 2, 5, 9, Genentech/Roche, 2, 5, Gilead, 2, 5, Gilead Science, 9, Gilead Sciences, Inc., 2, 5, 9, GSK, 5, Lilly, 2, 5, 9, Novartis, 2, 5, Pfizer, 2, 5, 9, Pfizer Inc, 2, 5, Pfizer, Inc., 9, Pzier, 9, RPharm, 5, Sanofi Genzyme, 2, 5, Vertex, 2, 5; **K. Kalunian**, AbbVie, 9, Abbvie, 5, Amgen, 5, AstraZeneca, 5, Biogen, 5, 9, BMS, 2, 9, Chemocentryx, 5, Eli Lilly, 5, 9, Equillium, 5, Exagen, 2, Genentech/Roche, 5, Gilead, 9, Gilead Sciences, Inc., 9, GSK, 5, Idosia, 2, Janssen, 5, Kirin, 2, MedImmune, 5, Nektar, 5, Pfizer, 2, Resolve, 2, Roche, 9, Takeda, 2, UCB, 2; **J. Gottenberg**, Abbvie, 8, BMS, 2, 5, Lilly, 5, 8, Pfizer, 2, 5, Roche, 8, Sanofi-Genzyme, 5, 8, UCB, 5, 8; **B. Bartok**, Gilead Sciences, Inc., 3, 4; **Y. Tan**, Gilead Sciences, Inc., 3, 4; **Y. Guo**, Gilead Sciences, Inc., 3, 4; **C. Tasset**, Galapagos, 1, 3, Galapagos NV, 3, 4; **J. Sundy**, Gilead Sciences, Inc., 3, 4; **K. de Vlam**, Celgene, 5, 8, Eli Lilly, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **D. Walker**, BMS, 8, Gilead Sciences, Inc., 8, Lilly, 8, Novartis, 8, Pfizer, 8; **T. Takeuchi**, AbbVie, 2, 5, 8, AbbVie GK, 2, 9, Asahi Kasei, 2, Asahikasei, 2, Asahikasei Pharma Corp., 2, Astellas, 2, 8, 9, Astellas Pharma Inc, 2, Astellas Pharma, Inc., 2, 5, 8, 9, Astra Zeneca, 2, AstraZeneca, 8, AYUMI, 2, 9, AYUMI Pharmaceutical Corporation, 2, BMS, 2, 8, Boehringer-ingelheim, 9, Bristol–Myers K.K., 9, Bristol-Myers, 2, Bristol-Myers Squibb, 8, Chugai, 2, 8, 9, Chugai Pharmaceutical Co, Ltd., 2, Daiichi Sankyo, 2, 8, 9, Daiichi Sankyo Co., Ltd., 2, Eisai, 2, 5, 8, 9, Eisai Co., Ltd., 2, Eli Lilly, 2, 8, Eli Lilly Japan, 9, Gilead Sciences, Inc., 9, GlaxoSmithKline K.K, 9, GSK, 8, Janssen, 2, 8, Janssen Pharmaceutical K.K, 9, Mitsubishi Tanabe, 2, 9, Mitsubishi Tanabe Pharma Co., 2, Mitsubishi-Tanabe Pharma Corp, 2, 8, 9, Nippon Kayaku, 2, Nipponkayaku, 2, 9, Nipponkayaku Co.Ltd., 2, Novartis, 2, 8, Novartis Pharma K.K, 2, 9, Novartis Pharma K.K., 2, Pfizer, 2, 8, Pfizer Japan, 2, 9, Pfizer Japan Inc., 2, Sanofi, 8, Sanofi K.K, 9, Shionogi & Co., 2, Shionogi & Co., LTD., 2, Taiho, 2, 8, 9, Taisho, 9, Taisho Toyama, 2, 8, Takahashi Industrial and Economic Research Foundation, 2, Takeda, 2, 8, Takeda Pharmaceutical Co., Ltd., 2, Teijin, 2, 8, UCB, 8, 9, UCB Japan, 9.

Abstract Number: 2876

Go-Dact: A Phase 3b Randomized Double-Blind Placebo-Controled Proof-Of-Concept Trial, of Golimumab Plus Methotrexate (MTX) versus MTX Monotherapy, in Improving Dactylitis, in MTX Naïve Psoriatic Arthritis Patients

Elsa Vieira-Sousa,[1] Pedro Alves,[2] Ana Maria Rodrigues,[3] Filipa Teixeira,[4] José Tavares-Costa,[5] Alexandra Bernardo,[6] Sofia Pimenta,[6] Fernando Pimentel-Santos,[7] João Lagoas Gomes,[8] Renata Aguiar,[9] Patrícia Pinto,[10] Taciana Videira,[10] Cristina Catita,[11] Helena Santos,[12] Joana Borges,[13] Graça Sequeira,[14] Célia Ribeiro,[14] Lídia Teixeira,[15] Pedro Ávila-Ribeiro,[16] Fernando M Martins,[17] Helena Canhão,[18] Ruy M Ribeiro,[19] and João Eurico Fonseca[16], [1]Rheumatology and Metabolic Bone Diseases, Hospital de Santa Maria - Centro Hospitalar Lisboa Norte, EPE | Rheumatology Research Unit, Instituto de Medicina Molecular - Faculty of Medicine, University of Lisbon, Lisbon Academic Medical Centre, Lisbon, Portugal,, Lisbon, Portugal, [2]Radiology Department, CHLC, Lisbon, Portugal, [3]Rheumatology Unit, , HSEIT, Ilha Terceira, Açores e FMUL, Centro Académico de Medicina de Lisboa, Lisbon, Portugal, [4]Rheumatology Department, ULSAM, Ponte de Lima, Portugal, [5]ULSAM, Ponte de Lima, Portugal, [6]Rheumatology Department, CHSJ, Porto, Portugal, [7]CEDOC, NOVA-Medical School | Hospital Egas Moniz, CHLO, Lisbon, Lisbon, Portugal, [8]Rheumatology Department, Hospital de Egas Moniz, Centro Hospitalar de Lisboa Ocidental; CEDOC, NOVA Medical School, Faculdade de Ciências Médicas, Lisbon., Lisbon, Portugal, [9]Rheumatology Department, CHBV, Aveiro, Portugal, [10]Rheumatology Department, CHVNG, Vila Nova de Gaia, Portugal, [11]Hospital Particular do Algarve, Faro, Portugal, [12]Instituto Português de Reumatologia (IPR), Lisbon, Portugal, [13]Instituto Português de Reumatologia, Lisbon, Portugal, [14]Rheumatology Unit, CHA, Faro, Portugal, [15]Rheumatology Department, HGO, Almada, Portugal, [16]Rheumatology and Bone Diseases Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte; Unidade de Investigação em Reumatologia, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa; Centro Académico de Medicina de Lisboa; Lisbon, Portugal., Lisbon, Portugal, [17]Portuguese Society of Rheumatology, Lisbon, Portugal, [18]CEDOC, EpiDoC Unit, NOVA Medical School, Lisbon, Lisbon, Portugal, [19]Laboratório de Biomatemática, FMUL, Lisbon, Portugal

SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical VII: Psoriatic Arthritis Treatment

Session Type: ACR Abstract Session

Session Time: 9:00AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) dactylitis is associated with an increased risk of erosions and higher disease activity. Dactylitis treatment strategies are however controversial due to the absence of evidence from randomized controlled trials studying dactylitis as a primary outcome. The objective of this trial was to assess the efficacy of golimumab in combination with methotrexate (MTX) versus MTX monotherapy in active PsA dactylitis.

Methods: GO-DACT was a proof-of-concept multicentric, investigator-initiated randomized, double-blind, placebo-controlled, parallel-design, phase 3b trial. PsA patients, fulfilling the ClASsification for Psoriatic ARthritis criteria, naïve to MTX and biologic disease modifying anti-rheumatic drugs (bDMARDs), with active dactylitis, were randomly allocated to receive subcutaneous injections of golimumab 50mg or placebo, administrated every four weeks for 24 weeks, both in combination with MTX. The primary endpoint was the change from baseline in the Dactylitis Severity Score (DSS) assessed at week 24. Key dactylitis secondary endpoints included DSS20, 50 and 70 response rates, changes and response rates in the Leeds Dactylitis Index (LDI20, 50 and 70) and changes in the magnetic resonance imaging (MRI) dactylitis score. Analysis was by intention to treat for the primary endpoint.

Results: 44 patients were centrally randomized, 21 to golimumab plus MTX and 23 to placebo plus MTX, for 24 weeks, and 1 patient from each arm dropped out. The median baseline DSS was 6 in each arm. The mean MTX dose reached in the golimumab plus MTX group was 16.3mg/week and in the MTX monotherapy group was 19.2mg/week. Patients treated with golimumab plus MTX experienced significantly greater improvements in the DSS at week 24

(median change of 5) as compared to the MTX group (median change of 2) (p=0.026). At week 24, significantly higher proportions of patients treated with golimumab plus MTX achieved DSS50/70 responses, as well as LDI20/50/70 responses (p< 0.05). At week 24, significantly lower median dactylitis MRI scores were observed in patients treated with golimumab plus MTX in comparison with those treated with MTX monotherapy (p=0.017). The median changes from baseline in the Disease Activity Score 28 (DAS28), the Disease Activity Index for PsA (DAPSA), the PsA Disease Activity Score (PASDAS) and the target Nail Psoriasis Severity Index (tNAPSI) at week 24, were significantly higher for those treated with golimumab plus MTX. Patient' inclusion was halted at 50% of recruitment due to a favorable interim analysis. There were no new safety issues for golimumab during this trial.

Conclusion: GO-DACT shows additional benefits from the combination of golimumab and MTX as first-line bDMARD therapy versus MTX monotherapy, in the treatment algorithm of active PsA dactylitis.

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Abstract Number: 2877

Safety and Efficacy Results from the Open Label Extension of a Phase 2 Trial of Risankizumab, a Selective IL-23p19 Inhibitor in Patients with Active Psoriatic Arthritis

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical VII: Psoriatic Arthritis Treatment

Session Type: ACR Abstract Session

Session Time: 9:00AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) is characterized by peripheral synovitis, enthesitis, dactylitis and spondylitis, and IL-23 is involved in the pathogenesis of these conditions either directly or indirectly. Risankizumab (RZB), a potent humanized IgG1 monoclonal antibody and selective IL23p19 inhibitor, exhibited superior efficacy vs placebo via ACR responses and PASI scores in patients (pts) with active PsA over 24 weeks (wks). Here, the objective is to report the safety and efficacy of RZB in pts who continued into the open-label extension (OLE, NCT02986373) after completing a 24-Wk Phase 2 study.

Methods: Pts who completed the 24-Wk double-blind Phase 2 study and met the inclusion criteria were eligible to enroll in this 52-Wk, single-arm, OLE and received 150 mg RZB every 12 wks for 36 wks. Safety and efficacy assessments (ACR and PASI responses, DAS28[CRP], Leeds Indices [dactylitis and enthesitis], and SF-36) were recorded at each visit (wks 0, 4, 12, 24, 36, 48, 52).

Results: Of 173 pts who completed the 24-Wk study, 145 (83.8%) enrolled in the OLE. The median age was 51 years and 61 (42.1%) pts were female. At baseline (BL, Week 0 of the 24-Wk study), 63 (44.4%) pts had psoriasis (PsO) ≥3% BSA, 40 (27.8%) / 73 (53.5%) showed presence of dactylitis/enthesitis, 35 (24.1%) had prior TNFi exposure and 83 (57.2%) were receiving concomitant MTX. Compared with response rates for pooled RZB data from the 24-Wk study, the ACR and PASI (in pts with PsO ≥3% BSA) response rates were higher/similar at Wk 52 (n/N: ACR20: 68/135 to 76/101; ACR50: 31/135 to 44/101; ACR70: 18/136 to 25/101; PASI90: 33/57 to 30/41; PASI100: 23/57 to 25/41; observed data). Mean change from BL (ΔBL) in DAS28[CRP] increased from -1.4 to -1.9 (Wk 52 mean: 2.7) and ΔBL in Leeds indices for dactylitis and enthesitis were -74.5 and -1.8, respectively. Pts also reported increase in ΔBL in physical and mental component summaries of SF-36 at Wk 52. There were no deaths, malignancies or cases of active tuberculosis in the study. A total of 60% pts had treatment-emergent adverse event (TEAEs), with viral upper respiratory tract infection being the most common (11.0%). Serious TEAEs and TEAEs leading to RZB discontinuation were low (3.4%).

Conclusion: Pts with active PsA treated with RZB maintained improvement in joint and skin symptoms throughout the OLE with no new or unexpected safety findings. These results were substantiated by enhanced patient quality-of-life.

Disclosure: K. Papp, AbbVie, 5, 8, Akros, 5, 6, 8, Allergan, 5, 8, Amgen, 5, 8, Anacor, 5, 6, 8, Kyowa Hakko Kirin, 5, 6, 8, Arcutis, 5, 8, Astellas, 5, 8, AstraZeneca, 5, 8, Baxalta, 5, 8, Baxter, 5, 8, BMS, 5, 8, Boehringer Ingelheim, 5, 8, CanFite, 5, 8, Celgene, 5, 8, Coherus, 5, 8, Demira, 5, 8, Dow Pharma, 5, 8, Eli Lilly, 5, 8, Forward Pharma, 5, 8, Galderma, 5, 8, Genentech, 5, 8, Gilead, 5, 8, GSK, 5, 8, InflaRx GmbH, 5, 8, Janssen, 5, 8, Leo, 5, 8, MedImmune, 5, 8, Meiji Seika Pharma, 5, 8, Merck Sharp & Dohme, 5, 8, Merck-Serono, 5, 8, Mitsubishi Pharma, 5, 8, Moberg Pharma, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, PRCL Research, 5, 8, Regeneron, 5, 8, Roche, 5, 8, Sanofi-Aventis/Genzyme, 5, 8, Takeda, 5, 8, UCB, 5, 8, Valeant/Bausch Health, 5, 8; **M. Gooderham**, AbbVie, 5, 8, Actelion, 5, 8, Akros Pharma Inc, 5, 8, Amgen, 5, 8, Arctuis Pharmaceuticals Inc, 5, 8, Boehringer Ingelheim, 5, 8, Bristol-Myers Squibb Co., 5, 8, Celgene, 5, 8, Dermira, 5, 8, Eli Lilly & Co, 5, 8, Galderma, 5, 8, Glenmark, 5, 8, GSK, 5, 8, Janssen, 5, 8, LEO Pharma, 5, 8, MedImmune, 5, 8, Merck & Co., 5, 8, Novartis, 5, 8, Pfizer, Inc, 5, 8, Regeneron, 5, 8, Roche, 5, 8, Sanofi Genzyme, 5, 8, Sun Pharmaceutical Industries, Inc, 5, 8, UCB, 5, 8, Valeant Pharmaceuticals Inc, 5, 8; **A. Morita**, AbbVie, 2, 5, 8, Astellas, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Janssen, 2, 5, 8, Kyowa Hakko Kirin Pharma, 2, 5, 8, Leo, 2, 5, 8, MedImmune, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Mitsubishi-Tanabe Pharma Corp, 2, 5, 8, Maruho Co, 2, 5, 8; **A. Kivitz**, AbbVie, 5, Amgen, 1, 4, 5, Boehringer Ingeleheim, 5, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 5, 8, Flexion Therapeutics, 8, Genzyme, 5, 8, Gilead, 1, 4, 5, Gilead Sciences, Inc., 4, Horizon, 8, Janssen, 5, Janssen Research & Development, LLC, 2, Merck, 8, Novartis, 1, 4, 8, Pfizer, 1, 4, 5, 8, Regeneron, 1, 5, 8, Sanofi, 1, 4, 5, 8, Sun Pharma, 5, SUN Pharma Advanced Research, 5, UCB, 5; **R. Sinvhal**, AbbVie, 3, 4; **A. Topp**, AbbVie, 3, 4; **G. Heap**, AbbVie, 3, 4; **A. Eldred**, AbbVie, 3, 4; **P. Mease**, Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, Roche, UCB, 2, 5, Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB, 8, AbbVie, 2, 5, 8, Abbvie, 2, 5, 8, Abbvie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer and UCB., 5, 8, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB, 2, Abbvie, Amgen, Brsitol Myers Squibb, Boehringer Ingelheim, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5, Abbvie, Amgen, Brsitol Myers Squibb, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, 8, Abbvie, Amgen, Brsitol Myers Squibb,Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2, Amgen, 2, 5, 6, 8, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, GSK, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, and UCB, 5, BMS, 2, 5, 8, Boehringer Ingelheim, 2, 5, Boerhinger Ingelheim, 5, Bristol Myers Squibb, 2, 5, 8, Bristol Myers Squibb Co., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 6, 8, Celgene, 2, 5, 6, 8, Celgene Corp., 2, 5, 8, CORRONA, 5, Eli Lilly, 2, 5, 8, Gal-

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Abstract Number: 2878

Randomized, Double-Blind, Placebo-Controlled, Multiple-Dose, Phase 2b Study to Demonstrate the Safety and Efficacy of Tildrakizumab, a High-Affinity Anti–Interleukin-23P19 Monoclonal Antibody, in Patients with Active Psoriatic Arthritis

Philip Mease,[1] Saima Chohan,[2] Ferran J. García Fructuoso,[3] Alice Gottlieb,[4] Richard C. Chou,[5] Alan Mendelsohn,[6] Rocco Ballerini,[6] and Michael E. Luggen[7], [1]Swedish Medical Center/Providence St Joseph Health, and University of Washington, Seattle, WA, [2]Arizona Arthritis and Rheumatology Research, PLLC, Phoenix, AZ, USA, Phoenix, AZ, [3]Hospital CIMA Sanitas, Barcelona, Spain, Barcelona, Spain, [4]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, USA, New York City, NY, [5]University at Buffalo School of Medicine and Biomedical Sciences, Buffalo, NY, USA, Buffalo, NY, [6]Sun Pharmaceutical Industries, Inc., Princeton, NJ, USA, Princeton, NJ, [7]Cincinnati Rheumatic Disease Study Group, Inc. and University of Cincinnati College of Medicine, Cincinnati, OH, USA, Cincinnati, OH

SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Clinical VII: Psoriatic Arthritis Treatment

Session Type: ACR Abstract Session

Session Time: 9:00AM–10:30AM

Background/Purpose: Tildrakizumab (TIL), a high-affinity anti–interleukin-23p19 monoclonal antibody, is approved for moderate-to-severe plaque psoriasis treatment and is under investigation for PsA. This study evaluated the 24-week efficacy and safety results from a randomized, double-blind, placebo-controlled, multiple-dose, phase 2b TIL study in patients with active PsA (NCT02980692).

	TIL 200 mg Q4W (N = 78)	TIL 200 mg Q12W (N = 79)	TIL 100 mg Q12W (N = 77)	TIL 20 mg Q12W (N = 78)	PBO (N = 79)
Patient demographics					
Age, years, median	50.0	49.0	50.0	47.5	47.0
Female, n (%)	46 (59.0)	37 (46.8)	47 (61.0)	41 (52.6)	44 (55.7)
White, n (%)	76 (97.4)	78 (98.7)	75 (97.4)	75 (96.2)	74 (93.7)
BMI, kg/m^2, median	30.0	29.3	27.8	28.9	27.8
Baseline disease characteristics					
Swollen joint count, median (range)	8.0 (3.0–35)	7.0 (3.0–45)	8.0 (0–38)	8.0 (3.0–38)	8.0 (3.0–42)
Tender joint count, median (range)	13.5 (3.0–64)	15.0 (4.0–63)	19.0 (3.0–59)	14.0 (4.0–54)	15.0 (3.0–64)
BSA ≥3%, n (%)	53 (67.9)	44 (55.7)	54 (70.1)	41 (52.6)	42 (53.2)
Physician GADA, mean ± SD	54.0 ± 16.1	55.4 ± 16.2	57.3 ± 17.3	59.4 ± 14.4	59.5 ± 15.6
Patient GADA, mean ± SD	57.8 ± 18.3	61.1 ± 20.7	60.3 ± 20.2	61.9 ± 17.4	65.2 ± 18.1
Patient's pain assessment, mean ± SD	55.4 ± 19.1	59.6 ± 23.5	59.2 ± 22.1	60.9 ± 19.7	64.2 ± 20.4

Table 1. Demographics and Baseline disease characteristics. BMI, body mass index; BSA, body surface area; GADA, global assessment of disease activity; Q4W, every 4 weeks; Q12W, every 12 weeks; PBO, placebo; SD, standard deviation; TIL, tildrakizumab.

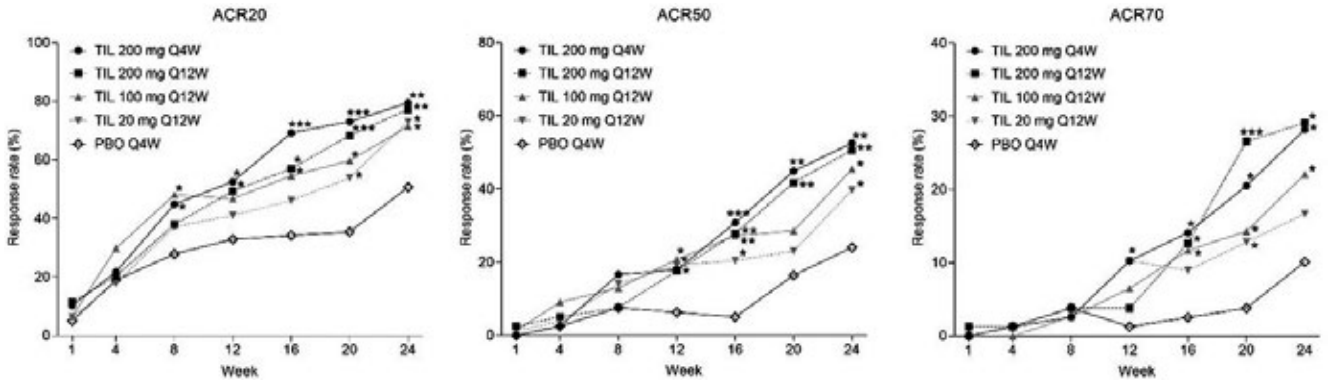

Figure 1. ACR 20/50/70 response rates. *P <0.05; **P <0.001; ***P <0.0001 vs PBO. PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

	TIL 200 mg Q4W (N = 78)	TIL 200 mg Q12W (N = 79)	TIL 100 mg Q12W (N = 77)	TIL 20 mg Q12W (N = 78)	PBO (N = 79)
PASI 75 [a], %	64.2***	79.6***	55.6***	46.3*	16.7
PASI 90 [a], %	47.2***	50.0***	38.9**	36.6*	7.1
Swollen joint count, median change from BL	−6.0*	−6.0	−6.0*	−6.0	−5.0
Tender joint count, median change from BL	−9.0	−10.0*	−11.0*	−10.0	−8.5

Table 2. Efficacy endpoints at week 24. aResponse rates only calculated in patients with BSA ≥3% at baseline, missing responses were imputed as nonresponses. *P <0.05; **P <0.001; ***P <0.0001 vs PBO. BL, baseline; BSA, Body Surface Area; PASI, Psoriasis Area and Severity Index; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

Methods: Patients with active PsA were randomized 1:1:1:1:1 to receive TIL (200 mg once every 4 weeks [Q4W] [n = 78], 200 mg every 12 weeks [Q12W] [n = 79], 100 mg Q12W [n = 77], 20 mg Q12W [n = 78] to week 24), or placebo (PBO) Q4W to week 24 (n = 79). Stable concomitant methotrexate or leflunomide use was permitted but not mandated. The primary efficacy endpoint was the proportion of patients who achieved a 20% reduction from baseline in ACR response criteria (ACR20) at week 24. Other outcome measurements included proportion of patients achieving ACR50/70 response and Psoriasis Area and Severity Index (PASI) 75, PASI 90, and changes in swollen and tender joint count at week 24. Safety assessments included monitoring of treatment-emergent adverse events (TEAEs).

Results: Of 500 patients screened, 391 patients met the inclusion criteria (including ≥18 years old, PsA diagnosis with symptoms for 6 months, and ≥3 tender and ≥3 swollen joints). Demographics and baseline disease characteristics are shown in Table 1. There were significantly greater proportions of ACR20/50/70 and PASI 75/90 responders with TIL vs PBO at week 24, and in some cases differences in parameters were noted as early as week 8 (Figure 1 and Table 2).

The most frequent TEAEs through week 24 included nasopharyngitis (pooled TIL arms: 5.4% [17/312]; PBO: 6.3% [5/79]); and diarrhoea (TIL: 1.3% [4/312]; PBO: 0). There were no reports of candidiasis, inflammatory bowel disease, major adverse cardiac events, or malignancy. No patients discontinued treatment due to TEAEs and no deaths were reported. Serious TEAEs occurred in 2.2% (7/312) of TIL-treated patients vs 2.5% (2/79) in PBO-treated patients.

Conclusion: By week 24, TIL was significantly more efficacious than PBO in the treatment of joint and skin manifestations of PsA. Furthermore, there was a clear separation between TIL and PBO as early as 8 weeks for ACR20 (TIL 200 mg Q4W and 100 mg Q12W) and 12 weeks for both ACR20 (TIL 200 mg doses) and ACR50 (all TIL groups).

Shortening the dosing interval from Q12W to Q4W for the 200-mg dose did not result in a measurable increase in skin or joint response scores. There was a low rate of TEAEs in the TIL-treated group.

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Abstract Number: 2879

Efficacy and Safety of Low-dose IL-2 in Rebuilting Immunity Re-equilibrium of Psoriatic Arthritis Patients

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SESSION INFORMATION

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Session Type: ACR Abstract Session

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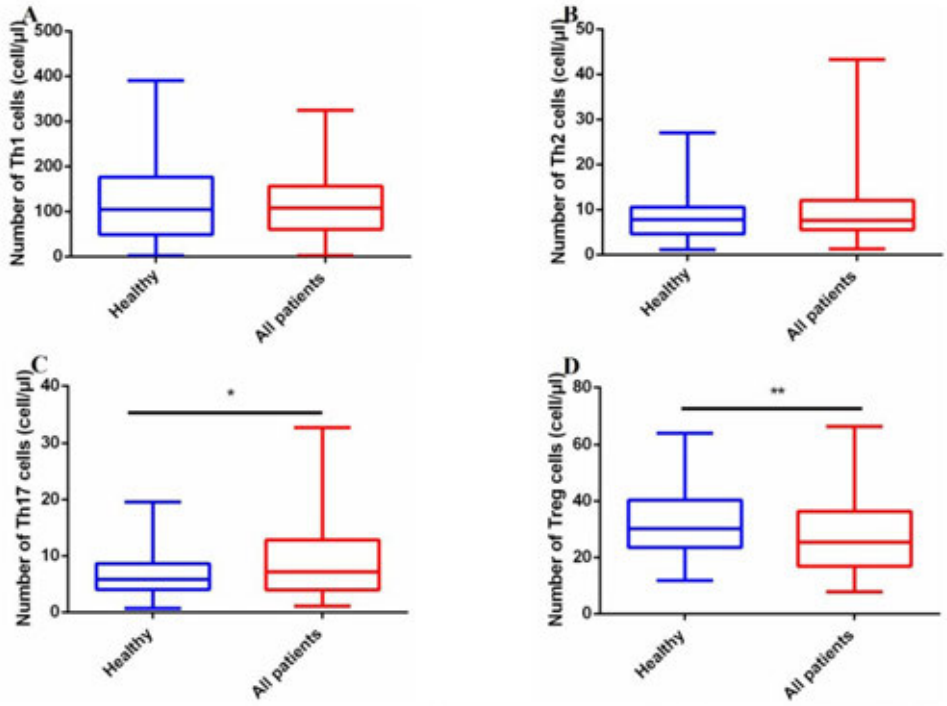

Figure 1: Comparison of absolute numbers of peripheral CD4⁺T cell subsets between PsA patients (n=95) and health controls (n=106). The level of Th17 was significantly increased while that of Tregs reduced in patients with PsA. Data were calculated and compared with Mann-Whitney *U* test. **P* < 0.05, ***P* <0.01, ****P* <0.001.

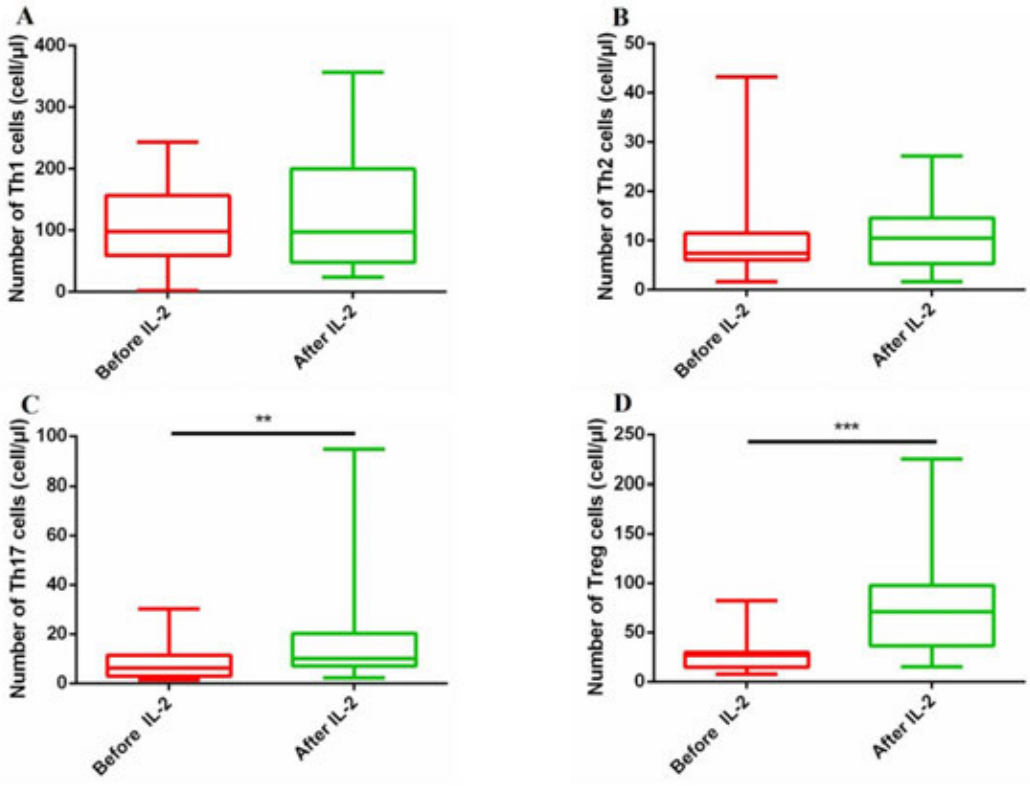

Figure 2: Comparative analysis the changes of CD4⁺T cell subsets in patients with PsA between pre- and post-treatment (n=22). Low-dose IL-2 markedly raised the absolute numbers of Treg and moderately increased the level of Th17 cells in PsA patients. **P* < 0.05, ***P* <0.01, ****P* <0.001.

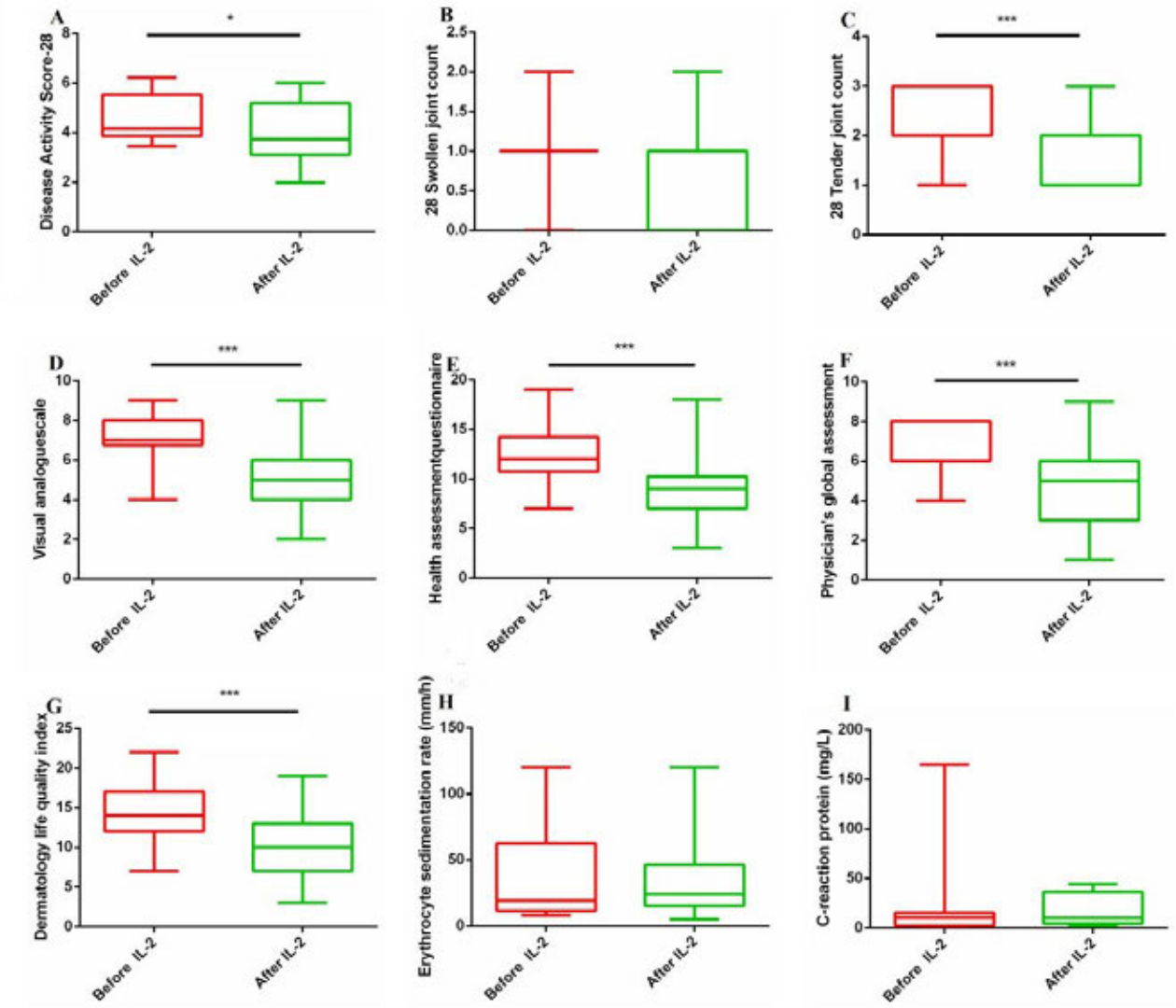

Figure 3: Comparative analysis the changes of PsA signs and symptoms between pre- and post-treatment (n=22). Data were presented as median(range) and calculated and compared with Mann-Whitney *U* test.(A-I) show that low-dose IL-2 treatment provided a significant decrease in 28 tender joint count, DAS28-ESR index, VAS index, PHGA index, DLQI index and HAQ index. $*P < 0.05$, $***P < 0.001$.

Background/Purpose: Psoriatic arthritis (PsA) is a T lymphocytes-mediated inflammatory condition. Although regulatory T cells (Tregs) isolated from blood and psoriatic skin have been showed a functional deficiency in suppressing effector T-cells in PsA, absolute quantitative status of peripheral Treg or Th17 cells is still unclear. On the other hand, recent studies have revealed that low-dose IL-2 alleviate**s** some of autoimmune disease activity by upregulating Treg cells, which is expected to control the development of PsA.This study aimed to assess the absolute numbers of peripheral lymphocyte subpopulations and the efficacy and safety of low-dose IL-2 therapy in PsA patients.

Methods: Total 95 PsA patients and 106 age-and sex-matched healthy controls were recruited. Of them, 22 cases received the treatment of low-dose IL-2 at 0.5 million IU per day for 5 days subcutaneously. The absolute numbers of lymphocyte subgroups and $CD4^+$T subsets in peripheral blood were measured by flow cytometry. The clinical mani-

festations and laboratory indicators as well as the levels of peripheral lymphocyte and $CD4^+$T subsets were compared before and after the treatment.

Results: Notably, the absolute numbers of lymphocyte subpopulations in peripheral blood such as NK, CD4+T, Th17 and Tregs in PsA patients were lower than those of healthy controls ($P< 0.05$). The absolute number of Treg was significantly and negatively correlated with the levels of disease indicators, including DAS28, the number of tender joints, visual analogue scale, physician's global assessment, dermatology life quality index, and health assessment questionnaire($P< 0.05$). After low-dose IL-2 treatment, compared with the baselines, there was a significant increase in the absolute numbers of NK ($P< 0.05$), CD4+T ($P< 0.01$), Th17 ($P< 0.01$) and Treg cells ($P< 0.001$). Interestingly, IL-2 markedly raised the level of Tregs in PsA patients even higher than that of healthy donors ($P< 0.001$), leading to re-balance of Th17 and Tregs. Further, low-dose IL-2 treatment rapid reduced the disease activity such as DAS28, the number of tender joints, visual analogue scale, physician's global assessment, dermatology life quality index, and health assessment questionnaire ($P< 0.05$).

Conclusion: Patients with PsA had an imbalance between pro- and anti-inflammatory cells, particularly the reduction of the absolute number of Tregs. Low-dose IL-2 combination treatments restored the decreased number of Treg cells and lowered disease activity indicators of these patients without over-treatment and evaluable side effect. Further studies are needed to evaluate the long-term immunoregulatory ability of IL-2 treatment.

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Abstract Number: 2880

Secukinumab Improves Axial Manifestations in Patients with Psoriatic Arthritis and Inadequate Response to NSAIDs: Primary Analysis of Phase 3 Trial

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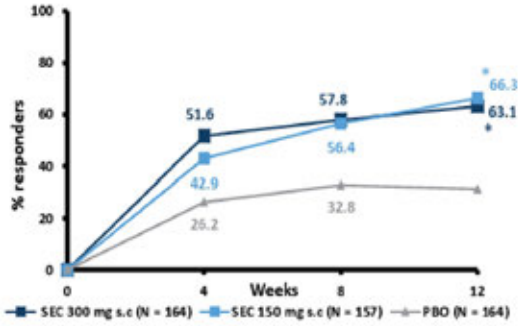
Background/Purpose: Secukinumab (SEC) has provided significant and sustained improvement in the signs and symptoms of active psoriatic arthritis (PsA) and ankylosing spondylitis[1]. Evidence is limited on the efficacy of biologics in the treatment of patients (pts) with PsA having axial manifestations that affect between 30–70% of pts[2], particularly as validated classification criteria for this subtype of PsA are not yet available; an effort to develop criteria is being undertaken by ASAS/GRAPPA. MAXIMISE is an ongoing study evaluating the efficacy and safety of secukinumab 300 mg or 150 mg in managing axial manifestations in pts with PsA. Here, we report the primary analysis results at Week (Wk) 12 from the MAXIMISE trial (NCT02721966).

Figure: ASAS20 Response rate through Week 12 (Full Analysis Set)



*P<0.001 vs placebo; ASAS, Assessment of Spondyloarthritis International Society; N, number of patients randomized

Table: Demographic/ BL Disease Characteristics

Mean (SD) unless specified	SEC 300 mg SC (N = 167)	SEC 150 mg SC (N = 165)	PBO (N = 166)
Age (years)	46.2 (12.3)	46.9 (11.5)	46.6 (11.5)
Male, n (%)	77 (46.1)	81 (49.1)	88 (53.0)
Evidence of current psoriasis, n (%)	152 (91.0)	147 (89.1)	153 (92.2)
Time since first axial symptoms (years)	6.8 (7.7)	7.4 (7.6)	7.7 (9.5)
Total back pain score, VAS	72.5 (13.8)	73.6 (15.3)	74.0 (13.7)
Inflammatory back pain parameters, n (%)			
Onset of back pain is insidious	150 (89.8)	147 (89.1)	152 (91.6)
Back pain improving with exercise	148 (88.6)	139 (84.2)	146 (88.0)
Back pain worsening with rest	152 (91.0)	151 (91.5)	157 (94.6)
Night pain with improvement upon getting up	147 (88.0)	147 (89.1)	143 (86.1)
Awakening due to back pain in 2nd half of night	143 (85.6)	145 (87.9)	137 (82.5)
Alternating buttock pain	102 (61.1)	98 (59.4)	101 (60.8)
Back pain improved after NSAID intake in past	136 (81.4)	134 (81.2)	138 (83.1)
BASDAI	7.3 (1.2)	7.2 (1.4)	7.3 (1.2)
HLA-B27 positive, n/M (%)	31/85 (36.5)	24/82 (29.3)	26/74 (35.1)

M, number of pts with available HLA-B27 status; N, number of randomised patients; SEC, secukinumab; BL, baseline; PBO, placebo; SC, subcutaneous; SD, standard deviation; VAS, visual analog scale; NSAID, nonsteroidal anti-inflammatory drug; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; HLA, human leukocyte.

Methods: This phase 3b, double blind, placebo (PBO)-controlled, multicenter 52-wk trial included 498 pts (aged ≥18 years) with PsA (CASPAR criteria), clinician-diagnosed axial involvements, spinal pain VAS > 40/100 and BASDAI > 4 despite trial of at least two NSAIDs. Pts were randomized to subcutaneous (SC) SEC (300/150 mg) or PBO weekly for 4 wks and every 4 wks thereafter. At Wk 12, PBO pts were re-randomized to SC SEC 300/150 mg. The primary endpoint was ASAS20 response with SEC 300 mg at Wk 12. The key secondary endpoint was ASAS20 response with SEC 150 mg at Wk 12 after superiority of 300 mg was established. Analyses used multiple imputation.

Results: Demographic and baseline (BL) disease characteristics were comparable across groups (Table). Primary and key secondary endpoints were met; ASAS20 response rates at Wk 12 were 63.1% (SEC 300 mg; P< 0.0001) and 66.3% (150 mg; P< 0.0001) versus 31.3% (PBO; Figure). ASAS20 responses in pts using concomitant methotrexate (MTX) were 65.1% [300 mg], 67.3% [150 mg] versus 33.9% [PBO]; corresponding values in pts without concomitant MTX use were 60.5%, 64.4% versus 27.1%. The safety profile was similar across groups through Wk 12.

Conclusion: MAXIMISE is the first randomized controlled trial evaluating the efficacy of a biologic in the management of the axial manifestations of psoriatic arthritis. Secukinumab 300 mg and 150 mg provided rapid and significant improvement in ASAS20 responses through Week 12 in patients with psoriatic arthritis with axial manifestations and inadequate responses to NSAIDs.

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Abstract Number: 2881

Dual Neutralization of IL-17A and IL-17F with Bimekizumab in Patients with Active Psoriatic Arthritis: Disease Activity and Remission in a 48-Week Phase 2b, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study

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Background/Purpose: The ultimate goal of therapy in patients with psoriatic arthritis (PsA) is clinical remission, defined as 'the absence of clinical and laboratory evidence of significant inflammatory disease activity'.[1,2] Since many patients with PsA may not achieve clinical remission, treatment recommendations recognise minimal or low disease activity as an important alternative treatment target.[1,2] Bimekizumab is in development for the treatment of psoriasis, PsA, and axial spondyloarthritis; it potently and selectively neutralizes both IL-17A and IL-17F.[3] The efficacy and

Table 1. Proportion of patients achieving MDA, VLDA, DAPSA remission and DAPSA LDA (full analysis set)

n (%)	Placebo (n=42)	Bimekizumab 16 mg (n=41)	Bimekizumab 160 mg (n=41)	Bimekizumab 160 mg [320 mg LD] (n=41)	Bimekizumab 320 mg (n=41)
MDA*					
Week 12	6 (14.3)	13 (31.7)	19 (46.3)	18 (43.9)	12 (29.3)
Week 24	17 (40.5)	23 (56.1)	20 (48.8)	23 (56.1)	15 (36.6)
Week 48	19 (45.2)	25 (61.0)	24 (58.5)	20 (48.8)	19 (46.3)
VLDA					
Week 12	1 (2.4)	1 (2.4)	6 (14.6)	8 (19.5)	4 (9.8)
Week 24	6 (14.3)	7 (17.1)	9 (22.0)	12 (29.3)	6 (14.6)
Week 48	8 (19.0)	11 (26.8)	15 (36.6)	11 (26.8)	9 (22.0)
DAPSA remission*					
Week 12	1 (2.4)	4 (9.8)	8 (19.5)	12 (29.3)	5 (12.2)
Week 24	12 (28.6)	9 (22.0)	14 (34.1)	19 (46.3)	8 (19.5)
Week 48	11 (26.2)	16 (39.0)	18 (43.9)	15 (36.6)	14 (34.1)
DAPSA LDA*					
Week 12	7 (16.7)	17 (41.5)	17 (41.5)	16 (39.0)	12 (29.3)
Week 24	13 (31.0)	20 (48.8)	14 (34.1)	13 (31.7)	14 (34.1)
Week 48	17 (40.5)	18 (43.9)	9 (22.0)	18 (43.9)	12 (29.3)

*Last observation carried forward (LOCF) analysis
DAPSA, disease activity index for psoriatic arthritis; MDA, minimal disease activity; VLDA, very low disease activity

safety of bimekizumab in patients with active PsA was assessed in a Phase 2b study over 48 weeks (NCT02969525);[4] disease activity outcomes are reported here.

Methods: Patients with active PsA, ≥3/76 swollen joint count and ≥3/78 tender joint count and fulfilling the Classification Criteria for PsA (CASPAR, score ≥3), were randomized (1:1:1:1:1) to receive subcutaneous bimekizumab 16 mg, 160 mg, 160 mg with 320 mg loading dose (160 mg [LD]), 320 mg, or placebo every 4 weeks (Q4W) for 12 weeks (double-blind period). After Week 12, patients receiving placebo or bimekizumab 16 mg were re-randomized (1:1) to receive bimekizumab 160 mg or 320 mg; all other patients continued on their previous dose (dose-blind period). The primary endpoint was a ≥50% improvement in American College of Rheumatology response criteria (ACR50) at Week 12; key results up to Week 48 have been reported previously.[4] Other and post-hoc efficacy variables included: minimal disease activity (MDA), very low disease activity (VLDA), disease activity index for psoriatic arthritis (DAPSA) remission, and DAPSA low disease activity (LDA).

Results: Of 206 patients randomized, 203 and 190 completed the double- and dose-blind periods, respectively. In patients receiving bimekizumab 160 mg, 160 mg (LD) or 320 mg throughout the study, 46.3–58.5% achieved MDA, 22.0–36.6% achieved VLDA, 34.1–43.9% achieved DAPSA remission and 22.0–43.9% achieved DAPSA LDA at Week 48 (Table 1). In general, disease activity improved across these measures from Week 12 to Week 24, with improvements typically maintained or further increased to Week 48.

Serious adverse events were reported by 9/204 (4.4%) patients up to Week 48 (8/204 [3.9%] receiving bimekizumab). The most common treatment-emergent adverse event up to Week 48 was nasopharyngitis (25/204 [12.1%]). Up to Week 48, oral candidiasis occurred in 10/204 (4.9%) patients (all on bimekizumab treatment). No deaths, cases of inflammatory bowel disease, uveitis, or major cardiovascular adverse events were reported.

Conclusion: Treatment with bimekizumab 160 mg, 160 mg (LD) or 320 mg throughout the study was associated with achievement of low and/or minimal disease activity. Disease activity measures generally improved to Week 24 and were maintained to Week 48. These data provide further support that neutralizing both IL-17F and IL-17A with bimekizumab is a promising therapeutic approach in patients with active PsA.

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Abstract Number: 2882

Prospective Demonstration That Attainment of the Lupus Low Disease Activity State Is Associated with Improved Health Related Quality of Life

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: SLE – Clinical VI: Epidemiology, Diagnosis, & Outcomes

Session Type: ACR Abstract Session

Session Time: 9:00AM–10:30AM

Background/Purpose: The Lupus Low Disease Activity State (LLDAS) is a treatment endpoint for SLE that has been shown in prospective validation studies to be associated with protection against disease flares and damage accrual. In addition to improved physician-measured outcomes, attainment of treatment endpoints should also result in improvement in patient-reported outcomes such as health related quality of life (HR-QoL). The objective of this study was to assess the effect of attainment of LLDAS on HR-QoL.

Methods: 1,735 SLE patients in 11 centres were prospectively recruited, and followed for (mean ± SD) 2.2 ± 0.9 years, totalling 12,717 visits. HR-QoL was captured using SF-36 at baseline and annually until completion of the study. At each visit LLDAS status was ascertained. Generalized estimating equations models were used to assess the association of LLDAS status with low SF-36 scores (threshold for low SF-36 based on the median across all visits). Time dependent Cox proportional hazard models were used to assess increasing proportion of cumulative time in LLDAS and protective association against low SF-36 scores.

Table 1: Association of cumulative time in LLDAS with PCS and MCS scores

% Cumulative time in LLDAS	N % patients	Low PCS* HR (p value)	Low MCS* HR (p value)
LLDAS 0 (no visit in LLDAS)	455 (26.2%)	0.97 (0.874)	1.07 (0.660)
LLDAS 25	1133(65.3%)	0.71 (0.013)	0.76 (0.037)
LLDAS 50	813 (46.9%)	0.65 (0.001)	0.78 (0.050)
LLDAS 75	544 (31.4%)	0.61 (0.002)	0.70 (0.011)
LLDAS 100 (all visits in LLDAS)	325 (18.7%)	0.44 (<0.001)	0.59 (0.003)

Results: LLDAS attainment was observed in 6091 (47.9%) visits. LLDAS status was associated with a significant protective effect against low physical component summary scores (PCS, RR 0.88, 95% CI 0.84-0.94, p< 0.001) and low mental component summary scores (MCS, RR 0.90, 95% CI 0.86-0.95, p< 0.001). Increasing proportions of cumulative time in LLDAS were associated with graded protective effect against low PCS and MCS scores (table 1).

Conclusion: In this large prospective cohort study, LLDAS was significantly associated with protection from low HR-QoL, as measured by SF-36. Importantly, increasing cumulative time in LLDAS was associated with a dose dependent protective effect against low SF-36 scores, providing further validation for the use of LLDAS as a treatment endpoint in SLE.

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Abstract Number: 2883

Systemic Lupus Erythematous Risk Alleles Drive Autoimmune Features in a Population Without Diagnosed Autoimmune Diseases

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: SLE – Clinical VI: Epidemiology, Diagnosis, & Outcomes
Session Type: ACR Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogeneous disease with > 100 known risk alleles. Some of these risk alleles associate with ACR SLE criteria such as renal disease. We examined if nine of these SLE risk alleles would identify autoimmune features in a population without diagnosed autoimmune diseases.

Methods: We investigated subjects from BioVU, a databank that links DNA extracted from routine, clinical blood samples to a de-identified electronic health record (EHR) with several decades of clinical data. BioVU contains 250,000 subjects, over 80,000 of which have been genotyped on Illumina MEGA chip. We selected individuals who had available data for 9 SLE risk single nucleotide polymorphisms (SNPs) (ITGAM rs1143683 and 1143679, STAT4 rs7574865, IRF5 rs10488631, IRF7 rs4963128, TFAF3IP2 rs13190932, PTPN2 rs2542151, UBE2L3 rs5754217, ICAM1-ICAM4-ICAM5 rs3093030), which have been associated with ACR SLE criteria. Subjects did not have ICD9 or ICD10 billing codes for autoimmune diseases including SLE, rheumatoid arthritis, Sjogren's syndrome, systemic sclerosis, or myositis. We compared subjects with or without these nine SLE risk SNPs using phenome-wide association studies

Table 1. SLE related PheWAS codes associated with SLE risk alleles in a population without diagnosed autoimmune diseases.

Gene SNP	SLE related PheWAS codes	Odds Ratio 95% Confidence Intervals	p value
ITGAM	Pleurisy, pleural effusion	1.09 (1.02 – 1.16)	0.01
rs1143683	Urinary complications	1.82 (1.10 – 2.99)	0.02
	Nephritis	1.50 (1.05 – 2.14)	0.03
	Symptoms and disorders of the joint	1.08 (1.01 – 1.17)	0.04
	Diseases of white blood cells	1.09 (1.01 – 1.19)	0.04
	Anemia of chronic disease	1.11(1.01 – 1.22)	0.05
STAT4	Joint effusions	1.28 (1.10 – 1.49)	0.002
rs7574865			
IRF7	Urinary complications	1.41 (1.02 – 1.96)	0.04
rs4963128	Dermatitis due to solar radiation	1.13 (1.01 – 1.29)	0.05
PTPN2	Other derangement of joint	1.25 (1.03 – 1.51)	0.03
rs2542151	Synovitis and tenosynovitis	1.14 (1.01 – 1.29)	0.03
UBE2L3	Alopecia	1.26 (1.02 – 1.55)	0.03
rs5754217			
ICAM1- ICAM4- ICAM5	Other arthropathies	1.10 (1.01 – 1.19)	0.02
	Proliferative glomerulonephritis	1.55 (1.07 – 2.25)	0.02
rs3093030	Raynaud's syndrome	1.36 (1.02 – 1.82)	0.04

(PheWAS). PheWAS is a technique that scans across EHR billing codes. Subjects with a SLE risk SNP and multiple codes corresponding to SLE ACR criteria were chart reviewed to determine if they had an undiagnosed autoimmune disease and assessed for other comorbidities.

Results: We identified 56,496 Caucasian subjects without billing codes for autoimmune diseases that had available genetic data for the 9 SLE risk SNPs. Of these subjects, 56% were female with a mean age of 53 years. Compared to subjects without the SNPs, subjects with the risk SNPs were more likely to have codes related to ACR SLE criteria including nephritis, arthritis, serositis, and hematologic disorders (Table 1, Figure 1). Subjects with the ITGAM

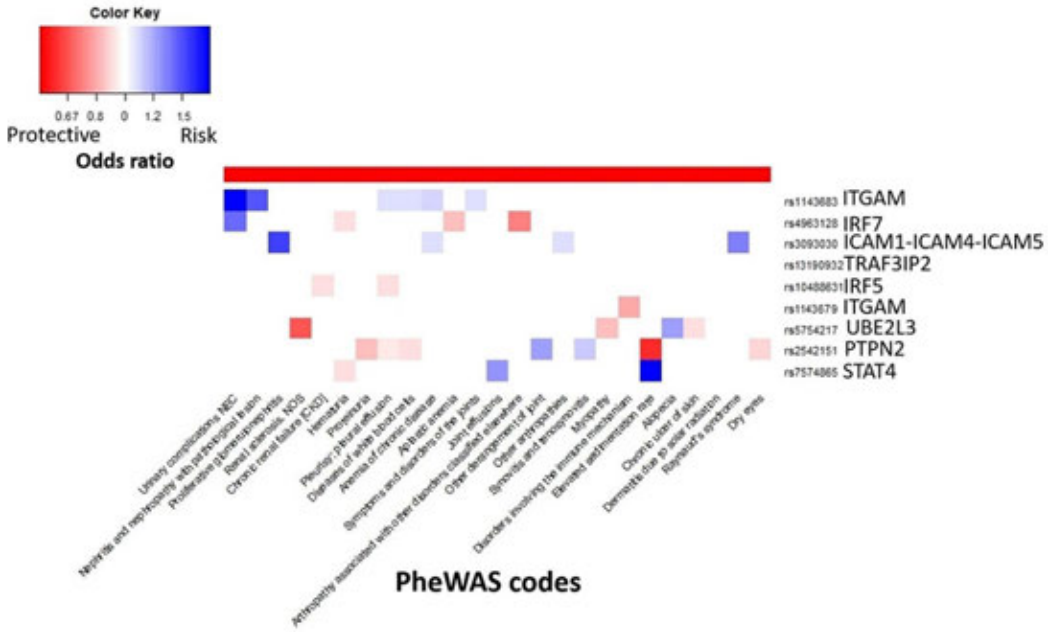

Figure 1. Heat map of SLE risk alleles and SLE related PheWAS codes in a population without diagnosed autoimmune diseases. Across the horizontal axis are PheWAS codes that represent SLE disease criteria and features organized by organ system (i.e. renal codes, codes related to hematologic diagnoses, codes related to arthritis). The nine SLE risk alleles with SNP number and gene name are labeled on the vertical axis. Odds ratio for each of the SLE risk alleles and PheWAS codes are shown per the above color key with non-significant associations in white on the heat map.

Table. Abnormal CB-CAPs compared to low C3/C4 in distinguishing SLE from other autoimmune rheumatic diseases

rs1143683 SNP were more likely to have codes related to nephritis (p = 0.03), arthritis (p = 0.04), and diseases of white blood cells (p = 0.04). Renal codes were also associated with IRF7 rs4963128 (p = 0.04) and ICAM1-ICAM4-ICAM5 rs3093030 (p = 0.02). On chart review of the 50 subjects with the greatest number of codes related to ACR SLE criteria, 2 subjects fit SLICC SLE criteria but were not formally diagnosed with SLE. Both of these subjects had renal biopsies suggestive of SLE nephritis. An additional two subjects had incomplete SLE and 1 subject ANCA-associated vasculitis, 1 amyloidosis, and 2 Henoch-Schonlein purpura. Notably, 45 (90%) of the subjects had renal disease with 19 requiring dialysis or a renal transplant.

Conclusion: Carriage of SLE risk alleles confers risk of SLE features in undiagnosed subjects. Some of these subjects may be pre-SLE or undiagnosed SLE cases or other autoimmune disease cases. The combination of SLE risk alleles plus early features of the disease may identify a population who are at high risk for developing clinical SLE who would be candidates for early treatment. Subjects with SLE risk alleles had a significant burden of renal disease. SLE risk alleles may share common pathways for renal disease and act as accelerants for organ damage.

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Abstract Number: 2884

Combined Trajectories of Fatigue and Disease Activity in an Inception Cohort of Lupus Patients over 10 Years

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: SLE – Clinical VI: Epidemiology, Diagnosis, & Outcomes

Session Type: ACR Abstract Session

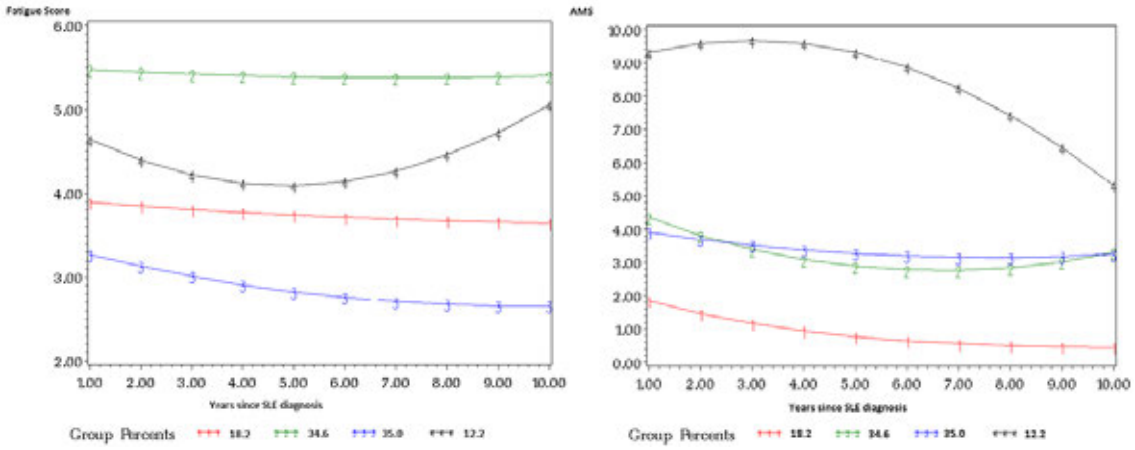
Session Time: 9:00AM–10:30AM

Background/Purpose: Fatigue is very common in SLE patients. We aim to: **1)** determine if different trajectories of fatigue associate with specific latent classes of disease activity and **2)** define the patient characteristics and associated factors in different latent classes.

Methods: This is a retrospective analysis on a prospectively collected dataset from an inception cohort and followed from 1997 to 2018. Fatigue levels was measured using Fatigue Severity Scale (FSS- scores range from 1-7, higher scores reflect more fatigue) and disease activity using the adjusted mean SLEDAI-2K (AMS). Ten-year cumulative SLE organ involvement were ascertained by SLEDAI-2K organ system. Joint latent class trajectory analysis for fatigue and AMS was performed using a group-based trajectory model in SAS PROC TRAJ. Each trajectory was fitted for the FSS and AMS. Models with the lowest Bayesian Information Criterion and groups containing > 9% of the total sample size were selected as the final models. Univariate and multivariate ordinal logistic regression analyses, using baseline variables, were performed to determine the predictors of both worse fatigue and AMS scores. This was performed on members with both latent class posterior probability ≥ 0.80.

Results: Among 280 inception patients with mean age of 35.8± 13.3 years, 4 latent classes (C) were created (figure 1): C1- very low disease activity and low fatigue (18.2%); C2 second lowest disease activity and highest fatigue trajectory (34.6%); C3 median disease activity and the lowest fatigue trajectory (35.0%); and C4 high disease activity

Figure 1. Trajectories of both fatigue (FSS) and disease activity (AMS) scores in an inception cohort of 280 patients over 10 years



	Descriptive Statistics	Univariate Regression		Multivariable regression	
Covariates at baseline visit	**Overall proportions n (%) or mean ± SD**	**Odds Ratio Estimate (95% CI)**	**p value**	**Odds Ratio Estimate (95% CI)**	**p value**
Mean age at SLE diagnosis	35.8 ± 13.3 years	0.98 (0.96,0.99)	0.01	0.98 (0.99,0.99)	0.01
Sex (Female)	252 (90.0%)	0.86 (0.39,1.91)	0.71		
Ethnicity (Caucasian vs. others)	163 (58.2%)	0.48 (0.29,0.79)	0.00	0.57 (0.34,0.94)	0.03
Education level (>high school or lower)	257 (91.8%)	1.75 (0.58,5.32)	0.32		
Marital status (married or common law vs. others)	127 (45.4%)	0.55 (0.34,0.91)	0.02		
Fibromyalgia	19 (6.8%)	0.39 (0.15,1.02)	0.06	0.41 (0.15,1.07)	0.07
Baseline SLEDAI	9.2 ± 7.5	1.05 (1.01,1.09)	0.00	1.04 (1.001,1.07)	0.04
SLICC score one year after diagnosis	0.3 ± 0.7	0.94 (0.64,1.38)	0.75		
Glucocorticoid use	238 (85.0%)	4.18 (1.98,8.84)	0.00	3.17 (1.45,6.92)	0.003
Antimalarial use	263 (93.9%)	1.39 (0.46,4.20)	0.56		
Immunosuppressive use	70 (25.0%)	1.36 (0.78,2.38)	0.28		

Table 1. Univariate and multivariate ordinal logistic regression analyses

and high fatigue trajectory (12.2%). C2 and C3 had similar AMS scores over time but different fatigue trajectories. C2 (highest fatigue) and C4 (high fatigue) had the highest proportion of individuals living with fibromyalgia (34.1% vs. 14.0% respectively) and cumulative glucocorticoid use at 10 years (37.2 ±15.7 grams vs. 44.4 ± 19.7 grams). SDI was highest in C4 (second lowest disease activity, highest fatigue score) with 67% of individuals having SDI >0. SDI was lowest in C3 (median disease activity, low fatigue score) with 53.2% of individuals having SDI >0. Cumulative organ involvement over 10 years showed that C4 included the most amount of individuals with central nervous system (43.8%), vasculitis (43.8%), renal (68.8), skin (100%), serosal (18.8%), immunologic (100%), and hematological (50%) manifestations; C2 had the most musculoskeletal findings (72.9%). Regression analyses showed that age at SLE diagnosis (OR: 0.98, 95% CI: 0.96; 0.99), Caucasian (OR 0.57, 95% CI: 0.34; 0.94), SLEDAI-2K scores (1.04, 95% CI: 1.00; 1.07) and glucocorticoid use (OR 3.2, 95% CI: 1.4; 6.9) were significantly associated with fatigue trajectories (Table 1).

Conclusion: There are **4 distinct joint classes of fatigue and disease activity trajectories**. Disease activity alone cannot fully explain fatigue trajectories over time. Trajectories with higher FSS and AMS scores, classes C2 and C4, are associated with more **fibromyalgia and cumulative glucocorticoid use**. Baseline SLEDAI-2K scores were more likely associated with worse trajectories of fatigue, being a Caucasian and older age at SLE diagnosis were associated with better fatigue trajectories.

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Abstract Number: 2885

An Integrated Gut Microbiomic and Plasma Metabolomic Analysis in Patients with Four Systemic Autoimmune Diseases

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: SLE – Clinical VI: Epidemiology, Diagnosis, & Outcomes

Session Type: ACR Abstract Session

Session Time: 9:00AM–10:30AM

Background/Purpose: Gut microbiota may be relevant in the regulation of immune processes and in the development of systemic autoimmune diseases (SADs). A reduction of microbiota diversity and a selective decrease of commensal pro-regolatory bacteria have been observed in systemic lupus erythematosus (SLE), Sjogren syndrome (SJS) and primary anti-phosholipid syndrome (PAPS). None studies have been performed on undifferentiated connective tissue disease (UCTD) and into an enlarged panel of SADs at the very same time, integrating microbiome data with the plasma metobolomic profile.

Objectives: to perform an integrated investigation of microbiomic and metabolomic profile in patients with SADs and healthy controls (HC) within the PRECISESADs study.

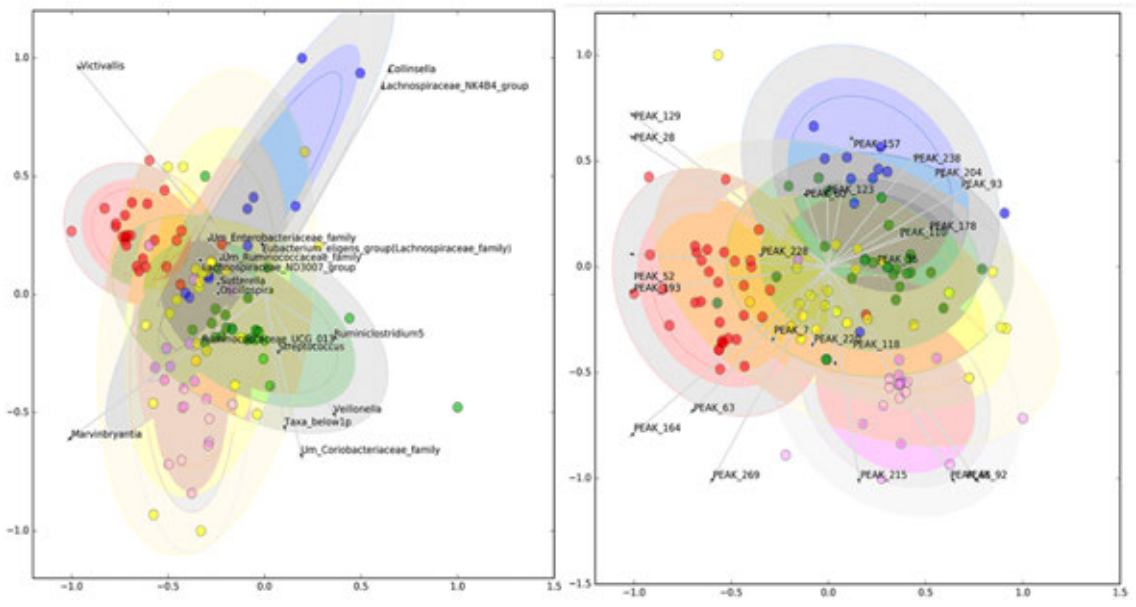

Figure 1. FreeViz multidimensional representation of microbiomic and metabolomic results

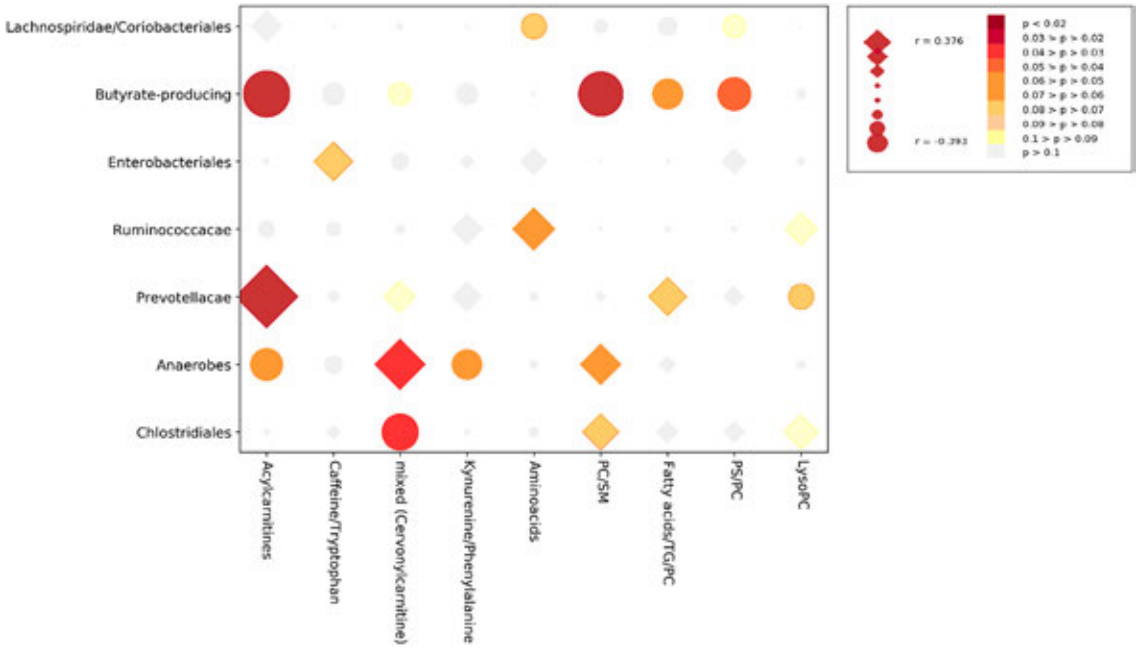

Figure 2. Cross-correlations

	SLE (n=29)	SjS (n=22)	PAPS (n=12)	UCTD (n=26)	HC (n=36)
Age, mean (SD)	48.14 (16.82)	65.14 (12.45)	41.82 (8.59)	52.23 (12.01)	52.47 (9.96)
Females, n (%)	26 (89.66)	22 (100)	9 (75)	23 (88.46)	24 (66.67)
Disease duration yrs, mean (SD)	14.98 (10.57)	10.30 (9.47)	11.87173 (6.13)	9.43 (5.09)	-
AutoAb profile, n (%)					
ANA	27 (93.10)	20 (90.90)	2 (16,67)	26 (100)	
Anti SSA/SSB	4 (13.79)	16 (72.72)	0(0)	3 (11.53)	
Anti dsDNA	13(44.82)	0 (0)	2 (16.67)	5 (19.23)	
Anti Sm	2 (6.90)	0 (0)	0 (0)	0 (0)	
Anti CLP	0 (0)	0 (0)	6 (50)	1(3.85)	
Anti B2GP	1 (3.45)	0 (0)	8 (66.67)	1 (3.85)	
RF	1 (3.45)	11 (50)	0 (0)	3 (11.54)	

Table. Clinical and demographic characteristics

Methods: a total of 125 subjects (29 SLE, 22 SJS, 12 PAPS, 26 UCTD, 36 HC) were enrolled (**Table 1**). Gut microbiome analysis through 16s-RNA sequencing on stool samples and metabolomic analysis on plasma samples with high-performance liquid chromatography coupled to electrospray ionization and quadrupole time-of-flight mass spectrometry (HPLC-MS-ESI-QTOF) were performed. Data mining algorithms were used to assess a single subset of microbiomic and metabolomic variables capable of to jointly distinguishing the groups of subjects. Microbial and metabolic signals were correlated adjusting for potential confounders (age, therapy) and corrected with stepwise procedure, minP. A Kruskall-Wallis (KW) test with a post hoc Dunn test were used for statistical analysis of microbial genera relative abundance and for metabolic peaks within groups.

Results: From 130 gut bacterial genera, a subset of 29 was able to jointly distinguish the study groups (AUROC=0.730±0.025). Similarly, of 254 metabolic peaks, 41 were able to discriminate study groups (AUROC=0.748±0.021). In both models, HC were well separated from SADs, while UCTD largely overlapped with other disease groups (Figure 1). The relative abundance of pro-tolerogenic bacterial strains such as Lachnospiraceae was

reduced in SADs (p=1.77E-06) while an increase of pro-inflammatory genera (Collinsella, Streptococcus, Clostridiales with p< 0.001) was observed. Metabolic alterations included mostly members of the carnitine family and phospholipids. Microbiomic genera significantly correlated with metabolic peaks as shown in Figure 2 and Acylcarnitines were directly correlated with a Prevotella-enriched cluster and inversely correlated with a butyrate-producing bacteria-enriched cluster. The latter was also inversely correlated with a phospholipid-enriched cluster.

Conclusion: A common microbiomic and metabolomic profile jointly distinguish SLE, PAPS, SJS, UCTD and HC. SADs are characterized by a reduction of pro-tolerogenic bacterial genera and the presence of correlations between microbial genera and metabolites support the hypothesis of an interaction between intestinal microbiota and metabolic functions.

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Abstract Number: 2886

Prevalence of Systemic Lupus Erythematosus in the United States: Preliminary Estimates from a Meta-Analysis of the Centers for Disease Control and Prevention Lupus Registries

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: SLE – Clinical VI: Epidemiology, Diagnosis, & Outcomes
Session Type: ACR Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: The heterogeneity of the clinical manifestations of systemic lupus erythematosus (SLE) and lack of a diagnostic test make SLE difficult for epidemiologists to study. The Centers for Disease Control and Prevention (CDC) supported five population-based SLE surveillance registries, using harmonized methodology, to better estimate incidence and prevalence of SLE in diverse areas in the United States (US). Leveraging these data, we performed a meta-analysis to estimate the general prevalence of SLE in the US.

Methods: The CDC registries were established in Michigan, Georgia, California, New York and the through the Indian Health Service (IHS). All registries used the 1997 revised ACR classification criteria for SLE as their primary case definition, and the surveillance time periods ranged from 2003 to 2009. Age-standardized prevalence was stratified by sex and race/ethnicity from the state-based registries; the American Indian/Alaska Native (AI/AN) estimate was based on the IHS registry that covered multiple states. For pooling data across the four sites with data on different racial/ethnic groups, we used Cochran's Q and I^2 statistic to test for heterogeneity across sites. Due to significant heterogeneity, we used a random effects model to calculate pooled prevalence, which allows for more variation across

Table 1. Sex, race and ethnicity-specific estimates for systemic lupus erythematosus prevalence in the United States (2003-2009), and estimated number of persons in the US living with SLE according to the ACR classification criteria (2017)

	FEMALE		MALE	
	Prevalence [a] per 100,000 (95% CI)	Estimated # in United States	Prevalence [a] per 100,000 (95% CI)	Estimated # in United States
Race				
Black	230.9 (178.2, 299.2)	55,089	26.7 (19.6, 36.4)	5,881
White	84.7 (68.4, 104.84)	108,472	8.9 (8.0, 10.1)	11,202
Asian/PI	84.4 (48.3, 147.4)	9,293	11.2 (5.7, 21.9)	1,138
AI/AN	271 (238, 307)	6,333	54 (36, 77)	1,270
Total [b]	***128.7 (113.3, 146.2)***	***179,186***	***14.6 (12.2, 17.5)***	***19,491***
Ethnicity				
Hispanic [c]	120.7 (84.0, 173.4)	35,205	18.0 (15.6, 20.8)	5,360

[a] Estimates for blacks and whites are based on pooled estimates from the four state-based registries; Asian/Pacific Islanders (Asian/PI) and Hispanics are based on pooled estimates from Michigan, California and New York; American Indian/Alaska Native (AI/AN) estimates are based on the IHS Registry.

[b] The pooled 'total' estimate includes black, white and Asian/Pacific Islanders (Asian/PI). Since the American Indian/Alaska Native (AI/AN) prevalence was based on one registry and was significantly higher, it was not included in the pooled prevalence.

[c] Hispanic ethnicity is not mutually exclusive from the race categories, i.e., all Hispanic persons are included in one of the race categories. Thus, the pooled estimates do not incorporate the Hispanic rates since that would lead to duplicate counting.

sites. We then extrapolated to the 2017 Census population data according to sex and race-stratified groups, including data from the IHS registry, and summed the stratum-specific estimates to provide a total population estimate of SLE cases in the US.

Results: The registries contributed 5,417 classified cases of SLE from a mix of urban and rural areas. From the meta-analysis of the four state-based registries, the overall prevalence was 72.8 (95%CI 65.3, 81.0) per 100,000 population. The prevalence among females was about 9 times higher than males (128.7 vs 14.6). In the meta-analysis, prevalence was highest among black females (230.9, 95%CI 178.2, 299.2), followed by Hispanic females (120.7, 95%CI 84.0, 173.4), white females (84.7, 95%CI 68.4, 104.8) and Asian/Pacific Islander females (84.4, 95%CI 48.3, 147.4). Among males, prevalence followed a similar pattern with the highest rates among black males (26.7, 95%CI 19.6, 36.4) followed by Hispanic males (18.0, 95%CI 15.6, 20.8), Asian/Pacific Islander males (11.2, 95%CI 5.7, 21.9), and white males (8.9, 95%CI 8.0, 10.1). The AI/AN prevalence estimates, which were not included in the meta-analysis, had the highest rates of SLE for both females (271, 95%CI 238, 307) and males (54, 95%CI 36, 77). Applying our sex- and race-specific prevalence estimates to the corresponding population denominators from 2017 Census data, we estimated that 198,677 persons (179,186 females and 19,491 males) in the US fulfill ACR SLE classification criteria, Table 1.

Conclusion: Using estimates from a coordinated network of population-based SLE registries, a more accurate prevalence estimate for the US was obtained. Our methods did not capture undiagnosed, "incomplete", or other forms of lupus such as cutaneous lupus. Other case definitions may yield different results.

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Abstract Number: 2887

Cell-bound Complement Activation Products in Combination with Low Complement C3 or C4 Have Superior Diagnostic Performance in Systemic Lupus Erythematosus

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SESSION INFORMATION

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Background/Purpose: Cell-bound complement activation products (CB-CAPs) are stable forms of classical complement activation ex-vivo, with high sensitivity and specificity for systemic lupus erythematosus (SLE). We sought to compare the performance of CB-CAPs to the gold standard low complement C3 or C4 in distinguishing SLE from other rheumatic diseases and healthy individuals.

Methods: Multiple academic centers in the United States contributed to the adult (>= 18 years) cross sectional cohort (n=1200) consisting of SLE (n=450), healthy individuals (n=252), and other rheumatic diseases (n=450; 189 RA, 88 Sjögren's, 90 fibromyalgia, and 83 other connective tissue diseases). Abnormal CB-CAPs status (erythro-

	Sensitivity	Specificity	AUC 95% CI	OR 95% CI	AIC
Low C3 (<81 mg/dl)	27%	97%	0.620 (0.599, 0.641)	10.9 (6.28,18.91)	1200
Low C4 (<12.9 mg/dl)	27%	97%	0.618 (0.596, 0.639)	9.57 (5.67,16.15)	1206
Low C3 or low C4	38%	93%	0.656 (0.632, 0.681)	8.34 (5.55,12.53)	1174
Abnormal EC4d (>14 net MFI)	43%	92%	0.675 (0.650, 0.700)	8.67 (5.9,12.72)	1153
Abnormal BC4d (>60 net MFI)	50%	94%	0.718 (0.693, 0.743)	14.95 (9.81,22.77)	1082
Abnormal EC4d or BC4d	62%	88%	0.746 (0.719, 0.772)	11.05 (7.95,15.37)	1067
Complement Score (>1)	45%	98%	0.812 (0.788, 0.836)	36.0 (18.76,68.98)	1037

Table. Abnormal CB-CAPs compared to low C3/C4 in distinguishing SLE from other autoimmune rheumatic diseases

cyte bound C4d [EC4d] and/or B-Lymphocyte bound C4d [BC4d] >99th percentile of normal healthy group) was determined using flow cytometry. Serum low C3 (< 81 mg/dl) and low C4 (< 12.9 mg/dl) levels was determined using immunoturbidimetry. Performance of the markers, either alone or in combination, to distinguish SLE from other rheumatic diseases and healthy controls were established using sensitivity, specificity, odds ratio (OR) and area under the curve (AUC) of the receiver operating characteristic curve (ROC). Youden Index (Sensitivity + Specificity – 100) and Akaike information criteria (AIC) were also calculated. The combination of 4 complement marker abnormalities was also evaluated using logistic regression and composite score cumulating the presence of these abnormalities was calculated.

Results: Abnormal CB-CAPs status yielded 62% sensitivity with 88% specificity in distinguishing SLE from the group with other diseases (Table). Youden index was 0.492±0.027. Low C3/C4 status yielded 38% sensitivity and 93% specificity in distinguishing SLE from the group with other diseases. Youden index for low C3/C4 (0.313±0.025) was significantly lower than the index associated with abnormal CB-CAPs status ($p< 0.01$). Specificity of low C3/C4 and abnormal CB-CAPs in distinguishing SLE from healthy individuals was 93% and 99%, respectively. AUC was significantly higher with BC4d (0.718) than with EC4d (0.675; $p< 0.01$), low C3 (0.620; $p< 0.01$), low C4 (0.618; $p< 0.01$) and low C3 and/or C4 status (0.656; $p< 0.01$). Average (SEM) composite score cumulating all 4 abnormalities (range 0-4) was higher in SLE (1.47±0.06) than disease control group (0.21±0.02) ($p< 0.01$) and healthy individuals (0.01±0.02) ($p< 0.01$). The cumulative complement scoring system yielded higher AUC (0.812), higher OR (36.0 CI95%: 18.8-69.0), lower AIC (1037) than low C3/C4 or abnormal CB- CAPS; score greater than 1 abnormality yielded 45% sensitivity and 98% specificity.

Conclusion: Our data suggest that the combination of CB-CAPs with low complement have superior diagnostic performance in SLE than either abnormality alone.

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Abstract Number: 2888

Deriving Accurate Prednisone Dosing from Electronic Health Records: Analysis of a Natural Language Processing Tool for Complex Prescription Instructions

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SESSION INFORMATION

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Session Time: 9:00AM–10:30AM

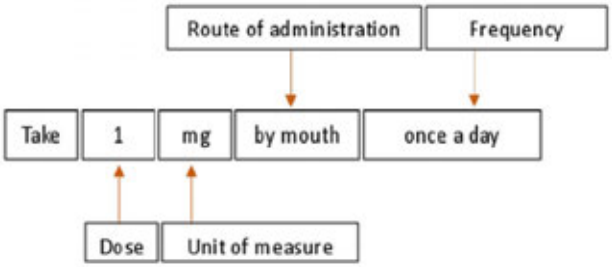

Figure 1. Sample sig from an electronic prescription. Electronic prescriptions are a potential data source for tracking prednisone use. The sig is the free-text portion of electronic prescriptions that conveys medication instructions for the patient, containing a maximum of 140 characters.

Background/Purpose: Prednisone is commonly used to treat rheumatic diseases, yet few comparative effectiveness studies on different dosing regimens are available. Electronic health records (EHR) and prescriptions are potential data sources for such research. However, a barrier to this work is organizing non-standardized prednisone "sigs", or free-text instructions within a prescription, into a standardized and analyzable format. Natural language processing (NLP) tools can potentially be used to extract accurate doses from complex sigs across large prescription data sets. In this study, we compared the daily prednisone dose derived from application of a commercially available NLP tool to manual review of prednisone sigs. Additionally, to understand if sigs accurately captured physicians' recommendations, we compared the prednisone dose derived from analysis of the sig alone to a review of the clinical notes.

Methods: Data for this study were derived from the EHR of an academic health center. 284 prescriptions from 113 randomly selected patients receiving prednisone in clinical encounters between January 1, 2018 and June 22, 2018 were analyzed. Two reviewers independently codified each prescription's sig into discrete structured data, which were used as the benchmark for comparison. An NLP tool, Sigmaster, was then used to automate this data extraction. Sigmaster uses a database of common sigs to map clinical text and translates this information into discrete data, such as dose, frequency, duration, and units. Its performance in determining patients' prednisone doses was assessed by applying it to the sig data and evaluating its output to our manual review-adjudicated benchmark. The validity of sigs as a data source was also evaluated by comparing daily doses of prednisone derived from our manual review of sigs with physician-recommended prednisone doses as recorded in clinical notes. Doses were considered concordant if they were an exact match.

Results: The NLP tool achieved 88.6% concordance with the manual review-derived sig interpretations. The most common reasons for discordance were ambiguous sigs ("Take 1 tab daily, or as directed") and sigs containing multiple phrases ("Take 1 tablet (5 mg total) by mouth daily. Take with one mg tablets to achieve prednisone taper"). However, only 50% of sigs were concordant with physician recommendations derived from clinical notes. The most common reasons for this latter discordance included failure to record tapers in sigs, inaccurate doses in sigs, and sigs with ranges larger than the dose recorded in the note. Given the discordance between manually reviewed sigs and clinical notes, application of the NLP tool to the sig alone would have captured the physician's recommendation in the note only 44% of the time.

Concordance of Dose Data Codified by the NLP tool vs. Manual Sig Review		Concordance of Dose Data Extracted from Clinical Notes vs. Prescription Sigs	
Classification	Unique Sigs (n=123)	Classification	Prescriptions (n=284)
NLP tool and manual sig review concordant	109 (88.6%)	Clinical note and sig concordant	142 (50%)
NLP tool and manual sig review discordant	14 (11.4%)	Clinical note and sig discordant	121 (42.6%)
		Unable to determine concordance	21 (7.4%)

Table. Concordance between NLP tool and manual review of sigs and concordance between manually reviewed sigs and clinical notes.

Conclusion: Although application of an NLP system to extract prednisone doses from complex prescription sigs had relatively high accuracy, significant discordance between sigs and physician notes suggests that sigs alone may be inadequate for research studies. Our study suggests that future NLP systems may need to create a hierarchy to capture physician-intent in glucocorticoid prescribing from EHRs, prioritizing data from clinical notes over prescription sigs alone.

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Abstract Number: 2889

From a Potential Solution to Part of the Problem: Analysis of Spending and Price Trends for Brand-Name and Generic Colchicine and Other Gout Medications

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Drug (Brand Name)	Total Spending in 2017[a]	# of Recipients in 2017	Change from 2012				
			Total Spending[a]	Total Spending, Rebate-Adjusted[b]	# of Recipients	Drug Prices	Drug Prices, Rebate-Adjusted[b]
Colchicine (All): 2012-2017	$307,882,574	504,548	19%	28%	37%	8%	16%
Colcrys: 2012-2014	$141,199,946	185,742	25%	19%	25%	6%	0%
Colcrys: 2015-2017			-11%	-16%	-22%	15%	9%
Generic: 2015-2017	$160,869,540	308,731	8%	8%	0%	1%	1%
Mitigare	$5,813,088	10,075	*n/a – data not reported until 2016*				
Febuxostat (Uloric)	$287,701,021	125,656	213%	174%	69%	59%	39%
Allopurinol (Generic)	$151,624,825	1,875,461	242%	242%	76%	80%	80%
Allopurinol (Zyloprim)	$202,733	288	10%	-4%	-16%	26%	10%
Probenecid (Generic)	$4,840,475	21,064	-6%	-6%	-14%	5%	5%
Probenecid/Colchicine (Generic)	$2,779,961	16,769	-12%	-12%	6%	-16%	-16%
Pegloticase (Krystexxa), Part D	$10,445,698	72	*n/a – data not reported until 2016*				
Pegloticase (Krystexxa), Part B[c]	$44,967,319	408	606%	606%	46%	463%	463%
Rasburicase (Elitek), Part B[c]	$9,867,790	1,292	69%	69%	72%	18%	18%
TOTAL: Medicare[d]	$810,444,607	-	98%	100%	-	81%	74%
TOTAL: Medicare and Medicaid[d]	$871,850,059	-	99%	100%	-		

Data pertains to Medicare Part D, unless otherwise indicated

[a]Amounts paid by Medicare, beneficiaries (as deductible, coinsurance, or copayment), and third-parties

[b]Applying time-varying manufacturers' rebates on brand-name drugs, ranging from 20% (year 2012) to 30% (year 2017); rebates not applied to generics nor drugs dispensed under Part B

[c]Amounts paid by Medicare, beneficiaries (as deductible, coinsurance, or copayment), and third-parties (e.g., supplemental Part B insurance plans)

[d]Excluding rasburicase. Pegloticase and rasburicase are both recombinant forms of urate oxidase, but only pegloticase is formally indicated for gout.

Spending and Utilization for Gout Drugs Covered Under Medicare Parts D and B

SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: Health Services Research II: Health Economics
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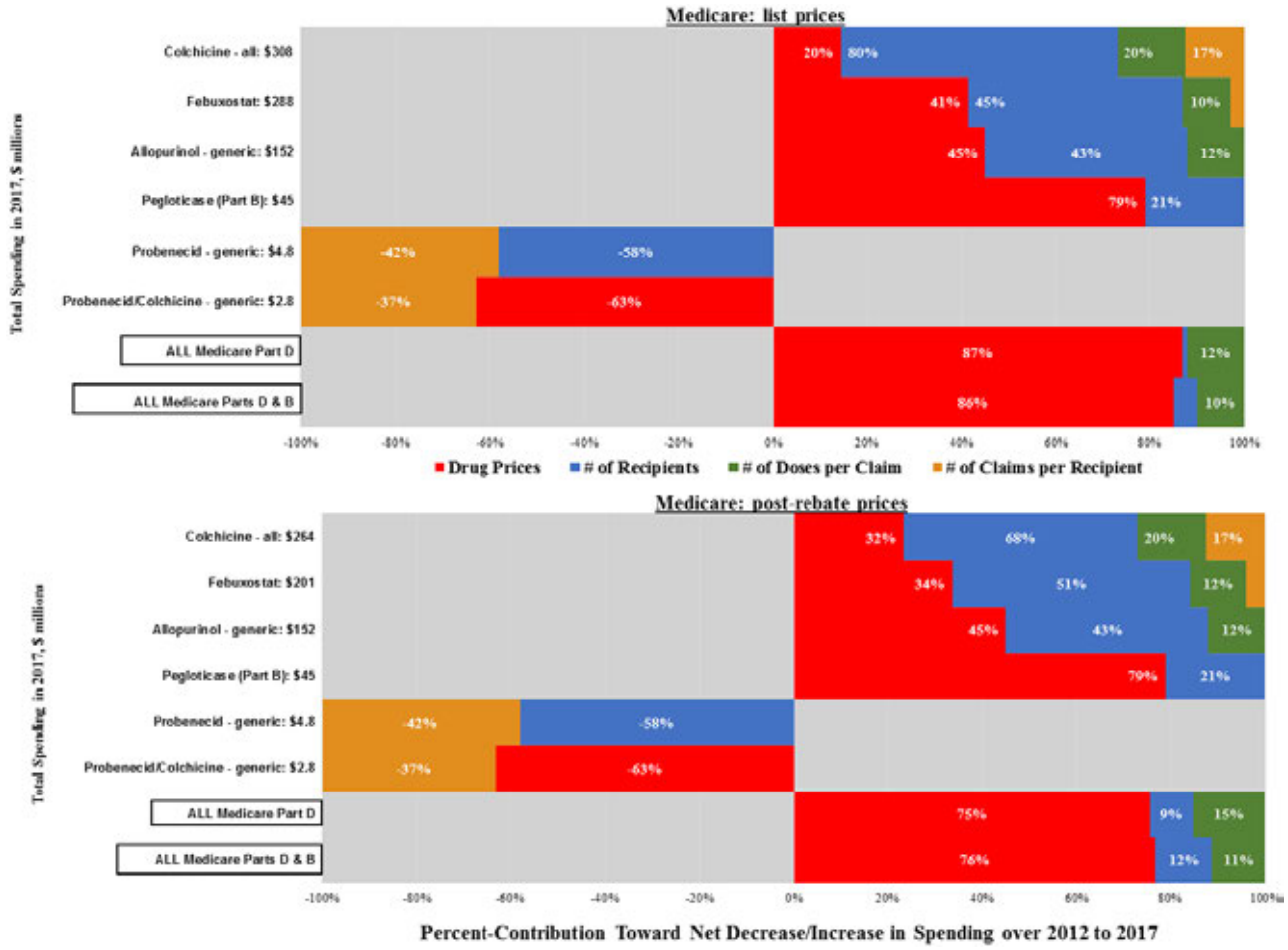
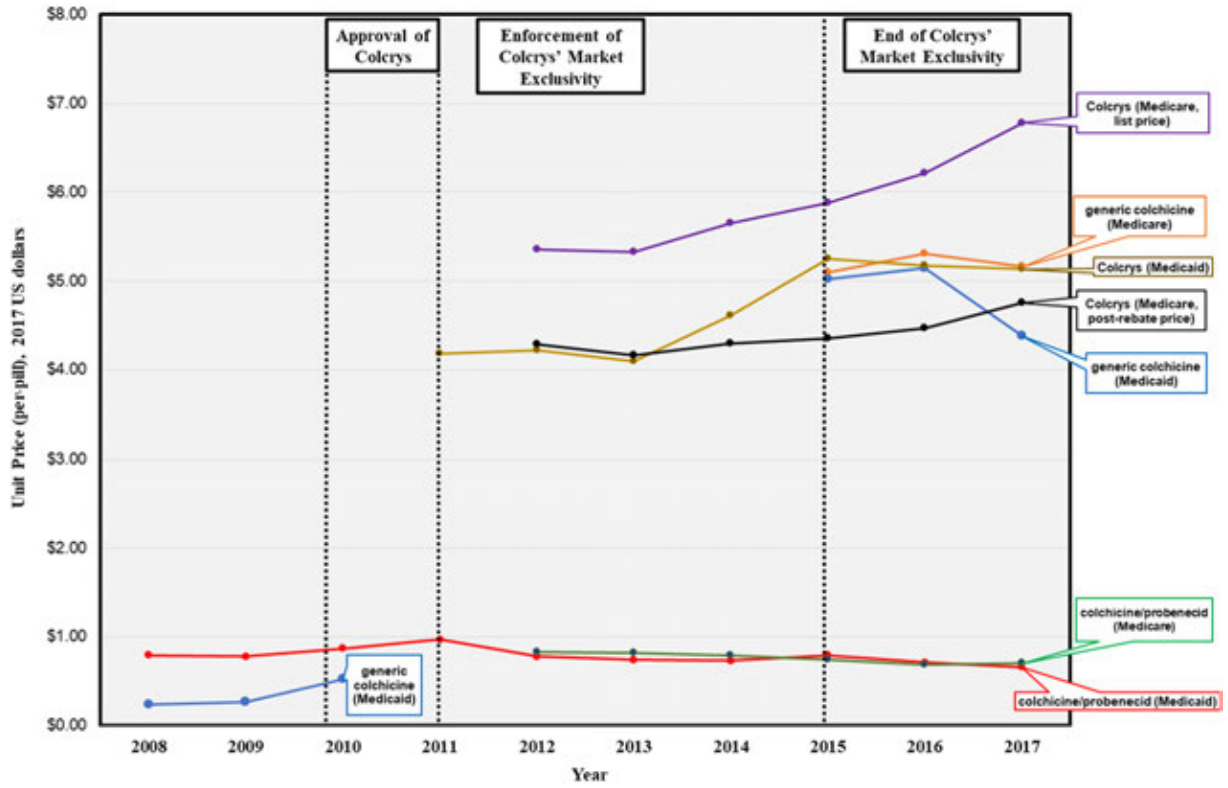
Background/Purpose: Gout affects >4 million US adults aged ≥ 65 years, but little is known about the scale and drivers of public spending on gout medications, including colchicine. Used for decades, its price rose drastically after one brand-name form (Colcrys) was granted market exclusivity from 2011-2014, as part of the FDA Unapproved Drugs Initiative.

We quantified changes in total spending and unit prices for gout drugs in Medicare and Medicaid, and key drivers. We also assessed colchicine prices and spending before, during, and after Colcrys' market exclusivity.

Methods: We used Medicare Parts B & D and Medicaid drug spending data for years 2012-2017, and Medicaid Drug Utilization Data for 2008-2017. These contain aggregated prescription claims for the > 42 million beneficiaries enrolled in Medicare Part B (fee-for-service) or Part D (stand-alone or Medicare Advantage plans) or Medicaid. We included 5 drugs in our main analysis (colchicine, probenecid, allopurinol, febuxostat and pegloticase) along with rasburicase (a urate kinase, like pegloticase, but not indicated for gout).



Component proportion of gout medication spending changes from 2012 to 2017, before and after adjustment for time-varying Medicare Part D rebates



Mean annual drug unit-prices (cost per-pill) for colchicine before, during, and after brand-name Colcrys' period of market exclusivity

Analysis: We calculated six-year changes in total spending and unit prices (mean cost/dose) for each drug and in aggregate, standardised to 2017 dollars, and assessed colchicine over 2012-2014 (Colcrys-only) and 2015-2017. We performed standard decomposition analyses to isolate four sources of spending growth: drug prices, uptake [# recipients], treatment intensity [mean # doses/claim], and annual # of claims/recipient.

We conducted our analysis including statutory Medicaid rebates (as these decrease public spending) and excluding and including estimated time-varying Medicare rebates for brand-name drugs (which are paid to Pharmacy Benefit Managers and Part D plans).

Results: From 2012-2017, public-payer and beneficiary spending on the five main gout drugs nearly doubled, from $439 to $872 million (**Table**). Colchicine accounted for 39% of 2017 spending, followed by febuxostat (35%), allopurinol (19%), pegloticase (6%) and probenecid (1%).

Spending on allopurinol and febuxostat increased ~200% over six years, driven nearly equally by growth in recipient numbers and unit prices (**Figure 1**). Pegloticase spending rose by 600%, mainly due to a > 5-fold unit-price hike (from $327 to $1,828 per-mg), while price hikes drove just 25% of spending growth for rasburicase.

Medicare spending on colchicine rose by 19% over the six years, from $258 to $308 million. Annual spending rose by 25% from 2012-2014 (Colcrys only) but changed little from 2015-2017 (Colcrys + generics) (**Table**).

Still, unit prices for the generics ($5.13/pill in 2017) were only marginally lower than Colcrys' ($6.78/pill), and considerably higher than colchicine before Colcrys' approval (~$0.50/pill) and the probenecid-colchicine combination pill in any year (~$0.70/pill) (**Figure 2**).

Trends were similar with and without Medicare price rebates (**Table, Figures**).

Conclusion: Main drivers of increased public spending were the substantial, > 5-fold price hikes for colchicine and pegloticase, and greater uptake of urate-lowering drugs (which may be positive). The re-entry of generic forms did little to mitigate the large financial burden colchicine now imposes on taxpayers and patients.

Disclosure: N. McCormick, None; **Z. Wallace**, National Institute of Arthritis, Musculoskeletal, and Skin Diseases, 2, Rheumatology Research Foundation, 2; **C. Yokose**, None; **A. Jorge**, None; **C. Sacks**, None; **J. Hsu**, None; **H. Choi**, AstraZeneca, 2, GSK, 5, Horizon, 5, Selecta, 5, Takeda, 5.

Abstract Number: 2890

The Effect of Rheumatoid Arthritis and Biologics on the Acquisition of Subsequent Diseases and Adverse Events: A Matched Longitudinal Population Study

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
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Background/Purpose: The direct and indirect effects of rheumatoid arthritis (RA) are difficult to measure in observational studies because:

(1) The inflammatory effects of RA are difficult to separate from underlying age-sex related risk of comorbid conditions

(2) Long-term large sample follow-up of patients is expensive, arduous, and difficult to standardize

(3) Limited methods for selecting appropriate non-diseased controls for matching with RA patients in case-control attribution studies

Our purpose was to utilize an administrative database over a long-term time horizon among a population of patients with identical insurance coverage with RA to separate the underlying age-sex related risk of acquisition of subsequent comorbid conditions, from conditions arising from RA related inflammation.

As a secondary exposure, we tested the plausibility of the introduction of biologics as an avoidance mechanism for subsequent comorbid conditions.

Methods: The study was a matched case-control cohort of adult RA patients from Ontario Canada, identified by validated algorithm. RA patients (cases) were matched 1-1 with age and sex matched controls, and re-matched 1-1 with a separate control group on age, sex, and available disease history using distance matrices.

The index date (exposure) of the match was the year of RA diagnosis for cases from 1995-2015 (Figure 1. Study Diagram).

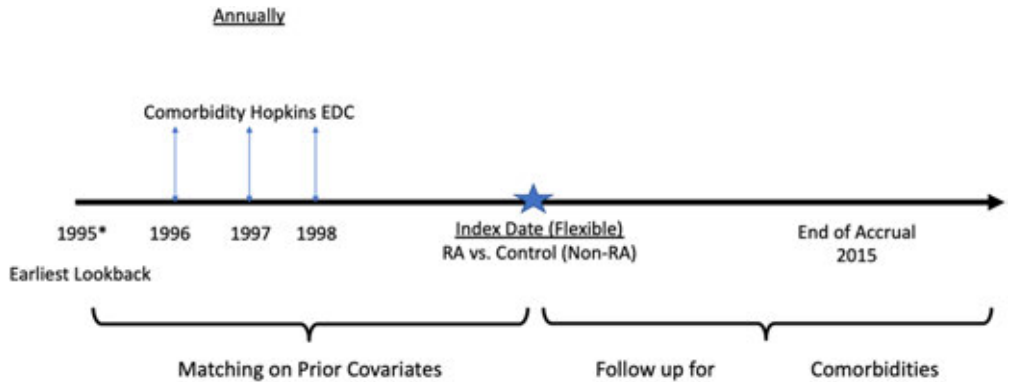

Figure 1. Study Diagram

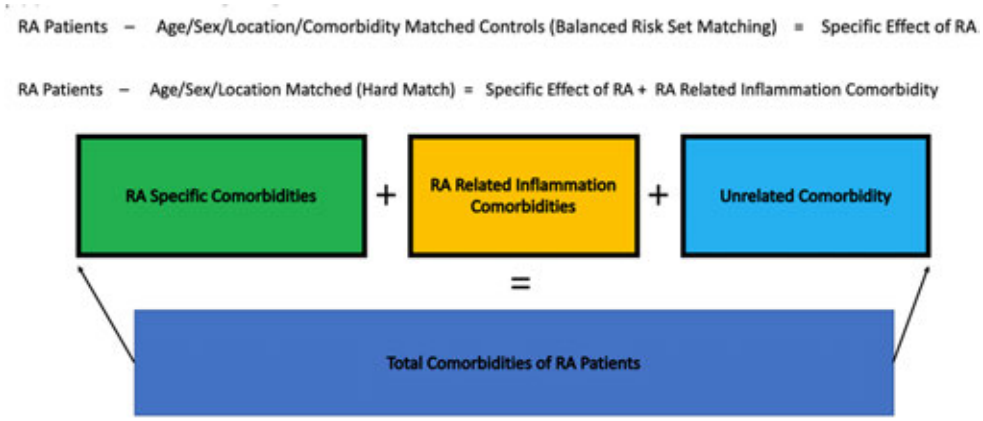

Figure 2. Matching Diagram

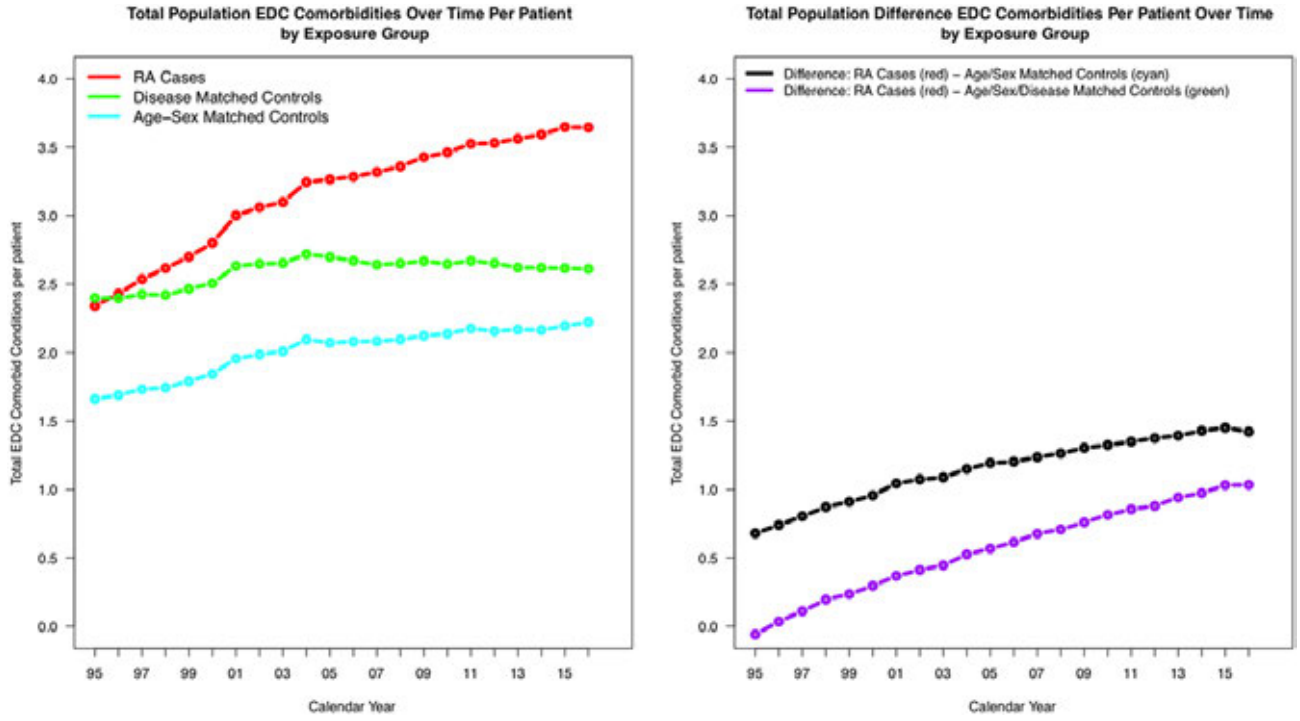

Figure 3. Per Capita Comorbid Conditions Over Time

The outcome variables were comorbidities accrued per patient in each year after diagnosis measured by Hopkins Expanded Diagnostic Clusters (EDC), a summary measure of administrative billing codes mapped on to clinical diagnosis of comorbidities.

The difference between the accrued comorbid conditions between each RAcase and age-sex hard matched control in each year yields the comorbidities assoiciated with RA patients (Figure 2. Matching Diagram) :

RA case - age/sex matched control = age-sex specific underlying risk of comorbid conditions.

The difference between each case and age-sex-disease history matched control yields the direct conferred risk by having RA.

The secondary outcome of modification of downstream disease acquisition was tested by using calendar year as an instrumental variable. From 1995-2001 no biologics were available with greater usage in each subsequent year. Biologics could plausible offset future comorbid conditions if the relative number of comorbid conditions of RA cases compared to similarly matched controls decreased over time.

Results: Of the 136,000 RA patients in Ontario, a random sample of 71,002 RA cases were matched with 71,002 Age/Sex and 71,002 Age/Sex/Medical History Matched Controls. Patients were 75% female, mean age=72, mean year of incidence 2005.

Figure 3. panel shows the per patient comorbidities in each year for all exposure years grouped together by match group. The right panel of Figure 3. shows the difference between RA cases and each matched control group.

Conclusion: This study separates the comorbidities of RA patients relative to age-sex, and age-sex-medical history matched controls. Although this study was a random sample of the population, the plausibility of biologics as a comorbidity avoidance mechanism at the population level may be detectable in administrative data with sufficient analytic tools.

Disclosure: M. Tatangelo, None; **G. Tomlinson**, None; **E. Keystone**, Abbvie, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 5, Astra-Zeneca, 5, Biotest, 5, BMS, 2, 5, 8, Celltrion, 5, Crescendo, 5, Crescendo Bioscience, 5, F. Hoffmann-La Roche Inc, 2, 5, 8, Genentech, 5, Genentech Inc., 5, Genzyme, 5, Gilead, 2, 5, Gilead Sciences, Inc., 5, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Merck, 5, 8, Pfizer, 2, 5, 8, Pfizer Pharmaceuticals, 2, 5, 8, Roche, 2, 5, 8, Sandoz, 5, Sanofi, 2, 5, 8, Sanofi-Aventis, 2, 8, UCB, 5, 8; **M. Paterson**, None; **N. Bansback**, None; **C. Bombardier**, AbbVie, 2, 5, AbbVie Medical, 2, Amgen, 2, ECHO Project Co-PI for Rheumatology, 9, Genzyme, 2, GSK, 5, 9, Hospira, 2, Janssen, 2, 5, Medexus, 2, Merck, 2, 5, Novartis, 2, 5, 9, Pfizer, 2, 5, 9, Schering, 2.

Abstract Number: 2891

Cost-effectiveness of Duloxetine for Knee OA Patients Whose Pain Can't Be Controlled by NSAIDs

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: Health Services Research II: Health Economics
Session Type: ACR/ARP Abstract Session
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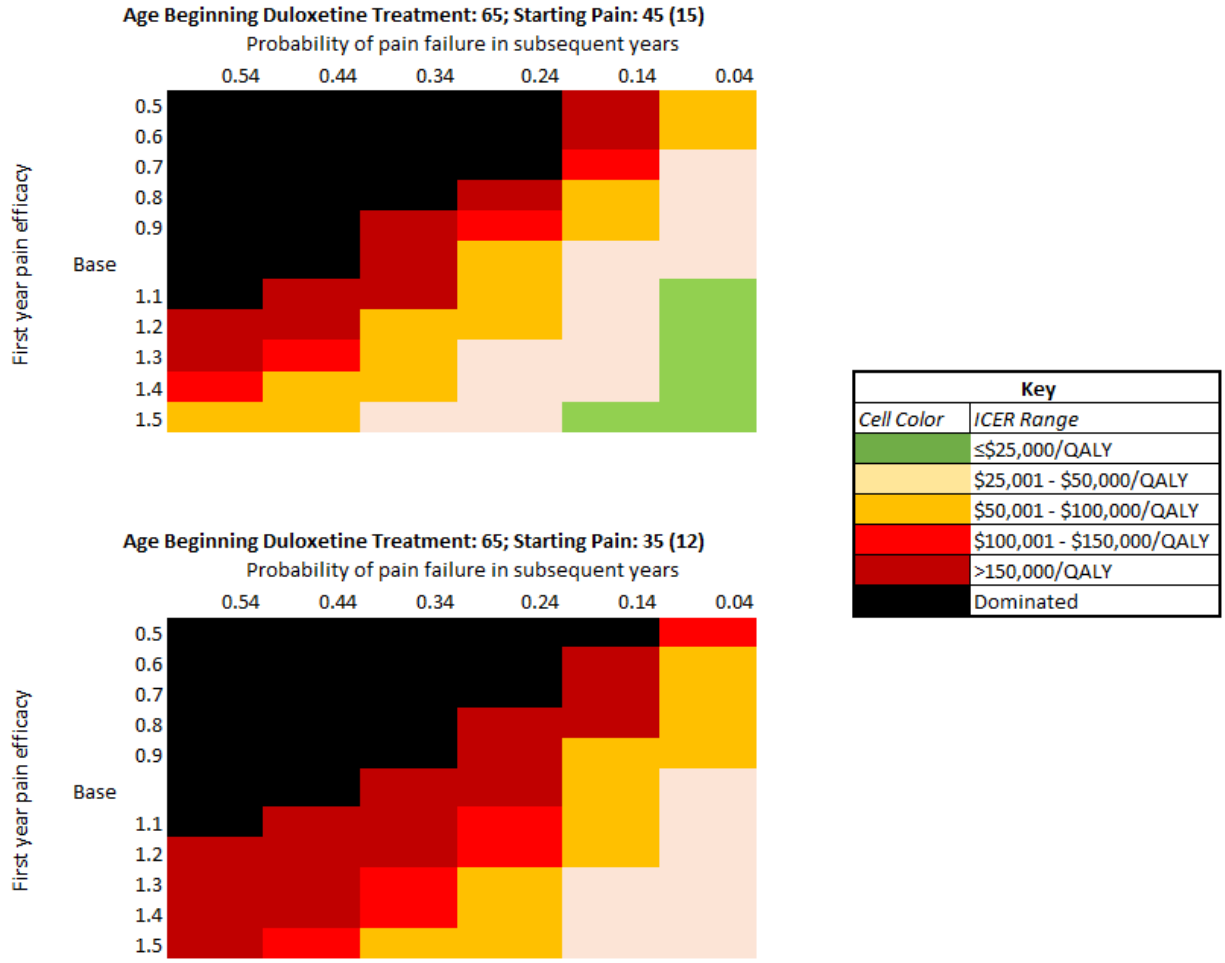

Two-way sensitivity analysis of probability of pain failure in subsequent years and pain efficacy of duloxetine for subjects beginning duloxetine treatment at age 65 with WOMAC pain 45 (top) and 35 (bottom).

Background/Purpose: Knee OA is a disabling condition affecting over 14 million adults in the US. NSAIDs provide only short-term pain relief, creating the need for additional pain management. Growing evidence indicates that chronic knee OA pain is associated with centralized pain pathways. Based on these considerations, ACR and OARSI recommend or conditionally recommend the use of duloxetine. The cost-effectiveness of generic duloxetine in the US has not been assessed in knee OA.

Methods: We used the Osteoarthritis Policy Model, a validated widely published microsimulation of knee OA, to evaluate the cost-effectiveness of adding duloxetine to usual care (UC) after NSAIDs fail to maintain pain relief for knee OA patients. The UC included intra-articular injections, tramadol, oxycodone, and total knee replacement (TKR). We generated the cohort with the demographic and clinical characteristics (age, BMI, and radiographic severity measured as Kellgren-Lawrence (KL) grade) of knee OA patients who failed NSAID treatment. We then conducted the evaluation of four different cohorts stratified by pain severity (starting WOMAC Pain (0-100, 100 is worst) scores of 25, 35, 45, and 55) and continued treatment with regimens that either did or did not contain duloxetine. We followed subjects until death, recording quality-adjusted life years (QALYs) accrued, total lifetime medical costs, likelihood of using opioids and/or TKR. We used national databases and previously published data to estimate the probability of KL progression, quality of life utilities (stratified by pain, number of comorbidities, age, and BMI), treatment efficacy, direct medical costs of knee OA treatments ($800 for NSAIDs and tramadol, $1,100 for oxycodone, and $1,200 for duloxetine), cost and risk of complications. We discounted costs and QALYs at 3%/year and used a healthcare perspective. We assessed cost-effectiveness by evaluating incremental cost-effectiveness ratios (ICERs) calculated as

the ratio of change in costs to change in QALYs for two competing strategies at a Willingness-to-Pay (WTP) threshold of $100,000/QALY.

Results: Adding duloxetine in addition to UC treatments in OA patients with high pain (45 (15) WOMAC points) resulted in adding 2 QALYS per 100 persons taking duloxetine and increased direct lifetime medical costs by $1,500 per person with resulting ICER of $81,000/QALY. Knee OA patients spent on average 2.25 years on duloxetine. Based on the age of starting duloxetine (56 vs. 75 years), duloxetine reduced the risk of opioid use by 7.2%-15.6% and reduced the use of TKR by 6.8% -12.5%. Duloxetine was not cost-effective (at $100,000 WTP) in those with lower pain (25 or 35 WOMAC points) with resulting ICERs of $580,000 and $148,000/QALY respectively. 2-way sensitivity analyses of pain efficacy and failure found the cost-effectiveness of duloxetine sensitive to both regardless of starting pain (Figure 1).

Conclusion: The addition of duloxetine to the UC for knee OA after failure of NSAIDs is cost-effective for those with high pain and may lead to appreciable reduction in risk of opioid use and utilization of TKR. Use of duloxetine in OA patients with mild pain is not justified based on cost-effectiveness.

Disclosure: J. Sullivan, None; **J. Katz**, Flexion, 2, Flexion Therapeutics, 2, Samumed, 2; **E. Losina**, Flexion, 2, Flexion Therapeutics, 2, Pfizer, 2, Pfizer Inc, 2, Regeneron, 5, Regeneron Pharmaceuticals, 5, Roche/Genentech, 2, Samumed, 2, TissueGene, 2, Velocity, 5, Velocity Pharaceutical Development, 5, Velocity Pharmaceutical Development, 5.

Abstract Number: 2892

Model-based Cost-Effectiveness Analyses Comparing Combinations of Urate Lowering Therapy and Anti-Inflammatory Treatment in Newly Diagnosed Gout Patients

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SESSION INFORMATION
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Session Type: ACR/ARP Abstract Session
Session Time: 9:00AM–10:30AM

Background/Purpose: To assess the cost-effectiveness of various combinations of urate lowering therapy (ULT) and anti-inflammatory treatment in the management of newly diagnosed gout patients, from the Dutch societal perspective.

Methods: The Anakinra versus Treatment as usual in the Treatment of ACute Gout (ATTACG) study was the primary data source for this study. Since only patients with crystal proven gout were included in that study, all patient satisfy the ACR/EULAR gout classification criteria.

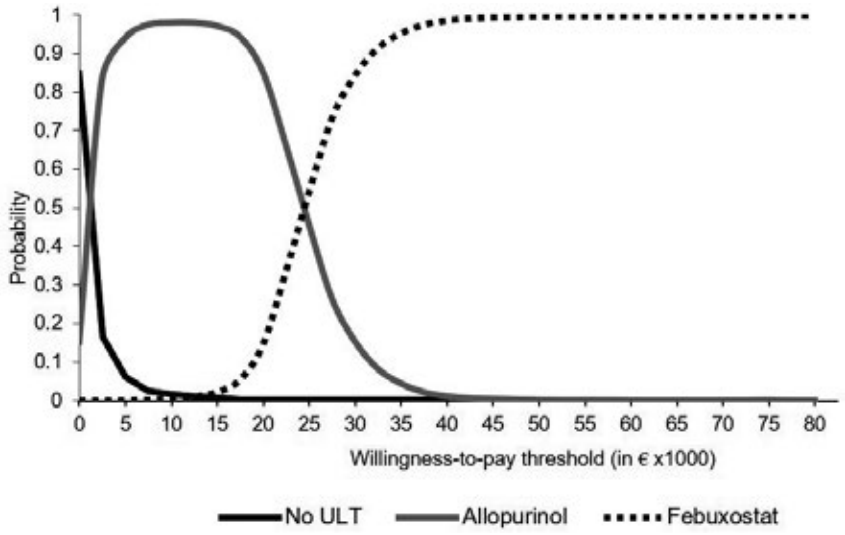
A probabilistic patient-level simulation estimating costs and quality-adjusted life years (QALYs) was performed to compare gout and hyperuricemia treatment strategies. Pain was the main determinant of both QALYs and costs,

	Costs (€)	Effects (QALY)	Δ Cost (€)	Δ Effect (QALY)	ICER (Δ€/Δ QALY)
Allopurinol					
Naproxen	4051.37	0.812493	-	-	-
Colchicine	4066.48	0.812356	15.11	-0.00014	Dominated
Prednisone	4074.27	0.812356	22.9	-0.00014	Dominated
Anakinra	4299.31	0.81274	247.94	0.00025	1,003,805.67

QALY = Quality adjusted life years; ICER = incremental cost-effectiveness ratio; ULT = urate lowering therapy;

	Costs (€)	Effects (QALY)	ΔC (€)	ΔE (QALY)	ICER (Δ€/Δ QALY)
Naproxen					
No ULT	4,031.19	0.78877	-	-	-
Allopurinol	4,063.94	0.81248	32.75	0.02371	1,381.27*
Febuxostat	4,385.40	0.82525	321.46	0.01277	25,173.06**

QALY = Quality adjusted life years; ICER = incremental cost-effectiveness ratio; ULT = urate lowering therapy;



ULT = urate lowering therapy; WTP = willingness-to-pay. Figure displays the CEAC for different ULT combined with naproxen as the anti-inflammatory agent.

with disutility assigned to patients who failed to reach the serum urate (SUA) target (< 0.36 mmol/L). Patients faced a daily risk of a gout flare, with a higher risk for patients who failed to achieve the SUA target level. Health states were no flare, severe pain, mild pain, moderate pain, or no pain in the presence of a flare. Model input was derived from patient level clinical trial data (i.e. SF-6D utility, indirect costs in €'s and pain transition probabilities), meta-analyses or from previously published health-economic evaluations. The results of probabilistic sensitivity analyses were presented using incremental cost-effectiveness ratios (ICERs), and summarized using cost-effectiveness acceptability curves (CEAC). Scenario analyses were performed for gout patients not necessarily experiencing a gout flare at model entry, and for patients with a higher daily flare probability.

Results: In the base case, the ICER for allopurinol versus no ULT was €1,381, when combined with naproxen. Febuxostat yielded the highest utility but also the highest costs (€4,385 vs. €4,063 for allopurinol), resulting in an ICER of €25,173 when compared to allopurinol, all combined with naproxen. No ULT with naproxen was not cost-effective, yielding the lowest utility. For the gout flare medications, comparable effects on utility were achieved. Combined with allopurinol, naproxen was the cheapest option (€4,051), and anakinra the most expensive (€4,299). The ICER of anakinra compared to naproxen, when combined with allopurinol was €1,003,805.67 . Colchicine and prednisone were dominated by naproxen when combined with any of the ULT options. Results of the scenario analyses did not

change the conclusions drawn from comparison of ULT and anti-inflammatory treatment. Results remained robust in scenario analyses.

Conclusion: Allopurinol and febuxostat were both cost-effective compared to No ULT. Febuxostat was cost-effective when compared to allopurinol in case of higher willingness-to-pay thresholds. Anakinra was not cost-effective at any regularly acceptable willingness-to-pay threshold. For treating acute gout flares, colchicine, naproxen and prednisone offered comparable health economic implications. However, naproxen was the favoured and dominant option.

Disclosure: C. van de Laar, None; **M. Oude Voshaar**, Swedish Oprhan Biovitrum AB, 2, Grünenthal B.V., 2; **C. Janssen**, Grünenthal B.V., 2, Swedish Oprhan Biovitrum AB, 2; **M. Janssen**, Grünenthal B.V., 8; **M. Al**, None; **M. van de Laar**, Abbvie, 2, 5, Eli Lilly and Company, 2, 5, 8, Merck, 2, 5, Pfizer, 2, 5, 8, Sanofi Genzym, 5, Grünenthal B.V., 2, Swedish Oprhan Biovitrum AB, 2.

Abstract Number: 2893

Long-term Clinical and Economic Benefits of a Short-term Physical Activity Intervention Among Inactive Knee Osteoarthritis Patients in US: A Model-based Evaluation

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SESSION INFORMATION
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Background/Purpose: The United States (US) knee osteoarthritis (OA) population has low levels of physical activity (PA), despite its well-defined health benefits. Interventions to promote PA are often stymied by concerns of lack of sustainability of intervention efficacy. We sought to evaluate lifetime benefits and cost-effectiveness of a short term (3-year) PA intervention in this population.

Methods: Using the validated computer microsimulation Osteoarthritis Policy Model, we examined the long-term clinical and economic impacts of a 3-year PA intervention for inactive adults, aged 55(5) (mean(SD)), with knee OA. The PA program was concurrent with standard of care (SOC), which included non-pharmacologic, pharmacologic, and surgical guideline-based regimens. The PA intervention, based on the SPARKS (Studying Physical Activity Rewards after Knee Surgery) trial, cost $287/person-year and incorporated wearable activity monitors, health coaching, and financial incentives for reaching predetermined PA goals. We considered 3 PA levels: inactive (< 30 minutes of moderate-to-vigorous PA/week), insufficiently active (30-149 min/week), and active (150+ min/week). Intervention efficacy was derived from the SPARKS data as the probability of increasing PA by at least one level, estimated as 0.38. We used accelerometry data from the Osteoarthritis Initiative to derive the impact of PA level on quality of life (QoL). Annual background medical cost savings for active ($714) and insufficiently active ($313) persons and reduction in incidence of cardiovascular disease (CVD) and type 2 diabetes mellitus (DM) compared to inactive persons were derived from the published literature. In sensitivity analyses we varied PA program cost, impact of PA on QoL, and PA-related background medical costs. All cost and QoL results were discounted by 3% annually. Cost-effectiveness of the PA program was defined using incremental cost-effectiveness ratios (ICERs), calculated as the difference in

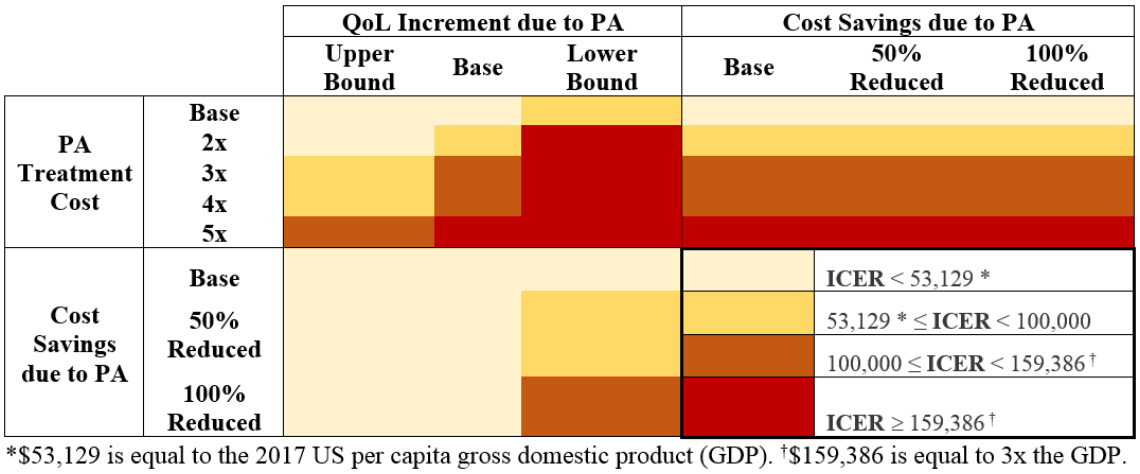

Figure. ICERs (USD/QALY) varying PA treatment cost and impact of PA on annual QoL and background medical costs

cost over the difference in accrued quality-adjusted life-years (QALYs) due to the PA program. This analysis was conducted from a healthcare systems perspective.

Results: The addition of a 3-year PA intervention to SOC for inactive adults with knee OA had an ICER of $16,000/QALY. Participation of 10% of the estimated 4 million inactive US adults with knee OA in such a program could prevent 212 cases of CVD and 319 cases of DM and save 7,476 quality-adjusted life years. Increasing cost of the PA program by 4x raised the ICER to $152,000/QALY (< 3x the US gross domestic product); varying QoL increment due to PA yielded ICERs from $10,000-58,000/QALY; varying background cost due to PA did not qualitatively affect ICERs. Results of two-way sensitivity analyses are presented in the Figure. Offering this program to all US adults with knee OA, regardless of baseline PA, yielded an ICER of $42,000/QALY.

Conclusion: A short-term PA intervention with no sustainability of efficacy beyond a 3-year time horizon in the knee OA population is cost-effective. Given its cost-effectiveness and clinical benefits, providers and payers may consider incorporating a PA intervention into usual care of knee OA patients.

Disclosure: G. Silva, None; **J. Sullivan**, None; **J. Katz**, Flexion, 2, Flexion Therapeutics, 2, Samumed, 2; **S. Messier**, None; **E. Losina**, Velocity, 5, Regeneron, 5, Flexion, 2, Samumed, 2, Pfizer, 2.

Abstract Number: 2894

CD6-ALCAM Signaling Is Upregulated in Kidneys with Lupus Nephritis and Is Associated with Disease Activity

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: SLE – Etiology & Pathogenesis II

Session Type: ACR Abstract Session

Session Time: 11:00AM–12:30PM

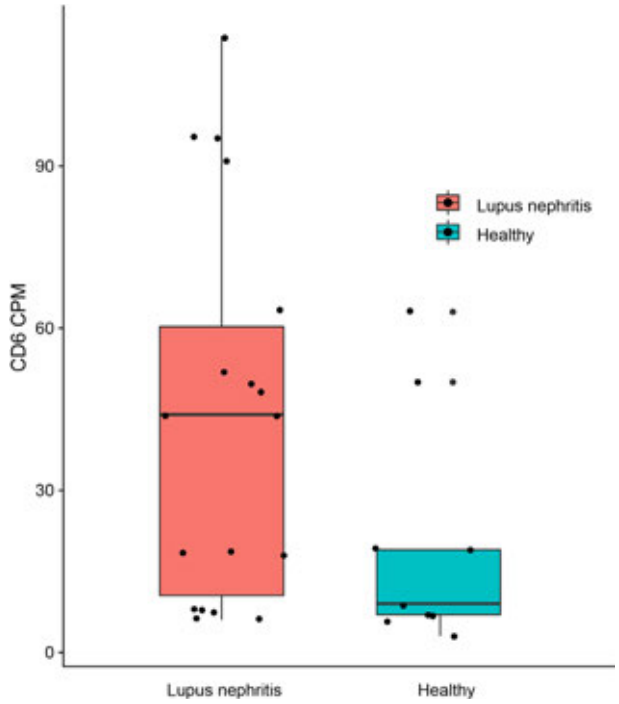

Figure 1. Numbers of CD6 expressing cells in LN (n = 19, red) and healthy control (n = 11, blue) biopsies by single-cell RNA-seq.

Background/Purpose: Lupus nephritis (LN) is a leading cause of morbidity and mortality in Systemic lupus erythematosus (SLE) patients. However, the pathogenesis of renal disease in lupus patients is not yet fully understood. CD6 is a co-stimulatory receptor, predominantly expressed on T cells, that binds to activated leukocyte cell adhesion molecule (ALCAM), a ligand expressed on antigen presenting cells (APCs) and various epithelial and endothelial tissues. The CD6/ALCAM pathway plays an integral role in modulating T cell activation, proliferation, differentiation and trafficking, and is central to immune mediated inflammation. The objectives of this research were to study the expression of CD6/ALCAM in kidneys of LN patients, and evaluate the potential of urine ALCAM as a disease biomarker in LN.

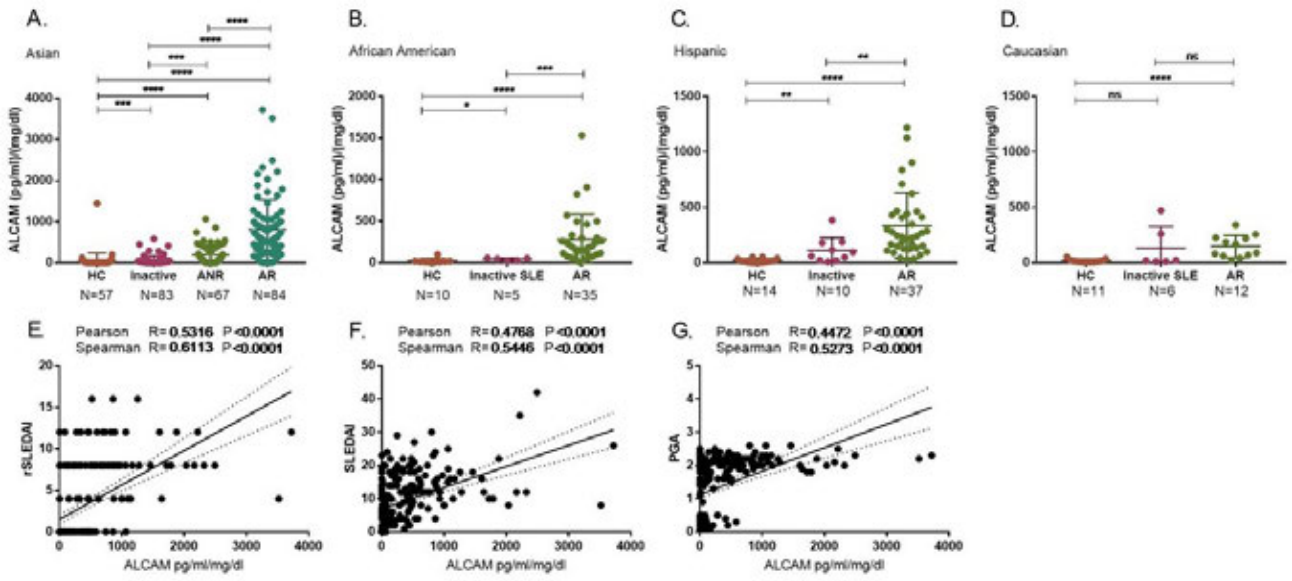

Figure 2. A-D: Cr-normalized urine ALCAM was significantly elevated in active LN patients of multiple ethnicities and discriminated patients with diverse disease activities. E-G: Urinary ALCAM correlated well with several clinical parameters including SLEDAI, renal domains of SLEDAI and PGA. HC, healthy controls, ANR, active non-renal lupus; AR, active renal lupus. *, p<0.05; **, p<0.01; ***; p<0.001; ****, p<0.0001.

Methods: Publicly available single-cell RNA sequencing (scRNA-seq) profiles of clinically indicated renal biopsies obtained from patients with active LN were acquired. scRNA-seq analysis was performed on these datasets using the Seurat package for R. Urine samples were collected from SLE patients of multiple ethnicities and diverse disease activities. ALCAM concentrations were assayed by ELISA then normalized to urine creatinine.

Results: Analysis of biopsies from 19 patients with LN and 11 healthy controls was performed. This analysis confirmed the expression of CD6 exclusively in T cells. ALCAM was expressed in both professional APCs such as macrophages, dendritic cells, and tubular cells. The number of CD6 expressing T cells was elevated in patients with LN compared to healthy controls ($p = 0.08$) (Figure 1). Patients with class III or IV LN trended towards having more CD6 expressing cells than controls. Furthermore, the number of ALCAM expressing tubular cells and macrophages were elevated in LN compared to healthy controls as well. Urine ALCAM was significantly elevated in patients with active LN when compared with controls across multiple ethnicities. In African American, Hispanic, and Asian patients, urine ALCAM further discriminated active LN from inactive SLE or active SLE patients without LN. Urine ALCAM correlated significantly with SLEDAI, rSLEDAI and PGA in Asian SLE patients (all $p< 0.0001$) (Figure 2).

Conclusion: Here, we demonstrate increased activity of the CD6/ALCAM pathway within the renal tissues of LN patients. More specifically, infiltrating T cells do indeed express *CD6* and the number of *CD6* expressing T cells are greater in renal biopsies from patients with LN vs. healthy controls, and in patients with proliferative vs. membranous LN. *ALCAM* expressing macrophages were also numerically elevated in patients with LN, suggesting increased activation of the CD6/ALCAM signaling pathway in LN. Patients with LN also had elevated levels of *ALCAM* expressing tubular cells, indicating these resident kidney cells may contribute to signaling and migration of T cells in the context of LN. Finally, urine ALCAM was significantly elevated in active LN patients in multiple ethnicities, and correlated well with clinical disease status, thus representing a promising biomarker for disease evaluation in LN. These data suggest that a targeted CD6-ALCAM therapy, such as itolizumab, may be a promising for the treatment of LN.

Disclosure: E. Der, None; **T. Zhang**, None; **C. Mok**, None; **R. Saxena**, None; **K. Polu**, Equillium, 3; **C. Mohan**, Equillium, 5, Equillium, Inc, 5; **C. Putterman**, Equillium, 5, Equillium, Inc, 2, 5, Exagen, 2.

Abstract Number: 2895

Complement Protein CL-K1 at High Concentrations Protects Against the Development of Lupus Nephritis

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Background/Purpose: Nephritis is a severe manifestation of systemic lupus erythematosus (SLE) that develops in 30 to 50 percent of the patients. At the time of diagnosis, it is not possible to predict which patients will develop nephritis.

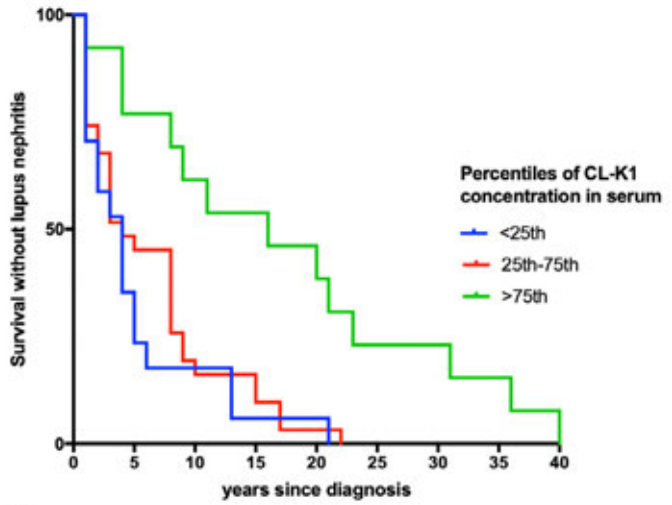

Fig.1

Time to development of lupus nephritis based on low, medium or high serum concentration of CL-K1.

CL-K1 (collectin kidney-1, collectin-11) is a soluble C-type lectin, with collagenous stalks like C1q, that through recognition of suitably spaced patterns of mannose glycans or negatively charged molecules can activate the complement system. It is found in low concentrations in the circulation in heteromeric complexes with collectin-10 (CL-L1). CL-K1 plays a role in the clearance of apoptotic cells through engagement of DNA displayed on the cell surface. Whereas other complement activating lectins, i.e., MBL, is produced only be hepatocytes, CL-K1 is widely distributed in several tissues in the bodyand it seems to distinguish itself by its capacity for production locally in different tissues.

We hypothesized that complement proteins like CL-K1, could play a role in modifying the local response to deposited DNA containing immunocomplexes, that cause inflammation and tissue damage in SLE, and hence play a protective role in the disease.

Methods: Patients included in the study fulfilled the 1997 ACR revised criteria for the classification of SLE. The cohort was included at two Danish university hospitals and has previously been described (1). A total of 372 SLE patients were included out of which 121 had biopsy verified nephritis. Disease onset was defined as the date of fulfillment of the 1997 ACR revised criteria for the classification of SLE. Lupus nephritis was defined by biopsy verified glomerulonephritis classified after the WHO classification system. Serum concentrations of complement proteins were measured in samples available from all included patients using in-house-developed time resolved immune fluorometric assays (TRIFMA).

Results: SLE patients with nephritis were clinically different from patients without this manifestation. They were on average younger at diagnosis (median: 27 vs 35, $p< 0.05$), a larger percentage was positive for anti-double-stranded-DNA (93 vs 85 %, $p >0.05$), and all patients with nephritis were positive for ANA (anti-nuclear antibody). Patients with nephritis had a lower concentration in serum of CL-K1 compared with patients without nephritis ($p< 0.05$). No difference was found for CL-L1. Amongst the SLE patients with nephritis, the patients with high concentrations in serum of CL-K1 had a significantly longer time from diagnosis to the onset of lupus nephritis (fig.1).

Conclusion: High serum concentrations of the complement protein CL-K1 were associated with delayed onset of lupus nephritis in a Danish cohort of 372 SLE patients. CL-K1 could play a protective role against the kidney inflammation and damage seen in lupus nephritis.

Ref. 1. Troldborg A *et al*. J Rheumatol. 2018;45(8):1136-1144

Disclosure: A. Troldborg, None; **A. Voss**, None; **S. Hansen**, None; **J. Jensenius**, None; **K. Stengaard-Pedersen**, None; **S. Thiel**, None.

Abstract Number: 2896

The Role of Alterations in the Splicing Machinery in the Pathogenesis of Lupus: Does It Impact Lupus Nephritis?

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: SLE – Etiology & Pathogenesis II

Session Type: ACR Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: The aim of this study was to evaluate whether alterations in the splicing machinery of immune cells could influence the development and activity of the disease and the kidney involvement in systemic lupus erythematosus (SLE) patients.

Methods: Monocytes, lymphocytes and neutrophils from 43 SLE patients and 34 healthy donors (HD) were purified by immunomagnetic selection. Then, 45 selected elements of the splicing machinery and a set of 48 genes related to inflammation, renal and cardiovascular disease (including interleukins, adipocytokines, chemokines, and oxidative stress markers, among others) were evaluated using a microfluidic qPCR array (Fluidigm). In parallel, an extensive clinical/serological evaluation was performed, comprising renal and CV involvement along with autoantibodies, and inflammatory molecules. Correlation and association studies and logistic models among those clinical and analytical parameters were developed. Separately, mechanistic *in vitro* studies were carried out by incubation of HD-leukocytes with purified anti-dsDNA-IgG from SLE patients.

Results: Altered expression of spliceosome components was demonstrated in the 3 leukocyte subsets: 29, 13 and 22 components were differentially expressed in monocytes, lymphocytes and neutrophils, respectively, vs HD. Intriguingly, any spliceosome component was commonly deregulated among the three leucocyte subsets except for PRPB8, a key component of the spliceosome, that acts as a scaffold protein essential for spliceosome assembly.

Correlation studies demonstrated multiple links among altered spliceosome components and the score of disease activity along with a number of inflammatory and oxidative stress mediators. Remarkably, the levels of those altered components were associated to the presence of lupus nephritis in the three leukocyte subsets. Moreover, we could build different logistic models to precisely identify patients with renal involvement, which integrated the concomitant alteration of: RNU12, RNU4ATAC and RNU6ATAC, in monocytes; RNU4, SRRM1 and U2AF2 in lymphocytes; and PRPF8, SF3B1 and KHDRBS1 in neutrophils.

On the other hand, a logistic model combining RNU6, CELF1 and RAVER1 could classify anti-dsDNA positivity in lymphocytes, thus suggesting the involvement of these autoantibodies in the splicing process. Finally, in vitro treatment of HD lymphocytes with anti-dsDNA promoted the decrease of several spliceosome components found altered in vivo in SLE lymphocytes, such as KHDRBS1, SRSF5 and TRA2B.

Conclusion: 1) The splicing machinery is profoundly altered in leukocytes from SLE patients and closely related to the development and activity of the disease. 2) Evaluation of specific components of the spliceosome in leukocytes subsets might be used to clinically typify kidney involvement. Ongoing studies would clarify the physiological implications of these findings, which may provide novel diagnostic-biomarkers and therapeutic-tools to treat SLE.

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Disclosure: C. Lopez-Pedrera, None; **A. Ibañez-Costa**, None; **M. Aguirre-Zamorano**, None; **L. Pérez-Sanchez**, None; **A. Patiño-Trives**, None; **M. Luque-Tevar**, None; **M. Abalos-Aguilera**, None; **I. Arias de la Rosa**, None; **N. Barbarroja**, None; **M. Espinosa**, None; **E. Collantes-Estevez**, None; **J. Castaño**, None; **R. Luque**, None; **C. Perez-Sanchez**, None.

Abstract Number: 2897

Increased CD69+ Tissue-resident Memory T (T_{RM}) Cells and STAT3 Expression in Cutaneous Lupus Erythematosus Patients Recalcitrant to Antimalarials

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: SLE – Etiology & Pathogenesis II
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Cutaneous lupus erythematosus (CLE) is an autoimmune disease with various subsets and clinical manifestations. T lymphocytes are the predominant cell type found in lesional skin, but plasmacytoid dendritic cells (pDCs) and myeloid dendritic cells (mDCs) also play an important role in the pathogenesis. Oral antimalarials, including hydroxychloroquine (HCQ) and quinacrine (QC) are first-line systemic therapy for all CLE sub-types. Although HCQ is effective in approximately 50% of patients, some patients still do not respond to antimalarials. Some of these patients benefit from additional QC, but there is a subset of patients who remain refractory to both antimalarials. Refractoriness poses a huge challenge as patients continue to have active disease despite antimalarial therapy. To better understand reasons for refractoriness in CLE, we investigated the immunologic characteristics of patients who responded to antimalarials versus those who did not.

Methods: One hundred fifteen patients with a diagnosis of CLE were recruited from the Autoimmune Skin Disease Center at the Hospital of the University of Pennsylvania. Sixty-five were well-characterized in terms of response to treatment as (i) HCQ-responders (n=22), (ii) HCQ+QC-responders (n=24), or (iii) HCQ+QC-nonresponders (n=19).

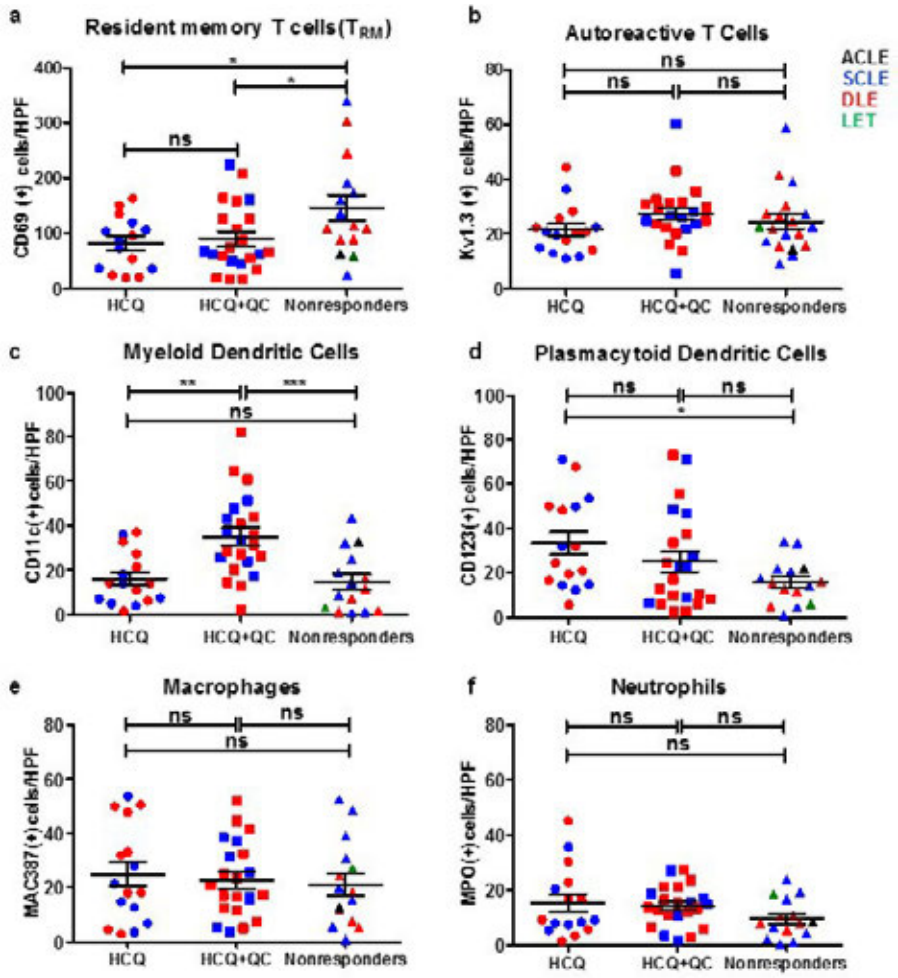

Figure 1. Immune Cell Quantification in HCQ-responders, HCQ+QC-responders, and Nonresponders. There was a significantly higher number of tissue-resident memory T (TRM) cells in nonresponders compared to HCQ-responders and HCQ+QC-responders ($p<0.05$, Figure 1a). There was a significantly higher number of mDCs in HCQ+QC-responders compared to the nonresponders ($p<0.001$, Figure 1c) and HCQ-responders ($p<0.01$, Figure 1c). There was a significantly higher number of pDCs in the HCQ-responders compared to the nonresponders ($p<0.05$, Figure 1d). There was no significant difference in the number of auto reactive T cells (Figure 1b) macrophages (Figure 1e) and number of neutrophils (Figure 1f) among the three groups.

Lesional skin was biopsied before starting treatment with antimalarials. We defined treatment failure to HCQ as continued skin activity requiring a second intervention after at least 2 months of HCQ therapy. Immunohistochemistry was used to characterize the inflammatory cells and cytokine expression in lesional skin biopsies from patients. Total RNA was extracted from these biopsies to analyze specific gene signatures. The patient's CLASI score – a measure of disease activity – at the time of the biopsy was also determined.

Results: Immunohistochemistry showed that CD69+ tissue-resident memory T (T_{RM}) cells were significantly higher in HCQ+QC-nonresponders compared to HCQ- and HCQ+QC-responders. mDCs were significantly higher in HCQ+QC-responders compared to HCQ- and HCQ+QC-nonresponders. There were significantly higher pDCs in the HCQ-responders compared to the nonresponders. There was no significant difference in the number of autoreactive T cells, macrophages, and neutrophils among the three groups (Figure 1). The HCQ+QC-nonresponder group was distinct from the other groups in that their CLASI scores correlated positively with the number of T_{RM} cells ($r=0.6254$, $p=0.017$) and macrophages ($r=0.5726$, $p=0.041$) (Figure 2). mRNA expression demonstrated high STAT3 expression in HCQ+QC-nonresponders (Figure 3). There was a significantly higher percentage of area stained for IL-17 in the HCQ+QC-responders compared to HCQ-responders and HCQ+QC-nonresponders while IL-22 expression was not significantly different between groups.

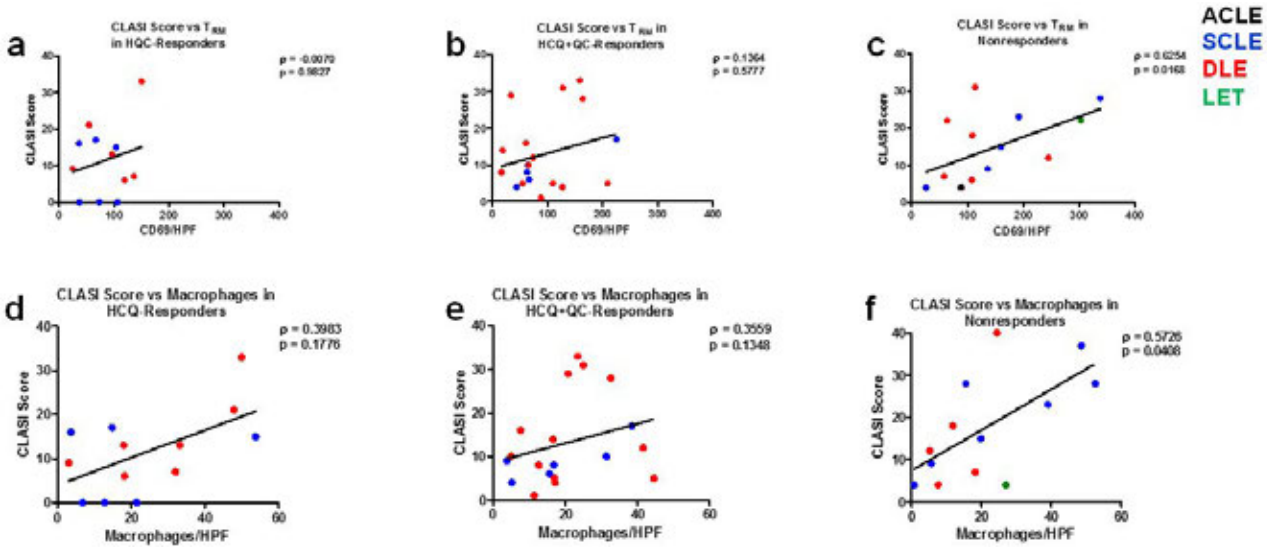

Figure 2. CLASI Score versus tissue-resident memory T (TRM) cells and Macrophages in HCQ-responders, HCQ+QC-responders, and Nonresponders. For the nonresponders, there was a significant positive correlation between the CLASI score with the number of tissue-resident memory T (TRM) cells and macrophages ($p<0.05$, Figures 3c&3f). There was no significant correlation between the CLASI score with the number of tissue-resident memory T (TRM) cells and macrophages counts in the HCQ-responders and HCQ+QC-responders.

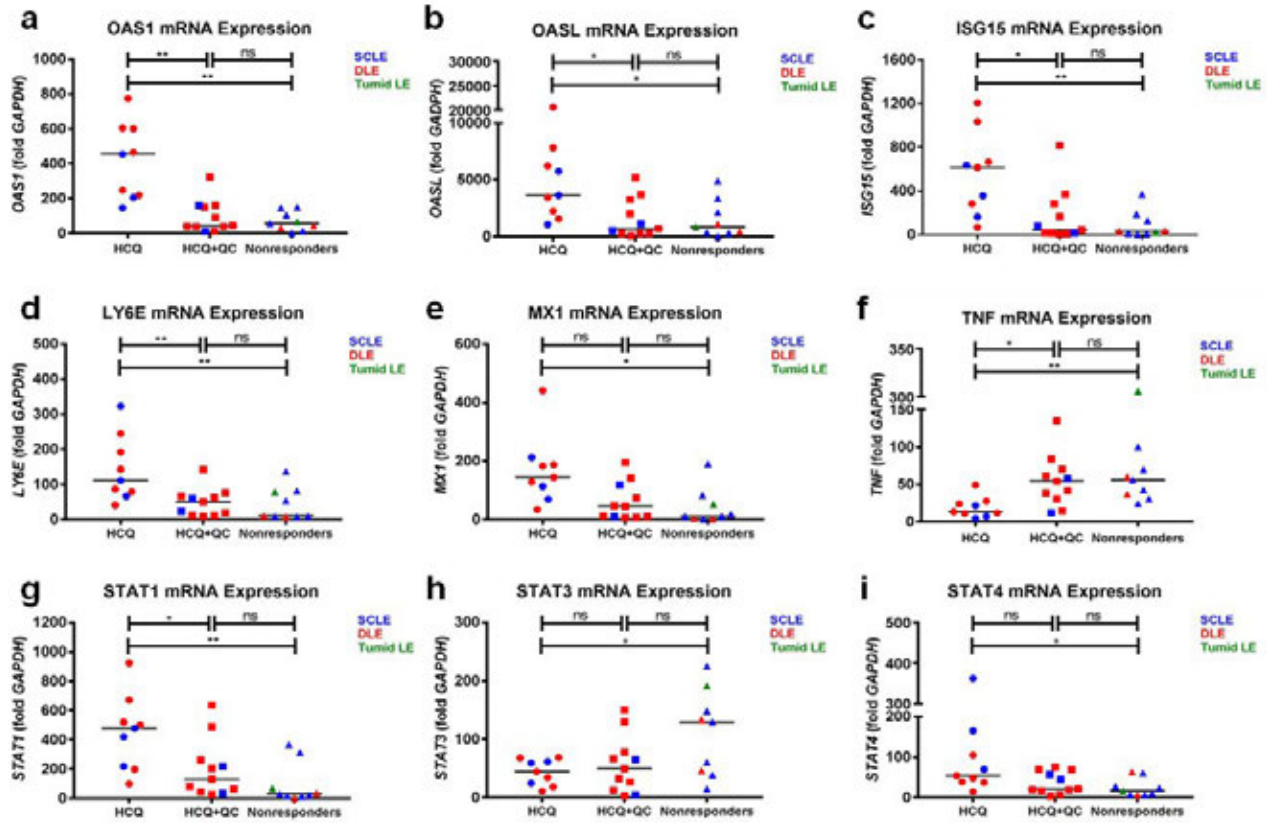

Figure 3. Type 1 Interferon, TNF, and STAT Gene Expression in HCQ-responders, HCQ+QC-responders, and Nonresponders. The nonresponders were found to have a significantly decreased type 1 IFN signature and elevated TNF-α expression compared to the HCQ-responders (OAS1 $p<0.01$; OASL $p<0.05$; ISG15 $p<0.01$; LY6E $p<0.01$; MX1 $p<0.05$; TNF $p<0.01$, Figures 4a-f). In terms of the STAT genes, the nonresponders had increased expression of STAT3 ($p<0.05$, Figure 4h) and decreased expression of STAT1 ($p<0.01$, Figure 4g) and STAT4 ($p<0.05$, Figure 4i) compared to the HCQ-responders. The nonresponders and HCQ+QC-responders had a similar expression profile for all analyzed genes.

Conclusion: An increased number of CD69+ T_{RM} cells and correlation between CD69+T_{RM} cells and macrophages with CLASI scores in the HCQ+QC-nonresponders, a finding not seen in either HCQ or HCQ+QC-responders, may indicate that CD69+ T_{RM} cells and macrophages are involved in antimalarial-refractory skin disease.

Disclosure: M. Zeidi, None; **K. Chen**, None; **K. Desai**, None; **H. Kim**, None; **S. Chakka**, None; **R. Lim**, None; **V. Werth**, Biogen, 2, 5, Corbus Pharmaceuticals, 2, 9, University of Pennsylvania, 9.

Abstract Number: 2898

Evaluation of the Transcriptome of Non-Lesional, Non-Sun Exposed Skin in Patients with Lupus Nephritis

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: SLE – Etiology & Pathogenesis II
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: The impact of renal injury in lupus nephritis (LN) is widespread with consequences to resident cells in other tissue beds, even non-lesional, non-sun exposed skin. Faithful reflection of a relevant renal tissue pathway in a more readily accessible compartment would allow for less invasive diagnostic alternatives. While ongoing studies are exploiting single cell RNA sequencing to link phenotype to "biotype" and identify cell specific pathways in the kidney, this study was initiated to address the hypothesis that these pathways may be reflected in uninvolved skin which is more likely to be serially biopsied.

Methods: Single cell RNAseq was performed on cell suspensions prepared from ~2 mm punch biopsies of non-lesional, non-sun-exposed skin from the buttocks of 5 healthy controls, 4 SLE patients without LN and 18 SLE patients with proteinuria (with skin biopsies obtained within 24 hrs of the kidney biopsy). Histology revealed Class III (*n=6*), Class III/V or IV/V mixed (*n=11*), Class V (*n=1*), and nephrosclerosis (*n=1*). Dissociation of cryostored skin biopsies with collagenase and trypsin enzymes was followed by scRNA-seq using the 10x Genomics platform using V2 and V3 reagents.

Results: We obtained 8,019 and 17,655 high-quality scRNA-seq profiles from single cell suspensions of control and SLE non-lesional, non-sun-exposed skin, respectively. A graph-based clustering method was applied and identified major clusters of cells as visualized by t-distributed stochastic neighbor embedding (tSNE). Differential gene expression analysis guided by established markers revealed these cell clusters as keratinocyte (KC), one smooth muscle cell cluster (SMC), fibroblast (FB), melanocyte (MEL), vascular endothelial cells (VEC), lymphatic endothelial cells (LEC), macrophages-dendritic cells (MAC-DC), T cells (TC) and sweat gland cells (SGC) (Figure 1A). Ranking cells by abundance, the result of the SLE skin cells was KC >FB >VEC >LEC, SMC, MAC-DC, TC, MEL and SGC. Overall, samples processed using the recent V3 single cell reagent kit showed higher genes and transcript captures compared to V2. However, these samples also captured more mitochondrial transcripts (Figure 1B). An analysis of gene expression changes in KC, SMC, and VSC from the LN patients versus controls demonstrated overexpression of interferon stimulated genes. However, the degree of interferon response varied in these cell types with KCs (basal KC, p=0.00312 and hair follicle KC, p=0.000012) showing the highest response followed by VECs (p=0.0043) and SMCs

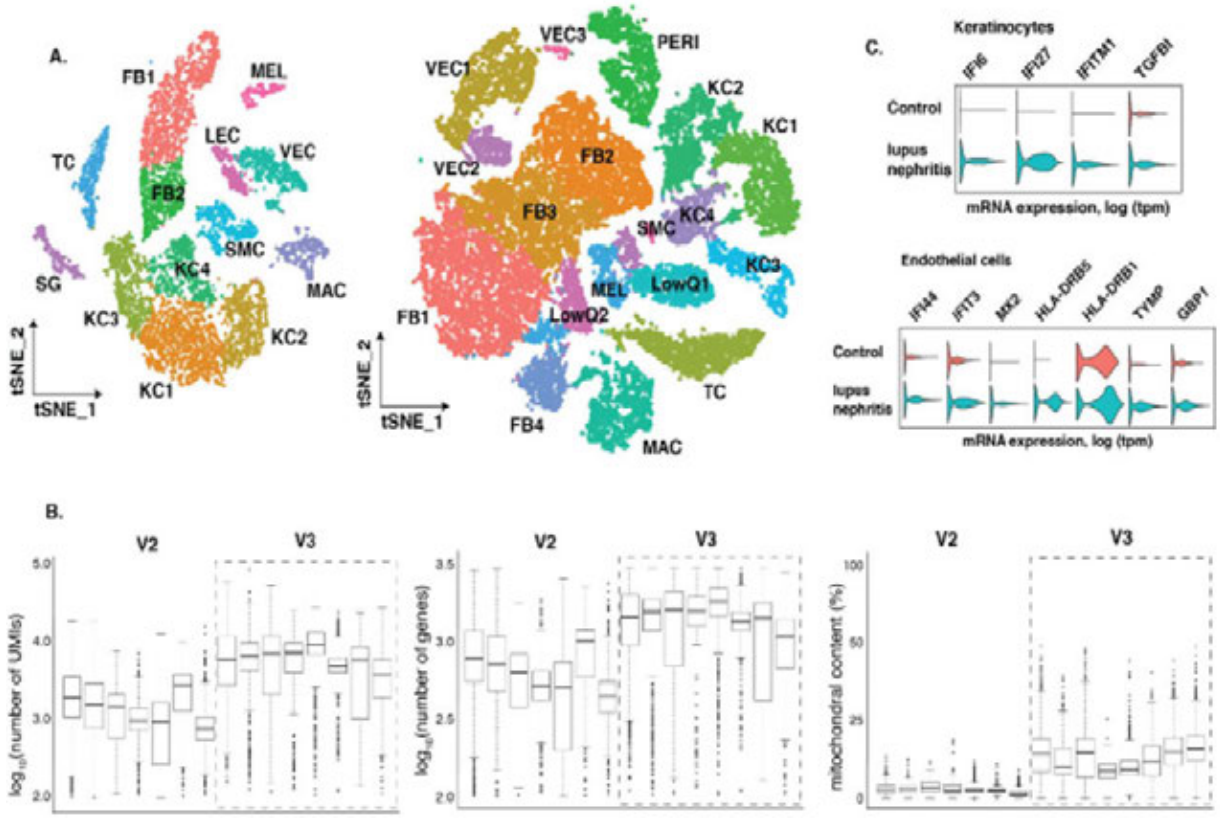

Figure 1. Single cell analysis of skin samples from SLE and healthy controls. A. tSNE plot showing 8019 (left) and 17,655 (right) cells processed using V2 and V3 reagents of 10x Genomics, respectively. B. Comparison of number of genes, transcripts (UMIs) and mitochondrial content in keratinocytes from samples processed on V2 and V3. C. Violin plots showing interferon induced and other differentially expressed genes in LN.

(p=0.0068). In addition to the interferon response signature, VECs from the LN patients also showed upregulation of MHC-II genes such as HLA-DRB5 and HLA-DRB1, suggesting increased antigen presentation capacity (Figure 1C).

Conclusion: scRNA-seq identifies major skin cell types and further clustering identifies rarer cell populations. KCs, SMCs, and VECs from the skin of LN patients reveal diverse IFN response states and additionally VECs also show higher antigen presentation potential. The V3 upgrade of 10x Genomics single cell reagents capture more genes and UMIs per cell, but also higher mitochondrial content compared to the V2 version.

Disclosure: H. Suryawanshi, None; **R. Clancy**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **E. Der**, None; **P. Izmirly**, GlaxoSmithKline, 5; **H. Belmont**, None; **C. Putterman**, Equillium, 5, Equillium, Inc, 2, 5, Exagen, 2; **J. Buyon**, Bristol Myers Squibb, 5, Exagen Diagnostics, 2; **T. Tuschl**, None.

Abstract Number: 2899

Transcriptomic Meta-analysis of Lupus Affected Tissues Reveals Shared Immune, Metabolic, and Biochemical Dysregulation

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	DLE	LA	LN Glom	LN TI
Antigen Presenting Cell	66.67%	75.00%	77.27%	63.64%
Monocyte	88.89%	100.00%	95.45%	59.09%
Myeloid Cell	77.78%	100.00%	81.82%	68.18%
Germinal Center B Cell	77.78%	100.00%	54.55%	77.27%
Plasma Cell	88.89%	75.00%	50.00%	45.45%

Table 1. Percentages of SLE Tissue Samples with GSVA enrichment of specific immune cell modules.

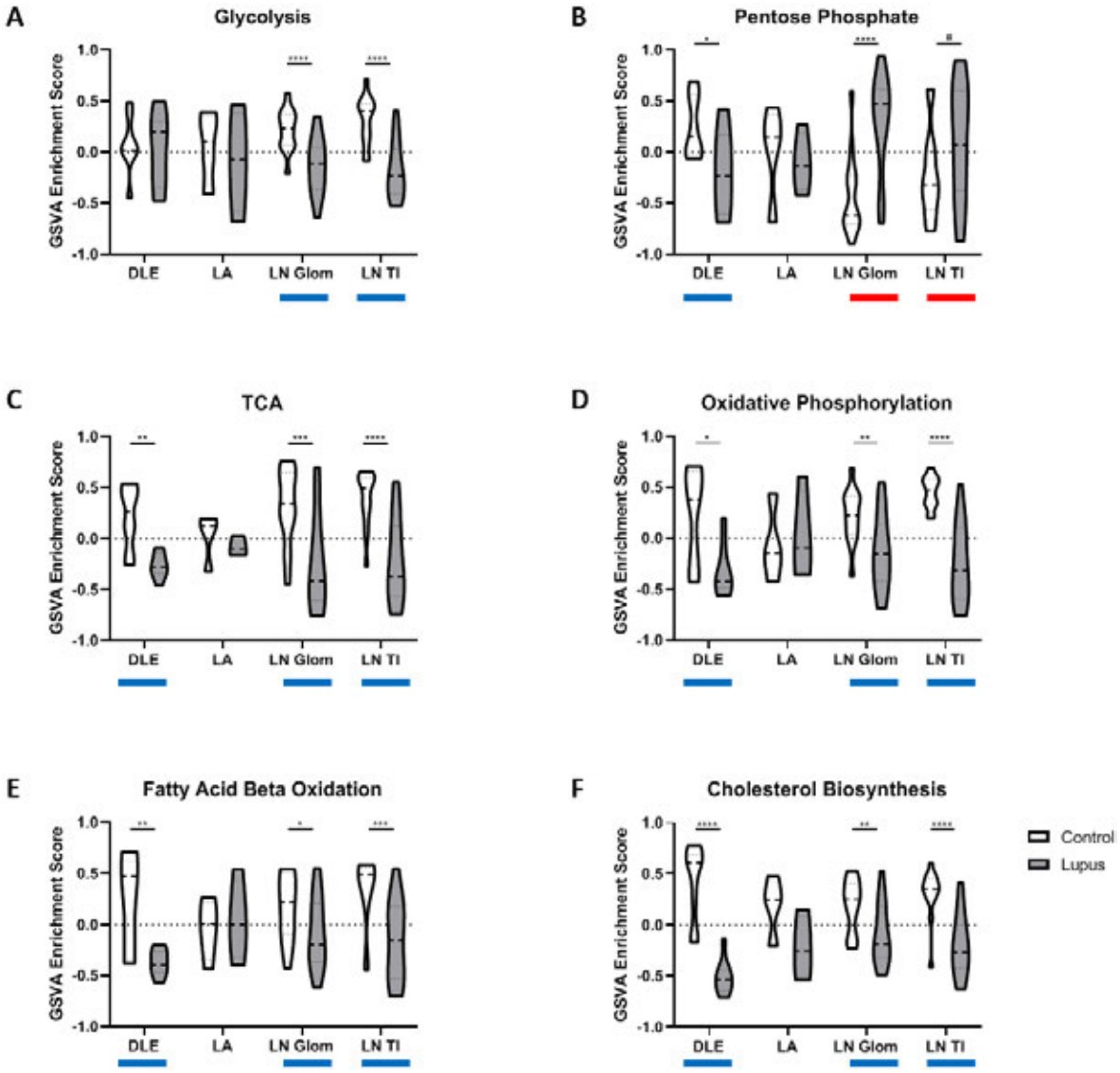

Figure 1. GSVA demonstrates metabolic dysregulation in individual SLE affected tissues. GSVA enrichment scores calculated for (A) glycolysis, (B) pentose phosphate, (C) tricarboxylic acid cycle (TCA), (D) oxidative phosphorylation, (E) fatty acid beta oxidation, and (F) cholesterol biosynthesis modules in DLE, LA, LN Glom and LN TI. Significant enrichment of tissue control to SLE affected tissue or SLE affected tissue to tissue control was determined using the Welch's t-test. Red bar represents enrichment of SLE tissue over control and blue bar represents enrichment of tissue control over SLE tissue. # $p < 0.1$ *$p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** < 0.0001.

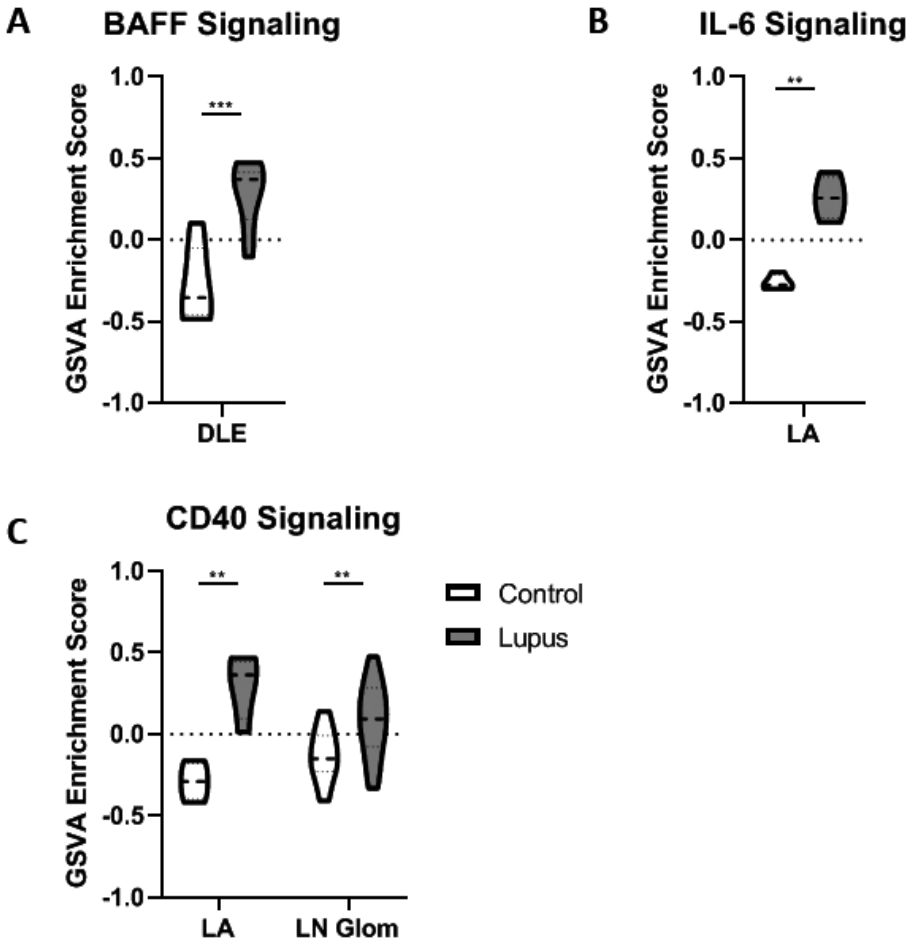

Figure 2. GSVA reveals potential pathways for therapeutic targeting in lupus affected tissues. Measures are shown for drug pathways significantly enriched in SLE affected tissue compared to control tissue as determined using the Welch's t-test for (A) B cell activating factor (BAFF), (B) interleukin (IL)-6, and (C) CD40 signaling in DLE, LA, and LN Glom. ** $p < 0.01$, *** $p < 0.001$.

SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: SLE – Etiology & Pathogenesis II
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) affects various organs and tissues, but whether pathologic processes in each organ are distinct or whether dysregulated molecular functions are found in common in all tissues is not known. We, therefore, conducted a meta-analysis of gene expression profiles in four affected SLE tissues to identify commonly dysregulated pathways.

Methods: Gene expression datasets for discoid lupus erythematosus (DLE), lupus arthritis (LA), lupus nephritis (LN) glomerulus (Glom), and LN tubulointerstitium (TI) were obtained from GEO. Differentially expressed genes (DEGs) were identified by LIMMA analysis for each dataset. DEGs from each tissue were analyzed with a multi-pronged bioinformatics approach to elucidate common immune cell infiltrates and common functional categories. These findings were then utilized to form modules of co-expressed genes to determine their enrichment using Gene Set Variation Analysis (GSVA).

Results: All tissues demonstrated the presence of immune cells with the fewest immune cell transcripts in LN TI. Analysis of bulk gene expression revealed enrichment of antigen presenting cells (APCs), monocytes, and myeloid cells in all four tissues. Notably, enrichment of B cells, plasma cells, germinal center (GC) B cells, and CD8 T cells was only detected in DLE and LA. All four tissues demonstrated upregulated immune activity, including interferon-stimulated genes, pattern recognition receptors (PRRs), and antigen presentation (MHC Class II). Pro-apoptosis genes were also found enriched in DLE, LN Glom, and LN TI. A generalized decrease in biochemical processes was found in all four tissues and a specific decrease in both fatty acid biosynthesis and the tricarboxylic acid cycle was found in DLE and LN. Ingenuity Pathway Analysis (IPA®) further confirmed the activation of Dendritic Cell Maturation, Interferon, NFAT Regulation of Immune Response, PRRs, and TH1 signaling pathways in all four tissues. Additionally, IPA demonstrated cholesterol biosynthesis was decreased in all tissues except LA.

To confirm the aforementioned cellular infiltrates and aberrant pathways, as well as additional pathways, were operative in individual SLE tissues, GSVA was used to analyze enrichment of gene modules in patient samples. As shown in **Table 1**, **Figure 1**, and **Figure 2**, specific abnormalities were found in the majority of tissues, including enrichment of myeloid cells/monocytes, APCs, and GC B cells, whereas others were observed in some but not all tissues.

Conclusion: Common cellular infiltrates and molecular pathways were found in all affected tissues, suggesting commonalities in lupus organ pathogenesis. However, certain cell types and signaling were predominant in some tissues over others and GSVA illustrated heterogeneity between patients. Together this analysis informs a tissue-specific model of lupus immunopathogenesis and metabolic dysfunction with common and unique features and highlights the importance of patient specific identification of dysfunctional pathways in lupus organ pathogenesis.

Disclosure: K. Kingsmore, None; **S. Heuer**, None; **E. Hubbard**, None; **M. Catalina**, None; **P. Bachali**, None; **P. Lipsky**, Horizon, 5, Janssen Research & Development, LLC, 2; **A. Grammer**, None.

Abstract Number: 2900

Interferon Signature Predicts Response to Tofacitinib in Haploinsufficiency of A20

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease III: Novel Therapies
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: The protein A20, encoded by *TNFAIP3*, represses signaling upstream of the inflammatory transcription factor nuclear factor (NF)-kB by regulating ubiquitination. Heterozygous loss-of-function mutations in *TNFAIP3* cause the systemic autoinflammatory disease Haploinsufficiency of A20 (HA20) [1]. Because no FDA-approved medications directly target NF-kB signaling, current HA20 therapies target NF-kB activating cytokines, with biological agents chosen based on clinical experience rather than mechanistic data [2].

Methods: HA20 patients were selected from NHGRI protocol 94-HG-0105 “Genetics and Pathophysiology of Autoinflammatory Disorders”. All patients had mutations in *TNFAIP3* diagnosed by targeted sequencing. Functional activity was confirmed using a reporter assay. Whole blood was extracted into PAXgene tubes, RNA was extracted,

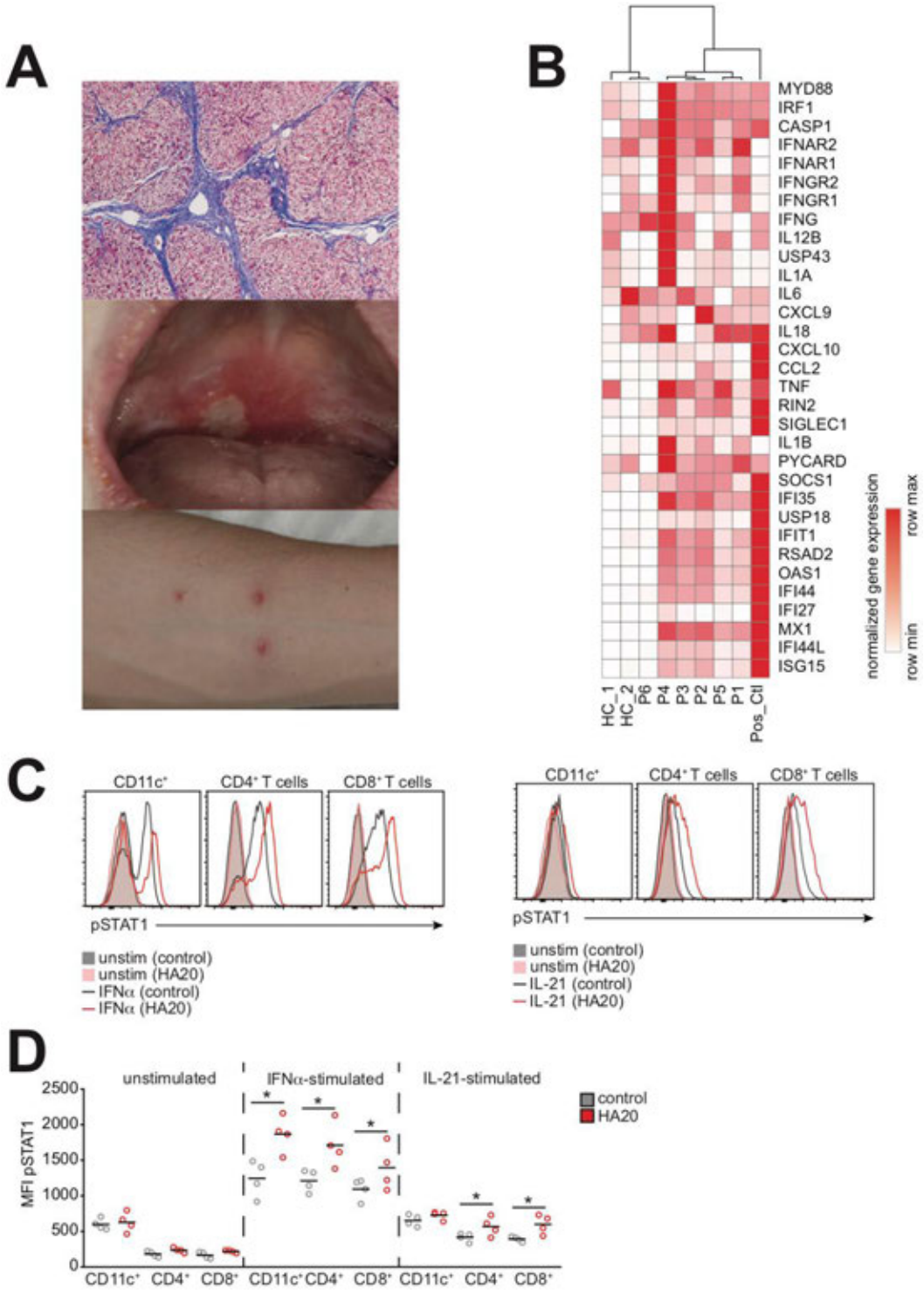

Figure 1. A. Clinical manifestations of HA20: hepatic fibrosis, nephritis, and orogenital ulcerations. B. Expression of interferon-stimulated genes. C-D. STAT1 phosphorylation in response to interferon (IFN)-α and Interleukin (IL)-21.

and Nanostring was used to assess expression of interferon-stimulated genes (ISGs). Peripheral blood mononuclear cells (PBMCs) were isolated and stored in liquid nitrogen. After thawing, cells were rested in R10 media for 2 hours, then in R0 media for 30 minutes before measuring STAT phosphorylation by flow cytometry. Patients were followed every 3-6 months during tofacitinib treatment. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were obtained by CLIA-certified clinical laboratories.

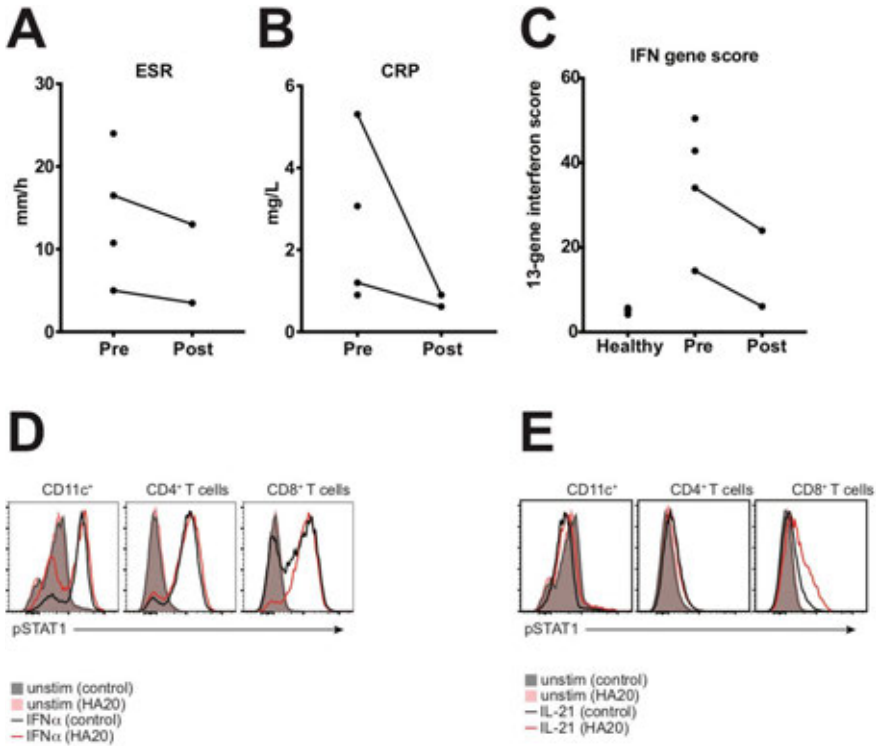

Figure 2. A-C. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and IFN gene score. D-E. Post tofacitinib treatment STAT1 phosphorylation in response to interferon (IFN)-α and Interleukin (IL)-21.

Results: ISG expression was measured on 5 patients with treatment-refractory active disease and 1 patient with inactive disease. Clinical manifestations were heterogeneous and included hepatic fibrosis, nephritis, and orogenital ulcerations (Fig 1A). All patients with active disease had increased expression of ISGs (Fig 1B). STAT1 phosphorylation was enhanced in response to both interferon (IFN)-α and Interleukin (IL)-21 (Fig 1C-D). STAT3 phosphorylation was not affected by HA20.

To date, 4 patients have undergone treatment with the JAK inhibitor tofacitinib, with treatment planned for the 5th patient. Treatment duration was 3-18 months at the time of analysis. All 4 patients reported improvements in clinical disease activity, and post-treatment data were available for 2 patients. Reduction in ESR, CRP, IFN gene score, and STAT1 phosphorylation were seen after treatment with tofacitinib (Fig 2). Tofacitinib was well-tolerated with no major adverse effects.

Conclusion: A group of treatment-refractory HA20 patients had increased expression of ISGs and enhanced STAT1 phosphorylation. Treatment with tofacitinib led to a clinical and immunological response. These results indicate that STAT1 signaling contributes to HA20 pathology, and that IFN signature predicts response to tofacitinib.

References:

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Disclosure: S. Blackstone, None; **D. Schwartz**, None; **N. Sampaio Moura**, None; **D. Stone**, None; **M. Waldman**, None; **P. Hoffmann**, None; **A. Jones**, None; **T. Romeo**, None; **K. Barron**, None; **J. Milner**, None; **D. Kastner**, None; **A. Ombrello**, None.

Abstract Number: 2901

Anakinra Treatment in Patients with Familial Mediterranean Fever: A Single-center Experience

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: Miscellaneous Rheumatic & Inflammatory Disease III: Novel Therapies

Session Type: ACR Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: The main goal of Familial Mediterranean Fever (FMF) treatment is to prevent attacks and subclinical inflammation. Mainstay of treatment is colchicine; however, 5-10% of patients are unresponsive to colchicine even in maximum tolerated dosage. Anakinra has been proven to be effective in controlled trials in terms of attack frequency and subclinical inflammation in colchicine resistant patients. The objective of this study is to review the patients followed in our single center with FMF who received Anakinra because of insufficient colchicine response.

Methods: The study is conducted in a tertiary rheumatology center experienced in autoinflammatory diseases. The patients are treated with at least one month of Anakinra in order to be included in the cohort. Patients with amyloidosis and pregnancy are not included. Genetic mutation of all patients was checked and recorded. Attack frequency, patient global assessment scales of disease severity (10-cm Visual Analogue Scale [VAS]), and acute phase reactants were recorded before and throughout Anakinra treatment. Treatment termination was also noted. Criteria of treatment termination were side effects, disease remission, inadequate response, pregnancy plan, and noncompliance.

Table 1: Demographic characteristics of the patients

Gender	69F, 37M
Mean age (years)	34.43±9.68
Mean time since the beginning of FMF symptoms (years)	21.68±10.7
Mean time since the initial FMF diagnosis (years)	12.47±7.49
Mean Colchicine dose before Anakinra*	2.34±1.02
Mean follow-up on Anakinra (months)	16.01±17.21
Comorbidities	24
Spondyloarthropathies	8
Inflammatory Bowel Disease	1
Rheumatoid Arthritis	1
Hypertension	6
Polyarteritis Nodosa	1
Psoriasis	1
Pericarditis	3
Asthma	2
Diabetes Mellitus	1

*97 patients were on colchicine.

Table 2. Reasons for Treatment Discontinuation

Causes of Treatment Discontinuation	n: 34
Insufficient Response	12
Remission	8
Noncompliance	3
Pregnancy plan	1
Side effect	10
Injection site reaction	2
Skin reaction	5
Increased liver enzymes	3
Leukopenia	4

Results: 106 patients diagnosed with FMF were treated with Anakinra. Table 1 represents the demographic characteristics and FMF-related clinical features of the patients. 45.92% of our patients had a homozygous M694V mutation. 83 of the 98 patients tested for MEFV carried at least one copy of M694V. Attack frequency decreased while on Anakinra treatment. Seventy five patients reported no attacks after anakinra treatment whereas 16 patients reported at least 50% decrease in the attack frequency. VAS score decreased from 7.49±2.03 to 3.08±2.82 ($p< 0.0001$). Currently, 70 patients are still on Anakinra treatment. Treatment of 34 patients was discontinued (32% of all patients). The reasons of Anakinra treatment discontinuation are shown in table 2. Insufficient response and side effects are the most common reasons for treatment discontinuation. All of the side effects observed were reversible and the patients alleviated after treatment cessation. In 4 patients, leukopenia was observed and was managed with dose reduction to alternating treatment. Treatment of 8 patients was successful enough that it was terminated due to remission.

Conclusion: In conclusion, in patients with colchicine treatment failure, anti-IL-1 agent Anakinra is shown to be effective and safe. The effectiveness of Anakinra stems from preventing attacks, and increasing the quality of life.

Disclosure: S. Ugurlu, None; **B. Egeli**, None; **B. Ergezen**, None; **O. Selvi**, None; **H. Ozdogan**, None.

Abstract Number: 2902

The Use and Safety of Rituximab in Connective Tissue Disease Associated Interstitial Lung Disease

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease III: Novel Therapies
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Interstitial Lung Disease (ILD) is the most common lung manifestation in Connective Tissue Diseases (CTD). It is present in most types of CTD, such as: Rheumatoid Arthritis (RA), Systemic Sclerosis (SSc), Systemic Lupus Erythematous (SLE), Inflammatory Myositis (IM), Mixed Connective Tissue Disease (MCTD), Sjogren Syndrome and Sarcoid. Despite it being so common, treatment has lacked to advance in the biologic era of Rheu-

Table 1. Patient Demographics

Baseline Characteristics of 24 Patients	
Age (Range)	25-67 years old
Average Age	48 years old
Sex (M/F)	4/20
Race	
Black	17
White	5
Hispanic	1
Asian	1
Prior Tobacco Use	6
Average Disease Time	7 years
Disease Breakdown	
SLE	4
IM	4
SSc	6
RA	4
Sarcoid	1
MTCD	4
Overlap (RA/IM)	1
ILD Pattern	
UIP	5
NSIP	12
Mixed	6
OP	1
Adverse Events	Tooth Abscess/Urticaria Rash/Hemolysis
Medication Combination	
RTX + MMF	17
RTX + AZA	4
RTX + PDN	10
RTX + HCQ	2
RTX + MTX	3
PFT Follow Up Range	4-24 months
Average follow up PFT	10 months

matology. CTD-ILD has different histological patterns, the most common being non-specific interstitial pneumonia (NSIP), usual interstitial pneumonia (UIP), and organizing pneumonia (OP). Literature has showed that Rituximab (RTX), a B lymphocyte depleting monoclonal antibody, can be useful in CTD-ILD. For that reason, we decided to evaluate the use and safety of RTX in patients who failed conventional immunosuppressant therapy.

Methods: In a retrospective chart review, we identified all patients with CTD-ILD expanding from 2015 to 2018, seen in the Rheumatology Clinic of University Medical Center New Orleans, Louisiana (UMCNO). This was done by performing a review of our clinical database by cross referencing International Classification of Diseases (ICD) 10 code J84.9 & 84.10, with M35.9, M05.10, M34.81, D89.89, M32.1, G72.4, M35.02, M35.0. Eighty charts were retrospec-

tively reviewed. Total of 24 patients were given RTX in addition to other immunosuppressive therapy. Data extracted from the chart included patient age, sex, race, tobacco history, CTD history, ILD histological pattern based on High Resolution Computer Tomography (HRCT) of the chest, pre and post pulmonary function test (PFT), other therapy used, and side effects after RTX.

Results: The patients average age was 48 years old. The study had a female to male ratio of 5:1, with 17 of 24 being of African descent. Of the 24, six had prior tobacco use. The most common CTD in our cohort was SSc with 6 of 24, then SLE, IM, RA and MCTD. There was one case of Sarcoid and another of an overlap of RA/IM. Average disease onset at time of RTX infusion was 7 years. The average PFT post RTX therapy was 10 months. NSIP was the most common ILD pattern seen in 12 of 24, then mixed pattern 6 of 24, UIP 5 of 24, and one OP. RTX was most commonly combined with Mycophenolate, 17 of 24 patients were receiving both therapies. Low dose prednisone (< 7.5mg/daily) was concurrently being given in 10 of 24 patients. Only 3 adverse events were encountered during chart review post RTX infusion: Tooth Abscess, Urticarial Rash, and Hemolysis. Pre and Post RTX PFTs are in the table below showing in average stability of the values.

Conclusion: As our data shows RTX is not only safe in CTD-ILD but also proves that it provides stability in lung function on repeat PFT at 10 months average. Our cohort was unique in that the majority were African Americans, and that it included a wide array of ILD patterns and CTD. We also demonstrated that it can be combined with other immunosuppressants and the side effect profile is not much different than using it by itself. As well as no clear trend towards improvement with any combination of immunosuppressants.

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Abstract Number: 2903

Cryopyrin-Associated Periodic Syndrome Treated with Canakinumab – Long-Term Follow-up Data Documents Sustained Safety and Remission

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease III: Novel Therapies
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Targeting the interleukin(IL)-1 pathway with anti-IL-1 drugs is a treatment option in patients with autoinflammatory diseases like monogenic periodic fever syndromes. The study aims to gain further insights into long-term effectiveness and safety of canakinumab (CAN), an anti-IL1 inhibitor, under routine clinical practice conditions in pediatric and adult patients with CAPS (cryopyrin-associated periodic syndrome, including Muckle-Wells syndrome [MWS], familial cold autoinflammatory syndrome [FCAS], neonatal onset multisystem inflammatory disease [NOMID]/chronic infantile neurological cutaneous and articular syndrome [CINCA]), FMF (familial Mediterranean

Table 1: Disease activity by patients` assessment.

	Mean disease activity, visual analog scale (VAS) 0–10 (SD [standard deviation])	Mean Fatigue, VAS 0–10 (SD)	Impairment of social life, %
Baseline, all patients, N=58	2.0 (2.0)	2.6 (2.5)	50.0
Baseline, analysis cohort 1, N=36	2.3 (2.0)	2.6 (2.3)	60.0
6 months, analysis cohort 1, N=36	1,9 (2.3)	2.7 (2.9)	30.0
Baseline, analysis cohort 2, N=15	1.9 (1.7)	2.6 (2.3)	30.8
6 months, analysis cohort 2, N=15	2.1 (2.7)	3.0 (3.4)	22.2
12 months, analysis cohort 2, N=15	2.3 (2.1)	3.2 (2.4)	28.5

Table 2: Patients with days absent in school or from work due to study indication.

	Days absent in school/from work during last 6 months, n (%)				Average number of days absent during last 6 months, (SD [standard deviation], number of patients included)
	Yes	No	Not appro-priate	Unknown	
Baseline, all patients, N=58	19 (33.3)	19 (33.3)	7 (12.3)	12 (21.1)	6.3 (4.2, n=16)
Baseline, analysis cohort 1, N=36	14 (38.9)	14 (38.9)	3 (8.3)	5 (13.9)	5.2 (2.3, n=12)
6 months, analysis cohort 1, N=36	8 (22.6)	18 (50.0)	0 (0.0)	10 (27.8)	20.6 (13.9, n=8)
Baseline, analysis cohort 2, N=15	5 (33.3)	9 (60.0)	0 (0.0)	1 (6.7)	5.3 (2.5, n=3)
6 months, analysis cohort 2, N=15	3 (23.1)	8 (61.5)	0 (0.0)	2 (15.4)	19.7 (16.3, n=3)
12 months, analysis cohort 2, N=15	5 (35.7)	7 (50.0)	1 (7.1)	1 (7.1)	2.8 (3.5, n=4)

Table 3: Analysis of hearing ability.

	Result of current audiogram compared to prior examination, n (%)			
	Improved	Worsened	Unchanged	Missing value
Baseline, all patients, N=58	1 (4.5)	1 (4.5)	20 (90.9)	34
Baseline, analysis cohort 1, N=36	1 (5.3)	1 (5.3)	17 (89.5)	17
6 months, analysis cohort 1, N=36	1 (6.7)	2 (13.3)	12 (80.0)	21
Baseline, analysis cohort 2, N=15	0 (0.0)	0 (0.0)	11 (100.0)	4
6 months, analysis cohort 2, N=15	1 (12.5)	0 (0.0)	7 (87.5)	5
12 months, analysis cohort 2, N=15	0 (0.0)	1 (14.3)	6 (85.7)	7

fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).

Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany with a 3-year follow-up enrolling pediatric (age ≥2 years) and adult patients with clinically confirmed diagnoses of CAPS,

FMF, TRAPS and HIDS/MKD who routinely received CAN. 6-monthly clinical assessment and evaluation of patient-reported outcomes is aligned with routine clinic visits. Endpoints were effectiveness and safety of CAN under standard clinical practice conditions.

Results: The interim analysis includes 58 CAPS patients (45.6% females; 41.4% participated in the β-Confident study) with prior long-term CAN treatment enrolled by September 2018. The mean age was 21.7 years (4.0–79.0 years) at baseline and the mean duration of prior CAN treatment was 5.2 years (0.0–11.0 years). 48 patients (82.7%) were diagnosed with MWS, the other patients had FCAS (N=1), NOMID/CINCA (N=6) or atypical CAPS (N=1) (subtype diagnosis of 2 patients not available). The following parameters were determined at baseline, month 6 and month 12: (1) disease activity by patients' assessment (table 1), (2) days absent in school/from work due to study indication (table 2), (3) hearing ability (table 3). The results demonstrate a sustained remission and control of disease in patients with long-term CAN treatment. Serious adverse events were reported for 4 patients including pyrexia (N=1), tonsillitis (N=2) and a delivery at week 31 (N=1).

Conclusion: An interim analysis of the RELIANCE study, the longest running real-life CAN registry, shows that long-term CAN treatment is safe and effective in CAPS patients.

Disclosure: J. Kuemmerle-Deschner, SOBI, 2, 8, Novartis, 2, 8; **N. Blank**, SOBI, 2, 8, Novartis, 2, 8; **M. Borte**, Pfizer, 2, Shire, 2; **I. Foeldvari**, Beyer, 5, BMS, 5, Glaxo, 5, Inventa, 5, Novartis, 5; **G. Horneff**, Chugai, 5, 8, GlaxoSmithKline, 5, 8, Novartis, 5, 8, Sanofi, 5, 8; **P. Oommen**, None; **C. Schuetz**, None; **F. Weller-Heinemann**, None; **J. Weber-Arden**, Novartis, 3; **T. Kallinich**, None.

Abstract Number: 2904

Rituximab as Rescue Therapy in Treatment-Refractory CTD-ILD

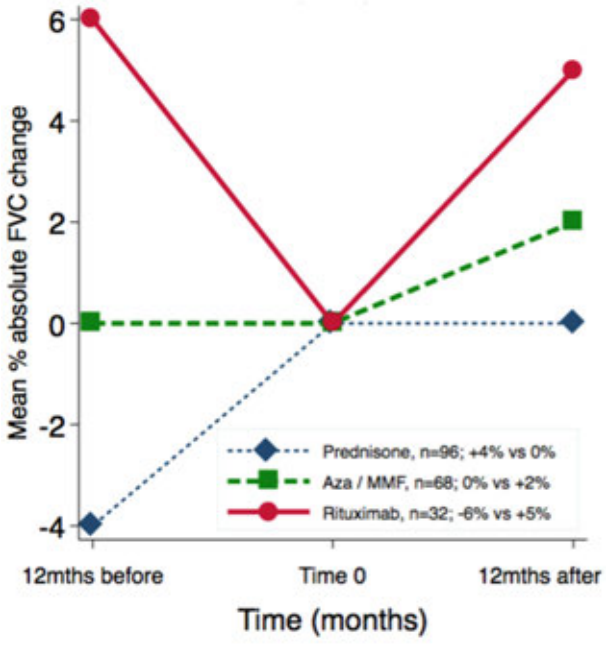
Julia Sun,[1] Charles Oshinsky,[2] Nicole Garcia,[3] Iazsmin Ventura,[3] Renea Jablonski,[4] Rekha Vij,[4] James Curran,[5] Mary Strek,[4] and Ayodeji Adegunsoye[4], [1]University of Chicago Department of Internal Medicine, Chicago, [2]University of Chicago, Department of Internal Medicine, Chicago, [3]University of Chicago, Chicago, [4]University of Chicago, Department of Pulmonary and Critical Care, Chicago, [5]University of Chicago, Department of Rheumatology, Chicago

SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease III: Novel Therapies
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is the leading cause of mortality and carries significant morbidity in connective tissue disease (CTD). Corticosteroids are often used as first line therapy, yet the use of additional immunosuppressive (IS) agents remains largely empiric. In this study we evaluated the effect of Rituximab (RTX) as rescue therapy on lung function in a cohort of patients with severe, progressive CTD-ILD.

Methods: We identified patients with CTD-ILD in the University of Chicago ILD registry who received conventional IS therapy with or without RTX from 2008 to 2018. Results of forced vital capacity (FVC) stratified by IS therapy pre- and post-RTX were compared.

Results: A total of 196 patients (65% female) with a mean age of 57.5 years were included. Rheumatoid arthritis (24.5%), mixed CTD (17.9%), and scleroderma (16.3%) were the most common CTD diagnosis. Of these, 96 received prednisone alone, 68 received azathioprine or mycophenolate without or without prednisone, and 32 received RTX in addition to these IS agents. In the RTX cohort, annualized FVC decline over 12 months pre-RTX was -6%, resulting



Time 0 = initiation of therapy in Rituximab cohort

in a mean FVC of 56% (95% CI=49%-62%) at the time of first RTX administration. One year post-RTX, there was a mean absolute increase of +5%, resulting in a post-RTX FVC of 61% (95% CI=49%-73%). In comparison, FVC remained stable to slightly improved in patients who did not receive RTX (0% in prednisone group; +2% in azathioprine/mycophenolate group) over this 12-month time period (Figure 1).

Conclusion: RTX may be an effective rescue therapy in patients with severe, progressive CTD-ILD refractory to conventional IS therapy.

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Abstract Number: 2905

Rilonacept in Recurrent Pericarditis: Efficacy and Safety Data from an Ongoing Phase 2 Pilot Clinical Trial

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: Miscellaneous Rheumatic & Inflammatory Disease III: Novel Therapies
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Recurrent pericarditis (RP) is characterized by the recurrence of pericarditis signs and symptoms after a symptom-free period of ≥4 to 6 weeks and affects 20-30 % of acute pericarditis patients. IL-1α/β, mediators of the inflammatory process, predominate in recurrent pericarditis (RP).

Table 1. Treatment with Rilonacept Resulted in Resolution of Pericardial Rub, ECG Changes, and Pericardial Effusion on Echocardiography

Time Point	Part 1 n/N (%)	Part 2 n/N (%)	Part 3 n/N (%)	Part 4 n/N (%)	Part 5 n/N (%)
Baseline					
Widespread ST elevation	2/12 (16.7)	0/3	0/6	0/1	0/3
PR depression	3/12 (25.0)	0/3	0/6	0/1	0/3
Pericardial rub	2/12 (16.7)	0/3	0/6	0/1	0/2
Fever	0/12	0/3	0/6	0/1	0/3
Pericardial effusion on ECHO	7/12 (58.3)	0/3	2/6 (33.3)	0/1	0/2
End of TP (visit 7)					
Widespread ST elevation	0/12	0/2	0/6	0/1	0/3
PR depression	1/12 (8.3)	0/2	0/6	0/1	0/3
Pericardial rub	0/11	0/2	0/6	0/1	0/3
Fever	0/12	0/2	0/6	0/1	0/3
Pericardial effusion on ECHO	1/12 (8.3)	0/2	1/6 (16.7)	0/1	0/3
Final visit					
Widespread ST elevation	0/7	0/2	0/2	0/0	0/0
PR depression	0/7	0/2	0/2	0/0	0/0
Pericardial rub	0/7	0/2	0/2	0/0	0/0
Fever	0/7	0/2	0/2	0/0	0/0
Pericardial effusion on ECHO	0/7	0/1	0/2	0/0	0/0

ECHO, echocardiography; TP, treatment period.

Figure 1. Rapid and Sustained Reductions in NRS Scores (Pain) and CRP Levels After the First Dose (Part 1

Table 1. Treatment with Rilonacept Resulted in Resolution of Pericardial Rub, ECG Changes, and Pericardial Effusion on Echocardiography

Time Point	Part 1 n/N (%)	Part 2 n/N (%)	Part 3 n/N (%)	Part 4 n/N (%)	Part 5 n/N (%)
Baseline					
Widespread ST elevation	2/12 (16.7)	0/3	0/6	0/1	0/3
PR depression	3/12 (25.0)	0/3	0/6	0/1	0/3
Pericardial rub	2/12 (16.7)	0/3	0/6	0/1	0/2
Fever	0/12	0/3	0/6	0/1	0/3
Pericardial effusion on ECHO	7/12 (58.3)	0/3	2/6 (33.3)	0/1	0/2
End of TP (visit 7)					
Widespread ST elevation	0/12	0/2	0/6	0/1	0/3
PR depression	1/12 (8.3)	0/2	0/6	0/1	0/3
Pericardial rub	0/11	0/2	0/6	0/1	0/3
Fever	0/12	0/2	0/6	0/1	0/3
Pericardial effusion on ECHO	1/12 (8.3)	0/2	1/6 (16.7)	0/1	0/3
Final visit					
Widespread ST elevation	0/7	0/2	0/2	0/0	0/0
PR depression	0/7	0/2	0/2	0/0	0/0
Pericardial rub	0/7	0/2	0/2	0/0	0/0
Fever	0/7	0/2	0/2	0/0	0/0
Pericardial effusion on ECHO	0/7	0/1	0/2	0/0	0/0

ECHO, echocardiography; TP, treatment period.

Methods: Participants with symptomatic or corticosteroid (CS)-dependent idiopathic or post-pericardiotomy RP receive subcutaneous rilonacept: 320 mg load, 160 mg weekly plus NSAIDs, colchicine and/or CS for the 6-week treatment period (TP). During optional 18-week treatment extension (EP), weekly rilonacept treatment continued while background therapy may be weaned. Primary endpoints are change in patient-reported pericardial pain (NRS, 11-point scale) and CRP in Parts 1, 2, 4 (symptomatic) and disease activity after CS taper in Parts 3, 5 (CS-dependent).

Results: As of Jan 23, 2019: 25 idiopathic RP patients enrolled (mean 3 episodes). Part 1: mean pericardial pain (NRS score) decreased from 4.6 (baseline) to 0.8 and CRP decreased from 4.9 mg/dL (baseline) to 0.30 mg/dL at 6 weeks (Figure 1); median 9 days to CRP normalization and objective pericarditis features (pericardial effusion, ECG changes, pericardial rub) resolved (Table 1). Parts 2, 4: reductions in NRS (Pain) and CRP were observed during the TP. Parts 3 and 5: pain and CRP remained low on rilonacept therapy during the TP and the effects of rilonacept on

NRS and CRP were maintained during CS-taper/discontinuation in EP among those that completed 24 weeks of therapy. Among the 11/25 who completed the EP; 4/4 on baseline CS successfully tapered off CS; 3/3 discontinued NSAIDs and 2/8 discontinued colchicine. AEs occurred in 23 participants (92%; 12/23 drug-related), most commonly mild transient injection site reactions (no discontinuations).

Conclusion: Data from this ongoing Phase 2 study suggest weekly rilonacept administration results in improvement in patient-reported pericardial pain and objective measures in patients with idiopathic RP. Improvements were durable, supporting CS tapering. AEs were consistent with the known safety profile of rilonacept. These data supported the design of a Phase 3, placebo-controlled, global RHAPSODY trial (NCT03737110).

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Abstract Number: 2906

DMARD-free Remission in Established Rheumatoid Arthritis: 2 Year Results of the TARA Trial

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: RA – Treatments V: Switching & Tapering RA Medications
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: In rheumatoid arthritis (RA) disease outcomes have improved enormously in the last decades. Due to early initiation of therapy, a treat-to-target approach and a growing arsenal of disease-modifying an-

	A. Tapering csDMARD first (n=94)	B. Tapering TNF-inhibitor first (n=95)
Baseline (T0)		
Age (years), mean (sd)	55.9 (14.1)	57.2 (10.6)
Gender, female, n(%)	66 (71)	58 (61)
Symptom duration (years), median (IQR)	6.0 (4.3-8.5)	6.3 (4.1-8.9)
ACPA positive, n(%)	61 (72)	65 (75)
RF positive, n(%)	49 (57)	56 (64)
2-year follow-up (T24)		
Cumulative flare, n(%)	57 (61)	59 (62)
DMARD free remission, n(%) *	15 (16)	8 (8)
Tapered, n(%) *	30 (32)	20 (21)
DAS, mean (sd)	1.39 (0.67)	1.30 (0.70)
ΔDAS (T24-T0), mean (sd)	0.41 (0.55)	0.33 (0.77)
HAQ-DI, mean (sd)	0.62 (0.53)	0.52 (0.51)
ΔHAQ-DI (T24-T0), mean (sd)	0.074 (0.40)	0.058 (0.31)
EQ5D, mean (sd)	0.81 (0.15)	0.83 (0.17)
ΔEQ5D (T24-T0), mean (sd)	-0.056 (0.15)	-0.035 (0.14)

*p<0.01.
ACPA: anti-citrullinated protein antibody; csDMARD: conventional synthetic disease modifying anti-rheumatic drug; DAS: disease activity score measured in 44 joints; EQ5D: European Quality of Life – 5 Dimensions; HAQ-DI: Health Assessment Questionnaire Disability Index; RF: rheumatoid factor.

Table 1. Baseline characteristics and results after 24 months.

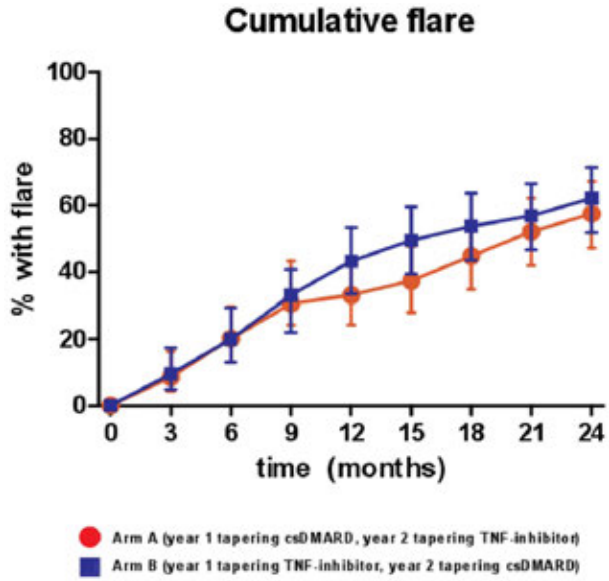

Figure 1. Cumulative flare rate over time. csDMARDs; conventional synthetic disease modifying antirheumatic drug.

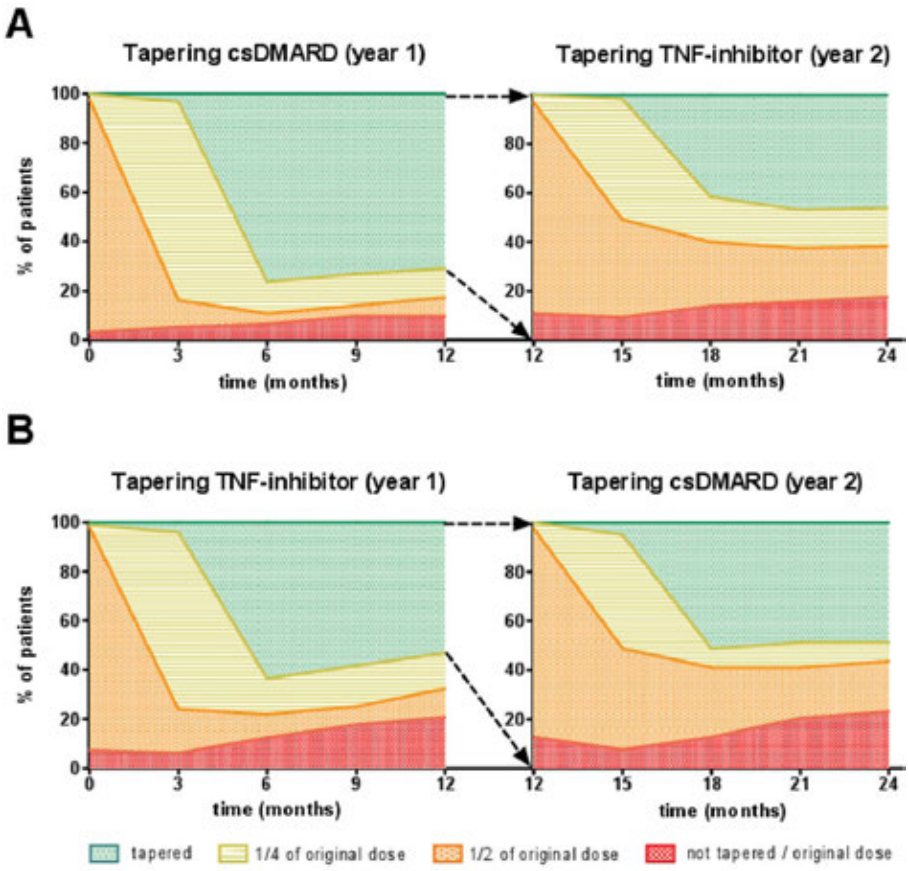

Figure 2. Overview of gradual tapering per time point indicated for tapering arm A and tapering arm B. Numbers indicate percentages of patients. Every 3 months the TNF-inhibitor or csDMARD was tapered until after 6 months the drug could be stopped. In case of a flare, defined as DAS>2.4 and/or SJC>1, patients were set back at their previous effective dose. No further tapering was allowed after having a flare. For the second year (T12 – T24), only tapering status was shown for patients who – according to protocol – should have tapered their medication in the second year. csDMARD; conventional synthetic disease modifying antirheumatic drug.

tirheumatic drugs (DMARDs) and biologicals, RA patients are in sustained remission more often. This raises the subsequent questions whether treatment should be continued, tapered or stopped. Although DMARD free remission (DFR) is nowadays achievable for increasing numbers of RA patients, the optimal tapering approach still needs to be defined. In this study, we want to evaluate the 2-year clinical effectiveness of two gradual tapering strategies, namely tapering DMARDs first followed by the TNF-inhibitor, or vice versa.

Methods: In this multicenter single-blinded randomised controlled trial RA patients with controlled disease for at least 3 consecutive months, defined as a DAS≤2.4 and a swollen joint count (SJC) ≤1, which was achieved with csDMARDs and a TNF-inhibitor were included. Eligible patients were randomised into gradual tapering csDMARDs followed by the TNF blocker or vice versa. Medication was tapered in three steps over the course of 6 months. After 12 months, the other DMARD was tapered. Gradual tapering was done by cutting the dosage into half, a quarter and thereafter it was stopped. The primary outcome for the clinical effectiveness was the number of patients with a disease flare, defined as DAS44 >2.4 and/or SJC >1. Secondary outcomes were DFR, disease activity, quality of life and functional ability. Outcomes were calculated in an intention-to-treat analysis, using all available data.

Results: A total of 189 patients were randomly assigned to tapering csDMARDs first (arm A) or tapering TNF-inhibitor first (arm B). The cumulative flare rate after 24 months in A was 61% (95% CI, 50% - 69%) and in B 62% (95% CI, 50%-70%) (p=0.35)(figure 1). In the second year the cumulative flare rate differs the most between the two groups between T12 and T18 (figure 1). Figure 2 shows an overview of how gradual tapering took place in the TARA study, and how many patients were at a certain point of tapering at the separate time-points (figure 2). This was indicated for both tapering arms (A and B), and for the first and second year (figure 2). In arm A there were significantly more patients able to taper their medication (n=30), and more patients reached DFR (n=15) (table 1). However, mean DAS, mean HAQ, and mean EQ5D over time, and after 2 years, did not differ between both tapering arms (table 1).

Conclusion: The order in which tapering and stopping medication was performed was not superior to each other based on flare rates, DAS and HAQ. However, patients that first tapered csDMARD reached DFR more often and more patients were able to taper their medication.

Disclosure: E. van Mulligen, None; **A. Weel**, None; **M. Kuijper**, None; **M. Hazes**, None; **A. van der Helm-van Mil**, None; **P. de Jong**, None.

Abstract Number: 2907

Clinical and Functional Outcomes Among Rheumatoid Arthritis Patients Switching Between JAK1-Selective Inhibitor Upadacitinib and Adalimumab Following Insufficient Response

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: RA – Treatments V: Switching & Tapering RA Medications

Session Type: ACR Abstract Session

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Table 1. Efficacy endpoints at 6-months following treatment switch

	All UPA 15 mg to ADA Switchers[1]			All ADA to UPA 15 mg Switchers[2]		
	Total group (n=252)	NR (n=126)	PR (n=126)	Total group (n=159)	NR (n=77)	PR (n=82)
ACR20[a]	159/232 (69)	67/113 (59)	92/119 (77)	118/146(81)	53/71 (75)	65/75 (87)
ACR50[a]	85/232 (37)	29/112 (26)	56/120 (47)	79/141 (56)	34/69 (49)	45/72 (63)
ACR70[a]	36/233 (16)	14/114 (12)	22/119 (19)	46/146 (32)	17/72 (24)	29/74 (39)
DAS28(CRP) ≤3.2	91/230 (40)	38/109 (35)	53/121 (44)	82/147 (56)	38/70 (54)	44/77 (57)
DAS28(CRP) <2.6	49/230 (21)	21/109 (19)	28/121 (23)	51/147 (35)	22/70 (31)	29/77 (38)
CDAI ≤10	95/234 (41)	41/114 (36)	54/120 (45)	77/146 (53)	33/70 (47)	44/76 (58)
CDAI ≤2.8	12/234 (5)	6/114 (5)	6/120 (5)	22/146 (15)	10/70 (14)	12/76 (16)
SDAI ≤11	96/229 (42)	41/109 (38)	55/120 (46)	77/145 (53)	33/69 (48)	44/76 (58)
SDAI ≤3.3	11/229 (5)	4/109 (4)	7/120 (6)	26/145 (18)	12/69 (17)	14/76 (18)
Mean change from baseline (95% CI)[b]						
DAS28(CRP)	-2.40 (-2.58, -2.22)	-2.10 (-2.36, -1.84)	-2.68 (-2.93, -2.44)	-2.88 (-3.11, -2.65)	-2.56 (-2.90, -2.22)	-3.17 (-3.49, -2.86)
HAQ-DI	-0.58 (-0.66, -0.49)	-0.52 (-0.64, -0.41)	-0.63 (-0.75, -0.51)	-0.73 (-0.83, -0.63)	-0.67 (-0.81, -0.53)	-0.78 (-0.93, -0.63)
CDAI	-27.28 (-29.35, -25.21)	-23.61 (-26.49, -20.73)	-30.82 (-33.69, -27.95)	-29.47 (-32.23, -26.71)	-24.95 (-28.35, -21.55)	-33.86 (-38.00, -29.73)
SDAI	-28.30 (-30.45, -26.15)	-24.52 (-27.47, -21.56)	-31.85 (-34.85, -28.84)	-31.02 (-33.86, -28.19)	-26.07 (-29.55, -22.59)	-35.83 (-40.04, -31.62)

UPA: upadacitinib; ADA: adalimumab; ACR: American College of Rheumatology; DAS28(CRP): 28-joint disease activity score based on C-reactive protein; CDAI: clinical disease activity index; SDAI: simplified disease activity index; CI: confidence interval; HAQ-DI: health assessment questionnaire disability index

[a]Responses are based on percent improvement in ACR criteria from original baseline at randomization; [b]mean change from *original* baseline at randomization.

NR: Non-responders were defined as patients who did not achieve ≥20% improvement in TJC or SJC at wks 14, 18 and 22.

PR: Partial responders were defined as patients who did not achieve CDAI LDA at wk 26.

[1]ADA dose: 40mg every other week; [2] UPA dose:15mg once daily.

Background/Purpose: The goal of RA treatment is to achieve clinical remission or, at minimum, low disease activity (LDA). Modification of initial csDMARD therapy with the addition of a biologic (b) DMARD, such as a tumor necro-

Table 2. Summary of adverse events during 3- and 6-months post treatment switch

	3-months post switch**		6-months post switch***	
Adverse events*	UPA 15 mg to ADA (n=252) n (%)	ADA to UPA 15 mg (n=159) n (%)	UPA 15 mg to ADA (n=252) n (%)	ADA to UPA 15 mg (n=159) n (%)
Any adverse event	125 (49.6)	64 (40.3)	155 (61.5)	92 (57.9)
Serious adverse event	6 (2.4)	6 (3.8)	17 (6.7)	14 (8.8)
Adverse event leading to discontinuation	7 (2.8)	3 (1.9)	15 (6.0)	8 (5.0)
Infection	41 (16.3)	30 (18.9)	76 (30.2)	49 (30.8)
Serious infection	2 (0.8)	4 (2.5)	5 (2.0)	6 (3.8)
Opportunistic infection	0	1 (0.6)	0	1 (0.6)
Herpes zoster	1 (0.4)	2 (1.3)	3 (1.2)	4 (2.5)
Hepatic disorder	8 (3.2)	4 (2.5)	15 (6.0)	5 (3.2)
Anemia	3 (1.2)	2 (1.3)	4 (1.6)	4 (2.5)
Neutropenia	4 (1.6)	2 (1.3)	5 (2.0)	2 (1.3)
Lymphopenia	1 (0.4)	1 (0.6)	2 (0.8)	1 (0.6)
Creatinine phosphokinase elevation (CPK)	2 (0.8)	0	3 (1.2)	1 (0.6)

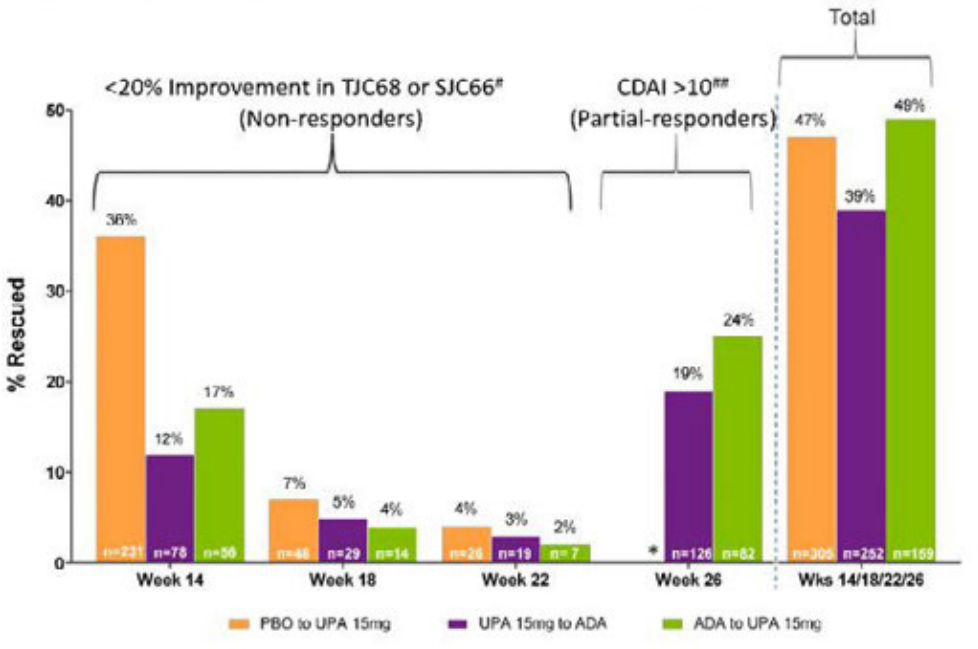
*Adverse events reported for all patients who switched treatments.
UPA: upadacitinib; ADA: adalimumab.
** for any of 3 months post switch adverse events, 95% confidence intervals were overlapping between the 2 switch groups.
*** for any of 6 months post switch adverse events, 95% confidence intervals were overlapping between the 2 switch groups. 6-months post-switch adverse event data include events from 3-months post-switch as well.

sis factor inhibitor (TNFi), or Janus Kinase inhibitor (JAKi) may be needed following an inadequate response (IR).[1] Switches in mechanism of action have been advocated in TNF- and JAK-IR patients (pts); however, controlled data describing switches between JAKi and TNFi are lacking.

Methods: In a phase 3, double-blind study of the JAK1-selective inhibitor upadacitinib (UPA) 15 mg once daily vs PBO or adalimumab (ADA) 40 mg every other week in MTX-IR pts (all on background MTX), pts without ≥20% improvements from baseline (BL) in tender or swollen joint counts by wks 14, 18, or 22 [non-responders (NR)] were switched from UPA to ADA and vice versa in a blinded fashion and without washout. Pts who did not achieve LDA according to CDAI (CDAI ≤10) at wk 26 [partial-responders (PR)] were switched to the alternate treatment as above. Post-hoc analyses assessed clinical outcomes (**Table 1**) at 3m(onth) and 6m (±2 wks) post-switch. Adverse events (AEs) were summarized as n% through 3m and 6m post-switch. Data were as observed.

Results: In total, 651 and 327 pts were randomized to receive UPA and ADA. 252 pts were switched from UPA to ADA (39%, NR:126; PR:126), and 159 were switched from ADA to UPA (49%, NR:77; PR:82) (Figure). At 6m post-switch, DAS28(CRP) < 2.6/CDAI ≤2.8 were achieved by 21%/5% of UPA to ADA pts, and 40%/41% achieved

Figure 1: Proportion of patients rescued at each treatment-switch timepoint



Treatment Switch:
Non-response at Weeks 14, 18, or 22 defined as not achieving ≥ 20% improvement in TJC (tender joint counts) or SJC (swollen joint counts) compared to baseline.
Partial-response at W26 defined as not achieving LDA (Low Disease Activity) according to CDAI (LDA defined as CDAI [Clinical Disease Activity Score]≤ 10).
* At Week 26, all placebo subjects who were not rescued prior to Week 26 were switched to UPA 15mg QD regardless of the response.

UPA dose: 15 mg QD; ADA dose: 40 mg every other week (eow)

DAS28(CRP) ≤3.2/CDAI ≤10. In pts who switched from ADA to UPA, 35%/15% achieved DAS28(CRP) < 2.6/CDAI ≤2.8 and 56%/53% achieved DAS28(CRP) ≤3.2/CDAI ≤10 at 6m post-switch. ACR20/50/70 (based on original BL) after switch are shown in Table 1. Mean change from the original BL in HAQ-DI were -0.58 and -0.73 for pts switching from UPA to ADA and ADA to UPA, respectively. The safety profiles of all pts who switched treatments appeared consistent with those observed for ADA and UPA during comparable periods. During 3m post-switch, the proportions (n%) of pts with serious AEs were 2.4% and 3.8% in the UPA-ADA and ADA-UPA groups, respectively; while serious infections were reported in 0.8% in the UPA-ADA group and in 2.5% in the ADA-UPA group. Safety at 6m overall was comparable to 3m post-switch (Table 2).

Conclusion: Data from this blinded, controlled study indicate that pts with initial insufficient response, either non-response or partial response, to either UPA or ADA may benefit from switching to the other therapy. No additional safety concerns were observed. These data suggest that a patient failing either UPA or ADA may respond to the alternate therapy.

References: 1) Singh, et al. *Arthritis Rheumatol*, 2016;68:1-26.

Disclosure: R. Fleischmann, AbbVie, 2, 5, Acea, 2, 5, Akros, 5, Amgen, 2, 5, AstraZeneca, 2, 5, BMS, 2, 5, Bristol-Myers Squibb, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, 5, Celltrion, 5, Celtrion, 2, 5, Centrexion, 2, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck-Serono, 2, 5, EMD Serono, 2, EMD-Serano, 2, EMD-Serono, 2, Genentech, 2, 5, Genetech, 2, GlaxoSmithKline, 2, 5, GSK, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Merck, 2, Nektar, 2, Novartis, 2, 5, Pfizer, 2, 5, Pfizer Inc, 2, 5, Regeneron, 2, Resolve, 2, Roche, 2, Samsung, 5, Sandoz, 5, Sanofi Genzyme, 2, Sanofi-Aventis, 2, 5, Sanofi-Aventis, 2, 5, Sanofi-Genzyme, 2, Selecta, 2, Tahio, 5, Taiho, 5, UCB, 2, 5; **M. Genovese**, AbbVie, 2, 5, Abbvie, 2, 5, AbbVie, Inc., 9, Astellas, 2, 5, Eli Lilly, 2, 5, Eli Lilly and Company, 2, 5, EMD Merck Serono, 2, 5, Gal-

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Abstract Number: 2908

Remission in Patients with Rheumatoid Arthritis Receiving Triple Therapy Compared to Biological Therapy - A Swedish Nationwide Register Study

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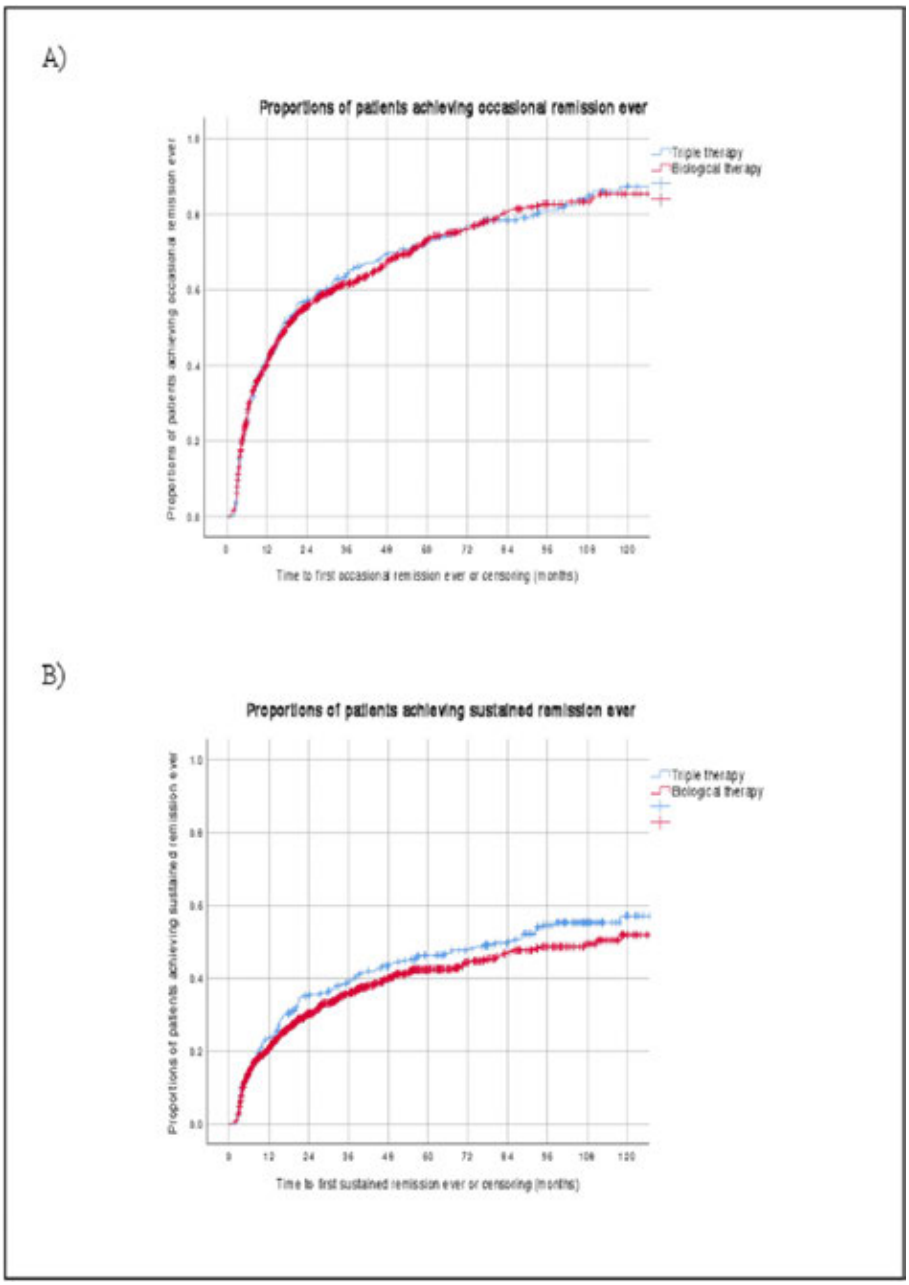
SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: RA – Treatments V: Switching & Tapering RA Medications
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Current treatment guidelines for rheumatoid arthritis (RA) recommend a treat-to-target approach with early treatment initiation of disease-modifying antirheumatic drugs (DMARDs), most commonly methotrexate (MTX), and treatment escalation in case of insufficient response. In this scenario, similar efficacy of biological DMARDs (bDMARDs) + MTX compared to conventional triple therapy (MTX + sulfasalazine + hydroxychloroquine) has been shown in randomized control trials. We aimed to compare occurrences of occasional and sustained remission in patients receiving triple therapy versus bDMARDs + MTX as first treatment strategy after MTX monotherapy, using real-life data from the Swedish national Rheumatology Quality Register (SRQ).

Methods: Adult patients with a clinical diagnosis of RA registered in the SRQ between 2000/01/01 and 2012/12/31 receiving triple therapy or any bDMARD + MTX as first treatment strategy after MTX monotherapy were included. ACR 1987 criteria were satisfied by 96.8% of patients. Occasional remission was defined as a disease activity score with 28 joint counts with erythrocyte sedimentation rate (DAS28) < 2.6 at one occasion and sustained remission as remission for ≥6 months. Per protocol analyses were used for occasional and sustained remission achieved during treatment at 12 and 24 months (*during*), and intention to treat analyses were used for occasional and sustained remission achieved at any time in the follow-up (*ever*). Propensity score adjusted regression analyses were performed.

Results: In total, 347 patients receiving triple therapy and 1156 patients receiving a bDMARD + MTX were included. Crude Kaplan Meier analyses of proportions of patients achieving occasional and sustained remission *ever* showed no statistically significant differences between triple therapy and bDMARDs + MTX (Figure). Propensity score adjusted odds ratios (ORs) (biological/triple therapy) with 95% confidence intervals (CIs) for occasional remission during treatment at 12 and 24 months



A) Occasional remission ever, Mantel-Cox p-value = 0.763. B) Sustained remission ever, Mantel-Cox p- value = 0.145. MTX = methotrexate; triple therapy = MTX + sulfasalazine + hydroxychloroquine/chloroquine; biological therapy = biological disease-modifying antirheumatic drug + MTX; censoring = last registered visit; DAS28 = disease activity score with 28 joint counts with erythrocyte sedimentation rate; remission = DAS28<2.6; sustained remission = remission for ≥6 months.

were 1.38 (95% CI 0.90-2.11) and 1.51 (95% CI 0.87-2.60) respectively. For sustained remission during treatment at 12 and 24 months, ORs were 1.34 (95% CI 0.86-2.10) and 1.22 (95% CI 0.70-2.14) respectively. For occasional and sustained remission *ever*, hazard ratios were 1.13 (95% CI 0.96-1.33) and 1.12 (95% CI 0.91-1.38) respectively.

Conclusion: In this nationwide Swedish register study, we found no statistically significant differences between triple therapy and bDMARDs + MTX as first treatment strategy after MTX monotherapy in odds of achieving occasional and sustained remission *during* treatment at 12 and 24 months, or *ever* in the follow-up. This suggests that in RA, conventional triple therapy is a good alternative to bDMARDs + MTX.

Disclosure: H. Källmark, None; **J. Einarsson**, None; **J. Nilsson**, None; **M. Kapetanovic**, Abbvie, 5, Pfizer, 2.

Abstract Number: 2909

Efficacy and Safety of the Selective Interleukin-1 Receptor Associated Kinase 4 Inhibitor, PF-06650833, in Patients with Active Rheumatoid Arthritis and Inadequate Response to Methotrexate

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
Session Title: RA – Treatments V: Switching & Tapering RA Medications
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Adaptive and innate immune pathways are involved in inflammation and pathogenesis of rheumatoid arthritis (RA). Toll-like receptor (TLR) stimulation activates the innate immune system, and may be involved in the pro-inflammatory response to ACPA protein complexes found in severe RA.[1] Interleukin (IL) receptor-associated kinase 4 (IRAK4) is a key signal transducer downstream of the myddosome-associated TLRs and IL-1 receptors. IRAK4 inhibition blocks inflammatory cytokine production, so is a potential therapeutic target for RA.[2] This study evaluated the efficacy and safety of PF-06650833, a highly selective, small molecule, reversible IRAK4 inhibitor in development for RA treatment.

Methods: In this Phase 2b, multicenter, randomized, double-blind, double-dummy, placebo and active-controlled parallel-group study, patients (pts) with moderately to severely active $ACPA^+$ RA and an inadequate response to methotrexate were randomized (6:6:6:5:5:5) to 12 weeks' dosing with PF-06650833 20 mg, 60 mg, 200 mg, 400 mg modified-release tablets once daily (QD), tofacitinib 5 mg twice daily, or placebo. The primary endpoint was change from baseline (CFB) at Week 12 in simplified disease activity index (SDAI). Secondary endpoints included ACR20, 50, and 70 responder rates and CFB in disease activity score 28 with 4 components-C-reactive protein (DAS28-4[CRP]) at Week 12. Adverse events (AEs) were also monitored.

Results: Overall, 269 pts from 19 countries were randomized and treated (PF-06650833 = 187; tofacitinib = 43; placebo = 39). Mean CFB in Week 12 SDAI was significantly higher in the PF-06650833 arms vs placebo ($p \leq 0.005$) using the primary Bayesian analysis with an informative placebo prior distribution and in the 200 mg and 400 mg groups with non-informative placebo prior distribution (sensitivity analysis; $p < 0.05$), suggesting improved response. Statistically significantly greater ACR50 response rate vs placebo was observed at Week 12 in 20/50 (40.0%) and 21/48 (43.8%) pts in the PF-06650833 200 mg and 400 mg group ($p=0.040$, $p=0.016$), respectively. Statistically significant CFB in DAS28-4(CRP) vs placebo was observed in PF-06650833 60 mg, 200 mg, and 400 mg QD groups at Week 12 ($p < 0.05$). Of 222 all-causality treatment-emergent AEs (TEAEs) reported across treatment groups, 8 were serious AEs (SAEs); 64 were treatment-related (reported in 48 pts; one was an SAE due to elevated liver transaminases, resolved) and were not dose-dependent. TEAEs of the system organ class (SOC) infections and infestations were most commonly reported (55/269 [20.4%] pts). Herpes zoster occurred in 3 pts (1 treatment-related). Twelve pts permanently discontinued due to TEAEs and no deaths occurred.

Conclusion: All PF-06650833 doses displayed improvement in clinical disease scores vs placebo at Week 12 in pts with moderate to severe RA. Infections and infestations were the most common TEAE SOC, and no deaths occurred.

Study sponsored by Pfizer Inc. Medical writing support was provided by Molly MacFadyen and Claire Cairney of CMC Connect and funded by Pfizer Inc.

1) Sokolove J et al. Arthritis Rheum 2011; 63: 53-62.
2) De Nardo D et al. J Biol Chem 2018; 293: 15195-15207.

Disclosure: S. Danto, Pfizer Inc, 1, 3; **N. Shojaee**, Pfizer Inc, 1, 3; **R. Singh**, Pfizer Inc, 1, 3; **Z. Manukyan**, Pfizer Inc, 1, 3; **J. Mancuso**, Pfizer Inc, 1, 3; **E. Peeva**, Pfizer Inc, 1, 3; **M. Vincent**, Pfizer Inc, 1, 3; **J. Beebe**, Pfizer Inc, 1, 3.

Abstract Number: 2910

Improving the Efficiency of Clinical Trial Recruitment Using Electronic Health Record Data, Natural Language Processing, and Machine Learning

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Session Title: RA – Treatments V: Switching & Tapering RA Medications
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Efficiently identifying eligible patients is an important component of a successful clinical trial. Billing codes from electronic health record (EHR) data are commonly used to first screen for potential patients, followed by labor-intensive chart review to identify the eligible patients by trial criteria. The objective of this study was to test whether a machine learning screening algorithm (ML-screen) incorporating ICD codes and data extracted from notes using natural language processing (NLP), could improve the efficiency for identifying eligible patients for an ongoing clinical trial.

Methods: We studied EHR data used for a clinical recruitment study of rheumatoid arthritis (RA) and cardiovascular disease recruiting from a tertiary care center (TCC) and a community hospital (CH). The target population were RA patients, age >35, about to initiate a tumor necrosis factor inhibitor, and not on a statin. Prior to this study all patients with ≥1 RA ICD codes (RA_{ICD}) and age >35 years were selected for chart review. The CH and TCC data sets were both manually reviewed as gold standard labels including 642 and 2387 patients, respectively. All notes were processed with NLP to obtain the number of mentions for the concept of RA and inflammatory arthritis. Three groups of features were considered for the ML-screen (**Table 1**): (1) inclusion criteria features, e.g. RA_{ICD}; (2) exclusion criteria features, e.g. # of electronic prescriptions for a statin; (3) the total # ICD codes as a proxy for healthcare utilization. For the ML-screen we considered features within a 2-year timeframe prior to the chart review as well as all years prior. The ML-screen combined two ML methods, random forest (RF) and penalized logistic regression. The goal for the ML-screen was to reduce the number of patients requiring chart review without excluding potentially eligible patients. The ML-screen was compared to alternative approaches using RA_{ICD} ≥1, RA_{ICD} ≥2, and RA_{ICD} ≥1+exclusion criteria features. To test whether the ML-screen can be successfully ported to other institutions, we trained at TCC and applied at CH, and vice versa.

Results: The current method reviewing all charts with RA_{ICD}≥1 yielded 346 (14.5%) eligible patients out of 2387 at TCC, and 74 (16.0%) out of 642 at CH. Applying the ML-screen would result in reviewing 33% less patients in TCC

Table 1.

Category	Feature	Description
Inclusionary features	RA_{ICD}	# RA ICD codes
	RA_{NLP}	# mentions for the concept of RA in the narrative notes
	IA_{NLP}	# of mentions for the concept of inflammatory arthritis in the narrative notes
	$RA_{ICD+NLP}$	the sum of RA_{ICD} and RA_{NLP}
Exclusionary features	JRA_{ICD}	ICD codes for juvenile rheumatoid arthritis
	SLE_{ICD}	ICD codes for systematic lupus erythematosus
	PsA_{ICD}	ICD codes for psoriatic arthritis
	$Melanoma_{ICD}$	ICD codes for melanoma
	$bDMARD_{COD}$	electronic prescriptions for biologic disease modifying anti-rheumatic drugs
	$Statin_{COD}$	electronic prescriptions for statin
Other	HU	Health care utilization, total # of ICD codes

Table 1. Features used in the ML-screen for clinical trial recruitment.

Table 2. Comparison of performance between a screen developed using machine learning vs ICD only screens

	ML-screen		$RA_{ICD} \geq 2$		$RA_{ICD} \geq 1$ & Exclusion		$RA_{ICD} \geq 1$	
Institution→	TCC	CH	TCC	CH	TCC	CH	TCC	CH
Sensitivity	0.98	1	0.98	0.78	0.73	0.78	1	1
PPV	0.22	0.29	0.15	0.36	0.3	0.36	0.15	0.16
n (%) of patients for review	1606(67.3)	258 (55.8)	2322 (97.3)	569(88.7)	828 (34.7)	222(34.6)	2387 (100)	642 (100)
% reduced compared to $RA_{ICD} \geq 1$	32.7	44.2	2.7	11.3	65.3	63.4	0	0

Table 2. Comparison of performance between a screen developed using machine learning vs ICD only screens

Table 3.

	TC	TC→ CH	CH	CH→ TC
Sensitivity	0.98	0.99	1.0	0.98
Positive predictive value	0.22	0.19	0.29	0.22
# patients for review	1606	355	258	1713
% reduced compared to $RA_{ICD} \geq 1$	32.7	25.6	44.2	28.2

Table 3. Comparison of performance for MLS algorithm across institutions

and 44% less in CH, compared to $RA_{ICD} \geq 1$, without screening out potentially eligible patients (**Table 2**). In contrast, $RA_{ICD} \geq 2$ high sensitivity 0.93-0.98, but did not reduce as many patients for chart review, 2.7-11.3%. The $RA_{ICD} \geq 1$+exclusion yielded a larger reduction of patients for review, 63-65%, however excluded approximately 22-27% of eligible patients. The ML-screen had similar performance when trained on one institution and tested on the other (**Table 3**).

Conclusion: The ML-screen incorporating EHR and NLP data can increase the efficiency of clinical trial recruitment by reducing the number of patients requiring chart review; importantly, this approach did not screen out eligible patients. Moreover, the ML-screen can be trained at one institution and applied at another for multi-center clinical trials.

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Abstract Number: 2911

A Randomised, Open Labelled Clinical Trial to Investigate Synovial Mechanisms Determining Response - Resistance to Rituximab versus Tocilizumab in Rheumatoid Arthritis Patients Failing TNF Inhibitor Therapy

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: RA – Treatments V: Switching & Tapering RA Medications

Session Type: ACR Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: Although biologic therapies have transformed the outlook for rheumatoid arthritis (RA), the lack of a major treatment response in over 50% of patients, the potential side effects and the high cost of these drugs have highlighted the need to define predictive markers of response and to stratify patients according to therapeutic outcome. B-cells are pivotal to RA pathogenesis, validated by the efficacy demonstrated by the B cell depleting agent rituximab (RTX). RTX is licensed for use following failure of conventional synthetic (cs)-DMARDs and TNF inhibitor (TNFi) therapy. However, in this increasing therapeutically resistant cohort only 30% of patients achieve an ACR50 response at 6 months. We have recently demonstrated in an early RA cohort[1]synovial heterogeneity with over 50% of patients showing low/absence of synovial B-cell infiltration. This prompted us to test the hypothesis that in these patients an alternative biologic agent targeting alternative pathways maybe more effective. We report results from the first pathobiology-driven randomised controlled trial (RCT) in RA (R4RA) evaluating whether patient stratification according to the synovial B-cell rich/poor status enriches for response/non response to RTX.

	Overall	Rituximab	Tocilizumab
N	161	82	79
Pathotype – N (%)			
Bpoor	79 (49.1)	38 (46.3)	41 (51.9)
Brich	64 (39.8)	33 (40.2)	31 (39.2)
GC	9 (5.6)	5 (6.1)	4 (5.1)
Unknown	9 (5.6)	6 (7.3)	3 (3.8)
Gender Female, N (%)	128 (79.5)	62 (75.6)	66 (83.5)
Age	55.7 (12.9)	55.2 (13.1)	56.1 (12.8)
Disease Duration (months)	9.0 [4.0, 19.0]	9.5 [4.0, 20.8]	9.0 [4.0, 18.0]
CDAI	29.8 [21.7, 40.6]	30.6 [22.8, 40.6]	29.4 [21.5, 40.3]
ESR (mm/h)	31.5 [17.0, 48.0]	34.0 [16.5, 50.0]	28.0 [18.0, 48.0]
CRP (mg/L)	11.0 [5.0, 27.5]	10.0 [5.0, 23.0]	15.1 [6.0, 32.5]
RF/ACPA Positive – N (%)	105 (67.3)	58 (72.5)	47 (61.8)
CCP/ACPA positive – N (%)	119 (76.8)	63 (79.7)	56 (73.7)
Tender Joint Count (28)	11.0 [6.0, 18.0]	10.5 [6.2, 18.8]	11.0 [6.0, 16.0]
Swollen Joint Count (28)	6.0 [3.0, 10.0]	6.0 [4.0, 9.0]	6.0 [3.0, 10.5]
DAS28 (ESR)	5.8 (1.2)	5.8 (1.2)	5.8 (1.3)
DAS28 (CRP)	5.3 (1.2)	5.3 (1.2)	5.3 (1.3)

*There were no significant differences among treatment groups at baseline.
Continuous variables are here reported as either mean(SD) or median[IQR], depending on normality
CDAI=Clinical disease activity index. DAS28 =28 joint count disease activity score. CRP=C-reactive protein. ESR=erythrocyte sedimentation rate.

Table 1. Patient demographics

Methods: R4RA is a 48 week phase IV open-label RCT conducted in 19 European centres that recruited patients failing or intolerant to csDMARD therapy and at least one TNFi. Synovial tissue was obtained at trial entry and classified histologically as B-cell rich (BCR) or B-cell poor (BCP). Patients were randomised to receive standard therapy with RTX or tocilizumab (TCZ) stratified according to histological classification. The study was powered to test in the BCP population superiority of TCZ over RTX at 16 weeks. The primary and co-primary end-points were defined respectively as Clinical Disease Activity Index (CDAI) ≥50% improvement from baselineand Major Treatment response (MTR)= CDAI improvement ≥ 50% and CDAI ≤10.1. Secondary outcomes included assessment of CDAI response in the BCR cohort where non-inferiority of RTX compared to TOCI was evaluated. Safety data up to week 48 is reported.

Results: The trial recruited to target with a power of 89.5%. 164 patients were randomised, 83 received RTX and 81 TCZ. 81/83 RTX and 73/81 TCZ patients completed treatment to week 16 (primary endpoint). Baseline characteristics were comparable among treatment groups (Tab 1). In the BCP population a numerically higher number of patients achieved the primary outcome and a statistically significantly higher number of patients achieved co-primary endpoint (MTR) as well as in a number of additional secondary endpoints in the TCZ group (Tab 2). In the BCR population there was no significant difference in the majority of endpoints (Tab 2). A higher number of adverse and serious adverse events such as infections in patients treated with TCZ compared to RTX were recorded (Tab 3).

	16 weeks			
	B cell poor		B cell rich	
	Rituximab	Tocilizumab	Rituximab	Tocilizumab
N	38	41	33	31
CDAI ≥50% improvement – N (%)	17 (44.7)	23 (56.1)	13 (39.4)	16 (51.6)
CDAI MTR – N (%)	9 (23.7)	19 (46.3) *	5 (15.2)	11 (35.5)
DAS28 (ESR)≤3.2 – N (%)	10 (26.3)	18 (43.9)	8 (24.2)	13 (41.9)
DAS28 (CRP) ≤3.2 – N (%)	12 (31.6)	19 (46.3)	12 (36.4)	13 (41.9)
DAS28 (ESR) ≤2.6 – N (%)	6 (15.8)	15 (36.6)*	2 (6.1)	11 (35.5) *
DAS28 (CRP) ≤2.6 – N (%)	7 (18.4)	13 (31.7)	4 (12.1)	9 (29.0)
Moderate or good EULAR response DAS28(ESR) – N (%)	25 (65.8)	36 (87.8)‡	25 (75.8)	27 (87.1)
Moderate or good EULAR response DAS28(CRP) – N (%)	22 (57.9)	32 (78.0)	23 (69.7)	25 (80.6)
CDAI ≤10.1– N (%)	11 (28.9)	19 (46.3)	7 (21.2)	12 (38.7)
Changes from baseline - LSM				
CDAI	12.11	15.71	13.21	14.21
DAS28(ESR)	1.46	2.56*	1.46	2.57*
DAS28(CRP)	1.31	1.96‡	1.47	2.03
HAQ	0.26	0.36	0.31	0.42
FACIT Fatigue Score	-1.57	-5.55*	-8.48	-7.75

Post primary endpoint only includes patients that stayed on the randomized medication. For secondary end points, no adjustments were made for multiple comparisons. A P value of 0.05 or less was considered to indicate statistical significance. CDAI: Clinical Disease Activity Index; DAS: Disease Activity Score; EULAR: European League against Rheumatism. LSM: Least-Squares Mean. MTR: Major treatment response (defined as CDAI ≥50% improvement and CDAI<10.1) Missing data were imputed with the use of Multiple Imputation of Chained Equation (MICE) ‡P≤0.05 for the comparison with Rituximab

Table 2. Primary and co-primary and Secondary Efficacy End Points after 16 weeks

	Rituximab (n=82)	Tocilizumab (n=79)	Total [1] (n=161)
Adverse Events - n (%)	284(46.5)	327(53.5)	659
Patients with adverse events - n (%)	62(47.7)	68(52.3)	135
Serious Adverse Events - n (%)	8(30.8)	18(69.2)	26
Patients with serious adverse events - n (%)	8(40)	12(60)	20
Infections - n (%)	3(50)	3(50)	6
Patients with serious infections - n (%)	3(50)	3(50)	6
Discontinuation of study drug because of serious adverse event - n (%)	2(50)	2(50)	4
Confirmed cancer - n (%) [2]	0(0)	0(0)	0
Deaths - n (%)	1(100)	0(0)	1

The total number of events/patients with events up to week 48 is reported. This includes some adverse events occurring before the first prescription of IMP
No cancer was observed during the treatment period. However, there was one kidney carcinoma after week 48

Table 3. Safety data from Weeks 0 to 48 (+30 days)

Conclusion: In a RA BCP population failing csDMARDs and TNFi therapy,TCZ is more effective than RTX in achieving both low levels and significant falls in disease activity. In a BCR RA population RTX is non inferior to TCZ for the majority of outcome measures evaluated.

1. Humby, M.Lewis et al Ann Rheum Dis. 2019 Mar 16. pii: annrheumdis-2018-214539.

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Abstract Number: 2912

Predictive Factors for Treatment Related Mortality and Event-Free Survival After Autologous Hematopoietic Stem Cell Transplantation for Systemic Sclerosis: Results of a Long Term Follow-up Multi-centre Study

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: Systemic Sclerosis & Related Disorder – Clinical III: Predictors of Outcome

Session Type: ACR Abstract Session

Session Time: 11:00AM–12:30PM

Table 1 Baseline characteristics

	N=92
Median (25-75 IQR) duration of follow up	4.6 (2.1 – 12.4) y
Diffuse SSc n (%)	88 (96)
Age years, mean (SD)	46 (10)
Female n (%)	43 (47)
Disease duration, years, median (IQR)	1.5 (0.9-3.0)
ANA positive, n (%)	88 (96)
• Antitopoisomerase	54 (59)
• Anti RNA polymerase III	4 (4)
ESR > 25 mm n (%) (n=66)	39 (59)
Baseline mRSS (n=86)	26.0 (10.1)
Pulmonary function (mean, SD)	
• FVC%pred, n=84	85(23)
• DLCO%pred, n=83	55 (16)
HCT-CI (mean, SD)	4.9 (1.3)
Pretreatment, n (%)	
• MTX	47 (51)
• MMF	9 (10)
• Cyclophosphamide pulses	38 (41)
• Prednisolon	22 (24)
Smoking ever, n (%)	54 (64)

Abbreviations: IQR: interquartile range; SSc: systemic sclerosis; SD: stand deviation ; ANA: antinuclear antibody; ESR: erythrocyte sedimentation rate; mRSS: modified Rodnan skin score; FVC %pred: forced vital capacity % predicted; DLCO %pred: diffusion capacity; HCT-CI: hematopoietic cell transplant comorbidity index; MTX: methotrexate; MMF: mycophenolate mofetil

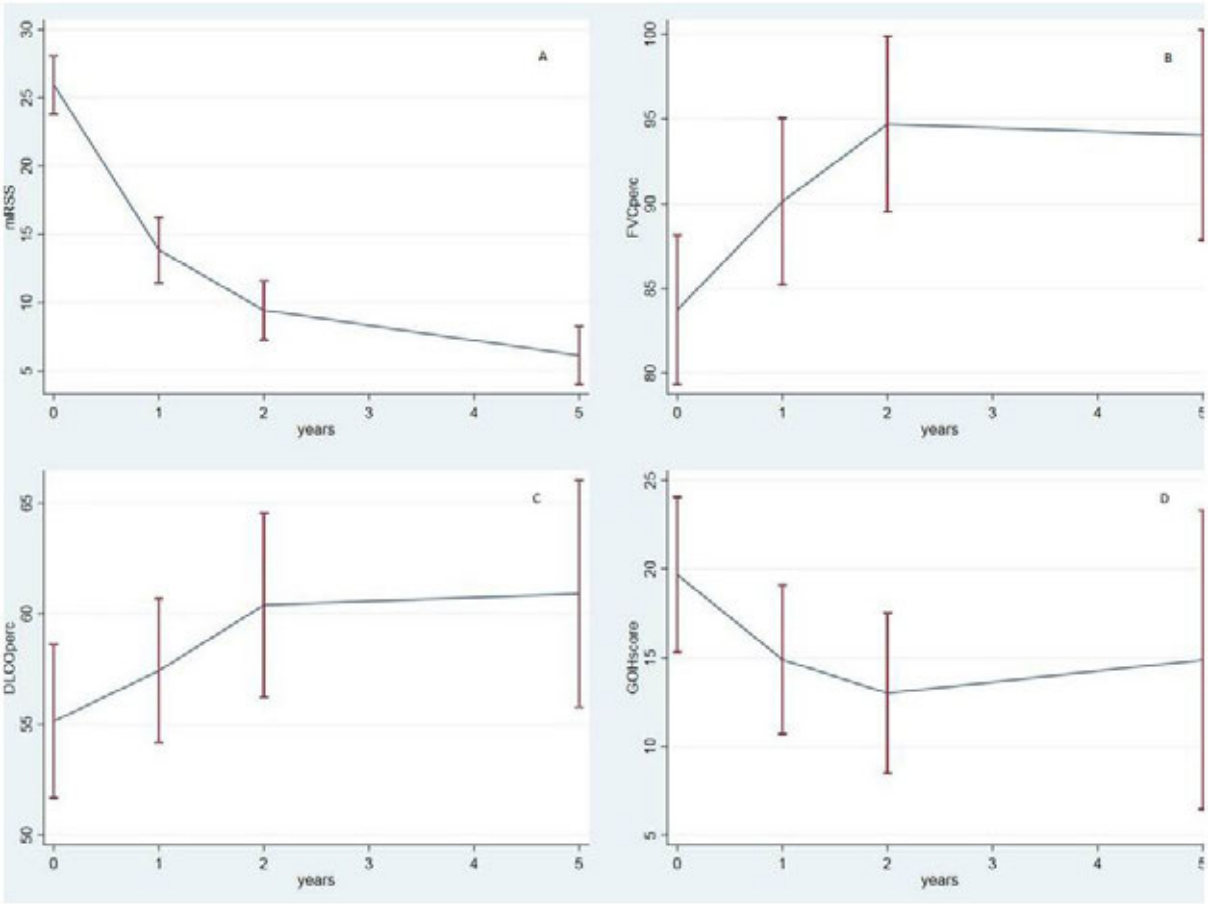

Figure 1. Course over time in patients surviving the first 5 years (n = 75) A skin involvement as measured by mRSS; B FVCpred: forced vital capacity % predicted; C DLCO pred: diffusion capacity % predicted; D Total Goh scores

Table 2 Association between baseline variables and occurrence of events (Univariate and multivariate Cox Hazard regression analysis), n= 92

	Univariate	Multivariate
Sex	**4.0 (1.4 to 11.0)**	**4.4 (1.4 to 13.4)**
Age, years	**1.1 (1.0 to 1.1)**	**1.1 (1.0 to 1.2)**
SSc Type	0.7 (0.1 to 3.6)	
Cyclofosfamide pretreatment	1.1 (0.4 to 2.6)	
Disease duration > 2 jaar	1.1 (0.5 to 2.7)	
HCT-CI	**1.4 (1.1 to 1.9)**	1.3 (0.9 to 1.8)
Smoking ever, n=84	1.4 (0.5 to 3.7)	
ESR > 25 mm, n=66	3.1 (0.9 to 10.9)	
FVC% pred < 70%, n= 84	0.9 (0.3 to 2.6)	
LVEF < 50%	**5.4 (1.2 to 23.6)**	**13.1 (2.0 to 89.0)**
DLCO % pred < 40%, n= 83	1.5 (0.5 to 4.1)	
Increase mRSS > 5 pre HSCT (n= 64)	**0.1 (0.0 – 0.7)**	0.3 (0.1 to 0.5)

Abbreviations: SSc: systemic sclerosis; HCT-CI: hematopoietic cell transplant comorbidity index; ESR: erythrocyte sedimentation rate; FVC % pred: forced vital capacity % predicted; LVEF: left ventricular ejection fraction; DLCO % pred: diffusion capacity % predicted; prog. mRSS: progression in skin involvement prior to stemceltransplantation;

Background/Purpose: Autologous hematopoietic stemcell transplantation (HSCT) has shown to improve survival of SSc patients with poor prognosis, but is hampered by treatment related mortality (TRM). Better selection of eligible patients could improve outcomes.

Objectives: 1. To evaluate event-free survival, TRM and response after HSCT in SSc and 2. To explore patient characteristics that associate with events.

Methods: Data on event-free survival of all patients treated with HSCT for SSc in the Netherlands between 1998 and 2017, performed as previously described (1) and with ≥ 1 year of follow-up were collected. Baseline characteristics including hematopoietic cell transplant comorbidity index (HCT-CI) (2) and left ventricular ejection fraction (LVEF) and data for skin involvement (modified Rodnan skin score (mRSS)), pulmonary function (forced vital capacity % predicted (FVC% pred), diffusion capacity % predicted (DLCO% pred)) and staging for interstitial lung disease on high resolution CT scan (HRCT) assessed according Goh (3) were collected at baseline and at 1,2, 5 years ; data for events and death were collected until end of study. All deaths were discussed in a consensus meeting (SB, MB, JV, MV) and classified as TRM, SSc progression or other. Event-free survival was defined as described before (4). Relapse was defined as an increase in mRSS of > 25% and > 5 points compared to the lowest value since HSCT, or either a ≥10% decline in FVC% pred, or ≥5 – < 10% decline in FVC% pred and ≥15% decline in DLCO% pred or initiation of immunosuppression (4). The association between event-free survival and baseline characteristics was examined by univariate Cox regression analysis. Factors with a significant association were entered in a multivariate analysis on imputed missing data.

Results: In total 92 patients were included (Table 1). Event-free survival estimates at 5, 10 and 15 years were 0.79, 0.79 and 0.68 respectively. Twenty deaths occurred, which were classified as TRM (n=10, 11%), SSc progression

(n=4, 4%) and other (n=6 7%). Relapse occurred in 22 patients in the first 5 years: skin relapse in 5, lung relapse in 11 and initiation of immunosuppression in 12 (in 7 patients without skin or lung relapse). FVC, DLCO, mRSS and Goh scores improved significantly over time in patients surviving the first 5 years (n=75) (Figure 1). Events were independently associated with male sex, LVEF < 50% and older age (table 2).

Conclusion: Event-free survival at 10 years after HSCT for SSc was 79%; male sex, lower LVEF and older age were identified as independent risk factors for events. Our data confirms efficacy of HSCT in improving survival and skin and lung involvement.
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Abstract Number: 2913

Serum Interferon Score Predicts Clinical Outcome at 12 Months in Diffuse Cutaneous Systemic Sclerosis as Measured by Global Ranked Composite Score (GRCS) and Composite Response Index in SSc (CRISS)

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SESSION INFORMATION
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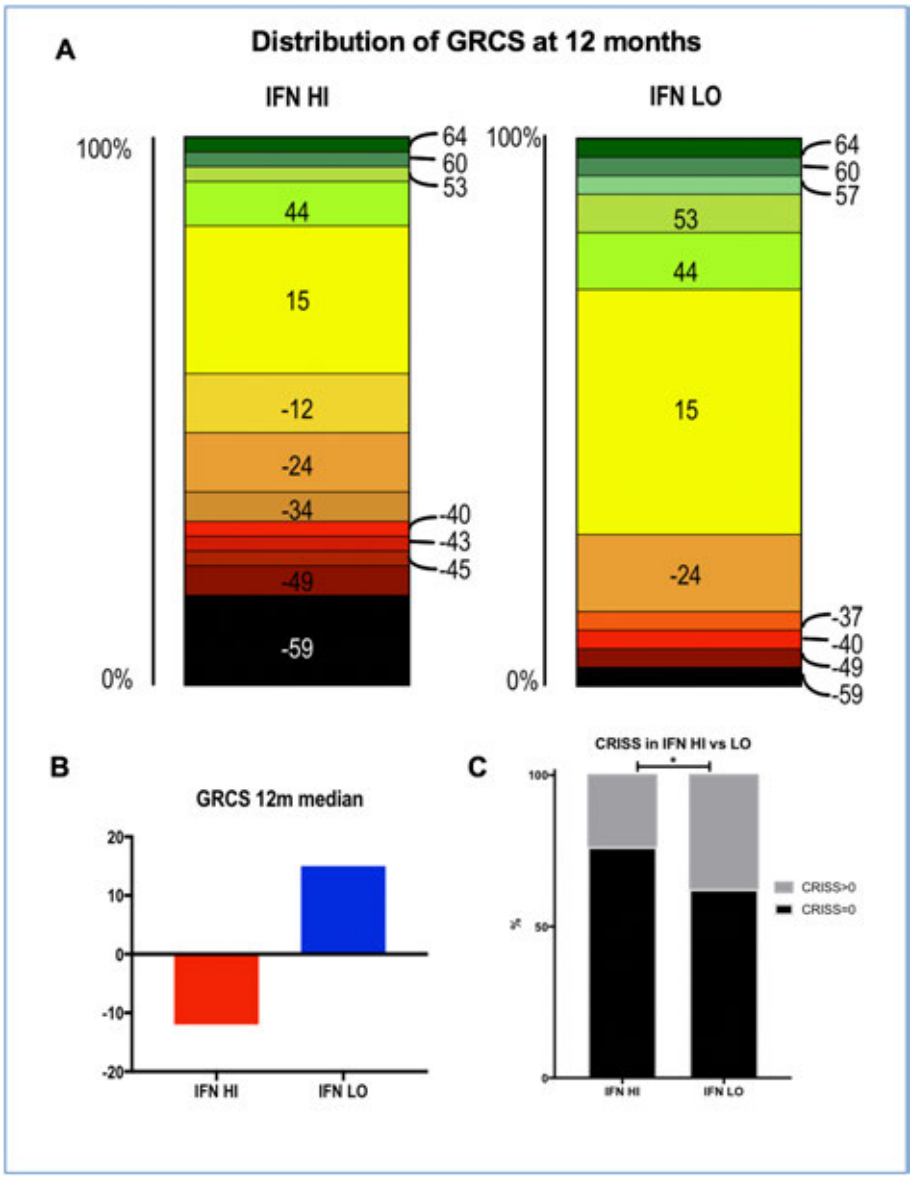
Session Type: ACR Abstract Session
Session Time: 11:00AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a highly heterogeneous disease orphan of effective disease modifying agents. The diffuse cutaneous clinical subset (dcSSc) is currently targeted in most clinical trials. Nevertheless, there is still high variability in clinical outcome within dcSSc, which is limiting effective clinical trial design and interpretation. Global Ranked Composite Score (GRCS) and Composite Response Index in SSc (CRISS) are two of the most recent attempts to capture overall response to treatment in dcSSc. Activation of interferon type 1 (IFN) pathway is associated with severe clinical manifestations in SSc. Microarray and proteomic studies have



Distribution of GRCS and CRISS in dcSSc patients stratified for serum Interferon Score. A: Distribution of GRCS in dcSSC patients with less than 6 years disease duration. HIght of color coded boxes reflects the proportion of patients with the GRCS score descibed in or on the side of the box. B: Median GRCS score in IFN HI (RED) or LO (Blue) dcSSc patients. C. Bar chart representing the proportion of patients with CRISS = 0 or higher than 0 in dcSSc patients stratified for their seum IFN score. * = P<0.05 according to Mann-Whytney test.

indicated that the serum concentration of CCL2, CCL8, CCL19, CXCL9, CXCL10, and CXCL11 are the most relevant serum measures of IFN induced activation of PBMCs. Here we aimed to determine whether their serum concentration of the above chemokines combined in a IFN score could be used to stratify patients with dcSSc for severe clinical outcome at 12 months as measured by GRCS and CRISS.

Methods: Serum concentration of CCL2, CCL8, CCL19, CXCL9, CXCL10, and CXCL11 was measured by Luminex xMAP technology (Myriad RBM) in 143 SSc patients and 35 healthy controls (HC). IFN score was calculated as the average of the natural logarithm of the above chemokines. GRCS were compared by Mann Whitney test and the effect size for the Mann Whitney test by Wilcoxon Paired ranked test, as described. Fisher exact test was used to analyse the proportion of patients with CRISS of 0% or >0%.

Results: All chemokines had a higher serum concentration in SSc vs HC ($p < 0.0001$ for all). Median IFN score was higher in SSc than HC (5.26 vs 4.70, $p < 0.0001$), but within SSc group, there was no difference associated with disease subset or duration. As with the dichotomization for IFN activity already described for RNA IFN Score, we defined IFN LO or HI patients as a score within or above mean + 2STDV of IFN Score of HCs. Sixty six 12-month outcome data of dcSSc patients were available for analysis. 37 were IFN HI and 29 IFN LO. GRCS ranged from -59 to 64. IFN HI patients had a worse outcome at 12 months with GRCS median score of -12 vs 15 in IFN LO ($p=0.0271$). Accordingly, GRCS favored IFN LO in 68.4% of 1073 (37*29) pairwise comparisons versus 31.6% of IFN HI ($p=0.0001$). 12 month CRISS was >0 in 24% of IFN HI vs 38% of IFN LO ($P=0.0464$).

Conclusion: Serum IFN Score predicts worse clinical outcome at 12 months in dcSSc. Stratification for IFN score could aid both in clinical trial design and clinical management. Moreover, here we show that GRCS and CRISS may be sufficiently sensitive to measure difference in composite outcome at 12 months in dcSSc in an observational setting.

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Abstract Number: 2914

Predictors to Develop Definite Systemic Sclerosis (SSc): Results from an International Multicentre Study on Very Early DiagnOsis of Systemic Sclerosis (VEDOSS)

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SESSION INFORMATION

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Session Type: ACR Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: The very early diagnosis of SSc is a challenge today. The aim of the VEDOSS project was to study in an at-risk population, the clinical signs that could predict the progression toward a definite SSc.

Indipendent predictors for progression into definite SSc	PPV	NPV
Disease specific abs ACA Scl70	70,2% 71% 60,7%	60,5% 52,3% 41,8%
NVC abnormalities	75%	50,4%
Puffy fingers (PF) PF + NVC abnormalities	**78,9%** 77,8%	**45,1%** 42%
PF + disease specific abs	**94,1%**	**43,9%**
Disease specifc abs + NVC abormalities	**82,2%**	**50,4%**

Methods: Patients with Raynaud phenomenon (RP), with or without anti-nuclear antibodies (abs) (ANA) were recruited for this longitudinal, observational study. Fulfilling the 2013 classification criteria at baseline was an exclusion criterion. Patients with ANA negative RP were recruited as controls. Patients had an annual assessment according to EUSTAR standards to determine organ involvement and severity. The endpoint was defined as fulfilment of the 2013 SSc classification criteria. The time to fulfilling 2013 classification criteria was evaluated with Kaplan-Meier analysis, and predictors of evolution were determined by univariate and multivariate Cox regression. The study was conducted in accordance with principals of Declaration of Helsinki.

Results: Out of 1,150 recruited patients, 35 were excluded due to non-RP at inclusion and 1.115 patients were analysed. After separating patients with missing ANA status (1), or already fulfilling ACR/EULAR 2013 (240) or ARA 1980 criteria at inclusion (110), the sample was distributed as followed: i) 237 patients (143 with follow up) RP/ANA negative (ANA^-/pRP), ii) 498 patients (401 with follow up) RP/ANA positive (ANA^+/pRP)): 87 had puffy fingers (PF), 199 had anti-centromere abs (ACA) positive, 45 had anti-topoisomerase-I abs (topo-I) positive and 182 had nailfold videocapillaroscopy (NVC) abnormalities at baseline. Out of 401 ANA^+/pRP patients, 7.4% within 1 year, 29.3% within 3 and 44.1% within 5 years satisfied the 2013 classification criteria. Out of the 143 ANA^-/pRP patients, none (0%) within 1 year, 4.6% within 3 years, and 4,6% within 5 years satisfied SSc criteria. After adjustment for age, the following baseline parameters were identified as independent predictors for progression into definite SSc by multivariate analysis: PF (OR=3.4 [2.0;5.6]), ACA (OR=2.6 [1.6;4.1]) and Topo-I (OR=3.1 [1.6;5.8]), and NVC abnormalities (OR=1.9 [1.3;2.9]) The presence of PF had a positive predictive value (PPV) of 79% . Combination of PF + specific

abs showed 94% PPV and disease specifc abs + NVC abormalities a 82,2% PPV to satisfy ACR/EULAR 2013 criteria within 5 years (Table 1).

Conclusion: The data show that 44% of VEDOSS patients develop, within 5 years of follow up, definite SSc according to classification criteria. At first visit, PF and SSc specific abs were identified as independent parameters predicting the development of definite SSc. These data may allow the risk stratification of patients with very early SSc in clinical practice and clinical studies.

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Abstract Number: 2915

Machine-learning Classification Identifies a Subset of Patients That Improve on Abatacept via Modulation of a CD28-Related Pathway

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SESSION INFORMATION

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Background/Purpose: We analyzed a phase 2 study designed to assess the efficacy of abatacept in patients with diffuse Systemic Sclerosis (SSc). In this work, we analyze data from ASSET and seek to confirm the hypothesis that patients in the inflammatory subset on abatacept show a significant decline in modified Rodnan Skin Score (mRSS), which is correlated to modulation of pathways related to the mechanism of action of abatacept.

Methods: SSc patients, who met 2013 ACR/EULAR criteria, were randomized to receive abatacept or placebo for 12 months. RNA sequencing was performed on 84 SSc patients at baseline, 3-month, and 6-month timepoints. Samples were assigned to an intrinsic gene expression subset (inflammatory, fibroproliferative, limited, or normal-like) using a Support Vector Machine (SVM) classifier. Treatment differences in longitudinal outcomes were assessed using linear

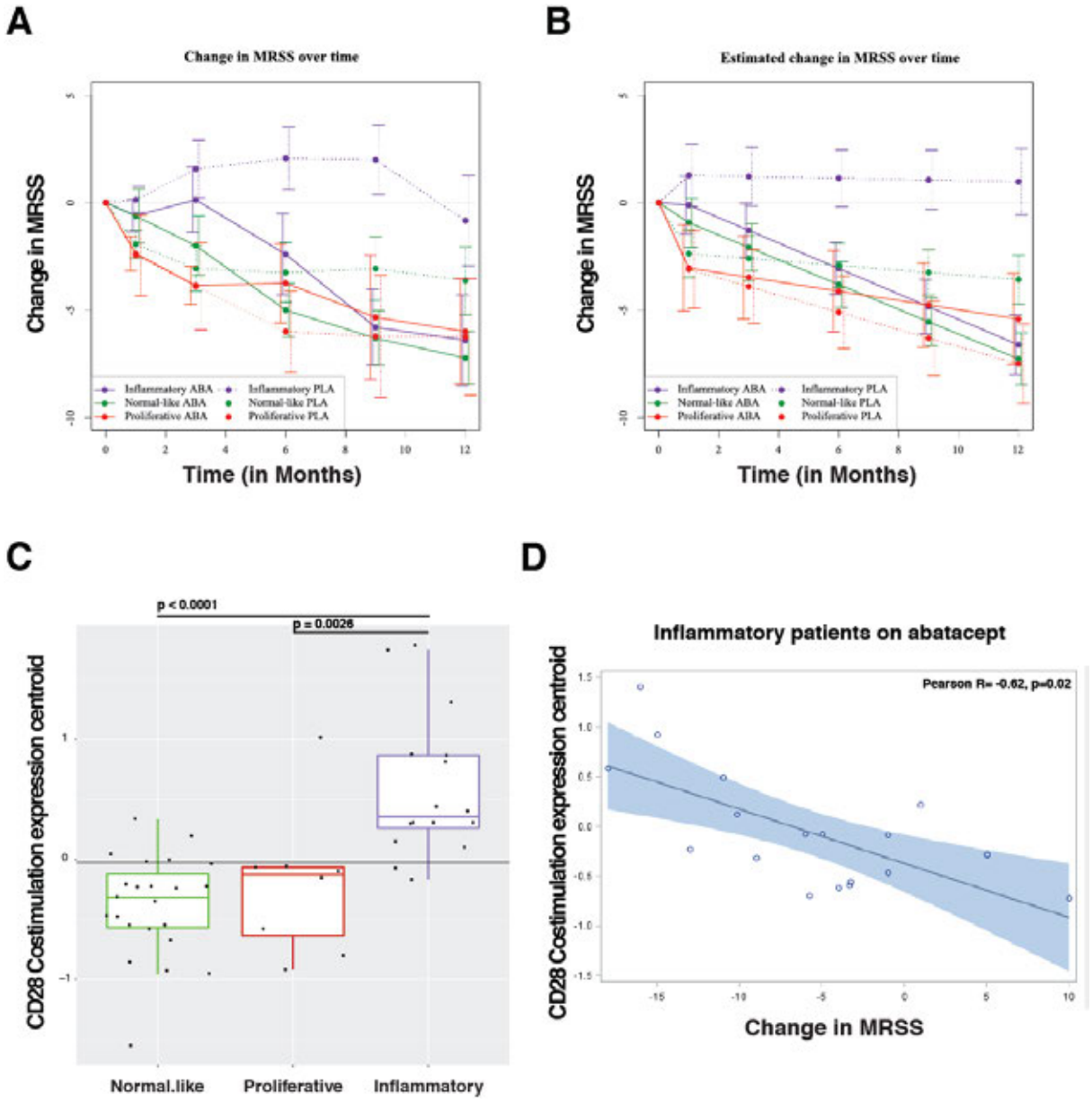

Figure 1. A) Observed average and B) estimated average change from baseline in MRSS in the placebo and abatacept group across intrinsic gene expression subsets. Estimates are obtained from a linear mixed model. C) Core expression genes from Costimulation of the CD28 family were log2 and median centered across the intrinsic subsets. An ANOVA found the means to be significantly different ($p<0.001$). P-values shown are using Tukey's test for multiple comparisons. D) Core gene expression from the Costimulation of the CD28 family were log2 and median centered for patients of the inflammatory subset on abatacept.

mixed effect models. Improvement was defined as a 5 point or >20% change in mRSS between baseline and 12 months. A machine-learning approach, trained on gene-gene relationships in the skin, was used to identify features beyond those simply differentially expressed. Gene Set Enrichment Analysis (GSEA) was used to identify pathways enriched in comparison groups.

Results: Patients were assigned to intrinsic subset at baseline (33 inflammatory, 18 fibroproliferative, and 33 normal-like). Differences in trajectory for intrinsic subsets are evident (Figures 1a, 1b). In the abatacept arm, change in mRSS was most pronounced for the inflammatory ($p< 0.001$) and normal-like ($p=0.03$) subsets when compared to placebo. The gene-gene network from skin, returned CD86 as being highly related to genes that decrease in abatacept improvers. For gene expression analyses, the dataset was parsed for quality and patients that completed the

trial, the remaining (n=140) biospecimens were analyzed. The pathway Costimulation by the CD28family decreases (FDR=5.88x10 -4) in patients that improve on abatacept; this decrease is specific to the inflammatory subset (FDR=0%) of patients. At baseline, patients in the inflammatory subset have an elevation in the Costimulation by the CD28 family pathway relative to proliferative (p = 0.0026) or normal-like (p=0.0001) patients (Figure 1c). In inflammatory patients, we see a correlation (R=-0.62, p=0.02) between DmRSS and baseline expression ofthe Costimulation by the CD28 family pathway (Figure 1d).

Conclusion: Abatacept shows the most benefit for inflammatory patients. CD28-related pathways are elevated in inflammatory patients relative to fibroproliferative or normal-like patients. Importantly, we find that the extent of improvement in inflammatory patients is directly correlated to their baseline expression of the *Costimulation by the CD28 family*pathway. We show that baseline gene expression can predict differential response to biological intervention by directly modulating pathways pertinent to a drug's mechanism of action. This data suggests that stratifying patients by baseline signatures may clarify the effects observed and act as a step towards precision medicine for future clinical practice.

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Abstract Number: 2916

Ancestry-Specific Classical *HLA* Alleles Define Phenotypic Subsets in the African American Scleroderma Population

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Table 1. Logistic regression and conditional analysis of *HLA* classical alleles in African American SSc clinical subsets.

		Frequency (%)		Unconditioned		Conditioned	
Subset	Allele	SSc	Controls	P-Value	OR (95% CI)	P-Value	OR (95% CI)
lcSSc v Controls SSc=354; Ctrl=946	***HLA-DRB1*08:04***	**21.8**	**9.3**	**1.13E-08**	**2.7 (1.9-3.8)**	**1.13E-08**	**2.7 (1.9-3.8)**
	*HLA-DQB1*03:19*	18.4	8.8	6.19E-06	2.3 (1.6-3.3)		
	*HLA-DRB4*01:01*	14.1	24.5	3.60E-05	0.4 (0.4-0.7)		
dcSSc v Controls SSc=516; Ctrl=946	***HLA-DRB1*08:04***	**25.0**	**9.3**	**1.39E-15**	**3.3 (2.5-4.5)**	**1.39E-15**	**3.3 (2.5-4.5)**
	*HLA-DQB1*03:19*	18.2	8.8	9.66E-08	2.4 (1.7-3.3)		
	HLA-DRB1*11:02	**14.9**	**7.1**	**2.00E-06**	**2.3 (1.6-3.3)**	**2.34E-07**	**2.6 (1.8-3.7)**
	*HLA-DRB4*01:01*	14.3	24.5	4.08E-06	0.5 (0.4-0.7)		
	HLA-DPB1*13:01	**18.2**	**9.7**	**4.37E-06**	**2.1 (1.5-2.8)**	**3.14E-05**	**2.0 (1.4-2.8)**
	*HLA-DPA1*01:03*	50.8	62.3	8.89E-06	0.6 (0.5-0.8)		
ILD+ SSc v Controls SSc=318; Ctrl=946	***HLA-DRB1*08:04***	**23.0**	**9.3**	**3.80E-09**	**2.9 (2.1-4.1)**	**3.80E-09**	**2.9 (2.1-4.1)**
	HLA-DPB1*13:01	**21.7**	**9.7**	**3.88E-07**	**2.5 (1.8-3.6)**	**6.26E-07**	**2.5 (1.8-3.6)**
	HLA-DQB1*03:19	**17.3**	**8.8**	**3.56E-05**	**2.2 (1.5-3.3)**	**1.18E-05**	**2.6 (1.7-3.9)**
	HLA-DQA1*01:02	**61.6**	**53.7**	**8.10E-03**	**1.4 (1.1-1.9)**	**2.18E-05**	**1.8 (1.4-2.4)**
PAH+ SSc v Controls SSc=285; Ctrl=946	***HLA-DRB1*08:04***	**23.5**	**9.3**	**1.40E-09**	**3.1 (2.2-4.4)**	**1.40E-09**	**3.1 (2.2-4.4)**
	HLA-DQA1*02:01	**8.1**	**20.0**	**3.10E-07**	**0.3 (0.2-0.5)**	**6.04E-06**	**0.4 (0.2-0.6)**
	*HLA-DRB1*11:02*	15.1	7.1	3.60E-05	2.5 (1.6-3.7)		
SRC+ SSc v Controls SSc=50; Ctrl=946	*HLA-DQB1*03:19*	26.0	8.8	ns			

ns = not significant at a threshold of P = 5 x 10^{-5}; independent associations by conditional regression analysis shown in bold.

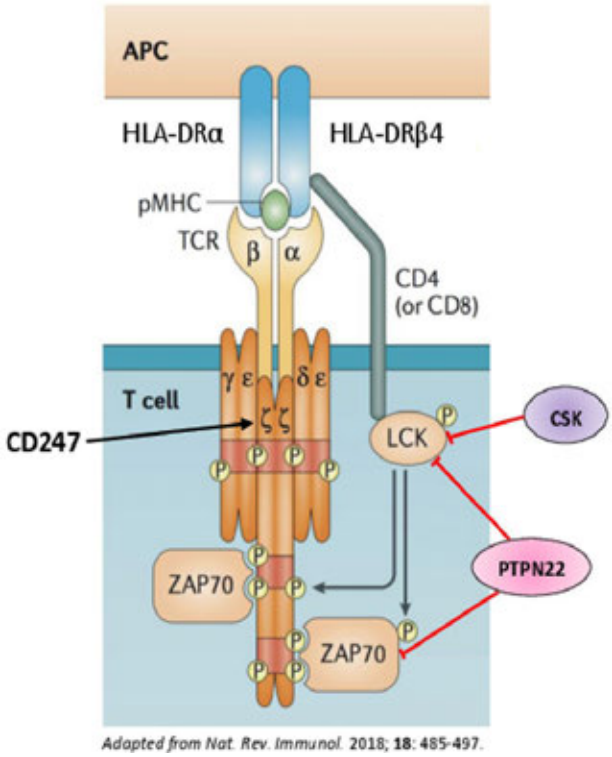

Figure 1. Scleroderma risk factors and the T cell receptor (TCR) signaling pathway. Three genes (CD247, CSK, and PTPN22) that have been previously implicated in scleroderma susceptibility are all involved in the initiation of the TCR signaling pathway. HLA-DRB4, which was identified in this study, is also involved in this pathway, suggesting an important role of TCR signaling in scleroderma pathogenesis.

Background/Purpose: Systemic sclerosis (SSc), or scleroderma, is a heterogeneous disease that is divided into limited cutaneous (lcSSc) and diffuse cutaneous (dcSSc) forms based on the extent of skin involvement, and internal organ involvement also adds to phenotypic variability. The three main internal organ complications are interstitial lung disease (ILD), pulmonary arterial hypertension (PAH) and scleroderma renal crisis (SRC).

Methods: We investigated classical *HLA* alleles and polymorphic amino acids for association with clinical subsets of SSc. A conditional association analysis with a Bonferroni-corrected significance threshold of P-value (P) < 0.00005 identified multiple subset-specific SSc risk factors in an African American cohort of 934 SSc patients and 946 unaffected controls.

Results: *HLA-DRB1*08:04*, an African-ancestry predominant allele, was the strongest risk factor with odds ratios (ORs) ranging from 2.7 to 3.3-fold in the lcSSc, dcSSc, ILD+ and PAH+ subsets of SSc. The allele *HLA-DPB1*13:01* also independently increased risk in the dcSSc and ILD+ subsets, with ORs of 2.0 (95% CI 1.4-2.8) and 2.5 (95% CI 1.8-3.6), respectively. There were no significant associations in the SRC+ subset at the chosen P threshold, but the strongest association was with *HLA-DQB1*03:19* (P = 0.0002), which is in linkage disequilibrium with *HLA-DRB1*08:04*. For the first time, a protective effect of *HLA-DRB4*01:01* was identified in SSc, with a stronger effect in the lcSSc subset (OR = 0.4, 95% CI 0.4-0.7) than in the dcSSc subset (OR = 0.5, 95% CI 0.4-0.7). The presence of this allele is also linked to *HLA-DRB1*07:01*, which has been reported as protective for SSc in European ancestry cohorts. Further stratification of clinical subsets by autoantibody status revealed more striking effects of certain alleles, despite the reduced sample size. On comparing the dcSSc with the lcSSc none of the alleles met the statistical significance threshold due to reduction in sample size. Interestingly, the top two associations were both class I *HLA* alleles, *HLA-A*74:01* (OR = 0.5, 95% CI 0.3-0.8) and *HLA-C*17:01* (OR = 1.7, 95% CI 1.1-2.6), and these associations

became even stronger upon comparing patients with dcSSc to those with CREST syndrome (OR = 0.4 and 2.0 and P = 0.0008 and 0.003, respectively).

Conclusion: This is the largest genetic study of African American SSc patients identifying classical *HLA* alleles increasing risk in clinical subsets of SSc. Class II *HLA* alleles are responsible for increasing risk for scleroderma in general and the class I *HLA* alleles play a more prominent role in defining the extent of skin involvement. Increased risk from the *HLA* genes along with previously implicated genes in SSc susceptibility (*CD247*, *CSK, PTPN22*) together with the newly identified role of *HLA-DRB4* point towards the important role of CD4 T cells and the relevance of T cell receptor (TCR) signaling in SSc pathogenesis.

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Abstract Number: 2917

Geographic Disparities in Systemic Sclerosis Mortality in the United States: 1999 to 2017

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SESSION INFORMATION

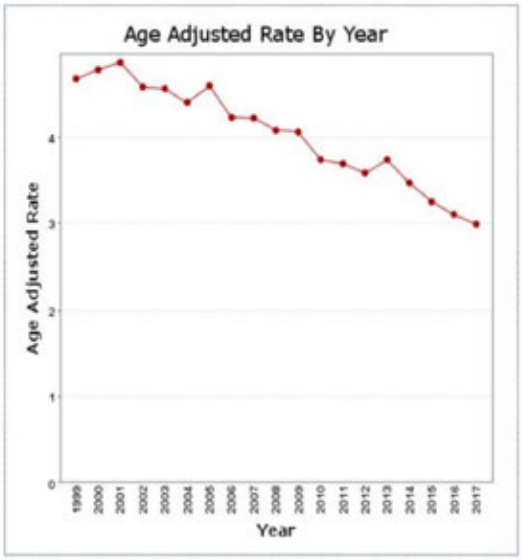
Session Date: Wednesday, November 13, 2019

Session Title: Systemic Sclerosis & Related Disorder – Clinical III: Predictors of Outcome

Session Type: ACR Abstract Session

Session Time: 11:00AM–12:30PM

Figure 1. Age-adjusted mortality rate for scleroderma as underlying cause of death by year.



Background/Purpose: Population mortality studies in the United States have previously reported a progressive increase in the scleroderma (SSc) mortality rates from 1959 to 2002. Identification of areas with clusters of higher mortality rates is important to implement targeted interventions and may provide clues about possible etiology factors, especially environmental. In this study, we aimed to estimate the mortality rates of patients with SSc and to determine whether there is a geographic variability in scleroderma mortality rates at the state level in the United States using publicly available data from 1999 to 2017.

Methods: To obtain mortality rates of scleroderma as the underlying cause of death, we used the CDC Wonder Underlying Cause of Death database and its query system, which contains data from 1999 to 2017. We used the corresponding ICD-10 codes for SSc for the queries. Age-adjusted rates were calculated by state and demographics, including, gender, race, and Hispanic ethnicity. Mortality rates were given as number of deaths per million. A linear regression model was applied to evaluate trends over time.

Results: During the 19-year period of our study, a total of 24,525 deaths had SSc as the underlying cause of death of an underlying population of 5,761,465,567. The age-adjusted mortality rate was 3.962 per million (95% CI: 3.912-4.012). The SSc-related mortality rates have progressively decreased from a rate of 4.679 (95%CI: 4.423 - 4.934) in 1999 to 2.993 (95% CI: 2.817 - 3.170) per million in 2017. Linear regression found a significant negative slope, indicating a trend to the decrease of age-adjusted mortality rates over time (Age-adjusted rate = - 0.1015*year + 207.8; $p < 0.0001$) (Figure 1).

There were more deaths in females than in males with a ratio: 4.1 to 1. The age-adjusted mortality rate was 5.885 (95% CI: 5.802 - 5.967) per million in females and 1.651 (95% CI: 1.604 - 1.698) per million in males. The highest age-adjusted mortality rate was in Blacks or African-Americans, at 5.703 per million (95% CI: 5.521 - 5.885), followed by American Indians or Alaska Native at 5.047 per million (95% CI: 4.428 - 5.667) (Table 1). Clusters of contiguous states with higher and lower mortality rates were identified. South Dakota was the state with the highest whereas Hawaii was the one with the lowest mortality rate. In Table 2, we list the states with the highest mortality rates.

Table 1. Age-adjusted mortality rate per million for scleroderma as underlying cause of death, by race and gender.

Race	Gender	Deaths	Population	Age-Adjusted Rate (95% CI)	% of Total Deaths
Black or African American	Female	2,981	406,808,112	7.867 (7.582 - 8.152)	12.155%
	Male	940	372,183,341	2.981 (2.784 - 3.179)	3.833%
	Total	**3,921**	**778,991,453**	**5.703 (5.521 – 5.885)**	**15.988%**
American Indian or Alaska Native	Female	224	36,894,044	7.660 (6.622 - 8.697)	0.913%
	Male	57	37,044,572	2.142 (1.585 - 2.832)	0.232%
	Total	**281**	**73,938,616**	**5.047 (4.428 – 5.667)**	**1.146%**
White	Female	16,118	2,326,457,753	5.620 (5.533 – 5.708)	65.721%
	Male	3,704	2,275,993,219	1.516 (1.466 - 1.565)	15.103%
	Total	**19,822**	**4,602,450,972**	**3.766 (3.713 – 3.819)**	**80.824%**
Asian or Pacific Islander	Female	413	158,995,020	2.887 (2.603 - 3.171)	1.684%
	Male	88	147,089,506	0.773 (0.615 - 0.960)	0.359%
	Total	**501**	**306,084,526**	**1.952 (1.777 – 2.128)**	**2.043%**
Total		**24,525**	**5,761,465,567**	**3.962 (3.912 – 4.012)**	**100%**

CI: Confidence interval.

Conclusion: Our study found a trend towards a decrease of mortality rate in SSc compared to previous studies, and a trend to a progressive decrease in mortality rates during the years of our study. In addition, we found relevant state-by-state variation in mortality with several geographical clusters with higher mortality rates. Further analyses of those geographical clusters are warranted in order to better understand the factors associated to the observed geographic disparities and to implement targeted interventions to decrease disparities.

Table 2. The 12 States with the highest mortality due to scleroderma as underlying cause of death with age-adjusted rates and 95% confidence interval.

	Deaths	Population	Age-Adjusted Rate per 1,000,000 (95% CI)
South Dakota	106	15,276,970	6.285 (5.076 – 7.495)
New Mexico	237	37,679,448	5.862 (5.108 – 6.616)
Montana	121	18,443,327	5.567 (4.563 - 6.571)
Colorado	457	93,127,301	5.152 (4.672 - 5.631)
Wyoming	54	10,296,319	4.818 (3.598 - 6.318)
New Jersey	837	165,736,728	4.582 (4.270 - 4.894)
District of Columbia	52	11,515,629	4.578 (3.409 - 6.019)
North Carolina	857	174,209,369	4.574 (4.265 - 4.882)
Louisiana	402	86,182,287	4.535 (4.087 - 4.982)
Iowa	302	57,386,432	4.523 (4.009 - 5.038)
Alaska	51	13,100,743	4.518 (3.283 - 6.066)
Minnesota	472	99,446,183	4.511 (4.101 - 4.921)

CI: Confidence Interval.

Disclosure: A. Rodriguez-Pla, None; **R. Simms**, None.

Abstract Number: 2918

Metabolic Signatures of Pathogenic T Cells in Medium and Large Vessel Vasculitis

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SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders III: Large Vessel Vasculitis Pathogenesis & Imaging

Session Type: ACR Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is an autoimmune vasculitis that causes aortic arch syndrome, blindnesss, and stroke. Embedded in granulomatous infiltrates, CD4 T cells persist over long periods in the inflamed vessel wall where they drive wall remodeling, intramural neoangiogenesis, intimal hyperplasia and luminal occulsion. To survive and function in a nonlymphoid tissue environment, T cells need access to nutrient supply and communicate with their surroundings through metabolic signals. Signaling pathways regulating the metabolic profile of tissue-residing T cells are currently unknown.

Methods: Metabolic gene expression was assessed in tissue biopsies from patients with temporal arteritis and in circulating CD4 T cells from patients with active GCA. Antibody blocking studies were performed in human artery-SCID chimeric mice. Effector cell differentiation was analyzed by detecting intracellular cytokines by flow cytometry. Intramural microvesssels and intimal thickness were quantified by immunohistochemistry.

Results: When compared to age-matched controls, CD4 T cells from GCA patients were characterized by high expression of the glucose transporter GLUT1 and induction of the glycolytic machinery ($P < 0.001$). Transcription factors relevant for glucose utilization, such as c-myc and HIF-1a, were strongly upregulated ($P < 0.001$). Tissue-residency of CD4 T cells was linked to $GLUT1^{hi}$ expression ($P < 0.001$). Upregulation of the metabolic machinery was dependent on CD28 signalinng via activation of the AKT signaling pathway. Costimulation through CD28 induced GLUT1 expression ($P < 0.01$), glycolytic enzymes ($P < 0.05$) and mitochondrial oxygen consumption ($P < 0.05$). Multiple disease-relevant processes required engagement of CD28 and enhanced glycolytic flux, including effector T cells differentiation into IFN-gamma producing Th1 cells and IL-21-producing Tfh cells, intramural neoangiogenesis and hyperplasia of the intimal layer. Notably, CD28 costimulation was needed to sustain $CD4^{+}CD103^{+}$ tissue-resident memory T cells that secure long-term persistence of vasculitic infiltrates.

Conclusion: CD4 T cells in GCA patients are metabolically reprogrammed, relying on massive upregulation of glucose uptake and breakdown. In the tissue microenvironment, unopposed CD28 costimulation enables optimal utilization of glucose. Pathogenic remodeling of the vessel wall is metabolically controlled, identifying new therapeutic opportunities through metabolic interference.

Disclosure: M. Akiyama, None; **H. Zhang**, None; **R. Watanabe**, None; **T. Maeda**, None; **G. Berry**, None; **J. Goronzy**, None; **C. Weyand**, Kiniska Pharmaceuticals, 2.

Abstract Number: 2919

Endothelial Protein C Receptor and Scavenger Receptor Class B Type 1 Negatively Regulate Vascular Inflammation and Are Major Autoantigens in Takayasu Arteritis

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SESSION INFORMATION

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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders III: Large Vessel Vasculitis Pathogenesis & Imaging

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Session Time: 11:00AM–12:30PM

Background/Purpose: Takayasu arteritis (TAK) is a chronic vasculitis which predominantly affects large vessels. Although anti-endothelial cell antibodies (AECA) had been reported to be involved in vascular inflammation in TAK,

their target antigens remained unclear. We had constructed an expression cloning system for specific identification of cell-surface antigens, which we named SARF. The aim of this study was to identify autoantigens expressed on the cell surface and to clarify their pathogenic relevance in TAK.

Methods: AECA activity against human umbilical vein endothelial cells (HUVEC) was measured and prototype AECA for SARF was determined. HUVEC cDNA library was inserted into rat myeloma cells by using retroviral vector, and cells expressing proteins derived from cDNA library of HUVEC were incubated with prototype AECA-IgG. Cells bound to AECA-IgG were sorted by flow cytometry, and inserted cDNA in sorted cells was analyzed to identify autoantigens. The prevalence of autoantibodies identified was measured among collagen diseases, and the clinical characteristics of patients with TAK were evaluated according to the presence of autoantibodies. To examine the pathogenic roles of identified autoantibodies, the activation of HUVEC and differentiation of Th17 cells were evaluated.

Results: We performed SARF by using nine TAK sera, and successfully completed in three patients. Four clones bound to the prototype AECA were established, and endothelial protein C receptor (EPCR) and scavenger receptor class B type 1 (SR-BI) were identified as novel autoantigens in TAK. Among 52 TAK patients, anti-EPCR or anti-SR-BI activity was observed in 18 (34.6%) or 19 (36.5%) patients, respectively, with minimal overlap. Their presence was mostly specific for TAK in collagen diseases. TAK was classified into 3 subtypes based on the activity of autoantibodies. Anti-EPCR positive group showed high prevalence of stroke, ulcerative colitis, and type II lesion. Anti-SR-BI positive group presented higher levels of inflammatory markers, type V lesion, and older age at onset. Aortic regurgitation (AR) was rare in anti-SR-BI group. Double-negative group presented higher rates of surgery for AR. In mechanistic studies, EPCR and SR-BI negatively regulated the upregulation of adhesion molecules on HUVEC upon stimulation. The expression of EPCR was induced upon Th17 differentiation, and its agonist suppressed Th17 differentiation. These functions of autoantigens were inhibited by autoantibodies, which resulted in the activation of endothelial cells and the promotion of Th17 differentiation.

Conclusion: EPCR and SR-BI were identified as novel autoantigens in TAK, and these autoantibodies were observed in 67.3% of TAK patients. These autoantibodies blocked the negative regulatory effects of their targets, and thus would contribute to the chronicity of vascular inflammation in TAK.

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Abstract Number: 2920

Comparison of Arterial Patterns of Disease in Takayasu's Arteritis and Giant Cell Arteritis

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Pennsylvania, Philadelphia, PA, [19]Department of Rheumatology, Auckland District Health Board, Auckland, New Zealand, [20]Mayo Clinic Rochester, Rochester, MN, [21]Mayo Clinic College of Medicine, Rochester, MN, [22]Norwich Medical School, University of East Anglia, Norwich, United Kingdom, [23]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) of the National Institutes of Health, Bethesda, MD, Bethesda, MD

SESSION INFORMATION

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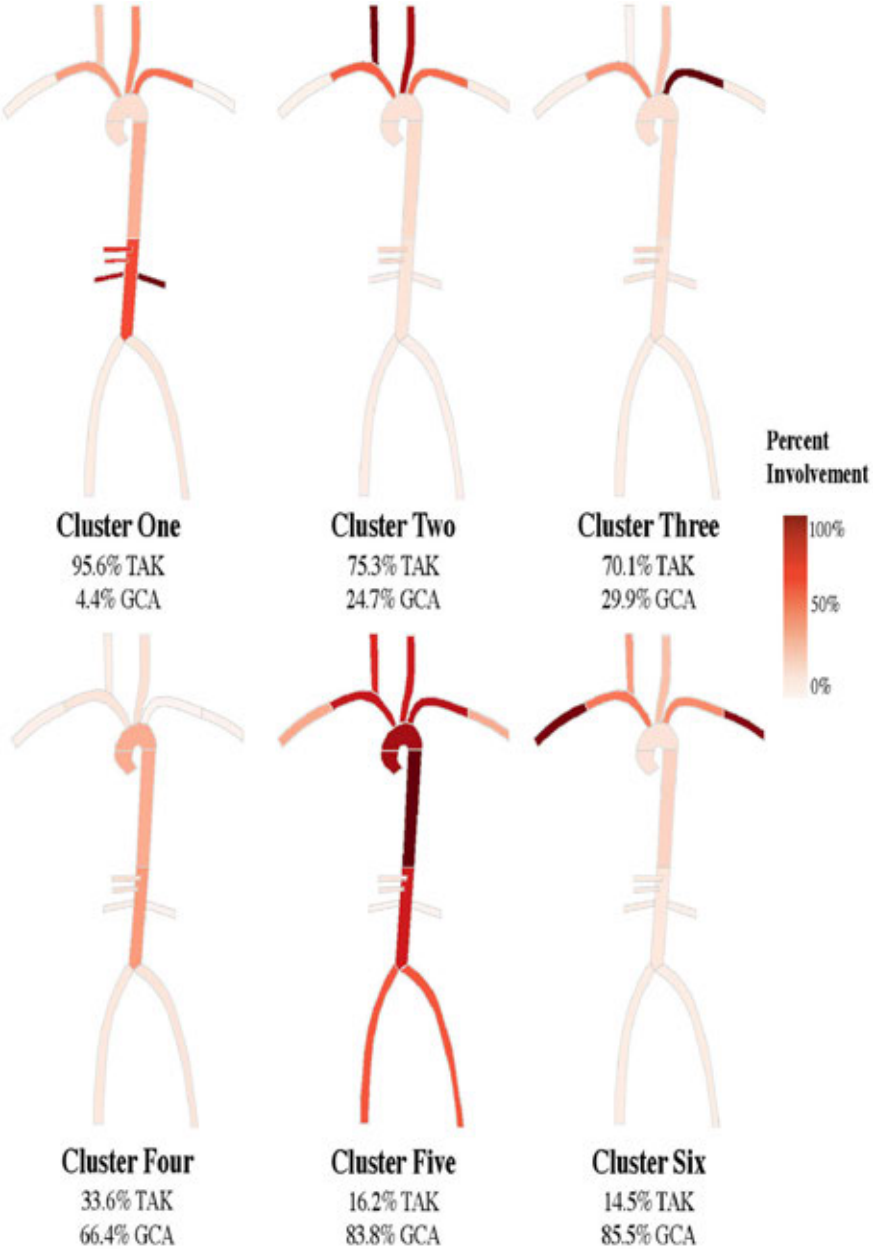

Heatmaps of the large arteries indicating the percent of patients in each cluster from the international cohort with involvement of the 11 arterial territories of interest (right and left carotid, subclavian, axillary, and renal arteries, mesenteric arteries, and descending and abdominal aorta). Increasingly darker red indicates an increasing percentage of patients in the cluster have involvement of the artery. The weighted proportion of patients with Takayasu's arteritis (TAK) and patients with giant cell arteritis (GCA) in each cluster are listed. Clusters One, Two, and Three were specific for TAK in the International (development) and North American (validation) cohorts. Clusters Four, Five, and Six were specific for GCA in the International cohort but only Clusters Four and Six was specific for GCA in the North American cohort.

Background/Purpose: Current classification criteria differentiate between Takayasu's arteritis (TAK) and giant cell arteritis (GCA), the two most common forms of large-vessel vasculitis, based primarily on clinical assessment, yet patients with TAK and GCA may differ in patterns of arterial disease. This study aimed to use computer-based algorithms to determine if patterns of arterial disease are useful to differentiate TAK from GCA with large-vessel involvement (LV-GCA).

Methods: Patients with TAK or LV-GCA were studied from four independent cohorts: a large, international cohort and three separate cohorts combined into one North America cohort. Case inclusion required evidence of large-vessel involvement, defined as stenosis, occlusion, or aneurysm by imaging or catheter-based angiography or ultrasound, or increased FDG uptake by positron-emission tomography (PET) in at least one of 11 specified arterial territories. K-means cluster analysis was performed to identify clusters of patients based on pattern of arterial involvement. Cluster groups were identified in the international cohort and independently validated in the combined North American cohort.

Results: A total of 1,068 patients were included (International: TAK=461, GCA=217; NA: TAK=225, GCA=165). Patients with TAK underwent angiography (95%), ultrasonography (28%), and/or PET imaging (14%). Patients with LV-GCA underwent angiography (50%), ultrasonography (52%), and/or PET imaging (58%). Six distinct clusters of patients were identified in the international cohort and validated in the North American cohort (Figure). Patients in Clusters One, Two, and Three were significantly more likely to have TAK, and patients in Clusters Four, Five, and Six were significantly more likely to have LV-GCA. Out of all study patients, involvement of the abdominal aorta and renal/mesenteric arteries was the most specific pattern for TAK (TAK: 134 (92%) vs GCA: 11 (8%), $p< 0.01$), while bilateral subclavian/axillary disease was the most specific pattern for GCA (GCA: 92 (80%) vs TAK: 23 (20%), $p< 0.01$). Among patients who underwent both angiography and PET, patients with TAK were more likely than patients with GCA to have damage by angiography without associated inflammation by PET (TAK: 52% vs GCA: 7%, $p< 0.001$), and patients with GCA were more likely than patients with TAK to have arterial FDG-uptake by PET without associated vascular damage (GCA: 80% vs TAK: 23%, $p< 0.001$).

Conclusion: These findings support the incorporation of arterial patterns of disease into classification criteria for large-vessel vasculitis and highlight shared and divergent vascular phenotypes between TAK and GCA.

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Abstract Number: 2921

High Resolution 3D Fast Spin-Echo T1 Black-Blood Imaging for the Diagnosis of Giant Cell Arteritis

Christine rodriguez,[1] Wagih Ben Hassen,[1] Pierre Seners,[2] Catherine Oppenheim,[1] and **Alexis Régent** [3], [1]Département d'imagerie, pôle Neuro Sainte Anne, GHT Paris – Psychiatrie & Neurosciences, 1 rue Cabanis, 75014 Paris, Paris, Ile-de-France, France, [2]Service de neurologie, pôle Neuro Sainte Anne, GHT Paris – Psychiatrie & Neurosciences, 1 rue Cabanis, 75014 Paris, Paris, Ile-de-France, France, [3]National Referral Center for Rare Systemic Autoimmune Diseases Paris Cochin, Paris, France

SESSION INFORMATION

Session Date: Wednesday, November 13, 2019

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders III: Large Vessel Vasculitis Pathogenesis & Imaging

Session Type: ACR Abstract Session

Session Time: 11:00AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is the most common form of vasculitis of large arteries affecting people older than 50 years. Temporal artery biopsy (TAB) is still considered as the gold standard for GCA diagnosis but it is invasive and its sensitivity ranges from 39 to 86%.Color Doppler Ultrasonography and PET-scanner have been proposed as alternative methods for GCA diagnosis but are not widespread in routine clinical practice. Recent recommendations suggest the use of MRI as an alternative method for GCA diagnosis. To our knowledge, there is no evaluation of 3D sequences in the diagnosis of GCA

Methods: We decided to evaluate the diagnostic performance of pre and post-contrast fat-suppressed 3D-Fast Spin echo T1-weighted black-blood magnetic resonance imaging (CUBE-T1), of the external carotid in the diagnosis process of GCA.

Results: Thirty-two patients (7 men, 25 women, mean±SD age 70.2±12.1 years) were included. The final diagnosis, blinded to CUBE T1 results, was GCA for 10 of them. 3D CUBE T1 displayed the arteries wall clearly, allowing an easy identification of parietal enhancement and the 3D TOF coregistration was helpful in image analysis. Intra- and inter-observer agreement for mural enhancement on CUBE T1 was 1 and 0.84, respectively.

Height of the 10 patients with GCA had a strong mural enhancement in CUBE-T1 (Figure 1), while none of the 22 patients without GCA had mural enhancement in MR images. Therefore, sensitivity was 80% and specificity was 100 %. The positive predictive value of post-contrast CUBE T1 was 100% and the negative predictive value was 92%. In our cohort, only 6 of the 10 GCA patients had a positive TAB. Therefore sensitivity of TAB was 60%. If TAB was used as the reference standard, MRI yielded a sensitivity of 100%. Two patients with a final diagnosis of GCA despite normal TAB had an arteritis on MRI and vessel enhancement was observed in occipital artery only for one patient.

Conclusion: We here demonstrate the feasibility and accuracy of a 3D post-contrast CUBE-T1 in the diagnosis of GCA. Indeed, we observed a sensitivity of 80%, which is higher than the 64.1% that was observed by Rhéaume et al. with 2D sequences on his series of 172 patients. We hypothesize that 3D MRI acquisition allowing multiplanar reconstructions together with the 3D TOF coregistration might explain the higher sensitivity and the excellent reproducibility. The reproducibility and short scan duration is a clear advantage of CUBE-T1 sequences with sub-millimetric voxels acquisition. Additional studies are required to confirm our preliminary results.

Disclosure: C. rodriguez, None; **W. Ben Hassen**, None; **P. Seners**, None; **C. Oppenheim**, None; **A. Régent**, None.

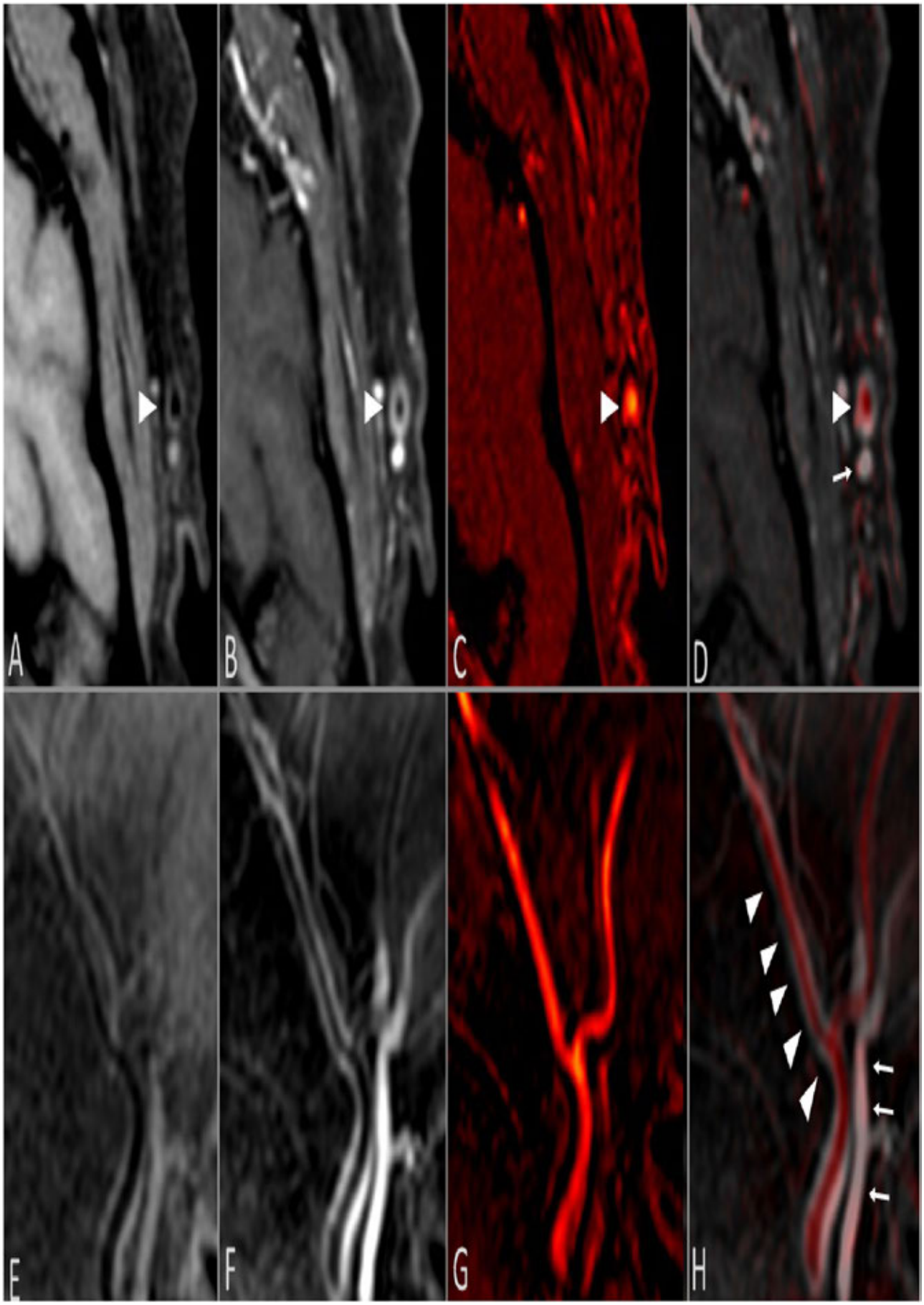

FIGURE 1. Mural enhancement of the left temporal artery in giant cell arteritis. Axial and sagittal reconstructions of CUBE T1 sequence before (A and E respectively) and after contrast injection (B and F respectively). 3D TOF sequence in axial and sagittal plane (C and G respectively) coregistered with post-contrast CUBE T1 sequence (D and H respectively), allowing a differentiation between the temporal artery in red (arrowhead) (C, G) and the temporal vein (arrows) (D, H). Strong mural enhancement of the temporal artery (arrowhead) (B, D, F, H).

Abstract Number: 2922

Imaging Acquisition Technique Influences Interpretation of Positron Emission Tomography Vascular Activity in Large-Vessel Vasculitis

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Background/Purpose: ^{18}F-flurodeoxyglucose (FDG) positron emission tomography (PET) is one of several imaging modalities used in the assessment of patients with large-vessel vasculitis (LVV). Conventionally PET images are obtained 1 hour after radiotracer injection; however, delayed imaging may be more sensitive to detect vascular inflammation.

The objectives of this study were to: 1) determine the impact of imaging acquisition time on interpretation of disease activity on FDG-PET in LVV and 2) assess the relationship between clinical features and image acquisition time.

Methods: An observational cohort of patients with giant cell arteritis (GCA) or Takayasu's arteritis (TAK) was prospectively recruited. Patients fulfilled the 1990 ACR Classification Criteria for TAK or modified 1990 ACR Criteria for GCA. Following injection, whole-body FDG-PET magnetic resonance imaging (MRI) was performed at one-hour uptake time followed by FDG-PET computed tomography (CT) at two-hours uptake time. A single reader with vascular imaging expertise interpreted the PET studies for evidence of active vasculitis. Patients were categorized as 1) both time points active (dual active), 2) both time points inactive (dual inactive), 3) only the one-hour time point active (early time point active), and 4) only the two-hour time point active (delayed active). Imaging and clinical assessments were performed blinded to each other within a 24-hour period.

Agreement was assessed by percent agreement, Cohen's kappa, and McNemar's test. Nominal logistic regression was used to study factors associated with the PET categories, including age, BMI, gender, LVV type, clinical status (active/remission), ESR, CRP, and treatment status (yes/no). Significant variables in the univariable model were included in multivariable regression.

Results: 79 patients (GCA=44, TAK=35) contributed 168 paired one and two-hour PET studies. A total of 94 out of 168 scans (56%) were interpreted as active at the one-hour time point, and 129 scans (77%) were interpreted as active at the two-hour time point ($p< 0.01$). Scans were interpreted as both active in 90 cases and both inactive in 35 cases (percent overall agreement=74%, cohen's kappa=0.45(fair agreement)). In discordant cases, delayed active only was observed in 39 cases versus early active only in 4 cases (McNemar's $p< 0.01$).

Associations between clinical variables and PET activity categories were also evaluated. Using multivariable nominal regression, clinically active disease was significantly more common in patients in the delayed active group (Odds

Clinical Features Associated with PET Activity Categories

Predictor Variable	Odds ratio	95% Confidence Interval	P-value
Dual active			
Clinically active disease	1.71	1.06—2.93	0.04
CRP (per 1mg/L)	1.05	1.00—1.14	0.12
Female gender	1.13	0.68—1.85	0.62
LVV type (GCA)	1.33	0.86—2.04	0.19
Delayed active only			
Clinically active disease	1.94	1.13—3.53	0.02
CRP (per 1mg/L)	1.01	0.92—1.08	0.88
Male gender	1.67	1.00—2.86	0.05
LVV type (TAK)	1.31	0.81—2.14	0.28

Ratio 1.94, 95%CI 1.13 – 3.53; p=0.02) and the dual active group (Odds Ratio 1.71, 95%CI 1.06 – 2.93; p=0.04) compared to the dual inactive group as shown in *Table 1*.

Conclusion: Imaging protocol significantly influences interpretation of PET activity in LVV. A substantial proportion of patients with LVV had PET activity only detected by delayed imaging. These patients were significantly more likely to have concomitant clinically-determined active disease. Imaging acquisition protocols should be standardized in LVV and encourage delayed imaging.

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Abstract Number: 2923

Clinical Subsets in Giant Cell Arteritis

K Bates Gribbons,[1] Cristina Ponte,[2] Anthea Craven,[3] Joanna Robson,[4] Ravi Suppiah,[5] Richard Watts,[6] Raashid Luqmani,[3] Peter Merkel,[7] and Peter C. Grayson[8], [1]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [2]Department of Rheumatology, Hospital de Santa Maria, Lisbon, Portugal, [3]University of Oxford, Oxford, United Kingdom, [4]Faculty of Health and Applied Sciences, University of the West of England, Bristol, United Kingdom, [5]Department of Rheumatology, Auckland District Health Board, Auckland, New Zealand, [6]Norwich Medical School, University of East Anglia, Norwich, United Kingdom, [7]University of Pennsylvania, Philadelphia, PA, [8]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) of the National Institutes of Health, Bethesda, MD, Bethesda, MD

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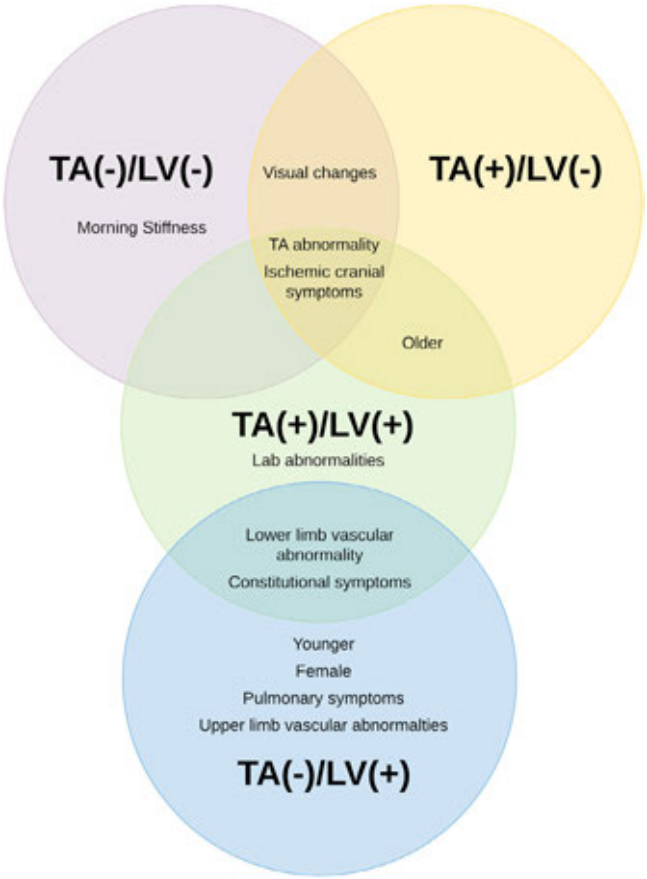
Background/Purpose: Giant cell arteritis (GCA) is a clinically heterogeneous disease. Disease subsets based upon cranial versus extracranial artery involvement have been proposed. The study objective was to determine if GCA subsets are associated with distinct clinical profiles or merely reflective of differential diagnostic assessment.



Clinical and demographic associations of patients with giant cell arteritis (GCA). Patients with TA(-)/LV(-) have a clinical diagnosis of GCA without evidence of temporal artery (TA) or large vessel (LV) involvement. Patients with TA(+)/LV(-) have evidence of TA involvement without evidence of LV involvement on imaging. Patients with TA(+)/LV(+) have evidence of both TA involvement and LV involvement on imaging. Patients with TA(-)/LV(+) have evidence of LV involvement on imaging without evidence of TA involvement.

Methods: Patients were included from a large international cohort with standardized data collection. Patients with a confirmed diagnosis of GCA were divided into four subsets based on a temporal artery (TA) abnormality [definite vasculitis by biopsy (TAB) or halo-sign positive ultrasound (TA-US)] and/or imaging evidence of large-vessel (LV, aorta and/or its primary branches) involvement on imaging: 1) patients with evidence of *both* LV involvement and TA abnormality (**TA(+)/LV(+) GCA**); 2) patients with TA abnormality without LV involvement (**TA(+)/LV(-) GCA**); 3) patients with LV involvement without TA abnormality (**TA(-)/LV(+) GCA**); and 4) patients with a clinical diagnosis of GCA without LV involvement or TA abnormality (**TA(-)/LV(-) GCA**).

Results: Out of 941 patients, 329 (35%) had TA-US, 705 (75%) had TAB, 536 (57%) had LV imaging, and 431 (46%) had both LV imaging and TA-US/TAB. GCA subsets had distinct clinical profiles (Figure). TA(+)/LV(-) GCA (n=480) had the highest burden of visual changes (e.g. amaurosis fugax, sudden ongoing visual loss; $p< 0.01$), other cranial ischemic symptoms (e.g. jaw claudication, scalp tenderness; $p< 0.01$), and TA abnormalities on physical examination ($p< 0.01$), with little evidence of other vascular exam abnormalities. Patients with TA(-)/LV(-) GCA (n= 245) were nearly indistinguishable from TA(+)/LV(-) GCA with a high prevalence of visual changes and other cranial ischemic symptoms ($p< 0.01$) but also had a high burden of musculoskeletal symptoms ($p=0.02$). Patients with TA(-)/LV(+) GCA (n=116) were younger ($p< 0.01$) and more frequently female ($p< 0.01$), with a lower burden of visual changes ($p< 0.01$) and cranial ischemic symptoms ($p< 0.01$), and a higher burden of vascular abnormalities (e.g. upper/lower limb claudication/pulse abnormality, arterial bruit, blood pressure differences; $p< 0.01$), constitutional (e.g. weight loss, night sweats; $p< 0.01$), and pulmonary symptoms (e.g. non-productive cough, dyspnea; $p< 0.01$). Patients with TA(+)/LV(+) GCA (n=100) were older and more likely to be male with a high prevalence of cranial ischemic symptoms like TA(+)/

LV(-) GCA and a high prevalence of lower-limb vascular abnormalities and constitutional symptoms like TA(-)/LV(+) GCA. Patients with TA(+)/LV(+) GCA also had the highest prevalence of lab abnormalities ($p< 0.01$). When analyses were restricted to 431 patients who had both TA assessment (TAB or TA-US) and LV assessment by imaging, the four subsets had similar patterns of clinical associations.

Conclusion: Patients with GCA can be divided into subsets based on temporal and extracranial artery involvement. Each subset has a unique clinical profile that is not explained by differences in diagnostic assessment. Longitudinal studies comparing immunologic differences and clinical outcomes across these subsets are warranted.

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Abstract Number: 2924

Does the Degree of Decline in Walking Speed Predict Mortality Risk Beyond the Present Level of Walking Speed in Knee Osteoarthritis?

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SESSION INFORMATION
Session Date: Wednesday, November 13, 2019
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Session Time: 11:00AM–12:30PM

Figure: Kaplan-Meier survival curves for adults with knee OA who were classified into one of four groups depending on the walking speed at one time-point (the 12-month visit) and degree of decline over the previous year (from baseline to 12-month visit).

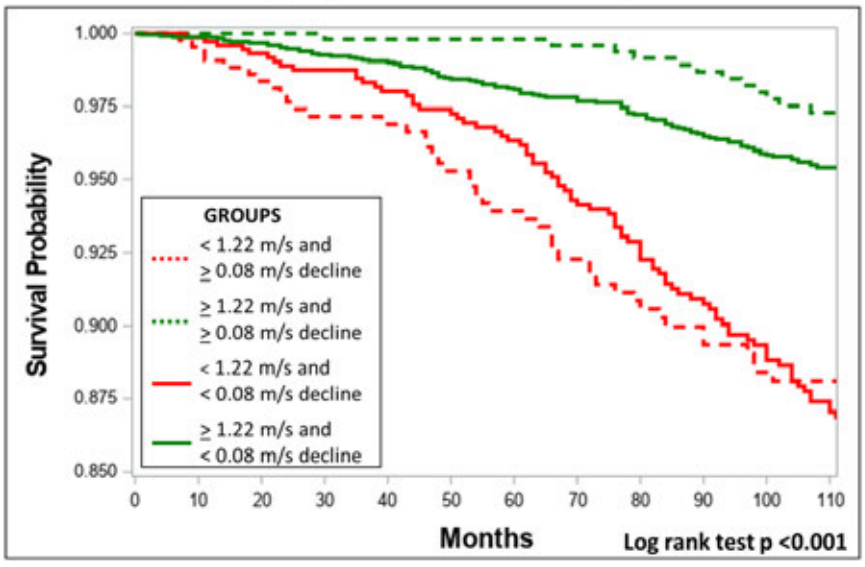

Table: Association of walking speed measured at one time-point and decline over past one year with the risk of mortality over 9 years among all the study participants (N=4229).

	<1.22 m/s and ≥0.08 m/s decline	≥1.22 m/s and ≥0.08 m/s decline	< 1.22 m/s and <0.08 m/s decline	≥1.22 m/s and <0.08 m/s decline
Sample size (N)	439	532	751	2507
Walking speed (m/s), Mean±SD				
one year prior to index date^	1.24±0.15	1.56±0.16	1.07±0.14	1.38±0.17
at index date^	1.06±0.15	1.41±0.14	1.10±0.11	1.45±0.16
Deaths % [n]	11.6 [51]	2.8 [15]	11.7 [88]	4.6 [116]
Unadjusted HR [95% CI]	**2.88 [2.07, 4.00]**	0.61 [0.34, 1.05]	**2.79 [2.12, 3.69]**	1.00 [Reference]
*Adjusted HR [95% CI]	**2.08 [1.46, 2.96]**	0.57 [0.32, 1.01]	**1.96 [1.44, 2.66]**	1.00 [Reference]

^ This study's index date is the 12-month follow-up OAI visit
*Adjusted for baseline age, BMI, sex, race, education, comorbidities, the presence of depression (≤ vs. >16), and symptomatic knee OA (yes or no), defined as presence of Kellgren–Lawrence grade ≥ 2 on x-ray in one or both knees, and pain, aching, or stiffness on most days of a month during the previous year.

Background/Purpose: Slow walking speed (WS) is a risk factor for mortality in well-functioning older adults and speeds slower than (<) 1.22 meters per second (m/s) are a risk factor for poor health outcomes in knee osteoarthritis (OA). WS is known to decline with age, with some declining faster than other, though it is unclear if the rate of decline in WS is additionally relevant for mortality risk in knee OA. If so, considering the degree of decline over a prior year in addition to the present level of WS may be important. Therefore, the purpose of this study was to investigate whether WS at one time-point, degree of decline in WS over past one year, or both predict mortality risk over 9 years in knee OA.

Methods: We used data from the Osteoarthritis Initiative. WS was measured from a 20-m walk test at baseline and the 12-month visit. The index date for this analysis is the 12-month visit. Walking < 1.22 m/s represents the inability to cross a street with a timed crosswalk, and change >0.08 m/s is considered to be a clinically meaningful decline. We classified people into one of four groups depending on the WS at one time-point (the 12-month visit) and degree of decline over the previous year (from baseline to 12-month visit): [1] < 1.22 m/s and >0.08 m/s decline, [2] at least (>) 1.22 m/s and >0.08 m/s decline, [3] < 1.22 m/s and < 0.08 m/s decline or [4] >1.22 m/s and >0.08 m/s decline. Mortality was assessed up to 9 years of follow-up. We used Kaplan-Meier curves to determine the survival probability for the four groups. We examined the association of the 4 groups with mortality using Cox proportional hazards regression, adjusting for potential confounders.

Results: Of 4229 participants in the analytic sample (58% female, age 62.3±9.2 years, BMI 28.5±4.8 kg/m2), 6% (n=270) died over 9 years. Groups with WS < 1.22 m/s at one time-point were at higher risk of mortality irrespective of history of decline in WS (Figure). Those walking < 1.22 m/s with and without decline had 108% and 96% greater risk of mortality compared with those walking >1.22 m/s without meaningful decline over previous year (Table). Those walking ≥1.22 m/s with decline had a lower risk of mortality than the group walking ≥1.22m/s without meaningful decline in WS, likely related to the latter having started with a higher WS at baseline.

Conclusion: Walking slower than 1.22 m/s was associated with increased mortality risk, irrespective of degree of decline in WS in adults with knee OA. Those walking at least 1.22 m/s who had a meaningful decline in WS over the prior year, did not have increased risk of mortality, and in fact had nonsignificant lower risk, suggesting a potential threshold effect such that WS assessed at one time-point may be sufficient to gauge mortality risk.

Disclosure: H. Master, None; **T. Neogi**, MerckSerono, 5, Novartis, 5; **L. Michael**, None; **L. Thoma**, None; **D. Voinier**, None; **M. Christiansen**, None; **J. Jakiela**, None; **L. Neely**, None; **D. White**, None.

Abstract Number: 2925

The Effects of Leisure Time Sitting and Sitting at Work on Worsening Radiographic Knee Osteoarthritis over Two Years: Data from the Osteoarthritis Initiative

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Background/Purpose: Sitting is associated with many poor health outcomes, which may include knee osteoarthritis (OA). When the knee is subject to minimal load, knee cartilage becomes thinner and may be more susceptible to damage. Thus, people who spend more time in **sitting**, whether during leisure time or during work, may be at greater risk for worsening structural damage in the knee. We examined the relation of time sitting to worsening radiographic OA over 2 years in a cohort of adults with or at risk for knee OA, assessing time spent sitting during leisure time and at work separately. We hypothesized that people with more leisure-time sitting **and** more sitting at work are at greater risk for worsening radiographic OA.

Methods: We used data from the Osteoarthritis Initiative (OAI). At study baseline, participants reported their leisure time sitting (hours/day) via the Physical Activity Scale for the Elderly (PASE). We dichotomized **leisure time sitting** as < 4 hours/day vs ≥4 hours/day, as this was the approximate mean for the sample. Participants also reported their **work activities** via the PASE as: sitting, sitting/standing/walking, walking/handling < 50 lbs, or walking/handling >50 lbs. We dichotomized work activities as "sitting only" vs "sitting and other activities". All OAI participants had bilateral knee radiographs obtained and scored for Kellgren and Lawrence (KL) grade at baseline, 1-year, and 2-year follow-up visits. We defined our outcome, **worsening radiographic OA over 2 years**, as an increase in KL grade from baseline to end of follow-up, including within-grade changes. We examined the relation of leisure time sitting with worsening radiographic OA using binomial regression with GEE, adjusting for potential confounders (age, sex, race, body mass index [BMI], and self-reported leisure time walking [hours/day]). We then repeated analyses of the effect of leisure time sitting on worsening ROA among those whose work involves "sitting only" and separately among those whose work involves "sitting and other activities".

Table: Siting and risk of worsening radiographic OA over 2 years.

	All OAI Participants n=5632 knees		Work: Primarily "Sitting" n=1641 knees		Work: "Sitting and Other Activities" n=3991 knees	
	% *(n/N)*	RR* *[95%CI]*	% *(n/N)*	RR* *[95%CI]*	% *(n/N)*	RR* *[95%CI]*
Leisure Time Sitting: <4 hours/day	9.2% (349/3804)	1.0 [REF]	7.0% (67/954)	1.0 [REF]	9.9% (282/2850)	1.0 [REF]
Leisure Time Sitting: ≥4 hours/day	11.3% (206/1828)	1.17 [0.98-1.39]	10.6% (73/687)	1.44 [1.01-2.06]	11.6% (133/1141)	1.12 [0.91-1.38]

*Adjusted for age, sex, race, BMI, and self-reported leisure time walking.

Results: We included 5632 knees in our analysis (2826 participants, BMI: 28.4 ± 4.8 kg/m2, age: 59.4 ± 8.6 years, 57% women, 83% white). People who spent ≥ 4 hours/day in leisure time sitting had greater risk (1.17[0.98-1.39]) of worsening radiographic OA over 2 years, compared with those who spent < 4 hours/day in leisure time sitting. Among participants who reported "sitting only" at work, those who spent ≥4 hours/day in leisure time sitting had greater risk (1.44[1.01-2.06] of worsening radiographic OA compared with those who spent < 4 hours/day in leisure time sitting. Conversely, among participants who reported "sitting and other activities" at work, there was no relationship between leisure time sitting and worsening radiographic OA (see Table).

Conclusion: People who spend at least 4 hours/day of leisure time sitting, and also primarily sit at work, may be at increased risk for worsening radiographic OA. Reducing leisure time sitting, and potentially reducing sitting at work, may be targets for intervention in people with or at risk for knee OA.

Disclosure: D. Voinier, None; **T. Neogi**, MerckSerono, 5, Novartis, 5; **H. Master**, None; **L. Thoma**, None; **M. Christiansen**, None; **J. Jakiela**, None; **L. Neely**, None; **D. White**, None.

Abstract Number: 2926

Knee Injury and Transitions Among States of Knee Osteoarthritis in the Johnston County Osteoarthritis Project: A Multi-State Time-To-Event Modeling Approach

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SESSION INFORMATION
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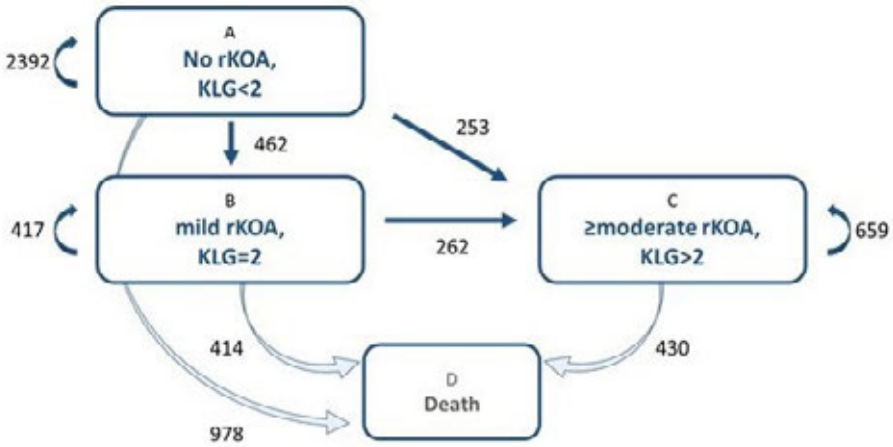

Figure 1. Four-state progressive model for knee OA status. The number of times each pair of transition states was observed at successive follow-up times is indicated next to its respective transition arrow. A curved arrow beside a state (A, B, or C) indicates no transition.

State transition	Normal	Overweight	Obese Class I	Obese Class II or III
A No rKOA → **B** mild rKOA	1.14 (0.60, 2.18)	1.29 (0.87, 1.90)	1.03 (0.65, 1.64)	*1.73 (0.96, 3.15)*
B mild rKOA → **C** ≥moderate rKOA	1.13 (0.43, 3.01)	1.45 (0.86, 2.44)	0.69 (0.41, 1.16)	0.91 (0.56, 1.47)
A No rKOA → **C** ≥moderate rKOA	1.05 (0.13, 8.81)	*3.38 (0.99, 11.5)*	*2.36 (0.99, 5.65)*	0.74 (0.14, 3.97)

*Adjusted for age, sex, race, self-reported diabetes, and self-reported cardiovascular disease.

Table 1. Adjusted* hazard ratios and 95% confidence intervals of the association of knee injury and radiographic knee osteoarthritis (rKOA) transitions for body mass index categories on modeled transition states, over the full follow-up period of 18 years.

Background/Purpose: Musculoskeletal injury is a known risk factor for osteoarthritis (OA). Cumulative effects of comorbid conditions on the association of injury and OA have not been previously examined. The purpose of this study was to clarify associations between knee injury and radiographic knee osteoarthritis (rKOA) and determine whether associations vary by sex, race, body mass index (BMI), diabetes mellitus (DM), and cardiovascular disease (CVD).

Methods: Data were from 4093 participants of the Johnston County Osteoarthritis Project who were enrolled during 1991-1997 (Original Cohort) and 2003-2004 (Enrichment Cohort). Data were from baseline and up to three follow-up study visits (over ~18 years). All knee radiographs were read for Kellgren-Lawrence grade (KLG) of 0-4. Using Markov multi-state models in a time-to-event approach, a progressive model included states of: (A) no rKOA (KLG< 2), (B) mild rKOA (KLG=2), and (C) ≥moderate rKOA (KLG >2 or total knee replacement; Figure 1). Hazard ratios and 95% confidence intervals (HR [95% CI]) were estimated to determine associations between knee injury and rKOA transitions, examining six variables as potential effect modifiers or covariates: age, sex, race (White, African-American), BMI (normal [< 25 kg/m2], overweight [25-< 30 kg/m2], obese class I [30-< 35 kg/m2], and obese class II [35+ kg/m2]), self-reported DM, and self-reported CVD.

Results: At baseline, participants had a mean age of 61 years (SD±10), were 63% women, and were 34% African American; 19% reported a prior knee injury, 40% were obese,13% reported DM, and 22% reported CVD. During the study period, 2738 participants had no transitions. In adjusted models, the hazards of incident mild and ≥moderate rKOA were higher among those with baseline knee injury (1.25 [0.99, 1.59] and 1.71 [0.99, 2.96], respectively). Knee injury was associated with incident mild rKOA among Whites (1.38 [1.04, 1.81]) but not among African Americans (0.93 [0.57, 1.51]). Associations did not differ between any transition states in interactions with sex or DM. Knee injury was not associated with incident rKOA transitions among individuals with normal BMI, but positive associations were observed in some higher BMI categories (Table 1). Among those without CVD, knee injury was associated with rKOA (1.48 [1.13, 1.93]). Among those with CVD, knee injury was not associated with rKOA but was associated with ≥moderate rKOA (4.15 [1.12, 15.4]).

Conclusion: The relationship of knee injury and rKOA transitions differs by race, CVD, and BMI. Maintaining a normal BMI in the setting of knee injury may mitigate the impact of a joint injury upon development of knee OA.

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Abstract Number: 2927

Dietary Patterns and Symptomatic Progression of Knee Osteoarthritis: Data from the Osteoarthritis Initiative

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Table 1. Factor Loading Matrix (correlations) for two Major Dietary Patterns in the Osteoarthritis Initiative

Foods or food groups	Western*	Prudent*
French fries	0.59	
Processed meats	0.58	
Refined grains	0.57	
Red meats	0.55	
Poultry	0.42	
Pizza	0.41	
Margarine	0.39	
Sugar-containing beverages	0.39	
Eggs	0.37	
Snacks	0.36	
Desserts and sweets	0.33	
Salad dressings	0.33	
High-fat dairy products	0.33	
Vegetables		0.77
Legumes		0.67
Fruit		0.55
Fish		0.52
Whole grains		0.47
Tomatoes		0.47
Potatoes other than French fries	0.30	0.37

*Absolute values of <0.30 were excluded from the table for simplicity.

Table 2. Odds ratios (OR) and 95% confident intervals (CI) for symptomatic progression of knee OA according to quartiles of dietary pattern scores

		Model 1[1]			Model 2[2]		
		OR (95% CI)	*P*	*P* trend	OR (95% CI)	*P*	*P* trend
Western[3]	Q1	1.00	Ref	**<0.01**	1.00	Ref	<0.01
	Q2	1.12 (0.94, 1.32)	0.21		1.02 (0.86, 1.21)	0.82	
	Q3	**1.23 (1.02, 1.47)**	**0.03**		1.11 (0.93, 1.34)	0.26	
	Q4	**1.44 (1.15, 1.82)**	**<0.01**		**1.37 (1.08, 1.72)**	**<0.01**	
Prudent[3]	Q1	1.00	Ref	0.11	1.00	Ref	0.12
	Q2	0.96 (0.81, 1.14)	0.64		0.96 (0.81, 1.13)	0.61	
	Q3	**0.83 (0.70, 0.99)**	**0.03**		**0.83 (0.70, 0.99)**	**0.04**	
	Q4	**0.85 (0.70, 1.03)**	**0.09**		0.90 (0.74, 1.08)	0.26	
Western - Prudent[3]	Q1	1.00	Ref	**<0.01**	1.00	Ref	**<0.01**
	Q2	**1.20 (1.02, 1.42)**	**0.03**		1.14 (0.96, 1.35)	0.13	
	Q3	**1.31 (1.11, 1.56)**	**<0.01**		**1.20 (1.01, 1.42)**	**0.04**	
	Q4	**1.39 (1.17, 1.66)**	**<0.01**		**1.31 (1.10, 1.56)**	**<0.01**	

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Background/Purpose: Osteoarthritis (OA) is a major source of disability worldwide yet dietary exposures that might be associated with its progression have not received significant research attention. We aimed to examine the prospective association of major dietary patterns derived by principal component analysis (PCA) with symptomatic progression of knee OA.

Methods: From the Osteoarthritis Initiative (OAI), 2,757 individuals with mild to moderate knee OA in at least one knee (defined as Kellgren-Lawrence (KL) grade of 1, 2, or 3) at baseline were followed annually up to 72 months. Dietary intake was assessed with a Block Brief Food Frequency Questionnaire completed at baseline. Two dietary patterns were identified by PCA: the prudent pattern characterized by high intakes of fruit/vegetables, legumes, whole grains, fish, etc.; the Western pattern characterized by high intakes of red / processed meats, refined grains, French fries, etc. (Table 1). A combined score was calculated as the difference between the Western and prudent pattern scores to evaluate the overall dietary quality since the two patterns are uncorrelated. We categorized the Western Ontario & McMaster Universities Arthritis Index (WOMAC) pain, disability and total scores at each time point into 5 grades: (zero and quartile thresholds based on baseline non-zero scores). Symptomatic progression, defined as either an increase in WOMAC grade or remaining in one of the two highest WOMAC grades, was evaluated at each follow-up time point. Generalized linear mixed models for repeated binary responses were developed to evaluate the associations after adjusting for age, sex, race, baseline K-L grades, injury/surgery, depression, pain medications and total energy intake. BMI and weight changes from baseline were additionally adjusted in separate models to assess the potential mediation effect.

Results: The progression increased significantly with higher Western pattern quartiles in a dose-response fashion (p trend < 0.01) (Table 2). In contrast, symptomatic knee OA progression generally decreased with a higher score of prudent dietary pattern. Consistent with a Western pattern, we observed a strong dose-response relationship between the combined score, which indicated not only high consumption of a Western diet but also low consumption of a prudent diet, and symptomatic knee OA progression (p trend < 0.01). The observed associations generally remained after additionally adjusting for BMI and weight change from baseline.

Conclusion: Adherence to a Western dietary pattern was associated with increased symptomatic knee OA progression, while following a prudent dietary pattern was associated with reduced knee OA progression. For participants already diagnosed with knee OA, eating a healthy diet rich in fruits, vegetables, fish, whole grains and legumes, lower in red/processed meats, refined grains and French fries, may slow symptomatic disease progression.

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Associations of Socioeconomic Status with Rheumatoid Arthritis (RA) Progression in African Americans with Early Disease

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Table 1. Baseline Characteristics in the Consortium for the Longitudinal Evaluation of African Americans with Early Rheumatoid Arthritis Registry (CLEAR) (n=194)

Characteristic	Baseline
Demographics	
Age, Mean (Std Dev)	51.07 (12.3)
Female, N (%)	166 (85.6%)
Months of Disease Duration, Mean (Std Dev)	14.05 (7.2)
Years of Follow up, Mean (Std Dev)	4.09 (0.7)
On Methotrexate and/or Leflunomide, N (%)	125 (64.4%)
Number of Comorbidities (Std Dev)	3.09 (2.2)
BMI, Mean (Std Dev)	31.83 (7.5)
Ever Smoker, N (%)	107 (55.2%)
SES Measures	
< HS Education, N (%)	58 (29.9%)
Household Income <$30k, N (%)	133 (68.6%)
Doesn't Own Home, N (%)	94 (48.5%)
Non-Professional Occupation, N (%)	101 (52.1%)
Block Group Poverty ≥20%, N (%)	92 (47.4%)

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Background/Purpose: In prior cross-sectional analyses of African Americans (AA) with RA, we observed that low education, income and home ownership were associated with clinical damage and patient reported outcomes (PROs) among those with mean disease duration of 7.8 years. However, when restricted to those with disease duration of < 2 years, associations with PROs remained, but were no longer observed with damage, most likely due to the low damage scores in individuals with early disease. Therefore, we hypothesize that socioeconomic status (SES) measures may be related to clinical progression and PRO worsening in AA with early RA.

Methods: We conducted analyses using data from 194 individuals with RA who completed a follow-up at 5 years of disease duration. Patients who had been diagnosed in the previous 2 years were enrolled from 5 medical centers in the southeastern US. SES measures were educational attainment (< high school diploma [< HS EDUC], or ≥HS); occupation (professional or not [Non-Pro OCC]); home ownership (yes or non-HOME); annual household income (≤$30,000 [≤$30K INC] or >$30K); and percent block group poverty (BGP ≥20% or < 20%). Outcomes were based on radiographs (erosion and JSN score) and PROs (Health Assessment Questionnaire [HAQ], self-rated pain and fatigue from visual analog scales [VAS] and the Rheumatology Attitudes Index [RAI]). Progression was defined as those who

Table 2. Outcome measures over time in the Consortium for the Longitudinal Evaluation of African Americans with Early Rheumatoid Arthritis Registry (CLEAR) (n=194)

	Baseline	60 Months
Patient Reported Outcomes		
HAQ Score, Mean (Std Dev)	1.39 (0.8)	1.25 (0.8)
Pain VAS, Mean (Std Dev)	6.10 (3.0)	5.82 (3.1)
Fatigue VAS, Mean (Std Dev)	5.89 (3.1)	5.61 (3.4)
RAI Score, Mean (Std Dev)	2.89 (1.1)	2.60 (1.0)
Radiographic Disease Scores		
Erosion Score, Mean (Std Dev)	1.27 (3.8)	2.12 (7.6)
JSN Score, Mean (Std Dev)	1.79 (5.0)	5.29 (12.6)

were in the highest quintile of disease progression (top 20% of increases in severity of outcome scores): erosions ≥1, JSN ≥7, HAQ ≥0.37, Pain and Fatigue VAS ≥3, RAI ≥0.4. We multiply imputed missing values of covariates. Multi-level logistic regression models with study site considered as a random effect were used to estimate odds ratios (OR) and 95% confidence intervals (CI) for the association between SES measures at baseline and progression. All models were adjusted for age, sex, BMI, number of comorbidities, smoking, disease duration at study entry, methotrexate/leflunomide use, and were simultaneously adjusted for other SES measures.

Results: Baseline demographics are shown in Table 1. At 5 years disease duration, mean outcome scores tended to increase for both erosion scores and JSN scores, but decreased for PROs (Table 2). We did not observe any association between SES measures and either erosion or JSN score progression (Table 3). However, < HS EDUC and Non-Pro OCC were both associated with worsening pain VAS, while non-HOME was inversely associated with worsening pain VAS, and non-Pro OCC was inversely associated with worsening RAI.

Conclusion: As with the previous cross-sectional analyses examining associations between SES measures and outcomes in AAs with < 2 years of disease who are being treated with RA therapies, we did not observe associations between SES and radiographic progression in adjusted analyses. However, some SES measures were associated with increased Pain VAS, after simultaneously adjusting for all SES measures and covariates. These results are possibly due to the relatively short disease duration (5 years) and length of follow-up (4 years) of the population and warrants further research with longer periods of follow-up.

Table 3. SES Predictors[†] of RA Radiographic and Patient Reported Outcomes Progression at 60 months in the Consortium for the Longitudinal Evaluation of African Americans with Early Rheumatoid Arthritis Registry (CLEAR) (n=194)

	Patient Reported Outcomes Progression							
	HAQ Score increased <0.37	HAQ Score increased ≥0.37	Pain VAS increased <3	Pain VAS increased ≥3	Fatigue VAS increased <3	Fatigue VAS increased ≥3	RAI Score increased <0.4	RAI Score increased ≥0.4
SES Measures[‡]								
	45/105	ref.	42/109	ref.	44/108	ref.	47/108	ref.
< HS Education	14/30	1.15 (0.77-1.71)	17/26	***1.75 (1.33-2.29)***	14/28	1.02 (0.74-1.41)	11/28	0.95 (0.71-1.28)
	104/46	ref.	105/46	ref.	103/50	ref.	107/48	ref.
Household Income <$30k	29/15	1.12 (0.74-1.70)	29/15	0.72 (0.46-1.13)	31/11	1.04 (0.76-1.41)	26/12	1.08 (0.76-1.54)
	74/76	ref.	77/74	ref.	73/79	ref.	76/80	ref.
Doesn't Own Home	20/24	0.90 (0.61-1.33)	18/26	***0.53 (0.33-0.85)***	21/21	0.84 (0.62-1.14)	18/20	0.84 (0.54-1.30)
	76/74	ref.	75/76	ref.	77/75	ref.	85/71	ref.
Non-Professional Occupation	25/19	1.17 (0.83-1.66)	26/17	***1.45 (1.05-2.00)***	24/18	1.19 (0.91-1.54)	16/22	***0.74 (0.56-0.99)***
	68/82	ref.	74/77	ref.	74/79	ref.	74/81	ref.
Block Group Poverty ≥20%	24/19	1.33 (0.76-2.33)	18/25	0.82 (0.58-1.17)	18/23	1.00 (0.69-1.46)	18/21	1.09 (0.66-1.80)

	Radiographic Progression			
	Erosion Score increased <1	Erosion Score increased ≥1	JSN Score increased <7	JSN Score increased ≥7
SES Measures[‡]				
	43/102	15/34	44/110	15/26
< HS Education	ref.	1.06 (0.45-2.47)	ref.	2.05 (0.76-5.49)
	100/45	34/15	108/46	26/15
Household Income <$30k	ref.	0.98 (0.39-2.45)	ref.	0.64 (0.24-1.67)
	70/75	24/25	73/80	21/20
Doesn't Own Home	ref.	0.89 (0.32-2.43)	ref.	0.84 (0.35-2.00)
	73/72	28/21	80/74	21/19
Non-Professional Occupation	ref.	1.36 (0.56-3.29)	ref.	0.97 (0.44-2.15)
	68/77	24/25	73/80	19/22
Block Group Poverty ≥20%	ref.	1.02 (0.43-2.40)	ref.	1.05 (0.42-2.64)

[†]Adjusted for age, sex, BMI, use of Methotrexate/Leflunomide, ever smoking, number of comorbidities; study site adjusted for as a random effect

[‡]All SES measures simultaneously adjusted in models

Disclosure: R. Cleveland, None; **E. Astrike-Davis**, None; **B. Jonas**, None; **L. Callahan**, None.

Abstract Number: 2929

Cannabis Use Among Patients in a Large US Rheumatic Disease Registry

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Background/Purpose: Legalization of cannabis use is rapidly increasing worldwide, raising the need to evaluate trends and medical implications. A systematic literature review showed inconsistent results on tolerability and safety of cannabis-based medicines for any chronic pain [1]. Additionally, little is known about the use and effectiveness of cannabis in rheumatic diseases [2]. We sought to evaluate the trends of cannabis use and associations with rheumatic disease characteristics in a US-wide registry.

Methods: Study patients were participants in FORWARD, The National Databank for Rheumatic Diseases, a longitudinal study of rheumatic disease outcomes, who indicated in a 2014 and/or 2019 questionnaire whether they had ever used marijuana, cannabis, or cannabidiol (hereafter cannabis) for symptom relief, and if so, whether they found it helpful. Demographics, disease activity/status assessments (PRO), medications, comorbidities, and diagnosis were compared between cannabis users and nonusers in 2014 and 2019. Significance was assessed using t-tests and Chi-square tests as appropriate. Choropleth maps were generated based on prevalence of cannabis use in each US state. Logistic regression models were generated to determine the probability of cannabis or opioid use by polysymptomatic distress (the score used to determine whether fibromyalgia criteria are met).

Results: Among the 11,006 unique respondents, the prevalence of past or current cannabis use has increased from 6.3% in 2014 to 17.6% in 2019. At both time points, patients reporting use were younger, had worse measures on all PROs, and were more likely to have a history of smoking cigarettes, have fibromyalgia, report a history of depression, and report opioid use (Table 1). In 2014, users were also less likely to be Caucasian, married, and have health insurance. In 2019 there were fewer demographic differences. Most patients reported that cannabis was helpful in relieving symptoms (74% in 2014 and 62% in 2019). Since 2014, prevalence of use increased in 49 of 50 US states, with the highest prevalence in and near states where cannabis use is legal (Figure 1). Logistic regression models indicate that the probability of cannabis use increases with increasing polysymptomatic distress, and the same is true for opioid use (Figure 2).

Conclusion: Reported cannabis use among patients with rheumatic diseases has increased significantly, and most patients stated it was helpful for symptom relief. Patients who tried cannabis tended to have worse pain, disease activity, and symptoms and were taking more analgesics. While interpretation of cannabis effectiveness is beyond our study's scope, the association with prior opioid use and polysymptomatic distress highlights areas for future work.

	2014			2019		
	Nonuser n=8873	User n=592	*p*	Nonuser n=3738	User n=799	*p*
Is cannabis helpful?						
Yes, %	-	74	-	-	62	-
No, %	-	8	-	-	14	-
Not sure, %	-	18	-	-	24	-
Demographics						
Age, years	64 ± 13	54 ± 12	**<0.001**	68.0 ± 11.1	63.3 ± 11.7	**<0.001**
Female, %	83	83	0.96	83	89	**<0.001**
Caucasian, %	90	86	**<0.01**	92	93	0.41
Education, years	14 ± 2	14 ± 2	0.07	15 ± 2	15 ± 2	0.57
Married, %	65	57	**<0.001**	66	67	0.51
Hx smoking, %	44	66	**<0.001**	37	51	**<0.001**
BMI	29 ± 7	30 ± 8	**0.03**	29 ± 7	29 ± 8	0.08
Disease Activity/Status Assessments						
Pain, 0-10	3.9 ± 2.8	5.5 ± 2.7	**<0.001**	3.4 ± 2.7	4.5 ± 2.7	**<0.001**
Global severity, 0-10	3.7 ± 2.5	4.9 ± 2.6	**<0.001**	3.4 ± 2.5	4.2 ± 2.5	**<0.001**
Fatigue, 0-10	4.2 ± 3.1	5.7 ± 3.1	**<0.001**	3.6 ± 2.9	4.8 ± 3.0	**<0.001**
Sleep disturbance, 0-10	3.7 ± 3.1	5.3 ± 3.2	**<0.001**	3.3 ± 2.9	4.3 ± 3.0	**<0.001**
SF-36 PCS, 0-100	38 ± 11	34 ± 10	**<0.001**	40 ± 11	37 ± 11	**<0.001**
SF-36 MCS, 0-100	50 ± 11	43 ± 13	**<0.001**	51 ± 11	47 ± 12	**<0.001**
HAQ-II	1.0 ± 0.7	1.1 ± 0.6	**<0.001**	0.9 ± 0.7	1.0 ± 0.7	**<0.001**
PAS-II	3.5 ± 2.2	4.7 ± 2.2	**<0.001**	3.2 ± 2.2	3.9 ± 2.2	**<0.001**
Medications						
Non-opioid analgesic, %	47	41	**<0.01**	47	46	0.71
Any opioid, %	28	42	**<0.001**	22	34	**<0.001**
Prednisone, %	22	22	0.94	19	20	0.86
Any cDMARD, %	56	55	0.52	53	50	0.15
Any bDMARD, %	33	35	0.31	32	33	0.76
Comorbidities						
RDCI, 0-9	2.1 ± 1.6	2.5 ± 1.8	**<0.001**	2.2 ± 1.7	2.5 ± 1.7	**<0.001**
Depression (ever), %	50	73	**<0.001**	50	64	**<0.001**
Hypertension (ever), %	65	55	**<0.001**	68	67	0.67
Cancer (ever), %	26	19	**<0.001**	33	32	0.55
Diagnosis						
Rheumatoid Arthritis, %	69	68	0.47	70	68	0.16
Osteoarthritis, %	18	15	**0.04**	18	19	0.51
Fibromyalgia (criteria), %	24	49	**<0.001**	17	30	**<0.001**
Lupus, %	5.4	9.0	**<0.001**	5.6	6.8	0.22
Psoriatic Arthritis, %	3.2	5.1	**0.02**	3.0	2.9	0.83
Ankylosing Spondylitis, %	1.2	2.5	**<0.01**	1.5	1.6	0.79

Table 1. Demographics, disease activity/status assessments, medications, comorbidities, and diagnoses among cannabis users and nonusers in 2014 and 2019. Values are mean +/- standard deviation unless indicated otherwise. Bold p values indicate statistical significance.

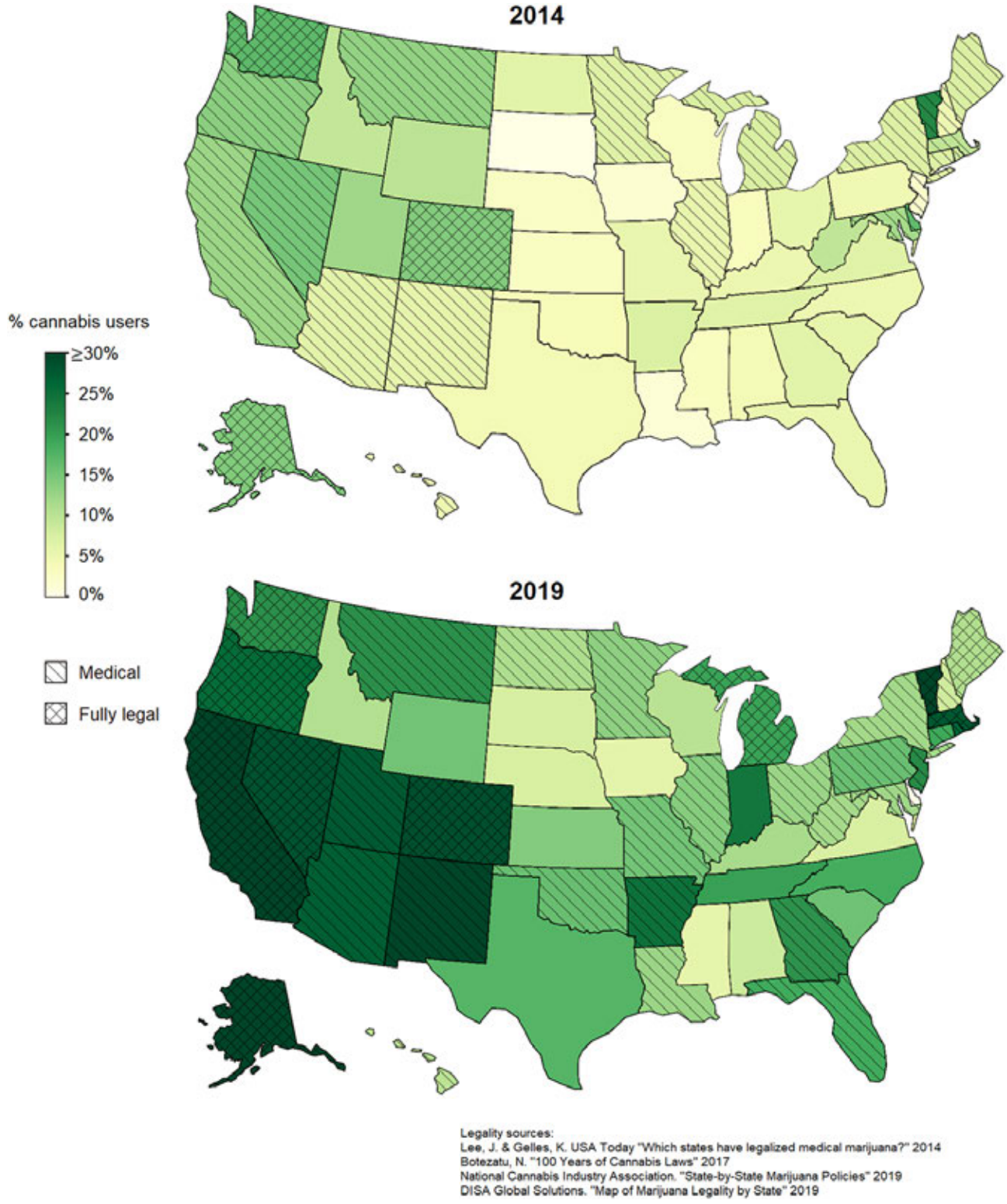

Figure 1. Prevalence of cannabis use in patients with rheumatic diseases and legality of cannabis by US state in 2014 and 2019. Mean n per state was 184 in 2014 and 88 in 2019. Maps were generated with Plotly.

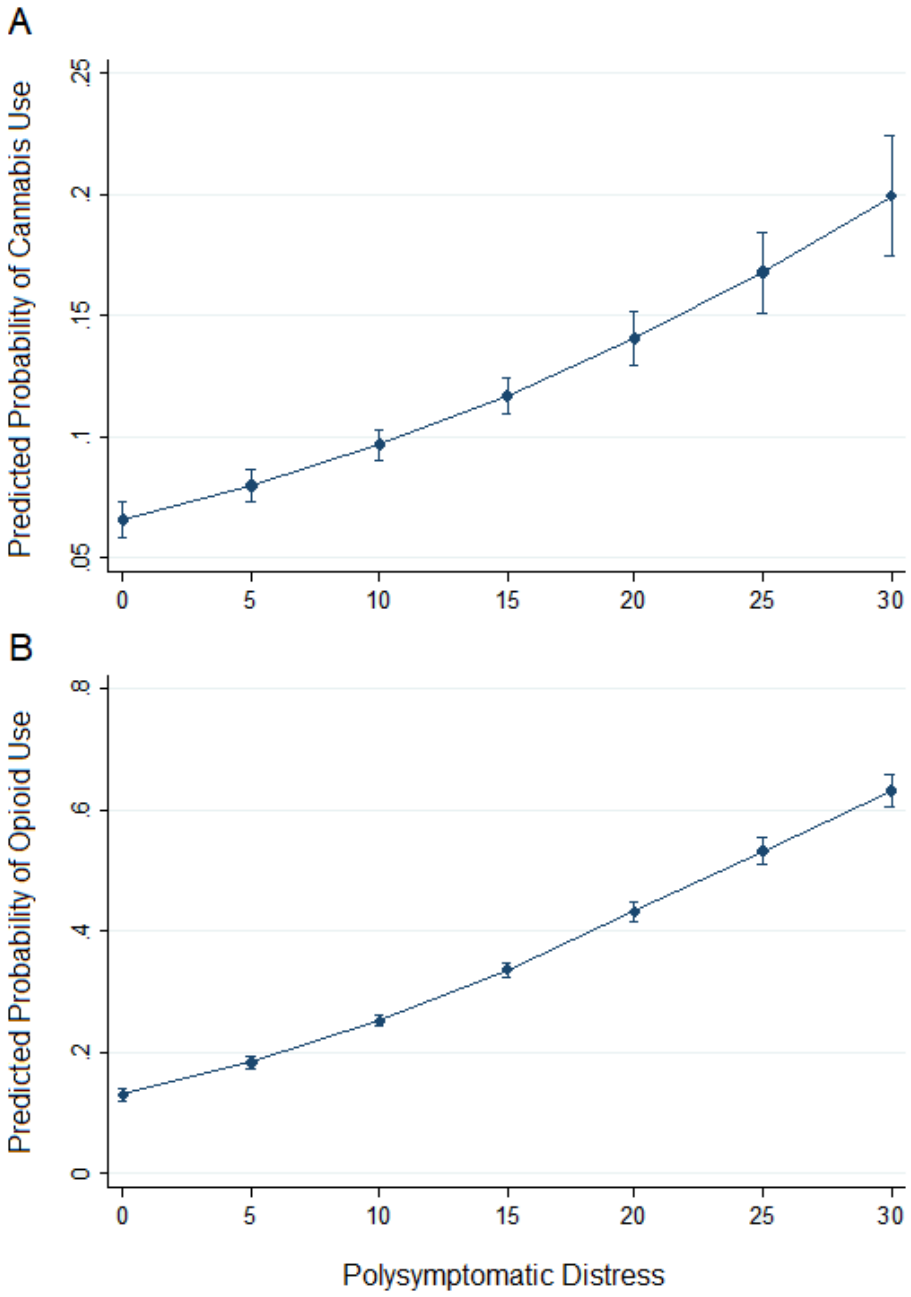

Figure 2. Adjusted predictions with 95% confidence intervals for cannabis use (A) and opioid use (B) by polysymptomatic distress score.

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1) Häuser W W, Petzke F Fitzcharles MA; Efficacy, tolerability and safety of cannabis-based medicines for chronic pain management - An overview of systematic reviews**.** European j Pain, volume 22, issue 3, 2018.

2) Fitzcharles MA, Niaki Z, Omid O, Hauser WW, Hazlewood G, et.al. A Pragmatic Approach for Medical Cannabis and Patients with Rheumatic Diseases**.**;2019 Jan 15; J. Rheumatol.

Disclosure: K. Wipfler, Option Care, 3; **T. Simon**, Bristol-Myers Squibb, 3; **P. Katz**, None; **F. Wolfe**, None; **K. Michaud**, Pfizer, 2, Rheumatology Research Foundation, 2.

Abstract Number: L01

Comparative Risk of Hospitalized Serious Infection in Patients with Psoriasis and Psoriatic Arthritis: A Population-Based Multi-Database Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Late-Breaking Abstracts ePoster

Session Type: Late-Breaking Abstract Poster Session

Session Time: 9:00AM–11:00AM

Background/Purpose: The risk of serious infection when using disease-modifying antirheumatic drugs (DMARDs), including biologic drugs is one of the major concerns for psoriasis/psoriatic arthritis (PsO/PsA) patients. Limited evidence exists on the comparative risk of infection among newer medications including ustekinumab (anti-IL-12/23), secukinumab and ixekizumab (anti IL-17), and a phosphodiesterase-4 inhibitor apremilast compared with TNF inhibitors (TNFi) in patients with PsO or PsA.

Methods: We conducted a cohort study using two large US claims databases, MarketScan (9/25/2009–12/31/2017) and Optum (9/25/2009–12/31/2018). We identified the initiators of one of the following biologic DMARDS: ustekinumab, secukinumab, ixekizumab, or TNFi, (i.e., adalimumab, etanercept, infliximab, certolizumab, golimumab). Apremilast, albeit not a biologic DMARDs (bDMARDs), was also included since it is a relatively new medication used to treat PsO and PsA. The index date was the date of the 1st dispensing for a given drug. We required a 6-month washout period to define new users of each study drug. Patients were required to have at least two PsO or two PsA diagnosis

MarketScan									
	Ustekinumab	Adalimumab	Apremilast	Certolizumab	Etanercept	Golimumab	Infliximab	Ixekizumab	Secukinumab
N	13,448	28,484	9,145	1,189	17,850	1,585	4,017	1,299	3,861
Age in years, mean (SD)	47.2 (12.7)	46.8 (12.5)	50.6 (12.6)	50.4 (11.3)	47.6 (12.5)	49.1 (11.3)	49.8 (12.5)	49.3 (11.7)	49.4 (11.5)
Female, %	48.7	48.8	56.9	63.7	50.7	58.9	59.2	46.8	52.6
Oral steroids	15.5	21.3	23.2	39.0	22.4	36.1	28.6	16.6	24.4
Antibiotic, %	41.0	41.4	46.7	50.9	42.0	47.5	38.8	43.0	44.7
Antiviral, %	3.8	3.6	4.5	4.6	3.7	4.9	3.4	3.7	3.5
Vaccination, %	11.7	14.1	15.1	18.1	14.4	18.4	17.8	12.9	14.3

Optum									
	Ustekinumab	Adalimumab	Apremilast	Certolizumab	Etanercept	Golimumab	Infliximab	Ixekizumab	Secukinumab
N	8,231	13,768	5,766	989	7,588	1,164	1,348	661	2,990
Age in years, mean (SD)	47.5 (13.3)	47.6 (13.2)	51.6 (13.7)	49.3 (12.6)	48.3 (13.4)	49.0 (11.8)	52.5 (13.5)	53.3 (13.2)	50.7 (12.8)
Female, %	47.2	47.0	53.8	60.9	48.6	55.9	57.9	47.5	51.5
Oral steroids	15.8	20.3	21.2	39.9	22.0	37.0	33.2	19.8	24.2
Antibiotic, %	39.7	40.2	44.2	42.8	40.9	46.8	41.7	44.6	42.0
Antiviral, %	3.8	3.6	4.1	5.0	3.8	5.2	3.7	3.9	3.9
Vaccination, %	16.5	17.8	19.6	25.1	16.9	21.1	22.7	18.9	20.0

Figure 1. Selected baseline characteristics before PS fine stratification weighting

during the 6-month baseline period. We excluded patients with a recent serious infection, rheumatoid arthritis, inflammatory bowel disease, malignancy, HIV, or organ transplant at baseline. Our primary outcome was a composite endpoint of hospitalized serious infection including bacterial, viral, or opportunistic infection. Follow-up time started from the day after the index date to the earliest date of the outcome, disenrollment, death, end of database, discontinuation, or switching to other study drugs. Propensity score (PS) was estimated as the predicted probability of receiving ustekinumab versus each of the aforementioned study drugs conditioning on >50 baseline characteristics. Cox proportional hazards regression estimated hazard ratios (HR) for serious infection associated with each study drug versus ustekinumab after controlling for confounding using PS-based fine stratification weights. Database-specific HRs were combined using a random-effects meta-analysis.

Results: We identified 123,383 PsO/PsA patients who initiated one of the study drugs. Among these, 61% had PsO, 22% had PsA, and 17% had both PsO and PsA. The mean (SD) age of the total cohort was 48.2 (12.8) years, and 50.6% were female (see **Figure 1)**. The crude incidence rate per 100 person-years was highest in Infliximab (2.47 in MarketScan and 3.17 in Optum) and the lowest ixekizumab (0.69 in MarketScan) and ustekinumab (1.03 in Optum). After the PS stratification, ustekinumab had lower risk of hospitalized serious infection compared to other bDMARDs or apremilast (**Figure 2**). However, our estimates comparing certolizumab and golimumab versus ustekinumab were imprecise due to a limited sample size even after combining results from the two databases.

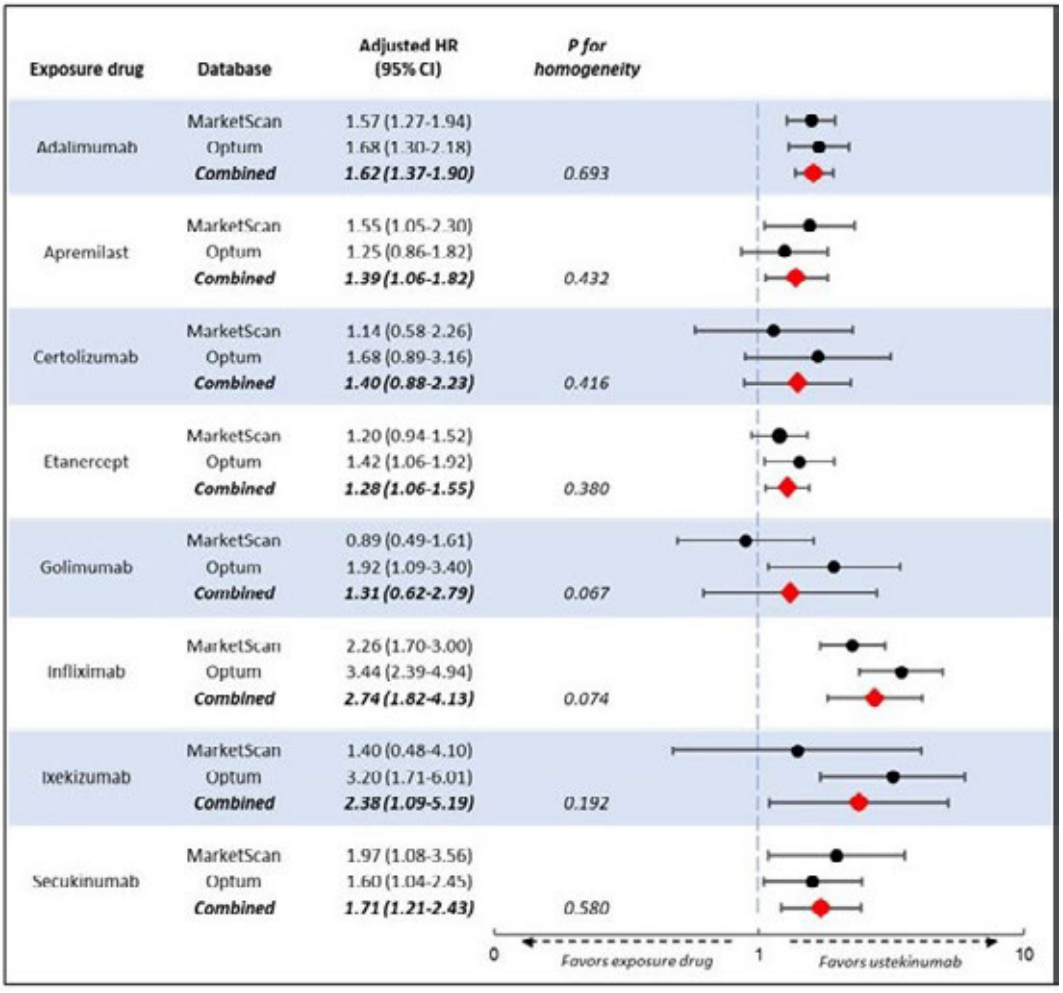

Figure 2. Forest plots for hazard ratios of serious infection of DMARDs comparing to ustekinumab

Conclusion: In this multi-database cohort of 123,383 PsO or PsA patients, ustekinumab initiators had a generally lower risk of hospitalized serious infection compared to TNFi, IL-17 therapy, and apremilast initiators.

Disclosure: Y. Jin, None; **H. Lee**, None; **M. Lee**, None; **J. Landon**, None; **J. Merola**, AbbVie, 2, 5, 8, Aclaris, 2, 5, Almirall, 2, 5, Amgen, 5, Biogen, 2, 5, Burrage Capital Management Boston Advisory Board, 6, Celgene, 2, 5, Dermavant, 2, 5, Eli Lilly, 2, 5, GSK, 2, 5, Incyte, 2, 5, Janssen, 2, 5, Leo Pharma, 2, 5, Merck Research Laboratories, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Regeneron, 5, Sanofi Regeneron, 2, 5, Sun Pharma, 2, 5, UCB, 2, 5; **R. Desai**, Merck, 2, Vertex, 2; **S. Kim**, AbbVie, 2, AstraZeneca, 2, Bristol-Myers Squibb, 2, Merck, 2, Pfizer, 2, research grants to Brigham and Women's Hospital from Pfizer, AbbVie, Bristol-Myers Squibb, and Roche for unrelated topics, 2, Roche, 2, Roche/Genentech, 2.

Abstract Number: L02

Multiple Industrial Air Pollutants and Anti-Citrullinated Protein Antibody Positivity

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Late-Breaking Abstracts ePoster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Studies of associations between industrial air emissions and rheumatic disease, or diseases-related serological biomarkers, are few. Moreover, previous evaluations typically studied individual (not mixed) emissions. We investigated associations between individual and combined exposures to industrial sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and fine particles matter ($PM_{2.5}$) on anti-citrullinated protein antibodies (ACPA), a characteristic biomarker for rheumatoid arthritis (RA).

Methods: Serum ACPA was determined for 7600 randomly selected CARTaGENE general population subjects in Quebec, Canada. Industrial SO_2, NO_2, and $PM_{2.5}$ concentrations, estimated by the California Puff (CALPUFF) atmospheric dispersion model, were assigned based on residential postal codes at the time of sera collection. Single-exposure logistic regressions were performed for ACPA positivity defined by 20 U/ml, 40 U/ml, and 60U/ml thresholds, adjusting for age, sex, French Canadian origin, smoking, and family income. Associations between regional overall $PM_{2.5}$ exposure and ACPA positivity were also investigated. The associations between the combined three industrial exposures and the ACPA positivity were assessed by weighted quantile sum (WQS) regressions.

Results: Significant associations between individual and combined industrial exposures and ACPA positivity (defined by the 20 U/ml and 40 U/ml thresholds) were seen with both single-exposure logistic and multi-exposure WQS regression models, for industrial emissions of $PM_{2.5}$ and SO_2, without clear associations for NO_2. The WQS model suggested that industrial $PM_{2.5}$ may have a stronger effect than the other exposures.

Model	Exposure variable	ACPA positivity defined by 20 units/ml (N positive =786)	ACPA positivity defined by 40 units/ml (N positive =292)	ACPA positivity defined by 60 units/ml (N positive =134)
Logistic	Industrial SO_2	1.03 (1.00 – 1.06)	1.03 (1.00 – 1.07)	1.03 (0.98 – 1.08)
	Industrial NO_2	1.01 (0.86 – 1.17)	1.14 (0.91 – 1.41)	0.90 (0.63 – 1.28)
	Industrial $PM_{2.5}$	1.19 (1.04 – 1.36)	1.21 (1.02 – 1.42)	1.17 (0.92 – 1.48)
	Regional overall $PM_{2.5}$	0.98 (0.95 – 1.01)	0.95 (0.91– 1.01)	0.94 (0.89– 1.01)
WQS	three industrial pollutants	1.36 (1.10 – 1.69)	1.43 (1.05 – 1.96)	1.33 (0.85– 2.10)

Conclusion: We noted positive associations between ACPA and industrial emissions of $PM_{2.5}$ and SO_2. Industrial $PM_{2.5}$ exposure may play a particularly important role in this regard.

Odds ratios - ORs (95% confidence intervals – CIs) from the single-pollutant logistic and the weighted quantile sum (WQS) regression models, adjusting by age, sex, ancestry, smoking, and family income.

Disclosure: N. Zhao, None; **A. Smargiassi**, None; **M. Hatzopoulou**, None; **I. Colmegna**, None; **M. Hudson**, None; **M. Fritzler**, Alexion Canada, 7, BioRad, 5, Dr. Fooke Laboratorien GmbH, 5, Euroimmun GmbH, 5, 7, ImmunoConcepts, 7, Inova Diagnostics, 5, 7, 8, Inova Diagnostics Inc. San diego, CA, 5, Inova Dx, Mikrogen GmbH, 5, Werfen International, 5; **P. Awadalla**, None; **S. Bernatsky**, None.

Abstract Number: L03

NYX-2925 Impacts Functional and Chemical Neuroimaging Biomarkers and Patient-reported Outcomes of Pain in Patients with Fibromyalgia

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Late-Breaking Abstracts ePoster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia (FM) is a chronic, debilitating disease typified by widespread musculoskeletal pain and accompanied by fatigue, sleep disturbance, memory issues, and mood disorders. FM has been described as the prototypical centralized chronic pain syndrome. NYX-2925 is a novel, non-opioid small-molecule modulator of the N-methyl-D-aspartate receptor (NMDAR) that is in Phase 2 development for fibromyalgia and painful diabetic peripheral neuropathy.

Methods: An exploratory Phase 2, placebo-controlled neuroimaging clinical trial was conducted in 22 right-handed female subjects with FM according to ACR 2010 criteria. Following a screening period, subjects received two weeks of placebo once-daily, followed by two weeks of 20 mg NYX-2925 once-daily, followed by two weeks of 200 mg NYX-2925 once-daily. Subjects underwent resting state functional connectivity magnetic resonance imaging (rs-fcMRI) and proton magnetic resonance spectroscopy (^{1}H-MRS) during screening and during the second week of each of the three dosing periods. Subjects and neuroimaging analysts were blinded to study drug and dose sequence.

Table 1: Patient reported measures of pain and fibromyalgia symptoms in Study NYX-2925-2002

	Placebo (Week 2)	20 mg NYX-2925 (Week 4)	200 mg NYX-2925 (Week 6)	Follow-up (Week 7)
Average Daily Pain	N=19	N=20	N=19	N=15
Change from baseline	-0.44	-0.51	-1.09	-0.79
p-value	0.0435	0.0921	0.0027	0.0404
Change from placebo	NA	0.10	-0.66	-0.38
p-value	NA	0.6829	0.0072	0.1358
Worst Daily Pain	N=19	N=20	N=19	N=15
Change from baseline	-0.34	-0.41	-0.98	-0.76
p-value	0.1477	0.1652	0.0169	0.0695
Change from placebo	NA	-0.13	-0.61	-0.39
p-value	NA	0.5547	0.0360	0.1197
Total FIQR Score	N=22	N=21	N=21	N=20
Change from baseline	-2.9	-3.8	-9.6	-0.4
p-value	0.2380	0.1389	0.0085	0.8712
Change from placebo	NA	-0.5	-6.3	2.4
p-value	NA	0.8746	0.0135	0.4339
Total $PROMIS_{FM}$ Fatigue Profile Score	N=22	N=21	N=21	N=20
Change from baseline	0.2	-3.2	-5.4	0.4
p-value	0.8702	0.1500	0.0081	0.7980
Change from placebo	NA	-3.4	-5.6	0.0
p-value	NA	0.2000	0.0049	>.9999

Testing for differences between treatment periods was performed using 2 sided paired t tests, comparing pre- and post-values based on analysis visits. The p-values were not corrected for multiple comparisons in this exploratory neuroimaging study.

Results: Neuroimaging showed that compared to placebo, administration of NYX-2925 resulted in statistically significant reductions of Glx/tCr (glutamate and glutamine ratio to total creatine) levels in key pain-regulating brain regions, including the dorsal anterior cingulate cortex (dACC) at rest (Placebo: 2.167+/-0.178; 20mg NYX-2925: 2.055+/-0.197; p=0.032) and the posterior insular cortex following an evoked pain stimulus (Placebo: 1.993+/-0.140; 200mg NYX-2925: 1.903+/-0.162; p=0.039). Greater concentrations of pain-evoked Glx pre-treatment in the posterior insular cortex were associated with greater reductions in patient reported sensitivity to evoked pain (increased pressure pain threshold) following 20mg NYX-2925 (r=0.58; p=0.009). In addition, 20mg NYX-2925 administration resulted in reduced connectivity between brain regions that are known to be associated with the processing of centralized chronic pain, including dACC to primary somatosensory cortex connectivity (p=0.030 Family Wise Error [FWE]).

Clinically meaningful and statistically significant clinical improvements were observed following treatment with 200mg NYX-2925 compared to baseline (Week 0) and placebo (Week 2) on the average daily pain score, worst daily pain score, total Revised Fibromyalgia Impact Questionnaire (FIQR) score, and $PROMIS_{FM}$ fatigue profile total score (Table 1). Clinical data further demonstrate that NYX-2925 is safe and well tolerated with no discontinuations due to treatment-emergent adverse events.

Conclusion: In this exploratory study, NYX-2925 demonstrated antinociceptive activity in neuroimaging evaluations. Clinically meaningful and statistically significant improvements were also observed in pain, fatigue, the overall intensity of fibromyalgia symptoms, and their impact on function. These data provide support for further evaluation of NYX-2925 for treating the hallmark symptoms of fibromyalgia.

Disclosure: S. Harte, Aptinyx, 1; **L. Arnold**, Aptinyx, 1; **E. Ichesco**, Aptinyx, 1; **C. Crumb**, None; **M. Suh**, Aptinyx, 1; **L. Sindelar**, Aptinyx, 1; **C. Kaplan**, None; **T. Larkin**, None; **A. Schrepf**, None; **D. Clauw**, Aptinyx, 2, 5, Daiichi Sankyo, 5, Eli Lilly, 5, Intec Pharma, 5, Nix Paterson LLP, 8, Pfizer, 1, 2, Pfizer Inc, 2, 5, 8, Samumed, 5, Theravance, 5, Tonix, 5, Williams & Connolly LLP, 8, Zynerba, 5; **S. Sainati**, Aptinyx, 1; **R. Harris**, Pfizer, 1, 2, Aptinyx, 1, 2.

Abstract Number: L04

Cardiovascular Disease Risk in Calcium Pyrophosphate Deposition Disease

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Late-Breaking Abstracts ePoster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Calcium pyrophosphate deposition (CPPD) disease results from precipitation of calcium pyrophosphate (CPP) crystals in joints. Prior studies demonstrated that vascular calcification is more common in patients with CPPD compared to those without CPPD. Vascular calcification is implicated in the development of cardiovascular disease, yet studies of cardiovascular risks in CPPD are lacking. We aimed to assess the risk of cardiovascular events and all-cause mortality in patients with CPPD vs. those without CPPD.

Methods: Using a retrospective cohort study design within the national Veterans Affairs (VA) database (2010-2014), we compared the risk of major adverse cardiovascular events (MACE) in US veterans with CPPD vs. veterans without CPPD. CPPD was defined by ≥1 ICD-9 code for chondrocalcinosis or calcium metabolism disorder (712.1-712.39 or 275.49; positive predictive value 91%).[1] CPPD patients were age and sex-matched 1:4 to patients without those ICD-9 codes (controls). Only males were included in the analysis, as MACE was extremely uncommon in females. All subjects had at least 1 healthcare encounter in the 365 days before index date, defined as the first ICD-9 code for CPPD or a matched date for controls, to allow for covariate assessment. Covariates were included if present during the study period prior to MACE.

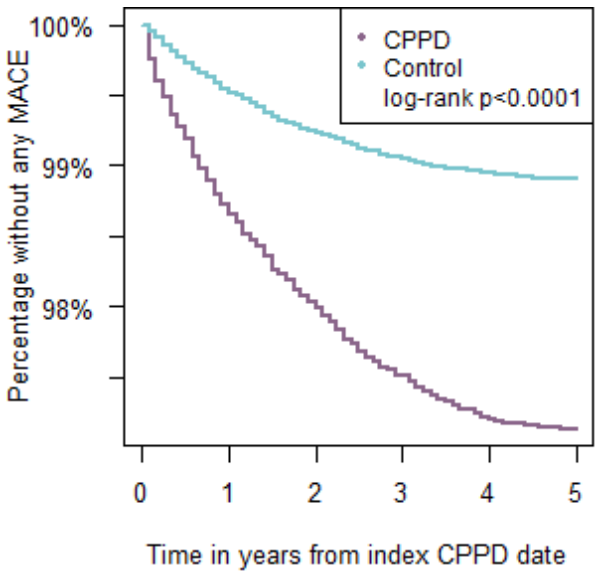

Figure 1. Percentage of patients without any MACE over time in CPPD and control groups

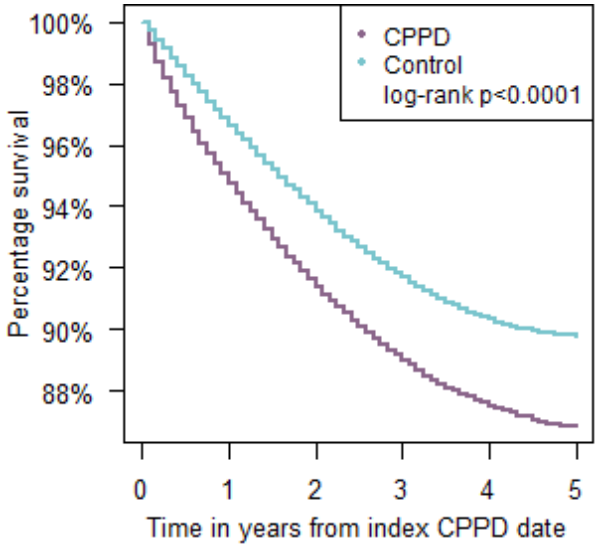

Figure 2. Percentage of patient survival over time in CPPD and control groups

The primary outcome was any MACE, defined by ICD-9 and/or procedure codes for myocardial infarction (MI), acute coronary syndrome (ACS), re-vascularization, or ischemic stroke. Secondary outcomes included individual types of MACE and all-cause mortality. We estimated incidence rates (IR) per 1,000 person-years and incidence rate ratios (IRR) for MACE and all-cause mortality. Stepwise Cox proportional hazards regression models were adjusted for traditional cardiovascular (CV) risk factors (hypertension, hyperlipidemia, diabetes, chronic kidney disease, peripheral vascular disease, smoking, obesity, gout, osteoarthritis, rheumatoid arthritis and prior history of MACE). Kaplan Meier curves and log-rank tests estimated the difference in MACE and mortality rates between groups.

Results: We identified 24,413 CPPD patients matched to 97,591 controls. MACE occurred in 702 (2.88%) patients with CPPD and 1069 (1.10%) controls (Figure 1). The IR of any MACE was nearly three times higher in patients with CPPD (IR 11.5 [95% CI 10.7-12.4]) compared to controls (4.3 [4.1-4.6]), with IRR 2.66 (2.42-2.93). The IRR for each individual type of MACE was also higher in CPPD vs. controls (Table 1). Findings were similar in adjusted Cox models.

The all-cause mortality rate was higher in patients with CPPD (IR 57.7 [55.7-59.7]) than controls (42.9 [42.0-43.7]) with IRR 1.35 (1.29-1.40). Cox analysis could not be performed because CPPD violated the proportional hazards assumption for mortality. In unadjusted survival analysis, time to death was shorter among CPPD patients than controls (log rank p< 0.0001) (Figure 2).

Conclusion: CPPD was associated with an increased risk of MACE after adjusting for known cardiovascular disease risk factors. Patients with CPPD also had a higher mortality rate compared to patients without CPPD.

Variable		CPPD		Controls		IRR (95% CI)
		n= 24,413 (%)	IR per 1000 PYs (95% CI)	n=97,591 (%)	IR per 1000 PYs (95% CI)	
Cardiovascular Event	MI	291 (1.19%)	4.7 (4.2-5.3)	400 (0.41%)	1.6 (1.5-1.8)	2.93 (2.52-3.40)
	ACS	486 (1.99%)	7.9 (7.2-8.6)	713 (0.73%)	2.9 (2.7-3.1)	2.75 (2.45-3.08)
	Re-vascularization	204 (0.84%)	3.3 (2.5-3.8)	337 (0.35%)	1.4 (1.2-1.5)	2.43 (2.04-2.89)
	Stroke	151 (0.62%)	2.4 (2.1-2.8)	244 (0.25%)	1.0 (0.9-1.1)	2.48 (2.02-3.04)
	Any MACE	702 (2.88%)	11.5 (10.7-12.4)	1069 (1.10%)	4.3 (4.1-4.6)	2.66 (2.42-2.93)

Table 1. Incidence rates (IR) and incidence rate ratios (IRR) of MACE comparing CPPD to control groups

Reference
1. Bartels CM, et al. J Clin Rheumatol 2015;21:189-92.

Disclosure: M. Bashir, None; **K. Sherman**, None; **S. Tedeschi**, None; **A. Rosenthal**, None.

Abstract Number: L05

Safety, Tolerability, Pharmacokinetics, and Clinical Outcomes Following Single-Dose IA Administration of UBX0101, a Senolytic MDM2/p53 Interaction Inhibitor, in Patients with Knee OA

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SESSION INFORMATION
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Background/Purpose: A non-drug biomarker study showed senescent cell (SnC) burden in OA synovial tissue to correlate with disease severity, inflammation, and knee pain (C. Yohn, Poster, this meeting). UBX0101 is a MDM2/p53 interaction inhibitor that can induce apoptosis of SnCs. Clearance of SnCs from joints by UBX0101 may create a pro-regenerative environment and lead to pain reduction. We assessed in a Phase 1 study the safety, pharmacokinetics (PK), and clinical outcomes of intra-articular (IA) UBX0101 treatment in patients (pts) with painful knee OA.

Methods: This was a Phase 1, double-blind, randomized, placebo-controlled, single, ascending dose (SAD) study in 48 pts randomized 3:1 to UBX0101 (dose range of 0.1 to 4.0 mg) or placebo IA. Key eligibility criteria included knee OA by ACR criteria, Kellgren-Lawrence grade (KLG) 1-4, and mean daily pain 4-9 on a Numeric Rating Scale (NRS, 0-10). Clinical outcomes through 12 weeks included WOMAC sub-scores for pain, function, and stiffness derived from the Knee Injury and Osteoarthritis Outcome Score (KOOS) Survey and NRS. PK modeling was used to pre-define low (0.1 to 0.4 mg) and high (1.0 to 4.0 mg) dose groups, predicted to achieve knee concentrations below and above pharmacological EC50 thresholds, respectively. Thirty additional subjects were randomized 2:1 to UBX0101 4.0 mg or placebo IA to assess the impact of UBX0101 on synovial fluid (SF) and plasma senescence-associated secretory phenotype (SASP) and OA disease biomarkers (BMKs). In this BMK sub-study, SF collected by arthrocentesis or lavage at Weeks 0 and 4 along with plasma were assayed using a custom multiplex panel. The SAD study design and sample size were chosen for evaluation of safety, while the BMK sub-study was sized to detect a meaningful change from baseline for BMKs.

Results: The SAD study population was balanced regarding demographic and baseline OA characteristics; mean age was 62 years, 67% were female, 89.6% white. Single IA doses of UBX0101 up to 4 mg were well-tolerated. Most adverse events (AEs) were mild. No serious AEs occurred and no AEs led to discontinuation. The plasma PK of UBX0101 following single IA injection demonstrated minor interpatient variability at all dose groups and systemic concentrations were low and further minimized by a ~4 hour half-life. Improvements in pain and function were dose-dependent, clinically meaningful, and durable through 12 weeks for the three highest UBX0101 doses of 1.0, 2.0, and 4.0 mg (table). A greater proportion (50%) of pts in the high dose group achieved a 50% decrease in WOMAC pain sub-score at Week 12 compared to the placebo and low dose groups (36% and 25%, respectively). SF/lavage fluid analyses in the BMK sub-study revealed modulation of multiple SASP/OA markers such as tissue remodeling and inflammatory factors, after one dose of UBX0101 IA compared to placebo.

Table: Clinical Outcomes at Week 12			
		UBX0101	
Endpoint	**Placebo (n=14)**	**Low doses, 0.1-0.4 mg (n=16)**	**High doses, 1.0-4.0 mg (n=18)**
WOMAC-A Pain			
Baseline, mean	1.87	2.14	1.86
LSM CFBL Week 12 (95% CI)	-0.74 (-1.14, -0.34)	-0.49 (-0.89, -0.10)	-1.09 (-1.38, -0.80)
p-value		0.43	**0.07**
Mean Daily Pain NRS			
Baseline, mean	6.47	6.29	6.31
LSM CFBL Week 12 (95% CI)	-1.96 (-3.14, -0.77)	-2.66 (-3.78, -1.55)	-3.95 (-4.74, -3.16)
p-value		0.42	**<0.01**
WOMAC-C Function			
Baseline, mean	1.93	2.05	1.94
LSM CFBL Week 12 (95% CI)	-0.72 (-1.12, -0.31)	-0.49 (-0.88, -0.10)	-1.05 (-1.36, -0.74)
p-value		0.43	0.13

WOMAC= Western Ontario and McMasters Universities Osteoarthritis Index (Likert) 0-4, LSM= Least-squares mean, CFBL=Change from baseline, CI=Confidence Interval, NRS=Numeric rating scale 0-10.

Conclusion: Single IA doses of UBX0101 up to 4.0 mg were well-tolerated by knee OA patients, and its PK was well-characterized. The activity of UBX0101 is supported by its effects on multiple BMKs, as well as the clinically meaningful and durable improvements in pain and function. UBX0101 as a senolytic agent may be an important future therapeutic option for pts with knee OA.

Disclosure: B. Hsu, UNITY Biotechnology, 1, 2, 3, Johnson & Johnson, 1; **J. Visich**, UNITY, 1, 2, 3; **M. Genovese**, UNITY, 1; **K. Walter**, UNITY Biotechnology, 1, 2; **M. An**, UNITY, 1, 2, 3; **R. Laberge**, UNITY, 1, 2, 3; **J. Dananberg**, UNITY Biotechnology, 1, 3, 4, 6, UNITY, 1, 2, 3.

Abstract Number: L06

Interferon-gamma (IFN-γ) Neutralization with Emapalumab and Time to Response in Patients with Macrophage Activation Syndrome (MAS) Complicating Systemic Juvenile Idiopathic Arthritis (s-JIA) who failed High-Dose Glucocorticoids

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SESSION INFORMATION

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Background/Purpose: MAS is a severe complication of rheumatic diseases, most frequently sJIA and adult-onset Still's disease. It is characterized by fever, hepatosplenomegaly, liver dysfunction, cytopenias, coagulation abnormalities and hyperferritinemia, potentially progressing to multiple organ failure and death. MAS is classified among the secondary forms of HLH. Overproduction of IFNγ is a major driver of hyperinflammation/hypercytokinemia in several MAS and HLH murine models. We assessed efficacy, safety and timing of response of clinical and laboratory parameters of the neutralizing IFNg monoclonal antibody emapalumab in patients with MAS.

Methods: In a pilot open-label single-arm international study (NCT03311854), patients with MAS (defined according to the 2016 criteria), on a background of sJIA and inadequate response to high-dose glucocorticoids, received emapalumab (first dose: 6 mg/kg; subsequent doses: 3 mg/kg twice weekly) for a total of 4 weeks or less upon achievement of complete response (CR). Serum concentrations of the IFNg-induced chemokine CXCL9 and of sIL2R were measured. Safety assessments included adverse events and laboratory abnormalities. CR (week 8) was defined as absence of MAS clinical signs AND white blood cell and platelet counts above lower limit of normal, LDH, AST/ALT< 1.5 x upper limit of normal, fibrinogen >100 mg/dL, and ferritin decreased by >80% or to < 2000 ng/mL, whichever was lower. Twin protocols (minimum 5 patients each) are in place in Europe and North America. We report on the first 6 patients recruited in Europe; subsequently 2 additional patients recruited in the US and 1 in Europe.

MAS features, median (range)	SCREENING	BASELINE
Physician VAS (1to10) of MAS activity	9.5 (7-10)	9.5 (8-10)
Ferritin (mg/L)	26 768 (1 071-192 584)	21 689 (716-192 584)
Platelets (x10^9/L)	173 (82-229)	133 (70-229)
WBC (x10^9/L)	5.78 (0.31-25.73)	7.83 (0.85-25.73)
ALT (IU/L)	166 (139-575)	156 (70-852)
LDH (IU/L)	2 553 (859-12 734)	2 063 (588-12 734)
Fibrinogen (mg/dL)	217 (137-341)	204 (110-465)
D-Dimers (mg/L)	10 940 (790-57 421)	10 615 (550-89 552)

Table 1. Baseline and screening disease parameters

	Baseline	Day 1	Day 2	Day3	Day 5	Day 7
Pt 1	3 413.7	2 909.2	1 302.3	997.5	538.4	407.8
Pt 2	13 259.4	16 298.7	21 962.0	20 266.3	1 656.1	461.8
Pt 3	1 518.2	2 672.3	774.0	405.1	228.0	192.2
Pt 4	98 120.5	43 211.9	11 132.4	NA	1 681.6	767.8
Pt 5	18 011.4	4 204.0	1 910.2	920.7	513.7	468.6
Pt 6	3 752.9	2 024.1	1 124.1	1 307.5	854.0	624.0
Median (Range)	8 506.1 (1 518.2-98 120.5)	3557.11 (2 024.1-43 211)	1 606.3 (774.0-21 962.0)	997.5 (405.1-20 266.3)	696.2 (228.0-1 681.6)	465.2 (192.2-767.8)

Table 2. Serum CXCL9 levels at baseline and during the first 7 days of treatments with emapalumab

Parameters	Days of treatment, median (range)
D-dimers to < 1000 mg/L	6.8 (1-49)
sIL-2R to < 2000 UI/ml	17.7 (6-37)
Ferritin < 500 mg/L	28.7 (9-35)
Physician VAS of MAS activity ≤ 1	37.0 (12-56)
All MAS laboratory parameters within range of complete response	23.8 (18-55)
Glucocorticoid tapering at < 1 mg/Kg PDN equivalent	49.0 (18-53)

Table 3. Time (days of treatment) of D-dimers to < 1000, sIL-2 receptor (sIL-2R) to < 2000 UI/ml, ferritin < 500 mg/L, physician VAS < 1, all MAS laboratory parameters within range of complete response and glucocorticoid tapering at < 1 mg/Kg PDN equivalent

Results: Six patients (4 females, median age 11 years, range: 2-25 years), who had failed methylprednisolone (in 2 patients plus cyclosporine A (CsA) and in 2 patients plus CsA and anakinra) received emapalumab (Table 1). CXCL9 showed initial substantial decrease between day 2 and 5, showing rapid IFNg neutralization (Table 2). In all patients but one (who presented a single measurement of 37.6 at SD 21) fever resolved (< 37.5) within 3 days. These effects were followed by progressive improvement in all MAS clinical and laboratory parameters (Table 3). CR was achieved in all patients after a median of 23.8 (18-55) days. Glucocorticoids were tapered in all patients (median % tapering -92%, range -45-98% at week 8). Emapalumab was well tolerated; no patient discontinued emapalumab. A CMV reactivation, reported as a serious event possibly related to emapalumab, resolved with treatment.

Conclusion: All 6 patients receiving emapalumab achieved CR. Progressive improvement and subsequent normalization of all clinical and laboratory parameters occurred following rapid and sustained CXCL9 decrease.

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Abstract Number: L07

A Serum Proteomic Signature Defines Transition from the Preclinical State to Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Anti-citrullinated protein antibodies (ACPA) are currently the primary biomarker for identifying individuals at increased risk for future RA development. However, we have recently shown in a prospective study that most unaffected ACPA+ individuals do not develop RA. We hypothesized that abnormalities in the serum

proteome may serve as additional biomarkers in the prediction risk for future disease onset. The aim of our study was to mine the serum proteome of individuals who ultimately developed RA to detect biomarkers that predict disease onset.

Methods: Using the SOMAscan (slow off-rate modified aptamer) array, SomaLogic, Boulder Co, we generated quantitative levels of 1307 proteins in serum samples from seventeen first-degree relatives (FDR) of Indigenous North American (INA) RA patients who developed inflammatory arthritis (IA) synovitis after having been followed prospectively for a mean of 3.2 years. All were ACPA+ at time of IA diagnosis. Each individual had two preclinical samples, one at the time of IA onset, and one at an earlier time point. We also analyzed samples from ACPA+ FDR (n = 63) and ACPA- FDR (n = 47) who did not develop inflammatory arthritis. Differentially expressed proteins were identified using ANOVA corrected for multiple comparisons. We applied a machine learning lasso regression model to identify a minimum set of proteins that classified patients who transition into clinical arthritis.

Results: Differential expression of 669 proteins (260 upregulated, 409 downregulated) were identified between pre-Transition samples (TR-pre) and ACPA negative FDR. ITGA2B and HIST1H3A were the highest upregulated proteins in TR-pre samples, while protease inhibitors SERPINA5 and ITIH4 were highly downregulated in the TR-pre samples. Compared with ACPA- FDR, overlap between TR-pre baseline and non-baseline samples of highly upregulated (log2 difference > 0.5) proteins was 60%, suggesting alterations in the serum proteome occur years before the development of RA. A lasso regression model identified a 23-marker panel that classified TR-pre samples from the larger pool of ACPA+ and ACPA- FDR serum samples. In a validation cohort (n = 34), the model correctly classified 31/34 samples (91.2% accuracy) with a sensitivity of 95.6% and specificity of 85.7%. Area under the curve (AUC) was 0.931 for the model. Transition scores were extracted from the model, which were higher in ACPA+ FDR compared to ACPA- FDR ($p < 0.001$). There were no differences in Transition score comparing TR-pre samples that were remote or close to the time of IA onset.

Conclusion: Compared to at-risk individuals who did not develop IA, clear and reproducible differences in the serum proteome are demonstrable in the serum samples of individuals who ultimately developed IA, even several years before the onset of clinically evident disease. Our findings suggest that a small serum biomarker panel can serve to accurately classify at-risk individuals who have a high likelihood of progressing to develop IA.

Transition scores generated from lasso model for FDR, binned by ACPA positivity (**** $p < 0.001$) and Transitioner samples binned by Remote and Imminent ($p = 0.897$) relative to the development of inflammatory arthritis (IA).

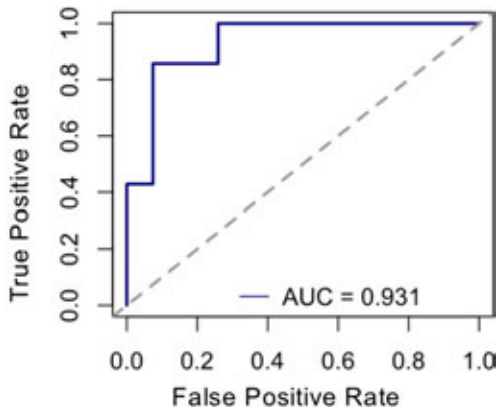
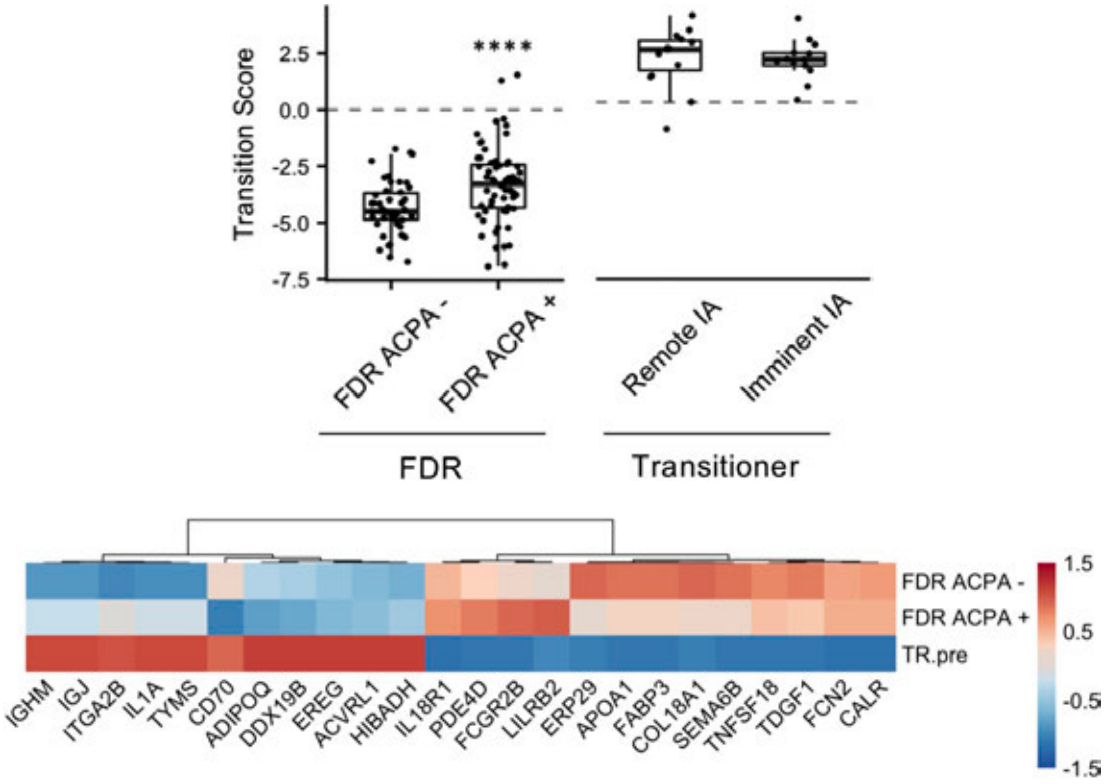


Figure 1. Area under the curve (AUC = 0.931) from a lasso model to identify pre-RA (pre-Transition) samples from FDR with and without ACPA positivity in a validation cohort (n = 34)



Representative heatmap of the average expression data by group, normalized for each protein included in the Transition Score. TR.pre: pre-RA samples, FDR ACPA - : First degree relatives without ACPA, FDR ACPA + : First degree relatives with elevated ACPA.

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Abstract Number: L08

Tapering of Conventional Synthetic Disease Modifying Anti-Rheumatic Drugs in Rheumatoid Arthritis Patients in Sustained Remission: Results from a Randomized Controlled Trial

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Background/Purpose: Sustained remission is the goal of rheumatoid arthritis (RA) care, and more patients reach and maintain this state on conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) after the implementation of treat-to-target strategies. The knowledge about whether csDMARDs can be tapered in RA remission is limited. The primary objective of the study was to assess the effect of tapering of csDMARDs on the risk of flares in RA patients in sustained clinical remission.

Methods: In the non-inferiority ARCTIC REWIND trial, RA patients in clinical remission for at least 12 months on stable csDMARD therapy were randomly assigned to continued stable csDMARD or half dose csDMARD, with visits

Table 1. Characteristics of patients at baseline.*

Characteristic	Stable csDMARD (N=78)	Half-dose csDMARD (N=78)
Age – years	55.1 (11.8)	55.5 (12.0)
Female sex – no. (%)	50 (64)	54 (69)
Time since first swollen joint – years	3.7 (1.8)	3.4 (1.4)
Positive for ACPA – no. (%)	57 (73)	63 (81)
Positive for rheumatoid factor – no. (%)	54 (69)	53 (68)
Body-mass index (kg/m2)	26.3 (4.5)	26.2 (4.0)
Current smoker – no. (%)	14 (18)	13 (17)
Measures of disease activity		
Disease Activity Score †	0.8 (0.4)	0.8 (0.3)
Simplified Disease Activity Index †	0.8 (0.5,1.6)	0.9 (0.3,2.1)
ACR/EULAR remission – no. (%)†	61 (78.2)	50 (64.9)
Swollen-joint count ‡	0.0 (0.0)	0.0 (0.0)
Tender-joint count (Ritchie Articular Index) ∫	0.0 (0.0,0.0)	0.0 (0.0,0.0)
Erythrocyte sedimentation rate, mm/hr	7.0 (4.0,14.0)	7.0 (4.0,13.0)
C-reactive protein, mg/liter	2.0 (1.0,3.0)	2.0 (1.0,3.0)
Patient's global assessment ¶	3.5 (1.0,10.0)	3.0 (1.0,10.0)
Investigator's global assessment ¶	1.0 (0.0,4.0)	0.0 (0.0,3.0)
Functional outcomes		
PROMIS Physical Function **	56.1 (7.4)	55.6 (7.5)
Fatigue visual-analogue scale ††	5.5 (1.0,24.0)	10.0 (2.0,29.0)
Pain visual-analogue scale ††	3.0 (1.0,9.0)	4.0 (1.0,10.0)
Radiographic joint damage		
Total van der Heijde modified Sharp score ‡‡	5.0 (2.0,11.5)	4.5 (2.0,8.5)
van der Heijde Sharp Erosion	2.0 (1.0,4.5)	2.0 (1.0,3.5)
van der Heijde Sharp Joint Space Narrowing	2.0 (0.5,8.0)	2.0 (0.5,6.0)
Ultrasound outcomes ∬		
Total power Doppler signal score	0.0 (0.0,0.0)	0.0 (0.0,0.0)
Total grey scale score	1.0 (0.0,2.0)	1.0 (0.0,3.0)
No power Doppler signal in any joint – no. (%)	72 (93.5)	71 (92.2)
Medication		
MTX monotherapy – no. (%)	61 (78.2)	65 (84.4)
Methotrexate monotherapy p.o. – no. (%)	51 (65.4)	51 (66.2)
Methotrexate monotherapy s.c. – no. (%)	10 (12.8)	14 (18.2)
MTX/sulfasalazine/hydroxychloroquine – no. (%)	10 (12.8)	6 (7.8)
Other mono- or duotherapies – no. (%)	7 (9.0)	6 (7.8)
Dose methotrexate in users, mg/week	19.0 (4.7)	19.5 (4.3)
Dose sulfasalazine in users, mg/day	1769.2 (438.5)	1562.5 (623.2)
Dose hydroxychlorochine in users, mg/day	400.0 (0.0)	377.8 (66.7)
Dose leflunomide in users, mg/day	20.0 (.)	20.0 (.)

* Full Analysis Set. Plus – minus values are means ± SD. Median values are given with interquartile range (IQR). † The Disease Activity Score for 44-joint counts (DAS) ranges from 0 to 10. The Simplified Disease Activity Index (SDAI) ranges from 0 to 86. ACR/EULAR remission is defined as tender joint count ≤1, swollen-joint count ≤1, CRP ≤1mg/dL and patient's global assessment ≤10. ‡ 44 swollen joint count ∫ Ritchie Articular Index ¶ The patient's and investigator's global assessments 0 to 100 mm. ** Patient-reported Outcomes Measurement Information Score (PROMIS) †† Fatigue and pain is self-reported on a visual analogue scale, 0 to 100 mm. ‡‡ Total van der Heijde modified Sharp based on radiographs of hands and feet, range from 0 to 448. ∬. Ultrasound examination was performed using 0-3 semi quantitative scoring systems for both grey-scale and power Doppler in 32 joints; ranges from 0 to 192 for total ultrasound score, and from 0 to 96 for grey-scale and power Doppler ultrasound score.

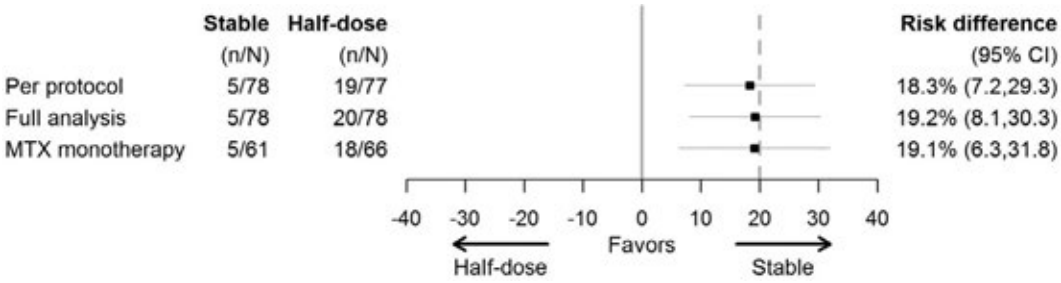

Figure 1. Non-inferiority plot of stable vs half-dose csDMARD treatment in per protocol set, full analysis set and in patients treated by methotrexate monotherapy, with the proportion of patients with a disease flare during the 12-month study period as outcome

every four months. Patients had to be in DAS remission at inclusion with no swollen joints (of 44 assessed). The primary endpoint was the proportion of patients with a disease flare during the 12-month study period (a combination of DAS > 1.6, a change in DAS > 0.6 and at least 2 swollen joints, or both the physician and patient agreed that a clinically significant flare had occurred). The non-inferiority margin was 20%, with a predefined superiority test if non-inferiority was not shown. The inferiority null-hypothesis was tested in the per-protocol population using mixed effect logistic regression. Radiographic joint damage at 0 and 12 months was scored by van der Heijde modified Sharp score (progression: ≥1 unit change/year). Clinicaltrials.gov number NCT01881308.

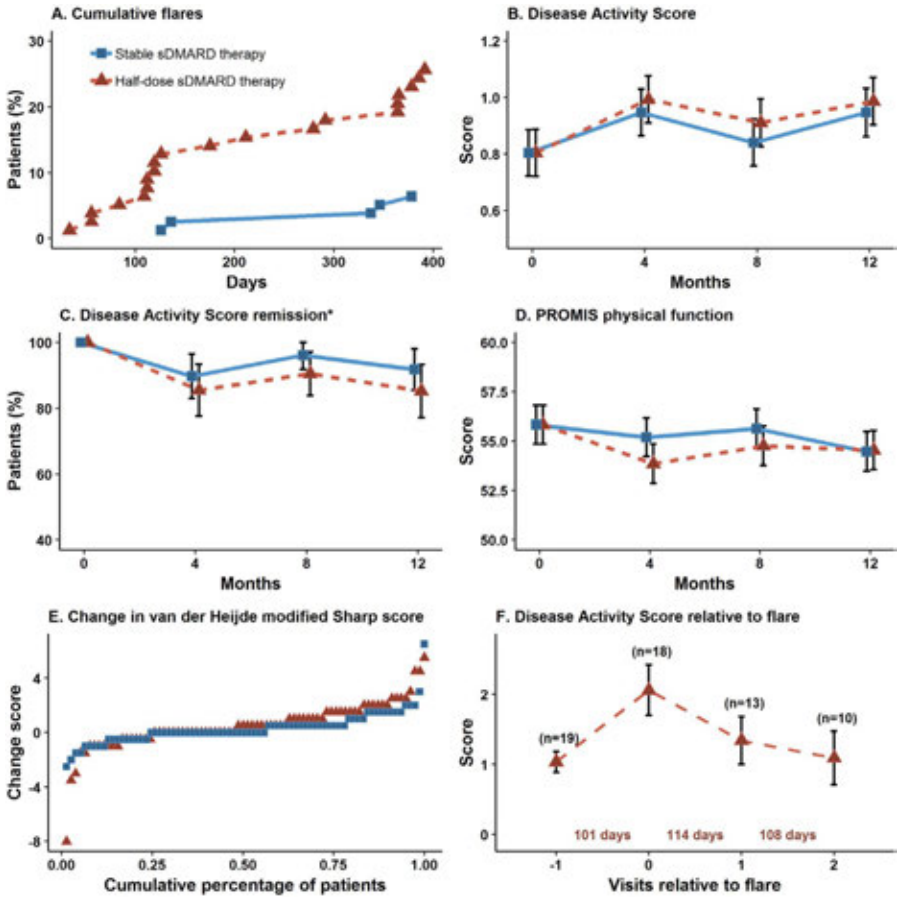

Figure 2 Secondary endpoints. Panel A shows the cumulative percentage of patients who have experienced flares. Panel B shows the Disease Activity Score. Panel C shows the percentage of patients in Disease Activity Score remission. Panel D shows the PROMIS physical function score. Panel E Panel F shows the cumulative probability plot for radiographic joint damage, scored by van der Heijde Sharp score. Panel F shows the Disease Activity Score at the visit before a flare occurred, at the flare visit and at visits after flare in the half-dose arm.

Results: We enrolled 160 patients, 155 received the allocated treatment strategy. Baseline characteristics were overall well balanced in the two arms (Table 1). 61/78 (78.2%) patients in the stable csDMARD arm and 65/78 (84.4%) in the half-dose csDMARD arm were methotrexate monotherapy users. In the primary analysis, 5/78 (6.4%) of patients in the stable csDMARD arm experienced a flare during the 12 months, compared to 19/77 (24.7%) in the half-dose csDMARD arm, giving a risk difference (95% confidence interval [CI]) of 18.3% (7.2% to 29.3%, Figure 1). Non-inferiority could not be claimed as the confidence interval crossed the non-inferiority margin. However, the confidence interval did not include the null, showing superiority of the stable arm over the half-dose arm, with similar results in methotrexate monotherapy users. In the stable arm, 2/5 (40.0%) adjusted DMARD medication following the flares, compared to 18/19 (94.7%) in the half-dose arm. No progression of radiographic joint damage was observed in 79.5% of patients on stable DMARDs and 62.7% in the half-dose arm, difference (95% CI) -17.7% (-33.0%, -2.3%, Figure 2E). At 12 months, 67 (91.8%) patients in the stable arm and 63 (85.1%) patients in the half-dose arm were in DAS remission (Figure 2), with similar results for other remission definitions. We observed 75 adverse events in the stable arm and 53 in the tapered arm, with serious adverse events in 2 (2.6%) of patients in the stable arm and in 4 (5.1%, including two serious infections) of patients in the tapered arm.

Conclusion: In RA patients in sustained remission on csDMARDs, continued csDMARD therapy with stable doses led to significantly fewer disease activity flares and less frequent radiographic joint damage progression than tapered csDMARD treatment.

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Abstract Number: L09

A Multicenter Randomized Study in Early Rheumatoid Arthritis to Compare Active Conventional Therapy versus Three Biological Treatments: 24 Week Efficacy and Safety Results of the NORD-STAR Trial

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

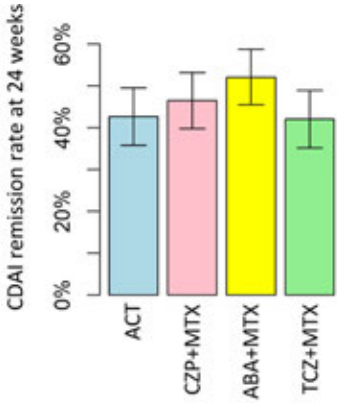
Session Title: Late-Breaking Abstracts ePoster

Session Type: Late-Breaking Abstract Poster Session

Session Time: 9:00AM–11:00AM

Background/Purpose: The optimal first-line treatment of patients (pts) with early rheumatoid arthritis (RA) is yet to be established. The primary aim was to assess and compare the proportion of pts who achieved remission with active conventional therapy (ACT) and with three different biologic therapies after 24 wks. Secondary aims were to assess and compare other efficacy measures and safety.

Methods: The investigator-initiated NORD-STAR trial (NCT01491815) was conducted in Sweden, Denmark, Norway, Finland, The Netherlands and Iceland. In this multicenter, randomized, open-label, blinded-assessor, phase 4 study pts with early RA (ACR/EULAR 2010 criteria, 18+ years old, < 24 months' symptom duration, disease activity score



Estimated CDAI remission rates at 24 weeks, intention-to-treat population, adjusted for gender, ACPA status, country, age, body-mass index and baseline DAS28-CRP, with 95% confidence intervals. ABA, abatacept; ACT, active conventional therapy; CZP, certolizumab-pegol; MTX, methotrexate; TCZ, tocilizumab.

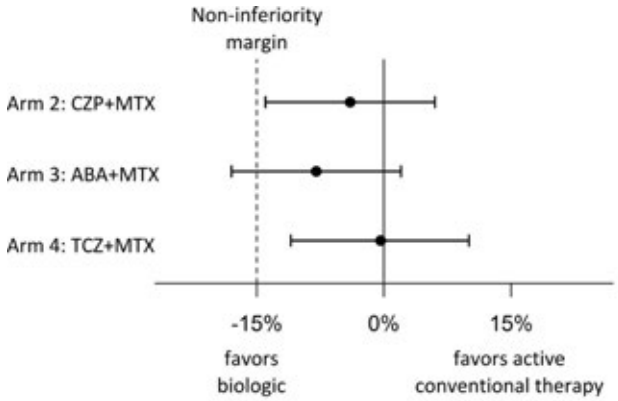
Figure 1.

(C-reactive protein, CRP (DAS28)) >3.2, ≥2 (of 66) swollen and ≥2 (68) tender joints, rheumatoid factor (RF) or anti-citrullinated protein antibody (ACPA) positive or CRP >10mg/L)) were recruited and randomized 1:1:1:1 (stratified by country, gender and ACPA). All received methotrexate (25 mg/week after one month). To this was added: Arm 1 (ACT): either oral prednisolone (tapered from 20 mg/d to 5 mg/d in 9 wks); or: sulphasalazine (2 g/day), hydroxychloroquine (35mg/kg/wk) and mandatory intra-articular (IA) triamcinolone hexacetonide (TCH) in ≤4 swollen joints (≤80

Table 1. Primary and key secondary outcomes at 24 weeks for the intention-to-treat (ITT) population.

	Arm 1: Active conventional therapy (ACT)	Arm 2: CZP+MTX	Arm 3: ABA+MTX	Arm 4: TCZ+MTX
No of patients in ITT population	200	203	204	188[§]
Table 1a	Remission and response rates			
CDAI remission	**42.0%**	**47.8%**	**52.5%**	**41.0%**
ACR/EULAR Boolean remission	34.0%	38.4%	37.3%	31.4%
DAS28 remission	63.5%	68.5%	69.6%	63.3%
SDAI remission	41.5%	49.8%	51.5%	42.6%
EULAR good response	71.5%	76.9%	79.9%	71.3%
Table 1b	Difference (95% CI) in rates with Arm 1 as the reference			
CDAI remission*	**Ref**	**4% (-5 to 13%)**	**9% (0.1 to 19%)**	**-1% (-10 to 9%)**
ACR/EULAR Boolean remission	Ref	4% (-6 to 13%)	5% (-5 to 14%)	-4% (-13 to 6%)
DAS28 remission	Ref	3% (-6 to 11%)	5% (-4 to 13%)	-1% (-10 to 8%)
SDAI remission	Ref	6% (-3 to 18%)	9% (-0.3 to 18%)	1% (-8 to 11%)
EULAR good response	Ref	4% (-4 to 14%)	8% (-2 to 18%)	0.4% (-10 to 11%)

*Primary outcome is **shown in bold.** Values in table 1a are unadjusted with NRI imputation. Values in table 1b are adjusted (for details see text) with NRI imputation; ABA: abatacept; ACR: American College of Rheumatology; ACT: active conventional therapy; CDAI: clinical disease activity index; CZP: certolizumab-pegol; DAS28: disease activity score (ESR); EULAR: European League Against Rheumatism; MTX: methotrexate; NRI: Non responder imputation; SDAI: simplified disease activity score; TCZ: tocilizumab. [§]17 Finnish patients allocated to Arm 4 did not receive Tocilizumab due to unavailability of the drug, and were excluded from the ITT population.



Non-inferiority analysis, per protocol population. Estimated differences in CDAI remission rates between Arm 1 (active conventional therapy) and Arms 2, 3 and 4 (biologic arms) as reference with 95% confidence intervals, adjusted for gender, ACPA status, country, age, body-mass index and baseline DAS28-CRP. ABA, abatacept; CZP, certolizumab-pegol, MTX, methotrexate; TCZ, tocilizumab.

Figure 2.

mg/visit up to wk 20); Arm 2 (CZP): certolizumab (CZP) 200 mg EOW SC (400 mg at 0, 2 and 4 wks); Arm 3 (ABA): abatacept 125 mg/wk SC; Arm 4 (TCZ): tocilizumab 8 mg/kg/4wks IV or 162 mg/wk SC. IA TCH was allowed in all arms up to wk 20. Primary outcome was clinical disease activity index remission (CDAI≤2.8) at wk 24 (ITT analysis). Dichotomous outcomes were analyzed by adjusted (stratification variables, age, body mass index (BMI) and baseline DAS28) logistic regression with non-responder imputation (NRI). Non-inferiority analyses (per protocol population) had a pre-specified margin of 15%.

Results: In total, 812 pts were randomized. At baseline age was 54.3±14.7 yrs (mean±SD), 31.2% were male, DAS28 5.0±1.1, 74.9% were RF positive and 81.9% ACPA positive, BMI 26.2±5.1 kg/m2, time since diagnosis 7 (1-18) days (median, IQR). Crude CDAI remission rates (ITT) were: ACT: 42.0%, CZP: 47.8%, ABA: 52.5%, TCZ: 41.0%. Figure 1 shows the estimated remission rates with 95% CI. Table 1 shows the primary and key secondary outcomes (ITT population). With ACT as the reference, the absolute difference in adjusted remission rate (delta) was 9% (95%CI: 0.1 to 19%) for ABA, 4% (-5 to 13%) for CZP and -1% (-10 to 9%) for TCZ. Differences in remission rates with CZP and TCZ, but not with ABA, remained within the pre-defined non-inferiority margin versus ACT (per-protocol population), Figure 2. Total numbers of (serious) adverse events (SAEs/total AEs) across ACT, CZP, ABA, TCZ were 13/552, 20/530, 10/527, 10/653, respectively.

Conclusion: High remission rates were found across all four treatment arms at 24 wks. Higher CDAI remission rate was observed for ABA versus ACT (delta 9%) and for CZP (4%), but not for TCZ (-1%). With the predefined 15% margin, ACT was non-inferior to CZP and TCZ, but not to ABA. These results underscore the efficacy and safety of active conventional therapy based on MTX combined with glucocorticoids and may guide future treatment strategies for early RA.

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Abstract Number: L10

Tocilizumab Effects on Coagulation Factor XIII in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Late-Breaking Abstracts ePoster
Session Type: Late-Breaking Abstract Poster Session
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease associated with a prothrombotic state. Tocilizumab, an interleukin-6 receptor inhibitor, is highly effective in controlling disease activity and thrombotic risk. Factor XIII (FXIII), involved in thrombotic complications, has been reported to be reduced in RA patients during maintenance treatment with tocilizumab, but no data are available before and after the drug administration. Thus, we investigated the effects of tocilizumab on FXIII, thrombin generation and inflammation in patients with RA naïve for the drug.

Methods: We studied fifteen consecutive adult patients with RA at baseline and four weeks after the onset of parenteral administration of tocilizumab, measuring disease activity and plasma levels of C-reactive protein (CRP), FXIII, and prothrombin fragments F1+2 by immunoenzymatic methods. Fifteen healthy subjects, sex-and age-matched with patients served as normal controls for laboratory measurements.

Results: At baseline, patients with established RA had a median DAS28 of 4.8 (3.2- 8.3) and, compared to healthy controls, had higher plasma levels of CRP ($p < 0.0001$), FXIII ($p = 0.017$) and F1+2 ($p < 0.0001$). Four weeks after starting treatment with tocilizumab, based on the EULAR response criteria, eight patients were classifiable as responders and seven as non-responders. In responders, we observed a statistically significant reduction not only of the values of DAS28 and CRP ($p = 0.012$ for both), but also of plasma levels of FXIII ($p = 0.05$) and F1+2 ($p = 0.025$). In nonresponders, all the studied parameters were unchanged. At baseline, patients with established RA had a median DAS28 of 4.8 (3.2- 8.3) and, compared to healthy controls, had higher plasma levels of CRP ($p < 0.0001$), FXIII ($p =$

0.017) and F1+2 ($p < 0.0001$). Four weeks after starting treatment with tocilizumab, based on the EULAR response criteria, eight patients were classifiable as responders and seven as non-responders. In responders, we observed a statistically significant reduction not only of the values of DAS28 and CRP ($p = 0.012$ for both), but also of plasma levels of FXIII ($p = 0.05$) and F1+2 ($p = 0.025$). In nonresponders, all the studied parameters were unchanged.

Conclusion: The decrease of FXIII and F1+2 levels after tocilizumab treatment observed only in those patients who responded to the drug indicates that the effect of tocilizumab on the prothrombotic state is linked to the control of inflammation and disease activity and not to a direct effect of the drug, thus contributing to the reduction of the cardiovascular risk.

Disclosure: R. Gualtierotti, None; **F. Ingegnoli**, None; **M. Boscolo**, None; **S. Griffini**, None; **E. Grovetti**, None; **M. Cugno**, None.

Abstract Number: L11

Maintenance of Remission Following Dose De-Escalation of Abatacept in Early, MTX-Naïve, ACPA-Positive Patients with RA: Results from a Randomized Phase IIIb Study

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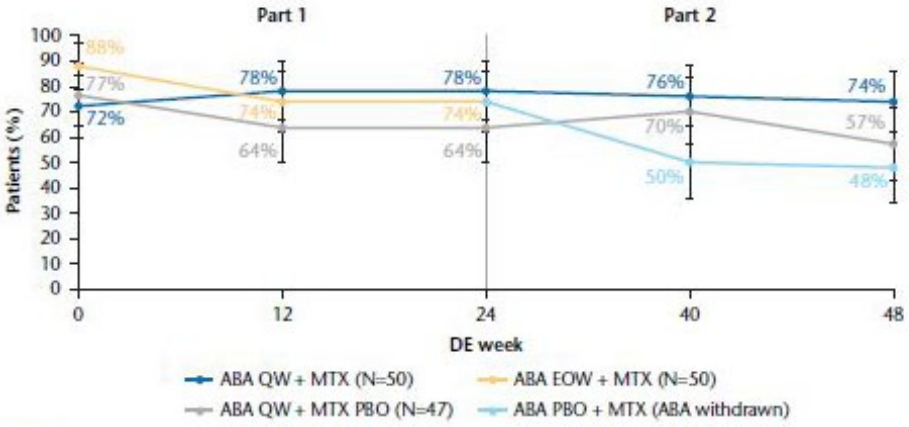
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Late-Breaking Abstracts ePoster
Session Type: Late-Breaking Abstract Poster Session
Session Time: 9:00AM–11:00AM

Background/Purpose: Although EULAR/ACR guidelines suggest tapering biologics following sustained remission in patients (pts) with RA, specific de-escalation (DE) regimens are not fully defined. The Phase IIIb Assessing Very Early Rheumatoid arthritis Treatment (AVERT)-2 trial (NCT02504268) is evaluating SC abatacept (ABA) + MTX versus ABA placebo (PBO) + MTX in ACPA-positive pts with early (ACR/EULAR 2010 criteria; disease duration ≤6 mths), active RA (SDAI >11). AVERT-2 was designed to investigate achievement of SDAI remission and a clinically meaningful dose DE strategy among pts in sustained remission who completed induction with ABA + MTX. We report results on the maintenance of remission during the DE period of AVERT-2.

Methods: Pts were randomized 3:2 to blinded SC ABA (125 mg once wkly [QW]) + MTX or ABA PBO + MTX induction treatment for 56 wks. Pts who completed induction with ABA + MTX and had sustained SDAI remission (≤3.3 at Wks 40 and 52) were re-randomized 1:1:1 to ABA QW + MTX for 48 wks, ABA every other wk (EOW) + MTX for 24 wks followed by ABA PBO + MTX for 24 wks, or ABA QW + MTX PBO for 48 wks in the DE period. MTX and oral corticosteroid doses in DE were stable. Pts with sustained SDAI remission who received ABA PBO + MTX during induction were not re-randomized and continued this treatment in the DE period in a blinded fashion; no comparisons between this arm and ABA arms were made. Endpoints: proportion of pts in SDAI remission, adjusted mean change from DE Day (D) 1 in SDAI score and safety to DE Wk 48; radiographic progression at DE Wk 48.

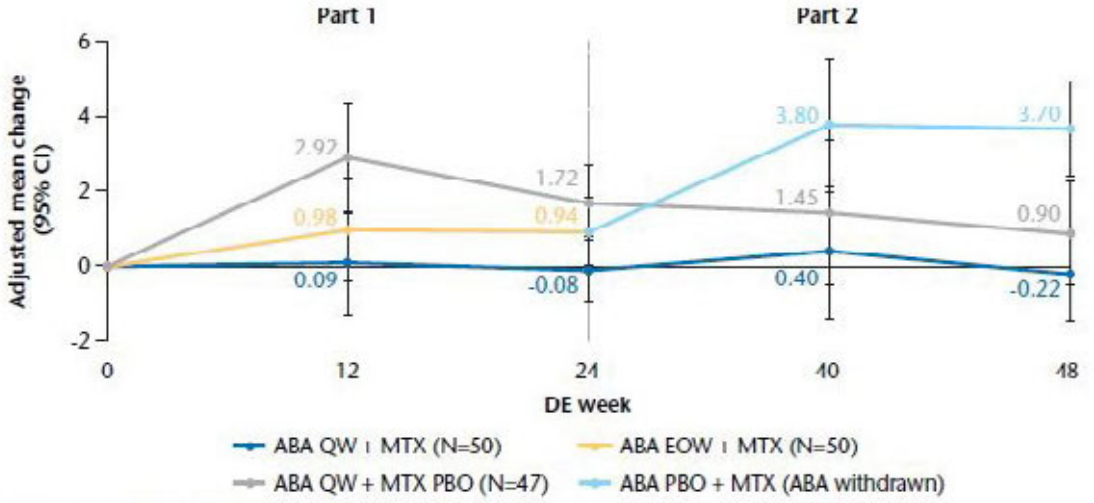
Figure 1. Proportion of re-randomized patients in SDAI remission (≤3.3) in the de-escalation period



Estimate of difference vs ABA QW + MTX (97.5% CI)					
ABA EOW + MTX (part 1)/ABA PBO + MTX (part 2)	16.0 (–1.6, 33.6)	–4.0 (–23.1, 15.1)	–4.0 (–23.1, 15.1)	–26.0 (–46.8, –5.2)	–26.0 (–47.1, –4.9)
ABA QW + MTX PBO	4.6 (–15.3, 24.4)	–14.2 (–34.6, 6.3)	–14.2 (–34.6, 6.3)	–5.8 (–26.0, 14.4)	–16.6 (–37.9, 4.8)

Missing values are imputed as not achieving remission. Patients receiving ABA EOW + MTX were switched to ABA PBO + MTX at DE Week 24, in a blinded manner.
ABA=abatacept; DE=de-escalation; EOW=every other week; MTX=methotrexate; QW=weekly; SDAI=simplified disease activity index.

Figure 2. Adjusted mean change in SDAI score in the de-escalation period among re-randomized patients



Adjusted mean difference from ABA QW + MTX (97.5% CI)				
ABA EOW + MTX (part 1)/ABA PBO + MTX (part 2)	0.89 (–1.38, 3.16)	1.01 (–0.47, 2.49)	3.40 (0.50, 6.30)	3.92 (1.84, 6.01)
ABA QW + MTX PBO	2.83 (0.47, 5.18)	1.79 (0.23, 3.36)	1.05 (–2.01, 4.12)	1.12 (–1.08, 3.32)

Estimates of adjusted mean changes are from a repeated measures mixed model which includes treatment group, time, time-by-treatment interaction, baseline value, and time-by-baseline value interaction. Patients receiving ABA EOW + MTX were switched to ABA PBO + MTX at DE Week 24, in a blinded manner. Number of patients with measurement at DE Weeks 0, 12, 24, 40 and 48, respectively: ABA QW + MTX: 50, 45, 42, 41, 42; ABA EOW + MTX/ABA PBO + MTX: 50, 45, 43, 41, 37; ABA + MTX PBO: 47, 39, 34, 33, 31.
ABA=abatacept; CI=confidence interval; DE=de-escalation; EOW=every other week; MTX=methotrexate; PBO=placebo; QW=weekly; SDAI=simplified disease activity index.

Results: 147 ABA + MTX–treated pts were re-randomized in the DE period (ABA QW + MTX, n=50; ABA EOW + MTX, n=50; ABA QW + MTX PBO, n=47); 37 pts with sustained remission who received ABA PBO + MTX during induction continued in DE period. Across the re-randomized arms, mean DAS28 (CRP), SDAI and HAQ-DI scores ranged from 1.63–1.79, 1.87–2.52 and 0.18–0.30, respectively, at DE D1. 74% of pts receiving ABA QW + MTX maintained remission at DE Wk 48 (Fig 1). Withdrawal of MTX (ABA QW + MTX PBO) led to an initial drop in remission rates to

Table 1. Radiographic progression* from DE Week −4 to DE Week 48 among re-randomized patients

	ABA QW + MTX (n=50)	ABA EOW + MTX/ ABA PBO + MTX (n=50)	ABA QW + MTX PBO (n=47)
Mean (SD) score at DE Day 1	4.11 (5.65)	8.67 (19.83)	4.96 (8.26)
Mean (SD) change from DE Day 1 at Week 104	0.21 (0.60)	0.28 (0.84)	−0.03 (0.73)
p value†	N/A	0.9736	0.0812
Patients without radiographic progression,‡ % (95% CI)	87.0 (77.2, 96.7)	84.1 (73.3, 94.9)	87.2 (76.7, 97.7)
Estimate of difference versus ABA QW + MTX (97.5% CI)	N/A	−2.9 (−19.5, 13.8)	0.2 (−16.1, 16.6)

Number of patients with assessments available at DE Week −4 and DE Week 48: ABA QW + MTX n=46, ABA EOW + MTX/ABA PBO + MTX n=44, ABA QW + MTX PBO n=39

*Measured using the modified total Sharp/van der Heijde total score

†p value is based on a rank-based non-parametric analysis of covariance model with treatment group and DE Week −4 rank score as covariates. For patients missing a DE Week 48 assessment, if DE Week −4 data and data collected during the DE period were available, imputation at DE Week 48 was done by linear extrapolation using the available assessments at DE Week −4 and time of discontinuation in DE

‡Change from DE Week −4 to DE Week 48 ≤0.5

ABA=abatacept; DE=de-escalation; EOW=every other week; N/A=not available; PBO=placebo; QW=once weekly

64%, with stabilization from DE Wk 12. After halving ABA dose to ABA EOW + MTX upon entry to the DE period, remission decreased from 88% at DE Wk 0 to 74% at DE Wk 24, and then further decreased to 48% at DE Wk 48 after ABA was fully withdrawn at DE Wk 24. At DE Wk 48, 59% of pts who received ABA PBO + MTX during induction maintained remission with this treatment. Adjusted mean change in SDAI score in the ABA arms in the DE period was numerically low, but varied between arms and increased following ABA withdrawal from the ABA EOW + MTX arm at DE Wk 24 (Fig 2). Sustained inhibition of structural damage was seen in all ABA arms (Table 1). Safety was similar across treatments with no new signals.

Conclusion: In the DE period of AVERT-2, combination therapy (abatacept + MTX) resulted in the best maintenance of remission and inhibition of structural damage progression in early seropositive pts with RA and sustained SDAI remission following abatacept + MTX treatment. Tapering of abatacept EOW + MTX to MTX only was associated with the greatest loss of remission. Abatacept-containing DE regimens should be investigated further as a viable option in clinical practice.

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Abstract Number: L12

Safety and Efficacy of Olokizumab in a Phase III Trial of Patients with Moderately to Severely Active Rheumatoid Arthritis Inadequately Controlled by Methotrexate - CREDO1 Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Late-Breaking Abstracts ePoster
Session Type: Late-Breaking Abstract Poster Session
Session Time: 9:00AM–11:00AM

Table 1. Demographic and Other Baseline Characteristics (intent-to-treat population)			
	OKZ q2w	**OKZ q4w**	**PBO**
Number of Subjects	**143**	**142**	**143**
Age, mean (SD) years	52.0(11.77)	49.1(12.07)	52.7(11.29)
Female/male, %	81.1/18.9	83.1/16.9	83.9/16.1
Duration of RA, mean (range) years	8.7(0.27-36.30)	7.3(0.32-35.52)	8.4(0.30-36.95)
MTX dose, mean (SD)[1]	16.1(3.35)	16.3(3.44)	16.1(3.65)
Glucocorticoid use, n (%)	52(36.4)	50(35.2)	41(28.7)
CRP, mean (SD) mg/L[2]	23.5(23.05)	22.7(22.68)	25.8(28.74)
Tender joint count, mean (SD)	24.4(11.40)	22.2(10.25)	24.0(11.34)
Swollen joint count, mean (SD)	14.8(6.52)	14.5(6.68)	14.6(6.85)
DAS28-CRP, mean (SD)	6.0(0.73)	5.9(0.71)	6.0(0.82)
HAQ-DI score, mean (SD)	1.74(0.471)	1.64(0.499)	1.78(0.493)
1 - 100% patients were on MTX; 2 - Upper Limit in Original Unit 6 mg/L			

Background/Purpose: Olokizumab (OKZ) is a new humanized monoclonal antibody targeting IL-6 [1, 2]. Here we present the results of the first phase III study of OKZ in patients with Rheumatoid Arthritis (RA).

Methods: This randomized, double-blind, placebo-controlled, multicenter study in patients with moderately to severely active RA despite methotrexate (MTX) (ClinicalTrials.gov Identifier NCT02760368, CREDO1) was carried out in Russia, Belarus and Bulgaria. Patients were randomized 1:1:1 to receive SC injections of OKZ 64 mg every 2 weeks (q2w), OKZ 64 mg once every 4 weeks (q4w), or placebo (PBO) for 24 weeks with continuation of their background MTX. Starting at Week (Wk) 14, non-responders were prescribed rescue medication (sulfasalazine and/or hydroxychloroquine) in addition to study treatment. After Wk 24, subjects either rolled over into an ongoing open-label study or entered the Safety Follow-Up Period. The primary endpoint was American College of Rheumatology 20% (ACR20) response at Wk 12. Secondary endpoints included: percentage of subjects with low disease activity, defined as Disease Activity Score 28-joint count - C-reactive protein (DAS28-CRP) < 3.2 at Wk 12, improvement of physical ability from baseline to Wk 12 measured by the Health Assessment Questionnaire-Disability Index (HAQ-DI), ACR50 response at Wk 24, and percentage of subjects with Clinical Disease Activity Index (CDAI) ≤2.8 (remission) at Wk 24. Safety outcomes, including adverse events (AEs), serious adverse events (SAEs) and laboratory abnormalities (via central lab) were assessed.

Results: A total of 428 patients were randomized to OKZ 64mg q2w (n = 143), OKZ 64mg q4w (n = 142), or PBO (n = 143). Baseline characteristics were comparable across treatment arms (Table 1).

The vast majority of patients completed 24 weeks of the study: 130 (90.9%) in q2w, 134 (94.4%) in q4w and 132 (92.3%) in PBO arms and enrolled to open label extension study CREDO4: 122 (85.3%), 127 (89.4%) and 126 (88.1%) patients, respectively.

Both regimens of OKZ were significantly better than placebo in all primary and secondary endpoints (Table 2).

Table 2. Key efficacy results (intent-to-treat population) NRI [1]			
	OKZ q2w	**OKZ q4w**	**PBO**
Number of Subjects	**143**	**142**	**143**
ACR20 Response, n (%) Wk 12 (primary endpoint)	91(63.6)***	100(70.4)***	37(25.9)
DAS28<3.2 Response, n (%) Wk 12	48(33.6)***	55(38.7)***	5(3.5)
HAQ-DI Wk 12			
LSM [2] (SE)	-0.54(0.041)	-0.56(0.042)	-0.20(0.042)
Treatment Comparison vs Placebo			
LSM Difference (SE)	-0.34***(0.059)	-0.36***(0.059)	
97.5% CI for LSM Difference	-0.47, -0.21	-0.49, -0.23	
ACR50 Response, n (%) Wk 24	61(42.7)***	69(48.6)***	11(7.7)
CDAI ≤2.8 Response, n (%) Wk 24	12(8.4)**	11(7.7)**	0
1 - NRI= Non-Responder Imputation; 2 - LSM=Least Squares Mean; **p-value difference from PBO <0.001; ***p-value difference from PBO <0.0001; SE=Standard Error			

Table 3. Number and percentage of key TESAE (Safety Population)			
	OKZ q2w	**OKZ q4w**	**PBO**
Number of Subjects	**143**	**142**	**142**
Subjects with at Least One TESAE	8(5.6%)	8(5.6%)	4(2.8%)
Serious Infections	4(2.8%)	0	2(1.4%)
Subcutaneous abscess	2(1.4%)	0	0
Gastroenteritis	0	0	1(0.7%)
Pneumonia	0	0	1(0.7%)
Pulmonary tuberculosis	1(0.7%)	0	0
Staphylococcal sepsis	1(0.7%)	0	0
Toxic shock syndrome	1(0.7%)	0	0
Herpes zoster	0	0	0
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	0	1(0.7%)	0
Cervix carcinoma stage II	0	1(0.7%)	0
Gastrointestinal disorders	0	1(0.7%)	0
Obstructive pancreatitis	0	1(0.7%)	0
Gastrointestinal perforation	0	0	0
Vascular disorders	0	1(0.7%)	0
Diabetic vascular disorder	0	1(0.7%)	0
Venous thromboembolism	0	0	0
Death	1(0.7%)	0	0

The key efficacy outcomes were maintained throughout the 24-week period of the study.

Overall incidence of treatment-emergent adverse events (TEAEs) was 58.0% in OKZ q2w arm; 57.0% in OKZ q4w arm and 43.7% in PBO, TEAEs leading to study treatment discontinuation were reported in 4.9%, 3.5% and 0.7% patients, respectively. There was one death due to septic shock in the OKZ q2w arm.

Incidence of treatment-emergent serious adverse events (TESAEs) were numerically higher in the OKZ groups, compared to placebo with no unexpected safety signals (Table 3).

Conclusion: In this Phase III trial, treatment with OKZ over a 24-week period was associated with significant improvements in the signs, symptoms and physical function of RA, with a safety profile consistent with Phase II data for OKZ and with the data for the agents with similar mechanism of action.

There were no discernible differences between the two regimens of OKZ in efficacy or safety outcomes.

Disclosure: E. Nasonov, None; **S. Fatenejad**, RPharm International, 1; **E. Korneva**, R-Pharm, 1; **D. Krechikova**, R-Pharm, 1; **A. Maslyansky**, None; **T. Plaksina**, R-Pharm, 1; **M. Stanislav**, R-Pharm, 5; **R. Stoilov**, R-Pharm, 1; **T. Tyabut**, R-Pharm, 1; **S. Yakushin**, R-Pharm, 1; **E. Zonova**, R-Pharm, 1; **M. Genovese**, UNITY, 1.

Abstract Number: L13

Guselkumab, an Anti-interleukin-23p19 Monoclonal Antibody, in Biologic-naïve Patients with Active Psoriatic Arthritis: Week 24 Results of the Phase 3, Randomized, Double-blind, Placebo-controlled Study

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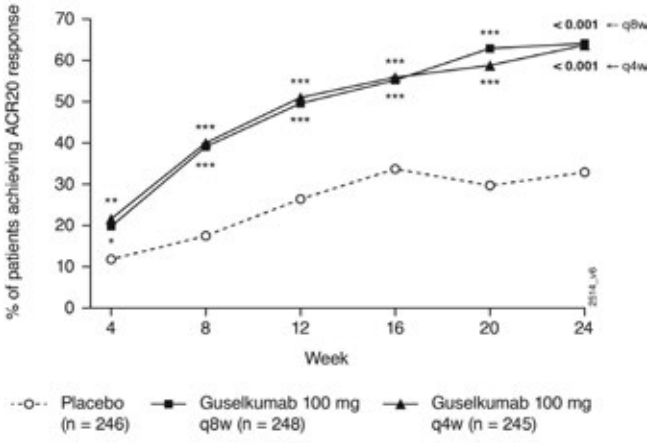
Figure – ACR20 response over time (see Table 1 for details of statistical testing)



unadjusted *p<0.05, **p<0.01, and ***p<0.001
bolded p values are adjusted

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019
Session Title: Late-Breaking Abstracts ePoster
Session Type: Late-Breaking Abstract Poster Session
Session Time: 9:00AM–11:00AM

Background/Purpose: Guselkumab (GUS), an anti-interleukin-23p19 monoclonal antibody, is approved for psoriasis (PsO). We assessed GUS efficacy and safety in DISCOVER-1 (ACR2019 Abstract ID697955) and DISCOVER-2, two Phase 3 trials in psoriatic arthritis (PsA).

Table 1. Efficacy in DISCOVER-2, a Randomized, Placebo-controlled, Phase 3 Study of GUS in Biologic-naïve Pts with PsA[1]

	Guselkumab 100 mg Q4W (N=245)	Guselkumab 100 mg Q8W (N=248)	Placebo (N=246)
Endpoints controlled for multiplicity			
Primary endpoint			
ACR20 response at W24, %	63.7	64.1	32.9
% difference vs placebo (95% CI)	*30.8 (22.4, 39.1)*	*31.2 (22.9, 39.5)*	
Adjusted p value[2]	*<0.001*	*<0.001*	
Major secondary endpoints			
IGA 0/1 + ≥2-grade decrease response at W24[3], %	68.5	70.5	19.1
% difference vs placebo (95% CI)	*49.8 (41.2, 58.4)*	*50.9 (42.2, 59.7)*	
Adjusted p value[2]	*<0.001*	*<0.001*	
HAQ-DI change at W24 LSmean (95% CI)	-0.40 (-0.46, -0.34)	-0.37 (-0.43, -0.31)	-0.13 (-0.19, -0.07)
LSmean difference vs placebo (95% CI)	-0.27 (-0.35, -0.19)	*-0.24 (-0.32, -0.15)*	
Adjusted p value[2]	*<0.001*	*<0.001*	
PsA-modified vdH-S change at W24, LSmean (95% CI)	0.29 (-0.05, 0.63)	0.52 (0.18, 0.86)	0.95 (0.61, 1.29)
LSmean difference vs placebo (95% CI)	*-0.66 (-1.13, -0.19)*	*-0.43 (-0.90, 0.03)*	
Adjusted p value[2]	*0.011*	*0.072*	
SF-36 PCS change at W24, LSmean (95% CI)	7.04 (6.14, 7.94)	7.39 (6.50, 8.29)	3.42 (2.53, 4.32)
LSmean difference vs placebo (95% CI)	*3.62 (2.39, 4.85)*	*3.97 (2.74, 5.20)*	
Adjusted p value[2]	*0.011*	*0.011*	
SF-36 MCS change at W24, LSmean (95% CI)	4.22 (3.14, 5.29)	4.17 (3.10, 5.23)	2.14 (1.07, 3.21)
LSmean difference vs placebo (95% CI)	*2.07 (0.60, 3.54)*	*2.02 (0.56, 3.49)*	
Adjusted p value[2]	*0.072*	*0.072*	
Endpoints not controlled for multiplicity			
ACR20 response at W16, %	55.9	55.2	33.7
% difference vs placebo (95% CI)	*22.2 (13.7, 30.7)*	*21.5 (13.1, 30.0)*	
Unadjusted p value[4]	*<0.001*	*<0.001*	
ACR50 response at W24, %	33.1	31.5	14.2
% difference vs placebo (95% CI)	*18.8 (11.5, 26.1)*	*17.2 (10.0, 24.4)*	
Unadjusted p value[4]	*<0.001*	*<0.001*	
ACR50 response at W16, %	20.8	28.6	9.3
% difference vs placebo (95% CI)	*11.5 (5.2, 17.7)*	*19.3 (12.6, 25.9)*	
Unadjusted p value[4]	*<0.001*	*<0.001*	
ACR70 response at W24, %	13.1	18.5	4.1
% difference vs placebo (95% CI)	*9.0 (4.1, 13.8)*	*14.5 (9.1, 19.9)*	
Unadjusted p value[4]	*<0.001*	*<0.001*	
DAS28-CRP change at W24, LSmean (95% CI)	-1.62 (-1.76, -1.49)	-1.59 (-1.72, -1.45)	-0.97 (-1.11, -0.84)
LSmean difference vs placebo (95% CI)	*-0.65 (-0.83, -0.47)*	*-0.61 (-0.80, -0.43)*	
Unadjusted p value[4]	*<0.001*	*<0.001*	
HAQ-DI improvement ≥0.35 at W24[5], n/N (%)	56.1	50.0	31.4
% difference vs placebo (95% CI)	24.4 (15.8, 33.0)	18.7 (10.0, 27.3)	
Unadjusted p value[4]	*<0.001*	*<0.001*	
PASI75 response at W24[3], %	78.3	79.0	23.0
% difference vs placebo (95% CI)	*55.4 (47.0, 63.8)*	*55.7 (47.2, 64.2)*	
Unadjusted p value[4]	*<0.001*	*<0.001*	
PASI90 response at W24[3], %	60.9	68.8	9.8
% difference vs placebo (95% CI)	*51.3 (43.2, 59.3)*	*58.6 (50.6, 66.6)*	
Unadjusted p value[4]	*<0.001*	*<0.001*	
PASI100 response at W24[3], %	44.6	45.5	2.7
% difference vs placebo (95% CI)	*42.2 (34.9, 49.6)*	*42.4 (34.8, 50.1)*	
Unadjusted p value[4]	*<0.001*	*<0.001*	
MDA response at W24, %	18.8	25.0	6.1
% difference vs placebo (95% CI)	12.7 (7.0, 18.4)	18.9 (12.8, 25.0)	
Unadjusted p value[4]	*<0.001*	*<0.001*	

Data were analyzed in randomized pts who received at least 1 dose of study drug according to the treatment assigned and based on composite estimand, where pts meeting treatment-failure criteria were considered nonresponders for binary endpoints and as having no improvement from baseline for continuous endpoints. Missing data were imputed as nonresponders for binary endpoints; multiple imputation was used to impute missing data for continuous endpoints. Treatment difference for binary endpoints was assessed via Cochran-Mantel-Haenszel test stratified by baseline use of non-biologic DMARDs (yes/no) and CRP prior to randomization (<2.0 vs ≥2.0 mg/dL). Treatment difference for continuous endpoints was assessed via an analysis of covariance model.

[1] Randomization was stratified by Week 0 DMARD use [Y/N] and CRP [<2.0 vs ≥2.0 mg/dL].

[2] Two multiplicity-controlled procedures were prespecified to satisfy different regulatory requirements. The adjusted p-values presented herein derive from the testing procedure in which: 1) the primary endpoint was first tested in sequence by dose at the ≤0.05 significance level, 2) the major secondary endpoints shown above were subsequentially tested for both GUS doses using a graphic procedure that specified testing sequences and alpha allocations, and 3) the overall type I error was controlled at p≤0.05 for the specified endpoints for both GUS doses.

[3] Assessed in 184, 176, and 183 pts with ≥3% BSA PsO and IGA score ≥2 at W0 in the guselkumab q4w, guselkumab q8w, and placebo groups, respectively .

[4] Unadjusted (nominal) p values are not controlled for multiplicity and are descriptive/supportive only; no statistical significance should be implied.

[5] Assessed in 228, 228, and 236 patients with HAQ-DI ≥0.35 at W0 in the guselkumab q4w, guselkumab q8w, and placebo groups, respectively.

Methods: In DISCOVER-2, adults with active PsA (≥5 swollen+≥5 tender joints; CRP ≥0.6mg/dL) despite non-biologic DMARDs and/or NSAIDs (biologic-naïve) were randomized (1:1:1) to GUS 100mg every 4 wks (Q4W); GUS 100mg at W0, W4, Q8W (Q8W); or placebo (PBO). Concomitant stable select non-biologic DMARDs, oral corticosteroids, and NSAIDs were allowed. At W16, patients (pts) with < 5% improvement in tender+swollen joints could initiate/increase the dose of permitted medications. The primary endpoint was W24 ACR20 response. Major secondary endpoints (MSEs) at W24 were Investigator's Global Assessment (IGA) PsO response (IGA=0/1 and ≥2-grade reduction) in pts with ≥3% BSA PsO&IGA ≥2 at W0; changes in HAQ-DI, PsA-modified van der Heijde-Sharp (vdH-S), and SF-36 PCS/MCS scores; resolution of enthesitis/dactylitis (using pooled DISCOVER-1&2 data); change in DAS28-CRP; and ACR50/70 responses. MSEs at W16 were ACR20/50 responses. Multiplicity-adjusted p-values for controlled endpoints, and nominal (unadjusted) p-values for uncontrolled endpoints, are presented. Adverse events (AEs) through W24 are reported.

Results: 739 treated pts in DISCOVER-2 with moderate-to-severe disease (mean swollen/tender joints: 12/21, median CRP: 1.2 mg/dL, mean BSA with PsO: 17.4%, IGA=3 or 4: 46.1% of pts) were analyzed. Significantly more GUS Q4W (63.7%) and Q8W (64.1%) vs PBO (32.9%) pts achieved ACR20 response at W24 (both adjusted p< 0.001). Both GUS doses separated from PBO by W4 (Figure). Among pts with ≥3% BSA PsO&IGA ≥2 at W0, significantly more GUS Q4W and Q8W vs PBO pts achieved IGA response at W24 (both adjusted p< 0.001). Significantly greater improvements from baseline in HAQ-DI (adjusted p< 0.001) and SF-36 PCS (adjusted p≤0.011) were seen with GUS Q4W and Q8W vs PBO at W24. Mean changes in total modified vdH-S scores at W24 were significantly lower for GUS Q4W (0.29) and numerically lower for GUS Q8W (0.52) vs. PBO (0.95; adjusted p=0.011 and p=0.072, respectively). Numerically larger mean improvements in SF-36 MCS scores were seen with GUS Q4W (4.22) and Q8W (4.17) than PBO (2.14; both adjusted p=0.072; Table 1). Among pooled DISCOVER-1&2 pts with the condition at baseline, significantly higher proportions of GUS Q4W and Q8W vs PBO pts had resolved enthesitis or dactylitis at W24 (all

Table 2. Summary of Dactylitis and Enthesitis Resolution at W24

	GUS 100 mg		Placebo
	Q4W	Q8W	
Endpoints controlled for multiplicity			
POOLED DISCOVER-1[1] and DISCOVER-2			
Resolution of dactylitis, n/N (%)	101/159 (63.5%)	95/160 (59.4%)	65/154 (42.2%)
[Diff vs PBO (95% CI)]	*[21.3 (10.5, 32.0)]*	*[18.0 (7.4, 28.6)]*	
Adjusted p value[2]	*0.011*	*0.030*	
Resolution of enthesitis, n/N (%)	109/243 (44.9%)	114/230 (49.6%)	75/255 (29.4%)
[Diff vs PBO (95% CI)]	*[14.6 (6.4, 22.7)]*	*[20.1 (11.8, 28.5)]*	
Adjusted p value[2]	*0.030*	*0.030*	
Endpoints not controlled for multiplicity			
DISCOVER-2 – biologic-naïve pts			
Resolution of dactylitis, n/N (%)	77/121 (63.6%)	63/111 (56.8%)	38/99 (38.4%)
[Diff vs PBO (95% CI)]	*[24.5 (11.8, 37.1)]*	*[18.7 (5.7, 31.7)]*	
Unadjusted p value[3]	*<0.001*	*0.007*	
Resolution of enthesitis, n/N (%)	74/170 (43.5%)	85/158 (53.8%)	54/178 (30.3%)
[Diff vs PBO (95% CI)]	*[12.3 (2.6, 22.1)]*	*[23.3 (13.1, 33.5)]*	
Unadjusted p value[3]	*0.017*	*<0.001*	

See Table 1 for details of statistical testing.

[1] 381 treated pts with active PsA (≥3 swollen+≥3 tender joints, CRP ≥0.3mg/dL), including 118 pts who previously received 1-2 tumor necrosis factor inhibitors, were analyzed in DISCOVER-1, which was similar to DISCOVER-2 in trial design with the exception of no radiographic evaluations. Subsets of the DISCOVER-1 patients presenting with dactylitis (N=142) and enthesitis (N=222) at baseline are included in these pooled analyses.

[2] p-values derive from multiplicity-controlled procedure (see Table 1).

[3] Unadjusted (nominal) p values are not controlled for multiplicity and are descriptive/supportive only; no statistical significance should be implied.

adjusted p< 0.05; Table 2). Numerically higher proportions of GUS Q4W and Q8W than PBO pts with PASI75/90/100 (among pts with ≥3% BSA PsO&IGA ≥2 at W0) and MDA responses at W24 (Table 1) were observed. Serious AEs and serious infections occurred in 18/739 (2.4%) and 5/739 (0.7%) pts, respectively, and no pt died through W24.

Conclusion: In pts with active PsA, GUS Q4W and Q8W significantly improved joint and skin symptoms, physical function, and quality of life, and resolved enthesitis/dactylitis. GUS Q4W significantly reduced radiographic damage progression vs. PBO. GUS was well tolerated, and observed AEs were consistent with GUS safety in PsO pts.

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Abstract Number: L14

Tofacitinib as Monotherapy Following Methotrexate Withdrawal in Patients with Psoriatic Arthritis Previously Treated with Open-label Tofacitinib + Methotrexate: A Randomized, Placebo-controlled Sub-study of OPAL Balance

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SESSION INFORMATION

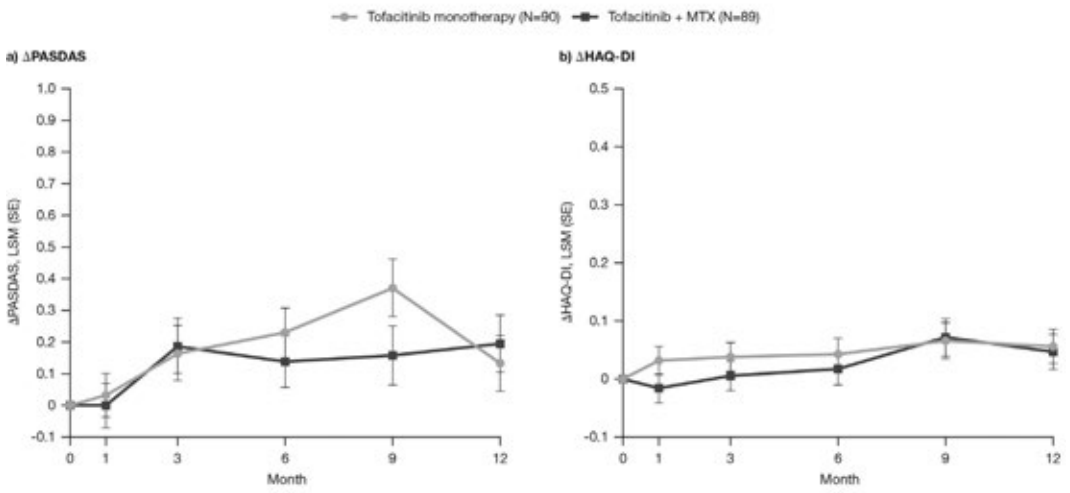
Session Date: Tuesday, November 12, 2019

Session Title: Late-Breaking Abstracts ePoster

Session Type: Late-Breaking Abstract Poster Session

Session Time: 9:00AM–11:00AM

Figure 1. LSM (SE) a) ΔPASDAS[a] and b) ΔHAQ-DI[a] up to Month 12 of the MTX withdrawal sub-study



[a]Primary endpoints at Month 6
Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction, and baseline value, without imputation for missing values; a common unstructured covariance matrix was used. The numbers of patients included in the repeated measures model from tofacitinib monotherapy and tofacitinib + MTX arms were 90 and 89, respectively, for both PASDAS and HAQ-DI. For each endpoint at each time point, the 95% CI of the LSM difference between the tofacitinib monotherapy and tofacitinib + MTX arms included 0
Δ, change from sub-study baseline; CI, confidence interval; HAQ-DI, Health Assessment Questionnaire-Disability Index; LSM, least squares mean; MTX, methotrexate; PASDAS, Psoriatic Arthritis Disease Activity Score, SE, standard error

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. Tofacitinib monotherapy has not been previously studied in PsA. This sub-study of OPAL Balance assessed tofacitinib 5 mg twice daily (BID) as monotherapy after MTX withdrawal vs with continued background MTX in patients (pts) with PsA.

Methods: OPAL Balance (NCT01976364) was an open-label (OL), long-term extension (LTE) study of tofacitinib in pts with PsA who had participated in Phase 3 studies (OPAL Broaden [NCT01877668]; OPAL Beyond [NCT01882439]). The MTX withdrawal sub-study was a multicenter, 12-month, randomized, double-blind, placebo (PBO)-controlled, parallel group, estimation study of pts who had completed ≥24 months' tofacitinib treatment in the LTE (5 mg BID; stable for ≥3 months) and were receiving oral MTX (7.5–20 mg/week; stable for ≥4 weeks) before sub-study entry. Pts remained on OL tofacitinib 5 mg BID and were randomized 1:1 to receive PBO (tofacitinib monotherapy; ie, underwent blinded MTX withdrawal) or MTX (tofacitinib + MTX; same stable doses) for 12 months. Primary endpoints were changes from sub-study baseline (BL; Δ) in Psoriatic Arthritis Disease Activity Score (PASDAS) and HAQ-Disability Index (HAQ-DI) at Month (M)6. Secondary efficacy endpoints (Table 1) were assessed at all time points. Safety (Table 2) was assessed throughout the sub-study. No specific statistical hypothesis was tested.

Results: Of 180 pts randomized, 179 were treated in the sub-study (tofacitinib monotherapy, n=90; tofacitinib + MTX, n=89). Demographics and BL characteristics were similar between tofacitinib monotherapy/tofacitinib + MTX (mean age, 53.1/51.8 yrs; female, 52.2%/55.1%; mean disease duration, 11.3/11.2 yrs; low disease activity [PASDAS ≤3.2], 70.0%/62.9%). At M6, least squares mean (LSM) (SE) ΔPASDAS was 0.229 (0.079) for tofacitinib monotherapy and 0.138 (0.081) for tofacitinib + MTX, and LSM ΔHAQ-DI were 0.043 (0.027) and 0.017 (0.028), respectively (primary endpoints; Figure 1; Table 1); no clinically meaningful differences were observed. In general, efficacy and patient-reported outcomes were similar between treatment arms at M6 and M12 (Table 1); rates of minimal disease activity were maintained regardless of MTX withdrawal. Rates of adverse events (AEs), serious AEs, discontinuations due to AEs, and AEs of special interest were comparable between treatment arms; laboratory changes were also similar, except that elevations in liver function enzymes were more common with tofacitinib + MTX (Table 2). One (1.1%) and two (2.2%) pts receiving tofacitinib + MTX met monitoring criteria for absolute neutrophil (< 1.2 x 10^3/

Table 1. Primary and secondary efficacy outcomes at Month 6 and Month 12 of the MTX withdrawal sub-study

	Month 6			Month 12		
	Tofacitinib monotherapy (N=90)	Tofacitinib + MTX (N=89)	Treatment difference[a] (95% CI)	Tofacitinib monotherapy (N=90)	Tofacitinib + MTX (N=89)	Treatment difference[a] (95% CI)
ΔPASDAS,[b] LSM (SE) [N1]	0.229 (0.079) [87]	0.138 (0.081) [81]	0.091 (-0.131, 0.313)	0.133 (0.088) [85]	0.194 (0.090) [82]	-0.061 (-0.309, 0.188)
ΔHAQ-DI,[b] LSM (SE) [N1]	0.043 (0.027) [88]	0.017 (0.028) [84]	0.026 (-0.051, 0.102)	0.056 (0.029) [86]	0.047 (0.030) [83]	0.010 (-0.073, 0.093)
MDA,[c] n (%) [N1]	44 (48.9) [88]	41 (46.1) [84]	2.8 (-11.8, 17.5)	40 (44.4) [83]	37 (41.6) [83]	2.9 (-11.6, 17.4)
%ΔBSA,[d] LSM (SE) [N1]	17.19 (21.16) [41]	41.51 (20.75) [42]	-24.33 (-83.35, 34.69)	41.75 (20.33) [38]	34.74 (19.91) [39]	7.02 (-49.73, 63.77)
ΔLEI,[d] LSM (SE) [N1]	-0.7 (0.28) [16]	-0.5 (0.29) [15]	-0.2 (-1.1, 0.6)	-0.3 (0.27) [15]	-0.5 (0.28) [15]	0.2 (-0.6, 1.0)
LEI,[e] mean (SE) [N1]	0.2 (0.10) [72]	0.2 (0.09) [69]	-	0.1 (0.06) [70]	0.2 (0.08) [68]	-
DSS,[e,f] mean (SE) [N1]	0.0 (0.00) [87]	0.0 (0.00) [78]	-	0.0 (0.01) [84]	0.0 (0.03) [77]	-
ΔPGA-PsO,[d] LSM (SE) [N1]	0.2 (0.12) [33]	-0.1 (0.11) [38]	0.3* (0.0, 0.6)	0.3 (0.15) [30]	0.0 (0.15) [33]	0.3 (-0.1, 0.7)
ΔTJC (66), LSM (SE) [N1]	0.5 (0.37) [88]	0.5 (0.37) [84]	0.0 (-1.0, 1.0)	0.5 (0.32) [84]	0.3 (0.32) [83]	0.2 (-0.7, 1.1)
ΔSJC (66), LSM (SE) [N1]	0.1 (0.15) [88]	0.0 (0.16) [84]	0.0 (-0.4, 0.5)	0.0 (0.14) [84]	0.1 (0.14) [83]	-0.1 (-0.5, 0.3)
ΔPain-VAS, LSM (SE) mm [N1]	4.07 (1.67) [88]	3.12 (1.71) [84]	0.95 (-3.78, 5.69)	3.35 (1.66) [86]	2.69 (1.69) [83]	0.66 (-4.03, 5.35)
ΔPGJS-VAS, LSM (SE) mm [N1]	1.83 (1.69) [88]	-0.22 (1.72) [84]	2.05 (-2.71, 6.81)	0.25 (1.76) [86]	2.15 (1.80) [82]	-1.90 (-6.86, 3.06)
ΔSF-36v2 PCS, LSM (SE) [N1]	-1.42 (0.47) [88]	-0.65 (0.48) [82]	-0.77 (-2.09, 0.55)	-1.00 (0.52) [86]	-1.52 (0.53) [83]	0.52 (-0.96, 2.00)
ΔSF-36v2 MCS, LSM (SE) [N1]	-0.89 (0.71) [88]	-0.23 (0.73) [82]	-0.66 (-2.66, 1.36)	-0.47 (0.68) [86]	-0.38 (0.69) [83]	-0.09 (-2.01, 1.84)
ΔSF-36v2 PF domain, LSM (SE) [N1]	-0.80 (0.57) [88]	-0.27 (0.59) [83]	-0.53 (-2.15, 1.08)	-1.02 (0.66) [86]	-1.01 (0.68) [83]	-0.01 (-1.89, 1.86)
ΔFACIT-F Total score, LSM (SE) [N1]	-2.0 (0.60) [88]	-1.3 (0.61) [84]	-0.7 (-2.4, 1.0)	-0.7 (0.64) [86]	-1.4 (0.66) [83]	0.8 (-1.1, 2.6)
ΔEQ-VAS, LSM (SE) mm [N1]	-1.9 (1.39) [88]	4.4 (1.41) [83]	-6.3* (-10.2, -2.4)	-1.9 (1.76) [86]	3.0 (1.82) [83]	-4.9 (-9.9, 0.2)

*95% CI excluded 0

[a]Tofacitinib monotherapy – tofacitinib + MTX. Reported as LSM difference (95% CI) for continuous endpoints and proportion difference (95% CI) for binary endpoints. For continuous endpoints, results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction, and baseline value, without imputation for missing values; a common unstructured covariance matrix was used

For binary endpoints, results were based on normal approximation to the difference in binomial proportions

[b]Primary endpoint at Month 6

[c]Missing response = non-response

[d]In patients whose BSA, LEI, or PGA-PsO was >0 at baseline for %ΔBSA, ΔLEI, and ΔPGA-PsO, respectively

[e]In patients whose LEI or DSS was 0 at baseline for mean LEI and DSS, respectively. Only sample means based on patients evaluable at each visit were reported

[f]LSM ΔDSS was not calculated due to the low number of patients with DSS >0 at baseline

95% CI for all treatment comparisons between tofacitinib monotherapy and tofacitinib + MTX included 0 unless noted otherwise

N is the number of patients randomized and treated; N1 is the number of patients evaluable at each visit if differing from the overall N

Δ, change from sub-study baseline; BSA, body surface area; CI, confidence interval; DSS, Dactylitis Severity Score; EQ, EuroQoL; FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; LEI, Leeds Enthesitis Index; LSM, least squares mean; MCS, Mental Component Summary; MDA, minimal disease activity; MTX, methotrexate; PASDAS, Psoriatic Arthritis Disease Activity Score; PCS, Physical Component Summary; PF, physical functioning; PGA-PsO, Physician's Global Assessment-Psoriasis; PGJS, Patient's Global Joint and Skin Assessment; SE, standard error; SF-36v2, Short Form-36 Health Survey (Version 2, Acute); SJC, swollen joint count; TJC, tender joint count; VAS, visual analog scale

mm^3) and lymphocyte (< 0.5 x 10^3/mm^3) counts, respectively; no pts met discontinuation criteria (ie, values were not confirmed).

Conclusion: In general, no clinically meaningful differences in efficacy and safety were observed in pts with PsA who received OL tofacitinib 5 mg BID as monotherapy after MTX withdrawal vs with continued MTX. No new safety risks were identified. Limitations include that the sub-study was designed as an estimation study and not powered for hypothesis testing, and only pts on long-term treatment who had responded well to, and tolerated, tofacitinib and MTX were included.

Table 2. Safety outcomes up to Month 12 of the MTX withdrawal sub-study

	Tofacitinib monotherapy (N=90)		Tofacitinib + MTX (N=89)	
Patients with AEs, n (%)	43 (47.8)		41 (46.1)	
Patients with SAEs, n (%)	4 (4.4)		3 (3.4)	
Patients who discontinued due to AEs, n (%)	3 (3.3)		4 (4.5)	
Deaths, n (%)	0		0	
Patients with AEs of special interest, n (%)				
Herpes zoster[a]	1 (1.1)		2 (2.2)	
Serious infections	0		2 (2.2)	
Opportunistic infections[b]	0		1 (1.1)[c]	
Malignancies (excluding NMSC)[b]	1 (1.1)[d]		1 (1.1)[e]	
NMSC[b]	0		0	
MACE[b]	0		0	
DVT[f]	0		0	
PE[f]	0		0	
ATE[f]	1 (1.1)[g]		0	
Gastrointestinal perforations[b]	0		0	
ILD[b]	0		0	
Patients with laboratory abnormalities,[h] n (%)				
ALT ≥2 x ULN	2 (2.2)		10 (11.2)	
ALT ≥3 x ULN	0		5 (5.6)	
AST ≥2 x ULN	1 (1.1)		7 (7.9)	
AST ≥3 x ULN	0		3 (3.4)	
ΔLaboratory values, mean (SE)	**Month 6**	**Month 12**	**Month 6**	**Month 12**
ANC, $10^3/mm^3$	0.09 (0.17)	0.12 (0.17)	-0.16 (0.21)	-0.24 (0.21)
ALC, $10^3/mm^3$	0.12 (0.05)	0.14 (0.05)	-0.06 (0.04)	-0.02 (0.05)
Platelets, $10^3/mm^3$	-1.84 (5.48)	13.98 (5.59)	-9.57 (5.19)	1.52 (4.93)
ALT, IU/L	-3.01 (1.62)	-2.71 (1.56)	4.53 (2.09)	2.46 (1.30)
AST, IU/L	-1.69 (1.13)	-1.51 (1.20)	3.08 (0.98)	1.69 (0.82)
Creatine kinase, U/L	-6.89 (14.44)	4.66 (21.86)	1.16 (10.97)	-18.52 (9.39)

[a]One serious event of pneumonia herpes viral was reported in a patient receiving tofacitinib + MTX; the other herpes zoster events were non-serious
[b]Reviewed by an independent adjudication committee
[c]One patient receiving tofacitinib + MTX reported an event of herpes zoster and an event of pneumonia herpes viral, both of which were adjudicated as opportunistic infections
[d]One event of bladder cancer
[e]One event of Bowen's disease
[f]Based on Standardized MedDRA Query terms
[g]One event of mild carotid occlusion (non-serious)
[h]In all patients, without regard to baseline abnormality
Δ, change from sub-study baseline; AE, adverse event; ALC, absolute lymphocyte count; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; ATE, arterial thromboembolism; DVT, deep vein thrombosis; ILD, interstitial lung disease; MACE, major adverse cardiovascular event; MedDRA, Medical Dictionary for Regulatory Activities; MTX, methotrexate; NMSC, non-melanoma skin cancer; PE, pulmonary embolism; SAE, serious adverse event; SE, standard error; ULN, upper limit of normal

Disclosure: P. Nash, AbbVie, 1, 2, 3, BMS, 1, 2, 3, Celgene, 1, 2, 3, Eli Lilly, 1, 2, 3, Gilead, 1, 2, 3, Janssen, 1, 2, 3, MSD, 1, 2, 3, Novartis, 1, 2, 3, Pfizer Inc, 1, 2, 3, Roche, 1, 2, 3, Sanofi, 1, 2, 3, UCB, 1; **L. Coates**, AbbVie, 1, 2, 3, Amgen, 1, 2, Celgene, 1, 2, Eli Lilly, 1, 2, 3, Galapagos, 1, Gilead, 1, Janssen, 1, Novartis, 1, 2, 3, Pfizer Inc, 1, 2, 3, UCB, 1; **P. Mease**, AbbVie, 1, 2, 3, Amgen, 1, 2, 3, Bristol-Myers Squibb, 1, 2, 3, Celgene, 1, 2, 3, Eli Lilly, 1, 2, 3, Galapagos, 1, Genentech, 1, Gilead, 1, Janssen, 1, 2, 3, Novartis, 1, 2, 3, Pfizer Inc, 1, 2, 3, Sun, 1, 2, UCB, 1, 2, 3, Boehringer Ingelheim, 1; **A. Kivitz**, AbbVie, 1, 2, Amgen, 1, Boehringer Ingelheim, 1, Celgene, 1, Flexion, 1, Genzyme, 1, 2, Gilead, 1, Horizon, 1, Janssen, 1, Merck, 1, Novartis, 1, Pfizer Inc, 1, 2, 3, Regeneron, 1, 2, Sanofi, 1, 2, 3, Sun Pharma, 1, UCB, 1, GSK, 1; **D. Gladman**, AbbVie, 1, 2, Amgen, 1, 2, BMS, 1, Celgene, 1, 2, Eli Lilly, 1, 2, Galapagos, 1, Gilead, 1, Janssen, 1, Novartis, 1, 2, Pfizer Inc, 1, 2, UCB, 1, 2; **F. Behrens**, Pfizer Inc, 1, 2, 3; **J. Wei**, AbbVie, 1, 2, BMS, 1, 2, Celgene, 1, 2, Chugai, 1, Eisai, 5, Janssen, 1, 2, Novartis, 1, 2, Pfizer Inc, 1, 2, Sanofi-Aventis, 1, UCB Pharma, 1, 2, Eli Lilly, 1; **D. Fleishaker**, Pfizer Inc, 1, 2; **J. Wu**, Pfizer Inc, 1, 3; **C. Wang**, Pfizer Inc, 1, 2; **A. Romero**, Pfizer Inc, 1, 3; **L. Fallon**, Pfizer Inc, 1, 3; **M. Hsu**, Pfizer Inc, 1, 3; **K. Kanik**, Pfizer Inc, 1, 2.

Abstract Number: L15

Efficacy, Safety, and Pharmacodynamic Effects of the Bruton's Tyrosine Kinase Inhibitor, Fenebrutinib (GDC-0853), in Moderate to Severe Systemic Lupus Erythematosus: Results of a Phase 2 Randomized Controlled Trial

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Table 1. Key Efficacy and Safety Results

	PBO (*n*=86)	FEN 150 mg QD (*n*=87)	FEN 200 mg BID (*n*=87)
Primary Endpoint			
SRI-4 Response at W48			
Responder, *n* (%)	38 (44)	44 (51)	45 (52)
Treatment difference vs. PBO (%)		6.4	7.5
95% CI		(-8.5, 21.2)	(-7.3, 22.4)
P-value		0.37	0.34
Additional Efficacy Results			
SLEDAI at W48[a]			
Reduction from baseline			
≥4 points, *n* (%)	62 (72)	68 (78)	70 (81)
Treatment difference vs. PBO (%)		6.1	8.4
BILAG at W48[a]			
Change from baseline			
Absence of new A and >1 new B domains, *n* (%)	83 (97)	84 (97)	84 (97)
Treatment difference vs. PBO (%)		0.0	0.0
PGA at W48[a]			
Change from baseline			
≤0.3 point increase , *n* (%)	83 (97)	82 (94)	83 (95)
Treatment difference vs. PBO (%)		-2.3	-1.1
BICLA Response at W48[b]			
Responder, *n* (%)	33/80 (41)	45/85 (53)	35/83 (42)
Treatment difference vs. PBO (%)		11.7	0.9
95% CI		(-3.4, 26.8)	(-14.2, 16.1)
P-value		0.086	0.879
Early Study Discontinuations, *n* (%)	22 (26)	21 (24)	22 (25)
Received Escape Therapy[c]**, *n* (%)**	8 (10)	7 (8.2)	10 (12)
Safety, *n* (%)			
Total number of patients with at least one			
AE	64 (76)	77 (89)	68 (77)
Serious AE	8 (10)	4 (5)	12 (14)
AE leading to death[d]	2 (2)	1 (1)	0

a- Note: SLEDAI, BILAG, and PGA are presented with the last observation carried forward. Study discontinuations are accounted for in the SRI-4 Response but not in the SRI-4 Components.
b- Based on the BICLA-Evaluable Population.
c- Escape therapy defined as receipt of SLE medications exceeding limits in protocol.
d- Deaths due to salivary gland tumor (150 mg QD); respiratory failure (PBO); infected skin ulcer (PBO).

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Late-Breaking Abstracts ePoster
Session Type: Late-Breaking Abstract Poster Session
Session Time: 9:00AM–11:00AM

Background/Purpose: Fenebrutinib (GDC-0853, FEN) is an oral, non-covalent, and highly selective inhibitor of Bruton's tyrosine kinase (BTK) in clinical development for autoimmune diseases. The efficacy, safety, and pharmacodynamic effects of fenebrutinib in patients with moderate-to-severe systemic lupus erythematosus (SLE) activity were assessed in this Phase 2, randomized, placebo-controlled, multi-center study.

Methods: Patients who met SLICC or revised ACR SLE criteria, had ≥1 serologic marker of SLE (ANA, anti-dsDNA, or anti-Smith), SLEDAI ≥6 (later amended to ≥8) at screening, and were on ≥1 standard of care (SOC) therapy (corticosteroid, antimalarial, and/or immunosuppressive) were included; patients with renal or CNS involvement, recent exposure to B cell depleting therapy, or who were receiving a calcineurin inhibitor were excluded. Enrolled patients were randomized to placebo, FEN 150 mg QD, or FEN 200 mg BID, for 48 weeks of therapy. Corticosteroid taper was recommended, with burst and taper permitted from week 0 to week 12 (W0 to W12) and W24 to W36. SRI-4 at W48 was the primary endpoint, comparing the FEN arms with placebo using a sample size of 240 patients targeted for 88% power. BICLA response at W48 was a secondary endpoint.

Table 2: Key Biomarker Results

	PBO	FEN 150 mg QD	FEN 200 mg BID
Median Biomarker Levels at Baseline			
Plasmabast signature (-ΔCt)	**1.29** (*n*=85)	**1.22** (*n*=87)	**1.34** (*n*=88)
CD19⁺ B cells (cells/µl)	**136** (*n*=63)	**140** (*n*=71)	**126** (*n*=70)
Anti-dsDNA# (IU/ml)	**154** (*n*=41)	**124** (*n*=47)	**180** (*n*=48)
Total IgG (g/L)	**14.1** (*n*=85)	**14.3** (*n*=86)	**15.0** (*n*=87)
C3 (g/L)	**1.03** (*n*=85)	**1.03** (*n*=87)	**1.03** (*n*=88)
C4 (g/L)	**0.18** (*n*=85)	**0.17** (*n*=87)	**0.16** (*n*=88)
Median (IQR) Change from Baseline at Week 48			
Plasmablast signature	**-19.7%** (-42.6 to 15.8) *n*=52	**-54.3%*** (-74.7 to -20.6) *n*=53	**-51.7%*** (-77.8 to -15.3) *n*=57
CD19⁺ B cells (cells/µl)	**-0.50** (-38.3 to 28.8) *n*=38	**-57.0*** (-128.0 to -6.0) *n*=49	**-57.5*** (-121.0 to -24.8) *n*=48
Anti-dsDNA# (IU/ml)	**+6.9** (-27.3 to 78.2) *n*=31	**-38.3*** (-91.7 to -3.9) *n*=36	**-75.7*** (-263.7 to -18.4) *n*=33
Total IgG (g/L)	**-0.20** (-1.30 to 1.55) *n*=65	**-1.25*** (-2.63 to 0.05) *n*=64	**-1.56*** (-3.73 to -0.68) *n*=64
C3 (g/L)	**-0.02** (-0.12 to 0.08) *n*=65	**+0.01** (-0.12 to 0.12) *n*=67	**-0.01** (-0.12 to 0.13) *n*=66
C4 (g/L)		**0.00** (-0.03 to 0.02) *n*=65	**+0.02*** (-0.01 to 0.05) *n*=67

Reference ranges: CD19+ B cells (80-616 cells/µl), Anti-dsDNA (<30 IU/ml), IgG (5.65-17.65 g/L), C3 (0.9-1.8 g/L), C4 (0.1-0.4 g/L)
#Patients who were positive at baseline (>30 IU/mL)
*Denotes significant versus PBO; Kruskal-Wallis false-discovery rate controlled two sided (*p*-value ≤0.05).

Results: This study enrolled 260 patients from 44 sites in 12 countries, with the majority of patients recruited in Latin America, USA, and Western Europe. At week 48, the SRI-4 response rates for FEN 150 mg QD and FEN 200 mg BID were 51% (95% CI: -8.5, 21.2) and 52% (95% CI: -7.3, 22.4), respectively, compared to 44% for the placebo arm (**Table 1**). The week 48 BICLA response rates for FEN 150 mg QD and FEN 200 mg BID were 53% (95% CI: -3.4, 26.8) and 42% (95% CI: -14.2, 16.1), respectively, compared to 41% for the placebo arm (**Table 1**). Safety results were similar between FEN and placebo, although more serious adverse events were observed in the FEN 200 mg BID arm (**Table 1**). Treatment with both doses of FEN significantly reduced levels of CD19+ B cells, anti-dsDNA autoantibodies, IgG, and a BTK-dependent RNA signature highly expressed in plasmablasts by week 48 compared to placebo; C4 levels modestly improved with FEN versus placebo (**Table 2**).

Conclusion: The primary endpoint of SRI-4 for FEN was not met despite evidence of strong BTK target and pathway inhibition. FEN had an acceptable safety profile.

Disclosure: D. Isenberg, Genentech, Inc., 1; **R. Furie**, Biogen, 5, GlaxoSmithKline, 2, 5, UCB Pharma, 2, 5, Genentech, Inc., 1; **N. Jones**, Genentech, Inc., 1, 2; **P. Guibord**, Hoffmann-La Roche Limited, 1, 2; **J. Galanter**, Genentech, Inc., 1, 2; **C. Lee**, Genentech, Inc., 1, 2, Eli Lilly, 1; **A. McGregor**, Genentech, Inc., 1; **B. Toth**, Genentech, Inc., 1, 2; **J. Rae**, Genentech, Inc., 1, 2; **O. Hwang**, Genentech, Inc., 1, 2; **P. Miranda**, Genentech, Inc., 1; **V. de Souza**, Genentech, Inc., 1; **J. Jaller-Raad**, Genentech, Inc., 1; **A. Maura Fernandes**, Genentech, Inc., 1; **R. Garcia Salinas**, Genentech, Inc., 1; **L. Chinn**, Genentech, Inc., 1, 2, 3; **M. Townsend**, Genentech, Inc., 1, 2; **A. Morimoto**, Genentech, Inc., 1, 2, 3; **K. Tuckwell**, Genentech, Inc., 1, 2.

Abstract Number: L16

GLCCI1 Polymorphism Is Associated with Prednisone Response in Giant Cell Arteritis: A Multicenter Prospective Study

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Late-Breaking Abstracts ePoster

Session Type: Late-Breaking Abstract Poster Session

Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is the most common cause of primary vasculitis in adults. Corticosteroids are the cornerstone of the treatment. However, approximately 50% of patients will relapse, and up to 86% will experience steroid-induced adverse events. The objective was to study the risk factors for relapse, including prednisolone clearance and glucocorticoid-induced transcript 1 (*GLCCI1*) promoter polymorphism (rs37972), which acts on steroid-induced apoptosis.

Methods: This multicenter prospective study included steroid-naive patients with a diagnosis of GCA, defined by ≥3/5 American College of Rheumatology (ACR) criteria (trial registration: NCT01400464). Patients received steroids, with a 10 to 16 months predefined taper schedule, with a planned follow-up of 18 months after inclusion. Genotyping of GLCCI1 (rs37972) and prednisolone clearance were performed between 14 and 28 days of treatment. Variables with p< 0.20 on univariate analysis were considered for multivariate analysis. Relapse was defined as the combination of inflammatory syndrome (C-reactive protein >15 mg/L or sedimentation rate >40 mm/h), GCA symptoms and resolution with increasing the dose of prednisone. The primary objective was the link between the prednisolone clearance and the risk of relapse.

Results: A total of 139 patients were included, but 20 were excluded from analysis (missing prednisolone clearance, n=18; cortico-resistant, n=2). Among the 119 patients (70 women), the mean age was 72.2 +/- 7.6 years with a median follow-up duration of 74 [32-82] months. Thirty-seven (31%) had polymyalgia rheumatica, the median C-reactive protein level and sedimentation rate were 78 [13-102] mg/L and 70 [35-94] mm/h, respectively, and 59 (49.6%) patients had at least one relapse. The mean prednisolone clearance was 7.2 +/- 6.7 L/h. For each increase of 1 unit of clearance, the relapse risk increased, although not significantly, by 2.6% (hazard-ratio, HR=1.026, IC95% 0.99-1.06) in univariate analysis. On multivariate analysis, only platelets were associated with a decreased risk of relapse (HR=0.98, IC95% 0.96-0.9997, for each increase of 10,000 platelets/mm^3, Tables 1 and 2).

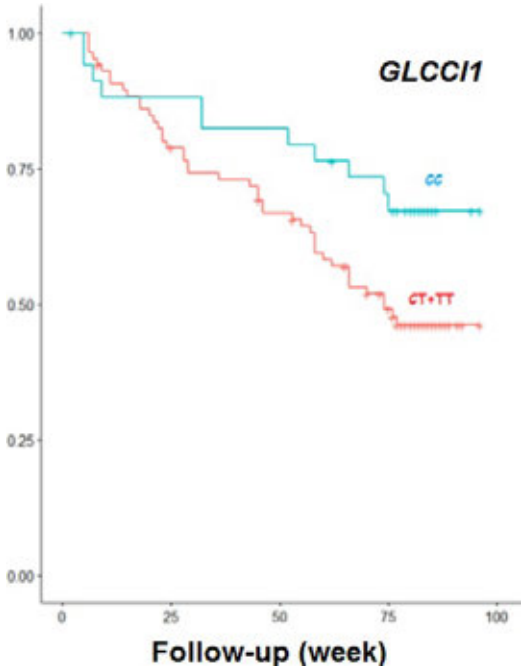
Additionally, based on an ancillary study among 121 patients who had a determination of *GLCCI1* rs37972 polymorphism, patients with a CC genotype experienced fewer relapses than patients with at least one T allele (Figure 1) in multivariate analysis adjusted for polymyalgia rheumatica (HR=0.498, IC95% 0.26-0.97, p=0.04).

Table 1: Univariate analysis of predictors of relapse in patients with giant cell arteritis

Other factors		*n*	HR	IC 95%	p
Sex	Male	49	1		
	Female	70	1.05	(0.60-1.83)	0.87
Age (per increase of 5 years)		119	0.97	(0.81-1.16)	0.75
High blood pressure	No	53	1		
	Yes	66	0.78	(0.45-1.36)	0.38
Diabetes	No	108	1		
	Yes	11	1.17	(0.47-2.95)	0.74
Fever (≥ 38°C)	No	94	1		
	Yes	24	0.85	(0.42-1.70)	0.65
Weight loss (> 4 kg)	No	82	1		
	Yes	37	0.91	(0.49-1.68)	0.76
Asthenia	No	26	1		
	Yes	92	0.76	(0.40-1.43)	0.40
Polymyalgia rheumatica	No	82	1		
	Yes	37	1.46	(0.83-2.58)	**0.19**
Hemoglobin level (per increase of 1 g/dL)		118	1.12	(0.91-1.38)	0.30
Sedimentation rate (per increase of 10 mm/h)		102	0.90	(0.83-0.98)	**0.020**
C-reactive protein (per increase of 50 mg/L)		117	1.07	(0.90-1.27)	0.44
Fibrinogen (per increase of 1 g/L)		98	0.85	(0.72-1.00)	**0.052**
Neutrophil (per increase of 1,000 cells/mm^3)		116	1.03	(0.96-1.11)	0.43
White blood cells (per increase of 1,000 cells/mm^3)		118	1.03	(0.96-1.10)	0.43
Platelets (per increase of 10,000 cells/mm^3)		118	0.98	(0.96-1.00)	**0.075**

Table 2: Multivariate analysis of predictors of relapse in patients with giant cell arteritis

Factors		Adjusted HR	IC 95%	p
By adjusting on all variables with a p-value <0.2 on univariate analysis (n=83)				
Clearance (per increase of 1 unit)		0.978	(0.91 - 1.06)	0.58
Polymyalgia rheumatica	No	1		
	Yes	1.46	(0.75 - 2.85)	0.27
Platelets (per increase of 10,000 cells/mm³)		0.98	(0.96 - 1.01)	0.17
Fibrinogen (per increase of 1 g/L)		0.87	(0.69 - 1.11)	0.27
Sedimentation rate (per increase of 10 mm/h)		0.97	(0.84 - 1.12)	0.68
By adjusting only on prednisolone clearance, polymyalgia rheumatica and platelets (n=118)				
Clearance (per increase of 1 unit)		1.016	(0.97 - 1.07)	0.51
Polymyalgia rheumatica	No	1		
	Yes	1.62	(0.92 - 2.89)	0.098
Platelets (per increase of 10,000 cells/mm³)		0.98	(0.96 – 0.9997)	**0.047**



Conclusion: To our knowledge, this study is the largest prospective study including steroid-naive GCA patients treated with uniform predefined taper schedule, and the first one assessing prednisolone clearance as a risk factor for relapse.

On multivariate analysis, a higher platelet count and a CC rs37972 polymorphism were associated with a decreased risk of relapse.

Further studies are needed to determine the effect of a steroid-sparing treatment as a first-line treatment in association with steroids in patients with the CT or TT rs37972 polymorphism.

Relapse-free survival in giant cell arteritis patients according to GLCCI1 rs37972 polymorphism

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Abstract Number: L17

Efficacy and Safety of Anifrolumab in Patients with Moderate to Severe Systemic Lupus Erythematosus: Results of the Second Phase 3 Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Late-Breaking Abstracts

Session Type: Late-Breaking Abstract Session

Session Time: 4:00PM–6:00PM

Background/Purpose: Anifrolumab, a human monoclonal antibody to the type I IFN receptor subunit 1, had robust efficacy in a phase 2 study in patients with active SLE. The first phase 3 trial, TULIP-1, did not meet its primary endpoint, SLE responder index (SRI[4]), but multiple other endpoints, including BILAG–based Composite Lupus Assessment (BICLA), suggested clinical benefit. We report results of the second phase 3 trial of anifrolumab.

Patient Characteristic	Placebo (n=182)	Anifrolumab 300 mg (n=180)
Age, years, mean (SD)	41.1 (11.47)	43.1 (11.95)
Female, n (%)	170 (93.4)	168 (93.3)
Time from initial SLE diagnosis to randomization (months), median (min, max)	78.0 (6, 494)	94.5 (6, 555)
SLEDAI-2K global score, mean (SD)	11.5 (3.88)	11.4 (3.64)
BILAG-2004 ≥1 A, n (%)	95 (52.2)	81 (45.0)
BILAG-2004 no A and ≥2 B, n (%)	78 (42.9)	91 (50.6)
PGA (0–3), mean (SD)	1.76 (0.397)	1.68 (0.411)
CLASI activity, mean (SD)	7.6 (7.75)	8.3 (7.94)
SDI, mean (SD)	0.5 (0.79)	0.5 (0.91)
Swollen joint count, mean (SD)	7.4 (6.55)	6.2 (5.65)
Tender joint count, mean (SD)	11.0 (7.89)	9.0 (7.07)
High type I IFNGS, n (%)	151 (83.0)	150 (83.3)
Elevated anti-dsDNA antibodies, n (%)	73 (40.1)	86 (47.8)
Abnormal complement concentration, n (%)		
C3	72 (39.6)	72 (40.0)
C4	46 (25.3)	49 (27.2)
Key baseline SLE treatments		
OCS (prednisone or equivalent), n (%)	151 (83.0)	141 (78.3)
OCS dosage ≥10 mg/d, n (%)	83 (45.6)	87 (48.3)
Immunosuppressants, n (%)	86 (47.3)	88 (48.9)
Antimalarials, n (%)	133 (73.1)	119 (66.1)

Abbreviations: anti-dsDNA = anti–double-stranded DNA; BILAG = British Isles Lupus Assessment Group; CLASI = Cutaneous Lupus Erythematosus Disease Area and Severity; IFNGS = interferon gene signature; OCS = oral corticosteroid; PBO = placebo; PGA = Physician's Global Assessment; SD = standard deviation; SDI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SLE = systemic lupus erythematosus; SLEDAI = SLE Disease Activity Index.

Table 1. Baseline Patient Demographics and Disease Characteristics

Endpoint	Placebo (n=182) n/N (%)*	Anifrolumab 300 mg (n=180) n/N (%)*	Difference (95% CI)*	Adjusted *P*-value/ Unadjusted *P*-value‡	Significant After Multiplicity Adjustment
Primary endpoint: BICLA response at wk 52†	57/182 (31.5)	86/180(47.8)	16.3 (6.3, 26.3)	0.001/ 0.001	NA
Key secondary endpoints:					
BICLA response at wk 52 in type I IFNGS test–high patients	46/151 (30.7)	72/150 (48.0)	17.3 (6.5, 28.2)	0.002/ 0.002	Yes
OCS reduction ≤7.5 mg/d sustained from wk 40 to wk 52§	25/83 (30.2)	45/87 (51.5)	21.2 (6.8, 35.7)	0.014/ 0.004	Yes
≥50% reduction in CLASI activity score from BL to wk 12¶	10/40 (25.0)	24/49 (49.0)	24.0 (4.3, 43.6)	0.039/ 0.017	Yes
≥50% reduction in both swollen and tender joints, BL to wk 52**	34/90 (37.5)	30/71 (42.2)	4.7 (–10.6, 20.0)	0.547/ 0.547	No
Annualized flare rate††	0.64	0.43	0.67‖ (0.48, 0.94)	0.081/ 0.020	No
Other secondary endpoint:					
SRI(4) at wk 52‡‡	68/182 (37.3)	100/180 (55.5)	18.2 (8.1, 28.3)	NA/ <0.001	NA

*Percentage response, the difference in response estimates, and the associated 95% CIs are weighted and are calculated using a stratified Cochran–Mantel–Haenszel approach with pre-specified stratification factors (SLEDAI-2K score at screening [<10 points vs ≥10 points], week 0 OCS dose [prednisone <10 mg/d vs ≥10 mg/d or equivalent] and type I IFN gene signature test result at screening [high vs low]).

†BICLA response is defined as reduction of all baseline BILAG-2004 A to B/C/D, baseline BILAG-2004 B to C/D, and no BILAG-2004 worsening in other organ systems (≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B items); no worsening (increase >0 points) from baseline SLEDAI-2K; <0.3-point increase in PGA from baseline, no use of restricted medications beyond protocol-allowed thresholds, and no discontinuation of investigational product.

‡Treatment comparison using a stratified Cochran–Mantel–Haenszel approach. *P*-values adjusted per weighted Holm procedure.

§In patients with baseline OCS prednisone ≥10 mg/d or equivalent.

¶In patients with CLASI activity score ≥10 at baseline.

**In patients with ≥6 swollen and ≥6 tender joints at baseline.

††Values are annualized flare rates rather than responder percentages. A flare is defined as either ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B items compared with the previous visit (ie, a worsening from an E, D, or C score to a B score in at least 2 organ systems or a worsening from an E, D, C, or B score to an A score in any 1 organ system compared with the previous visit).

‡‡SRI(4) response was defined as a ≥4-point reduction in SLEDAI-2K score, <1 new BILAG-2004 A or <2 new BILAG-2004 B organ domain scores, <0.3-point (10%) increase in PGA score from baseline, and no discontinuation of investigational product and no use of restricted medications beyond the protocol-allowed threshold.

‖Calculated as a rate ratio (anifrolumab/placebo).

BICLA = BILAG-based Composite Lupus Assessment; BILAG = British Isles Lupus Assessment Group; BL = baseline; CI = confidence interval; CLASI = Cutaneous Lupus Erythematosus Disease Area and Severity Index; IFNGS = interferon gene signature; NA = not applicable; OCS = oral corticosteroids; SRI = Systemic Lupus Erythematosus Responder Index.

Table 2. Primary and Secondary Efficacy Outcomes

Methods: TULIP-2 (NCT02446899) is a randomized, double-blind, placebo-controlled trial that evaluated efficacy and safety of IV anifrolumab 300 mg vs placebo every 4 weeks for 48 weeks in patients with moderate to severe SLE despite standard-of-care (SOC) treatment. Patients met ACR SLE criteria and had SLEDAI-2K ≥6 and BILAG ≥1 A or ≥2 B. The primary endpoint was BICLA response at week 52. SOC was stable except for mandatory attempts at oral corticosteroid (OCS) tapering to prednisone equivalent ≤7.5 mg/d for patients receiving ≥10 mg/d at baseline. Safety was also assessed.

Results: Of 365 randomized patients, 362 received ≥1 dose of study drug and were included in the analyses (anifrolumab, n=180; placebo, n=182). Baseline demographic and disease characteristics were similar between treatment groups (**Table 1**). Treatment completion was 85.0% for anifrolumab and 71.4% for placebo.

Anifrolumab was superior to placebo for BICLA response (47.8% vs 31.5%, respectively, *P*=0.001) and key secondary endpoints: OCS reduction (51.5% vs 30.2%; *P*=0.014) and Cutaneous Lupus Erythematosus Disease Area and Severity Index response (49.0% vs 25.0%; P=0.039); annualized flare rate was numerically lower in anifrolumab-treated patients (0.43 vs 0.64; rate ratio 0.67 [95% CI: 0.48, 0.94]; *P*=0.081; **Table 2**).

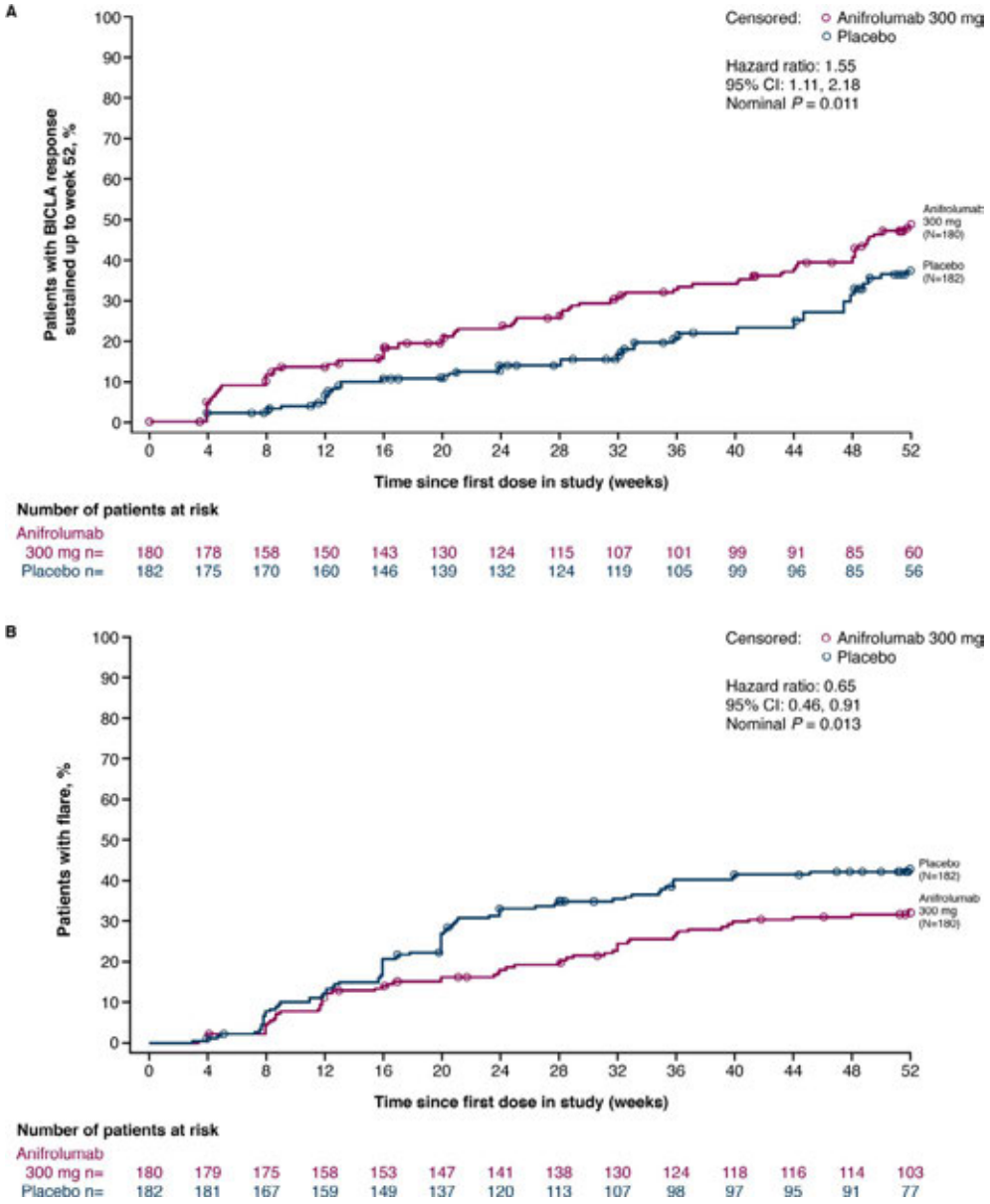

Figure. Time Course of Onset of BICLA Response Sustained Through Week 52* (A) and Time to First Flare,* Defined as Either ≥1 New BILAG A or ≥2 new BILAG B Items Compared With the Previous Visit (B)

Efficacy was further supported by numeric differences favoring anifrolumab in multiple secondary endpoints (unadjusted), including SRI(4) response (55.5% vs 37.3%; nominal *P*< 0.001) and higher thresholds of SRI(5–8), time to onset of BICLA response sustained to week 52 (hazard ratio [HR], 1.55; 95% CI: 1.11, 2.18; nominal *P*=0.011; **Figure 1A**), and time to first flare (HR, 0.65; 95% CI: 0.46, 0.91; nominal P=0.013; **Figure 1B**). In patients with high baseline IFN gene signature (IFNGS), anifrolumab induced neutralization of IFNGS by week 12 (median suppression 88.0%) that was maintained through week 52. Serum anti-dsDNA trended toward normalization with anifrolumab.

The safety profile of anifrolumab was similar to that of previous trials. Herpes zoster was more common in those receiving anifrolumab (7.2%) than placebo (1.1%). In contrast, serious adverse events were less frequent among anifrolumab- than placebo-treated patients (8.3% and 17.0%, respectively), as were adverse events leading to treatment discontinuation (2.8% and 7.1%). One death occurred in the anifrolumab group (pneumonia). Few patients (0.6%) developed antidrug antibodies.

Conclusion: Anifrolumab was superior to placebo for multiple efficacy endpoints, including overall disease activity, skin disease, and OCS tapering. No new safety signals were identified. TULIP-2 demonstrates efficacy of anifrolumab in moderate to severe SLE.

Writing assistance by Ellen Stoltzfus, PhD (Fishawack).

Disclosure: E. Morand, AstraZeneca, 1, 2, Bristol Myers Squibb, 1, Eli Lilly, 1, 2, Janssen, 1, 2, Merck Serono, 1, 2, UCB, 1, GSK, 1, CSL Inc, 1, Neovacs, 1, Wolf Biotherapeutics, 1, AbbVie, 1, Amgen, 1; **R. Furie**, AstraZeneca, 1, 2; **Y. Tanaka**, Daiichi-Sankyo, 1, 2, Astellas, 1, Chugai, 1, 2, Eli Lilly, 1, Pfizer, 1, Abbvie, 1, YL Biologics, 1, 2, Bristol-Myers Squibb, 1, 2, Takeda, 1, Mitsubishi-Tanabe, 1, 2, Novartis, 1, Eisai, 1, 2, Teijin, 1, Asahi-kasei, 1, Sanofi, 1, UCB, 1, Ono, 1, Janssen, 1; **I. Bruce**, AstraZeneca, 1, Eli Lilly, 1, Genzyme Sanofi, 2, GlaxoSmithKline, 2, 5, 8, GSK, 1, Iltoo, 1, MedImmune, 5, 8, Merck Serono, 1, Roche, 5, 8, Sanofi Genzyme, 1, UCB, 1, 2, 3; **A. Askanase**, GSK, 1, AstraZeneca, 1, Janssen, 1, Eli Lilly, 1, AbbVie, 1, Bristol-Myers Squibb, 1; **C. Richez**, Roche, 1, AstraZeneca, 1, Abbvie, 1, Glenmark, 1, Pfizer, 1, Bristol Myers Squibb, 1, Eli Lilly, 1, GSK, 1, Janssen, 1, UCB, 1; **S. Bae**, None; **P. Brohawn**, AstraZeneca, 1; **L. Pineda**, AstraZeneca, 1; **A. Berglind**, AstraZeneca, 3; **R. Tummala**, AstraZeneca, 3.

Abstract Number: L18

A Human Recombinant Fusion Protein Targeting B Lymphocyte Stimulator (BlyS) and a Proliferation-Inducing Ligand (APRIL), Telitacicept (RC18), in Systemic Lupus Erythematosus (SLE): Results of a Phase 2b Study

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SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 4:00PM–6:00PM

Background/Purpose: Telitacicept, also named RC18, is a novel recombinant fusion protein constructed with the extracellular domain of the human transmembrane activator and calcium modulator and cyclophylin ligand interactor (TACI) receptor and the Fc domain of human immunoglobulin (Ig) G1 targeting and neutralizing B lymphocyte stimulator (BLyS) and a proliferating-inducing ligand (APRIL). This phase 2b study evaluated the efficacy and safety of Telitacicept versus placebo in combination with standard therapy in SLE patients.

Methods: SLE patients aged 18 to 65 years with positive ANA and/or anti-dsDNA and with a SELENA-SLEDAI score ≥8 were randomized 1:1:1:1 to receive subcutaneous Telitacicept at 80 mg, 160 mg, 240 mg or placebo once a week in combination with standard therapy for 48 weeks. The primary endpoint was response rate of SLE Responder Index 4 (SRI4) at Week 48. The SRI4 response was defined as: ≥4 points reduction from baseline in SELENA-SLEDAI score, and no new BILAG A organ domain score or 1 new BILAG B organ domain score compared with baseline, and no worsening (increase of < 0.30 points from baseline) in Physician's Global Assessment (PGA). This trial is registered with ClinicalTrials.gov, number NCT02885610.

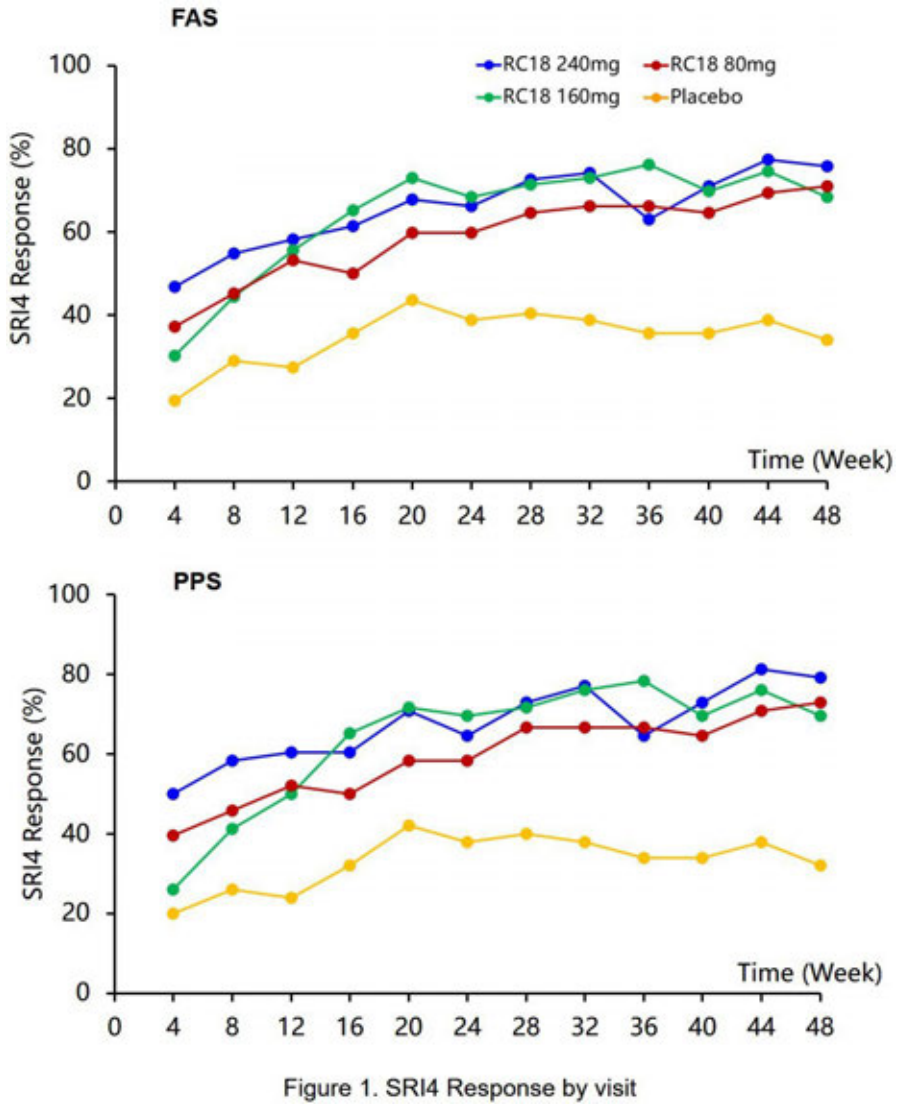


Figure 1. SRI4 Response by Visit

Results: 249 patients were randomized to receiving Telitacicept 80 mg (n=62), 160 mg (n=63), 240 mg (n=62) or placebo (n=62). Results from full analysis set (FAS) showed significantly higher response rates of SRI4 with Telitacicept 80mg (71.0%, p< 0.0001), 160 mg (68.3%, p=0.0001) and 240 mg (75.8%, p< 0.0001) than with placebo (33.9%) at Week 48; more patients had a reduction of ≥ 4 points in SELENA-SLEDAI score at Week 48 with Telitacicept 80mg (75.8%, p=0.003), 160 mg (77.8%, p=0.001) and 240 mg (79.0%, p< 0.001) than with placebo (50.0%); no worsening in PGA score was noted in more patients with Telitacicept 80mg (96.8%, p< 0.001), 160 mg (92.1%, p=0.013) and 240 mg (96.8%, p< 0.001) than with placebo (75.8%) at Week 48. Results from Per protocol set (PPS) were consistent with that from FAS. The incidences of AEs was 93.5%, 92.1%, 90.3%, 82.3% in the Telitacicept 240mg, 160mg, 80mg and placebo group. There were 13 SAEs in 8 subjects treated with 240mg Telitacicept, 16 SAEs in 10 subjects treated with 160mg Telitacicept, 12 SAEs in 8 subjects treated with 80mg Telitacicept, 12 SAEs in 10 subjects treated with placebo, the incidences of SAEs were 12.9%, 15.9%,12.9%, 16.1% in the Telitacicept 240mg, 160mg, 80mg and placebo groups, respectively. The incidence of AEs and SAEs was similar across groups (p >0.05). There was 1 death in Telitacicept 240mg group which was considered not related to the study drug. The most common AEs were upper respiratory tract infection and injection site reactions. 11 pregnancies occurred during the study in subjects received Telitacicept (4 on 240mg, 3 on 160 mg and 4 on 80 mg) while no pregnancy occurred in the placebo group. 1 pregnancy resulted in live birth and 10 in elective termination.

FAS				
	Placebo (N=62)	RC18 80mg (N=62)	RC18 160mg (N=63)	RC18 240mg (N=62)
SRI4 response, n (%) Observed difference (95% CI) vs. placebo p-value	21 (33.9)	44 (71.0) 37.1(20.8, 53.4) p<0.001	43 (68.3) 34.4(17.9, 50.8) p<0.001	47 (75.8) 41.9(26.0, 57.8) p<0.001
4-point reduction in SELENA SLEDAI, n (%) Observed difference (95% CI) vs. placebo p-value	31 (50.0)	47 (75.8) 25.8 (9.4, 42.2) 0.003	49 (77.8) 27.8 (11.6, 43.9) 0.001	49 (79.0) 29.0 (13.0, 45.1) <0.001
No New 1A/1B BILAG domain scores, n (%) Observed difference (95% CI) vs. placebo p-value	58(93.5)	61(98.4) 4.8 (-2.0, 11.7) 0.365	62 (98.4) 4.9 (-2.0, 11.7) 0.207	60 (96.8) 3.2 (-4.3, 10.8) 0.680
No worsening in PGA, n (%) Observed difference (95% CI) vs. placebo p-value	47 (75.8)	60 (96.8) 21.0 (9.4, 32.5) <0.001	58 (92.1) 16.3 (3.7, 28.8) 0.013	60 (96.8) 21.0 (9.4, 32.5) <0.001
PPS				
	Placebo (N=50)	RC18 80mg (N=48)	RC18 160mg (N=46)	RC18 240mg (N=48)
SRI4 response, n (%) Observed difference (95% CI) vs. placebo p-value	16 (32.0)	35 (72.9) 40.9 (22.9, 59.0) p<0.001	32 (69.6) 37.6 (19.0, 56.1) p<0.001	38 (79.2) 47.2 (29.9, 64.5) p<0.001
4-point reduction in SELENA SLEDAI, n (%) Observed difference (95% CI) vs. placebo p-value	25 (50.0%)	38 (79.2) 29.2 (11.2, 47.2) 0.003	35 (76.1) 26.1 (7.5, 44.6) 0.008	40 (83.3) 33.3 (15.9, 50.7) <0.001
No New 1A/1B BILAG domain scores, n (%) Observed difference (95% CI) vs. placebo p-value	48 (96.0)	48 (100.0) 4.0 (-1.4, 9.4) 0.495	45 (97.8) 1.8 (-5.0, 8.7) >0.999	47 (97.9) 1.9 (-4.9, 8.7) >0.999
No worsening in PGA, n (%) Observed difference (95% CI) vs. placebo p-value	38 (76.0)	47 (97.9) 21.9 (9.4, 34.4) 0.001	44 (95.7) 19.7 (6.4, 32.9) 0.006	48 (100.0) 24.0 (12.2, 35.8) <0.001

Table 1. SRI4 Response at Week 48

Conclusion: This phase 2b trial in patients with active SLE treated with Telitacicept in combination with standard therapy met the SRI4 primary endpoint. Telitacicept was well tolerated in SLE patients.

Disclosure: D. Wu, None; **J. Li**, None; **D. Xu**, None; **W. Wang**, RemeGen, Ltd., 1, 2; **L. Li**, RemeGen, Ltd., 1, 2; **J. Fang**, RemeGen, Ltd., 1, 2; **F. Zhang**, GlaxoSmithKline, 9.

Abstract Number: L19

Ianalumab (VAY736), a Dual Mode of Action Biologic Combining BAFF Receptor Inhibition with B Cell Depletion, for Treatment of Primary Sjögren's Syndrome: Results of an International Randomized, Placebo Controlled Dose Range Finding Study in 190 Patients

Simon Bowman,[1] Robert Fox,[2] Thomas Dörner,[3] Xavier Mariette,[4] Athena Papas,[5] Thomas Grader-Beck,[6] Benjamin A. Fisher,[7] Filipe Barcelos,[8] Salvatore De Vita,[9] Hendrik Schulze-Koops,[10] Robert J. Moots,[11] Guido Junge,[12] Janice Woznicki,[13] Monika Sopala,[12] Wen-Lin Luo,[13] and Wolfgang Hueber[12], [1]University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom, [2]Scripps Memorial Hospital and Research Institute, La Jolla, California, [3]Charite Universitätsmedizin Berlin and DRFZ, Berlin, Germany, [4]Center for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique – Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, Le Kremlin-Bicêtre, Université Paris Sud, INSERM, Paris, France, [5]Tufts School of Dental Medicine, Massachusetts, [6]Johns Hopkins University, Baltimore, [7]University Hospitals Birmingham NHS Foundation Trust, Birmingham Biomedical Research Centre, Birmingham, United Kingdom, [8]Nova Medical School, Hospital Cuf Descobertas, Instituto Português de Reumatologia,, Lisbon, Portugal, [9]Rheumatology Clinic, Udine University Hospital, Department of Medical Area, University of Udine, Udine, Italy, Udine, Italy, [10]Department of Rheumatology/Clinical Immunology, Ludwig-Maximilians-University Munich, Munich, Germany, [11]Institute of Ageing and Chronic Disease, Liverpool, United Kingdom, [12]Novartis Pharma AG, basel, Switzerland, [13]Novartis Pharmaceuticals Corporation, New Jersey

SESSION INFORMATION

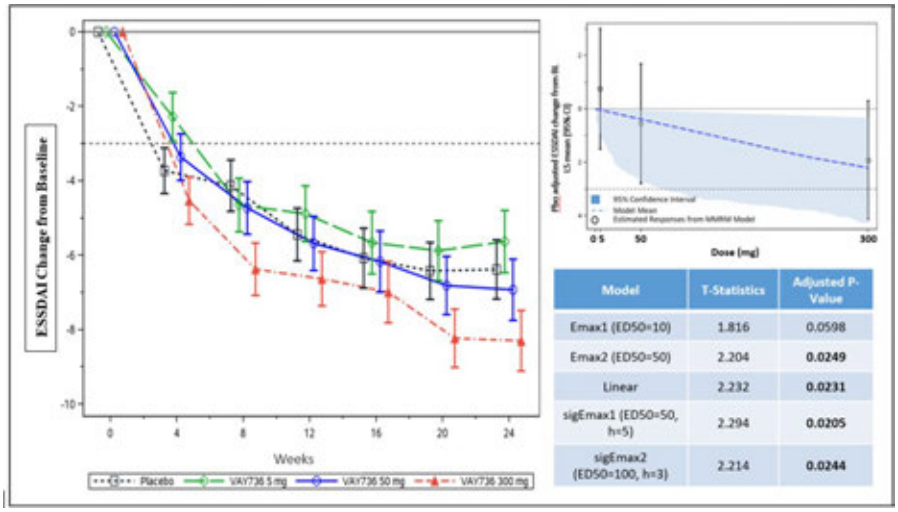
Session Date: Tuesday, November 12, 2019

Session Title: Late-Breaking Abstracts

Session Type: Late-Breaking Abstract Session

Session Time: 4:00PM–6:00PM

Background/Purpose: Primary Sjogren's syndrome (pSS) is a multi-organ autoimmune disease primarily affecting excretory glands and characterized by B-cell hyperactivity. No approved systemic treatments are available. Ianalumab (VAY736) is an anti-B-cell activating factor (BAFF) receptor fully human IgG1 monoclonal antibody, engineered for direct ADCC-mediated B-cell depletion, thus providing a dual mode of action and targeted approach to treat pSS. The current phase 2b study aimed at establishing a dose-response relationship over a wide range of VAY736 doses, using change from baseline (BL) in the EULAR Sjogren's Syndrome Disease Activity index (ESSDAI) over 24 Weeks (Wks) as the primary endpoint. Here we report Wk24 efficacy and safety. The study is ongoing with a second blinded treatment period up to Wk52.



Model	T-Statistics	Adjusted P-Value
Emax1 (ED50=10)	1.816	0.0598
Emax2 (ED50=50)	2.204	**0.0249**
Linear	2.232	**0.0231**
sigEmax1 (ED50=50, h=5)	2.294	**0.0205**
sigEmax2 (ED50=100, h=3)	2.214	**0.0244**

Methods: 190 patients with pSS were randomized 1:1:1:1 to monthly s.c. administrations of placebo (PBO) or one of three VAY736 doses; 5mg, 50mg and 300mg. First-dose premedication was 250mg IV methylprednisolone. To be eligible, patients had to fulfill the American European Consensus Group (AECG) criteria for pSS, be anti-Ro/SSA positive, have an ESSDAI ≥6 (on 7/12 domains: glandular, articular, lymphadenopathy, constitutional, cutaneous, hematologic, biologic), and EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI) ≥5. Statistical methods included MCP-Mod to assess the dose-response on change of ESSDAI (12 domains) from BL and responder analysis to calculate the proportion of patients with ≥3 points improvement on ESSDAI as secondary analysis. Secondary endpoints included ESSPRI, Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F), Physician's (PhGA) and Patient's Global Assessments (PGA), SF-36, stimulated salivary flow (sSF) and Schirmer's test.

Results: The primary endpoint of the study was met with a statistically significant dose-response for ESSDAI (**Figure 1**). The largest reduction in ESSDAI was 1.92 points over PBO for VAY736 300mg at Wk24. Secondary analysis on ESSDAI revealed for 300mg vs PBO responder rates of 42/47 (89.4%) vs 30/49 (61.2%), a difference of 28.1% (p=0.0019), while no differences were seen for 5mg and 50mg vs PBO. Consistent with this result, PhGA change from BL was significantly different between VAY736 300mg and PBO (p=0.022). A numerical trend for improvement of sSF for VAY736 300mg compared to PBO was notable at Wk24 (p=0.092). However, the secondary efficacy endpoints ESSPRI and FACIT-F showed no benefits over PBO for improvements in the burden of illness. PBO responses were generally high. Incidence of treatment emergent adverse events were comparable across PBO and active groups, whereby local injection reactions were most frequent, mostly mild and showed a dose-response.

Conclusion: The defined primary endpoint assessing ESSDAI was met, showing statistically significant dose-response for ianalumab with clinically important improvement over placebo at the highest tested dose. The preliminary safety profile was good. Future analysis will focus on PK and immunogenicity, salivary and tear flow parameters and the exploration of ESSDAI domains, and the ongoing-blinded treatment period up to Week 52.

ESSDAI Change from Baseline over Time up to Week 24 Reveals a Statistically Significant Dose Response Relationship

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Disclosure: S. Bowman, AstraZeneca, 1, Biogen, 1, BMS, 1, Celgene, 1, Medimmune, 1, MTPharma, 1, Novartis, 1, ONO, 1, UCB, 1, Xtlbio, 1; **R. Fox**, Novartis, 1, Pfizer, 1, Lilly, 1; **T. Dörner**, AbbVie, 5, Celgene, 5, Eli Lilly and Company, 5, 8, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Novartis Pharma AG, 5, Roche, 5, 8, Samsung, 5, 8, Sanofi, 2, UCB, 5, UCB Pharma, 2, 5; **X. Mariette**, Biogen, 2, Bristol-Myers Squibb, 5, GlaxoSmithKline, 5, Janssen, 5, LFB Pharmaceuticals, 5, OSE Immunotherapeutics, 2, Pfizer, 2, 5, UCB Pharma, 5, 8; **A. Papas**, Novartis, 1, 2; **T. Grader-Beck**, None; **B. Fisher**, Novartis, 1, Roche, 1, BMS, 1; **F. Barcelos**, None; **S. De Vita**, None; **H. Schulze-Koops**, Eli Lilly and Company, 1, 2, AbbVie, 1, 2, Amgen, 1, 2, Biogen, 1, 2, Hexal-Sandoz, 1, 2; **R. Moots**, Biogen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Chugai, 2, 5, 8, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Roche, 2, 5, 8, Sandoz, 2, 5, 8, UCB, 2, 5, 8; **G. Junge**, Novartis, 1, 2; **J. Woznicki**, Novartis, 1, 2; **M. Sopala**, Novartis, 1, 2; **W. Luo**, Novartis, 1, 2; **W. Hueber**, Novartis, 1, 2.

Abstract Number: L20

A Head-to-Head Comparison of Ixekizumab and Adalimumab in Biologic-Naïve Patients with Active Psoriatic Arthritis: Efficacy and Safety Outcomes from a Randomized, Open-Label, Blinded Assessor Study Through 52 Weeks

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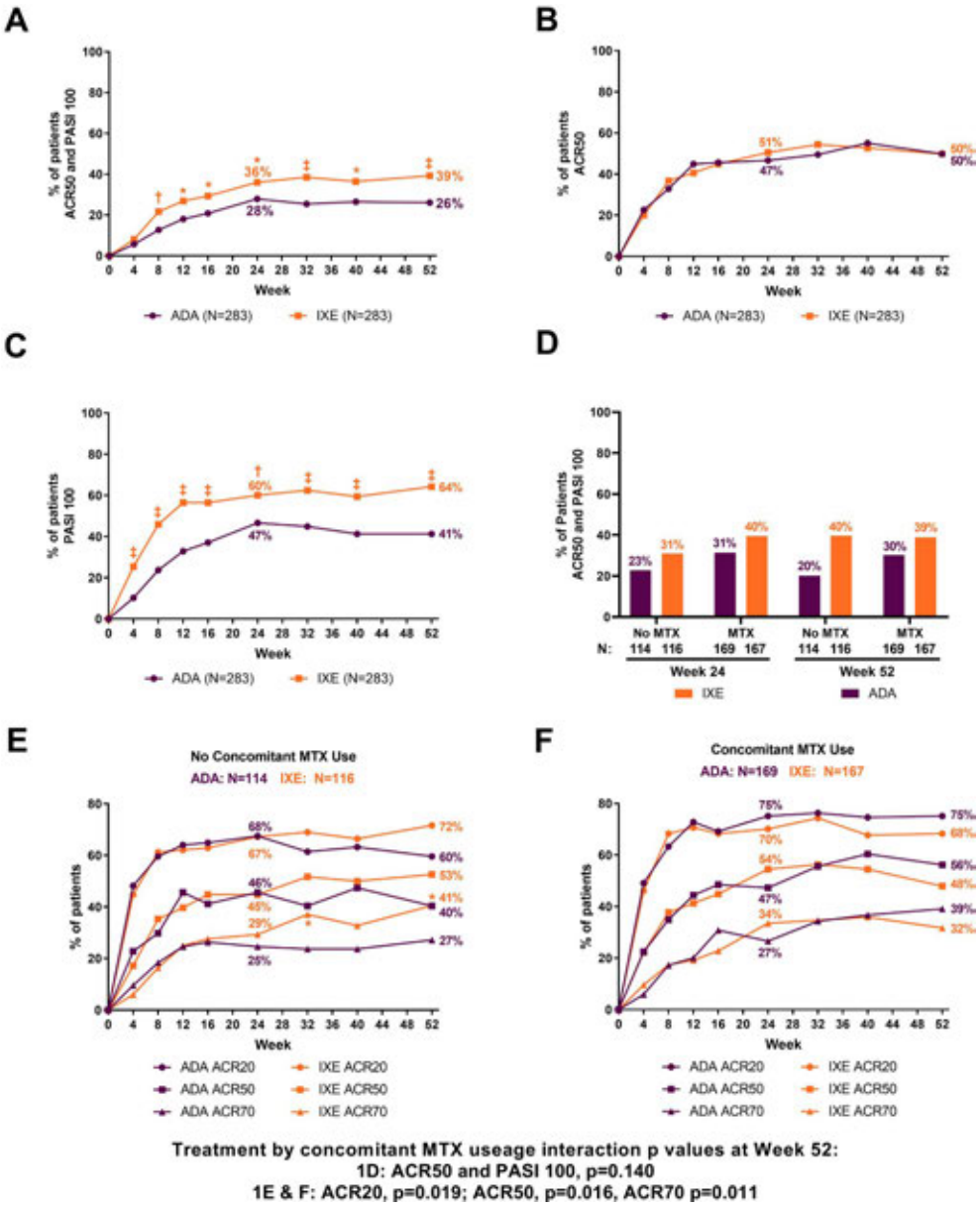

Figure 1. Percentage of patients achieving (A) simultaneous ACR50 and PASI100 response, (B) ACR50 response, and (C) PASI 100 through Week 52. (D) Percentage of patients achieving simultaneous ACR50 and PASI100 response at Week 24 and 52 by concomitant MTX use during the study. Percentage of patients achieving ACR20/50/70 response with (E) no concomitant MTX use or (F) concomitant MTX use through Week 52 of the study. Of 392 patients with concomitant csDMARDs use, 336 patients were on MTX and 56 were on other csDMARDs (leflunomide, sulfasalazine, or cyclosporine). *p<0.05, †p<0.01, ‡p<0.001.

SESSION INFORMATION

Session Date: Tuesday, November 12, 2019

Session Title: Late-Breaking Abstracts

Session Type: Late-Breaking Abstract Session

Session Time: 4:00PM–6:00PM

Background/Purpose: Multiple biologic DMARDs (bDMARDs) are available for treatment of PsA, but there are few direct comparisons of their efficacy and safety. Furthermore, efficacy of bDMARDs with or without concomitant MTX is one of the most clinically relevant questions for clinicians. Ixekizumab (IXE) was superior to adalimumab (ADA) at Week (Wk) 24 for simultaneous achievement of ACR50 and 100% improvement from baseline in the Psoriasis Area

	Week 24			Week 52		
	IXE N=283	ADA N=283	p-value	IXE N=283	ADA N=283	p-value
ACR20	195/283 (69)	204/283 (72)	0.403	197/283 (70)	195/283 (69)	0.791
ACR70	90/283 (32)	73/283 (26)	0.111	100/283 (35)	97/283 (34)	0.733
PASI75	227/283 (80)	195/283 (69)	0.002	222/283 (78)	194/283 (69)	0.008
PASI90	203/283 (72)	158/283 (56)	<0.001	206/283 (73)	153/283 (54)	<0.001
NAPSI=0[a]	111/191 (58)	88/177 (50)	0.082	129/191 (68)	104/177 (59)	0.060
MDA	135/283 (48)	100/283 (35)	0.003	134/283 (47)	116/283 (41)	0.108
VLDA	49/283 (17)	29/283 (10)	0.015	66/283 (23)	54/283 (19)	0.189
DAPSA LDA (≤14)	174/283 (61)	171/283 (60)	0.737	174/283 (61)	166/283 (59)	0.428
DAPSA Remission (≤4)	75/283 (27)	51/283 (18)	0.016	85/283 (30)	80/283 (28)	0.579
LEI=0[b]	95/159 (60)	81/147 (55)	0.432	98/159 (62)	84/147 (57)	0.392
SPARCC Enthesitis=0[c]	107/189 (57)	77/171 (45)	0.019	107/189 (57)	83/171 (49)	0.097
LDI-B=0[d]	37/42 (88)	54/58 (93)	0.658	35/42 (83)	47/58 (81)	0.620
HAQ-DI (≥0.35 CFB)[e]	168/252 (67)	166/254 (65)	0.741	168/252 (67)	164/254 (65)	0.605

Values are presented as n/N (%)
After the initial database lock and analysis run, nine patients who met baseline criteria for active psoriasis had baseline PASI=0 and BSA≥3% (a medical inconsistency). This inconsistency was not anticipated in the protocol or statistical analysis plan and was resolved using medical judgement. The primary analysis was re-run with these patients considered PASI100 responders if PASI=0 and BSA=0 at Week 24.
[a]Assessed for patients with NAPSI >0 at baseline.
[b]Assessed for patients with LEI score >0 at baseline.
[c]Assessed for patients with SPARCC Enthesitis Index score >0 at baseline
[d]Assessed for patients with LDI-B score >0 at baseline.
[e]Assessed for patients with HAQ DI score ≥0.35 at baseline. A response of ≥0.35 CFB is the minimal clinically important difference in HAQ-DI.
Abbreviations: ACR, American College of Rheumatology; ADA, adalimumab; CFB, change from baseline; DAPSA, Disease Activity in Psoriatic Arthritis; HAQ-DI, Health Assessment Questionnaire-Disability Index; IXE, ixekizumab; LDA, Low Disease Activity; LDI-B, Leeds Dactylitis Index-Basic; LEI, Leeds Enthesitis Index; MDA, Minimal Disease Activity; PASI, Psoriasis Area and Severity Index; SPARCC, Spondyloarthritis Research Consortium of Canada; VLDA, Very Low Disease Activity

and Severity Index (PASI100) (primary endpoint) in patients (pts) with active PsA (SPIRIT-H2H) (Mease et al, Ann Rheum Dis 2019). We report final 52-wk efficacy and safety, and efficacy in subgroups defined by concomitant MTX use in SPIRIT-H2H.

Methods: Pts with active PsA fulfilling Classification for Psoriatic Arthritis (CASPAR) criteria, ≥3/66 tender and ≥3/68 swollen joints, ≥3% psoriasis body surface area (BSA) involvement, no prior treatment with bDMARDs, and prior inadequate response to ≥1 conventional synthetic DMARD (csDMARD), were randomized 1:1 to open-label IXE or ADA (label dosing according to presence/absence of moderate-to-severe psoriasis [baseline BSA≥10%, PASI≥12, and static Physician's Global Assessment≥3]) through 52 wks. Outcomes included the percentage of pts achieving both ACR50 + PASI100 simultaneously, ACR20/50/70, PASI75/90/100, Nail Psoriasis Severity Index (NAPSI)=0, Minimal Disease Activity (MDA), Very Low Disease Activity (VLDA, defined as MDA 7/7), Disease Activity in Psoriatic Arthritis Low Disease Activity (DAPSA LDA), DAPSA remission, Leeds Enthesitis Index (LEI)=0, Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index=0, Leeds Dactylitis Index-Basic (LDI-B)=0, and HAQ-Disability Index (HAQ-DI) ≥0.35 change from baseline. Efficacy was also analyzed in subgroups based on concomitant MTX. Efficacy outcomes were analyzed using logistic regression with nonresponder imputation for missing data. There were no adjustments for multiple comparisons. Safety outcomes are summarized for pts who received ≥1 dose of study treatment.

	IXE N=283	ADA N=283
Treatment-emergent adverse events	209 (73.9)	194 (68.6)
Mild	95 (33.6)	85 (30.0)
Moderate	105 (37.1)	89 (31.4)
Severe	9 (3.2)	20 (7.1)
Serious adverse events	12 (4.2)	35 (12.4)
Discontinuations due to adverse events	12 (4.2)	21 (7.4)
Deaths	0	0
Adverse events of special interest		
Infections	119 (42.0)	111 (39.2)
Serious infections	5 (1.8)	8 (2.8)
Injection-site reactions	30 (10.6)	10 (3.5)
Allergic/hypersensitivity reactions	11 (3.9)	13 (4.6)
Potential anaphylaxis	1 (0.4)[a]	0
Cytopenias	9 (3.2)	12 (4.2)
Cerebrocardiovascular events	5 (1.8)	7 (2.5)
Malignancies	0	4 (1.4)
Depression	5 (1.8)	9 (3.2)
Inflammatory bowel disease	2 (0.7)[b]	0
Ulcerative Colitis	1 (0.4)[b,c]	0
Crohn's Disease	1 (0.4)[b,d]	0

[a]Patient experienced mild injection site pain, cough, and dizziness at the baseline visit, which was resolved on the same day.
[b]EPIdemiologique des Maladies de l'Appareil Digestif (EPIMAD) criteria for adjudication of suspected inflammatory bowel disease define "probable" and "definite" classifications as confirmed cases. Only 1 case met the EPIMAD criteria of confirmed inflammatory bowel disease.
[c]Event was reported as colitis ulcerative and was adjudicated as possible ulcerative colitis and did not meet the EPIMAD criteria of confirmed inflammatory bowel disease.
[d]Event was reported as colitis and was adjudicated as probable Crohn's disease.
Abbreviations: ADA, adalimumab; IXE, ixekizumab

Table 2. Safety outcomes at Week 52

Results: Overall, 87% (246/283) and 84% (237/283) of pts randomized to IXE and ADA, respectively, completed Wk 52. IXE provided significantly greater response than ADA for simultaneous ACR50 + PASI100 through Wk 52 (Figure 1A). IXE performed at least as well as ADA at Wk 52 for all other outcomes (Figure 1B, 1C, Table 1). Simultaneous ACR50 + PASI100 response was numerically greater with IXE than ADA, regardless of concomitant MTX use (Figure 1D). MTX use by treatment interaction was significant for ACR20/50/70 at Wk 52 (Figure 1E-F). Treatment-emergent adverse events (AEs) occurred in 73.9% (IXE) and 68.6% (ADA) of pts. Serious AEs occurred in 4.2% (IXE) and 12.4% (ADA) of pts, and discontinuations due to AEs occurred in 4.2% (IXE) and 7.4% (ADA) of patients; no deaths occurred. (Table 2).

Conclusion: IXE provided significantly greater simultaneous joint and skin improvement versus ADA as early as Wk 8 and through Wk 52. IXE performed at least as well as ADA across multiple PsA domains including musculoskeletal and skin domains through Wk 52. Safety outcomes for IXE and ADA were consistent with their previously established safety profiles.

Disclosure: J. Smolen, AbbVie, 2, 5, 8, AstraZeneca, 2, 5, 8, Celgene, 5, 8, Celltrion, 1, 2, Chugai, 1, 2, Eli Lilly and Company, 1, Gilead, 1, 2, ILTOO, 5, 8, Janssen, 1, 2, Novartis-Sandoz, 1, 2, Pfizer, 1, 2, Samsung, 5, 8, Sanofi, 5, 8, Kabi, 1, 2; **P. Nash**, AbbVie, 1, 2, 3, BMS, 1, 2, 3, Celgene, 1, 2, 3, Eli Lilly, 1, 2, 3, Gilead, 1, 2, 3, Janssen, 1, 2, 3, MSD, 1, 2, 3, Novartis, 1, 2, 3, Pfizer Inc, 1, 2, 3, Roche, 1, 2, 3, Sanofi, 1, 2, 3, UCB, 1; **H. Tahir**, Novartis, 1, 2, AbbVie, 1, Eli Lilly and Company, 1, 2; **H. Schulze-Koops**, Eli Lilly and Company, 1, 2, AbbVie, 1, 2, Amgen, 1, 2, Biogen, 1, 2, Hexal-Sandoz, 1, 2; **L. Li**, Eli Lilly and Company, 1, 2; **M. Hojnik**, Eli Lilly and Company, 3, 4; **A. Gellett**, Eli Lilly and Company, 1, 2; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **S. Pillai**, Eli Lilly and Company, 1, 2; **P. Mease**, AbbVie, 1, 2, 3, Amgen, 1, 2, 3, Bristol-Myers Squibb, 1, 2, 3, Celgene, 1, 2, 3, Eli Lilly, 1, 2, 3, Galapagos, 1, Genentech, 1, Gilead, 1, Janssen, 1, 2, 3, Novartis, 1, 2, 3, Pfizer Inc, 1, 2, 3, Sun, 1, 2, UCB, 1, 2, 3, Boehringer Ingelheim, 1.

Abstract Number: L21

Secukinumab 150 mg Significantly Improved Signs and Symptoms of Non-radiographic Axial Spondyloarthritis: Results from a Phase 3 Double-blind, Randomized, Placebo-controlled Study

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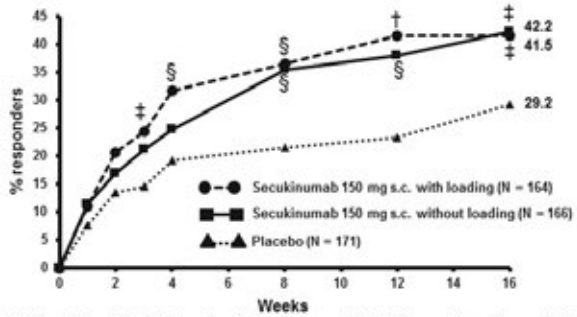
SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 4:00PM–6:00PM

Background/Purpose: Non-radiographic axial spondyloarthritis (nr-axSpA) and ankylosing spondylitis (AS) are considered part of the spectrum of axSpA. Patients (pts) are classified as nr-axSpA due to absence of definitive radiographic sacroiliitis but suffer from similar disease burden as pts with AS. NSAIDs are first-line therapy, and one anti-TNF therapy is approved for nr-axSpA pts with objective signs of inflammation in the US[1]. Secukinumab (SEC) provides significant and sustained improvement in signs and symptoms of pts with AS[2].

Methods: PREVENT (NCT02696031) is the first phase 3 study evaluating the efficacy and safety of SEC 150 mg with (LD) or without loading (NL) in pts with nr-axSpA. The study had 2 independent analysis plans as per EU (Week [Wk] 16) and US (Wk 52) regulatory requirements. Here, the Wk 16 efficacy results and safety to Wk 20 from the EU analysis plan are reported. This phase 3, double blind, placebo (PBO)-controlled, multicenter trial included 555 pts (aged ≥18 years) fulfilling the ASAS classification criteria for axSpA plus abnormal CRP and/or MRI, with no radiographic changes in the sacroiliac joints meeting modified New York Criteria. All images were assessed by central reading. Pts were randomized (1:1:1) to subcutaneous SEC 150 mg LD, 150 mg NL, or PBO. The LD group received SEC 150 mg at baseline (BL), Wks 1, 2, 3, and 4 , and then every 4 wks (q4wk) through Wk 52. NL group received SEC 150 mg at BL and PBO at Wks 1, 2, and 3, and then SEC 150 mg q4wk starting at Wk 4. PBO group received PBO at BL, Wks 1, 2, 3 and 4 and then q4wk. The primary endpoint was ASAS40 response with SEC 150 mg LD in anti-TNF-naïve pts at Wk 16. Secondary

Figure: ASAS40 response in anti-TNF-naïve patients through Week 16



†p<0.001; ‡p<0.01 and §p<0.05 vs placebo. (p values at Week 16 are adjusted for multiplicity of testing).
Data presented as non-responder imputation. N, number of anti-TNF-naïve patients randomized
ASAS, Assessment of Spondyloarthritis International Society; s.c., subcutaneous

Figure ASAS40 Response in Anti-TNF-naïve patients through Week 16

Table 1: Demographic and Baseline Disease Characteristics			
Characteristics Mean (SD), unless specified	**Secukinumab 150 mg with loading (N = 185)**	**Secukinumab 150 mg without loading (N = 184)**	**Placebo (N = 186)**
Age (years)	39.1 (11.5)	39.8 (11.7)	39.3 (11.5)
Male, n (%)	80 (43.2)	84 (45.7)	91 (48.9)
Anti-TNF-naïve, n (%)	164 (88.6)	166 (90.2)	171 (91.9)
Patients disease activity (median, 0-100 mm)	73.0	72.0	67.5
Time since onset of back pain (years)	8.7 (9.3)	8.6 (8.6)	8.4 (8.3)
Total Back pain (median, 0-100 mm)	74.0	72.5	71.0
BASDAI score	7.08 (1.3)	6.93 (1.4)	6.76 (1.24)
BASFI score	6.2 (2.0)	5.9 (2.0)	5.9 (1.9)
Abnormal CRP, n (%) of positive patients	104 (56.2)	107 (58.2)	105 (56.5)
Sacroiliac joint inflammation on MRI-yes, n (%)	132 (71.4)	134 (72.8)	139 (74.7)
HLA B-27 positive, n (%)	136 (73.5)	117 (63.6)	129 (69.4)
N, total number of randomized patients BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C-reactive protein; HLA, human leukocyte; MRI, Magnetic resonance imaging			

Table 1. Demographic and Baseline Disease Characteristics

Table 2: Secondary Efficacy Results# at Week 16			
Variables	**Secukinumab 150 mg with loading (N = 185)**	**Secukinumab 150 mg without loading (N = 184)**	**Placebo (N = 186)**
ASAS40, % responders	40.0‡	40.8‡	28.0
Total BASDAI, LS mean change from baseline (SE)	-2.4‡ (0.2)	-2.4‡ (0.2)	-1.5 (0.2)
BASDAI50, % responders	37.3‡	37.5‡	21.0
BASFI, LS mean change from baseline (SE)	-1.8‡ (0.2)	-1.6‡ (0.2)	-1.0 (0.2)
SF-36 PCS, LS mean change from baseline (SE)	5.7‡ (0.7))	5.6‡ (0.7)	2.9 (0.7)
ASQoL, LS mean change from baseline (SE)	-3.5‡ (0.4)	-3.6‡ (0.4)	-1.8 (0.4)
ASAS partial remission, % responders	21.6‡	21.2‡	7.0
‡P<0.05 vs. placebo (p values are adjusted for multiplicity of testing). Data presented as non-responder imputation (binary variables) and MMRM (continuous variables). #Pre-specified primary and secondary endpoints were analyzed according to a statistical hierarchy. Endpoints are shown in the order of testing. N, total number of randomized patients ASAS, Assessment of Spondyloarthritis International Society; ASQoL, Ankylosing Spondylitis Quality of Life; LS, least square; MMRM, mixed-model repeated measures; SE, standard error; SF-36 PCS, Short Form-36 physical component score			

Table 2. Secondary Efficacy Results# at Week 16

endpoints included ASAS40 response rates, total BASDAI, BASDAI50, BASFI, SF-36 PCS, ASQoL, and ASAS partial remission in the overall population. Analysis used NRI for binary and MMRM for continuous variables. Endpoints were analyzed according to a statistical hierarchy. Safety analyses included all pts who received ≥1 dose of study treatment.

Results: 94.6% (175/185; 150 mg LD), 96.2% (177/184; 150 mg NL) and 94.1% (175/186; PBO) pts completed 24 wks of treatment. Demographic and baseline disease characteristics were comparable across groups (**Table 1**). The primary and all secondary endpoints were met. At Wk 16, ASAS40 in anti-TNF-naïve pts was significantly higher in the SEC 150 mg LD group than PBO (**Figure**). SEC 150 mg LD and NL also showed significant improvement vs PBO in all secondary endpoints (**Table 2**). Three cases of serious infections/infestations (0.8%), and 1 case of Crohn's disease (0.3%) were reported with SEC. No cases of oesophageal candidiasis, major adverse cardiovascular events, malignancy or death were reported on any SEC dose up to Wk 20.

Conclusion: PREVENT is the first randomized controlled trial evaluating the efficacy and safety of SEC in pts with nr-axSpA. SEC 150 mg LD and NL provided significant improvement in signs and symptoms of nr-axSpA through Wk 16. The safety profile of SEC was consistent with the established safety profile across indications[3].

References:

1. van der Heijde D, et al. *Ann Rheu Dis*. 2017;76:978-991.
2. Lubrano E and Perrotta FM. *Ther Clin Risk Manag*. 2016;12:1587-92.
3. Deodhar A, et al. *Arth Res Ther*. 2019;21:111.

Disclosure: A. Deodhar, Abbvie, Amgen, Boehringer Ingelheim, BMS, Eli Lilly, GlaxoSmithKline, Janssen, Novartis AG, Pfizer, and UCB Pharma, 5, 8; **R. Blanco**, Janssen, 5, 8, MSD, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, AbbVie, 1, 2, 3,

Bristol-Myers, 1, 2; **E. Dokoupilova**, None; **M. van de Sande**, Novartis, 1, 2, 3, Eli Lilly, 1, 2, Boehringer Ingelheim, 1, Janssen, 1, Abbvie, 1, MSD, 1; **S. Hall**, Abbvie, UCB, JANSSEN, Merck, 1; **A. Wiksten**, Novartis, 1, 2; **B. Porter**, Novartis, 1, 3; **H. Richards**, Novartis, 1, 3; **S. Haemmerle**, Novartis, 1, 2; **J. Braun**, AbbVie, 1, 2, 3, Amgen, 1, 2, 3, BMS, 2, 5, 8, Boehringer, 2, 5, 8, Celltrion, 2, 5, 8, Centocor, 2, 5, 8, Chugai, 2, 5, 8, Medac, 2, 5, 8, MSD (Schering-Plough), 1, 2, 3, Mundipharma, 2, 5, 8, Novartis, 2, 5, 8, Pfizer (Wyeth, Hospira), 2, 5, 8, Roche, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, UCB Pharma, 2, 5, 8, Celgene, 1, 2, 3, EBEWE Pharma, 1, 2, 3.

Abstract Number: L22

Tofacitinib for the Treatment of Polyarticular Course Juvenile Idiopathic Arthritis: Results of a Phase 3 Randomized, Double-blind, Placebo-controlled Withdrawal Study

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Table 1. Demographics and disease characteristics at Part 1 baseline

	Pts in Part 1 (OLFAS)	Pts in Part 2 (DBFAS)	
	Tofacitinib[a] (N=225)	Tofacitinib[a] (N=88)	PBO (N=85)
Female, n (%)	169 (75.1)	66 (75.0)	64 (75.3)
Age (years), median (Q1, Q3)	13.0 (9.0, 15.0)	13.0 (9.0, 15.0)	13.0 (9.0, 15.0)
Race, n (%)			
White	196 (87.1)	76 (86.4)	74 (87.1)
Region, n (%)			
North America	96 (42.7)	31 (35.2)	41 (48.2)
South and Central America	47 (20.9)	22 (25.0)	15 (17.6)
Europe[b]	6 (2.7)	5 (5.7)	1 (1.2)
All other[c]	76 (33.8)	30 (34.1)	28 (32.9)
Primary JIA diagnosis, n (%)			
Extended oligoarthritis[d]	28 (12.4)	8 (9.1)	10 (11.8)
RF+ polyarthritis[d]	39 (17.3)	14 (15.9)	14 (16.5)
RF– polyarthritis[d]	104 (46.2)	45 (51.1)	42 (49.4)
Systemic JIA with active arthritis but without active systemic features[d]	13 (5.8)	5 (5.7)	4 (4.7)
PsA	20 (8.9)	7 (8.0)	8 (9.4)
ERA	21 (9.3)	9 (10.2)	7 (8.2)
Duration since onset of disease (years), median (Q1, Q3)	2.5 (1.0, 5.6)	2.5 (1.0, 5.7)	2.0 (1.0, 5.1)
Physician's global evaluation of overall disease activity, median (Q1, Q3)	6.0 (4.5, 7.5)	6.0 (4.5, 7.5)	6.0 (4.5, 7.5)
Joints with active arthritis, median (Q1, Q3)	10.0 (6.0, 15.0)	10.0 (7.0, 16.0)	9.0 (6.0, 14.0)
Joints with limited range of motion, median (Q1, Q3)	6.0 (3.0, 10.0)	6.0 (3.0, 12.0)	5.0 (3.0, 8.0)
CRP, median mg/dL (Q1, Q3)	0.3 (0.1, 1.0)	0.3 (0.1, 1.3)	0.2 (0.1, 0.9)
CHAQ-DI, median (Q1, Q3)	0.9 (0.3, 1.5)	0.8 (0.4, 1.4)	0.9 (0.3, 1.5)
Pt/parent assessment of overall wellbeing, median (Q1, Q3)	5.0 (3.0, 7.0)	5.0 (2.5, 7.0)	5.0 (3.0, 7.0)
JADAS27-CRP score, median (Q1, Q3)	20.1 (16.2, 26.6)	19.7 (16.2, 27.4)	20.1 (14.7, 25.4)

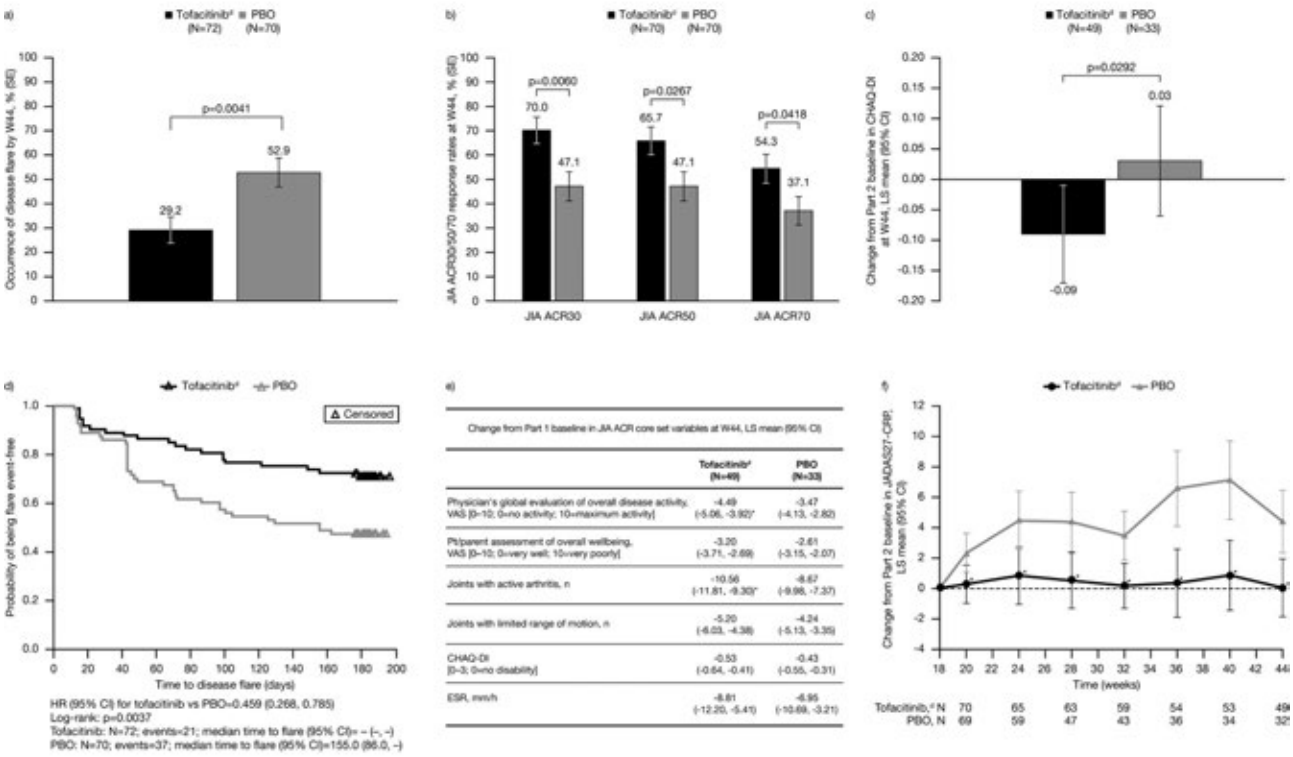
[a]5 mg BID or equivalent weight-based lower dose in pts < 40 kg
[b]Europe includes Belgium, Great Britain, Poland, and Spain
[c]All other includes Australia, Israel, Russia, Turkey, and Ukraine
[d]pcJIA, included in primary efficacy analysis
The OLFAS included enrolled pts who received ≥ 1 dose of study medication in Part 1 (18-week OL run-in phase); the DBFAS included pts randomized to Part 2 (26-week DB phase) who received ≥ 1 dose of study medication in Part 2 reported under randomized treatment; these analysis sets include pts with pcJIA, PsA, or ERA
BID, twice daily; CHAQ-DI; Childhood Health Assessment Questionnaire Disability Index; DB, double-blind; DBFAS, double-blind full analysis set; ERA, enthesitis-related arthritis; JADAS, Juvenile Arthritis Disease Activity Score; OL, open-label; OLFAS, open-label full analysis set; PBO, placebo; pcJIA, polyarticular course juvenile idiopathic arthritis; pt, patient; Q1, 25th percentile; Q3, 75th percentile

SESSION INFORMATION
Session Date: Tuesday, November 12, 2019
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 4:00PM–6:00PM

Background/Purpose: Tofacitinib is an oral JAK inhibitor that is being investigated for JIA. Here we assess the efficacy and safety of tofacitinib in patients (pts) with JIA.

Methods: This was a Phase 3, randomized, double-blind (DB), placebo (PBO)-controlled withdrawal study in pts aged 2 to < 18 years with polyarticular course JIA (pcJIA), PsA or enthesitis-related arthritis (ERA) (NCT02592434). In the 18-week, open-label (OL), run-in phase (Part 1), pts received tofacitinib. Pts achieving ≥ JIA ACR30 response[1] at Week (W)18 were randomized 1:1 in the DB phase (W18–44; Part 2) to continue receiving tofacitinib or withdraw tofacitinib and newly receive PBO. Tofacitinib was administered according to body weight: 2–4 mg BID oral solution in pts < 40 kg; 5 mg BID tablet or oral solution in pts ≥ 40 kg. The primary endpoint was occurrence of disease flare[2] by W44 (W26 of Part 2). Key secondary endpoints were JIA ACR50/30/70 response[1] rates and change (Δ) from Part 2 baseline (BL) in Childhood Health Assessment Questionnaire Disability Index (CHAQ-DI) at W44. The primary and key secondary endpoints were type 1 error-controlled with statistical significance declared at $p < 0.05$. Other efficacy endpoints included time to disease flare in Part 2, Δ from Part 1 BL in JIA ACR core set variables[1] at W44, and Δ from Part 2 BL in Juvenile Arthritis Disease Activity Score (JADAS27-CRP) during Part 2. Pts with PsA or ERA were exclud-

Figure 1. Efficacy of tofacitinib vs PBO in 142 pts with pcJIA in Part 2: a) occurrence of disease flare[a] by W44[b]; b) JIA ACR30/50/70 response[c] rates at W44[b]; c) mean change from Part 2 baseline in CHAQ-DI at W44[b]; d) Kaplan-Meier plot of time to flare in Part 2; e) mean change from Part 1 baseline in JIA ACR core set variables at W44; f) mean change from Part 2 baseline in JADAS27-CRP over time



*p < 0.05 tofacitinib vs PBO; nominal p values, not type 1 error-controlled
[a]Flare is defined as a worsening of ≥ 30% in ≥ 3 of the 6 variables of the JIA core set, with ≤ 1 variable improving by ≥ 30%[1]
[b]Type 1 error-controlled endpoints were tested sequentially as follows: occurrence of disease flare by W44 (primary endpoint); JIA ACR50/30/70 response rates at W44; change from Part 2 baseline in CHAQ-DI at W44. Using this gatekeeping approach, statistical significance could be claimed for the next endpoint only if the prior endpoint in the sequence met the requirements for significance
[c]The JIA ACR30/50/70 response criteria are: 3 out of 6 JIA core set variables improved ≥ 30%, 50%, and 70%, respectively, with ≤ 1 variable worsening by ≥ 30%. In pts with systemic JIA, the absence of spiking fever related to systemic JIA is also required[1]
[d]5 mg BID or equivalent weight-based lower dose in pts < 40 kg
[e]These data are for pts with pcJIA in Part 2 (26-week DB phase); pts with PsA or ERA are not included and were analyzed separately
BID, twice daily; CHAQ-DI, Childhood Health Assessment Questionnaire Disability Index; CI, confidence interval; DB, double-blind; JADAS, Juvenile Arthritis Disease Activity Score; LS mean, least squares mean; pcJIA, polyarticular course juvenile idiopathic arthritis; PBO, placebo; pts, patients; SE, standard error; W, Week

Table 2. Summary of treatment-emergent AEs, AEs of special interest, and laboratory abnormalities

	Part 1 (OLFAS)	Part 2 (DBSAS)		Entire tofacitinib exposure period
	Tofacitinib[a] (N=225)	Tofacitinib[a] (N=88)	PBO (N=85)	Tofacitinib[a] (N=225)
Pts with events, n (%)				
AEs	153 (68.0)	68 (77.3)	63 (74.1)	176 (78.2)
SAEs	7 (3.1)	1 (1.1)	2 (2.4)	8 (3.6)
Discontinuations due to AEs	26 (11.6)	16 (18.2)	29 (34.1)	42 (18.7)
Temporary dose reductions or discontinuations due to AEs	20 (8.9)	9 (10.2)	8 (9.4)	25 (11.1)
Most common AEs (≥ 5% of any treatment group)				
URTI	24 (10.7)	13 (14.8)	9 (10.6)	34 (15.1)
Headache	16 (7.1)	2 (2.3)	6 (7.1)	18 (8.0)
Nasopharyngitis	10 (4.4)	7 (8.0)	3 (3.5)	15 (6.7)
Nausea	13 (5.8)	1 (1.1)	1 (1.2)	14 (6.2)
Pyrexia	11 (4.9)	4 (4.5)	1 (1.2)	14 (6.2)
Disease progression	5 (2.2)	8 (9.1)	13 (15.3)	13 (5.8)
Vomiting	13 (5.8)	0	4 (4.7)	13 (5.8)
JIA	6 (2.7)	3 (3.4)	12 (14.1)	9 (4.0)
AEs of special interest				
Death	0	0	0	0
Gastrointestinal perforation[b]	0	0	0	0
Hepatic event[b]	3 (1.3)	0	0	3 (1.3)
Herpes zoster	2 (0.9)	0	0	2 (0.9)
ILD[b]	0	0	0	0
MACE[b]	0	0	0	0
Malignancy (including NMSC)[b]	0	0	0	0
MAS[b]	0	0	0	0
Opportunistic infection[b]	0	0	0	0
Serious infection	3 (1.3)	1 (1.1)[c]	1 (1.2)	4 (1.8)[c]
Thrombotic event (DVT, PE,[b] or ATE)	0	0	0	0
Tuberculosis[b]	0	0	0	0
Pts with lab test abnormalities, n (%)				
Hemoglobin (g/dL)				
< 0.8× LLN	1 (0.4)	1 (1.1)	3 (3.5)	
Lymphocytes (10^3/mm^3)				
< 0.8× LLN	7 (3.1)	5 (5.7)	1 (1.2)	
> 1.2× ULN	2 (0.9)	1 (1.1)	0	
Aspartate aminotransferase (U/L)				
> 1.0× ULN	25 (11.1)	12 (13.6)	9 (10.6)	
> 2.0× ULN	9 (4.0)	1 (1.1)	0	
> 3.0× ULN	4 (1.8)	0	0	
Alanine aminotransferase (U/L)				
> 1.0× ULN	33 (14.7)	14 (15.9)	11 (12.9)	
> 2.0× ULN	10 (4.4)	5 (5.7)	3 (3.5)	
> 3.0× ULN	5 (2.2)	1 (1.1)	2 (2.4)	
Cholesterol (mg/dL)				
> 1.3× ULN	2 (0.9)	0	0	

[a]5 mg BID or equivalent weight-based lower dose in pts < 40 kg

[b]Adjudicated events

[c]One SAE of pilonidal cyst repair was coded to surgical procedures instead of infections and was inadvertently not identified as a serious infection. Following adjudication, it was determined that the SAE did not meet opportunistic infection criteria; it is also included in the table as a serious infection

The OLFAS included pts enrolled who received ≥ 1 dose of study medication in Part 1 (18-week OL run-in phase); the DBSAS included pts who received ≥ 1 dose of study medication in Part 2 (26-week DB phase) reported under received treatment; these analysis sets include pts with pcJIA, PsA, or ERA

AE, adverse event; ATE, arterial thromboembolism; BID, twice daily; DB, double-blind; DBSAS, double-blind safety analysis set; DVT, deep vein thrombosis; ERA, enthesitis-related arthritis; ILD, interstitial lung disease; LLN, lower limit of normal; MACE, major adverse cardiovascular event; MAS, macrophage activation syndrome; OL, open-label; OLFAS, open-label full analysis set; PBO, placebo; pcJIA, polyarticular course juvenile idiopathic arthritis; PE, pulmonary embolism; pts, patients; SAE, serious adverse event; ULN, upper limit of normal; URTI, upper respiratory tract infection

ed from these efficacy analyses and analyzed separately. Time to flare was analyzed by the Kaplan-Meier method. Safety was evaluated throughout the study.

Results: 225 pts with pcJIA (n=184), PsA (n=20) or ERA (n=21) were enrolled and received OL tofacitinib in Part 1 (Table 1). At W18, 173/225 (76.9%) pts entered Part 2 (pcJIA [n=142], PsA [n=15], ERA [n=16]). In pts with pcJIA, occurrence of disease flare in Part 2 was significantly lower with tofacitinib (29.2%) vs PBO (52.9%) by W44 (p=0.0041; primary endpoint; Figure 1a). JIA ACR50/30/70 response rates (Figure 1b) and improvement from Part 2 BL in CHAQ-DI (Figure 1c) at W44 were greater with tofacitinib vs PBO. Time to disease flare was greater with tofacitinib vs PBO in Part 2 (Figure 1d). Tofacitinib had a greater effect vs PBO in reducing signs and symptoms of pcJIA, in terms of Δ from Part 1 BL in JIA ACR core set variables at W44 (Figure 1e). From early time points in Part 2, disease activity (assessed by JADAS27-CRP) worsened with PBO but remained stable with tofacitinib (Figure 1f). Safety was generally similar in pts receiving tofacitinib or PBO (Table 2): 77.3% and 74.1% had adverse events (AEs); 1.1% and 2.4% had serious AEs. There were no cases of death, opportunistic infection or tuberculosis.

Conclusion: In pts with pcJIA, treatment with tofacitinib vs PBO resulted in significantly fewer disease flares, improved time to flare, improvements in disease signs and symptoms and physical functioning, and a sustained clinically meaningful improvement in disease activity. The safety profile of tofacitinib was consistent with that in adults with RA.

1. Giannini EH et al. Arthritis Rheum 1997; 40: 1202-1209.
2. Brunner HI et al. J Rheumatol 2002; 29: 1058-1064.

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Patient Perspectives

Number: PP01

From Diagnosis to the Establishment of the Labalaba Foundation: My Journey from Surviving to Thriving

Chisa Nosamiefan ,[1] Courtnie Phillip,[2] and Candace Feldman[2], [1]The Labalaba Foundation, [2]Brigham and Women's Hospital, Massachusetts

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Perspectives Poster Session
Session Type: Poster Session (Sunday)
Session Time: 11:30AM–1:30PM

Background/Purpose: After having my youngest son in 1994, I developed discomfort in my fingers which I ignored. In 1997, I had pericarditis, and two years later, pleurisy. I was diagnosed with lupus at the Cleveland Hospital in Florida about 20 years ago, 4-5 years after my initial symptoms. My initial treatment was inconsistent, because I lived 4 hours away from the healthcare facility, and I did not have adequate health insurance. At this time, my symptoms were frequent fevers, weight loss, abdominal pain, and generalized myalgias. I took acetaminophen or naproxen and medicines like Zantac for the abdominal pain.

Treatment: I moved to Boston in 2008 and I started a consistent treatment regimen: prednisone, hydroxychloroquine, omeprazole, azathioprine, lisinopril, nifedipine. My disease also progressed. I experienced increased myalgias and developed blood clots and pulmonary hypertension. I continued to experience pericarditis and pleurisy. I was switched from azathioprine to mycophenolate mofetil, and warfarin and gabapentin were added. Abatacept was tried for my joints but I developed a rash. I was switched to belimumab.. Finding the right cocktail of drugs required the masterful skill of my healthcare team to move me from barely surviving with lupus, and now, well on the way to thriving despite lupus.

Maintenance: After setbacks to my health between 2008-2015 (falls, increased pain, hospitalizations, difficulty coping, and having to stop work) I began to improve. I earned my master's degree and started a consulting practice. I became active again with my Christian ministry and my stress level lessened, which seemed to be tied to reduced lupus activity. As a woman of Nigerian descent, it occurred to me that I had never met another Nigerian living with lupus. If lupus is prevalent in people of African descent in the US then it must be present in Africa and in Nigeria, the most populous African nation. I embarked on a fact finding trip and then started The Labalaba Foundation for Lupus Awareness and Advocacy in Nigeria. I also began to participate in Boston-based research studies and became a member of the Patient Advisory Board of the largest lupus center in New England.

Figure 1. Timeline of my journey with lupus, from my initial symptoms until the present time

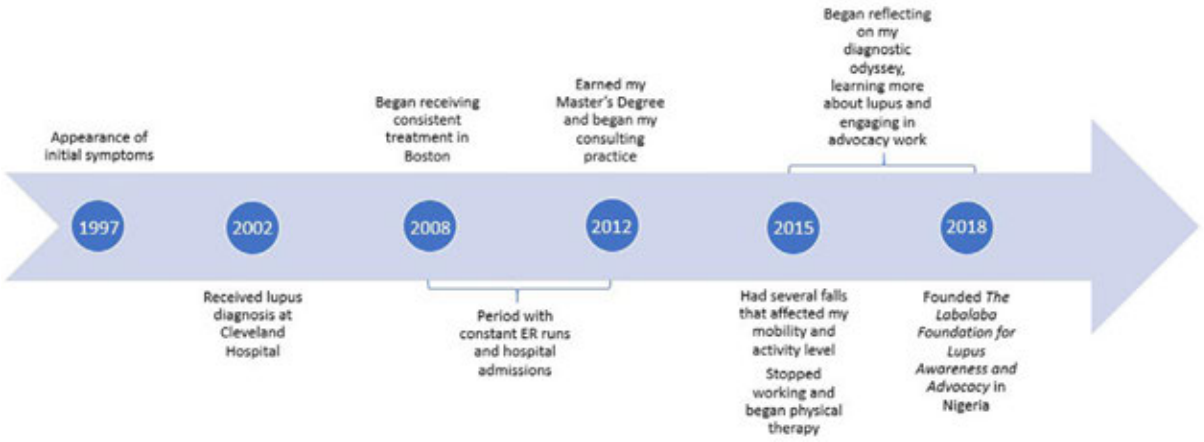


Figure 2. *The Labalaba Foundation for Lupus Awareness and Advocacy* programs and initiatives

Think Lupus Campaign	• Offers training to primary healthcare professionals - doctors, nurses, social workers and clinics to sensitize them to SLE symptoms and encourage the testing and consideration of a lupus diagnosis sooner
Erase Lupus Awareness Program	• Lupus educational workshops and seminars to raise awareness and foster early detection of lupus • Targets schools, community organizations, religious houses of worship, general public
The Pill Box Program	• A prescription assistance program that aims to to keep lupus patients, who are unable to afford their medications, on their medication and stable • It costs about 18,000 Naira ($50) per month for maintenance and 80,0000 Naira ($220) per month for a critical lupus patient.
"The Frank Talk"	• Caregivers roundtable meetings for support and discussions about the unique challenges that spouses, parents and others who care for lupus patients face on a daily basis
Free Individual and Family Counseling	• Relate Africa has a team of highly qualified professionals and has partnered with The Labalaba Foundation (TLF) to provide free counseling for lupus patients and their families
The Odelia Academic Scholarship for Pediatric SLE	• TLF annually awards an academic scholarship to a child living with lupus in honor of Odelia, an amazing girl who fought a hard fight with lupus

Chisa Nosamiefan, patient and founder of The Labalaba Foundation, pictured with Labalaba Champions in Nigeria

Quality of Life: My quality of life has drastically improved over the past three years. I am more active at home, I have socially re-engaged, I go shopping, and I travel. For many years I was unable to do this. Most amazing is that I am now a lupus advocate, educator and champion. Since I began helping lupus patients I have not been hospitalized. Lupus is a complex disease and the complexity goes beyond the clinical symptomatic manifestations. Each lupus manifestation is influenced by a patient's social circumstances and access to good medical care. The health and wellbeing of lupus patients may improve when definite steps are taken to address stress factors and other lifestyle triggers. Through my own journey and the creation of The Labalaba Foundation, I have taken charge of my health and hope to help others do the same.

Disclosure: C. Nosamiefan, None; **C. Phillip**, None; **C. Feldman**, None.

Number: PP02

Living and Adjusting to a Diagnosis of Rheumatoid Arthritis (RA) with an Interdisciplinary Team

Marie-Claude Beaulieu ,[1] Julie Robindaine,[2] Hélène Tremblay,[2] Stéphanie Demers Dubuc,[2] Patrick Liang,[3] and France Gervais[2], [1,2]Quebec, Canada, [3]Universite de Sherbrooke, Quebec, Canada

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Perspectives Poster Session
Session Type: Poster Session (Sunday)
Session Time: 11:30AM–1:30PM

Background/Purpose: RA affects all age groups and all occupational settings. I was diagnosed at age 58, while I was still very active at work, at sports and as a grandmother. I had to adapt to this new reality in several ways. Initially, the presentation was atypical (polymyalgia-like), and the disease was difficult to control with steroids. During steroid tapering, severe limitations in my hands, wrists, shoulders, ankles and feet associated with subtle hand synovitis (ultra sound exam negative once) made my rheumatologist suspect RA despite normal biomarkers. I started treatment with a combination of hydroxychloroquine and methotrexate injection, failed an anti-TNF and finally got sustained improvement with the addition of tofacitinib.

Treatment: I can attest how much an interdisciplinary team helps: rheumatologist, nurse, occupational therapist (OT) and physical therapist (PT) working with each other. Their support was especially important at the beginning of my disease, with the possibility to phone and ask questions to the specialized nurse to reduce my stress and improve my adherence to treatment. To overcome physical limitations, an OT provided orthotics for my hands, and several useful tips for energy conservation and activities of daily living. A PT gave me valuable tips and exercises to do at home. It would be particularly helpful if all patients should have access to these services early in their disease, although a supporting team may be important over all the disease stages, and particularly during flares or loss of efficacy of drugs. Our Faculty of Medicine in Sherbrooke developed a special teaching clinic “CURE” (OT and PT services) to give low-cost access to these services for patients without insurance. When receiving a diagnosis of arthritis, a grieving process ensues, a reorganization of daily activities is required and a lot of resilience to accept these changes is needed! I had to stop working temporarily and then returned to work progressively with adaptations and changes. The support of my rheumatologist was most important in this process.

Maintenance: My rheumatologist offered several effective treatments to slow down the progression of the disease, and we found together the winning combination (with trial and error). The availability and support from the interdisciplinary team, family and co-workers is very important, as there are good and bad periods. I need to keep hope, continue to be active, allow for rest periods, eat healthy and take the medication despite sometimes annoying side effects. Daily mindfulness meditation (offered to interested patients in our clinic) helps me a lot.

Quality of Life: It is very encouraging to regain control of one’s life through better control of the disease and to feel better and lead an almost normal life. However, I have to remain vigilant and be careful of infections since my immune system is weaker with the medication. The initial frequent consultations, regular check-ups, discouragement periods over my limitations and the frequent medication adjustments made me realize the importance of working as a team where the patient is a partner in care. Information about the disease and its treatments is important for the patient and health professionals as well.

Disclosure: M. Beaulieu, None; **J. Robindaine**, None; **H. Tremblay**, None; **S. Demers Dubuc**, None; **P. Liang**, None; **F. Gervais**, None.

Number: PP03

Bridging the Gap: Leveraging Social Media to Improve Patient Support; Build a Path to Collaborative Medicine

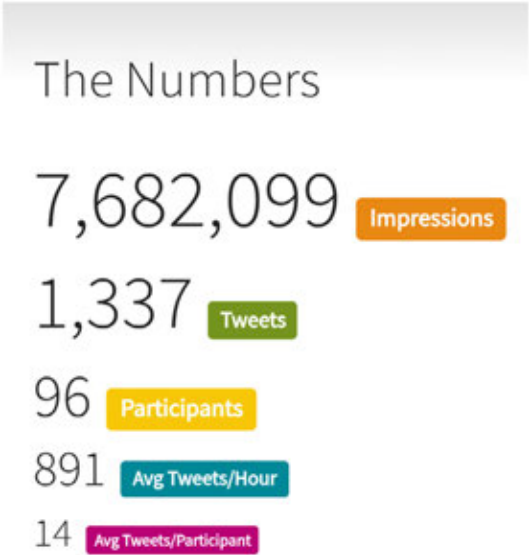
Carlene Harrison ,[1] and Tiffany Peterson[1], [1]Lupus and Allied Diseases Association, Inc.

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Perspectives Poster Session
Session Type: Poster Session (Sunday)
Session Time: 11:30AM–1:30PM

Background/Purpose: Due to the heterogeneous nature of disease presentation, when diagnosed with Systemic Lupus Erythematosus (SLE) patients often experience overwhelming feelings of isolation. This comes as a result of not knowing there are others, that may be experiencing the same types of symptoms. These sentiments proved true for two patients living six hours apart who would come to meet years later through their individual quests to attain more knowledge about SLE and find support from others facing the same challenges they met daily. Both Carly and Tiffany, patients diagnosed with SLE and secondary illnesses including Raynaud's Phenomenon, Fibromyalgia, and Nephritis within a year of each other, would come to connect years later through an online patient led community.

After spending years in search of resources for patients, Tiffany founded the online community #LupusChat to offer educational information about SLE to patients and provide a safe space for patients to feel supported. Through the years the community grew to include patients, advocates, physicians, scientists, industry leaders, and other partners in healthcare.

Treatment: SLE patients are treated with traditional interventions including immunosuppressants, corticosteroids, and antimalarials. Considerations are oftentimes only made in terms of treating the physical symptoms of the disease. This approach doesn't typically account for mental or emotional complications associated with SLE. This leads to a disconnect between patients and healthcare professionals, where patients feel physicians aren't empathetic to their needs outside of lab results and physicians complain of low treatment adherence and lack of interest in the patient's own medical care. Through online discussions with topics ranging from interpreting lab test results and connecting with doctors to becoming advocates, #LupusChat works to connect all healthcare stakeholders.



Maintenance: Both Tiffany and Carly found solace through the connections made from this online community. Starting out as solely a member of the community, Carly now joins Tiffany and two other Patient Advocates in curating discussions and sharing health literacy tools with the chronic illness community. They also work with groups like the patient founded national non-profit organization, Lupus and Allied Diseases Association, Inc. (LADA) on advocacy initiatives. This includes working with legislators at the state and federal level, attending and speaking at conferences, and educating patients on the importance of clinical trial participation.

Quality of Life: These patients have not only become advocates themselves, but have helped others to become empowered. Their roles in the Lupus community have also led them to become more adherent to their own treatment plans. They receive testimonials from other patients about the impact the community has had on their lives and how things like daily community medication reminders have impacted their health. Healthcare professionals have also become more involved in patient outreach and often seek their assistance in learning to use social media as a tool to educate patients. Through social media engagement, they amplify the Patient voice and help foster healthcare partnerships.

Disclosure: C. Harrison, Aurinia Pharmaceuticals Inc, 5; **T. Peterson**, Aurinia Pharmaceuticals Inc, 5.

Number: PP04

Reclaiming Medical Autonomy Through Healthcare Advocacy

Christele Felix[1], [1]LADA, Rosedale, New York

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Perspectives Poster Session
Session Type: Poster Session (Sunday)
Session Time: 11:30AM–1:30PM

Background/Purpose: When I received my diagnosis in 2007, I had never heard the word Lupus before and had no idea what it meant. I don't remember having any reaction to the news, because I did not know to be alarmed by the gravity of the situation. Newly diagnosed patients often cannot imagine the extent to which this health issue will take over their lives. I was diagnosed at 18 years old, while trying to juggle with young adulthood and an ambitious college career. I would soon discover that there was a lot to learn in managing a complex and long term condition like Lupus. In doing so I'd learn to raise my voice and help others raise theirs.

Treatment: Evolving as a chronic patient takes a lot of reevaluation on patients' part of what their priorities are. It takes some time, and is an ongoing experience, to learn how to appropriately manage stress and energy levels, in addition of staying on top of a complex treatment regiment and coordinating with a health team of multiple specialists. Very often, patients also learn a lot about patients' rights issues. I got involved in a support group as a quiet participant, observing and learning until I found my own voice. Pretty soon, and bolstered by the positive doctor-patient interactions with my rheumatologist and gastroenterologist, I became very vocal about patient-centered care and patient-centered research. My goals as I navigated this new life with chronic illness were to improve quality of life and make a better future for myself and for people living with similar conditions.

Maintenance: My background in research and education made it easier to piece together the medical jargon related to Lupus in medicine and research, and I have enjoyed educating myself so that I can educate others as well. As a result of this, I took a more active role in my care; my health and my quality of life have improved dramatically. My new-found drive to advocate on behalf of myself and others has influenced my personal health in a great way. Patients' motivation can falter in the face of such a long term condition, and it often takes years to figure out the right approach that works for each person. As patients find their voices and stand up for their rights and the rights of patients like them, they may discover that their personal health also improves for the better.

Quality of Life: My advocacy sustains me, both as an individual and as a patient. I believe that it is very important to let patients know that they have a voice that they can use if they so wish. Patient education starts with the patient itself, then gradually evolves to benefit others. As part of a community of patients and patient advocates, we give each other support and encouragement, as well as medicine reminders and helpful tips for people living with Lupus. Additionally, I constantly seek to have conversations with doctors and health professionals on ways to engage patients and improve their quality of life.

Disclosure: C. Felix, Aurinia Pharmaceuticals Inc, 5.

Number: PP05

Race for Relapsing Polychondritis Drives Awareness, Accelerates Research, and Improves the Quality of My Life: How Motorsports Help Me Overcome the Hopelessness of an Incurable, Rare Disease

Nancy Linn[1], [1]RPASF Inc.

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Perspectives Poster Session
Session Type: Poster Session (Sunday)
Session Time: 11:30AM–1:30PM

Background/Purpose: Like many other patients with a rare disease, I felt relieved when I finally received a diagnosis: relapsing polychondritis or "RP". However, once I started researching the disease, the scant information available wasn't encouraging. Most sources described RP as fatal – a shock to read at 54 years of age. Through a Facebook group for RP patients, I was introduced to physicians, specialists, and researchers, all of whom became essential for our future collaborations benefiting RP patients. However, I soon realized that my communications with doctors and other patients all revolved around RP, and I wanted a forum where we could engage outside the hopelessness of an incurable illness.

Treatment: In 2016, I founded Race for RP, an organization that partners with motorsports drivers and teams to support research, awareness, and quality care for RP patients. Since then, we've seen our logo zip across the finish line first, but the real victories have been solidifying the ties between care providers. For example, at one race, we invited the leader of an autoimmunity institute to have the organization's logo on a professional sports car. He accepted, and that car won the race, garnering international publicity and paving the way for future partnerships. At the same time, engaging with my community outside of hospitals and the Facebook group provides support centered on positive actions, like riding my bike for our cycling fundraisers.

Maintenance: In between getting news of more cartilage damaged, Race for RP gives me purpose and hope. Over Memorial Day Weekend, I was on my way to a friend's wedding instead of watching one of our professional drivers compete in a world-renowned automobile race – with our logo on the car! As I traveled to the wedding, I watched footage of the race on my phone. After losing cell service, I listened on satellite radio. Thankfully, the last lap was finished before the wedding reception, or I may have had to sneak into the bathroom to hear who won. The awareness generated by Race for RP's drivers and teams has been wonderfully distracting from the symptoms of the disease and sparked many positive, fun conversations with other autoimmune disease patients and motorsports enthusiasts. Race for RP has also improved my physical health through its collaboration with other organizations, which has provided me (and other patients) with access to specialists I never could've found on my own.

Quality of Life: Race for RP has greatly improved my quality of life, and one of my proudest moments was after last year's ACR/ARP Annual Meeting. There, Race for RP provided funding for 2 Exhibitor booths and hosted 2 affiliated educational events with highly regarded rheumatologists and epidemiologists. These awareness-generating events helped make RP the most searched disease (on a top search engine) in the host state. I feel this same pride when

Illustration of the Race for RP No. 153 Ferrari Challenge Car

After a Long Day of Riding on a Michigan Cycling Tour in Support of Race for RP

RACE FOR RP
RELAPSING POLYCHONDRITIS
RaceForRP.org

The Race for Relapsing Polychondritis Logo with Website Information

I see the Race for RP logo on race cars, mobile phones, windows of businesses in town, hats of a stranger, or the wristbands of my global friends. Race for RP is good for my health – mental and physical.

Disclosure: N. Linn, None.

Number: PP06

Art for Arthritis: A New Approach

Jennifer Walker[1], [1]Global Healthy Living Foundation, San Antonio, Texas

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Perspectives Poster Session
Session Type: Poster Session (Sunday)
Session Time: 11:30AM–1:30PM

Background/Purpose: Chronic 24/7 pain, fatigue, and swelling are all part of my journey with rheumatoid arthritis (RA) and Axial Spondyloarthritis (AxSpa). My RA is moderate to severe, and my AxSpa has taken 7 years to be properly diagnosed resulting in a loss of 3 inches in height, stenosis, osteophytes and a broken piece of disc floating near my spine. My experience is unique with only 1% of the population experiencing RA and 2% experiencing AxSpa. The coexistence of these diseases in one patient is exceptionally rare.

‘Spots’ - digital art

‘Rocks in a paper boat’ - digital art

Treatment: I am an expressive person finding myself discussing my diseases a lot due to the need for accommodation or pain levels. Constant exhaustion, lack of sleep, high pain levels, RA flares, bouts of back pain and episodes that leave me without the capacity to function is often too much for words. I found an amazing outlet in art to not only

'Unraveling' - digital art

express my journey but to reach out to others. It gives me the ability to look back on a piece of artwork and remember the pain and my resilience and power in the face of intense circumstances. I'm able to process my grief over lost abilities, deteriorating health, and describe my journey through art in a more universal way than just words. It fulfills my need to be creative but also my need to take control of my life and body in a way that makes sense, allowing me to accept where I am and heal. Art reminds me how powerful my mind and heart are, so I can pick myself up one more day and living for good instead of being lost in the pain. It helps me to listen to my body, enabling a more flexible reaction to pain episodes or flares. It gives me the chance to process what is happening so I don't fight the disease process; facing my body and my life with courage.

Maintenance: Creating art that expresses my pain and health struggles helps me trust my body. I began to publish these pieces on social media and the response has been overwhelming. Reminding me that I'm not alone on this journey and my body is telling the truth. Listening to my body in the first place got me diagnosed, getting me the medical help that I need. After being diagnosed with RA and fibromyalgia 9 years ago, I was angry and frustrated ending up in the hospital from a panic attack. The last 4 months have been an intense struggle and expressing that through art has helped me to admit how bad my body and my pain levels have been when I wanted to run away from the downswing

in my health. As a patient with multiple chronic illnesses I go through a cycle of acceptance and grief. My health and body took an upturn when I learned to not fight the cycles of flares, pain and disease.

Quality of Life: Listening to my body for cues allowed me to function more because I rested or pushed when needed. I learned my patterns and strengths, allowing accomplishing more when I do have energy without overdoing it. These diseases won't go away and I no longer fight that, increasing my quality of life. Because I have accepted my body I can also create art in a very vulnerable and open way that reaches out to others. My art allows me to show my life and struggles in a way that makes the abled folks stop and take notice. Visual representation helps other patients point to a piece that validates their pain and creates better connections with their loved ones. Patients need to know that what we experience is normal - my art helps me to see that so I can cope better daily.

This piece represents the places on my body that are always in pain. This pain causes constant fatigue and the need to adapt. I created this piece right before I was diagnosed with AxSpa. I had a lot of frustration because my lower back pain was not really acknowledged or treated. After diagnosis this reminded me to always trust my body's signals about something being wrong. This is piece #1 in my fatigue series. This piece received 490 likes and 409 shares on the CreakyJoints Facebook page.

This piece helped me express frustration from intense pain, a rough day at work, and some intense gastro issues that have been amping up lately. It got over 575 views on my Facebook page.

This is #10 in my fatigue series. This series takes input from other people with autoimmune diseases and illustrates what fatigue feels like for them so they can use these images to speak with loved ones and/or HCPs. I love this piece.

Disclosure: J. Walker, None.

Number: PP07

Coming to Terms with Lupus: How Learning to Listen to My Body and Letting it Tell Me What to Do Improved My Quality of Life

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Perspectives Poster Session
Session Type: Poster Session (Sunday)
Session Time: 11:30AM–1:30PM

Background/Purpose: A diagnosis in my teens of epilepsy resulted in shifting my dreams of being a teacher, but after successful brain surgery I began living what was a normal life. But medical issues continued to come and go. I went to the hospital several times and no one could figure out what was wrong. In fact, some did more harm than good. A cardiac catherization led to emergency surgery. Then my husband and I decided to find an answer, no matter what. After visiting many specialists, we found a rheumatologist who listened. I was tested for leukemia, MS, and others, but not lupus. Meanwhile, I was swollen and sore all the time with severe fatigue and weakness throughout my body. Finally, I asked the rheumatologist to test for lupus. He still didn't think it was lupus, but after more tests I was diagnosed. Listening to my body and my own instincts led to a diagnosis!

Treatment: After being diagnosed with SLE and other autoimmune diseases my rheumatologist started me on several medications and a couple worked. I began swimming and playing volleyball to keep moving. Then I moved

and the first doctor I met pushed chemo, even though I was in remission. That was the last day I saw this doctor. I contacted a patient advocacy group that pointed me to a new rheumatologist who listened to me and suggested keeping the status quo. After a year, she started to wean me off some of the medications. I learned you can find the right doctor by searching and speaking up.

Maintenance: As my rheumatologist decreased some medications, my neurologist increased some vitamins and minerals. Their working together and sharing information is key to my mental and physical health. I have learned to deal with three main issues:

- Sensitivity to sunlight
- Burning of my face
- Body aches

These all got more severe since my lupus diagnosis and I took on a new perspective of life through this challenge.

Quality of Life: I have learned that in order to succeed through my day, I must listen closely to my body. For instance, despite loving the sun, I now avoid it as much as possible. I have learned to always wear a hat, sunglasses and use a lot of sunblock with high UV protection. Often, I just stay inside. When I feel my face burning, I don't go out. A cool, wet washcloth on my cheeks and eyes helps the symptoms subside. The key is to feel it coming on. If I catch it early, I can usually continue my day without much impact. If I'm out, I find a cool, dark place to minimize the flare. Part of my daily life is dealing with different aches - fingers swelling, joints aching, body fatigue. Every day is different, and when I push myself, I pay for it the next day. I now know that when my body tells me to slow down, I must listen. I don't like to stop, or even slow down, but I know that in order to live with lupus I have no choice. Swimming is one way I have adapted to this new normal. The water helps support my body and relaxes the pain. Walking our dogs is another way to exercise but not put too much stress on my body. Every day I listen carefully to what my body is telling me. What can I do today, what should I do differently? Think back to yesterday…what did I do, and how is it affecting me today? Understanding my body has been one of the most beneficial things in my fight with lupus.

Disclosure: D. Schwartz, None; **D. Gross**, None.

Number: PP08

Framework for Enhancing Patient-Physician Communication in the Context of Rare Disease

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Perspectives Poster Session
Session Type: Poster Session (Sunday)
Session Time: 11:30AM–1:30PM

Background/Purpose: For over two years, I experienced a variety of symptoms including: joint aches, sinus congestion, shortness of breath and chronic cough. An episode of hemoptysis led to laryngoscopy and a diagnosis of subglottic stenosis. Test results showed a high ANCA titer. Referral to a rheumatologist resulted in a diagnosis in 2012

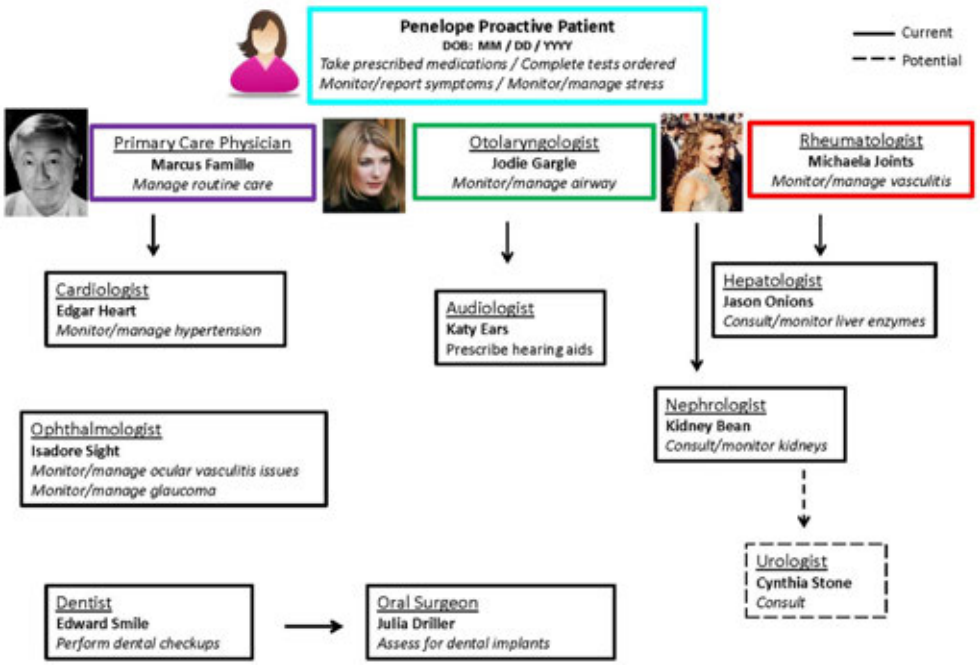

Figure 1. org chart

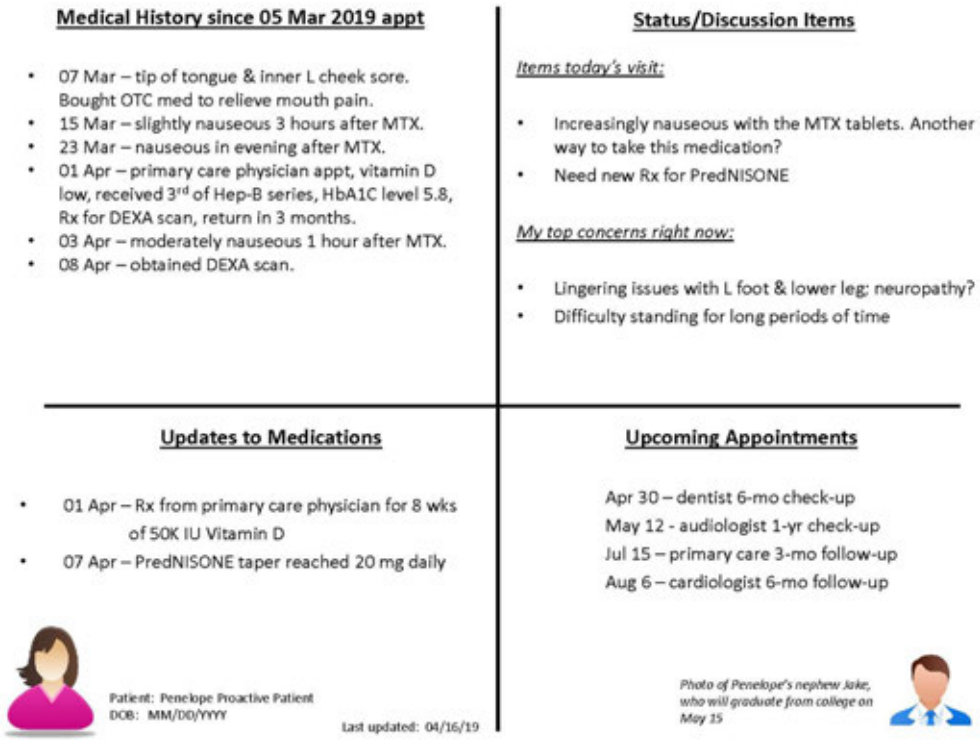

Figure 2. quad chart

of Granulomatosis with Polyangiitis (GPA), a rare disease with estimated incidence of 10-12 per million in the U.S. (Banerjee and Grayson, 2017). I've been hospitalized twice with relapses and received serial rituximab.

Treatment: To provide a framework for enhancing patient-physician communication, I applied work tools I use regularly: 1) an org chart, 2) a quad chart, and 3) a risk chart. I made my org chart about 6 months after diagnosis, updating

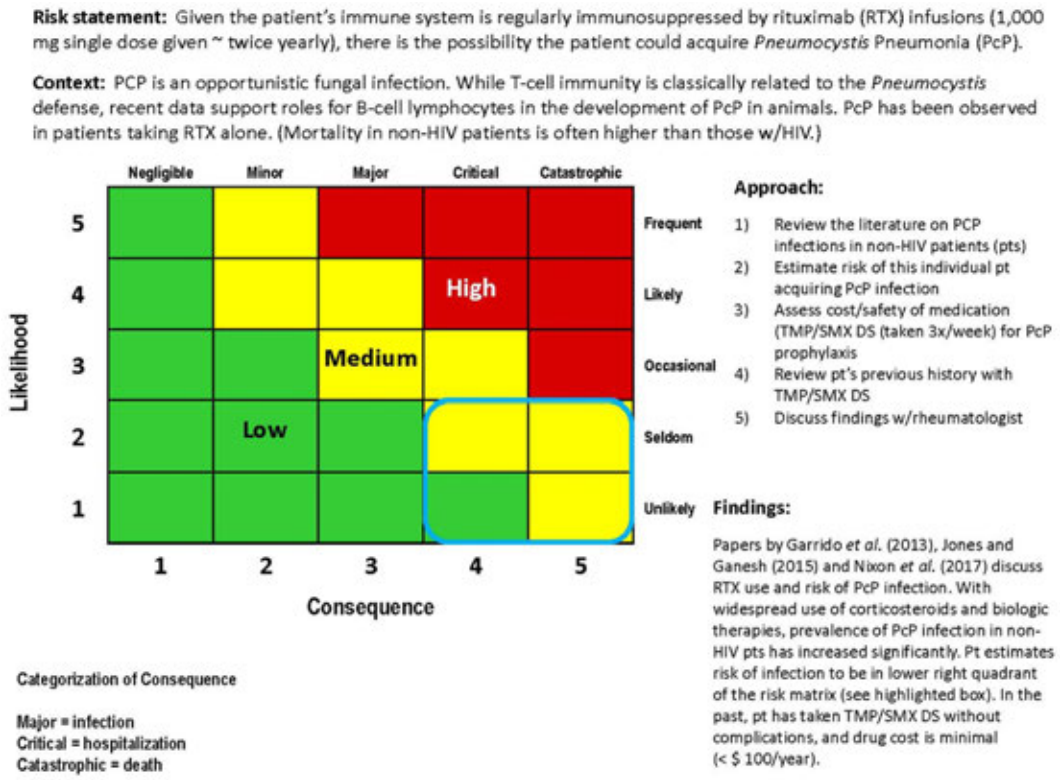

Figure 3. risk chart

it in 2018 to add photos. The chart lists my physicians, their specialties, and their roles in managing my health. I use a quad chart as a briefing tool for clinic visits to list medical history, updates to medications, topics I want to cover, and upcoming appointments. I made a risk chart to assess the likelihood of acquiring *Pneumocystis* pneumonia given I was having rituximab infusions. I used the chart with my rheumatologist in the shared decision-making process regarding trimethoprim/sulfamethoxazole for prophylaxis.

Maintenance: KQ: I first met this patient in 2015 during my rheumatology fellowship and became her clinical rheumatologist in 2017. The charts she provides help to inform and enhance our communications and coordination. The org chart provides an overview of other specialists involved in care and the quad chart highlights her main concerns to be discussed at the clinic visit. Additionally, her quad chart always includes a picture of a family member so that we discuss other important events going on in her life. These charts are an easy way to make sure we are addressing the patient's health needs in an organized and efficient manner.

IH: Use of these tools has positively impacted communication with my physicians. With my org chart, a new doctor may see at a glance my medical team, as well as their faces. The quad chart provides a systematic way to organize my thoughts prior to a clinic appointment. The risk chart provides an assessment of benefits and risks for a given course of action as an aid to discussion with my physician.

I have a rare disease that all physicians learned about in medical school but most never experience in clinical practice. Consistent briefing tools for my clinic visits enhance the efficiency and effectiveness of the patient-physician interaction.

Quality of Life: I'm grateful my GPA remains quiescent. I appreciate my team of medical professionals who work in partnership with me to monitor and treat this rare, chronic, and potentially life-threatening disease. Shortly after diag-

nosis, I became a member of the Vasculitis Foundation, a patient advocacy group. In 2014, I joined a natural history study in the Vasculitis Translational Research Program at the National Institutes of Health. My six-word memoir is: “Thanks to research, living with vasculitis.”

Reference: Shubhasree Banerjee and Peter C. Grayson. Vasculitis around the world: Epidemiologic insights into causality and a need for global partnerships. J Rheumatol 2017;44(2):136-139

Disclosure: I. Hakkarinen, None; **K. Quinn**, None.

Number: PP09

Journeying Towards Hope: Making a Difference in The Lives of Lupus Patients in Mauritius

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SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Perspectives Poster Session
Session Type: Poster Session (Sunday)
Session Time: 11:30AM–1:30PM

Background/Purpose: Growing up in the small island of Mauritius, I received the unexpected diagnosis of lupus at the young age of 13. The journey that followed was an arduous one filled with perseverance and survival. During these past 22 years, I have been overwhelmed with feelings of hopelessness. The hardest aspect of having lupus as a teen is the inevitable sense of isolation from the normal world. Living with lupus is challenging and disturbing from the moment of diagnosis. There were times when my condition did not allow me to attend school or pain and other physical restrictions prevented me from participating in school activities. I felt frightened, angry and depressed but with the support of my mother, I soon realised that living a life paralysed with fear was not living at all. Gradually, I had to accommodate my life to this dreadful disease, to adjust to the impact of strong daily medications and to resolve stress, pain, depression and fatigue.

Treatment: It took me two to three years to get to grips with lupus, but my grasp was strengthened by contact with other people who have the disease. Life with lupus is a Journey. Throughout the years, I found out that sharing my story with others helped in ending the isolation and depression created by the disease. I, therefore, made it a priority to

Educating others and raising awareness of lupus will save lives. The Quality of Life Programme

The Quality of Life Programme has been established to assist those patients who have needs not covered by community resources of assistance. We consider requests for help with home health care, child care, certain medications, transportation, personal care items or other products and services which will help alleviate some of the trauma of living with Lupus.

Spread Awareness

Raising public awareness of lupus to increase understanding and support for those affected by this autoimmune disease.

educate others and raise consciousness about lupus and other autoimmune diseases. Passionate about this awareness, my goal has been to ensure that all the work achieved ultimately benefited every individual affected by Lupus.

Maintenance: In 2000, my mother, Babs and I founded Lupus Alert, a non-profit organization in Mauritius providing moral, emotional and financial support to people living with lupus as well as spreading awareness of the disease to the public. Our goal is to provide lupus education to others including teachers, friends, family members and even health and government professionals who are not aware of its symptoms and complications. Lupus Alert also provides patient services and community awareness promotion to advance research initiatives.

Quality of Life: Lupus awareness in Mauritius has become a passion for me and all the work achieved has ultimately benefitted every individual who is touched by this disease. As a patient, I encourage other patients to accept and talk

openly about their illness. By providing a network of support for patients throughout the island I have been able to reach out to patients and their families teaching them how to manage and cope with lupus and provide the best opportunity for improving quality of life for patients and for controlling morbidity and mortality. In Mauritius, it has been particularly difficult to make the Health Authority recognise lupus as a significant public health issue. Through a wide awareness campaign, we have been able to create a synergy which today responds to the needs of those affected by this destructive illness. The mutual confidence between physicians and patients has improved and proved to be a large element in the effectiveness and the economy of healthcare. The next step now is to continue enhancing the progress made in creating local awareness about the disease and strengthening the position of Lupus Alert as a beacon of hope and support for the entire community of lupus patients in Mauritius and beyond.

Disclosure: D. Kalla, None.

Number: PP10

The Practice of Reiki and Meditation in Maintaining Medical Compliance and Decreased Anxiety in an Adult with Juvenile Rheumatoid Arthritis

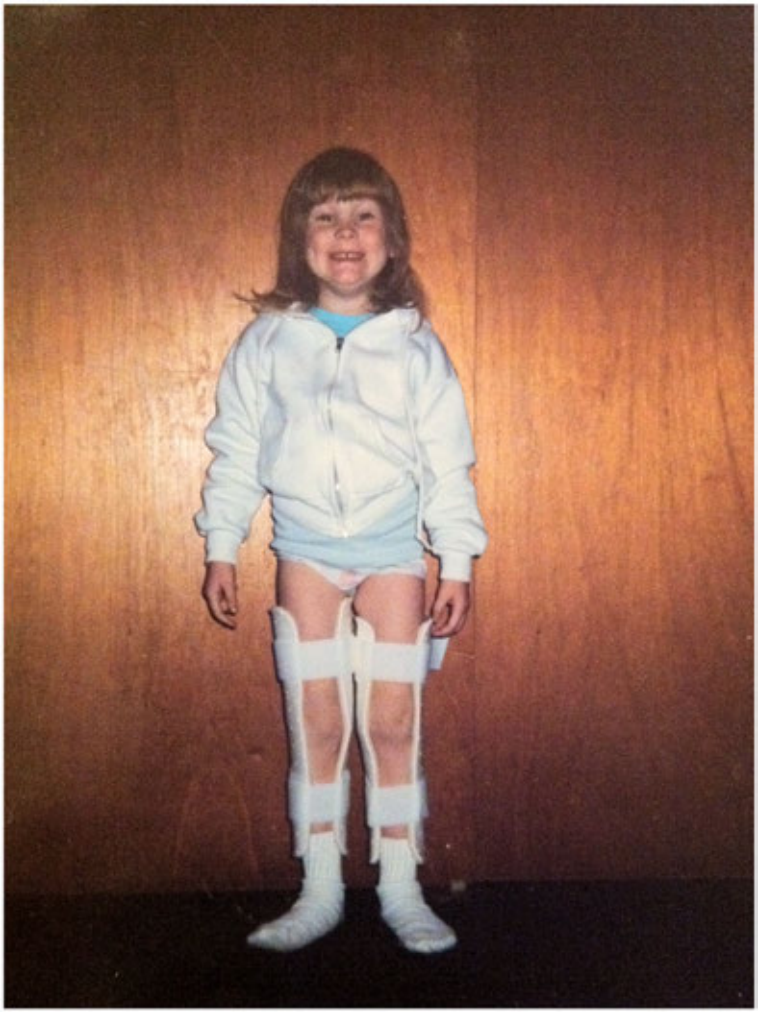
Shannan O'Hara-Levi [1], [1]Staten Island, New York

SESSION INFORMATION
Session Date: Sunday, November 10, 2019
Session Title: Patient Perspectives Poster Session
Session Type: Poster Session (Sunday)
Session Time: 11:30AM–1:30PM

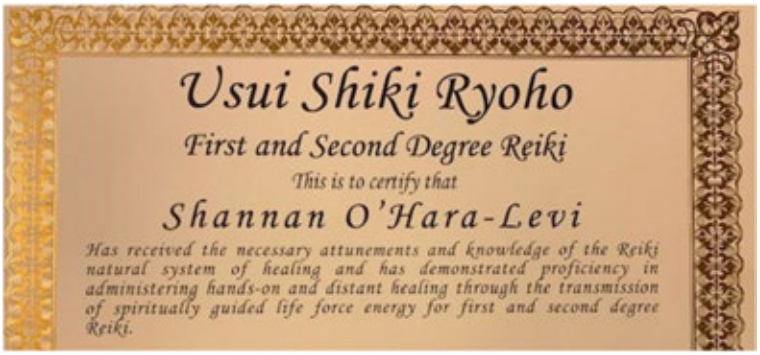
Background/Purpose: Up until a few years ago, my 30+ year journey with Polyarticular Juvenile Rheumatoid was treated mostly with medication management alone. I was diagnosed at age 3 with Polyarticular Juvenile Rheumatoid Arthritis. At time of diagnosis I was expected to be in a wheelchair by age 6. With the help of NSAIDs, prednisone and Gold Injections, this was not the case. Eventually, I began trials of various drug cocktails that included those previously listed with the addition of DMARDs and a rotation of various supplements including shark cartilage and vitamins. The ever changing trials of these cocktails continued until my mid-teenage years when biologic medication came to market. After being unsuccessful long term on any one medication, disease progression continued and I underwent bilateral shoulder replacement surgery in 2018. The integration of additional treatment options such as diet, exercise and mindfulness was the logical next step in my treatment journey.

Treatment: Through desperation in search of a better quality of life due to the progression of my illness, I was introduced to Reiki and meditation. I have added meditation and Reiki into my care plan in addition to current medication treatments and surgical interventions. Meditation and Reiki have enabled me to become more empowered and less fearful of the future of illness. I have studied and become certified as a Reiki Practitioner as well as regularly meditate through various Apps, walking mediation and mindfulness practice.

Maintenance: In order to fully feel the benefits of mediation and Reiki, I practice regularly as well as attend classes, certifications and educate myself about furthering my practice in this approach. By ensuring that mediation and Reiki are a regular part of my current lifestyle, I am able to be more present in the care of my illness and work better with my medical team. This also helps me stay more compliant with medications and medical appointments as my anxiety has decreased regarding these major parts of my life.



Shannan with JRA



Reiki Certification

Meditation Tools

Quality of Life: Although physical disease progression continues, I have had a better sense of control of fear and anxiety related to my illness. By practicing Reiki, I feel empowered and more peaceful. Regular meditation has allowed me to reflect on my disease and anxiety related to it. Without incorporating these practices into my treatment plan, I believe that my illness complications may have worsened. These practices have allowed me peace and acceptance with what is and the ability to play a strong, more active role in my disease management on a daily basis.

Disclosure: S. O'Hara-Levi, None.

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